Copper-Catalyzed Enantioselective Allylic Substitution Reactions with Organoaluminum and Boron Based Reagents Promoted by Chiral Sulfonate Bearing N-Heterocyclic Carbenes

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COPPER-CATALYZED ENANTIOSELECTIVE ALLYLIC SUBSTITUTION REACTIONS WITH ORGANOALUMINUM AND BORON BASED REAGENTS PROMOTED BY CHIRAL SULFONATE BEARING N-HETEROCYCLIC CARBENES

A dissertation

By

FANG GAO

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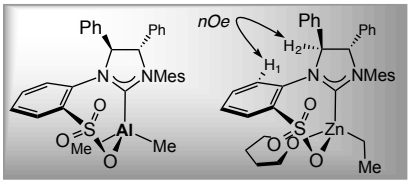
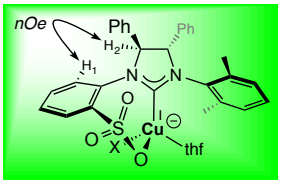
Abstract

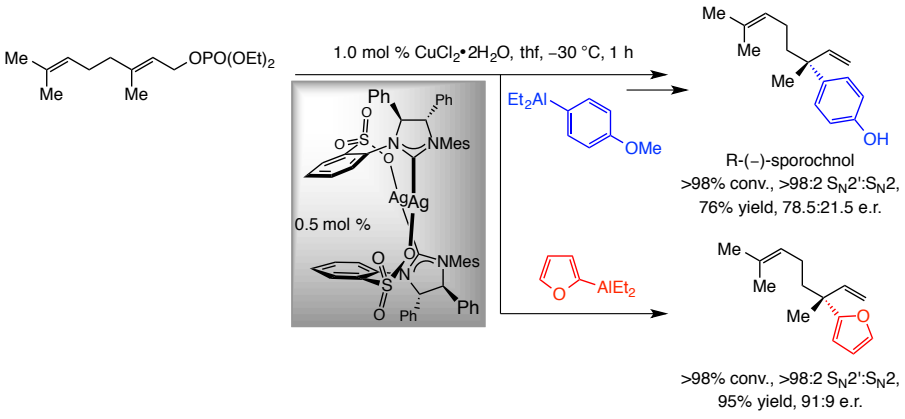
Chapter 1. A Review of Catalytic Enantioselective Allylic Substitution (EAS) with Chiral Sulfonate Containing N-heterocyclic Carbenes (NHC). A comprehensive review of enantioselective allylic substitution reactions, which are promoted by a chiral *N*-heterocyclic carbene metal complex that features a unique sulfonate motif, is provided in this chapter. Reactions are classified into two categories. One class of transformations is catalyzed by a series of easily modifiable sulfonate bearing NHC–Cu complexes, with which a range of nucleophilic organometallic reagents (i.e., organozinc-, aluminum-, magnesium- and boron-based) that carry different carbon-based units are readily utilized in efficient and highly selective C-C bond forming processes. Another set of reactions exclude the use of a copper salt; catalytic amount of a sulfonate containing imidazolinium salt is capable of promoting additions of alkyl Grignard, zinc and aluminum species to easily available allylic

electrophiles in a site- and enantioselective fashion. The mechanistic scenarios of both catalytic systems that account for the observed experimental data are discussed in detail.

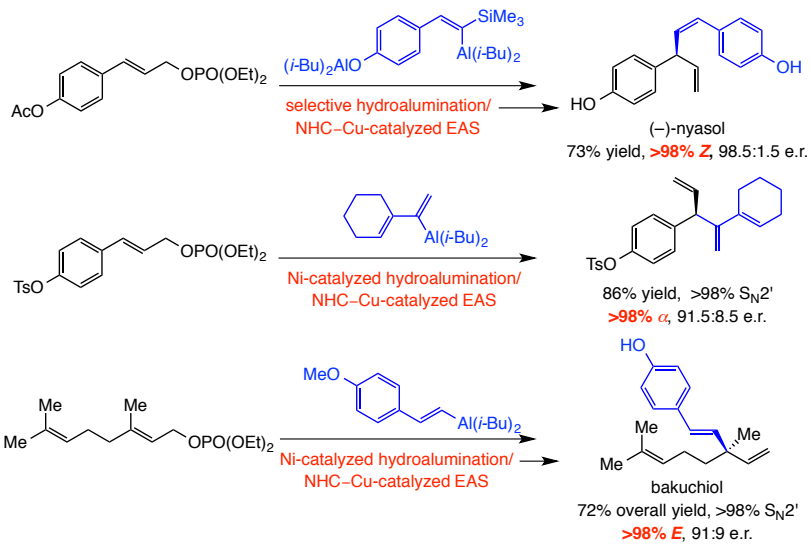




Chapter 2. Cu-Catalyzed Enantioselective Allylic Substitutions with Aryl- and Heteroarylaluminum Reagents. In this chapter, the first examples of EAS reactions of aryl- and heteroaryl-substituted dialkylaluminum reagents to a wide range of trisubstituted allylic phosphates are demonstrated through a facile and selective catalysis rendered possible by an in situ generated sulfonate containing NHC–Cu complex, delivering enantiomerically enriched olefin products that bear an all carbon quaternary stereogenic center. The requisite organometallic species are easily prepared from either the corresponding aryl- and heteroaryl halides, or through efficient and site selective deprotonation at the C-2 position of furan and thiophene; such aluminum entities are readily used in situ without the requirement of purification. Application to small molecule natural product synthesis is also carried out to illustrate the utility of the present protocol.



Chapter 3. Cu-Catalyzed Enantioselective Allylic Substitutions with Alkenylaluminum Reagents. This chapter focuses on our research towards construction of enantioenriched tertiary and quaternary stereogenic centers that are substituted with two further functionalizable alkenes. The first combination of the study involves the addition of stereochemically well-defined trisubstituted alkenylaluminum reagents to disubstituted allylic phosphates; the transformation commences with a silyl-directed stereoselective hydroalumination and finishes with an enantioselective Cu-catalyzed EAS promoted by a sulfonate bearing NHC. Such reactions deliver molecules that feature silicon containing trisubstituted olefin adjacent to the tertiary stereogenic center; subsequent conversion of the versatile silicon group to a proton reveals the first set of examples that incorporate pure *Z* alkene in Cu-catalyzed EAS. The stereoselective and concise synthesis of naturally occurring small molecule nyasol demonstrates the utility of the above method. On a different front, Ni-catalyzed site-selective hydroalumination of terminal alkynes has opened new possibility of introducing 1,1-disubstituted olefins in Cu-catalyzed EAS in the formation of tertiary stereogenic center containing enantioenriched organic building blocks. Such catalytic hydrometallation procedure also allows efficient access to alkenylaluminums that are derived from the conventionally problematic aromatic alkynes. The importance of efficient and selective synthesis of terminal aryl-substituted alkenylaluminum species is showcased in NHC–Cu-catalyzed EAS reactions that construct all-carbon quaternary stereogenic centers; a three-step convergent synthesis of natural product bakuchiol in enantiomerically enriched form highlights the potential of the current protocol in chemical synthesis.



Chapter 4 Cu-Catalyzed Enantioselective Allylic Substitutions with Alkenylboronic Acid Pinacol Ester Reagents and Applications in Natural Product Synthesis. Within this chapter, we disclose the efficient utilization of alkenylboron reagents in Cu-catalyzed EAS reactions, which lead to highly site and enantioselective formations of molecules that contain both tertiary and quaternary carbon stereogenic centers. Unlike their aluminum-based counterparts, the use of boron-based reagents allows effective delivery of sensitive organic function groups, such as a carbonyl, which would be incompatible in the hydrometallation process with dibal-H. Our efforts accumulate to the first report of incorporation of all carbon quaternary centers that are substituted with unsaturated ester and aldehyde units in the EAS products; such a method facilitates the concise diastereo- and enantioselective synthesis of Pummerer's ketone and it's *trans* isomer. Further development of the above protocol towards the construction of tertiary stereogenic centers requires the design of new chiral sulfonate-containing imidazolinium salts as the ligand precursors and has lead to the employment of a broader range of alkenylboron species, which feature readily

functionalizable motifs. Subsequent demonstrations in enantioselective synthesis of a variety of small molecule natural products showcase the utility.

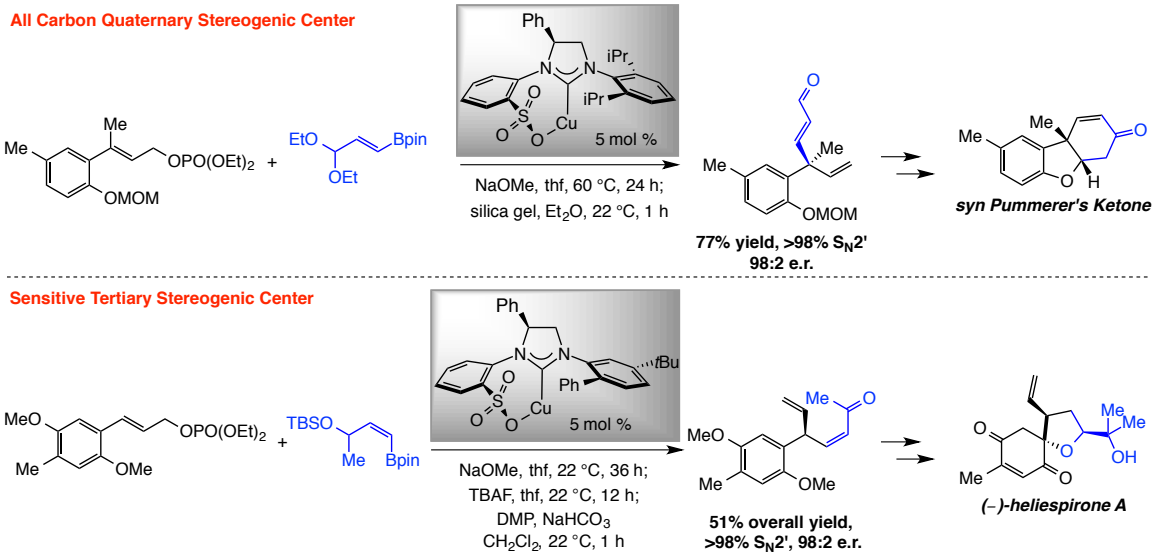


Table of Contents

Chapter 1

A Review of Catalytic Enantioselective Allylic Substitution (EAS) with Chiral Sulfonate Containing N-heterocyclic Carbenes (NHC)

1.1 Introduction

Catalytic enantioselective allylic substitution (EAS) reactions are of prominent utility in chemical synthesis.[1] Such transformations generate a stereogenic center adjacent to an alkene. Copper was known as a prestigious transition metal to promote allylic substitution reactions in association with "hard" organometallic nucleophiles.[2] The enantioselective variants started to emerge since 1995, when Bäckvall reported the first example involving Grignard reagents.[3] As the interest in enantioselective catalysis grows over the past two decades, a number of catalyst systems were also devised to address the problems in Cu-catalyzed EAS reactions. The most prominent ones among them are

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(1) For reviews on allylic substituion reactions catalyzed by other transition metals and with "soft" nucleophiles, see: (a) Trost, B. M.; Lee, C. In *Catalytic Asymmetric Synthesis*; Oijima, I., Ed.; Wiley-VCH: Weinheim, Germany, 2000; Chapter 8E. (b) Trost, B. M.; Crawley, M. L. *Chem. Rev.* **2003**, *103*, 2921–2944. (c) Stanley, L. M.; Hartwig, J. F. *Acc. Chem. Res.* **2010** *43*, 1461–1475. (d) Trost, B. M. *Org. Process Res. Dev.* **2012**, *16*, 185–194. (e) Tosatti, P.; Nelson, A.; Marsden, S. P. *Org. Biomol. Chem.* **2012**, *10*, 3147–3163.

(2) For reviews on Cu-catalyzed allylic alkylation reactions that involve "hard" alkyl- or arylmetal-based reagents, see: (a) Hoveyda, A. H.; Hird, A. W.; Kacprzynski, M. A. *Chem. Commun.* **2004**, 1779–1785. (b) Yorimitsu, H.; Oshima, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 4435–4439. (c) Falciola, C. A.; Alexakis, A. *Eur. J. Org. Chem.* **2008**, 3765–3780. (d) Alexakis, A.; Bäckvall, J.-E.; Krause, N.; Pàmies, O.; Diéguez, M. *Chem. Rev.* **2008**, *108*, 2796–2823. (e) Harutyunyan, S. R.; den Hartog, T.; Geurts, K.; Minnaard, A. J.; Feringa, B. L. *Chem. Rev.* **2008**, *108*, 2824–2852. (f) Lu, Z.; Ma, S. *Angew. Chem., Int. Ed.* **2008**, *47*, 258–297. (g) Langlois, J. -B.; Alexakis, A. *Topics in Organometallic Chemistry* **2012**, *38*, 235–268.

(3) van Klaveren, M.; Persson, E. S. M.; Grove, D. M.; Bäckvall, J. E.; van Koten, G. *Tetrahedron Lett.* **1995**, *36*, 3059–3062.

phosphine[4] and amino acid[5] based copper complexes; EAS reactions in the presence of these catalysts proceed efficiently in connection with alkyl Grignard or zinc reagents. Very recently, Feringa and co-workers began to employ highly reactive alkyllithiums in Cu-catalyzed EAS reactions in which a Cu-phosphoramidite complex served as the catalyst.[6]

N-heterocyclic carbenes (NHC),[7] on the other hand, were only introduced as chiral ligands on Cu[8] to facilitate EAS reactions slightly over a decade ago. Our group has synthesized and characterized two generations of phenoxide-based bidentate NHC ligands, which store the stereochemical information in a Binol unit[9] and an optically pure biphenylethylene diamine moiety,[10] respectively. The corresponding copper complexes derived from such entities exhibit superior reactivity and selectivity profiles compared to those that contain amino acid based chiral ligands; over a magnitude of TON increase

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(4) (a) ref. 2. For an additional review dedicated to widely used phosphoramidite ligands, see: (b) Teichert, J. F.; Feringa, B. L. *Angew. Chem., Int. Ed*. **2010**, *49*, 2486–2528.
(5) (a) Luchaco-Cullis, C.; Mizutani, H.; Murphy, K. E.; Hoveyda, A. H. *Angew. Chem., Int. Ed*. **2001**, *40*, 1456–1460. b) Murphy, K. E.; Hoveyda; A. H. *J. Am. Chem. Soc*. **2003**, *125*, 4690–4691; (c) Kacprzynski, M. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2004**, *126*, 10676–10681. (d) Murphy, K. E.; Hoveyda, A. H. *Org. Lett.* **2005**, *7*, 1255–1258.
(6) (a) Pérez, M.; Fañanás-Mastral, M.; Bos, P. H.; Rudolph, A. Harutyunyan, S. R.; Feringa, B. L. *Nature Chemistry* **2011**, *3*, 377–381. (b) Fañanás-Mastral, M.; Pérez, M.; Bos, P. H.; Rudolph, A. Harutyunyan, S. R.; Feringa, B. L. *Angew. Chem., Int. Ed*. **2012**, *51*, 1922–1925. (c) Pérez, M.; Fañanás-Mastral, M.; Hornillos, V.; Rudolph, A.; Bos, P. H.; Harutyunyan, S. R.; Feringa, B. L. *Chem. Eur. J.* **2012**, *18*, 11880–11883.
(7) For recent reviews on *N*-heterocyclic carbenes as catalysts in organic synthesis, see: (a) Enders, D.; Niemeier, O.; Henseler, A. *Chem. Rev.* **2007**, *107*, 5606–5655. (b) Marion, N.; Díez-González, S.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2007**, *46*, 2988–3000. For representative reviews on *N*-heterocyclic carbenes as ligands in metal catalyzed processes, see: (c) Kantchev, E. A. B.; O'Brien, C. J.; Organ, M. G. *Angew. Chem., Int. Ed.* **2007**, *46*, 2768–2813. (d) Gade, L. H.; Bellemin-Laponnaz, S. *Top. Organomet. Chem.* **2007**, *21*, 117–157. (e) Tekavec, T. N.; Louie, J. *Top. Organomet. Chem.* **2007**, *21*, 159–192. (f) Díez-González, S.; Marion, N. Nolan, S. P. *Chem. Rev.* **2009**, *109*, 3612–3676. (g) Wang, F.; Liu L.-j; Wang, W.; Li, S.; Shi, M. *Coord. Chem. Rev*. **2012**, *256*, 804–853.
(8) Egbert, J. D.; Cazin, C. S. J.; Nolan, S. P. *Catal. Sci. Technol*. **2013**, *3*, 912–926.
(9) Larsen, A. O.; Leu, W.; Oberhuber, C. N.; Campbell, J. E.; Hoveyda, A. H. *J. Am. Chem. Soc*. **2004**, *126*, 11130–11131.
(10) Van Veldhuizen, J. J.; Campbell, J. E.; Guidici, R. E.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2005**, *127*, 6877–6882.

was observed in the EAS reactions with dialkylzinc reagents. Since these discoveries, another set of carbenes that bear an alkoxide secondary binding site appeared in the literature[11] along with a few examples of EAS promoted by Cu complexes derived from monodentate NHCs;[12] in these cases, alkyl Grigard or zinc reagents are effective nucleophilic partners. Pertinent to the context of this review, we will focus the discussion on sulfonate containing N-heterocyclic carbenes[13] as ligands on Cu to effect EAS reactions. More detailed information of the reactions delineated above can be found in previous review articles related to copper catalyzed allylic substitution.[2]

1.2 Additions of Alkyl Metal Reagents in Cu-catalyzed EAS Promoted by Sulfonate Containing NHCs

Shortly after its discovery in 2007, the sulfonate bearing NHC was investigated in two ongoing studies to help gauge its ability in promoting Cu-catalyzed EAS in comparison with existing Cu catalysts that derived from bidentate phenoxide based carbene ligands. One of them involved the addition of dialkylzinc reagents to a silyl-

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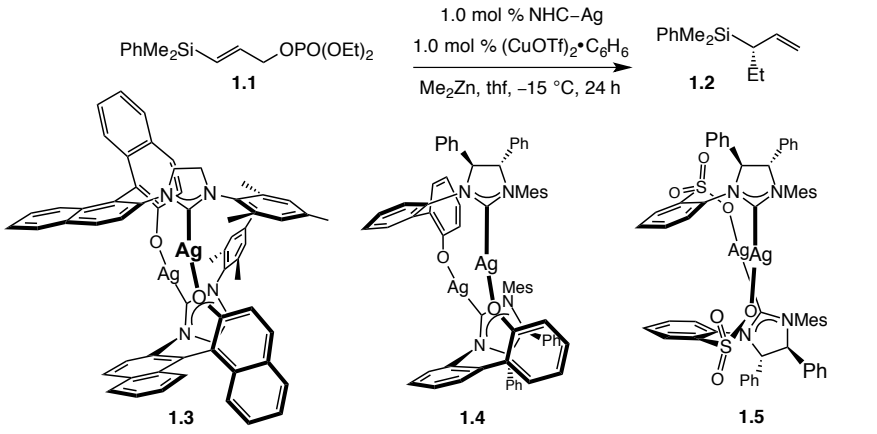
(11) (a) Martin, D.; Kehrli, S.; d'Augustin, M.; Clavier, H.; Mauduit, M.; Alexakis, A. *J. Am. Chem. Soc.* **2006**, *128*, 8416–8417. (b) Germain, N.; Magrez, M.; Kehrli, S.; Mauduit, M.; Alexakis, A. *Eur. J. Org. Chem.* **2012**, 5301–5306. (c) Magrez, M.; Le Guen, Y.; Baslé, O.; Crévisy, C.; Mauduit, M. *Chem. Eur. J.* **2013**, *19*, 1199–1203.
(12) (a) Seo, H.; Hirsch-Weil, D.; Abboud, K. A.; Hong, S. *J. Org. Chem.* **2008**, *73*, 1983–1986. (b) Selim, K. B.; Yamada, K-i.; Tomioka, K. *Chem. Commun.* **2008**, 5140–5142. (c) Selim, K. B.; Matsumoto, Y.; Yamada, K-I.; Tomioka, K. *Angew. Chem. Int. Ed.* **2009**, *48*, 8733–8735.
(13) For the first disclosure of these NHCs, see: (a) Brown, M. K.; May, T. L.; Baxter, C. A.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 1097–1100. For their applications in Cu-catalyzed conjugate additions, see: (b) May, T. L.; Brown, M. K.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2008**, *47*, 7358–7362. (c) Brown, M. K.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2008**, *130*, 12904–12906. (d) May, T. L.; Dabrowski, J. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 736–739. (e) Dabrowski, J. A.; Villaume, M. T.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2013**, *52*, 8156–8159.

substituted allyic phosphate.[14] As shown in Scheme 1.1, in the presence of 2 mol % of in situ formed Cu complexes generated from treatment of phenoxide based NHC–Ag complexes **1.3** and **1.4** with $(CuOTf)_2 \bullet C_6H_6$, the desired EAS reactions of diethylzinc proceed to >98% conversions within 24 h at –15 ˚C, affording ethyl substituted allylsilane in exceptional site and enantioselectivity levels (>98% S_N2', >97:3 e.r.). Interestingly, essentially the same result was obtained with the newly discovered sulfonate carbene (**1.5**) as the promoter under these conditions (98% conv., >98% S_N2', 96:4 e.r., Scheme 1.1).

Scheme 1.1. Cu-Catalyzed Enantioselective Allylic Substitution with Et_2Zn.

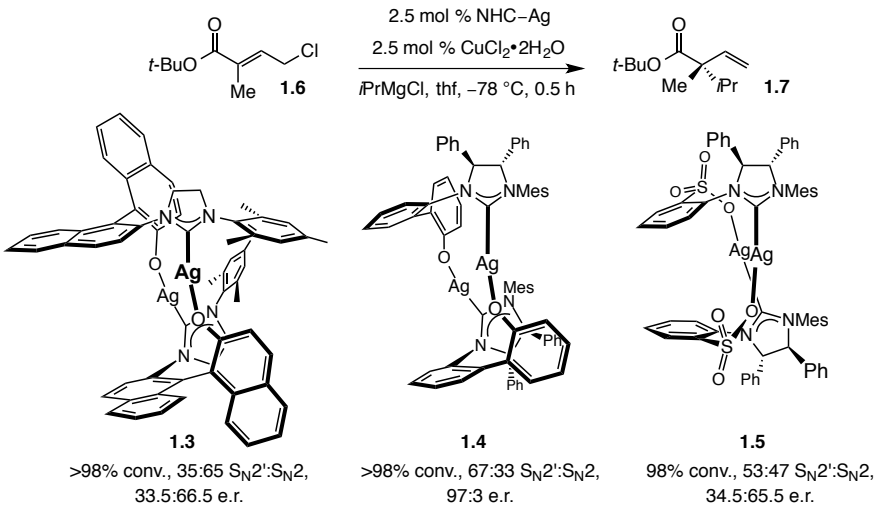


In the other case, where we concerned the addition of a secondary Grignard reagent in the formation of quaternary stereogenic center containing enantioenriched molecules,[15] the sulfonate ligated NHC–Cu catalyst was able to effect the transformation with high efficiency even at –78 ˚C for a short period of time (98% conversion in 30 minutes); the selectivities, however, were not as good as that in which **1.4** served as the

(14) Kacprzynski, M. A.; May, T. L.; Kazane, S. A.; Hoveyda, A. H. *Angew. Chem., Int. Ed*. **2007**, *46*, 4554–4558.
(15) Unpublished results obtained by Yumin Lee and Kyoko Mandai in our group

chiral ligand (53% S_N2', 34.5:65.5 e.r. with **1.5** vs. 67% S_N2', 97:3 e.r. with **1.4**, Scheme 1.2). Although comparable levels of efficiency and selectivity were observed with this new class of catalysts, it would be much more appealing to explore their full potentials in Cu-catalyzed EAS reactions, especially in cases where activity and selectivity profiles superior to previously known catalyst systems can be revealed.

Scheme 1.2. Cu-Catalyzed Enantioselective Allylic Substitution with *i*PrMgCl.

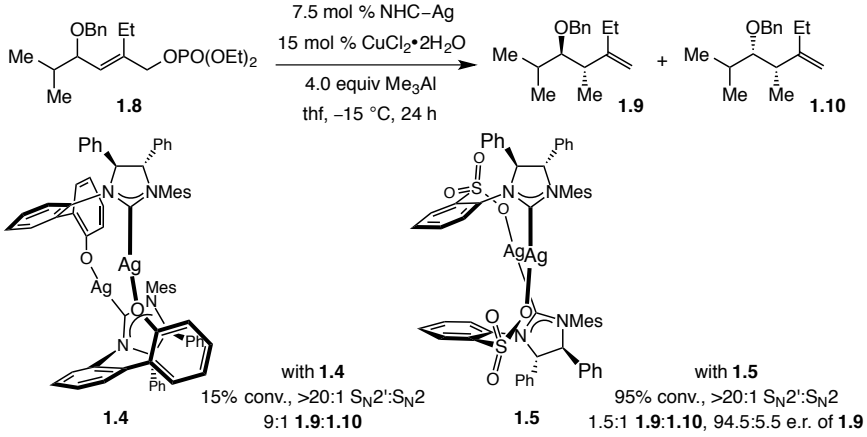


With this contention, we turned to a much less widely employed class of substrates in Cu-catalyzed EAS reactions: a trisubstituted allylic phosphate with a substituent at the β carbon. Our special interest in this class of substrates also evolved from their potential application in the synthesis of natural product baconipyrone C (cf. Scheme 1.4),[16] a piece of which can be prepared from a double allylic substitution with a nucleophilic methyl group. Preliminary results have shown that treatment of the advanced model compound **1.8** (Scheme 1.3) with dimethylzinc under previously reported catalytic conditions fails to provide any conversion of the substrate. Clearly, in order to address the

(16) For alternative enantioselective synthesis of this molecule, see: (a) Paterson, I.; Chen, D. Y.; Acena, J. L.; Franklin, A. S. *Org. Lett.* **2000**, *2*, 1513–1516. (b) Yadav, J. S.; Sathaiah, K.; Srinivas, R. *Tetrahedron* **2009**, *65*, 3545–3552. (c) Beye, G. E.; Ward, D. E. *J. Am. Chem. Soc.* **2010**, *132*, 7210–7215.

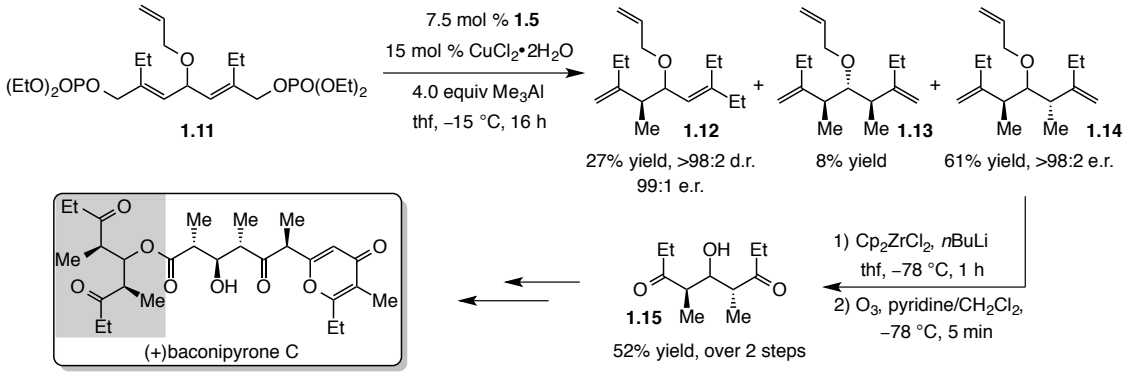
issue, either a more reactive methyl surrogate is introduced or a more efficient class of promoters is invented. As illustrated in Scheme 1.3, Me_3Al, a more Lewis acidic reagent, was examined in Cu-catalyzed EAS reactions with allylic phosphate **1.8**. After an extensive screening, we have found that with 15 mol % of an in situ generated NHC–Cu complex derived from **1.4**, a small quantity of products is obtained (15% conv., 9:1 **1.9**:**1.10**, >20:1 S_N2':S_N2, Scheme 1.3). Low conversion as well as the preference for the formation of one diastereo isomer all point to a possible match/mismatch scenario of the chiral catalyst and the stereogenic center resided α to the incipient C-C bond. In contrast, when the sulfonate containing **1.5** is used under otherwise identical conditions, 95% conversion of compound **1.8** is observed, furnishing an almost equal mixture of diastereomers (1.5:1 **1.9**:**1.10**), indicating override of the substrate preference with catalyst control. Furthermore, the desired compound **1.9** is formed in excellent site selectivity (>20:1) and enantioselectivity (95.5:4.5 e.r., Scheme 1.3). Such an unforeseen activity and selectivity levels of this new class of NHCs to facilitate Cu-catalyzed EAS reactions, especially in combination with Al-based organometallic reagents, is the unique feature brought in through the incorporation of a sulfonate moiety into the catalyst structure (see below for more detailed discussion).

Scheme 1.3. Cu-Catalyzed Enantioselective Allylic Substitution with Me_3Al.



With the tool in hand, we have carried out the double allylic substitution reactions for the synthesis of baconipyrone C.[17] In the presence of 7.5 mol % of **1.5** and 15 mol % of air stable $CuCl_2•2H_2O$, Bisallylic phosphate **1.11** is converted to the desired triene **1.14** in 61% yield and as a single enantiomer; 27% yield of a mono methyl adduct **1.12** is isolated from the reaction mixture along with small quantity of a meso diastereomer **1.13** (8% yield, Scheme 1.4). Upon deprotection of the allyl group and ozonolysis of the remaining two olefins, diketone **1.15** is furnished in 52% yield over two steps.

Scheme 1.4. Cu-Catalyzed Double EAS with Me_3Al Reagent and Its Application to the Synthesis of Baconipyrone C.



Access of molecules bearing an all carbon quaternary stereogenic center in an enantioselective fashion is of great interest, yet challenging. EAS reactions that deliver

(17) Gillingham, D. G.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 3860–3864.

such entities through the incorporation of a simple alkyl group are rare; most of the cases utilize expensive dialkylzinc reagents and the substrate scope is limited. The more atom economical alkyl Grignard reagent suffers from low site selectivity in Cu-catalyzed EAS reactions (cf. Scheme 1.2). The much less expensive and commercially available trialkylaluminum species, therefore, are promising candidates for the above purposes if a class of efficient catalysts can be secured for such difficult transformations.[18] As demonstrated in Scheme 1.5, triethylaluminum readily serves as the nucleophilic coupling partner in EAS reactions with the ester substituted allylic phosphate **1.16** with only 2 mol % in situ formed NHC–Cu complex derived from **1.5**. The α vinylic ester **1.17** is furnished in >98% conversion, >98% S_N2' and 92:8 enantiomer ratio. Additional catalyst modification has revealed **1.19** as a more selective variant (94:6 e.r.) to effect the EAS reactions with trialkylaluminums, whereas the other representative classes of carbenes (cf. **1.4** and **1.18**, Scheme 1.5) are much less effective promoters. Additional cases of **1.20** and **ent-1.17** showcase the scope of the above transformations.[19]

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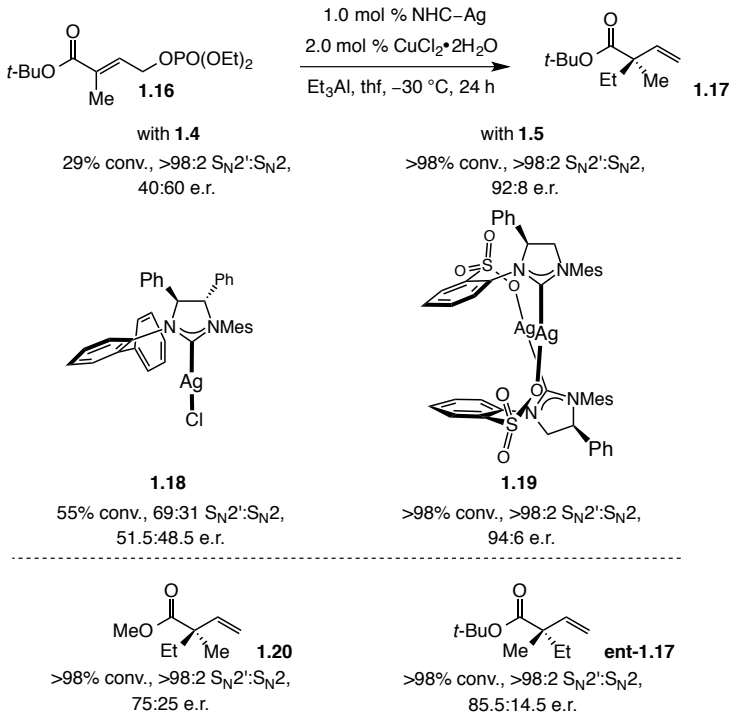
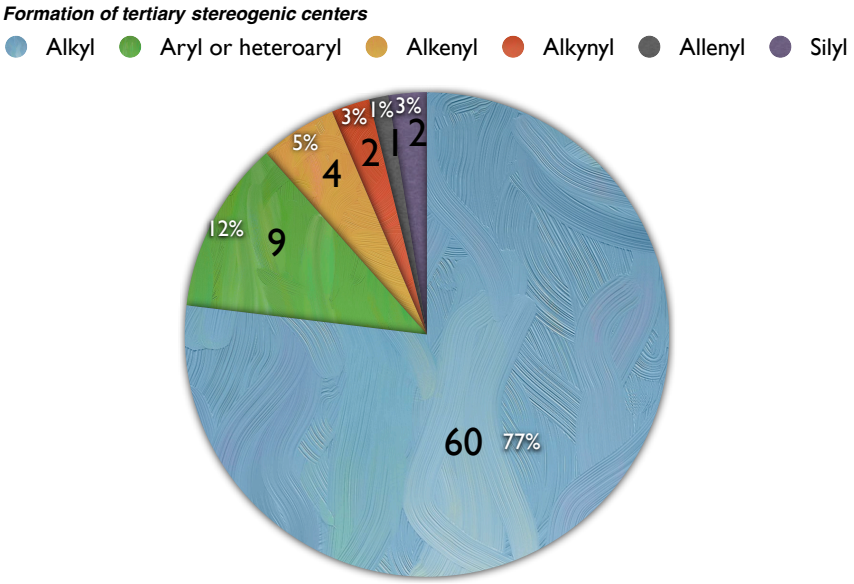
(18) Das, J. P.; Marek, I. *Chem. Commun.* **2011**, *47*, 4593–4623.
(19) Unpublished results acquired by Yunmi Lee and Kyoko Mandai in our group.

Scheme 1.5. Cu-Catalyzed EAS with Trialkylaluminum Reagents.



While the Cu-catalyzed EAS reactions with *alkylmetals* have gained more extensive attention from chemists worldwide, their variants that couple the more useful aryl-, heteroaryl-, alkenyl-, alkynyl-, allyl- and allenyl units are much less developed.[1, 2] During the 18 years of advancement (summarized in Figure 1.1 and 1.2), one can easily deduce the imbalance in the progress towards the exploration of the full potential of Cu-catalyzed EAS. At least two contributing factors that account for the relative underdevelopment in the coupling reactions with the more complex carbon-based nucleophiles are noteworthy. The first one concerns the readily availability of these nucleophilic organometallic reagents; unlike commercially available alkylmetals, most of the higher order species require in house preparation, the procedures of which sometimes are either not trivial to follow or need to be developed. Moreover, the proper choice of which metal reagent as the target is also of great value and will affect the synthetic

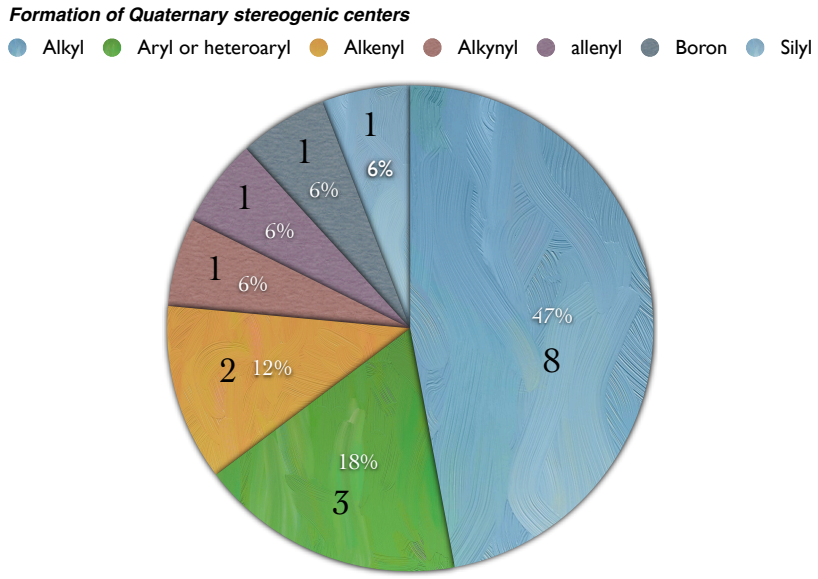
Figure 1.1. Statistic Distribution of Cu-Catalyzed EAS by Nucleophilic Reagents.



efficiency as well as method development. For example, aryl Grignard is more attractive for its atom economy but harder to control in a catalytic reaction due to its higher reactivity compared to diarylzinc or triarylaluminum, reactions with which often have to waste one or more valuable groups on the metal. Ideally, one would like to be able to use an organometallic reagent that is easy to prepare and use directly without further purification, contains one transferrable valuable group and one or multiple "dummy" ligands that are of less value and has appropriate reactivity profile, which is suitable for catalysis. The second factor that is equally, if not more important, regards the development of catalysts capable of promoting EAS reactions with the more complex organometallic species. More ligands are available for the additions of an alkyl group to allylic electrophiles,[2] whereas precedents for the incorporation of other nucleophiles

through Cu catalysis are very rare.[20] Thus, design and identification of a class of chiral ligands that can promote the addition of a range of carbon nucleophiles (i.e., aryl-, alkenyl-, alkynyl-, allyl- and allenyl et al.) are challenging but highly desirable.

Figure 1.2. Statistic Distribution of Cu-Catalyzed EAS by Nucleophilic Reagents.



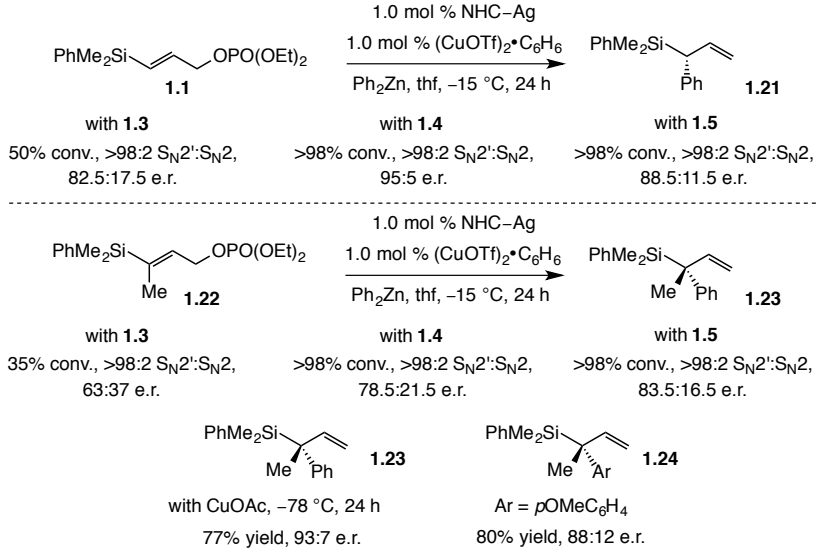
1.3 Additions of Aryl and Heteroaryl Metal Reagents in Cu-catalyzed EAS Promoted by Sulfonate Containing NHCs

In 2007, a project was initiated in these laboratories to probe the possibility of carrying out Cu-catalyzed EAS with diarylzinc reagents.[14] As indicated in Scheme 1.6, three representative bidentate NHCs are able to facilitate EAS reactions with catalyst loading as low as 2 mol %, furnishing phenyl substituted tertiary stereogenic center containing enantioenriched allylsilanes in exceptional site selectivity (>98% S_N2' in all cases). Unlike the reactions shown in Scheme 1.1 with Et_2Zn, the ligand precursor **1.3**,

(20) (a) ref. 12 (b) and (c). (b) Alexakis, A.; Hajjaji, S. E.; Polet, D.; Rathgeb, X. *Org. Lett.* **2007**, *9*, 3393–3395. (c) Falciola, C. A.; Alexakis, A. *Chem. Eur. J.* **2008**, *14*, 10615–10627; (d) Polet, D.; Rathgeb, X.; Falciola, J C.; Langlois, A. B.; Hajjaji, S. E.; Alexakis, A. *Chem. Eur. J.* **2009**, *15*, 1205–1206.

which is based on chiral binol structure, is much less effective when more sterically encumbered Ph_2Zn is used (50% conv., Scheme 1.6). In contrast, Cu complexes derived from **1.5** and **1.4** remain active, delivering compound **1.21** in high efficiency and 88.5:11.5–95:5 e.r. Similar results are observed with more difficult substrates; trisubstituted allylic phosphate **1.22** is readily converted to a tertiary allylsilane **1.23** with the highest enantioselectivity obtained when Cu complex generated from sulfonate containing **1.5** serves as the catalyst. The enantiomer ratio can be further improved at lower temperature without loss of reactivity (93:7 e.r. at –78 ˚C, Scheme 1.6). Substituted diarylzinc can also be employed under these conditions, resulting in the introduction of various aromatic units through the formation of sterically congested C-C bonds (e.g., **1.24**).

Scheme 1.6. Cu-Catalyzed Enantioselective Allylic Substitution with Diarylzinc Reagents.



The drawback of the above protocol, as mentioned in the previous context, resides in the waste of half of the valuable group on zinc. Tomioka and coworkers, since then, have reported methods that take the advantage of the atom economical aryl Grignard reagents in Cu-catalyzed EAS reactions;[12b, c] a class of monodentate chiral NHCs are

synthesized to promote such transformations, generating molecules that bear a tertiary aryl substituted stereocenter. This elegant catalyst system, however, has not been reported effective in the preparation of quaternary stereogenic center containing enantioenriched organic building blocks. Additionally, due to the nature of high reactivity associated with Grignard reagents, undesired linear (S_N2) products are often seen in various quantities in the reaction mixtures.

We have carried out a study that takes the advantage of using Grignard reagent and at the same time buffers the undesired high reactivity. As illustrated in Scheme 1.7, the treatment of the PhMgCl solution with neat Et_2AlCl in dioxane results in a salt metathesis reaction with the equilibrium driven towards the formation of Et_2AlPh **1.25** by precipitation of $MgCl_2$•dioxane complex.[21] The supernatant of the resulting suspension can be used directly without further purification in the subsequent Cu-catalyzed EAS reactions.[22] In the presence of 1 mol % in situ formed NHC–Cu complex derived from the sulfonate containing **1.5**, allylic phosphate **1.16** is fully consumed at –30 ˚C within 30 minutes to afford ester **1.26** that bears an all carbon quaternary stereogenic center in >98% site selectivity and 89.5:10.5 e.r. Although there are two ethyl groups on the mixed aluminum reagent, only the transfer of the phenyl unit observed. Therefore, suitable and

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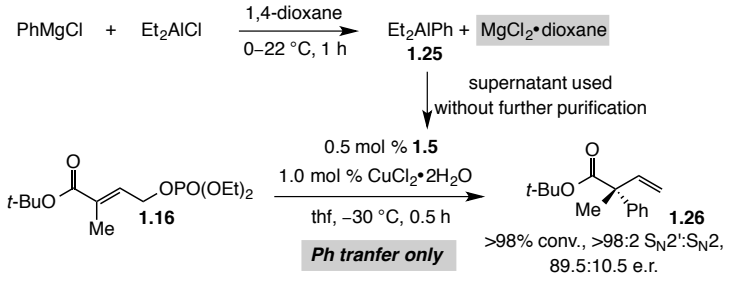
(21) For previous reports regarding preparation of dialkyl arylaluminum reagents, see: (a) Belgardt, T.; Storre, J.; Roesky, H.W.; Noltemeyer, M.; Schmidt, H.-G. *Inorg. Chem.* **1995**, *34*, 3821–3822. (b) Bumagin, N. A.; Ponomaryov, A. B.; Beletskaya, I. P. *Tetrahedron Lett.* **1985**, *26*, 4819–4822. (c) Lu, B. Z. F.; Jin, Y.; Zhang, X.; Wu, S.; Wald, A.; Senanayake, C. H. *Org. Lett.* **2005**, *7*, 1465–1468. For a catalytic enantioselective reaction involving Me_2(aryl)Al reagents, see: (d) Siewert, J.; Sandmann, R.; von Zezschwitz, P. *Angew. Chem. Int. Ed.* **2007**, *46*, 7122–7124.

(22) Gao, F.; Lee, Y.; Mandai, K.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2010**, *49*, 8370–8374.

less valuable "dummy" ligands on the metal were identified and this phenomenon turns out to be generally applicable in other classes of Al-based reagents.[23]

Scheme 1.7. In Situ Formed Et_2AlAr From Grignard Reagents.



Based on the preliminary discovery, we have continued to explore more systematically the utilization of aryllithium, another class of atom economical reagents, in Cu-catalyzed EAS reactions. Similar principles can be applied with minor adjustment of the conditions in generating the mixed arylaluminums; again the supernatant is usable without any additional purification, with which the Cu-catalyzed EAS furnishes the aryl addition products exclusively in all cases. The screening of representative NHCs demonstrates two points that merit further discussion. 1) EAS reactions of **1.16** with all NHCs as the promoters proceed to completion within one hour at –30 °C and >98% selectivities for the branched ester **1.17** are observed except for that with the monodentate *N*-heterocyclic carbene (83% S_N2' with **1.18**, Scheme 1.8). 2) The optimal enantiomer ratio is obtained when the sulfonate containing NHC **1.5** serves as the ligand, whereas the monodentate NHC delivers ester **1.17** essentially as a racemate. Additional examples (cf. **1.27**–**1.29**, Scheme 1.8) highlight the scope of this transformation; various aryl adducts are synthesized in 71–97% yield and 91.5:8.5–97:3 e.r.

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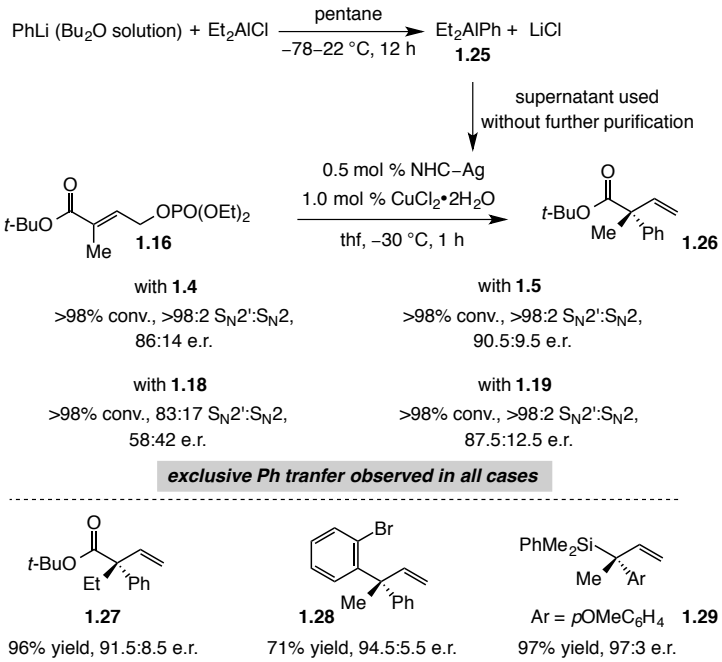
(23) For the more favored transfer of an aryl unit versus an alkyl group of an Al-based reagent, see: (a) Mole, T.; Surtees, J. R. *Aus. J. Chem.* **1964**, *17*, 310–314. (b) Merino, E.; Melo, R. P. A.; Ortega-Guerra, M.; Ribagorda, M.; Carreño, M. C. *J. Org. Chem.* **2009**, *74*, 2824–2831. (c) Gao, H.; Knochel, P. *Synlett* **2009**, 1321–1325. (d) ref. 21 (b) and (c).

Scheme 1.8. Cu-Catalyzed EAS with In Situ Formed Et_2AlAr Reagents.



The utility of the method was showcased in a concise synthesis of natural product sporochnol[24] as evidenced in Scheme 1.9. Lithium halogen exchange facilely provides the requisite aryllithium, which is subsequently treated with Et_2AlCl in pentane to generate mixed diethyl *p*-methoxyphenylaluminum reagent **1.30**. Upon exposure of the supernatant solution to the readily accessible allylic phosphate **1.31**, which derives from geraniol, in the presence of 1.0 mol % in situ formed sulfonate bearing NHC–Cu complex of **1.5**, methyl ether of sporochnol is delivered in excellent efficiency and site selectivity, albeit with moderate e.r. value (76% yield over two steps, >98% S_N2', 78.5:21.5 e.r., Scheme 1.9).

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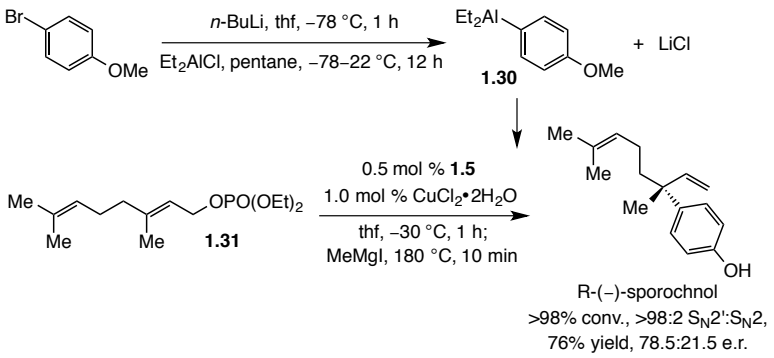
(24) For isolation and selected previous syntheses, see: (a) Shen, Y. C.; Tsai, P. I.; Fenical W.; Hay, M. E. *Phytochemistry* **1993**, *52*, 71–75. (b) Takahashi, M.; Shioura, Y.; Murakami T.; Ogasawara, K.; *Tetrahedron: Asymmetry* **1997**, *8*, 1235–1242. (c) Fadel, A.; Vandromme, L. *Tetrahedron: Asymmetry* **1999**, *10*, 1153–1162. (d) Alibés, R.; Busqué, F.; Bardaji, G. G.; de March, P.; Figueredo, M.; Font, J. *Tetrahedron: Asymmetry* **2006**, *17*, 2632–2632.

Scheme 1.9 Efficient Synthesis of Natural Product *R*-(–)-Sporochnol.

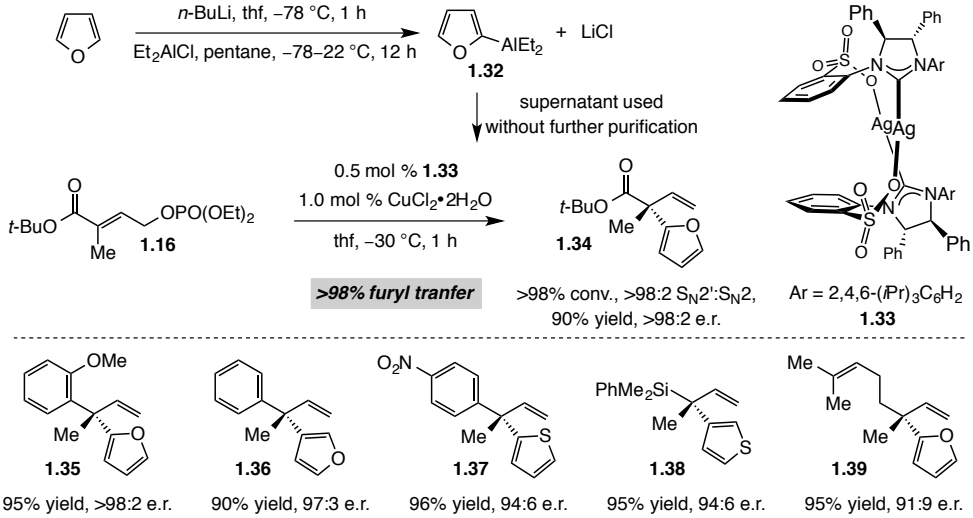


The above strategy also proved beneficial in the addition of heteroaromatic groups, a class of entities, which are of great value in organic synthesis and pharmaceutical industry but virtually unexplored in Cu-catalyzed EAS reactions. As shown in Scheme 1.10, taking the advantage of the acidity of the C2 proton of furan, *n*-BuLi is used to generate the 2-furyllithium, which is readily converted to the diethyl 2-furylaluminum **1.32** under the conditions of Et_2AlCl treatment.[25] A furan substituted all carbon quaternary stereogenic center containing ester **1.34** is obtained under the standard catalytic conditions in 90% yield, >98% S_N2' and >98:2 e.r. within one hour; exclusive incorporation of the furan over the ethyl group is noteworthy. To ensure the highest enantioselectivity observed, we have introduced a modified sulfonate NHC–Ag complex that exhibits larger steric presence around the Cu center (i.e., **1.33**, Scheme 1.10); such change, as compared to the results in Scheme 1.8, probably is in response to the reduced size of the furyl-based nucleophile vs. the regular phenyl variant. Additional cases (cf. **1.35**–**1.39**, Scheme 1.10) exemplified the scope of the transformation; the heterocyclic compounds, which feature a vinyl substituted quaternary stereogenic center, are furnished

(25) For use of furyl- and thienylaluminum reagents in enantioselective additions to carbonyls, see: (a) Wu, K-H.; Chuang, D-W.; Chen, C-A.; Gau, H-M. *Chem. Commun.* **2008**, 2343–2345. (b) Biradar, D. B.; Zhou, S.; Gau, H-M. *Org. Lett.* **2009**, *11*, 3386–3389.

in exceptional efficiency (90–96% yield) and 91:9–>98:2 enantiomer ratio. The corresponding furyl or thiophenyl units are initially obtained through either direct deprotonation (C2 isomers) or lithium/halogen exchange with 3-bromo substituted precursors.

Scheme 1.10. Cu-Catalyzed EAS with In Situ Formed Heterocyclic Aluminum Reagents.



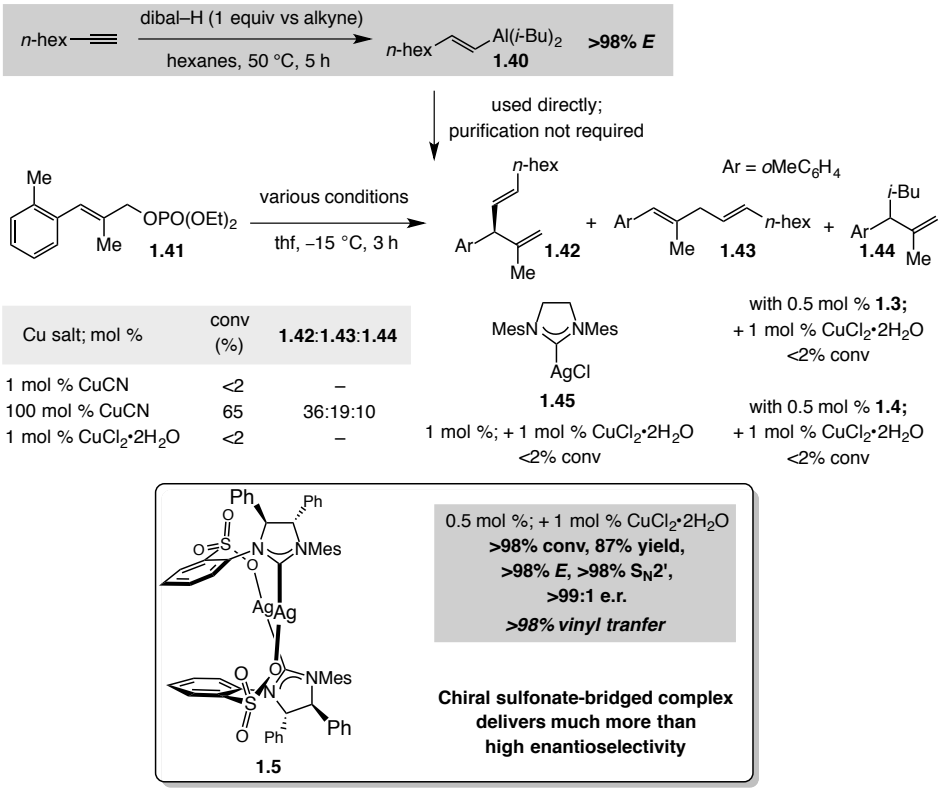
1.4 Additions of Alkenylaluminum Reagents in Cu-catalyzed EAS Promoted by Sulfonate Containing NHCs

Another important sets of EAS reactions include the addition of an olefin-based nucleophile;[26] such transformations deliver 1,4-dienes with a stereocenter in between the

(26) For examples of catalytic enantioselective vinyl additions to carbonyls, see: (a) Oppolzer, W.; Radinov, R. N. *J. Am. Chem. Soc.* **1993**, *115*, 1593–1594. (b) Miller, K. M.; Huang, W.-S.; Jamison, T. F. *J. Am. Chem. Soc.* **2003**, *125*, 3442–3443. (c) Li, H.; Walsh, P. J. *J. Am. Chem. Soc.* **2004**, *126*, 6538–6539. (d) Tomita, D.; Wada, R.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2005**, *127*, 4138–4139. (e) Yang, Y.; Zhu, S.-F.; Zhou, C.-Y.; Zhou, Q.-L. *J. Am. Chem. Soc.* **2008**, *130*, 14052–14053. (f) Kerrigan, M. H.; Jeon, S.-J.; Chen, Y. K.; Carroll, P. J.; Walsh, P. J. *J. Am. Chem. Soc.* **2009**, *131*, 8434–8445. (g) Biradar, D. B.; Gau, H.-M. *Org. Lett.* **2009**, *11*, 499–502. For examples of catalytic enantioselective vinyl additions to aldimines, see: (h) Patel, S. J.; Jamison, T. F. *Angew. Chem. Int. Ed.* **2004**, *43*, 3941–3944. (i) Kong, J.-R.; Cho, C.-W.; Krische, M. J. *J. Am. Chem. Soc.* **2005**, *127*, 11269–11276. (j) Ngai, M.-Y.; Barchuk, A.; Krische, M. J. *J. Am. Chem. Soc.* **2007**, *129*, 12644–12645. (k) Lou, S.; Schaus, S. E. *J. Am. Chem. Soc.* **2008**, *130*, 6922–6923. (l) Nakao, Y.; Takeda, M.; Chen, J.; Salvi, L.; Hiyama, T.; Ichikawa, Y.; Shintani,

two functionalizable alkenes. These structure motifs are either often present in natural products themselves or can be further derivatized to afford more complex multi functional group containing molecules, especially so if the two differently substituted olefins were able to be transformed selectively. However, no such attempt has been reported before 2008; challenges may arise again from both the proper choice of the nucleophilic alkenylmetal reagents and the availability of a class of ligands capable of facilitating the EAS reactions.

Scheme 1.11. Cu-Catalyzed EAS with In Situ Formed Akenylaluminum Reagents.



R.; Hayashi, T. *Chem. Lett.* **2008**, *37*, 290–291. For examples of catalytic enantioselective vinyl conjugate additions to unsaturated carbonyls, see: (m) Oi, S.; Taira, A.; Honma, Y.; Inoue, Y. *Org. Lett.* **2003**, *5*, 97–99. (n) Oi, S.; Sato, T.; Inoue, Y. *Tetrahedron Lett.* **2004**, *45*, 5051–5055. (o) Otomaru, Y.; Hayashi, T. *Tetrahedron: Asymmetry* **2004**, *15*, 2647–2651. (p) Nicolaou, K. C.; Tang, W.; Dagneau, P.; Faraoni, R.; *Angew. Chem. Int. Ed.* **2005**, *44*, 3874–3879. (q) Nakao, Y.; Chen, J.; Imanaka, H.; Hiyama, T.; Ichikawa, Y.; Duan, W.-L.; Shintani, R.. Hayashi, T. *J. Am. Chem. Soc.* **2007**, *129*, 9137–9143. (r) Vuagnoux-d_Augustin, M.; Alexakis, A. *Chem. Eur. J.* **2007**, *13*, 9647–9662. (s) Lee, K.-s.; Hoveyda, A. H. *J. Org. Chem.* **2009**, *74*, 4455–4462.

We have devised a project targeting this problem taking the advantage of our recent progress in the use of Al-based organometallic reagents (cf. aryl(diethyl)aluminum in Section 1.3) in combination with the sulfonate bearing NHC–Cu complexes as catalysts in allylic substitution. Our inspiration came from a reaction known in literature for over half a century; treatment of a terminal alkyne with one equivalent of di*iso*butylaluminum hydride in hydrocarbon solvent results in hydroalumination reaction across the triple bond.[27] Exclusive *trans* 1,2-disubstituted alkenylaluminum species thus generated can be used directly without further purification as a homogeneous solution with calculated concentration assuming minimal solvent evaporation. The class of substrates of our choice is the trisubstituted allylic phosphates that bear a β-substitution, which are notoriously unreactive in Cu-catalyzed EAS reactions. Indeed, as evidenced in Scheme 1.11, most of the representative conditions tested are ineffective at all in promoting such transformations, including catalytic amount of copper salts, in situ mixing of monodentate Ag-carbene **1.45**, bidentate phenoxide-based NHC–Ag complexes (cf. **1.3** and **1.4**) with $CuCl_2 \bullet 2H_2O$; <2% conversion of allylic phosphate **1.41** are observed in all cases. In contrast, in the presence of 1.0 mol % in situ generated sulfonate-bridged Cu complex derived from **1.5**, the EAS reaction proceeds to completion within 3 h at –15 ˚C, affording the desired 1,4-diene **1.42** in 87% yield and >98:2 e.r. No detection of any linear byproduct (<2% S_N2) or the incorporation of the isobutyl group (>98% vinyl transfer).[28] The drastic increase in reactivity observed with the introduction of a sulfonate secondary binding point is noteworthy; the new chiral

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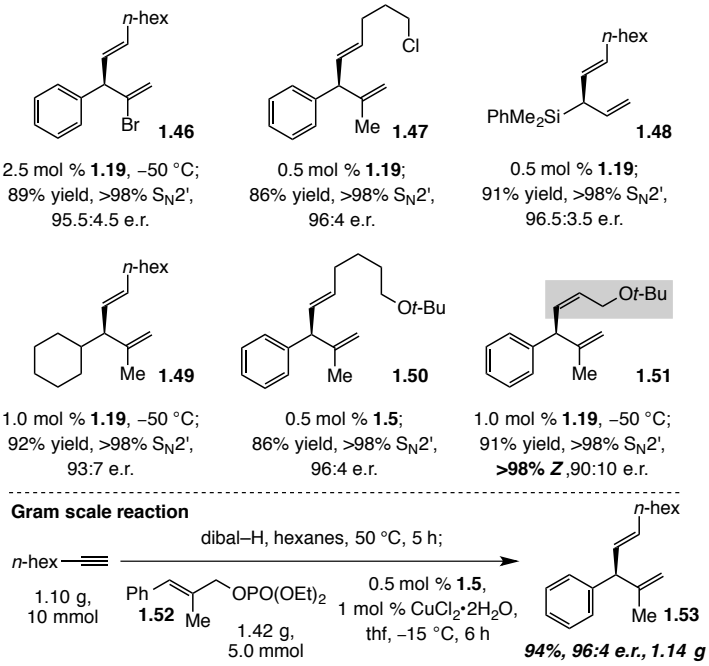
(27) For a review on hydroaluminations of alkynes and alkenes, see: Eisch, J. J. In Comprehensive Organic Synthesis; Trost, B. M., Fleming, I., Schreiber, S. L., Eds.; Pergamon, Oxford, 1991; Vol. 8, pp 733–766.
(28) Lee, Y.; Akiyama, K.; Gillingham, D. G.; Brown, M. K.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2008**, *130*, 446–447.

catalyst (i.e., **1.5**, Scheme 1.11) not only provides high enantioselectivity but also induces exceptional reactivity in Cu-catalyzed EAS.

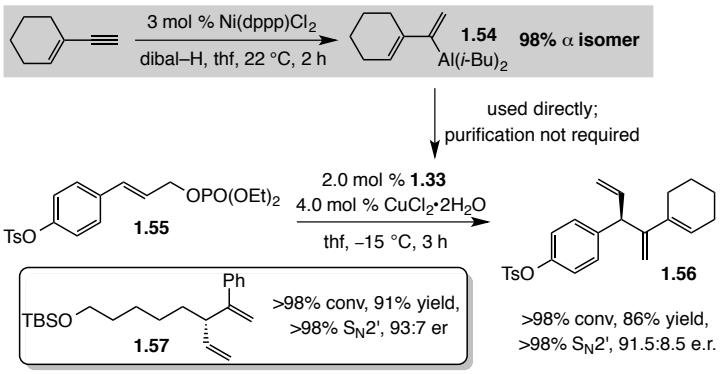
Scheme 1.12 Scope of Cu-Catalyzed EAS with Alkenylaluminum Reagents.



Additional examples (cf. **1.46**–**1.51**) shown in Scheme 1.12 highlight the generality of the above protocol. A few points merit further mention: 1) The EAS reaction tolerates vinylbromide, alkylchloride, alkylether and allylsilane functionalities. 2) Aryl- as well as alkyl-substituted allylic phosphates serve as good substrates; high yields and excellent site selectivity (>98% S_N2' in all cases) are usually obtained. 3) A simply modified **1.19** can help secure the optimal e.r. value whenever **1.5** does not deliver satisfied selectivity. 4) Hydroalumination of *t*-butyl propargyl ether generates alkenylaluminum reagent in exclusive *Z* isomer and such stereochemical information can be transferred without loss of isomeric purity through Cu-catalyzed EAS (cf. >98% *Z* in **1.51**). 5) The reaction can be easily performed at gram scale with minimal use of organic solvent to furnish the desired 1,4-diene product **1.53** in 94% yield and 96:4 e.r.

Traditional hydroalumination with dibal-H proceeds through cis Al-H addition and with di*iso*butylaluminum residing only at the terminus of a resulting alkene. The availability of regioisomeric alkenylaluminum species would on the other hand significantly improve the scope of the NHC–Cu catalyzed EAS reactions. In order to realize such a scenario, a Ni-catalyzed hydroalumination protocol was developed;[29] as shown in Scheme 1.13, with 3 mol % of an inexpensive and commercially available Ni salt, regioselectivity of the traditional uncatalyzed hydroalumination is completely reversed (98% α isomer; cf. **1.54**). The 1,1-disubstituted alkenes that bear a secondary C-Al bond prove to be efficient coupling partners in EAS reactions promoted with low loadings of a chiral silver complex **1.33**, which again features the sulfonate motif. An assortment of differently substituted 1,4-dienes (i.e., **1.56–1.57**, Scheme 1.13) are therefore furnished in high yields (86–91%) and good levels of site and enantioselectivity (>98% S_N2' and 91.5:8.5–93:7 e.r.).

Scheme 1.13 Cu-Catalyzed EAS with 1,1-Disubstituted Alkenylaluminum Reagents.



(29) (a) Gao. F.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 10961–10963. For related selectivity reversal in Ni-catalyzed H-P and H-S addition to terminal alkynes, see: (b) Han, L.-B.; Zhang, C.; Yazawa, H.; Shimada, S. *J. Am. Chem. Soc.* **2004**, *126*, 5080–5081.

Besides catalysis, selective hydroalumination can also be achieved from substrate control. Silicon substituted internal alkynes are established to be a unique class of substrates for uncatalyzed hydroalumination.[30] As demonstrated in Scheme 1.14, under seemingly very similar conditions, acetylene **1.58** undergoes hydroalumination with complete conversions within two hours, however delivering two distinct products (**1.59** vs. **1.60**) in >98% selectivities. The only difference is the existence of a coordinating solvent thf. Rationales for such a phenomenon likely consist of three aspects: 1) the availability of an empty p orbital in the aluminum metal significantly delocalizes the electron density in the double bond, thus rendering it a more single bond character; 2) the phenyl as well as the silicon substituents stabilize the incipient carbocation and lower the energy barrier towards to the formation of such entities (cf. **1.62**); 3) the steric repulsion between the sizable Si and an aryl unit further facilitate the projected isomerization of the kinetically generated *Z* isomer (from cis H-Al addition across triple bond) to the thermodynamically more favored *E* isomer. The role of thf molecule is therefore to occupy the empty p orbital of the aluminum and shuts down the isomerization pathway.

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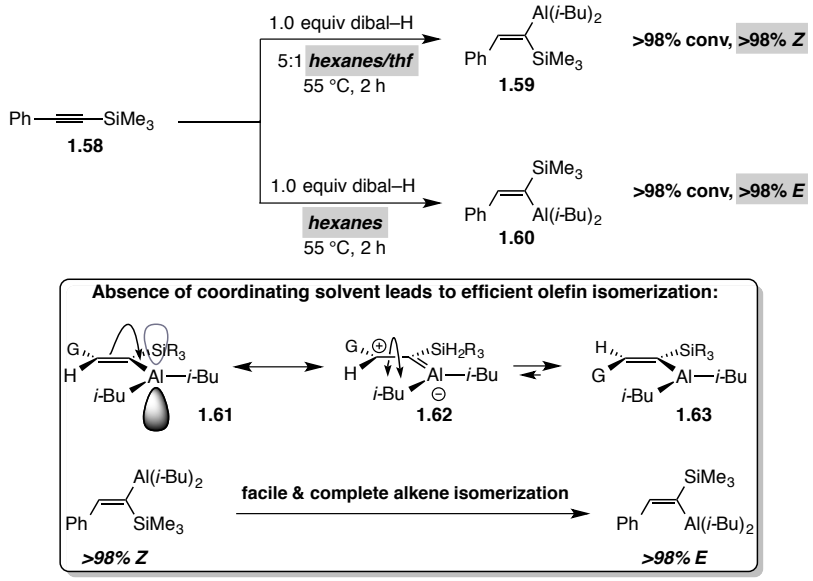
(30) For a review regarding stereoselective synthesis through the use of Si-containing compounds, see: (a) Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev.* **1997**, *97*, 2063–2192. For related examples, see: (b) Eisch, J. J.; Foxton, M. W. *J. Org. Chem.* **1971**, *36*, 3520–3526. (c) Eisch, J. J.; Rhee, S-G. *J. Am. Chem. Soc.* **1975**, *97*, 4673–4682. For a related review, see: (d) ref. 27.

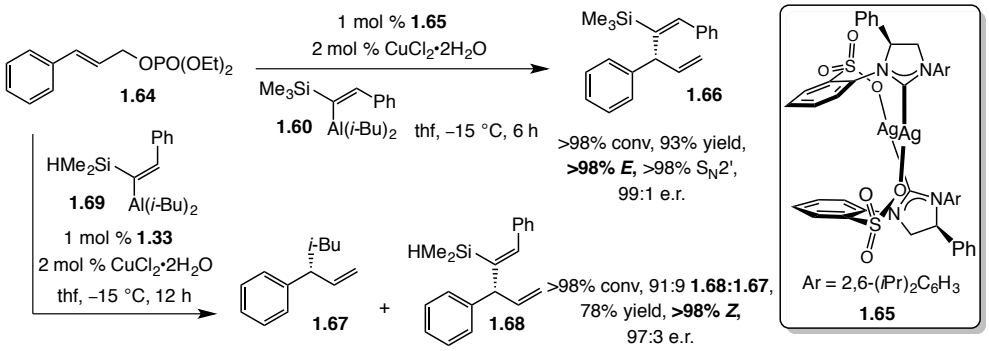
Scheme 1.14 Solvent Controlled Stereoselective Synthesis of Si Containing Alkenylaluminums.



Despite the congested nature of these trisubstituted alkenylaluminum species, the NHC–Cu catalyzed EAS reactions with them are still very efficient and highly selective.[31] With 1 mol % of a modified Ag complex **1.65**, 1,4-diene **1.66**, which bears a well defined trisubstituted alkene, is afforded in 93% yield, exceptional site (>98%) and enantioselectivity (99:1 e.r., Scheme 1.15). The addition of the *Z* isomeric alkenylaluminum requires the combination of a slightly smaller silicon group (HMe_2Si vs. Me_3Si) and NHC–Ag **1.33** for optimal enantioselectivity; a small quantity of transfer of an isobutyl group (cf. **1.67**) is also observed under such conditions.

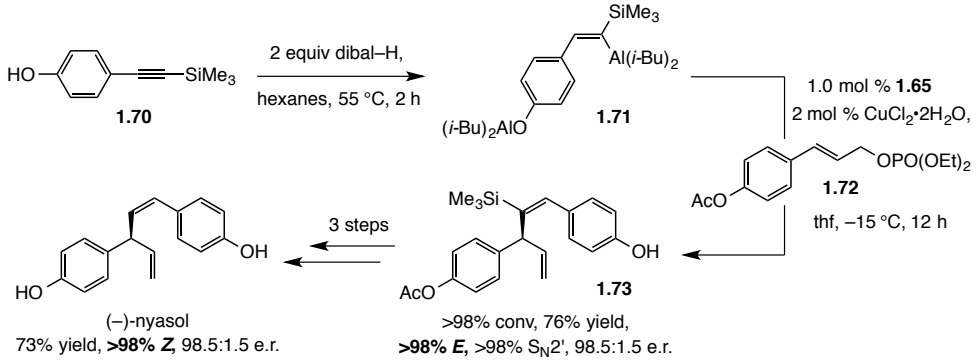
(31) Akiyama, K.; Gao, F.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2010**, *49*, 419–423.

Scheme 1.15 Cu-Catalyzed EAS with Si Containing Akenylaluminum Reagents.



The utility of the above method is demonstrated through the concise total synthesis of natural product (–)-nyasol.[32] Hydroalumination of a phenol containing alkynylsilane **1.70** results in a bis-aluminum compound **1.71**, which is readily involved in the NHC–Cu catalyzed EAS with an acetate bearing allylic phosphate **1.72** to furnish the alkenylsilane **1.73** in complete control of selectivity levels (>98% *E*, >98% S_N2' and 98.5:1.5 e.r., Scheme 1.16). The silicon group is later protonated to reveal the *cis* olefin (>98% *Z*) equipped in the final target.

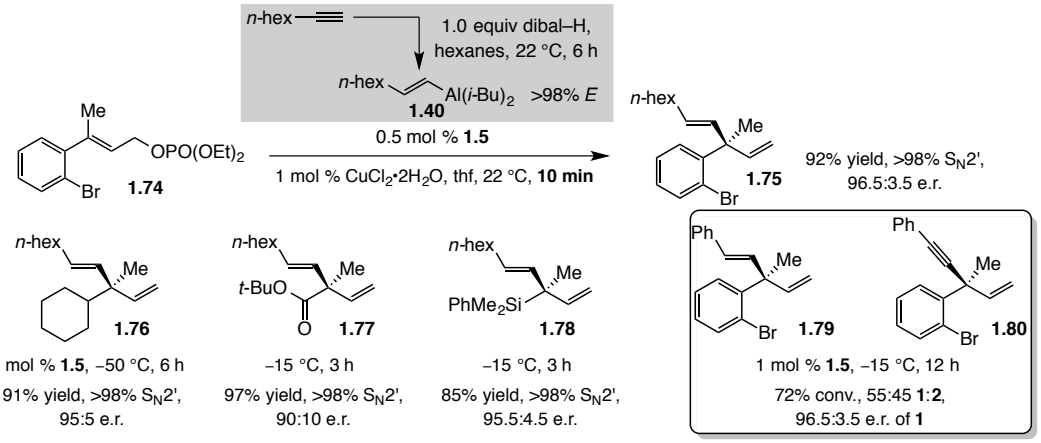
Scheme 1.16 Efficient and Enantioselective Synthesis of Natural Product *R*-(–)-Nyasol.



(32) For a previous enantioselective synthesis of di-O-methyl ether of nyasol, involving a Wittig olefination that proceeds with 3:2 Z:E selectivity, and related natural products, see: (a) Quan, W.-G.; Yu, B.-X.; Zhang, J.-Y.; Liang, Q.-R.; Sun, Y.-Q.; She, X.-G.; Pan, X.-F. *Chin. J. Chem.* **2007**, *25*, 688–693. For another synthesis using Ir-catalyzed vinylation chemistry, see: (b) Hamilton, J. Y.; Sarlah, D.; Carreira, E. M. *J. Am. Chem. Soc.* **2013**, *135*, 994−997.

The formation of sterically demanding all carbon quaternary stereogenic center with alkenylaluminum reagents is also efficient under NHC–Cu catalysis.[33] As shown in Scheme 1.17, as low as 1 mol % of an in situ formed Cu catalyst (derived from **1.5**) is sufficient to promote the formation of 1,4-diene **1.75**; the reaction is complete in ten minutes at ambient temperature and the product is affored in 96.5:3.5 e.r. Additional examples (**1.76**–**1.78**) illustrate the scope of this transformation. One shortcoming of the traditional hydroalumination is the impractical synthesis of aryl-substituted alkenylaluminum species; such an issue is highlighted in our attempt to prepare compound **1.79**, which is accompanied with an inseparable byproduct **1.80**, which derives from catalytic addition of the corresponding alkynylaluminum reagent generated during the course of uncatalyzed hydroalumination process of phenylacetylene.[34]

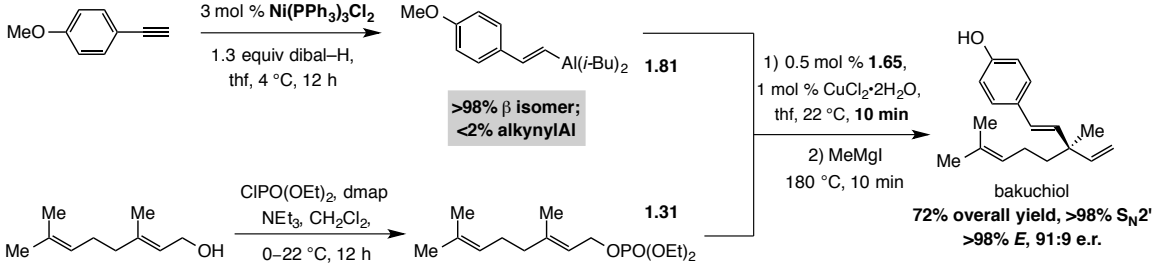
Scheme 1.17 Formation of Quaternary Stereogenic Centers through Cu-Catalyzed EAS with Alkenylaluminum Reagents.



(33) Gao, F.; McGrath, K. P.; Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 14315−14320.
(34) (a) Zweifel, G.; Snow, J. T.; Whitney, C. C. *J. Am. Chem. Soc.* **1968**, *90*, 7139−7140. (b) Uhl, W.; Er, E.; Hepp, A.; Kösters, J.; Grunenberg, J. *Organometallics* **2008**, *27*, 3346−3351. (c) Uhl, W.; Er, E.; Hepp, A.; Kösters, J.; Layh, M.; Rohling, M.; Vinogradov, A.; Würthwein, E.-U.; Ghavtadze, N. *Eur. J. Inorg. Chem.* **2009**, 3307−3316.

To address this issue, we sought to Ni catalysis again, for a potential acceleration effect to out compete the adventitious deprotonation pathway.[35] The synthesis of natural product bakuchiol in Scheme 1.18 showcases the significance of having such a protocol in hand. Through an extensive screening, commercial $Ni(PPh_3)_2Cl_2$ is identified as the optimal catalyst to carry out the desired hydroalumination reaction of *p*-methoxy phenylacetylene with no detectable formation of alkynylalane. Coupling of alkenylaluminum **1.81** with a geraniol derived allylic phosphate **1.31** under the standard conditions delivers bakuchiol in 72% overall yield and high selectivity levels after demethylation (>98% S_N2', >98% *E* and 91:9 e.r.).[36]

Scheme 1.18 Ni-Catalyzed Hydroalumination/Cu-Catalyzed EAS Sequence in the Synthesis of Bakuchiol.



1.5 Additions of Alkynylaluminum Reagents in Cu-catalyzed EAS Promoted by Sulfonate Containing NHCs

The coupling of an alkyne group with an allylic phosphate to afford a "skipped" enyne is an unexplored territory in Cu-catalyzed EAS reactions. In fact, an alkynyl ligand

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(35) Eisch, J. J.; Foxton, M. W. *J. Organomet. Chem.* **1968**, *12*, P33–P36. (a) Eisch, J. J.; Sexsmith, S. R.; Fichter, K. C. *J. Organomet. Chem.* **1990**, *382*, 273–293. (b) Eisch, J. J.; Ma, X.; Singh, M.; Wilke, G. *J. Organomet. Chem.* **1997**, *527*, 301–304.

(36) For previous enantioselective syntheses of bakuchiol, see: (a) Takano, S.; Shimazaki, Y.; Ogasawara, K. *Tetrahedron Lett.* **1990**, *31*, 3325– 3326. (b) Du, X.-L.; Chen, H.-L.; Feng, H.-J.; Li, Y.-C. *Helv. Chim. Acta* **2008**, *91*, 371–378. (c) Esumi, T.; Shimizu, H.; Kashiyama, A.; Sasaki, C.; Toyota, M.; Fukuyama, Y. *Tetrahedron Lett.* **2008**, *49*, 6846–6849. (d) Bequette, J. P.; Jungong, C. S.; Novikov, A. V. *Tetrahedron Lett.* **2009**, *50*, 6963–6964.

on copper used to be considered much less readily transferrable compared to other organic ligands (e.g., an alkenyl unit).[37] Due to the discovery outlined above (cf. **1.80** in Scheme 1.17), we surmised that the unique sulfonate containing NHCs might be able to serve as effective promoters for such transformations as long as a clean synthesis of alkynylaluminum reagents is available. Micouin and coworkers have reported an effective method for the preparation of alkynylalanes.[38] The conditions described are almost the same as in traditional hydroalumination except for the introduction of 5 mol % Et_3N to the reaction media; such a variation completely tunes the reactivity of dibal-H towards deprotonation of the terminal alkyne. The observed reactivity profile is attributed to a small amount, but highly reactive, Et_3N bound Al ate complex. With the proper reagents in hand, we have carried out the study to determine the efficiency, selectivity and scope of EAS involving an alkyne unit.[39] As shown in Scheme 1.19, in the presence of only 1 mol % NHC–Cu complex derived from **1.5**, a range of alkynes and allylic phosphates can be effectively coupled with EAS reactions, furnishing a variety of enynes that bear a quaternary stereogenic center (**1.83–1.87**) in 82–97% yield and high enantioselectivity levels (93:7–99:1 e.r.). An interesting aspect is that, in contrast to the previous studies,[37] transfer of the alkyl (*i*Bu) ligands on Al is never observed. The utility of the alkyne moiety is demonstrated through the efficient Au catalyzed cyclization of the *t*-butyl ester containing enyne product,[40] with cyclic lactone **1.88** as a representative.

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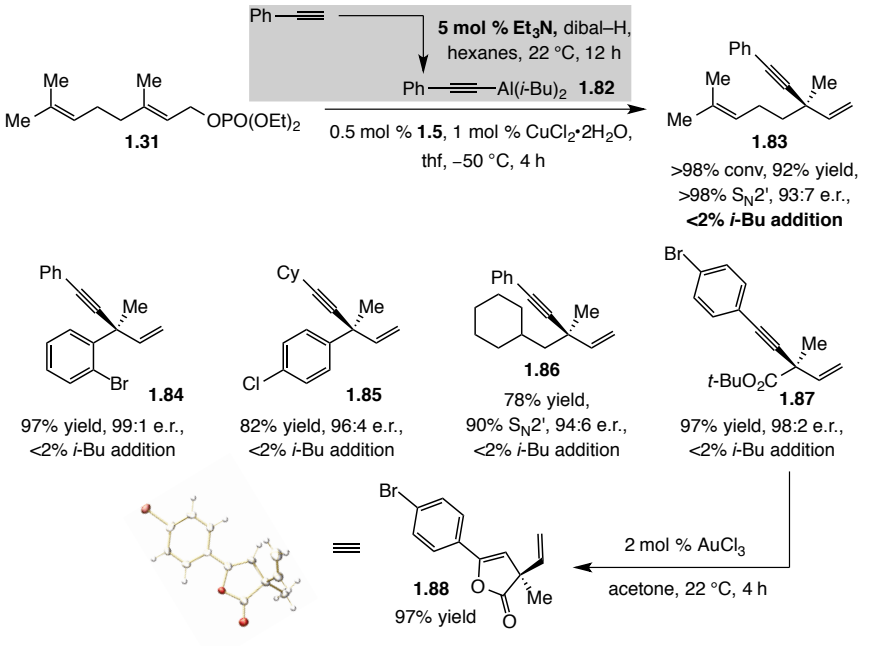
(37) (a) Modern Acetylene Chemistry; Stang, P. J., Diederich, F., Eds.; Wiley-VCH: Weinheim, Germany, 1995. (b) Acetylene Chemistry: Chemistry, Biology and Material Science; Stang, P. J., Diederich, F., Tykwinski, R., Eds.; Wiley-VCH, Weinheim, Germany, 2005.
(38) (a) Binger, P. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 686. (b) Feuvrie, C.; Blanchet, J.; Bonin, M.; Micouin, L. *Org. Lett.* **2004**, *6*, 2333–2336.
(39) Dabrowski, J. A.; Gao. F.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 4778−4781.
(40) For Au-catalyzed intramolecular addition of carboxylic acids to terminal alkynes, see: (a) Genin, E.; Toullec, P. Y.; Antoniotti, S.; Brancour, C.; Genêt, J.-P.; Michelet, V. *J. Am. Chem. Soc.* **2006**, *128*, 3112–

Scheme 1.19 Catalytic Generation of Alkynylaluminums and Their Utilities in Cu-Catalyzed EAS.



Subsequently, the formation of alkyne-substituted tertiary stereogenic center containing enantioenriched molecules through Cu-catalyzed EAS is our next focus.[41] As the findings in Scheme 1.20 indicates, treatment of an ester bearing allylic phosphate **1.89** under the aforementioned alkynyl addition conditions catalyzed by copper complex of **1.19** furnishes a "skipped" enyne **1.90** with a sensitive benzylic C-H bond in 90% yield and 95:5 e.r. The corresponding EAS product derived from a regular 1,2-disubstituted allylic phosphate is cleanly formed under these conditions as well; it is, however, somewhat unstable towards isolation by silica gel chromatography. Additional cases, including an alkyl-substituted enoate **1.92**, a heterocycle containing enyne **1.93** and a highly functionalized ester **1.94**, showcase the scope of this approach, allowing access to a large number of enantiomerically enriched enynes, which are applicable in an efficient

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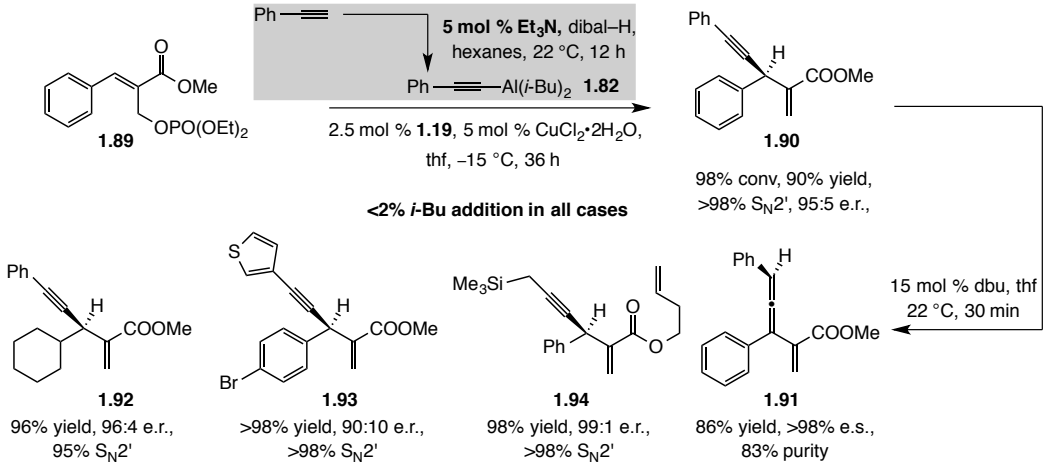
3113. For intramolecular Au catalyzed additions of methyl esters to allenes, see: (b) Liu, L.-P.; Xu, B.; Mashuta, M. S.; Hammond, G. B. *J. Am. Chem. Soc.* **2008**, *130*, 17642–17643. For Bi-catalyzed cyclizations of carboxylic esters to internal alkynes, see: (c) Komeyama, K.; Takahashi, K.; Takaki, K. *Org. Lett.* **2008**, *10*, 5119–5122.

(41) Dabrowski, J. A.; Haeffner, F.; Hoveyda A. H. *Angew. Chem., Int. Ed.* **2013**, *52*, 7694–7699.

isomerization reaction to deliver trisubstituted allenes without loss of optical purity (usually >98% e.s., cf. **1.91**); such processes are catalyzed by an inexpensive small organic base (dbu) and proceed to completion at ambient temperature within 30 minutes.

Scheme 1.20 Cu-Catalyzed EAS with Alkynylaluminums and Their Applications in Allene Synthesis.



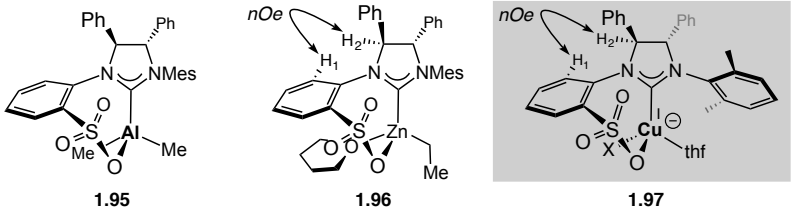
1.6 Proposed Mechanistic Working Models of Sulfonate Containing N-heterocyclic Carbene Copper Complex in Catalytic EAS with Aluminum Based Reagents

The highly efficient EAS reactions with a range of nucleophilic organometallic reagents (especially Al based), promoted by this unique class of bidentate *N*-heterocyclic carbenes, prompt us to understand the mechanistic insights that are attributed to the sulfonate motif. To begin with, we want to establish the identity of the catalytically active species especially since dimeric Ag-complexes are used to generate the Cu based catalysts. For three reasons that we believe that the complexes in action are monomeric: 1) simply examining the crystal structure of the dimeric Ag-complex **1.5**[42] suggests that the corresponding dimeric copper species are too sterically congested and without enough

(42) To review the crystal structure, see ref. 13 (a).

coordinating sites for both substrates and the nucleophilic partners to bind at the same time. It would be much more likely for the catalysts to become active if the dimeric structures equilibrate to their monomeric counterparts first. 2) Although the crystal structures of the copper complexes are difficult to obtain, the related Al (**1.95**) and Zn (**1.96**) based crystals were secured and their monomeric structures were shown in Figure 1.3.[43] A critical difference was discovered compared to the dimeric Ag complexes; the secondary ligating sulfonate group points in the same direction with the backbone Ph unit (cf. Ag complexes shown in the previous schemes for comparison). Such a counterintuitive finding, as we reasoned, derives from the small seven-membered ring formed in the monomeric bidentate NHC metal complexes; the ring strain bends the sulfonate containing N-Ar unit of the heterocycle, forcing the ortho C-H bond opposite to the sulfonate intruding into the congested backbone region. Such an unfavored steric interaction can be alleviated if the C-H is in closer proximity to the backbone C-H instead of the larger phenyl ring. Based on these rationales, we propose that the corresponding copper catalysts bear similar monomeric structures (cf. **1.97**). 3) The solution nOe studies (highlighted in Figure 1.3) further support the unique structure feature of the sulfonate containing bidentate NHC metal complexes.

Figure 1.3. Proposed Monomeric Sulfonate Containing NHC–Cu Structure in Solution.



1.95 **1.96** **1.97**

(43) Lee, Y.; Li, B.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 11625–11633.

Based on the established active catalytic species, the following catalytic cycle, involving the additions of various organoaluminum reagents in Cu-catalyzed EAS reactions, is proposed (Scheme 1.21). The tetrahedron NHC–Cu(I) complex **1.100**, which has two available coordination sites (solvent bound when not in action), can accept the transfer of groups with better polarizability among the organic ligands on the aluminum metal (e.g., aryl, alkenyl and alkynyl vs. alkyl). The transfer is further facilitated due to the large space available at the left back quadrant of the Cu complex, a feature attributed to the syn relationship of the sulfonate moiety and the backbone Ph group. The resulting ate complex **1.101** can closely bind the cationic dialkylaluminum through the equatorially disposed sulfonate oxygen; such an orientation of the Al cation can chelate with the substrate phosphate oxygen, activating and organizing the allylic phosphate coordination from the front right site of the complex (as in **1.98**). The resulting intimate relationship between the substrate and the non-sulfonate bearing N-Ar substituent allows modifications to be done to fine tune the enantioselectivity levels (as observed in numerous cases in the previous experimental sections). The following steps along the catalytic cycle remain controversial.[44] Both an oxidative addition/reductive elimination

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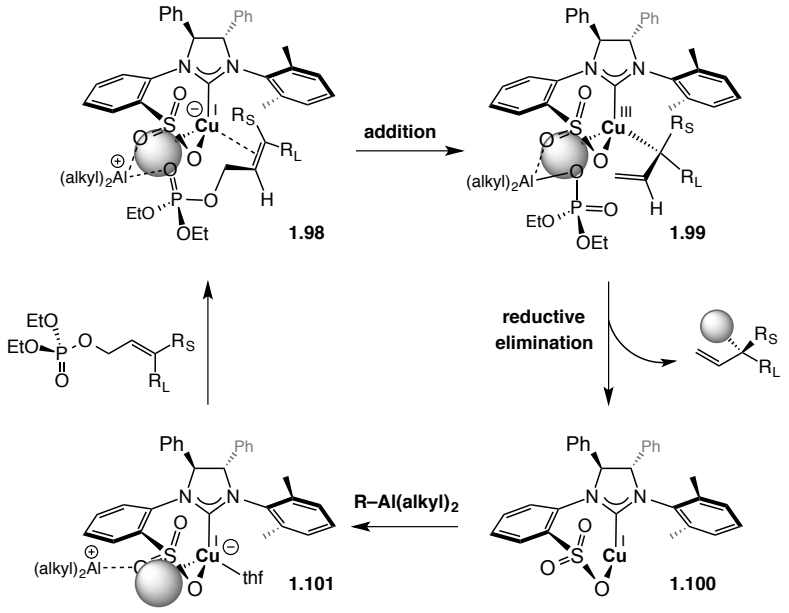
(44) An NHC-Cu-catalyzed EAS process might proceed through a Cu(I) mechanism (direct transfer of the vinyl unit) or a pathway that involves a Cu(III) complex (cuprate addition followed by alkyl-vinyl reductive elimination). It is not clear at present which pathway is energetically preferred. Although previous mechanistic studies point to Cu(III) mechanism being operative, such investigations were in connection to alkyl- or allylcopper complexes, considered allyl halides as substrates, and did not involve a catalyst. The more polarized nature of a Cu-C bond in a vinylmetal complex, particularly a strongly Lewis base-activated NHC–Cu-vinyl complex, and the associated steric demands of forming a Cu(III)-substituted quaternary carbon, could favor the Cu(I) pathway. For recent reports regarding the mechanism of non-catalytic allylic substitution reactions with alkyl- and allylcopper reagents, see: (a) Sofia, A.; Karlström, E.; Bäckvall, J.-E. *Chem. Eur. J.* **2001**, *7*, 1981–1989. (b) Yoshikai, N.; Zhang, S.-L.; Nakamura, E. *J. Am. Chem. Soc.* **2008**, *130*, 12862–12863. (c) Bartholomew, E. R.; Bertz, S. H.; Cope, S.; Murphy, M.; Ogle, C. A. *J. Am. Chem. Soc.* **2008**, *130*, 11244–11245. For a recent review on the mechanism of nucleophilic organoCu(I) reactions, see: (d) Yoshikai, N.; Nakamura, E. *Chem. Rev.* **2012**, *112*, 2339–2372.

sequence and a direct transfer of the organic group to the γ position of the allylic phosphate are plausible to complete the cycle.

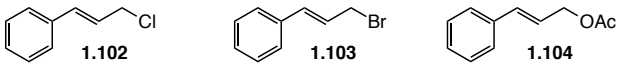
Scheme 1.21. A General Mechanistic Model for Cu-Catalyzed EAS with Aluminum Reagents.



A few experimental evidences to support the above chelation scenario are collected. As illustrated in Scheme 1.22, substrates that bear less potent coordinating leaving groups are examined and proved to be much less efficient (<10% conv. of halogen containing **1.102** and **1.103** and acetate bearing **1.104** vs. allylic phosphate, Part 1, Scheme 1.22). In part 2, NHC ligands, either monodentate (cf. **1.18**) or bidentate (cf. **1.4**), that lack the properly disposed chelating oxygen are much less efficient promoters for the Cu-catalyzed EAS reactions with alkenylaluminums. Additionally, trisubstituted allylic phosphate **1.107** with *Z* olefin geometry is an effective substrate but delivers product **1.108** enriched in the opposite enantiomer and with lower enantioselectivity (30:70 e.r. vs. 98:2 e.r., part 3, Scheme 1.22), suggesting the validity of the proposed stereochemical determining complex **1.98** (Scheme 1.21).

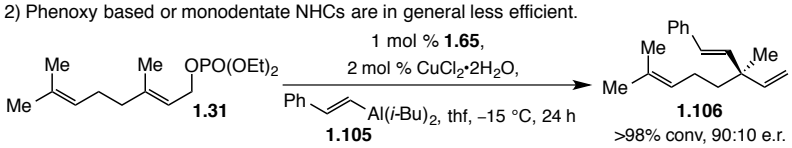
Scheme 1.22 Supporting Evidences for The Proposed Mechanistic Model.

1) Leaving groups that fail to provide chelate are ineffective.



1.102 **1.103** **1.104**

2) Phenoxy based or monodentate NHCs are in general less efficient.

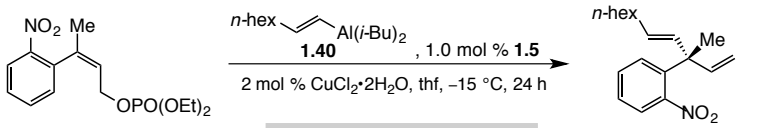


1.31 **1.105** **1.106**

>98% conv, 90:10 e.r.

with 1 mol % **1.4**	with 2 mol % **1.18**
27% conv, 71:29 e.r.	5–10% conv

3) *Z*-allylic phosphates serve as less effective substrates.



1.107

E isomer under such condtions: >98% conv, 98:2 e.r.

1.108

>98% conv, 30:70 e.r.

1.7 Effective Utilizations of Organoboronic Acid Pinacol Esters in Cu-catalyzed EAS Promoted by Sulfonate Containing NHCs

The trend of identifying milder conditions to conduct highly selective organic transformations has emerged to a greater extent ever. Enantioselective copper catalyzed allylic substitution, for the past almost two decades, centered on the use of reactive organometallic reagents (i.e., organolithium, Grignard, aluminum or zinc species) to achieve efficiency and at the same time control various selectivity parameters.[2] The above reviewed sulfonate containing *N*-heterocyclic carbene Cu catalysts also exhibit a harmonic relationship with Al based nucleophilic reagents through a crucial chelation rendered possible by the cationic aluminum species. An interesting question then arises to challenge the proposed working model (Section 1.6): what if the Lewis acidic Al cations are no longer available; can the same NHC–Cu system still provide similar efficiency and selectivity? One set of reagents that is of great importance and can be informative to answer the above question corresponds to organoboron species, especially since recent

advances in their synthesis[45] have delivered more facile access of these robust and user-friendly nucleophilic surrogates.

Allenylboronic acid pinacol ester was chosen for investigation in NHC-Cu catalyzed EAS reactions for two reasons. The first one relates to the much less Lewis acidic boron center (i.e., B was substituted with at least two oxygen atoms; the delocalization of lone pair electrons to the empty p orbital of the B center significantly reduces its acidity) compared to cationic Al. The efficiency and selectivity with this reagent (cf. **1.109**) can help reveal the role of the proposed chelating metal. Second, the enantioselective additions of an allenyl unit in Cu-catalyzed EAS reactions are unknown and the best precursor for such transformations is the commercially available allenylBpin, due to the instability and the difficulty in preparation of the corresponding allenyl metals. As shown in Scheme 1.23, in the presence of 10 mol % in situ formed NHC–Cu complexes, the consumption of the allenylBpin reagent is feasible through a proper activation from stoichiometric amount of NaOMe;[46] the supposedly generated OMe substituted borate complex is nucleophilic enough for ligand transfer to the Cu catalysts. The EAS reactions are conducted at ambient temperature with extended reaction time compared to the previously investigated organoaluminum reagents (e.g., 24 h vs 10 minutes with alkenylaluminums in Scheme 1.17). Surprisingly, the EAS reactions with monodentate (i.e., **1.111** and **1.112**) or oxygen based bidentate (i.e., **1.113** and **1.114**) imidazolinium salts almost exclusively give linear achiral allenyl adduct when exposed to

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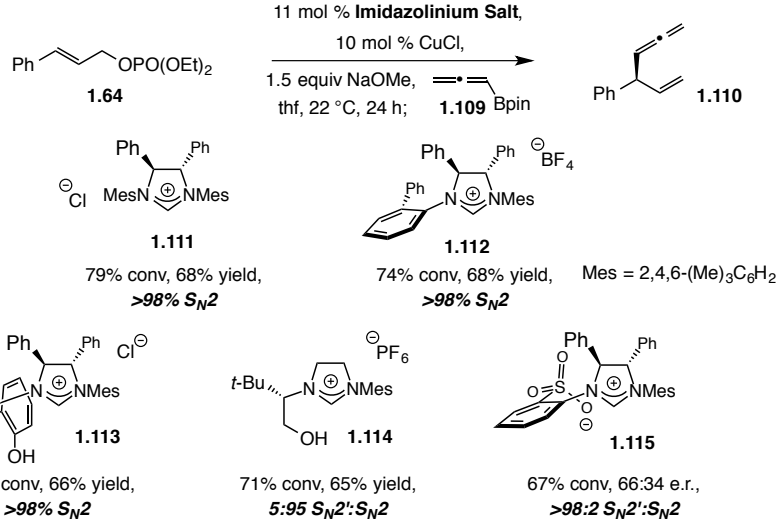
(45) For recent selected reviews, see: (a) Ishiyama, T.; Miyaura, N. *The Chemical Record* **2004**, *3*, 271–280. (b) Jiao, J.; Nishihara, Y. *J. Organometallic Chem*. **2012**, *721–722*, 3–16. (c) Ishiyama, Tatsuo, and Norio Miyaura. "Metal Catalyzed Borylation of C-H and C-Halogen Bonds of Alkanes, Alkenes, and Arenes for the Synthesis of Boronic Esters." *Boronic Acids: Preparation and Applications in Organic Synthesis, Medicine and Materials (Volume 1 and 2), Second Edition* (2012): 135-169.
(46) Ohishi, T.; Nishiura, M.; Hou, Z. *Angew. Chem. Int. Ed*. **2008**, *47*, 5792–5795.

an allylic phosphate **1.64**. On the contrary, the sulfonate bearing imidazolinium salt **1.115** is able to deliver >98% branched product **1.110** in 66:34 enantiomer ratio.[47] As suggested in this study, the drastic ligand effect may come from the ability of the mildly Lewis basic sulfonate oxygen to retain the cuprate character of the active Cu complex (i.e., NHC keeps its bidentate ligation with the copper center) under the specific reaction conditions involving allenylBpin. The rationale for alkoxide and phenoxide based carbenes to be less effective ligands can be formulated as the following: these bidentate chelating oxygens are relatively more Lewis basic and therefore capable of performing the similar role of NaOMe in promoting allenyl transfer. However, such an intramolecular allenyl group delivery will result in the break of the O-Cu bonds (a new O-Bpin bond formed instead), a crucial ligation for keeping the copper centers as ate complexes.

Scheme 1.23 Amazing Ligand Effect in Cu-Catalyzed EAS with Allenylboron Reagents.



Even though an impressive site selective allenyl allylic substitution is achieved with imidazolinium salt **1.115**, the differentiation of the enantiotopic faces of the

(47) Jung, B.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2012**, *134*, 1490–1493.

substrate is no longer prominent (66:34 e.r.). Apparently, new modifications of NHCs are needed for this class of reactions to be synthetically useful. To direct our design, we first set forth to acquire certain hypothesis to explain the observed much lower efficiency and enantioselectivity when the same combination of substrate and chiral ligand is used towards the EAS with allenylBpin reagent as opposed to organoaluminums. As demonstrated in Figure 1.4, in addition to the chelate activation of the phosphate leaving group, the Lewis acidic metal also serves as an anchor to lock the approaching direction of the olefin substrate relative to the copper center (cf. **1.116**). Upon the removal of the bridging metal, the relatively linear shaped allylic phosphate no longer has preference for one of the two available coordination sites in a tetrahedron Cu(I) complex and the anti-sulfonate substrate coordination mode (cf. **1.118** vs. **1.117**) becomes competitive and thus lowers the enantioselectivity, especially when the ortho substituent is a small methyl group. Our initial attempts to install larger groups (bigger than *i*Pr) at the *ortho* position of the symmetrical N-Ar unit result in failure because of the ineffective Pd-catalyzed C-N couplings with sterically congested aryl halides.[48] We then revised our design direction to target introducing sizable substituents at the *meta* positions of the N-Ar moiety since, after a careful analysis of the molecular model, the approaching mode syn to the sulfonate is found to impose strong steric interaction between the substrate and the *meta* substituent (cf. **1.119**). Such modifications should encourage allylic phosphate

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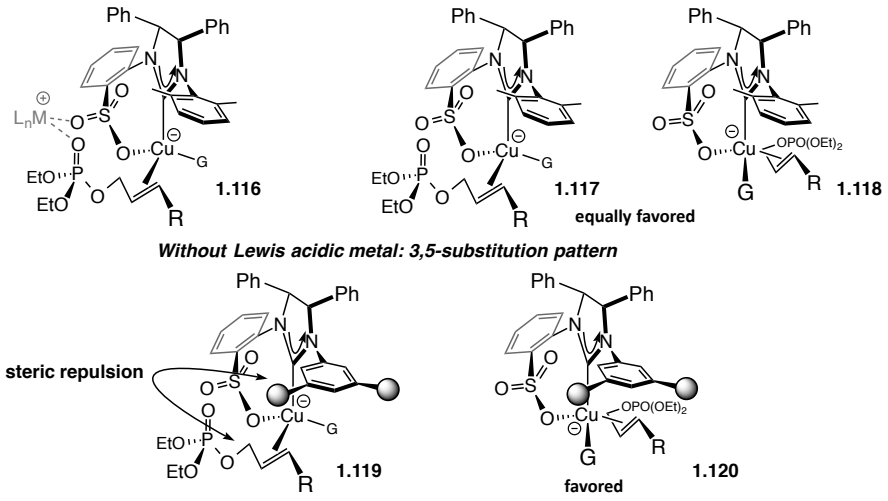
(48) For recent reviews on C-N coupling reactions, see: (a) Gwilherm, E.; Blanchard, N.; Toumi, M. *Chem. Rev*. **2008**, *108*, 3054–3131. (b) Monnier, F.; Taillefer, M. *Angew. Chem. Int. Ed*. **2009**, *48*, 6954–6971. (c) Marcel, K.; Dubbaka, S. R.; Brade, K.; Knochel, P. *Eur. J. Org. Chem*. **2007**, *25* 4166-4176. (d) Lei, J.; Buchwald, S. L. Metal Catalyzed Cross Coupling Reactions, Second Edition (2004): 699–760. (e) Klinkenberg, J. L.; Hartwig, J. F. *Angew. Chem. Int. Ed*. **2011**, *50*, 86–95. (f) Lemen, G. S.; Wolfe, J. P. Palladium-Catalyzed sp2 C–N Bond Forming Reactions: Recent Developments and Applications. (2013): 1–53.

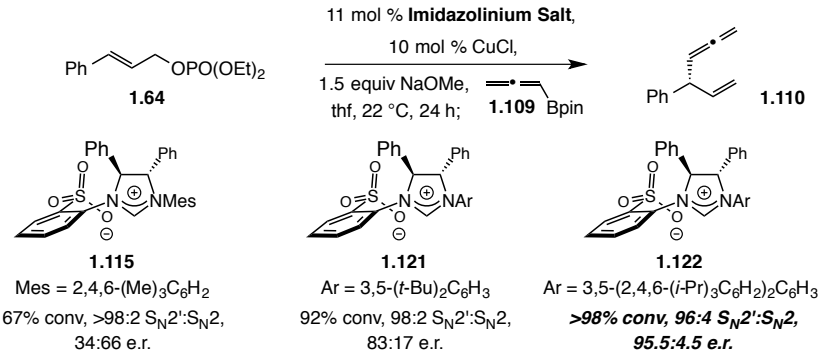
coordination *anti* to the sulfonate (cf. **1.120**). Furthermore, the synthesis involving the C-N couplings of less sterically demanding aryl bromides is much more efficient.

Figure 1.4 Design of New Sulfonate Containing Imidazolinium Salts with Improved Enantioselectivity.



The above hypothesis is challenged through EAS reactions with two modified bis-*meta* substituted imidazolinium salts (cf. **1.121** and **1.122**) and the results are presented in Scheme 1.24. As the groups at the *meta* position become larger (i.e., from *t*-Bu to tri*iso*propylphenyl), the enantiomer ratio improves to 95.5:4.5 for the synthesis of **1.110** and in consistent with our analysis, the opposite enantiomer is now dominant in the product mixture.

Scheme 1.24 Enantioselective Construction of Allene Containing Tertiary Stereocenter.



The construction of allene containing all-carbon quaternary stereogenic center through Cu-catalyzed EAS reactions is also illustrated in Scheme 1.25. In the presence of 10 mol % of an in situ generated Cu complex derived from **1.115**, trisubstituted allylic phosphate **1.123** is converted to allenyl adduct **1.124** in 74% yield and 93.5:6.5 e.r. with again complete control of site selectivity (>98% S_N2'). Interestingly, the optimal NHC for disubstituted allylic phosphates delivers product **1.124** in 33:67 e.r., favoring the opposite enantiomer. Similar analysis through molecular model suggests that the additional methyl group on the olefin substrate imposes more severe steric interaction with *ortho* methyl unit on the N-Ar (cf. **1.128**); the approaching mode syn to the sulfonate (cf. **1.127**) now becomes more energetically favored. On the other hand, because of the upward pointing methyl group, the originally more favored complex with anti-sulfonate coordination (cf. **1.130**) when **1.122** serves as the ligand now becomes much less populated in the reaction mixture. The utility of the allene is further demonstrated through a formal synthesis of α-cuparenone; the advanced ketone intermediate **1.126** can be accessed from the quaternary center bearing enantiomerically enriched allene **1.125** through an efficient Cu-catalyzed protoboration/oxidation sequence.[49]

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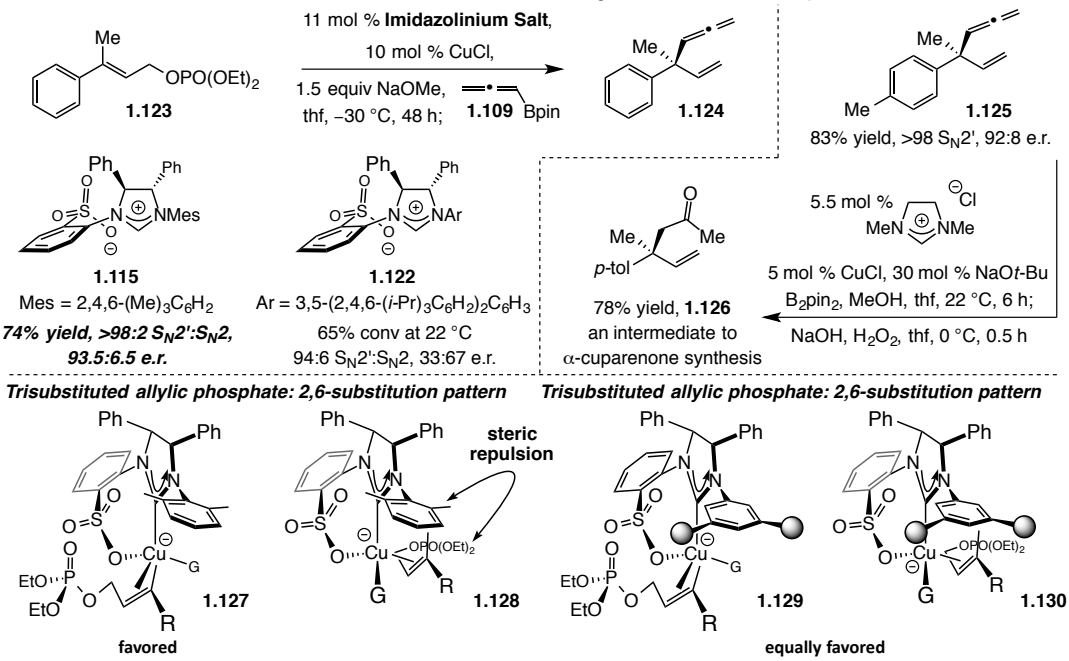
(49) For Cu-catalyzed protoboration of allenes, see: (a) Meng, F.; Jung, B.; Haeffner, F.; Hoveyda, A. H. *Org. Lett.* **2013**, *15*, 1414–1417. (b) Yuan, W.; Ma, S. *Adv. Synth. Catal.* **2012**, *354*, 1867–1872. For protoboration of alkynes to synthesize alkenylborons, see: (c) Kim, H. R.; Jung, I. G.; Yoo, K.; Jang, K.; Lee, E. S.; Yun, J.; Son, S. U. *Chem. Commun.* **2010**, *46*, 758–760. (d) Semba, K.; Fujihara, T.; Terao, J.; Tsuji, Y. *Chem. Eur. J.* **2012**, *18*, 4179–4184. (e) Moure, A. L.; Array_as, R. G.; G_ardenas, D. J.; Alonso, I.; Carretero, J. C. *J. Am. Chem. Soc.* **2012**, *134*, 7219–7222. (f) Park, J. K.; Ondrusek, B. A.; McQuade, D. T. *Org. Lett.* **2012**, *14*, 4790–4793. (g) Jang, H.; Zhugralin, A. R.; Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 7859–7871.

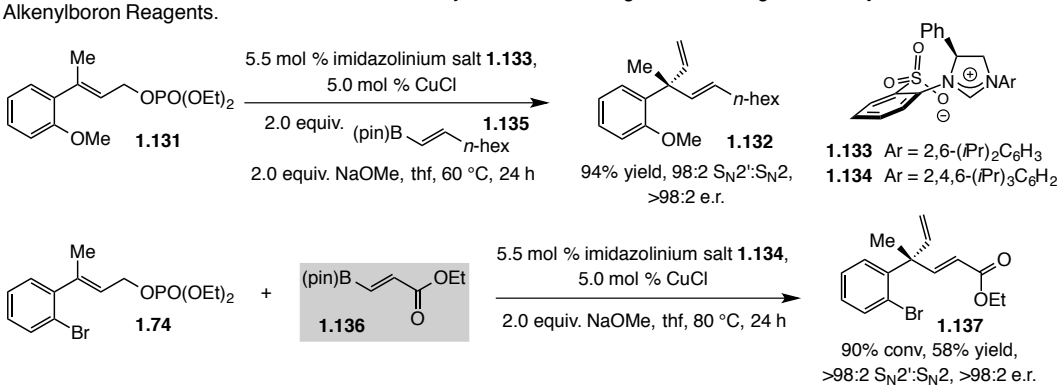
Scheme 1.25 Enantioselective Construction of Allene Containing All Carbon Quaternary Stereocenter.



Another incentive for us to pursue the EAS methods that involve organoboron reagents, besides the understanding of the fundamentals of sulfonate containing *N*-heterocyclic carbene promoted reactions, is the functional group compatibility that is provided through the use of these less nucleophilic reagents. Even though there are Al based protocols to deliver various alkenyl units in Cu-catalyzed EAS reactions (cf. Section 1.4), we surmised that the incorporations of functional group bearing alkenyl units can only be realized by utilizing alkenylboron reagents. As shown in Scheme 1.26, the initial examination of the feasibility of such a transformation starts with a model EAS reaction involving a commercially available alkyl substituted alkenylboronic acid pinacol ester **1.135**. With 5.0 mol % in situ formed Cu complex derived from imidazolinium salt **1.133**, allylic phosphate **1.131** is converted to the 1,4-diene **1.132** in 94% yield, 98% S_N2' and as a single enantiomer. Stoichiometric amount of NaOMe is again used to activate the alkenylboron reagent and an elevated temperature (60 °C) is required to achieve

appreciable conversion.[50] This observation is in consistent with the lack of the Lewis acidic metal chelate in the present system. A more rewarding discovery is listed in Scheme 1.26 as well; an ester bearing commercially available alkenylBpin **1.136** is effectively employed under similar conditions with a slightly modified imidazolinium salt **1.134** (cf. 58% yield, >98% S_N2' and >98:2 e.r. of **1.137**, Scheme 1.26). This represents the first example of having a carbonyl functionality on the nucleophilic partner in the Cu-catalyzed allylic substitution reactions.

Scheme 1.26. Formation of All Carbon Quaternary Center Containing Dienes through Cu-Catalyzed EAS with Alkenylboron Reagents.



The significance of introducing α,β-unsaturated conjugate acceptor in EAS reactions is further demonstrated through concise syntheses of syn and anti Pummerer's Ketones.[51] In these cases, a commercially available acetal containing alkenylboron reagent **1.139** serves as the surrogate of an enal. As illustrated in Scheme 1.27, unsaturated aldehyde **1.140** is prepared in 77% overall yield after a mild hydrolysis of the

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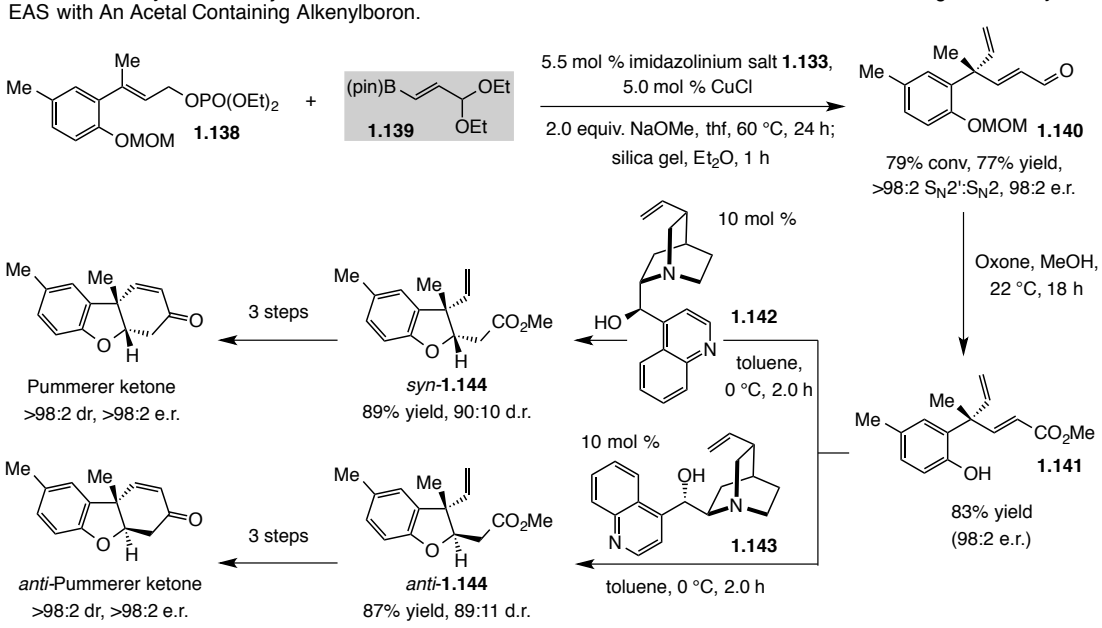
(50) (a) Gao, F.; Carr, J. L.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2012**, *51*, 6613–6617. For a recent enantioselective version promoted by an NHC–Cu complex involving the more reactive arylboronic acid neopentyl glycol esters (vs. pinacol esters), see: (b) Shintani, R.; Takatsu, K.; Takeda, M.; Hayashi, T. *Angew. Chem. Int. Ed.* **2011**, *50*, 8656–8659.

(51) For a previous synthesis of racemic syn Pummerer's ketone, see: Vierfond, J.-M.; Reynet, A.; Moskowitz, H.; Thal, C. *Synth. Commun.* **1992**, *22*, 1783–1792. For other related references, see: (b) Pummerer, R.; Melamed, D.; Puttfarcken, H. *Ber. Dtsch. Chem. Ges.* **1922**, *55*, 3116–3132. (c) Opioid Analgesics Chemistry and Receptors (Eds.: Casy, A. F.; Parfitt, R. T.), Plenum, New York, 1986. (d) Winternitz, F.; Autia, N. J.; Tumlirova, M.; Lacharette, R. *Bull. Soc. Chim. Fr.* **1956**, 1817. (e) Barton, D. H. R.; Deflorin, A. M.; Edwards, O. E. *J. Chem. Soc.* **1956**, 530–534.

crude mixture obtained from Cu-catalyzed EAS of allylic phosphate **1.138**; the resulting enal is highly enriched in optical purity (98:2 e.r.) and can be oxidized with Oxone in methanol[52] to furnish the desired enoate **1.141** with concurrent removal of the MOM protecting group. The utility of the conjugate acceptor is emphasized through Chichona alkaloid (cf. **1.142** and **1.143**) catalyzed intramolecular oxy Michael cyclization of **1.141**;[53] the relative stereochemistry is determined by the choice of pseudo enantiomers of these commercially available organic bases. Syn and anti benzofuran **1.144** are generally obtained in 87–89% yield and in 89:11–90:10 d.r. and are readily carried over to the final targets in three more steps;[50] syn and anti isomers of Pummerer's ketone are afforded as single diastereomers after purification and in enantiomeric pure form.

Scheme 1.27 Synthesis of *Syn* and *Anti* Pummerer's Ketone Via An Enal Intermediate Obtained through Cu-Catalyzed EAS with An Acetal Containing Alkenylboron.



(52) Travis, B. R.; Sivakumar, M.; Hollist, G. O.; Borhan, B. *Org. Lett.* **2003**, *5*, 1031–1034.
(53) For related enantioselective intramolecular conjugate additions catalyzed by derivatives of cinchona alkaloids, see: Biddle, M. M.; Lin, M.; Scheidt, K. A. *J. Am. Chem. Soc.* **2007**, *129*, 3830–3831 and references cited therein.

1.8 Enantioselective Boron and Silicon Allylic Substitution Catalyzed by Sulfonate Containing NHC–Cu Complexes

The enantioselective delivery of a heteroatom to the γ carbon of an allylic electrophile is an important class of reactions,[54] especially if the resulting C-heteroatom bond is convertible to a range of new C-C or C-heteroatom bonds through one or a set of simple chemical transformations without loss of stereochemical information. C-B bond belongs to this category since a number of reactions are available to utilize C-B bond for the formations of C-O, C-N and C-C bond;[55] the resulting enantioenriched allylic alcohols, amines and carbon frameworks are useful building blocks in organic synthesis. Recent advances in Cu-catalyzed protoboration of alkenes[56] and alkynes[57] have paved the way for the testing of boron allylic substitution reactions catalyzed by copper complexes.[58] Since the protoboration reactions of alkenes are known to be promoted by simple monodentate N-heterocyclic carbene ligands (e.g., commercially available bis-mesityl imidazolinium salt) with great efficiency, we set forth to investigate Cu-catalyzed

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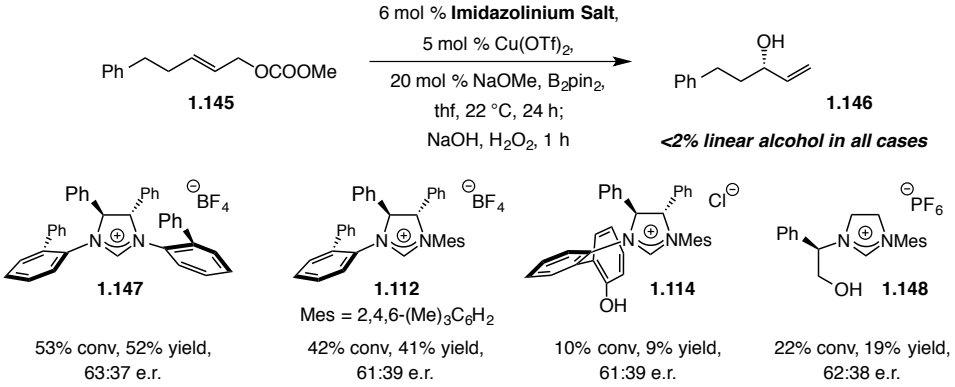
(54) (a) ref. 1 (c), (b) Trost, B. M.; Zhang T.; Sieber, J. D. *Chem. Sci.* **2010**, *1*, 427–440.
(55) For selected reviews, see: (a) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. Organic Syntheses via Boranes; Wiley-Interscience: New York, 1975. (b) Brown, H. C.; Singaram, B. *Acc. Chem. Res.* **1988**, *21*, 287–293. (c) Crudden, C. M.; Edwards, D. *Eur. J. Org. Chem*. **2003**, 4695–4712.
(56) (a) Mun, S.; Lee, J.-E.; Yun, J. *Org. Lett.* **2006**, *8*, 4887–4889. (b) Lillo, V.; Fructos, M. R.; Ramírez, J.; Braga, A. A. C.; Maseras, F.; Díaz-Requejo, M. M.; Pérez, P. J.; Fernández, E. *Chem. Eur. J.* **2007**, *13*, 2614–2621. (c) Lee, Y. Hoveyda, A. H. *J. Am. Chem. Soc*. **2009**, *131*, 3160–3161. (d) Noh, D.; Chea, H.; Ju, J.; Yun, J. *Angew. Chem. Int. Ed.* **2009**, *48*, 6062–6064. (e) Corberán, R.; Mszar, N. W.; Hoveyda, A. H. *Angew. Chem. Int. Ed*. **2011**, *50*, 7079–7082. (f) Yoshida, H.; Kageyuki, I.; Takaki, K. *Org. Lett*. **2013**, *15*, 952–955. (g) Meng, F.; Jang, H.; Hoveyda, A. H. *Chem. Eur. J*. **2013**, *19*, 3204–3214.
(57) (a) ref. 49 (c)–(g). (b) Lee, Y.; Jang, H.; Hoveyda, A. H. *J. Am. Chem. Soc*. **2009**, *131*, 18234–18235. (c) Jung, H.-Y.; Yun, J. *Org. Lett.* **2012**, *14*, 2606–2609.
(58) For catalytic enantioselective synthesis of R-substituted allyl boronates (tertiary C-B), see: (a) Gao, X.; Hall, D. G. *J. Am. Chem. Soc.* **2003**, *125*, 9308–9309. (b) Pelz, N. F.; Woodward, A. R.; Burks, H. E.; Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc.* **2004**, *126*, 16328–16329. (c) Gerdin, M.; Moberg, C. *Adv. Synth. Catal.* **2005**, *347*, 749–753. (d) Carosi, L.; Hall, D. G. *Angew. Chem., Int. Ed.* **2007**, *46*, 5913–5915. (e) Peng, F.; Hall, D. G. *Tetrahedron Lett.* **2007**, *48*, 3305–3309. For examples of Cu-catalyzed allylic substitutions that deliver allylborons, see: (f) Ito, H.; Ito, S.; Sasaki, Y.; Matsuura, K.; Sawamura, M. *J. Am. Chem. Soc.* **2007**, *129*, 14856–14857. (g) Park, J. K.; Lackey, H. H.; Ondrusek, B. A.; McQuade, D. T. *J. Am. Chem. Soc.* **2011**, *133*, 2410–2413.

enantioselective boron allylic substitutions (BAS) with a variety of monodentate and bidentate NHCs.

Scheme 1.28 Inefficient Boron Allylic Substitution with Monodentate and Alkoxide Based Bidentate NHCs.



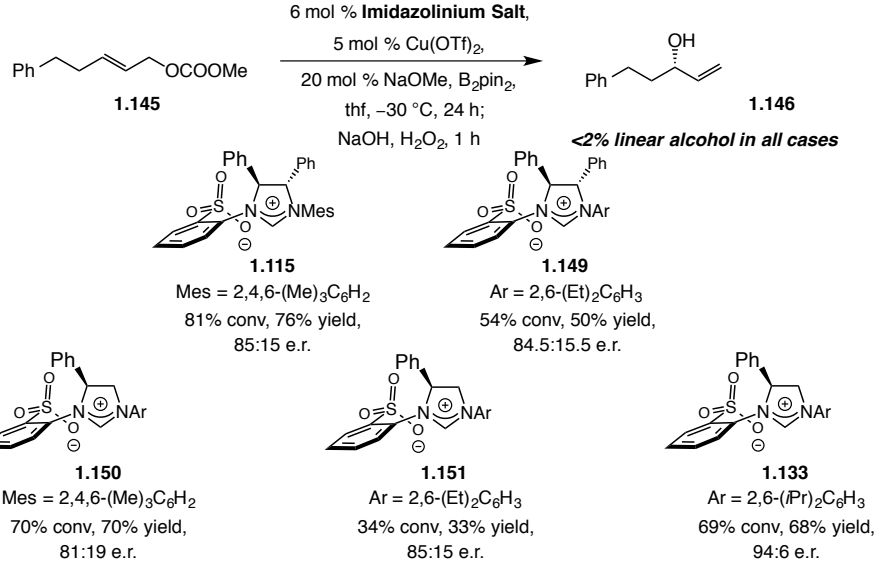
Representative data are presented in Scheme 1.28.[59] With 5 mol % in situ formed NHC–Cu complexes derived from C2 and C1 monodentate imidazolinium salts **1.147** and **1.112**, the BAS reactions proceed with reasonable efficiency, affording allylic alcohol **1.146** after oxidation of the crude mixture in 41–52% yield but in 61:39–63:37 enantiomer ratios. The corresponding reactions with pheoxy (cf. **1.114**) and alkoxy (cf. **1.148**) based imidazolinium salts are more sluggish and non selective (up to 19% yield and 62:38 e.r. obtained in Scheme 1.28). A few points regarding this class of transformations merit further discussion: 1) the reagent used for the delivery of a Bpin unit is a commercially available pinacolato diboron (B_2pin_2). 2) Compared to the EAS reactions with organoBpin reagents (cf. Section 1.7), the BAS only requires catalytic amount of NaOMe to initiate the catalytic cycle. The remaining methoxy anion needed for the generation of MeOBpin byproduct comes from the carbonate leaving group in the substrate; after each catalytic cycle, the resulting NHC–Cu-OCOOMe decomposes to

(59) Guzman-Martinez, A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 10634–10637.

NHC–Cu-OMe and CO_2. The success of these conditions is based on the fact that the crucial catalytically active NHC–Cu-Bpin species are more reactive than their carbon counterparts (e.g., NHC–Cu-alkenyl), which require the more reactive allylic phosphates (vs. allylic carbonate) for efficient Cu-catalyzed allylic substitution reactions. 3) In all cases, there is no observed formation of undesired linear alcohol.

The same transformations are examined with sulfonate containing *N*-heterocyclic carbenes and the results are listed in Scheme 1.29. In contrast, BAS reactions with these promoters are more effective, affording 33–76% yield of the desired branched alcohol product at lower temperature (–30 ºC) and with significantly higher enantioselectivities (≥81:19 e.r.). As the trend extrapolated from the data in Scheme 1.29 reveals, the modified NHCs with mono phenyl backbone (vs. diphenyl substituted five membered ring) and a larger symmetric N-Ar unit (from mesityl to di*iso*propyl phenyl) are more effective in inducing stereogenecity in the formation of allylic alcohol **1.146**; BAS with **1.133** delivers the product in 68% yield and in 94:6 e.r.

Scheme 1.29. Efficient Boron Allylic Substitution with Sulfonate Based Bidentate Imidazolinium Salts.



Furthermore, trisubstituted allylic carbonates are also effective substrates in NHC–Cu-catalyzed BAS reactions; such transformations furnish otherwise difficult-to-synthesize tertiary allylborons.[60] As shown in Scheme 1.30, the addition of a Bpin unit to an allylic carbonate **1.152** derived from geraniol delivers, after oxidation, natural product linalool in 82% yield and 97:3 enantiomer ratio; in the course of this process, sulfonate containing **1.115** serves as the optimal ligand on copper. Several additional points are noteworthy: 1) compared to BAS of disubstituted allylic carbonates, reactions with trisubstituted allylic carbonates are facilitated with extra amount of NaOMe (80 mol % vs. 20 mol % in Scheme 1.28–1.29). Such a requirement may be because of the need for better in situ catalyst synthesis and more efficient B_2pin_2 activation when a more difficult substrate class is involved. 2) The scope of the BAS is relatively general, but is limited when a strong electron withdrawing substituent is present on the phenyl ring (cf. <2% conv to **1.154**). Substrate that bears an ethyl group is also a less effective coupling partner in Cu-catalyzed BAS; tertiary allylic alcohol **1.155** is afforded in 80:20 e.r. along with 20% linear achiral product. 3) These derived tertiary allylBpins are very robust and can be purified through silica gel column chromatography to generate isolable and reasonably stable organoBpin products, which are highly versatile reagents in catalysis,[61] in high yield and enantiomeric purity (cf. **1.156** and **1.157** in Scheme 1.30).

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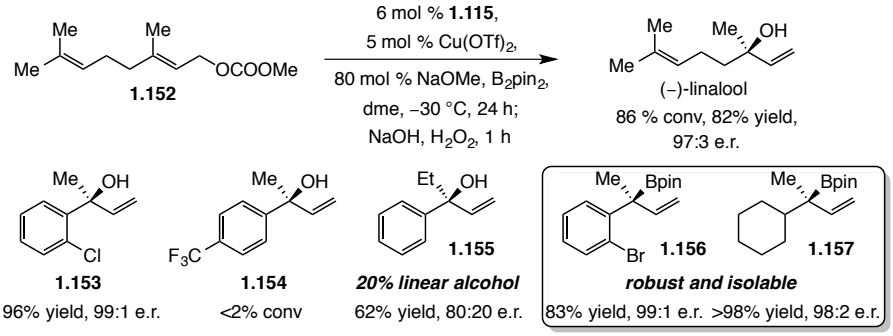
(60) (a) Stymiest, J. L.; Bagutski, V.; French, R. M.; Aggarwal, V. K. *Nature* **2008**, *456*, 778–782. (b) Bagutski, V.; Ros, A.; Aggarwal, V. K. *Tetrahedron* **2009**, *65*, 9956–9960. (c) Nave, S.; Sonawane, R. P.; Elford, T. G.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2010**, *132*, 17096–17098.

(61) For an application of such enantiomerically enriched tertiary allylboronic acid pinacol esters, see: Silverio, D. L.; Torker, S.; Piyugina, T.; Vieira, E. M.; Snapper, M. L.; Haeffner, F.; Hoveyda, A. H. *Nature* **2013**, *494*, 216–221.

Scheme 1.30. Synthesis of Tertiary Allylboron through Cu-Catalyzed Boron Allylic Substitution.



The ability to synthesize enantiomerically enriched allylsilanes is also desirable especially since a range of less sterically congested allylBpins (e.g., cases in Scheme 1.28–1.29) are not isolable by simple column chromatography. The corresponding allylsilanes, on the other hand, are readily prepared through Cu-catalyzed EAS[62] and isolated in high yields (>70%) and excellent enantioselectivities (≥94:6 e.r.), as the data shown in Scheme 1.31 indicates. In these cases, the sulfonate bearing **1.115** serves as the optimal ligand on copper and a commercially available $PhMe_2SiBpin$ reagent is used as the surrogate for the silicon unit. The scope of such transformations is broad; substrates that contain an electron withdrawing (**1.160**), an electron donating (**1.159**), a *N*-heterocycle (**1.161**) and a simple alkyl substituent (**1.162**) are well tolerated. Recent disclosures regarding similar transformations utilize chiral monodentate NHC–Cu complexes to achieve enantioselective silicon allylic substitution;[63] a number of cases that feature enantioenriched secondary as well as tertiary allylsilanes are reported with good efficiency and selectivity levels.

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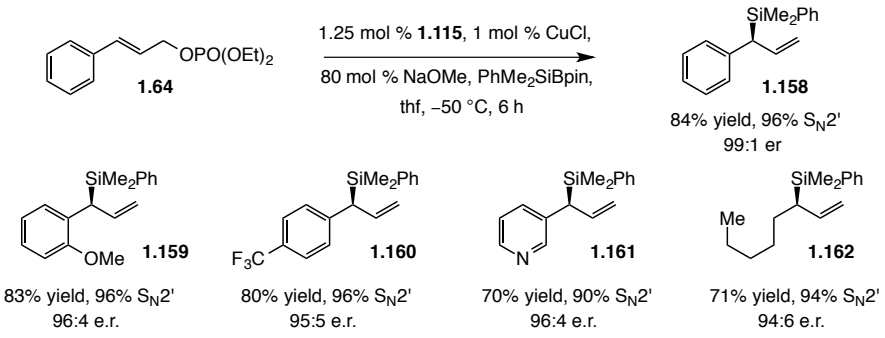
(62) Unpublished results obtained by Hao Wu from our group.

(63) For recent examples of enantioselective silyl allylic substitution, see: (a) Delvos, L. B.; Vyas, D. J.; Oestreich, M. *Angew. Chem. Int. Ed.* **2013**, *52*, 4650–4653. (b) Takeda, M.; Shintani, R.; Hayashi, T. *J. Org. Chem.* **2013**, *78*, 5007–5017.

Scheme 1.31. Synthesis of Enantioenriched Allylsilane through Cu-Catalyze Silicon Allylic Substitution.



1.9 Enantioselective Allylic Substitution Catalyzed by Sulfonate Containing N-heterocyclic Carbenes under Cu Free Conditions

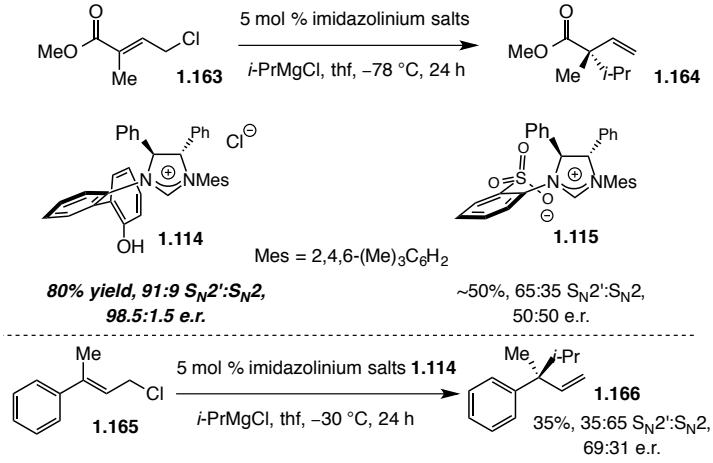
Although copper metal is privileged towards additions to activated olefin substrates (e.g., allylic phosphate) with organometallic nucleophiles, some recent discoveries have demonstrated the possibility of accomplishing allylic substitution reactions without the presence of Cu.[64] In the following segment, we will discuss the role of sulfonate containing N-heterocyclic carbenes in promoting these transformations as well as their comparison with other known carbene promoters.

In 2006, the first examples of enantioselective allylic substitution without the use of a copper complex are disclosed;[64a] the reactions are especially effective in coupling trisubstituted ester containing allylic chlorides with alkylmagnesium halides. As shown in Scheme 1.32, in the presence of 5 mol % imidazolinium salt **1.114**, allylchloride **1.163** is converted to enantioenriched ester **1.164** in 80% yield, 91% S_N2' selectivity and in 98.5:1.5 e.r. On the contrary, the use of sulfonate containing **1.115**, the copper free allylic

(64) (a) Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2006**, *128*, 15604–15605. (b) ref. 43. (c) Jackowski, O.; Alexakis, A. *Angew. Chem. Int. Ed.* **2010**, *49*, 3346–3350. (d) Grassi, D.; Dolka, C.; Jackowski, O.; Alexakis, A. *Chem. Eur. J.* **2013**, *19*, 1466–1475.

substitution proceeds to ~50% conversion as a mixture of branched and linear products (35:65 S_N2':S_N2) with the desired **1.164** in racemic form. Reactions promoted by the phenoxide containing **1.114** are less efficient and selective when trisubstituted allylic chlorides bearing no ester functionality serve as the substrates (cf. **1.165** in Scheme 1.32). The essential role of the ester moiety in this class of reactions will be discussed later.

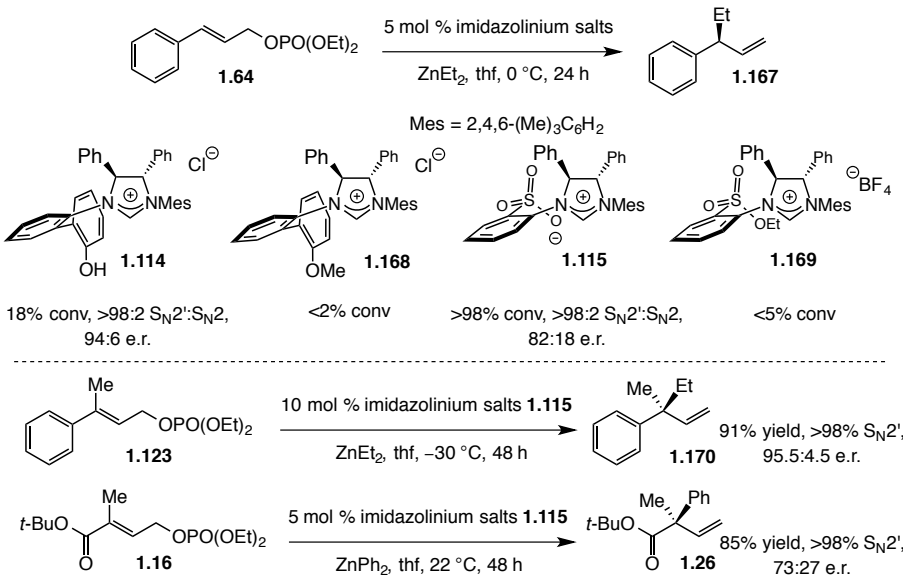
Scheme 1.32 Cu Free Enantioselective Allylic Substitutions of Allylic Chloride with Grignard Reagents.



Later, a copper free EAS method targeting allylic substrates bearing more general substituents (i.e., groups not limited to an ester) is reported;[43] these reactions utilize alkyl or arylzinc reagents in combination with allylic phosphates. Representative cases are presented in Scheme 1.33. The synthesis of alkene **1.167** is site (>98% S_N2') and enantioselective (94:6 e.r.) when alkoxide based **1.114**, optimal promoter in the previous Grignard additions, is used, but proceeds sluggishly to 18% conversion after 24 hours at ambient temperature. In contrast, the use of sulfonate containing **1.115** results in a very efficient reaction (>98% conversion) towards the formation of **1.167**, albeit in lower enantioselectivity (82:18 e.r.). Additional data reveal the essentialness of the bidentate nature of the N-heterocyclic carbenes; copper free EAS reactions with protected **1.168** and **1.169** deliver only traces of desired products, if any. Furthermore, when it comes to

the additions of Et_2Zn to trisubstituted allylic phosphate **1.123**, imidazolinium salt **1.115** can serve as the optimal promoter, EAS with which furnishes a quaternary stereogenic center containing alkene **1.170** in 91% yield and 94.5:5.5 e.r. The first example of copper free EAS reactions with Ph_2Zn is also disclosed with the formation of **1.26** as a representative (85% yield and 73:27 e.r., Scheme 1.33).

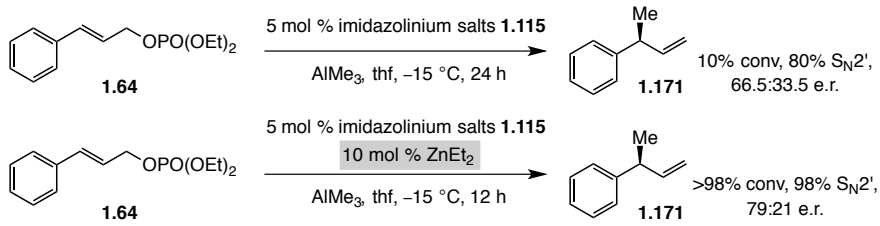
Scheme 1.33 Cu Free Enantioselective Allylic Substitutions with Dialkylzinc Reagents.



The synergistic relationship between organoaluminum reagents and sulfonate containing NHCs prompt us to investigate Cu free EAS reactions with Al based species. As shown in Scheme 1.34, with 5 mol % **1.115**, EAS reaction with $AlMe_3$ proceeds to only 10% conversion at –15 ºC after one day. The product **1.171** is obtained in 66.5:33.5 e.r. with 80% regioisomeric purity. However, with the addition of 10 mol % $ZnEt_2$, the desired transformation occurs to completion within 12 hours under the same conditions, affording **1.171** in higher enantiomer ratio (79:21) without any detectable linear side product. It seems that, based on the results above, the formation of active catalysts that

bear the chiral bidentate NHC is ineffective with the less basic $AlMe_3$ and the more basic Et_2Zn serves to deprotonate the imidazolinium salt prior to the catalyst formation.

Scheme 1.34. Cu Free Enantioselective Allylic Substitutions with Trialkylaluminum Reagents.



The above proposal is further supported during the processes of preparing the corresponding sulfonate containing NHC–Zn[65] and NHC–Al[66] complexes. As shown in Scheme 1.35, treatment of imidazolinium salt **1.115** with 3.0 equivalents of Et_2Zn in tetrahydrofuran for 24 hours at ambient temperature results in the formation of complex **1.96**, the crystal structure of which is subsequently secured to confirm the identity of the metal complex. On the other hand, under the similar conditions, reactions with Me_3Al fail to deliver the corresponding Al complex **1.95**; such ineffectiveness of the complex formation is not inherent because **1.95** can be accessed through treatment of Zn complex **1.96** with excess Me_3Al (see Scheme 1.35 for details and the crystal structure of **1.95**). Therefore, it is more likely that the low basicity of Me_3Al is responsible for the inefficient formation of sulfonate bearing NHC–Al complex. The valuable crystal structures are essential not only in the understanding of fundamentals of Cu free allylic substitution reactions, but also in revealing key structure features of related metal

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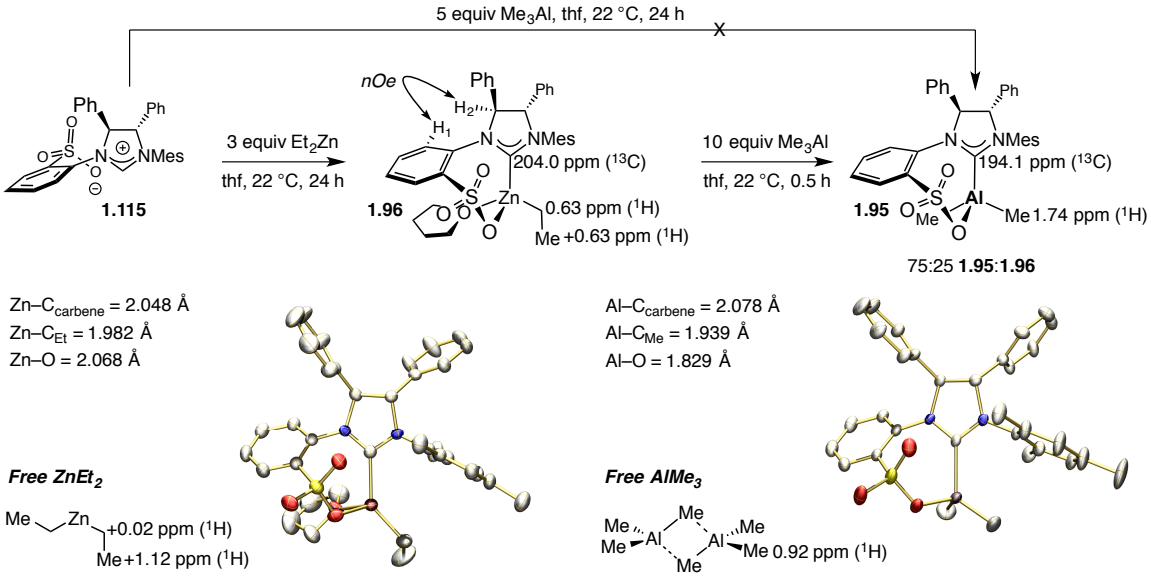
(65) For reports regarding X-ray structures of monodentate NHC–Zn(II) complexes, see: (a) Arduengo, A. J., III.; Rasika Dias, H. V. R.; Davidson, F.; Harlow, R. L. *J. Organomet. Chem.* **1993**, *462*, 13–18. (b) Wang, D.; Wurst, K.; Buchmeiser, M. R. *J. Organomet. Chem.* **2004**, *689*, 2123–2130.
(66) For a report regarding the X-ray structure of a monodentate NHC–$AlMe_3$ complex, see: (a) Li, X.-W.; Su, J.; Robinson, G. H. *Chem. Commun.* **1996**, 2683–2684. For an X-ray structure of an NHC–AlH_3, see: (b) Arduengo, A. J., III.; Rasika Dias, H. V.; Calabrese, J. C.; Davidson, F. *J. Am. Chem. Soc.* **1992**, *114*, 9724–9725.

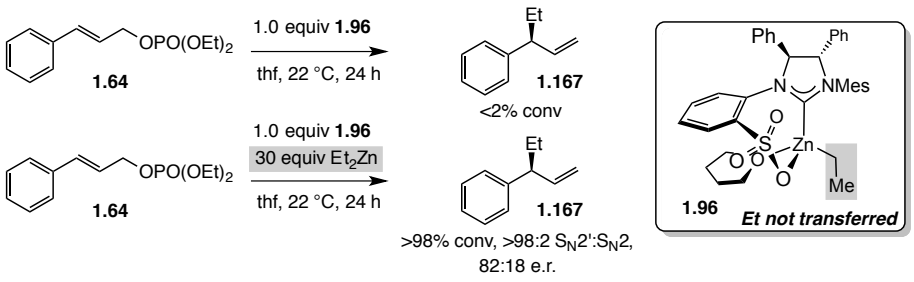
complexes (e.g., Cu complexes discussed in the Section 1.6) that are derived from the sulfonate containing N-heterocyclic carbenes. Several characteristics merit discussion in further details: 1) the sulfonate group chelate to the metal centers in such a fashion that it points to the same direction as the backbone phenyl substituent. The solution nOe of the two highlighted protons (cf. **1.96**) suggests that the observed syn orientation in the crystal structures is not limited to the solid state; these metal complexes when solvated are very likely to exhibit the same structures as they are found in the crystals. 2) Compared to the unbound $ZnEt_2$ or $AlMe_3$, the NHC complexed Zn or Al species possess more nucleophilic alkyl groups within their structural frameworks, probably due to the strong electron donating effect from the carbene association. The proton chemical shifts of the ethyl group in **1.96** and methyl group in **1.95** move significantly upfield (i.e., –0.63 ppm vs. +0.02 ppm in free $ZnEt_2$ and –1.74 ppm vs. –0.92 ppm in free $AlMe_3$) implying higher electron density located on these carbon-based nucleophiles. 3) Both Zn and the Al complexes are neutral and tetrahedron in geometry with two additional ligands bound to the metal centers besides the sulfonate carbene.

Scheme 1.35 Synthesis, Isolation and Characterization of Sulfonate Containing NHC–Zn and Al Complexes.



To continue probing the mechanistic details for Cu free allylic substitution reactions, treatment of allylic phosphate **1.64** with stoichiometric isolated Zn complex **1.96** is examined (Scheme 1.37). To our surprise, no detectable (<2% conv.) Et addition product **1.167** is obtained after 24 hours at 22 ºC. The reactivity, however, is restored with the addition of 30 equivalents of extra Et_2Zn; essentially the same result is achieved as under the catalytic conditions (>98% conv., >98% S_N2' and 82:18 e.r. of **1.167**). The above control experiments suggest that the bound Et group in **1.96** is not likely to be the one transferred to the γ position of the allylic phosphate.

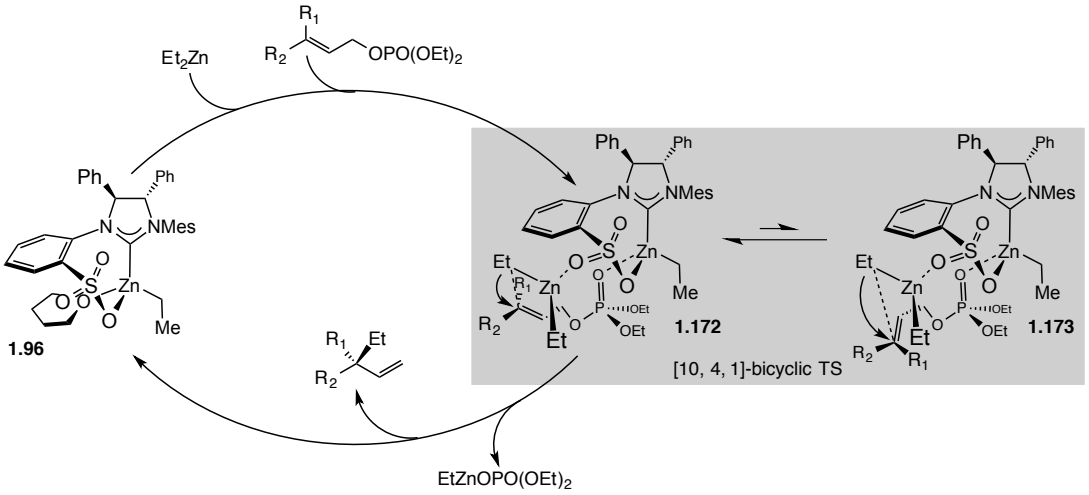
Scheme 1.36. Resubjection of the Isolated NHC–Zn Complex to Cu Free EAS Conditions.



With these information in hand, and considering the neutral and enhanced Lewis acidic character of NHC coordinated Zn metal, the following catalytic cycle is proposed and the central role of NHC–Zn complex **1.96** is established as a chiral Lewis acid with a secondary Lewis basic site (i.e., the sulfonate oxygen) for nucleophile delivery (Scheme 1.37). Unlike the more nucleophilic cuprate, which tends to associate with electrophilic olefins, the Lewis acidic Zn site is proposed to more favorably interact with the phosphate oxygen; such coordination can readily occur from the spacious back binding pocket (cf. **1.172** and **1.173**). The properly oriented sulfonate oxygen can serve to bring in another molecule of Et_2Zn and activates it towards direct transfer of an ethyl unit to the γ carbon of allylic phosphate. The highly organized transition state exhibits a [10, 4, 1]

bicyclic structure; the strain and the rigidity of the smaller seven membered chelate ring (i.e., the ring originally existed in the bidentate NHC–Zn complex) dictate the energetic preference for the left structure **1.172**, which delivers the observed major enantiomer (see Scheme 1.37 for details), whereas the more geometrically constrained **1.173** is much less populated in the reaction media.

Scheme 1.37 Proposed Catalytic Cycle Involving Bifunctional Catalysis in Cu Free EAS.

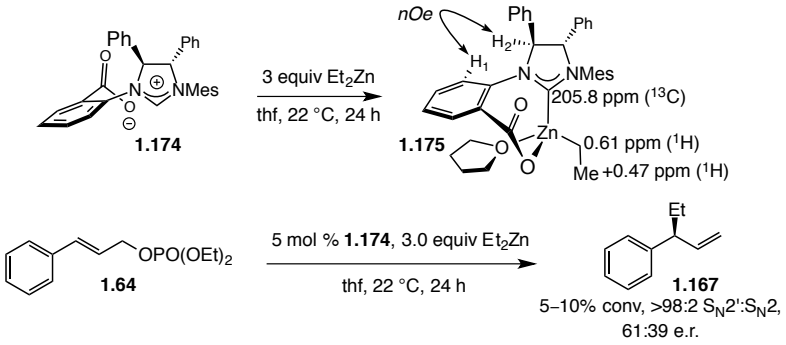


The potential evidence for the proposed bifunctional[67] Lewis base delivery of nucleophiles is described in Scheme 1.38. A carboxylate containing imidazolinium salt **1.174** is prepared and its corresponding Zn complex **1.175** is obtained through treatment of **1.174** with 3.0 equivalents of Et_2Zn in tetrahydrofuran (thf).[43] Similar structure is assigned to **1.175** based on extensive spectroscopic evidences. The catalytic activity of the new Zn complex **1.175** is then evaluated under the same circumstance towards the Cu free EAS with Et_2Zn to a 1,2-disubstituted allylic phosphate **1.64**. As shown in Scheme

(67) For recent reviews on bifunctional enantioselective catalysis, see: (a) Ma, J.-A.; Cahard, D. *Angew. Chem., Int. Ed.* **2004**, *43*, 4566–4583. (b) Nájera, C.; Sansano, J. M.; Saá, J. M. *Eur. J. Org. Chem.* **2009**, 2385–2400. For additional examples of bifunctional enantioselective catalysis, see: (c) ref. 5 (c). (d) Kanai, M.; Kato, N.; Ichikawa, E.; Shibasaki, M. *Synlett* **2005**, 1491–1508. (e) Carswell, E. L.; Snapper, M. L.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2006**, *45*, 7230–7233. (f) Paull, D. H.; Abraham, C. J.; Scerba, M. T.; Alden-Danforth, E.; Lectka, T. *Acc. Chem. Res.* **2008**, *41*, 655–663. (g) Friel, D. K.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2008**, *130*, 9942–9951.

1.38, ethyl-substituted allylbenzene **1.167** is obtained after 24 hours only in ~5–10% conversion and in 61:39 e.r. The lack of the properly resided Lewis basic binding site diminishes the efficiency in nucleophile delivery and also disrupts the organized transition state en route higher levels of differentiation of the two enantiotopic faces of the substrate alkene.

Scheme 1.38. Evidence for the Proposed Involvement of Equatorially Disposed Sulfonate Oxygen.



Having established the unique structures of sulfonate bearing NHC metal complexes, it is now feasible to discuss the lower efficiency and selectivity levels in Cu free EAS with Grignard reagents when imidazolinium **1.115** serves as the catalytic promoter (vs. phenoxide based **1.114**). There are two very different approaches towards rationalizing the ineffectiveness of sulfonate containing NHCs in coupling allylic chlorides and alkylmagnesium halides. The first possibility concerns the fact that, as a good leaving group, the sulfonate unit can be readily displaced by strongly nucleophilic Grignard reagents; such a scenario is not likely to occur when milder organozinc or aluminum species are used. The resulting bis alkyl group substituted Mg center associates with only a monodentate carbene ligand, the flexible nature of which reduces the ability

of the NHC–Mg complex[68] to efficiently induce stereogenicity. Also, the non-rigid structure diminishes the rate for proper nucleophile delivery by the sulfonate oxygen, resulting in a sluggish reaction between allylchloride and Grignard reagents. The second approach assumes the intact of the bidentate chelation under the catalytic conditions, with the detailed analysis provided in Scheme 1.39. As represented by complexes **1.176** and **1.177**, the phenoxy oxygen chelates from the opposite side of the phenyl backbone[69] and thus delivers alkyl Grignard reagents from the backside of the complexes, whereas the Lewis basic ester group on the substrate coordinates to the Lewis acidic Mg center from the open site opposite to the phenoxy unit. Such a transition state, based on the above assumption, favors the S_N2' addition product due to the relative ease in the formation of a seven membered ring compared to eight (leading to cyclopropane product) or nine (leading to S_N2 product) membered rings. Additionally, the flat phenoxide bearing N-Ar substituent imposes enough steric presence to differentiate the enantiotopic faces of the allylic chloride (cf. less favored **1.177**), therefore delivering the desired product in high enantioselectivity (cf. Scheme 1.32). In contrast, transition structures of sulfonate containing NHC–Mg complexes are represented by **1.178** and **1.179**, both of which are energetically similar because of the tilt of the N-Ar substituent rendered by the smaller chelate ring. Furthermore, the transition states that lead to the formation of S_N2', S_N2 and cyclopropane products go through nine, ten and eleven membered rings, which are equally difficult to achieve due to the ring strain. Thus, Cu free EAS with representative

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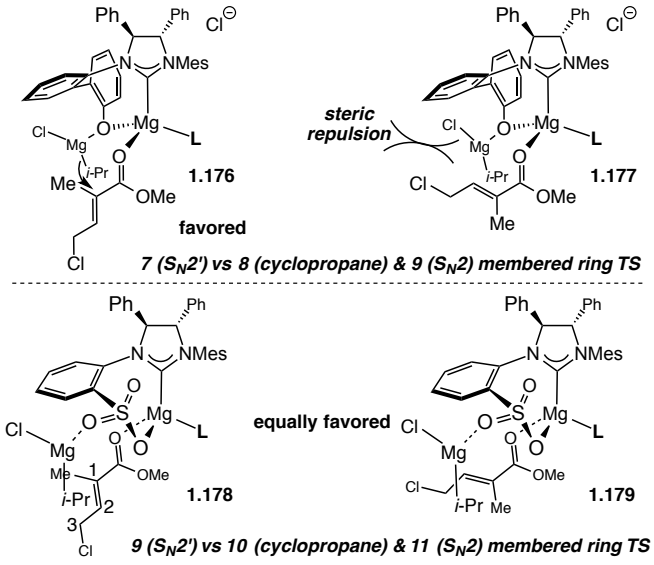
(68) For X-ray structures of monodentate NHC–Mg complexes, see: (a) Schumann, H.; Gottfriedsen, J.; Glanz, M.; Dechert, S.; Demtschuk, J. *J. Organomet. Chem.* **2001**, 617–618, 588–600. (b) ref. 65 (a).
(69) For the crystal structure of NHC–Cu complex that bears the phenoxide secondary chelate, see: ref. 9 and 10.

imidazolinium salt **1.115** affords a mixture of various products and with the desired chiral molecule in low enantiomeric purity (cf. Scheme 1.32).

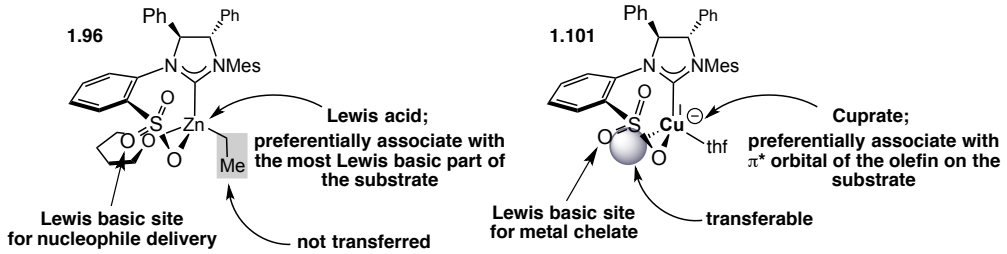
Scheme 1.39 Stereochemical Models Accounted for the Differences between Phenoxide and Sulfonate Based Bidentate Carbenes in EAS with Alkyl Grignard Reagents.



1.10 Conclusions

To conclude this section, the sulfonate containing *N*-heterocyclic carbenes are capable of promoting both Cu-catalyzed enantioselective allylic substitutions with various organozinc, aluminum and boron reagents and Cu free EAS with organozinc and aluminum nucleophiles. Most of the organic groups incorporated (i.e., heteroaryl, alkenyl, alkynyl, functionalized alkenyl and allenyl) through Cu-catalyzed EAS, promoted by this class of carbenes, are difficult-to-access otherwise. Distinct structural features of the catalysts in both Cu-catalyzed (cf. **1.101**) and Cu free (cf. **1.96**) protocols are summarized in Scheme 1.40.

Scheme 1.40. Comparison of Cu Free and Cu-Catalyzed EAS systems: Key Features of the Catayst Structures.



The ate complex nature of NHC–Cu species renders them preferentially associate with the olefin part of the substrate, whereas the neutral Zn or Mg complexes serve as the Lewis acids to bind substrates through their Lewis basic oxygen atoms. The copper complex then undergoes oxidative addition/reductive elimination to transfer the organic ligands on Cu, whereas the Cu free system bears a non-transferrable alkyl ligand on the metal center. Lastly, the sulfonate chelate through Lewis acidic cationic metal species (i.e., Al) with allylic phosphates in Cu-catalyzed enantioselective allylic substitutions, whereas the same Lewis base helps to deliver nucleophiles through coordination to neutral organometallic reagents (e.g., Et_2Zn).

Chapter 2

Cu-Catalyzed Enantioselective Allylic Substitutions with Aryl- and Heteroarylaluminum Reagents

2.1 Introduction

Catalytic enantioselective allylic substitution (EAS) reactions[1] are among the most versatile classes of transformations in organic chemistry: such processes deliver enantiomerically enriched products bearing a stereogenic center adjacent to a readily functionalizable olefin from easily available prochiral substrates. Despite significant progress made in the past almost two decades, a majority of the studies published from chemists worldwide focuses on the additions of an alkyl group enantioselectively through Cu-catalysis with the choice of proper nucleophilic "hard" alkyl metal reagents and mostly deliver products with a tertiary stereogenic center.[2] The Hoveyda group has devised chiral amino acid-based[3] and bidentate N-heterocyclic carbene (NHC) Cu

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(1) For reviews on allylic substitution reactions catalyzed by other transition metals and with "soft" nucleophiles, see: (a) Trost, B. M.; Lee, C. In *Catalytic Asymmetric Synthesis*; Oijima, I., Ed.; Wiley-VCH: Weinheim, Germany, 2000; Chapter 8E. (b) Trost, B. M.; Crawley, M. L. *Chem. Rev.* **2003**, *103*, 2921–2944. (c) Stanley, L. M.; Hartwig, J. F. *Acc. Chem. Res.* **2010** *43*, 1461–1475. (d) Trost, B. M. *Org. Process Res. Dev.* **2012**, *16*, 185–194. (e) Tosatti, P.; Nelson, A.; Marsden, S. P. *Org. Biomol. Chem.* **2012**, *10*, 3147–3163.

(2) For reviews on Cu-catalyzed allylic alkylation reactions that involve "hard" alkyl- or arylmetal-based reagents, see: (a) Hoveyda, A. H.; Hird, A. W.; Kacprzynski, M. A. *Chem. Commun.* **2004**, 1779–1785. (b) Yorimitsu, H.; Oshima, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 4435–4439. (c) Falciola, C. A.; Alexakis, A. *Eur. J. Org. Chem.* **2008**, 3765–3780. (d) Alexakis, A.; Bäckvall, J.-E.; Krause, N.; Pàmies, O.; Diéguez, M. *Chem. Rev.* **2008**, *108*, 2796–2823. (e) Harutyunyan, S. R.; den Hartog, T.; Geurts, K.; Minnaard, A. J.; Feringa, B. L. *Chem. Rev.* **2008**, *108*, 2824–2852. (f) Lu, Z.; Ma, S. *Angew. Chem., Int. Ed.* 2**008**, *47*, 258–297. (g) Langlois, J. -B.; Alexakis, A. *Topics in Organometallic Chemistry* **2012**, *38*, 235–268.

(3) (a) Luchaco-Cullis, C.; Mizutani, H.; Murphy, K. E.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2001**, *40*, 1456–1460. b) Murphy, K. E.; Hoveyda; A. H. *J. Am. Chem. Soc.* **2003**, *125*, 4690–4691; (c) Kacprzynski, M. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2004**, *126*, 10676–10681. (d) Murphy, K. E.; Hoveyda, A. H. *Org. Lett.* **2005**, *7*, 1255–1258.

complexes[4] that promote EAS processes with dialkylzinc reagents and generate difficult-to-access quaternary carbon stereogenic centers[5] with high site- and enantioselectivity. Work from other research groups has also emerged to challenge this compelling problem, but almost always with alkyl metal reagents.[6] On the other hand, catalytic EAS transformations involving aryl nucleophiles and which furnish quaternary carbon centers are scarce,[7] and protocols that effectively utilize heteroaryl metal reagents to incorporate heterocycles through Cu-catalyzed EAS do not exist (including those that furnish tertiary C–C bonds). Only two reported cases of aryl additions by catalytic EAS that generate quaternary carbons besides the study delineated in this chapter have appeared. One pioneering investigation corresponds to a class of Si-substituted allylic electrophiles and involves diarylzinc reagents,[4c] which are relatively difficult to prepare in high purity and offer only one of the aryl units. The second disclosure with a limited scope of examples deals with arylboronic acid neopentylglycol esters and transfers the corresponding aryl

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(4) (a) Larsen, A. O.; Leu, W.; Oberhuber, C. N.; Campbell, J. E.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2004**, *126*, 11130–11131. (b) Van Veldhuizen, J. J.; Campbell, J. E.; Guidici, R. E.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2005**, *127*, 6877–6882. (c) Kacprzynski, M. A.; May, T. L.; Kazane, S. A.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 4554–4558.

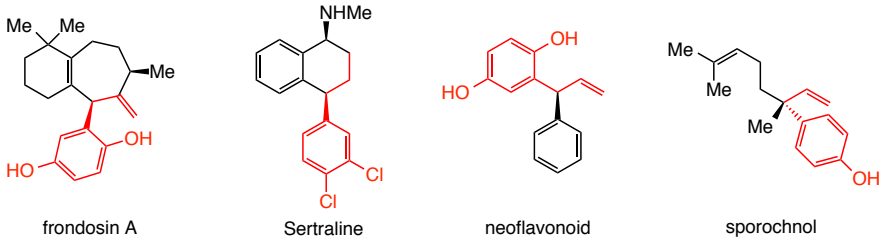
(5) Das, J. P.; Marek, I. *Chem. Commun.* **2011**, *47*, 4593–4623.

(6) (a) Seo, H.; Hirsch-Weil, D.; Abboud, K. A.; Hong, S. *J. Org. Chem.* **2008**, *73*, 1983–1986. (b) Fañanás-Mastral, M.; Pérez, M.; Bos, P. H.; Rudolph, A. Harutyunyan, S. R.; Feringa, B. L. *Angew. Chem., Int. Ed.* **2012**, *51*, 1922–1925.

(7) (a) ref. 4 (c). (b) Shintani, R.; Takatsu, K.; Takeda, M.; Hayashi, T. *Angew. Chem. Int. Ed.* **2011**, *50*, 8656–8659. For examples of enantioselective conjugate addition reactions that involve arylmetal reagents, see: with Rh-based catalysts and arylboronic acids, (c) Shintani, R.; Duan, W.-L.; Hayashi, T. *J. Am. Chem. Soc.* **2006**, *128*, 5628–5629. With Cu-based catalysts and arylaluminum reagents, (d) May, T. L.; Brown, M. K.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2008**, *47*, 7358–7362. (e) Hawner, C.; Li, K.; Cirriez, V.; Alexakis, A. *Angew. Chem. Int. Ed.* **2008**, *47*, 8211–8214. (f) Dabrowski, J. A.; Villaume, M. T.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2013**, *52*, 8156–8159. With Rh-based catalysts and sodium tetraarylborates, (g) Shintani, R.; Tsutsumi, Y.; Nagaosa, M.; Nishimura, T.; Hayashi, T. *J. Am. Chem. Soc.* **2009**, *131*, 13588–13589. With Rh-based catalysts and triarylboroxines, (h) Shintani, R.; Takeda, M.; Nishimura, T.; Hayashi, T. *Angew. Chem. Int. Ed.* **2010**, *49*, 3969–3971. With Rh-based catalysts and arylaluminum reagents, (i) Hawner, C.; Müller, D.; Gremaud, L.; Felouat, A.; Woodward, S.; Alexakis, A. *Angew. Chem. Int. Ed.* **2010**, *49*, 7769–7772. With Pd-based catalysts and arylboronic acids, (j) Kikushima, K.; Holder, J. C.; Gatti, M.; Stoltz, B. M. *J. Am. Chem. Soc.* **2011**, *133*, 6902–6905. (k) Gottumukkala, A. L.; Matcha, K.; Lutz, M.; de Vries, J. G.; Minnaard, A. J. *Chem. Eur. J.* **2012**, *18*, 6907–6914.

unit to allylic phosphates with an alkoxide based NHC–Cu catalyst.[7b] Alternative methods can, in principle, provide access to some of the products enantioselectively but in a rather constrained fashion.[8]

Figure 2.1: Aryl-substituted Stereogenic Center Containing Natural Products.



frondosin A | Sertraline | neoflavonoid | sporochnol

Since aryl-substituted tertiary as well as quaternary stereogenic centers are abundant motifs in a variety of naturally occurring molecules (Figure 2.1), we would like to explore and hopefully introduce a set of efficient catalytic EAS processes that involve the use of commercial or easily prepared aryllithium or heteroaryllithium reagents in connection with Et_2AlCl[9] and generate quaternary carbon stereogenic centers with our readily modifiable *N*-heterocyclic carbenes as the chiral promoters. The ideal scenario of the proposed reactions should meet the criteria of delivering the desired aryl group in an atom economical fashion, catalyzed by abundant and inexpensive metals at low catalyst loadings and finally affording a wide range of desired EAS products in high efficiency and selectivity levels.

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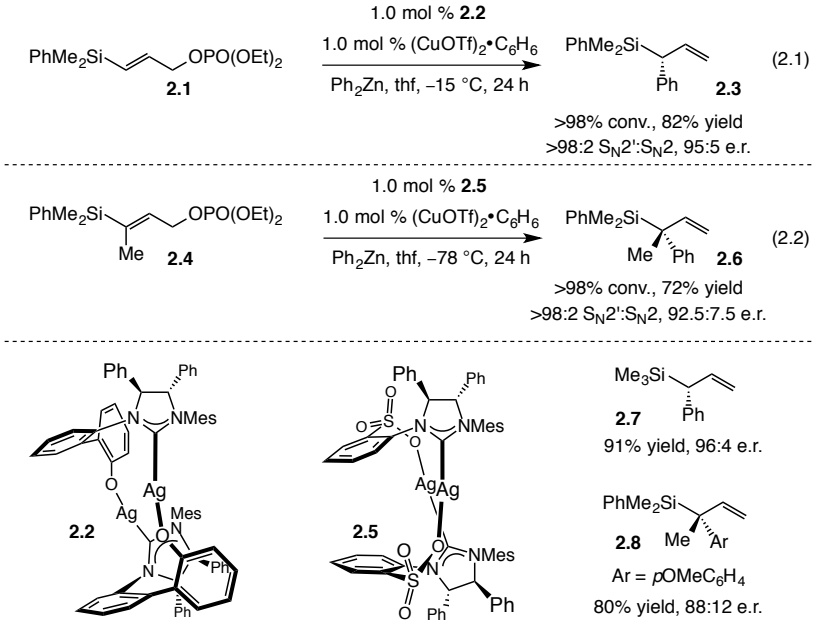
(8) Ni-catalyzed reactions of styrenes with ethylene furnish enantiomerically enriched products with a benzylic vinyl unit at an all-carbon quaternary stereogenic center. See: Smith, C. R.; Lim, H. J.; Zhang, A.; RajanBabu, T. V. *Synthesis* **2009**, 2089–2100 and references cited therein.

(9) For previous reports regarding preparation of dialkyl arylaluminum reagents, see: (a) Belgardt, T.; Storre, J.; Roesky, H.W.; Noltemeyer, M.; Schmidt, H.-G. *Inorg. Chem.* **1995**, *34*, 3821–3822. (b) Bumagin, N. A.; Ponomaryov, A. B.; Beletskaya, I. P. *Tetrahedron Lett.* **1985**, *26*, 4819–4822. (c) Lu, B. Z. F.; Jin, Y.; Zhang, X.; Wu, S.; Wald, A.; Senanayake, C. H. *Org. Lett.* **2005**, *7*, 1465–1468. For a catalytic enantioselective reaction involving Me_2(aryl)Al reagents, see: (d) Siewert, J.; Sandmann, R.; von Zezschwitz, P. *Angew. Chem. Int. Ed.* **2007**, *46*, 7122–7124.

2.2 Background

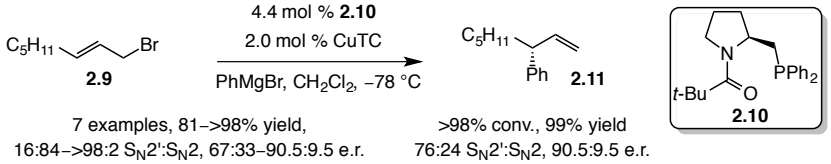
The very first examples of Cu-catalyzed enantioselective allylic substitution reactions that involve aryl metal reagents are reported by Hoveyda and co-workers in 2007;[4c] the corresponding transformations deal with a specific class of silyl-substituted allylic phosphates and generate enantioenriched allylsilanes with tertiary as well as quaternary stereogenic centers (Scheme 2.1). As shown in Eq 2.1, silyl-substituted allylic phosphate **2.1**, when subjected to diphenylzinc in the presence of 2.0 mol % in situ generated NHC–Cu complex of Ag dimer **2.2**, is converted to Ph-substituted allylsilane **2.3** in 82% yield, complete site selectivity and 95:5 e.r.; the reaction proceeds to >98% conversion within 24 h at –15 ^{o}C with tetrahydrofuran (thf) as the solvent. The protocol is applicable to synthesize quaternary stereogenic center bearing allylsilane as well; as the finding in Eq 2.2 indicates, with a different sulfonate containing N-heterocyclic carbene (cf. **2.5**) as the optimal promoter, product **2.6** is furnished in 72% yield and 92.5:7.5 e.r. with trisubstituted allylic phosphate **2.4** serving as the substrate. Additional cases of allylsilanes **2.7** and **2.8** demonstrate the scope of the method.

Scheme 2.1: Cu-Catalyzed Enantioselective Allylic Substitution with Diarylzinc Reagents.



After the above report, Tomioka group has shown that allylic bromides can react with PhMgBr under Cu catalysis to deliver Ph-substituted tertiary stereogenic center bearing molecules;[10] for a specific instance, alkene **2.11** is afforded in quantitative yield and 90.5:9.5 e.r., but with moderate site selectivity (24% inseparable linear product obtained). An amide containing chiral phosphine is used in combination with CuTC to catalyze the targeted transformations, furnishing a number of examples (with mostly PhMgBr) that appear as mixtures of regioisomers, with moderate enantioselectivity levels of the desired branched alkenes.

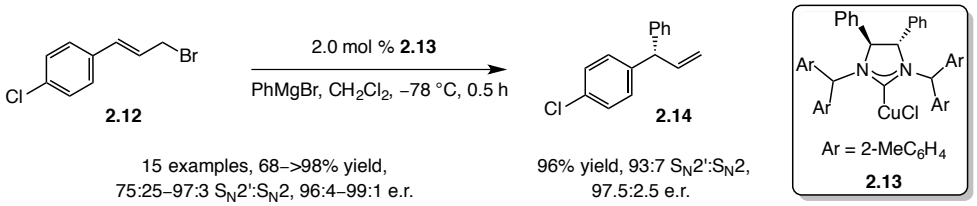
Scheme 2.2: Phosphine–Cu-Catalyzed EAS with Aryl Grignard Reagents.



(10) Selim, K. B.; Yamada, K-i.; Tomioka, K. *Chem. Commun.* **2008**, 5140–5142.

The same research group was able to improve its previous Cu-catalyzed EAS procedure by utilization of an enantiomerically pure monodentate NHC–Cu complex (cf. **2.13** in Scheme 2.3).[11] With 2.0 mol % of the isolated Cu catalyst, allylbromide **2.12** is transformed into Ph-substituted allylbenzene **2.14** when exposed to phenyl Grignard; the reaction occurs at –78 °C and completes within 30 minutes, giving the desired **2.14** in 96% yield, 93:7 S_N2':S_N2 and 97.5:2.5 enantiomer ratio. A wider substrate scope is demonstrated in this study and the products are often afforded enriched in the desired regioisomer and with increased optical purity.

Scheme 2.3: Monodentate NHC–Cu-Catalyzed EAS with Aryl Grignard Reagents.

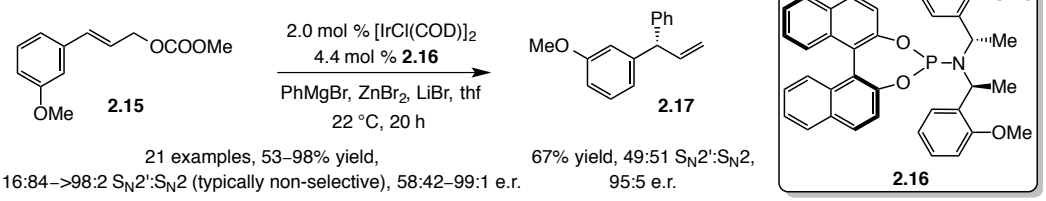


In 2007, Alexakis and colleagues described a related method for the enantioselective incorporation of an aromatic unit through allylic substitution reactions of allylic carbonates.[12] Such transformations, however, are catalyzed by an in situ formed Ir-phosphoramidite complex and utilize phenyl Grignard reagents combined with $ZnBr_2$ and LiBr. As showcased in Scheme 2.4, in the presence of 4 mol % the Ir catalyst derived from phosphoramidite **2.16**, allylic carbonate **2.15** is converted to Ph bearing allylbenzene **2.17** in 67% yield, 95:5 e.r., but as a non-selective mixture of regioisomers (49:51 S_N2':S_N2). Most of the cases examined in this study result in very low preference for the formation of the branched products, presumably because of the facile

(11) Selim, K. B.; Matsumoto, Y.; Yamada, K-I.; Tomioka, K. *Angew. Chem. Int. Ed.* **2009**, *48*, 8733–8735
(12) (a) Alexakis, A.; Hajjaji, S. E.; Polet, D.; Rathgeb, X. *Org. Lett.* **2007**, *9*, 3393–3395. (b) Polet, D.; Rathgeb, X.; Falciola, J C.; Langlois, A. B.; Hajjaji, S. E.; Alexakis, A. *Chem. Eur. J.* **2009**, *15*, 1205–1206.

isomerization of the allyl-Ir intermediates to position the large Ir complex at the less hindered terminus before Ph-allyl reductive elimination.

Scheme 2.4: Phosphine–Ir Complexes in EAS with Arylzinc Reagents.



21 examples, 53–98% yield, 16:84–>98:2 $S_N2':S_N2$ (typically non-selective), 58:42–99:1 e.r.

67% yield, 49:51 $S_N2':S_N2$, 95:5 e.r.

After the work in this chapter was published, Hayashi and Shintani disclosed the first set of experiments of Cu-catalyzed EAS reactions with arylboronic acid neopentylglycol esters (Scheme 2.5).[7b] As the example in Eq 2.3 illustrates, disubstituted allylic phosphate **2.18** serves as an effective substrate in the EAS reaction with 5 mol % Cu-complex of an hydroxy based imidazolinium salt **2.20**;[13] phenylboron reagent **2.19** is successfully incorporated into diaryl-substituted chiral olefin **2.21**, which is obtained in 91% yield, 99% S_N2' selectivity and 95.5:4.5 e.r. Stoichiometric amount of NaOMe is required as an activator to effect transmetallation from organoboron to copper due to the relatively low nucleophilicity of the boron based reagents (see Chapter 1 & 4 for more details). Among many efficient and enantioselective cases, one instance that couples an alkenylboronic acid neopentylglycol ester with Ph-substituted allylic phosphate delivers the desired 1,4-diene **2.22** in diminished e.r. value (86.5:13.5, Scheme 2.5). Processes that construct quaternary stereogenic centers are explored as well with a specific case shown in Eq 2.4 (89% yield of **2.25** in complete site selectivity and 95:5 e.r.).

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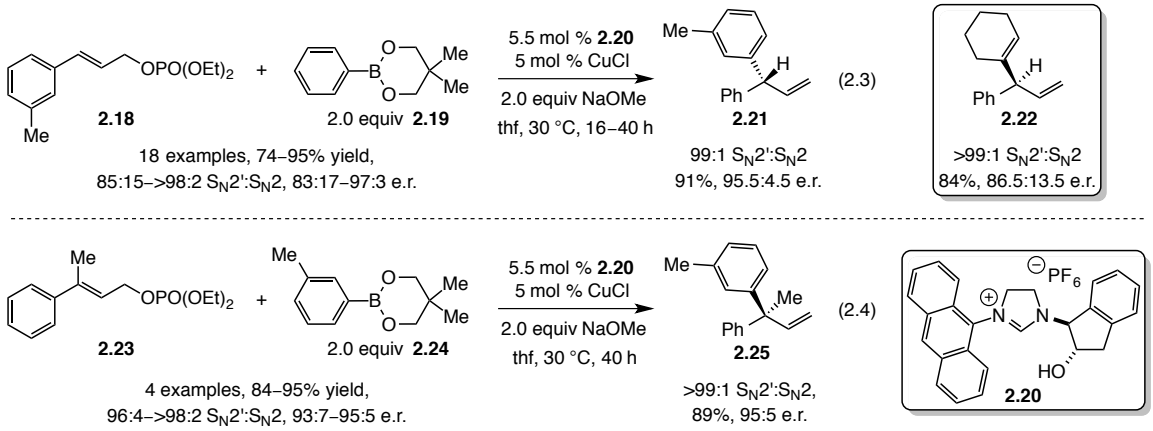
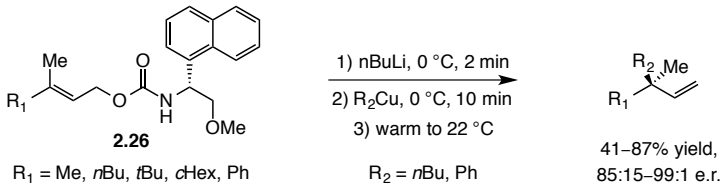
(13) (a) Martin, D.; Kehrli, S.; d'Augustin, M.; Clavier, H.; Mauduit, M.; Alexakis, A. *J. Am. Chem. Soc.* **2006**, *128*, 8416–8417. (b) Magrez, M.; Le Guen, Y.; Baslé, O.; Crévisy, C.; Mauduit, M. *Chem. Eur. J.* **2013**, *19*, 1199–1203.

Scheme 2.5. Enantioselective Cu–catalyzed Allylic Subsitution with Arylboronic Acid Neopentylglycol Esters



Very recently, Denmark and co-workers delineated a chiral auxiliary strategy to synthesize similar enantiomerically enriched molecules that bear an all carbon quaternary stereogenic center.[14] The key component of this process is the enantiopure allylic carbamate as exemplified through a general structure **2.26**. Treatment of **2.26** with *n*BuLi at 0 ^{o}C for two minutes removes the acidic proton of the carbamate moiety; such a transformation puts a Lewis acidic lithium cation, which potentially interacts with the methoxy substituent to rigidify the structure of the chiral auxiliary in achieving high levels of stereogenicity induction. Subsequent reaction with a PhCu delivers the desired olefin products in 85:15–99:1 e.r. (Scheme 2.6).

Scheme 2.6. Enantioselective Synthesis of Ph-Substituted Quaternary Stereogenic Center through Chiral Auxiliary Approach



(14) Denmark, S. E.; Marble, L. K. *Heterocycles*, **2014**, *88*, ASAP.

2.3 Initial Identification of the Optimal Chiral Cu Catalyst for Additions of Monoaryl- Dialkylaluminum Reagents

We began our research with the contention of developing a protocol that only requires mono-aryl metal reagents for the sake of atom economy, and decided to take advantage of the higher propensity of transferring an aryl unit of an (aryl)dialkylaluminum to the catalytically active copper center;[15] reaction of an aryllithium or aryl Grignard with a commercially available and inexpensive dialkylaluminum halide (e.g., Et_2AlCl) would deliver the reagent of interest.[7d, 7f, 9] Thus, we first examined EAS reactions with phenyl(diethyl)aluminum, synthesized and used in situ without further purification from commercial phenyllithium (in Bu_2O); the additions of the resulting aluminum reagents **2.27** to allylic phosphate **2.28** was investigated in the presence of 1 mol % in situ generated NHC–Cu catalysts of a few representative chiral promoters (Scheme 2.7). As the findings in Scheme 2.7 illustrates, transformation with the chiral NHC–Cu complex, obtained from C_1 symmetric monodentate Ag agent **2.30**,[16] is efficient (>98% conversion in one hour), but delivers the desired product **2.29** in a non-selective fashion (83:17 site selectivity and 58:42 e.r.). The corresponding C_2 symmetric Ag based varient **2.31** serves as a much more effective ligand on copper, furnishing **2.29** in complete site selectivity and improved enantiomer ratio (87.5:12.5). Reaction with phenoxide containing bidentate Cu catalyst of NHC–Ag **2.2**[4b] is equally efficient and

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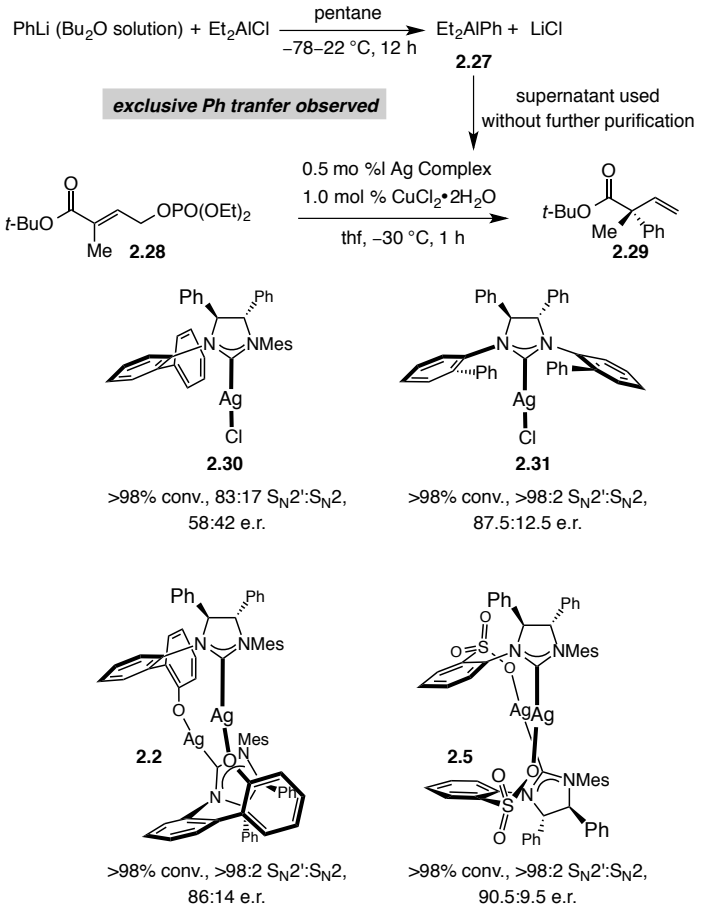
(15) For the more favored transfer of an aryl unit versus an alkyl group of an Al-based reagent, see: (a) Mole, T.; Surtees, J. R. *Aus. J. Chem.* **1964**, *17*, 310–314. (b) Merino, E.; Melo, R. P. A.; Ortega-Guerra, M.; Ribagorda, M.; Carreño, M. C. *J. Org. Chem.* **2009**, *74*, 2824–2831. (c) Gao, H.; Knochel, P. *Synlett* **2009**, 1321–1325. (d) ref. 9 (b) and (c).
(16) Lee, K.-s.; Hoveyda, A. H. *J. Org. Chem.* **2009**, *74*, 4455–4462.

selective. When the sulfonate bearing **2.5**[17] is utilized to promote the C–C bond forming processes, higher enantiomeric purity of the resulting ester product is observed (90.5:9.5 e.r. vs. 86:14 e.r. with **2.2**). One noteworthy aspect of this protocol that needs additional

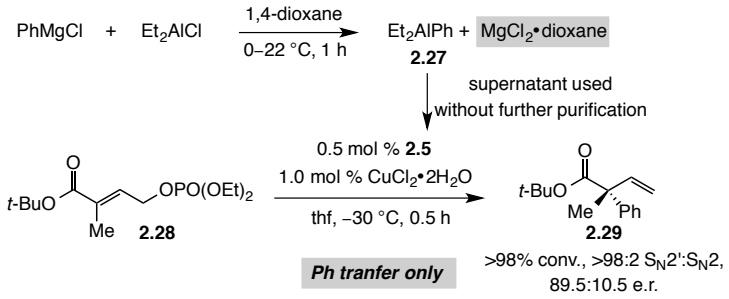
Scheme 2.7. Identification of the Optimal Catalyst in Cu-Catalyzed EAS with In Situ Formed Et_2AlPh Reagents.



(17) For the first disclosure of these NHCs, see: (a) Brown, M. K.; May, T. L.; Baxter, C. A.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 1097–1100. For Cu-catalyzed EAS with these sulfonate bearing NHCs, see: (b) ref. 4 (c). (c) Gillingham, D. G.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 3860–3864. (d) Lee, Y.; Akiyama, K.; Gillingham, D. G.; Brown, M. K.; Hoveyda, A. H. *J. Am. Chem. Soc*. **2008**, *130*, 446–447. (e) Gao, F.; Lee, Y.; Mandai, K.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2010**, *49*, 8370–8374. (f) Gao. F.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 10961–10963. (g) Akiyama, K.; Gao, F.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2010**, *49*, 419–423. (h) Gao, F.; McGrath, K. P.; Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 14315−14320. (i) Guzman-Martinez, A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 10634–10637. (j) Dabrowski, J. A.; Gao. F.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 4778−4781. (k) Jung, B.; Hoveyda, A. H. *J. Am. Chem. Soc*. **2012**, *134*, 1490–1493. (l) Gao, F.; Carr, J. L.; Hoveyda, A. H. *Angew. Chem. Int. Ed*. **2012**, *51*, 6613–6617. (m) Dabrowski, J. A.; Haeffner, F.; Hoveyda A. H. *Angew. Chem., Int. Ed.* **2013**, *52*, 7694–7699.

mention is that all reactions proceed with exclusive transfer of the aromatic component of the mixed aluminum reagent (Ph:Et transfer = >98:2). This feature is only pertinent to Et_2AlPh reagent **2.27**; the Cu-catalyzed EAS reactions with reagents that are derived from commercial Me_2AlCl and iBu_2AlCl provide alkylation products that correspond to the transfer of a Me or *i*Bu group, and result in diminished enantioselectivity levels (73:27 e.r. with Me_2AlPh and 88:12 e.r. with iBu_2AlPh vs. 90.5:9.5 in Scheme 2.7). It should be noted that PhMgCl could also be used to access reagent **2.27** with similar efficiency and effectiveness; mixing of phenyl Grignard with Et_2AlCl in dioxane at 0 °C followed by allowing the resulting suspension to stir at ambient temperature for an additional hour furnishes the desired Et_2AlPh in the supernatant. The choice of solvent is based on the efficient removal of $MgCl_2$ salt via a solvent/salt complex. Thus, EAS reaction with the aluminum species obtained through the above procedure delivers **2.29** in >98% conv., >98% S_N2' and 89.5:10.5 e.r. (Scheme 2.8) under otherwise identical conditions as outlined in Scheme 2.7. The related PhMgBr, on the other hand, although is transformable to the diethylphenyl aluminum **2.27**, and applicable in the subsequent EAS with similar selectivity, the efficiency of the C-C bond formation is somewhat suffered while using the supernatant prepared with it (68% conv. to **2.29** vs. >98% conv. with PhMgCl).

Scheme 2.8: EAS with In Situ Formed Et_2AlPh From Grignard Reagents.

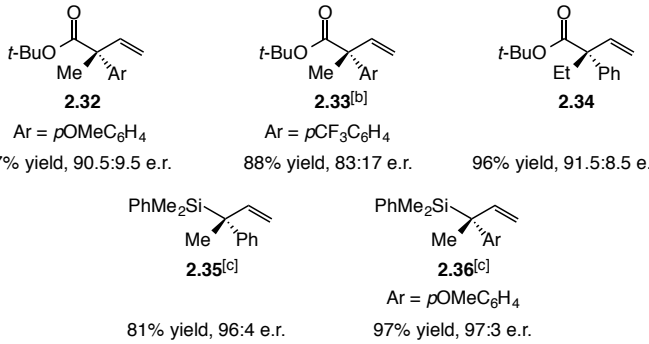


2.4 Scope of NHC–Cu-Catalyzed EAS with Arylaluminums

With the optimal conditions in hand, we then turned our attention to examine an assortment of aryllithium reagents, either purchased or prepared by well-established procedures through metal-halogen exchange with the corresponding bromides, in site-selective (>98% S_N2'), efficient (81–97% yield) and enantioselective Cu-catalyzed EAS reactions (83:17–97:3 e.r., Figure 2.2). Additions of electronically varied nucleophilic aryl units to α,β-unsaturated esters (cf. **2.32** and **2.33**, Figure 2.2) afford the EAS product in 87–88% yield and 83:17–90.5:9.5 e.r. value; a larger Et substituent on the trisubstituted alkene is tolerated under the standard conditions, furnishing ester **2.34** in 96% yield and 91.5:9.5 enantiomer ratio. Reactions with Si-substituted allylic phosphates deliver the desired quaternary stereogenic center containing allylsilanes in up to 97:3 e.r. (cf. **2.35** and **2.36**, Figure 2.2); higher catalyst loading (2 mol % in situ formed NHC–Cu vs. 1 mol % with α,β-unsaturated ester substrates), however, is needed for complete conversion and high yield of the desired products. A few notable points merit further discussion. 1) All transformations proceed with >98% S_N2' selectivity. 2) EAS of α,β-unsaturated ester with arylaluminum reagent that bears an electron withdrawing substituent (e.g., CF_3 in **2.33**) requires the use of phenoxide based Ag complex **2.2** in combination of a copper salt to ensure the highest enantioselectivity. The reason for such a specific need in this particular case is unclear at this moment. 3) Metal halides can be detrimental to enantioselectivity. For example, when the synthesis of **2.34** is performed with an added equiv. of LiCl, the desired product is obtained in ~70:30 e.r. Arylaluminum solutions are allowed to stand for 30 minutes to one hour to permit precipitation of inorganic lithium salts to occur prior to the supernatant being utilized. 4)

The reactions that afford Si-substituted quaternary carbons are substantially more efficient than those previously reported involving diarylzincs.[4c] For example, with $(p\text{OMeC}_6\text{H}_4)_2\text{Zn}$ (related to the preparation of **2.36**), 2.5 mol % **2.5** and 24 hours of reaction time are needed (vs. 1.0 mol % and three hours needed in Figure 2.2), and the desired product is isolated in 88:12 e.r. (vs. 97:3 e.r. with the diethylaryl aluminum reagent). Furthermore, the air-stable $\text{CuCl}_2\bullet 2\text{H}_2\text{O}$ salt utilized in the current protocol can be handled under less rigorously inert atmosphere as opposed to the $(\text{CuOTf})_2\bullet\text{C}_6\text{H}_6$ required for reactions with diarylzincs.

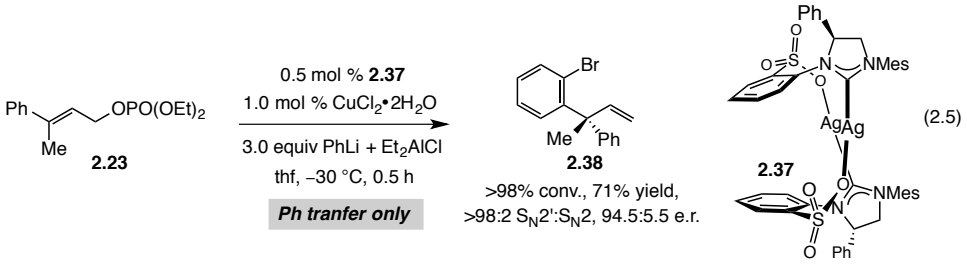
Figure 2.2: Additional Examples of Cu-Catalyzed EAS with Et_2AlAr Reagents.[a]



[a] Reactions performed under conditions identical to Scheme 2.7. [b] 0.75 mol % **2.2** and 1.5 mol % $\text{CuCl}_2\bullet 2\text{H}_2\text{O}$ used. [c] 1.0 mol % **2.5** and 2.0 mol % $\text{CuCl}_2\bullet 2\text{H}_2\text{O}$ used.

Aryl-substituted allylic phosphates are also effective substrates in NHC–Cu-catalyzed EAS reactions. As the case in Eq 2.5 indicates, subjection of trisubstituted allylic phosphate **2.23** to the catalytic C-C bond forming processes, with 1 mol % in situ generated Cu complex of **2.37**, incorporates again exclusively the phenyl group of the mixed organoaluminum reagent, affording diaryl-substituted product **2.38** in 71% yield and 94.5:5.5 e.r. The advantage of using Ag complex **2.37** instead of the biphenyl backbone containing **2.5** is the higher enantiomeric purity (vs. 90:10 e.r. with **2.5**) as well as >98% Ph transfer (26% Et addition with **2.5**) observed with the former NHC ligand. Although the products obtained through the aforementioned transformations (Figure 2.2

and Eq 8), in principle, can be accessed by additions of alkylmetal reagents to the related aryl-substituted substrates (e.g., Ar, silyl-substituted; Ar, ester-substituted and Ar_1, Ar_2-substituted allylic phosphates), such processes remain largely unexplored (the only reported variant involves dialkylzinc reagents to an ester bearing substrate).[3d] Moreover, the latter processes will be less likely favorable due to the complicated substrate synthesis, which relies on stereocontrol in HWE reactions that lead to the crucial trisubstituted olefins, as well as the difficulty in enantiotopic face differentiation of the substrates that bear alkene substituents similar in size (i.e., Ar vs. silyl, ester or a different Ar unit).



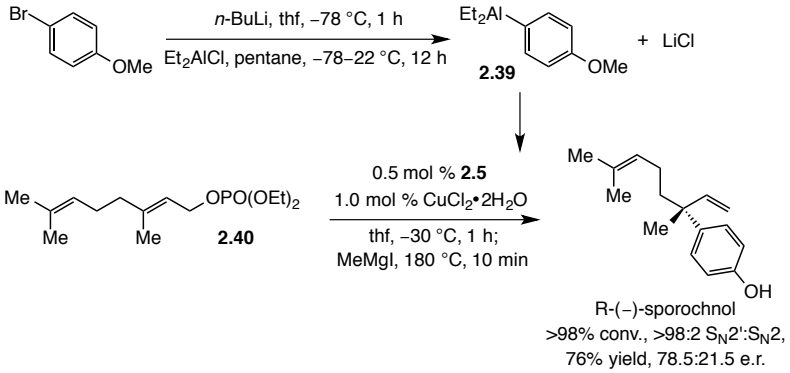
2.5 Synthesis of Natural Product Sporochnol through Cu-Catalyzed EAS

The EAS transformation with allylic phosphate **2.40** and the aryl(diethyl)aluminum **2.39**, which bears a *p*-methoxyaryl unit, affords natural product *R*-(–)-sporochnol (Scheme 2.9).[18] The requisite aluminum species **2.39** is prepared

(18) For isolation and selected previous syntheses, see: (a) Shen, Y. C.; Tsai, P. I.; Fenical W.; Hay, M. E. *Phytochemistry* **1993**, *52*, 71–75. (b) Takahashi, M.; Shioura, Y.; Murakami T.; Ogasawara, K.; *Tetrahedron: Asymmetry* **1997**, *8*, 1235–1242. (c) Fadel, A.; Vandromme, L. *Tetrahedron: Asymmetry* **1999**, *10*, 1153–1162. (d) Alibés, R.; Busqué, F.; Bardaji, G. G.; de March, P.; Figueredo, M.; Font, J. *Tetrahedron: Asymmetry* **2006**, *17*, 2632–2632.

according to the standard procedure starting with lithium/halogen exchange of *n*BuLi with *p*-methoxy bromobenzene. Again, the use of the resulting supernatant in the Cu-catalyzed coupling with geraniol derived allylic phosphate **2.40** delivers the targeted molecule in 76% overall yield and 78.5:21.5 e.r. after removal of methyl ether. Compared to a more enantioselective (91:9 e.r.) previous alternative synthesis of the same natural product involving an aryl-substituted allylic phosphate with di(2-methyl-2-pentenyl)Zn, promoted by 10 mol % of an amino acid-based chiral Cu complex,[3a] the current route depicted in Scheme 2.9 is superior on several fronts. First, 1.0 mol % of the NHC–Cu complex is required for a reaction that is complete in one hour at –30 °C versus 10 mol % of the amino acid–Cu complex for 48 hours at –78 °C (lower temperature required for maximum enantioselectivity in the latter synthesis). Second, the aluminum reagent, which combines an easily accessible aryllithium and commercially available Et_2AlCl, is considerably more practical than the preparation, purification and use of the aforementioned dialkylzinc reagent. Third, allylic phosphate **2.40** required in the present synthesis, which is easily accessed in one step from commercial geraniol competes favorably to the previously involved aryl-substituted allylic phosphate, which is prepared in three steps through Horner-Wadsworth-Emmons olefination, reduction of ester and followed by phosphorylation.

Scheme 2.9. Efficient Synthesis of Natural Product *R*-(–)Sporochnol.

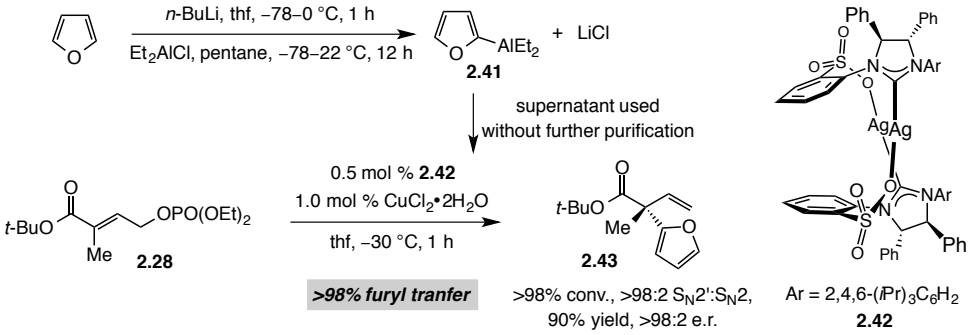


2.6 NHC–Cu-Catalyzed EAS with Heteroarylaluminum Reagents

Heterocycles are among the most important motifs in pharmaceutical industry. The involvement of heterocyclic nucleophiles in Cu-catalyzed enantioselective allylic substitution reactions is unknown previous to our study delineated below.[17e] Having effected the efficient and enantioselective introduction of various aryl(diethyl)aluminum reagents in Cu-catalyzed EAS, we then probed the possibility of catalytic enantioselective additions of heterocyclic units, preferentially through the use of reagents similar to those used in the above sections. Towards this end, we take the advantage of efficient and site-selective deprotonation of furan (Scheme 2.10) to secure the 2-furyllithium species prior to a similar subjection to Et_2AlCl to afford (2-furyl)$Al(Et)_2$ **2.41**, which can be utilized without isolation or purification in a highly group- (<2% Et addition), site- (>98% S_N2') and enantioselective (>98:2 e.r.) process, converting allylic phosphate **2.28** to α-furyl substituted ester **2.43** within one hour at –30 ºC with 1.0 mol % Cu catalyst derived from Ag complex **2.42**. When the less hindered variant **2.5** is utilized in this case, **2.43** is obtained with equally high efficiency (>98% conv.), group- and site-selectivity (>98%

S_N2', >98% furyl addition) but in diminished e.r. value (90.5:9.5 vs. >98:2 in Scheme 2.10).

Scheme 2.10. Cu-Catalyzed EAS with In Situ Formed Heterocyclic Furylaluminum Reagents.



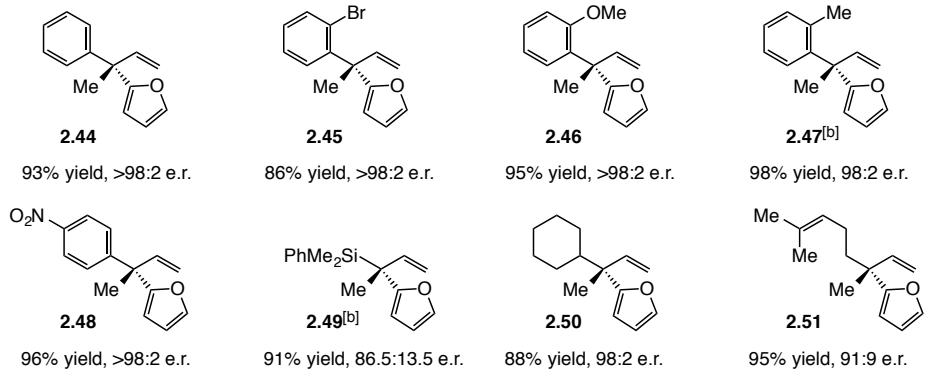
The results summarized in Figure 2.3 illustrate that 2-furyl- and 2-thienyl(diethyl)aluminum,[19] furnished in the same fashion, participate in effective EAS reactions with a range of allylic phosphates catalyzed by small quantity of in situ synthesized Cu catalyst of **2.5**. From the first half of the examples shown in Scheme 2.10, we demonstrate that EAS reactions with 2-furyl(diethyl)aluminum **2.41** are highly efficient (>98% conv. in one hour with 0.5–1.0 mol % chiral NHC–Ag(I) complex), affording desired biaryl-substituted quaternary stereogenic center containing products **2.44**–**2.51** in 86–98% yield after purification with complete site-selectivity in all cases (>98% S_N2'). Enantioselectivity levels are exceptional (≥98:2 e.r.) with substrates that bear an electron- withdrawing (cf. **2.45** and **2.48**), donating (cf. **2.46**) and sizable (cf. **2.47**) aryl substituent, or a cyclohexane ring (cf. **2.50**). Reactions with silyl- or long chain aliphatic substituted allylic phosphates are less enantioselective, delivering **2.49** and **2.51** in 86.5:13.5 and 91:9 e.r., respectively, with formation of the former compound requiring

(19) For use of furyl- and thienylaluminum reagents in enantioselective additions to carbonyls, see: (a) Wu, K-H.; Chuang, D-W.; Chen, C-A.; Gau, H-M. *Chem. Commun.* **2008**, 2343–2345. (b) Biradar, D. B.; Zhou, S.; Gau, H-M. *Org. Lett.* **2009**, *11*, 3386–3389.

increased catalyst loading (2 mol % NHC–Cu). The second half of the data indicates that EAS reactions with 2-thienyl(diethyl)aluminum are equally applicable to an assortment of allylic phosphates, including one that bears a carboxylic ester (cf. **2.55**), providing facile and selective preparation of thiophene-substituted enantiomerically enriched molecules (94–98% yield and 81:19–98:2 e.r. for **2.52**–**2.57**, Figure 2.3). These results put forth the first examples of Cu-catalyzed EAS reactions with heterocyclic metal reagents.

Figure 2.3: Additional Examples of Cu-Catalyzed EAS with 2-Furyl- and 2-Thienyl(diethyl)aluminum Reagents.[a]

2-Furyl Additions



2.44 93% yield, >98:2 e.r.

2.45 86% yield, >98:2 e.r.

2.46 95% yield, >98:2 e.r.

2.47[b] 98% yield, 98:2 e.r.

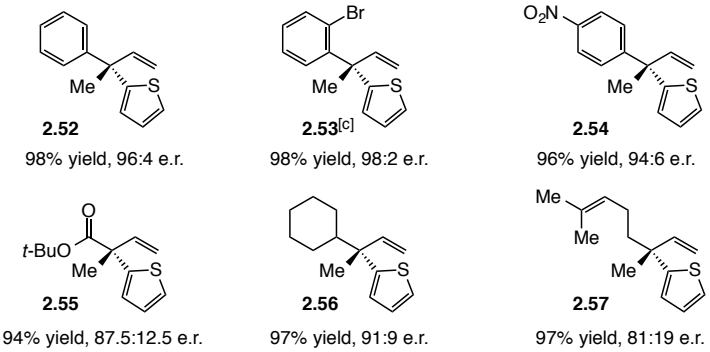
2.48 96% yield, >98:2 e.r.

2.49[b] 91% yield, 86.5:13.5 e.r.

2.50 88% yield, 98:2 e.r.

2.51 95% yield, 91:9 e.r.

2-Thienyl Additions



2.52 98% yield, 96:4 e.r.

2.53[c] 98% yield, 98:2 e.r.

2.54 96% yield, 94:6 e.r.

2.55 94% yield, 87.5:12.5 e.r.

2.56 97% yield, 91:9 e.r.

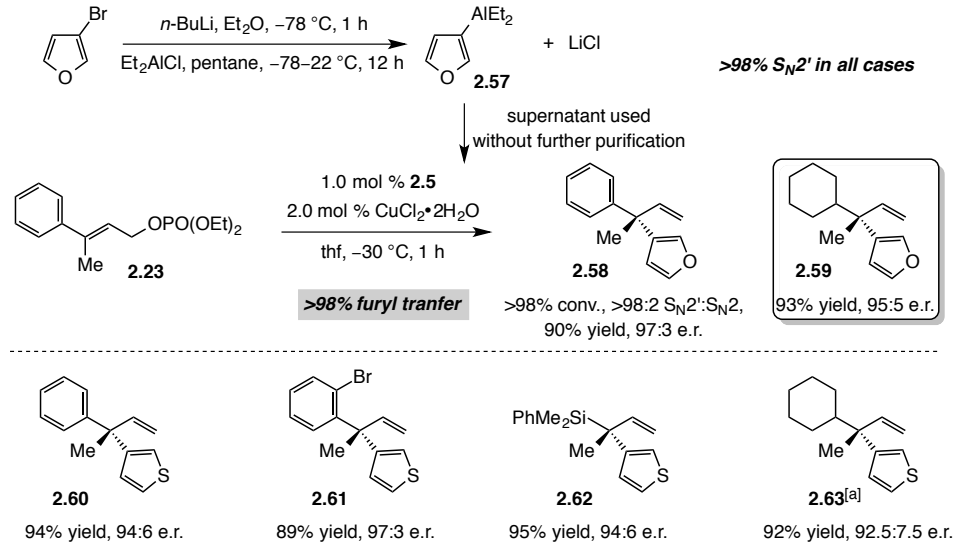
2.57 97% yield, 81:19 e.r.

[a] Reactions performed under conditions identical to Scheme 2.10 expect with Ag complex **2.5**; >98% S_N2' selectivity in all cases. [b] 1.0 mol % **2.5** and 2.0 mol % $CuCl_2 \cdot 2H_2O$ used. [c] 1.5 mol % **2.5** and 3.0 mol % $CuCl_2 \cdot 2H_2O$ used.

The NHC–Cu-catalyzed EAS reactions can be performed with regioisomeric 3-furyl- and 3-thienyl(diethyl)aluminum (Scheme 2.11); the sequence begins with the corresponding readily available (3-bromo)heterocyclic precursors, which are converted to

the derived heteroarylaluminum reagents through a simple metal-halogen exchange/subjection to Et_2AlCl procedure. Subsequent transformations of, for example, allylic phosphate **2.23** with the derived 3-furyl(diethyl)aluminum **2.57** proceed readily with 1.0 mol % chiral NHC–Ag complex **2.5**, to afford the EAS product **2.58** in 90% yield, with >98% site selectivity and 97:3 e.r. Cyclohexyl-substituted allylic phosphate is equally effective under these conditions, delivering **2.59** in 93% and 95:5 e.r. Additional cases, in which 3-thienyl(diethyl)aluminum reagent is utilized, further showcase the scope of Cu-catalyzed EAS processes, which are able to furnish all carbon quaternary center containing 3-thiophene derivatives in excellent efficiency (89–95% yield) and high enantioselectivites (92.5:7.5–97:3 e.r., cf. **2.60**–**2.63** in Scheme 2.11).

Scheme 2.11. EAS with In Situ Formed Heterocyclic 3-Furylaluminums from Lithium/Halogen Exchange.

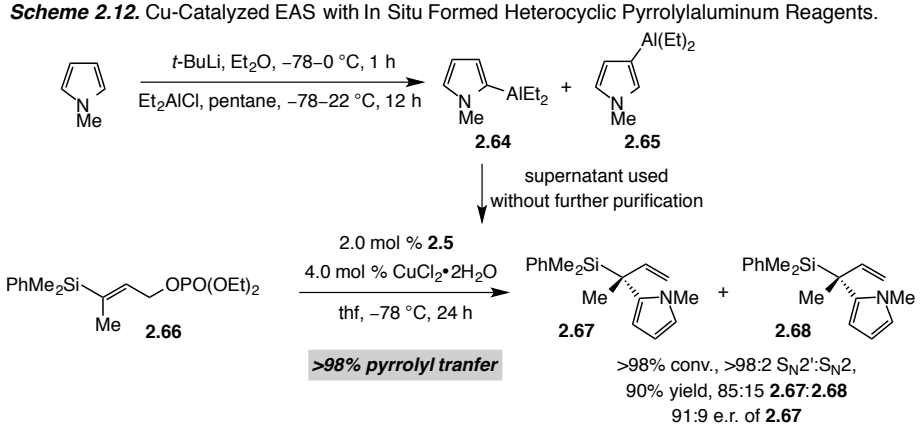


[a] Reactions performed at –50 °C for 3 h under otherwise identical conditions.

The ability to introduce a pyrrole site-selectively through Cu-catalyzed EAS will further enhance the synthetic utility of the present catalytic protocol. As demonstrated in Scheme 2.12, we examined the possibility of such a contention employing the same

strategy; deprotonation of *N*-methyl pyrrole with *t*BuLi in diethyl ether[20] results in a mixture of regioisomeric lithium species as represented by their Al counterparts **2.64** and **2.65** after treatment with Et_2AlCl under standard conditions. As expected, based on the previous observation of the facile reactions with both 2- and 3-heterocyclic metal reagents, subjection of such a reagent mixture with allylic phosphate **2.66** under slightly modified conditions transfers both nucleophilic species at a similar rate, affording 2- and 3-pyrrolyl-substituted EAS products **2.67** and **2.68** in 85:15 ratio, with combined yield of 90%, exclusive S_N2' selectivity and 91:9 e.r. for major isomer **2.67**.

Scheme 2.12. Cu-Catalyzed EAS with In Situ Formed Heterocyclic Pyrrolylaluminum Reagents.



2.7 Conclusion

In this chapter, we have addressed a longstanding shortcoming in an important class of enantioselective C–C bond forming reactions. The present investigations introduce efficient and highly selective NHC–Cu-catalyzed EAS processes that allow access to a number of enantioenriched versatile organic molecules, which contain aryl- or heteroaryl-substituted quaternary carbon stereogenic centers, through the use of simple

(20) The corresponding deprotonation reactions with nBuLi as under conditions described in Scheme 2.10 are very sluggish, affording a mixture of products in low conversion (<30%).

combinations of commercially available or easily accessible organolithium reagents and Et_2AlCl in an atom economical fashion. Utility of the method is demonstrated through a concise enantioselective synthesis of natural product sporochnol. Moreover, the studies outlined herein offer additional evidence regarding the modular and uniquely behaved sulfonate-bridged bidentate *N*-heterocyclic carbene–based copper complexes to continuously provide effective solutions to difficult problems resided in enantioselective allylic substitution and catalysis in general.

2.8 Experimental

General. Infrared (IR) spectra were recorded on a Bruker FT-IR Alpha (ATR mode) spectrophotometer, ν_{max} in cm^{-1}. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). ^1H NMR spectra were recorded on a Varian Unity INOVA 400 (400 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on a Varian Unity INOVA 400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: 77.16 ppm). High-resolution mass spectrometry was performed on a Micromass LCT ESI-MS (positive mode) at the Mass Spectrometry Facility, Boston College. Enantiomer ratios were determined by GLC analysis (Alltech Associated Chiral dex GTA column (30 m x 0.25 mm) and Betadex 120 column (30 m x 0.25 mm)) and HPLC analysis (high-performance liquid chromatography) with a

Shimadzu chromatograph (Chiral Technologies Chiralcel OD (4.6 x 250 mm), Chiral Technologies Chiralpak AD (4.6 x 250 mm), Chiral Technologies Chiralcel OB-H (4.6 x 250 mm), Chiral Technologies Chiralcel OJ-H (4.6 x 250 mm), Chiral Technologies Chiralcel OD-H (4.6 x 250 mm), or Chiral Technologies Chiralpak AD-H (4.6 x 250 mm)) in comparison with authentic racemic materials. Specific rotations were measured on a Rudolph Research Analytical Autopol IV Polarimeter.

Unless otherwise noted, all reactions were carried out with distilled and degassed solvents under an atmosphere of dry N_2 in oven- (135 ºC) or flame-dried glassware with standard dry box or vacuum-line techniques. Pentane and dichloromethane (Fisher Scientific) were purified by passing through two alumina columns under a positive pressure of dry argon by a modified Innovative Technologies purification system. Tetrahydrofuran (Aldrich Chemical Co.) was purified by distillation from sodium benzophenone ketyl immediately prior to use unless otherwise specified. All work-up and purification procedures were carried out with reagent grade solvents (purchased from Fisher Scientific) under air. All substrates are prepared according to previously reported procedures;[21] all substrates possess *E*-olefin geometry and purities are established by ^{1}H NMR analysis (400 MHz).

2.8.1 Reagents and Ligands

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(21) (a) C. A. Luchaco-Cullis, H. Mizutani, K. E. Murphy, A. H. Hoveyda, *Angew. Chem. Int. Ed.* **2001**, *40*, 1456–1460. (b) M. A. Kacprzynski, T. L. May, S. A. Kazane, A. H. Hoveyda, *Angew. Chem. Int. Ed.* **2007**, *46*, 4554–4558. (c) Y. Lee, A. H. Hoveyda, *J. Am. Chem. Soc.* **2006**, *128*, 15604–15605. (d) F. Gao, K. P. McGrath, Y. Lee, A. H. Hoveyda, *J. Am. Chem. Soc.* **2010**, *132*, 14315–14320.

Ag-NHC complex 2.2: prepared according to a previously reported procedure.[22]

Ag-NHC complex 2.5: prepared according to a previously reported procedure.[23]

Ag-NHC complex 2.37: prepared according to a previously reported procedure.[24]

Ag-NHC complex 2.42: prepared according to a previously reported procedure.[25]

Ag-NHC complex 2.30 and 2.31: prepared according to a previously reported procedure.[26]

9-Borabicyclo[3.3.1]nonane (0.5 M in thf): purchased from Aldrich Chemical Co. and used as received.

4-Bromoanisole: purchased from Aldrich Chemical Co. and purified by distillation over CaH_2.

3-Bromofuran: purchased from Aldrich Chemical Co. and purified by distillation over sodium.

3-Bromothiophene: purchased from Aldrich Chemical Co. and purified by distillation over CaH_2.

1-Bromo-4-(trifluoromethyl)benzene: purchased from Aldrich Chemical Co. and purified by distillation over CaH_2.

***n*-Butyllithium (15% in hexanes):** purchased from Strem Chemicals Inc. and titrated before use.

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(22) J. J. Van Veldhuizen, J. E. Campbell, R. E. Giudici, A. H. Hoveyda, *J. Am. Chem. Soc.* **2005**, *127*, 6877–6882.

(23) M. K. Brown, T. L. May, C. A. Baxter, A. H. Hoveyda, *Angew. Chem. Int. Ed.* **2007**, *46*, 1097–1100.

(24) Y. Lee, K. Akiyama, D. G. Gillingham, M. K. Brown, A. H. Hoveyda, *J. Am. Chem. Soc.* **2008**, *130*, 446–447.

(25) K. Akiyama, F. Gao, A. H. Hoveyda, *Angew. Chem. Int. Ed.* **2010**, 49, 419–423.

(26) K-s. Lee, A. H. Hoveyda, *J. Org. Chem.* **2009**, *74*, 4455–4462.

***t*-Butyllithium (16% in pentane):** purchased from Strem Chemicals Inc. and titrated before use.

Copper(II) dichloride bishydrate: purchased from Aldrich Chemical Co. and used as received.

Diethylaluminum chloride: purchased from Aldrich Chemical Co. and used as received.

Diethylphenylaluminum 2.27: prepared according to a previously reported procedure.[27]

Furan: purchased from Aldrich Chemical Co. and purified by distillation over sodium.

Hydrogen peroxide (35% wt solution in water): purchased from Aldrich Chemical Co. and used as received.

Magnesium turning: purchased from Strem Chemicals Inc. and used as received.

Methylmagnesium iodide: prepared from iodomethane and Mg turning in Et_2O.

***N*-Methylpyrrole:** purchased from Aldrich Chemical Co. and purified by distillation over CaH_2.

Phenyllithium (2.0 M in Bu_2O): purchased from Acros Organics and titrated before use.

Sodium perborate tetrahydrate: purchased from Aldrich Chemical Co. and used as received.

Thiophene: purchased from Aldrich Chemical Co. and purified by distillation over CaH_2.

2.8.2 Experimental Procedures for the Preparation of Diethylaryl- and Heteroarylaluminum Reagents

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(27) T. L. May, M. K. Brown, A. H. Hoveyda, *Angew. Chem. Int. Ed.* **2008**, *47*, 7358–7362.

■ **Representative Experimental Procedure for the Preparation of Diethylarylaluminum Reagents:**[27] Under a N_2 atmosphere, 4-bromoanisole (626 μL, 5.0 mmol) and tetrahydrofuran (thf, 700 μL) are placed in a flame-dried round bottom flask equipped with a stir bar. The solution is allowed to cool to –78 °C (dry ice/acetone bath). *n*-Butyllithium (1.61 M in hexanes, 3.10 mL, 5.0 mmol) is added through a syringe dropwise over ten minutes and the resulting mixture is allowed to stir at –78 °C for 1 h. Pentane (3.0 mL), followed by diethylaluminum chloride (690 μL, 5.5 mmol) is added to the solution through syringes and the suspension of white precipitate is allowed to warm to 22 °C and stir for 12 h. After that time, the resulting mixture is allowed to stand for 30 minutes to assist with the settling of white solid (LiCl) and the colorless supernatant (diethyl(4-methoxyphenyl)aluminum **2.39**, 0.616 M) is used directly without further purification.

■ **Experimental Procedure for the Preparation of Diethyl(2-furyl)aluminum Reagent 2.41:** Under a N_2 atmosphere, furan (727 μL, 10.0 mmol) and tetrahydrofuran (thf, 1.4 mL) are added to a flame-dried round bottom flask equipped with a stir bar through syringes. The solution is allowed to cool to –78 °C (dry ice/acetone bath). *n*-Butyllithium (1.61 M in hexanes, 6.21 mL, 10.0 mmol) is added through a syringe and the resulting yellow solution is allowed to stir at 0 °C for 1 h, after which time the solution is allowed to cool to –78 °C again. Pentane (5.6 mL), followed by diethylaluminum chloride (1.38 mL, 11.0 mmol) is added to the solution through syringes and the mixture is allowed to warm to 22 °C and stir for 12 h. The resulting mixture is allowed to stand for 30 minutes to assist with the settling of white solid (LiCl) and the clear yellow supernatant (diethyl(2-furyl)aluminum **2.41**, 0.653 M) is used directly

without further purification.

■ **Diethyl(2-thienyl)aluminum Reagent:** prepared the same way as diethyl(2-furyl)aluminum reagent and used as supernatant without further purification.

■ **Experimental Procedure for the Preparation of Diethyl(3-furyl)aluminum Reagent 2.57:** Under a N_2 atmosphere, 3-bromofuran (449 μL, 5.0 mmol) and diethyl ether (Et_2O, 3.1 mL) are added to a flame-dried round bottom flask equipped with a stir bar through syringes. The solution is allowed to cool to –78 °C (dry ice/acetone bath). *n*-Butyllithium (1.61 M in hexanes, 3.1 mL, 5.0 mmol) is added through a syringe and the resulting yellow mixture is allowed to stir at –78 °C for 1 h. Diethylaluminum chloride (690 μL, 5.5 mmol) is added to the solution through a syringe and the mixture is allowed to warm to 22 °C and stir for 12 h. The resulting mixture is allowed to stand for 30 minutes to assist with the settling of white solid (LiCl) and the clear yellow supernatant (diethyl(3-furyl)aluminum **2.57**, 0.681 M) is used directly without further purification.

■ **Diethyl(3-thienyl)aluminum Reagent:** prepared the same way as diethyl(3-furyl)aluminum reagent and used as supernatant without further purification.

■ **Experimental Procedure for the Preparation of Diethyl(2-pyrrolyl)aluminum Reagent 2.64:** Under an N_2 atmosphere, *N*-methylpyrrole (444 μL, 5.0 mmol) and diethyl ether (Et_2O, 3.1 mL) are added to a flame-dried round bottom flask equipped with a stir bar through syringes. The solution is allowed to cool to –78 °C (dry ice/acetone bath). *t*-Butyllithium (1.62 M in pentane, 3.1 mL, 5.0 mmol) is added through a syringe and the resulting yellow solution is allowed to stir at 0 °C for 1 h. White solid is generated and the mixture is allowed to cool to –78 °C. Diethylaluminum chloride (690 μL, 5.5 mmol) is added to the solution through a syringe and the mixture is allowed to

warm to 22 °C and stir for 12 h. The resulting mixture is allowed to stand for 30 minutes to assist with the settling of white solid (LiCl) and the clear orange supernatant (diethyl(2-pyrrolyl)aluminum **2.64**, 0.682 M) is used directly without further purification.

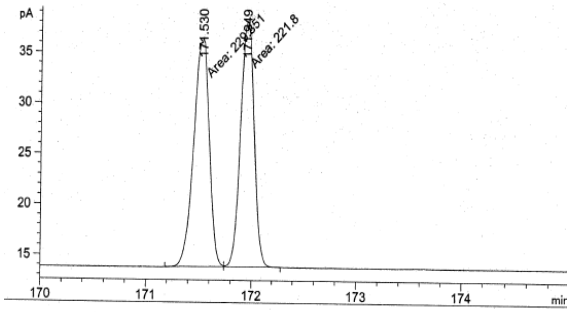
2.8.3 Experimental Procedures and Charaterization Data for Cu-Catalyzed EAS with Diethylarylaluminum Reagents

■ **Representative Experimental Procedure for Cu-Catalyzed Enantioselective Allylic Substitution Reactions of Diethylarylaluminum Reagents to Allylic Phosphates:** In an N_2 filled glove box, an oven-dried vial (8 mL, 17 x 60 mm) with a magnetic stir bar is charged with NHC–Ag(I) complex **2.5** (0.9 mg, 7.5 x 10^{-4} mmol) and sealed with a septum before removal from the glove box. To the vial under an N_2 atmosphere are added tetrahydrofuran (thf, 0.5 mL) and a solution of $CuCl_2$•$2H_2O$ (0.02 M in thf, 75 μL, 1.50 x 10^{-3} mmol). The light blue solution is allowed to stir at 22 °C for 30 minutes and a solution of *(E)-tert*-butyl-4-(diethoxyphosphoryloxy)-2-methylbut-2-enoate **2.28** (46.2 mg, 0.150 mmol) in thf (0.5 mL) is added through a syringe. After stirring for 10 minutes, the reaction mixture is allowed to cool to –78 °C (dry ice/acetone bath). A solution of diethylphenylaluminum reagent **2.27** (0.622 M in pentane, 723 μL, 0.450 mmol) is added slowly through a syringe. The vial is transferred to a –30 °C cryocool. After 1 h, the reaction solution is allowed to cool to –78 °C and quenched by addition of a saturated aqueous solution of Rochelle's salt (potassium sodium tartrate, 2 mL). The aqueous layer is washed with Et_2O (3 x 1 mL) and the combined organic layers are passed through a short plug of $MgSO_4$ and silica gel. The filtrate is concentrated under reduced pressure to provide colorless oil residue, which is purified by silica gel

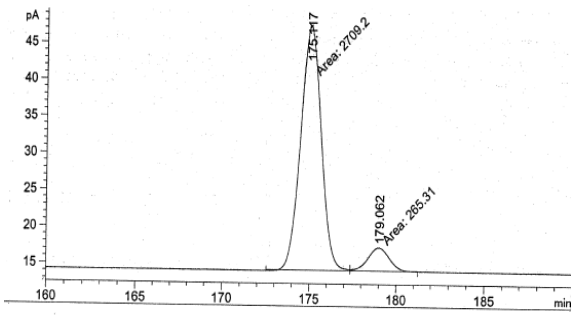
column chromatography (30:1 pentane:Et_2O) to afford product **2.29** as colorless oil (34.2 mg, 0.147 mmol, 98% yield). **(*R*)-*tert*-Butyl 2-methyl-2-phenylbut-3-enoate** (**2.29**): The compound has been previously reported and spectra data match those previously described).[28] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.22 (5H, m), 6.37 (1H, dd, *J* = 17.6, 10.8 Hz), 5.25 (1H, dd, *J* = 10.8, 1.2 Hz), 5.13 (1H, dd, *J* = 17.6, 1.2 Hz), 1.58 (3H, s), 1.41 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.0, 144.3, 141.7, 128.4, 126.7, 126.5, 114.6, 81.1, 54.4, 28.0, 23.6. Specific Rotation: $[\alpha]_D^{20}$ +3.49 (*c* 1.06, $CHCl_3$) for an enantiomerically enriched sample of 90.5:9.5 e.r.

Proof of Stereochemistry: Literature value ($[\alpha]_D^{20}$ –3.05 (*c* 0.747, $CHCl_3$), 94.5:5.5 e.r.) is assigned to the (*S*) enantiomer.[28]

Enantiomeric purity is determined by GLC analysis in comparison with authentic racemic material (91.1:8.9 e.r. shown; *β*-dex column, 15 psi, 90 °C).



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	171.530	MF	0.1688	229.85078	22.69767	50.89121
2	171.949	FM	0.1523	221.80048	24.27510	49.10879



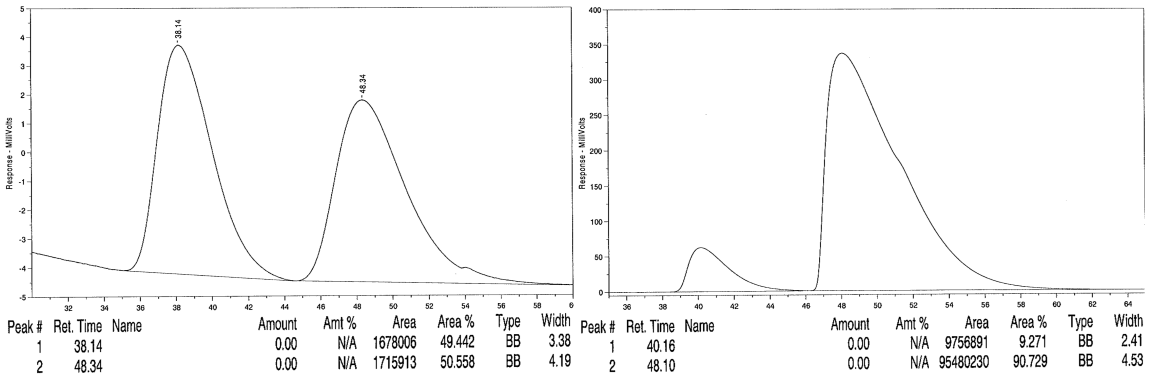
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	175.117	MF	1.3493	2709.19824	33.46421	91.08054
2	179.062	FM	1.3937	265.30994	3.17263	8.91946

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	171.530	50.9	1	175.117	91.1
2	171.949	49.1	2	179.062	8.9

(28) K. E. Murphy, A. H. Hoveyda, *Org. Lett*. **2005**, *7*, 1255–1258.

(*R*)-*tert*-Butyl 2-(4-methoxyphenyl)-2-methylbut-3-enoate (2.32). IR (neat): 2979 (w), 1721 (s), 1610 (w), 1510 (s), 1367 (m), 1247 (s), 1161 (s), 1122 (s), 1034 (m), 920 (w), 831 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.19 (2H, d, *J* = 8.8 Hz), 6.84 (2H, d, *J* = 9.2 Hz), 6.37 (1H, dd, *J* = 17.6, 10.4 Hz), 5.22 (1H, dd, *J* = 10.8, 1.2 Hz), 5.11 (1H, dd, *J* = 17.2, 0.8 Hz), 3.78 (3H, s), 1.54 (3H, s), 1.40 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.2, 158.3, 142.0, 136.3, 127.7, 114.3, 113.7, 81.0, 55.4, 53.7, 28.0, 23.6; HRMS (ESI+): Calcd for $C_{16}H_{26}N_1O_3$ $[M+NH_4]^+$: 280.1913, Found: 280.1914. Specific Rotation: $[\alpha]_D^{20}$ –4.11 (*c* 1.72, $CHCl_3$) for an enantiomerically enriched sample of 90.5:9.5 e.r.

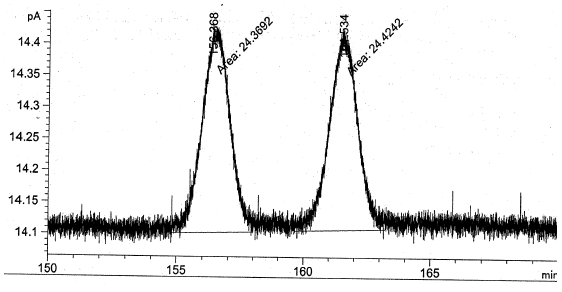
Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived methyl ester derivative, which was prepared by deprotection of *tert*-butyl ester with trifluoroacetic acid in CH_2Cl_2, followed by methylation of the derived acid with MeI and K_2CO_3 in dmf (90.7:9.3 e.r. shown; Chiralcel OB-H column, 99.8/0.2 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



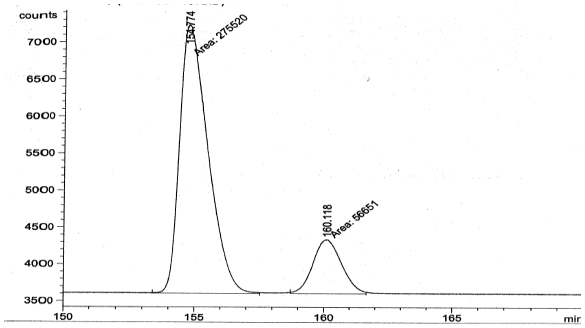
Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	38.14	49.4	1	40.16	9.3
2	48.34	50.6	2	48.10	90.7

(*R*)-*tert*-Butyl 2-methyl-2-(4-(trifluoromethyl)phenyl)but-3-enoate (2.33). IR (neat): 1725 (m), 1369 (m), 1324 (s), 1253 (m), 1161 (s), 1121 (s), 1078 (s), 1016 (s), 924 (m), 842 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.56 (2H, d, *J* = 8.8 Hz), 7.38 (2H, d, *J* = 8.4 Hz), 6.33 (1H, dd, *J* = 17.6, 17.2 Hz), 5.30 (1H, d, *J* = 11.6 Hz), 5.15 (1H, d, *J* = 17.6 Hz), 1.58 (3H, s), 1.41 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.0, 148.0, 140.6, 128.8 (q, *J* = 32.0 Hz), 126.8, 126.1 (q, *J* = 270.9 Hz), 125.1 (q, *J* = 4.4 Hz), 115.2, 81.4, 54.3, 27.7, 23.3; HRMS (ESI+): Calcd for $C_{16}H_{23}F_3N_1O_2$ $[M+NH_4]^+$: 318.1681, Found: 318.1693. Specific Rotation: $[\alpha]_D^{20}$ +2.30 (*c* 1.57, $CHCl_3$) for an enantiomerically enriched sample of 83:17 e.r.

Enantiomeric purity was determined by GLC analysis in comparison with authentic racemic material (82.9:17.1 e.r. shown; *β*-dex column, 15 psi, 90 °C).



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	156.368	MM	1.2207	24.36917	3.32720e-1	49.94365
2	161.534	MM	1.2957	24.42416	3.14172e-1	50.05635



Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	154.774	MM	1.2624	2.75520e5	3637.60327	82.94522
2	160.118	MM	1.2801	5.66510e4	737.60937	17.05478

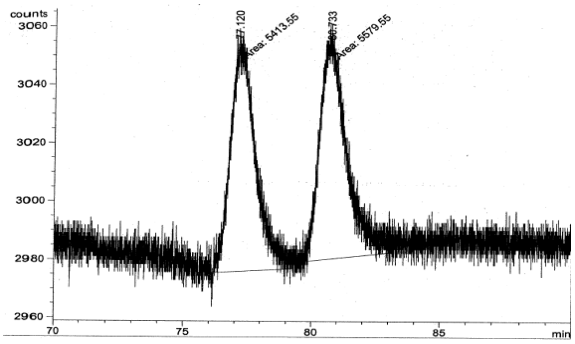
Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	156.368	49.9	1	154.774	82.9
2	161.534	50.1	2	160.118	17.1

(*R*)-*tert*-Butyl 2-ethyl-2-phenylbut-3-enoate (2.34): The compound has been previously reported and spectra data match those described.[28] ^1H NMR (400 MHz, $CDCl_3$): δ 7.31–7.18 (5H, m), 6.35 (1H, dd, *J* = 17.6, 10.8 Hz), 5.25 (1H, dd, *J* = 11.2, 1.2 Hz), 4.97

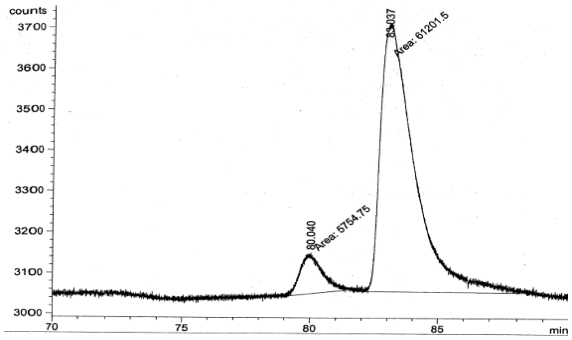
(1H, dd, *J* = 17.6, 1.2 Hz), 2.15 (1H, dq, *J* = 14.0, 7.6 Hz), 2.06 (1H, dq, *J* = 13.6, 7.2 Hz), 1.39 (9H, s), 0.84 (3H, t, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.6, 142.7, 140.3, 128.1, 127.4, 126.6, 115.7, 81.0, 58.5, 29.5, 28.0, 9.5. Specific Rotation: $[\alpha]_D^{20}$ –12.4 (*c* 1.00, $CHCl_3$) for an enantiomerically enriched sample of 91:9 e.r.

Proof of Stereochemistry: Literature value ($[\alpha]_D^{20}$ +14.3 (*c* 0.493, $CHCl_3$), 89.5:10.5 e..r) is assigned to the (*S*) enantiomer.[28]

Enantiomeric purity was determined by GLC analysis in comparison with authentic racemic material obtained from the derived methyl ester derivative, which was prepared by deprotection of *tert*-butyl ester with trifluoroacetic acid in CH_2Cl_2, followed by methylation of the derived acid with MeI and K_2CO_3 in dmf (91.4:8.6 e.r. shown; Chiral dex GTA column, 15 psi, 90 ºC).



Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	77.120	MM	1.0694	5413.54980	84.37312	49.24500
2	80.733	MM	1.1414	5579.54541	81.47540	50.75500



Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	80.040	MM	0.9496	5754.75000	101.00825	8.59479
2	83.037	MM	1.5399	6.12015e4	662.41803	91.40521

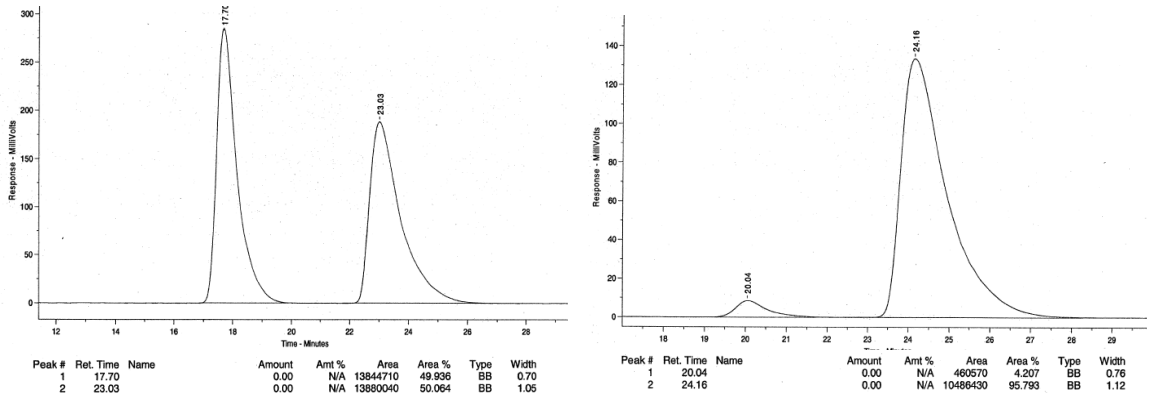
Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	77.120	49.2	1	80.040	8.6
2	80.733	50.8	2	83.037	91.4

(*R*)-Dimethyl(phenyl)(2-phenylbut-3-en-2-yl)silane (2.35): The compound has been previously reported and spectra data match those described.[21b] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37–7.06 (10H, m), 6.47 (1H, dd, *J* = 17.2, 10.8 Hz), 5.09 (1H, dd, *J* = 10.8,

1.6 Hz), 4.94 (1H, dd, *J* = 17.2, 1.2 Hz), 1.46 (3H, s), 0.24 (3H, s), 0.23 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.5, 143.1, 136.6, 135.0, 129.2, 127.9, 127.4, 126.6, 124.7, 111.4, 37.6, 19.0, –5.1, –5.2. Specific Rotation: $[\alpha]_D^{20}$ –15.7 (*c* 1.00, $CHCl_3$) for an enantiomerically enriched sample of 96:4 e.r.

Proof of Stereochemistry: Literature value ($[\alpha]_D^{20}$ –17.1 (*c* 0.513, $CHCl_3$), 92.5:7.5 e.r.) is assigned to the (*R*) enantiomer.[21b]

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (95.8:4.2 e.r. shown; Chiralcel OD column, 98/2 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



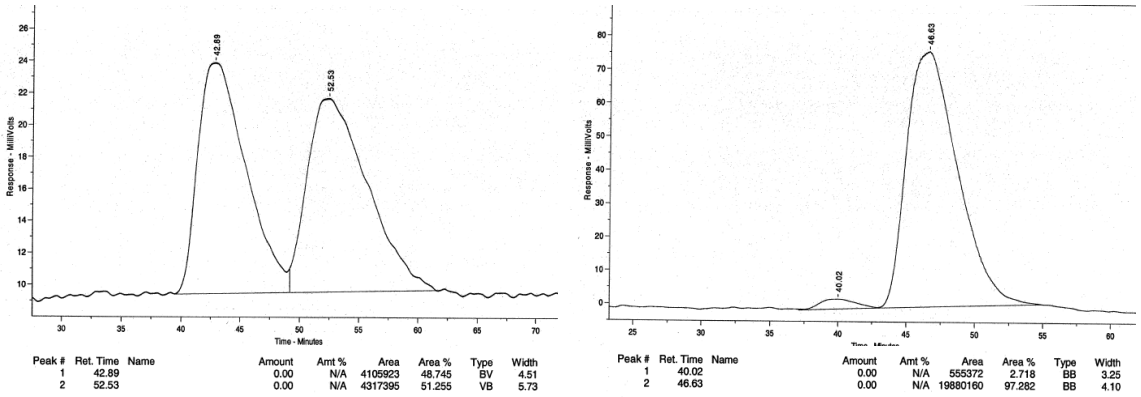
Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	17.70	49.9	1	20.04	4.2
2	23.03	50.1	2	24.16	95.8

(*R*)-(2-(4-Methoxyphenyl)but-3-en-2-yl)dimethyl(phenyl)silane (2.36): The compound has been previously reported and spectra data match those described.[21b] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.26 (5H, m), 6.99 (2H, d, *J* = 8.8 Hz), 6.76 (2H, d, *J* = 8.8 Hz), 6.41 (1H, dd, *J* = 17.2, 10.8 Hz), 5.07 (1H, dd, *J* = 10.8, 1.6 Hz), 4.98 (1H, dd, *J* = 17.2,

1.2 Hz), 3.78 (3H, s), 1.43 (3H, s), 0.24 (3H, s), 0.23 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.0, 143.4, 137.7, 136.9, 135.1, 129.3, 127.7, 127.5, 113.4, 111.3, 55.4, 36.8, 19.4, –5.0, –5.0. Specific Rotation: $[\alpha]_D^{20}$ –22.9 (*c* 2.22, $CHCl_3$) for an enantiomerically enriched sample of 97:3 e.r. sample.

Proof of Stereochemistry: Literature value ($[\alpha]_D^{20}$ –4.38 (*c* 0.213, $CHCl_3$), 95:5 e.r.) is assigned to the (*R*) enantiomer.[21b]

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (97.3:2.7 e.r. shown; Chiralcel AD column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).

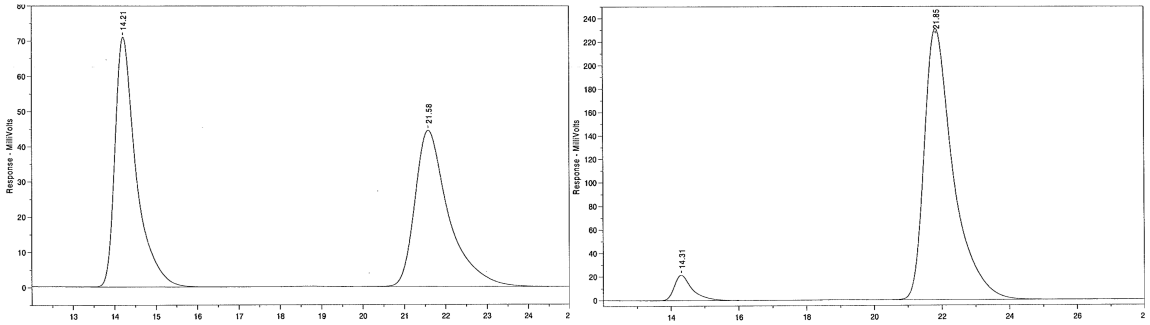


Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	42.89	48.7	1	40.02	2.7
2	52.53	51.3	2	46.63	97.3

(*R*)-1-Bromo-2-(2-phenylbut-3-en-2-yl)benzene (2.38): IR (neat): 3084 (w), 3057 (w), 2977 (w), 1492 (w), 1467 (m), 1446 (m), 1425 (w), 1020 (m), 918 (m), 753 (s), 698 (s), 601 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (1H, dd, *J* = 8.0, 1.6 Hz), 7.53 (1H, dd, *J* = 8.0, 1.6 Hz), 7.33 (1H, ddd, *J* = 7.2, 7.2, 1.6 Hz), 7.29–7.23 (2H, m), 7.20–7.16 (1H,

m), 7.13–7.08 (3H, m), 6.66 (1H, dd, *J* = 17.6, 10.8 Hz), 5.19 (1H, ddd, *J* = 10.8, 0.8, 0.4 Hz), 4.99 (1H, dd, *J* = 17.2, 0.8 Hz), 1.87 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.4, 146.1, 145.1, 141.7, 135.7, 129.8, 128.6, 128.3, 128.2, 127.3, 127.0, 125.8, 124.3, 113.4, 51.5, 26.6; HRMS (ESI+): Calcd for $C_{16}H_{16}Br_1$ $[M+H]^+$: 287.0435, Found: 287.0439. Specific Rotation: $[\alpha]_D^{20}$ –17.3 (*c* 0.57, $CHCl_3$) for an enantiomerically enriched sample of 94.5:5.5 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (94.5:5.5 e.r. shown; Chiralcel OD column, 95/5 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	14.21		0.00	N/A	2510528	49.987	BB	0.50
2	21.58		0.00	N/A	2511803	50.013	BB	0.80

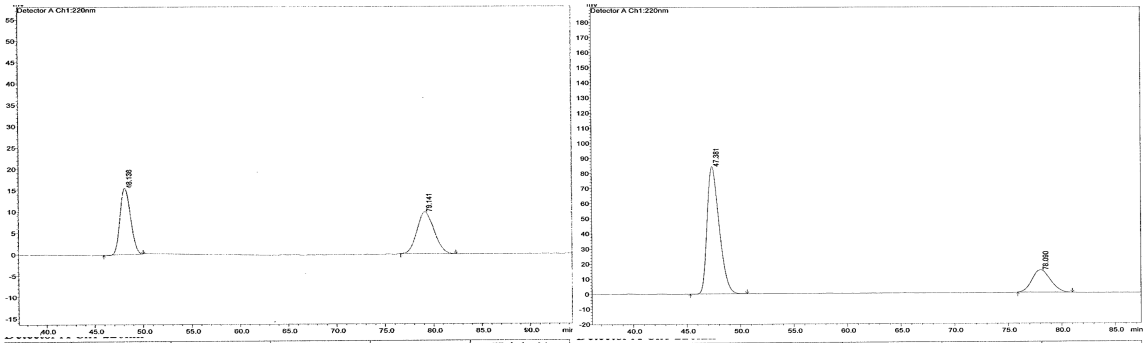
Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	14.31		0.00	N/A	795098	5.496	BB	0.52
2	21.85		0.00	N/A	13672790	94.504	BB	0.84

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	14.21	50.0	1	14.31	5.5
2	21.58	50.0	2	21.85	94.5

2.8.4 Experimental Procedures and Charaterization Data for Synthesis of R-(–)-Sporochnol

(*R*)-1-(3,7-Dimethylocta-1,6-dien-3-yl)-4-methoxybenzene (sporochnol methyl ether, not shown in Scheme 2.9). IR (neat): 2966 (m), 2927 (m), 2857 (w), 2835 (w), 1610 (w), 1511 (s), 1463 (w), 1295 (w), 1249 (s), 1182 (m), 1038 (m), 913 (w), 828 (m), 649 (w), 545 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.25–7.22 (2H, m), 6.87–6.83 (2H, m), 6.02 (1H, dd, *J* = 17.6, 10.8 Hz), 5.11–5.07 (2H, m), 5.03 (1H, dd, *J* = 17.2, 1.2 Hz), 3.80 (3H, s), 1.91–1.67 (4H, m), 1.66 (3H, s), 1.53 (3H, s), 1.36 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.7, 147.4, 139.7, 131.4, 127.7, 124.9, 113.5, 111.6, 55.4, 43.8, 41.3, 25.8, 25.2, 23.4, 17.7; HRMS (ESI+): Calcd for $C_{17}H_{25}O_1$ $[M+H]^+$: 245.1905, Found: 245.1905. Specific Rotation: $[\alpha]_D^{20}$ –2.57 (*c* 0.79, $CHCl_3$) for an enantiomerically enriched sample of 78.5:21.5 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with $NaBO_3$•$4H_2O$) in comparison with authentic racemic material (78.7:21.3 e.r. shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	48.136	1165079	15488	49.308	61.288
2	79.141	1197761	9783	50.692	38.712
Total		2362840	25271	100.000	100.000

Peak#	Ret. Time	Area	Height	Area %	Height %
1	47.381	6604615	84345	78.684	85.068
2	78.090	1789235	14805	21.316	14.932
Total		8393850	99151	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	48.136	49.3	1	47.381	78.7
2	79.141	50.7	2	78.090	21.3

■ **Enantioselective Synthesis of *R*-(–)-sporochnol (Scheme 2.9): Procedure for Demethylation of Sporochnol Methyl Ether.** A flame-dried 6-dram vial is charged with sporochnol methyl ether (17.4 mg, 0.071 mmol) and a stir bar. The vial is sealed with a septum and purged with N_2 flow for 10 minutes. Freshly prepared MeMgI in diethyl ether (890 μL, 0.356 mmol) is added to the reaction vessel and solvent is carefully removed under reduced pressure. The resulting mixture is heated in a 180 °C oil bath for 10 minutes (white smoke generated as the reaction goes on and disappears in 10 minutes), after which time, it is allowed to cool to 22 °C and diluted with Et_2O (5 mL). A saturated solution of NH_4Cl is added to quench the reaction and layers are separated. The aqueous layer is washed with Et_2O (5 mL x 3) and the combined organic layers are dried with anhydrous $MgSO_4$, filtered and concentrated *in vacuo* to afford a slightly yellow oil, which is subjected to silica gel chromatography (10:1 hexanes:ethyl acetate) to furnish the desired product as colorless oil (14.1 mg, 0.061 mmol, 86% yield). ***R*-(–)-Sporochnol:** The compound has been previously reported and spectra data match those previously described.[36] IR (neat): 3332 (br), 2966 (w), 2922 (w), 2857 (w), 1611 (w), 1511 (s), 1439 (w), 1374 (w), 1232 (m), 1178 (m), 1013 (w), 912 (m), 828 (s), 651 (w), 541 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.20–7.17 (2H, m), 6.78–6.75 (2H, m), 6.00 (1H, dd, J = 17.6, 10.8 Hz), 5.10–5.00 (3H, m), 4.68 (1H, s), 1.86–1.61 (4H, m), 1.66 (3H, s), 1.52 (3H, s), 1.35 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.5, 147.3, 139.9, 131.4, 130.0, 124.8, 114.9, 111.6, 43.8, 41.3, 25.8, 25.1, 23.4, 17.7; HRMS (ESI+): Calcd for $C_{16}H_{23}O_1$ $[M+H]^+$: 231.1749, Found: 231.1751. Specific Rotation: $[\alpha]_D^{20}$ –2.03 (*c* 0.82, $CHCl_3$) for an enantiomerically enriched sample of 78.5:21.5 e.r.

Proof of Stereochemistry: Literature value ($[\alpha]_D^{20}$ –2.5 (*c* 1.00, $CHCl_3$), 98.5:1.5 e.r.) is assigned to the (*R*) enantiomer.[29]

2.8.5 Experimental Procedures and Charaterization Data for Cu-Catalyzed EAS with Diethylheteroarylaluminum Reagents

■ **Representative Experimental Procedure for Cu-Catalyzed Enantioselective Allylic Substitution Reactions of Diethylheteroarylaluminum Reagents to Allylic Phosphates:** In an N_2 filled glove box, an oven-dried vial (8 mL, 17 x 60 mm) with a magnetic stir bar is charged with NHC–Ag(I) complex **2.42** (1.3 mg, 7.5 x 10^{-4} mmol) and sealed with a septum before removal from the glove box. To the vial under an N_2 atmosphere are added tetrahydrofuran (thf, 0.5 mL) and a solution of $CuCl_2 \bullet 2H_2O$ (0.02 M in thf, 75 μL, 1.50 x 10^{-3} mmol). The light blue solution is allowed to stir at 22 °C for 30 minutes and a solution of *(E)-tert*-butyl-4-(diethoxyphosphoryloxy)-2-methylbut-2-enoate **2.28** (46.2 mg, 0.150 mmol) in thf (0.5 mL) is added through a syringe. After stirring for 10 minutes, the reaction mixture is allowed to cool to –78 °C (dry ice/acetone bath). A solution of diethyl(2-furyl)aluminum reagent **2.41** (0.653 M in pentane, 689 μL, 0.450 mmol) is added slowly through a syringe. The vial is transferred to a –30 °C cryocool. After 1 h, the reaction solution is allowed to cool to –78 °C and quenched by addition of a saturated aqueous solution of Rochelle's salt (potassium sodium tartrate, 2 mL). The aqueous layer is washed with Et_2O (3 x 1 mL) and the combined organic layers are passed through a short plug of $MgSO_4$ and silica gel. The filtrate is concentrated under reduced pressure to provide colorless oil residue, which is purified by silica gel

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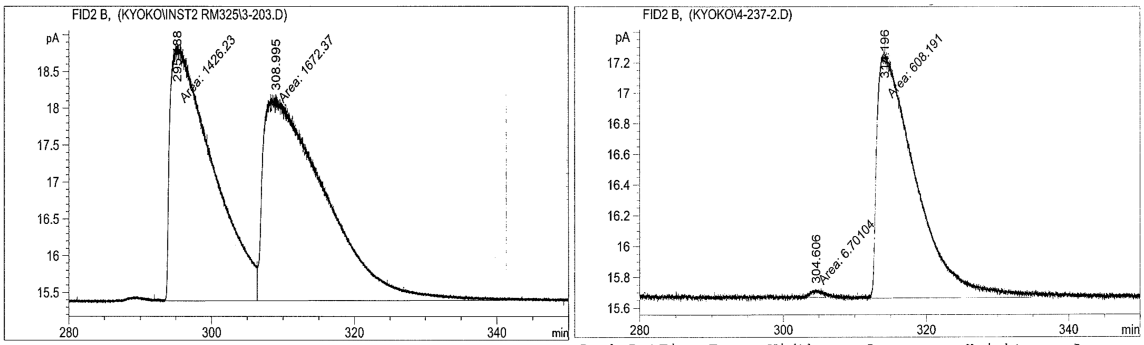
(29) A. Fadel, L. Vandromme, *Tetrahedron: Asymmetry* **1999**, *10*, 1153–1162.

column chromatography (30:1 pentane:Et_2O) to afford product **2.43** as colorless oil (30.0 mg, 0.135 mmol, 90% yield). **(*R*)-*tert*-Butyl 2-(furan-2-yl)-2-methylbut-3-enoate** (**2.43**): IR (neat): 2980 (w), 1729 (s), 1368 (m), 1253 (m), 1155 (s), 1116 (m), 1012 (w), 929 (w), 801 (w), 733 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.35–7.33 (1H, m), 6.29 (1H, dd, *J* = 3.2, 1.6 Hz), 6.27 (1H, dd, *J* = 17.6, 10.8 Hz), 6.13 (1H, dd, *J* = 3.2, 0.8 Hz), 5.20 (1H, dd, *J* = 10.4, 0.8 Hz), 5.09 (1H, dd, *J* = 17.2, 0.8 Hz), 1.59 (3H, s), 1.40 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 156.2, 141.8, 139.3, 114.9, 110.2, 106.0, 81.5, 51.2, 28.0, 21.6; HRMS (ESI+): Calcd for $C_{13}H_{19}O_3$ $[M+H]^+$: 223.1334, Found: 223.1329. Specific Rotation: $[\alpha]_D^{20}$ –2.38 (*c* 1.00, $CHCl_3$) for an enantiomerically enriched sample of 99:1 e.r.

Enantiomeric purity was determined by GLC analysis in comparison with authentic racemic material (98.9:1.1 e.r. shown; Chiral dex GTA column, 10 psi, 50 ºC).



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	295.188	MF	6.7887	1426.23059	3.50149	46.02822
2	308.995	FM	9.9466	1672.36975	2.80224	53.97178

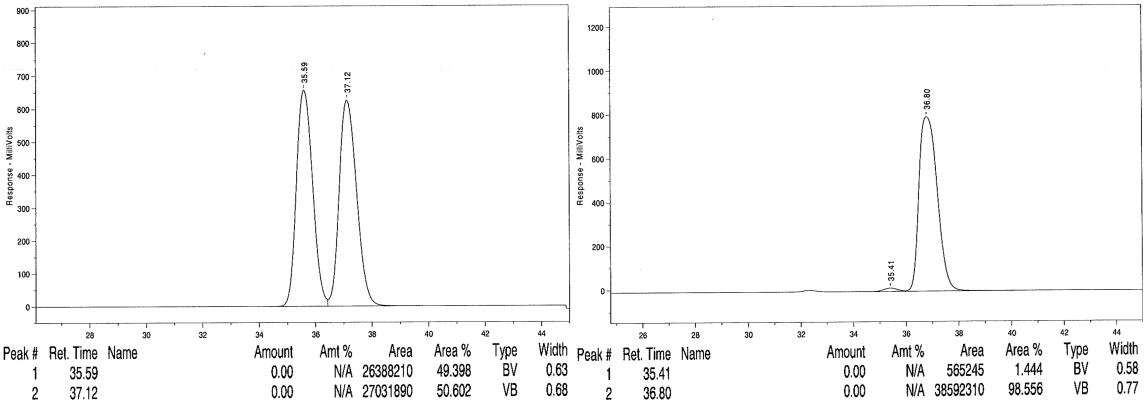
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	304.606	MM	1.6802	6.70104	6.64691e-2	1.08979
2	314.196	MM	6.0701	608.19061	1.66992	98.91021

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	295.188	46.0	1	304.606	1.1
2	308.995	54.0	2	314.196	98.9

(*S*)-2-(2-Phenylbut-3-en-2-yl)furan (2.44). IR (neat): 3085 (w), 3058 (w), 2979 (w), 2936 (w), 1491 (w), 1445 (w), 1409 (w), 1155 (w), 1009 (m), 922 (m), 759 (m), 730 (s),

697 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.38–7.37 (1H, m), 7.33–7.28 (2H, m), 7.25–7.18 (3H, m), 6.38 (1H, dd, *J* = 17.2, 10.4 Hz), 6.35–6.34 (1H, m), 6.13 (1H, dd, *J* = 3.2, 0.8 Hz), 5.23 (1H, dd, *J* = 10.8, 1.2 Hz), 5.01 (1H, dd, *J* = 17.6, 1.2 Hz), 1.77 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.6, 145.8, 143.5, 141.7, 128.2, 127.1, 126.5, 113.7, 109.9, 106.3, 47.4, 25.2; HRMS (ESI+): Calcd for $C_{14}H_{15}O_1$ $[M+H]^+$: 199.1123, Found: 199.1122. Specific Rotation: $[\alpha]_D^{20}$ –26.8 (*c* 1.19, $CHCl_3$) for an enantiomerically enriched sample of 99:1 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with $NaBO_3$•$4H_2O$) in comparison with authentic racemic material (98.6:1.4 e.r. shown; Chiralcel AD-H column, 97/3 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).

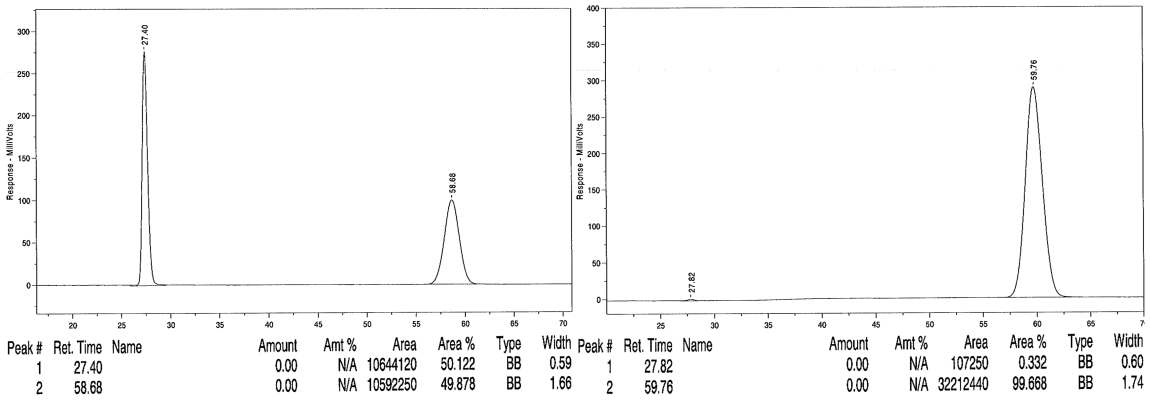


Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	35.59	49.4	1	35.41	1.4
2	37.12	50.6	2	36.80	98.6

(*S*)-2-(2-(2-Bromophenyl)but-3-en-2-yl)furan (2.45). IR (neat): 3059 (w), 2979 (w), 2939 (w), 1465 (w), 1427 (w), 1408 (w), 1368 (w), 1017 (m), 1009 (m), 922 (m), 799 (w), 751 (s), 723 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.55 (1H, dd, *J* = 7.6, 0.8 Hz),

7.34–7.24 (3H, m), 7.09 (1H, td, *J* = 7.6, 1.6 Hz), 6.45 (1H, dd, *J* = 17.2, 10.4 Hz), 6.33 (1H, dd, *J* = 3.2, 2.0 Hz), 6.05 (1H, d, *J* = 3.2 Hz), 5.20 (1H, d, *J* = 10.4 Hz), 4.97 (1H, d, *J* = 17.2 Hz), 1.88 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.9, 144.0, 142.9, 141.0, 135.4, 129.8, 128.4, 127.2, 123.7, 113.7, 110.5, 106.3, 48.6, 24.3; HRMS (ESI+): Calcd for $C_{14}H_{14}Br_1O_1$ $[M+H]^+$: 277.0228, Found: 277.0217. Specific Rotation: $[\alpha]_D^{20}$ –39.8 (*c* 1.73, $CHCl_3$) for an enantiomerically enriched sample of 99.5:0.5 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with $NaBO_3$•$4H_2O$) in comparison with authentic racemic material (99.7:0.3 e.r. shown; Chiralcel OJ-H column, 95/5 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).

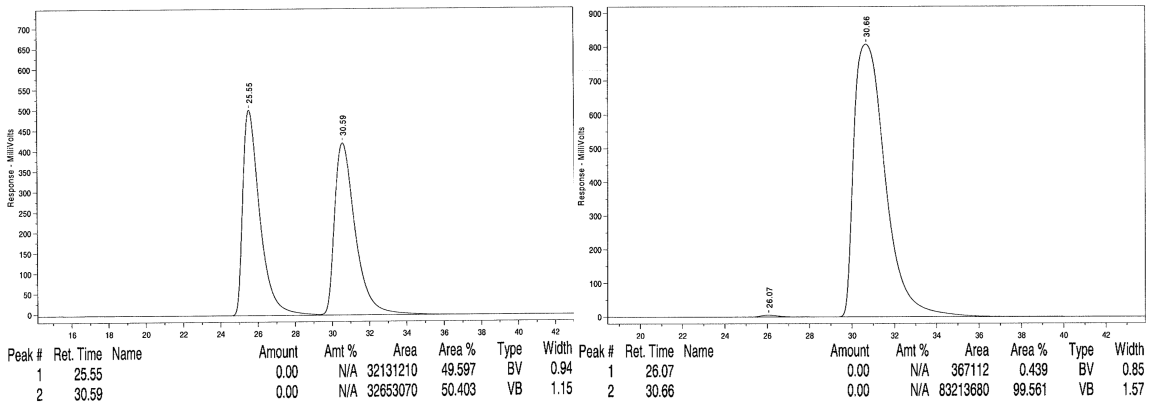


Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	27.40	50.1	1	27.82	0.3
2	58.68	49.9	2	59.76	99.7

(*S*)-2-(2-(2-Methoxyphenyl)but-3-en-2-yl)furan (2.46). IR (neat): 3081 (w), 2978 (w), 2936 (w), 2834 (w), 1598 (w), 1581 (w), 1488 (m), 1460 (m), 1434 (m), 1242 (s), 1027 (m), 1007 (m), 883 (m), 751 (s), 726 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.30 (1H, m), 7.26–7.21 (1H, m), 7.05 (1H, dd, *J* = 7.6, 1.6 Hz), 6.92–6.86 (2H, m), 6.41 (1H,

dd, *J* = 17.7, 10.8 Hz), 6.32–6.30 (1H, m), 6.02 (1H, dd, *J* = 3.2, 0.8 Hz), 5.13 (1H, dt, *J* = 10.4, 0.4 Hz), 4.93 (1H, dd, *J* = 17.2, 1.2 Hz), 3.62 (3H, s), 1.81 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.5, 157.9, 143.5, 140.6, 134.0, 128.3, 128.1, 120.5, 112.5, 112.4, 110.0, 104.6, 55.5, 46.2, 23.7; HRMS (ESI+): Calcd for $C_{15}H_{17}O_2$ $[M+H]^+$: 229.1229, Found: 229.1227. Specific Rotation: $[\alpha]_D^{20}$ –20.6 (*c* 1.52, $CHCl_3$) for an enantiomerically enriched sample of 99.5:0.5 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with $NaBO_3$•$4H_2O$) in comparison with authentic racemic material (99.6:0.4 e.r. shown; Chiralcel OJ-H column, 96/4 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).

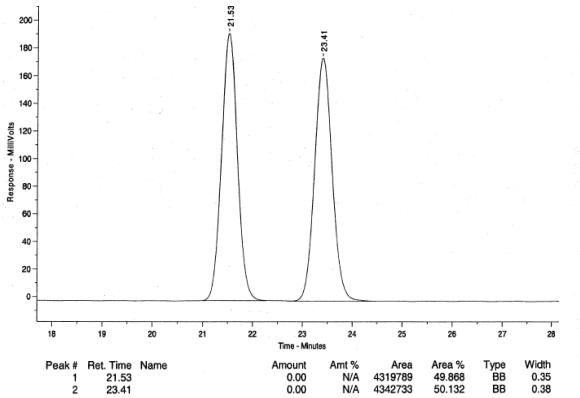


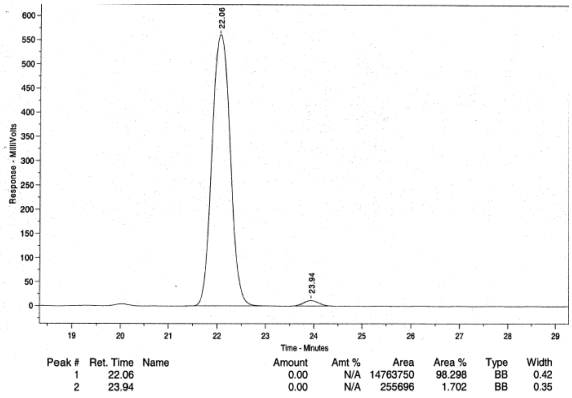
Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	25.55	49.6	1	26.07	0.4
2	30.59	50.4	2	30.66	99.6

(*S*)-2-(2-*o*-Tolylbut-3-en-2-yl)furan (2.47). IR (neat): 3059 (w), 3015 (w), 2978 (w), 2933 (w), 2876 (w), 1499 (w), 1486 (w), 1456 (w), 1153 (w), 1008 (m), 922 (m), 750 (m), 724 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34–7.33 (1H, m), 7.31–7.28 (1H, m), 7.20–7.16 (2H, m), 7.16–7.10 (1H, m), 6.48 (1H, dd, *J* = 17.2, 10.4 Hz), 6.33 (1H, dd, *J* =

3.2, 1.6 Hz), 6.05 (1H, dd, *J* = 2.8, 0.8 Hz), 5.16 (1H, dd, *J* = 10.4, 0.8 Hz), 4.92 (1H, dd, *J* = 17.2, 1.2 Hz), 1.99 (3H, s), 1.79 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.4, 143.6, 143.1, 141.0, 137.3, 132.3, 127.6, 126.9, 125.8, 113.0, 110.2, 105.1, 47.5, 25.8, 21.0; HRMS (ESI+): Calcd for $C_{15}H_{17}O_1$ $[M+H]^+$: 213.1279, Found: 213.1273. Specific Rotation: $[\alpha]_D^{20}$ –21.1 (*c* 1.92, $CHCl_3$) for an enantiomerically enriched sample of 98:2 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with $NaBO_3$•$4H_2O$) in comparison with authentic racemic material (98.3:1.7 e.r. shown; Chiralpak AD-H column, 95/5 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



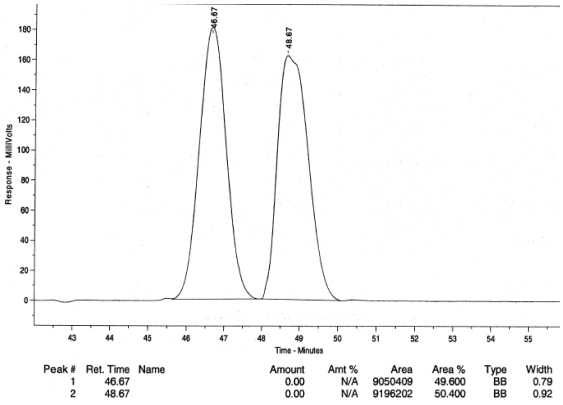


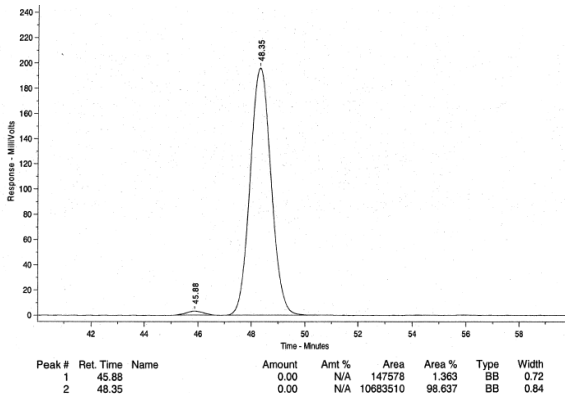
Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	21.53	49.9	1	22.06	98.3
2	23.41	50.1	2	23.94	1.7

(*S*)-2-(2-(4-Nitrophenyl)but-3-en-2-yl)furan (2.48). IR (neat): 1603 (w), 1514 (s), 1344 (s), 1316 (w), 1154 (w), 1110 (w), 1011 (m), 925 (m), 851 (m), 734 (m), 699 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15–8.11 (2H, m), 7.38–7.37 (1H, m), 7.33–7.30 (2H, m), 6.36–6.35 (1H, m), 6.32 (1H, dd, *J* = 17.6, 10.8 Hz), 6.18 (1H, dd, *J* = 3.2, 0.8 Hz), 5.29 (1H, dd, *J* = 10.4, 0.8 Hz), 5.03 (1H, dd, *J* = 17.6, 0.8 Hz), 1.77 (3H, s); ^{13}C NMR

(100 MHz, $CDCl_3$): δ 158.0, 153.3, 146.6, 142.2, 142.1, 128.1, 123.5, 115.0, 110.2, 106.8, 47.6, 25.3; HRMS (ESI+): Calcd for $C_{14}H_{14}N_1O_3$ $[M+H]^+$: 244.0974, Found: 244.0985. Specific Rotation: $[\alpha]_D^{20}$ –21.1 (*c* 1.92, $CHCl_3$) for an enantiomerically enriched sample of 98.5:1.5 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with $NaBO_3$•$4H_2O$) in comparison with authentic racemic material (98.6:1.4 e.r. shown; Chiralpak AD-H column, 93/7 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



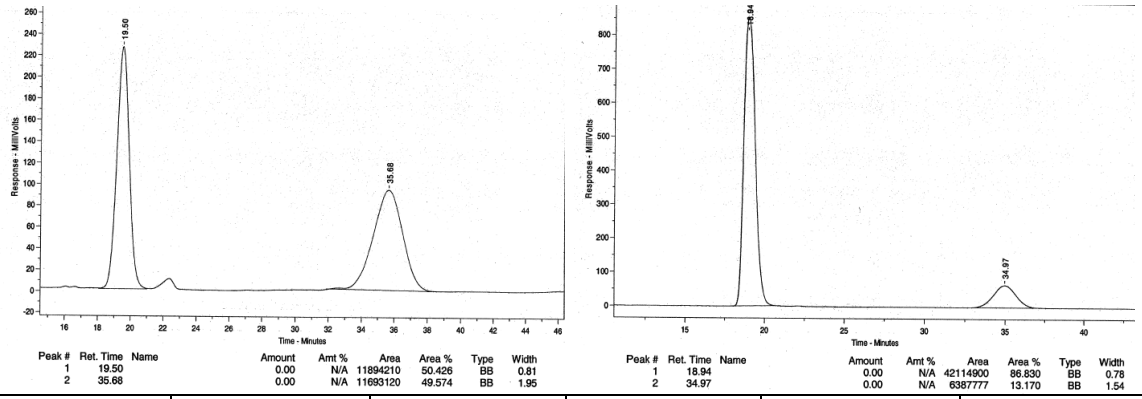


Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	46.67	49.6	1	45.88	1.4
2	48.67	50.4	2	48.35	98.6

(*R*)-(2-(Furan-2-yl)but-3-en-2-yl)dimethyl(phenyl)silane (2.49). IR (neat): 3079 (w), 3050 (w), 3010 (w), 2959 (w), 2929 (w), 1624 (w), 1500 (w), 1192 (m), 1160 (w), 1015 (w), 923 (w), 901 (w), 833 (m), 816 (s), 772 (m), 723 (s), 699 (s), 654 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.37–7.27 (6H, m), 6.28–6.27 (1H, m), 6.26 (1H, dd, *J* = 17.6, 10.8 Hz), 5.77–5.76 (1H, m), 5.03 (1H, dd, *J* = 10.8, 1.6 Hz), 4.84 (1H, dd, *J* = 17.6, 1.2 Hz), 1.35 (3H, s), 0.36 (3H, s), 0.30 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9, 140.6,

140.4, 136.3, 134.6, 129.2, 127.3, 111.2, 110.3, 103.4, 35.8, 17.7, –4.9, –5.0; HRMS (ESI+): Calcd for $C_{16}H_{21}O_1Si_1$ $[M+H]^+$: 257.1362, Found: 257.1366. Specific Rotation: $[\alpha]_D^{20}$ –4.00 (*c* 1.37, $CHCl_3$) for an enantiomerically enriched sample of 85:15 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (86.8:13.2 e.r. shown; Chiralcel OJ-H column, 95/5 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).

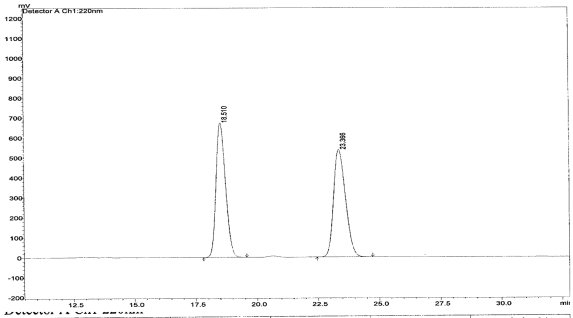


Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	19.50	50.4	1	18.94	86.8
2	35.68	49.6	2	34.97	13.2

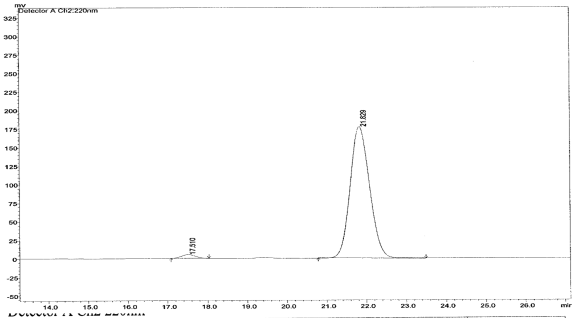
(*S*)-2-(2-Cyclohexylbut-3-en-2-yl)furan (2.50). IR (neat): 2980 (w), 2926 (s), 2853 (m), 1635 (w), 1503 (w), 1450 (w), 1416 (w), 1370 (w), 1152 (w), 1014 (m), 914 (m), 802 (w), 731 (s), 598 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.34–7.33 (1H, m), 6.27–6.26 (1H, m), 6.11 (1H, dd, *J* = 17.6, 10.8 Hz), 5.99–5.97 (1H, m), 5.08 (1H, dd, *J* = 10.8, 1.6 Hz), 4.98 (1H, dd, *J* = 17.6, 1.2 Hz), 1.78–1.59 (5H, m), 1.42–1.37 (1H, m), 1.30 (3H, s), 1.27–0.87 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.0, 143.4, 140.9, 112.9, 109.7, 104.9, 46.2, 45.6, 28.2, 27.9, 27.2, 27.1, 26.8, 18.4; HRMS (ESI+): Calcd for $C_{14}H_{21}O_1$

$[M+H]^+$: 205.1592, Found: 205.1595. Specific Rotation: $[\alpha]_D^{20}$ –84.2 (*c* 1.37, $CHCl_3$) for an enantiomerically enriched sample of 98:2 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with $NaBO_3 \bullet 4H_2O$) in comparison with authentic racemic material (98.1:1.9 e.r. shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.510	18276583	673977	49.965	55.615
2	23.366	18302480	537885	50.035	44.385
Total		36579063	1211862	100.000	100.000



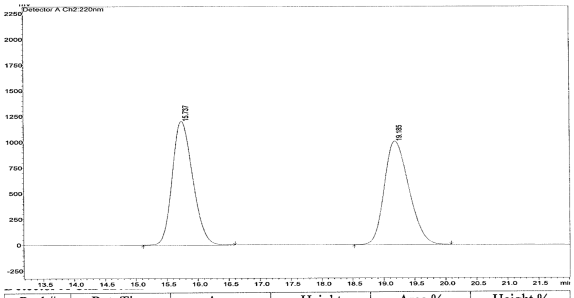
Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.510	116121	4948	1.894	2.721
2	21.829	6014012	176883	98.106	97.279
Total		6130133	181831	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	18.510	50.0	1	17.510	1.9
2	23.366	50.0	2	21.829	98.1

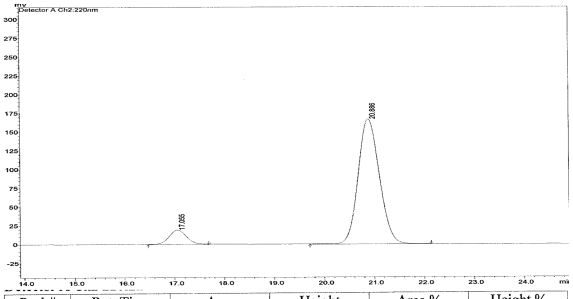
(*R*)-2-(3,7-Dimethylocta-1,6-dien-3-yl)furan (2.51). IR (neat): 2970 (w), 2925 (w), 2857 (w), 1504 (w), 1452 (w), 1412 (w), 1376 (w), 1260 (w), 1156 (w), 1074 (w), 1012 (m), 916 (m), 799 (m), 730 (s), 598 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.34–7.33 (1H, m), 6.29–6.27 (1H, m), 6.05–5.98 (2H, m), 5.10–5.04 (2H, m), 4.99 (1H, dd, *J* = 17.6, 1.2 Hz), 1.91–1.76 (2H, m), 1.67 (3H, d, *J* = 1.2 Hz), 1.55 (3H, d, *J* = 0.4 Hz), 1.37 (3H, s), 1.35–1.21 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.6, 144.5, 141.2, 131.6, 124.5, 112.4, 109.9, 104.6, 42.3, 40.0, 25.8, 23.3, 22.8, 17.7; HRMS (ESI+): Calcd for

$C_{14}H_{21}O_1$ [M+H]$^+$: 205.1592, Found: 205.1596. Specific Rotation: $[\alpha]_D^{20}$ –19.6 (*c* 2.43, $CHCl_3$) for an enantiomerically enriched sample of 91:9 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with $NaBO_3$•$4H_2O$) in comparison with authentic racemic material (91.1:8.9 e.r. shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.737	27692584	1203170	49.947	54.495
2	19.185	27751479	1004698	50.053	45.505
Total		55444063	2207868	100.000	100.000

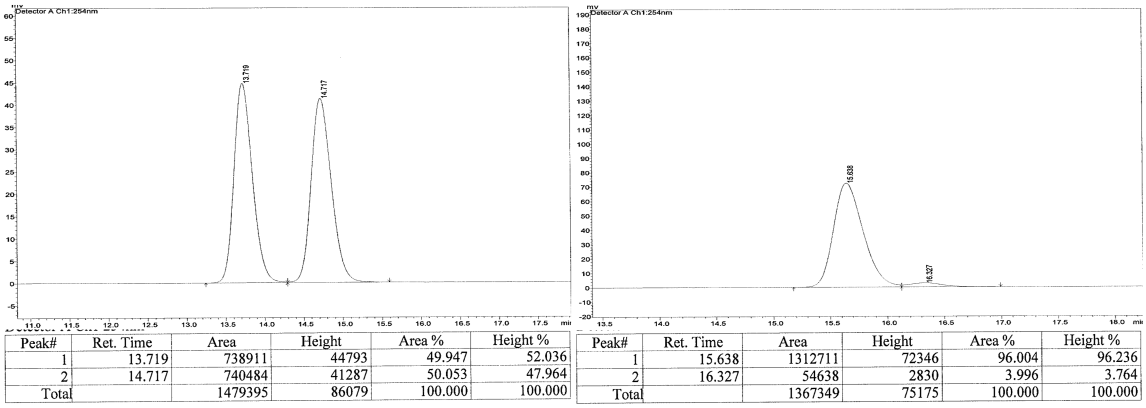


Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.055	485131	19400	8.906	10.430
2	20.886	4961994	166592	91.094	89.570
Total		5447124	185991	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	15.737	49.9	1	17.055	8.9
2	19.185	50.1	2	20.886	91.1

(*S*)-2-(2-Phenylbut-3-en-2-yl)thiophene (2.52). IR (neat): 3084 (w), 3059 (w), 2976 (w), 2931 (w), 1634 (w), 1599 (w), 1491 (w), 1444 (w), 1407 (w), 1370 (w), 1237 (w), 999 (w), 918 (m), 853 (w), 828 (w), 759 (m), 692 (s), 527 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30–7.25 (4H, m), 7.24–7.19 (2H, m), 6.95 (1H, dd, *J* = 5.2, 3.6 Hz), 6.79 (1H, dd, *J* = 3.6, 1.2 Hz), 6.38 (1H, dd, *J* = 17.2, 10.4 Hz), 5.20 (1H, dd, *J* = 10.8, 1.2 Hz), 4.96 (1H, dd, *J* = 17.2, 1.2 Hz), 1.87 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.0, 147.5, 146.1, 128.2, 127.4, 126.6, 126.5, 125.0, 124.1, 113.5, 48.5, 28.8; HRMS (ESI+): Calcd for $C_{14}H_{15}S_1$ [M+H]$^+$: 215.0895, Found: 215.0892. Specific Rotation: $[\alpha]_D^{20}$ –22.6 (*c* 0.31, $CHCl_3$) for an enantiomerically enriched sample of 96:4 e.r.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (96.0:4.0 e.r. shown; Chiralcel OD-H column, 100/0 hexanes/*i*-PrOH, 0.5 mL/min, 254 nm).



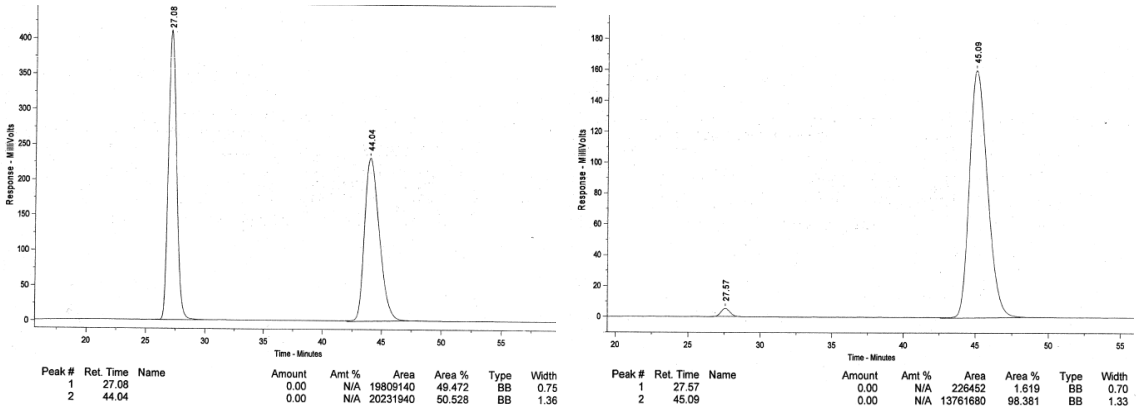
Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.719	738911	44793	49.947	52.036
2	14.717	740484	41287	50.053	47.964
Total		1479395	86079	100.000	100.000

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.638	1312711	72346	96.004	96.236
2	16.327	54638	2830	3.996	3.764
Total		1367349	75175	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	13.719	49.9	1	15.638	96.0
2	14.717	50.1	2	16.327	4.0

(*S*)-2-(2-(2-Bromophenyl)but-3-en-2-yl)thiophene (2.53). IR (neat): 3064 (w), 2974 (w), 2933 (w), 1463 (w), 1430 (w), 1406 (w), 1368 (w), 1348 (w), 1018 (m), 910 (m), 852 (w), 824 (w), 805 (w), 753 (m), 732 (m), 689 (s), 644 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.57 (1H, dd, *J* = 7.6, 1.6 Hz), 7.52 (1H, dd, *J* = 8.0, 1.6 Hz), 7.30 (1H, td, *J* = 7.6, 1.2 Hz), 7.19 (1H, dd, *J* = 4.4, 1.2 Hz), 7.12 (1H, td, *J* = 7.6, 1.6 Hz), 6.93 (1H, dd, *J* = 4.8, 3.2 Hz), 6.67 (1H, dd, *J* = 3.6, 1.2 Hz), 6.58 (1H, dd, *J* = 17.6, 10.8 Hz), 5.20 (1H, dd, *J* = 10.4, 0.4 Hz), 4.97 (1H, dd, *J* = 17.2, 0.4 Hz), 1.99 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.5, 145.4, 145.1, 135.7, 129.6, 128.5, 127.1, 126.7, 124.5, 124.4, 123.4, 113.4, 49.5, 27.9; HRMS (ESI+): Calcd for $C_{14}H_{14}Br_1S_1$ $[M+H]^+$: 293.0000, Found: 293.0006. Specific Rotation: $[\alpha]_D^{20}$ –26.0 (*c* 2.93, $CHCl_3$) for an enantiomerically enriched sample of 98:2 e.r.

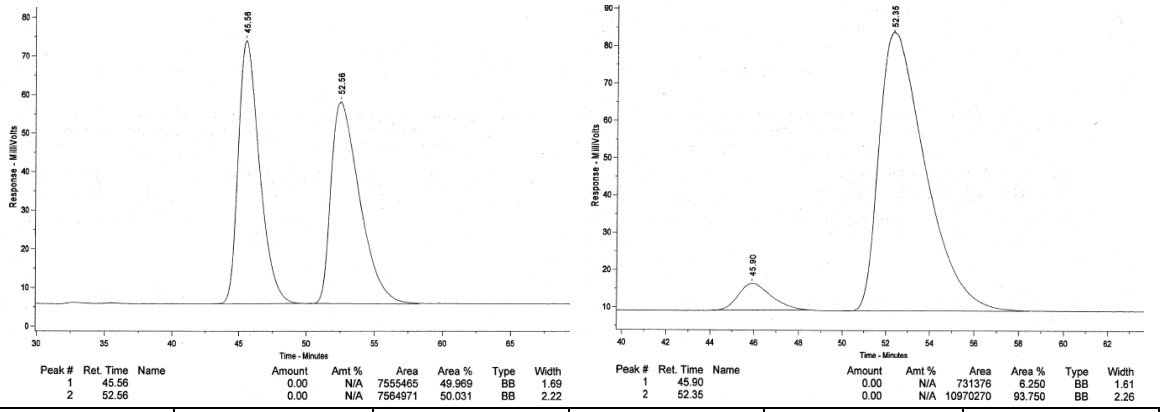
Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with $NaBO_3 \bullet 4H_2O$) in comparison with authentic racemic material (98.4:1.6 e.r. shown; Chiralcel OJ-H column, 94/6 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	27.08	49.5	1	27.57	1.6
2	44.04	50.5	2	45.09	98.4

(*S*)-2-(2-(4-Nitrophenyl)but-3-en-2-yl)thiophene (2.54). IR (neat): 3081 (w), 2977 (w), 2935 (w), 1602 (w), 1513 (s), 1342 (s), 1238 (w), 1012 (w), 924 (w), 849 (m), 830 (w), 804 (w), 694 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.14–8.11 (2H, m), 7.43–7.41 (2H, m), 7.25–7.22 (1H, m), 6.98–6.96 (1H, m), 6.81–6.78 (1H, m), 6.35 (1H, ddd, J = 17.2, 10.4, 0.8 Hz), 5.27 (1H, dd, J = 10.4, 0.4 Hz), 4.98 (1H, d, J = 17.2 Hz), 1.89 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.9, 151.1, 146.6, 144.7, 128.4, 126.7, 125.3, 124.7, 123.3, 114.7, 48.7, 28.6; HRMS (ESI+): Calcd for $C_{14}H_{14}N_1O_2S_1$ $[M+H]^+$: 260.0745, Found: 260.0754. Specific Rotation: $[\alpha]_D^{20}$ –2.70 (*c* 2.38, $CHCl_3$) for an enantiomerically enriched sample of 94:6 e.r.

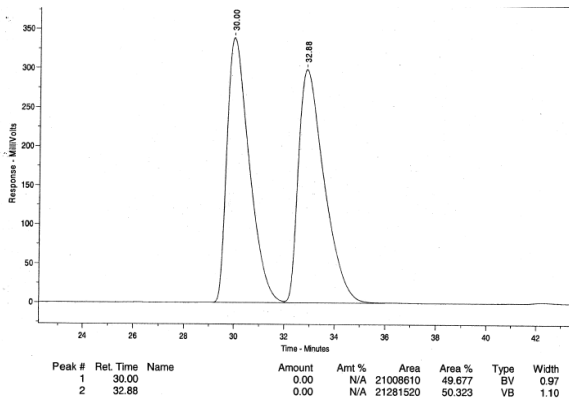
Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with $NaBO_3 \bullet 4H_2O$) in comparison with authentic racemic material (93.8:6.2 e.r. shown; Chiralcel OD column, 96/4 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).

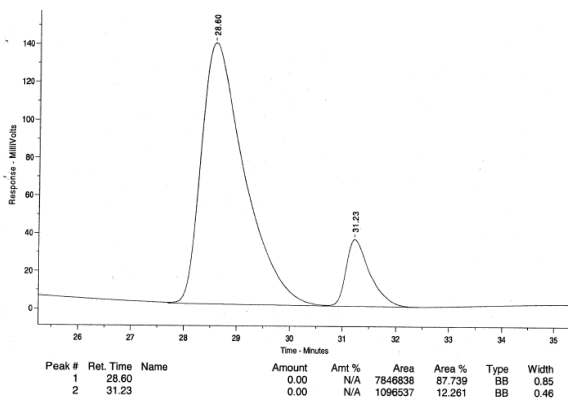


Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	45.56	50.0	1	45.90	6.2
2	52.56	50.0	2	52.35	93.8

(*S*)-*tert*-Butyl 2-methyl-2-(thiophen-2-yl)but-3-enoate (2.55). IR (neat): 2978 (w), 2935 (w), 1724 (s), 1455 (w), 1432 (w), 1419 (w), 1367 (m), 1253 (s), 1237 (m), 1154 (s), 1113 (s), 920 (m), 877 (m), 693 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.20–7.18 (1H, m), 6.95–6.92 (2H, m), 6.38 (1H, dd, *J* = 17.2, 10.4 Hz), 5.20 (1H, dd, *J* = 11.2, 0.8 Hz), 5.15 (1H, d, *J* = 17.2 Hz), 1.70 (3H, s), 1.42 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.5, 147.6, 141.5, 126.4, 124.4, 124.3, 114.1, 81.6, 51.8, 27.9, 24.3; HRMS (ESI+): Calcd for $C_{13}H_{19}O_2S_1$ $[M+H]^+$: 239.1106, Found: 239.1105. Specific Rotation: $[\alpha]_D^{20}$ –2.41 (*c* 1.75, $CHCl_3$) for an enantiomerically enriched sample of 79:21 e.r.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (87.7:12.3 e.r. shown; Chiralcel OD column, 100% hexanes, 0.5 mL/min, 220 nm).

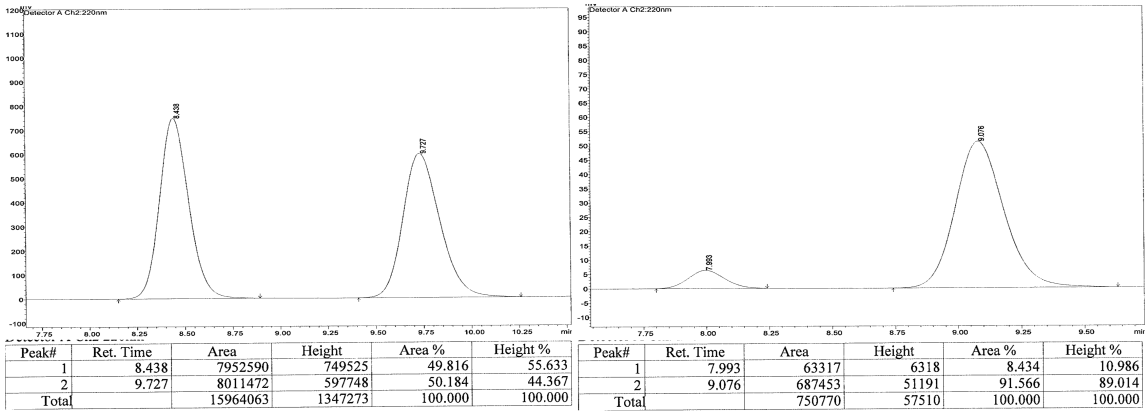




Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	30.00	49.7	1	28.60	87.7
2	32.88	50.3	2	31.23	12.3

(*S*)-2-(2-Cyclohexylbut-3-en-2-yl)thiophene (2.56). IR (neat): 2978 (w), 2923 (s), 2851 (m), 1449 (w), 1372 (w), 1235 (w), 1008 (w), 914 (w), 850 (w), 821 (w), 689 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.15 (1H, dd, *J* = 5.2, 0.8 Hz), 6.93 (1H, dd, *J* = 5.2, 3.6 Hz), 6.80 (1H, dd, *J* = 3.6, 1.2 Hz), 6.14 (1H, dd, *J* = 17.6, 10.8 Hz), 5.11 (1H, dd, *J* = 10.8, 1.2 Hz), 5.05 (1H, dd, *J* = 17.2, 1.2 Hz), 1.76–1.57 (6H, m), 1.42 (3H, s), 1.27–0.91 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.2, 145.3, 126.3, 123.0, 122.8, 112.6, 49.6, 46.8, 28.2, 28.0, 27.2, 27.1, 26.8, 21.5; HRMS (ESI+): Calcd for $C_{14}H_{21}S_1$ $[M+H]^+$: 221.1364, Found: 221.1367. Specific Rotation: $[\alpha]_D^{20}$ –38.4 (*c* 0.34, $CHCl_3$) for an enantiomerically enriched sample of 91.5:8.5 e.r.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (91.6:8.4 e.r. shown; Chiralcel OJ-H column, 99/1 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



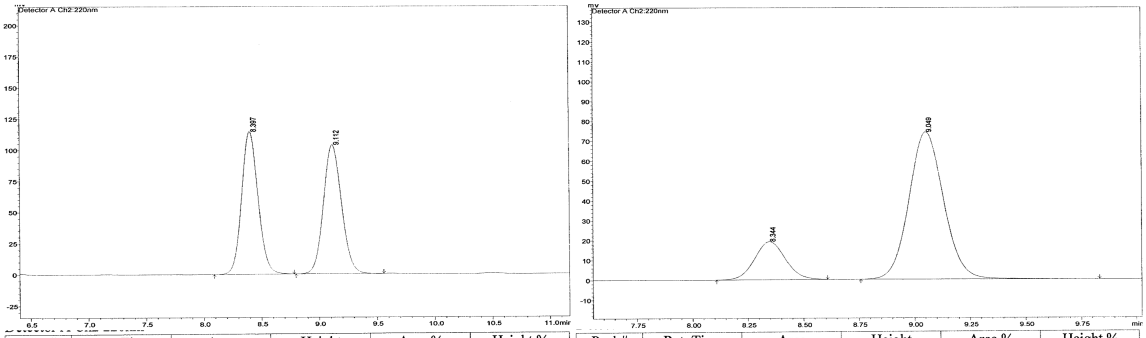
Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.438	7952590	749525	49.816	55.633
2	9.727	8011472	597748	50.184	44.367
Total		15964063	1347273	100.000	100.000

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.993	63317	6318	8.434	10.986
2	9.076	687453	51191	91.566	89.014
Total		750770	57510	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	8.438	49.8	1	7.993	8.4
2	9.727	50.2	2	9.076	91.6

(*R*)-2-(3,7-Dimethylocta-1,6-dien-3-yl)thiophene (2.57). IR (neat): 2967 (m), 2925 (m), 2856 (w), 1439 (w), 1375 (w), 1235 (w), 916 (w), 849 (w), 825 (w), 692 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.16 (1H, dd, *J* = 4.8, 0.8 Hz), 6.94 (1H, dd, *J* = 5.2, 4.0 Hz), 6.83 (1H, dd, *J* = 3.6, 1.2 Hz), 6.08 (1H, dd, *J* = 17.6, 10.8 Hz), 5.13–5.05 (3H, m), 1.96–1.88 (2H, m), 1.85–1.71 (2H, m), 1.68 (3H, s), 1.56 (3H, s), 1.47 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.7, 146.4, 131.7, 126.5, 124.4, 123.2, 123.0, 112.0, 43.5, 43.0, 25.9, 25.8, 23.5, 17.7; HRMS (ESI+): Calcd for $C_{14}H_{21}S_1$ $[M+H]^+$: 221.1364, Found: 221.1374. Specific Rotation: $[\alpha]_D^{20}$ –9.44 (*c* 0.35, $CHCl_3$) for an enantiomerically enriched sample of 81:19 e.r.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (81.4:18.6 e.r. shown; Chiralcel OJ-H column, 99/1 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



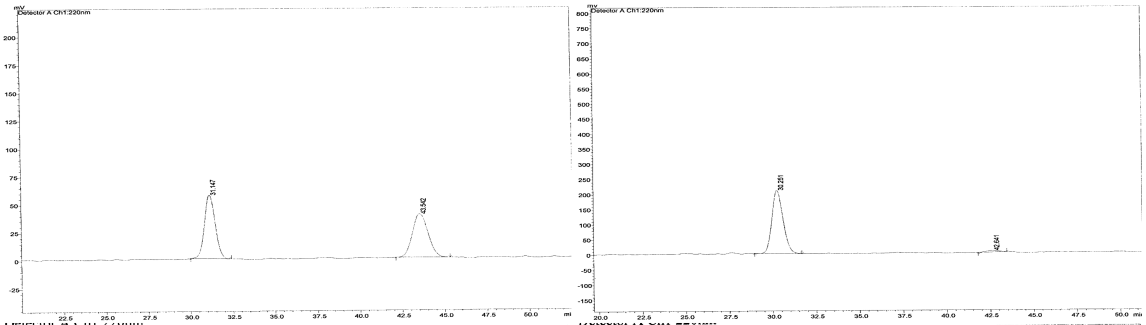
Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.397	1131598	114524	50.104	52.537
2	9.112	1126887	103464	49.896	47.463
Total		2258485	217988	100.000	100.000

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.344	184239	19103	18.561	20.502
2	9.049	808373	74073	81.439	79.498
Total		992612	93176	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	8.397	50.1	1	8.344	18.6
2	9.112	49.9	2	9.049	81.4

(*S*)-3-(2-Phenylbut-3-en-2-yl)furan (2.58). IR (neat): 2976 (w), 1636 (w), 1599 (w), 1492 (w), 1445 (w), 1409 (w), 1368 (w), 1160 (w), 1060 (w), 1025 (m), 1000 (w), 954 (w), 918 (m), 873 (m), 785 (m), 758 (m), 728 (w), 698 (s), 599 (s), 553 (w), 532 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.39–7.38 (1H, m), 7.30–7.28 (4H, m), 7.23–7.19 (1H, m), 7.16–7.15 (1H, m), 6.26 (1H, dd, *J* = 17.6, 10.8 Hz), 6.19–6.18 (1H, m), 5.16 (1H, dd, *J* = 10.8, 1.2 Hz), 4.98 (1H, dd, *J* = 17.2, 1.2 Hz), 1.70 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.9, 145.6, 143.1, 139.5, 132.5, 128.2, 127.3, 126.4, 113.1, 110.7, 44.7, 27.2; HRMS (ESI+): Calcd for $C_{14}H_{15}O_1$ $[M+H]^+$: 199.1123, Found: 199.1120. Specific Rotation: $[\alpha]_D^{20}$ –4.32 (*c* 0.47, $CHCl_3$) for an enantiomerically enriched sample of 97:3 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with $NaBO_3$•$4H_2O$) in comparison with authentic racemic material (97.1:2.9 e.r. shown; Chiralcel OJ-H column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



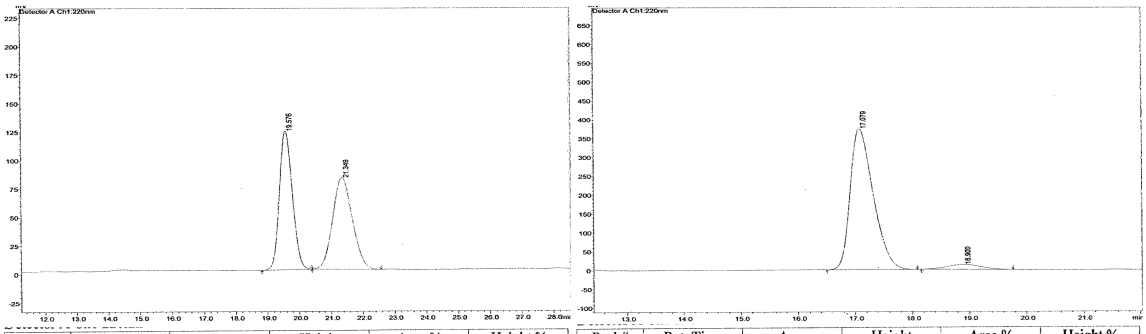
Peak#	Ret. Time	Area	Height	Area %	Height %
1	31.147	2492465	56684	50.213	59.499
2	43.542	2471302	38585	49.787	40.501
Total		4963767	95269	100.000	100.000

Peak#	Ret. Time	Area	Height	Area %	Height %
1	30.251	9369543	209214	97.075	97.190
2	42.641	282271	6049	2.925	2.810
Total		9651815	215263	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	31.147	50.2	1	30.251	97.1
2	43.542	49.8	2	42.641	2.9

(*S*)-3-(2-Cyclohexylbut-3-en-2-yl)furan (2.59). IR (neat): 2925 (s), 2853 (m), 1635 (w), 1501 (w), 1450 (w), 1413 (w), 1370 (w), 1159 (w), 1060 (w), 1027 (w), 914 (w), 873 (m), 778 (m), 726 (w), 600 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (1H, dd, *J* = 1.6, 1.6 Hz), 7.13 (1H, dd, *J* = 1.6, 0.8 Hz), 6.30 (1H, dd, *J* = 0.8, 0.8 Hz), 6.02 (1H, dd, *J* = 17.2, 10.8 Hz), 5.04 (1H, dd, *J* = 10.8, 1.6 Hz), 4.98 (1H, dd, *J* = 17.2, 1.6 Hz), 1.74–1.56 (6H, m), 1.48–1.40 (1H, m), 1.25 (3H, s), 1.22–1.02 (2H, m), 0.98–0.86 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.2, 142.7, 138.8, 132.4, 112.3, 109.7, 47.3, 42.5, 28.00, 27.98, 27.21, 27.18, 26.8, 20.4; HRMS (ESI+): Calcd for $C_{14}H_{21}O_1$ $[M+H]^+$: 205.1592, Found: 205.1600. Specific Rotation: $[\alpha]_D^{20}$ –9.48 (*c* 0.27, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with $NaBO_3$•$4H_2O$) in comparison with authentic racemic material (95.0:5.0 e.r. shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



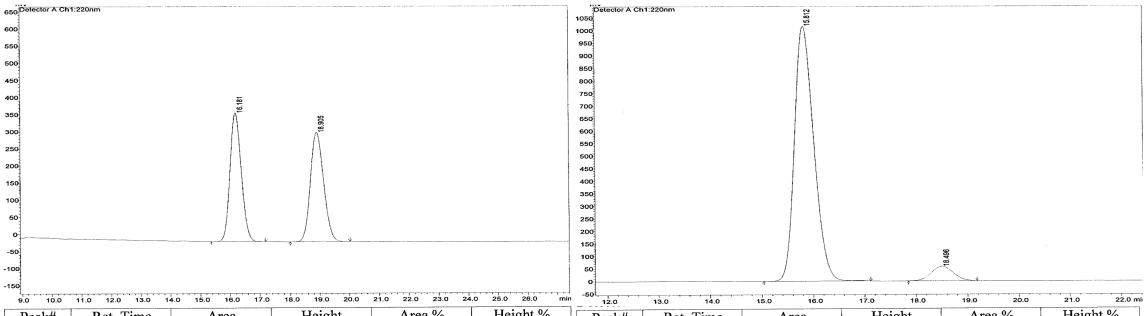
Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.576	3447725	121592	49.930	60.225
2	21.349	3457334	80305	50.070	39.775
Total		6905058	201897	100.000	100.000

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.079	10488798	373578	95.031	96.501
2	18.900	548394	13545	4.969	3.499
Total		11037192	387123	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	19.576	49.9	1	17.079	95.0
2	21.349	50.1	2	18.900	5.0

(*S*)-3-(2-Phenylbut-3-en-2-yl)thiophene (2.60). IR (neat): 2974 (w), 1491 (w), 1444 (w), 1367 (w), 1000 (w), 918 (m), 838 (m), 755 (m), 698 (s), 664 (s), 528 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.31–7.18 (6H, m), 6.97–6.96 (1H, m), 6.85–6.83 (1H, m), 6.36 (1H, ddd, *J* = 17.2, 10.4, 0.8 Hz), 5.17 (1H, dd, *J* = 10.8, 1.2 Hz), 4.92 (1H, dd, *J* = 17.2, 1.2 Hz), 1.79 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.0, 147.6, 146.0, 128.2, 127.5, 126.3, 125.3, 120.9, 113.1, 48.2, 27.5; HRMS (ESI+): Calcd for $C_{14}H_{15}S_1$ $[M+H]^+$: 215.0895, Found: 215.0899. Specific Rotation: $[\alpha]_D^{20}$ –6.69 (*c* 0.28, $CHCl_3$) for an enantiomerically enriched sample of 94:6 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with $NaBO_3$•$4H_2O$) in comparison with authentic racemic material (94.0:6.0 e.r. shown; Chiralcel OD-H column, 95/5 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.181	9900097	375875	49.934	54.083
2	18.905	9926390	319123	50.066	45.917
Total		19826487	694998	100.000	100.000

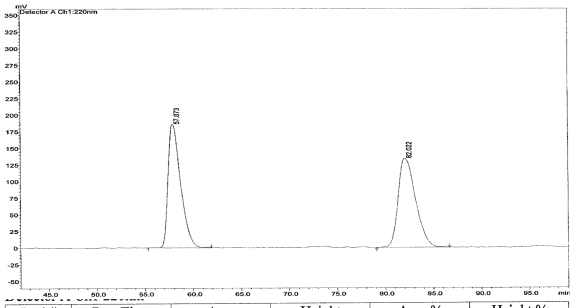
Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.812	26806961	1017664	93.953	94.607
2	18.496	1725290	58017	6.047	5.393
Total		28532252	1075681	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	16.181	49.9	1	15.812	94.0
2	18.905	50.1	2	18.496	6.0

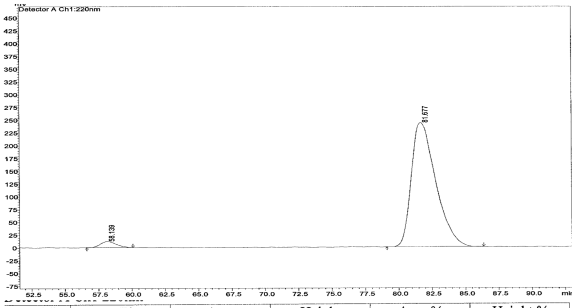
(*R*)-3-(2-(2-Bromophenyl)but-3-en-2-yl)thiophene (2.61). IR (neat): 2974 (w), 1633 (w), 1464 (w), 1409 (w), 1367 (w), 1231 (w), 1198 (w), 1173 (w), 1084 (w), 1019 (m), 917 (m), 838 (m), 750 (s), 652 (m), 455 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.55 (1H, dd, *J* = 7.6, 1.6 Hz), 7.51 (1H, dd, *J* = 8.0, 2.0 Hz), 7.30 (1H, ddd, *J* = 8.0, 7.2, 1.6 Hz), 7.23 (1H, dd, *J* = 5.2, 3.2 Hz), 7.10 (1H, ddd, *J* = 7.6, 7.2, 1.6 Hz), 6.90 (1H, dd, *J* = 3.2, 1.6 Hz), 6.74 (1H, dd, *J* = 5.2, 1.2 Hz), 6.56 (1H, dd, *J* = 17.6, 10.8 Hz), 5.17 (1H, dd, *J* = 10.4, 0.8 Hz), 4.94 (1H, dd, *J* = 17.2, 0.8 Hz), 1.91 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.2, 145.7, 145.1, 135.7, 129.5, 128.3, 127.6, 127.2, 125.1, 124.2, 120.7, 113.1, 49.3, 26.6; HRMS (ESI+): Calcd for $C_{14}H_{14}Br_1S_1$ $[M+H]^+$: 293.0000, Found: 292.9987. Specific Rotation: $[\alpha]_D^{20}$ –22.7 (*c* 1.19, $CHCl_3$) for an enantiomerically enriched sample of 97:3 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation

with $NaBO_3 \bullet 4H_2O$) in comparison with authentic racemic material (97.0:3.0 e.r. shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	57.873	16932633	186036	50.063	58.098
2	82.022	16889813	134172	49.937	41.902
Total		33822446	320208	100.000	100.000

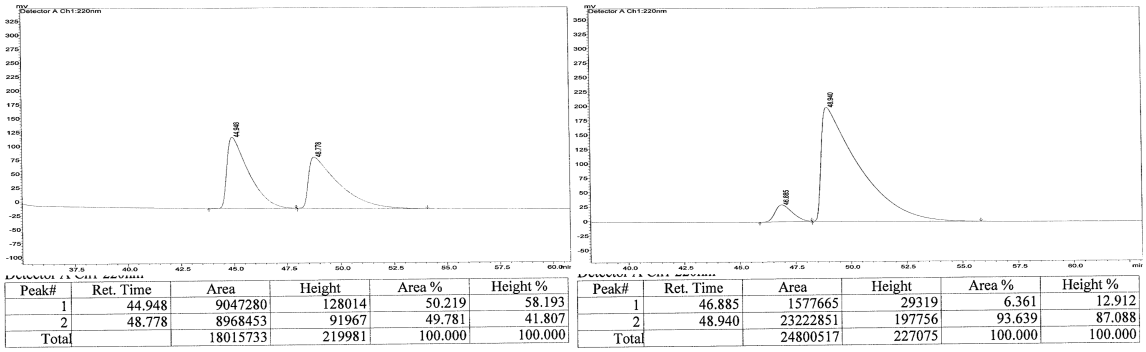


Peak#	Ret. Time	Area	Height	Area %	Height %
1	58.139	959740	11782	3.026	4.632
2	81.677	30758578	242577	96.974	95.368
Total		31718318	254359	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	57.873	50.1	1	58.139	3.0
2	82.022	49.9	2	81.677	97.0

(*R*)-Dimethyl(phenyl)(2-(thiophen-3-yl)but-3-en-2-yl)silane (2.62). IR (neat): 2959 (w), 1620 (w), 1427 (w), 1366 (w), 1247 (m), 1112 (m), 998 (w), 830 (s), 810 (s), 773 (s), 734 (s), 699 (s), 653 (s), 567 (m), 472 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.39–7.34 (1H, m), 7.31–7.25 (4H, m), 7.20 (1H, dd, *J* = 5.2, 2.8 Hz), 6.80 (1H, dd, *J* = 5.2, 1.6 Hz), 6.65 (1H, dd, *J* = 3.2, 1.6 Hz), 6.36 (1H, dd, *J* = 17.2, 10.8 Hz), 5.05 (1H, dd, *J* = 10.4, 1.2 Hz), 4.90 (1H, dd, *J* = 17.6, 1.2 Hz), 1.44 (3H, s), 0.26 (6H, d, *J* = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.5, 142.8, 136.5, 134.9, 129.3, 127.4, 127.2, 124.5, 117.9, 110.8, 36.7, 19.4, –5.2, –5.4; HRMS (ESI+): Calcd for $C_{16}H_{21}S_1Si_1$ $[M+H]^+$: 273.1133, Found: 273.1132. Specific Rotation: $[\alpha]_D^{20}$ –18.7 (*c* 0.41, $CHCl_3$) for an enantiomerically enriched sample of 94:6 e.r.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (93.6:6.4 e.r. shown; Chiralcel OD-H column, 100% hexanes, 0.2 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	44.948	9047280	128014	50.219	58.193
2	48.778	8968453	91967	49.781	41.807
Total		18015733	219981	100.000	100.000

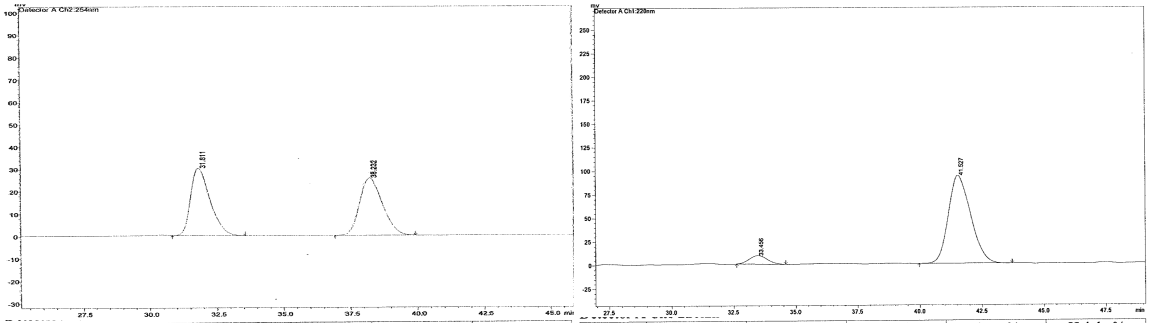
Peak#	Ret. Time	Area	Height	Area %	Height %
1	46.885	1577665	29319	6.361	12.912
2	48.940	23222851	197756	93.639	87.088
Total		24800517	227075	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	44.948	50.2	1	46.885	6.4
2	48.778	49.8	2	48.940	93.6

(*S*)-3-(2-Cyclohexylbut-3-en-2-yl)thiophene (2.63). IR (neat): 2981 (w), 2926 (s), 2852 (m), 1449 (w), 913 (w), 770 (w), 652 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.25 (1H, ddd, *J* = 5.2, 3.2, 0.4 Hz), 7.02 (1H, ddd, *J* = 5.2, 1.6, 0.4 Hz), 6.91 (1H, ddd, *J* = 2.8, 1.2, 0.4 Hz), 6.13 (1H, dd, *J* = 17.2, 10.8 Hz), 5.08 (1H, ddd, *J* = 11.2, 1.6, 0.4 Hz), 4.99 (1H, dd, *J* = 17.6, 1.2 Hz), 1.75–1.58 (5H, m), 1.50–1.44 (1H, m), 1.34 (3H, s), 1.25–1.01 (3H, m), 0.99–0.86 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.6, 145.3, 126.8, 125.0, 119.5, 112.4, 47.8, 46.1, 28.2, 28.0, 27.3, 27.2, 26.8, 20.6; HRMS (ESI+): Calcd for $C_{14}H_{21}S_1$ $[M+H]^+$: 221.1364, Found: 221.1371. Specific Rotation: $[\alpha]_D^{20}$ +1.39 (*c* 0.72, $CHCl_3$) for an enantiomerically enriched sample of 92.5:7.5 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation

with $NaBO_3 \bullet 4H_2O$) in comparison with authentic racemic material (92.7:7.3 e.r. shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	31.811	1512039	29972	49.910	53.962
2	38.232	1517487	25571	50.090	46.038
Total		3029526	55544	100.000	100.000

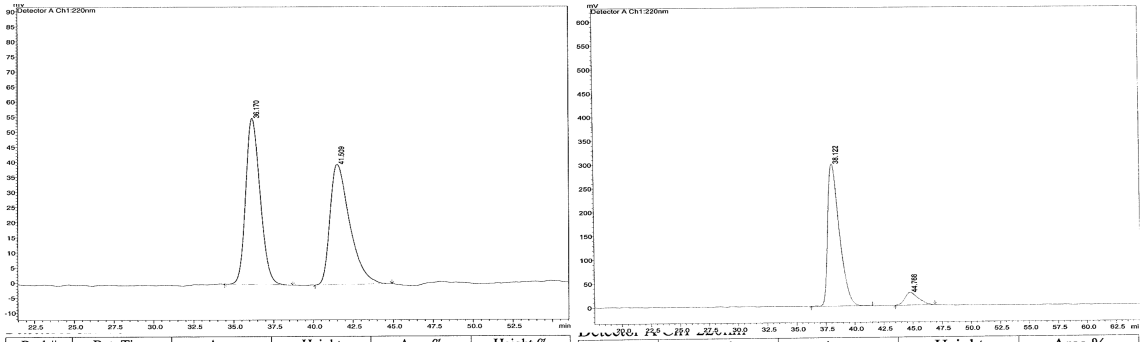
Peak#	Ret. Time	Area	Height	Area %	Height %
1	33.456	455015	9027	7.286	8.835
2	41.527	5790473	93152	92.714	91.165
Total		6245489	102179	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	31.811	49.9	1	33.456	7.3
2	38.232	50.1	2	41.527	92.7

(*R*)-2-(2-(Dimethyl(phenyl)silyl)but-3-en-2-yl)-1-methyl-1*H*-pyrrole (2.67). IR (neat): 3070 (w), 2961 (w), 1617 (w), 1480 (w), 1427 (w), 1409 (w), 1294 (w), 1249 (w), 1109 (w), 1002 (w), 891 (w), 822 (m), 777 (w), 736 (w), 701 (s), 654 (w), 474 (w), 445 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.55–7.52 (2H, m), 7.37–7.30 (3H, m), 6.47 (1H, dd, *J* = 2.8, 2.0 Hz), 6.10–6.03 (2H, m), 5.99 (1H, dd, *J* = 3.6, 2.8 Hz), 5.07 (1H, dd, *J* = 10.8, 1.2 Hz), 4.73 (1H, dd, *J* = 17.6, 1.2 Hz), 3.41 (3H, s), 1.50 (3H, s), 0.47 (3H, s), 0.43 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.2, 137.6, 135.4, 135.1, 129.1, 127.5, 123.3, 112.2, 108.4, 105.9, 36.7, 33.8, 20.6, –3.7, –3.8; HRMS (ESI+): Calcd for $C_{17}H_{24}N_1Si_1$ $[M+H]^+$: 270.1678, Found: 270.1666. Specific Rotation: $[\alpha]_D^{20}$ +41.9 (*c* 0.67, $CHCl_3$) for an enantiomerically enriched sample of 85:15 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation

with $NaBO_3 \bullet 4H_2O$) in comparison with authentic racemic material (90.7:9.3 e.r. shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	36.170	3473016	55040	50.223	57.994
2	41.509	3442157	39866	49.777	42.006
Total		6915173	94906	100.000	100.000

Peak#	Ret. Time	Area	Height	Area %
1	38.122	20939460	298663	90.723
2	44.768	2141304	26979	9.277
Total		23080764	325642	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
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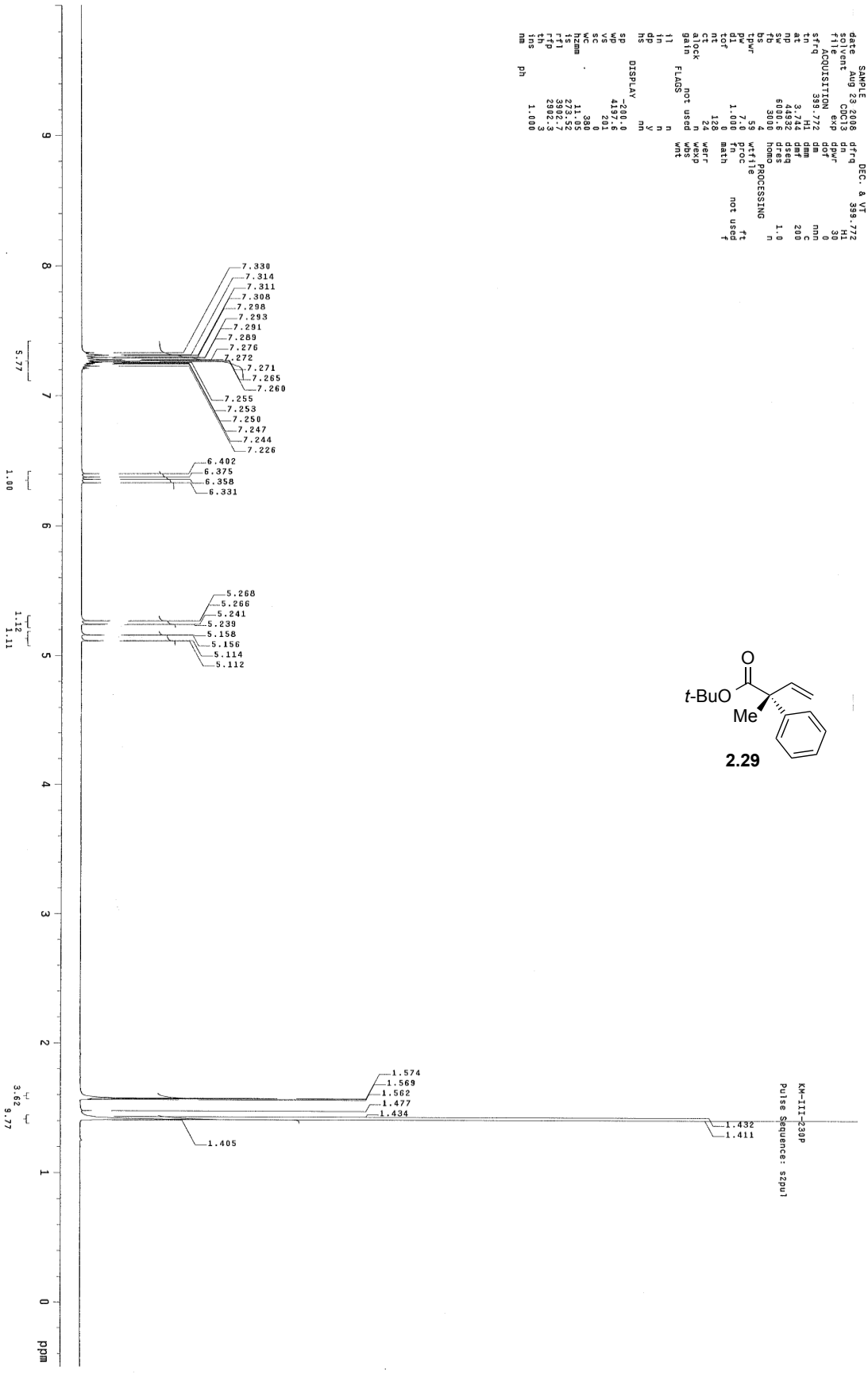
2	41.509	49.8	2	44.768	9.3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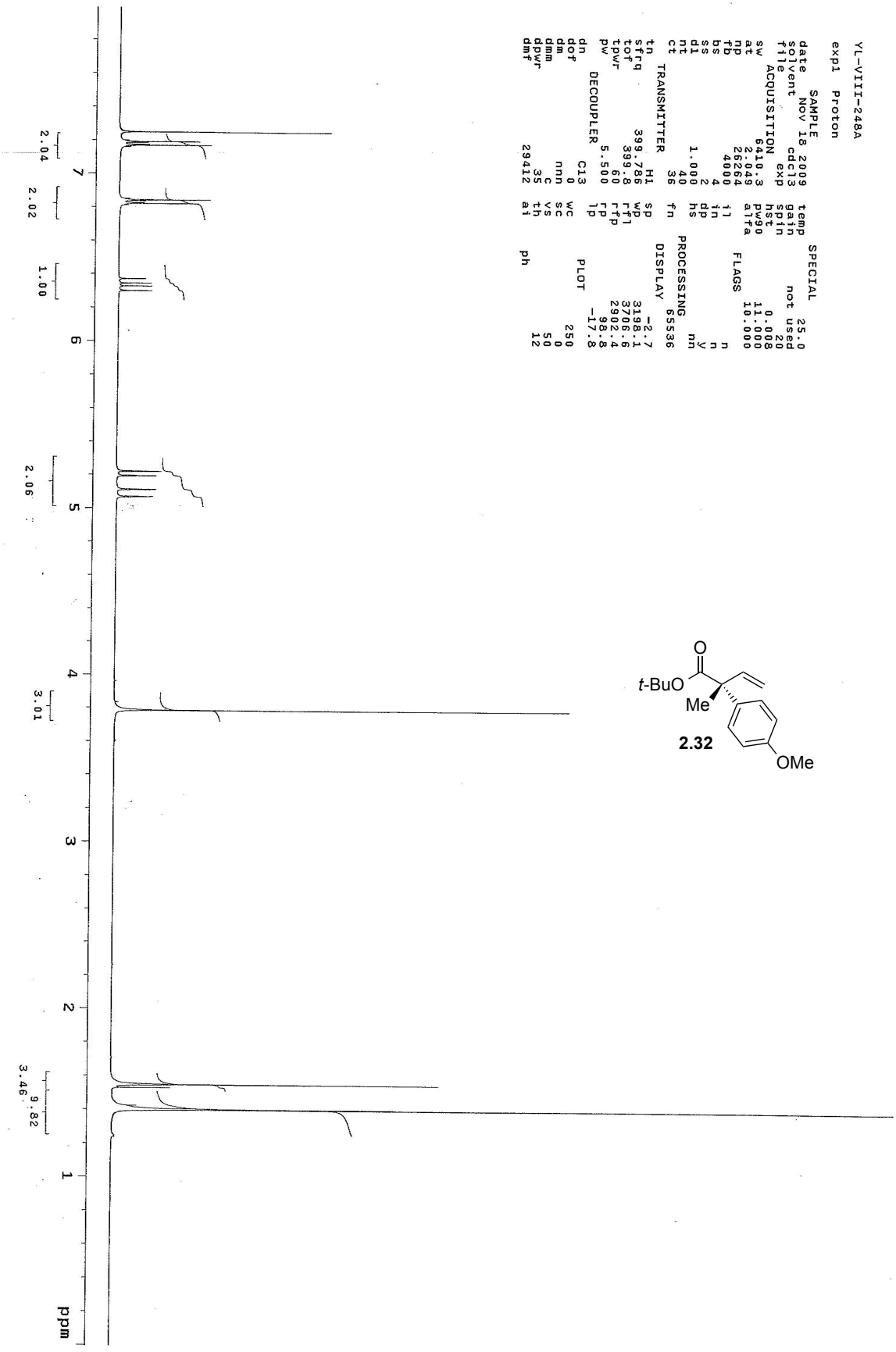
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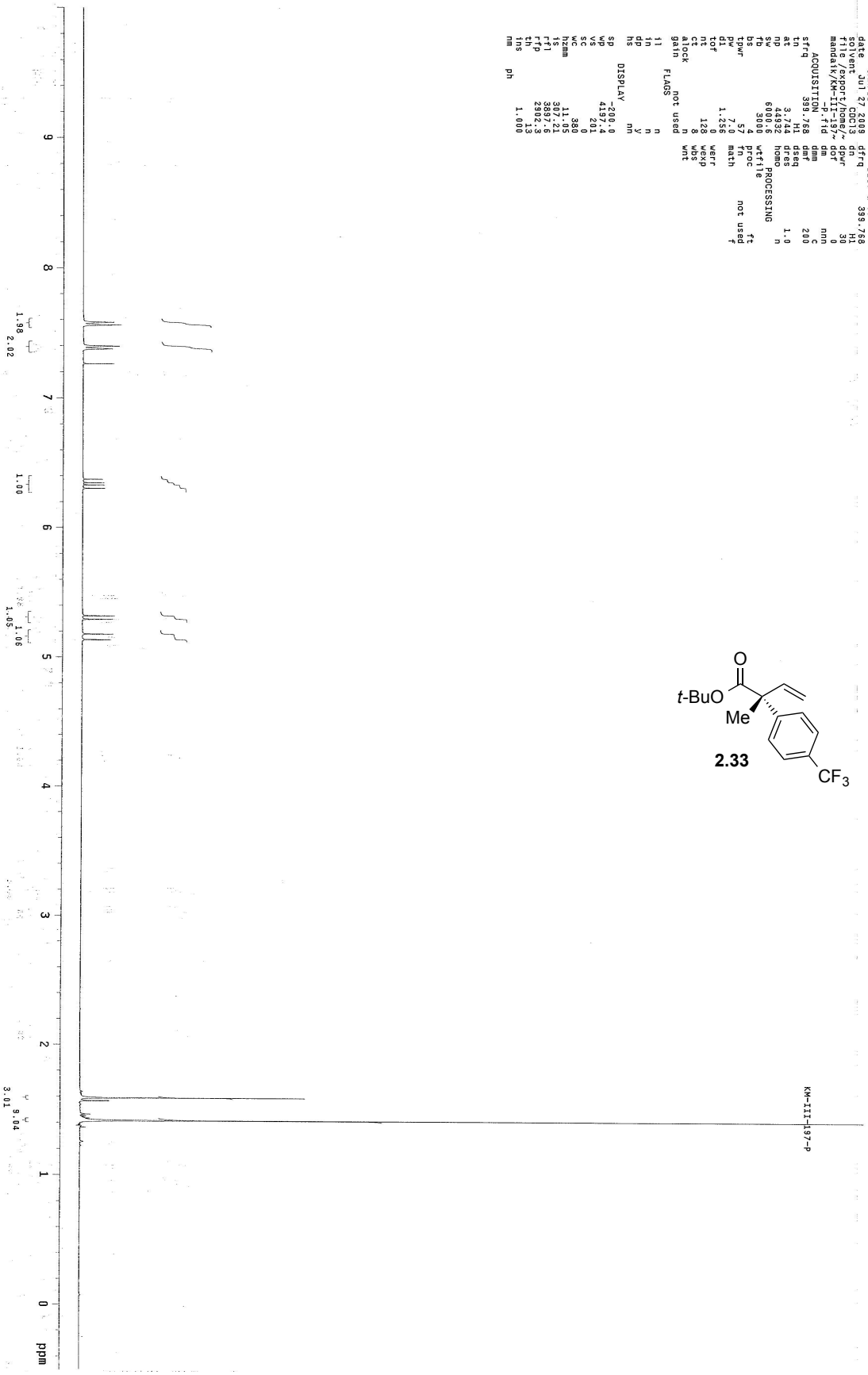
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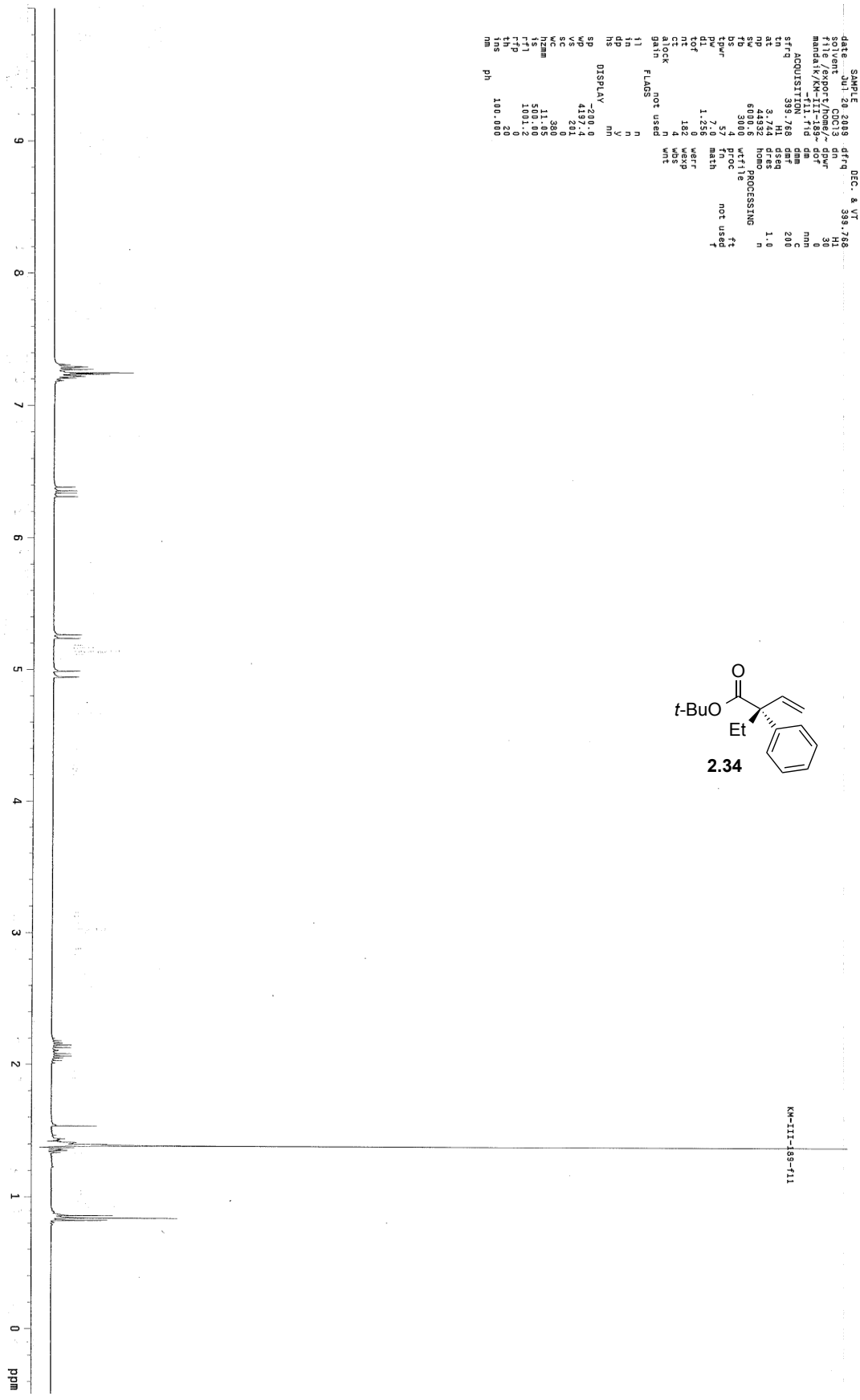
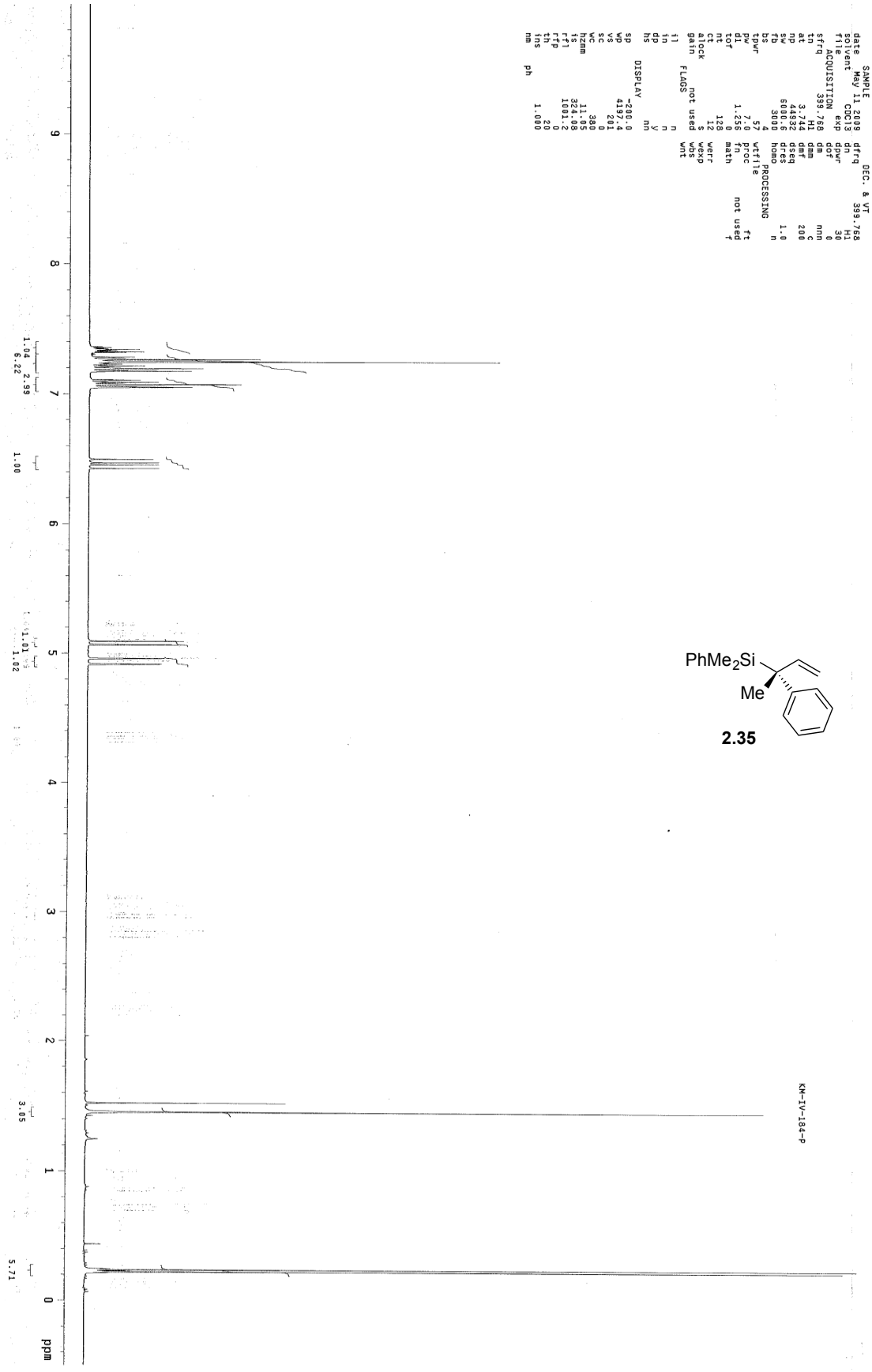
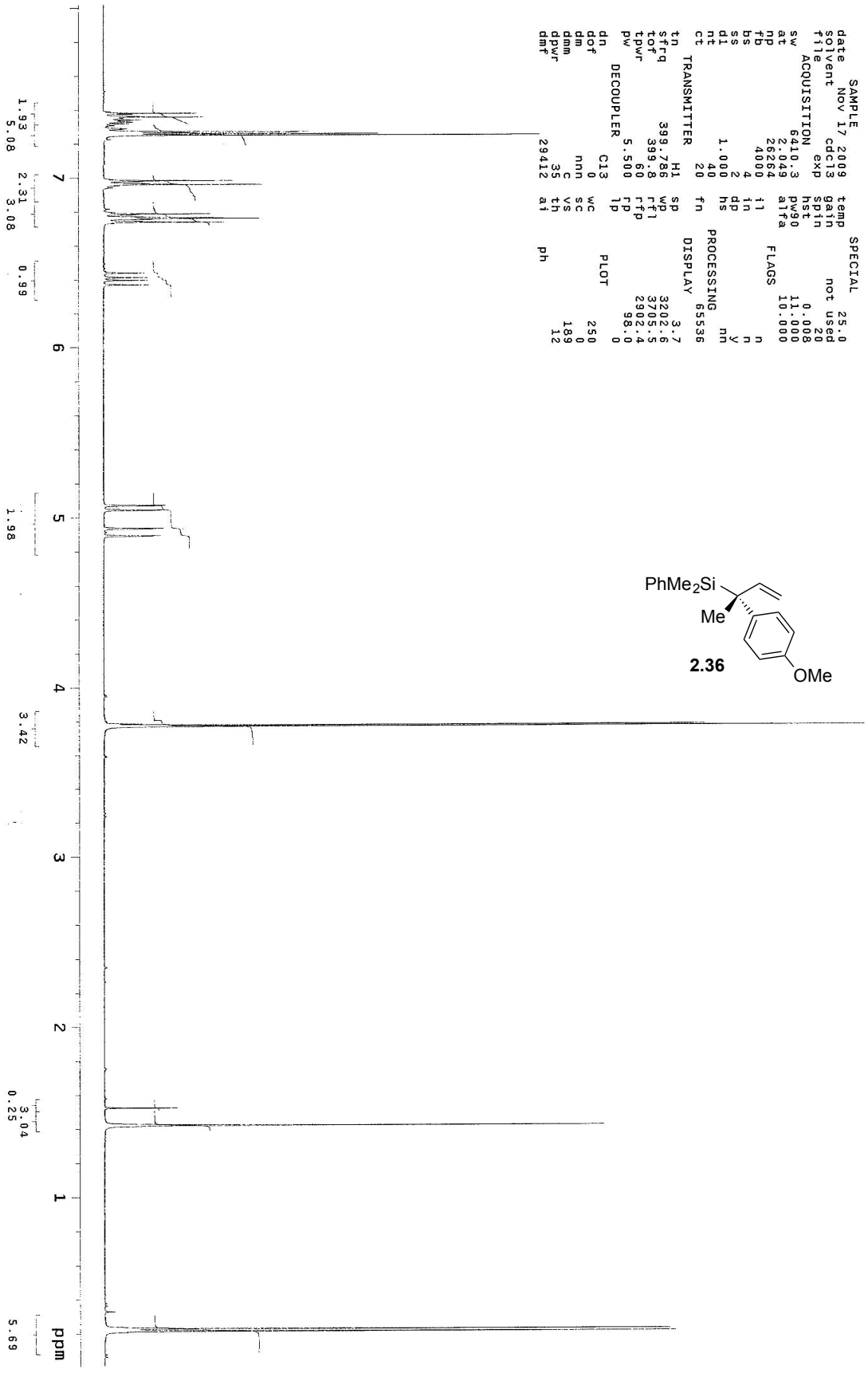
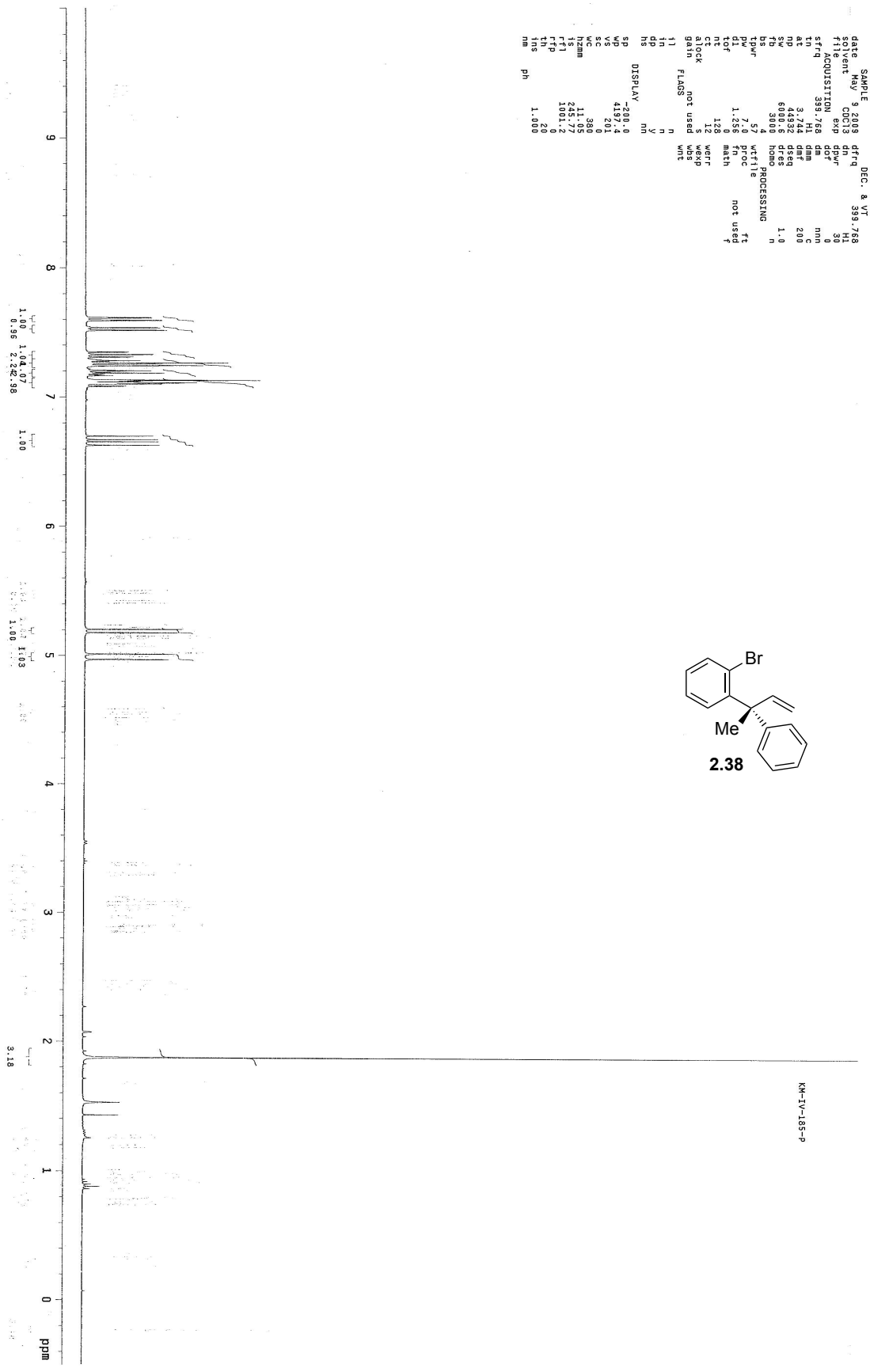
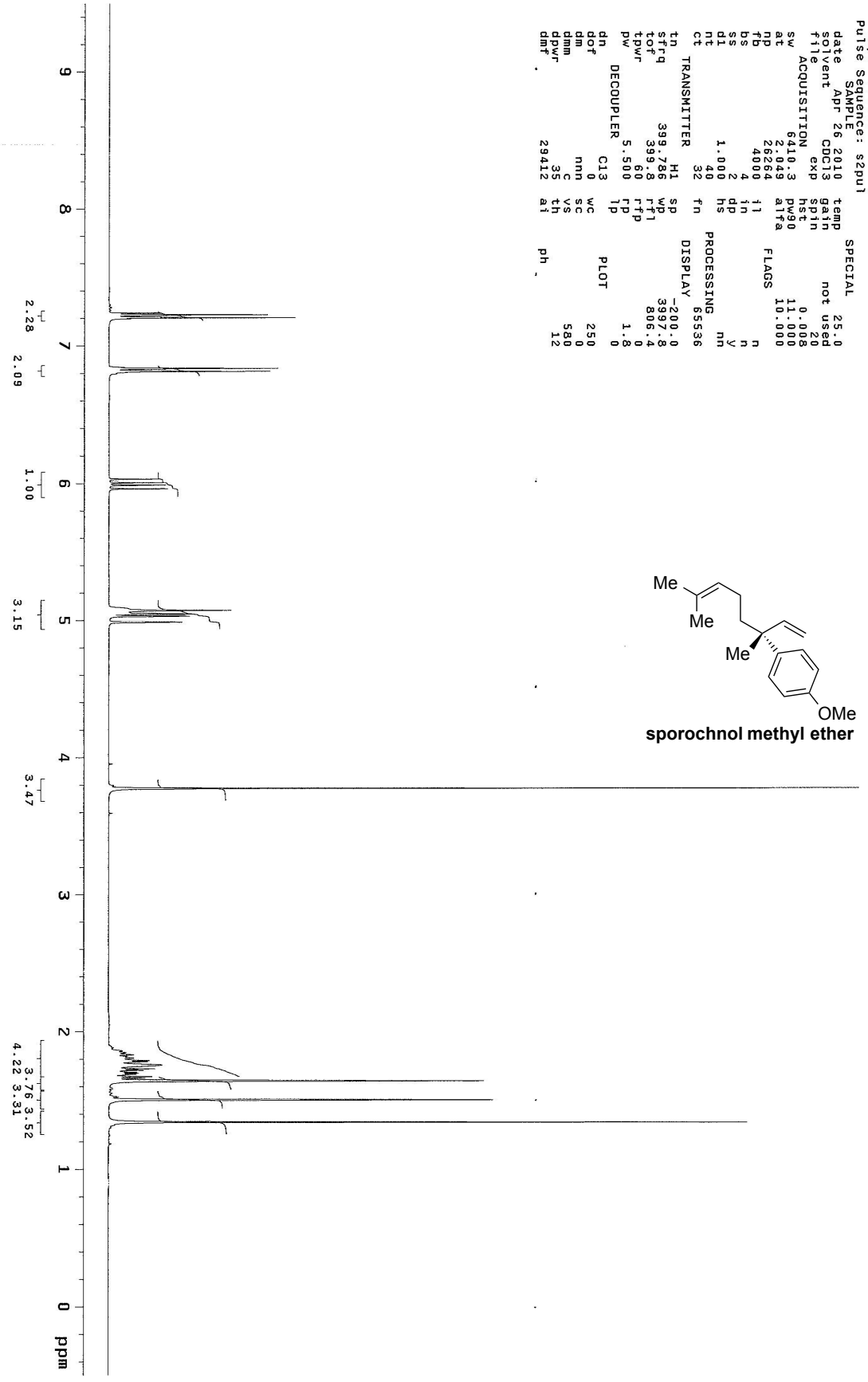
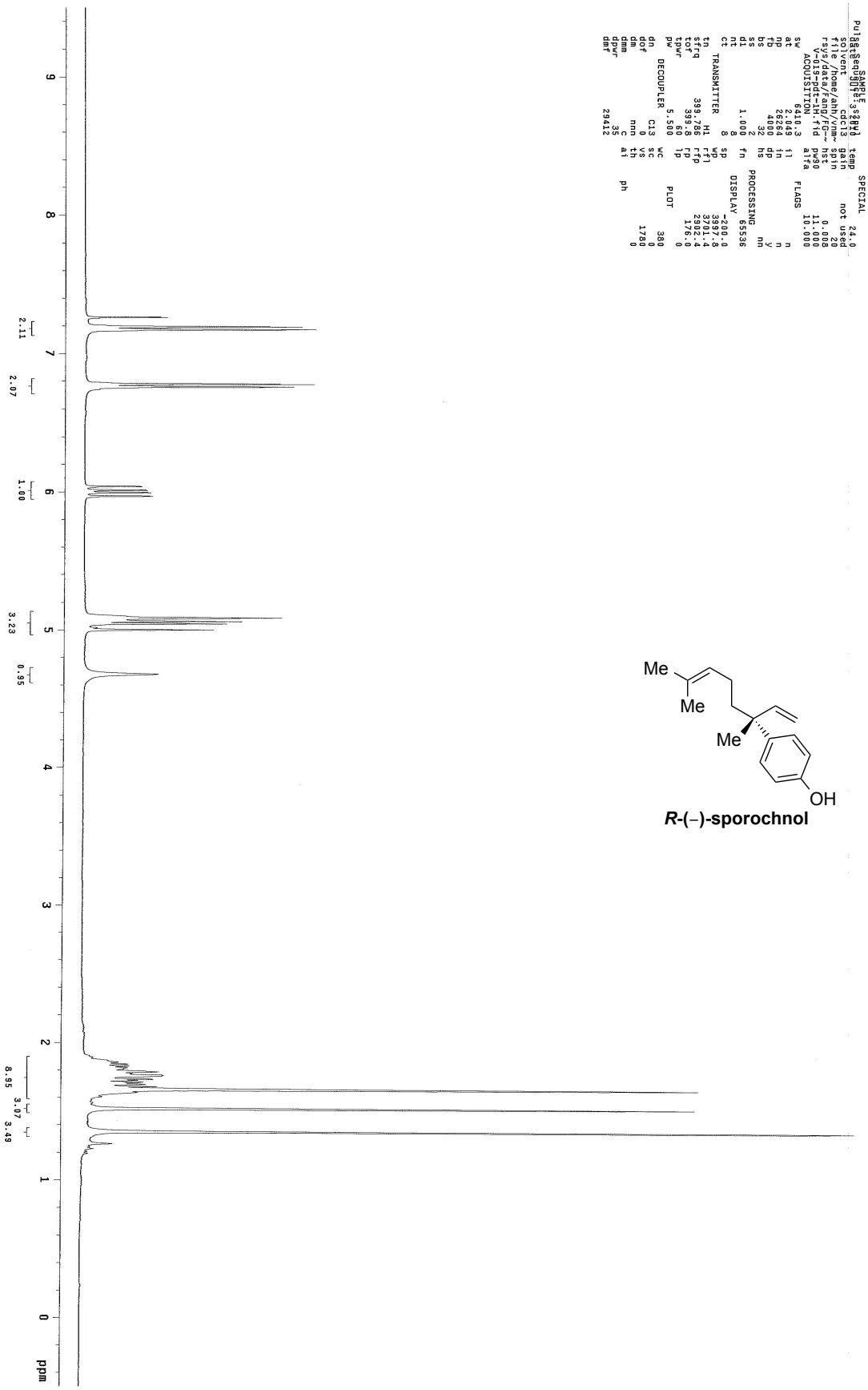

KM-III-189-f11
expl stdih
SAMPLE
date Jul 20 2009
solvent CDCl3
file /export/home/~
manda1k/KM-III-189~
ACQUISITION
sfrq 399.768
tn H1
at 3.744
np 44932
sw 6009.6
fb 3004
bs 4
tpwr 57
pw 7.0
d1 1.256
nt 182
ct 4
alock n
gain not used
FLAGS
fl n
in n
dp y
hs nn
DISPLAY
sp -210.0
wp 4197.4
vs 201
sc 0
wc 380
hzmm 11.05
is 500.00
rfl 1001.2
rfp 0
th 20
ins 100.000
nm
ph
DEC. & VT
dfrq 399.768
dn H1
dof 30
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn not used
math f
wexp
wbs
wnt
O
t-BuO
Et
2.34
KM-III-189-f11
9
8
7
6
5
4
3
2
1
0
ppm

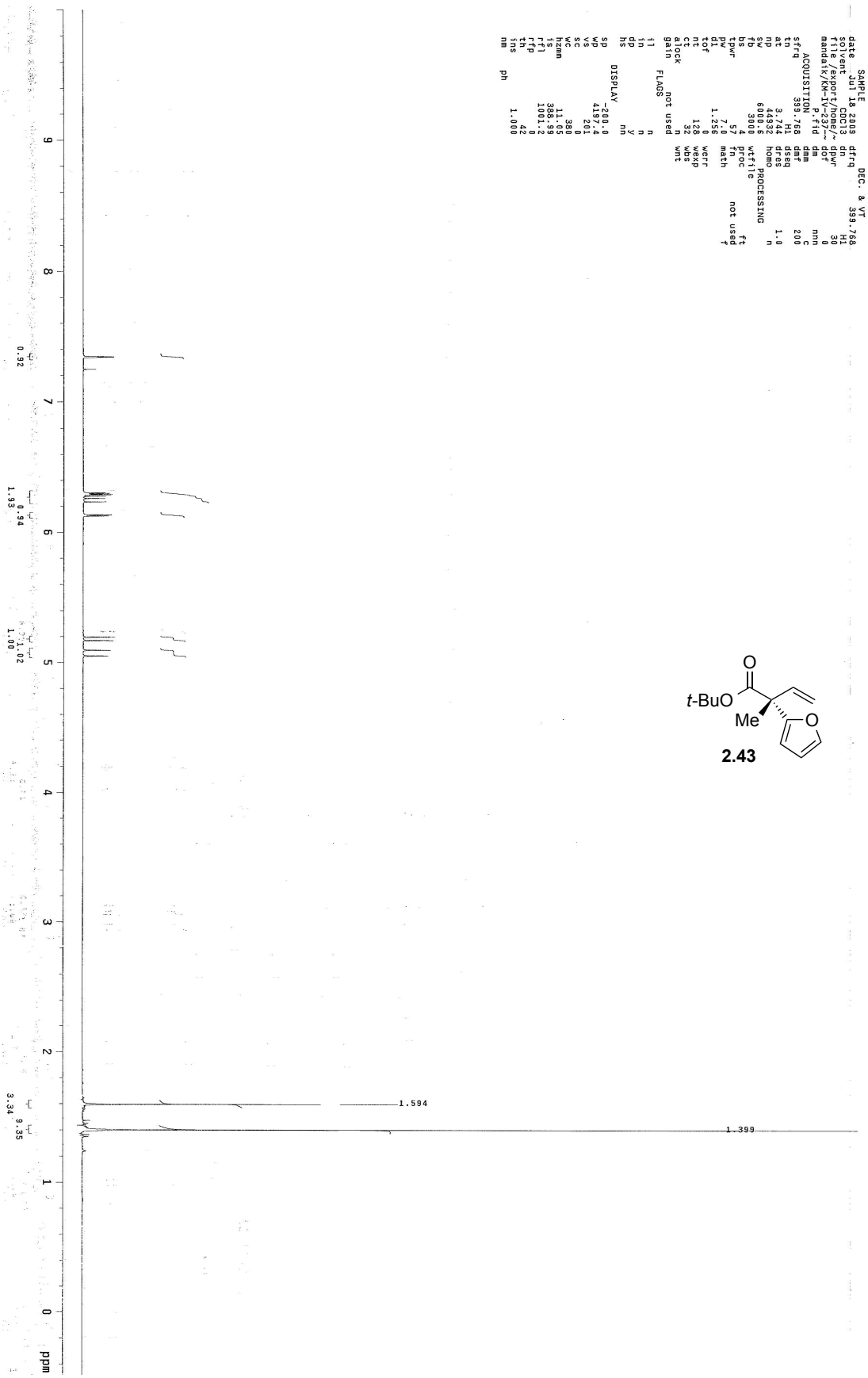

KM-IV-184-P
expl stdih
SAMPLE
date May 11 2009
solvent CDCl3
file ACQUISITION
sfrq 399.768
tn H1
at 3.744
np 44932
sw 6009.615
fb 3006
bs 4
tpwr 57
pw 7.0
d1 1.256
nt 128
ct 12
alock n
gain s
FLAGS
not used wexp
wbs
wnt
il n
in n
dp y
hs nn
DISPLAY
sp -200.0
wp 4197.4
vs 201
sc 0
wc 380
hzcm 11.905
hz/pt 0.183112
rfl 1001.2
rfp 0
th 20
ins 1.000
nm
ph
DEC. & VT
dfrq
dn
dpwr
dof
dm
dmm
dmf
dseq
homo
PROCESSING
wtfile
proc
ft
fn
not used
math
f
PhMe2Si
Me
2.35
KM-IV-184-P
ppm
1.04
2.99
6.22
1.00
1.01
1.02
3.05
5.71

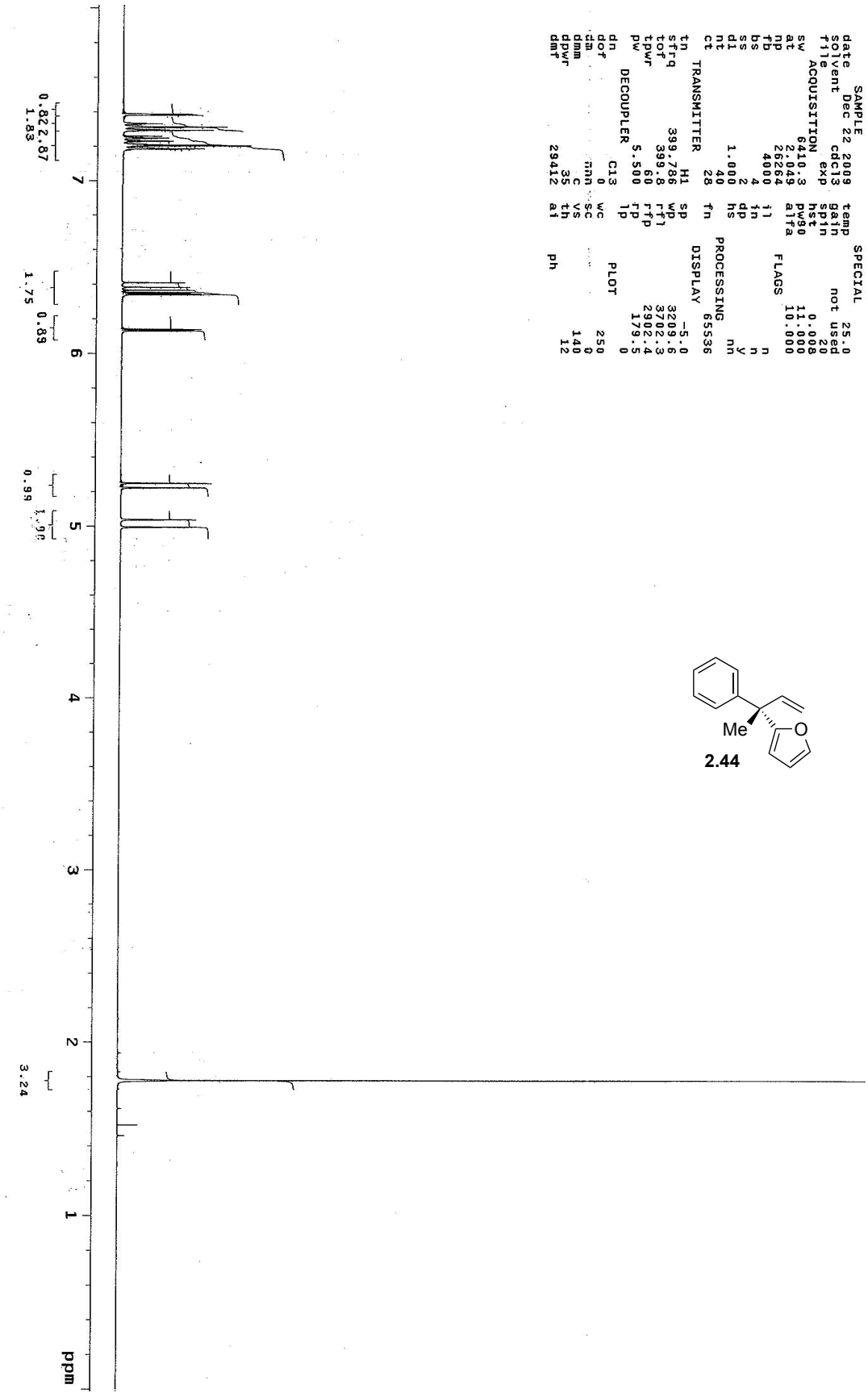

YL-VIII-249A
exp1 Proton
SAMPLE
date Nov 17 2009
solvent cdcl3
file
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4000
bs 4
ss 2
d1 1.000
nt 40
ct 20
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
temp 25.0
gain not used
spin 20
hst
pw90 11.000
alfa 10.000
FLAGS
il n
in n
dp y
hs nn
PROCESSING
fn 65536
DISPLAY
sp 3.7
wp 3202.6
rfl 3705.5
rfp 2902.4
rp 98.0
lp 0
PLOT
wc 250
sc 0
vs 189
th 12
ai
ph
PhMe2Si
Me
OMe
2.36
1.93
5.08
2.31
3.08
0.99
1.98
3.42
3.04
0.25
5.69
ppm

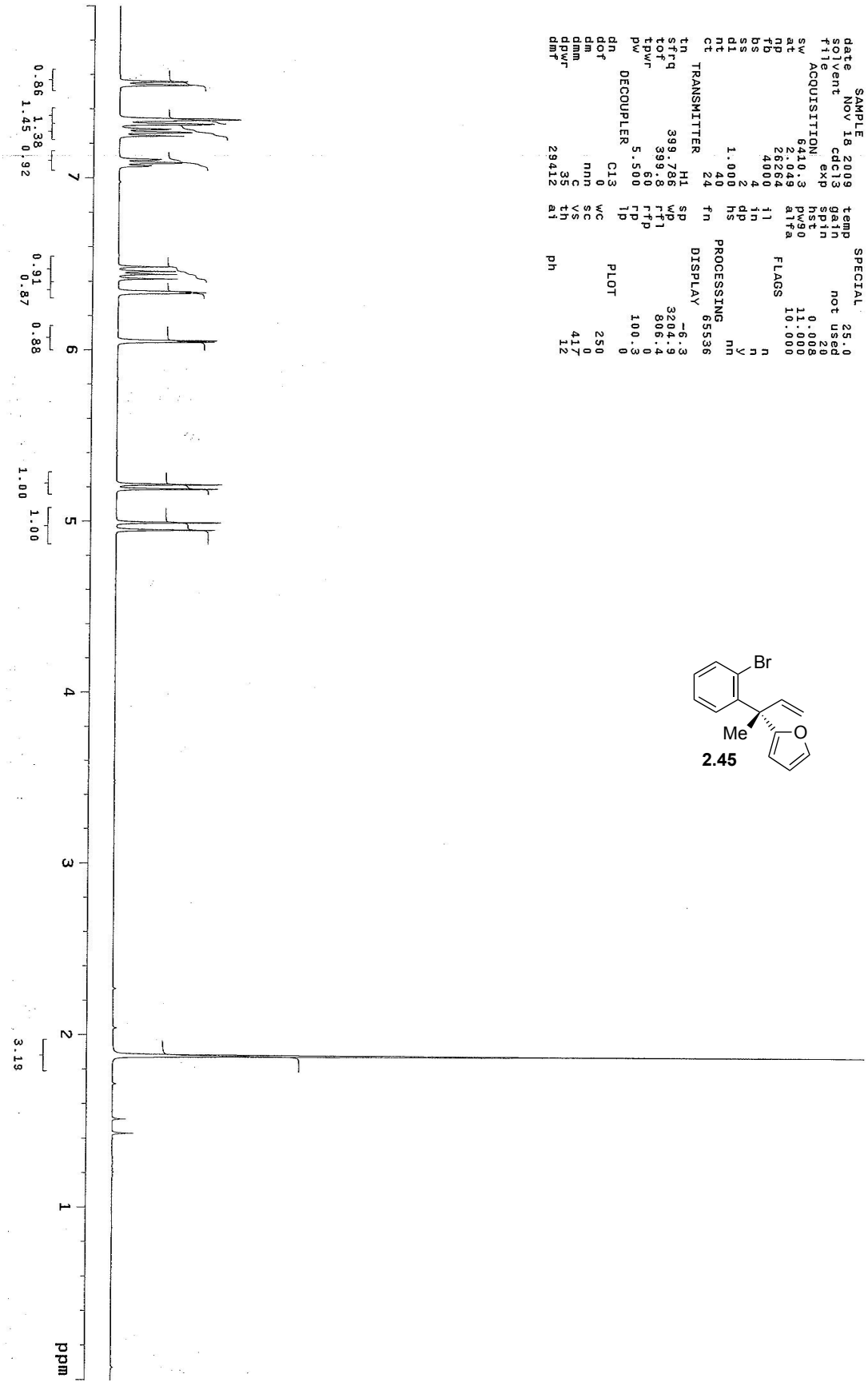

KM-IV-185-P
expl stdih
SAMPLE
date May 9 2009
solvent CDCl3
file
ACQUISITION
sfrq 399.768
tn H1
at 3.744
np 44992
sw 6009.6
fb 3010
bs 4
tpwr 57
pw 7.0
dl 1.256
d1 0
hst 128
ct 12
alock s
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -200.0
wp 4197.4
vs 201
sc 0
wc 380
hzpmm 11.95
rfl 2457.7
rfp 1601.2
th 20
ins 0
nm 1.000
ph
DEC. & VT
dfrq 399.768
dn H1
dpwr 30
dof 0
dm nnn
tm c
amf 200
dmm
dmf
homo 1.0
PROCESSING n
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt
Br
Me
2.38
KM-IV-185-P
1.00
1.04
1.07
0.96
2.24
2.98
1.00
1.00
1.03
3.18
9
8
7
6
5
4
3
2
1
0
ppm

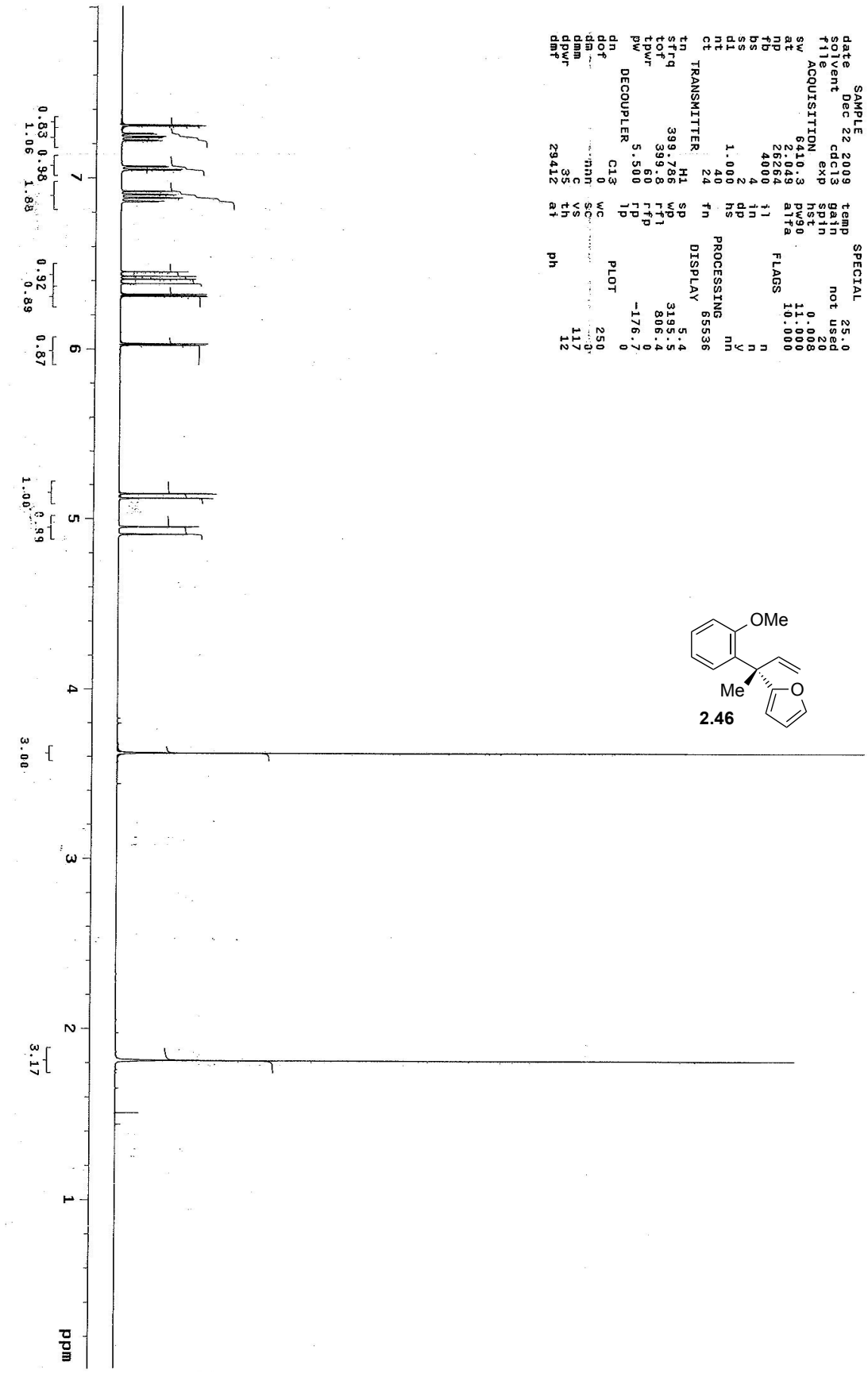

FG-IV-230-pdt-1H
File: exp
exp3 Proton
Pulse Sequence: s2pul
SAMPLE
date Apr 26 2010
solvent CDCl3
file
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4000
bs 4
ss 2
d1 1.000
nt 40
ct 32
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
temp
gain
spin
hst
pw90
alfa
FLAGS
PROCESSING
fn 65536
DISPLAY
sp -200.0
wp 3997.8
rfl 806.4
rfp 0
rp 1.8
lp 0
PLOT
wc 250
sc 0
vs 580
th 12
ai
ph
SPECIAL
25.0
not used
20
0.008
11.000
10.000
n
n
y
nn
Me
Me
Me
OMe
sporochnol methyl ether
2.28
2.09
1.00
3.15
3.47
3.76 3.52
4.22 3.31
ppm

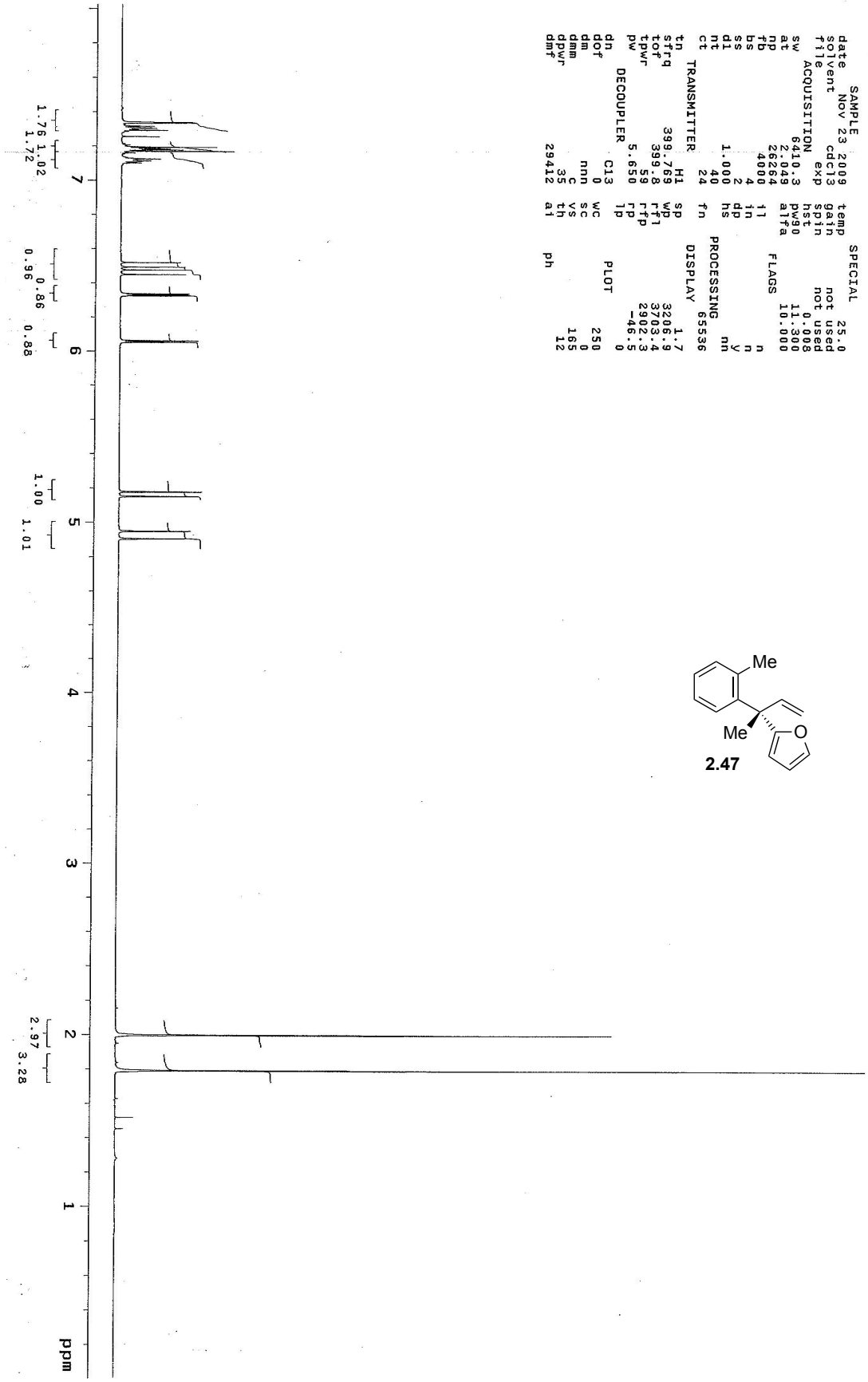

Sample: FG-V-019-pdt
Sample_ID: ahh_0703_03
File: /home/ahh/vnmrsys/data/Fang/FG-V-019-pdt-1H.fid
SAMPLE
SPECIAL
Pulse Sequence: s2pul
solvent cdcl3
file /home/ahh/vnmr
rsys/data/Fang/FG-
V-019-pdt-1H.fid
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 400
bs 32
ss 2
d1 1.000
nt 8
ct 8
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 50
pw 5.500
DECOUPLER
C13
dn
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
temp 24.0
gain not used
spin 20
0
hs nn
PROCESSING
fn 65536
DISPLAY
sp -200.0
wp 3897.8
rfl 3701.4
rfp 2902.4
rp 176.0
lp 0
PLOT
wc 380
sc
vs 0
th 1780
ph
al
0
11.000
10.000
FLAGS
n
n
y
y
nn
Me
Me
Me
OH
R-(−)-sporochnol
ppm
2.11
2.07
1.00
3.23
0.95
8.95
3.07
3.49

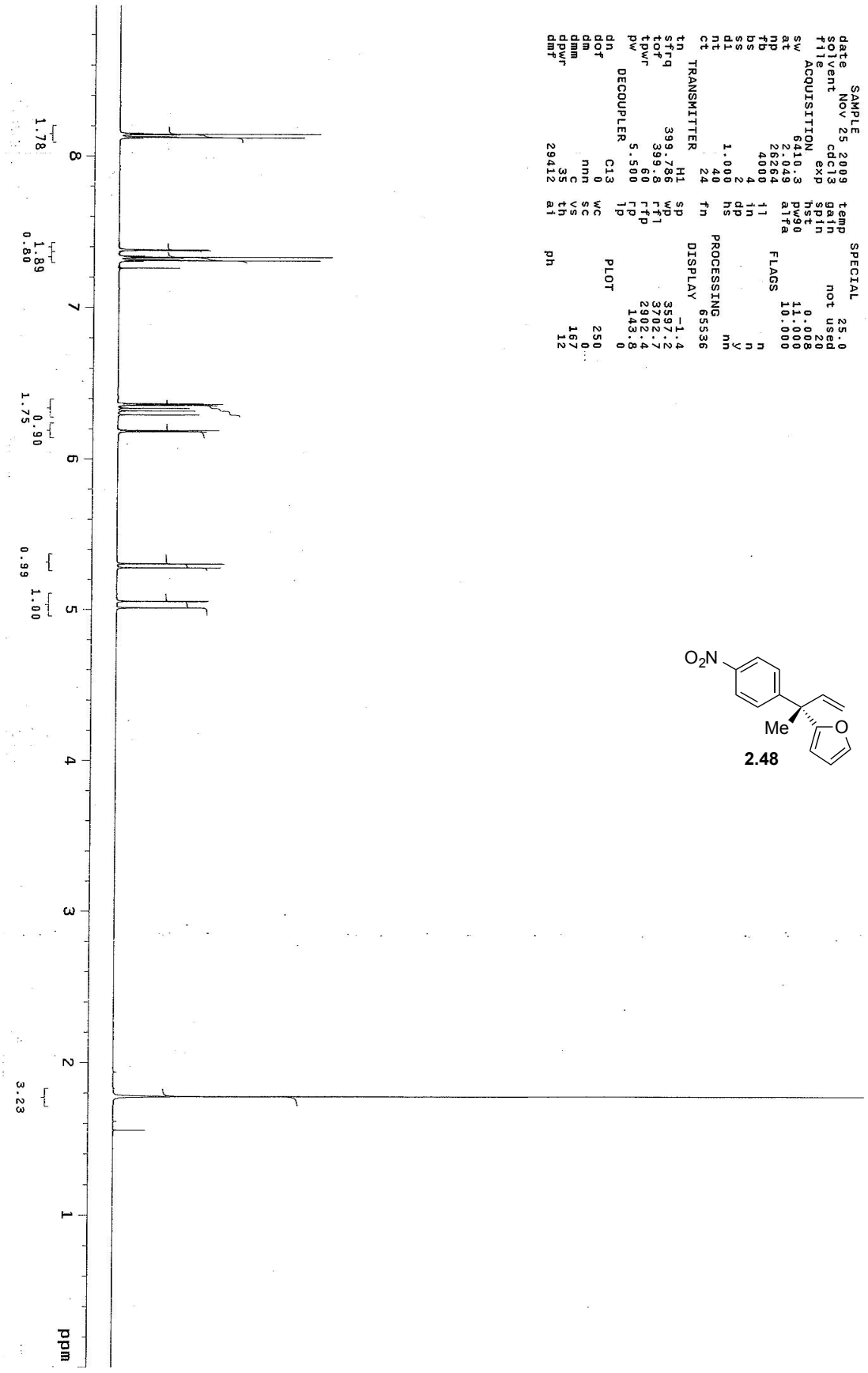

KM-IV-237-P
expl stdlh
SAMPLE
date Jul 18 2009
solvent CDCl3
file /export/home/~
mandaik/KM-IV-237~
ACQUISITION
sfrq 399.768
tn H1
at 3.744
np 44932
sw 6000.6
fb 300.4
bs 57
tpwr 57
pw 7.0
d1 1.256
tof 0
nt 128
ct 32
alock n
gain wnt
FLAGS
not used
il n
in n
dp y
hs nn
DISPLAY
sp -200.0
wp 4197.4
vs 201
sc 0
wc 380
hzmm 11.05
is 388.92
rfl 1001.0
rfp 0
th 42
ins 1.000
nm
ph
DEC. & VT
dfrq 399.768
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt
1.594
1.399
0.92
0.94
1.93
1.02
1.00
3.34
9.35
ppm
t-BuO
Me
O
O
2.43


YL-VIII-286A
exp26 proton
SAMPLE
date Dec 22 2009
solvent cdcl3
file
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4000
bs 4
ss 2
d1 1.000
nt 40
ct 28
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
SPECIAL
temp 25.0
gain not used
spin 20
hst 0.008
pw90 11.000
alfa 10.000
FLAGS
il n
in n
dp y
hs nn
PROCESSING
fn 65536
DISPLAY
sp -5.0
wp 3209.6
rfl 3702.3
rfp 2902.4
rp 179.5
lp 0
PLOT
wc 250
sc 0
vs 140
th 12
ph
Me
O
2.44
0.82
2.87
1.83
1.75
0.89
0.99
1.00
3.24
7
6
5
4
3
2
1
ppm


YL-KM-4-240B
expl Proton
SAMPLE
date Nov 18 2009
solvent cdcl3
file expl
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4000
bs 4
ss 2
d1 1.000
nt 40
ct 24
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
temp 25.0
gain not used
spin 20
hst 0.008
pw90 11.000
atfa 10.000
FLAGS
il n
in n
dp y
hs nn
PROCESSING
fn 65536
DISPLAY
sp -6.3
wp 3204.9
rfl 806.4
rfp 0
rp 0
lp 100.3
PLOT
wc 250
sc 0
vs 417
th 12
ph
ai
0.86 1.38 1.45 0.92
0.91 0.87 0.88
1.00 1.00
3.19
7 6 5 4 3 2 1
ppm
Br
Me
O
2.45

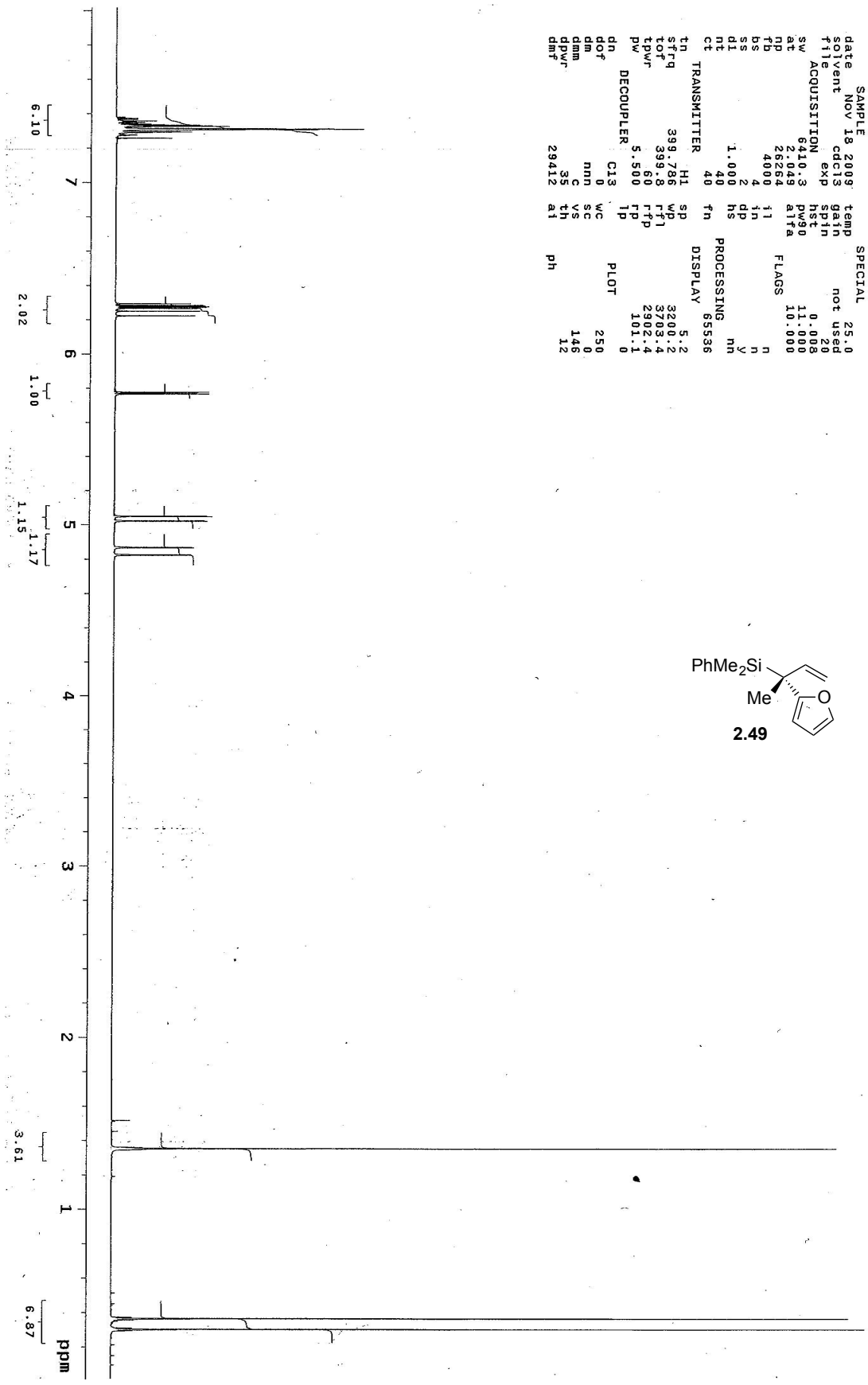

YL-VIII-287A
exp26 Proton
SAMPLE
date Dec 22 2009
solvent cdcl3
file exp
ACQUISITION
sw 6410.3
at 2.043
np 26264
fb 4000
bs 4
ss 2
d1 1.000
nt 40
ct 24
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
temp
gain
spin
hst
pw90
atfa
FLAGS
fl
in
dp
hs
PROCESSING
fn
DISPLAY
sp
wp
rfl
rfp
rp
lp
PLOT
wc
sc
vs
th
at
ph
SPECIAL
25.0
not used
20
0.008
11.000
10.000
n
n
y
nn
65536
5.4
3195.5
806.4
0
-176.7
0
250
117
12
0.83 0.98
1.06 1.88
0.92
0.89
0.87
1.00 0.99
3.00
3.17
7
6
5
4
3
2
1
ppm
OMe
Me
O
2.46

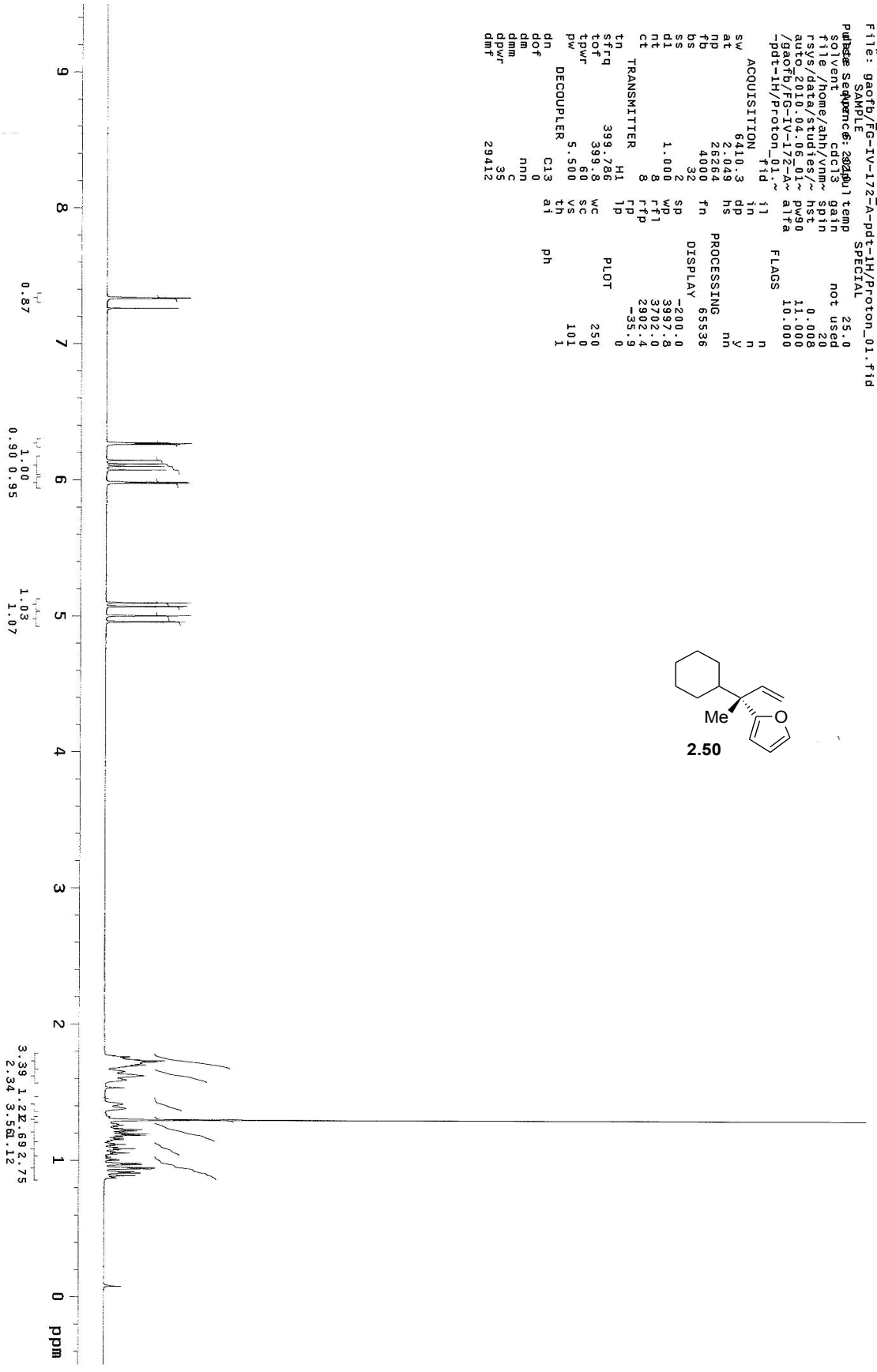

YL-VIII-263-1H
exp1 Proton
SAMPLE
date Nov 23 2009
solvent cdcl3
file exp
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4000
bs 4
ss 2
d1 1.000
nt 40
ct 24
TRANSMITTER
tn H1
sfrq 399.769
tof 399.8
tpwr 59
pw 5.650
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
SPECIAL
temp 25.0
gain not used
spin not used
hst 0.008
pw90 11.300
alfa 10.000
FLAGS
ll n
in n
dp y
hs nn
PROCESSING
fn 65536
DISPLAY
sp 1.7
wp 3206.9
rfl 3703.4
rfp 2902.3
rp -46.5
lp 0
PLOT
wc 250
sc 0
vs 165
th 12
ph
Me
Me
O
2.47
1.76 1.02
1.72
0.96 0.86
0.88
1.00
1.01
2.97
3.28
7
6
5
4
3
2
1
ppm

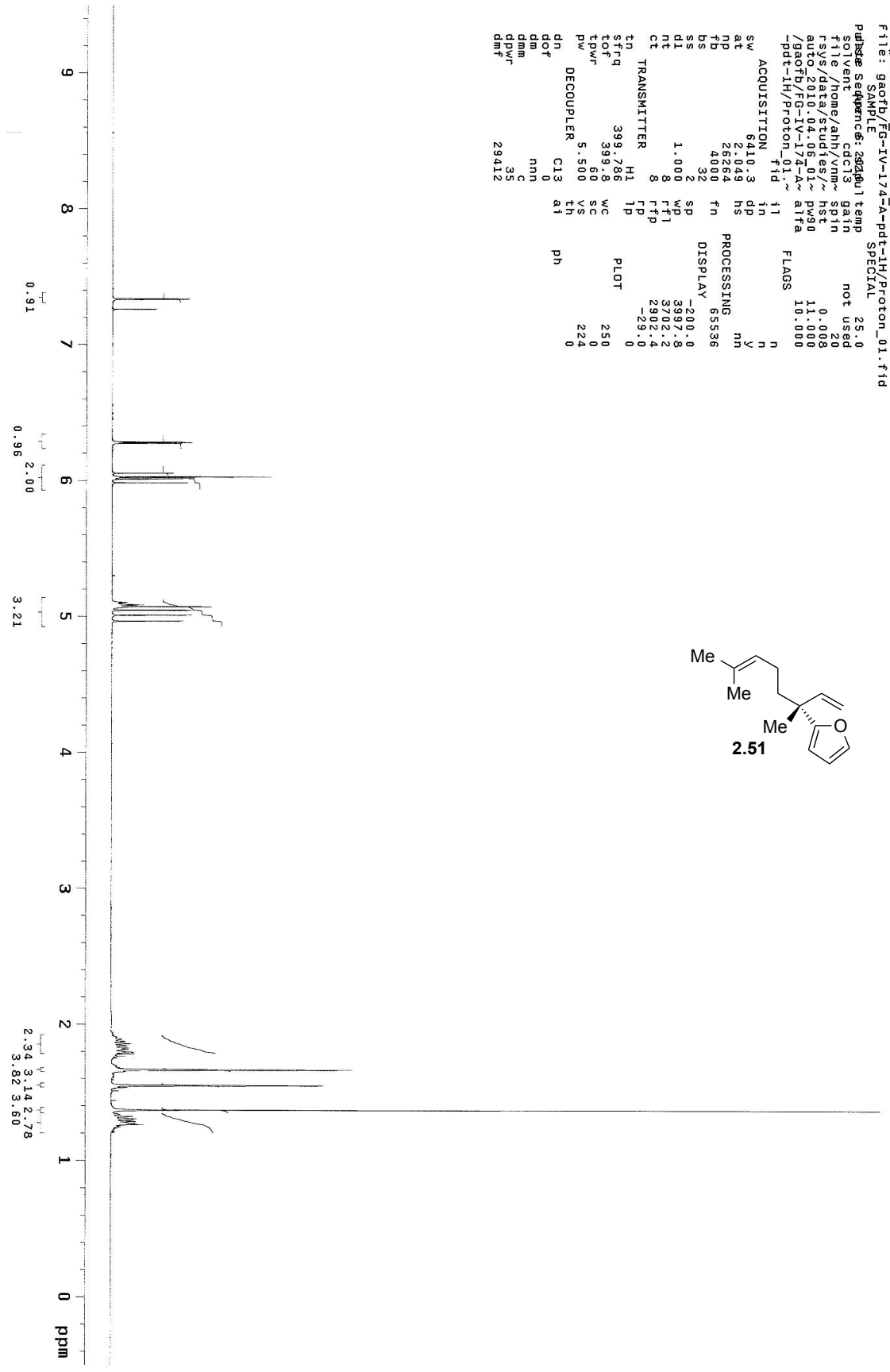

YL-VIII-268B
exp145 Proton
SAMPLE
date Nov 25 2009
solvent cdcl3
file exp
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4000
bs 4
ss 2
d1 1.000
nt 40
ct 24
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
temp
gain
spin
hst
pw90
alfa
FLAGS
PROCESSING
fn
DISPLAY
sp
wp
rfl
rfp
rp
lp
PLOT
sc
vs
th
ai
ph
SPECIAL
25.0
not used
20
0.008
11.000
10.000
n
n
y
nn
65536
-1.4
3597.2
3702.7
2902.4
143.8
0
250
0
167
12
1.78
1.89
0.80
0.90
1.75
0.99
1.00
3.23
ppm

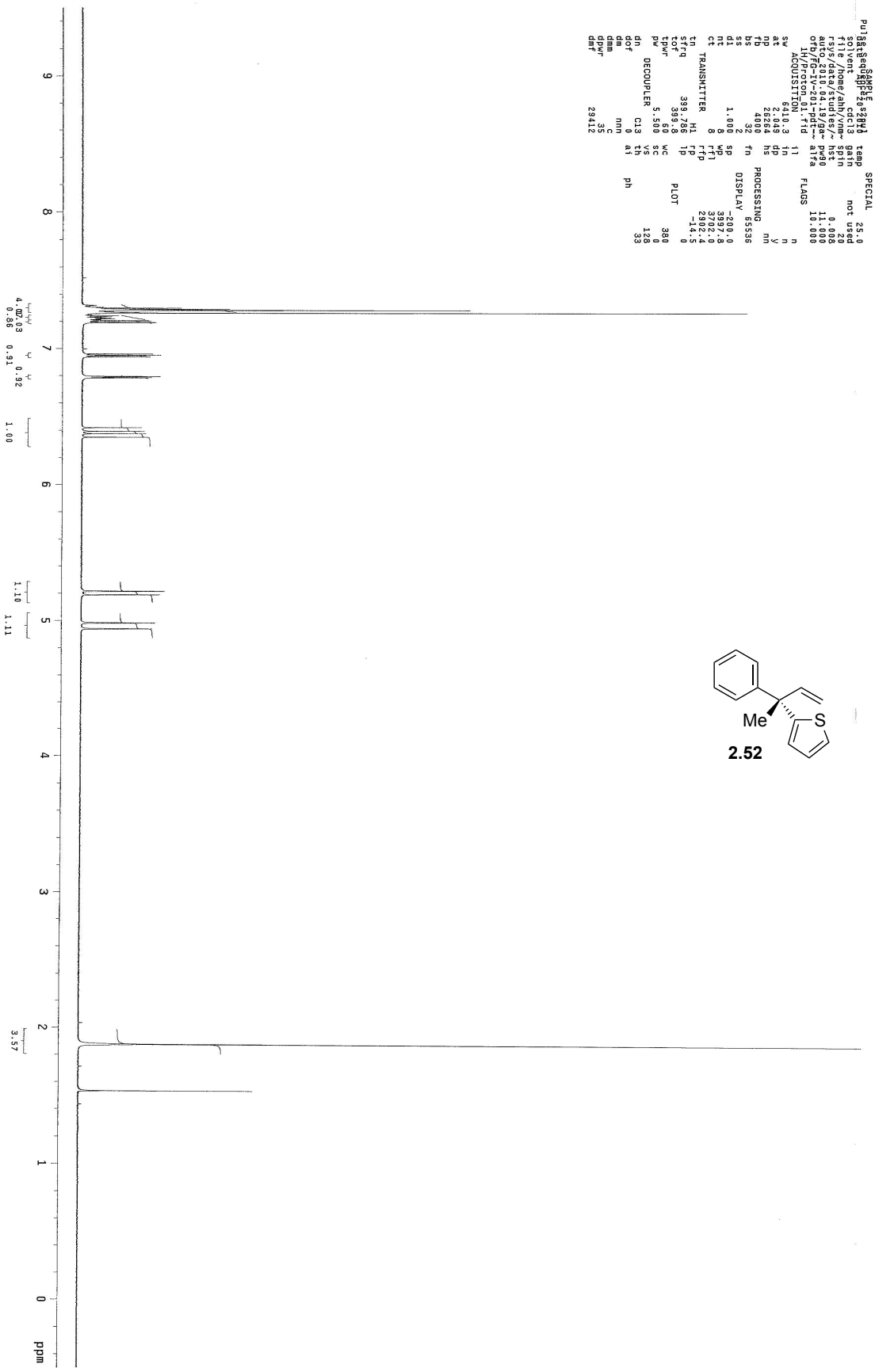
O2N
Me
O

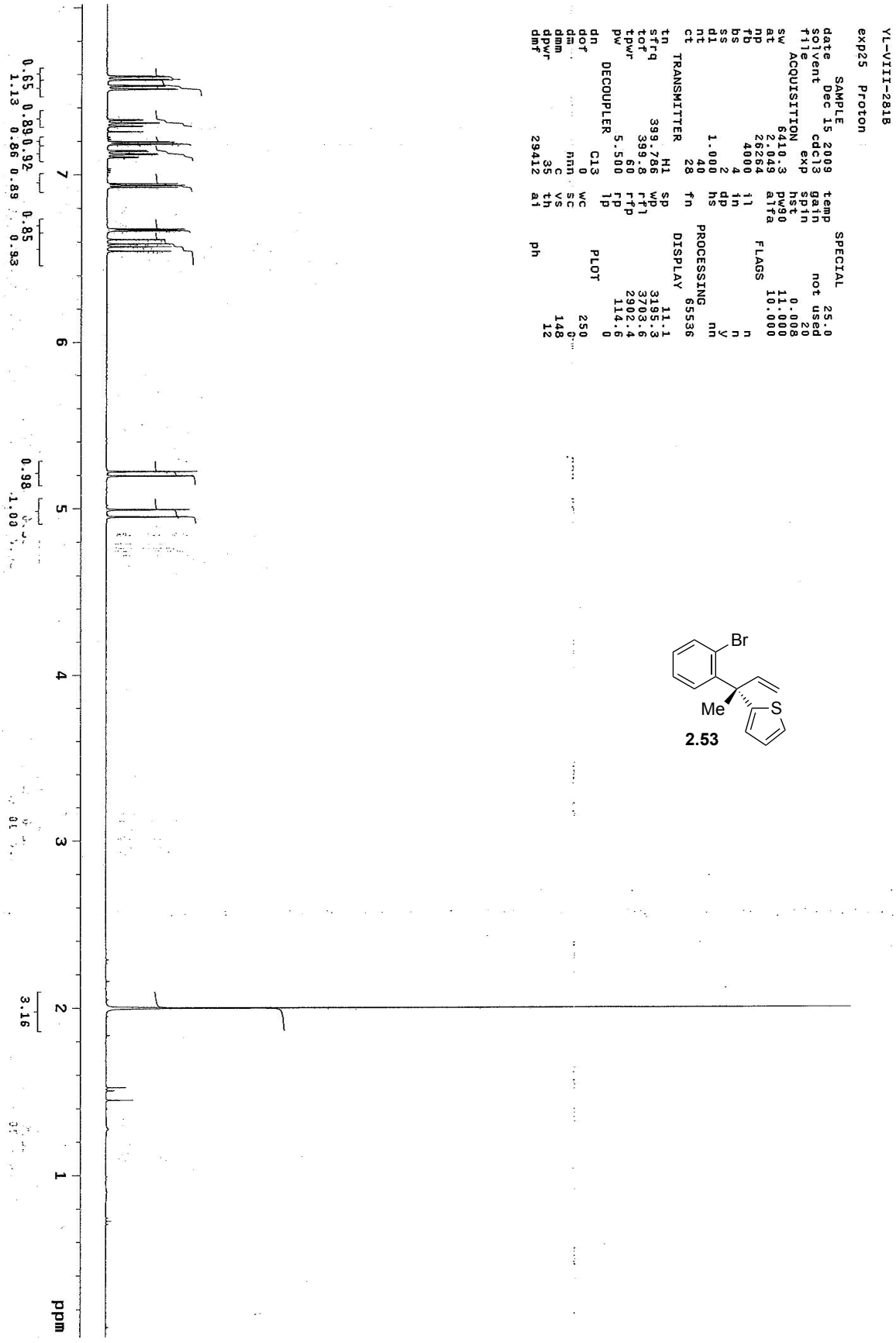
2.48


YL-KM--4-238A
expl Proton
SAMPLE
date Nov 18 2009
solvent cdcl3
file exp
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4000
bs 4
ss 2
d1 1.000
nt 40
ct 40
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
temp
gain
spin
hst
pw90
alfa
FLAGS
PROCESSING
fn
DISPLAY
sp
wp
rfl
rfp
rp
lp
PLOT
wc
sc
vs
th
ai
ph
SPECIAL
25.0
not used
20
0.008
11.000
10.000
n
n
y
nn
65536
5.2
3200.2
3703.4
2902.4
101.1
0
250
0
146
12
6.10
2.02
1.00
1.15
1.17
3.61
6.87
ppm
PhMe2Si
Me
O
2.49


Sample: FG-IV-172-A-pdt-1H
Sample_ID: gaorfb_20100406_001
File: gaorfb/FG-IV-172-A-pdt-1H/Proton_01.fid
SAMPLE
Pulse Sequence: s2pul
solvent cdcl3
file /home/ahh/vnm~
rsys/data/studies/~
auto_2010.04.06_01~
/gaorfb/FG-IV-172-A~
-pdt-1H/Proton_01.~
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4000
bs 32
ss 2
d1 1.000
nt 8
ct 8
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
temp 25.0
gain not used
spin 20
hst 0.008
pw90 11.000
alfa 10.000
FLAGS
il n
in n
dp y
hs nn
PROCESSING
fn 65536
DISPLAY
sp -200.0
wp 3997.8
rfl 3702.0
rfp 2902.4
rp -35.9
lp 0
PLOT
wc 250
sc 0
vs 101
th 1
ai
ph
Me
O
2.50
0.87
1.00
0.90 0.95
1.03
1.07
3.39 1.22 2.69 2.75
2.34 3.56 1.12
9
8
7
6
5
4
3
2
1
0
ppm


Sample: FG-IV-174-A-pdt-1H
Sample ID: Proton_002
File: gaofb/FG-IV-174-A-pdt-1H/Proton_01.fid
SAMPLE
Pulse Sequence: s2pul
solvent cdcl3
file /home/ahh/vnm~
rsys/data/studies/~
auto 2010_04_06_01~
/gaofb/FG-IV-174-A~
-pdt-1H/Proton_01.~
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4000
bs 32
ss 2
d1 1.000
nt 8
ct 8
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
temp 25.0
gain not used
spin 20
hst 0.008
pw90 11.000
atfa 10.000
FLAGS
il n
in n
dp y
hs nn
PROCESSING
fn 65536
DISPLAY
-200.0
3597.8
3202.2
2902.4
-29.0
PLOT
wc 250
sc 0
vs 224
th 0
ai ph
0.91
2.00
0.96
3.21
2.34
3.14
2.78
3.82
3.60
Me
Me
Me
O
2.51
9
8
7
6
5
4
3
2
1
0
ppm


Me
S
2.52
ppm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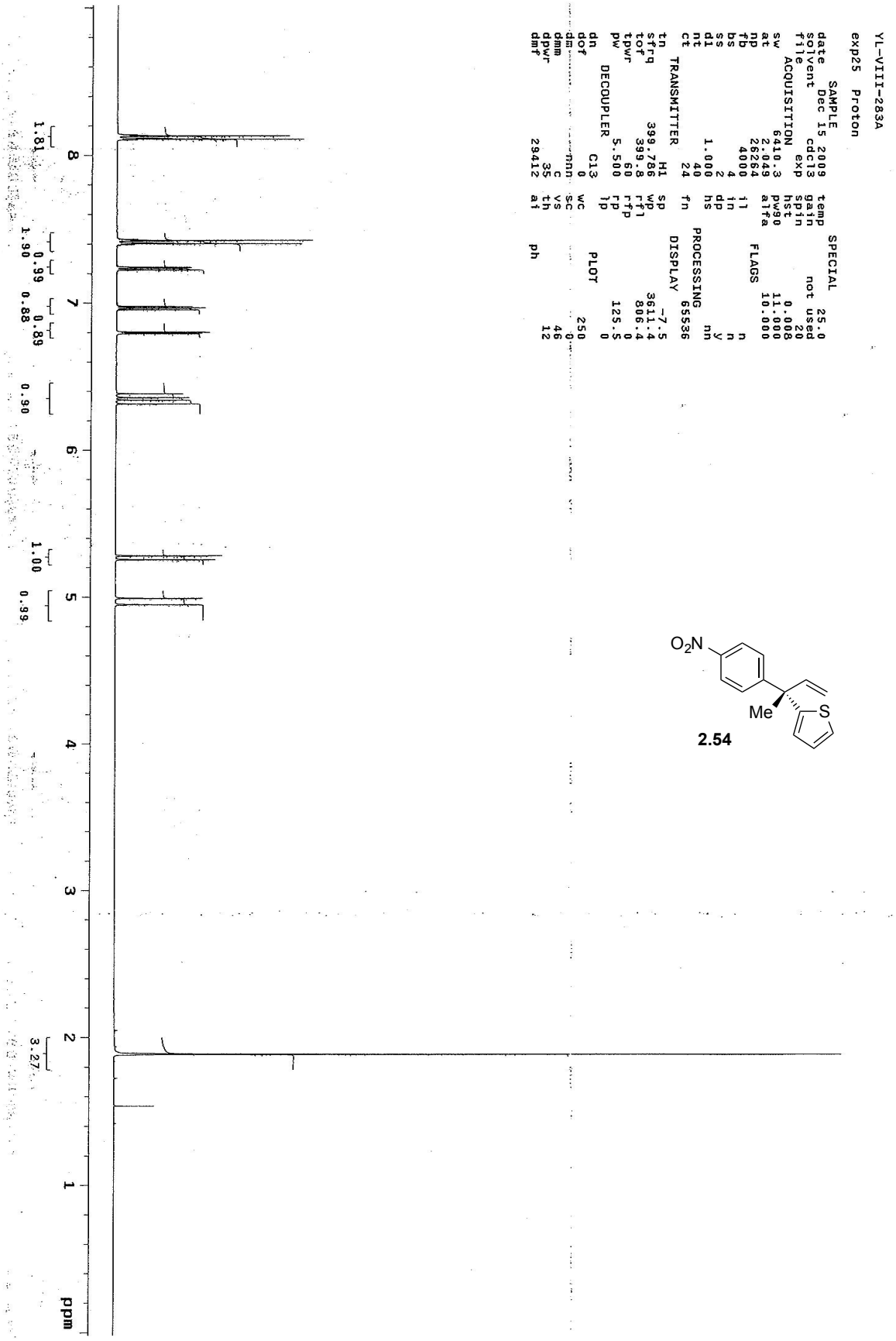
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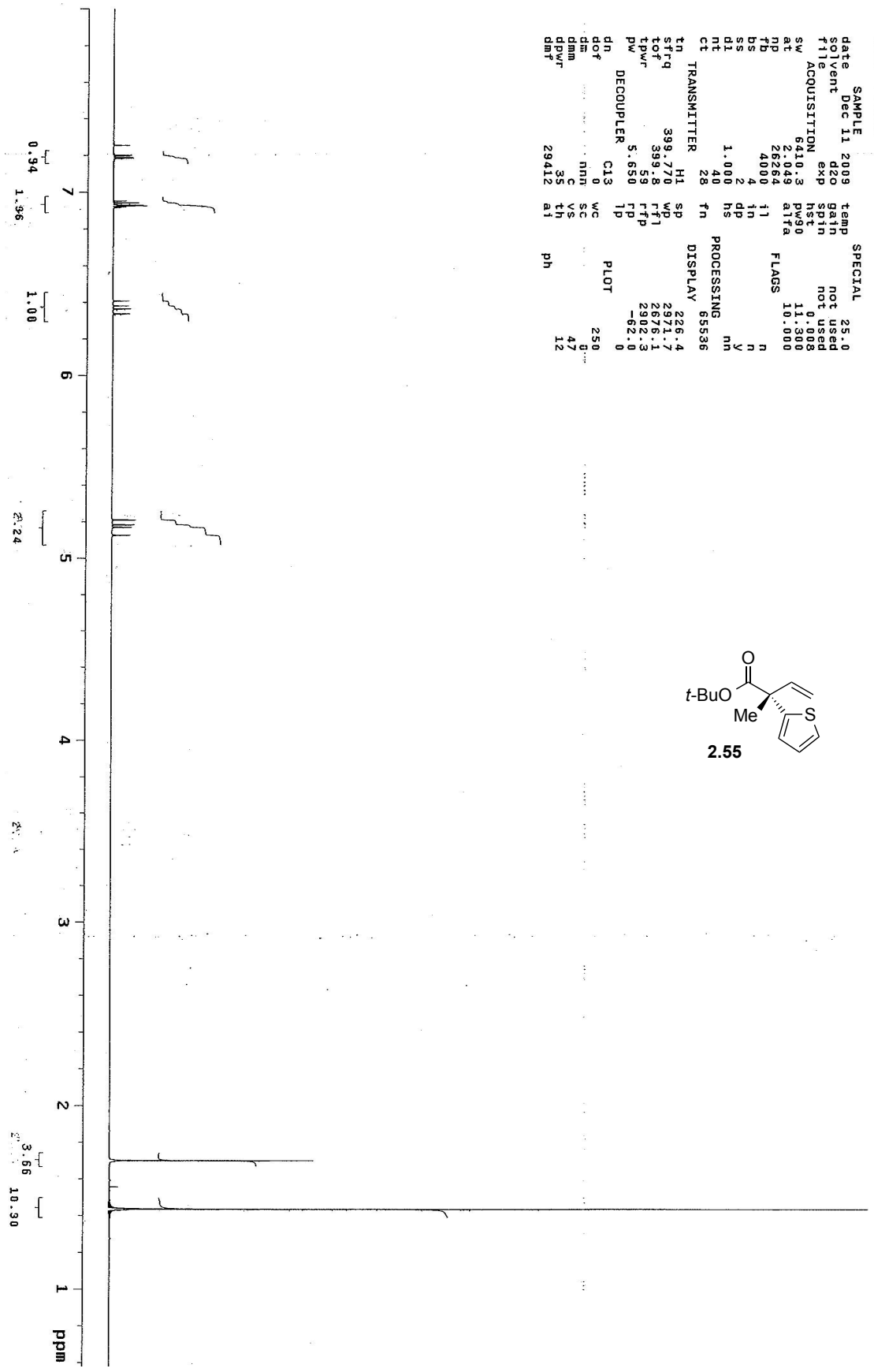
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th
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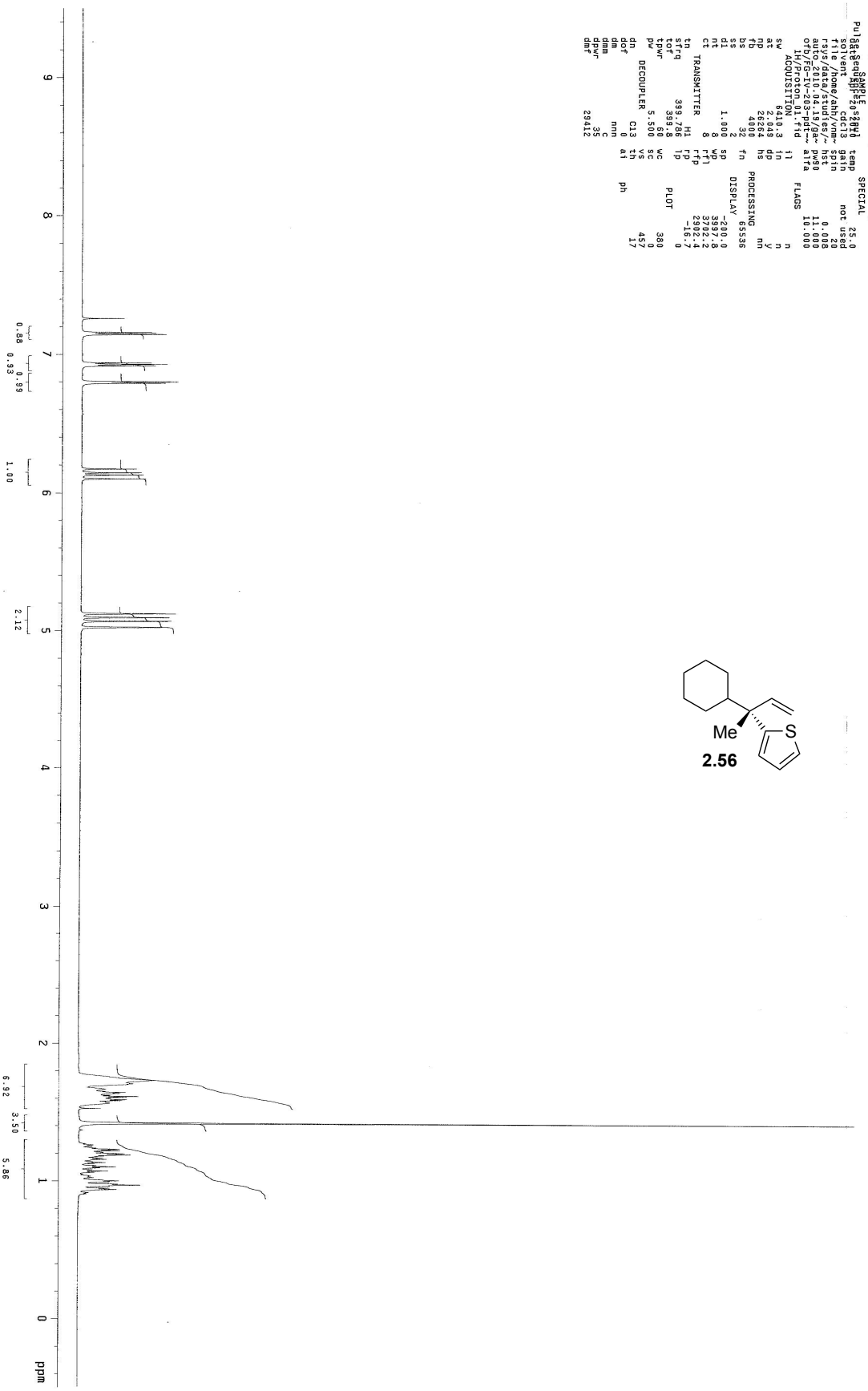
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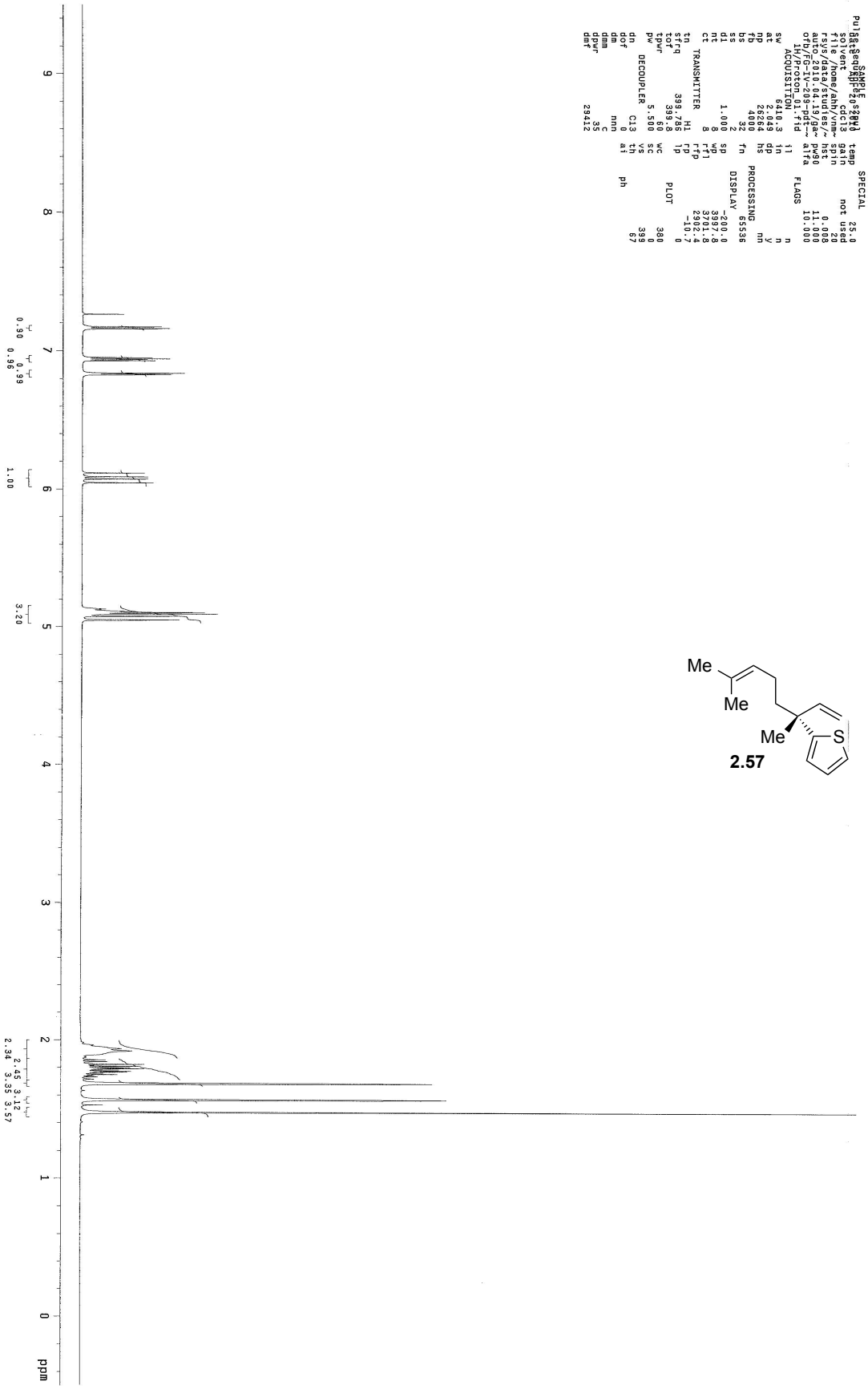
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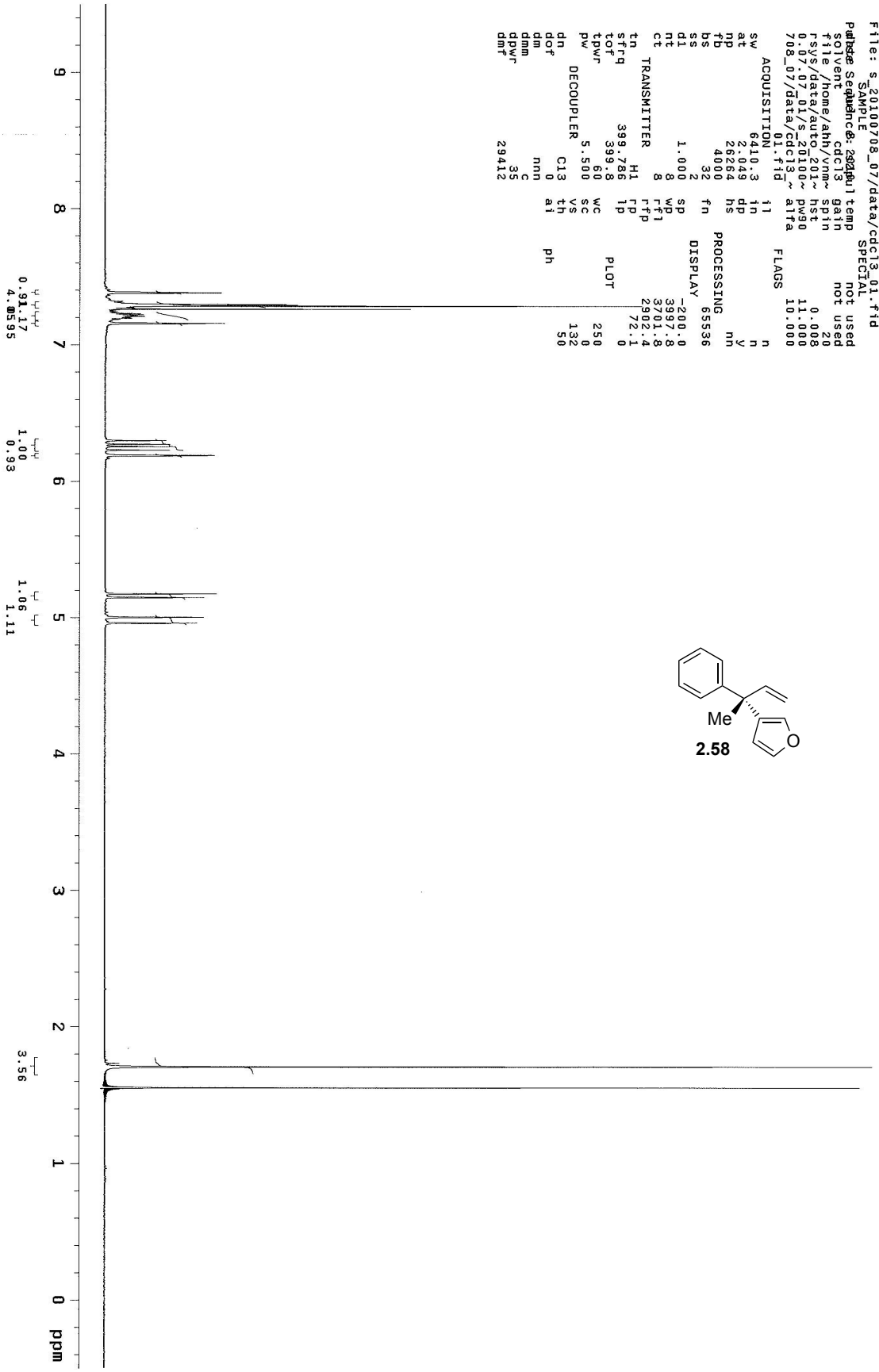
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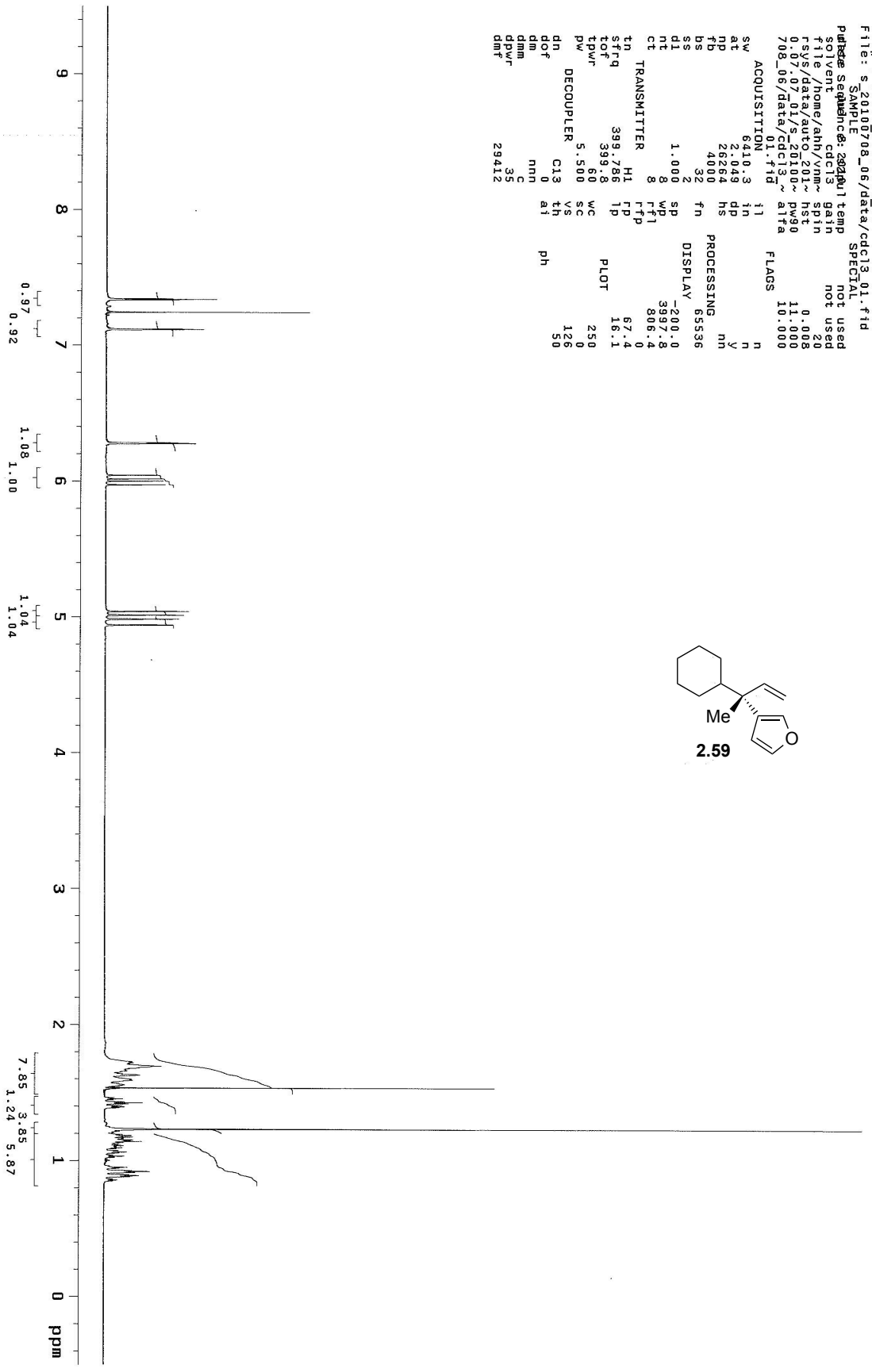
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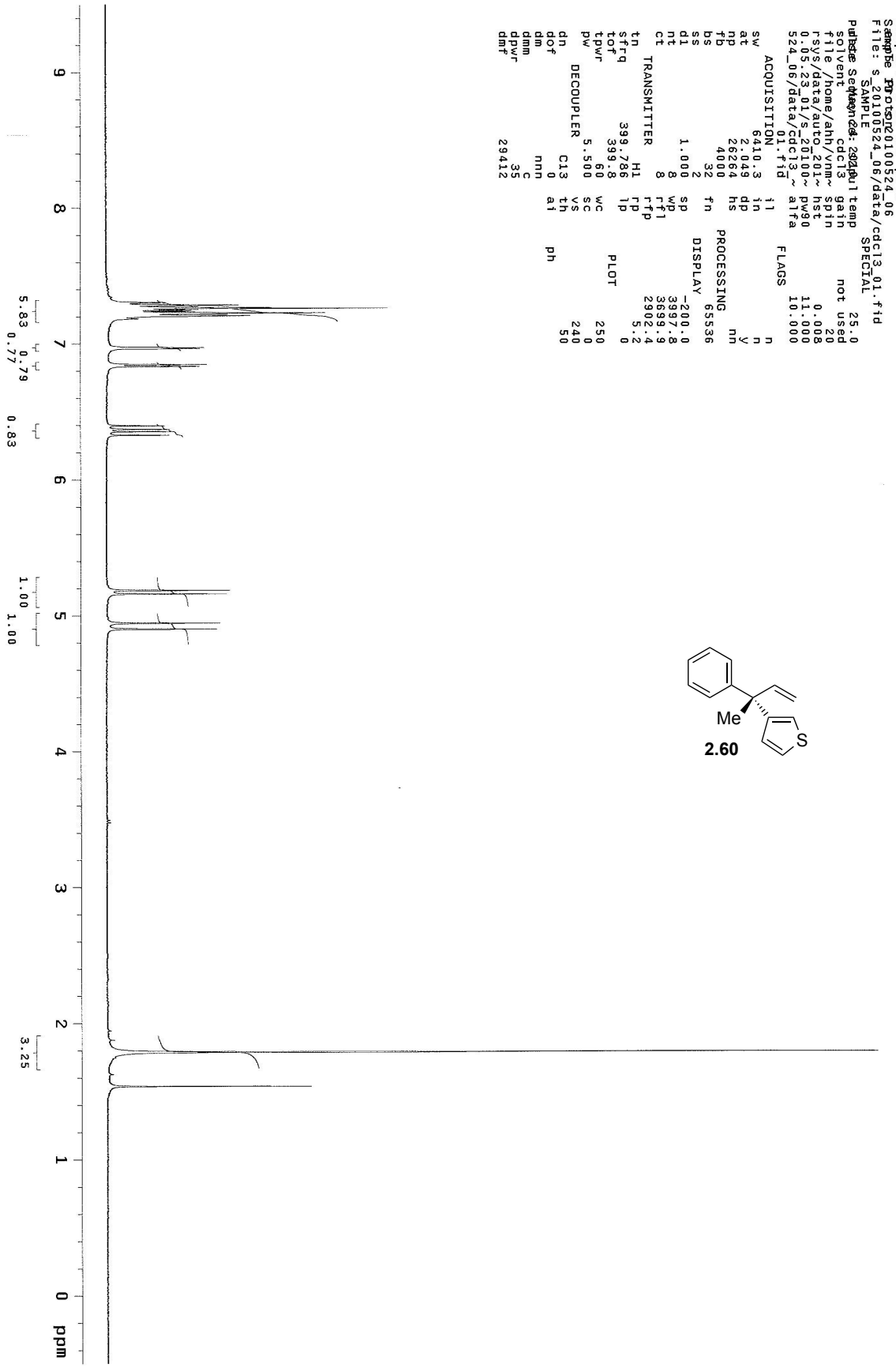
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fb 4000
bs 32
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nt 8
ct 8
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tn H1
sfrq 399.786
tof 399.8
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pw 5.500
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dof 0
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dmm c
dpwr 35
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3699.9
2902.4
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250
0
240
50
wc
sc
vs
th
ai
ph
Me
S
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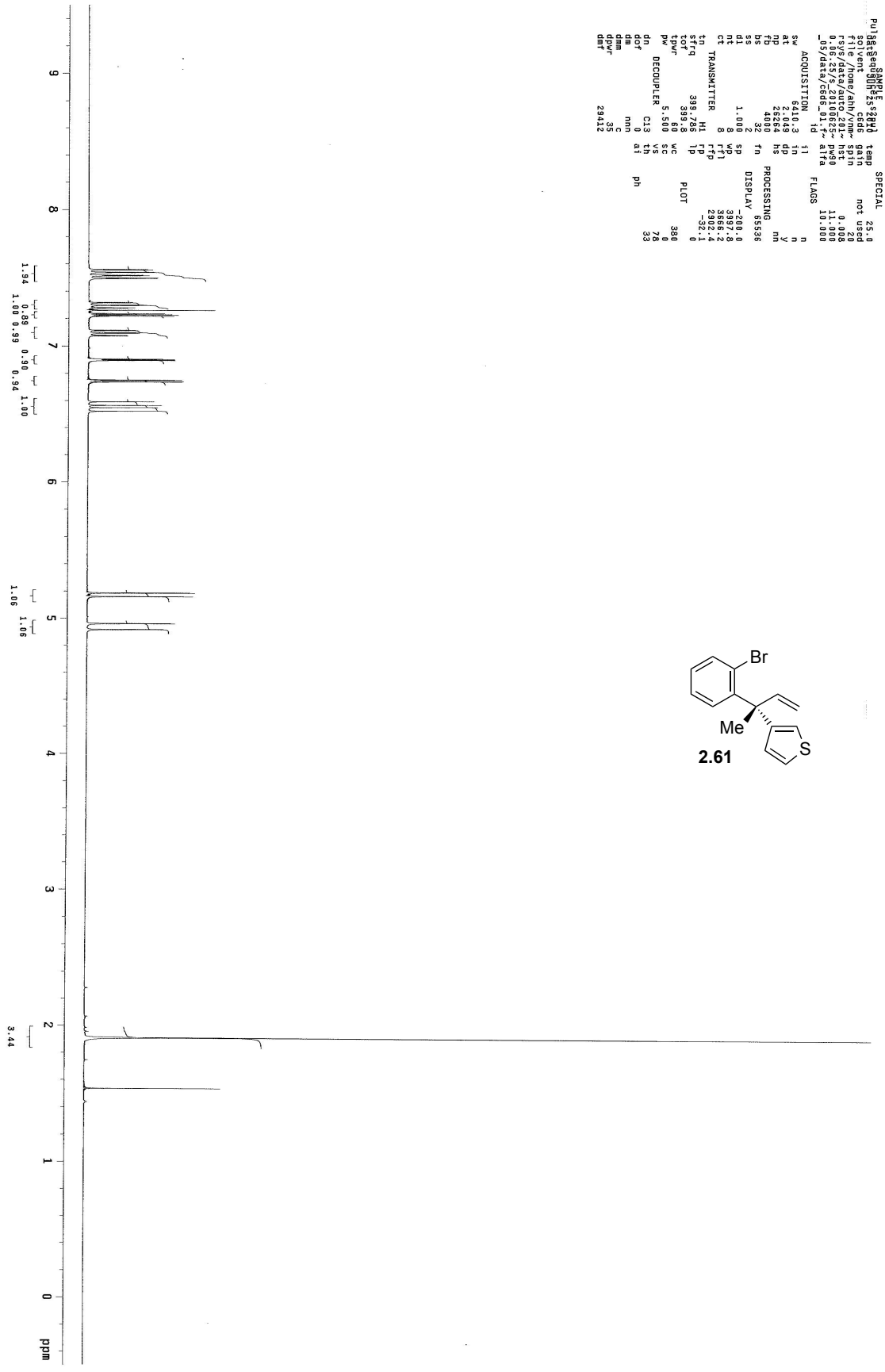
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TRANSMITTER rfp 2902.4
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dof 0 ai
dm nnn ph
dmm c
dmf 35
dpwr 29412
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0.90
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1.00
0.99
0.94
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Me
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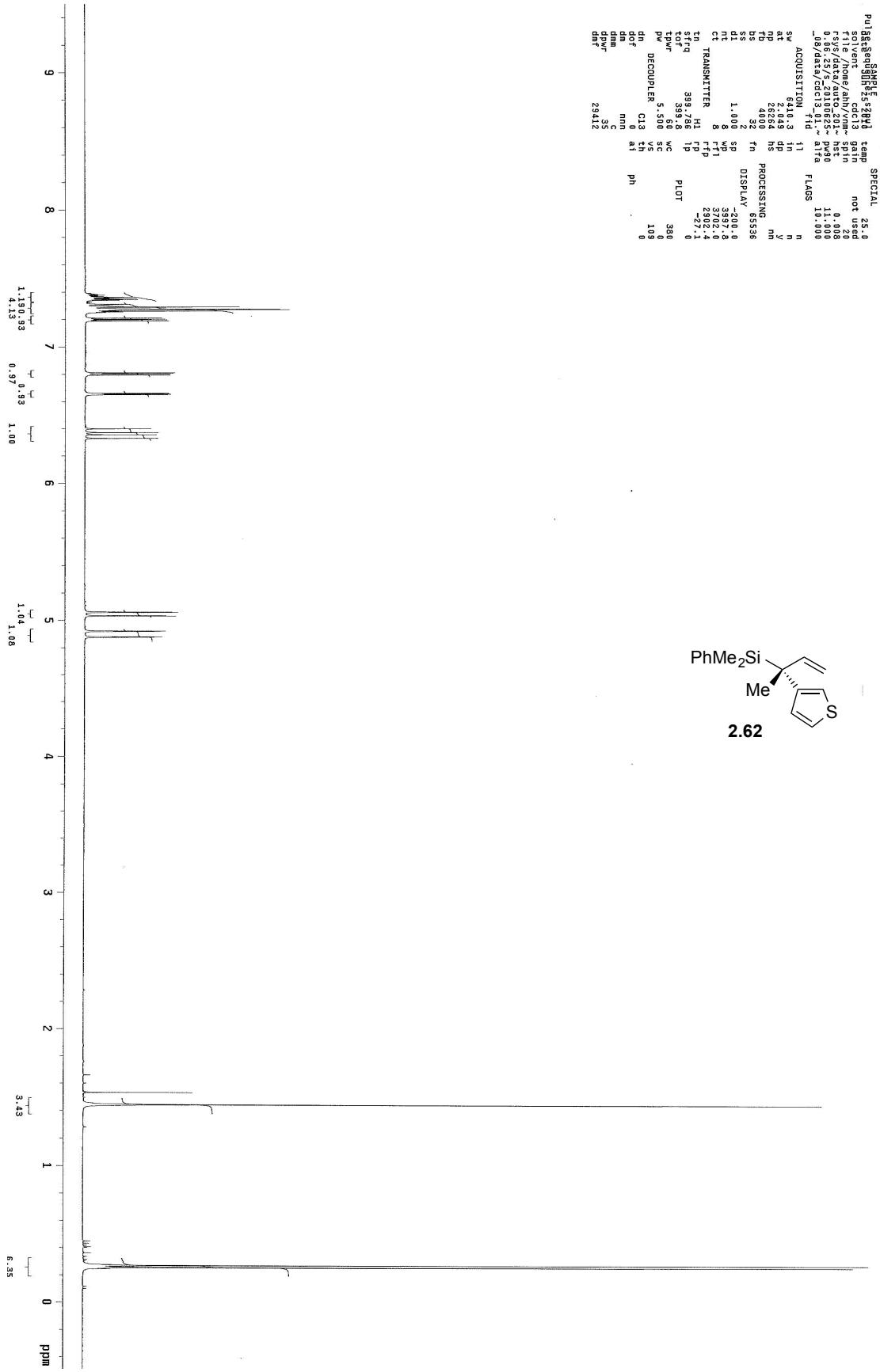
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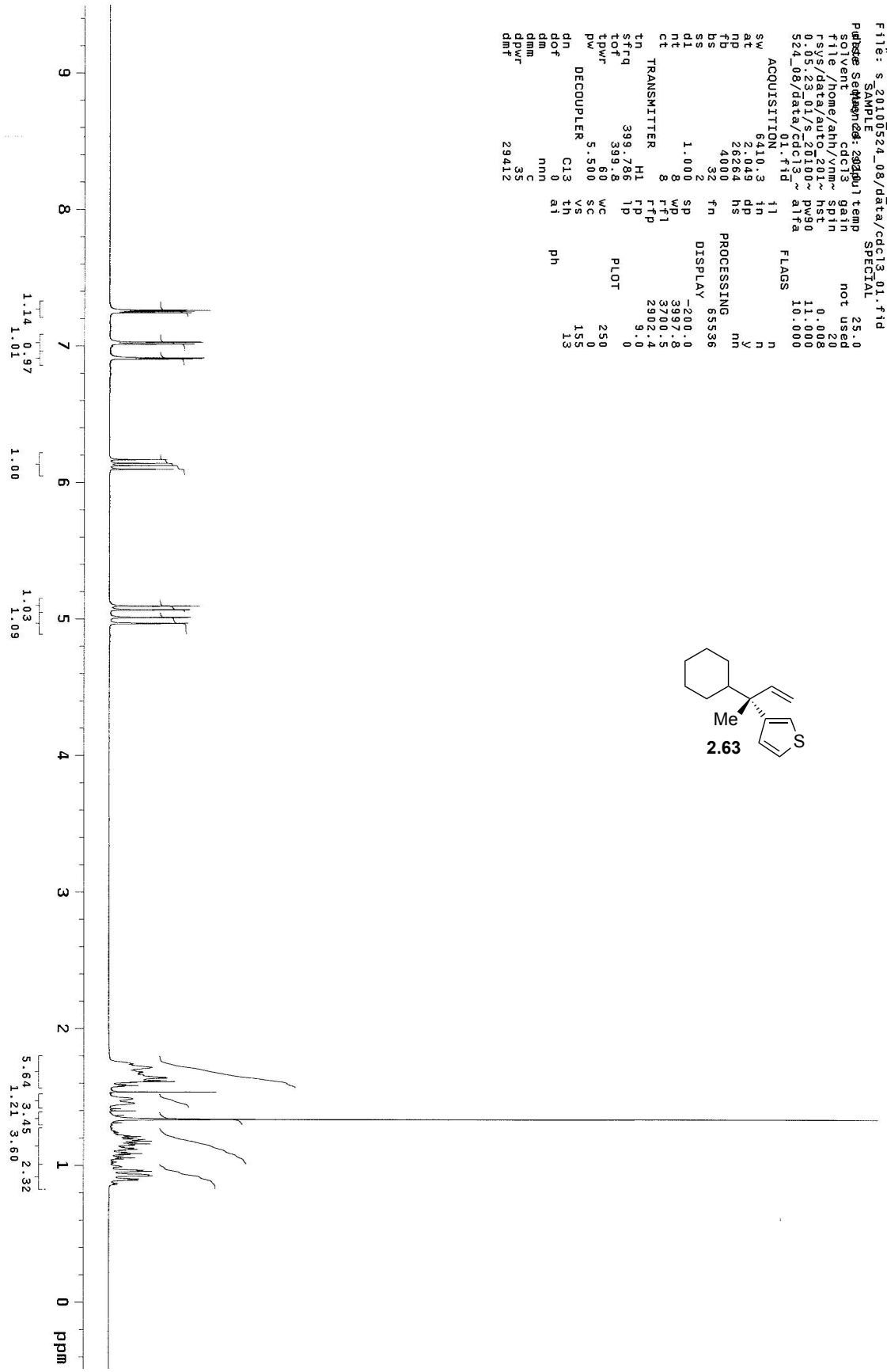
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S
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7
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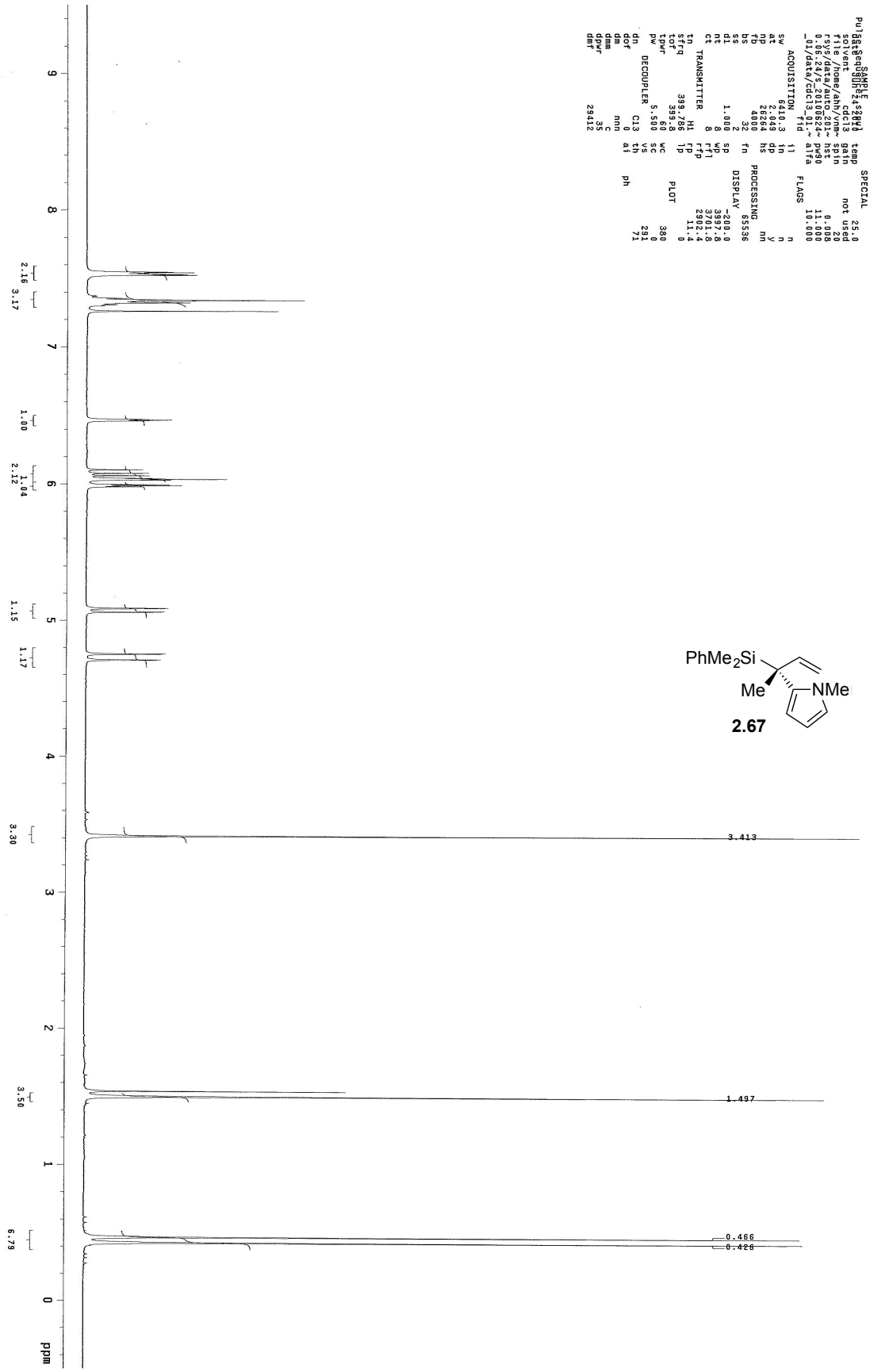
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1.17
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6.79
ppm

Chapter 3

Cu-Catalyzed Enantioselective Allylic Substitutions with Alkenylaluminum Reagents

3.1 Introduction

Catalytic enantioselective addition of alkenyl groups to C-based electrophiles constitutes a versatile class of C-C bond forming processes; up to date, the corresponding reactions with carbonyls,[1] imines[2] and α,β-unsaturated conjugate acceptors[3] have been introduced. Catalytic enantioselective allylic substitution (EAS) reactions,[4] on the other

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(1) For examples of catalytic enantioselective alkenyl additions to carbonyls, see: (a) Oppolzer, W.; Radinov, R. N. *J. Am. Chem. Soc.* **1993**, *115*, 1593–1594. (b) Miller, K. M.; Huang, W.-S.; Jamison, T. F. *J. Am. Chem. Soc.* **2003**, *125*, 3442–3443. (c) Li, H.; Walsh, P. J. *J. Am. Chem. Soc.* **2004**, *126*, 6538–6539. (d) Tomita, D.; Wada, R.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2005**, *127*, 4138–4139. (e) Yang, Y.; Zhu, S.-F.; Zhou, C.-Y.; Zhou, Q.-L. *J. Am. Chem. Soc.* **2008**, *130*, 14052–14053. (f) Kerrigan, M. H.; Jeon, S.-J.; Chen, Y. K.; Carroll, P. J.; Walsh, P. J. *J. Am. Chem. Soc.* **2009**, *131*, 8434–8445. (g) Biradar, D. B.; Gau, H.-M. *Org. Lett.* **2009**, *11*, 499–502.

(2) For examples of catalytic enantioselective alkenyl additions to aldimines, see: (a) Patel, S. J.; Jamison, T. F. *Angew. Chem. Int. Ed.* **2004**, *43*, 3941–3944. (b) Kong, J.-R.; Cho, C.-W.; Krische, M. J. *J. Am. Chem. Soc.* **2005**, *127*, 11269–11276. (c) Ngai, M.-Y.; Barchuk, A.; Krische, M. J. *J. Am. Chem. Soc.* **2007**, *129*, 12644–12645. (d) Lou, S.; Schaus, S. E. *J. Am. Chem. Soc.* **2008**, *130*, 6922–6923. (e) Nakao, Y.; Takeda, M.; Chen, J.; Salvi, L.; Hiyama, T.; Ichikawa, Y.; Shintani, R.; Hayashi, T. *Chem. Lett.* **2008**, *37*, 290–291.

(3) For examples of catalytic enantioselective alkenyl conjugate additions to unsaturated carbonyls, see: (a) Oi, S.; Taira, A.; Honma, Y.; Inoue, Y. *Org. Lett.* **2003**, *5*, 97–99. (b) Oi, S.; Sato, T.; Inoue, Y. *Tetrahedron Lett.* **2004**, *45*, 5051–5055. (c) Otomaru, Y.; Hayashi, T. *Tetrahedron: Asymmetry* **2004**, *15*, 2647–2651. (d) Nicolaou, K. C.; Tang, W.; Dagneau, P.; Faraoni, R.; *Angew. Chem. Int. Ed.* **2005**, *44*, 3874–3879. (e) Nakao, Y.; Chen, J.; Imanaka, H.; Hiyama, T.; Ichikawa, Y.; Duan, W.-L.; Shintani, R.. Hayashi, T. *J. Am. Chem. Soc.* **2007**, *129*, 9137–9143. (f) Vuagnoux-d_Augustin, M.; Alexakis, A. *Chem. Eur. J.* **2007**, *13*, 9647–9662. (g) Lee, K.-s.; Hoveyda, A. H. *J. Org. Chem.* **2009**, *74*, 4455–4462. (h) May, T. L.; Dabrowski, J. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 736–739. (i) Müller, D.; Tissot, M.; Alexakis, A. *Org. Lett.* **2011**, *13*, 3040–3043. (j) Müller, D.; Alexakis, A. *Org. Lett.* **2012**, *14*, 1842–1845. (k) Müller, D.; Alexakis, A. *Chem. Commun.* **2012**, *48*, 12037–12049. (l) Cottet, P.; Müller, D.; Alexakis, A. *Org. Lett.* **2013**, *15,* 828–831. (m) Müller, D.; Alexakis, A. *Org. Lett.* **2013**, *15*, 1594–1597.

(4) For reviews on allylic substituion reactions catalyzed by other transition metals and with "soft" nucleophiles, see: (a) Trost, B. M.; Lee, C. In *Catalytic Asymmetric Synthesis*; Oijima, I., Ed.; Wiley-VCH: Weinheim, Germany, 2000; Chapter 8E. (b) Trost, B. M.; Crawley, M. L. *Chem. Rev.* **2003**, *103*, 2921–2944. (c) Stanley, L. M.; Hartwig, J. F. *Acc. Chem. Res.* **2010** *43*, 1461–1475. (d) Trost, B. M. *Org.*

hand, have only experienced very limited development in terms of utilizing an olefin-based nucleophilic reagent.[5] Among various imaginable organometallic species, alkyl metals are most widely explored in Cu-catalyzed EAS reactions,[6] followed by small numbers of additions involving aryl nucleophiles.[7] Moreover, rare examples are available that deal with the formation of difficult-to-access quaternary stereogenic centers.[8] Therefore, the development of efficient and enantioselective protocols, which effectively incorporate an alkene moiety through Cu-catalyzed allylic substitution to deliver enantioenriched 1,4-dienes bearing tertiary as well as quaternary stereogenic centers, is highly desirable especially since such motifs are often found in many naturally occurring molecules (cf. representative natural products in Figure 3.1).

Process Res. Dev. **2012**, *16*, 185–194. (e) Tosatti, P.; Nelson, A.; Marsden, S. P. *Org. Biomol. Chem.* **2012**, *10*, 3147–3163.

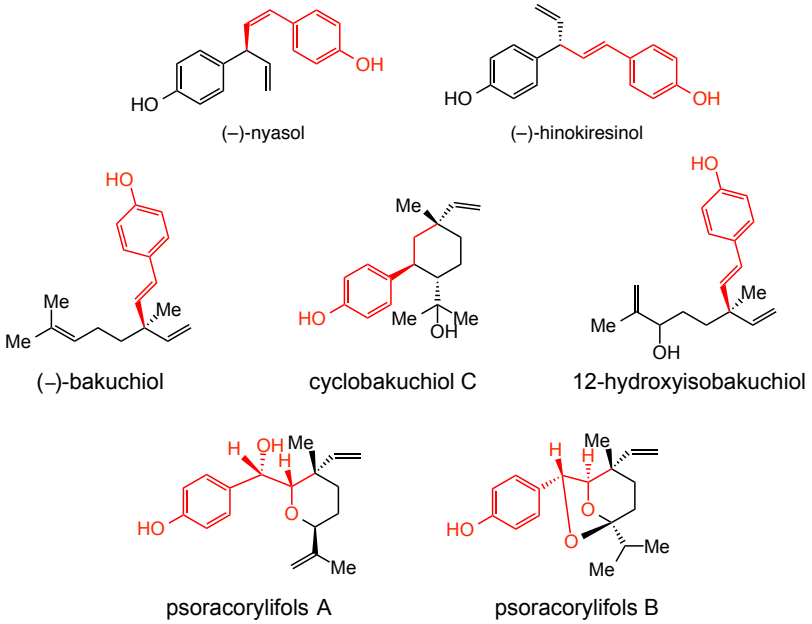
(5) For recent advances in enantioselective allylic substitution involving alkenyl metal reagents, see: (a) Lee, Y.; Akiyama, K.; Gillingham, D. G.; Brown, M. K.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2008**, *130*, 446–447. (b) Gao, F.; McGrath, K. P.; Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 14315−14320. (c) Akiyama, K.; Gao, F.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2010**, *49*, 419–423. (d) Shintani, R.; Takatsu, K.; Takeda, M.; Hayashi, T. *Angew. Chem. Int. Ed.* **2011**, *50*, 8656–8659. (e) Hamilton, J. Y.; Sarlah, D.; Carreira, E. M. *J. Am. Chem. Soc.* **2013**, *135*, 993–997. For a related study involving additions of an allene group, see: (f) Jung, B.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2012**, *134*, 1490–1493.

(6) For reviews on Cu-catalyzed allylic alkylation reactions that involve "hard" alkyl- or arylmetal-based reagents, see: (a) Hoveyda, A. H.; Hird, A. W.; Kacprzynski, M. A. *Chem. Commun.* **2004**, 1779–1785. (b) Yorimitsu, H.; Oshima, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 4435–4439. (c) Falciola, C. A.; Alexakis, A. *Eur. J. Org. Chem.* **2008**, 3765–3780. (d) Alexakis, A.; Bäckvall, J.-E.; Krause, N.; Pàmies, O.; Diéguez, M. *Chem. Rev.* **2008**, *108*, 2796–2823. (e) Harutyunyan, S. R.; den Hartog, T.; Geurts, K.; Minnaard, A. J.; Feringa, B. L. *Chem. Rev.* **2008**, *108*, 2824–2852. (f) Lu, Z.; Ma, S. *Angew. Chem., Int. Ed.* 2**008**, *47*, 258–297. (g) Langlois, J. -B.; Alexakis, A. *Topics in Organometallic Chemistry* **2012**, *38*, 235–268.

(7) For examples, see: (a) Kacprzynski, M. A.; May, T. L.; Kazane, S. A.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 4554–4558. (b) Alexakis, A.; Hajjaji, S. E.; Polet, D.; Rathgeb, X. *Org. Lett.* **2007**, *9*, 3393–3395. (c) May, T. L.; Brown, M. K.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2008**, *47*, 7358–7362. (d) Selim, K. B.; Yamada, K-i.; Tomioka, K. *Chem. Commun.* **2008**, 5140–5142. (e) Falciola, C. A.; Alexakis, A. *Chem. Eur. J.* **2008**, *14*, 10615–10627; (f) Selim, K. B.; Matsumoto, Y.; Yamada, K-I.; Tomioka, K. *Angew. Chem. Int. Ed.* **2009**, *48*, 8733–8735. (g) Polet, D.; Rathgeb, X.; Falciola, J C.; Langlois, A. B.; Hajjaji, S. E.; Alexakis, A. *Chem. Eur. J.* **2009**, *15*, 1205–1206. (h) Gao, F.; Lee, Y.; Mandai, K.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2010**, *49*, 8370–8374. (i) ref. 5 (d).

(8) Das, J. P.; Marek, I. *Chem. Commun.* **2011**, *47*, 4593–4623.

Figure 3.1. Natural Products that Bear an Aryl-substituted Alkene Adjacent to A Tertiary or Quaternary Stereogenic Center.



In addition to the challenging identifications of a set of chiral ligands that are applicable in promoting such proposed reactions, we envision that readily accessibility to the requisite alkenyl metal reagents would offer higher chance of success in reaction development. The Hoveyda group has recently reported the use of alkyl-substituted alkenylaluminum reagents in the formation of tertiary C-C bond through Cu-catalyzed EAS;[5a] hydroalumination of the corresponding terminal alkynes[9] provides the nucleophiles, which can be easily employed in the subsequent bond forming processes without further purification. Although it is effective with alkyl-substituted acetylenes, such reactions are unreliable towards utilization of aryl alkynes, which bear more acidic protons.[10] In order to secure a broad scope of catalyzed EAS with alkenyl metals, new

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(9) For a review on hydroaluminations of alkynes and alkenes, see: Eisch, J. J. In Comprehensive Organic Synthesis; Trost, B. M., Fleming, I., Schreiber, S. L., Eds.; Pergamon, Oxford, 1991; Vol. 8, pp 733–766.
(10) (a) Zweifel, G.; Snow, J. T.; Whitney, C. C. *J. Am. Chem. Soc.* **1968**, *90*, 7139−7140. (b) Uhl, W.; Er, E.; Hepp, A.; Kösters, J.; Grunenberg, J. *Organometallics* **2008**, *27*, 3346−3351. (c) Uhl, W.; Er, E.; Hepp, A.; Kösters, J.; Layh, M.; Rohling, M.; Vinogradov, A.; Würthwein, E.-U.; Ghavtadze, N. *Eur. J. Inorg. Chem.* **2009**, 3307−3316.

procedures have to be introduced to address the inefficiency assoaciated with hydroalumination of aryl-substituted triple bonds. Here in this chapter, we describe our efforts in developing catalytic C-C bond forming reactions between allylic phosphates with various substitution patterns and alkenylaluminums; the novel catalytic synthesis of the nucleophilic reagents are also delineated.

3.2 Background

In 2008, the Hoveyda laboratories have devised a project targeting the additions of alkenyl metal reagents to allylic phosphates,[5a] taking the advantage of recent progress in the use of Al-based organometallic reagents (cf. the synthesis of baconipyrone C[11] in Section 1.2 of Chapter 1) in combination with the sulfonate bearing NHC–Cu complexes as catalysts in allylic substitution. The inspiration of the chosen surrogate of a nucleophilic alkenyl unit came from a reaction known in literature for over half a century; treatment of a terminal alkyne with one equivalent of di*iso*butylaluminum hydride in hydrocarbon solvent results in hydroalumination reaction across the triple bond.[9] Exclusive *trans* 1,2-disubstituted alkenylaluminum species thus generated can be used directly without further purification as a homogeneous solution. The class of substrates that we pick is the trisubstituted allylic phosphates that bear a β-substitution, which are notoriously unreactive in Cu-catalyzed EAS reactions.[12] Indeed, as evidenced in Scheme 3.1, most of the representative conditions tested are ineffective at all in promoting such transformations, including catalytic amount of copper salts, in situ mixing of

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(11) Gillingham, D. G.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 3860–3864.
(12) Falciola, C. A.; Tissot-Croset, K.; Alexakis, A. *Angew. Chem., Int. Ed.* **2006**, *45*, 5995-5998.

monodentate Ag-carbene **3.6**, bidentate phenoxide-based NHC–Ag complexes (cf. **3.7**[13] and **3.8**[14]) with $CuCl_2 \bullet 2H_2O$; <2% conversion of allylic phosphate **3.2** are observed in all cases. In contrast, in the presence of 1.0 mol % in situ generated sulfonate-bridged Cu complex derived from **3.9**,[15] the EAS reaction proceeds to completion within three hours at –15 ˚C, affording the desired 1,4-diene **3.3** in 87% yield and >98:2 e.r. No detection of any linear byproduct (<2% S_N2) or the incorporation of the isobutyl group (>98% alkenyl transfer). The drastic increase in reactivity observed with the introduction of a sulfonate secondary binding point is noteworthy; the new chiral catalyst (i.e., **3.9**, Scheme 3.1) not only provides high enantioselectivity but also induces exceptional reactivity in Cu-catalyzed EAS with alkenylaluminum reagents.

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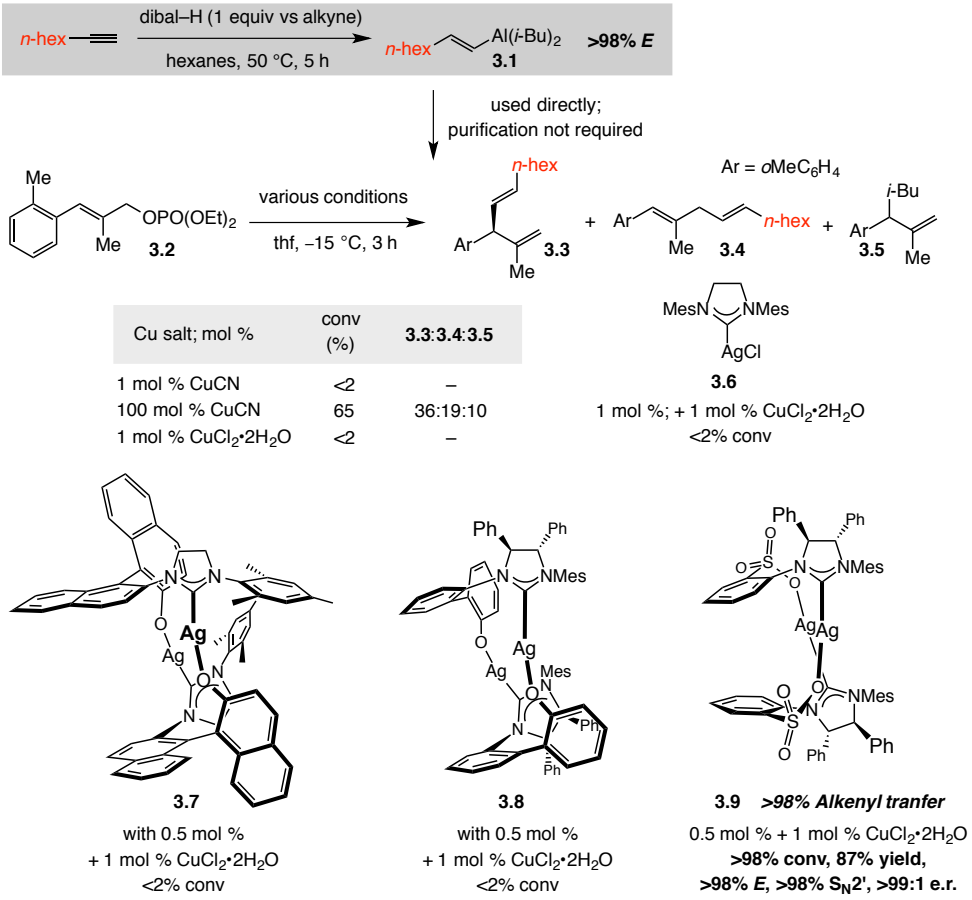
(13) Larsen, A. O.; Leu, W.; Oberhuber, C. N.; Campbell, J. E.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2004**, *126*, 11130–11131.
(14) Van Veldhuizen, J. J.; Campbell, J. E.; Guidici, R. E.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2005**, *127*, 6877–6882.
(15) For the first disclosure of these NHCs, see: (a) Brown, M. K.; May, T. L.; Baxter, C. A.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 1097–1100. For their applications in Cu-catalyzed conjugate additions, see: (b) ref. 7 (c). (c) Brown, M. K.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2008**, *130*, 12904–12906. (d) ref. 3 (h). (e) Dabrowski, J. A.; Villaume, M. T.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2013**, *52*, 8156–8159.

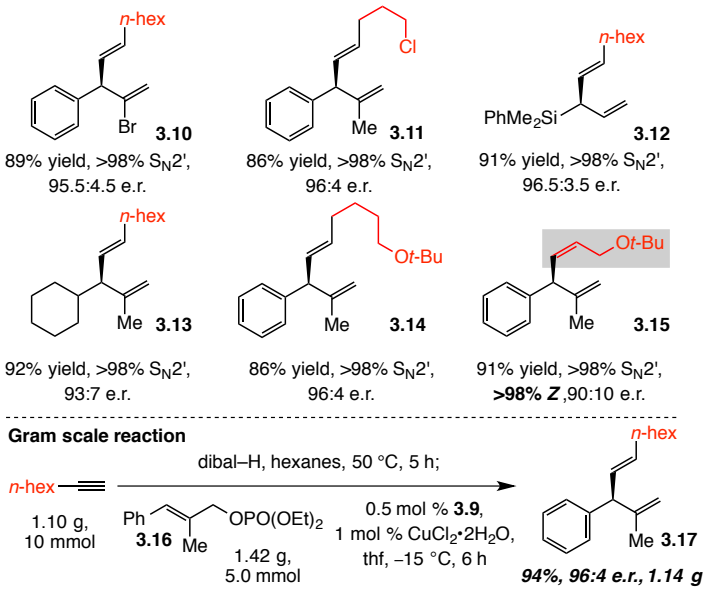
Scheme 3.1. Cu-Catalyzed EAS with In Situ Formed Alkyl-substituted Akenylaluminum Reagents.



Additional examples (cf. **3.10**–**3.15**) shown in Scheme 3.2 highlight the generality of the above protocol. A few points merit further mention: 1) The EAS reaction tolerates vinylbromide, alkylchloride, alkylether and allylsilane functionalities. 2) Aryl- as well as alkyl-substituted allylic phosphates serve as good substrates; high yields (86–92%) and excellent site selectivity (>98% S_N2' in all cases) are usually obtained. 3) The modular nature of the NHC allow maximal secure of the e.r. value whenever **3.9** does not deliver satisfied selectivity. 4) Hydroalumination of *t*-butyl propargyl ether generates alkenylaluminum reagent in exclusive *Z* isomer and such stereochemical information can be transferred without loss of isomeric purity through Cu-catalyzed EAS (cf. >98% *Z* in

3.15). 5) The reaction can be easily performed at gram scale with minimal use of organic solvent to furnish the desired 1,4-diene product **3.17** in 94% yield and 96:4 e.r.

Scheme 3.2. Scope of Cu-Catalyzed EAS with Alkenylaluminum Reagents.

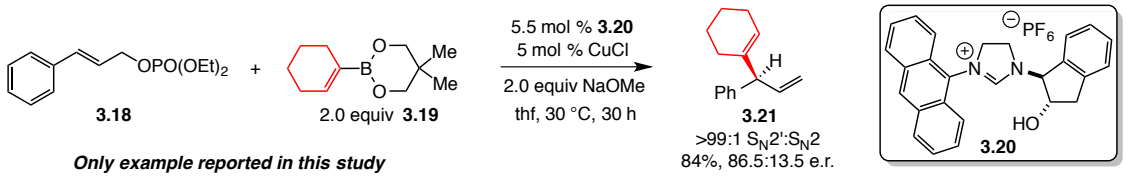


In 2011, Hayashi and co-workers disclosed the first examples of NHC–Cu-catalyzed enantioselective allylic substitution reactions of arylboronic acid neopentyl glycol esters to a number of allylic phosphates.[5d] Among many cases centered on aryl additions, one example of the formation of a cyclohexenyl substituted tertiary stereogenic center containing compound has been delineated. As shown in Scheme 3.3, subjection of boron reagent **3.19** to the reaction with substrate **3.18** in the presence of 5 mol % of an in situ generated NHC–Cu complex, derived from an alkoxide containing bidentate imidazolinium salt **3.20**,[16] results in the formation of 1,4-diene **3.21** that bears tertiary stereocenter in 84% yield and 86.5:13.5 enantiomer ratio. Such transformations, albeit

(16) (a) Martin, D.; Kehrli, S.; d'Augustin, M.; Clavier, H.; Mauduit, M.; Alexakis, A. *J. Am. Chem. Soc.* **2006**, *128*, 8416–8417. (b) Germain, N.; Magrez, M.; Kehrli, S.; Mauduit, M.; Alexakis, A. *Eur. J. Org. Chem.* **2012**, 5301–5306. (c) Magrez, M.; Le Guen, Y.; Baslé, O.; Crévisy, C.; Mauduit, M. *Chem. Eur. J.* **2013**, *19*, 1199–1203.

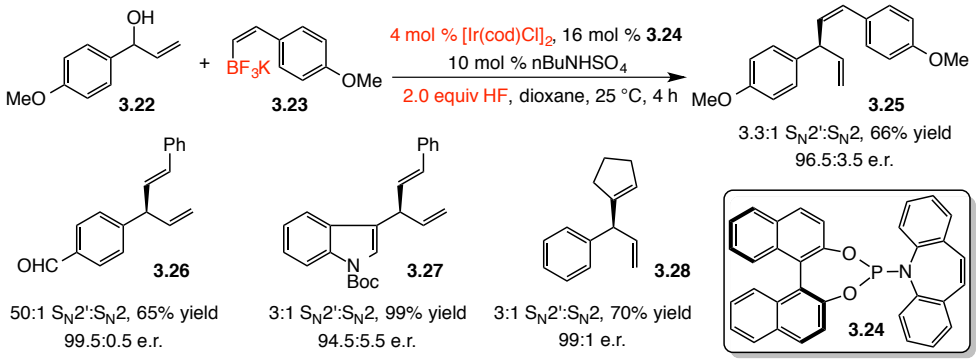
lower in selectivity, demonstrate the potential of utilizing robust and much less nucleophilic organoboron reagents, activated by alkoxide base, in Cu-catalyzed EAS.

Scheme 3.3. Enantioselective Cu–catalyzed Allylic Subsitution with Cyclic Alkenylboronic Acid Neopentylglycol Esters.



Carreira and colleagues have recently showcased that Ir-phosphoramidite complexes can induce stereogenicity in the coupling reactions of racemic secondary aryl-substituted allylic alcohols and sp2 and sp hybridized potassium trifluoroborate salts.[5e] One case that is directly pertinent to the interest of this chapter is analyzed in Scheme 3.4. Racemic allylic alcohol **3.22**, which is derived from the corresponding aromatic aldehyde through reactions with the vinyl Grignard reagent, reacts with potassium alkenyltrifluoroborate **3.23** in the presence of 8 mol % in situ formed Ir complex of phosphoramidite **3.24** to deliver 1,4-diene **3.25** in 66% yield and 96.5:3.5 e.r. Site selectivity of this transformation, however, is only moderate, affording ~23% achiral linear adduct; such phenomena can also be observed in the cases of the formations of compounds **3.27** and **3.28**. Furthermore, the use of boron based nucleophilic reagents demonstrates the good level of compatibility with functional groups, such as an aldehyde (cf. **3.26**, Scheme **3.3**); although in this particular case with trifluoroborate salt, stoichiometric hydrogen fluoride is required to achieve efficiency.

Scheme 3.4. Ir–catalyzed Enantioselective Allylic Subsitution with Potassium Alkenyltrifluoroborate.



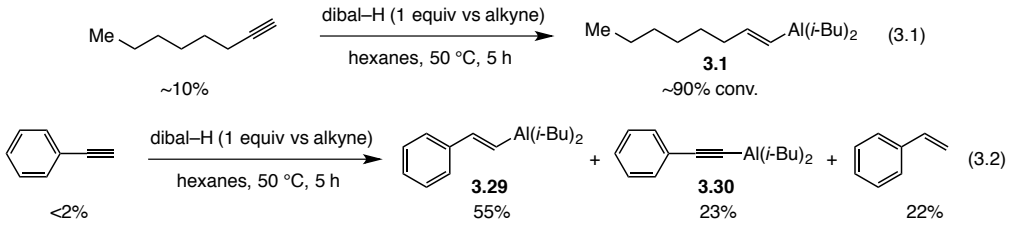
3.3 NHC–Cu-catalyzed EAS with Silyl-substituted Alkenylaluminum Reagents

3.3.1 Identification of Efficient Protocols for Hydroalumination of Silyl-substituted Acetylenes

One shortcoming of the traditional hydroalumination is the impractical synthesis of aryl-substituted alkenylaluminum species; such an issue is highlighted in Scheme 3.5, in which the data suggest that whereas the treatment of dibal-H with 1-octyne results in 90% conversion cleanly to the desired trans-alkenylaluminum reagent **3.1**, the corresponding reaction with phenylacetylene delivers a mixture of products. The more acidic proton (by ~1000 times) of aryl-substituted alkyne causes the adventitious deprotonation when it meets the basic alkenylaluminum **3.29** generated during the course of the reaction; alkynylaluminum **3.30** is thus formed as an accompany along with styrene.[10] Such a complication will subsequently be reflected in the product mixture after Cu-catalyzed EAS (see below), which furnishes a pair of inseparable compounds that

derive from the additions of both the alkenyl- and alkynylaluminum reagents[17] simultaneously.

Scheme 3.5. Different Reactivity Profiles of Hydroalumination of Alkyl- vs. Aryl-substituted Acetylenes.



The first resort that we seek to address this issue is to protect the aromatic acetylenes with a silicon group at the terminus. Selective hydroalumination can be achieved with silicon substituted internal alkynes, the silyl group of which controls the regioselectivity of the uncatalyzed hydroalumination.[18] As demonstrated in Scheme 3.6, under seemingly very similar conditions, acetylene **3.31** undergoes hydroalumination with complete conversions within two hours, however delivering two distinct products (**3.32** vs. **3.33**) in >98% selectivities. The only difference is the existence of a coordinating solvent thf. Rationales for such a phenomenon likely consist of three aspects: 1) the availability of an empty p orbital in the aluminum metal significantly delocalizes the electron density in the double bond, thus rendering it a more single bond character; 2) the phenyl as well as the silicon substituents stabilize the incipient carbocation and lower the energy barrier towards to the formation of such entities (cf. **3.35**); 3) the steric repulsion between the sizable Si and an aryl unit further facilitate the

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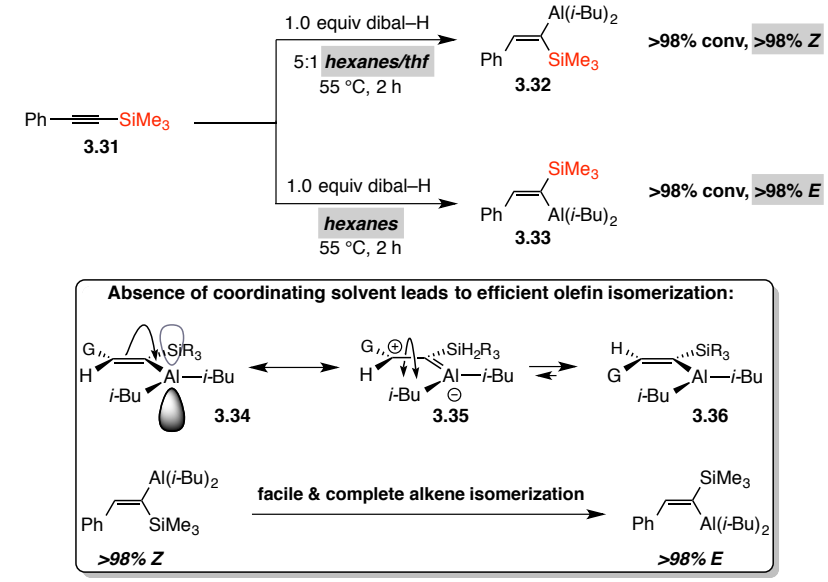
(17) For Cu-catalyzed EAS with alkynylaluminum reagents, see: (a) Dabrowski, J. A.; Gao. F.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 4778−4781. (b) Dabrowski, J. A.; Haeffner, F.; Hoveyda A. H. *Angew. Chem., Int. Ed.* **2013**, *52*, 7694–7699.

(18) For a review regarding stereoselective synthesis through the use of Si-containing compounds, see: (a) Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev.* **1997**, *97*, 2063–2192. For related examples, see: (b) Eisch, J. J.; Foxton, M. W. *J. Org. Chem.* **1971**, *36*, 3520–3526. (c) Eisch, J. J.; Rhee, S-G. *J. Am. Chem. Soc.* **1975**, *97*, 4673–4682. For a related review, see: (d) ref. 27.

projected isomerization of the kinetically generated *Z* isomer (from cis H-Al addition across triple bond) to the thermodynamically more favored *E* isomer. The role of thf molecule is therefore to occupy the empty p orbital of the aluminum and shuts down the isomerization pathway.

Scheme 3.6. Solvent Controlled Stereoselective Synthesis of Si Containing Alkenylaluminums.



3.3.2 Identification of Optimal Catalysts and Scope Study of EAS with *E* Silyl-substituted Alkenylaluminum Reagents

Despite the congested nature of these trisubstituted alkenylaluminum species, the NHC–Cu catalyzed EAS reactions with them can be very efficient and highly selective.[5c] The screening data correspond to various representative chiral *N*-heterocyclic carbene promoters are delineated in Table 3.1; unlike the ineffective transformations (<7% conv., entries, 1–2 and 7) catalyzed by Cu complexes derived from monodentate Ag-carbene **3.40** or bidentate phenoxide based NHC–Ag species **3.7** and **3.8**, the EAS with 1 mol % **3.9** and 2.0 mol % $CuCl_2$•$2H_2O$ proceeds to completion in six hours, delivering 1,4-diene **3.41**, which bears a well defined trisubstituted alkene, in 87% yield, exceptional site (>98% S_N2') and good enantioselectivity (95:5 e.r., entry 3). Further ligand modifications

have lead to the identification of more sterically congested Ag-carbene **3.39** as the optimal promoter for this reaction, furnishing the desired product in 93% yield and excellent optical purity (99:1 e.r., entry 6).

Figure 3.2. Addiitional NHC–Ag Complexes Examined in Ligand Screening.

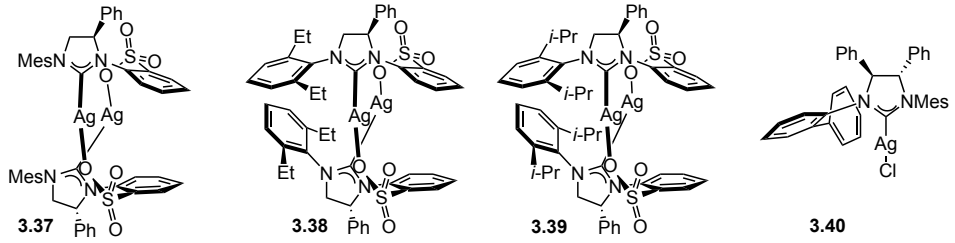
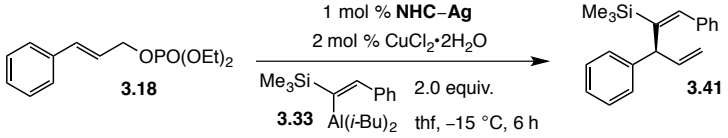


Table 3.1. Initial Screening of NHC–Ag Complexes in EAS with *E* Alkenylaluminum Reagent.[a]



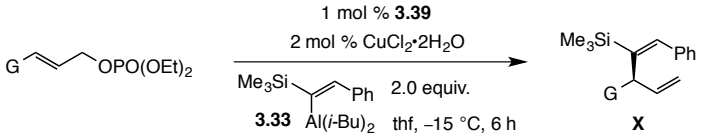
Entry	NHC–Ag	Conv. [%][b]	Yield [%][c]	$S_N2':S_N2$[b]	e.r.[d]
1	**3.7**	5	--	>98:2	--
2	**3.8**	7	--	>98:2	--
3	**3.9**	>98	87	>98:2	5:95
4	**3.37**	90	80	>98:2	96.5:3.5
5	**3.38**	>98	94	>98:2	98:2
6	**3.39**	>98	93	>98:2	99:1
7[e]	**3.40**	5	--	>98:2	--

[a] Reactions were performed under N_2 atmosphere. [b] Determined through analysis of 400 MHz ^{1}H NMR spectra of unpurified mixtures. [c] Yields of isolated products after purification (±5%). [d] Determined by HPLC analysis (±2%); see the experimentals for details. [e] 2 mol % **3.40** and 2.0 mol % $CuCl_2$•$2H_2O$ used.

With the optimal catalyst in hand, we examined the scope of NHC–Cu-catalyzed enantioselective allylic substitutions. Subjection of 2.0 equivalents of Alkenylaluminum **3.33**, prepared and used in situ, to aryl- and alkyl-substituted allylic phosphates, in the presence of 1.0 mol% NHC–Ag complex **3.39** and 2.0 mol% $CuCl_2$•$2H_2O$, results in complete substrate consumption in all cases (Table 3.2). 1,4-Dienes **3.41**–**3.51** are generated with >98% site selectivity (S_N2'), in 82–>98% yield and in 94:6–99:1 e.r. Regardless of the steric (entries 3–4) or electronic attributes (entries 2 and 7) of aryl substituents of the allylic phosphates, EAS reactions occur efficiently and with high

selectivities. Alkyl-substituted substrates (entries 10–11, Table 3.2) can be used effectively as well in Cu-catalyzed EAS processes, albeit with somewhat lower enantioselectivity levels (94:6 e.r.). In all the transformations examined, there is >98% preservation of *E* olefin geometry found in the nucleophilic precursors, and products derived from the addition of an *i*Bu unit of the Al-based reagent are not detected (<2% by 400 MHz ^{1}H NMR analysis). It is thus a notable attribute of this class of transformations that the overall process, beginning with the silyl-substituted alkyne and ending with the enantiomerically enriched dienes, requires five distinct issues of selectivity to be addressed: site- and stereoselectivity in generation of the alkenylaluminums (Scheme 3.6), followed by site- (S_N2' vs. S_N2), group- (vinyl- vs. *i*Bu addition) and, finally, enantioselectivity of allylic substitution reactions.

Table 3.2. Scheme of Cu-Catalyzed EAS with *E* Alkenylaluminum Reagent **3.33**.[a]



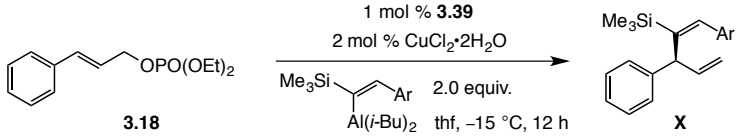
Entry	G	X	Yield [%][c]	*E*:*Z*[b]	e.r.[d]
1	Ph	**3.41**	93	>98:2	99:1
2	*o*MeOC$_6$H$_4$	**3.42**	82	>98:2	98:2
3	*o*NO$_2$C$_6$H$_4$	**3.43**	89	>98:2	>99:1
4	*o*MeC$_6$H$_4$	**3.44**	96	>98:2	99:1
5	*m*BrC$_6$H$_4$	**3.45**	95	>98:2	99:1
6	*p*ClC$_6$H$_4$	**3.46**	94	>98:2	98.5:1.5
7	*p*NO$_2$C$_6$H$_4$	**3.47**	87	>98:2	97.5:2.5
8	*p*MeC$_6$H$_4$	**3.48**	92	>98:2	>99:1
9	*p*TsOC$_6$H$_4$	**3.49**	>98	>98:2	99:1
10	(CH$_2$)$_2$Ph	**3.50**	88	>98:2	94:6
11	*c*Hex	**3.51**	88	>98:2	94:6

[a] Reactions were performed under N_2 atmosphere. >98% conversion and >98:2 S_N2':S_N2 in all cases. [b] Determined through analysis of 400 MHz ^{1}H NMR spectra of unpurified mixtures. [c] Yields of isolated products after purification (±5%). [d] Determined by HPLC analysis (±2%); see the experimentals for details.

Sequential hydroalumination/Cu-catalyzed EAS can be performed with silyl-substituted alkynes bearing different aryl units (Table 3.3). Irrespective of the steric or electronic characteristics of the aromatic alkynes, substrate controlled hydroalumination

proceeds effectively and in complete selectivity for the isomerized *E* trisubstituted alkenylaluminums. The subsequent catalytic C-C bond forming processes deliver desired diene products (cf. **3.52**–**3.56**) with complete site- and group-selectivity and in 92:8–99:1 e.r. Only in one instance is the final product **3.55** isolated as a mixture of *E* and *Z* isomers (entry 4, 88:12 *E*:*Z*). The incomplete alkenylaluminum isomerization may be due to destabilization of the zwitterionic structure (**3.35** in Scheme 3.6) by the electron withdrawing *p*-CF_3 unit.

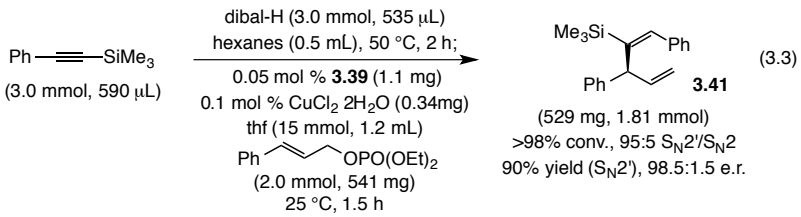
Table 3.3. Scope of Cu-Catalyzed EAS with *E* Alkenylaluminum Reagents.[a]



Entry	Ar	X	t (h)	Yield [%][c]	*E*:*Z*[b]	e.r.[d]
1	*o*$MeOC_6H_4$	**3.52**	12	94	>98:2	92:8
2	*m*MeC_6H_4	**3.53**	6	82	>98:2	99:1
3	*p*FC_6H_4	**3.54**	12	70	>98:2	97:3
4	*p*$CF_3C_6H_4$	**3.55**	12	70[e]	88:12	97:3[e]
5	*p*MeC_6H_4	**3.56**	6	91	>98:2	99:1

[a] Reactions were performed under N_2 atmosphere. >98% conversion and >98:2 S_N2':S_N2 in all cases. [b] Determined through analysis of 400 MHz ^1H NMR spectra of unpurified mixtures. [c] Yields of isolated products after purification (±5%). [d] Determined by HPLC analysis (±2%); see the experimentals for details. [e] Data pertain to pure *E* isomer.

The gram-scale preparation of 1,4-diene **3.41**, as illustrated in Eq. 3.3, underscores the exceptional efficiency and reliable selectivities of this single-pot class of reactions. More than half a gram of **3.41** (90% yield) can be synthesized in 98.5:1.5 e.r. and 95:5 site selectivity (S_N2':S_N2) through a transformation, which requires only 0.05 mol % (1.1 mg) of chiral NHC–Ag complex **3.39** in total 2 ml of organic solvent.

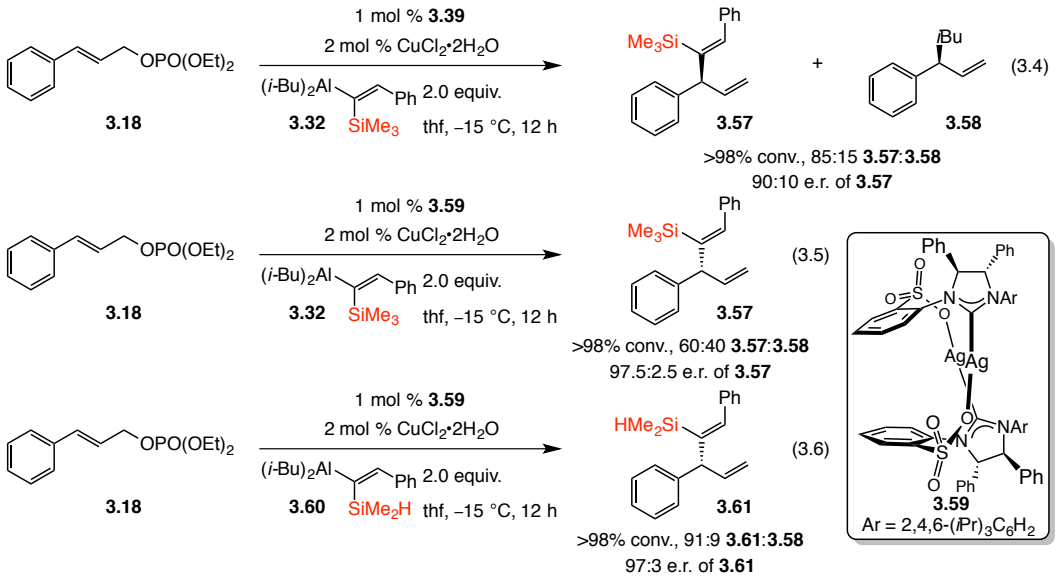


(3.3)

3.3.3 Identification of Optimal Catalysts and Scope Study of EAS with *Z* Silyl-substituted Alkenylaluminum Reagents

While the reactions with E alkenylaluminum reagents are highly effective, we observe reduced selectivity levels of the EAS product **3.57** derived from the addition of *Z* alkenylaluminum reagent **3.32** under the same conditions. As shown in Eq. 3.4, Scheme 3.7, the conversion of allylic phosphate **3.18** proceeds to completion in 12 h with 2 mol % Cu catalyst of **3.39**, furnishing desired product in 90:10 e.r. (vs. 99:1 e.r. with the E alkenylaluminum **3.33**) mixed with 15% of an *iso*butyl adduct **3.58**. Additional ligand screening reveals that improved enantiomer ratio (97.5:2.5 e.r.) can be achieved with copper complex generated from **3.59**; the group selectivity, however, suffers to a greater extent under these conditions, affording **3.57** in only 60% of the crude product mixture (Eq. 3.5). To address this inefficiency, we surmised that a smaller silyl substituent on the aluminum reagents might help with transfer of the targeted alkenyl unit, based on the assumption that the relatively hindered stereochemical environment engendered by the use of **3.59** may accommodate only a smaller nucleophilic coupling partner (see section 3.6 for mechanistic discussion). Indeed, the dimethylsilyl hydride substituent introduced in alkenylaluminum reagent **3.60** benefits the corresponding Cu-catalyzed EAS reactions, allowing the formation of desired alkenyl adduct **3.61** in 97:3 e.r. and higher group selectivity (91% alkenyl transfer vs. 9% *iso*butyl transfer, Eq 3.6).

Scheme 3.7. Optimization of Cu-Catalyzed EAS with *Z* Alkenylaluminum Reagents.

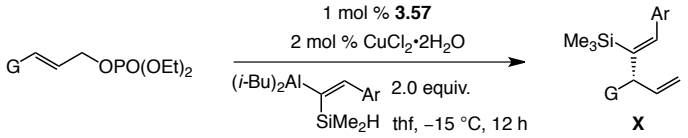


Having established the conditions for additions of the *Z* alkenylaluminum reagents, such as **3.60** (Scheme 3.7), obtained site selectively through kenetic syn aluminum hydride addition to silyl-substituted aryl alkynes. We continued the method development by investigating its response to an assortment of aromatic acetylenes and substituted allylic phosphates. As the results in Table 3.4 illustrates, a wide range of enantiomerically enriched 1,4-dienes (cf. **3.61**–**3.70**) can be obtained through enantioselective Cu-catalyzed allylic substitution with this set of stereochemically defined alkenylaluminum reagents. Similar to reactions with *E* isomeric reagents (Tables 3.2–3.3 and Eq 3.3), when various aryl-substituted allylic phosphates are used, high site- (>98% S_N2') and enantioselectivities are observed (95.5:4.5–98.5:1.5 e.r.). In all instances except one (*Z*:*E*= 90:10, entry 7),[19] there is >98% *Z* selectivity in the derived

(19) Generation of a minor amount of *E* alkene (**3.67** formed with 90:10 *Z*:*E* selectivity) in the reaction shown in entry 7 of Table 3.4 might be caused by olefin isomerization facilitated by the *p*MeO substituent. The inability of the substrate in entry 2 (Table 3.4), containing an *o*-methoxyphenyl group (**3.62** formed with >98% Z selectivity) might be because the corresponding resonance structure suffers from destabilization as a result of the attendant allylic strain.

trisubstituted alkenes. Several points regarding the data in Table 3.4 merit further discussion: 1) In contrast to reactions of *E* alkenylaluminums, 7–28% of the products derived from addition of an *i*Bu group are observed (Table 3.4). The origin of such group selectivity differences remains to be clarified, but is likely due to subtle variations in equilibria involving the formation of vinyl- vs. *iso*butylcopper species as well as the relative facility with which such complexes undergo EAS transformations (i.e., only C–C bond formation is irreversible). 2) Cu-catalyzed allylic substitution with Ag complex **3.9**, which proves to be optimal in reactions with *E* alkenylaluminum reagents (Tables 3.2–3.3 and Eq 3.3), furnishes similar efficiency and site-selectivity when in combination with the HMe_2Si containing *Z* isomeric aluminum species (vs. **3.39**). However, enantioselectivity is diminished significantly; as an example, the formation of **3.61** shown in entry 1 of Table 3.4 results in 86.5:13.5 e.r. when **3.9** is used, whereas in the presence of **3.39** the desired 1,4-diene is isolated in 97:3 e.r. The amount of *iso*butyl adduct is slightly lower with Cu catalyst of **3.9** (96:4 vs. 91:9 with **3.39**). On the other hand, when **3.39** is used to promote EAS reactions of *E* alkenylaluminum **3.33** to allylic phosphate **3.18**, under otherwise identical conditions, only 53% conversion is observed and **3.41** is obtained in 94.5:5.5 e.r. (vs. >98% conv. and >99:1 e.r. with **3.9**). The rationale for such selectivity differences is unclear at this moment.

Table 3.4. Scope of Cu-Catalyzed EAS with *Z* Alkenylaluminum Reagents.[a]

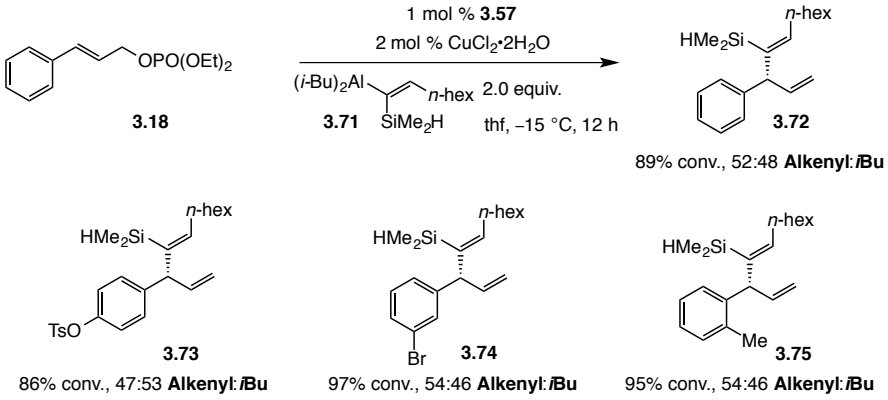


Entry	G	Ar	**X**	Yield [%][c]	Alkenyl:*i*Bu[b]	e.r.[d]
1	Ph	Ph	**3.61**	78	91:9	97:3
2	Ph	*o*MeOC$_6$H$_4$	**3.62**	68	72:28	97.5:2.5
3	Ph	*o*MeC$_6$H$_4$	**3.63**	61	76:24	97:3
4	Ph	*m*CF$_3$C$_6$H$_4$	**3.64**	86	91:9	95.5:4.5
5	Ph	*p*CF$_3$C$_6$H$_4$	**3.65**	71	75:25	96.5:3.5
6	Ph	*p*FC$_6$H$_4$	**3.66**	85	90:10	98:2
7	Ph	*p*OMeC$_6$H$_4$	**3.67**	75	80:20	98.5:1.5
8	*p*NO$_2$C$_6$H$_4$	Ph	**3.68**	81	93:7	97:3
9	*p*TsOC$_6$H$_4$	Ph	**3.69**	81	90:10	98:2
10	*p*MeC$_6$H$_4$	Ph	**3.70**	84	87:13	98:2

[a] Reactions were performed under N_2 atmosphere. >98% conversion, >98:2 S_N2':S_N2 and >98% *Z* isomer in all cases except in entry 7 (90:10 *Z*:*E*). [b] Determined through analysis of 400 MHz ^{1}H NMR spectra of unpurified mixtures. [c] Yields of isolated products after purification (±5%). [d] Determined by HPLC analysis (±2%); see the experimentals for details.

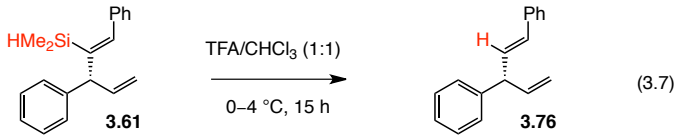
As the ineffective isomerization observed with alkyl-substituted alkynes towards the synthesis of corresponding *E* alkenylaluminums (i.e., variants of **3.33**) further indicates the crucial role of aromatic substituents and therefore limits the scope in that aspect, the related alkyl-substituted *Z* isomeric species can be prepared efficiently, in complete stereochemical control and available for the subsequent Cu-catalyzed EAS. The reactions with these aluminum reagents (cf. **3.71**), however, are less prone to transfer the alkenyl units but rather delivering the *iso*butyl group instead. As the several cases shown in Scheme 3.8 demonstrates, roughly half of the product mixtures are undesired *i*Bu adducts. Such a drastic contrast (vs. aryl-substituted, e.g., **3.60**) is unexpected and a little bit counterintuitive; as one would anticipate that the electron donating alkyl-substituents might facilitate the corresponding alkenyl transfer compared to aryl-substituted variants.

Scheme 3.8. Non-Selective Cu-Catalyzed EAS with Alkyl-substituted Alkenylaluminum Reagent.



3.3.4 Representative Funtionalization of EAS Products and Application in the Synthesis of Nyasol

Protodesilylation of the enantiomerically enriched silyl-substituted 1,4-diene **3.61** is showcased in Eq 3.7; such process converts the silicon containing trisubstituted olefin products to the *trans* 1,2-disubstituted alkenyl adducts in good yield (89% in Eq. 3.7), as represented by **3.76**, which equals to the compounds expected from the pertinent EAS transformations starting with alkenylaluminum reagents that are not accessible through hydroalumination of aryl-substituted terminal alkynes.



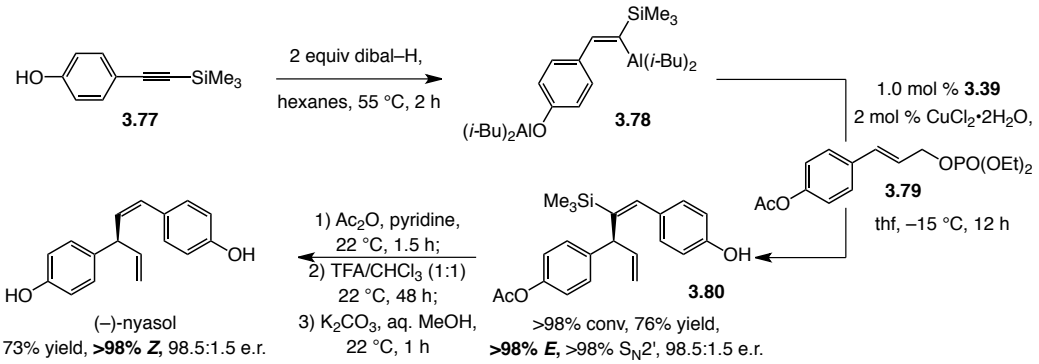
(3.7)

The first enantioselective synthesis of nyasol was then realized (Scheme 3.9). Pd-catalyzed cross-coupling[20] of commercially available trimethylsilylacetylene with 4-iodophenol delivers the silyl-alkyne **3.77**, required for site- and stereoselective hydroalumination in 76% yield. Treatment of **3.77** with dibal-H at 55 °C for two hours

(20) For a review of Sonogashira-type coupling processes, see: Chinchilla, R.; Nájera, C. *Chem. Rev.* **2007**, *107*, 874–922.

delivers alkenylaluminum **3.78**, which is subsequently used in Cu-catalyzed allylic substituion of an acetate-bearing allylic phosphate **3.79**. Such single-vessel operation affords silyl-substituted 1,4-diene **3.80** in 76% yield, >98% site selectivity and 98.5:1.5 e.r. Complete control of alkene selectivity (>98% *E*), as well as >98% alkenyl transfer (<2% *i*Bu addition) is observed. (–)-Nyasol is obtained after three manipulations in 73% overall yield from **3.80**; the sequence includes protodesilylation with trifluoroacetic acid of phenol protected substrate, followed by simple removal of the two acetates (42% overall yield from commercially available trimethylsilylacetylene).[21]

Scheme 3.9. Efficient and Enantioselective Synthesis of Natural Product *R*-(–)-Nyasol.



3.4 Development of Efficient and Site Selective Catalytic Hydroalumination of Terminal Alkynes

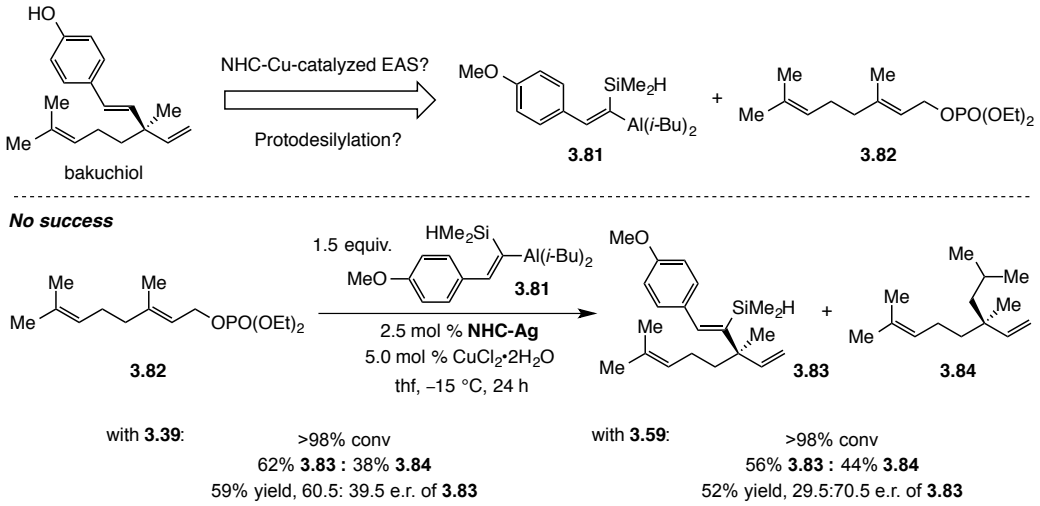
3.4.1 The Need for Alkenylaluminum Reagents That Do Not Bear A Silicon Substituent

Next, we have tried to incorporate the silicon containing alkenylaluminum reagents into enantioenriched 1,4-dienes that bear a quaternary stereogenic center; such a

(21) For a previous enantioselective synthesis of di-O-methyl ether of nyasol, involving a Wittig olefination that proceeds with 3:2 Z:E selectivity, and related natural products, see: (a) Quan, W.-G.; Yu, B.-X.; Zhang, J.-Y.; Liang, Q.-R.; Sun, Y.-Q.; She, X.-G.; Pan, X.-F. *Chin. J. Chem.* **2007**, *25*, 688–693. For another synthesis using Ir-catalyzed vinylation chemistry, see: (b) Hamilton, J. Y.; Sarlah, D.; Carreira, E. M. *J. Am. Chem. Soc.* **2013**, *135*, 994−997.

protocol would allow facile access to the targeted natural product bakuchiol (Scheme 3.10).[22] Our initial attempt involved Cu-catalyzed EAS reactions of aluminum reagent **3.81** to a geraniol derived allylic phosphate **3.82**; the outcome shown in Scheme 3.10 suggests that, with both optimal Cu catalysts of **3.39** and **3.59**, the C-C bond formations proceed with little discrimination of transferring which nucleophilic ligand on aluminum. The desired sterically congested 1,4-diene **3.83** is afforded in only 56–62% of the product mixtures and with low enantioselectivity levels (69.5:30.5–71.5:28.5 e.r.). Stabilization of electron density at the vinylic carbon by the silyl substituent likely retards the rate of alkenyl transfer, resulting in the formation of 38–44% of **3.84** in the product mixture.

Scheme 3.10. Is Silyl-substituted Alkenylaluminums Applicable in Construction of Quaternary Center?

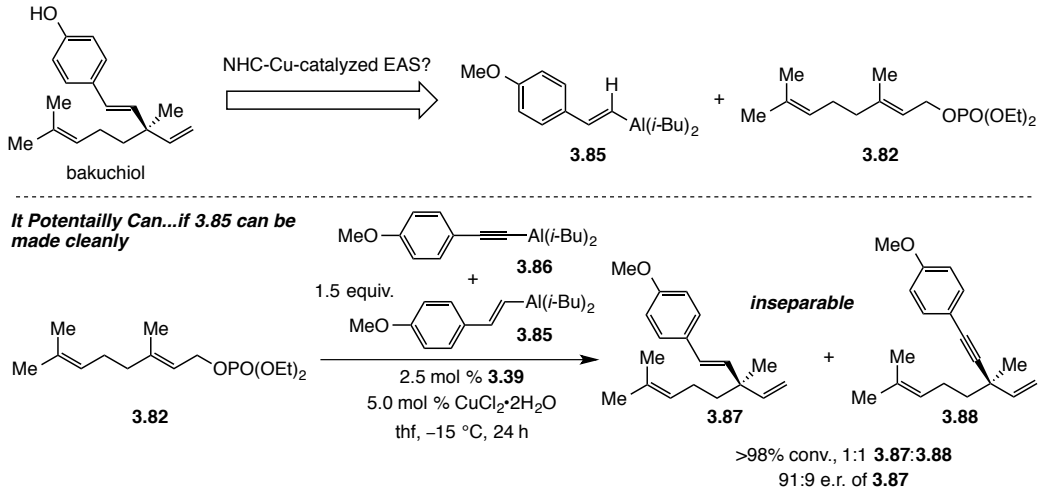


Our second resort relies on the hope that, even with a mixture of alkenyl- and alkynylaluminum species generated through the conventional impractical hydroalumination of aryl alkynes, the NHC–Cu-catalyzed EAS reactions can selectively incorporate the desired alkenyl unit rather than the "dummy" alkynyl ligand when it is

(22) For previous enantioselective syntheses of bakuchiol, see: (a) Takano, S.; Shimazaki, Y.; Ogasawara, K. *Tetrahedron Lett.* **1990**, *31*, 3325– 3326. (b) Du, X.-L.; Chen, H.-L.; Feng, H.-J.; Li, Y.-C. *Helv. Chim. Acta* **2008**, *91*, 371–378. (c) Esumi, T.; Shimizu, H.; Kashiyama, A.; Sasaki, C.; Toyota, M.; Fukuyama, Y. *Tetrahedron Lett.* **2008**, *49*, 6846–6849. (d) Bequette, J. P.; Jungong, C. S.; Novikov, A. V. *Tetrahedron Lett.* **2009**, *50*, 6963–6964.

ligated to the copper.[23] As the results illustrated in Scheme 3.11 indicate, such an assumption is invalid in this particular experimental setting; exposure of the reagent mixture of **3.85** and **3.86** to allylic phosphate **3.82** under standard allylic substitution reaction conditions similar to those used in the previous discoveries[5a,c] has lead to EAS products as an inseparable mixture (1:1 in ratio of **3.87**:**3.88**, Scheme 3.11). Although good enantioselectivity of **3.87** is obtained (91:9 e.r.), the above scenario is far from synthetically useful. One fact that further exacerbates the inefficient reagent synthesis is the faster formation of alkynyl adduct **3.88** relative to the desired **3.87** (from a roughly 2:1 alkenylaluminum:alkynylaluminum mixture in Scheme 3.5 to 1:1 product mixture, Scheme 3.11). Nonetheless, however important the discovery of catalytic EAS that involves an alkyne is,[24] we still need to address the issue of effective preparation of alkenylaluminum reagents derived from aryl-substituted terminal acetylenes.

Scheme 3.11. Can Non Silyl-substituted Alkenylaluminums Solve the Problem?



3.4.2 Identification of Effective Catalysts for Site Selective Hydroalumination of Terminal Alkynes

(23) Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, L. A. *Tetrahedron* **1984**, *40*, 5005–5038.
(24) (a) ref. 17. For more details, see: (b) Dabrowski, J. A. thesis, 2013.

Our investigations began with the search for an effective hydroalumination catalyst, which accelerates the desired H-Al addition to out compete the adventitious deprotonation, a phenomenon presumably due to the elongated time of exposure of the remaining alkyne to the alkenylaluminum reagent. We focused on commercially available Ni-based complexes, owing in part to the study by Eisch regarding hydroaluminations of a small number of disubstituted alkynes involving $Ni(acac)_2$.[25] In this study, they have shown that the presence of small quantity of a commercial Ni salt dramatically increases the reaction rate of H-Al addition across the internal triple bonds (up to 60 times seen for the catalytic hydroalumination of phenylpropyne).

The outcome of our initial catalyst screening, with phenylacetylene serving as the substrate, is summarized in Table 3.5.[26] Reactions with simple nickel salts, such as, $NiCl_2•6H_2O$, $Ni(cod)_2$ and $Ni(acac)_2$ and 1.3 equiv of dibal–H in tetrahydrofuran (thf)[27] at 22 °C for two hours lead to efficient hydrometallation (entries 1–3) but with a modest preference for the terminal vinylaluminum (43–69% of **3.89**) along with 13–19% of 1,3-diene **3.91**. For the first time, we observed the formation of alkenylaluminums that bear the C-Al bond at the benzylic position (14–33% **3.90**); such a discovery provides new organometallic species that otherwise cannot be genenrated through conventional method (i.e., uncatalyzed hydroalumination). While the use of tetrakis(triphenylphosphine)Ni(0) complex furnishes non selective hydrometallation (entry 4), reaction with 3 mol % $Ni(PPh_3)_2Cl_2$ delivers the desired terminal alkenyl metal species in 92.5% selectivity;

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(25) (a) Eisch, J. J.; Foxton, M. W. *J. Organomet. Chem.* **1968**, *12*, P33–P36. (b) Eisch, J. J.; Sexsmith, S. R.; Fichter, K. C. *J. Organomet. Chem.* **1990**, *382*, 273–293. (c) Eisch, J. J.; Ma, X.; Singh, M.; Wilke, G. *J. Organomet. Chem.* **1997**, *527*, 301–304.
(26) Gao. F.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 10961–10963.
(27) Reactions can also be performed in toluene with similar efficiency, but might result in slight diminish in selectivity levels.

7.5% of the internal alkenylaluminum is formed with no detection of the undesired homo-coupling product **3.91** (entry 5). Additional PPh_3 slows down the hydroalumination reaction but without much diminish in site selectivity (entry 6). Efforts regarding in situ formation of Ni-phosphine complexes of various Ni salts and phosphines lead to efficient consumption of phenylacetylene but in low selectivity levels together with significant amounts of **3.91** (entries 7–10). It must be noted that in the absence of a catalyst, dibal–H reacts with phenylacetylene at 50 °C (hexanes or toluene) to afford ~50% of the *β*-alkenylaluminum (**3.89**) along with 25% styrene and 25% alkynylaluminum (due to deprotonation of the alkyne substrate by the vinylaluminum). There is, however, <2% reaction when phenyacetylene is treated with dibal–H in thf (at 22 °C, in 2 h), which allows catalytic pathway to operate with minimal background reaction. More importantly, as depicted in entries 11–15 of Table 3.5, when the Ni catalyst bears a bidentate phosphine ligand, the facile hydrometallation process occurs with complete reversal of site selectivity.[28] The internal alkenylaluminum (**3.90**) is formed efficiently (>98% conv) and with complete α selectivity (**3.89**:**3.90** = <2:>98) when Ni(dppp)Cl_2 is used (entry 12); such a highly selective and efficient protocol not only allows access to important organic building blocks (see below) but also prompts reaction development that effectively utilizes these organometallic entities.[29]

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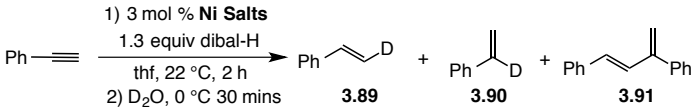
(28) For related selectivity reversal in Ni-catalyzed H-P and H-S addition to terminal alkynes, see: Han, L.-B.; Zhang, C.; Yazawa, H.; Shimada, S. *J. Am. Chem. Soc.* **2004**, *126*, 5080–5081.

(29) (a) ref. 3 (m). For the use of alkenylaluminums derived from this study in enantioselective conjugate additions to acyclic enones with the construction of quaternary stereogenic centers, see: McGrath, K. P.; Hoveyda, A. H. manuscript in preparation, 2013.

Table 3.5. Catalysts Screening for Ni-Catalyzed Hydroalumination of Phenylacetylene.[a]

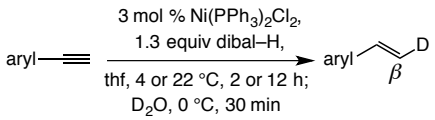


Entry	Ni Salt	Conv (%)	**3.89 : 3.90 : 3.91** (%)
1	$NiCl_2$•$6H_2O$	95	43 : 33 : 19
2	$Ni(cod)_2$	>98	69 : 14 : 17
3	$Ni(acac)_2$	97	66 : 18 : 13
4	$Ni(PPh_3)_4$	>98	55 : 32 : 13
5	*$Ni(PPh_3)_2Cl_2$*	*>98*	*92.5 : 7.5 : <2*
6	$Ni(PPh_3)_2Cl_2$ + 30 mol % PPh_3	83	78 : 5 : <2
7	$NiCl_2$•$6H_2O$ + (*o*-tol)$_3$P	>98	78 (1+2) : 22
8	$NiCl_2$•$6H_2O$ + Cy_3P	>98	74 : 19 : 7
9	$NiCl_2$•$6H_2O$ + $EtPPh_2$	82	42 : 40 : <2
10	$Ni(cod)_2$ + $EtPPh_2$	97	54 : 31 : <2[c]
11	$Ni(dppe)Cl_2$	92	3 : 89 : <2
12	*$Ni(dppp)Cl_2$*	*>98*	*2 : >98 : <2*
13	$NiCl_2$•$6H_2O$ + dppb	61	3 : 58 : <2
14	$NiCl_2$•$6H_2O$ + dppf	83	5 : 78 : <2
15	$Ni(dcpe)Cl_2$	91	24 : 64 : 3

[a] All reactions performed under N_2 atomsphere; <2% deprotonation determined for all cases that proceed to completion. [b] Determined by analysis of 400 MHz ^{1}H NMR. [c] 12% deprotonation observed; see the experimentals for details.

Ni-catalyzed hydroaluminations can be performed with a considerable range of aryl alkynes (Table 3.6), affording the β-alkenylaluminum isomer efficiently and with high selectivity in the presence of 3 mol % $Ni(PPh_3)_2Cl_2$. Reactions are conducted at 4–22 °C and require 2–12 hours. Alkynes bearing electron-donating (entries 1–3) or electron-withdrawing units (entries 4–8) or sterically congested aryl acetylenes (entries 9) are suitable substrates. N- or S-containing heterocycle-substituted alkynes readily undergo hydroalumination with moderate to high site selectivity (85.5:14.5–96:4 β:α, entries 10–11). An additional aspect regarding the cases in Table 3.6 is noteworthy: only in reactions involving certain *o*-substituted aryl acetylenes and N-bearing heterocyclic substrate (entries 7–10), 5~10% adventitious alkyne deprotonation is observed.

Table 3.6. *β*-Selective Ni-Catalyzed Hydroalumination of Arylacetylenes.[a]

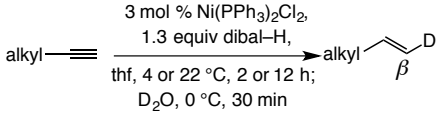


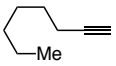
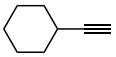
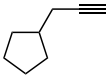
Entry	Aryl	Temp (°C); Time (h)[b]	Conv (%)[c]	β:α[c]
1	*o*-$OMeC_6H_4$	4; 12	>98	97:3
2	*m*-$OMeC_6H_4$	22; 2	>98	94:6
3	*p*-$OMeC_6H_4$	4; 12	>98	>98:2
4	*m*-$CF_3C_6H_4$	4; 12	>98	98:2
5	*p*-$CF_3C_6H_4$	22; 2	>98	88:12
6	*p*-FC_6H_4	22; 2	>98	92:8
7	*o*-ClC_6H_4	22; 2	>98[d]	95.5:4.5
8	*o*-BrC_6H_4	4; 12	>98[d]	96:4
9	*o*-MeC_6H_4	4; 12	83[d]	>98:2
10	3-pyridyl	22; 2	>98[d]	85.5:14.5
11	3-thienyl	22; 2	>98	96:4

[a] Reactions under N_2 atm. [b] Reaction times correspond to hydroalumination portion of the process (not including D_2O quench). [c] By analysis of 400 MHz ^1H NMR spectra of unpurified mixtures (after D_2O). [d] 5~10% alkynylaluminum oberved.

β-Selective catalytic hydroaluminations of alkyl-substituted alkynes proceed as readily (Table 3.7) as with aryl-substituted variants with similar trends in efficiency and exceptional site selectivity (>98% *β* in all instances). Alkynes bearing a linear (entries 1–3), α- (entry 4) or *β*-branched (entry 5) alkyl unit serve as effective substrates. As mentioned before, without a catalyst, alkyl-substituted substrates react relatively efficiently (vs. aryl alkynes) with dibal–H to generate the terminal or *β*-vinylaluminums (>98% selectivity). Such uncatalyzed reactions, however, proceed to ~80% conversion after six hours at 22 °C and must be heated to 55 °C for 2 h to achieve maximum ~90% alkyne consumption (additional time does not improve conversion). The Ni-catalyzed processes (entries 3–5, Table 3.7), in contrast, are complete in two hours at ambient temperature.

Table 3.7. β-Selective Ni-Catalyzed Hydroalumination of Alkylacetylenes.[a]

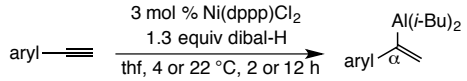


Entry	Aryl	Temp (°C); Time (h)[b]	Conv (%)[c]	β:α[c]
1		22; 2	95	>98:2
2		4; 12	94	>98:2
3		22; 2	>98	>98:2
4		22; 2	>98	>98:2
5		22; 2	>98	>98:2

[a] Reactions under N_2 atm. [b] Reaction times correspond to hydroalumination portion of the process (not including D_2O quench). [c] By analysis of 400 MHz ^1H NMR spectra of unpurified mixtures (after D_2O).

α-Selective catalytic hydroaluminations with Ni(dppp)Cl_2 occur also with significant range of aryl-acetylenes (Table 3.8). Under same conditions as described in Table 3.6, benzylic alkenylaluminum reagents are usually afforded in 95–>98% site selectivities and in excellent efficiencies (>98% conversion in all cases). None of the transformations with Ni(dppp)Cl_2 generate the alkynylaluminum side product, which, is obtained in significantly larger amounts in the absence of a catalyst (see above). Furthermore, catalytic hydrometallations promoted with Ni(dppp)Cl_2 are more selective than Ni(PPh_3)$_2Cl_2$.

Table 3.8. α-Selective Ni-Catalyzed Hydroalumination of Arylacetylenes.[a]

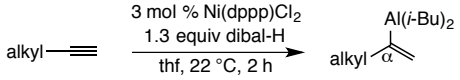


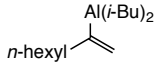
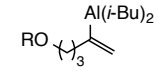
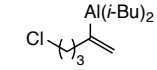
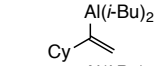
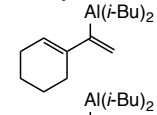
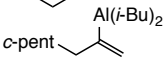
Entry	Aryl	T (°C)	t (h)	Conv (%)[b]	α:β[b]
1	Ph	22	2	>98	>98:2
2	*o*-$OMeC_6H_4$	4	12	>98	98:2
3	*m*-$OMeC_6H_4$	22	2	>98	>98:2
4	*p*-$OMeC_6H_4$	4	12	>98	>98:2
5	*m*-$CF_3C_6H_4$	4	12	>98	95:5
6	*p*-$CF_3C_6H_4$	22	2	>98	97:3
7	*p*-FC_6H_4	22	2	>98	>98:2
8	*o*-ClC_6H_4	22	2	>98	>98:2
9	*o*-BrC_6H_4	22	2	>98	>98:2
10	*o*-MeC_6H_4	4	12	>98	>98:2
11	3-pyridyl	22	2	>98	>98:2
12	3-thienyl	22	2	>98	>98:2

[a] Reactions under N_2 atm. [b] By analysis of 400 MHz ^1H NMR spectra of unpurified mixtures (after D_2O); <2% alkynylalane.

We have also demonstrated that a variety of alkyl-substituted acetylenes undergo α-selective hydroalumination reactions efficiently (>98% conv. in all cases) and with high levels of site preferences (96.5:3.5–>98:2 α:*β*, Table 3.9). Functional groups, such as a free alcohol (cf. entry 2), silyl ether (cf. entry 3), alkyl halide (cf. entry 4) and conjugated enyne (entry 6), are well tolerated under Ni-catalysis. Only in the formation of dienylaluminum species as shown in entry 6 can we observe the competitive alkyne deprotonation in ~5%.

Table 3.9. α-Selective Ni-Catalyzed Hydroalumination of Alkylacetylenes.[a]



Entry	Product		Conv (%)[b]	α:β[b]
1			>98	>98:2
2		R = H	>98	97:3
3		R = TBS	>98	>98:2
4			>98	>98:2
5			>98	>98:2
6			>98[c]	98:2
7			>98	96.5:3.5

[a] Reactions under N_2 atm. [b] By analysis of 400 MHz ^{1}H NMR spectra of unpurified mixtures (after D_2O); <2% alkynylalane; 2.3 equiv dibal-H in entry 2; 3 h for entry 4. [c] Performed at 4 °C for 12 h; ~5% alkyne deprotonation observed.

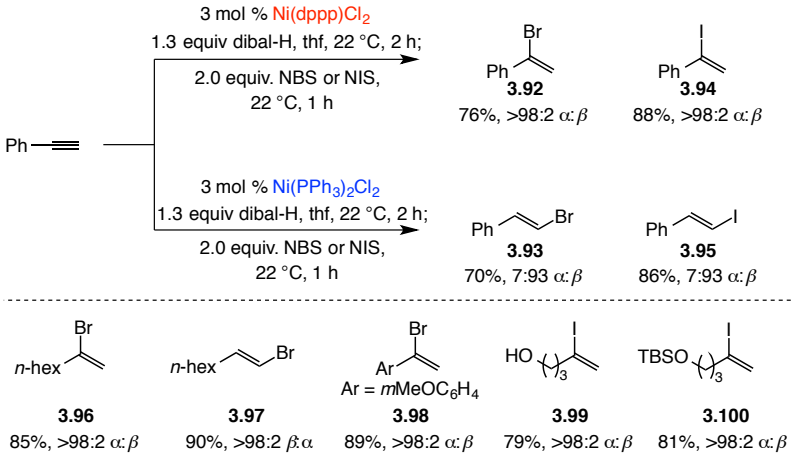
3.4.3 Representative Functionalizations of Derived α and β-Substituted Alkenylaluminum Reagents

Next, we examined reactions of the two isomeric phenyl-substituted alkenylaluminums with electrophiles other than a proton (or deuterium). Synthesis of alkenyl halides was investigated first.[30] As illustrated in Scheme 3.12, direct treatment of the internal or terminal alkenyl metal products, derived from Ni-catalyzed hydrometallation of phenylacetylene, with N-bromo- or N-iodosuccinamide, gives rise to the formation of alkenyl bromides **3.92** and **3.93** or iodides **3.94** and **3.95** in complete transfer of selectivity information and 70–88% yield after chromatography. The >98%

(30) (a) Haloboration/protodeboration of alkyl-substituted alkynes: Hara, S.; Dojo, H.; Takinami, S.; Suzuki, A. *Tetrahedron Lett*. **1983**, *24*, 731–734. (b) Cr-mediated conversion of aldehydes to vinyl iodides: Takai, K.; Nitta, K.; Utimoto, K. *J. Am. Chem. Soc*. **1986**, *108*, 7408–7410. (c) Terminal alkynes to β-vinyl iodides by TMSI/protodesilylation: Kamiya, N.; Chikami, Y.; Ishii, Y. *Synlett* **1990**, 675–676. (d) Ketones and aldehydes to vinyl iodides with phosphitohalides: Spaggiari, A.; Vaccari, D.; Davoli, P.; Torre, G.; Prati, F. *J. Org. Chem*. **2007**, *72*, 2216–2219. (e) Terminal alkynes (no branched alkyl-substituted cases) to iodides by HI addition (generated from iodine/hydrophosphine): Kawaguchi, S-i.; Ogawa, A. *Org. Lett.* **2010**, *12*, 1893–1895.

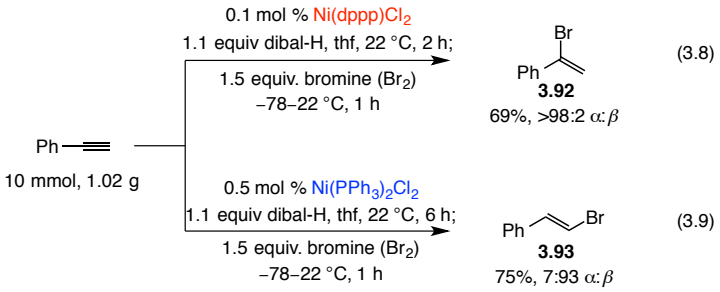
selectivities observed with Ni(dppp)Cl_2, are especially noteworthy from a practical viewpoint because the two alkenyl halide isomers are difficult to separate. Additionally, the synthesis of alkyl-substituted α- or *β*-alkenyl bromides **3.96–3.97** demonstrates the generality of such transformations; halogen-containing products can be efficiently prepared cleanly in high yields (85–90%). A few points regarding the effective preparations of compounds **3.98–3.100** merit further discussion: 1) the methyl-phenylether functionality preserved in the formation of **3.98** cannot survive the harsh procedure that requires the use of BBr_3/HOAc;[30a] even though such protocol has been shown to deliver similar products in good efficiency. 2) It must be also noted that the access to α-alkenyliodide bearing an acid labile unit (e.g., silyl ether **3.100**) is not feasible through the previously reported TMSI/protodesilylation procedure.[31] 3) Free alcohol does not intervene the desired conversion of secondary alkenylaluminum reagents to the corresponding alkenyliodide; **3.99** is thus obtained in 79% yield and as a single regioisomer.

Scheme 3.12. One Pot Synthesis of α or β-substituted Alkenylhalides.



(31) (a) ref. 30 (c) and (d). (b) Morrill, C.; Funk, T. W.; Grubbs, R. H. *Tetrahedron Lett.* **2004**, *45*, 7733–7736.

Catalytic hydroalumination reactions can be performed in commercial grade undistilled thf and with Ni salts that are used as received (purification not required); for example, alkenyliodide **3.94** (Scheme 3.12) is obtained in 83% yield and >98% α selectivity under such conditions. Similarly, the alkyl-substituted alkenyliodide derived through catalytic hydroalumination of 1-octyne is synthesized in 89% yield and 96% α selectivity when the same conditions are used. The Ni-catalyzed protocols are amenable to scale up, and require minimal catalyst loadings. For example, hydroalumination of 1.02 g phenylacetylene proceeds efficiently in the presence of only 0.5 mol % $Ni(PPh_3)_2Cl_2$, delivering alkenyl bromide **3.93** in 75% yield after treatment of the resulting aluminum reagent with 1.5 equivalents of inexpensive bromine (Eq. 3.9); site selectivity remains intact. With $Ni(dppp)Cl_2$, catalyst loading can be dropped further to 0.1 mol % (>98% conversion in 2 h); pure α-alkenyl bromide **3.92** is isolated in 69% yield (Eq. 3.8).



Alkenylboronic acid pinacol esters are members of another important class of compounds readily prepared through Ni-catalyzed alkyne hydroalumination; representative examples are illustrated in Scheme 3.13.[32] Subjection of alkenylaluminum

(32) For recent selected reviews, see: (a) Ishiyama, T.; Miyaura, N. *The Chemical Record* **2004**, *3*, 271–280. (b) Jiao, J.; Nishihara, Y. *J. Organometallic Chem*. **2012**, *721–722*, 3–16. (c) Ishiyama, Tatsuo, and Norio Miyaura. "Metal Catalyzed Borylation of C-H and C-Halogen Bonds of Alkanes, Alkenes, and

products, generated through α- and *β*-selective hydrometallation processes of phenylacetylene, to reactions with commercially available and inexpensive methoxy(pinacolato)boron affords alkenylboron **3.101** and **3.102** in >98% and 94% selectivity and 75% and 88% yield (pure isomers) after purification, respectively. The reaction of the sterically more congested α-alkenylaluminum requires elevated temperatures (>98% conv. at 80 ºC vs. ~30% conv. at 22 °C). Additional cases, such as **3.104** and **3.105**, showcase the scope in synthesizing alkenylborons that bear benzylic C-B bond. As the efficient formations of alkenylborons **3.103**, **3.106** and **3.107** indicate, similar procedures may be applied to alkyl-substituted alkynes;[33] the corresponding products are obtained in 68–82% yield and >95% site selectivity. Two relevant aspects regarding synthesis of alkenylborons through Ni-catalyzed hydrolaluminations merit further mention: (1) Hydroborations of terminal alkynes with pinacolborane (HBpin), affording terminal C–B bonds exclusively, require freshly prepared reagent and strictly anhydrous dichloromethane (<2% conv. in thf or toluene).[34] In contrast, conversion of 1-octyne to the derived α-alkenylboron **3.103** can easily be performed in undistilled commercial grade thf (65% yield of pure α product, 96:4 α:*β*). (2) There are non-catalytic as well as metal-catalyzed hydroborations of alkynes that furnish terminal *β*-alkenylborons either exclusively or as the predominant isomer (>90%).[35,36] Such

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Arenes for the Synthesis of Boronic Esters." *Boronic Acids: Preparation and Applications in Organic Synthesis, Medicine and Materials (Volume 1 and 2), Second Edition* (2012): 135–169.

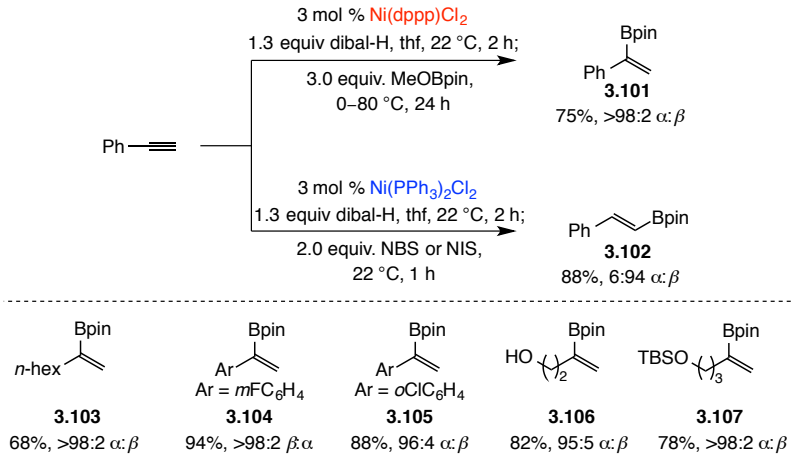
(33) An NHC–Cu-catalyzed hydroboration of a propargyl ether and a propargyl amide was recently reported to proceed with ~90% α-selectivity: Lee, Y.; Jang, H.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 18234–18235.

(34) Tucker, C. E.; Davidson, J.; Knochel, P. *J. Org. Chem.* **1992**, *57*, 3482–3485.

(35) Alkyl-substituted α-alkenylborons can be prepared from terminal alkynes by treatment with BBr_3 and 15–20 equiv HOAc to generate the α-alkenylbromide, followed by metal/halogen exchange and subjection to *i*-propoxypinacolborane. This procedure, however, is not tolerant of acid-sensitive functional groups (cf. **3.107**). See: (a) Ref 30 (a). (b) Moran, W. J.; Morken, J. P. *Org. Lett.* **2006**, *8*, 2413–2415. A Cu-mediated

processes require expensive Rh- or Ir-based catalysts[37] or the sensitive Cp_2ZrHCl.[38] (3) After this work was developed, alkenylboron synthesis from terminal alkynes based on Cu-catalyzed protoboration, which delivers both α and *β* isomers in good efficiency and selectivity levels, appeared in literature.[39]

Scheme 3.13. One Pot Synthesis of α or β-substituted Alkenylborons.



As the first group that introduce alkenylaluminum reagents into Cu-catalyzed EAS reactions, we have no doubt considered the use of previously unavailable α-alkenylaluminum reagents in such C-C bond forming processes. Additions of substantially wider range of alkenyl units can be realized if we can develop an efficient

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(1.1 equiv CuCl, KOAc, LiCl or a phosphine) hydroboration of only *alkyl*-substituted alkynes has been reported to afford up to 91% α-alkenylboron (typically 9–71%). See: (c) Takahashi, K.; Ishiyama, T.; Miyaura, N. *J. Organomet. Chem.* **2001**, *625*, 47–53.

(36) For a Cu-catalyzed hydroboration of phenylacetylene to afford **3.102**, see: Lee, J. E.; Kwon, J.; Yun, J. *Chem. Commun.* **2008**, 733–734. This procedure is ineffective with alkyl-substituted alkynes.

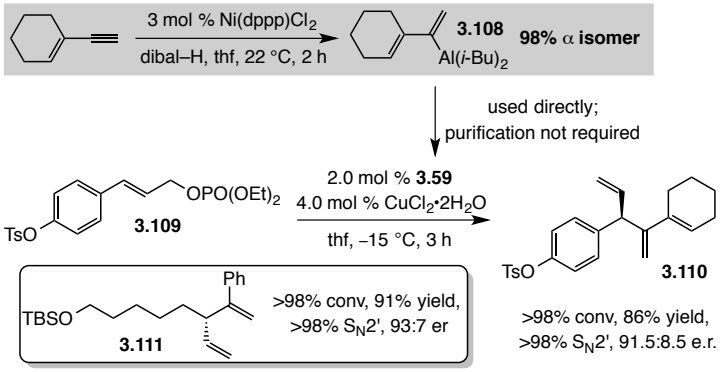
(37) (a) Pereira, S.; Srebnik, M. *Tetrahedron Lett.* **1996**, *37*, 3283–3286. (b) Ohmura, T.; Yamamoto, Y.; Miyaura, N. *J. Am. Chem. Soc.* **2000**, *122*, 4990–4991.

(38) (a) Huang, Z.; Negishi, E-i. *Org. Lett.* **2006**, *8*, 3675–3678. (b) Wang, Y. D.; Kimball, G.; Prashad, A. S.; Wang, Y. *Tetrahedron Lett.* **2005**, *46*, 8777–8780.

(39) For Cu-catalyzed protoboration of allenes, see: (a) Meng, F.; Jung, B.; Haeffner, F.; Hoveyda, A. H. *Org. Lett.* **2013**, *15*, 1414–1417. (b) Yuan, W.; Ma, S. *Adv. Synth. Catal.* **2012**, *354*, 1867–1872. For protoboration of alkynes to synthesize alkenylborons, see: (c) Kim, H. R.; Jung, I. G.; Yoo, K.; Jang, K.; Lee, E. S.; Yun, J.; Son, S. U. *Chem. Commun.* **2010**, *46*, 758–760. (d) Semba, K.; Fujihara, T.; Terao, J.; Tsuji, Y. *Chem. Eur. J.* **2012**, *18*, 4179–4184. (e) Moure, A. L.; Array_as, R. G.; G_ardenas, D. J.; Alonso, I.; Carretero, J. C. *J. Am. Chem. Soc.* **2012**, *134*, 7219–7222. (f) Park, J. K.; Ondrusek, B. A.; McQuade, D. T. *Org. Lett.* **2012**, *14*, 4790–4793. (g) Jang, H.; Zhugralin, A. R.; Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 7859–7871.

and enantioselective catalyst that effects such transformations, which are only limited at this time to the incorporation of alkyl-substituted *β*-alkenylaluminums.[5a] Cu-catalyzed enantioselective allylic substituions in Scheme 3.14 illustrate the above point. An olefin-substituted α-alkenylaluminum **3.108**, obtained through the α-selective Ni-catalyzed process, can be used to synthesize 1,4-diene **3.110** with high efficiency (86% yield) and in 91.5:8.5 e.r. when Ag-carbene **3.59** serves as the ligand precusor in connection with $CuCl_2 \bullet 2H_2O$. The additional 1,4-diene **3.111**, which derives from an alkyl-substituted allylic phosphate, is also rendered feasible because the requisite α-alkenylaluminum can now be easily prepared.

Scheme 3.14. Cu-Catalyzed EAS with 1,1-Disubstituted Alkenylaluminum Reagents.



3.4.4 Initial Mechanistic Considerations for Ni-catalyzed Hydroalumination

A rationale regarding the ligand dependent reversal of site selectivity during the course of phosphine–Ni-catalyzed alkyne hydroalumination must await extensive mechanistic investigations; initial studies do imply that Ni(0) complexes are involved (vs Ni(II)). Thus, subjection of phenylacetylene to the reaction conditions shown in Table 3.5, but with 3 mol % $Ni(cod)_2$ and 6 mol % PPh_3, leads to the formation of **3.89** in 96% selectivity (4% **3.90**; >98% conv.). Similarly, in the presence of 3 mol % $Ni(dppp)Cl_2$, pre-treated with 6 mol % MeMgI (to generate Ni(0)(dppp) complex in situ),

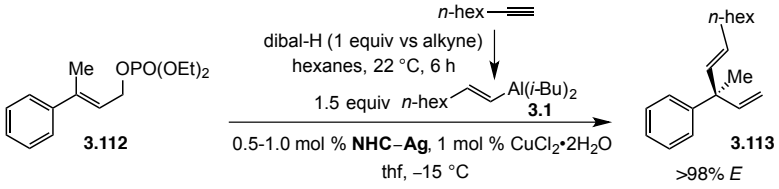
hydroalumination gives **3.90** that is formed in 97% selectivity (3% **3.89**, >98% conv.). It is plausible to propose that reactions proceed via an Al–Ni hydride [(*i*-Bu)$_2$Al–Ni–H]; addition of Ni–H across the triple bond followed by subsequent alkenyl–Al reductive elimination regenerates the Ni(0) catalysts.[25b,c]

3.5 NHC–Cu-catalyzed EAS Reactions with Non Silyl-substituted Alkenylaluminum Reagents to Construct Quaternary Stereogenic Center

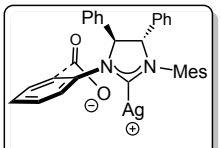
3.5.1 Identification of NHC–Cu Catalysts for Enantioselective Allylic Substitution of Alkyl-substituted Alkenylaluminum Reagents to Trisubstituted Allylic Phosphates

Having established efficient protocols that allow access to broader scope of alkenylaluminum nucleophilic coupling partners, we then proceed to identify catalytic conditions en route the synthesis of bakuchiol by first evaluating the feasibility of Cu-catalyzed EAS to construct quaternary stereogenic centers. We focus our attention on easily accessible alkyl-substituted alkenylaluminums for their previous utilizations in the synthesis of tertiary center containing 1,4-dienes enantioselectively.[5a] Initial screening data in Table 3.10 point to Cu complexes derived from sulfonate-containing bidentate Ag carbenes (entries 3–5) as equally optimal (see below for further discussion), furnishing **3.113** in 76–84% yield and 93.5:6.5–95:5 e.r.[5b] The inefficiency of the EAS with a carboxylate bearing Ag complex **3.114** is noteworthy.

Table 3.10. Ligand Screening for Cu-catalyzed EAS with Alkenylaluminum Reagent **3.1**.[a]



Entry	NHC–Ag	Time (h)	Conv. [%][b]	Yield [%][c]	$S_N2':S_N2$[b]	e.r.[d]
1	**3.40**	120	58	--	43:57	61:39
2	**3.8**	24	30	--	>98:2	89.5:10.5
3	**3.9**	3	>98	76	>98:2	93.5:6.5
4	**ent-3.37**	3	>98	84	>98:2	95:5
5	**ent-3.39**	3	>98	80	>98:2	95:5
6	**3.114**	24	49	--	71:29	53.5:46.5



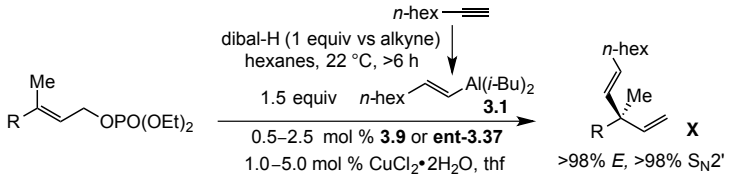
3.114

Mes = 2,4,6-MeC_6H_2

[a] Reactions were performed under N_2 atmosphere. [b] Determined through analysis of 400 MHz ^{1}H NMR spectra of unpurified mixtures. [c] Yields of isolated products after purification (±5%). [d] Determined by HPLC analysis (±2%); see the experimentals for details.

A considerable range of allylic phosphates undergo facile EAS reactions in the presence of 0.5–2.5 mol % **3.9** or **ent-3.37** with *n*hexyl-substituted alkenylaluminum **3.1** to furnish the desired 3,3-disubstituted 1,4-dienes **3.113**–**3.124** in 89:11–98:2 e.r. and 77–97% yield (Table 3.11). Aryl-substituted substrates (entries 1–12) bearing electron-donating (entries 7–8) and -withdrawing substituents (entries 4–6 and 9–12), as well as those that carry sterically demanding *ortho* units (entries 3–10), serve as effective starting materials. Reactions with aryl-substituted allylic phosphates are sufficiently enantioselective to be performed at 22 °C and are complete in 0.5 h (entries 2, 6, 8, 10, 12). Transformations that involve alkyl-substituted electrophiles (entries 13–14 and 17–18, Table 3.11) must be performed at –50 °C for maximum enantioselectivity (92.5:7.5–95:5 e.r.) and might require longer reaction times (6–24 h vs. 10 min–3 h). The Cu-catalyzed process can also be used to access 1,4-dienes containing a carboxylic ester or silyl- substituted quaternary carbon stereogenic center at the C3 position (entries 15–16).

Table 3.11. Cu-Catalyzed EAS of 1-Octyne Derived Alkenylaluminum Reagents to Allylic Phosphates.[a]



Entry	Substrate [R]	NHC-Ag[I]; mol %	X	Temp [°C]	Time [h]	Yield [%][b]	e.r.[c]
1	Ph	**ent-3.37**; 0.5	**3.113**	–15	3	84	95:5
2	Ph	**ent-3.37**; 0.5	**3.113**	22	10 min	82	94:6
3	*o*MeC_6H_4	**3.9**; 2.0	**3.115**	–15	3	87	96.5:3.5
4	*o*$CF_3C_6H_4$	**3.9**; 2.5	**3.116**	–15	3	96	98:2
5	*o*BrC_6H_4	**3.9**; 1.0	**3.117**	–15	3	87	98:2
6	*o*BrC_6H_4	**3.9**; 1.0	**3.117**	22	10 min	92	96.5:3.5
7	*o*$MeOC_6H_4$	**3.9**; 0.5	**3.118**	–15	3	86	98.5:1.5
8	*o*$MeOC_6H_4$	**3.9**; 0.5	**3.118**	22	30 min	83	97.5:2.5
9	*o*$NO_2C_6H_4$	**3.9**; 2.0	**3.119**	–15	3	97	97.5:2.5
10	*o*$NO_2C_6H_4$	**3.9**; 2.0	**3.119**	22	10 min	89	96.5:3.5
11	*p*$NO_2C_6H_4$	**3.9**; 0.5	**3.120**	–15	3	92	94.5:5.5
12	*p*$NO_2C_6H_4$	**3.9**; 0.5	**3.120**	22	10 min	91	94.5:5.5
13	Cy	**3.9**; 2.0	**3.121**	–50	6	91	95:5
14	Cy	**3.9**; 0.5	**3.121**	22	10 min	93	93:7
15	$PhMe_2Si$	**3.9**; 0.5	**3.122**	–15	3	85	95.5:4.5
16	CO_2*t*Bu	**ent-3.37**; 0.5	**3.123**	–15	3	82	91:9
17[d]	$(CH_3)_2CHCH_2CH_2$	**3.9**; 1.0	**3.124**	–50	24	77	92.5:7.5
18	$(CH_3)_2CHCH_2CH_2$	**ent-3.37**; 0.5	**3.124**	22	10 min	84	89:11

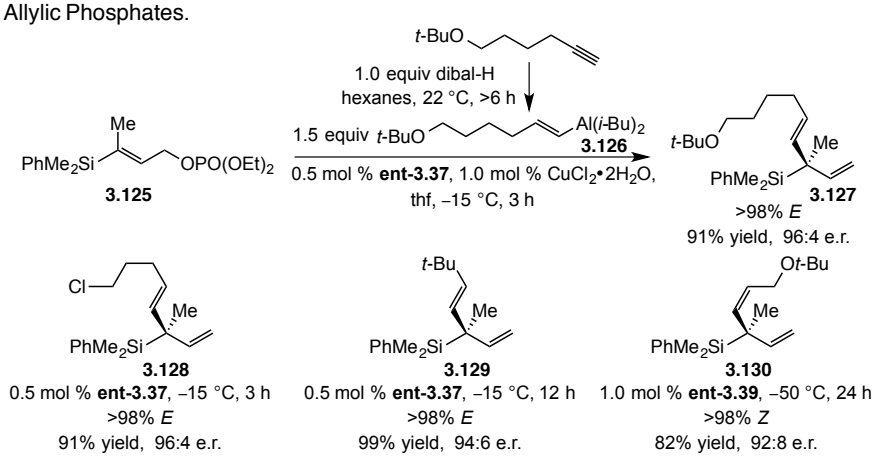
[a] Reactions were performed under N_2 atmosphere; >98% conv. in all cases. [b] Yields of isolated products after purification (±5%). [c] Determined by HPLC analysis (±2%); see the experimentals for details. [d] 91% conv. in this case.

As the results in Scheme 3.15 indicate, synthesis of 1,4-dienes **3.127**–**3.130** (Scheme 3.15) through Cu-catalyzed EAS reactions can be efficient and highly selective with a variety of in situ generated alkenylaluminum reagents through conventional hydroalumination with diabl-H, including one that contains a halide (**3.128**), a sterically demanding *tert*-butyl substituent (**3.129**), or heteroatom units (**3.127**–**3.128**). Propargyl ether containing aluminum reagents that are formed in >98% *Z* olefin isomer can be realized under non-catalytic conditions.[40] Subsequent transformations retain the alkene geometry and proceed to give 82% yield and 92:8 e.r. of allylsilane **3.130**. The

(40) For directed (*Z*-selective) hydroalumination of terminal propargyl ethers (cf., **3.130**), see: Alexakis, A.; Duffault, J. M. *Tetrahedron Lett.* **1988**, *29*, 6243–6246.

availability of a small set of chiral catalysts permits facile modifications to be done with the conditions, ensuring the highest enantiomer ratio value for each substrate.

Scheme 3.15. Cu-Catalyzed EAS of Alkenylaluminum Reagents Derived from Various Alkynes to Allylic Phosphates.

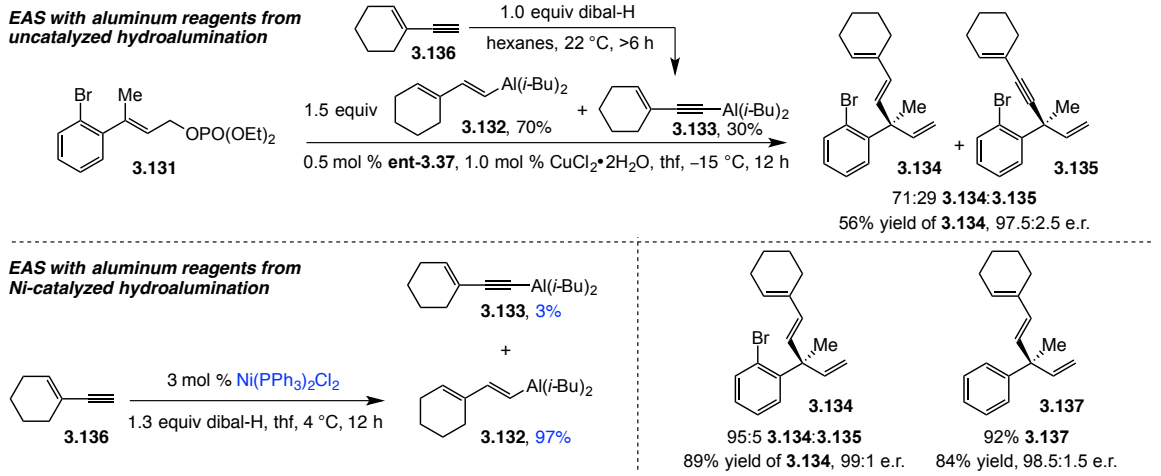


3.5.2 Catalytic EAS of Alkenyl- and Aryl-substituted Aluminum Reagents Derived from Ni-Catalyzed Hydroalumination

In contrast to NHC–Cu-catalyzed reactions that involve alkyl-substituted alkenylaluminum reagents, when the alkenylmetal is derived from an enyne through conventional hydroalumination (e.g., **3.132**, Scheme 3.16), desired product **3.134** is contaminated with alkynyl addition product **3.135**. Presumably, during hydroalumination, the alkenylmetal serves as an effective base to deprotonate the starting alkyne (cf. Scheme 3.5), affording alkynylaluminum and the corresponding protonated alkene. The above complication is completely transferred in EAS reaction with allylic phosphate **3.131**, furnishing a 7:3 mixture of alkenyl- vs. alkynyl adduct from 7:3 mixture of alkenyl- vs. alkynylaluminum reagent. In the course of searching for an effective solution to the problem of efficient alkenylaluminum synthesis with minimal alkynylaluminum presence, we resort to recently discovered catalytic variants with 3.0 mol % of commercially available $Ni(PPh_3)_2Cl_2$; hydroalumination of dibal-H with enyne **3.136** thus

proceeds efficiently (within 12 h at 4 °C) to afford the desired organometallic reagent with high selectivity (>98% β isomer) and with 3% alkyne deprotonation. Subsequent EAS with these reagents deliver the desired 1,4-diene **3.134** in 89% yield and 99:1 e.r.; the amount of alkynyl addition side product is reduced to 5% (vs. 29%). Formation of the 1,4-diene **3.137** further strengthens the reliability of the present protocol in minimizing undesired side product, while maintaining high levels of enantioselectivity; this contention is substantiated by reactions of aryl alkynes, described below.

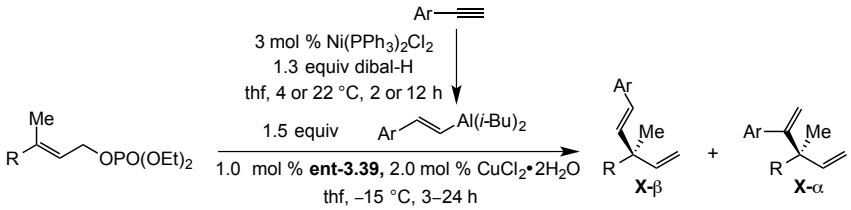
Scheme 3.16. Cu-Catalyzed EAS of Alkenylaluminum Reagents Derived from Conjugated Alkynes to Allylic Phosphates.



As the data in Table 3.12 illustrate, an assortment of aryl-substituted alkynes is readily and selectively converted to the derived β-alkenylaluminums, which are then used in situ for highly efficient as well as site- and enantioselective EAS reactions (78–92% yield of pure β product, >98% S_N2', 87:13–98:2 e.r.). In stark contrast to the process involving uncatalyzed hydroalumination (~50% alkynyl addition; Scheme 3.11), the transformations illustrated in Table 3.12 afford minimal quantity of products derived from alkynylaluminum addition (<2% by 400 MHz ^{1}H NMR analysis of the unpurified mixture). In cases where the alkyne substrate contains a sterically demanding *o*-substituted aryl group (entries 4 and 12), ~10% of the alkynyl addition product is formed,

likely as a result of diminution in the rate of catalytic hydroalumination. Moreover, in cases where the aryl unit of the alkyne bears an electron-withdrawing *p*-CF_3 substituent is >10% of the α-alkenyl adduct observed (13% and 15% in entries 3 and 11, respectively); otherwise, the desired *β*-substituted 1,4-diene products are obtained in >92% selectivity. It is notable that the presence of the Ni catalyst enhances the rate of hydroalumination such that higher conversion is attained for the overall process (alkenylaluminum formation/EAS). For an instance, the transformation corresponds to entry 5 of Table 3.12 proceeds to only 72% conversion with aluminum reagent formed from uncatalyzed hydroalumination under otherwise identical conditions, probably because of lower amounts of available active alkenylaluminum species generated during the impractical synthesis.

Table 3.12. Cu-Catalyzed EAS of Aryl-Substituted Alkenylaluminum Reagents Derived from Ni-Catalyzed Hydroalumination of Various Arylacetylenes to Allylic Phosphates.[a]

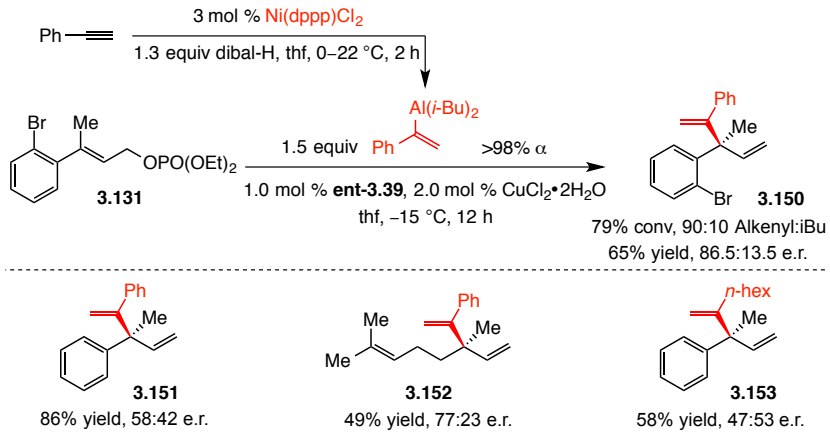


Entry	Substrate [R]	Arylacetylene [Ar]	X	Time [h]	β:α[b]	Yield [%][c]	e.r.[d]
1	Ph	Ph	**3.138**	3	95:5	78	96:4
2	Ph	*p*$MeOC_6H_4$	**3.139**	6	>98:2	84	96.5:3.5
3	Ph	*p*$CF_3C_6H_4$	**3.140**	3	87:13	82	94:6
4	Ph	*o*MeC_6H_4	**3.141**	6	>98:2	88[e]	95:5
5	*o*BrC_6H_4	Ph	**3.142**	3	96:4	91	98:2
6	*o*MeC_6H_4	*p*$MeOC_6H_4$	**3.143**	3	>98:2	82	98:2
7	*o*$NO_2C_6H_4$	Ph	**3.144**	24	>98:2	92	98:2
8	*p*$NO_2C_6H_4$	Ph	**3.145**	3	92:8	84	93:7
9	*p*$CF_3C_6H_4$	*p*$MeOC_6H_4$	**3.146**	3	>98:2	89	94:6
10	$(CH_3)_2CHCH_2CH_2$	Ph	**3.147**	3	93:7	81	90:10
11	$(CH_3)_2CHCH_2CH_2$	*p*$CF_3C_6H_4$	**3.148**	3	85:15	79	87:13
12	$(CH_3)_2CHCH_2CH_2$	*o*MeC_6H_4	**3.149**	6	>98:2	85[e]	91:9

[a] Reactions under N_2 atm. >98% conversion and >98% S_N2' in all cases. [b] By analysis of 400 MHz ^1H NMR spectra of unpurified mixtures. [c] Yield of isolated and purified β products. [d] Enantiomer ratio corresponds to β products; determined by HPLC analysis. See experimentals for details. [e] 5~10% alkynylaluminum oberved.

The encouraging results with the additions of *β*-alkenylaluminums to construct sterically encumbered quaternary stereogenic center containing enantioenriched 1,4-dienes have prompted us to engage in applying such Cu-catalyzed EAS protocols for the incorporation of α-alkenylaluminums,[41] which can be efficiently and highly selectively synthesized through catalytic hydroalumination; the data towards this end are summarized in Scheme 3.17. Subjection of the cleanly formed benzylic alkenylaluminum reagents to catalytic EAS in the presence of 1.0 mol % **ent-3.39** affords highly congested 1,4-diene **3.150** that bears a C3 quaternary carbon in 65% yield and 86.5:13.5 e.r.; the conversion of allylic **3.131** is incomplete even after 12 h (79%), underlining the difficulty in the formation of this C-C bond. Additional cases examined (cf. **3.151**–**3.153**) indicate that although appreciable efficiency can be achieved in this class of transformations, the enantioselectivity levels are low (53:47–77:23 e.r.).

Scheme 3.17. Cu-Catalyzed EAS with α-Alkenylaluminum Reagents.



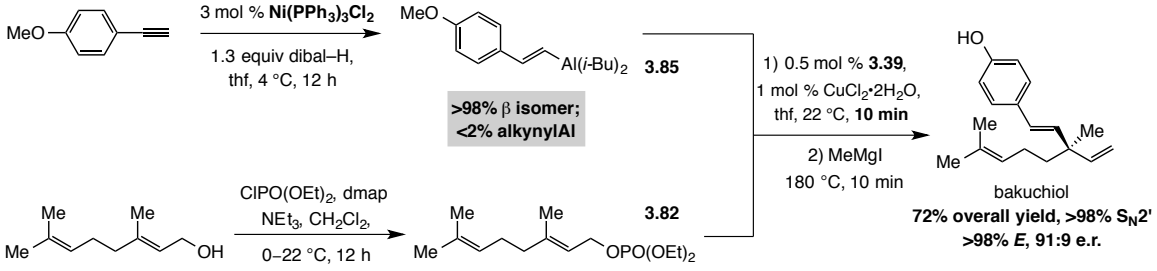
3.5.3 Concise Total Synthesis of Natural Product Bakuchiol

The utility of the sequential site selective Ni-catalyzed hydroalumination of terminal alkyne/NHC–Cu-catalyzed EAS is highlighted in the concise synthesis of

(41) The α-alkenylaluminum has been successfully used in Cu-catalyzed EAS to construct tertiary stereogenic centers, see: ref. 26.

enantiomerically enriched bakuchiol[22] shown in Scheme 3.18. The three-vessel process, involving geraniol and a commercially available terminal acetylene as starting materials, proceeds in 72% overall yield. Again, the sequence benefits from the highly site selective formation of *β*-alkenylaluminum **3.85** (>98% selectivity and <2% alkynylalane observed). The route depicted in Scheme 3.18 is substantially more concise than the most efficient of the previously reported approaches, the shortest of which requires 10 steps and delivers the target in 49% yield.[22]

Scheme 3.18. Ni-Catalyzed Hydroalumination/Cu-Catalyzed EAS Sequence in the Synthesis of Bakuchiol.



3.6 Mechanistic Insights in Sulfonate Containing NHC–Cu-catalyzed EAS Reactions with Alkenylaluminum Reagents

The highly efficient EAS reactions with a range of nucleophilic alkenylaluminum reagents, promoted by the unique class of sulfonate containing bidentate *N*-heterocyclic carbenes, prompt us to understand the mechanistic insights regarding these transformations. To begin with, we want to establish the identity of the catalytically active species especially since dimeric Ag-complexes are used to generate the Cu based catalysts. For three reasons that we believe that the complexes in action are monomeric: 1) simply examining the crystal structure of the dimeric Ag-complex **3.9**[42] suggests that

(42) To review the crystal structure, see: ref. 15 (a).

the corresponding dimeric copper species are too sterically congested and without enough coordinating sites for both substrates and the nucleophilic partners to bind at the same time. It would be much more likely for the catalysts to become active if the dimeric structures equilibrate to their monomeric counterparts first. 2) Although the crystal structures of the copper complexes are difficult to obtain, the related Al (**3.154**) and Zn (**3.155**) based crystals were secured and their monomeric structures were shown in Figure 3.3.[43] A critical difference was discovered compared to the dimeric Ag complexes; the secondary ligating sulfonate group points in the same direction with the backbone Ph unit (cf. Ag complexes shown in Figure 3.2 for comparison). Such a counterintuitive finding, as we reasoned, derives from the small seven-membered ring formed in the monomeric bidentate NHC metal complexes; the ring strain bends the sulfonate containing N-Ar unit of the heterocycle, forcing the ortho C-H bond opposite to the sulfonate intruding into the congested backbone region. Such an unfavored steric interaction can be alleviated if the C-H is in closer proximity to the backbone C-H instead of the larger phenyl ring. Based on these rationales, we propose that the corresponding copper catalysts bear similar monomeric structures (cf. **3.156**). 3) The solution nOe studies (highlighted in Figure 3.3) further support the unique structure feature of the sulfonate containing bidentate NHC metal complexes. One additional aspect merits further discussion: take a closer look at the tetrahedron Cu(I) complex, we find that the two available coordination sites (ones that are other from the two binding points of sulfonate NHC) experience steric environment imposed by the second N-Ar group differently, due to the unsymmetrical nature of the these two sites relative to the symmetric N-Ar ring (cf. side view in **3.157**). Thus, the site

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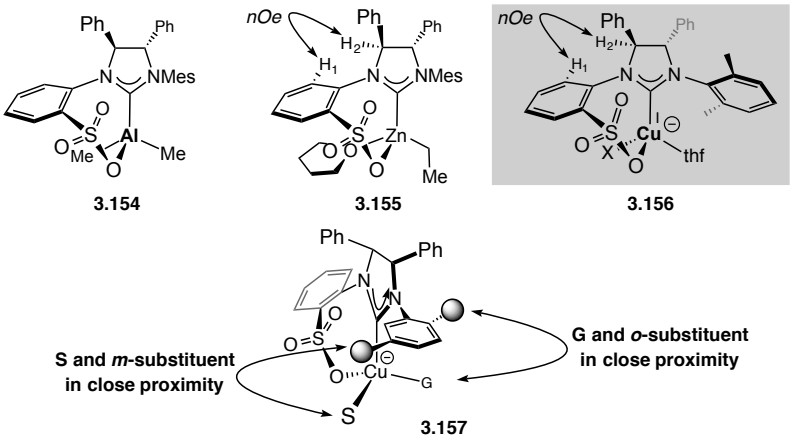
(43) Lee, Y.; Li, B.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 11625–11633.

denoted as G feels the steric presence of an ortho-substituent on the N-Ar unit, whereas the S site is in closer proximity to a meta-substituent.

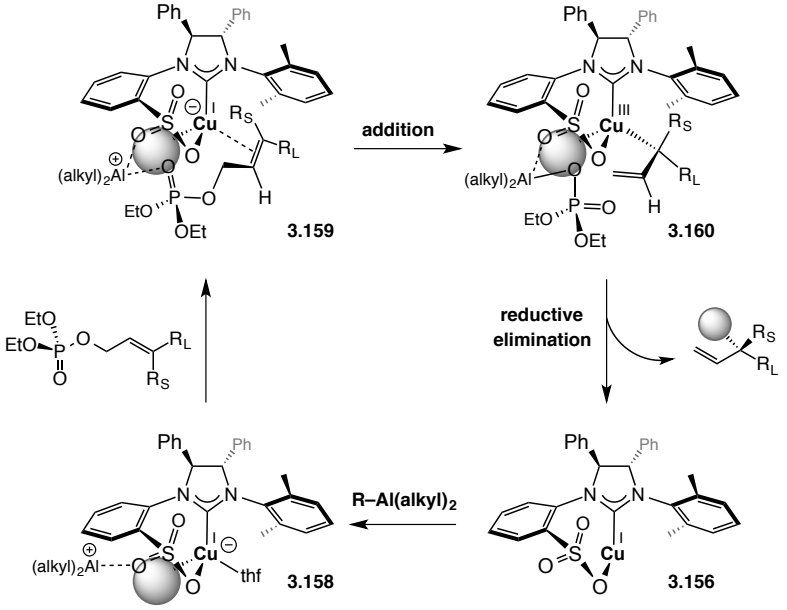
Figure 3.3. Proposed Monomeric Sulfonate Containing NHC–Cu Structure in Solution.



Based on the established active catalytic species, the following catalytic cycle, involving the additions of various alkenylaluminum reagents in Cu-catalyzed EAS reactions, is proposed (Scheme 3.19). The tetrahedron NHC–Cu(I) complex **3.156**, which has two available coordination sites (solvent bound when not in action), can accept the transfer of groups with better polarizability among the organic ligands on the aluminum metal (e.g., alkenyl vs. alkyl). The transfer is further facilitated due to the large space available at the left back quadrant of the Cu complex, a feature attributed to the syn relationship of the sulfonate moiety and the backbone Ph group. The resulting ate complex **3.158** can closely bind the cationic dialkylaluminum through the equatorially disposed sulfonate oxygen; such an orientation of the Al cation can chelate with the substrate phosphate oxygen, activating and organizing the allylic phosphate coordination from the front right site of the complex (as in **3.159**). The resulting intimate relationship between the substrate and the non-sulfonate bearing N-Ar substituent allows modifications to be done to fine tune the enantioselectivity levels (as observed in

numerous cases in the previous experimental sections). The following steps along the catalytic cycle remain controversial.[44] Both an oxidative addition/reductive elimination sequence and a direct transfer of the organic group to the γ position of the allylic phosphate are plausible to complete the cycle.

Scheme 3.19. A General Mechanistic Model for Cu-Catalyzed EAS with Aluminum Reagents.



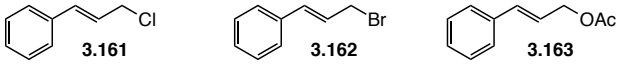
A few experimental evidences to support the above chelation scenario are collected. As illustrated in Scheme 3.20, substrates that bear less potent coordinating leaving groups are examined and proved to be much less efficient (<10% conv. of halogen containing **3.161** and **3.162** and acetate bearing **3.163** vs. allylic phosphate, Part

(44) An NHC-Cu-catalyzed EAS process might proceed through a Cu(I) mechanism (direct transfer of the vinyl unit) or a pathway that involves a Cu(III) complex (cuprate addition followed by alkyl-vinyl reductive elimination). It is not clear at present which pathway is energetically preferred. Although previous mechanistic studies point to Cu(III) mechanism being operative, such investigations were in connection to alkyl- or allylcopper complexes, considered allyl halides as substrates, and did not involve a catalyst. The more polarized nature of a Cu-C bond in a vinylmetal complex, particularly a strongly Lewis base-activated NHC–Cu-vinyl complex, and the associated steric demands of forming a Cu(III)-substituted quaternary carbon, could favor the Cu(I) pathway. For recent reports regarding the mechanism of non-catalytic allylic substitution reactions with alkyl- and allylcopper reagents, see: (a) Sofia, A.; Karlström, E.; Bäckvall, J.-E. *Chem. Eur. J.* **2001**, *7*, 1981–1989. (b) Yoshikai, N.; Zhang, S.-L.; Nakamura, E. *J. Am. Chem. Soc.* **2008**, *130*, 12862–12863. (c) Bartholomew, E. R.; Bertz, S. H.; Cope, S.; Murphy, M.; Ogle, C. A. *J. Am. Chem. Soc.* **2008**, *130*, 11244–11245. For a recent review on the mechanism of nucleophilic organoCu(I) reactions, see: (d) Yoshikai, N.; Nakamura, E. *Chem. Rev.* **2012**, *112*, 2339–2372.

1, Scheme 3.20). In part 2, NHC ligands, either monodentate (cf. **3.40**) or bidentate (cf. **3.8**), that lack the properly disposed chelating oxygen are much less efficient promoters for the Cu-catalyzed EAS reactions with alkenylaluminums. Additionally, trisubstituted allylic phosphate **3.165** with *Z* olefin geometry is an effective substrate but delivers product **3.166** enriched in the opposite enantiomer and with lower enantioselectivity (30:70 e.r. vs. 98:2 e.r. with *E* allylic phosphate, part 3, Scheme 3.20), suggesting the validity of the proposed stereochemical determining complex **3.159** (Scheme 3.19).

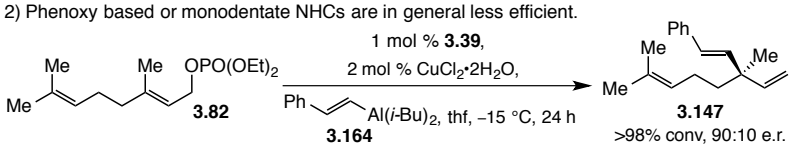
Scheme 3.20. Supporting Evidences for The Proposed Mechanistic Model.

1) Leaving groups that fail to provide chelate are ineffective.



3.161 **3.162** **3.163**

2) Phenoxy based or monodentate NHCs are in general less efficient.

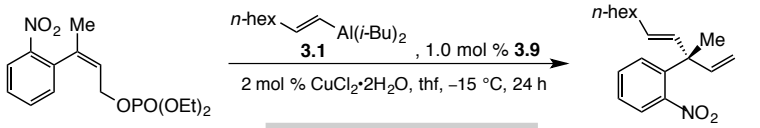


3.82 **3.164** **3.147**

>98% conv, 90:10 e.r.

with 1 mol % **3.8**	with 2 mol % **3.40**
27% conv, 71:29 e.r.	5–10% conv

3) *Z*-allylic phosphates serve as less effective substrates.



3.165

E isomer under such condtions: >98% conv, 98:2 e.r.

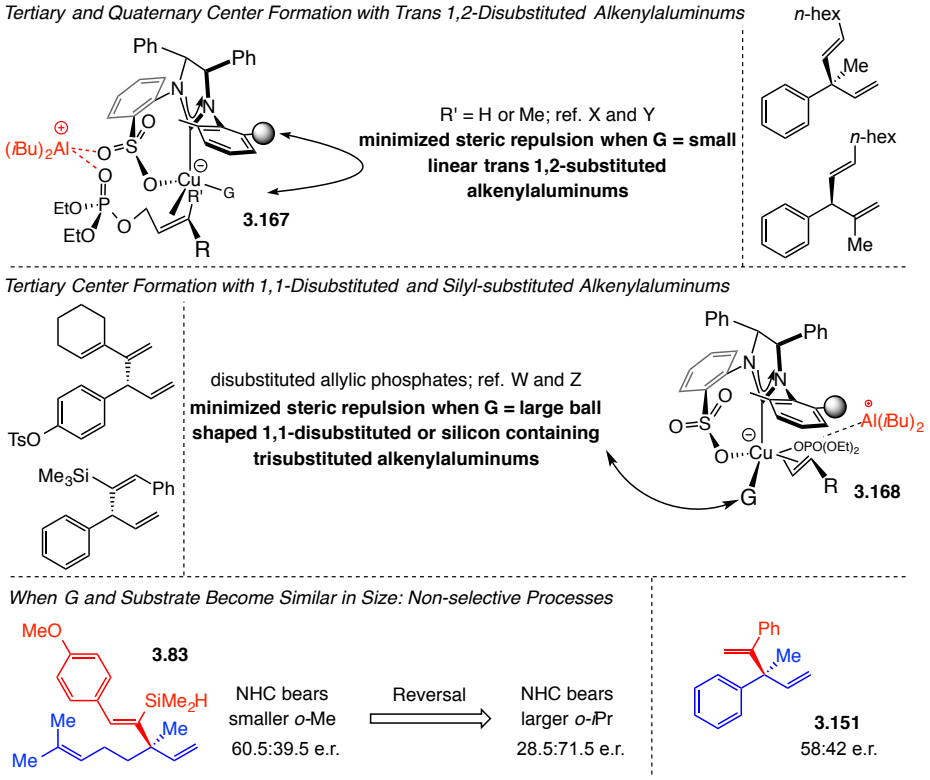
3.166

>98% conv, 30:70 e.r.

The above-suggested general catalytic cycle invokes a key metal chelate activation rendered possible through the proper positioning of the sulfonate equatorial oxygen and the Lewis basic oxygen of the phosphate unit (cf. Scheme 3.19). Such a proposal is substantiated by a few related experimental evidences, which, although still circumstantial, agree with numerous observations during the reaction development involving these sulfonate containing NHCs and organoaluminum reagents. Even though we are relatively comfortable with the above-proposed mechanistic scenario, exceptions do exist. As the stereochemical models summarized in Figure 3.4 indicate, we think that

there might be two operating systems that govern the stereochemical outcomes in the final 1,4-diene products. When allylic phosphates are coupled with small linear 1,2-*trans*-alkenylaluminum reagents, either in the formation of tertiary or quaternary stereogenic centers, the chelate model (cf. **3.167**) dominates. Such a preference derives from 1) the chelate activation and 2) the minimized steric repulsion between the ligated alkenyl unit and the *ortho*-substituent of the N-Ar group on the chiral carbenes. However, when Cu-catalyzed EAS is trying to generate a C-C bond with sterically congested silicon containing trisubstituted alkenylaluminums, another stereochemical model that alleviates the projected steric repulsion, as indicated in **3.167**, starts to operate (cf. **3.168**), delivering the 1,4-dienes with the opposite sense of stereogenicity induction. If the above proposal holds valid, the coupling reactions of nucleophiles and electrophilic alkenes with smaller size difference would be less selective. Indeed, as the synthesis of compounds **3.83** and **3.151** suggests, under the same catalytic conditions, the couplings between trisubstituted allylic phosphates and silyl-substituted alkenylaluminums as well as the reactions to construct quaternary carbon centers with internal alkenylaluminum reagents are much less enantioselective. Moreover, the data pertinent to the formation of **3.83** as shown in Figure 3.4 further support the above contention; as the change, from a smaller *o*-Me substituted N-Ar to a more hindered aromatic ring that bears *o*-*i*Pr group, occurs, the sense of absolute stereochemical induction reverses (from 60.5:39.5 e.r. to 28.5:71.5 e.r.), implying the increasing steric repulsion becomes severer such that it overcomes the preference associated with the chelate activation.

Figure 3.4. Stereochemical Models for Silyl- and Non Silyl-substituted Alkenylaluminum Reagents.



3.7 Conclusions

We have demonstrated in this chapter that a large number of differently substituted alkenylaluminum reagents can be utilized in efficient and enantioselective Cu-catalyzed EAS reaction of an assortment of allylic phosphates, furnishing several classes of enantioenriched 1,4-dienes that bear a C3 tertiary or quaternary stereogenic center. Specifically, we have explored hydroalumination of silyl-substituted alkynes, the products of which are readily incorporated into dienes that feature stereochemical well defined trisubstituted alkenylsilanes[45] in almost optical pure form; several fronts in

(44) For representative examples in catalytic cross-couplings involving sp2 hybridized C-Si bond, see: (a) Hatanaka, Y.; Hiyama, T. *J. Org. Chem.* **1988**, *53*, 918–920. (b) Tamao, K.; Kobayashi, K.; Ito, Y. *Tetrahedron Lett.* **1989**, *30*, 6051–6054. (c) Denmark, S. E.; Pan, W. *Org. Lett.* **2003**, *5*, 1119–1122. (d) Denmark, S. E.; Tymonko, S. A. *J. Am. Chem. Soc.* **2005**, *127*, 8004–8005. (e) Nakao, Y.; Imanaka, H.;

selectivity are effectively addressed to allow the development of an efficient and highly selective protocol. Furthermore, we have identified two sets of distinct conditions that convert terminal alkynes, either alkyl- or aryl-substituted, to terminal and internal alkenylaluminum reagents, addressing the long-standing challenge associated with the impractical reactions of dibal-H with aromatic acetylenes. New classes of synthetically useful building blocks (e.g., alkenyl halides and borons) are rendered easily accessible through simple conversions of the C-Al bonds. Finally, the use of the above introduced alkenylaluminum reagents in the formation of difficult-to-access quaternary stereogenic center containing 1,4-dienes is developed under Cu-catalysis promoted by a collection of chiral *N*-heterocyclic carbenes. Stereo- and enantioselective synthesis of naturally occurring nyasol and bakuchiol further underscores the utilities of the methods outlined in this chapter.

3.8 Experimentals

3.8.1 Representative Experimental Procedures for Cu-catalyzed EAS with Silicon Containing Trisubstituted Alkenylaluminum Reagents and Characterization Data of New Compounds

General. Infrared (IR) spectra were recorded on a Nicolet 210 spectrophotometer, ν_{max} in cm^{-1}. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). ^1H NMR spectra were recorded on a Varian Unity INOVA 400 (400 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as

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Sahoo, A. K.; Yada, A.; Hiyama, T. *J. Am. Chem. Soc.* **2005**, *127*, 6952–6953. (f) Denmark, S. E.; Baird, J. D. *Chem. Eur. J.* **2006**, *12*, 4954–4963.

the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, sept = septuplet, br = broad, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on a Varian Unity INOVA 400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: 77.16 ppm). High-resolution mass spectrometry was performed on a Micromass LCT ESI-MS (positive mode) at the Mass Spectrometry Facility, Boston College. Enantiomer ratios were determined by analytical liquid chromatography (HPLC) on a Shimadzu chromatograph (Chiral Technologies Chiralpak AS (4.6 x 250 mm), Chiral Technologies Chiralpak OD (4.6 x 250 mm), Chiral Technologies Chiralpak OD-R (4.6 x 250 mm) or Chiral Technologies Chiralpak AD (4.6 x 250 mm)) in comparison with authentic racemic materials. Optical rotations were measured on a Rudolph Research Analytical Autopol IV Polarimeter.

Unless otherwise noted, all reactions were carried out with distilled and degassed solvents under an atmosphere of dry N_2 in oven (135 ^oC) and flame-dried glassware with standard dry box or vacuum-line techniques. All work-up and purification procedures were carried out with reagent grade solvents (purchased from Doe & Ingalls) in air. Substrates were prepared by known procedures.[46] All substrates possess *E*-olefin geometry (>98%); purity was established by ^1H NMR analysis (400 MHz).

■ Reagents and Ligands:

Acetic acid: Purchased from Fisher and used as received.

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(46) Luchaco-Cullis, C. A.; Mizutani, H.; Murphy, K. E.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2001**, *40*, 1456–1460.

Acetic anhydride: Purchased from Acros and used as received.

9-Borabicyclo[3.3.1]nonane: Purchased from Aldrich and used without further purification.

Chlorodiethylphosphate: Purchased from Aldrich and used as received.

Chloroform: Purchased from Fisher Scientific and distilled from CaH_2 under N_2.

Copper (II) chloride dihydrate: Purchased from Aldrich and used without further purification.

Di-*t*-butyl dicarbonate: Purchased from Advanced Chem Tech and used as received.

Diisobutyl aluminum hydride (neat): Purchased from Aldrich and used as received.

2,6-Diisopropylaniline: Purchased from Aldrich and used as received.

4-Dimethylaminopyridine: Purchased from Advanced Chem Tech used as received.

***N*,*N*'-Dimethylformamide** (anhydrous): Purchased from Aldrich and used as received.

***N*,*N*'-Dimethylmethylene ammonium iodide**: Purchased from Lancaster and used as received.

1-(Dimethylsilyl)-2-phenylacetylene: Purchased from Aldrich and used after distillation from CaH_2 under N_2.

1,4-Dioxane (anhydrous): Purchased from Aldrich and used as received.

[(4-Fluorophenyl)ethynyl]trimethylsilane: Purchased from Aldrich and used after distillation from CaH_2 under N_2.

Hydrogen peroxide (35% wt solution in water): Purchased from Aldrich and used without further purification.

4-Iodophenol: Purchased from Aldrich and used without further purification.

Methanol (extra dry with molecular sieves**)**: Purchased from Acros and used as received.

Palladium acetate: Purchased from Strem (99% purity) and used as received.

Phenylethynyltrimethylsilane: Purchased from Aldrich and used after distillation from CaH_2 under N_2.

Potassium carbonate: Purchased from Aldrich and used as received.

Pyridine (anhydrous): Purchased from Aldrich and used as received.

Racemic-2,2'-bis(diphenylphosphino)-1,1'-binapthyl (*rac*-binap): Purchased from Aldrich (99% purity) and used as received.

Silver (I) oxide: Prepared by previously reported methods.[47]

Sodium *tert*-butoxide (98%): Purchased from Strem and used as received.

Sodium hydride (60% dispersion): Purchased from Strem and used as received.

Tetrahydrofuran: Distilled under N_2 from sodium benzophenone ketyl.

Triethylamine: Purchased from Aldrich and distilled from CaH_2 under N_2.

Trifluoroacetic acid: Purchased from Acros and used as received.

Trimethylsilyl acetylene: Purchased from Acros and used without further purification.

2-(Trimethylsilylethynyl)anisole: Purchased from Aldrich and used after distillation from CaH_2 under N_2.

4-(Trimethylsilylethynyl)toluene: Prepared by a known procedure.[48]

3-(Trimethylsilylethynyl)toluene: Prepared by a known procedure.[48]

1-(Trimethylsilylethynyl)-4-(trifluoromethyl)benzene: Purchased from Aldrich and used after distillation from CaH_2 under N_2.

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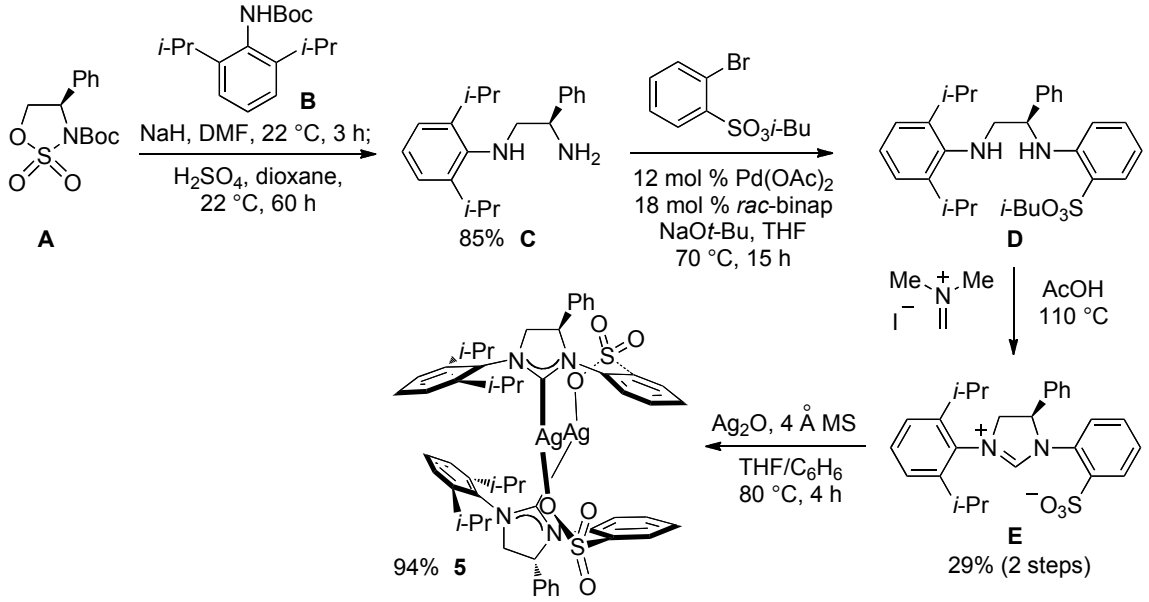
(47) May, T. L.; Brown, M. K.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2008**, *47*, 7358-7362.
(48) Leventis, N.; Rawashdeh, A. M.; Elder, I. A.; Yang, J.; Dass, A.; Sotiriou-Leventis, C. *Chem. Mater.* **2004**, *16*, 1493-1506.

Benzene, Dichloromethane, Diethyl ether, and Hexanes: Purified by being passed through two alumina columns under a positive pressure of dry argon by a modified Advanced ChemTech purification system.

Scheme 1. Synthesis of NHC-Ag **5**



(2,6-Diisopropylphenyl)-carbamic acid tert-butyl ester (B):[49] To a solution of 2,6-diisopropylaniline (3.80 mL, 20.0 mmol) in water (100 mL) was added $(Boc)_2O$ (4.36 g, 22.0 mmol) in one portion. After allowing to stir for 48 hours, the mixture was extracted with Et_2O (100 mL x 3), the combined organic layers were washed with 1N HCl (100 mL x 3), dried over $MgSO_4$, and evaporated under reduced pressure. The resulting residue was dried under vacuum to afford a light red solid in 73% yield (4.03 g, 14.5 mmol).

IR (neat): 3310 (w), 2960 (m), 2929 (w), 2868 (w), 1686 (s), 1591 (w), 1503 (s), 1390 (w), 1364 (m), 1248 (s), 1164 (s), 1055 (s), 1025 (m), 937 (w), 918 (w), 840 (w), 801 (w), 774 (w), 721 (m), 617 (m), 458 (w), 417 (w) cm^{-1}; This compound was isolated as a

(49) Chankeshwara, S. V.; Chakraborti, A. K. *Org. Lett.* **2006**, *8*, 3259-3262.

mixture of rotomers. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 (1H, t, *J* = 7.2 Hz, Ar**H**), 7.13 (2H, d, *J* = 7.2 Hz, Ar**H**) 5.80 (0.6H, brs, ArN**H**), 5.63 (0.4H, brs, ArN**H**), 3.30-3.10 (2H, m, ArC**H**$(CH_3)_2$), 1.49 (5.4H, s, ArOCOC(C**H**$_3)_3$), 1.35 (3.6H, s, ArOCOC(C**H**$_3)_3$), 1.20 (12H, d, *J* = 6.8 Hz, ArCH(C**H**$_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.6, 146.8, 131.1, 127.9, 123.3, 79.6, 28.6, 28.2, 23.5; HRMS (ESI+) Calcd for $C_{17}H_{28}N_1O_2$ $[M+H]^+$: 278.2120. Found: 278.2118.

(*R*)-N2-(2,6-Diisopropyl-phenyl)-1-phenyl-ethane-1,2-diamine (C): To a two necked, 100 mL flask was added NaH (60% dispersion, 640 mg, 16.0 mmol), *tert*-butyl-2,6-diisopropylphenylcarbamate **B** (3.88 g, 14.0 mmol) and DMF (35.0 mL) under N_2. After allowing the solution to stir at 22 °C for 30 min, sulfonamide **A**[50] (2.99 g, 10.0 mmol) was added as a solid in one portion and the resulting mixture was allowed to stir for 15 h. A distillation head was equipped and DMF was removed under reduced pressure (~3 mmHg) with gentle heating (<60 °C). Dioxane (35.0 mL) was added followed by concentrated H_2SO_4 (2.0 mL, ~18 M). The resulting solution was allowed to stir at 22 °C for 60 hours. (The reaction was monitored by TLC analysis and an additional portion of H_2SO_4 (1.0 mL) was added after stirring 18 hours. A saturated aqueous solution of Na_2CO_3 was added until pH = ~10. CH_2Cl_2 (100 mL) was added and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (100 mL x 3), and the organic layers were combined, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc from 20/1 to 1/1) to afford the desired product in 85% yield (2.53 g, 8.53 mmol)

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(50) Sulfonamide **A** was prepared by previously reported procedure; see; Ref. 47.

IR (neat): 3368 (w), 2959 (s), 2866 (w), 1760 (w), 1692 (w), 1588 (w), 1491 (w), 1449 (s), 1382 (w), 1362 (w), 803 (m), 751 (s), 699 (s), 575 (w), 529 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.41-7.27 (5H, m, Ar**H**), 7.09-6.98 (3H, m, Ar**H**), 4.20 (1H, t, J = 6.2 Hz, $NH_2C\mathbf{H}Ph$), 3.13 (2H, dsept, J = 6.8, 1.0 Hz, $ArC\mathbf{H}(CH_3)_2$), 3.07-3.02 (2H, m, $ArNHC\mathbf{H}_2$), 2.21 (brs, 3H, $N\mathbf{H}CH_2CH(Ph)N\mathbf{H}_2$) 1.17 (12H, d, J = 6.8 Hz, $ArCH(C\mathbf{H}_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.2, 143.0, 142.5, 128.6, 127.4, 126.3, 123.7, 123.4, 59.1, 56.3, 27.4, 24.1; HRMS (ESI+) Calcd for $C_{20}H_{29}N_2$ $[M+H]^+$: 297.2330. Found: 297.2328; $[\alpha]^{20}_D$ –24.9 (c = 1.19, $CHCl_3$).

Imidazolinium salt (E): To a 150 mL round bottom flask in a N_2-filled glove box was added $Pd(OAc)_2$ (308 mg, 1.37 mmol), *rac*-binap (1.28 g, 2.05 mmol), and NaO*t*-Bu (1.97 g, 20.5 mmol). The flask was fitted with a reflux condenser, capped with a septum and removed from the glove box. A solution of diamine **C** (3.40 g, 11.4 mmol) and isobutyl-2-bromobenzenesulfonate[51] (4.02 g, 13.7 mmol) in thf (50 mL) was added through a syringe and the resulting red solution was allowed to stir at 60 °C for 20 h. The reaction mixture was allowed to cool to 22 °C before filtered through filter paper, and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (petroleum ether/Et_2O from 100/1 to 20/1) to afford a mixture of diamine **D** and isobutylbenzenesulfonate (3.89 g). The resulting mixture was used in next step.

A 150 mL round bottom flask was charged with a mixture of diamine **D** and isobutylbenzenesulfonate (3.89 g) and *N*,*N'*-dimethylmethylene ammonium iodide (5.46 g, 29.5 mmol), and acetic acid (40 mL); the flask was equipped with a reflux condenser

(51) The compound was prepared by a previously reported procedure; see; Brown, M. K.; May, T. L.; Baxter, C. A.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2007**, *46*, 1097–1100.

and the solution was allowed to stir at 110 °C for 2.5 h. The reaction mixture was transfered to a 500 mL flask, and neutralized by the addition of sat. $NaHCO_3$ (aq.). The aqueous layer was washed with CH_2Cl_2 (100 mL x 3), and the combined organic layers were washed with sat. Na_2SO_3 (aq.), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH from100/1 to 20/1). The yellow residue was further purified by trituration with pentane to afford imidazolinium salt **E** as a white solid in 29% yield (over two steps, 1.54 g, 3.33 mmol).

IR (neat): 3457 (br), 2962 (w), 2927 (w), 2869 (w), 1619 (s), 1585 (m), 1458 (w), 1386 (w), 1365 (w), 1333 (w), 1234 (s), 1199 (s), 1141 (w), 1090 (m), 1055 (w), 1022 (m), 935 (w), 888 (w), 865 (w), 808 (w), 757 (s), 729 (w), 703 (m), 651 (w), 610 (s), 564 (m), 537 (w), 498 (w), 451 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.81 (1H, s, N=C**H**N), 8.12 (1H, dd, *J* = 8.0, 1.6 Hz, Ar**H**), 7.50-7.43 (6H, m, Ar**H**), 7.30-7.25 (3H, m, Ar**H**), 7.08 (1H, td, *J* = 8.0, 1.6 Hz, Ar**H**), 6.65 (1H, dd, *J* = 8.0, 1.2 Hz, Ar**H**), 6.25 (1H, dd, *J* = 12.0, 10.0 Hz, NCH_2C**H**(Ph)N), 4.81 (1H, t, *J* = 12.0 Hz, NC**H**$_2$CH(Ph)N), 4.11 (1H, dd, *J* = 11.6, 9.6 Hz, NC**H**$_2$CH(Ph)N), 3.64 (1H, sept, *J* = 6.8 Hz, ArC**H**$(CH_3)_2$), 3.18 (1H, sept, *J* = 6.8 Hz, ArC**H**$(CH_3)_2$), 1.40 (3H, d, *J* = 6.8 Hz, $ArCH(C$**H**$_3)_2$), 1.32 (3H, d, *J* = 6.8 Hz, $ArCH(C$**H**$_3)_2$), 1.29 (3H, d, *J* = 6.8 Hz, $ArCH(C$**H**$_3)_2$), 1.24 (3H, d, *J* = 6.8 Hz, $ArCH(C$**H**$_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.7, 148.1, 145.6, 143.7, 135.9, 131.2, 130.5, 130.0, 129.7, 129.6, 129.5, 128.2, 126.6, 125.5, 124.5, 68.2, 61.3, 28.8, 28.0, 24.8, 24.7, 24.7, 24.6; HRMS (ESI+) Calcd for $C_{27}H_{31}N_2O_3S_1$ $[M+H]^+$: 463.2044. Found: 463.2055; $[\alpha]^{20}_D$ –130.0 (*c* = 0.96, $CHCl_3$).

NHC-Ag complex (3.39): Imidazolinium salt **E** (50.0 mg, 0.108 mmol), Ag_2O (50.0 mg, 0.215 mmol), and oven-dried 4 Å molecular sieves (powdered) were weighed out into an oven-dried 25 mL vial wrapped with aluminum foil. Tetrahydrofuran (1.0 mL), followed immediately by benzene (1.0 mL), were added through a syringe resulting in a black heterogeneous mixture. The vial was capped and sealed with electrical tape, which was allowed to stir at 80 °C. After 4 h, the mixture was allowed to cool to 22 °C and filtered through a short plug of Celite 545 eluted with thf (ca 4 mL) the solution was concentrated under vacuum to afford the desired product as a white solid in 94% yield (57.9 mg, 0.0508 mmol).

IR (neat): 3435 (br), 3059 (w), 3027 (w), 2960 (w), 2923 (w), 2867 (w), 1479 (s), 1445 (w), 1333 (w), 1274 (w), 1194 (s), 1137 (m), 1091 (m), 1055 (w), 1022 (s), 867 (w), 805 (w), 756 (s), 700 (m), 663 (w), 608 (s), 564 (m), 548 (m), 458 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.91 (1H, br, Ar**H**), 8.12 (1H, dd, *J* = 8.0, 1.6 Hz, Ar**H**), 7.34-7.17 (6H, m, Ar**H**), 7.08-7.06 (2H, m, Ar**H**), 6.94 (1H, d, *J* = 6.4 Hz, Ar**H**), 6.60 (1H, br, Ar**H**), 6.06-5.98 (2H, br, Ar**H**, $NCH_2C\mathbf{H}(Ph)N$), 4.29 (1H, br, $NC\mathbf{H}_2CH(Ph)N$), 3.65 (1H, dd, *J* = 11.2, 7.2 Hz, $NC\mathbf{H}_2CH(Ph)N$), 3.21 (1H, br, $ArC\mathbf{H}(CH_3)_2$), 3.23 (1H, br, $ArC\mathbf{H}(CH_3)_2$), 1.42 (3H, br, $ArCH(C\mathbf{H}_3)_2$), 1.23-1.10 (6H, br, $ArCH(C\mathbf{H}_3)_2$), 0.73 (3H, br, $ArCH(C\mathbf{H}_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.4, 205.5, 148.5, 145.9, 143.5, 139.8, 135.4, 134.7, 130.6, 130.0, 129.4, 128.9, 128.5, 128.2, 128.0, 125.3, 123.3, 68.3, 62.7, 28.3, 27.3, 25.6, 25.1, 24.6, 24.2; HRMS (ESI+) Calcd for $C_{27}H_{29}N_2O_3S_1Ag_1Na_1$ $[M+Na]^+$: 591.0848. Found: 591.0859; $[\alpha]^{20}_D$ –106.1 (*c* = 0.36, $CHCl_3$).

NHC-Ag complex (3.59): Prepared from the same procedure as described for NHC–Ag complex **3.39** in 87% yield as a pale yellow solid. The imidazolinium salt is prepared according to a known procedure.[52]

IR (neat): 3448 (br), 3065 (w), 2961 (w), 2927 (w), 2923 (w), 2870 (w), 2247 (w), 1473 (m), 1450 (m), 1226 (m), 1197 (m), 1138 (w), 1093 (w), 1022 (w), 905 (s), 725 (s), 698 (s), 646 (m), 612 (m), 561 (w), 540 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (1H, d, *J* = 7.6 Hz, Ar**H**), 7.26-7.18 (6H, m, Ar**H**), 7.09-7.07 (4H, m, Ar**H**), 6.97-6.95 (2H, m, Ar**H**), 6.51-6.45 (3H, m, Ar**H**), 6.22 (1H, d, *J* = 7.6 Hz, NCH(Ph)C**H**(Ph)N), 4.97 (1H, d, *J* = 12.0 Hz, NC**H**(Ph)CH(Ph)N), 3.29 (1H, brs, ArC**H**$(CH_3)_2$), 2.89 (2H, brs, ArC**H**$(CH_3)_2$), 1.54 (6H, brs, ArCH(C**H**$_3)_2$), 1.27 (6H, brs, ArCH(C**H**$_3)_2$), 0.60 (3H, brs, ArCH(C**H**$_3)_2$), 0.22 (3H, brs, ArCH(C**H**$_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.7, 204.9, 149.0, 148.4, 145.2, 143.5, 138.6, 135.5, 133.6, 131.0, 130.6, 130.2, 129.7, 128.9, 128.8, 128.6, 128.4, 128.0, 122.2, 121.1, 79.5, 72.7, 68.1, 33.9, 28.7, 28.0, 27.5, 26.6, 24.9, 24.0, 23.9, 21.5; HRMS (ESI+) Calcd for $C_{36}H_{39}N_2O_3S_1Ag_1Na_1$ $[M+Na]^+$: 709.1630. Found: 709.1646; $[\alpha]^{20}_D$ –11.75 (*c* = 0.80, $CHCl_3$).

Preparation of ethynyldimethylsilanes: A variety of aryl-substituted ethylnyldimethylsilanes were prepared according to a known procedure.[53]

Preparation of allylic phosphate substrates: Allylic alcohols were prepared from the corresponding aldehydes by a two-step Horner-Wadsworth-Emmons

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(52) Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 3160–3161.
(53) Maifeld, S. V.; Lee, D. *Org. Lett.* **2005**, *7*, 4995–4998.

olefination[54]/DIBAL-H reduction[55] sequence. Allylic alcohols were converted to the corresponding allylic phosphates using a known procedure.[46] The compounds that have not been reported are assigned below.

2-Methoxycinnamyl diethyl phosphate (Table 3.2, entry 2): IR (neat): 2982 (w), 2909 (w), 2838 (w), 1597 (w), 1489 (m), 1462 (m), 1438 (w), 1242 (s), 1163 (w), 1022 (s), 964 (s), 817 (m), 750 (s), 732 (s), 528 (m), 462 (m), cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.46 (1H, dd, *J* = 8.0, 2.0 Hz, Ar**H**), 7.28 (1H, dt, *J* = 8.0, 1.5 Hz, Ar**H**), 7.02 (1H, d, *J* = 16.0 Hz, ArC**H**=CH), 6.96 (1H, dt, *J* = 8.0, 1.0 Hz, Ar**H**), 6.90 (1H, dd, *J* = 8.0, 1.0 Hz, Ar**H**), 6.36 (1H, dt, *J* = 16.5, 6.0 Hz, ArCH=C**H**), 4.74 (2H, ddd, *J* = 8.0, 6.5, 1.5 Hz, CH=CHC**H**$_2$), 4.17 (4H, dq, *J* = 7.5, 7.5 Hz, PO(OC**H**$_2$CH$_3$)$_2$), 3.88 (3H, s, ArOC**H**$_3$), 1.37 (6H, td, *J* = 7.5, 1.0 Hz, PO(OCH$_2$C**H**$_3$)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.1, 129.4, 129.2, 127.4, 125.2, 124.3 (d, *J* = 6.7 Hz), 120.8, 111.0, 68.7 (d, *J* = 5.2 Hz), 63.9 (d, *J* = 6.0 Hz), 55.5, 16.3 (d, *J* = 6.7 Hz); HRMS (ESI+) Calcd for $C_{14}H_{25}N_1O_5P_1$ $[M+NH_4]^+$: 318.1470. Found: 318.1471.

Phosphoric acid 3-(3-bromo-phenyl)-allyl ester diethyl ester (Table 3.2, entry 5): IR (neat): 2982 (w), 1591 (w), 1562 (w), 1475 (w), 1261 (s), 1165 (w), 1010 (s), 960 (s), 816 (m), 773 (m), 680 (m), 522 (m), 433 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.53 (1H, t, *J* = 1.8 Hz, Ar**H**), 7.39 (1H, dq, *J* = 8.0, 0.8 Hz, Ar**H**), 7.29 (1H, d, *J* = 7.6 Hz, Ar**H**), 7.19 (1H, t, *J* = 7.8 Hz, Ar**H**), 6.60 (1H, d, *J* = 16.0 Hz, ArC**H**=CH), 6.30 (1H, dt, *J* = 16.0, 6.0 Hz, ArCH=C**H**), 4.69 (2H, ddd, *J* = 7.8, 7.2, 1.6 Hz, CH=CH-C**H$_2$**), 4.13 (4H, dq, *J* = 7.6, 7.2 Hz, PO(C**H$_2$**CH$_3$)$_2$), 1.34 (6H, td, *J* = 7.2, 0.8 Hz, PO(CH$_2$C**H$_3$**)$_2$); ^{13}C

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(54) Nestl, B. M.; Glueck, S. M.; Hall, M.; Kroutil, W.; Stuermer, R.; Hauer, B.; Faber, K. *Eur. J. Org. Chem.* **2006**, 4573–4577.

(55) Clive, D. L. J.; Stoffman, E. J. L. *Chem. Comm.* **2007**, *21*, 2151–2153.

NMR (100 MHz, $CDCl_3$): δ 138.1, 132.0, 130.9, 130.1, 129.4, 125.2, 125.1, 122.7, 67.4 (d, *J* = 5.3 Hz), 63.8 (d, *J* = 5.6 Hz), 16.1 (d, *J* = 6.9 Hz); HRMS (ESI+) Calcd for $C_{13}H_{19}Br_1O_4P_1$ $[M+H]^+$: 349.0204. Found: 349.0201.

Phosphoric acid 3-(4-chloro-phenyl)-allyl ester diethyl ester (Table 1, entry 6): IR (neat): 2982 (w), 1491 (w), 1262 (s), 1007 (s), 962 (s), 795 (m), 747 (w), 679 (w), 505 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.32 (2H, dd, *J* = 6.4, 2.8 Hz, Ar**H**), 7.29 (2H, dd, *J* = 6.4, 2.8 Hz, Ar**H**), 6.63 (1H, dt, *J* = 16.0, 1.2 Hz, ArC**H**=CH), 6.28 (1H, dt, *J* = 16.0, 5.8 Hz, ArCH=C**H**), 4.68 (2H, ddd, *J* = 16.0, 6.4, 1.4 Hz, CH=CHC**H**$_2$), 4.13 (4H, dq, *J* = 8.0, 7.0 Hz, PO(OC**H**$_2$CH$_3$)$_2$), 1.34 (6H, td, *J* = 7.0, 0.8 Hz, PO(OCH$_2$C**H**$_3$)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 134.5, 133.8, 132.4, 128.8, 127.8, 124.2 (d, *J* = 6.5 Hz), 67.6 (d, *J* = 5.7 Hz), 63.8 (d, *J* = 5.7 Hz), 16.1 (d, *J* = 6.4 Hz); HRMS (ESI+) Calcd for $C_{13}H_{19}Cl_1O_4P_1$ $[M+H]^+$: 305.0709. Found: 305.0706.

Toluene-4-sulfonic acid 4-[3-(diethoxy-phosphoryloxy)-propenyl]-phenyl ester (Table 1, entry 8): IR (neat): 2983 (w), 1597 (w), 1501 (m), 1370 (m), 1264 (m), 1197 (m), 1176 (m), 1152 (m), 1091 (m), 1011 (s), 965 (s), 860 (s), 811 (s), 731 (m), 708 (m), 659 (m), 548 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.69 (2H, d, *J* = 8.0 Hz, Ar**H**), 7.30 (2H, d, *J* = 8.0 Hz, Ar**H**), 7.29 (2H, d, *J* = 8.8 Hz, Ar**H**), 6.93 (2H, d, *J* = 8.8 Hz, Ar**H**), 6.61 (1H, d, *J* = 15.6 Hz, ArC**H**=CH), 6.24 (1H, dt, *J* = 16.0, 6.0 Hz, ArCH=C**H**), 4.67 (2H, ddd, *J* = 8.4, 6.0, 1.2 Hz, CH=CHC**H**$_2$), 4.13 (4H, dq, *J* = 6.8, 6.8 Hz, PO(OC**H**$_2$CH$_3$)$_2$), 2.44 (3H, s, ArC**H**$_3$), 1.33 (6H, td, *J* = 7.0, 0.8 Hz, PO(OCH$_2$C**H**$_3$)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.2, 145.3, 135.0, 132.3, 132.1, 129.7, 128.4, 127.7, 124.7 (d, *J* = 6.5 Hz), 122.5, 67.5 (d, *J* = 5.3 Hz), 63.8 (d, *J* = 5.7 Hz), 21.6, 16.1 (d, *J* =

6.5 Hz); HRMS (ESI+) Calcd for $C_{20}H_{29}N_1O_7P_1S_1$ $[M+NH_4]^+$: 458.1402. Found: 458.1404.

Representative procedure for the synthesis of *E*-alkenylaluminum reagents (Table 3.2–3.3):[56] Under a N_2 atmosphere, phenylethynyltrimethylsilane (1.18 mL, 6.00 mmol) and hexanes (3.75 mL) were added to 10 mL round bottom flask equipped with a reflux condenser. The solution was allowed to cool to 0 °C and dibal–H (1.07 mL, 6.00 mmol) was added through a syringe. The solution was allowed to stir at 55 °C (oil bath) for 2 h. The resulting solution was used without further purification.

General Procedure for Cu-catalyzed Enantioselective Alkenyl Additions to Allylic Phosphates (Table 3.2–3.3): A 10 mL test tube equipped with a stir bar was charged with NHC-Ag **3.39** (2.3 mg, 0.0020 mmol) in a N_2 filled glovebox. The test tube was sealed with a septum and removed from the glovebox. Tetrahydrofuran (2.0 mL) and a solution of $CuCl_2$•$2H_2O$ (0.01M in THF, 400 μL, 0.004 mmol) was added to the test tube at 22 °C. The blue solution was allowed to cool to –78 °C (dry ice/acetone), followed by addition of the vinylaluminum reagent (1.0 M in hexane, 300 μL, 0.300 mmol) and substrate (0.200 mmol). The mixture was allowed to warm to –15 °C for 6 h, after which time, the reaction was quenched by addition of a saturated aqueous solution of Rochelle's salt (3.0 mL) and allowed to stir for 1 h at 22 °C. The organic layer was separated, and the aqueous layer was washed with Et_2O (1.0 mL x 3). The combined organic layers were passed through a short plug of $MgSO_4$, and concentrated under reduced pressure. The

(56) Negishi, E.; Takahashi, T.; Baba, S. *Org. Synth., Coll.* **1993**, *8*, 295–297.

resulting yellow residue was purified by silica gel column chromatography to give products as clear oil.

General Procedure for Cu-catalyzed Enantioselective Alkenyl Additions to Allylic Phosphates (Table 3.4): A 10 mL Schlenk tube equipped with a stir bar was charged with dibal–H (71 μL, 0.40 mmol) and tetrahydrofuran (65 μL, 0.80 mmol) under N_2. Alkynyldimethylsilanes (0.40 mmol) in hexanes (325μL) were added to the reaction vassel. After allowing to stir at 55 °C for 2 hours, the solution was allowed to cool to -78 °C (dry ice/acetone) and a solution of NHC–Ag **3.59** (2.7 mg, 0.0020 mmol) and $CuCl_2$•$2H_2O$ (0.68 mg, 0.0040 mmol) in THF (2.4 mL) was added through a syringe. After allowing the solution to stir for 10 min, the substrate (0.20 mmol) was added and the solution was allowed to warm to –15 °C (freezer) and sit for 12 hours. The reaction was quenched with a saturated aqueous solution of Rochelle's salt (3.0 mL) and allowed to stir for 1 hour at 22 °C. The organic layer was separated and the aqueous layer was washed with Et_2O (1 mL x 3). The combined organic layers were passed through a short plug of $MgSO_4$, and concentrated under reduced pressure. The resulting yellow residue was purified by silica gel column chromatography to afford the desired products as clear oil.

General Procedure for Hydroboration-Oxidation of 1,4-Dienes: To a 10 mL test tube charged with 1,4-diene **3.44** (27.6 mg, 0.0900 mmol) in THF (1.0 mL) was added a 0.1 M THF solution of 9-BBN (1.0 mL, 0.100 mmol) under N_2 at 22 °C. The reaction mixture was allowed to stir for 15 h. The mixture was quenched by the addition of 30% wt H_2O_2 solution (300 μL), and 2 N NaOH (aq.) (300 μL), and allowed to stir for 30 min. A saturated solution of NaCl (1 mL) was added and the resulting mixture was extracted

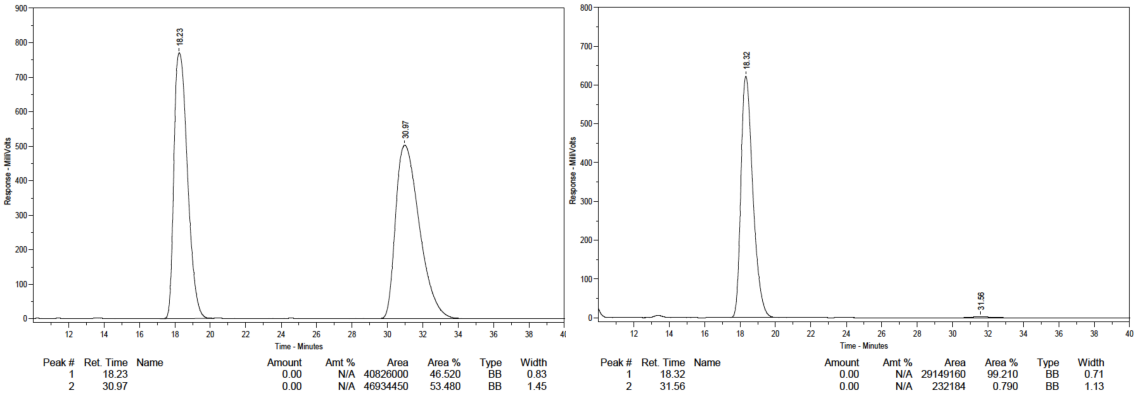
with Et_2O (3 x 2 mL). Combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Et_2O/Hexanes 1/4) to afford the desired alcohol in 73% yield (21.2 mg, 0.0653 mmol) as clear oil.

(*S*,*E*)-(1-Benzylidene-2-phenyl-but-3-enyl)-trimethylsilane (3.41): IR (neat): 3078 (w), 3058 (w), 3024 (w), 2953 (w), 2895 (w), 1634 (w), 1599 (w), 1491 (m), 1446 (m), 1405 (w), 1247 (s), 1062 (w), 1020 (w), 955 (w), 916 (m), 832 (s), 755 (s), 695 (s), 628 (m), 550 (w), 494 (w), 476 (w), 452 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.36-7.19 (10H, m, Ar**H**), 7.10 (1H, s, C=C**H**Ph), 6.31 (1H, ddd, *J* = 17.2, 10.0, 7.2 Hz, CC**H**=CHH), 5.31 (1H, dt, *J* = 10.4, 1.6 Hz, CH=C**H**H), 5.17 (1H, dt, *J* = 16.8, 1.6 Hz, CH=C**H**H), 4.95 (1H, d, *J* = 7.2 Hz, PhC**H**CH=CH_2), –0.02 (9H, s, Si(C**H**$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.5, 142.8, 139.7, 139.2, 138.2, 128.3, 128.1, 128.0, 128.0, 126.8, 126.0, 117.1, 50.1, 0.7; HRMS (ESI+): Calcd for $C_{20}H_{25}Si_1$ $[M+H]^+$: 293.1726. Found: 293.1717; Specific Rotation: $[\alpha]_D^{20}$ –67.2 (*c* = 0.64, $CHCl_3$) for an enantiomerically enriched sample of 99:1 *e.r.*

(*S*,*E*)-3,5-Diphenyl-4-trimethylsilanyl-pent-4-en-1-ol: The compound was prepared by hydroboration-oxidation of **3.41** using 9-BBN as described above. IR (neat): 3334 (br), 3057 (w), 3024 (w), 2950 (w), 2892 (w), 1599 (w), 1491 (w), 1445 (w), 1406 (w), 1247 (m), 1053 (w), 1025 (w), 911 (w), 831 (s), 753 (s), 696 (s), 634 (w), 582 (w), 519 (w), 486 (w), 443 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.37–7.18 (10H, m, Ar**H**), 7.06 (1H, s, C=C**H**Ph), 4.41 (1H, dd, *J* = 9.2, 6.0 Hz, ArC**H**CH_2CH_2OH), 3.67-3.55 (2H, m, ArCHCH_2C**H**$_2$OH), 2.32 (1H, dddd, *J* = 14.4, 7.2, 7.2, 7.2 Hz, ArCHC**H**$_2CH_2OH$), 2.01-1.92 (1H, m, ArCHC**H**$_2CH_2OH$), –0.07 (9H, s, Si(C**H**$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$):

δ 147.6, 143.0, 139.8, 138.4, 128.4, 128.1, 127.7, 126.9, 126.0, 61.2, 41.0, 34.9, 0.6; HRMS (ESI+): Calcd for $C_{20}H_{27}OSi_1$ $[M+H]^+$: 311.1831. Found: 311.1841; Specific Rotation: $[\alpha]_D^{20}$ –318.3 (*c* = 1.19, $CHCl_3$) for an enantiomerically enriched sample of 99:1 *e.r.*

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (chiralpak OD column (25 cm x 0.46 cm), 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm). Retention time: major peak at 18.32 min, minor peak at 31.56 min.

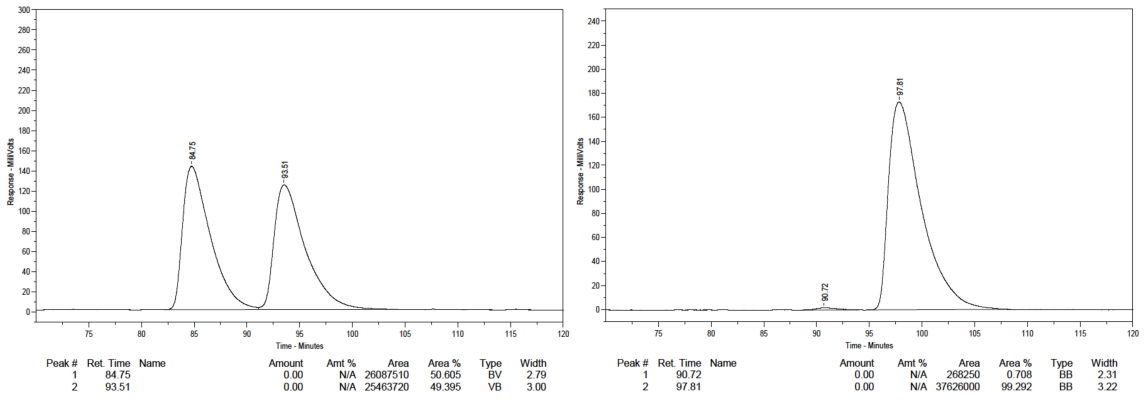


(*S*,*E*)-(1-Benzylidene-2-o-tolyl-but-3-enyl)-trimethylsilane (3.44): IR (neat): 3058 (w), 3020 (w), 2951 (w), 2925 (w), 2895 (w), 2854 (w), 1634 (w), 1568 (w), 1487 (w), 1459 (w), 1443 (w), 1404 (w), 1246 (m), 1133 (w), 1018 (m), 942 (m), 833 (s), 754 (s), 728 (w), 697 (s), 628 (m), 571 (w), 495 (w), 446 (w), 396 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.36–7.30 (5H, m, Ar**H**), 7.30–7.22 (1H, m, Ar**H**), 7.15 (1H, td, *J* = 7.2, 1.6 Hz, Ar**H**), 7.10 (1H, td, *J* = 7.2, 1.6 Hz, Ar**H**), 7.09 (1H, s, PhC**H**=C), 7.03 (1H, d, *J* = 7.6 Hz, Ar**H**), 6.36 (1H, ddd, *J* = 17.6, 10.4, 4.4 Hz, CC**H**=CHH), 5.39 (1H, ddd, *J* = 10.8, 2.4, 2.0 Hz, CH=C**H**H), 5.24 (1H, ddd, *J* = 17.6, 2.2, 1.8 Hz, CH=C**H**H), 4.79–4.77 (1H, m, ArC**H**CH=CH_2), 1.85 (3H, s, ArC**H**$_3$), –0.16 (9H, s, Si(C**H**$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.4, 141.2, 140.8, 138.1, 130.2, 128.2, 128.0, 126.9, 126.5, 125.4, 116.8, 47.9, 19.3, 0.2; HRMS (ESI+): Calcd for $C_{21}H_{27}Si_1$ $[M+H]^+$: 307.1882. Found:

307.1892; Specific Rotation: $[\alpha]_D^{20}$ +35.7 (*c* = 0.74, $CHCl_3$) for an enantiomerically enriched sample of 99:1 *e.r.*

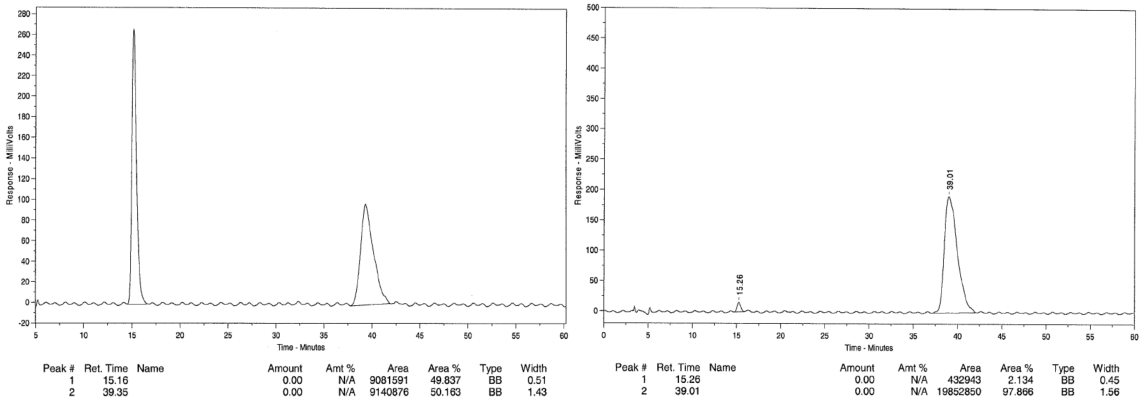
(*S*,*E*)-5-Phenyl-3-o-tolyl-4-trimethylsilanyl-pent-4-en-1-ol: The compound was prepared by hydroboration-oxidation of **3.44** using 9-BBN as described above. IR (neat): 3320 (br), 3060 (w), 3020 (w), 2949 (w), 2892 (w), 1488 (w), 1459 (w), 1443 (w), 1245 (m), 1026 (m), 918 (w), 832 (s), 754 (s), 697 (s), 636 (w), 624 (w), 511 (w), 477 (w), 441 (w), 406 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.38–7.37 (5H, m, Ar**H**), 7.29–7.25 (1H, m, Ar**H**), 7.18 (1H, t, *J* = 7.2 Hz, Ar**H**), 7.10 (1H, t, *J* = 7.2 Hz, Ar**H**), 7.05 (1H, d, *J* = 7.2 Hz, Ar**H**), 6.90 (1H, s, C=C**H**Ph), 4.30 (1H, dd, *J* = 11.2, 4.0 Hz, ArC**H**CH_2CH_2OH), 3.74–3.57 (2H, m, $ArCHCH_2C\mathbf{H}_2OH$), 2.66–2.56 (1H, m, $ArCHC\mathbf{H}_2CH_2OH$), 2.12–2.04 (1H, m, $ArCHC\mathbf{H}_2CH_2OH$), 1.89 (3H, s, $ArC\mathbf{H}_3$), –0.15 (9H, s, $Si(C\mathbf{H}_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.7, 139.3, 139.0, 138.9, 138.4, 130.7, 128.5, 128.1, 126.8, 126.3, 126.2, 125.5, 60.9, 39.7, 36.6, 19.7, 0.2; HRMS (ESI+): Calcd for $C_{21}H_{29}O_1Si_1$ $[M+H]^+$: 325.1988. Found: 325.1997; Specific Rotation: $[\alpha]_D^{20}$ –36.0 (*c* = 1.19, $CHCl_3$) for an enantiomerically enriched sample of 99:1 *e.r.*

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (chiralpak OD-R column (25 cm x 0.46 cm), 99.5/0.5 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm). Retention time: minor peak at 90.72 min, major peak at 97.81 min.



(*S*,*E*)-(3-(2-Methoxyphenyl)-1-phenylpenta-1,4-dien-2-yl)trimethylsilane (3.42): IR (neat): 3057 (w), 2952 (w), 2833 (w), 1585 (w), 1489 (m), 1462 (m), 1241 (s), 1111 (w), 1020 (m), 916 (m), 832 (s), 752 (s), 697 (s), 627 (m), 581 (w), 485 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.35–7.31 (4H, m, Ar**H**), 7.24–7.22 (2H, m, Ar**H**), 7.19 (1H, dt, *J* = 8.0, 1.0 Hz, Ar**H**), 7.03 (1H, s, C=C**H**Ph), 6.90 (1H, dt, *J* = 7.5, 1.0 Hz, Ar**H**), 6.75 (1H, dd, *J* = 7.5, 1.0 Hz, Ar**H**), 6.26 (1H, ddd, *J* = 17.5, 10.5, 5.0 Hz, ArCHC**H**=CHH), 5.27 (1H, dt, *J* = 11.0, 2.0 Hz CH=C**H**H), 5.14 (1H, dt, *J* = 17.0, 2.0 Hz, CH=CH**H**), 5.04 (1H, d, *J* = 2.0 Hz, ArC**H**CH=CH_2), 3.63 (3H, s, ArOC$\mathbf{H}_3$), –0.13 (9H, s, Si(C$\mathbf{H}_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.3, 143.6, 140.7, 140.3, 139.3, 131.5, 129.0, 128.3, 127.9, 127.7, 126.6, 120.0, 116.4, 110.3, 55.0, 44.8, 0.5; HRMS (ESI+): Calcd for $C_{21}H_{27}O_1Si_1$ $[M+H]^+$: 323.1831. Found: 323.1842; Specific Rotation: $[\alpha]_D^{20}$ –90.5 (*c* = 1.24, $CHCl_3$) for an enantiomerically enriched sample of 98:2 *e.r.*

Enantiomeric purity was determined by HPLC analysis of the derived primary alcohol after hydroboration of the title compound with 9-BBN in comparison with authentic racemic material (chiralpak OD column (25 cm x 0.46 cm), 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm). Retention time: minor peak 15.26 min, major peak 39.01 min.

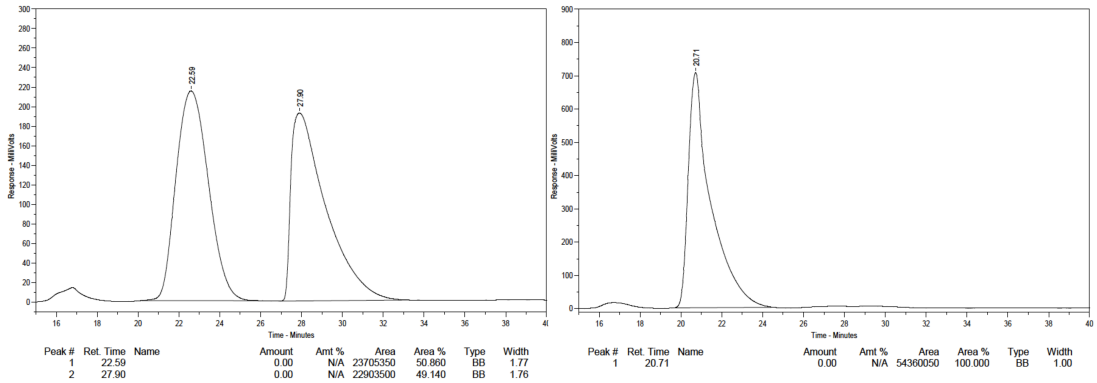


Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	15.16		0.00	N/A	9081591	49.837	BB	0.51
2	39.35		0.00	N/A	9140876	50.163	BB	1.43

Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	15.26		0.00	N/A	432943	2.134	BB	0.45
2	39.01		0.00	N/A	19852850	97.866	BB	1.56

(*S*,*E*)-[1-Benzylidene-2-(2-nitrophenyl)-but-3-enyl]-trimethylsilane (3.43): IR (neat): 3078 (w), 3023 (w), 2953 (w), 2895 (w), 1605 (w), 1525 (s), 1443 (w), 1406 (w), 1354 (s), 1247 (s), 1018 (m), 921 (m), 833 (s), 781 (m), 756 (s), 743 (s), 695 (s), 648 (w), 626 (m) 566 (w), 492 (w), 459 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (1H, dd, *J* = 7.6, 0.8 Hz, Ar**H**), 7.48–7.42 (2H, m, Ar**H**), 7.32–7.20 (6H, m, Ar**H**), 7.04 (1H, s, C=C**H**Ph), 6.21 (1H, ddd, *J* = 17.2, 10.4, 6.0 Hz, ArCHC**H**=CHH), 5.48 (1H, d, *J* = 6.0 Hz, ArC**H**CH=CH_2), 5.38 (1H, dt, *J* = 10.4, 1.2 Hz, CH=C**H**H), 5.22 (1H, dt, *J* = 17.2, 1.6 Hz, CH=C**H**H), –0.04 (9H, s, Si(C**H**$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.8, 142.5, 141.7, 138.1, 137.8, 136.6, 131.6, 130.2, 128.2, 127.8, 127.3, 127.0, 124.3, 118.2, 45.6, 0.4; HRMS (ESI+): Calcd for $C_{20}H_{24}N_1O_2Si_1$ $[M+H]^+$: 338.1576. Found: 338.1572; Specific Rotation: $[\alpha]_D^{20}$ +178.3 (*c* = 0.70, $CHCl_3$) for an enantiomerically enriched sample of >98:2 *e.r.*

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (chiralpak AD column (25 cm x 0.46 cm), 99/1 hexanes/*i*-PrOH, 0.2 mL/min, 220 nm). Retention time: major peak at 20.71, minor peak is too small to integrate.

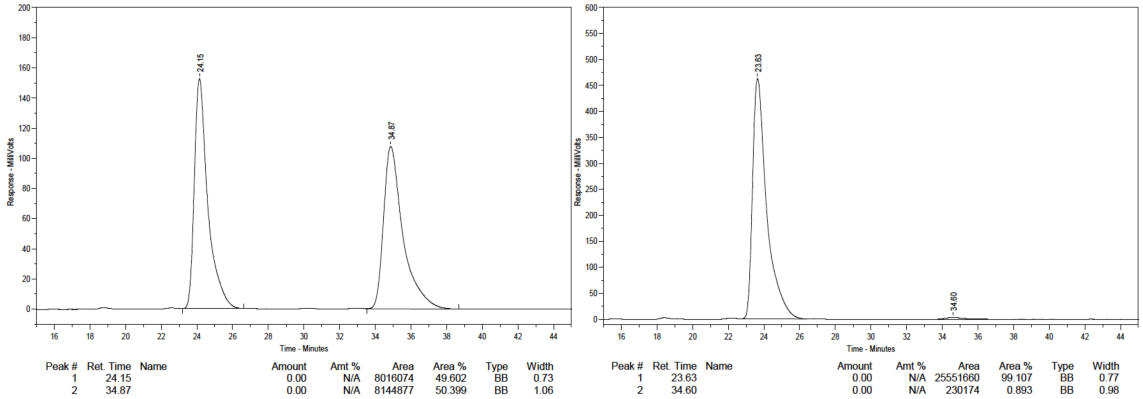


(*S*,*E*)-[1-Benzylidene-2-(3-bromophenyl)-but-3-enyl]-trimethylsilane (3.45): IR (neat): 3077 (w), 3058 (w), 3020 (w), 2953 (w), 2894 (w), 1590 (w), 1563 (w), 1491 (w),

1470 (w), 1443 (w), 1419 (w), 1406 (w), 1247 (m), 1073 (w), 1021 (w), 995 (w), 919 (m), 832 (s), 778 (m), 758 (s), 695 (s), 630 (m), 570 (w), 491 (w), 433 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.34–7.30 (4H, m, Ar**H**), 7.26–7.22 (3H, m, Ar**H**), 7.14–7.12 (2H, m, Ar**H**), 7.09 (1H, s, C=C**H**Ph), 6.21 (1H, ddd, *J* = 17.2, 10.0, 7.2 Hz, CHC**H**=CHH), 5.30 (1H, dt, *J* = 10.4, 1.2 Hz, CH=C**H**H), 5.14 (1H, dt, *J* = 17.2, 1.2 Hz, CH=C**H**H), 4.87 (1H, d, *J* = 7.2 Hz, ArC**H**CH=CH_2), –0.02 (9H, s, Si(C**H**$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.4, 144.8, 140.4, 138.4, 137.9, 131.1, 129.5, 129.1, 128.3, 128.2, 126.9, 126.6, 122.3, 117.8, 49.9, 0.7; HRMS (ESI+): Calcd for $C_{20}H_{24}Br_1Si_1$ $[M+H]^+$: 373.0810. Found: 373.0804; Specific Rotation: $[\alpha]_D^{20}$ –71.2 (*c* = 0.80, $CHCl_3$) for an enantiomerically enriched sample of 99:1 *e.r.*

(*S*,*E*)-3-(3-Bromophenyl)-5-phenyl-4-trimethylsilanyl-pent-4-en-1-ol: The compound was prepared by hydroboration-oxidation of **3.45** using 9-BBN as described above. IR (neat): 3344 (br), 3057 (w), 3021 (w), 2950 (w), 2892 (w), 1590 (w), 1563 (w), 1473 (w), 1442 (w), 1415 (w), 1247 (m), 1027 (m), 832 (s), 777 (w), 758 (s), 697 (s), 664 (w), 634 (m), 590 (w), 426 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.41 (1H, brs, Ar**H**), 7.38-7.14 (8H, m, Ar**H**), 7.09 (1H, s, C=C**H**Ph), 4.37 (1H, dd, *J* = 9.6, 6.0 Hz, ArC**H**CH_2CH_2OH), 3.66-3.53 (2H, m, $ArCHCH_2C$**H**$_2$OH), 2.27 (1H, dddd, *J* = 13.6, 6.8, 6.8, 6.8 Hz, ArCHC**H**$_2CH_2OH$), 1.98–1.89 (1H, m, ArCHC**H**$_2CH_2OH$), –0.04 (9H, s, Si(C**H**$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.8, 145.7, 140.5, 138.1, 130.9, 129.6, 129.1, 128.5, 128.0, 127.0, 126.3, 122.4, 60.9, 40.9, 34.9, 0.7; HRMS (ESI+): Calcd for $C_{20}H_{26}Br_1O_1Si_1$ $[M+H]^+$: 391.0916. Found: 391.0926; Specific Rotation: $[\alpha]_D^{20}$ –283.8 (*c* = 1.49, $CHCl_3$) for an enantiomerically enriched sample of 99:1 *e.r.*

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (chiralpak OD column (25 cm x 0.46 cm), 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm). Retention time: major peak at 23.63 min, minor peak at 34.60 min.

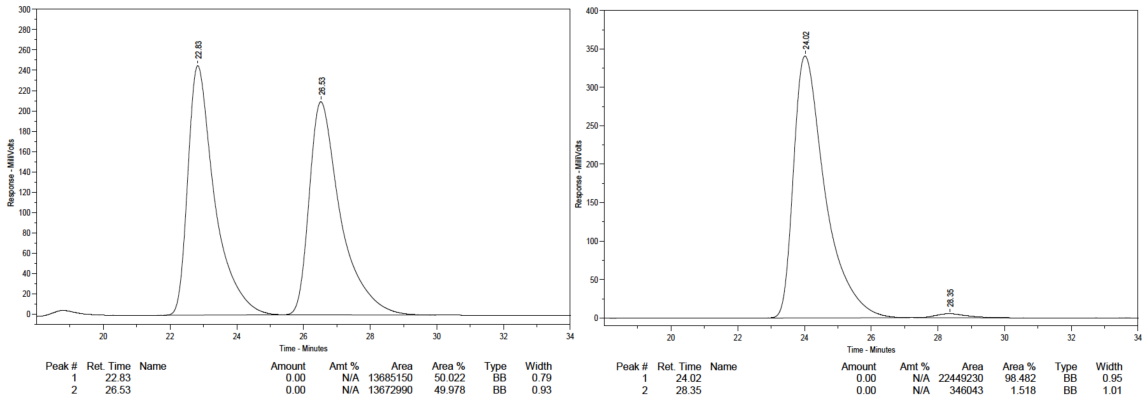


(*S*,*E*)-[1-Benzylidene-2-(4-chlorophenyl)-but-3-enyl]-trimethylsilane (3.46): IR (neat): 3077 (w), 3022 (w), 2954 (w), 2895 (w), 1634 (w), 1588 (m), 1571 (w), 1488 (s), 1443 (w), 1404 (w), 1247 (s), 1091 (m), 1070 (w), 1014 (m), 995 (w), 918 (m), 832 (s), 757 (s), 725 (w), 696 (s), 630 (m), 574 (m), 472 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.33–7.29 (2H, m, Ar**H**) 7.26–7.21 (5H, m, Ar**H**), 7.15–7.11 (2H, m, Ar**H**), 7.07 (1H, s, C=C**H**Ph), 6.21 (1H, ddd, *J* = 17.2, 10.0, 7.2 Hz, CC**H**=CHH), 5.28 (1H, dt, *J* = 10.4, 1.4 Hz, CH=C**H**H), 5.14 (1H, dt, *J* = 17.2, 1.4 Hz, CH=C**H**H), 4.85 (1H, d, *J* = 7.2 Hz, ArC**H**CH=CH_2), –0.03 (9H, s, Si(C**H**$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.0, 141.4, 140.2, 138.7, 138.0, 131.9, 129.4, 128.3, 128.2, 128.1, 126.9, 117.5, 49.6, 0.7; HRMS (ESI+): Calcd for $C_{20}H_{24}Cl_1Si_1$ $[M+H]^+$: 327.1336. Found: 327.1344; Specific Rotation: $[\alpha]_D^{20}$ –107.7 (*c* = 0.86, $CHCl_3$) for an enantiomerically enriched sample of 98.5:1.5 *e.r.*

(*S*,*E*)3-(4-Chlorophenyl)-5-phenyl-4-trimethylsilanyl-pent-4-en-1-ol: The compound was prepared by hydroboration-oxidation of **3.46** using 9-BBN as described above. IR (neat): 3331 (br), 2950 (w), 1489 (m), 1442 (w), 1403 (w), 1248 (m), 1091 (m), 1050 (w),

1027 (w), 1012 (m), 832 (s), 758 (s), 696 (s), 633 (w), 581 (w), 546 (w), 469 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.37–7.25 (7H, m, Ar**H**), 7.20 (2H, d, *J* = 8.8 Hz, Ar**H**), 7.07 (1H, s, C=C**H**Ph), 4.35 (1H, dd, *J* = 9.2, 6.0 Hz, ArC**H**CH_2CH_2OH), 3.66–3.53 (2H, m, $ArCHCH_2C\mathbf{H}_2OH$), 2.27 (1H, dddd, *J* = 13.6, 6.8, 6.8, 6.8 Hz, $ArCHC\mathbf{H}_2CH_2OH$), 1.99-1.90 (1H, m, $ArCHC\mathbf{H}_2CH_2OH$), –0.05 (9H, s, $Si(C\mathbf{H}_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.1, 141.7, 140.3, 138.2, 131.7, 129.1, 128.5, 128.2, 128.0, 127.0, 61.0, 40.5, 34.9, 0.7; HRMS (ESI+): Calcd for $C_{20}H_{26}Cl_1O_1Si_1$ $[M+H]^+$: 345.1441. Found: 345.1441; Specific Rotation: $[\alpha]_D^{20}$ –346.5 (*c* = 1.58, $CHCl_3$) for an enantiomerically enriched sample of 98.5:1.5 *e.r.*

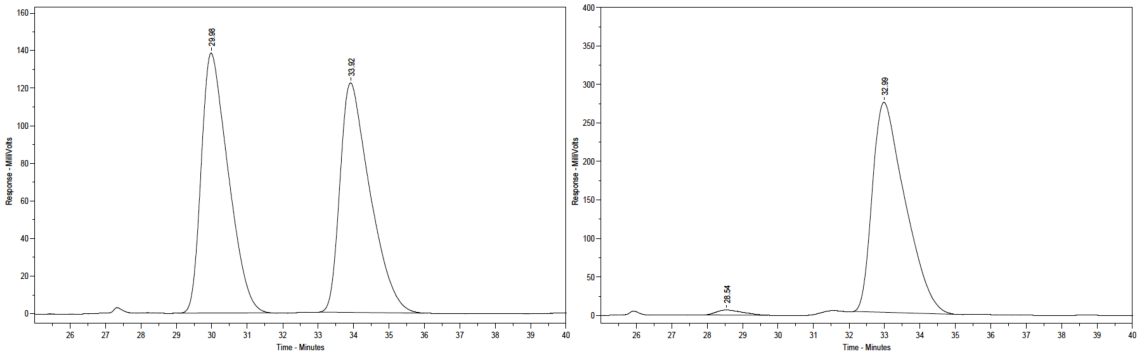
Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (chiralpak OD column (25 cm x 0.46 cm), 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm). Retention time: major peak at 24.02 min, minor peak at 28.35 min.



(*S*,*E*)-[1-Benzylidene-2-(4-nitrophenyl)-but-3-enyl]-trimethylsilane (3.47): IR (neat): 3077 (w), 3057 (w), 3020 (w), 2954 (w), 2895 (w), 1594 (m), 1516 (s), 1490 (m), 1443 (w), 1407 (w), 1342 (s), 1248 (s), 1108 (w), 1070 (w), 1014 (w), 995 (w), 920 (m), 831 (s), 757 (s), 696 (s), 629 (m), 573 (m), 547 (w), 481 (w), 461 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.13 (2H, dt, *J* = 8.8, 2.2 Hz, Ar**H**), 7.38–7.30 (4H, m, Ar**H**), 7.27–7.22 (3H, m, Ar**H**), 7.13 (1H, s, C=C**H**Ph), 6.24 (1H, ddd, *J* = 17.2, 10.0, 7.6 Hz,

ArCHC**H**=CHH), 5.36 (1H, dt, *J* = 10.0, 1.2 Hz, CH=C**H**H), 5.20 (1H, dt, *J* = 17.2, 1.6 Hz, CH=C**H**H), 4.95 (1H, d, *J* = 7.6 Hz, ArC**H**CH=CH_2), –0.02 (9H, s, Si(C**H**$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.0, 146.4, 144.2, 141.1, 137.7, 128.7, 128.3, 128.1, 127.1, 123.2, 118.5, 50.3, 0.7; HRMS (ESI+): Calcd for $C_{20}H_{24}NO_2Si_1$ $[M+H]^+$: 338.1576. Found: 338.1572; Specific Rotation: $[\alpha]_D^{20}$ –166.1 (*c* = 0.89, $CHCl_3$) for an enantiomerically enriched sample of 98:2 *e.r.*

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (chiralpak OD column (25 cm x 0.46 cm), 99/1 hexanes/*i*-PrOH, 0.2 mL/min, 220 nm). Retention time: minor peak at 28.54 min, major peak at 32.99 min.



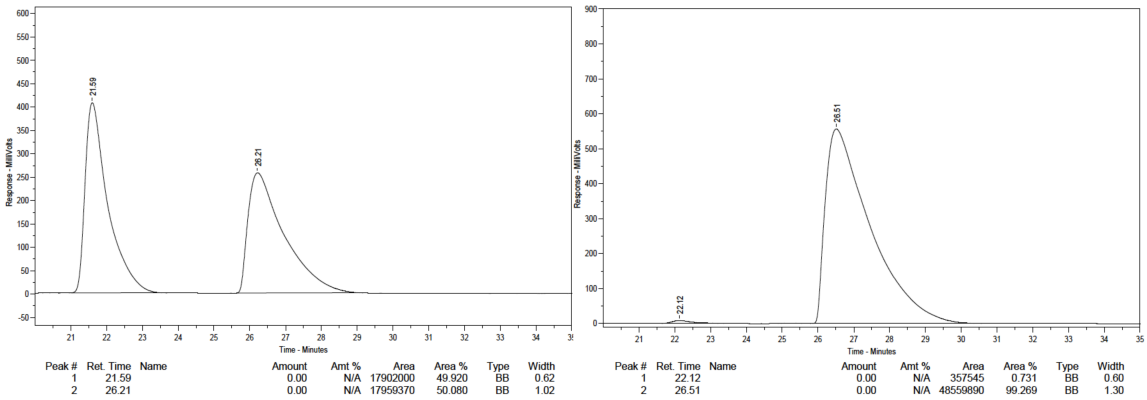
Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	29.98		0.00	N/A	7304348	50.393	BB	0.83
2	33.92		0.00	N/A	7190523	49.607	BB	0.91

Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	28.54		0.00	N/A	339535	1.905	BB	0.85
2	32.99		0.00	N/A	17485050	98.095	BB	1.01

(*S*,*E*)-Toluene-4-sulfonic acid 4-(3-phenyl-2-trimethylsilanyl-1-vinyl-allyl)-phenyl ester (3.49): IR (neat): 3076 (w), 3056 (w), 2954 (br), 2895 (w), 1597 (w), 1497 (s), 1444 (w), 1405 (w), 1373 (s), 1248 (m), 1198 (s), 1176 (s), 1153 (s), 1092 (s), 1017 (m), 919 (m), 833 (s), 812 (w), 755 (s), 722 (w), 698 (s), 666 (s), 631 (m), 550 (s), 514 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (2H, dt, *J* = 8.4, 1.6 Hz, Ar**H**), 7.34–7.20 (7H, m, Ar**H**), 7.08 (2H, dd, *J* = 8.8, 0.8 Hz, Ar**H**), 7.04 (1H, s, C=C**H**Ph), 6.86 (2H, dt, *J* = 8.8, 2.0 Hz, Ar**H**), 6.20 (1H, ddd, *J* = 17.2, 10.0, 7.2 Hz, ArCHC**H**=CHH), 5.28 (1H, dt, *J* = 10.0, 1.2 Hz, CH=C**H**H), 5.13 (1H, dt, *J* = 17.2, 1.2 Hz, CH=C**H**H), 4.85 (1H, d, *J* = 6.8 Hz, ArC**H**CH=CH_2), 2.42 (3H, s, ArC**H**$_3$), –0.09 (9H, s, Si(C**H**$_3$)$_3$); ^{13}C NMR (100

MHz, $CDCl_3$): δ 147.9, 145.1, 145.0, 142.0, 140.2, 138.5, 137.9, 132.1, 129.6, 129.1, 128.6, 128.2, 128.1, 126.9, 121.9, 117.6, 49.5, 21.6, 0.7; HRMS (ESI+): Calcd for $C_{27}H_{31}O_3S_1Si_1$ $[M+H]^+$: 463.1763. Found: 463.1752; Specific Rotation: $[\alpha]_D^{20}$ –62.1 (*c* = 0.69, $CHCl_3$) for an enantiomerically enriched sample of 99:1 *e.r.*

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (chiralpak OD column (25 cm x 0.46 cm), 99/1 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm). Retention time: minor peak at 22.12 min, major peak at 26.51 min.

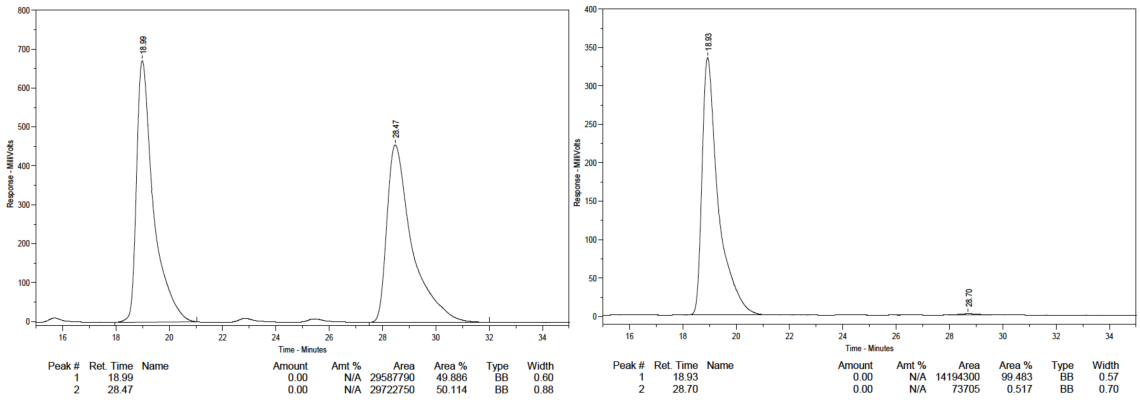


(*S*, *E*)-(1-Benzylidene-2-*p*-tolyl-but-3-enyl)-trimethylsilane (3.48): IR (neat): 3077 (w), 3054 (w), 3020 (w), 2953 (w), 2922 (w), 2895 (w), 1634 (w), 1588 (w), 1509 (w), 1491 (w), 1443 (w), 1405 (w), 1247 (m), 1070 (w), 1019 (w), 995 (w), 916 (m), 832 (s), 783 (w), 756 (s), 697 (s), 631 (m), 601 (w), 561 (w), 548 (w), 488 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.33–7.21 (5H, m, Ar**H**), 7.12–7.07 (4H, m, Ar**H**), 7.06 (1H, s, C=C**H**Ph), 6.27 (1H, ddd, *J* = 17.2, 10.0, 7.2 Hz, ArCHC**H**=CHH), 5.26 (1H, ddd, *J* = 10.0, 2.0, 1.2 Hz, CH=C**H**H), 5.13 (1H, dt, *J* = 17.2, 1.6 Hz, CH=C**H**H), 4.89 (1H, d, *J* = 7.2 Hz, ArC**H**CH=CH_2), 2.32 (3H, s, ArC$\mathbf{H}_3$), –0.02 (9H, s, Si(C$\mathbf{H}_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.7, 139.7, 139.6, 139.5, 138.2, 135.5, 128.7, 128.3, 128.1, 127.9, 126.7, 116.8, 49.8, 20.9, 0.7; HRMS (ESI+): Calcd for $C_{21}H_{27}Si_1$ $[M+H]^+$: 307.1882.

Found: 307.1873; Specific Rotation: $[\alpha]_D^{20}$ –102.0 (*c* = 0.80, $CHCl_3$) for an enantiomerically enriched sample of >98:2 *e.r.*

(*S*,*E*)-5-Phenyl-3-p-tolyl-4-trimethylsilanyl-pent-4-en-1-ol: The compound was prepared by hydroboration-oxidation of **3.48** using 9-BBN as described above. IR (neat): 3337 (br), 3053 (w), 3020 (w), 2949 (w), 2892 (w), 1586 (w), 1511 (w), 1489 (w), 1442 (w), 1406 (w), 1247 (m), 1027 (m), 831 (s), 756 (s), 698 (s), 633 (w), 604 (w), 515 (w), 470 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.37–7.22 (5H, m, Ar**H**), 7.17 (2H, d, *J* = 8.0 Hz, Ar**H**), 7.10 (2H, d, *J* = 8.0 Hz, Ar**H**), 7.05 (1H, s, C=C**H**Ph), 4.36 (1H, dd, *J* = 9.2, 6.0 Hz, ArC**H**CH_2CH_2OH), 3.66–3.54 (2H, m, $ArCHCH_2C\mathbf{H}_2OH$), 2.33 (3H, s, Ar$C\mathbf{H}_3$), 2.35–2.27 (1H, m, $ArCHC\mathbf{H}_2CH_2OH$), 1.99–1.90 (1H, m, $ArCHC\mathbf{H}_2CH_2OH$), -0.05 (9H, s, $Si(C\mathbf{H}_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.8, 139.9, 139.6, 138.4, 135.5, 128.8, 128.4, 128.1, 127.6, 126.8, 61.3, 40.6, 35.0, 20.9, 0.7; HRMS (ESI+): Calcd for $C_{21}H_{29}O_1Si_1$ $[M+H]^+$: 325.1988. Found: 325.1973; Specific Rotation: $[\alpha]_D^{20}$ –362.5 (*c* = 1.11, $CHCl_3$) for an enantiomerically enriched sample of >98:2 *e.r.*

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (chiralpak OD column (25 cm x 0.46 cm), 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm). Retention time: major peak at 18.93 min, minor peak at 28.70 min.

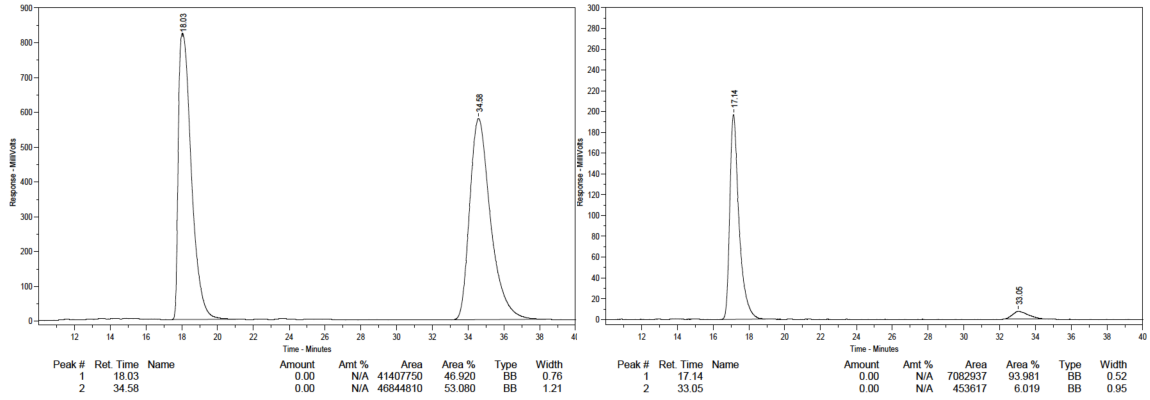


(*R*,*E*)-(1-Benzylidene-2-phenethyl-but-3-enyl)-trimethylsilane (3.50): IR (neat): 3060 (w), 3025 (w), 2950 (w), 2858 (w), 1632 (w), 1602 (w), 1586 (w), 1493 (w), 1453 (w), 1443 (w), 1407 (w), 1247 (m), 1070 (w), 1028 (w), 993 (w), 960 (w), 912 (m), 831 (s), 758 (s), 695 (s), 632 (m), 569 (w), 487 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.30–7.04 (10H, m, Ar**H**), 6.95 (1H, s, C=C**H**Ph), 5.94 (1H, ddd, *J* = 17.2, 10.4, 6.4 Hz, CC**H**=CHH), 5.06 (1H, dt, *J* = 10.4, 1.6 Hz, CH=C**H**H), 5.00 (1H, dt, *J* = 17.2, 1.6 Hz, CH=C**H**H), 3.59 (1H, q, *J* = 7.2 Hz, $ArCH_2CH_2C\mathbf{H}CH=CH_2$), 2.55–2.39 (2H, m, $PhC\mathbf{H}_2CH_2$), 1.90–1.76 (2H, m, $PhCH_2C\mathbf{H}_2$), 0.02 (9H, s, $Si(C\mathbf{H}_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.7, 142.3, 141.8, 139.7, 138.7, 128.4, 128.3, 128.2, 128.0, 126.4, 125.5, 114.8, 45.4, 36.1, 33.9, 1.3; HRMS (ESI+): Calcd for $C_{22}H_{29}Si_1$ $[M+H]^+$: 321.2039. Found: 321.2025; Specific Rotation: $[\alpha]_D^{20}$ +77.7 (*c* = 1.03, $CHCl_3$) for an enantiomerically enriched sample of 94:6 *e.r.*

(*R*,*E*)-3-Phenethyl-5-phenyl-4-trimethylsilanyl-pent-4-en-1-ol: The compound was prepared by hydroboration-oxidation of **3.50** using 9-BBN as described above. IR (neat): 3339 (br), 3059 (w), 3024 (w), 2944 (w), 2859 (w), 1601 (w), 1584 (w), 1492 (w), 1453 (w), 1406 (w), 1248 (m), 1051 (w), 1028 (w), 915 (w), 831 (s), 760 (s), 696 (s), 634 (m), 574 (w), 515 (w), 486 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.30–7.08 (10H, m, Ar**H**), 7.00 (1H, s, C=C**H**Ph), 3.56–3.44 (2H, m, $CHCH_2C\mathbf{H}_2OH$), 3.03 (1H, ddd, *J* = 14.8, 8.8, 6.4 Hz, $PhCH_2CH_2C\mathbf{H}CH_2CH_2OH$), 2.59 (1H, ddd, *J* = 14.0, 9.6, 6.8 Hz, $PhC\mathbf{H_2}CH_2CHCH_2CH_2OH$), 2.46 (1H, ddd, *J* = 14.0, 9.6, 6.8 Hz, $PhC\mathbf{H_2}CH_2CHCH_2CH_2OH$), 1.81-1.62 (4H, m, $PhCH_2C\mathbf{H_2}CHC\mathbf{H_2}CH_2OH$), 0.25 (9H, s, $Si(C\mathbf{H}_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.0, 142.4, 140.7, 138.8, 128.3, 128.2, 126.5, 125.7, 61.3, 37.8, 37.1, 34.3, 1.4; HRMS (ESI+): Calcd for $C_{22}H_{30}O_1Si_1Na$

$[M+Na]^+$: 361.1964. Found: 361.1960; Specific Rotation: $[\alpha]_D^{20}$ –89.0 (*c* = 1.31, $CHCl_3$) for an enantiomerically enriched sample of 94:6 *e.r.*

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (chiralpak OD-R column (25 cm x 0.46 cm), 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm). Retention time: major peak at 17.14 min, minor peak at 33.05 min.



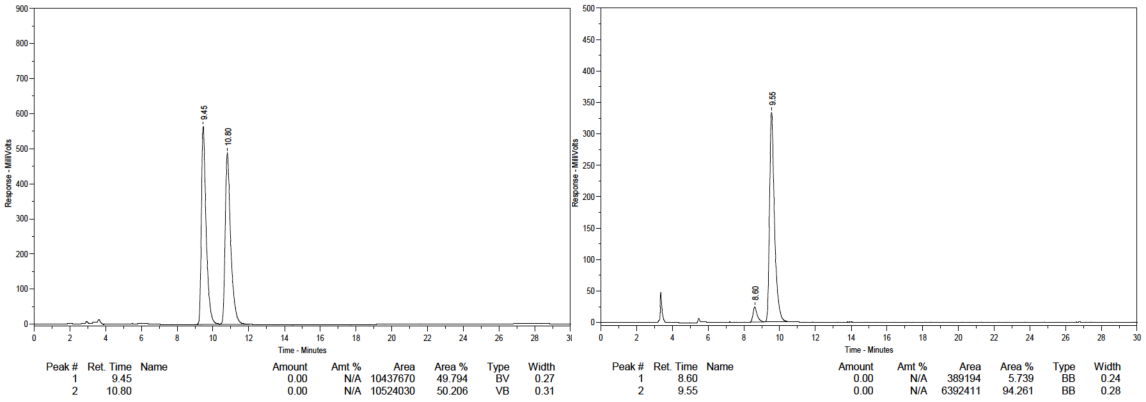
Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	18.03		0.00	N/A	41407750	46.920	BB	0.76
2	34.58		0.00	N/A	46844810	53.080	BB	1.21

Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	17.14		0.00	N/A	7082937	93.981	BB	0.52
2	33.05		0.00	N/A	453617	6.019	BB	0.95

(*S*,*E*)-(1-Benzylidene-2-cyclohexyl-but-3-enyl)-trimethylsilane (3.51): IR (neat): 3074 (w), 2921 (m), 2849 (m), 1490 (w), 1447 (w), 1407 (w), 1247 (m), 1061 (w), 1028 (w), 933 (w), 909 (m), 889 (w), 831 (s), 758 (s), 721 (w), 697 (s), 657 (w), 633 (w), 480 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.32–7.28 (2H, m, Ar**H**), 7.21–7.15 (3H, m, Ar**H**), 6.90 (1H, s, C=C**H**Ph), 5.86 (1H, ddd, *J* = 17.2, 10.4, 8.6 Hz, CyCHC**H**=CHH), 4.97 (1H, ddd, *J* = 10.0, 2.0, 0.8 Hz, CyCH=C**H**H), 4.89 (1H, ddd, *J* = 17.2, 2.0, 1.2 Hz, CyCH=C**H**H), 3.14 (1H, t, *J* = 7.2 Hz, CyC**H**CH=CH_2), 1.76–1.50 (5H, m, Cy**H**), 1.34 (1H, qt, *J* = 11.2, 3.2 Hz, Cy**H**) 1.20–0.95 (3H, m, Cy**H**), 0.70–0.50 (2H, m, Cy**H**), 0.20 (9H, s, Si($C\mathbf{H}_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.6, 140.8, 139.6, 139.3, 128.4, 127.9, 126.2, 114.8, 53.1, 39.9, 32.0, 31.6, 26.4, 26.3, 1.3; HRMS (ESI+): Calcd for $C_{20}H_{31}Si_1$ $[M+H]^+$: 299.2195. Found: 299.2201; Specific Rotation: $[\alpha]_D^{20}$ +168.8 (*c* = 0.70, $CHCl_3$) for an enantiomerically enriched sample of 94:6 *e.r.*

(*S*,*E*)-3-Cyclohexyl-5-phenyl-4-trimethylsilanyl-pent-4-en-1-ol: The compound was prepared by hydroboration-oxidation of **3.51** using 9-BBN as described above. IR (neat): 3314 (br), 2921 (m), 2849 (w), 1585 (w), 1490 (w), 1447 (w), 1406 (w), 1247 (m), 1051 (w), 1030 (w), 1009 (w), 974 (w), 956 (w), 914 (w), 890 (w), 831 (s), 759 (s), 700 (s), 685 (w), 634 (m), 567 (w), 526 (w), 490 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.34–7.16 (5H, m, Ar**H**), 7.00 (1H, s, C=C**H**Ph), 3.53–3.48 (1H, m, CyCHCH$_2$C**H**$_2$OH), 3.43–3.36 (1H, m, CyCHCH$_2$C**H**$_2$OH), 2.61 (1H, td, *J* = 10.8, 3.6 Hz, Cy**H**CH$_2$CH$_2$OH), 1.91–1.60 (7H, m, **Cy**CHC**H**$_2$CH$_2$OH), 1.47–1.09 (4H, m, **Cy**CHCH$_2$CH$_2$OH), 0.87-0.68 (2H, m, **Cy**CHCH$_2$CH$_2$OH), 0.22 (9H, s, Si(C**H**$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.9, 140.6, 138.9, 128.3, 128.1, 126.4, 61.7, 43.8, 41.2, 34.7, 33.2, 31.3, 26.7, 26.5, 1.4; HRMS (ESI+): Calcd for $C_{20}H_{33}O_1Si_1$ $[M+H]^+$: 317.2301. Found: 317.2299; Specific Rotation: $[\alpha]_D^{20}$ –109.1 (*c* = 1.05, $CHCl_3$) for an enantiomerically enriched sample of 94:6 *e.r.*

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (chiralpak OD-R column (25 cm x 0.46 cm), 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm). Retention time: minor peak at 8.60 min, major peak at 9.55 min.

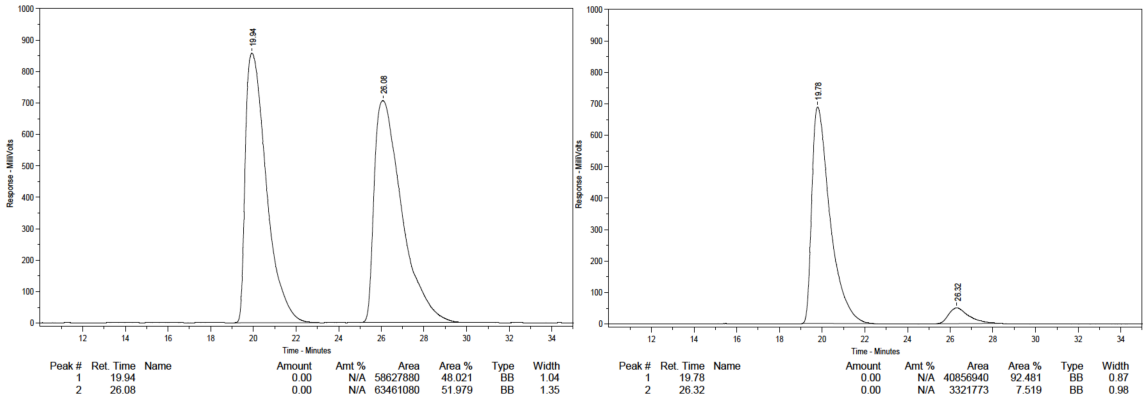


(*S*,*E*)-[1-(2-Methoxybenzylidene)-2-phenyl-but-3-enyl]-trimethylsilane (3.52): IR (neat): 3077 (w), 3059 (w), 3024 (w), 2953 (w), 2895 (w), 2834 (w), 1598 (w), 1484 (w), 1462 (w), 1434 (w), 1406 (w), 1291 (w), 1246 (s), 1175 (w), 1161 (w), 1108 (w), 1048 (w), 1028 (w), 996 (w), 916 (w), 831 (s), 746 (s), 698 (s), 630 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.27–7.14 (7H, m, Ar**H**), 7.05 (1H, s, C=C**H**Ar), 6.88–6.83 (2H, m, Ar**H**), 6.26 (1H, ddd, *J* = 17.2, 10.4, 7.2 Hz, PhCHC**H**=CHH), 5.25 (1H, dt, *J* = 10.0, 1.2 Hz, CH=C**H**H), 5.11 (1H, dt, *J* = 17.2, 1.6 Hz, CH=C**H**H), 4.81 (1H, d, *J* = 7.6 Hz, PhC**H**CH=CH_2), 3.83 (3H, s, ArOC**H**$_3$), –0.05 (9H, s, Si(C**H**$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.2, 145.0, 143.1, 139.4, 136.2, 129.4, 128.2, 128.1, 127.9, 127.3, 125.8, 119.9, 116.8, 110.6, 55.5, 50.5, 0.8; HRMS (ESI+): Calcd for $C_{21}H_{27}O_1Si_1$ $[M+H]^+$: 323.1831. Found: 323.1828; Specific Rotation: $[\alpha]_D^{20}$ –38.7 (*c* = 0.80, $CHCl_3$) for an enantiomerically enriched sample of 92:8 *e.r.*

(*S*,*E*)-5-(2-Methoxyphenyl)-3-phenyl-4-trimethylsilanyl-pent-4-en-1-ol: The compound was prepared by hydroboration-oxidation of **3.52** using 9-BBN as described above. IR (neat): 3369 (br), 3059 (w), 3025 (w), 2950 (w), 1599 (w), 1484 (w), 1462 (w), 1434 (w), 1289 (w), 1241 (s), 1174 (w), 1160 (w), 1109 (w), 1048 (w), 1025 (m), 831 (s), 746 (s), 698 (s), 634 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.31–7.15 (7H, m, Ar**H**), 6.96 (1H, s, C=C**H**Ar), 6.93–6.89 (2H, m, Ar**H**), 4.20 (1H, dd, *J* = 9.6, 5.6 Hz, PhC**H**CH_2CH_2OH), 3.83 (s, 3H, ArOC**H**$_3$), 3.57 (2H, t, *J* = 6.4 Hz, PhCHCH_2C**H**$_2$OH), 2.28–2.20 (1H, m, PhCHC**H**$_2CH_2OH$), 1.99–1.90 (1H, m, PhCHC**H**$_2CH_2OH$), –0.08 (9H, s, Si(C**H**$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.9, 147.8, 143.5, 136.4, 129.4, 128.4, 128.0, 127.8, 127.4, 125.9, 120.3, 110.7, 61.4, 55.4, 42.0, 35.0, 0.7; HRMS (ESI+): Calcd

for $C_{21}H_{29}O_2Si_1$ $[M+H]^+$: 341.1937. Found: 341.1938; Specific Rotation: $[\alpha]_D^{20}$ –290.4 (*c* = 0.23, $CHCl_3$) for an enantiomerically enriched sample of 92:8 *e.r.*

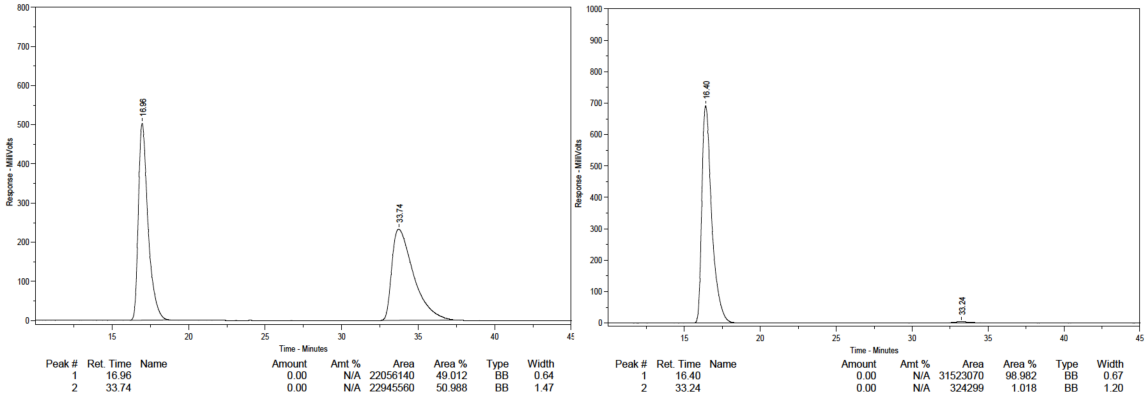
Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (chiralpak OD column (25 cm x 0.46 cm), 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm). Retention time: major peak at 19.78 min, minor peak at 26.32 min.



(*S*,*E*)-Trimethyl-[1-(3-methyl-benzylidene)-2-phenyl-but-3-enyl]-silane (3.53): IR (neat): 3080 (w), 3058 (w), 3025 (w), 2953 (w), 2921 (w), 2895 (w), 1599 (w), 1491 (w), 1447 (w), 1405 (w), 1246 (m), 1023 (w), 995 (w), 915 (m), 831 (s), 788 (w), 753 (s), 735 (w), 696 (s), 633 (w), 575 (w), 554 (w), 480 (w), 457 (w), 438 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.27–7.03 (9H, m, Ar**H**), 7.02 (1H, s, C=C**H**Ar), 6.27 (1H, ddd, *J* = 17.2, 10.0, 7.2 Hz, PhCHC**H**=CHH), 5.27 (1H, ddd, *J* = 10.4, 2.0, 1.2 Hz, CH=C**H**H), 5.13 (1H, dt, *J* = 17.2, 1.6 Hz, CH=C**H**H), 4.92 (1H, d, *J* = 7.2 Hz, PhC**H**CH=CH_2), 2.30 (3H, s, ArC**H**$_3$), –0.07 (9H, s, Si(C**H**$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.3, 143.0, 139.9, 139.3, 138.1, 137.6, 129.1, 128.1, 128.0, 127.5, 126.0, 125.2, 117.0, 50.1, 21.4, 0.7; HRMS (ESI+): Calcd for $C_{21}H_{27}Si_1$ $[M+H]^+$: 307.1882. Found: 307.1871; Specific Rotation: $[\alpha]_D^{20}$ –55.4 (*c* = 0.66, $CHCl_3$) for an enantiomerically enriched sample of 99:1 *e.r.*

(*S*,*E*)-3-Phenyl-5-*m*-tolyl-4-trimethylsilanyl-pent-4-en-1-ol: The compound was prepared by hydroboration-oxidation of **3.53** using 9-BBN as described above. IR (neat): 3332 (br), 3085 (w), 3057 (w), 3025 (w), 2950 (w), 2892 (w), 1600 (w), 1493 (w), 1447 (w), 1406 (w), 1247 (m), 1024 (w), 907 (w), 831 (s), 752 (s), 732 (m), 697 (s), 636 (w), 592 (w), 438 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.28–7.04 (9H, m, Ar**H**), 7.02 (1H, s, C=C**H**Ar), 4.41 (1H, dd, J = 9.6, 6.4 Hz, PhC**H**CH_2CH_2OH), 3.64–3.57 (2H, m, $PhCHCH_2C\mathbf{H}_2OH$), 2.33 (3H, s, Ar$C\mathbf{H}_3$), 2.38–2.26 (1H, m, $PhCHC\mathbf{H}_2CH_2OH$), 1.99-1.91 (1H, m, $PhCHC\mathbf{H}_2CH_2OH$), –0.09 (9H, s, $Si(C\mathbf{H}_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.2, 143.1, 139.9, 138.3, 138.0, 128.8, 128.3, 128.1, 127.8, 127.6, 126.0, 125.1, 61.2, 41.0, 34.9, 21.4, 0.6; HRMS (ESI+): Calcd for $C_{21}H_{29}O_1Si_1$ $[M+H]^+$: 325.1988. Found: 325.1988; Specific Rotation: $[\alpha]_D^{20}$ –304.0 (c = 1.21, $CHCl_3$) for an enantiomerically enriched sample of 99:1 *e.r.*

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (chiralpak OD column (25 cm x 0.46 cm), 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm). Retention time: major peak at 16.40 min, minor peak at 33.24 min.

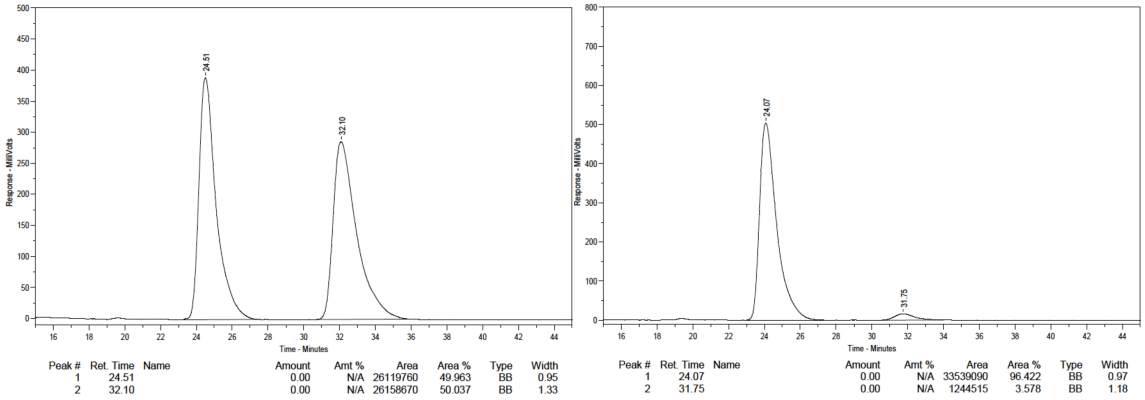


(*S*,*E*)-[1-(4-Fluoro-benzylidene)-2-phenyl-but-3-enyl]-trimethylsilane (3.54): IR (neat): 3080 (w), 3060 (w), 2954 (w), 2895 (w), 1635 (w), 1601 (w), 1504 (s), 1448 (w), 1407 (w), 1247 (m), 1221 (m), 1157 (w), 1093 (w), 1062 (w), 1021 (w), 995 (w), 918

(w), 830 (s), 782 (w), 755 (m), 739 (s), 698 (s), 617 (w), 554 (w), 521 (w), 495 (w), 458 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.29–7.16 (7H, m, Ar**H**), 7.01–6.96 (3H, m, Ar**H**, C=C**H**Ar), 6.27 (1H, ddd, *J* = 17.2, 10.0, 7.2 Hz, CHC**H**=CHH), 5.28 (1H, dt, *J* = 10.4, 1.6 Hz, CH=C**H**H), 5.13 (1H, dt, *J* = 16.8, 1.6 Hz, CH=C**H**H), 4.85 (1H, d, *J* = 7.2 Hz, PhC**H**CH=CH_2), –0.05 (9H, s, Si(C**H**$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.7 (d, *J* = 244.8 Hz), 145.7, 142.7, 139.1, 138.6, 134.1 (d, *J* = 3.4 Hz), 129.9 (d, *J* = 8.0 Hz), 128.1, 128.0, 126.2, 117.1, 115.0 (d, *J* = 21.3 Hz), 50.1, 0.6; ^{19}F NMR (376 MHz, $CDCl_3$): δ –115.7 (tt, *J* = 9.0, 5.3 Hz); HRMS (ESI+): Calcd for $C_{21}H_{24}F_1Si_1$ $[M+H]^+$: 311.1631. Found: 311.1619; Specific Rotation: $[\alpha]_D^{20}$ –57.2 (*c* = 1.06, $CHCl_3$) for an enantiomerically enriched sample of 96.5:3.5 *e.r.*

(*S*,*E*)-5-(4-Fluorophenyl)-3-phenyl-4-trimethylsilanyl-pent-4-en-1-ol: The compound was prepared by hydroboration-oxidation of **3.54** using 9-BBN as described above. IR (neat): 3332 (br), 3085 (w), 3059 (w), 3027 (w), 2950 (w), 2893 (w), 1601 (w), 1503 (s), 1447 (w), 1406 (w), 1247 (m), 1221 (m), 1156 (w), 1093 (w), 1054 (w), 1024 (w), 972 (w), 910 (w), 831 (s), 754 (m), 739 (s), 697 (s), 640 (w), 622 (w), 571 (w), 533 (w), 494 (w), 443 (w), 421 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.29–7.15 (7H, m, Ar**H**), 7.02 (2H, tt, *J* = 8.8, 2.0 Hz, Ar**H**), 6.97 (1H, s, C=C**H**Ar), 4.29 (1H, dd, *J* = 8.8, 6.4 Hz, PhC**H**CH_2CH_2OH), 3.67–3.54 (2H, m, $PhCHCH_2C$**H**$_2OH$), 2.33 (1H, dddd, *J* = 13.6, 6.8, 6.8, 6.8 Hz, $PhCHC$**H**$_2CH_2OH$), 2.00–1.92 (1H, m, $PhCHC$**H**$_2CH_2OH$), –0.08 (9H, s, Si(C**H**$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.7 (d, *J* = 244.8 Hz), 148.0, 142.8, 138.6, 134.3 (d, *J* = 3.2 Hz), 129.9 (d, *J* = 8.0 Hz), 128.2, 127.7, 126.1, 115.3 (d, *J* = 20.9 Hz), 61.3, 41.1, 35.0, 0.6; ^{19}F NMR (376 MHz, $CDCl_3$): δ –115.6 (tt, *J* = 8.8, 5.3 Hz); HRMS

(ESI+): Calcd for $C_{20}H_{26}F_1O_1Si_1$ $[M+H]^+$: 329.1737. Found: 329.1743; Specific Rotation: $[\alpha]_D^{20}$ –267.5 (*c* = 1.17, $CHCl_3$) for an enantiomerically enriched sample of 96.5:3.5 *e.r.* Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (chiralpak OD column (25 cm x 0.46 cm), 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm). Retention time: major peak at 24.07 min, minor peak at 31.75 min.

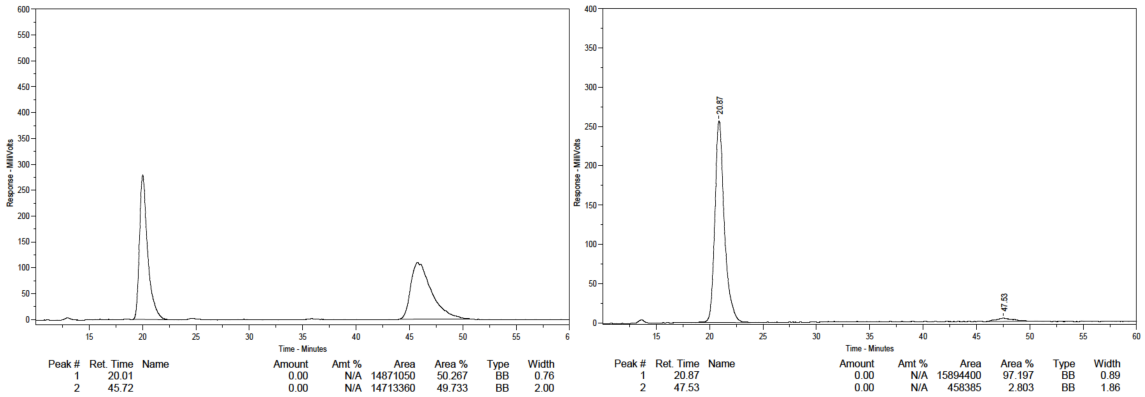


(*S*,*E*)-Trimethyl-[2-phenyl-1-(4-trifluoromethyl-benzylidene)-but-3-enyl]-silane (3.55): IR (neat): 3082 (w), 3061 (w), 2955 (w), 2897 (w), 1616 (w), 1600 (w), 1492 (w), 1448 (w), 1408 (w), 1321 (s), 1248 (m), 1163 (m), 1123 (s), 1107 (w), 1066 (s), 1016 (m), 919 (w), 832 (s), 756 (s), 699 (m), 641 (m), 597 (w), 554 (w), 507 (w), 458 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.55 (2H, d, *J* = 8.4 Hz, Ar**H**), 7.37 (2H, d, *J* = 8.4 Hz, Ar**H**), 7.29–7.24 (2H, m, Ar**H**), 7.20–7.15 (3H, m, Ar**H**), 7.05 (1H, s, C=C**H**Ar), 6.26 (1H, ddd, *J* = 17.2, 10.0, 7.2 Hz, CHC**H**=CHH), 5.29 (1H, ddd, *J* = 10.4, 1.6, 1.2 Hz, CH=C**H**H), 5.12 (1H, dt, *J* = 17.2, 1.6 Hz, CH=C**H**H), 4.80 (1H, d, *J* = 7.2 Hz, PhC**H**CH=CH_2), –0.03 (9H, s, Si(C**H**$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.0, 142.3, 141.9, 138.9, 138.2, 128.6, 128.5 (q, *J* = 32.3 Hz), 128.1, 127.9, 126.3, 125.0 (q, *J* = 3.8 Hz), 124.2 (q, *J* = 270.6 Hz), 117.4, 50.3, 0.6; ^{19}F NMR (376 MHz, $CDCl_3$): δ –62.87; HRMS (ESI+): Calcd for $C_{21}H_{24}F_3Si_1$ $[M+H]^+$: 361.1599. Found: 361.1591; Specific

Rotation: $[\alpha]_D^{20}$ –46.7 (*c* = 0.81, $CHCl_3$) for an enantiomerically enriched sample of 97:3 *e.r.*

(*S*,*E*)-3-Phenyl-5-(4-trifluoromethylphenyl)-4-trimethylsilanyl-pent-4-en-1-ol: The compound was prepared by hydroboration-oxidation of **3.55** using 9-BBN as described above. IR (neat): 3337 (br), 3086 (w), 3060 (w), 2952 (w), 2894 (w), 1615 (w), 1600 (w), 1494 (w), 1447 (w), 1407 (w), 1321 (s), 1248 (m), 1163 (m), 1122 (s), 1065 (s), 1016 (m), 833 (s), 755 (m), 697 (m), 640 (m), 596 (w), 525 (w), 443 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.57 (2H, d, *J* = 8.0 Hz, Ar**H**), 7.41 (2H, d, *J* = 8.0 Hz, Ar**H**), 7.29–7.16 (5H, m, Ar**H**), 7.00 (1H, s, C=C**H**Ar), 4.29 (1H, t, *J* = 7.6 Hz, PhC**H**CH_2CH_2OH), 3.66-3.52 (2H, m, $PhCHCH_2C\mathbf{H}_2OH$), 2.27 (1H, dddd, *J* = 13.6, 6.8, 6.8, 6.8 Hz, $PhCHC\mathbf{H}_2CH_2OH$), 2.04–1.95 (1H, m, $PhCHC\mathbf{H}_2CH_2OH$), –0.05 (9H, s, $Si(C\mathbf{H}_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.0, 142.4, 142.2, 138.1, 128.8 (q, *J* = 32.2 Hz), 128.6, 128.2, 127.7, 126.2, 125.2 (q, *J* = 3.8 Hz), 124.1 (q, *J* = 270.6 Hz), 61.3, 41.4, 35.0, 0.6; ^{19}F NMR (376 MHz, $CDCl_3$): δ –62.87; HRMS (ESI+): Calcd for $C_{21}H_{26}F_3O_1Si_1$ $[M+H]^+$: 379.1705. Found: 379.1705; Specific Rotation: $[\alpha]_D^{20}$ –224.1 (*c* = 0.96, $CHCl_3$) for an enantiomerically enriched sample of 97:3 *e.r.*

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (chiralpak OD column (25 cm x 0.46 cm), 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm). Retention time: major peak at 20.87 min, minor peak at 47.53 min.

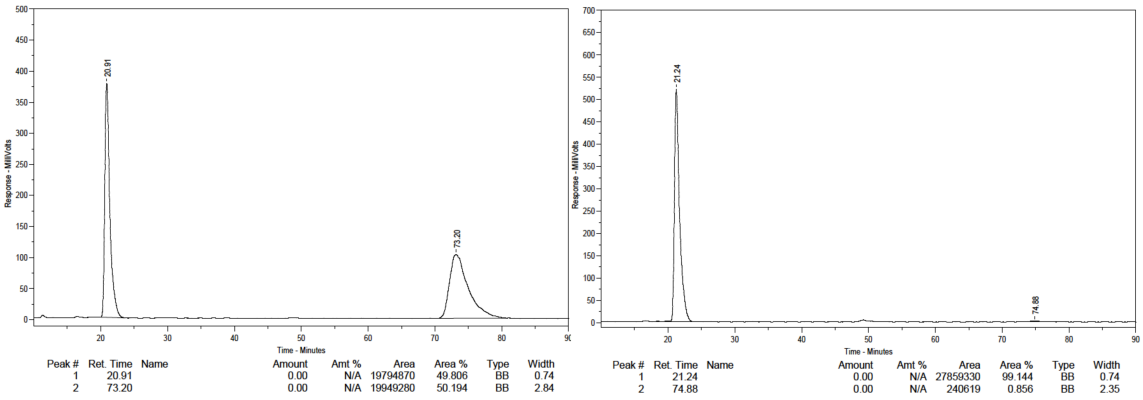


(*S*,*E*)-Trimethyl-[1-(4-methyl-benzylidene)-2-phenyl-but-3-enyl]-silane (3.56): IR (neat): 3079 (w), 3058 (w), 3023 (w), 2953 (w), 2920 (w), 2894 (w), 1635 (w), 1599 (w), 1507 (w), 1492 (w), 1447 (w), 1406 (w), 1246 (s), 1020 (w), 995 (w), 950 (w), 916 (m), 830 (s), 807 (m), 773 (m), 754 (s), 737 (m), 698 (s), 620 (w), 554 (w), 492 (w), 455 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.15 (7H, m, Ar**H**) 7.11 (2H, d, *J* = 8.0 Hz, Ar**H**), 7.03 (1H, s, C=C**H**Ar), 6.28 (1H, ddd, *J* = 17.2, 10.0, 7.2 Hz, PhCHC**H**=CHH), 5.27 (1H, dt, *J* = 10.0, 1.6 Hz, CH=C**H**H), 5.14 (1H, dt, *J* = 17.2, 1.6 Hz, CH=C**H**H), 4.94 (1H, d, *J* = 7.2 Hz, PhC**H**CH=CH_2), 2.32 (3H, s, ArC**H**$_3$), –0.06 (9H, s, Si(C**H**$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.8, 142.9, 139.7, 139.3, 136.5, 135.2, 128.8, 128.3, 128.1, 128.0, 126.0, 117.0, 50.1, 21.1, 0.7; HRMS (ESI+): Calcd for $C_{21}H_{27}Si_1$ $[M+H]^+$: 307.1882. Found: 307.1876; Specific Rotation: $[\alpha]_D^{20}$ –63.3 (*c* = 0.73, $CHCl_3$) for an enantiomerically enriched sample of 99:1 *e.r.*

(*S*,*E*)-3-Phenyl-5-*p*-tolyl-4-trimethylsilanyl-pent-4-en-1-ol: The compound was prepared by hydroboration-oxidation of **3.56** using 9-BBN as described above. IR (neat): 3321 (br), 3053 (w), 3023 (w), 2891 (w), 1600 (w), 1507 (w), 1494 (w), 1446 (w), 1406 (w), 1246 (m), 1021 (m), 831 (s), 752 (s), 737 (m), 697 (s), 643 (w), 626 (w), 572 (w), 539 (w), 493 (w), 441 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.13 (9H, m, Ar**H**), 7.02 (1H, s, C=C**H**Ar), 4.42 (1H, dd, *J* = 9.6, 5.6 Hz, PhC**H**CH_2CH_2OH), 3.65–3.56 (2H,

m, PhCHCH$_2$C**H**$_2$OH), 2.32 (3H, s, ArC**H**$_3$), 2.37–2.26 (1H, m, PhCHC**H**$_2$CH$_2$OH), 1.98-1.89 (1H, m, PhCHC**H**$_2$CH$_2$OH), –0.09 (9H, s, Si(C**H**$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.0, 143.1, 139.8, 136.6, 135.4, 129.1, 128.1, 128.0, 127.7, 126.0, 61.2, 40.9, 34.9, 21.1, 0.6; HRMS (ESI+): Calcd for $C_{21}H_{29}O_1Si_1$ $[M+H]^+$: 325.1988. Found: 325.1986; Specific Rotation: $[\alpha]_D^{20}$ –346.9 (*c* = 1.21, $CHCl_3$) for an enantiomerically enriched sample of 99:1 *e.r.*

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (chiralpak OD column (25 cm x 0.46 cm), 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm). Retention time: major peak at 21.24 min, minor peak at 74.88 min.



(*R*,*Z*)-(1-Benzylidene-2-phenyl-but-3-enyl)-dimethylsilane (3.61): IR (neat): 3079 (w), 3058 (w), 3024 (w), 2957 (w), 2122 (w), 1633 (w), 1598 (w), 1491 (w), 1449 (w), 1247 (m), 1073 (w), 1029 (w), 999 (w), 886 (s), 834 (m), 747 (s), 695 (s), 665 (w), 637 (w), 598 (w), 560 (w), 495 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.22 (11H, m, Ar**H**, C=C**H**Ph), 6.21 (1H, ddd, *J* = 17.2, 10.0, 7.2 Hz, CC**H**=CHH), 5.23 (1H, ddd, *J* = 10.4, 1.6, 1.2 Hz, CH=C**H**H), 4.99 (1H, dt, *J* = 17.2, 1.6Hz, C=C**H**H), 4.42 (1H, d, *J* = 6.8 Hz, PhC**H**CH=CH$_2$), 4.07 (1H, dq, *J* = 4.0, 4.0 Hz, Si(CH$_3$)$_2$**H**), –0.03 (3H, d, *J* = 4.0 Hz, Si(C**H**$_3$)$_2$H), –0.13 (3H, d, *J* = 3.6 Hz, Si(C**H**$_3$)$_2$H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.8, 143.6, 142.0, 140.8, 139.6, 129.0, 128.5, 128.2, 127.8, 127.0, 126.4, 116.2, 55.9, –

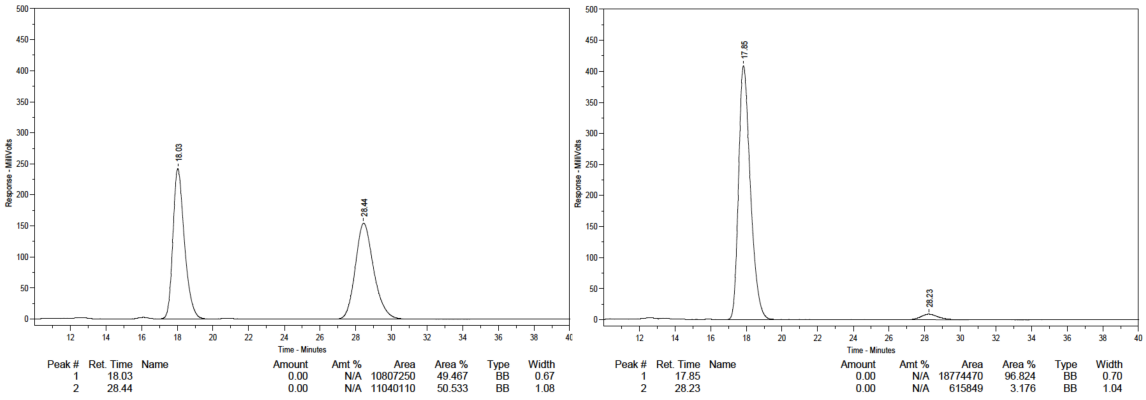
2.8, –2.9; HRMS (ESI+): Calcd for $C_{19}H_{23}Si_1$ $[M+H]^+$: 279.1569. Found: 279.1578; Specific Rotation: $[\alpha]_D^{20}$ +20.7 (*c* = 0.30, $CHCl_3$) for an enantiomerically enriched sample of 97:3 *e.r.*

(*S*,*E*)-Penta-1,4-diene-1,3-diyldibenzene (3.76): A 5 mL vial was charged with **3.61** (14.8 mg, 0.067 mmol), and $CHCl_3$ (0.5 mL). The solution was allowed to cool to 0 °C, at which temperature trifluoroacetic acid (0.5 mL) was added. The reaction mixture was allowed to stir at 4 °C for 15 h. After 15 h, the reaction mixture was diluted with Et_2O (1 mL), and carefully neutralized by addition of a saturated aqueous solution of $NaHCO_3$ (aq) (~ 5 mL). The aqueous layer was extracted with Et_2O (3 x 5.0 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting yellow oil was purified by silica gel column chromatography (hexane/Et_2O = 20/1) to afford the desired product in 89% yield (8.3 mg, 0.035 mmol). IR (neat): 3080 (w), 3059 (w), 3025 (w), 2976 (w), 2924 (w), 2855 (w), 1634 (w), 1598 (w), 1492 (w), 1448 (w), 1406 (w), 1073 (w), 1028 (w), 965 (m), 915 (m), 741 (s), 691 (s), 594 (w), 552 (w), 491 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.38–7.18 (10H, m, Ar**H**), 6.46–6.36 (2H, m, C**H**=C**H**Ph), 6.11 (1H, ddd, *J* = 17.2, 10.0, 6.8 Hz, CHC**H**=CHH), 5.18 (1H, dt, *J* = 10.4, 1.6 Hz, CH=C**H**H), 5.13 (1H, dt, *J* = 17.2, 1.6 Hz, CH=C**H**H), 4.42 (1H, d, *J* = 6.4 Hz, PhC**H**CH=CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.6, 140.0, 137.3, 131.7, 130.6, 128.5, 128.4, 128.0, 127.2, 126.5, 126.2, 115.6, 52.3; HRMS (ESI+): Calcd for $C_{17}H_{17}$ $[M+H]^+$: 221.1330. Found: 221.1331; Specific Rotation: $[\alpha]_D^{20}$ +3.3 (*c* = 0.60, $CHCl_3$) for an enantiomerically enriched sample of 97:3 *e.r.*

(*S*)-3,5-Diphenyl-pent-4-en-1-ol: The compound was prepared by hydroboration-oxidation of **3.76** using 9-BBN as described above. The resulting alcohol product serves

as the proof of absolute stereochemistry of 1,4-dienes from *Z*-vinylaluminum additions to allylic phosphates. [57] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34–7.16 (10H, m, Ar**H**), 6.43 (1H, d, *J* = 16.0 Hz, CH=C**H**Ph), 6.33 (1H, dd, *J* = 16.0, 7.6 Hz, C**H**=CHPh), 3.68–3.61 (3H, m, PhC**H**CH_2CH_2OH, $PhCHCH_2C\mathbf{H}_2OH$), 2.14–2.00 (2H, m, $PhCHC\mathbf{H}_2CH_2OH$); HRMS (ESI+): Calcd for $C_{17}H_{19}O_1$ $[M+H]^+$: 239.1436. Found: 239.1437; Specific Rotation: $[\alpha]_D^{20}$ –10.5 (*c* = 0.21, $CHCl_3$) for an enantiomerically enriched sample of 97:3 *e.r.*

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (chiralpak OD column (25 cm x 0.46 cm), 95/5 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm). Retention time: major peak at 17.85 min, minor peak at 28.23 min.

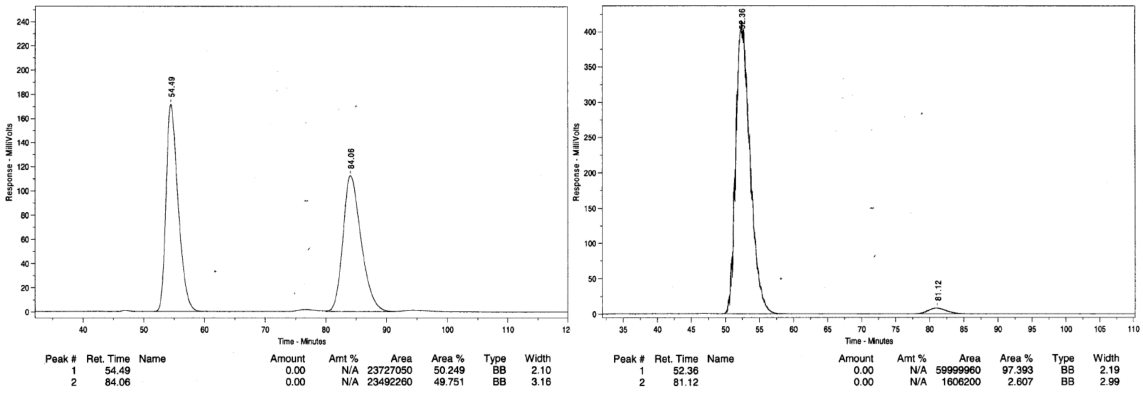


(*R*,*Z*)-(1-(2-Methoxyphenyl)-3-phenylpenta-1,4-dien-2-yl)dimethylsilane (3.62): IR (neat): 3059 (w), 3025 (w), 3001 (w), 2955 (w), 2926 (w), 2853 (w), 2834 (w), 2126 (w), 1592 (w), 1485 (m), 1462 (m), 1243 (s), 1075 (m), 999 (m), 884 (s), 836 (m), 750 (s), 700 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.19 (8H, m, Ar**H**, C=C**H**Ar), 6.92–6.84 (2H, m, Ar**H**), 6.24 (1H, ddd, *J* = 17.2, 10.0, 6.0 Hz, CHC**H**=CHH), 5.21 (1H, dt, *J*

[57] The analytical data for the compound is identical with that previously reported; see; P. von-Matt, G. C. Lloyd-Jones, A. B. E. Minidis, A. Pfaltz, L. Macko, M. Neuburger, M. Zehnder, H. Rueegger, P. S. Pregosin, *Helv. Chim. Acta.* **1995**, *78*, 265-284.

= 10.0, 1.2 Hz, CH=C**H**H), 4.98 (1H, dt, *J* = 17.2, 1.2 Hz, CH=CH**H**), 4.41 (1H, d, *J* = 6.0 Hz, PhC**H**CH=CHH), 3.96 (1H, dq, *J* = 4.0, 4.0 Hz, CH_3CH_3Si**H**), 3.83 (3H, s, OC**H₃**), –0.10 (3H, d, *J* = 4.0 Hz, C**H₃**CH_3SiH), –0.21 (3H, d, *J* = 4.0 Hz, CH_3C**H₃**SiH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.6, 143.8, 142.7, 141.5, 140.3, 130.7, 129.6, 129.5, 129.1, 128.7, 126.8, 120.3, 116.5, 110.6, 56.3, 55.9, –2.5, –2.6; HRMS (ESI+): Calcd for $C_{20}H_{25}O_1Si_1$ $[M+H]^+$: 309.1675. Found: 309.1661; Specific Rotation: $[\alpha]_D^{20}$ +31.8 (*c* = 0.81, $CHCl_3$) for an enantiomerically enriched sample of 97.5:2.5 *e.r.*

Enantiomeric purity was determined by HPLC analysis of the derived primary alcohol after hydroboration of title compound with 9-BBN in comparison with authentic racemic material (chiralpak OD column (25 cm x 0.46 cm), 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm). Retention time: Major peak at 52.36 min, minor peak at 81.12 min.



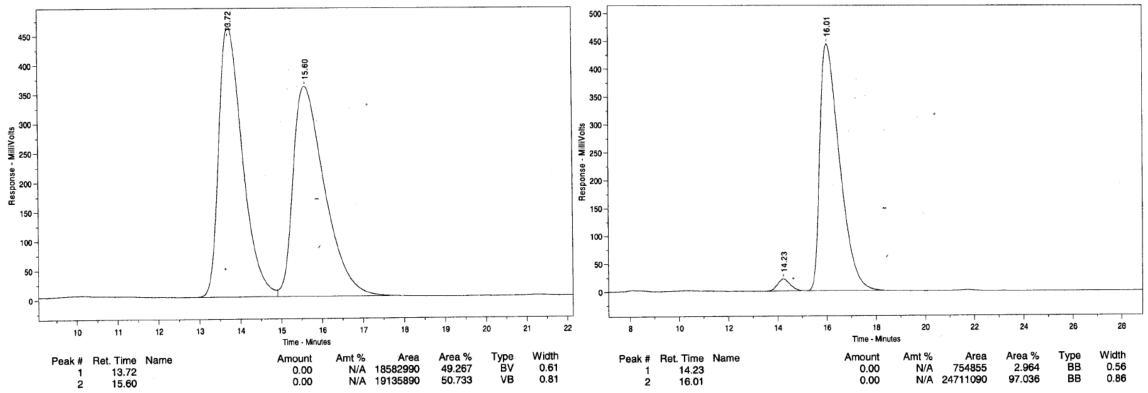
Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	54.49		0.00	N/A	23727050	50.249	BB	2.10
2	84.06		0.00	N/A	23492260	49.751	BB	3.16

Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	52.36		0.00	N/A	59999960	97.393	BB	2.19
2	81.12		0.00	N/A	1606200	2.607	BB	2.99

(*R*,*Z*)-Dimethyl(3-phenyl-1-*o*-tolylpenta-1,4-dien-2-yl)silane (3.63): IR (neat): 3060 (w), 3024 (w), 2956 (w), 2902 (w), 2118 (w), 1633 (w), 1599 (w), 1490 (w), 1450 (w), 1246 (m), 883 (s), 836 (m), 760 (m), 746 (s), 698 (s), 454 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37–7.29 (5H, m, Ar**H**), 7.27–7.14 (5H, m, Ar**H**, C=C**H**Ar), 6.25 (1H, ddd, *J* = 17.2, 10.4, 6.4 Hz, CHC**H**=CHH), 5.24 (1H, dt, *J* = 10.4, 1.2 Hz, CH=C**H**H), 5.04 (1H, dt, *J* = 17.2, 1.2 Hz, CH=CH**H**), 4.43 (1H, d, *J* = 6.4 Hz, PhC**H**CH=CHH), 3.92 (1H, dq, *J* = 4.0, 4.0 Hz, CH_3CH_3Si**H**), 2.23 (3H, s, PhC**H₃**), –0.14 (3H, d, *J* = 4.0 Hz,

C**H**$_3$CH$_3$SiH), –0.23 (3H, d, J = 4.0 Hz, CH$_3$C**H**$_3$SiH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.8, 143.6, 142.4, 140.9, 139.5, 136.2, 129.5, 129.2, 129.1, 128.4, 127.5, 126.5, 125.3, 116.3, 56.0, 20.1, –2.9, –3.0; HRMS (ESI+): Calcd for $C_{20}H_{25}O_1$ $[M+H]^+$: 293.1726. Found: 293.1712; Specific Rotation: $[\alpha]_D^{20}$ +17.9 (c = 1.31, $CHCl_3$) for an enantiomerically enriched sample of 97:3 *e.r.*

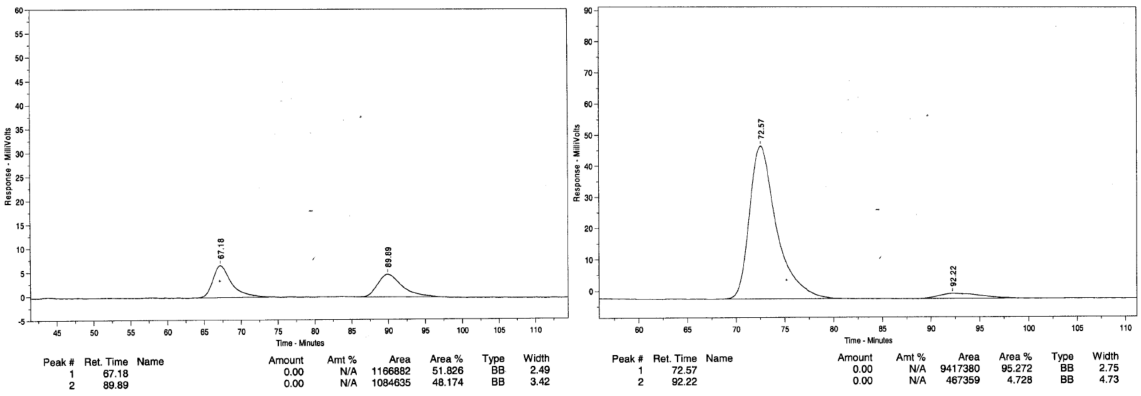
Enantiomeric purity was determined by HPLC analysis of the derived primary alcohol after hydroboration of title compound with 9-BBN in comparison with authentic racemic material (chiralpak AS column (25 cm x 0.46 cm), 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm). Retention time: minor peak 14.23 min, major peak 16.01 min.



(*R*,*Z*)-Dimethyl(3-phenyl-1-(3-(trifluoromethyl)phenyl)penta-1,4-dien-2-yl)silane: (3.64): IR (neat): 3061 (w), 3027 (w), 2960 (w), 2903 (w), 2130 (w), 1634 (w), 1600 (w), 1491 (w), 1450 (w), 1428 (w), 1328 (s), 1250 (w), 1205 (w), 1163 (m), 1123 (s), 1071 (m), 999 (w), 878 (s), 837 (m), 797 (m), 754 (m), 698 (s), 514 (w), 458 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55–7.51 (2H, m, Ar**H**), 7.46–7.43 (2H, m, Ar**H**), 7.38–7.34 (2H, m, Ar**H**), 7.28–7.24 (3H, m, Ar**H**), 7.20 (1H, s, C=C**H**Ar), 6.20 (1H, ddd, J = 17.2, 10.0, 7.2 Hz, CHC**H**=CHH), 5.25 (1H, dt, J = 10.0, 1.2 Hz, CH=C**H**H), 5.02 (1H, dt, J = 17.2, 1.2 Hz, CH=CH**H**), 4.44 (1H, d, J = 7.2 Hz, PhC**H**CH=CHH), 4.04 (1H, dq, J = 4.0, 4.0 Hz, CH$_3$CH$_3$Si**H**), –0.01 (3H, d, J = 4.0 Hz, C**H**$_3$CH$_3$SiH), –0.13 (3H, d, J = 4.0

Hz, $CH_3C\mathbf{H_3}SiH$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.8, 142.4, 142.1, 140.9, 140.8, 132.3, 129.5, 128.9, 128.8, 127.1, 125.9, 125.8, 124.2, 124.1, 117.1, 56.4, –2.5, –2.7; HRMS (ESI+): Calcd for $C_{20}H_{22}F_3Si_1$ $[M+H]^+$: 347.1443. Found: 347.1431; Specific Rotation: $[\alpha]_D^{20}$ +22.7 (*c* = 2.56, $CHCl_3$) for an enantiomerically enriched sample of 95.5:4.5 *e.r.*

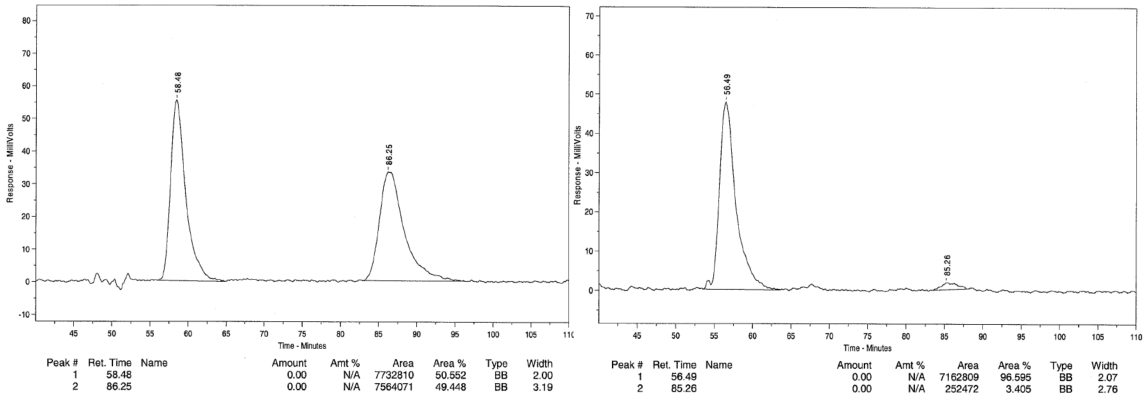
Enantiomeric purity was determined by HPLC analysis of the derived primary alcohol after hydroboration of title compound with 9-BBN in comparison with authentic racemic material (chiralpak OD column (25 cm x 0.46 cm), 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm). Retention time: major peak at 72.57 min, minor peak at 92.22 min.



(*R*,*Z*)-Dimethyl(3-phenyl-1-(4-(trifluoromethyl)phenyl)penta-1,4-dien-2-yl)silane: (3.65): IR (neat): 3062 (w), 3027 (w), 2960 (w), 2904 (w), 2137 (w), 1616 (w), 1491 (w), 1406 (w), 1321 (s), 1250 (w), 1163 (m), 1122 (s), 1065 (s), 1017 (m), 881 (s), 834 (s), 765 (m), 699 (s), 599 (m), 511 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.57 (2H, d, *J* = 8.5 Hz, Ar**H**), 7.38–7.33 (4H, m, Ar**H**), 7.26–7.24 (3H, m, Ar**H**), 7.19 (1H, s, C=C**H**Ar), 6.19 (1H, ddd, *J* = 17.0, 10.5, 7.0 Hz, CHC**H**=CHH), 5.25 (1H, dt, *J* = 10.5, 1.5 Hz, CH=C**H**H), 5.00 (1H, dt, *J* = 17.0, 1.5 Hz, CH=CH**H**), 4.43 (1H, d, *J* = 7.5 Hz, PhC**H**CH=CHH), 4.04 (1H, dq, *J* = 4.0, 4.0 Hz, $CH_3CH_3Si\mathbf{H}$), –0.02 (3H, d, *J* = 4.0 Hz, $C\mathbf{H_3}CH_3SiH$), –0.14 (3H, d, *J* = 4.0 Hz, $CH_3C\mathbf{H_3}SiH$); ^{13}C NMR (100 MHz, $CDCl_3$): δ

146.6, 143.4, 142.2, 141.8, 140.6, 129.3, 129.2, 129.0, 128.5, 126.8, 124.9 (q, J = 3.8 Hz), 124.4 (q, J = 270.9 Hz), 116.8, 56.0, –2.8, –2.9; HRMS (ESI+): Calcd for $C_{20}H_{22}F_3Si_1$ $[M+H]^+$: 347.1443. Found: 347.1458; Specific Rotation: $[\alpha]_D^{20}$ +18.7 (*c* = 2.22, $CHCl_3$) for an enantiomerically enriched sample of 96.5:3.5 *e.r.*

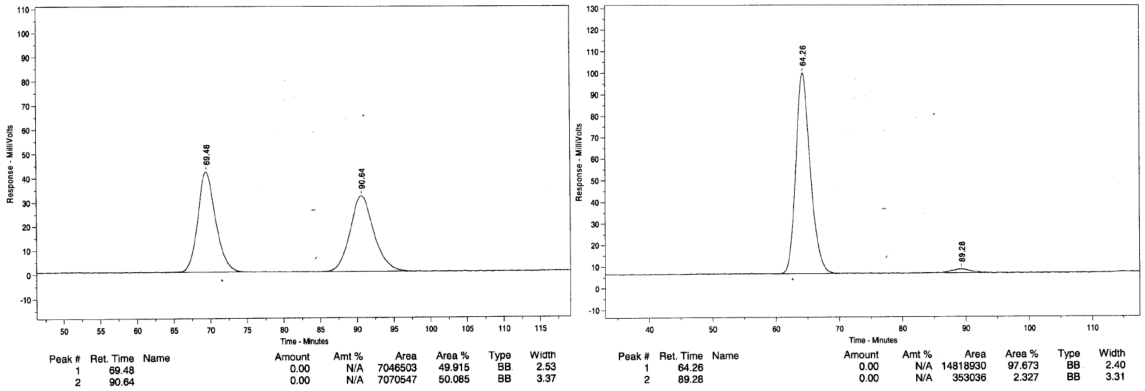
Enantiomeric purity was determined by HPLC analysis of the derived primary alcohol after hydroboration of title compound with 9-BBN in comparison with authentic racemic material (chiralpak OD column (25 cm x 0.46 cm), 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm). Retention time: major peak at 56.49 min, minor peak at 85.26 min.



(*R*,*Z*)-(1-(4-fluorophenyl)-3-phenylpenta-1,4-dien-2-yl)dimethylsilane: (3.66): IR (neat): 3060 (w), 3026 (w), 2959 (w), 2901 (w), 2131 (w), 1601 (w), 1503 (s), 1450 (w), 1248 (m), 1222 (s), 1155 (m), 881 (s), 833 (s), 757 (s), 698 (s), 510 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.35–7.31 (2H, m, Ar**H**), 7.26–7.21 (5H, m, Ar**H**), 7.14 (1H, s, C=C**H**Ar), 7.02–6.98 (2H, m, Ar**H**), 6.18 (1H, ddd, J = 17.2, 10.4, 7.2 Hz, CHC**H**=CHH), 5.22 (1H, dt, J = 10.4, 1.2 Hz, CH=C**H**H), 4.98 (1H, dt, J = 17.2, 1.2 Hz, CH=CH**H**), 4.39 (1H, d, J = 6.8 Hz, PhC**H**CH=CHH), 4.04 (1H, dq, J = 4.0, 4.0 Hz, CH_3CH_3Si**H**), –0.04 (3H, d, J = 4.0 Hz, C**H₃**CH_3SiH), –0.15 (3H, d, J = 4.0 Hz, CH_3C**H₃**SiH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.1 (d, J = 244.8 Hz), 144.4, 142.6,

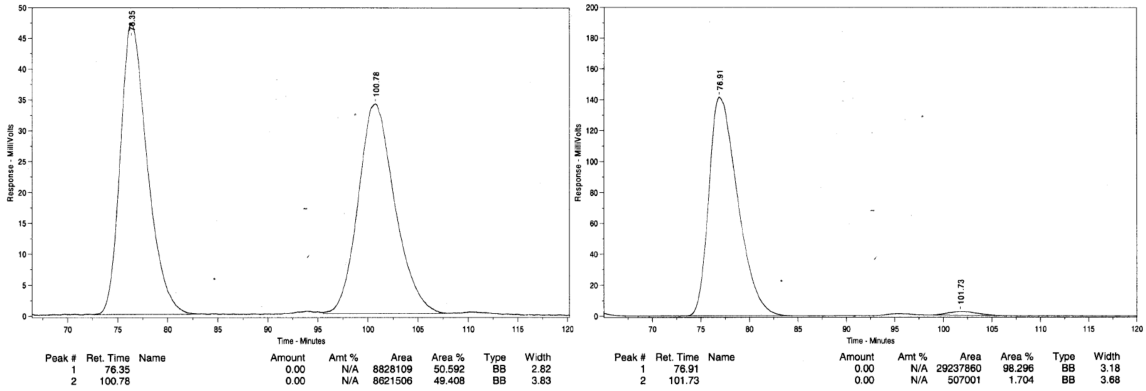
142.1, 140.9, 135.9, 130.3 (d, J = 7.6 Hz), 129.2, 128.5, 126.6, 116.5, 114.9 (d, J = 21.3 Hz), 56.0, –2.7, –2.9; HRMS (ESI+): Calcd for $C_{19}H_{20}F_1Si_1$ $[M\text{-}H]^+$: 295.1318. Found: 295.1313; Specific Rotation: $[\alpha]_D^{20}$ +25.7 (c = 0.52, $CHCl_3$) for an enantiomerically enriched sample of 98:2 *e.r.*

Enantiomeric purity was determined by HPLC analysis of the derived primary alcohol after hydroboration of title compound with 9-BBN in comparison with authentic racemic material (chiralpak OD column (25 cm x 0.46 cm), 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm). Retention time: major peak at 64.26 min, minor peak at 89.28 min.



(*R*,*Z*)-(1-(4-Methoxyphenyl)-3-phenylpenta-1,4-dien-2-yl)dimethylsilane: (3.67): The data was measured with 10% unseparable *E*-alkenylaluminum addition product. IR (neat): 3059 (w), 3026 (w), 2955 (w), 2904 (w), 2834 (w), 2123 (w), 1607 (m), 1491 (s), 1297 (w), 1245 (s), 1173 (m), 1034 (m), 999 (w), 882 (s), 830 (s), 755 (s), 698 (s), 552 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.34–7.30 (2H, m, Ar**H**), 7.28–7.20 (5H, m, Ar**H**), 7.14 (1H, s, C=C**H**Ar), 6.88-6.84 (2H, m, Ar**H**), 6.20 (1H, ddd, J = 17.2, 10.4, 6.8 Hz, CHC**H**=CHH), 5.21 (1H, dt, J = 10.4, 1.2 Hz, CH=C**H**H), 4.97 (1H, dt, J = 17.2, 1.2 Hz, CH=CH**H**), 4.39 (1H, d, J = 6.8 Hz, PhC**H**CH=CHH), 4.09 (1H, dq, J = 4.0, 3.6 Hz, CH_3CH_3Si**H**), 3.81 (3H, s, OC**H₃**), –0.02 (3H, d, J = 4.0 Hz, C**H₃**CH_3SiH), –0.12 (3H, d, J = 3.6 Hz, CH_3C**H₃**SiH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.9, 143.4, 142.4, 141.2,

132.4, 130.0, 129.2, 128.4, 126.5, 116.2, 113.8, 113.4, 56.1, 55.4, –2.6, –2.8; HRMS (ESI+): Calcd for $C_{20}H_{25}O_1Si_1$ $[M+H]^+$: 309.1675. Found: 309.1659; Specific Rotation: $[\alpha]_D^{20}$ +47.7 (*c* = 2.31, $CHCl_3$) for an enantiomerically enriched sample of 98.5:1.5 *e.r.* Enantiomeric purity was determined by HPLC analysis of the derived primary alcohol after hydroboration of title compound with 9-BBN in comparison with authentic racemic material (chiralpak OD column (25 cm x 0.46 cm), 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm). Retention time: major peak at 76.91 min, minor peak at 101.73 min.

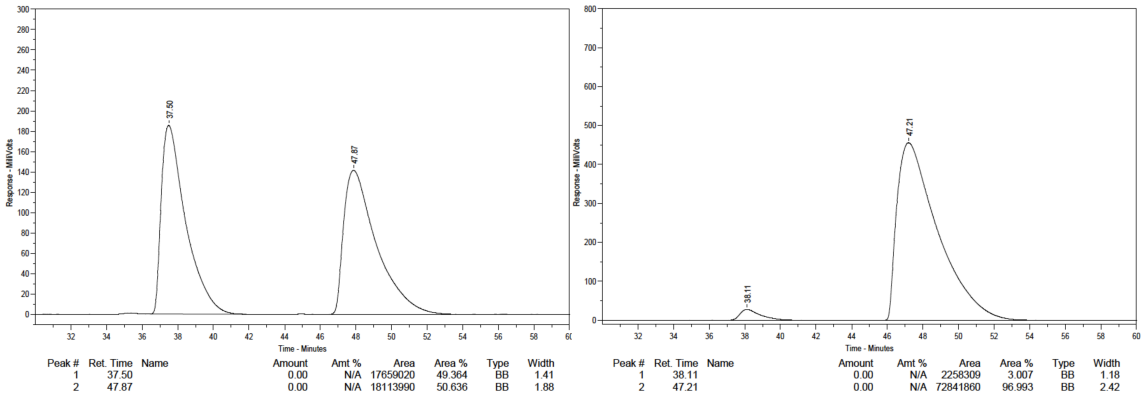


(*R*,*Z*)-[1-Benzylidene-2-(4-nitrophenyl)-but-3-enyl]-dimethylsilane (3.68): The data was measured with 7% unseparable *iso*-butyl addition product. IR (neat): 3078 (w), 3057 (w), 3020 (w), 2957 (w), 2920 (w), 2854 (w), 2121 (m), 1594 (m), 1516 (s), 1490 (m), 1342 (s), 1248 (m), 1108 (w), 888 (s), 833 (s), 850 (s), 835 (s) 748(s), 696 (s), 605 (w), 506 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.18 (2H, d, *J* = 8.8 Hz, Ar**H**), 7.42 (2H, d, *J* = 8.8 Hz, Ar**H**), 7.31–7.22 (5H, m, Ar**H)**, 7.19 (1H, s, C=C**H**Ph), 6.16 (1H, ddd, *J* = 17.2, 10.4, 6.8 Hz, CHC**H**=CHH), 5.28 (1H, dt, *J* = 10.4, 1.2 Hz, CH=C**H**H), 4.98 (1H, dt, *J* = 17.2, 1.2 Hz, CH=C**H**H), 4.50 (1H, d, *J* = 6.8 Hz, PhC**H**CH=CH_2), 4.03 (1H, dq, *J* = 4.0, 4.0 Hz, $Si(CH_3)_2$**H**), –0.04 (3H, d, *J* = 3.6 Hz, $Si(CH_3)_2H$), –0.13 (3H, d, *J* = 4.0 Hz, $Si(CH_3)_2H$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.1, 146.7, 145.1, 142.6, 139.3, 139.0, 129.7, 128.4, 127.9, 127.4, 123.5, 117.5, 55.7, –2.8, –2.9; HRMS (ESI+): Calcd

for $C_{19}H_{21}N_1O_2Si_1$ $[M]^+$: 323.1356. Found: 323.1354; Specific Rotation: $[\alpha]_D^{20}$ +8.1 (*c* = 0.37, $CHCl_3$) for an enantiomerically enriched sample of 97:3 *e.r.*

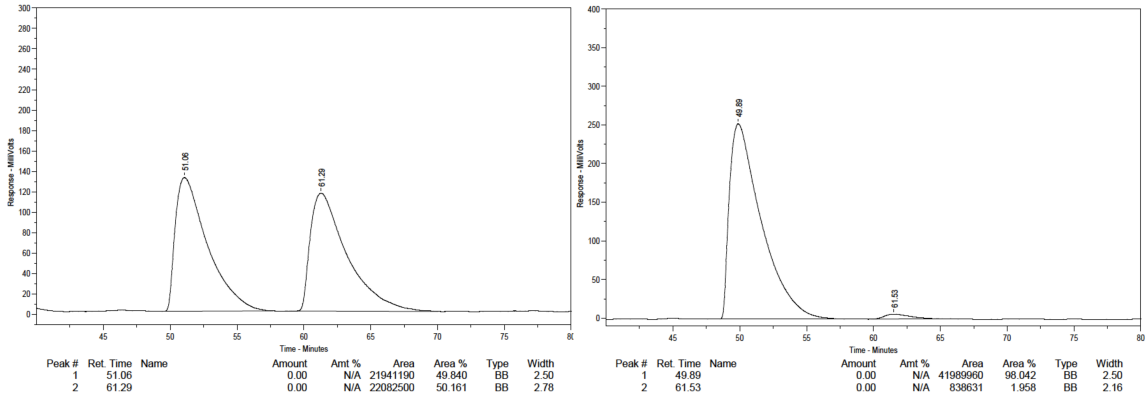
(*S*,*Z*)-1-Nitro-4-(1-phenylpenta-1,4-dien-3-yl)benzene: The compound was prepared by protodesilylation of **3.68** in TFA/$CHCl_3$ as described above. IR (neat): 3079 (w), 3025 (w), 2925 (w), 2850 (w), 1634 (w), 1596 (m), 1514 (s), 1447 (w), 1409 (w), 1341 (s), 1179 (w), 1108 (w), 1014 (w), 966 (m), 921 (m), 850 (m), 798 (w), 744 (m), 691 (s), 604 (w), 513 (w), 490 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.17 (2H, dt, *J* = 8.8, 2.4 Hz, Ar**H**), 7.42 (2H, dt, *J* = 8.8, 2.4 Hz, Ar**H**), 7.37–7.21 (5H, m, Ar**H**), 6.45 (1H, d, *J* = 16.4 Hz, CH=C**H**Ph), 6.33 (1H, dd, *J* = 16.0, 6.8 Hz, C**H**=CHPh), 6.06 (1H, ddd, *J* = 17.2, 10.4, 6.8 Hz, CHC**H**=CHH), 5.26 (1H, dt, *J* = 10.0, 1.2 Hz, CH=C**H**H), 5.16 (1H, dt, *J* = 17.2, 1.2 Hz, CH=C**H**H), 4.32 (1H, t, *J* = 6.8 Hz, PhC**H**CH=CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.1, 146.7, 138.4, 136.7, 131.9, 129.8, 128.9, 128.6, 127.7, 126.3, 123.8, 117.0, 52.0; HRMS (ESI+): Calcd for $C_{17}H_{16}N_1O_2$ $[M+H]^+$: 266.1181. Found: 266.1174; Specific Rotation: $[\alpha]_D^{20}$ +2.1 (*c* = 0.55, $CHCl_3$) for an enantiomerically enriched sample of 97:3 *e.r.*

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (chiralpak OD column (25 cm x 0.46 cm), 99/1 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm). Retention time: minor peak at 38.11 min, major peak at 47.21 min.



(*R*,*Z*)-Toluene-4-sulfonic acid 4-(2-dimethylsilanyl-3-phenyl-1-vinyl-allyl)-phenyl ester (3.69): The data was measured with 10% unseparable *iso*-butyl addition product. IR (neat): 3076 (w), 3054 (w), 3024 (w), 2958 (w), 2924 (w), 2870 (w), 2129 (w), 1633 (w), 1597 (w), 1497 (m), 1372 (w), 1248 (w), 1197 (m), 1175 (s), 1151 (s), 1092 (m), 1017 (w), 860 (s), 812 (m), 749 (m), 697 (s), 663 (s), 564 (m), 549 (s), 503 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.66 (2H, d, *J* = 8.0 Hz, Ar**H**), 7.31-7.19 (7H, m, Ar**H**), 7.14 (2H, d, *J* = 8.8 Hz, Ar**H**), 7.13 (1H, s, C=C**H**Ph), 6.92 (2H, d, *J* = 8.4 Hz, Ar**H**), 6.11 (1H, ddd, *J* = 17.2, 10.4, 6.8 Hz, CHC**H**=CHH), 5.20 (1H, d, *J* = 10.0 Hz, CH=C**H**H), 4.91 (1H, dt, *J* = 17.2, 1.2 Hz, CH=C**H**H), 4.34 (1H, d, *J* = 7.2 Hz, PhC**H**CH=CH_2), 3.98 (1H, dq, *J* = 4.0, 4.0 Hz, $Si(CH_3)_2$**H**), 2.41 (3H, s, ArC$\mathbf{H}_3$), –0.10 (3H, d, *J* = 4.0 Hz, $Si(C\mathbf{H}_3)_2H$), –0.22 (3H, d, *J* = 3.6 Hz, $Si(C\mathbf{H}_3)_2H$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.1, 145.2, 144.0, 143.4, 141.1, 140.2, 139.3, 132.2, 130.1, 129.6, 128.5, 128.4, 127.8, 127.1, 122.1, 116.6, 55.2, 21.6, –2.8, –2.9; HRMS (ESI+): Calcd for $C_{26}H_{27}O_3S_1Si_1$ $[M-H]^+$: 447.1450, Found: 447.1456; Specific Rotation: $[\alpha]_D^{20}$ +4.3 (*c* = 0.33, $CHCl_3$) for an enantiomerically enriched sample of 98:2 *e.r.*

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (chiralpak OD column (25 cm x 0.46 cm), 99.5/0.5 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm). Retention time: major peak at 49.89 min, minor peak at 61.53 min.

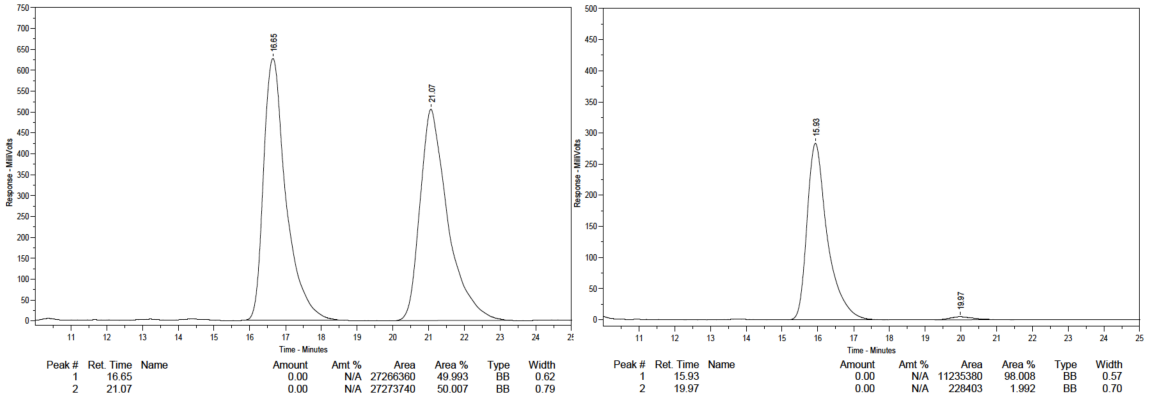


(*R*,*Z*)-(1-Benzylidene-2-p-tolyl-but-3-enyl)-dimethylsilane (3.70): IR (neat): 3077 (w), 3053 (w), 3020 (w), 2973 (w), 2956 (w), 2920 (w), 2901 (w), 2864 (w), 2125 (w), 1632 (w), 1592 (w), 1572 (w), 1509 (w), 1491 (w), 1443 (w), 1406 (w), 1247 (m), 998 (w), 888 (s), 833 (s), 815 (w), 746 (s), 696 (s), 661 (w), 640 (w), 591 (w), 555 (w), 525 (w), 491 (m), 450 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.33–7.14 (10H, m, Ar**H**, C=C**H**Ph), 6.19 (1H, ddd, *J* = 17.2, 10.0, 7.2 Hz, CHC**H**=CHH), 5.20 (1H, ddd, *J* = 10.4, 1.6, 1.2 Hz, CH=C**H**H), 4.98 (1H, dt, *J* = 17.2, 1.2 Hz, CH=C**H**H), 4.37 (1H, dd, *J* = 7.2, 1.2 Hz, PhC**H**CH=CH_2), 4.05 (1H, dq, *J* = 4.0, 4.0 Hz, Si$(CH_3)_2$**H**), 2.34 (3H, s, ArC**H**$_3$), –0.03 (3H, d, *J* = 3.6 Hz, Si(C**H**$_3)_2$H), –0.13 (3H, d, *J* = 4.0 Hz, Si(C**H**$_3)_2$H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.0, 143.4, 141.0, 139.7, 139.0, 135.9, 129.0, 128.9, 128.5, 127.7, 126.9, 115.9, 55.5, 21.0, -2.7, -2.9; HRMS (ESI+): Calcd for $C_{20}H_{25}Si_1$ $[M+H]^+$: 293.1726. Found: 293.1719; Specific Rotation: $[\alpha]_D^{20}$ +34.4 (*c* = 0.98, $CHCl_3$) for an enantiomerically enriched sample of 98:2 *e.r.*

(*R*,*Z*)-4-Dimethylsilanyl-5-phenyl-3-p-tolyl-pent-4-en-1-ol: The compound was prepared by hydroboration-oxidation of **3.70** using 9-BBN as described above. IR (neat): 3317 (br), 3051 (w), 3020 (w), 2923 (w), 2857 (w), 2128 (w), 1728 (w), 1592 (w), 1510 (w), 1491 (w), 1442 (w), 1042 (m), 884 (s), 834 (m), 815 (m), 655 (w), 638 (w), 566 (w), 486 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.30–7.20 (6H, m, Ar**H**, C=C**H**Ph), 7.15 (2H, d, *J* = 8.0 Hz, Ar**H**), 7.10 (2H, d, *J* = 8.0 Hz, Ar**H**), 3.96 (1H, dq, *J* = 4.0, 4.0 Hz, Si$(CH_3)_2$**H**), 3.75 (1H, t, *J* = 7.6 Hz, ArC**H**CH_2CH_2OH), 3.70–3.59 (2H, m, ArCHCH_2C**H**$_2$OH), 2.31 (3H, s, ArC**H**$_3$), 2.22 (1H, dddd, *J* = 13.6, 6.8, 6.8, 6.8 Hz, ArCHC**H**$_2CH_2OH$), 2.10–2.01 (1H, m, ArCHC**H**$_2CH_2OH$), –0.11 (3H, d, *J* = 3.6 Hz, Si(C**H**$_3)_2$H), –0.24 (3H, d, *J* = 4.0 Hz, Si(C**H**$_3)_2$H); ^{13}C NMR (100 MHz, $CDCl_3$): δ

145.1, 141.1, 140.0, 139.7, 135.9, 129.0, 128.6, 128.4, 127.8, 126.9, 61.4, 47.9, 37.5, 21.0, –2.7, –2.9; HRMS (ESI+): Calcd for $C_{20}H_{28}O_1Si_1$ $[M+H]^+$: 311.1831. Found: 311.1822; Specific Rotation: $[\alpha]_D^{20}$ –40.0 (*c* = 0.31, $CHCl_3$) for an enantiomerically enriched sample of 98:2 *e.r.*

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (chiralpak OD column (25 cm x 0.46 cm), 95/5 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm). Retention time: major peak at 15.93 min, minor peak at 19.97 min.



Enantioselective Total Synthesis of (–)-Naysol.

(*E*)-Acetic acid 4-[3-(diethoxy-phosphoryloxy)-propenyl]-phenyl ester (3.79): A 10 mL test tube was charged with (*E*)-acetic acid 4-(3-hydroxy-propenyl)-phenyl ester[58] (192 mg, 1.00 mmol), 4-dimethylaminopyridine (24.4 mg, 0.200 mmol), CH_2Cl_2 (2.0 mL), and triethylamine (170 µL, 1.20 mmol). The solution was allowed to cool to 0 °C, and chlorodiethylphosphate (173 µL, 1.20 mmol) was added to the mixture. After allowing the solution to stir at 22 °C for 15 h, the reaction was quenched by addition of sat. NH_4Cl (aq.) (2.0 mL). The layers were separated and the aqueous layer was washed

[58] The alcohol was prepared as described in the literature by Mizoroki-Heck reaction from 4-iodophenyl acetate and allyl alcohol; see: A. S. Paraskar, A. Sudalai, *Tetrahedron*, **2006**, *62*, 5756-5762.

with Et_2O (1.0 mL x 3). The combined organic layers were passed through a short plug of $MgSO_4$, and concentrated under reduced pressure. The resulting yellow oil was purified by silica gel column chromatography (hexanes/EtOAc = 1/1) to give the product as light yellow oil in 92% yield (303 mg, 0.920 mmol).

IR (neat): 2984 (w), 2931 (w), 1757 (m), 1501 (m), 1601 (w), 1506 (m), 1443 (w), 1369 (m), 1262 (m), 1190 (s), 1165 (s), 1097 (w), 1007 (s), 963 (s), 909 (s), 853 (m), 800 (m), 746 (w), 658 (w), 593 (w), 517 (m), 454 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.37 (2H, dt, *J* = 8.8, 2.4 Hz, Ar**H**), 7.03 (2H, dt, *J* = 8.8, 2.4 Hz, Ar**H**), 6.64 (1H, d, *J* = 16.0 Hz, ArC**H**=CH), 6.23 (1H, dt, *J* = 15.6, 6.0 Hz, ArCH=C**H**), 4.66 (2H, ddd, *J* = 8.4, 6.0, 1.2 Hz, CH=CHC**H**$_2$), 4.11 (4H, dq, *J* = 7.2, 7.2 Hz, PO(OC**H**$_2$CH$_3$)$_2$), 2.27 (3H, s, ArOCOC**H**$_3$), 1.32 (6H, td, *J* = 7.2, 1.2 Hz, PO(OCH$_2$C**H**$_3$)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.3, 150.4, 133.8, 132.7, 127.6, 123.8 (d, *J* = 6.5 Hz), 121.7, 67.7 (d, *J* = 5.4 Hz), 63.8 (d, *J* = 5.7 Hz), 21.0, 16.1 (d, *J* = 6.8 Hz); HRMS (ESI+) Calcd for $C_{15}H_{22}O_6P_1$ $[M+H]^+$:329.1154. Found: 329.1153.

(*S*,*E*)-Acetic acid 4-[3-(4-hydroxyphenyl)-2-trimethylsilanyl-1-vinyl-allyl]-phenyl ester (3.80): A 10 mL Schlenk tube equipped with a stir bar was charged with 4-hydroxyphenylethynyltrimethylsilane **3.77**[59] (76.1 mg, 0.400 mmol) under N_2. Hexanes (1.0 mL) and dibal–H (143 μL, 0.80 mmol) were added to the reaction vessel at 0 °C. After stirring at 55 °C for 2 h, the solution was allowed to cool to −78 °C (dry ice/acetone) and a solution of NHC–Ag **3.39** (2.3 mg, 0.002 mmol) and $CuCl_2$•$2H_2O$ (0.68 mg, 0.004 mmol) in THF (2.4 mL) was added through a syringe. After allowing the solution to stir for 10 min, substrate **3.79** (65.7 mg, 0.200 mmol) was added at that

(59) The compound was prepared by Sonogashira coupling from 4-iodophenol and trimethylsilylacetylene; see: Yashima, E.; Huang, S.; Matsuhima, T.; Okamoto, Y. *Macromolecules*, **1995**, *28*, 4184–4193.

temperature. The reaction mixture was allowed to warm to –15 °C (freezer) and sit for 12 h. The reaction was quenched by addition of a saturated aqueous solution of Rochelle's salt (3.0 mL) and the resulting mixture was allowed to stir for 1 hour at 22 °C. The layers were separated and the aqueous layer was washed with Et_2O (1.0 mL x 3). The combined organic layers were passed through a short plug of $MgSO_4$ and concentrated under reduced pressure. The resulting yellow residue was purified by silica gel column chromatography (hexane/Et_2O = 10/1) to give the product as clear oil (55.7 mg, 0.152 mmol, 76%).

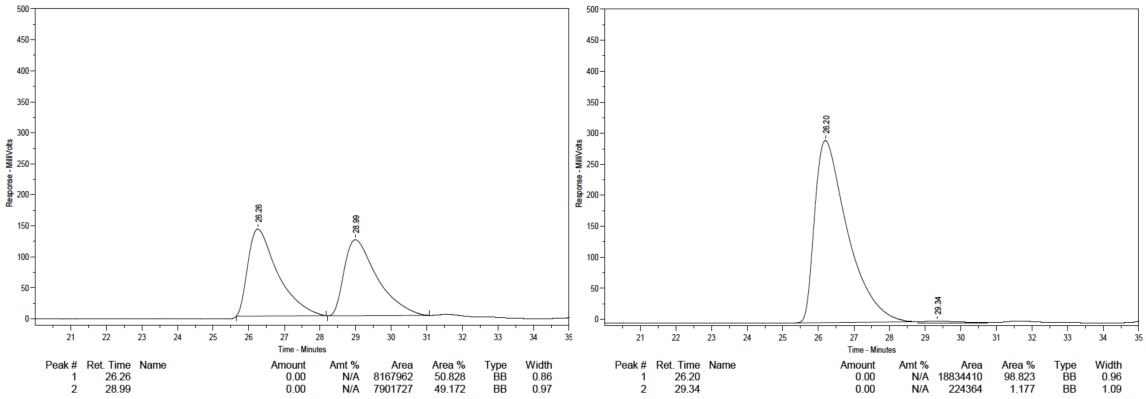
IR (neat): 3405 (w), 3077 (w), 3033 (w), 2954 (w), 2895 (w), 1757 (w), 1735 (w), 1608 (w), 1505 (m), 1433 (w), 1369 (w), 1196 (s), 1165 (m), 1100 (w), 1072 (w), 1016 (w), 909 (m), 888 (w), 832 (s), 780 (w), 755 (w), 729 (s), 687 (w), 647 (w), 582 (w), 551 (w), 508 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.19 (2H, d, *J* = 8.0 Hz, Ar**H**), 7.13 (2H, d, *J* = 8.0 Hz, Ar**H**), 6.98 (2H, dt, *J* = 8.8, 2.4 Hz, Ar**H**), 6.97 (1H, s, C=C**H**Ar), 6.74 (2H, dt, *J* = 8.8, 2.4 Hz, Ar**H**), 6.23 (1H, ddd, *J* = 17.2, 10.0, 7.2 Hz, ArCHC**H**=CHH), 5.26 (1H, dt, *J* = 10.0, 1.6 Hz, CH=C**H**H), 5.12 (1H, dt, *J* = 17.2, 1.6 Hz, CH=C**H**H), 4.88 (1H, d, *J* = 7.2 Hz, ArC**H**CH=CH_2), 2.27 (3H, s, ArOCOC**H**$_3$), –0.06 (9H, s, Si(C**H**$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 154.5, 148.9, 143.8, 140.6, 139.5, 139.1, 130.5, 129.8, 128.9, 121.0, 117.3, 115.0, 49.6, 21.1, 0.7; HRMS (ESI+): Calcd for $C_{22}H_{27}O_3Si_1$ $[M+H]^+$: 367.1723. Found: 367.1745; Specific Rotation: $[\alpha]_D^{20}$ –63.7 (*c* = 2.85, $CHCl_3$) for an enantiomerically enriched sample of 98.5:1.5 *e.r.*

(*S*,*E*)-Acetic acid 4-[3-(4-acetoxy-phenyl)-2-trimethylsilanyl-1-vinyl-allyl]-phenyl ester (S1): A 10 mL test tube was charged with **3.80** (37.5 mg, 0.102 mmol), pyridine (0.7 mL), and acetic anhydride (19.2 μL, 0.204 mmol) under N_2. The reaction mixture

was allowed to stir at 22 °C for 2 h. The reaction was quenched by addition of 1N HCl (aq.) (1.5 mL), washed with Et_2O (3 x 1.0 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The resulting yellow oil was purified by silica gel column chromatography (hexane/Et_2O = 20/1) to afford the desired product in 94% yield (39.3 mg, 0.096 mmol).

IR (neat): 3077 (w), 3034 (w), 2954 (w), 2896 (w), 1760 (s), 1634 (w), 1602 (w), 1501 (s), 1409 (w), 1367 (m), 1247 (w), 1187 (s), 1164 (s), 1103 (w), 1072 (w), 1044 (w), 1015 (m), 910 (s), 834 (s), 756 (m), 687 (w), 631 (w), 613 (w), 592 (w), 582 (w), 551 (w), 511 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.26 (2H, d, *J* = 8.4 Hz, Ar**H**), 7.18 (2H, d, *J* = 8.8 Hz, Ar**H**), 7.04–6.97 (5H, m, Ar**H**, C=C**H**Ar), 6.23 (1H, ddd, *J* = 17.2, 10.0, 7.2 Hz, ArCHC**H**=CHH), 5.27 (1H, dt, *J* = 10.0, 1.6 Hz, CH=C**H**H), 5.13 (1H, dt, *J* = 17.2, 1.6 Hz, CH=C**H**H), 4.86 (1H, d, *J* = 7.2 Hz, ArC**H**CH=CH_2), 2.27 (3H, s, ArOCOC**H**$_3$), 2.26 (3H, s, ArOCOC**H**$_3$), –0.04 (9H, s, Si(C**H**$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.3, 149.4, 149.0, 145.7, 140.2, 139.0, 138.9, 135.6, 129.3, 128.9, 121.2, 121.0, 117.4, 49.6, 21.1, 0.7; HRMS (ESI+): Calcd for $C_{24}H_{29}O_4Si_1$ $[M+H]^+$: 409.1835. Found: 409.1843; Specific Rotation: $[\alpha]_D^{20}$ –60.7 (*c* = 0.57, $CHCl_3$) for an enantiomerically enriched sample of 98.5:1.5 *e.r.*

Enantiomeric purity was determined by HPLC analysis of the derived primary alcohol after hydroboration of title compound with 9-BBN in comparison with authentic racemic material (chiralpak OD column (25 cm x 0.46 cm), 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm). Retention time: major peak at 26.20 min, minor peak at 29.34 min.



(*R*,*Z*)Acetic acid 4-[3-(4-acetoxy-phenyl)-1-vinyl-allyl]-phenyl ester (S2): A 5 mL vial was charged with **S1** (37.7 mg, 0.092 mmol), $CHCl_3$ (1.5 mL), and trifluoroacetic acid (1.5 mL). The reaction mixture was allowed to stir at 22 °C for 48 h. After 48 h, the reaction mixture was diluted with Et_2O, and carefully neutralized by addition of sat. $NaHCO_3$ (aq). The organic layer was extracted with Et_2O (3 x 1.0 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting yellow oil was purified by silica gel column chromatography (hexane/Et_2O = 20/1) to afford the desired product in 73% yield (22.6 mg, 0.067 mmol).

IR (neat): 3079 (w), 3012 (w), 2960 (w), 2927 (w), 2855 (w), 1755 (s), 1633 (w), 1601 (w), 1503 (m), 1429 (w), 1367 (m), 1187 (s), 1163 (s), 1143 (w), 1014 (m), 908 (s), 875 (w), 846 (m), 749 (w), 684 (w), 594 (w), 562 (w), 540 (w), 511 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.27 (2H, dt, *J* = 8.4, 2.4 Hz, Ar**H**), 7.22 (2H, dt, *J* = 8.8, 2.4 Hz, Ar**H**), 7.04 (2H, dt, *J* = 8.4, 2.0 Hz, Ar**H**), 7.01 (2H, dt, *J* = 8.4, 2.0 Hz, Ar**H**), 6.58 (1H, d, *J* = 11.2 Hz, ArC(CH=CH_2)CH=C**H**Ar), 6.00 (1H, ddd, *J* = 17.6, 10.0, 6.0 Hz, C**H**=CHH), 5.76 (1H, dd, *J* = 11.6, 10.0, ArC(CH=CH_2)C**H**=CHAr), 5.21–5.16 (2H, m, ArCH=C**HH**), 4.54 (1H, dd, *J* = 10.0, 6.0 Hz, ArC**H**CH=CH_2), 2.29 (3H, s, ArOCOC**H**$_3$), 2.27 (3H, s, ArOCOC**H**$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.5, 169.4, 149.5, 149.2, 140.5, 139.9, 134.6, 132.7, 129.5, 128.6, 121.5, 121.3, 115.7, 46.9, 21.1;

HRMS (ESI+): Calcd for $C_{21}H_{21}O_4$ $[M+H]^+$: 337.1440. Found: 337.1454; Specific Rotation: $[\alpha]_D^{20}$ –181.7 (*c* = 0.95, $CHCl_3$) for an enantiomerically enriched sample of 98.5:1.5 *e.r.*

(–)-Nyasol (cis-hinokiresinol)[60]: To a 10 mL test tube charged with **S2** (14.2 mg, 0.042 mmol) in MeOH (2.0 mL) was added a solution of K_2CO_3 (100 mg in 1.0 mL H_2O). The reaction mixture was allowed to stir at 22 °C for 1 h. A solution of 1N HCl (2.0 mL) was added doropwise. The solution was washed with Et_2O (3 x 1.0 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/AcOEt = 4/1) to give (–)-nyasol in >98% yield (10.7 mg, 0.042 mmol).

IR (neat): 3300 (br), 3011 (w), 2975 (w), 2960 (w), 2927 (w), 1633 (m), 1508 (s), 1440 (w), 1365 (w), 1225 (s), 1169 (s), 1098 (m), 994 (w), 913 (m), 874 (w), 829 (s), 732 (m), 647 (w), 622 (w), 584 (w), 541 (w), 513 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.17 (2H, dt, *J* = 8.4, 2.4 Hz, Ar**H**), 7.11 (2H, dt, *J* = 8.8, 2.4 Hz, Ar**H**), 6.79 (2H, dt, *J* = 8.8, 2.4 Hz, Ar**H**), 6.78 (2H, dt, *J* = 8.4, 2.4 Hz, Ar**H**), 6.52 (1H, d, *J* = 11.6 Hz, ArC(CH=CH_2)CH=C**H**Ar), 6.01 (1H, ddd, *J* = 16.8, 10.4, 6.0 Hz, C**H**=CHH), 5.68 (1H, dd, *J* = 11.6, 10.0 Hz, ArC(CH=CH_2)C**H**=CHAr), 5.17–5.14 (2H, m, ArCH=C**HH**), 4.76 (1H, s, ArO**H**), 4.67 (1H, s, ArO**H**), 4.49 (1H, dd, *J* = 10.0, 6.0 Hz, ArC**H**CH=CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.4, 153.9, 140.6, 135.6, 131.7, 130.0, 129.9, 128.8, 128.5, 115.3, 115.1, 115.0, 46.8; HRMS (ESI+): Calcd for $C_{17}H_{17}O_2$ $[M+H]^+$: 253.1229. Found:

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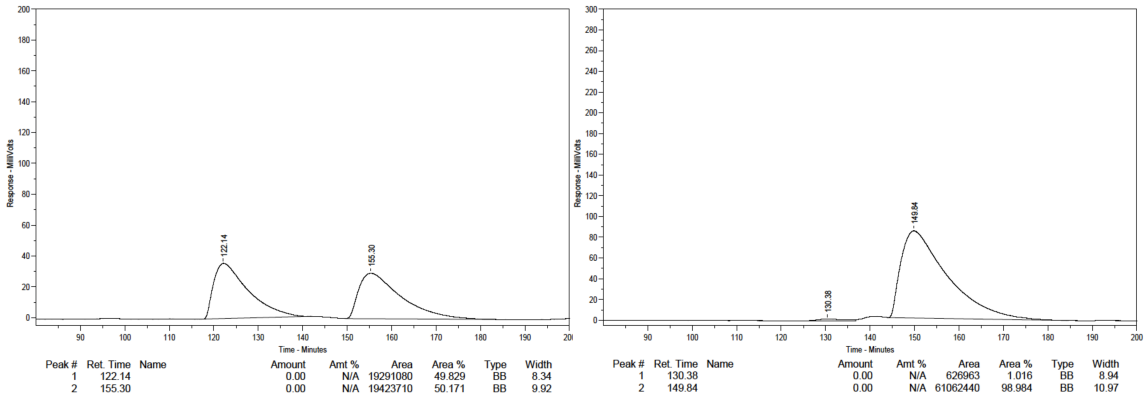
(60) The analytical data of this compound is identical with previously reported data, for ^1H and ^{13}C, see: Iida, Y.; Oh, K-B.; Saito, M.; Matsuoka, H.; Kurata, H.; Natsume, M.; Abe, H. *J. Agric. Food. Chem.* **1999**, *47*, 584–587. For a report on the specific rotation: $[\alpha]_D^{22}$= –198 (*c* = 0.13, MeOH), see: Jeong, S-J.; Higuchi, R.; Ono, M.; Kuwano, M.; Kim, Y -C.; Miyamoto, T. *Biol. Pharm. Bull.* **2003**, *26*, 1721–1724.

253.1233; Specific Rotation: $[\alpha]_D^{20}$ –201.9 (*c* = 0.42, $CHCl_3$) for an enantiomerically enriched sample of 98.5:1.5 *e.r.*

(*R,Z*)-4,4'-(5-hydroxypent-1-ene-1,3-diyl)diphenol: The compound was prepared by hydroboration-oxidation of (–)-nyasol using 9-BBN (3 equiv) as described above. IR (neat): 3270 (br), 2927 (w), 2443 (br), 1607 (m), 1508 (s), 1443 (w), 1382 (w), 1242 (s), 1170 (m), 1102 (w), 1013 (w), 829 (s), 728 (w), 701 (w), 624 (w), 577 (w), 550 (w), 517 (w) cm^{-1}; ^1H NMR (400 MHz, CD_3OD): δ 7.10 (2H, d, *J* = 8.4 Hz, Ar**H**), 7.08 (2H, d, *J* = 8.4 Hz, Ar**H**), 6.74-6.70 (4H, m, Ar**H**), 6.36 (1H, d, *J* = 11.2 Hz, CH=C**H**Ar), 5.69 (1H, t, *J* = 11.0 Hz, C**H**=CHAr), 3.91 (1H, dt, *J* = 10.0, 7.2 Hz, ArC**H**CH_2CH_2OH), 3.44 (2H, td, *J* = 6.8, 2.0 Hz, $ArCHCH_2C\mathbf{H}_2OH$), 1.91–1.81 (2H, m, $ArCHC\mathbf{H}_2CH_2OH$); ^{13}C NMR (100 MHz, CD_3OD): δ 157.3, 156.6, 137.2, 135.1, 131.0, 130.1, 129.3, 129.2, 116.3, 115.9, 60.9, 41.8, 40.7; HRMS (ESI+): Calcd for $C_{17}H_{18}O_3$ $[M]^+$: 270.1256. Found: 270.1246; Specific Rotation: $[\alpha]_D^{20}$ –324.2 (*c* = 0.71, CH_3OH) for an enantiomerically enriched sample of 98.5:1.5 *e.r.*

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (chiralpak OD column (25 cm x 0.46 cm), 95/5 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm). Retention time: minor peak at 130.38 min, major peak at 149.84 min.



Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	122.14		0.00	N/A	19291080	49.829	BB	8.34
2	155.30		0.00	N/A	19423710	50.171	BB	9.92

Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	130.38		0.00	N/A	626963	1.016	BB	8.94
2	149.84		0.00	N/A	61062440	98.984	BB	10.97

3.8.2 Representative Experimental Procedures for Ni-catalyzed Hydroalumination of Terminal Alkynes and Characterization Data of New Compounds

General. Infrared (IR) spectra were recorded on a Bruker FT-IR Alpha (ATR mode) spectrophotometer, ν_{max} in cm^{-1}. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). ^{1}H NMR spectra were recorded on a Varian Unity INOVA 400 (400 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, sep = septet, bs = broad singlet, bd = broad doublet, bt = broad triplet, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on a Varian Unity INOVA 400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 77.16 ppm). High-resolution mass spectrometry was performed on a JEOL AccuTOF DART (positive mode) at the Mass Spectrometry Facility, Boston College. Unless otherwise noted, all reactions were carried out with distilled and degassed solvents under an atmosphere of dry N_2 in oven- (135 °C) or flame-dried glassware with standard dry box or vacuum-line techniques. Tetrahydrofuran (thf) was purified by distillation from sodium benzophenone ketyl immediately prior to use (the use of unpurified solvent could cause erosion of selectivity by up to 5%, especially for alkyl-substituted alkynes). Except where noted, all work-up and purification procedures were carried out in air. All solvents were purchased from Fisher.

Reagent grade (97%) di-*iso*-butylaluminum hydride (dibal–H) was purchased from Aldrich and used as received. Alkynes were purchased from Aldrich and distilled prior to use (or could be used as received without any purification, in some cases with minor erosion of selectivity (<5%)). Deuterium oxide (D incorporation >99.96% with sure seal cap) was purchased from Cambridge Isotope Laboratories, Inc. and used as received. *N*-Bromosuccinimide was purchased from Aldrich and recrystallized from hot water before use. *N*-Iodosuccinimide was purchased from Aldrich and used as received. 2-Methoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (MeO–Bpin) was purchased from Aldrich and used as received. Bromine (Br_2) was purchased from Aldrich and treated with basic alumina for 2 hours and filtered through a plug of basic alumina prior to use. Nickel(II) acetylacetonate ($Ni(acac)_2$) and tetrakis(triphenylphosphine)nickel(0) ($Ni(PPh_3)_4$) were purchased from Aldrich and used as received. Nickel(II) chloride hexahydrate ($NiCl_2 \bullet 6H_2O$), bis(triphenylphosphine)nickel(II) chloride ($Ni(PPh_3)_2Cl_2$), 1,2-bis(diphenylphosphino)ethane nickel(II) chloride ($Ni(dppe)Cl_2$), and 1,3-bis(diphenylphosphino)propane nickel(II) chloride ($Ni(dppp)Cl_2$) were purchased from Strem and used as received. Bis(1,5-cyclooctadiene)nickel(0) ($Ni(cod)_2$) was purchased from Strem and purified in a N_2 dry box (commercial solid $Ni(cod)_2$ was washed with anhydrous diethyl ether and recrystallized from dry toluene at –50 °C). 1,4-Bis(diphenylphosphino)butane nickel(II) chloride ($Ni(dppb)Cl_2$) was prepared according to a known procedure.[61] Dichloro[1,1'-bis(diphenylphosphino)ferrocene]nickel(II) ($Ni(dppf)Cl_2$) was prepared based on a reported procedure.[62]

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(61) Wille, A.; Tomm, S.; Frauenrath, H. *Synthesis*, **1998**, 305–308.

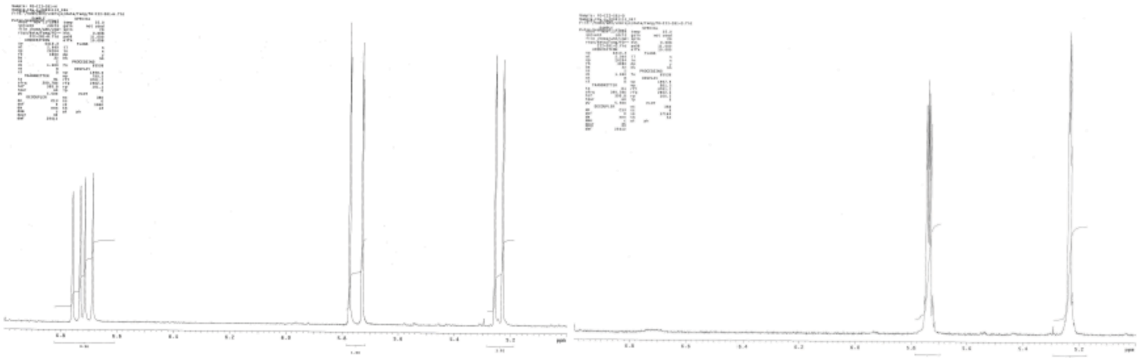
(62) Grant, G. J.; Carter, S. M.; Russell, A. L.; Poullaos, I. M.; VanDerveer D. G. *J. Organomet. Chem.* **2001**, *637-639*, 683–690.

■ **Representative Procedure for Ni(dppp)Cl_2 Catalyzed Hydroalumination of Terminal Alkynes:** Commercial grade 1,3-bis(diphenylphosphino)propane nickel(II) chloride (Ni(dppp)Cl_2, 16.3 mg, 0.0300 mmol) is placed in an oven-dried 13x100 test tube equipped with a stir bar. The test tube is sealed with a septum and purged with N_2 for approximately ten minutes. Tetrahydrofuran (thf, 1.0 mL) is added through a syringe, followed by dropwise addition of commercial grade di-*iso*-butylaluminum hydride (dibal–H, 232 μL, 1.30 mmol) at 22 °C (gas evolution occurs as dibal–H was added). The resulting black solution is allowed to cool to 0 °C (ice bath) before phenylacetylene (110 μL, 1.00 mmol) is added slowly over five minutes (please note that reaction is exothermic). The resulting black solution is allowed to warm to 22 °C and stir for an additional two hours. An aliquot of reaction mixture is removed by a syringe and quenched by adding this into a solution of saturated aqueous Rochelle's salt (sodium potassium tartrate; 1.0 mL) at 0 °C (ice bath) and allowed to stir at 0 °C for 30 minutes. The aqueous layer is washed with Et_2O (1.0 mL x 3) and the combined organic layers are passed through a plug of anhydrous $MgSO_4$ and concentrated *in vacuo* to afford the *protonated* product as yellow oil. The remaining reaction mixture is subjected to dropwise addition of D_2O at 0 °C (ice bath) and the resulting mixture is allowed to stir at 0 °C for additional 30 minutes. The aqueous layer is washed with Et_2O (1.0 mL x 3) and the combined organic layers are passed through a plug of anhydrous $MgSO_4$ and concentrated *in vacuo* to afford the crude *deuterated* product as yellow oil. The crude products are subjected to ^{1}H NMR analysis.

α-Deuteriostyrene (3.90): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.40 (2H, m), 7.34–7.30

(2H, m), 7.27–7.23 (1H, m), 5.74 (1H, dt, J = 2.8, 1.2 Hz), 5.23 (1H, dt, J = 1.6, 1.2 Hz). The spectroscopic data match those reported previously.[63]

Site selectivity (>98:<2 α:β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).



Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	6.72	0.93	48.2	1	6.70	<0.02	<2.0
3	5.24	1.00	51.8	3	5.23	0.98	>98.0

α-Deuterio-1-methoxy-2-vinylbenzene (Table 3.8, entry 2): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (1H, dd, J = 7.6, 1.6 Hz), 7.24 (1H, ddd, J = 8.0, 8.0, 1.6 Hz), 6.94 (1H, dd, J = 7.6, 7.6 Hz), 6.87 (1H, d, J = 8.4 Hz), 5.73 (1H, dt, J = 1.6, 1.2 Hz), 5.26 (1H, dt, J = 1.6, 1.6 Hz), 3.85 (3H, s). The spectroscopic data match those reported previously.[64]

Site selectivity (98:2 α:β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).

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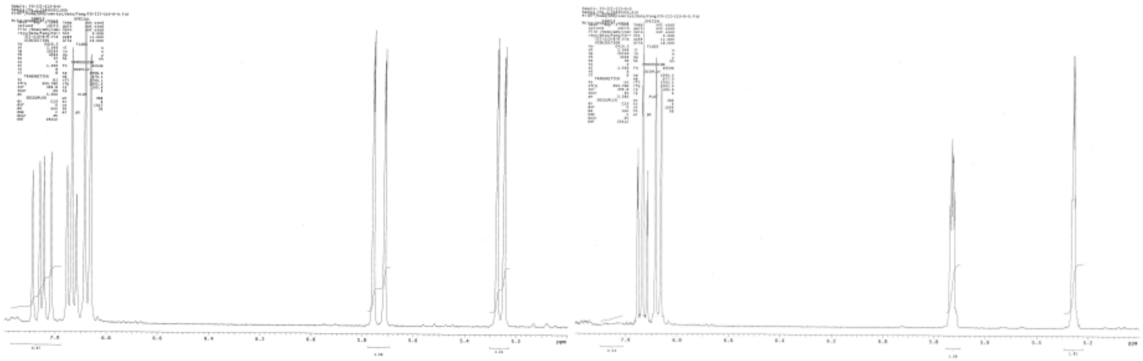
(63) Liard, A.; Marek, I. *J. Org. Chem.* **2000**, *65*, 7218–7220.

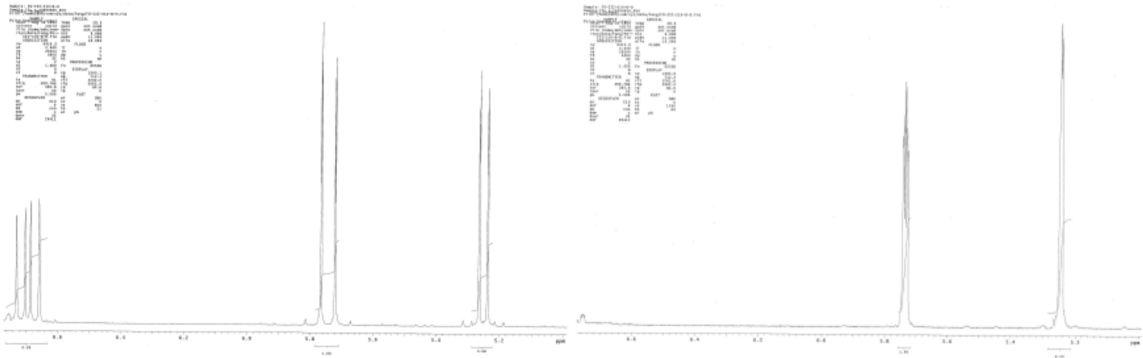
(64) The spectroscopic data for the corresponding protonated alkene: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (1H, dd, J = 7.6, 1.6 Hz), 7.24 (1H, ddd, J = 8.0, 8.0, 1.6 Hz), 7.05 (1H, dd, J = 17.6, 11.2 Hz), 6.94 (1H, dd, J = 7.6, 7.6 Hz), 6.87 (1H, d, J = 8.4 Hz), 5.74 (1H, dd, J = 18.0, 1.6 Hz), 5.26 (1H, dd, J = 11.2, 1.6 Hz), 3.85 (3H, s); these data match the ^{1}H NMR spectra of the commercially available material.



Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	7.05	0.97	49.0	1	7.05	0.02	1.9
4	5.26	1.01	51.0	4	5.26	1.02	98.1

α-Deuterio-1-methoxy-3-vinylbenzene (Table 3.8, entry 3): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 (1H, dd, J = 7.6, 7.6 Hz), 7.02–7.00 (1H, m), 6.95 (1H, dd, J = 2.0, 2.0 Hz), 6.82 (1H, ddd, J = 8.4, 2.4, 0.8 Hz), 5.74 (1H, dt, J = 2.4, 0.8 Hz), 5.25 (1H, d, J = 1.2 Hz), 3.82 (3H, s). The spectroscopic data match those reported previously.[65]

Site selectivity (>98:<2 α:β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).

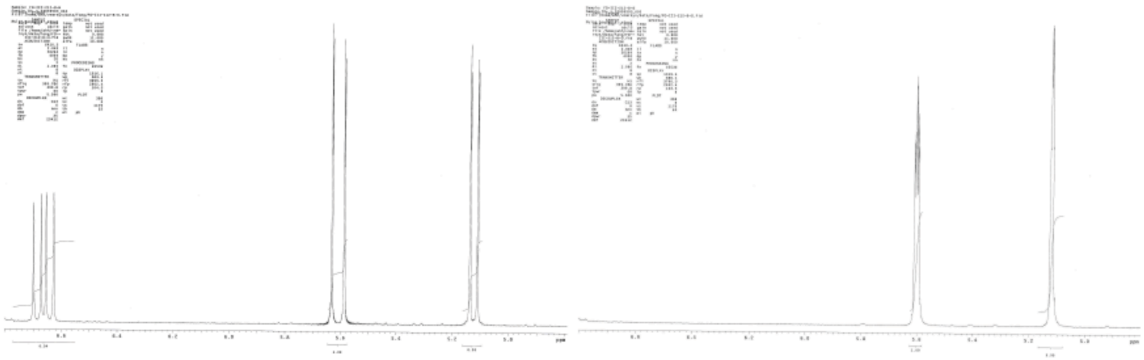


Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	6.69	0.99	50.3	1	6.69	<0.02	<0.02
3	5.25	0.98	49.7	3	5.25	0.99	>98.0

(65) The spectroscopic data for the corresponding protonated alkene: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 (1H, dd, J = 7.6, 7.6 Hz), 7.02–7.00 (1H, m), 6.95 (1H, dd, J = 2.0, 2.0 Hz), 6.82 (1H, ddd, J = 8.4, 2.4, 0.8 Hz), 6.69 (1H, dd, J = 17.6, 11.2 Hz), 5.74 (1H, dd, J = 17.6, 1.2 Hz), 5.25 (1H, dd, J = 11.2, 0.8 Hz), 3.82 (3H, s); these data match the ^{1}H NMR spectra of the commercially available material.

α-Deuterio-1-methoxy-4-vinylbenzene (Table 3.8, entry 4): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (2H, ddd, *J* = 8.8, 2.0, 2.0 Hz), 6.86 (2H, ddd, *J* = 8.8, 2.0, 2.0 Hz), 5.60 (1H, dt, *J* = 2.4, 0.8 Hz), 5.12 (1H, dt, *J* = 1.6, 1.2 Hz), 3.81 (3H, s). The spectroscopic data match those reported previously.[66]

Site selectivity (>98:<2 α:β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).



Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	6.66	0.94	48.7	1	6.66	<0.02	<2.0
3	5.12	0.99	51.3	3	5.12	0.98	>98.0

α-Deuterio-1-(trifluoromethyl)-3-vinylbenzene (Table 3.8, entry 5): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (1H, s), 7.59–7.56 (1H, m), 7.51 (1H, d, *J* = 8.0 Hz), 7.44 (1H, dd, *J* = 7.6, 7.6 Hz), 5.82 (1H, bt, *J* = 2.4 Hz), 5.36 (1H, bt, *J* = 1.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.4, 135.4 (t, *J* = 24.6 Hz), 131.1 (q, *J* = 32.0 Hz), 129.5, 129.1, 124.5 (q, *J* = 3.7 Hz), 124.3 (q, *J* = 270.9 Hz), 123.1 (q, *J* = 3.8 Hz), 115.8; HRMS (ESI$^+$): Calcd for $C_9H_7D_1F_3$ $[M+H]^+$: 174.0641; Found: 174.0641.

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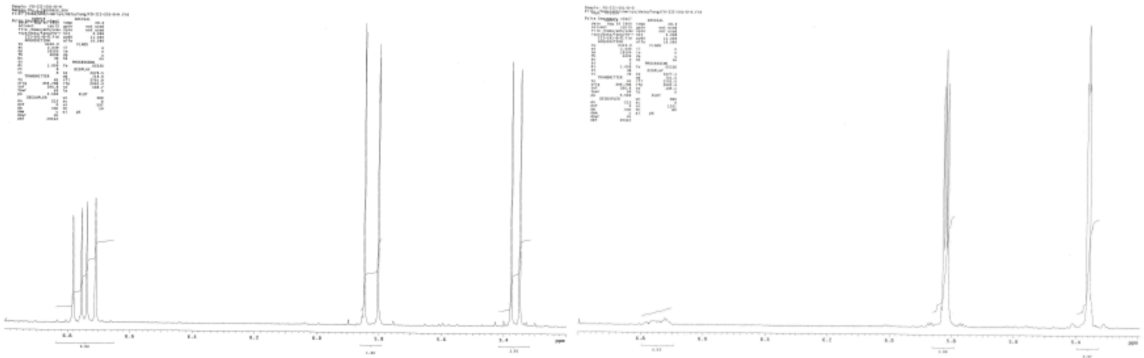
(66) The spectroscopic data for the corresponding protonated alkene: ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.35 (2H, ddd, *J* = 8.8, 2.0, 2.0 Hz), 6.86 (2H, ddd, *J* = 8.8, 2.0, 2.0 Hz), 6.66 (1H, dd, *J* = 17.6, 10.8 Hz), 5.61 (1H, dd, *J* = 17.6, 0.8 Hz), 5.12 (1H, dd, *J* = 10.8, 0.8 Hz), 3.81 (3H, s); these data match the ^{1}H NMR spectra of the commercially available material.

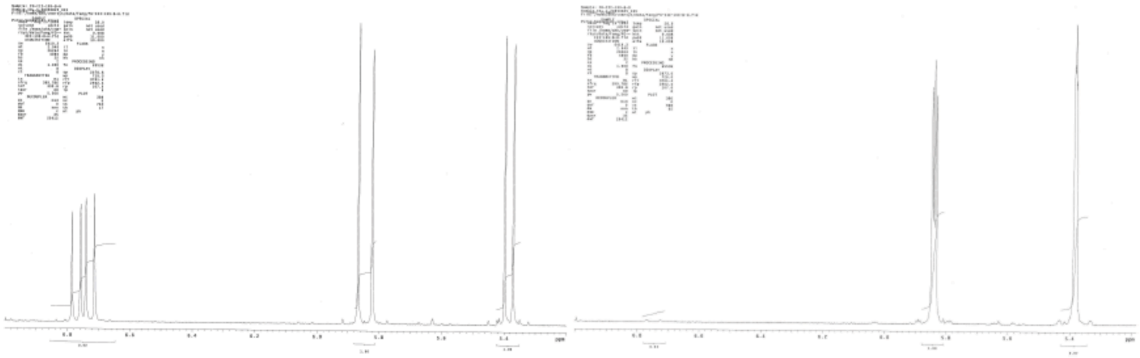
Site selectivity (95:5 α:*β*) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).



Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	6.74	0.94	48.2	1	6.74	0.05	4.9
3	5.36	1.01	51.8	3	5.36	0.97	95.1

α-Deuterio-1-(trifluoromethyl)-4-vinylbenzene (Table 3.8, entry 6): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (2H, d, *J* = 8.4 Hz), 7.50 (2H, d, *J* = 8.4 Hz), 5.84 (1H, bt, *J* = 2.8 Hz), 5.38 (1H, bt, *J* = 1.2 Hz). The spectroscopic data match those reported previously.[67] Site selectivity (97:3 α:*β*) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).

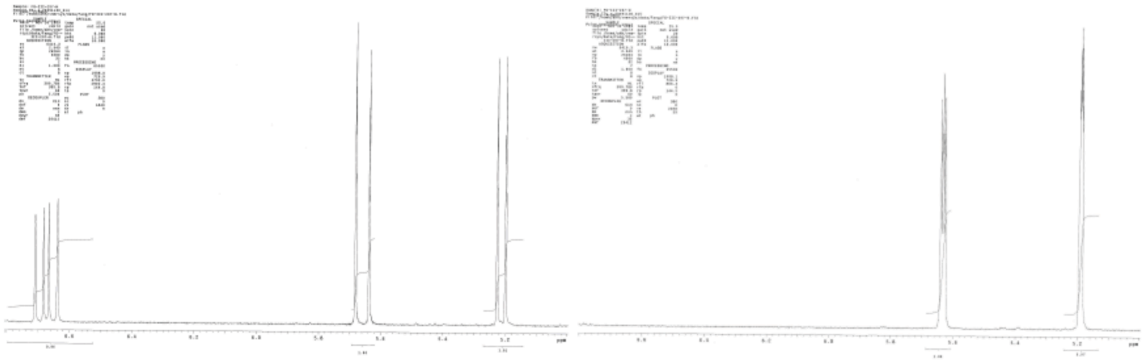
(67) The spectroscopic data for the corresponding protonated alkene: ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.58 (2H, d, *J* = 8.4 Hz), 7.50 (2H, d, *J* = 8.4 Hz), 6.75 (1H, dd, *J* = 17.6, 11.2 Hz), 5.85 (1H, d, *J* = 17.6 Hz), 5.39 (1H, d, *J* = 11.2 Hz); these data match the ^{1}H NMR spectra of the commercially available material.



Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	6.75	0.92	47.9	1	6.75	0.03	3.0
3	5.39	1.00	52.1	3	5.38	0.97	97.0

α-Deuterio-1-fluoro-4-vinylbenzene (Table 3.8, entry 7): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.35 (2H, m), 7.03–6.98 (2H, m), 5.63 (1H, ddt, J = 2.8, 0.8, 0.8 Hz), 5.19 (1H, ddt, J = 0.8, 0.8, 0.8 Hz). The spectroscopic data match those reported previously.[68]

Site selectivity (>98:<2 α*:β*) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).

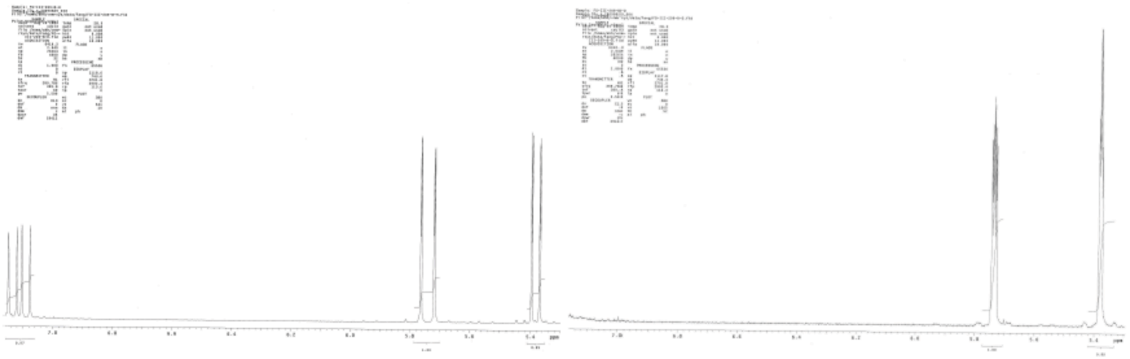


Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	6.67	0.96	47.9	1	6.66	<0.02	<2.0
3	5.21	1.01	52.1	3	5.19	0.97	>98.0

(68) The spectroscopic data for the corresponding protonated alkene: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.35 (2H, m), 7.03–6.98 (2H, m), 6.67 (1H, dd, J = 17.6, 10.8 Hz), 5.66 (1H, ddd, J = 17.6, 0.8, 0.8 Hz), 5.21 (1H, ddd, J = 11.2, 0.8, 0.8 Hz); these data match the ^{1}H NMR spectra of the commercially available material.

α-Deuterio-1-chloro-2-vinylbenzene (Table 3.8, entry 8): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (1H, dd, J = 7.6, 2.0 Hz), 7.35 (1H, dd, J = 7.6, 2.0 Hz), 7.26–7.17 (2H, m), 5.74 (1H, dt, J = 2.8, 1.2 Hz), 5.38 (1H, dt, J = 1.6, 0.8 Hz). The spectroscopic data match those reported previously.[69]

Site selectivity (>98:<2 α:β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).



Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	7.11	0.97	49.5	1	7.11	<0.02	<2.0
3	5.38	0.99	50.5	3	5.38	0.99	>98.0

α-Deuterio-1-bromo-2-vinylbenzene (Table 3.8, entry 9): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (2H, d, J = 8.0 Hz), 7.28 (1H, dd, J = 8.0, 8.0 Hz), 7.11 (1H, ddd, J = 7.6, 7.6, 1.6 Hz), 5.69 (1H, bt, J = 2.4 Hz), 5.36 (1H, bd, J = 1.6 Hz). The spectroscopic data match those reported previously.[70]

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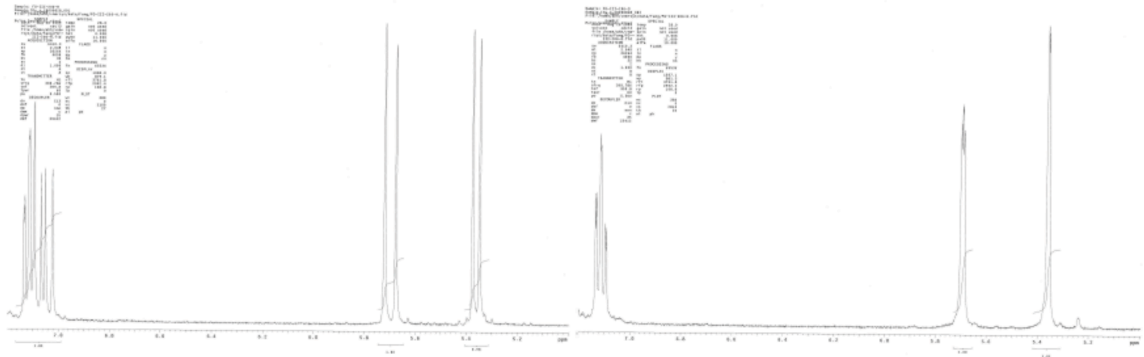
(69) The spectroscopic data for the corresponding protonated alkene: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (1H, dd, J = 7.6, 2.0 Hz), 7.35 (1H, dd, J = 7.6, 2.0 Hz), 7.26–7.17 (2H, m), 7.11 (1H, dd, J = 17.6, 10.8 Hz), 5.74 (1H, dd, J = 17.6, 1.2 Hz), 5.38 (1H, dd, J = 11.2, 1.2 Hz); these data match the ^{1}H NMR spectra of the commercially available material.

(70) The spectroscopic data for the corresponding protonated alkene: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (2H, d, J = 8.0 Hz), 7.28 (1H, dd, J = 8.0, 8.0 Hz), 7.14–7.02 (2H, m), 5.70 (1H, d, J = 17.2 Hz), 5.36 (1H, d, J = 11.2 Hz); these data match the ^{1}H NMR spectra of the commercially available material.

Site selectivity (>98:<2 α:β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).

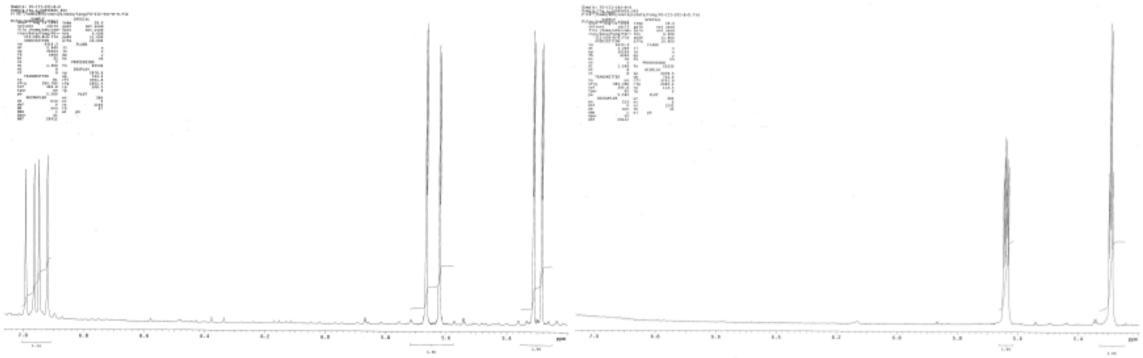


Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
2	7.05	0.93	48.7	2	7.05	<0.02	<2.0
4	5.36	0.98	51.3	4	5.36	1.01	>98.0

α-Deuterio-1-methyl-2-vinylbenzene (Table 3.8, entry 10): ^{1}H NMR (400 MHz, $CDCl_3$): 7.49–7.47 (1H, m), 7.19–7.15 (3H, m), 5.64 (1H, dt, *J* = 2.8, 1.6 Hz), 5.29 (1H, dt, *J* = 1.6, 1.6 Hz), 2.36 (3H, s). The spectroscopic data match those reported previously.[71]

Site selectivity (>98:<2 α:β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).

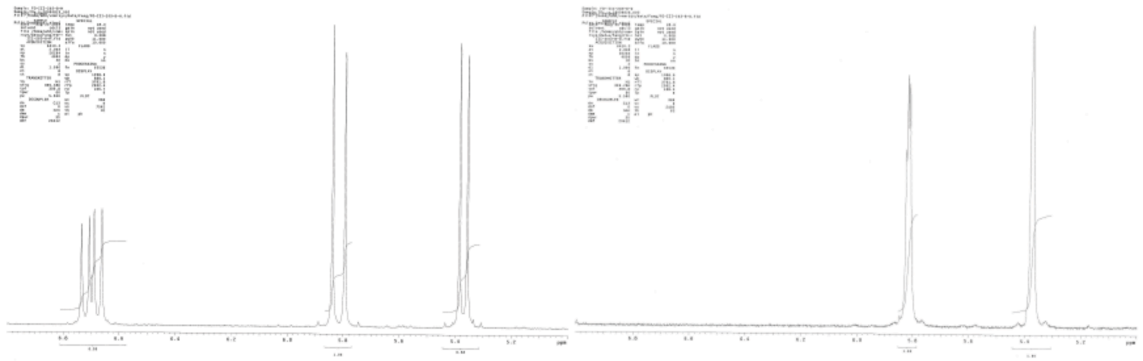
(71) The spectroscopic data for the corresponding protonated alkene: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49–7.47 (1H, m), 7.19–7.15 (3H, m), 6.96 (1H, dd, *J* = 17.6, 11.2 Hz), 5.64 (1H, ddd, *J* = 17.6, 0.8, 0.8 Hz), 5.30 (1H, ddd, *J* = 10.8, 0.8, 0.8 Hz), 2.36 (3H, s); these data match the ^{1}H NMR spectra of the commercially available material.



Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	6.96	1.14	53.3	1	6.95	<0.02	<2.0
3	5.30	1.00	46.7	3	5.29	1.00	>98.0

α-Deuterio-3-vinylpyridine (Table 3.8, entry 11): ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.61 (1H, s), 8.48 (1H, d, J = 3.2 Hz), 7.72 (1H, d, J = 7.6 Hz), 7.24 (1H, dd, J = 7.6, 2.0 Hz), 5.82 (1H, bt, J = 2.4 Hz), 5.38 (1H, bs). The spectroscopic data match those reported previously.[72]

Site selectivity (>98:<2 α:β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).

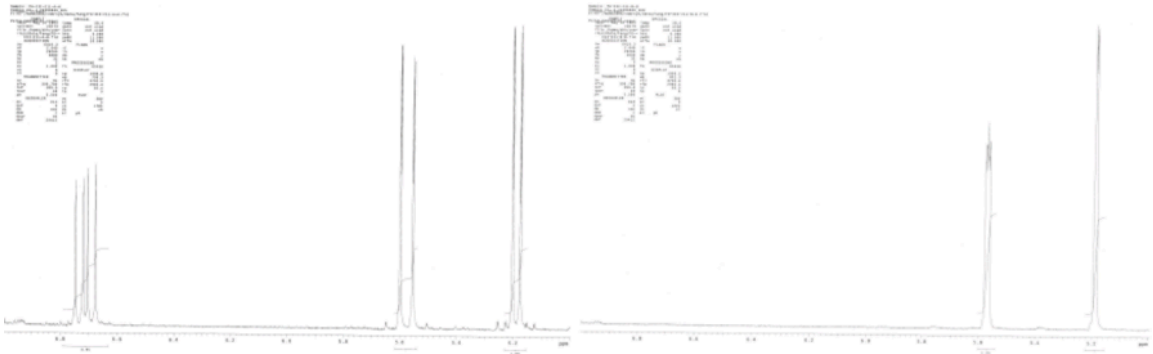


Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	6.70	0.99	50.3	1	6.70	<0.02	<2.0
3	5.37	0.98	49.7	3	5.38	1.00	>98.0

(72) The spectroscopic data for the corresponding protonated alkene: ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.61 (1H, s), 8.48 (1H, d, J = 3.2 Hz), 7.72 (1H, d, J = 7.6 Hz), 7.24 (1H, dd, J = 7.6, 2.0 Hz), 6.70 (1H, dd, J = 17.6, 10.8 Hz), 5.82 (1H, d, J = 17.6 Hz), 5.37 (1H, d, J = 10.8 Hz); these data match the ^{1}H NMR spectra of the commercially available material.

α-Deuterio-3-vinylthiophene (Table 3.8, entry 12): ^{1}H NMR (400 MHz, $CDCl_3$): 7.28–7.23 (2H, m), 7.18–7.17 (1H, m), 5.57 (1H, bt, J = 2.8 Hz), 5.19 (1H, bd, J = 1.6 Hz). The spectroscopic data match those reported previously.[73]

Site selectivity (>98:<2 α:β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).



Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	6.71	0.95	48.7	1	6.71	<0.02	<2.0
3	5.19	1.00	51.3	3	5.19	0.98	>98.0

2-Deuterio-oct-1-ene (Table 3.9, entry 1): ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.98 (1H, bs), 4.92 (1H, bs), 2.03 (2H, bt, J = 7.2 Hz), 1.39–1.24 (8H, m), 0.88 (3H, t, J = 6.4 Hz). The spectroscopic data match those reported previously.[74]

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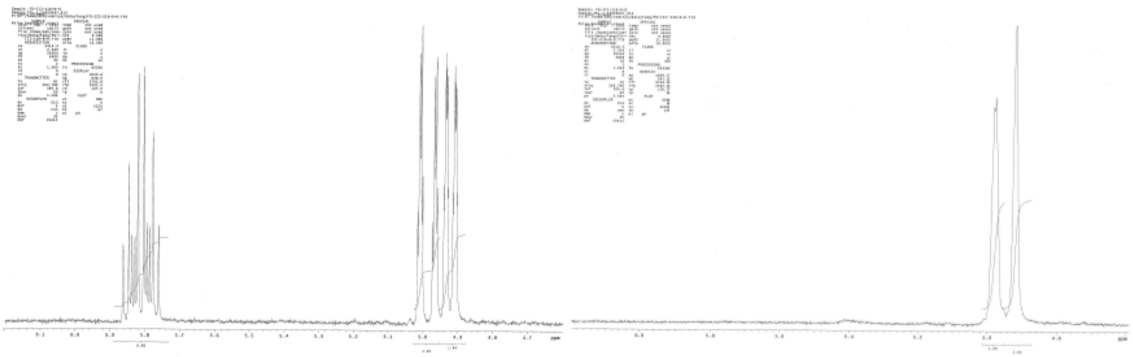
(73) The spectroscopic data for the corresponding protonated alkene: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.23 (2H, m), 7.18–7.17 (1H, m), 6.71 (1H, dd, J = 17.6, 10.8 Hz), 5.58 (1H, dd, J = 17.6, 1.2 Hz), 5.19 (1H, dd, J = 10.8, 1.2 Hz); this matches the data reported previously. See: Tominaga, Y.; Lee, M. L.; Castle, R. N. *J. Heterocyclic Chem.* **1981**, *18*, 967–972.

(74) The spectroscopic data for the corresponding protonated alkene: ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.81 (1H, ddt, J = 16.8, 10.0, 6.4 Hz), 4.99 (1H, ddt, J = 16.8, 2.0, 1.6 Hz), 4.92 (1H, ddt, J = 10.0, 1.2, 1.2 Hz), 2.04 (2H, dtt, J = 7.6, 7.6, 1.2 Hz), 1.39–1.24 (8H, m), 0.88 (3H, t, J = 6.4 Hz); these data match the ^{1}H NMR spectra of the commercially available material.

Site selectivity (>98:<2 α:β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).

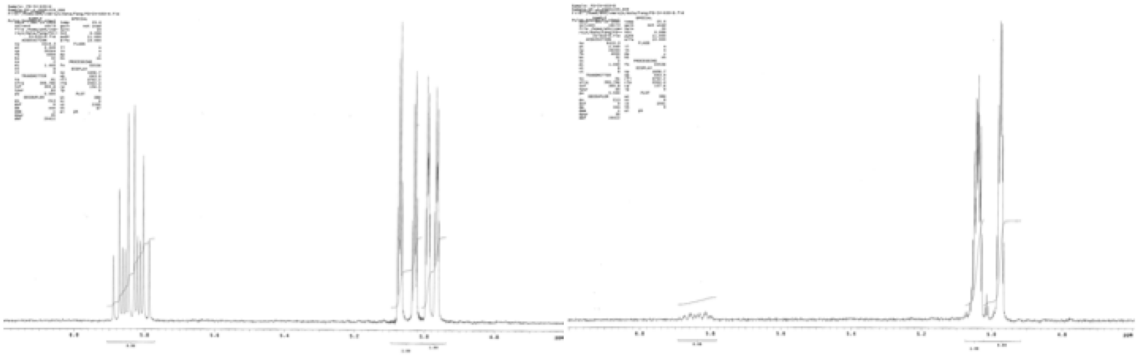


Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	5.81	0.98	48.5	1	5.81	<0.02	<2.0
3	4.92	1.04	51.5	3	4.92	1.02	>98.0

4-Deuterio-pent-4-en-1-ol **(Table 3.9, entry 2):** ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.05–5.03 (1H, m), 4.99–4.97 (1H, m), 3.67 (2H, t, *J* = 6.4 Hz), 2.15 (2H, t, *J* = 7.6 Hz), 1.68 (2H, tt, *J* = 7.6, 6.8 Hz), 1.29 (1H, br). The spectroscopic data match those reported previously.[75]

Site selectivity (97:3 α:β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).

(75) The spectroscopic data for the corresponding protonated alkene: ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 5.84 (1H, ddt, *J* = 16.8, 10.0, 6.8 Hz), 5.08–5.02 (1H, m), 5.00–4.96 (1H, m), 3.67 (2H, t, *J* = 6.4 Hz), 2.15 (2H, t, *J* = 7.6 Hz), 1.68 (2H, tt, *J* = 7.6, 6.8 Hz), 1.29 (1H, br); these data match the ^{1}H NMR spectra of the commercially available material.

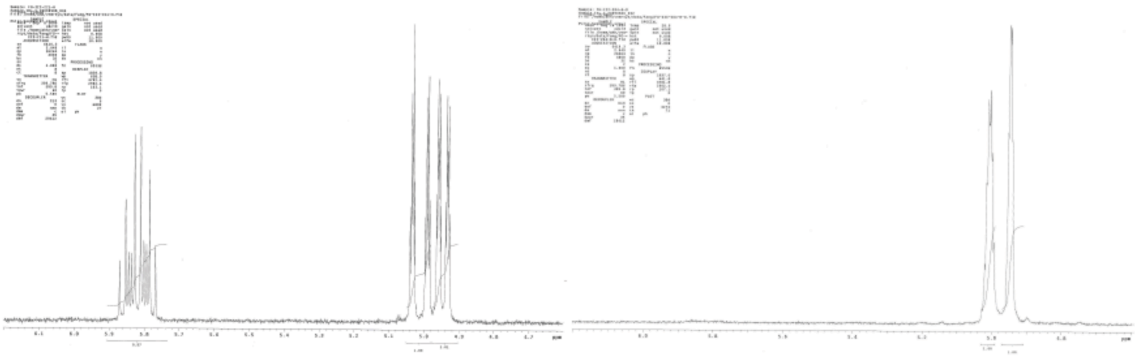


Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	5.84	0.96	49.0	1	5.84	0.03	2.9
3	4.98	1.00	51.0	3	4.98	0.99	97.1

***tert*-Butyldimethyl(4-deuterio-pent-4-en-1-yloxy)silane (Table 3.9, entry 3):** ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.01–5.00 (1H, m), 4.95–4.94 (1H, m), 3.60 (2H, t, J = 6.8 Hz), 2.08 (2H, bt, J = 7.2 Hz), 1.63–1.56 (2H, m), 0.88 (9H, s), 0.04 (6H, s). The spectroscopic data match those reported previously.[76]

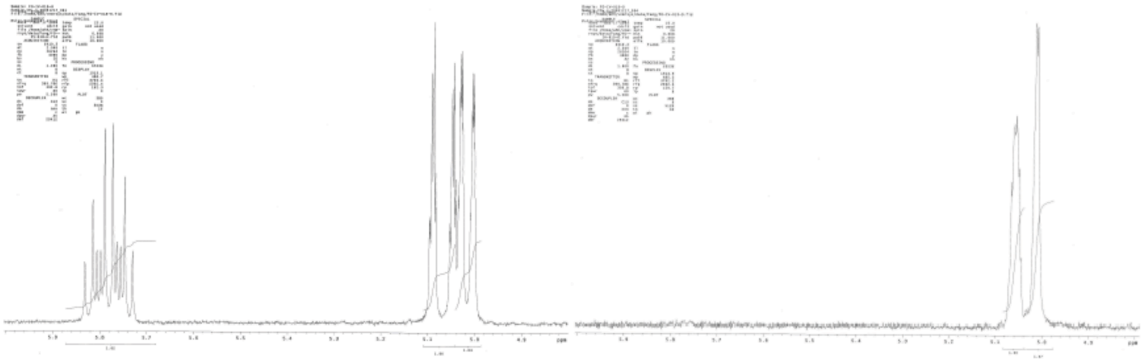
Site selectivity (>98:<2 α:β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).

(76) The spectroscopic data for the corresponding protonated alkene: ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.82 (1H, ddt, J = 16.8, 10.4, 6.8 Hz), 5.04–4.98 (1H, m), 4.97–4.93 (1H, m), 3.61 (2H, t, J = 6.4 Hz), 2.10 (2H, dtt, J = 7.2, 7.2, 1.2 Hz), 1.64–1.57 (2H, m), 0.89 (9H, s), 0.04 (6H, s); this matches the data reported previously. See: Grotjahn, D. B.; Larsen, C. R.; Gustafson, J. L.; Nair, R.; Sharma, A. *J. Am. Chem. Soc.* **2007**, *129*, 9592–9593.



Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	5.82	0.97	48.5	1	5.82	<0.02	<2.0
3	4.95	1.01	51.5	3	4.95	1.00	>98.0

2-Deuterio-5-chloropent-1-ene (Table 3.9, entry 4): ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.07–5.05 (1H, m), 5.01 (1H, bd, J = 1.2 Hz), 3.55 (2H, t, J = 6.4 Hz), 2.14 (2H, bt, J = 7.2 Hz), 1.89–1.84 (2H, m). The spectroscopic data match those reported previously.[77] Site selectivity (>98:<2 α:β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).

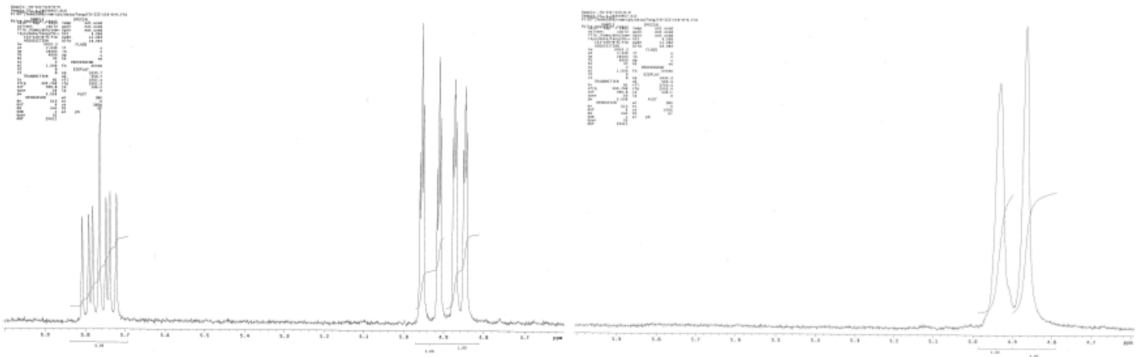


Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	5.78	1.02	49.5	1	5.78	<0.02	<2.0
3	5.01	1.04	50.5	3	5.01	1.07	>98.0

(77) The spectroscopic data for the corresponding protonated alkene: ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.78 (1H, ddt, J = 17.2, 10.4, 6.8 Hz), 5.10–5.04 (1H, m), 5.04–5.00 (1H, m), 3.55 (2H, t, J = 6.4 Hz), 2.21 (2H, dt, J = 6.8, 6.8 Hz), 1.89–1.84 (2H, m); this matches the data reported previously. See: Kabalka, G. W.; Gooch, E. E. *J. Org. Chem.* **1980**, *45*, 3578–3580.

(1-Deuteriovinyl)cyclohexane (Table 3.9, entry 5): ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.93 (1H, bs), 4.87 (1H, bs), 1.97–1.89 (1H, m), 1.73–1.58 (4H, m), 1.31–1.02 (6H, m). The spectroscopic data match those reported previously.[78]

Site selectivity (>98:<2 α:β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).



Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	5.77	0.98	48.3	1	5.78	<0.02	<2.0
3	4.86	1.05	51.7	3	4.87	1.02	>98.0

(1-Deuteriovinyl)cyclohex-1-ene (Table 3.9, entry 6): ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.75 (1H, bs), 5.05 (1H, bs), 4.88 (1H, bs), 2.15–2.12 (4H, m), 1.71–1.57 (4H, m). The spectroscopic data match those reported previously.[79]

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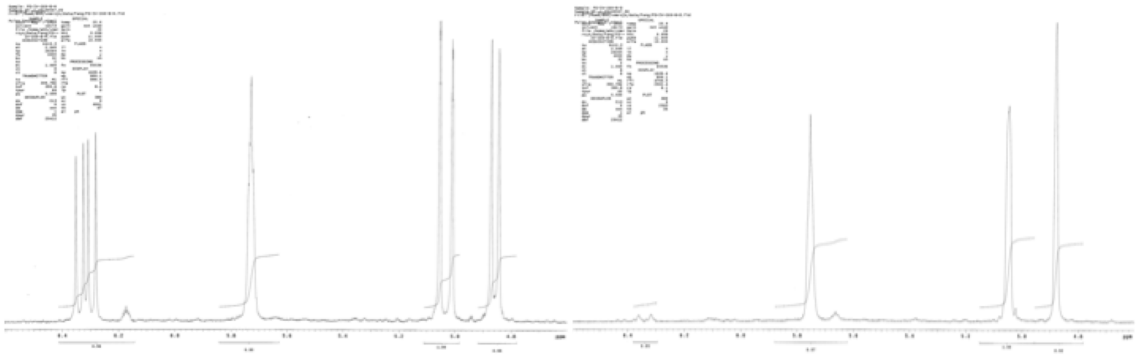
(78) The spectroscopic data for the corresponding protonated alkene: ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.77 (1H, ddd, J = 17.2, 10.4, 6.8 Hz), 4.93 (1H, ddd, J = 17.2, 2.0, 2.0 Hz), 4.86 (1H, ddd, J = 10.8, 2.0, 2.0 Hz), 1.97–1.89 (1H, m), 1.73–1.58 (4H, m), 1.31–1.02 (6H, m); these data match the ^{1}H NMR spectra of the commercially available material.

(79) The spectroscopic data for the corresponding protonated alkene: ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.32 (1H, dd, J = 17.2, 10.8 Hz), 5.74–5.72 (1H, m), 5.03 (1H, ddd, J = 16.8, 0.8, 0.4 Hz), 4.86 (1H, d, J = 10.4 Hz), 2.15–2.12 (4H, m), 1.71–1.57 (4H, m); these data match the ^{1}H NMR spectra of the commercially available material.

Site selectivity (98:2 α*:*β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).

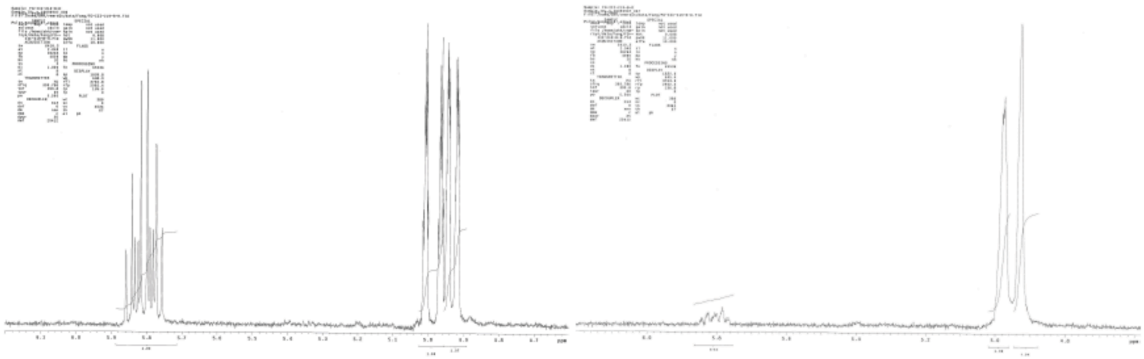


Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	6.32	0.96	49.5	1	6.32	0.02	2.1
4	4.86	0.98	50.5	4	4.88	0.92	97.9

(2-Deuterioallyl)cyclopentane (Table 3.9, entry 7): ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.98 (1H, bt, *J* = 1.2 Hz), 4.93 (1H, bs), 2.03 (2H, bd, *J* = 6.0 Hz), 1.77-1.69 (1H, m), 1.63-1.48 (6H, m), 1.17-1.09 (2H, m). The spectroscopic data match those reported previously.[80]

Site selectivity (96.5:3.5 α*:*β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).

(80) The spectroscopic data for the corresponding protonated alkene: ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.81 (1H, ddt, *J* = 17.2, 9.6, 7.6 Hz), 5.02–4.96 (1H, m), 4.95–4.91 (1H, m), 2.05 (2H, dd, *J* = 6.8, 6.8 Hz), 1.77–1.69 (1H, m), 1.63–1.48 (6H, m), 1.17–1.09 (2H, m); these data match the ^{1}H NMR spectra of the commercially available material.



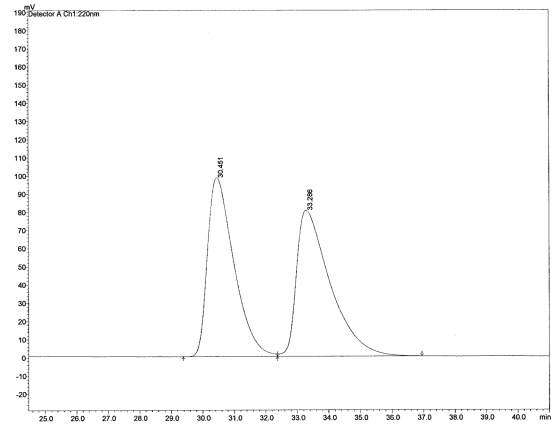
Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	5.81	1.00	48.3	1	5.81	0.04	3.7
3	4.93	1.07	51.7	3	4.93	1.04	96.3

■ **Representative Procedure for Ni-catalyzed Hydroalumination of Terminal Alkynes and Functionalization of the Resulting Vinylaluminum Reagent with NHC–Cu Catalyzed Enantioselective Allylic Alkylation**:

A 13 x 100 mm test tube equipped with a stir bar is charged with NHC–Ag complex (2.8 mg, 0.0020 mmol) in an N_2-filled glovebox. The test tube is sealed with a septum and removed from the glovebox. Tetrahydrofuran (1.0 mL) and a solution of $CuCl_2 \bullet 2H_2O$ (0.02 M in thf, 200 μL, 0.004 mmol) are added to the test tube at 22 °C. The resulting blue solution is allowed to cool to –78 °C (dry ice/acetone), followed by the addition of the vinylaluminum reagent **3.89** (0.745 M in thf, 200 μL, 0.150 mmol) and a solution of (*E*)-4-(3-((diethoxyphosphoryl)oxy)prop-1-en-1-yl)phenyl 4-methylbenzenesulfonate in thf (44.0 mg, 0.100 mmol in 1.0 mL thf). The mixture is allowed to warm to –15 °C and stir for 3 h, after which time, the reaction is quenched by addition of a saturated aqueous solution of Rochelle's salt (2.0 mL) and allowed to stir for 1 h at 22 °C. Layers are separated, and the aqueous layer is washed with Et_2O (2.0 mL x 3). The combined organic layers are passed through a short plug of $MgSO_4$, and concentrated under reduced

pressure. The resulting yellow oil is purified by silica gel chromatography to give the product as colorless oil (36.3 mg, 0.0930 mmol, 93%). **(*S*, *E*)-4-(1-Phenylpenta-1, 4-dien-3-yl)phenyl 4-methylbenzenesulfonate:** IR (neat): 3060 (w), 3027 (w), 1635 (w), 1499 (s), 1373 (s), 1198 (s), 1177 (s), 1153 (s), 1093 (w), 1018 (w), 969 (w), 921 (s), 864 (m), 814 (s), 752 (m), 694 (m), 670 (m), 567 (s), 552 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (2H, ddd, *J* = 8.4, 2.0, 1.6 Hz), 7.37–7.34 (2H, m), 7.32–7.28 (4H, m), 7.24–7.20 (1H, m), 7.19–7.16 (2H, m), 6.93 (2H, ddd, *J* = 8.4, 3.2, 2.0 Hz), 6.40 (1H, d, *J* = 16.0 Hz), 6.32 (1H, dd, *J* = 16.0, 6.4 Hz), 6.04 (1H, ddd, *J* = 17.2, 10.4, 6.8 Hz), 5.19 (1H, ddd, *J* = 10.4, 1.6, 1.2 Hz), 5.10 (1H, ddd, *J* = 17.2, 1.6, 1.2 Hz), 4.19 (1H, dd, *J* = 6.8, 6.8 Hz), 2.45 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.3, 145.4, 141.7, 139.6, 137.2, 132.7, 131.2, 131.2, 129.9, 129.3, 128.7, 128.7, 127.6, 126.4, 122.5, 116.3, 51.8, 21.9; HRMS (ESI^+): Calcd for $C_{24}H_{23}S_1O_3$ $[M+H]^+$: 391.1368; Found: 391.1385. Specific rotation: $[\alpha]_D^{20}$ –3.32 (*c* = 1.25, $CHCl_3$) for an enantiomerically enriched sample of 93:7 e.r.

Enantiomer ratio was determined by HPLC analysis in comparison with authentic racemic material (chiralcel column OD-H, 99% hexanes: 1% *iso*propanol, 1.0 mL/min, 220nm). A sample with 96:4 e.r. is shown below:



PeakTable

Detector A Ch1 220nm

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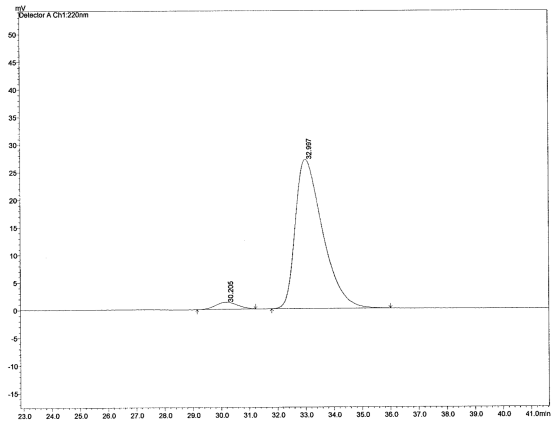

PeakTable

Detector A Ch1 220nm

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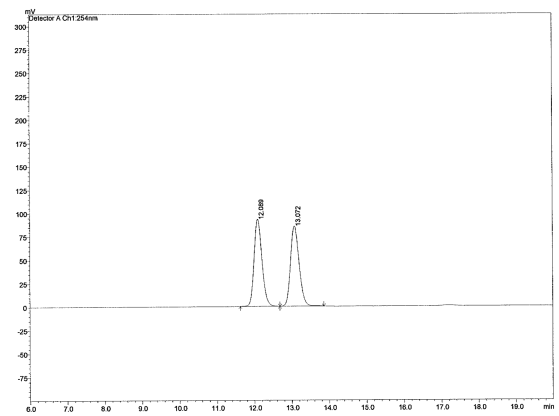
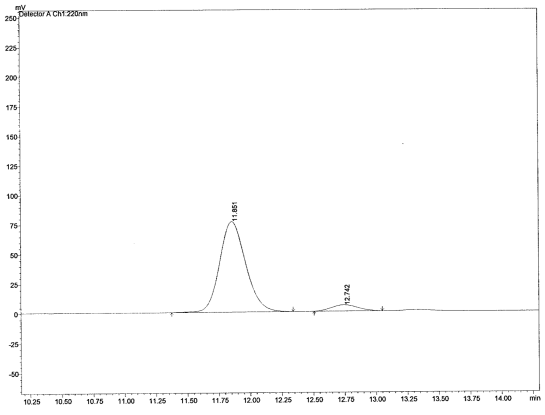
2	32.997	1821225	27024	96.393	95.534
Total		1889376	28287	100.000	100.000

(*S*)-*tert*-Butyldimethyl((7-phenyl-6-vinyloct-7-en-1-yl)oxy)silane (3.111): IR (neat): 2929 (m), 2856 (m), 1471 (w), 1254 (m), 1099 (s), 1005 (w), 912 (m), 834 (s), 774 (s), 703 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.38–7.35 (2H, m), 7.33–7.29 (2H, m), 7.28–7.24 (1H, m), 5.83 (1H, ddd, J = 17.0, 10.0, 8.0 Hz), 5.28 (1H, d, J = 1.6 Hz), 5.09–5.03 (3H, m), 3.58 (2H, t, J = 6.8 Hz), 3.19 (1H, ddd, J = 8.4, 8.4, 8.4 Hz), 1.63–1.57 (1H, m), 1.53–1.46 (3H, m), 1.39–1.27 (4H, m), 0.90 (9H, s), 0.05 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.0, 142.7, 141.7, 128.2, 127.3, 126.8, 114.8, 112.8, 63.4, 48.8, 34.1, 32.9, 27.4, 26.1, 25.9, 18.5, –5.11; HRMS (ESI^+): Calcd for $C_{22}H_{37}Si_1O_1$ $[M+H]^+$: 345.2614; Found: 345.2607. Specific rotation: $[\alpha]_D^{20}$ +5.82 (c = 0.91, $CHCl_3$) for an enantiomerically enriched sample of 93:7 e.r.

Enantiomer ratio was determined by HPLC analysis in comparison with authentic racemic material (chiralcel column OD-H, 100% hexanes, 0.5 mL/min, 220nm). A sample with 93:7 e.r. is shown below:





PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.089	1363072	92781	50.067	52.114
2	13.072	1359406	85253	49.933	47.886
Total		2722478	178035	100.000	100.000

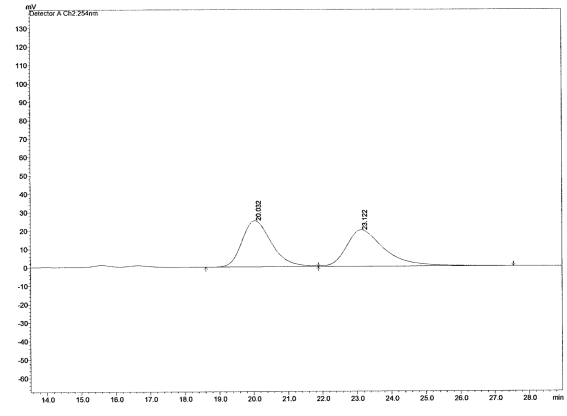
PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.851	1104189	76379	93.581	93.568
2	12.742	75738	5251	6.419	6.432
Total		1179927	81629	100.000	100.000

(*R*)-4-(2-(Cyclohex-1-en-1-yl)penta-1, 4-dien-3-yl)phenyl 4-methylbenzenesulfonate (3.110): IR (neat): 2928 (m), 2858 (w), 1599 (w), 1499 (s), 1375 (s), 1198 (s), 1177 (s), 1153 (s), 1094 (m), 1019 (w), 919 (w), 866 (s), 814 (m), 747 (m), 666 (m), 578 (m), 552 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (2H, dd, *J* = 8.4, 2.0 Hz), 7.29–7.26 (2H, m), 7.09 (2H, dd, *J* = 8.8, 2.0 Hz), 6.90–6.87 (2H, m), 6.04 (1H, ddd, *J* = 16.8, 10.0, 6.4 Hz), 5.74 (1H, t, *J* = 4.0 Hz), 5.26 (1H, s), 5.10 (1H, ddd, *J* = 10.0, 1.6, 1.2 Hz), 4.84 (1H, s), 4.75 (1H, ddd, *J* = 16.8, 1.6, 1.2 Hz), 4.42 (1H, d, *J* = 6.8 Hz), 2.44 (3H, s), 2.16–1.97 (4H, m), 1.64–1.47 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.7, 148.1, 145.3, 141.6, 140.8, 135.7, 132.6, 129.8, 129.7, 128.7, 125.8, 122.1, 116.0, 112.1, 51.2, 26.7, 25.9, 23.0, 22.2, 21.8; HRMS (ESI^+): Calcd for $C_{24}H_{27}S_1O_3$ $[M+H]^+$: 395.1681; Found: 395.1677. Specific rotation: $[\alpha]_D^{20}$ –37.44 (*c* = 1.95, $CHCl_3$) for an enantiomerically enriched sample of 91.5:8.5 e.r.

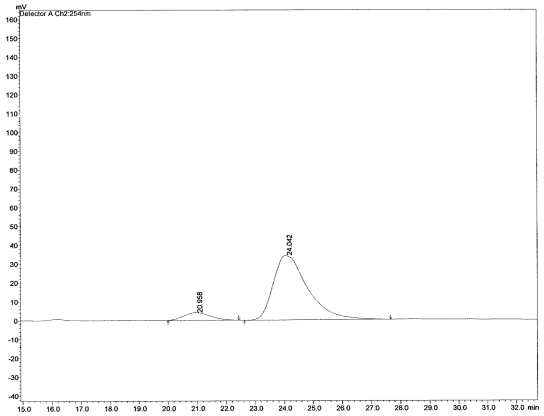
Enantiomer ratio was determined by HPLC analysis in comparison with authentic racemic material (chiralcel column OJ-H, 98.5% hexanes: 1.5% *iso*propanol, 1.0 mL/min, 254nm). A sample with 91.5:8.5 e.r. is shown below:



PeakTable

Detector A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.032	1494292	25057	49.590	55.805
2	23.122	1519026	19844	50.410	44.195
Total		3013318	44901	100.000	100.000



PeakTable

Detector A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.958	253618	4071	8.316	10.661
2	24.042	2796223	34120	91.684	89.339
Total		3049841	38191	100.000	100.000

■ Representative Procedure for Ni(dppp)Cl_2 Catalyzed Hydroalumination of Terminal Alkynes and Functionalization of the Resulting alkenylaluminum Reagent with *N*-bromosuccinamide or *N*-iodosuccinamide

Commercial grade 1,3-bis(diphenylphosphino)propane nickel(II) chloride (Ni(dppp)Cl_2, 16.3 mg, 0.0300 mmol) is placed in an oven-dried 13x100 test tube equipped with a stir bar. The test tube is sealed with a septum and purged with N_2 for approximately ten minutes. Tetrahydrofuran (thf, 1.0 mL) is added through a syringe, followed by dropwise addition of dibal–H (232 μL, 1.30 mmol) at 22 °C (gas evolution occurs as dibal–H is added). The resulting black solution is allowed to cool to 0 °C (ice bath) before 1-ethynyl-3-methoxybenzene (127 μL, 1.00 mmol) is added slowly over five minutes (reaction is exothermic). The resulting black solution is allowed to warm to 22 °C and stir for an additional two hours. In a separate 10 mL pear shape flask, a solution (orange color) of *N*-bromosuccinamide (356.0 mg, 2.0 mmol) in thf (3.0 mL) is prepared and transferred with a syringe into hydroalumination reaction mixture at 0 ^{o}C (ice bath). The

resulting dark brown solution is allowed to warm up to 22 ^{o}C and stir for one hour. At this point, the reaction is quenched by adding the mixture into a separatory funnel, which contains a saturated solution of Rochelle's salt (sodium potassium tartrate; 5.0 mL) and Et_2O (5.0 mL). The organic layer is separated and the aqueous layer is washed with Et_2O (5.0 mL x 2). The combined organic layers are dried with anhydrous $MgSO_4$, filtered and concentrated *in vacuo* to afford yellow oil, which is purified by basified (with triethylamine) silica gel chromatography or basic alumina (100% hexanes) to furnish the desired product **3.98** as light yellow oil (185.4 mg, 0.87 mmol, 87% yield). **1-(1-Bromovinyl)-3-methoxybenzene (3.98):** The compound is sensitive to acidic condition (It will decompose in regular chloroform; therefore, chloroform basified with K_2CO_3 is needed to acquire the NMR spectra). IR (neat): 2924 (s), 2853 (m), 1577 (m), 1485 (m), 1463 (m), 1428 (m), 1288 (m), 1259 (s), 1164 (w), 1045 (m), 883 (m), 780 (w), 707 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (1H, dd, *J* = 8.0, 8.0 Hz), 7.18 (1H, ddd, *J* = 7.6, 1.6, 0.8 Hz), 7.13 (1H, dd, *J* = 2.4, 2.4 Hz), 6.88 (1H, ddd, *J* = 8.4, 2.4, 1.2 Hz), 6.12 (1H, d, *J* = 2.0 Hz), 5.78 (1H, d, *J* = 2.4 Hz), 3.84 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.5, 140.1, 130.8, 129.4, 119.9, 118.1, 114.8, 113.3, 55.5; HRMS (ESI^+): Calcd for $C_9H_{10}Br_1O_2$ $[M+OH]^+$: 228.9864; Found: 228.9874.

(1-Iodovinyl)benzene (3.94): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53–7.49 (2H, m), 7.34–7.28 (3H, m), 6.47 (1H, d, *J* = 1.6 Hz), 6.09 (1H, d, *J* = 2.0 Hz); HRMS (ESI^+): Calcd for $C_8H_8I_1$ $[M+H]^+$: 230.9671; Found: 230.9671. The spectroscopic data match those reported previously.[81]

2-Bromooct-1-ene (3.96): IR (neat): 2956 (m), 2928 (s), 2858 (m), 1713 (w), 1629 (m),

(81) Cheung, L. L. W.; Yudin, A. K. *Org. Lett.* **2009**, *11*, 1281–1284.

1459 (w), 1188 (w), 882 (s), 726 (w), 640 (w), 568 (w), 531 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.55 (1H, d, *J* = 1.6 Hz), 5.38 (1H, d, *J* = 1.2 Hz), 2.41 (2H, dt, *J* = 7.2, 0.8 Hz), 1.57–1.51 (2H, m), 1.34–1.24 (6H, m), 0.91–0.86 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.1, 116.3, 41.6, 31.7, 28.2, 28.0, 22.7, 14.2; HRMS (ESI^+): Calcd for $C_8H_{16}Br_1$ $[M+H]^+$: 191.0435; Found: 191.0435.

4-Iodopent-4-en-1-ol (3.99): The compound is prepared through the use of the general halogenation procedure except that 2.3 equiv of dibal–H and 3.0 equiv of *N*-iodosuccinamide are used (iodination occurs at 0 ^oC for one hour). IR (neat): 3316 (b), 2941 (m), 2874 (w), 1617 (m), 1429 (w), 1184 (w), 1112 (w), 1057 (s), 1037 (s), 894 (s), 494 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.07 (1H, q, *J* = 1.2 Hz), 5.72 (1H, s), 3.67 (2H, t, *J* = 6.4 Hz), 2.50 (2H, dt, *J* = 7.2, 0.8 Hz), 1.78 (2H, tt, *J* = 7.6, 6.4 Hz), 1.47 (1H, bs); ^{13}C NMR (100 MHz, $CDCl_3$): δ 126.0, 111.6, 61.3, 41.8, 32.1; HRMS (ESI^+): Calcd for $C_5H_{10}I_1O_1$ $[M+H]^+$: 212.9776; Found: 212.9773.

***tert*-Butyl((4-iodopent-4-en-1-yl)oxy)dimethylsilane (3.100):** IR (neat): 2952 (w), 2928 (w), 2856 (w), 1617 (w), 1471 (w), 1253 (m), 1098 (s), 969 (w), 891 (w), 832 (s), 773 (s), 661 (w), 494 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.03 (1H, q, *J* = 1.6 Hz), 5.70 (1H, s), 3.62 (2H, t, *J* = 6.4 Hz), 2.47 (2H, dt, *J* = 7.2, 1.2 Hz), 1.72 (2H, tt, *J* = 7.6, 6.4 Hz), 0.90 (9H, s), 0.05 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 125.7, 112.1, 63.1, 41.9, 32.2, 26.1, 18.4, –5.2; HRMS (ESI^+): Calcd for $C_{11}H_{24}I_1O_1Si_1$ $[M+H]^+$: 327.0641; Found: 327.0633.

■ Representative Procedure for $Ni(dppp)Cl_2$ Catalyzed Hydroalumination of Terminal Alkynes and Functionalization of the Resulting *Internal* Alkenylaluminum

Reagent with Bromine:

Commercial grade 1,3-bis(diphenylphosphino)propane nickel dichloride ($Ni(dppp)Cl_2$, 5.4 mg, 0.0100 mmol) is placed in a flame-dried 50 mL round bottom flask. The vessel is sealed with a septum and purged with N_2 for approximately ten minutes. Tetrahydrofuran (thf, 10.0 mL) is added through a syringe followed by dropwise addition of dibal–H (1.96 mL, 11.0 mmol) at 22 °C (gas evolution occurs as dibal–H is introduced). The resulting light brown solution is allowed to cool to 0 °C (ice bath) before phenylacetylene (1.10 mL, 10.0 mmol) is added slowly over approximately five minutes (reaction is exothermic). The resulting light brown solution is allowed to warm to 22 °C and stir for two hours. The mixture is allowed to cool to –78 °C (dry ice-acetone bath), and bromine (Br_2; 0.771 mL, 15.0 mmol) is added through a syringe slowly in a dropwise manner (reaction is vigorous) over approximately ten minutes. Tetrahydrofuran (thf, 5.0 mL) is used to wash off the residue on the sidewall of the flask. The resulting yellow solution is allowed to warm to 22 °C and kept at this temperature for one additional hour before the reactions is quenched at 0 °C through dropwise addition of a saturated solution of Rochelle's salt (sodium potassium tartrate; 10.0 mL) over a period of ten minutes. The mixture is allowed to stir at 22 °C for 30 minutes and layers are separated. The aqueous layer is washed with Et_2O (20.0 mL x 3) and the combined organic layers are dried over anhydrous $MgSO_4$, filtered and concentrated under vacuum to give light yellow oil. Purification with basified (with triethylamine) silica gel chromatography (100% hexanes) affords **3.92** as light yellow oil (1.26 g, 6.60 mmol, 69% yield). **(1-Bromovinyl)benzene (3.92):** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61–7.58 (2H, m), 7.37–7.32 (3H, m), 6.12 (1H, d, J = 2.0 Hz), 5.78 (1H, d, J = 2.0 Hz). The

spectroscopic data match those reported previously.[82]

■ **Representative Procedure for Ni(dppp)Cl_2 catalyzed Hydroalumination of Terminal Alkynes and Functionalization of the Resulting Vinylaluminum Reagent with MeO-Bpin**:

Commercial grade 1,3-bis(diphenylphosphino)propane nickel(II) chloride (Ni(dppp)Cl_2, 16.3 mg, 0.0300 mmol) is placed in an flame-dried 10 mL round bottom flask equipped with a stir bar and a refluxing condenser. The apparatus is sealed with a septum and purged with N_2 for approximately ten minutes. Tetrahydrofuran (thf, 3.0 mL) is added through a syringe, followed by dropwise addition of dibal–H (232 μL, 1.30 mmol) at 22 °C (gas evolution occurs as dibal–H is added). The resulting black solution is allowed to cool to 0 °C (ice bath) before phenylacetylene (110 μL, 1.00 mmol) is added slowly over five minutes (reaction is exothermic). The resulting black solution is allowed to warm to 22 °C and stir for an additional two hours. After two hours, 2-methoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (MeO-Bpin; 492 μL, 3.00 mmol) is added dropwise through a syringe into the reaction solution at 0 °C (ice bath). The resulting solution is allowed to be heated to 80 °C and stir for 24 hours before the reaction is quenched by dropwise addition of water (3.0 mL) at 0 °C (ice bath). The mixture is allowed to warm to 22 °C and stir for one additional hour before it is washed with Et_2O (5.0 mL x 3). The combined organic layers are passed through a plug of anhydrous $MgSO_4$ and concentrated under vacuum to afford yellow oil, which is purified by silica gel chromatography (40/1 hexanes/ethyl acetate) to afford the desired product **3.101** as

(82) Spaggiari, A.; Vaccari, D.; Davoli, P.; Torre, G.; Prati, F. *J. Org. Chem.* **2007**, *72*, 2216–2219.

colorless oil (173.0 mg, 0.752 mmol, 75% yield). **4,4,5,5-Tetramethyl-2-(1-phenylvinyl)-1,3,2-dioxaborolane (3.101):** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49–7.46 (2H, m), 7.34–7.29 (2H, m), 7.27–7.22 (1H, m), 6.08–6.05 (2H, m), 1.33 (12H, s); HRMS (ESI^+): Calcd for $C_{14}H_{20}B_1O_2$ $[M+H]^+$: 231.1556; Found: 231.1568. The spectroscopic data match those reported previously.[83]

2-(1-(3-Fluorophenyl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.104): Purification of this compound from a byproduct *iso*butyl-Bpin could be tedious. IR (neat): 2979 (w), 1578 (w), 1372 (m), 1316 (m), 1238 (m), 1142 (s), 933 (w), 868 (m), 844 (w), 788 (w), 743 (w), 673 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29–7.26 (2H, m), 7.24–7.21 (1H, m), 6.96–6.91 (1H, m), 6.11 (2H, bs), 1.33 (12H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.9 (d, J = 243.3 Hz), 143.7 (d, J = 8.2 Hz), 132.0, 129.6 (d, J = 8.9 Hz), 122.9 (d, J = 2.3 Hz), 114.2 (d, J = 21.6 Hz), 113.8 (d, J = 21.6 Hz), 84.1, 24.9; HRMS (ESI^+): Calcd for $C_{14}H_{19}B_1O_2F_1$ $[M+H]^+$: 249.1462; Found: 249.1472.

2-(1-(2-Chlorophenyl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.105): The compound is prepared as described in the general procedure, except that the reaction is carried out with 5 equivalent of MeOBpin and heated for 48 hours (all characterizations are carried out in the presence of 4% corresponding β isomer). IR (neat): 2979 (m), 2932 (w), 1471 (m), 1371 (s), 1319 (s), 1262 (m), 1210 (m), 1145 (s), 1101 (m), 1046 (m), 966 (m), 849 (m), 745 (m), 698 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.32 (1H, m), 7.25–7.17 (3H, m), 6.12 (1H, bd, J = 3.2 Hz), 5.85 (1H, bd, J = 2.8 Hz), 1.31 (12H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.8, 132.7, 132.7, 129.8, 129.1, 128.4, 127.1, 84.1, 24.9; HRMS (ESI^+): Calcd for $C_{14}H_{19}B_1O_2Cl_1$ $[M+H]^+$: 265.1167; Found: 265.1167.

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(83) Takagi, J.; Takahashi, K.; Ishiyama, T.; Miyaura, N. *J. Am. Chem. Soc.* **2002**, *124*, 8001–8006.

4,4,5,5-Tetramethyl-2-(oct-1-en-2-yl)-1,3,2-dioxaborolane (3.103): The compound is prepared as described in the general procedure, except that the reaction is carried out at 0 °C for 24 h. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.75 (1H, d, *J* = 3.2 Hz), 5.59 (1H, bs), 2.14 (2H, t, *J* = 7.6 Hz), 1.43–1.36 (2H, m), 1.34–1.22 (6H, m), 1.27 (12H, s), 0.88 (3H, t, *J* = 6.4 Hz); HRMS (ESI$^+$): Calcd for $C_{14}H_{28}B_1O_2$ $[M+H]^+$: 239.2182; Found: 239.2188. The spectroscopic data match those reported previously.[84]

3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-ol (3.106): The compound is prepared as described in the general procedure, except that the reaction is carried out at 22 °C for 24 h. IR (neat): 3422 (br), 2978 (m), 2932 (w), 1617 (w), 1429 (m), 1370 (s), 1309 (s), 1213 (w), 1141 (s), 1048 (m), 948 (w), 863 (m), 672 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.90 (1H, bd, *J* = 3.6 Hz), 5.71 (1H, bs), 3.68 (2H, t, *J* = 6.0 Hz), 2.43 (2H, t, *J* = 6.0 Hz), 2.03 (1H, bs), 1.27 (12H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 132.5, 83.9, 62.7, 39.5, 24.9; HRMS (ESI$^+$): Calcd for $C_{10}H_{20}B_1O_3$ $[M+H]^+$: 199.1506; Found: 199.1509.

***tert*-Butyldimethyl((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-1-yl)oxy)silane (3.107):** The compound is prepared as described in the general procedure, except that the reaction is carried out at 22 °C for 24 h. IR (neat): 2954 (w), 2929 (w), 2857 (w), 1369 (m), 1308 (m), 1253 (m), 1142 (s), 1097 (s), 968 (w), 939 (w), 833 (s), 773 (s), 669 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.77 (1H, d, *J* = 3.6 Hz), 5.61 (1H, bs), 3.60 (2H, t, *J* = 6.8 Hz), 2.17 (2H, t, *J* = 8.0 Hz), 1.65 (2H, tt, *J* = 7.6, 7.6 Hz), 1.26 (12H, s), 0.90 (9H, s), 0.05 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 129.3, 83.4, 63.1, 32.5, 31.7, 26.1, 24.9, 18.5, –5.1; HRMS (ESI$^+$): Calcd for $C_{17}H_{36}B_1O_3Si_1$ $[M+H]^+$:

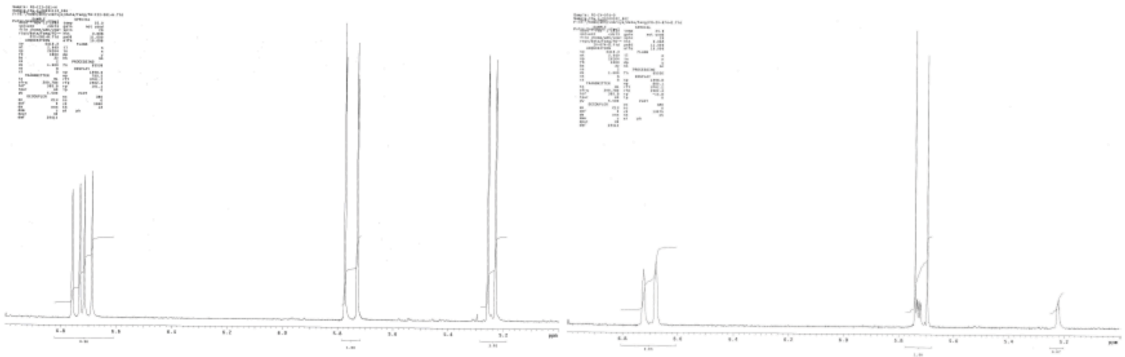
(84) Moran, M. J.; Morken, J. P. *Org. Lett.* **2006**, *8*, 2413–2415.

327.2527; Found: 327.2540.

■ **Characterization Data of the Terminal Alkenylaluminums Derived from Hydroalumination of Terminal Alkynes Catalyzed by $Ni(PPh_3)_2Cl_2$**:

(*E*)-*β*-Deuteriostyrene (3.89): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.40 (2H, m), 7.34–7.30 (2H, m), 7.27–7.23 (1H, m), 6.70 (1H, bd, *J* = 17.2 Hz), 5.72 (1H, d, *J* = 17.2 Hz). The spectroscopic data match those reported previously.[63]

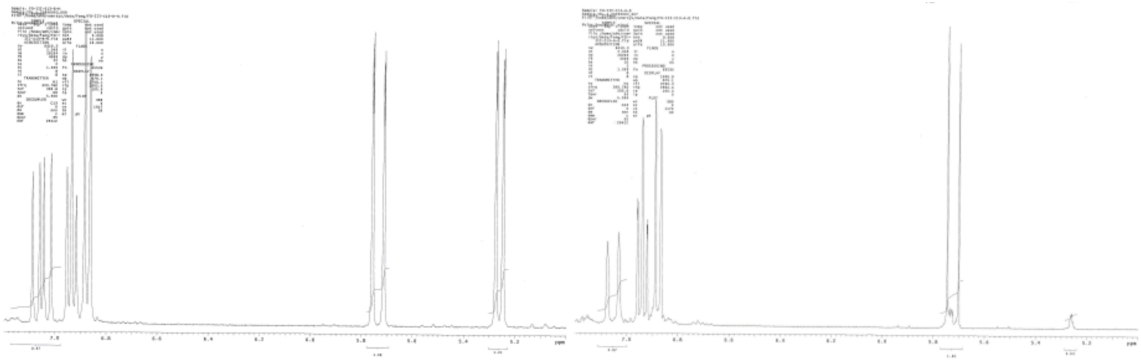
Site selectivity (7:93 α:*β*) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).



Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	6.72	0.93	48.2	1	6.70	0.93	93.0
3	5.24	1.00	51.8	3	5.23	0.07	7.0

(*E*)-*β*-Deuterio-1-methoxy-2-vinylbenzene (Table 3.6, entry 1): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (1H, dd, *J* = 7.6, 1.6 Hz), 7.24 (1H, ddd, *J* = 8.0, 8.0, 1.6 Hz), 7.05 (1H, bd, *J* = 17.6 Hz), 6.94 (1H, dd, *J* = 7.6, 7.6 Hz), 6.87 (1H, d, *J* = 8.4 Hz), 5.72 (1H, d, *J* = 18.0 Hz), 3.85 (3H, s). The spectroscopic data match those reported previously.[64]

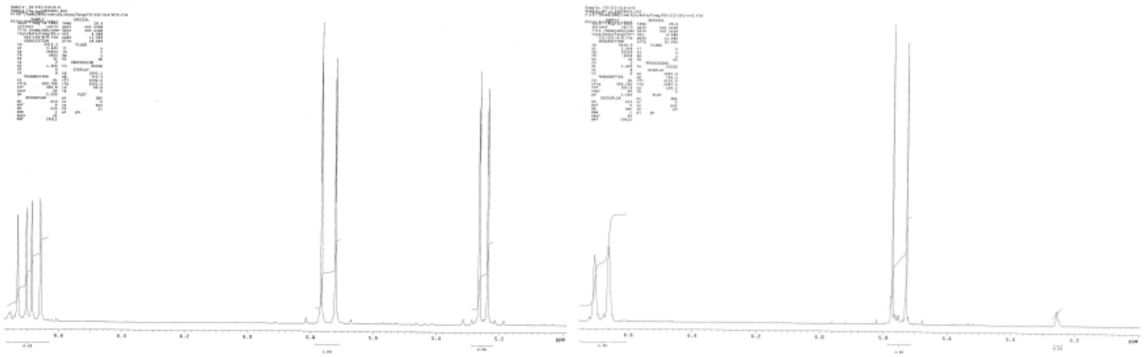
Site selectivity (3:97 α:*β*) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).



Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	7.05	0.97	49.0	1	7.05	0.97	97.0
4	5.26	1.01	51.0	4	5.26	0.03	3.0

(*E*)-*β*-Deuterio-1-methoxy-3-vinylbenzene (Table 3.6, entry 2): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 (1H, dd, *J* = 7.6, 7.6 Hz), 7.02–7.00 (1H, m), 6.95 (1H, dd, *J* = 2.0, 2.0 Hz), 6.82 (1H, ddd, *J* = 8.4, 2.4, 0.8 Hz), 6.69 (1H, bd, *J* = 17.6 Hz), 5.73 (1H, d, *J* = 17.6 Hz), 3.82 (3H, s). The spectroscopic data match those reported previously.[65]

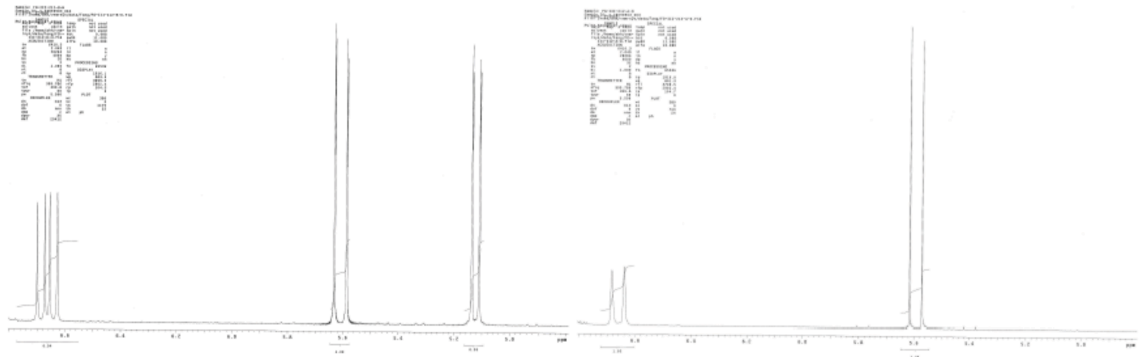
Site selectivity (6:94 α:*β*) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).



Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	6.69	0.99	50.3	1	6.69	1.00	94.3
3	5.25	0.98	49.7	3	5.25	0.06	5.7

(*E*)-*β*-Deuterio-1-methoxy-4-vinylbenzene (Table 3.6, entry 3): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (2H, ddd, *J* = 8.8, 2.0, 2.0 Hz), 6.86 (2H, ddd, *J* = 8.8, 2.0, 2.0 Hz), 6.66 (1H, bd, *J* = 17.6 Hz), 5.59 (1H, d, *J* = 17.6 Hz), 3.81 (3H, s). The spectroscopic data match those reported previously.[66]

Site selectivity (<2:>98 α:*β*) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).

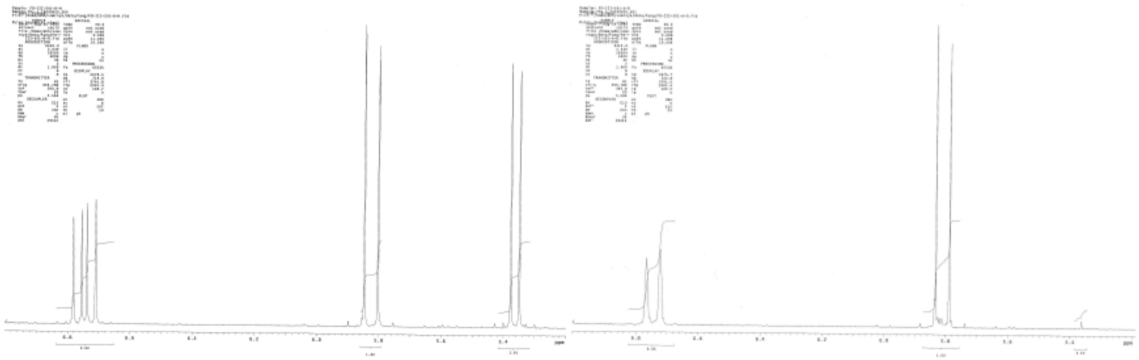


Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	6.66	0.94	48.7	1	6.66	1.02	>98.0
3	5.12	0.99	51.3	3	5.12	<0.02	<2.0

(*E*)-*β*-Deuterio-1-(trifluoromethyl)-3-vinylbenzene (Table 3.6, entry 4): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (1H, s), 7.59–7.56 (1H, m), 7.51 (1H, d, *J* = 8.0 Hz), 7.44 (1H,

dd, J = 7.6, 7.6 Hz), 6.74 (1H, bd, J = 17.6 Hz), 5.81 (1H, d, J = 17.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.4, 135.6, 131.1 (q, J = 32.0 Hz), 129.5, 129.1, 124.5 (q, J = 3.7 Hz), 124.3 (q, J = 270.9 Hz), 123.1 (q, J = 4.4 Hz), 115.6 (t, J = 24.6 Hz); HRMS (ESI^+): Calcd for $C_9H_7D_1F_3$ $[M+H]^+$: 174.0641; Found: 174.0642.

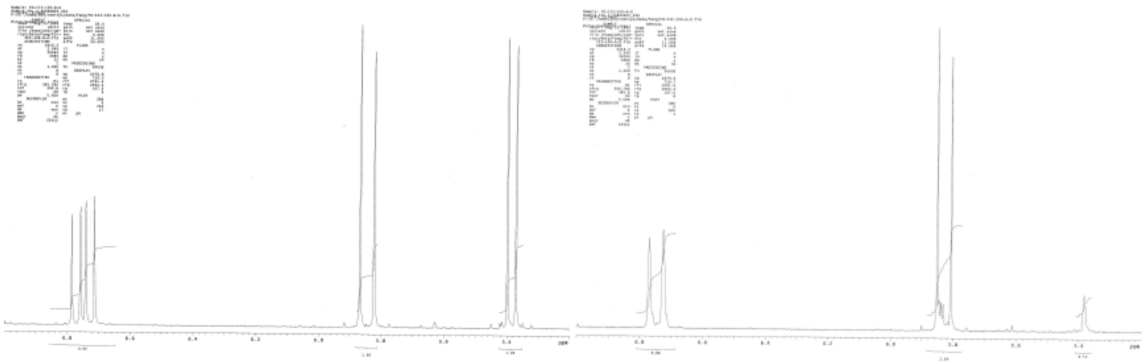
Site selectivity (2:98 α:β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).



Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	6.74	0.94	48.2	1	6.74	0.96	98.0
3	5.36	1.01	51.8	3	5.36	0.02	2.0

(*E*)-β-Deuterio-1-(trifluoromethyl)-4-vinylbenzene (Table 3.6, entry 5): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (2H, d, J = 8.4 Hz), 7.50 (2H, d, J = 8.4 Hz), 6.75 (1H, bd, J = 17.6 Hz), 5.83 (1H, d, J = 17.6 Hz). The spectroscopic data match those reported previously.[67]

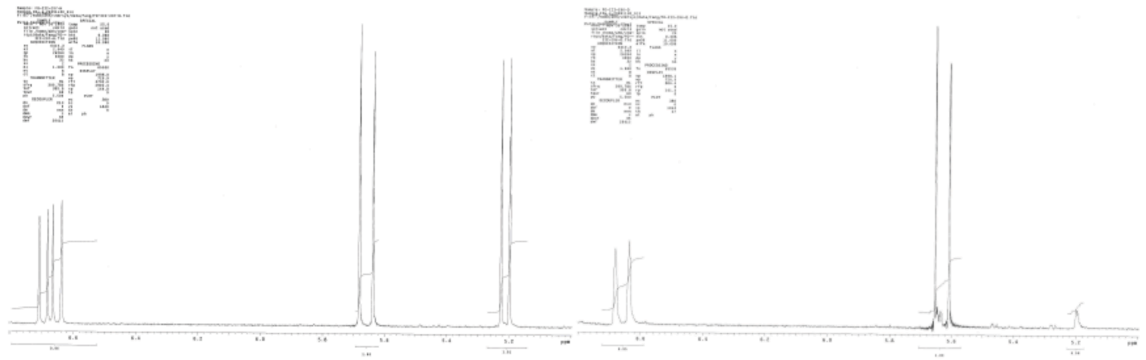
Site selectivity (12:88 α:β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).



Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	6.75	0.92	47.9	1	6.75	0.88	88.0
3	5.39	1.00	52.1	3	5.38	0.12	12.0

(*E*)-*β*-Deuterio-1-fluoro-4-vinylbenzene (Table 3.6, entry 6): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.35 (2H, m), 7.03–6.98 (2H, m), 6.66 (1H, bd, J = 17.6 Hz), 5.63 (1H, dd, J = 17.6, 0.4 Hz). The spectroscopic data match those reported previously.[68]

Site selectivity (8:92 α:β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).

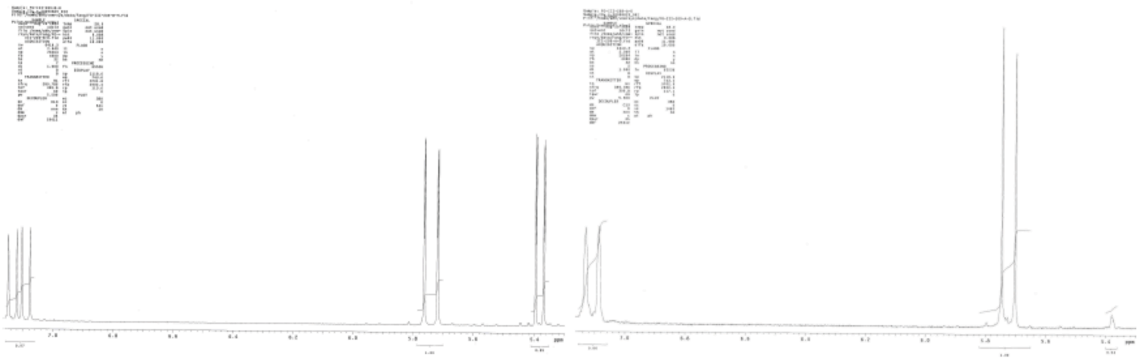


Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	6.67	0.96	47.9	1	6.66	0.95	92.2
3	5.21	1.01	52.1	3	5.19	0.08	7.8

(*E*)-*β*-Deuterio-1-chloro-2-vinylbenzene (Table 3.6, entry 7): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (1H, dd, J = 7.6, 2.0 Hz), 7.35 (1H, dd, J = 7.6, 2.0 Hz), 7.26–7.17 (2H, m), 7.11 (1H, bd, J = 17.6 Hz), 5.72 (1H, d, J = 18.0 Hz). The spectroscopic data match

those reported previously.[69]

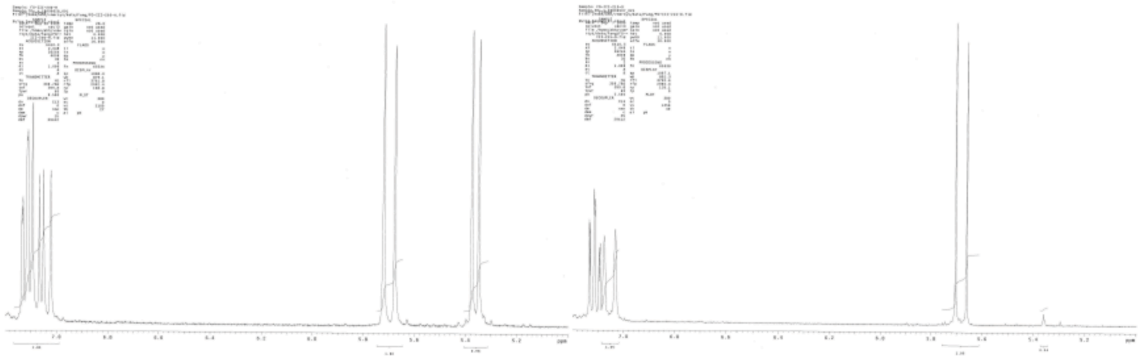
Site selectivity (4.5:95.5 α*:*β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).



Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	7.11	0.97	49.5	1	7.11	0.86	95.5
3	5.38	0.99	50.5	3	5.38	0.04	4.5

(*E*)-β-Deuterio-1-bromo-2-vinylbenzene (Table 3.6, entry 8): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (2H, d, *J* = 8.0 Hz), 7.28 (1H, dd, *J* = 8.0, 8.0 Hz), 7.11 (1H, ddd, *J* = 7.6, 7.6, 1.6 Hz), 7.05 (1H, bd, *J* = 17.6 Hz), 5.68 (1H, d, *J* = 17.6 Hz). The spectroscopic data match those reported previously.[70]

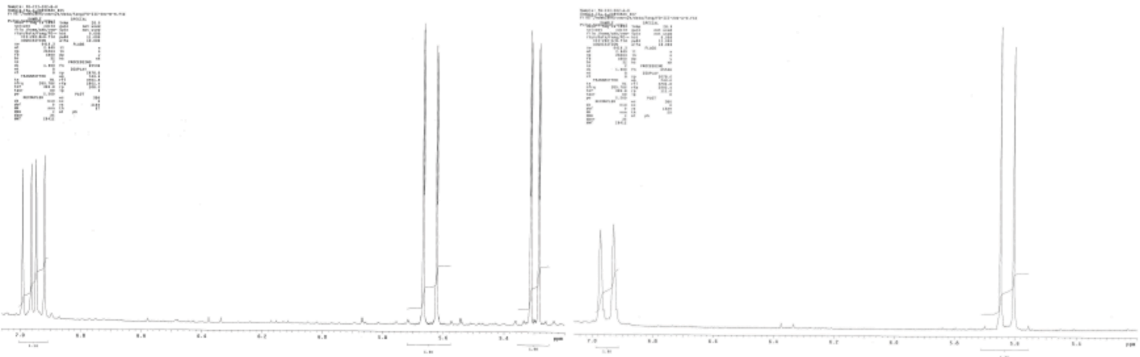
Site selectivity (4:96 α*:*β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).



Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
2	7.05	0.93	48.7	2	7.05	1.05	96.3
4	5.36	0.98	51.3	4	5.36	0.04	3.7

(*E*)-*β*-Deuterio-1-methyl-2-vinylbenzene (Table 3.6, entry 9): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49–7.47 (1H, m), 7.19–7.15 (3H, m), 6.95 (1H, bd, J = 17.6 Hz), 5.63 (1H, d, J = 17.2 Hz), 2.36 (3H, s). The spectroscopic data match those reported previously.[71]

Site selectivity (<2:>98 α:*β*) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).

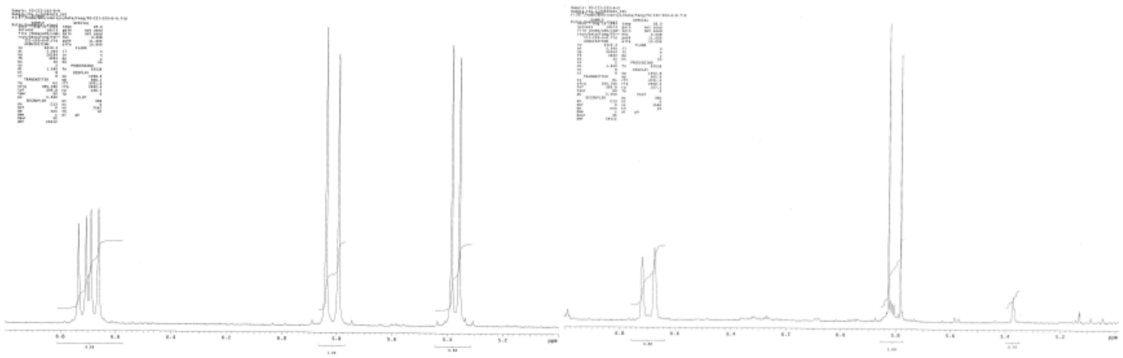


Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	6.96	1.14	53.3	1	6.95	1.06	>98.0
3	5.30	1.00	46.7	3	5.29	<0.02	<2.0

(*E*)-*β*-Deuterio-3-vinylpyridine (Table 3.6, entry 10): ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.61 (1H, s), 8.48 (1H, d, J = 3.2 Hz), 7.72 (1H, d, J = 7.6 Hz), 7.24 (1H, dd, J = 7.6, 2.0 Hz), 6.70 (1H, bd, J = 17.6 Hz), 5.80 (1H, d, J = 17.6 Hz). The spectroscopic data match

those reported previously.[72]

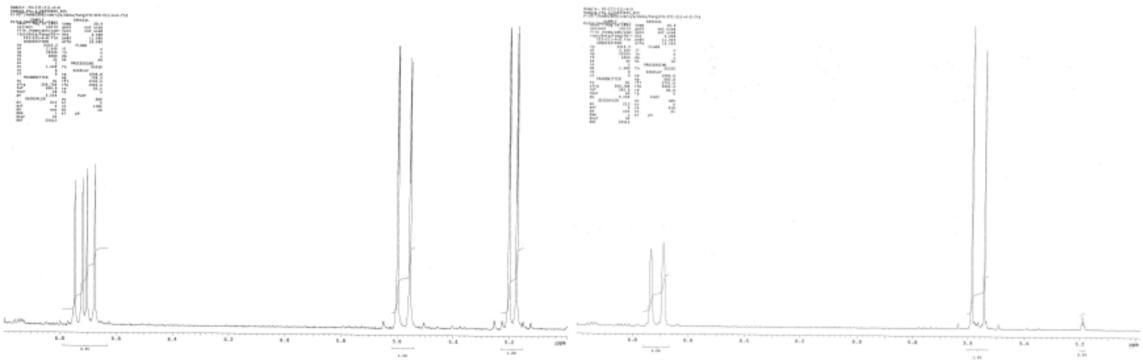
Site selectivity (14.5:85.5 α:β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).



Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	6.70	0.99	50.3	1	6.70	0.88	85.4
3	5.37	0.98	49.7	3	5.38	0.15	14.6

(*E*)-β-Deuterio-3-vinylthiophene (Table 3.6, entry 11): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.23 (2H, m), 7.18–7.17 (1H, m), 6.71 (1H, bd, J = 17.6 Hz), 5.56 (1H, d, J = 17.6 Hz). The spectroscopic data match those reported previously.[73]

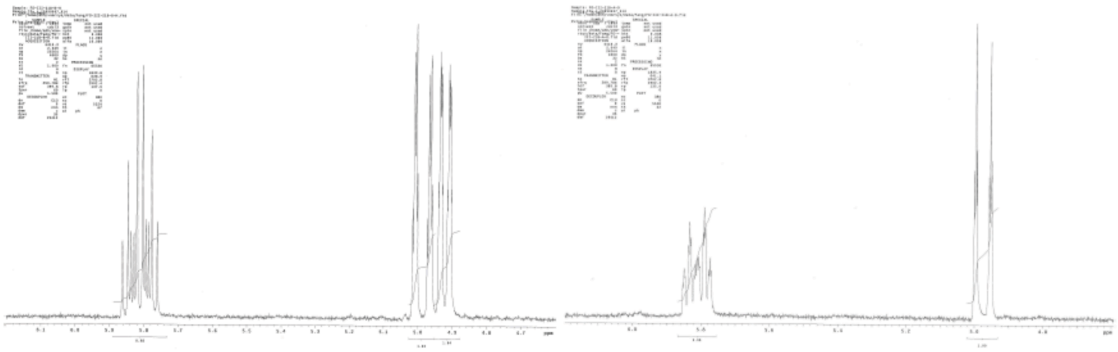
Site selectivity (4:96 α:β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).



Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	6.71	0.95	48.7	1	6.71	0.96	96.0
3	5.19	1.00	51.3	3	5.19	0.04	4.0

(*E*)-1-Deuterio-oct-1-ene (Table 3.7, entry 1): ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.85–5.77 (1H, m), 4.98 (1H, dt, *J* = 17.2, 1.6 Hz), 2.04 (2H, dtt, *J* = 7.6, 7.6, 1.2 Hz), 1.39–1.24 (8H, m), 0.88 (3H, t, *J* = 6.4 Hz). The spectroscopic data match those reported previously.[74]

Site selectivity (<2:>98 α*:β*) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).

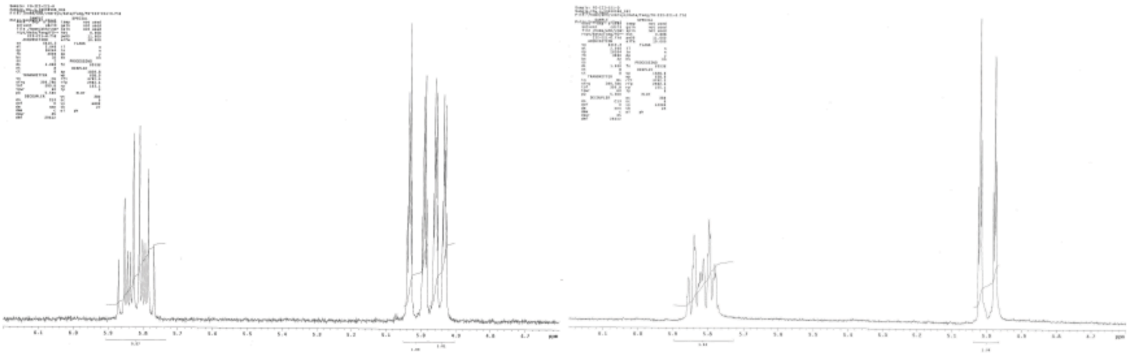


Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	5.81	0.98	48.5	1	5.81	0.98	>98.0
3	4.92	1.04	51.5	3	4.92	<0.02	<2.0

(*E*)-*tert*-Butyldimethyl(5-deuterio-pent-4-en-1-yloxy)silane (Table 3.7, entry 2): ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.86–5.78 (1H, m), 5.00 (1H, dt, *J* = 16.8, 1.6 Hz), 3.61 (2H,

t, J = 6.4 Hz), 2.10 (2H, dtt, J = 7.2, 7.2, 1.2 Hz), 1.64–1.57 (2H, m), 0.89 (9H, s), 0.04 (6H, s). The spectroscopic data match those reported previously.[76]

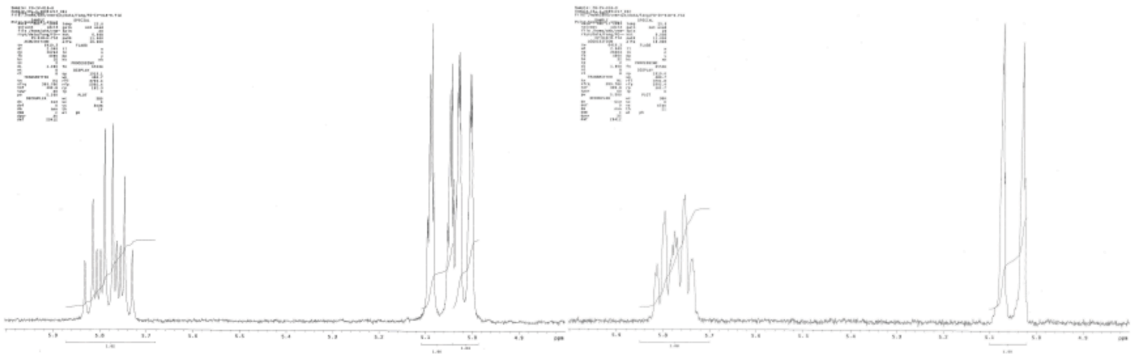
Site selectivity (<2:>98 α:β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).



Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	5.82	0.97	48.5	1	5.82	1.04	>98.0
3	4.95	1.01	51.5	3	4.95	<0.02	<2.0

(*E*)-1-Deuterio-5-chloropent-1-ene (Table 3.7, entry 3): ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.81–5.74 (1H, m), 5.05 (1H, dt, J = 17.2, 1.6 Hz), 3.55 (2H, t, J = 6.4 Hz), 2.21 (2H, dt, J = 6.8, 6.8 Hz), 1.89–1.84 (2H, m). The spectroscopic data match those reported previously.[77]

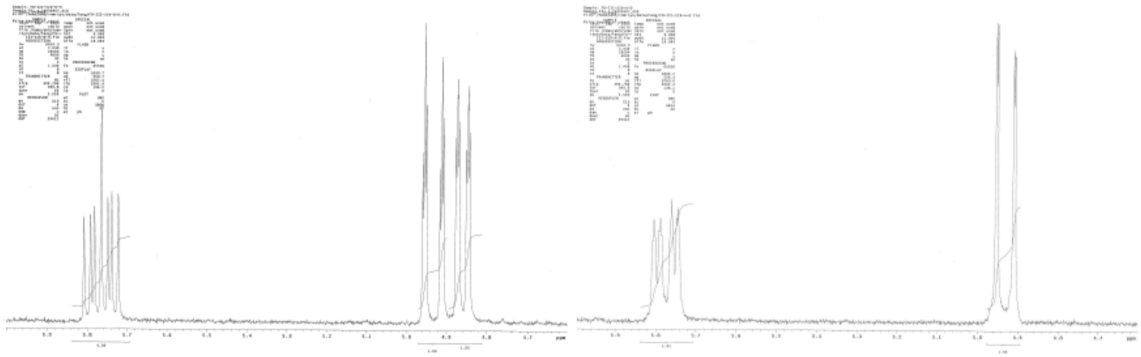
Site selectivity (<2:>98 α:β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).



Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	5.78	1.02	49.5	1	5.78	1.08	>98.0
3	5.01	1.04	50.5	3	5.01	<0.02	<2.0

(*E*)-(2-Deuteriovinyl)cyclohexane (Table 3.7, entry 4): ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.78 (1H, dd, *J* = 17.2, 6.0 Hz), 4.93 (1H, dd, *J* = 17.6, 1.6Hz), 1.97–1.89 (1H, m), 1.73–1.58 (4H, m), 1.31–1.02 (6H, m). The spectroscopic data match those reported previously.[78]

Site selectivity (<2:>98 α:*β*) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).

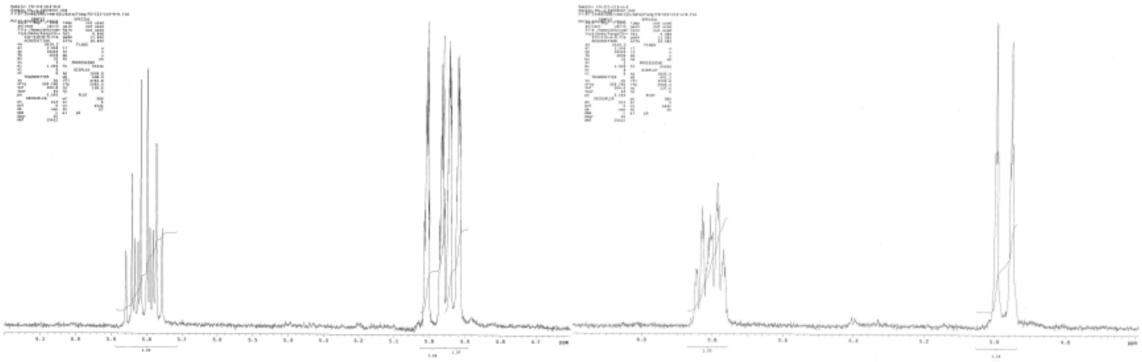


Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	5.77	0.98	48.3	1	5.78	1.01	>98.0
3	4.86	1.05	51.7	3	4.87	<0.02	<2.0

(*E*)-(3-deuterioallyl)cyclopentane (Table 3.7, entry 5): ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.85–5.77 (1H, m), 4.97 (1H, dt, *J* = 17.2, 1.2 Hz), 2.05 (2H, dd, *J* = 6.8, 6.8 Hz), 1.77–

1.69 (1H, m), 1.63–1.48 (6H, m), 1.17–1.09 (2H, m). The spectroscopic data match those reported previously.[80]

Site selectivity (<2:>98 α:β) was determined by analysis of 400 MHz ^{1}H NMR spectra of the unpurified reaction mixtures through comparison of the protonated sample (below left) with deuterated sample (below right).



Peak #	Chemical shift (ppm)	Area	Area (%)	Peak #	Chemical shift (ppm)	Area	Area (%)
1	5.81	1.00	48.3	1	5.81	1.05	>98.0
3	4.93	1.07	51.7	3	4.93	<0.02	<2.0

■ **Representative Procedure for $Ni(PPh_3)_2Cl_2$ catalyzed Hydroalumination of Terminal Alkynes and Functionalization of the Resulting *Terminal* Alkenylaluminum Reagent with Bromine**:

Commercial grade bis(triphenylphosphine)nickel dichloride ($Ni(PPh_3)_2Cl_2$, 32.7 mg, 0.0500 mmol) is placed in a flame-dried 50 mL round bottom flask equipped with a stir bar. The flask is sealed with a septum and purged with N_2 for approximately ten minutes. Tetrahydrofuran (thf, 10.0 mL) is added through a syringe, followed by dropwise addition of dibal–H (1.96 mL, 11.0 mmol) at 22 °C (gas evolution occurs as dibal–H is added). The resulting black solution is allowed to cool to 0 °C (ice bath) before phenylacetylene (1.10 mL, 10.0 mmol) is added slowly over five minutes (reaction is

exothermic). The resulting black solution is allowed to warm to 22 °C and stir for additional six hours. The solution is allowed to cool to –78 °C (dry ice-acetone bath), and bromine (Br_2; 0.771 mL, 15.0 mmol) is added through a syringe slowly in a dropwise manner (vigorous reaction occurs) over a period of approximately ten minutes. Tetrahydrofuran (thf, 5.0 mL) is used to wash off the residue on the sidewall of the flask. The resulting light brown solution is allowed to warm to 22 °C and kept at this temperature for one hour before the reaction is quenched at 0 °C through dropwise addition of a saturated solution of Rochelle's salt (sodium potassium tartrate; 10.0 mL) over ten minutes. The mixture is allowed to stir at 22 °C for 30 minutes and the layers are separated. The aqueous layer is washed with Et_2O (20.0 mL x 3) and the combined organic layers are dried over anhydrous $MgSO_4$, filtered and concentrated under vacuum to furnish yellow oil, which is purified through silica gel chromatography (100% hexanes) to afford **3.93** as light yellow oil in 75% yield (1.37g, 7.48 mmol) and as a 93:7 mixture (**3.93**:**3.92**). **(*E*)-(2-bromovinyl)benzene (3.93):** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.27 (5H, m), 7.11 (1H, d, J = 13.6 Hz), 6.77 (1H, d, J = 14.0 Hz); The spectroscopic data match those reported previously.[85]

(*E*)-(2-iodovinyl)benzene (3.95): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (1H, d, J = 14.8 Hz), 7.35–7.26 (5H, m), 6.83 (1H, d, J = 14.8 Hz); HRMS (ESI^+): Calcd for $C_8H_8I_1$ $[M+H]^+$: 230.9671; Found: 230.9672. The spectroscopic data match those reported previously.[63]

(*E*)-4,4,5,5-tetramethyl-2-styryl-1,3,2-dioxaborolane (3.102): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50–7.47 (2H, m), 7.40 (1H, d, J = 18.4 Hz), 7.36–7.29 (3H, m), 6.17 (1H, d,

(85) Bull, J. A.; Mousseau, J. J.; Charette, A. B. *Org. Lett.* **2008**, *10*, 5485–5488.

J = 18.4 Hz), 1.32 (12H, s); HRMS (ESI^+): Calcd for $C_{14}H_{20}B_1O_2$ $[M+H]^+$: 231.1556; Found: 231.1549. The spectroscopic data match those reported previously.[86]

3.8.3 Representative Experimental Procedures for Cu-catalyzed EAS with Non Silyl-substitued *Trans* 1,2-Alkenylaluminum Reagents to Construct Quaternary Stereogenic Centers and Characterization Data of New Compounds

General. Infrared (IR) spectra were recorded on a Nicolet 210 spectrophotometer, ν_{max} in cm^{-1}. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). ^1H NMR spectra were recorded on a Varian Unity INOVA 400 (400 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on a Varian Unity INOVA 400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: 77.16 ppm). High-resolution mass spectrometry was performed on a Micromass LCT ESI-MS (positive mode) at the Mass Spectrometry Facility, Boston College. Enantiomer ratios were determined by analytical liquid chromatography (HPLC) on a Shimadzu chromatograph (Chiral Technologies Chiralpak AS (4.6 x 250 mm), Chiral Technologies Chiralcel OD (4.6 x 250 mm), Chiral Technologies Chiralcel OD-R (4.6 x 250 mm), Chiral Technologies Chiralcel OJ-H (4.6 x 250 mm), or Chiral

(86) Tucker, C. E.; Davidson, J.; Knochel, P. *J. Org. Chem.* **1992**, *57*, 3482–3485.

Technologies Chiralcel OD-H (4.6 x 250 mm)) in comparison with authentic racemic materials. Optical rotations were measured on a Rudolph Research Analytical Autopol IV Polarimeter.

Unless otherwise noted, all reactions were carried out with distilled and degassed solvents under an atmosphere of dry N_2 in oven- (135 ^oC) or flame-dried glassware with standard dry box or vacuum-line techniques. All work-up and purification procedures were carried out with reagent grade solvents (purchased from Fisher Inc.) in air.

■ **Reagents and Ligands:**

3-(*tert*-Butoxy)prop-1-yne: Purchased from Acros and used after distillation from CaH_2 under N_2.

Chlorodiethylphosphate: Purchased from Aldrich and used as received.

5-Chloropent-1-yne: Purchased from Aldrich and used after distillation from CaH_2 under N_2.

Copper (II) chloride dihydrate: Purchased from Aldrich and used without further purification.

Di*iso*butyl aluminum hydride (dibal-H, neat): Purchased from Aldrich and used as received.

4-Dimethylaminopyridine: Purchased from Advanced Chem Tech used as received.

3,3-Dimethylbut-1-yne: Purchased from Aldrich and used after distillation from CaH_2 under N_2.

1-Ethynylcyclohex-1-ene: Purchased from Aldrich and used after distillation from CaH_2 under vacuum.

1-Ethynyl-4-methoxybenzene: Purchased from Aldrich and used after distillation from CaH_2 under vacuum.

1-Ethynyl-2-methylbenzene: Purchased from Aldrich and used after distillation from CaH_2 under vacuum.

1-Ethynyl-4-(trifluoromethyl)benzene: Purchased from Aldrich and used after distillation from CaH_2 under vacuum.

1-Octyne: Purchased from Aldrich and used after distillation from CaH_2 under N_2.

Phenylacetylene: Purchased from Aldrich and used after distillation from CaH_2 under vaccum.

Tetrahydrofuran: Distilled under N_2 from sodium benzophenone ketyl.

Triethylamine: Purchased from Aldrich and distilled from CaH_2 under N_2.

Dichloromethane, diethyl ether, and hexanes: Purified by being passed through two alumina columns under a positive pressure of dry argon with a modified Advanced ChemTech purification system.

Alkyl-substituted vinylaluminum reagents: Prepared according to a known literature procedure. [87]

Chiral NHC-Ag Complex 1a: Prepared based on a previously reported procedure.[88]

Chiral NHC-Ag Complex 1b: Prepared based on a previously reported procedure.[89]

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Chiral NHC-Ag Complex 1c: Prepared based on a previously reported procedure.[90]

■ **Preparation of trisubstituted allylic phosphate substrates:** Allylic alcohols were synthesized from the corresponding ketones by a two-step Horner-Wadsworth-Emmons olefination[91]/dibal–H reduction sequence.[92] Allylic alcohols were converted to the corresponding allylic phosphates based on well-established methods.[93] Physical attributes of compounds that have not been reported in the past are presented below.

(*E*)-Diethyl (3-phenylbut-2-en-1-yl) phosphate. IR (neat): 2982 (w), 2908 (w), 1495 (w), 1478 (w), 1445 (w), 1391 (w), 1261 (m), 1165 (w), 1125 (w), 1100 (w), 1062 (w), 1004 (s), 969 (s), 879 (w), 821 (m), 758 (m), 696 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$); δ 7.42–7.39 (2H, m), 7.36–7.32 (2H, m), 7.30–7.28 (1H, m), 5.95 (1H, dt, *J* = 6.8, 1.2 Hz), 4.77 (2H, dd, *J* = 8.0, 7.6 Hz), 4.13 (4H, dq, *J* = 7.2, 1.2 Hz), 2.12 (3H, s), 1.36-1.32 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.5, 140.5, 128.5, 127.8, 126.0, 122.0 (d, *J* = 6.7 Hz), 64.5 (d, *J* = 5.2 Hz), 63.9 (d, *J* = 6.0 Hz), 16.35 (d, *J* = 3.0 Hz), 16.27; HRMS (ESI+): Calcd for $C_{14}H_{22}O_5P_1$ $[M+OH]^+$: 301.1205, Found: 301.1207.

(*E*)-Diethyl (3-(*o*-tolyl)but-2-en-1-yl) phosphate. IR (neat): 2982 (w), 2931 (w), 1486 (w), 1445 (w), 1381 (w), 1263 (w), 1263 (m), 1166 (w), 1103 (w), 1029 (s), 1009 (s), 977 (s), 881 (w), 827 (w), 761 (w), 729 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$); δ 7.28–7.22

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(3H, m), 7.17–7.15 (1H, m), 5.63 (1H, dt, J = 6.8, 1.2 Hz), 4.84 (2H, dd, J = 8.0, 7.6 Hz), 4.27–4.19 (4H, m), 2.37 (3H, s), 2.10 (3H, s), 1.47–1.43 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$), δ 144.4, 142.5, 134.8, 130.5, 128.1, 127.4, 126.0, 124.0 (d, J = 6.7 Hz), 64.3 (d, J = 6.0 Hz), 64.0 (d, J = 5.9 Hz), 20.0, 18.7, 16.5 (d, J = 6.7 Hz); HRMS (ESI+): Calcd for $C_{15}H_{24}O_5P_1$ $[M+OH]^+$: 315.1361, Found: 315.1370.

(*E*)-3-(2-Bromophenyl)but-2-enyl diethyl phosphate. IR (neat): 2983 (w), 2905 (w), 1468 (w), 1426 (w), 1378 (w), 1270 (m), 1166 (w), 1026 (s), 979 (s), 887 (w), 823 (w), 758 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$); δ 7.56–7.53 (1H, m), 7.29–7.24 (1H, m), 7.17–7.11 (2H, m), 5.59 (1H, dt, J = 5.2, 1.2 Hz), 4.74 (2H, dd, J = 6.8, 0.8 Hz), 4.14 (4H dq, J = 7.2, 0.8 Hz), 2.05–2.04 (3H, m), 1.37–1.34 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.1, 141.9, 132.9, 129.8, 128.8, 127.5, 125.2 (d, J = 6.7 Hz), 121.8, 63.9 (d, J = 6.7 Hz), 18.1, 16.3 (d, J = 6.7 Hz); HRMS (ESI+): Calcd for $C_{14}H_{21}Br_1O_5P_1$ $[M+OH]^+$: 379.0310, Found: 379.0332.

(*E*)-Diethyl (3-(4-nitrophenyl)but-2-en-1-yl) phosphate. IR (neat): 2984 (w), 2911 (w), 1595 (w), 1515 (m), 1444 (w), 1391 (w), 1369 (w), 1343 (s), 1263 (m), 1165 (w), 1106 (w), 1062 (w), 1005 (s), 974 (s), 853 (s), 818 (m), 747 (m), 695 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$); δ 8.21–8.17 (2H, m), 7.56–7.52 (2H, m), 6.07 (1H, dt, J = 6.4, 1.2 Hz), 4.78 (2H, dd, J = 6.4, 0.8 Hz), 4.18–4.10 (4H, m), 2.14–2.13 (3H, m), 1.37–1.33 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.9, 147.3, 138.2, 126.8, 125.9 (d, J = 6.7 Hz), 123.8, 64.1 (d, J = 4.5 Hz), 64.1 (d, J = 5.2 Hz), 16.3 (d, J = 4.5 Hz), 16.3 (d, J = 2.2 Hz); HRMS (ESI+): Calcd for $C_{14}H_{24}N_2O_6P$ $[M+NH_4]^+$: 347.1372, Found: 347.1379.

(*E*)-Diethyl (3-(4-(trifluoromethyl)phenyl)but-2-en-1-yl) phosphate. IR (neat): 2986 (w), 2934 (w), 2910 (w), 1616 (w), 1445 (w), 1411 (w), 1394 (w), 1324 (s), 1265 (m), 1164 (m), 1115 (s), 1059 (m), 1006 (s), 975 (s), 847 (m), 819 (m), 749 (w), 724 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$); δ 7.60–7.57 (2H, m), 7.50–7.48 (2H, m), 6.00 (1H, dt, *J* = 5.6, 1.6 Hz), 4.79–4.75 (2H, m), 4.17–4.10 (4H, m), 2.12 (3H, s), 1.37–1.32 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.0, 139.1, 129.7 (q, *J* = 32.0 Hz), 128.8 (q, *J* = 82.1 Hz), 126.3, 125.4 (q, *J* = 3.8 Hz), 124.1 (d, *J* = 6.7 Hz), 64.2 (d, *J* = 5.3 Hz), 64.0 (d, *J* = 5.9 Hz), 17.8, 16.3 (d, *J* = 6.7 Hz); HRMS (ESI+): Calcd for $C_{15}H_{21}F_3O_5P_1$ $[M+OH]^+$: 369.1079, Found: 369.1084.

(*E*)-3-Cyclohexylbut-2-enyl diethyl phosphate. IR (neat): 2982 (w), 2925 (m), 2853 (w), 1663 (w), 1448 (w), 1392 (w), 1369 (w), 1261 (m), 1166 (w), 1098 (w), 1069 (w), 1024 (s), 1001 (s), 972 (s), 881 (w), 852 (w), 830 (w), 801 (m), 747 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$); δ 5.37 (1H, ddt, *J* = 6.8, 2.4, 1.2 Hz), 4.57 (2H, t, *J* = 7.6 Hz), 4.14–4.06 (4H, m), 1.87 (1H, t, *J* = 11.6 Hz), 1.77–1.69 (5H, m), 1.67 (3H, s), 1.35–1.30 (6H, m), 1.28–1.11 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.6, 117.4 (d, *J* = 6.7 Hz), 64.4 (d, *J* = 5.9 Hz), 63.7 (d, *J* = 5.2 Hz), 47.3, 31.7, 26.7, 26.4, 16.3 (d, *J* = 6.7 Hz), 15.0; HRMS (ESI+): Calcd for $C_{14}H_{28}O_5P_1$ $[M+OH]^+$: 307.1674, Found: 307.1681.

(*E*)-3, 7-Dimethylocta-2, 6-dienyl diethyl phosphate (10, Scheme 4). IR (neat): 2981 (w), 2912 (w), 1669 (w), 1444 (w), 1383 (w), 1261 (m), 1166 (w), 1100 (w), 1027 (s), 972 (s), 886 (w), 818 (m), 801 (m), 746 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$); δ 5.41–5.38 (1H, m), 5.10–5.06 (1H, m), 4.56 (2H, t, *J* = 7.6 Hz), 4.14–4.07 (4H, m), 2.13–2.02 (4H, m), 1.69 (6H, d, *J* = 10.0 Hz), 1.60 (3H, s), 1.35–1.31 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.7, 132.0, 123.8, 119.1 (d, *J* = 6.7 Hz), 64.2 (d, *J* = 5.2 Hz), 63.7 (d, *J* = 5.9

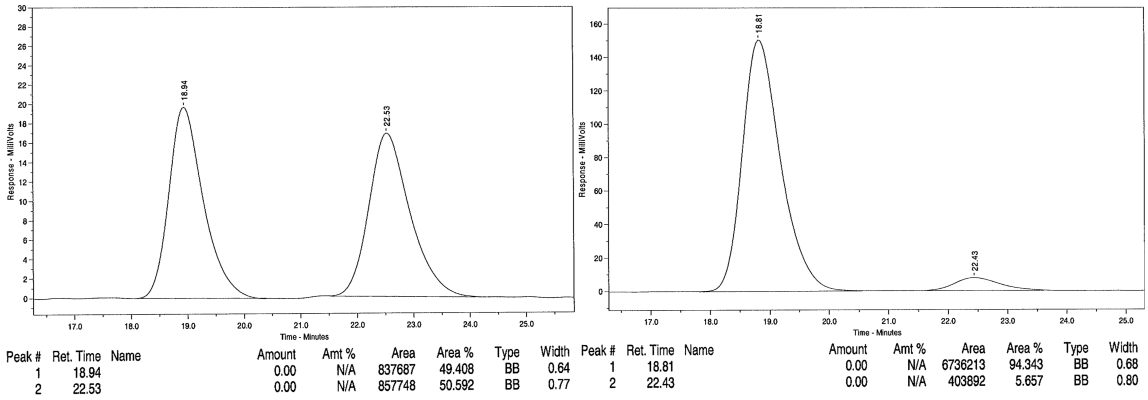
Hz), 39.6, 26.4, 25.8, 17.8, 16.6, 16.3 (d, J = 6.7 Hz); HRMS (ESI+): Calcd for $C_{14}H_{28}O_5P_1$ $[M+OH]^+$: 307.1674, Found: 307.1673.

(*E*)-*tert*-Butyl 4-((diethoxyphosphoryl)oxy)-2-methylbut-2-enoate. IR (neat): 2980 (w), 2934 (w), 1708 (m), 1657 (w), 1479 (w), 1457 (w), 1392 (w), 1368 (w), 1333 (w), 1252 (m), 1171 (w), 1134 (m), 1100 (w), 1017 (s), 889 (w), 848 (w), 819 (w), 730 (w), 670 (w), 511 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.66–6.63 (1H, m), 4.68–4.63 (2H, m), 4.13–4.05 (4H, m), 1.78 (3H, s), 1.44 (9H, s), 1.33–1.28 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 134.0 (d, J = 7.5 Hz), 132.2, 80.9, 64.0 (d, J = 6.0 Hz), 63.9 (d, J = 5.2 Hz), 28.1, 16.2 (d, J = 6.7 Hz), 12.9; HRMS (ESI+): Calcd for $C_{13}H_{26}O_6P_1$ $[M+H]^+$: 309.1467, Found: 309.1453.

■ **General Procedure for Cu-catalyzed Enantioselective Allylic Substitutions with Alkyl-substituted Alkenylaluminum Reagents (Table 3.11 and Scheme 3.15):** A 13 x 100 mm test tube equipped with a stir bar is charged with NHC•Ag complex **3.9** (1.2 mg, 0.0010 mmol) in an N_2-filled glovebox. The test tube is sealed with a septum and removed from the glovebox. Tetrahydrofuran (1.0 mL) and a solution of $CuCl_2•2H_2O$ (0.02M in thf, 100 μL, 0.002 mmol) are added to the test tube at 22 °C. The resulting blue solution is allowed to cool to –78 °C (dry ice/acetone bath), followed by the addition of the vinylaluminum reagent (1.0 M in hexanes, 300 μL, 0.30 mmol) and a solution of (*E*)-diethyl (3-phenylbut-2-en-1-yl) phosphate (56.9 mg, 0.200 mmol) in thf (1.0 mL). The mixture is allowed to warm to –15 °C and sit in a freezer for 3 h, after which time, the reaction is quenched by the addition of a saturated aqueous solution of Rochelle's salt (2.0 mL) at –78 °C and the resulting mixture is allowed to warm to 22 °C and stir for 1 h.

The layers are separated, and the aqueous layer is washed with Et_2O (2.0 mL x 3). The combined organic layers are passed through a short plug of $MgSO_4$, and concentrated under reduced pressure. The resulting yellow oil is purified by silica gel chromatography to give the product as colorless oil (39.8 mg, 0.164 mmol, 82% yield). **(*R*, *E*)-(3-Methylundeca-1,4-dien-3-yl)benzene (3.113).** IR (neat): 3083 (w), 2957 (m), 2925 (s), 2871 (m), 2854 (s), 1633 (w), 1599 (w), 1492 (m), 1460 (m), 1445 (m), 975 (m), 914 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.36–7.29 (4H, m), 7.22–7.18 (1H, m), 6.09 (1H, dd, *J* = 17.6, 10.8 Hz), 5.67 (1H, dt, *J* = 15.6, 1.6 Hz), 5.43 (1H, dt, *J* = 15.6, 6.8 Hz), 5.12 (1H, dd, *J* = 10.8, 1.6 Hz), 5.02 (1H, dd, *J* = 17.2, 1.6 Hz), 2.09 (2H, dtd, *J* = 6.8, 6.8, 1.2 Hz), 1.49 (3H, s), 1.42–1.27 (8H, m), 0.90 (3H, t, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.2, 146.0, 137.0, 129.1, 128.2, 127.3, 126.1, 112.4, 47.6, 32.9, 31.9, 29.7, 29.1, 25.9, 22.9, 14.3; HRMS (ESI+): Calcd for $C_{18}H_{27}$ $[M+H]^+$: 243.2113, Found: 243.2118. Elemental Analysis: Calcd for $C_{18}H_{26}$: C, 89.19; H, 10.81; Found: C, 89.35; H, 10.60. Optical Rotation: $[\alpha]_D^{20}$ –5.31 (*c* 1.50, $CHCl_3$) for an enantiomerically enriched sample of 94.5:5.5 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (94.3:5.7 e.r. shown; Chiralcel OD column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).

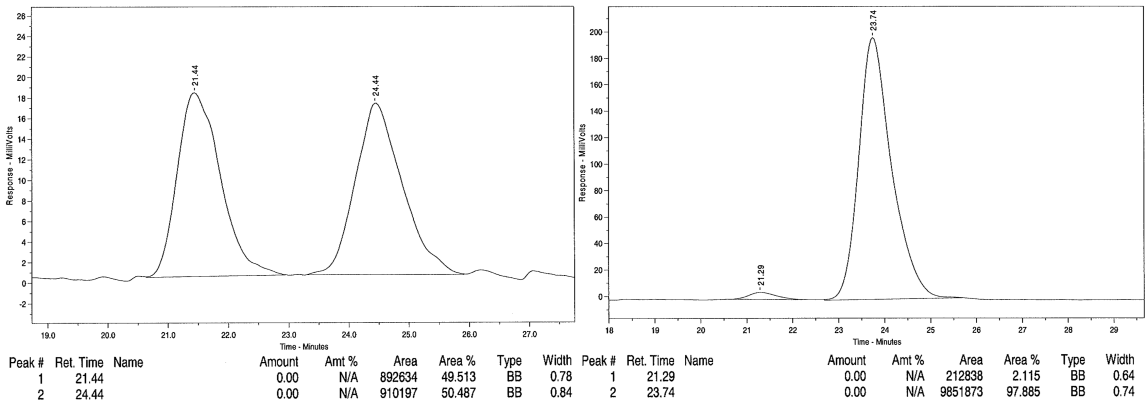


Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	18.94	49.4	1	18.81	94.3
2	22.53	50.6	2	22.43	5.7

(*R*, *E*)-1-Bromo-2-(3-methylundeca-1,4-dien-3-yl)benzene (3.117). IR (neat): 2956 (w), 2923 (m), 2853 (w), 1463 (m), 1431 (w), 1267 (w), 1019 (m), 987 (w), 966 (m), 944 (m), 754 (s), 734 (m), 724 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (1H, dd, *J* = 8.0, 1.2 Hz), 7.46 (1H, dd, *J* = 8.0, 1.6 Hz), 7.25 (1H, dt, *J* = 8.0, 0.8 Hz), 7.06 (1H, dq, *J* = 7.2, 0.8 Hz), 6.19 (1H, dd, *J* = 17.2, 10.8 Hz), 5.74 (1H, dt, *J* = 15.6, 0.8 Hz), 5.30 (1H, dt, *J* = 15.6, 6.8 Hz), 5.10 (1H, dt, *J* = 10.8, 0.9 Hz), 4.93 (1H, dd, *J* = 17.6, 0.8 Hz), 2.07 (2H, dtd, *J* = 7.2, 7.2, 1.6 Hz), 1.62 (3H, s), 1.39–1.26 (8H, m), 0.88 (3H, t, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.8, 145.5, 136.4, 135.6, 129.8, 129.5, 128.0, 127.1, 124.0, 112.8, 48.8, 32.9, 31.9, 29.5, 29.1, 26.3, 22.8, 14.3. Elemental Analysis: Calcd for $C_{18}H_{25}Br_1$: C, 67.29; H, 7.84; Found: C, 67.34; H, 7.84. Optical Rotation: $[\alpha]_D^{20}$ –9.71 (*c* = 1.12, $CHCl_3$) for an enantiomerically enriched sample of 96.5:3.5 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation

with H_2O_2) in comparison with authentic racemic material (97.9:2.1 e.r. shown; Chiralcel OD column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



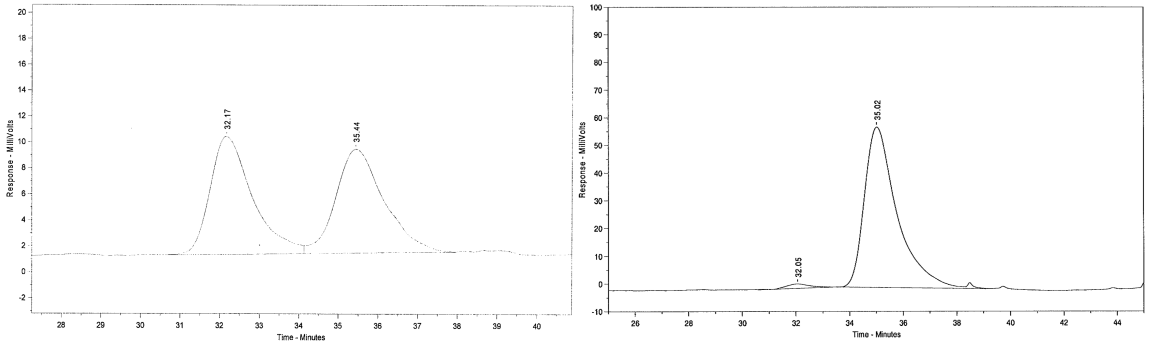
Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	21.44		0.00	N/A	892634	49.513	BB	0.78
2	24.44		0.00	N/A	910197	50.487	BB	0.84

Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	21.29		0.00	N/A	212838	2.115	BB	0.64
2	23.74		0.00	N/A	9851873	97.885	BB	0.74

Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	21.44	49.5	1	21.29	2.1
2	24.44	50.5	2	23.74	97.9

(*R*, *E*)-1-(3-Methylundeca-1,4-dien-3-yl)-2-(trifluoromethyl)benzene (3.116). IR (neat): 2957 (w), 2925 (w), 2855 (w), 1488 (w), 1304 (s), 1268 (m), 1166 (s), 1129 (s), 1034 (s), 912 (m), 765 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.70 (1H, dd, *J* = 8.0, 1.6 Hz), 7.63 (1H, d, *J* = 8.0 Hz), 7.46 (1H, dq, *J* = 8.0, 0.8 Hz), 7.35–7.31 (1H, m), 6.14 (1H, ddd, *J* = 17.6, 10.8, 0.8 Hz), 5.72 (1H, dd, *J* = 15.6, 0.8 Hz), 5.28 (1H, dt, *J* = 15.6, 6.8 Hz), 5.06 (1H, dd, *J* = 10.8, 0.8 Hz), 4.88 (1H, dd, *J* = 17.2, 0.8 Hz), 2.05 (2H, dtd, *J* = 6.8, 6.8, 1.2 Hz), 1.57 (3H, s), 1.38–1.26 (8H, m), 0.89 (3H, t, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.5, 145.9, 137.3, 131.4, 130.6, 129.2 (q, *J* = 30.7 Hz), 128.6, 128.6, 128.5, 124.7 (q, *J* = 272.8 Hz), 111.7, 48.7, 32.9, 31.9, 29.4, 29.1, 27.4, 22.8, 14.3; HRMS (ESI+): Calcd for $C_{19}H_{26}F_3$ $[M+H]^+$: 311.1987, Found: 311.1979. Optical Rotation: $[\alpha]_D^{20}$ –13.3 (*c* = 1.00, $CHCl_3$) for an enantiomerically enriched sample of 98:2 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (98.0:2.0 e.r. shown; Chiralcel OD column, 99.5/0.5 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	32.17		0.00	N/A	676400	49.958	BV	1.09
2	35.44		0.00	N/A	677548	50.042	VB	1.23

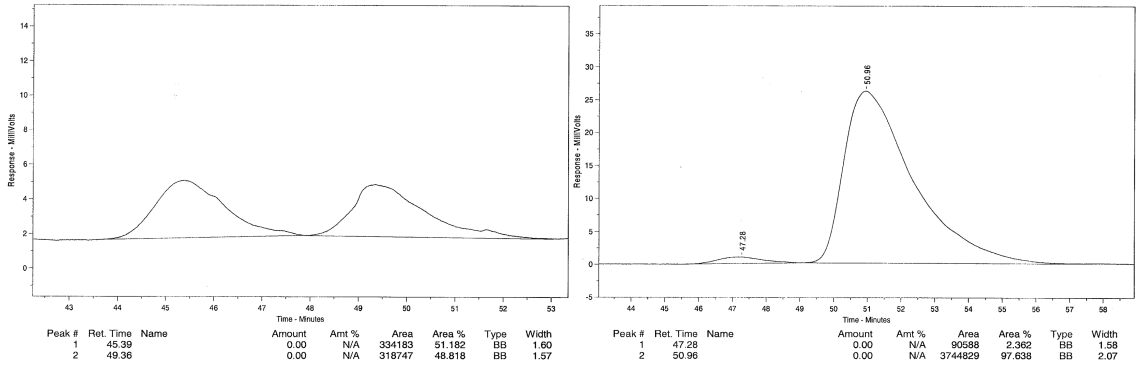
Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	32.05		0.00	N/A	99439	1.972	BB	1.52
2	35.02		0.00	N/A	4943837	98.028	BB	1.21

Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	32.17	50.0	1	32.05	2.0
2	35.44	50.0	2	35.02	98.0

(*R*, *E*)-1-(3-Methylundeca-1,4-dien-3-yl)-2-nitrobenzene (3.119). IR (neat): 2956 (w), 2925 (m), 2855 (w), 1531 (s), 1367 (m), 974 (w), 916 (w), 850 (w), 751 (s), 650 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.53 (1H, dd, *J* = 7.2, 1.2 Hz), 7.47–7.39 (2H, m), 7.32 (1H, dt, *J* = 7.2, 1.2 Hz), 6.01 (1H, dd, *J* = 17.2, 10.6 Hz), 5.58 (1H, d, *J* = 16.4 Hz), 5.44 (1H, dt, *J* = 16.4, 6.0 Hz), 5.13 (1H, d, *J* = 10.6 Hz), 5.02 (1H, d, *J* = 17.6 Hz), 2.01 (2H, dt, *J* = 6.0, 6.0 Hz), 1.62 (3H, s), 1.40–1.24 (8H, m), 0.88 (3H, t, *J* = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.3, 143.8, 139.3, 134.3, 131.2, 130.5, 130.2, 127.5, 124.4, 112.9, 47.4, 32.8, 31.9, 29.3, 29.2, 25.7, 22.9, 14.3; HRMS (ESI+): Calcd for $C_{18}H_{26}N_1O_2$ $[M+H]^+$: 288.1964, Found: 288.1961. Elemental Analysis: Anal Calcd for $C_{18}H_{25}N_1O_2$:

C, 75.22; H, 8.77; N, 4.87; Found: C, 75.49; H, 9.04; N, 5.05. Optical Rotation: $[\alpha]_D^{20}$ +0.71 (*c* 1.00, $CHCl_3$) for an enantiomerically enriched sample of 97.5:2.5 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (97.6:2.4 e.r. shown; Chiralcel OD column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 254 nm).

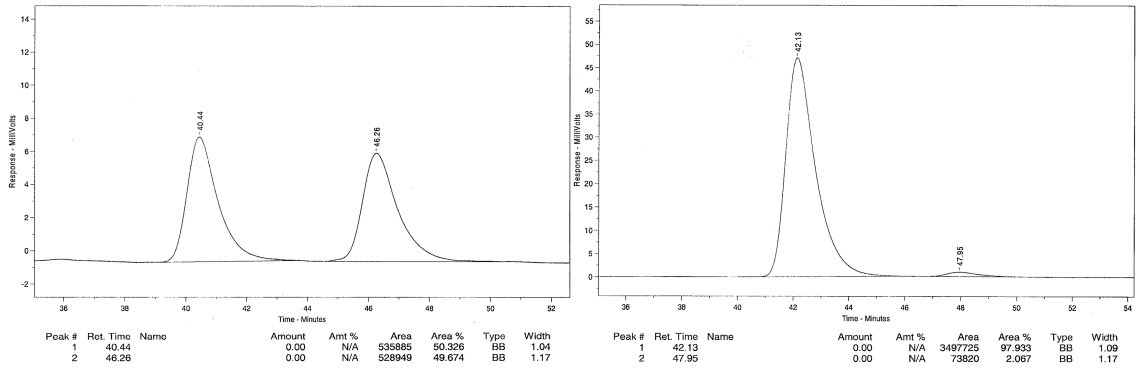


Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	45.39	51.2	1	47.28	2.4
2	49.36	48.8	2	50.96	97.6

(*R*, *E*)-1-Methoxy-2-(3-methylundeca-1,4-dien-3-yl)benzene (3.118). IR (neat): 2956 (w), 2924 (m), 2853 (w), 1487 (m), 1461 (m), 1434 (m), 1241 (s), 1031 (m), 967 (w), 909 (m), 748 (s), 670 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.27 (1H, dd, *J* = 7.6, 1.6 Hz), 7.21 (1H, dt, *J* = 7.6, 1.6 Hz), 6.91–6.86 (2H, m), 6.18 (1H, dd, *J* = 17.2, 10.4 Hz), 5.73 (1H, dt, *J* = 15.6, 1.2 Hz), 5.32 (1H, dt, *J* = 15.6, 6.0 Hz), 5.01 (1H, dd, *J* = 10.4, 1.6 Hz,), 4.91 (1H, dd, *J* = 17.2, 1.2 Hz), 3.76 (3H, s), 2.04 (2H, dt, *J* = 6.0, 6.0 Hz), 1.53 (3H, s), 1.35–1.27 (8H, m), 0.88 (3H, t, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.3, 146.3, 137.1, 135.7, 128.3, 127.9, 127.8, 120.5, 112.3, 111.2, 55.3, 46.5, 33.0, 32.0, 29.9,

29.1, 24.8, 22.9, 14.3; HRMS (ESI+): Calcd for $C_{19}H_{29}O_1$ $[M+H]^+$: 273.2218, Found: 273.2219. Optical Rotation: $[\alpha]_D^{20}$ –3.36 (*c* 1.00, $CHCl_3$) for an enantiomerically enriched sample of 98:2 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (97.9:2.1 e.r. shown; Chiralcel OD-R column, 99/1 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).

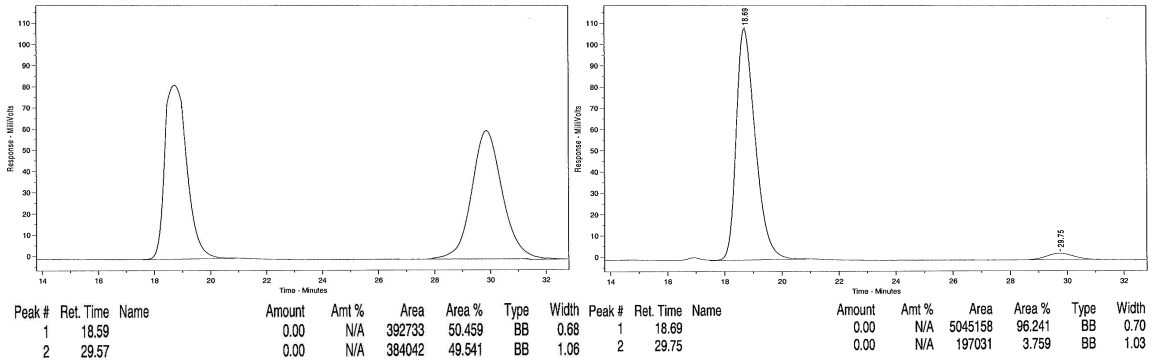


Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	40.44	50.3	1	42.13	97.9
2	46.26	49.7	2	47.95	2.1

(*R*, *E*)-1-Methyl-2-(3-methylundeca-1,4-dien-3-yl)benzene (3.115). IR (neat): 3014 (m), 2957 (m), 2853 (m), 1631 (w), 1485 (w), 1456 (m), 972 (m), 910 (m), 759 (s), 728 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.40–7.37 (1H, m), 7.17–7.12 (3H, m), 6.14 (1H, dd, *J* = 17.2, 10.4 Hz), 5.73 (1H, dt, *J* = 15.6, 1.6 Hz), 5.28 (1H, dt, *J* = 15.6, 6.8 Hz), 5.06 (1H, dd, *J* = 10.4, 1.2 Hz), 4.90 (1H, dd, *J* = 17.6, 1.2 Hz), 2.33 (3H, s), 2.05 (2H, dtd, *J* = 6.8, 6.8, 1.6 Hz), 1.53 (3H, s), 1.38–1.27 (8H, m), 0.89 (3H, t, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.3, 144.5, 137.6, 137.2, 132.4, 128.6, 127.6, 126.5,

125.6, 111.9, 48.1, 33.0, 31.9, 29.6, 29.1, 27.5, 22.9, 22.8, 14.3; HRMS (ESI+): Calcd for $C_{19}H_{29}$ $[M+H]^+$: 257.2269, Found: 257.2274. Optical Rotation: $[\alpha]_D^{20}$ –7.58 (*c* 1.26, $CHCl_3$) for an enantiomerically enriched sample of 96.5:3.5 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (96.2:3.8 e.r. shown; Chiralpak AS column, 99.5/0.5 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).

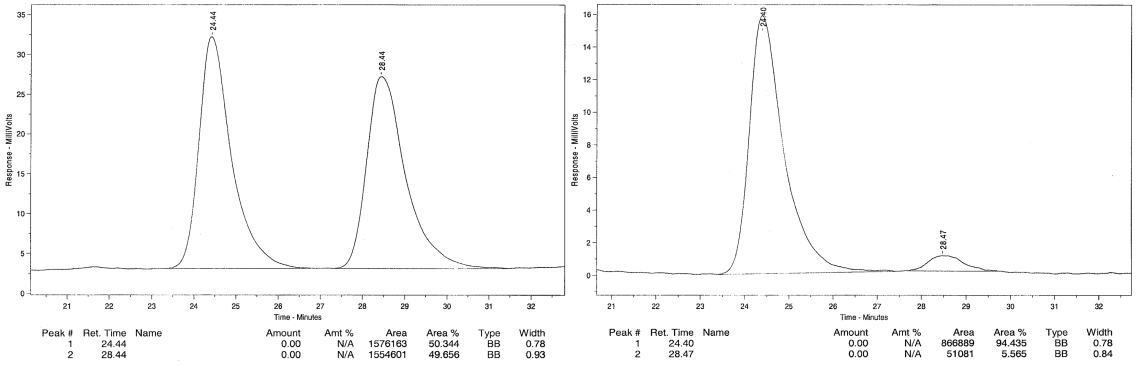


Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	18.59	50.5	1	18.69	96.2
2	29.57	49.5	2	29.75	3.8

(*R*, *E*)-1-(3-Methylundeca-1,4-dien-3-yl)-4-nitrobenzene (3.120). IR (neat): 2956 (w), 2926 (m), 2855 (w), 1597 (w), 1518 (s), 1492 (w), 1459 (w), 1345 (s), 1216 (w), 1111 (w), 1014 (w), 1000 (w), 976 (w), 920 (w), 852 (m), 755 (s), 701 (m), 668 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.14 (2H, d, *J* = 6.8 Hz), 7.48 (2H, d, *J* = 9.2 Hz), 6.03 (1H, dd, *J* = 17.6, 10.6 Hz), 5.62 (1H, d, *J* = 15.6 Hz), 5.43 (1H, dt, *J* = 16.0, 6.8 Hz), 5.18 (1H, d, *J* = 10.6 Hz), 5.03 (1H, d, *J* = 17.6 Hz), 2.08 (2H, dt, *J* = 7.2, 7.2 Hz), 1.50 (3H, s), 1.43–1.27 (8H, m), 0.89 (3H, t, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.0,

146.5, 144.6, 135.7, 130.7, 128.4, 123.5, 113.8, 48.0, 32.9, 31.9, 29.6, 29.1, 26.0, 22.9, 14.3; HRMS (ESI+): Calcd for $C_{18}H_{26}N_1O_2$ $[M+H]^+$: 288.1964, Found: 288.1949. Elemental Analysis: Anal Calcd for $C_{18}H_{25}N_1O_2$: C, 75.22; H, 8.77; N, 4.87; Found: C, 75.49; H, 8.90; N, 4.98. Optical Rotation: $[\alpha]_D^{20}$ –7.54 (*c* = 1.00, $CHCl_3$) for an enantiomerically enriched sample of 94.5:5.5 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (94.4:5.6 e.r. shown; Chiralcel OD-R column, 98/2 hexanes/*i*-PrOH, 1.0 mL/min, 240 nm).

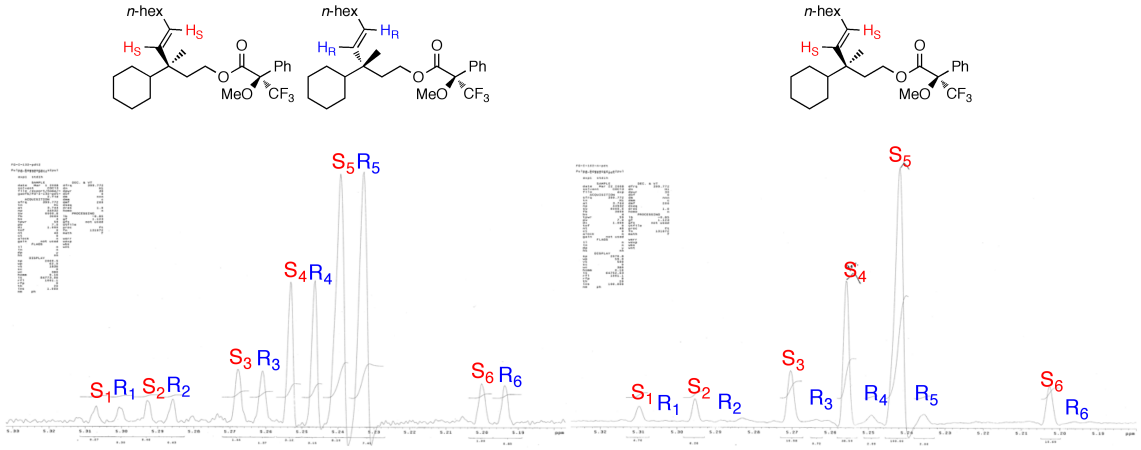


Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	24.44	50.3	1	24.40	94.4
2	28.44	49.7	2	28.47	5.6

(*S*, *E*)-(3-Methylundeca-1,4-dien-3-yl)cyclohexane (3.121). IR (neat): 2922 (s), 2852 (s), 1450 (m), 1000 (w), 973 (m), 910 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.82 (1H, dd, *J* = 17.6, 10.8 Hz), 5.40 (1H, dt, *J* = 15.6, 1.2 Hz), 5.28 (1H, dt, *J* = 15.6, 6.4 Hz), 4.97 (1H, dd, *J* = 10.8, 1.6 Hz), 4.89 (1H, dd, *J* = 17.6, 1.6 Hz), 2.01 (2H, dt, *J* = 6.4, 6.4 Hz), 1.75-1.69 (4H, m), 1.64–1.61 (1H, m), 1.36–1.19 (8H, m), 1.18–1.05 (4H, m), 1.01

(3H, s), 0.94–0.86 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.4, 137.0, 128.3, 111.6, 47.4, 45.3, 33.2, 31.9, 29.9, 29.2, 28.0, 27.4, 27.0, 22.9, 20.2, 14.3; HRMS (ESI+): Calcd for $C_{18}H_{33}$ $[M+H]^+$: 249.2582, Found: 249.2591. Elemental Analysis: Anal Calcd for $C_{18}H_{32}$: C, 87.02; H, 12.98; Found: C, 87.30; H, 13.26. Optical Rotation: $[\alpha]_D^{20}$ –16.3 (*c* 1.00, $CHCl_3$) for an enantiomerically enriched sample of 93:7 e.r.

Enantiomeric purity was determined by ^{1}H NMR analysis in comparison with authentic racemic material obtained from the derived Mosher ester,[94] which was synthesized by hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2. The corresponding alcohol was esterified according to published procedure.[95] (See ^{1}H NMR spectra for racemic and enantiomerically enriched Mosher esters in the appendix, 94.9:5.1 er shown).



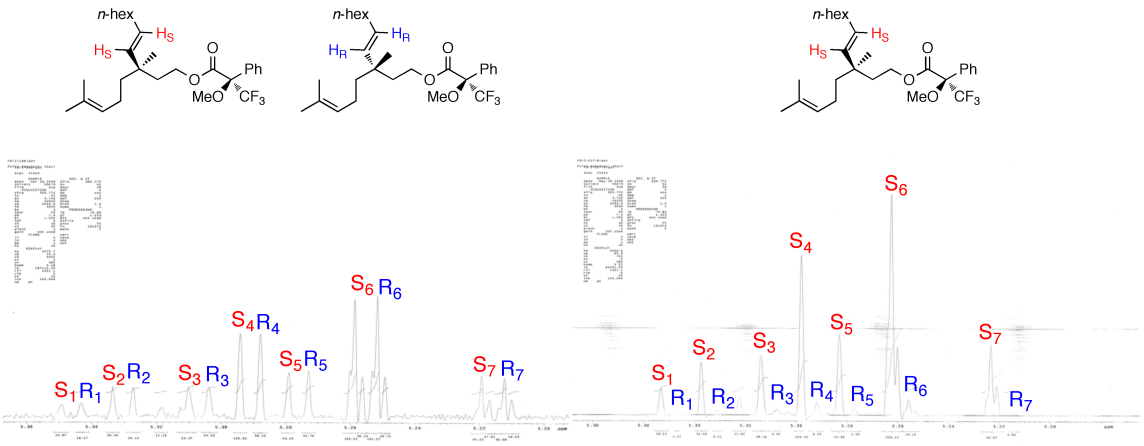
Peak#	ppm	Area%	Peak#	ppm	Area%
S_4	5.253	99.51	S_4	5.254	100.0

(94) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543–2549.
(95) Fujii, M.; Fukumura, M.; Hori, Y.; Hirai, Y.; Akita, H.; Nakamura, K.; Toriizukaa, K.; Idaa, Y. *Tetrahedron; Asymmetry* **2006**, *17*, 2292–2298.

R_4	5.246	100.0	R_4	5.247	5.42

(*R*, *E*)-2,6-Dimethyl-6-vinyltetradeca-2,7-diene (3.124). IR (neat): 2960 (m), 2923 (s), 2854 (m), 1634 (w), 1455 (m), 1376 (w), 1459 (w), 972 (s), 911 (s), 837 (w), 724 (w), 681 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.80 (1H, dd, J = 17.6, 10.8 Hz), 5.40–5.29 (2H, m), 5.09 (1H, tt, J = 7.2, 1.6 Hz), 4.97–4.91 (2H, m), 2.03–1.98 (2H, m), 1.89 (2H, dt, J = 6.8, 6.8 Hz), 1.67 (3H, s), 1.58 (3H, s), 1.38–1.27 (10H, m), 1.07 (3H, s), 0.88 (3H, t, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.8, 137.3, 131.4, 128.1, 125.0, 111.3, 42.5, 41.9, 35.2, 34.2, 32.1, 31.3, 28.0, 23.7, 23.6, 23.0, 17.9, 14.6; HRMS (ESI+): Calcd for $C_{18}H_{33}$ $[M+H]^+$: 249.2582, Found: 249.2588. Optical Rotation: $[\alpha]_D^{20}$ –8.37 (*c* 1.48, $CHCl_3$) for an enantiomerically enriched sample of 92.5:7.5 e.r.

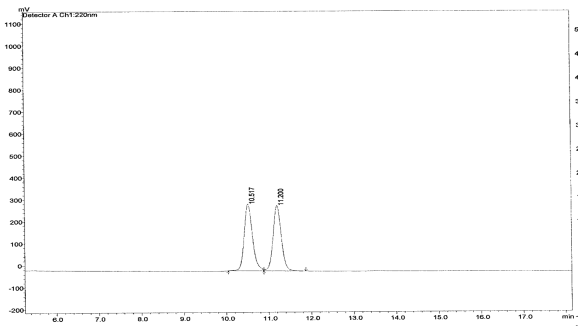
Enantiomeric purity was determined by ^1H NMR analysis in comparison with authentic racemic material obtained from the derived Mosher ester,[94] which was synthesized by hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2. The corresponding alcohol was esterified according to published procedure.[95] (See ^1H NMR spectra for racemic and enantiomerically enriched Mosher esters in the appendix, 92.2:7.8 er shown).



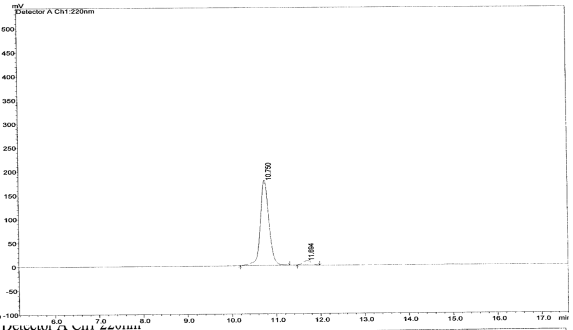
Peak#	ppm	Area%	Peak#	ppm	Area%
S_4	5.294	100.0	S_4	5.295	100.0
R_4	5.288	98.16	R_4	5.289	8.50

(*R*, *E*)-*tert*-Butyl 2-methyl-2-vinyldec-3-enoate (3.123). IR (neat): 2958 (w), 2926 (m), 2855 (w), 1726 (s), 1456 (w), 1409 (m), 1250 (s), 1160 (s), 1123 (s), 971 (m), 915 (m), 850 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.04 (1H, dd, *J* = 18.0, 10.0 Hz), 5.60 (1H, dt, *J* = 16.0, 0.8 Hz), 5.47 (1H, dt, *J* = 15.6, 6.8 Hz), 5.08–5.04 (2H, m), 2.03 (2H, dtd, *J* = 7.6, 7.6, 0.8 Hz), 1.42 (9H, s), 1.37–1.24 (8H, m), 1.32 (3H, s), 0.87 (3H, t, *J* = 6.8 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.2, 141.7, 132.6, 130.3, 113.4, 80.7, 51.4, 32.8, 31.9, 29.5, 28.9, 28.1, 22.8, 21.6, 14.3; HRMS (ESI+): Calcd for $C_{17}H_{31}O_2$ $[M+H]^+$: 267.2324, Found: 267.2325. Optical Rotation: $[\alpha]_D^{20}$ –11.4 (*c* 0.91, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (95.2:4.8 e.r. shown; Chiralcel OD-H column, 99.8/0.2 hexanes/*i*-PrOH, 0.3 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.517	4119220	303701	50.726	50.567
2	11.200	4001372	296892	49.274	49.433
Total		8120592	600593	100.000	100.000



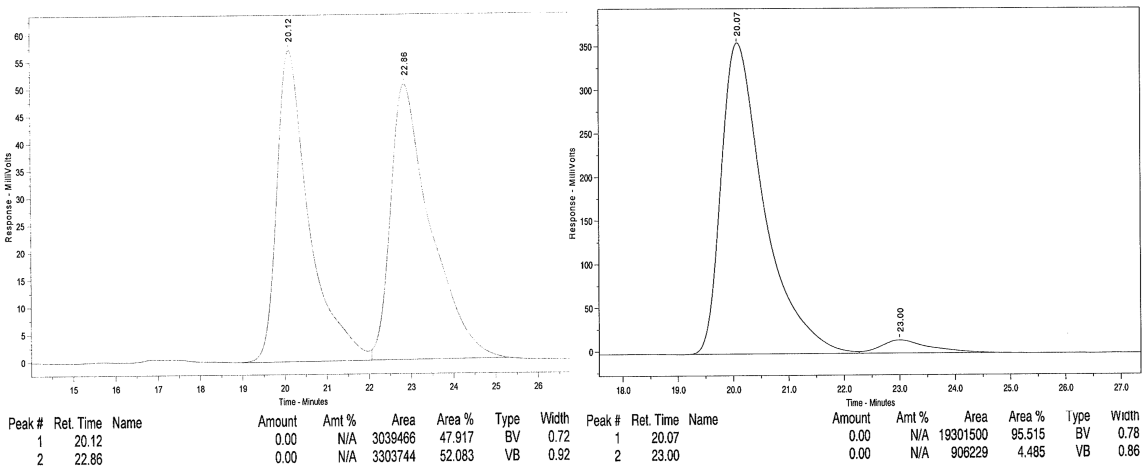
Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.750	2389805	178017	95.248	95.147
2	11.694	119231	9081	4.752	4.853
Total		2509035	187098	100.000	100.000

Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%

1	10.52	50.7	1	10.75	95.2
2	11.20	49.3	2	11.69	4.8

(*R*, *E*)-Dimethyl(3-methylundeca-1,4-dien-3-yl)(phenyl)silane (3.122). IR (neat): 2956 (w), 2925 (w), 2856 (w), 1724 (w), 1427 (w), 1251 (w), 1117 (w), 1052 (w), 1026 (w), 998 (w), 829 (m), 811 (m), 790 (m), 773 (m), 698 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49–7.47 (2H, m), 7.39–7.31 (3H, m), 5.93 (1H, dd, *J* = 17.6, 10.8 Hz), 5.54 (1H, dt, *J* = 15.6, 1.2 Hz), 5.16 (1H, dt, *J* = 15.2, 7.2 Hz), 4.92 (1H, dd, *J* = 10.8, 1.2 Hz), 4.75 (1H, dd, *J* =17.2, 0.8 Hz), 2.03 (2H, dt, *J* = 6.8, 6.8 Hz), 1.36–1.23 (8H, m), 1.11 (3H, s), 0.89 (3H, t, *J* = 6.8 Hz), 0.28 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.3, 136.8, 135.0, 133.9, 129.2, 127.4, 126.8, 109.9, 36.2, 33.4, 32.0, 30.2, 29.1, 22.9, 17.9, 14.3, –5.8; HRMS (ESI+): Calcd for $C_{20}H_{33}Si_1$ $[M+H]^+$: 301.2352, Found: 301.2348. Optical Rotation: $[\alpha]_D^{20}$ –3.56 (*c* 0.46, $CHCl_3$) for an enantiomerically enriched sample of 95.5:4.5 e.r.

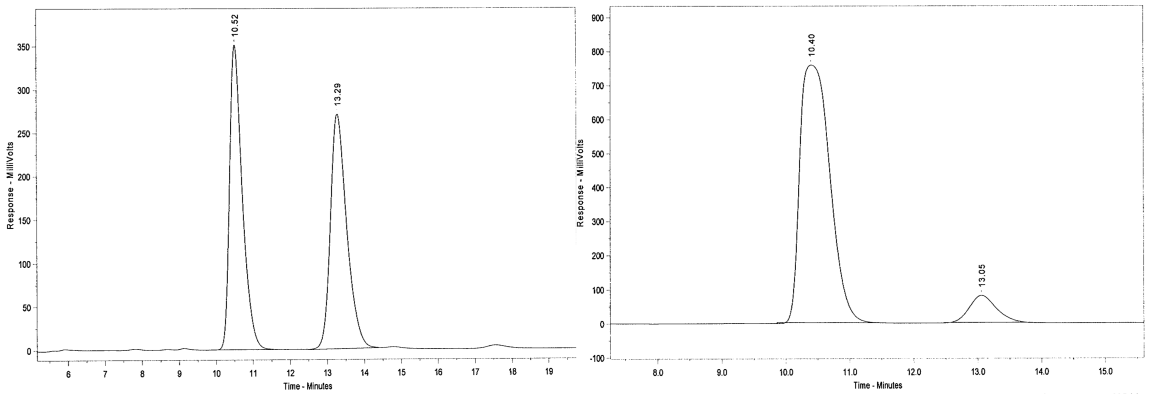
Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (95.5:4.5 e.r. shown; Chiralcel OD column, 99.5/0.5 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	20.12	47.9	1	20.07	95.5
2	22.86	52.1	2	23.00	4.5

(*R*, *E*)-Dimethyl(phenyl)(3,6,6-trimethylhepta-1,4-dien-3-yl)silane (3.129). IR (neat): 2956 (m), 1427 (w), 1247 (m), 1113 (m), 976 (m), 894 (m), 810 (s), 772 (s), 734 (s), 698 (s), 473 (m), 404 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.47–7.45 (2H, m), 7.36–7.32 (3H, m), 5.92 (1H, dd, J = 17.6, 10.8 Hz), 5.42 (1H, d, J = 16.0 Hz), 5.15 (1H, d, J = 16.0 Hz), 4.91 (1H, dd, J = 10.4, 1.2 Hz), 4.74 (1H, dd, J =17.2, 1.2 Hz), 1.09 (3H, s), 0.98 (9H, s), 0.25 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.5, 137.4, 136.8, 134.9, 129.2, 128.6, 127.4, 109.8, 35.8, 33.3, 30.2, 17.8, –6.0; HRMS (ESI+): Calcd for $C_{18}H_{29}Si_1$ $[M+H]^+$: 273.2039, Found: 273.2027. Optical Rotation: $[\alpha]_D^{20}$ +10.82 (*c* 3.58, $CHCl_3$) for an enantiomerically enriched sample of 91:9 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (91.5:8.5 e.r. shown; Chiralcel OD column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



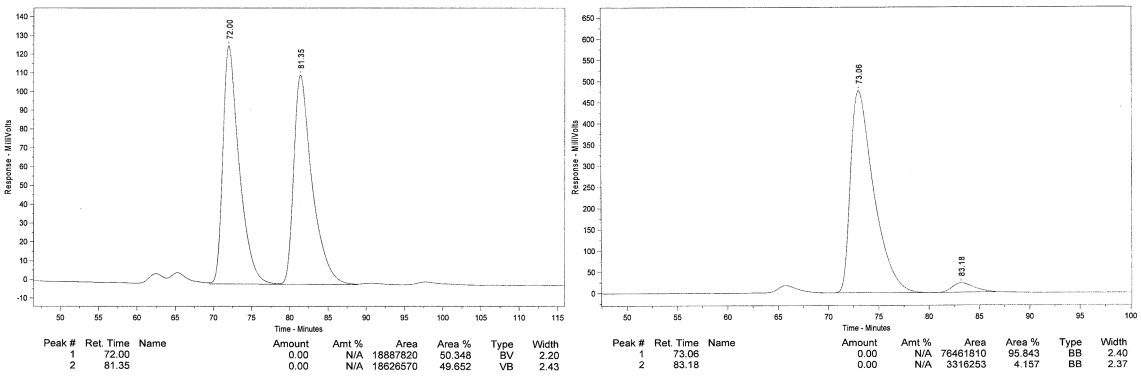
Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	10.52		0.00	N/A	8350070	50.130	BB	0.35
2	13.29		0.00	N/A	8306865	49.870	BB	0.46

Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	10.40		0.00	N/A	24754270	91.494	BB	0.52
2	13.05		0.00	N/A	2301415	8.506	BB	0.45

Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	10.52	50.1	1	10.40	91.5
2	13.29	49.9	2	13.05	8.5

(*R*, *E*)-(9-(*tert*-Butoxy)-3-methylnona-1,4-dien-3-yl)dimethyl(phenyl)silane (3.127). IR (neat): 2970 (m), 2927 (m), 2860 (w), 1621 (w), 1427 (w), 1361 (m), 1248 (m), 1198 (m), 1081 (m), 972 (m), 894 (m), 830 (s), 810 (s), 773 (s), 735 (s), 699 (s), 654 (m), 472 (m), 409 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.48–7.46 (2H, m), 7.36–7.32 (3H, m), 5.91 (1H, dd, J = 17.2, 10.8 Hz), 5.54 (1H, d, J = 15.6 Hz), 5.15 (1H, dt, J = 15.6, 7.2 Hz), 4.91 (1H, dd, J = 10.8, 1.2 Hz), 4.74 (1H, dd, J = 17.2, 1.2 Hz), 3.33 (2H, t, J = 7.6 Hz), 2.04 (2H, dt, J = 7.2, 7.2 Hz), 1.54–1.49 (2H, m), 1.43–1.39 (2H, m), 1.20 (9H, s), 1.10 (3H, s), 0.26 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.3, 136.8, 135.0, 134.1, 129.2, 127.5, 126.6, 110.0, 72.6, 61.7, 36.4, 33.3, 30.5, 29.9, 27.8, 26.9, 17.9, –5.8; HRMS (ESI+): Calcd for $C_{22}H_{36}O_1Si_1Na_1$ $[M+Na]^+$: 367.2433, Found: 367.2420. Optical Rotation: $[\alpha]_D^{20}$ –0.11 (*c* 1.43, $CHCl_3$) for an enantiomerically enriched sample of 96:4 e.r.

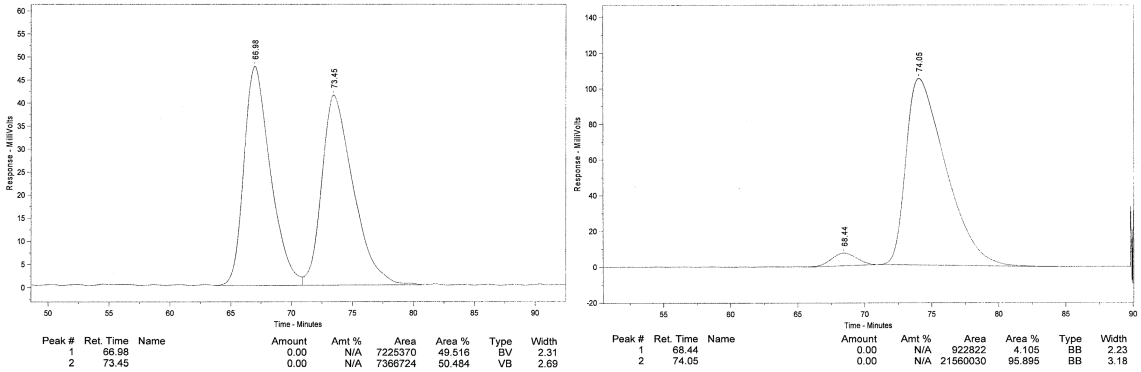
Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (95.8:4.2 e.r. shown; Chiralcel OD column, 99/1 hexanes/*i*-PrOH, 0.2 mL/min, 220 nm).



Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	72.00	50.3	1	72.06	95.8
2	81.35	49.7	2	83.18	4.2

(*R*, *E*)-(8-Chloro-3-methylocta-1,4-dien-3-yl)dimethyl(phenyl)silane (3.128). IR (neat): 2957 (w), 1621 (w), 1427 (w), 1247 (m), 1112 (m), 974 (m), 896 (m), 810 (s), 773 (s), 735 (s), 699 (s), 653 (s), 471 (m), 409 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.47–7.45 (2H, m), 7.37–7.33 (3H, m), 5.91 (1H, dd, J = 17.6, 11.2 Hz), 5.61 (1H, d, J = 15.2 Hz), 5.06 (1H, dt, J = 15.6, 6.4 Hz), 4.92 (1H, dd, J = 11.2, 1.2 Hz), 4.75 (1H, dd, J = 17.6, 1.2 Hz), 3.49 (2H, t, J = 6.8 Hz), 2.18 (2H, dt, J = 6.4, 6.4 Hz), 1.80 (2H, q, J = 7.2 Hz), 1.10 (3H, s), 0.27 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.0, 136.6, 135.8, 134.9, 129.3, 127.6, 124.4, 110.2, 44.7, 36.7, 32.7, 30.4, 17.9, –5.8, –5.8; HRMS (ESI+): Calcd for $C_{17}H_{25}Cl_1Si_1Na_1$ $[M+Na]^+$: 315.1312, Found: 315.1319. Optical Rotation: $[\alpha]_D^{20}$ +0.92 (*c* 2.76, $CHCl_3$) for an enantiomerically enriched sample of 96:4 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (95.9:4.1 e.r. shown; Chiralpak AS column, 99/1 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).

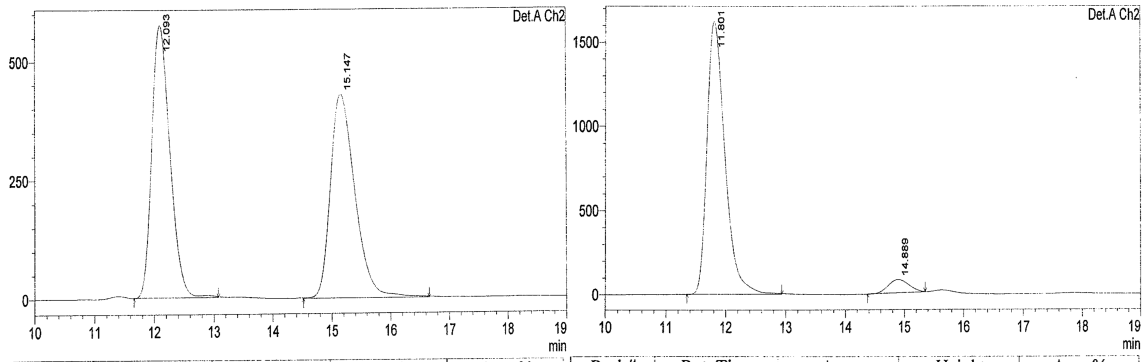


Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	66.98	49.5	1	68.44	4.1
2	73.45	50.5	2	74.05	95.9

(*R*, *Z*)-(6-(*tert*-Butoxy)-3-methylhexa-1,4-dien-3-yl)dimethyl(phenyl)silane (3.130). IR (neat): 2971 (m), 1363 (m), 1248 (m), 1196 (m), 1111 (m), 1069 (m), 892 (m), 808 (s), 773 (s), 735 (s), 700 (s), 654 (m), 474 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.53–7.51 (2H, m), 7.38–7.33 (3H, m), 6.04 (1H, dd, *J* = 17.2, 10.4 Hz), 5.47 (1H, d, *J* = 12.4 Hz), 5.40, (1H, dt, *J* = 11.6, 5.6 Hz), 4.97 (1H, d, *J* = 10.8 Hz), 4.81 (1H, dd, *J* = 17.6, 0.8 Hz), 3.87 (1H, dd, *J* = 11.2, 5.6 Hz), 3.77 (1H, ddd, *J* = 12.0, 6.0, 1.2 Hz), 1.25 (3H, s), 1.14 (9H, s), 0.32 (3H, s), 0.31 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.6, 136.4, 135.0, 133.9, 129.3, 127.9, 127.6, 110.3, 72.9, 58.8, 37.2, 27.8, 19.2, –5.9; HRMS (ESI+): Calcd for $C_{19}H_{30}O_1Si_1Na_1$ $[M+Na]^+$: 325.1964, Found: 325.1973. Optical

Rotation: $[\alpha]_D^{20}$ –26.78 (*c* 1.63, $CHCl_3$) for an enantiomerically enriched sample of 94.8:5.2 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (94.8:5.2 e.r. shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %
1	12.093	12146934	573358	49.406
2	15.147	12439114	429052	50.594
Total		24586047	1002410	100.000

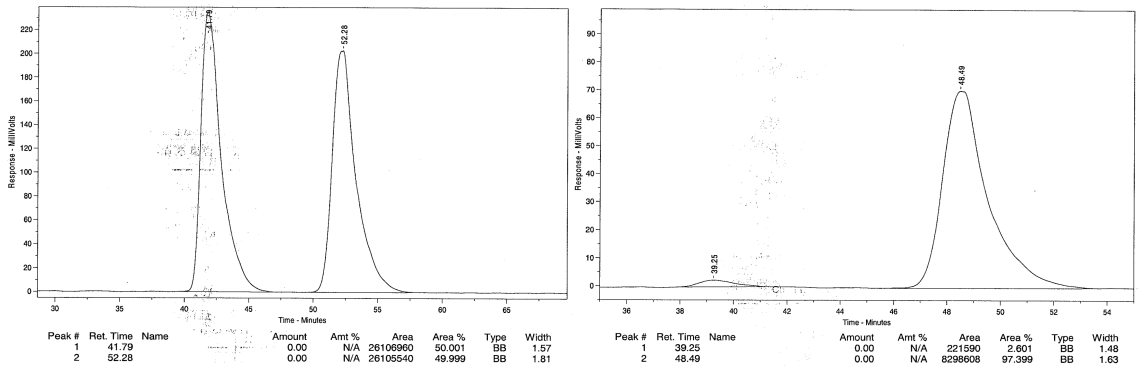
Peak#	Ret. Time	Area	Height	Area %
1	11.801	33980596	1619852	94.790
2	14.889	1867747	78323	5.210
Total		35848343	1698175	100.000

Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	12.09	49.4	1	11.80	94.8
2	15.15	50.6	2	14.89	5.2

(*R*, *E*)-1-Bromo-2-(1-(cyclohex-1-en-1-yl)-3-methylpenta-1,4-dien-3-yl)benzene (3.134). IR (neat): 2925 (m), 1463 (m), 1018 (s), 963 (s), 911 (s), 791 (w), 756 (s), 645 (m), 454 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.58 (1H, dd, *J* = 8.0, 1.6 Hz), 7.46 (1H, dd, *J* = 8.0, 1.6 Hz), 7.26 (1H, dt, *J* = 7.6, 1.2 Hz), 7.08 (1H, dt, *J* = 8.0, 1.6 Hz), 6.22 (1H, dd, *J* = 17.2, 10.4 Hz), 5.92 (2H, s), 5.66–5.64 (1H, m), 5.13 (1H, dd, *J* = 10.8, 1.2 Hz), 4.97 (1H, dd, *J* = 17.6, 0.8 Hz), 2.22–2.18 (2H, m), 2.13–2.09 (2H, m), 1.70–1.65 (2H, m), 1.66 (3H, s), 1.63–1.59 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.9,

145.2, 135.9, 135.6, 132.9, 132.2, 129.7, 128.5, 128.1, 127.2, 124.0, 112.9, 48.7, 26.1, 26.0, 24.8, 22.83, 22.78; HRMS (ESI+): Calcd for $C_{18}H_{22}Br_1$ $[M+H]^+$: 317.0905, Found: 317.0906. Optical Rotation: $[\alpha]_D^{20}$ –27.4 (*c* 1.29, $CHCl_3$) for an enantiomerically enriched sample of 97.5:2.5 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (97.4:2.6 e.r. shown; Chiralcel OD column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).

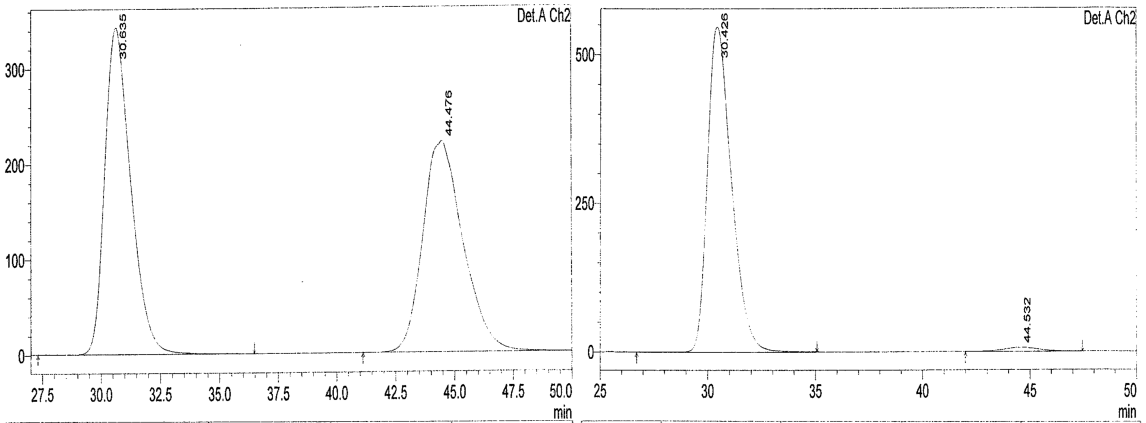


Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	41.79	50.0	1	39.25	2.6
2	52.28	50.0	2	48.49	97.4

(*R*, *E*)-1-Bromo-2-(3-methyl-1-phenylpenta-1,4-dien-3-yl)benzene (3.142). IR (neat): 3080 (w), 3057 (w), 3024 (w), 2971 (w), 2918 (w), 2849 (w), 1630 (w), 1597 (w), 1491 (w), 1464 (w), 1427 (w), 1368 (w), 1018 (m), 963 (m), 912 (m), 746 (s), 690 (s), 646 (w), 458 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.61 (1H, dd, *J* = 8.0, 1.6 Hz), 7.51 (1H, dd, *J* = 7.6, 1.6 Hz), 7.38 (2H, dd, *J* = 8.4, 1.2 Hz), 7.32–7.27 (3H, m), 7.21 (1H, tt, *J* = 6.8, 2.0 Hz), 7.11, (1H, dt, *J* = 8.0, 2.0 Hz), 6.57 (1H, d, *J* = 16.0 Hz), 6.33–6.25 (2H, m),

5.19 (1H, dd, J = 10.4, 0.8 Hz), 5.04 (1H, dd, J = 17.6, 1.2 Hz), 1.75 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.4, 144.6, 137.9, 137.2, 135.6, 131.7, 129.7, 128.7, 128.5, 128.2, 127.2, 126.3, 123.9, 113.4, 49.0, 26.0; HRMS (ESI+): Calcd for $C_{18}H_{18}Br_1$ $[M+H]^+$: 313.0592, Found: 313.0589. Optical Rotation: $[\alpha]_D^{20}$ –31.12 (*c* 0.91, $CHCl_3$) for an enantiomerically enriched sample of 98:2 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (98.2:1.8 e.r. shown; Chiralcel OJ-H column, 95/5 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %
1	30.635	26267229	342739	50.004
2	44.476	26263306	221259	49.996
Total		52530535	563998	100.000

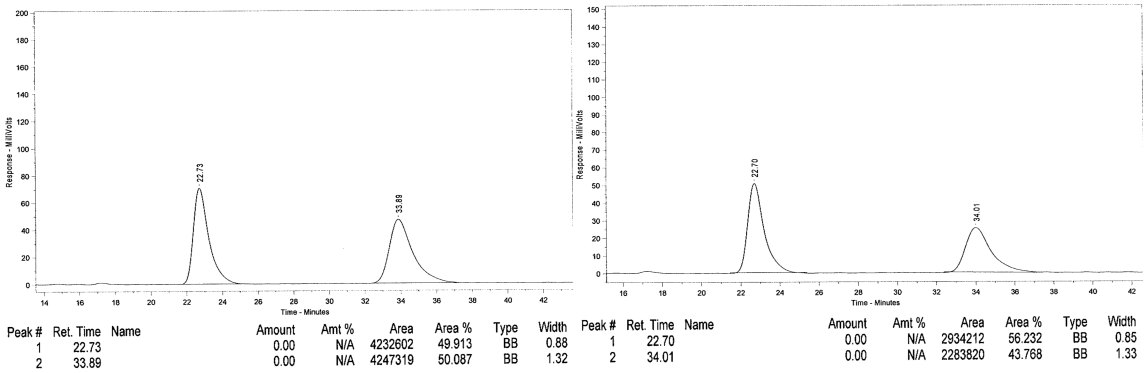
Peak#	Ret. Time	Area	Height	Area %
1	30.426	41880649	546331	98.173
2	44.532	779598	6637	1.827
Total		42660247	552968	100.000

Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	30.64	50.0	1	30.43	98.2
2	44.48	50.0	2	44.53	1.8

(*R*, *Z*)-(1-(4-Methoxyphenyl)-3,7-dimethyl-3-vinylocta-1,6-dien-2-yl)trimethylsilane (3.83). IR (neat): 2964 (w), 2929 (w), 2835 (w), 1609 (w), 1505 (s), 1464 (w), 1283 (w), 1244 (s), 1172 (m), 1038 (m), 911 (w), 835 (s), 763 (s), 679 (w), 646 (w), 573 (w), 514

(w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.20 (1H, s), 7.04 (2H, dd, *J* = 8.8, 1.2 Hz), 6.80 (2H, d, *J* = 8.8 Hz), 5.95 (1H, dd, *J* = 17.6, 10.8 Hz), 5.14–5.09 (1H, m), 5.04–4.97 (2H, m), 3.80 (3H, s), 1.94 (2H, dt, *J* = 8.0, 8.0 Hz), 1.75–1.68 (4H, m), 1.60–1.50 (4H, m), 1.23 (3H, s), –0.09 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.5, 149.5, 148.2, 141.8, 134.1, 131.3, 129.9, 125.1, 113.2, 112.1, 55.4, 47.7, 39.9, 25.9, 25.7, 23.7, 17.9, 3.9; HRMS (ESI+): Calcd for $C_{22}H_{35}O_1Si_1$ $[M+H]^+$: 343.2457, Found: 343.2457.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (56.2:43.8 e.r. shown; Chiralcel OD column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	22.73	49.9	1	22.70	56.2
2	33.89	50.1	2	34.01	43.8

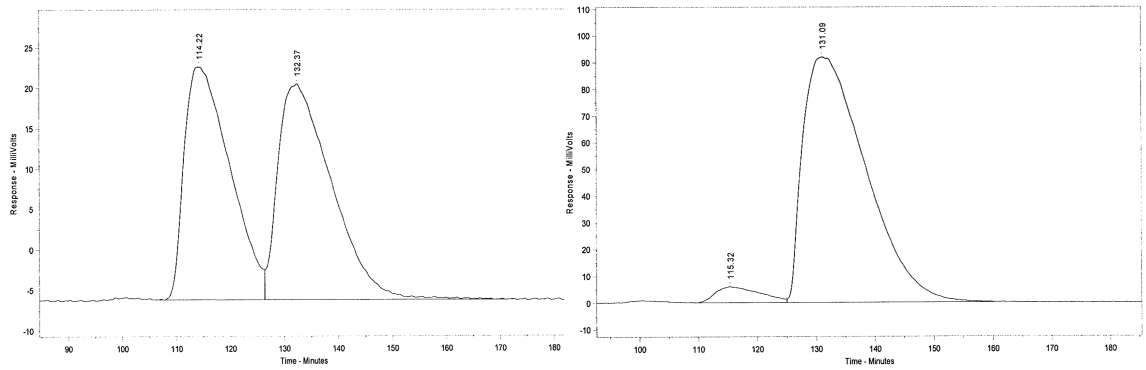
■ **General Procedure for $Ni(PPh_3)_2Cl_2$-catalyzed Hydroalumination of Aryl-substituted Terminal Alkynes (Table 3.12, Scheme 3.16 and 3.18):** Commercial grade bis(triphenylphosphine)nickel dichloride ($Ni(PPh_3)_2Cl_2$, 19.6 mg, 0.0300 mmol) is placed

in an oven-dried 13 x 100 mm test tube equipped with a stir bar. The test tube is sealed with a septum and purged with N_2 for approximately ten minutes. Tetrahydrofuran (thf, 1.0 mL) is added through a syringe, followed by dropwise addition of dibal–H (232 μL, 1.3 mmol) at 22 °C (gas evolution occurs as dibal–H is added). The resulting black solution is allowed to cool to 0 °C (ice bath) before phenylacetylene (110 μL, 1.0 mmol) is added slowly over five minutes (reaction is exothermic). The resulting black solution is allowed to warm to 22 °C and stir for additional two hours and used without further purification.

■ **General Procedure for Cu-catalyzed Enantioselective Allylic Substitutions with Aryl-substituted Vinylaluminum Reagents (Table 3.12 and Scheme 3.16 and 3.18):** A 13 x 100 mm test tube equipped with a stir bar is charged with NHC–Ag complex **ent-3.39** (2.3 mg, 0.0020 mmol) in an N_2-filled glovebox. The test tube is sealed with a septum and removed from the glovebox. Tetrahydrofuran (1.0 mL) and a solution of $CuCl_2$•$2H_2O$ (0.02M in thf, 200 μL, 0.0040 mmol) are added to the test tube at 22 °C. The resulting blue solution is allowed to cool to –78 °C (dry ice/acetone), followed by the addition of the aryl-substituted vinylaluminum reagent (0.745 M in thf, 403 μL, 0.300 mmol) and a solution of (*E*)-diethyl (3-phenylbut-2-en-1-yl) phosphate (56.9 mg, 0.200 mmol) in thf (1.0 mL). The mixture is allowed to warm to –15 °C and sit in a freezer for 3 h, after which time, the reaction is quenched by addition of a saturated aqueous solution of Rochelle's salt (2.0 mL) at –78 °C and the resulting mixture is allowed to warm to 22 °C and stir for 1 h. The layers are separated, and the aqueous layer is washed with Et_2O (2.0 mL x 3). The combined organic layers are passed through a short plug of $MgSO_4$, and concentrated under reduced pressure. The resulting yellow oil is purified by silica

gel chromatography to give the product as colorless oil (36.6 mg, 0.156 mmol, 78% yield). **(*R*, *E*)-(3-Methylpenta-1,4-diene-1,3-diyl)dibenzene (3.138).** IR (neat): 3082 (w), 3057 (w), 3025 (w), 2973 (w), 2917 (w), 2872 (w), 2849 (w), 1633 (w), 1598 (w), 1492 (m), 1445 (m), 1408 (w), 1368 (w), 1072 (w), 1029 (w), 971 (m), 916 (m), 748 (s), 694 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.34–7.29 (4H, m), 7.28–7.22 (4H, m), 7.18–7.13 (2H, m), 6.39 (1H, d, J = 16.0 Hz), 6.29 (1H, d, J = 16.0 Hz), 6.09 (1H, dd, J = 17.6, 10.4 Hz), 5.11 (1H, dd, J = 10.8, 1.2 Hz), 5.00 (1H, dd, J = 17.6, 1.2 Hz), 1.55 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.5, 145.2, 137.7, 137.3, 131.7, 128.7, 128.4, 128.2, 127.4, 127.3, 126.4, 113.2, 48.0, 25.7; HRMS (ESI+): Calcd for $C_{18}H_{19}$ $[M+H]^+$: 235.1487, Found: 235.1476. Optical Rotation: $[\alpha]_D^{20}$ +33.80 (*c* 2.02, $CHCl_3$) for an enantiomerically enriched sample of 96:4 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (95.6:4.4 e.r. shown; Chiralpak AS column, 99/1 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	114.22		0.00	N/A	17014080	47.981	BV	9.66
2	132.37		0.00	N/A	18446020	52.019	VB	10.87

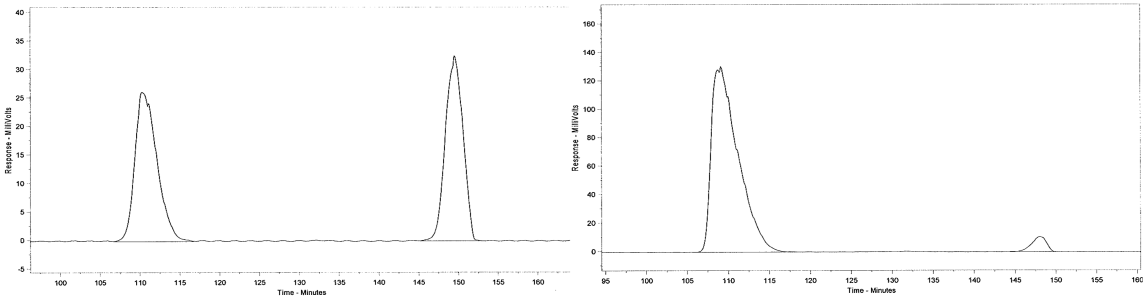
Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	115.32		0.00	N/A	3135952	4.376	BV	9.13
2	131.09		0.00	N/A	68528960	95.624	VB	11.91

Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%

1	114.22	48.0	1	115.32	4.4
2	132.37	52.0	2	131.09	95.6

(*R*, *E*)-1-Methyl-2-(3-methyl-3-phenylpenta-1,4-dien-1-yl)benzene (3.141). Spectra are taken in the presence of 12% alkynyl adduct. IR (neat): 3059 (w), 3021 (w), 2958 (m), 2924 (m), 2854 (m), 1634 (w), 1600 (w), 1490 (m), 1459 (m), 1378 (w), 1029 (w), 951 (m), 916 (m), 747 (s), 698 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.48–7.46 (1H, m), 7.42–7.38 (2H, m), 7.37–7.32 (2H, m), 7.26–7.21 (2H, m), 7.19–7.14 (2H, m), 6.59 (1H, d, *J* = 16.0 Hz), 6.33 (1H, d, *J* = 16.0 Hz), 6.20 (1H, dd, *J* = 17.2, 10.4 Hz), 5.21 (1H, dd, *J* = 10.8, 1.2 Hz), 5.10 (1H, dd, *J* = 17.6, 1.2 Hz), 2.33 (3H, s), 1.64 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.6, 145.3, 138.8, 137.0, 135.5, 132.1, 130.3, 128.3, 127.4, 127.3, 126.4, 126.2, 125.8, 113.2, 48.1, 25.8, 20.0; HRMS (ESI+): Calcd for $C_{19}H_{21}$ $[M+H]^+$: 249.1643, Found: 249.1643. Optical Rotation: $[\alpha]_D^{20}$ –29.53 (*c* 1.63, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (95.9:4.1 e.r. shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



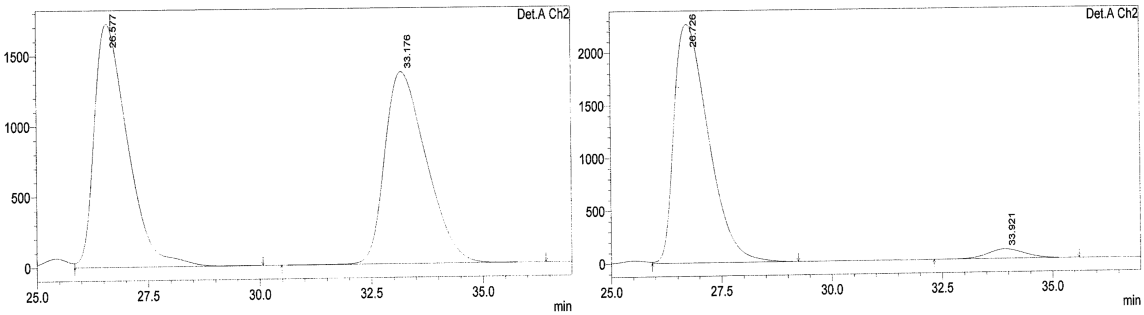
Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	110.25		0.00	N/A	5077918	50.217	BB	2.99
2	149.52		0.00	N/A	5034133	49.784	BB	2.51

Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	109.14		0.00	N/A	29436000	95.854	BB	3.51
2	148.03		0.00	N/A	1273114	4.146	BB	1.99

Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	110.25	50.2	1	109.14	95.9
2	149.52	49.8	2	148.03	4.1

(*R*, *E*)-1-Methoxy-4-(3-methyl-3-phenylpenta-1,4-dien-1-yl)benzene (3.139). IR (neat): 3082 (w), 3056 (w), 3030 (w), 3021 (w), 2970 (w), 2933 (w), 2835 (w), 1607 (m), 1510 (s), 1443 (w), 1280 (w), 1246 (s), 1174 (m), 1034 (m), 972 (w), 917 (w), 808 (w), 762 (m), 700 (m), 533 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.39–7.30 (6H, m), 7.22 (1H, tt, *J* = 6.4, 2.0 Hz), 6.88–6.84 (2H, m), 6.33 (2H, s), 6.17 (1H, dd, *J* = 17.6, 10.4 Hz), 5.18 (1H, dd, *J* = 10.4, 1.2 Hz), 5.07 (1H, dd, *J* = 17.2, 1.2 Hz), 3.81 (3H, s), 1.60 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.1, 146.7, 145.4, 135.2, 130.4, 128.3, 127.6, 127.5, 127.4, 126.3, 114.1, 113.0, 55.5, 47.9, 25.8; HRMS (ESI+): Calcd for $C_{19}H_{21}O_1$ $[M+H]^+$: 265.1592, Found: 265.1590. Optical Rotation: $[\alpha]_D^{20}$ +24.49 (*c* 1.16, $CHCl_3$) for an enantiomerically enriched sample of 96.5:3.5 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (95.9:4.1 e.r. shown; Chiralcel OD-H column, 97/3 hexanes/*i*-PrOH, 1.0 mL/min, 254 nm).



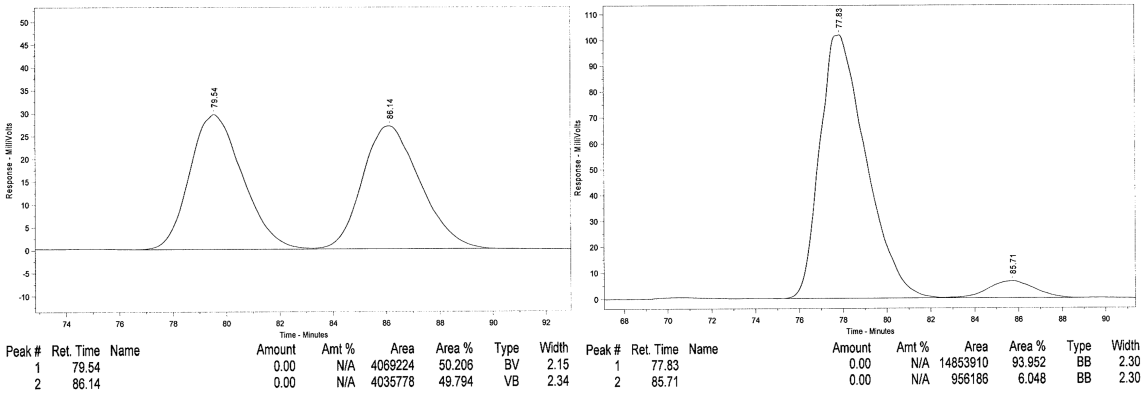
Peak#	Ret. Time	Area	Height	Area %
1	26.577	89643798	1722114	50.446
2	33.176	88057866	1364330	49.554
Total		177701664	3086445	100.000

Peak#	Ret. Time	Area	Height	Area %
1	26.726	122902957	2263135	95.916
2	33.921	5233178	90344	4.084
Total		128136135	2353479	100.000

Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	26.58	50.4	1	26.73	95.9
2	33.18	49.6	2	33.92	4.1

(*R*, *E*)-1-(3-Methyl-3-phenylpenta-1,4-dien-1-yl)-4-(trifluoromethyl)benzene (3.140). IR (neat): 2924 (m), 2854 (w), 1615 (w), 1323 (s), 1165 (m), 1125 (s), 1067 (s), 1016 (w), 975 (w), 919 (w), 815 (w), 762 (w), 699 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.56 (2H, d, *J* = 8.4 Hz), 7.48 (2H, d, *J* = 8.4 Hz), 7.38–7.32 (4H, m), 7.27–7.22 (1H, m), 6.57 (1H, d, *J* = 16.0 Hz), 6.40 (1H, d, *J* = 16.0 Hz), 6.17 (1H, dd, *J* = 17.6, 10.4 Hz), 5.22 (1H, dd, *J* = 10.8, 1.2 Hz), 5.09 (1H, dd, *J* = 17.6, 1.2 Hz), 1.63 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.0, 144.8 (q, *J* = 5.2 Hz), 141.2 (q, *J* = 1.5 Hz), 140.0 (q, *J* = 3.0 Hz), 132.1, 129.2 (q, *J* = 32.0 Hz), 128.5, 127.3, 127.1 (q, *J* = 3.8 Hz), 126.6 (q, *J* = 4.5 Hz), 125.7 (q, *J* = 10.4 Hz), 124.4 (q, *J* = 270.0 Hz), 113.6 (q, *J* = 3.0 Hz), 48.1, 25.6; HRMS (ESI+): Calcd for $C_{19}H_{18}F_3$ $[M+H]^+$: 303.1361, Found: 303.1373. Optical Rotation: $[\alpha]_D^{20}$ –26.78 (*c* 2.47, $CHCl_3$) for an enantiomerically enriched sample of 94:6 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (94.0:6.0 e.r. shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



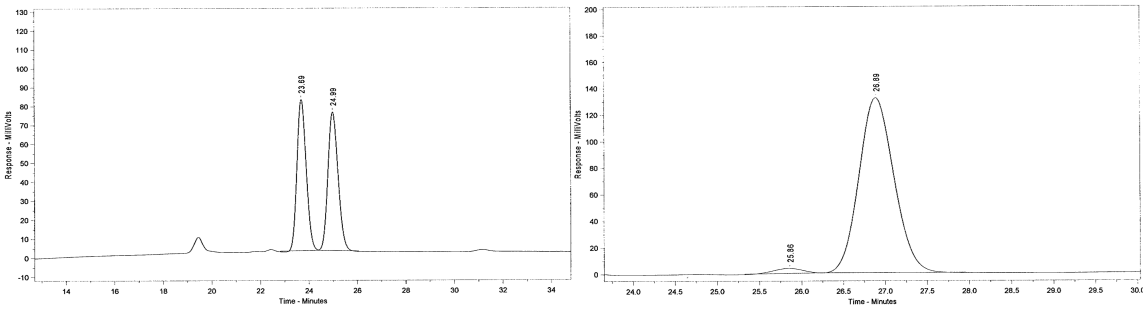
Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	79.54		0.00	N/A	4069224	50.206	BV	2.15
2	86.14		0.00	N/A	4035778	49.794	VB	2.34

Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	77.83		0.00	N/A	14853910	93.952	BB	2.30
2	85.71		0.00	N/A	956186	6.048	BB	2.30

Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	79.54	50.2	1	77.83	94.0
2	86.14	49.8	2	85.71	6.0

(*R*, *E*)-1-(3-Methyl-1-phenylpenta-1,4-dien-3-yl)-2-nitrobenzene (3.144). IR (neat): 3082 (w), 3026 (w), 2925 (w), 2854 (w), 1528 (s), 1366 (s), 971 (m), 909 (s), 852 (m), 777 (m), 731 (s), 692 (s), 649 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.59 (1H, dd, J = 8.0, 1.2 Hz), 7.50–7.46 (2H, m), 7.38–7.29 (5H, m), 7.23 (1H, tt, J = 6.4, 1.6 Hz), 6.40 (1H, d, J = 16.4 Hz), 6.35 (1H, d, J = 16.4 Hz), 6.10 (1H, dd, J = 17.6, 10.4 Hz), 5.18 (1H, d, J = 10.8 Hz), 5.13 (1H, d, J = 17.6 Hz), 1.79 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.4, 142.7, 138.8, 137.2, 134.8, 131.4, 130.4, 128.8, 128.7, 127.8, 127.6, 126.5, 124.5, 113.8, 47.7, 25.6; HRMS (ESI+): Calcd for $C_{18}H_{18}N_1O_2$ $[M+H]^+$: 280.1338, Found: 280.1327. Optical Rotation: $[\alpha]_D^{20}$ –23.19 (*c* 1.71, $CHCl_3$) for an enantiomerically enriched sample of 98:2 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (97.8:2.2 e.r. shown; Chiralcel OD-H column, 99.5/0.5 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



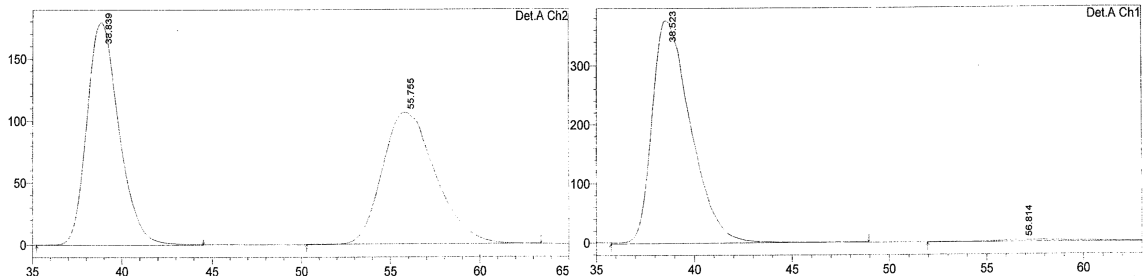
Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	23.69		0.00	N/A	2109513	49.710	BB	0.42
2	24.99		0.00	N/A	2134112	50.290	BB	0.46

Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	25.86		0.00	N/A	85797	2.192	BB	0.44
2	26.89		0.00	N/A	3828763	97.808	BB	0.45

Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	23.69	49.7	1	25.86	2.2
2	24.99	50.3	2	28.89	97.8

(*R*, *E*)-1-(1-(4-Methoxyphenyl)-3-methylpenta-1,4-dien-3-yl)-2-methylbenzene (3.143). IR (neat): 3000 (w), 2968 (w), 2932 (w), 2835 (w), 1607 (m), 1510 (s), 1248 (s), 1175 (m), 1036 (m), 972 (w), 915 (w), 815 (w), 759 (w), 730 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.42–7.40 (1H, m), 7.29–7.25 (2H, m), 7.19–7.13 (3H, m), 6.85–6.80 (2H, m), 6.38 (1H, d, *J* = 16.0 Hz), 6.25–6.15 (2H, m), 5.11 (1H, dd, *J* = 10.8, 1.2 Hz), 4.95 (1H, dd, *J* = 17.2, 1.2 Hz), 3.80 (3H, s), 2.33 (3H, s), 1.62 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.8, 145.4, 144.1, 137.4, 135.5, 132.3, 130.5, 127.5, 127.2, 126.9, 126.5, 125.6, 113.9, 112.3, 55.3, 48.2, 27.0, 22.6; HRMS (ESI+): Calcd for $C_{20}H_{21}O_1$ $[M+H]^+$: 277.1592, Found: 277.1598. Optical Rotation: $[\alpha]_D^{20}$ –14.23 (*c* 1.07, $CHCl_3$) for an enantiomerically enriched sample of 98:2 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (98.1:1.9 e.r. shown; Chiralcel OJ-H column, 95/5 hexanes/*i*-PrOH, 1.0 mL/min, 254 nm).



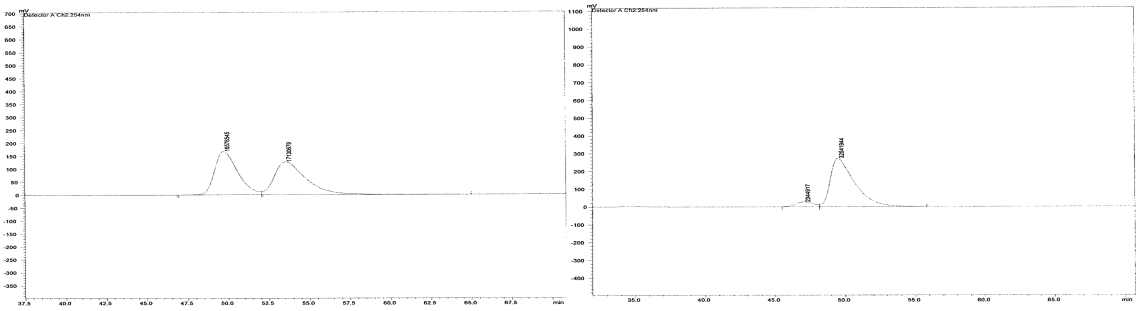
Peak#	Ret. Time	Area	Height	Area %
1	38.839	22537602	179456	50.954
2	55.755	21693733	106012	49.046
Total		44231335	285468	100.000

Peak#	Ret. Time	Area	Height	Area %
1	38.523	51401863	376815	98.122
2	56.814	983787	3129	1.878
Total		52385650	379944	100.000

Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	38.84	51.0	1	38.52	98.1
2	55.76	49.0	2	56.81	1.9

(*R*, *E*)-1-(3-Methyl-1-phenylpenta-1,4-dien-3-yl)-4-nitrobenzene (3.145). IR (neat): 3082 (w), 3026 (w), 2974 (w), 2931 (w), 2852 (w), 1596 (m), 1514 (s), 1343 (s), 1111 (w), 1068 (w), 971 (m), 919 (m), 852 (s), 748 (s), 735 (s), 692 (s), 613 (w), 537 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.19–8.15 (2H, m), 7.55–7.52 (2H, m), 7.40–7.37 (2H, m), 7.34–7.31 (2H, m), 7.27–7.25 (1H, m), 6.44–6.35 (2H, m), 6.14 (1H, dd, *J* = 17.6, 10.8 Hz), 5.27 (1H, dd, *J* = 10.4, 0.8 Hz), 5.10 (1H, dd, *J* = 17.6, 0.8 Hz), 1.64 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.2, 146.6, 143.8, 137.0, 135.5, 129.5, 128.8, 128.4, 127.8, 126.5, 123.6, 114.5, 48.3, 25.8; HRMS (ESI+): Calcd for $C_{18}H_{18}N_1O_2$ $[M+H]^+$: 280.1338, Found: 280.1339. Optical Rotation: $[\alpha]_D^{20}$ –20.37 (*c* 2.42, $CHCl_3$) for an enantiomerically enriched sample of 93:7 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (93.7:6.3 e.r. shown; Chiralcel OJ-H column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 254 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	49.706	16576545	166872	49.178	56.845
2	53.528	17130679	126687	50.822	43.155
Total		33707225	293559	100.000	100.000

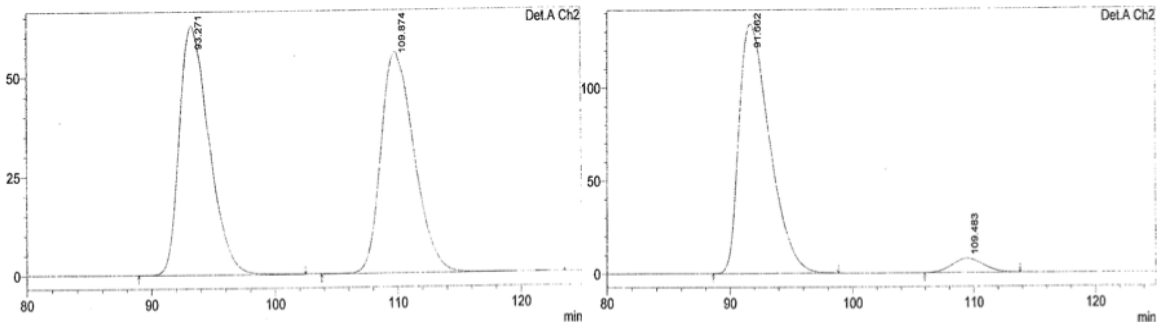
Peak#	Ret. Time	Area	Height	Area %	Height %
1	47.062	2344917	27231	6.721	9.125
2	49.485	32541944	271196	93.279	90.875
Total		34886861	298427	100.000	100.000

Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	49.71	49.2	1	47.06	6.7
2	53.53	50.8	2	49.49	93.3

(*R*, *E*)-1-Methoxy-4-(3-methyl-3-(4-(trifluoromethyl)phenyl)penta-1,4-dien-1-yl)benzene (3.146). IR (neat): 2957 (w), 2926 (w), 2854 (w), 1608 (w), 1511 (m), 1326 (s), 1248 (m), 1165 (m), 1123 (s), 1076 (m), 1036 (w), 1016 (w), 973 (w), 921 (w), 841 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.56 (2H, d, *J* = 8.0 Hz), 7.48 (2H, d, *J* = 8.0 Hz), 7.34–7.30 (2H, m), 6.87–6.84 (2H, m), 6.32 (1H, d, *J* = 16.4 Hz), 6.26 (1H, d, *J* = 16.4 Hz), 6.13 (1H, dd, *J* = 17.2, 10.4 Hz), 5.22 (1H, dd, *J* = 10.8, 1.2 Hz), 5.07 (1H, dd, *J* = 17.6, 1.2 Hz), 3.81 (3H, s), 1.60 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.3, 150.9, 144.6, 134.2, 130.1, 128.6 (q, *J* = 32.0 Hz), 128.4, 127.8, 127.6, 125.2 (q, *J* = 3.7 Hz), 124.4 (q, *J* = 270.1 Hz), 114.2, 113.8, 55.5, 48.0, 25.8; HRMS (ESI+): Calcd for

$C_{20}H_{20}F_3O_1$ $[M+H]^+$: 333.1466, Found: 333.1480. Optical Rotation: $[\alpha]_D^{20}$ –22.91 (*c* 1.11, $CHCl_3$) for an enantiomerically enriched sample of 94:6 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (94.0:6.0 e.r. shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %
1	93.271	10594147	62857	50.263
2	109.874	10483365	55838	49.737
Total		21077512	118695	100.000

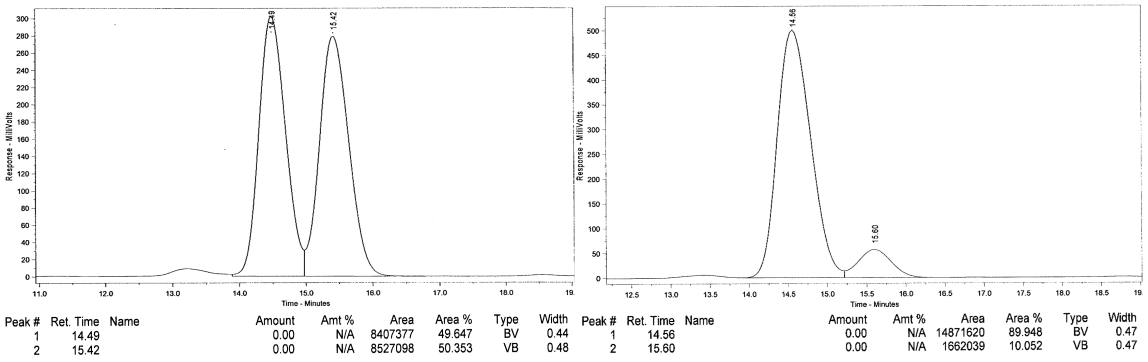
Peak#	Ret. Time	Area	Height	Area %
1	91.650	18888094	106429	93.976
2	109.481	1210681	6303	6.024
Total		20098775	112731	100.000

Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	93.27	50.3	1	91.65	94.0
2	109.87	49.7	2	109.48	6.0

(*R*, *E*)-(3,7-Dimethyl-3-vinylocta-1,6-dien-1-yl)benzene (3.147). IR (neat): 3082 (w), 3059 (w), 3026 (w), 2966 (w), 2915 (w), 2854 (w), 1633 (w), 1598 (w), 1492 (w), 1447 (w), 1374 (w), 968 (m), 912 (m), 831 (w), 745 (s), 691 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.39–7.37 (2H, m), 7.33–7.29 (2H, m), 7.21 (1H, tt, *J* = 6.4, 1.6 Hz), 6.34 (1H, d, *J* = 16.8 Hz), 6.22 (1H, d, *J* = 16.0 Hz), 5.91 (1H, dd, *J* = 17.2, 10.8 Hz), 5.15–5.11 (1H, m), 5.08–5.02 (2H, m), 1.98 (2H, dt, *J* = 7.6, 7.6 Hz), 1.69 (3H, s), 1.60 (3H, s), 1.55–1.50 (2H, m), 1.23 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.9, 138.05, 138.03,

131.5, 128.6, 127.4, 127.1, 126.2, 124.9, 112.2, 42.8, 41.4, 25.8, 23.5, 23.4, 17.8; HRMS (ESI+): Calcd for $C_{18}H_{25}$ $[M+H]^+$: 241.1956, Found: 241.1945. Optical Rotation: $[\alpha]_D^{20}$ +23.80 (*c* 1.83, $CHCl_3$) for an enantiomerically enriched sample of 90:10 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (89.9:10.1 e.r. shown; Chiralcel OD-H column, 95/5 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).

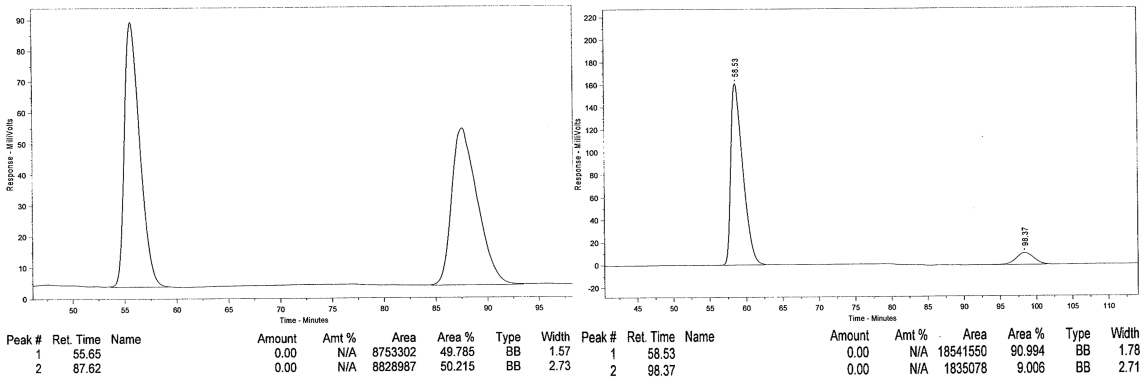


Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	14.49	49.6	1	14.56	89.9
2	15.42	50.4	2	15.60	10.1

(*R*, *E*)-1-(3,7-Dimethyl-3-vinylocta-1,6-dien-1-yl)-2-methylbenzene (3.149). Spectra are taken in the presence of 14% alkynyl adduct. IR (neat): 3019 (w), 2967 (m), 2921 (m), 2856 (w), 1636 (w), 1602 (w), 1511 (w), 1484 (w), 1457 (m), 1376 (w), 1248 (w), 1036 (w), 972 (m), 914 (m), 748 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.43–7.40 (1H, m), 7.20–7.11 (3H, m), 6.53 (1H, d, *J* = 16.4 Hz), 6.07 (1H, d, *J* = 16.4 Hz), 5.92 (1H, dd, *J* = 17.6, 10.8 Hz), 5.16–5.10 (1H, m), 5.08–5.02 (2H, m), 2.34 (3H, s), 1.98 (2H, dt, *J* = 7.6, 7.6 Hz), 1.69 (3H, s), 1.60 (3H, s), 1.53–1.50 (2H, m), 1.23 (3H, s); ^{13}C NMR (100

MHz, $CDCl_3$): δ 146.0, 143.6, 139.6, 137.4, 135.3, 132.1, 131.5, 130.2, 127.0, 126.2, 124.9, 112.2, 43.0, 42.4, 41.4, 25.8, 23.7, 23.4, 17.8; HRMS (ESI+): Calcd for $C_{19}H_{27}$ $[M+H]^+$: 255.2113, Found: 255.2115. Optical Rotation: $[\alpha]_D^{20}$ –23.46 (*c* 1.02, $CHCl_3$) for an enantiomerically enriched sample of 91:9 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (91.0:9.0 e.r. shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	55.65		0.00	N/A	8753302	49.785	BB	1.57
2	87.62		0.00	N/A	8828987	50.215	BB	2.73

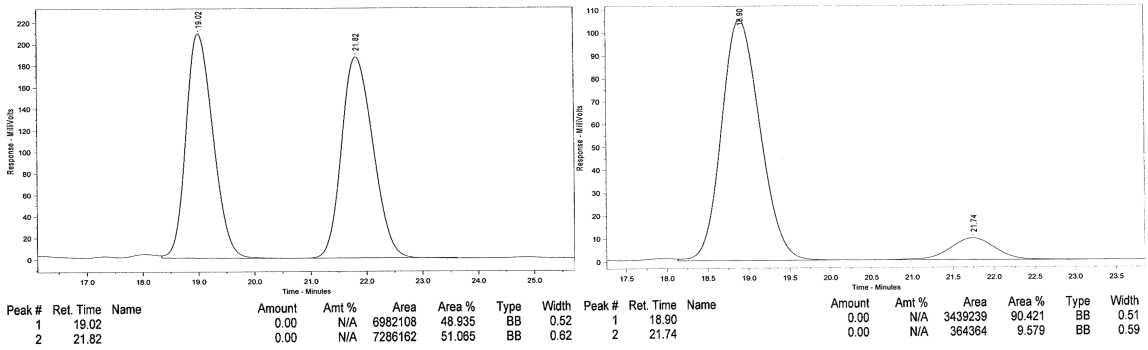
Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	58.53		0.00	N/A	18541550	90.994	BB	1.78
2	98.37		0.00	N/A	1835078	9.006	BB	2.71

Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	55.65	49.8	1	58.53	91.0
2	87.62	50.2	2	98.37	9.0

(*R*, *E*)-1-(3,7-Dimethyl-3-vinylocta-1,6-dien-1-yl)-4-methoxybenzene (bakuchiol methylether). IR (neat): 2965 (m), 2916 (m), 1608 (m), 1510 (s), 1456 (w), 1280 (s), 1247 (m), 1037 (m), 970 (w), 913 (w), 815 (w), 527 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.31–7.29 (2H, m), 6.86–6.84 (2H, m), 6.27 (1H, d, *J* = 16.4 Hz), 6.07 (1H, d, *J* = 16.4 Hz), 5.89 (1H, dd, *J* = 17.2, 10.8 Hz), 5.14–5.10 (1H, m), 5.06–5.00 (2H, m), 3.81 (3H, s), 1.96 (2H, dt, *J* = 7.6, 7.6 Hz), 1.68 (3H, s), 1.59 (3H, s), 1.53–1.48 (2H, m),

1.21 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.9, 146.2, 136.0, 131.4, 130.9, 127.3, 126.7, 124.9, 114.1, 112.0, 55.5, 42.7, 41.5, 25.8, 23.5, 23.4, 17.8; HRMS (ESI+): Calcd for $C_{19}H_{27}O_1$ $[M+H]^+$: 271.2062, Found: 271.2064. Optical Rotation: $[\alpha]_D^{20}$ –25.16 (*c* 1.91, $CHCl_3$) for an enantiomerically enriched sample of 91:9 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (90.4:9.6 e.r. shown; Chiralcel OD-H column, 97/3 hexanes/*i*-PrOH, 0.8 mL/min, 220 nm).



Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	19.02		0.00	N/A	6982108	48.935	BB	0.52
2	21.82		0.00	N/A	7286162	51.065	BB	0.62

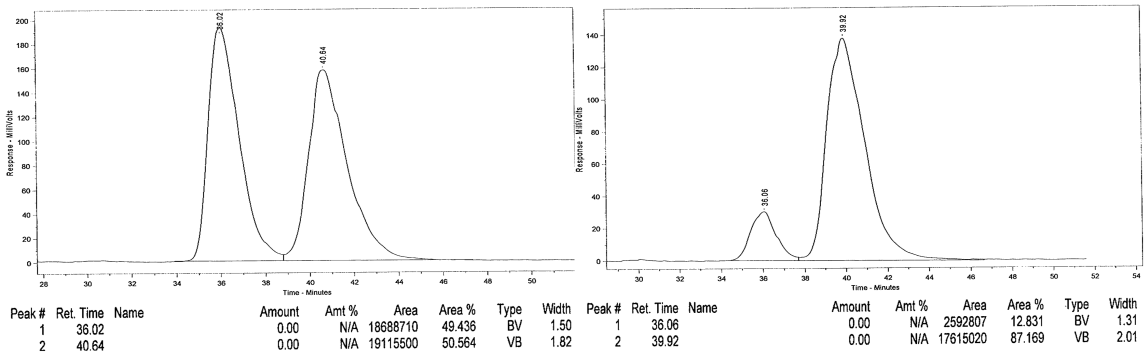
Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	18.90		0.00	N/A	3439239	90.421	BB	0.51
2	21.74		0.00	N/A	364364	9.579	BB	0.59

Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
1	19.02	48.9	1	18.90	90.4
2	21.82	51.1	2	21.74	9.6

(*R*, *E*)-1-(3,7-Dimethyl-3-vinylocta-1,6-dien-1-yl)-4-(trifluoromethyl)benzene (3.148). IR (neat): 2969 (w), 2919 (w), 1616 (w), 1453 (w), 1413 (w), 1376 (w), 1323 (s), 1164 (m), 1124 (s), 1067 (m), 1016 (w), 973 (w), 916 (w), 817 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (2H, d, *J* = 8.4 Hz), 7.44 (2H, d, *J* = 8.4 Hz), 6.36 (1H, d, *J* = 16.0 Hz), 6.30 (1H, d, *J* = 16.0 Hz), 5.89 (1H, ddd, *J* = 17.2, 10.4, 0.8 Hz), 5.12–5.06 (2H, m), 5.03 (1H, dd, *J* = 17.2, 1.2 Hz), 1.96 (2H, dt, *J* = 7.2, 7.2 Hz), 1.68 (3H, s), 1.58 (3H, s), 1.55–

1.50 (2H, m), 1.23 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.4, 141.5 (q, J = 1.4 Hz), 140.9, 131.7, 128.9 (q, J = 32.0 Hz), 126.4, 126.2, 125.6 (q, J = 3.7 Hz), 124.7, 124.4 (q, J = 270.1 Hz), 112.6, 43.0, 41.3, 25.8, 23.4, 23.3, 17.8; HRMS (ESI+): Calcd for $C_{19}H_{24}F_3$ $[M+H]^+$: 309.1830, Found: 309.1830. Optical Rotation: $[\alpha]_D^{20}$ +13.68 (*c* 1.41, $CHCl_3$) for an enantiomerically enriched sample of 87:13 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with H_2O_2) in comparison with authentic racemic material (87.2:12.8 e.r. shown; Chiralcel OJ-H column, 99/1 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



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Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
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2	39.92		0.00	N/A	17615020	87.169	VB	2.01

Peak#	Ret. Time	Area%	Peak#	Ret. Time	Area%
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2	40.64	50.6	2	39.92	87.2

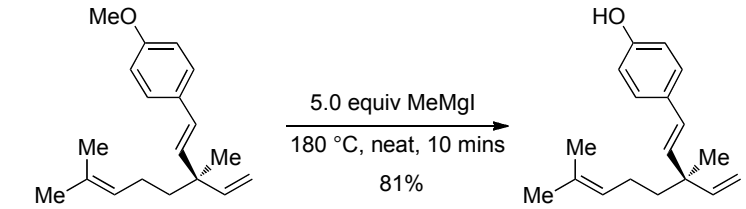
■ **Stereochemistry Proof and Enantioselective Total Synthesis of *R*-(–)-bakuchiol (Scheme 6): Procedure for Demethylation of Bakuchiol Methyl Ether.** A flame-dried 6-dram vial is charged with bakuchiol methyl ether (21.4 mg, 0.079 mmol) and a stir bar. The vial is sealed with a septum and purged with N_2 flow for 10 minutes. Freshly

prepared MeMgI in diethyl ether (990 μL, 0.396 mmol) is added to the reaction vessel and solvent is carefully removed under reduced pressure. Neat reaction mixture is allowed to be heated in a 180 ^{o}C oil bath for 10 minutes (white smoke generated as the reaction goes on and disappears in 10 minutes), after which time, the vessel is allowed to cool to 22 ^{o}C and diluted with diethyl ether (5 mL). A saturated solution of NH_4Cl is added to quench the reaction and layers are separated. The aqueous layer is washed with Et_2O (5 mL x 3) and the combined organic layers are dried with anhydrous $MgSO_4$, filtered and concentrated *in vacuo* to afford crude product as slightly yellow oil. The crude is subjected to silica gel chromatography (10:1 hexanes:ethyl acetate) to furnish the desired product as colorless oil (16.4 mg, 0.064 mmol, 81% yield). ***R*-(–)-bakuchiol.** IR (neat): 3345 (br), 2966 (m), 2919 (m), 2862 (w), 1609 (m), 1511 (s), 1441 (m), 1374 (w), 1235 (m), 1171 (m), 970 (m), 914 (m), 813 (w), 527 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27–7.24 (2H, m), 6.79–6.76 (2H, m), 6.25 (1H, d, *J* = 16.0 Hz), 6.06 (1H, d, *J* = 16.0 Hz), 5.88 (1H, dd, *J* = 17.2, 10.8 Hz), 5.13–5.09 (1H, m), 5.05–4.99 (2H, m), 4.74 (1H, br), 1.96 (2H, dt, *J* = 7.6, 7.6 Hz), 1.68 (3H, s), 1.58 (3H, s), 1.52–1.47 (2H, m), 1.20 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.8, 146.1, 136.0, 131.5, 131.1, 127.5, 126.6, 125.0, 115.5, 112.0, 42.7, 41.4, 25.8, 23.5, 23.4, 17.8; HRMS (ESI+): Calcd for $C_{18}H_{25}O_1$ $[M+H]^+$: 257.1905, Found: 257.1903. Optical Rotation: $[\alpha]_D^{20}$ –23.81 (*c* 1.14, $CHCl_3$) for an enantiomerically enriched sample of 91:9 e.r.

Stereochemistry Correlation: bakuchiol derived from bakuchiol methyl ether in entry 12, Table 2 is determined to be *R*-(–)-bakuchiol by comparison with the data previously

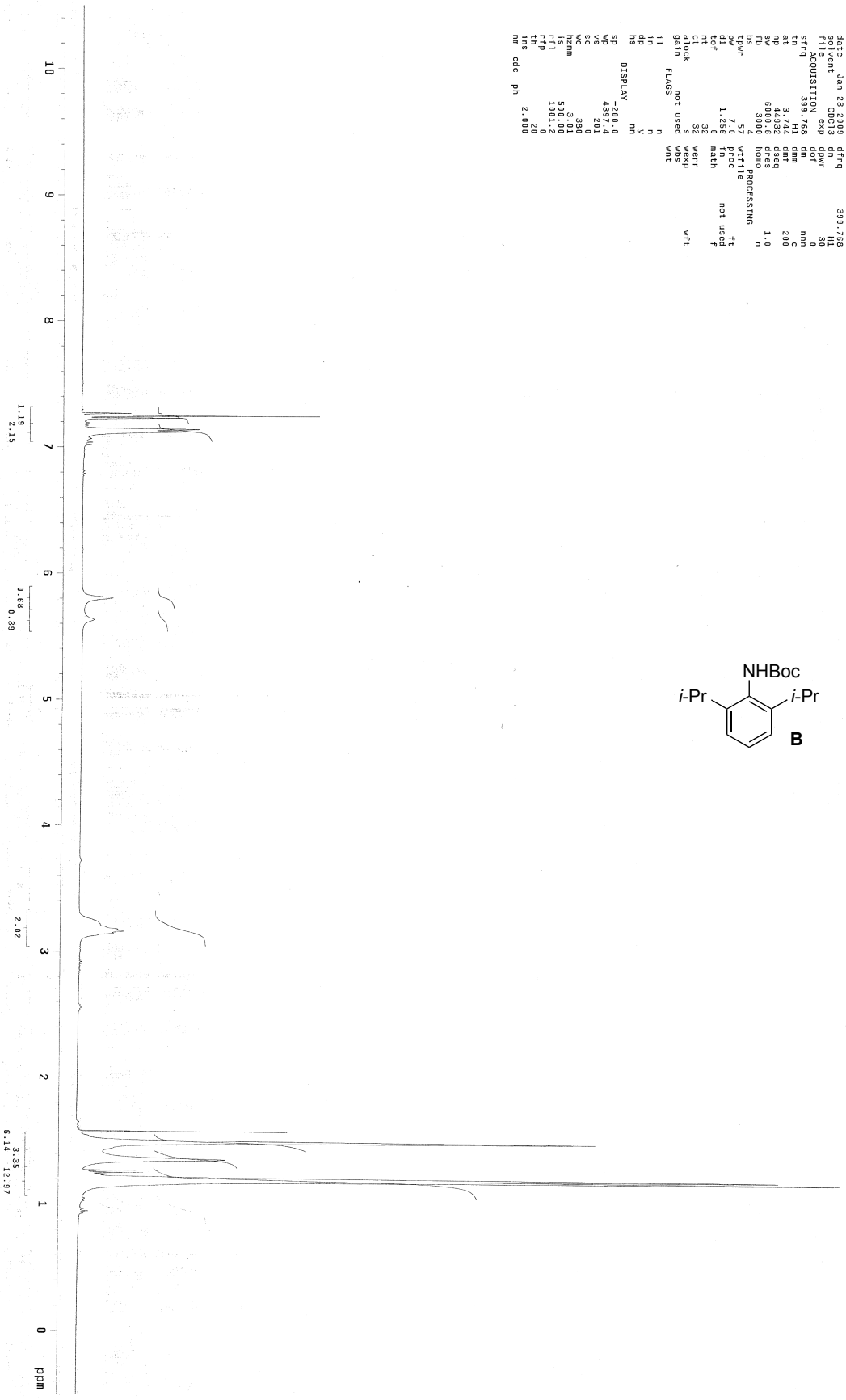
reported.[96] All the compounds generated in this study therefore are assigned as *R* enantiomer in analogy with bakuchiol methyl ether.

Scheme S1. Demethylation of R-(—)–Bakuchiol Methyl Ether and Stereochemistry Proof



R-(—)–bakuchiol methyl ether R-(—)–bakuchiol

(96) Du, X-L.; Chen, H-L.; Feng, H-J.; Li, Y-C. *Helv. Chim. Acta* **2008**, *91*, 371–378.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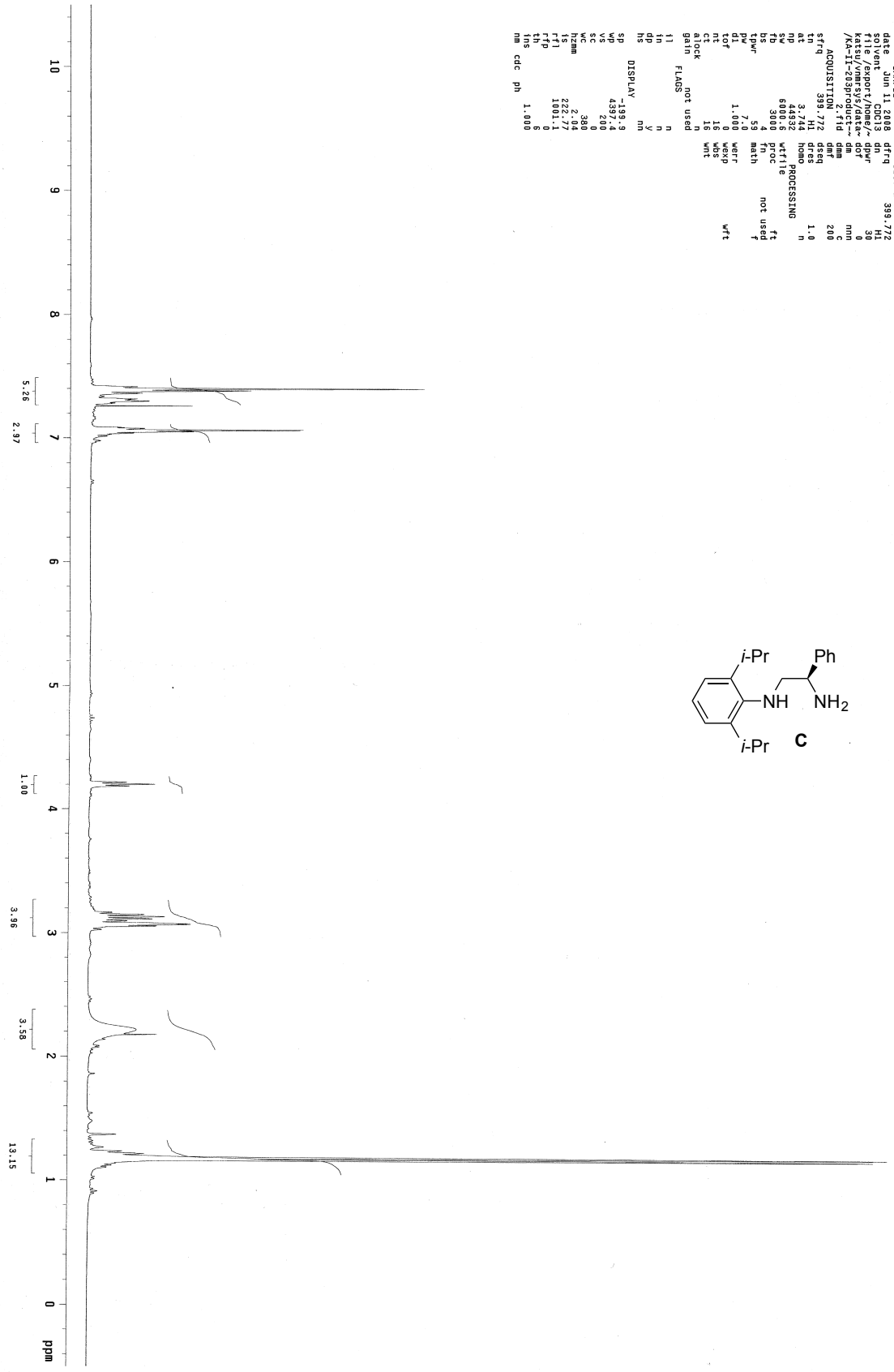
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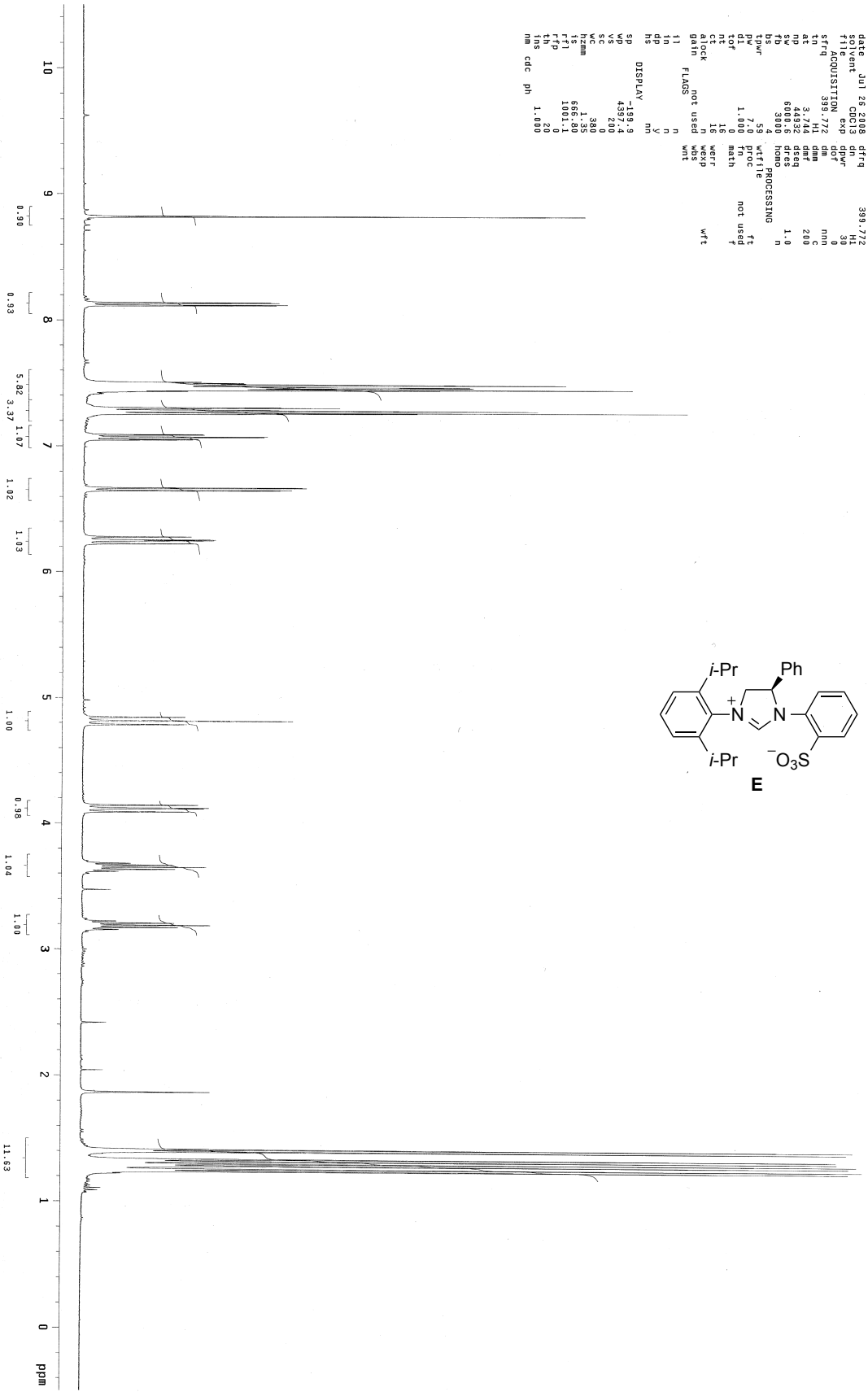
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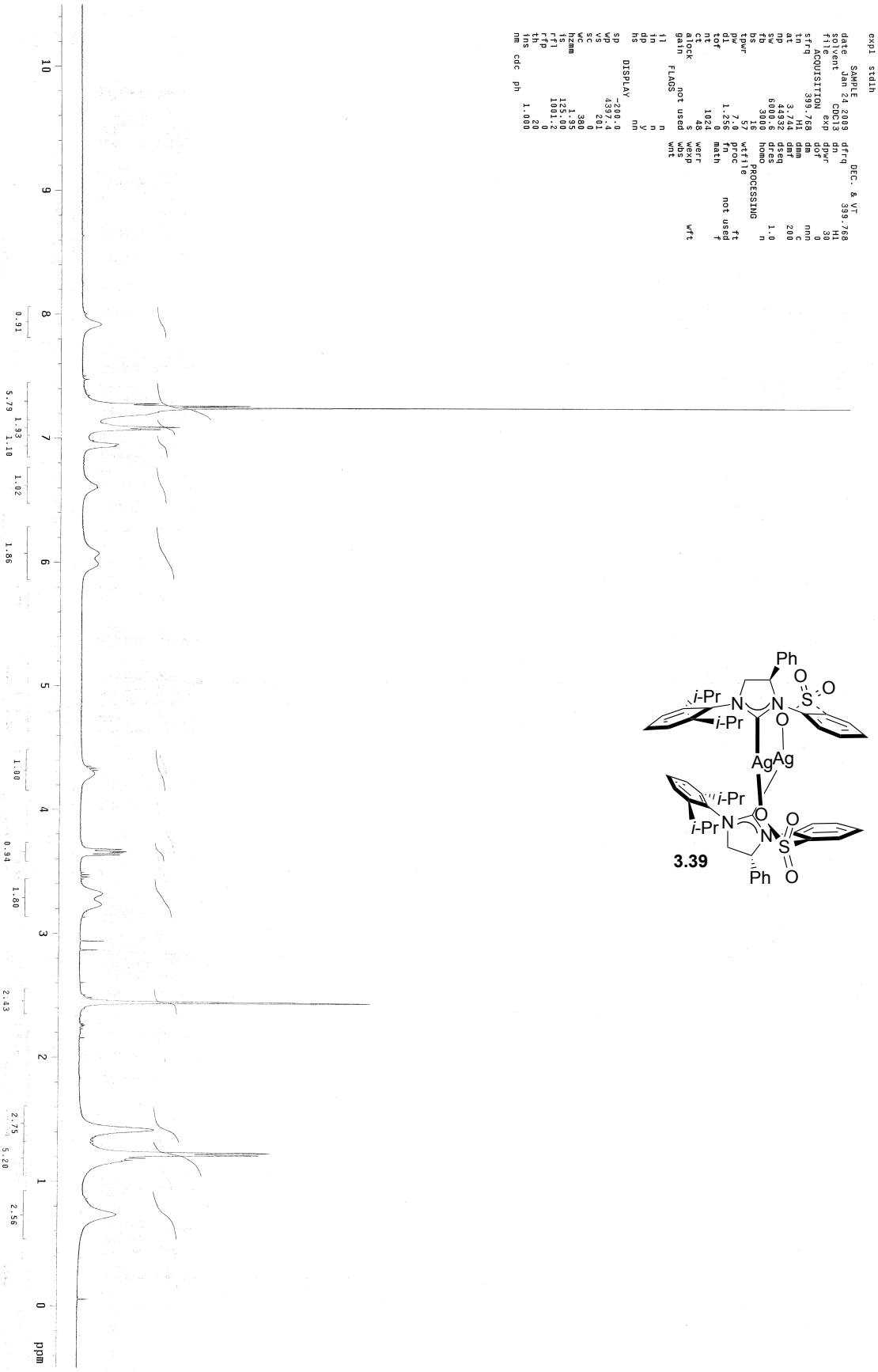
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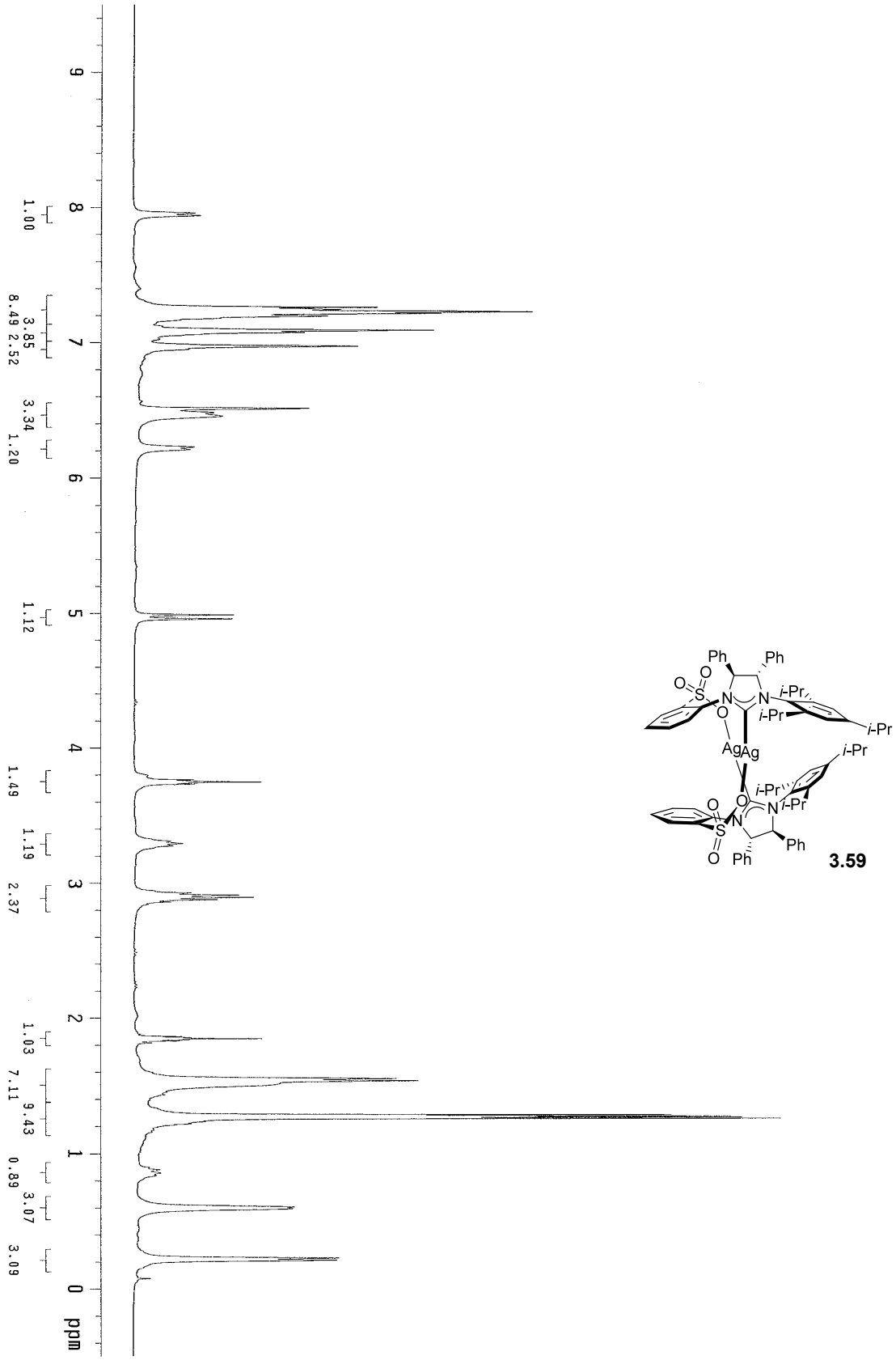
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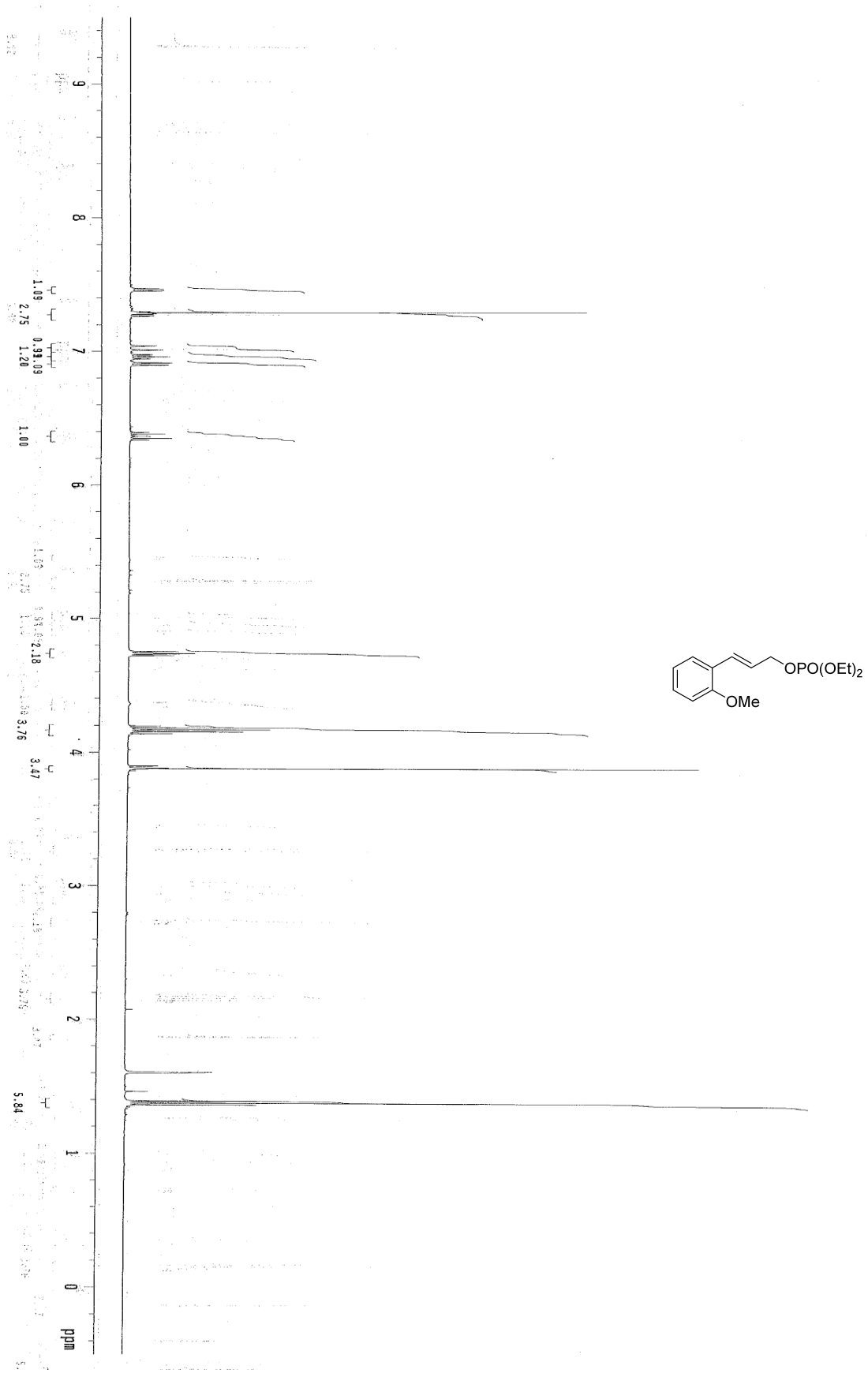
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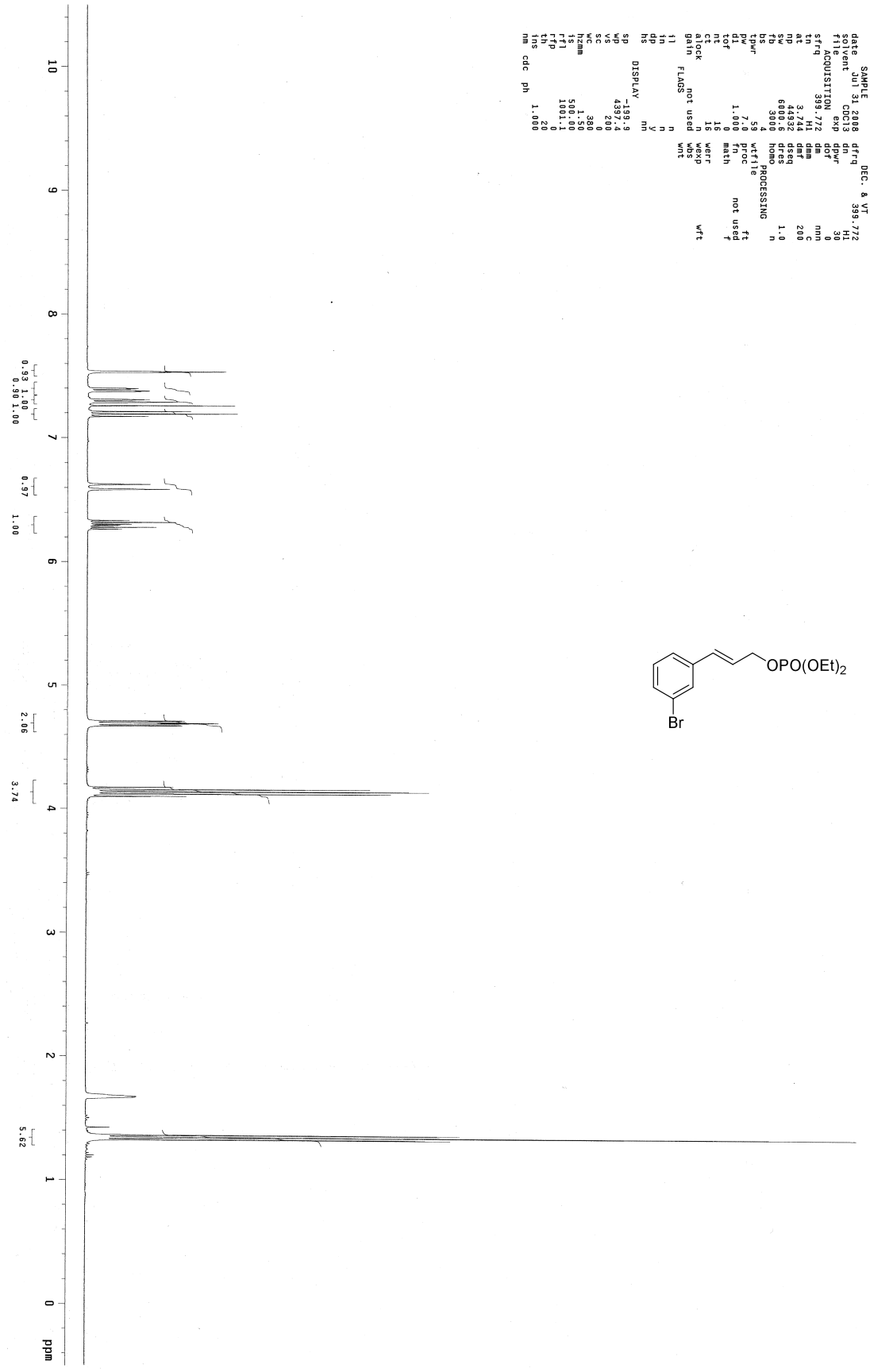
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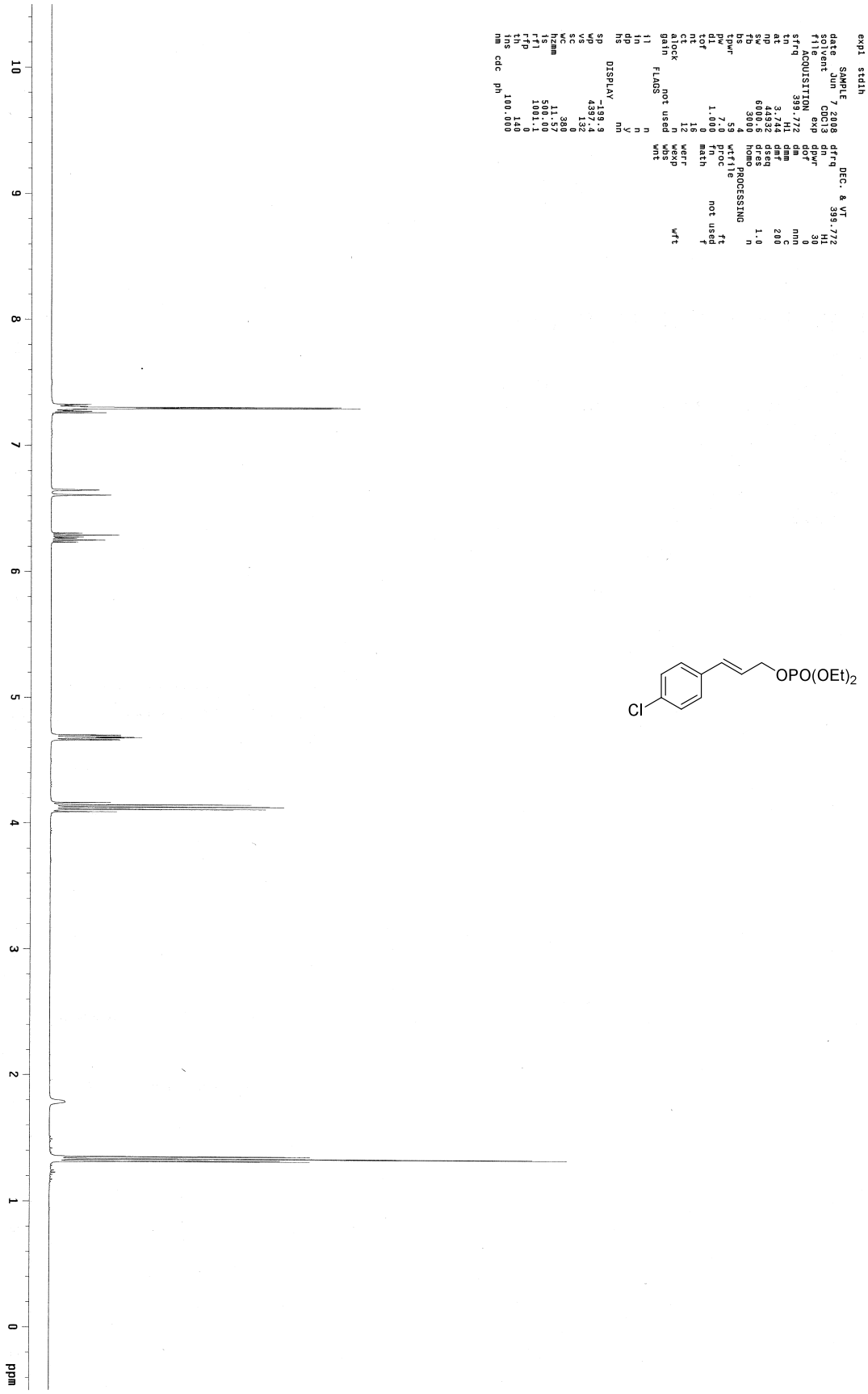
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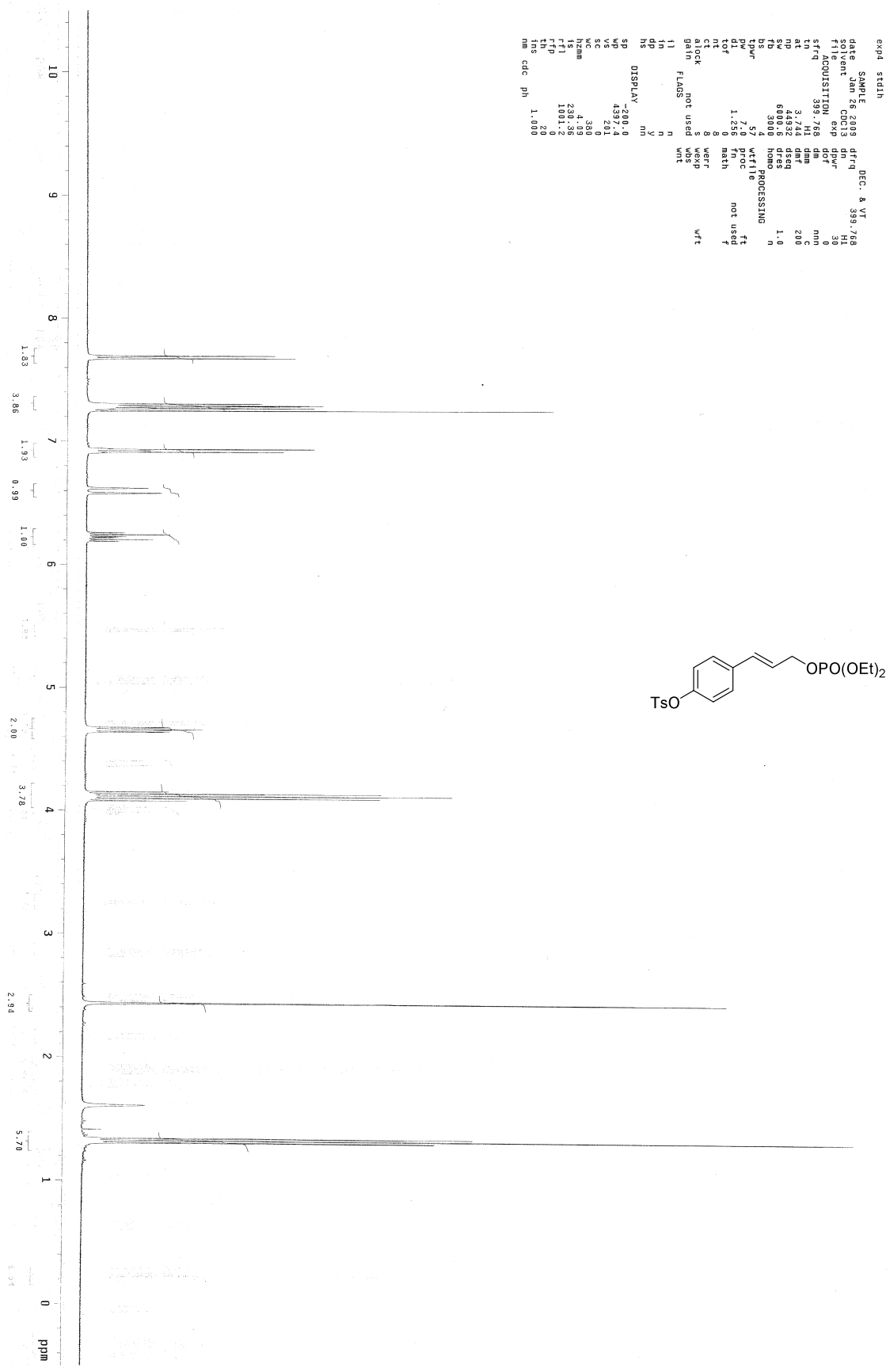
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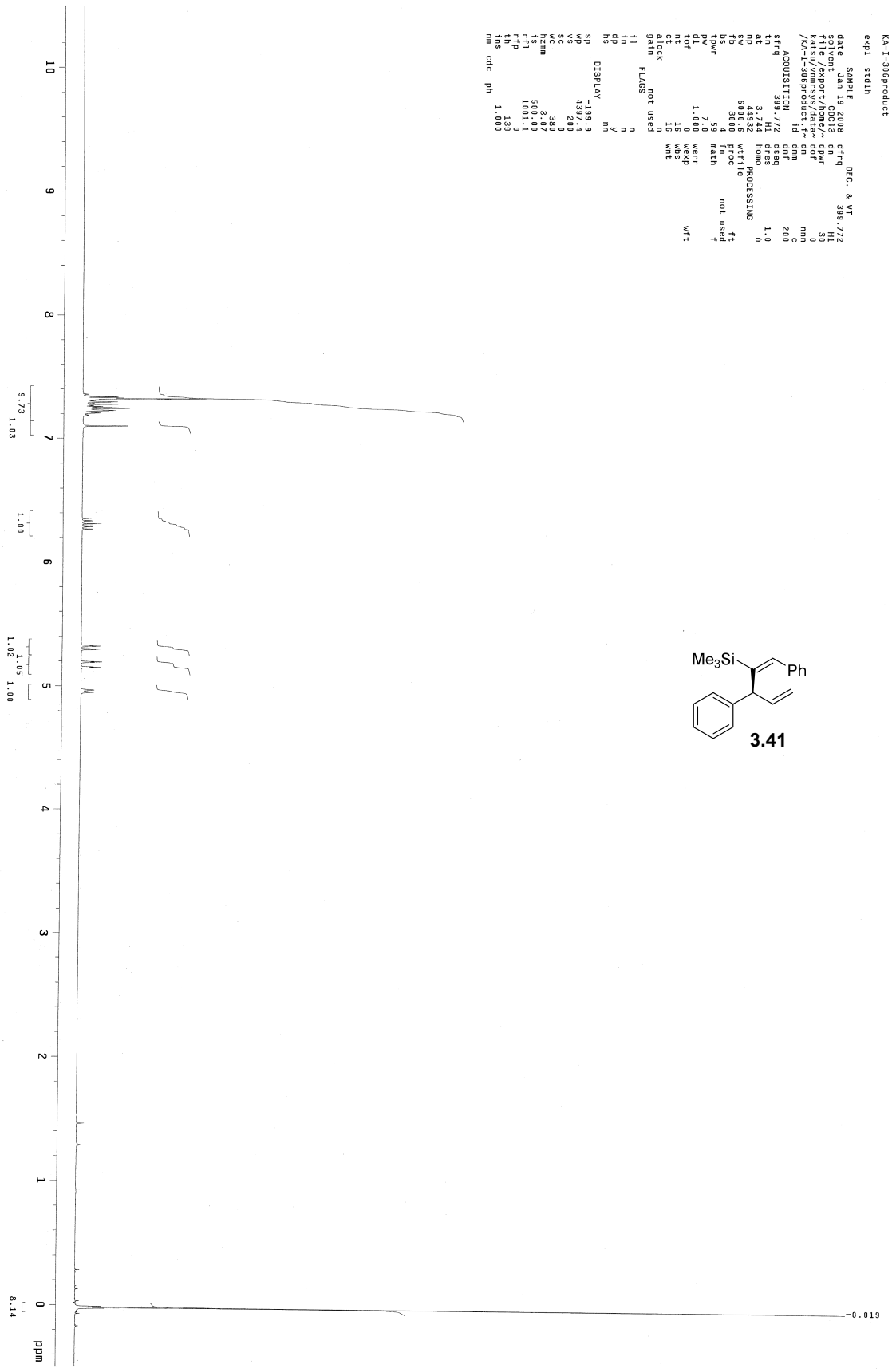
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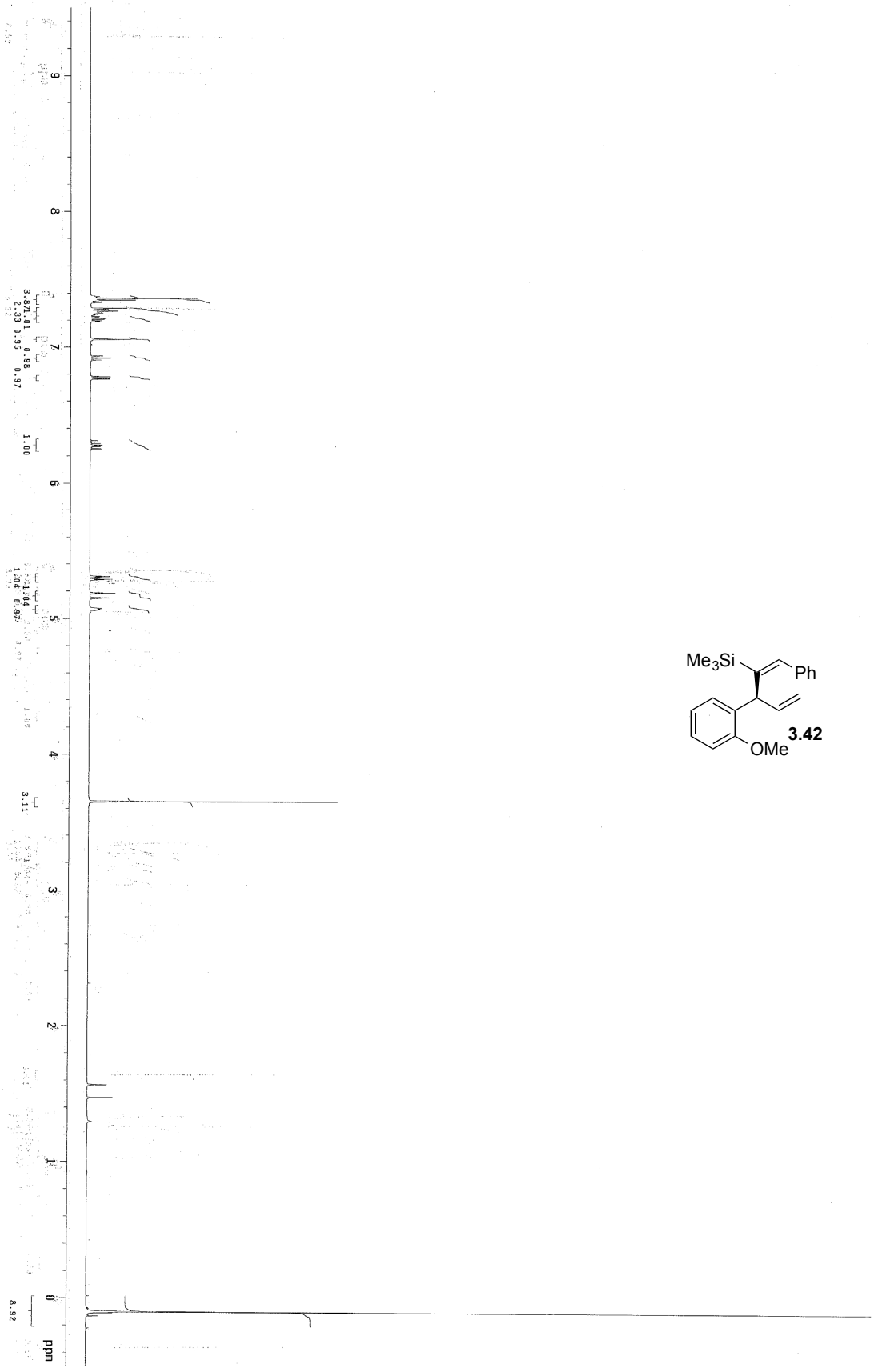
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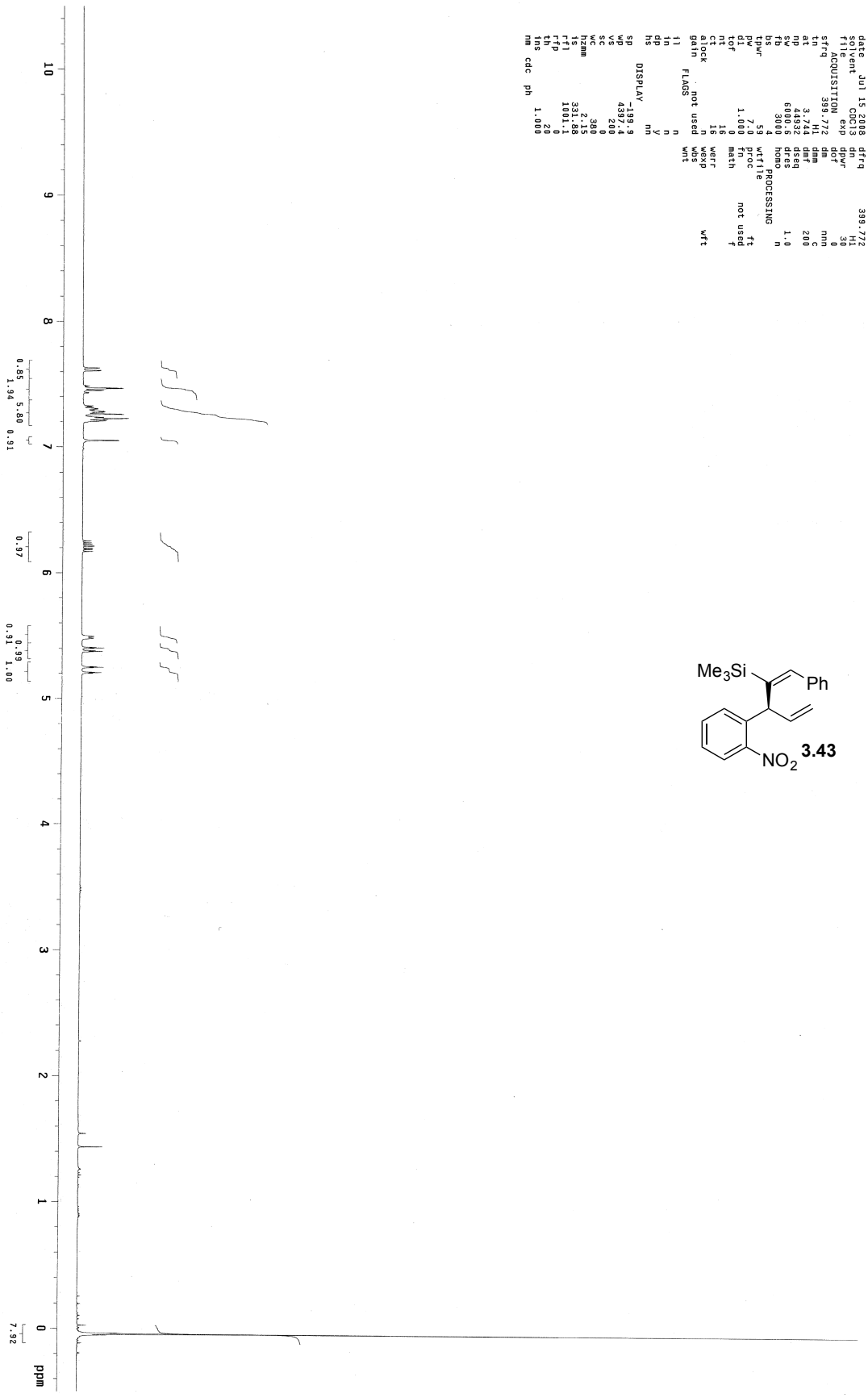
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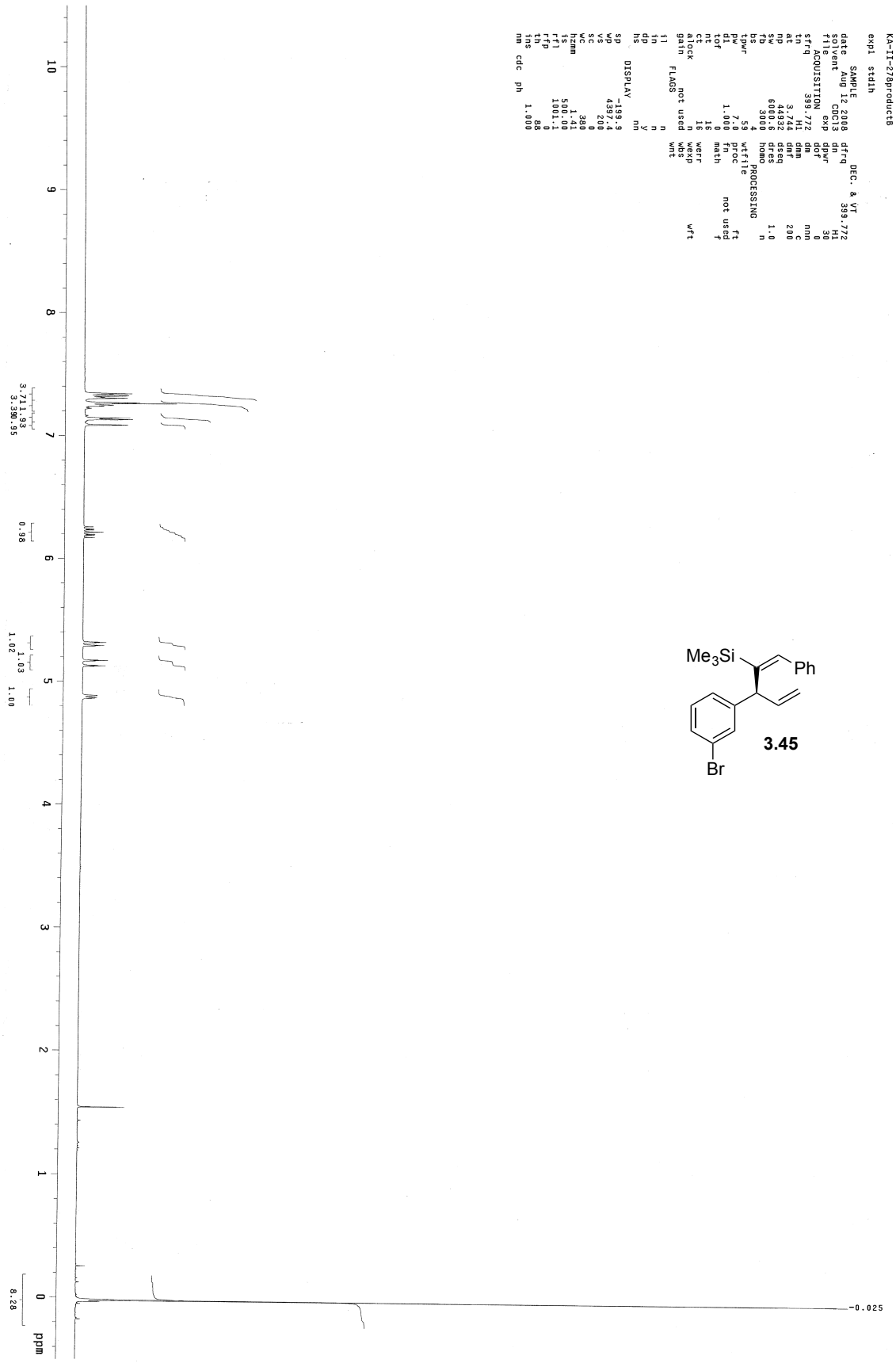
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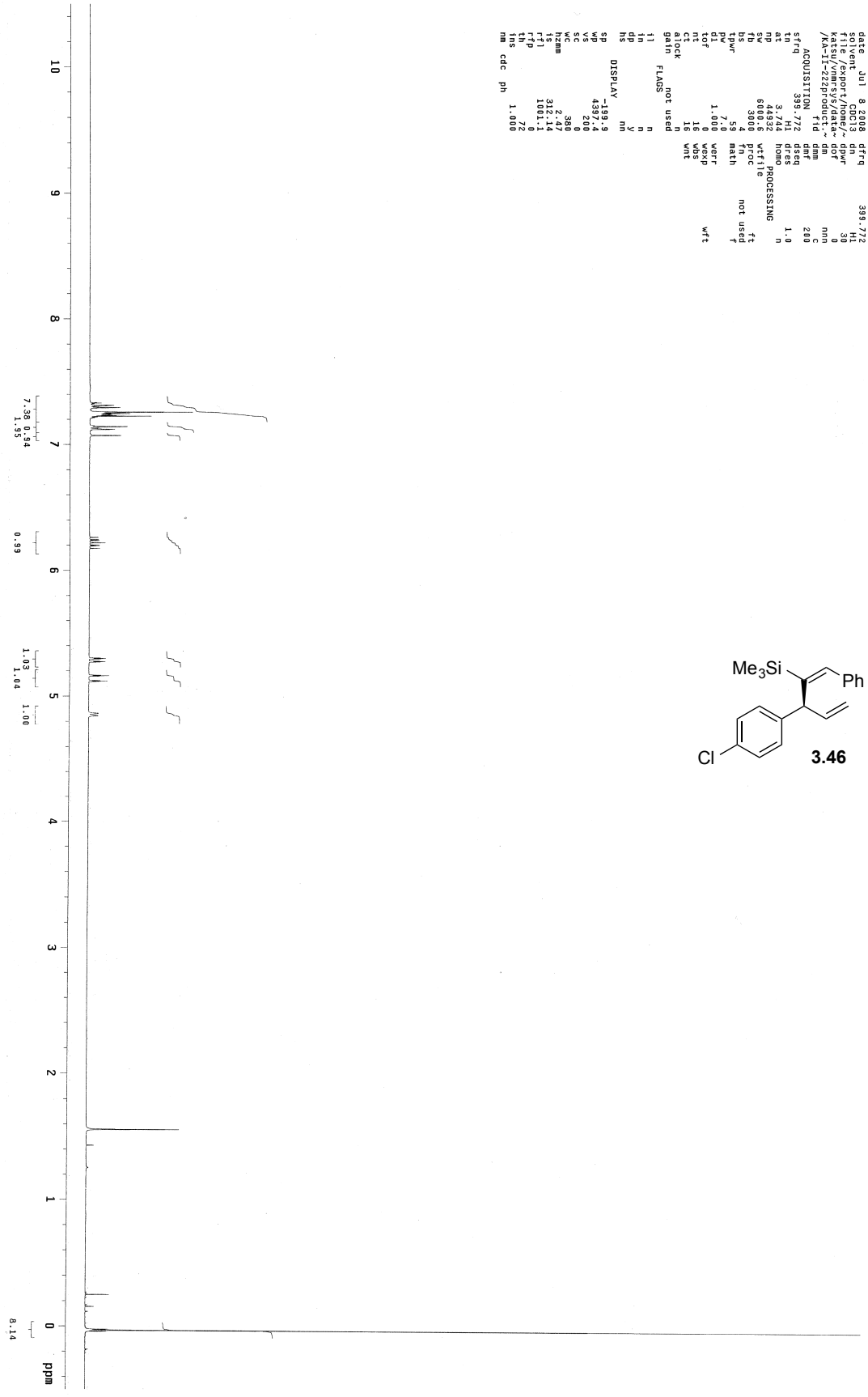
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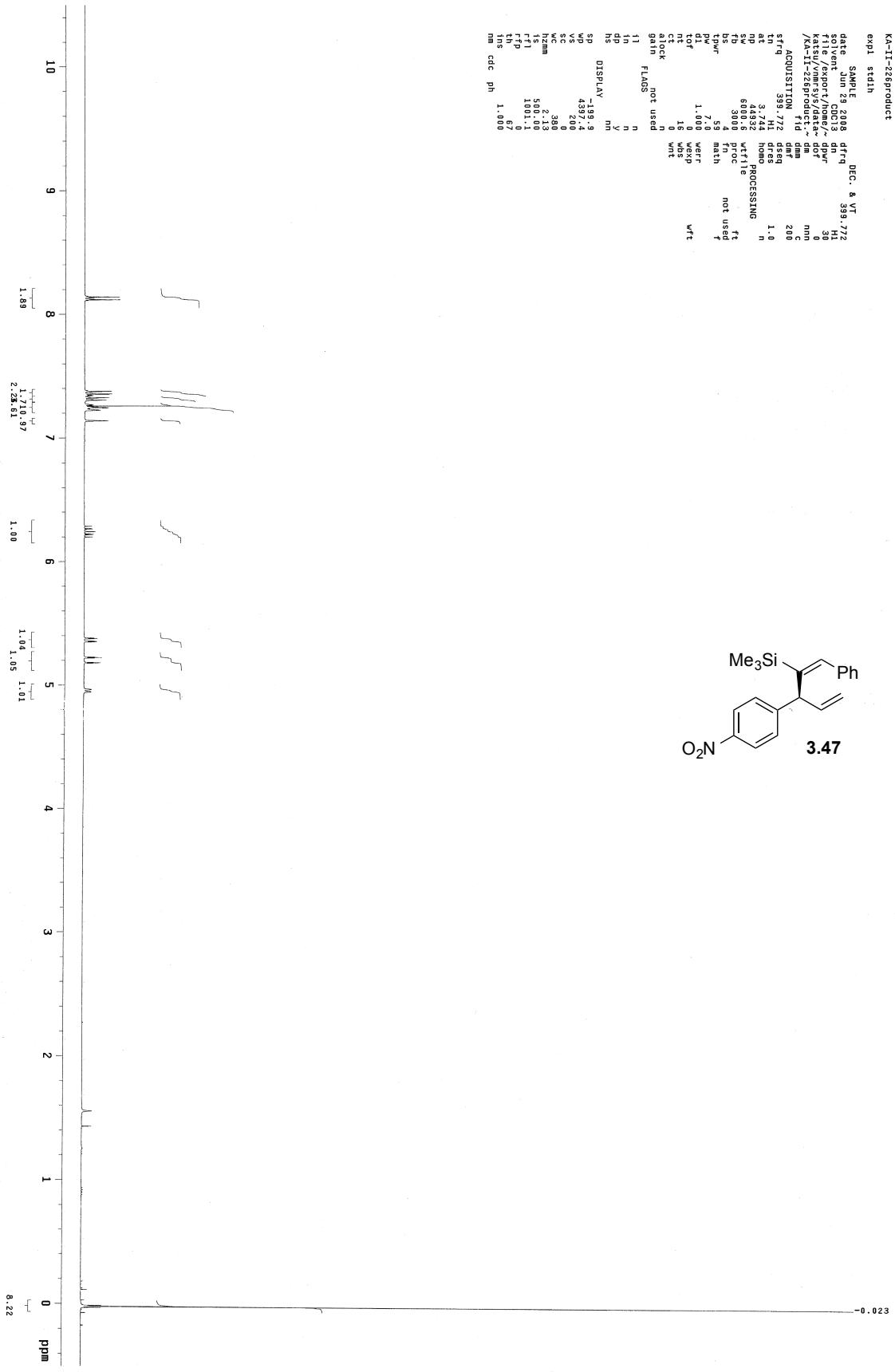
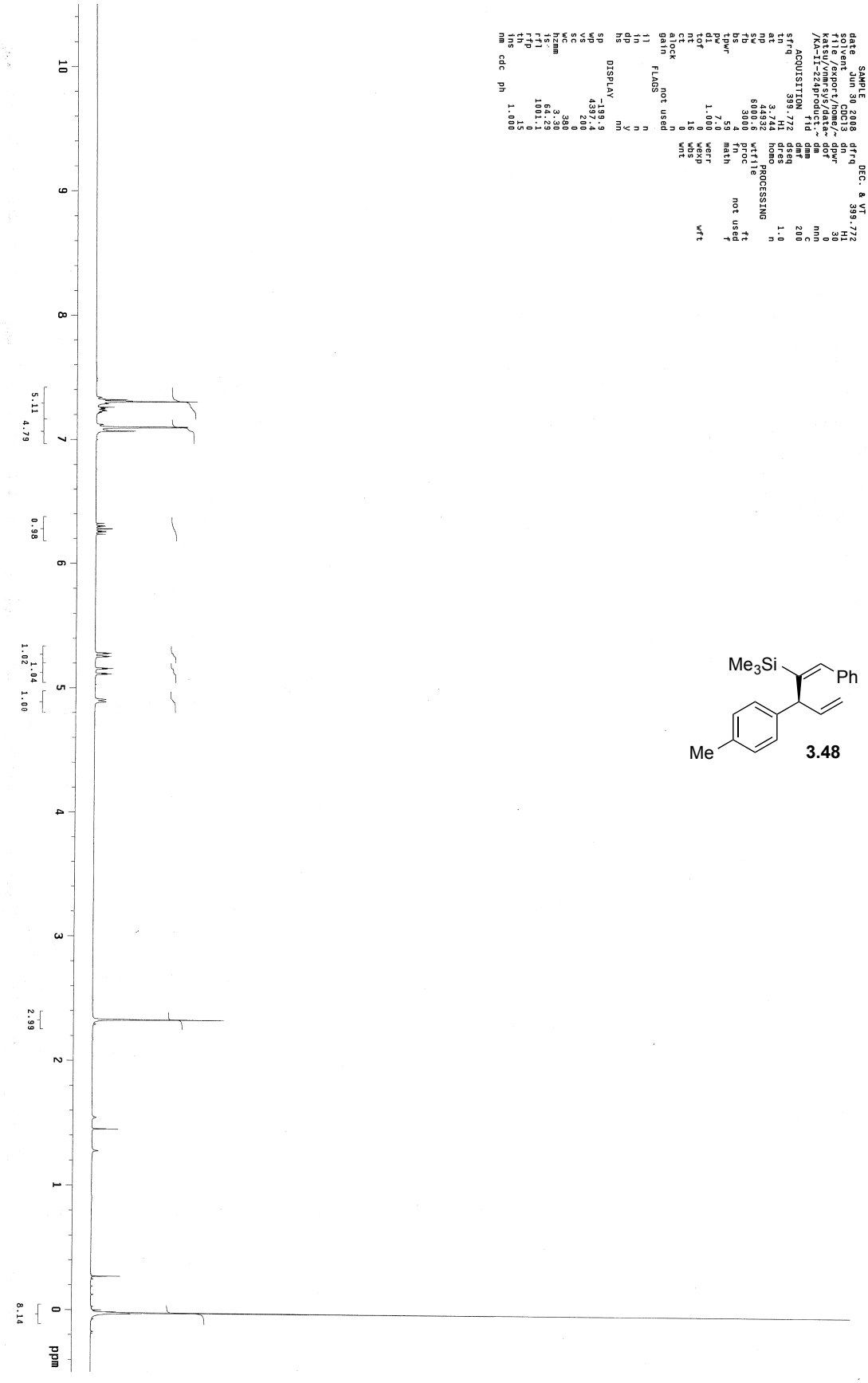
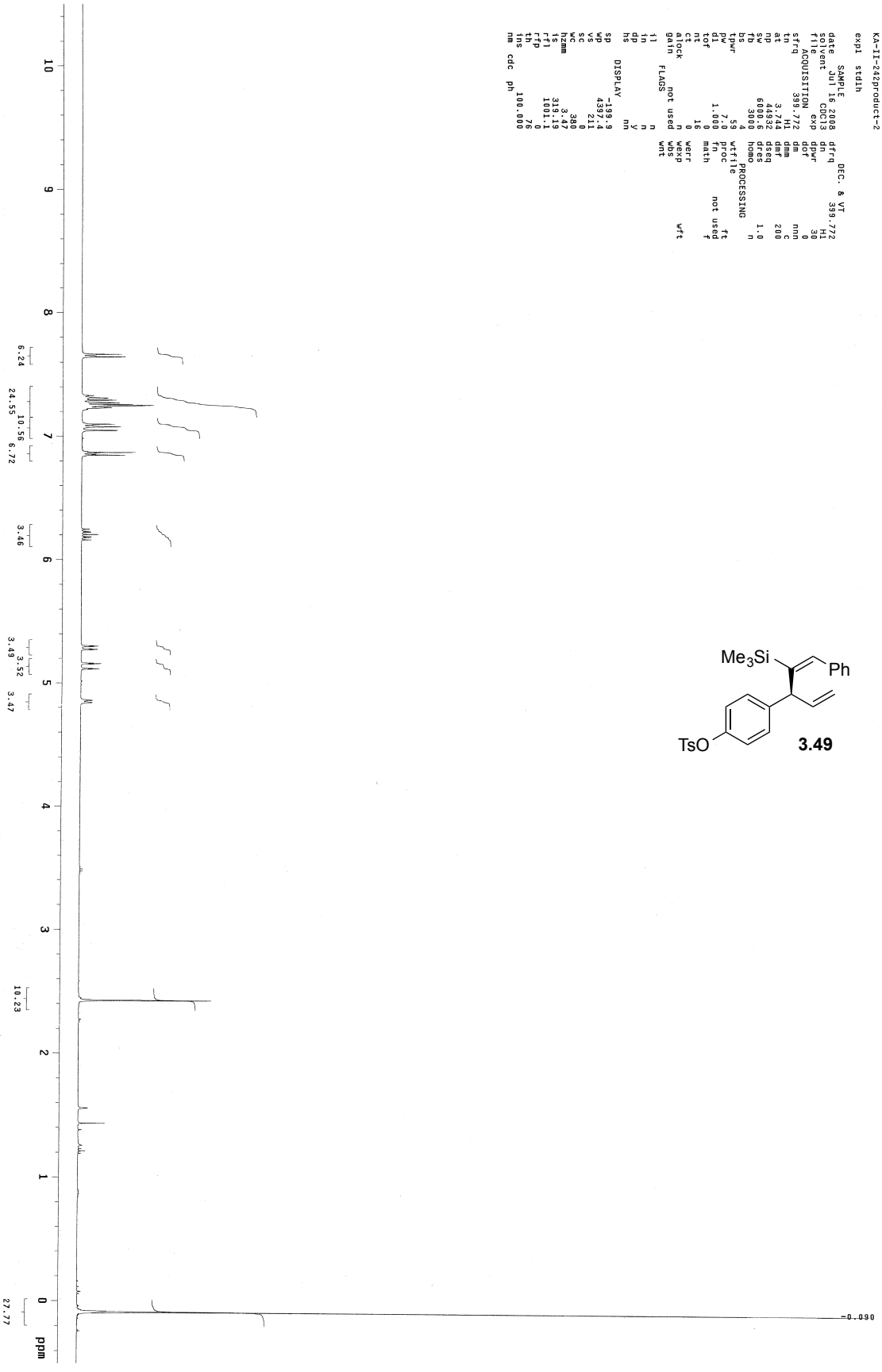
Cl
3.46

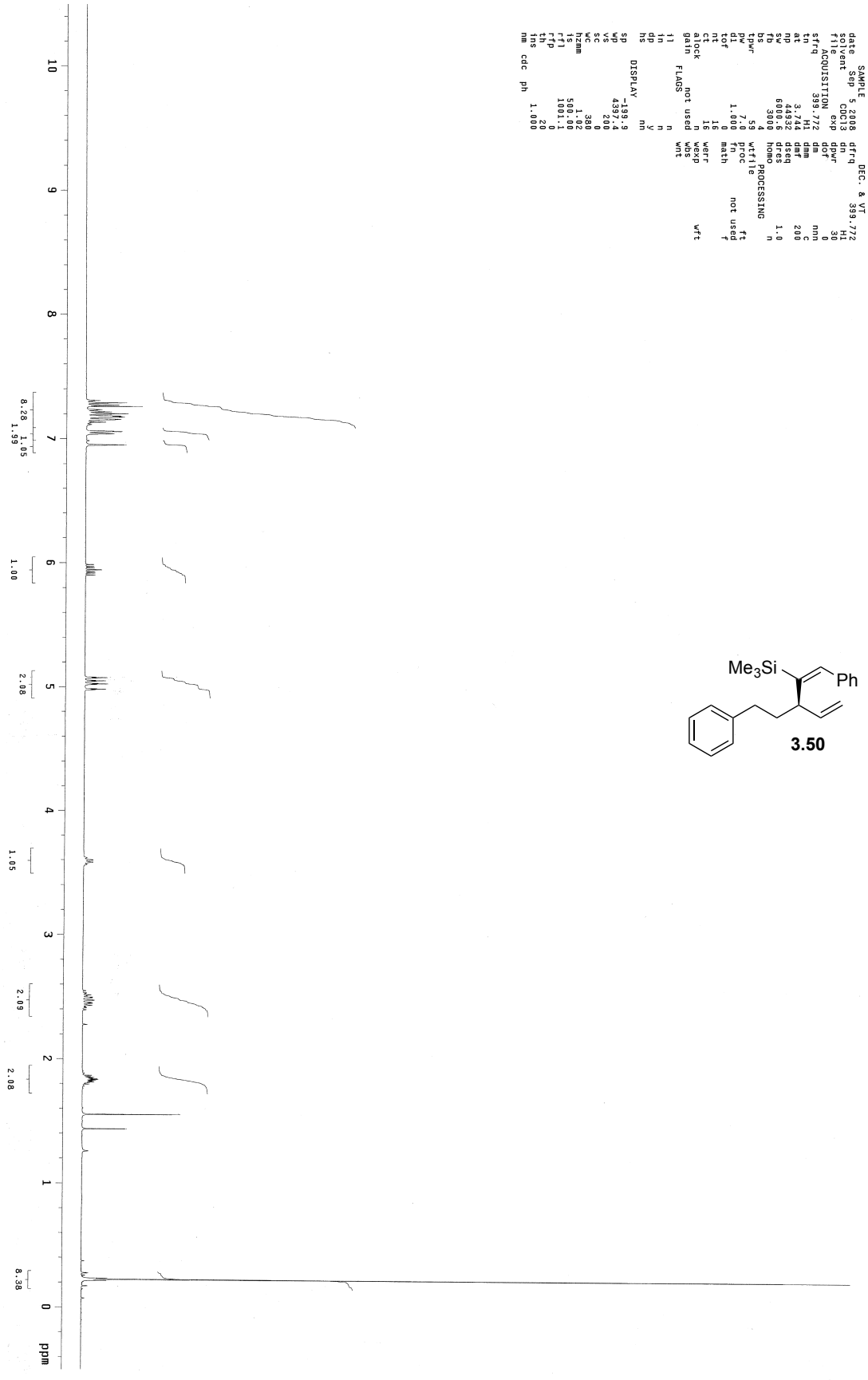

KA-II-226product
expl stdih
SAMPLE
date Jun 29 2008
solvent CDCl3
file /export/home/...
/KA-II-226product.~
ACQUISITION
sfrq 399.772
tn H1
at 3.744
np 44932
sw 6000.6
fb 30004
bs 4
tpwr 59
pw 7.0
d1 1.000
d2 0
tof 18
nt 0
ct 0
alock n
gain n
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -199.9
wp 4397.4
vs 200
sc 0
wc 380
hzmm 22.233
is 500.00
rfl 1001.1
rfp 0
th 67
lvl 1.000
dfrq 399.772
dn H1
dof 0
dm nnn
dmm c
dmf 200
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn
math
not used f
werr
wexp
wbs
wnt wft
1.89
1.71
0.97
2.23
1.61
1.00
1.04
1.05
1.01
8.22
-0.023
ppm
Me3Si
Ph
O2N
3.47


KA-II-224product
expl stdih
SAMPLE
date Jun 30 2008
solvent CDCl3
file /export/home/~ dpwr
katsu/vnmrsys/data~ dof
/KA-II-224product.~ dm
ACQUISITION fid dmm
sfrq 399.772 dmf
tn H1 dseq
at 3.744 homo
np 44932 PROCESSING
sw 6010.6 wrfile
fb 3008.4 proc
bs 4 fn
tpwr 59 math
pw 7.0 wexp
d1 1.000 wbs
nt 16 wnt
ct 0
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -199.9
wp 4397.4
vs 200
sc 300
wc 3.30
hzmm 64.29
is 1001.1
rfl 0
rfp 15
th 1.000
ins
nm cdc ph
DEC. & VT
399.772
H1
30
0
nnn
c
200
1.0
n
ft
not used
f
wft
5.11
4.79
0.98
1.02
1.04
1.00
2.99
8.14
10
9
8
7
6
5
4
3
2
1
0
ppm

Me3Si
Ph
Me

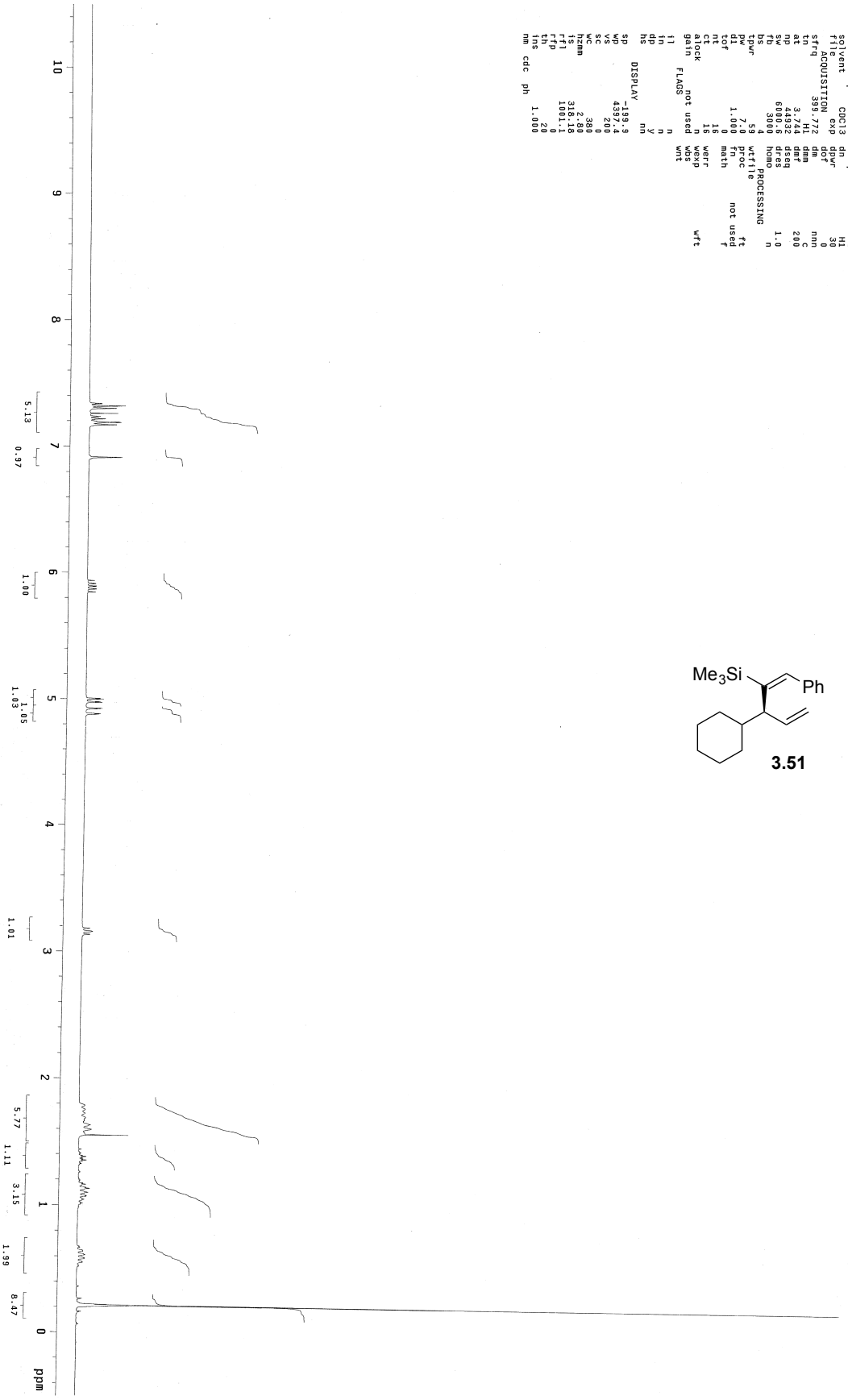
3.48

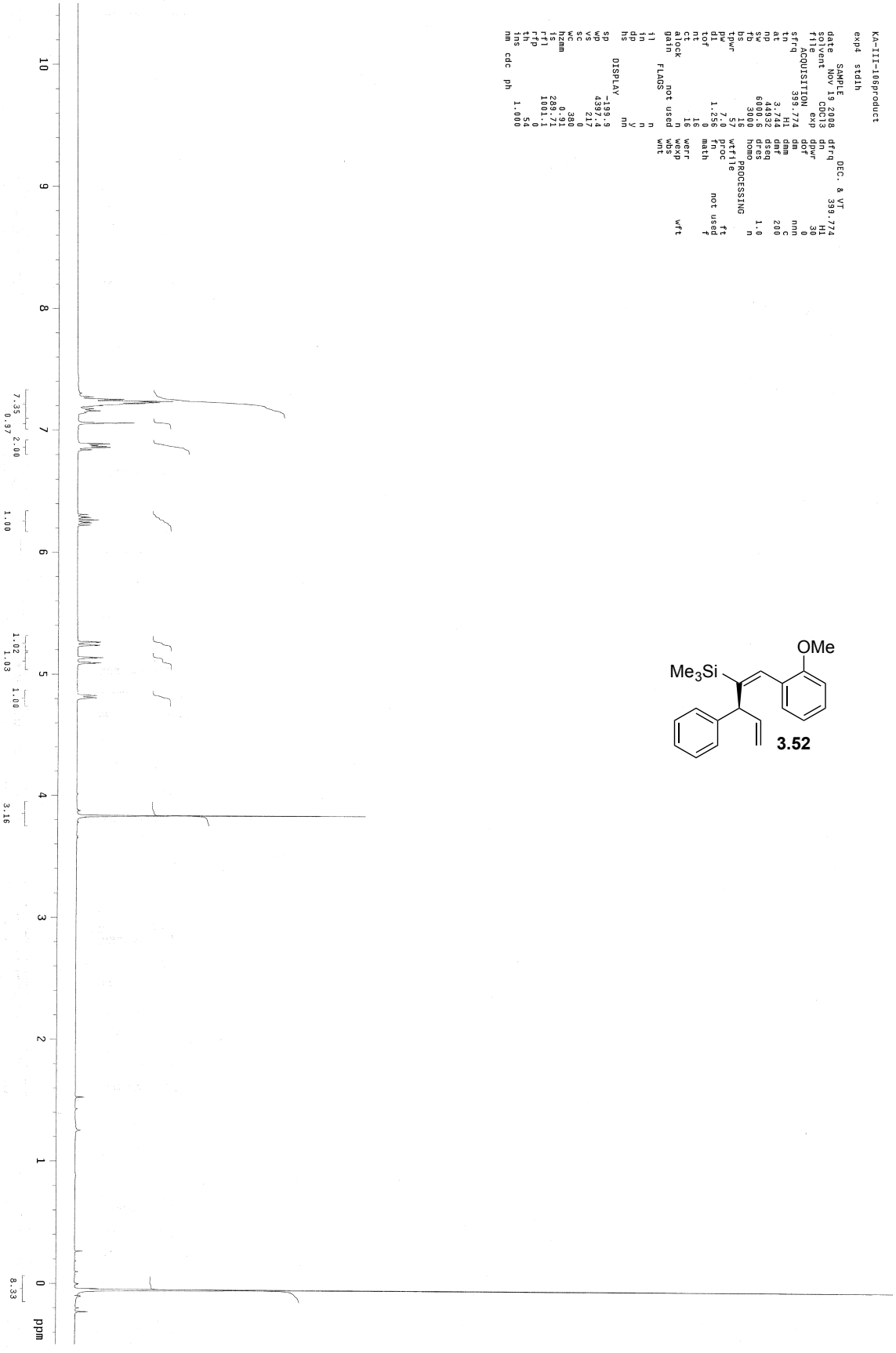

KA-II-244product-2
expl stdih
SAMPLE
date 1oul 16 2008
solvent CDCl3
file ACQUISITION
sfrq 399.772
tn C13
at 3.744
np 44932
sw 6000.6
fb 3000
bs 59
tpwr 59
pw 7.0
pw1 1.000
tof 10
nt 0
ct 0
alock n
gain n
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -199.9
wp 4397.4
vs 211
sc 0
wc 380
hzmm 3.47
ts 319.49
rfl 1001.1
rfp 0
th 76
ins 0
nm cdc ph
100.000
DEC. & VT
dfrq 399.772
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt
wft
Me3Si
Ph
TsO
3.49
6.24
24.55
10.56
6.72
3.46
3.49
3.52
3.47
10.23
27.77
0.090
ppm

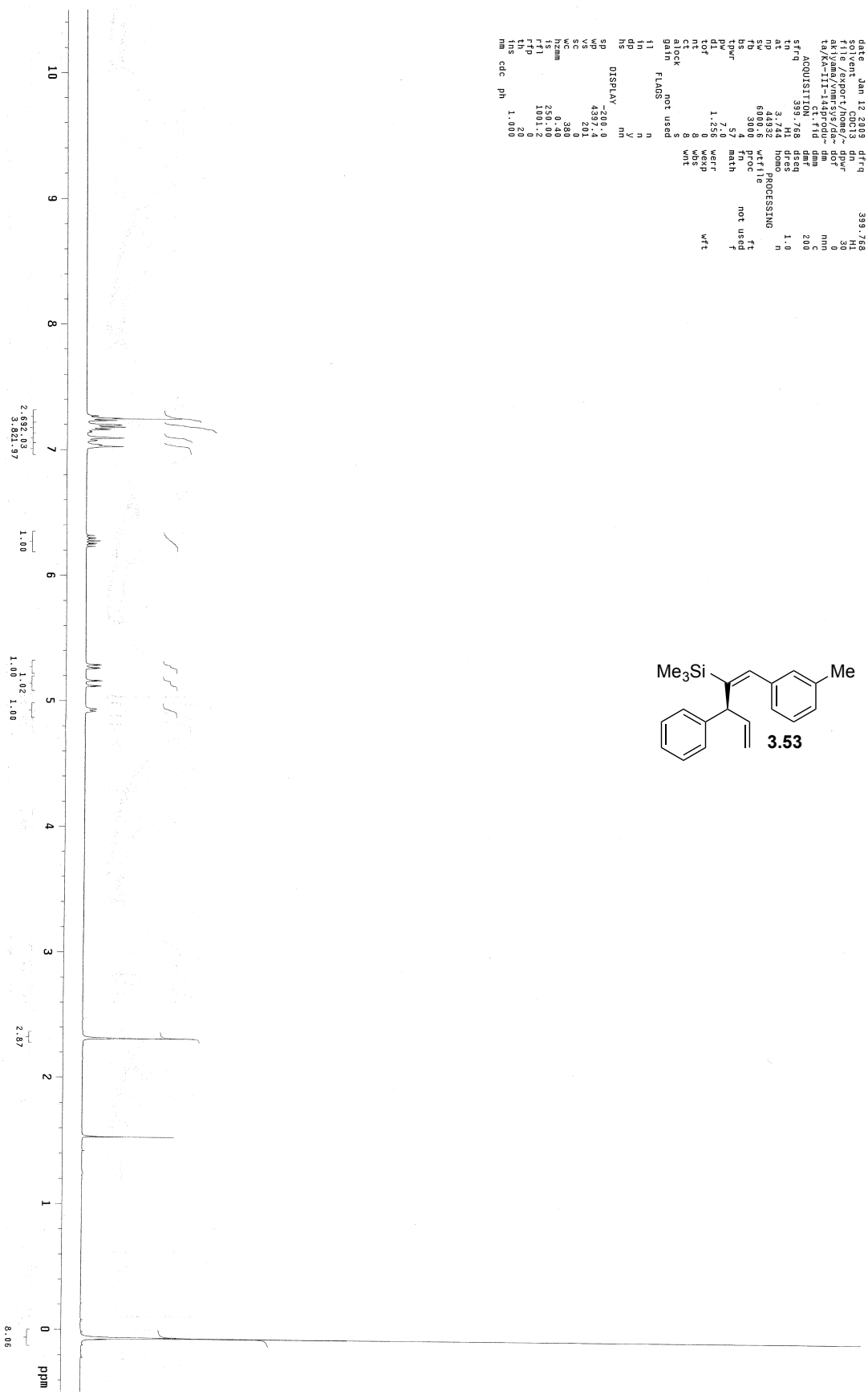

Ka-III-4product
expl stdih
SAMPLE
date Sep 5 2008
solvent CDCl3
file exp
ACQUISITION
sfrq 399.772
tn H1
at 3.754
np 44932
sw 6000.6
fb 3000
bs 4
tpwr 59
pw 7.5
d1 1.000
tof 0
nt 16
ct 16
alock n
gain wft
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -199.9
wp 4397.4
sc 20
wc 380
hzmm 1.02
is 500.00
rfl 1001.1
rfp 0
th 20
ins 1.000
nm cdc ph
DEC. & VT
dfrq 399.772
dn H1
dof 30
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt
wft
8.28
1.99
1.05
1.00
2.08
1.05
2.09
2.08
8.38
10
9
8
7
6
5
4
3
2
1
0
ppm

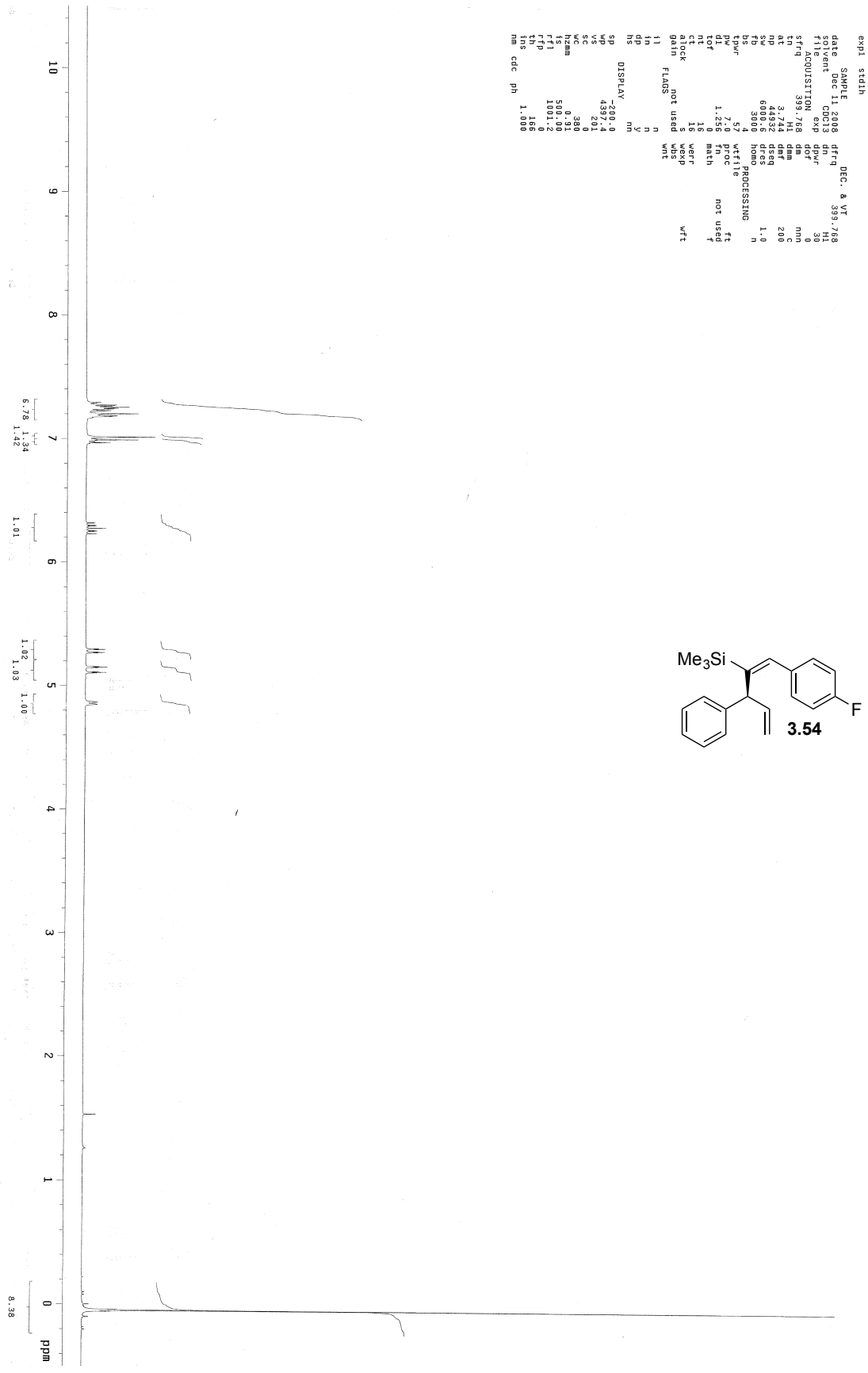
Me3Si
Ph

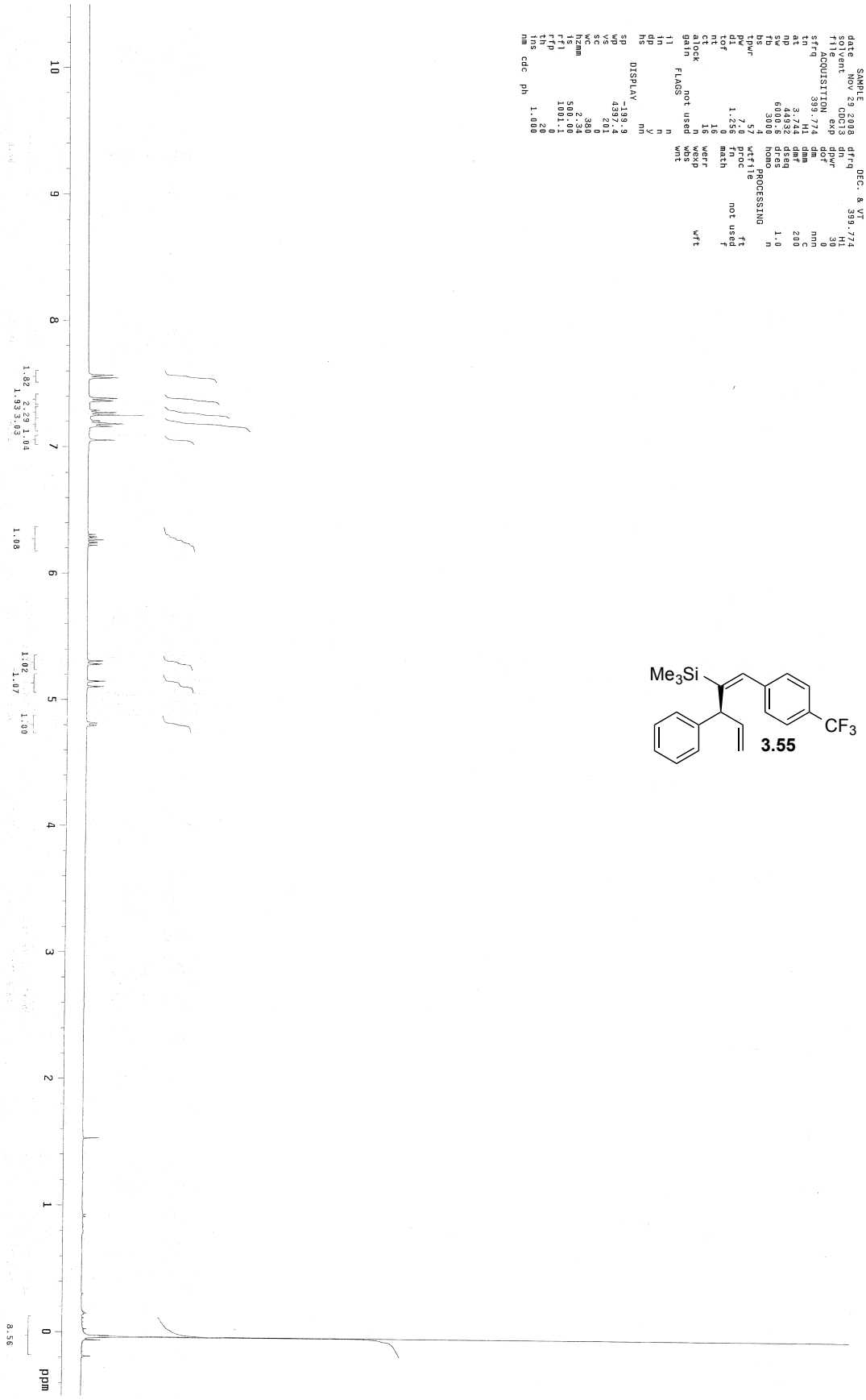
3.50

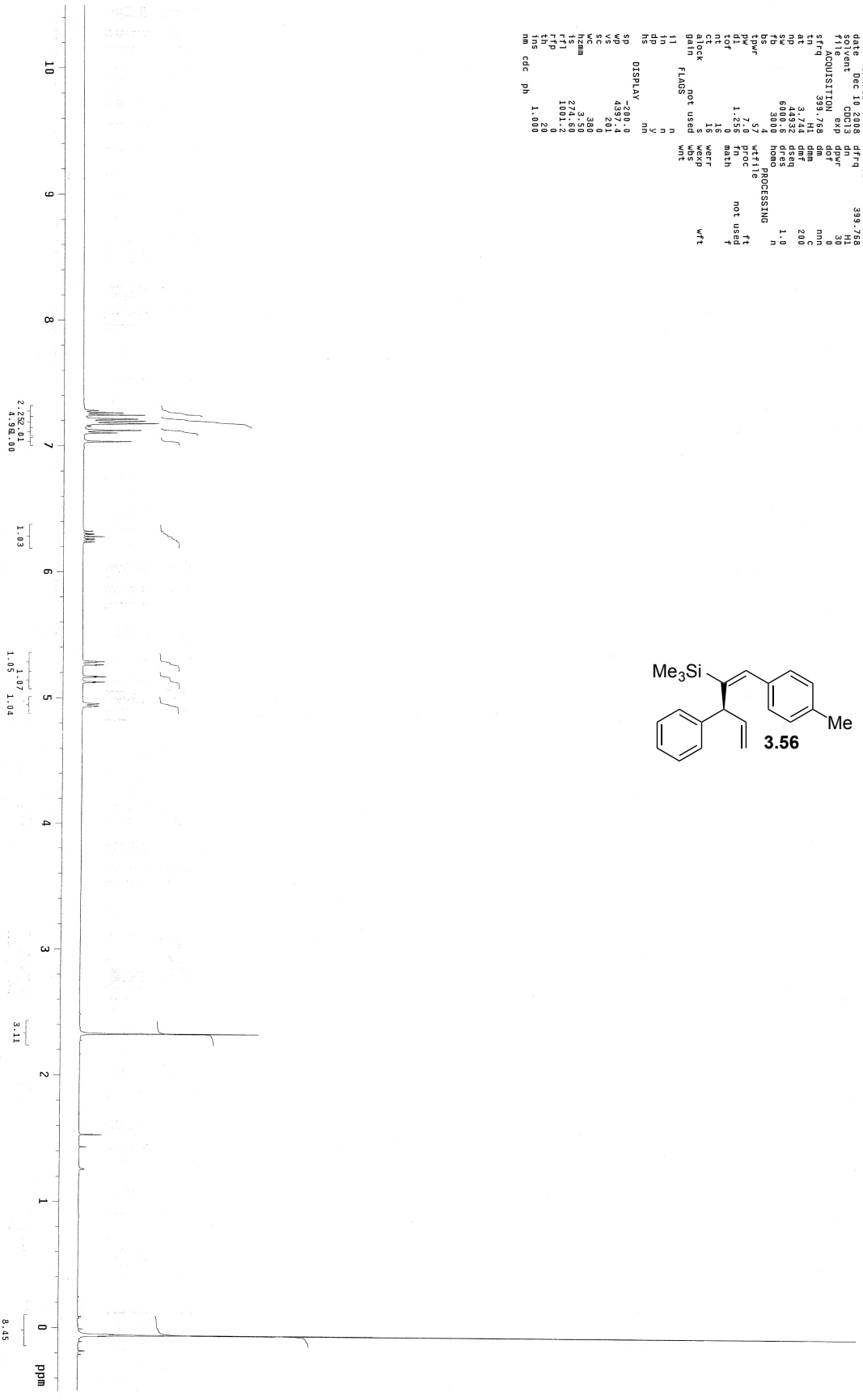

KA-III-3product
expl stdln
SAMPLE
date Sep 6 2008
solvent CDCl3
file ACQUISITION
sfrq 399.772
tn H1
at 3.744
np 44932
sw 6000.6
fb 3004
bs
tpwr 59
pw 7.0
dl 1.000
tl
nt 16
ct 16
alock n
gain
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -199.9
wp 4397.4
vs 200
sc 0
wc 380
hzmm 2.80
is 318.18
rfl 1001.1
rfp 0
th 20
ins 1.000
nm cdc ph
DEC. & VT
dfrq 399.772
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn not used
math f
werr
wexp
wbs wft
wnt
Me3Si
Ph
3.51
10
9
8
7
6
5
4
3
2
1
0
ppm
5.13
0.97
1.00
1.03
1.05
1.01
5.77
1.11
3.15
1.99
8.47

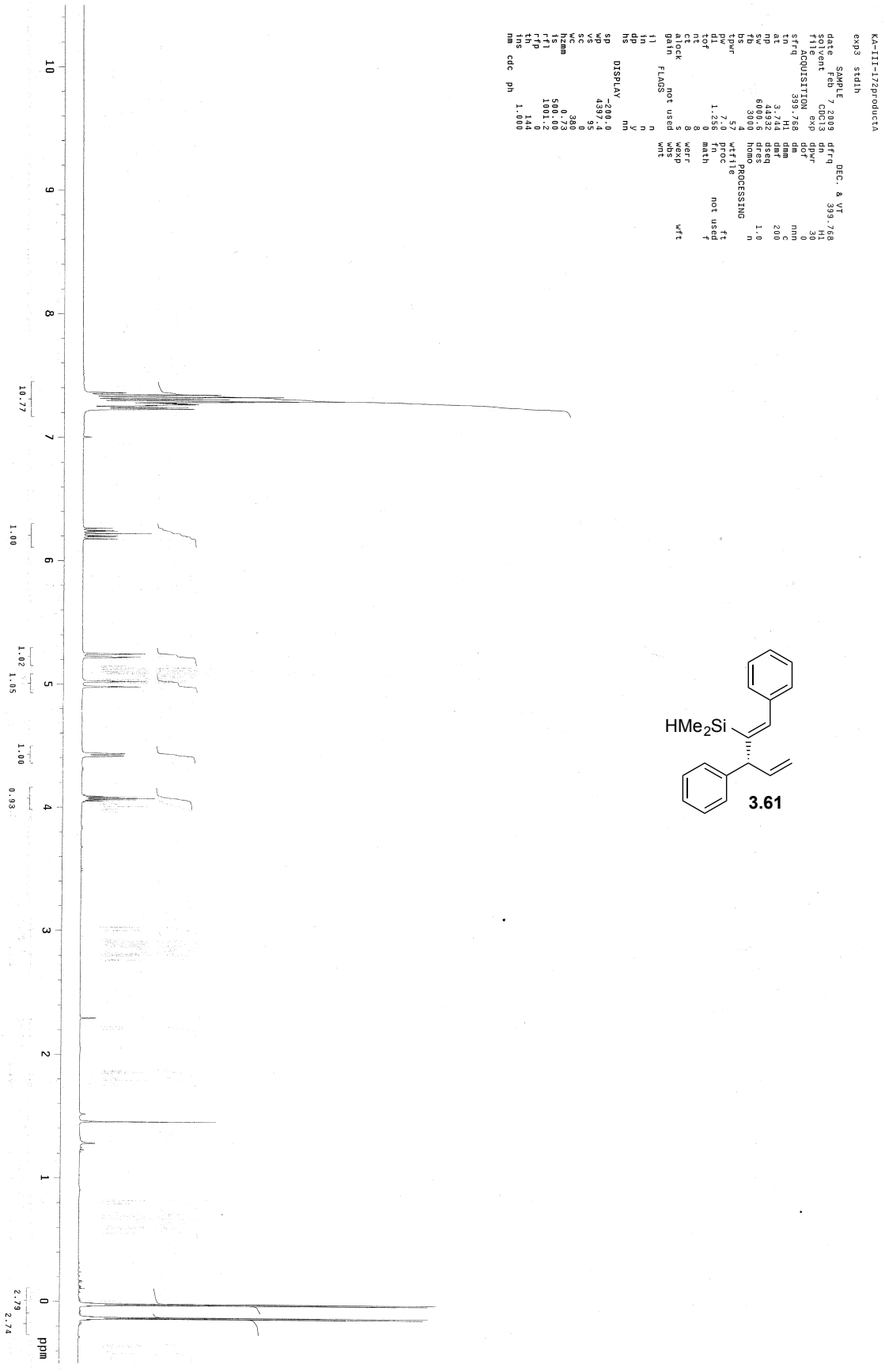

KA-III-106product
exp4 std1h
SAMPLE
date Nov 19 2008
solvent CDCl3
file exp
ACQUISITION
sfrq 399.774
tn H1
at 3.744
np 44932
sw 6000.6
fb 3000
bs 16
tpwr 57
pw 7.5
d1 1.256
tof 0
nt 16
ct 16
alock n
gain n
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -199.9
wp 4397.4
vs 217
sc 0
wc 380
hzmm 0.91
is 289.71
rfl 1001.1
rfp 0
th 54
ins 1.000
nm cdc ph
DEC. & VT
dfrq 399.774
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn not used
math f
werr
wdisp
wbs
wnt wft
OMe
Me3Si
3.52
10
9
8
7
6
5
4
3
2
1
0
ppm
7.35
0.97
2.00
1.00
1.02
1.03
1.00
3.16
8.33

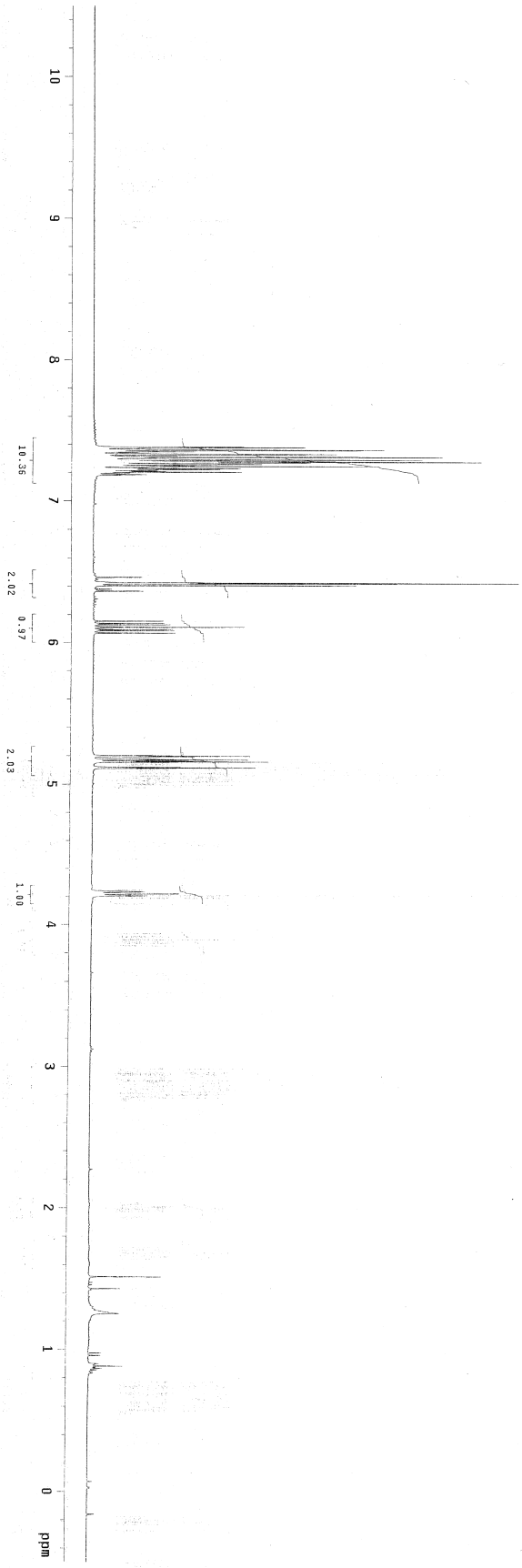

Ka-III-143product
exp4 std1h
SAMPLE
date DEC. & VT
solvent CDCl3 dn H1
file /export/home/~ dpwr 30
akiyama/ynmrsys/da~ dof 0
ta/KA-III-144produ~ dm nnn
ACQUISITION dmm c
sfrq 399.768 dmf 200
tn H1 dres 1.0
at 3.744 homo n
np 44932 PROCESSING
sw 6009.6 wtfile
fb 3000 proc ft
bs 4 fn not used
tpwr 57 math f
pw 7.0 werr
pl 1.25 wexp wft
nt 8 wbs
ct 8 wnt
alock s
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -200.0
wp 4397.4
vs 201
sc 0
wc 380
hzmm 0.010
is 250.40
rfl 1001.2
rfp 0
th 20
ins 1.000
nm cdc ph
2.692.03
3.821.97
1.00
1.00 1.02 1.00
2.87
8.06
10 9 8 7 6 5 4 3 2 1 0 ppm
Me3Si
Me
3.53


KA-III-133product
expl stdih
SAMPLE
date Dec 11 2008
solvent CDCl3
file ACQUISITION
sfrq 399.768
tn H1
at 3.744
np 44932
sw 6009.6
fb 3906
bs 4
tpwr 57
pw 7.0
pl1 1.25
nt 16
ct 16
alock n
gain n
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -200.0
wp 4397.4
vs 201
sc 0
wc 380
hzmm 0.91
is 500.00
rfl 1001.2
rfp 0
th 166
ins 1.000
nm cdc ph
DEC. & VT
dfrq 399.768
dn H1
dpwr 30
dof 0
dm nnn
tm c
at 200
dmf
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
math not used
wexp
wbs
wnt wft
Me3Si
F
3.54
10
9
8
7
6
5
4
3
2
1
0
ppm
6.78
1.34
1.42
1.01
1.02
1.03
1.00
8.38

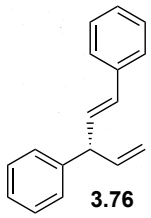

KA-III-116product
exp3 stdlh
SAMPLE
date Nov 29 2008
solvent CDCl3
file
ACQUISITION
sfrq 399.774
tn H1
at 3.744
nt 8
sw 6009.6
fb 3000
bs 4
tpwr 57
pw 7.0
d1 1.250
tof 16
ct 16
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -199.9
wp 4397.4
vs 201
sc 0
wc 380
hzmm 2.34
is 500.00
rfl 1001.1
rfp 0
th 20
ins 1.000
nm cdc ph
DEC. & VT
dfrq 399.774
dn H1
dof 0
dm nnn
dmm c
dmf 200
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn not used
math
werr
wexp
wbase wft
wnt
Me3Si
CF3
3.55
1.82 2.29 1.04
1.93 3.03
1.08
1.02 1.00
1.07
8.56
ppm


KA-III-130product
exp2 std1h
SAMPLE
date Dec 10 2018
solvent CDCl3
file exp
ACQUISITION
sfrq 399.768
tn H1
at 3.744
np 44032
sw 6000.6
fb 3000
bs 4
tpwr 57
pw 7.0
pw1 1.256
tof 0
nt 16
ct 16
alock n
gain n
FLAGS
il n
in n
dp y
hs
DISPLAY
sp -200.0
wp 4397.4
sc 201
wc 360
hzmm 3.50
is 274.60
rfl 1001.2
rfp 0
th 20
ins 1.000
nm
cdc
DEC. & VT
dfrq 399.768
dn H1
dpwr 50
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn not used
math f
werr
wdisp
wbs wft
wnt
Me3Si
Me
3.56
2.252.01
4.98.00
1.03
1.03 1.04
1.07
3.11
8.45
ppm

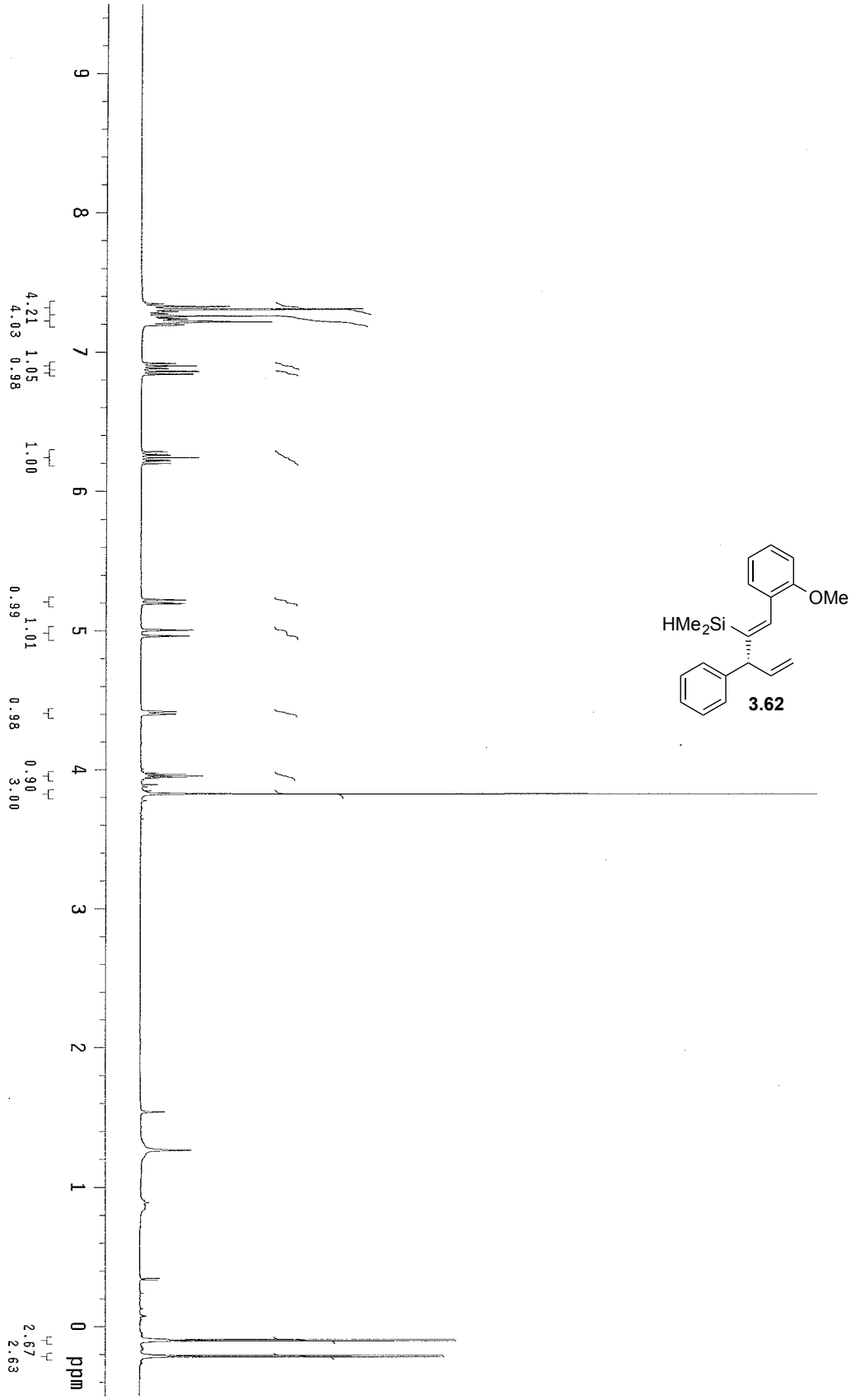

KA-III-172productA
exp3 std1h
SAMPLE
date Feb 7 2009
solvent CDCl3
file exp
ACQUISITION
sfrq 399.768
tn H1
at 3.744
np 44932
sw 6000.6
fb 3000
bs
tpwr 57
pw 7.0
d1 1.256
tof 0
nt 8
ct 8
alock s
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -200.0
wp 4397.4
vs 95
sc 0
wc 380
hzmm 0.73
ins 500.00
rfl 1001.2
rfp 0
th 144
ins 1.000
nm cdc ph
DEC. & VT
dfrq 399.768
dn H1
dpwr 30
dof 0
nnn
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn not used
math f
wexp
wbs
wnt wft
10.77
1.00
1.02
1.05
1.00
0.93
2.79
2.74
10
9
8
7
6
5
4
3
2
1
0
ppm
HMe2Si
3.61

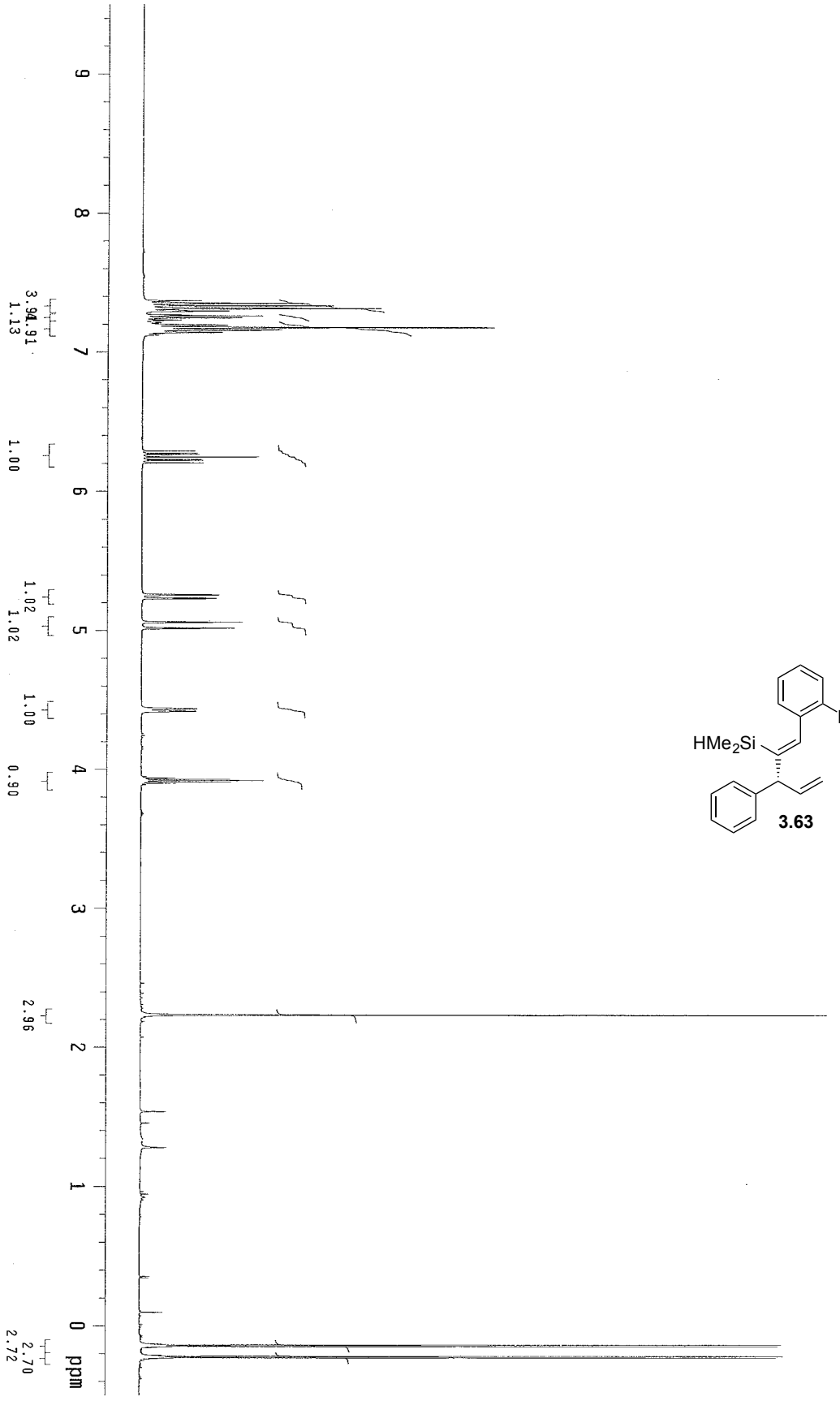


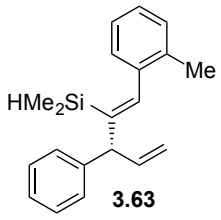

```
KA-III-181productA

exp4  std1h

          SAMPLE
date      Feb 11 2009
solvent   CDCl3
file      exp
ACQUISITION
sfrq      399.768
tn        H1
at        3.741
np        44932
sw        6000.6
fb        3000
bs        4
tdpr      1
pw        7.0
d1        1.256
tof       0
nt        16
ct        16
alock     s
gain      not used
FLAGS
il        n
in        n
dp        y
hs        nn
DISPLAY
sp        -200.0
wp        4397.4
vs        96
sc        0
wc        380
hzmm      0.35
is        250.00
rfl       1001.2
rfp       0
th        20
ins       0
nm  cdc   ph
          1.000
                    DEC. & VT
date      399.768
dn        H1
dpwr      30
dof       0
dm        nnn
dmm       c
dmf       200
dseq
dres      1.0
homo      n
PROCESSING
wtfile
proc      ft
fn        not used
math
werr
wexp
wbs       wft
wnt
```



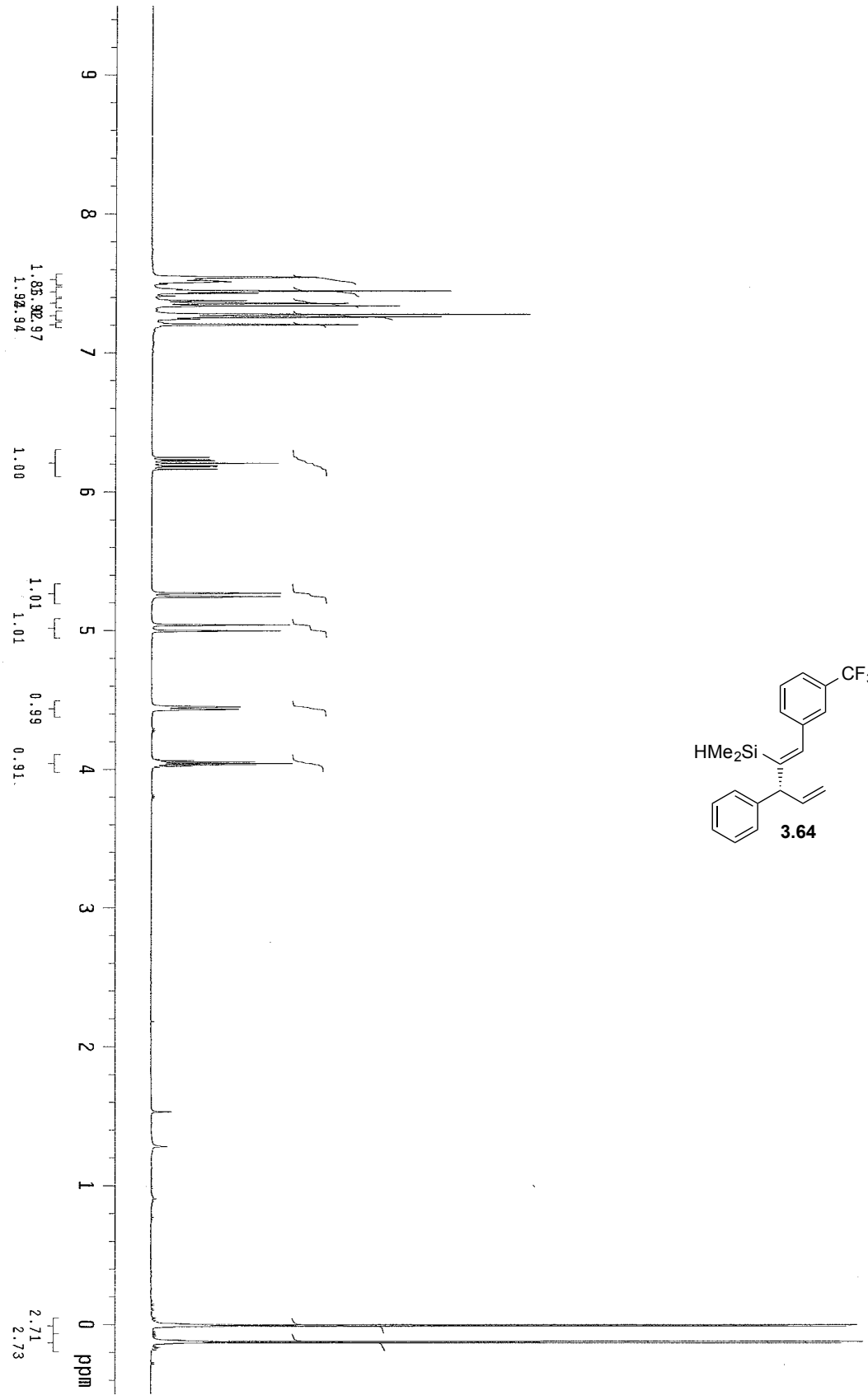
3.76


OMe
HMe2Si
3.62
ppm


9
8
7
6
5
4
3
2
1
0
ppm
3.94
4.91
1.13
1.00
1.02
1.02
1.00
0.90
2.96
2.70
2.72

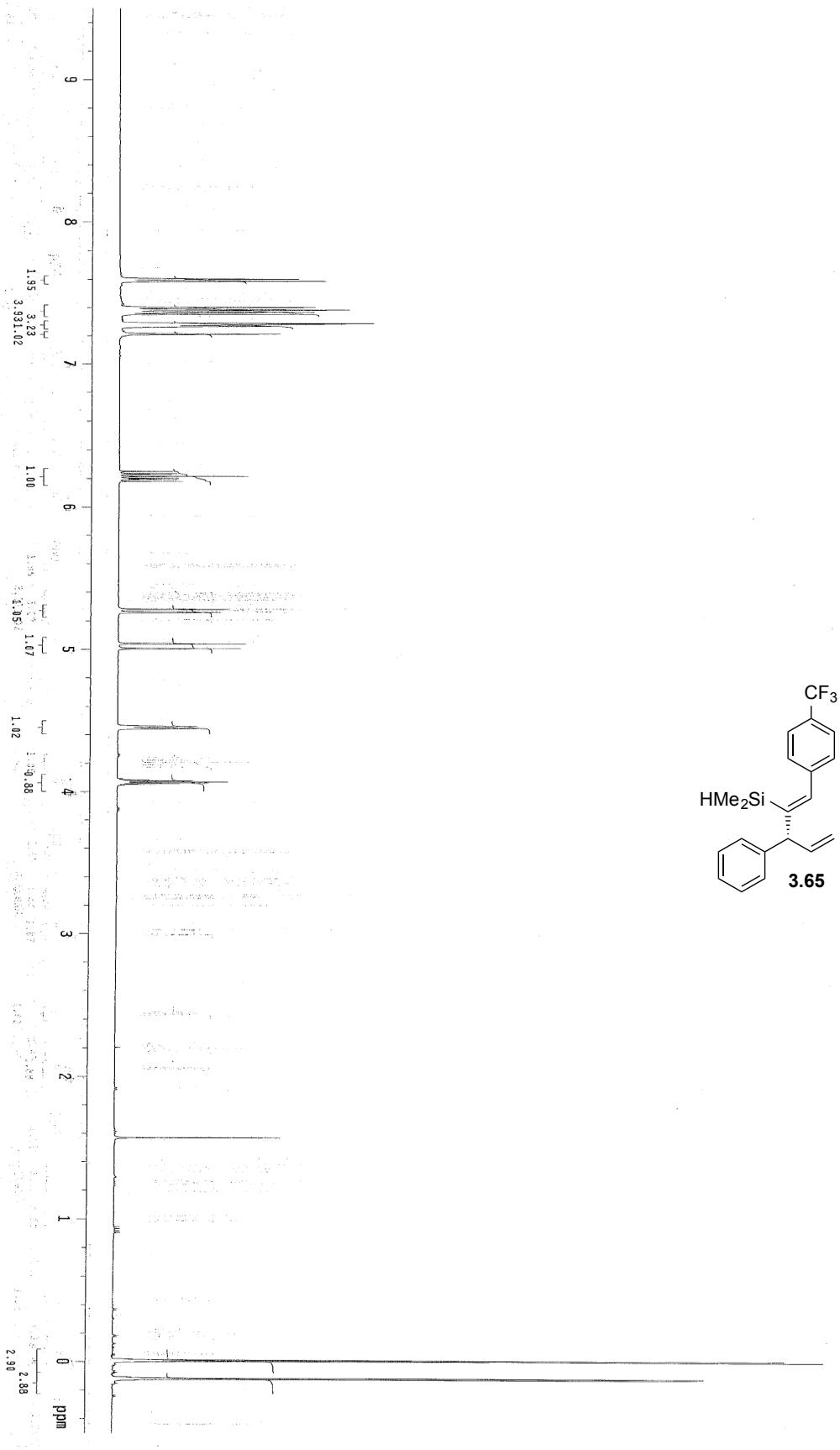

Me
HMe2Si

3.63


9
8
7
6
5
4
3
2
1
0 ppm
1.85
2.00
2.97
1.92
2.94
1.00
1.01
1.01
0.99
0.91
2.71
2.73

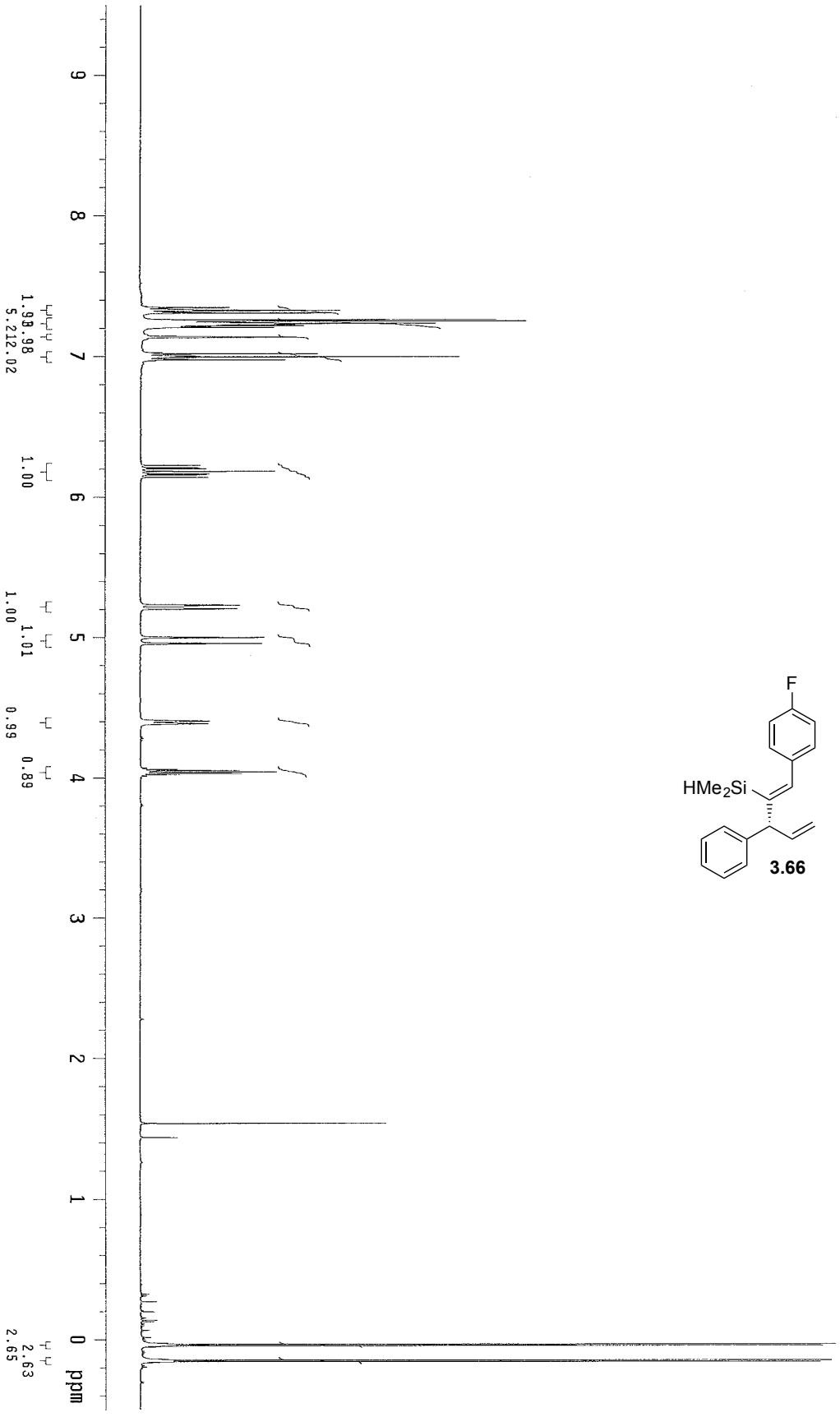
CF3
HMe2Si

3.64


9
8
7
6
5
4
3
2
1
0
ppm
1.95
3.23
3.93
1.02
1.00
1.05
1.07
1.02
0.88
2.90
2.88

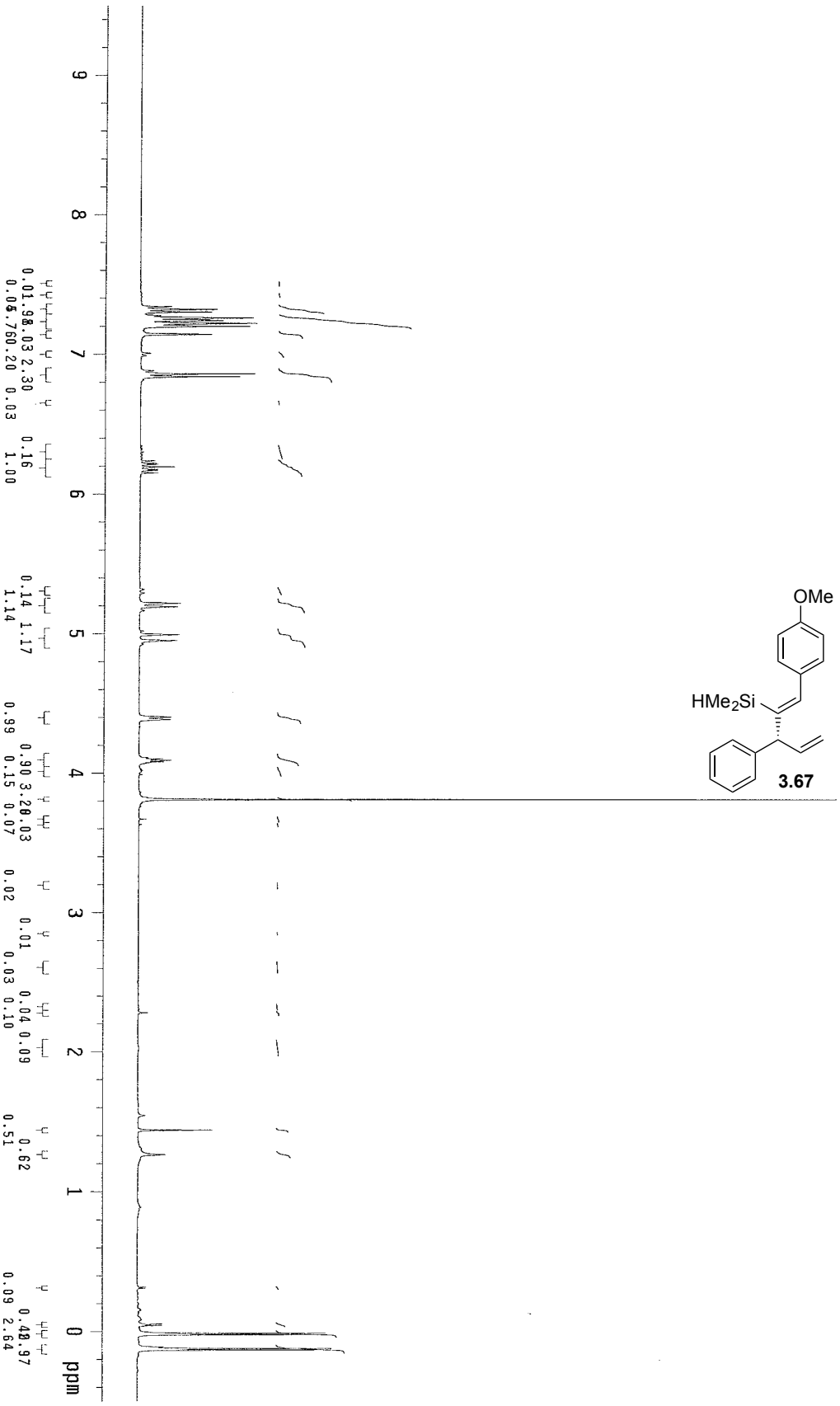
CF3
HMe2Si

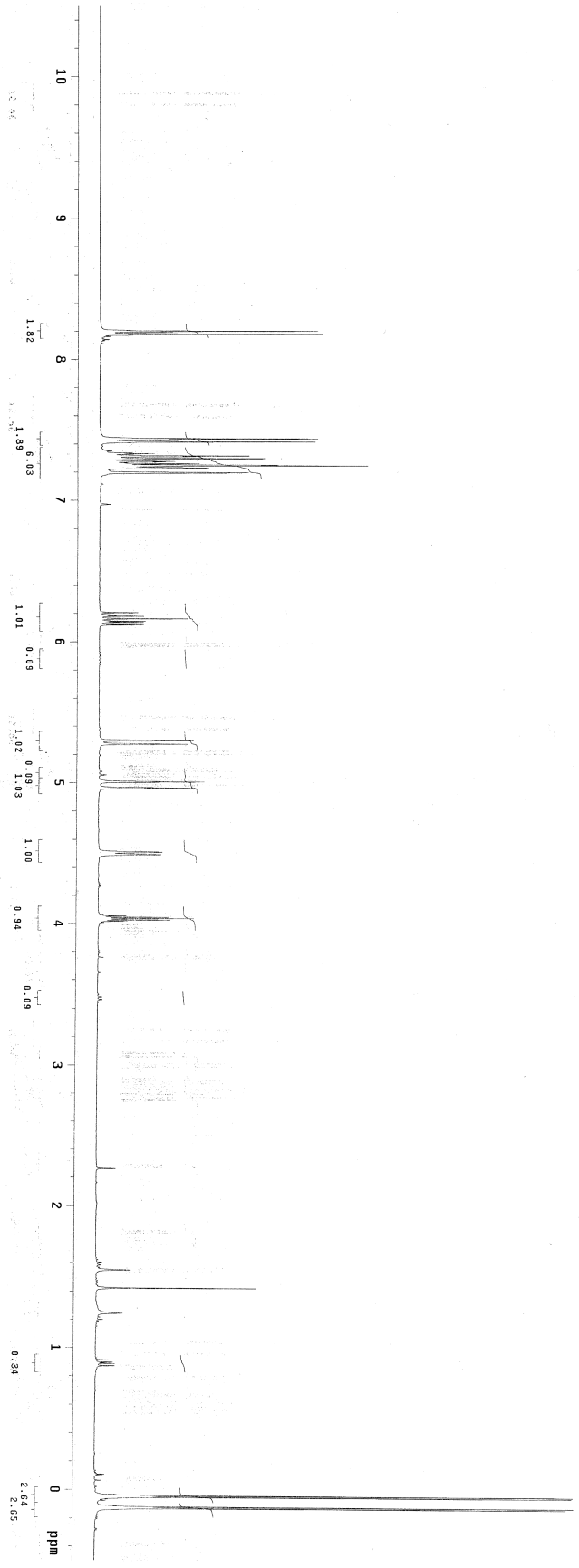
3.65

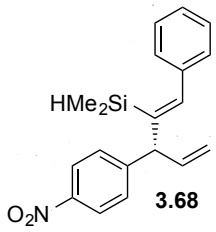

9
8
7
6
5
4
3
2
1
0
ppm
1.98
1.98
5.21
2.02
1.00
1.00
1.01
0.99
0.89
2.63
2.65

F
HMe2Si

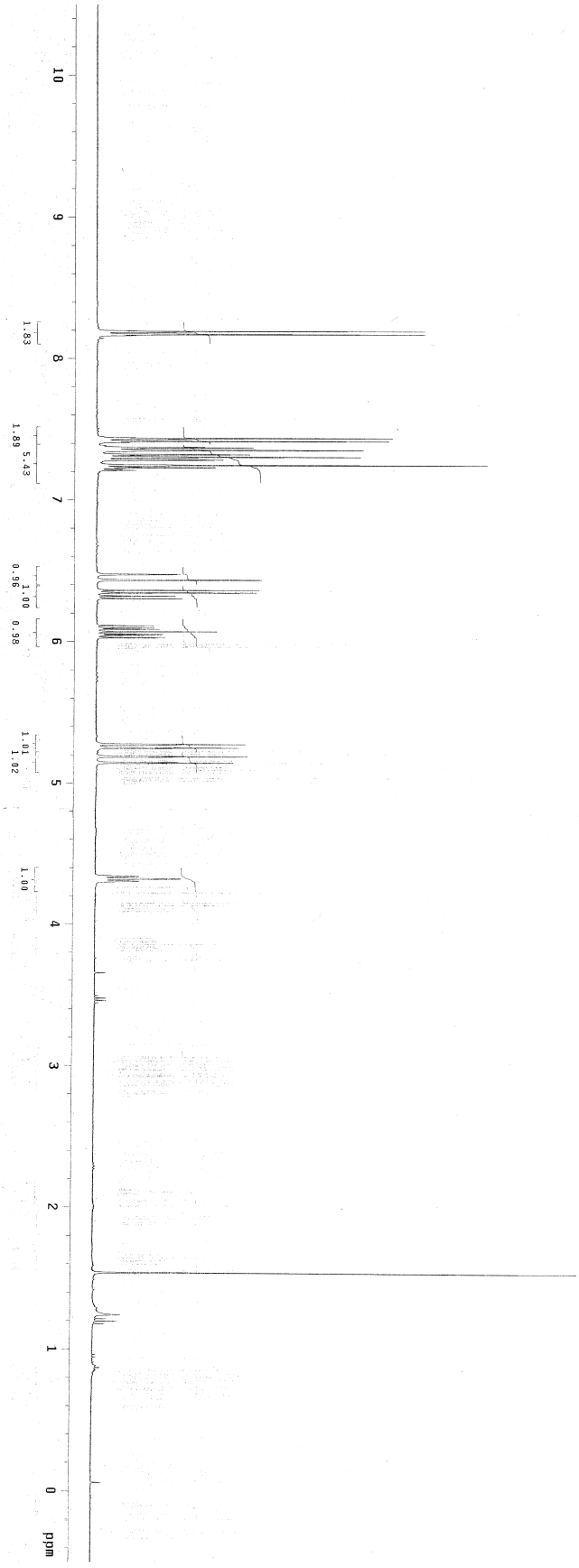
3.66


OMe
HMe2Si
3.67
ppm

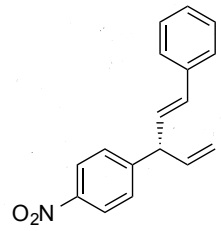

KA-III-171productA
exp4 std1h
SAMPLE
date Feb 9 2009
solvent CDCl3
file ACQUISITION
sfrq 399.768
tn H1
at 3.744
np 16032
sw 6410.3
fb 3900
bs 4
tpwr 57
pw 7.0
d1 1.250
tof 0
nt 16
ct 16
alock s
gain wexp
FLAGS not used wshim
wnt
il n
in n
dp y
hs nn
DISPLAY
sp -200.0
wp 4397.4
vs 112
sc 0
wc 380
hzmm 1.54
is 96.13
rfl 1001.2
rfp 0
th 20
ins 1.000
nm cdc ph
DEC. & VT
dfrq 399.768
dn H1
dpwr 30
dpwr 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
ft
ftpkg f
not used
math
werr
wexp
wft
1.82
1.89
6.03
1.01
0.09
1.02
0.09
1.03
1.00
0.94
0.09
0.34
2.64
2.65
10
9
8
7
6
5
4
3
2
1
0
ppm

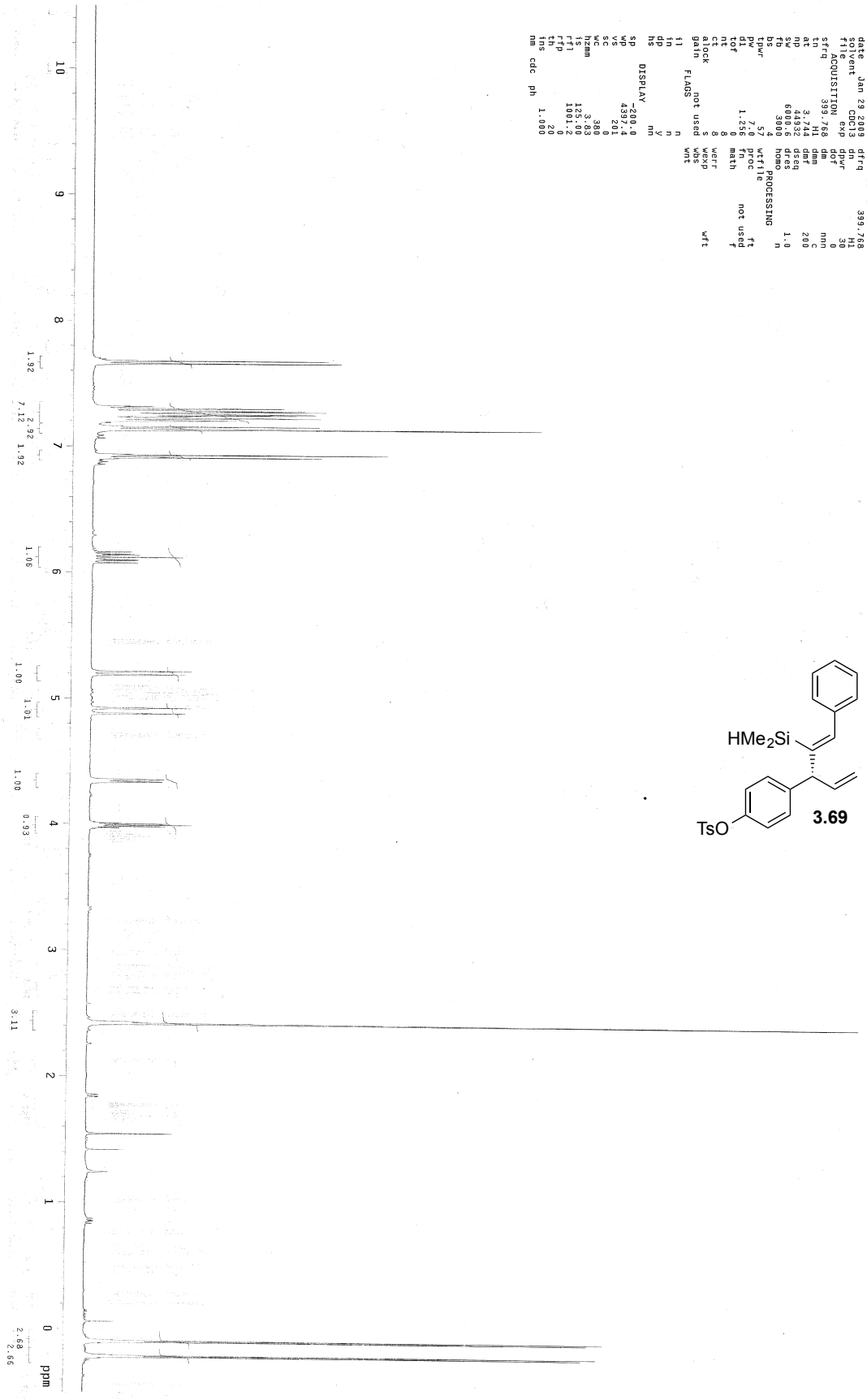

HMe2Si
O2N

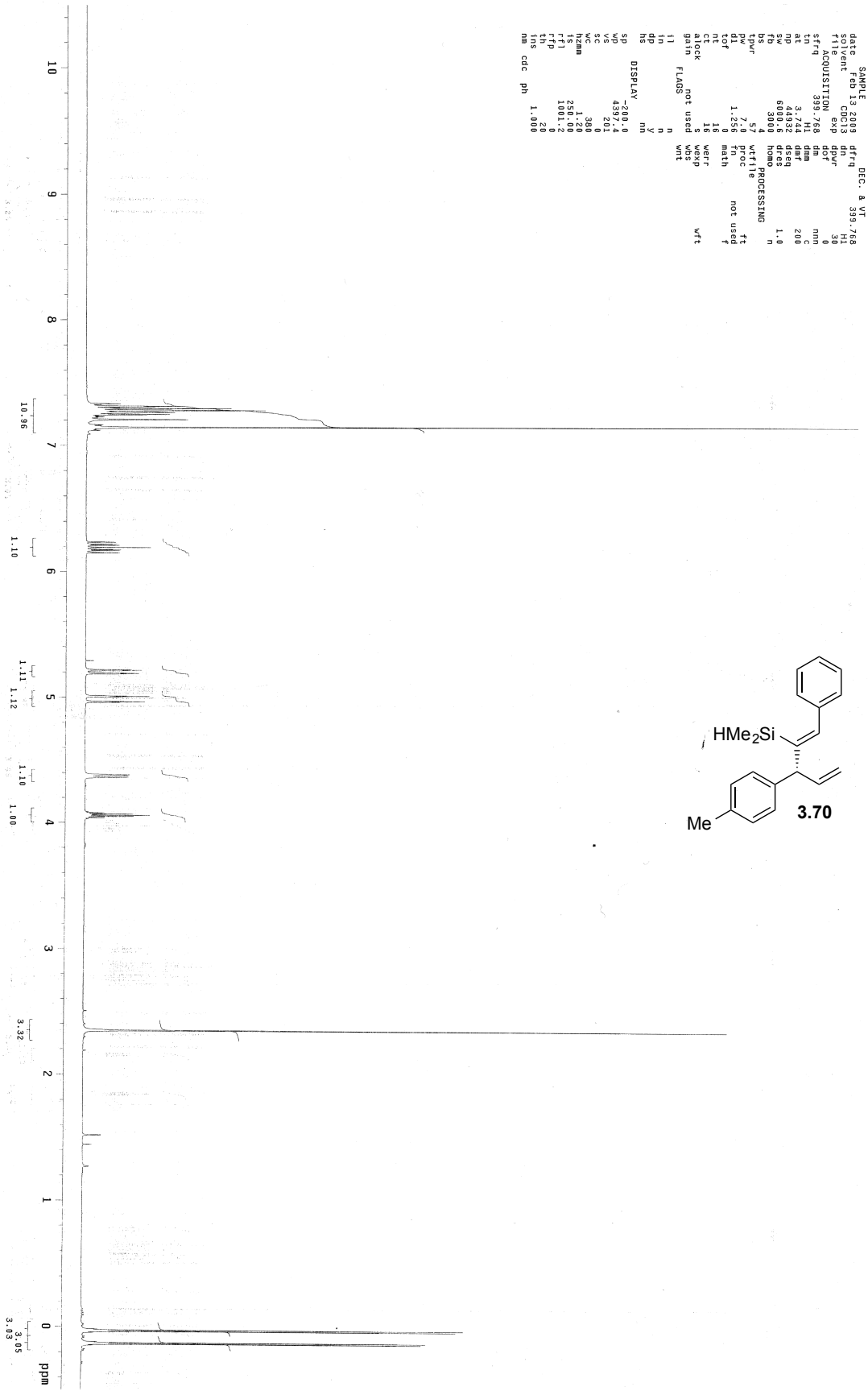
3.68

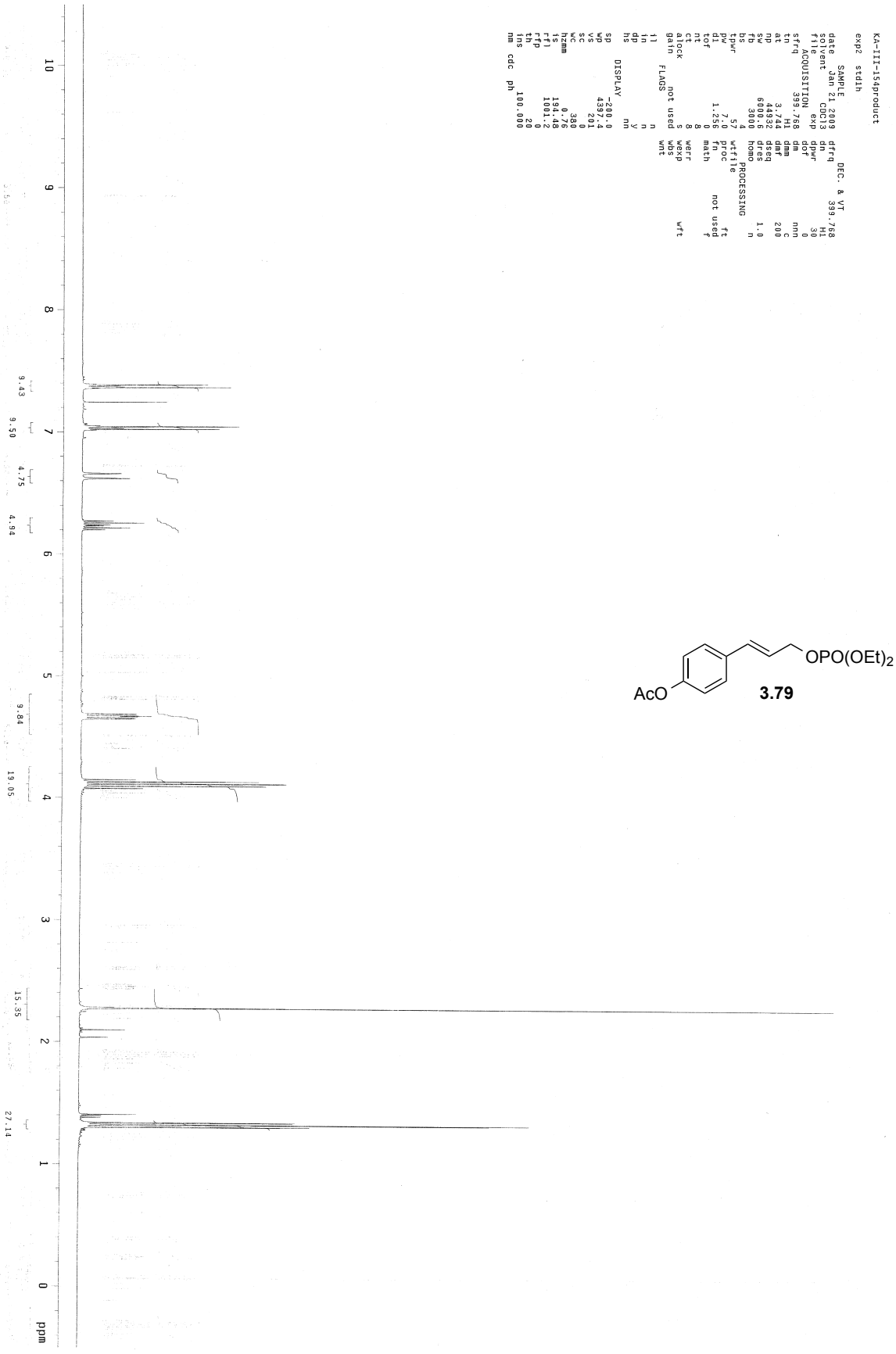


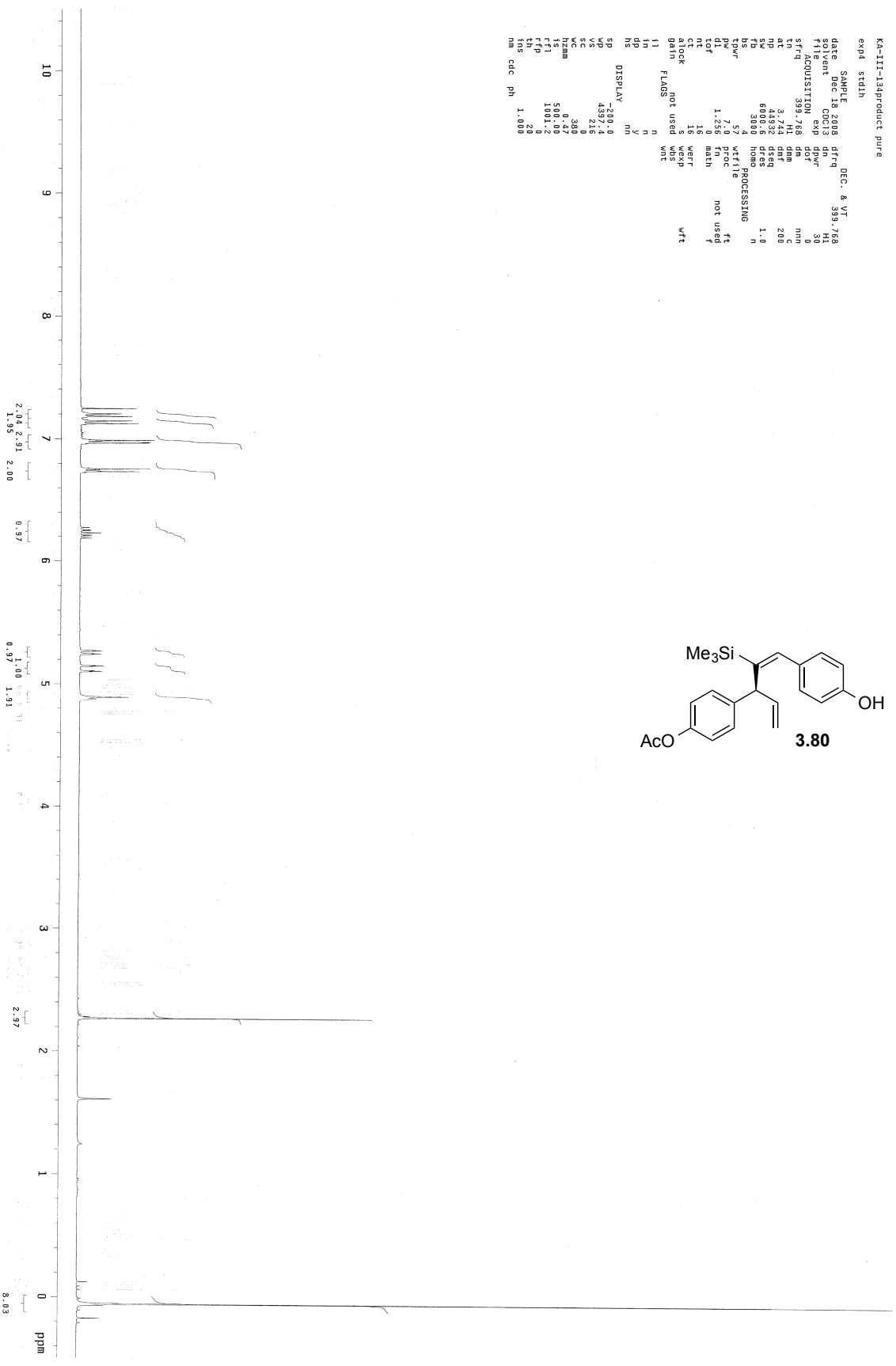

```
KA-III-180product

exp3  stdih

                    SAMPLE
date                Feb 11 2009
solvent             CDCl3
file                acquisition
                    exp
sfrq                399.768
tn                  H1
at                  3.744
np                  44932
sw                  6010.5
fb                  3000
bs                  4
tpwr                57
pw                  7.0
pw1                 1.256
                    16
                    16
ct                  0
alock               s
gain                not used
                    FLAGS
il                  n
in                  n
dp                  y
hs                  nn
                    DISPLAY
sp                  -200.0
wp                  4397.4
vs                  112
sc                  0
wc                  350
hzmm                2.04
is                  125.00
rfl                 1001.2
rfp                 0
th                  20
ins                 1.000
nm  cdc  ph

                                    DEC. & VT
                                    dfrq        399.768
                                    dn          H1
                                    dpwr        30
                                    dof         0
                                    dm          nnn
                                    dmm         c
                                    dmf         200
                                    dseq
                                    homo        1.0
                                    homo        n
                                    PROCESSING
                                    wtfile
                                    proc        ft
                                    fn          not used
                                    math        f
                                    werr
                                    wexp
                                    wbs         wft
                                    wnt
```

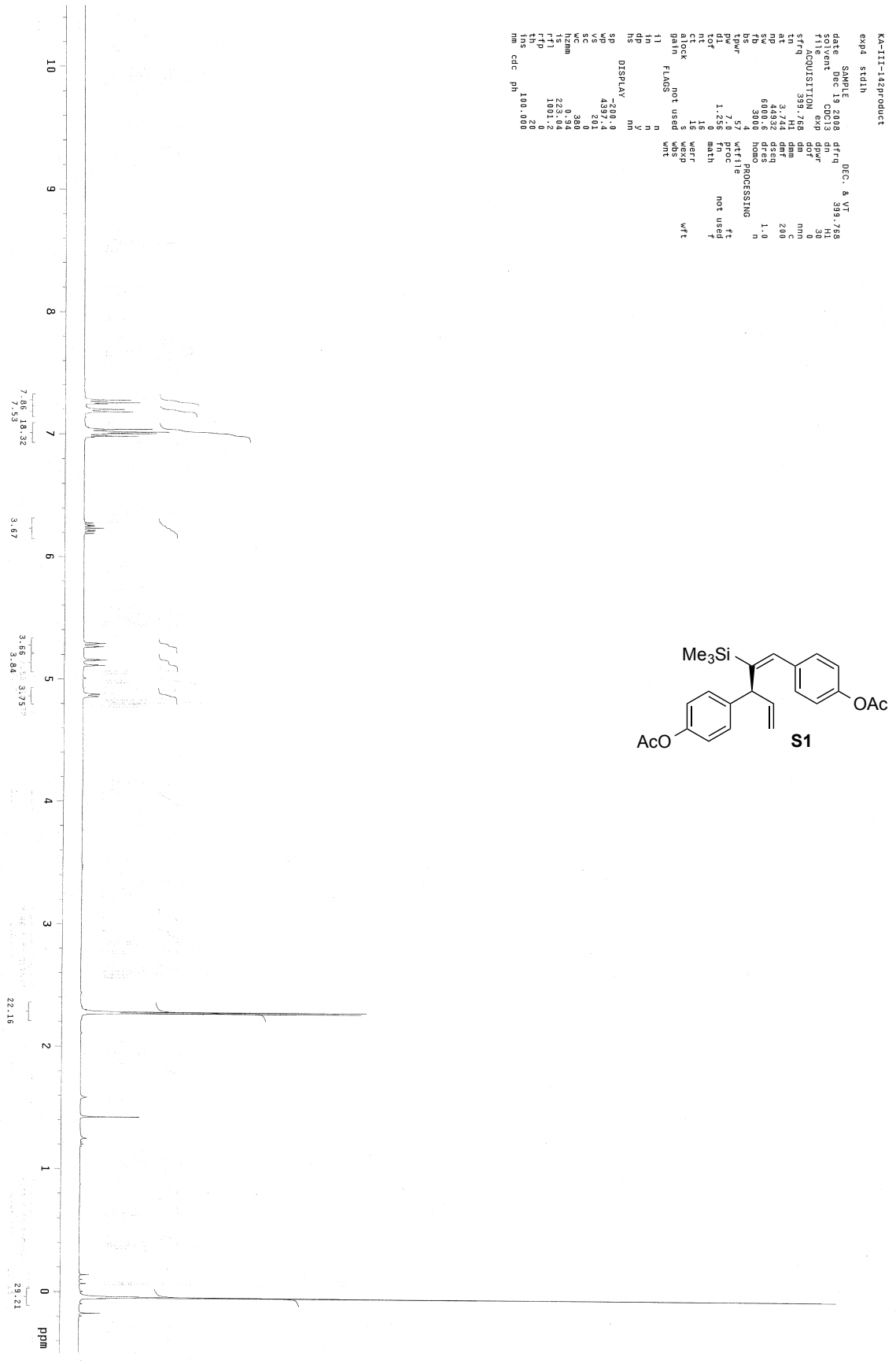


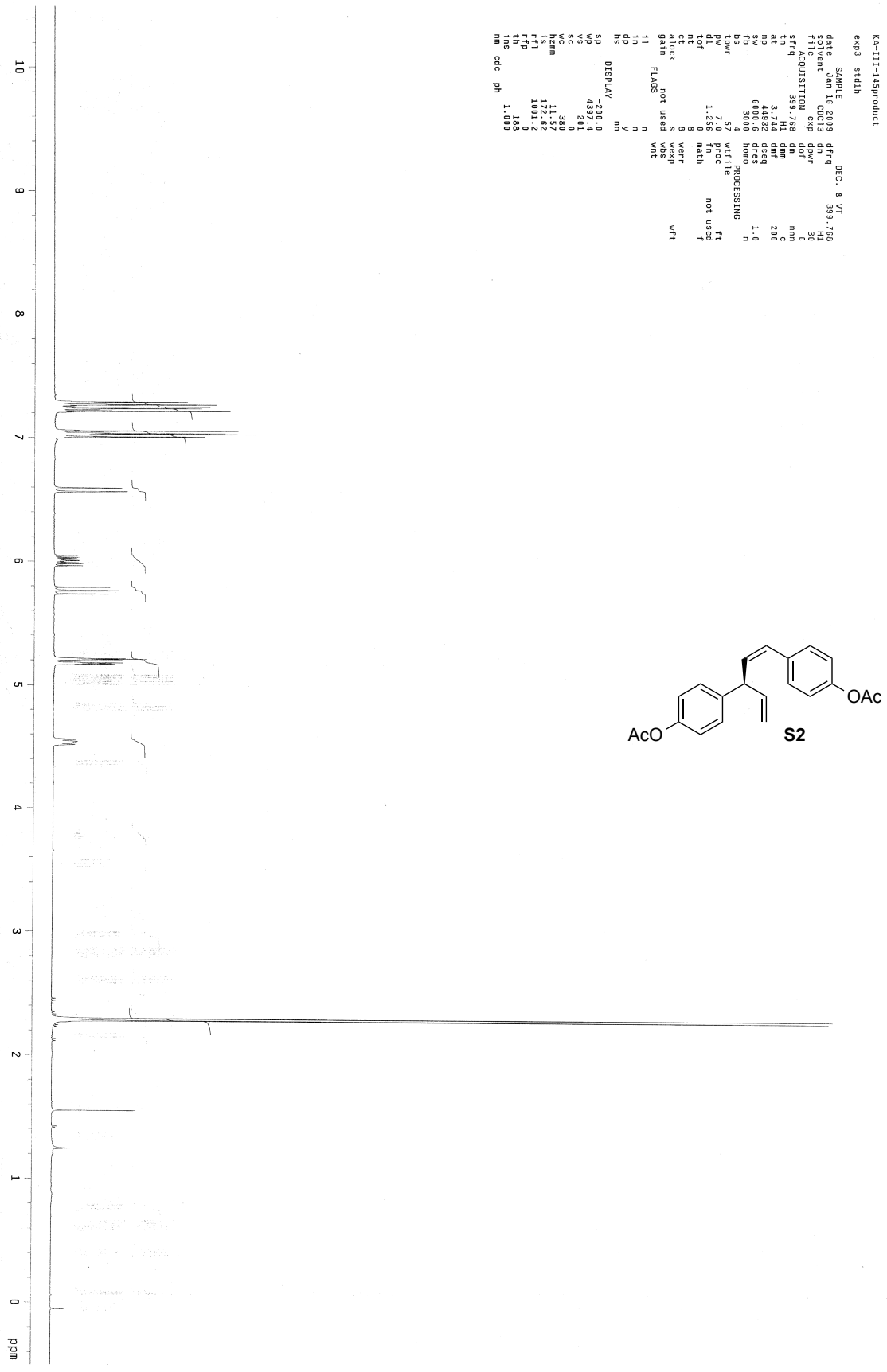

KA-III-153productC
exp3 std1h
SAMPLE
date Jan 29 2009
solvent CDCl3
file Exp
ACQUISITION
sfrq 399.768
tn H1
at 3.744
nt 4
sw 6000.6
fb 3000
bs 4
tpwr 57
pw 7.0
d1 1.256
tof 0
nt 8
ct 8
alock s
gain
FLAGS
not used
il n
in n
dp y
hs nn
DISPLAY
sp -200.0
wp 4397.4
vs 2
sc 0
wc 380
hzmm 3.83
fp 125.00
rfl 1001.4
rfp 0
th 20
ins 1.000
nm cdc ph
DEC. & VT
dfrq 399.768
dn H1
dof 0
nnn
c 200
dmf
dmm
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt
wft
HMe2Si
TsO
3.69
ppm

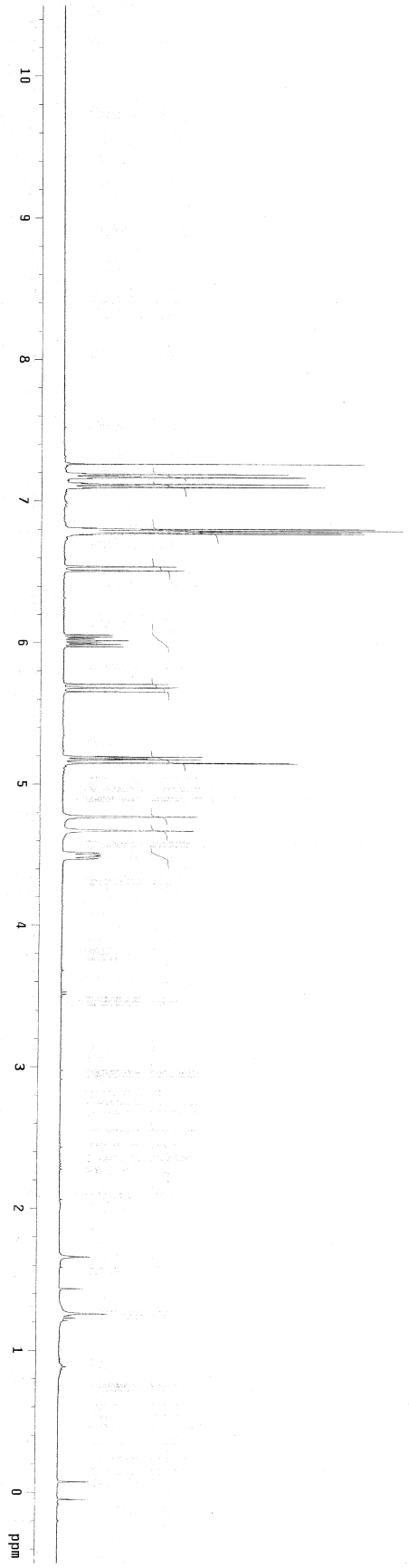

KA-III-185productA
exp4 std1h
SAMPLE
date Feb 13 2019
solvent CDCl3
file exp
ACQUISITION
sfrq 399.768
tn H1
at 3.744
np 44932
sw 6000.6
fb 3000
bs 4
tpwr 57
pw 7.5
d1 1.256
tof 0
nt 16
ct 16
alock n
gain 50
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -200.0
wp 4397.4
sc 20.1
wc 380
hzmm 1.20
is 250.00
rfl 1001.2
rfp 0
th 20
ins 1.000
nm cdc ph
DEC. & VT
dfrq 399.768
dn H1
dof 30
dm nnn
dmm c
dmf 200
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt wft
HMe2Si
Me
3.70
10.96
1.10
1.11
1.12
1.10
1.00
3.32
3.05
3.03
ppm


KA-III-154product
exp2 std1h
SAMPLE
date Jan 21 2009
solvent CDCl3
file exp
ACQUISITION
sfrq 399.768
tn H1
at 3.741
np 44932
sw 6000.6
fb 3000
bs 4
tdpwr 57
pw 7.0
d1 1.256
tof 0
nt 8
ct 8
alock n
gain FLAGS not used
n
n
y
nn
DISPLAY
-200.0
4397.4
20.1
0
380
0.76
194.48
1001.2
20
100.000
cdc ph
DEC. & VT
dfrq 399.768
dn H1
dpwr 30
dof 0
nnn
c 200
dmm
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn not used
math f
wtr
werr
wexp wft
wbs
wnt
9.43
9.50
4.75
4.94
9.84
19.05
15.35
27.14
10
9
8
7
6
5
4
3
2
1
0
ppm
OPO(OEt)2
AcO
3.79

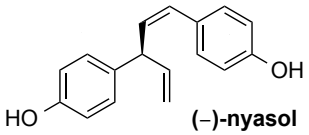

KA-III-134product pure
exp4 std1h
SAMPLE
date Dec 18 2008
solvent CDCl3
file ACQUISITION
sfrq 399.768
tn H1
at 3.744
np 44932
sw 6000.6
fb 300.4
bs 57
tpwr 57
pw 7.0
pl 1.256
nt 16
ct 16
alock s
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -200.0
wp 4397.4
vs 216
sc 0
wc 387
hzmm 0.87
fs 500.00
rfl 1001.2
rfp 0
th 20
lns 1.000
nm cdc ph
dfrq DEC. & VT 399.768
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn not used
math f
wexp
wbs wft
wnt
Me3Si
OH
AcO
3.80
ppm


KA-III-142product
exp4 stdih
SAMPLE
date Dec 19 2013
solvent CDCl3
file ACQUISITION
sfrq 399.768
tn H1
at 3.744
nt 44932
sw 6000.6
fb 3000
bs 54
tpwr 57
pw 7.0
d1 1.256
tof 0
nt 16
ct 16
alock n
gain n
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -200.0
wp 4397.4
vs 2011
sc 0
wc 380
hzmm 0.94
is 223.04
rfl 1001.2
rfp 0
th 20
ins 100.000
nm cdc ph
DEC. & VT
dfrq 399.768
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt
wft
Me3Si
OAc
AcO
S1
ppm
7.86 18.32
7.53
3.67
3.86 3.75
3.84
22.16
29.21

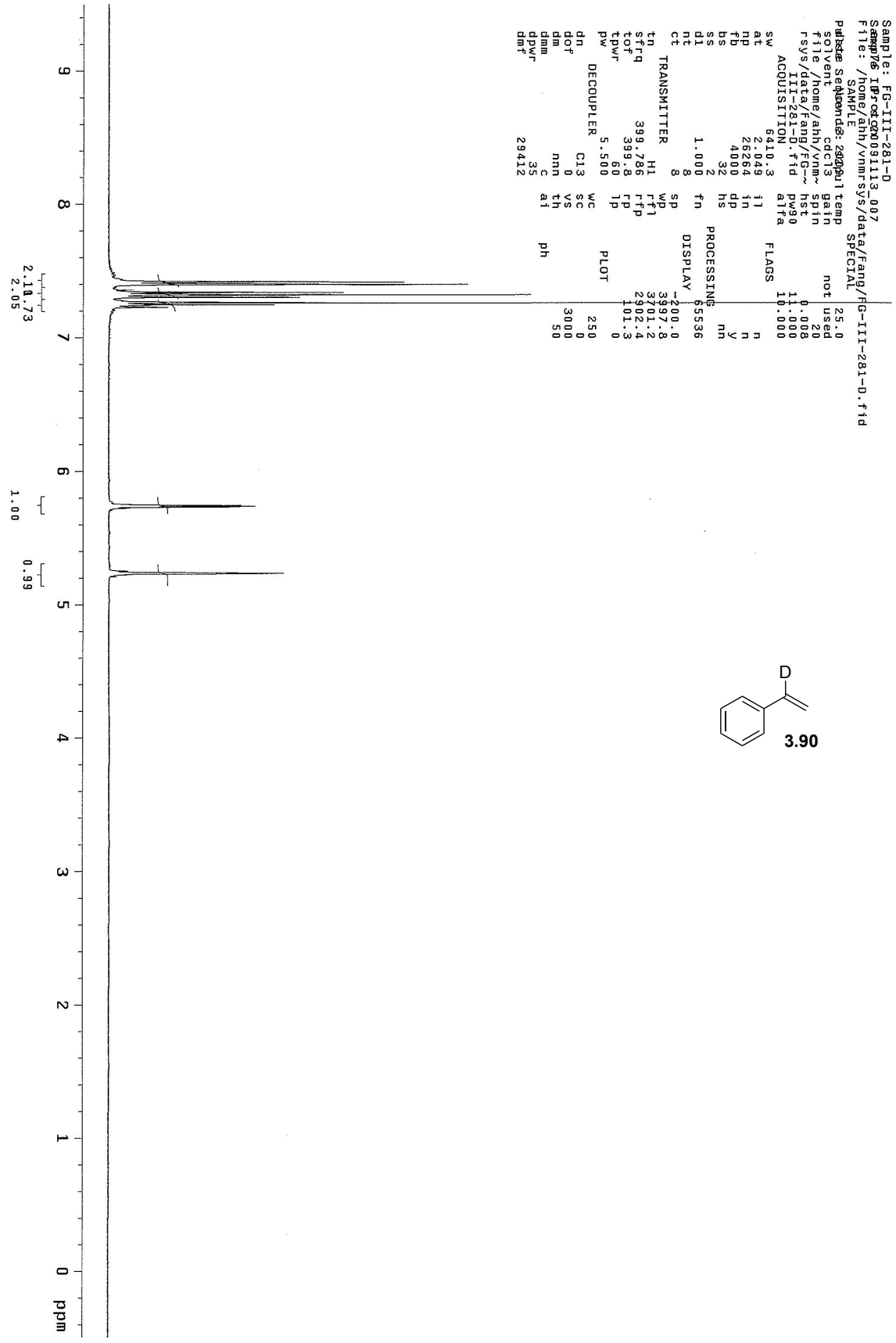

Ka-III-145product
exp3 std1h
SAMPLE
date Jan 16 2009
solvent CDCl3
file exp
ACQUISITION
sfrq 399.768
tn H1
at 3.744
np 43232
sw 6000.6
fb 3000
bs 4
tpwr 57
pw 7.700
dl 1.258
tof 8
nt 8
ct 8
alock s
gain wexp
FLAGS not used
il n
in n
dp y
hs nn
DISPLAY
sp -200.0
wp 4397.4
vs 201
sc 30.0
wc 11.59
hzmm 172.62
fs 1001.2
rfl 0
rfp 188
th 1.000
nm cdc ph
dfrq DEC. & VT
dn 399.768
nn 30
np 0
ni nnn
ns c
lb 200
gb 1.0
vs n
PROCESSING
wtfile
proc ft
math not used
werr
wexp
wbs wft
wnt
OAc
AcO
S2
10
9
8
7
6
5
4
3
2
1
0
ppm




```
KA-III-167productA
exp3  stdih

      SAMPLE                    DEC. & VT
date  Jan 29 2009         dfrq  399.768
solvent   CDCl3           dn    H1
file      exp             dpwr  30
ACQUISITION               dof   0
sfrq  399.768             dm    nnn
tn    H1                  dmm   c
at    3.744               dmf   200
np    44932               dseq
sw    6009.6              dres  1.0
fb    9000                homo  n
bs    16              PROCESSING
tpwr  57              wtfile
pw    7.0             proc      ft
p1    1.256           fn        not used
dl                    math
tof   0
nt    16              werr
ct    16              wexp
alock s               wbs       wft
gain                  wnt
      not used
      FLAGS
il          n
in          n
dp          y
hs          nn
      DISPLAY
sp    -200.0
wp    4397.4
vs    76
sc    0
wc    380
hzmm  11.57
hs    1221.0
rfl   3856.9
rfp   2902.3
th    20
ins   100.000
nm  cdc  ph
```



(–)-nyasol


Sample: FG-III-281-D
Sample 76 IPrSc 20091113_007
File: /home/ahh/vnmrsys/data/Fang/FG-III-281-D.fid
SAMPLE
Pulse Sequence: s2pul temp 25.0
solvent cdcl3 gain not used
file /home/ahh/vnm~ spin 20
rsys/data/Fang/FG-~ hst 0.008
III-281-D.fid pw90 11.000
ACQUISITION alfa 10.000
sw 6410.3 FLAGS
at 2.049 il n
np 26264 in n
fb 4000 dp y
bs 32 hs nn
ss 2 PROCESSING
d1 1.000 fn 65536
nt 8 DISPLAY
ct 8 sp -200.0
wp 3997.8
TRANSMITTER rfl 3701.2
tn H1 rfp 2902.4
sfrq 399.786 rp 101.3
tof 399.8 lp 0
tpwr 60 PLOT
pw 5.500 wc 250
DECOUPLER sc 0
dn C13 vs 3000
dof 0 th 50
dm nnn ph
dmm c ai
dpwr 35
dmf 29412
D
3.90
ppm
9
8
7
6
5
4
3
2
1
0
2.10
1.73
2.05
1.00
0.99

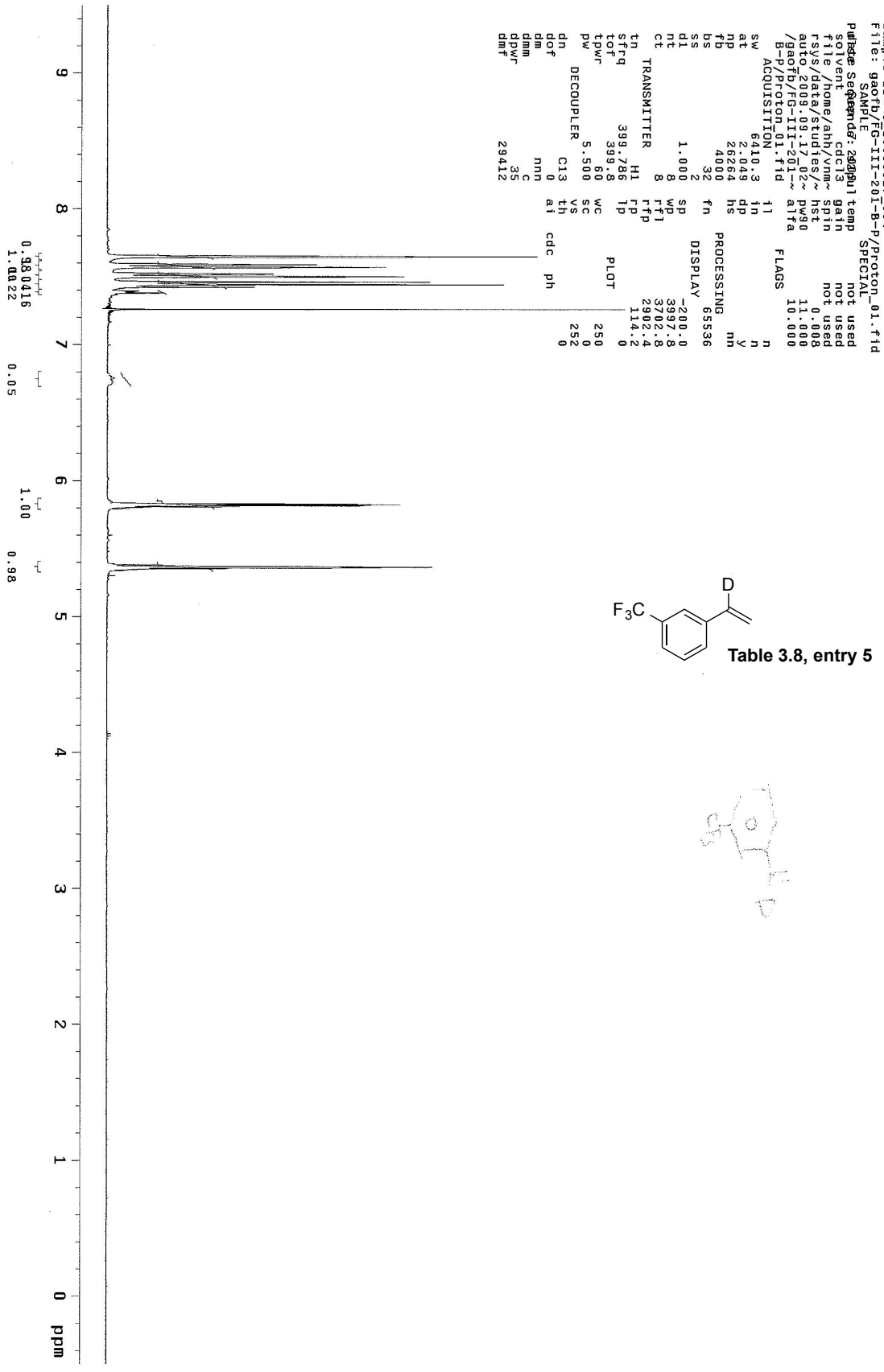
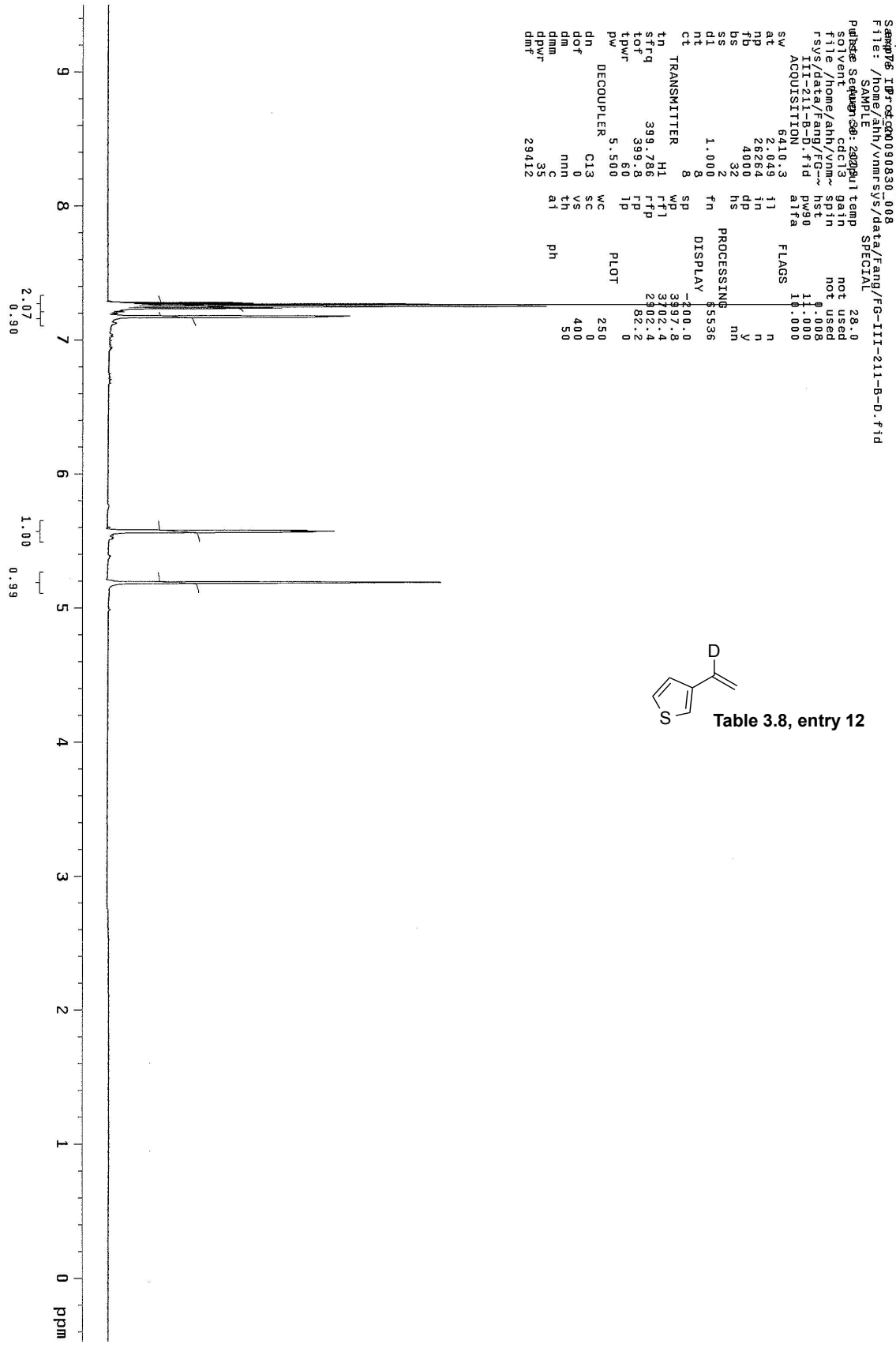
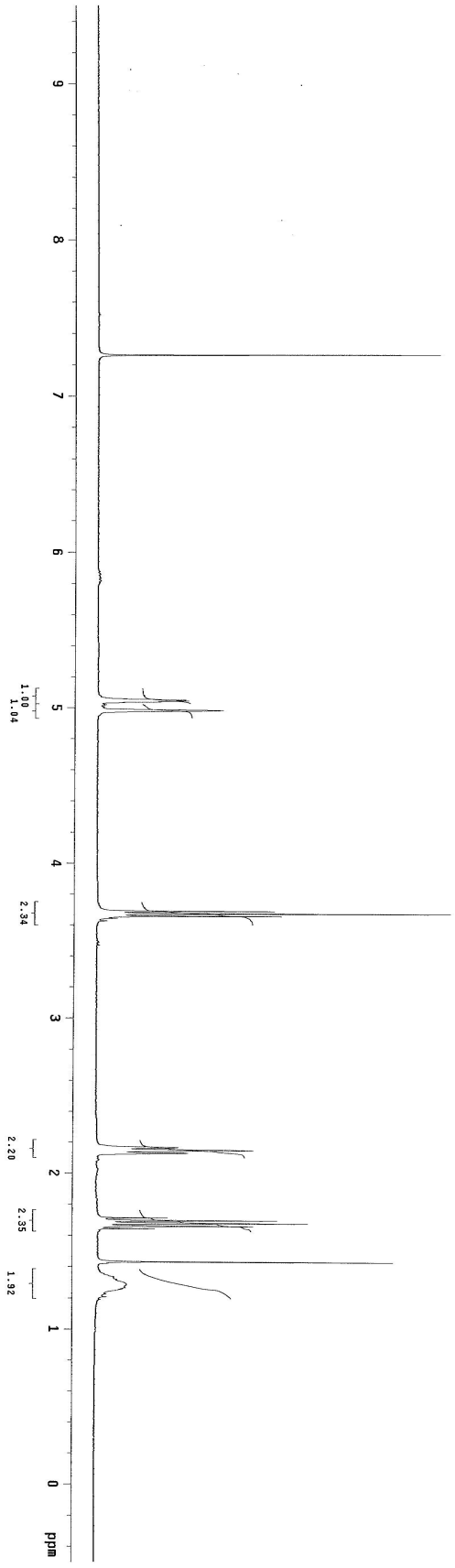


Table 3.8, entry 5


Sample: FG-III-211-B-D
Solvent: cdcl3
File: /home/ahh/vnmrsys/data/Fang/FG-III-211-B-D.fid
SAMPLE
Pulse Sequence: s2pul temp
solvent gain
file /home/ahh/vnm~ spin
rsys/data/Fang/FG~ hst
III-211-B-D.fid pw90
ACQUISITION FLAGS
sw 6410.3 fl n
at 2.049 in n
np 26264 dp y
fb 4000 hs nn
bs 32
ss 2 PROCESSING
d1 1.000 fn 65536
nt 8 DISPLAY
ct 8 sp -200.0
wp 3597.8
TRANSMITTER rfl 3702.4
tn H1 rfp 2902.4
sfrq 399.786 rp 82.2
tof 399.8 lp 0
tpwr 60
pw 5.500 PLOT
DECOUPLER wc 250
C13 sc 0
dn 0 vs 400
dof nnn th 50
dm ph
dmm al
dpwr 35
dmf 29412
28.0
not used
not used
0.008
11.000
10.000
D
S
Table 3.8, entry 12
2.07
0.90
1.00
0.99
ppm




```
Sample: FG-IV-032-D-pdt
SampleID: fgrp_001102_004
File: /home/ahh/vmrsys/data/fang/FG-IV-032-D-pdt.fid

PulseSequence: s2pul                    temp          SPECIAL
                                        temp          25.0
solvent    cdcl3                        spin          not used
file /home/ahh/vnmr                     hst                0.008
rsys/data/fang/FG~                      pw90              11.000
IV-032-D-pdt.fid                        alfa              10.000
ACQUISITION                       FLAGS
sw      6210.3                    il          n
at      2.604                     in          n
np      26264                     dp          y
fb      4000                      hs          nn
bs      32
ss      2                 PROCESSING
d1      1.000             fn      65536
nt      8                 DISPLAY
ct      8                 sp      -200.0
TRANSMITTER               wp      3997.8
tn      H1                rfl     3702.2
sfrq    399.788           rfp     2982.4
tof     3990.0            lp      1024.6
tpwr    60                lp      -14.3
pw      5.500
DECOUPLER                 PLOT
dn      C13               wc      380
dof     0                 sc      0
dm      nnn               vs      200
dmm     c                 ai      1
dpwr    35                ph
dmf     29412
```

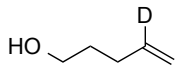


Table 3.9, entry 2

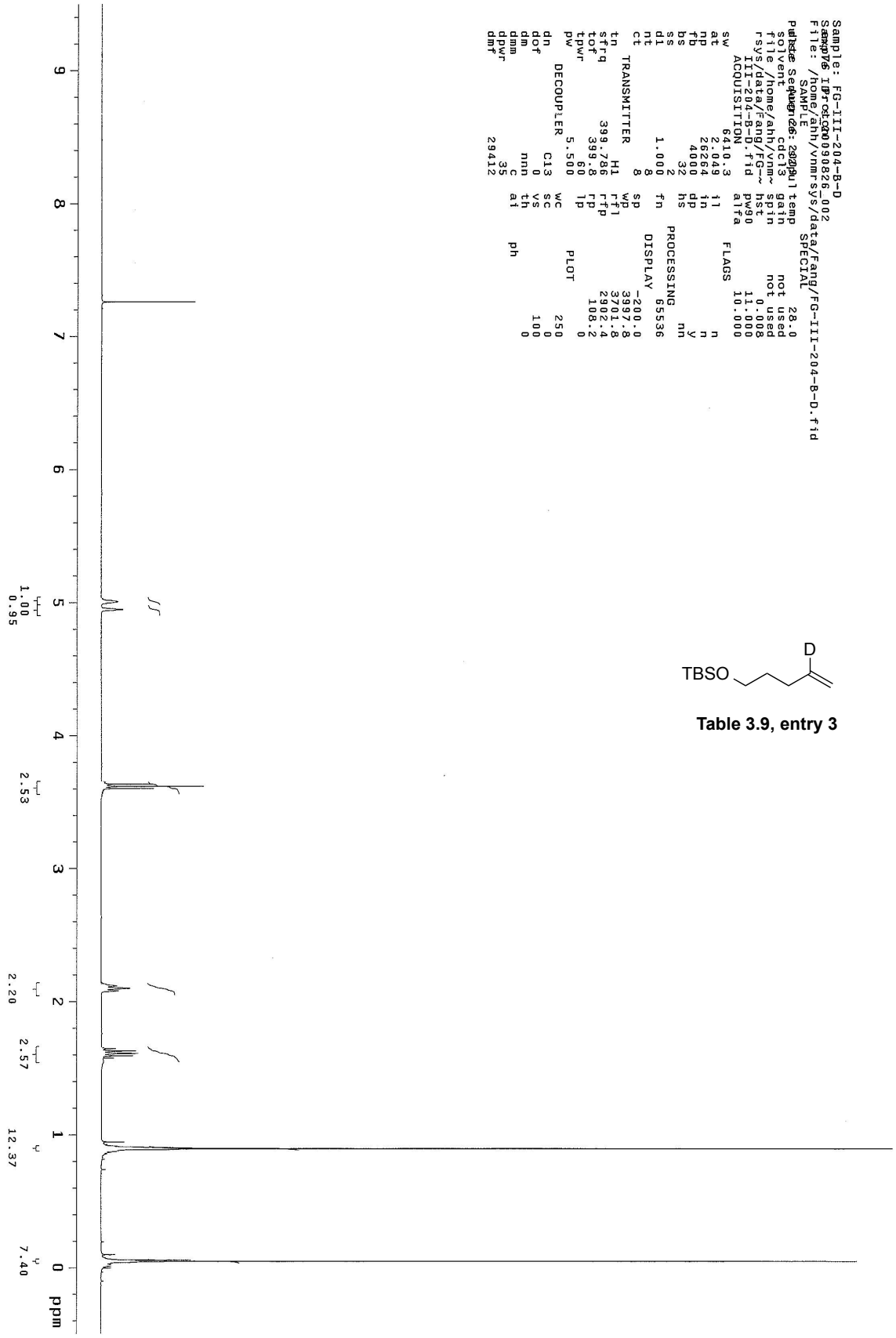


Table 3.9, entry 3

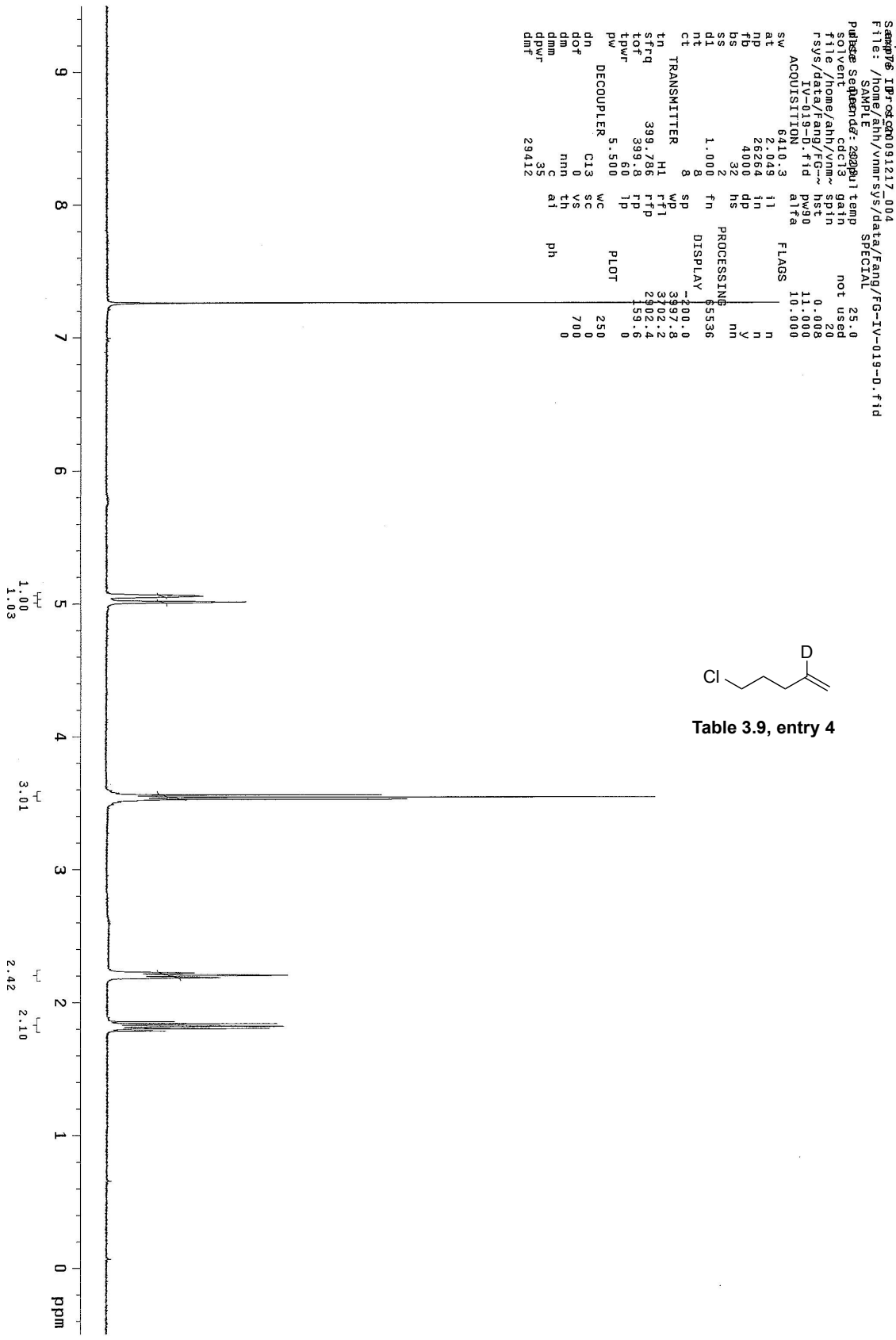
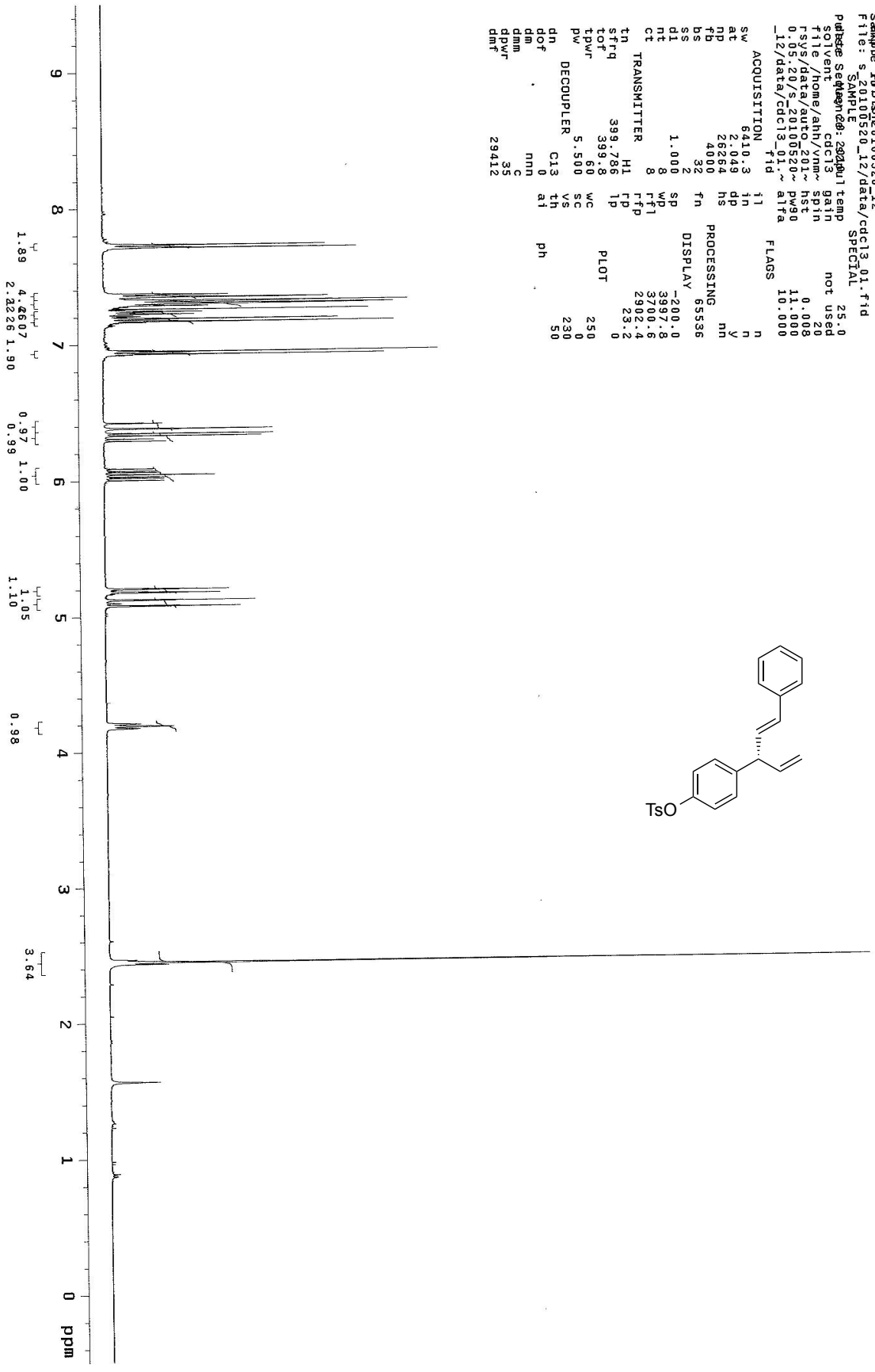
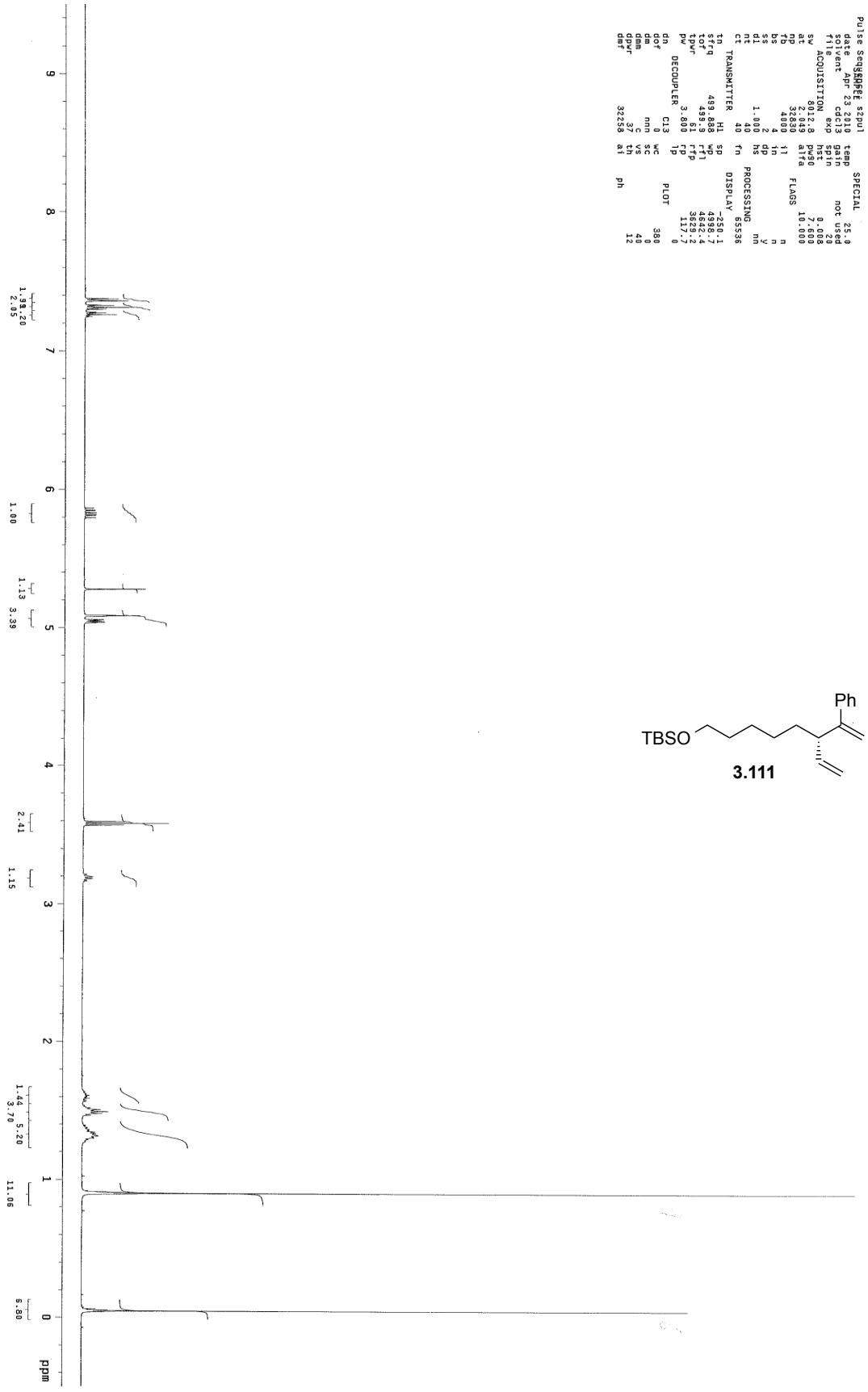
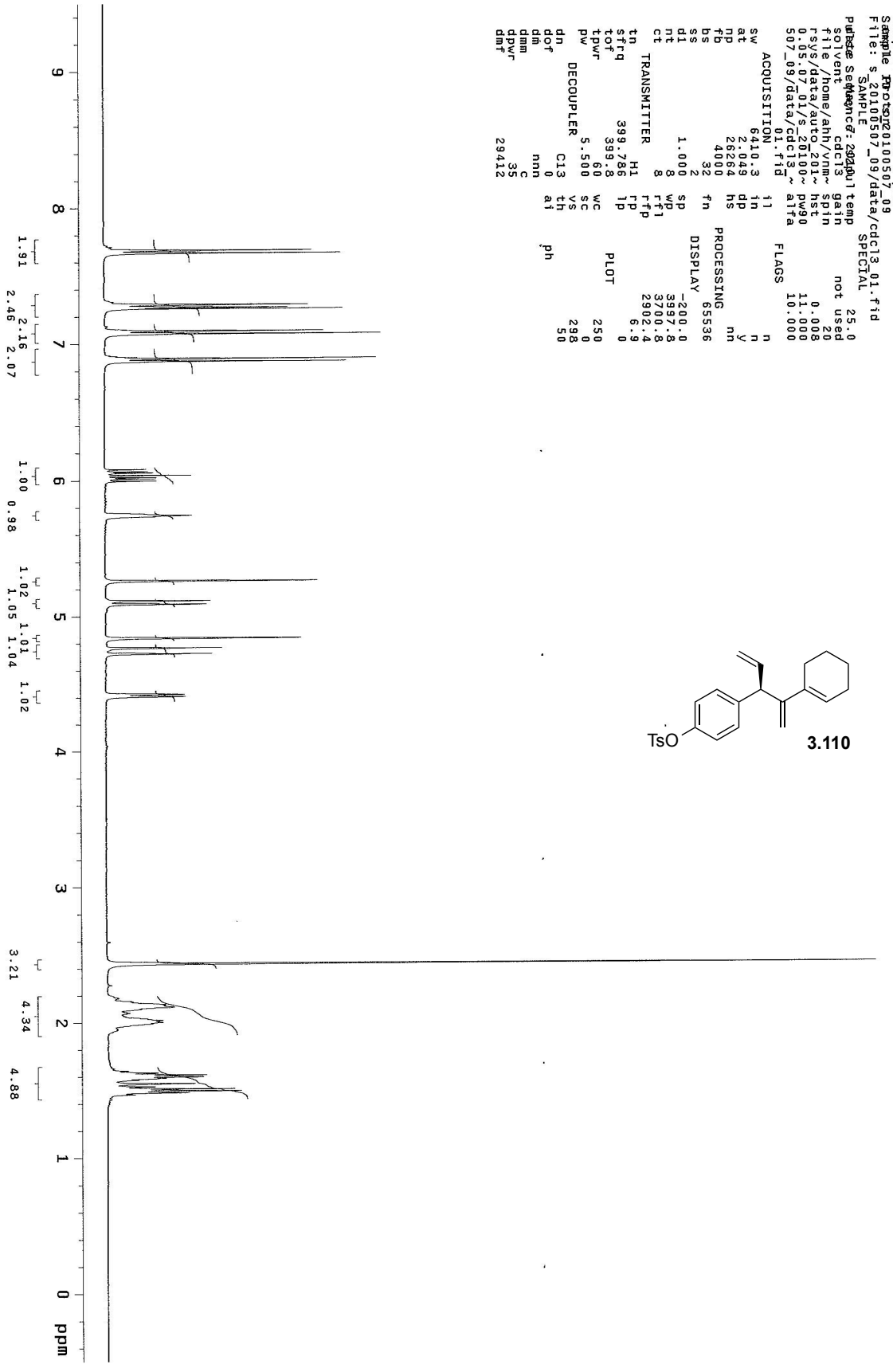
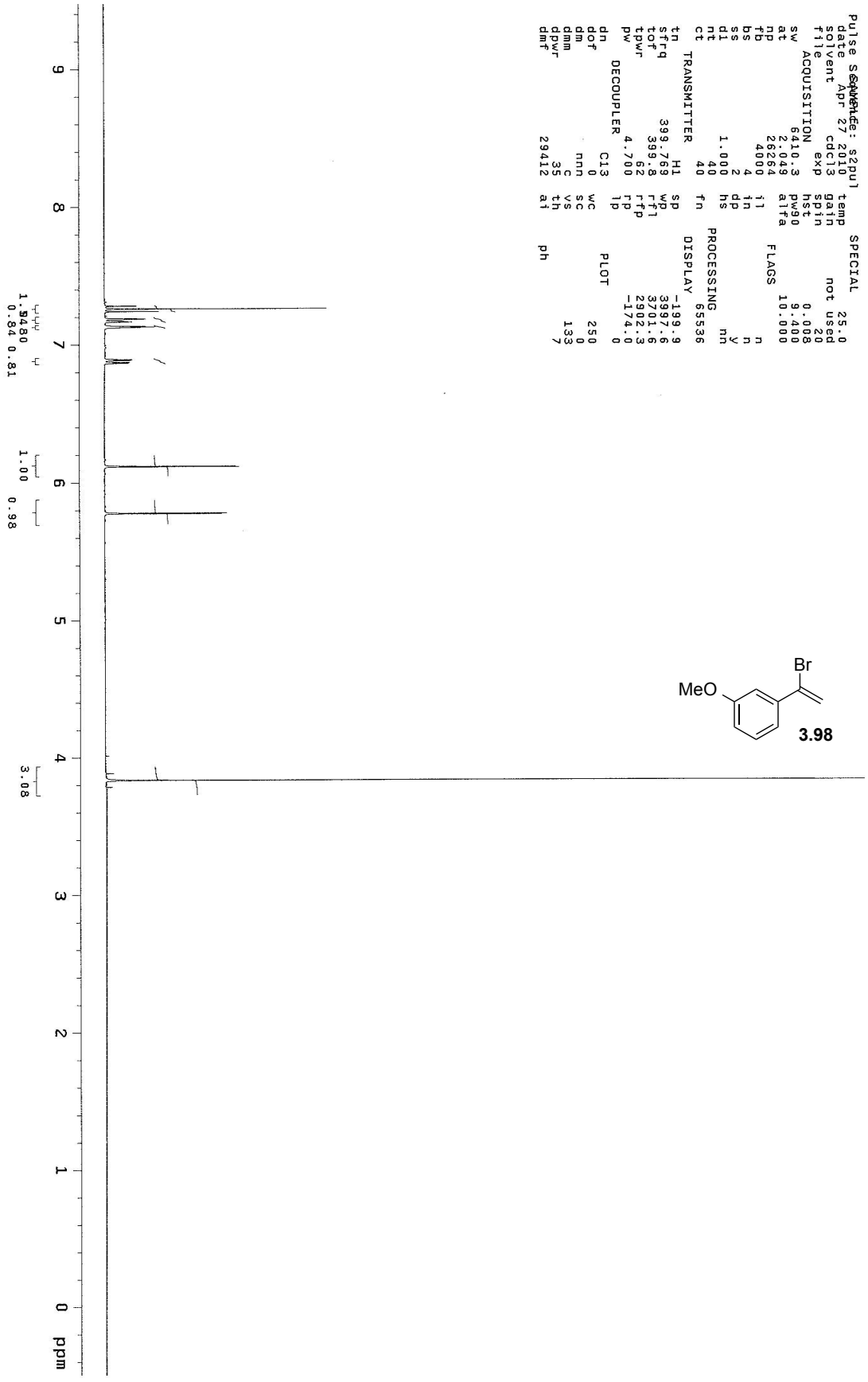


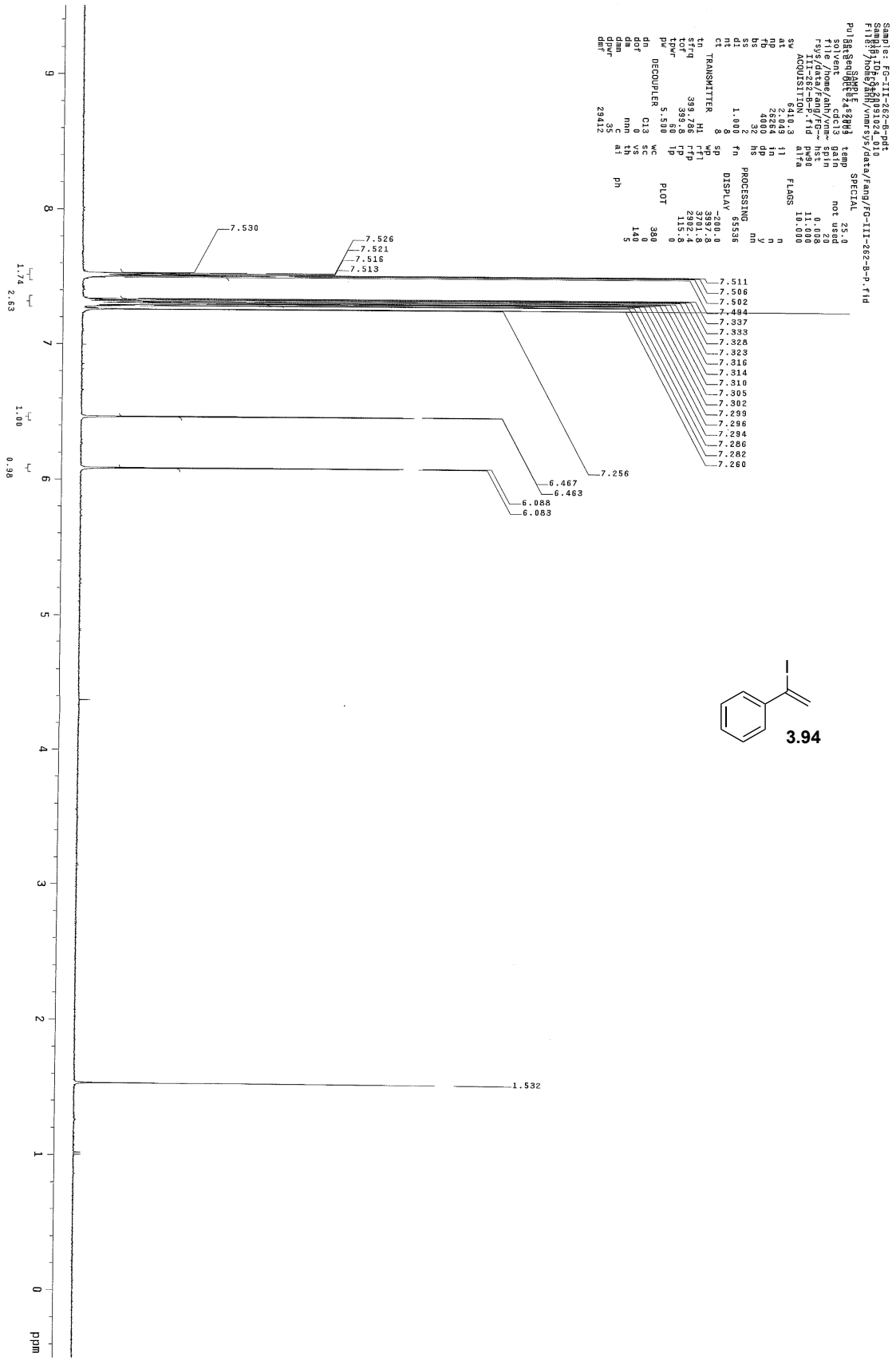
Table 3.9, entry 4

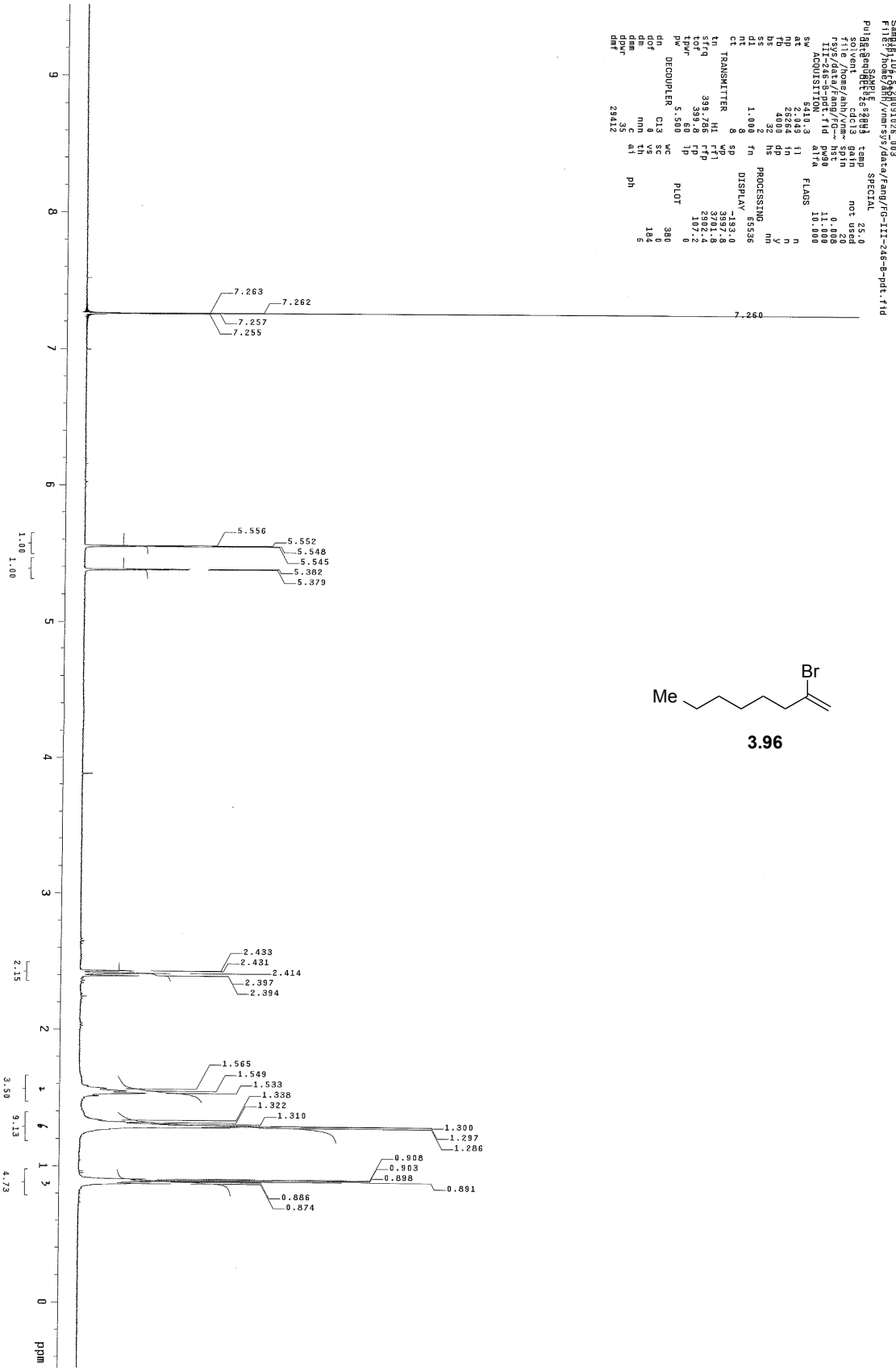

Sample: FG-IV-281-A-pdt
Sample Id: FG-IV-281-A-pdt
File: s_20100520_12/data/cdcl3_01.fid
SAMPLE
Pulse Sequence: 2pul
solvent cdcl3
file /home/ahh/vnm~
rsys/data/auto_201~
0.05.20/s_20100520~
_12/data/cdcl3_01.~
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4000
bs 32
ss 2
d1 1.000
nt 8
ct 8
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
Expt: 20100520_12
temp 25.0
gain not used
spin 20
hst 0.008
pw90 11.000
alfa 10.000
FLAGS
il n
in n
dp y
hs nn
PROCESSING
fn 65536
DISPLAY
sp -200.0
wp 3997.8
rfl 3700.6
rfp 2902.4
rp 23.2
lp 0
PLOT
wc 250
sc 0
vs 230
th 50
ai ph
TsO
ppm
1.89
4.46
2.82
2.26
1.90
0.97
1.00
0.99
1.05
1.10
0.98
3.64


Sample: FG-IV-227-A-pdt-1H
File: exp2
Pulse Sequence: SHAPE s2pul
date Apr 23 2010
solvent cdcl3
file exp
ACQUISITION
sw 8012.8
at 2.013
np 32830
fb 4000
bs 4
ss 2
ns 1.00
nt 40
ct 40
TRANSMITTER
tn H1
sfrq 499.881
tof 439.8
tpwr 61
pw 3.800
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dmf 32258
SPECIAL
temp 25.0
gain not used
spin 20
hst 9.008
pw90 7.600
alfa 10.000
FLAGS
il n
in n
dp y
hs nn
PROCESSING
fn 65536
DISPLAY
sp -250.1
wp 4542.4
rfl 4542.4
rfp 3629.2
rp 117.7
lp 0
PLOT
wc 380
sc 0
vs 40
th 12
ph
1.98 2.20
2.05
1.00
1.13 3.39
2.41
1.15
1.44 5.20
3.70
11.06
6.80
ppm
Ph
TBSO
3.111


Sample: FG-IV-258-B-pdt
Sample Proton 20100507_09
File: s_20100507_09/data/cdcl3_01.fid
SAMPLE
Pulse Sequence: 2010 solvent temp 25.0
solvent cdcl3 gain not used
file /home/ahh/vnm~ spin 20
rsys/data/auto_201~ hst 0.008
0.05.07_01/s_20100~ pw90 11.000
507_09/data/cdcl3_~ alfa 10.000
01.fid FLAGS
ACQUISITION
sw 6410.3 il n
at 2.049 in n
np 26264 dp y
fb 4000 hs nn
bs 32 PROCESSING
ss 2 fn 65536
d1 1.000 DISPLAY
nt 8 sp -200.0
ct 8 wp 3997.8
rfl 3700.8
TRANSMITTER rfp 2902.4
tn H1 rp 6.9
sfrq 399.786 lp 0
tof 399.8 PLOT
tpwr 60 wc 250
pw 5.500 sc 0
DECOUPLER vs 298
dn C13 th 50
dof 0 ai
dm nnn ph
dmm c
dpwr 35
dmf 29412
TsO
3.110
ppm
1.91
2.16
2.46
2.07
1.00
0.98
1.02
1.05
1.01
1.04
1.02
3.21
4.34
4.88

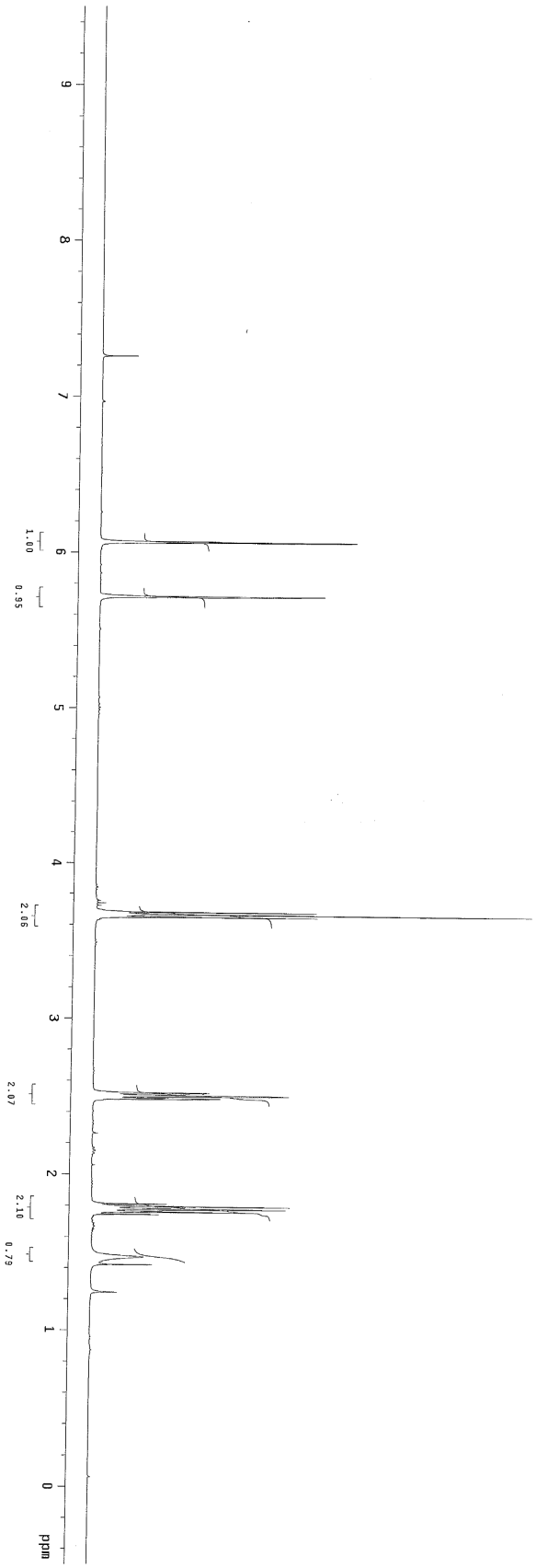

Sample: FG-IV-235-pdt
Exp1 exp proton
Pulse Sequence: s2pul
date Apr 27 2010
solvent cdcl3
file
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4000
bs
ss
d1 1.000
nt 40
ct 40
TRANSMITTER
tn H1
sfrq 399.769
tof 399.8
tpwr 62
pw 4.700
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
temp
gain
spin
hst
pw90
alfa
FLAGS
i1
in
dp
hs
fn
PROCESSING
DISPLAY
PLOT
sc
vs
th
at
ph
SPECIAL
25.0
not used
20
0.008
9.400
10.000
n
n
y
nn
65536
-199.9
3997.6
3701.6
2902.3
-174.0
0
250
0
133
7
Br
MeO
3.98
1.54
1.80
0.84
0.81
1.00
0.98
3.08
9
8
7
6
5
4
3
2
1
0
ppm

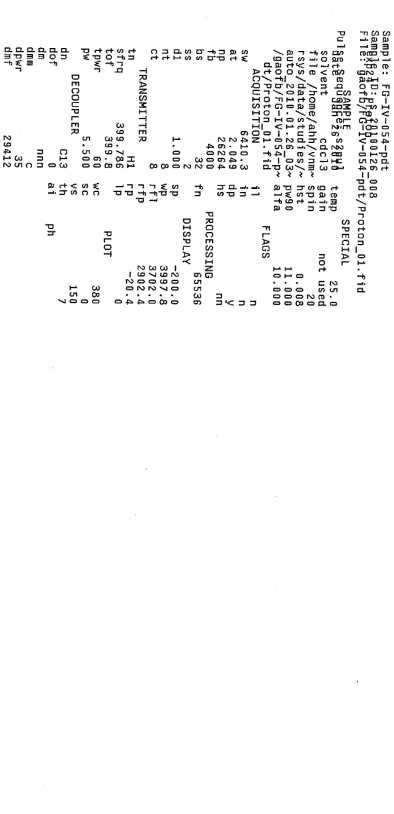

7.530
7.526
7.521
7.516
7.513
7.511
7.506
7.502
7.494
7.337
7.333
7.328
7.323
7.316
7.314
7.310
7.305
7.302
7.299
7.296
7.294
7.286
7.282
7.260
7.256
6.467
6.463
6.088
6.083
1.532
1.74
2.63
1.00
0.98
ppm
I
3.94

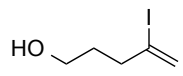

7.263
7.262
7.257
7.255
7.260
5.556
5.552
5.548
5.545
5.382
5.379
2.433
2.431
2.414
2.397
2.394
1.565
1.549
1.533
1.338
1.322
1.310
1.300
1.297
1.286
0.908
0.903
0.898
0.891
0.886
0.874
1.00
1.00
2.15
3.50
9.13
4.73
ppm

Br
Me

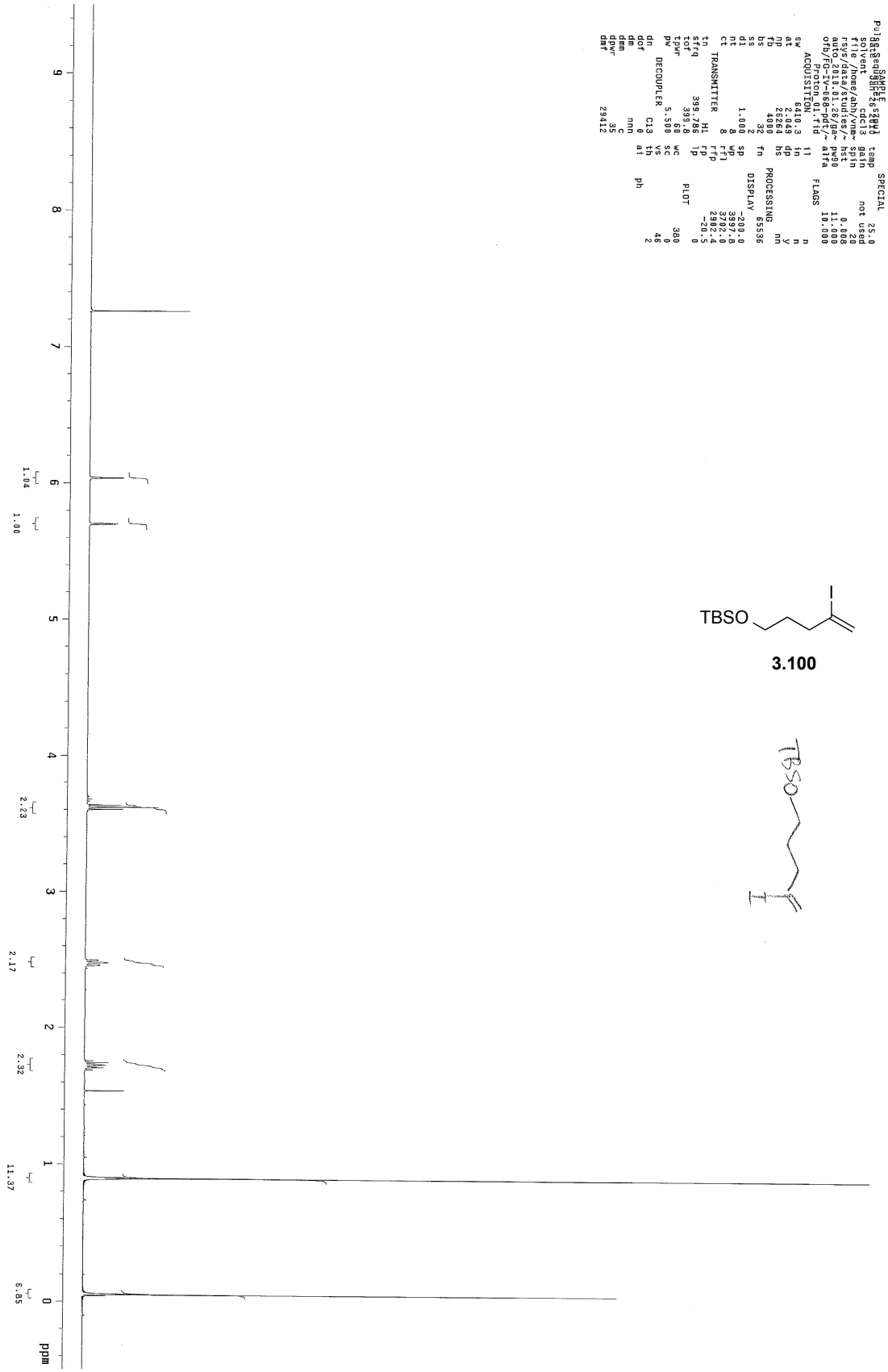
3.96







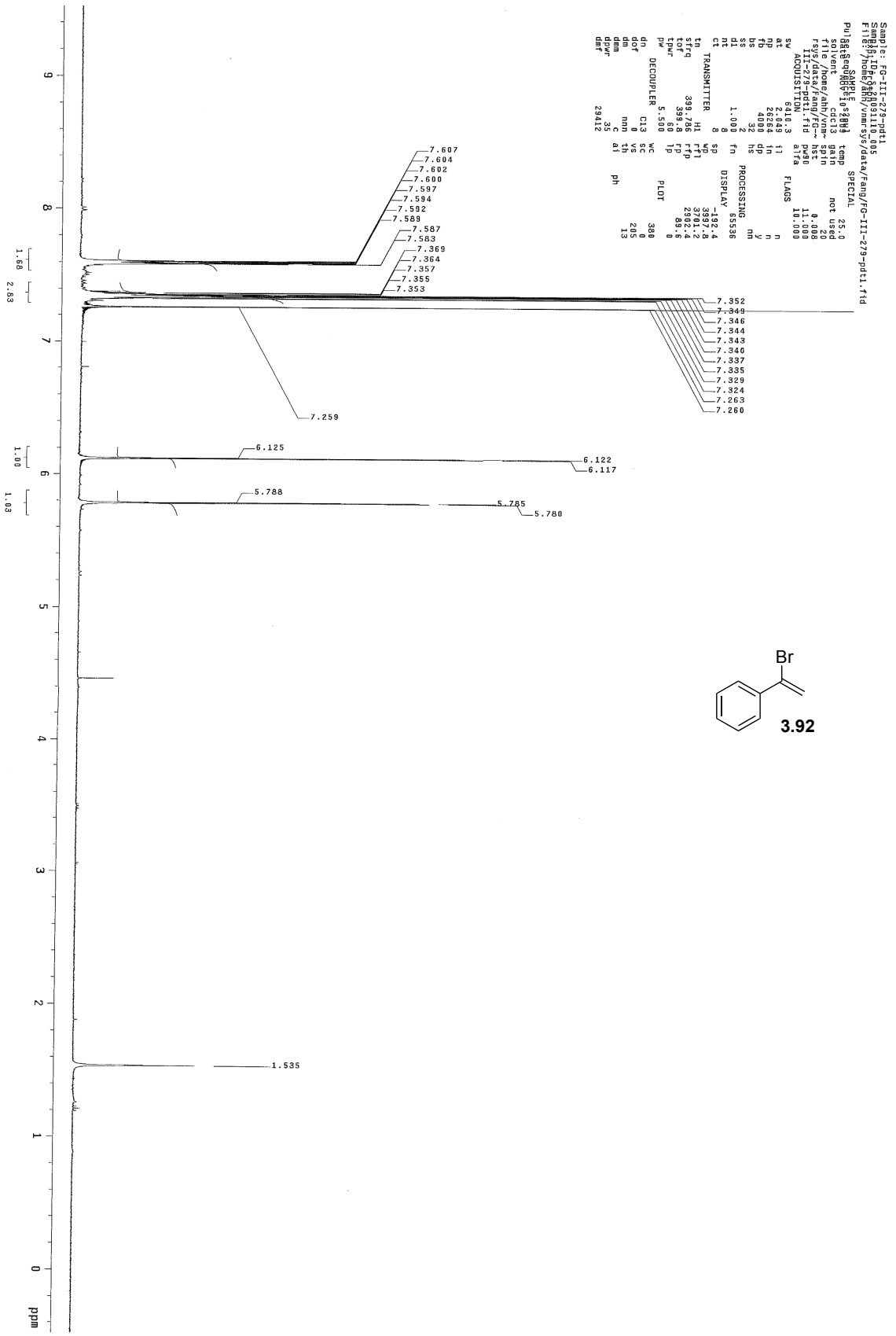
3.99

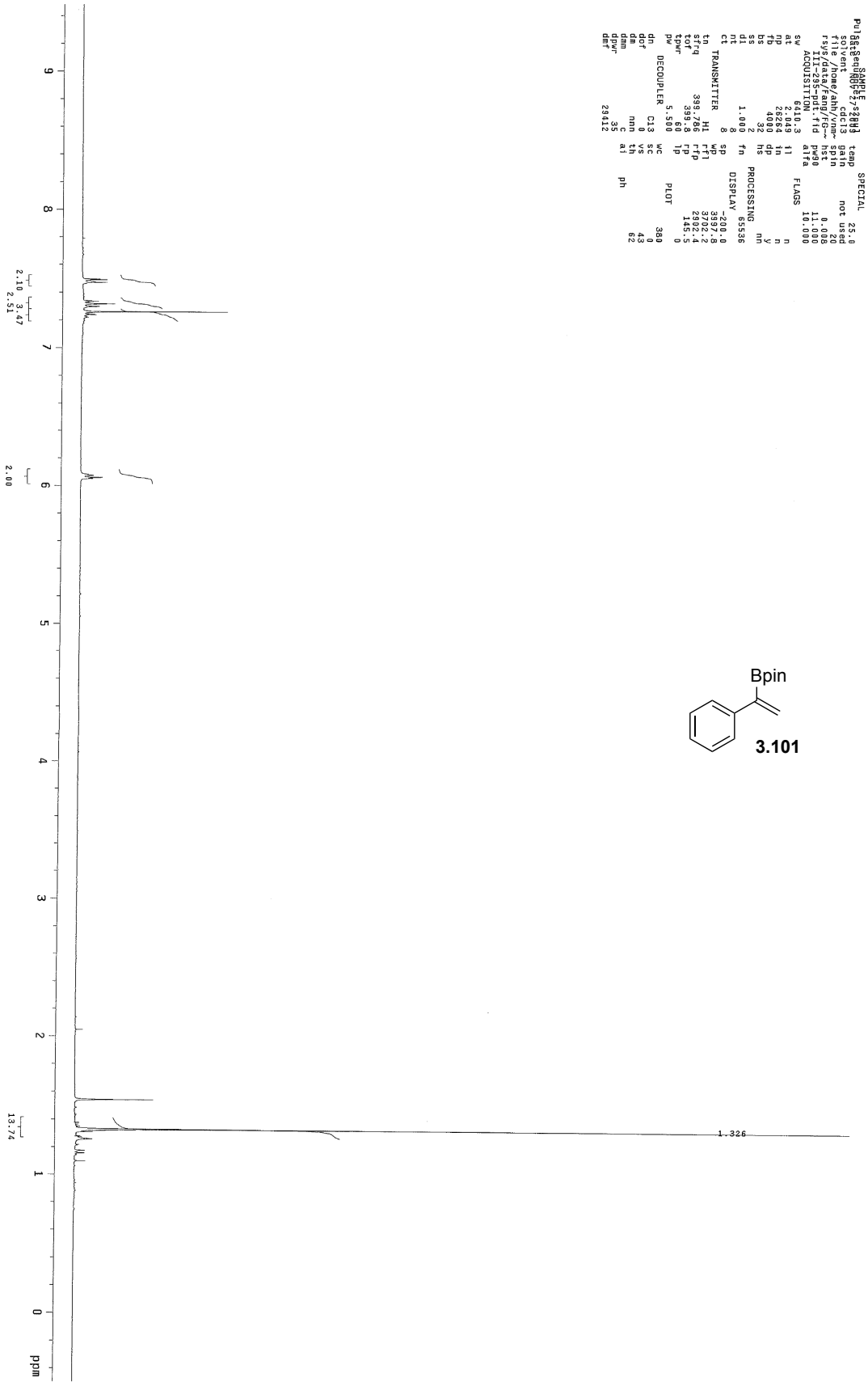

Sample: FG-IV-068-pdt
SampleID: ea20100126_002
File: /data/FG/FG-IV-068-pdt/Proton_01.fid
Pulse Sequence: SAMPLE sp02 SPECIAL
solvent cdcl3 gain not used
file /home/anh/vnmr spin 20
rs /data/FG/FG-IV-068 ns 16 temp 25.0
auto 2010/01/26/ac~ pw90 11.000
ofb/FG-IV-068-pdt/~ aif a 10.000
Proton_01.fid FLAGS
ACQUISITION PROCESSING DISPLAY PLOT
sw 6410.3 fl n
at 2.043 fn n
np 26264 hs y
fb 4000 nn
bs 32 65536
ss 2 -200.0
d1 1.000 sp 397.8
nt 8 wp 3703.0
ct 8 rfl 3702.0
TRANSMITTER rfp 2902.4
tn H1 rp -20.5
sfrq 399.786 lp 0
tof 3537.60 wc 380
tpwr 60 sc 0
pw 5.500 vs 46
dn C13 th 2
dof 0 at
dm nnn ph
dmm c
dpwr 35
dmf 29412
1.04
1.00
2.23
2.17
2.32
11.37
6.85
ppm

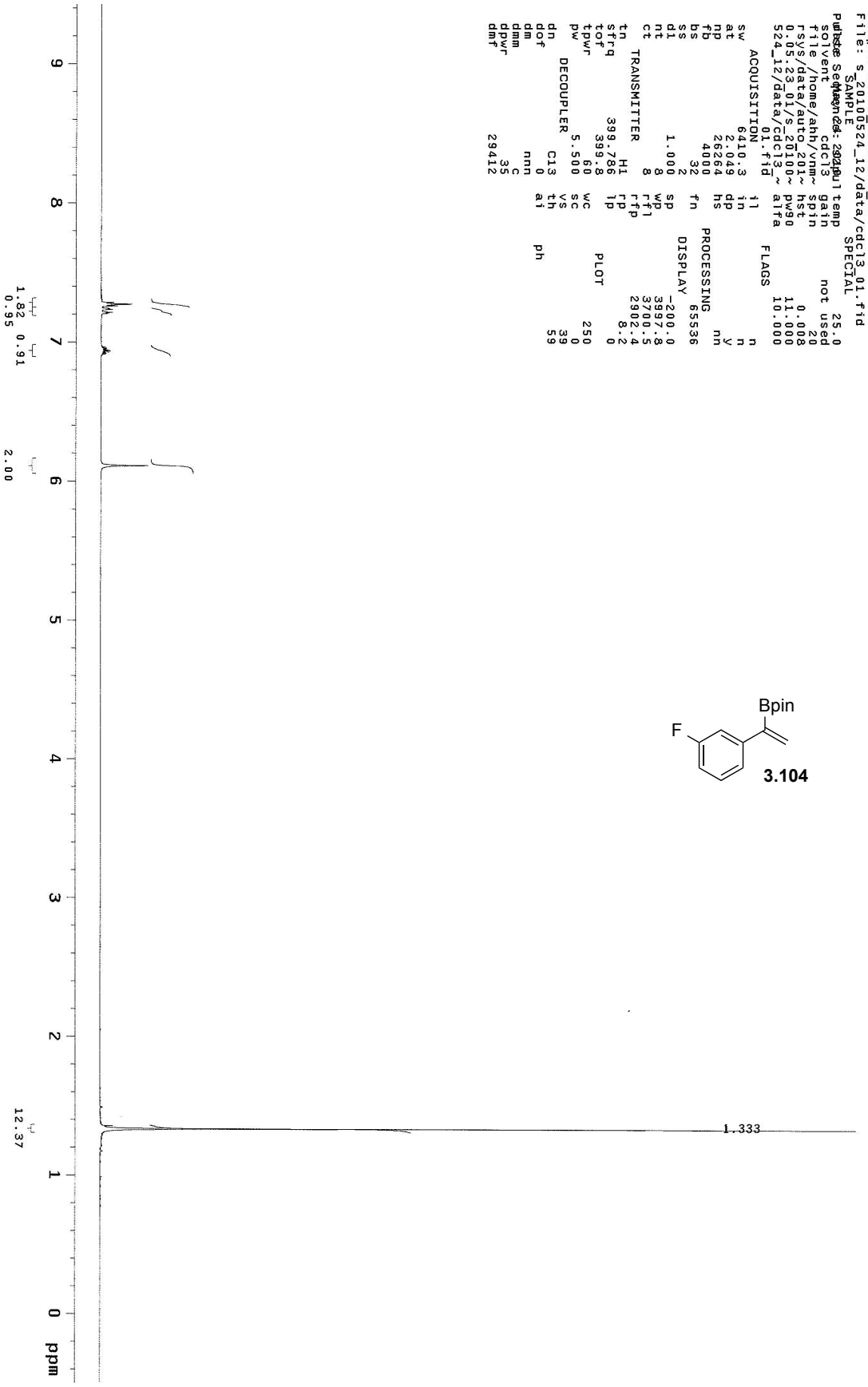
TBSO
I

3.100

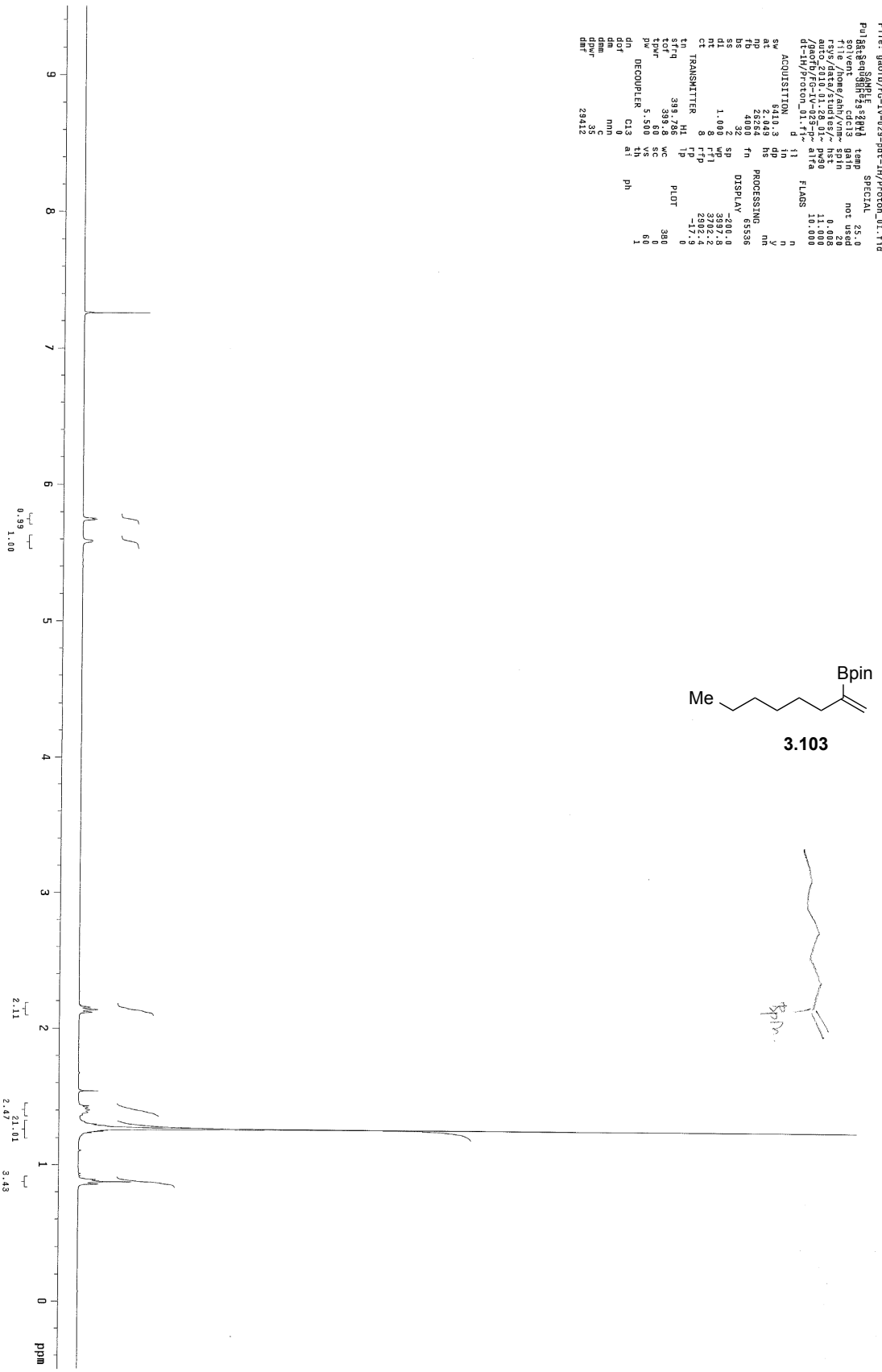
TBSO
I

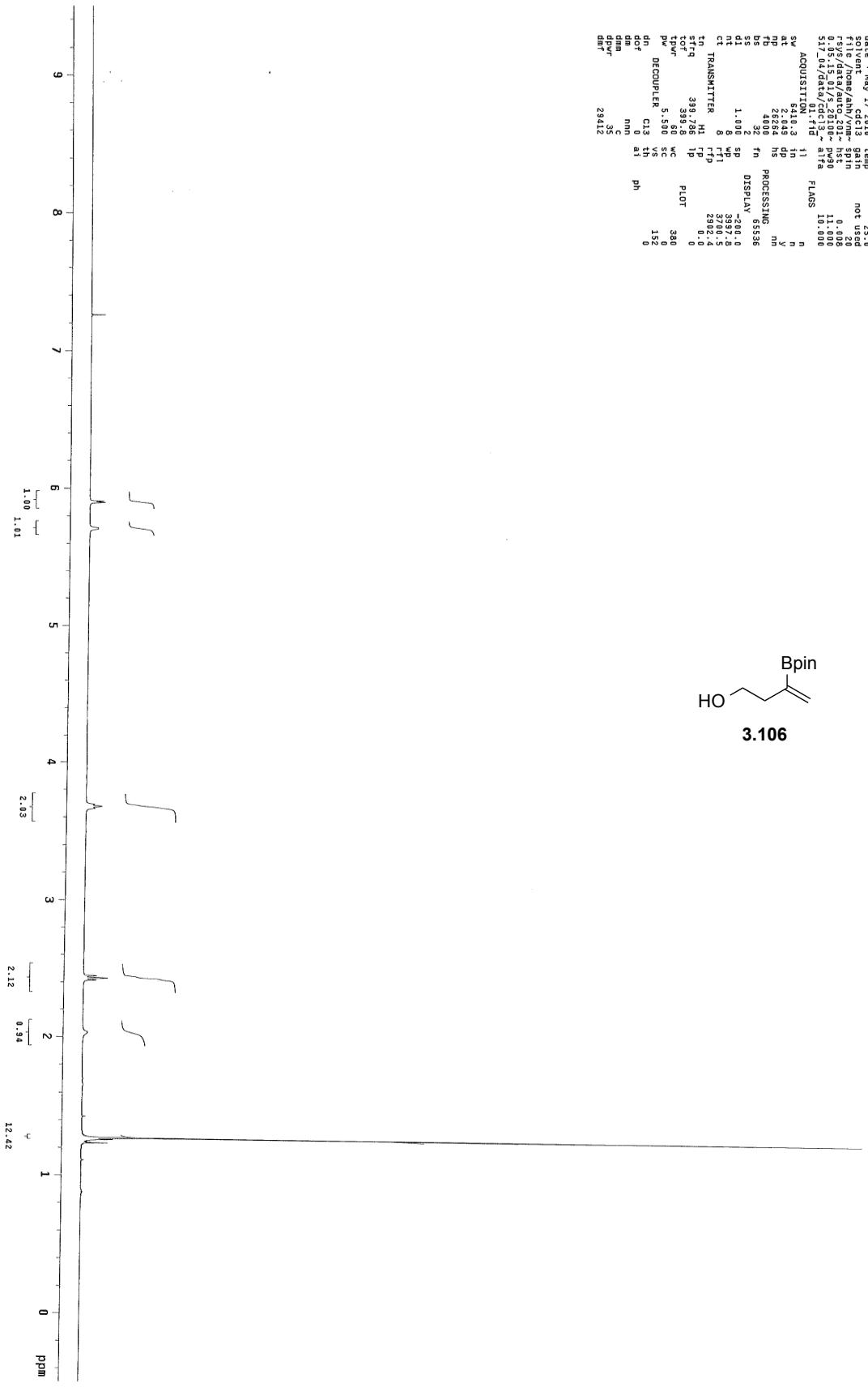

7.607
7.604
7.602
7.600
7.597
7.594
7.592
7.589
7.587
7.583
7.369
7.364
7.357
7.355
7.353
7.352
7.349
7.346
7.344
7.343
7.340
7.337
7.335
7.329
7.324
7.263
7.260
7.259
6.125
6.122
6.117
5.788
5.785
5.780
1.535
1.68
2.83
1.00
1.03
ppm
Br
3.92

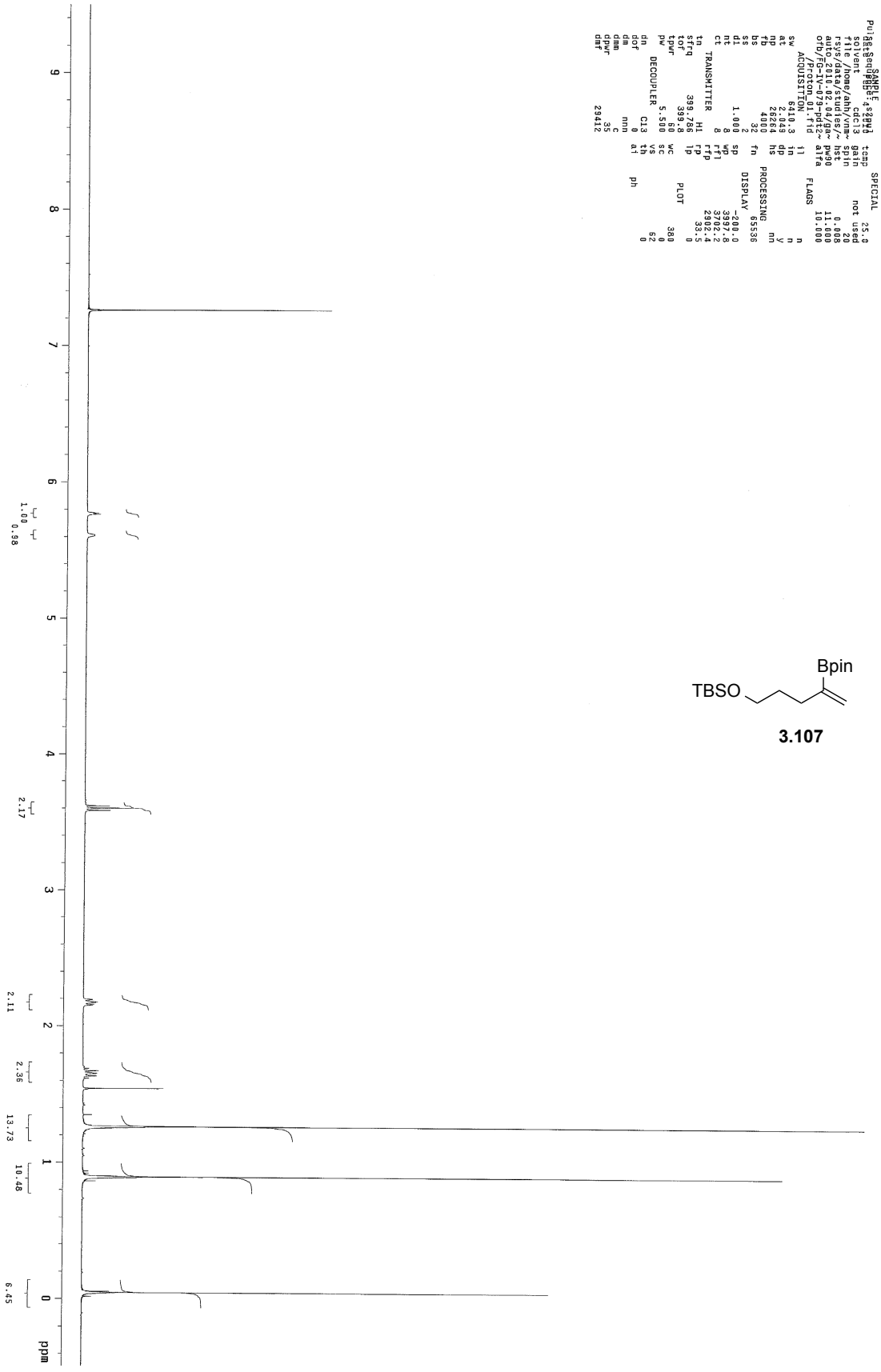

Sample: FG-III-295-pdt
Sample ID: fa20091127_009
File: /home/ANH/vnmrsys/data/Fang/FG-III-295-pdt.fid
Pulse Sequence: s2pul
Solvent: cdcl3
File Name: /home/ANH/vnmrsys/data/Fang/FG-III-295-pdt.fid
Experiment: s2pul
Data Collected on: ROBOT-7 at 25.0
SAMPLE
temp 25.0
gain not used
spin not used
hst 0.008
pw90 11.000
alfa 10.000
ACQUISITION
sw 6410.3
at 2.048
np 26264
fb 4000
bs 32
ss 2
d1 1.000
nt 8
ct 0
FLAGS
il n
in n
dp y
hs nn
PROCESSING
fn 65536
DISPLAY
sp -200.0
wp 3597.8
rfl 3702.2
rfp 2902.4
lp 145.5
PLOT
wc 380
sc 0
vs 43
th 62
TRANSMITTER
tn H1
sfrq 399.786
tof 359.60
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
ph
ai
Bpin
3.101
1.326
13.74
2.10
3.47
2.51
2.00
ppm


Sample: FG-IV-284-pdt
Sample Protocol: 20100524_12
File: s_20100524_12/data/cdc13_01.fid
Pulse Sequence: s2pul SAMPLE SPECIAL
solvent cdc13 gain not used 25.0
file /home/anh/vnm~ spin 20
rsys/data/auto_201~ hst 0.008
0.05.23_01/s_20100~ pw90 11.000
524_12/data/cdc13_~ alfa 10.000
01.fid FLAGS
ACQUISITION
6410.3 il n
2.049 in n
26264 dp y
4000 hs nn
32 fn 65536
2 PROCESSING
1.000 sp -200.0
8 wp 3997.8
8 rfl 3700.5
TRANSMITTER rfp 2902.4
H1 rp 8.2
399.786 lp 0
399.8 PLOT
60 wc 250
5.500 sc 0
DECOUPLER vs 39
C13 th 59
0 ai
nnn ph
c
35
29412
DISPLAY
Bpin
F
3.104
1.333
12.37
1.82
0.91
0.95
2.00
ppm


SM-VI-249-F
SM-VI-249-F
Sample: FG-IV-284-pdt
Sample_ [illegible]
File: s_20100527_08/data/cdcl3_01.fid
SAMPLE
Pulse Sequence: [illegible]
solvent cdcl3
file /home/ahh/vnm~
rsys/data/auto_201~
0.05.27/s_20100527~
_08/data/cdcl3_01.~
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4000
bs 32
ss 2
d1 1.000
nt 8
ct 8
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
temp 25.0
gain not used
spin 20
hst 0.008
pw90 11.000
alfa 10.000
FLAGS
il n
in n
dp y
hs nn
PROCESSING
fn 65536
DISPLAY
sp -199.9
wp 3997.8
rfl 1426.1
rfp 623.7
rp -11.8
lp 0
PLOT
wc 250
sc 0
vs 81
th 1
ai
ph
Cl
Bpin
3.105
1.03
2.87
1.00
1.00
12.22
ppm

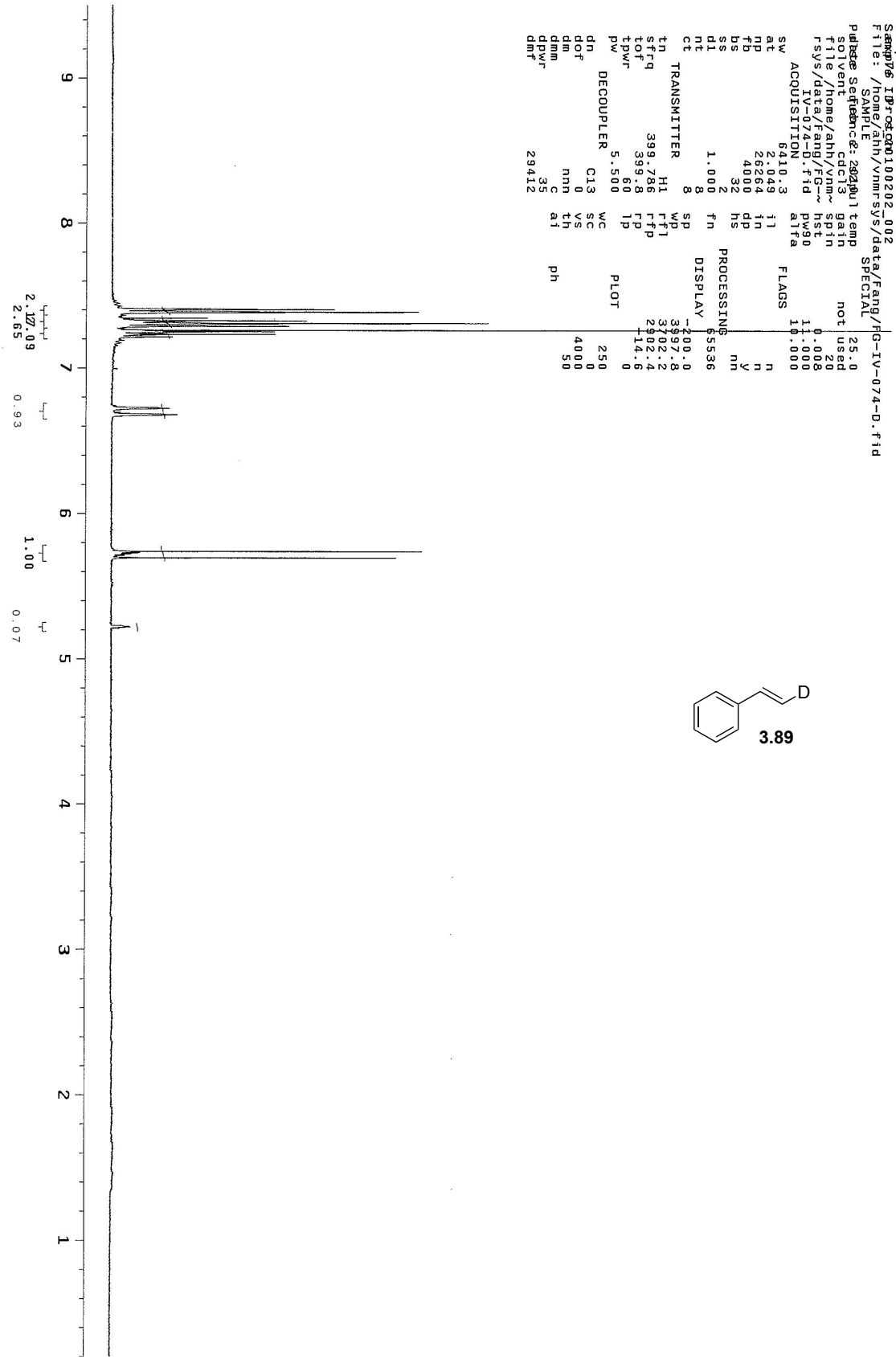

Sample: FD-IV-025-pdt-1H
Sample: FD-IV-025-pdt-1H
File: gaor7b/FD-IV-025-pdt-1H/proton_01.fid
Pulse Sequence: s2pul
solvent
file /home/ahh/vnm
exp /data/studies/
/gaor7b/FD-IV-025-p
dt-1H/proton_01.fi
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4000
bs 32
ss 2
d1 1.000
nt 8
ct 8
TRANSMITTER
tn H1
sfrq 399.787
tof 399.6
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
SPECIAL
temp
gain
spin
hst
pw90
alfa
FLAGS
il n
in n
dp y
hs nn
PROCESSING
fn 65536
DISPLAY
sp -200.0
wp 3302.8
wp1 3302.8
rfp 2982.4
rp -17.9
lp 0
PLOT
wc 380
sc 0
vs 60
th 1
ai
ph
Me
Bpin
3.103
0.99
1.00
2.11
2.47
21.01
3.43
ppm


Sample: FG-IV-273-pdi2
SAMPLE
date 1287671284
solvent cdcl3
file /home/ahh/vnm~
rsys/data/auto_201~
S17_04/data/01.fid
ACQUISITION
sw 6410.3
at 2.049
np 14000
fb 4600
bs 32
ss 2
d1 1.000
ct 8
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
FLAGS
il n
in n
dp y
hs nn
PROCESSING
fn 65536
DISPLAY
sp -200.0
wp 3990.5
rfp 3992.4
rp 290.0
lp 0.0
PLOT
wc 380
sc 0
vs 152
th 0
ai
ph
Pulse Sequence: s2pul
temp SPECIAL
gain
spin not used
hst 20
pw90 0.008
alfa 11.000
10.000
25.0
Bpin
HO
3.106
1.00
1.01
2.03
2.12
0.94
12.42
ppm


Sample: FG-IV-079-pdt2
Sample#: 3
File: gaorb/FG-IV-079-pdt2/proton_01.fid
Pulse Sequence: SAMPLE.s2pul
solvent: CDCl3
fidname: /home/ahuynh/vnmrsys/data/students/~
rsys/data/students/~
auto_2010.02.04/ga~
orb/FG-IV-079-pdt2~
/Proton_01.fid
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4000
bs 32
ss 1
d1 1.000
nt 8
ct 8
TRANSMITTER
tn H1
sfrq 399.781
tof 339.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
temp SPECIAL 25.0
gain not used
spin 0.000
hst 11.000
pw90 10.000
alfa FLAGS
fl n
in n
dp y
hs nn
PROCESSING
fn 65536
DISPLAY
sp -200.0
wp 3397.8
rfl 3702.2
rfp 2902.4
lp 33.5
0
PLOT
wc 380
sc 0
vs 62
th 0
al ph
ppm
1.00
0.98
2.17
2.11
2.36
13.73
10.48
6.45

Bpin
TBSO

3.107


Sample: FG-IV-074-D
Sampl
File: /home/ahh/vnmrsys/data/Fang/FG-IV-074-D.fid
SAMPLE
Pulse Sequence: s2pul
solvent cdcl3
file /home/ahh/vnm~
rsys/data/Fang/FG~
IV-074-D.fid
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4000
bs 32
ss 2
d1 1.000
nt 8
ct
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
temp
gain
spin
hst
pw90
alfa
FLAGS
fn
PROCESSING
DISPLAY
sp
wp
rfl
rfp
rp
lp
PLOT
wc
sc
vs
th
ai
ph
25.0
not used
20
0.008
11.000
10.000
n
n
y
nn
65536
-200.0
3997.8
3702.2
2902.4
-14.6
0
250
0
400
50
2.65
2.17
2.09
0.93
1.00
0.07
D
3.89

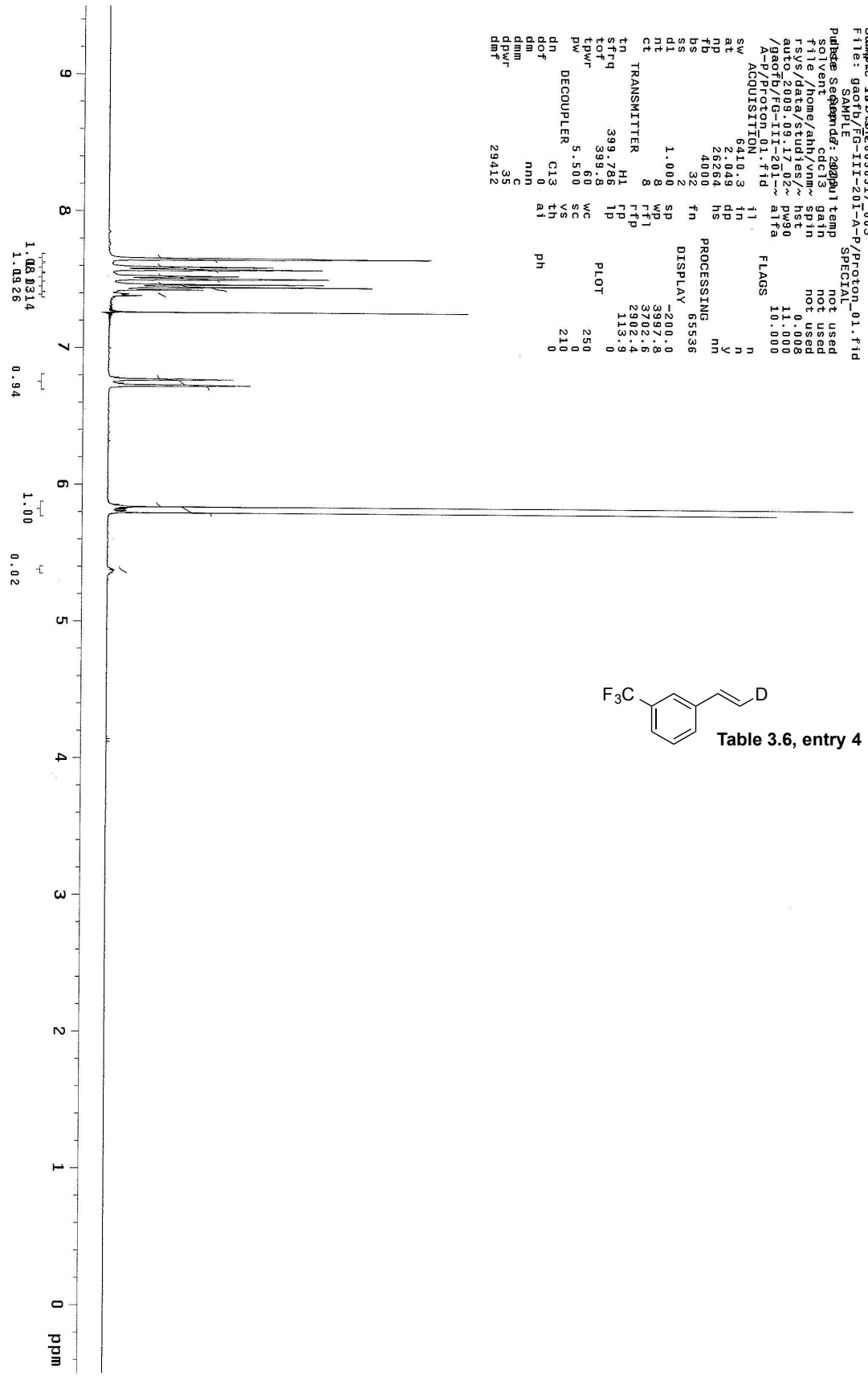


Table 3.6, entry 4

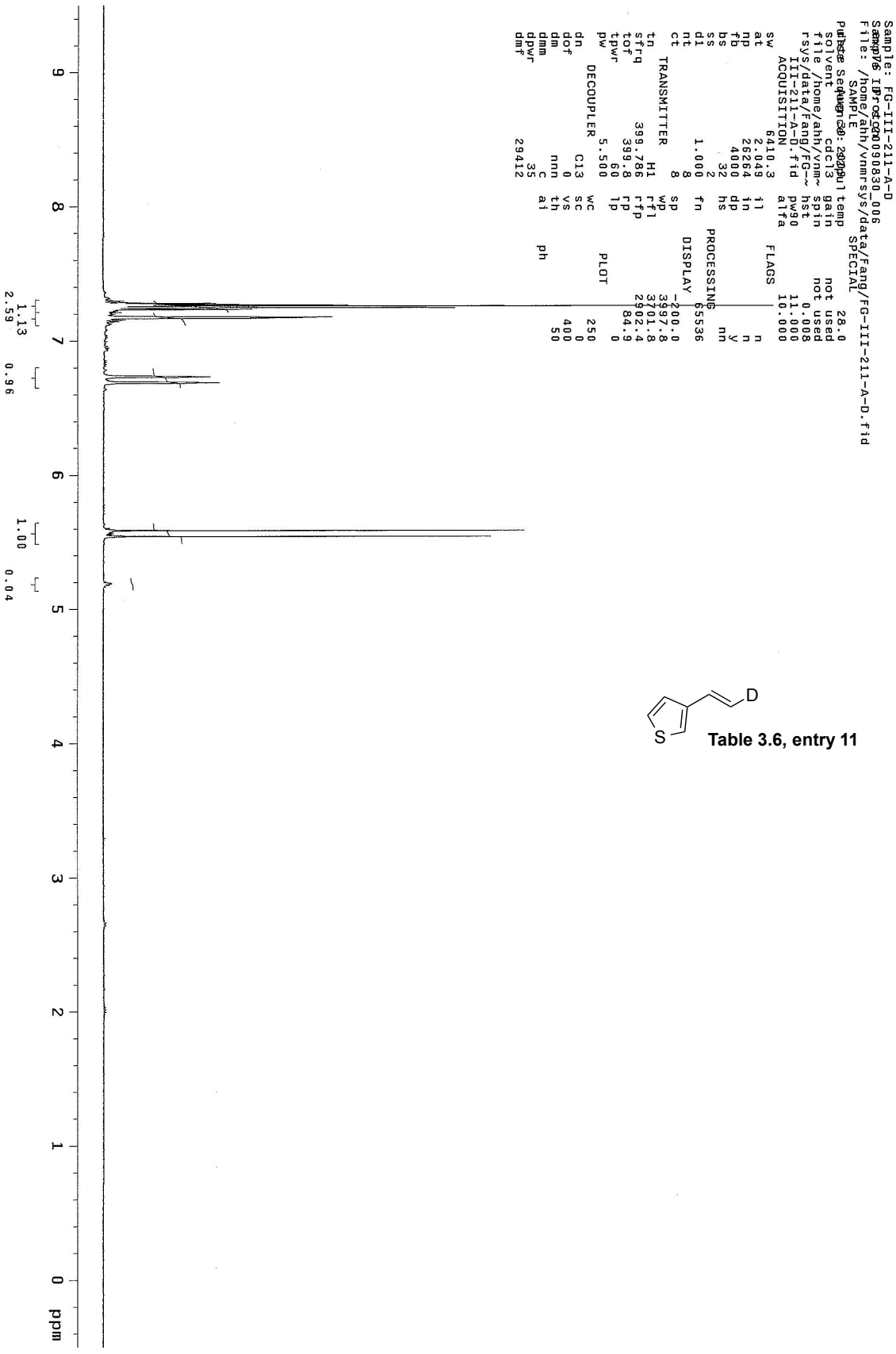


Table 3.6, entry 11

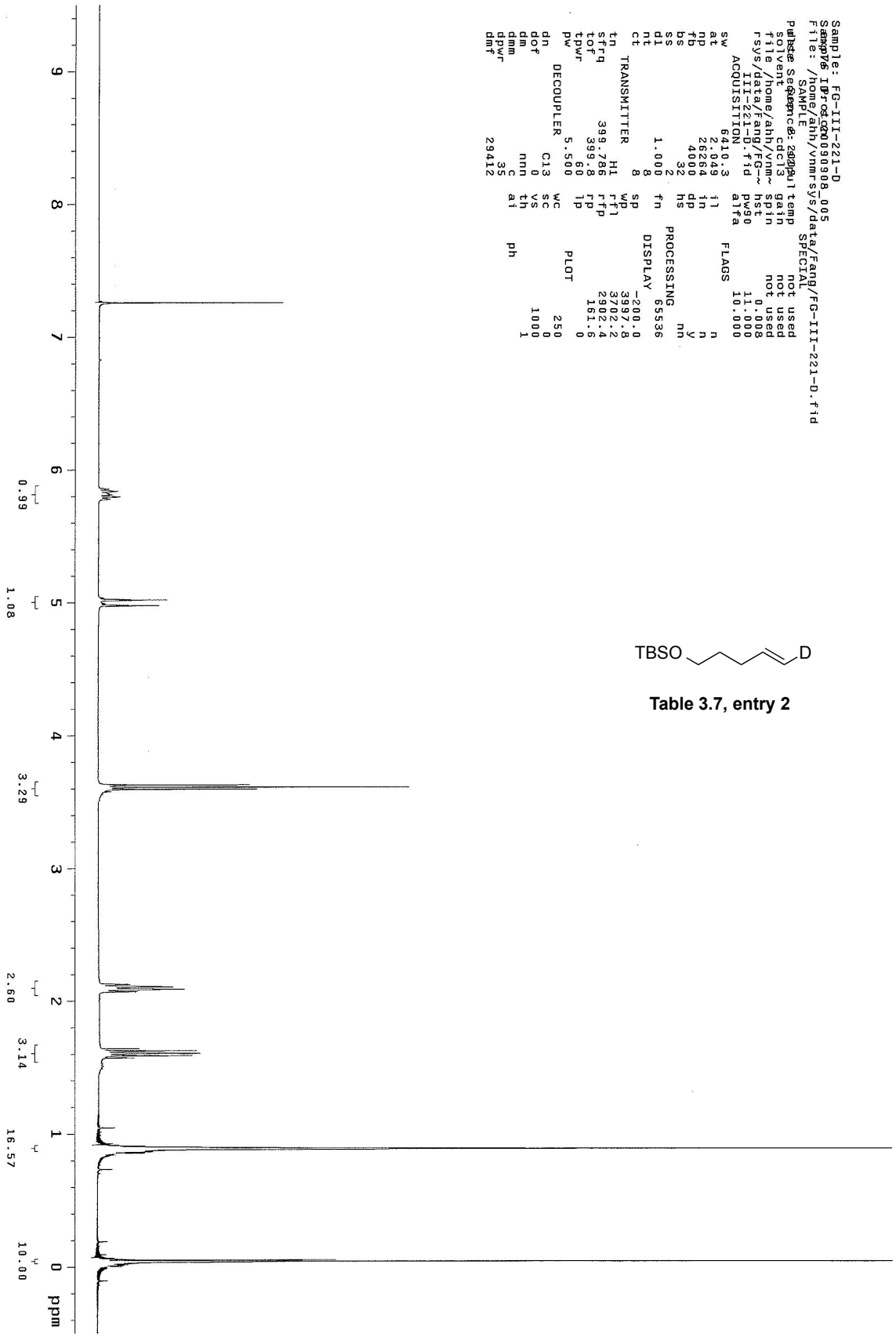


Table 3.7, entry 2

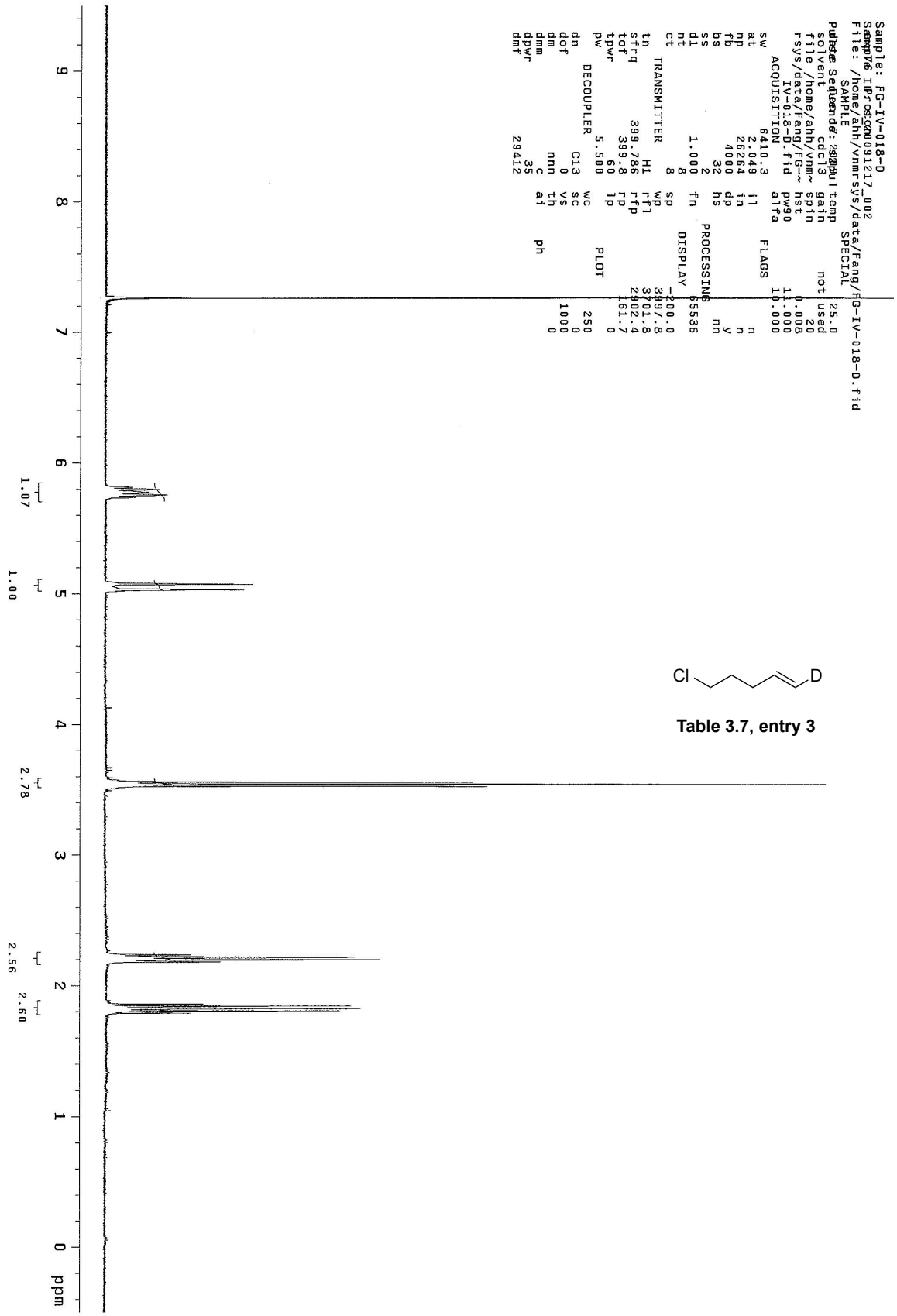
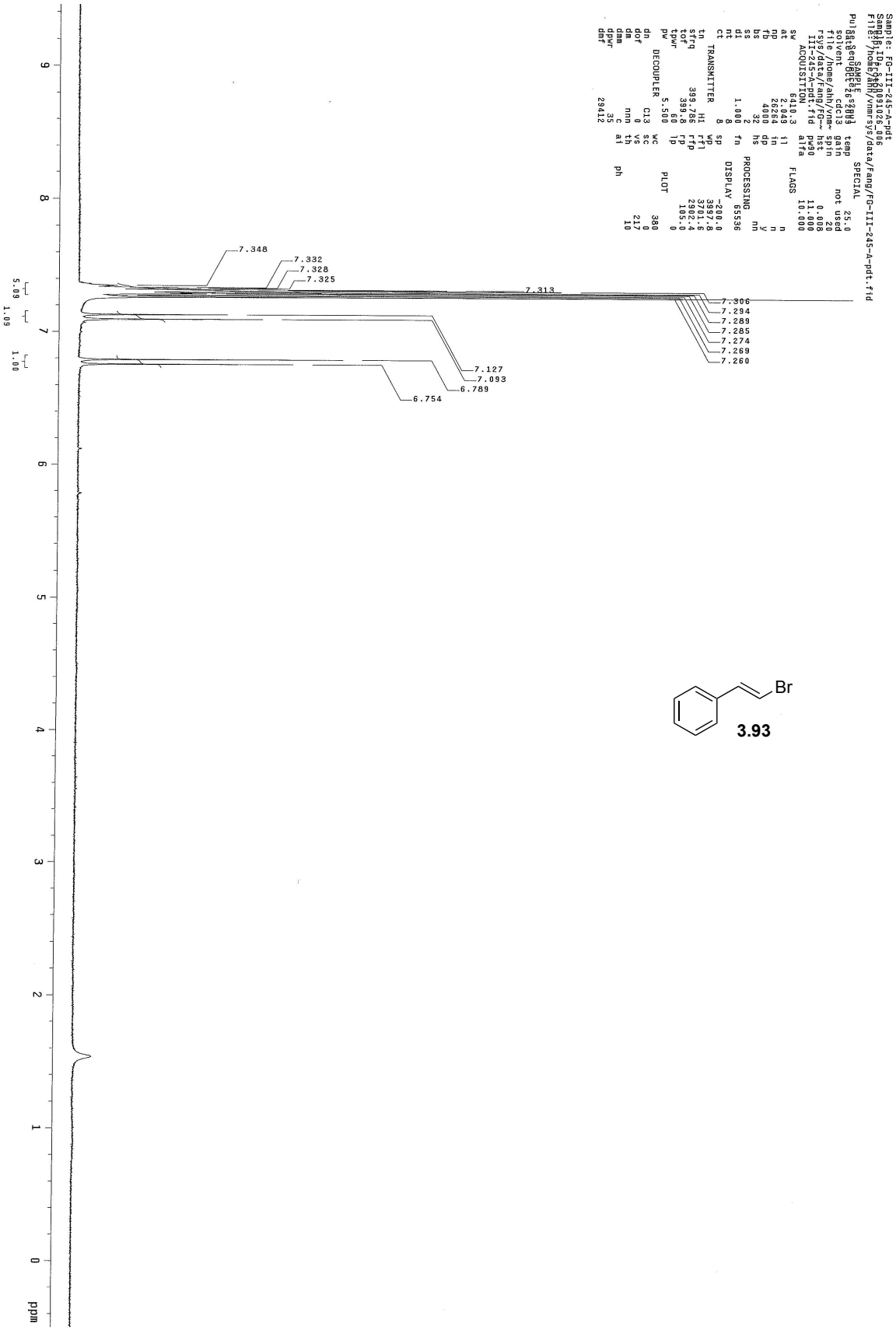
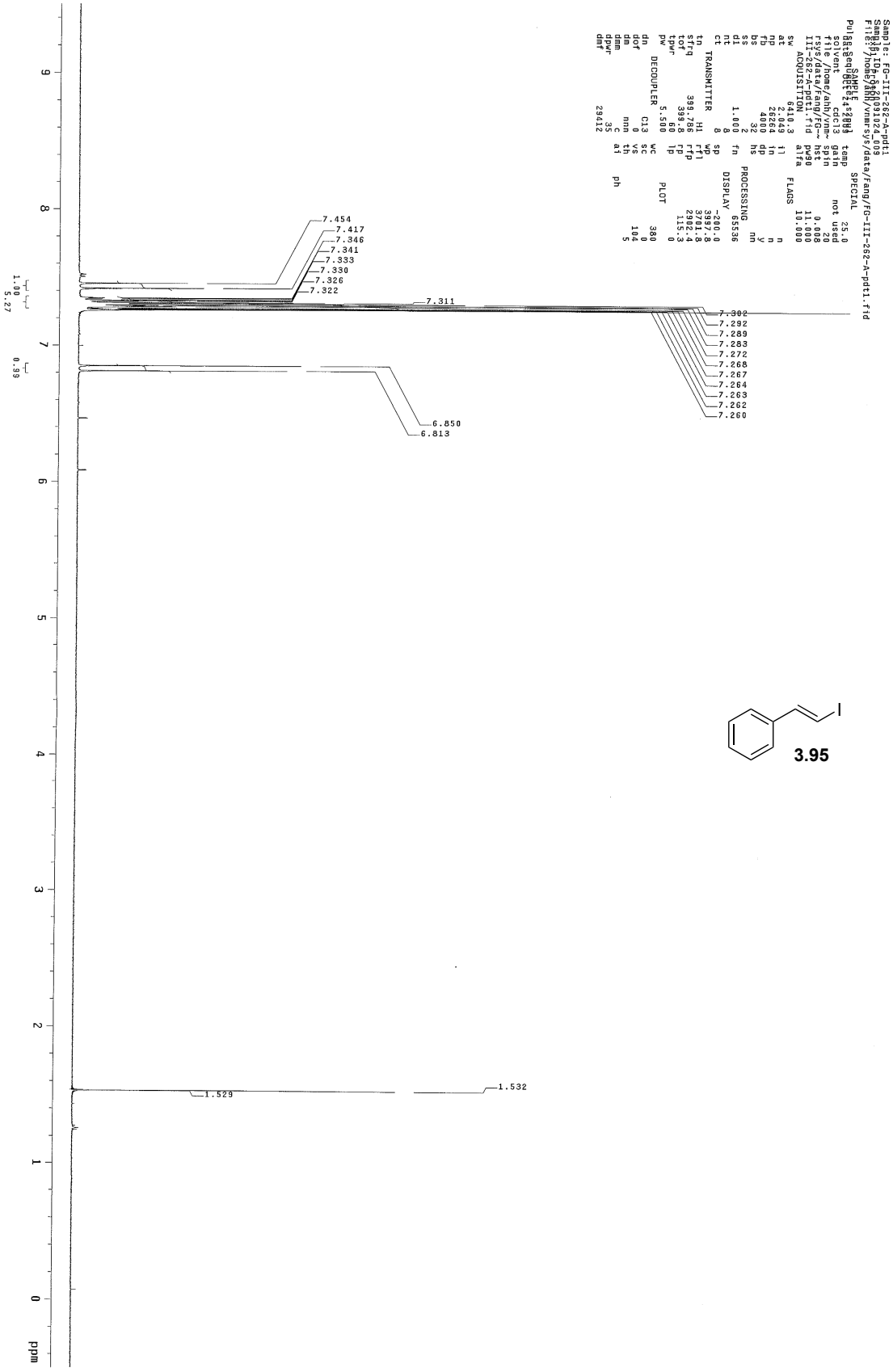
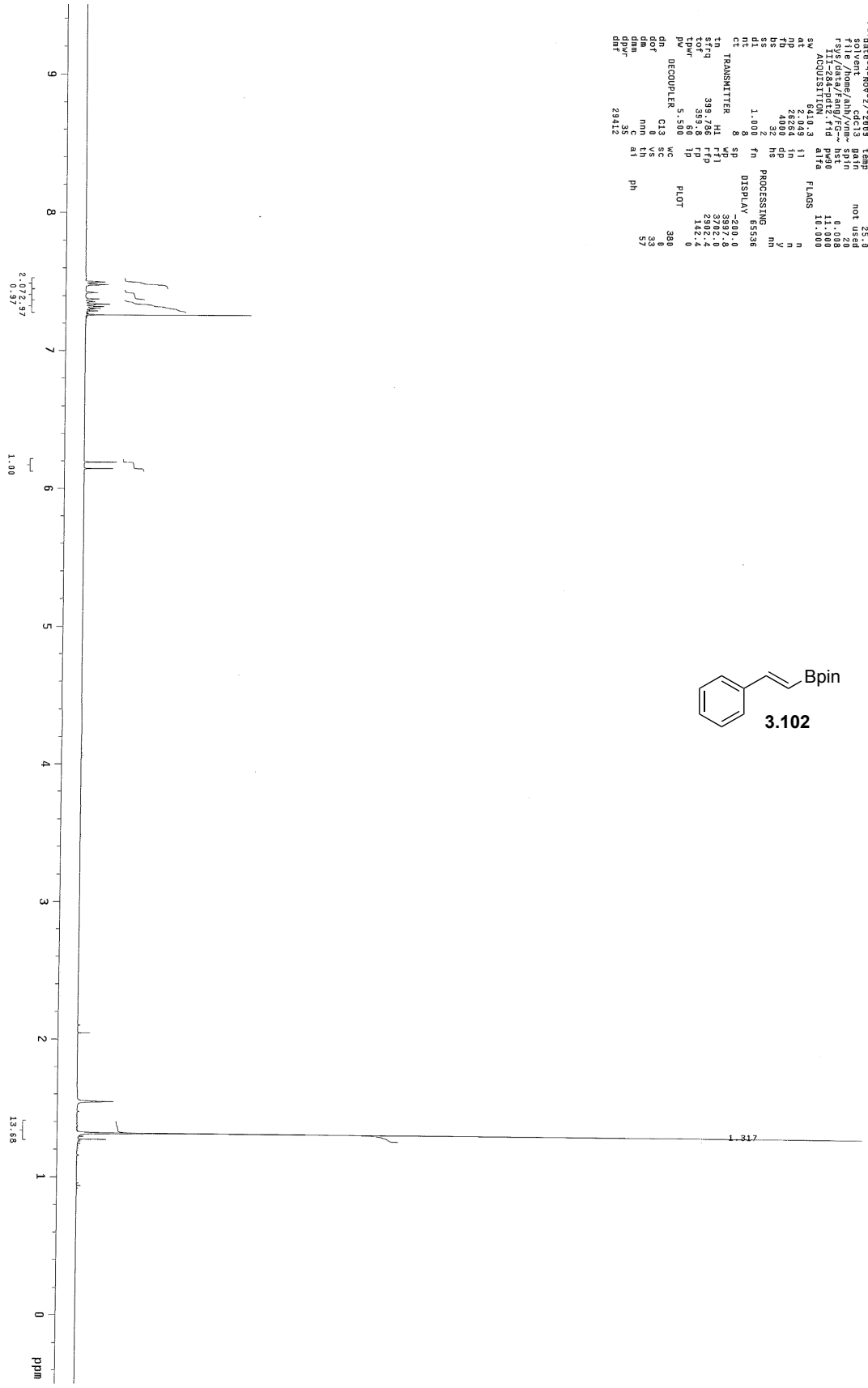
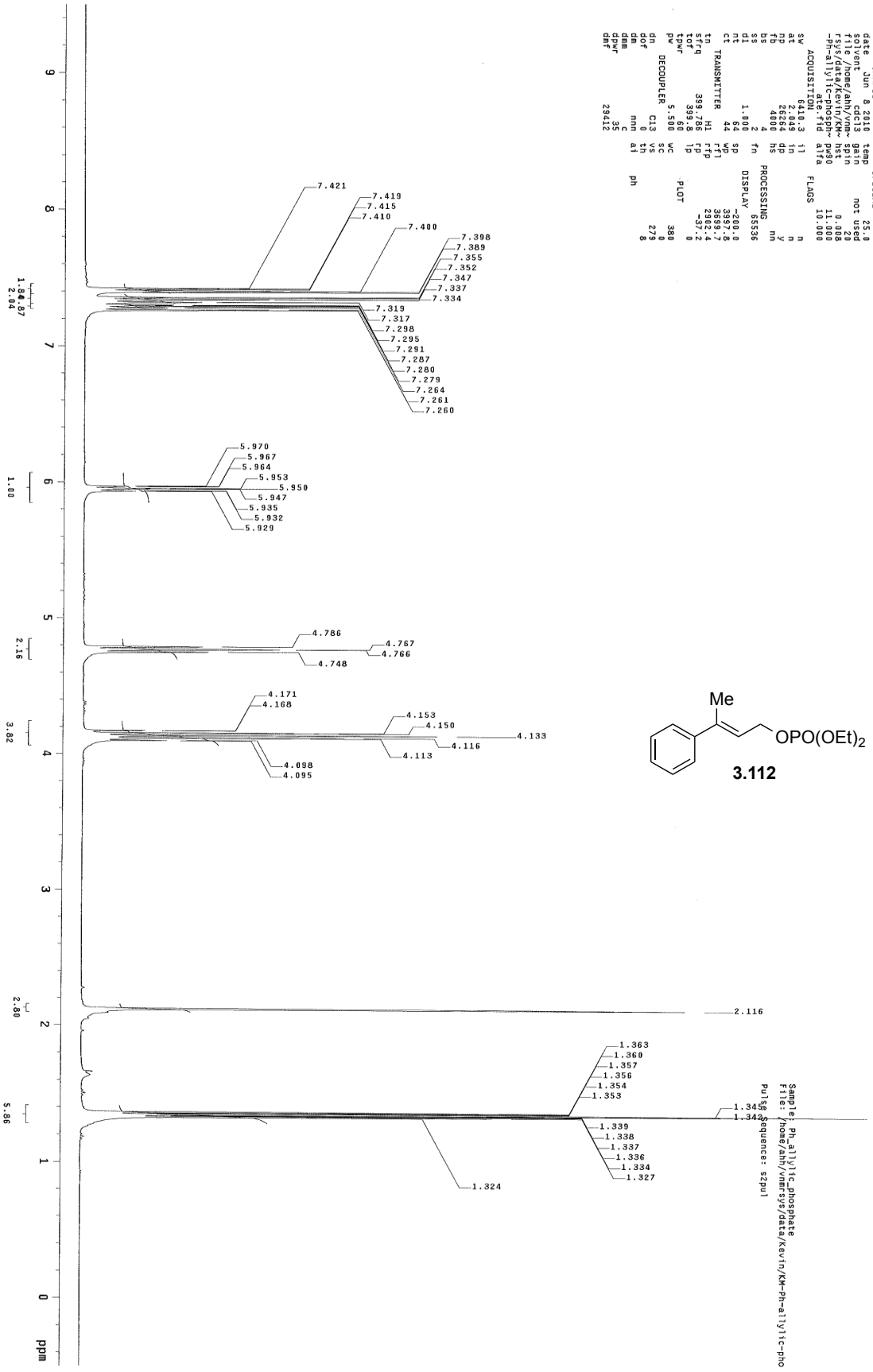


Table 3.7, entry 3


Sample: FG-III-245-A-pdt
Sample ID: 61209102c.006
File (Pfile): /home/ahh/vnmrsys/data/Fang/FG-III-245-A-pdt.fid
Pulse Sequence: s2pul
SAMPLE
Solvent: cdcl3
File: /home/ahh/vnmrsys/data/Fang/FG-III-245-A-pdt.fid
SPECIAL
temp 25.0
gain not used
spin 20
hst 0.008
pw90 11.000
alfa 10.000
FLAGS
sw 6410.3
at 2.049
np 26264
fb 4000
bs 32
ss 2
d1 1.000
nt 8
ct 8
TRANSMITTER
th nl
sfrq 399.788
tof 339.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dmf 29412
il n
in n
dp y
hs nn
PROCESSING
fn 65536
DISPLAY
sp -200.0
wp 3997.8
rfl 3701.6
rfp 292.4
lp 105.0
PLOT
wc 380
sc 0
vs 217
ts 10
ph
al
7.348
7.332
7.328
7.325
7.313
7.306
7.284
7.280
7.265
7.274
7.269
7.260
7.127
7.093
6.789
6.754
5.09
1.09
1.00
ppm
Br
3.93

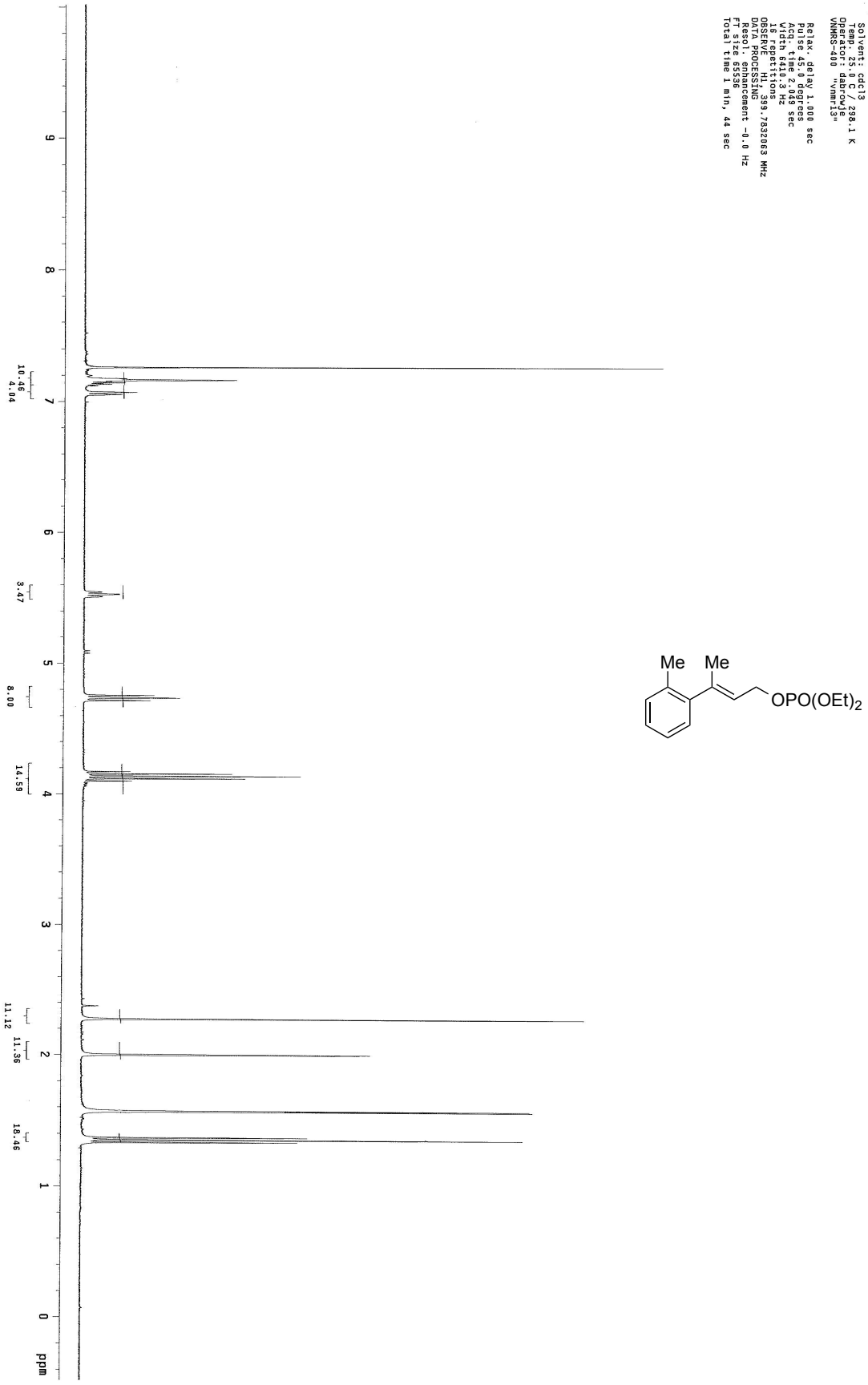

7.454
7.417
7.346
7.341
7.333
7.330
7.326
7.322
7.311
7.302
7.292
7.289
7.283
7.272
7.268
7.267
7.264
7.263
7.262
7.260
6.850
6.813
1.532
1.529
1.00
5.27
0.99
ppm
I
3.95

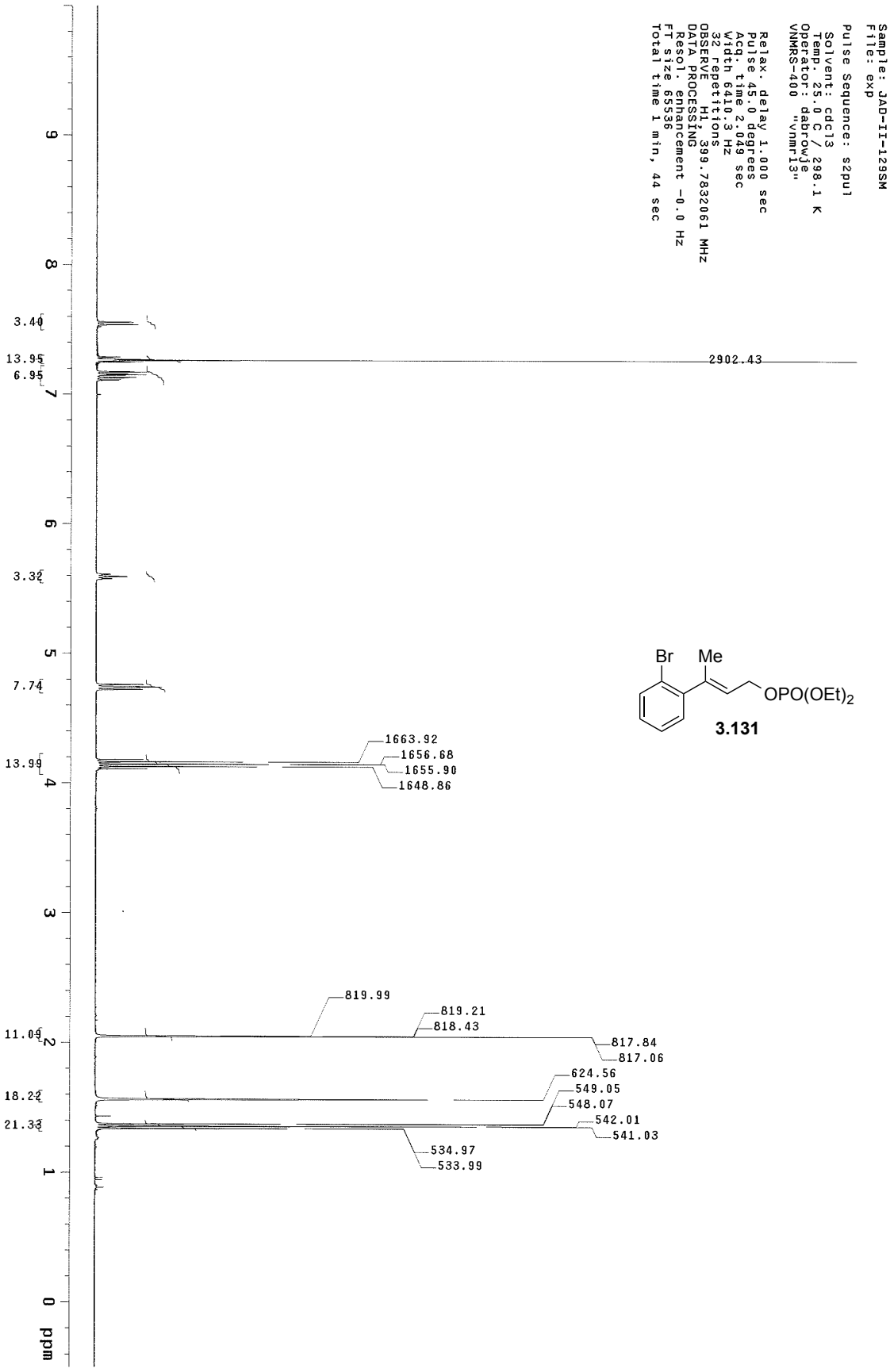

Sample: FG-III-284-pdt2
Solvent: CDCl3
File: /home/ahh/vnmrsys/data/fang/FG-III-284-pdt2.fid
Pulse Sequence: s2pul
solvent cdc13 temp SPECIAL
file /home/ahh/vnm~ spin not used
rsys/data/fang/FG~ hst 0.000
III-284-pdt2.fid pw90 11.000
ACQUISITION at 10.3 FLAGS 10.000
sw 6410.3 il n
np 26264 in n
fb 4000 dp y
bs 32 hs nn
ss 2 PROCESSING
d1 1.000 fn 65536
nt 8 DISPLAY
ct 8 sp -200.0
TRANSMITTER wp 3997.8
tn H1 rfl 3702.0
sfrq 399.781 rfp 2102.4
tof 339.8 rp 142.4
tpwr 60 lp 0
pw 5.500
PLOT
DECOUPLER wc 380
dn C13 sc 39
dof 0 vs 57
dm nnn th
dmm c ai
dpwr 35 ph
dmf 29412
Bpin
3.102
2.072.97
0.97
1.00
13.68
1.317
ppm

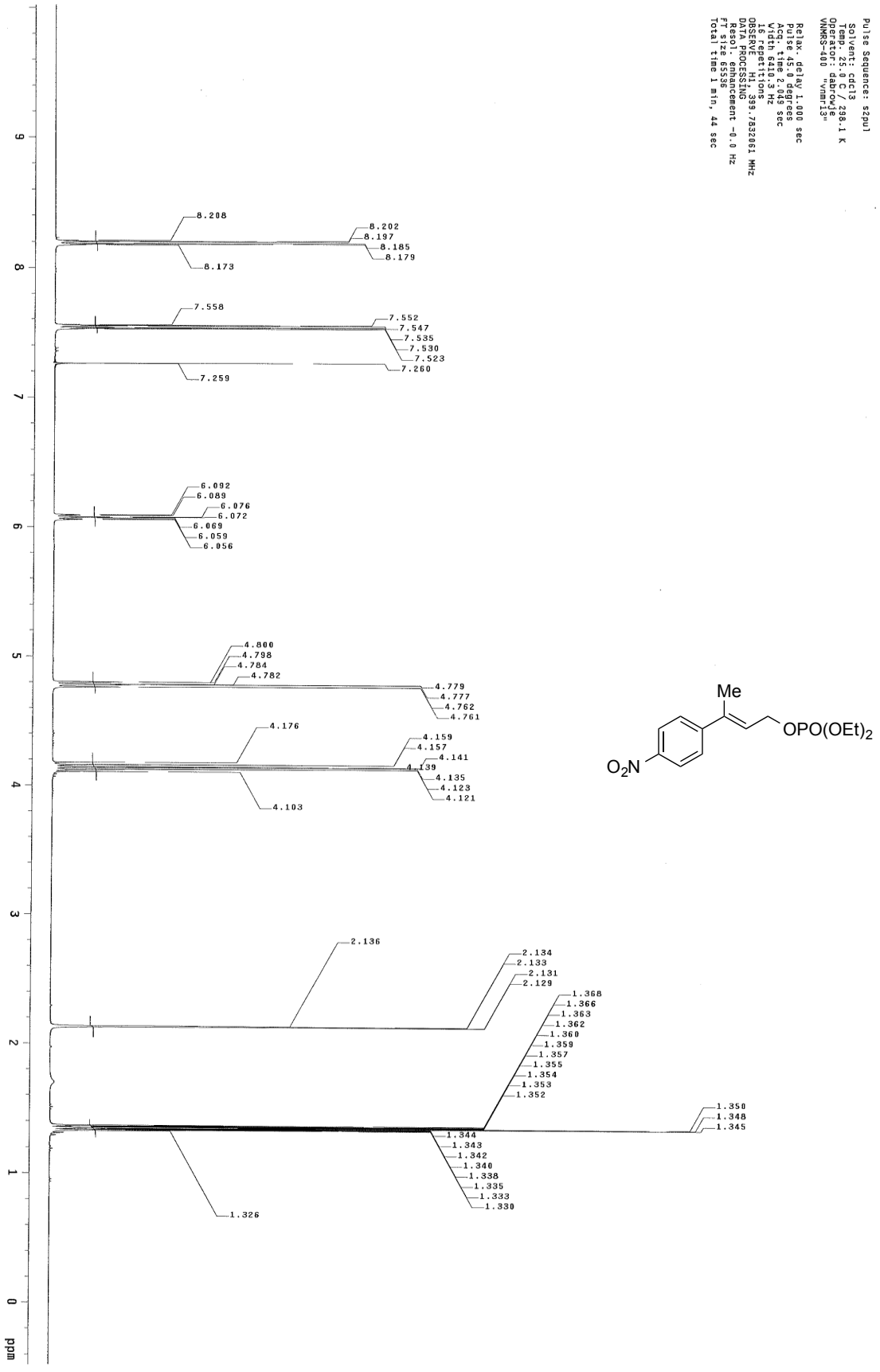

7.421
7.419
7.415
7.410
7.400
7.398
7.389
7.355
7.352
7.347
7.337
7.334
7.319
7.317
7.298
7.295
7.291
7.287
7.280
7.279
7.264
7.261
7.260
5.970
5.967
5.964
5.953
5.950
5.947
5.935
5.932
5.929
4.786
4.767
4.766
4.748
4.171
4.168
4.153
4.150
4.133
4.116
4.113
4.098
4.095
2.116
1.363
1.360
1.357
1.356
1.354
1.353
1.345
1.342
1.339
1.338
1.337
1.336
1.334
1.327
1.324
1.87
2.04
1.00
2.16
3.82
2.80
5.86
ppm
exp20 Proton
date SAMPLE
solvent Jun 8 2010
file /home/ahh/vnmr
rsys/data/Kevin/KM
-Ph-allylic-phosph
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4000
bs
ss 2
d1 1.000
nt 64
ct 44
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
ai
ph
temp SPECIAL
gain 25.0
spin not used
hst 20
pw90 9.108
alfa 11.000
FLAGS 10.000
n n
n n
y nn
PROCESSING
65536
DISPLAY
-200.0
3997.8
2889.7
-32.2
0
PLOT
380
279
8
Sample: Ph_allylic_phosphate
File: /home/ahh/vnmrsys/data/Kevin/KM-Ph-allylic-pho
Pulse Sequence: s2pul

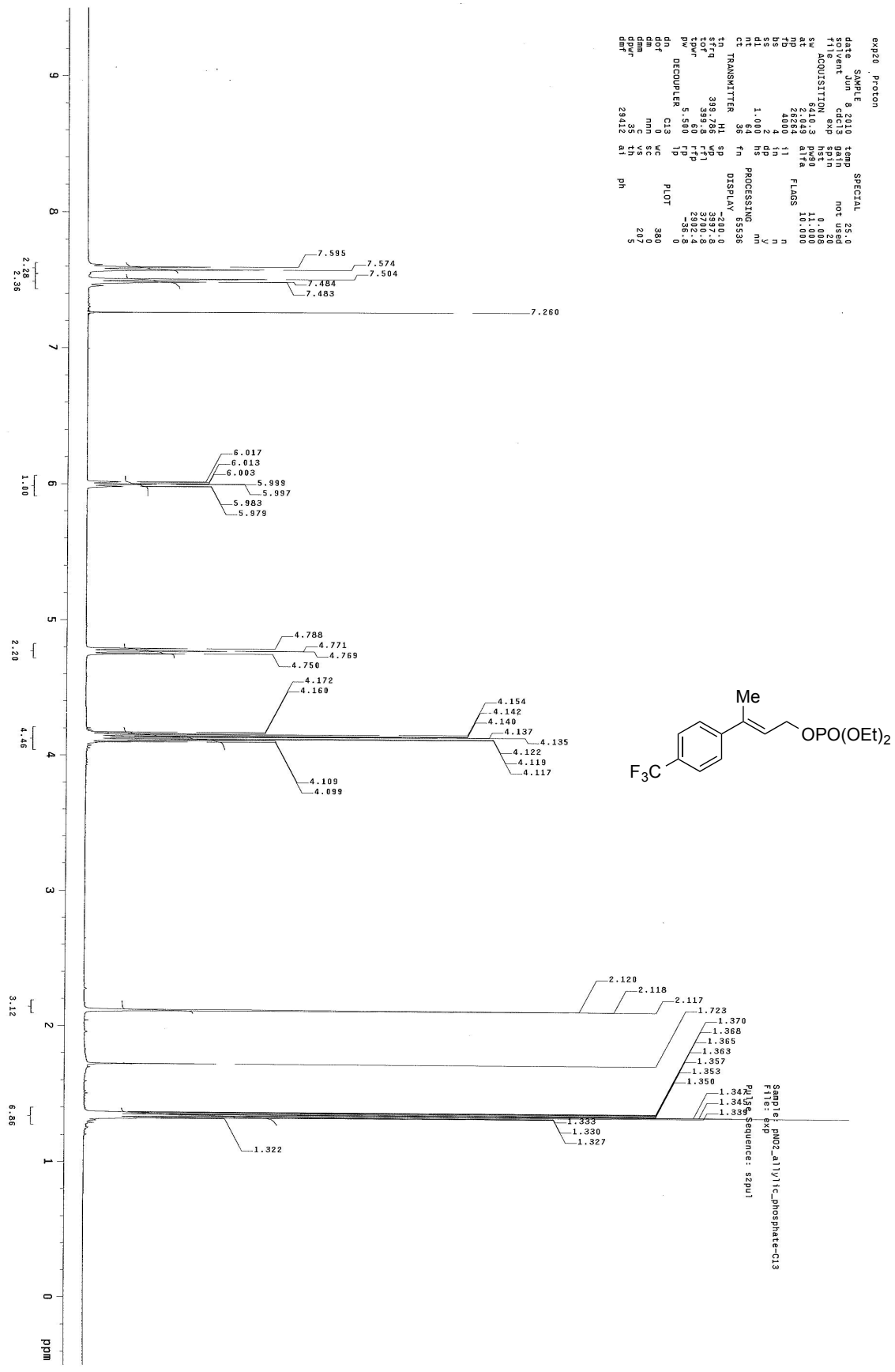
Me
OPO(OEt)2

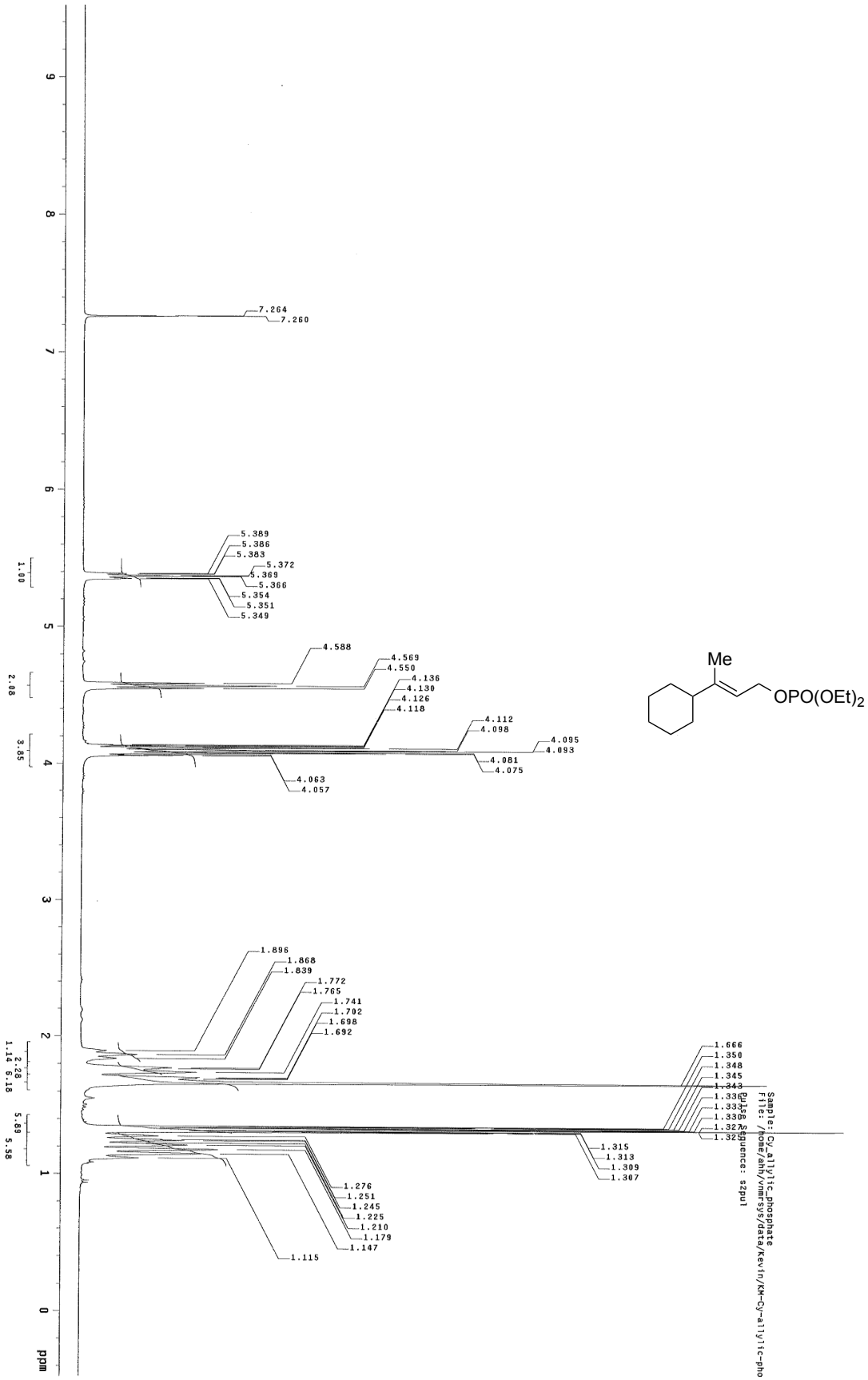
3.112

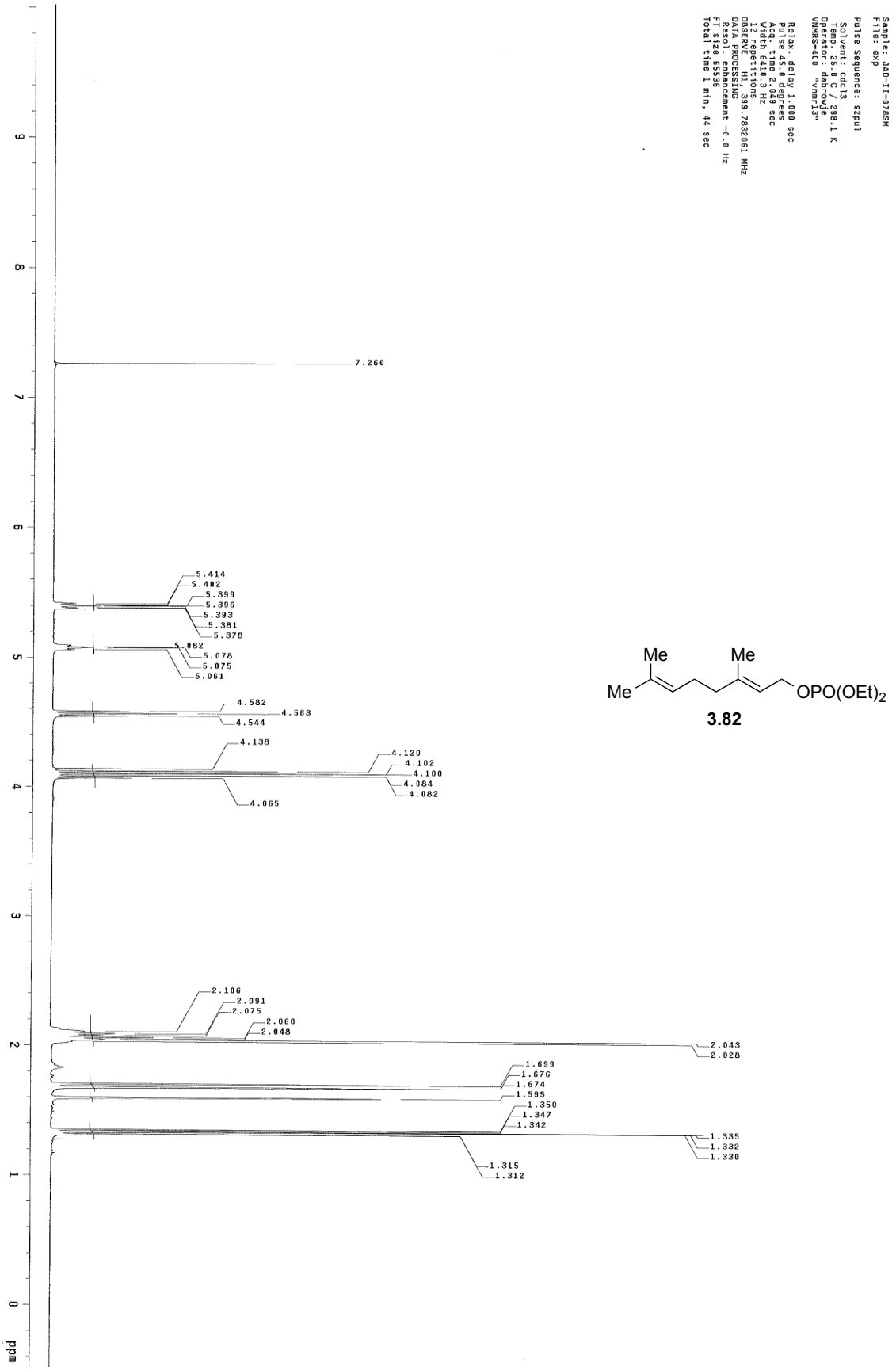

Sample: JAD-II-058SM
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: dabrowje
VNMRS-400 "vmmr13"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.009 sec
Width 6410.3 Hz
16 repetitions
OBSERVE H1, 399.7832063 MHz
DATA PROCESSING
Resol. enhancement -0.1 Hz
FT size 65536
Total time 1 min, 44 sec
10.46
4.04
3.47
8.00
14.59
11.12
11.36
18.46
ppm
Me
Me
OPO(OEt)2


Sample: JAD-II-129SM
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: dabrowje
VNMRS-400 "vnmr13"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 6410.3 Hz
32 repetitions
OBSERVE H1, 399.7832061 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 1 min, 44 sec
3.40
13.95
6.95
2902.43
3.32
7.74
13.99
1663.92
1656.68
1655.90
1648.86
11.06
819.99
819.21
818.43
817.84
817.06
18.22
624.56
549.05
548.07
21.33
542.01
541.03
534.97
533.99
Br
Me
OPO(OEt)2
3.131
ppm


Sample: JAD-II-pNO2
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: dabrowje
VNMRS-400 "vnmrl3"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.043 sec
Width 6410.3 Hz
16 repetitions
OBSERVE H1, 399.7832861 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 1 min, 44 sec
8.208
8.202
8.197
8.185
8.179
8.173
7.558
7.552
7.547
7.535
7.530
7.523
7.260
7.259
6.092
6.089
6.076
6.072
6.069
6.059
6.056
4.800
4.798
4.784
4.782
4.779
4.777
4.762
4.761
4.176
4.159
4.157
4.141
4.139
4.135
4.123
4.121
4.103
2.136
2.134
2.133
2.131
2.129
1.368
1.366
1.363
1.362
1.360
1.359
1.357
1.355
1.354
1.353
1.352
1.350
1.348
1.345
1.344
1.343
1.342
1.340
1.338
1.335
1.333
1.330
1.326
Me
OPO(OEt)2
O2N
ppm

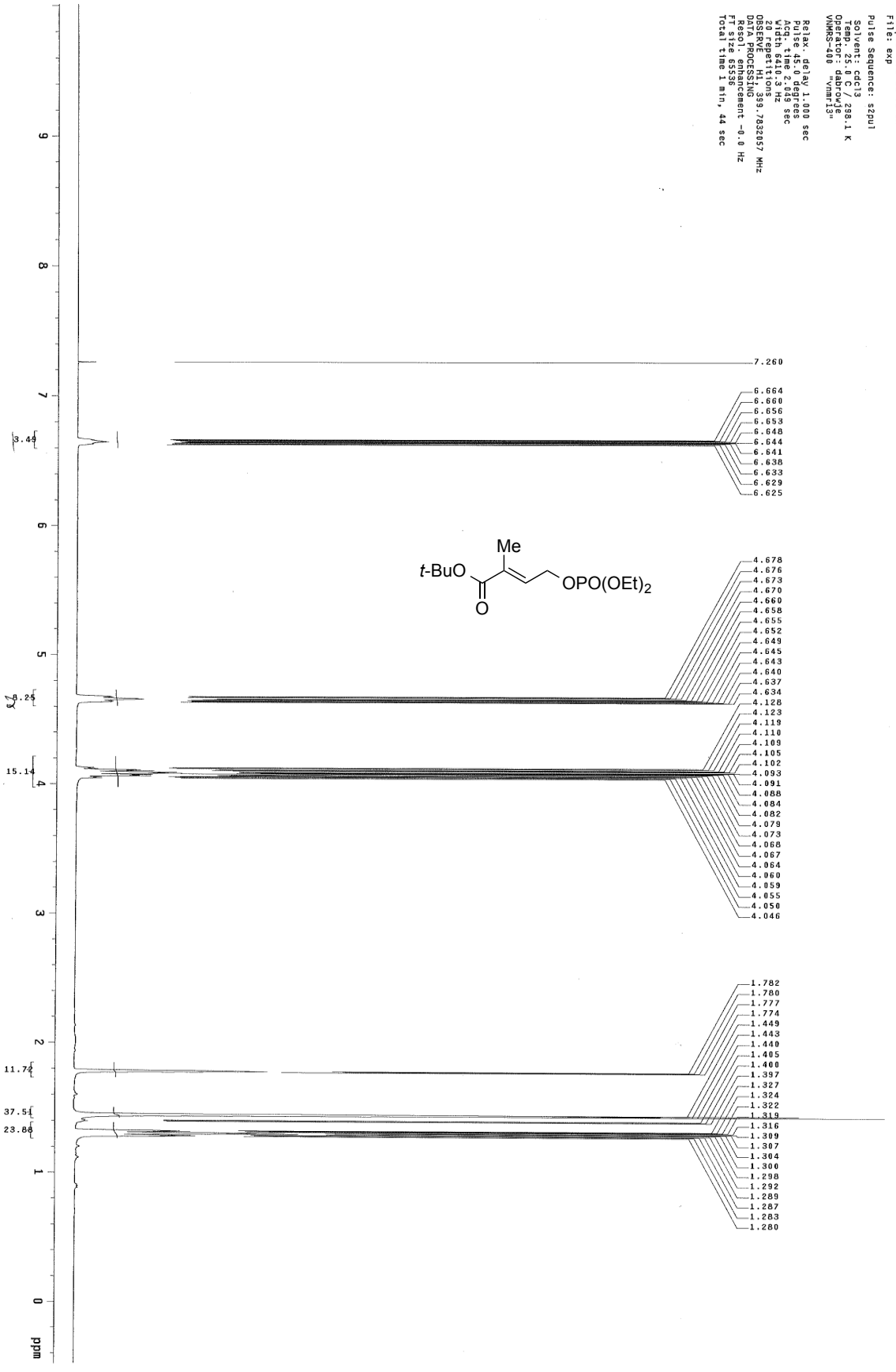

exp20 Proton
SAMPLE
date Jun 8 2010
solvent cdcl3
file exp
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4000
bs 2
ss 1
d1 1.000
nt 64
ct 36
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
PLOT
ph
temp SPECIAL
gain 25.0
spin not used
hst 20
pw90 0.008
aq 11.000
FLAGS 10.000
il n
in n
dp y
hs nn
PROCESSING
fn 65536
DISPLAY
wp 4000.0
sp 399.8
rfl 3700.8
rfp 2902.4
rp -36.8
lp 0
380
0
207
5
7.595
7.574
7.504
7.484
7.483
7.260
6.017
6.013
6.003
5.999
5.997
5.983
5.979
4.788
4.771
4.769
4.750
4.172
4.160
4.154
4.142
4.140
4.137
4.135
4.122
4.119
4.117
4.109
4.099
2.120
2.118
2.117
1.723
1.370
1.368
1.365
1.363
1.357
1.353
1.350
1.345
1.343
1.339
1.333
1.330
1.327
1.322
2.28
2.36
1.00
2.20
4.46
3.12
6.86
ppm
Me
OPO(OEt)2
F3C
PULSE Sequence: szpul
Sample: pNO2_allylic_phosphate-C13
File: exp

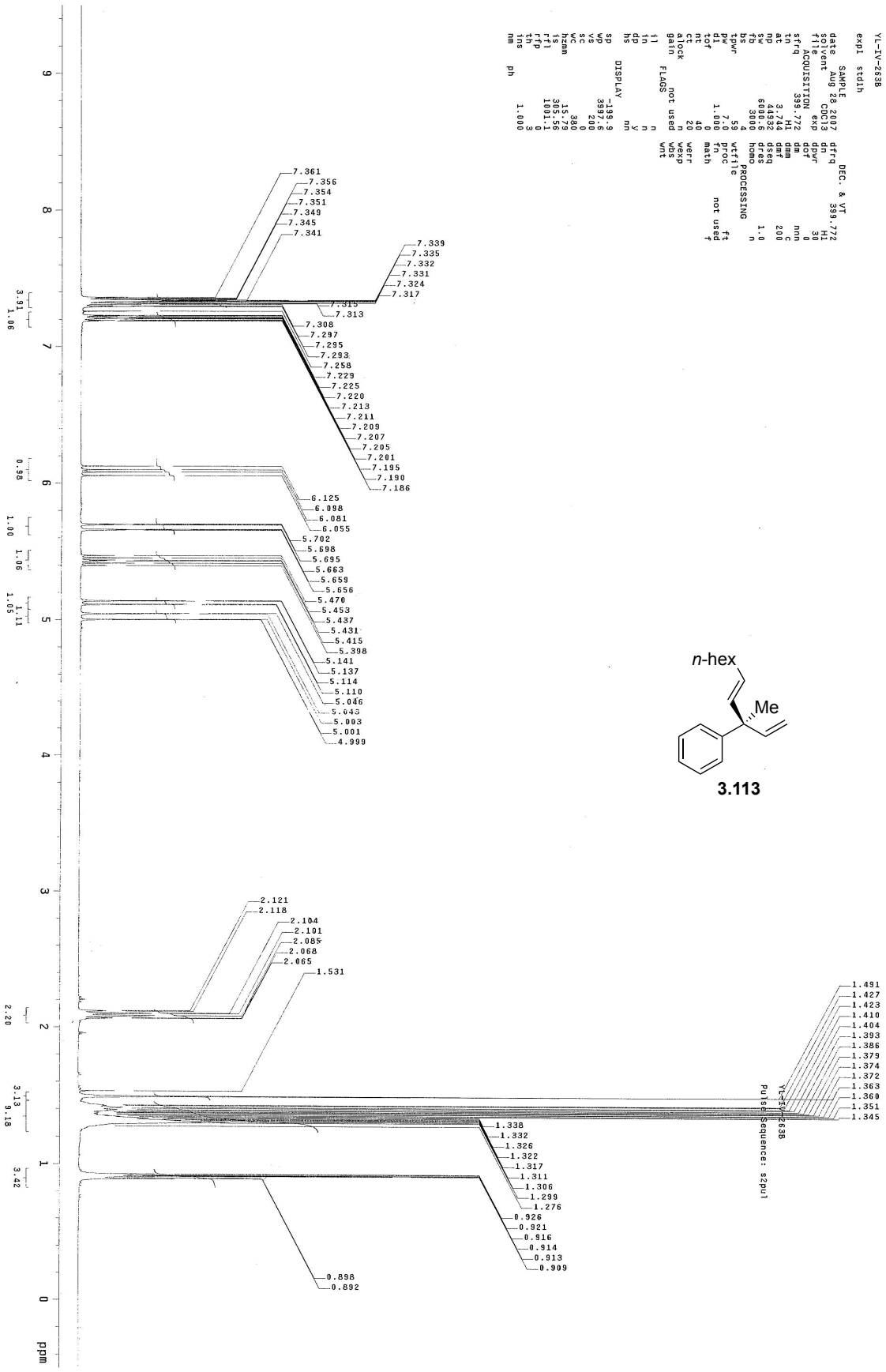

7.264
7.260
5.389
5.386
5.383
5.372
5.369
5.366
5.354
5.351
5.349
4.588
4.569
4.550
4.136
4.130
4.126
4.118
4.112
4.098
4.095
4.093
4.081
4.075
4.063
4.057
1.896
1.868
1.839
1.772
1.765
1.741
1.702
1.698
1.692
1.666
1.350
1.348
1.345
1.343
1.338
1.334
1.330
1.327
1.323
1.315
1.313
1.309
1.307
1.276
1.251
1.245
1.225
1.210
1.179
1.147
1.115
1.00
2.08
3.85
1.14
6.18
2.28
5.89
5.58
ppm
Me
OPO(OEt)2
Sample: Cy_allylic_phosphate
File: /home/ahh/vnmrsys/data/kevin/KM-Cy-allylic-pho
Pulse Sequence: s2pul

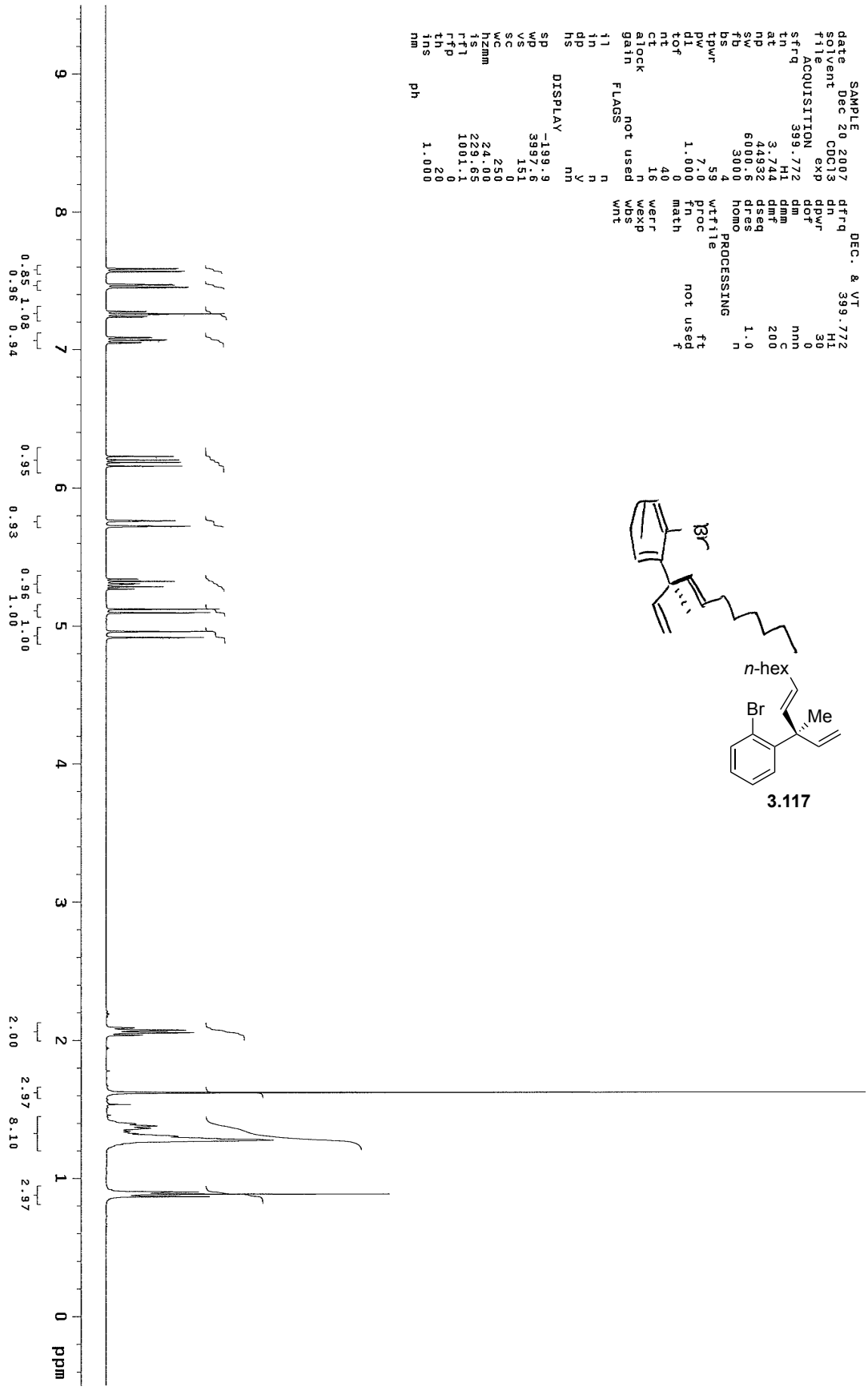

Sample: JAD-II-078SM
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: daurova
VNMRS-400 "vnmrj3"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 6410.3 Hz
12 repetitions
OBSERVE H1, 399.7832061 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 44 sec
7.260
5.414
5.402
5.399
5.396
5.393
5.381
5.378
5.082
5.078
5.075
5.061
4.582
4.563
4.544
4.138
4.120
4.102
4.100
4.084
4.082
4.065
2.106
2.091
2.075
2.060
2.048
2.043
2.028
1.699
1.676
1.674
1.595
1.350
1.347
1.342
1.335
1.332
1.330
1.315
1.312
ppm

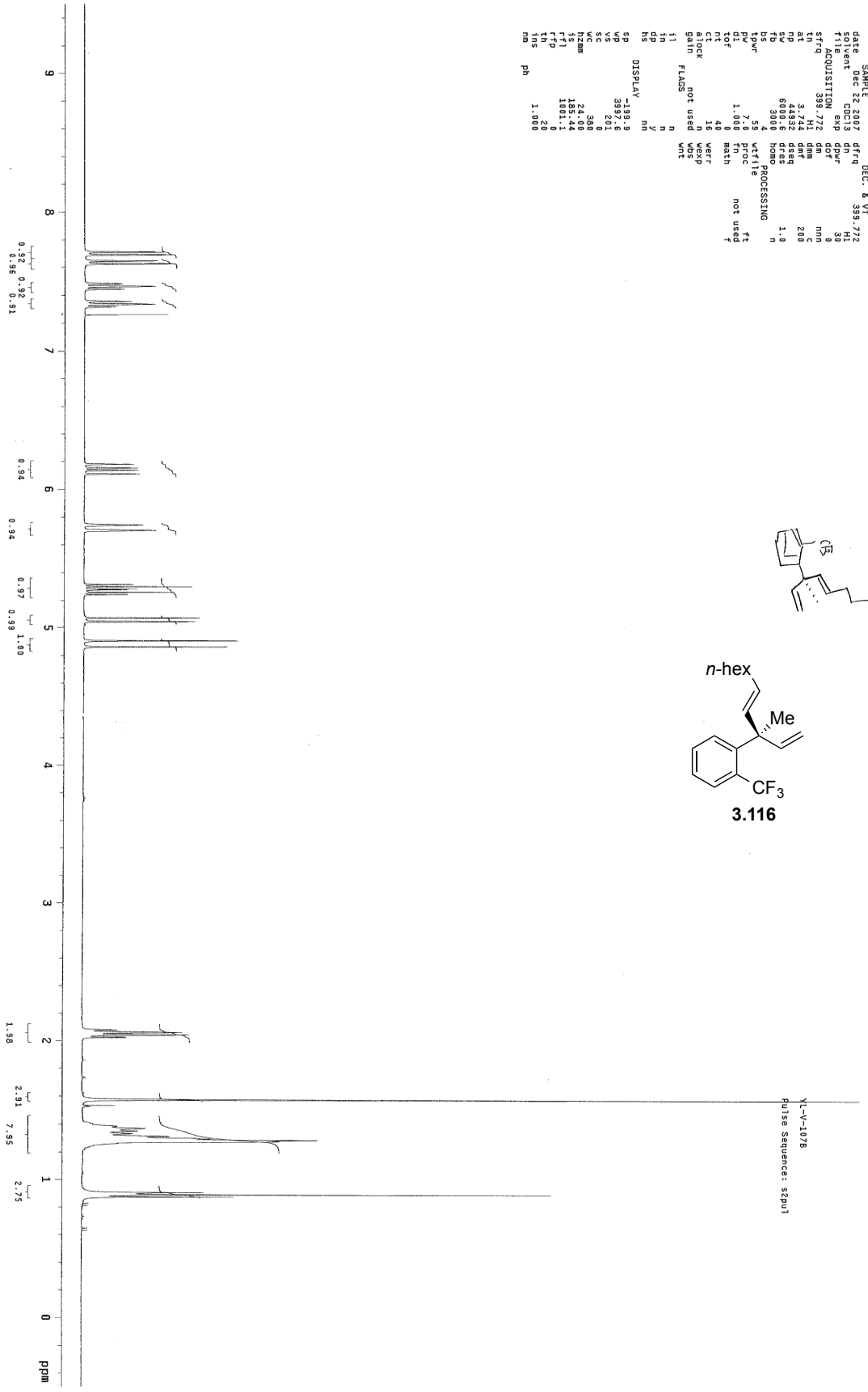
Me
Me
Me
OPO(OEt)2

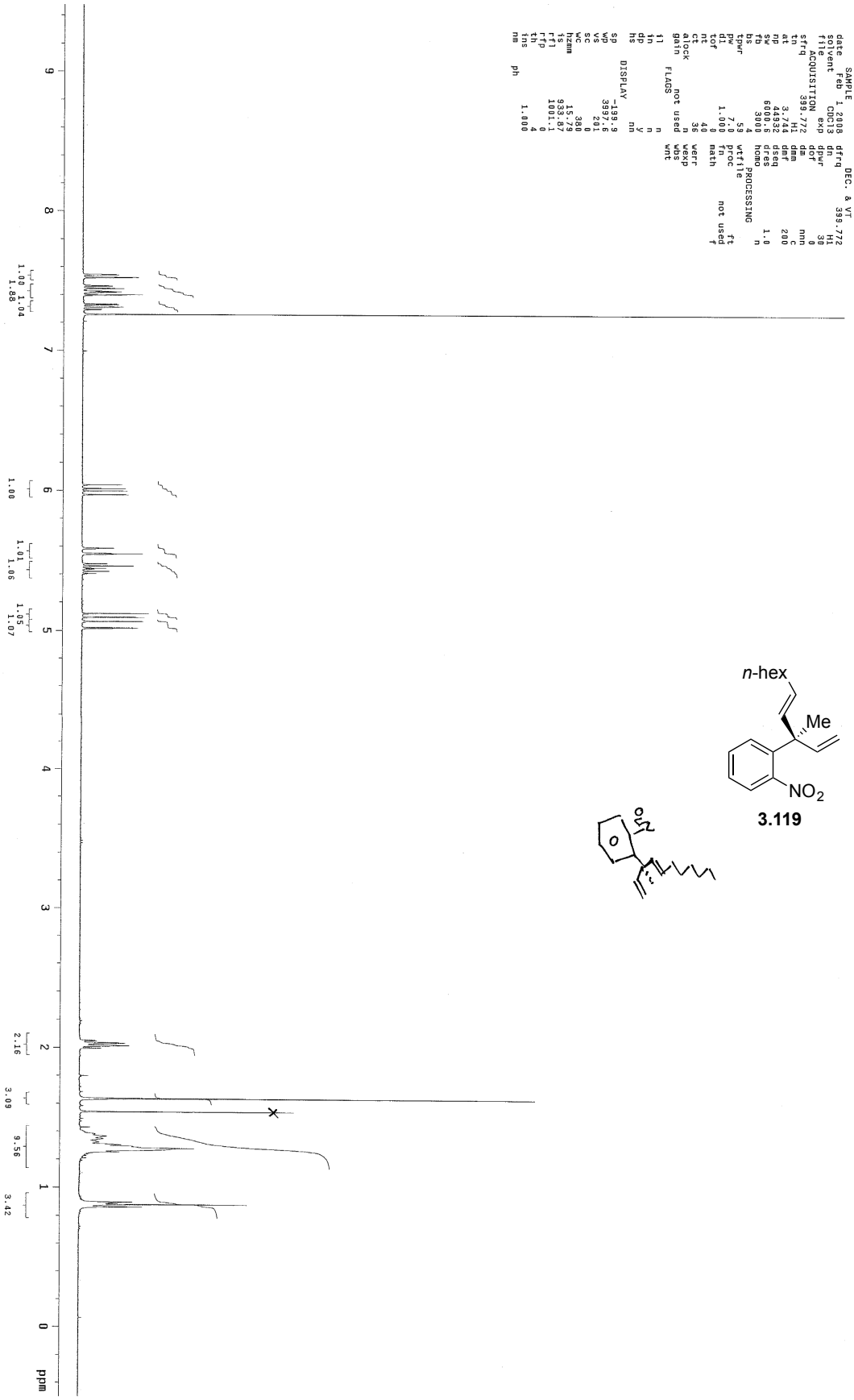
3.82

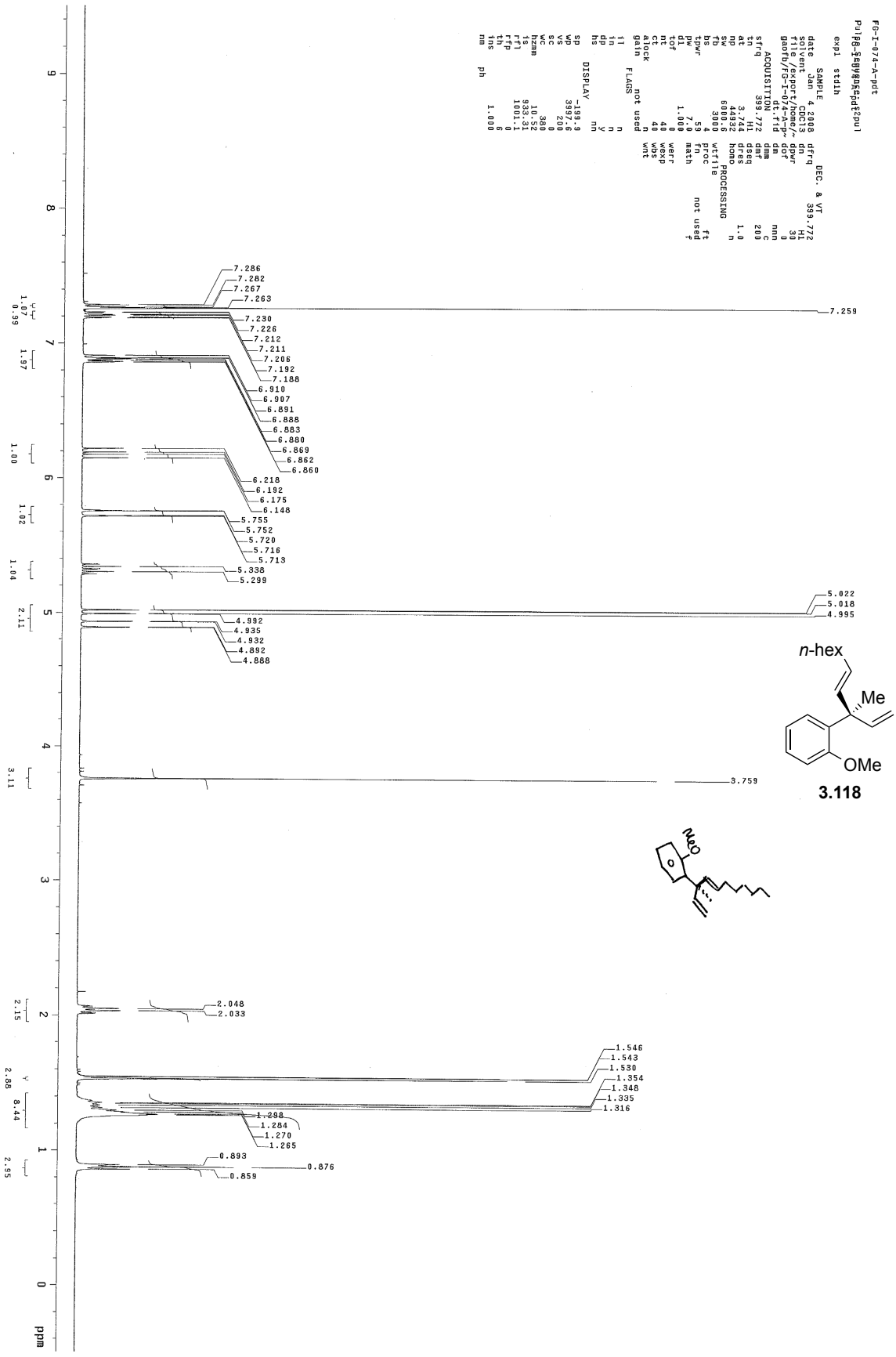

Sample: JAD-I-087SM
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: dabrow18
VNMRS-400 "vnmr13"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 6410.3 Hz
28 repetitions
OBSERVE H1, 399.7832057 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 1 min, 44 sec
7.260
6.664
6.660
6.656
6.653
6.648
6.644
6.641
6.638
6.633
6.629
6.625
4.678
4.676
4.673
4.670
4.660
4.658
4.655
4.652
4.649
4.645
4.643
4.640
4.637
4.634
4.128
4.123
4.119
4.110
4.109
4.105
4.102
4.093
4.091
4.088
4.084
4.082
4.079
4.073
4.068
4.067
4.064
4.060
4.059
4.055
4.050
4.046
1.782
1.780
1.777
1.774
1.449
1.443
1.440
1.405
1.400
1.397
1.327
1.324
1.322
1.319
1.316
1.309
1.307
1.304
1.300
1.298
1.292
1.289
1.287
1.283
1.280
3.49
8.25
15.14
11.74
37.51
23.88
Me
t-BuO
OPO(OEt)2
O
ppm


7.361
7.356
7.354
7.351
7.349
7.345
7.341
7.339
7.335
7.332
7.331
7.324
7.317
7.315
7.313
7.308
7.297
7.295
7.293
7.258
7.229
7.225
7.220
7.213
7.211
7.209
7.207
7.205
7.201
7.195
7.190
7.186
6.125
6.098
6.081
6.055
5.702
5.698
5.695
5.663
5.659
5.656
5.470
5.453
5.437
5.431
5.415
5.398
5.141
5.137
5.114
5.110
5.046
5.045
5.003
5.001
4.999
2.121
2.118
2.104
2.101
2.085
2.068
2.065
1.531
1.491
1.427
1.423
1.410
1.404
1.393
1.386
1.379
1.374
1.372
1.363
1.360
1.351
1.345
1.338
1.332
1.326
1.322
1.317
1.311
1.306
1.299
1.276
0.926
0.921
0.916
0.914
0.913
0.909
0.898
0.892
ppm
3.91
1.06
0.58
1.00
1.06
1.11
1.05
2.20
3.13
9.18
3.42
n-hex
Me
3.113


YL-V-143A
exp2 stdih
SAMPLE
date Dec 20 2007
solvent CDCl3
file
ACQUISITION
sfrq 399.772
tn H1
at 3.744
np 44932
sw 6000.6
fb 3000
bs 4
tpwr 59
pw 7.0
pl 1.000
tof 0
nt 40
ct 16
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -199.9
wp 3997.6
vs 151
sc 0
wc 250
hzmm 24.00
is 229.65
rfl 1001.1
rfp 0
th 20
ins 1.000
nm
ph
dfrq DEC. & VT
dn 399.772
dpwr H1
dof 30
dm 0
nnn
c 200
dmm
dmf
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn not used
math f
wexp
wbs
wnt
n-hex
Br
Me
3.117
9
8
7
6
5
4
3
2
1
0
ppm
0.85 1.08 0.94
0.96
0.95
0.93
0.96 1.00
1.00
2.00
2.97 8.10
2.97


YL-V-107B
exp2 stdih
SAMPLE
date Dec 22 2017
solvent CDCl3
file exp
ACQUISITION
sfrq 399.772
tn H1
at 3.277
nt 8
np 44932
sw 6000.6
fb 3000
bs 4
tpwr 51
pw 7.8
d1 1.000
tof 40
nt 16
ct 0
alock n
gain n
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -199.9
wp 3997.6
vs 201
sc 0
wc 380
hzmm 24.00
is 185.44
rfl 1001.1
rfp 0
th 20
ins 1.000
nm
ph
DEC. & VT
dfrq 399.772
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn not used
math
wer
wexp
wbs
wnt
YL-V-107B
Pulse Sequence: s2pul
n-hex
Me
CF3
3.116
ppm
0.82
0.96
0.92
0.91
0.94
0.94
0.97
0.99
1.00
1.98
2.91
7.95
2.75


n-hex
Me
NO2
3.119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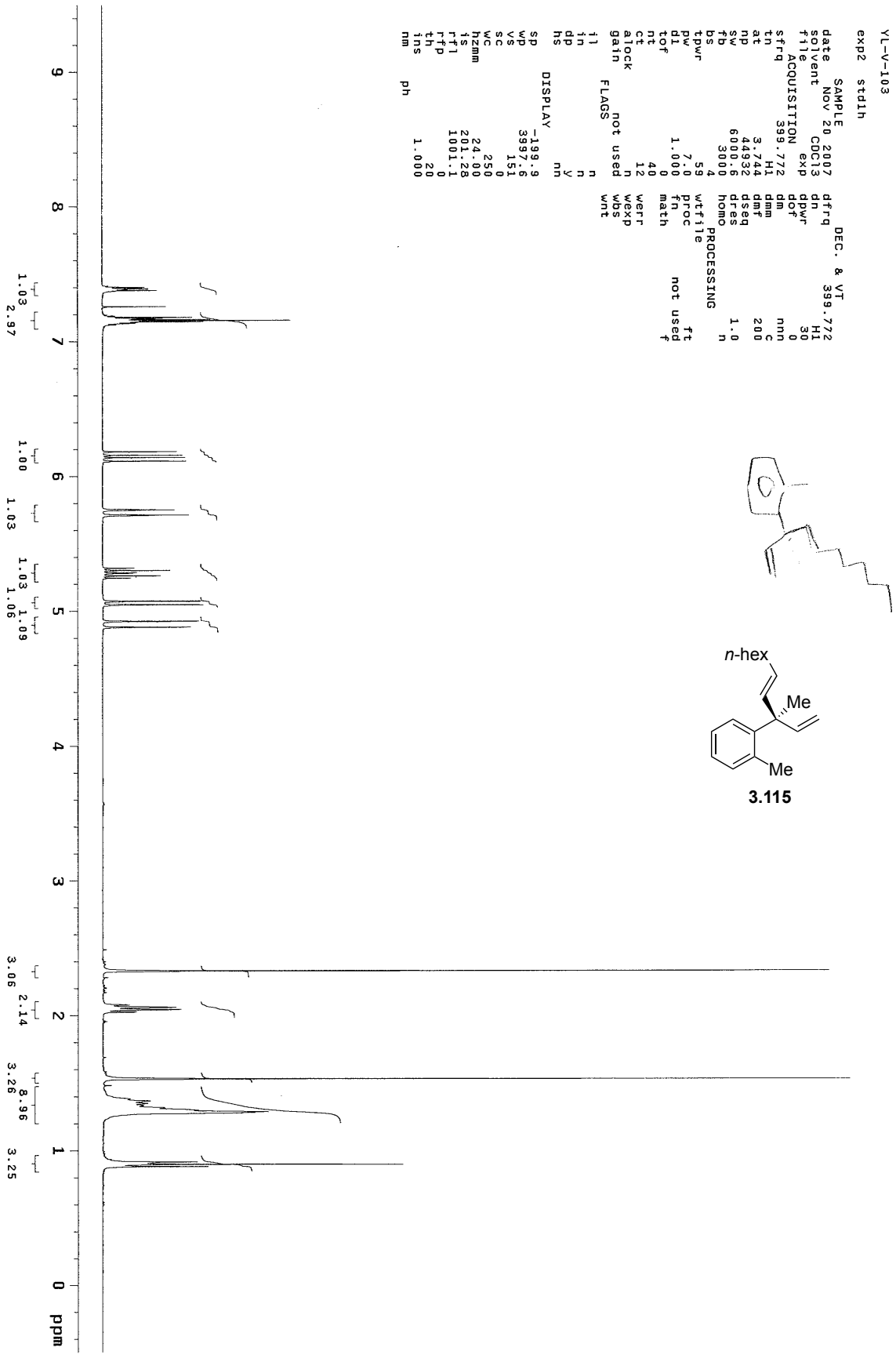
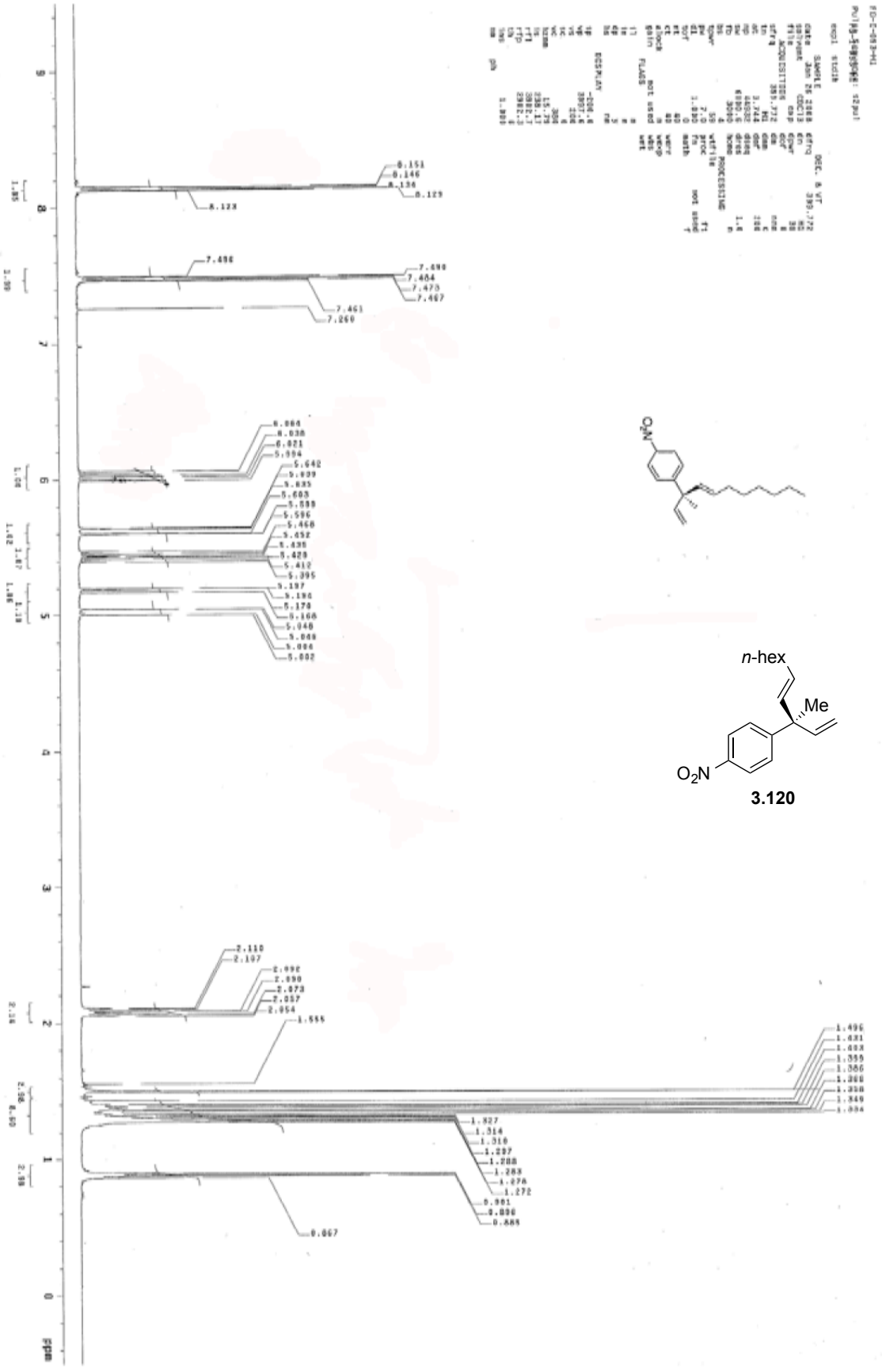
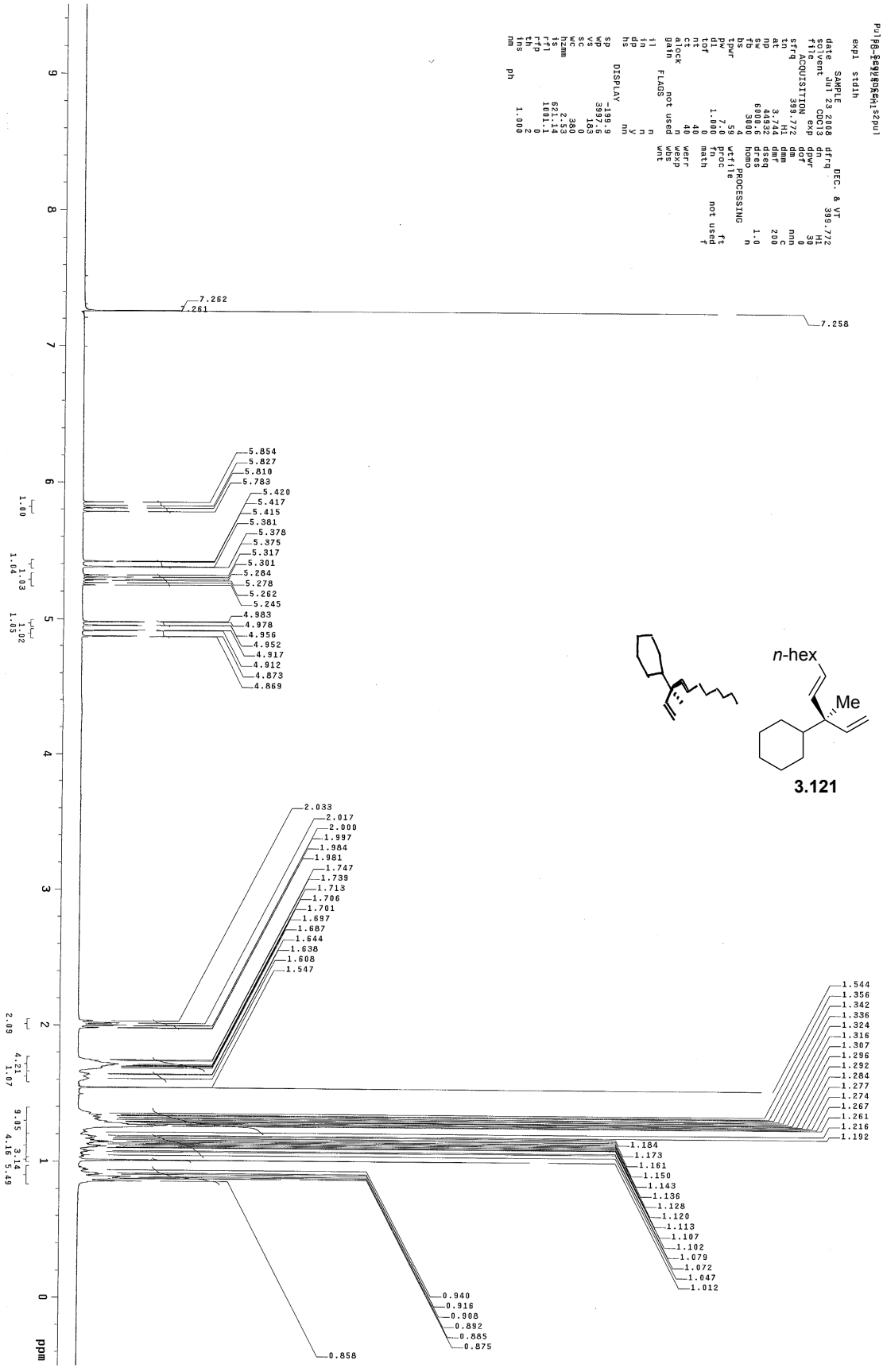
7.259
7.230
7.226
7.212
7.211
7.206
7.192
7.188
6.910
6.907
6.891
6.888
6.883
6.880
6.869
6.862
6.860
6.218
6.192
6.175
6.148
5.755
5.752
5.720
5.716
5.713
5.338
5.299
5.022
5.018
4.995
4.992
4.935
4.932
4.892
4.888
3.759
2.048
2.033
1.546
1.543
1.530
1.354
1.348
1.335
1.316
1.298
1.284
1.270
1.265
0.893
0.876
0.859
ppm
n-hex
Me
OMe
3.118
MeO


YL-V-103
exp2 stdih
SAMPLE
date Nov 20 2007
solvent CDCl3
file exp
ACQUISITION
sfrq 399.772
tn H1
at 3.744
np 44932
sw 6000.6
fb 3000
bs 4
tpwr 59
pw 7.0
d1 1.000
tof 0
nt 40
ct 12
alock n
gain n
FLAGS
not used
wnt
il n
in n
dp y
hs nn
DISPLAY
sp -199.9
wp 3997.6
vs 151
sc 0
wc 250
hzmm 24.00
is 201.28
rfl 1001.1
rfp 0
th 20
ins 1
nm 1.000
ph
DEC. & VT
dfrq 399.772
dn H1
dpwr 30
dof 0
nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn not used
math f
wexp
wbs
n-hex
Me
Me
3.115
9
8
7
6
5
4
3
2
1
0
ppm
1.03
2.97
1.00
1.03
1.03
1.06
1.09
3.06
2.14
3.26
8.96
3.25



3.120


7.262
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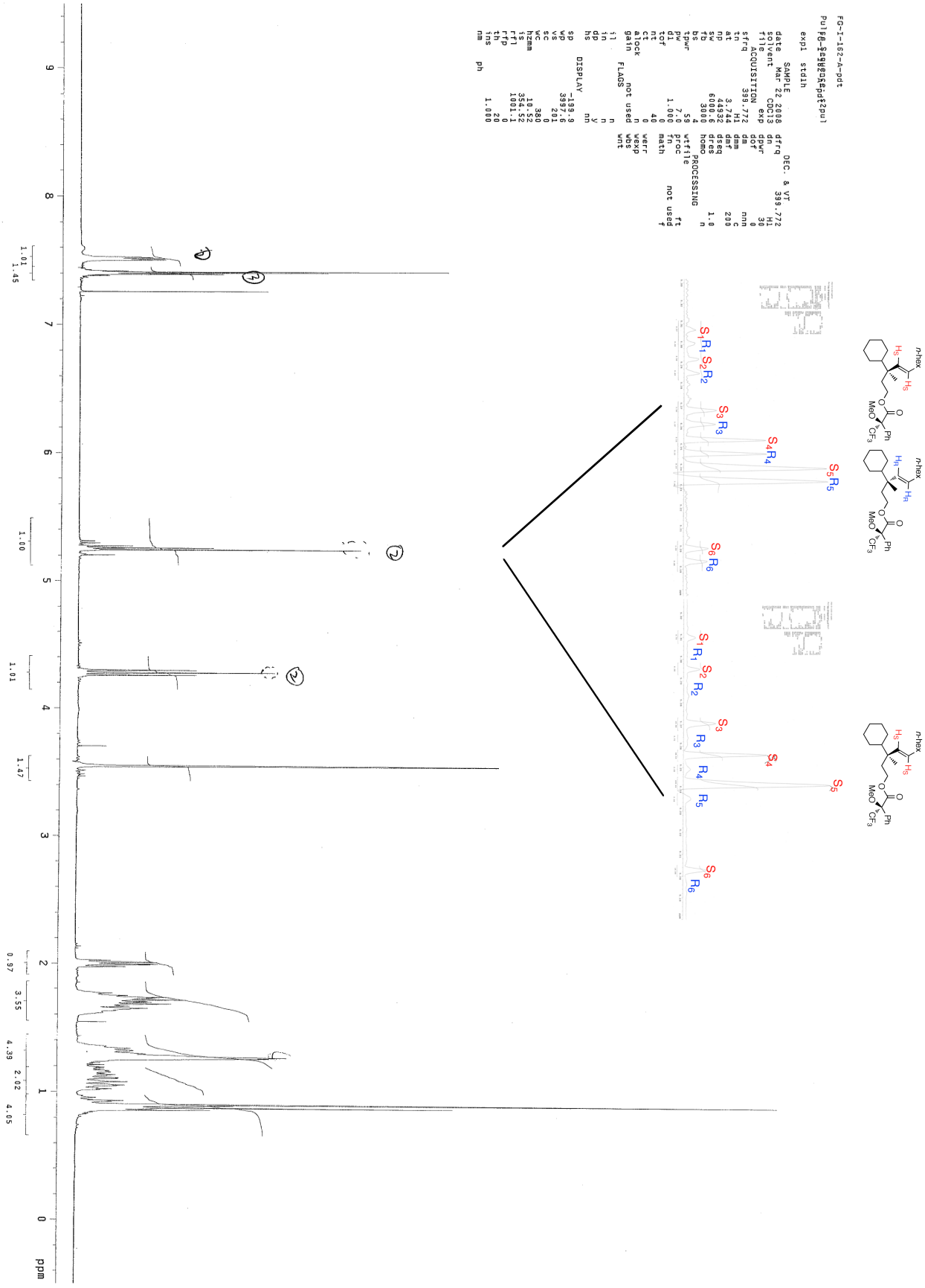
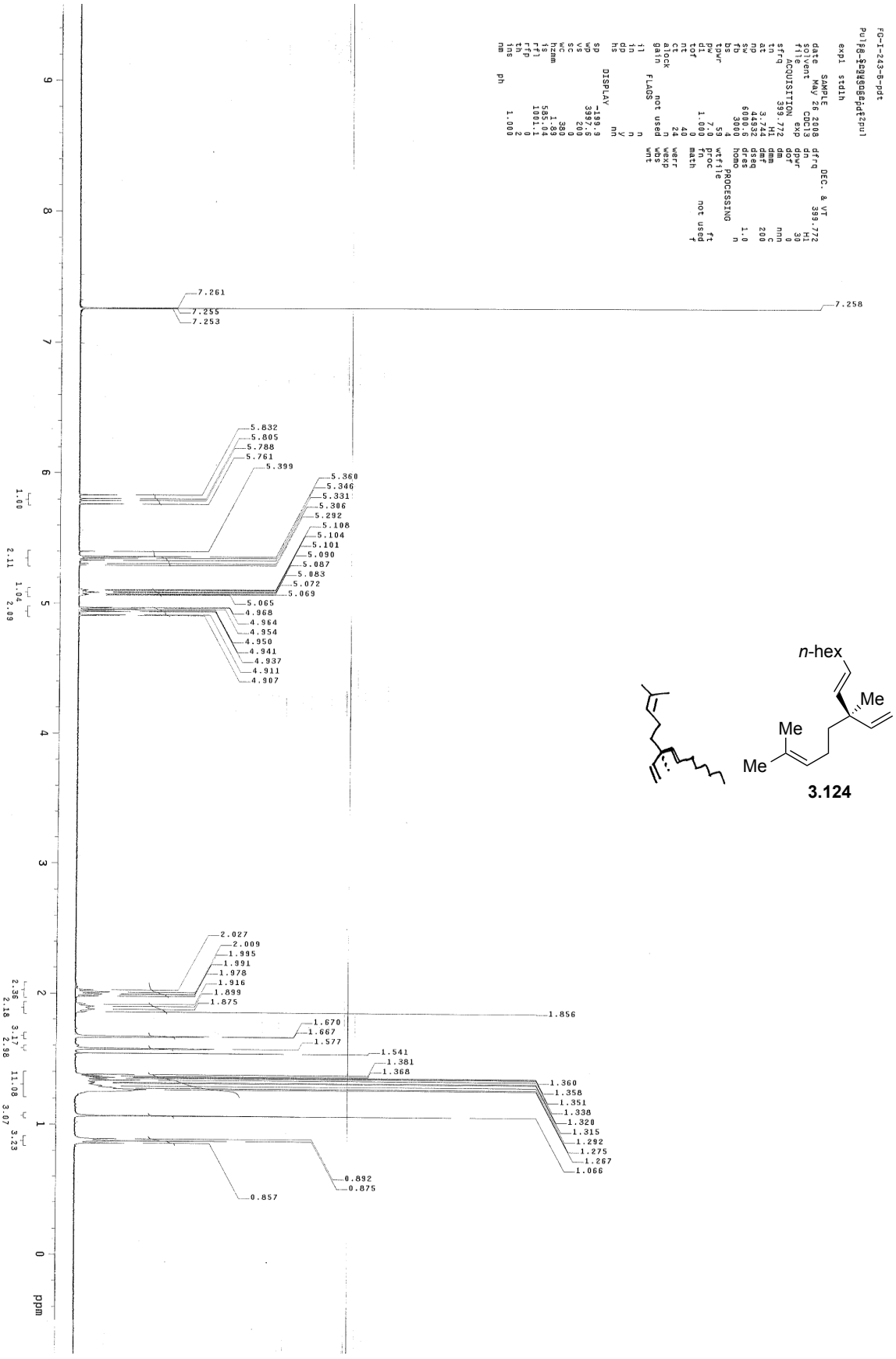
7.258
5.854
5.827
5.810
5.783
5.420
5.417
5.415
5.381
5.378
5.375
5.317
5.301
5.284
5.278
5.262
5.245
4.983
4.978
4.956
4.952
4.917
4.912
4.873
4.869
2.033
2.017
2.000
1.997
1.984
1.981
1.747
1.739
1.713
1.706
1.701
1.697
1.687
1.644
1.638
1.608
1.547
1.544
1.356
1.342
1.336
1.324
1.316
1.307
1.296
1.292
1.284
1.277
1.274
1.267
1.261
1.216
1.192
1.184
1.173
1.161
1.150
1.143
1.136
1.128
1.120
1.113
1.107
1.102
1.079
1.072
1.047
1.012
0.940
0.916
0.908
0.892
0.885
0.875
0.858
ppm
n-hex
Me

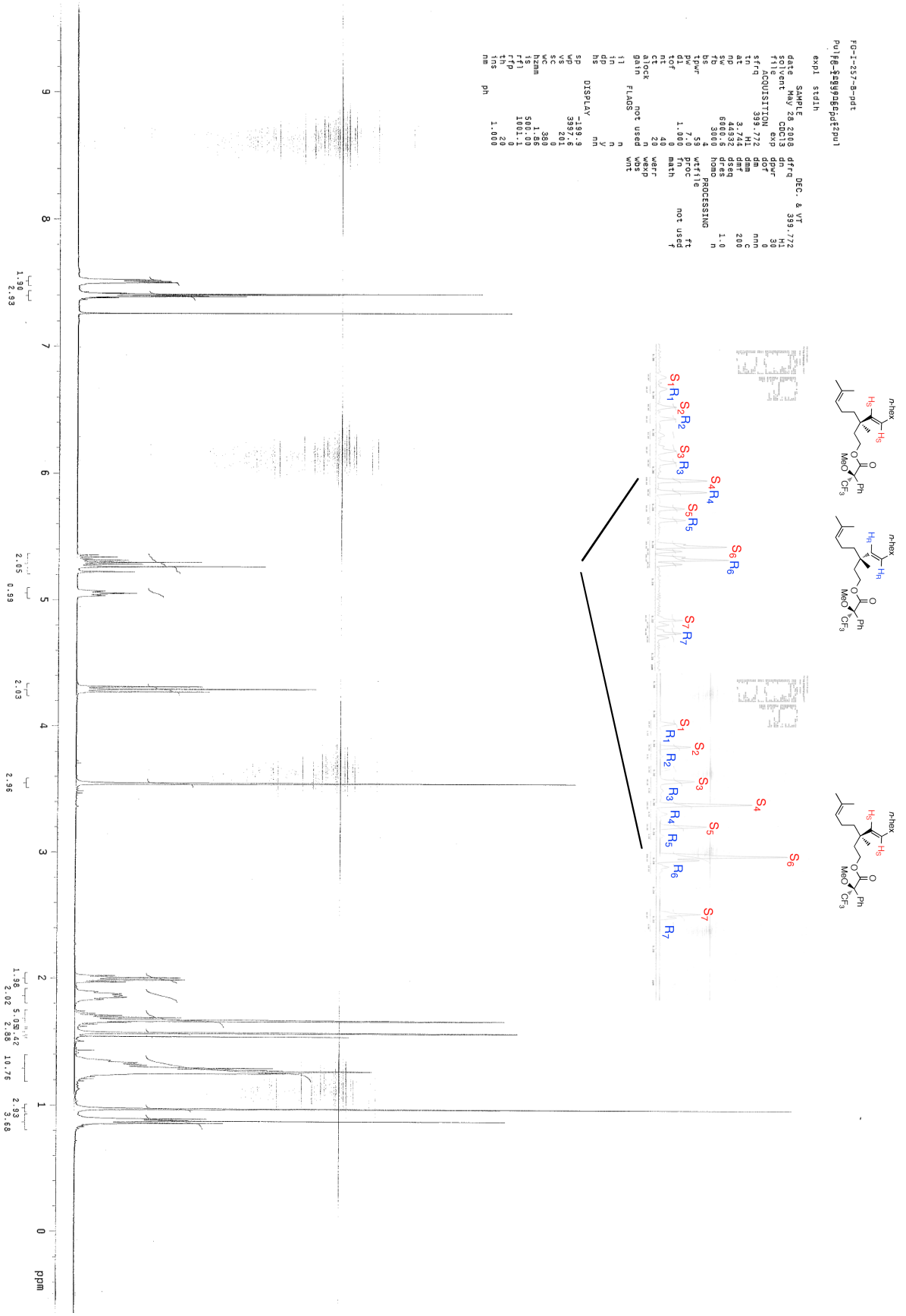
3.121

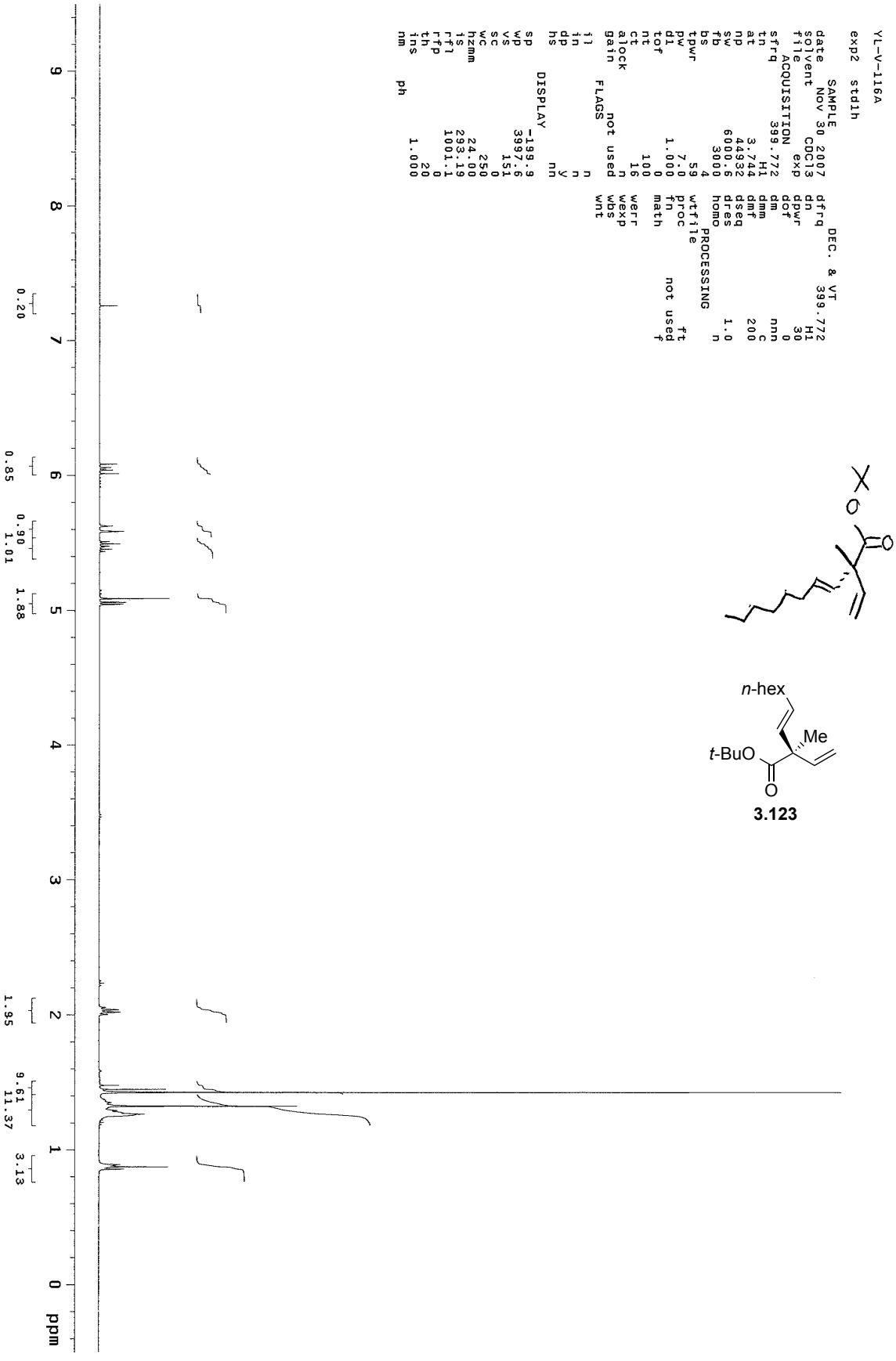

FG-1-162-A-pdt
Pulprog FG-1-162-A-pdt$2pul
expl stdih
SAMPLE
date Mar 22 2008
solvent CDCl3
file ACQUISITION
sfrq 399.772
tn H1
at 3.744
np 44932
sw 6000.6
fb 300.4
bs 59
tpwr 59
pw 7.0
d1 1.000
nt 40
ct 0
alock n
gain n
FLAGS
not used
wbs
wnt
il n
in n
dp y
hs nn
DISPLAY
sp -199.9
wp 3997.6
vs 201
sc 0
wc 380
hzmm 10.52
is 354.52
rfl 1001.1
rfp 0
th 20
ins 1.000
nm ph
DEC. & VT
dfrq 399.772
dn H1
dpwr 30
dof 0
dm nnn
dmm 200
dmf
dseq
dres 1.0
homo n
PROCESSING
wtfile
ft
not used f
proc
fn
math
werr
wexp
wbs
wnt
S1R1 S2R2
S3R3
S4R4
S5R5
S6R6
S1R1
S2R2
S3
R3
S4
R4
R5
S5
S6
R6
nhex
Hs
Ph
MeO
CF3
Hn
ppm
1.01
1.45
1.00
1.01
1.47
0.97
3.55
4.39
2.02
4.05

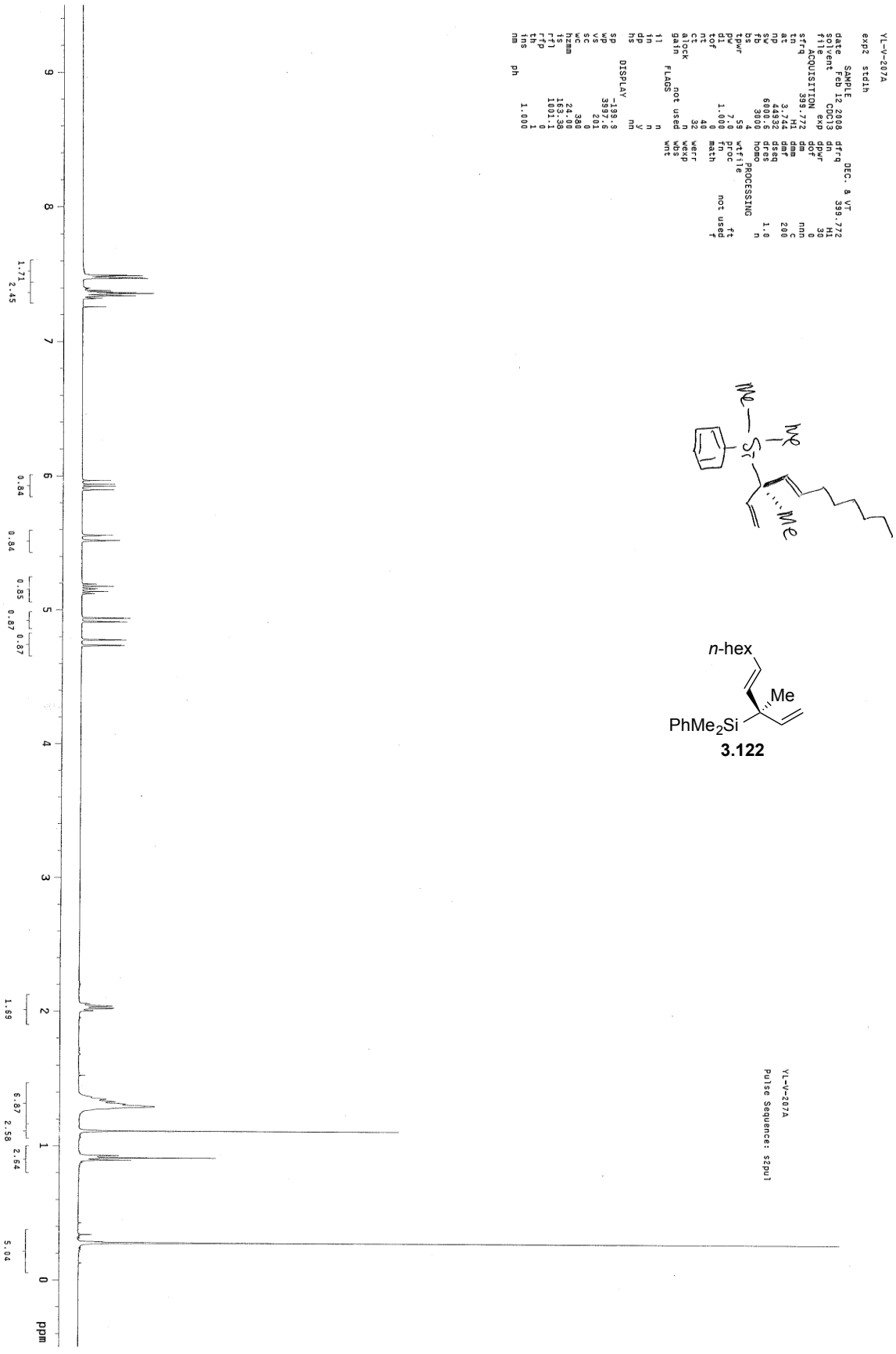

FG-I-243-B-pdt
Pulse Sequence: s2pul
exp1 std1h
SAMPLE
date May 26 2008
solvent CDCl3
file ACQUISITION
399.772 dfrq
DEC. & VT
399.772 H1
sfrq
tn H1
at 3.74
nuc1 off
sw 6000.6
fb 3000
bs 4
tpwr 59
pw 7.03
pl1 1.00
tof 0
nt 40
ct 24
alock wexp
gain wns
FLAGS not used
il n
in y
dp n
hs nn
DISPLAY
sp -199.9
wp 3997.5
vs 2210
sc 0
wc 380
hzmm 1.83
vs 585.04
rfl 1001.0
rfp 0
th 2
ins 1.000
nm
ph
dfrq 399.772
dn H1
dpwr 30
dof 0
nnn
c 200
dmf
dmm
dm
math
ft
not used f
PROCESSING
wtfile
proc
werr
wdw
wnt
7.261
7.255
7.253
7.258
5.832
5.805
5.788
5.761
5.399
5.360
5.346
5.331
5.306
5.292
5.108
5.104
5.101
5.090
5.087
5.083
5.072
5.069
5.065
4.968
4.964
4.954
4.950
4.941
4.937
4.911
4.907
2.027
2.009
1.995
1.991
1.978
1.916
1.899
1.875
1.856
1.670
1.667
1.577
1.541
1.381
1.368
1.360
1.358
1.351
1.338
1.328
1.315
1.292
1.275
1.267
1.066
0.892
0.875
0.857
1.00
2.11
1.04
2.09
2.36
2.18
3.17
2.98
11.08
3.07
3.23
ppm

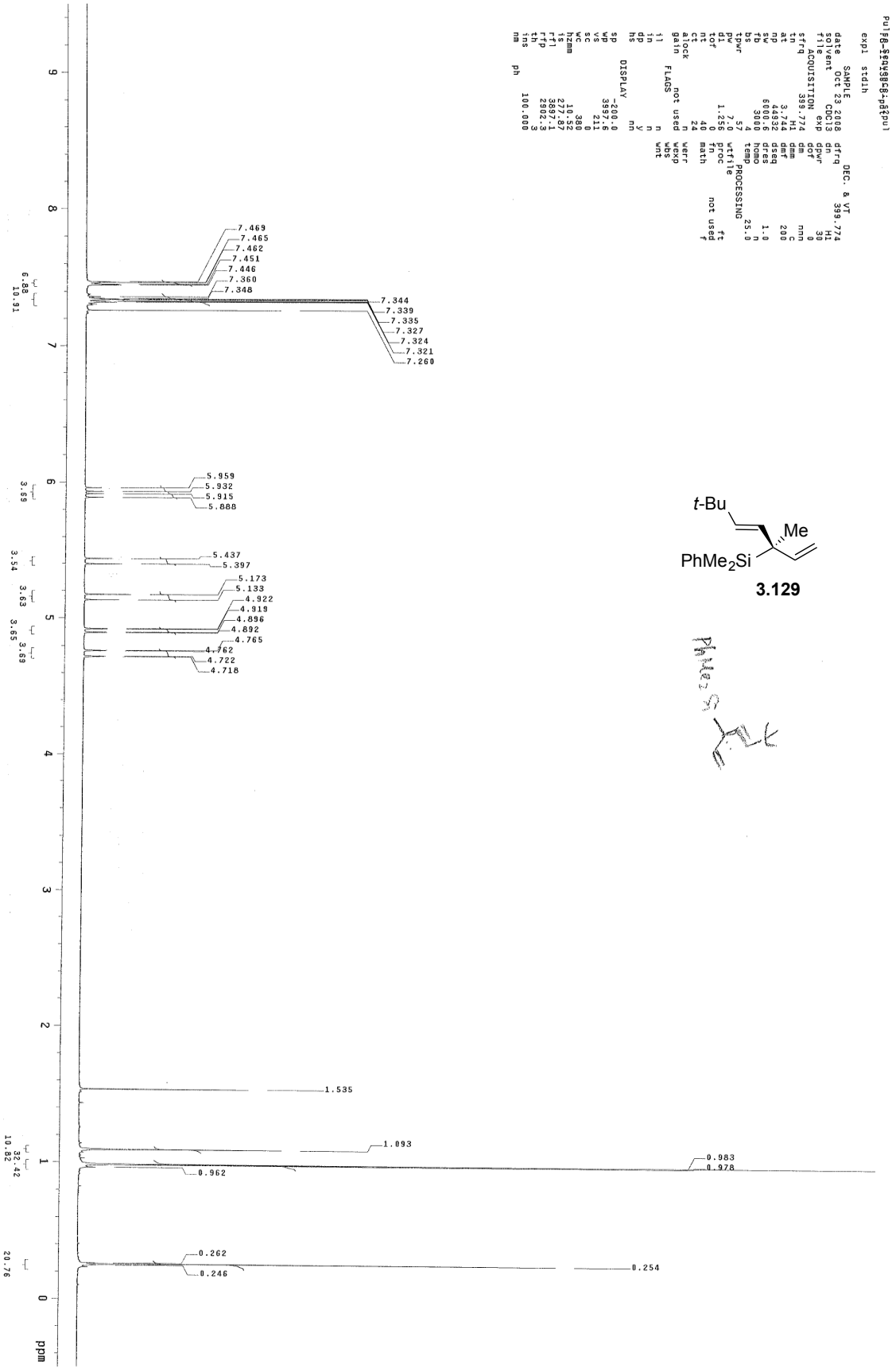
n-hex
Me
Me
Me

3.124


FG-I-257-B-pdt
Pulse Sequence: s2pul
expl stdin
SAMPLE
date May 28 2008
solvent CDCl3
file exp
ACQUISITION
sfrq 399.772 MHz
tn H1
at 3.234 sec
np 44934
sw 6000.6 dfrq 399.772 MHz
fb 3000 homo dfrq 1.0
bs 4 n dfrm
tpwr 59 wtfile PROCESSING
pw 7.9 proc ft
d1 1.000 proc math
tof 0.0 not used f
nt 40 wer
ct 20 wexp
alock wbs
gain not used wnt
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -199.9
wp 399.61
vs 20
sc 0
wc 380
hzmm 1.86
hs 100.0
100.1
rfl 0
rfp 0
th 20
ins 1.000
nm
ph
ppm
1.98
2.93
2.05
0.99
2.03
2.96
1.98
2.02
5.03
2.88
10.76
2.93
3.68
S1R1
S2R2
S3R3
S4R4
S5R5
S6R6
S7R7
S1
R1
S2
R2
S3
R3
S4
R4
S5
R5
S6
R6
S7
R7
nhex
Hs
MeO
Ph
CF3
nhex
HR
MeO
Ph
CF3
nhex
Hs
MeO
Ph
CF3

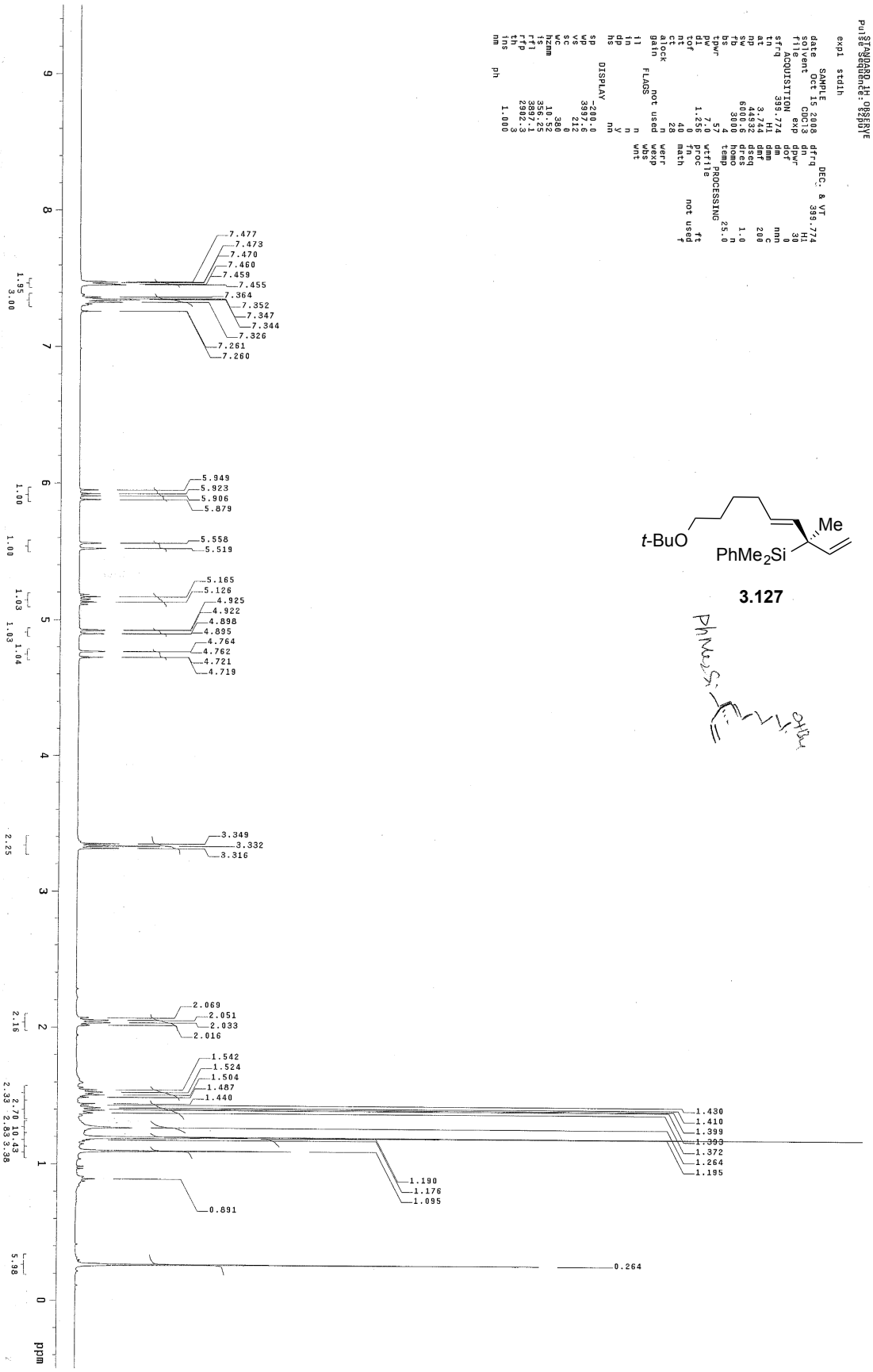

YL-V-116A
exp2 std1h
SAMPLE
date Nov 30 2007
solvent CDCl3
file
ACQUISITION
sfrq 399.772
tn H1
at 3.744
np 44932
sw 6000.6
fb 3000
bs 4
tpwr 59
pw 7.0
d1 1.000
tof 0
nt 100
ct 16
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -199.9
wp 3997.6
vs 151
sc 0
wc 250
hzmm 24.00
is 293.19
rfl 1001.1
rfp 0
th 20
ins 1.000
nm
ph
dfrq DEC. & VT
dn 399.772
dpwr H1
dof 30
dm 0
dmm nnn
dmf c
dseq 200
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn not used
math f
wexp
wbs
wnt
n-hex
Me
t-BuO
O
O
3.123
9
8
7
6
5
4
3
2
1
0
ppm
0.20
0.85
0.90
1.01
1.88
1.95
9.61
11.37
3.13

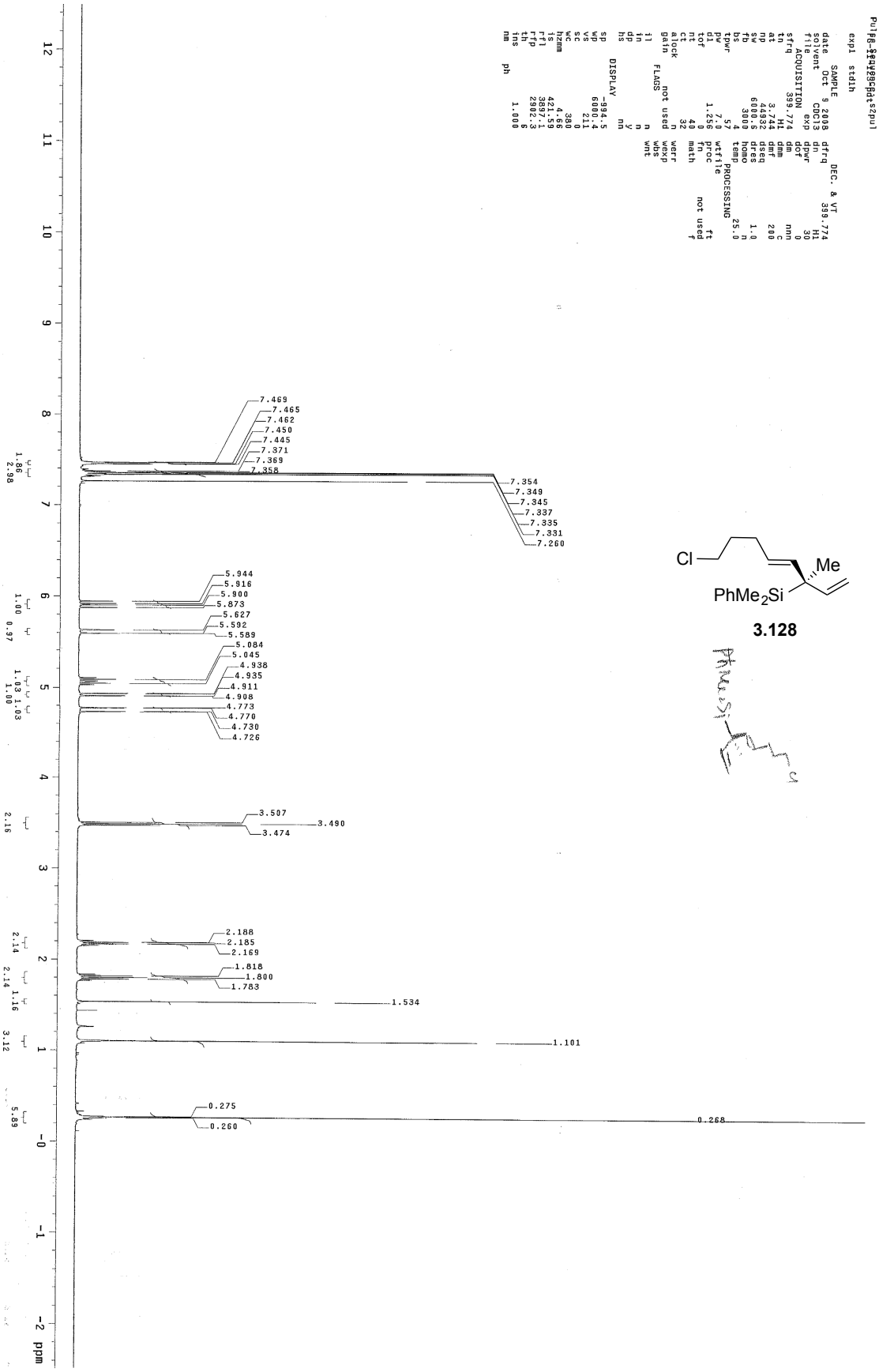

YL-V-207A
exp2 stdih
SAMPLE
date Feb 12 2008
solvent CDCl3
file ACQUISITION
sfrq 399.772
tn H1
at 3.744
np 44932
sw 6009.0
fb 3900
bs 4
tpwr 59
pw 7.0
dl 1.000
nt 40
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -198.9
wp 399.6
vs 201
sc 0
wc 380
hzmm 24.00
ftsize 163.98
rfl 1801.1
rfp 0
th 1
ins 1.000
nm ph
DEC. & VT
dfrq 399.772
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
ft
math not used
werr
wexp
wbs
wnt
Me
Me
Si
Me
n-hex
Me
PhMe2Si
3.122
YL-V-207A
Pulse Sequence: szpul
1.71
2.45
0.84
0.84
0.85
0.87
0.87
1.69
6.87
2.58
2.64
5.04
9
8
7
6
5
4
3
2
1
0
ppm


7.469
7.465
7.462
7.451
7.446
7.360
7.348
7.344
7.339
7.335
7.327
7.324
7.321
7.260
5.959
5.932
5.915
5.888
5.437
5.397
5.173
5.133
4.922
4.919
4.896
4.892
4.765
4.762
4.722
4.718
1.535
1.093
0.983
0.978
0.962
0.262
0.246
0.254
ppm

t-Bu
Me
PhMe2Si

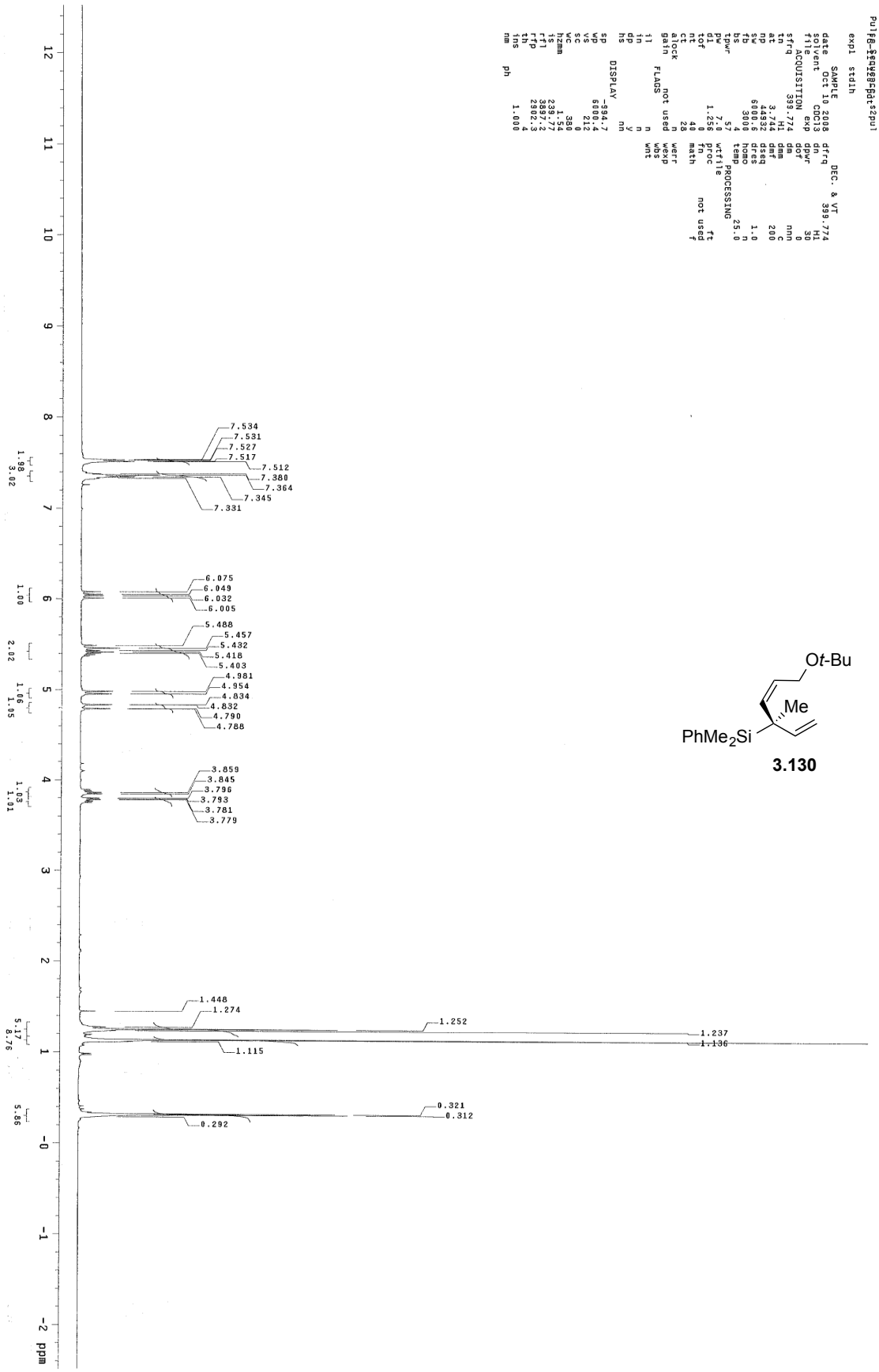
3.129


STANDARD 1H OBSERVE
Pulse Sequence: STANDARD 1H OBSERVE
SAMPLE
date Oct 15 2008
solvent CDCl3
file ACQUISITION
sfrq 399.774
tn H1
at 3.744
np 44932
sw 6000.6
fb 30864
bs 4
tpwr 57
pw 7.0
d1 1.256
do 0
nt 40
ct 28
alock n
gain n
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -280.0
wp 3997.6
vs 212
sc 0
wc 360
hzmm 10.52
vsadj 356.25
lb 3887.1
rfl 2392.3
rfp 0
th 1
ins 1.000
nm
ph
dfrq DEC. & VT
dn 399.774
dpwr H1
dof 30
dm nnn
dmf 0
dseq 200
dres 1.0
homo n
temp 25.0
PROCESSING
wtfile
proc ft
math not used
werr
wexp
wbs
wnt
7.477
7.473
7.470
7.460
7.459
7.455
7.364
7.352
7.347
7.344
7.326
7.261
7.260
5.949
5.923
5.906
5.879
5.558
5.519
5.165
5.126
4.925
4.922
4.898
4.895
4.764
4.762
4.721
4.719
3.349
3.332
3.316
2.069
2.051
2.033
2.016
1.542
1.524
1.504
1.487
1.440
1.430
1.410
1.399
1.393
1.372
1.264
1.195
1.190
1.176
1.095
0.891
0.264
1.95
3.00
1.00
1.00
1.03
1.03
1.04
2.25
2.16
2.33
2.70
10.43
2.83
3.38
5.98
ppm
t-BuO
Me
PhMe2Si
3.127


7.469
7.465
7.462
7.450
7.445
7.371
7.369
7.358
7.354
7.349
7.345
7.337
7.335
7.331
7.260
5.944
5.916
5.900
5.873
5.627
5.592
5.589
5.084
5.045
4.938
4.935
4.911
4.908
4.773
4.770
4.730
4.726
3.507
3.490
3.474
2.188
2.185
2.169
1.818
1.800
1.783
1.534
1.101
0.275
0.260
0.268
ppm

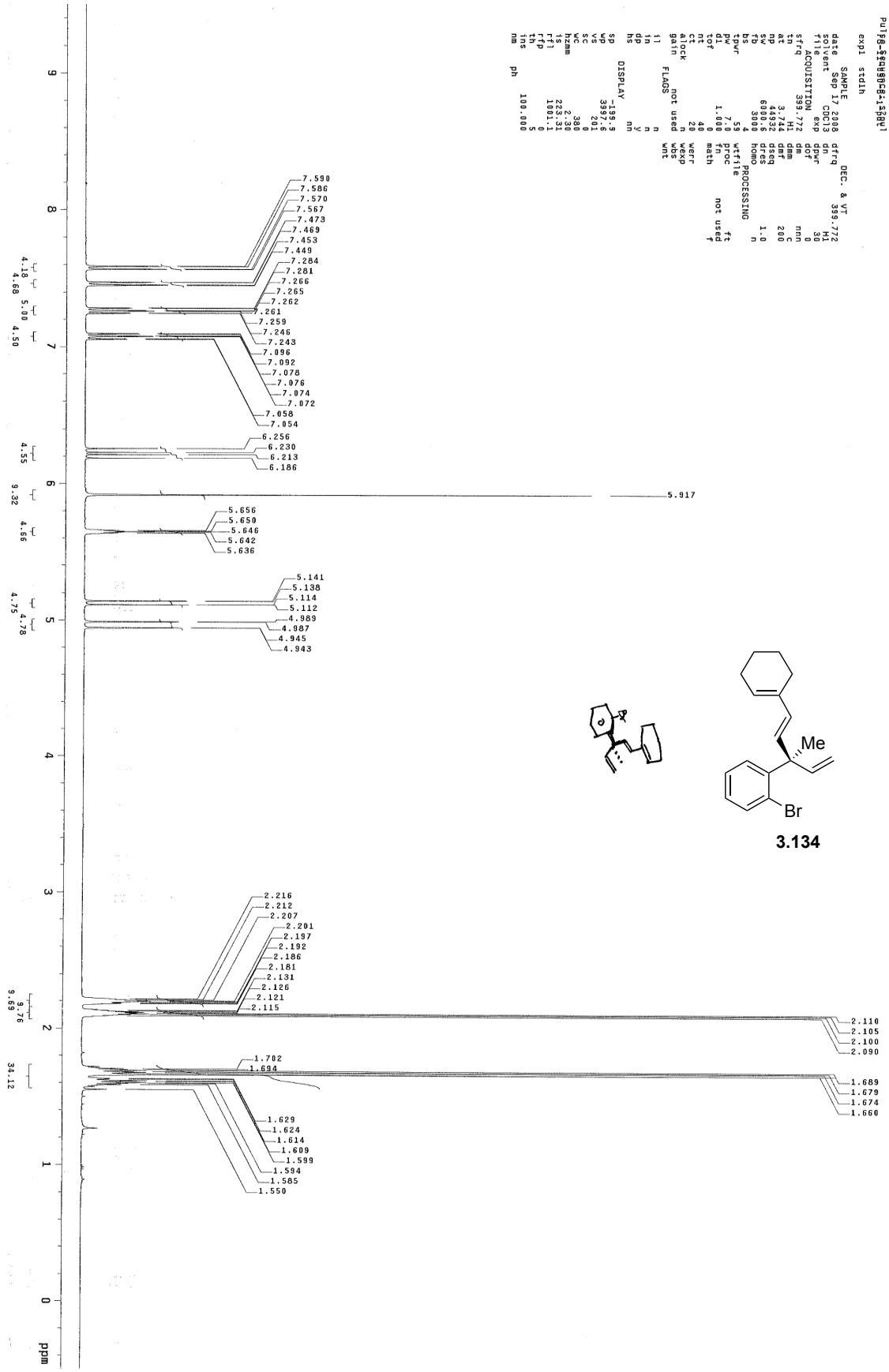
Cl
Me
PhMe2Si

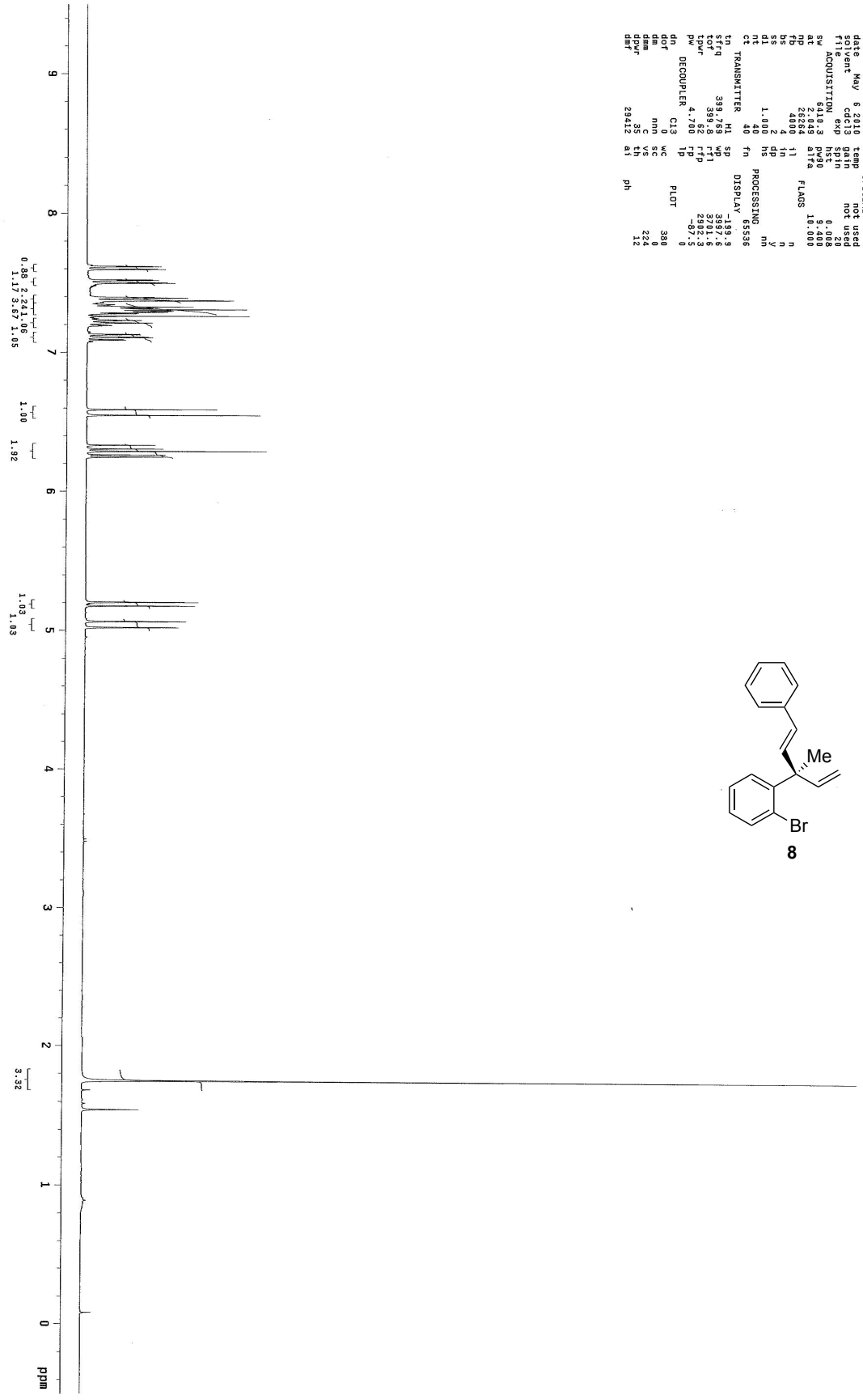
3.128

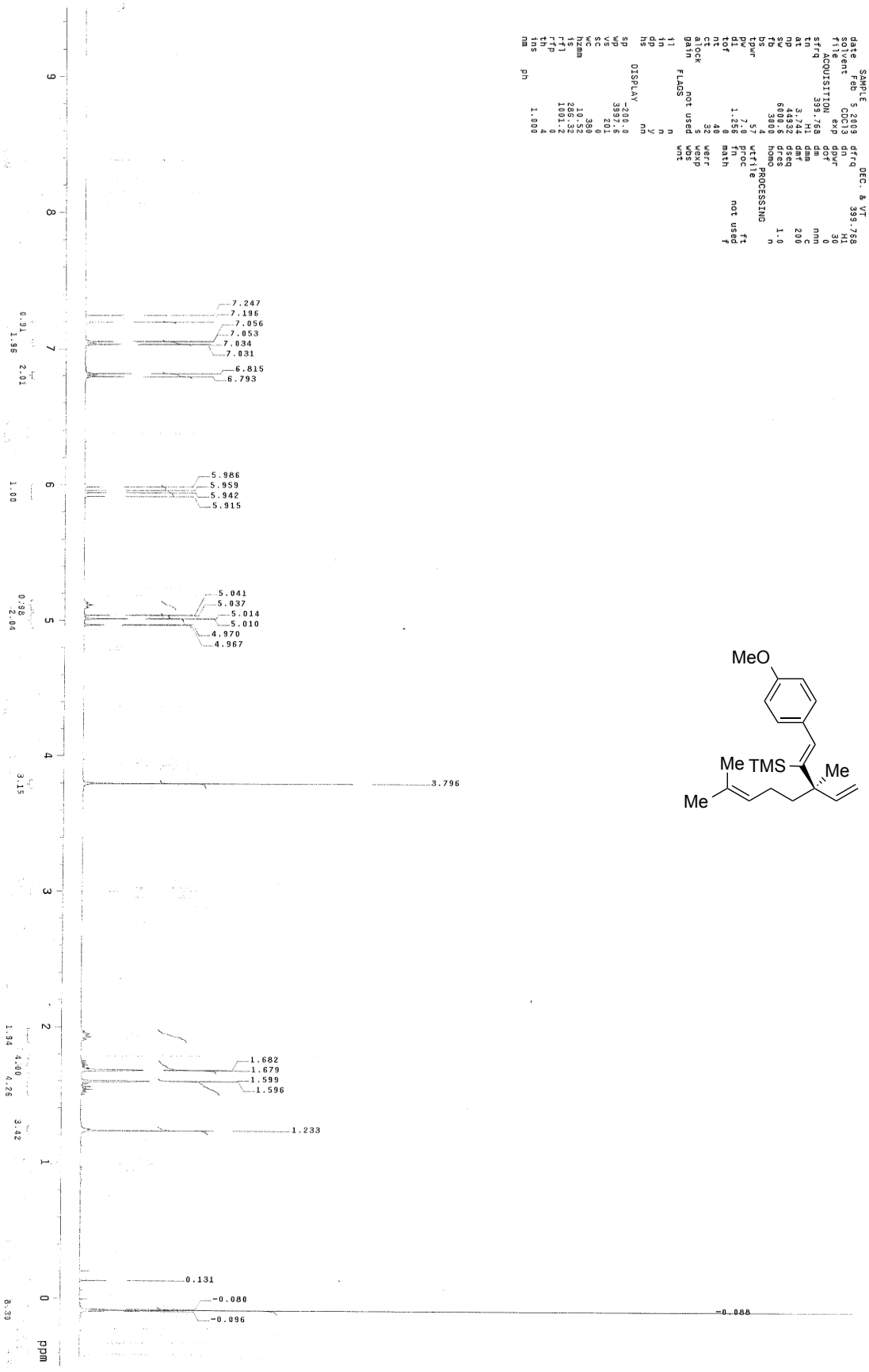

7.534
7.531
7.527
7.517
7.512
7.380
7.364
7.345
7.331
6.075
6.049
6.032
6.005
5.488
5.457
5.432
5.418
5.403
4.981
4.954
4.834
4.832
4.790
4.788
3.859
3.845
3.796
3.793
3.781
3.779
1.448
1.274
1.252
1.237
1.136
1.115
0.321
0.312
0.292
1.99
3.02
1.00
2.02
1.06
1.05
1.03
1.01
5.17
8.76
5.86
ppm

Ot-Bu
Me
PhMe2Si

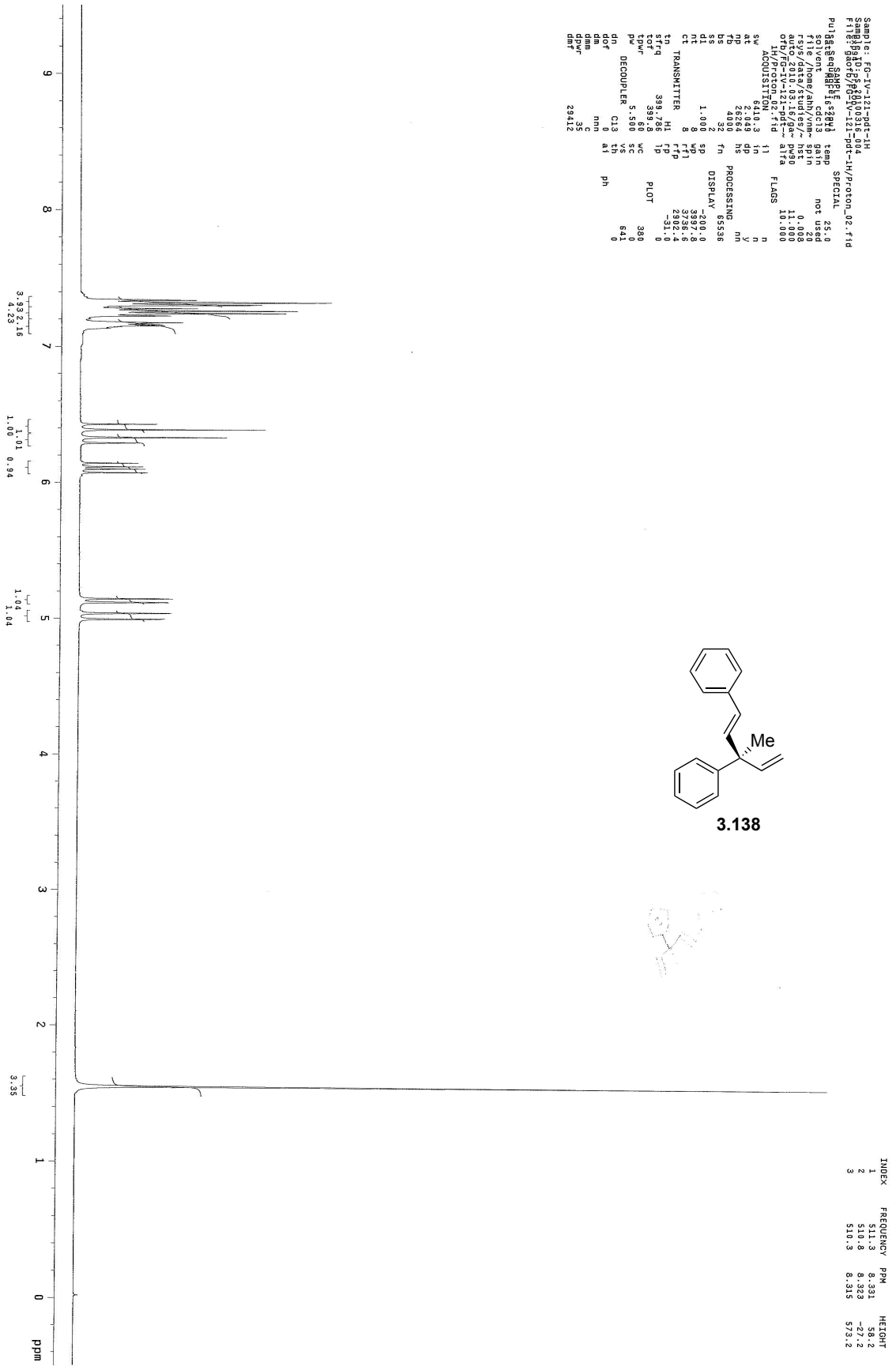
3.130


7.590
7.586
7.570
7.567
7.473
7.469
7.453
7.449
7.284
7.281
7.266
7.265
7.262
7.261
7.259
7.246
7.243
7.096
7.092
7.078
7.076
7.074
7.072
7.058
7.054
6.256
6.230
6.213
6.186
5.917
5.656
5.650
5.646
5.642
5.636
5.141
5.138
5.114
5.112
4.989
4.987
4.945
4.943
2.216
2.212
2.207
2.201
2.197
2.192
2.186
2.181
2.131
2.126
2.121
2.115
2.110
2.105
2.100
2.090
1.702
1.694
1.689
1.679
1.674
1.660
1.629
1.624
1.614
1.609
1.599
1.594
1.585
1.550
Me
Br
3.134
ppm


Sample: FG-IV-218-pdt
File: exp
Pulse Sequence: s2pul
Solvent: CDCl3
ACQUISITION
sw 6410.3
at 2.048
np 26264
fb 4000
bs 4
ss 2
d1 1.000
nt 40
ct 40
TRANSMITTER
tn H1
sfrq 399.789
tof 339.62
tpwr 52
pw 4.700
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
SAMPLE
date 6 2010
solvent MeOy
file exp
pw90 hst
alfa
FLAGS
il
in
dp
hs
PROCESSING
fn
DISPLAY
sp
wp
rfl
rfp
rp
lp
PLOT
wc
sc
vs
th
ai
ph
SPECIAL
temp
gain
spin
65536
-199.9
3997.6
3701.6
2982.3
-87.5
0
300
0
224
12
not used
not used
20
0.008
9.400
10.000
n
n
y
nn
Me
Br
8
ppm
0.88 2.24 1.06
1.17 3.67 1.05
1.00
1.92
1.03
1.03
3.32

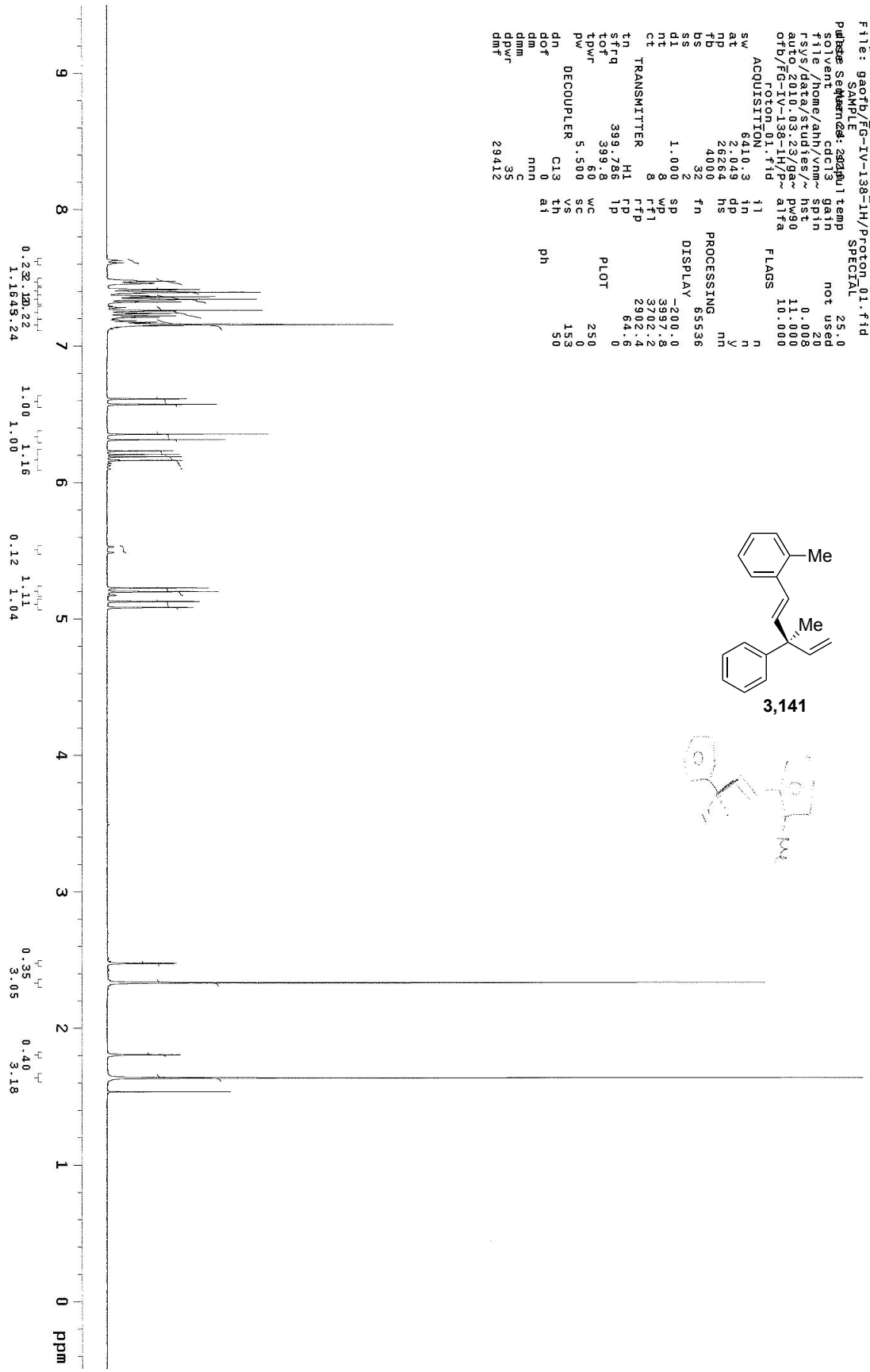

FG-IIFG-I-pt2-rdt-1H
exp1 stdin
SAMPLE
date Feb 5 2009
solvent CDCl3
file ACQUISITION
sfrq 399.768
tn H1
at 3.744
np 44932
sw 6000.6
fb 30014
bs 30
tpwr 57
pw 7.0
tof 1.256
nt 40
ct 32
alock n
gain n
FLAGS not used
fl n
fn n
dp y
hs nn
DISPLAY
sp 2010.0
wp 3991.3
vs 2101
sc 0
wc 380
hzmm 10.52
vs 2101.32
rfl 1001.0
rfp 4
th 4
ins 1.000
nm
ph
DEC. & VT
dfrq 399.768
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo PROCESSING
wtfile
proc ft
fn math
not used f
werr
wexp
wbs
wnt
7.247
7.196
7.056
7.053
7.034
7.031
6.815
6.793
5.986
5.959
5.942
5.915
5.041
5.037
5.014
5.010
4.970
4.967
3.796
1.682
1.679
1.599
1.596
1.233
0.131
-0.080
-0.096
-0.088
0.91
1.96
2.01
1.00
0.98
2.04
3.15
1.94
4.00
4.26
3.42
8.39
ppm

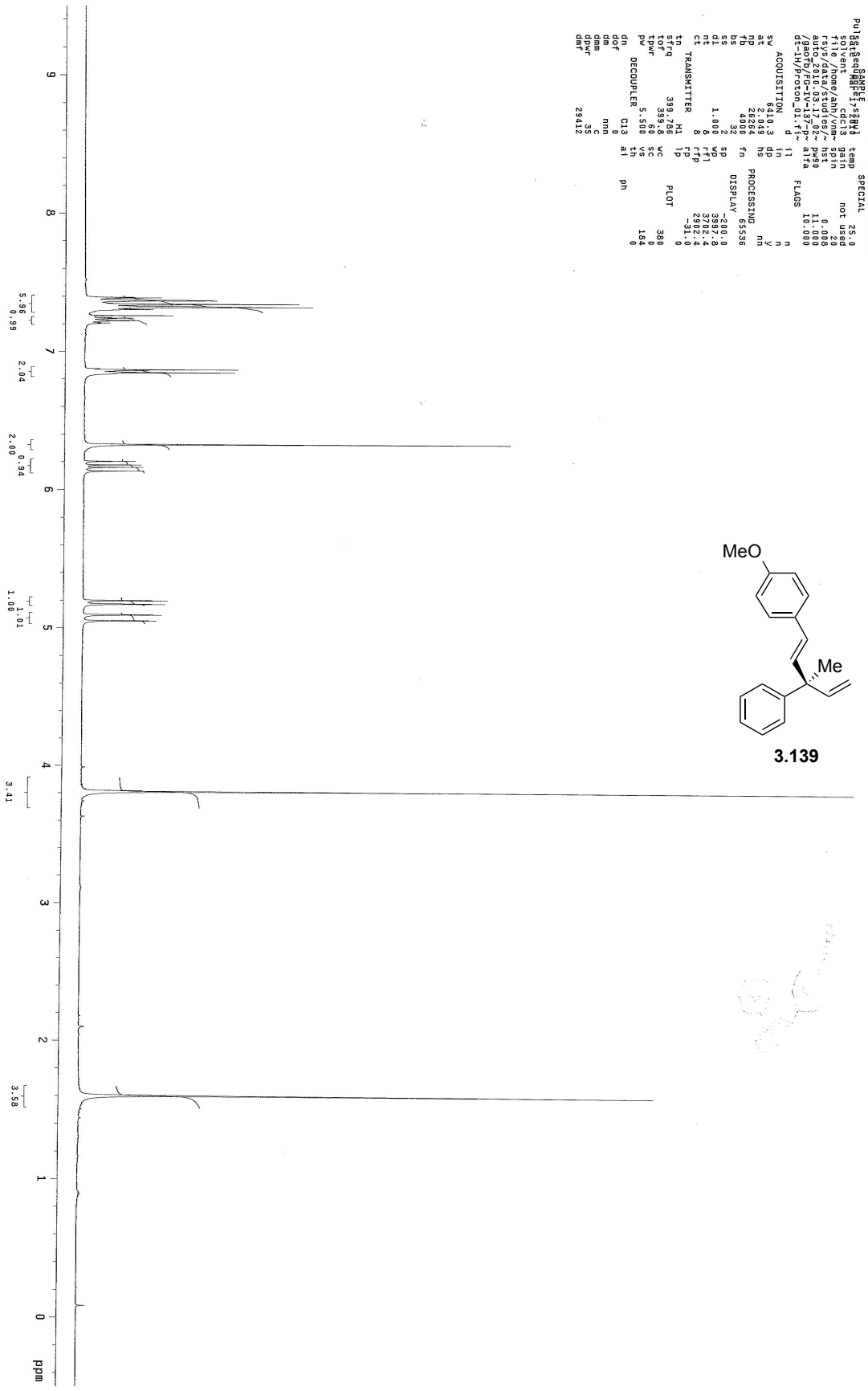
MeO
Me TMS
Me
Me

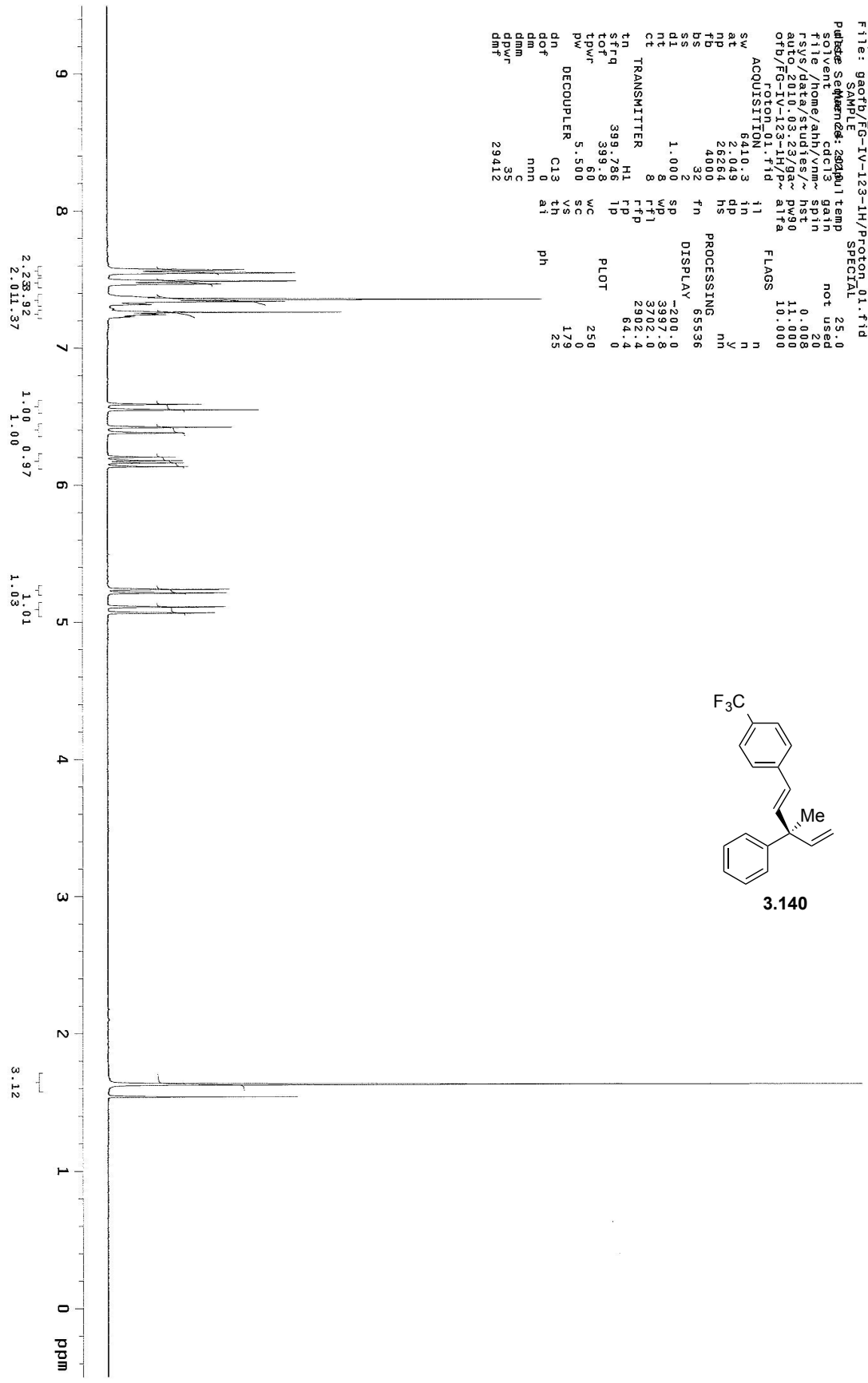



```
Sample: FG-IV-121-pdt-1H
Solvent: CDCl3
File: /home/ahh/vnmrsys/data/studies/~~~~~~~~~~/FG-IV-121-pdt-1H/proton_02.fid
Pulse Sequence: s2pul
solvent  cdcl3
file  /home/ahh/vnmrsys/data/studies/~~~~~~~~~~/FG-IV-121-pdt-1H/proton_02.fid
  1H/Proton_02.fid
ACQUISITION
  sw          6410.3
  at          2.049
  np          26284
  fb          4000
  bs          32
  ss          2
  d1          1.000
  ct          8
TRANSMITTER
  tn          H1
  sfrq        399.8
  tof         3593.6
  tpwr        60
  pw          5.500
DECOUPLER
  dn          C13
  dof         0
  dm          nnn
  dmm         c
  dpwr        35
  dmf         29412
  temp        25.0
  gain        not used
  spin        20
  hst         0.008
  pw90        11.000
  alfa        10.000
FLAGS
  il          n
  in          n
  dp          y
  hs          nn
PROCESSING
  fn          65536
DISPLAY
  sp          -200.0
  wp          3597.8
  rfl         3736.6
  rfp         2902.4
PLOT
  wc          380
  sc          0
  vs          641
  th          0
  al          ph
```

INDEX	FREQUENCY	PPM	HEIGHT
1	511.3	8.331	58.2
2	510.8	8.323	-27.2
3	510.3	8.315	573.2


Sample: FG-IV-138-1H
Sample ID: proton_01_00324_004
File: gaofb/FG-IV-138-1H/proton_01.fid
SPECIAL
25.0
not used
0.008
11.000
10.000
n
n
y
nn
65536
-200.0
3997.8
3702.2
2902.4
64.6
0
250
0
153
50
Me
Me
3,141
ppm


MeO
Me
3.139
ppm


Sample: FG-IV-123-1H
Sample ID: rsys/data/studies/~/2010_0324_002
File: gaofb/FG-IV-123-1H/Proton_01.fid
SAMPLE
Pulse Sequence: s2pul
solvent cdcl3
file /home/ahh/vnmr~
rsys/data/studies/~
auto_2010.03.23/ga~
ofb/FG-IV-123-1H/P~
proton_01.fid
ACQUISITION
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1.00
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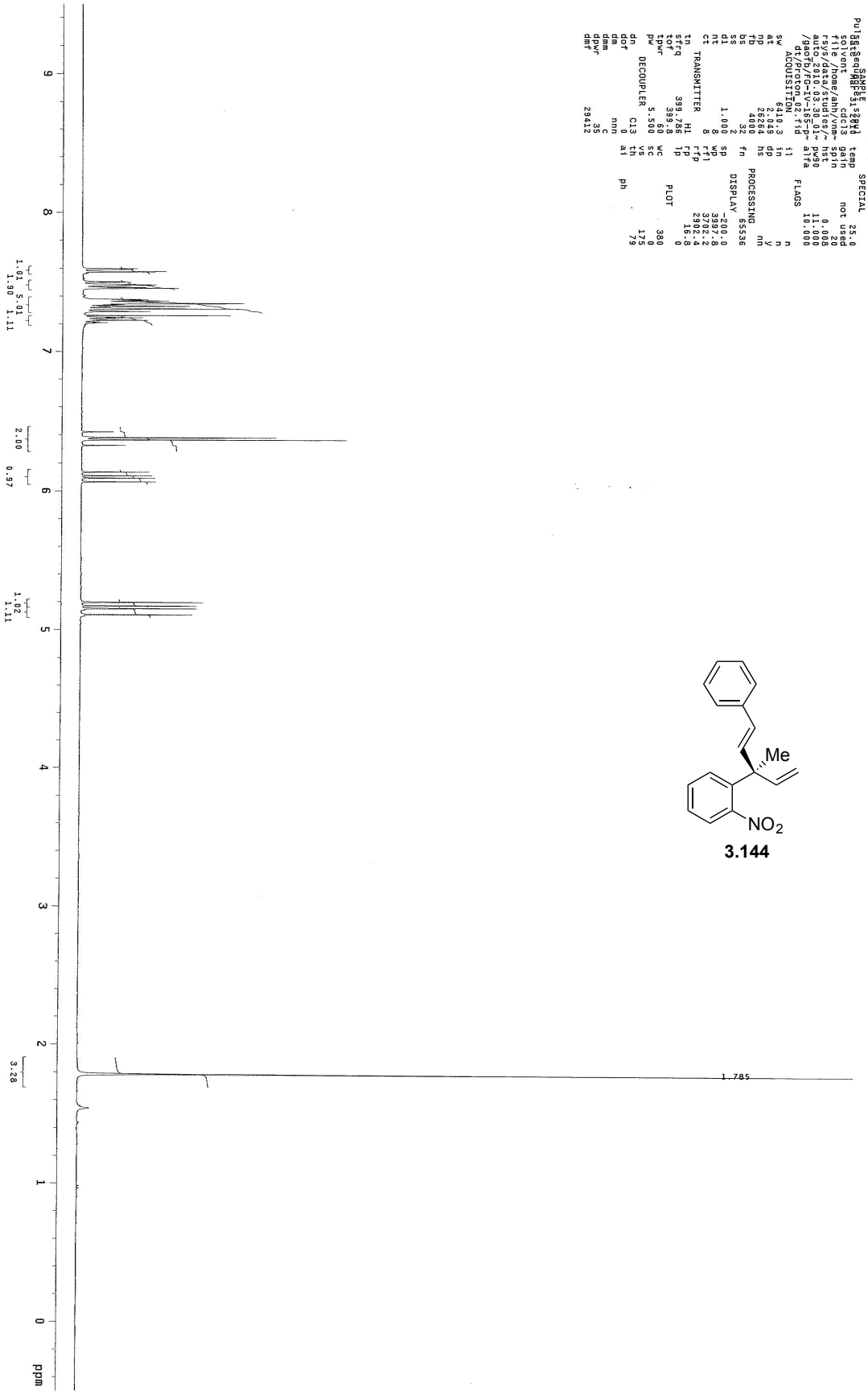
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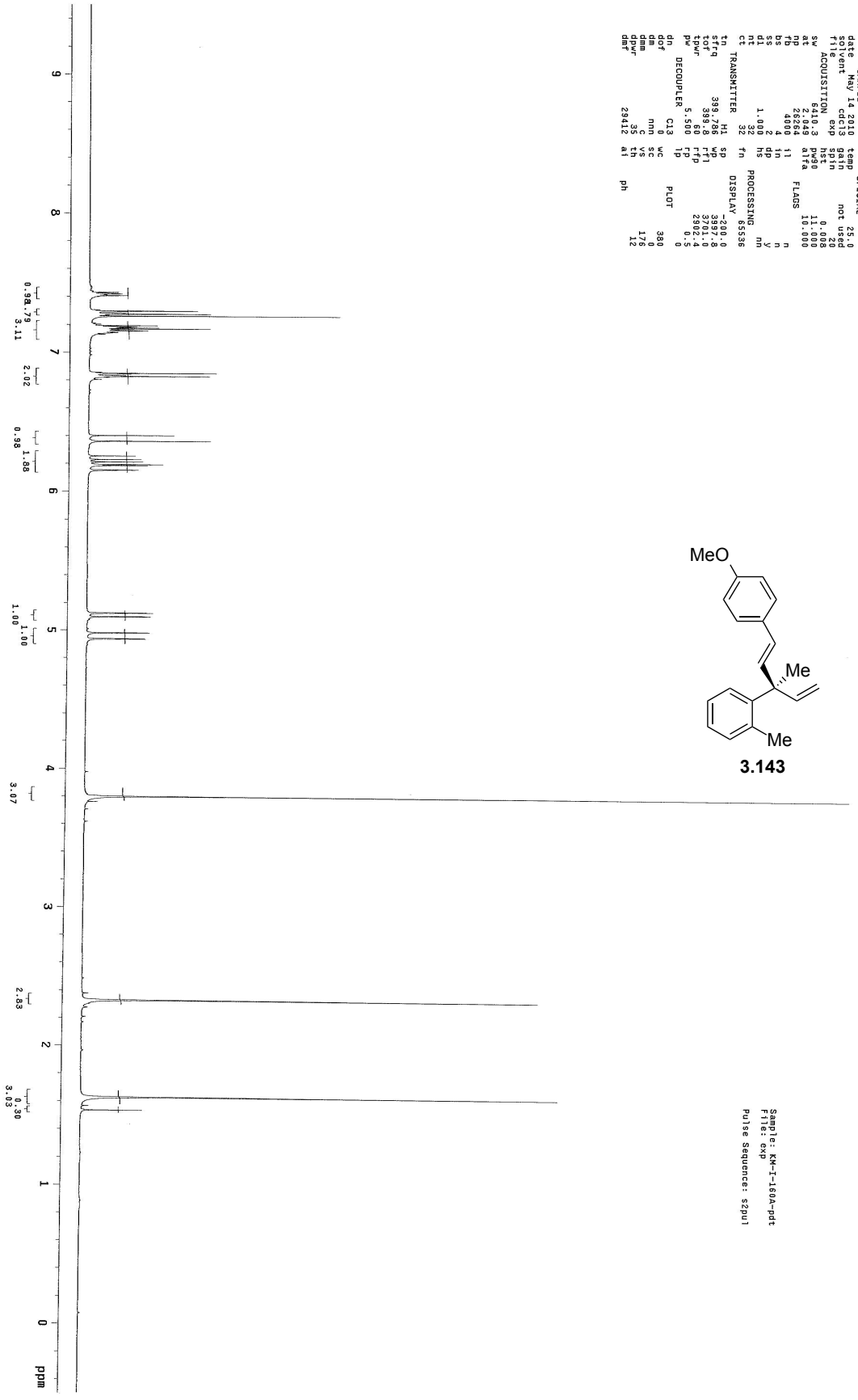
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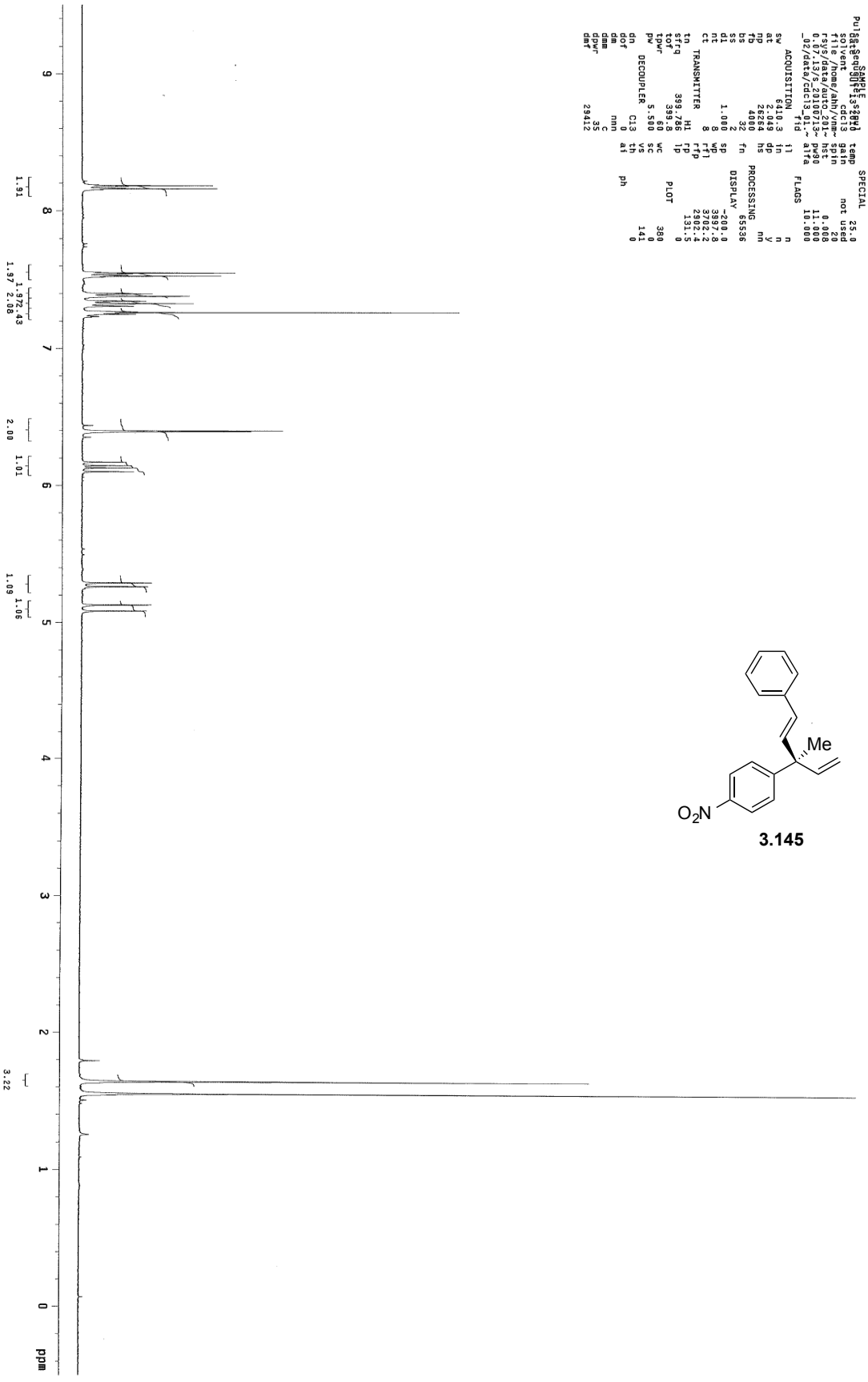
3.03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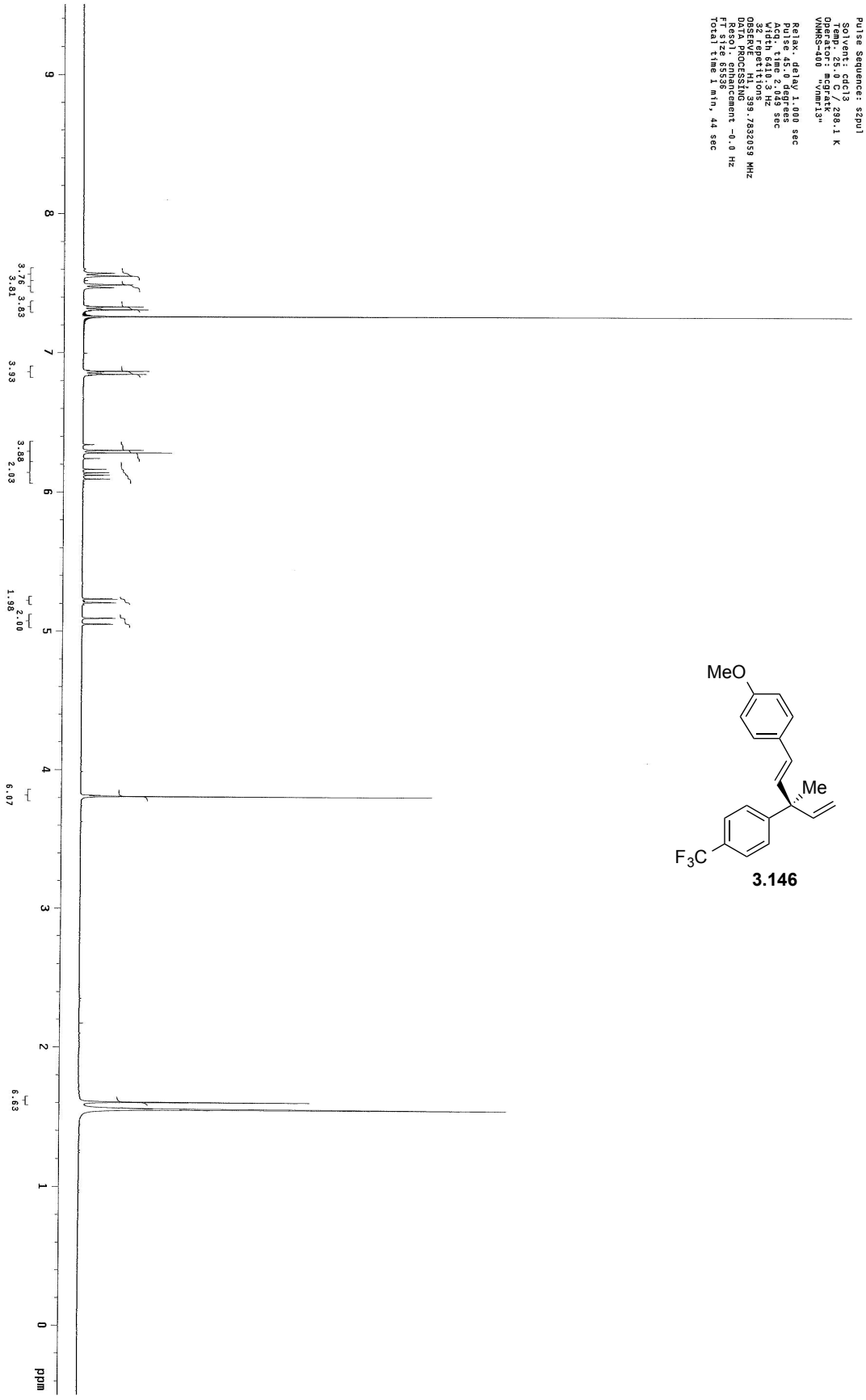
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Pulse 45.0 degrees
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32 repetitions
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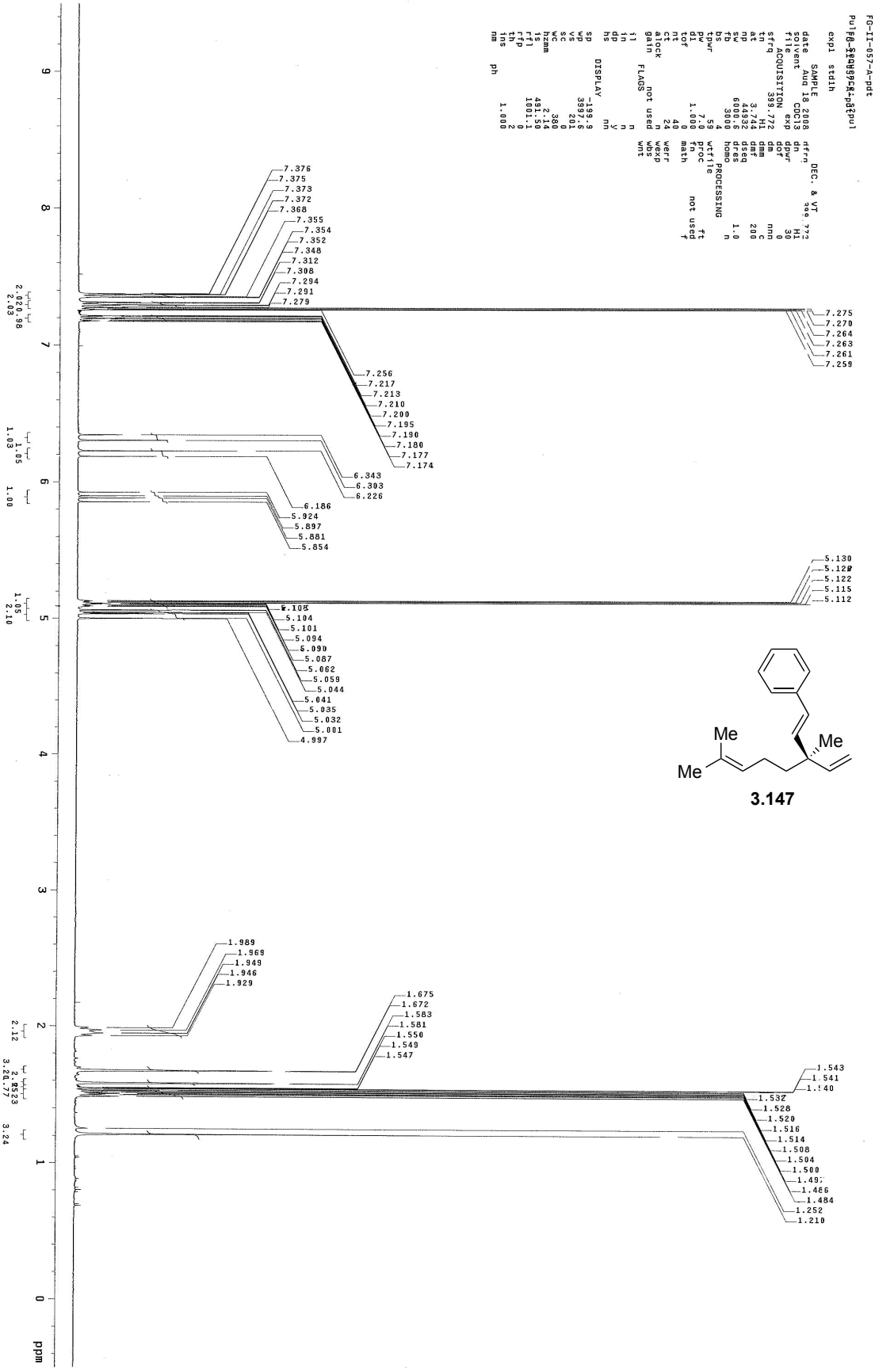
3.146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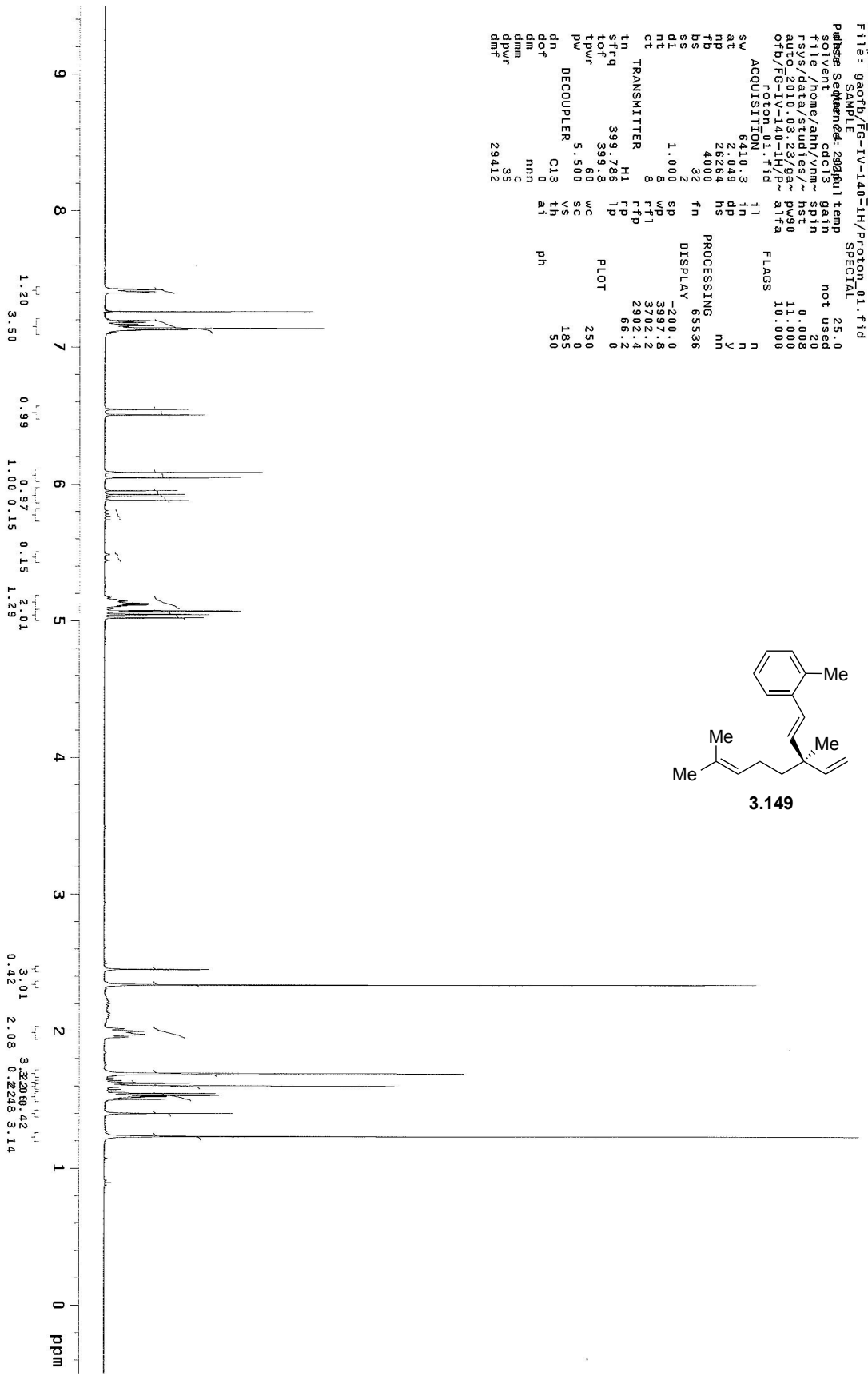
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tof 399.8
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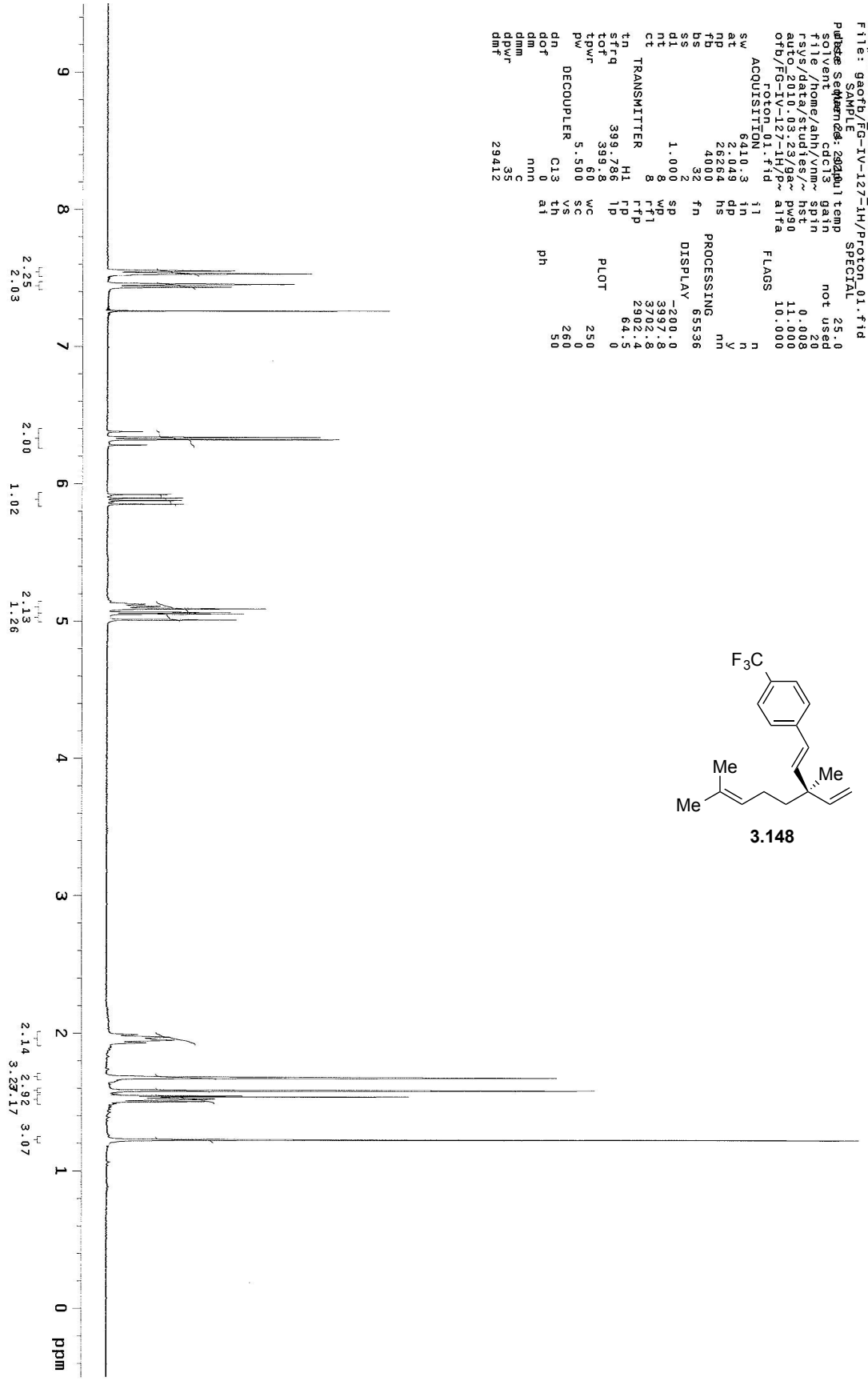
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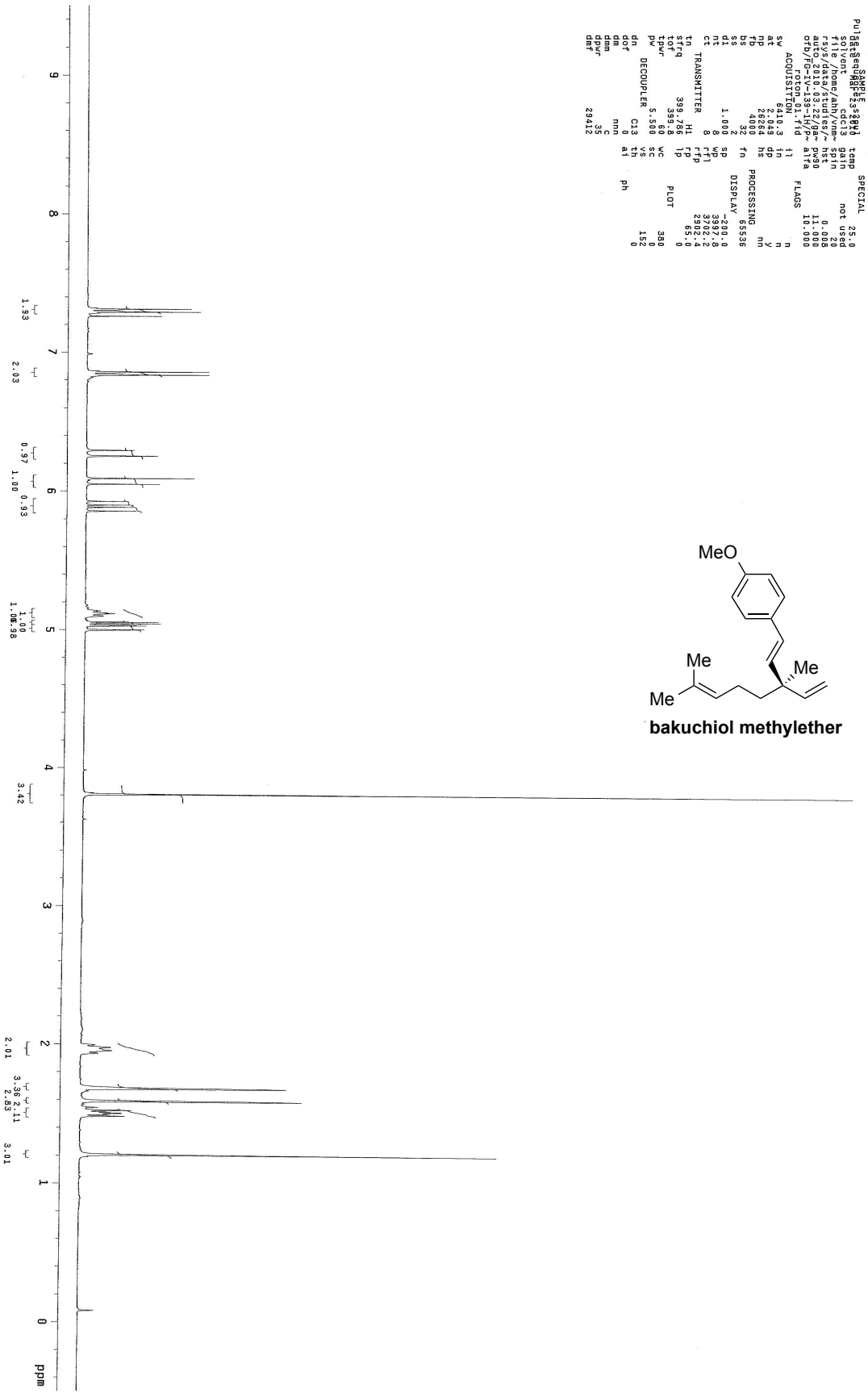
ppm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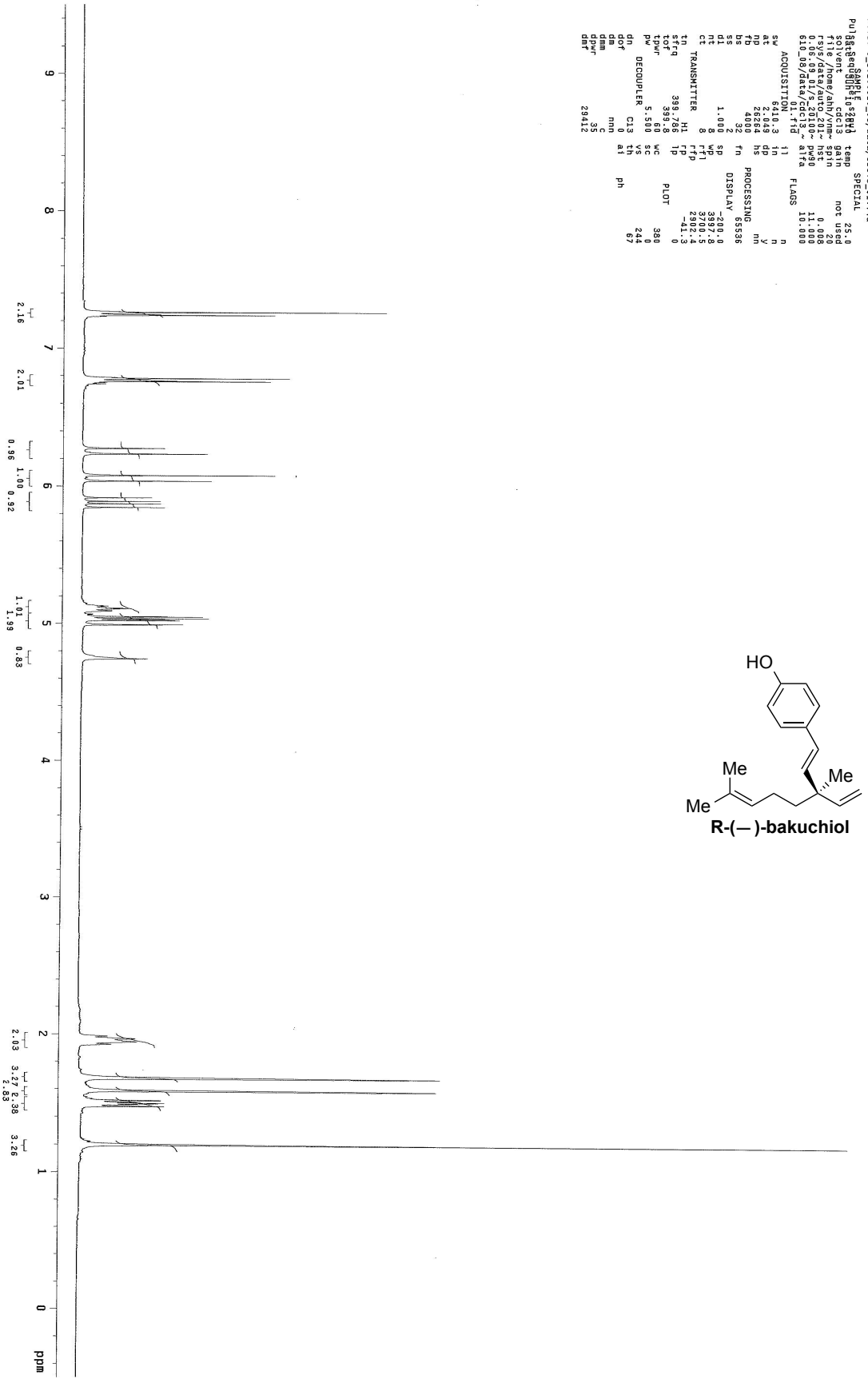
bakuchiol methylether
ppm


HO
Me
Me
Me
R-(—)-bakuchiol

Chapter 4

Cu-Catalyzed Enantioselective Allylic Substitutions with Alkenylboronic Acid Pinacol Ester Reagents and Applications in Natural Product Synthesis

4.1 Introduction

Enantioselective allylic substitution (EAS) reactions catalyzed by chiral copper complexes to deliver tertiary as well as difficult-to-access all-carbon quaternary stereogenic centers are known territories for "hard" organometallic reagents as the nucleophilic partners.[1] While the last decade has seen considerable developments in Cu-catalyzed EAS with organometallic reagents, there are still shortcomings that need to be addressed for achieving genuinely broad scope of these important transformations.[1] One major drawback derives from the sensitivity associated with common organometallic species; the fresh preparation is often required prior to the EAS reactions to ensure quality of the crucial nucleophile. The second limitation corresponds to the less functional group compatible processes in the synthesis of most organometallic reagents that are of great significance in Cu-catalyzed EAS reactions, resulting in the contrived

---

(1) For reviews on Cu-catalyzed allylic alkylation reactions that involve "hard" alkyl- or arylmetal-based reagents, see: (a) Hoveyda, A. H.; Hird, A. W.; Kacprzynski, M. A. *Chem. Commun.* **2004**, 1779–1785. (b) Yorimitsu, H.; Oshima, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 4435–4439. (c) Falciola, C. A.; Alexakis, A. *Eur. J. Org. Chem.* **2008**, 3765–3780. (d) Alexakis, A.; Bäckvall, J.-E.; Krause, N.; Pàmies, O.; Diéguez, M. *Chem. Rev.* **2008**, *108*, 2796–2823. (e) Harutyunyan, S. R.; den Hartog, T.; Geurts, K.; Minnaard, A. J.; Feringa, B. L. *Chem. Rev.* **2008**, *108*, 2824–2852. (f) Lu, Z.; Ma, S. *Angew. Chem., Int. Ed.* 2**008**, *47*, 258–297.

ability in the incorporation of useful functionalities on the nucleophilic partners.[2] One specific example is outlined in Scheme 4.1, in our attempt to dissect the targeted Pummerer's ketone,[3] we have found that a late stage ring closing metathesis (RCM)[4] of advanced intermediate **4.1** would secure the synthesis; the requisite enone can be accessed from an enoate bearing enantiomerically enriched compound **4.2**, which features the core structure of a typical Cu-catalyzed EAS of a trisubstituted allylic phosphate with a nucleophilic α,β-unsaturated ester equivalent. Despite the advances accomplished in EAS reactions with alkenylaluminum reagents developed in these laboratories, the availability of such ester containing alkenylalanes is problematic due to the reductive function of diisobutylaluminum hydride (dibal-H) used in hydroalumination of an alkyne.[5] To address this issue, a functional group more compatible surrogate that can carry the enoate unit is highly desirable.

---

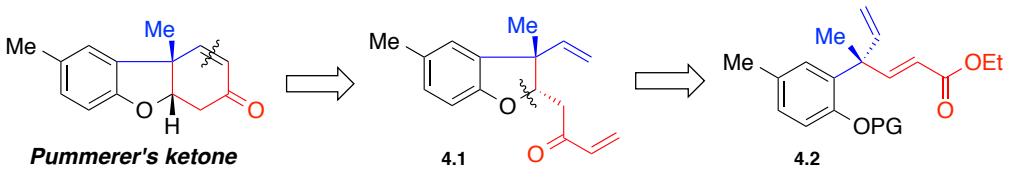
(2) For selected studies on organo Grignard and Zinc reagents that contain certain functional groups, see: (a) Piller, F. M.; Appukkuttan, P.; Gavryushin, A.; Mattew, H.; Knochel, P. *Angew. Chem., Int. Ed.* **2008**, *47*, 6802–6806. (b) Closoki, G. C.; Rohbogner, C. J.; Knochel, P. *Angew. Chem., Int. Ed.* **2007**, *46*, 7861–7864. (c) Metzger, A.; Schade, M. A.; Knochel, P. *Org. Lett.* **2008**, *10*, 1107–1110. (d) Wunderlich, S. H.; Knochel, P. *Org. Lett.* **2008**, *10*, 4705–4707.

(3) For a previous synthesis of racemic syn Pummerer's ketone, see: Vierfond, J.-M.; Reynet, A.; Moskowitz, H.; Thal, C. *Synth. Commun.* **1992**, *22*, 1783–1792. For other related references, see: (b) Pummerer, R.; Melamed, D.; Puttfarcken, H. *Ber. Dtsch. Chem. Ges.* **1922**, *55*, 3116–3132. (c) Opioid Analgesics Chemistry and Receptors (Eds.: Casy, A. F.; Parfitt, R. T.), Plenum, New York, 1986. (d) Winternitz, F.; Autia, N. J.; Tumlirova, M.; Lacharette, R. *Bull. Soc. Chim. Fr.* **1956**, 1817. (e) Barton, D. H. R.; Deflorin, A. M.; Edwards, O. E. *J. Chem. Soc.* **1956**, 530–534.

(4) For recent review articles on olefin metathesis, see: (a) Hoveyda, A. H.; Malcomson, S. J.; Meek, S. J.; Zhugralin, A. R. *Angew. Chem., Int. Ed.* **2010**, *49*, 34–44. (b) Hoveyda, A. H.; Zhugralin, A. R. *Nature*, **2007**, *450*, 243–251. (c) Schrock, R. R.; Hoveyda, A. H. *Angew. Chem., Int. Ed. Engl.* **2003**, *42*, 4592–4633.

(5) For a review on hydroaluminations of alkynes and alkenes, see: Eisch, J. J. In Comprehensive Organic Synthesis; Trost, B. M., Fleming, I., Schreiber, S. L., Eds.; Pergamon, Oxford, 1991; Vol. 8, pp 733–766.

Scheme 4.1. Retrosynthetic Analysis of Pummerer's Ketone.



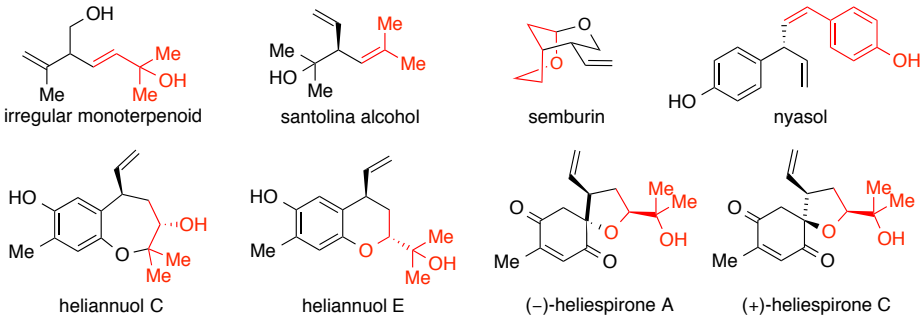
In this context, we have turned our attention to the much less reactive, but functional group tolerable organoboron reagents, especially the air and moisture stable and isolable alkenylboronic acid pinacol esters (alkenylBpin)[6] for the potential application in the synthesis of Pummerer's ketone. Another incentive that consolidates our pursuit along this line comes from the recent achievements in the effective synthesis of alkenylBpin entities; for examples, Cu-catalyzed site selective protoboration of terminal acetylenes[7] or allenes,[8] Rh-, or Ru-catalyzed *trans* hydroboration of alkynes,[9] Mo-catalyzed *Z* selective cross metathesis of an olefin and commercially available vinylBpin[10] and other related protocols,[11] in combination, have provided access to virtually all imaginable alkenylboron reagents with high efficiency and selectivity levels. However promising it looks, challenges with the utilization of organoboron species in Cu-catalyzed EAS still lie ahead. Unlike alkenylmetal reagents, which are nucleophilic

---

(6) Hall, D. G. In Boronic Acids: Preparation and Applications in Organic Synthesis and Medicine; Wiley-VCH: Weinheim, 2005.
(7) (a) Kim, H. R.; Jung, I. G.; Yoo, K.; Jang, K.; Lee, E. S.; Yun, J.; Son, S. U. *Chem. Commun.* **2010**, *46*, 758–760. (b) Semba, K.; Fujihara, T.; Terao, J.; Tsuji, Y. *Chem. Eur. J.* **2012**, *18*, 4179–4184. (c) Moure, A. L.; Array_as, R. G.; G_ardenas, D. J.; Alonso, I.; Carretero, J. C. *J. Am. Chem. Soc.* **2012**, *134*, 7219–7222. (d) Park, J. K.; Ondrusek, B. A.; McQuade, D. T. *Org. Lett.* **2012**, *14*, 4790–4793. (e) Jang, H.; Zhugralin, A. R.; Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 7859–7871.
(8) (a) Meng, F.; Jung, B.; Haeffner, F.; Hoveyda, A. H. *Org. Lett.* **2013**, *15*, 1414–1417. (b) Yuan, W.; Ma, S. *Adv. Synth. Catal.* **2012**, *354*, 1867–1872.
(9) Ohmura, T.; Yamamoto, Y.; Miyaura, N. *J. Am. Chem. Soc.* **2000**, *122*, 4990–4991. Gunanathan, C.; Hölscher, M.; Pan, F.; Leitner, W. *J. Am. Chem. Soc.* **2012**, *134*, 14349–14352.
(10) Kiesewetter, E. T.; O'Brien, R. V.; Yu, E. C.; Meek, S. J.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2013**, *135*, 6026–6029.
(11) (a) Roush, W. R.; Ando, K.; Powers, D. B.; Palkowitz, A. D.; Halterman, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 6339–6348. (b) Ramachandran, P. V.; Pratihar, D.; Biswas, D. *Chem. Commun.* **2005**, 1988–1989. (c) Molander, G. A.; Ellis, N. M. *J. Org. Chem.* **2008**, *73*, 6841–6844.

enough to transfer ligands to catalytically active NHC–Cu complexes, alkenylBpins are significantly less reactive and unlikely to do ligand transfer without help from external promoters; the identification of such species is crucial to the success of developing an efficient C-C bond forming reactions employing organoboron reagents.[12] Additionally, whether the existing chiral *N*-heterocyclic carbenes are effective in inducing stereogenicity in Cu-catalyzed EAS reactions with alkenylBpins remains unknown, especially since the reaction media lack highly Lewis acidic cationic metal entities that are essential in the previous EAS involving alkenylaluminum reagents.[13] Nonetheless, the development of such methods will have great impacts in expanding the scope of the current Cu-catalyzed EAS reactions with organometallic species by introducing further functionalizable handles that are not compatible with the existing protocols, benefiting the potential synthesis of a variety of natural products with the representatives shown in Scheme 4.2.

Scheme 4.2. Representative Natural Products that Bear Functionalized Olefins.



(12) For recent reviews of cross coupling reactions involving organoboron reagents to make C-C bonds, see: (a) ref. 6. (b) Suzuki, A. *J. Organomet. Chem.* **2002**, *653*, 83–90. (c) Negishi, E.-i.; Huang, Z.; Wang, G.; Mohan, S.; Wang, C.; Hattori, H. *Acc. Chem. Res.* **2008**, *41*, 1474–1485. (d) Tobisu, M.; Chatani, N. *Angew. Chem., Int. Ed.* **2009**, *48*, 3565–3568.

(13) (a) Lee, Y.; Akiyama, K.; Gillingham, D. G.; Brown, M. K.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2008**, *130*, 446–447. (b) Gao, F.; McGrath, K. P.; Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 14315−14320. (c) Akiyama, K.; Gao, F.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2010**, *49*, 419–423.

4.2 Background

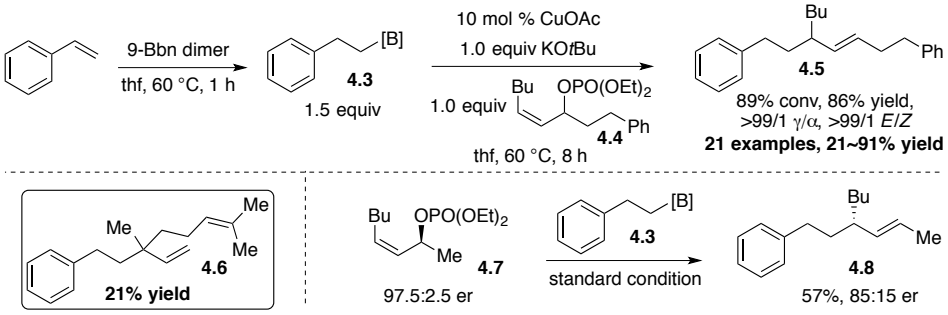
4.2.1 Cu-catalyzed Allylic Substitution with Trialkylboranes

In 2010, Sawamura and co-workers reported Cu-catalyzed allylic substitution reactions of alkylborane reagents to a number of *cis* disubstituted allylic phosphates.[14] As shown in Scheme 4.3, subjection of alkylborane **4.3**, derived from hydroboration of styrene with 9-Bbn, to the reaction with allylic phosphate **4.4** in the presence of 10 mol % of CuOAc results in the formation of alkene **4.5** in 86% yield as a single olefin isomer (>99:1 γ/α, >99:1 *E*/*Z*). One noteworthy aspect of this study is that stoichiometric amount of *t*BuOK is utilized presumably acting as an activating agent to promote alkyl group transfer from borane to copper. The synthesis of a variety of products has been shown viable through this method; several limitations, however, remain to be addressed. For example, a quaternary stereogenic center containing diene **4.6** was only obtained in 21% yield under standard condition. Furthermore, transfer of stereogenicity from an enantioenriched allylic phosphate is incomplete; for example, synthesis of alkene **4.8** from allylic phosphate **4.7** resulted in limited success due to the significant loss of enantiomer ratio during the Cu-catalyzed allylic substitution process (from 97.5:2.5 e.r. to 85:15 e.r.).

---

(14) Ohmiya, H.; Yokobori, U.; Makida, Y.; Sawamura, M. *J. Am. Chem. Soc.* **2010**, *132*, 2895−2897.

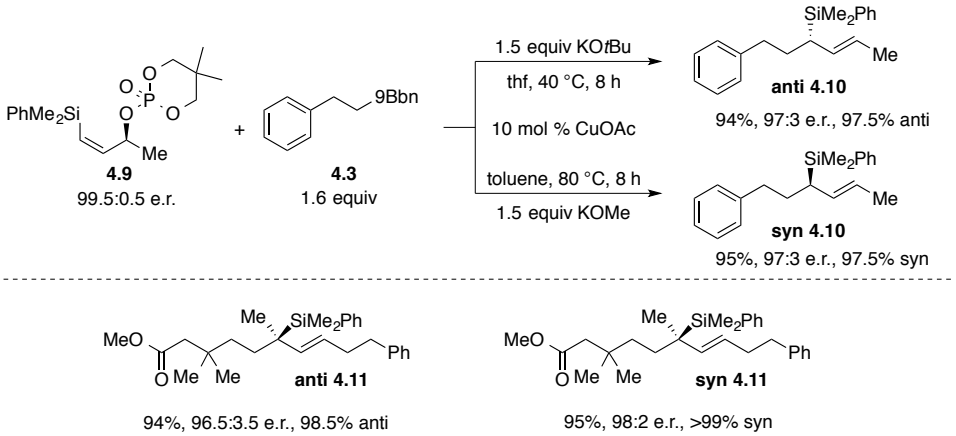
Scheme 4.3. Cu–catalyzed Addition of Alkylborane Reagents to Allylic Phosphates



Although the diastereoselective Cu-catalyzed allylic substitution with alkylborane reagents is less effective (cf. Scheme 4.3), Sawamura and co-workers have developed a selective protocol to access enantiomerically enriched allylsilanes through similar catalytic processes in 2012.[15] As illustrated in Scheme 4.4, exposure of enantiopure silyl-substituted allylic phosphate **4.9** to the same trialkylborane **4.3** in the presence of catalytic amount of CuOAc delivers both enantiomers of the resulting allylsilane **4.10** in high levels of the transfer of stereogenicity (97:3 e.r. in both cases); retention of stereochemical information is achieved when KOMe serves as the promoter and toluene as the solvent, whereas inversion of the stereogenic center is observed while employing KO*t*Bu in tetrahydrofuran (thf). Moreover, such transformations are not limited to the construction of tertiary silyl-substituted stereocenters; as further showcased in Scheme 4.4, quaternary center containing enantiomerically enriched allylsilanes **4.11** can be furnished under the same conditions with respectable levels of efficiency and selectivity (94% yield and 96.5:3.5 e.r. for the formation of **anti 4.11** and 95% yield and 98:2 e.r. for **syn 4.11**).

(15) Nagao, K.; Yokobori, U.; Makida, Y.; Ohmiya, H.; Sawamura, M. *J. Am. Chem. Soc.* **2012**, *134*, 8982−8987.

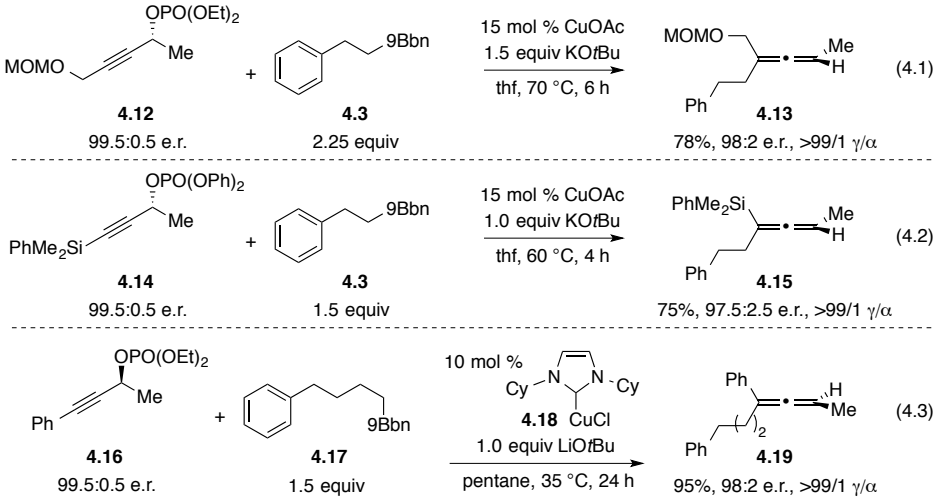
Scheme 4.4. Cu–catalyzed Addition of Alkylborane Reagents to Silyl-Substituted Allylic Phosphates



Enantiomerically enriched trisubstituted allenes can be accessed through Cu-catalyzed diastereoselective allylic substitution reactions of propargyl phosphates. In 2011, Sawamura group disclosed a protocol that converts propargyl phosphates (represented by **4.12**) to trisubstituted allenes with little erosion in stereogenicity transfer;[16] as shown in Eq 4.1 of Scheme 4.5, with 15 mol % of CuOAc, DAS reactions proceed to completion in six hours at 70 ^{o}C, delivering trisubstituted allene **4.13** in 78% yield and 98:2 enantiomer ratio. Later, the same group has adapted the above procedure to the synthesis of optically active silyl-substituted allenes (cf. **4.15** in Eq 4.2 of Scheme 4.5).[17] Lalic and co-workers have described similar reactions catalyzed by an isolated NHC–Cu complex under slightly different conditions. As demonstrated in Eq 4.3, 10 mol % of biscyclohexyl substituted unsaturated *N*-heterocyclic carbene bearing Cu complex **4.18** is sufficient to catalyze allylic substitution reactions of propargyl phosphate **4.16** with alkylborane reagent **4.17** derived from hydroboration of the corresponding terminal olefin with 9-Bbn. Desired allene **4.19** is obtained in 95% yield and 98:2 e.r.

(16) Ohmiya, H.; Yokobori, U.; Makida, Y.; Sawamura, M. *Org. Lett.* **2011**, *13*, 6312−6315.
(17) Yokobori, U.; Ohmiya, H.; Sawamura, M. *Organometallics* **2012**, *31*, 7909−7913.

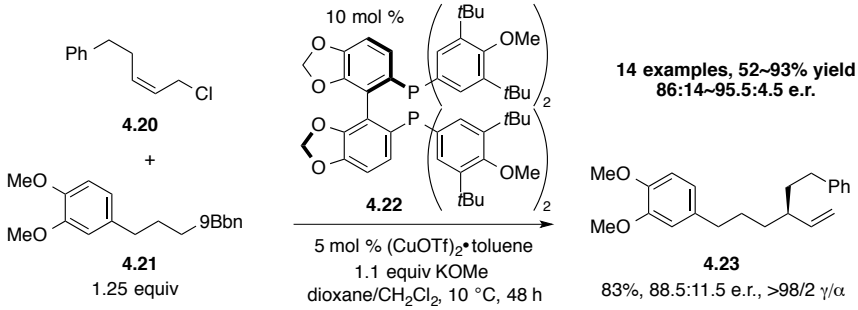
Scheme 4.5. Cu–catalyzed Addition of Alkylborane Reagents to Propargyl Phosphates



The first examples of enantioselective allylic substitution involving trialkylboranes were published by Sawamura and co-workers in 2012.[18] As shown in Scheme 4.6, unlike the previous non-enantioselective reactions, which utilize allylic phosphates as effective substrates, the enantioselective variants require the use of allylchlorides as the electrophilic coupling partners. As such, EAS reactions in the presence of 10 mol % of an in situ generated bisphosphine Cu complex derived from chiral ligand **4.22** proceed to complete conversion after 48 h at 10 ^{o}C, affording alkene **4.23** in 83% yield and 88.5:11.5 e.r. as a single regioisomer (>98:2 γ/α). A number of examples, including enantiomerically enriched allylsilanes, are reported in mostly moderate yields and enantioselectivities (only four cases with >95:5 e.r.).

(18) Shido, Y.; Yoshida, M.; Tanabe, M.; Ohmiya, H.; Sawamura, M. *J. Am. Chem. Soc.* **2012**, *134*, 18573−18576.

Scheme 4.6. Enantioselective Cu–catalyzed Addition of Alkylborane Reagents to Allylic Chlorides



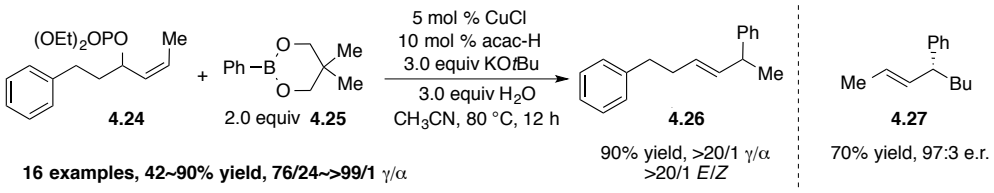
4.2.2 Cu-catalyzed Allylic Substitution with Organoboronic Acid Neopentylglycol Esters

While alkyl-9Bbn reagents are prominent in delivering desired alkyl groups, aromatic group substituted dialkylboranes are less readily available. In order to achieve additions of an aromatic unit in Cu-catalyzed allylic substitution reactions, Sawamura group has introduced the use of commercially available or easily accessible arylboronic acid neopentylglycol esters in their racemic synthesis of tertiary arylsubstituted stereocenter containing internal olefins.[19] As illustrated in Scheme 4.7, the combination of 5 mol % CuCl and 10 mol % acetylacetone under basic conditions serves as the active catalyst in allylic substitutions of *Z*-allylic phosphate **4.24**. Such transformations occur in the presence of 2.0 equivalent of boron reagent **4.25**, again activated by stoichiometric amount of KO*t*Bu, furnishing exclusive *E* alkene **4.26** in 90% yield and complete regioselectivity (>20:1 γ/α). The water additive is crucial, reactions without which only afford complex mixture. Although the role of such an additive is not explicitly discussed in the paper, it is plausible that it helps to hydrolyze the neopentylglycol ester to boronic acid, which is the actual reagent that can be utilized by the employed copper catalyst.

(19) Ohmiya, H.; Yokokawa, N.; Sawamura, M. *Org. Lett.* **2010**, *12*, 2438−2440.

Control experiments have shown that allylic phosphates undergo substitution reactions in the presence of the corresponding phenylboronic acid, albeit in lower yield (62%). The optimal conditions may benefit from a controlled release of the sensitive but active boronic acid rendered possible by the basic aqueous media. Two examples of efficient transfers of stereogenicity are described as well with highly enantioenriched compound **4.27** as a representative (Scheme 4.7).

Scheme 4.7. Cu–catalyzed Allylic Subsitution with Arylboronic Acid Neopentylglycol Esters

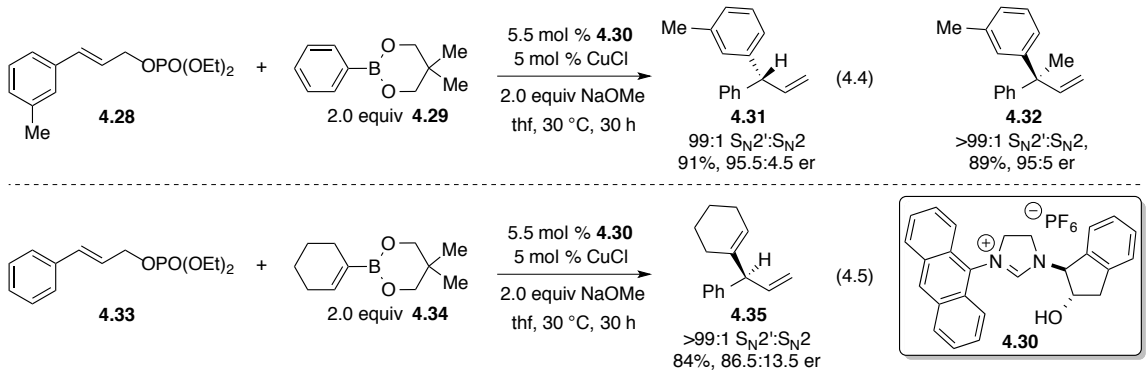


In 2011, Hayashi and co-workers disclosed the first examples of NHC–Cu-catalyzed enantioselective allylic substitution reactions of arylboronic acid neopentyl glycol esters to a number of allylic phosphates.[20] As shown in Eq 4.4, Scheme 4.8, subjection of boron reagent **4.29** to the reaction with substrate **4.28** in the presence of 5 mol % of an in situ generated NHC–Cu complex, derived from an alkoxide containing bidentate imidazolinium salt **4.30**, results in the formation of bisaryl-substituted tertiary stereocenter containing molecule **4.31** in 91% yield and 95.5:4.5 enantiomer ratio. Such transformations are also applicable in the formation of all carbon quaternary stereogenic center bearing compounds; for instance, alkene **4.32** can be synthesized in 89% yield and 95:5 e.r. as a single regioisomer. Among many cases centered around aryl additions, one example of the formation of a cyclohexenyl substituted tertiary stereogenic center

(20) Shintani, R.; Takatsu, K.; Takeda, M.; Hayashi, T. *Angew. Chem. Int. Ed.* **2011**, *50*, 8656–8659.

containing compound has been delineated; the EAS reaction furnishes 1,4-diene adduct **4.35** in 84% yield and moderate enantioselectivity (86.5:13.5 e.r.).

Scheme 4.8. Enantioselective Cu–catalyzed Allylic Subsitution with Arylboronic Acid Neopentylglycol Esters

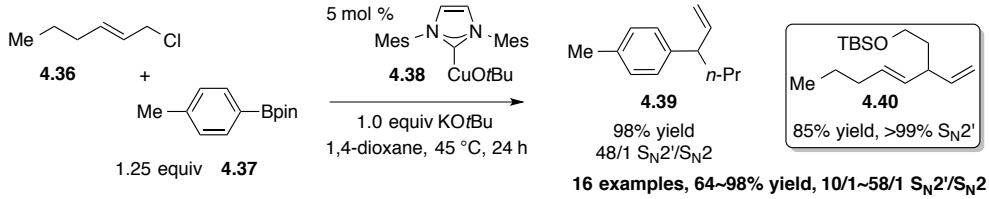


4.2.3 Cu-catalyzed Allylic Substitution with Organoboronic Acid Pinacol Esters

Lalic group published the first set of studies exploring the possibility of using NHC–Cu-alkoxide catalysts for allylic substitutions of allylic chlorides with sterically more hindered, but more air-stable arylboronic acid pinacol esters (vs. neopentylglycol esters).[21] As demonstrated in Scheme 4.9, in the presence of 5 mol % of the isolable carbene copper *tert*butoxide **4.38**, the substitution reaction of allylchloride **4.36** with commercially available *p*-tolBpin **4.37** proceeds to completion at 45 °C after 24 h, affording racemic **4.39** in almost quantitative yield and high site selectivity (48:1 S_N2':S_N2). In particular, one example pertinent to this chapter involving alkenylboronic acid pinacol ester has also been demonstrated; 1,4-diene adduct **4.40** that bears a tertiary stereocenter is furnished in 85% yield and >99% S_N2' selectivity.

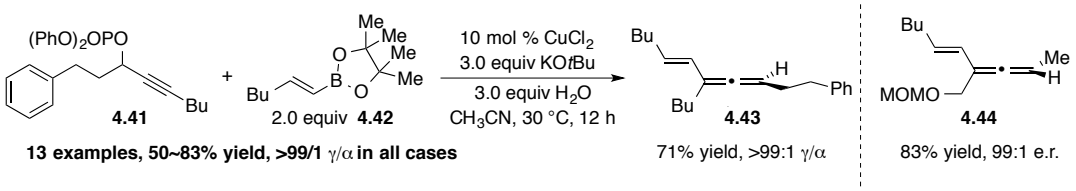
(21) Whittaker, A. M.; Rucker, R. P.; Lalic, G. *Org. Lett.* **2010**, *12*, 3216–3218.

Scheme 4.9. Cu–catalyzed Allylic Subsitution with Arylboronic Acid Pinacol Esters



Following the initial observation by Lalic and et al., Sawamura and colleagues have demonstrated the additions of alkenylboronic acid pinacol esters to propargyl phosphates under copper catalysis.[22] With 10 mol % $CuCl_2$ as the catalyst, allene **4.43** can be synthesized in 71% yield from propargyl phosphate **4.41** and excess 1,2-*trans* disubstituted alkenylBpin **4.42**; again, the super stoichiometric amount of KO*t*Bu and water are needed to ensure a clean transformation, presumably causing hydrolysis of the hindered and thus less reactive pinacol esters to reveal the actual intermediates for alkenyl group transfer. In addition to the racemic synthesis of olefin containing trisubstituted allenes, the preparation of enantiomerically enriched allenes through stereogenicity relay is also showcased in this study; for instance, compound **4.44** is readily furnished under the standard conditions starting with an optically pure propargyl phosphate substrate (83% yield and 99:1 e.r., Scheme 4.10). The quantitative transfer of stereochemical information is noteworthy.

Scheme 4.10. Cu–catalyzed Allylic Subsitution of AlkenylBpins to Propargyl Phosphates



(22) Yang, M.; Yokokawa, N.; Ohmiya, H.; Sawamura, M. *Org. Lett.* **2012**, *14*, 816–819.

The first examples of Cu-catalyzed allylic substitution reactions that utilize organoboronic acid pinacol esters were reported in 2012 by the Hoveyda group.[23] The nucleophilic unit that is of choice in this study is an allenylBpin because of two reasons. One focuses on the versatile utilities of an allene functional group, the additions of which in Cu-catalyzed EAS are unknown. The other takes the advantage of the commercial availability and the reasonable stability of allenylBpin over allenyl metal species. As shown in Scheme 4.11, with 10 mol % in situ generated *N*-heterocyclic carbene Cu complexes, EAS reactions consume allylic phosphate **4.33** to 71–79% after 24 h at ambient temperature when salts **4.47**–**4.50** serve as the ligands on copper; surprisingly, these reactions, whether with monodentate (i.e., **4.47** and **4.48**) or oxygen based bidentate (i.e., **4.49** and **4.50**) imidazolinium salts, give almost exclusively linear achiral allenyl adduct instead of desired compound **4.46** (>95% S_N2 selectivity, Scheme 4.11). On the contrary, the sulfonate bearing imidazolinium salt **4.51** is able to furnish >98% branched product **4.46** in 67% conversion and 66:34 e.r. Further modifications have led to the optimal sulfonate containing imidazolinium salt **4.52**, which is capable of promoting the EAS to completion under the same conditions and affording the desired product in 95.5:4.5 enantiomer ratio and 96:4 site selectivity. One notable point that requires further emphasis is that the reaction with **4.52** delivers allene **4.46** enriched in the opposite enantiomer compared to that with a very similar sulfonate containing imidazolinium salt **4.51**. The substitution pattern of the N-Ar unit in these NHCs apparently affects to a great extent the stereochemical outcome of the Cu-catalyzed EAS with organoboron reagents. For detailed discussion regarding this contrast, please refer to content in Chapter 1.

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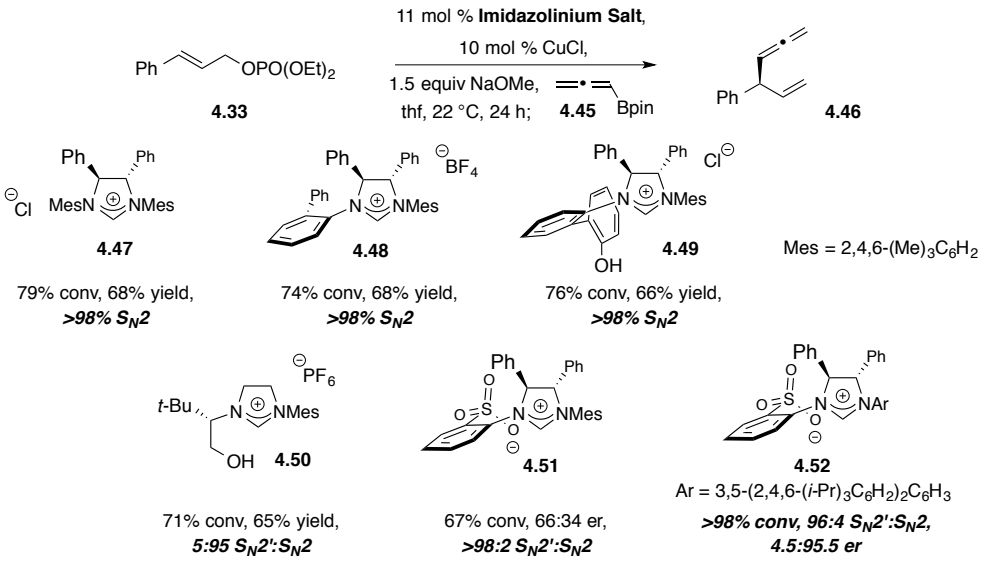
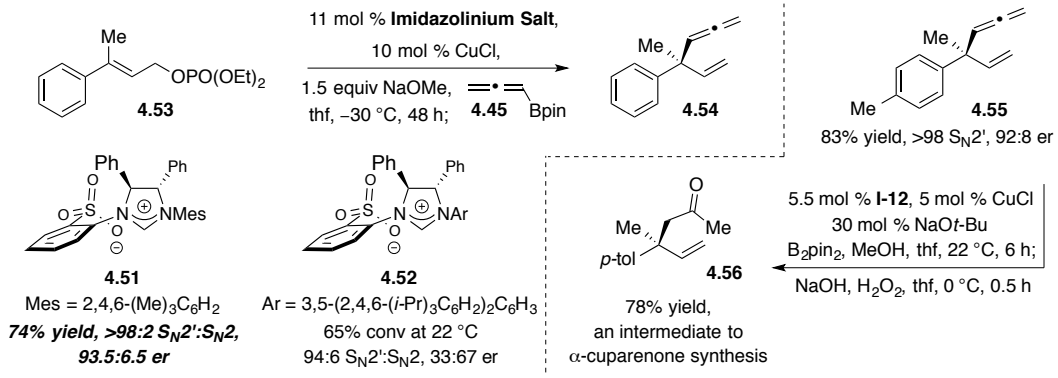
(23) Jung, B.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2012**, *134*, 1490–1493.

Scheme 4.11. Enantioselective Cu–catalyzed Allylic Subsitution of AllenylBpins to Allylic Phosphates



The construction of allene containing all-carbon quaternary stereogenic center through Cu-catalyzed EAS reactions is also illustrated in this study. As the Scheme 4.12 illustrated, in the presence of 10 mol % of an in situ generated Cu complex derived from **4.51**, trisubstituted allylic phosphate is converted to allenyl adduct **4.54** in 74% yield and 93.5:6.5 e.r. with again complete control of site selectivity. Interestingly, the optimal NHC ligand for allene additions to disubstituted allylic phosphates delivers product **4.54** in only 33:67 e.r., still favoring the opposite enantiomer. The utility of the allene is further demonstrated through a formal synthesis of α-cuparenone; the advanced ketone intermediate **4.56** can be accessed from the quaternary center bearing enantiomerically enriched allene **4.55** through an efficient Cu-catalyzed protoboration/oxidation sequence.

Scheme 4.12. Enantioselective Construction of Allene Containing All Carbon Quaternary Stereocenter.



4.2.4 Other Metal Catalyzed Allylic Substitution with Organoboron Reagents

Allylic substitution reactions are powerful due to the concomitant formation of a stereogenic center as well as a functionalizable alkene, and therefore attract attentions from synthetic chemists worldwide. Consequently, attempts to develop such methods are not limited in only the Cu regime. In fact, one of the early examples that utilize arylboronic acid to conduct diastereoselective allylic substitution with a palladium catalyst were reported in 2008 by Sawamura and co-workers.[24] Secondary allylic acetates are effective substrates for this transformation and various arylboronic acids, including those that bear an ester or aldehyde functionality, were shown to be valid coupling partners in the presence of 10 mol % of a Pd-1,10-phenanthroline complex. The above reactions can also be applied in the transfer of stereogenicity when an enantioenriched allylacetate serves as the substrate; the levels of retaining stereochemical information vary depending on the subtle differences in the substitution pattern of each substrate. Later, the same group demonstrated the employment of engineered silyl-substituted allylic esters as substrates under similar conditions to synthesize aryl-substituted

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(24) (a) Ohmiya, H.; Makida, Y.; Tanaka, T.; Sawamura, M. *J. Am. Chem. Soc.* **2008**, *130*, 17276–17277. For a related example, see: (b) Li, C.; Xing, J.; Zhao, J.; Huyuh, P.; Zhang, W.; Jiang, P.; Zhang, Y. Z.; *Org. Lett.* **2012**, *14*, 390–393.

allylsilanes; transfer of stereogenicity is also available for this method.[25] Recent works from the Morken group have advanced the enantioselective couplings of allylboronic acid pinacol esters with allylic carbonates under Pd catalysis; the 1,5-hexdienes that contain a tertiary or quaternary stereocenter are prepared in high efficiency and excellent levels of enantioselectivity.[26] Diastereo-control is also accessible when 1,2-disubstituted allylBpins are used in combination with substituted allylchlorides; two consecutive stereocenters are set in a single transformation and the products are generally high in optical purity.[27] In 2012, Morken and co-workers have described another protocol, in which enantiopure secondary propargyl acetates were shown to be effective substrates in the production of enantiomerically enriched 1,5-enynes in the presence of a Pd-rac-binap complex.[28] Besides the use of palladium, Carreira and colleagues have recently showcased that Ir-phosphoramidite complexes can induce stereogenicity in the coupling reactions of racemic secondary aryl-substituted allylic alcohols and sp2 and sp hybridized potassium trifluoroborate salts.[29] One case that is directly pertinent to the interest of this chapter is analyzed in Scheme 4.13. Racemic allylic alcohol **4.57**, which is derived from the corresponding aromatic aldehyde through reactions with the vinyl Grignard reagent, reacts with potassium alkenyltrifluoroborate **4.58** in the presence of 8 mol % in situ formed Ir complex of phosphoramidite **4.60** to deliver 1,4-diene **4.59** in 66% yield and 96.5:3.5 e.r. Site selectivity of this transformation, however, is only moderate, affording

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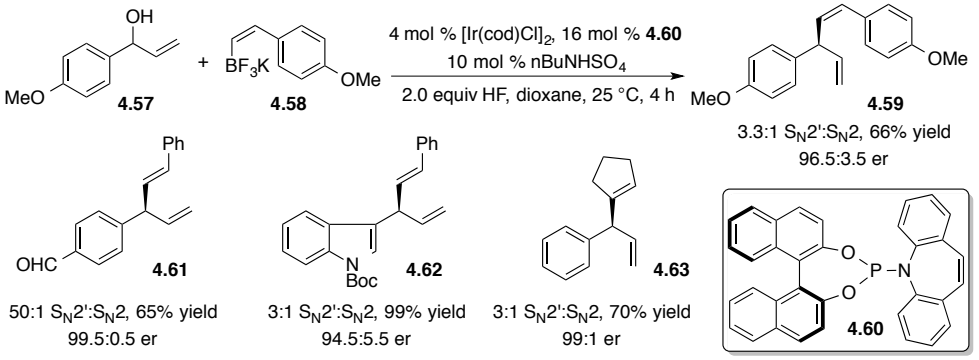
(25) Li, D.; Tanaka, T.; Ohmiya, H.; Sawamura, M. *Org. Lett.* **2010**, *12*, 3344–3347.
(26) (a) Zhang, P.; Brozek, L. A.; Morken, J. P. *J. Am. Chem. Soc.* **2010**, *132*, 10686–10688. (b) Zhang, P.; Le, H.; Kyne, R. E.; Morken, J. P. *J. Am. Chem. Soc.* **2011**, *133*, 9716–9719. (c) Le, H.; Kyne, R. E.; Brozek, L. A.; Morken. J. P. *Org. Lett.* **2013**, *15*, 1432–4135.
(27) Brozek, L. A.; Ardolino, M. J.; Morken, J. P. *J. Am. Chem. Soc.* **2011**, *133*, 16778–16781.
(28) Ardolino, M. J.; Morken, J. P. *J. Am. Chem. Soc.* **2012**, *134*, 8770–8773.
(29) (a) Hamilton, J. Y.; Sarlah, D.; Carreira, E. M. *J. Am. Chem. Soc.* **2013**, *135*, 993–997. (b) Hamilton, J. Y.; Sarlah, D.; Carreira, E. M. *Angew. Chem. Int. Ed.* **2013**, *52*, 7532–7535.

~23% achiral linear adduct; such phenomena can also be observed in the cases of the formations of compounds **4.62** and **4.63**. Again, the use of boron based nucleophilic reagents demonstrates the good level of compatibility with functional groups, such as an aldehyde (cf. **4.61**, Scheme 4.13), although in the particular case of trifluoroborate salt, stoichiometric hydrogen fluoride is required to achieve efficiency.

Scheme 4.13. Ir–catalyzed Enantioselective Allylic Subsitution with Potassium Alkenyltrifluoroborate



In summary, the ability to conduct allylic substitution reaction with organoboron based reagents provides significant advancement in terms of robustness of the reagents, easy handling during the reaction set up and the most important aspect---functional group compatibility and should be pursuit in the near future targeting higher efficiency, more variants that induce enantioselectivity through the use of small quantity of chiral catalysts, and broader scope both in regard of the electrophilic allylic substrates and the nucleophilic organoboron species. Particularly, enantioselective methods that centered around the efficient utilization of air and moisture insensitive, readily isolable and storable organoboronic acid pinacol esters, the preparation of which also see great progress in the past a few years,[30] are highly desirable.

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(30) For recent selected reviews, see: (a) Ishiyama, T.; Miyaura, N. *The Chemical Record* **2004**, *3*, 271–280. (b) Jiao, J.; Nishihara, Y. *J. Organometallic Chem*. **2012**, *721–722*, 3–16. (c) Ishiyama, Tatsuo, and Norio Miyaura. "Metal Catalyzed Borylation of C-H and C-Halogen Bonds of Alkanes, Alkenes, and

4.3 NHC–Cu-catalyzed Enantioselective Construction of Quaternary Center Containing 1,4-Dienes through Allylic Substitution with Alkenylboronic Acid Pinacol Esters

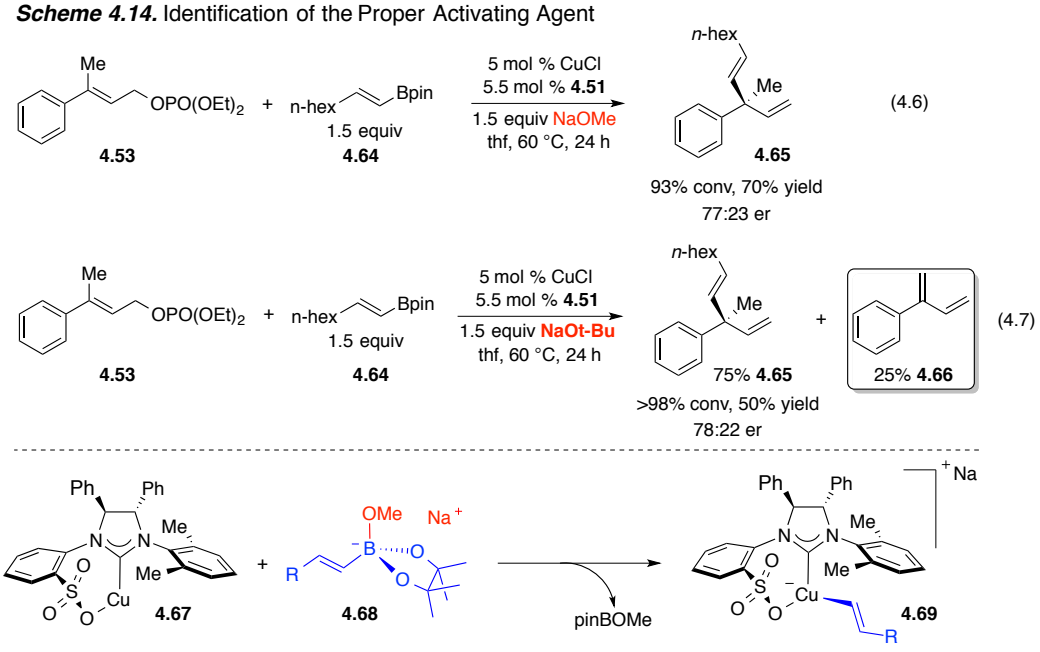
4.3.1 Identification of the Optimal Reaction Conditions

Cu-catalyzed EAS protocols that deal with the formation of quaternary stereogenic center containing enantiomerically enriched organic molecules with alkenylboron reagents are scarce, with only one example reported from the Hayashi group in 2011 (86.5:13.5 e.r., cf. Scheme 4.8). Therefore, we hope that with our chiral *N*-heterocyclic carbene ligands, an efficient and enantioselective Cu-catalyzed method can be developed for the coupling of an alkenylboron reagent and a trisubstituted prochiral allylic phosphate. We began our research with the efforts of trying to identify efficient reaction conditions, in which a commercially available alkenylBpin **4.64** (cf. Scheme 4.14) can be utilized in combination with substrate **4.53**. As shown in Scheme 4.14, with 5 mol % of the in situ generated NHC–Cu complex derived from sulfonate bearing imidazolinium salt **4.51**, the EAS reaction proceeds to 93% conversion at 60 ºC after 24 h in the presence of 1.5 equivalent of NaOMe base, furnishing the desired quaternary stereogenic center containing 1,4-diene **4.65** in 70% yield and 77:23 e.r. (Eq 4.6). The corresponding transformation performed at ambient temperature is much less efficient and equally enantioselective (~25% conv. and 77:23 e.r., not shown). Cu-catalyzed EAS

Arenes for the Synthesis of Boronic Esters." *Boronic Acids: Preparation and Applications in Organic Synthesis, Medicine and Materials (Volume 1 and 2), Second Edition* (2012): 135-169.

with the more basic NaO*t*Bu[31] delivers 50% yield of the desired alkenyl adduct in 78:22 e.r. but along with ~25% of an undesired 1,3-diene **4.66** (Eq. 4.7), presumably formed from the deprotonation of the allylic phosphate followed by elimination of the phosphate group from the resulting allyl anion. Thus, NaOMe is chosen as the activating agent, the role of which is showcased in Scheme 4.14 as well; we believe that the more nucleophilic ate complex of the trivalent boron reagent (cf. **4.68**) is responsible for the transfer of the alkneyl unit to the neutral bidentate NHC–Cu complex **4.67** to give the cuprate **4.69** prior to the substrate coordination.

Scheme 4.14. Identification of the Proper Activating Agent

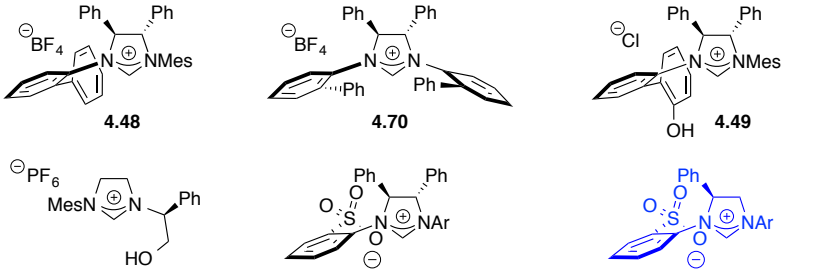


Next, we put forth to identify the optimal NHCs in terms of higher enantioselectivity for Cu-catalyzed EAS reactions, with the representative imidazolinium salt precursors outlined in Figure 4.1. The substrate for our ligand screening is an *ortho*-

(31) For the use of NaOtBu to activate arylboron reagents towards additions to CO_2 under Cu catalysis, see: Ohishi, T.; Nishiura, M.; Hou, Z. *Angew. Chem. Int. Ed.* **2008**, *47*, 5792–5795.

substituted allylic phosphate **4.77**, which can serve as a model compound *en route* to the synthesis of Pummerer's ketone, the target molecule proposed in Section 4.1. As the data in Table 4.1 illustrated, monodentate NHC–Cu complexes derived from C_1- or C_2-symmetric imidazolinium salts[32] **4.48** and **4.70** have led to good conversions, but moderate yields of a mixture of regioisomers (~86:14 S_N2':S_N2); up to 80:20 enantiomer ratio is observed (entries 1–2, Table 4.1). Minimal yield (12%) is obtained when phenoxide based bidentate Cu complex[33] that is derived from **4.49** is utilized (entry 3). 1,4-Diene **4.78** is formed with higher site selectivity (93:7 S_N2':S_N2, entry 4, Table 4.1) when the amino acid derived, alkoxide based salt[34] **4.71** serves as the ligand precursor; however, the reaction is not enantioselective (52:48 e.r.).

Figure 4.1. Representative Imidazolinium Salts Used in the Study



We then examined sulfonate-containing **4.51**,[35] the Cu-complex of which promotes the addition of alkenylBpin **4.64** with high efficiency (>98% conv., 95% yield), affording the desired product in improved selectivities (98% S_N2', 90:10 e.r., entry 5,

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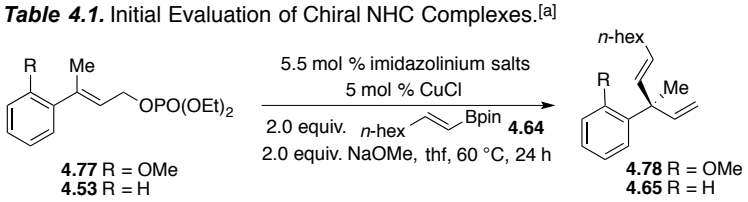
(32) Lee, K.-s.; Hoveyda, A. H. *J. Org. Chem.* **2009**, *74*, 4455–4462.
(33) Van Veldhuizen, J. J.; Campbell, J. E.; Guidici, R. E.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2005**, *127*, 6877–6882.
(34) (a) Martin, D.; Kehrli, S.; d'Augustin, M.; Clavier, H.; Mauduit, M.; Alexakis, A. *J. Am. Chem. Soc.* **2006**, *128*, 8416–8417. (b) Magrez, M.; Le Guen, Y.; Baslé, O.; Crévisy, C.; Mauduit, M. *Chem. Eur. J.* **2013**, *19*, 1199–1203.
(35) Brown, M. K.; May, T. L.; Baxter, C. A.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 1097–1100.

Table 4.1). Catalysts derived from more sterically hindered **4.72** and **4.73** further increase the enantioselectivity (97:3–99:1 e.r., entry 6–7) without diminution in reactivity (90% and 91% yield, respectively) and site selectivities (98:2–99:1 S_N2': S_N2). Further examination of sulfonate containing salts **4.74**, **4.75** and **4.76**, the mono-Ph variants of **4.51**, **4.72** and **4.73** has led to similar results for the Cu-catalyzed EAS reactions between alkenylBpin **4.64** and allylic phosphate **4.77** compared to their corresponding diphenyl counterparts (entries 8–10, Table 4.1); excellent enantioselectivity levels are again observed with sterically demanding *N*-heterocyclic carbene copper complexes (up to 99:1 e.r.). Another set of ligand screening data obtained with a simple Ph substituted substrate **4.53** under the same conditions with sulfonate containing NHC–Cu complexes, however, has revealed a few interesting observations. EAS reactions with mesityl bearing imidazolinium salts **4.51** and **4.74**, whether they contain diphenyl or mono-Phbackbone, afford 1,4-diene **4.65** in almost the same results (86–90% yield, 99% S_N2' and 77:23 e.r. in both cases, entries 11 and 14, Table 4.1). In contrast, when the transformations are carried out with sterically more hindered salts **4.72** and **4.73**, which are proved to be optimal for the EAS of substrate **4.77**, only racemic **4.65** are delivered in both cases, albeit still with high efficiencies and site selectivities (entries 12–13, Table 4.1). These findings led us to investigate the mono-Ph variants **4.75** and **4.76**, both of which are competent as catalyst precursors to promote highly selective (up to 99:1 e.r. and 98% S_N2') EAS with substrate **4.77**. Interestingly, the in situ formed Cu complexes are more effective in catalyzing the formation of 1,4-diene **4.65** with improved levels of enantioselectivity (up to 86:14 e.r. in entries 15–16 vs. up to 56:44 e.r. in entries 12–13, Table 4.1). It seems that even slight variations in the ligand structure can cause dramatic

differences when different substrates are utilized under the same reaction conditions. Fortunately, we are able to identify a set of mono-Ph backbone bearing imidazolinium salts as optimal NHC precursors that provide consistent levels of enantioselectivity while varying the structure of the allylic phosphates.

Table 4.1. Initial Evaluation of Chiral NHC Complexes.[a]



4.77 R = OMe
4.53 R = H

4.78 R = OMe
4.65 R = H

Entry	Substrate	Imidazolinium salt	Conv. (%)[b]	Yield (%)[c]	$S_N2':S_N2$[b]	e.r.[d]
1	**4.77**	**4.48**	92	59	87:13	73:27
2	**4.77**	**4.70**	87	51	86:14	80:20
3	**4.77**	**4.49**	58	12	80:20	na
4	**4.77**	**4.71**	89	60	93:7	52:48
5	**4.77**	**4.51**	>98	95	98:2	90:10
6	**4.77**	**4.72**	>98	90	98:2	97:3
7	**4.77**	**4.73**	>98	91	99:1	99:1
8	**4.77**	**4.74**	95	87	99:1	73:27
9	**4.77**	**4.75**	*>98*	*94*	*98:2*	*98.5:1.5*
10	**4.77**	**4.76**	>98	86	98:2	99:1
11	**4.53**	**4.51**	>98	90	99:1	77:23
12	**4.53**	**4.72**	95	92	99:1	56:44
13	**4.53**	**4.73**	>98	95	99:1	52:48
14	**4.53**	**4.74**	92	86	99:1	77:23
15	**4.53**	**4.75**	>98	86	98:2	83:17
16	**4.53**	**4.76**	*>98*	*90*	*98:2*	*86:14*

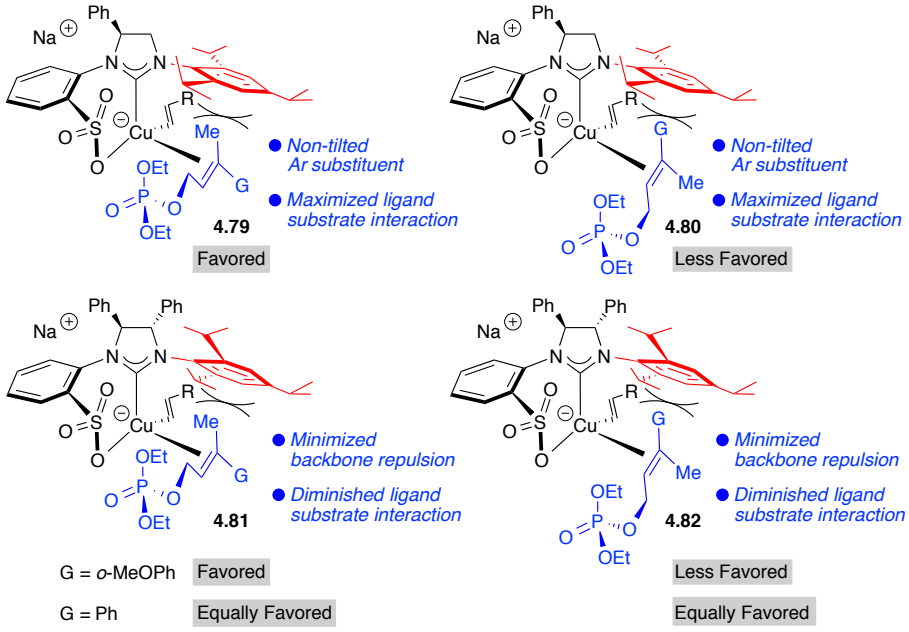
[a] Reactions were performed under N_2 atmosphere. [b] Determined through analysis of 400 MHz ^{1}H NMR spectra of unpurified mixtures. [c] Yields of isolated products after purification (±5%). [d] Determined by HPLC analysis (±2%); see the Supporting Information for details. na = not applicable.

4.3.2 Stereochemical Models That Account for the Observed Enantioselectivities

The above preliminary studies have established that, unlike their aluminum counterparts, reactions with boron-based reagents have to be conducted at elevated temperature to obtain appreciable conversion (i.e., –50—15 °C with alkenylaluminums[13] vs 60 °C with alkenylBpins). Such observations are consistent with the lack of Lewis acid activation in the absence of a chelating metal (i.e., cationic dialkylaluminum species, cf. Chapters 1 and 3). Without the Al bridge, substrate coordination is no longer fixed to the binding site adjacent to the ligated sulfonate unit and the orientation of the substrate can change as well while interacting with the copper center; these complicating factors

potentially contribute to the diminished enantioselectivity with alkenylBpin compared to reactions with alkenylaluminum reagent (83:17 e.r. with boron vs. 95:5 with Al in the formation of product **4.65**, cf. Chapter 3 and Table 4.1). Nonetheless, the observed major enantiomer is the same as that with vinylaluminum reagents, suggesting that the favored mode of substrate coordination remains the same as in the EAS with alkenylaluminum reagents (cf. structure **4.79** in Scheme 4.15). The more severe steric repulsion between the *ortho* substituent and a trisubstituted allylic phosphate renders backside substrate approaching much less prevalent (for detailed analysis, see Chapter 1). Furthermore, the orientation of the phosphate unit can be rendered favorable due to the secondary orbital interaction between the alkenyl-Cu σ-bond and the LUMO of the substrate, which has a bigger lobe at the γ carbon.[36]

Scheme 4.15. Variations In the Backbone of the NHC–Cu Complexes Impact the Enantioselectivity Levels of Different Substrates.

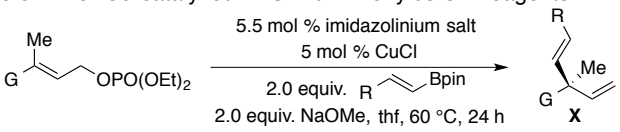


(36) For a recent review on the mechanism of nucleophilic organoCu(I) reactions, see: Yoshikai, N.; Nakamura, E. *Chem. Rev.* **2012**, *112*, 2339–2372.

Based on the above established hypothetical mode of stereochemical induction, we set forth to rationale the observed difference in the behavior of salts **4.73** and **4.76** (i.e., entry 13 vs. entry 16, Table 4.1; similar conclusion can be drawn for the difference between **4.72** and **4.75**, which are omitted for clarity), only varied by a Ph group on the backbone. We surmised that when Cu-complex derived from **4.73** is investigated, the strong steric repulsion between the backbone Ph and the proximal *i*Pr substituent would force the symmetrical aryl unit to tilt (i.e., **4.81** and **4.82** in Scheme 4.15), which exposes the front quadrant to a higher extent compared to the complex derived from **4.76**, the tri*iso*propylphenyl group of which remains flat during the course of the reaction (i.e., **4.79** and **4.80** in Scheme 4.15). Such tilt reduces the energy gap between the substrate coordination mode represented in complex **4.81** and its competing mode, as depicted in complex **4.82**, in which the bigger olefin substituent is pointing towards the aromatic moiety of the ligand. Thus, when a more difficult-to-differentiate substrate, such as **4.53** (G=Ph), is used, enantioselectivity is minimal (52:48 e.r. in entry 13 of Table 4.1); whereas in **4.77** (G=*o*-MeOPh), the effective size difference between a methyl unit and an *o*-methoxyphenyl group is large enough to compensate for the reduction in energy gap so that the EAS reaction with **4.77** remains selective (99:1 e.r., entry 6, Table 1).

4.3.3 The Substrate Scope of NHC–Cu-Catalyzed EAS

Table 4.2. Scope of NHC–Cu-catalyzed EAS with Alkenylboron Reagents.[a]



Entry	G	R	X	Imidazolinium salt	Conv. (%)[b]	Yield (%)[c]	$S_N2':S_N2$[b]	e.r.[d]
1	*o*$OMeC_6H_4$;	*n*-hex;	**4.83**	**4.75**	98	94	98:2	98.5:1.5
2	*o*MeC_6H_4;	*n*-hex;	**4.84**	**4.75**	87	82	96:4	92:8
3	*o*$NO_2C_6H_4$;	*n*-hex;	**4.85**	**4.51**	82	50	98:2	87:13
4	*o*BrC_6H_4;	*n*-hex;	**4.86**	**4.75**	87	85	98:2	99:1
5	Ph;	*n*-hex;	**4.87**	**4.76**	>98	90	98:2	86:14
6	*p*ClC_6H_4;	*n*-hex;	**4.88**	**4.75**	>98	>98	98:2	84:16
7	*m*BrC_6H_4;	*n*-hex;	**4.89**	**4.75**	>98	97	94:6	80:20
8	*o*BrC_6H_4;	$Cl(CH_2)_3$;	**4.90**	**4.75**	96	91	99:1	99:1
9	*m*BrC_6H_4;	*c*propyl;	**4.91**	**4.76**	>98	99	96:4	79:21
10	*o*BrC_6H_4;	Ph;	**4.92**	**4.75**	98	98	>98:2	99:1
11	*p*ClC_6H_4;	*p*$OMeC_6H_4$;	**4.93**	**4.76**	>98	91	99:1	81:19
12	Cy;	Ph;	**4.94**	**4.75**	>98	75	99:1	85:15
13	CO_2*t*Bu;	Ph;	**4.95**	**4.75**	>98	93	>98:2	87:13

[a] Reactions were performed under N_2 atmosphere. [b] Determined through analysis of 400 MHz ^{1}H NMR spectra of unpurified mixtures. [c] Yields of isolated products after purification (±5%). [d] Determined by HPLC analysis (±2%); see the Supporting Information for details.

With optimal imidazolinium salts **4.75** and **4.76** in hand, we continued to expand the scope of current protocol. As shown in entries 1–4, Table 4.2, substrates bearing an electron donating (entry 1), an electron withdrawing (entries 3–4)[37] or sterically hindered *o*-substituent (entry 2) are effective; the corresponding EAS reactions deliver desired diene products in high efficiency (50–94% yield) and enantioselectivities (87:13–99:1 e.r.). The NHC–Cu-catalyzed processes with aryl-substituted allylic phosphates that contain no, *meta*- or *para*-substituent proceed to completion under the standard conditions, resulting in somewhat decreased enantioselectivities (80:20–86:14 e.r. in entries 5–7, Table 4.2). Additionally, a variety of alkenylboron reagents can be utilized in Cu-catalyzed EAS. Entities, such as chlorine or cyclopropyl containing aliphatic alkenes, styrene or substituted styrene, are effectively incorporated into the enantiomerically enriched 1,4-dienes **4.90**–**4.93** (91–99% yields, 79:21–99:1 e.r., entries 8–11).

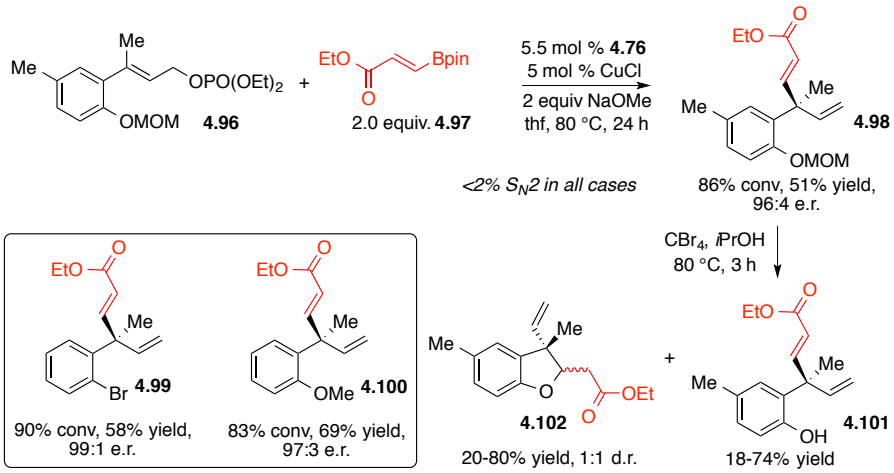
(37) With *o*-NO_2-phenyl substituted allylic phosphate, reactions involving NHC–Cu complex derived from **4.75** proceed sluggishly and with diminished site selectivity (~50% conv. and 80:20 $S_N2':S_N2$).

Cyclohexyl-substituted allylic phosphate participates in Cu-catalyzed EAS to furnish the desired styrenyl adduct **4.94** in 75% yield and 85:15 enantiomer ratio (entry 12). Moreover, a *t-butyl*ester moiety is also tolerated under such conditions (entry 13, Table 4.2). Notably, Site selectivity levels in all cases remain high (>94% S_N2').

4.3.4 EAS Reactions with Ester Containing AlkenylBpin Reagents

Having established the scope, the stage is now set for the synthesis of Pummerer's ketone. Upon treatment with a commercially available ester-containing alkenylboron reagent **4.97**, a MOM protected allylic phosphate **4.96** is transformed through NHC–Cu-catalyzed EAS into desired enoate **4.98** (Scheme 4.16); the reaction proceeds to 86% conversion at 80 °C after 24 h, delivering **4.98** in 51% yield and 96:4 e.r. when **4.76** is used as the *N*-heterocyclic carbene precursor.[38] Similar protocols can be applied to a number of substrates, affording unsaturated esters **4.99** and **4.100** in 58% and 69% yield, and 99:1 and 97:3 e.r., respectively. The above cases put forth the first examples in Cu-catalyzed EAS reactions that feature the addition of nucleophiles that contain a carbonyl

Scheme 4.16. Enantioselective Additions of An Ester Containing Alkenylboron Reagent.

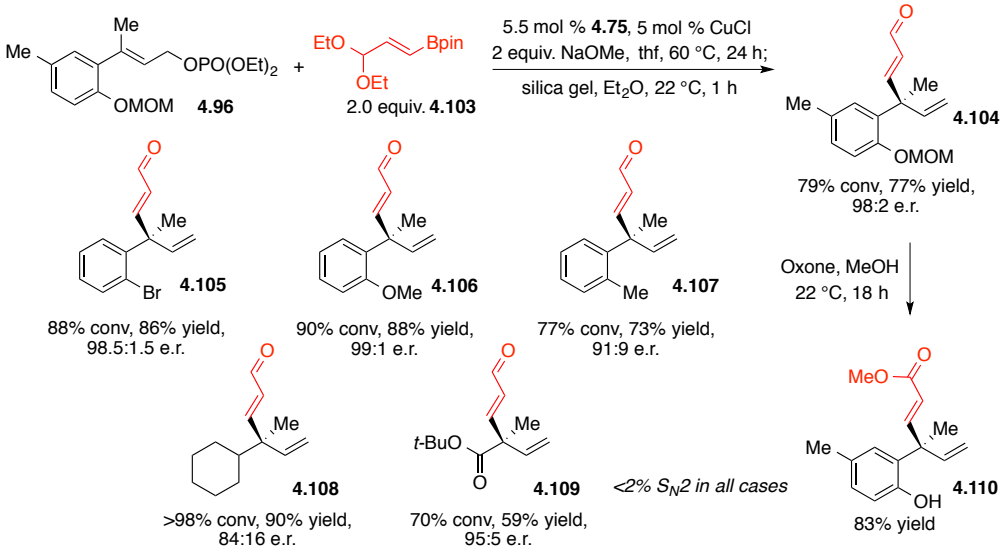


(38) When the catalyst derived from **4.75** is used, **4.98** is isolated in 42% yield (>98% S_N2', 96:4 e.r.). The results obtained with **4.75** or **4.76** are often similar but the outcome can be, at times, slightly different.

functionality. Among many deprotection strategies of the MOM group to reveal the free phenol, only an adapted procedure[39] that uses CBr_4 in *i*PrOH is successful in converting **4.98** to the desired compound **4.101**, however, in irreproducible yields (18–74%, Scheme 4.16). The major byproduct observed is the cyclized benzofuran **4.102** with minimal induction of diastereoselectivity (1:1 dr). Such an observation suggests that the substrate controlled diastereoselective functionalization adjacent to a quaternary stereogenic center is of great difficulty due to the intrinsic similarity of substituents on the carbon (i.e., in this case, differentiation between a methyl and a vinyl unit is not possible). Therefore, in order to preferentially produce one diastereo isomer, we need to resort help from a catalytic procedure, in which a chiral catalyst can override the stereochemical preference of the enantioenriched substrate.

4.3.5 EAS Reactions with Acetal Containing AlkenylBpin Reagents

Scheme 4.17. Enantioselective Additions of An Acetal Containing Alkenylboron Reagent.



(39) Lee, A. S-Y.; Hu, Y-J.; Chu, S-F. *Tetrahedron*, **2001**, *57*, 2121–2126.

Because of the unreliable synthesis of the phenol containing enoate **4.101**, a slightly modified route that explores the idea of using an acetal containing alkenylBpin reagent **4.103** in Cu-catalyzed EAS is subjected to investigation, the product derived from which is also synthetically valuable and could serve as a potential intermediate for the synthesis of Pummerer's ketone. As shown in Scheme 4.17, EAS reaction of allylic phosphate **4.96** with **4.103**, in the presence of 5 mol % of in situ generated NHC–Cu complex derived from **4.75**, affords enal **4.104**, after silica gel treatment of the crude reaction mixture, in 77% yield (79% conv.) and 98:2 e.r.[40] Enals **4.105**–**4.107**, synthesized from the corresponding aryl-substituted allylic phosphates, are furnished in high efficiency (73–88% yields) and excellent levels of enantioselectivity (91:9–99:1 e.r., Scheme 4.17). Alkyl-substituted substrate is also effective under the standard conditions; high yield of the 1,4-diene **4.108** (90%) is obtained. The enantiomeric purity, however, is diminished compared to the products derived from aryl-substituted substrates (84:16 e.r.). In addition, highly functionalized dicarbonyl compound **4.109** is prepared in 95:5 enantiomer ratio and in 59% yield (70% conv.).[39] With the efficient formation of **4.104**, the synthesis can be further carried out through a concurrent oxidation of the enal functionality and oxidative deprotection of the MOM group with Oxone in Methanol to give desired phenol **4.110** in 67–90% yields (average to 83% over five attempts, Scheme 4.17).[41]

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(40) Further attempts (i.e., 80 ºC or increased equivalents of reagent **4.103** or prolonged reaction time) to improve conversion did not lead to higher yields; instead, more byproduct formation complicated the reaction and subsequent isolation.

(41) Travis, B. R.; Sivakumar, M.; Hollist, G. O.; Borhan, B. *Org. Lett.* **2003**, *5*, 1031–1034.

4.3.6 Diastereo- and Enantioselective Synthesis of Syn and Anti Pummerer's Ketones

Considering the low diastereoselectivity in the benzofuran formation by substrate control (cf. Scheme 4.16), we envision a diastereoselective process promoted by a chiral catalyst. Inspired by related studies on cinchona alkaloid catalyzed intramolecular conjugate additions of phenol,[42] we are able to discover that oxy-Michael cyclization is complete within two hours when phenol **4.110** is treated with 10 mol % of the commercially available and inexpensive cinchonidine at 0 °C in toluene, leading to the formation of **syn-4.111** in 90:10 d.r. favoring the syn isomer (referring to the relative stereochemistry of the vinyl group and the ester functionality; Scheme 4.18). Conversion of **syn-4.111** to the Weinreb amide **syn-4.112** is efficient (78% yield); a small quantity of β-eliminated phenol **4.113** is obtained under the basic conditions (~20%). Treatment of unsaturated amide **4.113** with the same cyclization protocol using cinchonidine (10 mol % in toluene) affords **syn-4.112** in 91:9 d.r. and 87% yield. The subsequent addition of vinyl Grignard furnishes the corresponding enone in >98% yield. Finally, ring closing metathesis (RCM) with phosphine free Ru carbene **4.114**,[43] at ambient temperature, gives rise to enantiopure *syn* Pummerer's ketone (99:1 e.r., Scheme 4.18).[44]

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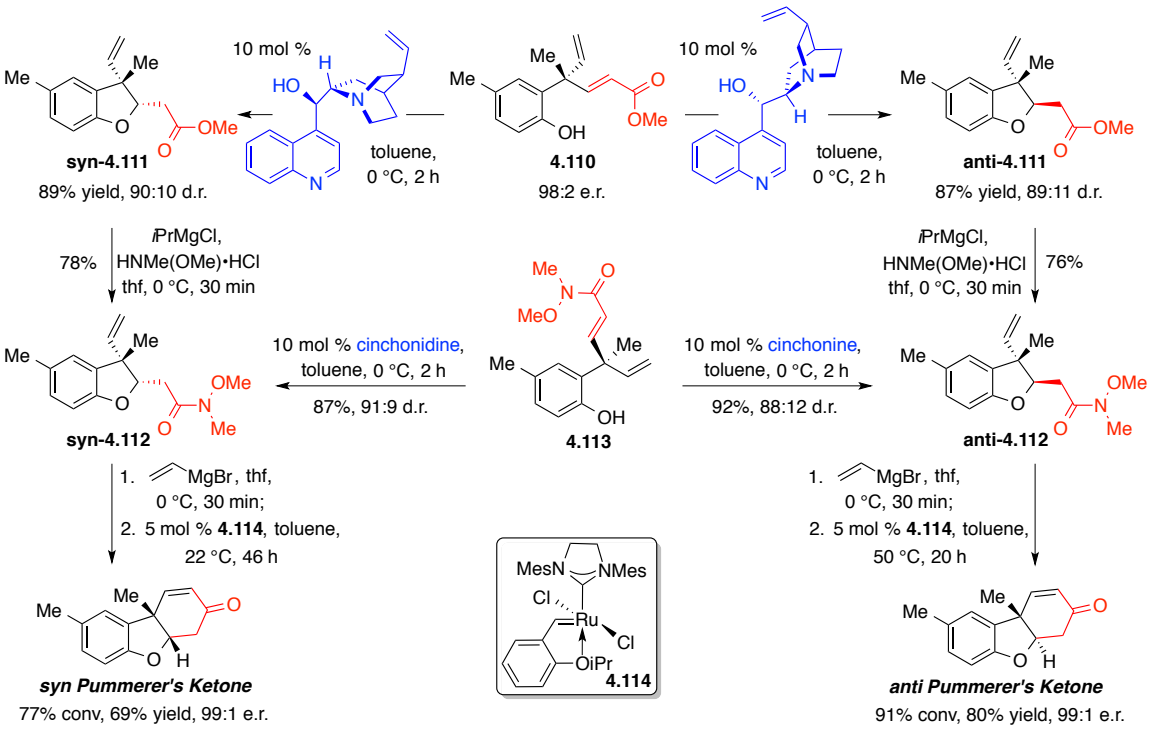
(42) For related enantioselective intramolecular conjugate additions catalyzed by derivatives of cinchona alkaloids, see: (a) Biddle, M. M.; Lin, M.; Scheidt, K. A. *J. Am. Chem. Soc.* **2007**, *129*, 3830–3831 and references cited therein. (b) Merschaert, A.; Delbeke, P.; Daloze, D.; Dive, G. *Tetrahedron Lett*. **2004**, *45*, 4697–4701. (c) Sekino, E.; Kumamoto, T.; Tanaka, T.; Ikeda, T.; Ishikawa, T. *J. Org. Chem*. **2004**, *69*, 2760–2767;

(43) Garber, S. B.; Kingsbury, J. S.; Gary, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168–8179.

(44) Syn Pummerer's Ketone is prone to racemization; RCM performed at 50 °C results in ~60:40 er after purification, albeit >98% conv. and an improved yield (90%) is observed. See experimentals for more details of the proposed mechanism of racemization.

Scheme 4.18. Synthetic Applications to Syn and Anti Pummerer's Ketones.



Previous syntheses of Pummerer's ketone employed similar strategies, in which the six membered enone rings were formed prior to the construction of the furan moiety.[45] Such strategies cannot provide access to the *anti* isomer of Pummerer's ketone due to the inherent energy preference for the formation of the less strained *cis* fused polycyclic molecule;[46] indeed, only *syn* Pummerer's ketone was detected from previous syntheses. As demonstrated in Scheme 4.18, our route, which consists of the diastereoselective phenol conjugate addition that furnishes both diastereomers of **4.111** by changing the identity of the chiral catalyst (cinchonine is used for the formation of **anti-4.111**), can

(45) For a previous non-enantioselective synthesis of Pummerer's ketone, see: Vierfond, J.-M.; Reynet, A.; Moskowitz, H.; Thal, C. *Synth. Commun.* **1992**, *22*, 1783–1792. For other related references, see: (b) Pummerer, R.; Melamed, D.; Puttfarcken, H. *Ber. Dtsch. Chem. Ges.* **1922**, *55*, 3116–3132. (c) Opioid Analgesics Chemistry and Receptors (Eds.: Casy, A. F.; Parfitt, R. T.), Plenum, New York, 1986. (d) Winternitz, F.; Autia, N. J.; Tumlirova, M.; Lacharette, R. *Bull. Soc. Chim. Fr.* **1956**, 1817. (e) Barton, D. H. R.; Deflorin, A. M.; Edwards, O. E. *J. Chem. Soc.* **1956**, 530–534.

(46) Preliminary calculations have shown that syn Pummerer's ketone is 7.6 kcal/mol lower in energy than anti Pummerer's ketone.

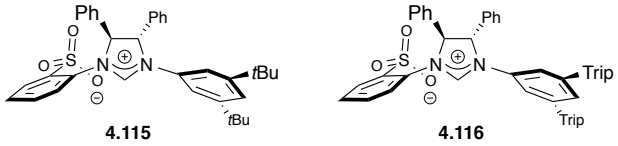
lead us to the efficient and enantioselective synthesis of *anti* Pummerer's ketone. Use of essentially the same synthetic sequence with the RCM performed at elevated temperature (21% conv. at 22 ºC) accomplishes the synthesis of the target molecule again in exceptional optical purity (99:1 e.r.).

4.4 NHC–Cu-catalyzed Enantioselective Construction of Tertiary Stereocenter Containing 1,4-Dienes through Couplings of Allylic Phosphates with A Range of Alkenylboronic Acid Pinacol Esters

4.4.1 Identification of the Optimal Reaction Conditions

Having established the protocol for enantioselective EAS reactions to construct all carbon quaternary stereogenic centers, we then turned to methods that can deliver 1,4-dienes that bear a stereogenic C-H bond. Related cases, although a bit more abundant compared to the literature articles regarding the formation of quaternary center containing molecules, are still relatively scarce.[13a, c, 29a] What we would like to address in this section is a general coupling protocol that can fuse a broad range of readily available alkenylBpin reagents (e.g., trans- and cis-1,2-disbustituted, 1,1-disubstituted, heterocyclic, trisubstituted and the non-substituted vinylBpin) with various electrophilic allylic phosphates. In order to achieve the goal, the identification of a small collection of chiral catalysts must be conducted due to the different requirements of the shape of the binding pockets associated with different combinations of coupling partners employed in the EAS reactions. Two additional sulfonate containing enantiomerically pure imidazolinium salts are listed in Figure 4.2.

Figure 4.2. Additional Imidazolinium Salts Used in the Study

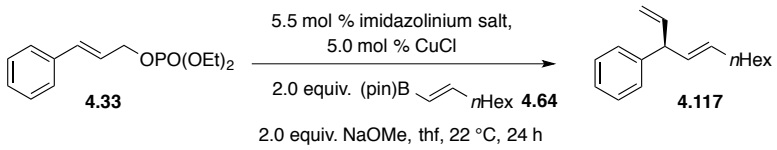


4.115 **4.116**

We initiate the study by evaluating again effects of representative chiral *N*-heterocyclic carbenes as ligands on copper to promote additions of alkenylBpin **4.64** to a simple allylic phosphate **4.33**. As shown in Table 4.3, EAS with C_1 or C_2 symmetric monodentate NHCs proceeds sluggishly at ambient temperature after 24 h, affording the desired product in 31% and 59% yield, 67% and 79% S_N2' selectivity, 45:55 e.r. and 74:26 e.r., respectively (entries 1–2). The reaction with a phenoxide based bidentate carbene Cu complex gives <2% conversion of the substrate (entry 3). Low efficiency (30% yield) is also observed with an alkoxide containing bidentate NHC, albeit with >98% site selectivity and reasonable enantioselectivity (78:22 e.r., entry 4). Next, we started to evaluate the chiral sulfonate bearing carbene copper complexes (entries 5–10, Table 4.3). To our delight, when a mesityl substituted salt **4.51** is used, the corresponding EAS reaction furnishes the 1,4-diene **4.117** in 90% yield, >98% S_N2', however, essentially as a racemic mixture (entry 5). The more sterically demanding tri*iso*propylphenyl unit containing salt **4.73** is able to improve the enantiomer ratio to 86:14 while retaining high levels of efficiency and site selectivity (entry 6). It is noteworthy that the monoPh variants **4.74** and **4.75**, especially the latter of which proves to be optimal in catalyzing quaternary center forming EAS, deliver the alkenyl adduct in diminished enantioselectivity levels (43:57–34:66 e.r., entries 9–10). At this point, we seek solutions from NHCs that feature 3,5-substitution patterns; the rationale for this effort finds support in NHC–Cu-catalyzed allene additions to *trans* 1,2-disubstituted

allylic phosphates to create tertiary stereogenic centers, wherein a 3,5-triisopropylphenyl substituted sulfonate bearing imidazolinium salt operates to provide the optimal enantioselectivity and, even more interestingly, enriched in the opposite enantiomer compared to the results with 2,6-substituted carbene copper species (for detailed discussion of the stereochemical models with these sulfonate bearing NHC–Cu complexes that can shed light on the present study, please refer to Chapter 1). In agreement with the previous findings involving allene transfer in Cu-catalyzed EAS, reactions with imidazolinium salt that carry a 3,5-di*tert*butylphenyl N-Ar unit proceed effectively, delivering **4.117**[23] in 87:13 e.r. (entry 7). Moreover, use of more sterically present salt **4.116** further improves the enantiomer ratio (92:8 e.r., entry 8).

Table 4.3: Initial Examination of Various Chiral NHC–Cu Complexes.[a]



Entry	Imidazolinium salt	Conv. [%][b]	Yield [%][c]	$S_N2':S_N2$[b]	e.r.[d]
1	**4.70**	38	31	67:33	45:55
2	**4.48**	76	59	79:21	74:26
3	**4.49**	<2	--	--:--	--:--
4	**4.71**	38	30	>98:2	78:22
5	**4.51**	91	90	>98:2	41:59
6	**4.73**	86	84	97:3	86:14
7	**4.115**	98	93	98:2	87:13
8	**4.116**	97	97	98:2	92:8
9	**4.74**	93	88	>98:2	43:57
10	**4.75**	72	70	98:2	34:66

[a] Reactions were performed under N_2 atmosphere. [b] Determined through analysis of 400 MHz ^{1}H NMR spectra of unpurified mixtures. [c] Yields of isolated products after purification (±5%). [d] Determined by HPLC analysis (±2%); see the Supporting Information for details.

4.4.2 Cu-catalyzed EAS with *trans* 1,2-Disubstituted AlkenylBpin Reagents

As the catalytic conditions have been discovered for the additions of alkenylBpin **4.64**, we decided to target nucleophiles that are specifically beneficial from the use of functional group compatible boron reagents, since the corresponding EAS reactions with alkenylaluminums are more practical and inexpensive while dealing with the additions of

simple, unfunctionalized alkenyl moieties.[13] One particular reagent of interest is the acetal containing alkenylBpin **4.103**; the product generated from the Cu-catalyzed EAS with such a reagent is synthetically useful and can lead to the corresponding enal as well. The associated challenge, therefore, concerns the potential loss of induced stereochemistry information because of the seemingly labile C-H bond adjacent to the unsaturated carbonyl. As illustrated in Scheme 4.19, EAS of allylic phosphate **4.33** with alkenylBpin **4.103** occurs in 88% conversion at 22 ºC after 24 h, delivering the enal product **4.118** after silica gel hydrolysis in 85% yield and 91:9 e.r. Thus, the suggested epimerization does not take place under milder acidic hydrolysis conditions within one hour. An *ortho*-Br-substituted enal **4.119** is also furnished in 86% yield, 95% S_N2' selectivity and 94:6 e.r. The formation of carboxylic ester **4.120** showcases the possibility of isolating the acetal containing diene as a single regioisomer in 92:8 e.r., albeit in only moderate yield (52%). Additionally, the efficient hydrolysis to reveal a para-NO_2-substituted "skipped" enal **4.122** is notable because of the much higher propensity of the very acidic C-H to undergo either isomerization reactions or product epimerization; fortunately, under the standard conditions within one hour, the desired enal[47] is obtained in 90% overall yield, almost complete site selectivity (98%) and no loss of the stereochemical information (93:7 e.r., >98% enantiospecificity, Scheme 4.19).

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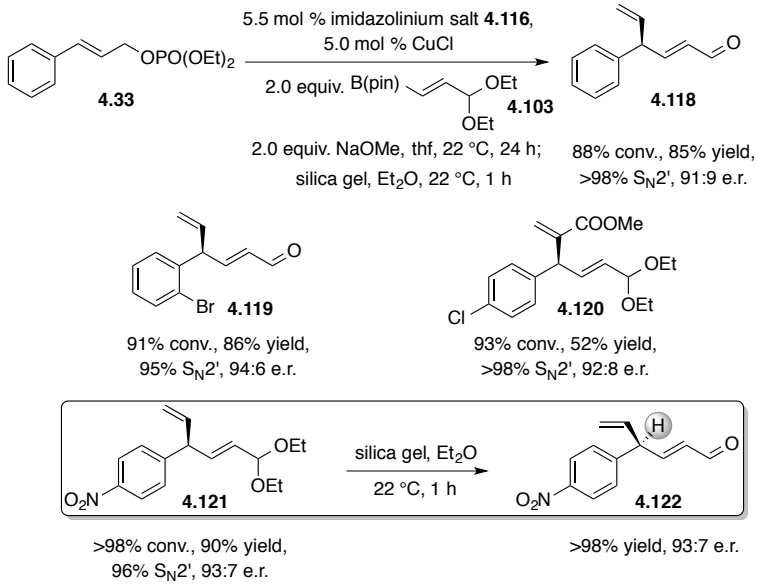
(47) The benchtop stability of this compound has not been rigorously tested; potential decomposition or loss of the stereochemical purity may occur upon prolonged standing.

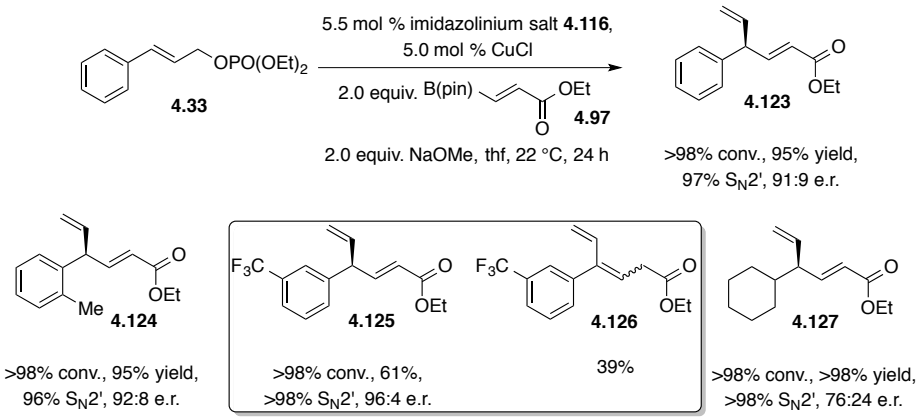
Scheme 4.19: NHC-Cu-catalyzed EAS with Acetal Containing *trans* 1,2-Disubstituted AlkenylBpin Reagents to Construct Tertiary Stereogenic Centers.



γ-Substituted enantiomerically enriched unsaturated esters are interesting building blocks in chemical synthesis. The present protocol is capable of delivering such entities through the additions of an ester containing **4.97** in the presence of 5 mol % of in situ formed Cu catalyst derived from **4.116**. The representative enoate **4.123** is furnished in 95% yield, 97% S_N2' selectivity and 91:9 e.r.; the acidic γ proton survives the basic reaction media of EAS. Additional cases, in which a sterically hindered aryl allylic phosphate (cf. **4.124**) or an alkyl-substituted substrate (**4.127**) is utilized, further demonstrate the generality of the desired transformations. An instance, however, is shown to be less compatible with the standard Cu-catalyzed coupling procedure; the synthesis of a trifluoromethyl bearing enoate **4.125** is highly selective (>98% site selectivity and 96:4 e.r., Scheme 4.20), but along with 39% of the isomerized conjugated

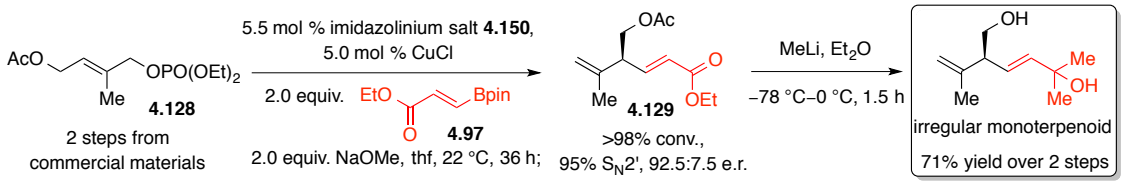
diene **4.126**,[48] presumably because of the increased acidity rendered by the strong electron withdrawing CF_3 substituent.

Scheme 4.20: NHC-Cu-catalyzed EAS with Ester Containing *trans* 1,2-Disubstituted AlkenylBpin Reagents to Construct Tertiary Stereogenic Centers.



The synthetic utility of the aforementioned protocol is highlighted in Scheme 4.21. A readily available trisubstituted allylic phosphate **4.128** is converted to enantiomerically enriched enoate **4.129** in the presence of 5 mol % in situ generated Cu catalyst of unsymmetrical imidazolinium salt **4.150**; the reaction proceeds to completion after 36 h at ambient temperature and affords the diene adduct in 95% S_N2' selectivity and 92.5:7.5 enantiomer ratio. The crude reaction mixture is subjected to excess methyllithium in diethylether to reveal the masked primary alcohol as well as to deliver the tertiary allylic alcohol motif; 71% yield of the irregular monoterpenoid[49] is obtained over two steps.

Scheme 4.21: Concise Synthesis of An Irregular Monoterpenoid through Cu-catalyzed EAS.



(48) Such an impurity is not separable from the desired unsaturated ester **4.125**.
(49) (a) Sy, L.-K.; Brown, G. D. *Phytochemistry* **2001**, *58*, 1159–1166. (b) Araki, S.; Kambe, S.; Kameda, K.; Hirashita, T. *Synthesis* **2003**, *5*, 751–754.

4.4.3 Cu-catalyzed EAS with *cis* 1,2-Disubstituted AlkenylBpin Reagents

The involvement of a *cis* organometallic reagent in Cu-catalyzed allylic substitution is virtually unknown,[50] which raises an interesting question of whether the *cis* olefin geometry can be preserved during the course of the reaction. Another challenge that one has to face is the lack of efficient methods in the preparation of alkenyl metals that bear a *cis* alkene.[51] Recent advances in catalytic Z selective cross metathesis of vinylboronic acid pinacol ester with terminal olefins have provided effective access to *cis* alkenylBpin reagents.[10] Additionally, the Rh-catalyzed trans hydroboration of terminal acetylenes as well as other recent developments serves as efficient alternatives.[9a] In this regard, we began to investigate NHC–Cu-catalyzed EAS reactions that utilize a commercial cis propenylBpin **4.130** to construct a tertiary stereogenic center (Table 4.4). Various *trans* 1,2-disubstituted allylic phosphates serve as effective substrates under the standard catalytic conditions with imidazolinium salt **4.116** as the optimal ligand precursor. Electron- donating (entry 2), withdrawing (entry 3) and sterically demanding (entry 4) substituents are well tolerated, furnishing desired 1,4-dienes that bear a preserved *cis* alkene functionality in 76–82% yield,[52] complete site selectivity (>98% in all cases) and 95:5–98:2 e.r. (entries 1–4, Table 4.4). Trisubstituted allylic phosphates that contain an ester functional group are also examined in Cu-catalyzed EAS protocol

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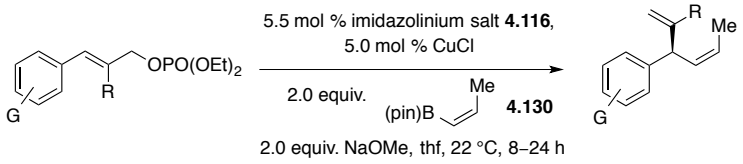
(50) For two reported isolated examples that bear a cis allyl *t*butylether moiety, see: ref. 13 (a) and (b).
(51) Studies of cis alkenyl Grignard and lithium reagents have been carried out, see: (a) Yoshino, T.; Manabe, Y.; Kikuchi, Y. *J. Am. Chem. Soc.* **1964**, *86*, 4670–4673. (b) Neumann, H.; Seebach, D. *Tetrahedron Lett*. **1976**, *52*, 4839–4842. However, concerns about their stereochemical stability have lead to further investigations in isomerization processes of these alkenyl metals, see: (c) Yoshino, T.; Manabe, Y. *J. Am. Chem. Soc.* **1963**, *85*, 2860–2861. (d) Curtin, D. Y.; Koehl, W. J. *J. Am. Chem. Soc.* **1962**, *84*, 1967–1973.
(52) EAS reactions with cis propenylBpin **4.130** proceed to completion usually within eight hours, which is significantly shorter than other cases (often require 24 h). Such a phenomenon may be attributed to its smaller size.

with **4.130**. Again, a range of representative *cis* alkene containing unsaturated esters are accessible efficiently (74–90% yield) and selectively (96:4–97:3 e.r., cf. **4.135**–**4.137** in entries 5–7). An unique feature associated with these transformations is the use of only 1 mol % of the sulfonate bearing imidazolinium salt **4.116** in combination with 10 mol % commercially available CuCl as the optimal conditions.[53] The methyl substituted allylic phosphates, on the other hand, require the use of a modified unsymmetrical imidazolinium salt **4.150**, which is consistent with the observation in Scheme 4.21. Slightly diminished enantioselective levels (87:13–95:5 e.r.) are obtained in synthesizing this class of 1,4-dienes; the Z olefin geometry, nevertheless, remains intact in all cases (entries 8–10).

Table 4.4: NHC–Cu-catalyzed EAS with *cis* Me-substituted Vinylboron Reagents.[a]



Entry	G, R	Conv. [%][b]	Yield [%][c]	$S_N2':S_N2$[b]	e.r.[d]
1	H, H; **4.131**	90	76	>98:2	95:5
2	*o*-OMe, H; **4.132**	>98	82	>98:2	97:3
3	*m*-CF_3, H; **4.133**	95	76	>98:2	98:2
4	*o*-Me, H; **4.134**	92	78	>98:2	98:2
5[e]	*p*-CF_3;, COOMe **4.135**	>98	81	>98:2	97:3
6[e]	*o*-OMOM, COOMe; **4.136**	95	74	>98:2	97:3
7[e]	*p*-Me, COOMe; **4.137**	93	90	>98:2	96:4
8[f]	H, Me; **4.138**	86	77	98:2	91:9
9[f]	*o*-Me, Me; **4.139**	89	87	98:2	87:13
10[f]	*p*-NO_2, Me; **4.140**	>98	96	>98:2	95:5

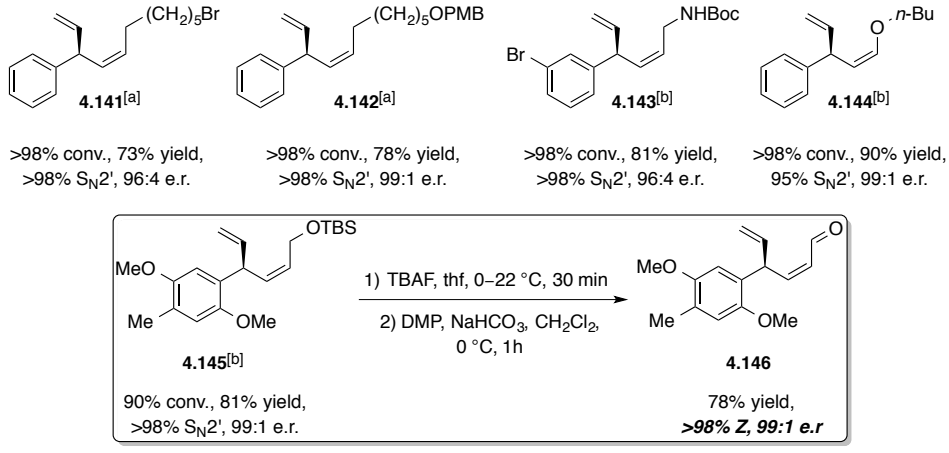
[a] Reactions were performed under N_2 atmosphere. [b] Determined through analysis of 400 MHz ^{1}H NMR spectra of unpurified mixtures. [c] Yields of isolated products after purification (±5%). [d] Determined by HPLC analysis (±2%); see the Supporting Information for details. [e] Reactions were performed with 1 mol % of **4.116**, 10 mol % of CuCl, 1.5 equiv NaOMe and at 60 °C. [f] Reactions were performed with imidazolinium salt **4.150** under otherwise identical conditions.

Additional examples that employ other alkyl-substituted *cis* alkenylBpins than propenyl based **4.130** are outlined in Figure 4.3; Z selective olefin cross metathesis

(53) Reactions with standard 5.5 mol % NHC and 5.0 mol % CuCl combination proceed to lower conversion. Rationale may arise from the unique structure of the substrate, which has two possible Lewis basic oxygen possible for a potential chelate activation rendered by excess Cu salt.

provides accesss to these boron reagents. As illustrated, a halogen atom and PMB ether are tolerated under the conditions described in Table 4.4, delivering *cis* alkenes **4.141** and **4.142** in complete site selectivity and 96:4 and 99:1 e.r., respectively. One notable point with these transformations is the reversal of stoichiometry of the alkenylboron reagents and the allylic phosphates; such a feature ensures that when a more precious alkenylBpin is utilized in Cu-catalyzed EAS, maximum utility of the reagent is possible with a little excess of the electrophile. The somewhat diminished yields (73–78%) suffer from the adventitious protonation of alkenyl-Cu species by trace amount of moisture. The compatibility with a *cis* allylic amide (**4.143**), allylic silylether (**4.145**) and alkylvinyl ether (**4.144**) further demonstrates the generality of the present method; EAS reactions are capable of incorporating such entities into the versatile 1,4-diene products in 81–90% yields, >95% S_N2' selectivity and 96:4–99:1 enantiomer ratios. The subsequent conversion of the Z allylic silylether, in an efficient two-step sequence, to Z enal **4.146** with complete retention of the alkene geometry is noteworthy.

Figure 4.3: Additional Examples of EAS with *cis* 1,2-Disubstituted Alkenylboron Reagents.

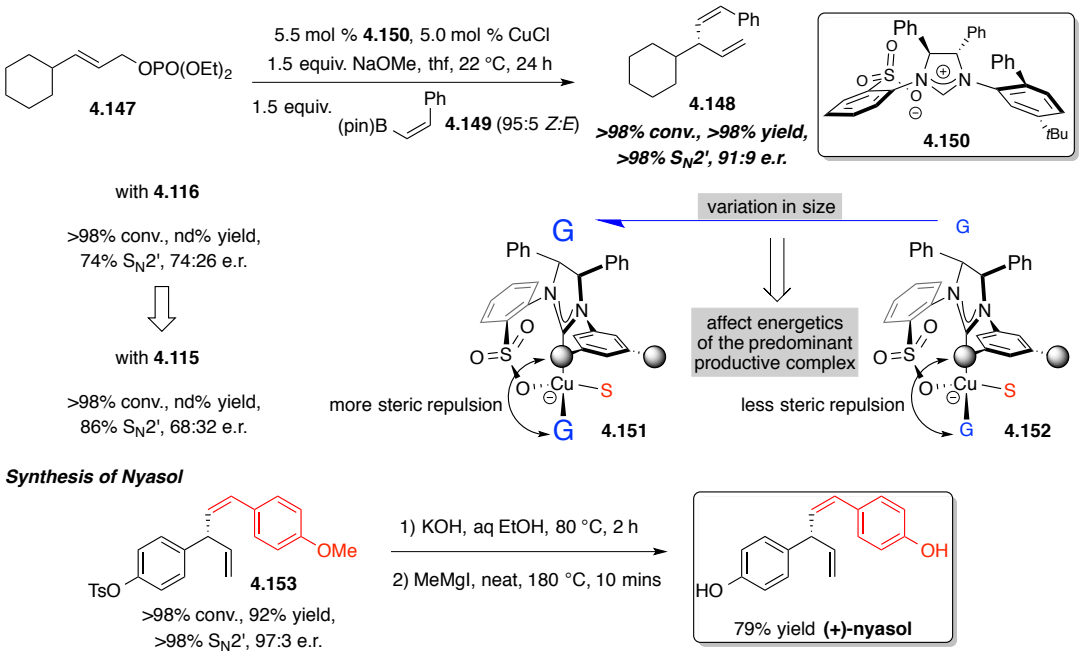


[a] Reactions were performed with 1.0 equiv alkenylBpin, 1.25 equiv NaOMe and 1.25 equiv of allylic phosphates. [b] Reactions were performed with 1.5 equiv alkenylBpin and 1.5 equiv NaOMe under otherwise identical conditions as in Table 4.4.

When it comes to the additions of a *cis* aryl-substituted alkenylBpin reagent, the optimal Cu catalyst that is derived from 3,5-(2,4,6-tri*iso*propylphenyl)-phenyl containing imidazolinium salt **4.116** becomes a sluggish promoter of the EAS reaction. For instance, the coupling between allylic phosphate **4.147** and alkenylBpin **4.149**, in the presence of 5 mol % of Cu complex of **4.116**, proceeds to complete conversion at 22 ºC after 24 h, but only furnishing 74% desired regioisomer and in 74:26 e.r. (Scheme 4.22). The hypothesis for such incompetence is showcased in Scheme 4.22; the active stereochemical model associated with NHC–Cu complex of **4.116** puts the relatively smaller *cis* alkenyl unit (cf. G in **4.152**) underneath one of the large tri*iso*propylphenyl substituent so that the more sizable allylic phosphate is placed in the open coordination site *anti* to the sulfonate chelate (for details regarding such a binding preference, please refer to Chapter 1). As the effective size of the alkenyl unit gets larger (i.e., an aromatic substituted Z alkene), it imposes more severe steric repulsion with the large substituent at the *meta* position of the N-Ar of the carbene ligand, increasing the energy of the preferred mode of reaction (cf. **4.151** in Scheme 4.22). As a result, the energetic gap becomes smaller and the competitive mode, in which the substrate and G group switch positions, starts to operate, thus lowering the enantioselectivity and overall efficiency of the transformation. Based on the above analysis, reduction of the size of the *meta* substituent may be helpful in achieving couplings with **4.149**; the result with 3,5-di*tert*butyl N-Ar containing salt **4.115** is somewhat promising with improved site selectivity (86%). Complete removal of interacting *meta t*Bu group and installment of an *ortho* Ph substituent (cf. **4.150**) restores high efficiency and selectivity levels for Cu-catalyzed coupling of **4.147** and **4.149** (>98% yield, >98% S_N2' and 91:9 e.r., Scheme 4.22). The newly introduced *o*-Ph

substituent plays the role of interacting with the more extended linear allylic phosphate so that the competitive mode remains higher in energy. With the identification of the modified optimal imidazolinium salt **4.150**, we carried out the synthesis of natural product nyasol. The advanced intermediate **4.153**, which is constructed by coupling of a *p*-methoxyphenyl substituted alkenylBpin (prepared using cross metathesis) and a *p*-OTs bearing allylic phosphate, is readily accessible under the new catalytic conditions and is obtained in 92% yield and 97:3 e.r. It is further converted to (+)-nyasol[54] after consecutive removal of the tosyl group and the methylaryl ether in a two-step sequence in 79% overall yield.

Scheme 4.22: Change of Optimal Imidazolinium Salt for Additions of Aryl-substituted cis AlkenylBpin.



(54) For isolation and selected previous syntheses, see: (a) Shen, Y. C.; Tsai, P. I.; Fenical W.; Hay, M. E. *Phytochemistry* **1993**, *52*, 71–75. (b) Takahashi, M.; Shioura, Y.; Murakami T.; Ogasawara, K.; *Tetrahedron: Asymmetry* **1997**, *8*, 1235–1242. (c) Fadel, A.; Vandromme, L. *Tetrahedron: Asymmetry* **1999**, *10*, 1153–1162. (d) Alibés, R.; Busqué, F.; Bardaji, G. G.; de March, P.; Figueredo, M.; Font, J. *Tetrahedron: Asymmetry* **2006**, *17*, 2632–2632.

The ability to introduce versatile alkenyl groups in Cu-catalyzed EAS allows us to further investigate the synthetic utilities of the building blocks generated from such transformations. The heliannuol family of natural products[55] and the related heliespirones[56] are suitable targets to challenge the EAS protocols involving cis alkenylBpins; we surmised that it is possible for us to quickly access one common intermediate **4.158** that could lead to all four naturally occurring molecules shown in Scheme 4.23. The sequence starts with an inconsequential 4:1 diastereomer mixture of diene **4.154**, which is obtained through NHC–Cu-catalyzed coupling reaction between a racemic cis alkenylBpin and the corresponding allylic phosphate (79% yield, 98:2 e.r., Scheme 4.23). The subsequent deprotection of the silylether and oxidation of the resulting secondary allylic alcohol gives enantioenriched Z enone **4.155** in 65% yield over two steps (98% e.r.). Methyl addition to the ketone at –78 ºC affords the desired Z tertiary allylic alcohol **4.156** in 92% yield, which is subjected to Ti(O*i*Pr)$_4$ mediated directed epoxidation reaction to deliver epoxy alcohol **4.157** in 76% yield and 92:8 diastereomeric ratio. Site selective $LiBH_4$ opening of the epoxide, again mediated by Ti(O*i*Pr)$_4$,[57] results in the desired 1,2-diol **4.158** in 55% yield after 18 h at 50 ºC. This diol has been demonstrated in the previous reports to be applicable in the synthesis of heliespirone A & C[56] and heliannuol E[55e] in short steps. Meanwhile, we are attempting to

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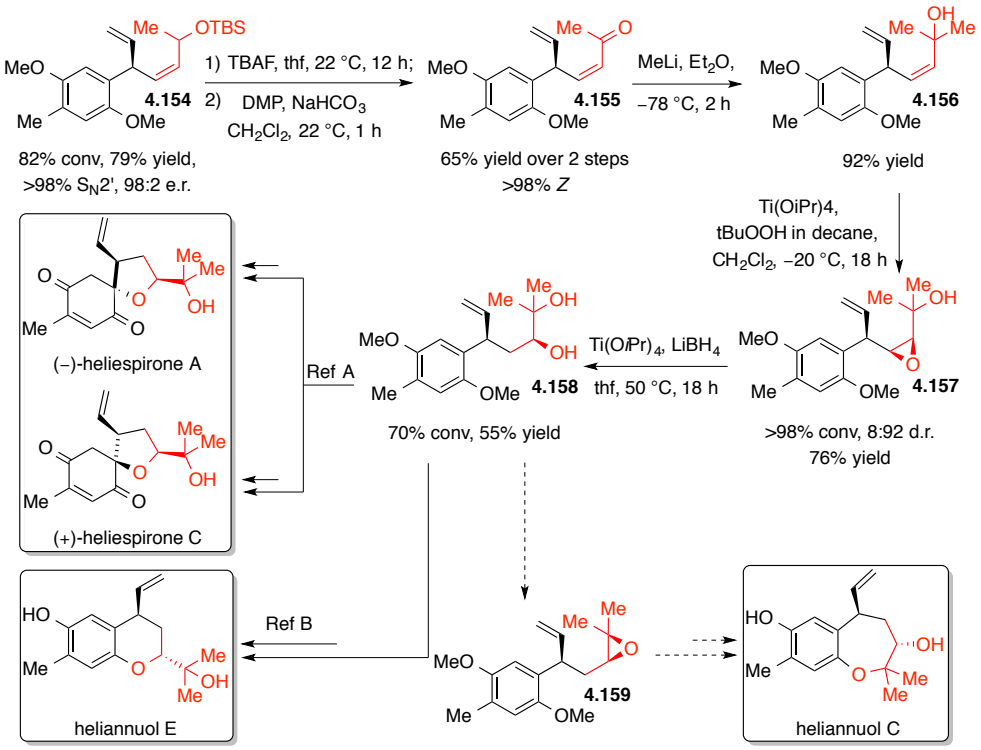
(55) For isolation, see: (a) Masías, F. A.; Molinillo, J. M. G.; Varela, R. M.; Torres, A. *J. Org. Chem.* **1994**, *59*, 8261–8266. For previous synthesis of haliennuol C, see: (b) Kamei, T.; Shindo, M.; Shishido, K. *Tetrahedron Lett.* **2003**, *44*, 8505–8507. (c) Vyvyan, J. R.; Oaksmith, J. M.; Parks, B. W.; Peterson, E. M. *Tetrahedron Lett.* **2005**, *46*, 2457–2460. (d) Biswas, B.; Sen, P. K.; Venkateswaran, R. V. *Tetrahedron Lett.* **2006**, *47*, 4019–4021. For previous synthesis of haliennuol E, see: (e) Liu, Y.; Huang, C.; Liu, B. *Tetrahedron Lett.* **2011**, *52*, 5802–5804.
(56) Huang, C.; Liu, B. *Chem. Commun.* **2010**, *46*, 5280–5282 and references cited therein.
(57) Dai, L.-x.; Lou, B.-l.; Zhang, Y.-z.; Guo, G.-z. *Tetrahedron Lett.* **1986**, *27*, 4343–4346.

complete the synthesis of heliannuol C as well through a proposed epoxide intermediate **4.159** from the enantiomerically enriched diol **4.158**.

Scheme 4.23: Applications to Syntheses of Heliannuols C&E and Heliespirones A&C.



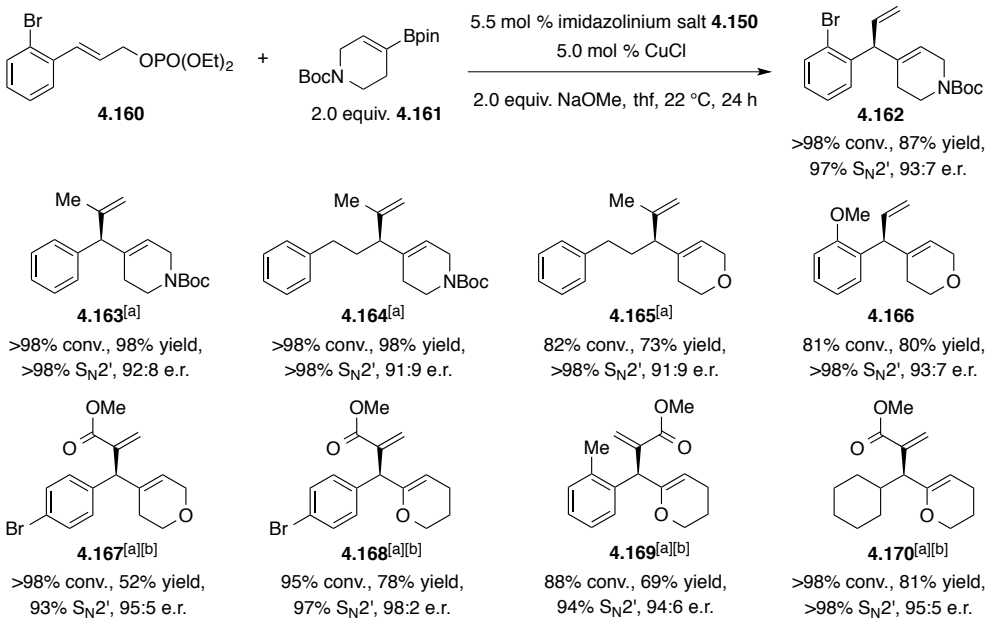
4.4.4 Cu-catalyzed EAS with Heterocyclic AlkenylBpin Reagents

There are examples of additions of carbocycles through enantioselective allylic substitution in the literature; one of them involves a chiral NHC–Cu complex reported by Hayashi (cf. Scheme 4.8 for one specific example with low enantioselectivity value).[20] However, cases, in which the additions of heterocyclic alkenylboron reagents are realized, are not known in enantioselective allylic substitution to date.[1] Here in Scheme 4.24, we described the first examples that couple such entities with a range of allylic phosphates enantioselectively. For a specific instance, an *o*-Brphenyl substituted allylic phosphate **4.160** is converted to a Boc protected dihydropiperidine **4.162** in 87% yield, 97% S_N2' selectivity and 93:7 e.r. when the reaction is carried out in the presence of 5

mol % Cu catalyst of imidazolinium salt **4.150**. The commercially available heterocyclic alkenylBpin reagent **4.161** serves as the nucleophile. EAS reactions with **4.161** are also applicable to trisubstituted allylic phosphates, but have to be performed at elevated temperature (60 ºC) to ensure complete conversions; representative products **4.163** and **4.164** are delivered in almost quantitative yields and 91:9–92:8 e.r. Dihydropyran group can also be incorporated through Cu-catalyzed EAS into 1,4-dienes that are from three different classes of allylic phosphate substrates (cf. **4.165**–**4.167** in Scheme 4.24); the corresponding transformations are efficient (52–80% yield) and selective (93%–>98% S_N2' and 91:9–95:5 e.r.). An isomeric dihydropyran is also suitable for the additions to allylic phosphates through Cu-catalyzed EAS; however, only the products that bear the ester functionality can be isolated and obtained in analytic pure form.[58] The resulting enoates are furnished in 69–81% yield and 94:6–98:2 e.r. with high site selectivity as usual (>94% S_N2', cf. **4.168**–**4.170**). Again, with these ester substituted allylic phosphates, EAS reactions are carried out with only 2.5 mol % chiral salt **4.150** and 25 mol % CuCl.

(58) Other products, derived from additions of this oxygen containing heterocyclic alkenylBpin reagent to either disubstituted or trisubstituted allylic phosphates that do not bear an ester functionality, can be observed by crude NMR and formed cleanly; However, any attempt of isolation through silica gel column is unsuccessful, resulting in complete product decomposition.

Scheme 4.24: NHC–Cu-catalyzed EAS with Heterocyclic Alkenylboron Reagents.



[a] Reactions were performed at 60 °C under otherwise identical conditions. [b] Reactions were performed with 2.5 mol % **4.150** and 25 mol % CuCl at 60 °C under otherwise identical conditions .

The advantage of having a heterocyclic structure in the 1,4-diene product is showcased in the diastereo- and enantioselective synthesis of naturally occurring small molecule semburin (Scheme 4.25).[59] EAS reaction that couples a silyl ether bearing allylic phosphate and a dihydropyran moiety occurs in high efficiency, delivering the 1,4-diene **4.171** in quantitative yield, albeit in lower enantioselectivity (83:17 e.r.) when imidazolinium salt **4.150** is used. Oxidation of the dihydropyran unit with PCC at 80 °C for 12 h gives enantiomerically enriched lactone **4.172** in 78% yield. The subsequent conjugate reduction with silane catalyzed by an achiral monodentate carbene copper system results in minimal diastereoselectivity (~1:1 d.r.).[60] We then turned our attention to identify a chiral monodentate *N*-heterocyclic carbene ligand that could induce the

(59) Kawamura, M.; Ogasawara, K. *Tetrahedron Lett.* **1995**, *36*, 3369.
(60) Jurkauskas, V.; Sadighi, J. P.; Buchwald, S. L. *Org. Lett.* **2003**, *5*, 2417.

diastereoselective conjugate reduction;[61] after an extensive screening, tetrafluoroborate salt **4.173**[62] was revealed as the optimal ligand on copper to deliver product **4.174** in 92% yield as a 78:22 diastereomer mixture and with 96:4 e.r. of the major isomer. Deprotection of the silylether by tetrabutylammonium fluoride at 0 ºC for 30 minutes generates the desired compound **4.175** along with a constitutional isomer **4.176**, both of which can be converted to the final target semburin through a two-step sequence in 65% overall yield. Isolation of the desired natural product from the minor isosemburin (derived from the minor diastereomer of **4.174**) is tedious and the volatility issue can further diminish the yield of semburin; therefore, a more enantioselective chiral sulfonate containing carbene for the preparation of **4.171** can substantially benefit the efficiency of the entire synthetic sequence.

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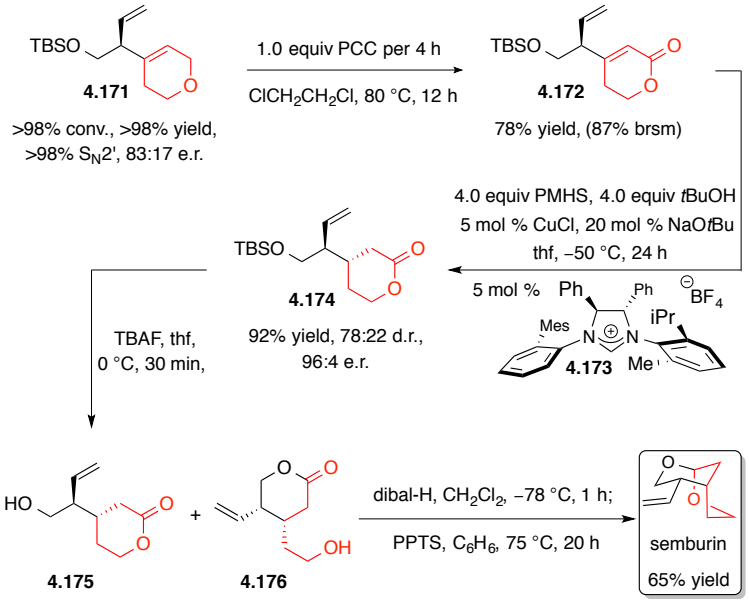
(61) For an example with chiral phosphine Cu complex, see: Hughes, G.; Kimura, M.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 11253. This protocol, however, provides the desired lactone 4.174 in lower yield (~60%); unidentified byproduct formation causes the reduced efficiency.

(62) (a) Vieira, E. M.; Haeffner, F.; Snapper, M. L; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2012**, *51*, 6618–6621. (b) Vieira, E. M.; Snapper, M. L; Hoveyda, A. H. *J. Am., Chem. Soc.* **2011**, *133*, 3332–3335.

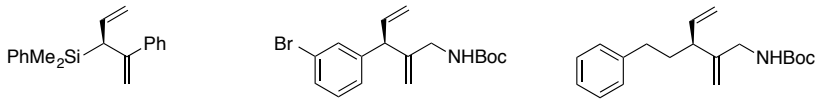
Scheme 4.25: Enantioselective Synthesis of Natural Product Semburine.



4.4.5 Cu-catalyzed EAS with 1,1-Disubstituted AlkenylBpin Reagents

In Figure 4.4, we demonstrate cases where 1,1-disubstituted alkenylBpin reagents are effectively incorporated into 1,4-diene products bearing differently substituted tertiary stereogenic centers. Specifically, allylsilane **4.177** is synthesized in 93% yield and 97:3 e.r. through EAS reaction catalyzed by Cu catalyst of sulfonate containing imidazolinium salt **4.116** at ambient temperature within 24 h. Enantioenriched allylic Boc amides **4.178** and **4.179** are furnished in 84% and 89% yield, and 98:2 and 80:20 e.r., respectively, by coupling the corresponding alkenylBpin with aryl and alkyl-substituted allylic phosphates at 60 °C under otherwise identical conditions as in the formation of **4.177**. Complete site selectivity is observed in all cases (>98% S_N2').

Figure 4.4: Additional Examples of EAS with 1,1-Disubstituted Alkenylboron Reagents.[a]



4.177[b]
>98% conv., 93% yield,
>98% S_N2', 97:3 e.r.

4.178
>98% conv., 89% yield,
>98% S_N2', 98:2 e.r.

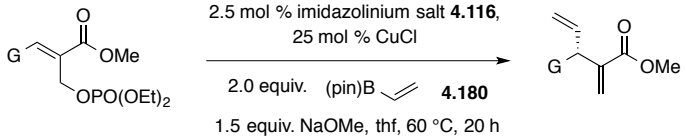
4.179
>98% conv., 84% yield,
>98% S_N2', 80:20 e.r.

[a] Reactions were performed at 60 °C under otherwise identical conditions as those in Scheme 4.24. [b] Reactions were performed at 22 °C under otherwise identical conditions .

4.4.6 Cu-catalyzed EAS with Unsubstituted VinylBpin Reagents

Unsubstituted vinyl group is probably the most common olefin motif that resides adjacent to a stereogenic center within many natural products. The reliable organometallic surrogates of such an entity, however, are limited due to the instability issues associated with them. Commercially available vinylboronic acid pinacol ester, on the other hand, can potentially serve as an ideal nucleophile because of the robustness and the ease of handling. In this section, we delineate our efforts in utilizing such a reagent in NHC–Cu-catalyzed EAS reactions to construct a tertiary stereogenic center (Table 4.5). A representative enoate product **4.181** is obtained in 85% yield, complete site selectivity and exceptional enantiomer ratio (99:1, entry 1); the reaction is carried out with 2.5 mol % imidazolinium salt **4.116** and 25 mol % CuCl at 60 °C for 20 h. The scope of the reaction is general, tolerating sterically demanding naphthal substitution on the substrates (entries 2–3), and electron withdrawing (entries 4–5 and 7) as well as donating substituent (entries 6 and 8) on the aryl-substituted allylic phosphates. The vinyl bearing enantioenriched enoates are furnished in 43–82% yields, uniformly high site selectivity and 97:3–99:1 e.r. values. When an alkyl-substituted allylic phosphate serves as the substrate, an alternative imidazolinium salt **4.150** becomes optimal in terms of enantioselectivity; the desired diene **4.189** is delivered in 66% yield and 94:6 e.r. Even more interestingly, the major enantiomer shows opposite sense of stereochemical induction to the one synthesized with salt **4.116**; the reason for such an intriguing contrast is unclear at this moment.

Table 4.5: NHC–Cu-catalyzed EAS with Vinylboron Reagents.[a]

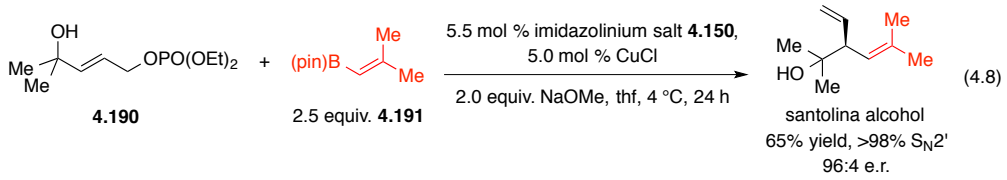


Entry	G	Conv. [%][b]	Yield [%][c]	$S_N2':S_N2$[b]	e.r.[d]
1[e]	Ph; **4.181**	>98	85	>98:2	99:1
2	2-naphthal; **4.182**	85	69	>98:2	99:1
3[e]	1-naphthal; **4.183**	76	55	>98:2	99:1
4[f]	*p*-BrC_6H_4; **4.184**	82	49	>98:2	98:2
5[e]	*p*-$CF_3C_6H_4$; **4.185**	>98	68	>98:2	98:2
6	*o*-$OMeC_6H_4$; **4.186**	92	82	>98:2	97:3
7	*o*-BrC_6H_4; **4.187**	80	43	>98:2	98:2
8[g]	*o*-$OMOMC_6H_4$; **4.188**	83	79	>98:2	98:2
9[h]	Cy; **4.189**	83	66	>98:2	6:94

[a] Reactions were performed under N_2 atmosphere. [b] Determined through analysis of 400 MHz ^{1}H NMR spectra of unpurified mixtures. [c] Yields of isolated products after purification (±5%). [d] Determined by HPLC analysis (±2%); see the Supporting Information for details. [e] 10 mol % **4.116** and 10 mol % CuCl used. [f] 1.0 mol % **4.116** and 10 mol % CuCl used. [g] 3.0 equiv vinylBpin reagent used. [h] 1.0 mol % **4.150** and 10 mol % CuCl is used and the product is afforded as the opposite enantiomer of that obtained from reactions promoted with **4.116**.

4.4.7 Cu-catalyzed EAS with Trisubstituted AlkenylBpin Reagents

Trisubstituted alkenylBpin reagents are usable as well in Cu-catalyzed EAS reaction; the one step enantioselective synthesis of santolina alcohol[63] showcases the utility of this class of transformations. As shown in Eq 4.8, in the presence of 5 mol % in situ generated Cu complex of imidazolinium salt **4.150**, the tertiary alcohol containing allylic phosphate **4.190** is transformed to santolina alcohol when exposed to the commercially available alkenylBpin **4.191**; high levels of selectivity (96:4 e.r. and >98% S_N2') are observed as the reaction is performed at 0 °C for 24 h. Moderate yield of the target molecule is a consequence of its relatively volatile nature.



(4.8)

(63) Santolina alcohol is a component in plant essential oils from various origins and now a commercially available natural product used as a analytical standard for terpene analysis.

4.5 Conclusion

In this chapter, we have demonstrated two general protocols that address long lasting challenges in C-C bond formations through allylic substitution reactions catalyzed by abundant copper; several distinct enantiomerically pure sulfonate containing N-heterocyclic carbenes are developed to suit a variety of substrate/nucleophile combinations, providing products in generally high efficiency, site selectivity and enantioselectivity. The first set of conditions allow access to quaternary stereogenic center containing 1,4-dienes; the utilization of air and moisture insensitive, readily available alkenylboronic acid pinacol esters further advances the method by introducing functionalities that are otherwise difficult-to-access through previously reported procedures. The second part of the study deals with the couplings of different classes of versatile alkenylBpin reagents with a range of allylic phosphates; two optimal imidazolinium salts are identified to fulfill the needs when drastically different substrate/alkenylBpin combinations are targeted. Additionally, the applications to efficient, diastereo- and enantioselective synthesis of naturally occurring molecules, which are from distinct origins, have been outlined in details to showcase the utilities of the present methods.

4.6 Experimentals

4.6.1 Representative Experimental Procedures for Cu-catalyzed EAS with Alkenylboron Reagents to Construct All Carbon Quaternary Stereogenic Center and Characterization Data of New Compounds

General. Infrared (IR) spectra were recorded on a Bruker FT-IR Alpha (ATR mode) spectrophotometer, ν_{max} in cm^{-1}. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). ^{1}H NMR spectra were recorded on a Varian Unity INOVA 400 (400 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on a Varian Unity INOVA 400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: 77.16 ppm). High-resolution mass spectrometry was performed on a Micromass LCT ESI-MS (positive mode) at the Mass Spectrometry Facility, Boston College. Enantiomer ratios were determined by GLC analysis (gas liquid chromatography) with an Agilent chromatograph (Alltech Associated Chiral dex CD-BDM column (30 m x 0.25 mm)), HPLC analysis (high-performance liquid chromatography) with a Shimadzu chromatograph (Chiral Technologies Chiralcel OD-H (4.6 x 250 mm), Chiral Technologies Chiralpak AD-H (4.6 x 250 mm), Chiral Technologies Chiralcel OJ-H (4.6 x 250 mm) Chiral Technologies Chiralpak AS-H (4.6 x 250 mm)) and SFC analysis (supercritical fluid chromatography) with a Thar chromatograph (Chiral Technologies Chiralcel OD-H (4.6 x 250 mm)) in comparison with authentic racemic materials. Specific rotations were measured on a Rudolph Research Analytical Autopol IV Polarimeter.

Unless otherwise noted, all reactions were carried out with distilled and degassed solvents under an atmosphere of dry N_2 in oven- (135 °C) or flame-dried glassware with

standard dry box or vacuum-line techniques. Toluene and dichloromethane (Fisher Scientific) were purified by passing through two alumina columns under a positive pressure of dry argon by a modified Innovative Technologies purification system. Tetrahydrofuran (Aldrich Chemical Co.) was purified by distillation from sodium benzophenone ketyl immediately prior to use unless otherwise specified. All work-up and purification procedures were carried out with reagent grade solvents (purchased from Fisher Scientific) under air. All substrates are prepared according to previously reported procedures and the characterization data of the unknown compounds will be disclosed within this text;[64] all substrates possess *E*-olefin geometry and purities are established by ^{1}H NMR analysis (400 MHz).

■ **Reagents and Imidazolinium Salts:**

9-Borabicyclo[3.3.1]nonane (0.5 M in thf): purchased from Aldrich Chemical Co. and used as received.

(*E*)-2-(5-Chloropent-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane: purchased from Aldrich Chemical Co. and purified by distillation over CaH_2.

Cinchonidine: purchased from Aldrich Chemical Co. and used as received.

Cinchonine: purchased from Aldrich Chemical Co. and used as received.

Copper(I) chloride: purchased from Strem Chemicals Inc. and used as received.

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(64) (a) C. A. Luchaco-Cullis, H. Mizutani, K. E. Murphy, A. H. Hoveyda, *Angew. Chem. Int. Ed.* **2001**, *40*, 1456–1460; (b) M. A. Kacprzynski, T. L. May, S. A. Kazane, A. H. Hoveyda, *Angew. Chem. Int. Ed.* **2007**, *46*, 4554–4558; (c) Y. Lee, A. H. Hoveyda, *J. Am. Chem. Soc.* **2006**, *128*, 15604–15605; (d) F. Gao, K. P. McGrath, Y. Lee, A. H. Hoveyda, *J. Am. Chem. Soc.* **2010**, *132*, 14315–14320; (e) J. A. Dabrowski, F. Gao, A. H. Hoveyda, *J. Am. Chem. Soc.* **2011**, *133*, 4778–4781.

(*E*)-2-(3,3-Diethoxyprop-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.103): generously donated to us by Frontier Scientific Inc. and used as received.

Di*iso*butylaluminum hydride (neat): purchased from Aldrich Chemical Co. and used as received.

***N,O*-Dimethylhydroxylamine hydrochloride:** purchased from Aldrich Chemical Co. and used as received.

(*E*)-Ethyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (4.97): generously donated to us by Frontier Scientific Inc. and used as received.

Imidazolinium salts 4.48 and 4.70: prepared according to a previously reported procedure.[65]

Imidazolinium salt 4.49: prepared according to a previously reported procedure.[66]

Imidazolinium salt 4.71: prepared according to a previously reported procedure.[67]

Imidazolinium salt 4.51: prepared according to a previously reported procedure.[68]

Imidazolinium salts 4.72 and 4.73: prepared according to a previously reported procedure.[69]

Imidazolinium salt 4.74: prepared according to a previously reported procedure.[70]

Imidazolinium salt 4.75: prepared according to a previously reported procedure.[71]

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(65) K-s. Lee, A. H. Hoveyda, *J. Org. Chem.* **2009**, *74*, 4455–4462.
(66) J. J. Van Veldhuizen, J. E. Campbell, R. E. Giudici, A. H. Hoveyda, *J. Am. Chem. Soc.* **2005**, *127*, 6877–6882.
(67) D. Martin, S. Kehrli, M. d'Augustin, H. Clavier, M. Mauduit, A. Alexakis, *J. Am. Chem. Soc.* **2006**, *128*, 8416–8417.
(68) M. K. Brown, T. L. May, C. A. Baxter, A. H. Hoveyda, *Angew. Chem. Int. Ed.* **2007**, *46*, 1097–1100.
(69) Y. Lee, A. H. Hoveyda, *J. Am. Chem. Soc.* **2009**, *131*, 3160–3161.
(70) Y. Lee, K. Akiyama, D. Gillingham, M. K. Brown, A. H. Hoveyda, *J. Am. Chem. Soc.* **2008**, *130*, 446–447.

***Iso*propyl alcohol (HPLC grade):** purchased from Fisher Scientific and used as received.

***Iso*-propylmagnesium chloride (~1.0 M solution in thf):** prepared from *iso*propyl chloride and Mg turnings in thf and used immediately after titration.

(*E*)-2-(4-Methoxystyryl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane: prepared according to a previously reported procedure.[72]

Methyl alcohol (extra dry): purchased from Acros Organics and used as received from an Acroseal container.

Oxone: purchased from Aldrich Chemical Co. and used as received.

Phosphine free Ru carbene complex 4.114: purchased from Materia Inc. and purified by column chromatography followed by recrystallization before use.

Sodium methoxide: purchased from Strem Chemicals Inc. and used as received.

Sodium perborate tetrahydrate: purchased from Aldrich Chemical Co. and used as received.

(*E*)-4,4,5,5-Tetramethyl-2-(oct-1-en-1-yl)-1,3,2-dioxaborolane (4.64): purchased from Aldrich Chemical Co. and purified by distillation over CaH_2.

(*E*)-4,4,5,5-Tetramethyl-2-styryl-1,3,2-dioxaborolane: purchased from Aldrich Chemical Co. and purified by distillation over CaH_2.

Vinylmagnesium bromide (1.0 M solution in thf): purchased from Aldrich Chemical Co. and used immediately after titration.

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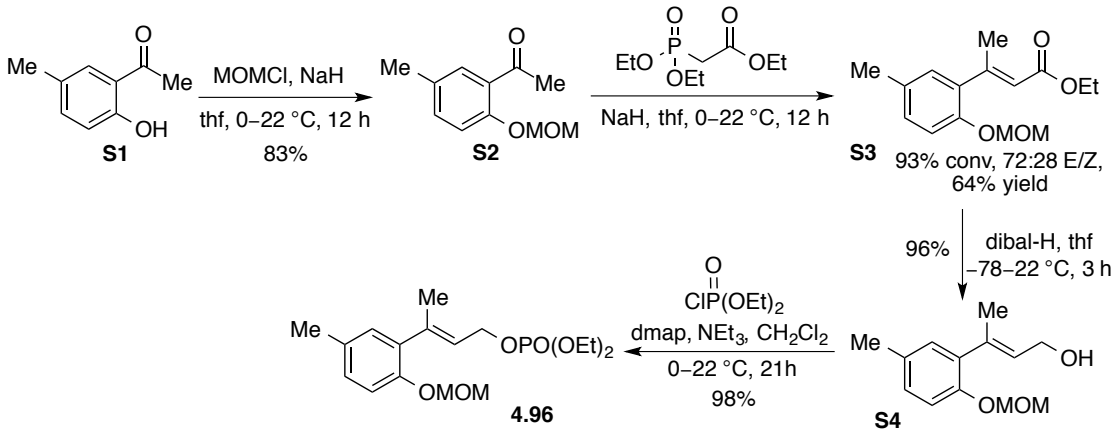
(71) K. Akiyama, F. Gao, A. H. Hoveyda, *Angew. Chem. Int. Ed.* **2010**, *49*, 419–423.
(72) F. Gao, A. H. Hoveyda, *J. Am. Chem. Soc.* **2010**, *132*, 10961–10963.

■ **Tri-substituted Allylic Phosphate 4.96:** The compound is prepared according to previous reported procedures;[64] detailed reaction sequence is shown in Scheme S1.

Scheme S1. Synthesis of Tri-substituted Allylic Phosphate **4.96**



(*E*)-Diethyl (3-(2-(methoxymethoxy)-5-methylphenyl)but-2-en-1-yl) phosphate (4.96): IR (neat): 2982 (w), 2909 (w), 1495 (w), 1395 (w), 1262 (m), 1157 (w), 973 (s), 811 (m), 730 (m), 523 (w), 486 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.03–6.95 (3H, m), 5.65 (1H, dt, *J* = 6.8, 1.2 Hz), 5.12 (2H, s), 4.73 (2H, dd, *J* = 7.6, 7.6 Hz), 4.14 (1H, dq, *J* = 7.2, 7.2 Hz), 3.45 (3H, s), 2.27 (3H, s), 2.06 (3H, d, *J* = 0.8 Hz), 1.35 (6H, t, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.1, 140.9, 134.2, 131.4, 130.2, 129.1, 123.8 (d, *J* = 6.7 Hz), 115.0, 94.9, 64.2 (d, *J* = 6.0 Hz), 63.8 (d, *J* = 5.2 Hz), 56.2, 20.6, 17.7, 16.3 (d, *J* = 6.7 Hz); HRMS (ESI+): Calcd for $C_{17}H_{28}P_1O_6$ $[M+H]^+$: 359.16235, Found: 359.16154.

■ **Imidazolinium Salt 4.76:** The compound is prepared through the same reaction sequence as described in a previous report;[70] the requisite tri-*iso*propylaniline is

synthesized according to a known procedure.[73] Characterization data: IR (neat): 2962 (m), 2970 (w), 1624 (s), 1590 (m), 1461 (m), 1287 (w), 1240 (s), 1202 (s), 1090 (m), 1022 (m), 761 (w), 726 (w), 702 (w), 612 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.79 (1H, s), 8.13 (1H, d, *J* = 7.6 Hz), 7.51–7.42 (5H, m), 7.29–7.25 (1H, m), 7.12–7.05 (3H, m), 6.67 (1H, d, *J* = 8.0 Hz), 6.25 (1H, dd, *J* = 12.0, 9.6 Hz), 4.80 (1H, dd, *J* = 12.0, 12.0 Hz), 4.10 (1H, dd, *J* = 11.2, 10.0 Hz), 3.60 (1H, septet, *J* = 6.8 Hz), 3.17 (1H, septet, *J* = 6.8 Hz), 2.93 (1H, septet, *J* = 6.8 Hz), 1.39 (3H, d, *J* = 6.4 Hz), 1.33–1.26 (15H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9, 152.1, 147.8, 145.5, 143.7, 136.1, 130.7, 130.2, 129.85, 129.83, 129.78, 129.73, 128.4, 127.4, 126.7, 123.6, 122.6, 68.3, 61.5, 34.5, 29.0, 28.3, 25.0, 24.90, 24.87, 23.97, 23.95; HRMS (ESI+): Calcd for $C_{30}H_{37}N_2O_3S_1$ $[M+H]^+$: 505.25249, Found: 505.25327. Specific Rotation: $[\alpha]_D^{20}$ +98.3 (*c* 1.53, $CHCl_3$) for an enantiomerically pure sample.

■ **Representative Experimental Procedure for Cu-Catalyzed Enantioselective Allylic Substitution (EAS) with Alkenylboron Reagents:** In an N_2-filled glove box, an oven-dried 1-dram vial (15 x 45 mm) with a magnetic stir bar is charged with imidazolinium salt **4.75** (5.1 mg, 0.011 mmol), NaOMe (21.6 mg, 0.400 mmol) and CuCl (1.0 mg, 0.010 mmol). The vial is sealed with a cap (phenolic open top cap with a red PFTE/white silicon septum) and electrical tape before removal from the glove box. To the vial under an N_2 atmosphere is added tetrahydrofuran (thf, 0.5 mL) and the resulting suspension is allowed to stir at 22 °C for one hour. The suspension turns from off-white

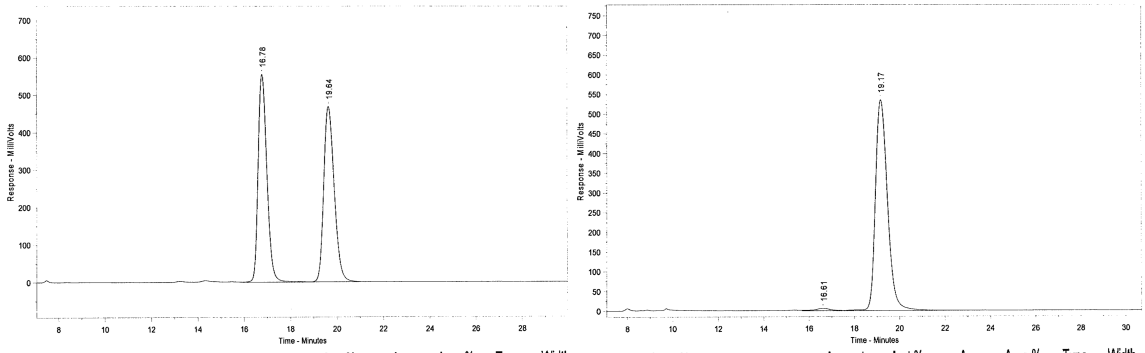
(73) J-Y. Liu, Y. Zheng, Y-G. Li, L. Pan, Y-S. Li, N-H. Hu, *J. Organometallic Chem.* **2005**, *690*, 1233–1239.

to light yellow during catalyst formation. Meanwhile, in a separate vial, (*E*)-diethyl (3-(2-methoxyphenyl)but-2-en-1-yl) phosphate **4.77** (62.9 mg, 0.200 mmol) and (*E*)-4,4,5,5-tetramethyl-2-(oct-1-en-1-yl)-1,3,2-dioxaborolane **4.64** (95.3 mg, 0.400 mmol) are weighted out and the vial is sealed and purged with N_2 flow for 10 min before thf (0.5 mL) is added through a syringe. The stock solution is transferred through a syringe to the reaction vessel that contains the in situ-formed catalyst and the resulting yellow solution is allowed to warm to 60 °C in an oil bath and kept stirring for an additional 24 h. The mixture is allowed to cool to ambient temperature before it is passed through a short plug of silica gel eluted with Et_2O. The filtrate is concentrated under reduced pressure to provide a yellow oil residue, which is purified by silica gel column chromatography (100:1 hexanes:Et_2O) to afford product **4.78** as colorless oil (51.4 mg, 0.189 mmol, 94% yield). **(*R*,*E*)-1-Methoxy-2-(3-methylundeca-1,4-dien-3-yl)benzene (4.78).** The product has been previously reported and spectra data match those previously described.[64d] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (1H, dd, *J* = 7.6, 1.6 Hz), 7.21 (1H, ddd, *J* = 8.0, 8.0, 1.6 Hz), 6.91–6.86 (2H, m), 6.19 (1H, dd, *J* = 17.6, 10.4 Hz), 5.74 (1H, dt, *J* = 15.6, 1.2 Hz), 5.32 (1H, dt, *J* = 15.6, 6.8 Hz), 5.01 (1H, dd, *J* = 10.4, 1.2 Hz), 4.91 (1H, dd, *J* = 17.2, 1.2 Hz), 3.76 (3H, s), 2.04 (2H, dt, *J* = 6.4, 6.4 Hz), 1.53 (3H, s), 1.37–1.27 (8H, m), 0.88 (3H, t, *J* = 6.4 Hz). Specific Rotation: $[\alpha]_D^{20}$ –3.82 (*c* 0.820, $CHCl_3$) for an enantiomerically enriched sample of 98.5:1.5 e.r.

Proof of Stereochemistry: Literature value ($[\alpha]_D^{20}$ –3.36 (*c* 1.00, $CHCl_3$), 98:2 e.r.) is assigned to the (*R*) enantiomer.[64d]

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation

with $NaBO_3•4H_2O$) in comparison with authentic racemic material (98.5:1.5 e.r. shown; Chiralcel OJ-H column, 99/1 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	16.78		0.00	N/A	14640510	49.781	BV	0.40
2	19.64		0.00	N/A	14769170	50.219	VB	0.48

Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	16.61		0.00	N/A	296045	1.476	BV	0.52
2	19.17		0.00	N/A	19765800	98.524	VB	0.56

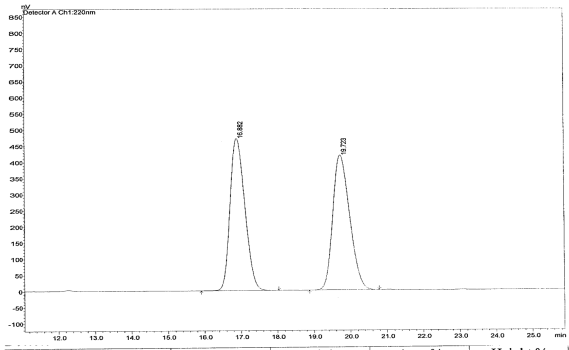
Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	16.78	49.8	1	16.61	1.5
2	19.64	50.2	2	19.17	98.5

(*R*,*E*)-(3-Methylundeca-1,4-dien-3-yl)benzene (4.65). The compound has been previously reported and spectra data match those described.[64d] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34–7.27 (4H, m), 7.21–7.17 (1H, m), 6.07 (1H, dd, *J* = 17.6, 10.8 Hz), 5.66 (1H, dt, *J* = 16.0, 1.6 Hz), 5.41 (1H, dt, *J* = 15.6, 6.8 Hz), 5.10 (1H, dd, *J* = 10.4, 1.2 Hz), 5.00 (1H, dd, *J* = 17.6, 1.2 Hz), 2.10–2.04 (2H, m), 1.47 (3H, s), 1.40–1.25 (8H, m), 0.90–0.87 (3H, m). Specific Rotation: $[\alpha]_D^{20}$ –6.38 (*c* 0.627, $CHCl_3$) for an enantiomerically enriched sample of 86:14 e.r.

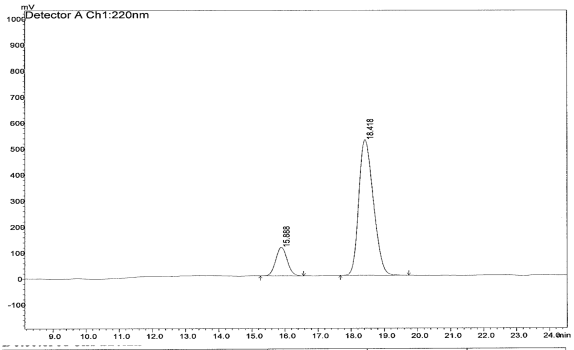
Proof of Stereochemistry: Literature value ($[\alpha]_D^{20}$ –5.31 (*c* 1.50, $CHCl_3$), 94.5:5.5 e.r.) is assigned to the (*R*) enantiomer.[64d]

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with $NaBO_3•4H_2O$) in comparison with authentic racemic material (86:14 e.r. shown;

Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm). The trace shown is obtained from compound derived from EAS with *R* enantiomer of catalyst.



Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.882	13335495	470693	49.812	53.009
2	19.723	13436279	417264	50.188	46.991
Total		26771774	887958	100.000	100.000



Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.888	2644505	110094	14.209	17.431
2	18.418	15966941	521516	85.791	82.569
Total		18611447	631610	100.000	100.000

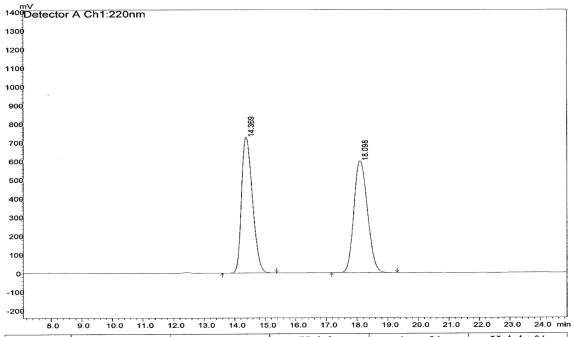
Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	16.88	49.8	1	15.89	14.2
2	19.72	50.2	2	18.42	85.8

(*R*,*E*)-1-Methyl-2-(3-methylundeca-1,4-dien-3-yl)benzene (4.84). The compound has been previously reported and spectra data match those described.[64d] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.35 (1H, m), 7.18–7.10 (4H, m), 6.13 (1H, dd, *J* = 17.6, 10.4 Hz), 5.71 (1H, dt, *J* = 16.0, 1.6 Hz), 5.26 (1H, dt, *J* = 15.6, 6.8 Hz), 5.04 (1H, ddd, *J* = 10.8, 0.8, 0.4 Hz), 4.88 (1H, dd, *J* = 17.6, 1.2 Hz), 2.31 (3H, s), 2.06–2.00 (2H, m), 1.51 (3H, s), 1.36–1.25 (8H, m), 0.89–0.86 (3H, m). Specific Rotation: $[\alpha]_D^{20}$ –6.06 (*c* 1.67, $CHCl_3$) for an enantiomerically enriched sample of 92:8 e.r.

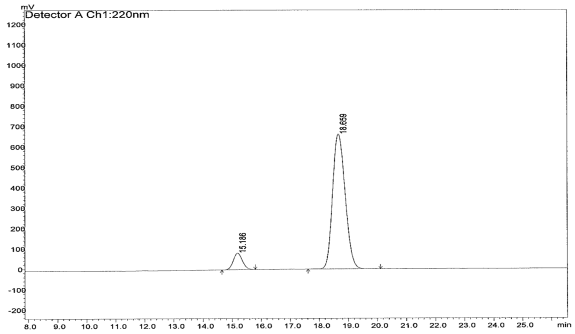
Proof of Stereochemistry: Literature value ($[\alpha]_D^{20}$ –7.58 (*c* 1.26, $CHCl_3$), 96.5:3.5 e.r.) is assigned to the (*R*) enantiomer.[64d]

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation

with $NaBO_3•4H_2O$) in comparison with authentic racemic material (92:8 e.r. shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.369	18062372	729086	49.533	54.900
2	18.098	18402871	598949	50.467	45.100
Total		36465243	1328034	100.000	100.000



Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.186	1775924	81352	8.192	10.961
2	18.659	19901994	660860	91.808	89.039
Total		21677918	742212	100.000	100.000

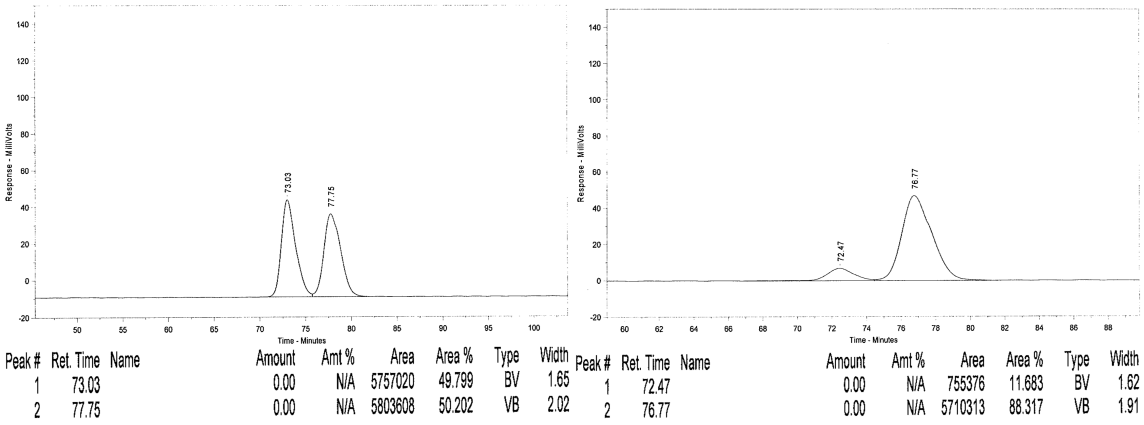
Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	14.37	49.5	1	15.19	8.2
2	18.10	50.5	2	18.66	91.8

(*R*,*E*)-1-(3-Methylundeca-1,4-dien-3-yl)-2-nitrobenzene (4.85). The compound has been previously reported and spectra data match those described.[64d] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (1H, dd, *J* = 8.0, 1.2 Hz), 7.47–7.40 (2H, m), 7.31 (1H, ddd, *J* = 8.8, 7.2, 1.6 Hz), 6.00 (1H, dd, *J* = 17.2, 10.4 Hz), 5.57 (1H, dt, *J* = 15.6, 1.6 Hz), 5.44 (1H, dt, *J* = 15.6, 6.4 Hz), 5.11 (1H, dd, *J* = 10.8, 0.8 Hz), 5.04 (1H, dd, *J* = 17.2, 0.8 Hz), 2.05–2.00 (2H, m), 1.64 (3H, s), 1.38–1.27 (8H, m), 0.90–0.86 (3H, m). Specific Rotation: $[\alpha]_D^{20}$ +1.75 (*c* 0.42, $CHCl_3$) for an enantiomerically enriched sample of 87:13 e.r.

Proof of Stereochemistry: Literature value ($[\alpha]_D^{20}$ +0.71 (*c* 1.00, $CHCl_3$), 97.5:2.5 e.r.) is assigned to the (*R*) enantiomer.[64d]

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation

with $NaBO_3$•$4H_2O$) in comparison with authentic racemic material (88:12 e.r. shown; Chiralcel OJ-H column, 99/1 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



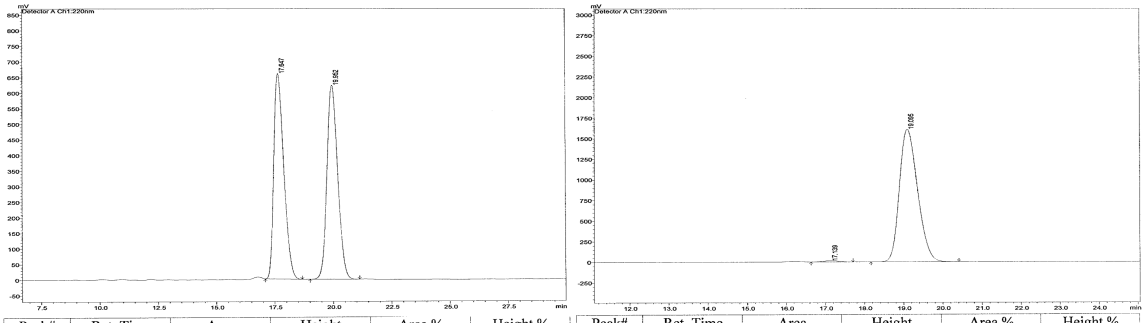
Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	73.03	49.8	1	72.47	11.7
2	77.75	50.2	2	76.77	88.3

(*R*,*E*)-1-Bromo-2-(3-methylundeca-1,4-dien-3-yl)benzene (4.86). The compound has been previously reported and spectra data match those described.[64d] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (1H, dd, *J* = 7.6, 1.6 Hz), 7.45 (1H, dd, *J* = 8.0, 1.6 Hz), 7.25 (1H, ddd, *J* = 7.6, 7.6, 1.6 Hz), 7.06 (1H, ddd, *J* = 7.6, 7.6, 1.6 Hz), 6.18 (1H, dd, *J* = 17.6, 10.8 Hz), 5.73 (1H, dt, *J* = 15.6, 1.6 Hz), 5.30 (1H, dt, *J* = 16.0, 7.2 Hz), 5.10 (1H, dd, *J* = 10.4, 1.2 Hz), 4.93 (1H, dd, *J* = 17.6, 1.2 Hz), 2.08–2.03 (2H, m), 1.61 (3H, s), 1.39–1.24 (8H, m), 0.89–0.86 (3H, m). Specific Rotation: $[\alpha]_D^{20}$ –9.60 (*c* 2.31, $CHCl_3$) for an enantiomerically enriched sample of 99:1 e.r.

Proof of Stereochemistry: Literature value ($[\alpha]_D^{20}$ –9.71 (*c* 1.12, $CHCl_3$), 96.5:3.5 e.r.) is assigned to the (*R*) enantiomer.[64d]

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation

with $NaBO_3 \bullet 4H_2O$) in comparison with authentic racemic material (99:1 e.r. shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.647	19707158	659980	49.628	51.427
2	19.952	20002403	623349	50.372	48.573
Total		39709561	1283329	100.000	100.000

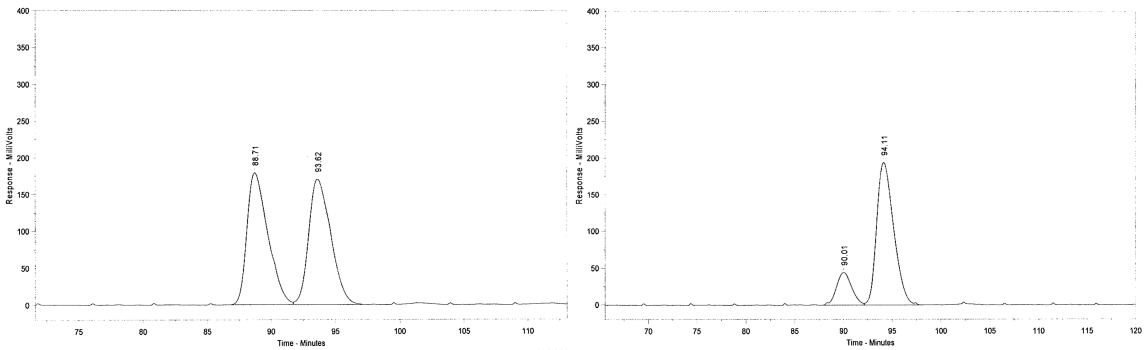
Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.139	405913	15768	0.778	0.971
2	19.095	51745903	1607766	99.222	99.029
Total		52151817	1623534	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	17.65	49.6	1	17.14	0.8
2	20.0	50.4	2	19.1	99.2

(*R*,*E*)-1-Chloro-4-(3-methylundeca-1,4-dien-3-yl)benzene (**4.88**)**.** IR (neat): 2957 (m), 2925 (s), 2854 (m), 1490 (s), 1459 (m), 1096 (s), 1013 (s), 975 (s), 916 (s), 826 (s), 747 (w), 723 (w), 613 (w), 562 (w), 532 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.25 (4H, s), 6.03 (1H, dd, *J* = 17.2, 10.4 Hz), 5.62 (1H, dt, *J* = 15.6, 1.2 Hz), 5.40 (1H, dt, *J* = 15.6, 6.8 Hz), 5.12 (1H, dd, *J* = 10.8, 1.2 Hz), 4.99 (1H, dd, *J* = 17.2, 1.2 Hz), 2.10–2.04 (2H, m), 1.45 (3H, s), 1.41–1.26 (8H, m), 0.91–0.88 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.7, 145.5, 136.5, 131.9, 129.6, 128.8, 128.2, 112.8, 47.3, 32.8, 31.8, 29.6, 29.0, 26.0, 22.8, 14.2; HRMS (ESI+): Calcd for $C_{18}H_{26}Cl_1$ $[M+H]^+$: 277.17230, Found: 277.17033. Specific Rotation: $[\alpha]_D^{20}$ –2.37 (*c* 2.41, $CHCl_3$) for an enantiomerically enriched sample of 83:17 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation

with $NaBO_3$•$4H_2O$) in comparison with authentic racemic material (83:17 e.r. shown; Chiralcel OD-H column, 99.5/0.5 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



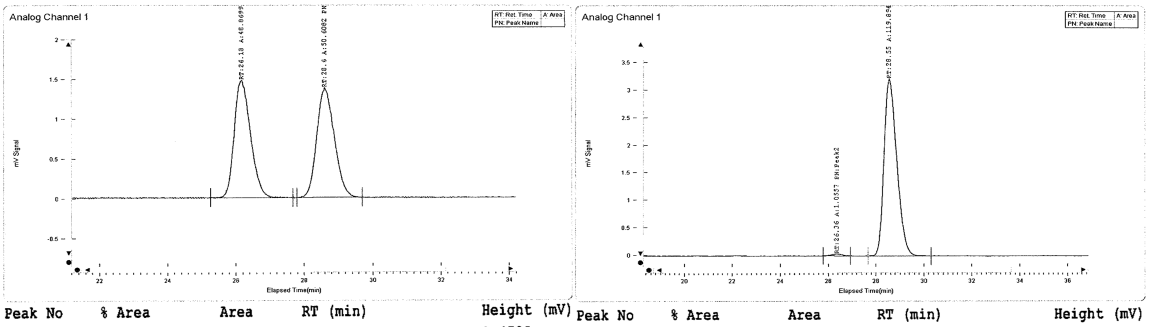
Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	88.71		0.00	N/A	20397850	49.871	BV	1.76
2	93.62		0.00	N/A	20503730	50.129	VB	1.89

Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	90.01		0.00	N/A	4798192	16.887	BV	1.69
2	94.11		0.00	N/A	23616130	83.113	VB	1.89

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	88.71	49.9	1	90.01	16.9
2	93.62	50.1	2	94.11	83.1

(*R*,*E*)-1-Bromo-2-(8-chloro-3-methylocta-1,4-dien-3-yl)benzene (4.90). IR (neat): 2956 (w), 2934 (w), 1463 (m), 1429 (m), 1303 (w), 1269 (w), 1018 (s), 946 (m), 913 (m), 755 (s), 735 (m), 648 (m), 456 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.58 (1H, dd, *J* = 8.0, 1.6 Hz), 7.45 (1H, dd, *J* = 8.0, 1.6 Hz), 7.29–7.25 (1H, m), 7.10–7.06 (1H, m), 6.19 (1H, dd, *J* = 17.6, 10.4 Hz), 5.83 (1H, dt, *J* = 15.6, 1.6 Hz), 5.25 (1H, dt, *J* = 16.0, 7.2 Hz), 5.12 (1H, dd, *J* = 10.4, 0.8 Hz), 4.94 (1H, dd, *J* = 18.0, 1.2 Hz), 3.55 (2H, t, *J* = 7.2 Hz), 2.23 (2H, ddt, *J* = 7.2, 7.2, 1.2 Hz), 1.87 (2H, tt, *J* = 6.4, 6.4 Hz), 1.62 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.4, 145.2, 138.1, 135.6, 129.7, 128.1, 127.3, 127.1, 123.9, 112.9, 48.8, 44.7, 32.2, 29.9, 26.4; HRMS (ESI+): Calcd for $C_{15}H_{19}Br_1Cl_1$ $[M+H]^+$: 315.03292, Found: 315.03124. Specific Rotation: $[\alpha]_D^{20}$ –14.66 (*c* 2.40, $CHCl_3$) for an enantiomerically enriched sample of 99:1 e.r.

Enantiomeric purity is determined by SFC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with $NaBO_3 \bullet 4H_2O$) in comparison with authentic racemic material (99:1 e.r. shown; Chiralcel OD-H column, 5% *i*-PrOH in supercritical CO_2 flow, 3.0 mL/min, 220 nm, 30 °C oven temperature).



Peak No	% Area	Area	RT (min)	Height (mV)
1	49.1263	48.8699	26.18	1.4735
2	50.8737	50.6082	28.6	1.3766

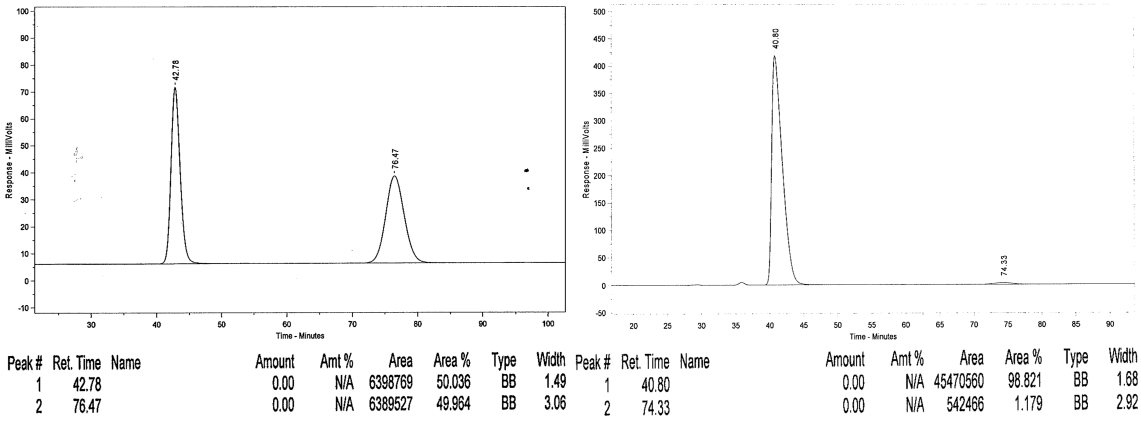
Peak No	% Area	Area	RT (min)	Height (mV)
1	0.8729	1.0557	26.36	0.0367
2	99.1271	119.8948	28.55	3.2165

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	26.18	49.1	1	26.36	0.9
2	28.60	50.9	2	28.55	99.1

(*R*,*E*)-1-Bromo-2-(3-methyl-1-phenylpenta-1,4-dien-3-yl)benzene (4.92). The compound has been previously reported and spectra data match those described.[64d] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (1H, dd, *J* = 8.0, 1.2 Hz), 7.50 (1H, dd, *J* = 7.6, 1.2 Hz), 7.39–7.37 (2H, m), 7.32–7.27 (3H, m), 7.21 (1H, ddd, *J* = 6.4, 1.2, 1.2 Hz), 7.13–7.09 (1H, m), 6.56 (1H, d, *J* = 16.4 Hz), 6.33–6.24 (2H, m), 5.18 (1H, dd, *J* = 10.4, 1.2 Hz), 5.04 (1H, dd, *J* = 17.6, 0.8 Hz), 1.75 (3H, s). Specific Rotation: $[\alpha]_D^{20}$ –22.59 (*c* 2.57, $CHCl_3$) for an enantiomerically enriched sample of 99:1 e.r.

Proof of Stereochemistry: Literature value ($[\alpha]_D^{20}$ –31.12 (*c* 0.91, $CHCl_3$), 98:2 e.r.) is assigned to the (*R*) enantiomer.[64d]

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with $NaBO_3 \bullet 4H_2O$) in comparison with authentic racemic material (99:1 e.r. shown; Chiralcel OJ-H column, 95/5 hexanes/*i*-PrOH, 0.8 mL/min, 220 nm).



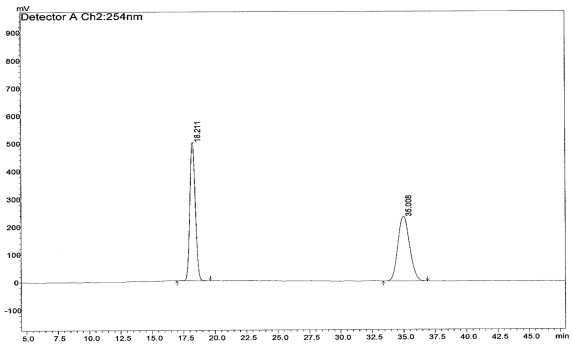
Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	42.78		0.00	N/A	6398769	50.036	BB	1.49
2	76.47		0.00	N/A	6389527	49.964	BB	3.06

Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	40.80		0.00	N/A	45470560	98.821	BB	1.68
2	74.33		0.00	N/A	542466	1.179	BB	2.92

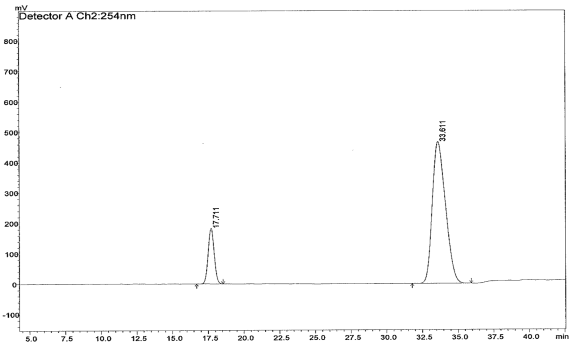
Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	42.78	50.0	1	40.80	98.8
2	76.47	50.0	2	74.33	1.2

(*S*,*E*)-(3-Cyclohexyl-3-methylpenta-1,4-dien-1-yl)benzene (4.94). IR (neat): 2924 (s), 2851 (m), 1632 (w), 1599 (w), 1494 (w), 1447 (m), 1412 (w), 1370 (w), 1000 (w), 969 (m), 909 (m), 744 (s), 691 (s), 607 (w), 514 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.40–7.37 (2H, m), 7.33–7.29 (2H, m), 7.22–7.18 (1H, m), 6.33–6.24 (2H, m), 5.94 (1H, dd, *J* = 17.2, 10.8 Hz), 5.08 (1H, dd, *J* = 10.8, 1.6 Hz), 5.00 (1H, dd, *J* = 17.2, 1.6 Hz), 1.79–1.74 (4H, m), 1.67–1.64 (1H, m), 1.36–0.94 (9H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.3, 138.2, 137.9, 128.6, 127.5, 127.0, 126.2, 112.5, 47.7, 45.9, 28.1, 27.2, 26.8, 20.0; HRMS (ESI+): Calcd for $C_{18}H_{25}$ $[M+H]^+$: 241.19563, Found: 241.19538. Specific Rotation: $[\alpha]_D^{20}$ –50.03 (*c* 1.62, $CHCl_3$) for an enantiomerically enriched sample of 85:15 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with $NaBO_3 \bullet 4H_2O$) in comparison with authentic racemic material (85:15 e.r. shown; Chiralpak AS-H column, 98/2 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.211	15103407	499723	49.837	68.137
2	35.008	15202449	233686	50.163	31.863
Total		30305856	733409	100.000	100.000

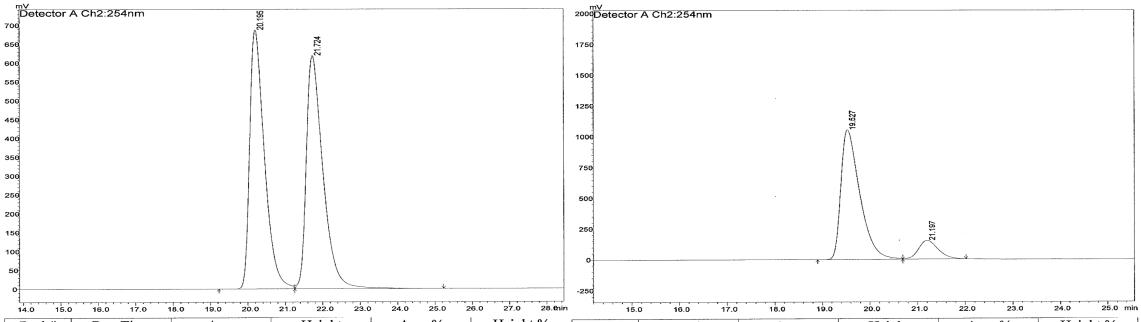


Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.711	5408527	183289	15.278	28.211
2	33.611	29991707	466418	84.722	71.789
Total		35400233	649706	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	18.21	49.8	1	17.71	15.3
2	35.01	50.2	2	33.61	84.7

(*R*,*E*)-*tert*-Butyl 2-methyl-4-phenyl-2-vinylbut-3-enoate (4.95). IR (neat): 2978 (w), 2933 (w), 1723 (s), 1456 (w), 1367 (m), 1248 (s), 1153 (s), 1107 (s), 968 (m), 918 (m), 847 (m), 745 (s), 692 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.40–7.37 (2H, m), 7.33–7.29 (2H, m), 7.25–7.21 (1H, m), 6.43 (2H, s), 6.14 (1H, ddd, J = 17.2, 10.4, 0.8 Hz), 5.19–5.14 (2H, m), 1.47 (3H, s), 1.46 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.6, 141.0, 137.4, 132.8, 129.1, 128.7, 127.5, 126.5, 114.2, 81.2, 51.8, 28.1, 21.6; HRMS (ESI+): Calcd for $C_{17}H_{23}O_2$ $[M+H]^+$: 256.16980, Found: 259.16647. Specific Rotation: $[\alpha]_D^{20}$ –16.40 (*c* 0.847, $CHCl_3$) for an enantiomerically enriched sample of 87:13 e.r.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (87:13 e.r. shown; Chiralcel OD-H column, 100/0 hexanes/*i*-PrOH, 0.5 mL/min, 254 nm).



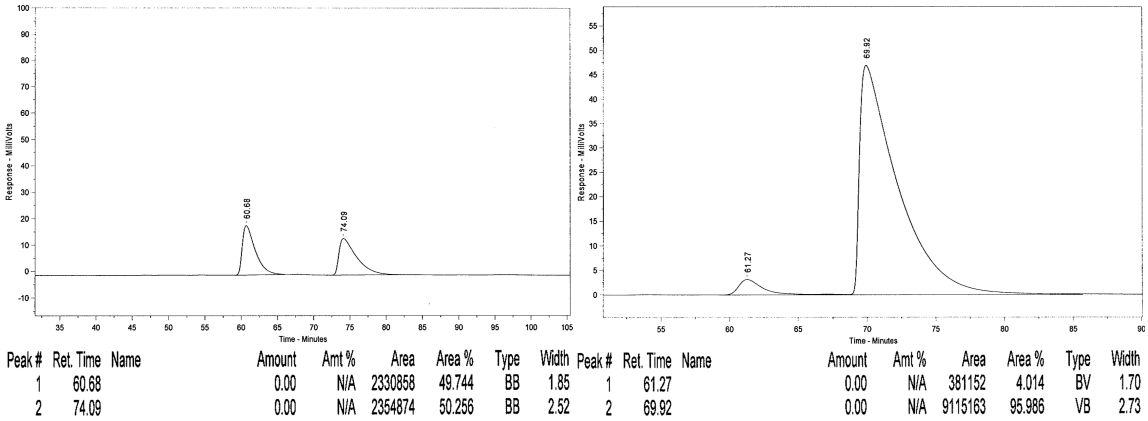
Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.195	18810561	687792	49.474	52.625
2	21.724	19210225	619183	50.526	47.375
Total		38020786	1306975	100.000	100.000

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.527	29145682	1052236	87.069	87.400
2	21.197	4328625	151698	12.931	12.600
Total		33474306	1203934	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	20.20	49.5	1	19.53	87.1
2	21.72	50.5	2	21.2	12.9

(*R*,*E*)-Ethyl 4-(2-(methoxymethoxy)-5-methylphenyl)-4-methylhexa-2,5-dienoate (4.98). IR (neat): 2978 (w), 2932 (w), 1717 (s), 1648 (w), 1496 (m), 1401 (w), 1367 (w), 1307 (m), 1287 (m), 1267 (m), 1242 (m), 1230 (m), 1198 (m), 1157 (s), 1079 (m), 1067 (m), 1002 (s), 922 (m), 812 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (1H, d, *J* = 15.6 Hz), 7.04–6.98 (3H, m), 6.18 (1H, dd, *J* = 17.6, 10.8 Hz), 5.73 (1H, d, *J* = 15.6 Hz), 5.13 (1H, d, *J* = 10.4 Hz), 5.08 (2H, s), 5.03 (1H, d, *J* = 17.6 Hz), 4.17 (2H, q, *J* = 6.8 Hz), 3.41 (3H, s), 2.28 (3H, s), 1.60 (3H, s), 1.26 (3H, t, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 155.8, 153.2, 143.5, 133.2, 130.8, 128.7, 128.6, 118.4, 114.7, 113.1, 94.2, 60.3, 56.2, 46.6, 24.0, 20.9, 14.4; HRMS (ESI+): Calcd for $C_{18}H_{25}O_4$ $[M+H]^+$: 305.17528, Found: 305.17534. Specific Rotation: $[\alpha]_D^{20}$ –12.32 (*c* 1.71, $CHCl_3$) for an enantiomerically enriched sample of 96:4 e.r.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (96:4 e.r. shown; Chiralcel OD-H column, 100/0 hexanes/*i*-PrOH, 0.8 mL/min, 220 nm). The trace shown is obtained from compound derived from EAS with *R* enantiomer of catalyst.



Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	60.68		0.00	N/A	2330858	49.744	BB	1.85
2	74.09		0.00	N/A	2354874	50.256	BB	2.52

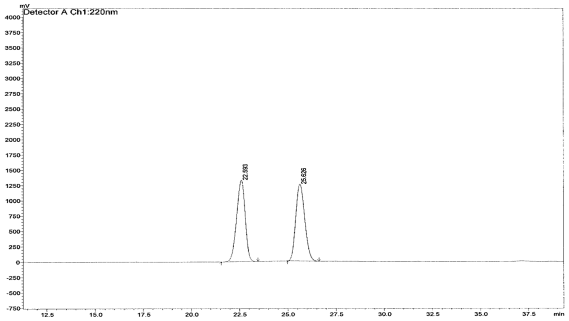
Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	61.27		0.00	N/A	381152	4.014	BV	1.70
2	69.92		0.00	N/A	9115163	95.986	VB	2.73

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	60.68	49.7	1	61.27	4.0
2	74.09	50.3	2	69.9	96.0

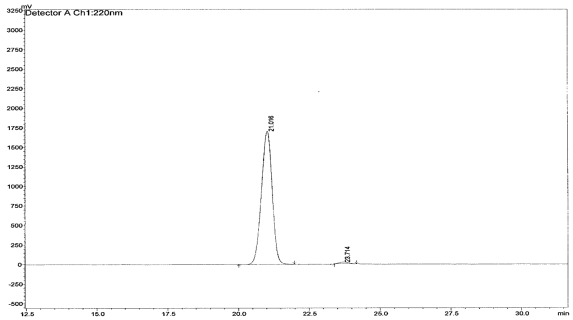
(*R*,*E*)-Ethyl 4-(2-bromophenyl)-4-methylhexa-2,5-dienoate (4.99). IR (neat): 2978 (w), 1713 (s), 1646 (m), 1466 (m), 1367 (m), 1305 (s), 1288 (s), 1267 (s), 1163 (s), 1020 (s), 979 (m), 916 (m), 860 (w), 754 (s), 727 (s), 645 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (1H, dd, *J* = 8.0, 0.8 Hz), 7.41 (1H, dd, *J* = 8.0, 1.2 Hz), 7.35–7.27 (2H, m), 7.12 (1H, ddd, *J* = 7.6, 7.6, 1.2 Hz), 6.19 (1H, dd, *J* = 17.6, 10.8 Hz), 5.68 (1H, d, *J* = 16.4 Hz), 5.20 (1H, dd, *J* = 10.8, 0.4 Hz), 5.01 (1H, d, *J* = 17.2 Hz), 4.19 (2H, q, *J* = 7.2 Hz), 1.68 (3H, s), 1.28 (3H, t, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.0, 154.6, 143.8, 143.0, 135.5, 129.5, 128.7, 127.4, 123.9, 120.0, 114.5, 60.5, 49.2, 25.8, 14.4; HRMS (ESI+): Calcd for $C_{15}H_{18}O_2Br_1[M+H]^+$: 309.04902, Found: 309.04586. Specific

Rotation: $[\alpha]_D^{20}$ –12.12 (*c* 1.36, $CHCl_3$) for an enantiomerically enriched sample of 99:1 e.r.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (99:1 e.r. shown; Chiralcel OD-H column, 99.5/0.5 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.593	41058396	1327470	50.411	51.437
2	25.626	40388793	1253278	49.589	48.563
Total		81447189	2580748	100.000	100.000



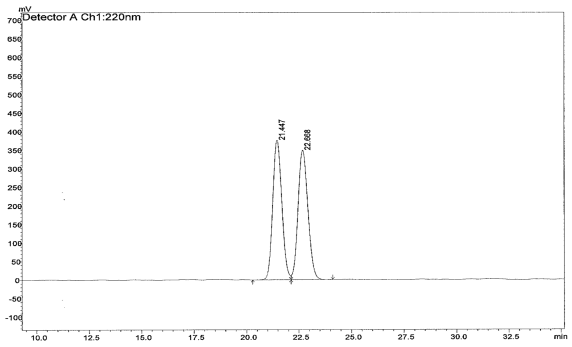
Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.016	45122907	1702028	98.916	98.712
2	23.714	494360	22210	1.084	1.288
Total		45617266	1724238	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	22.59	50.4	1	21.02	98.9
2	25.63	49.6	2	23.71	1.1

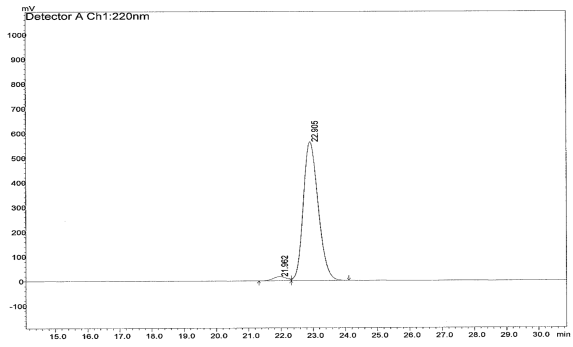
(*R*,*E*)-Ethyl 4-(2-methoxyphenyl)-4-methylhexa-2,5-dienoate (4.100). IR (neat): 2978 (w), 2836 (w), 1713 (s), 1647 (m), 1597 (w), 1581 (w), 1489 (m), 1462 (m), 1435 (m), 1366 (m), 1305 (m), 1288 (m), 1266 (m), 1242 (s), 1027 (s), 917 (m), 850 (w), 791 (w), 752 (s), 668 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.29 (1H, d, *J* = 16.0 Hz), 7.26–7.22 (2H, m), 6.93–6.86 (2H, m), 6.17 (1H, dd, *J* = 17.6, 10.8 Hz), 5.70 (1H, d, *J* = 16.0 Hz), 5.11 (1H, dd, *J* = 10.8, 1.2 Hz), 5.00 (1H, dd, *J* = 17.2, 1.2 Hz), 4.17 (2H, q, *J* = 6.8 Hz), 3.74 (3H, s), 1.58 (3H, s), 1.27 (3H, t, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.5, 157.8, 155.8, 143.5, 133.4, 128.4, 127.8, 120.6, 118.4, 113.1, 112.3, 60.3, 55.3, 46.6, 24.0, 14.4; HRMS (ESI+): Calcd for $C_{16}H_{21}O_3$ $[M+H]^+$: 261.14907, Found:

261.14492. Specific Rotation: $[\alpha]_D^{20}$ –23.32 (*c* 0.667, $CHCl_3$) for an enantiomerically enriched sample of 97:3 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from dibal-H reduction of the unsaturated ester) in comparison with authentic racemic material (97:3 e.r. shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.447	11441678	376830	50.075	51.891
2	22.668	11407259	349361	49.925	48.109
Total		22848936	726192	100.000	100.000



Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.962	477539	16709	2.564	2.884
2	22.905	18147969	562670	97.436	97.116
Total		18625508	579379	100.000	100.000

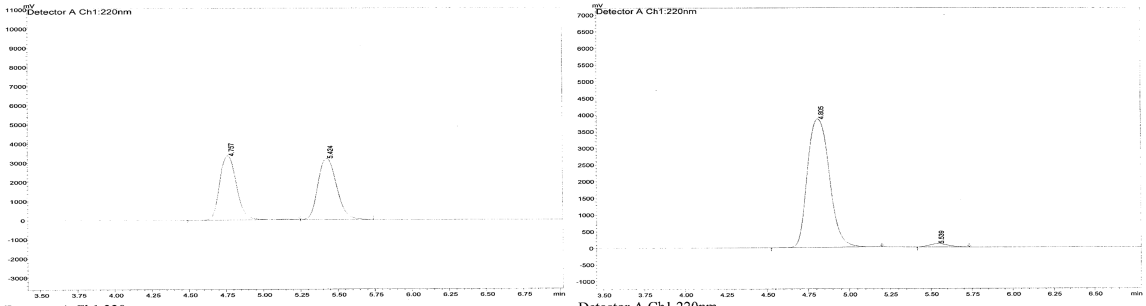
Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	21.45	50.1	1	21.96	2.6
2	22.67	49.9	2	22.91	97.4

■ **Representative Procedure for Cu-Catalyzed Enantioselective Allylic Substitution Reactions with Acetal Containing Alkenylboron 4.103:** The set up and work-up procedures are the same as described above in the general experimental procedure. The purification is adapted as follows: (1) A brief column chromatography can be performed to obtain the corresponding acetal containing product (instead of an enal); partial hydrolysis, however, does occur during the chromatography (~20%). Preliminary treatment of the silica gel with Et_3N prevents the partial hydrolysis. Accordingly, the acetal product can be obtained in similar yield as its enal counterpart reported in Scheme

4.17. (2) If the filtrate (before solvent removal *in vacuo*) is treated with silica gel (ca. ~100 mg/ 0.2 mmol of substrate) and the resulting suspension is allowed to stir at ambient temperature for one hour, the corresponding enal is efficiently generated. The resulting suspension may be filtered through a cotton plug to remove silica gel eluted with Et_2O. The combined organic filtrate is concentrated *in vacuo* to afford the unpurified product as yellow or brown oils, which is purified by column chromatography to furnish the desired enal as colorless oil.

(*R*,*E*)-4-(2-(Methoxymethoxy)-5-methylphenyl)-4-methylhexa-2,5-dienal (4.104). IR (neat): 2974 (w), 2824 (w), 1687 (s), 1625 (w), 1496 (m), 1237 (m), 1199 (w), 1143 (m), 1076 (m), 997 (m), 921 (m), 813 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.57 (1H, d, *J* = 7.6 Hz), 7.14 (1H, d, *J* = 16.0 Hz), 7.07–7.00 (3H, m), 6.20 (1H, dd, *J* = 17.6, 10.8 Hz), 6.06 (1H, dd, *J* = 16.0, 8.0 Hz), 5.19 (1H, dd, *J* = 10.4, 0.8 Hz), 5.09–5.05 (3H, m), 3.40 (3H, s), 2.29 (3H, s), 1.61 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.5, 165.7, 153.1, 142.8, 132.5, 131.0, 129.8, 129.1, 128.5, 114.7, 113.7, 94.3, 56.3, 47.2, 23.9, 20.9; HRMS (ESI+): Calcd for $C_{16}H_{20}O_3$ $[M+H]^+$: 260.14124, Found: 260.14216. Specific Rotation: $[\alpha]_D^{20}$ –35.49 (*c* 1.19, $CHCl_3$) for an enantiomerically enriched sample of 98:2 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived unsaturated ester **14** (obtained from oxidation of **20** with 0.5 equiv of Oxone in absolute EtOH) in comparison with authentic racemic material (98:2 e.r. shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.757	26421008	3350680	48.556	51.198
2	5.424	27992916	3193842	51.444	48.802
Total		54413924	6544523	100.000	100.000

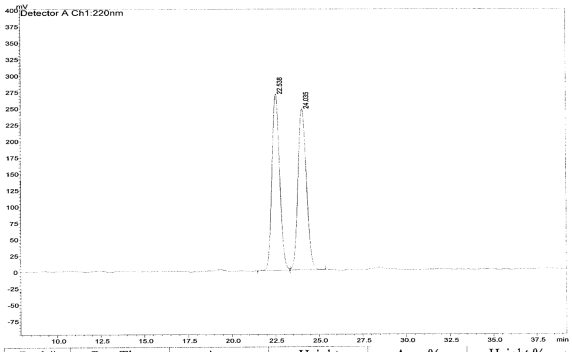
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.805	35749901	3857946	97.743	97.406
2	5.539	825557	102737	2.257	2.594
Total		36575458	3960683	100.000	100.000

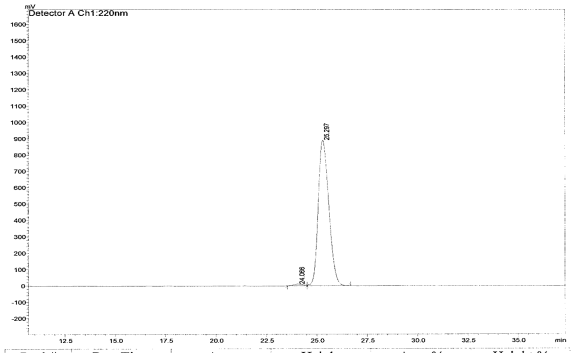
Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	4.76	48.6	1	4.81	97.7
2	5.42	51.4	2	5.54	2.3

(*R*,*E*)-4-(2-Bromophenyl)-4-methylhexa-2,5-dienal (4.105). IR (neat): 2978 (w), 2812 (w), 2728 (w), 1687 (s), 1622 (w), 1466 (w), 1428 (w), 1126 (w), 1020 (w), 975 (w), 922 (w), 761 (w), 740 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.61 (1H, d, *J* = 7.6 Hz), 7.60 (1H, dd, *J* = 7.6, 1.2 Hz), 7.43 (1H, dd, *J* = 8.0, 1.6 Hz), 7.34–7.30 (1H, m), 7.21–7.13 (2H, m), 6.23 (1H, dd, *J* = 17.6, 10.8 Hz), 5.99 (1H, dd, *J* = 16.0, 7.6 Hz), 5.25 (1H, d, *J* = 10.4 Hz), 5.06 (1H, d, *J* = 17.6 Hz), 1.72 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.2, 164.0, 143.4, 142.5, 135.6, 131.2, 129.4, 129.0, 127.6, 123.8, 114.9, 49.7, 25.7; HRMS (ESI+): Calcd for $C_{13}H_{14}Br_1O_1$ $[M+H]^+$: 265.02280, Found: 265.02318. Specific Rotation: $[\alpha]_D^{20}$ –39.45 (*c* 0.313, $CHCl_3$) for an enantiomerically enriched sample of 99:1 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from dibal-H reduction of the enal) in comparison with authentic racemic material (99:1 e.r. shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.538	8329684	269546	50.320	52.274
2	24.035	8223591	246096	49.680	47.726
Total		16553275	515643	100.000	100.000

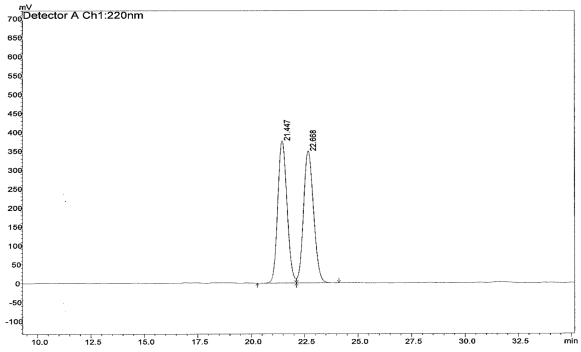


Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.066	346878	10942	1.051	1.214
2	25.297	32660547	890735	98.949	98.786
Total		33007425	901677	100.000	100.000

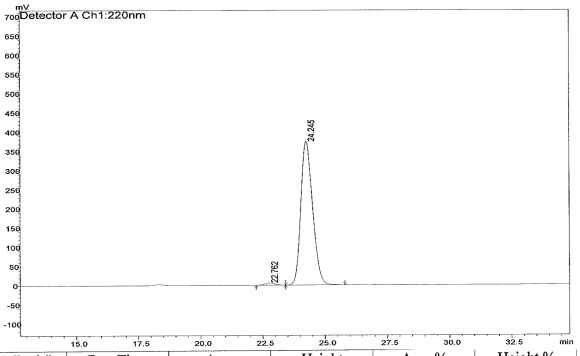
Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	22.54	50.3	1	24.07	1.1
2	24.04	49.7	2	25.30	98.9

(*R*,*E*)-4-(2-Methoxyphenyl)-4-methylhexa-2,5-dienal (4.106). IR (neat): 2971 (w), 2935 (w), 1687 (s), 1490 (m), 1459 (w), 1436 (w), 1245 (m), 1128 (w), 1027 (w), 756 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.55 (1H, d, *J* = 7.6 Hz), 7.28–7.24 (2H, m), 7.12 (1H, d, *J* = 16.0 Hz), 6.92 (1H, ddd, *J* = 7.6, 7.6, 1.2 Hz), 6.88 (1H, dd, *J* = 8.8, 1.2 Hz), 6.19 (1H, dd, *J* = 17.6, 10.8 Hz), 6.01 (1H, dd, *J* = 15.6, 7.6 Hz), 5.16 (1H, dd, *J* = 10.4, 0.8 Hz), 5.04 (1H, dd, *J* = 17.2, 0.8 Hz), 3.73 (3H, s), 1.61 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.7, 165.9, 157.5, 142.8, 132.7, 129.8, 128.8, 127.7, 120.8, 113.6, 112.1, 55.2, 47.1, 23.8; HRMS (ESI+): Calcd for $C_{14}H_{17}O_2$ $[M+H]^+$: 217.12285, Found: 217.12207. Specific Rotation: $[\alpha]_D^{20}$ –55.60 (*c* 0.193, $CHCl_3$) for an enantiomerically enriched sample of 99:1 e.r.

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from dibal-H reduction of the enal) in comparison with authentic racemic material (99:1 e.r. shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.447	11441678	376830	50.075	51.891
2	22.668	11407259	349361	49.925	48.109
Total		22848936	726192	100.000	100.000



Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.762	163173	5765	1.313	1.519
2	24.245	12260236	373651	98.687	98.481
Total		12423409	379416	100.000	100.000

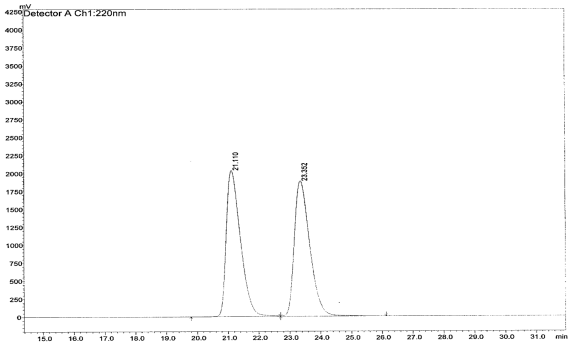
Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	21.45	50.0	1	22.76	1.3
2	22.67	50.0	2	24.25	98.7

(*R*,*E*)-1-(6,6-Diethoxy-3-methylhexa-1,4-dien-3-yl)-2-methoxybenzene (S5, acetal derivative of 4.106). IR (neat): 2973 (m), 2928 (m), 2876 (m), 1489 (m), 1462 (m), 1436 (w), 1370 (w), 1337 (w), 1288 (w), 1244 (s), 1134 (m), 1052 (s), 1031 (m), 996 (m), 914 (w), 752 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.21 (2H, m), 6.92–6.87 (2H, m), 6.22 (1H, dd, *J* = 17.6, 10.4 Hz), 6.16 (1H, dd, *J* = 16.0, 0.8 Hz), 5.42 (1H, dd, *J* = 16.0, 5.6 Hz), 5.06 (1H, dd, *J* = 10.4, 1.6 Hz), 4.97 (1H, dd, *J* = 17.6, 0.8 Hz), 4.93 (1H, dd, *J* = 5.6, 0.4 Hz), 3.77 (3H, s), 3.68–3.61 (2H, m), 3.55–3.48 (2H, m), 1.59 (3H, s), 1.24–1.20 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.9, 145.1, 141.5, 134.5, 128.03, 127.97, 125.0, 120.4, 112.0, 111.9, 102.3, 60.85, 60.82, 55.1, 46.2, 24.5, 15.4; HRMS (ESI+): Calcd for $C_{16}H_{21}O_2$ $[M+H]^+$: 245.15415, Found: 245.15529. Specific Rotation: $[\alpha]_D^{20}$ –6.80 (*c* 1.687, $CHCl_3$) for an enantiomerically enriched sample of 99:1 e.r.

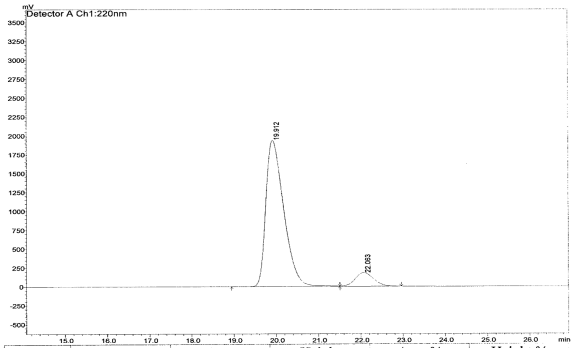
Enantiomeric purity is determined by converting the title compound to **4.106** and following the same derivatization strategy and HPLC analysis (cf. **4.106**).

(*R*,*E*)-4-Methyl-4-(*o*-tolyl)hexa-2,5-dienal (4.107). IR (neat): 2976 (w), 2930 (w), 2816 (w), 2727 (w), 1688 (s), 1623 (w), 1487 (w), 1456 (w), 1124 (w), 980 (w), 921 (w), 763 (m), 730 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.61 (1H, d, *J* = 8.0 Hz), 7.34–7.31 (1H, m), 7.22–7.11 (4H, m), 6.16 (1H, dd, *J* = 17.2, 10.4 Hz), 6.00 (1H, dd, *J* = 16.0, 7.6 Hz), 5.20 (1H, dd, *J* = 10.8, 0.8 Hz), 4.98 (1H, dd, *J* = 17.2, 0.4 Hz), 2.24 (3H, s), 1.64 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.1, 164.6, 143.0, 141.7, 137.1, 132.6, 130.5, 127.5, 127.3, 126.1, 114.4, 49.1, 26.5, 22.7; HRMS (ESI+): Calcd for $C_{14}H_{17}O_1$ $[M+H]^+$: 201.12794, Found: 201.12865. Specific Rotation: $[\alpha]_D^{20}$ –10.14 (*c* 1.33, $CHCl_3$) for an enantiomerically enriched sample of 91:9 e.r.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (91:9 e.r. shown; Chiralcel OD-H column, 99.8/0.2 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.110	65191763	2035475	49.835	51.904
2	23.352	65623218	1886116	50.165	48.096
Total		130814981	3921591	100.000	100.000



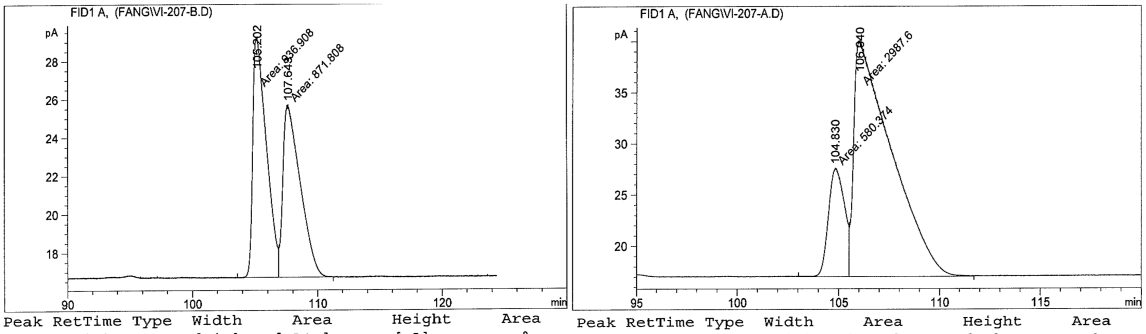
Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.912	57045646	1939504	91.150	91.385
2	22.063	5538834	182839	8.850	8.615
Total		62584480	2122343	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	21.11	49.8	1	19.91	91.2
2	23.35	50.2	2	22.06	8.9

(*S*,*E*)-4-Cyclohexyl-4-methylhexa-2,5-dienal (4.108). IR (neat): 2928 (s), 2854 (m), 1692 (s), 1626 (w), 1450 (w), 1414 (w), 1372 (w), 1142 (w), 1108 (w), 1008 (w), 981

(w), 916 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.54 (1H, d, *J* = 7.6 Hz), 6.82 (1H, d, *J* = 16.0 Hz), 6.05 (1H, dd, *J* = 15.6, 7.6 Hz), 5.83 (1H, dd, *J* = 17.6, 10.8 Hz), 5.12 (1H, dd, *J* = 10.8, 0.8 Hz), 4.98 (1H, dd, *J* = 17.2, 0.8 Hz), 1.77–1.64 (4H, m), 1.37 (1H, tt, *J* = 12.0, 2.8 Hz), 1.26–0.90 (9H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.3, 165.3, 142.6, 130.9, 114.3, 47.1, 47.0, 28.0, 27.9, 27.00, 26.97, 26.6, 18.9; HRMS (ESI+): Calcd for $C_{13}H_{21}O_1$ $[M+H]^+$: 193.15924, Found: 193.15949. Specific Rotation: $[\alpha]_D^{20}$ –39.40 (*c* 0.807, $CHCl_3$) for an enantiomerically enriched sample of 84:16 e.r.

Enantiomeric purity is determined by GLC analysis in comparison with authentic racemic material (84:16 e.r. shown; Chiral dex CD-BDM column, 100 ºC, 15 psi).



Peak RetTime Type	Width	Area	Height	Area
# [min]	[min]	[pA*s]	[pA]	%
1 105.202 MF	1.2432	936.90845	12.56088	51.79962
2 107.643 FM	1.6122	871.80847	9.01288	48.20038

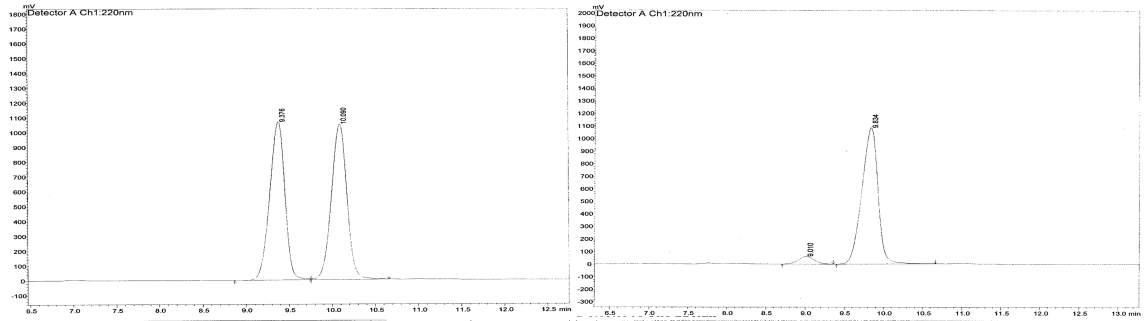
Peak RetTime Type	Width	Area	Height	Area
# [min]	[min]	[pA*s]	[pA]	%
1 104.830 MF	0.9087	580.37421	10.64436	16.26620
2 106.040 FM	2.1434	2987.60205	23.23061	83.73380

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	105.20	51.8	1	104.83	16.3
2	107.64	48.2	2	106.04	83.7

(*R*,*E*)-*tert*-Butyl 2-methyl-5-oxo-2-vinylpent-3-enoate (4.109). IR (neat): 2979 (m), 2935 (w), 1728 (s), 1695 (s), 1369 (m), 1252 (m), 1149 (s), 1122 (s), 980 (w), 925 (w), 847 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.59 (1H, d, *J* = 8.0 Hz), 7.03 (1H, d, *J* = 16.0 Hz), 6.13 (1H, dd, *J* = 16.0, 7.6 Hz), 6.02 (1H, dd, *J* = 17.6, 10.8 Hz), 5.24 (1H, d, *J* = 10.8 Hz), 5.16 (1H, dd, *J* = 17.2, 0.4 Hz), 1.459 (9H, s), 1.458 (3H, s); ^{13}C NMR (100

MHz, $CDCl_3$): δ 193.9, 171.7, 158.9, 138.6, 131.5, 116.0, 82.3, 52.4, 28.0, 21.0; HRMS (ESI+): Calcd for $C_{12}H_{19}O_3$ $[M+H]^+$: 211.13342, Found: 211.13393. Specific Rotation: $[\alpha]_D^{20}$ –12.39 (*c* 0.067, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (95:5 e.r. shown; Chiralcel OD-H column, 99.8/0.2 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm). The trace shown is obtained from compound derived from EAS with the *R* enantiomer of catalyst.



Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.376	13092716	1068682	49.819	50.420
2	10.090	13188042	1050885	50.181	49.580
Total		26280758	2119567	100.000	100.000

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.010	839250	60095	5.131	5.252
2	9.834	15517204	1084125	94.869	94.748
Total		16356455	1144220	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	9.38	49.8	1	9.01	5.1
2	10.09	50.2	2	9.8	94.9

■ **Procedure for Oxidation of Enal and Deprotection of MOM group with Oxone/MeOH (Scheme 4.17):** A flame-dried 6-dram vial (23 x 85 mm) is charged with enal **4.104** (17.9 mg, 0.069 mmol), Oxone (42.3 mg, 0.069 mmol) and a stir bar. The vial is sealed with a septum and purged with N_2 flow for 10 minutes. Methyl alcohol (2.0 mL) is added to the vessel through a syringe. The resulting suspension is allowed to stir at 22 °C for 18 hours before the reaction is quenched by passing the mixture through a plug of celite eluted with Et_2O. The filtrate is concentrated *in vacuo* to afford a yellow residue,

which is subjected to rapid silica gel chromatography (4:1 hexanes:Et_2O; partial cyclization occurs during purification) to furnish the desired product **4.110** as colorless oil (15.3 mg, 0.062 mmol, 90% yield). **(*R*,*E*)-Methyl 4-(2-hydroxy-5-methylphenyl)-4-methylhexa-2,5-dienoate (4.110).** IR (neat): 3408 (br), 2977 (w), 2951 (w), 1723 (s), 1698 (s), 1646 (m), 1509 (m), 1437 (m), 1412 (w), 1314 (s), 1291 (s), 1262 (m), 1208 (s), 1176 (m), 1013 (w), 919 (w), 816 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.26 (1H, d, *J* = 16.0 Hz), 7.01–6.95 (2H, m), 6.75 (1H, d, *J* = 8.0 Hz), 6.17 (1H, dd, *J* = 17.6, 10.8 Hz), 5.78 (1H, d, *J* = 16.0 Hz), 5.34 (1H, dd, *J* = 10.8, 0.8 Hz), 5.25 (1H, dd, *J* = 17.6, 0.8 Hz), 5.20 (1H, s), 3.74 (3H, s), 2.28 (3H, s), 1.59 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.2, 152.8, 152.0, 143.0, 130.2, 129.5, 128.6, 128.3, 119.8, 117.9, 115.7, 51.8, 46.8, 24.4, 20.9; HRMS (ESI+): Calcd for $C_{15}H_{19}O_3$ $[M+H]^+$: 247.13342, Found: 247.13362. Specific Rotation: $[\alpha]_D^{20}$ –1.22 (*c* 0.573, $CHCl_3$) for an enantiomerically enriched sample of 98:2 e.r. Enantiomeric purity is determined in correlation with its precursor (assuming no racemization occurs in this step) and further confirmed after the complete synthesis of Pummerer ketone (99:1 e.r.).

■ **Enantioselective Synthesis of *syn* and *anti*-Pummerer Ketone (Scheme 4.18):**

1) Representative Procedure for Cinchona Alkaloid-Catalyzed Intramolecular Phenol Conjugate Addition. A flame-dried 1-dram vial (15 x 45 mm) is charged with freshly prepared phenol **4.110** (11.9 mg, 0.048 mmol) and a stir bar. The vial is sealed with a septum and purged with N_2 flow for 10 minutes before 0.5 mL toluene is added through a syringe. Cinchonidine (1.4 mg, 0.0048 mmol) is weighted out into a separate flame-dried 1-dram vial (15 x 45 mm) and suspended in toluene (0.5 mL). Both vials are

allowed to cool to 0 °C in an ice bath and the solution of phenol **4.110** is transferred to the catalyst-containing vessel through a syringe or a cannula. The resulting solution is allowed to stir at 0 °C for an additional two hours before it is passed through a plug of celite to remove any remaining solid eluted with Et_2O. The filtrate is concentrated under reduced pressure to afford a colorless residue, which is purified by silica gel chromatography (10:1 hexanes:Et_2O), furnishing the desired product as colorless oil (10.6 mg, 0.043 mmol, 89% yield). **Methyl 2-((2*S*,3*S*)-3,5-dimethyl-3-vinyl-2,3-dihydrobenzofuran-2-yl)acetate (*syn*-4.111):** The characterization is carried out in the presence of 10% ***anti*-4.111**. IR (neat): 2954 (w), 2923 (w), 2864 (w), 1742 (s), 1489 (s), 1437 (w), 1309 (w), 1257 (w), 1200 (m), 1172 (m), 1000 (m), 924 (w), 873 (w), 811 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.95–6.93 (1H, m), 6.82–6.81 (1H, m), 6.71 (1H, d, *J* = 8.0 Hz), 5.82 (1H, dd, *J* = 17.2, 10.4 Hz), 5.16 (1H, dd, *J* = 10.8, 1.2 Hz), 4.94 (1H, dd, *J* = 17.2, 1.2 Hz), 4.76 (1H, dd, *J* = 9.2, 4.0 Hz), 3.74 (3H, s), 2.70 (1H, dd, *J* = 16.0, 9.6 Hz), 2.56 (1H, dd, *J* = 16.0, 4.0 Hz), 2.27 (3H, s), 1.46 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.6, 156.4, 139.9, 133.7, 130.4, 129.0, 124.6, 115.5, 109.8, 88.9, 52.1, 50.4, 36.4, 23.7, 21.0; HRMS (ESI+): Calcd for $C_{15}H_{19}O_3$ $[M+H]^+$: 247.13342, Found: 247.13399. Specific Rotation: $[\alpha]_D^{20}$ –65.90 (*c* 0.213, $CHCl_3$) for an enantiomerically enriched sample of 99:1 e.r. Enantiomeric purity is determined after the completion of the synthesis of *syn*-Pummerer ketone (99:1 e.r.).

Methyl 2-((2*R*,3*S*)-3,5-dimethyl-3-vinyl-2,3-dihydrobenzofuran-2-yl)acetate (*anti*-4.111). Compound characterization is carried out in the presence of 11% ***syn*-4.111**. IR (neat): 2953 (w), 2921 (w), 1742 (s), 1488 (s), 1436 (w), 1313 (w), 1251 (w), 1203 (m), 1169 (m), 997 (m), 922 (w), 878 (w), 811 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.94–

6.92 (1H, m), 6.80–6.79 (1H, m), 6.71 (1H, d, *J* = 8.0 Hz), 5.99 (1H, dd, *J* = 17.2, 10.8 Hz), 5.25–5.19 (2H, m), 4.81 (1H, dd, *J* = 9.6, 4.0 Hz), 3.74 (3H, s), 2.78 (1H, dd, *J* = 16.0, 9.6 Hz), 2.59 (1H, dd, *J* = 15.6, 4.0 Hz), 2.27 (3H, s), 1.20 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.5, 156.2, 142.0, 135.1, 130.6, 129.0, 124.2, 115.0, 109.8, 87.2, 52.1, 50.5, 34.8, 21.0, 19.6; HRMS (ESI+): Calcd for $C_{15}H_{19}O_3$ $[M+H]^+$: 247.13342, Found: 247.13445. Specific Rotation: $[\alpha]_D^{20}$ +61.14 (*c* 0.227, $CHCl_3$) for an enantiomerically enriched sample of 99:1 e.r. Enantiomeric purity is determined after the completion of the synthesis of *anti*-Pummerer ketone (99:1 e.r.).

2) Procedure for Weinreb Amide Formation from Ester 4.111. A flame-dried 2-dram vial (17 x 60 mm) is charged with benzofuran ***syn*-4.111** (40.5 mg, 0.164 mmol), *N,O*-dimethylhydroxylamine hydrochloride (32.1 mg, 0.319 mmol) and a stir bar. The vial is sealed with a septum and purged with N_2 flow for 10 minutes. Tetrahydrofuran (thf, 1.5 mL) is added through a syringe and the suspension is allowed to cool to 0 °C in an ice bath. Freshly prepared *i*PrMgCl (765 μL, 0.658 mmol, 0.86 M in thf) is added through a syringe in a dropwise fashion over a 20 minutes period to the above mixture. The resulting solution is allowed to stir at 0 °C for an additional 10 minutes before being treated with a saturated solution of NH_4Cl (1.0 mL) to quench the reaction. At this point, EtOAc (1.0 mL) is added to dilute the mixture and the layers are separated. The aqueous layer is washed with EtOAc (1.0 mL x 3) and the combined organic layers are dried with anhydrous $MgSO_4$, filtered and concentrated *in vacuo* to afford a colorless oil, which is subjected to silica gel chromatography (1:1 hexanes:Et_2O) to furnish the desired product ***syn*-4.112** as colorless oil (35.2 mg, 0.128 mmol, 78% yield). **Note:** Two possible scenarios can be applied in regard to the use of free phenol **4.113**, a byproduct resulting

from the Weinreb amide formation: (1) Phenol **4.113** can be isolated and subjected to cyclization condition described above. (2) The resulting unpurified mixture obtained above can be directly subjected to cinchona alkaloid catalyzed cyclization process (up to 92% yield of the desired **4.112** can be obtained after isolation). **2-((2*S*,3*S*)-3,5-Dimethyl-3-vinyl-2,3-dihydrobenzofuran-2-yl)-*N*-methoxy-*N*-methylacetamide (*syn*-4.112).** Compound characterization is carried out in the presence of 10% ***anti*-4.112**. IR (neat): 2970 (w), 2935 (w), 1666 (s), 1488 (s), 1419 (m), 1390 (w), 1255 (w), 1218 (w), 1122 (w), 1006 (m), 926 (w), 810 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.93–6.90 (1H, m), 6.81–6.80 (1H, m), 6.70 (1H, d, *J* = 8.4 Hz), 6.02 (1H, dd, *J* = 17.6, 10.8 Hz), 5.23–5.18 (2H, m), 4.93 (1H, dd, *J* = 9.6, 3.6 Hz), 3.72 (3H, s), 3.24 (3H, s), 3.06–3.00 (1H, m), 2.55 (1H, dd, *J* = 15.6, 3.2 Hz), 2.27 (3H, s), 1.24 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.6, 140.4, 133.9, 130.2, 128.9, 124.7, 115.2, 109.7, 89.1, 61.5, 50.4, 33.8, 32.3, 30.5, 23.9, 21.0; HRMS (ESI+): Calcd for $C_{16}H_{22}N_1O_3$ $[M+H]^+$: 276.15997, Found: 276.15966. Specific Rotation: $[\alpha]_D^{20}$ –50.18 (*c* 0.267, $CHCl_3$) for an enantiomerically enriched sample of 99:1 e.r.

2-((2*R*,3*S*)-3,5-Dimethyl-3-vinyl-2,3-dihydrobenzofuran-2-yl)-*N*-methoxy-*N*-methylacetamide (*anti*-4.112). The characterization is carried out in the presence of 11% ***syn*-4.112**. IR (neat): 2968 (w), 2937 (w), 1666 (s), 1487 (s), 1421 (m), 1390 (w), 1253 (w), 1218 (w), 1122 (w), 1008 (m), 923 (w), 810 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.94–6.92 (1H, m), 6.83–6.82 (1H, m), 6.70 (1H, d, *J* = 8.0 Hz), 5.88 (1H, dd, *J* = 17.2, 10.4 Hz), 5.15 (1H, dd, *J* = 10.4, 1.2 Hz), 4.95 (1H, dd, *J* = 17.2, 1.2 Hz), 4.88 (1H, dd, *J* = 8.8, 4.0 Hz), 3.68 (3H, s), 3.22 (3H, s), 2.98–2.92 (1H, m), 2.55 (1H, dd, *J* = 16.0, 4.0 Hz), 2.28 (3H, s), 1.48 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.4, 142.4, 135.2,

130.4, 128.9, 124.2, 114.7, 109.7, 87.3, 61.5, 50.5, 32.3, 32.1, 30.5, 21.0, 19.9; HRMS (ESI+): Calcd for $C_{16}H_{22}N_1O_3$ $[M+H]^+$: 276.15997, Found: 276.16006. Specific Rotation: $[\alpha]_D^{20}$ +59.49 (*c* 0.240, $CHCl_3$) for an enantiomerically enriched sample of 99:1 e.r.

3) Procedure for reaction of Vinylmagnesium Bromide with the Weinreb Amides: Formation of Unsaturated Enone. A flame-dried 2-dram vial (17 x 60 mm) is charged with amide **4.112** (16.8 mg, 0.061 mmol) and a stir bar. The vial is sealed with a septum and purged with N_2 flow for 10 minutes. Tetrahydrofuran (thf, 1.0 mL) is added through a syringe and the resulting solution is allowed to cool to 0 °C in an ice bath. Freshly titrated vinylmagnesium bromide (111 μL, 0.122 mmol, 1.1 M in thf) is added to the mixture through a syringe. The colorless solution is allowed to stir for another 30 min at 0 °C before the reaction is quenched by addition of a saturated solution of NH_4Cl (1.0 mL). The layers are separated and the aqueous layer is washed with Et_2O (1.0 mL x 3). The combined organic layers are dried with anhydrous $MgSO_4$, filtered and concentrated *in vacuo* to afford a colorless oil, which is purified by silica gel chromatography (4:1 hexanes:Et_2O) to furnish the desired enone as colorless oil (14.6 mg, 0.060 mmol, 98% yield). **Note:** the isolated products are immediately used in the following Ru-catalyzed RCM reactions due to the potential instability of the enone.

4) Procedure for Ru-Catalyzed Ring Closing Metathesis Reactions. A flame-dried 6-dram vial is charged with *syn* enone (6.8 mg, 0.028 mmol) and a stir bar. The vial is sealed with a septum and purged with N_2 flow for 10 minutes. Toluene (0.5 mL) is added through a syringe followed by the addition of a stock solution of Ru complex **4.114** (500 μL, 0.0014 mmol, 2.8 x 10^{-3} M in toluene). The resulting light green solution is allowed to stir at ambient temperature for 46 hours. At this time, the mixture is allowed to pass

through a plug of silica gel eluted with 1:1 mixture of hexanes:Et_2O. The filtrate is concentrated *in vacuo* to afford a dark green residue, which is subjected to silica gel chromatography (silica pre-treated with 3% by volume Et_3N; 4:1 hexanes:Et_2O; rapid chromatography required) to furnish the desired *syn*-Pummerer ketone as white solid (4.1 mg, 0.019 mmol, 69% yield).

***syn*-Pummerer's ketone.** The ^1H and ^{13}C NMR of the title compound is known[74] and matches the data acquired with the synthetic material. IR (neat) 2963 (w) 2925 (w) 1682 (s) 1488 (m) 1234 (m) 1004 (m) 811 (w) 794 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.01–6.98 (2H, m), 6.72 (1H, d, J = 8.0 Hz), 6.46 (1H, dd, J = 10.0, 2.0 Hz), 5.92 (1H, d, J = 10.4 Hz), 4.70–4.68 (1H, m), 3.04 (1H, ddd, J = 17.2, 2.4, 0.8 Hz), 2.79 (1H, dd, J = 17.6, 3.6 Hz), 2.32 (3H, s), 1.57 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.2, 156.8, 149.7, 132.3, 131.2, 129.8, 125.9, 123.3, 110.2, 86.7, 45.2, 37.7, 21.6, 21.1; HRMS (ESI+): Calcd for $C_{14}H_{15}O_2$ $[M+H]^+$: 215.10720, Found: 215.10690. Specific Rotation: $[\alpha]_D^{20}$ –174.26 (*c* 0.082, $CHCl_3$) for an enantiomerically enriched sample of 99:1 e.r.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (99:1 e.r. shown; Chiralpak AD-H column, 99.5/0.5 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).

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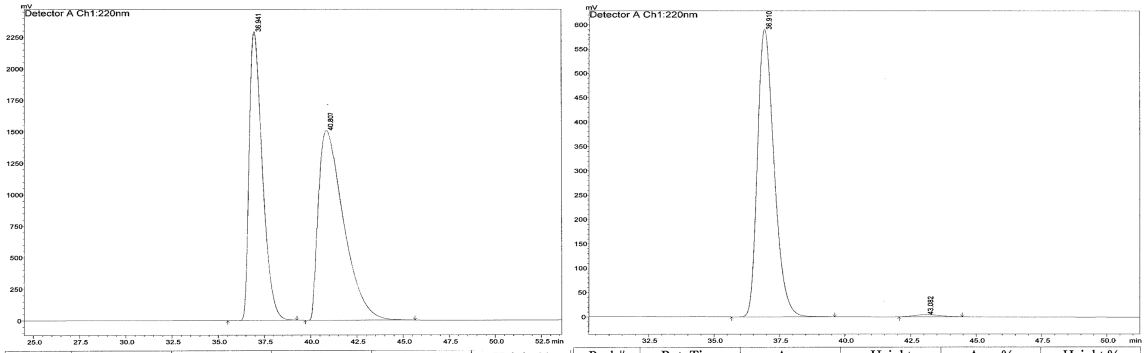
(65) J. –M. Vierfond, A. Reynet, H. Moskowitz, C. Thal, *Synthetic Communication* **1992**, *22*, 1783-1792.



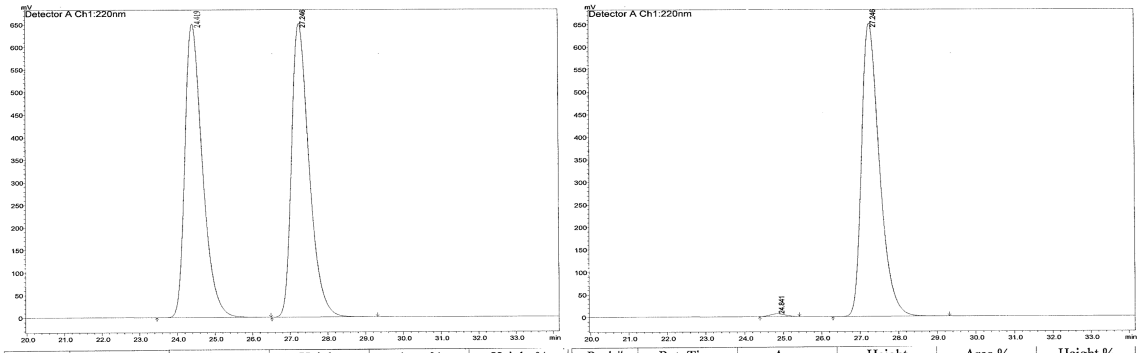
Peak#	Ret. Time	Area	Height	Area %	Height %
1	36.941	114393416	2291680	49.661	59.353
2	40.807	117611494	1569419	50.339	40.647
Total		232004910	3861099	100.000	100.000

Peak#	Ret. Time	Area	Height	Area %	Height %
1	36.910	26160245	590428	98.876	99.265
2	43.082	297419	4372	1.124	0.735
Total		26457664	594800	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	36.94	49.7	1	36.91	98.9
2	40.81	50.3	2	43.08	1.1

***anti*-Pummerer's ketone.** IR (neat): 2963 (w), 2922 (w), 2865 (w), 1682 (s), 1478 (m), 1258 (w), 1232 (w), 1196 (m), 1095 (w), 1019 (m), 810 (m), 781 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (1H, d, *J* = 9.6 Hz), 7.03 (1H, s), 6.93 (1H, dd, *J* = 8.0, 0.8 Hz), 6.77 (1H, d, *J* = 8.0 Hz), 5.96 (1H, d, *J* = 9.6 Hz), 4.39 (1H, dd, *J* = 14.0, 5.6 Hz), 3.06–2.90 (2H, m), 2.27 (3H, s), 1.19 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.5, 157.3, 152.3, 134.1, 131.6, 130.4, 128.9, 122.2, 111.4, 85.0, 47.0, 39.5, 24.3, 21.2; HRMS (ESI+): Calcd for $C_{14}H_{15}O_2$ $[M+H]^+$: 215.10720, Found: 215.10857. Specific Rotation: $[\alpha]_D^{20}$ +75.60 (*c* 0.073, $CHCl_3$) for an enantiomerically enriched sample of 99:1 e.r.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (99:1 e.r. shown; Chiralpak AD-H column, 99.5/0.5 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm). The trace shown is obtained from compound derived from EAS with *R* enantiomer of catalyst.



Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.419	20927207	174513	50.257	47.722
2	27.606	20713396	191176	49.743	52.278
Total		41640603	365689	100.000	100.000

Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.841	165156	6135	0.776	0.933
2	27.246	21108391	651628	99.224	99.067
Total		21273547	657763	100.000	100.000

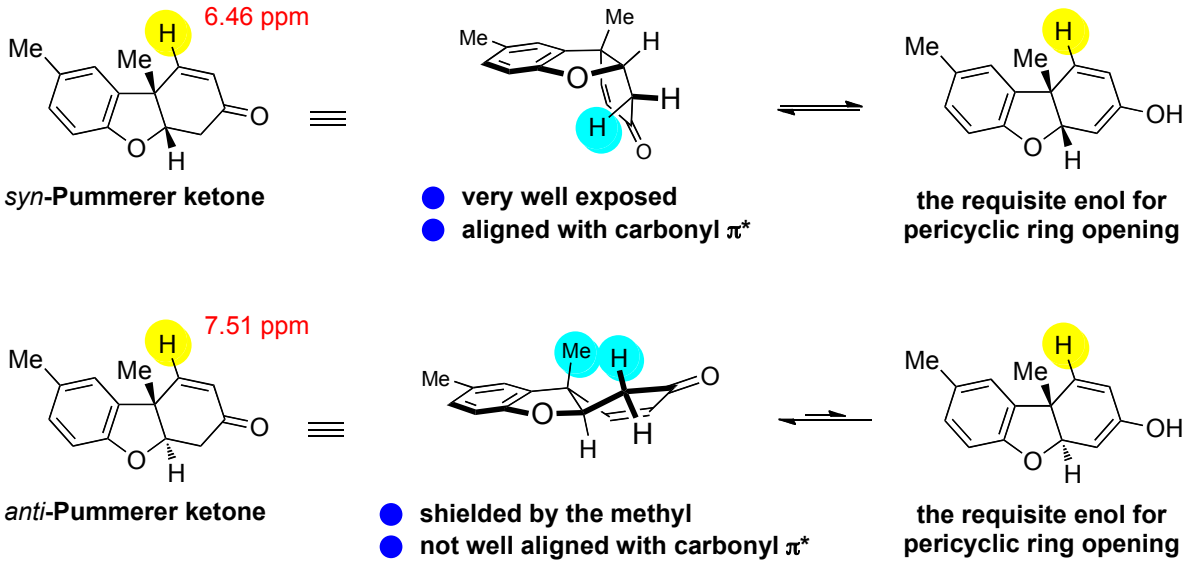
Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	24.42	50.3	1	24.84	0.8
2	27.61	49.7	2	27.25	99.2

■ Proposed Racemization of *syn*-Pummerer Ketone through Pericyclic Rearrangement:

The racemization observed for *syn*-pummerer ketone can be explained through a process that begins with enolization and formation of the conjugated cyclic diene; this is followed by thermal pericyclic ring-opening and then closing causing racemizatyion of the enantiomerically enriched sample (see Scheme S3, below). Only *syn*-pummerer ketone undergoes racemization, whereas *anti* isomer is relatively stable to high temperatures. The latter difference can be rationalized as follows: As illustrated in Scheme S2, enolization of *syn*-Pummerer ketone is expected to be substantially more facile (vs its *anti* isomer). The α-proton in the *syn*-Pummerer ketone is not sterically congested and the C–H σ bond properly aligned with the C=O π*. In contrast, the suitably aligned α-proton in the *anti*-Pummerer ketone is shielded by the proximal methyl unit and therefore the rate of proton transfer is likely slower. Chemical shift of the highlighted enone proton

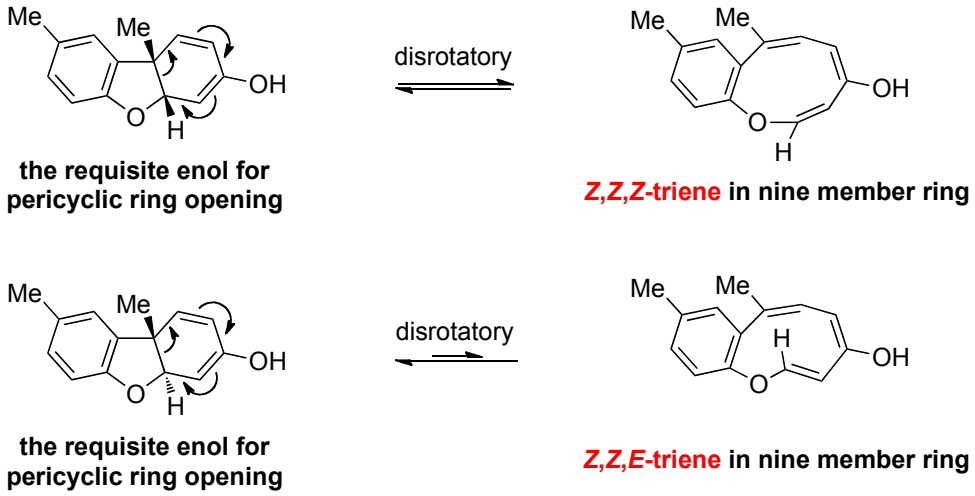
(yellow colored) in *syn*-Pummerer ketone is 6.46 ppm, a value that is typically associated with simple olefin, indicating that the enol form contributes to a much higher degree than it is in the *anti*-isomer (7.51 ppm for the same proton, Scheme S2).

Scheme S2. Proposed Difference in Enolization between *syn*- and *anti*-Pummerer Ketone



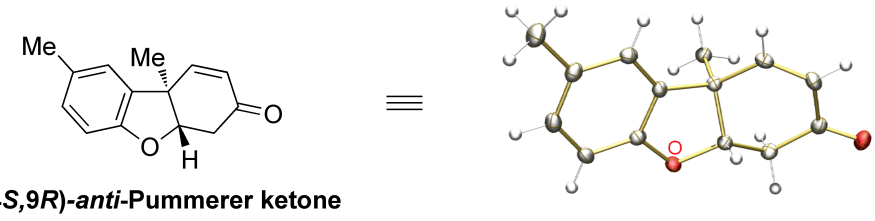
The following observations are consistent with the above scenario for racemization: (1) Product purification with silica gel that has not been pre-treated with Et_3N leads to substantial decrease in enantiomeric purity (from 99:1 e.r. to 75:25 e.r.). In stark contrast, use of silica gel that has been carefully treated with base leads to little or no loss of enantiomeric purity. (2) Ru-catalyzed RCM at 22 °C provides enantiomerically pure *syn*-Pummerer ketone, whereas when the cyclization is performed at 50 °C, the desired compound is obtained in 60:40 e.r.

Scheme S3. Proposed Difference in Racemization between *syn*- and *anti*-Pummerer Ketone



■ **Proof of Relative and Absolute Stereochemistry: Crystal Structure of *anti*-Pummerer Ketone.** The crystal structure is secured for *anti*-Pummerer ketone (99:1 e.r., 4*S*,9*R*) that is synthesized with *R* enantiomer of imidazolinium salt **4.76**. Therefore, the proposed structure of *anti*-Pummerer ketone in Scheme 5 (99:1 er, 4*R*,9*S*) in the main text is substantiated. For details, refer to the crystallography data attached.

Figure S1. Crystal Structure of (4*S*,9*R*)-*anti*-Pummerer Ketone



4.6.2 Representative Experimental Procedures for Cu-catalyzed EAS with Alkenylboron Reagents to Construct Tertiary Stereogenic Center and Characterization Data of New Compounds

General. Infrared (IR) spectra were recorded on a Bruker FT-IR Alpha (ATR mode) spectrophotometer, ν_{max} in cm^{-1}. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). ^{1}H NMR spectra were recorded on a Varian Unity INOVA 400 (400 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on a Varian Unity INOVA 400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: 77.16 ppm). High-resolution mass spectrometry was performed on a Micromass LCT ESI-MS (positive mode) at the Mass Spectrometry Facility, Boston College. Enantiomer ratios were determined by GLC analysis (gas liquid chromatography) with an Agilent chromatograph (Alltech Associated Chiral dex CD-BDM column (30 m x 0.25 mm)), HPLC analysis (high-performance liquid chromatography) with a Shimadzu chromatograph (Chiral Technologies Chiralcel OD-H (4.6 x 250 mm), Chiral Technologies Chiralpak AD-H (4.6 x 250 mm), Chiral Technologies Chiralcel OJ-H (4.6 x 250 mm) Chiral Technologies Chiralpak AS-H (4.6 x 250 mm)) in comparison with authentic racemic materials. Specific rotations were measured on a Rudolph Research Analytical Autopol IV Polarimeter.

Unless otherwise noted, all reactions were carried out with distilled and degassed solvents under an atmosphere of dry N_2 in oven- (135 °C) or flame-dried glassware with standard dry box or vacuum-line techniques. Diethylether, benzene and dichloromethane (Fisher Scientific) were purified by passing through two alumina columns under a

positive pressure of dry argon by a modified Innovative Technologies purification system. Tetrahydrofuran (Aldrich Chemical Co.) was purified by distillation from sodium benzophenone ketyl immediately prior to use unless otherwise specified. All work-up and purification procedures were carried out with reagent grade solvents (purchased from Fisher Scientific) under air. All substrates are prepared according to previously reported procedures and the characterization data of the unknown compounds will be disclosed within this text;[75] all substrates possess *E*-olefin geometry and purities are established by ^{1}H NMR analysis (400 MHz). Allylic phosphate **4.128** is prepared according to a previously reported procedure[75b] from the corresponding alcohol, which has been disclosed before.[76] Allylic phosphates that lead to **4.145**[77a] and **4.190**[77b] are synthesized according to the general phosphorylation procedure[75] from the corresponding alcohols reported in previous studies.[77]

■ **Reagents and Imidazolinium Salts:**

9-Borabicyclo[3.3.1]nonane (0.5 M in thf): purchased from Aldrich Chemical Co. and used as received.

(*Z*)-2-(8-Bromonon-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane: prepared

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(75) (a) Kacprzynski, M. A.; May T. L.; Kazane, S. A.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2007**, *49*, 4554–4558. (b) Lee, Y.; Akiyama, K.; Gillingham, D. G.; Brown, M. K.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2008**, *130*, 446–447. (c) Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 11625–11633. (d) Akiyama, K.; Gao, F.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2010**, *49*, 419–423. (e) Jung, B.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2012**, *134*, 1490–1493. (f) Dabrowski, J. A.; Haeffner, F.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2013**, *52*, 7694–7699. And references cited within these papers.
(76) Zhao, Y.-J.; Loh, T.-P. *Tetrahedron* **2008**, *64*, 4972–4978.
(77) (a) Sato, K.; Yoshimura, T.; Shindo, M.; Shishido, K. *J. Org. Chem.* **2001**, *66*, 309–314. (b) Grigorjeva, L.; Jirgenson, A. *Eur. J. Org. Chem.* **2012**, 5307–5316.

according to a previously disclosed procedure.[78]

***tert*-Butanol:** purchased from Aldrich Chemical Co. and used as received.

(*Z*)-2-(2-Butoxyvinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane: prepared according to a previously disclosed procedure.[78]

***tert*-Butyl hydroperoxide solution (5.0~6.0 M in decane):** purchased from Aldrich Chemical Co. and used as received.

***tert*-Butyl (2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)carbamate:** prepared according to a previously disclosed procedure.[79]

***tert*-Butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydropyridine-1(2*H*)-carboxylate (4.161):** purchased from Frontier Scientific Inc. and used as received.

***tert*-Butyl (*Z*)-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)carbamate:** prepared according to a previously disclosed procedure.[78]

(*Z*)-*tert*-Butyldimethyl((3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)oxy)silane: prepared according to a previously reported procedure.[4]

(*Z*)-*tert*-butyldimethyl((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-2-yl)oxy)silane: prepared according to a previously disclosed procedure. [80]

Copper(I) chloride: purchased from Strem Chemicals Inc. and used as received.

Dess-Martin Periodinane: purchased from TCI America and used as received.

1,2-Dichloroethane: purchased from Aldrich Chemical Co. and used as received.

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(78) Kiesewetter, E. T.; O'Brien, R. V.; Yu, E. C.; Meek, S. J.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2013**, *135*, 6026–6029.
(79) Jang, H.; Zhugralin, A. R.; Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 7859–7871.
(80) Ohmura, T.; Yamamoto, Y.; Miyaura, N. *J. Am. Chem. Soc.* **2000**, *122*, 4990–4991.

(*E*)-2-(3,3-Diethoxyprop-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.103): generously donated to us by Frontier Scientific Inc. and used as received.

2-(3,4-Dihydro-2*H*-pyran-6-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane: purchased from Frontier Scientific Inc. and used as received.

2-(3,6-Dihydro-2*H*-pyran-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane: purchased from Frontier Scientific Inc. as a dark brown oil and used as a white solid after purification through silica gel column chromatography.

Di*iso*butylaluminum hydride (neat): purchased from Aldrich Chemical Co. and used as received.

Ethanol (200 proof): purchased from Fisher Scientific and used as received.

(*E*)-Ethyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (4.97): generously donated to us by Frontier Scientific Inc. and used as received.

Imidazolinium salt 4.115 and 4.116: prepared according to a previously reported procedure.[75e]

Imidazolinium salt 4.150: prepared according to a previously reported procedure.[81]

Imidazolinium salt 4.173: prepared according to a previously reported procedure.[82]

Imidazolinium salts 4.48 and 4.70: prepared according to a previously reported procedure.[83]

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(81) Corberán, R.; Mszar, N. W.; Hoveyda, A. H. **2011**, *50*, 7079–7082.
(82) Vieira, E. M.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 3332–3335.
(83) Lee, K-s.; Hoveyda, A. H. *J. Org. Chem.* **2009**, *74*, 4455–4462.

Imidazolinium salt 4.49: prepared according to a previously reported procedure.[84]

Imidazolinium salt 4.71: prepared according to a previously reported procedure.[85]

Imidazolinium salt 4.51: prepared according to a previously reported procedure.[86]

Imidazolinium salt 4.73: prepared according to a previously reported procedure.[87]

Imidazolinium salt 4.74: prepared according to a previously reported procedure.[75b]

Imidazolinium salt 4.75: prepared according to a previously reported procedure.[75d]

Lithium borohydride solution (2.0 M in tetrahydrofuran): purchased from Aldrich Chemical Co. and used as received.

(*Z*)-2-(9-((4-Methoxybenzyl)oxy)non-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane: prepared according to a previously reported procedure.[78]

(*Z*)-2-(4-Methoxystyryl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane: prepared according to a previously reported procedure.[78]

Methyllithium (1.6 M solution in diethylether): purchased from Acros Organics and used as received from an Acroseal container.

Methylmagnesium iodide (~1.0 M solution in Et_2O): prepared from methyl iodide and Mg turnings in diethylether and used immediately after titration.

Poly(methylhydrosiloxane): purchased from Aldrich Chemical Co. and used as received.

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(84) Van Veldhuizen, J. J.; Campbell, J. E.; Giudici, R. E.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2005**, *127*, 6877–6882.
(85) Martin, D.; Kehrli, S.; d'Augustin, M.; Clavier, H.; Mauduit, M.; Alexakis, A. *J. Am. Chem. Soc.* **2006**, *128*, 8416–8417.
(86) Brown, M. K.; May, T. L.; Baxter, C. A.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2007**, *46*, 1097–1100.
(87) Y. Lee, A. H. Hoveyda, *J. Am. Chem. Soc.* **2009**, *131*, 3160–3161.

Potassium hydroxide: purchased from Fisher Scientific and used as received.

Pyridinium chlorochromate: purchased from Aldrich Chemical Co. and used as received.

Pyridinium *p*-toluenesulfonate: purchased from Aldrich Chemical Co. and used as received.

Sodium bicarbonate: purchased from Fisher Scientific and used as received.

Sodium methoxide: purchased from Strem Chemicals Inc. and used as received.

Sodium perborate tetrahydrate: purchased from Aldrich Chemical Co. and used as received.

Tetrabutylammonium fluoride (1.0 M solution in tetrahydrofuran): purchased from Aldrich Chemical Co. and used as received.

4,4,5,5-Tetramethyl-2-(2-methylprop-1-en-1-yl)-1,3,2-dioxaborolane (4.191): purchased from Frontier Scientific Inc. and used as received.

(*E*)-4,4,5,5-Tetramethyl-2-(oct-1-en-1-yl)-1,3,2-dioxaborolane (4.64): purchased from Aldrich Chemical Co. and purified by distillation over CaH_2.

4,4,5,5-Tetramethyl-2-(1-phenylvinyl)-1,3,2-dioxaborolane: purchased from Aldrich Chemical Co. and used as received.

(*Z*)-4,4,5,5-Tetramethyl-2-(prop-1-en-1-yl)-1,3,2-dioxaborolane (4.130): purchased from Aldrich Chemical Co. and used as received.

(*Z*)-4,4,5,5-Tetramethyl-2-styryl-1,3,2-dioxaborolane (4.149): prepared according to a previously reported procedure.[78]

Titanium(IV) *iso*propoxide: purchased from Aldrich Chemical Co. and used as received.

Vinylboronic acid pinacol ester (4.180): purchased from Aldrich Chemical Co. and used immediately after vacuum transfer under N_2 atmosphere.

■ Characterization Data for New Allylic Phosphates

(*E*)-4-((diethoxyphosphoryl)oxy)-3-methylbut-2-en-1-yl acetate (4.128): IR (neat): 2985 (w), 2934 (w), 1737 (s), 1444 (w), 1368 (w), 1230 (s), 1166 (w), 1004 (s), 955 (s), 877 (m), 801 (m), 750 (w), 590 (w), 506 (m), 421 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.66–5.62 (1H, m), 4.60 (2H, dd, *J* = 7.2, 0.8 Hz), 4.22 (2H, d, *J* = 6.4 Hz), 4.09 (4H, ddq, *J* = 7.6, 6.8, 0.8 Hz), 2.02 (3H, s), 1.73 (3H, d, *J* = 0.8 Hz), 1.31 (6H, dt, *J* = 6.8, 0.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.0, 136.0 (d, *J* = 7.6 Hz), 122.0, 71.5 (d, *J* = 5.3 Hz), 63.9 (d, *J* = 6.0 Hz), 60.6, 21.0, 16.0 (d, *J* = 6.8 Hz), 13.8; HRMS (ESI+): Calcd for $C_{11}H_{21}P_1Na_1O_6$ $[M+Na]^+$: 303.0968, Found: 303.0966.

(*E*)-3-(2,5-dimethoxy-4-methylphenyl)allyl diethyl phosphate: IR (neat): 2984 (w), 2937 (w), 2833 (w), 1508 (m), 1466 (m), 1401 (m), 1271 (m), 1211 (s), 1038 (s), 975 (s), 860 (w), 818 (w), 543 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.97 (1H, d, *J* = 15.6 Hz), 6.90 (1H, s), 6.70 (1H, s), 6.29 (1H, dt, *J* = 16.0, 6.0 Hz), 4.70 (2H, ddd, *J* = 8.0, 5.6, 1.6 Hz), 4.14 (4H, dq, *J* = 7.2, 7.2 Hz), 3.81 (3H, s), 3.80 (3H, s), 2.22 (3H, s), 1.35 (6H, dt, *J* = 7.2, 0.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.0, 151.1, 129.4, 128.2, 123.2 (d, *J* = 6.9 Hz), 122.8, 114.7, 109.0, 68.8 (d, *J* = 5.3 Hz), 63.9 (d, *J* = 6.0 Hz), 56.4, 56.1, 16.6, 16.3 (d, *J* = 6.9 Hz); HRMS (ESI+): Calcd for $C_{16}H_{25}P_1O_6$ $[M]^+$: 344.13887, Found: 344.13780.

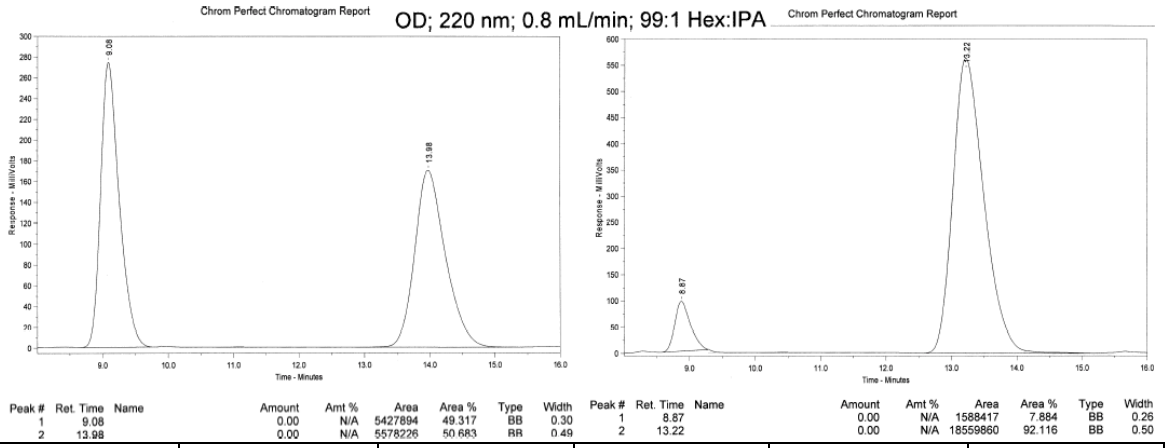
(*E*)-diethyl (4-hydroxy-4-methylpent-2-en-1-yl) phosphate (4.190): IR (neat): 3410 (w), 2972 (w), 2925 (w), 1464 (w), 1372 (w), 1256 (m), 1164 (w), 1019 (s), 968 (s), 802 (m), 547 (w), 526 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.93 (1H, dt, *J* = 15.6, 1.2 Hz), 5.78 (1H, dt, *J* = 15.6, 6.0 Hz), 4.51 (2H, ddd, *J* = 8.0, 5.6, 0.8 Hz), 4.10 (4H, dq, *J* = 7.2, 7.2 Hz), 1.33 (6H, dt, *J* = 7.2, 0.8 Hz), s), 1.31 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.5, 121.4 (d, *J* = 6.9 Hz), 70.5, 67.6 (d, *J* = 5.3 Hz), 63.9 (d, *J* = 6.1 Hz), 29.7 (d, *J* = 8.3 Hz), 16.3 (d, *J* = 6.8 Hz); HRMS (ESI+): Calcd for $C_{10}H_{21}P_1Na_1O_5$ $[M+Na]^+$: 275.1019, Found: 275.1017.

■ **Representative Experimental Procedure for Cu-Catalyzed Enantioselective Allylic Substitution (EAS) with Trans 1,2-Disubstituted Alkenylboron Reagents (Table 1):** In an N_2-filled glove box, an oven-dried 1-dram vial (15 x 45 mm) with a magnetic stir bar is charged with imidazolinium salt **4.116** (4.7 mg, 0.0055 mmol), NaOMe (10.8 mg, 0.200 mmol) and CuCl (0.5 mg, 0.005 mmol). The vial is sealed with a cap (phenolic open top cap with a red PFTE/white silicon septum) and electrical tape before removal from the glove box. To the vial under an N_2 atmosphere is added tetrahydrofuran (thf, 0.5 mL) and the resulting suspension is allowed to stir at 22 °C for one hour. The suspension turns from off-white to light yellow during catalyst formation. Meanwhile, in a separate vial, cinnamyl diethyl phosphate **4.33** (27.0 mg, 0.100 mmol) and (*E*)-4,4,5,5-tetramethyl-2-(oct-1-en-1-yl)-1,3,2-dioxaborolane **4.64** (47.6 mg, 0.200 mmol) are weighted out and the vial is sealed and purged with N_2 flow for 10 min before thf (0.5 mL) is added through a syringe. The stock solution is transferred through a syringe to the reaction vessel that contains the in situ-formed catalyst and the resulting

yellow solution is allowed to stir at 22 °C for additional 24 h. After that time, the mixture is passed through a short plug of silica gel eluted with Et_2O. The filtrate is concentrated under reduced pressure to provide a yellow oil residue, which is purified by silica gel column chromatography (100% hexanes) to afford product **4.117** as colorless oil (22.1 mg, 0.0968 mmol, 97% yield). **(*S*,*E*)-Undeca-1,4-dien-3-ylbenzene (4.117, Table 4.3).** The product has been previously reported and spectra data match those previously described.[75b] ^{1}H NMR (400 MHz, CDCl3): δ 7.31–7.28 (2H, m), 7.21–7.18 (3H, m), 6.02 (1H, ddd, *J* = 16.8, 10.0, 6.8 Hz), 5.60 (1H, ddt, *J* = 15.6, 7.2, 1.6 Hz), 5.50 (1H, ddt, *J* = 15.2, 6.8, 0.8 Hz), 5.11 (1H, d, *J* = 10.0 Hz), 5.05 (1H, d, *J* = 17.2 Hz), 4.06 (1H, dd, *J* = 6.8, 6.8 Hz), 2.05 (2H, dt, *J* = 7.2, 7.2 Hz), 1.37–1.25 (8H, m), 0.88 (3H, t, *J* = 7.2 Hz). Specific Rotation: $[\alpha]_D^{20}$ +15.1 (*c* 0.467, $CHCl_3$) for an enantiomerically enriched sample of 92:8 er.

Proof of Stereochemistry: Literature value ($[\alpha]_D^{20}$ –11.0 (*c* 1.49, $CHCl_3$), 89.5:10.5 er) is assigned to the (*R*) enantiomer.[75b]

Enantiomeric purity is determined by HPLC analysis of the derived primary alcohol (obtained from hydroboration of the terminal olefin with 9-BBN, followed by oxidation with $NaBO_3 \bullet 4H_2O$) in comparison with authentic racemic material (92:8 er shown; Chiralcel OD column, 99/1 hexanes/*i*-PrOH, 0.8 mL/min, 220 nm).



Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	9.08	49.3	1	8.87	7.9
2	13.98	50.7	2	13.22	92.1

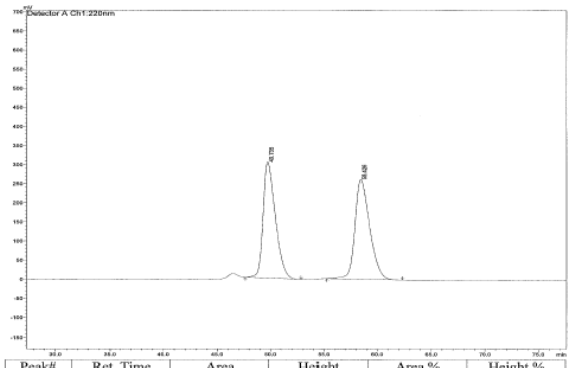
■ **Representative Experimental Procedure for Cu-Catalyzed Enantioselective Allylic Substitution (EAS) with Acetal-Containing Trans 1,2-Disubstituted Alkenylboron Reagents (Scheme 4.19):** In this section, the reactions are performed following the same representative procedure as described for Table 4.3. The specific differences are included within the characterization data of each compound.

(*S*,*E*)-1-(6,6-Diethoxyhexa-1,4-dien-3-yl)-4-nitrobenzene (4.121, Scheme 4.19). Same procedure as described in Table 4.3 is followed. The title compound is isolated by column chromatography with basified silica gel (5% NEt_3). IR (neat): 2976 (w), 2928 (w), 2876 (w), 1598 (w), 1521 (s), 1346 (s), 1133 (w), 1052 (m), 996 (w), 854 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.19–8.16 (2H, m), 7.39–7.35 (2H, m), 6.04–5.95 (2H, m), 5.58 (1H, ddd, *J* = 17.2, 5.2, 1.6 Hz), 5.22 (1H, ddd, *J* = 10.4, 1.2, 1.2 Hz), 5.10 (1H, ddd, *J* = 17.2, 1.2, 1.2 Hz), 4.93 (1H, dd, *J* = 6.0, 0.8 Hz), 4.20 (1H, dd, *J* = 6.8, 6.8 Hz), 3.67–3.60 (2H, m), 3.54–3.45 (2H, m), 1.24–1.19 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.9, 146.9, 138.3, 134.1, 130.2, 129.1, 124.0, 117.3, 101.0, 61.2, 51.5, 15.39, 15.40;

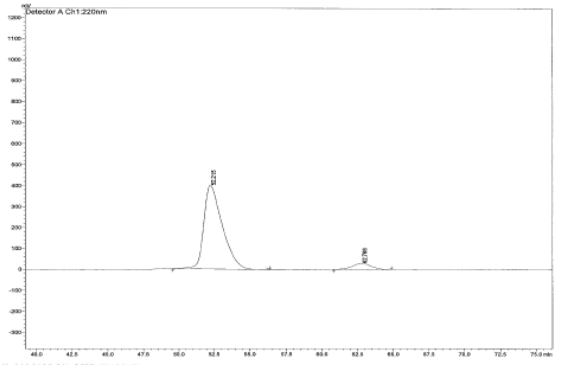
HRMS (ESI+): Calcd for $C_{14}H_{16}N_1O_3$ $[M–OEt]^+$: 246.11302, Found: 246.11300. Specific Rotation: $[\alpha]_D^{20}$ +3.79 (*c* 0.327, $CHCl_3$) for an enantiomerically enriched sample of 93:7 er. Enantiomeric purity is determined by HPLC analysis of the derived enal (see below).

(*S*,*E*)-4-(4-Nitrophenyl)hexa-2,5-dienal (4.122, Scheme 4.19). Same procedure as described in Table 4.3 is followed. The crude reaction mixture is dissolved in Et_2O and treated with solid silica gel (ca. 100 mg). The resulting suspension is allowed to stir at 22 ^oC for one hour before it is passed through a cotton plug eluted with Et_2O. Solvent is removed by rotory evaporation to afford a yellow oil residue, which is purified by regular column chromatography. IR (neat): 2985 (w), 2827 (w), 1699 (s), 1634 (w), 1472 (m), 1433 (w), 1166 (w), 1031 (m), 985 (w), 927 (m), 754 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.61 (1H, dd, *J* = 8.0, 2.8 Hz), 8.24–8.20 (2H, m), 7.41–7.37 (2H, m), 6.96 (1H, dd, *J* = 16.0, 6.8 Hz), 6.15 (1H, ddd, *J* = 17.2, 7.6, 1.6 Hz), 6.03 (1H, ddd, *J* = 17.2, 10.4, 6.8 Hz), 5.36 (1H, dd, *J* = 10.0, 0.8 Hz), 5.20 (1H, dd, *J* = 17.2, 0.8 Hz), 4.45 (1H, dd, *J* = 6.8, 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.2, 155.7, 147.4, 147.2, 136.1, 133.9, 129.2, 124.3, 118.9, 51.7; HRMS (ESI+): Calcd for $C_{12}H_{12}N_1O_3$ $[M+H]^+$: 218.08172, Found: 218.08203. Specific Rotation: $[\alpha]_D^{20}$ +17.2 (*c* 0.492, $CHCl_3$) for an enantiomerically enriched sample of 93:7 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (93:7 er shown; Chiralcel OJ-H column, 95/5 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	49.735	24237585	303774	49.411	53.799
2	58.426	24815053	260872	50.589	46.201
Total		49052638	564646	100.000	100.000

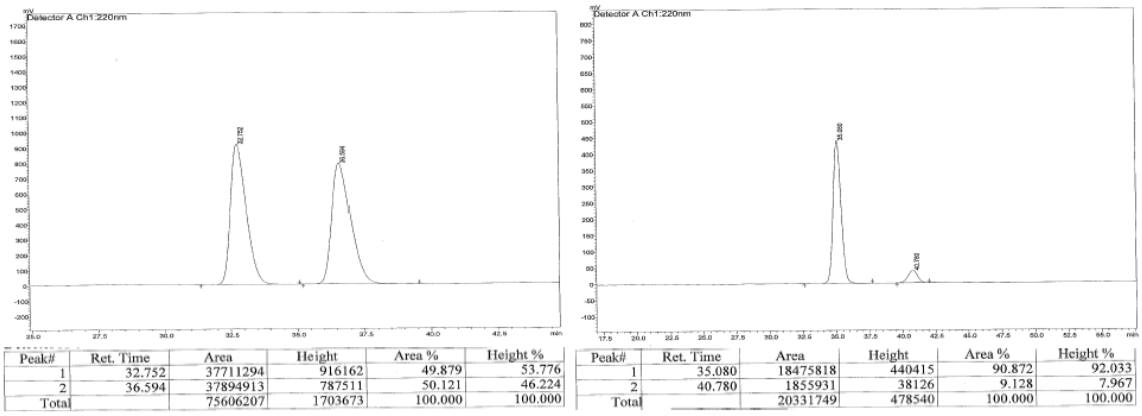


Peak#	Ret. Time	Area	Height	Area %	Height %
1	52.215	36366606	400479	93.233	93.057
2	62.768	2639421	29878	6.767	6.943
Total		39006027	430356	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	49.74	49.4	1	52.22	93.2
2	58.43	50.6	2	62.77	6.8

(*S*,*E*)-4-Phenylhexa-2,5-dienal (4.118, Scheme 4.19). The title compound is prepared using the same procedure as with **4.122**. IR (neat): 3083 (w), 3061 (w), 3029 (w), 2980 (w), 2818 (w), 2735 (w), 1687 (s), 1631 (w), 1600 (w), 1492 (w), 1453 (w), 1111 (m), 978 (m), 923 (m), 758 (m), 701 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.51 (1H, d, *J* = 8.0 Hz), 7.31–7.26 (2H, m), 7.23–7.19 (1H, m), 7.13 (2H, dd, *J* = 8.4, 1.2 Hz), 6.92 (1H, dd, *J* = 15.6, 6.8 Hz), 6.09–5.94 (2H, m), 5.19 (1H, ddd, *J* = 10.4, 1.2, 1.2 Hz), 5.07 (1H, ddd, *J* = 17.2, 1.6, 0.8 Hz), 4.25 (1H, dd, *J* = 6.8, 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.8, 158.3, 140.1, 137.6, 133.1, 129.1, 128.2, 127.5, 117.5, 52.2; HRMS (ESI+): Calcd for $C_{12}H_{13}O_1$ $[M+H]^+$: 173.09664, Found: 173.09718. Specific Rotation: $[\alpha]_D^{20}$ +16.0 (*c* 0.807, $CHCl_3$) for an enantiomerically enriched sample of 91:9 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (91:9 er shown; Chiralcel OJ-H column, 99/1 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	32.752	37711294	916162	49.879	53.776
2	36.594	37894913	787511	50.121	46.224
Total		75606207	1703673	100.000	100.000

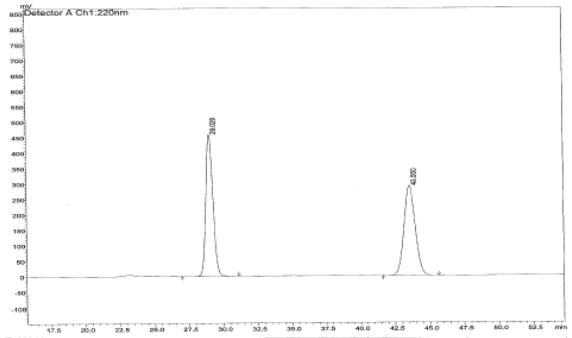
Peak#	Ret. Time	Area	Height	Area %	Height %
1	35.080	18475818	440415	90.872	92.033
2	40.780	1855931	38126	9.128	7.967
Total		20331749	478540	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	32.75	49.9	1	35.08	90.8
2	36.59	50.1	2	40.78	9.1

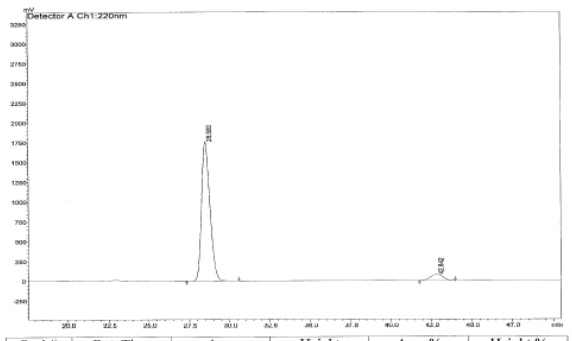
(*S*,*E*)-1-Bromo-2-(6,6-diethoxyhexa-1,4-dien-3-yl)benzene (Scheme 4.19). The title compound is prepared using the same procedure as with **4.121**. IR (neat): 2975 (m), 2929 (w), 2878 (w), 1468 (w), 1439 (w), 1339 (w), 1300 (w), 1133 (m), 1051 (s), 1022 (w), 996 (m), 920 (w), 754 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (1H, dd, *J* = 8.0, 1.6 Hz), 7.27 (1H, ddd, *J* = 7.6, 7.2, 1.2 Hz), 7.21 (1H, dd, *J* = 7.6, 2.0 Hz), 7.08 (1H, ddd, *J* = 9.2, 7.2, 1.6 Hz), 6.02–5.93 (2H, m), 5.55 (1H, ddd, *J* = 16.0, 5.2, 1.6 Hz), 5.20 (1H, ddd, *J* = 10.4, 1.6, 1.6 Hz), 5.08 (1H, ddd, *J* = 17.2, 1.6, 1.6 Hz), 4.93 (1H, ddd, *J* = 5.2, 0.8, 0.8 Hz), 4.62 (1H, ddd, *J* = 6.4, 6.0, 0.8 Hz), 3.68–3.59 (2H, m), 3.54–3.45 (2H, m), 1.23–1.18 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.2, 138.4, 134.5, 133.2, 129.8, 129.7, 128.2, 127.7, 124.9, 116.7, 101.3, 61.0, 49.9, 15.42, 15.40; HRMS (ESI+): Calcd for $C_{14}H_{16}O_1Br_1$ $[M+H–EtOH]^+$: 279.03845, Found: 279.03902. Specific Rotation: $[\alpha]_D^{20}$ –18.5 (*c* 0.780, $CHCl_3$) for an enantiomerically enriched sample of 94:6 er. Enantiomeric purity is determined by HPLC analysis of the derived enal (see below).

(*S*,*E*)-4-(2-Bromophenyl)hexa-2,5-dienal (4.119, Scheme 4.19). The title compound is prepared using the same procedure as with **4.122**. IR (neat): 3063 (w), 2981 (w), 2816 (w), 2734 (w), 1691 (s), 1630 (w), 1469 (w), 1437 (w), 1122 (w), 1023 (w), 979 (w), 926 (w), 756 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.60 (1H, d, *J* = 7.6 Hz), 7.60 (1H, dd, *J* = 8.0, 1.2 Hz), 7.32 (1H, ddd, *J* = 7.6, 7.6, 1.2 Hz), 7.21–7.13 (2H, m), 6.95 (1H, dd, *J* = 15.6, 6.0 Hz), 6.11 (1H, ddd, *J* = 15.6, 7.6, 1.6 Hz), 6.02 (1H, ddd, *J* = 17.2, 10.4, 6.4 Hz), 5.32 (1H, ddd, *J* = 10.0, 1.2, 0.8 Hz), 5.16 (1H, ddd, *J* = 17.2, 1.6, 0.8 Hz), 4.89–4.85 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.7, 157.0, 139.2, 136.3, 133.8, 133.5, 129.7, 129.1, 128.1, 124.8, 118.3, 50.5; HRMS (ESI+): Calcd for $C_{12}H_{12}Br_1O_1$ $[M+H]^+$: 251.00715, Found: 251.00766. Specific Rotation: $[\alpha]_D^{20}$ –14.6 (*c* 0.467, $CHCl_3$) for an enantiomerically enriched sample of 94:6 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (94:6 er shown; Chiralcel OJ-H column, 99/1 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.029	16311175	458748	49.983	61.187
2	43.550	16322571	291001	50.017	38.813
Total		32633745	749750	100.000	100.000

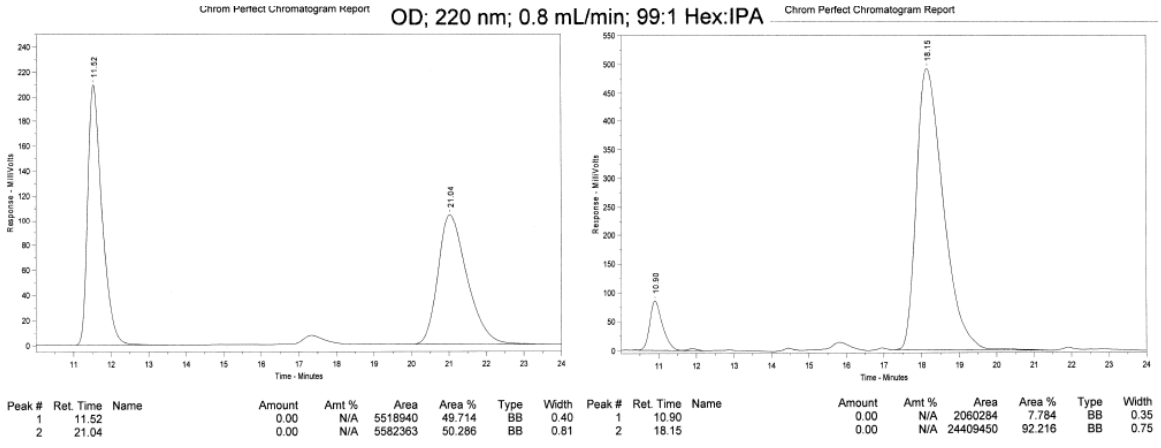


Peak#	Ret. Time	Area	Height	Area %	Height %
1	28.500	64083321	1759240	93.871	95.766
2	42.842	4184373	77787	6.129	4.234
Total		68267694	1837027	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	29.03	50.0	1	28.50	93.9
2	43.55	50.0	2	42.84	6.1

Methyl (*S*,*E*)-3-(4-chlorophenyl)-6,6-diethoxy-2-methylenehex-4-enoate (4.120, Scheme 4.19). The title compound is prepared using the same procedure as with **4.121**, except in the presence of 2.5 mol % **4.116**, 25 mol % CuCl and 1.5 equiv NaOMe. IR (neat): 2972 (w), 2928 (w), 2870 (w), 1720 (s), 1599 (w), 1488 (m), 1340 (s), 1243 (s), 1234 (m), 1134 (w), 1128 (s), 1080 (m), 1052 (s), 997 (m), 825 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (2H, d, *J* = 8.4 Hz), 7.12 (2H, d, *J* = 8.4 Hz), 6.37 (1H, app s), 6.06 (1H, ddd, *J* = 15.6, 6.8, 1.2 Hz), 5.60 (1H, t, *J* = 1.2 Hz), 5.38 (1H, ddd, *J* = 15.6, 4.8, 1.6 Hz), 4.91 (1H, dt, *J* = 5.2, 0.8 Hz), 4.65 (1H, br d, *J* = 6.8 Hz), 3.68 (3H, s), 3.64–3.55 (2H, m), 3.51–3.43 (2H, m), 1.19 (6H, dt, *J* = 7.2, 0.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 143.6, 139.4, 134.3, 133.9, 130.7, 126.9, 124.5, 124.1, 100.9, 61.1, 52.1, 50.5, 15.39, 15.41; HRMS (ESI$^+$): Calcd for $C_{16}H_{18}{}^{35}ClO_3$ $[M–OEt]^+$: 293.0945, Found: 293.0921.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (92:8 er shown; Chiralcel OD column, 99/1 hexanes/*i*-PrOH, 0.8 mL/min, 220 nm).



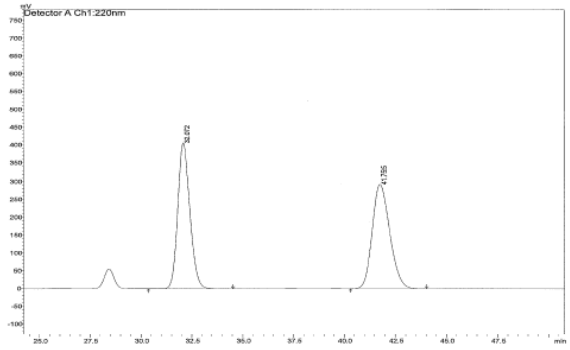
Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	11.52	49.7	1	10.90	7.8

2	21.04	50.3	2	18.15	92.2

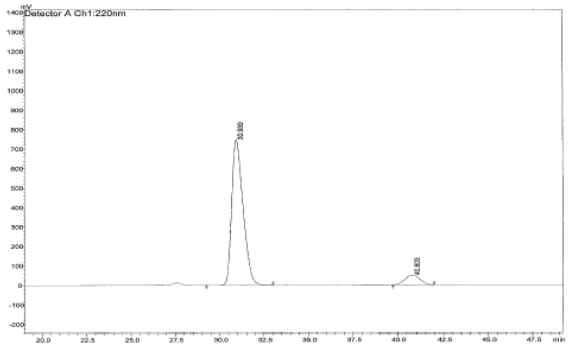
■ **Representative Experimental Procedure for Cu-Catalyzed Enantioselective Allylic Substitution (EAS) with Ester-Containing Trans 1,2-Disubstituted Alkenylboron Reagents (Scheme 4.20):** In this section, the reactions are performed following the same representative procedure as described for Table 4.3. Compound **4.125** and **4.126** are inseparable mixture by column chromatography; therefore, the yield is determined by ^{1}H NMR with an internal standard.

Ethyl (*S*,*E*)-4-phenylhexa-2,5-dienoate (4.123, Scheme 4.20). IR (neat): 2980 (w), 1718 (s), 1651 (w), 1493 (w), 1452 (w), 1367 (w), 1312 (w), 1265 (m), 1231 (w), 1172 (m), 1041 (w), 986 (w), 922 (w), 700 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.29 (1H, m), 7.24–8.20 (1H, m), 7.18–7.09 (3H, m), 6.00 (1H, ddd, *J* = 17.2, 10.4, 6.8 Hz), 5.81 (1H, dd, *J* = 16.0, 1.6 Hz), 5.18 (1H, dd, *J* = 11.2, 1.2 Hz), 5.09 (1H, dd, *J* = 17.2, 1.2 Hz), 4.19–4.13 (3H, m), 1.25 (3H, t, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 149.4, 140.7, 138.3, 128.9, 128.2, 127.2, 122.2, 116.9, 60.5, 51.8, 14.4; HRMS (ESI+): Calcd for $C_{14}H_{16}N_1O_3$ $[M+H]^+$: 217.12285, Found: 217.12381. Specific Rotation: $[\alpha]_D^{20}$ +5.78 (*c* 1.45, $CHCl_3$) for an enantiomerically enriched sample of 92.5:7.5 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (92.5:7.5 er shown; Chiralcel OJ-H column, 99.5/0.5 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	32.072	17157511	405517	49.999	58.158
2	41.755	17157991	291752	50.001	41.842
Total		34315502	697269	100.000	100.000

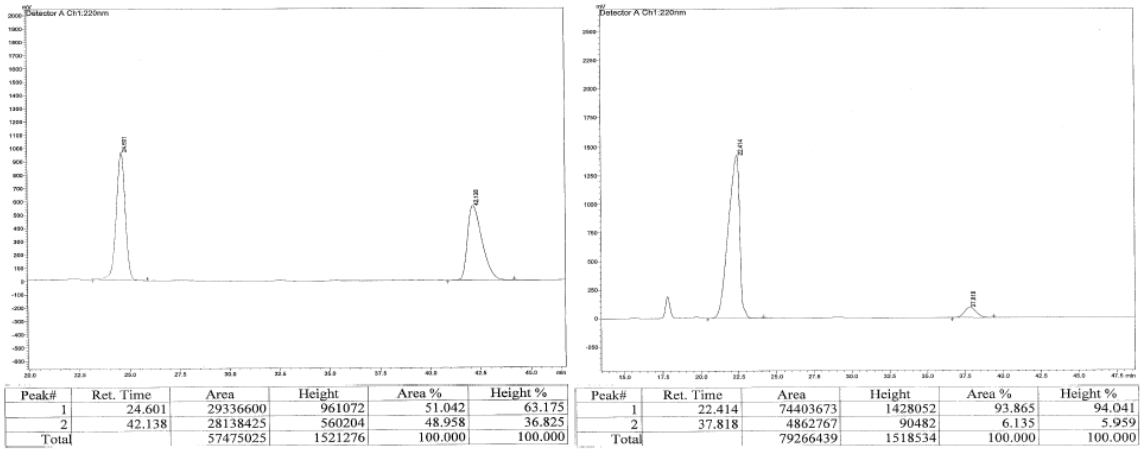


Peak#	Ret. Time	Area	Height	Area %	Height %
1	30.939	32967222	745842	92.590	93.921
2	40.803	2638491	48277	7.410	6.079
Total		35605713	794119	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	32.07	50.0	1	30.94	92.6
2	41.76	50.0	2	40.80	7.4

Ethyl (*S*,*E*)-4-(*o*-tolyl)hexa-2,5-dienoate (4.124, Scheme 4.20). IR (neat): 3065 (w), 2980 (w), 1718 (s), 1650 (w), 1489 (w), 1462 (w), 1367 (w), 1309 (w), 1264 (m), 1234 (w), 1179 (m), 1040 (m), 987 (w), 922 (w), 759 (w), 729 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.22–7.11 (5H, m), 6.00 (1H, ddd, *J* = 16.4, 10.0, 6.4 Hz), 5.80 (1H, dd, *J* = 15.6, 1.6 Hz), 5.23 (1H, ddd, *J* = 10.4, 1.2, 1.2 Hz), 5.07 (1H, ddd, *J* = 17.2, 1.6, 1.2 Hz), 4.43–4.39 (1H, m), 4.19 (2H, q, *J* = 6.8 Hz), 2.32 (3H, s), 1.27 (3H, t, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 149.3, 136.6, 137.9, 136.2, 130.8, 128.0, 127.1, 126.5, 122.3, 117.0, 60.5, 47.5, 19.6, 14.4; HRMS (ESI+): Calcd for $C_{15}H_{19}O_2$ $[M+H]^+$: 231.13850, Found: 231.13894. Specific Rotation: $[\alpha]_D^{20}$ +7.96 (*c* 0.950, $CHCl_3$) for an enantiomerically enriched sample of 94:6 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (94:6 er shown; Chiralcel OD-H column, 99.5/0.5 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.601	29336600	961072	51.042	63.175
2	42.138	28138425	560204	48.958	36.825
Total		57475025	1521276	100.000	100.000

Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.414	74403673	1428052	93.865	94.041
2	37.818	4862767	90482	6.135	5.959
Total		79266439	1518534	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	24.60	51.0	1	22.41	93.9
2	42.14	49.0	2	37.82	6.1

Ethyl (*R*,*E*)-4-cyclohexylhexa-2,5-dienoate (Scheme 4.20). IR (neat): 2979 (w), 2924 (s), 2852 (m), 1718 (s), 1651 (w), 1449 (w), 1367 (w), 1308 (w), 1265 (s), 1243 (m), 1209 (m), 1171 (s), 1143 (m), 1096 (w), 1070 (m), 1043 (m), 991 (m), 915 (w), 726 (w), 670 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.90 (1H, dd, *J* = 15.6, 8.4 Hz), 5.77 (1H, dd, *J* = 15.6, 0.8 Hz), 5.72 (1H, ddd, *J* = 17.2, 10.0, 8.4 Hz), 5.07 (1H, ddd, *J* = 10.4, 2.0, 0.8 Hz), 5.01 (1H, ddd, *J* = 17.2, 2.0, 0.8 Hz), 4.18 (2H, q, *J* = 7.2 Hz), 2.65 (1H, ddd, *J* = 8.4, 8.0, 7.6 Hz), 1.73–1.60 (5H, m), 1.44–1.35 (1H, m), 1.28 (3H, t, *J* = 7.2 Hz), 1.26–1.05 (3H, m), 1.00–0.87 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.8, 150.3, 138.0, 121.6, 116.6, 60.3, 53.4, 41.6, 30.9, 30.6, 26.50, 26.47, 26.46, 14.4; HRMS (ESI+): Calcd for $C_{14}H_{23}O_2$ $[M+H]^+$: 223.16980, Found: 223.16916. Specific Rotation: $[\alpha]_D^{20}$ +6.77 (*c* 1.43, $CHCl_3$) for an enantiomerically enriched sample of 76:24 er.

Ethyl (*S*,*E*)-4-(2,5-dimethoxy-4-methylphenyl)hexa-2,5-dienoate (Scheme 4.20). IR (neat): 2980 (w), 2938 (w), 2831 (w), 1717 (s), 1650 (w), 1505 (m), 1465 (m), 1397 (m), 1367 (w), 1309 (w), 1265 (w), 1209 (s), 1179 (m), 1045 (s), 986 (w), 921 (w), 863 (w),

762 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.13 (1H, dd, *J* = 15.6, 6.4 Hz), 6.71 (1H, s), 6.60 (1H, s), 6.04 (1H, ddd, *J* = 16.8, 10.4, 6.4 Hz), 5.80 (1H, dd, *J* = 15.6, 1.6 Hz), 5.19 (1H, ddd, *J* = 10.4, 1.6, 1.2 Hz), 5.11 (1H, ddd, *J* = 17.2, 1.6, 1.2 Hz), 4.61 (1H, ddd, *J* = 6.0, 6.0, 1.2 Hz), 4.17 (2H, q, *J* = 7.2 Hz), 3.768 (3H, s), 3.766 (3H, s), 2.21 (3H, s), 1.27 (3H, t, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.9, 152.0, 150.7, 149.8, 138.2, 126.8, 126.2, 121.7, 116.6, 114.7, 111.5, 60.4, 56.5, 56.3, 44.6, 16.3, 14.4; HRMS (ESI+): Calcd for $C_{17}H_{23}O_4$ $[M+H]^+$: 291.15963, Found: 291.15862. Specific Rotation: $[\alpha]_D^{20}$ +18.2 (*c* 1.65, $CHCl_3$) for an enantiomerically enriched sample of 98:2 er.

■ **Synthesis of Irregular Monoterpenoid from Enoate 4.129 (Scheme 4.21):** Enoate **4.129** is prepared following the procedure described in Scheme 4.20 with the exception that imidazolinium salt **4.150** is used as the optimal ligand on copper. **4.129** cannot be separated from alkenylboron **4.97** and thus the characterization is carried out after the transformation into the natural product.

To an oven-dried 2-dram vial equipped with a magnetic stir bar is charged with enoate **4.129** (ca. 32.0 mg, 0.141 mmol). The vessel is evacuated and refilled with N_2 three times; under N_2 atmosphere, diethyl ether (1.5 mL) is added through a syringe. The solution is allowed to cool to –78 °C in a dry ice/acetone bath followed by dropwise addition of MeLi solution (353 μL, 0.564 mmol, 1.6 M in Et_2O) over 5 minutes. The resulting solution is allowed to stir at –78 °C for an additional hour; then it is allowed to warm to 0 °C and kept stirring at this temperature for another 30 minutes before it is quenched by addition of saturated NH_4Cl solution (1.0 mL). The layers are separated and the aqueous layer is washed with Et_2O (3 x 1.0 mL). The combined organic layers are dried over anhydrous $MgSO_4$, filtered and volatiles removed under reduced pressure to

afford a crude yellowish oil residue, which is purified by silica gel column chromatography (3:1 hexanes/ethyl acetate) to deliver the irregular monoterpenoid as colorless oil (17.0 mg, 0.100 mmol, 71% yield). **(*R*,*E*)-5-Methyl-2-(prop-1-en-2-yl)hex-3-ene-1,5-diol (irregular monoterpenoid, Scheme 4.21).** The compound has been previously isolated and the spectral data match those reported.[88] IR (neat): 3334 (s), 2970 (s), 2922 (m), 2874 (w), 1645 (w), 1453 (w), 1374 (s), 1230 (w), 1152 (s), 1042 (s), 973 (s), 891 (s), 604 (w), 548 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.74 (1H, dd, *J* = 15.6, 0.8 Hz), 5.56 (1H, dd, *J* = 15.6, 8.0 Hz), 4.90 (1H, ddd, *J* = 2.8, 1.6, 1.2 Hz), 4.81 (1H, dd, *J* = 0.8, 0.4 Hz), 3.66 (1H, dd, *J* = 10.4, 7.2 Hz), 3.58 (1H, dd, *J* = 10.8, 7.2 Hz), 2.89 (1H, dt, *J* = 7.2, 7.2 Hz), 1.73 (3H, d, *J* = 0.8 Hz), 1.32 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.8, 140.8, 125.6, 112.5, 70.8, 63.9, 52.4, 30.1, 29.9, 20.9; HRMS (ESI+): Calcd for $C_{10}H_{17}O_1$ $[M+H–H_2O]^+$: 153.12794, Found: 153.12809. Specific Rotation: $[\alpha]_D^{20}$ –23.1 (*c* 0.267, $CHCl_3$) for an enantiomerically enriched sample of 92.5:7.5 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (92.5:7.5 er shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).

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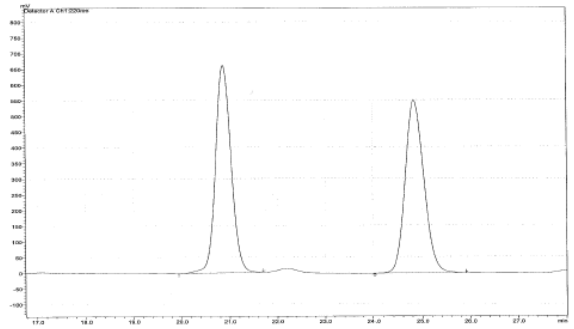
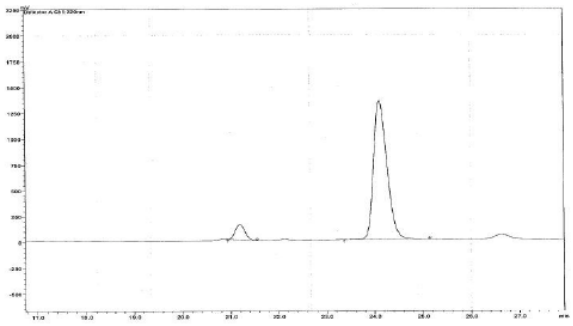
(88) (a) Sy, L.-K.; Brown, G. D. *Phytochemistry* **2001**, *58*, 1159–1166. (b) Araki, S.; Kambe, S.; Kameda, K.; Hirashita, T. *Synthesis* **2003**, *5*, 751–754.



Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.868	14908942	660924	50.032	54.563
2	24.832	14889622	550382	49.968	45.437
Total		29798564	1211306	100.000	100.000



Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.288	4744242	149163	7.475	9.979
2	24.140	58721733	1345546	92.525	90.021
Total		63465975	1494709	100.000	100.000

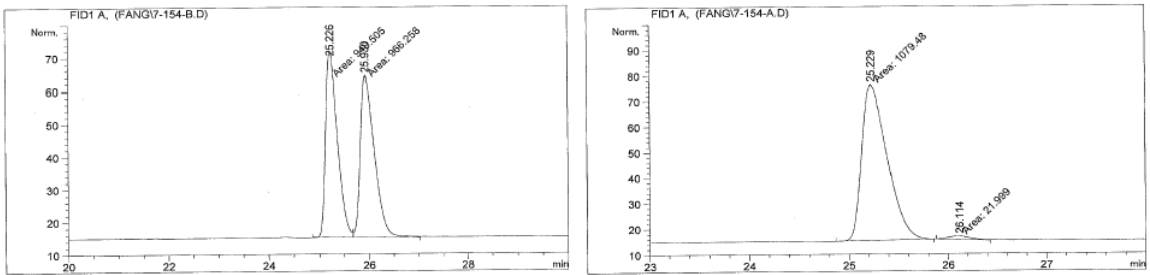
Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	20.87	50.0	1	21.29	7.5
2	24.83	50.0	2	24.14	92.5

■ **Representative Experimental Procedure for Cu-Catalyzed Enantioselective Allylic Substitution (EAS) with Methyl-Substituted Cis 1,2-Disubstituted Alkenylboron Reagents (Table 4.4):** In this section, the reactions are performed following the same representative procedure as described for Table 4.3. The specific differences are included within the characterization data of each compound.

(*S*,*Z*)-1-(Hexa-1,4-dien-3-yl)-3-(trifluoromethyl)benzene (4.133, Table 4.4). The title compound is prepared in 8 h at 22 °C following the general procedure. IR (neat): 3020 (w), 2980 (w), 2921 (w), 1444 (w), 1328 (s), 1248 (w), 1162 (s), 1121 (s), 1072 (s), 993 (w), 917 (m), 801 (m), 777 (w), 720 (m), 701 (s), 682 (w), 655 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.49–7.41 (4H, m), 5.97 (1H, ddd, *J* = 16.8, 10.4, 6.4 Hz), 5.72–5.64 (1H, m), 5.58–5.52 (1H, m), 5.18–5.12 (2H, m), 4.42 (1H, dd, *J* = 8.4, 6.8 Hz), 1.71 (3H, dd, *J* = 6.8, 2.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.7, 139.6, 131.3, 130.88, 130.9 (q, *J* = 32.0 Hz), 129.0, 125.7, 124.5 (q, *J* = 3.7 Hz), 123.3 (q, *J* = 3.7 Hz), 123.2 (q, *J* = 245.0 Hz), 115.6, 46.5, 13.2; HRMS (ESI+): Calcd for $C_{13}H_{14}F_3$ $[M+H]^+$: 227.10476,

Found: 227.10569. Specific Rotation: $[\alpha]_D^{20}$ –8.76 (*c* 1.14, $CHCl_3$) for an enantiomerically enriched sample of 98:2 er.

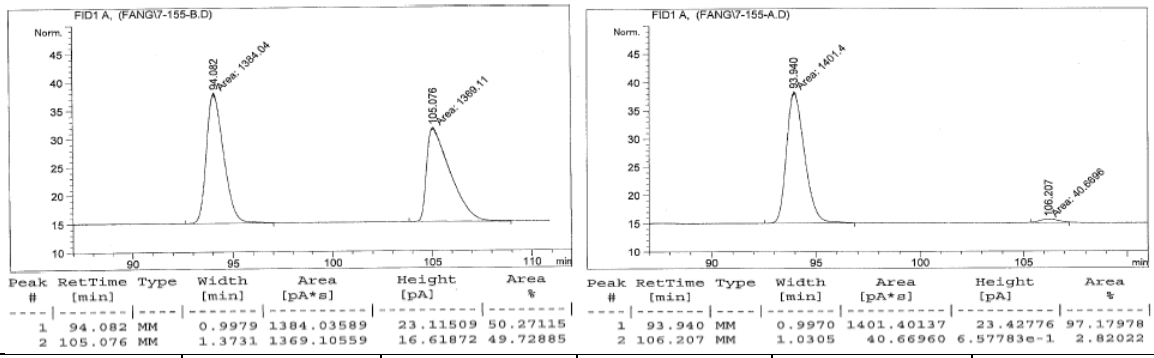
Enantiomeric purity is determined by GLC analysis in comparison with authentic racemic material (98:2 er shown; CDB/DM column, 80 ºC, 15 psi).



Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	25.23	49.3	1	25.23	98.0
2	25.93	50.7	2	26.11	2.0

(*S*,*Z*)-1-(Hexa-1,4-dien-3-yl)-2-methoxybenzene (4.132, Table 4.4). The title compound is prepared in 8 h at 22 ºC following the general procedure. IR (neat): 3078 (w), 3012 (w), 2936 (w), 2835 (w), 1634 (w), 1598 (w), 1586 (w), 1490 (s), 1463 (m), 1438 (m), 1288 (w), 1238 (s), 1105 (m), 1051 (m), 1030 (s), 993 (w), 912 (m), 855 (w), 750 (s), 715 (s), 662 (m), 577 (w), 492 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.21–7.17 (2H, m), 6.92 (1H, ddd, *J* = 7.5, 7.5, 1.0 Hz), 6.87 (1H, dd, *J* = 8.5, 1.0 Hz), 6.04 (1H, ddd, *J* = 17.0, 10.0, 5.5 Hz), 5.60–5.53 (2H, m), 5.11–5.05 (2H, m), 4.82–4.79 (1H, m), 3.84 (3H, s), 1.71 (3H, d, *J* = 5.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.8, 140.7, 132.5, 131.6, 128.5, 127.3, 124.7, 120.9, 114.0, 111.0, 55.6, 39.8, 13.1; HRMS (ESI+): Calcd for $C_{13}H_{17}O_1$ $[M+H]^+$: 189.12794, Found: 189.12772. Specific Rotation: $[\alpha]_D^{20}$ +87.3 (*c* 1.03, $CHCl_3$) for an enantiomerically enriched sample of 97:3 er.

Enantiomeric purity is determined by GLC analysis in comparison with authentic racemic material (97:3 er shown; CDB/DM column, 80 ºC, 15 psi).



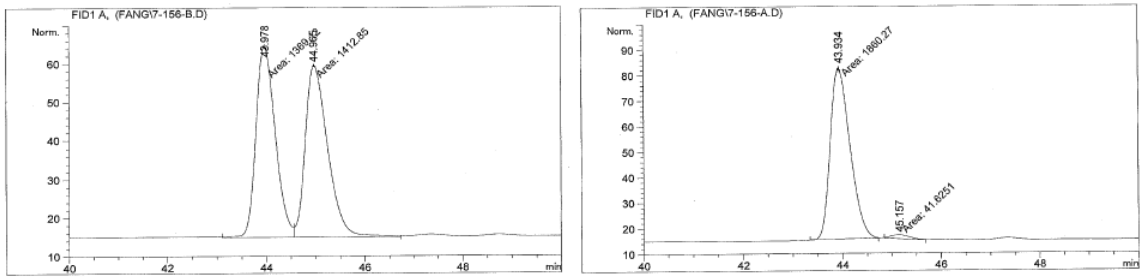
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	94.082	MM	0.9979	1384.03589	23.11509	50.27115
2	105.076	MM	1.3731	1369.10559	16.61872	49.72885

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	93.940	MM	0.9970	1401.40137	23.42776	97.17978
2	106.207	MM	1.0305	40.66960	6.57783e-1	2.82022

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	94.08	50.3	1	93.94	97.2
2	105.08	49.7	2	106.21	2.8

(*S*,*Z*)-1-(Hexa-1,4-dien-3-yl)-2-methylbenzene (**4.134, Table 4.4).** The title compound is prepared in 8 h at 22 ºC following the general procedure. IR (neat): 3066 (w), 3018 (w), 2975 (w), 2916 (w), 1634 (w), 1487 (m), 1461 (m), 1396 (w), 1369 (w), 993 (m), 915 (s), 848 (w), 794 (w), 753 (s), 728 (s), 658 (w), 547 (w), 454 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.22–7.10 (4H, m), 6.02 (1H, ddd, J = 17.0, 10.0, 5.0 Hz), 5.65–5.58 (1H, m), 5.51–5.46 (1H, m), 5.13–5.06 (2H, m), 4.54–4.51 (1H, m), 2.35 (3H, s), 1.70 (3H, dd, J = 6.5, 2.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.1, 140.4, 135.9, 131.5, 130.5, 127.4, 126.4, 126.3, 124.9, 114.5, 43.0, 19.6, 13.2; HRMS (ESI+): Calcd for $C_{13}H_{17}$ $[M+H]^+$: 173.13303, Found: 173.13231. Specific Rotation: $[\alpha]_D^{20}$ +0.67 (*c* 0.90, $CHCl_3$) for an enantiomerically enriched sample of 98:2 er.

Enantiomeric purity is determined by GLC analysis in comparison with authentic racemic material (98:2 er shown; CDB/DM column, 80 ºC, 15 psi).



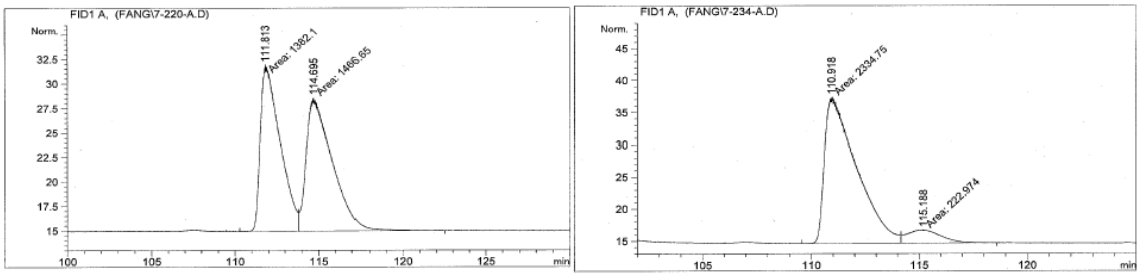
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	43.978	MF	0.4559	1369.12305	50.04856	49.21411
2	44.965	FM	0.5260	1412.84937	44.76710	50.78589

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	43.934	MM	0.4576	1860.26843	67.74814	97.81139
2	45.157	MM	0.4507	41.62508	1.53918	2.18861

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	43.98	50.0	1	43.93	97.8
2	44.97	50.0	2	94.11	2.1

(*R*,*Z*)-(2-Methylhexa-1,4-dien-3-yl)benzene (4.138, Table 4.4). The title compound is prepared with **4.150** in 24 h at 22 ºC following the general procedure. IR (neat): 3062 (w), 3022 (w), 2971 (w), 2917 (w), 1644 (w), 1599 (w), 1491 (w), 1450 (w), 1371 (w), 1073 (w), 1032 (w), 893 (m), 755 (m), 739 (m), 697 (s), 536 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.32–7.28 (2H, m), 7.26–7.18 (3H, m), 5.74–5.68 (1H, m), 5.66–5.58 (1H, m), 4.90–4.86 (2H, m), 4.29 (1H, d, *J* = 9.2 Hz), 1.68 (3H, dd, *J* = 6.4, 1.6 Hz), 1.66 (3H, dd, *J* = 0.8, 0.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.4, 143.3, 131.9, 128.5, 128.0, 126.3, 124.9, 111.8, 50.2, 21.3, 13.1; HRMS (ESI+): Calcd for $C_{13}H_{17}$ $[M+H]^+$: 173.13303, Found: 173.13295. Specific Rotation: $[\alpha]_D^{20}$ +21.2 (*c* 0.970, $CHCl_3$) for an enantiomerically enriched sample of 91:9 er.

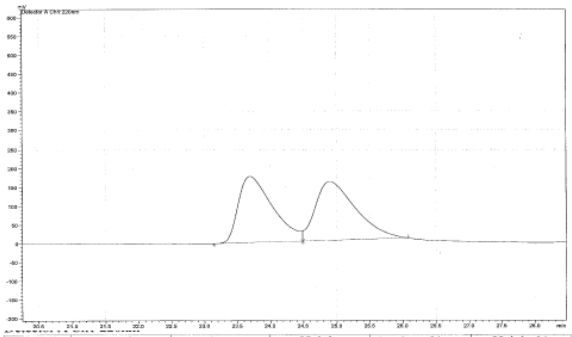
Enantiomeric purity is determined by GLC analysis in comparison with authentic racemic material (91:9 er shown; CDB/DM column, 60 ºC, 15 psi).



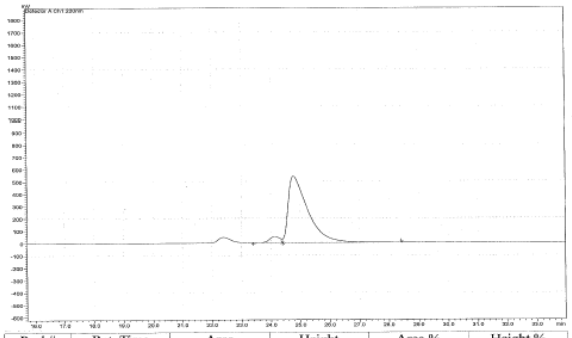
Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	111.81	48.5	1	110.92	91.3
2	114.70	51.5	2	115.19	8.7

(*R*,*Z*)-1-(2-Methylhexa-1,4-dien-3-yl)-4-nitrobenzene (4.140, Table 4.4). The title compound is prepared with **4.150** in 24 h at 22 °C following the general procedure. IR (neat): 3078 (w), 3020 (w), 2973 (w), 2917 (w), 2856 (w), 1646 (w), 1596 (w), 1518 (s), 1448 (w), 1343 (s), 1109 (w), 1015 (w), 899 (m), 847 (m), 744 (w), 696 (m), 539 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 8.16 (2H, dd, *J* = 8.0, 2.5 Hz), 7.39 (2H, dd, *J* = 8.0, 2.5 Hz), 5.72–5.62 (2H, m), 4.95 (1H, s), 4.87 (1H, s), 4.38 (1H, d, *J* = 9.0 Hz), 1.68 (3H, d, *J* = 6.0 Hz), 1.65 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.1, 146.6, 145.9, 130.2, 128.9, 126.6, 123.8, 113.2, 50.1, 21.2, 13.2; HRMS (ESI+): Calcd for $C_{13}H_{15}N_1O_2$ $[M]^+$: 217.1103, Found: 217.1099. Specific Rotation: $[\alpha]_D^{20}$ +147 (*c* 2.11, $CHCl_3$) for an enantiomerically enriched sample of 95:5 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (95:5 er shown; Chiralcel OD-H column, 100/0 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.692	6410323	175707	49.330	52.949
2	24.894	6584433	156134	50.670	47.051
Total		12994756	331840	100.000	100.000

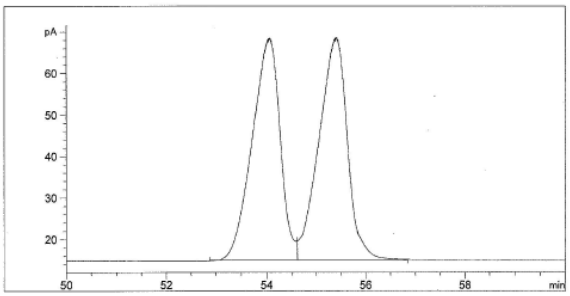


Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.126	1246131	49221	4.743	8.376
2	24.767	25026124	538447	95.257	91.624
Total		26272255	587668	100.000	100.000

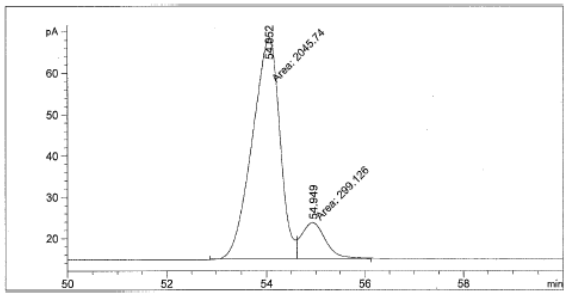
Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	23.69	49.3	1	24.13	4.7
2	24.89	50.7	2	24.77	95.3

(*R*,*Z*)-1-Methyl-2-(2-methylhexa-1,4-dien-3-yl)benzene (4.139, Table 4.4). The title compound with **4.150** is prepared in 24 h at 22 ºC following the general procedure. IR (neat): 3067 (w), 3018 (w), 2970 (w), 2915 (w), 2858 (w), 1646 (w), 1487 (m), 1449 (m), 1371 (w), 1052 (w), 1033 (w), 894 (s), 751 (s), 721 (s), 705 (s), 463 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.21–7.09 (4H, m), 5.62–5.56 (2H, m), 4.89 (1H, s), 4.76 (1H, s), 4.39 (1H, d, J = 6.5 Hz), 2.33 (3H, s), 1.68–1.66 (6H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 147.3, 141.6, 136.3, 132.3, 130.4, 127.4, 126.2, 126.1, 124.7, 111.7, 46.4, 22.3, 19.7, 13.2; HRMS (ESI+): Calcd for $C_{14}H_{18}$ $[M]^+$: 186.1409, Found: 186.1408. Specific Rotation: $[\alpha]_D^{20}$ +130 (*c* 1.31, $CHCl_3$) for an enantiomerically enriched sample of 87:13 er.

Enantiomeric purity is determined by GLC analysis in comparison with authentic racemic material (87:13 er shown; CDB/DM column, 80 ºC, 15 psi).



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	54.069	MF	0.6364	2245.56255	56.93786	49.84947
2	55.549	FM	0.6374	2259.12371	56.79375	50.15053

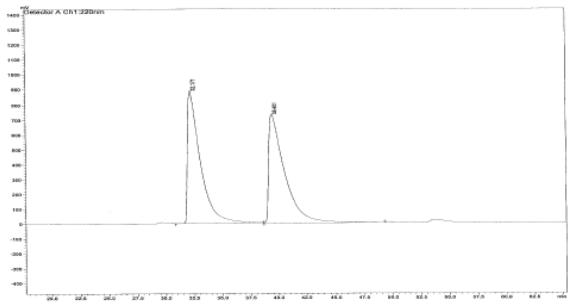


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	54.052	MF	0.6321	2045.73645	53.93697	87.24336
2	54.949	FM	0.5674	299.12561	8.78665	12.75664

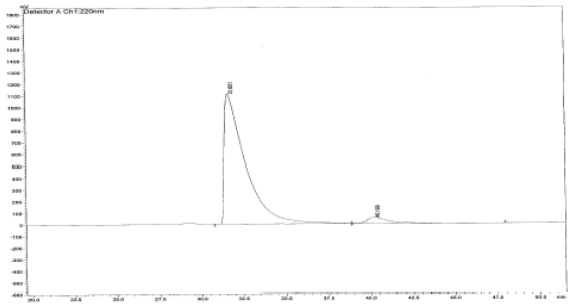
Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	54.07	49.8	1	54.05	87.2
2	55.55	50.2	2	54.95	12.8

Methyl (*S*,*Z*)-2-methylene-3-(*p*-tolyl)hex-4-enoate (4.137, Table 4.4). The title compound is prepared with 1.0 mol % **4.116**, 10 mol % CuCl and 1.5 equiv NaOMe in 24 h at 60 ºC following the general procedure. IR (neat): 3019 (w), 2950 (w), 2921 (w), 1721 (s), 1627 (w), 1512 (m), 1436 (m), 1315 (m), 1244 (s), 1190 (m), 1144 (s), 945 (m), 811 (s), 740 (s), 680 (w), 529 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.12–7.08 (4H, m), 6.28 (1H, dd, *J* = 1.2, 0.8 Hz), 5.66–5.56 (3H, m), 4.86 (1H, d, *J* = 8.0 Hz), 3.68 (3H, d, *J* = 0.8 Hz), 2.30 (3H, s), 1.70 (3H, dd, *J* = 5.6, 0.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.5, 143.4, 139.9, 136.0, 131.5, 129.3, 127.7, 125.5, 125.2, 52.0, 44.0, 21.2, 13.2; HRMS (ESI+): Calcd for $C_{15}H_{19}O_2$ $[M+H]^+$: 231.13850, Found: 231.13787. Specific Rotation: $[\alpha]_D^{20}$ –17.8 (*c* 1.40, $CHCl_3$) for an enantiomerically enriched sample of 96:4 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (95.5:4.5 er shown; Chiralcel OD-H column, 100/0 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	32.171	71045914	887170	49.476	54.754
2	39.401	72550866	733122	50.524	45.246
Total		143596780	1620292	100.000	100.000

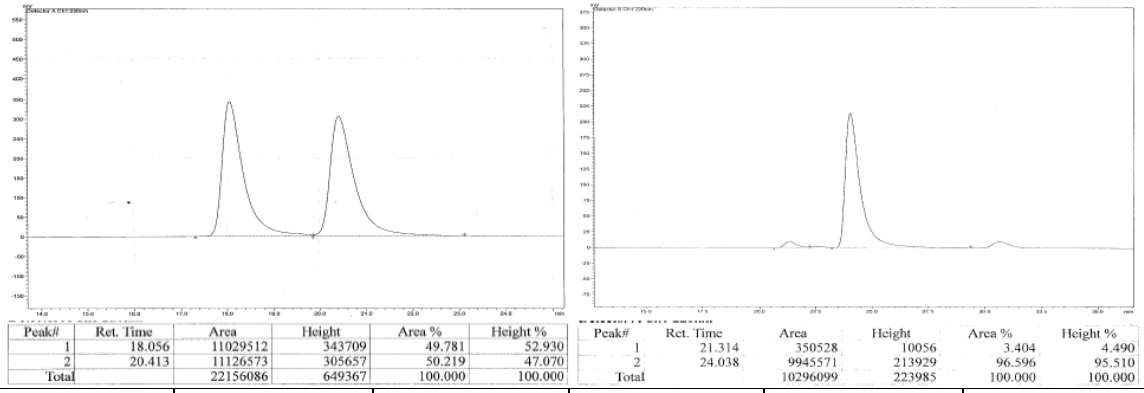


Peak#	Ret. Time	Area	Height	Area %	Height %
1	31.601	96792729	1109805	95.354	95.589
2	40.199	4716070	51213	4.646	4.411
Total		101508799	1161018	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	32.17	49.5	1	31.60	95.4
2	39.40	50.5	2	40.20	4.6

Methyl (*S*,*Z*)-2-methylene-3-(4-(trifluoromethyl)phenyl)hex-4-enoate (4.135, Table 4.4). The title compound is prepared with 1.0 mol % **4.116**, 10 mol % CuCl and 1.5 equiv NaOMe in 24 h at 60 ºC following the general procedure. IR (neat): 3021 (w), 2954 (w), 2917 (w), 2849 (w), 1723 (s), 1617 (w), 1438 (w), 1418 (w), 1324 (s), 1251 (w), 1162 (m), 1121 (s), 1068 (s), 1019 (w), 953 (w), 832 (w), 733 (w), 604 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54 (2H, d, *J* = 8.0 Hz), 7.33 (2H, d, *J* = 8.0 Hz), 6.35 (1H, d, *J* = 2.5 Hz), 5.71–5.56 (3H, m), 4.93 (1H, d, *J* = 9.0 Hz), 3.68 (3H, s), 1.70 (3H, dd, *J* = 6.5, 2.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.0, 147.1, 142.4, 128.6 (q, *J* = 32 Hz), 128.2, 126.7, 126.2, 125.6 (q, *J* = 3.7 Hz), 124.2 (q, *J* = 269 Hz), 52.1, 44.3, 13.3; HRMS (ESI+): Calcd for $C_{15}H_{15}F_3O_2$ $[M]^+$: 284.1024, Found: 284.1029. Specific Rotation: $[\alpha]_D^{20}$ +135 (*c* 1.70, $CHCl_3$) for an enantiomerically enriched sample of 97:3 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (97:3 er shown; Chiralcel OD-H column, 100/0 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



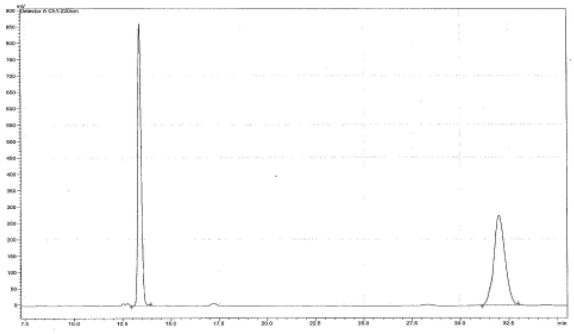
Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.056	11029512	343709	49.781	52.930
2	20.413	11126573	305657	50.219	47.070
Total		22156086	649367	100.000	100.000

Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.314	350528	10056	3.404	4.490
2	24.038	9945571	213929	96.596	95.510
Total		10296099	223985	100.000	100.000

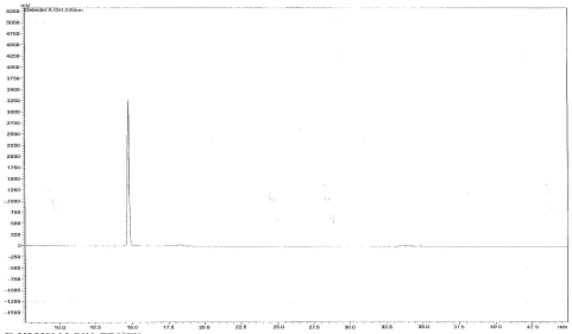
Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	18.06	49.8	1	21.31	3.4
2	20.41	50.2	2	24.04	96.6

Methyl (*S*,*Z*)-3-(2-(methoxymethoxy)phenyl)-2-methylenehex-4-enoate (4.136, Table 4.4). The title compound is prepared with 1.0 mol % **4.116**, 10 mol % CuCl and 1.5 equiv NaOMe in 24 h at 60 ºC following the general procedure. IR (neat): 2951 (w), 2917 (w), 2849 (w), 2826 (w), 1722 (s), 1488 (m), 1403 (m), 1317 (w), 1231 (s), 1200 (m), 1150 (s), 1078 (m), 1001 (s), 923 (w), 754 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.17–7.14 (2H, m), 7.06 (1H, d, *J* = 8.0 Hz), 6.94 (1H, dd, *J* = 8.0, 7.5 Hz), 6.25 (1H, s), 5.64–5.50 (3H, m), 5.30 (1H, d, *J* = 9.5 Hz), 5.20 (2H, s), 3.68 (3H, s), 3.46 (3H, s), 1.71 (3H, d, *J* = 6.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.5, 154.3, 143.4, 132.0, 130.8, 128.1, 127.6, 125.9, 124.9, 121.8, 114.3, 94.3, 66.0, 56.1, 52.0, 13.2; HRMS (ESI+): Calcd for $C_{16}H_{20}O_4$ $[M]^+$: 276.1362, Found: 276.1368. Specific Rotation: $[\alpha]_D^{20}$ +98.3 (*c* 2.54, $CHCl_3$) for an enantiomerically enriched sample of 97:3 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (97:3 er shown; Chiralcel OD-H column, 99.5/0.5 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.388	10520048	859915	49.960	69.159
2	31.989	10537033	273544	50.040	22.000
Total		24677740	1243396	100.000	100.000



Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.718	27992522	3259557	96.808	99.435
2	33.925	923067	18531	3.192	0.565
Total		28915589	3278088	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	13.39	50.0	1	14.72	96.8
2	31.99	50.0	2	33.93	3.2

■ **Representative Experimental Procedure for Cu-Catalyzed Enantioselective Allylic Substitution (EAS) with Alkyl-Substituted Cis 1,2-Disubstituted Alkenylboron Reagents (Figure 4.3):** In this section, the reactions are performed following the same representative procedure as described for Table 4.3. The specific differences are included within the characterization data of each compound.

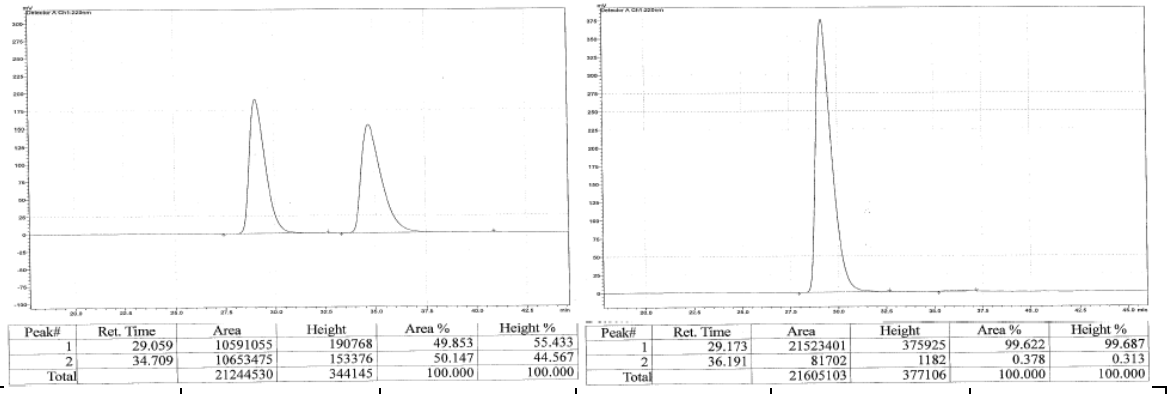
(*S*,*Z*)-*tert*-Butyl((4-(2,5-dimethoxy-4-methylphenyl)hexa-2,5-dien-1-yl)oxy)dimethylsilane (4.145, Figure 4.3). The title compound is prepared in the presence of 1.5 equiv of the corresponding alkenylboron reagent (96% *Z*) and 1.5 equiv of NaOMe following the same representative procedure. IR (neat): 2952 (w), 2929 (w), 2855 (w), 1502 (m), 1464 (m), 1396 (m), 1252 (w), 1205 (s), 1087 (s), 1046 (s), 1004 (m), 914 (w), 834 (s), 774 (s), 715 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.68 (1H, s), 6.63 (1H, s), 6.00 (1H, ddd, *J* = 17.6, 10.0, 5.2 Hz), 5.63–5.53 (2H, m), 5.12–5.08 (2H, m), 4.67 (1H, dd, *J* = 8.8, 7.2 Hz), 4.39 (1H, dd, *J* = 13.6, 5.2 Hz), 4.28 (1H, dd, *J* = 14.0, 4.4 Hz), 3.774 (3H, s), 3.769 (3H, s), 2.20 (3H, s), 0.90 (9H, s), 0.07 (6H, s); ^{13}C NMR

(100 MHz, $CDCl_3$): δ 152.0, 150.4, 140.4, 130.8, 130.6, 129.7, 125.4, 114.6, 114.5, 111.0, 60.0, 56.4, 56.2, 40.3, 26.1, 18.5, 16.3, –4.98, –.5.00; HRMS (ESI+): Calcd for $C_{21}H_{35}O_3Si_1$ $[M+H]^+$: 363.23555, Found: 363.23475. Specific Rotation: $[\alpha]_D^{20}$ +85.5 (*c* 1.17, $CHCl_3$) for an enantiomerically enriched sample of 99:1 er. Enantiomeric purity is determined by HPLC analysis of the derived *Z* allylic alcohol (see below).

(*S*,*Z*)-4-(2,5-Dimethoxy-4-methylphenyl)hexa-2,5-dien-1-ol (Figure 4.3). To a 2-dram vial equipped with a magnetic stir bar is charged with **4.145** (27.4 mg, 0.0756 mmol). The vessel is evacuated and refilled with N_2 three times; under N_2 atmosphere, tetrahydrofuran (thf, 1.0 mL) is added through a syringe. The solution is allowed to cool to 0 °C in an ice bath followed by dropwise addition of tetrabutylammonium fluoride solution (151 μL, 0.151 mmol, 1.0 M in thf). The resulting light yellow solution is allowed to warm to 22 °C and stir for an additional 30 minutes before it is quenched by addition of saturated NH_4Cl solution (1.0 mL). The layers are separated and the aqueous layer is washed with EtOAc (3 x 1.0 mL). The combined organic layers are dried over anhydrous $MgSO_4$, filtered and volatiles removed under reduced pressure to afford a crude yellowish oil residue, which is purified by silica gel column chromatography (3:1 hexanes/ethyl acetate) to deliver the title compound as colorless oil (18.8 mg, 0.0756 mmol, >98% yield). IR (neat): 3371 (m), 2997 (w), 2933 (w), 2848 (w), 1501 (m), 1464 (m), 1395 (m), 1316 (w), 1236 (w), 1205 (s), 1041 (s), 915 (m), 861 (w), 767 (w), 695 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.71 (1H, s), 6.65 (1H, s), 6.04 (1H, ddd, *J* = 16.8, 10.4, 4.8 Hz), 5.76 (1H, dddd, *J* = 11.2, 7.6, 6.4, 0.8 Hz), 5.60 (1H, dddd, *J* = 10.4, 10.4, 1.2, 1.2 Hz), 5.18–5.12 (2H, m), 4.83–4.80 (1H, m), 4.35 (1H, dd, *J* = 12.4, 7.6 Hz), 4.17–4.11 (1H, m), 3.81 (3H, s), 3.78 (3H, s), 2.20 (3H, s), 1.78 (1H, bs); ^{13}C NMR (100

MHz, $CDCl_3$): δ 152.3, 150.1, 140.2, 133.9, 129.3, 128.6, 125.7, 115.2, 114.8, 110.8, 58.6, 56.6, 56.2, 39.7, 16.3; HRMS (ESI+): Calcd for $C_{15}H_{19}O_2$ $[M+H-H_2O]^+$: 231.13850, Found: 231.13793. Specific Rotation: $[\alpha]_D^{20}$ +198.2 (*c* 1.05, $CHCl_3$) for an enantiomerically enriched sample of 99:1 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (99:1 er shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 0.8 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.059	10591055	190768	49.853	55.433
2	34.709	10653475	153376	50.147	44.567
Total		21244530	344145	100.000	100.000

Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.173	21523401	375925	99.622	99.687
2	36.191	81702	1182	0.378	0.313
Total		21605103	377106	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	29.06	49.9	1	29.17	99.6
2	34.71	50.1	2	36.19	0.4

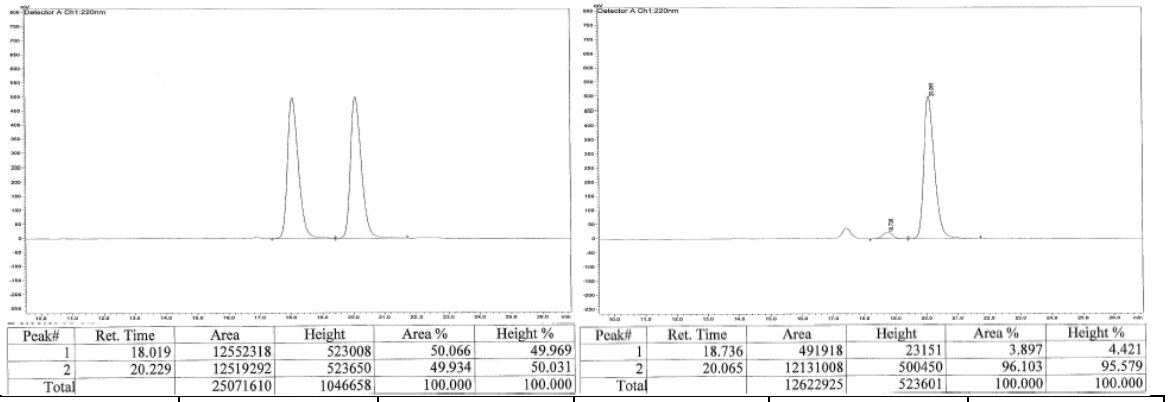
(*S*,*Z*)-4-(2,5-Dimethoxy-4-methylphenyl)hexa-2,5-dienal (4.146, Figure 4.3). To a 2-dram vial equipped with a magnetic stir bar is charged with the above allylic alcohol (18.8 mg, 0.0756 mmol) and solid sodium bicarbonate (50.8 mg, 0.605 mmol). The vessel is evacuated and refilled with N_2 three times; under N_2 atmosphere, CH_2Cl_2 (1.0 mL) is added through a syringe. The solution is allowed to cool to 0 ^oC in an ice bath followed by addition of Dess-Martin periodinane (48.1 mg, 0.113 mmol) in one portion as a solid. The resulting white suspension is allowed to stir for an additional 60 minutes before it is quenched by passing the suspension through a celite plug eluted with EtOAc.

The volatiles are removed under reduced pressure to afford a crude colorless oil residue, which is purified by silica gel column chromatography (8:1 hexanes/ethyl acetate) to deliver **4.146** as colorless oil (14.5 mg, 0.0590 mmol, 78% yield). IR (neat): 2936 (w), 2849 (w), 2831 (w), 1767 (w), 1678 (s), 1504 (m), 1466 (m), 1397 (m), 1207 (s), 1044 (s), 998 (w), 921 (w), 863 (w), 785 (s), 697 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 10.25 (1H, d, *J* = 8.0 Hz), 6.70 (1H, s), 6.67 (1H, s), 6.60 (1H, dd, *J* = 11.2, 11.2 Hz), 6.11 (1H, ddd, *J* = 17.6, 10.4, 5.2 Hz), 5.93 (1H, dd, *J* = 10.8, 8.0 Hz), 5.46–5.42 (1H, m), 5.28 (1H, d, *J* = 10.8 Hz), 5.20 (1H, d, *J* = 17.2 Hz), 3.79 (3H, s), 3.76 (3H, s), 2.21 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.2, 152.1, 151.4, 150.5, 138.6, 129.0, 126.8, 126.6, 116.8, 114.2, 110.7, 56.3, 56.0, 40.2, 16.4; HRMS (ESI+): Calcd for $C_{15}H_{19}O_3$ $[M+H]^+$: 247.13342, Found: 247.13346. Specific Rotation: $[\alpha]_D^{20}$ +297 (*c* 0.327, $CHCl_3$) for an enantiomerically enriched sample of 99:1 er. Enantiomeric purity is further confirmed by converting the title compound to the corresponding enone **4.155**, **Scheme 4.23** (see below).

(*S*,*Z*)-(11-Bromoundeca-1,4-dien-3-yl)benzene (4.141, Figure 4.3). The title compound is prepared with 1.0 equiv of the alkenylboron reagent (96% *Z*) as the limiting reagent, 1.25 equiv of NaOMe and 1.25 equiv of the corresponding allylic phosphate following the same representative procedure. The compound was characterized with 6% *E* isomer. IR (neat): 3081 (w), 3006 (w), 2929 (m), 2855 (m), 1634 (w), 1600 (w), 1492 (w), 1451 (w), 1256 (w), 1230 (w), 944 (w), 915 (m), 851 (w), 741 (m), 699 (s), 563 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.33–7.28 (2H, m), 7.26–7.18 (3H, m), 5.99 (1H, ddd, *J* = 17.6, 10.0, 6.4 Hz), 5.58–5.48 (2H, m), 5.14–5.08 (2H, m), 4.34 (1H, dd, *J* = 6.8, 6.8 Hz), 3.39 (2H, t, *J* = 7.2 Hz), 2.19–2.09 (2H, m), 1.87–1.80 (2H, m), 1.46–1.26 (6H, m); ^{13}C

NMR (100 MHz, $CDCl_3$): δ 143.8, 140.7, 131.0, 130.5, 128.6, 127.8, 126.4, 114.8, 47.1, 34.1, 32.9, 29.4, 28.5, 28.2, 27.4; HRMS (ESI+): Calcd for $C_{17}H_{24}Br_1$ $[M+H]^+$: 307.10614, Found: 307.10584. Specific Rotation: $[\alpha]_D^{20}$ +57.5 (*c* 0.740, $CHCl_3$) for an enantiomerically enriched sample of 96:4 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (96:4 er shown; Chiralcel OD-H column, 100/0 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.019	12552318	523008	50.066	49.969
2	20.229	12519292	523650	49.934	50.031
Total		25071610	1046658	100.000	100.000

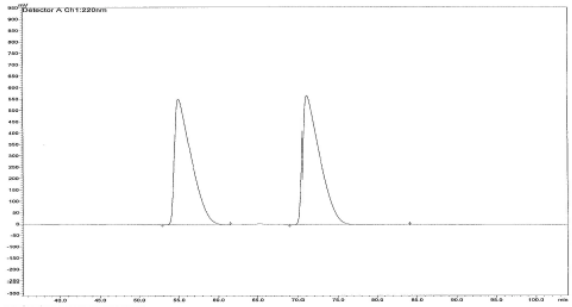
Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.736	491918	23151	3.897	4.421
2	20.065	12131008	500450	96.103	95.579
Total		12622925	523601	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	18.02	50.1	1	18.74	3.9
2	20.23	49.9	2	20.07	96.1

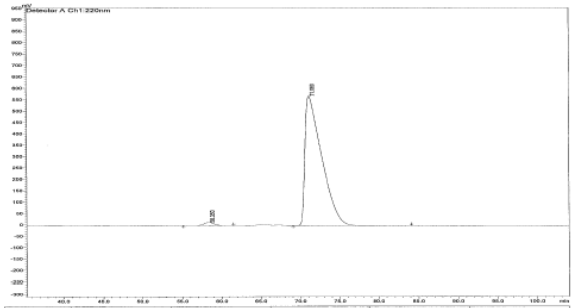
(*S*,*Z*)-1-Methoxy-4-(((9-phenylundeca-7,10-dien-1-yl)oxy)methyl)benzene (4.142, Figure 4.3). The title compound is prepared with 1.0 equiv of the alkenylboron reagent (97% *Z*) as the limiting reagent, 1.25 equiv of NaOMe and 1.25 equiv of the corresponding allylic phosphate following the same representative procedure. The compound was characterized with 7% *E* isomer. IR (neat): 3057 (w), 2930 (m), 2854 (m), 1612 (w), 1512 (s), 1453 (w), 1362 (w), 1301 (w), 1246 (s), 1172 (w), 1097 (m), 1036 (m), 914 (w), 820 (m), 741 (m), 699 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.32–7.17 (7H, m), 6.88 (2H, d, *J* = 8.8 Hz), 6.03–5.95 (1H, m), 5.57–5.48 (2H, m), 5.13–5.09 (2H,

m), 4.43 (2H, s), 4.34 (1H, dd, *J* = 7.6, 7.6 Hz), 3.80 (3H, s), 3.42 (2H, t, *J* = 6.8 Hz), 2.17–2.07 (2H, m), 1.59 (2H, dt, *J* = 13.2, 6.0 Hz), 1.44–1.26 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.2, 143.9, 140.7, 131.0, 130.8, 130.7, 129.4, 128.6, 127.8, 126.3, 114.7, 113.9, 72.7, 70.3, 55.4, 47.1, 29.9, 29.6, 29.3, 27.5, 26.2; HRMS (ESI+): Calcd for $C_{25}H_{33}O_2$ $[M+H]^+$: 365.24806, Found: 365.24830. Specific Rotation: $[\alpha]_D^{20}$ +41.2 (*c* 0.650, $CHCl_3$) for an enantiomerically enriched sample of 99:1 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (99:1 er shown; Chiralcel OD-H column, 99.5/0.5 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	55.050	72130372	585095	49.963	49.916
2	71.322	72237530	587054	50.037	50.084
Total		144367902	1172149	100.000	100.000



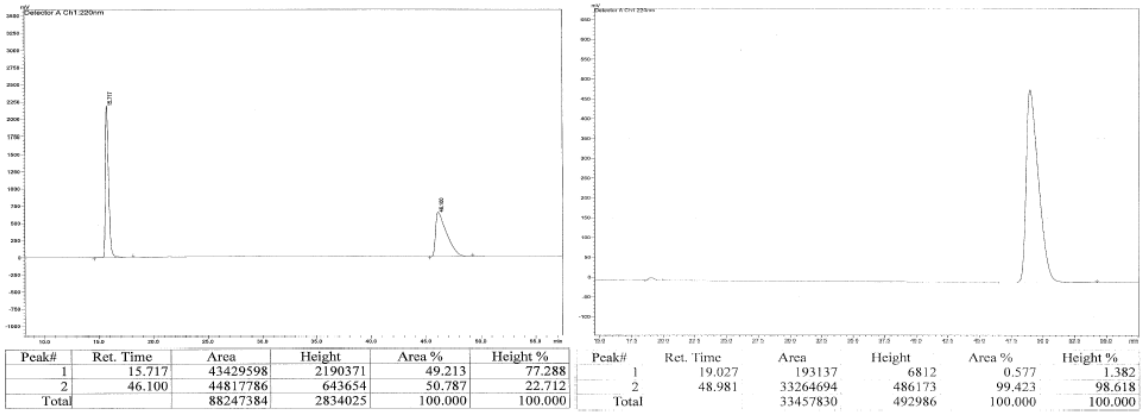
Peak#	Ret. Time	Area	Height	Area %	Height %
1	58.350	1130322	13035	1.340	2.244
2	71.060	83242530	567984	98.660	97.756
Total		84372853	581019	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	55.05	50.0	1	58.35	1.3
2	71.32	50.0	2	71.06	98.7

(*S*,*Z*)-(1-Butoxypenta-1,4-dien-3-yl)benzene (4.144, Figure 4.3). The title compound is prepared in the presence of 1.5 equiv of the corresponding alkenylboron reagent (>98% *Z*) and 1.5 equiv of NaOMe following the same representative procedure. IR (neat): 3083 (w), 3029 (w), 2959 (m), 2931 (m), 2872 (m), 1660 (m), 1492 (w), 1452 (w), 1372 (w), 1275 (w), 1102 (s), 994 (w), 913 (m), 744 (m), 699 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.24 (4H, m), 7.21–7.16 (1H, m), 6.07–5.97 (2H, m), 5.13 (1H, ddd, *J* =

17.6, 1.6, 1.2 Hz), 5.08 (1H, ddd, J = 10.4, 2.0, 1.2 Hz), 4.58–4.57 (2H, m), 3.76 (2H, dddd, J = 16.8, 12.4, 9.6, 6.4 Hz), 1.64–1.57 (2H, m), 1.44–1.35 (2H, m), 0.93 (3H, t, J = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.3, 144.4, 141.1, 128.5, 127.7, 126.2, 114.2, 108.0, 72.3, 44.0, 32.0, 19.2, 14.0; HRMS (ESI+): Calcd for $C_{14}H_{17}O_2$ $[M+H]^+$: 217.15924, Found: 217.15902. Specific Rotation: $[\alpha]_D^{20}$ +79.2 (*c* 1.64, $CHCl_3$) for an enantiomerically enriched sample of 99:1 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (99:1 er shown; Chiralcel OD-H column, 100/0 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.717	43429598	2190371	49.213	77.288
2	46.100	44817786	643654	50.787	22.712
Total		88247384	2834025	100.000	100.000

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.027	193137	6812	0.577	1.382
2	48.981	33264694	486173	99.423	98.618
Total		33457830	492986	100.000	100.000

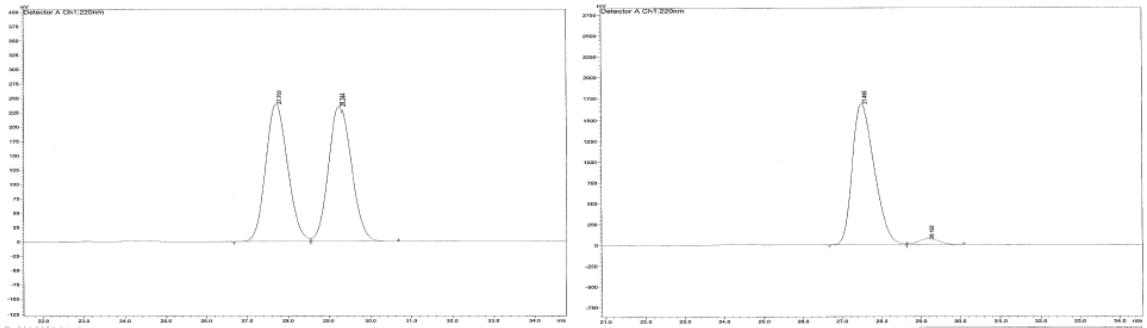
Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	15.72	49.2	1	19.03	0.6
2	46.10	50.8	2	48.98	99.4

tert-Butyl (*S*,*Z*)-(4-(3-bromophenyl)hexa-2,5-dien-1-yl)carbamate (4.143, Figure 4.3).

The title compound is prepared in the presence of 1.5 equiv of the corresponding alkenylboron reagent (>98% *Z*) and 1.5 equiv of NaOMe following the same representative procedure. IR (neat): 3062 (w), 3022 (w), 2971 (w), 2917 (w), 1644 (w), 1599 (w), 1491 (w), 1450 (w), 1371 (w), 1073 (w), 1032 (w), 893 (m), 755 (m), 739 (m),

697 (s), 536 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.36–7.33 (2H, m), 7.19–7.13 (2H, m), 5.93 (1H, ddd, *J* = 17.2, 10.0, 6.4 Hz), 5.67–5.55 (2H, m), 5.17–5.10 (2H, m), 4.50 (1H, bs), 4.36 (1H, bdd, *J* = 7.6, 7.6 Hz), 3.83 (2H, dd, *J* = 5.6, 5.6 Hz), 1.45 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.9, 145.4, 139.3, 133.1, 130.9, 130.3, 129.8, 127.3, 126.5, 122.9, 116.0, 77.4, 46.8, 37.9, 28.6; HRMS (ESI+): Calcd for $C_{13}H_{17}$ $[M+H–Boc]^+$: 251.03096, Found: 251.03077. Specific Rotation: $[\alpha]_D^{20}$ +99.1 (*c* 1.21, $CHCl_3$) for an enantiomerically enriched sample of 96:4 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (96:4 er shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	27.700	8954626	240033	50.122	50.497
2	29.244	8910868	235309	49.878	49.503
Total		17865494	475342	100.000	100.000

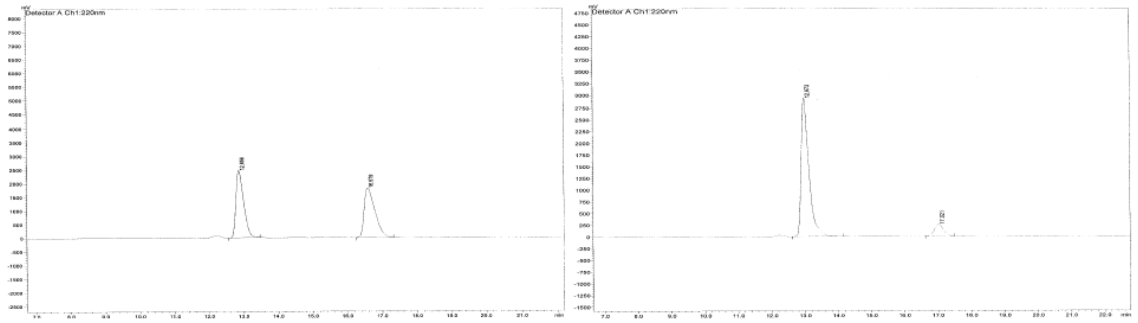
Peak#	Ret. Time	Area	Height	Area %	Height %
1	27.495	65605465	1678893	96.012	95.897
2	29.192	2725106	71826	3.988	4.103
Total		68330571	1750719	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	27.70	50.1	1	27.50	96.0
2	29.24	49.9	2	29.19	4.0

■ **Representative Experimental Procedure for Cu-Catalyzed Enantioselective Allylic Substitution (EAS) with Aryl-Substituted Cis 1,2-Disubstituted Alkenylboron Reagents (Scheme 4.22):** In this section, the reactions are performed following the same representative procedure as described for Table 4.3. The specific differences are included within the characterization data of each compound.

(*R*,*Z*)-(3-Cyclohexylpenta-1,4-dien-1-yl)benzene (4.148, Scheme 4.22). The title compound is prepared in the presence of 1.5 equiv of the corresponding alkenylboron reagent (95% *Z*) and 1.5 equiv of NaOMe following the same representative procedure. IR (neat): 3078 (w), 3058 (w), 3023 (w), 2921 (s), 2850 (s), 1633 (m), 1600 (w), 1493 (m), 1447 (s), 1415 (w), 1261 (w), 1074 (w), 1029 (w), 994 (m), 971 (w), 911 (s), 812 (m), 768 (s), 698 (s), 652 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.32–7.18 (5H, m), 6.52 (1H, d, *J* = 11.6 Hz), 5.80 (1H, ddd, *J* = 17.6, 10.8, 7.2 Hz), 5.58 (1H, dd, *J* = 11.6, 10.4 Hz), 5.07–5.01 (2H, m), 3.11–3.04 (1H, m), 1.74–1.57 (5H, m), 1.33–1.02 (4H, m), 0.95–0.83 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.1, 137.9, 133.7, 129.5, 128.8, 128.2, 126.6, 114.9, 48.3, 42.0, 30.8, 30.5, 26.7, 26.6; HRMS (ESI+): Calcd for $C_{17}H_{23}$ $[M+H]^+$: 227.17998, Found: 227.18093. Specific Rotation: $[\alpha]_D^{20}$ –171 (*c* 1.58, $CHCl_3$) for an enantiomerically enriched sample of 91:9 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (91:9 er shown; Chiralcel OD-H column, 100/0 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.856	38227803	2467504	49.850	57.566
2	16.579	38457304	1818903	50.150	42.434
Total		76685107	4286407	100.000	100.000

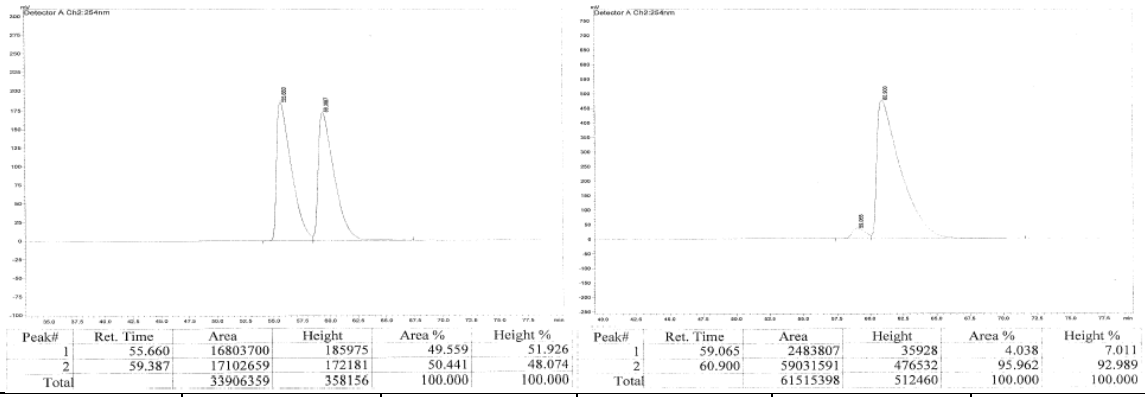
Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.973	48037031	2932785	91.031	91.970
2	17.021	4732933	256068	8.969	8.030
Total		52769964	3188853	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	12.86	49.9	1	12.97	91.0

2	16.58	50.1	2	17.02	9.0

(*S*,*Z*)-4-(1-(4-Methoxyphenyl)penta-1,4-dien-3-yl)phenyl 4-methylbenzenesulfonate (4.153, Scheme 4.22). The title compound is prepared in the presence of 1.5 equiv of the corresponding alkenylboron reagent (93% *Z*) and 1.5 equiv of NaOMe following the same representative procedure. IR (neat): 3008 (w), 2956 (w), 2927 (w), 2837 (w), 1607 (m), 1509 (s), 1490 (s), 1372 (s), 1303 (w), 1248 (s), 1198 (s), 1176 (s), 1153 (s), 1093 (s), 1033 (m), 1018 (m), 922 (w), 864 (s), 839 (s), 815 (m), 750 (m), 669 (m), 570 (s), 552 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.73–7.70 (2H, m), 7.30 (2H, dd, *J* = 8.8, 0.8 Hz), 7.21–7.13 (4H, m), 6.93–6.85 (4H, m), 6.56 (1H, d, *J* = 11.6 Hz), 5.99 (1H, ddd, *J* = 16.8, 10.4, 6.0 Hz), 5.63 (1H, dd, *J* = 11.2, 10.0 Hz), 5.20–5.15 (2H, m), 4.54 (1H, dd, *J* = 9.6, 6.0 Hz), 3.81 (3H, s), 2.45 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.8, 148.2, 145.4, 142.5, 140.0, 132.7, 130.9, 129.90, 129.86, 129.5, 129.0, 128.6, 122.5, 115.9, 113.9, 55.4, 47.1, 21.9; HRMS (ESI+): Calcd for $C_{25}H_{25}O_4S_1$ $[M+H]^+$: 421.14735, Found: 421.14770. Specific Rotation: $[\alpha]_D^{20}$ +60.7 (*c* 1.81, $CHCl_3$) for an enantiomerically enriched sample of 97:3 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (96:4 er shown; Chiralcel OD-H column, 99.5/0.5 hexanes/*i*-PrOH, 0.5 mL/min, 254 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	55.660	16803700	185975	49.559	51.926
2	59.387	17102659	172181	50.441	48.074
Total		33906359	358156	100.000	100.000

Peak#	Ret. Time	Area	Height	Area %	Height %
1	59.065	2483807	35928	4.038	7.011
2	60.900	59031591	476532	95.962	92.989
Total		61515398	512460	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	55.66	49.6	1	59.07	4.0
2	59.39	50.4	2	60.90	96.0

(–)-Nyasol: To a 10-mL round bottom flask with a magnetic stir bar is charged with **4.153** (40.2 mg, 0.0956 mmol); the flask is equipped with a reflux condenser and the whole apparatus is sealed with a septum and purged with N_2 for fve minutes. EtOH (2.0 mL) is added through a syringe followed by the addition of 2N solution of KOH (112 mg in 1.0 mL H_2O). The resulting solution is allowed to warm to 80 °C and stir for one hour, after which it is allowed to cool to ambient temperature and quenched by the addition of a solution of 1N HCl (2.0 mL). The solution was washed with EtOAc (3 x 1.0 mL); the combined organic layers are dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to afford a yellow oil residue, which is dried under high vacuum. After that, the crude mixture is placed in a flame-dried 6-dram vial with a magnetic stir bar and this vessel is sealed with a septum and purged with N_2 flow for 10 minutes. Freshly prepared MeMgI in diethyl ether (956 μL, 0.478 mmol) is added to the reaction vessel through a syringe and solvent is carefully removed under reduced pressure. The resulting mixture is allowed to warm to 180 °C in an oil bath and kept for 10 minutes (white smoke generated as the reaction goes on and disappears in 10 minutes), after

which time it is allowed to cool to 22 °C and diluted with EtOAc (5.0 mL). A saturated solution of NH_4Cl (2.0 mL) is added to quench the reaction and layers are separated. The aqueous layer is washed with EtOAc (3 x 2.0 mL) and the combined organic layers are dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo* to afford a brown oil residue, which is subjected to silica gel chromatography (4:1 hexanes:ethyl acetate) to furnish (–)-nyasol. (19.1 mg, 0.0755 mmol, 79% yield). The product has been previously reported and spectra data match those previously described.[89] IR (neat): 3300 (br), 2975 (w), 2961 (w), 2928 (w), 1634 (m), 1509 (s), 1440 (w), 1366 (w), 1224 (s), 1168 (s), 1099 (m), 913 (m), 829 (s), 732 (m), 649 (w), 623 (w), 542 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.17 (2H, dt, *J* = 8.4, 2.4 Hz), 7.10 (2H, dt, *J* = 8.8, 2.4 Hz), 6.79 (2H, dt, *J* = 8.8, 2.4 Hz), 6.78 (2H, dt, *J* = 8.4, 2.4 Hz), 6.52 (1H, d, *J* = 11.6 Hz), 6.00 (1H, ddd, *J* = 16.8, 10.4, 6.0 Hz), 5.68 (1H, dd, *J* = 11.6, 10.0 Hz), 5.16–5.14 (2H, m), 4.75 (1H, s), 4.66 (1H, s), 4.49 (1H, dd, *J* = 10.0, 6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.5, 153.9, 140.6, 135.5, 131.8, 130.0, 129.9, 128.7, 128.4, 115.4, 115.2, 115.0, 46.7; HRMS (ESI+): Calcd for $C_{17}H_{17}O_2$ $[M+H]^+$: 253.12285. Found: 253.12318. Specific rotation: $[\alpha]_D^{20}$ +195 (*c* 0.947, $CHCl_3$) for an enantiomerically enriched sample of 97:3 er. Assuming the enantiomeric purity is kept the same as compound **4.153** (see above).

Proof of Stereochemistry: Literature value ($[\alpha]_D^{20}$ –201.9 (*c* 0.42, $CHCl_3$), 98.5:1.5 er) is assigned to the (*R*) enantiomer.[75d]

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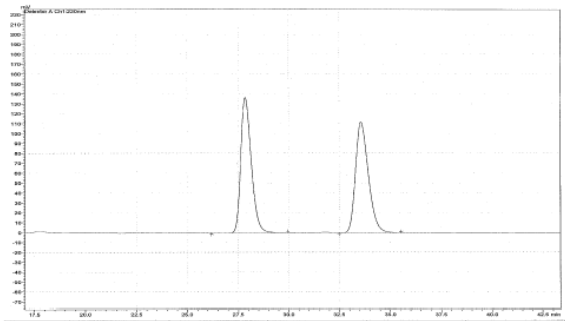
(89) (a) Ref 1d. (b) Iida, Y.; Oh, K-B.; Saito, M.; Matsuoka, H.; Kurata, H.; Natsume, M.; Abe, H. *J. Agric. Food. Chem.* **1999**, *47*, 584–587. (c) Jeong, S-J.; Higuchi, R.; Ono, M.; Kuwano, M.; Kim, Y-C.; Miyamoto, T. *Biol. Pharm. Bull.* **2003**, *26*, 1721–1724.

■ **Formal Synthesis of Heliespirone A and Heliannuol E (Scheme 4.23):** In this section, the synthesis of compound **4.154** is performed at 22 ^{o}C for 36 h following the same representative procedure as described for Table 4.3. Silyl ether **4.154** is formed as a 4:1 inconsequential diastereomer mixture in 79% yield. The mixture is subsequently deprotected; the resulting secondary alcohol is oxidized to deliver the *Z* enone and the compound is characterized at this stage (for procedure details, see below).

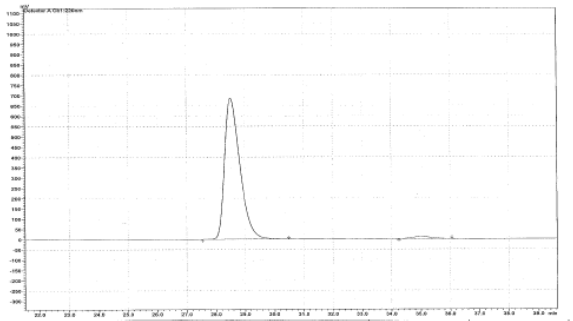
To a 2-dram vial equipped with a magnetic stir bar is charged with **4.154** (29.8 mg, 0.0791 mmol). The vessel is evacuated and refilled with N_2 three times; under N_2 atmosphere, tetrahydrofuran (thf, 1.0 mL) is added through a syringe. The solution is allowed to cool to 0 ^{o}C in an ice bath followed by dropwise addition of tetrabutylammonium fluoride solution (158 μL, 0.158 mmol, 1.0 M in thf). The resulting light yellow solution is allowed to warm to 22 ^{o}C and stir for an additional 12 h before it is quenched by addition of saturated NH_4Cl solution (1.0 mL). The layers are separated and the aqueous layer is washed with EtOAc (3 x 1.0 mL). The combined organic layers are dried over anhydrous $MgSO_4$, filtered and volatiles removed under reduced pressure to afford a crude yellowish oil residue. The residue is directly placed into a 2-dram vial equipped with a magnetic stir bar and solid sodium bicarbonate (53.2 mg, 0.633 mmol) is added to the reaction vessel. The vessel is evacuated and refilled with N_2 three times; under N_2 atmosphere, CH_2Cl_2 (1.0 mL) is added through a syringe. The solution is allowed to cool to 0 ^{o}C in an ice bath followed by addition of Dess-Martin periodinane (50.5 mg, 0.119 mmol) in one portion as a solid. The resulting white suspension is allowed to warm to 22 ^{o}C and stir for an additional 60 minutes before it is quenched by passing the suspension through a celite plug eluted with EtOAc. The volatiles are

removed under reduced pressure to afford a crude colorless oil residue, which is purified by silica gel column chromatography (8:1 hexanes/ethyl acetate) to deliver the *Z* enone **4.155** as colorless oil (13.4 mg, 0.0514 mmol, 65% yield). **(*S*,*Z*)-5-(2,5-Dimethoxy-4-methylphenyl)hepta-3,6-dien-2-one (4.155, Scheme 4.23).** IR (neat) 2932 (m) 2850 (w) 1694 (m) 1611 (w) 1504 (m) 1465 (m) 1397 (m), 1209 (s), 1176 (m), 1045 (s), 916 (w), 866 (w) 789 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 6.74 (1H, s), 6.69 (1H, s), 6.27 (1H, dd, *J* = 11.5, 10.0 Hz), 6.14 (1H, d, *J* = 11.5 Hz), 6.09 (1H, ddd, *J* = 17.0, 10.0, 6.0 Hz), 5.52–5.49 (1H, m), 5.14–5.09 (2H, m), 3.79 (3H, s), 3.75 (3H, s), 2.25 (3H, s), 2.19 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.2, 152.0, 151.1, 146.5, 139.2, 128.5, 126.7, 126.0, 115.3, 114.9, 111.8, 56.4, 56.2, 43.3, 31.7, 29.8; HRMS (ESI+): Calcd for $C_{16}H_{21}O_3$ $[M+H]^+$: 261.14907, Found: 261.14862. Specific Rotation: $[\alpha]_D^{20}$ +119.7 (*c* 0.670, $CHCl_3$) for an enantiomerically enriched sample of 98:2 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (98:2 er shown; Chiralcel OD-H column, 99.5/0.5 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	27.850	4944303	136601	50.024	54.969
2	33.561	4939639	111904	49.976	45.031
Total		9883942	248505	100.000	100.000



Peak#	Ret. Time	Area	Height	Area %	Height %
1	28.513	25098393	686930	98.118	98.467
2	35.013	481389	10697	1.882	1.533
Total		25579783	697628	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	27.85	50.0	1	28.51	98.1

2	33.56	50.0	2	35.01	1.9

To an oven-dried 2-dram vial equipped with a magnetic stir bar is charged with enone **4.155** (52.2 mg, 0.201 mmol). The vessel is evacuated and refilled with N_2 three times; under N_2 atmosphere, diethyl ether (1.5 mL) is added through a syringe. The solution is allowed to cool to –78 ^oC in a dry ice/acetone bath followed by dropwise addition of MeLi solution (251 μL, 0.402 mmol, 1.6 M in Et_2O) over 5 minutes. The resulting solution is allowed to stir at –78 ^oC for additional two hours; then it is allowed to warm to 22 ^oC and quenched by addition of saturated NH_4Cl solution (1.0 mL). The layers are separated and the aqueous layer is washed with Et_2O (3 x 1.0 mL). The combined organic layers are dried over anhydrous $MgSO_4$, filtered and volatiles removed under reduced pressure to afford a crude yellowish oil residue, which is purified by silica gel column chromatography (6:1 hexanes/ethyl acetate) to deliver **4.156** as colorless oil (51.1 mg, 0.185 mmol, 92% yield). **(*S*,*Z*)-5-(2,5-Dimethoxy-4-methylphenyl)-2-methylhepta-3,6-dien-2-ol (4.156, Scheme 4.23).** IR (neat): 3500 (w), 2972 (w), 2830 (w), 1768 (w), 1504 (m), 1466 (m), 1397 (m), 1208 (s), 1045 (m), 1001 (w), 957 (w), 916 (w), 863 (w), 778 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.71 (1H, s), 6.67 (1H, s), 6.06 (1H, ddd, *J* = 17.2, 10.4, 4.4 Hz), 5.57 (1H, d, *J* = 11.2 Hz), 5.38–5.27 (2H, m), 5.23–5.17 (2H, m), 3.82 (3H, s), 3.78 (3H, s), 3.15 (1H, bs), 2.20 (3H, s), 1.39 (3H, s), 1.35 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.3, 150.0, 140.6, 137.0, 130.3, 129.7, 125.6, 115.2, 114.4, 110.9, 71.7, 56.3, 56.2, 39.9, 32.0, 30.8, 16.3; HRMS (ESI+): Calcd for $C_{17}H_{23}O_2$ [M+H–H_2O]$^+$: 259.16980, Found: 259.16932. Specific Rotation: $[\alpha]_D^{20}$ +183.9 (*c* 0.560, $CHCl_3$) for an enantiomerically enriched sample of 98:2 er. Assuming the enantiomeric purity is kept the same as the *Z* enone **4.155** (see above).

To an oven-dried 2-dram vial equipped with a magnetic stir bar is charged with tertiary alcohol **4.156** (51.1 mg, 0.185 mmol). The vessel is evacuated and refilled with N_2 three times; under N_2 atmosphere, CH_2Cl_2 (2.0 mL) is added through a syringe. The solution is allowed to cool to –20 ^oC in a cryogenic bath followed by dropwise addition of titanium (IV) isopropoxide (110 μL, 0.370 mmol). The resulting solution is allowed to stir at –20 ^oC for additional 10 minutes, after which time tert-butyl peroxide (~5.5 M in decane, 101 μL, 0.555 mmol) is added through a syringe. The solution is allowed to stir at –20 ^oC for additional 18 h before it is quenched by addition of 0.1 M HCl solution (2.0 mL). The resulting mixture is allowed to warm to ambient temperature and stir for another 30 minutes. Layers are separated and the aqueous layer is washed with Et_2O (3 x 1.0 mL). The combined organic layers are dried over anhydrous $MgSO_4$, filtered and volatiles removed under reduced pressure to afford a crude colorless oil residue, which is purified by silica gel column chromatography (4:1 hexanes/ethyl acetate) to deliver **4.157** as colorless oil (41.1 mg, 0.141 mmol, 76% yield). **2-((2*S*,3*S*)-3-((*R*)-1-(2,5-Dimethoxy-4-methylphenyl)allyl)oxiran-2-yl)propan-2-ol (4.157, Scheme 4.23).** In the crude mixture, ~15% mono epoxidation at the terminal alkene is also observed. The major epoxidation product is obtained as a 92:8 diastereomer mixture; the minor diastereomer can be separated away from the desired **4.157**. IR (neat): 3489 (w), 3455 (w), 2972 (m), 2831 (w), 1505 (m), 1466 (m), 1397 (m), 1210 (s), 1044 (s), 998 (w), 968 (w), 922 (w), 866 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.74 (1H, s), 6.69 (1H, s), 6.16 (1H, ddd, *J* = 17.2, 10.4, 6.4 Hz), 5.21 (1H, ddd, *J* = 17.6, 1.6, 1.6 Hz), 5.16 (1H, ddd, *J* = 10.4, 1.6, 1.2 Hz), 4.29–4.24 (1H, m), 3.78 (6H, s), 3.41 (1H, dd, *J* = 9.6, 4.0 Hz), 2.82 (1H, d, *J* = 4.4 Hz), 2.21 (3H, s), 1.36 (3H, s), 1.10 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.3,

150.2, 139.1, 126.8, 126.3, 115.7, 115.2, 112.1, 68.5, 63.9, 61.1, 56.6, 56.2, 41.2, 29.7, 25.9, 16.4; HRMS (ESI+): Calcd for $C_{17}H_{25}O_4$ $[M+H]^+$: 293.17528, Found: 293.17594. Specific Rotation: $[\alpha]_D^{20}$ +25.8 (*c* 0.387, $CHCl_3$) for an enantiomerically enriched sample of 98:2 er.

To an oven-dried 2-dram vial equipped with a magnetic stir bar is charged with epoxy alcohol **4.157** (41.1 mg, 0.141 mmol). The vessel is evacuated and refilled with N_2 three times; under N_2 atmosphere, tetrahydrofuran (thf, 1.0 mL) is added through a syringe. The vessel is charged with titanium (IV) isopropoxide (83 μL, 0.282 mmol) in a dropwise fashion and the resulting solution is allowed to age at 22 °C for 10 minutes before $LiBH_4$ solution (282 μL, 0.564 mmol, 2 M in thf) is introduced through a syringe. The resulting solution is allowed to warm to 50 °C and stir for additional 18 h, after which time it is allowed to cool to ambient temperature and quenched by addition of 0.1 M HCl solution (1.0 mL). The mixture is allowed to stir for another 30 minutes. Layers are separated and the aqueous layer is washed with EtOAc (3 x 1.0 mL). The combined organic layers are dried over anhydrous $MgSO_4$, filtered and volatiles removed under reduced pressure to afford a crude yellow oil residue, which is purified by silica gel column chromatography (1:1 hexanes/ethyl acetate) to deliver **4.158** as colorless oil (22.8 mg, 0.0776 mmol, 55% yield). **(3*S*,5*R*)-5-(2,5-Dimethoxy-4-methylphenyl)-2-methylhept-6-ene-2,3-diol (4.158, Scheme 4.23).** The compound has been previously prepared and the spectral data match those reported.[90] ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.70 (1H, s), 6.66 (1H, s), 6.03 (1H, ddd, *J* = 18.0, 10.4, 9.6 Hz), 5.17–5.10 (2H, m), 3.90 (1H, dt, *J* = 9.6, 4.8 Hz), 3.80 (3H, s), 3.78 (3H, s), 3.52 (1H, dd, *J* = 9.2, 4.0 Hz), 2.19 (3H, s), 2.08 (1H, d, *J* = 4.4 Hz),

(90) Huang, C.; Liu, B. *Chem. Commun.* **2010**, *46*, 5280–5282.

2.06 (1H, bs), 1.94 (1H, dd, *J* = 14.0, 10.0 Hz), 1.64–1.58 (1H, m), 1.21 (3H, s), 1.15 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.0, 150.4, 140.4, 131.3, 125.2, 115.5, 114.8, 110.9, 76.4, 73.1, 56.5, 56.2, 40.6, 37.2, 26.3, 23.7, 16.3; HRMS (ESI+): Calcd for $C_{17}H_{26}O_4$ $[M]^+$: 294.18311, Found: 294.18332. Specific Rotation: $[\alpha]_D^{20}$ –33.3 (*c* 0.0330, $CHCl_3$) for an enantiomerically enriched sample of 98:2 er.

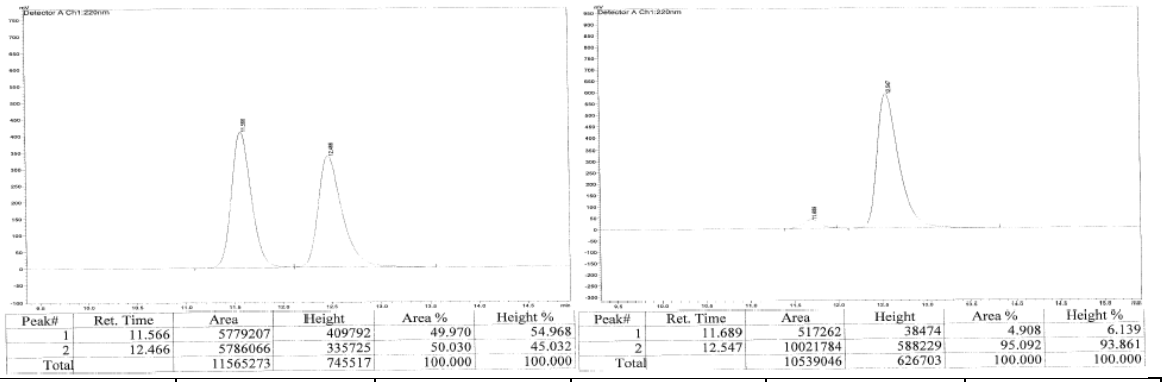
Proof of Stereochemistry: Literature value ($[\alpha]_D^{20}$ +36.3 (*c* 0.25, $CHCl_3$), 98:2 er) is assigned to the (3*R*, 5*S*) enantiomer.[90]

■ **Representative Experimental Procedure for Cu-Catalyzed Enantioselective Allylic Substitution (EAS) with Heterocyclic-Substituted Alkenylboron Reagents (Scheme 4.24):** In this section, the reactions are performed following the same representative procedure as described for Table 4.3. The specific differences are included within the characterization data of each compound.

***tert*-Butyl (*S*)-4-(1-(2-bromophenyl)allyl)-3,6-dihydropyridine-1(2*H*)-carboxylate (4.162, Scheme 4.24).** IR (neat): 2976 (w), 2827 (w), 2837 (w), 1696 (s), 1467 (w), 1415 (m), 1365 (m), 1286 (w), 1240 (m), 1171 (s), 1112 (m), 1022 (w), 921 (w), 754 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (1H, dd, *J* = 8.0, 1.2 Hz), 7.25 (1H, ddd, *J* = 7.6, 7.6, 1.6 Hz), 7.16 (1H, dd, *J* = 8.0, 2.0 Hz), 7.09–7.05 (1H, m), 5.96 (1H, ddd, *J* = 17.2, 10.4, 6.8 Hz), 5.37 (1H, bs), 5.18 (1H, ddd, *J* = 10.4, 1.6, 1.2 Hz), 4.95 (1H, ddd, *J* = 17.2, 1.6, 1.2 Hz), 4.40 (1H, d, *J* = 6.8 Hz), 3.90 (2H, bs), 3.48–3.36 (2H, m), 1.98 (2H, bs), 1.44 (9H, bs); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.1, 140.6, 137.9, 137.2 (broad), 133.2, 129.7, 128.2, 127.5, 125.7, 121.0 (broad), 117.1, 79.7, 54.5, 43.6 (broad), 41.2 (broad), 40.0 (broad), 28.6; HRMS (ESI+): Calcd for $C_{14}H_{17}Br_1N_1$ $[M+H–Boc]^+$: 278.05444,

Found: 278.05322. Specific Rotation: $[\alpha]_D^{20}$ –30.1 (*c* 1.99, $CHCl_3$) for an enantiomerically enriched sample of 93:7 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (95:5 er shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.566	5779207	409792	49.970	54.968
2	12.466	5786066	335725	50.030	45.032
Total		11565273	745517	100.000	100.000

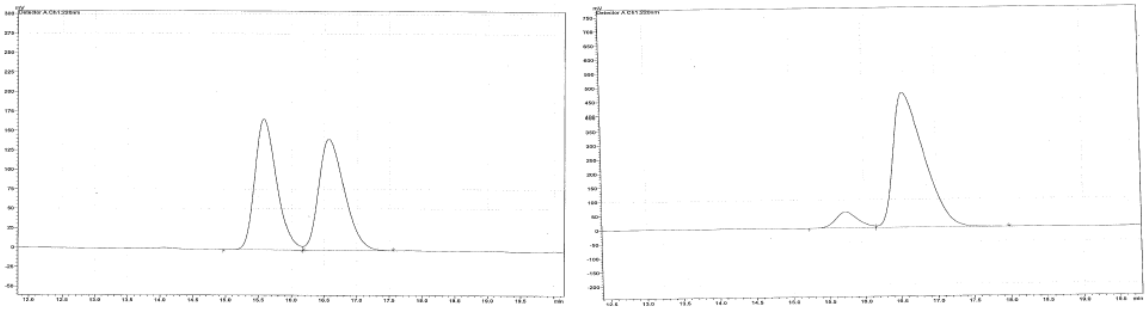
Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.689	517262	38474	4.908	6.139
2	12.547	10021784	588229	95.092	93.861
Total		10539046	626703	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	11.57	50.0	1	11.69	4.9
2	12.47	50.0	2	12.55	95.1

***tert*-Butyl (*S*)-4-(2-methyl-1-phenylallyl)-3,6-dihydropyridine-1(2*H*)-carboxylate (4.163, Scheme 4.24).** The title compound is prepared at 60 ºC for 24 h following the same representative procedure. IR (neat): 2975 (m), 2928 (m), 2853 (w), 1699 (s), 1417 (m), 1365 (w), 1338 (w), 1285 (w), 1241 (m), 1173 (s), 1110 (m), 959 (w), 897 (w), 865 (w), 770 (w), 701 (w), 656 (w), 539 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.31–7.27 (2H, m), 7.24–7.20 (1H, m), 7.17–7.14 (2H, m), 5.24 (1H, bs), 5.00 (1H, dd, *J* = 1.5, 1.0 Hz), 4.62 (1H, s), 3.89–3.86 (3H, m), 3.48 (2H, t, *J* = 6.0), 2.12 (2H, bs), 1.73 (3H, s), 1.46 (9H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 155.1, 145.7, 140.8, 129.2, 128.3, 126.6, 125.4, 121.2, 113.7, 79.6, 59.7, 43.5, 29.9, 28.6, 25.3, 23.3; HRMS (ESI+): Calcd for

$C_{16}H_{18}N_1O_2$ $[M–C_4H_9]^+$: 256.1338, Found: 256.1327. Specific Rotation: $[\alpha]_D^{20}$ +8.90 (*c* 1.91, $CHCl_3$) for an enantiomerically enriched sample of 92:8 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (92:8 er shown; Chiralpak AD-H column, 99.7/0.3 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.573	3880503	168086	49.828	54.066
2	16.563	3907369	142807	50.172	45.934
Total		7787871	310892	100.000	100.000

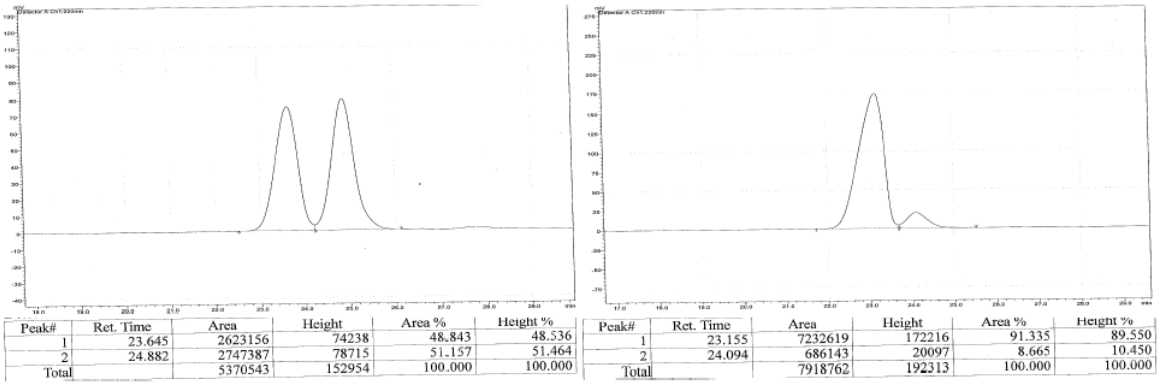
Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.734	1215729	56101	8.026	10.602
2	16.552	13931014	473037	91.974	89.398
Total		15146742	529138	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	15.57	49.8	1	15.73	8.0
2	16.56	50.2	2	16.55	92.0

***tert*-Butyl (*S*)-4-(2-methyl-5-phenylpent-1-en-3-yl)-3,6-dihydropyridine-1(2*H*)-carboxylate (4.164, Scheme 4.24).** The title compound is prepared at 60 ºC for 24 h following the same representative procedure. IR (neat): 2975 (m), 2930 (m), 2859 (w), 1699 (s), 1418 (m), 1365 (w), 1285 (w), 1241 (m), 1173 (s), 1111 (m), 892 (w), 770 (w), 700 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.30–7.25 (2H, m), 7.20–7.15 (3H, m), 5.45 (1H, bs), 4.87 (1H, dd, *J* = 1.5, 1.0 Hz), 4.78 (1H, bs), 3.88 (2H, dt, *J* = 6.0, 2.5 Hz), 3.51–3.44 (2H, m), 3.39 (1H, ddd, J = 12.5, 6.5, 4.5 Hz), 2.61–2.51 (3H, m), 2.13 (1H, ddt, *J* = 7.0, 4.0, 3.5 Hz), 1.83 (2H, ddt, *J* = 9.0, 7.5, 2.0 Hz), 1.60 (3H, s), 1.47 (9H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 155.1, 145.7, 142.6, 128.6, 128.4, 125.9, 125.3, 119.4, 111.9, 79.6, 53.2, 43.5, 34.0, 31.8, 28.6, 26.3, 25.3, 20.5; HRMS (ESI+): Calcd for

$C_{18}H_{22}N_1O_2$ $[M–C_4H_9]^+$: 284.1651, Found: 284.1689. Specific Rotation: $[\alpha]_D^{20}$ –16.1 (*c* 2.68, $CHCl_3$) for an enantiomerically enriched sample of 91:9 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (91:9 er shown; Chiralpak AD-H column, 99.7/0.3 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



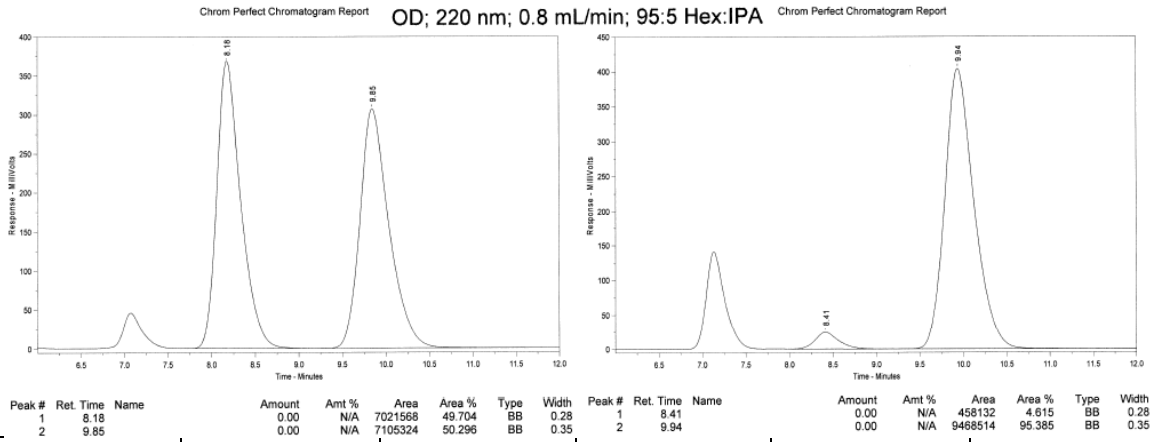
Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.645	2623156	74238	48.843	48.536
2	24.882	2747387	78715	51.157	51.464
Total		5370543	152954	100.000	100.000

Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.155	7232619	172216	91.335	89.550
2	24.094	686143	20097	8.665	10.450
Total		7918762	192313	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	23.65	48.8	1	23.16	91.3
2	24.88	51.2	2	24.09	8.7

Methyl (*S*)-2-((4-bromophenyl)(3,6-dihydro-2*H*-pyran-4-yl)methyl)acrylate (4.167, Scheme 4.24). The title compound is prepared with 2.5 mol % **4.150** and 25 mol % CuCl at 60 ºC for 24 h following the same representative procedure. IR (neat): 2956 (w), 2924 (w), 2835 (m), 1720 (s), 1598 (w), 1486 (s), 1464 (m), 1340 (s), 1287 (w), 1243 (s), 1233 (m), 1132 (s), 1128 (m), 1052 (s), 917 (m), 828 (w), 749 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.44 (2H, d, *J* = 8.4 Hz), 7.05 (2H, d, *J* = 8.4 Hz), 6.40 (1H, app s), 5.34 (1H, t, *J* = 1.2 Hz), 5.28 (1H, dt, *J* = 2.8, 1.2 Hz), 4.54 (1H, br s), 4.15 (2H, dtt, *J* = 11.2, 5.2, 2.8 Hz), 3.73 (3H, s), 3.86–3.71 (2H, m), 2.18–1.95 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 140.3, 138.9, 136.6, 131.5, 130.7, 126.9, 121.9, 120.8, 65.8, 64.7, 52.3, 49.6, 28.2; HRMS (ESI$^+$): Calcd for $C_{16}H_{18}{}^{79}BrO_3$ $[M+H]^+$: 337.04393, Found: 337.04357.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (95:5 er shown; Chiralcel OD column, 95/5 hexanes/*i*-PrOH, 0.8 mL/min, 220 nm).

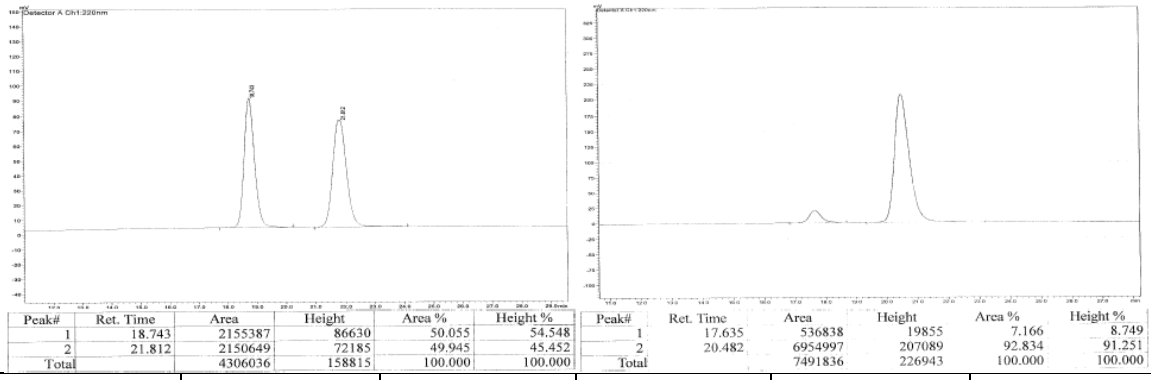


Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	8.18	49.7	1	8.41	4.6
2	9.85	50.3	2	9.94	95.4

(*S*)-4-(1-(2-Methoxyphenyl)allyl)-3,6-dihydro-2*H*-pyran (4.166, Scheme 4.24). IR (neat): 2956 (w), 2922 (m), 2834 (m), 1634 (w), 1598 (w), 1490 (s), 1463 (m), 1439 (w), 1288 (w), 1243 (s), 1130 (s), 1031 (m), 917 (m), 754 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21 (1H, ddd, *J* = 9.2, 7.6, 2.0 Hz), 7.13 (1H, dd, *J* = 7.6, 2.0 Hz), 6.92 (1H, ddd, *J* = 7.2, 7.2, 0.8 Hz), 6.88 (1H, dd, *J* = 8.0, 1.2 Hz), 6.05 (1H, ddd, *J* = 17.2, 10.0, 7.2 Hz), 5.46–5.44 (1H, m), 5.12 (1H, ddd, *J* = 11.2, 2.0, 1.2 Hz), 4.95 (1H, ddd, *J* = 16.8, 1.6, 1.6 Hz), 4.40 (1H, d, *J* = 6.8 Hz), 4.19–4.16 (2H, m), 3.81 (3H, s), 3.74 (2H, ddd, *J* = 22.0, 11.2, 5.6 Hz), 2.02–1.98 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.4, 139.0, 137.1, 129.9, 128.7, 127.6, 121.7, 120.6, 115.9, 110.9, 65.9, 64.7, 55.8, 48.0, 28.4; HRMS (ESI+): Calcd for $C_{15}H_{19}O_2$ $[M+H]^+$: 231.13850, Found: 231.13929. Specific

Rotation: $[\alpha]_D^{20}$ –15.2 (*c* 1.28, $CHCl_3$) for an enantiomerically enriched sample of 93:7 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (93:7 er shown; Chiralcel OJ-H column, 99.5/0.5 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.743	2155387	86630	50.055	54.548
2	21.812	2150649	72185	49.945	45.452
Total		4306036	158815	100.000	100.000

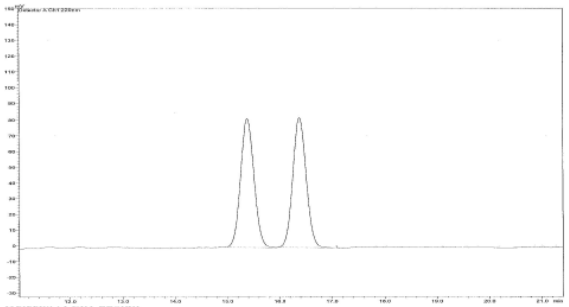
Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.635	536838	19855	7.166	8.749
2	20.482	6954997	207089	92.834	91.251
Total		7491836	226943	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	18.74	50.1	1	17.64	7.2
2	21.81	49.9	2	20.48	92.8

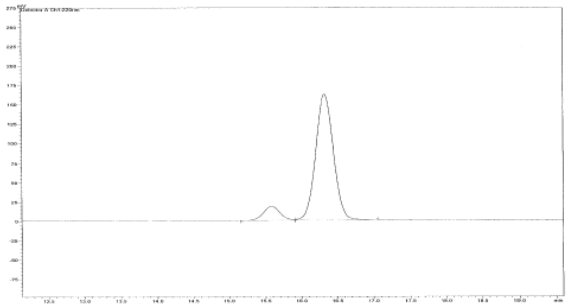
(*S*)-4-(2-Methyl-5-phenylpent-1-en-3-yl)-3,6-dihydro-2*H*-pyran (4.165, Scheme 4.24). The title compound is prepared at 60 °C for 24 h following the same representative procedure. IR (neat): 3063 (w), 3025 (w), 2928 (m), 2849 (m), 1643 (w), 1603 (w), 1495 (w), 1453 (m), 1371 (w), 1234 (w), 1126 (s), 1029 (w), 971 (w), 890 (m), 851 (w), 747 (m), 698 (s), 572 (w), 478 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.31–7.26 (2H, m), 7.20–7.16 (3H, m), 5.53–5.50 (1H, m), 4.89–4.88 (1H, m), 4.80–4.79 (1H, m), 4.18–4.16 (2H, m), 3.80–3.71 (2H, m), 2.60–2.55 (3H, m), 2.08–1.99 (1H, m), 1.95–1.82 (3H, m), 1.63 (3H, dd, *J* = 1.2, 0.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.7, 142.7, 136.3, 128.6, 128.5, 125.9, 121.2, 112.0, 65.7, 64.8, 53.2, 34.0, 31.6, 26.5, 20.4; HRMS (ESI+): Calcd

for $C_{13}H_{21}O_1$ [M+H]$^+$: 243.17489, Found: 243.17497. Specific Rotation: $[\alpha]_D^{20}$ –11.1 (*c* 1.13, $CHCl_3$) for an enantiomerically enriched sample of 91:9 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (91:9 er shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.390	1248844	81178	50.117	49.531
2	16.382	1243017	82714	49.883	50.469
Total		2491861	163892	100.000	100.000



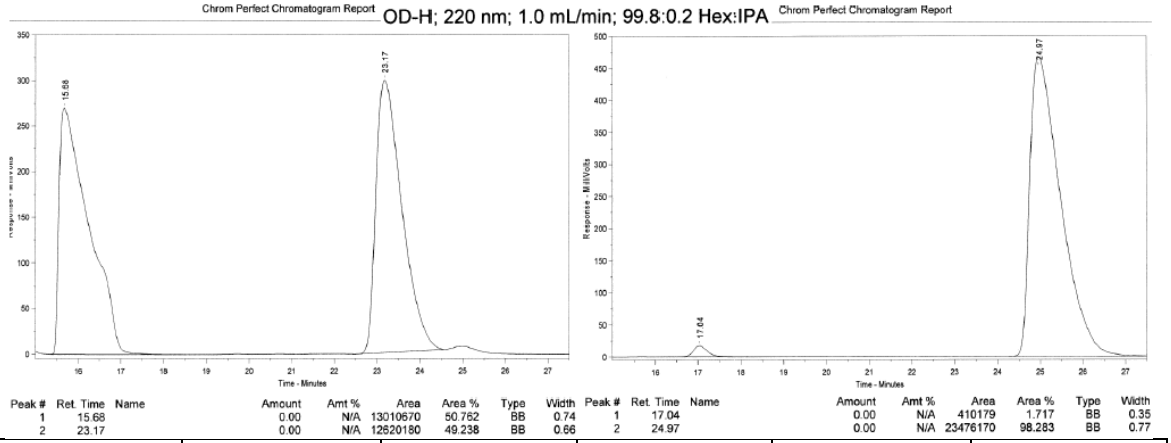
Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.580	292938	18490	9.476	10.250
2	16.317	2798312	161899	90.524	89.750
Total		3091250	180390	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	15.39	50.1	1	15.58	9.5
2	16.38	49.9	2	16.32	90.5

Methyl (*S*)-2-((4-bromophenyl)(3,4-dihydro-2*H*-pyran-6-yl)methyl)acrylate (4.168, Scheme 4.24). The title compound is prepared with 2.5 mol % **4.150** and 25 mol % CuCl at 60 ºC for 24 h following the same representative procedure. IR (neat): 1720 (s), 1490 (m), 1240 (s), 1230 (m), 1150 (m), 1130 (s), 1080 (m), 1060 (s), 1010 (m), 820 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 (2H, d, *J* = 8.4 Hz), 7.11 (2H, d, *J* = 8.4 Hz), 6.38 (1H, app s), 5.52 (1H, t, *J* = 1.2 Hz), 4.59 (1H, s), 4.47 (1H, t, *J* = 3.6 Hz), 3.96 (2H, dd, *J* = 5.2, 4.8 Hz), 3.71 (3H, s), 2.04–2.00 (2H, m), 1.79 (2H, dt, *J* = 10.4, 5.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.3, 152.6, 140.6, 138.9, 131.5, 130.7, 127.2, 120.8, 99.9, 66.6, 52.2, 50.9, 22.3, 20.5; HRMS (ESI$^+$): Calcd for $C_{16}H_{18}{}^{79}BrO_3$ [M+H]$^+$: 337.0439, Found: 337.0441.

Proof of Stereochemistry: The absolute stereochemistry is secured by X-ray crystallography of the title compound (see the last section).

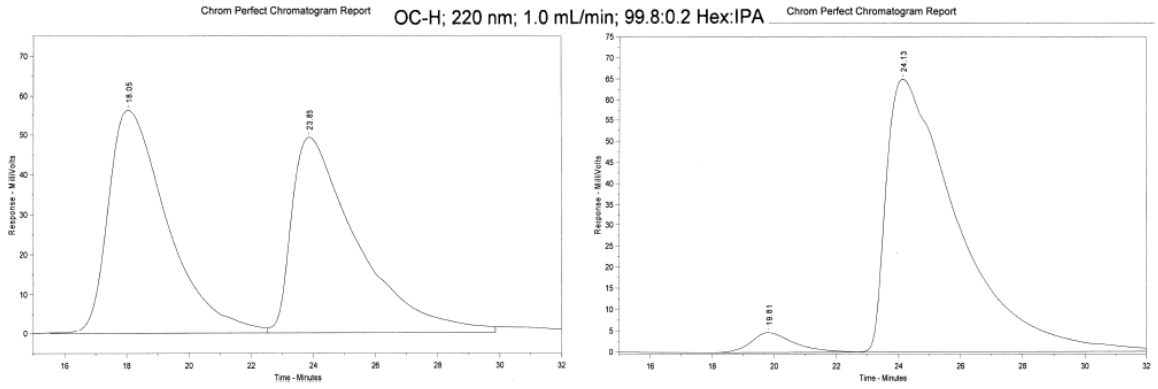
Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (98:2 er shown; Chiralcel OD-H column, 99.8/0.2 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	15.68	50.8	1	17.04	1.7
2	23.17	49.2	2	24.97	98.3

Methyl (*S*)-2-((3,4-dihydro-2*H*-pyran-6-yl)(*o*-tolyl)methyl)acrylate (4.169, Scheme 4.24). The title compound is prepared with 2.5 mol % **4.150** and 25 mol % CuCl at 60 ºC for 24 h following the same representative procedure. IR (neat,): 1720 (s), 1290 (w), 1250 (m), 1230 (m), 1150 (m), 1130 (s), 1060 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19–7.13 (4H, m), 6.36 (1H, dd, *J* = 1.2, 0.8 Hz), 5.43 (1H, t, *J* = 1.2 Hz), 4.79 (1H, br s), 4.39 (1H, t, *J* = 4.0 Hz), 3.99 (2H, dd, *J* = 6.0, 4.0 Hz), 3.72 (3H, s), 2.30 (3H, s), 2.05–2.00 (2H, m), 1.81 (2H, dt, *J* = 10.4, 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.5, 153.5, 140.6, 137.9, 136.9, 130.6, 127.7, 126.9, 126.8, 125.8, 99.8, 66.6, 52.1, 47.8, 22.4, 20.6, 19.5; HRMS (ESI^+): Calcd for $C_{17}H_{21}O_3$ $[M+H]^+$: 273.1491, Found: 273.1487.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (96:4 er shown; Chiralcel OC-H column, 99.8/0.2 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



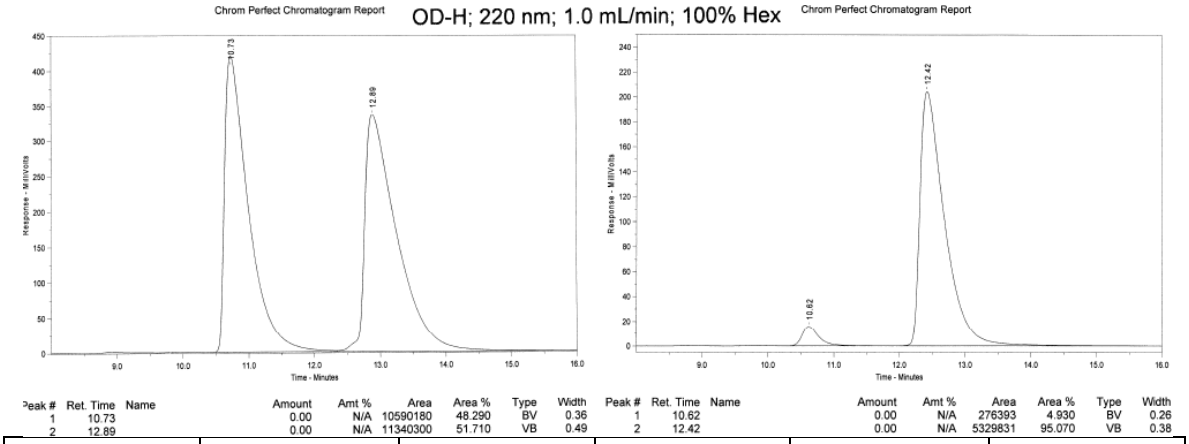
Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	18.05		0.00	N/A	7474935	50.538	BV	1.94
2	23.86		0.00	N/A	7315933	49.463	VB	2.02

Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	19.81		0.00	N/A	457057	4.186	BV	1.41
2	24.13		0.00	N/A	10462770	95.814	VB	2.30

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	18.05	50.5	1	19.81	4.2
2	23.86	49.5	2	24.13	95.8

Methyl (*S*)-2-(cyclohexyl(3,4-dihydro-2*H*-pyran-6-yl)methyl)acrylate (4.170, Scheme 4.24). The title compound is prepared with 2.5 mol % **4.150** and 25 mol % CuCl at 60 ºC for 24 h following the same representative procedure. IR (neat) 2930 (m), 2850 (w), 1720 (s), 1670 (w), 1250 (s), 1230 (w), 1150 (m), 1120 (w), 1090 (w), 1060 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.24 (1H, dd, *J* = 1.6, 0.8 Hz), 5.80 (1H, dd, *J* = 1.6, 0.8 Hz), 4.58 (1H, t, *J* = 3.6 Hz), 3.97–3.86 (2H, m), 3.74 (3H, s), 2.99 (1H, d, *J* = 10.4 Hz), 1.99–1.94 (2H, m), 1.82–1.57 (8H, m), 1.30–1.07 (3H, m), 0.96–0.76 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 153.1, 140.9, 124.9, 98.0, 66.3, 52.0, 50.9, 39.2, 31.6, 31.1, 26.7, 26.5, 26.4, 22.6, 20.6; HRMS (ESI^+): $[M+H]^+$ Calcd for $C_{16}H_{25}O_3$: 265.1804, found 265.1811.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (95:5 er shown; Chiralcel OD-H column, 100/0 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	10.73	48.3	1	10.62	4.9
2	12.89	51.7	2	12.42	95.1

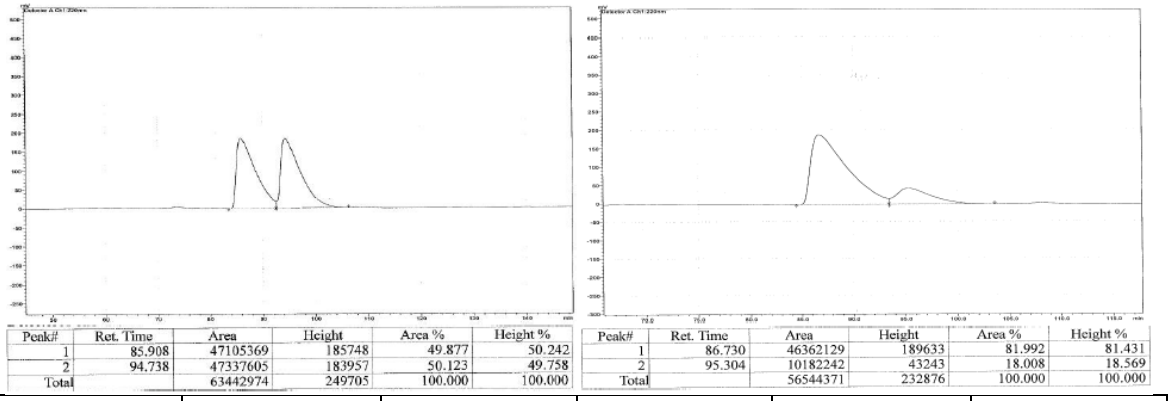
■ **Diastereo- and Enantioselective Synthesis of Semburin (Scheme 4.25):** In this section, the EAS product **4.171** is prepared with imidazolinium salt **4.150** following the same representative procedure as described for Table 4.3. **(*S*)-*tert*-Butyl((2-(3,6-dihydro-2*H*-pyran-4-yl)but-3-en-1-yl)oxy)dimethylsilane (4.171, Scheme 4.25).** IR (neat): 2955 (w), 2928 (w), 2888 (w), 2855 (w), 1472 (w), 1384 (w), 1362 (w), 1253 (m), 1100 (s), 1005 (w), 915 (w), 833 (s), 773 (s), 665 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.82–5.73 (1H, m), 5.49–5.47 (1H, m), 5.10–5.05 (2H, m), 4.13 (2H, ddd, *J* = 5.2, 2.4, 0.8 Hz), 3.81–3.72 (2H, m), 3.67 (2H, ddd, *J* = 22.0, 10.0, 6.4 Hz), 2.81 (1H, dt, *J* = 7.6, 7.6 Hz), 2.11–2.05 (2H, m), 0.88 (9H, s), 0.04 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.9, 135.4, 121.8, 116.1, 65.7, 64.8, 64.6, 53.1, 27.2, 26.0, 18.4, –5.16, –5.22; HRMS (ESI+): Calcd for $C_{15}H_{29}O_2Si_1$ $[M+H]^+$: 269.19368, Found: 269.19423. Specific Rotation:

$[\alpha]_D^{20}$ +15.8 (*c* 1.83, $CHCl_3$) for an enantiomerically enriched sample of 83:17 er. Enantiomeric purity is determined by HPLC analysis of the derived lactone (see below).

To a 2-dram vial equipped with a magnetic stir bar is charged with dihydropyran **4.171** (53.7 mg, 0.200 mmol). The vessel is evacuated and refilled with N_2 three times; under N_2 atmosphere, dichloroethane (2.0 mL) is added through a syringe. The vessel is charged with pyridinium chlorochromate (PCC, 43.1 mg, 0.200 mmol) in one portion as a solid. The resulting orange suspension is sealed with a teflon-lined cap and allowed to warm to 80 ^oC and stir for 4 h (the orange suspension turns to dark brown suspension). After that time, another equivalent of PCC (43.1 mg, 0.200 mmol) is added to the above reaction mixture and resulting dark brown suspension is sealed again and allowed to stir at 80 ^oC for another 4 h. The third equivalent of PCC is introduced the same way and the reaction is quenched 4 hours later by addition of *i*PrOH (2.0 mL). The mixture is allowed to cool to ambient temperature and stir for another 30 minutes, after which time it is passed through a plug of celite eluted with EtOAc. The volatiles are removed under reduced pressure to afford a crude brown oil residue, which is purified by silica gel column chromatography (4:1 hexanes/ethyl acetate) to deliver **4.172** as colorless oil (44.1 mg, 0.156 mmol, 78% yield). **(*S*)-4-(1-((*tert*-Butyldimethylsilyl)oxy)but-3-en-2-yl)-5,6-dihydro-2*H*-pyran-2-one (4.172, Scheme 4.25).** IR (neat): 2954 (m), 2929 (m), 2896 (w), 2857 (m), 1727 (s), 1471 (w), 1420 (w), 1257 (m), 1220 (m), 1102 (s), 1086 (s), 1003 (w), 922 (w), 838 (s), 777 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.88–5.87 (1H, m), 5.77 (1H, ddd, *J* = 18.0, 10.4, 7.6 Hz), 5.21 (1H, ddd, *J* = 10.4, 1.2, 1.2 Hz), 5.16 (1H, ddd, *J* = 17.2, 1.2, 1.2 Hz), 4.36 (2H, t, *J* = 6.0 Hz), 3.80–3.72 (2H, m), 3.09 (1H, dt, *J* = 6.4, 6.4 Hz), 2.43 (2H, dt, *J* = 6.0, 0.8 Hz), 0.87 (9H, s), 0.04 (6H, d, *J* = 0.8 Hz); ^{13}C

NMR (100 MHz, $CDCl_3$): δ 164.8, 161.2, 134.7, 118.5, 117.3, 66.3, 64.4, 52.7, 26.6, 25.9, 18.3, –5.31, –5.38; HRMS (ESI+): Calcd for $C_{15}H_{27}O_3Si_1$ $[M+H]^+$: 283.17295, Found: 283.17397. Specific Rotation: $[\alpha]_D^{20}$ +5.33 (*c* 0.912, $CHCl_3$) for an enantiomerically enriched sample of 83:17 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (83:17 er shown; Chiralcel OD-H column, 99.8/0.2 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	85.908	47105369	185748	49.877	50.242
2	94.738	47337605	183957	50.123	49.758
Total		63442974	249705	100.000	100.000

Peak#	Ret. Time	Area	Height	Area %	Height %
1	86.730	46362129	189633	81.992	81.431
2	95.304	10182242	43243	18.008	18.569
Total		56544371	232876	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	85.91	49.9	1	86.73	82.0
2	94.74	50.1	2	95.30	18.0

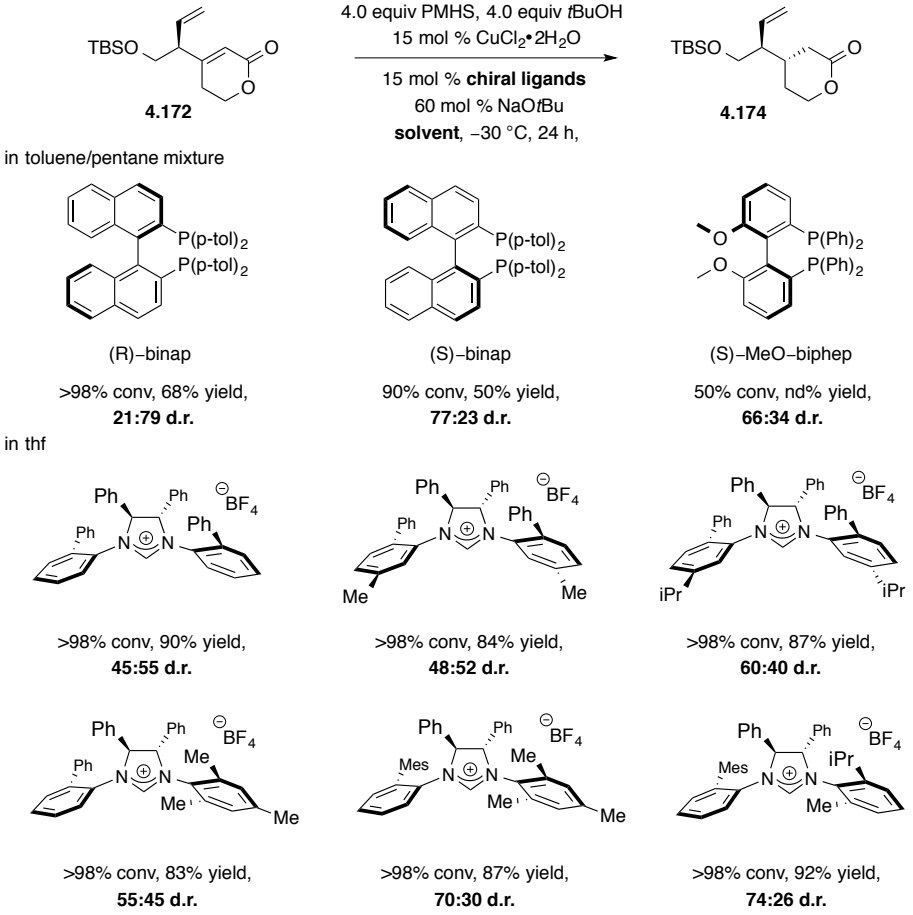
In an N_2-filled glove box, an oven-dried 1-dram vial (15 x 45 mm) with a magnetic stir bar is charged with imidazolinium salt **4.173** (3.2 mg, 0.0050 mmol), NaO*t*Bu (1.9 mg, 0.020 mmol) and CuCl (0.5 mg, 0.005 mmol). The vial is sealed with a cap (phenolic open top cap with a red PFTE/white silicon septum) and electrical tape before removal from the glove box. To the vial under an N_2 atmosphere is added tetrahydrofuran (thf, 0.5 mL) and the resulting suspension is allowed to stir at 22 °C for one hour. The suspension turns from off-white to light yellow during catalyst formation. Poly(methylhydrosiloxane) (PMHS, 24.1 mg, 0.400 mmol) is introduced into the reaction

vessel through a micro syringe (the light yellow suspension turns to orange solution immediately). Meanwhile, in a separate vial, lactone **4.172** (28.2 mg, 0.100 mmol) and *t*BuOH (29.6 mg, 0.400 mmol) are weighted out and the vial is sealed and purged with N_2 flow for 10 min before thf (0.5 mL) is added through a syringe. Both vials are allowed to cool to –50 ^{o}C in a dry ice/acetone bath and the substrate solution is transferred through a syringe to the reaction vessel that contains the in situ-formed catalyst. The resulting bright yellow solution is allowed to stir at –50 °C for additional 24 h. After that time, the mixture is passed through a short plug of silica gel eluted with Et_2O when it is still cold. The filtrate is concentrated under reduced pressure to provide a yellow oil residue, which is purified by silica gel column chromatography (4:1 hexanes/etheyl acetate) to afford product **4.174** as colorless oil (26.2 mg, 0.0921 mmol, 92% yield). **(*S*)-4-((*S*)-1-((*tert*-Butyldimethylsilyl)oxy)but-3-en-2-yl)tetrahydro-2*H*-pyran-2-one (4.174, Scheme 4.25).** The compound is characterized in the presence of 22% minor diastereomer. IR (neat): 2954 (w), 2928 (w), 2897 (w), 2857 (w), 1738 (s), 1472 (w), 1401 (w), 1252 (m), 1218 (m), 1079 (s), 1001 (m), 918 (w), 834 (s), 774 (s), 666 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.64 (1H, ddd, *J* = 17.2, 10.0, 9.6 Hz), 5.15 (1H, dd, *J* = 10.4, 1.6 Hz), 5.09 (1H, ddd, *J* = 17.2, 2.0, 0.8 Hz), 4.43–4.36 (1H, m), 4.24 (1H, ddd, *J* = 11.6, 10.8, 3.6 Hz), 3.67 (1H, dd, *J* = 10.4, 4.8 Hz), 3.59 (1H, dd, *J* = 10.4, 6.0 Hz), 2.64–2.60 (1H, m), 2.29–2.20 (2H, m), 2.10 (1H, ddd, J = 14.8, 6.0, 4.8 Hz), 1.98–1.92 (1H, m), 1.70–1.60 (1H, m), 0.87 (9H, s), 0.03 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9, 136.2, 118.4, 68.7, 63.8, 50.9, 33.7, 31.5, 27.2, 26.0, 18.4, –5.3, –5.4; HRMS (ESI+): Calcd for $C_{15}H_{29}O_3Si_1$ $[M+H]^+$: 285.18860, Found: 285.18790. Specific Rotation: $[\alpha]_D^{20}$ –27.2 (*c* 1.00, $CHCl_3$) for an enantiomerically enriched sample of 96:4 er (major diastereomer).

Enantiomeric purity is determined by GLC analysis of natural product semburin (see below).

■ Screening Data for Cu-Catalyzed Enantioselective Reduction of Unsaturated Lactone with Poly(methylhydrosiloxane):

Scheme S4. Screening Data of Various Phosphines and NHCs for Cu-Catalyzed Reduction



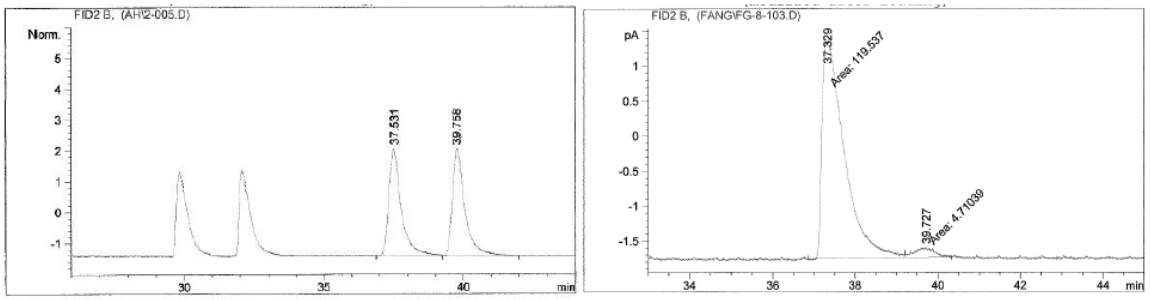
A flame-dried 6-dram vial (23 x 85 mm) is charged with lactone **4.174** (26.2 mg, 0.0921 mmol) and a stir bar. The vial is sealed with a septum and purged with N_2 flow for 10 minutes. CH_2Cl_2 (1.0 mL) is added to the vessel through a syringe. The vial is allowed to cool to –78 °C in a dry ice/acetone bath followed by dropwise addition of a CH_2Cl_2 solution of di*iso*butyl aluminum hydride (0.5 M stock solution, 202 μL, 0.101 mmol). The resulting solution is allowed to stir for one hour at –78 °C before the reaction is

quenched by addition of methyl alcohol (0.5 mL). The solution is then allowed to warm to 22 °C; saturated Rochelle's salt solution (1.0 mL) is added. The mixture is allowed to stir until two clear layers formed and the aqueous layer is washed with Et_2O (3 x 1.0 mL). The combined organic layers are dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo* to afford a colorless oil residue. To another 6-dram vial (23 x 85 mm) is charged with the residue and pyridinium *p*-toluenesulfonate (25.4 mg, 0.101 mmol) and a stir bar. The vial is sealed with a septum and purged with N_2 flow for 10 minutes before 1.0 mL benzene is added through a syringe. The septum is quickly switched to a teflon-lined cap and the resulting suspension is allowed to warm to 80 °C and stir for additional 20 h, after which time the reaction is quenched by passing through a plug of silica gel eluted with Et_2O. The filtrate is concentrated under reduced pressure to afford a colorless oil residue, which is purified by preparative thin-layer chromatography to separate the diastereomers (100% CH_2Cl_2), furnishing the desired natural product as colorless oil (9.2 mg, 0.0599 mmol, 65% yield). Note: the separation of diastereomers can be tedious. Usually the first half of the TLC band is collected and the second half is resubjected to preparative TLC. The process is repeated two more times to maximize the yield (semburin can be volatile; minimum Et_2O should be used to retrieve the natural product and careful evaporation should be performed). **Semburin (Scheme 4.25).** The title natural product has been previously reported and the spectral data match those described before.[91] ^{1}H NMR (500 MHz, C_6D_6): δ 5.38 (1H, ddd, *J* = 17.5, 11.0, 6.5 Hz), 5.31 (1H, d, *J* = 1.0 Hz), 4.91 (1H, ddd, *J* = 10.5, 1.5, 1.0 Hz), 4.79 (1H, ddd, *J* = 17.5, 1.5, 1.5 Hz),

(91) (a) Sakai, T.; Nakagawa, Y.; Iwashita, T.; Naoki, H.; Sakan, T. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 3477–3482. (b) Kawamura, M.; Ogasawara, K. *Tetrahedron Lett*. **1995**, *36*, 3369–3372.

4.06 (1H, dd, *J* = 12.0, 11.5 Hz), 3.73–3.66 (2H, m), 3.42–3.37 (1H, m), 2.39–2.32 (1H, m), 1.70–1.57 (3H, m), 1.36–1.25 (2H, m); ^{13}C NMR (125 MHz, C_6D_6): δ 137.8, 115.6, 92.4, 61.6, 60.3, 44.0, 30.3, 25.9, 23.9; HRMS (ESI+): Calcd for $C_9H_{15}O_2$ $[M+H]^+$: 155.10720, Found: 155.10705. Specific Rotation: $[\alpha]_D^{20}$ +1.49 (*c* 0.267, $CHCl_3$) for an enantiomerically enriched sample of 96:4 er.

Enantiomeric purity is determined by GLC analysis in comparison with authentic racemic material (96:4 er shown; CDGTA column, 100 ºC, 15 psi).



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	37.531	MM	0.5234	108.93215	3.47582	50.00478
2	39.758	MM	0.5221	108.72426	3.47049	49.95522

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	37.329	MF	0.6348	119.53748	3.13850	96.20888
2	39.727	FM	0.5367	4.71039	1.46288e-1	3.79112

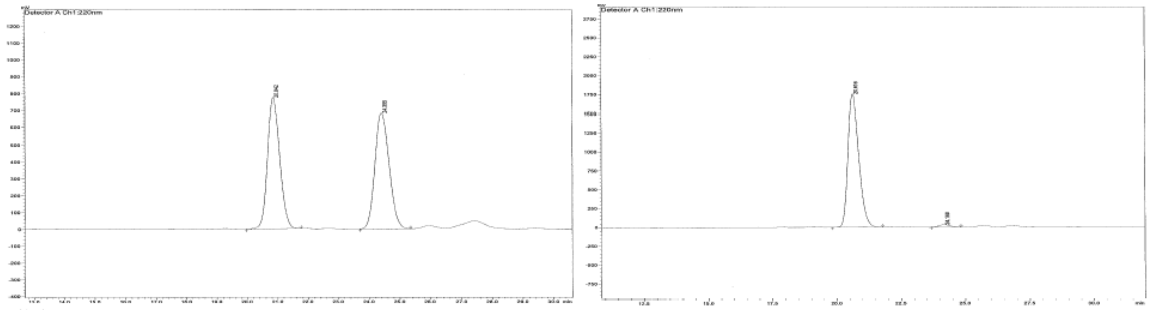
Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	37.53	50.0	1	37.33	96.2
2	39.76	50.0	2	39.73	3.8

■ **Representative Experimental Procedure for Cu-Catalyzed Enantioselective Allylic Substitution (EAS) with 1,1-Disubstituted Alkenylboron Reagents (Figure 4.4):** In this section, the reactions are performed following the same representative procedure as described for Table 4.3. The specific differences are included within the characterization data of each compound.

***tert*-Butyl (*R*)-(3-(3-bromophenyl)-2-methylenepent-4-en-1-yl)carbamate (4.178, Figure 4.4).** The title compound is prepared at 60 ºC for 24 h following the same general procedure. IR (neat): 3348 (w), 2977 (w), 2928 (w), 1701 (s), 1567 (w), 1508 (m), 1473

(w), 1391 (w), 1366 (m), 1271 (m), 1169 (s), 1073 (w), 1049 (w), 997 (w), 945 (m), 862 (w), 781 (w), 702 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.37–7.33 (2H, m), 7.18 (1H, dd, *J* = 7.6, 7.6 Hz), 7.13 (1H, ddd, *J* = 7.6, 1.2, 1.2 Hz), 6.05 (1H, ddd, *J* = 17.2, 10.0, 7.2 Hz), 5.20–5.17 (2H, m), 4.99–4.94 (2H, m), 4.55 (1H, bs), 4.00 (1H, d, *J* = 7.2 Hz), 3.64 (2H, bs), 1.43 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.2, 148.7, 146.0, 138.6, 132.9, 130.5, 128.9, 127.7, 126.1, 117.4, 111.4, 79.1, 45.3, 40.8, 28.4; HRMS (ESI+): Calcd for $C_{12}H_{14}Br_1N_1$ $[M+H–Boc]^+$: 251.03096, Found: 251.03035. Specific Rotation: $[\alpha]_D^{20}$ +67.1 (*c* 0.532, $CHCl_3$) for an enantiomerically enriched sample of 98:2 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (98:2 er shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.842	21899279	773288	50.080	53.108
2	24.395	21829267	682790	49.920	46.892
Total		43728546	1456077	100.000	100.000

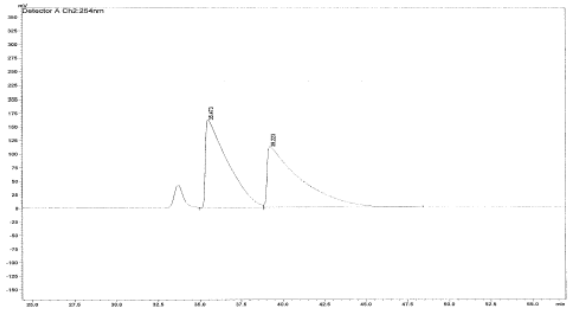
Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.616	51552876	1752120	98.177	98.222
2	24.168	957452	31710	1.823	1.778
Total		52510328	1783829	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	20.84	50.1	1	20.62	98.2
2	24.40	49.9	2	24.17	1.8

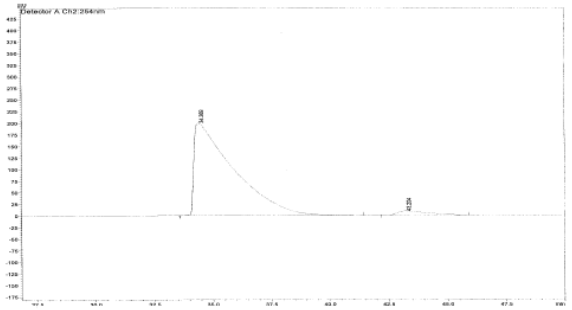
(*S*)-Dimethyl(phenyl)(2-phenylpenta-1,4-dien-3-yl)silane (4.177, Figure 4.4). IR (neat): 3070 (w), 3052 (w), 3023 (w), 2958 (w), 2898 (w), 1616 (w), 1491 (w), 1426 (w), 1301 (w), 1249 (m), 1112 (m), 995 (w), 897 (m), 830 (s), 813 (s), 772 (s), 724 (s), 696 (s), 654 (s), 469 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.46–7.42 (2H, m), 7.36–7.18

(8H, m), 5.98 (1H, ddd, *J* = 17.6, 12.4 9.2 Hz), 5.21 (1H, dd, *J* = 0.8, 0.8 Hz), 4.98–4.93 (2H, m), 4.83 (1H, s), 3.14 (1H, d, *J* = 9.6 Hz), 0.252 (3H, s), 0.246 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.1, 144.4, 138.9, 137.2, 134.4, 129.2, 128.2, 127.6, 127.3, 126.6, 112.6, 111.9, 42.7, –3.7, –4.4; HRMS (ESI+): Calcd for $C_{19}H_{23}Si_1$ $[M+H]^+$: 279.15690, Found: 279.15733. Specific Rotation: $[\alpha]_D^{20}$ –144 (*c* 1.73, $CHCl_3$) for an enantiomerically enriched sample of 97:3 er.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (97:3 er shown; Chiralcel OD-H column, 100/0 hexanes/*i*-PrOH, 0.5 mL/min, 254 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	35.473	14992124	161331	49.612	59.098
2	39.223	15226647	111657	50.388	40.902
Total		30218771	272988	100.000	100.000



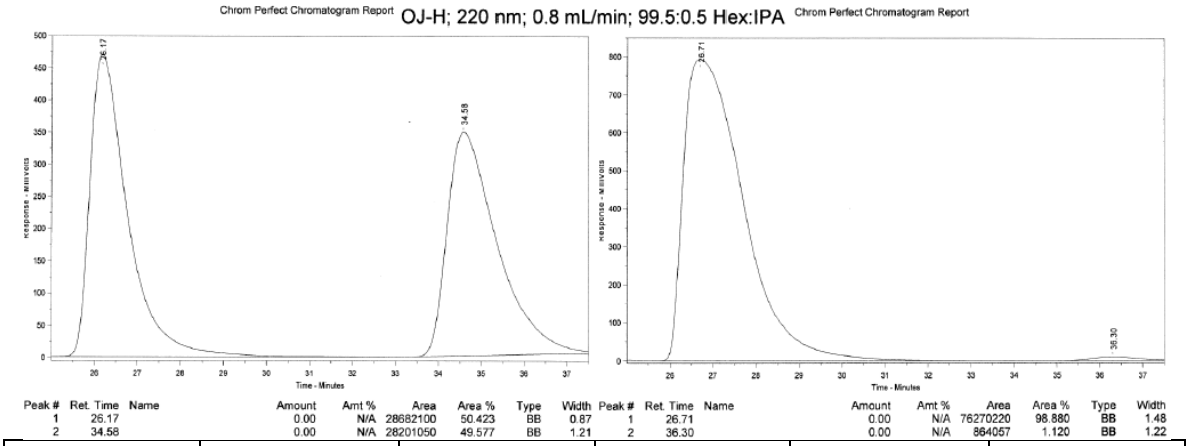
Peak#	Ret. Time	Area	Height	Area %	Height %
1	34.369	23361038	199627	96.840	95.764
2	43.204	762258	8830	3.160	4.236
Total		24123296	208457	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	35.47	49.6	1	34.37	96.8
2	39.23	50.4	2	43.20	3.2

■ **Representative Experimental Procedure for Cu-Catalyzed Enantioselective Allylic Substitution (EAS) with Unsubstituted Alkenylboron Reagents (Table 4.5):** In a nitrogen-filled glovebox, an oven-dried vial equipped with a magnetic stir bar is charged with imidazolinium salt **4.116** (2.1 mg, 0.0025 mmol), NaOMe (8.1 mg, 0.15 mmol) and CuCl (2.5 mg, 0.025 mmol). The vial is sealed with a screw cap fitted with a Teflon septum and removed from the glovebox. Tetrahydrofuran (thf, 0.5 mL) is added

and the suspension is allowed to stir for 2 h at 22 °C. After this time, a solution of methyl (*E*)-2-(((diethoxyphosphoryl)oxy)methyl)-3-(naphthalen-2-yl)acrylate (37.8 mg, 0.100 mmol) and vinylboronic acid pinacol ester (**4.180**, 30.8 mg, 0.200 mmol) in thf (0.4 mL) is prepared in an oven-dried vial equipped with a septum. The solution is transferred to the vessel that contains the catalyst solution, with the vial further rinsed with thf (0.1 mL). The septum-fitted screw cap is rapidly exchanged for a standard screw cap, the vial sealed with electrical tape and allowed to warm to 60 °C and kept stirring for 20 h. After this time the reaction mixture is allowed to cool to ambient temperature and partitioned between water and ethyl acetate. The aqueous solution is washed with more ethyl acetate (3 x 1.0 mL). The combined organic layers are dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The oil residue is purified by silica gel column chromatography (50:1 to 25:1 hexanes:diethyl ether) to deliver the desired product **4.182** as colorless oil (17.4 mg, 0.0690 mmol, 69% yield). **Methyl (*S*)-2-methylene-3-(naphthalen-2-yl)pent-4-enoate (4.182, Table 4.5).** IR (neat): 1720 (s), 1190 (s), 1100 (s), 920 (m), 900 (m), 820 (s), 750 (s), 470 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.82–7.77 (3H, m), 7.63 (1H, br d, *J* = 1.2 Hz), 7.46 (1H, ddd, *J* = 7.2, 7.2, 2.8 Hz), 7.43 (1H, ddd, *J* = 7.2, 6.4, 2.8 Hz), 7.33 (1H, d, *J* = 8.4, 1.2 Hz), 6.42 (1H, dd, *J* = 0.8, 0.4 Hz), 7.17 (1H, ddd, *J* = 17.2, 10.0, 6.8 Hz), 5.64 (1H, t, *J* = 1.2 Hz), 5.23 (1H, dt, *J* = 10.0, 1.2 Hz), 4.99 (1H, dt, *J* = 17.2, 1.2 Hz), 4.84 (1H, d, *J* = 6.8 Hz), 3.68 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.3, 142.5, 138.9, 138.4, 133.6, 132.5, 128.2, 127.9, 127.7, 127.3, 127.0, 126.6, 126.1, 125.7, 117.1, 52.1, 50.3; HRMS (ESI^+): Calcd for $C_{17}H_{17}O_2$ $[M+H]^+$: 253.1229, Found: 253.1233.

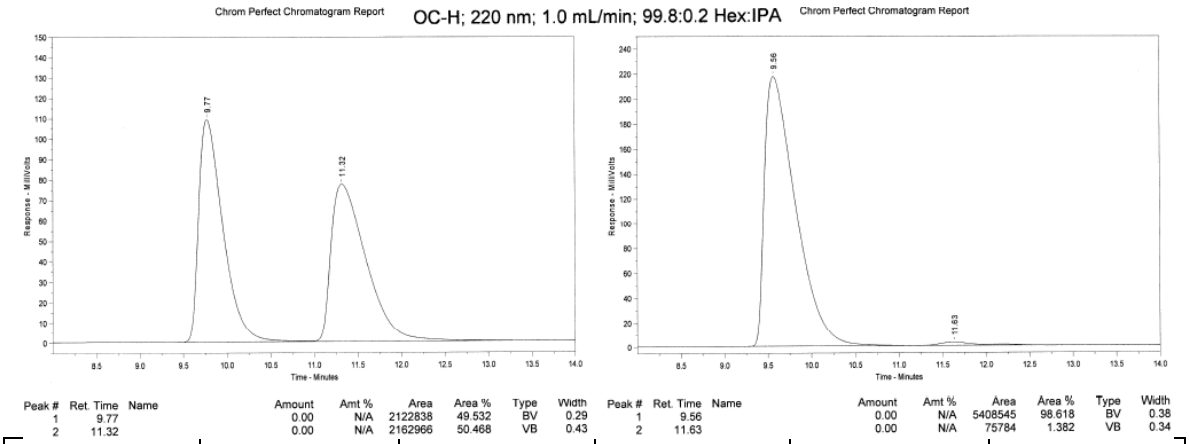
Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (99:1 er shown; Chiralcel OJ-H column, 99.5/0.5 hexanes/*i*-PrOH, 0.8 mL/min, 220 nm).



Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	26.17	50.4	1	26.71	98.9
2	34.58	49.6	2	36.30	1.1

Methyl (*S*)-2-methylene-3-phenylpent-4-enoate (4.181, Table 4.5). The title compound is prepared with 10 mol % imidazolinium salt **4.116** and 10 mol % CuCl following the same representative procedure. IR (neat): 1720 (s), 1440 (w), 1250 (m), 1140 (m), 920 (w), 700 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32–7.28 (2H, m), 7.24–7.18 (3H, m), 6.36 (1H, dd, *J* = 1.0, 0.6 Hz), 6.10 (1H, ddd, *J* = 17.0, 10.0, 6.8 Hz), 5.58 (1H, t, *J* = 1.2 Hz), 5.18 (1H, dt, *J* = 10.4, 1.2 Hz), 4.95 (1H, dt, *J* = 17.0, 1.2 Hz), 4.67 (1H, br d, *J* = 6.8 Hz), 3.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 142.7, 140.8, 139.0, 128.6, 128.5, 126.7, 126.4, 116.8, 52.1, 50.3; HRMS (ESI^+): $[M+H]^+$ Calcd for $C_{13}H_{15}O_2$: 203.10720, found 203.10777.

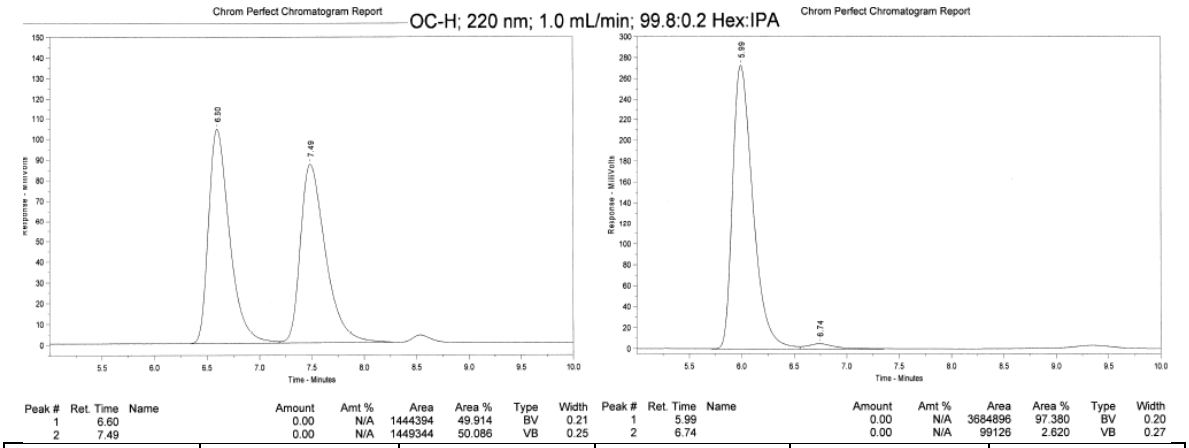
Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (99:1 er shown; Chiralcel OC-H column, 99.8/0.2 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	9.77	49.5	1	9.56	98.6
2	11.32	50.5	2	11.63	1.4

Methyl (*S*)-2-methylene-3-(4-(trifluoromethyl)phenyl)pent-4-enoate (4.185, Table 4.5). The title compound is prepared with 10 mol % imidazolinium salt **4.116** and 10 mol % CuCl following the same representative procedure. IR (neat): 1720 (m), 1320 (s), 1250 (w), 1160 (m), 1120 (s), 1070 (s), 1000 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.56 (2H, d, *J* = 8.2 Hz), 7.31 (2H, d, *J* = 8.2 Hz), 6.42 (1H, s), 6.08 (1H, ddd, *J* = 17.2, 10.0, 6.8 Hz), 5.64 (1H, s), 5.23 (1H, br d, *J* = 10.0 Hz), 4.94 (1H, dt, *J* = 17.2, 1.2 Hz), 4.71 (1H, br d, *J* = 6.8 Hz), 3.69 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.9, 145.0, 141.9, 138.2, 129.3, 128.9, 127.0, 125.6, 125.5, 125.5, 117.6, 52.2, 50.2, 24.9; HRMS (ESI^+): Calcd for $C_{14}H_{14}F_3O_2$ $[M+H]^+$: 271.0946, Found: 271.0939.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (97:3 er shown; Chiralcel OC-H column, 99.8/0.2 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



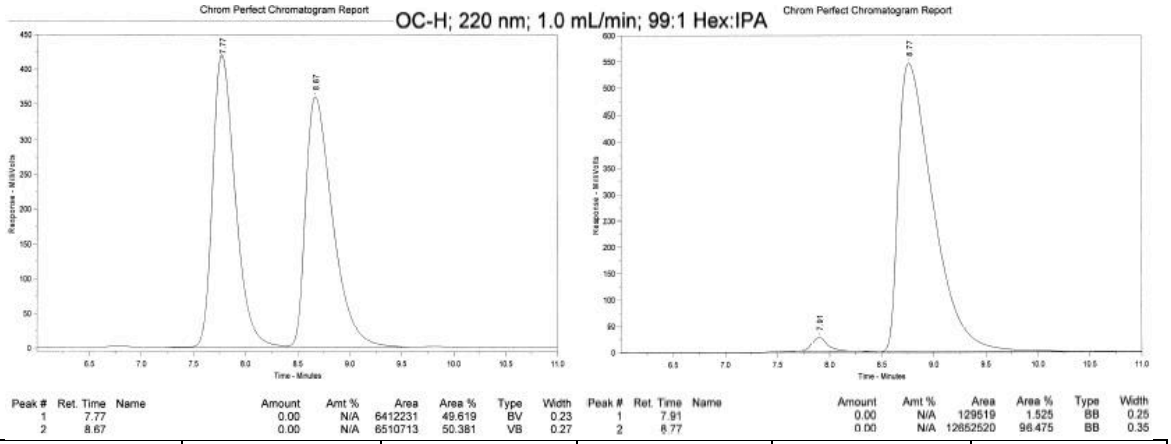
Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	6.60		0.00	N/A	1444394	49.914	BV	0.21
2	7.49		0.00	N/A	1449344	50.086	VB	0.25

Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	5.99		0.00	N/A	3684896	97.380	BV	0.20
2	6.74		0.00	N/A	99126	2.620	VB	0.27

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	6.60	49.9	1	5.99	97.4
2	7.49	50.1	2	6.74	2.6

Methyl (*S*)-3-(2-(methoxymethoxy)phenyl)-2-methylenepent-4-enoate (4.188, Table 4.5). The title compound is prepared with 3.0 equiv of vinylBpin following the same representative procedure. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (1H, ddd, *J* = 8.0, 7.2, 1.6 Hz), 7.11 (1H, dd, 7.6, 1.6 Hz), 7.08 (1H, dd, *J* = 8.0, 1.2 Hz), 6.96 (1H, ddd, *J* = 7.6, 7.2, 1.2 Hz), 6.34 (1H, dd, *J* = 1.2, 0.8 Hz), 6.06 (1H, ddd, *J* = 17.2, 10.4, 6.4 Hz), 5.49 (1H, dd, *J* = 1.2, 0.8 Hz), 5.19 (2H, s), 5.18 (1H, dt, *J* = 10.4, 1.6 Hz), 5.11 (1H, br dd, *J* = 6.4, 0.8 Hz), 4.94 (1H, dt, *J* = 17.2, 1.6 Hz), 3.70 (3H, s), 3.46 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.4, 154.6, 142.4, 138.4, 130.1, 128.9, 128.0, 126.2, 121.7, 116.6, 114.4, 94.4, 56.2, 52.0, 43.1; HRMS (ESI^+): Calcd for $C_{15}H_{19}O_4$ $[M+H]^+$: 263.1283.

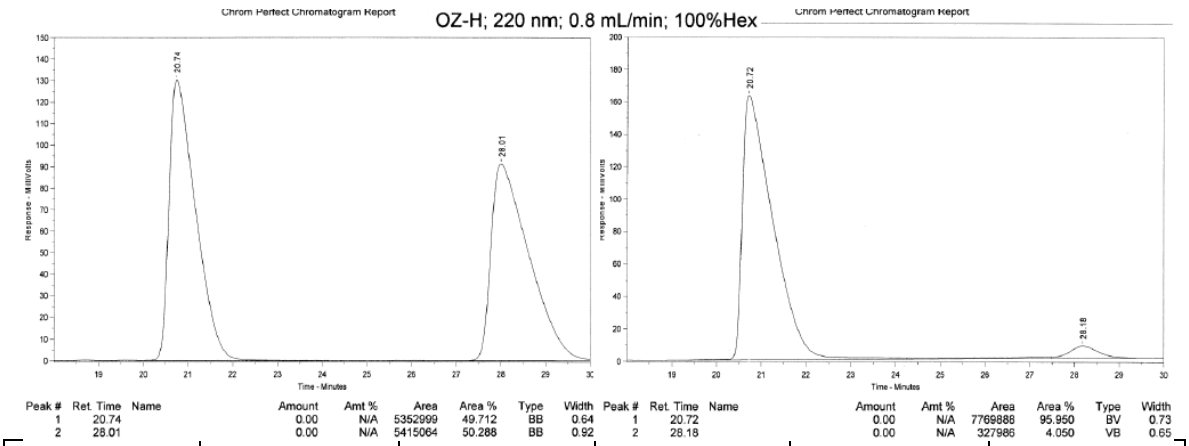
Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (92.5:7.5 er shown; Chiralcel OC-H column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	7.77	49.6	1	7.91	1.5
2	8.67	50.4	2	8.77	98.5

Methyl (*R*)-3-cyclohexyl-2-methylenepent-4-enoate (4.189, Table 4.5). The title compound is prepared with 1 mol % imidazolinium salt **4.150** and 10 mol % CuCl following the same representative procedure. IR (neat): 2920 (m), 2850 (w), 1720 (s), 1250 (m), 1190 (w), 1160 (m), 1130 (m), 910 (w), cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.20 (1H, d, *J* = 1.2 Hz), 5.84 (1H, dddd, *J* = 17.6, 13.2, 9.2, 6.4 Hz), 5.51 (1H, t, *J* = 1.2 Hz), 5.03 (1H, dt, *J* = 17.6, 1.2 Hz), 5.00 (1H, dt, *J* = 13.2, 1.3 Hz), 3.75 (3H, s), 2.96 (1H, t, *J* = 9.2 Hz), 1.82–1.60 (5H, m), 1.58–1.48 (1H, m), 1.25–1.05 (3H, m), 0.93–7.90 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.7, 142.7, 139.5, 125.0, 116.0, 52.8, 51.9, 40.3, 31.5, 30.8, 26.6, 26.5, 26.4; HRMS (ESI^+): Calcd for $C_{13}H_{21}O_2$ $[M+H]^+$: 209.1542, Found: 209.1550.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (96:4 er shown; Chiralcel OZ-H column, 100/0 hexanes/*i*-PrOH, 0.8 mL/min, 220 nm).



Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	20.74	49.7	1	20.72	96.0
2	28.01	50.3	2	28.18	4.0

Methyl (*S*)-3-(2-methoxyphenyl)-2-methylenepent-4-enoate (4.186, Table 4.5). IR (neat): 1720 (m), 1490 (m), 1440 (w), 1240 (s), 1110 (m), 1030 (w), 760 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.23 (1H, ddd, *J* = 8.0, 7.6, 2.0 Hz), 7.21 (1H, dd, 7.6, 2.0 Hz), 6.93 (1H, dd, *J* = 7.6, 1.2 Hz), 6.87 (1H, dd, *J* = 8.4, 1.2 Hz), 6.31 (1H, dd, *J* = 1.2, 0.4 Hz), 6.06 (1H, ddd, *J* = 17.2, 10.4, 6.8 Hz), 5.46 (1H, t, *J* = 1.2 Hz), 5.17 (1H, dt, *J* = 10.4, 1.6 Hz), 5.09 (1H, br d, *J* = 5.6 Hz), 4.94 (1H, dt, *J* = 17.2, 1.6 Hz), 3.82 (3H, s), 3.70 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.3, 156.9, 142.2, 138.3, 129.3, 128.6, 127.8, 125.9, 120.3, 116.3. 110.8, 55.6, 51.9, 42.8; HRMS (ESI^+): Calcd for $C_{14}H_{17}O_3$ $[M+H]^+$: 233.1178, Found: 233.1186.

Methyl (*S*)-2-methylene-3-(naphthalen-1-yl)pent-4-enoate (4.183, Table 4.5). The title compound is prepared with 10 mol % imidazolinium salt **4.116** and 10 mol % CuCl

following the same representative procedure. IR (neat): 1720 (s), 1440 (w), 1240 (m), 1130 (s), 920 (m), 800 (m), 790 (s), 780 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (1H, d, *J* = 8.4 Hz), 7.85 (1H, dd, *J* = 7.2, 2.0 Hz), 7.76 (1H, d, *J* = 8.0 Hz), 7.51 (1H, ddd, *J* = 8.4, 7.2, 2.0 Hz), 7.46 (1H, ddd, *J* = 7.2, 6.8, 1.6 Hz), 7.42 (1H, dd, *J* = 8.0, 7.2 Hz), 7.34 (1H, dd, 7.2, 1.2 Hz), 6.37 (1H, dd, *J* = 0.8, 0.4 Hz), 6.18 (1H, ddd, *J* = 17.4, 10.0, 6.4 Hz), 5.52 (1H, d, *J* = 6.4 Hz), 5.43 (1H, t, *J* = 1.2 Hz), 5.27 (1H, dt, *J* = 10.0, 1.6 Hz), 5.01 (1H, dt, *J* = 17.2, 1.6 Hz), 3.73 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.5, 142.2, 138.4, 137.0, 134.2, 131.7, 128.9, 127.7, 127.2, 126.3, 125.7, 125.3, 123.9, 117.4, 52.2, 45.3; HRMS (ESI^+): Calcd for $C_{17}H_{17}O_2$ $[M+H]^+$: 253.1229, Found: 253.1230.

Methyl (*S*)-3-(4-bromophenyl)-2-methylenepent-4-enoate (4.184, Table 4.5). The title compound is prepared with 1 mol % imidazolinium salt **4.116** and 10 mol % CuCl following the same representative procedure. IR (neat): 1720 (s), 1490 (w), 1250 (m), 1140 (m), 1010 (w), 920 (w), 820 (w) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 (2H, d, *J* = 8.4 Hz), 7.07 (2H, d, *J* = 8.4 Hz), 6.38 (1H, app s), 6.05 (1H, dddd, *J* = 17.0, 10.4, 6.8, 0.8 Hz), 5.60 (1H, t, *J* = 1.2 Hz), 5.20 (1H, dt, *J* = 10.4, 1.2 Hz), 4.93 (1H, dt, *J* = 17.2, 1.2 Hz), 4.61 (1H, br d, *J* = 6.8 Hz), 3.69 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0, 142.2, 139.9, 138.5, 131.7, 130.4, 126.6, 120.7, 117.3, 52.2, 49.8; HRMS (ESI^+): Calcd for $C_{13}H_{14}{}^{79}Br_1O_2$ $[M+H]^+$: 281.0177, Found: 281.0179.

Methyl (*S*)-3-(2-bromophenyl)-2-methylenepent-4-enoate (4.187, Table 4.5). IR (neat): 1720 (s), 1470 (w), 1440 (w), 1250 (m), 1140 (w), 760 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (1H, dd, *J* = 8.0, 1.2 Hz), 7.26 (1H, ddd, *J* = 7.6, 7.2, 1.2 Hz), 7.16 (1H, dd, *J* = 7.6, 2.0 Hz), 7.10 (1H, ddd, *J* = 8.0, 7.2, 2.0 Hz), 6.41 (1H, app t, *J* = 1.2 Hz), 6.00 (1H, ddd, *J* = 17.2, 10.4, 6.4 Hz), 5.50 (1H, t, *J* = 1.2 Hz), 5.25 (1H, dt, *J* =

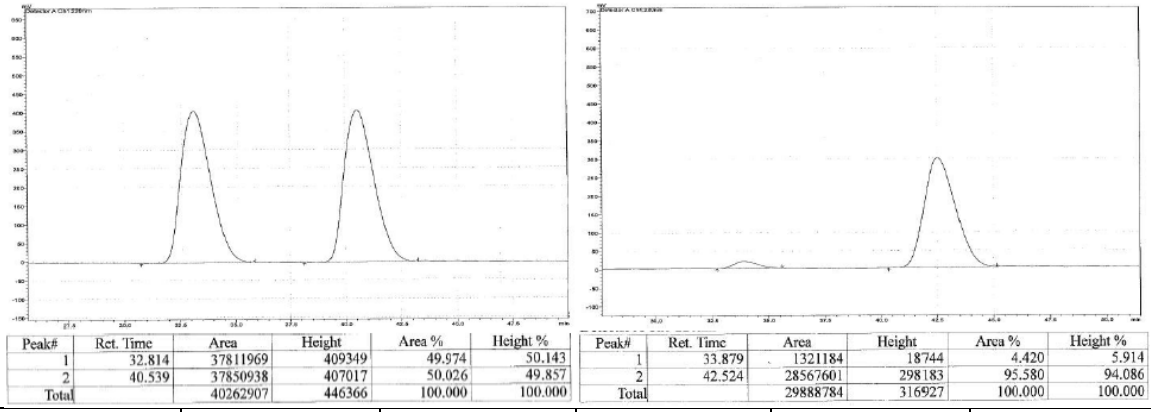
10.4, 1.4 Hz), 5.12 (1H, br d, *J* = 6.4 Hz), 4.94 (1H, dt, *J* = 17.2, 1.2 Hz), 3.70 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0, 141.6, 140.1, 137.3, 133.4, 129.5, 128.4, 127.4, 127.0, 125.5, 117.6, 52.2, 49.2; HRMS (ESI$^+$): Calcd for $C_{13}H_{14}{}^{79}BrO_2$ $[M+H]^+$: 281.0177, Found: 281.0178.

■ **Synthesis of Santolina Alcohol (Eq. 4.8):** In this section, the synthesis of santolina alcohol is performed with 2.5 equiv of the corresponding alkenylboron reagent at 4 ^oC for 24 h following the same representative procedure as described for Table 4.3. The product is volatile and therefore the loss of santolina alcohol occurs during the work-up and isolation processes.

(*S*)-2,5-Dimethyl-3-vinylhex-4-en-2-ol (santolina alcohol, Eq. 4.8). The compound is commercially available and the spectral data match those collected from a commercial sample. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.84–5.75 (1H, m), 5.16 (1H, dddd, *J* = 10.0, 2.4, 1.6, 0.8 Hz), 5.11–5.06 (2H, m), 2.98 (1H, dd, *J* = 9.2, 8.8 Hz), 1.76 (3H, d, *J* = 1.6 Hz), 1.69 (1H, bs), 1.66 (3H, d, *J* = 1.2 Hz), 1.18 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.1, 135.0, 122.8, 116.6, 72.7, 54.7, 27.1, 26.8, 26.4, 18.4; HRMS (ESI+): Calcd for $C_{10}H_{17}$ $[M+H–H_2O]^+$: 137.13303, Found: 137.13342. Specific Rotation: $[\alpha]_D^{20}$ +3.24 (*c* 0.440, $CHCl_3$) for an enantiomerically enriched sample of 96:4 er.

Proof of Stereochemistry: Specific rotation value ($[\alpha]_D^{20}$ +15.0 (neat), >98:2 er) from Aldrich Chemical Co. is assigned to the (*S*) enantiomer.

Enantiomeric purity is determined by HPLC analysis in comparison with authentic racemic material (96:4 er shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 0.8 mL/min, 220 nm).



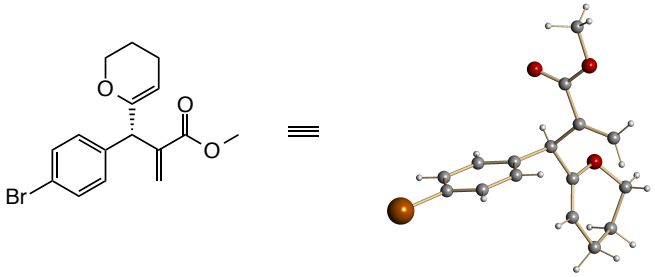
Peak#	Ret. Time	Area	Height	Area %	Height %
1	32.814	37811969	409349	49.974	50.143
2	40.539	37850938	407017	50.026	49.857
Total		40262907	446366	100.000	100.000

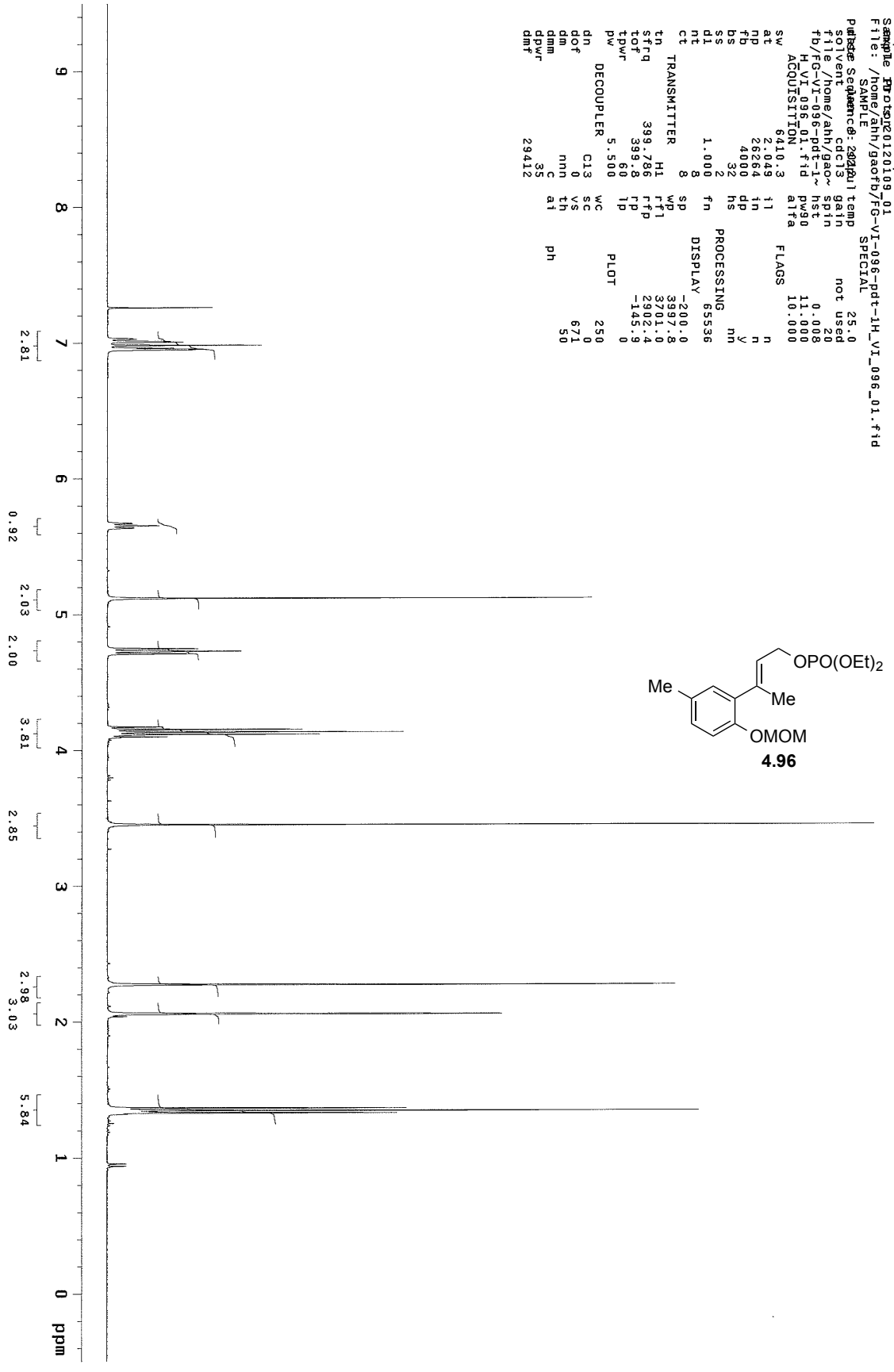
Peak#	Ret. Time	Area	Height	Area %	Height %
1	33.879	1321184	18744	4.420	5.914
2	42.524	28567601	298183	95.580	94.086
Total		29888784	316927	100.000	100.000

Peak #	Time (mins)	Area (%)	Peak #	Time (mins)	Area (%)
1	32.81	50.0	1	33.88	4.4
2	40.54	50.0	2	42.52	95.6

■ **Proof of Absolute Stereochemistry: Crystal Structure of 4.168 (Scheme 4.24).** The crystal structure secured for **4.168** is assigned to the (*S*) enantiomer.

Figure S2. Crystal Structure of Compound **4.168**

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Sample ID: Proton20120109_01
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solvent cdcl3 gain not used
file /home/ahh/gao~ spin 20
fb/FG-VI-096-pdt-1~ hst 0.008
H_VI_096_01.fid pw90 11.000
ACQUISITION FLAGS 10.000
sw 6410.3 il n
at 2.049 in n
np 26264 dp y
fb 4000 hs nn
bs 32
ss 2 PROCESSING
d1 1.000 fn 65536
nt 8 DISPLAY
ct 8 sp -200.0
wp 3997.8
TRANSMITTER rfl 3701.0
tn H1 rfp 2902.4
sfrq 399.786 rp -145.9
tof 399.8 lp 0
tpwr 60
pw 5.500 PLOT
DECOUPLER wc 250
sc 0
dn C13 vs 671
dof 0 th 50
dm nnn
dmm c ph
dpwr a1
dmf 35
29412
OPO(OEt)2
Me
Me
OMOM
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9
8
7
6
5
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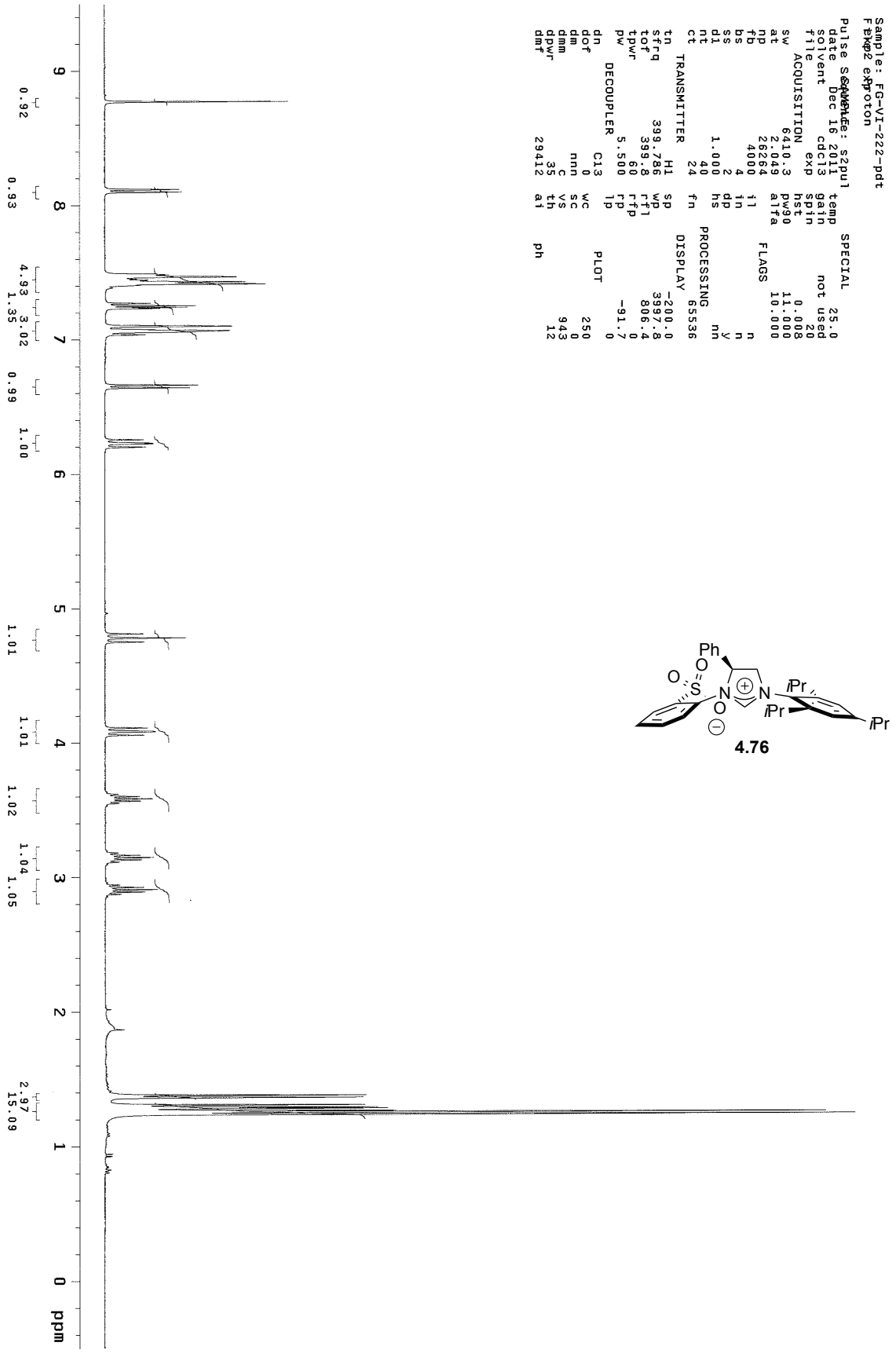
2.00
3.81
2.85
2.98
3.03
5.84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file
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fb
bs 4
ss 2
d1 1.000
nt 40
ct 24
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
temp
gain
spin
hst
pw90
alfa
FLAGS
il
in
dp
hs
PROCESSING
fn
DISPLAY
sp
wp
rfl
rfp
rp
lp
PLOT
wc
sc
vs
th
ai
ph
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20
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10.000
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n
y
nn
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806.4
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-91.7
0
250
0
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12
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0.93
4.93
3.02
1.35
0.99
1.00
1.01
1.01
1.02
1.04
1.05
2.97
15.09
9
8
7
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ppm

Ph
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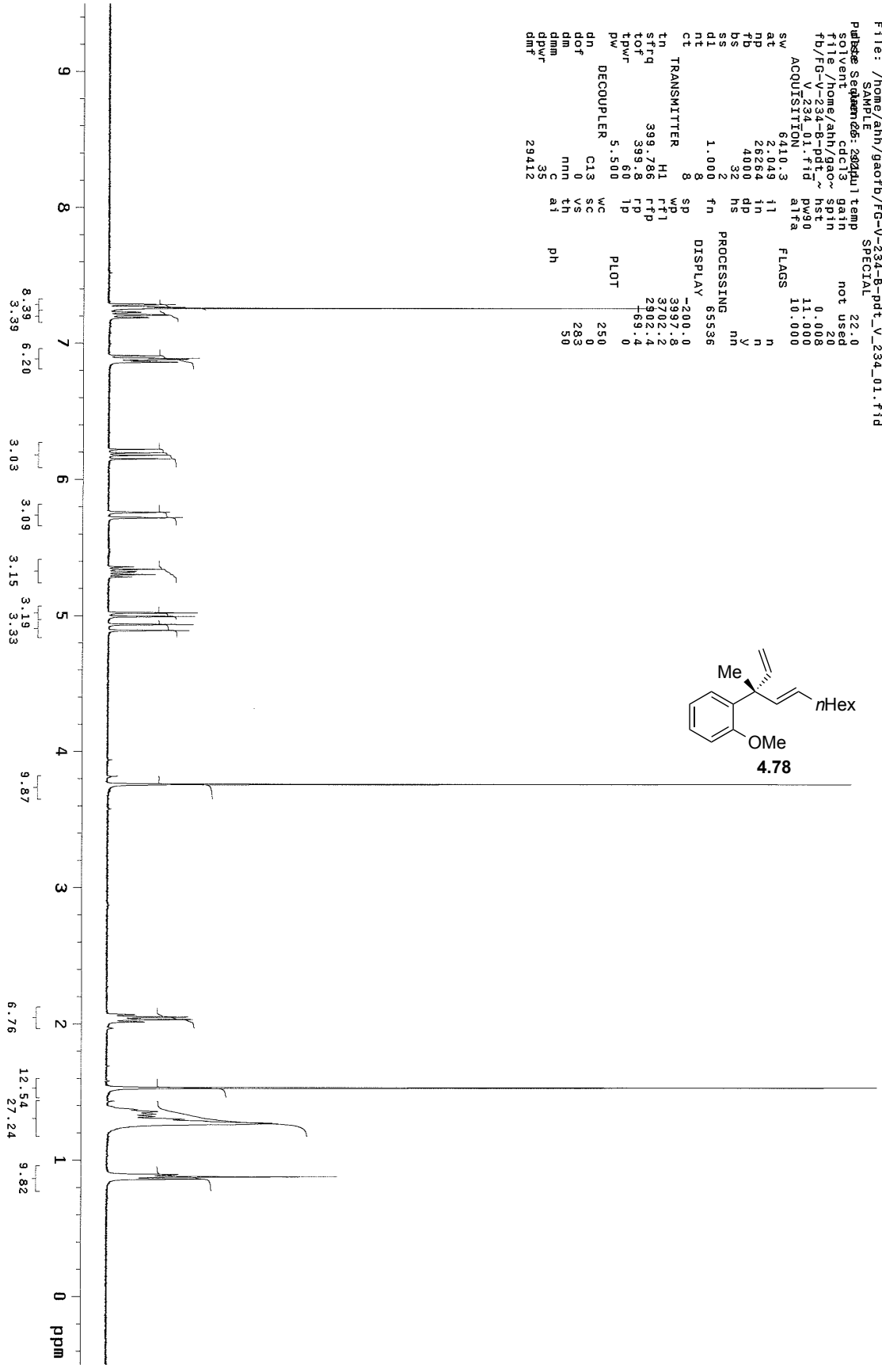
N
N
O
iPr
iPr
iPr

4.76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Sample Proton 20110125_02
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solvent cdcl3 not used
file /home/ahh/gao~ spin 20
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at 2.049 in n
np 26264 dp n
fb 4000 hs y
bs 32 nn
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d1 1.000 fn PROCESSING 65536
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ct 8 sp -200.0
wp 3997.8
TRANSMITTER rfl 3702.2
tn H1 rfp 2902.4
sfrq 399.786 rp -69.4
tof 399.8 lp 0
tpwr 60
pw 5.500 PLOT
DECOUPLER wc 250
sc 0
dn C13 vs 283
dof 0 th 50
dm nnn ph
dmm c
dpwr ai
dmf 35
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Me
nHex
OMe
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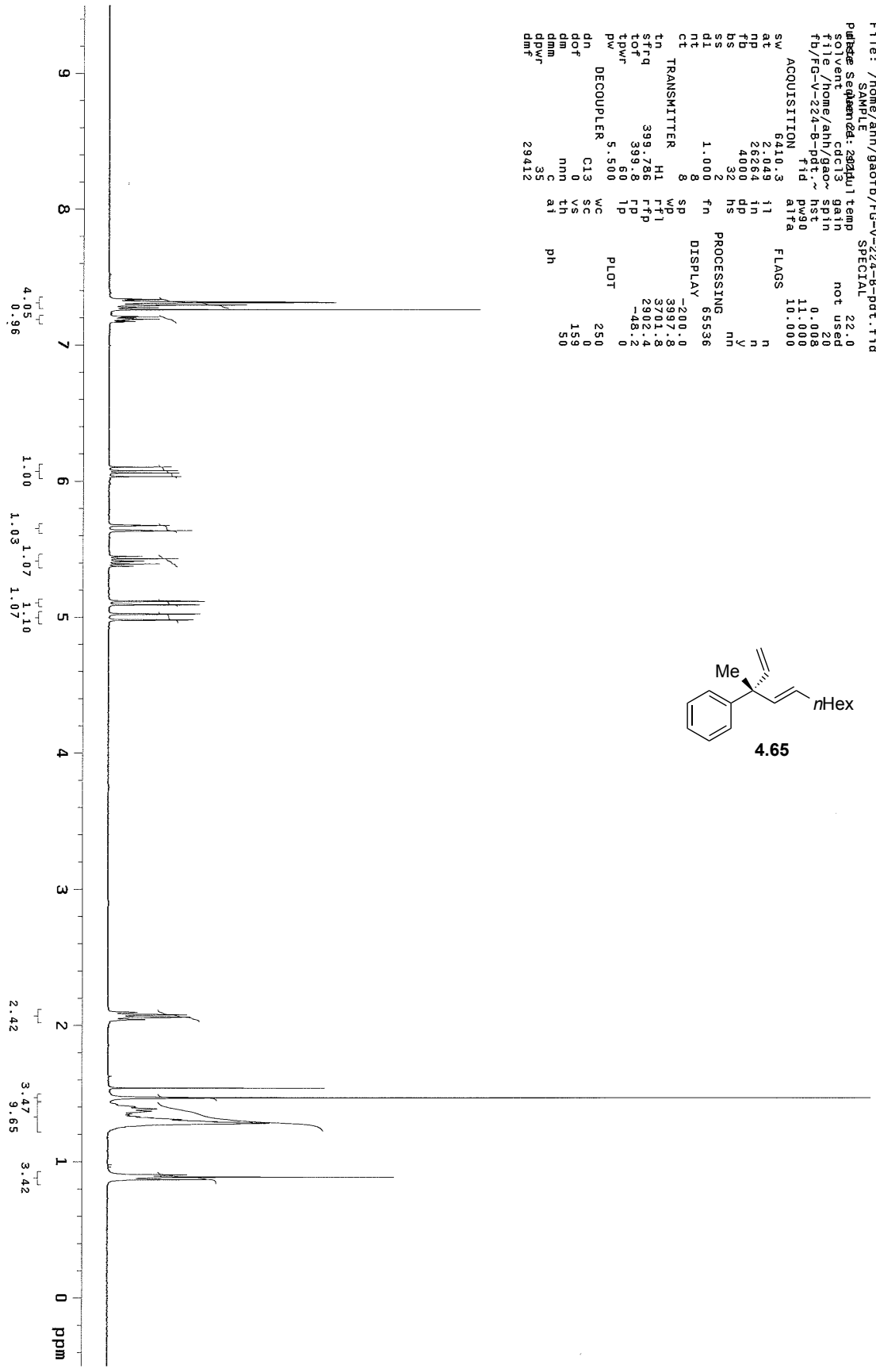
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Solvent: chloroform-d
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solvent cdcl3
file /home/ahh/gao~
fb/FG-V-224-B-pdt.~
ACQUISITION
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at 2.049
np 26264
fb 4000
bs 32
ss 2
d1 1.000
nt 8
ct 8
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
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dm nnn
dmm c
dpwr 35
dmf 29412
temp 22.0
gain not used
spin 20
hst 0.008
pw90 11.000
alfa 10.000
FLAGS
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n
y
nn
PROCESSING
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DISPLAY
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3701.8
2902.4
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0
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sc 0
vs 159
th 50
PLOT
ph
at
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nHex
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4.05
0.96
1.00
1.03
1.07
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2
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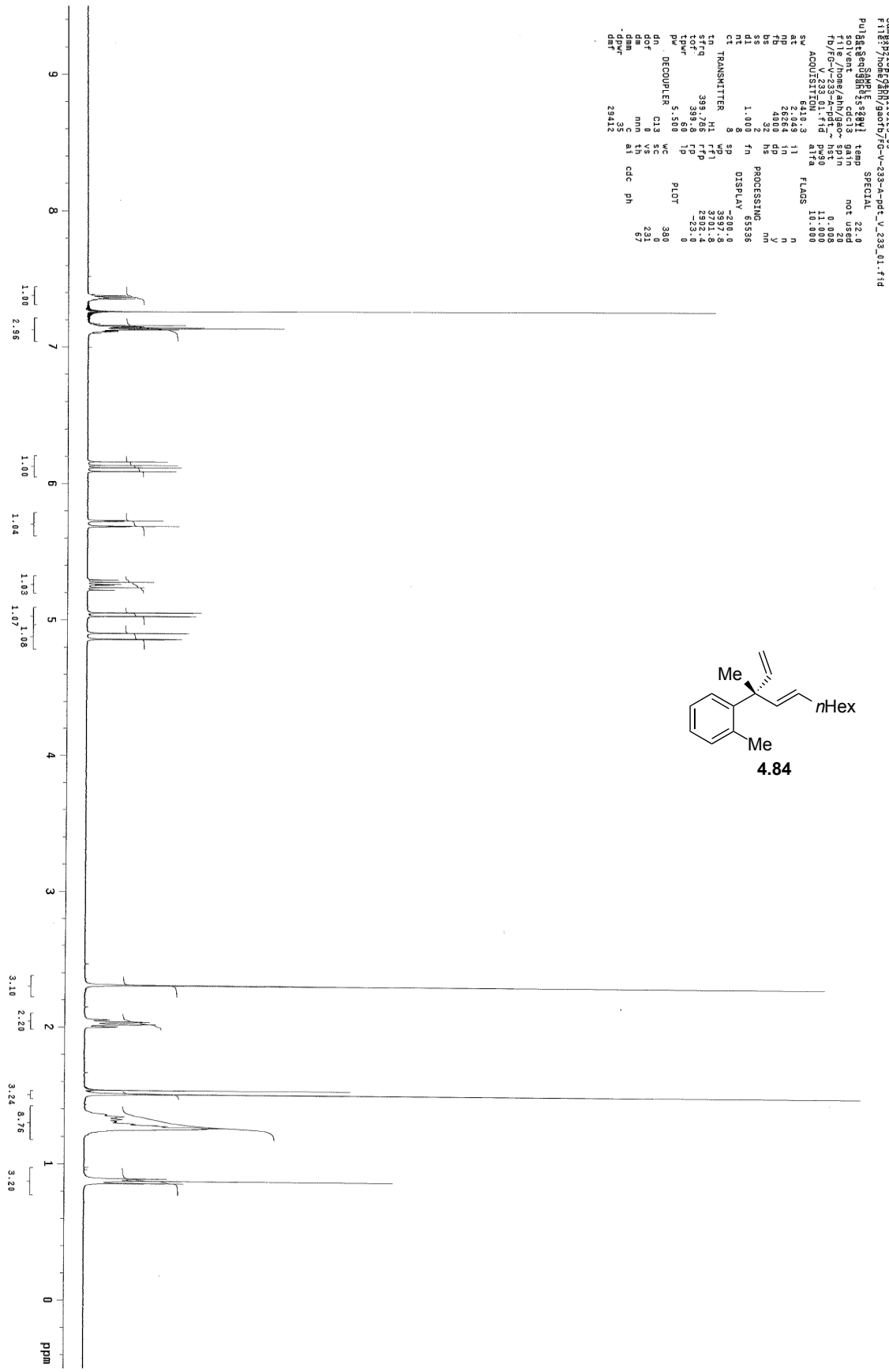
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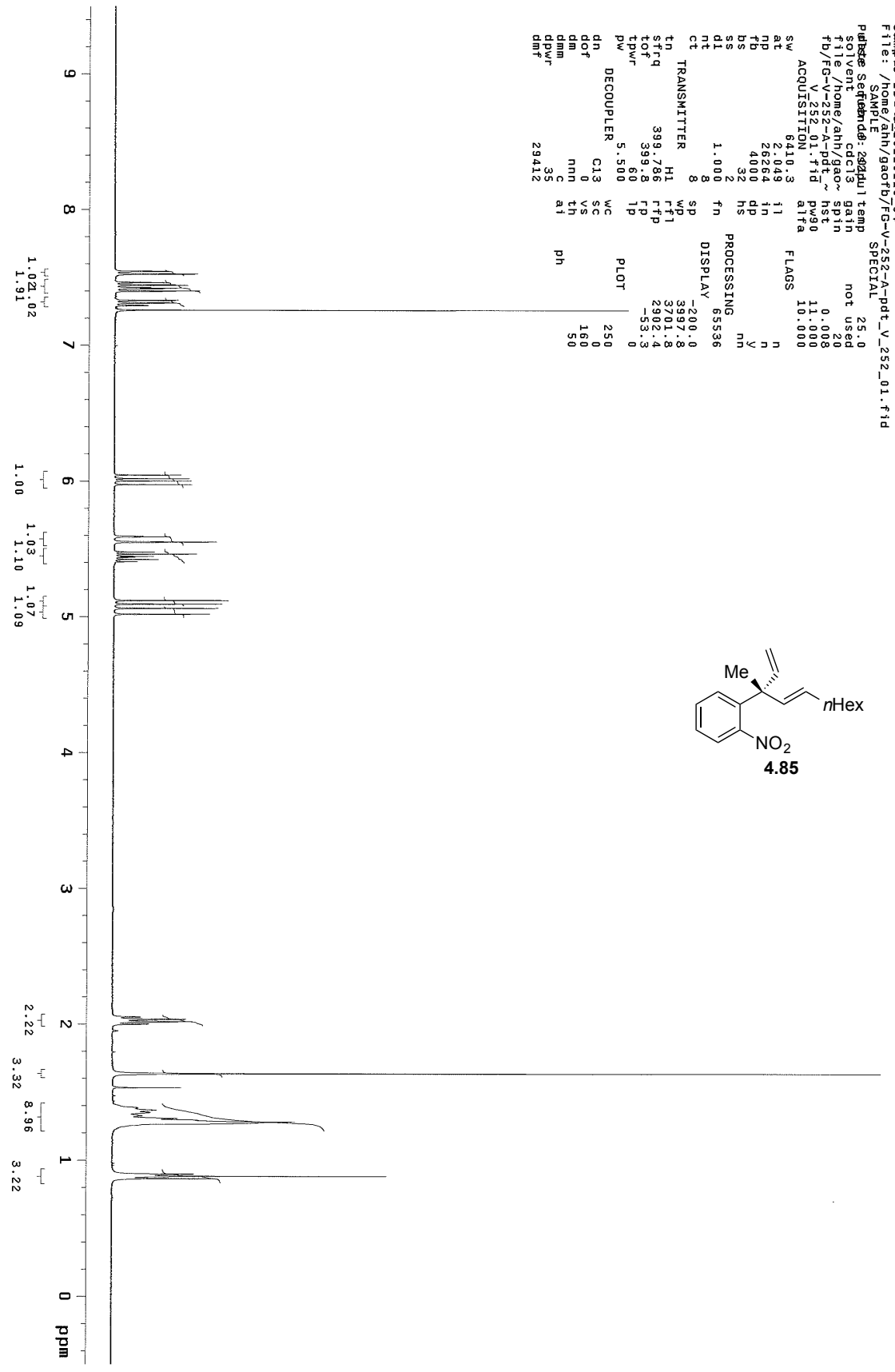
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Solvent: cdcl3
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np 26264
fb 4000
bs 32
ss 2
d1 1.000
nt 8
ct 8
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 60
pw 5.500
DECOUPLER
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temp 25.0
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hs nn
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rfl 3701.8
rfp 2902.4
rp -53.3
lp 0
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sc 0
vs 160
th 50
ai
ph
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nHex
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8
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6
5
4
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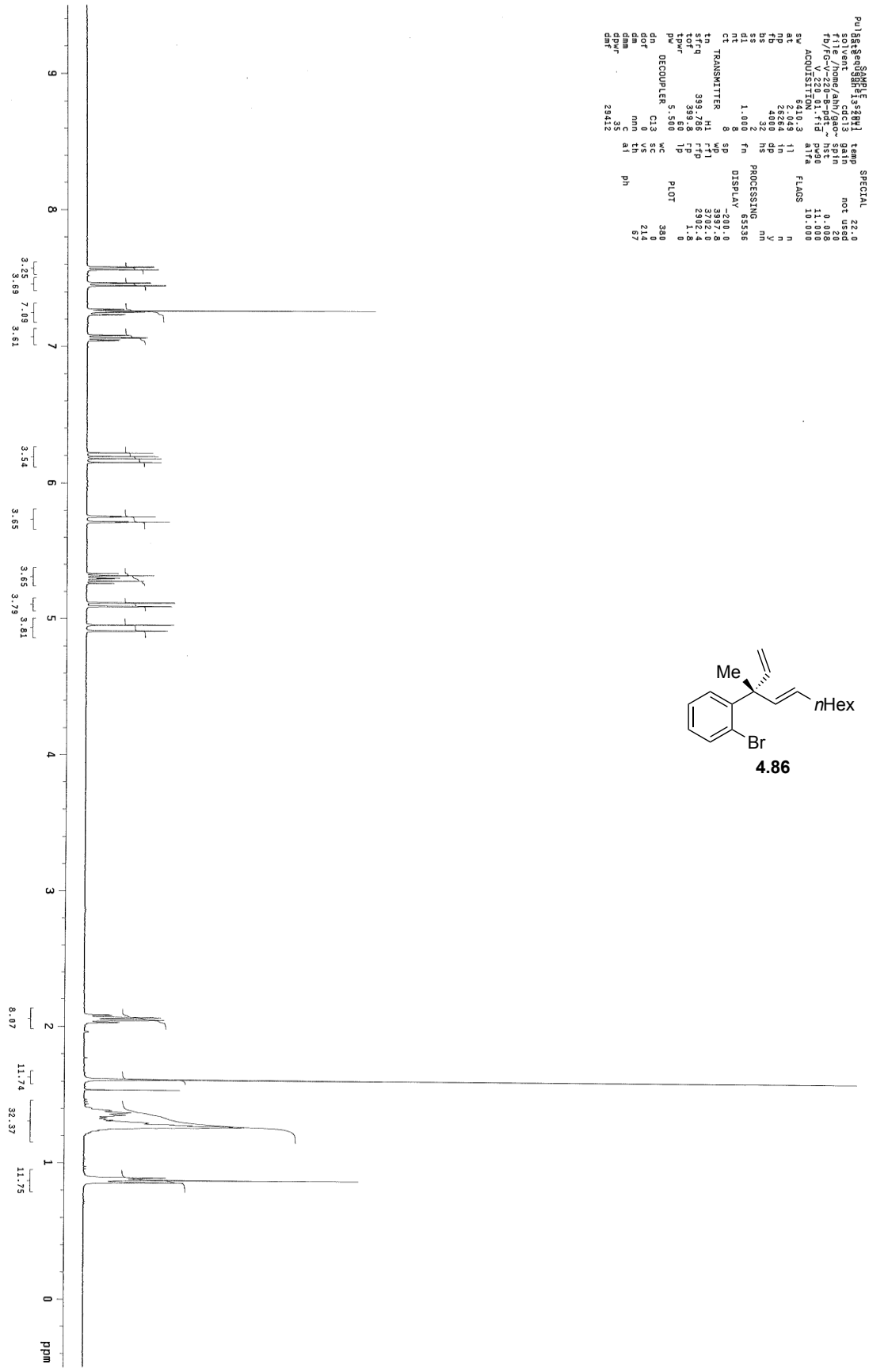
3.22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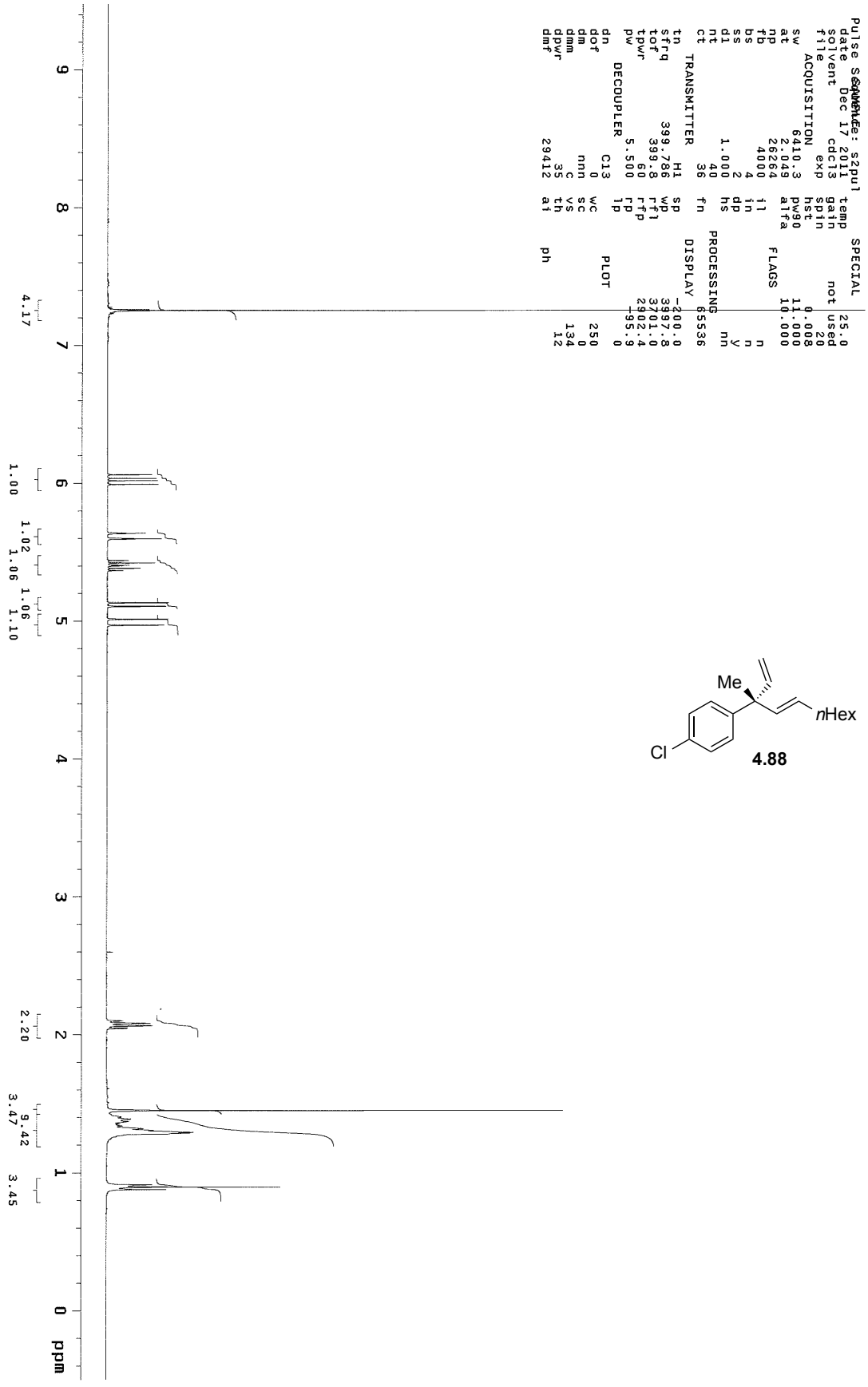
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date Dec 17 2011
solvent cdcl3
file exp
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nt 40
ct 36
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tof 399.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
temp
gain
spin
hst
pw90
alfa
FLAGS
il
in
dp
hs
fn
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lb
wc
sc
vs
th
ai
ph
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20
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11.000
10.000
n
n
y
nn
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3997.8
3701.0
2402.4
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1.06
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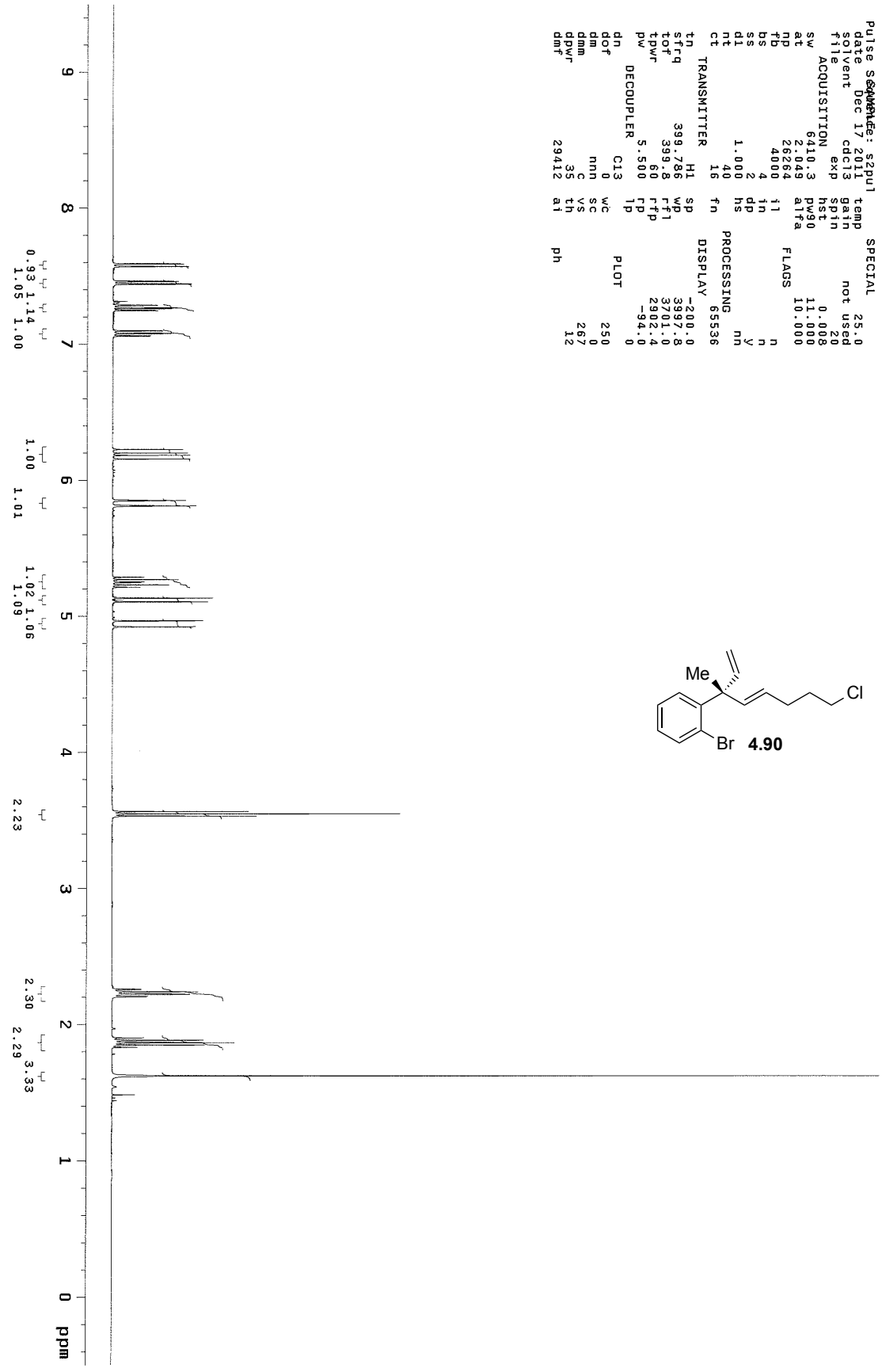
0
ppm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date Dec 17 2011
solvent cdcl3
file exp
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np 26264
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ss 2
d1 1.000
nt 40
ct 16
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tof 399.8
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pw 5.500
DECOUPLER
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dp y
hs nn
PROCESSING
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DISPLAY
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rfl 3701.0
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rp -94.0
lp 0
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sc 0
vs 267
th 12
ai
ph
Me
Cl
Br
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9
8
7
6
5
4
3
2
1
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ppm
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1.00
1.01
1.02 1.06
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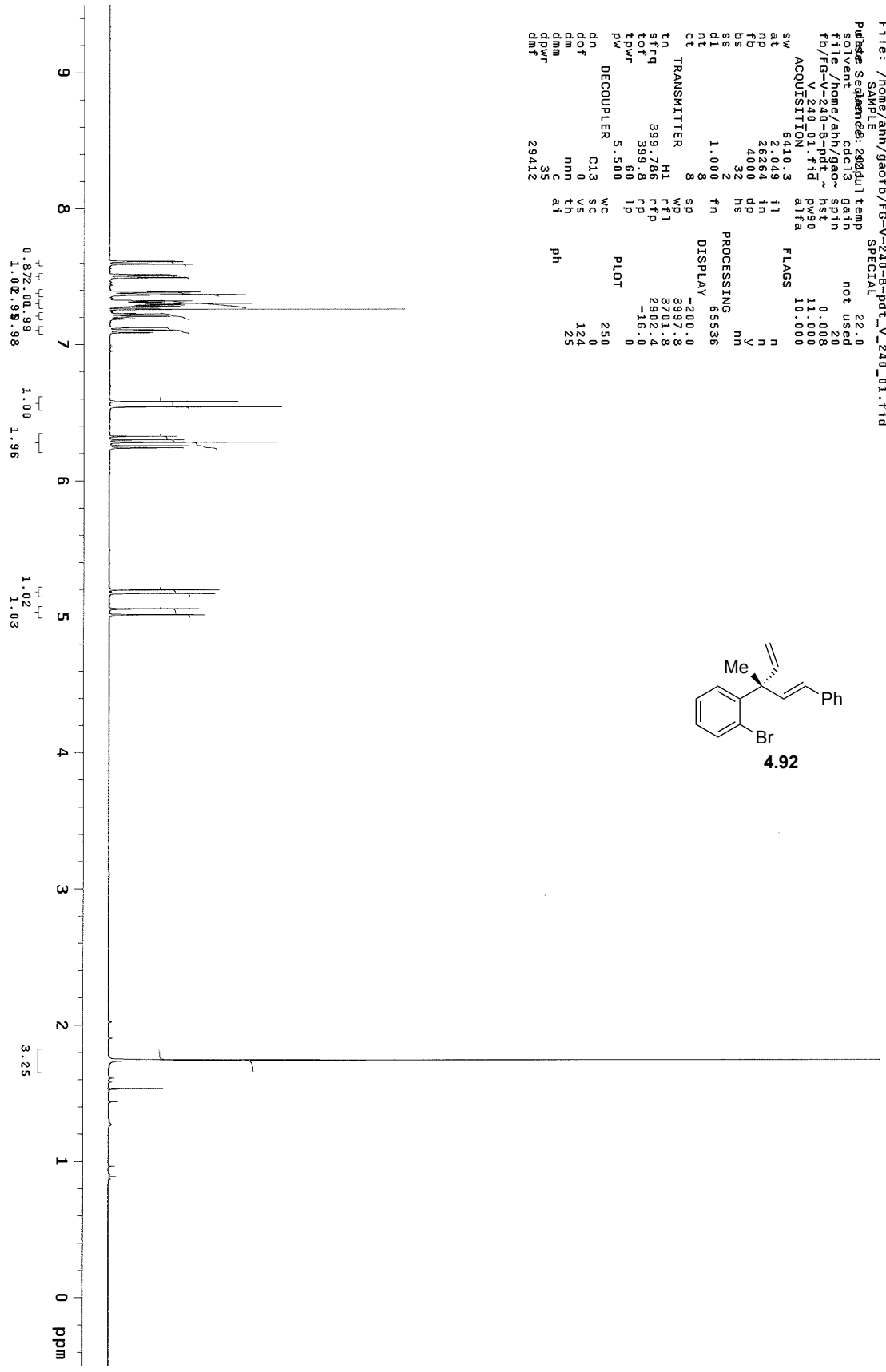
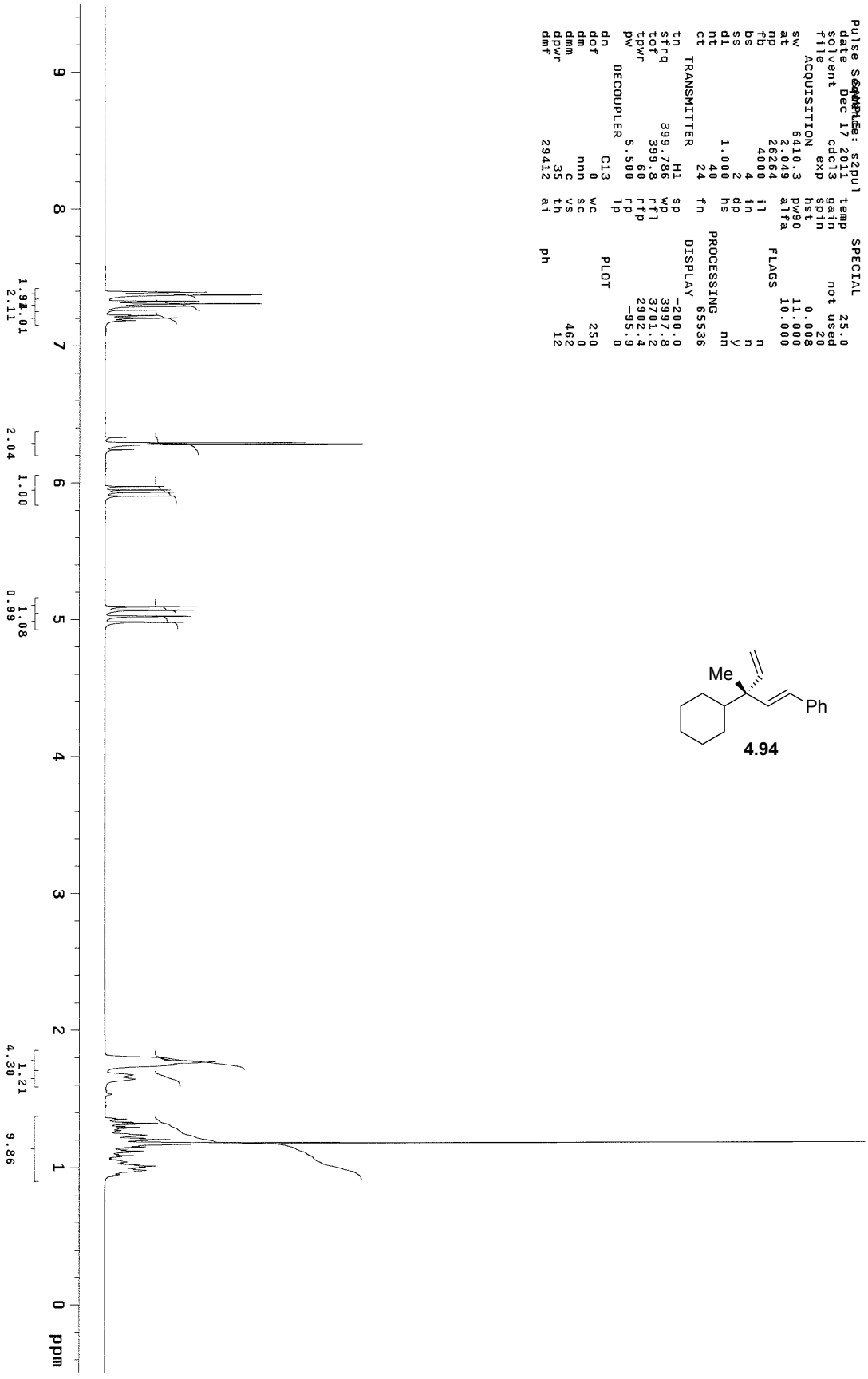
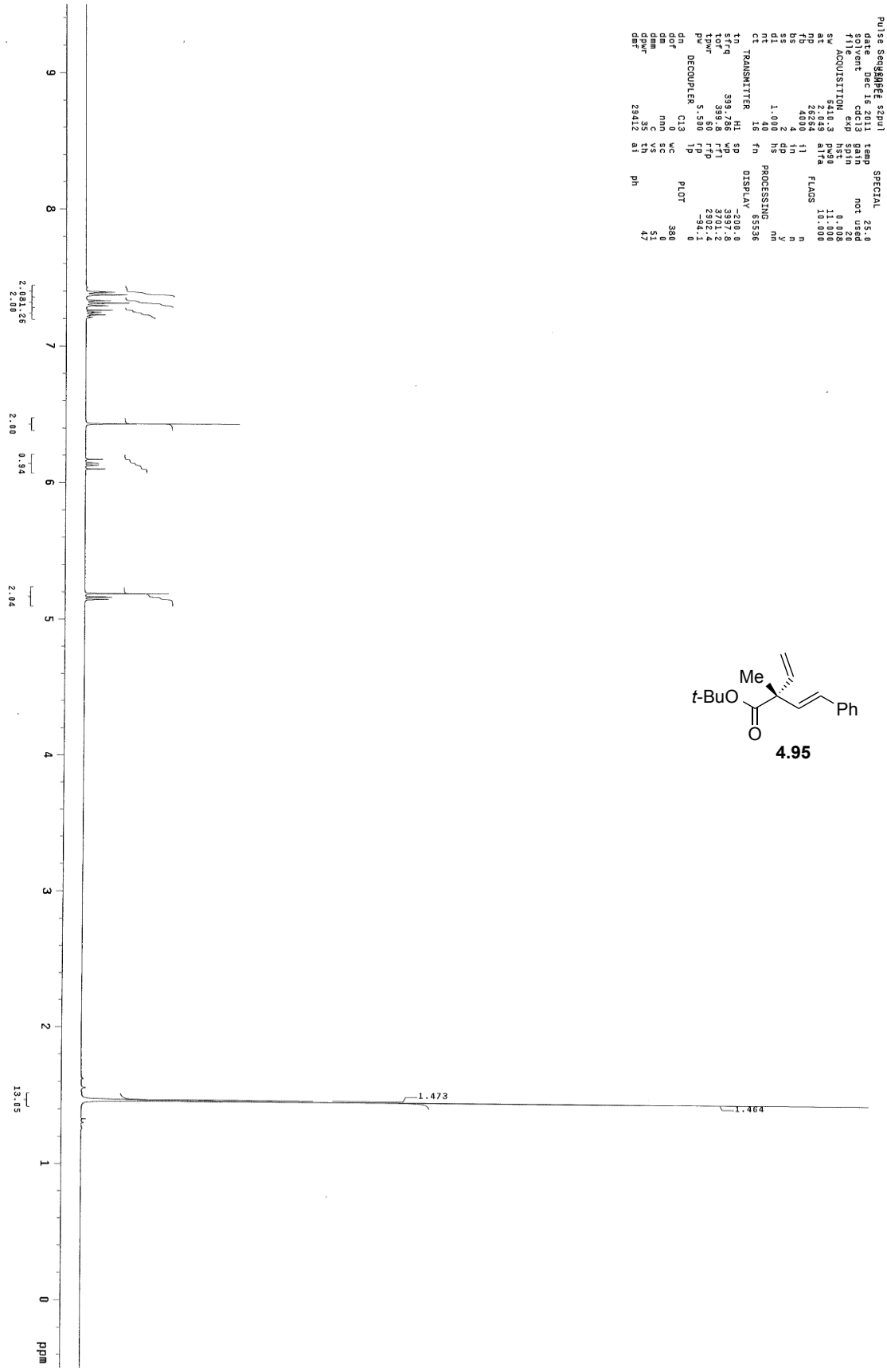
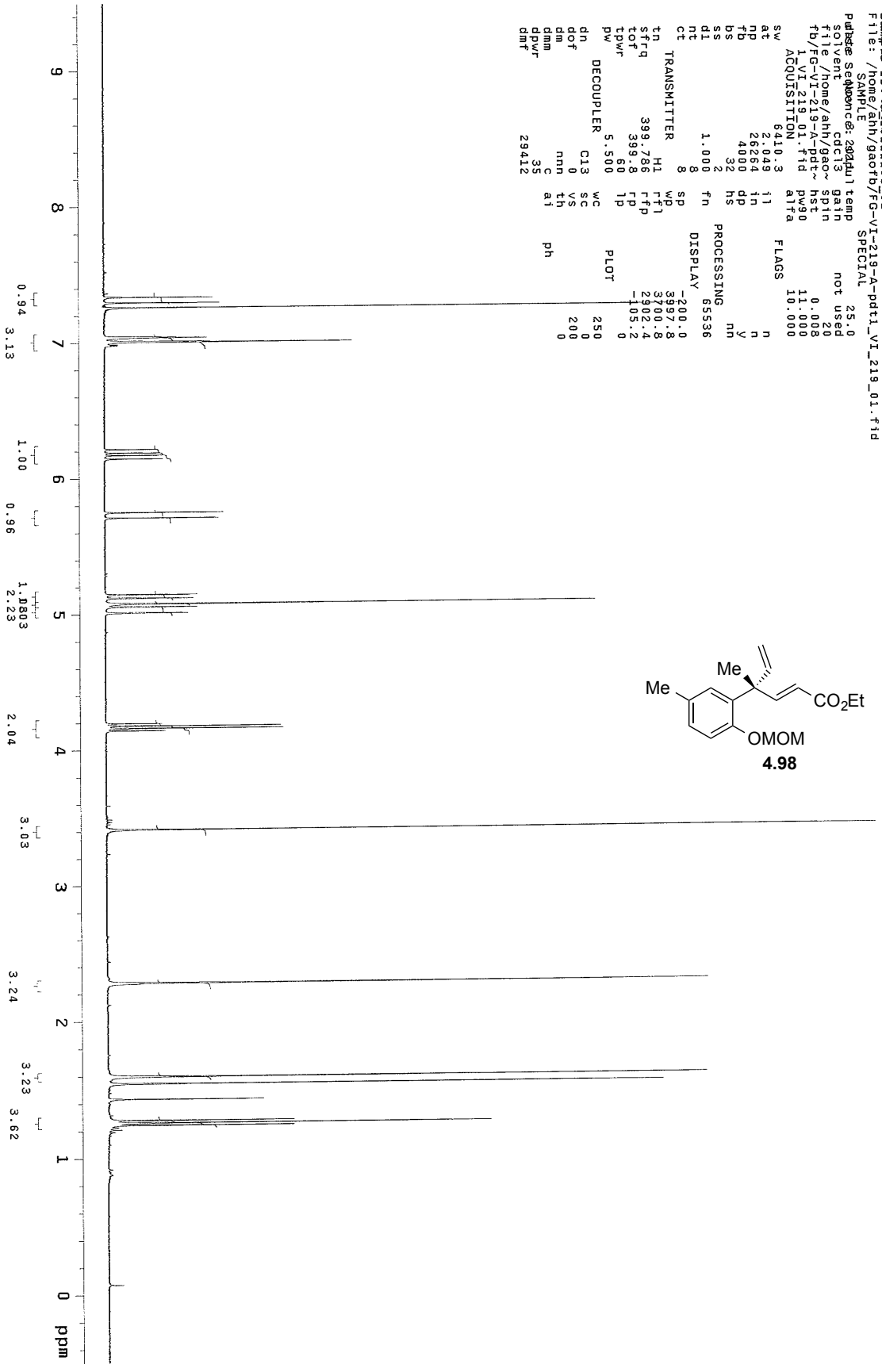
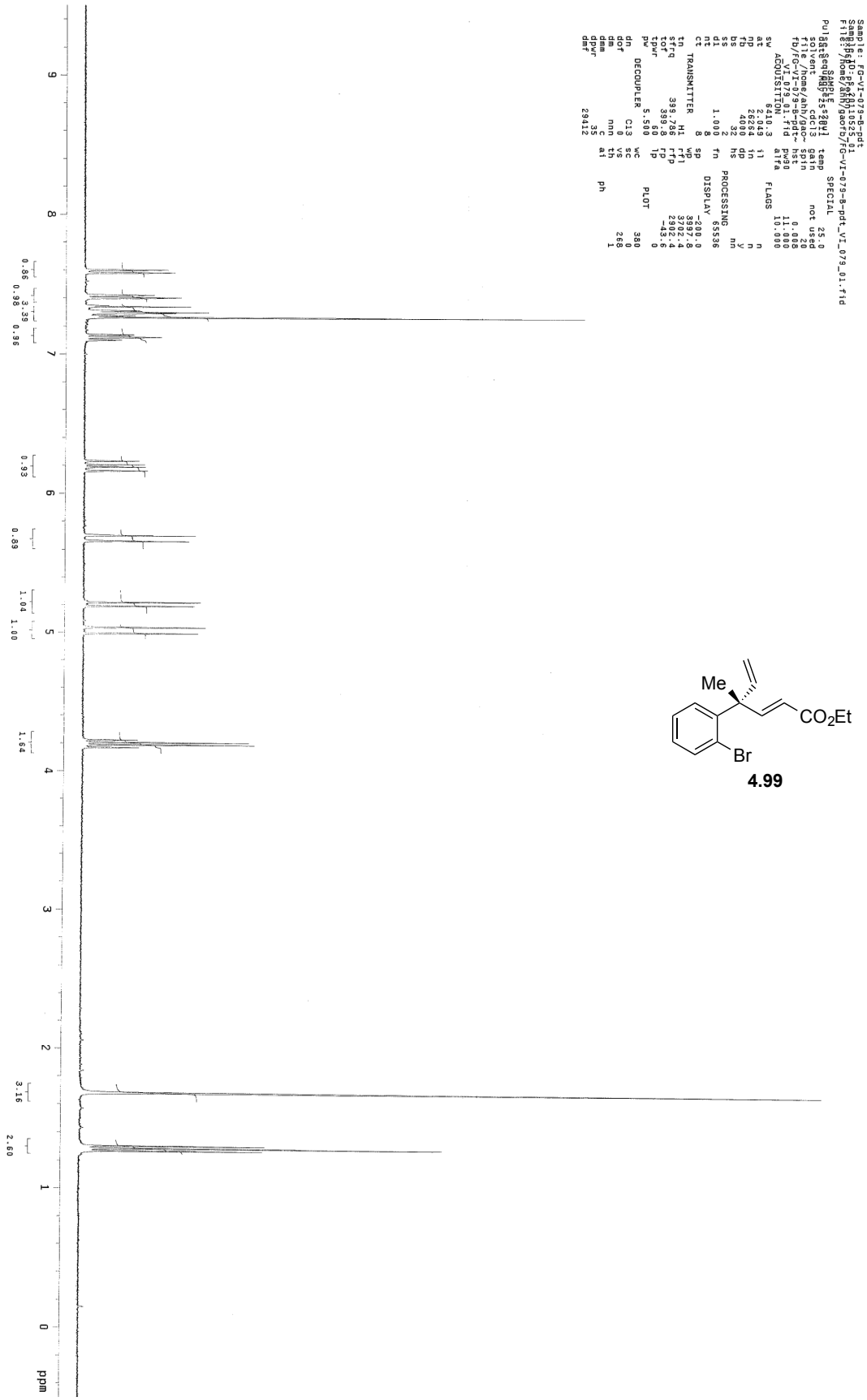
2.29
3.33

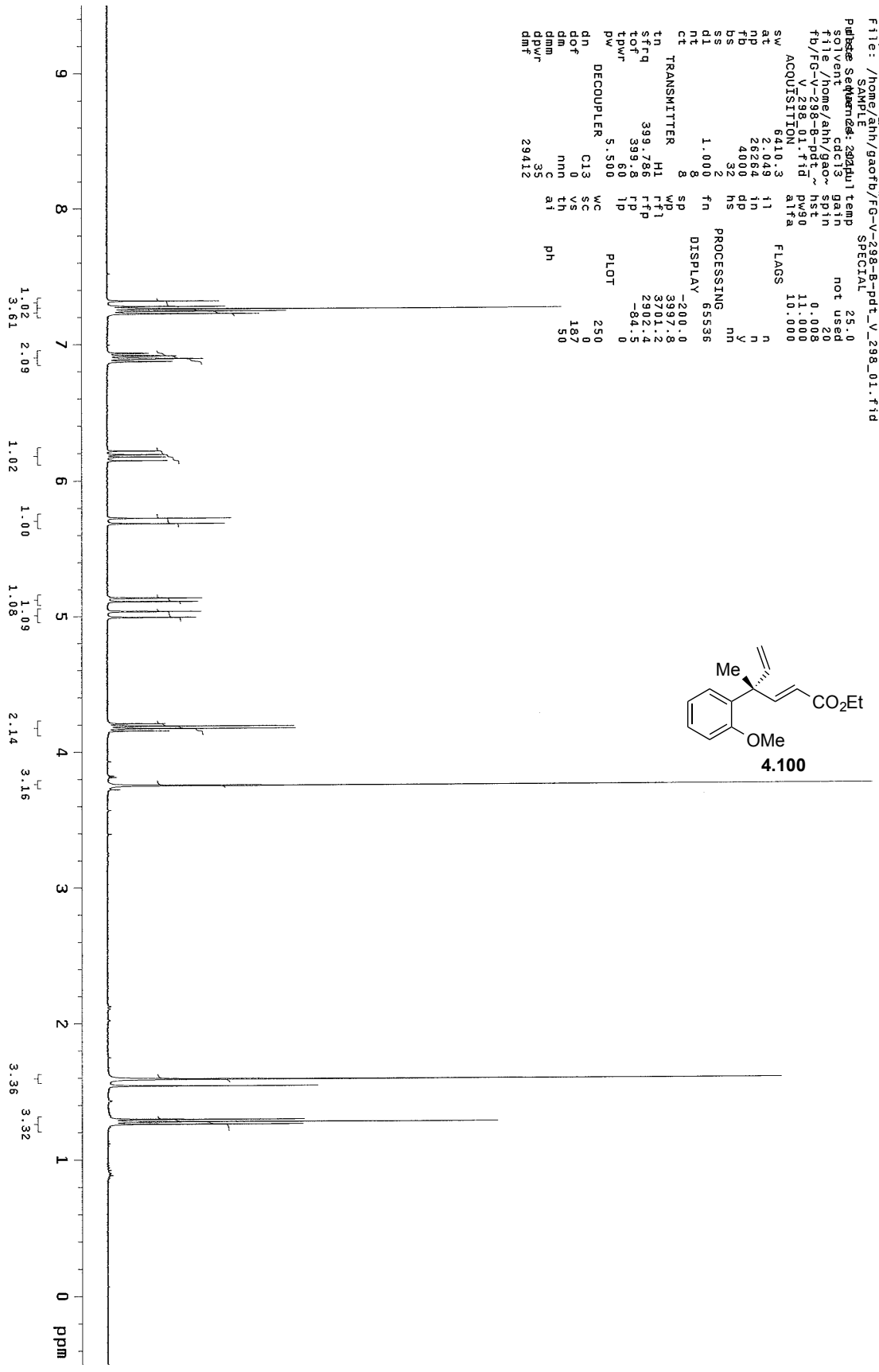

Sample: FG-V-240-B-pdt-1H
Sample Description: Proton 20110128_11
File: /home/anh/gaofb/FG-V-240-B-pdt_V_240_01.fid
SAMPLE
Pulse Sequence: zg30 SPECIAL
solvent cdcl3
file /home/anh/gao~ spin not used
fb/FG-V-240-B-pdt_~ hst 20
V_240_01.fid pw90 0.008
ACQUISITION alfa 11.000
6410.3 FLAGS 10.000
sw 2.049 il n
at 26264 in n
np 4000 dp y
fb 32 hs nn
bs 2 PROCESSING
ss 1.000 fn 65536
d1 8 DISPLAY
nt 8 sp -200.0
ct TRANSMITTER wp 3997.8
tn H1 rfl 3701.8
sfrq 399.786 rfp 2902.4
tof 399.8 rp -16.0
tpwr 60 lp 0
pw 5.500 PLOT
DECOUPLER wc 250
dn C13 sc 0
dof 0 vs 124
dm nnn th 25
dmm c ai
dpwr 35 ph
dmf 29412
0.87
2.00
1.99
1.02
2.99
1.98
1.00
1.96
1.02
1.03
3.25
9
8
7
6
5
4
3
2
1
0
ppm
Me
Ph
Br
4.92

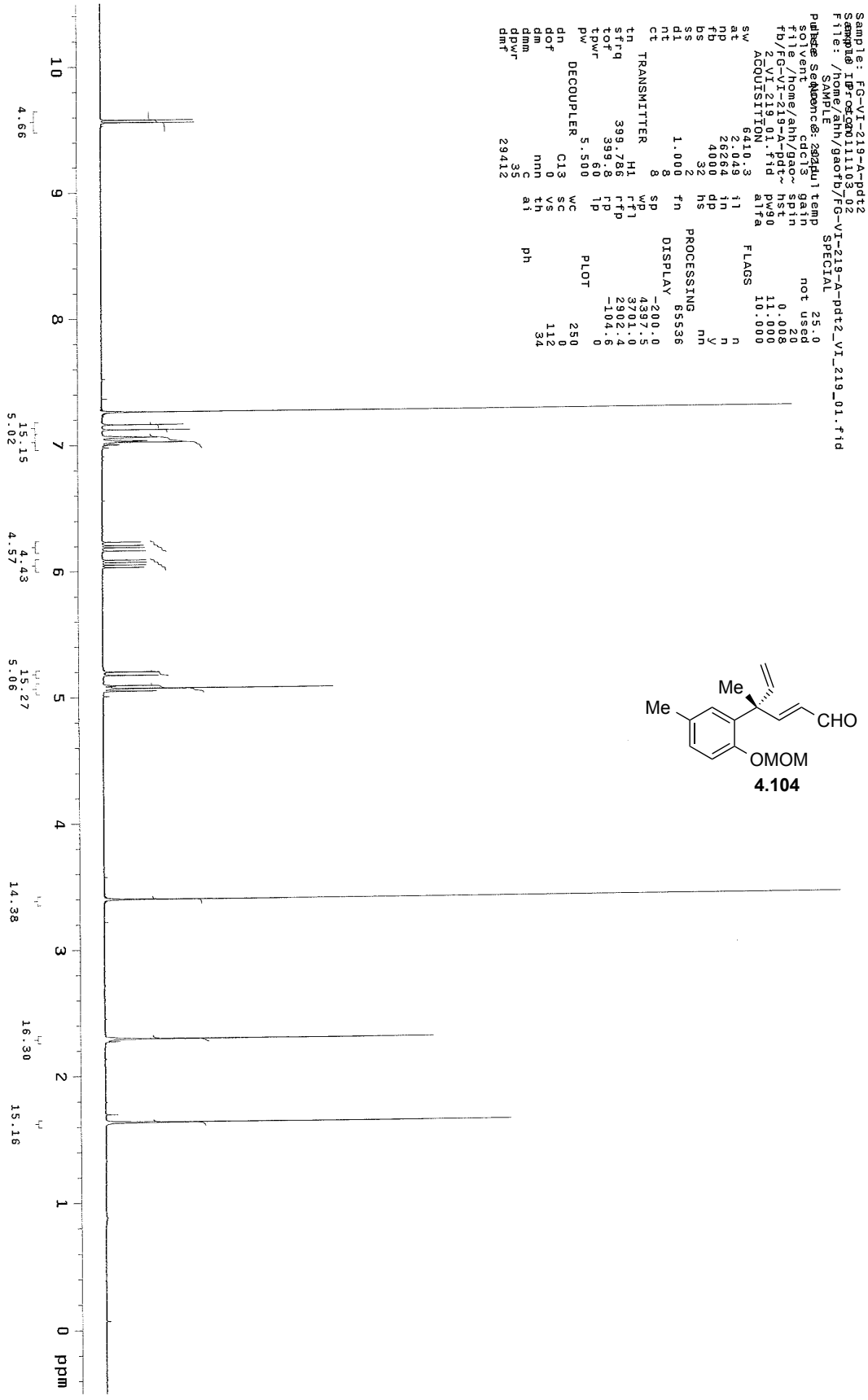

Sample: FG-V-253-B-pdt
Exp: 2 exp proton
Pulse Sequence: s2pul SPECIAL
date Dec 17 2011 temp 25.0
solvent cdcl3 gain not used
file exp spin 20
ACQUISITION hst 0.008
sw 6410.3 pw90 11.000
at 2.049 alfa 10.000
np 26264 FLAGS
fb 4000 il n
bs 4 in n
ss 2 dp y
d1 1.000 hs nn
nt 40 PROCESSING
ct 24 fn 65536
TRANSMITTER DISPLAY
tn H1 sp -200.0
sfrq 399.786 wp 3997.8
tof 399.8 rfl 3701.2
tpwr 60 rfp 2902.4
pw 5.500 rp -95.9
DECOUPLER lp 0
dn C13 PLOT
dof 0 wc 250
dm nnn sc 0
dmm c vs 462
dpwr 35 th 12
dmf 29412 ai
ph
Me
Ph
4.94
1.94
1.01
2.11
2.04
1.00
1.08
0.99
1.21
4.30
9.86
9
8
7
6
5
4
3
2
1
0
ppm

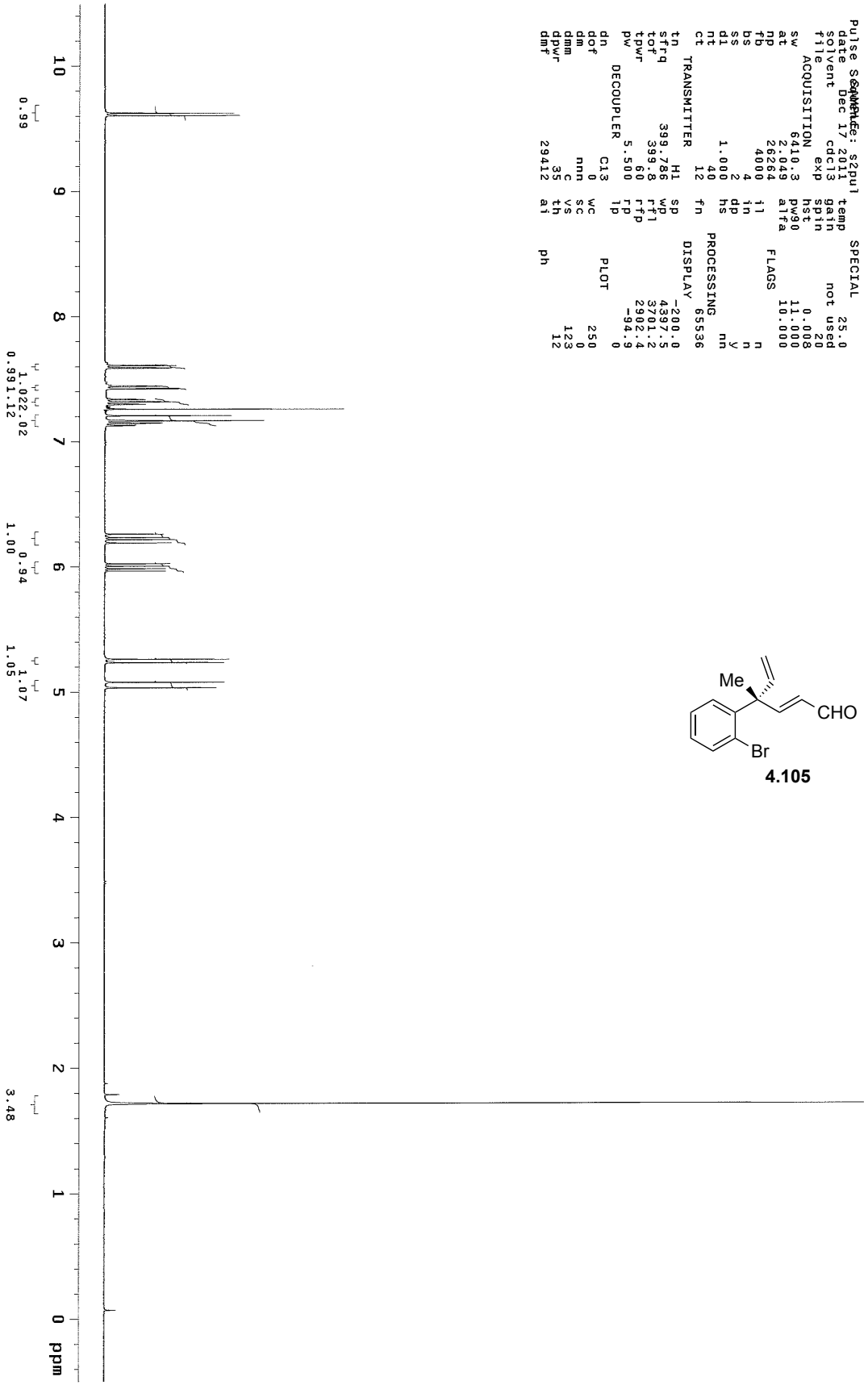

Sample: FG-V-255-B-pdt
Exp: 1HPproton
Pulse Sequence: s2pul
solvent
file
ACQUISITION
sw
at
np
fb
bs
ss
d1
nt
ct
TRANSMITTER
tn
sfrq
tof
tpwr
pw
DECOUPLER
dn
dof
dm
dmm
dmf
dpwr
PLOT
SPECIAL
FLAGS
PROCESSING
DISPLAY
ppm
2.081.26
2.00
0.94
2.04
13.05
1.473
1.464
Me
t-BuO
Ph
O
4.95

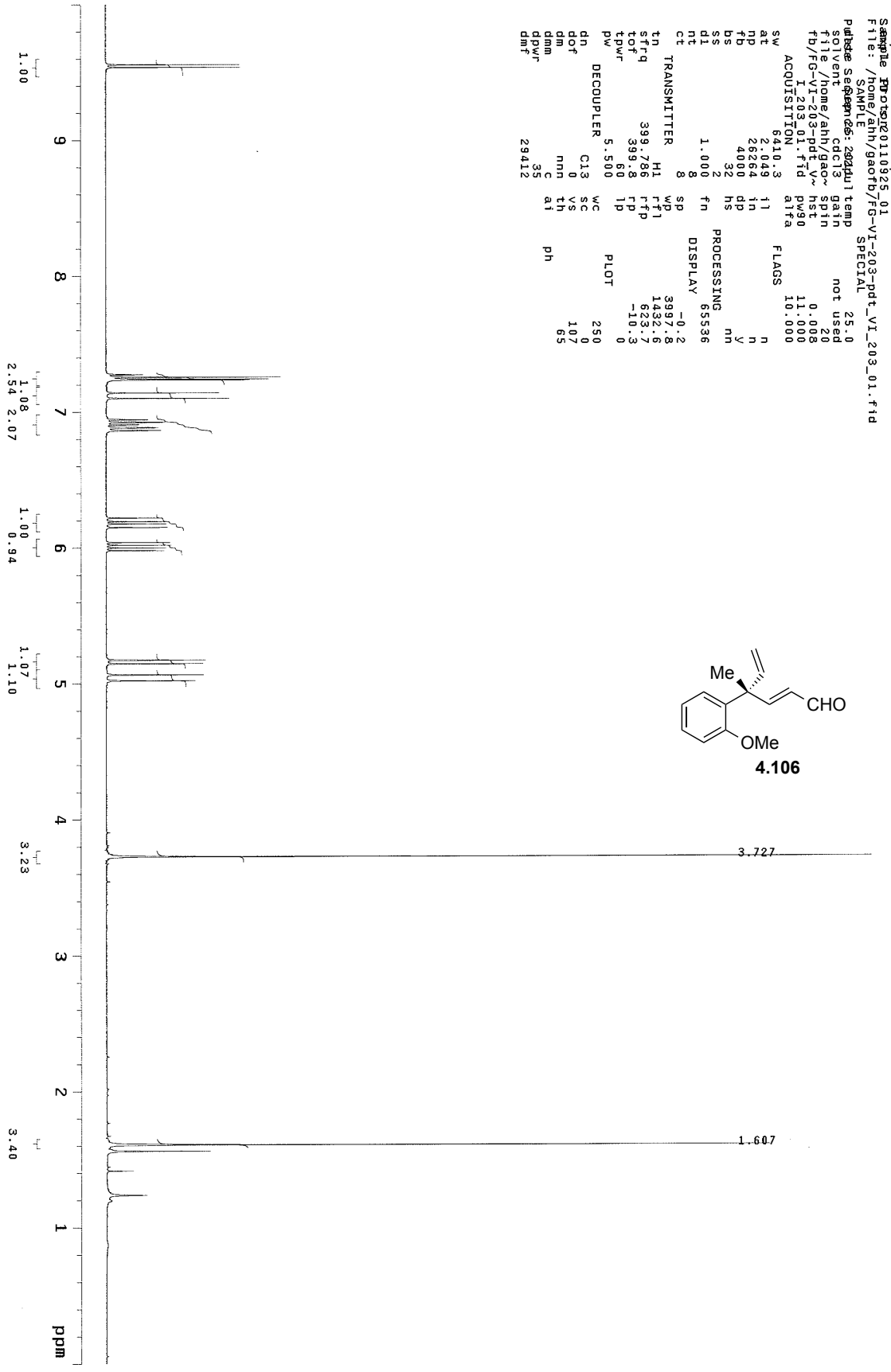

Me
Me
CO2Et
OMOM
4.98
ppm
0.94
3.13
1.00
0.96
1.88
2.23
2.04
3.03
3.24
3.23
3.62

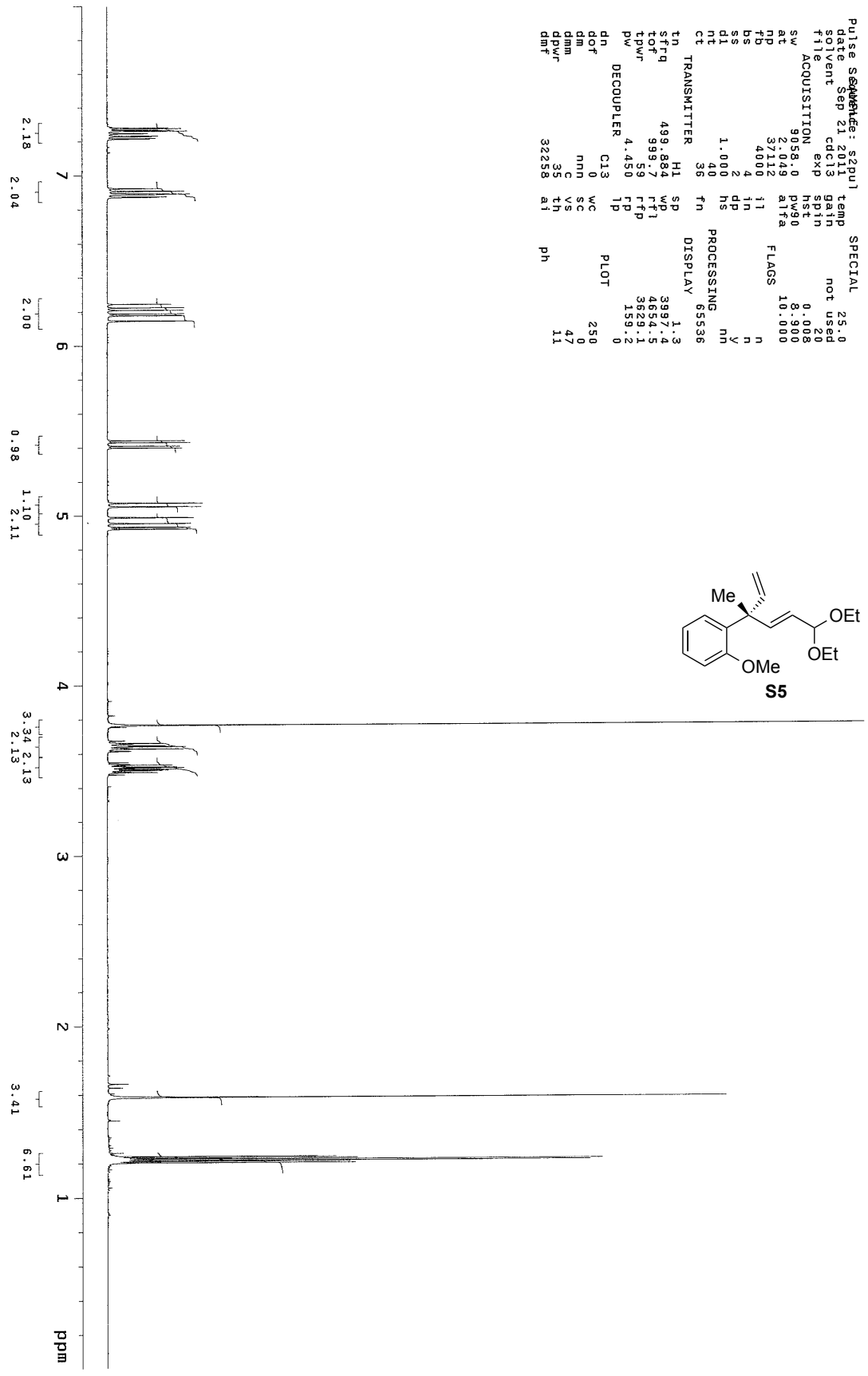

Me
CO2Et
Br
4.99
ppm

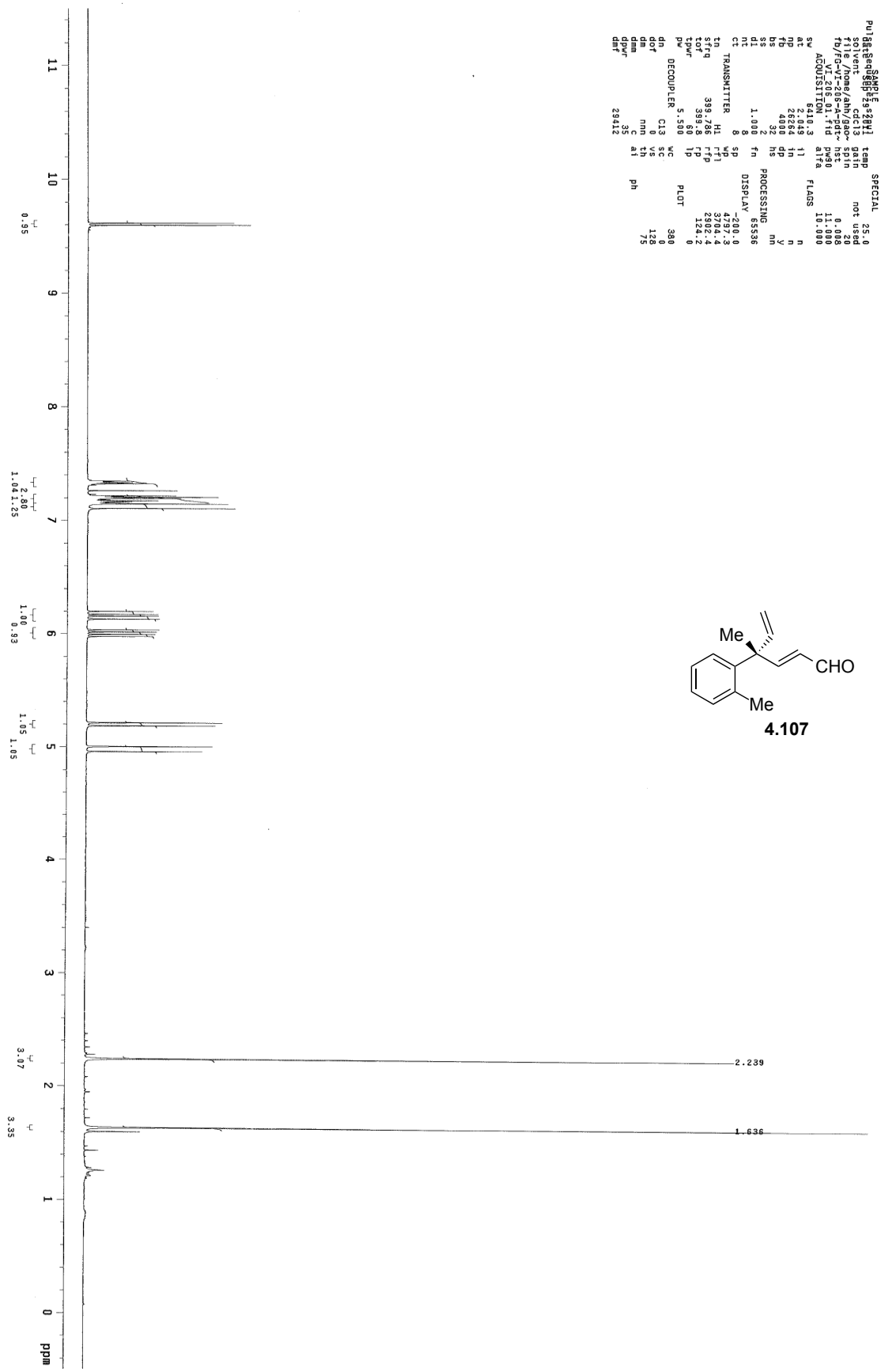

Me
CO2Et
OMe
4.100
ppm
0
1
2
3
4
5
6
7
8
9
3.61
1.02
2.09
1.02
1.00
1.08
1.09
2.14
3.16
3.36
3.32

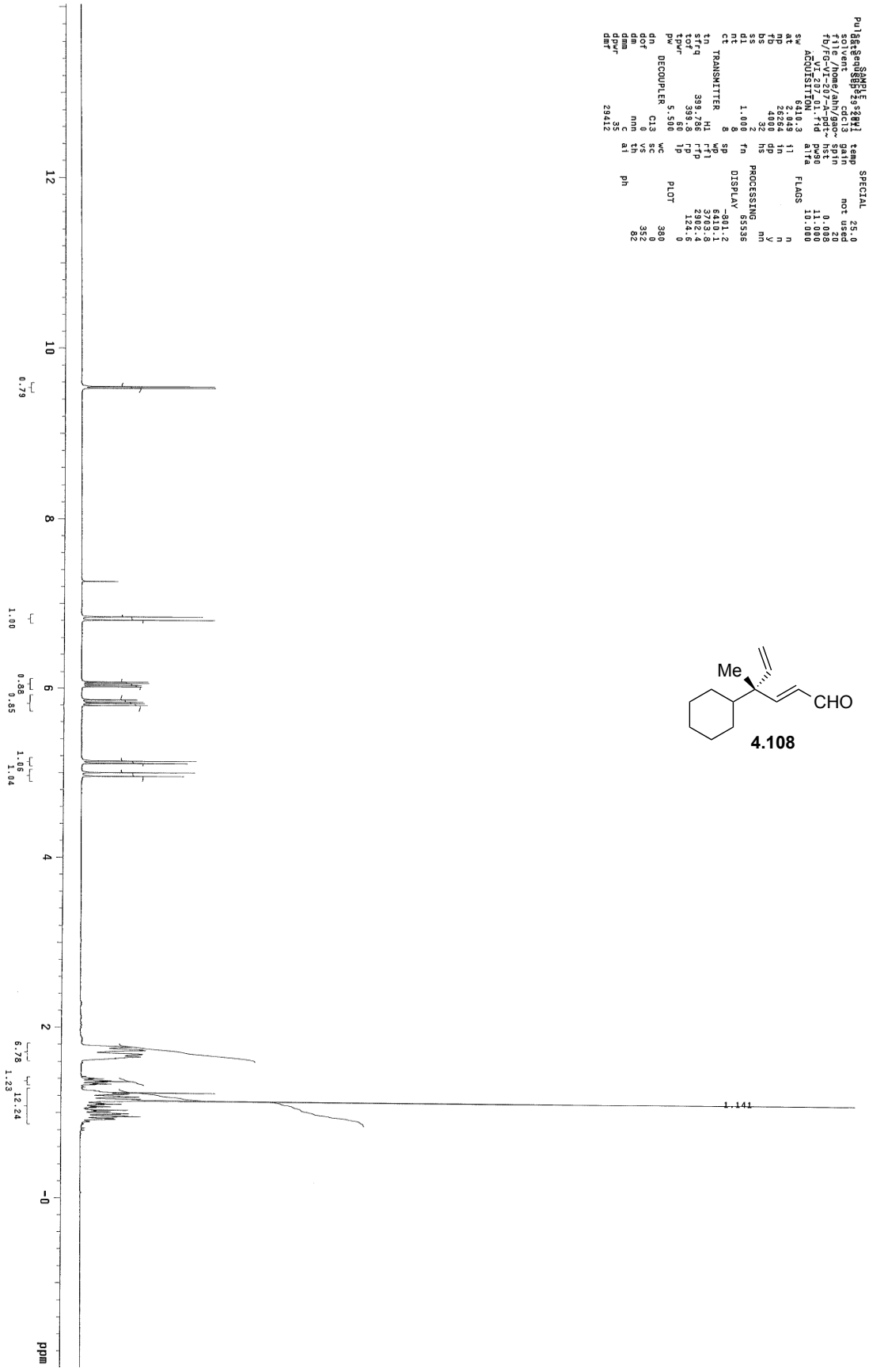

Sample: FG-VI-219-A-pdt2
Sample IPrSeCO111103_02
File: /home/ahh/gaofb/FG-VI-219-A-pdt2_VI_219_01.fid
SAMPLE
SPECIAL
solvent cdcl3
file /home/ahh/gao~
fb/FG-VI-219-A-pdt~
2_VI_219_01.fid
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4000
bs 32
ss 2
d1 1.000
nt 8
ct 8
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
temp 25.0
gain not used
spin 20
hst 0.008
pw90 11.000
alfa 10.000
FLAGS
n
y
nn
PROCESSING
65536
DISPLAY
-200.0
4397.5
3701.0
2902.4
-104.6
0
PLOT
250
0
112
34
ph
4.66
5.02
15.15
4.57
4.43
5.06
15.27
14.38
16.30
15.16
Me
Me
CHO
OMOM
4.104

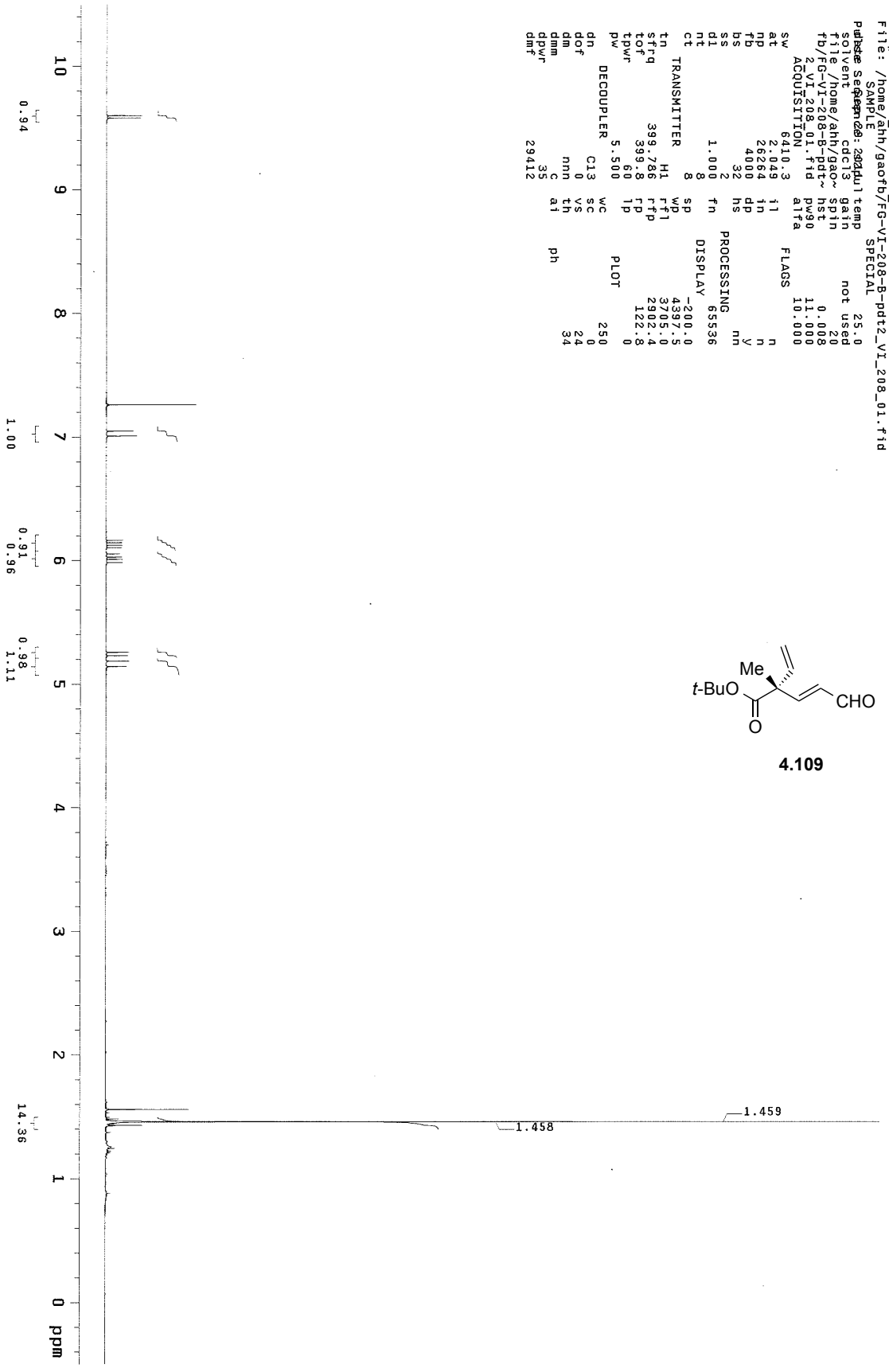

Sample: FG-V-288-pdt-1H
Exp2 exp1oton
Pulse Sequence: s2pul
date Dec 17 2011
solvent cdcl3
file exp
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4000
bs 4
ss 2
d1 1.000
nt 40
ct 12
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
temp
gain
spin
hst
pw90
alfa
FLAGS
il
in
dp
hs
fn
PROCESSING
sp
wp
rfl
rfp
rp
lp
PLOT
wc
sc
vs
th
ai
ph
SPECIAL
25.0
not used
20
0.008
11.000
10.000
n
n
y
nn
65536
DISPLAY
200.0
4397.5
3701.2
2902.4
-94.9
0
250
0
123
12
Me
CHO
Br
4.105
0.99
1.02
0.99
1.12
1.00
0.94
1.05
1.07
3.48
10
9
8
7
6
5
4
3
2
1
0 ppm

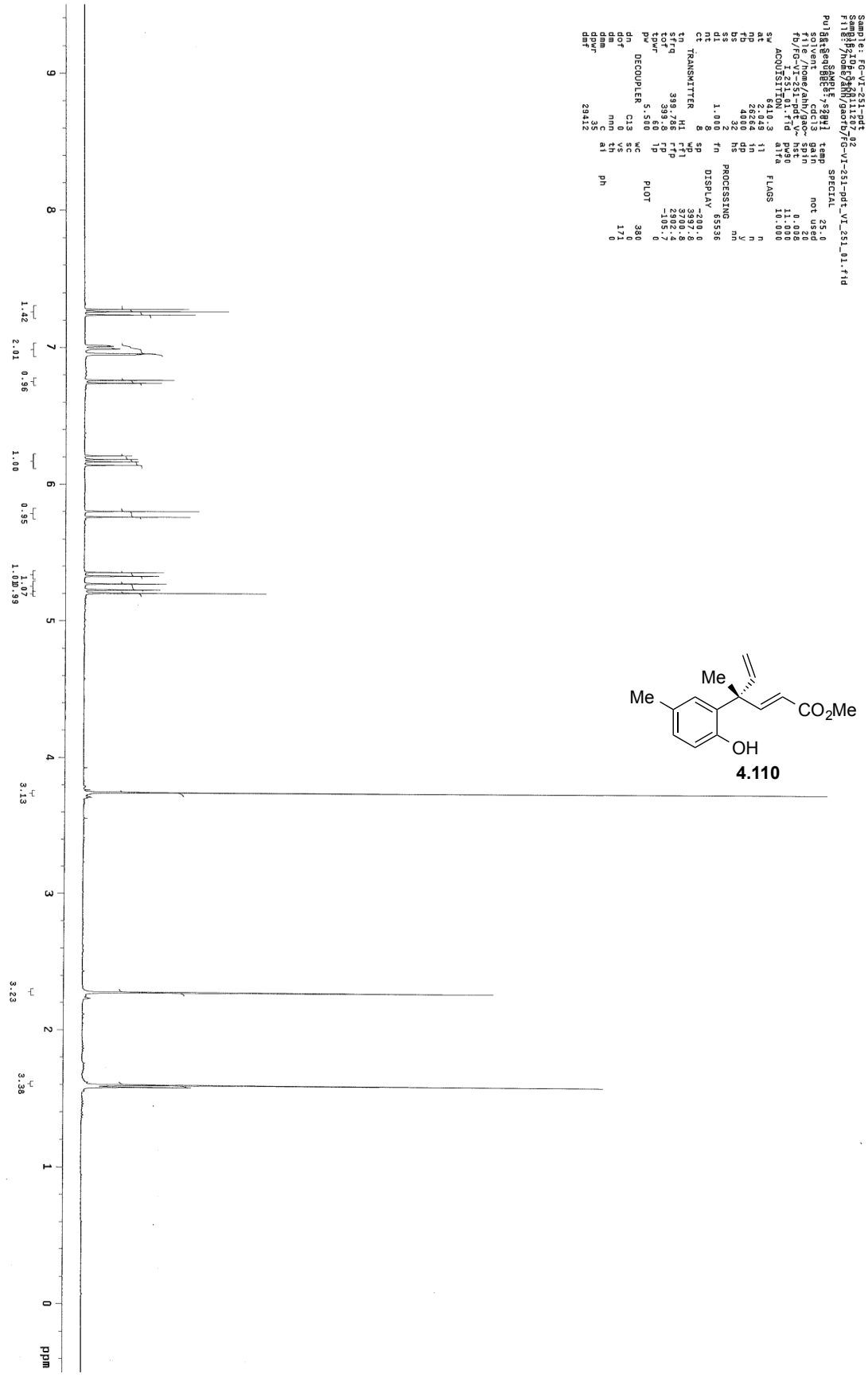

Sample: FG-VI-203-pdt
Sample ID: proton20110925_01
File: /home/ahh/gaofb/FG-VI-203-pdt_VI_203_01.fid
SAMPLE
SPECIAL
25.0
not used
20
0.008
11.000
10.000
FLAGS
n
n
y
nn
PROCESSING
65536
DISPLAY
-0.2
3997.6
1432.6
623.7
-10.3
0
PLOT
250
0
107
65
Me
CHO
OMe
4.106
3.727
1.607
1.00
1.08
2.54
2.07
1.00
0.94
1.07
1.10
3.23
3.40
ppm

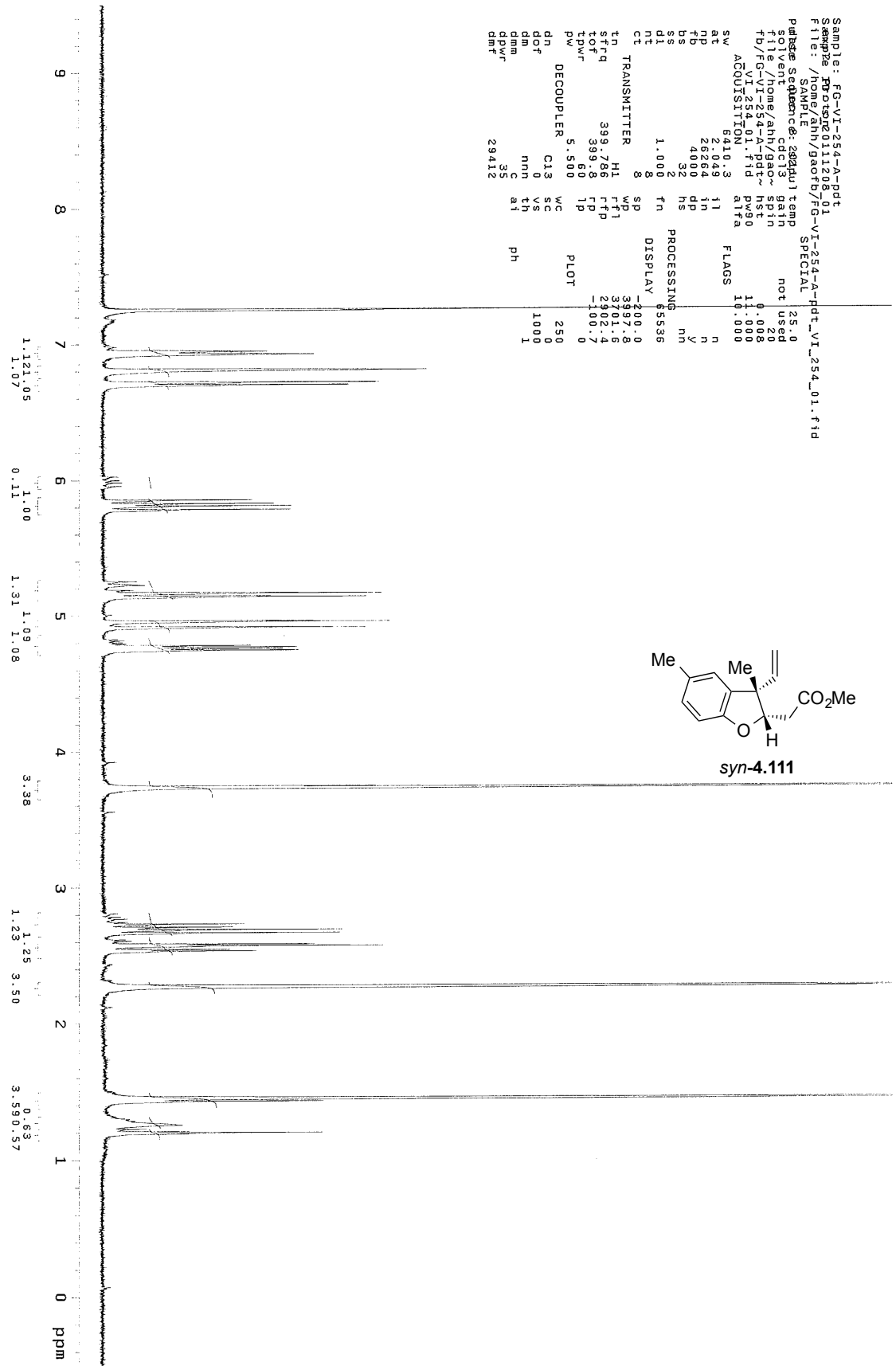

Sample: FG-VI-198-A-pdt2
Expt: exp1 proton
Pulse Sequence: s2pul SPECIAL
date Sep 21 2011 temp 25.0
solvent cdcl3 gain not used
file exp spin 20
ACQUISITION hst 0.008
sw 9058.0 pw90 8.900
at 2.049 alfa 10.000
np 37112 FLAGS
fb 4000 il n
bs 4 in n
ss 2 dp y
d1 1.000 hs nn
nt 40 PROCESSING
ct 36 fn 65536
TRANSMITTER DISPLAY
tn H1 sp 1.3
sfrq 499.884 wp 3997.4
tof 999.7 rfl 4654.5
tpwr 59 rfp 3629.1
pw 4.450 rp 159.2
DECOUPLER lp 0
dn C13 PLOT
dof 0 wc 250
dm nnn sc 0
dmm c vs 47
dpwr 35 th 11
dmf 32258 ai
ph
Me
OEt
OEt
OMe
S5
2.18
2.04
2.00
0.98
1.10
2.11
3.34
2.13
2.13
3.41
6.61
7
6
5
4
3
2
1
ppm

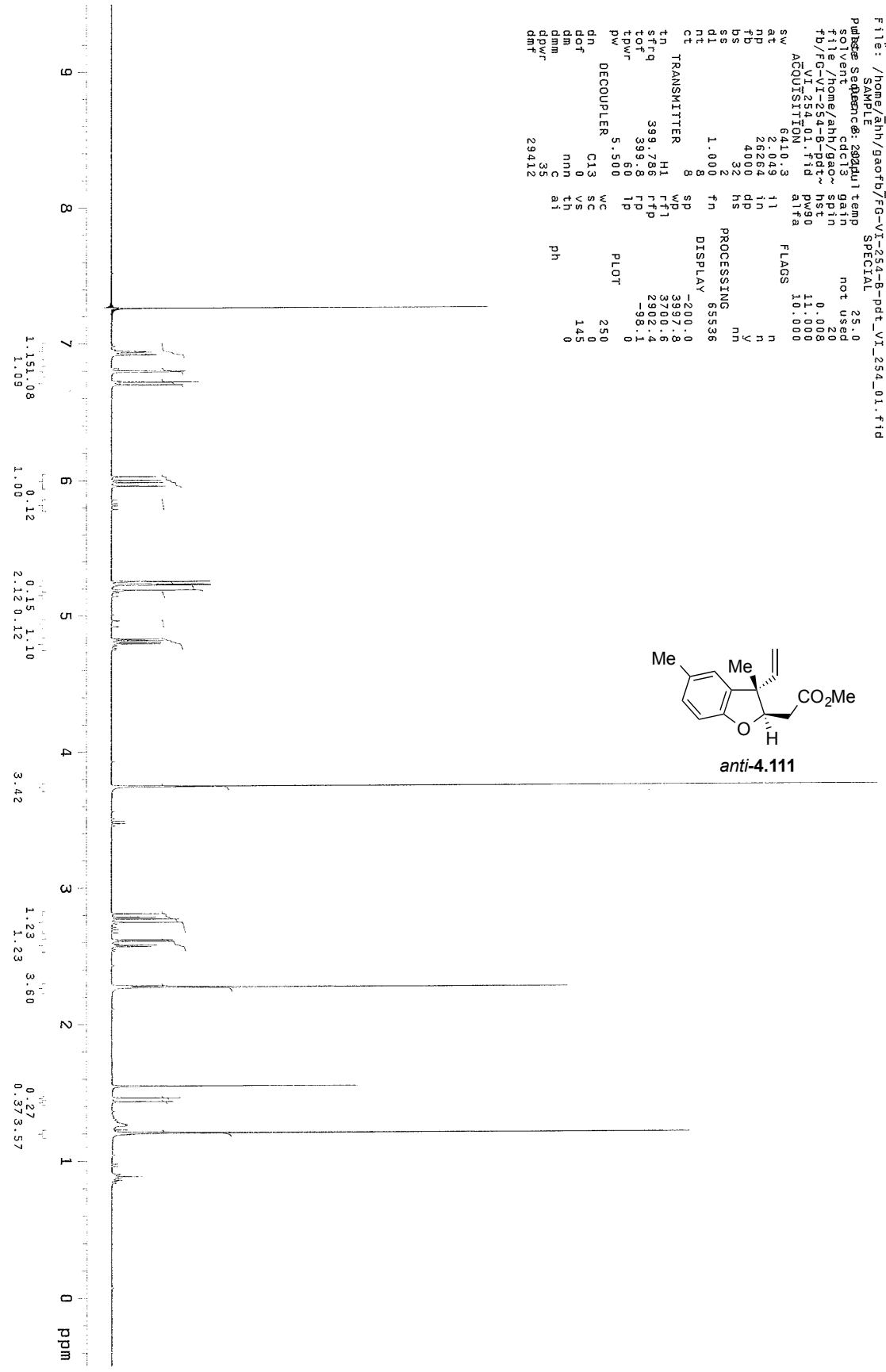

Sample: FG-VI-206-A-pdt
Solvent: cdcl3
File: /home/ahh/gaor0/FG-VI-206-A-pdt_VI_206_01.fid
Pulse Sequence: s2pul
SAMPLE
temp 25.0
gain SPECIAL
spin
hst not used
pw90 20
alfa 11.000
FLAGS 10.000
sw 4810.3
at 2.043
np 26264
fb 4000
bs 32
ss 2
d1 1.006
nt 8
ct 8
TRANSMITTER
tn H1
sfrq 399.786
tof -2513.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dmf 35
29412
il n
in n
dp y
hs nn
PROCESSING
fn DISPLAY 65536
sp -200.0
wp 4797.3
rfl 3704.4
rfp 2902.4
lp 124.2
PLOT
wc 380
sc 0
vs 128
th 75
ph
2.239
1.636
Me
CHO
Me
4.107

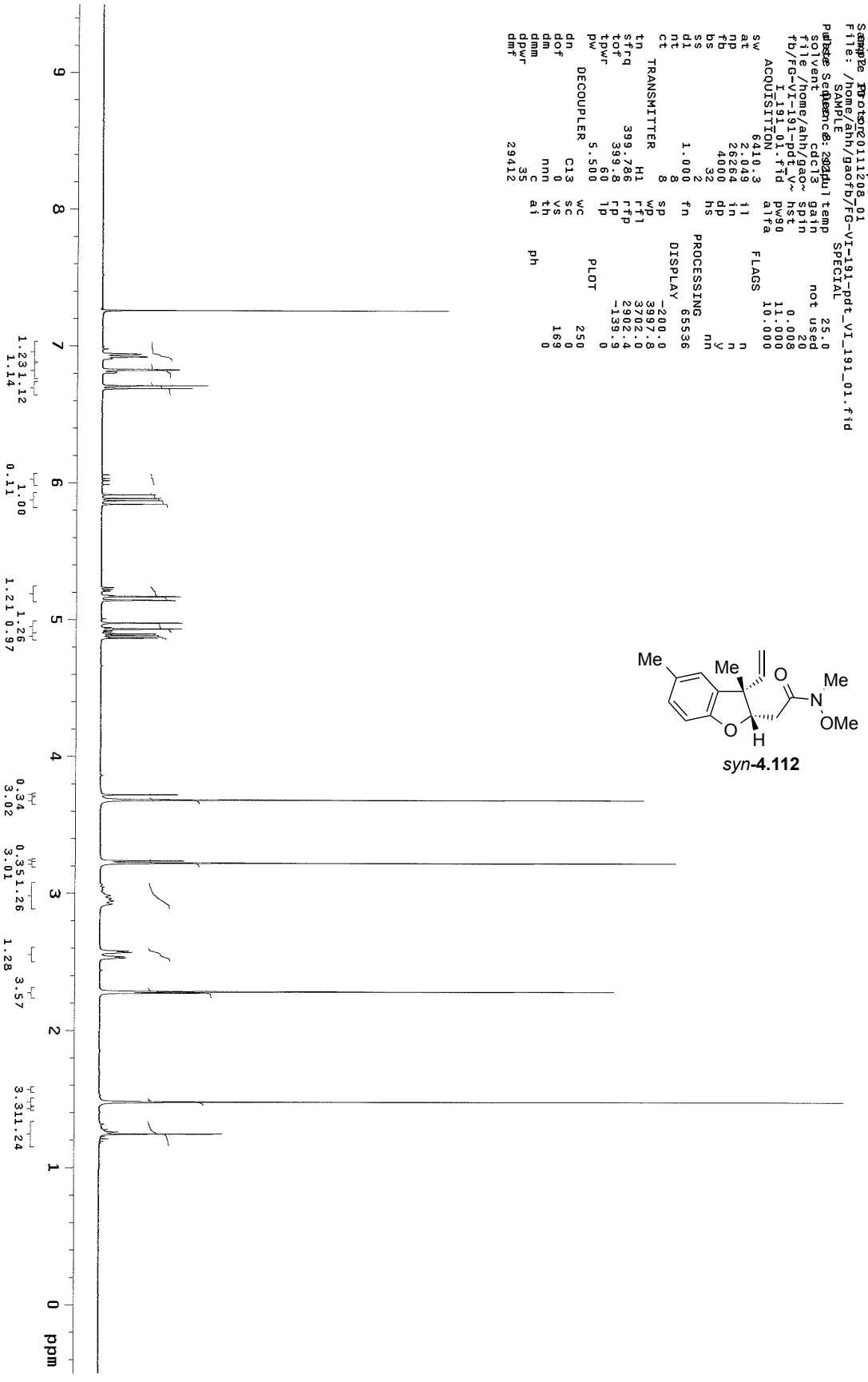

Sample: FG-VI-207-A-pdt
Solvent: cdcl3
File: /home/ahh/gaov/FG-VI-207-A-pdt_VI_207_01.fid
Pulse Sequence: s2pul
solvent cdcl3
file /home/ahh/gaov
fb/FG-VI-207-A-pdt~
VI_207_01.fid
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4000
bs 32
ss
d1 1.000
nt 8
ct 8
TRANSMITTER
tn H1
sfrq 399.796
tof 399.8
tpwr 60
pw 5.500
DECOUPLER
C13
dn
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
SPECIAL
temp 25.0
gain not used
spin 20
hst 0.008
pw90 11.000
alfa 10.000
FLAGS
n
n
y
nn
PROCESSING
fn 65536
DISPLAY
sp -801.2
wp 6410.1
rfl 3203.8
rfp 3202.4
rp 124.6
lp 0
PLOT
wc 380
sc 0
vs 352
th 82
ph
ai
Me
CHO
4.108
1.141
12.24
6.78
1.23
1.06
1.04
0.88
0.85
1.00
6.79
12
10
8
6
4
2
-0
ppm


Sample: FG-VI-208-B-pdt2
Sample IPrOSCON110929_03
File: /home/ahh/gaofb/FG-VI-208-B-pdt2_VI_208_01.fid
SAMPLE SPECIAL
Pulse Sequence: 2pulse temp 25.0
solvent cdcl3 gain not used
file /home/ahh/gao~ spin 20
fb/FG-VI-208-B-pdt~ hst 0.008
2_VI_208_01.fid pw90 11.000
ACQUISITION alfa 10.000
6410.3 FLAGS
sw 2.049 il n
at 26264 in n
np 4000 dp y
fb 32 hs nn
bs 2 PROCESSING
ss 1.000 fn 65536
d1 8 DISPLAY -200.0
nt 8 sp 4397.5
ct wp 3705.0
TRANSMITTER rfl 2902.4
tn H1 rfp 122.8
sfrq 399.786 rp 0
tof 399.8 lp
tpwr 60 PLOT
pw 5.500 wc 250
DECOUPLER sc 0
dn C13 vs 24
dof 0 th 34
dm nnn
dmm c ph
dpwr ai
dmf 35
29412
Me
t-BuO
CHO
O
4.109
1.459
1.458
0.94
1.00
0.91
0.96
0.98
1.11
14.36
10
9
8
7
6
5
4
3
2
1
0
ppm

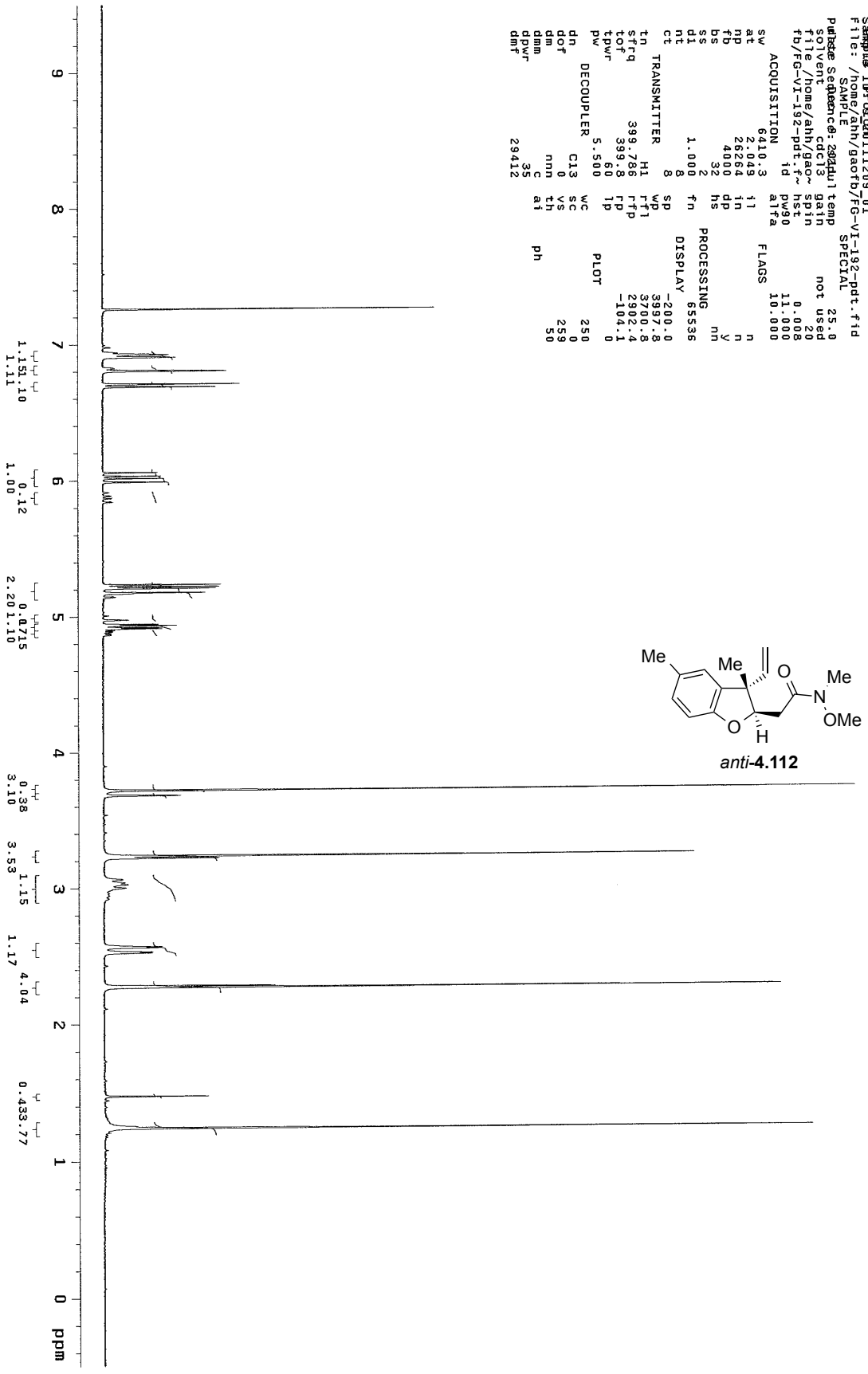

Me
Me
CO2Me
OH
4.110
ppm

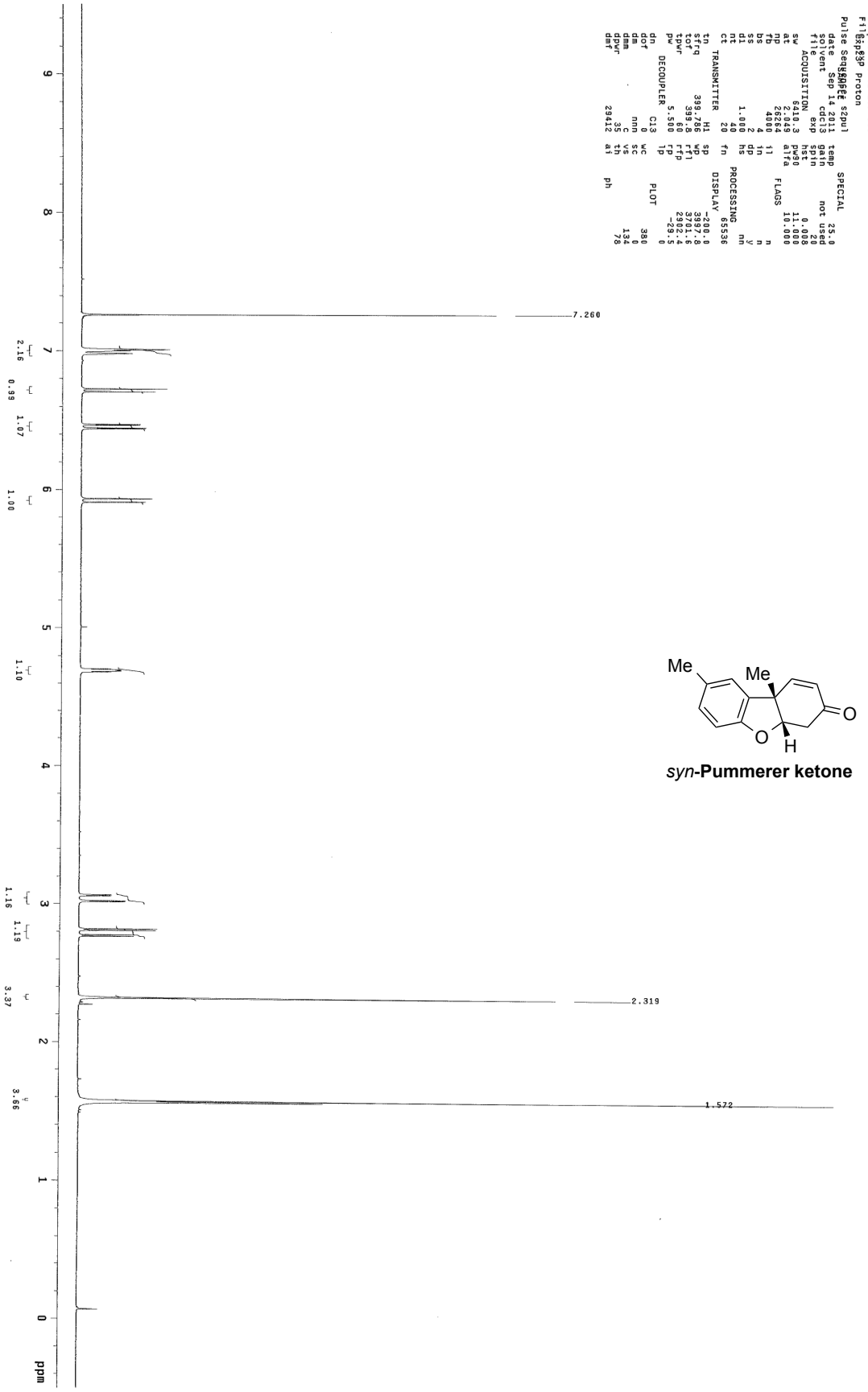

Me
Me
CO2Me
O
H
syn-4.111


Sample: FG-VI-254-B-pdt
Sample ID: 20111208_02
File: /home/ahh/gaofb/FG-VI-254-B-pdt_VI_254_01.fid
SAMPLE
PROTON
SPECIAL
pulse sequence: 2pul
solvent: cdcl3
file: /home/ahh/gao~
fb/FG-VI-254-B-pdt~
VI_254_01.fid
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4000
bs 32
ss 2
d1 1.000
nt 8
ct 8
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
temp 25.0
gain not used
spin 20
hst 0.008
pw90 11.000
alfa 10.000
FLAGS
il n
in n
dp y
hs nn
PROCESSING
fn 65536
DISPLAY
sp -200.0
wp 3997.8
rfl 3700.6
rfp 2902.4
rp -98.1
lp 0
PLOT
wc 250
sc 0
vs 145
th 0
ph
ai
1.15 1.10
2.12 0.12
0.12
1.00
1.51 1.08
1.09
3.42
1.23 3.60
1.23
0.27
0.37 3.57
Me
Me
CO2Me
O
H
anti-4.111
9
8
7
6
5
4
3
2
1
0
ppm

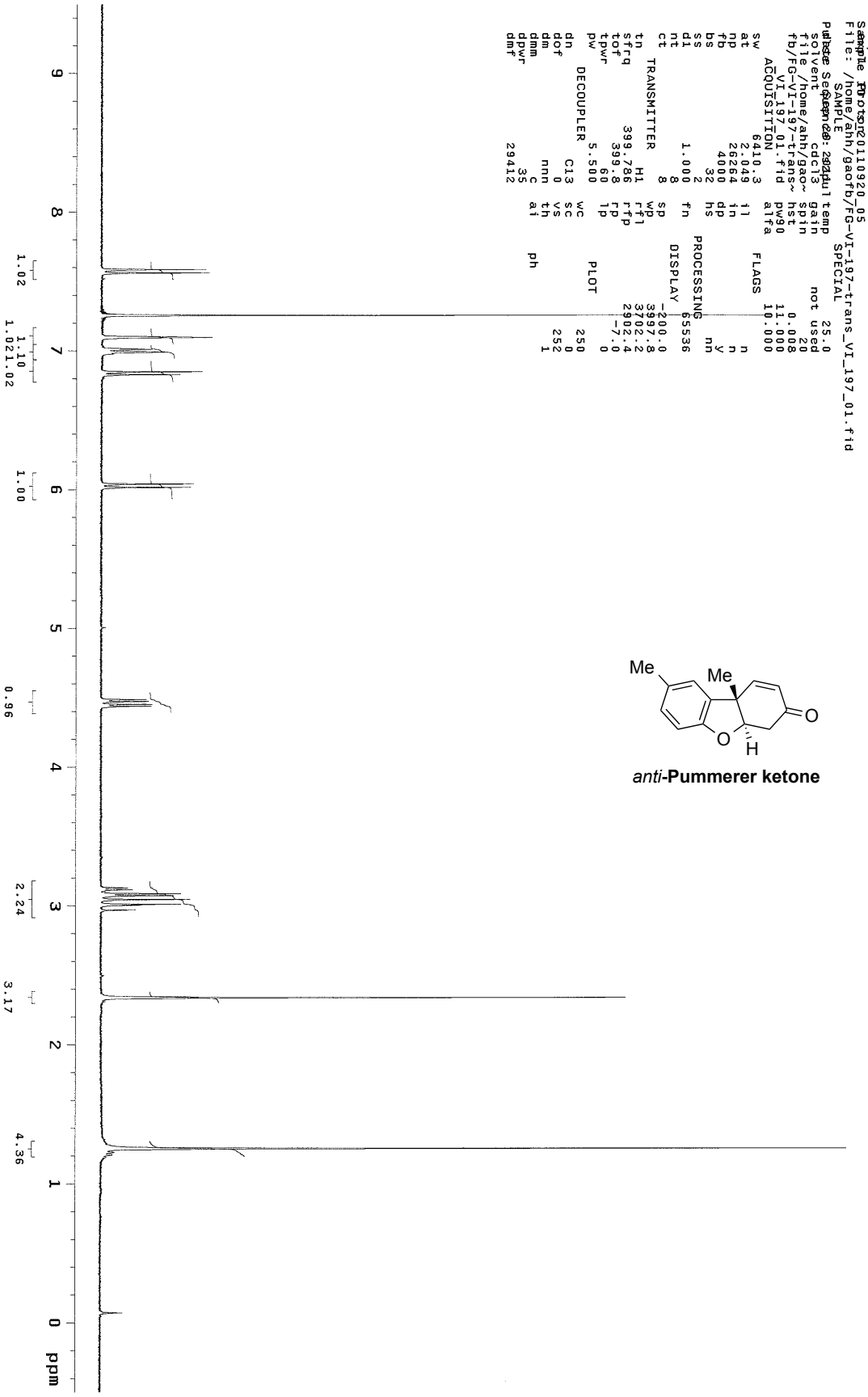

Sample: FG-VI-191-pdt
Sample ID: FG-VI-191-pdt
File: /home/ahh/gaofb/FG-VI-191-pdt_VI_191_01.fid
SAMPLE
Pulse Sequence: 2D pul temp 25.0
solvent cdcl3 gain not used 20
fb/FG-VI-191-pdt_v~ hst 0.008
file /home/ahh/gao~ spin 11.000
I_191_01.fid pwg0 10.000
ACQUISITION FLAGS
sw 6410.3 il n
at 2.049 in n
np 26264 dp y
fb 4000 hs nn
bs 32
ss 2 PROCESSING
d1 1.000 fn 65536
nt 8 DISPLAY
ct 8 sp -200.0
wp 3997.8
TRANSMITTER rfl 3702.0
tn H1 rfp 2902.4
sfrq 399.786 rp -139.9
tof 399.8 lp 0
tpwr 60 PLOT
pw 5.500 wc 250
DECOUPLER sc 0
dn C13 vs 169
dof 0 th 0
dm nnn ph
dmm c ai
dpwr 35
dmf 29412
Me
Me
O
Me
N
OMe
O
H
ppm
0
1
2
3
4
5
6
7
8
9
1.23 1.12
1.14
1.00
0.11
1.21 0.97
1.26
0.34
3.02
0.35 1.26
3.01
1.28
3.57
3.31 1.24

syn-**4.112**

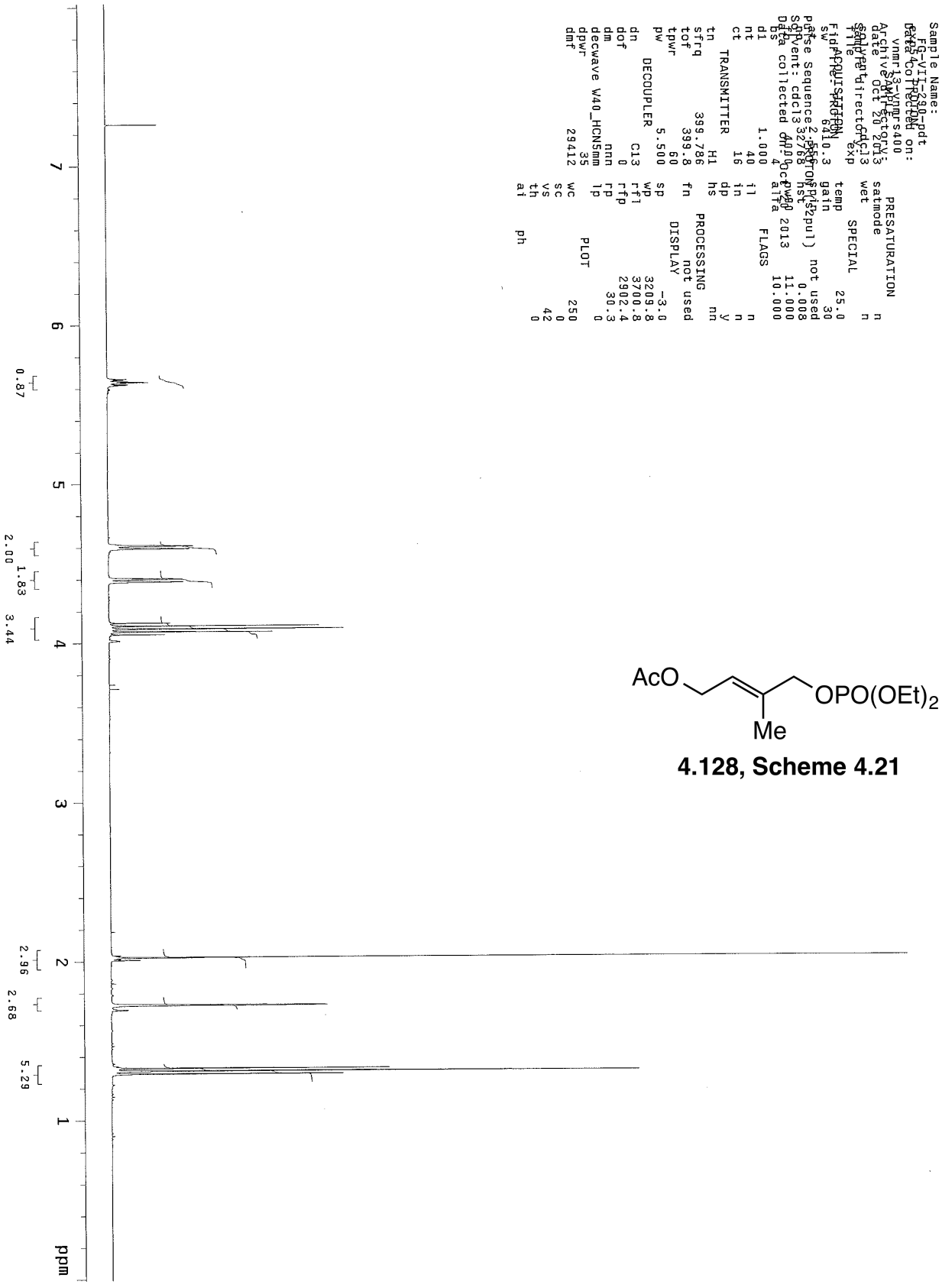

Sample: FG-VI-192-pdt
Sample ID: osc01112103_01
File: /home/anh/gaofb/FG-VI-192-pdt.fid
SAMPLE
Pulse Sequence: 2pul temp
solvent cdcl3 gain not used 20
file /home/anh/gao~ spin 25.0
fb/FG-VI-192-pdt.f~ hst 0.008
1d pw90 11.000
ACQUISITION alfa 10.000
6410.3 FLAGS
sw 2.049 il n
at 26264 in n
np 4000 dp y
fb 32 hs nn
bs 2 PROCESSING
ss 1.000 fn 65536
d1 8 DISPLAY
nt 8 sp -200.0
ct wp 3997.8
TRANSMITTER rfl 3700.8
tn H1 rfp 2902.4
sfrq 399.786 rp -104.1
tof 399.8 lp 0
tpwr 60 PLOT
pw 5.500 wc 250
DECOUPLER sc 0
dn C13 vs 259
dof 0 th 50
dm nnn ai ph
dmm c
dpwr 35
dmf 29412
Me
Me
O
Me
N
OMe
O
H
anti-4.112
1.15
1.10
1.11
0.12
1.00
0.07
2.20
1.10
0.38
3.10
1.15
3.53
1.17
4.04
0.43
3.77
ppm



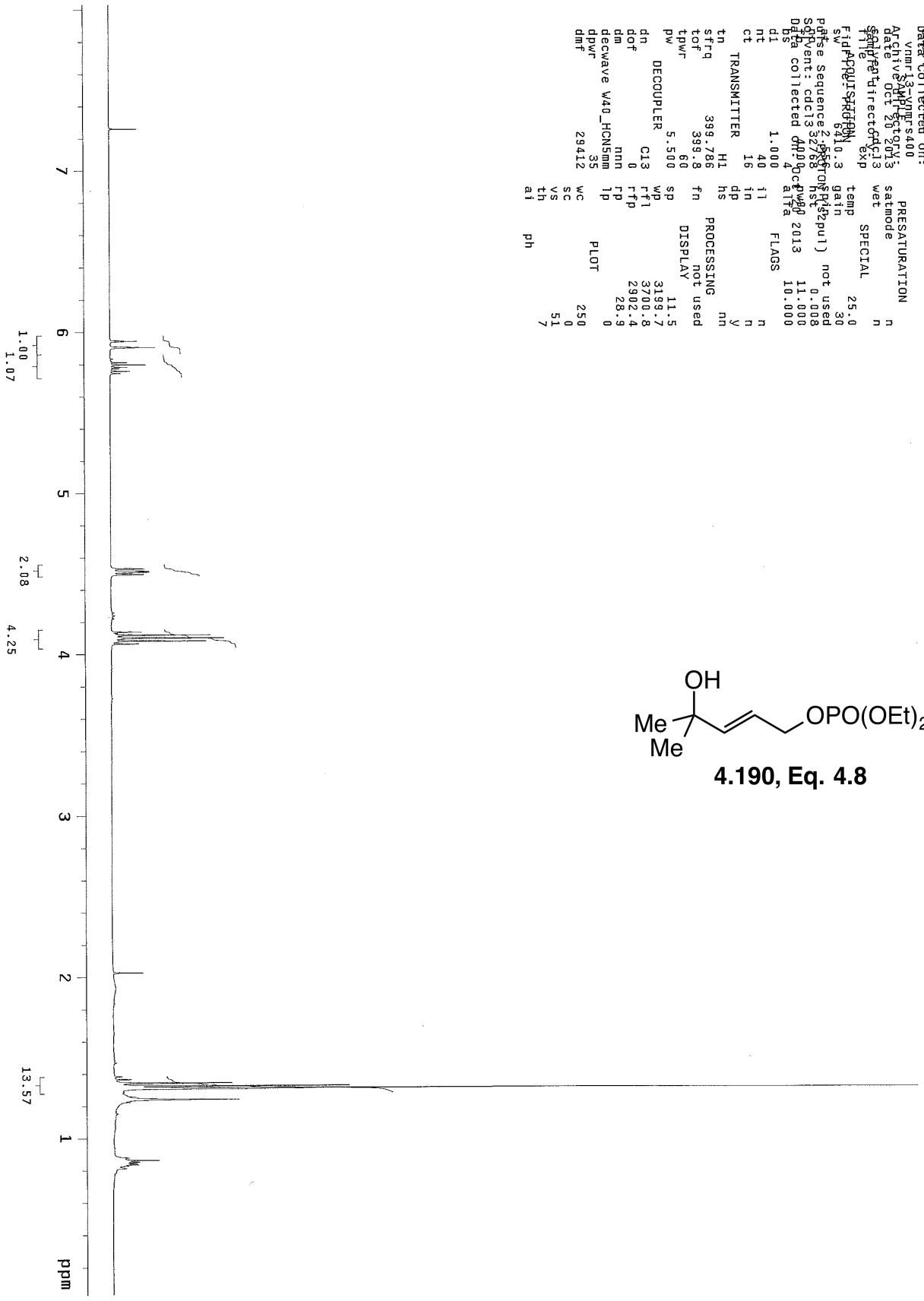
syn-**Pummerer ketone**



anti-**Pummerer ketone**

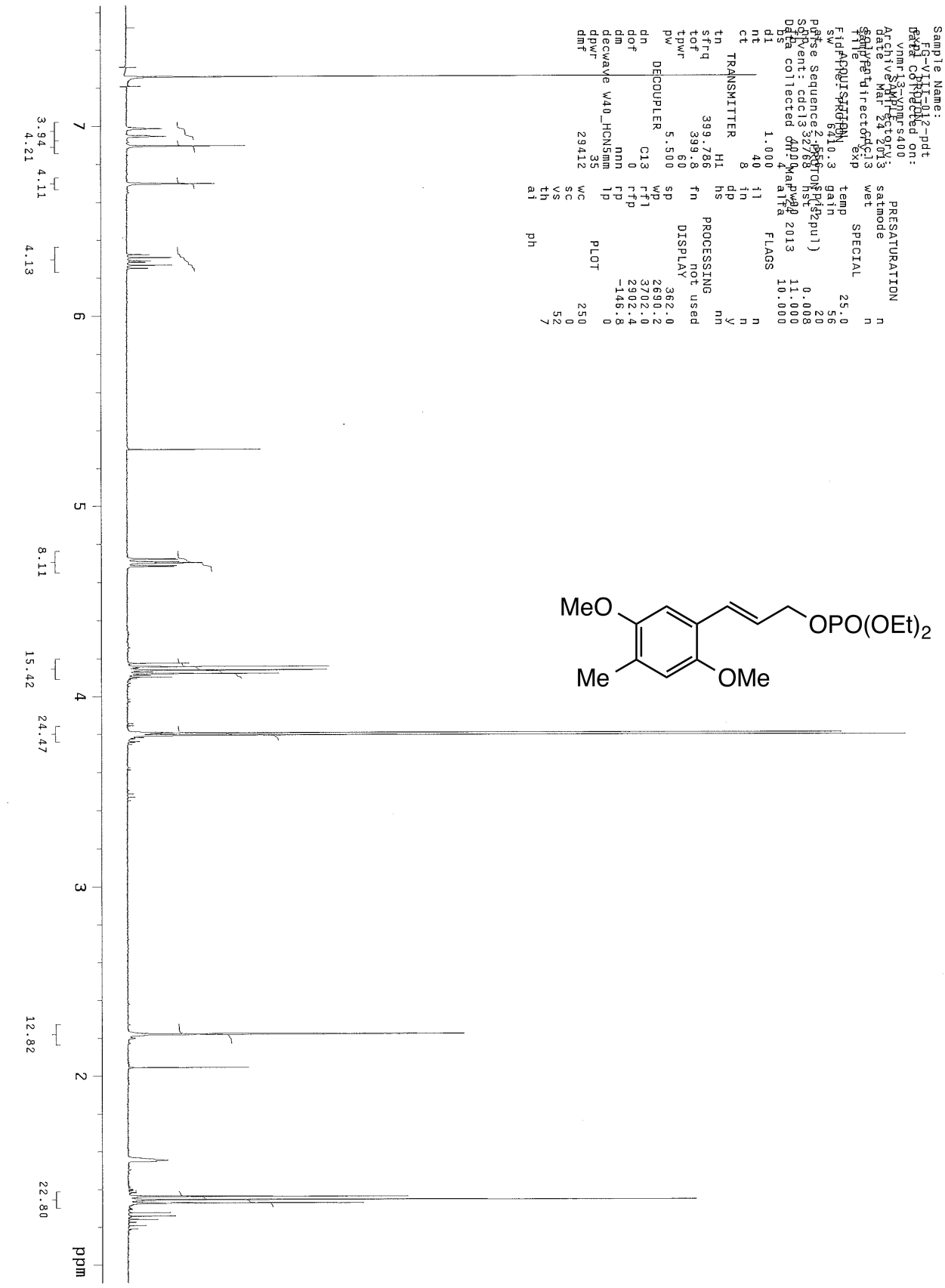


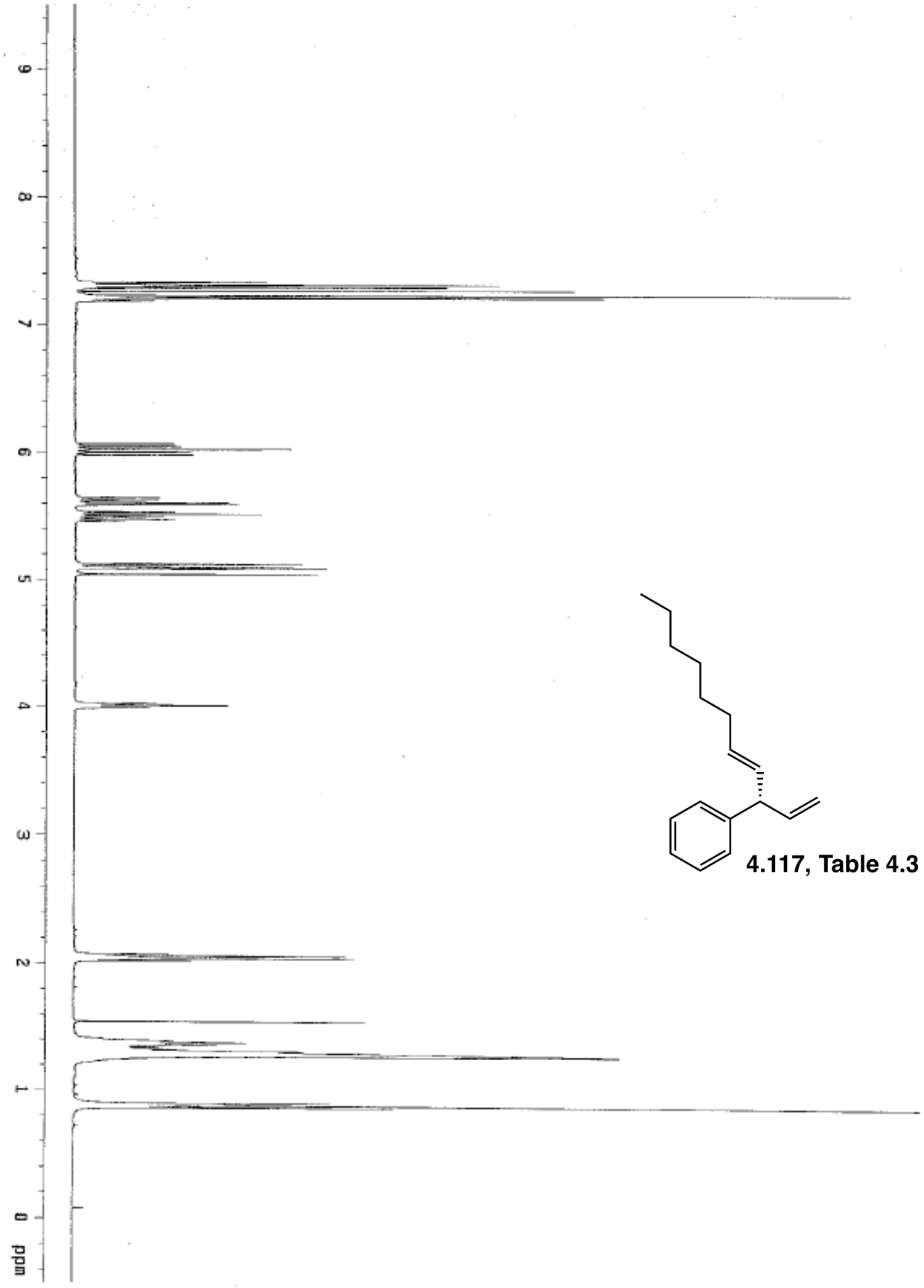
4.128, Scheme 4.21


Sample Name:
FG-VII-040-pdt
Data Collection on:
Archive directory:
Archive file:
Date
Sample directory:
File
Fid acquisition
Pulse Sequence
Solvent: cdcl3
Data collected on:
PRESATURATION
SPECIAL
FLAGS
PROCESSING
DISPLAY
PLOT
TRANSMITTER
DECOUPLER
ppm
1.00
1.07
2.08
4.25
13.57

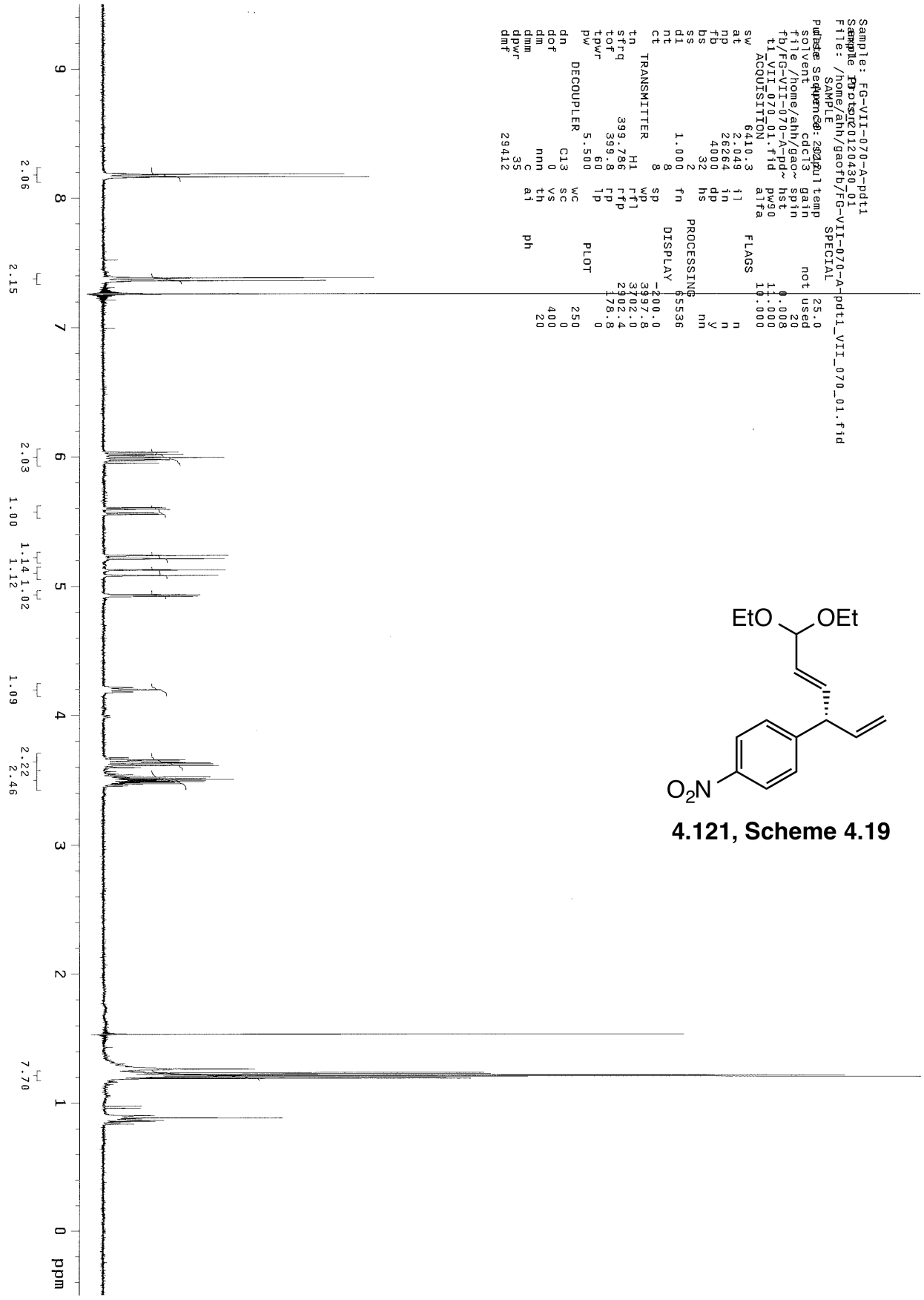
OH
Me
Me
OPO(OEt)2

4.190, Eq. 4.8

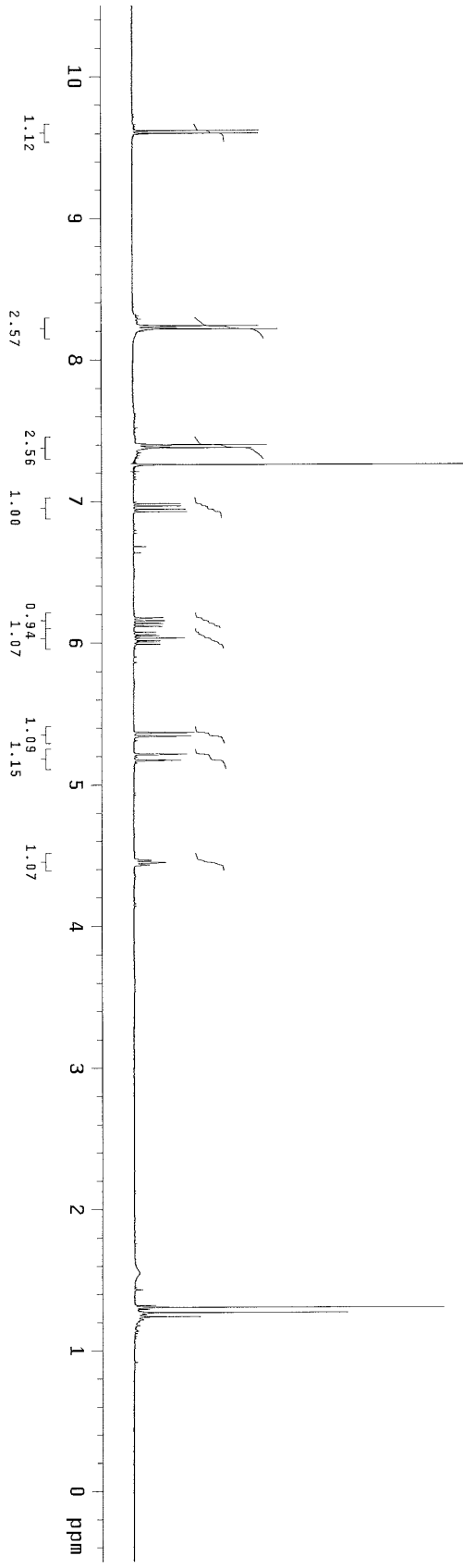

Sample Name:
FG-VIII-012-pdt
Data Collected on:
vnmrs13-vnmrs400
Archive directory:
Mar 24 2013
Title
Fid FROM SPECTRUM
Pulse Sequence: s2pul
Solvent: cdcl3
Data collected on: Mar 24 2013
PRESATURATION
satmode n
wet n
SPECIAL
temp 25.0
gain 56
hst 20
0.008
11.000
10.000
FLAGS
n
n
y
nn
PROCESSING
not used
DISPLAY
362.0
2690.2
3702.0
2902.4
-146.8
0
PLOT
250
0
52
7
MeO
OPO(OEt)2
Me
OMe
3.94
4.21
4.11
4.13
8.11
15.42
24.47
12.82
22.80
ppm



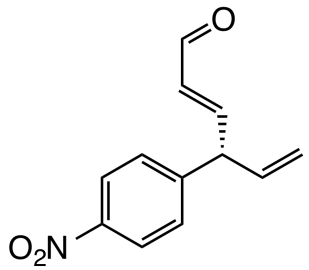
4.117, Table 4.3



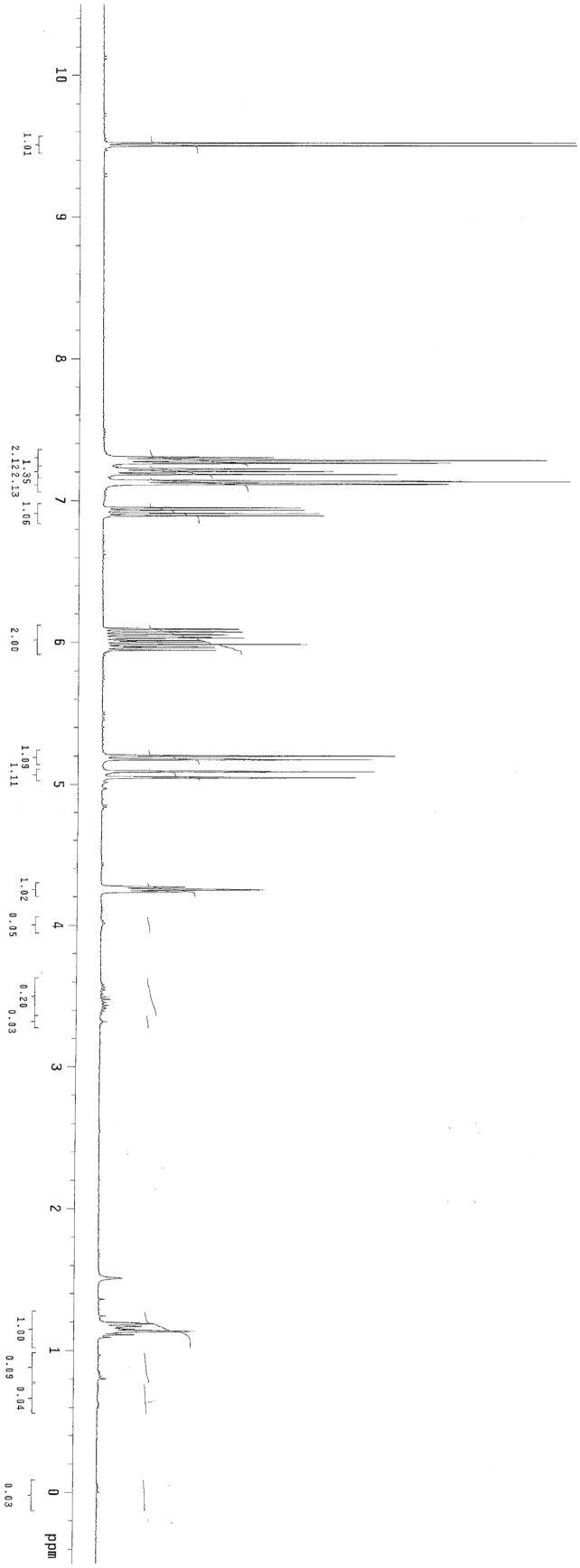
4.121, Scheme 4.19



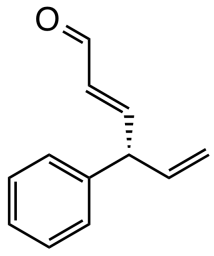

```
Sample: FG-VII-070-B-pdt2
Exp: 1 exp proton

Pulse Sequence: s2pul          SPECIAL
date  Apr 30 2012  temp          25.0
solvent     cdcl3  gain      not used
file         exp   spin            20
ACQUISITION        hst           0.008
sw          6410.3 pw90         11.000
at             2.049 alfa       10.000
np           26264          FLAGS
fb            4000  il            n
bs               4  in            n
ss               2  dp            y
d1           1.000  hs           nn
nt              40
ct              20  fn        65536
TRANSMITTER        DISPLAY
tn              H1  sp         -200.0
sfrq     399.786  wp         4397.5
tof        399.8  rfl        3701.8
tpwr          60  rfp        2902.4
pw         5.500  rp         -175.2
DECOUPLER          lp            0
dn              C13          PLOT
dof               0  wc          250
dm              nnn  sc            0
dmm               c  vs          100
dpwr             35  th           12
dmf           29412  ai
                     ph
```



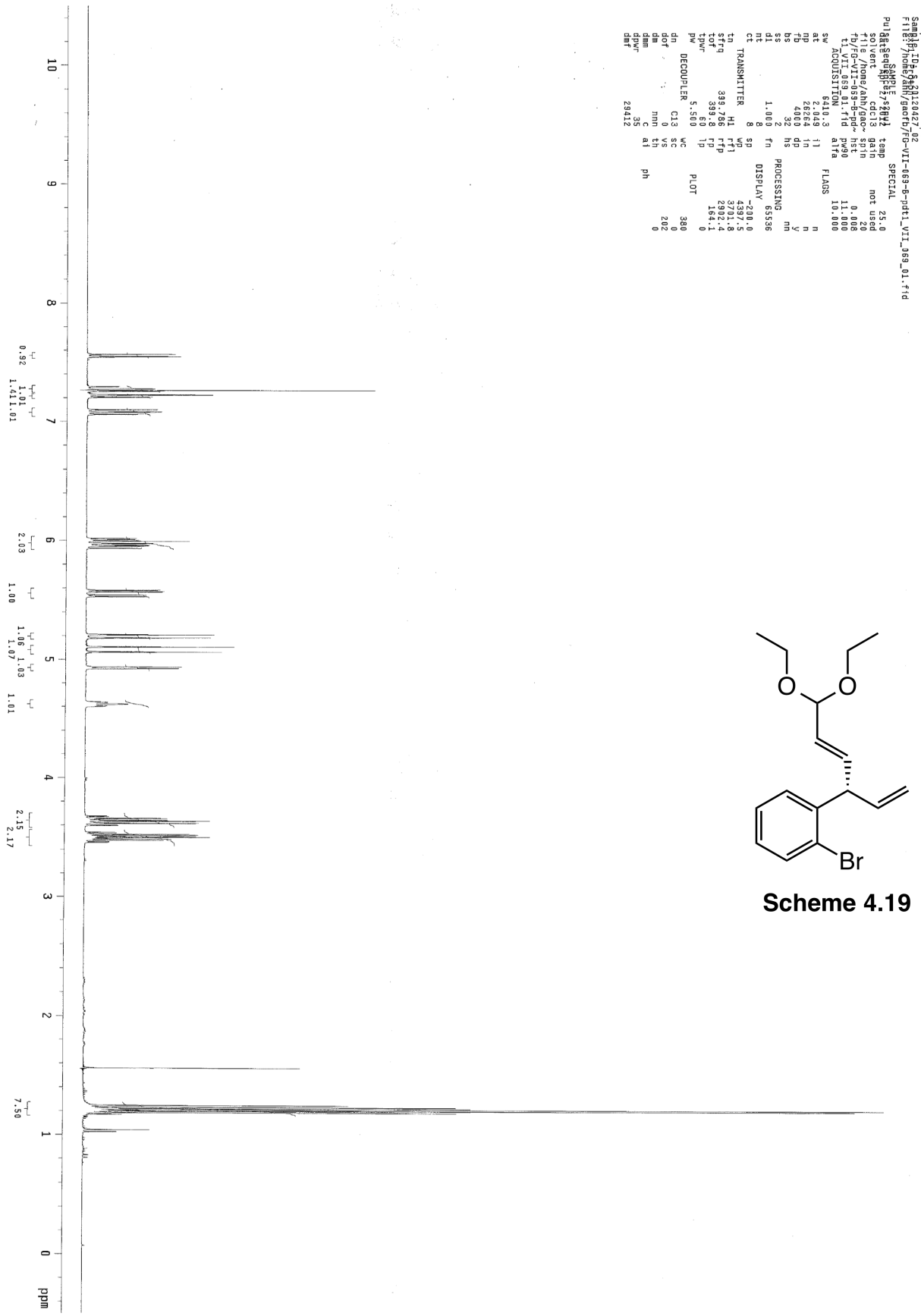
4.122, Scheme 4.19



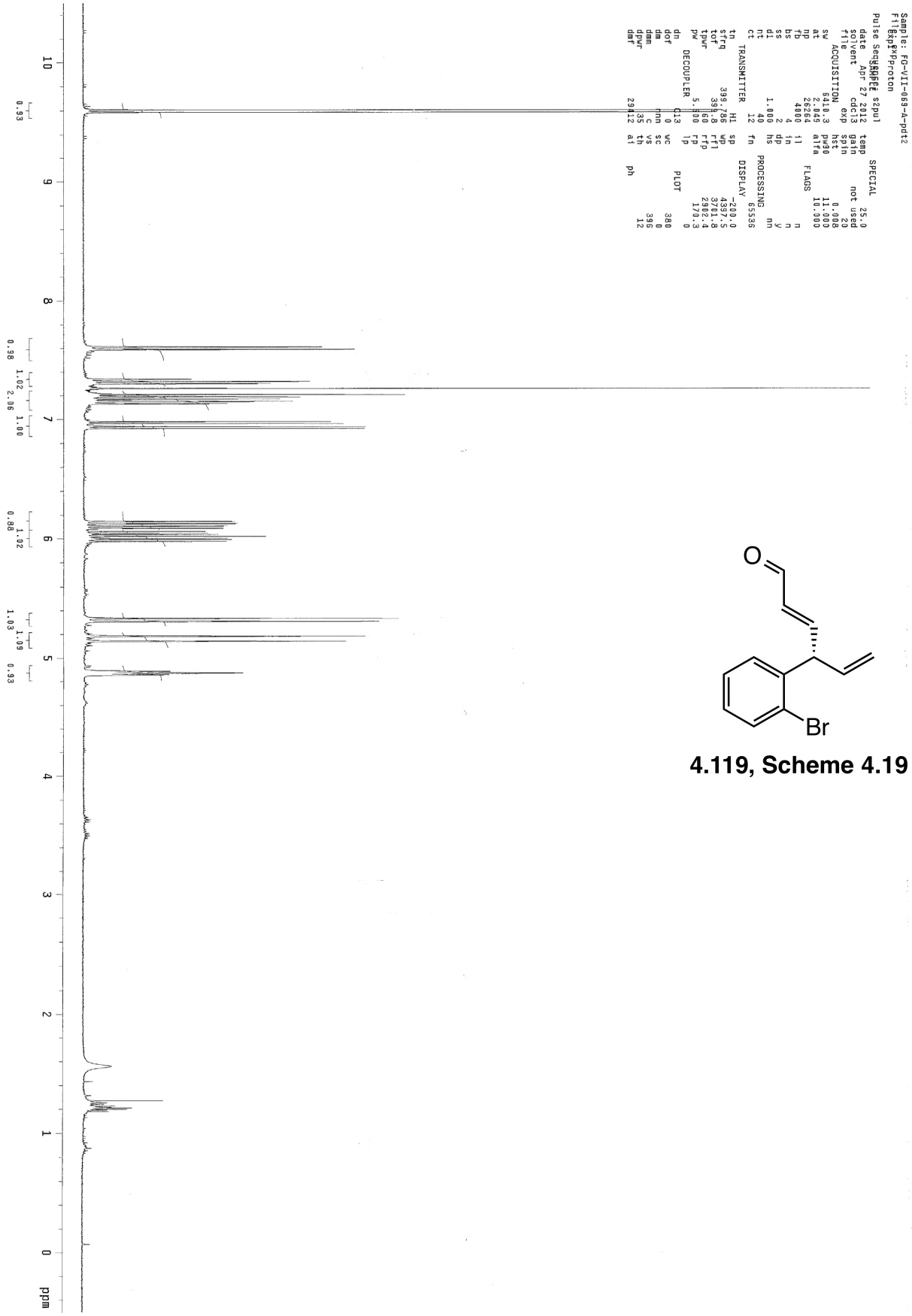

```
Sample: FG-VII-067-A-pdt2
Sample ID: FG-VII-067-A-pdt2
File: /home/amy/gaotb/FG-VII-067-A-pdt2_VII_067_01.fid

PulseSeq SAMPLE.62mhz  temp    SPECIAL    25.0
solvent    cdcl3     gain          not used
fb/FG-VII-067-A-pdt~ bsfrq              0.008
tl_VII_067_01.fid    pw90              11.000
ACQUISITION          alfa              10.000
sw          6410.3   FLAGS
at             2.049  il          n
np            26264   in          n
fb             4000   dp          y
bs               32   hs         nn
ss                1   PROCESSING
dl1           1.000   fn      65536
nt                8   DISPLAY
ct                8   sp        -199.9
TRANSMITTER       H1  wp       4397.5
tn           399.786  rfl       830.0
sfrq         399.8    rfp         0
tof               0   lp         91.3
tpwr             60   lp          0
pw          5.500     PLOT
DECOUPLER             wc        380
dn              C13   sc          0
dof               0   vs        400
dm              nnn   th          1
dmm               c   ph
dmf              35   al
dpwr          29412
```



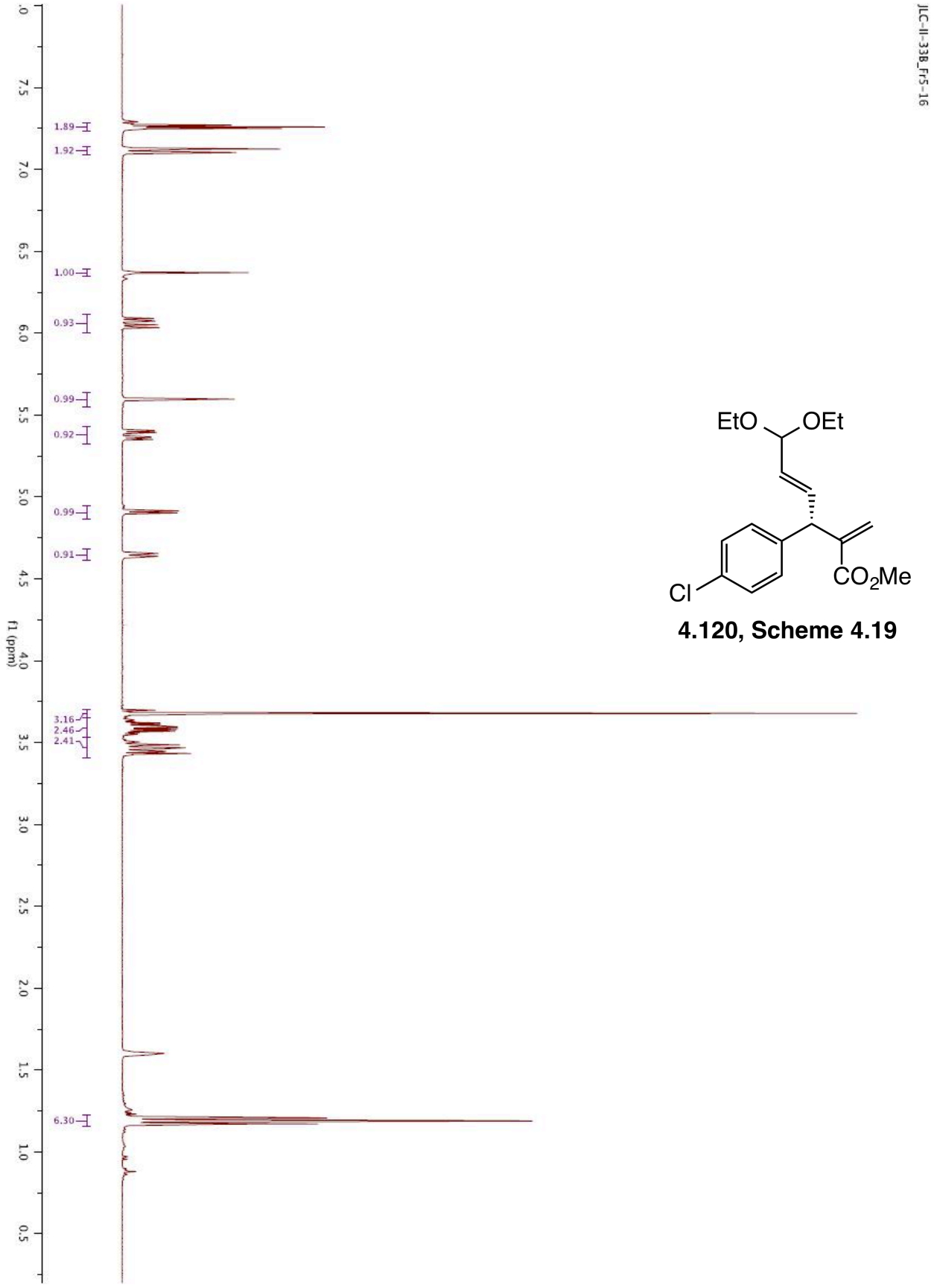
4.118, Scheme 4.19


Sample: FG-VII-069-B-pdt1
Sample_ID: S_20120427_02
File: /home/ahb/gaofb/FG-VII-069-B-pdt1_VII_069_01.fid
SAMPLE
Pulse Sequence: s2pul
solvent: cdcl3
file: /home/ahb/gao~
fb/FG-VII-069-B-pd~
tl_VII_069_01.fid
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4912
bs 32
ss 2
d1 1.000
nt 8
ct 8
TRANSMITTER
tn H1
sfrq 399.786
tof 399.673
tpwr 61
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 55
dmf 29412
SPECIAL
temp 25.0
gain not used
spin 20
hst 0.008
pw90 11.000
alfa 10.000
FLAGS
il n
in y
dp y
hs nn
PROCESSING
fn 65536
DISPLAY
wp -200.0
rfl 4397.5
rfp 3701.8
rlp 2902.4
lp 164.1
PLOT
wc 380
sc 0
vs 202
th 0
ph
ppm
0.92
1.01
1.41
1.01
2.03
1.00
1.06
1.07
1.03
1.01
2.15
2.17
7.50
O
O
Br

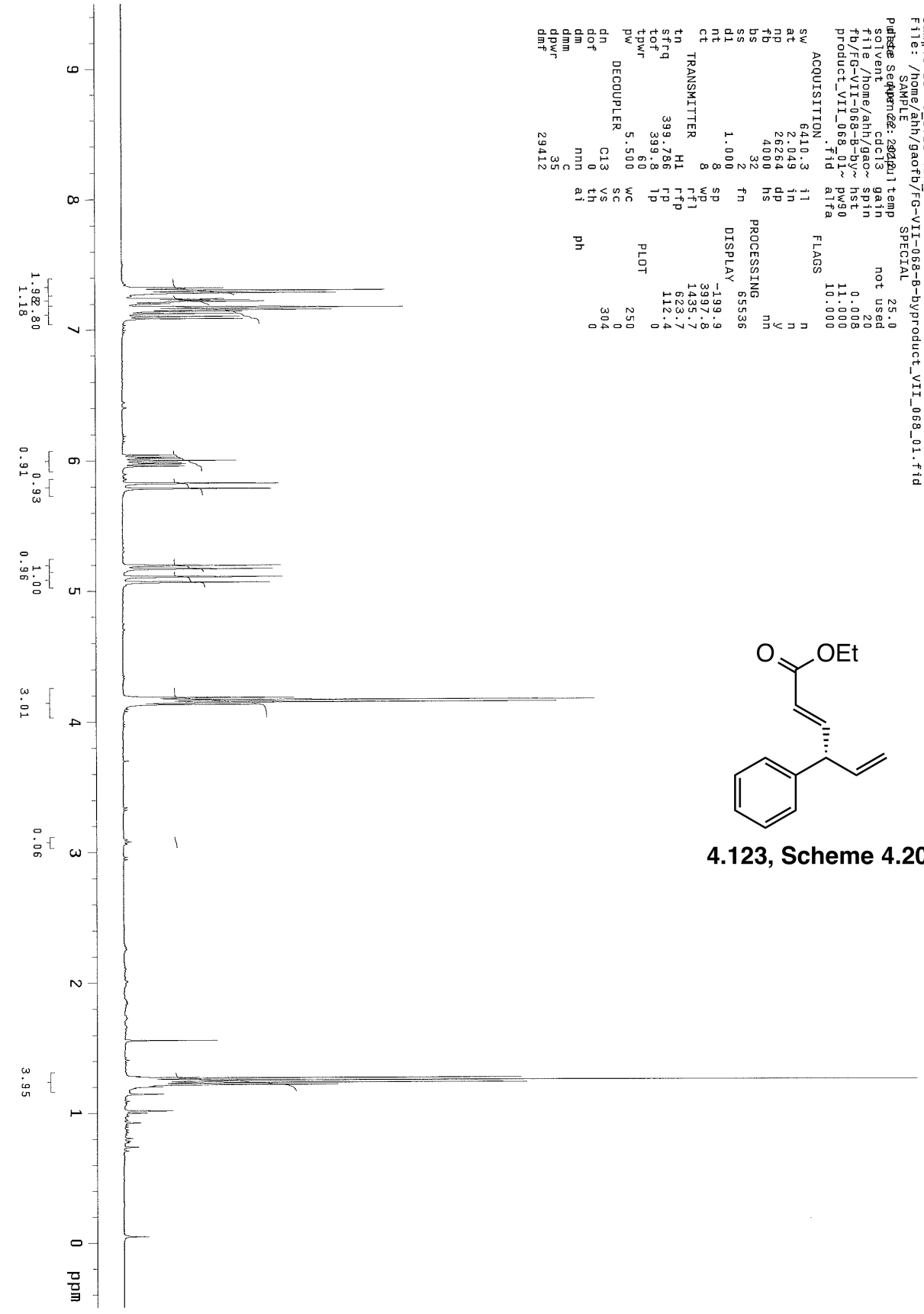
Scheme 4.19



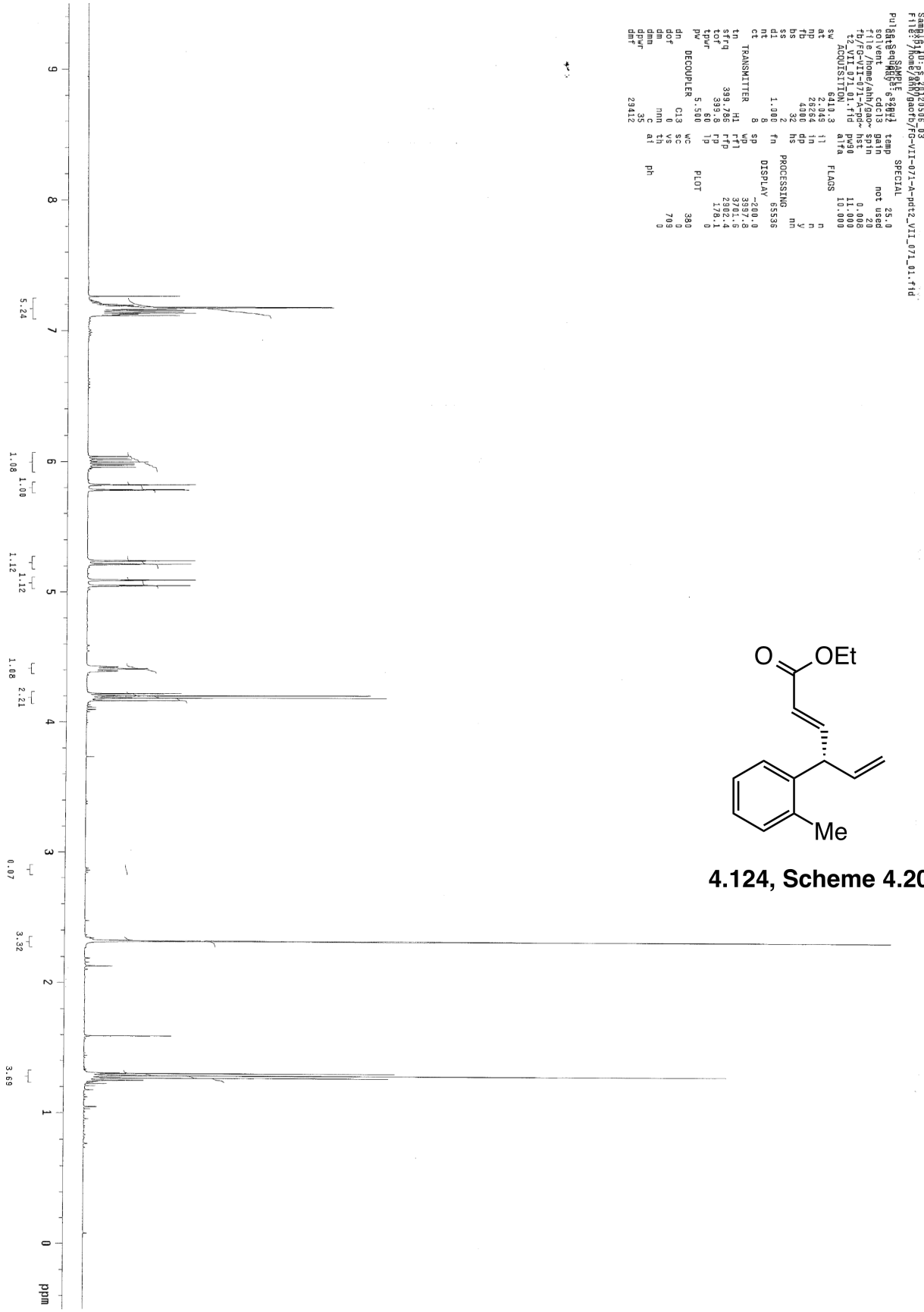
4.119, Scheme 4.19



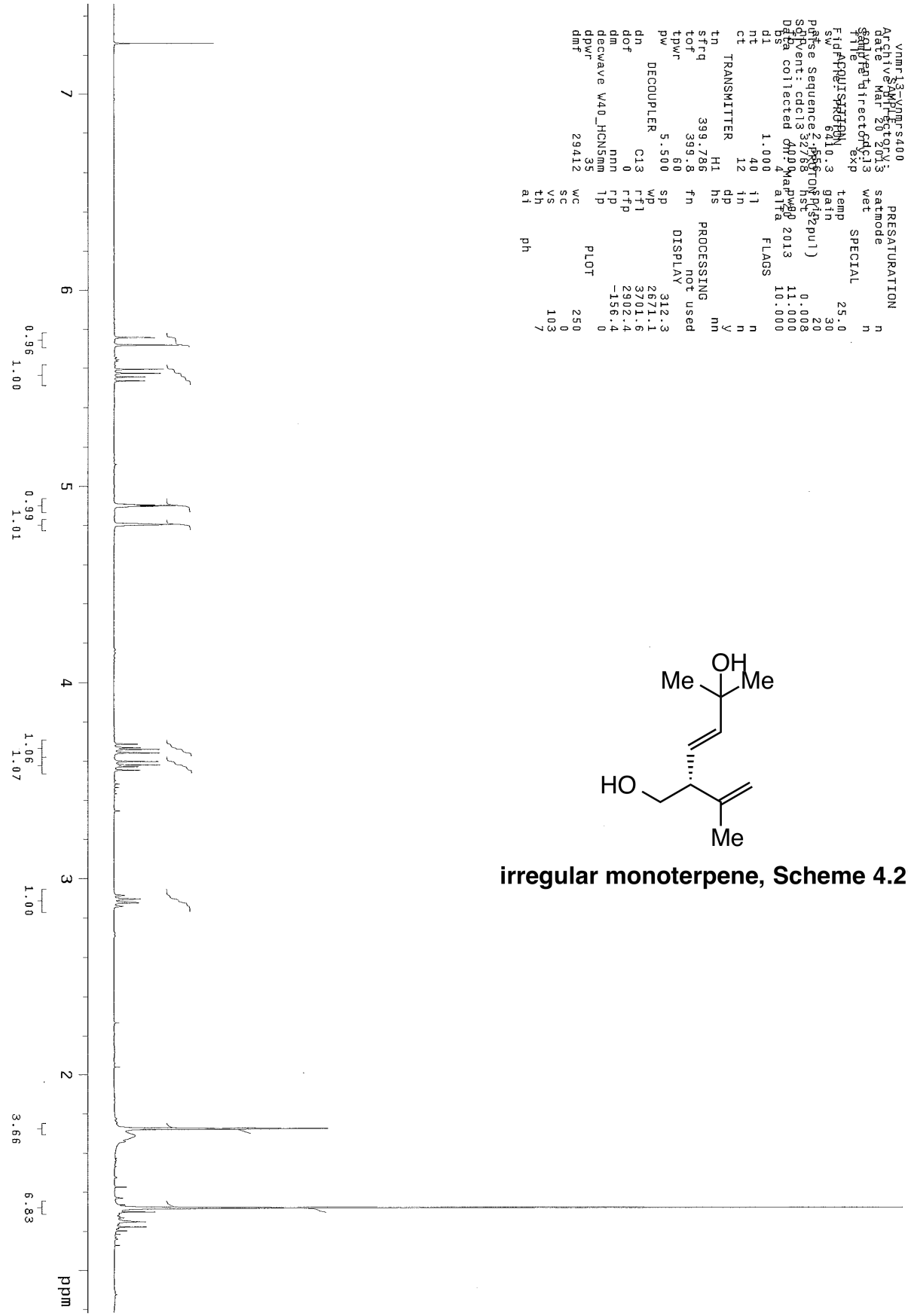
4.120, Scheme 4.19



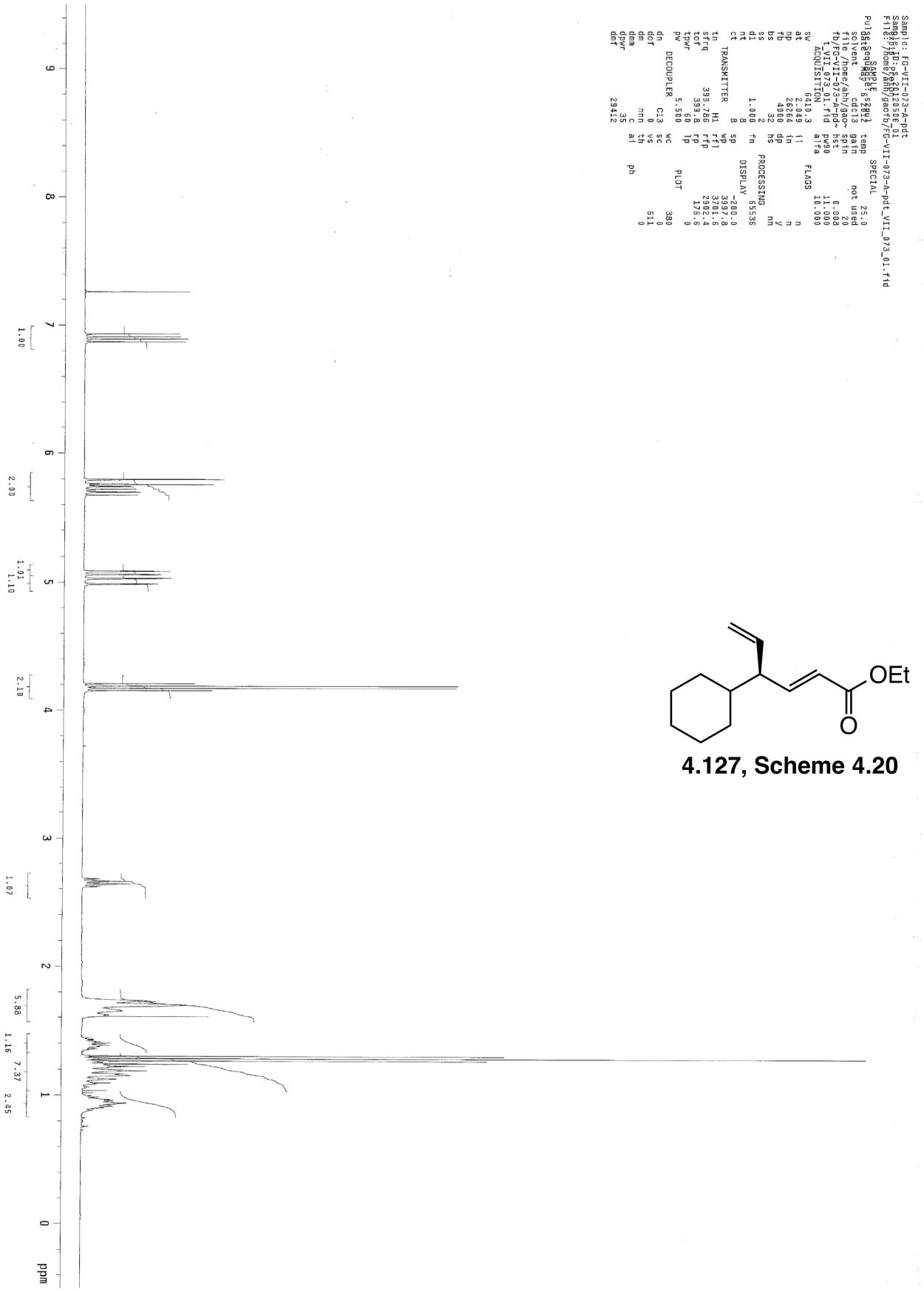
4.123, Scheme 4.20



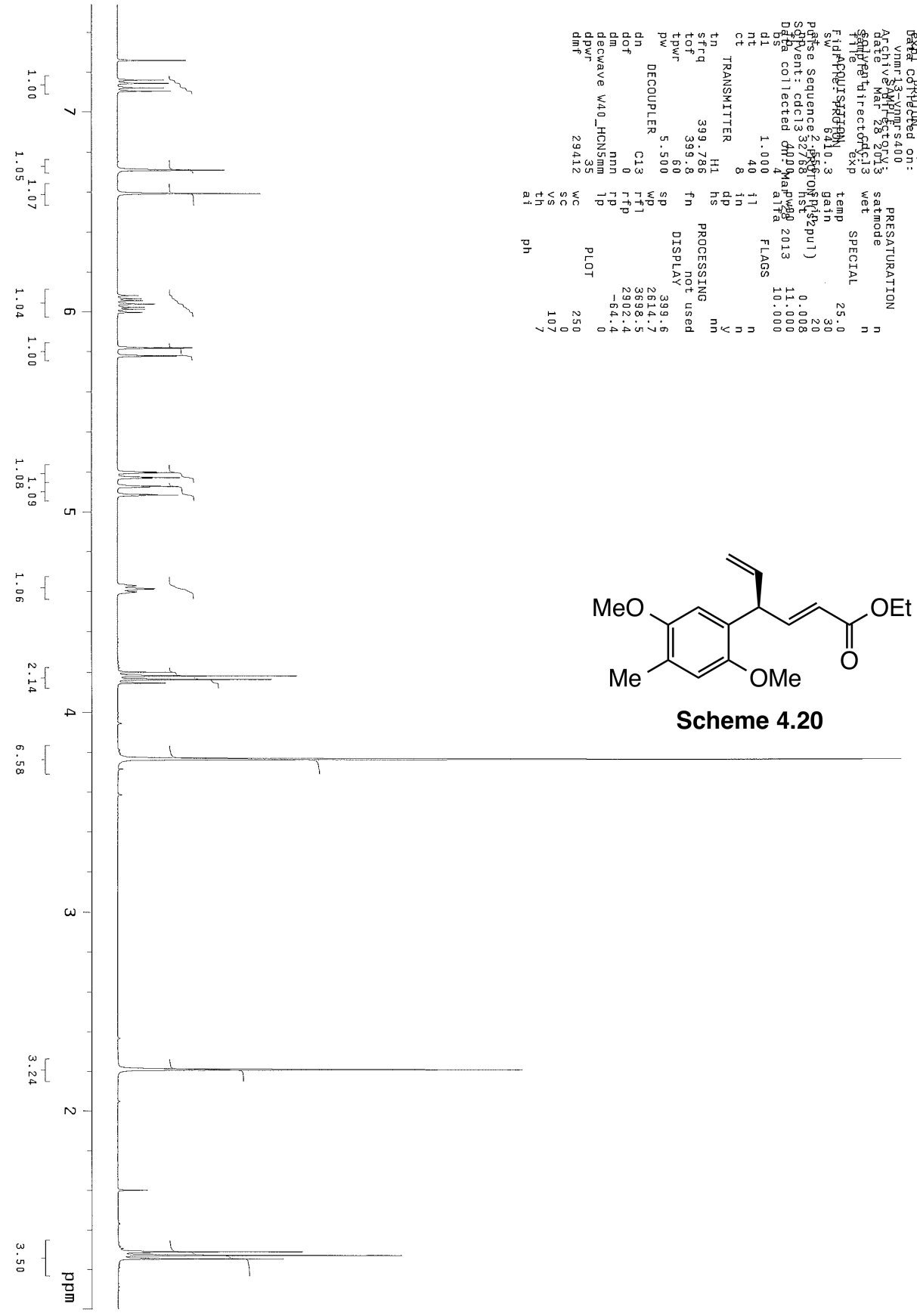
4.124, Scheme 4.20



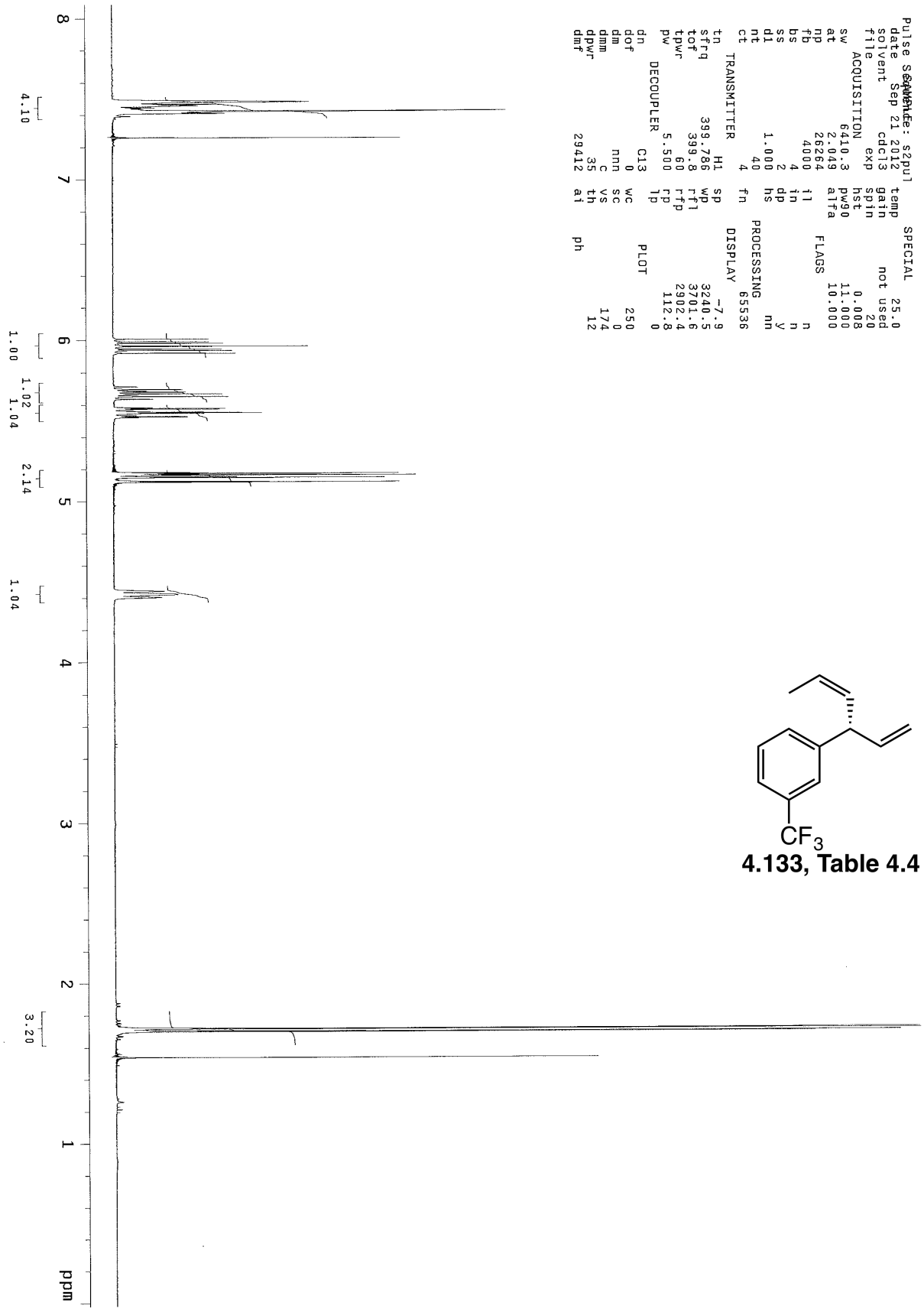
irregular monoterpene, Scheme 4.21



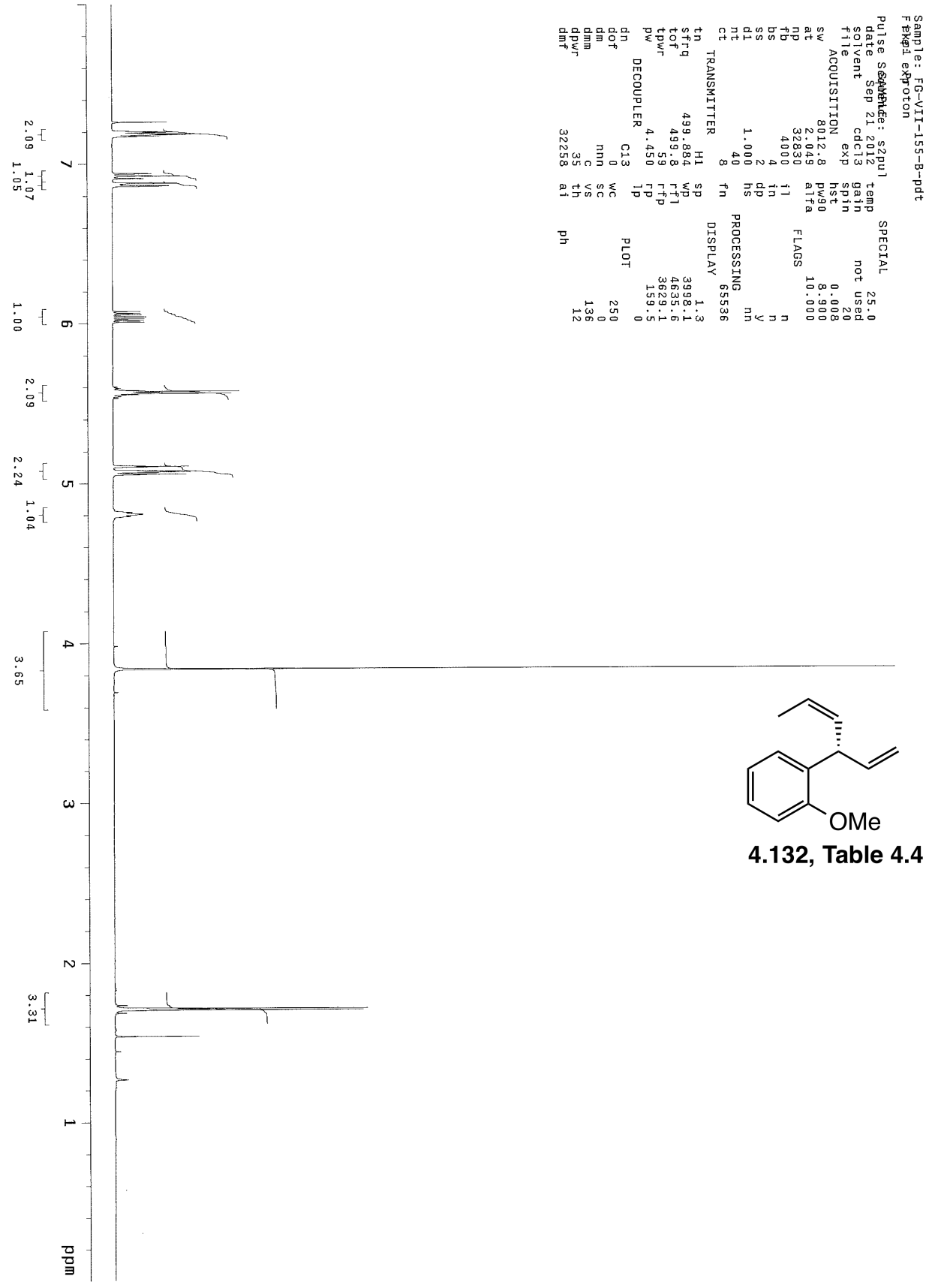
4.127, Scheme 4.20


Sample Name:
FG-VTR-013-B-pdt
Data collected on:
vnmrs13-vnmrs400
Archive directory
date Mar 28 2013
solvent chcl3
file exp
ACQUISITION
sw 6410.3
Pulse Sequence: s2pul
solvent: cdcl3
Data collected on: Apr 2 2013
ds 1.000
nt 40
ct 8
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
decwave W40_HCN5mm
dpwr 35
dmf 29412
PRESATURATION
satmode n
wet n
SPECIAL
temp 25.0
gain 30
20
hst 0.008
alfa 11.000
FLAGS 10.000
il n
in n
dp y
hs nn
PROCESSING
not used
DISPLAY
sp 399.6
wp 2614.7
rfl 3898.5
rfp 2902.4
lp -64.4
PLOT 0
wc 250
sc 0
vs 107
th 7
ai
ph
MeO
OEt
Me
OMe
O
7
6
5
4
3
2
ppm
1.00
1.05
1.07
1.04
1.00
1.08
1.09
1.06
2.14
6.58
3.24
3.50

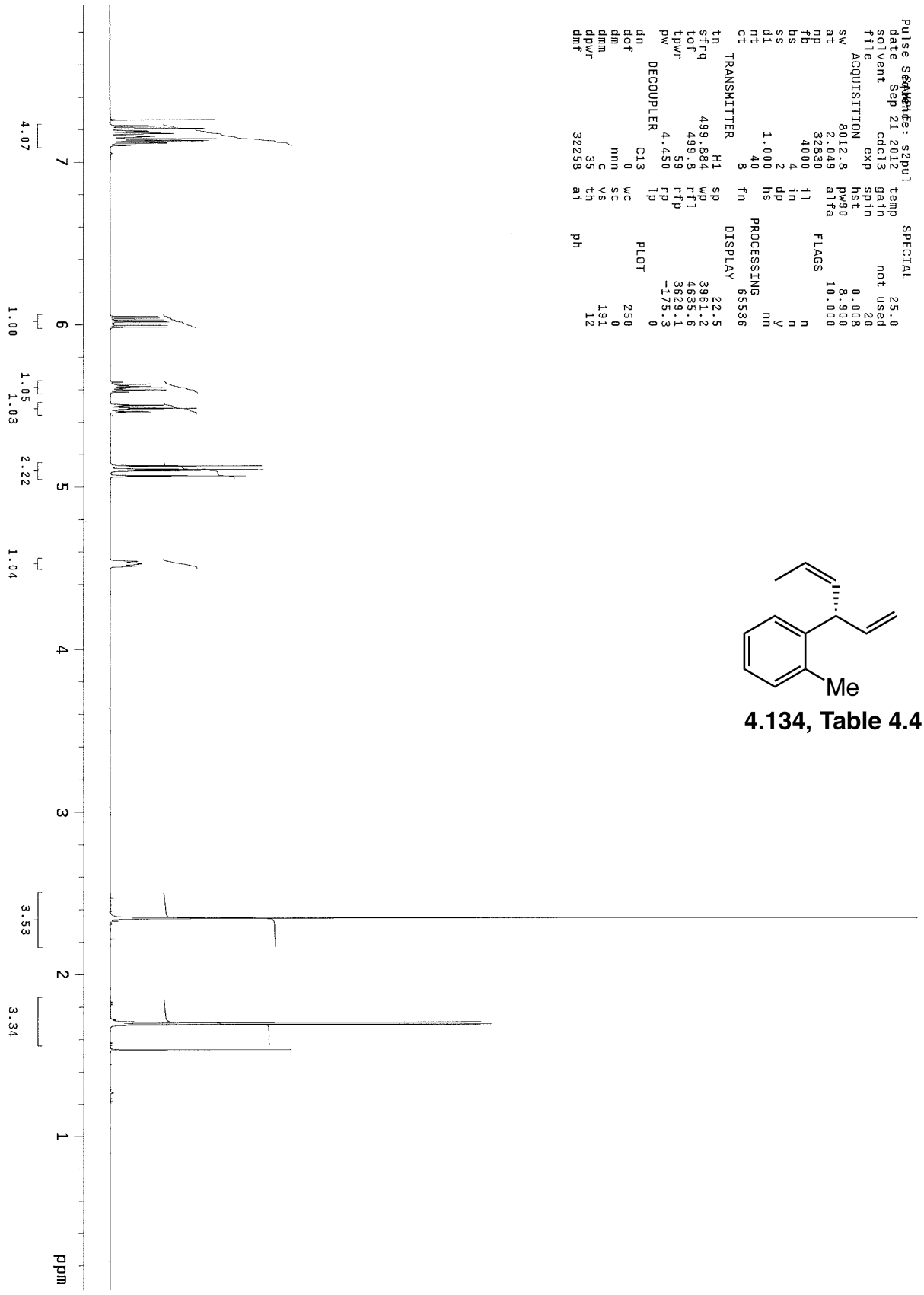
Scheme 4.20

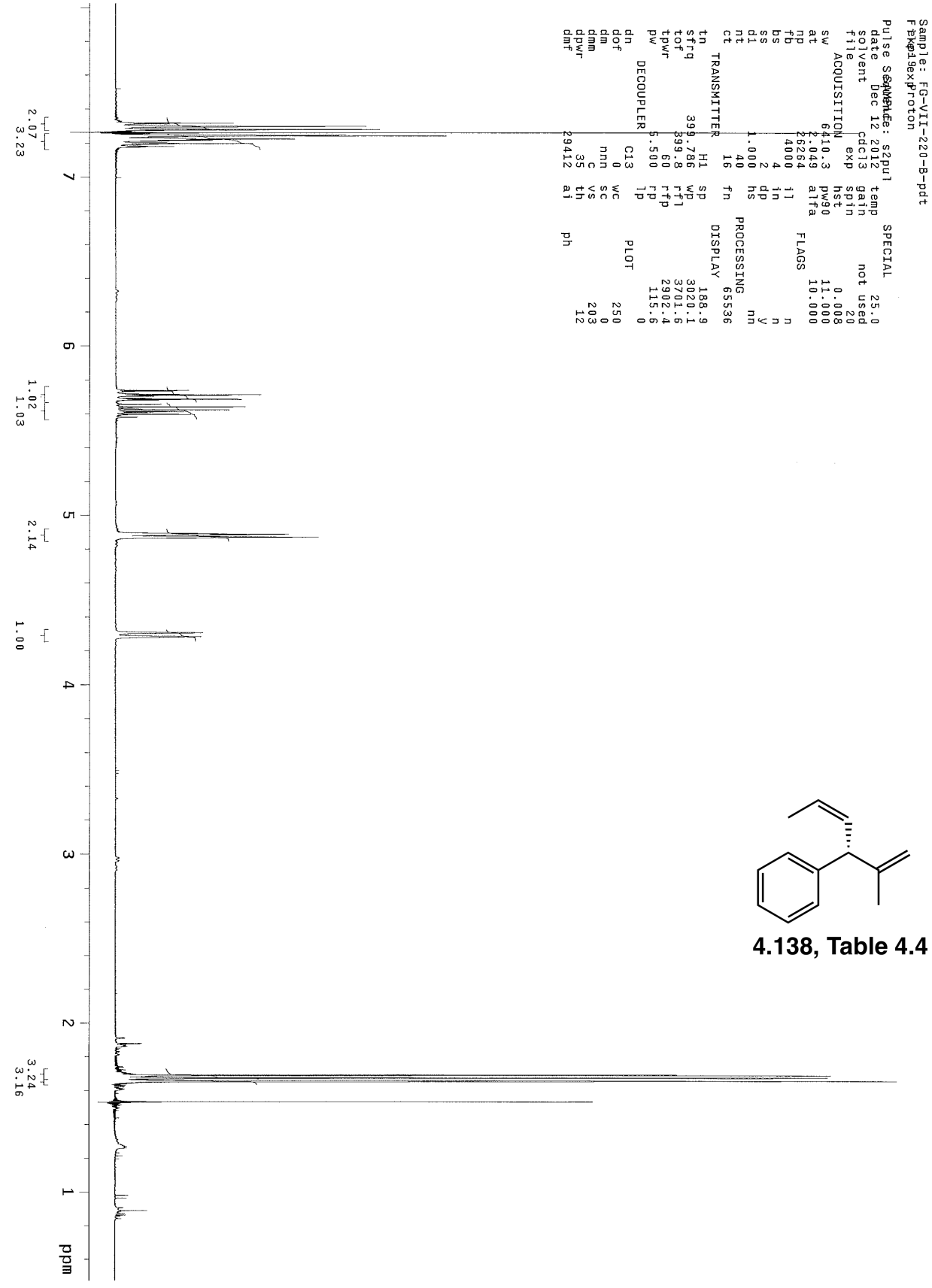


4.133, Table 4.4

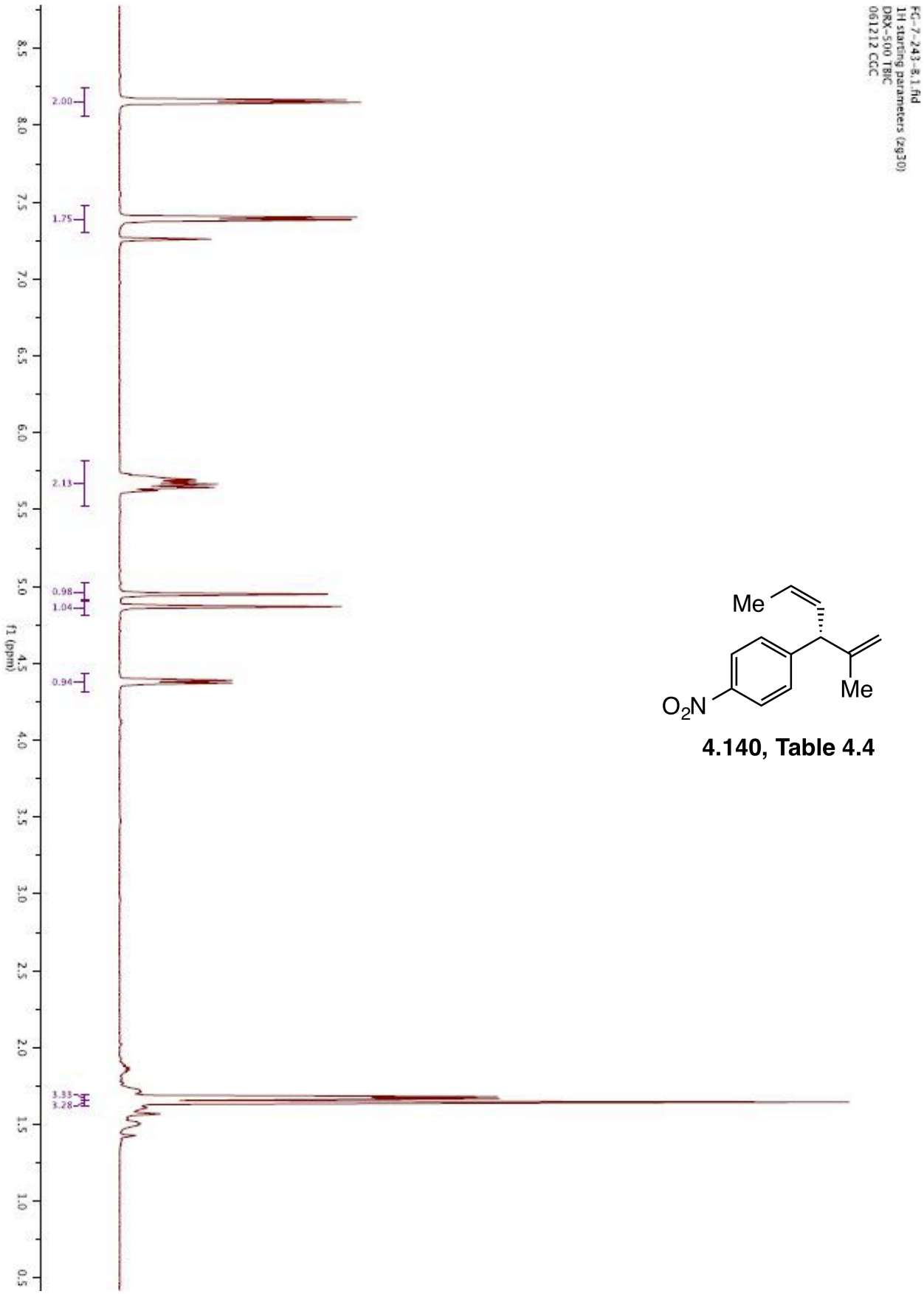


4.132, Table 4.4

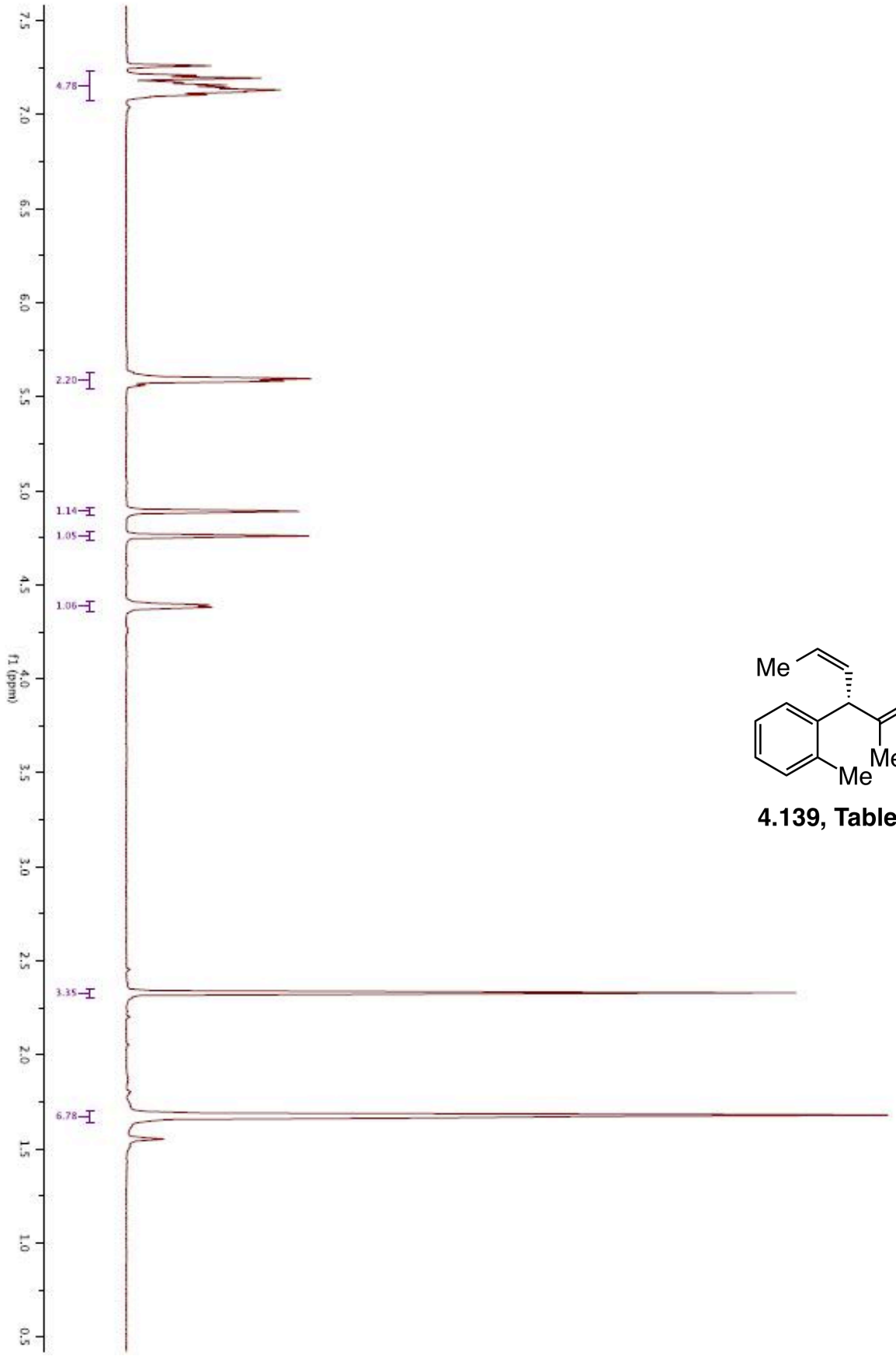

Sample: FG-VII-156-B-pdt
File: exp1.fid
Pulse Sequence: s2pul
date Sep 21 2012
solvent cdcl3
file exp
ACQUISITION
sw 8012.8
at 2.049
32830
np 4000
fb 4
bs 2
ss 1.000
d1 40
nt 8
ct
TRANSMITTER
tn H1
sfrq 499.884
tof 499.8
tpwr 59
pw 4.450
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 32258
SPECIAL
temp 25.0
gain not used
spin 20
hst 0.008
pw90 8.900
alfa 10.000
FLAGS
il n
in n
dp y
hs nn
PROCESSING
fn 65536
DISPLAY
sp 22.5
wp 3961.2
rfl 4635.6
rfp 3629.1
rp -175.3
lp 0
PLOT
wc 250
sc 0
vs 191
th 12
ph
al
Me
4.134, Table 4.4
4.07
1.00
1.05
1.03
2.22
1.04
3.53
3.34
7
6
5
4
3
2
1
ppm

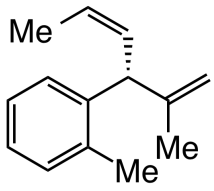


4.138, Table 4.4

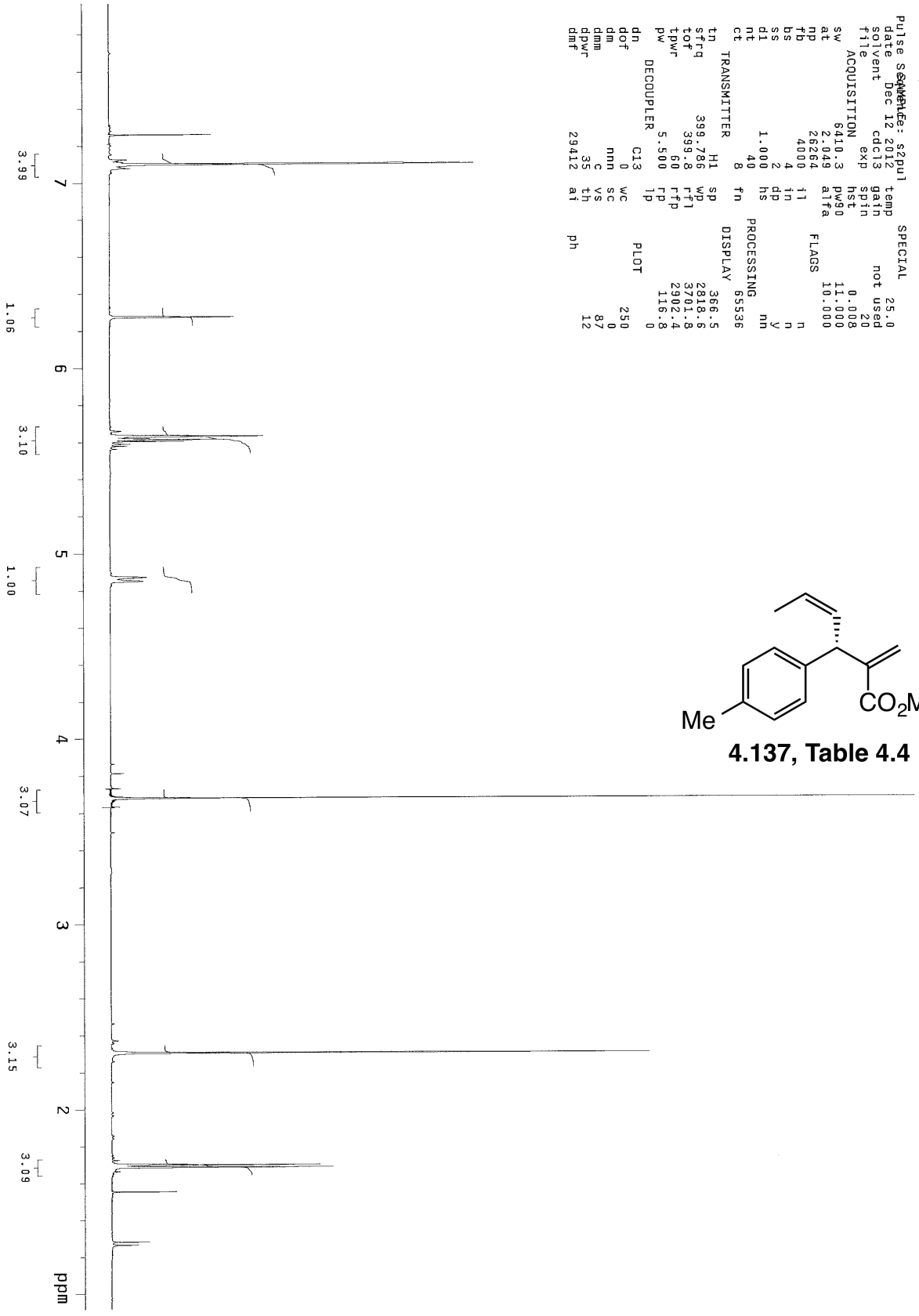


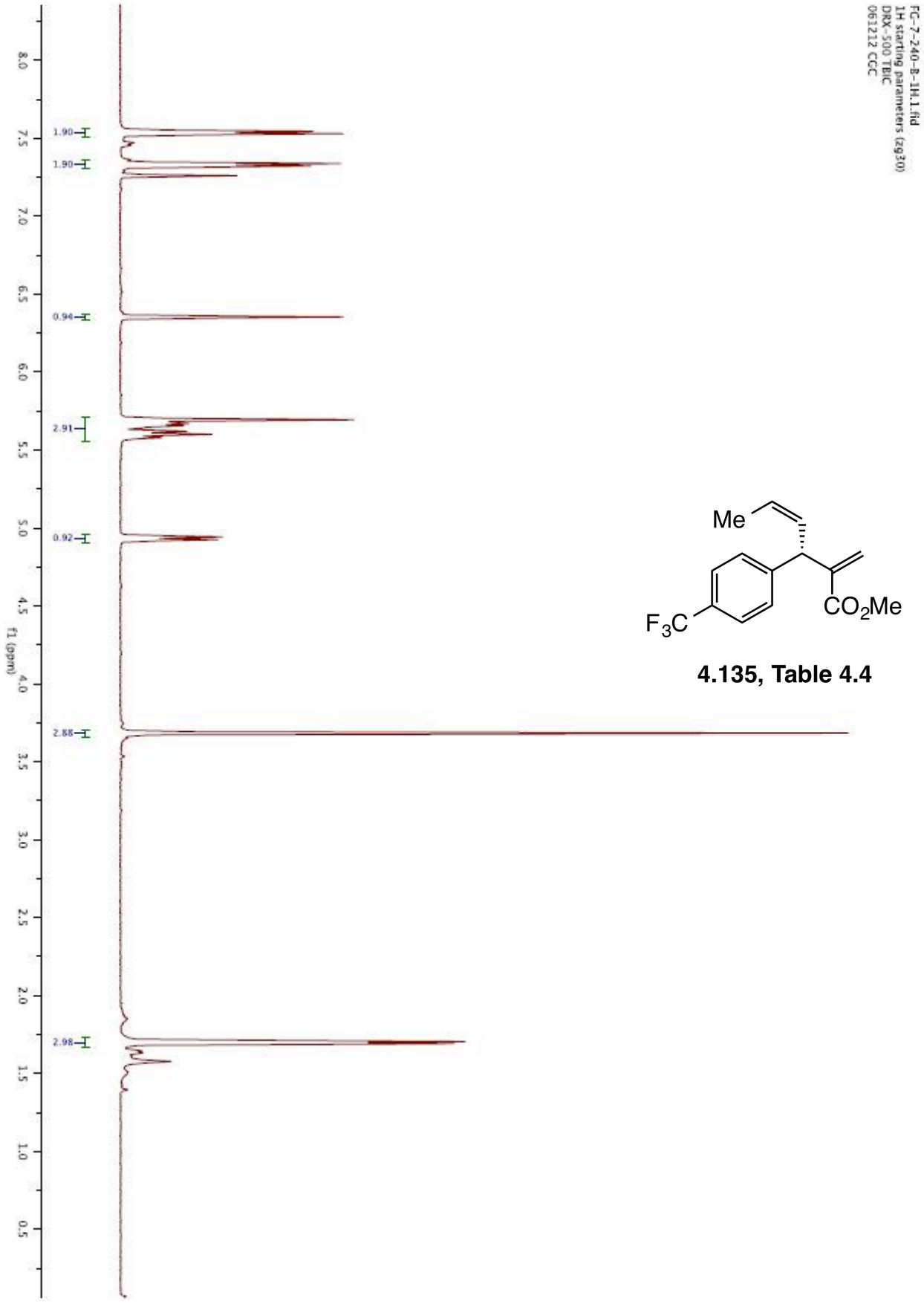
4.140, Table 4.4



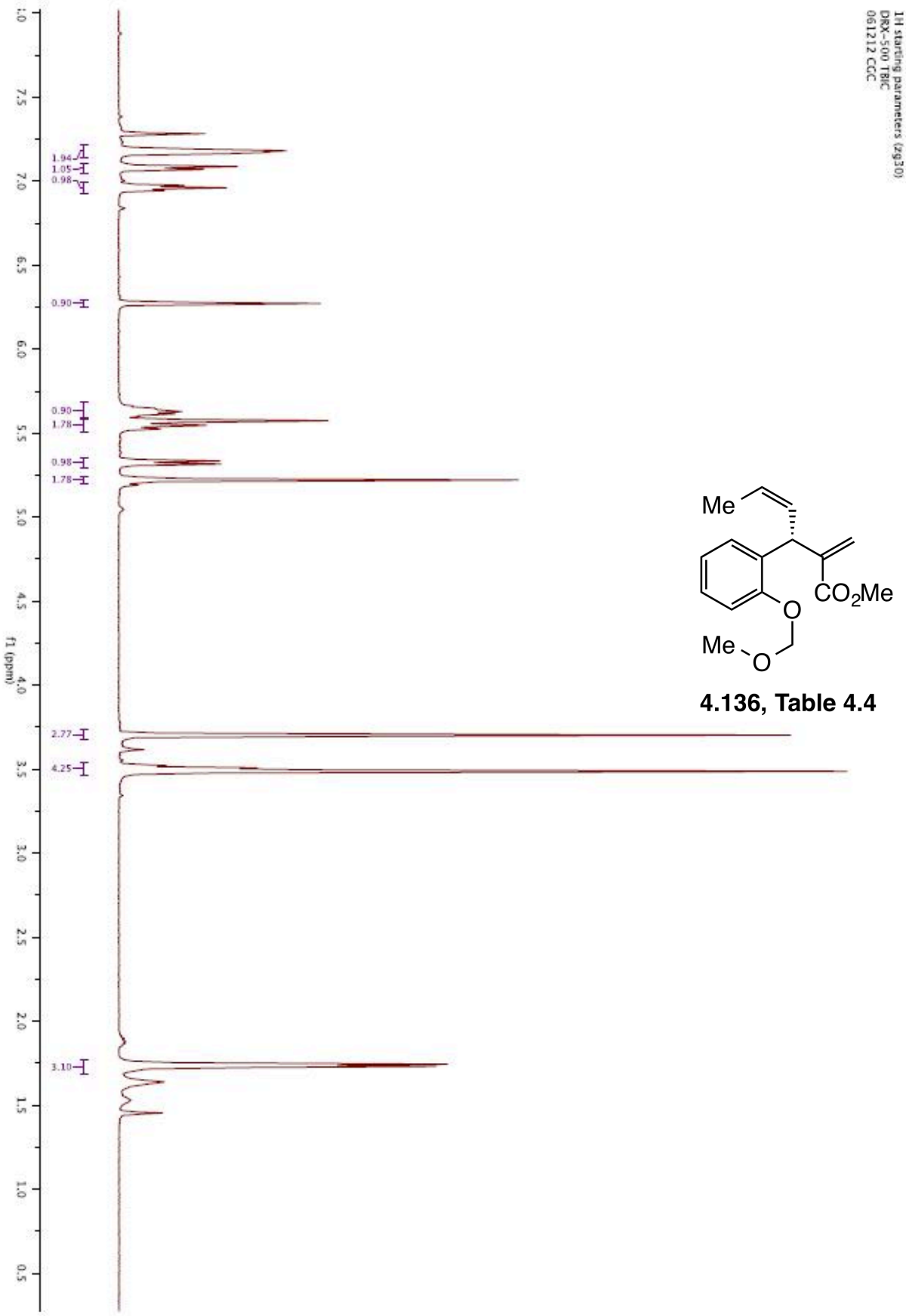


4.139, Table 4.4

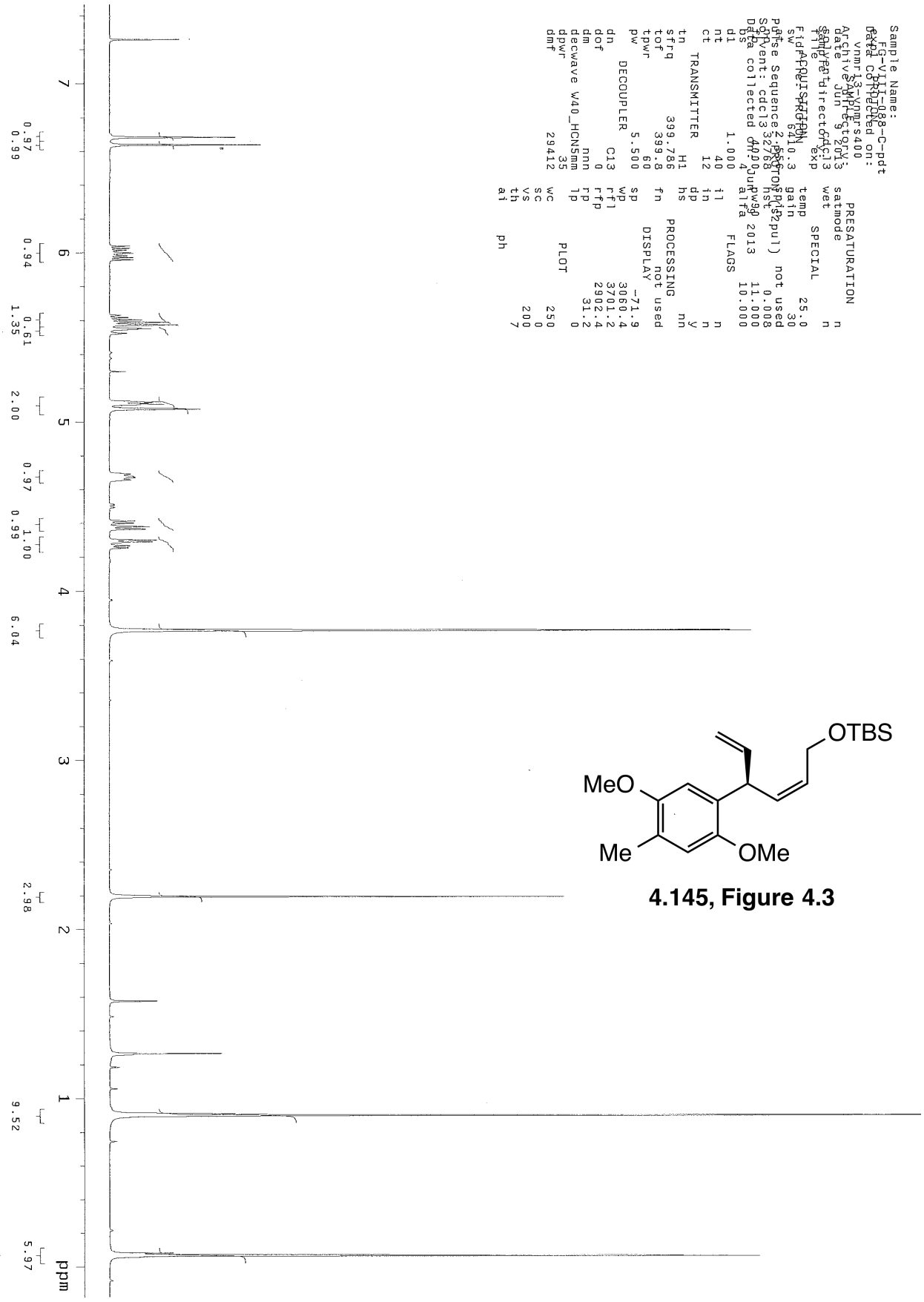

Sample: FG-VII-219-A-pdt
Exp: 1Sexp Proton
Pulse Sequence: s2pul SPECIAL
date Dec 12 2012 temp 25.0
solvent cdcl3 gain not used
file exp spin 20
ACQUISITION hst 0.008
6410.3 pw90 11.000
sw 2.049 alfa 10.000
at 26264 FLAGS
np 4000 il n
fb 4 in n
bs 2 dp y
ss 1.000 hs nn
d1 PROCESSING
nt 40 lb 65536
ct 8 fn DISPLAY
TRANSMITTER 366.5
tn H1 sp 2818.6
sfrq 399.786 wp 3701.8
tof 399.8 rfl 2902.4
tpwr 60 rfp 116.8
pw 5.500 rp 0
DECOUPLER lp
dn C13 PLOT
dof 0 wc 250
dm nnn sc 0
dmm c vs 87
dpwr 35 th 12
dmf 29412 ai
ph
3.99
1.06
3.10
1.00
3.07
3.15
3.09
7
6
5
4
3
2
ppm
Me
CO2Me
4.137, Table 4.4



4.135, Table 4.4



4.136, Table 4.4



4.145, Figure 4.3

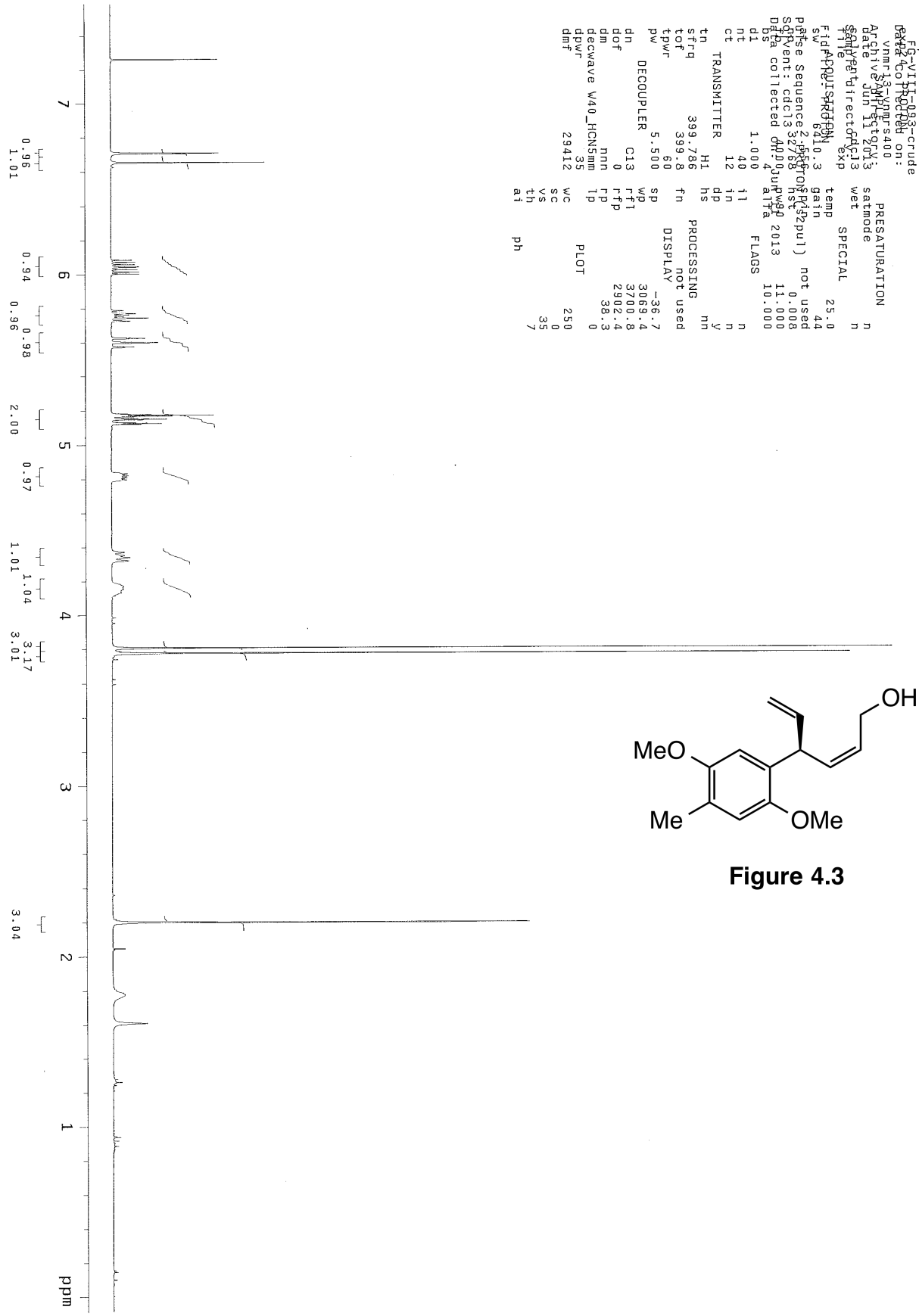
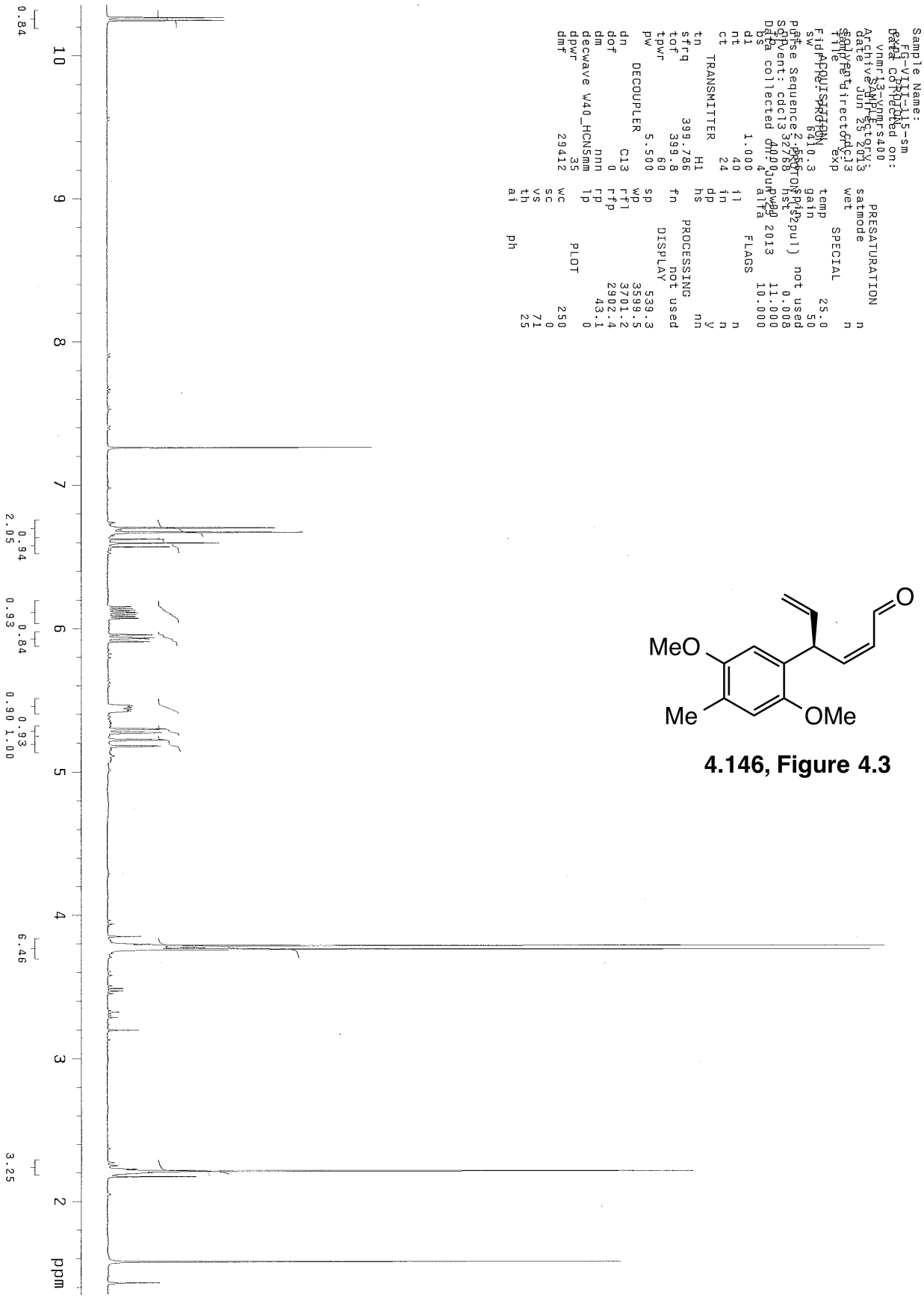
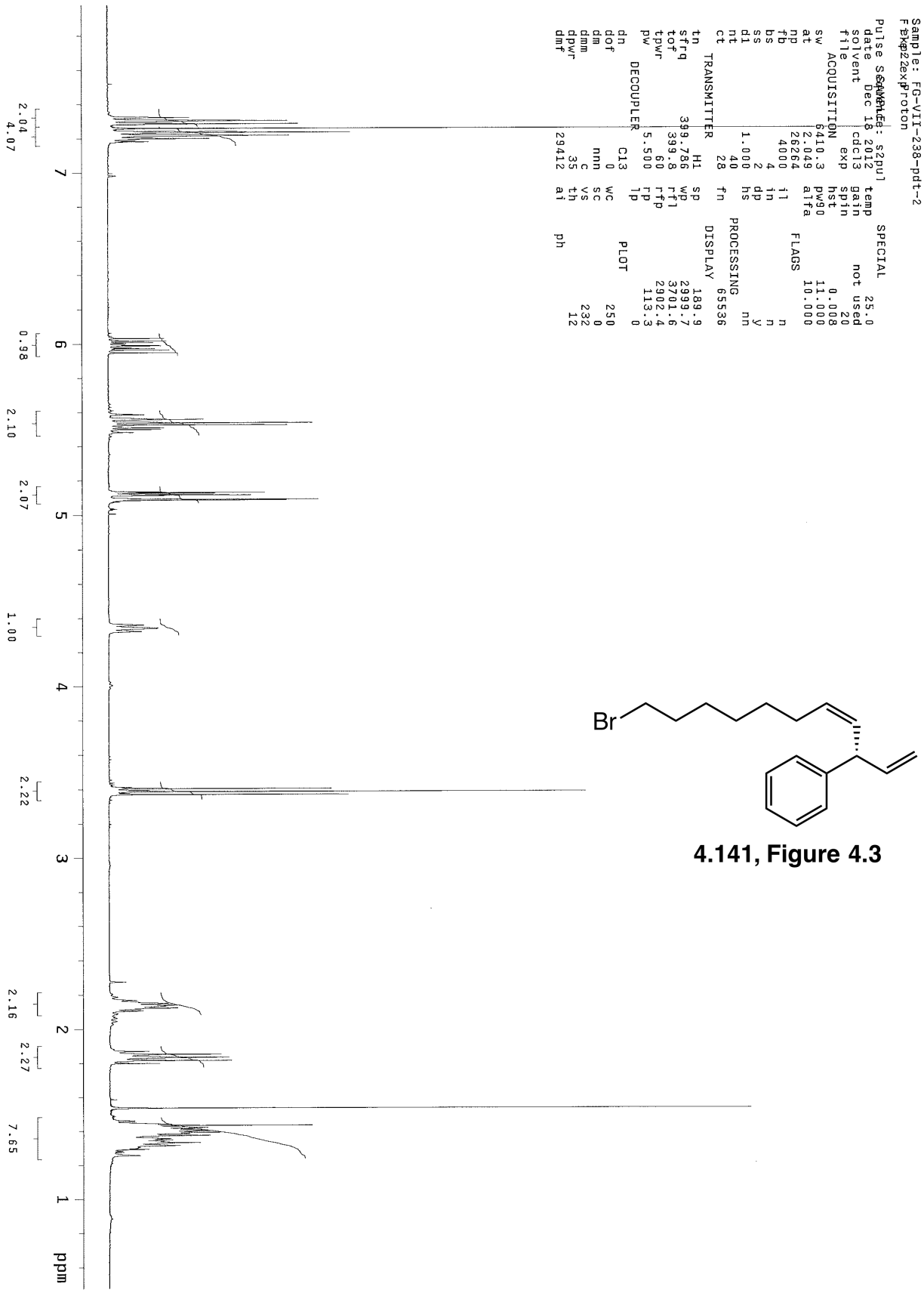

Sample Name:
FG_VIII-109-3-crude
Data Collected on:
vnmrs400
Archive directory:
Jun 11 2013
exp
cdcl3
PRESATURATION
n
wet
n
SPECIAL
25.0
44
temp
gain
not used
0.008
11.000
10.000
FLAGS
n
n
y
nn
PROCESSING
not used
DISPLAY
-36.7
3069.4
3700.8
2902.4
38.3
0
250
0
35
7
ph
OH
MeO
Me
OMe
7
6
5
4
3
2
1
ppm
0.96
1.01
0.94
0.96
0.98
2.00
0.97
1.01
1.04
3.17
3.01
3.04

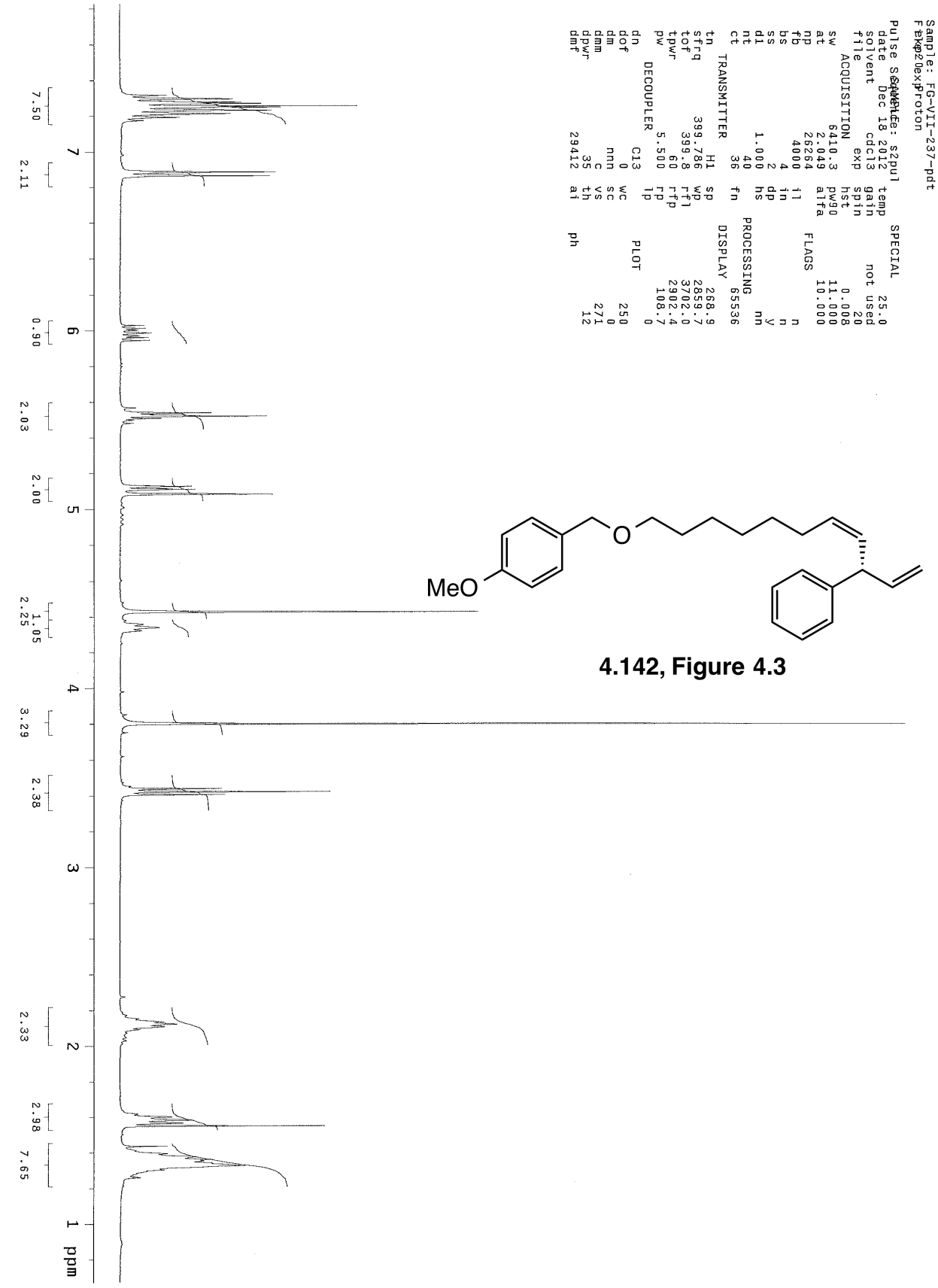
Figure 4.3



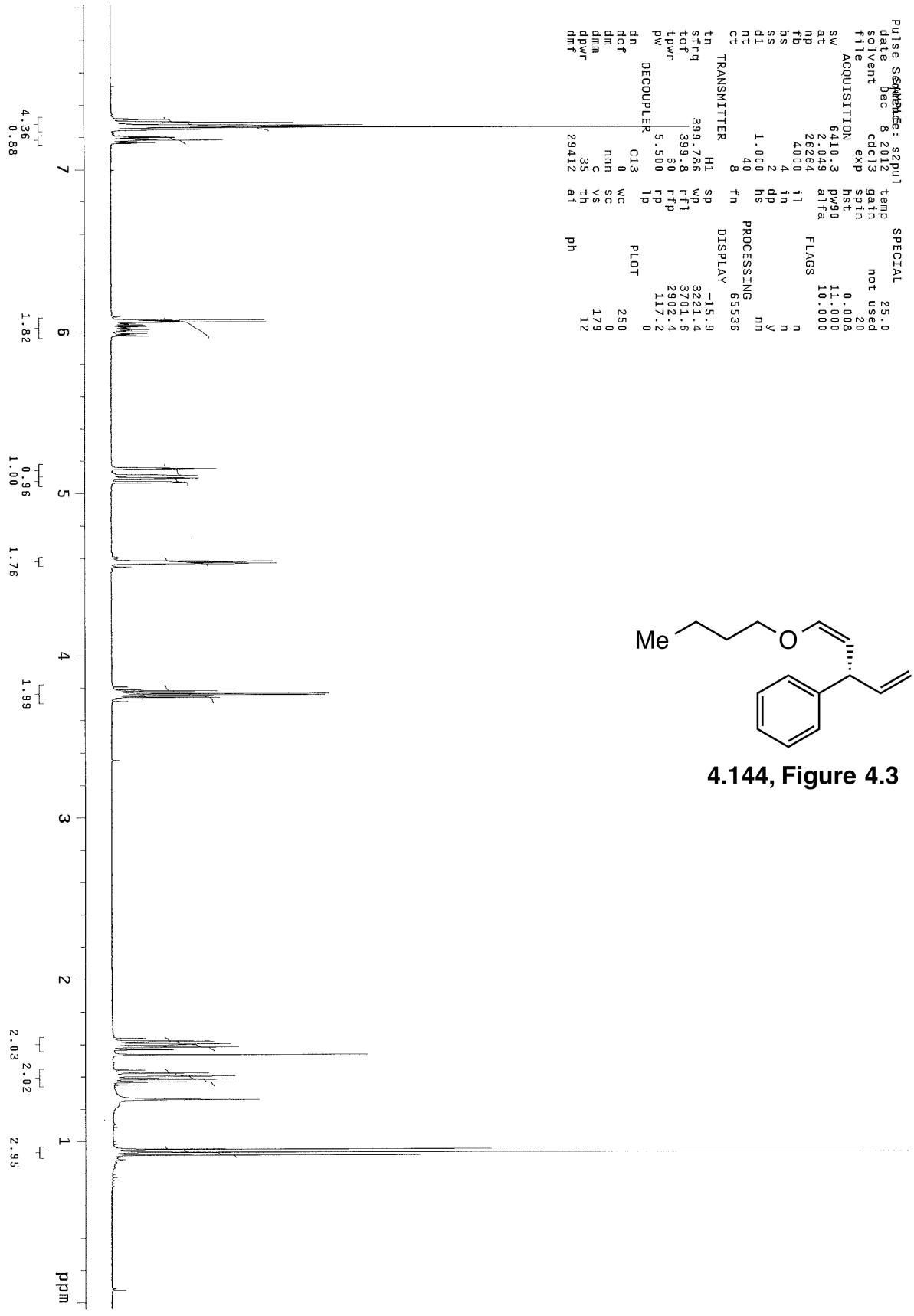
4.146, Figure 4.3



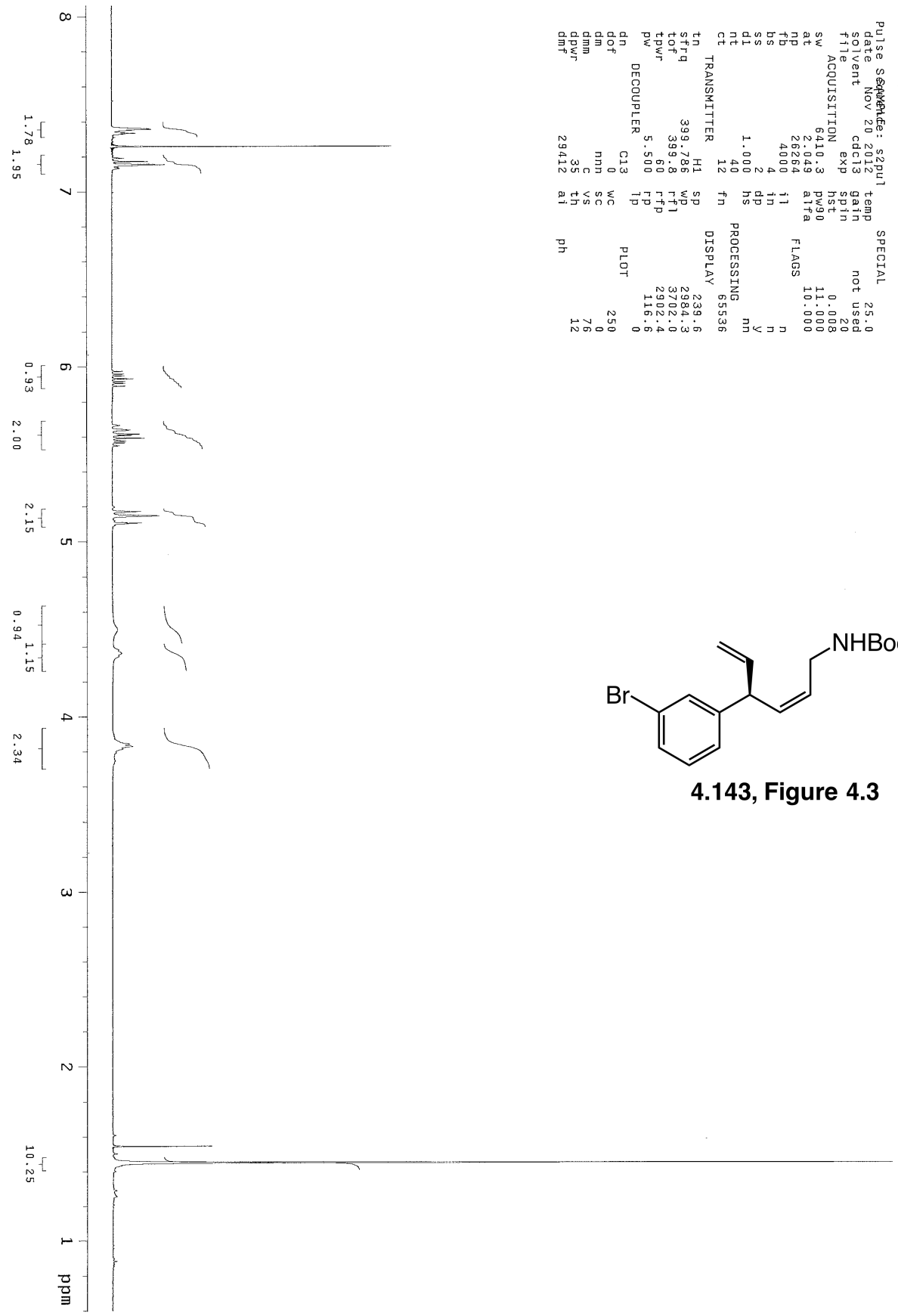
4.141, Figure 4.3



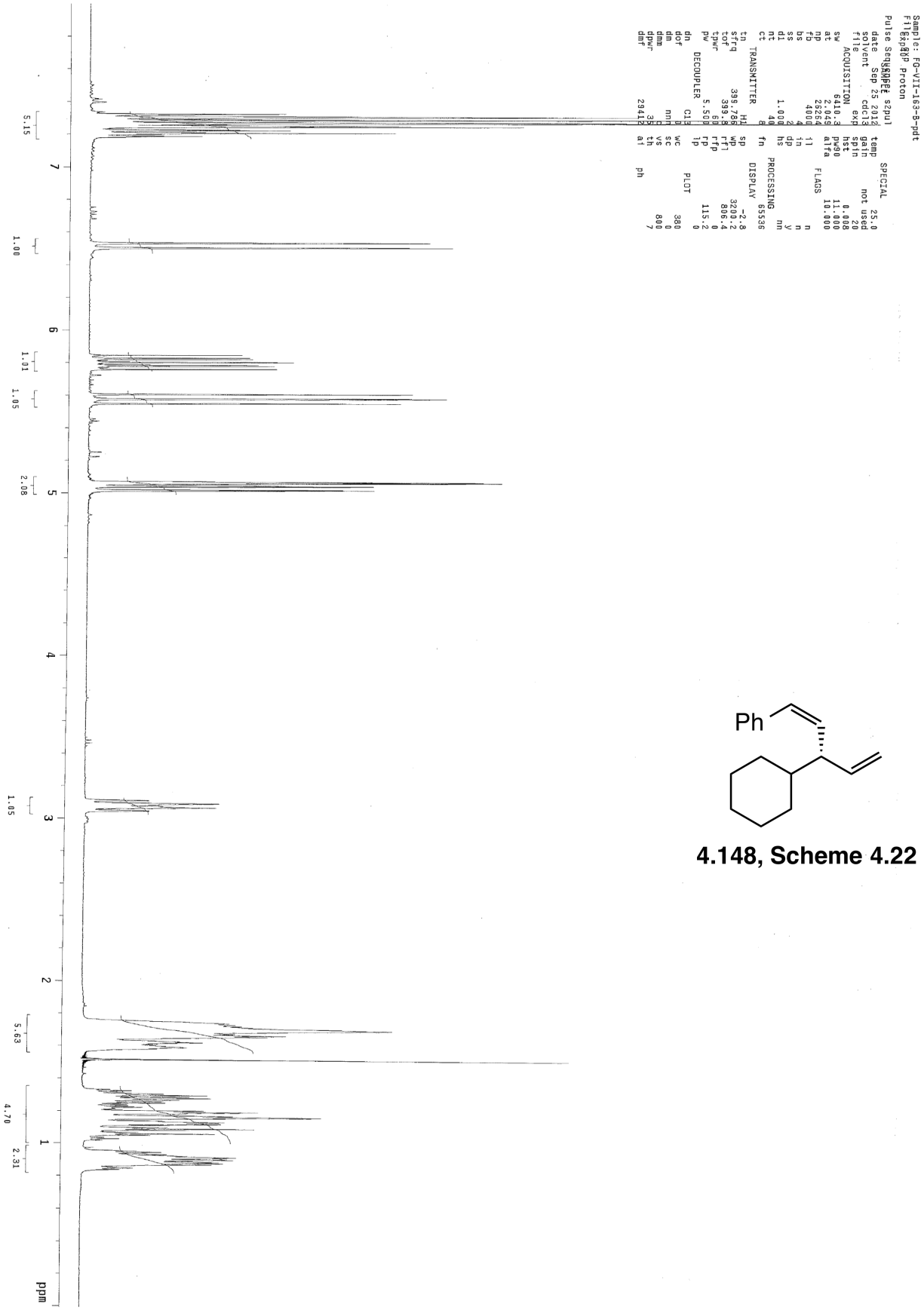
4.142, Figure 4.3



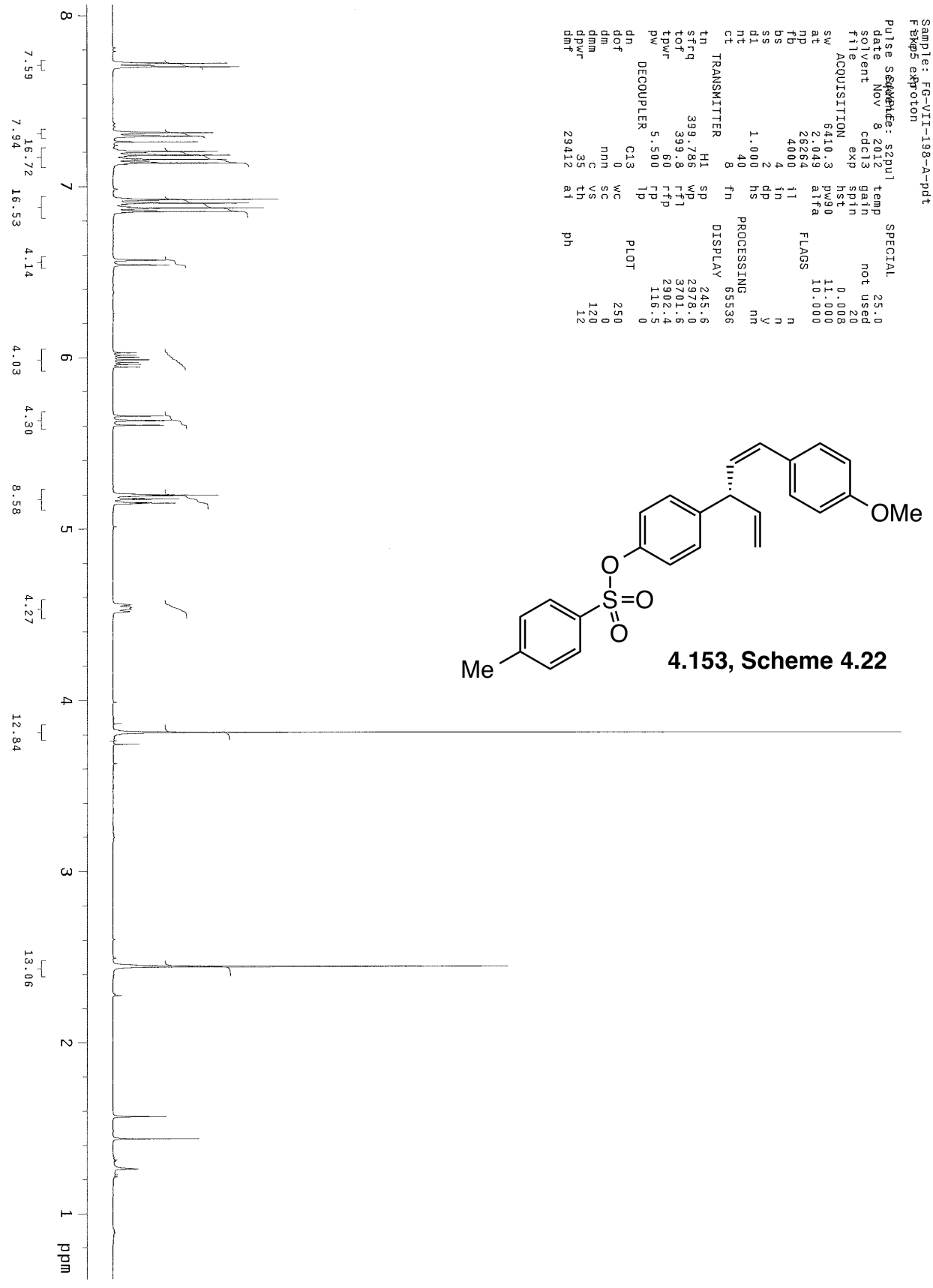
4.144, Figure 4.3

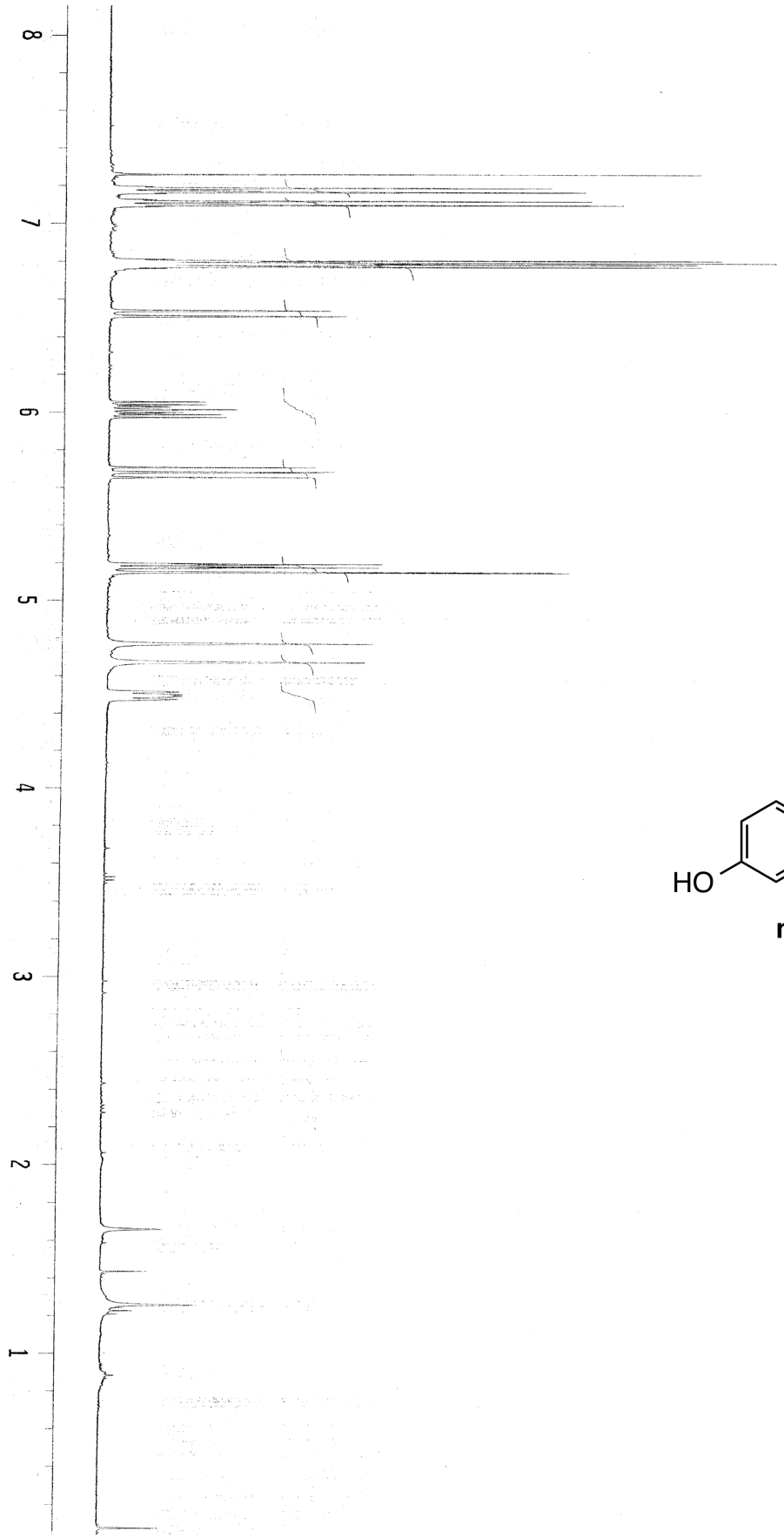


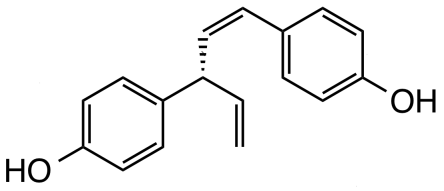
4.143, Figure 4.3



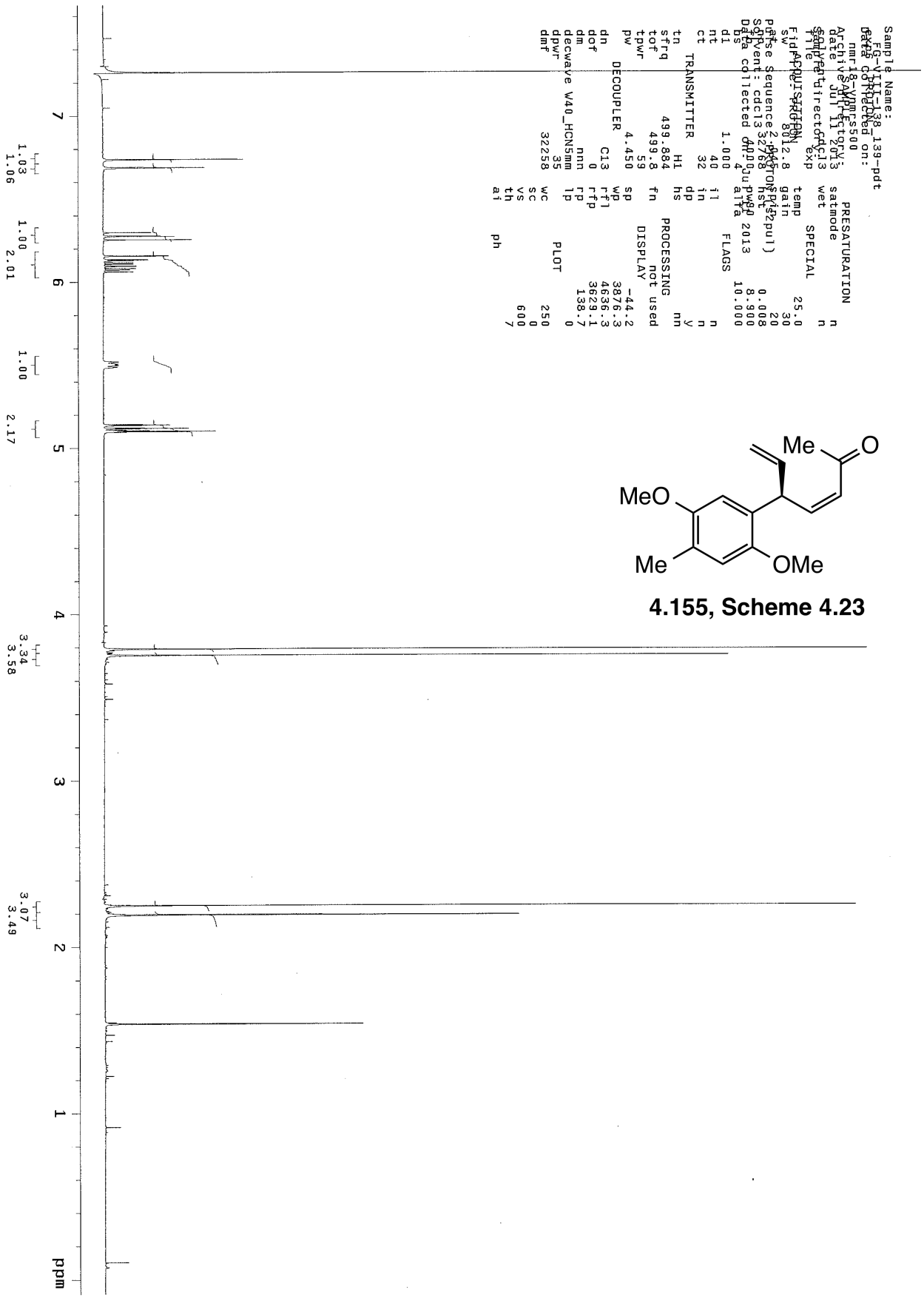
4.148, Scheme 4.22


Sample: FG-VII-198-A-pdt
Exp5 exp1proton
Pulse Sequence: s2pul
date Nov 8 2012
solvent cdcl3
file
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4000
bs 4
ss 2
d1 1.000
nt 40
ct 8
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
SPECIAL
temp 25.0
gain not used
spin 20
hst 0.008
pw90 11.000
alfa 10.000
FLAGS
il n
in n
dp y
hs nn
PROCESSING
fn 65536
DISPLAY
sp 245.6
wp 2978.0
rfl 3701.6
rfp 2902.4
rp 116.5
lp 0
PLOT
wc 250
sc 0
vs 120
th 12
ai
ph
OMe
O
S
O
O
Me
4.153, Scheme 4.22
8
7
6
5
4
3
2
1
ppm
7.59
16.72
7.94
16.53
4.14
4.03
4.30
8.58
4.27
12.84
13.06

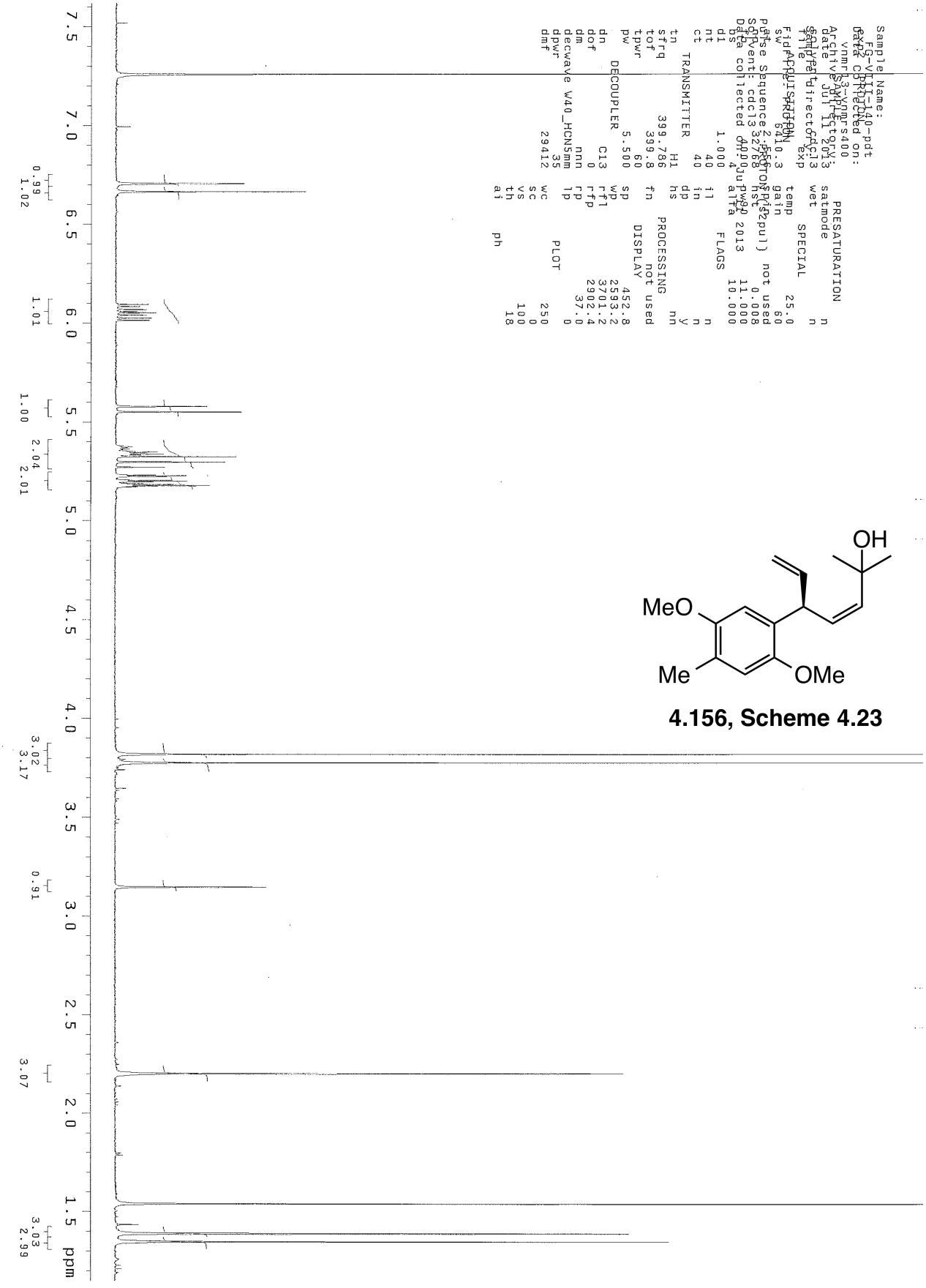




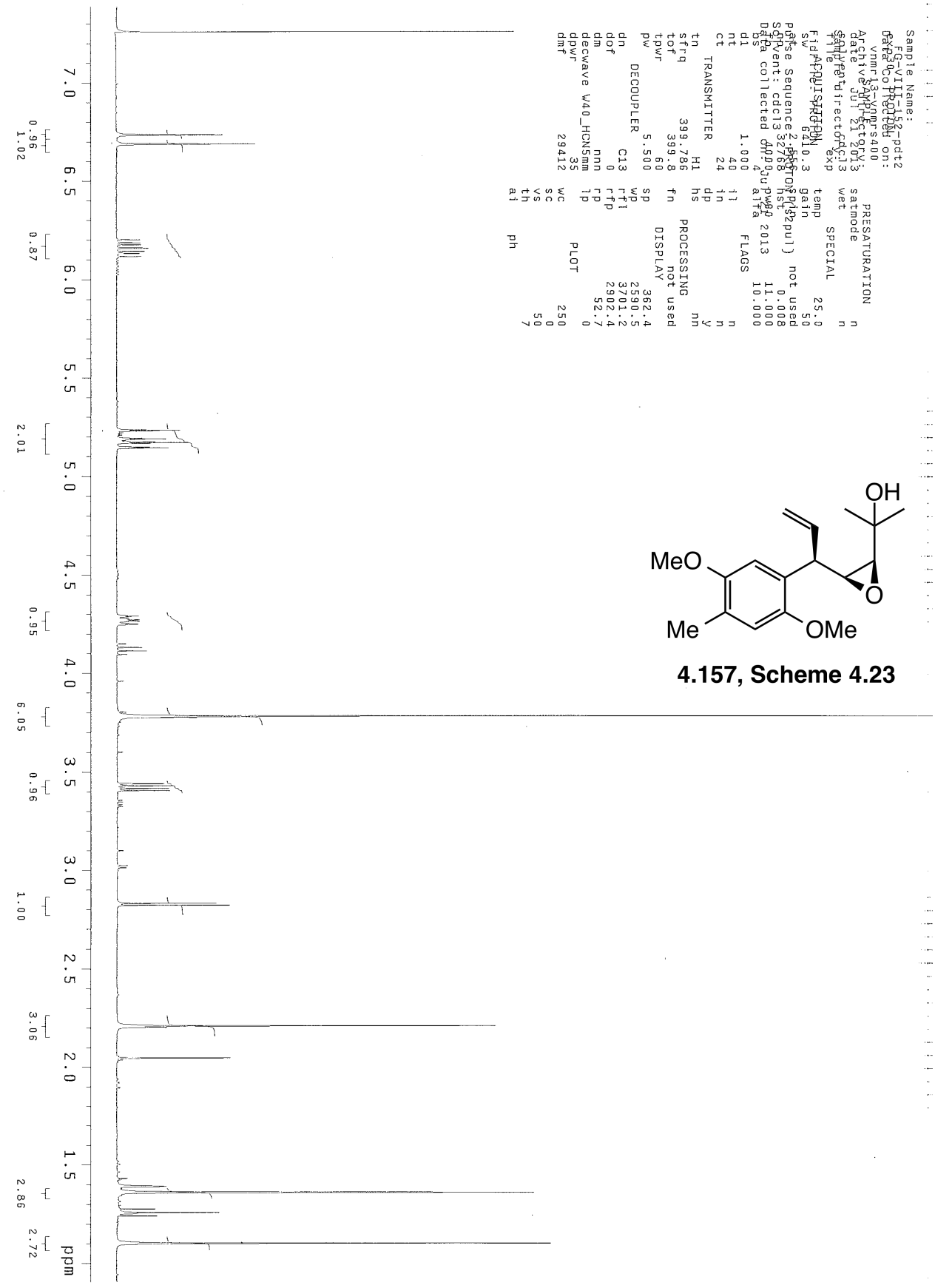
nyasol, Scheme 4.22



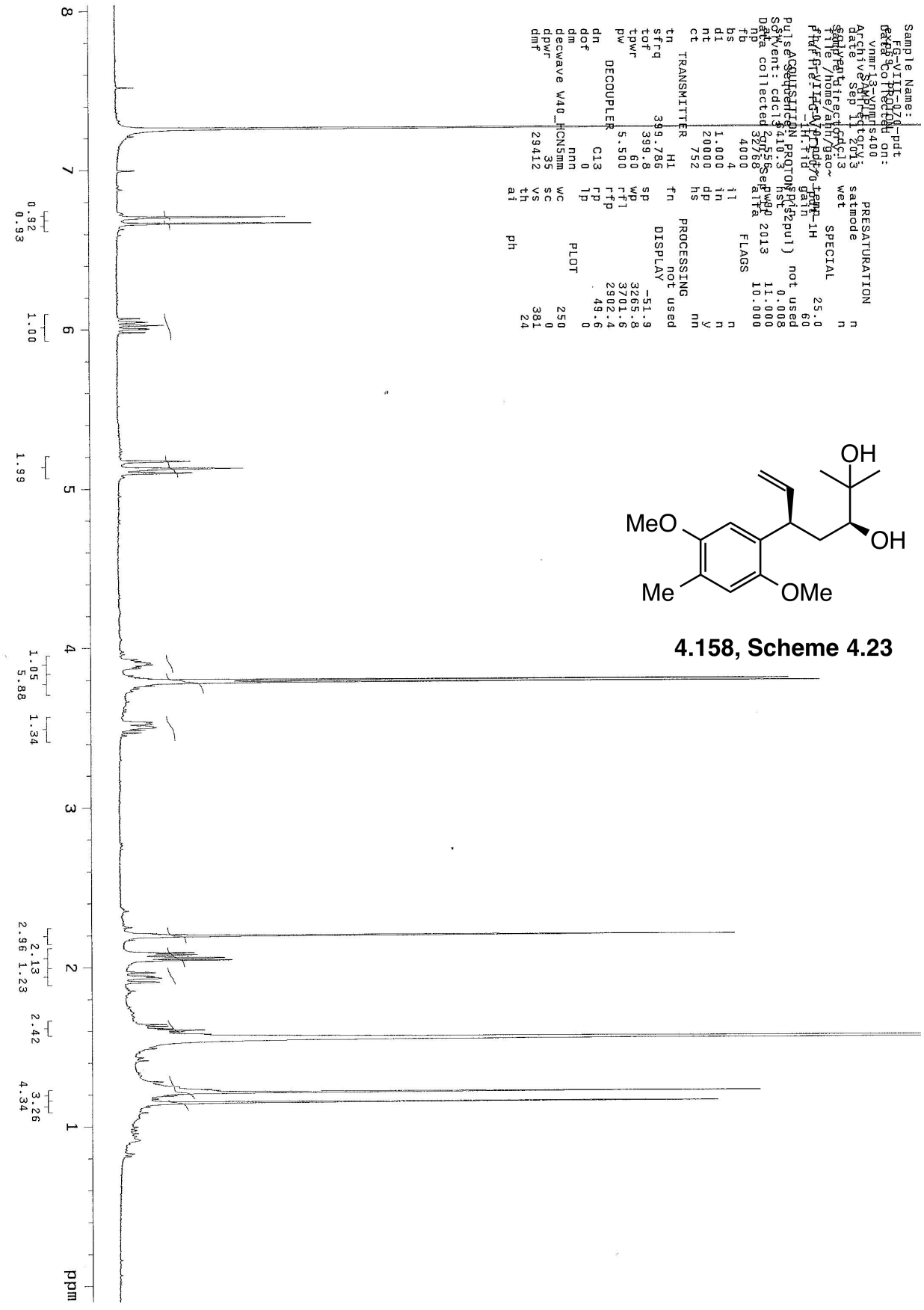
4.155, Scheme 4.23



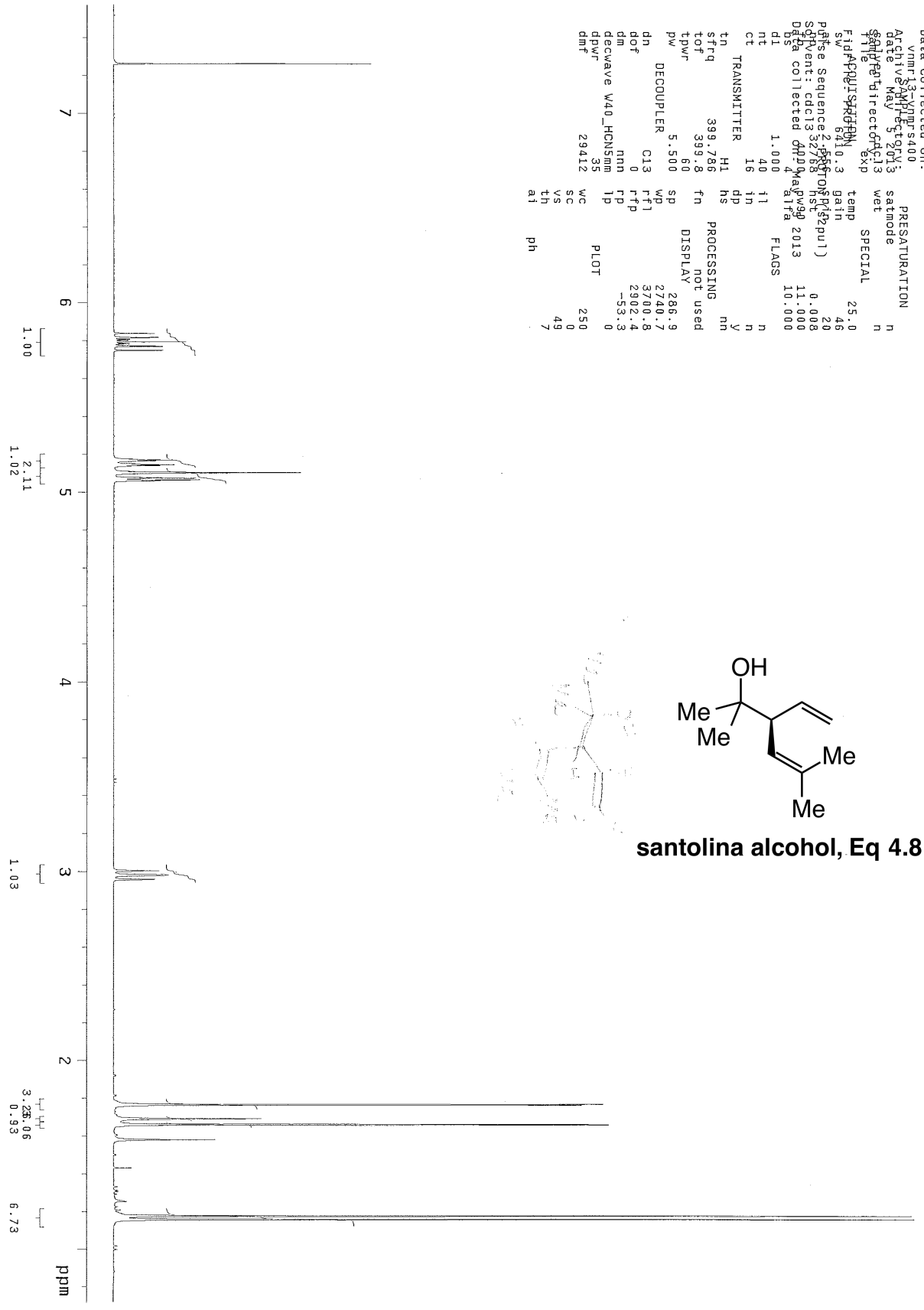
4.156, Scheme 4.23



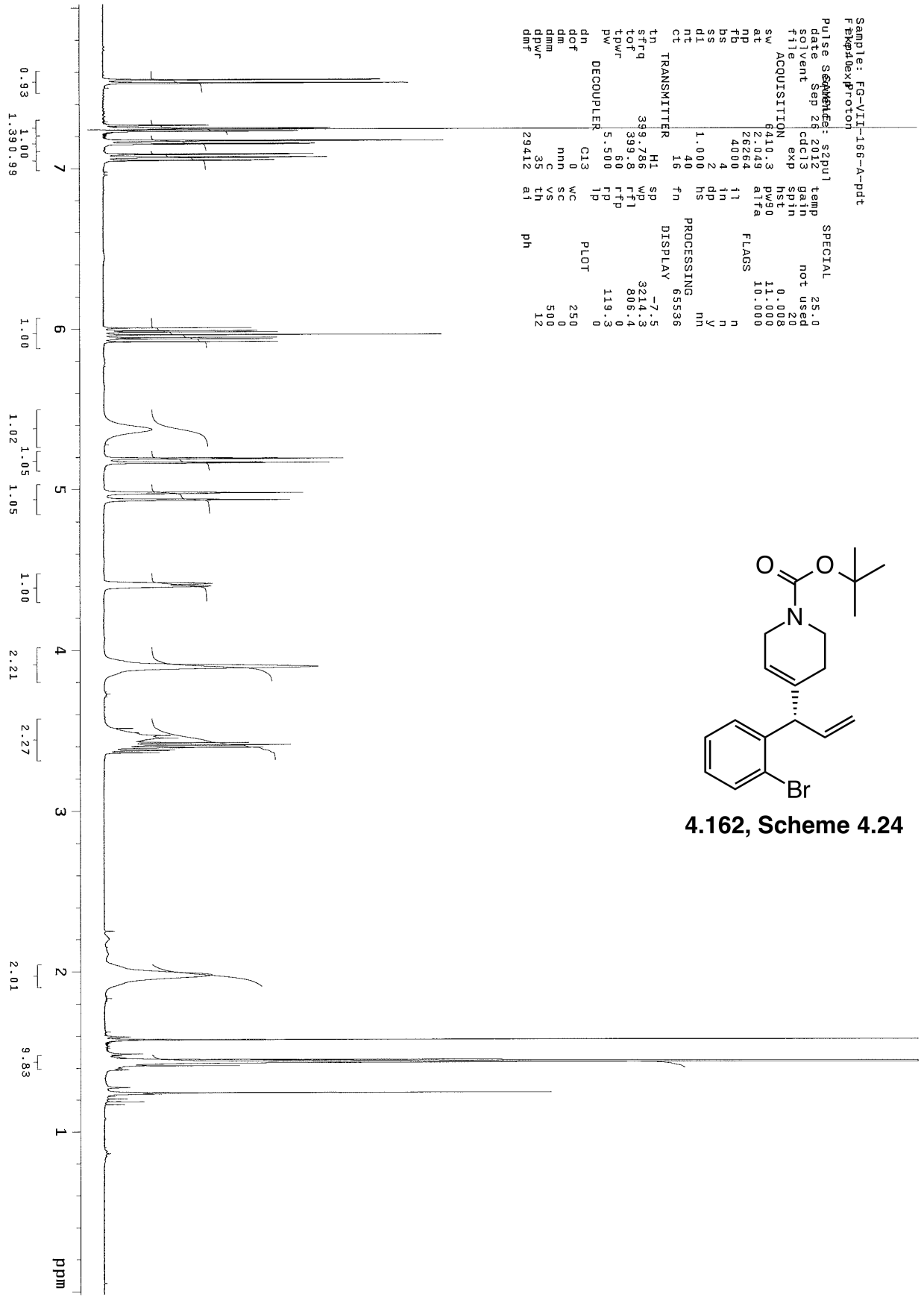
4.157, Scheme 4.23



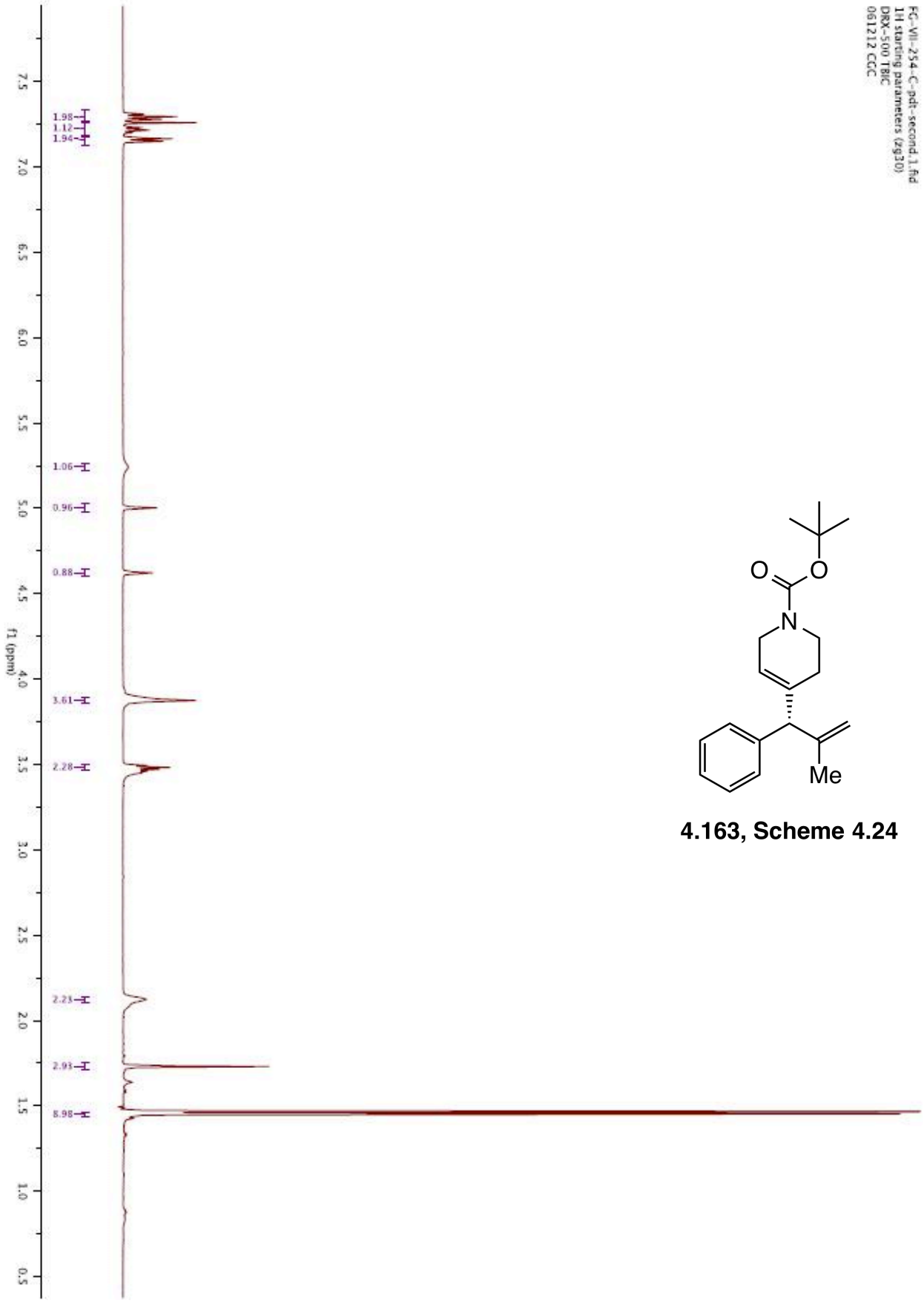
4.158, Scheme 4.23



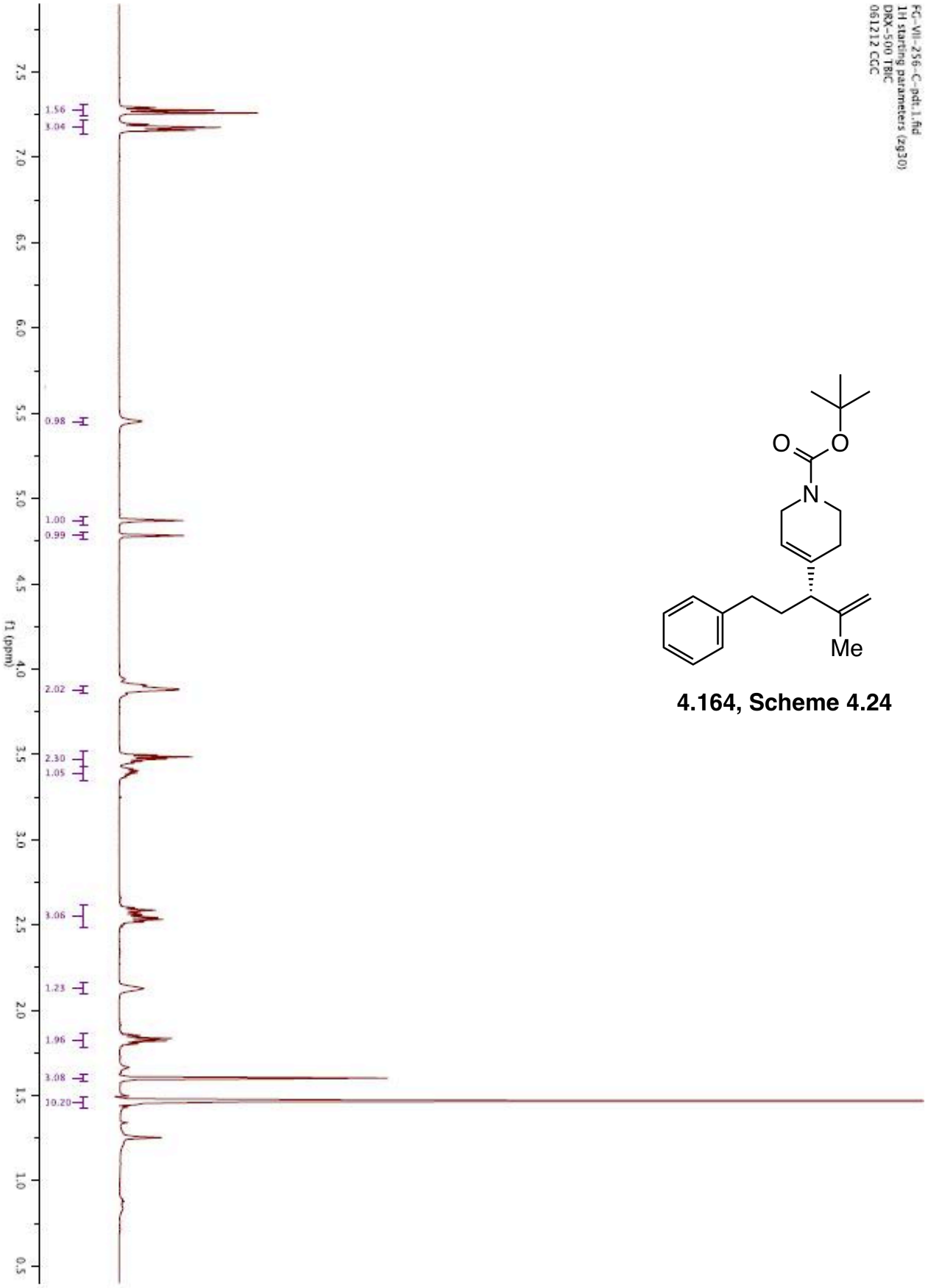
santolina alcohol, Eq 4.8



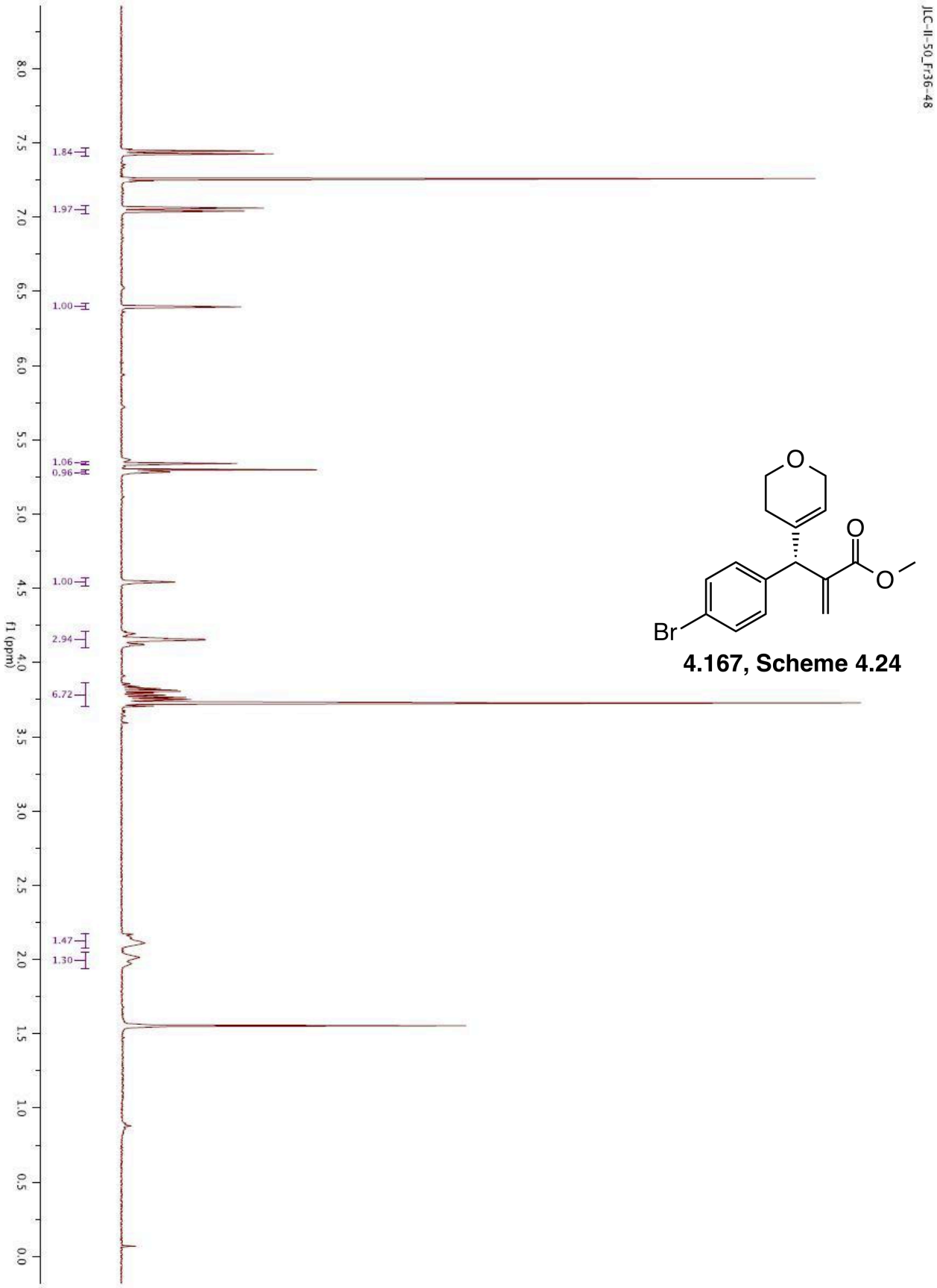
4.162, Scheme 4.24



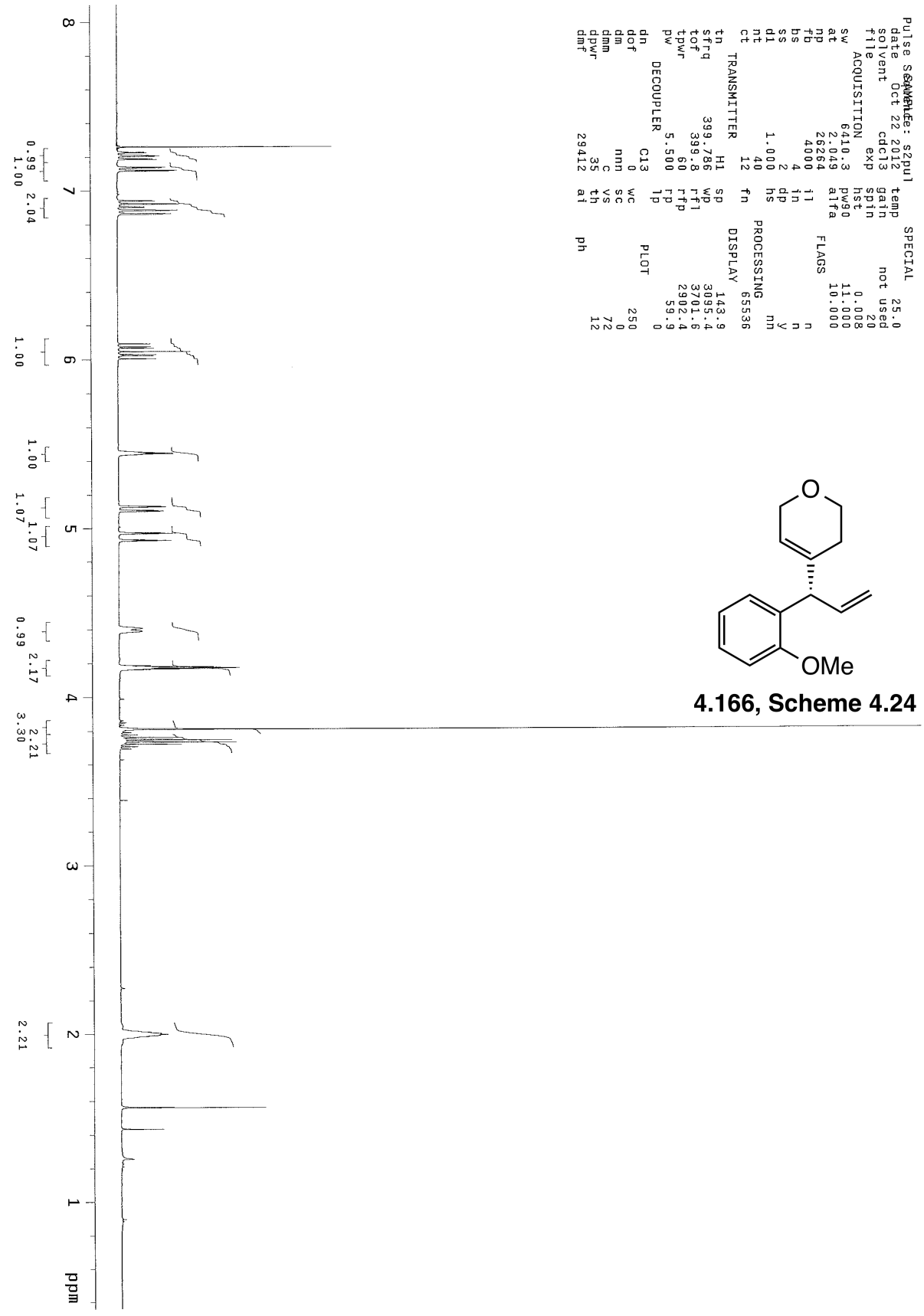
4.163, Scheme 4.24

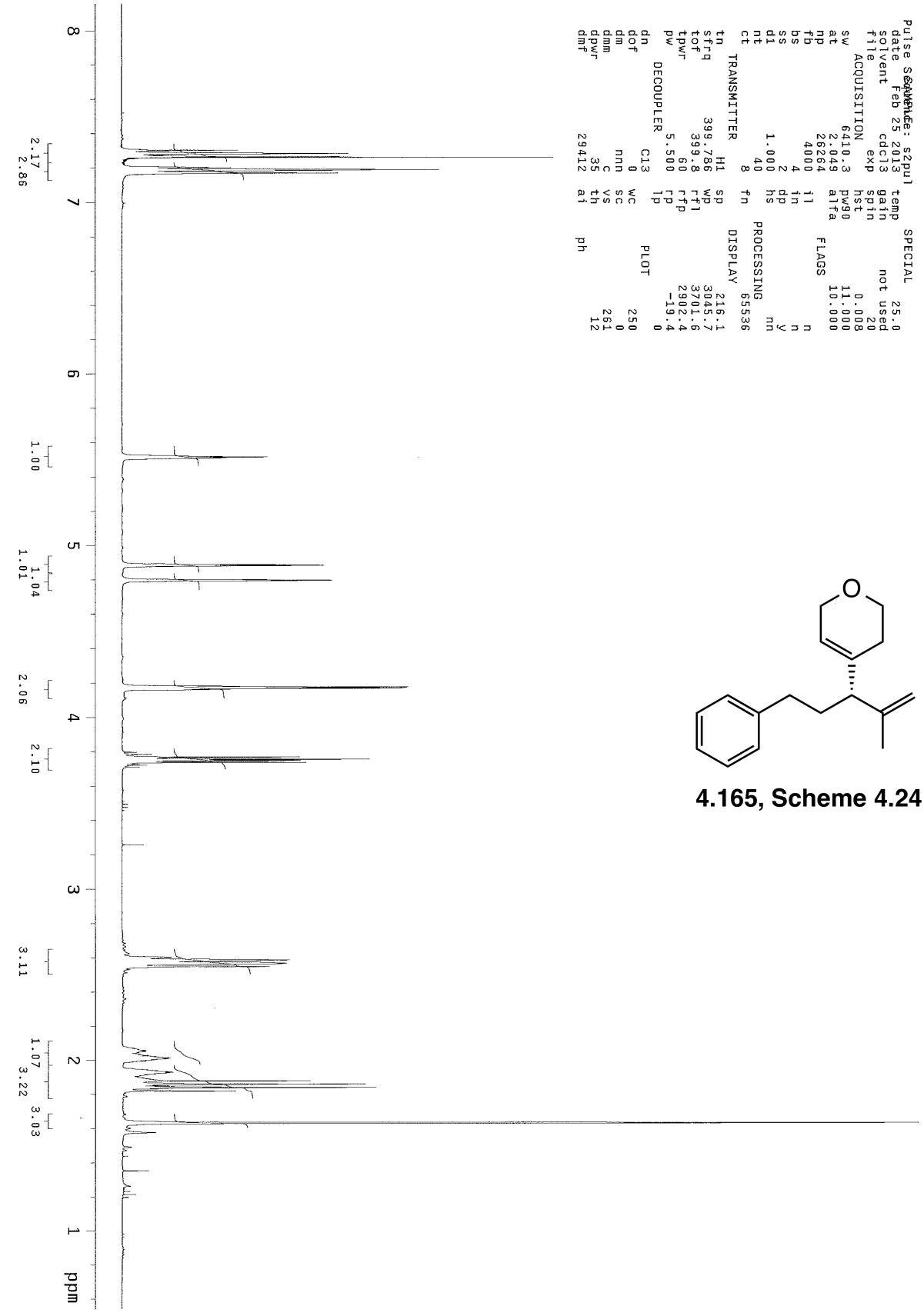


4.164, Scheme 4.24

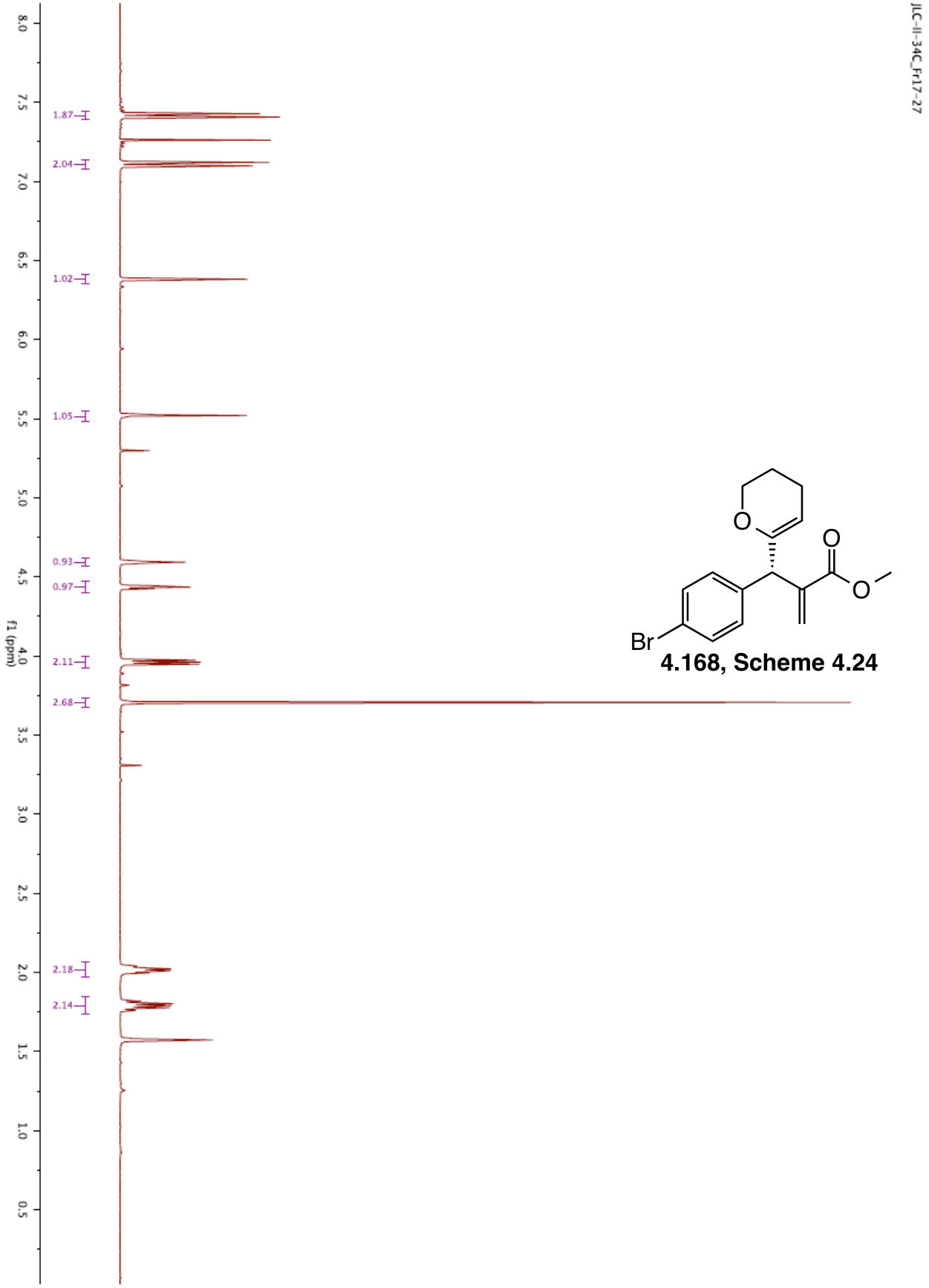


4.167, Scheme 4.24

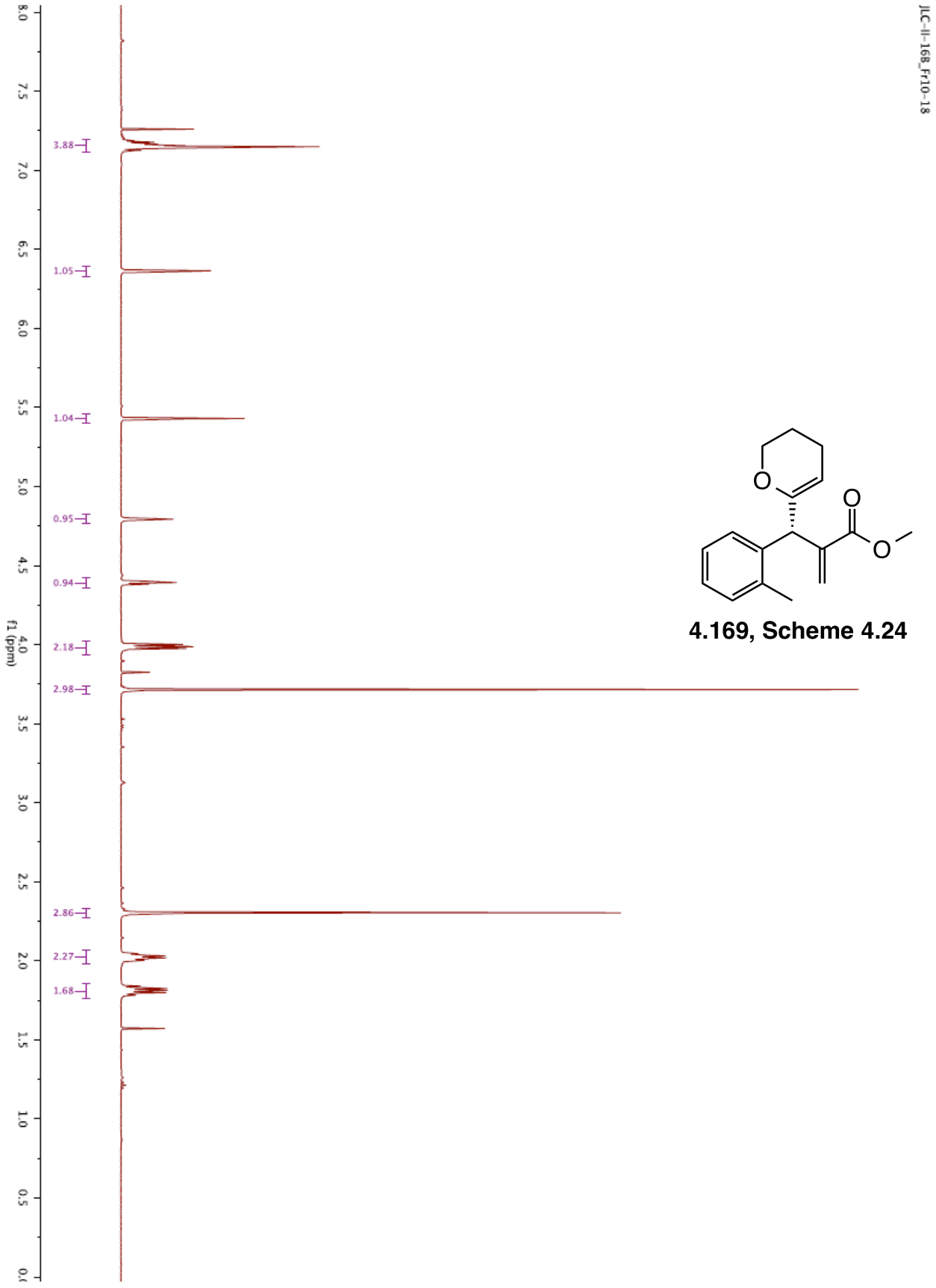

Sample: FG-VII-192-B-pdt
Exp1 exp proton
Pulse Sequence: s2pul SPECIAL
date Oct 22 2012 temp 25.0
solvent cdcl3 gain not used
file exp spin 20
ACQUISITION hst 0.008
sw 6410.3 pw90 11.000
at 2.049 alfa 10.000
np 26264 FLAGS
fb 4000 il n
bs 4 in n
ss 2 dp y
d1 1.000 hs nn
nt 40 PROCESSING
ct 12 fn 65536
TRANSMITTER DISPLAY
tn H1 sp 143.9
sfrq 399.786 wp 3095.4
tof 399.8 rfl 3701.6
tpwr 60 rfp 2902.4
pw 5.500 rp 59.9
DECOUPLER lp 0
dn C13 PLOT
dof 0 wc 250
dm nnn sc 0
dmm c vs 72
dpwr 35 th 12
dmf 29412 al
ph
O
OMe
4.166, Scheme 4.24
8
7
6
5
4
3
2
1
ppm
0.99
2.04
1.00
1.00
1.00
1.07
1.07
0.99
2.17
2.21
3.30
2.21



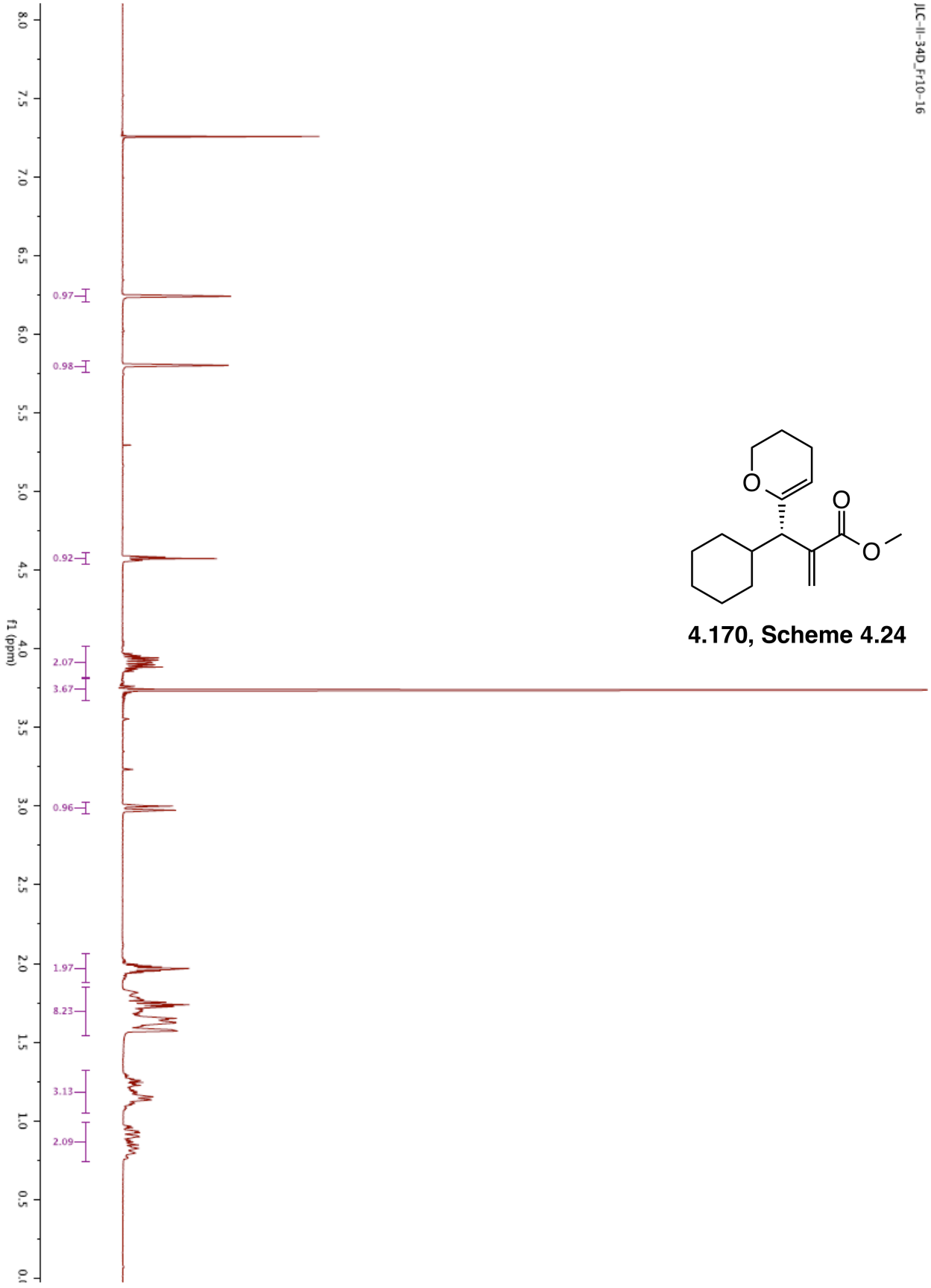
4.165, Scheme 4.24



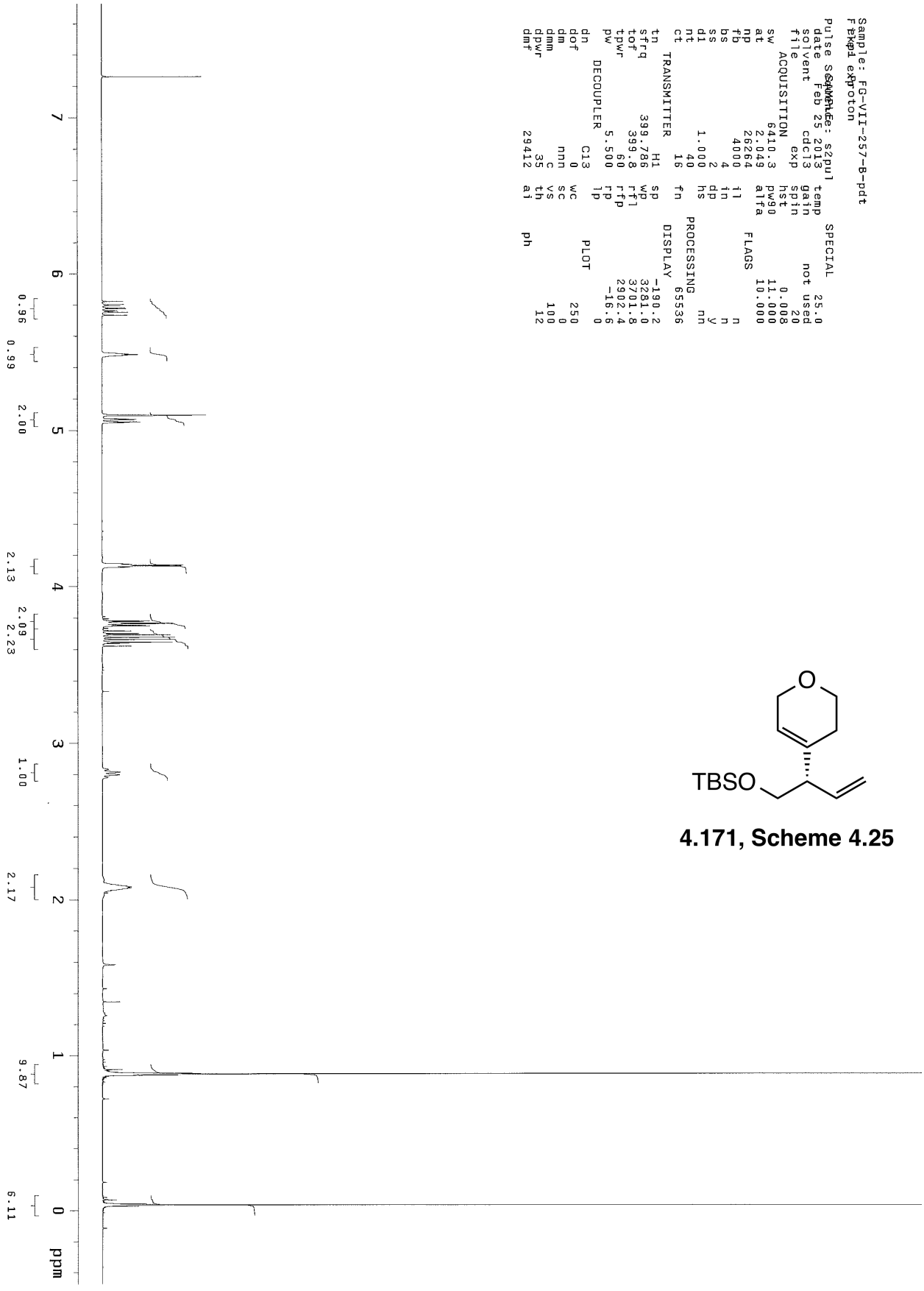
4.168, Scheme 4.24



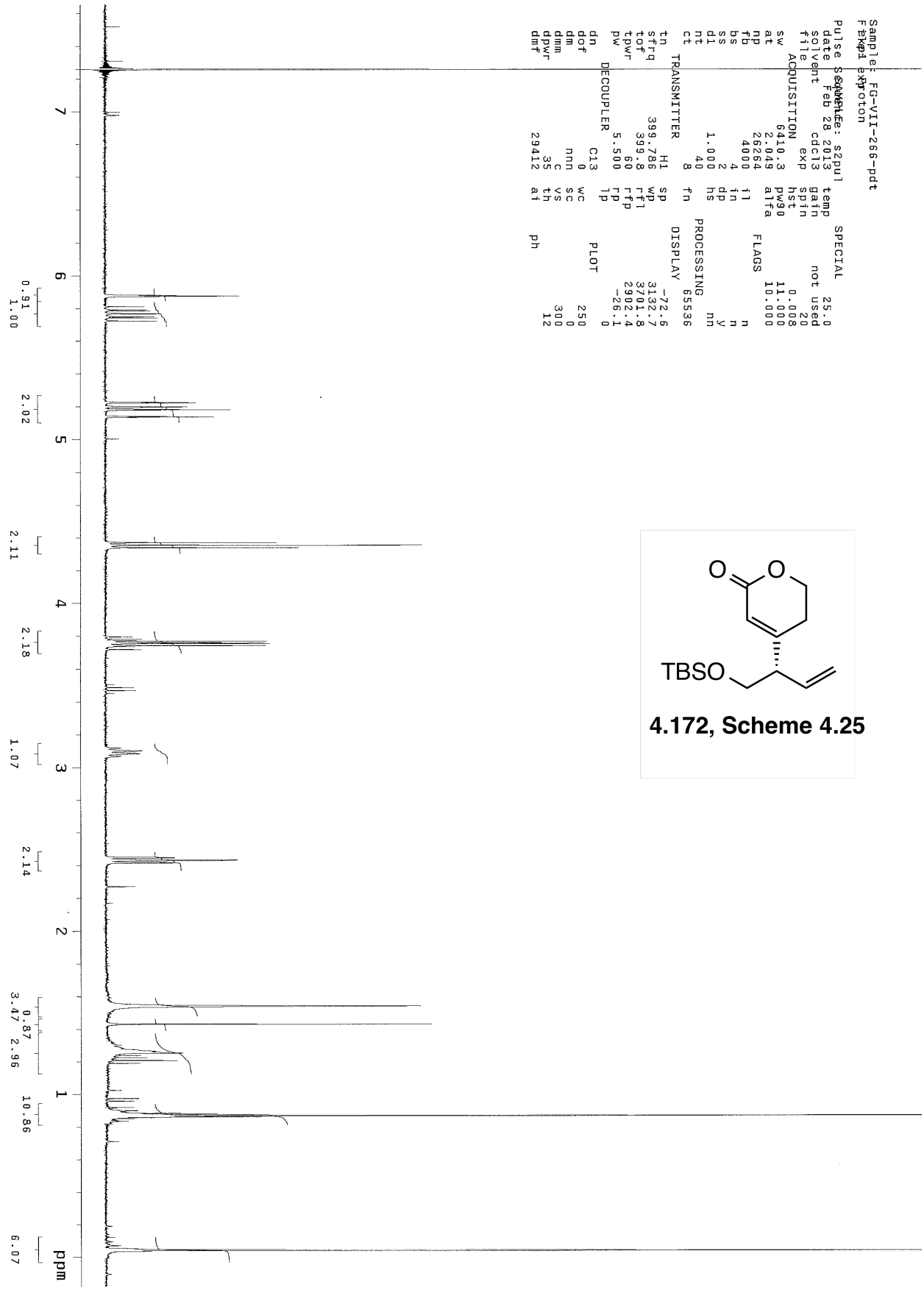
4.169, Scheme 4.24

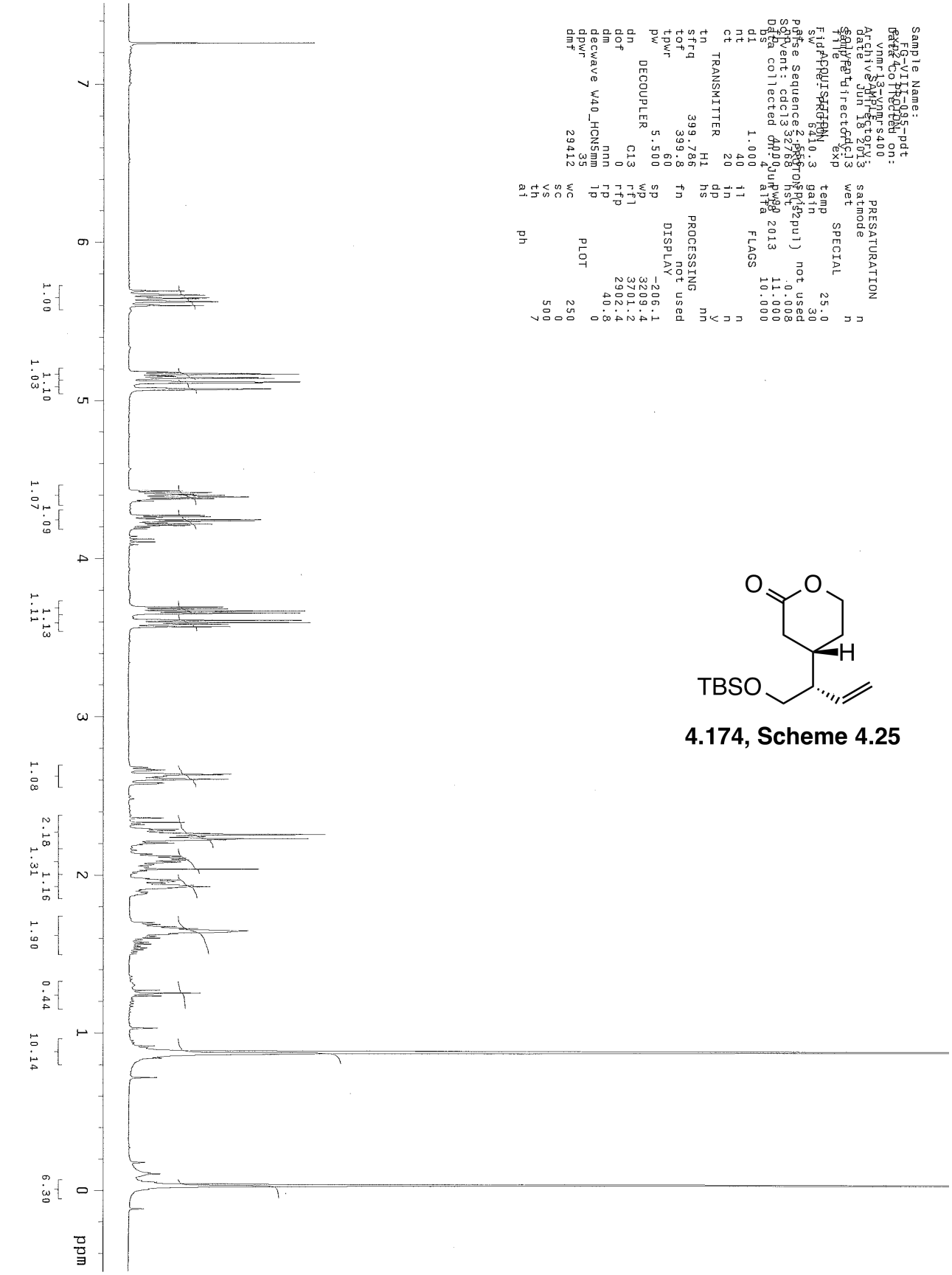


4.170, Scheme 4.24

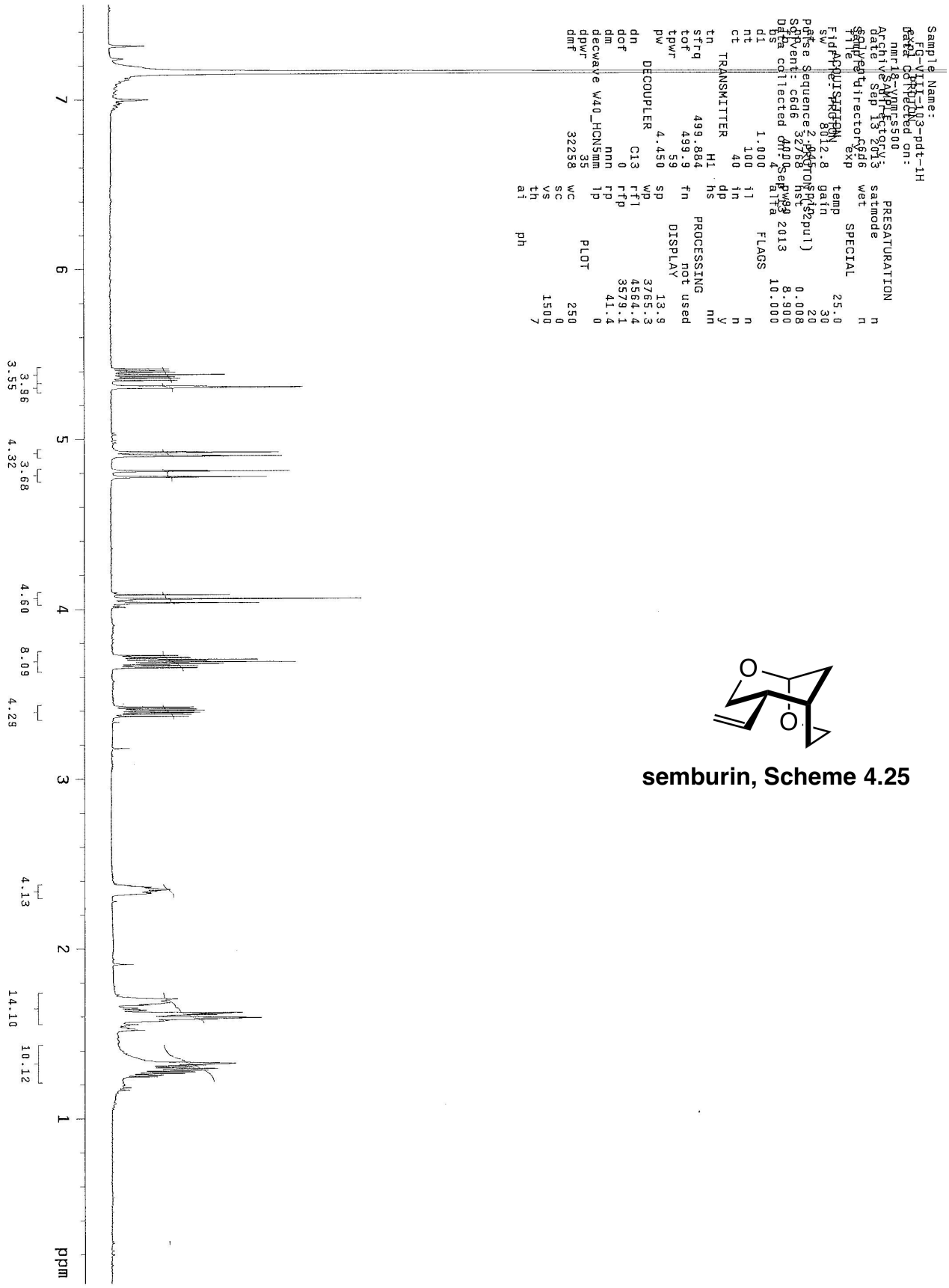


4.171, Scheme 4.25

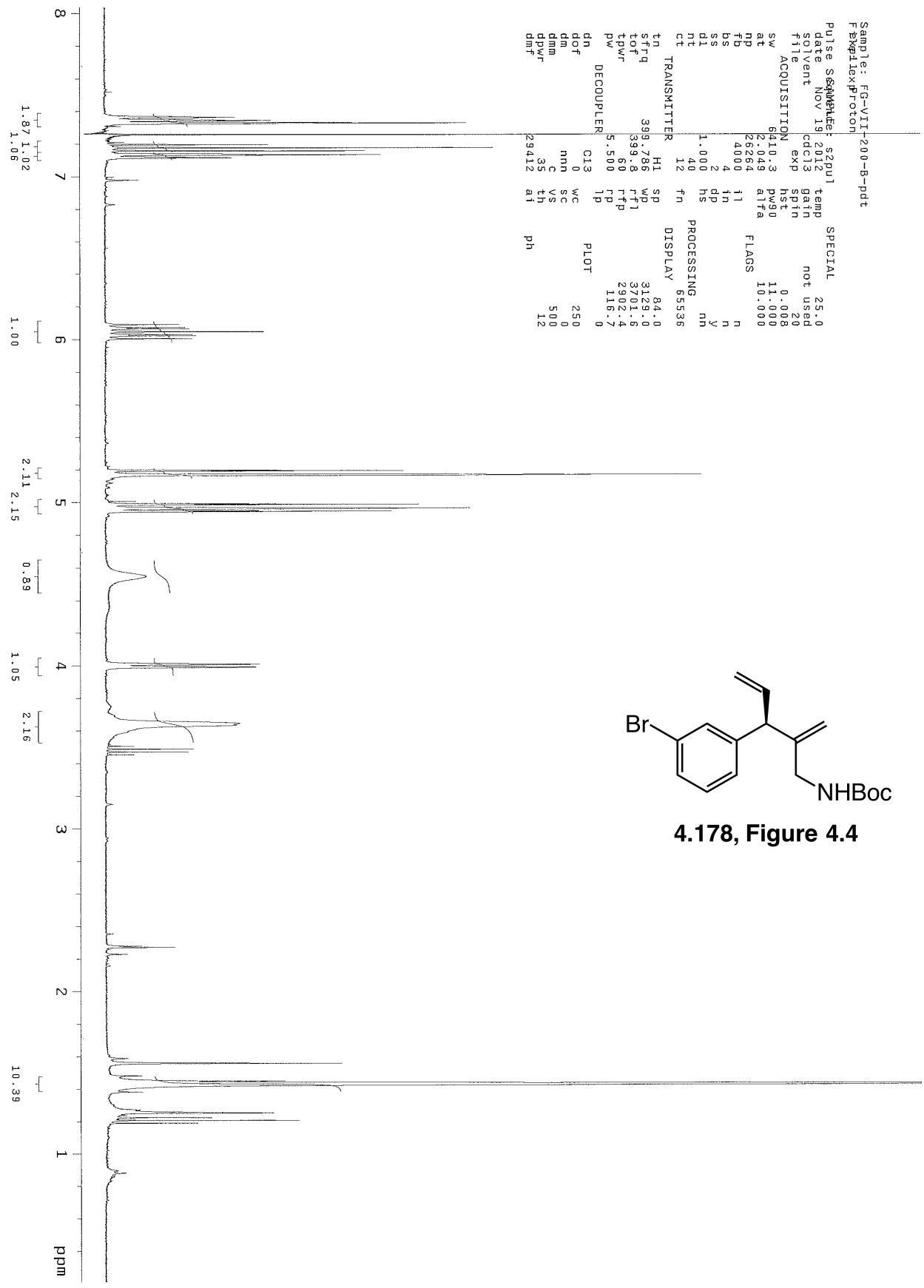

Sample: FG-VII-266-pdt
Exp1 exp proton
Pulse Sequence: s2pul
date Feb 28 2013
solvent cdcl3
file exp
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4000
bs 4
ss 2
d1 1.000
nt 40
ct 8
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 60
pw 5.500
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
temp
gain
spin
hst
pw90
alfa
FLAGS
il
in
dp
hs
fn
PROCESSING
DISPLAY
sp
wp
rfl
rfp
rp
lp
PLOT
wc
sc
vs
th
ai
ph
SPECIAL
25.0
not used
20
0.008
11.000
10.000
n
n
y
nn
65536
-72.6
3132.7
3701.8
2902.4
-26.1
0
250
0
300
12
O
O
TBSO
4.172, Scheme 4.25
7
6
5
4
3
2
1
ppm
0.91
1.00
2.02
2.11
2.18
1.07
2.14
0.87
3.47
2.96
10.86
6.07



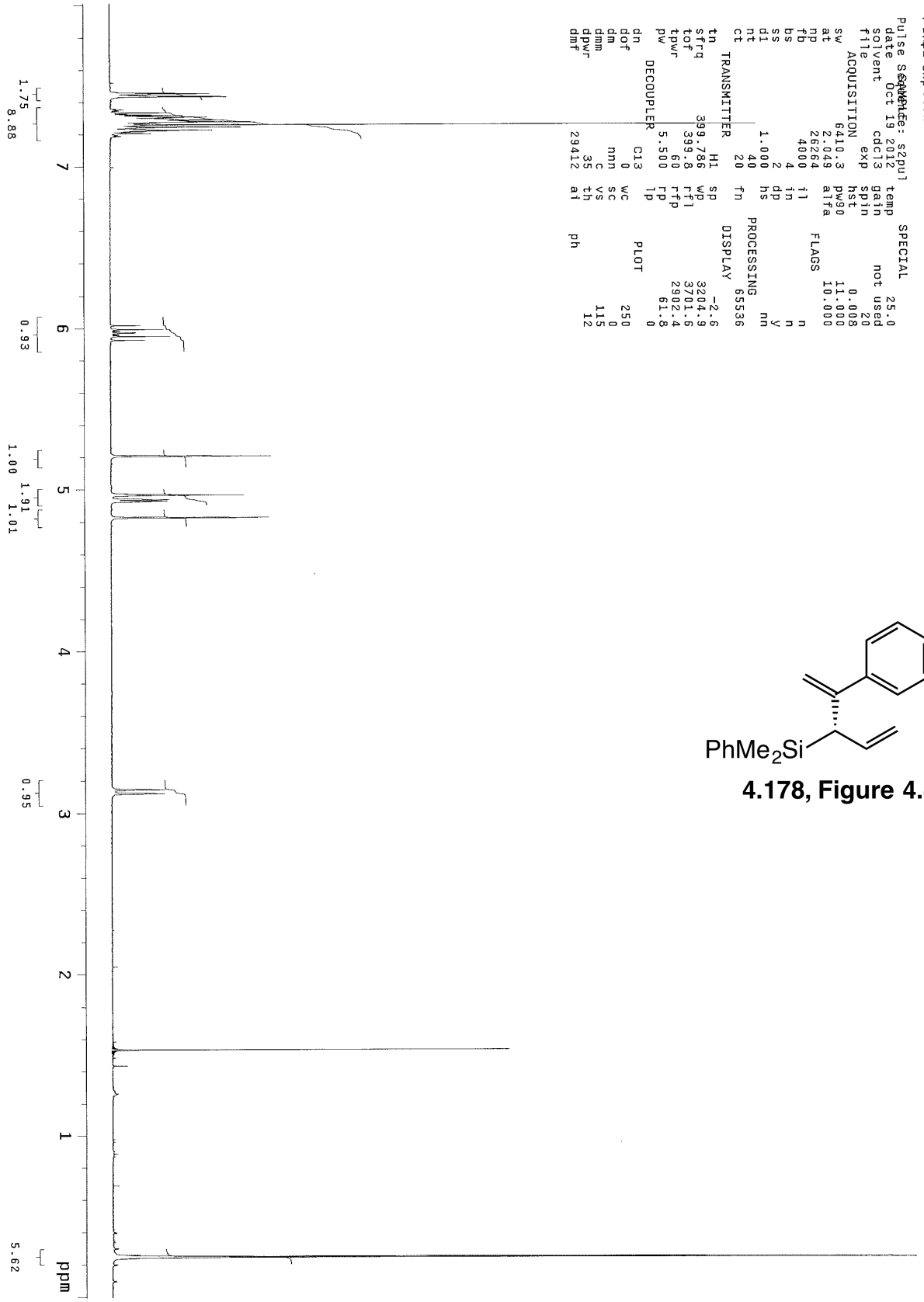
4.174, Scheme 4.25



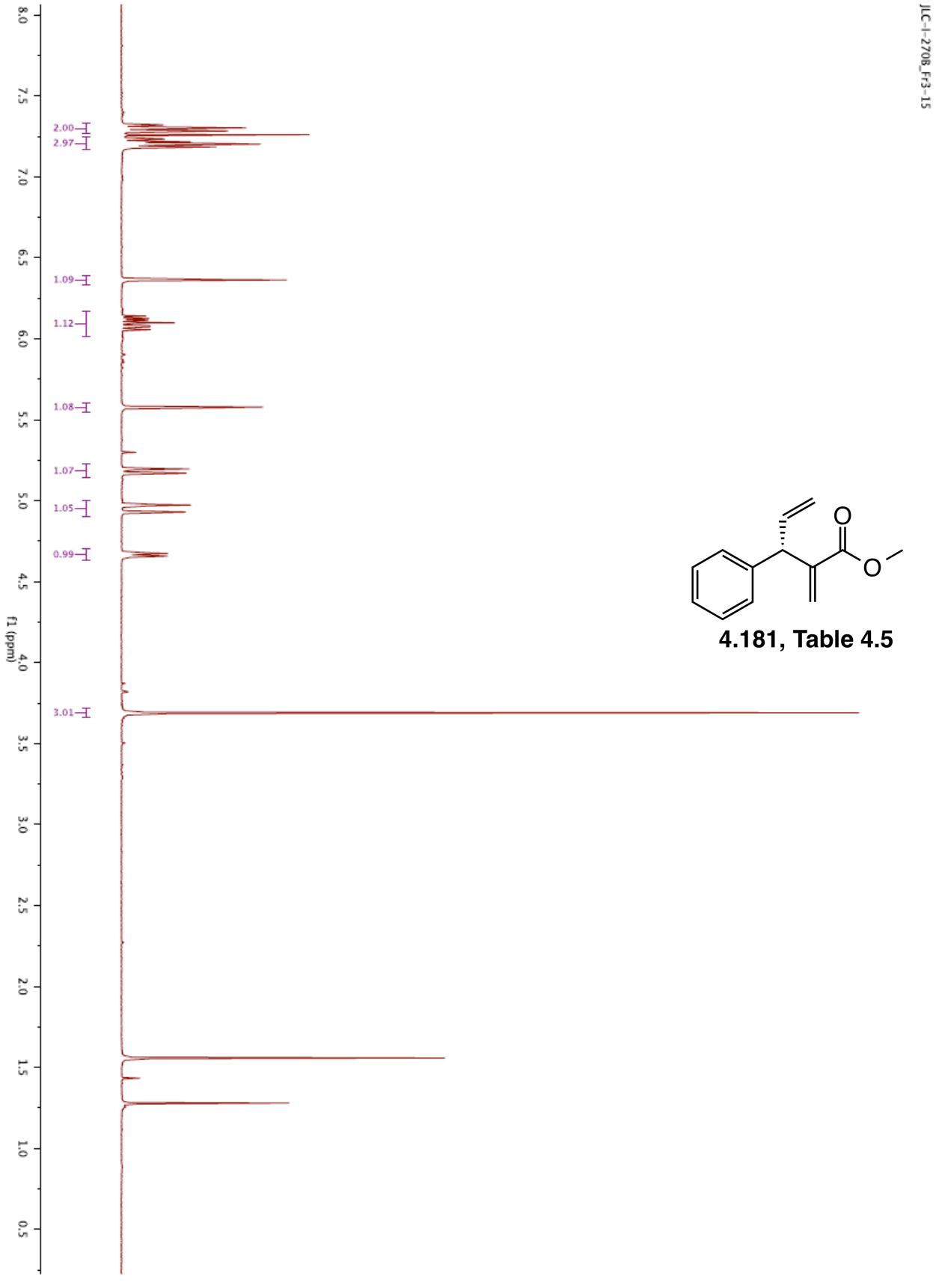
semburin, Scheme 4.25



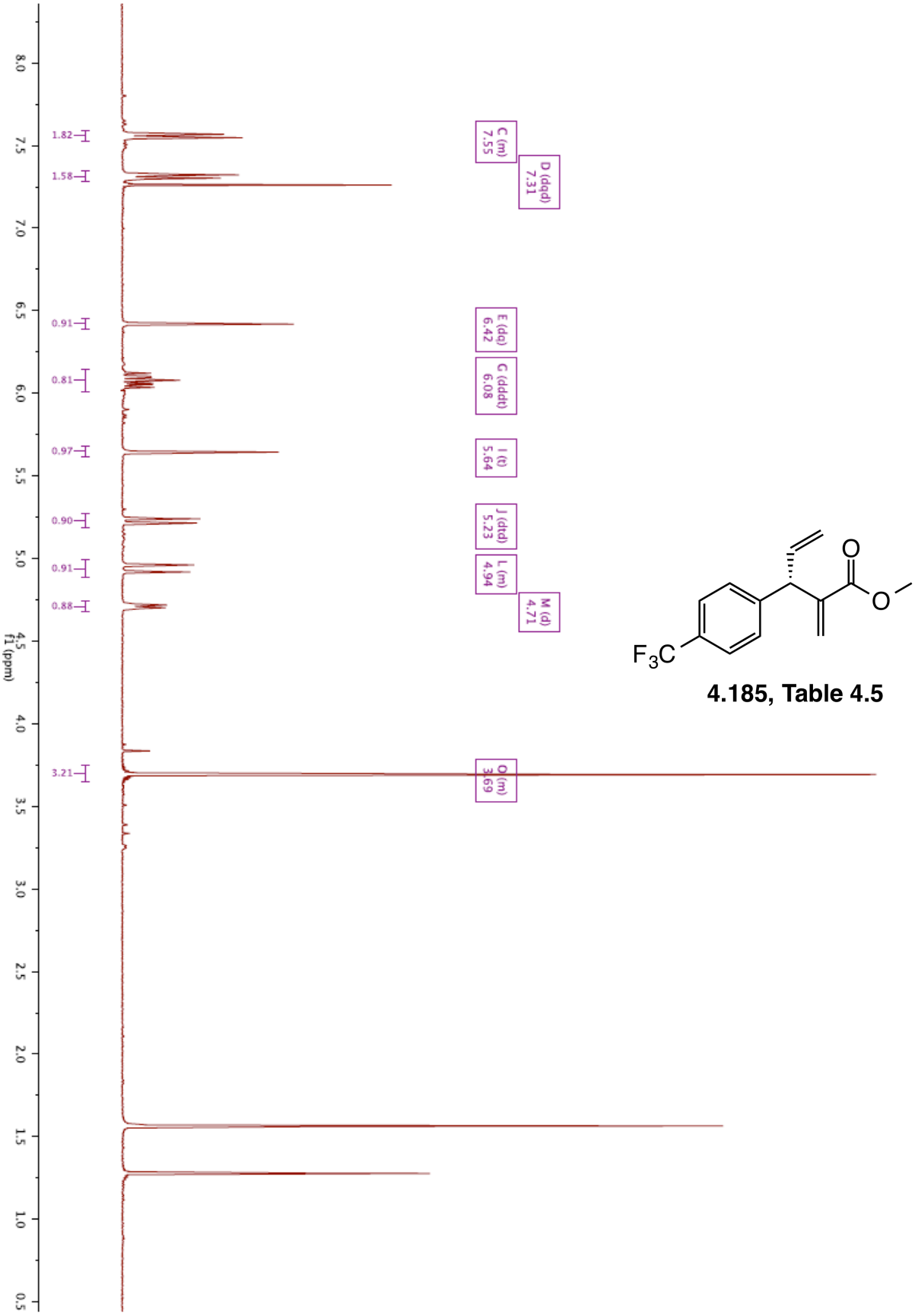
4.178, Figure 4.4



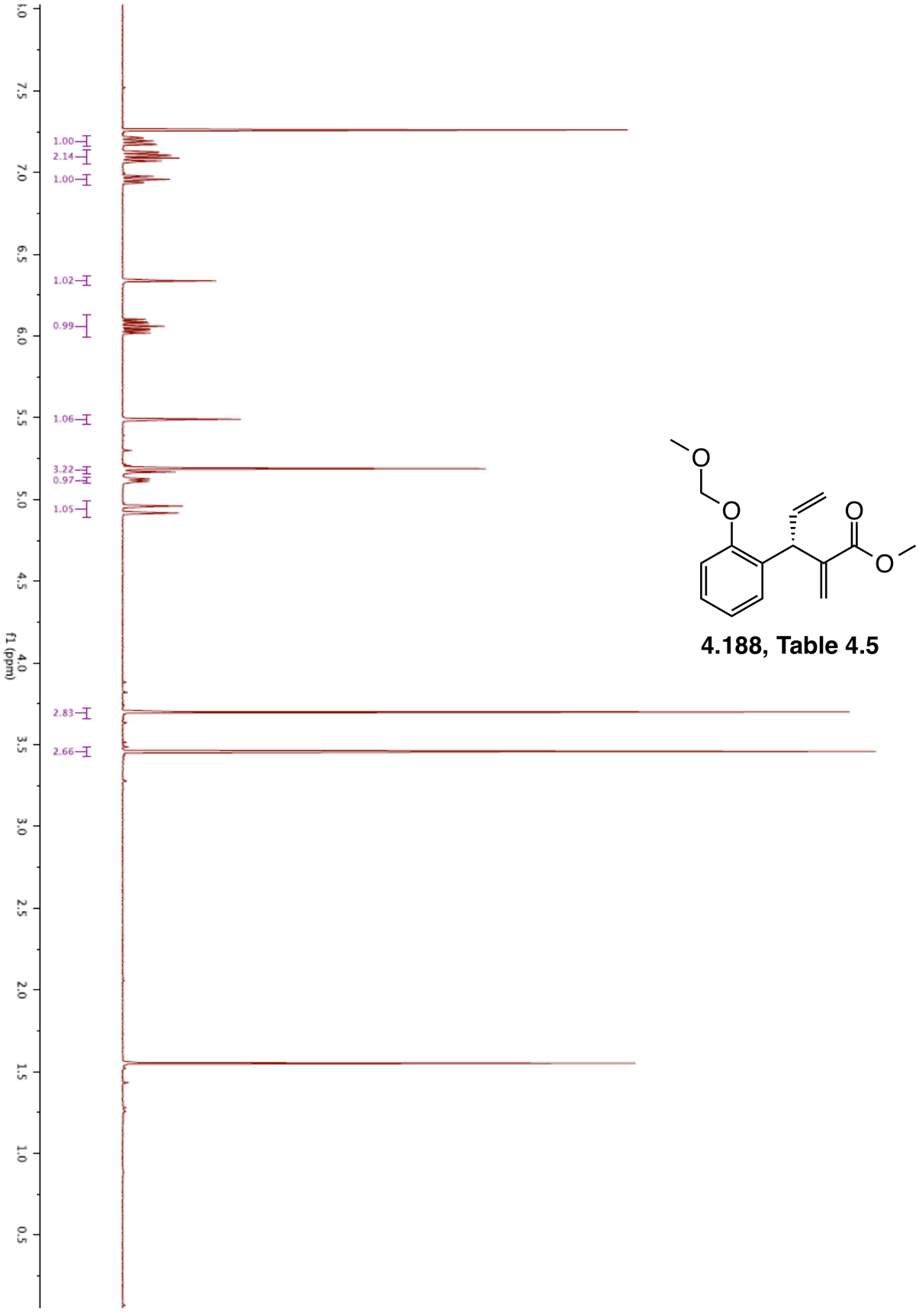
4.178, Figure 4.4



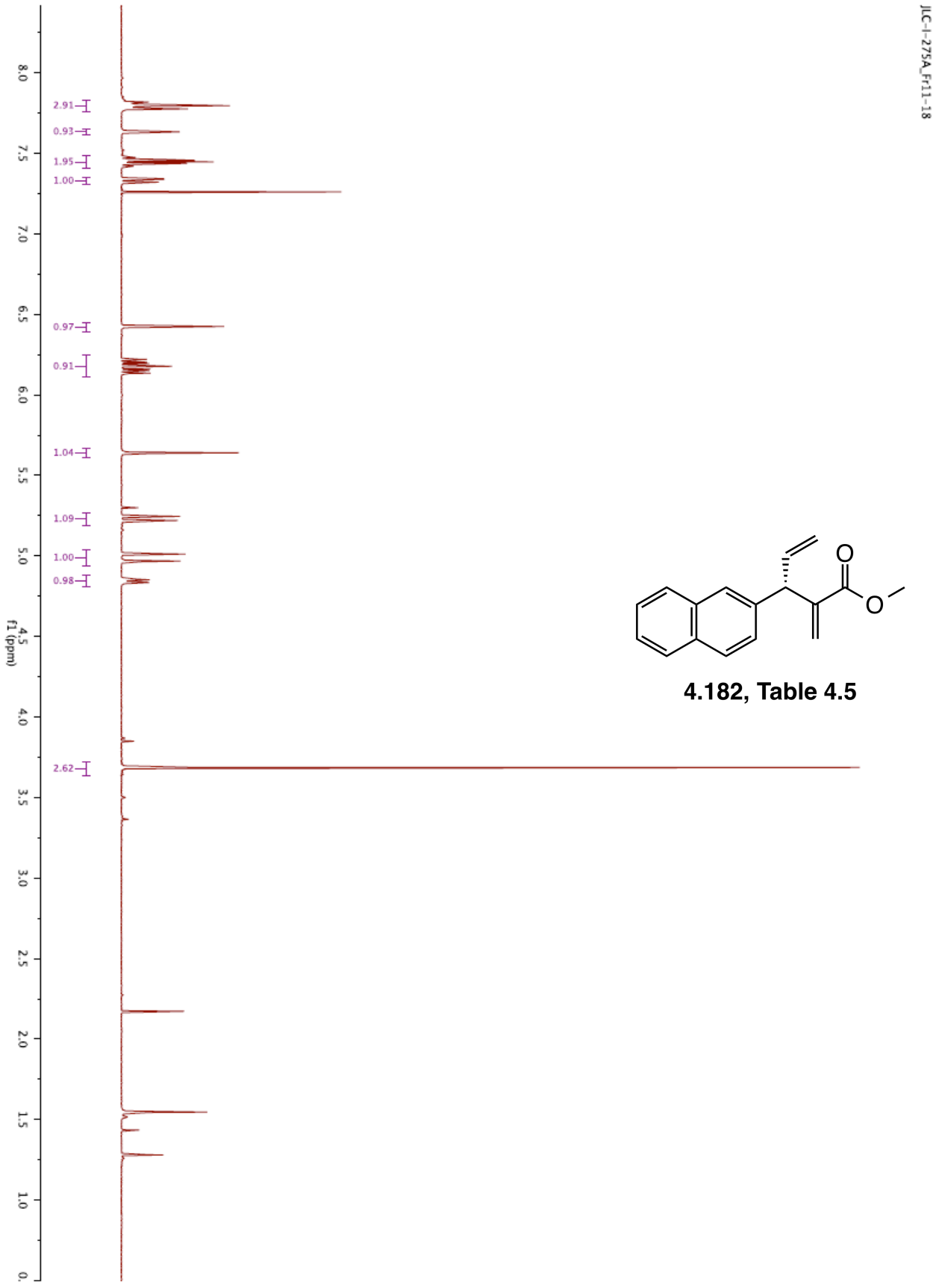
4.181, Table 4.5



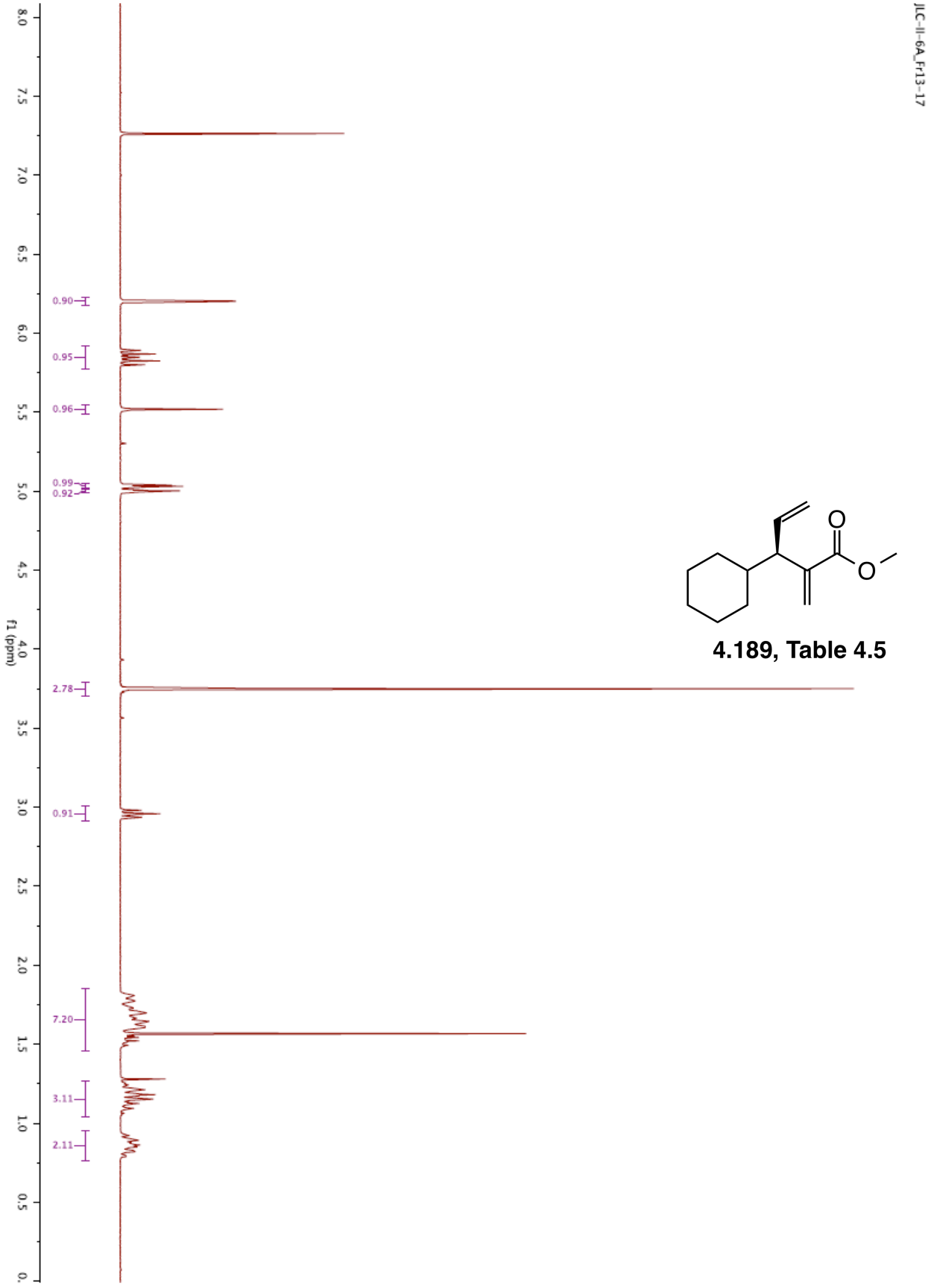
4.185, Table 4.5



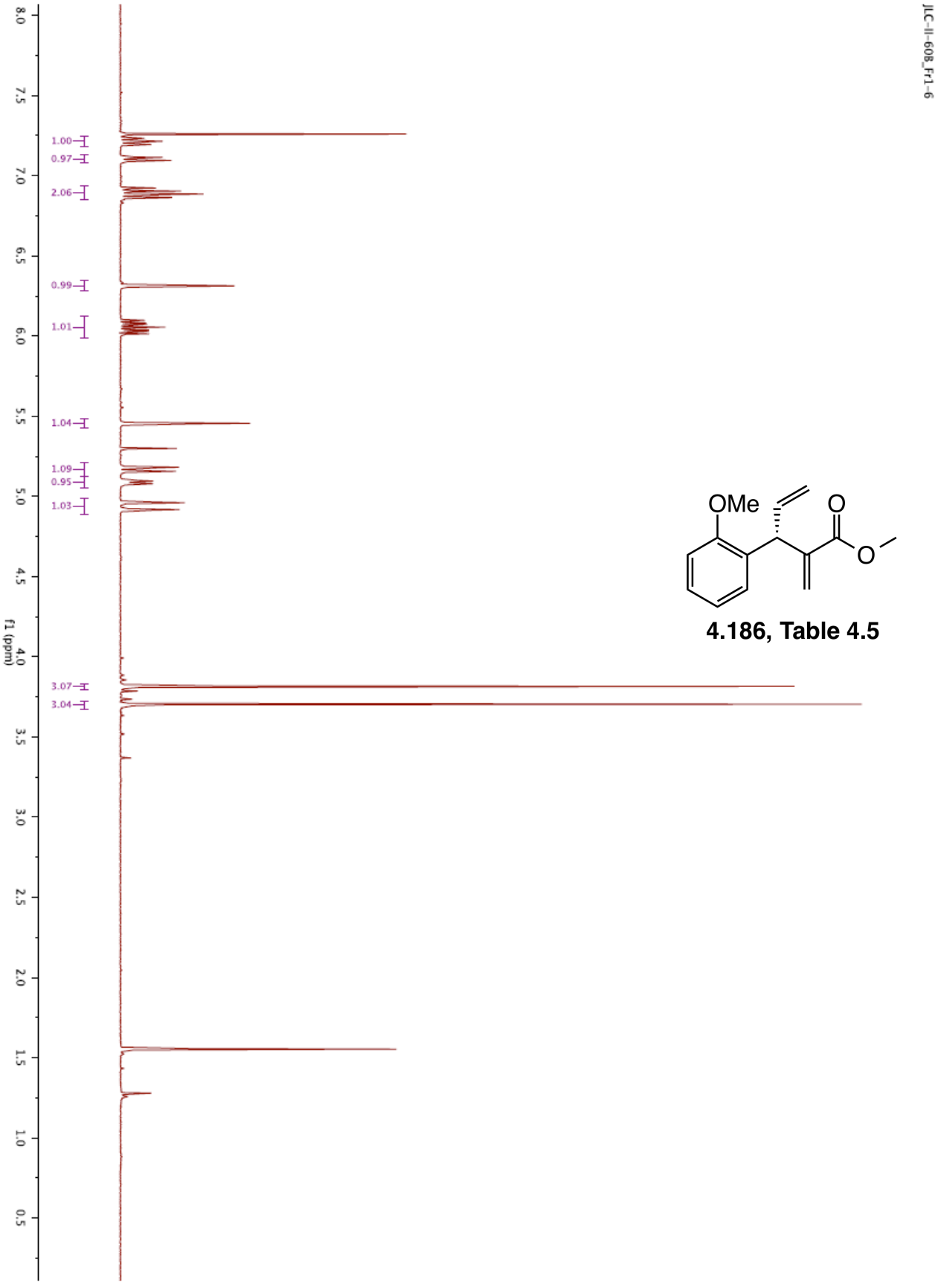
4.188, Table 4.5



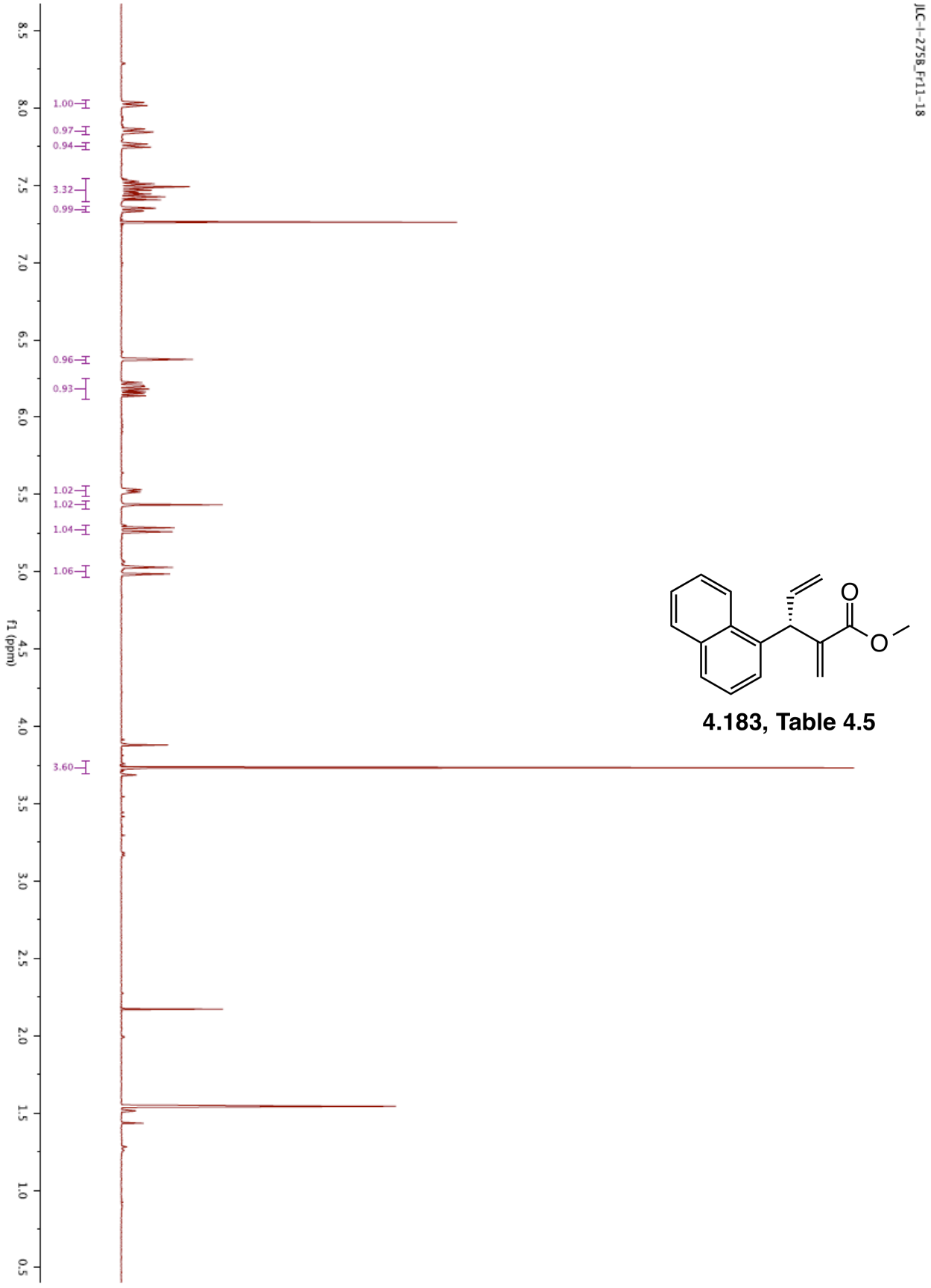
4.182, Table 4.5



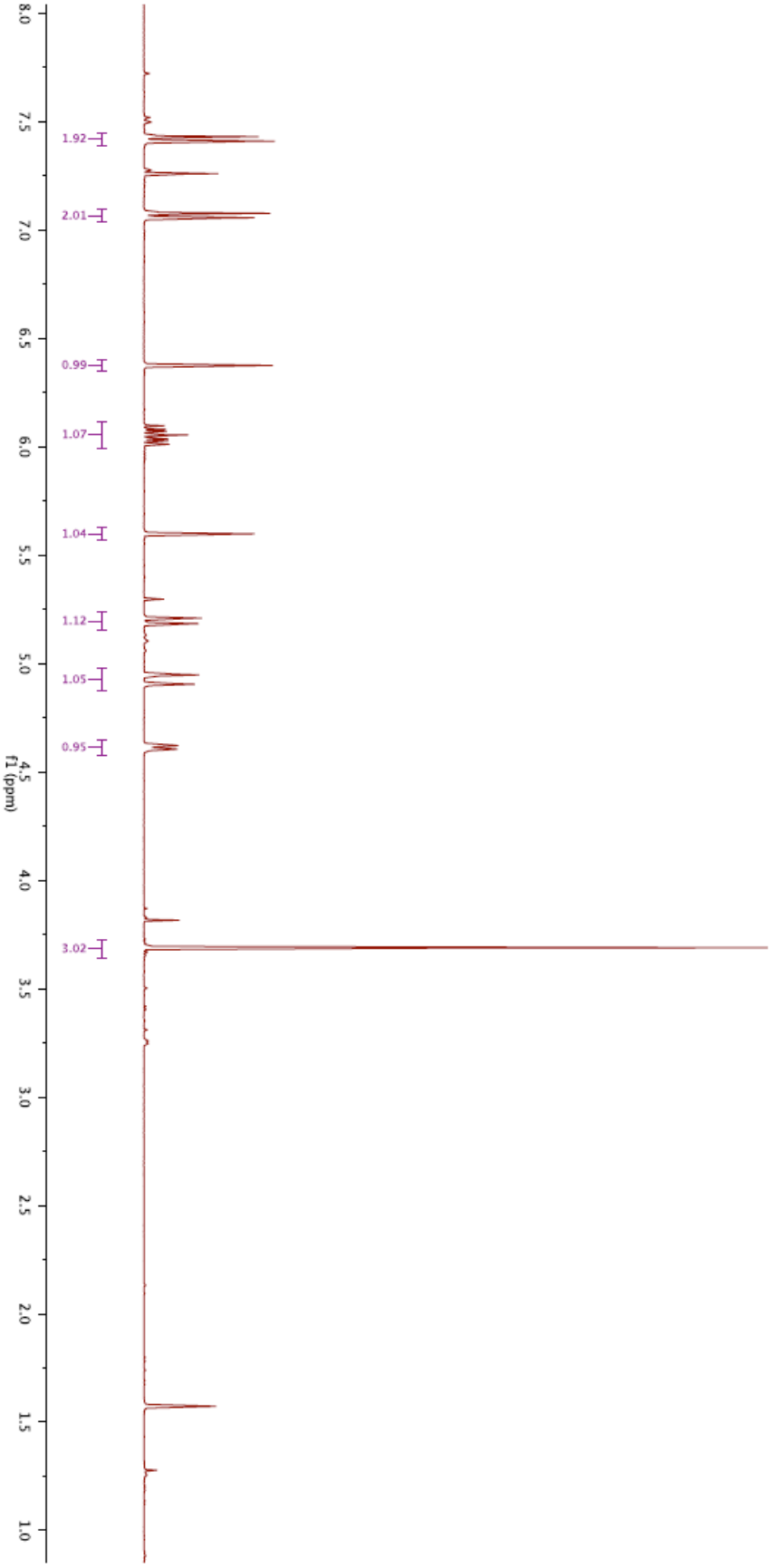
4.189, Table 4.5

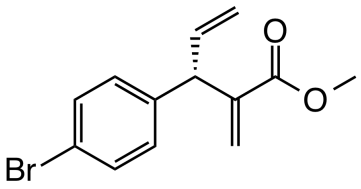


4.186, Table 4.5

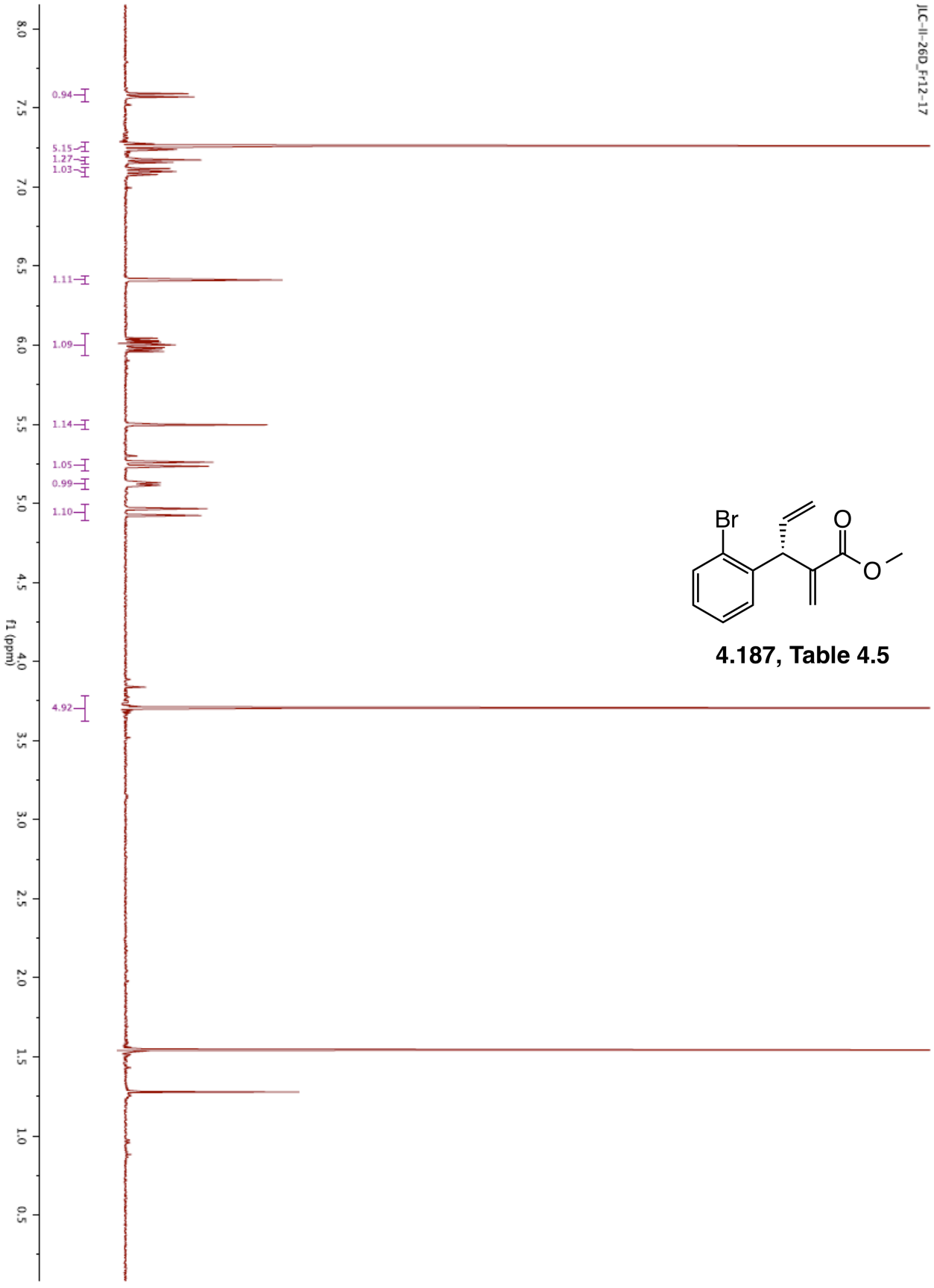


4.183, Table 4.5





4.184, Table 4.5



4.187, Table 4.5