Design of Copper-Catalyzed Multicomponent Reactions and Applications to Natural Product Synthesis

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DESIGN OF COPPER-CATALYZED MULTICOMPONENT REACTIONS AND APPLICATIONS TO NATURAL PRODUCT SYNTHESIS

A dissertation

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DESIGN OF COPPER-CATALYZED MULTICOMPONENT REACTIONS AND APPLICATIONS TO NATURAL PRODUCT SYNTHESIS

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Abstract

Chapter 1. Ligand-Controlled Site-Selective NHC–Cu-Catalyzed Protoboration of Monosubstituted Allenes. Site-selective proto–boryl additions to monosubstituted allenes promoted by NHC–Cu complexes are disclosed. Synthetically useful 1,1-disubstituted and Z-trisubstituted alkenylboron compounds are afforded in high efficiency (71%–92% yield) and site selectivity (88% to >98%) through proper choice of NHC ligands. Mechanistic study with the assistance of DFT calculations indicates that protonation of 2-boron-substituted allylcopper complex occurs through six-membered cyclic transition state. The utility of this protocol is demonstrated through application to fragment synthesis of an antibiotic macrolide natural product elansolid A.

Chapter 2. Cu-Catalyzed Chemoselective Copper–Boron Additions to Monosubstituted Allenes Followed by Allyl Additions to Carbonyl Compounds. The first examples of catalytic generation of 2-boron-substituted allylcopper species and their in situ use for C–C bond formation are described. The reactions are performed in the

presence of bisphosphine– or NHC–Cu complexes at 22 ºC. High-value alcohol-containing alkenylboron compounds are provided in high efficiency (68–92% yield after oxidation) and stereoselectivity (88:12 to >98:2 dr). The reactions proceed with exclusive γ-addition mode through a cyclic six-membered transition state. Enantioselectivity can be achieved with chiral bisphosphine ligands in up to 97:3 enantiomeric ratio.

Chapter 3. Chemo-, Site- and Enantioselective Copper–Boron Additions to 1,3-Enynes Followed by Site- and Diastereoselective Additions of the Resulting Allenylcopper Complexes to Aldehydes. Catalytic enantioselective multicomponent reactions involving 1,3-enynes, aldehydes and $B_2(pin)_2$ are described. The resulting products contain a primary C–B(pin) bond, as well as alkyne- and hydroxyl-substituted tertiary stereogenic centers. A critical feature is high enantioselectivity of the initial Cu–B addition to an alkyne-substituted terminal alkene. The key mechanistic issues are investigated by DFT calculations. Reactions are promoted in the presence of the Cu complex of an enantiomerically pure C_1-symmetric bisphosphine and are complete in 8 h at ambient temperature. Products are generated in 66–94% yield (after oxidation or catalytic cross-coupling), 90:10 to >98:2 diastereomeric ratio, and 85:15–99:1 enantiomeric ratio. Aryl-, heteroaryl-, alkenyl-, and alkyl-substituted aldehydes and enynes are suitable substrates. Utility is demonstrated through catalytic alkylation and arylation of the organoboron compounds as well as applications to synthesis of fragments of tylonolide and mycinolide IV.

Chapter 4. Multifunctional Alkenylboron Compounds through Single-Catalyst-Controlled Multicomponent Reactions and Their Applications in Scalable Natural Product Synthesis. A facile multicomponent catalytic process that begins with a chemo-,

site- and diastereoselective copper–boron addition to a monosubstituted allene followed by addition of the resulting boron-substituted organocopper intermediate to an allylic phosphate, generating products that contain a stereogenic center, a monosubstituted alkene and an easily functionalizable *Z*-trisubstituted alkenylboron group in up to 89% yield with >98% branch selectivity and stereoselectivity and an enantiomeric ratio greater than 99:1. The copper-based catalyst is derived from a robust heterocyclic salt that can be prepared in multigram quantities from inexpensive starting materials and without costly column chromatography purification. The utility of the method is demonstrated through enantioselective synthesis of gram quantities of two natural products, rottnestol and herboxidiene/GEX1A.

Chapter 5. Cu-Catalyzed Enantioselective Allyl and Propargyl 1,6-Conjugate Additions through 3,3'-Reductive Elimination. Catalytic enantioselective 1,6-conjugate additions of allyl-type nucleophiles promoted by NHC–Cu complexes are reported. Propargyl and 2-boron allyl 1,6-conjugate products are formed in high efficiency, diastereo- and enantioselectivity. The unique mechanistic feature is that the transformations proceed through Cu-catalyzed 3,3'-reductive elimination, that is unprecedented for copper catalysis. Further mechanistic study and application to complex molecule synthesis will be conducted.

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Chapter 1

Ligand-Controlled Site-Selective NHC–Cu-Catalyzed Protoboration of Monosubstituted Allenes

1.1 Introduction

Alkenylboron compounds play a critical role in chemical synthesis, most notably as cross-coupling partners;[1] therefore it is an attractive objective to develop methods for efficient, site- and stereoselective synthesis of such building blocks. Especially, protocols that are promoted by a catalyst are of great value, in which variations of structures of catalysts can lead to different selectivity profiles. Although significant progresses have been made in this area, the majority of Cu-catalyzed processes employ alkynes as substrates.[2] In 2011, Hoveyda and co-workers demonstrated that terminal alkynes can be converted to α- and β-alkenylboron compounds selectively through adjustment of structures of the NHC ligands of a Cu–based catalyst.[3] Reactions proceed with site-selective Cu–B addition followed by protonation of the alkenylcopper intermediate by

(1) For applications of alkenylboron compounds in cross-coupling reactions, see: (a) Hall, D. G. In *Boronic Acids: Preparation and Applications in Organic Synthesis and Medicine*; Wiley–VCH: Weinheim, **2005**. (b) Tobisu, M.; Chatani, N. *Angew. Chem., Int. Ed.* **2009**, *48*, 3565–3568. For syntheses of cyclic and acyclic alkenylborons through Pd-catalyzed cross-coupling reactions involving alkenyl bromides and triflates, see: (c) Takagi, J.; Takahashi, K.; Ishiyama, T.; Miyaura, N. *J. Am. Chem. Soc.* **2002**, *124*, 8001–8006. For a review on applications of alkenyltrifluoroboron reagents, prepared via alkenylborons, see: (d) Molander, G. A.; Ellis, N. *Acc. Chem. Res.* **2007**, *40*, 275–286.

(2) For a Cu-catalyzed hydroboration of phenylacetylene, see (a) Lee, J. E.; Kwon, J.; Yun, J. *Chem. Commun.* **2008**, 733–734. This procedure is ineffective with alkyl-substituted alkynes. For synthesis of alkenylboron entities through Cu-catalyzed protoboration of alkynes, see: (b) Kim, H. R.; Jung, I. G.; Yoo, K.; Jang, K.; Lee, E. S.; Yun, J.; Son, S. U. *Chem. Commun.* **2010**, *46*, 758–760. (c) Semba, K.; Fujihara, T.; Terao, J.; Tsuji, Y. *Chem. Eur. J.* **2012**, *18*, 4179–4184. (d) Moure, A. L.; Arrayás, R. G.; Gárdenas, D. J.; Alonso, I.; Carretero, J. C. *J. Am. Chem. Soc.* **2012**, *134*, 7219–7222. (e) Park, J. K.; Ondrusek, B. A.; McQuade, D. T. *Org. Lett.* **2012**, *14*, 4790–4793. (f) Moure, A. L.; Mauleon, P.; Arrayás, R. G.; Carretero, J. C. *Org. Lett.* **2013**, *15*, 2054–2057.

(3) Jang, H.; Zhugralin, A. R.; Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 7859–7871.

MeOH. Allenes are another important class of unsaturated hydrocarbons that can serve as substrates for copper–boron additions. Development of such protocols provides possible access to not only two isomeric alkenylboron compounds,[4] but also allylboron entities.[5] More recently, in conjunction with studies regarding NHC–Cu-catalyzed enantioselective allylic substitution reactions, Hoveyda group demonstrated that the resulting monosubstituted allenes undergo protoboration in the presence of a Cu-based catalyst, delivering a 9:1 mixture of 1,1-disubstituted and trisubstituted alkenylboron products.[6]

Our interest in establishing a catalytic process to access either 1,1-disubstituted or trisubstittuted alkenylboron products in high selectivity originates from not only its wide applications in organic synthesis, but also the mechanistic question regarding impact of catalyst structures on selectivity. We would like to identify catalysts derived from abundant inexpensive metal salts at low catalyst loading and easily accessible ligands to afford a wide range of alkenylboron compounds.

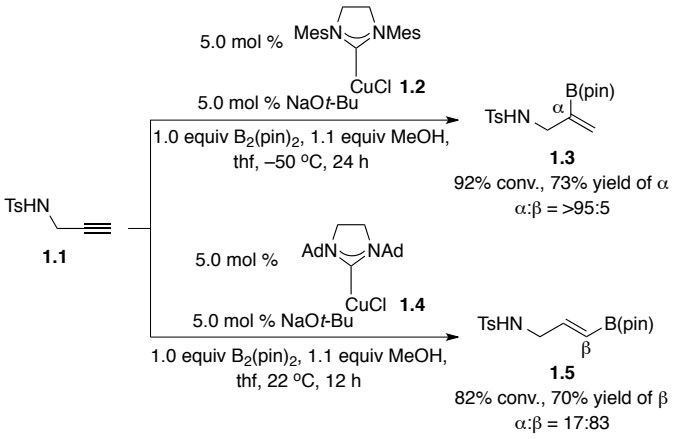
1.2 Background

The first example of Cu-catalyzed site-selective protoboration of terminal alkynes is reported by Hoveyda and co-workers.[3] As shown in Scheme 1.1, reaction of propargylic amine **1.1** with $B_2(pin)_2$ and MeOH in the presence of NHC–Cu complex **1.2** delivers 1,1-disubstituted alkenylboron **1.3** in >95% site selectivity wtih 73% yield of

(4) (a) Yuan, W.; Ma, S. *Adv. Synth. Catal.* **2012**, *354*, 1867–1872. (b) Semba, K.; Shinomiya, M.; Fujihara, T.; Terao, J.; Tsuji, Y. *Chem. Eur. J.* **2013**, *19*, 7125–7132.
(5) Jang, H.; Jung, B.; Hoveyda, A. H. *Org. Lett.* **2014**, *16*, 4658–4661.
(6) Jung, B.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2012**, *134*, 1490–1493.

pure α-product **1.3**. Variation of the Cu complex bearing N–Mes to that derived from adamantyl-containing imidazolinium salt (complex **1.4**) leads to formation of 1,2-disubstituted alkenylboron **1.5**. The reaction proceeds to 82% conversion within 12 h at 22 °C with tetrahydrofuran (thf) as solvent. However, the substrate scope is limited to propargylic alcohols or amines and aryl alkynes.

Scheme 1.1: NHC–Cu-Catalyzed Site-Selective Protoboration of Alkynes



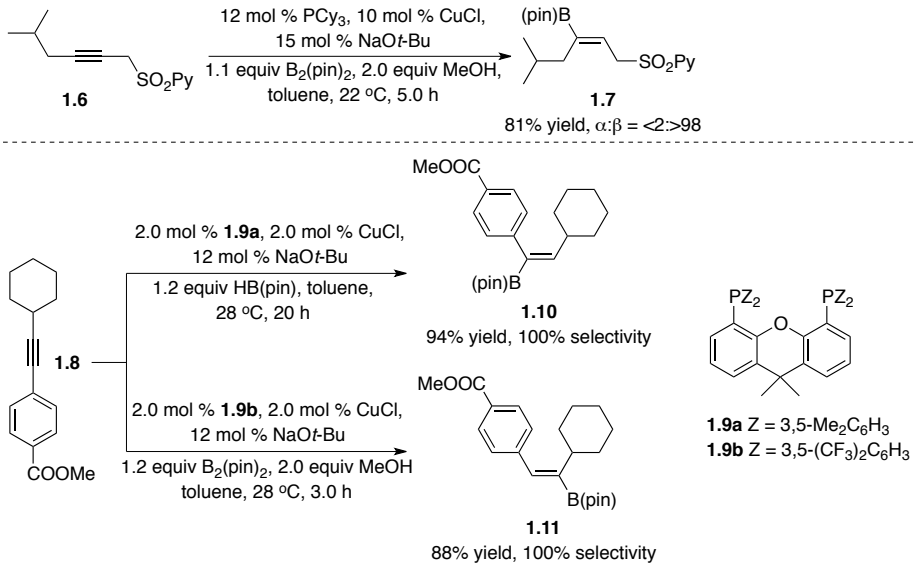
Mes = 2,4,6-trimethylphenyl, Ad = adamantyl

Subsequently, a variety of protocols regarding Cu-catalyzed protoboration of internal alkynes have been developed. As illustrated in Scheme 1.2, internal alkynes that carry directing groups (e.g. alcohols, ethers, 2-pyridylsulfide and 2-pyridylsulfone) at allylic position undergo Cu–B addition followed by protonation to generate β-alkenylboron products in high site selectivity.[2b] In the presence of 10 mol % Cy_3P–Cu complex, reaction of alkyne **1.6** affords trisubstituted alkenylboron **1.7** in 81% yield and complete site selectivity.

Tsuji and co-workers also reported a catalytic protocol that either isomers of alkenylboron can be accessed in high site selectivity (Scheme 1.2).[2c] Reaction of internal alkyne **1.8** with in situ generated copper hydride from phosphine–Cu complex derived

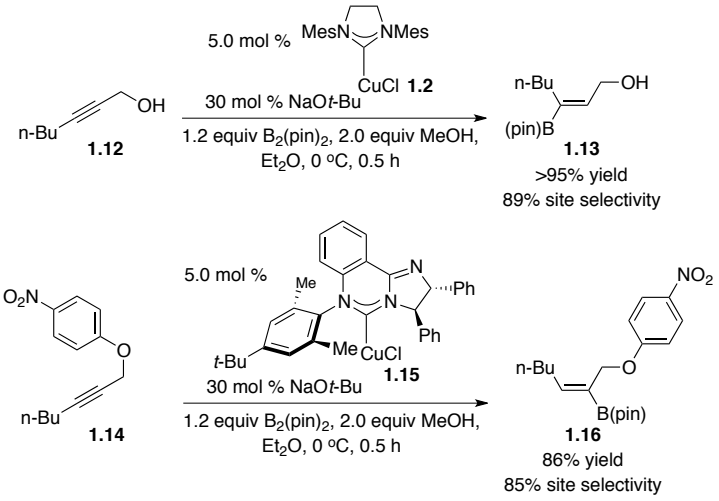
from **1.9a** provides **1.10** in 94% yield with complete selectivity. In contrast, electronically modified phosphine–Cu complex generated from **1.9b** promotes Cu–B addition/protonation of alkyne **1.8** delivering **1.11** in 88% yield with complete selectivity.

Scheme 1.2: Phosphine–Cu-Catalyzed Site-Selective Protoboration of Alkynes



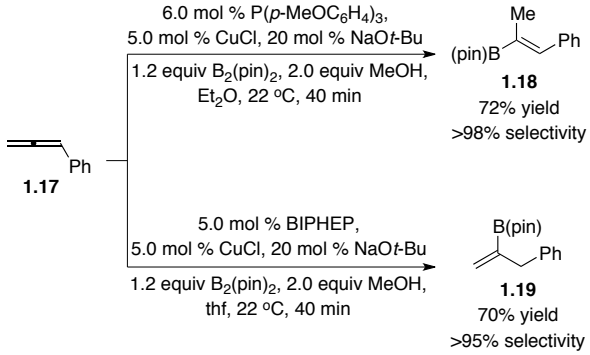
Later, McQuade and co-workers developed a catalytic site-selective protoboration of internal alkynes promoted by NHC–Cu complexes (Scheme 1.3).[2e] Site selectivity can be switched through simple protection of the propargylic alcohol moiety as *para*-nitrophenyl ether. Propargylic alcohol **1.12** undergoes site-selective protoboration to give trisubstituted alkenylboron **1.13** in >95% NMR yield and 89% selectivity in the presence of Cu complex **1.2**. Reaction of the corresponding *para*-nitrophenylether derivative **1.14** promoted by NHC–Cu complex **1.15** furnishes the other isomeric product **1.16** in 86% yield and 85% site selectivity. However, the range of substrates is limited.

Scheme 1.3: NHC–Cu-Catalyzed Site-Selective Protoboration of Alkynes



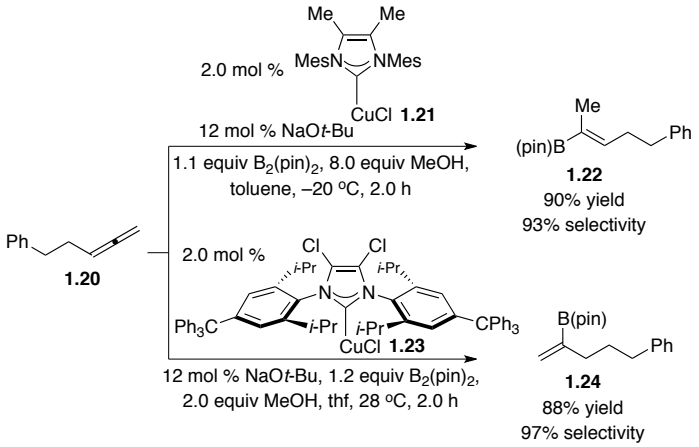
Ma and co-workers developed the first examples of Cu-catalyzed protoboration of allenes (Scheme 1.4).[4a] Phenyl-substituted allene **1.17** is transformed to trisubstituted alkenylboron **1.18** in 72% yield with >98% site selectivity when exposed to 5.0 mol % Cu catalyst derived from electron-rich P(*p*-$MeOC_6H_4)_3$. With bidentate phosphine–Cu complex generated from 2,2'-bis(diphenylphosphino)biphenyl (BIPHEP), 1,1-disubstituted alkenylboron **1.19** is formed in 70% yield with >95% selectivity. Most cases in this study are limited to aryl-substituted allenes, and no mechanistic rationale for site selectivity is discussed.

Scheme 1.4: Phosphine–Cu-Catalyzed Site-Selective Protoboration of Allenes



In the meantime of this study, Tsuji and co-workers described an NHC–Cu-catalyzed process that furnishes either 1,1-disubstituted or trisubstituted alkenylboron selectively by appropriate choice of the catalysts.[4b] As the examples shown in Scheme 1.5, monosubstituted allene **1.20** is converted to trisubstituted alkenylboron **1.22** in 90% yield and 93% site selectivity upon exposure to 2.0 mol % NHC–Cu complex **1.21**. Moreover, reaction of **1.20** in the presence of 2.0 mol % of a more sterically hindered Cu complex **1.23** delivers 1,1-disubstituted alkenylboron **1.24** in 88% yield and 97% site selectivity.

Scheme 1.5: NHC–Cu-Catalyzed Site-Selective Protoboration of Allenes

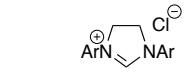


1.3 Identification of the Optimal Catalysts for Site-Selective NHC–Cu-Catalyzed Protoboration of Monosubstituted Allenes

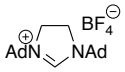
We first examined the influence of catalyst structure on site selectivity. With styrene-containing allene **1.29** as standard substrate, the reactions occur chemoselectively favoring addition to allene moiety (<2% addition to alkene, Table 1.1). NHC–Cu complexes that carry sterically more hindered aryl groups deliver higher selectivity for

1,1-disubstituted alkenylboron **1.30** (entries 1–4, Table 1.1). Especially, in the presence of Cu complex derived from **1.27**, a 90:10 mixture of products are formed in 73% yield. The selectivity in favor of **1.31** is improved when allene **1.29** is exposed to Cu complexes containing N–alkyl moiety. Reducing the size of the alkyl units on NHCs results in better selectivity for trisubstituted alkenylboron **1.31** with complete *Z* selectivity; reaction promoted by N–Me-containing NHC–Cu complex affords **1.31** in 94% selectivity.

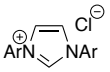
Table 1.1: Ligand Screen for NHC–Cu-Catalyzed Site-Selective Protoboration of Allenes[a]



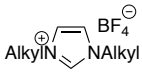
1.25a, Ar = Mes [2,4,6-$(Me)_3C_6H_2$]
1.25b, Ar = 2,6-$(i\text{-}Pr)_2C_6H_3$



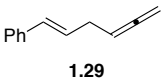
1.26, Ad = adamantyl



1.27, Ar = 2,6-$(i\text{-}Pr)_2C_6H_3$



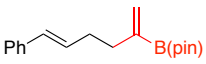
1.28a, Alkyl = adamantyl
1.28b, Alkyl = cyclohexyl
1.28c, Alkyl = *i*-Bu
1.28d, Alkyl = *i*-Pr
1.28e, Alkyl = Me (Cl salt)



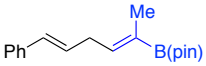
1.29

5.0 mol % NHC precursor
5.0 mol % CuCl, 40 mol % NaO*t*-Bu,
1.1 equiv $B_2(pin)_2$, 6.0 equiv MeOH,
thf, 22 °C, 8.0 h

<2% product from aryl alkene reaction



1.30



1.31

Entry	NHC precursor	Conv (%)[b]	Yield (%)[c]	**1.30**:**1.31**[b]	*Z*/*E* (**1.31**)[d]
1	**1.25a**	>98	74	84:16	>98:2
2	**1.25b**	94	75	88.5:11.5	>98:2
3	**1.26**	>98	78	68:32	>98:2
4	**1.27**	>98	73	90:10	>98:2
5	**1.28a**	>98	80	56:44	>98:2
6	**1.28b**	73	58	22:78	>98:2
7	**1.28c**	73	60	10:90	>98:2
8	**1.28d**	89	69	16:84	>98:2
9	**1.28e**	79	62	6:94	>98:2

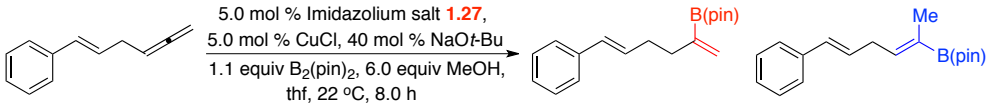
[a] Reactions were performed under N_2 atmosphere. [b] Determined through analysis of 400 MHz ^1H NMR spectra of unpurified product mixtures. [c] Yields of isolated and purified products (mixture of **1.30** and **1.31**, ±5%). [d] Analyzed by 400 MHz ^1H NMR spectra of purified materials.

It is noteworthy that copper–boron addition to **1.29** is highly chemselective, as protoboration of β-alkyl styrenes proceeds with similar efficiency,[7] suggesting that less hindered and more Lewis acidic allene moiety coordinates more efficiently with the NHC–Cu–B(pin) complex compared with aryl alkenes.[8] Another observation that supports this hypothesis is that although Cu–B addition to monosubstituted allenes/1,2-addition of the resulting allylcopper species to enals requires 8.0 h, the enal is fully consumed within 4.0 h in the absence of an allene.[9] With the assistance of DFT calculations in the latter transformation, association of allene with the Cu complex is indeed significant more exothermic (by ~10 kcal/mol). The lower efficiency of sterically less congested catalysts in entries 6–8 (Table 1.1) is probably due to the more competitive association of aryl alkene with the Cu complexes and shorter longevity of the catalysts.

Attempts to further improve site selectivity for generation of 1,1-disubstituted alkenylborons lead to investigation of temperature effects. Decreasing reaction temperature from 22 °C to –15 and 4 °C results in lower selectivity (entries 1 and 2, respectively, Table 1.2). Heating the reaction to 40 °C does not increase the site selectivity any further (entry 4, Table 1.2).

(7) Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 3160–3161.
(8) Dang, L.; Lin, Z.; Marder, T. B. *Organometallics* **2008**, *27*, 4443–4454.
(9) Meng, F.; Jang, H.; Jung, B.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2013**, *52*, 5046–5051.

Table 1.2: Temperature Effects on Site Selectivity for NHC–Cu-Catalyzed Protoboration of Allenes[a]



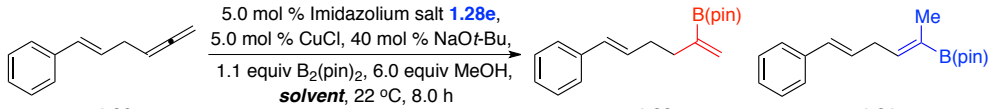
1.29 **1.30** **1.31**

Entry	Temperature (°C)	Conv. (%)[b]	Yield (%)[c]	**1.30**:**1.31**[b]
1	–15	>98	81	78:22
2	4	>98	80	72:28
3	22	>98	73	90:10
4	40	>98	72	90:10

[a–c]See Table 1.1.

Reactions promoted by NHC–Cu complex derived from **1.28e** in different solvents are also explored. Reaction performed in CH_2Cl_2 is not effective at all (entry 1, Table 1.3). With dimethoxyethane (DME) as solvent, efficiency and site selectivity of the reaction is slightly lower (entry 2, Table 1.3). Reaction in dioxane delivers slightly better efficiency and selectivity (entry 3, Table 1.3).

Table 1.3: Solvent Screen for NHC–Cu-Catalyzed Protoboration of Allenes[a]



1.29 **1.30** **1.31**

Entry	Solvent	Conv. (%)[b]	Yield (%)[c]	**1.30**:**1.31**[b]	*Z*/*E* (**1.31**)[d]
1	CH_2Cl_2	13	nd[d]	nd[d]	>98:2
2	DME	68	52	8:92	>98:2
3	dioxane	84	66	5:95	>98:2

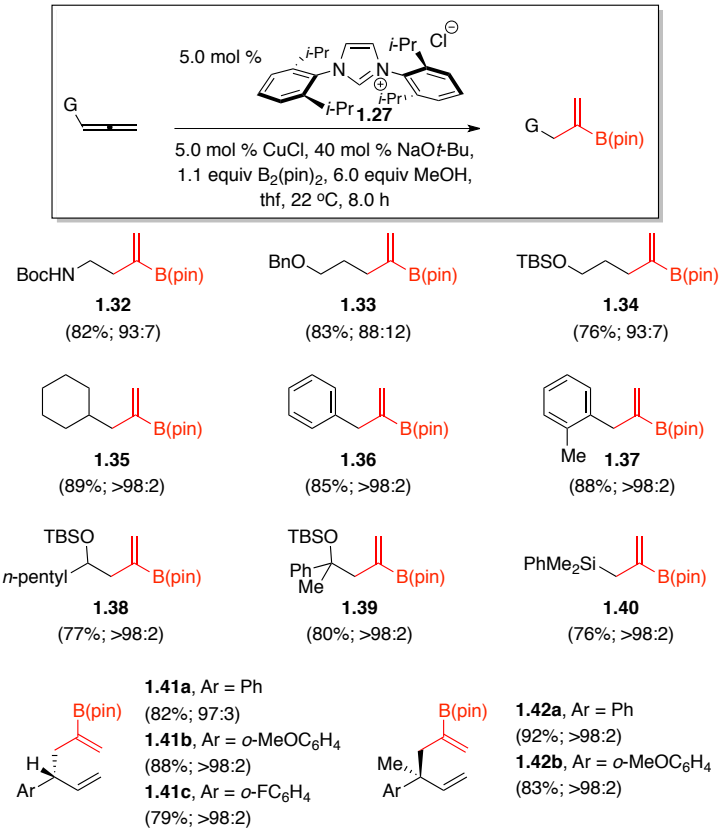
[a–c]See Table 1.1. [d]Not determined.

1.4 Scope of NHC–Cu-Catalyzed Protoboration of Monosubstituted Allenes

A wide range of alkyl- and aryl-substituted allenes are suitable substrates in the catalytic protoboration with Cu complex derived from **1.27** (Scheme 1.6). Protected alcohols and amines are well tolerated in this protocol (cf. **1.32**-**1.34**, **1.38**-**1.39**). Transformations of sterically hindered substrates, including those bearing a quaternary

center (cf. **1.38**-**1.40**, **1.42a**-**b**), not only proceed with high efficiency but also are more selective than those that contain less congested linear substrates (cf. **1.32**-**1.34**).

Scheme 1.6: Synthesis of 1,1-Disubstituted Alkenylborons through NHC–Cu-Catalyzed Protoboration of Allenes[a]

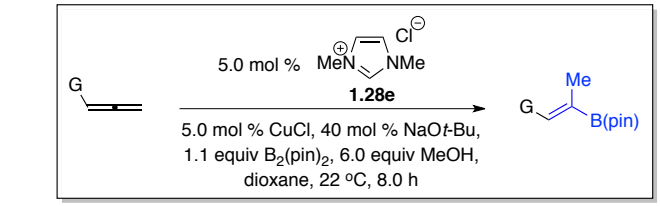


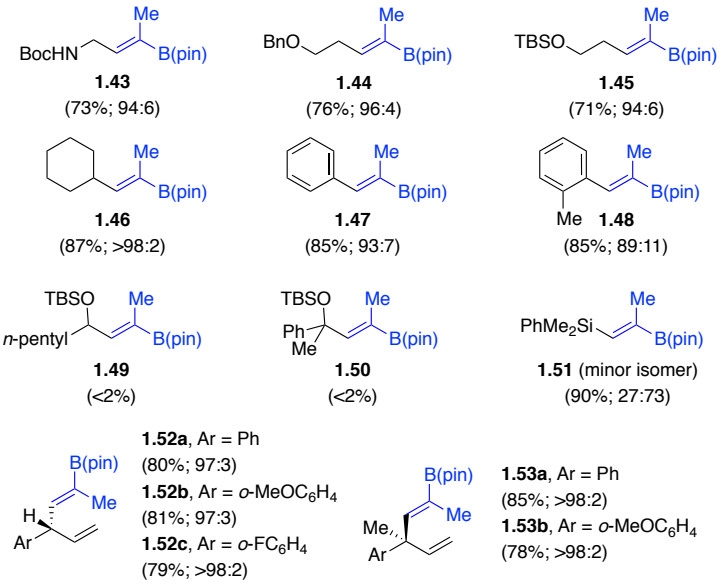
[a] >98% conversion in all cases; same conditions as those in Table 1.1; site selectivity in parenthesis.

NHC–Cu complex in situ generated from imidazolium salt **1.28e** promotes the protoboration with a variety of monosubstituted allenes in high efficiency and site selectivity, delivering trisubstituted alkenylboron products exclusively as *Z* isomers (Scheme 1.7). Less congested linear substrates provide better site selectivity compared with those catalyzed by Cu complex derived from **1.27**. Allenes that carry sizable substituents can be less selective; reaction of *o*-tolyl containing allene generates **1.48** in 85% yield and 89% selectivity (vs. 93% with phenyl-substituted allene). Moreover, silyl-

substituted alkenylboron **1.51** is delivered with a preference for the 1,1-disubstituted isomer (73% of mixture). Contrary to the reactions in Scheme 1.6, allyl ethers are not suitable substrates; <2% conversion to desired protoboration products is observed.

Scheme 1.7: Synthesis of Trisubstituted Alkenylborons through NHC–Cu-Catalyzed Protoboration of Allenes[a]





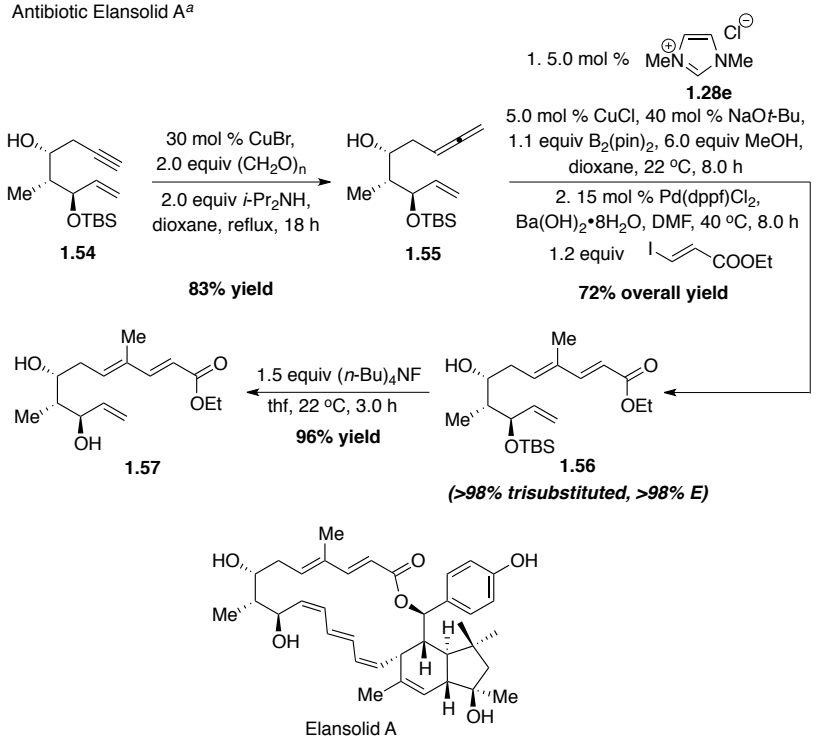
[a] >98% conversion in all cases; same conditions as those in Table 1.1; site selectivity in parenthesis.

1.5 Application of the Catalytic Protoboration Method to Natural Product Fragment Synthesis

To demonstrate its utility, we applied this method to synthesis of the C1–C10 fragment of macrolide elansolid A, which was isolated by Müller and co-workers

recently.[10] The synthesis commences with Crabbé homologation of terminal alkyne **1.54**, illustrating that highly functionalized allenes such as **1.55** can be easily accessed. NHC–Cu-catalyzed protoboration followed by Pd-catalyzed cross-coupling of the resulting trisubstituted alkenylboron with single purification affords triene **1.56** in 72% overall yield as a single stereoisomer, implying that the mild reaction conditions tolerate highly functionalized substrates. Removal of the silyl group in **1.56** delivers diol **1.57**, which constitutes a potential method for total synthesis of natural product elansolid A.

Scheme 1.8: Application to Stereoselective Synthesis of the C1–C10 Fragment of Macrolide Antibiotic Elansolid A[a]



1.6 Mechanistic Rationale for Site Selectivity of NHC–Cu-Catalyzed Protoboration of Monosubstituted Allenes

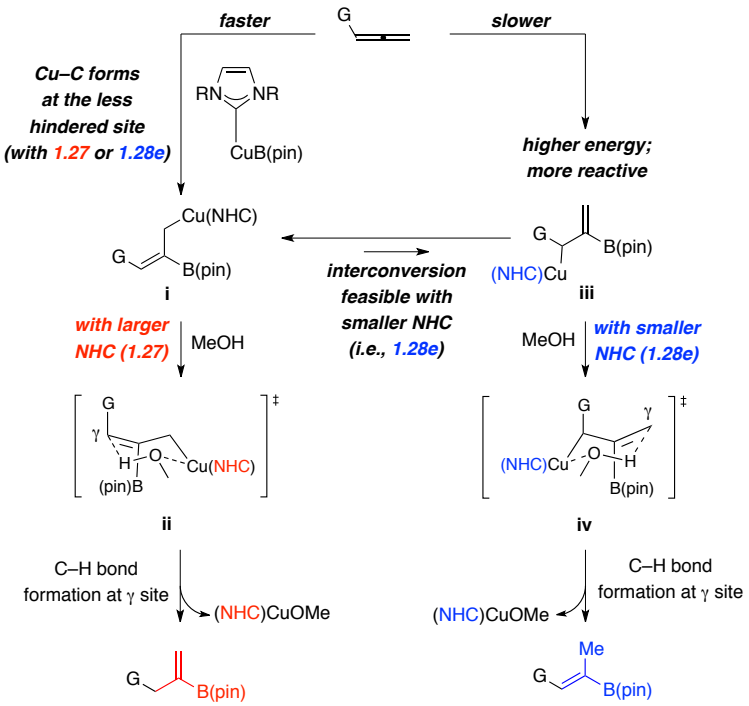
(10) Steinmetz, H.; Gerth, K.; Jansen, R.; Schläger, N.; Dehn, R.; Reinecke, S.; Kirschning, A.; Müller, R. *Angew. Chem., Int. Ed.* **2011**, *50*, 532–536.

The trends in site selectivity with NHC–Cu complexes that have different steric profiles can be rationalized by the pathways outlined in Scheme 1.9 with assistance of DFT calculations. Initial Cu–B addition places the Cu center at less congested carbon of the monosubstituted allene to generate allylcopper complex **i**. Subsequent γ-protonation via six-membered transition state delivers 1,1-disubstituted alkenylboron preferentially when Cu complex in situ generated from larger NHC ligand is used (e.g. **1.27**). With catalyst derived from smaller ligand **1.28e**, the barrier for isomerization to more hindered allylcopper complex **iii** bearing a secondary Cu–C bond is lower, and the isomerization pathway to **iii** becomes feasible. The allyl–Cu(I) complexes might exist in the η^1 form as there is no empty d orbital in a Cu(I) center to accommodate the π electron of the alkene, supported by theoretical studies.[11] The η^1 to η^1 interconversion may proceed by an intramolecular process where the B(pin) can engender a steric barrier. It is also possible that two molecules of the allylcopper complexes are involved during the exchange process, which underscores the significance of a smaller NHC to the rate of interconversion. Moreover, DFT calculations indicate that allylcopper complex **iii** is of higher energy, and can undergo protonaton via **iv** to provide trisubstituted alkenylboron more rapidly (Curtin-Hammett kinetics). The greater reactivity of allylcopper **iii** results from higher energy of HOMO of the more substituted Cu–C bond. Furthermore, as the energy of trisubstituted alkenylboron is lower, the activation barrier to furnish such entities would be lower (Hammond's postulate). Protonation proceeds via six-membered transition state **iv**, which allows for minimization of steric repulsion between allene substituent (G) and the B(pin) and NHC–Cu units, leading to high stereoselectivity.

(11) For a related report regarding allylzinc systems, see: Lichtenberg, C.; Engel, J.; Spaniol, T. P.; Englert, U.; Raabe, G.; Okuda, J. *J. Am. Chem. Soc.* **2012**, *134*, 9805–9811.

Based on this hypothesis, with larger NHC ligand **1.27**, kinetically generated allylcopper complex **i** undergoes protonation faster than equilibration between **i** and **iii**, providing 1,1-disubstituted alkenylborons (non-Curtin–Hammett). With Cu complex bearing smaller ligands, more facile protonation of the allylcopper complex **iii** determines the major product.

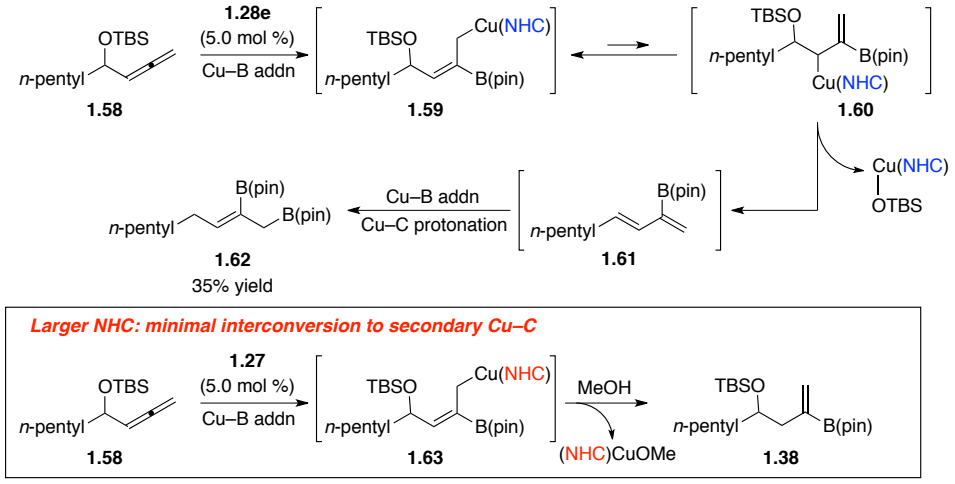
Scheme 1.9: Mechanistic Rationle for the Site Selectivity Trends



The hypothesis described above also provides an explanation for several other observations. For less congested substrates, the activation barrier of isomerization of **i** to **iii** is lower. Protonation of allylcopper complex **iii** becomes more competitive and therefore site selectivity is reduced. As the barrier of protonation of allylcopper **iii** is lower than that of **i**, high selectivity is observed when smaller ligand **1.28e** is employed. As illustrated in Scheme 1.10, the reason why no desired allyl ethers products **1.49**-**1.50** in the presence of smaller ligand **1.28e** are obtained is likely that the corresponding

allylcopper complexes **iii** such as **1.60** might undergo facile elimination followed by a second protoboration of the resulting dienes, affording allylboron products (cf. **1.62**). With larger NHC derived from **1.27**, isomerization of allylcopper complex **1.63** is disfavored, minimizing the elimination process. After γ-protonation, 1,1-disubstituted alkenylboron **1.38** can be generated efficiently. The unusual site selectivity of silyl-containing substrate favoring 1,1-disubstituted alkenylboron is likely due to hyperconjugative stabilization of electron density at adjacent Cu–C bond by the low-lying C–Si σ* orbitals in **iv**, which lowers the energy of transition state **iv** and elevates the activation barrier of protonation. Pathway via **ii** becomes more competitive, and Curtin–Hammett pathway is therefore disfavored.

Scheme 1.10: Effect of Site Selectivity on Efficiency



1.7 Conclusion

In this chapter, we have developed a catalyst-controlled site-selective protoboration of monosubtituted allenes.[12] The investigation described above not only presents a reliable method to access 1,1-disubstituted or trisubstituted alkenylboron compounds efficiently and selectively, but also provides additional mechanistic insights into the effect of catalyst structures on selectivity. The catalysts can be prepared through simple combination of commercially available imidazolium salts, inexpensive and abundant copper salts and base. A wide range of substrates, the monosubstitued allenes, can be synthesized in high efficiency. Utility of the method is demonstrated through a stereoselective synthesis of C1–C10 fragment of antibiotic macrolide elansolid A. Moreover, the method demonstrates a catalytic site- and stereoselective route to access the 2-boron-substituted allylcopper complexes, providing an opportunity for in situ trap of the organocopper intermediate with electrophiles to form C–C bonds.

1.8 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 ($CDCl_3$: δ 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br s = broad singlet, m = multiplet, app. = apparent), and coupling

(12) Meng, F.; Jung, B.; Haeffner, F.; Hoveyda, A. H. *Org. Lett.* **2013**, *15*, 1414–1417.

constant (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. 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. Solvents were purified under a positive pressure of dry argon by a modified Innovative Technologies purification system: toluene, benzene and hexanes were purified through a copper oxide and alumina column; CH_2Cl_2 and Et_2O were purged with Ar and purified by passage through two alumina columns. Tetrahydrofuran (Aldrich Chemical Co.) was purified by distillation from sodium benzophenone ketyl immediately prior to use unless otherwise specified. Methanol (Aldrich Chemical Co.) was distilled over CaH_2. All work-up and purification procedures were carried out with reagent grade solvents (purchased from Fisher Scientific) in air.

1.8.1 Reagents and Ligands

Allenes: prepared according to a previously reported procedure.[13]

(13) (a) Crabbé, P.; Fillion, H.; André, D.; Luche, J.-L. *J. Chem. Soc., Chem. Commun.* **1979**, 859–860. (b) Searles, S.; Li, Y.; Nassim, B.; Lopes, M.-T. R.; Tran, P. T.; Crabbé, P. *J. Chem. Soc., Perkin Trans. 1*, **1984**, 747–751. (c) Inoue, A.; Kondo, J.; Shinokubo, H.; Oshima, K. *Chem. Eur. J.* **2002**, *8*, 1730–1740. (d) Baird, M. S.; Nizovtsev, A. V.; Bolesov, I. G. *Tetrahedron* **2002**, *58*, 1581–1593. (e) Tenaglia, A.; Buono, G. *Org. Lett.* **2011**, *13*, 308–311. (f) Jung, B.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2012**, *134*, 1490–1493.

Allenylboronic acid pinacol ester: purchased from Frontier Scientific, Inc. and used as received.

Barium hydroxide octahydrate: purchased from Aldrich Chemical Co. and used as received.

[1,1'-Bis(diphenylphosphino)ferrocene]dichloropalladium (II): purchased from Strem Chemicals Inc. and used as received.

Bis(pinacolato)diboron: purchased from Frontier Scientific, Inc. and recrystallized from pentane.

Copper (I) bromide: purchased from Strem Chemicals Inc. and used as received.

Copper (I) chloride: purchased from Strem Chemicals Inc. and used as received.

Diisopropylamine: purchased from Aldrich Chemical Co. and used as received.

Dimethylformamide: purchased from Acros Organics Co. and used as received.

Dioxane: purchased from Aldrich Chemical Co. and used as received.

Imidazolium or imidazolinium salts (1.25a-b, 1.26-1.27, 1.28a-e): purchased from Aldrich Chemical Co. and used as received.

Paraformaldehyde: purchased from Aldrich Chemical Co. and used as received.

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

Tetrabutylammonium fluoride solution (1.0 M in thf): purchased from Acros Organics Co. and used as received.

1.8.2 Experimental Procedures and Characterization Data for Synthesis of 1,1-Disubstituted Alkenylborons through NHC–Cu-Catalyzed Protoboration of Allenes

■ **Representative Experimental Procedure for Synthesis of 1,1-Disubstituted Alkenylborons through NHC–Cu-Catalyzed Protoborations of Allenes:** In a N_2-filled glove box, an oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with imidazolium salt **1.27** (2.1 mg, 0.0050 mmol, 5.0 mol %), CuCl (0.5 mg, 0.005 mmol, 5.0 mol%), NaO*t*-Bu (3.8 mg, 0.040 mmol, 40 mol %) and tetrahydrofuran (thf, 0.5 mL). The vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the solution was allowed to stir at 22 °C for one hour. Bis(pinacolato)diboron (27.9 mg, 0.11 mmol, 1.1 equiv) was added to the solution, causing it to turn dark brown immediately. The vial was re-sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and removed from the glove box. The mixture was allowed to stir at 22 °C for 30 min under an atmosphere of N_2. Allene **1.29** (15.6 mg, 0.10 mmol, 1.0 equiv) and MeOH (24.6 μL, 0.60 mmol, 6.0 equiv) were added through syringes. The resulting solution was allowed to stir at 22 °C for eight hours before the reaction was quenched by passing the mixture through a short plug of celite and silica gel and eluted with Et_2O (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide a yellow oil, which was purified by silica gel chromatography (hexanes:Et_2O=100:1) to afford the mixture of **1.30** and **1.31** as a colorless oil (20.8 mg, 0.073 mmol of **1.30** and **1.31**, 73% yield of **1.30** and **1.31**).

(*E*)-4,4,5,5-Tetramethyl-2-(6-phenylhexa-1,5-dien-2-yl)-1,3,2-dioxaborolane (1.30). IR (neat): 3025 (w), 2977 (m), 2927 (w), 1427 (m), 1368 (s), 1308 (s), 1213 (m), 1138 (s), 963 (m), 834 (m), 739 (m), 692 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.31–7.28 (2H,

m), 7.26–7.22 (2H, m), 7.17–7.12 (1H, m), 6.35 (1H, d, J = 15.6 Hz), 6.21 (1H, dt, J = 15.6, 6.8 Hz), 5.79 (1H, d, J = 3.2 Hz), 5.62 (1H, d, J = 3.2 Hz), 2.33–2.31 (4H, m), 1.23 (12H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.1, 130.9, 130.0, 129.8, 128.6, 126.9, 126.1, 83.5, 35.5, 33.0, 24.9; HRMS (ESI$^+$): Calcd for $C_{18}H_{26}B_1O_2$ $[M+H]^+$: 285.2026; Found: 285.2028.

***tert*-Butyl (3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)carbamate (1.32).** IR (neat): 3368 (br), 2977 (m), 2930 (w), 1703 (m), 1511 (m), 1366 (m), 1308 (m), 1140 (s), 1056 (w), 967 (m), 862 (m), 833 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.87 (1H, d, J = 2.4 Hz), 5.68 (1H, d, J = 2.4 Hz), 4.82 (1H, br s), 3.21 (2H, q, J = 4.8 Hz), 2.32 (2H, t, J = 4.8 Hz), 1.43 (9H, s), 1.27 (12H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.1, 132.1, 83.8, 79.2, 40.7, 35.6, 28.6, 24.9; HRMS (ESI$^+$): Calcd for $C_{15}H_{29}B_1N_1O_4$ $[M+H]^+$: 298.2190; Found: 298.2198.

2-(5-(Benzyloxy)pent-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.33). IR (neat): 3062 (w), 2978 (m), 2929 (m), 2855 (m), 1453 (m), 1369 (s), 1308 (s), 1141 (s), 969 (w), 860 (m), 736 (m), 697 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36–7.32 (4H, m), 7.29–7.25 (1H, m), 5.78 (1H, d, J = 2.8 Hz), 5.62 (1H, d, J = 2.8 Hz), 4.50 (2H, s), 3.48 (2H, t, J = 5.2 Hz), 2.23 (2H, t, J = 6.0 Hz), 1.80–1.71 (2H, m), 1.26 (12H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.9, 129.5, 128.5, 127.8, 127.6, 83.5, 72.9, 70.2, 32.0, 29.3, 24.9; HRMS (ESI$^+$): Calcd for $C_{18}H_{28}B_1O_3$ $[M+H]^+$: 303.2132; Found: 303.2136.

***tert*-Butyldimethyl((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-1-yl)oxy)silane (1.34).** IR (neat): 2978 (m), 2955 (m), 2857 (m), 1369 (s), 1309 (s), 1254 (m), 1143 (s), 1100 (s), 969 (w), 836 (s), 775 (s), 671 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400

MHz): δ 5.77 (1H, d, *J* = 2.4 Hz), 5.61 (1H, d, *J* = 2.4 Hz), 3.60 (2H, t, *J* = 5.2 Hz), 2.17 (2H, t, *J* = 6.0 Hz), 1.68–1.62 (2H, m), 1.26 (12H, s), 0.89 (9H, s), 0.04 (6H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 129.3, 83.5, 63.1, 32.5, 31.7, 26.1, 24.9, 18.5, –5.1; HRMS (ESI^+): Calcd for $C_{17}H_{36}B_1O_3Si_1$ $[M+H]^+$: 327.2527; Found: 327.2533.

2-(3-Cyclohexylprop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.35). IR (neat): 2978 (w), 2921 (m), 2850 (m), 1367 (s), 1305 (s), 1208 (m), 1142 (s), 966 (m), 863 (m), 738 (w), 671 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.77 (1H, d, *J* = 3.6 Hz), 5.54 (1H, d, *J* = 3.6 Hz), 2.04 (2H, d, *J* = 7.2 Hz), 1.73–1.60 (6H, m), 1.26 (12H, s), 1.22–1.11 (3H, m), 0.89–0.83 (2H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 130.0, 83.4, 43.4, 37.8, 33.3, 26.8, 26.5, 24.8; HRMS (ESI^+): Calcd for $C_{15}H_{28}B_1O_2$ $[M+H]^+$: 251.2182; Found: 251.2185.

4,4,5,5-Tetramethyl-2-(3-phenylprop-1-en-2-yl)-1,3,2-dioxaborolane (1.36). IR (neat): 3028 (w), 2978 (m), 2927 (w), 1426 (m), 1362 (s), 1308 (s), 1272 (m), 1134 (s), 944 (m), 861 (m), 745 (m), 699 (s), 553 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.33–7.29 (2H, m), 7.26–7.19 (3H, m), 5.89 (1H, d, *J* = 3.2 Hz), 5.59 (1H, d, *J* = 3.2 Hz), 3.54 (2H, s), 1.25 (12H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 140.8, 129.9, 129.3, 128.2, 125.8, 83.6, 41.5, 24.8; HRMS (ESI^+): Calcd for $C_{15}H_{22}B_1O_2$ $[M+H]^+$: 245.1713; Found: 245.1710.

4,4,5,5-Tetramethyl-2-(3-(*o*-tolyl)prop-1-en-2-yl)-1,3,2-dioxaborolane (1.37). IR (neat): 3064 (w), 2977 (m), 2928 (w), 1422 (m), 1361 (s), 1307 (s), 1214 (w), 1135 (s), 946 (m), 862 (m), 740 (s), 627 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.14–7.10 (4H, m), 5.84 (1H, d, *J* = 2.4 Hz), 5.32 (1H, d, *J* = 2.4 Hz), 3.47 (2H, s), 2.26 (3H, s), 1.26 (12H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.7, 136.8, 130.1, 130.0, 129.8, 126.1, 125.8,

83.6, 38.3, 24.9, 19.6; HRMS (ESI$^+$): Calcd for $C_{16}H_{24}B_1O_2$ [M+H]$^+$: 259.1869; Found: 259.1879.

***tert*-Butyldimethyl((2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)non-1-en-4-yl)oxy)silane (1.38).** IR (neat): 2977 (m), 2928 (m), 2856 (m), 1462 (m), 1387 (s), 1308 (s), 1272 (m), 1143 (s), 1052 (m), 1005 (m), 834 (s), 773 (s), 670 (m), 579 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.82 (1H, d, *J* = 3.2 Hz), 5.62 (1H, d, *J* = 3.2 Hz), 3.81–3.76 (1H, m), 2.35 (1H, dd, *J* = 10.4, 3.6 Hz), 2.24 (1H, dd, *J* = 10.4, 6.0 Hz), 1.34–1.32 (3H, m), 1.30–1.23 (14H, m), 1.23–1.19 (4H, m), 1.17–1.09 (2H, m), 0.88 (9H, s), 0.08–0.06 (6H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 132.0, 83.5, 72.0, 44.5, 36.6, 32.1, 26.1, 25.1, 25.0, 24.9, 22.8, 14.2, –4.02, –4.03; HRMS (ESI$^+$): Calcd for $C_{21}H_{44}B_1O_3Si_1$ [M+H]$^+$: 383.3153; Found: 383.3155.

***tert*-Butyldimethyl((2-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-2-yl)oxy)silane (1.39).** IR (neat): 2977 (m), 2958 (m), 2856 (m), 1462 (m), 1304 (s), 1253 (m), 1140 (s), 1001 (s), 916 (w), 829 (s), 772 (s), 678 (s), 577 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.41–7.38 (2H, m), 7.26–7.22 (2H, m), 7.18–7.13 (1H, m), 5.82 (1H, d, *J* = 4.0 Hz), 5.47 (1H, d, *J* = 4.0 Hz), 2.58 (2H, app. d, *J* = 4.0 Hz), 1.59 (3H, s), 1.11 (12H, s), 0.91 (9H, s), 0.04 (3H, s), –0.17 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 148.5, 134.1, 127.6, 126.4, 126.2, 83.4, 77.4, 50.8, 27.7, 26.3, 24.9, 18.6, –1.6, –2.3; HRMS (ESI$^+$): Calcd for $C_{17}H_{24}B_1O_2$ [M–TBSO]$^+$: 271.1869; Found: 271.1862.

Dimethyl(phenyl)(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)silane (1.40). IR (neat): 3068 (w), 2978 (m), 2928 (w), 1426 (m), 1371 (s), 1309 (s), 1247 (m), 1143 (s), 952 (w), 833 (s), 699 (m), 603 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.54–7.51 (2H,

m), 7.35–7.32 (3H, m), 5.68 (1H, d, *J* = 3.6 Hz), 5.38 (1H, d, *J* = 3.6 Hz), 1.92 (2H, s), 1.21 (12H, s), 0.27 (6H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 139.3, 134.0, 128.9, 127.7, 83.5, 24.9, 24.4, –3.1; HRMS (ESI$^+$): Calcd for $C_{17}H_{28}B_1O_2Si_1$ $[M+H]^+$: 303.1952; Found: 303.1964.

(*S*)-4-Phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,5-hexadiene (1.41a). IR (neat): 3061 (w), 3027 (w), 2977 (m), 2929 (w), 1624 (w), 1600 (w), 1492 (w), 1448 (m), 1410 (m), 1367 (s), 1343 (m), 1306 (s), 1272 (m), 1212 (m), 1164 (m), 1139 (s), 1111 (m), 1076 (w), 1029 (w), 992 (w), 961 (w), 942 (m), 912 (m), 860 (s), 834 (m), 755 (m), 698 (s), 670 (s), 578 (m), 520 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.29–7.26 (2H, m), 7.21–7.15 (3H, m), 5.97 (1H, ddd, *J* = 17.4, 10.0, 7.6 Hz), 5.78 (1H, d, *J* = 3.2 Hz), 5.53 (1H, d, *J* = 3.2 Hz), 5.00 (1H, dd, *J* = 10.0, 1.2 Hz), 4.98 (1H, dd, *J* = 17.4, 1.2 Hz), 3.53 (1H, td, *J* = 7.6, 7.0 Hz) 2.58 (2H, dd, *J* = 7.0, 2.8 Hz), 1.24 (12H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 144.4, 142.1, 131.3, 128.6, 128.4, 128.0, 126.1, 114.4, 83.4, 49.9, 41.5, 24.9; HRMS (ESI$^+$): Calcd for $C_{18}H_{26}B_1O_2$ $[M+H]^+$: 285.2025; Found: 285.2021; specific rotation: $[\alpha]_D^{23.2}$ +0.17 (*c* = 1.20, $CHCl_3$).

(*S*)-4-(2-Methoxyphenyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,5-hexadiene (1.41b). IR (neat): 3064 (w), 2977 (m), 2934 (m), 2835 (w), 1635 (w), 1617 (w), 1598 (w), 1585 (w), 1491 (s), 1463 (m), 1437 (m), 1366 (s), 1306 (s), 1239 (s), 1212 (m), 1164 (m), 1139 (s), 1107 (m), 1052 (m), 1030 (s), 995 (w), 970 (m), 939 (m), 910 (m), 861 (s), 832 (w), 808 (w), 783 (w), 750 (s), 671 (s), 578 (m), 517 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.17–7.12 (2H, m), 6.89 (1H, dd, *J* = 7.6, 1.2 Hz), 6.83 (1H, d, *J* = 7.6 Hz), 6.01 (1H, ddd, *J* = 17.4, 10.0, 7.4 Hz), 5.73 (1H, d, *J* = 3.6 Hz), 5.49 (1H, d, *J* = 3.6 Hz), 4.99–4.94 (2H, m), 3.98 (1H, td, *J* = 7.6, 7.4 Hz), 3.80 (3H, s), 2.58 (1H, d, *J* =

7.6 Hz), 2.53 (1H, d, J = 7.6 Hz), 1.25 (12H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.9, 141.6, 132.5, 130.4, 128.1, 126.8, 120.4, 113.9, 110.7, 83.2, 55.3, 42.3, 40.0, 24.7; HRMS (ESI^+): Calcd for $C_{19}H_{28}B_1O_3$ $[M+H]^+$: 315.2131; Found: 315.2129; specific rotation: $[\alpha]_D^{24.6}$ +5.5 (c = 1.70, $CHCl_3$).

(*S*)-4-(2-Fluorophenyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,5-hexadiene (1.41c). IR (neat): 3065 (w), 2978 (m), 2929 (w), 1637 (w), 1616 (w), 1583 (w), 1489 (m), 1445 (m), 1425 (m), 1388 (m), 1367 (s), 1308 (s), 1252 (s), 1225 (s), 1165 (m), 1139 (s), 1110 (m), 1036 (w), 992 (m), 970 (m), 942 (m), 914 (m), 861 (s), 827 (m), 802 (w), 753 (s), 737 (m), 679 (m), 578 (w), 555 (w), 520 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.18 (1H, dd, J = 7.6, 7.6 Hz), 7.16–7.11 (1H, m), 7.05 (1H, dd, J = 7.6, 7.6 Hz), 7.03–6.94 (1H, m), 6.00 (1H, ddd, J = 17.2, 10.4, 7.2 Hz), 5.75 (1H, d, J = 3.6 Hz), 5.49 (1H, d, J = 3.6 Hz), 5.04–4.99 (2H, m), 3.90 (1H, td, J = 7.6, 7.2 Hz), 2.64 (1H, d, J = 8.4 Hz), 2.54 (1H, d, J = 8.4 Hz), 1.25 (12H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 160.8 (d, J_{CF} = 244.1 Hz), 140.8, 131.4, 130.9 (d, J_{CF} = 14.1 Hz), 129.2 (d, J_{CF} = 5.2 Hz), 127.5 (d, J_{CF} = 8.2 Hz), 124.0 (d, J_{CF} = 3.8 Hz), 115.5, 115.3, 114.7, 83.5, 42.6 (d, J_{CF} = 1.4 Hz), 40.5, 24.9; HRMS (ESI^+): Calcd for $C_{18}H_{25}B_1F_1O_2$ $[M+H]^+$: 303.1931; Found: 303.1940; specific rotation: $[\alpha]_D^{22.1}$ +0.17 (c = 1.20, $CHCl_3$).

(*R*)-4-Methyl-4-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,5-hexadiene (1.42a). IR (neat): 3084 (w), 3059 (w), 2976 (m), 2930 (w), 1635 (w), 1612 (w), 1493 (w), 1443 (m), 1423 (m), 1365 (s), 1305 (s), 1268 (w), 1212 (m), 1192 (m), 1164 (m), 1140 (s), 1112 (m), 1072 (w), 1029 (w), 1002 (w), 977 (m), 959 (m), 947 (m), 911 (m), 864 (m), 833 (w), 758 (m), 722 (m), 697 (s), 670 (w), 579 (w), 537 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.34 (2H, d, J = 7.6 Hz), 7.27 (2H, dd, J = 7.6, 7.6 Hz), 7.15 (1H,

app. d, J = 7.6 Hz), 6.11 (1H, dd, J = 17.6, 10.8 Hz), 5.82 (1H, d, J = 1.8 Hz), 5.40 (1H, d, J = 1.8 Hz), 5.07 (1H, d, J = 10.8 Hz), 5.01 (1H, d, J = 17.6 Hz), 2.64 (1H, ABq, J = 12 Hz), 1.30 (3H, s), 1.19 (12H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.9, 146.6, 132.9, 128.0, 126.9, 125.8, 112.3, 83.4, 45.6, 44.9, 24.7, 24.1; HRMS (ESI^+): Calcd for $C_{19}H_{28}B_1O_2$ $[M+H]^+$: 299.2182; Found: 299.2192; specific rotation: $[\alpha]_D^{21.2}$ +3.70 (c = 2.70, $CHCl_3$).

(*R*)-4-Methyl-4-(2-methoxyphenyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,5-hexadiene (1.42b). IR (neat): 3060 (w), 2976 (m), 2931 (w), 2833 (w), 1633 (w), 1597 (w), 1580 (w), 1488 (m), 1461 (m), 1433 (m), 1364 (s), 1342 (m), 1303 (s), 1238 (s), 1213 (m), 1190 (m), 1164 (m), 1140 (s), 1070 (m), 1049 (m), 1029 (s), 976 (m), 960 (m), 944 (m), 907 (m), 863 (w), 827 (m), 793 (w), 749 (s), 725 (m), 712 (m), 670 (m), 579 (w), 518 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.19–7.15 (2H, m), 6.86–6.84 (2H, m), 6.33 (1H, dd, J = 17.6, 10.8 Hz), 5.76 (1H, d, J = 3.2 Hz), 5.35 (1H, d, J = 3.2 Hz), 4.96 (1H, d, J = 10.8 Hz), 4.90 (1H, d, J = 17.6 Hz), 3.82 (3H, s), 2.80 (1H, ABq, J = 12.4 Hz), 1.38 (3H, s), 1.17 (12H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.4, 147.0, 135.4, 132.4, 128.0, 127.4, 120.3, 111.9, 111.0, 83.3, 55.1, 44.5, 43.2, 25.0, 24.6, 23.5; HRMS (ESI^+): Calcd for $C_{20}H_{30}B_1O_3$ $[M+H]^+$: 329.2288; Found: 329.2289; specific rotation: $[\alpha]_D^{21.7}$ –15.8 (c = 2.30, $CHCl_3$).

1.8.3 Experimental Procedures and Characterization Data for Synthesis of Trisubstituted Alkenylborons through NHC–Cu-Catalyzed Protoboration of Allenes

■ **Representative Experimental Procedure for Synthesis of Trisubstituted Alkenylborons through NHC–Cu-Catalyzed Protoborations of Allenes:** In a N_2-filled glove box, an oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with imidazolium salt **1.28e** (0.7 mg, 0.005 mmol, 5.0 mol %), CuCl (0.5 mg, 0.005 mmol, 5.0 mol%), NaO*t*-Bu (3.8 mg, 0.040 mmol, 40 mol %) and dioxane (0.5 mL). The vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the solution was allowed to stir at 22 °C for one hour. Bis(pinacolato)diboron (27.9 mg, 0.11 mmol, 1.1 equiv) was added to the solution, causing it to turn dark brown immediately. The vial was re-sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and removed from the glove box. The mixture was allowed to stir at 22 °C for 30 min under an atmosphere of N_2. Allene **1.29** (15.6 mg, 0.10 mmol, 1.0 equiv) and MeOH (24.6 μL, 0.60 mmol, 6.0 equiv) were added through syringes. The resulting solution was allowed to stir at 22 °C for eight hours before the reaction was quenched by passing the mixture through a short plug of celite and silica gel and eluted with Et_2O (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide a yellow oil, which was purified by silica gel chromatography (hexanes:Et_2O=100:1) to afford the mixture of **1.30** and **1.31** as a colorless oil (18.8 mg, 0.066 mmol of **1.30** and **1.31**, 66% yield of **1.30** and **1.31**).

4,4,5,5-Tetramethyl-2-((2*Z*,5*E*)-6-phenylhexa-2,5-dien-2-yl)-1,3,2-dioxaborolane (1.31). IR (neat): 3025 (w), 2977 (m), 2928 (w), 1627 (m), 1410 (m), 1368 (s), 1303 (s), 1145 (s), 964 (m), 856 (m), 742 (m), 692 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.35–7.32 (2H, m), 7.30–7.27 (2H, m), 7.21–7.17 (1H, m), 6.43–6.38 (2H, m), 6.21 (1H, dt, *J* = 15.6, 6.8 Hz), 3.05 (2H, t, *J* = 6.8 Hz), 1.75 (3H, s), 1.26 (12H, s); ^{13}C NMR ($CDCl_3$,

100 MHz): δ 142.8, 137.7, 130.5, 128.4, 127.9, 126.9, 126.0, 83.2, 32.3, 24.8, 13.9; HRMS (ESI$^+$): $C_{18}H_{26}B_1O_2$ $[M+H]^+$: 285.2026; Found: 285.2035.

(*Z*)-*tert*-Butyl (3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-2-en-1-yl)carbamate (1.43). IR (neat): 3360 (br), 2977 (m), 2929 (m), 1702 (s), 1517 (m), 1370 (s), 1309 (s), 1248 (m), 1168 (s), 1142 (s), 1023 (w), 862 (m), 780 (w), 667 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.22 (1H, td, *J* = 6.0, 1.6 Hz), 4.54 (1H, br s), 3.88–3.84 (2H, m), 1.71 (3H, s), 1.43 (9H, s), 1.26 (12H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.0, 141.8, 83.6, 79.6, 39.0, 28.6, 24.9, 14.2; HRMS (ESI$^+$): Calcd for $C_{15}H_{29}B_1N_1O_4$ $[M+H]^+$: 298.2190; Found: 298.2201.

(*Z*)-2-(5-(Benzyloxy)pent-2-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.44). IR (neat): 2977 (m), 2926 (m), 2856 (m), 1495 (m), 1370 (s), 1304 (m), 1213 (m), 1135 (s), 1029 (w), 859 (m), 736 (m), 698 (m), 669 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35–7.31 (4H, m), 7.30–7.27 (1H, m), 6.31 (1H, td, *J* = 6.8, 2.0 Hz), 4.53 (2H, s), 3.53 (2H, t, *J* = 7.2 Hz), 2.48 (2H, app. qd, *J* = 7.2, 1.2 Hz), 1.70 (3H, s), 1.26 (12H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 141.9, 138.6, 128.5, 127.8, 127.6, 83.3, 73.0, 69.3, 29.5, 24.9, 14.2; HRMS (ESI$^+$): Calcd for $C_{18}H_{28}B_1O_3$ $[M+H]^+$: 303.2132; Found: 303.2140.

(*Z*)-*tert*-Butyldimethyl((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-3-en-1-yl)oxy)silane (1.45). IR (neat): 2978 (m), 2954 (m), 2929 (m), 2857 (m), 1634 (m), 1369 (s), 1303 (s), 1255 (s), 1136 (s), 1099 (s), 1006 (w), 939 (m), 835 (s), 775 (s), 669 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.28 (1H, td, *J* = 5.2, 1.6 Hz), 3.66 (2H, t, *J* = 7.2 Hz), 2.37 (2H, app. qd, *J* = 8.0, 0.8 Hz), 1.70 (3H, s), 1.26 (12H, s), 0.89 (9H, s), 0.05

(6H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 142.0, 83.3, 62.5, 32.7, 26.1, 24.9, 18.6, 14.1, –5.1; HRMS (ESI$^+$): Calcd for $C_{17}H_{36}B_1O_3Si_1$ $[M+H]^+$: 327.2527; Found: 327.2537.

(*Z*)-2-(1-Cyclohexylprop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.46). IR (neat): 2978 (m), 2923 (m), 2850 (m), 1631 (m), 1368 (s), 1300 (s), 1226 (w), 1142 (s), 1087 (m), 987 (m), 863 (m), 692 (m), 580 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.12 (1H, dd, *J* = 8.8, 1.2 Hz), 2.40–2.31 (1H, m), 1.72–1.60 (9H, m), 1.27–1.17 (13H, m), 1.16–1.04 (3H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 152.0, 83.2, 37.7, 32.4, 26.2, 26.1, 24.9, 14.0; HRMS (ESI$^+$): Calcd for $C_{15}H_{28}B_1O_2$ $[M+H]^+$: 251.2182; Found: 251.2177.

(*Z*)-4,4,5,5-Tetramethyl-2-(1-phenylprop-1-en-2-yl)-1,3,2-dioxaborolane (1.47). IR (neat): 3024 (w), 2977 (m), 2929 (w), 1617 (m), 1447 (m), 1366 (s), 1308 (s), 1207 (m), 1144 (s), 1103 (s), 960 (m), 924 (w), 864 (m), 751 (m), 698 (m), 667 (m), 554 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.46–7.38 (4H, m), 7.31–7.26 (2H, m), 2.05 (3H, d, *J* = 2.0 Hz), 1.37 (12H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 142.5, 138.1, 129.5, 128.2, 127.2, 83.6, 25.0, 16.0; HRMS (ESI$^+$): Calcd for $C_{15}H_{22}B_1O_2$ $[M+H]^+$: 245.1713; Found: 245.1720.

(*Z*)-4,4,5,5-Tetramethyl-2-(1-(*o*-tolyl)prop-1-en-2-yl)-1,3,2-dioxaborolane (1.48). IR (neat): 2977 (m), 2928 (w), 1619 (m), 1482 (m), 1366 (s), 1307 (s), 1214 (m), 1145 (s), 1099 (s), 959 (m), 864 (m), 744 (s), 669 (s), 580 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.30–7.28 (1H, m), 7.21–7.13 (4H, m), 2.28 (3H, s), 1.80 (3H, s), 1.33 (12H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 142.0, 137.3, 136.4, 129.9, 129.1, 127.2, 125.2, 83.6, 25.0, 20.0, 15.8; HRMS (ESI$^+$): Calcd for $C_{16}H_{24}B_1O_2$ $[M+H]^+$: 259.1869; Found: 259.1874.

(*S*,*Z*)-4,4,5,5-Tetramethyl-2-(4-phenylhexa-2,5-dien-2-yl)-1,3,2-dioxaborolane (1.52a). IR (neat): 3081 (w), 3060 (w), 3026 (w), 2977 (m), 2929 (w), 1624 (m), 1600 (w), 1492 (w), 1450 (w), 1407 (m), 1367 (s), 1340 (m), 1303 (s), 1271 (m), 1235 (w), 1213 (w), 1137 (s), 1111 (m), 1097 (m), 1076 (w), 1029 (m), 993 (m), 977 (m), 959 (m), 914 (m), 860 (s), 834 (w), 756 (m), 743 (m), 698 (s), 669 (s), 578 (w), 542 (w), 520 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.32–7.28 (2H, m), 7.26–7.23 (2H, m), 7.20–7.18 (1H, m), 6.45 (1H, d, *J* = 9.2 Hz), 6.00 (1H, ddd, *J* = 17.4, 10.0, 8.0 Hz), 5.12–5.08 (2H, m), 4.44 (1H, dd, *J* = 9.2, 8.0 Hz), 1.78 (3H, s), 1.26 (12H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 145.9, 143.2, 139.7, 128.6, 128.0, 126.4, 126.1, 115.0, 83.3, 48.5, 24.9, 14.3; HRMS (ESI^+): Calcd for $C_{18}H_{26}B_1O_2$ $[M+H]^+$: 285.2025; Found: 285.2025; specific rotation: $[\alpha]_D^{21.5}$ +80.0 (*c* = 1.10, $CHCl_3$).

(*S*,*Z*)-2-(4-(2-Methoxyphenyl)hexa-2,5-dien-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.52b). IR (neat): 3078 (w), 2977 (m), 2930 (w), 2836 (w), 1624 (m), 1598 (w), 1585 (w), 1491 (m), 1463 (m), 1438 (w), 1407 (m), 1369 (s), 1339 (m), 1304 (s), 1242 (s), 1214 (w), 1142 (s), 1102 (m), 1051 (w), 1030 (m), 995 (w), 959 (w), 914 (w), 862 (m), 835 (w), 784 (w), 753 (m), 693 (w), 672 (m), 578 (w), 519 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.22 (1H, app. dd, *J* = 7.6, 1.6 Hz), 7.16 (1H, dd, *J* = 7.6, 7.6 Hz), 6.91 (1H, dd, *J* = 7.6, 7.6 Hz), 6.84 (1H, d, *J* = 7.6 Hz), 6.41 (1H, d, *J* = 8.8 Hz), 6.02 (1H, ddd, *J* = 17.4, 10.0, 6.0 Hz), 5.08–5.03 (2H, m), 4.88 (1H, dd, *J* = 8.8, 6.0 Hz), 3.81 (3H, s), 1.76 (3H, s), 1.24 (12H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.9, 146.2, 139.9, 131.9, 128.8, 127.3, 120.8, 114.4, 110.9, 83.2, 77.1, 55.6, 41.2, 24.9, 14.2; HRMS (ESI^+): Calcd for $C_{19}H_{28}B_1O_3$ $[M+H]^+$: 315.2131; Found: 315.2136; specific rotation: $[\alpha]_D^{22.1}$ +35.4 (*c* = 1.28, $CHCl_3$).

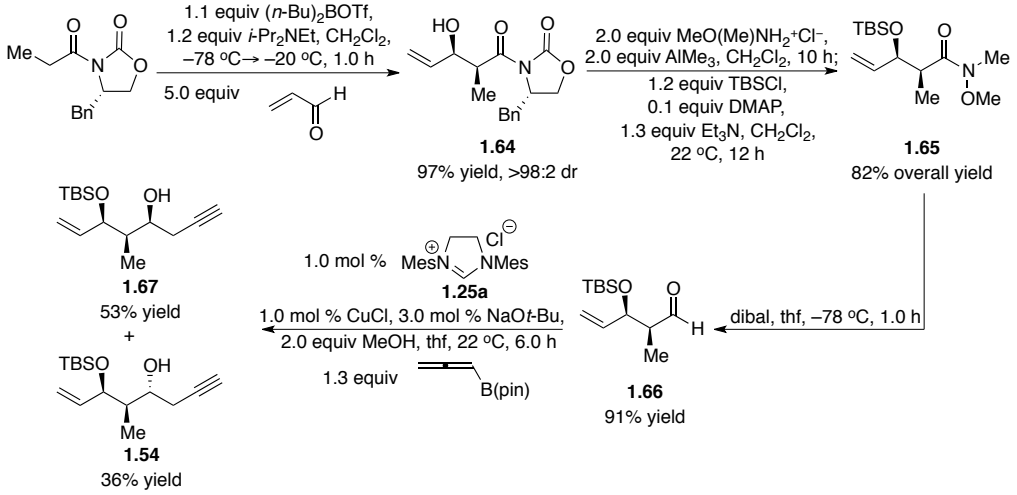
(*S*,*Z*)-2-(4-(2-Fluorophenyl)hexa-2,5-dien-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.52c). IR (neat): 2978 (m), 2925 (w), 1626 (m), 1581 (w), 1488 (m), 1454 (m), 1408 (m), 1369 (s), 1339 (m), 1305 (s), 1272 (w), 1228 (m), 1143 (s), 1094 (m), 1034 (w), 966 (w), 919 (w), 859 (m), 802 (w), 754 (m), 692 (w), 670 (m), 579 (w), 552 (w), 521 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.26 (1H, dd, J = 7.6, 7.6 Hz), 7.20–7.14 (1H, m), 7.08 (1H, dd, J = 7.6, 7.6 Hz), 7.00 (1H, dd, J = 7.6, 7.6 Hz), 6.42 (1H, d, J = 9.2 Hz), 6.01 (1H, ddd, J = 17.2, 10.4, 7.6 Hz), 5.11–5.06 (2H, m), 4.74 (1H, dd, J = 9.2, 7.6 Hz), 1.76 (3H, s), 1.25 (12H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 160.6 (d, J_{CF} = 244 Hz), 144.5, 138.7, 130.2 (d, J_{CF} = 14.8 Hz), 129.5 d, J_{CF} = 5.2 Hz), 127.9 (d, J_{CF} = 8.2 Hz), 124.3 (d, J_{CF} = 3.0 Hz), 115.6, 115.4, 115.2, 83.4, 41.4 (d, J_{CF} = 2.2 Hz), 24.9, 14.2; HRMS (ESI^+): Calcd for $C_{18}H_{25}B_1F_1O_2$ $[M+H]^+$: 303.1931; Found: 303.1928; specific rotation: $[\alpha]_D^{20.8}$ +56.2 (c = 1.60, $CHCl_3$).

(*R*,*Z*)-4,4,5,5-Tetramethyl-2-(4-methyl-4-phenylhexa-2,5-dien-2-yl)-1,3,2-dioxaborolane (1.53a). IR (neat): 3083 (w), 3057 (w), 2976 (m), 2929 (w), 1617 (m), 1599 (w), 1491 (w), 1445 (m), 1406 (m), 1368 (s), 1337 (s), 1303 (s), 1271 (m), 1213 (m), 1144 (s), 1102 (s), 1075 (w), 1028 (w), 1001 (m), 964 (s), 913 (s), 860 (s), 834 (w), 822 (w), 765 (m), 732 (w), 700 (s), 668 (s), 578 (w), 539 (w), 522 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.32 (2H, d, J = 7.6 Hz), 7.27 (2H, dd, J = 7.6, 7.6 Hz), 7.16 (1H, app. d, J = 7.6 Hz), 6.52 (1H, s), 6.24 (1H, dd, J = 17.6, 10.8 Hz), 5.12 (1H, d, J = 10.8 Hz), 5.04 (1H, d, J = 17.6 Hz), 1.52 (3H, s), 1.33 (3H, s), 1.27 (12H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 151.2, 147.9, 144.4, 128.2, 127.0, 125.8, 112.4, 83.4, 48.4, 28.8, 24.9, 16.0; HRMS (ESI^+): Calcd for $C_{19}H_{28}B_1O_2$ $[M+H]^+$: 299.2182; Found: 299.2178; specific rotation: $[\alpha]_D^{21.5}$ –45.4 (c = 1.10, $CHCl_3$).

(*R*,*Z*)-2-(4-(2-Methoxyphenyl)-4-methylhexa-2,5-dien-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.53b). IR (neat): 2976 (m), 2932 (w), 2833 (w), 1617 (m), 1596 (w), 1580 (w), 1488 (m), 1459 (m), 1434 (m), 1406 (m), 1369 (s), 1334 (s), 1298 (s), 1272 (m), 1241 (s), 1214 (m), 1145 (s), 1125 (s), 1094 (s), 1070 (m), 1048 (w), 1028 (m), 1008 (m), 964 (m), 910 (m), 860 (s), 835 (w), 822 (w), 792 (w), 750 (s), 726 (w), 689 (m), 668 (s), 578 (w), 520 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.30 (1H, d, *J* = 7.6 Hz), 7.19 (1H, dd, *J* = 7.6, 7.6 Hz), 6.90 (1H, dd, *J* = 7.6, 7.6 Hz), 6.86 (1H, d, *J* = 7.6 Hz), 6.58 (1H, s), 6.34 (1H, dd, *J* = 17.6, 10.8 Hz), 5.06 (1H, d, *J* = 10.8 Hz), 5.00 (1H, d, *J* = 17.6 Hz), 3.72 (3H, s), 1.57 (3H, s), 1.27 (3H, s), 1.24 (12H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 157.7, 152.8, 144.4, 136.6, 127.4, 127.2, 120.7, 112.7, 111.7, 83.1, 55.6, 46.5, 25.3, 24.9, 14.7; HRMS (ESI^+): Calcd for $C_{20}H_{30}B_1O_3$ $[M+H]^+$: 329.2288; Found: 329.2298; specific rotation: $[\alpha]_D^{21.8}$ –53.9 (*c* = 2.50, $CHCl_3$).

1.8.4 Stereoselective Synthesis of C1–C10 Fragment of Antibiotic Macrolide Elansolid A

Scheme S1: Stereoselective Synthesis of Homopropargyl Alcohol **1.54**.



Experimental Procedure for Synthesis of 1.64: The experimental procedure has been reported previously.[14]

Imide 1.64. The title compound has been previously reported and spectral data match those described.[14] ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36–7.26 (3H, m), 7.22–7.20 (2H, m), 5.86 (1H, ddd, *J* = 17.2, 10.4, 5.6 Hz), 5.36 (1H, dt, *J* = 17.2, 1.6 Hz), 5.23 (1H, dt, *J* = 10.4, 1.6 Hz), 4.74–4.69 (1H, m), 4.52–4.50 (1H, m), 4.26–4.18 (2H, m), 3.88 (1H, qd, *J* = 6.8, 3.2 Hz), 3.26 (1H, dd, *J* = 13.6, 3.2 Hz), 2.85 (1H, d, *J* = 3.2 Hz), 2.80 (1H, dd, *J* = 13.6, 9.6 Hz), 1.25 (3H, d, *J* = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.8, 153.2, 137.4, 135.2, 129.6, 129.1, 127.6, 116.5, 72.7, 66.4, 55.3, 42.6, 38.0, 11.1.

Experimental Procedure for Synthesis of 1.65: The experimental procedure has been reported previously.[14]

Weinreb Amide 1.65. The title compound has been previously reported and spectral data match those described.[14] ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.82 (1H, ddd, *J* = 17.2, 10.4, 6.4 Hz), 5.18 (1H, dt, *J* = 17.2, 1.2 Hz), 5.05 (1H, dt, *J* = 10.4, 1.2 Hz), 4.25–4.21 (1H, m), 3.64 (3H, s), 3.13 (3H, s), 3.02–2.97 (1H, m), 1.17 (3H, d, *J* = 6.8 Hz), 0.87 (9H, s), 0.07 (3H, s), 0.03 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.0, 140.2, 115.4, 75.9, 61.6, 42.9, 32.2, 26.0, 18.4, 14.7, –4.1, –4.7.

Experimental Procedure for Synthesis of 1.66: The experimental procedure has been reported previously.[14]

Aldehyde 1.66. The title compound has been previously reported and spectral data match those described.[14] ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.76 (1H, d, *J* = 1.2 Hz), 5.82 (1H, ddd,

(14) (a) Evans, D. A.; Bender, S. L.; Morris, J. *J. Am. Chem. Soc.* **1988**, *110*, 2506–2526; (b) Evans, D. A.; Gage, J. R.; Leighton, J. L. *J. Am. Chem. Soc.* **1992**, *114*, 9434–9453.

J = 17.2, 10.4, 6.0 Hz), 5.25 (1H, dt, *J* = 17.2, 1.6 Hz), 5.17 (1H, dt, *J* = 10.4, 1.6 Hz), 4.55–4.51 (1H, m), 2.54–2.43 (1H, qdd, *J* = 6.8, 4.4, 1.2 Hz), 1.06 (3H, d, *J* = 6.8 Hz), 0.88 (9H, s), 0.05 (3H, s), 0.03 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 204.8, 138.5, 116.1, 73.7, 52.7, 25.9, 18.3, 8.4, –4.1, –4.9.

Experimental Procedure for Synthesis of 1.54: In a N_2-filled glove box, an oven-dried round bottom flask (25 mL) with a magnetic stir bar was charged with imidazolinium salt **1.25a** (6.8 mg, 0.020 mmol, 1.0 mol %), CuCl (2.0 mg, 0.020 mmol, 1.0 mol%), NaO*t*-Bu (5.8 mg, 0.060 mmol, 3.0 mol %) and tetrahydrofuran (thf, 10 mL). The vessel was sealed with a septum and removed from glove box. The solution was allowed to stir at 22 °C for one hour. AllenylB(pin) (467 μL, 2.60 mmol, 1.3 equiv), aldehyde **1.66** (457 mg, 2.00 mmol, 1.0 equiv) and MeOH (162 μL, 4.00 mmol, 2.0 equiv) were added to the solution through syringes. The mixture was allowed to stir at 22 °C for six hours before the reaction was quenched by passing the mixture through a short plug of silica gel and eluted with Et_2O (3 × 10 mL). The filtrate was concentrated *in vacuo* to provide a yellow oil, which was purified by silica gel chromatography (hexanes:ethyl acetate = 30:1) to afford the desired product **1.54** and **1.67** as a colorless oil (**1.54:** 194.4 mg, 0.724 mmol, 36% yield; **1.67:** 285.1 mg, 1.062 mmol, 53% yield).

Homopropargyl alcohol 1.54. IR (neat): 3458 (br), 3312 (w), 2955 (w), 2929 (w), 2886 (w), 2857 (w), 1471 (w), 1462 (w), 1405 (w), 1389 (w), 1361 (w), 1252 (m), 1122 (w), 1078 (m), 1026 (m), 992 (m), 957 (w), 924 (m), 833 (s), 774 (s), 671 (m), 628 (s), 586 (w), 539 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.89 (1H, ddd, *J* = 17.2, 10.4, 6.0 Hz), 5.24 (1H, ddd, *J* = 17.2, 1.6, 1.6 Hz), 5.19 (1H, ddd, *J* = 10.4, 1.6, 1.6 Hz), 4.36–4.33 (1H, m), 4.15 (1H, d, *J* = 2.4 Hz), 3.73–3.68 (1H, m), 2.48 (1H, ddd, *J* = 16.8, 4.0, 2.8 Hz),

2.30 (1H, ddd, J = 16.8, 6.0, 2.8 Hz), 2.01 (1H, dd, J = 2.8, 2.8 Hz), 1.94 (1H, ddd, J = 9.6, 6.6, 3.2 Hz), 0.90 (9H, s), 0.81 (3H, d, J = 6.8 Hz), 0.09 (3H, s), 0.05 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 137.1, 116.4, 81.1, 77.8, 71.7, 70.2, 42.8, 25.9, 25.4, 18.2, 12.5, –4.3, –5.0; HRMS (ESI^+): Calcd for $C_{15}H_{29}O_2Si_1$ $[M+H]^+$: 269.1937; Found: 269.1930; specific rotation: $[\alpha]_D^{21.7}$ +20.7 (c = 2.00, $CHCl_3$).

Experimental Procedure for Synthesis of 1.55: An oven-dried round bottom flask (10 mL) equipped with a reflux condenser and a magnetic stir bar was charged with homopropargyl alcohol (100 mg, 0.370 mmol, 1.0 equiv), paraformaldehyde (23 mg, 0.74 mmol, 2.0 equiv), CuBr (17 mg, 0.12 mmol, 0.30 equiv), diisopropylamine (0.10 mL, 0.74 mmol, 2.0 equiv) and dioxane (2 mL) under N_2 atmosphere. The resulting mixture was allowed to stir at 110 °C for eight hours and the reaction was quenched by addition of saturated aqueous Na_2CO_3 solution (5 mL). The aqueous layer was washed with diethyl ether (3 × 5 mL) and the combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography (hexanes:Et_2O = 10:1) to afford homoallenyl alcohol **1.55** (87 mg, 0.31 mmol, 83%) as a colorless oil.

Homoallenyl alcohol 1.55. IR (neat): 3447 (br), 2955 (w), 2929 (w), 2886 (w), 2857 (w), 1955 (w), 1471 (w), 1462 (w), 1405 (w), 1388 (w), 1360 (w), 1252 (m), 1188 (w), 1079 (m), 1023 (m), 993 (m), 958 (w), 922 (m), 832 (s), 773 (s), 678 (m), 584 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.90 (1H, ddd, J = 17.2, 10.8, 6.4 Hz), 5.25–5.17 (3H, m), 4.66 (2H, ddd, J = 6.8, 3.2, 2.4 Hz), 4.34–4.31 (1H, m), 4.03 (1H, s), 3.69–3.64 (1H, m), 2.36–2.28 (1H, m), 2.13–2.04 (1H, m), 1.85–1.77 (1H, m), 0.90 (9H, s), 0.79 (3H, d, J = 7.2 Hz), 0.09 (3H, s), 0.05 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 209.2, 137.1, 116.1,

86.0, 78.0, 74.1, 72.8, 42.9, 34.3, 25.7, 18.0, 12.4, –4.5, –5.2; HRMS (ESI$^+$): Calcd for $C_{16}H_{31}O_2Si_1$ $[M+H]^+$: 283.2088; Found: 283.2093; specific rotation: $[\alpha]_D^{21.2}$ +23.0 (*c* = 0.75, $CHCl_3$).

Experimental Procedure for Synthesis of 1.56: In a N_2-filled glove box, an oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with imidazolium salt **1.28e** (1.7 mg, 0.013 mmol, 5.0 mol %), CuCl (1.2 mg, 0.013 mmol, 5.0 mol %), NaO*t*Bu (9.2 mg, 0.096 mmol, 40 mol %) and dioxane (0.5 mL). The reaction vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the solution was allowed to stir at 22 °C for one hour. Bis(pinacolato)diboron (68 mg, 0.27 mmol, 1.1 equiv) was added to the solution and the vial was re-sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and removed from the glove box. The resulting solution was allowed to stir at 22 °C for 30 min under N_2 atmosphere. The solution of allene **1.55** (68 mg, 0.24 mmol, 1.0 equiv) and MeOH (58 μL, 1.4 mmol, 6.0 equiv) in dioxane (2.0 mL) was added to the mixture through syringes and the resulting mixture was allowed to stir at 22 °C for eight hours. The reaction was quenched by passing the mixture through a short plug of celite and silica gel and eluted with diethyl ether (3 × 5 mL). The filtrate was concentrated under reduced pressure with gentle heating to afford yellow oil, which was used in the next step without further purification. An oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with the crude mixture, $Pd(dppf)Cl_2$ (26 mg, 0.036 mmol, 15 mol %), $Ba(OH)_2 \cdot 8H_2O$ (114 mg, 0.360 mmol, 1.50 equiv), (*E*)-iodo-ethylacrylate[15] (66 mg, 0.29 mmol, 1.2 equiv) and dmf (2.0 mL) under N_2 atmosphere. The vessel was sealed with a cap and the resulting solution was allowed

(15) Trost, B.M.; Papillon, J. P. N.; Nussbaumer, T. *J. Am. Chem. Soc.* **2005**, *127*, 17921–17937.

to stir at 40 °C for eight hours. The reaction was quenched by addition of H_2O (2 mL) and the aqueous layer was washed with diethyl ether (3 × 5 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography (hexanes:Et_2O = 3:1) to afford **1.56** (66 mg, 0.17 mmol, 72%) as a colorless oil.

Triene 1.56. IR (neat): 3496 (br), 2955 (w), 2930 (w), 2894 (w), 2856 (w), 1710 (s), 1620 (m), 1462 (m), 1389 (m), 1366 (m), 1304 (s), 1252 (s), 1163 (s), 1094 (s), 1029 (s), 1004 (s), 981 (m), 921 (m), 833 (s), 774 (s), 671 (w), 583 (w) cm^{-1}: ^1H NMR ($CDCl_3$, 400 MHz): δ 7.36 (1H, d, *J* = 15.6 Hz), 6.09 (1H, t, *J* = 7.2 Hz), 5.90 (1H, ddd, *J* = 17.2, 10.8, 6.4 Hz), 5.78 (1H, d, *J* = 15.6 Hz), 5.24 (1H, d, *J* = 17.2 Hz), 5.19 (1H, d, *J* = 10.8 Hz), 4.29 (1H, m), 4.21 (1H, d, *J* = 1.6 Hz), 4.19 (2H, q, *J* = 7.2 Hz), 3.72 (1H, m), 2.44 (1H, m), 2.31 (1H, m), 1.79 (3H, s), 1.28 (3H, t, *J* = 7.2 Hz), 0.91 (9H, s), 0.78 (3H, d, *J* = 7.2 Hz), 0.08 (6H, d, *J* = 16 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.7, 149.6, 138.2, 136.8, 134.3, 116.6, 115.7, 78.3, 73.1, 60.2, 43.3, 34.6, 25.9, 18.2, 14.4, 13.1, 12.6, -4.3, -5.0; HRMS (ESI^+): Calcd for $C_{21}H_{39}O_4Si_1$ $[M+H]^+$: 383.2617; Found: 383.2604; specific rotation: $[\alpha]_D^{21}$ +23.9 (*c* = 1.15, $CHCl_3$).

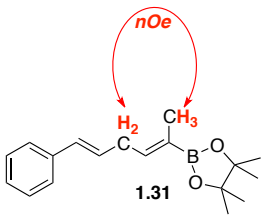
Experimental Procedure for Synthesis of 1.57: An oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with triene **1.56** (30 mg, 0.078 mmol, 1.0 equiv) and thf (1.0 mL) under N_2 atmosphere. Tetra(*n*-butyl)ammonium fluoride (0.12 mL of 1.0 M thf solution, 0.12 mmol, 1.5 equiv) was added to the solution and the resulting mixture was allowed to stir at 22 °C for 1.5 hour. The reaction was quenched by addition of saturated aqueous NH_4Cl solution (1 mL) and the aqueous layer was extracted with diethyl ether (3 × 2 mL). The combined organic layers were washed with brine (10 mL),

dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography (hexanes:Et_2O = 1:1) to afford diol **1.57** (20 mg, 0.075 mmol, 96%) as a colorless oil.

Diol 1.57. IR (neat): 3399 (br), 2978 (m), 2923 (m), 1706 (s), 1693 (s), 1620 (s), 1444 (m), 1394 (m), 1367 (m), 1305 (s), 1268 (s), 1171 (s), 1117 (m), 1094 (m), 1033 (s), 979 (s), 921 (m), 855 (m), 711 (w), 581 (w), 541 (w) cm^{-1}: ^1H NMR ($CDCl_3$, 400 MHz): δ 7.34 (1H, d, *J* = 15.6 Hz), 5.99 (1H, t, *J* = 7.2 Hz), 5.93 (1H, ddd, *J* = 17.2, 10.8, 6.4 Hz), 5.82 (1H, d, *J* = 15.6 Hz), 5.30 (1H, d, *J* = 17.2 Hz), 5.22 (1H, d, *J* = 10.8 Hz), 4.43 (1H, m), 4.21 (2H, q, *J* = 7.2 Hz), 3.77 (1H, m), 2.74 (1H, d, *J* = 3.6 Hz), 2.67 (1H, d, *J* = 4.8 Hz), 2.46 (2H, m), 1.81 (3H, s), 1.30 (3H, t, *J* = 7.2 Hz), 0.91 (3H, d, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.6, 149.1, 138.3, 137.1, 135.4, 116.5, 115.8, 75.0, 74.4, 60.4, 42.1, 35.0, 14.4, 12.6, 12.1; HRMS (ESI^+): Calcd for $C_{15}H_{25}O_4$ $[M+H]^+$: 269.1753; Found: 269.1745; specific rotation: $[\alpha]_D^{20}$ +35.0 (*c* = 0.50, $CHCl_3$).

■ Proof of Stereochemistry of the Olefin in β-Alkenylborons

The geometry of the double bond in compound **1.31** was assigned as *Z* based on nOe study.



1.8.5 Theoretical Studies Regarding Mechanism

***Part 1*. Computational protocol:**

Geometry optimizations and frequency calculations were carried out by using the gradient-corrected Density Functional Theory (DFT) BP86 functional[16] and the basis set used was constructed as following: The core electrons on the copper ion were described by using the Los Alamos effective core pseudo-potential (ECP), as implemented in the double-zeta quality LANL2DZ basis set.[17] The valence electrons were augmented with polarization functions of d-type, described by one Gaussian function with an exponent value of $\alpha = 0.451$. All other elements were described by using the split-valence 6-31G** basis set. Tetrahydrofuran was simulated by means of the PCM method[18]. The results of harmonic frequency calculations on the optimized geometries showed that all of them are real[19] except for the transition state structures, which have one imaginary frequency. Free energies were computed at 298.15 K and 1.0 atm. by using the unscaled frequencies. The structures involved in the dimeric η_1–η_1 isomerization process were computed by using the BP86/LANL2DZ method and solvation was not considered. All calculations were carried out with the Gaussian09 computer program.[20]

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(16) Perdew, J. P. *Phys. Rev. B.* **1986**, *33*, 8822.
(17) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 270–83.
(18) Tomasi, J.; Mennucci, B. ; Cammi, R. *Chem. Rev.* **2005**, *105*, 2999–3093.
(19) The geometry optimized trisubstituted olefin product showed one very small imaginary frequency of 7i cm^{-1}.
(20) Gaussian 09, Revision A.02, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S.S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.;

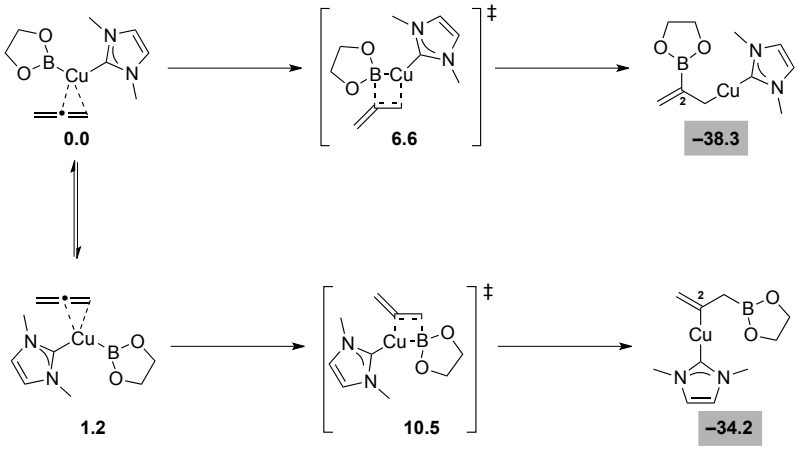
Part 2. **Chemical models used in the computations:**

The precursor of N-heterocyclic carbene (NHC) used in these computational studies is N,N-dimethylimidazolium salt (**1.28e**). The allenes used in these studies are propadiene, methylpropadiene and compound **1.41a**. 1,3,2-dioxaborolane was used as the model of 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (pinacolatoboron, B(pin)), except for compound **1.41a**, where the full model of B(pin) was used.

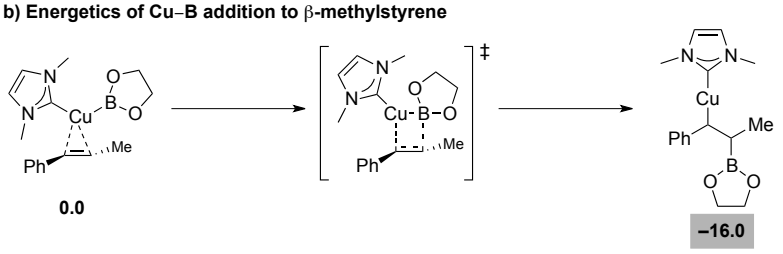
Part 3. **Regioselective Cu–B addition to allene and β-methylstyrene (C_2–B vs C_1–B);**[21] values are in kcal/mol

Scheme S2. Energetics of Site-Selective Cu–B additions to allene and *β*-methylstyrene

a) Energetics of Cu–B addition to allene



b) Energetics of Cu–B addition to β-methylstyrene

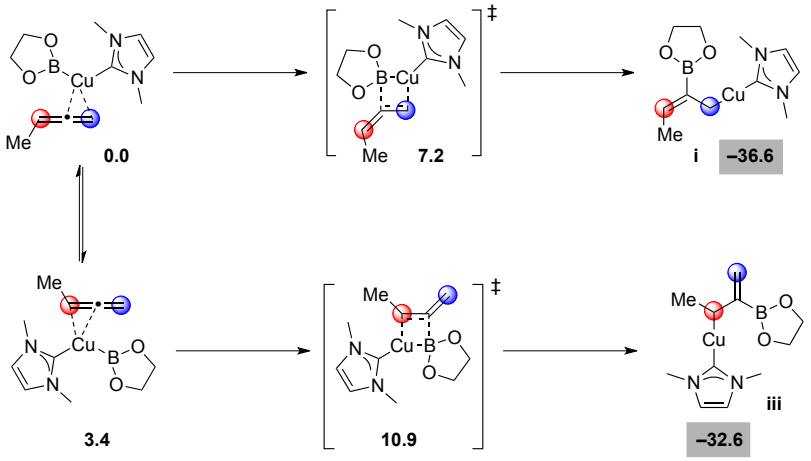


Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford CT, 2009.

(21) Numbers are relative free energies in kcal/mol (298 K).

Part 4. **Site Selective Cu–C bond formation** (intermediate **i** vs intermediate **iii** in Scheme 1.9); values are in kcal/mol

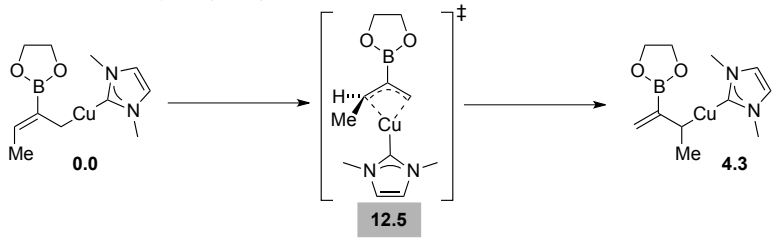
Scheme S3. Energetics of Site-Selective Cu-B Addition to Methyl-Substituted Allene



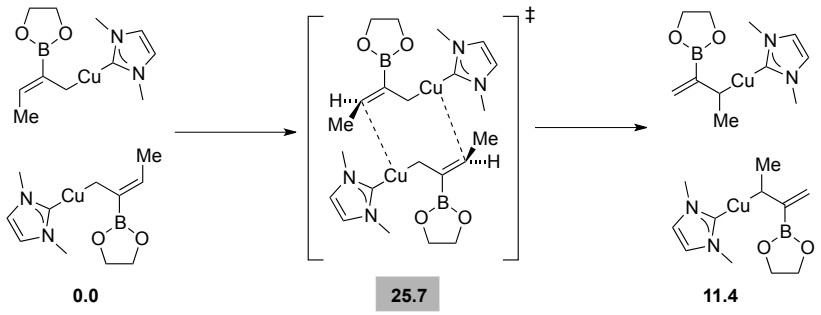
Part 5. **η^1–η^1 isomerization of NHC–Cu–allyl complex** (intramolecular vs intermolecular isomerization);[22] values are in kcal/mol

Scheme S4. Unimolecular or Bimolecular Isomerization Pathway of Cu-allyl Complex **i** to **iii**

a) Unimolecular pathway for η^1-to-η^1 isomerization



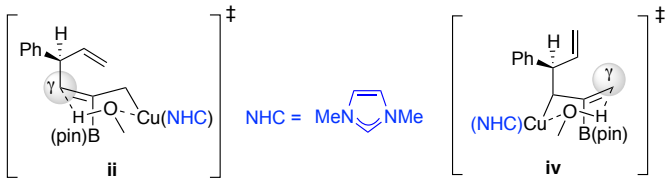
b) Bimolecular pathway for η^1-to-η^1 isomerization



(22) In case of bimolecular isomerization, the value for free energy of activation was computed as $\mathbf{G}_{TS\text{-}dimer} - 2*\mathbf{G}_{monomer}$ in the gas phase.

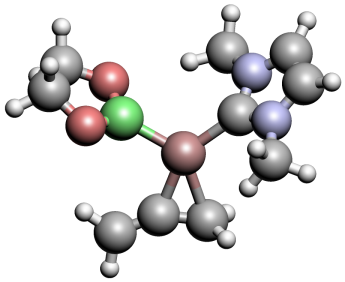
Part 6. Energy Difference Between the Transition States for γ-Protonation for Synthesis of Product 1.41a (Scheme 1.6)

Scheme S5. Energy Difference Between Transition States Leading to **2.41a** (with **2.28e**)



$\Delta\Delta G^{\neq} = \Delta G^{\neq}_{iv} - \Delta G^{\neq}_{ii} = -1.3$ kcal/mol

GS1_propadiene



H -2.517 0.867 2.790

C -2.710 1.231 1.768

H -4.636 -0.764 1.260

H -3.686 1.739 1.741

H -1.921 1.940 1.479

C -3.722 -0.809 0.673

N -2.697 0.125 0.811

C -3.310 -1.698 -0.283

H -3.802 -2.571 -0.704

C -1.642 -0.153 -0.023

H 3.151 2.072 -0.136

H -0.591 2.601 -1.979

Cu 0.109 0.752 -0.189

N -2.042 -1.286 -0.687

H -0.171 -1.803 -1.470

C -0.198 2.728 -0.963

C 2.400 2.757 -0.540

C -1.236 -1.948 -1.715

H 2.737 3.758 -0.845

C 1.117 2.407 -0.657

H -0.807 3.332 -0.279

H -1.469 -3.023 -1.722

H -1.449 -1.526 -2.711

B 1.694 -0.451 0.245

O 2.550 -0.363 1.350

O 2.066 -1.517 -0.592

C 3.482 -1.483 1.319

C 3.280 -2.131 -0.068

H 4.115 -1.917 -0.760

H 3.142 -3.224 -0.017

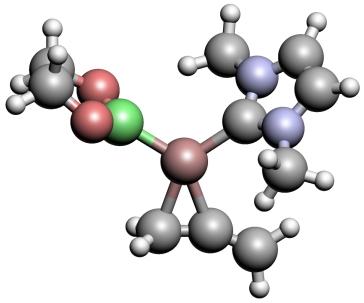
H 4.507 -1.106 1.472

H 3.237 -2.174 2.146

Sum of electronic and thermal Free Energies=   -871.572951

hartree

GS2_propadiene



H -2.150 0.040 2.886

C -2.633 0.333 1.940

H -3.934 -2.098 1.343

H -3.719 0.417 2.098

H -2.234 1.303 1.609

C -3.079 -1.838 0.724

N -2.366 -0.653 0.893

C -2.479 -2.510 -0.308

H -2.720 -3.460 -0.776

C -1.320 -0.563 0.007

H -2.985 2.124 -0.825

H 0.852 3.227 0.450

Cu 0.096 0.799 -0.125

N -1.409 -1.721 -0.724

H 0.483 -1.596 -1.601

C 0.440 2.810 -0.478

C -2.179 2.865 -0.858

C -0.495 -2.055 -1.818

H -2.473 3.896 -1.113

C -0.911 2.551 -0.604

H 1.086 2.888 -1.361

H -0.386 -3.148 -1.880

H -0.878 -1.675 -2.780

B 1.975 0.045 0.179

O 2.692 0.052 1.385

O 2.717 -0.593 -0.833

C 3.942 -0.675 1.207

C 4.022 -0.971 -0.307

H 4.799 -0.370 -0.814

H 4.209 -2.036 -0.527

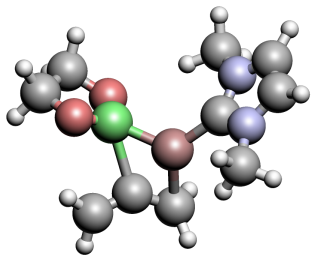
H 4.779 -0.052 1.567

H 3.909 -1.597 1.817

Sum of electronic and thermal Free Energies=   -871.571058

hartree

TS1_propadiene



H -2.644 1.660 2.371

C -2.834 1.759 1.290

H -4.870 -0.189 1.092

H -3.805 2.254 1.133

H -2.039 2.367 0.834

C -3.919 -0.428 0.624

N -2.839 0.450 0.638

C -3.506 -1.544 -0.054

H -4.033 -2.461 -0.306

C -1.749 -0.085 -0.005

H 2.978 1.946 0.967

H 0.562 1.545 -2.583

Cu -0.006 0.691 -0.232

N -2.182 -1.320 -0.421

H -0.303 -1.977 -1.053

C 0.661 2.143 -1.666

C 2.612 2.330 0.012

C -1.360 -2.248 -1.198

H 3.134 3.189 -0.430

C 1.574 1.767 -0.650

H 0.325 3.184 -1.731

H -1.530 -3.277 -0.844

H -1.610 -2.188 -2.270

B 1.718 -0.292 0.244

O 2.406 -0.361 1.456

O 2.182 -1.238 -0.681

C 3.527 -1.273 1.270

C 3.170 -2.068 -0.001

H 4.032 -2.227 -0.669

H 2.716 -3.048 0.231

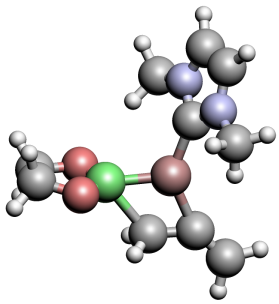
H 4.450 -0.677 1.143

H 3.634 -1.907 2.165

Sum of electronic and thermal Free Energies=   -871.562379

hartree

TS2_propadiene



H -2.305 0.535 2.837

C -2.648 0.959 1.879

H -4.559 -0.999 1.163

H -3.671 1.347 1.999

H -1.976 1.780 1.583

C -3.643 -0.973 0.579

N -2.628 -0.050 0.822

C -3.223 -1.750 -0.467

H -3.710 -2.573 -0.984

C -1.572 -0.233 -0.037

Cu 0.058 0.754 -0.125

N -1.957 -1.292 -0.822

H -0.081 -1.678 -1.659

C 0.618 2.608 -0.544

H 2.307 1.976 0.717

C -1.143 -1.824 -1.915

C 1.789 1.788 -0.236

C 0.474 3.894 -0.902

H -1.349 -2.898 -2.035

H -1.367 -1.303 -2.861

B 1.757 -0.333 0.215

O 2.324 -0.584 1.465

O 2.304 -1.141 -0.788

C 3.208 -1.731 1.330

C 3.386 -1.916 -0.193

H 4.350 -1.514 -0.556

H 3.301 -2.968 -0.513

H 4.157 -1.521 1.852

H 2.731 -2.607 1.806

H -0.514 4.333 -1.100

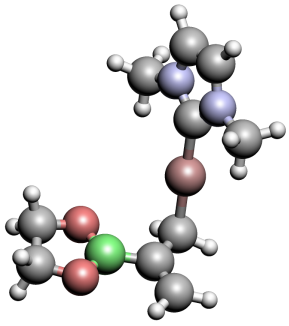
H 1.324 4.591 -1.020

H 2.484 1.557 -1.058

Sum of electronic and thermal Free Energies=   -871.556257

hartree

PRODUCT1_propadiene



H 2.541 -1.900 2.511

C 2.669 -1.951 1.418

H 4.834 -0.210 1.902

H 3.488 -2.647 1.177

H 1.738 -2.308 0.956

C 4.075 0.138 1.206

N 2.957 -0.622 0.876

C 3.974 1.308 0.499

H 4.628 2.175 0.460

C 2.148 0.033 -0.020

H -3.296 -2.591 0.868

H -1.480 -0.441 -2.334

Cu 0.495 -0.583 -0.812

N 2.798 1.223 -0.238

H 1.363 1.920 -1.578

C -1.182 -1.213 -1.599

C -2.582 -2.544 0.039

C 2.308 2.269 -1.138

H -2.184 -3.504 -0.320

C -2.194 -1.353 -0.506

H -1.022 -2.167 -2.139

H 2.131 3.202 -0.580

H 3.040 2.456 -1.940

B -2.843 -0.053 0.080

O -3.763 -0.048 1.124

O -2.567 1.223 -0.400

C -4.234 1.309 1.293

C -3.272 2.173 0.436

H -3.801 2.900 -0.202

H -2.536 2.719 1.053

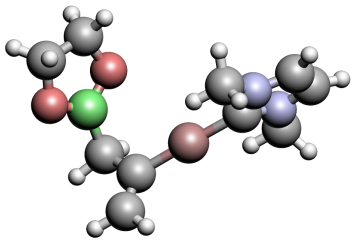
H -5.279 1.372 0.940

H -4.210 1.577 2.363

Sum of electronic and thermal Free Energies=   -871.633961

hartree

PRODUCT2_propadiene



H -1.689 -2.816 1.706

C -1.829 -1.744 1.912

H -4.365 -2.292 0.810

H -2.393 -1.623 2.851

H -0.848 -1.257 2.009

C -3.804 -1.478 0.359

N -2.541 -1.103 0.805

C -4.115 -0.640 -0.680

H -4.998 -0.585 -1.311

C -2.039 -0.051 0.079

Cu -0.341 0.854 0.282

N -3.031 0.217 -0.834

H -1.982 1.786 -1.715

C 1.324 1.783 0.489

H 3.311 2.239 -0.346

C -2.947 1.274 -1.843

C 2.440 1.578 -0.547

C 1.577 2.608 1.539

H -3.002 0.843 -2.855

H -3.767 1.997 -1.708

B 2.886 0.066 -0.528

O 3.928 -0.413 0.252

O 2.250 -0.930 -1.260

C 3.971 -1.854 0.110

C 2.929 -2.184 -0.994

H 3.401 -2.537 -1.928

H 2.189 -2.936 -0.670

H 4.995 -2.161 -0.165

H 3.717 -2.315 1.081

H 0.839 2.796 2.331

H 2.539 3.142 1.656

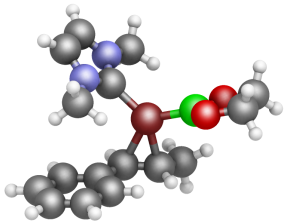
H 2.064 1.816 -1.561

Sum of electronic and thermal Free Energies=   -871.627383

hartree

Addition of NHC-Cu-B(pin) to styrene

Ground state



H -5.303 1.572 -1.076

C -2.805 2.666 -0.365

C -4.541 0.871 -0.744

N -3.266 1.277 -0.366

C 1.386 -1.799 2.652

C 2.424 -3.329 -1.549

O 2.909 -2.431 -0.519

C -4.570 -0.493 -0.614

H -5.364 -1.210 -0.807

C 0.898 -3.069 -1.617

C -2.483 0.209 0.002

B 1.809 -1.907 0.149

C 1.921 -0.997 1.437

N -3.311 -0.875 -0.164

O 0.601 -2.316 -0.411

Cu -0.669 0.233 0.657

C 1.182 0.366 1.337

C -2.918 -2.254 0.138

H -1.820 -2.302 0.162

H -3.299 -2.924 -0.648

H -3.328 -2.568 1.111

H -1.742 2.671 -0.082

H -3.381 3.262 0.361

H -2.918 3.105 -1.369

H 0.614 -2.459 -2.493

H 0.304 -3.997 -1.623

H 2.939 -3.109 -2.498

H 2.660 -4.367 -1.252

C 1.807 1.418 0.480

C 2.694 1.140 -0.597

C 1.520 2.796 0.714

C 2.055 3.815 -0.081

C 2.912 3.510 -1.158

C 3.226 2.163 -1.401

H 0.855 3.055 1.550

H 2.982 0.103 -0.805

H 3.905 1.899 -2.221

H 3.332 4.305 -1.782

H 1.808 4.860 0.142

H 1.500 -1.214 3.584

H 1.918 -2.757 2.791

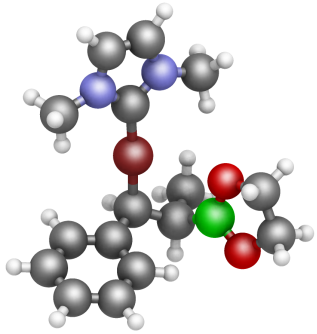
H 0.310 -2.019 2.531

H 3.007 -0.821 1.615

H 1.071 0.779 2.362

Sum of electronic and thermal Free Energies= -1103.809897 hartree

Product



H 0.424 5.056 0.265

C -1.119 3.073 1.565

C 0.571 4.029 -0.060

N -0.131 2.960 0.492

C -1.394 -1.602 2.702

C -3.970 -1.519 -1.909

O -2.571 -1.146 -1.746

C 1.389 3.499 -1.022

H 2.093 3.975 -1.700

C -4.689 -0.907 -0.688

C 0.223 1.765 -0.087

B -2.392 -0.576 -0.476

C -0.410 -1.695 1.552

N 1.162 2.124 -1.022

O -3.620 -0.470 0.199

Cu -0.600 -0.002 0.295

C 0.848 -1.071 1.601

C 1.842 1.176 -1.905

H 1.280 0.232 -1.898

H 2.867 0.977 -1.552

H 1.874 1.578 -2.929

H -1.766 2.184 1.527

H -1.730 3.976 1.413

H -0.628 3.128 2.550

H -5.309 -0.032 -0.959

H -5.329 -1.633 -0.158

H -4.342 -1.123 -2.870

H -4.046 -2.622 -1.936

C 1.997 -1.379 0.738

C 1.914 -2.252 -0.381

C 3.260 -0.791 1.017

C 4.381 -1.057 0.220

C 4.278 -1.918 -0.889

C 3.036 -2.512 -1.180

H 3.351 -0.118 1.878

H 0.959 -2.726 -0.629

H 2.941 -3.188 -2.037

H 5.153 -2.127 -1.513

H 5.342 -0.593 0.466

H -1.249 -0.674 3.282

H -1.257 -2.453 3.397

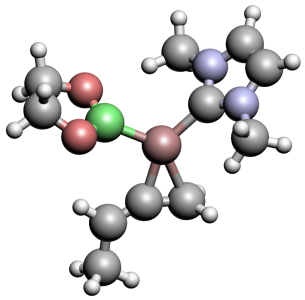
H -2.435 -1.621 2.341

H -0.537 -2.566 0.898

H 1.052 -0.390 2.439

Sum of electronic and thermal Free Energies= -1103.784402 hartree

GS1_methylpropadiene



H 2.483 -1.025 2.886

C 2.530 -1.560 1.924

H 4.935 -0.299 1.155

H 3.318 -2.327 1.973

H 1.561 -2.041 1.729

C 4.051 -0.064 0.567

N 2.805 -0.632 0.827

C 3.878 0.778 -0.498

H 4.585 1.409 -1.031

C 1.845 -0.166 -0.037

H -3.352 -0.826 0.070

H -0.032 -2.668 -1.684

Cu -0.099 -0.522 -0.084

N 2.531 0.707 -0.844

H 0.860 1.650 -1.678

C -0.417 -2.563 -0.662

C -2.896 -1.767 -0.262

C 1.908 1.442 -1.947

C -3.833 -2.923 -0.535

C -1.566 -1.830 -0.392

H 0.016 -3.240 0.086

H 2.443 2.391 -2.098

H 1.944 0.855 -2.880

B -1.248 1.121 0.273

O -2.125 1.316 1.349

O -1.265 2.230 -0.591

C -2.678 2.662 1.271

C -2.264 3.182 -0.121

H -3.284 -3.820 -0.862

H -4.569 -2.661 -1.317

H -4.416 -3.182 0.369

H -3.108 3.197 -0.836

H -1.819 4.191 -0.089

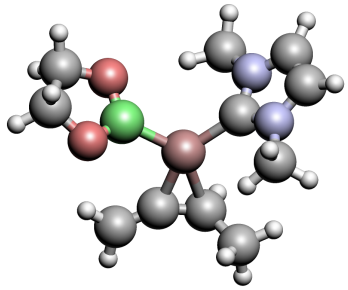
H -3.772 2.613 1.405

H -2.254 3.270 2.091

Sum of electronic and thermal Free Energies=   -910.865989

hartree

GS2_methylpropadiene



H -2.446 -0.098 3.052

C -2.551 0.474 2.116

H -4.388 -1.536 1.388

H -3.482 1.061 2.152

H -1.694 1.154 2.012

C -3.533 -1.398 0.732

N -2.559 -0.427 0.965

C -3.156 -2.060 -0.406

H -3.625 -2.881 -0.942

C -1.572 -0.460 0.011

H 3.020 2.094 -0.080

H -0.698 2.267 -1.966

Cu 0.127 0.547 -0.139

N -1.961 -1.479 -0.824

H -0.127 -1.729 -1.795

C -0.348 2.512 -0.952

C 2.240 2.722 -0.520

C -1.197 -1.880 -2.007

H 2.522 3.732 -0.854

C 0.985 2.285 -0.649

C -1.265 3.389 -0.115

H -1.383 -2.944 -2.215

H -1.490 -1.283 -2.886

B 1.814 -0.535 0.251

O 2.805 -0.262 1.207

O 2.154 -1.672 -0.503

C 3.806 -1.320 1.167

C 3.480 -2.127 -0.106

H 4.190 -1.924 -0.929

H 3.454 -3.217 0.068

H 4.812 -0.868 1.145

H 3.718 -1.930 2.086

H -2.298 3.001 -0.096

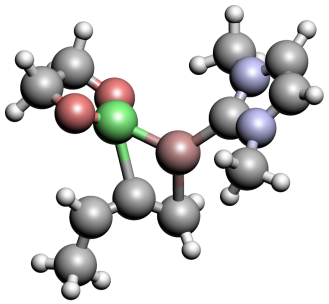
H -1.308 4.416 -0.530

H -0.904 3.470 0.923

Sum of electronic and thermal Free Energies=   -910.860586

hartree

TS1_methylpropadiene



H 2.510 -1.913 2.400

C 2.686 -2.084 1.326

H 5.061 -0.583 1.026

H 3.552 -2.752 1.200

H 1.796 -2.554 0.881

C 4.165 -0.176 0.564

N 2.933 -0.823 0.628

C 3.964 0.976 -0.149

H 4.655 1.761 -0.444

C 1.955 -0.105 -0.016

H -3.036 -1.075 1.110

H -0.712 -1.395 -2.483

Cu 0.089 -0.527 -0.174

N 2.613 1.005 -0.486

H 0.887 2.002 -1.108

C -0.880 -1.890 -1.517

C -2.804 -1.604 0.179

C 1.973 2.052 -1.282

C -3.787 -2.655 -0.279

C -1.682 -1.284 -0.514

H -0.726 -2.975 -1.503

H 2.352 3.038 -0.971

H 2.179 1.907 -2.356

B -1.398 0.794 0.276

O -2.044 1.062 1.485

O -1.675 1.771 -0.694

C -2.962 2.170 1.254

C -2.463 2.816 -0.052

H -3.535 -3.025 -1.286

H -4.822 -2.263 -0.295

H -3.797 -3.524 0.408

H -3.281 3.121 -0.726

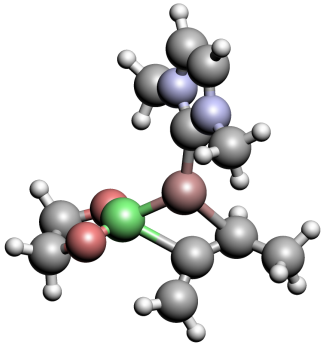
H -1.813 3.691 0.135

H -3.988 1.767 1.153

H -2.934 2.854 2.118

Sum of electronic and thermal Free Energies= -910.854474 hartree

TS2_methylpropadiene



H -2.652 1.031 2.689

C -2.832 1.335 1.645

H -4.918 -0.487 1.086

H -3.787 1.877 1.582

H -2.016 1.994 1.312

C -3.970 -0.661 0.584

N -2.867 0.170 0.761

C -3.582 -1.644 -0.287

H -4.132 -2.484 -0.705

C -1.786 -0.267 0.034

H 2.904 1.492 1.468

H 0.602 1.652 -2.155

Cu -0.013 0.470 -0.020

N -2.250 -1.392 -0.605

H -0.383 -1.981 -1.328

C 0.715 2.164 -1.185

C 2.596 2.024 0.565

C -1.445 -2.190 -1.530

H 3.168 2.916 0.276

C 1.578 1.594 -0.224

C 0.337 3.635 -1.159

H -1.648 -3.259 -1.369

H -1.677 -1.929 -2.576

B 1.701 -0.601 0.247

O 2.371 -0.909 1.433

O 2.201 -1.326 -0.845

C 3.522 -1.729 1.080

C 3.202 -2.254 -0.333

H 4.076 -2.252 -1.004

H 2.771 -3.272 -0.315

H 4.428 -1.093 1.091

H 3.642 -2.531 1.826

H -0.656 3.814 -1.610

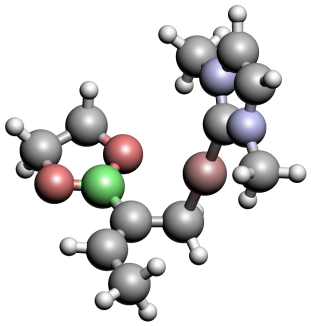
H 1.061 4.264 -1.719

H 0.318 4.015 -0.123

Sum of electronic and thermal Free Energies=   -910.848663

hartree

PRODUCT1_methylpropadiene



H 3.931 2.157 -1.225

C 3.678 1.766 -0.227

H 5.384 -0.337 -1.011

H 4.500 1.987 0.472

H 2.754 2.245 0.130

C 4.379 -0.614 -0.702

N 3.438 0.324 -0.291

C 3.768 -1.839 -0.625

H 4.139 -2.835 -0.851

C 2.245 -0.270 0.046

H -2.897 2.012 -1.589

H -1.385 0.743 2.195

Cu 0.627 0.558 0.703

N 2.475 -1.607 -0.169

H 0.540 -2.166 0.368

C -1.057 1.337 1.323

C -2.201 2.198 -0.762

C 1.476 -2.653 0.058

C -1.480 3.521 -0.748

C -2.008 1.213 0.174

H -0.902 2.384 1.645

H 1.304 -3.223 -0.869

H 1.812 -3.339 0.852

B -2.788 -0.122 -0.018

O -3.722 -0.343 -1.030

O -2.626 -1.231 0.811

C -4.321 -1.639 -0.804

C -3.430 -2.308 0.274

H -0.380 3.375 -0.702

H -1.735 4.128 0.144

H -1.707 4.130 -1.639

H -4.015 -2.771 1.087

H -2.760 -3.076 -0.155

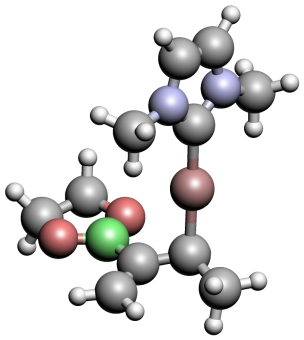
H -5.362 -1.498 -0.456

H -4.345 -2.205 -1.751

Sum of electronic and thermal Free Energies=   -910.924843

hartree

PRODUCT2_methylpropadiene



H -1.769 -0.938 3.140

C -1.957 -0.021 2.560

H -4.434 -1.273 2.068

H -2.582 0.666 3.154

H -1.000 0.466 2.325

C -3.859 -0.973 1.196

N -2.621 -0.346 1.296

C -4.126 -1.095 -0.142

H -4.980 -1.523 -0.662

C -2.094 -0.067 0.058

H 3.309 1.171 2.132

H 1.556 1.384 -1.724

Cu -0.422 0.811 -0.356

N -3.044 -0.539 -0.815

H -1.978 0.047 -2.505

C 1.284 1.731 -0.707

C 2.683 1.713 1.415

C -2.923 -0.464 -2.272

C 2.187 1.094 0.296

C 1.206 3.263 -0.661

H -2.911 -1.476 -2.708

H -3.764 0.107 -2.695

B 2.603 -0.396 0.058

O 3.245 -1.185 1.010

O 2.387 -1.071 -1.141

C 3.607 -2.434 0.375

C 2.819 -2.441 -0.959

H 3.435 -2.749 -1.820

H 1.927 -3.093 -0.916

H 4.700 -2.450 0.215

H 3.337 -3.274 1.037

H 2.211 3.738 -0.716

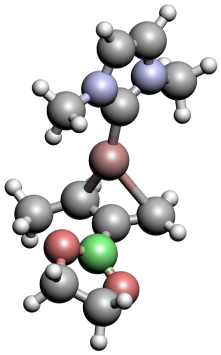
H 0.741 3.634 0.272

H 0.603 3.659 -1.497

H 2.467 2.762 1.653

Sum of electronic and thermal Free Energies=   -910.917961 hartree

Monomeric $\eta^1 - \eta^1$ isomerization TS



H -1.330 3.220 -0.011

C -1.633 2.526 0.790

H -4.378 2.607 0.129

H -0.739 2.034 1.203

H -2.145 3.088 1.586

C -3.866 1.661 -0.025

N -2.517 1.484 0.271

C -4.320 0.464 -0.513

H -5.308 0.161 -0.851

C -2.099 0.207 -0.026

H 0.562 -2.606 1.351

H 0.393 -2.794 -1.197

Cu -0.374 -0.555 0.213

N -3.232 -0.404 -0.512

H -2.263 -2.106 -1.228

C 0.998 -1.878 -1.234

C 1.084 -1.634 1.279

C -3.278 -1.806 -0.925

C 1.850 -1.268 2.540

C 1.548 -1.308 -0.059

H 1.333 -1.547 -2.219

H -3.617 -2.450 -0.097

H -3.964 -1.918 -1.778

B 2.545 -0.112 -0.312

O 3.454 -0.124 -1.359

O 2.596 1.055 0.441

C 4.099 1.174 -1.397

C 3.696 1.856 -0.066

H 5.189 1.037 -1.496

H 3.731 1.726 -2.281

H 4.512 1.844 0.678

H 3.356 2.896 -0.200

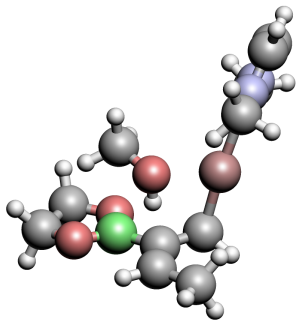
H 2.675 -1.982 2.759

H 1.189 -1.272 3.425

H 2.298 -0.264 2.470

Sum of electronic and thermal Free Energies=   -910.904923 hartree

Protonation GS1_methylpropadiene



C	1.788	3.110	-1.486
H	1.654	0.662	2.804
C	0.606	0.713	2.452
H	-0.046	0.867	3.328
O	0.389	1.807	1.557
H	1.020	1.688	0.801
H	0.343	-0.263	1.995
H	-5.237	0.604	1.496
C	-2.838	1.987	0.978
C	-4.481	0.068	0.928
N	-3.244	0.623	0.622
C	2.437	1.952	-0.769
C	4.473	-1.386	1.197
O	3.836	-0.146	0.809
C	-4.490	-1.192	0.387
H	-5.251	-1.969	0.401
C	3.577	-2.497	0.594
C	-2.466	-0.245	-0.104

B 2.883 -0.446 -0.161

C 2.080 0.634 -0.957

N -3.259 -1.361 -0.236

O 2.732 -1.814 -0.364

Cu -0.716 0.025 -0.882

C 0.983 0.196 -1.860

C -2.846 -2.581 -0.932

H 0.814 0.891 -2.704

H 1.169 -0.817 -2.264

H -1.857 -2.396 -1.377

H -3.567 -2.826 -1.728

H -2.780 -3.424 -0.226

H -1.738 2.020 1.056

H -3.284 2.251 1.949

H -3.188 2.703 0.216

H 4.155 -3.282 0.078

H 2.935 -2.978 1.355

H 5.498 -1.405 0.784

H 4.538 -1.437 2.297

H 2.127 4.082 -1.094

H 0.683 3.071 -1.402

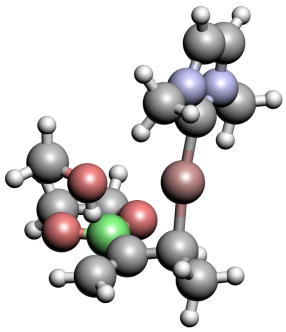
H 3.266 2.181 -0.086

H 2.004 3.095 -2.574

Sum of electronic and thermal Free Energies= -1026.61199

hartree

Protonation GS2_methylpropadiene



H 1.418 -2.604 -3.151

C 0.710 -1.924 -2.632

H -0.194 -1.837 -3.258

O 0.312 -2.429 -1.356

H 1.073 -2.256 -0.737

H 1.184 -0.927 -2.562

H -5.059 -0.218 -1.417

C -2.891 -1.926 -0.845

C -4.219 0.224 -0.888

H 2.613 -2.913 0.874

N -3.076 -0.499 -0.565

H 3.464 -1.978 -0.496

C 2.762 -1.965 0.343

C 2.836 2.758 -0.466

O 2.196 1.800 0.414

C -4.023 1.498 -0.421

H -4.655 2.381 -0.470

C 3.399 1.910 -1.637

C -2.159 0.278 0.100

B 2.558 0.526 -0.010

C 2.180 -0.786 0.764

N -2.767 1.509 0.176

O 3.311 0.539 -1.179

Cu -0.466 -0.228 0.880

C 1.201 -0.669 1.865

C -2.163 2.682 0.809

H 1.361 0.276 2.420

C 1.082 -1.868 2.811

H -1.172 2.389 1.185

H -2.787 3.028 1.648

H -2.051 3.498 0.076

H -1.811 -2.138 -0.912

H -3.375 -2.170 -1.803

H -3.347 -2.535 -0.048

H 4.450 2.150 -1.871

H 2.800 2.016 -2.559

H 3.631 3.279 0.096

H 2.093 3.504 -0.796

H 2.061 -2.156 3.253

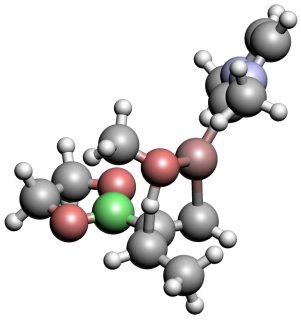
H 0.698 -2.769 2.296

H 0.389 -1.655 3.644

Sum of electronic and thermal Free Energies= -1026.604540

hartree

Protonation TS1_methylpropadiene



C -1.853 -3.150 -1.451

H -0.663 -2.348 2.986

C -0.519 -1.454 2.344

H 0.266 -0.829 2.808

O -0.141 -1.817 1.018

H -1.169 -2.002 0.424

H -1.468 -0.875 2.358

H 5.433 -0.124 0.786

C 3.201 -1.856 0.773

C 4.489 0.298 0.447

N 3.312 -0.442 0.404

C -2.226 -1.977 -0.553

C -4.008 1.650 1.261

O -3.700 0.363 0.671

C 4.176 1.557 0.006

H 4.791 2.446 -0.107

C -3.203 2.674 0.422

C 2.259 0.308 -0.063

B -2.630 0.543 -0.195

C -1.935 -0.631 -0.972

N 2.819 1.542 -0.300

O -2.249 1.875 -0.322

Cu 0.443 -0.300 -0.374

C -0.949 -0.274 -1.937

C 2.069 2.693 -0.803

H -0.605 -1.021 -2.667

H -0.919 0.762 -2.293

H 1.044 2.355 -1.013

H 2.531 3.073 -1.728

H 2.045 3.497 -0.050

H 2.130 -2.090 0.899

H 3.737 -2.034 1.718

H 3.635 -2.495 -0.013

H -3.841 3.223 -0.295

H -2.662 3.407 1.042

H -5.097 1.820 1.218

H -3.696 1.637 2.321

H -2.145 -4.111 -0.995

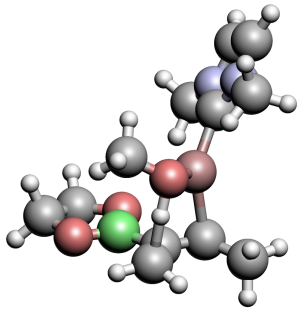
H -0.761 -3.194 -1.629

H -3.163 -2.090 0.010

H -2.330 -3.098 -2.453

Sum of electronic and thermal Free Energies= -1026.600965 hartree

Protonation TS2_methylpropadiene



H 0.437 -2.468 -3.224

C 0.321 -1.600 -2.542

H -0.511 -0.981 -2.921

O 0.041 -2.020 -1.205

H 1.053 -2.259 -0.734

H 1.252 -0.998 -2.596

H -5.280 0.454 -0.659

C -3.355 -1.620 -0.683

C -4.265 0.724 -0.379

H 2.242 -3.152 0.702

N -3.222 -0.196 -0.362

H 3.167 -2.210 -0.586

C 2.321 -2.227 0.112

C 3.044 2.570 -0.113

O 2.205 1.618 0.588

C -3.729 1.928 -0.000

H -4.186 2.908 0.106

C 3.675 1.758 -1.272

C -2.039 0.386 0.027

B 2.546 0.344 0.135

C 1.983 -0.986 0.750

N -2.378 1.701 0.243

O 3.460 0.372 -0.912

Cu -0.332 -0.487 0.288

C 1.062 -0.850 1.832

C -1.428 2.726 0.680

H 1.060 0.116 2.353

C 0.618 -2.049 2.654

H -0.437 2.256 0.765

H -1.730 3.133 1.658

H -1.386 3.544 -0.056

H -2.346 -2.019 -0.874

H -3.981 -1.739 -1.581

H -3.818 -2.164 0.156

H 4.756 1.943 -1.386

H 3.180 1.955 -2.240

H 3.804 2.958 0.589

H 2.427 3.413 -0.465

H 1.461 -2.497 3.224

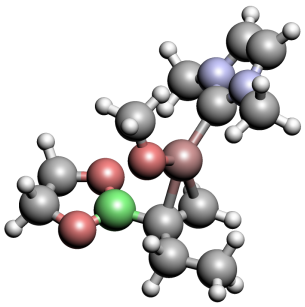
H 0.210 -2.860 2.023

H -0.163 -1.772 3.383

Sum of electronic and thermal Free Energies=   -1026.600753

hartree

Protonation PRODUCT1_methylpropadiene



C 1.233 3.362 -1.324

H -0.204 1.270 3.698

C -0.293 0.529 2.866

H -1.390 0.354 2.728

O 0.369 0.976 1.719

H 2.038 2.346 0.421

H 0.115 -0.431 3.275

H -5.292 -0.015 0.252

C -3.139 1.768 0.706

C -4.294 -0.385 0.031

N -3.151 0.388 0.218

C 2.064 2.244 -0.680

C 3.949 -1.450 0.976

O 3.581 -0.161 0.424

C -3.870 -1.599 -0.439

H -4.426 -2.495 -0.703

C 3.111 -2.479 0.176

C -2.014 -0.299 -0.127

B 2.438 -0.349 -0.337

C 1.645 0.814 -1.012

N -2.481 -1.526 -0.528

O 2.079 -1.692 -0.473

Cu -0.168 0.377 -0.020

C 0.664 0.498 -1.964

C -1.620 -2.618 -0.984

H 0.159 1.275 -2.550

H 0.562 -0.525 -2.340

H -0.573 -2.312 -0.841

H -1.800 -2.831 -2.050

H -1.817 -3.527 -0.394

H -2.105 2.009 0.997

H -3.799 1.861 1.582

H -3.477 2.462 -0.080

H 3.707 -2.991 -0.602

H 2.641 -3.240 0.819

H 5.036 -1.599 0.860

H 3.704 -1.457 2.053

H 1.601 4.351 -1.003

H 0.170 3.290 -1.032

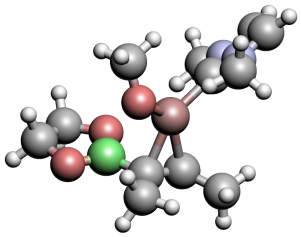
H 3.128 2.365 -0.967

H 1.281 3.331 -2.427

Sum of electronic and thermal Free Energies= -1026.624227

hartree

Protonation PRODUCT2_methylpropadiene



H -0.170 -2.113 -3.441

C -0.151 -1.222 -2.765

H -1.191 -0.802 -2.785

O 0.306 -1.562 -1.489

H 1.916 -2.624 0.118

H 0.487 -0.465 -3.288

H -5.194 0.003 -0.523

C -3.035 -1.834 -0.647

C -4.201 0.397 -0.322

H 1.264 -2.838 1.770

N -3.059 -0.398 -0.355

H 2.978 -2.413 1.536

C 1.955 -2.241 1.152

C 3.328 2.119 -0.636

O 2.229 1.552 0.121

C -3.783 1.666 -0.018

H -4.340 2.593 0.093

C 4.100 0.896 -1.191

C -1.929 0.328 -0.071

B 2.496 0.189 0.277

C 1.624 -0.757 1.157

N -2.399 1.601 0.131

O 3.633 -0.226 -0.400

Cu -0.117 -0.438 0.024

C 0.665 -0.169 2.005

C -1.546 2.747 0.447

H 0.678 0.927 2.078

C -0.122 -0.869 3.091

H -0.499 2.416 0.397

H -1.766 3.125 1.458

H -1.708 3.554 -0.284

H -1.989 -2.109 -0.866

H -3.669 -2.045 -1.522

H -3.407 -2.411 0.216

H 5.192 0.992 -1.080

H 3.869 0.702 -2.253

H 3.948 2.731 0.044

H 2.929 2.771 -1.430

H 0.427 -0.837 4.053

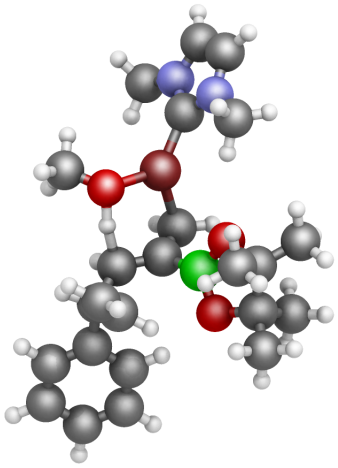
H -0.319 -1.929 2.862

H -1.092 -0.372 3.258

Sum of electronic and thermal Free Energies= -1026.624247

hartree

Protonation 2.41a TS1



H	0.083	-1.742	0.966
O	-1.017	-1.871	1.417
H	-2.321	-3.490	1.607
C	-1.253	-3.237	1.748
H	-0.991	-3.446	2.806
H	-0.657	-3.924	1.111
H	3.001	3.667	1.084
H	0.864	4.382	2.129
H	3.623	3.934	-0.567
H	-6.701	1.002	0.194
H	2.497	5.112	0.158
H	1.214	2.626	2.191
C	2.738	4.038	0.082
C	-4.003	1.531	0.849
C	0.489	3.383	1.852
C	-5.973	0.241	-0.079

H -0.459 3.210 2.389

H -0.817 0.194 -2.161

N -4.610 0.385 0.172

H -0.454 -1.616 -2.099

C -0.449 -0.651 -1.565

C 1.563 3.264 -0.521

O 1.909 1.831 -0.538

C -6.130 -0.972 -0.694

H -7.021 -1.472 -1.066

C 0.236 3.279 0.339

H -0.406 5.335 0.009

C -3.895 -0.707 -0.262

H 2.258 3.451 -2.562

B 0.743 1.117 -0.294

C 0.569 -0.421 -0.593

H 1.137 4.754 -2.076

C 1.345 3.675 -1.987

N -4.859 -1.533 -0.795

C -0.805 4.312 -0.100

O -0.312 1.932 0.095

H -1.701 4.231 0.536

H 2.666 0.678 3.753

Cu -1.988 -0.972 -0.148

H 0.508 3.119 -2.440

C 1.201 -1.511 0.099

H 2.892 0.703 1.304

C 2.530 -0.234 3.162

H -1.110 4.165 -1.147

C -4.574 -2.829 -1.408

H 2.294 -1.150 3.719

C 2.646 -0.233 1.822

H 1.152 -2.465 -0.463

C 2.491 -1.462 0.946

C 3.759 -1.676 0.100

H 3.511 0.110 -1.110

C 4.132 -0.772 -0.920

C 4.578 -2.801 0.326

C 5.290 -0.991 -1.683

C 5.733 -3.028 -0.442

H 5.565 -0.276 -2.467

H 6.350 -3.913 -0.250

C 6.095 -2.121 -1.451

H 6.994 -2.292 -2.052

H -4.434 2.466 0.458

H -2.921 1.517 0.651

H -4.177 1.479 1.936

H -5.085 -3.637 -0.860

H -3.487 -2.990 -1.365

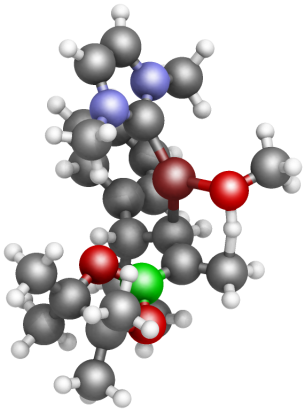
H -4.901 -2.838 -2.460

H 2.436 -2.330 1.634

H 4.304 -3.512 1.117

Sum of electronic and thermal Free Energies= -1492.092671 hartree

Protonation 2.41a TS2



H 0.756 -1.154 2.822

O 0.002 -1.980 2.513

H -0.468 -3.138 4.206

C -0.856 -2.285 3.613

H -0.965 -1.419 4.298

H -1.863 -2.557 3.246

H 5.612 1.604 -0.418

H 4.514 1.580 -2.632

H 6.357 0.287 0.528

H -4.921 -2.663 -1.542

H 6.329 0.192 -1.253

H 3.526 2.232 -1.288

C 5.755 0.514 -0.367

C -4.177 -0.999 0.607

C 3.568 1.465 -2.078

C -3.855 -2.546 -1.364

H 2.736 1.648 -2.777

H 2.520 -0.087 3.159

N -3.352 -1.772 -0.320

H 0.906 0.601 3.738

C 1.473 0.130 2.917

C 4.418 -0.229 -0.290

O 3.667 0.291 0.861

C -2.772 -3.053 -2.030

H -2.710 -3.705 -2.898

C 3.429 0.050 -1.491

H 4.445 -1.023 -3.091

C -1.977 -1.769 -0.308

H 5.178 -1.843 0.935

B 2.324 0.289 0.518

C 1.194 0.574 1.581

H 5.266 -2.186 -0.816

C 4.650 -1.726 -0.025

N -1.642 -2.567 -1.377

C 3.453 -0.996 -2.608

O 2.113 -0.002 -0.827

H 2.709 -0.736 -3.379

H 1.627 4.822 1.023

Cu -0.766 -0.852 0.891

H 3.695 -2.273 0.040

C -0.073 1.113 1.186

H 0.278 4.008 -0.840

C 1.177 3.823 1.058

H 3.221 -2.003 -2.230

C -0.263 -2.894 -1.741

H 1.367 3.220 1.952

C 0.436 3.359 0.036

H -0.711 1.439 2.030

C -0.249 1.995 -0.060

C -1.727 2.221 -0.397

H -2.122 3.395 1.383

C -2.553 2.970 0.469

C -2.293 1.718 -1.586

C -3.907 3.188 0.169

C -3.645 1.941 -1.897

H -4.530 3.772 0.857

H -4.061 1.545 -2.830

C -4.460 2.674 -1.017

H -5.513 2.853 -1.259

H 0.399 -2.119 -1.326

H -0.164 -2.909 -2.837

H 0.025 -3.879 -1.336

H -3.511 -0.545 1.353

H -4.905 -1.655 1.110

H -4.708 -0.197 0.069

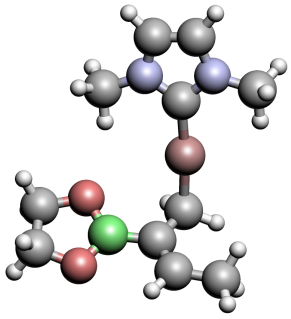
H -1.663 1.144 -2.276

H 0.204 1.477 -0.927

Sum of electronic and thermal Free Energies= -1492.094777

hartree

MONOMER1



Cu 0.616 0.725 0.626

C -1.089 1.460 1.244

O -2.066 -1.405 0.564

B -2.668 -0.237 0.010

C -2.113 1.196 0.173

O -3.840 -0.571 -0.718

C -2.561 2.156 -0.719

C -4.000 -2.048 -0.737

C -2.951 -2.573 0.295

H 4.051 -2.851 -0.723

C 3.708 -1.835 -0.547

C 4.376 -0.630 -0.675

H 5.397 -0.419 -0.983

N 2.402 -1.529 -0.118

C 2.217 -0.154 0.034

N 3.458 0.378 -0.319

H 4.583 2.051 0.366

C 3.745 1.824 -0.316

H 2.840 2.346 0.034

H 3.993 2.173 -1.334

H 1.627 -3.155 1.018

C 1.345 -2.522 0.157

H 0.409 -1.987 0.392

H 1.184 -3.160 -0.731

H -3.802 -2.404 -1.764

H -5.039 -2.291 -0.458

H -2.336 -3.401 -0.098

H -3.413 -2.880 1.251

H -3.295 1.864 -1.483

C -2.076 3.592 -0.728

H -2.528 4.173 -1.552

H -0.970 3.639 -0.835

H -2.313 4.109 0.226

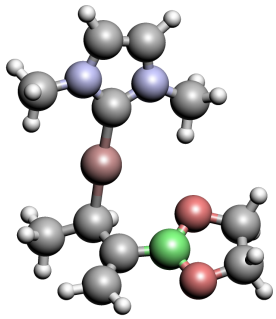
H -0.995 2.531 1.508

H -1.293 0.876 2.167

Sum of electronic and thermal Free Energies=   -910.817443

hartree

MONOMER2



H 5.270 -0.681 0.972

C 4.257 -0.817 0.603

C 3.607 -1.956 0.162

H 3.961 -2.980 0.079

N 3.330 0.240 0.499

C 2.101 -0.197 0.003

N 2.302 -1.564 -0.196

H 1.526 -2.780 -1.763

C 1.263 -2.461 -0.739

H 0.305 -1.914 -0.764

H 1.159 -3.351 -0.093

H 2.692 2.227 0.646

C 3.597 1.641 0.872

H 3.820 1.721 1.950

H 4.445 2.042 0.288

H -3.415 1.737 1.928

C -2.702 2.129 1.193

O -3.758 -0.649 0.913

H -2.444 3.194 1.277

B -2.637 -0.163 0.194

C -2.158 1.313 0.216

O -2.025 -1.211 -0.557

C -1.158 1.762 -0.814

H -1.403 1.299 -1.798

C -1.010 3.292 -0.968

C -2.870 -2.435 -0.440

C -3.865 -2.118 0.719

Cu 0.508 0.804 -0.378

H -3.380 -2.592 -1.408

H -2.216 -3.298 -0.225

H -3.585 -2.612 1.667

H -4.911 -2.363 0.470

H -1.993 3.786 -1.146

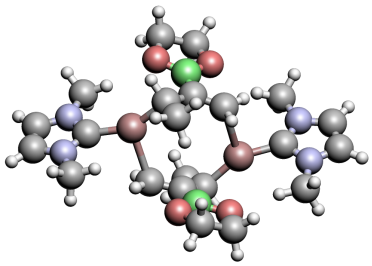
H -0.344 3.541 -1.816

H -0.579 3.763 -0.060

Sum of electronic and thermal Free Energies=   -910.808365

hartree

DIMERIC TS



H -6.698 -2.541 -0.060

C -6.056 -1.664 -0.082

C -6.362 -0.325 0.079

H -7.313 0.162 0.273

N -4.664 -1.739 -0.293

C -4.066 -0.474 -0.282

N -5.149 0.382 -0.045

H -5.681 2.343 -0.671

C -5.013 1.846 0.056

H -3.968 2.119 -0.167

H -5.267 2.187 1.077

H -3.960 -3.230 -1.641

C -3.924 -2.985 -0.563

H -2.873 -2.868 -0.253

H -4.371 -3.814 0.014

H 2.024 2.244 -0.641

C 1.372 1.525 -1.157

O 0.306 3.877 0.317

H 1.855 0.833 -1.859

B -0.534 2.948 -0.350

C -0.009 1.747 -1.180

O -1.905 3.298 -0.185

Cu 2.427 0.081 0.551

C -0.975 0.954 -1.977

H -1.739 1.618 -2.440

C -0.373 -0.016 -3.010

C -1.983 4.594 0.548

C -0.536 4.831 1.083

H 1.934 -1.020 2.613

C 1.204 -0.364 2.088

O 1.562 -3.210 0.936

C 0.868 0.892 2.912

B 0.291 -2.584 1.063

C 0.045 -1.154 1.609

O -0.743 -3.467 0.636

Cu -2.262 0.075 -0.706

C -1.281 -0.719 1.651

C -0.133 -4.717 0.112

C 1.364 -4.632 0.542

H 6.922 -1.334 -1.589

C 6.220 -0.631 -1.147

C 6.366 0.711 -0.847

H 7.217 1.374 -0.981

N 4.915 -0.992 -0.756

C 4.212 0.090 -0.215

N 5.145 1.133 -0.284

H 5.690 2.865 0.819

C 4.864 2.501 0.183

H 3.936 2.478 0.776

H 4.724 3.188 -0.670

H 5.076 -3.101 -0.596

C 4.332 -2.338 -0.889

H 3.457 -2.408 -0.219

H 4.011 -2.523 -1.931

H -0.257 -4.727 -0.986

H -0.660 -5.580 0.554

H 2.062 -4.873 -0.278

H 1.591 -5.266 1.418

H -2.303 5.374 -0.166

H -2.730 4.499 1.355

H -0.436 4.591 2.157

H -0.169 5.854 0.896

H 0.325 0.499 -3.714

H -1.167 -0.498 -3.613

H 0.211 -0.823 -2.521

H 0.164 0.668 3.749

H 0.386 1.672 2.286

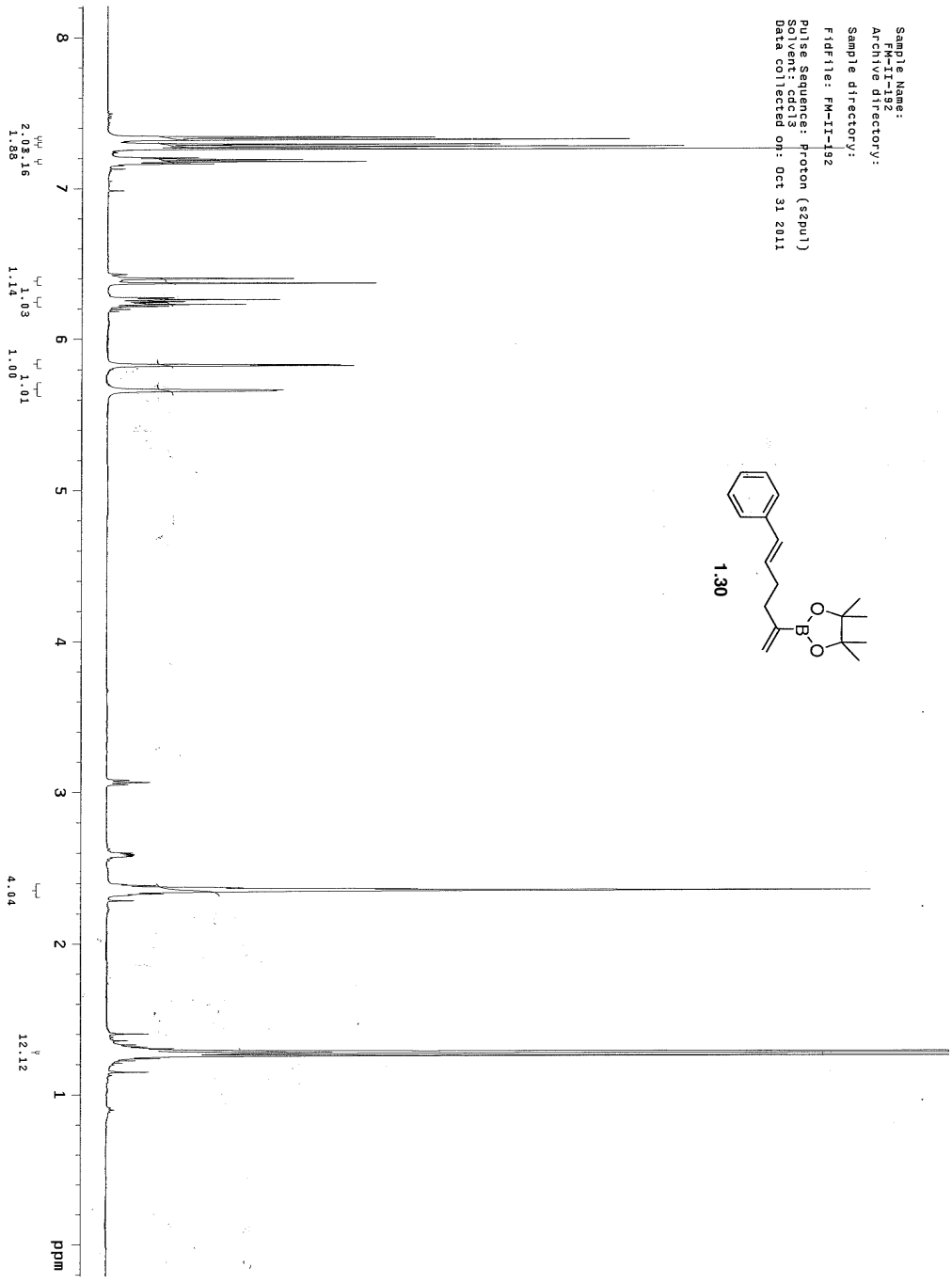
H 1.783 1.339 3.348

H -2.103 -1.400 1.406

H -1.565 0.241 2.104

Sum of electronic and thermal Free Energies=   -1821.593890

Hartree

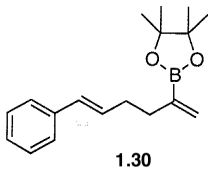

Sample Name:
FM-I-192
Archive directory:
Sample directory:
FidFile: FM-I-192
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Oct 31 2011
1.30
O
B
O
8
7
6
5
4
3
2
1
ppm
2.08
1.88
1.14
1.03
1.00
1.01
4.04
12.12

Sample Name:
FM-III-215-CNMR
Archive directory:

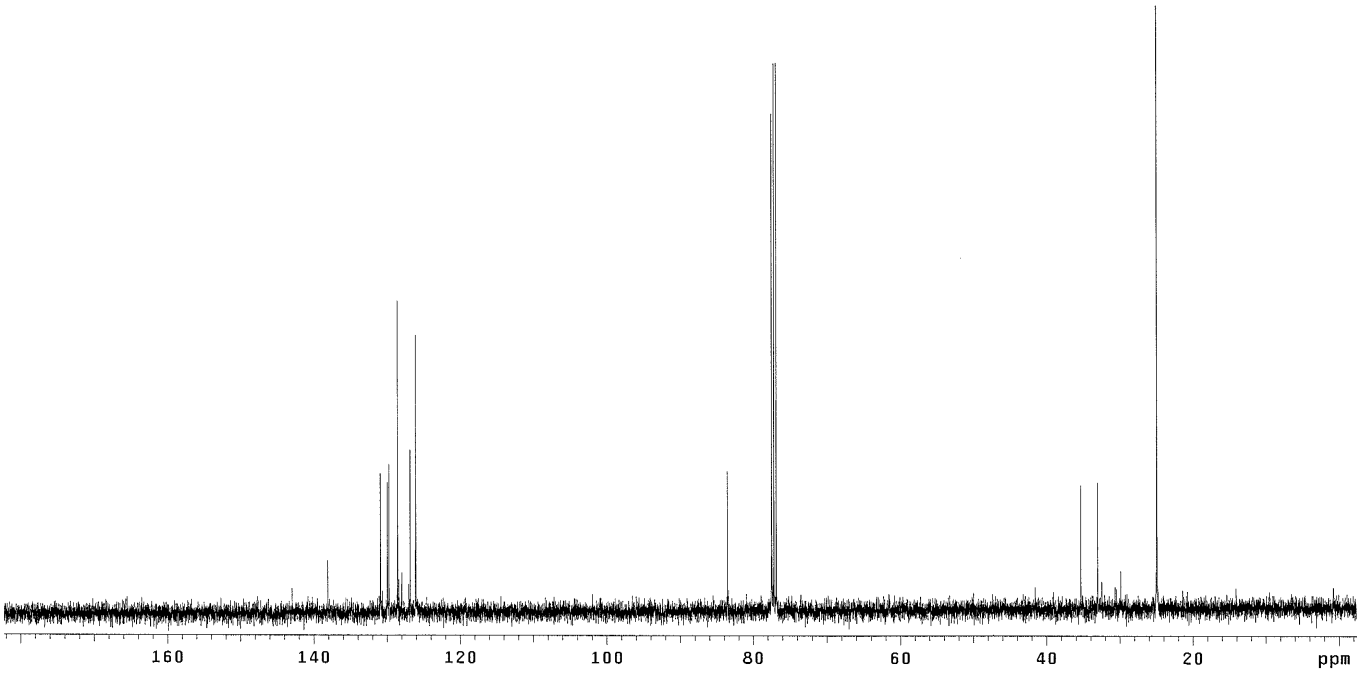
Sample directory:

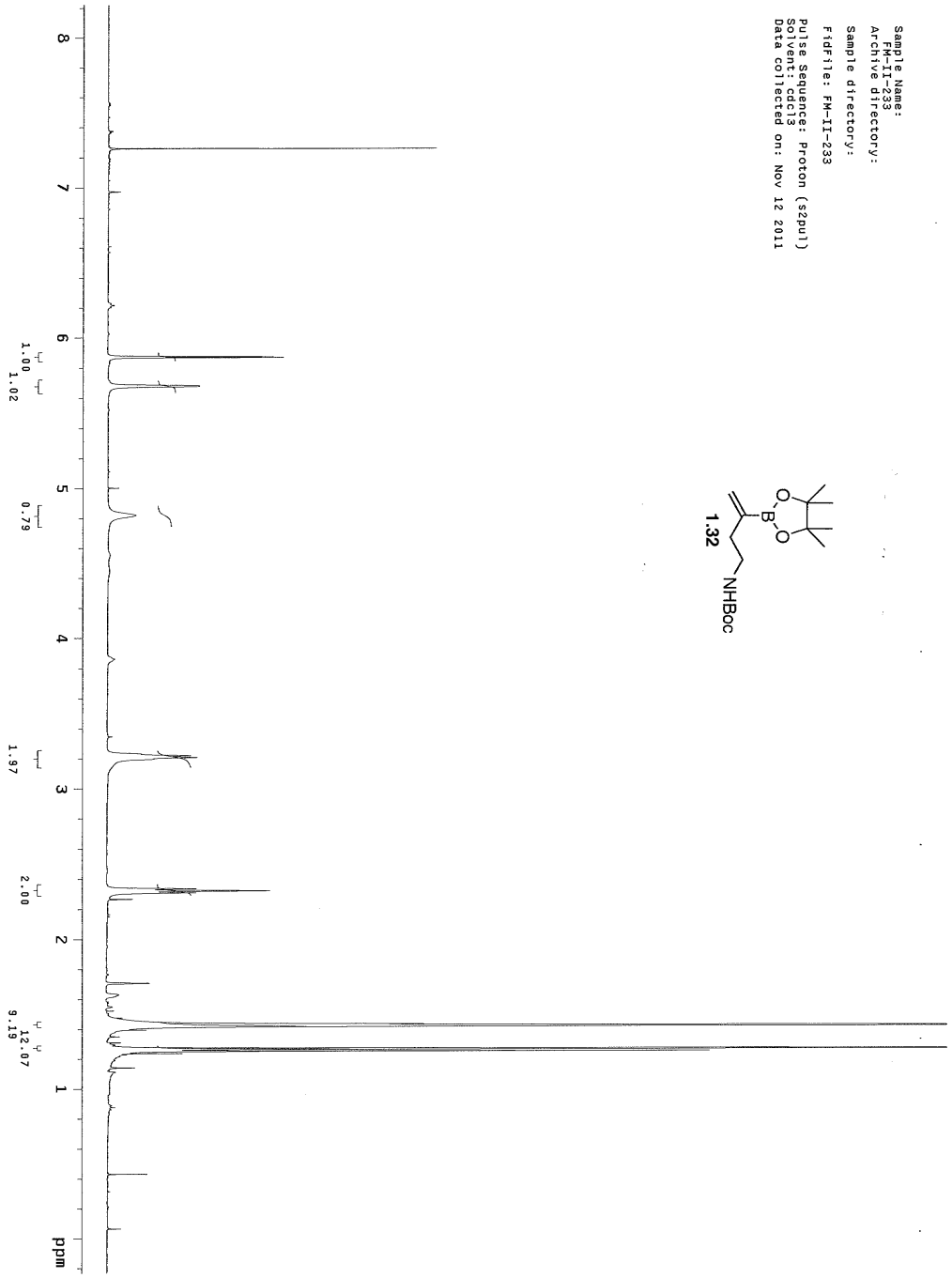
FidFile: FM-III-215-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Apr 6 2012



1.30




Sample Name:
FM-II-233
Archive directory:
Sample directory:
FidFile: FM-II-233
Pulse Sequence: Proton (szpul)
Solvent: cdcl3
Data collected on: Nov 12 2011
1.32
NHBoc
8
7
6
5
4
3
2
1
ppm
1.00
1.02
0.79
1.97
2.00
12.07
9.19

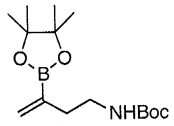
Sample Name:

Archive directory:

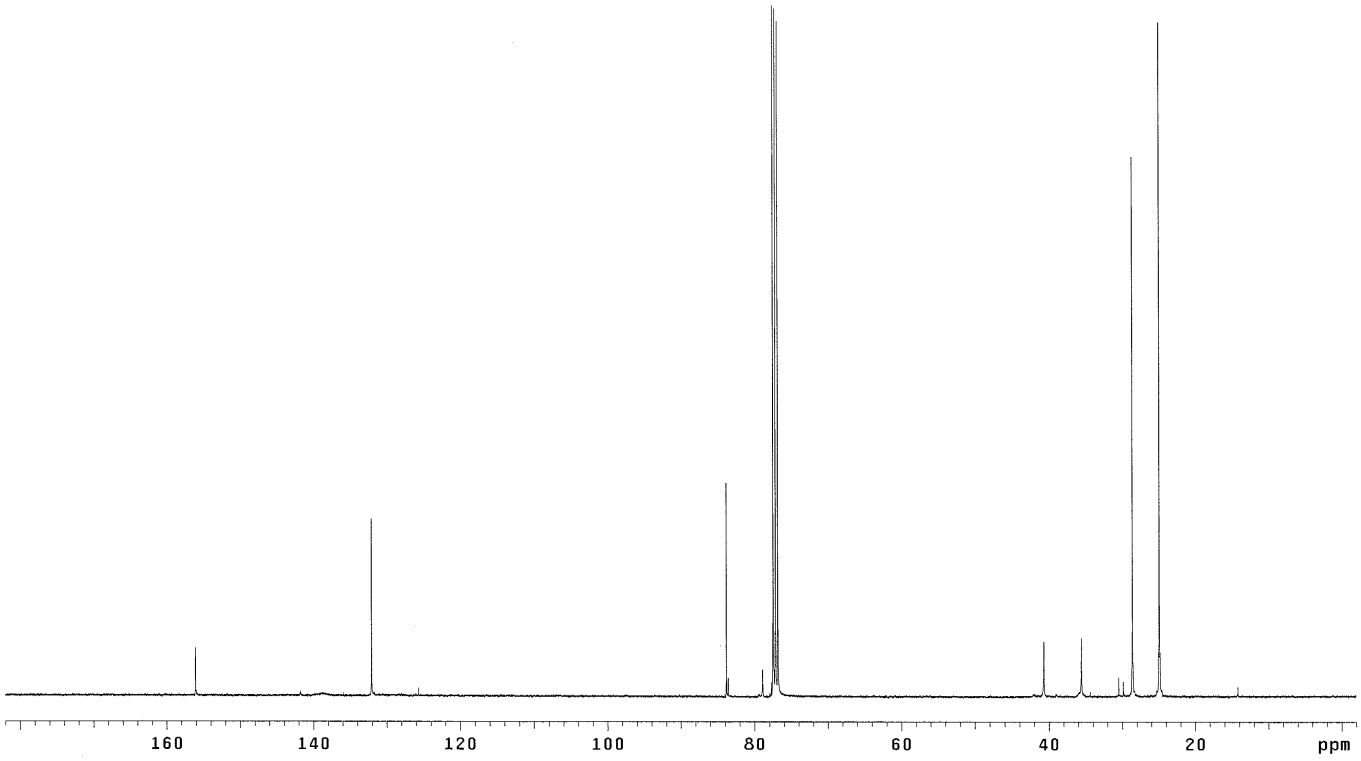
Sample directory:

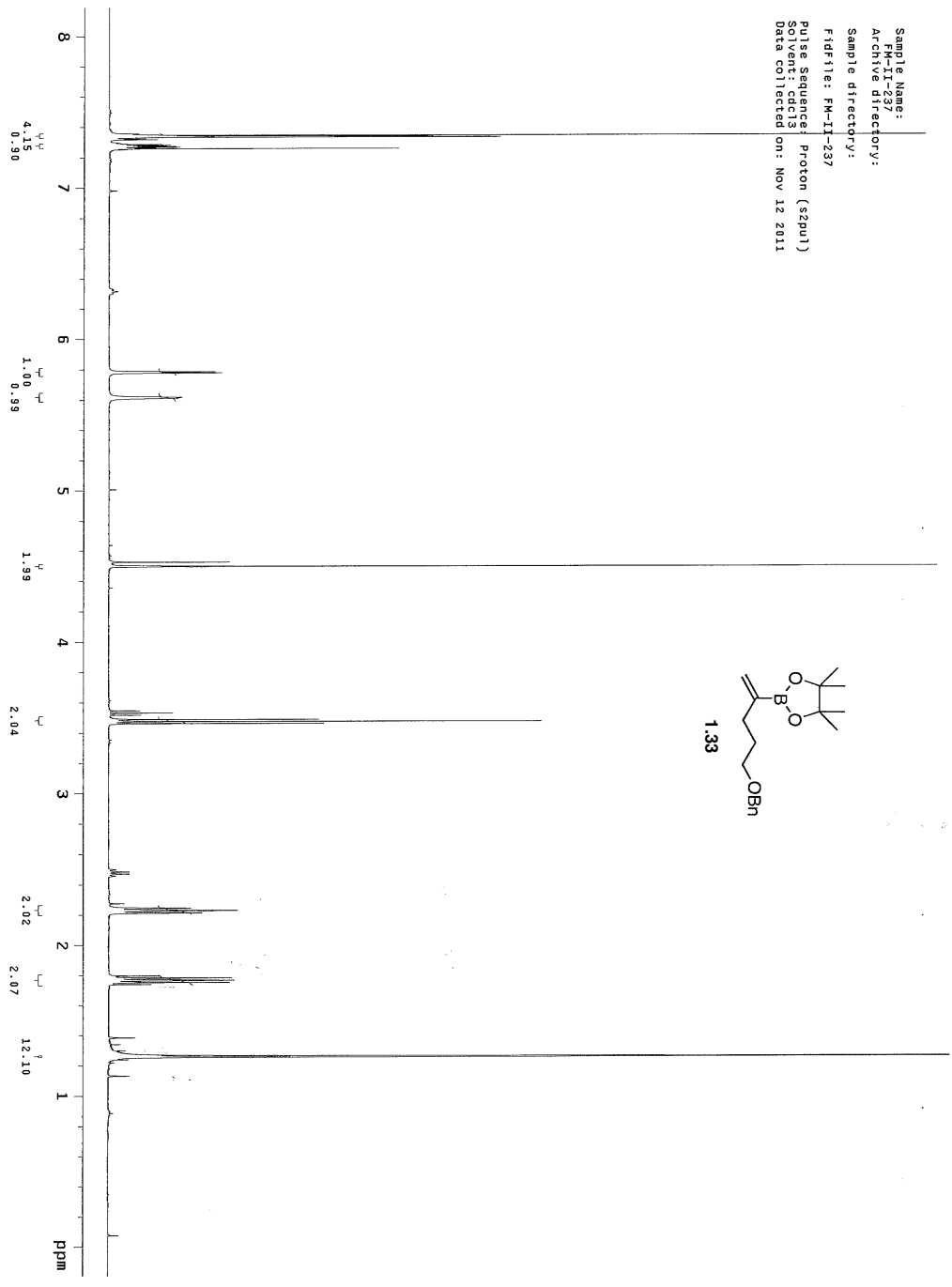
FidFile: FM-II-233-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Nov 13 2011



1.32



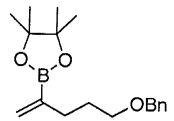

Sample Name:
FM-II-237
Archive directory:
Sample directory:
FidFile: FM-II-237
Pulse Sequence: Proton (s2pul)
Solvent: CDCl3
Data collected on: Nov 12 2011
1.33
OBn
ppm

Sample Name:
FM-II-237-CNMR
Archive directory:

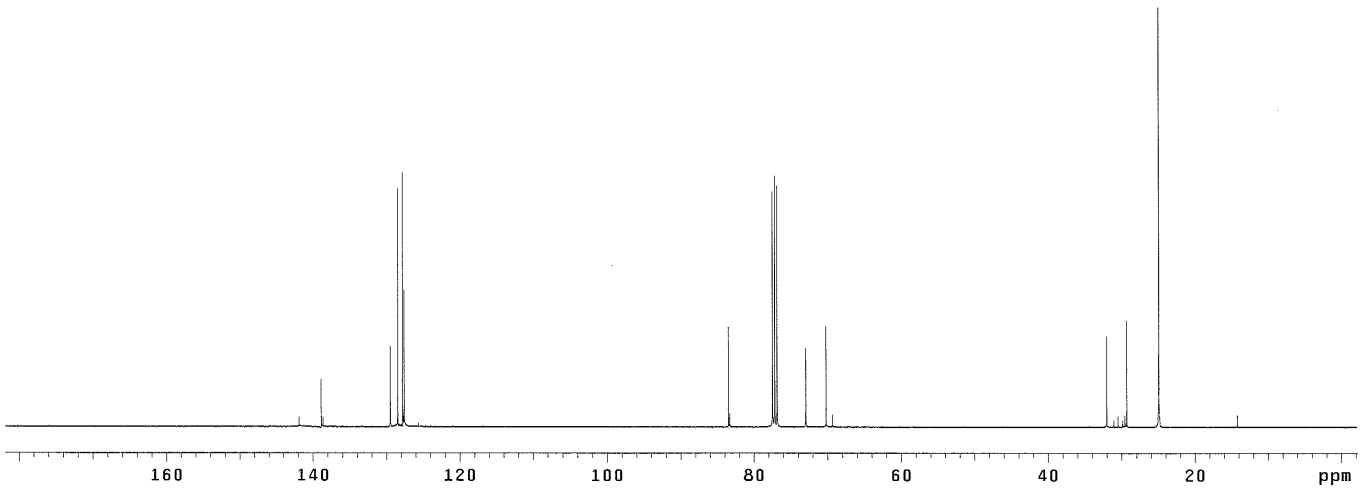
Sample directory:

FidFile: FM-II-237-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Nov 14 2011



1.33

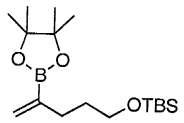


Sample Name:
FM-II-239
Archive directory:

Sample directory:

FidFile: FM-II-239

Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Nov 12 2011



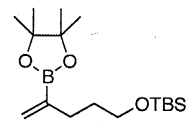
1.34

Sample Name:
FM-II-240-CNMR
Archive directory:

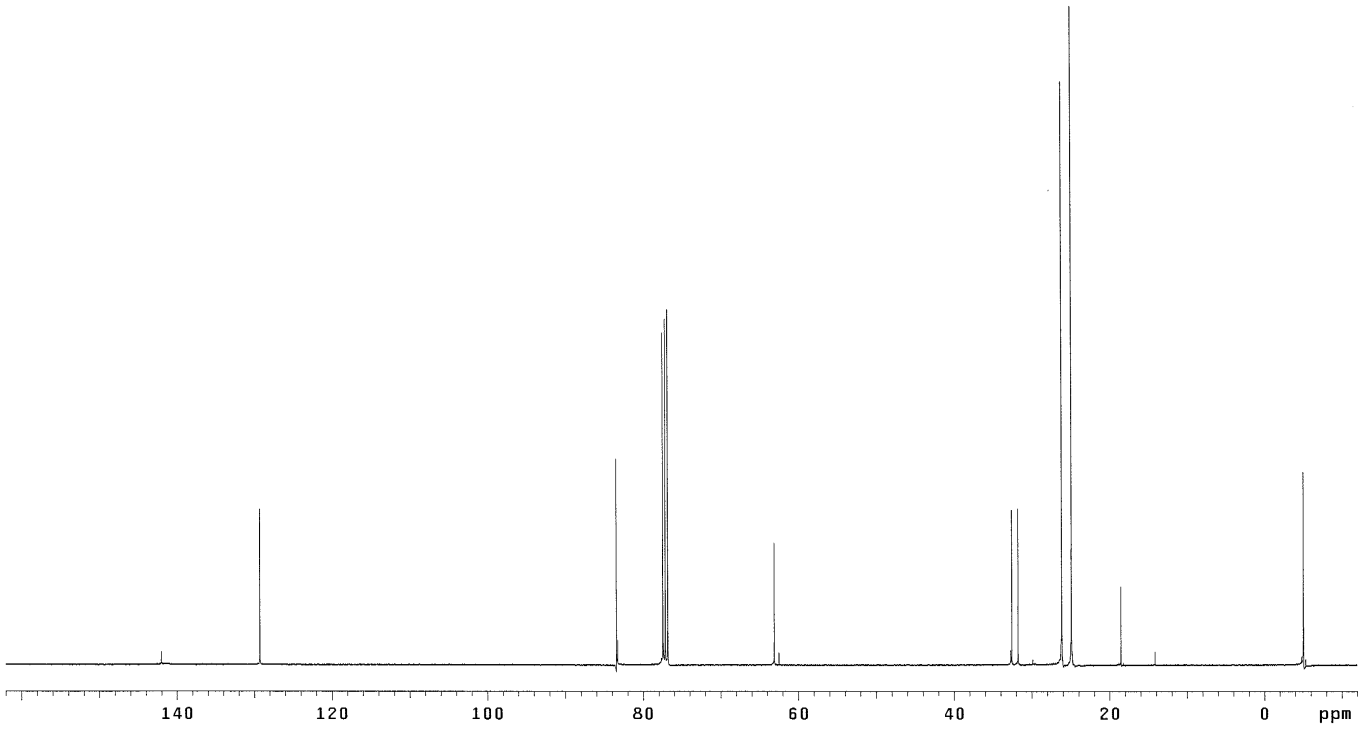
Sample directory:

FidFile: FM-II-240-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Jan 9 2012



1.34

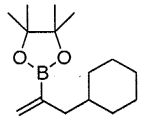


Sample Name:
FM-IV-155
Archive directory:

Sample directory:

FidFile: FM-IV-155

Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Jul 18 2012



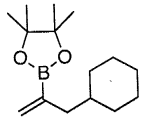
1.35

Sample Name:
FM-IV-155
Archive directory:

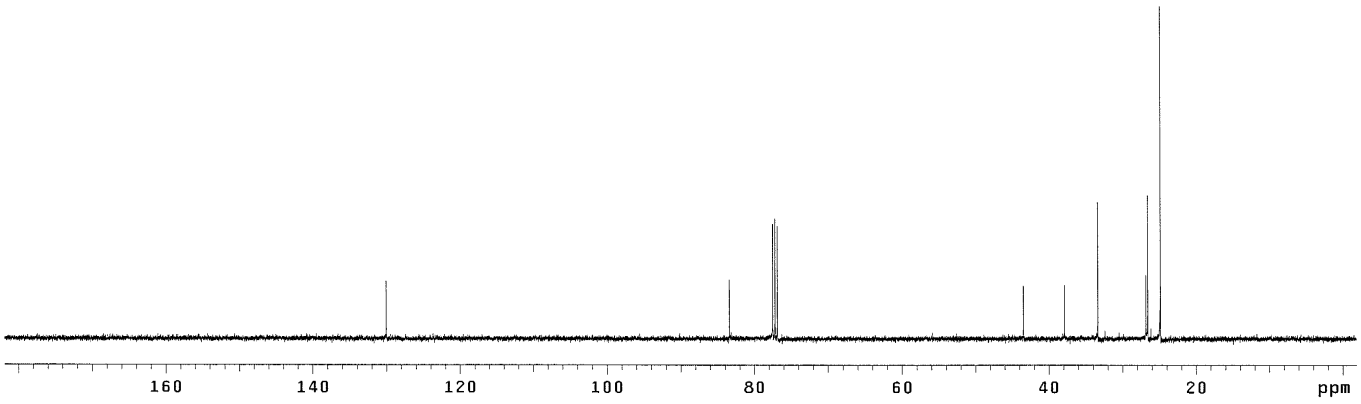
Sample directory:

FidFile: FM-IV-155-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Jul 18 2012



1.35

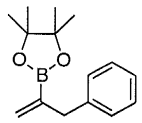


Sample Name:
FM-IV-119
Archive directory:

Sample directory:

FidFile: FM-IV-119

Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Jul 18 2012



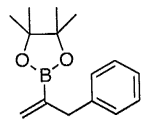
1.36

Sample Name:
FM-IV-119
Archive directory:

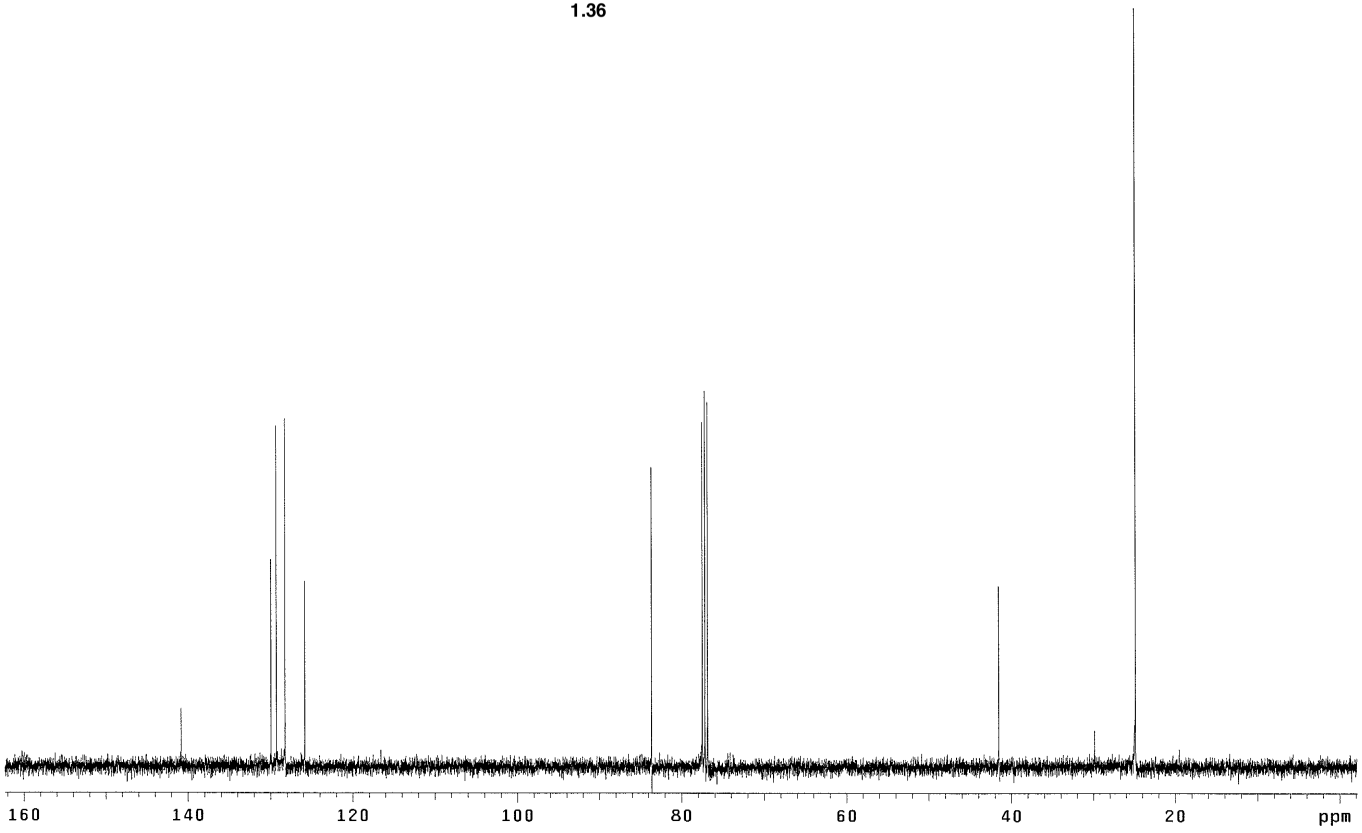
Sample directory:

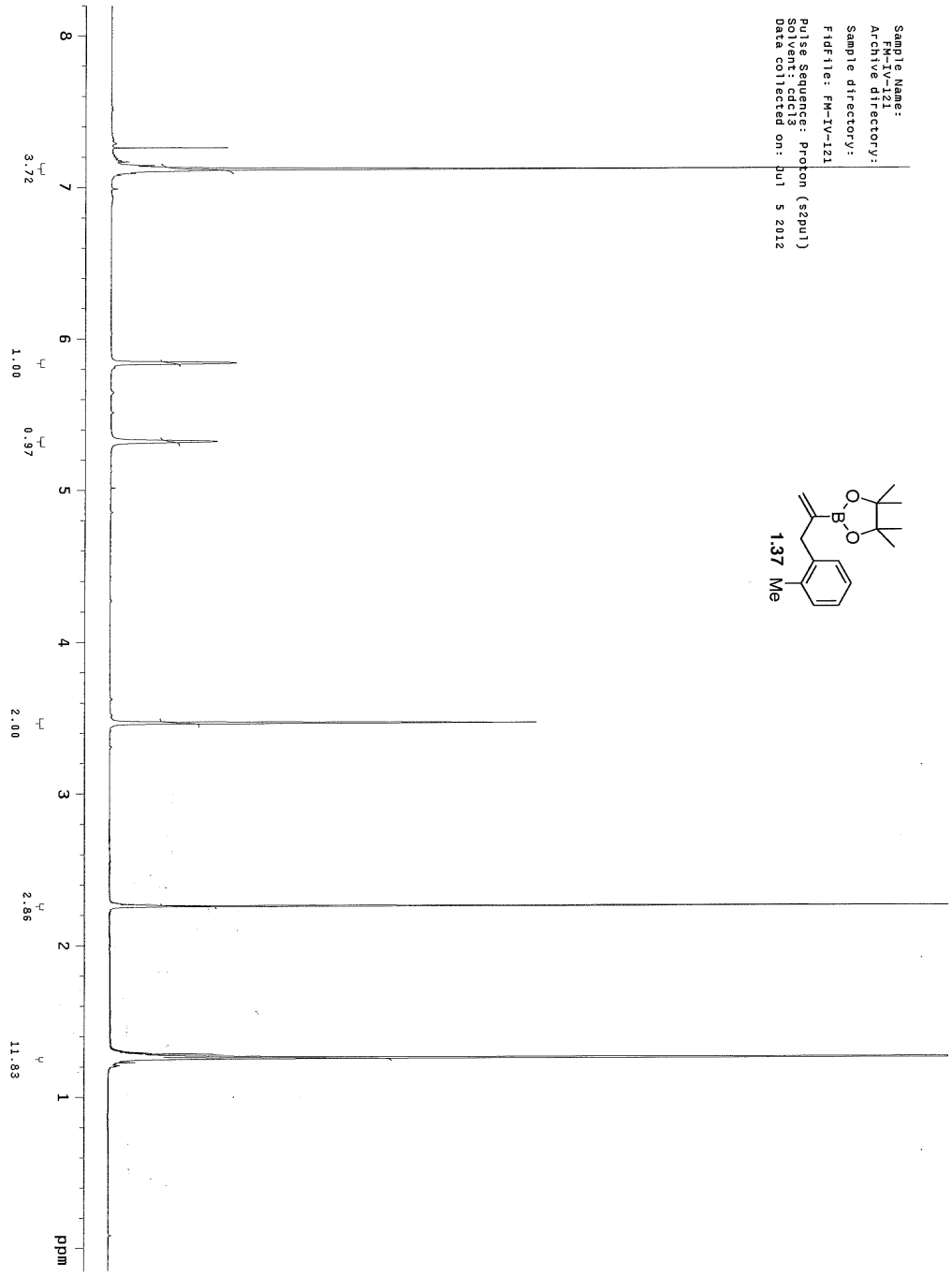
FidFile: FM-IV-119-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Jul 18 2012



1.36



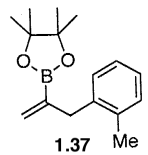

Sample Name:
FM-IV-121
Archive directory:
Sample directory:
FidFile: FM-IV-121
Pulse Sequence: Proton (szpul)
Solvent: cdcl3
Data collected on: Jul 5 2012
1.37 Me
3.72
1.00
0.97
2.00
2.86
11.83
ppm

Sample Name:
FM-IV-121
Archive directory:

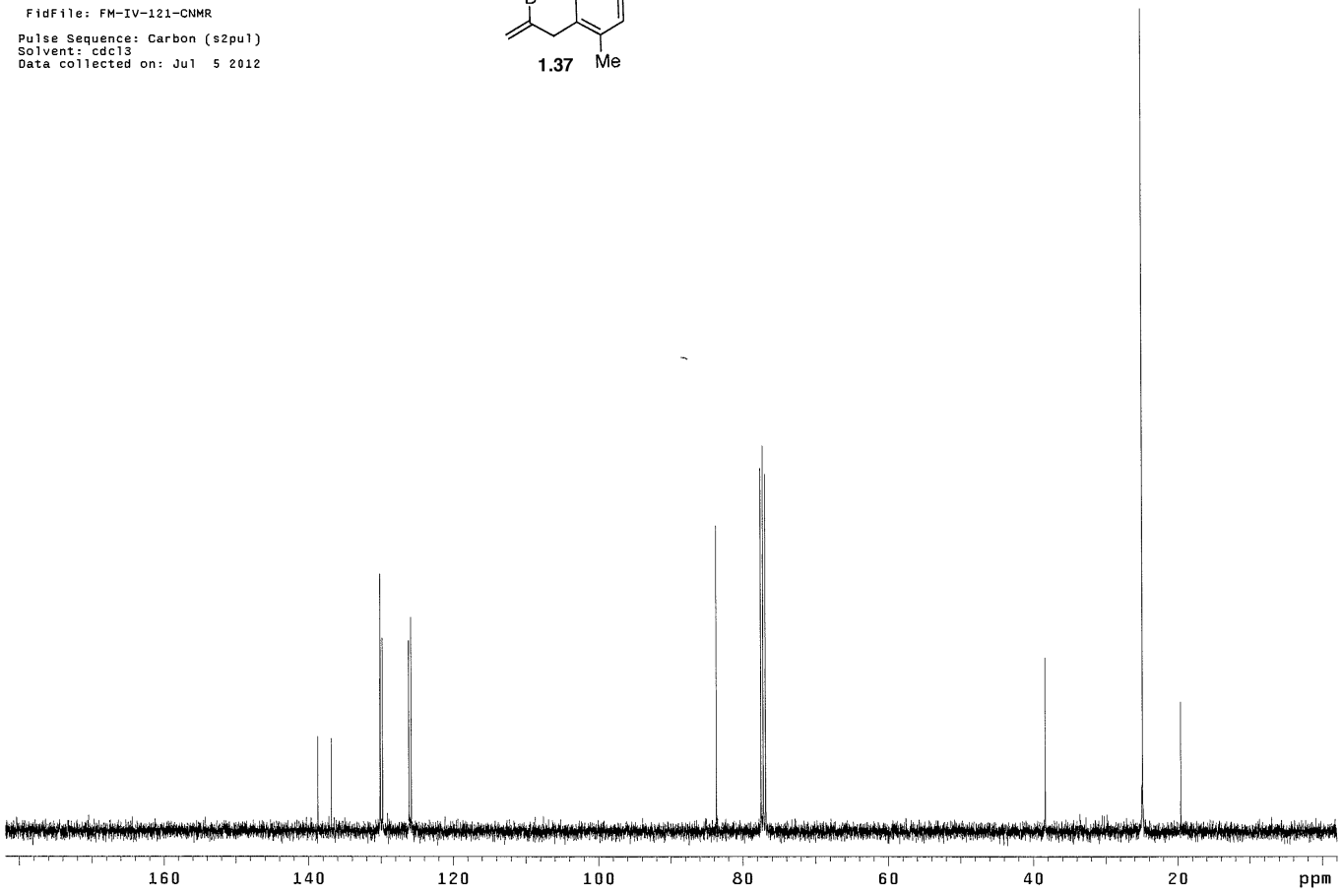
Sample directory:

FidFile: FM-IV-121-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Jul 5 2012



1.37

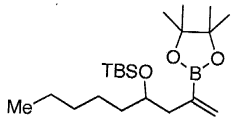


Sample Name:
FM-IV-162
Archive directory:

Sample directory:

FidFile: FM-IV-162

Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Jul 18 2012



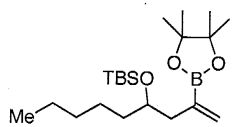
1.38

Sample Name:
FM-IV-162
Archive directory:

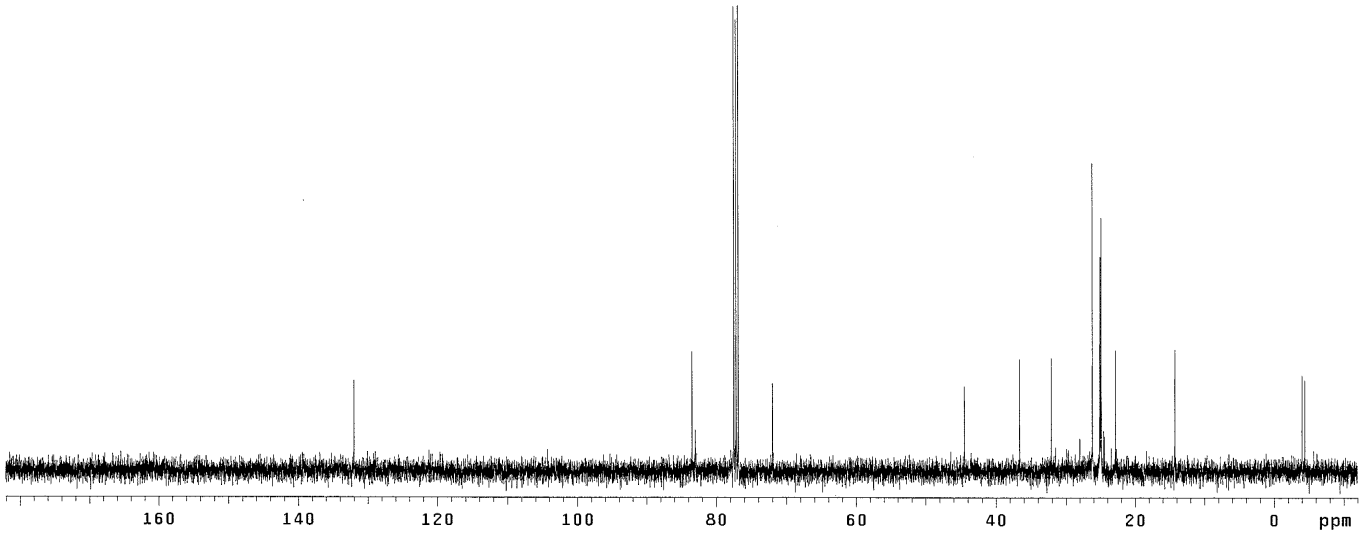
Sample directory:

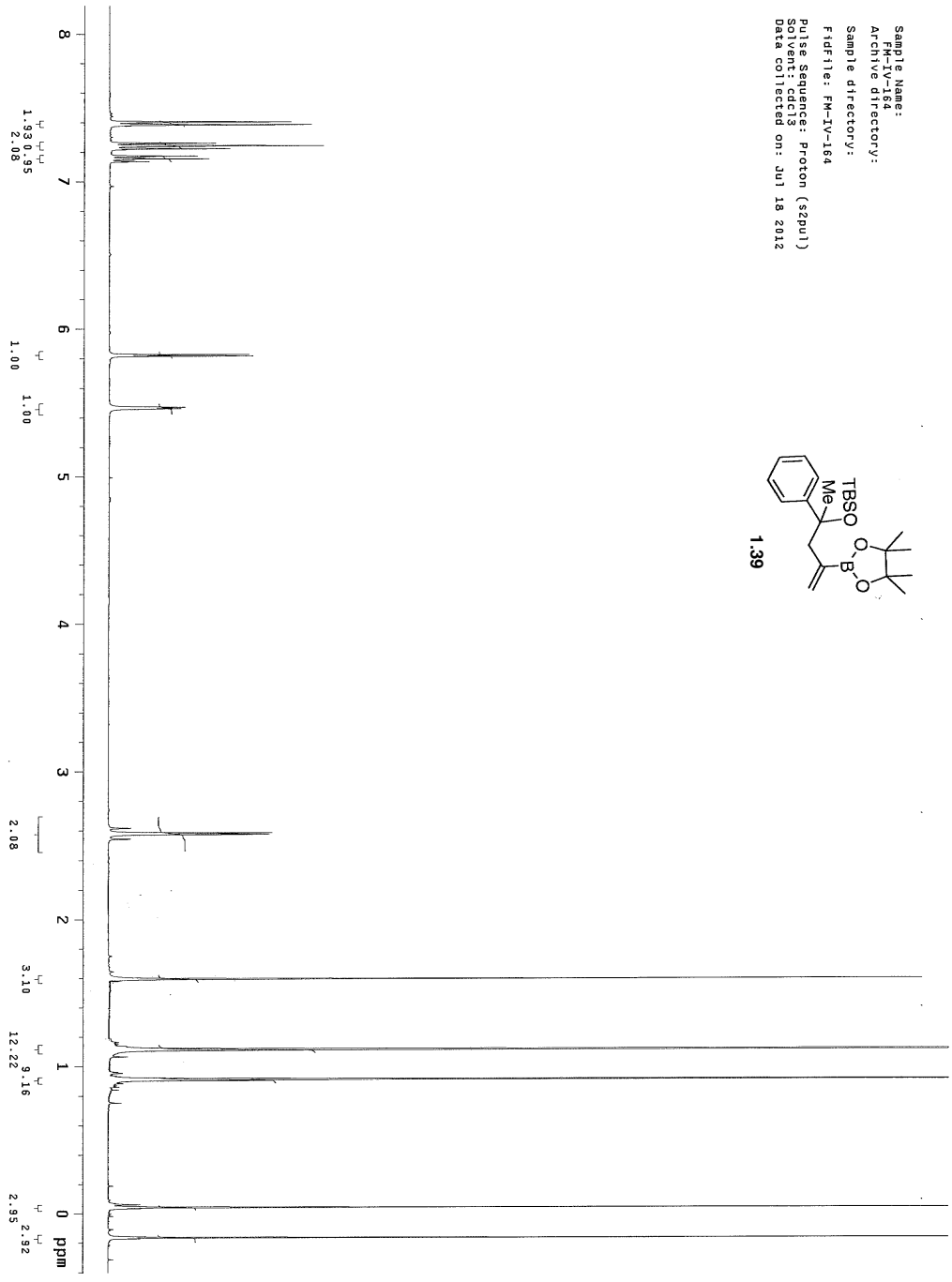
FidFile: FM-IV-162-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Jul 18 2012



1.38



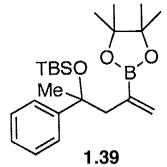

Sample Name:
FM-IV-164
Archive directory:
Sample directory:
FidFile: FM-IV-164
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Jul 18 2012
TBSO
Me
O
B
O
1.39
8
7
6
5
4
3
2
1
0 ppm
1.93
0.95
2.08
1.00
1.00
2.08
3.10
12.22
9.16
2.95
2.92

Sample Name:
FM-IV-164
Archive directory:

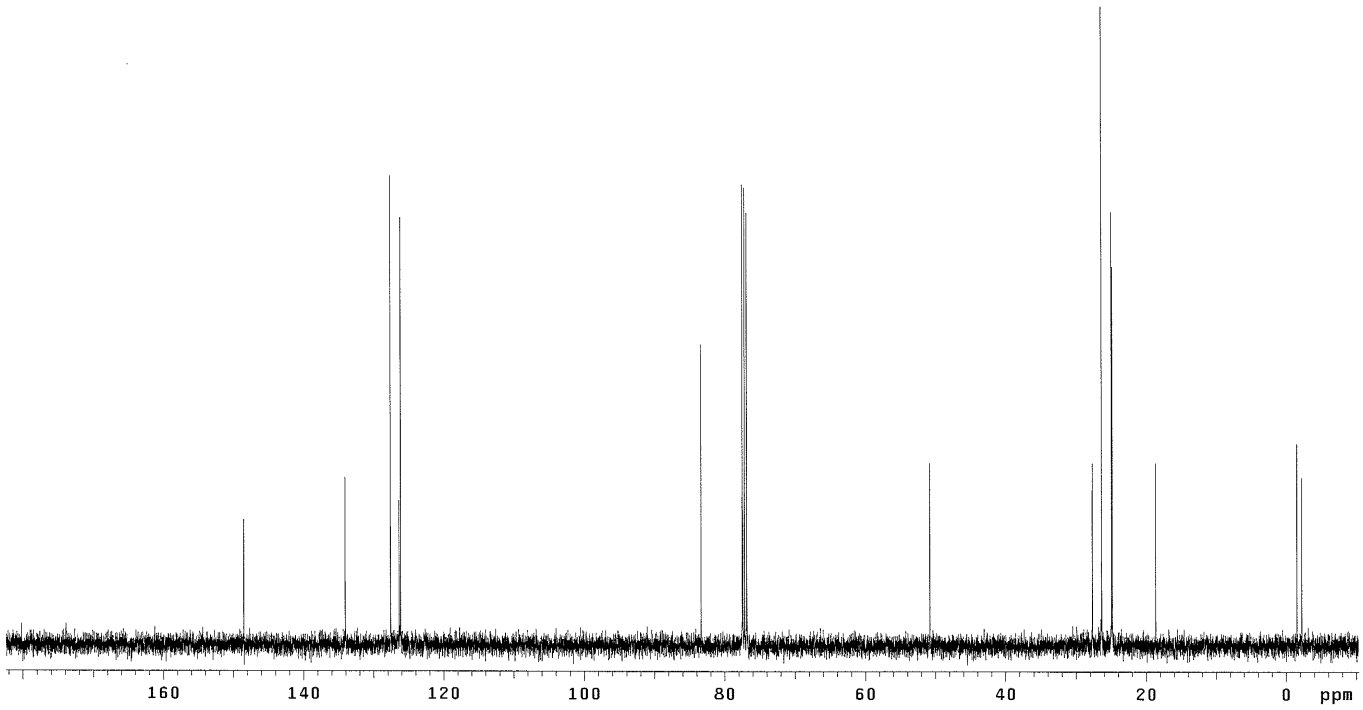
Sample directory:

FidFile: FM-IV-164-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Jul 18 2012



1.39

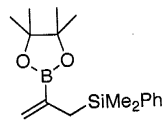


Sample Name:
FM-IV-151
Archive directory:

Sample directory:

FidFile: FM-IV-151

Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Jul 18 2012



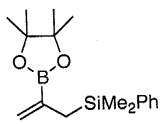
1.40

Sample Name:
FM-IV-151
Archive directory:

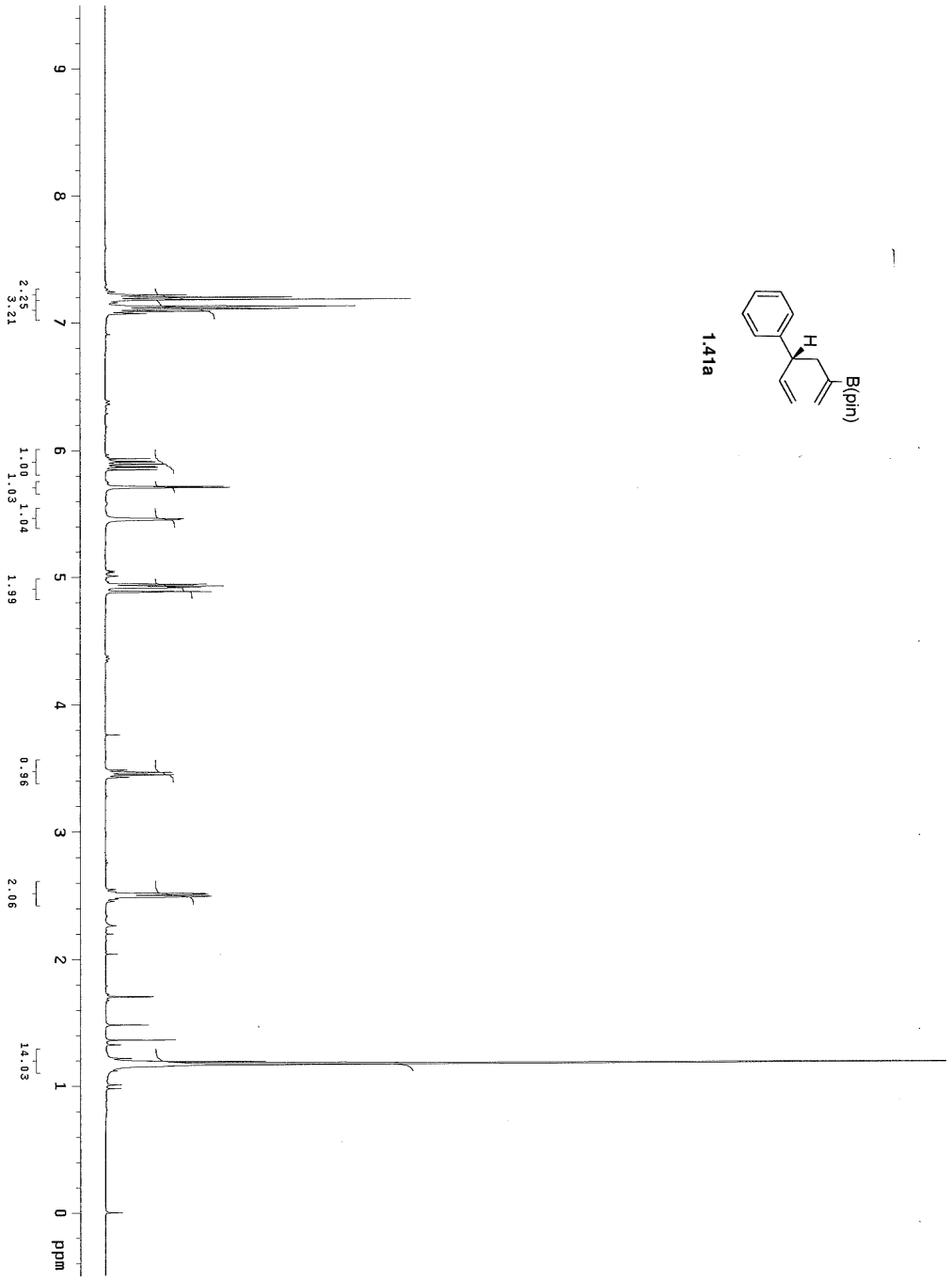
Sample directory:

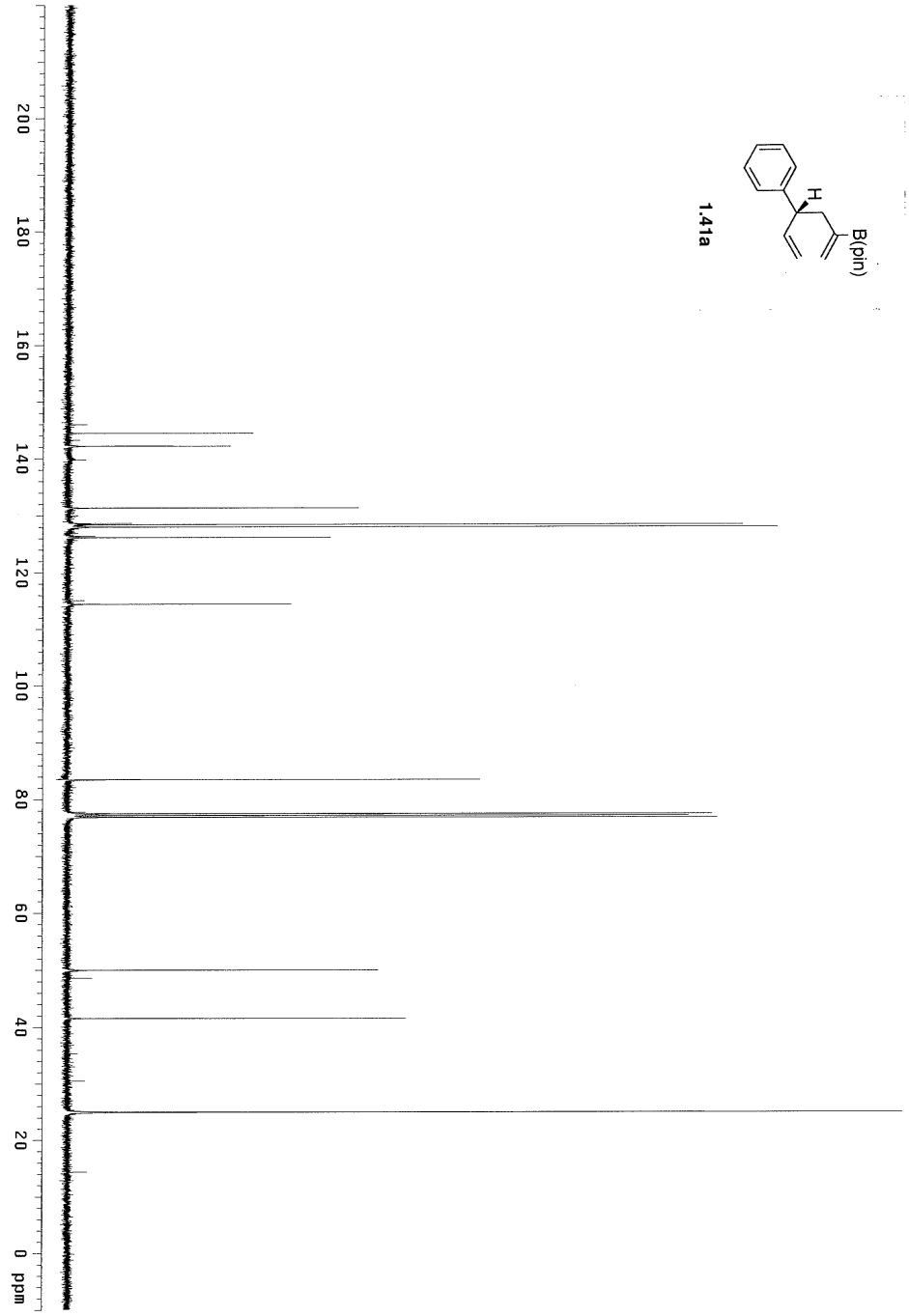
FidFile: FM-IV-151-CNMR

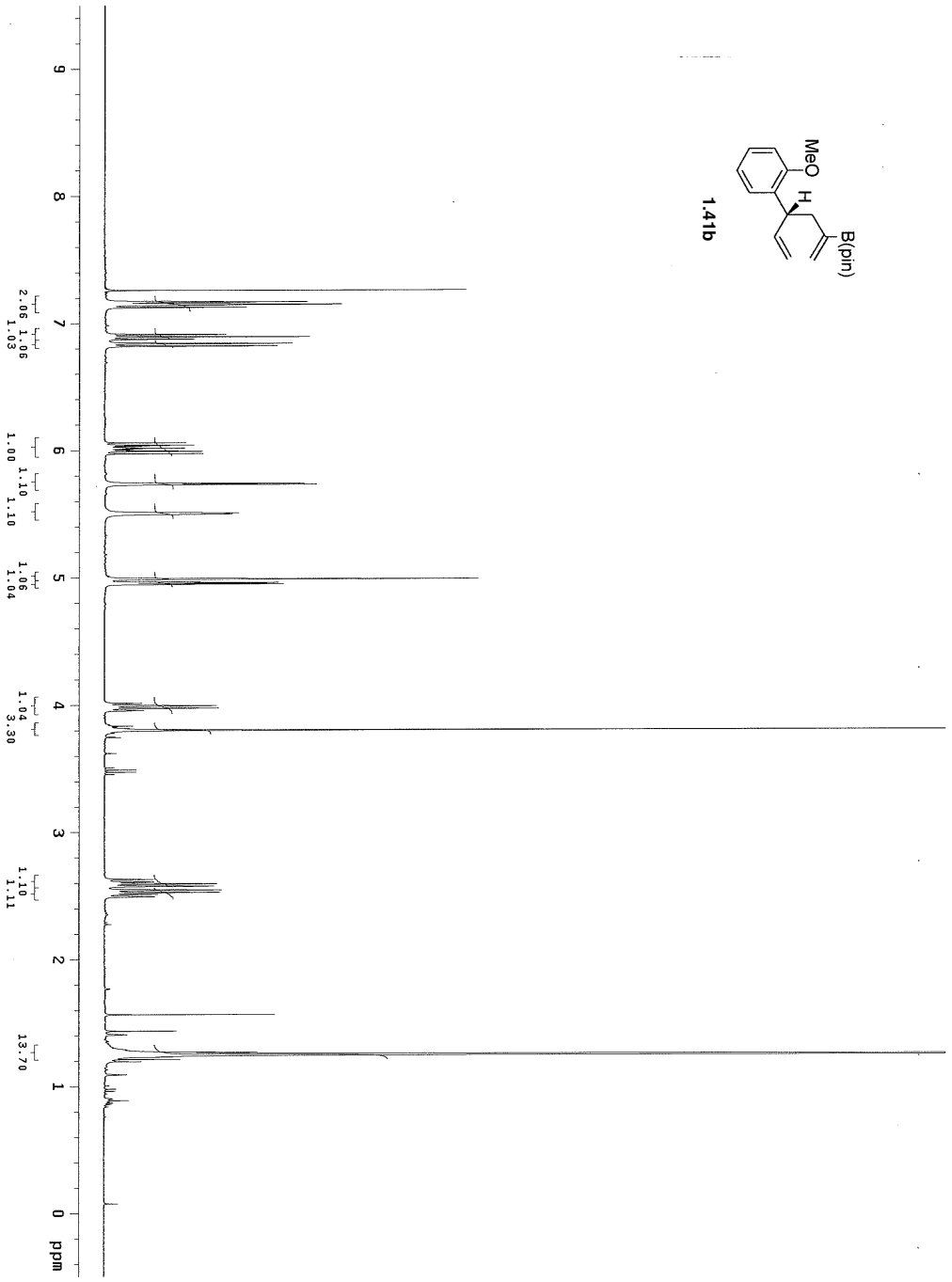
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Jul 18 2012

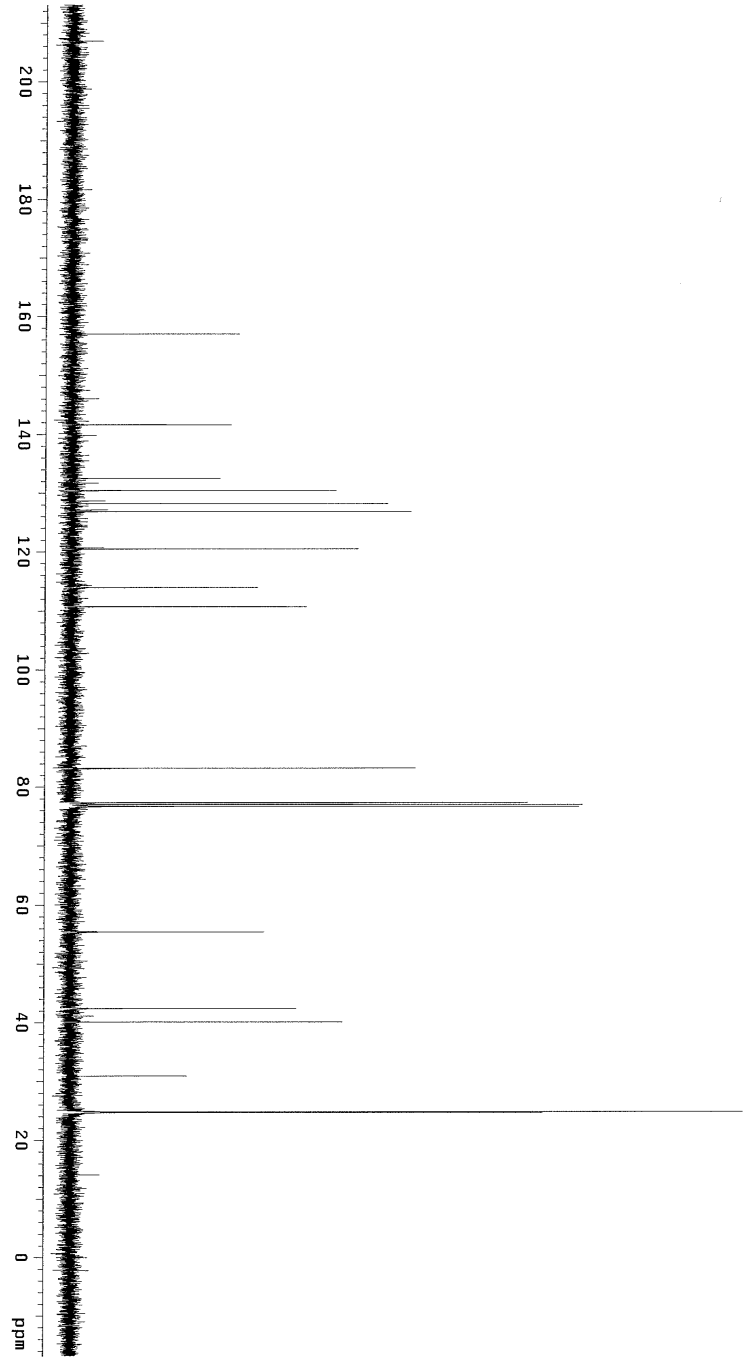


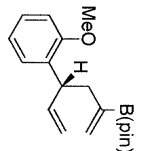
1.40


B(pin)
H
1.41a
9
8
7
6
5
4
3
2
1
0
ppm
2.29
3.21
1.00
1.03
1.04
1.99
0.96
2.06
14.03

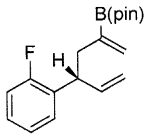

B(pin)
H
1.41a
200
180
160
140
120
100
80
60
40
20
0
ppm


MeO
H
B(pin)
1.41b
ppm



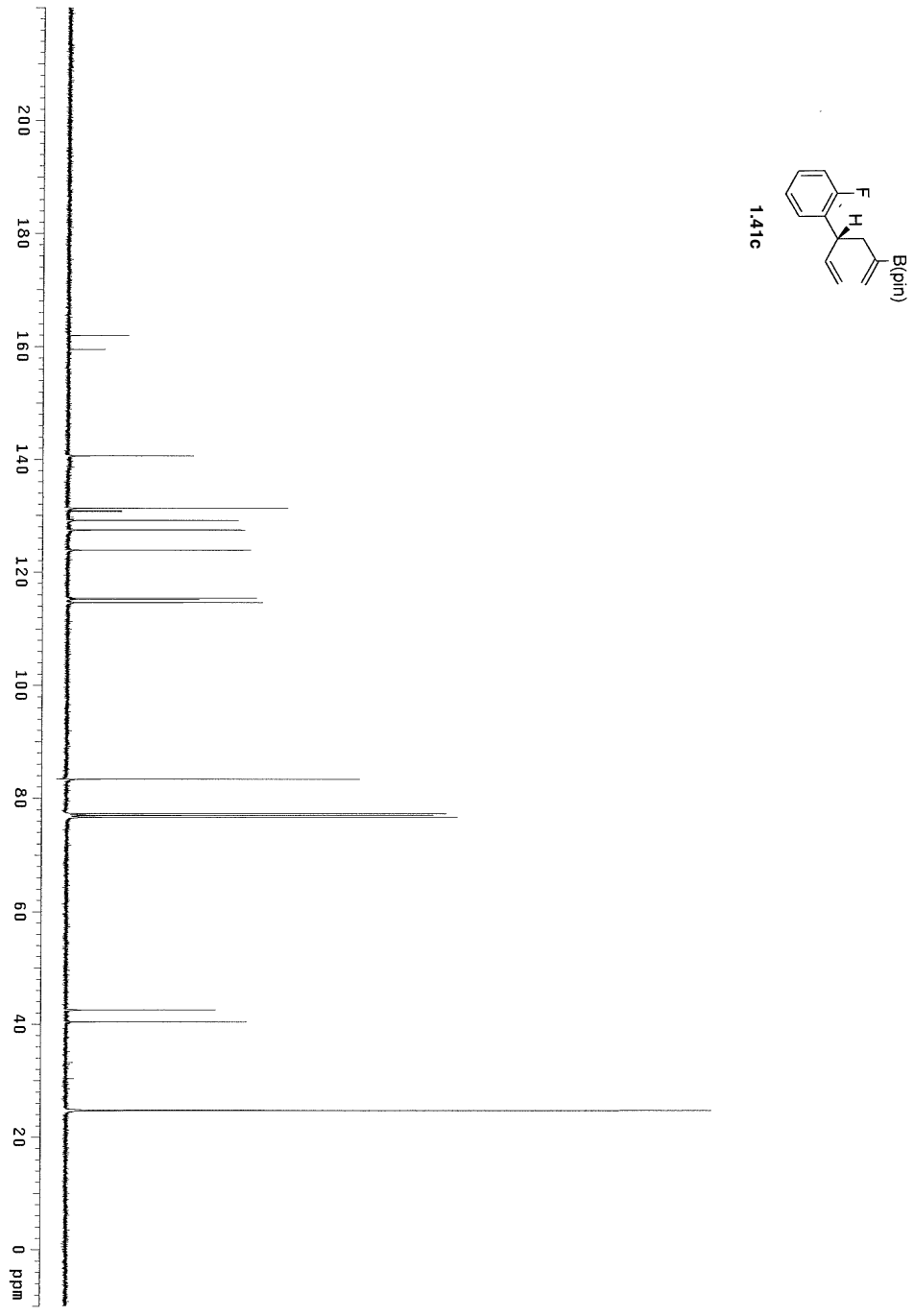


1.41b

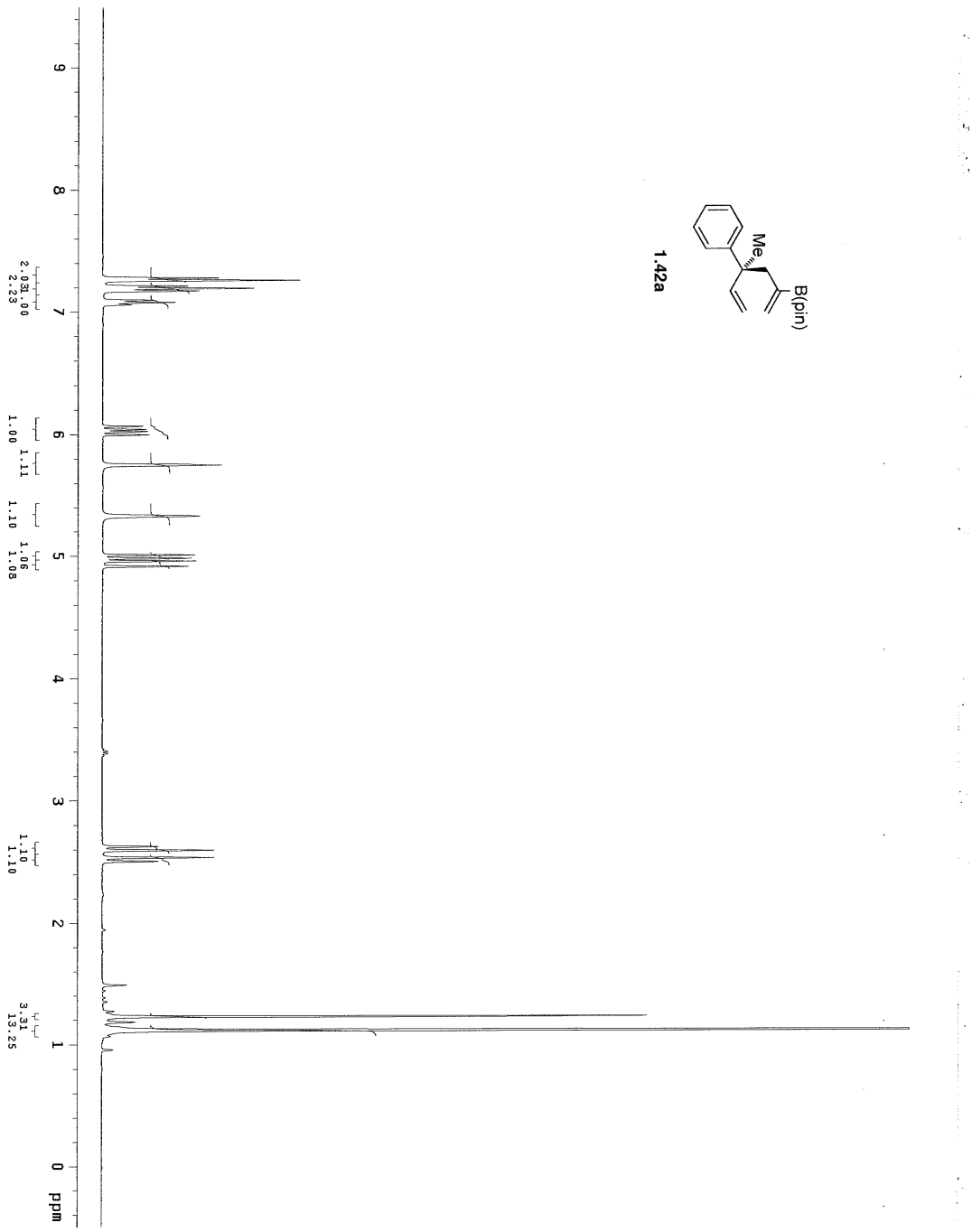

B(pin)
F
H

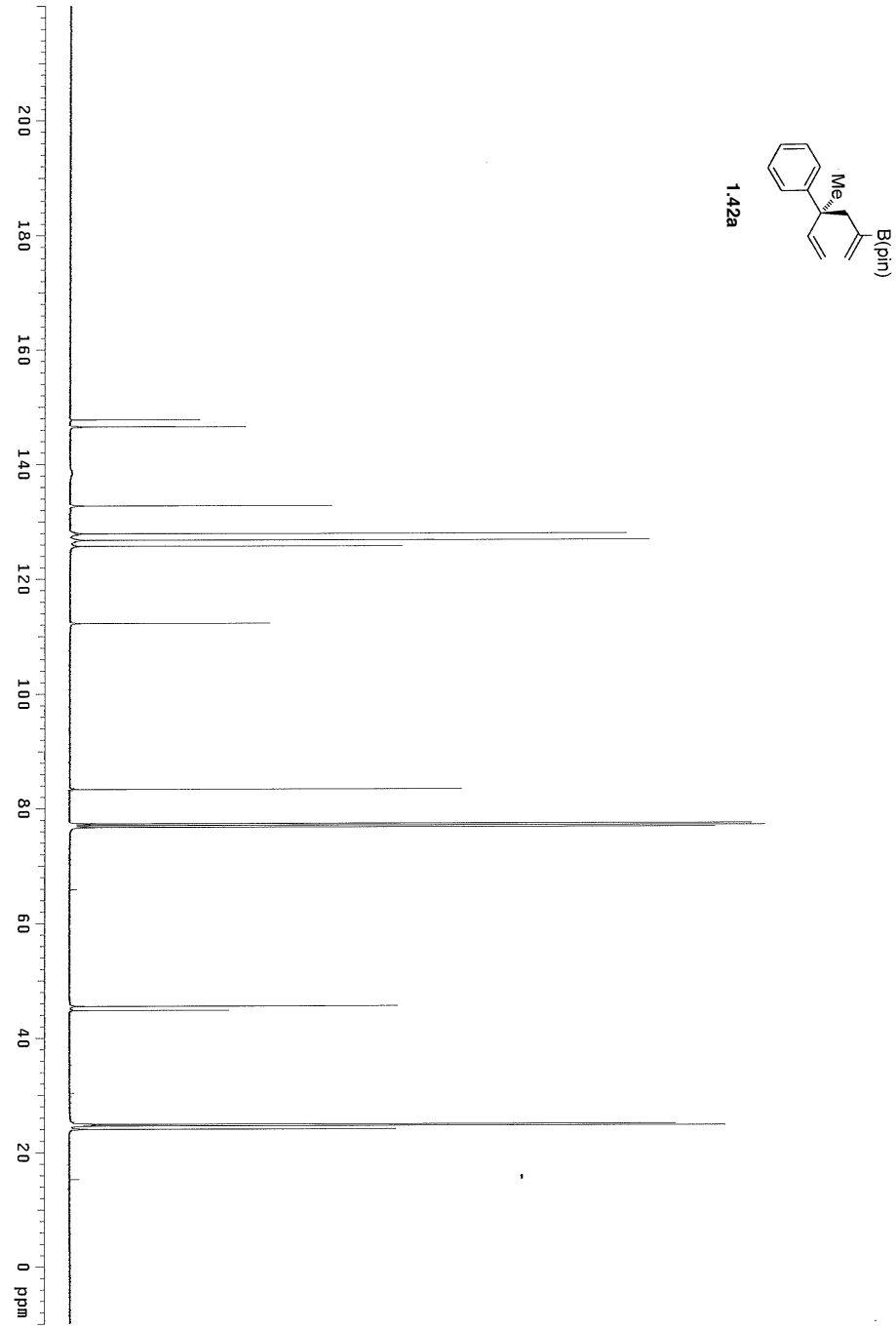
1.41c

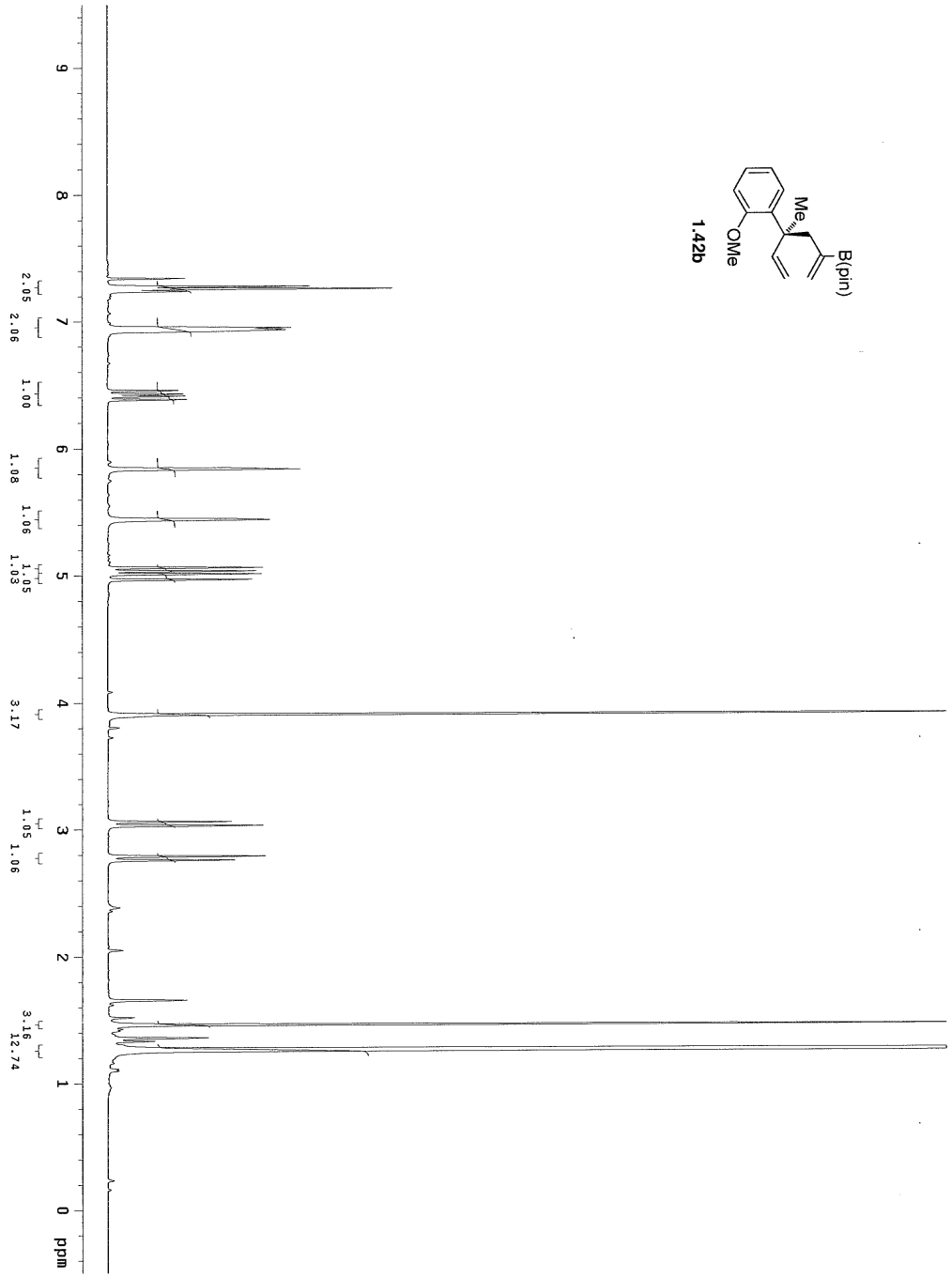
9
8
7
6
5
4
3
2
1
0
ppm
1.11
0.91
0.04
6.01
1.00
1.07
1.08
2.07
1.01
1.11
1.11
13.53

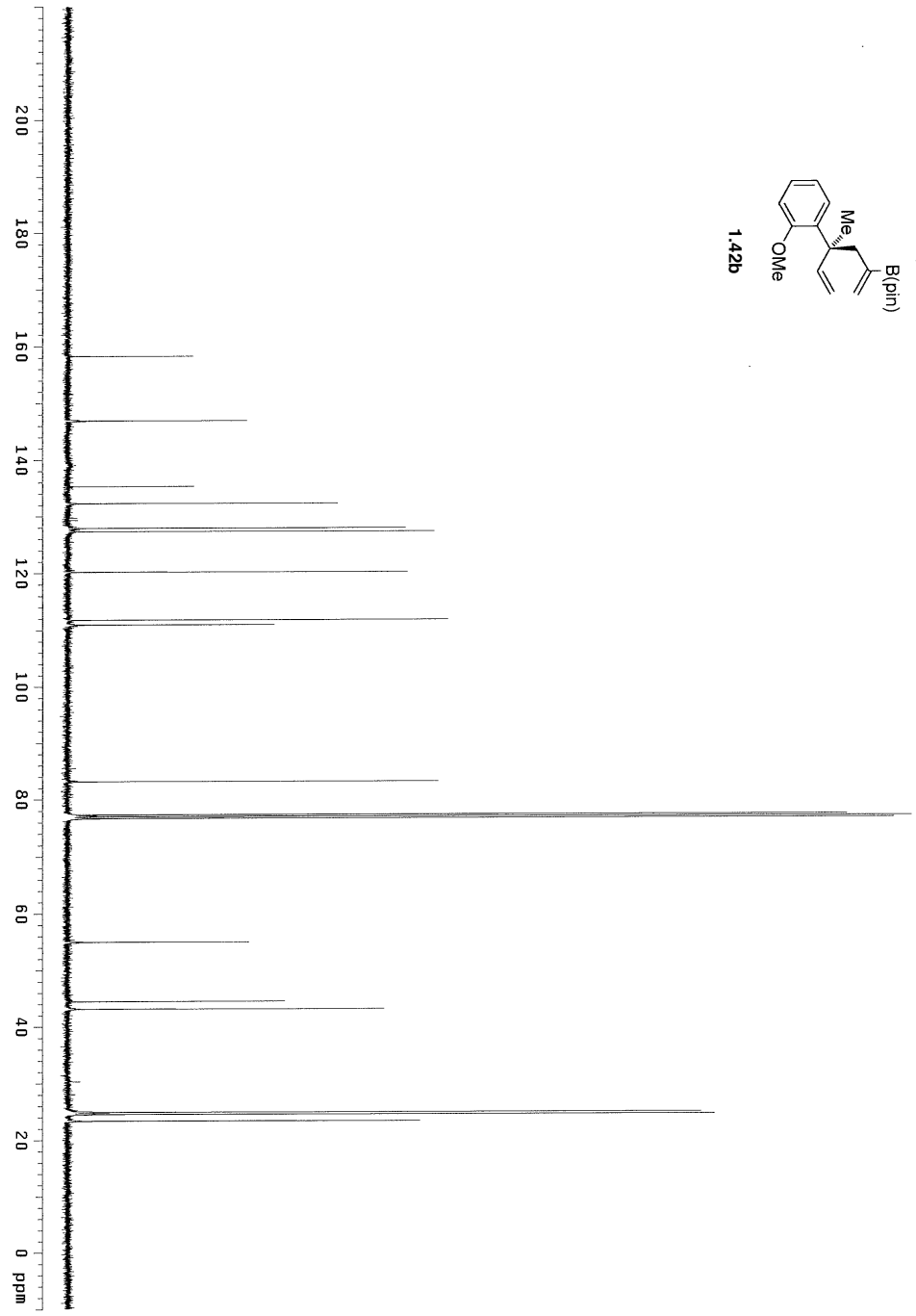


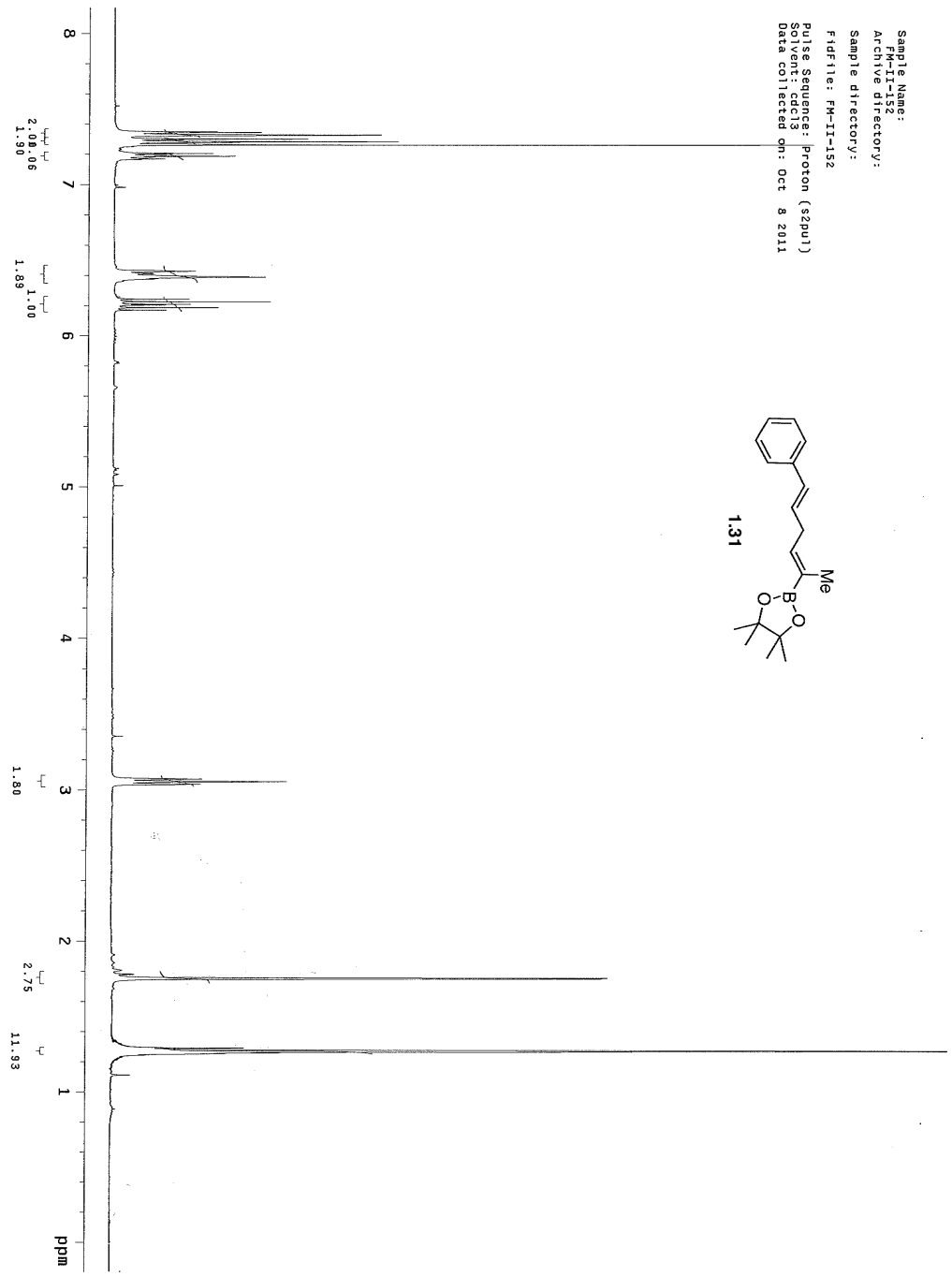
1.41c


B(pin)
Me
1.42a
9
8
7
6
5
4
3
2
1
0
ppm
2.03
2.23
1.00
1.00
1.11
1.10
1.06
1.08
1.10
1.10
3.31
13.25


Me
B(pin)
1.42a
200
180
160
140
120
100
80
60
40
20
0
ppm


B(pin)
Me
OMe
1.42b
9
8
7
6
5
4
3
2
1
0
ppm
2.05
2.06
1.00
1.08
1.06
1.05
1.03
3.17
1.05
1.06
3.16
12.74


Me
OMe
B(pin)
1.42b
200
180
160
140
120
100
80
60
40
20
0
ppm

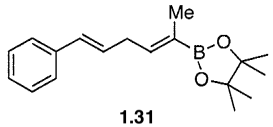

Sample Name:
FM-II-152
Archive directory:
Sample directory:
FidFile: FM-II-152
Pulse Sequence: proton (s2pul)
Solvent: cdcl3
Data collected on: Oct 8 2011
1.31
Me
B
O
O
8
7
6
5
4
3
2
1
ppm
2.08
1.90
1.00
1.89
1.80
2.75
11.93

Sample Name:
FM-II-152
Archive directory:

Sample directory:

FidFile: FM-II-152-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Oct 11 2011



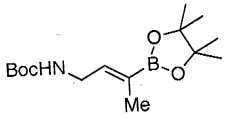
1.31

Sample Name:
FM-II-242
Archive directory:

Sample directory:

FidFile: FM-II-242

Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Nov 19 2011



1.43

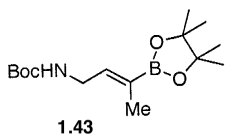
STANDARD 1H OBSERVE - profile

Sample Name:
FM-II-242-CNMR
Archive directory:

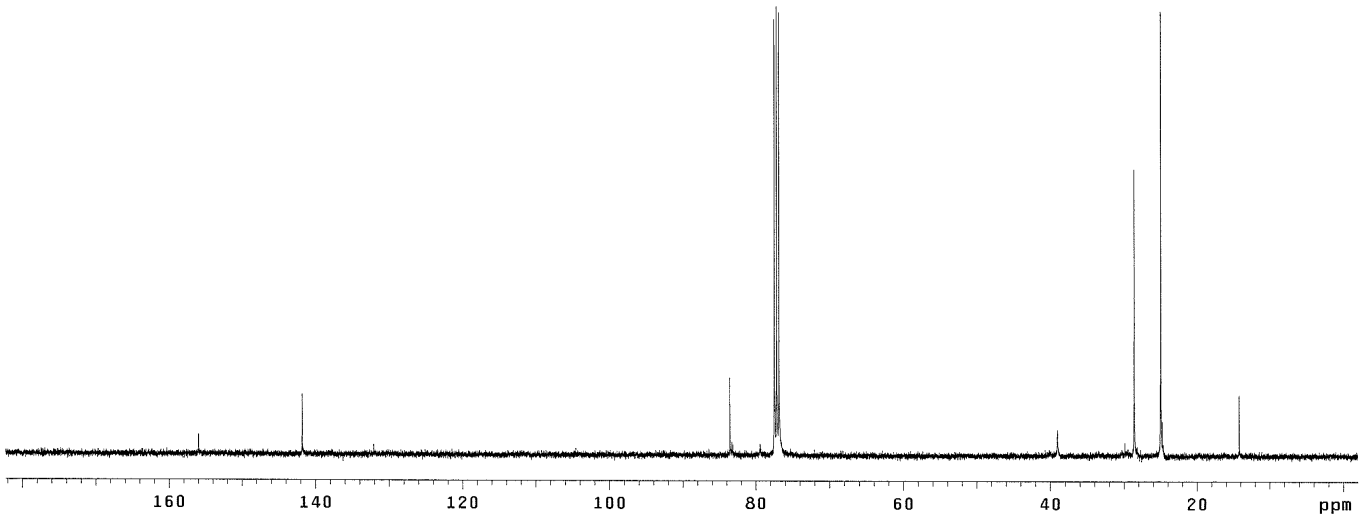
Sample directory:

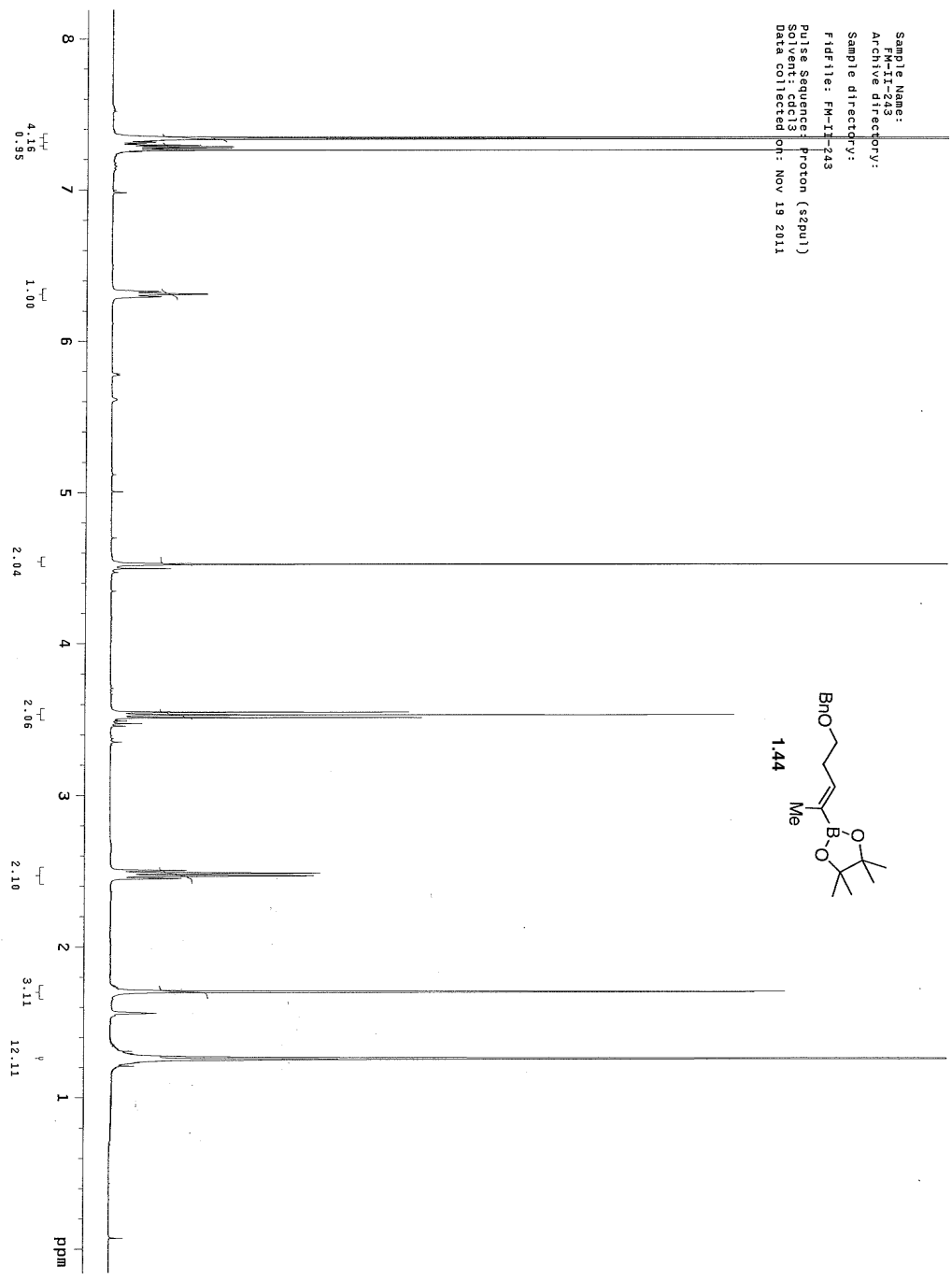
FidFile: FM-II-242-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Jan 17 2012



1.43



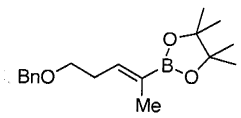

Sample Name:
FM-II-243
Archive directory:
Sample directory:
FidFile: FM-II-243
Pulse Sequence: proton (s2pul)
Solvent: cdcl3
Data collected on: Nov 19 2011
BnO
Me
B
O
O
1.44
8
7
6
5
4
3
2
1
ppm
4.16
0.95
1.00
2.04
2.06
2.10
3.11
12.11

Sample Name:
FM-II-243-CNMR
Archive directory:

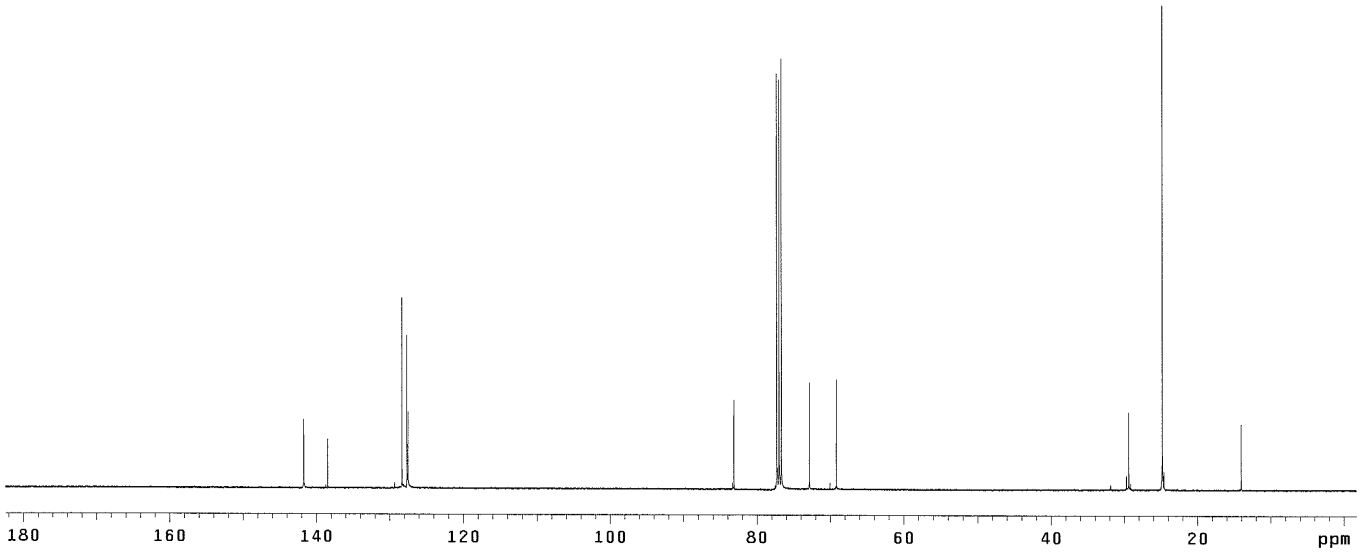
Sample directory:

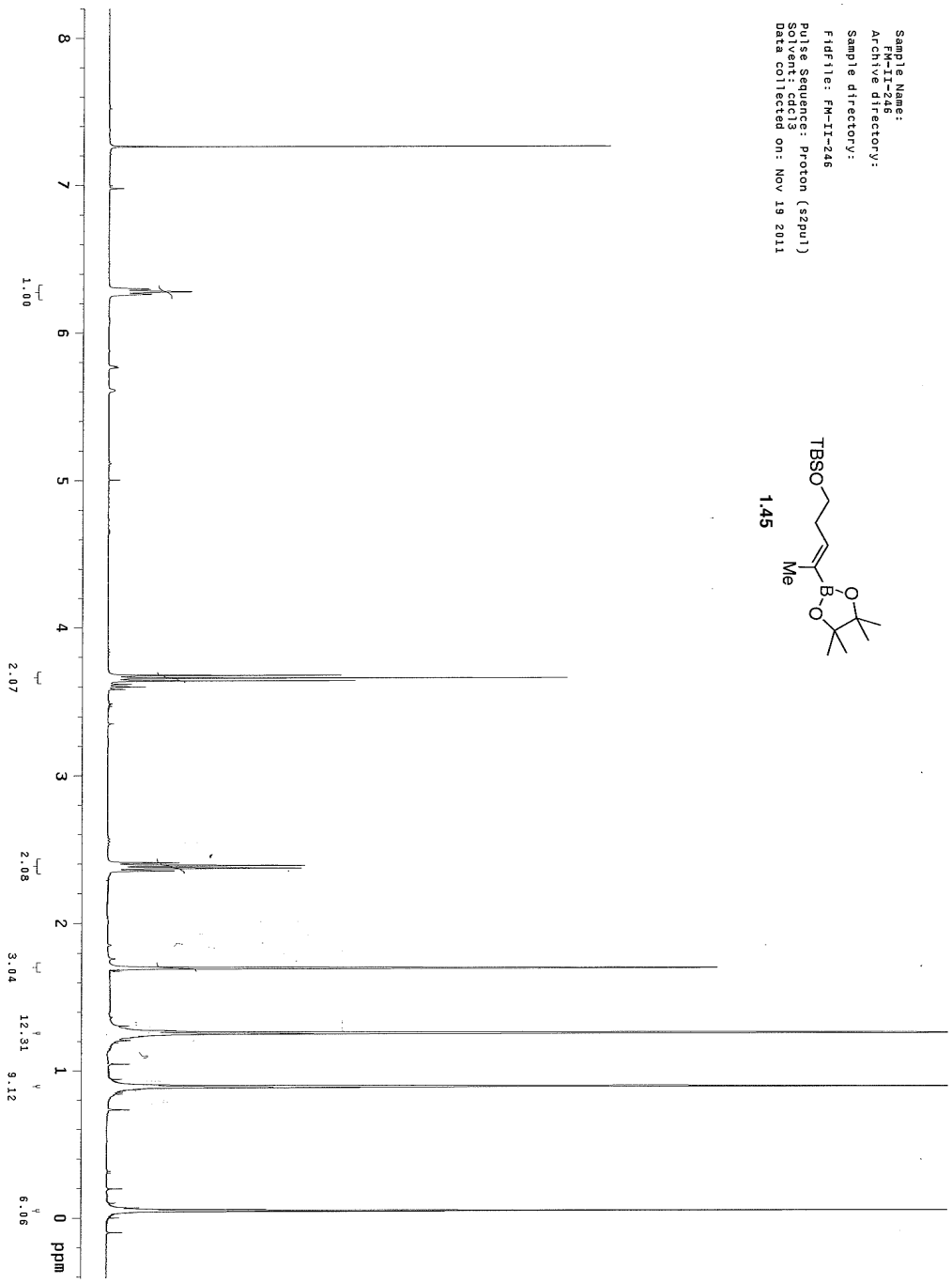
FidFile: FM-II-243-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Jan 16 2012



1.44




Sample Name:
FM-II-246
Archive directory:
Sample directory:
FidFile: FM-II-246
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Nov 19 2011
TBSO
Me
B
O
O
1.45
8
7
6
5
4
3
2
1
0 ppm
1.00
2.07
2.08
3.04
12.31
9.12
6.06

STANDARD 1H OBSERVE - profile

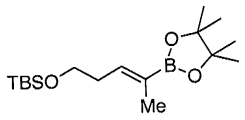
Sample Name:

Archive directory:

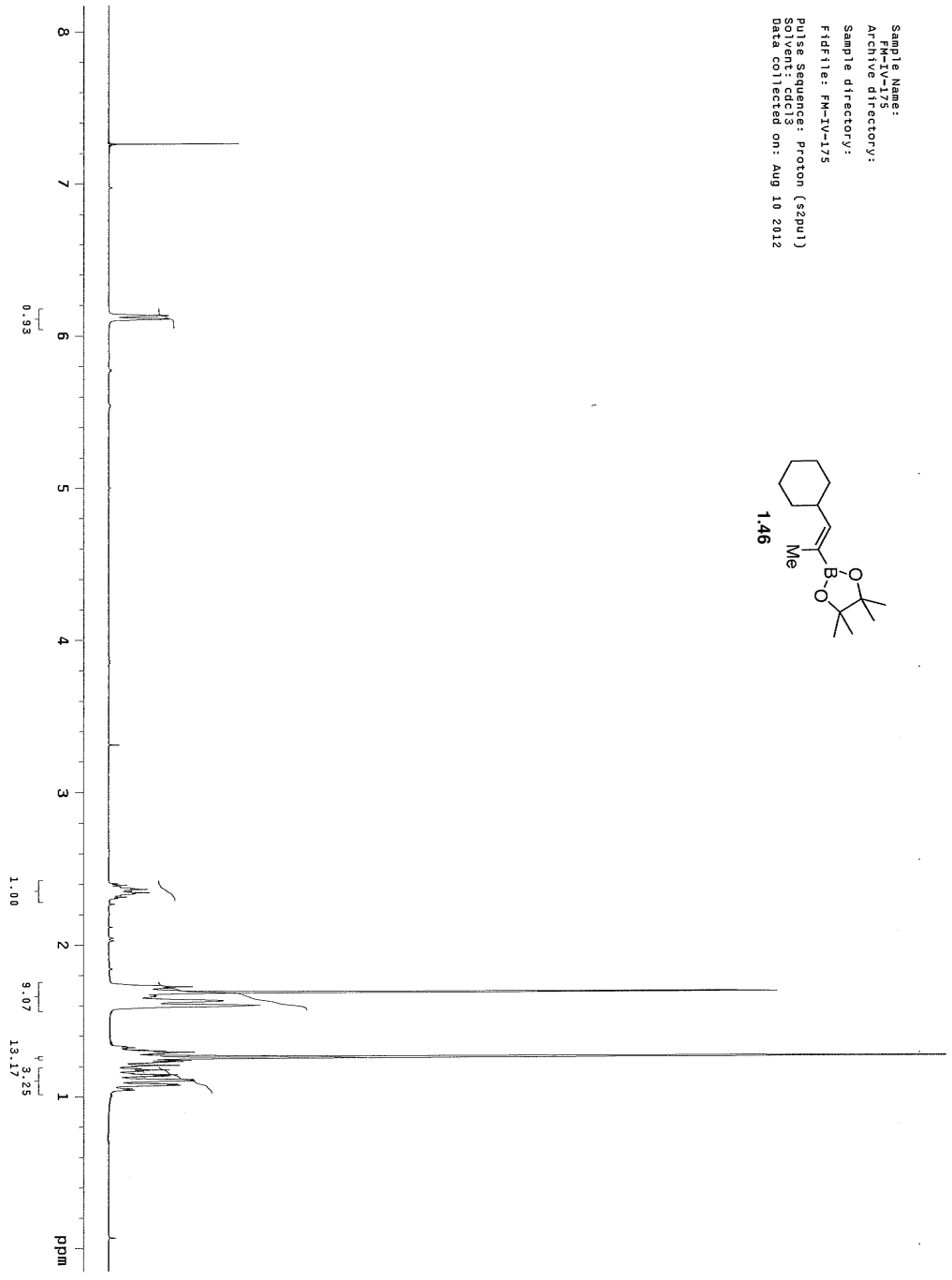
Sample directory:

FidFile: FM-II-246-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: d2o
Data collected on: Jan 12 2012



1.45

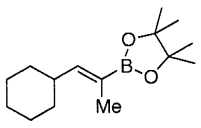

Sample Name:
FM-IV-175
Archive directory:
Sample directory:
FidFile: FM-IV-175
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Aug 10 2012
1.46
Me
B
O
O
8
7
6
5
4
3
2
1
ppm
0.93
1.00
9.07
3.25
13.17

Sample Name:
FM-IV-175
Archive directory:

Sample directory:

FidFile: FM-IV-175-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Aug 10 2012



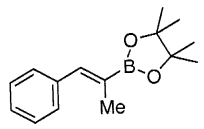
1.46

Sample Name:
FM-IV-128
Archive directory:

Sample directory:

FidFile: FM-IV-128

Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Jul 18 2012



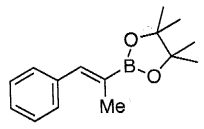
1.47

Sample Name:
FM-IV-120
Archive directory:

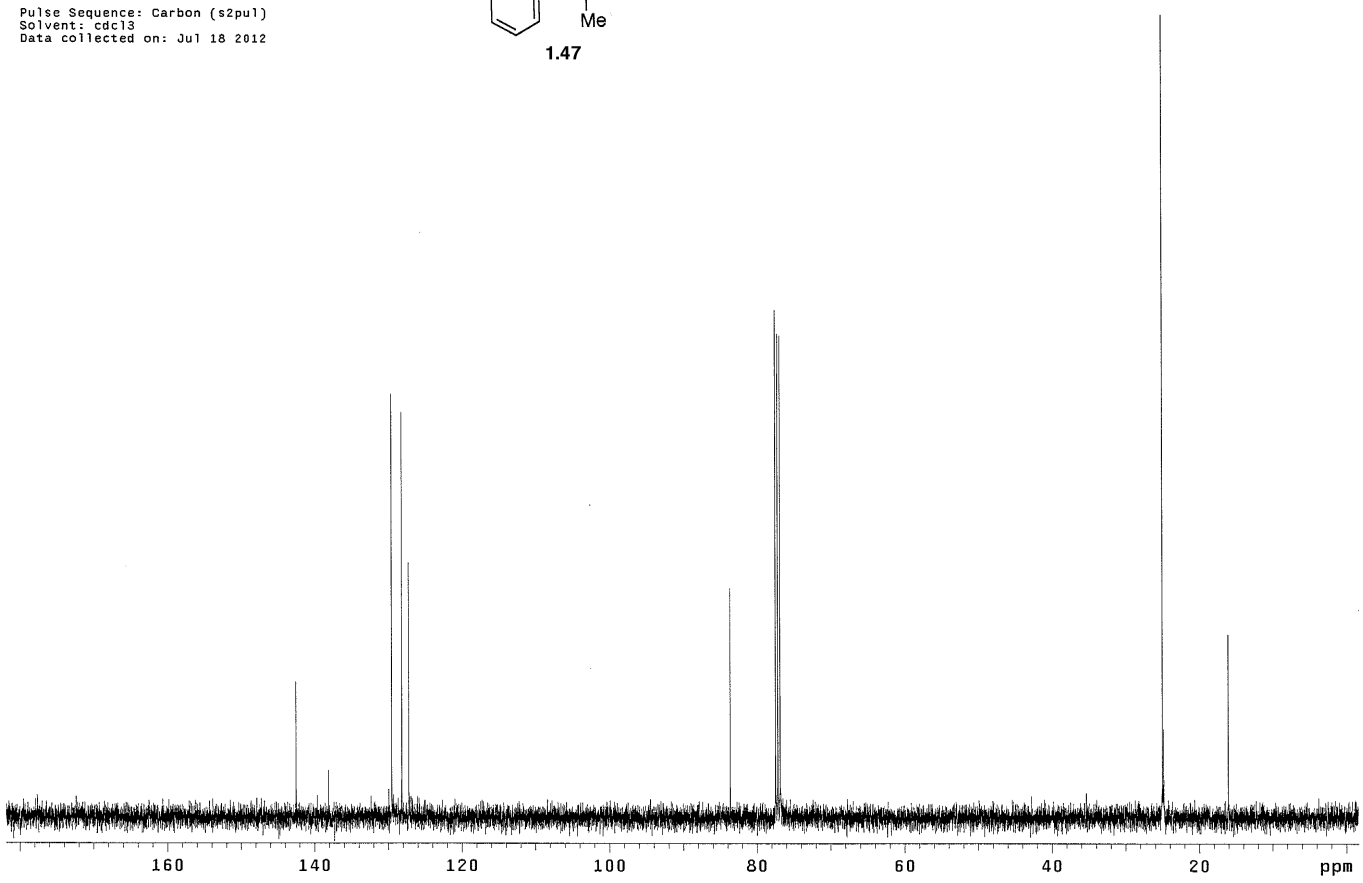
Sample directory:

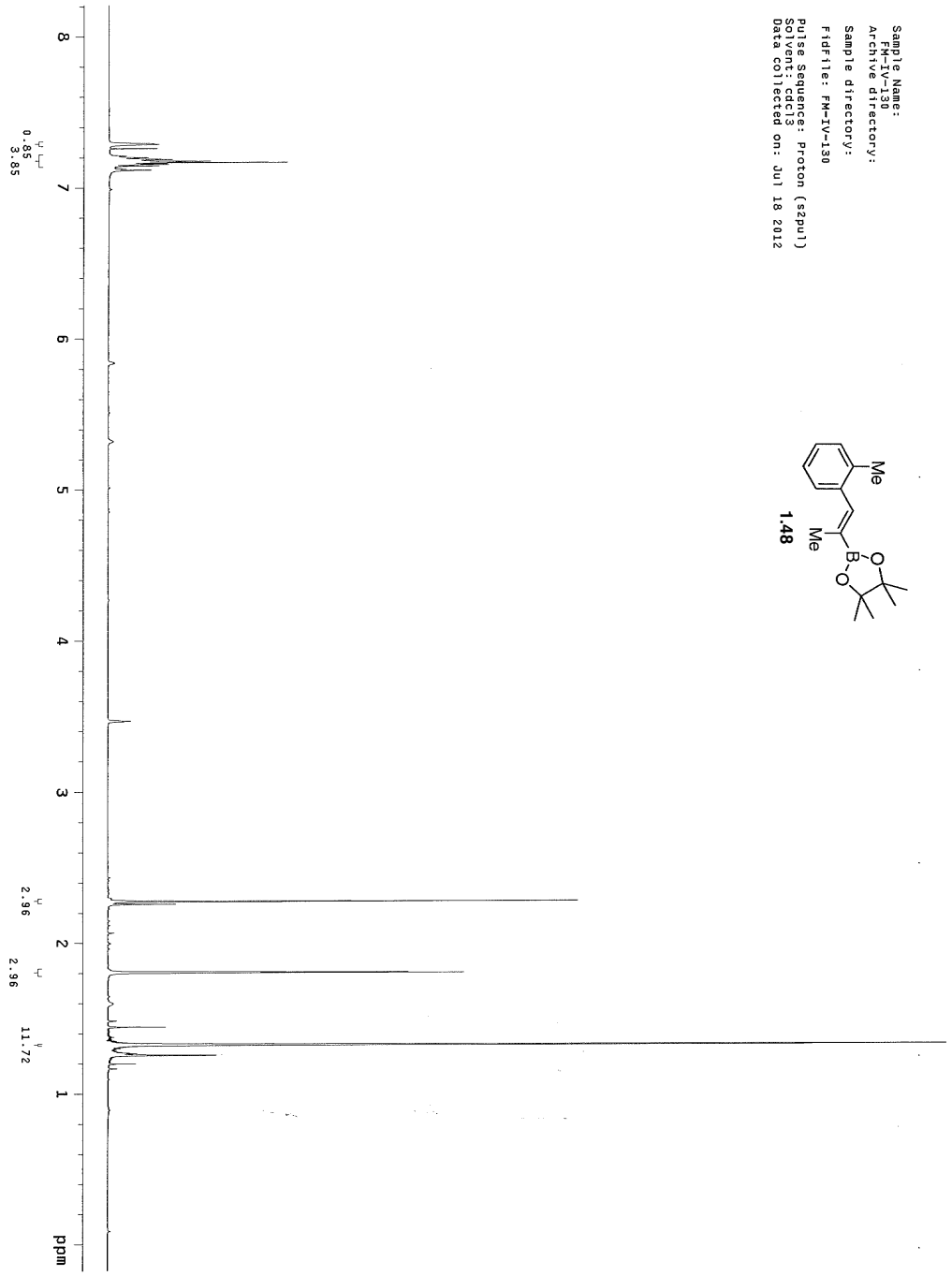
FidFile: FM-IV-128-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Jul 18 2012



1.47



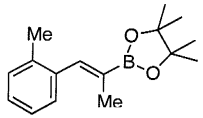

Sample Name:
FM-IV-130
Archive directory:
Sample directory:
FidFile: FM-IV-130
Pulse Sequence: proton (s2pul)
Solvent: cdcl3
Data collected on: Jul 18 2012
Me
Me
B
O
O
1.48
8
7
6
5
4
3
2
1
ppm
0.85
3.85
2.96
2.96
11.72

Sample Name:
FM-IV-129
Archive directory:

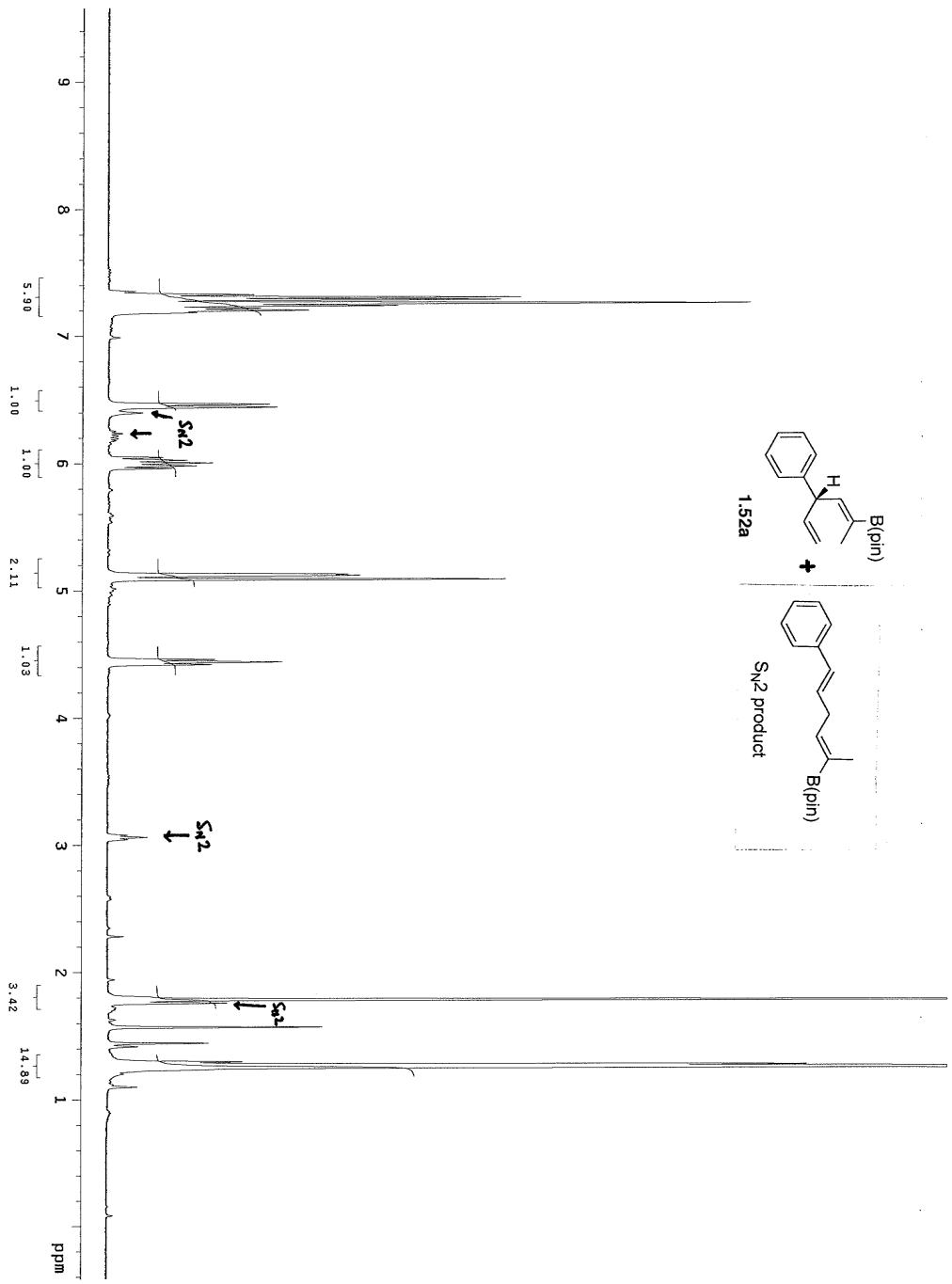
Sample directory:

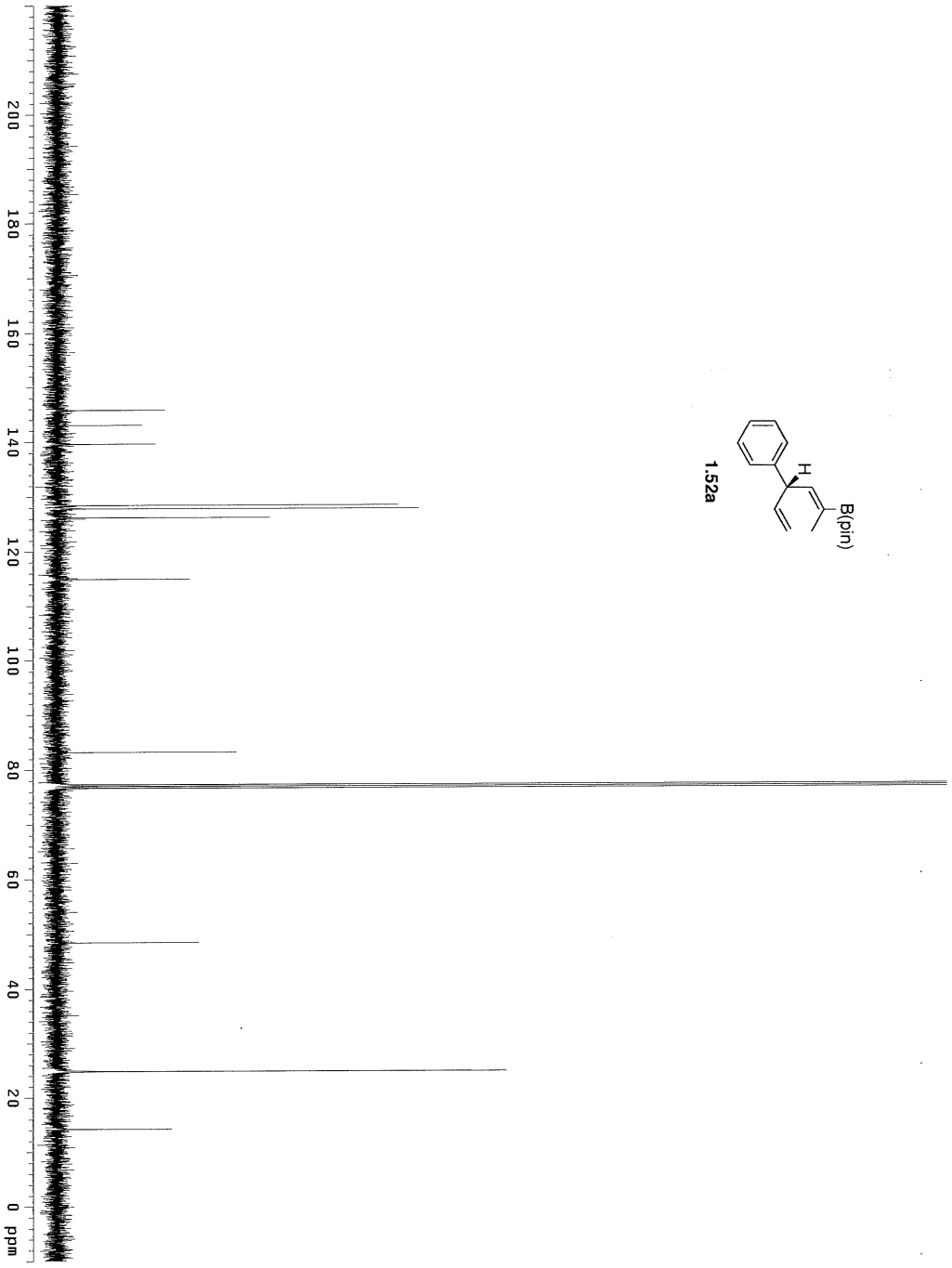
FidFile: FM-IV-130-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Jul 18 2012

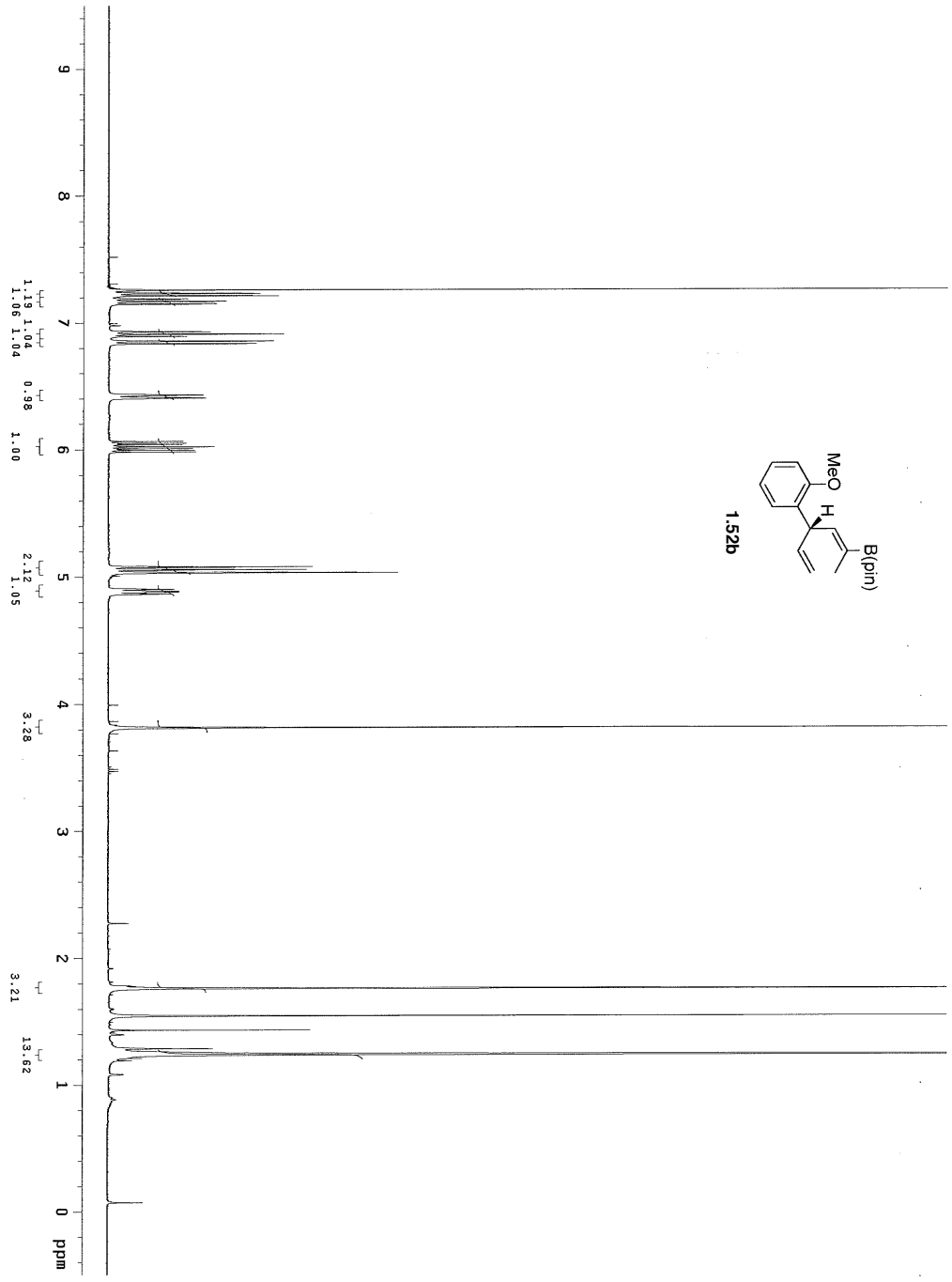


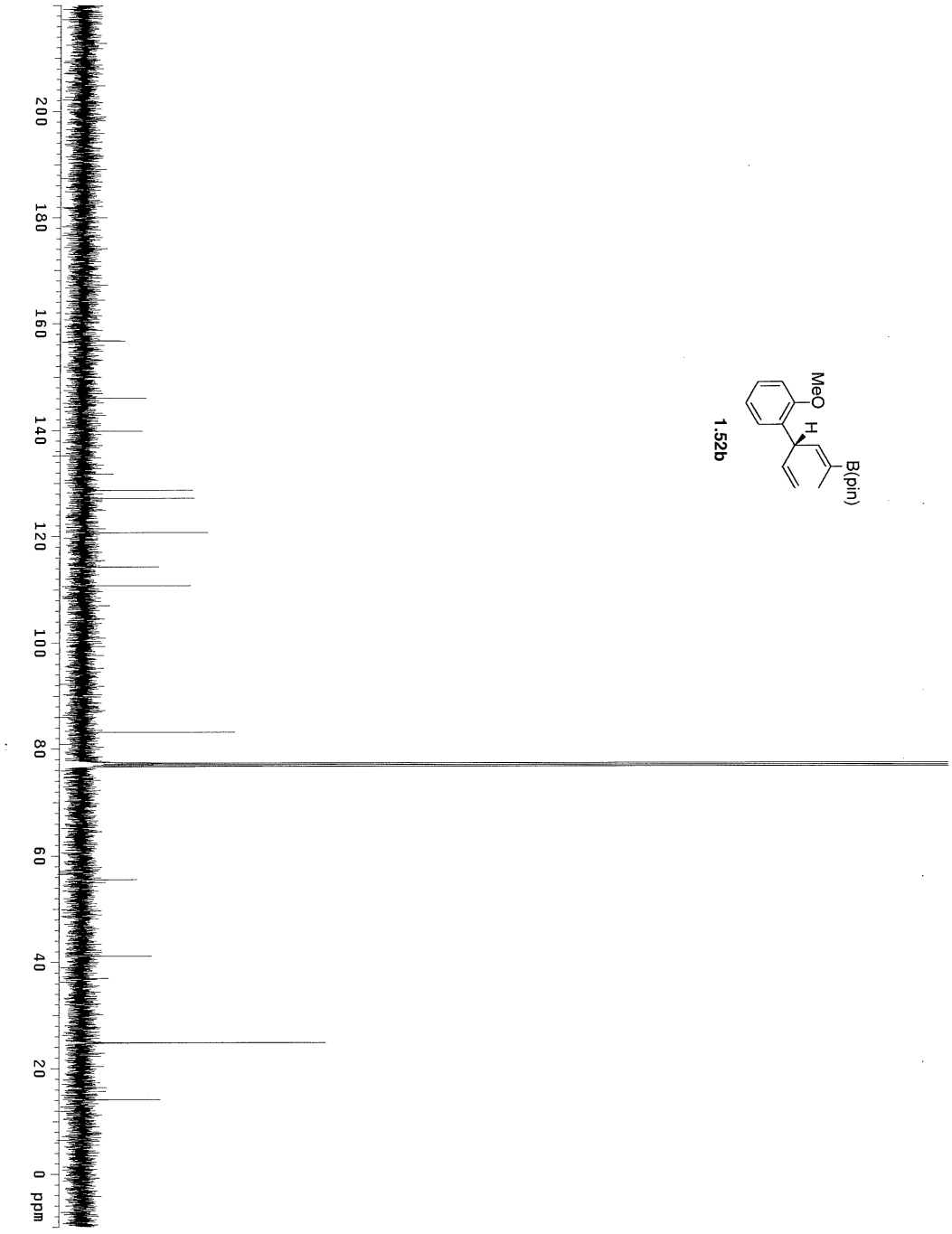
1.48

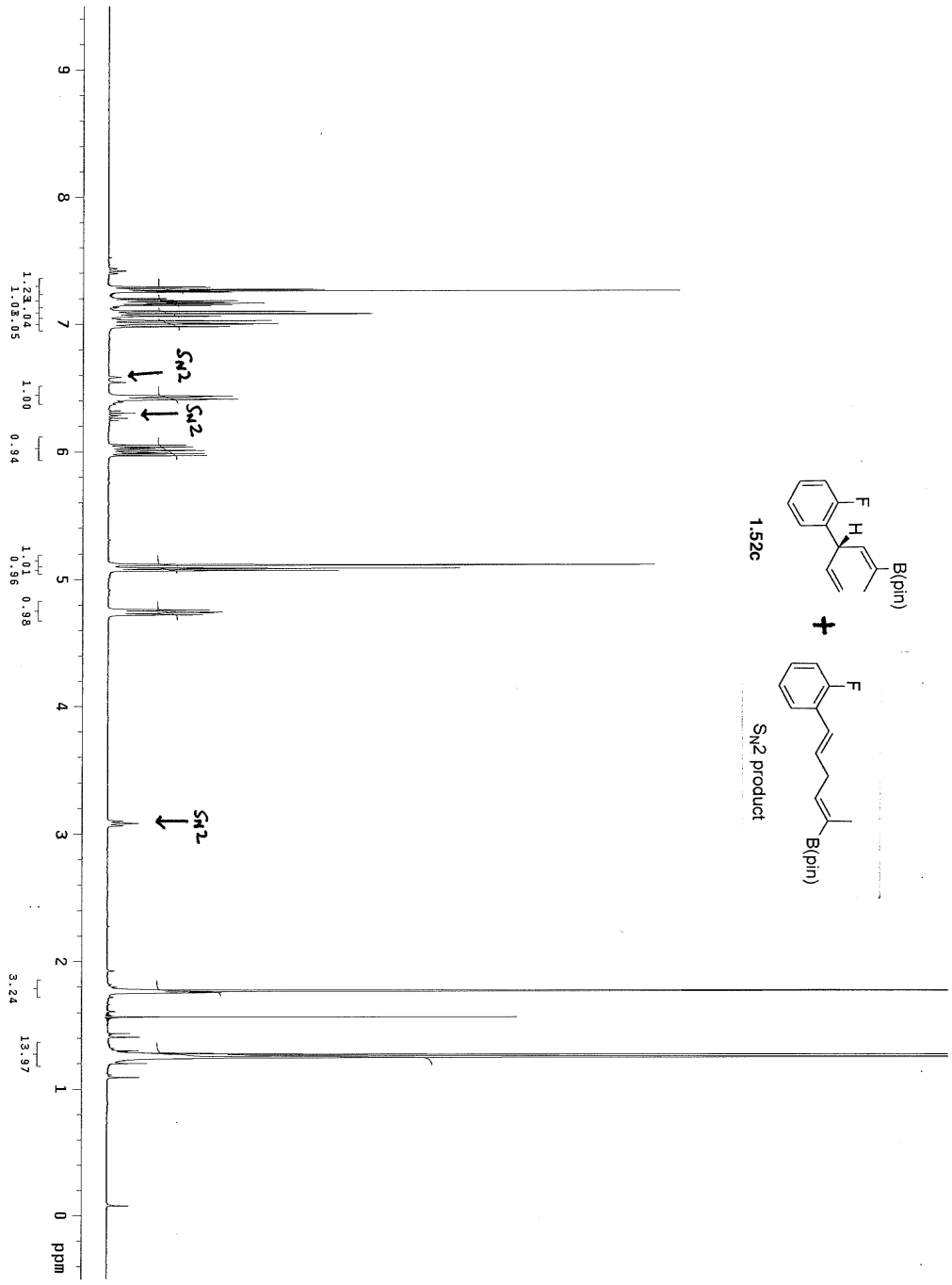

B(pin)
H
1.52a
+
B(pin)
SN2 product
SN2
SN2
SN2
5.90
1.00
1.00
2.11
1.03
3.42
14.89
ppm

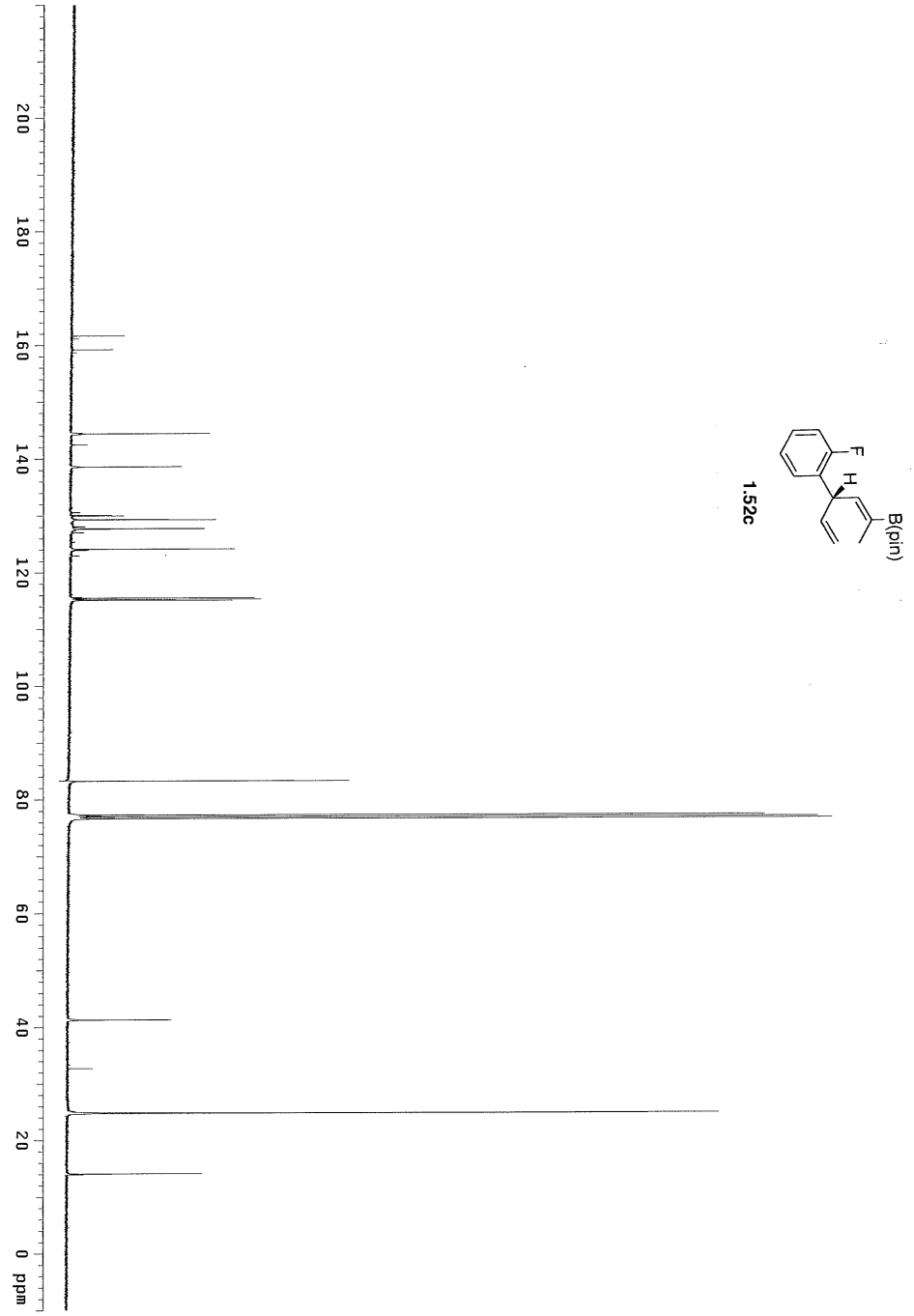


1.52a

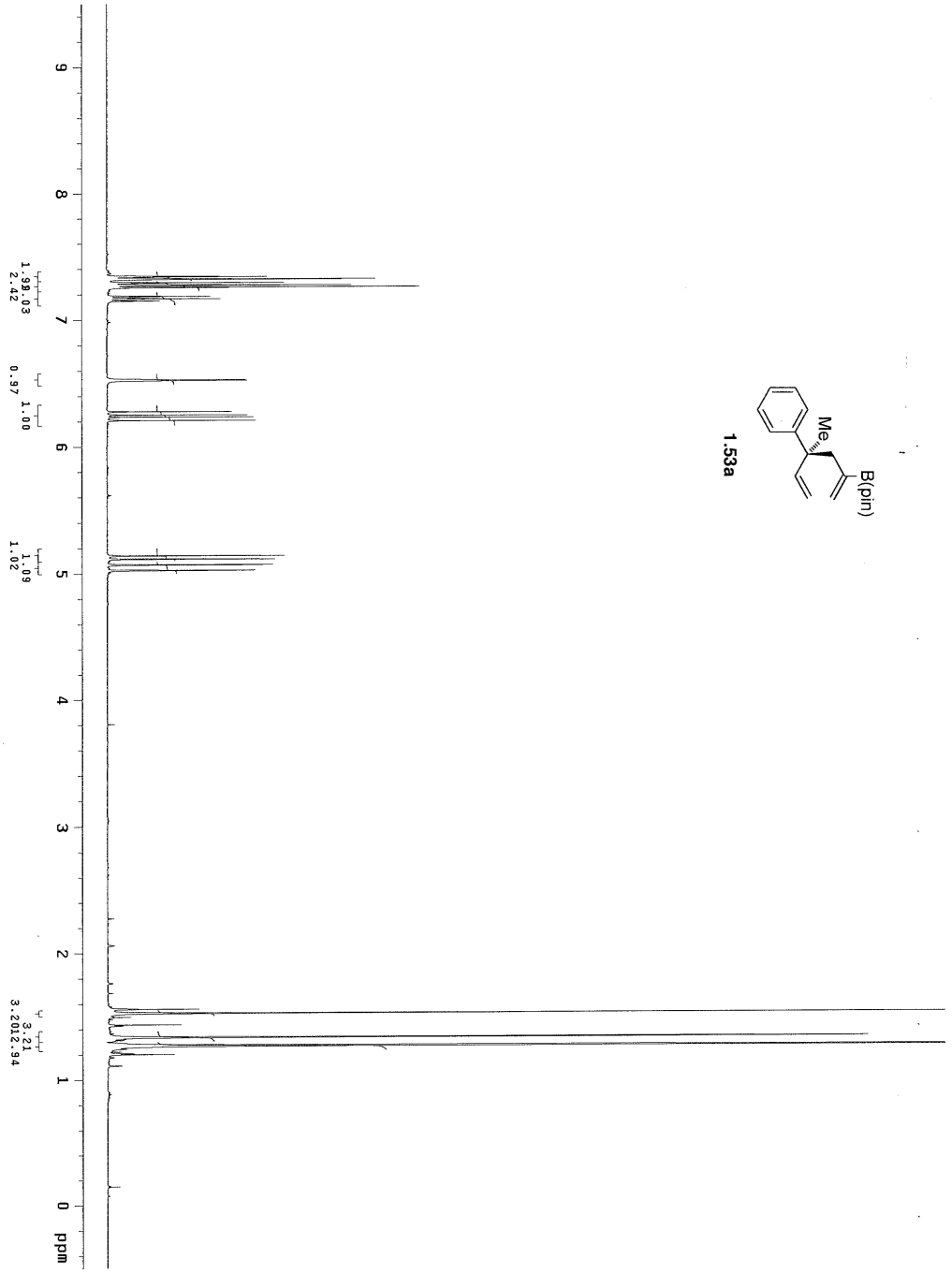

MeO
H
B(pin)
1.52b
9
8
7
6
5
4
3
2
1
0
ppm
1.19 1.04
1.06 1.04
0.98
1.00
2.12
1.05
3.28
3.21
13.62

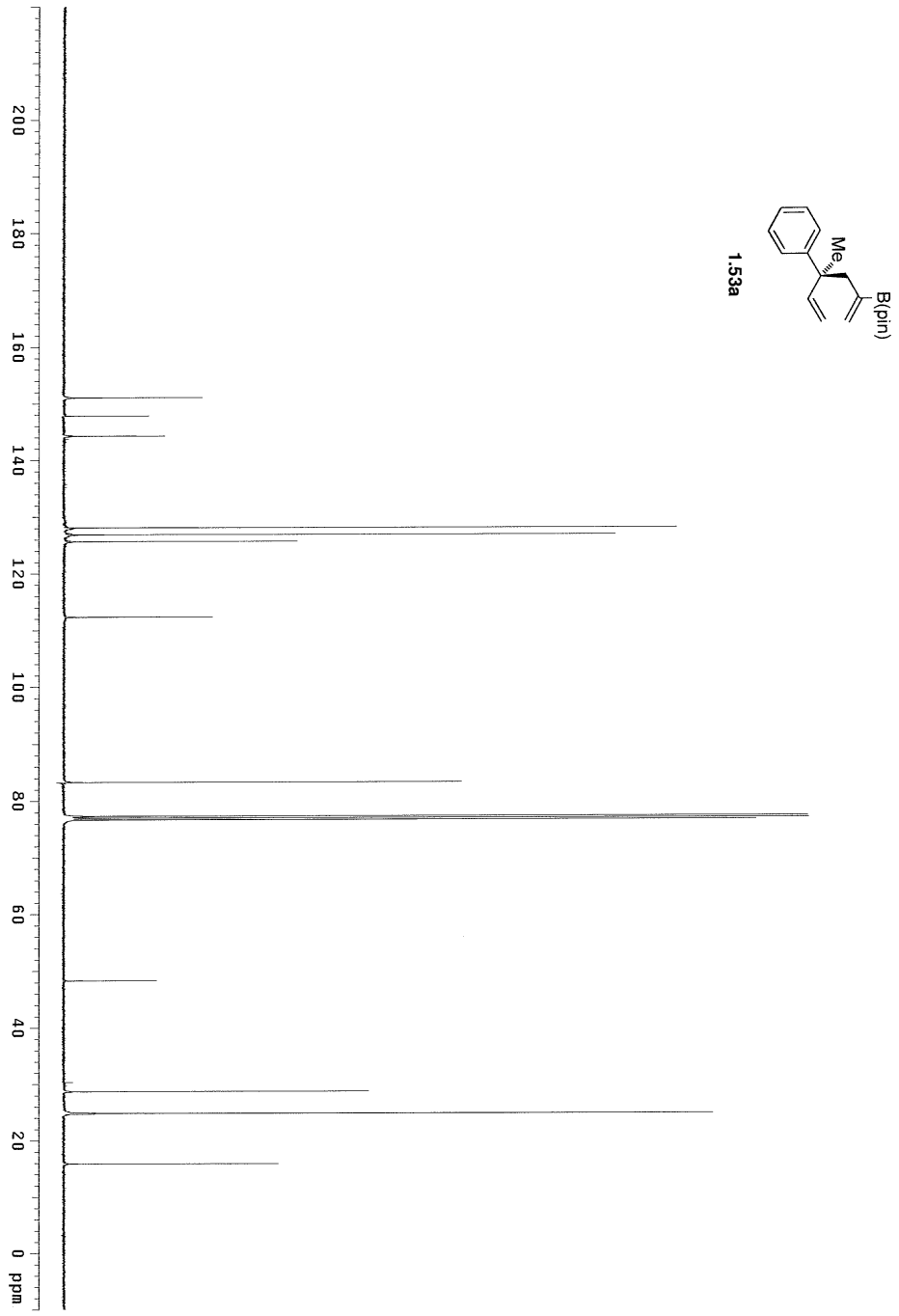

MeO
H
B(pin)
1.52b
200
180
160
140
120
100
80
60
40
20
0 ppm

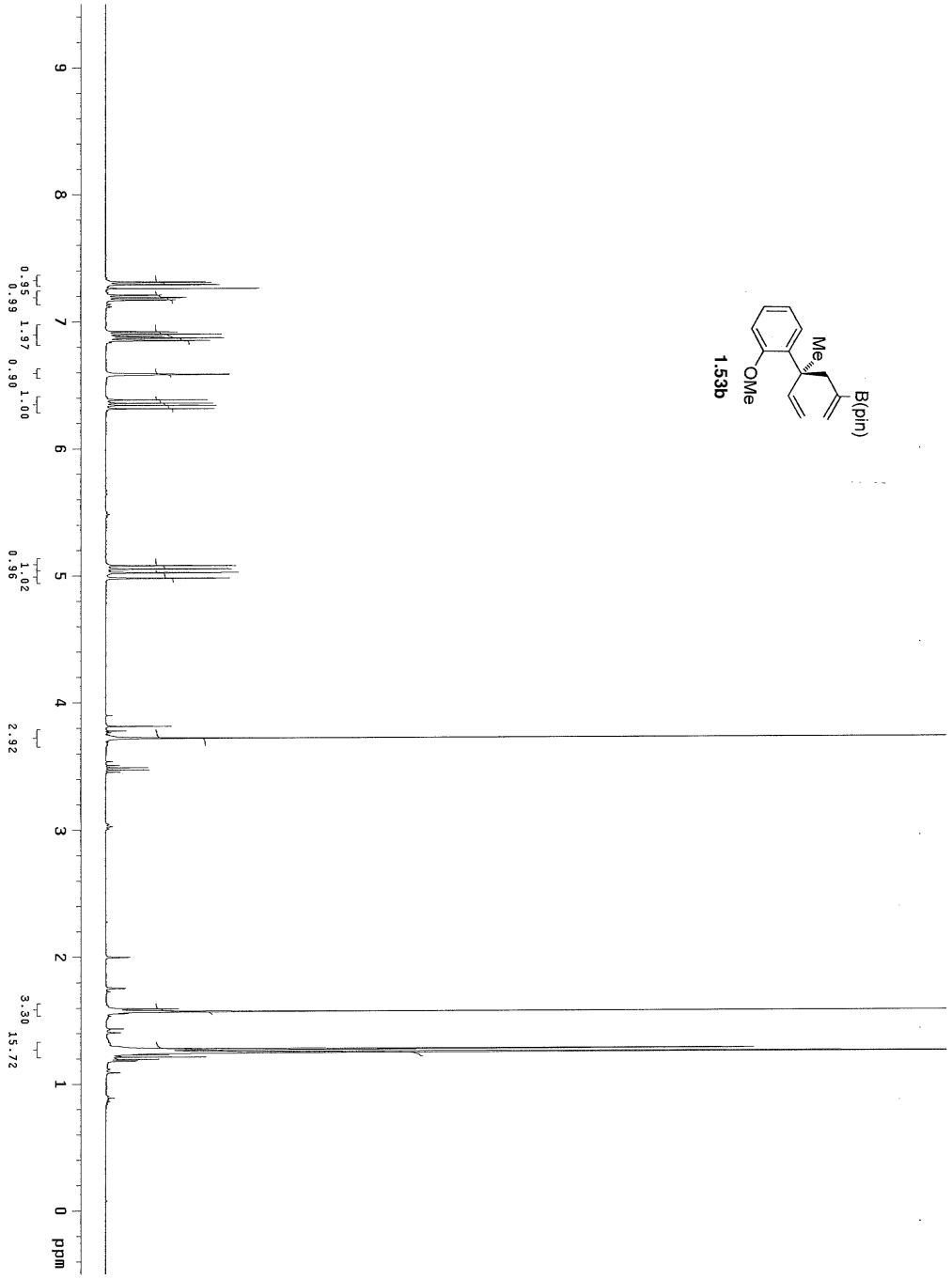

B(pin)
F
H
1.52c
+
F
B(pin)
SN2 product
SN2
SN2
SN2
1.23
1.03
1.00
0.94
1.01
0.96
0.98
3.24
13.97
ppm

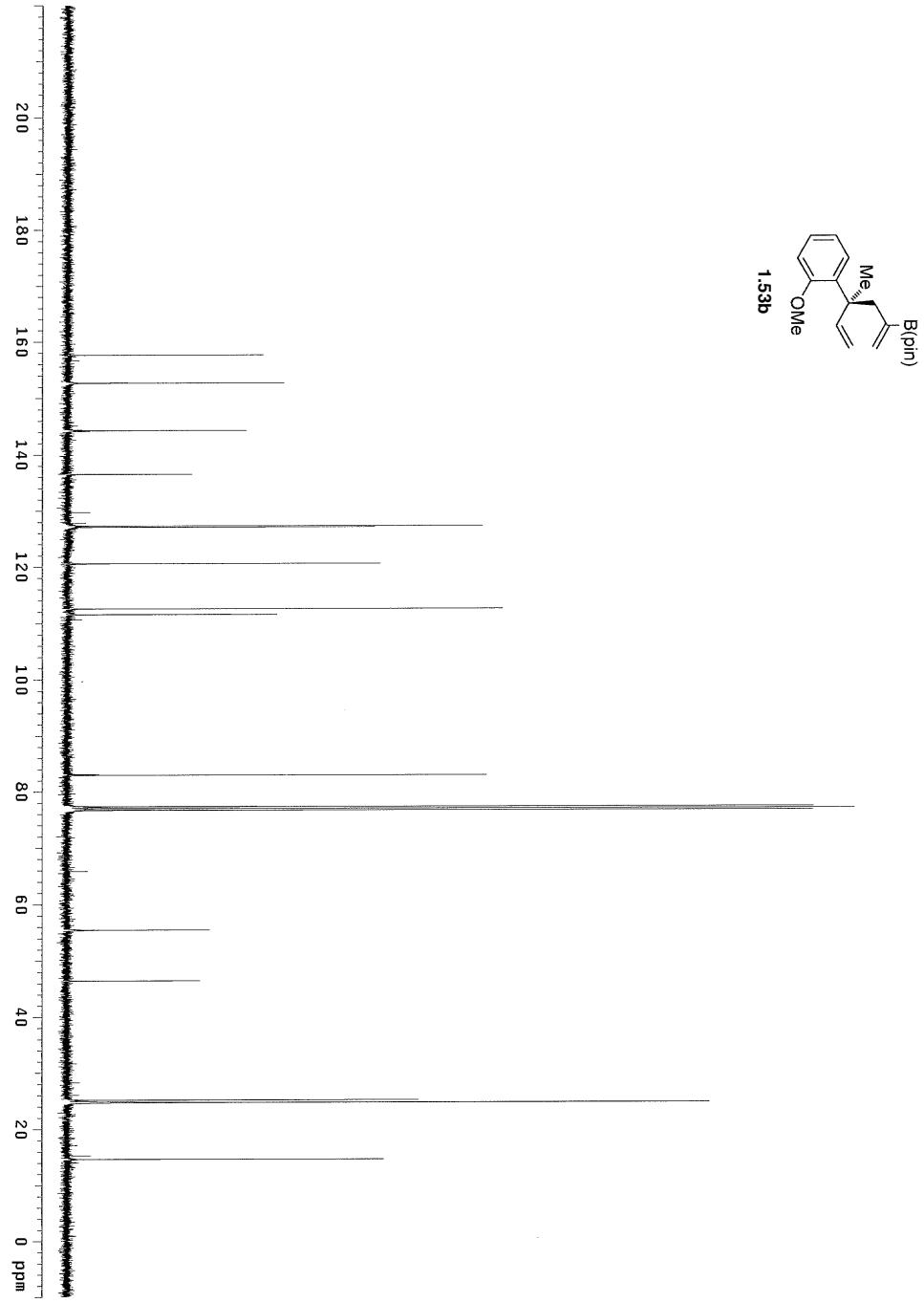


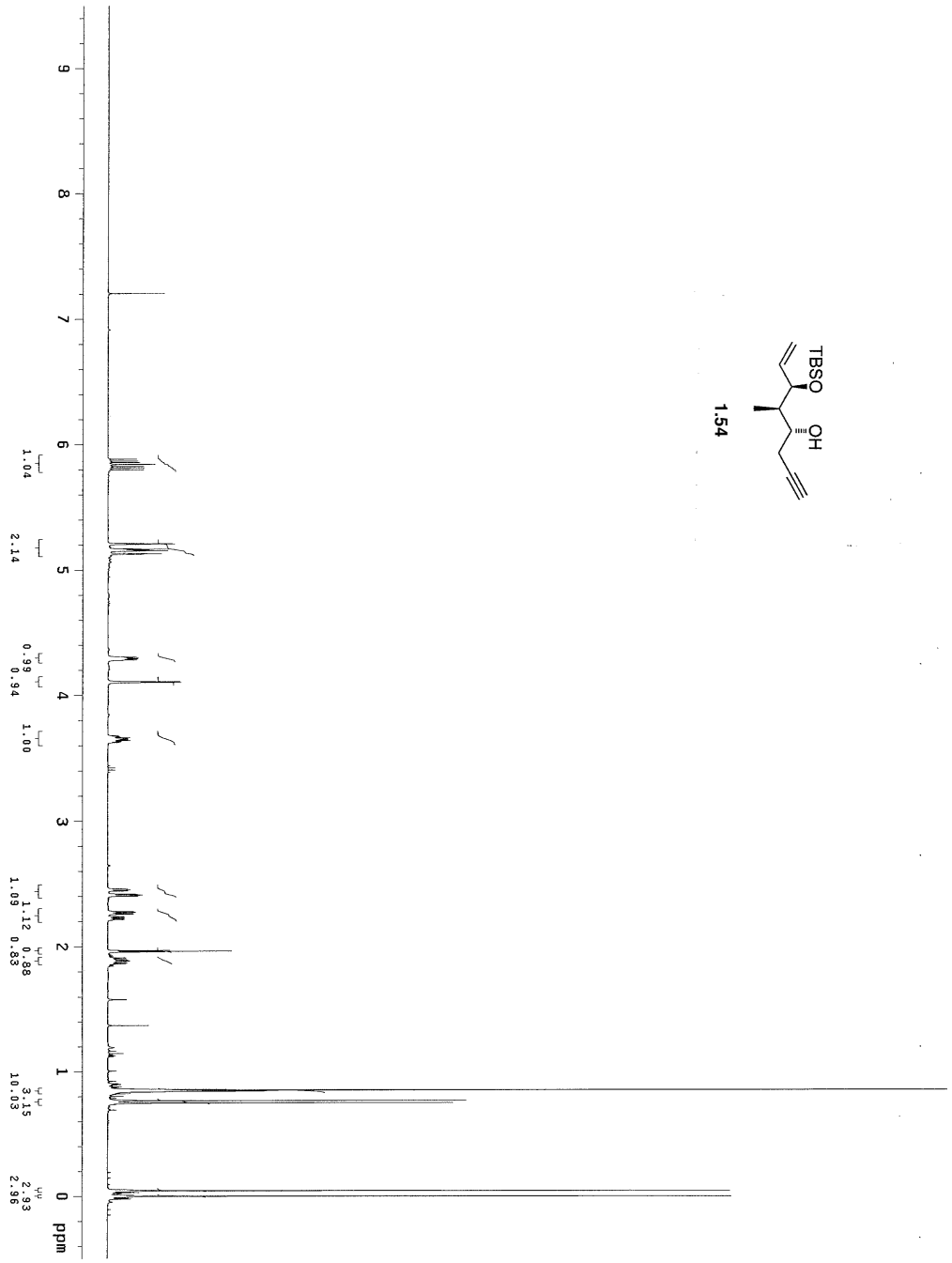
1.52c

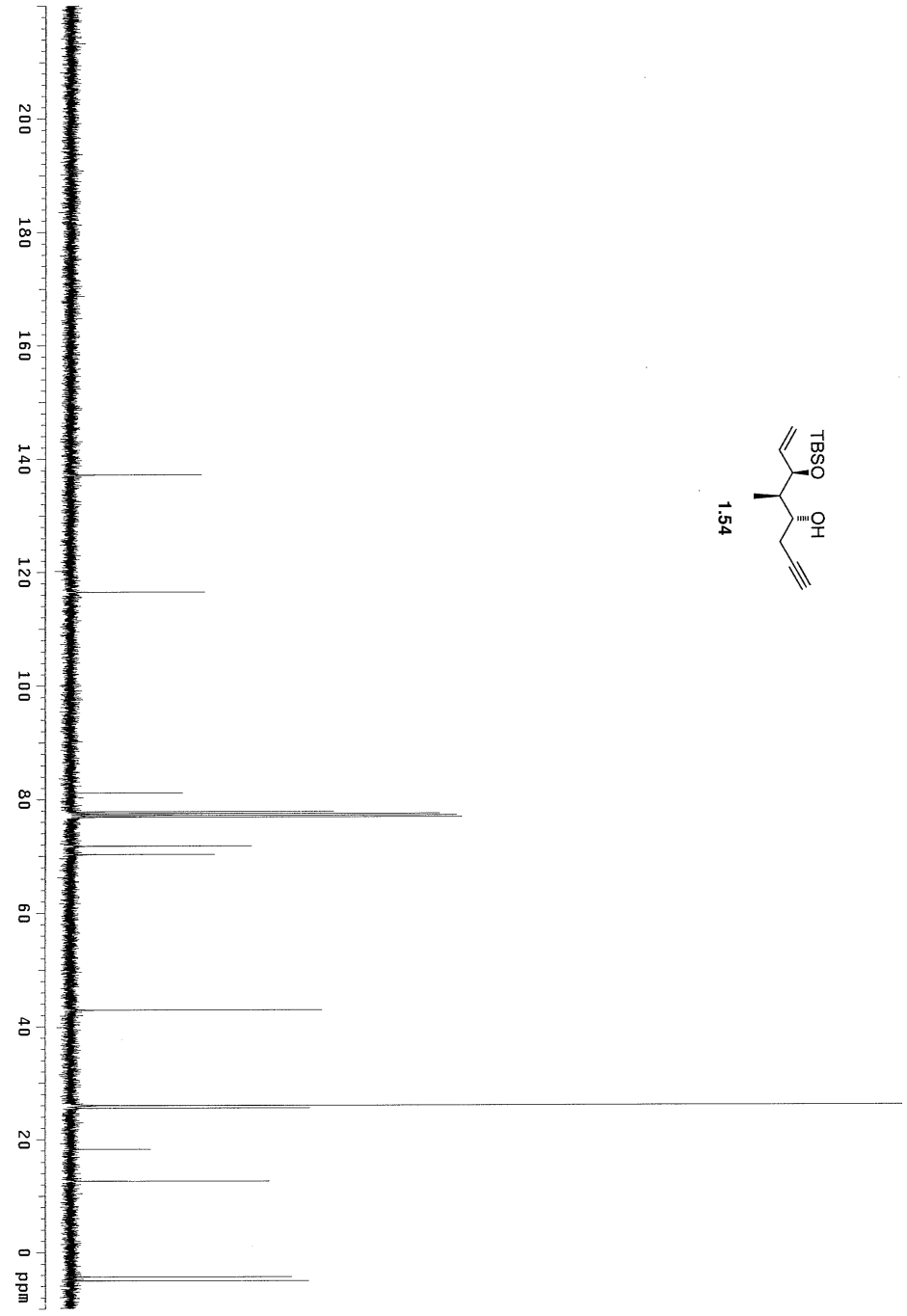

B(pin)
Me
1.53a
9
8
7
6
5
4
3
2
1
0
ppm
1.98
1.03
2.42
0.97
1.00
1.09
1.02
3.21
3.20
12.94

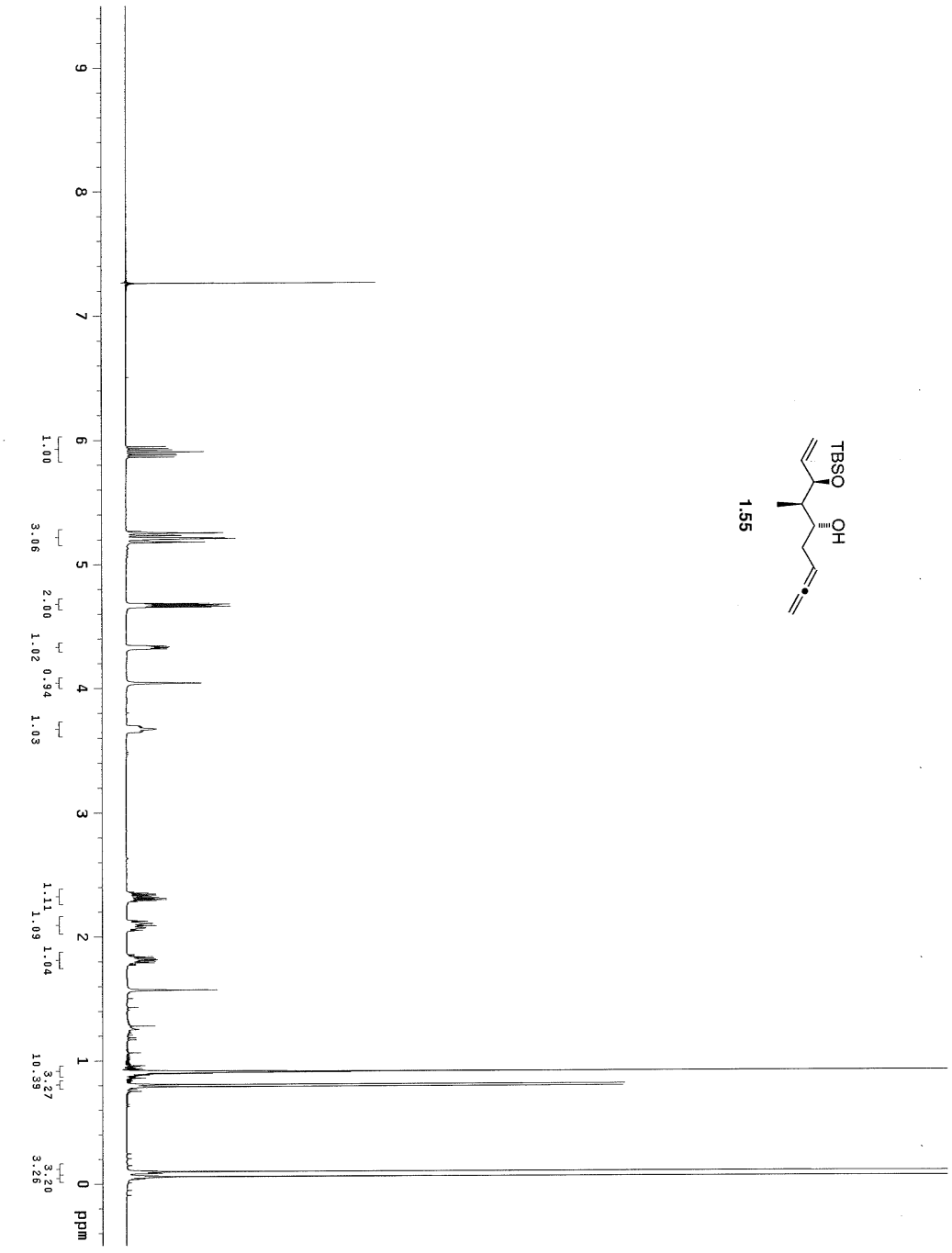

200
180
160
140
120
100
80
60
40
20
0 ppm
Me
B(pin)
1.53a

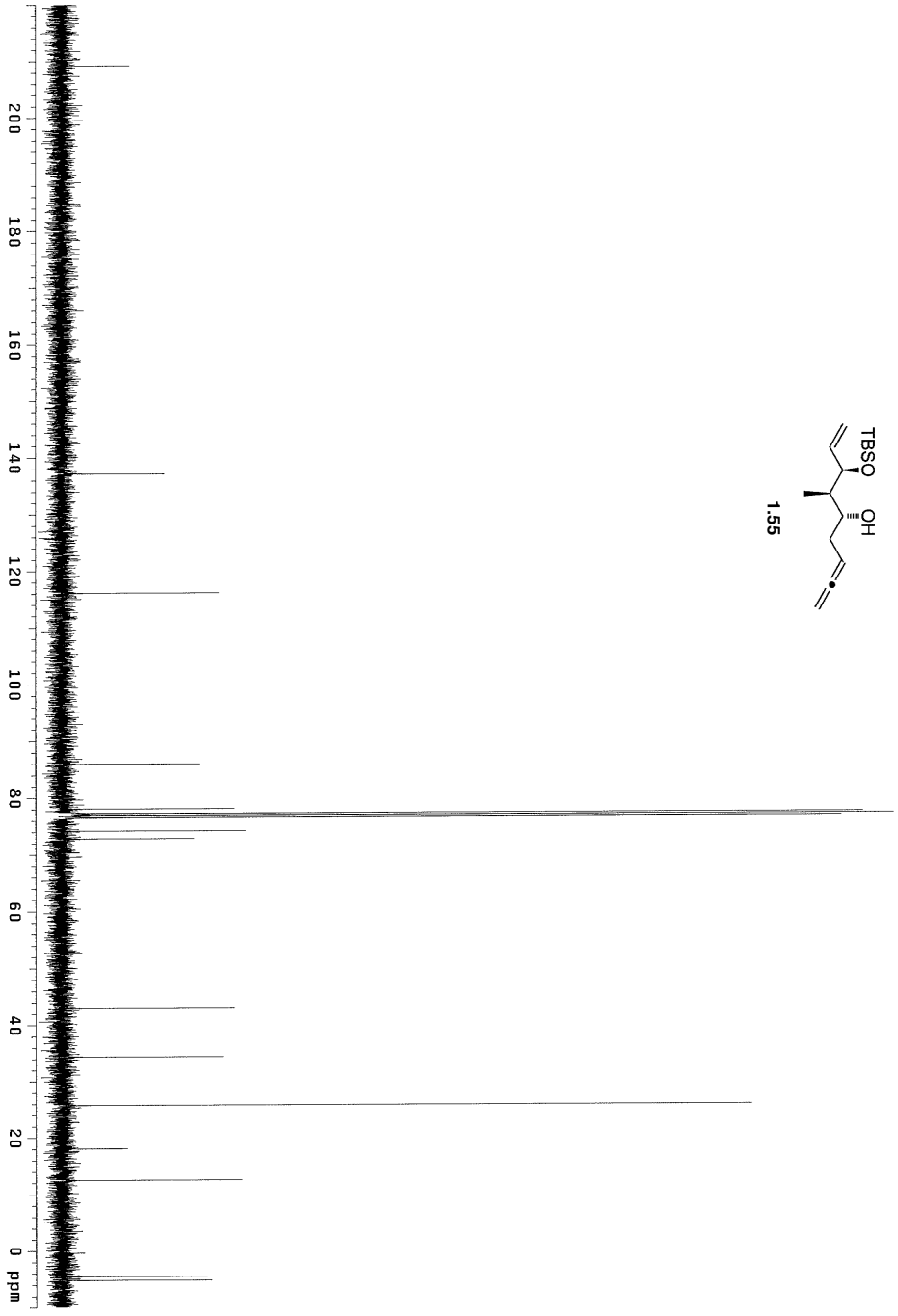

B(pin)
Me
OMe
1.53b
ppm

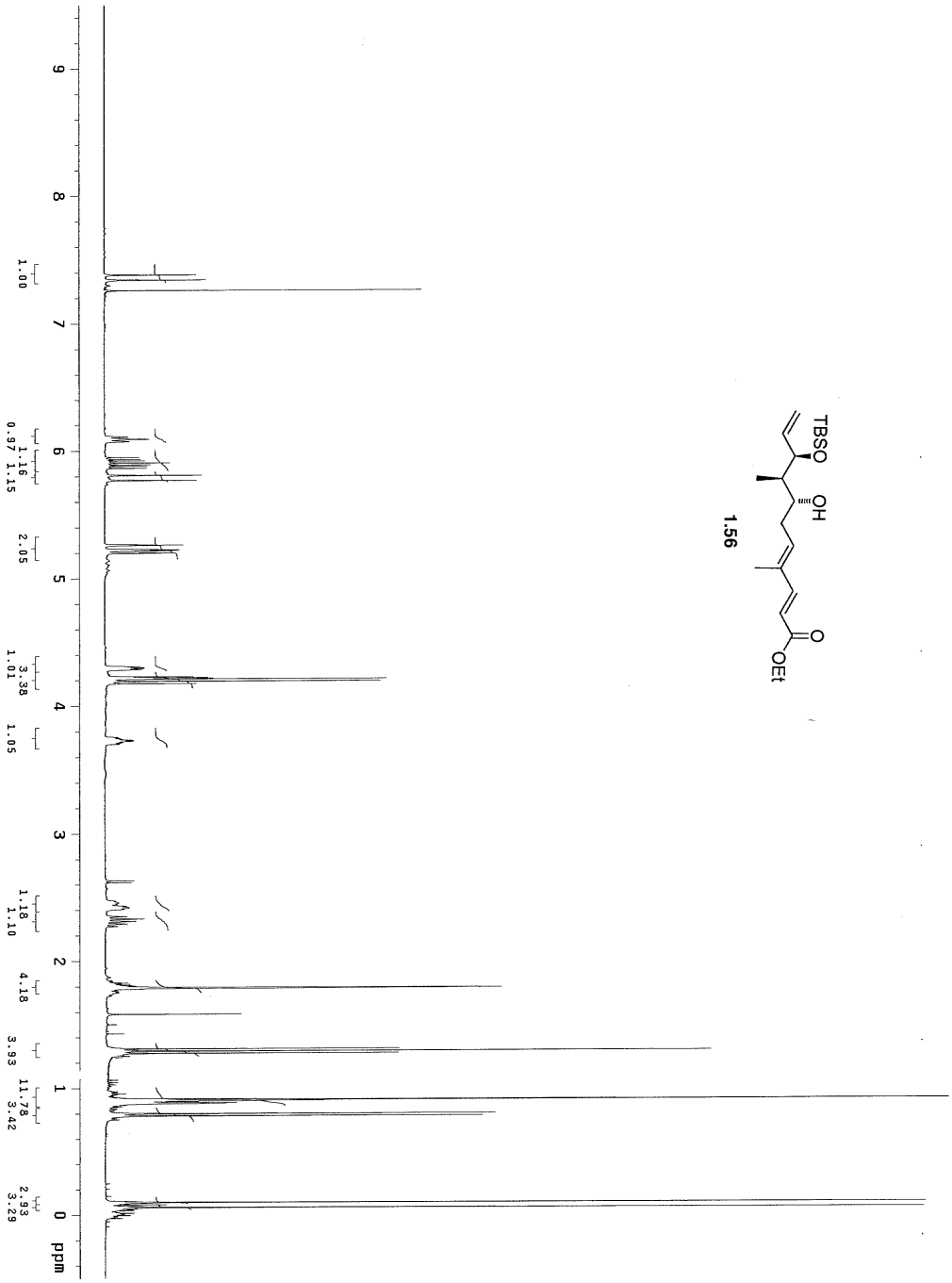

B(pin)
Me
OMe
1.53b
200
180
160
140
120
100
80
60
40
20
0 ppm

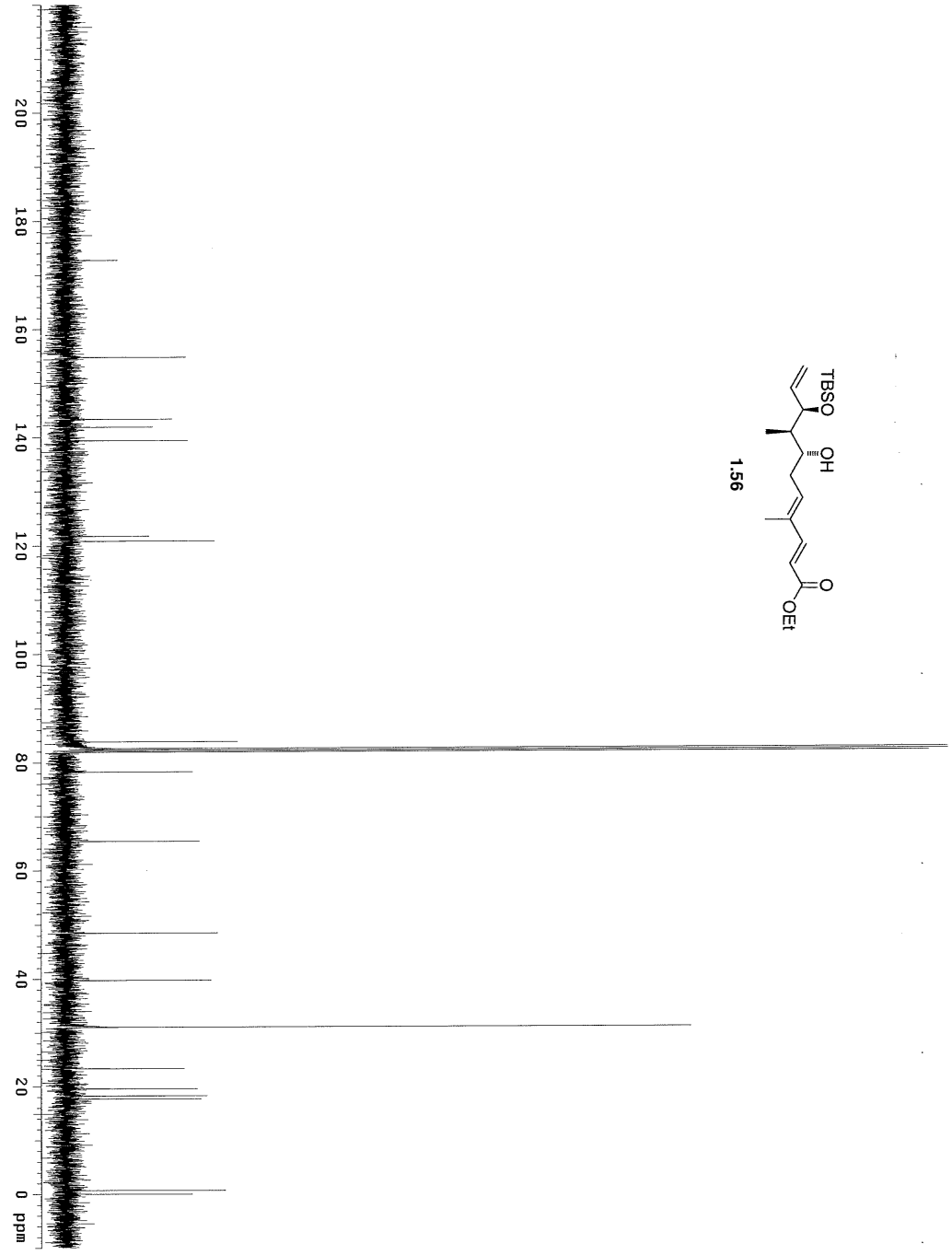

TBSO
OH
1.54
9
8
7
6
5
4
3
2
1
0
ppm
1.04
2.14
0.99
0.94
1.00
1.09
1.12
0.88
0.83
3.15
10.03
2.93
2.96

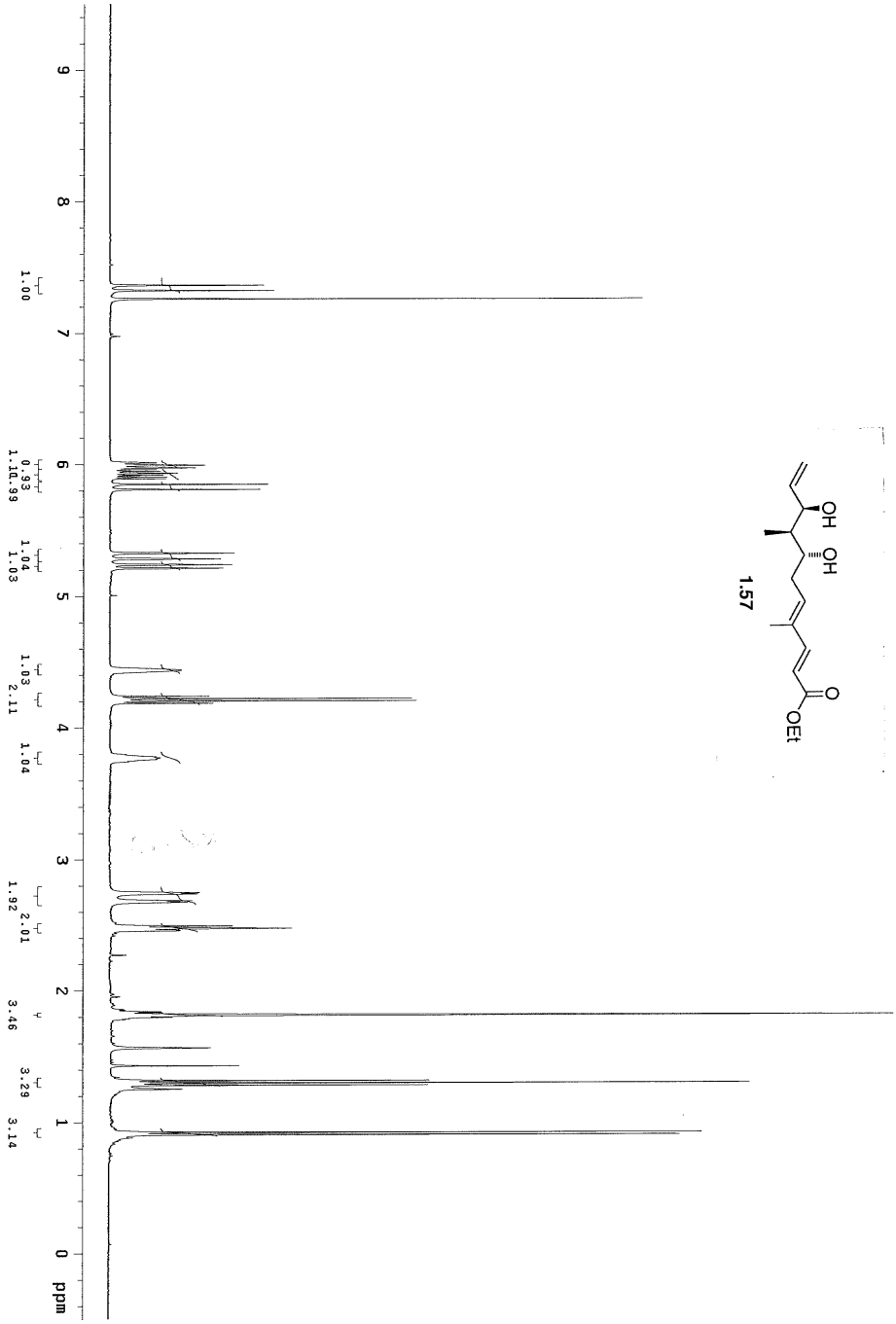

TBSO
OH
1.54
200
180
160
140
120
100
80
60
40
20
0
ppm

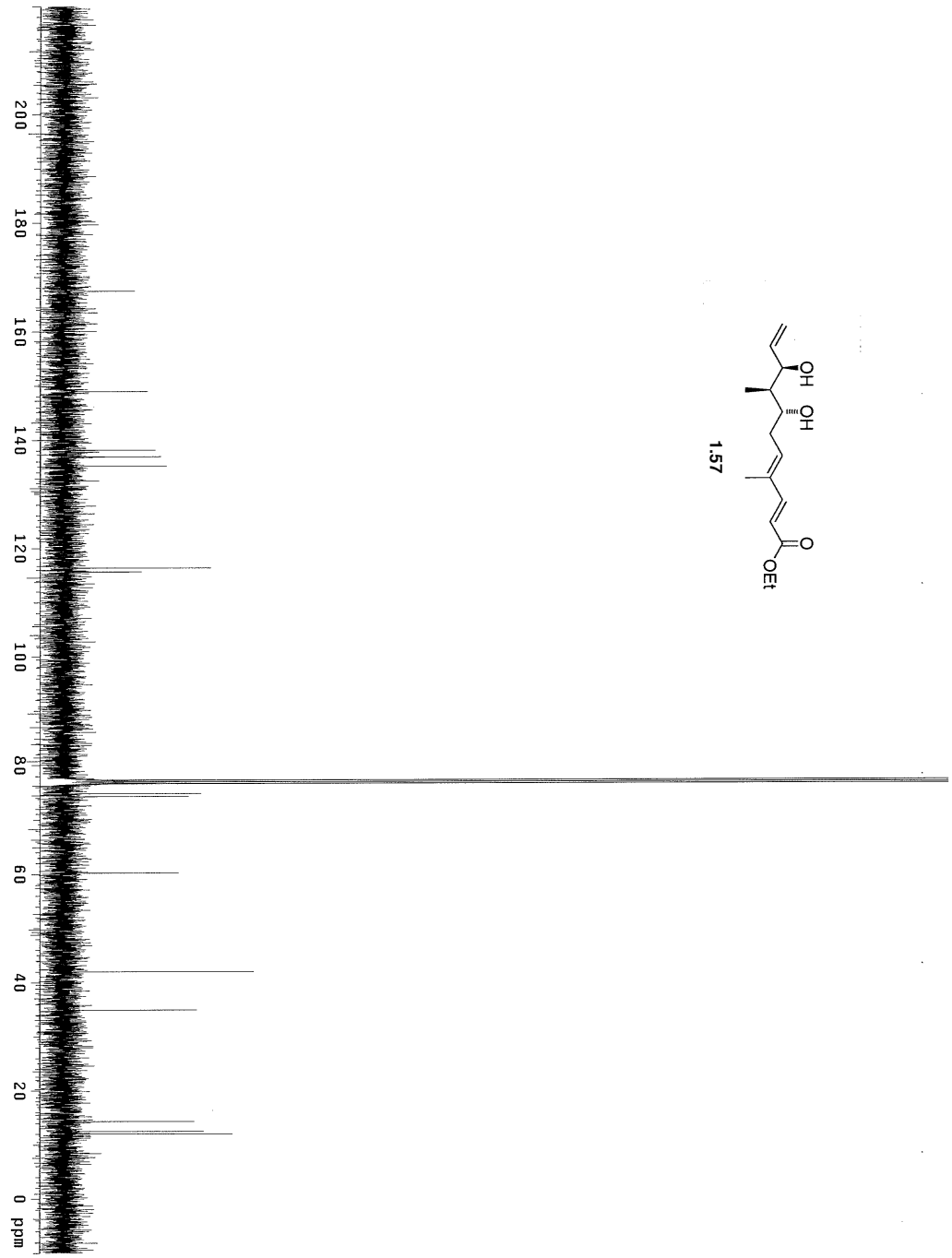

TBSO
OH
1.55
9
8
7
6
5
4
3
2
1
0
ppm
1.00
3.06
2.00
1.02
0.94
1.03
1.11
1.09
1.04
3.27
10.39
3.20
3.26


TBSO
OH
1.55
200
180
160
140
120
100
80
60
40
20
0
ppm


TBSO
OH
O
OEt
1.56
ppm


TBSO
OH
O
OEt
1.56
200
180
160
140
120
100
80
60
40
20
0
ppm


OH
OH
O
OEt
1.57
ppm

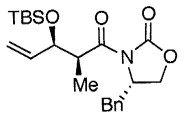

OH
OH
O
OEt
1.57
200
180
160
140
120
100
80
60
40
20
0 ppm

Sample Name:
FM-IV-224
Archive directory:

Sample directory:

FidFile: FM-IV-224

Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Aug 16 2012



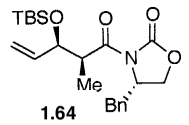
1.64

Sample Name:
FM-IV-224
Archive directory:

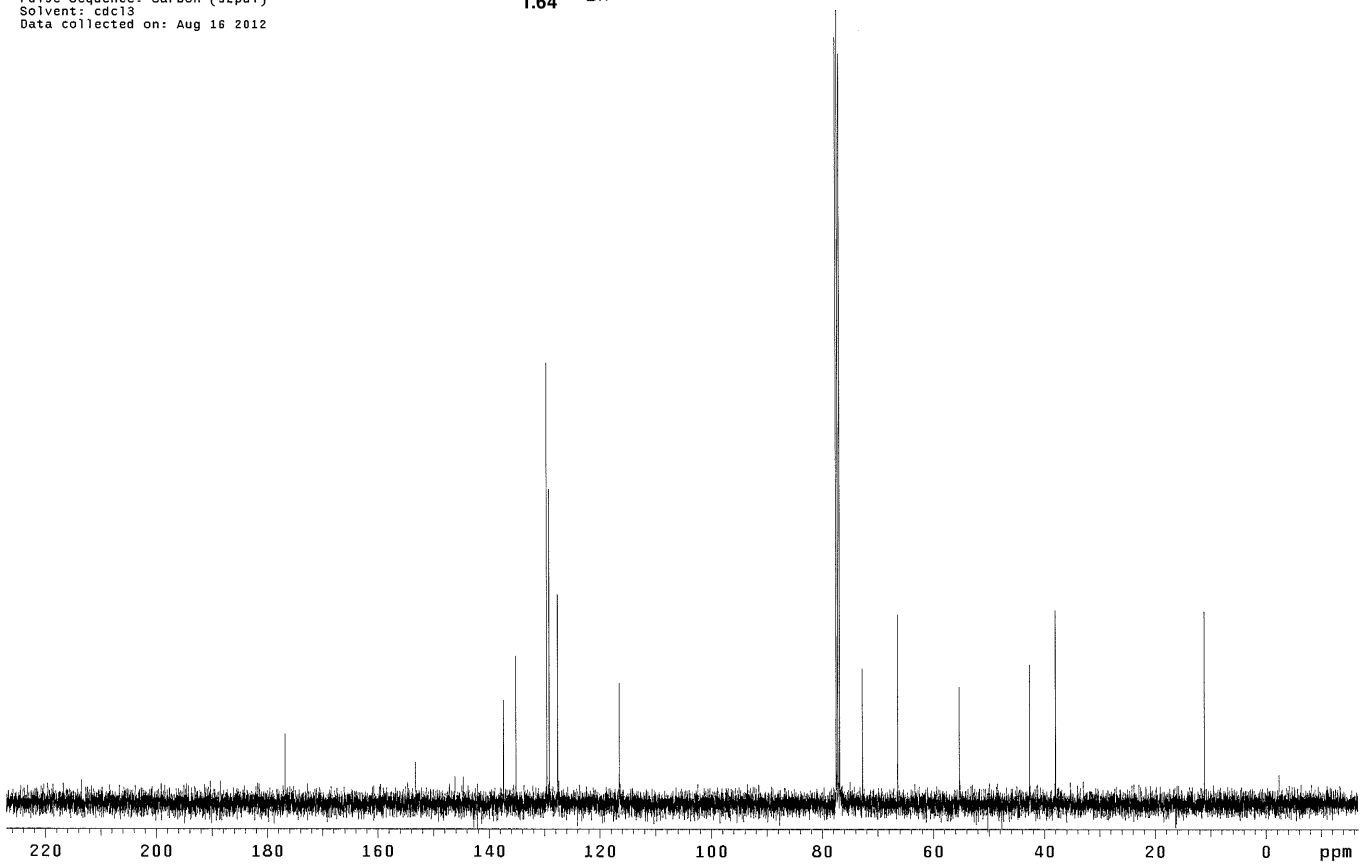
Sample directory:

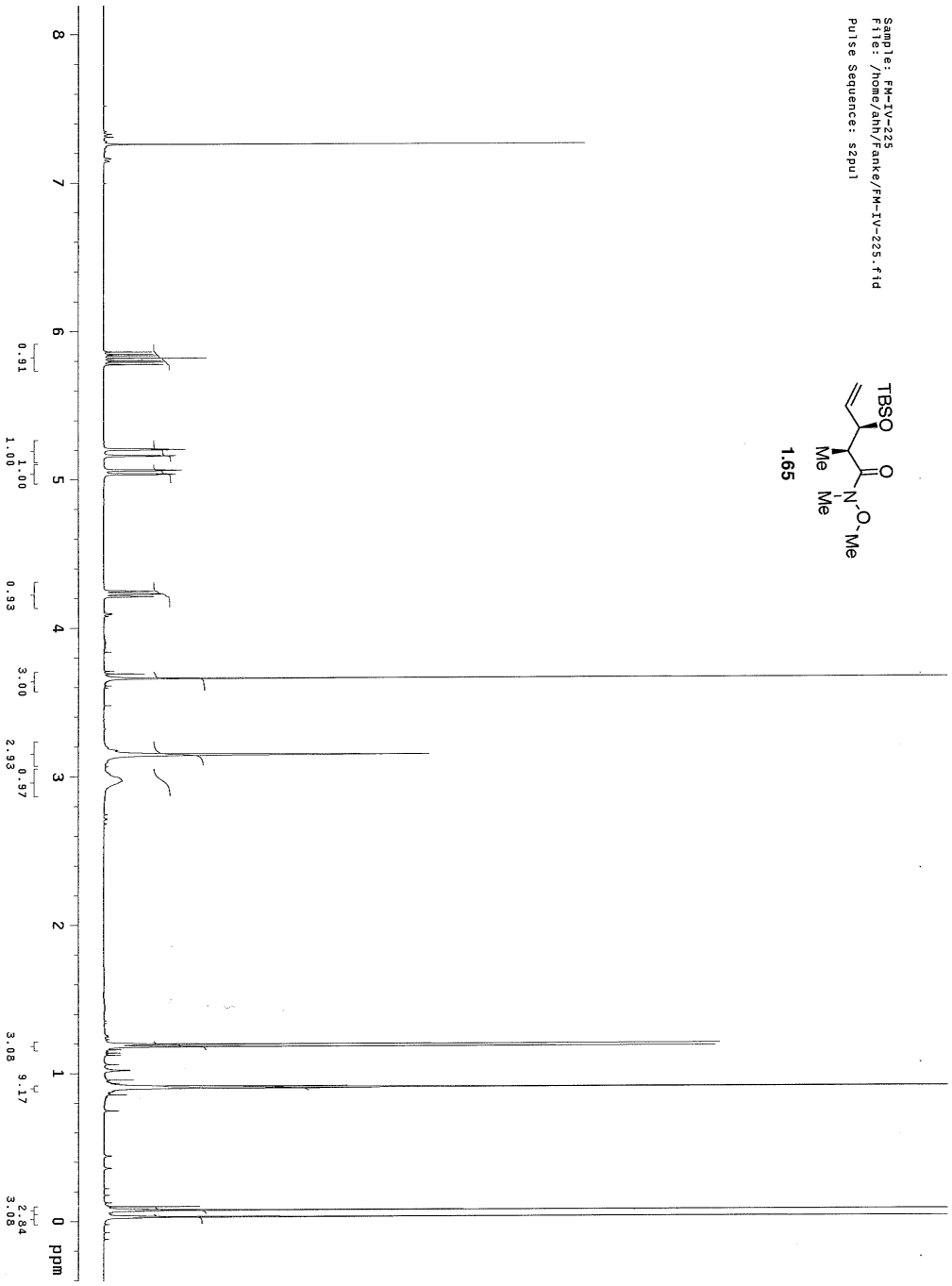
FidFile: FM-IV-224-CNMR

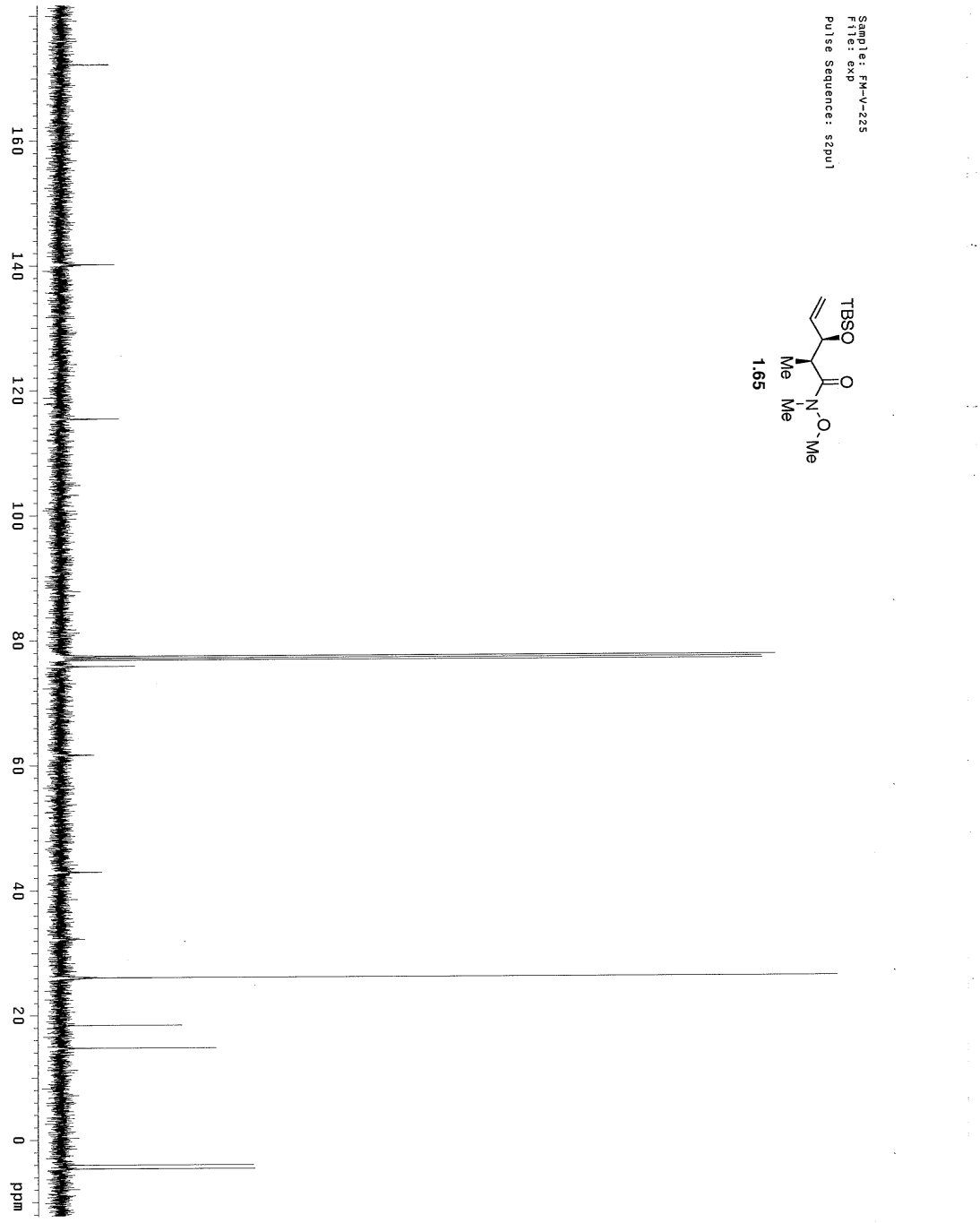
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Aug 16 2012

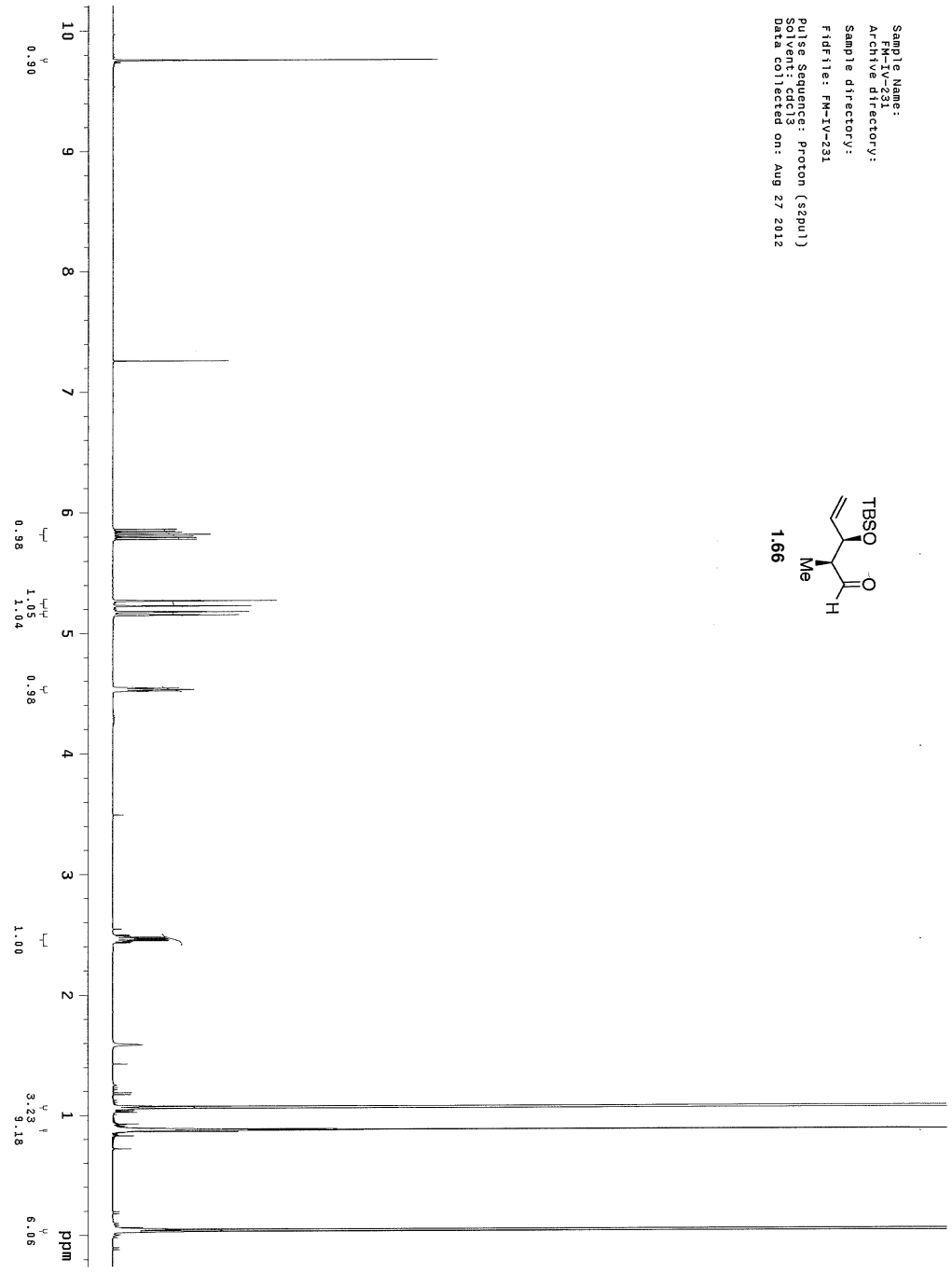


1.64




Sample: FM-IV-225
File: /home/ahh/Franke/FM-IV-225.fid
Pulse Sequence: s2pul
TBSO
O
N
O
Me
Me
Me
1.65
8
7
6
5
4
3
2
1
0
ppm
0.91
1.00
1.00
0.93
3.00
2.93
0.97
3.08
9.17
2.84
3.08


Sample: FM-V-225
File: exp
Pulse Sequence: s2pul
TBSO
O
N
O
Me
Me
Me
1.65
160
140
120
100
80
60
40
20
0
ppm

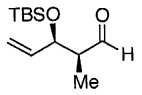

Sample Name:
FM-IV-231
Archive directory:
Sample directory:
FidFile: FM-IV-231
Pulse Sequence: proton (s2pul)
Solvent: cdcl3
Data collected on: Aug 27 2012
TBSO
O
H
Me
1.66
10
9
8
7
6
5
4
3
2
1
ppm
0.90
0.98
1.05
1.04
0.98
1.00
3.23
9.18
6.06

Sample Name:
FM-IV-231
Archive directory:

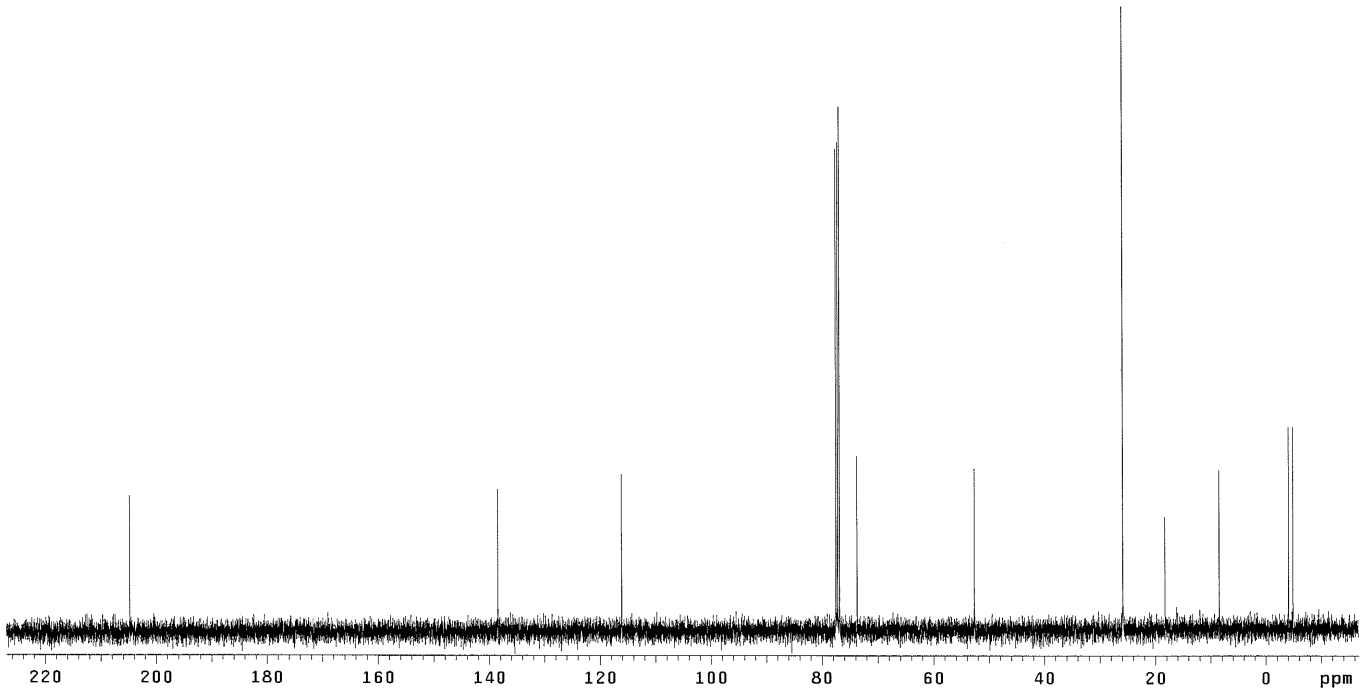
Sample directory:

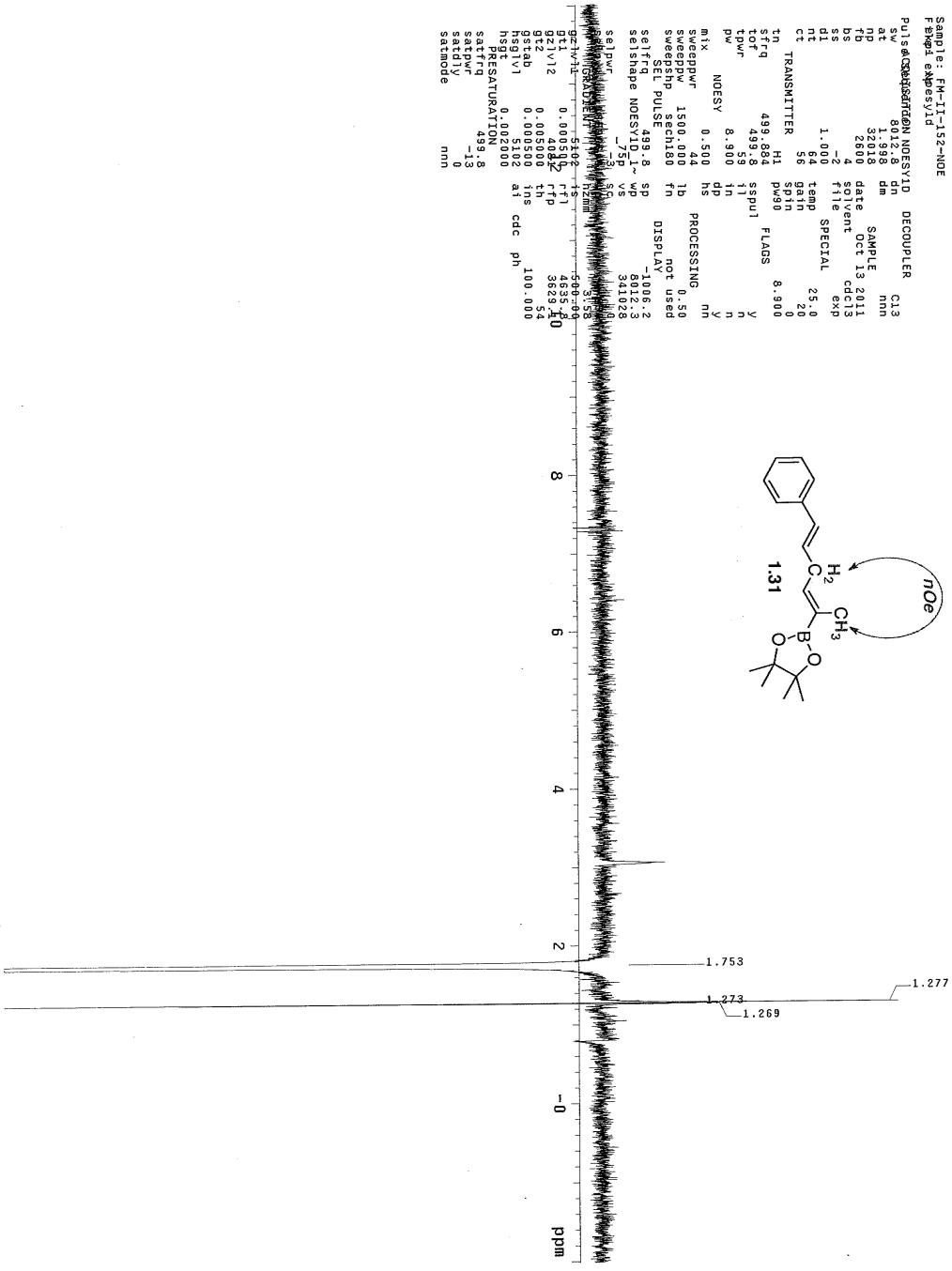
FidFile: FM-IV-231-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Aug 27 2012



1.66




1.31
nOe
1.753
1.277
1.273
1.269
ppm

Chapter 2

Cu-Catalyzed Chemoselective Copper–Boron Additions to Monosubstituted Allenes Followed by Allyl Additions to Carbonyl Compounds

2.1 Introduction

Enantioselective transformations that entail chemoselective catalytic generation of reactive organometallic reagents followed by fusion with a third substrate are of high demand in organic synthesis;[1] such processes may provide access to otherwise difficult-to-access intermediates and products. Wasteful and costly procedures for isolation/purification of sensitive intermediates are unnecessary. Highly functionalized organic molecules can be delivered in a more efficient and operationally simpler fashion.[2] Successful design of such single-catalyst-controlled protocols requires the catalyst to react with the substrates in a desired sequence. As the organometallic intermediate has the catalyst structure incorporated, further control of reactivity and selectivity of the subsequent reaction is possible. The single catalyst must also address all the selectivity issues in each stage of the multistep reaction.

(1) For reviews on catalytic multicomponent reactions, see (a) Ramón, D. J.; Yus, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 1602–1634. (b) Ruijter, E.; Scheffelaar, R.; Orru, R. V. *Angew. Chem., Int. Ed.* **2011**, *50*, 6234–6246. For a review on applications of multicomponent reactions in natural products synthesis, see: (c) Touré, B. B.; Hall, D. G. *Chem. Rev.* **2009**, *109*, 4439–4486.

(2) For a relevant discussion, see: Bower, J. F.; Kim, I. S.; Patman, R. L.; Krische, M. J. *Angew. Chem., Int. Ed.* **2009**, *48*, 34–46. 2-Substituted allylmetal species cannot be accessed by Ir- and Ru-catalyzed reductive couplings with allenes, and there are no related processes involving ketones.

Pioneering investigations by Krische and co-workers lead to identification of enantioselective multicomponent processes that fuse hydrogen and unsaturated hydrocarbons with aldehydes or imines catalyzed by phosphine–Ir or Ru complexes,[3] however, the scope of electrophiles is limited to those activated substrates. Ketones are not reactive in this system. Only a hydrogen atom can be incorporated into the final products.

In 2013, Hoveyda and co-workers described a method for catalytic generation of 2-boron-substituted allylcopper complexes from monosubstituted allenes.[4] After in situ protonation, 1,1-disubstituted or trisubstituted alkenylboron compounds are delivered in high selectivity. We are interested in introduction of a catalytic system that utilizes the allylcopper complexes generated catalytically from monosubstituted allenes in situ to form C–C bonds.[5] Aldehydes and ketones are an important class of electrophiles,[6] since the corresponding allyl addition products, homoallylic alcohols, are motifs that exist widely in natural products and pharmaceuticals.[7] The proposed protocol also provides an opportunity to incorporate a boron group into the final product that can be further functionalized. The ideal scenario of the designed multicomponent reactions meets the

(3) For representative examples of Ir- and Ru-catalyzed reductive allylation, see: (a) Ngai, M.-Y.; Barchuk, A.; Krische, M. J. *J. Am. Chem. Soc.* **2007**, *129*, 12644–12645. (b) Hassan, A.; Krische, M. J. *Org. Process Res. Dev.* **2011**, *15*, 1236–1242.

(4) (a) Meng, F.; Jung, B.; Haeffner, F.; Hoveyda, A. H. *Org. Lett.* **2013**, *15*, 1414–1417. For related studies, see: (b) Yuan, W.; Ma, S. *Adv. Synth. Catal.* **2012**, *354*, 1867–1872. (c) Semba, K.; Shinomiya, M.; Fujihara, T.; Terao, J.; Tsuji, Y. *Chem. Eur. J.* **2013**, *19*, 7125–7132.

(5) For an overview of three-component coupling reactions with allenes, delivering reagents that can be used in allyl addition processes, see: Jeganmohan, M.; Cheng, C.-H. *Chem. Commun.* **2008**, 3101–3117.

(6) For catalytic reductive coupling reactions of allenes and aldehydes, involving in situ generated allylmetal intermediates, promoted by Ir or Ru complexes, see: (a) Skucas, E.; Bower, M. J.; Krische, M. *J. J. Am. Chem. Soc.* **2007**, *129*, 12678–12679. (b) Zbieg, J. R.; McInturff, E. L.; Leung, J. C.; Krische, M. J. *J. Am. Chem. Soc.* **2011**, *133*, 1141–1144.

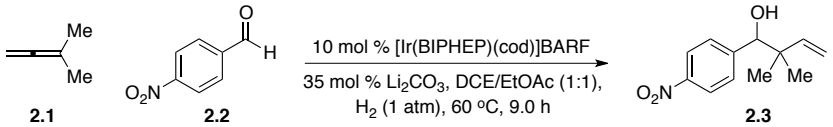
(7) For reviews on catalytic enantioselective allylation of carbonyl compounds and imines, see: Yus, M.; González-Gómez, J. C.; Foubelo, F. *Chem. Rev.* **2011**, *111*, 7774–7854.

criteria of efficient delivery of the desired products in a chemo-, site- and stereoselective fashion, promoted by commercially available or easily accessible ligands and abundant and inexpensive metals at low catalyst loadings.

2.2 Background

The first examples of catalytic multicomponent reactions that fuse hydrogen and allenes with aldehydes are reported by Krische and co-workers in 2007;[3a] the corresponding transformations involve an in situ generated allylmetal complex from an allene and hydrogen. As shown in Scheme 2.1, reaction of allene **2.1** with a cationic iridium hydride complex delivers the corresponding allyl iridium complex, which subsequently adds to aldehyde **2.2** to generate homoallylic alcohol **2.3** in 82% yield. The same group later described an enantioselective version of this multicomponent reaction. Chiral Ir complex formed from $[Ir(cod)Cl]_2$, (*S*)-SEGPHOS, allyl acetate, 3-nitrobenzoic acid and cesium carbonate prove to be optimal.[8]

Scheme 2.1: Ir-Catalyzed Reductive Coupling of Hydrogen, Allenes and Aldehydes



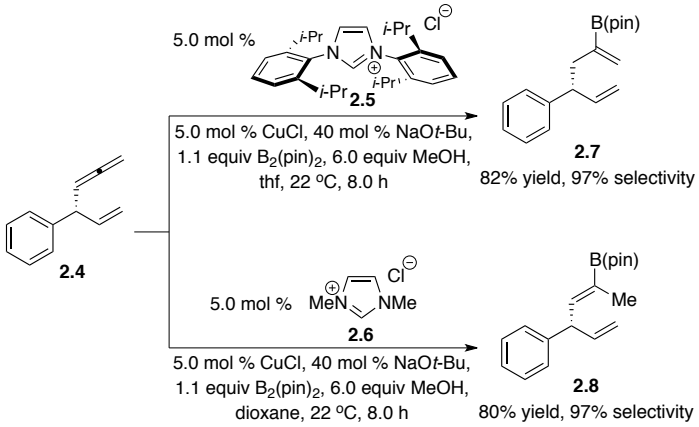
BARF = $B(3,5\text{-}(CF_3)_2C_6H_3)_4$
BIPHEP = 2,2'-Bis(diphenylphosphino)-1,1'-biphenyl

Another method for catalytic generation of allylmetal complexes from unsaturated hydrocarbons involves copper catalysis.[4] Formation of 2-boron-substituted allylcopper complexes through Cu–B addition to monosubstituted allenes followed by γ-protonation leads to 1,1-disubstituted or trisubstituted alkenylboron compounds in high efficiency and

(8) Han, S. B.; Kim, I. S.; Han, H.; Krische, M. J. *J. Am. Chem. Soc.* **2009**, *131*, 6916–6917.

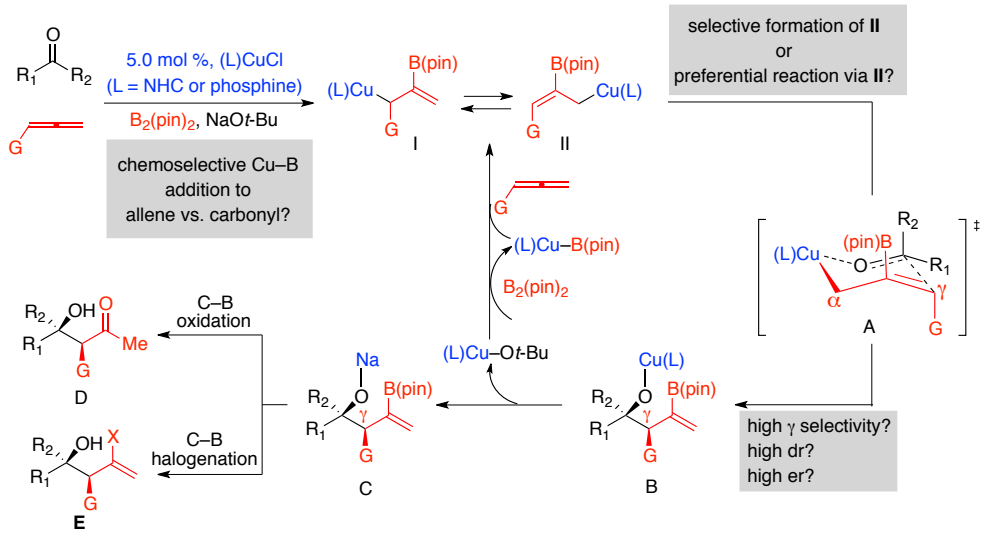
selectivity. As illustrated in Scheme 2.2, reaction of allene **2.4** affords 1,1-disubstituted alkenylboron **2.7** in 82% yield and 97% site selectivity upon exposure to NHC–Cu complex derived from **2.5**. Moreover, in the presence of smaller NHC–Cu complex in situ generated from imidazolium salt **2.6**, trisubstituted alkenylboron **2.8** is delivered in 80% yield and 97% site selectivity.

Scheme 2.2: NHC–Cu-Catalyzed Site-Selective Protoboration of Allenes



In addition to protonation, we wondered if addition of the allylcopper complex formed in situ to carbonyl compounds could proceed efficiently. The requisite for such multicomponent process is that Cu–B addition to allenes must be chemoselective in the presence of carbonyl compounds. The proposed transformation commences with chemoselective Cu–B addition to an allene, delivering a mixture of 2-boron-substituted allylcopper complexes **I** and **II** (Scheme 2.3). Equilibration to thermodynamically more stable **II** could be expected to be more rapid than addition to a carbonyl, which might occur via an organized six-membered transition state **A** to afford copper alkoxide **B**. Release of product **C** and regeneration of the L–Cu–O*t*Bu complex close the catalytic cycle. The carbon–boron bond in the final product **C** can be converted to carbon–oxygen, carbon–halogen or carbon–carbon bonds.

Scheme 2.3: Proposed Catalytic Cycle for Chemoselective Cu–B Addition to an Allene Followed by Addition to Carbonyl Compounds



2.3 Identification of the Optimal Achiral Catalysts and Scope for Cu-Catalyzed Cu–B Additions to Allenes Followed by Carbonyl Additions

We first evaluated how Cu catalysts derived from different types of ligands influence on chemo-, site- and stereoselectivity. Reactions of benzaldehyde **2.9a** and allene **2.11a** with $B_2(pin)_2$ in the presence of NHC–Cu complexes derived from **2.14a**-**b** or **2.15a**-**b** afford, after oxidative work-up,[9] β-hydroxyketone **2.12a** with complete γ-selectivity and 92:8 and 94:6 d.r. but in 36–42% yield and 30–41% yield, respectively (Table 2.1, entries 1–4).[10] Low yields originate from competitive Cu–B addition to aldehyde, when NHCs are employed as ligands.[11] With Cu complexes in situ generated from mono- or bidentate phosphine, chemoselectivity improves and the desired product is formed in higher yields with similar diastereoselectivity (78–80% yield, 93:7–95:5 d.r.,

(9) The alkenylboron products are unstable to silica gel due to boron chelation with neighboring alcohol.
(10) For direct Ti-catalyzed aldol addition involving ketones and aryl aldehydes, see: Mahrwald, R.; Schetter, B. *Org. Lett.* **2006**, *8*, 281–284.
(11) Laitar, D. S.; Tsui, E. Y.; Sadighi, J. P. *J. Am. Chem. Soc.* **2006**, *128*, 11036–11037.

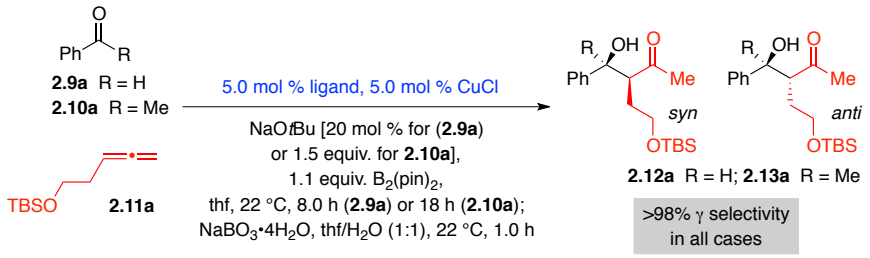
entries 5–7, Table 2.1). In sharp contrast, both NHC- and phosphine-based catalysts promote efficient allyl addition to ketone **2.10a** (entries 8–14, Table 2.1),[12] consistent with a sluggish NHC–Cu–B(pin) addition to ketone.[13] Complete γ-selectivity is observed and diastereoselectivity is high despite the diminished size difference between the ketone substitutents (vs. those of aldehyde); unfavorable diaxial interactions in **A** are likely less severe due to relatively long incipient bonds.[14] It is noteworthy that the stronger σ-donors, NHC ligands, lead to more nucleophilic Cu–B(pin) complexes, resulting in more competitive 1,2-addition to aldehydes and lower chemoselectivity, compared with phosphine ligands.

(12) Excess NaO*t*-Bu is needed for reactions with ketones, presumably because L–Cu–B(pin) regeneration by reaction of the more sterically congested Cu–alkoxide B with $B_2(pin)_2$ is slower via σ-bond metathesis and must proceed by alkoxide-assisted ligand exchange, see: Gao, F.; Carr, J. L.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2012**, *51*, 6613–6617.

(13) Treatment of ketone **3.10a** to reaction conditions in entry 11 of Table 3.1 but in the absence of allene **3.11a** results in <2% conversion after 18 h. For a precedence of NHC–Cu–B(pin) addition to ketone at elevated temperature, see: McIntosh, M. L.; Moore, C. M.; Clark, T. B. *Org. Lett.* **2010**, *12*, 1996–1999.

(14) Further Cu–B additions to alkenylboron products do not occur, see: Lee, Y.; Jang, H.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 18234–18235.

Table 2.1: Screening of Representative Catalyst Types[a]



Entry	Substrate	Ligand	Conv. (%)[b]	*syn*:*anti*[b]	Yield (%)[c]
1	**2.9a**	**2.14a**	47	92:8	36
2	**2.9a**	**2.15a**	42	94:6	30
3	**2.9a**	**2.14b**	66	92:8	42
4	**2.9a**	**2.15b**	58	94:6	41
5	**2.9a**	PPh_3	>98	93:7	78
6	**2.9a**	PCy_3	>98	93:7	80
7	**2.9a**	*rac*-binap	>98	95:5	80
8	**2.10a**	**2.14a**	>98	91:9	76
9	**2.10a**	**2.15a**	>98	92:8	80
10	**2.10a**	**2.14b**	>98	94:6	70
11	**2.10a**	**2.15b**	>98	93:7	83
12	**2.10a**	PPh_3	76	90:10	64
13	**2.10a**	PCy_3	>98	91:9	79
14	**2.10a**	*rac*-binap	>98	94:6	85

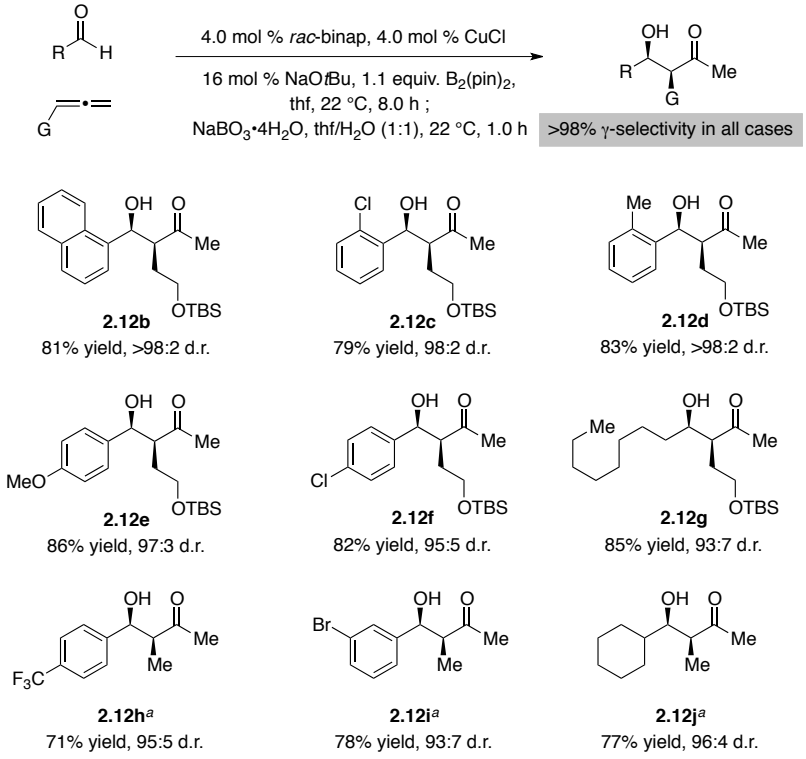
[a] Performed under N_2 atm. [b] Determined by analysis of 400 MHz ^{1}H NMR spectra of unpurified mixtures (±2%).
[c] Yields of isolated and purified products (±5%; major isomer for entries 1–7 and both isomers for entries 8–14).

Ar = Mes [2,4,6-$(Me)_3C_6H_2$] Ad = adamantyl

With the optimal conditions in hand, we turn our attention to examination of an assortment of allenes and aldehydes. A variety of aryl-substituted aldehydes are suitable subtrates including those containing an electron-donating group or an electron-withdrawing group (cf. **2.12b**-**f**, Scheme 2.4). Reactions of sterically congested aryl aldehydes in the presence of 4.0 mol % *rac*-binap and 4.0 mol % CuCl deliver the desired products **2.12b** and **2.12d** in 81% and 83% yield as a single diastereomer, respectively. Transformations with alkyl-substituted aldehydes are facile and selective (cf. **2.12g** and **2.12j**, Scheme 2.4). Reactions of aldehydes with a strong electron-withdrawing

substituent require a large excess of allene (5.0 equiv), otherwise B(pin) addition to aldehyde predominates. Methyl-substituted allene is effective as well (cf. **2.12h**-**j**, Scheme 2.4).

Scheme 2.4: Substrate Scope for Cu–B Addition to Allenes/Aldehyde Additions

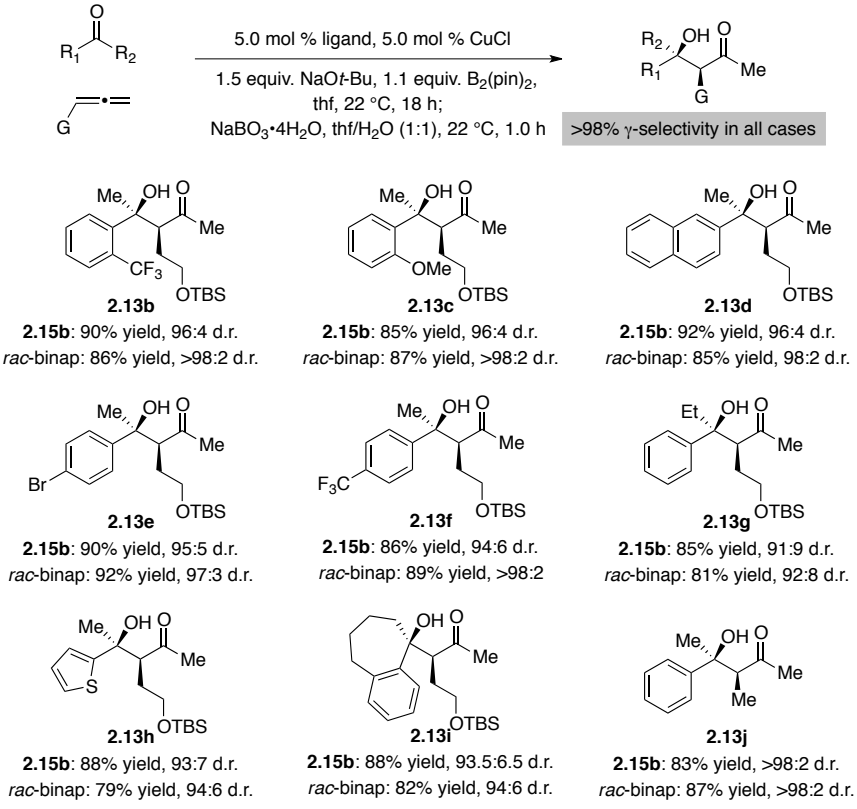


[a] Reactions conducted with 5.0 equiv of allene

A wide range of aryl ketones can be converted to products that contain tertiary hydroxyl groups (Scheme 2.5). Substrates with sterically hindered (cf. **2.13b**-**d**), electron-withdrawing (cf. **2.13b**, **2.13e**-**f**) and electron-donating (cf. **2.13c**) groups react efficiently and selectively. Ethyl ketone transforms in high efficiency albeit lower diastereoselectivity, presumably due to diminished size difference between an ethyl group and a phenyl group (cf. **2.13g**). Heterocyclic and cyclic ketones are suitable substrates as well (**2.13h** and **2.13i**). Facile and selective access to **2.13j** provides an attractive alternative to a propionate ketone aldol process. In all cases, selective

generation of trisubstituted enolate would be difficult. Unlike reaction with aliphatic aldehydes, the use of alkyl-substituted ketones leads predominately to side reactions. It is plausible that the lower electrophilicity of aliphatic ketones renders enolization of ketones by NaO*t*-Bu and following undesired transformations more competitive. Instead, the use of less basic NaOPh leads to formation of desired products in high efficiency and selectivity.

Scheme 2.5: Substrate Scope for Cu–B Addition to Allenes/Ketone Additions

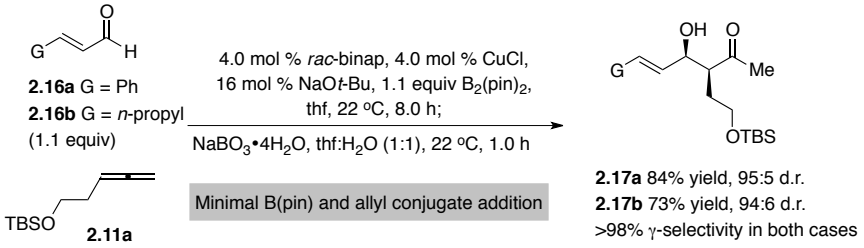


α,β-Unsaturated aldehydes are a more challenging class of electrophiles; possible competitive B(pin) or allyl conjugate addition leads to further complication in addition to 1,2-addition.[15] However, subjection of enals **2.16a** and **2.16b** to the reaction conditions

(15) For Cu-catalyzed B(pin) 1,4-additions to unsaturated carbonyls, see: Hartmann, E.; Vyas, D. J.; Oestreich, M. *Chem. Commun.* **2011**, *47*, 7917–7932.

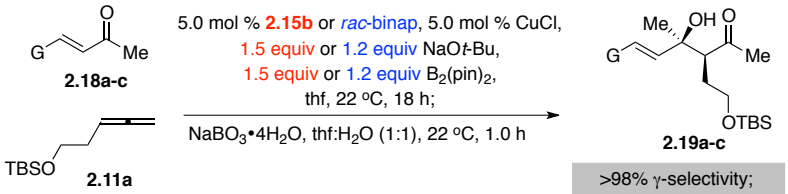
results in clean formation of allylic alcohols **2.17a** and **2.17b** in 84% and 73% yield with 95:5 d.r. and 94:6 d.r., respectively. In sharp contrast, reaction of enal **2.16a** in the absence of allene **2.11a** under otherwise identical reaction conditions leads to complete consumption of **2.16a** in only 4.0 h (vs. >98% conv. for the synthesis of **2.17a** and **2.17b** in 8.0 h). High chemoselectivity in favor of reaction initiating with addition to the allene in spite of a slower rate of transformation with an enal might be due to a substantially faster rate of the allene coordination to Cu.[4a]

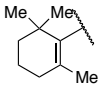
Scheme 2.6: Catalytic Cu–B Addition to Allenes Followed by Reactions with α,β-Unsaturated Aldehydes



Reactions of α,β-unsaturated ketones proceed with high diastereoselectivities in spite of the diminished size difference between the carbonyl substituents (vs. aryl ketones, Table 2.2). With either 5.0 mol % of **2.15a** or *rac*-binap, tertiary allylc alcohols are generated in 53–77% yield; the remaining mass balance is attributed to B(pin) 1,4-addition products. Similar with those cases in Table 2.1, the Cu catalyst derived from a phosphine ligand is more chemoselective (entries 2 and 4 vs. entries 1 and 3, Table, 2.2). Dienones are also suitable substrates. Higher efficiency in formation of **2.18c** results from the presence of the congested cyclic substituent, which disfavors the B(pin) 1,4-addition (entries 5 and 6, Table 2.2). The catalyst derived from an NHC ligand provides higher diastereoselectivity, probably because the large phosphine ligand has stronger destabilizing interaction in the transition state.

Table 2.2: Catalytic Multicomponent Reactions with α,β-Unsaturated Ketones[a]



Entry	Substrate	G	Ligand	d.r.[b]	Yield (%)[c]
1	**2.18a**	Ph	**2.15b**	>98:2	64
2	**2.18a**	Ph	*rac*-binap	91:9	68
3	**2.18b**	*n*-pentyl	**2.15b**	>98:2	53
4	**2.18b**	*n*-pentyl	*rac*-binap	91.5:8.5	77
5	**2.18c**		**2.15b**	90:10	86
6	**2.18c**		*rac*-binap	87:13	81

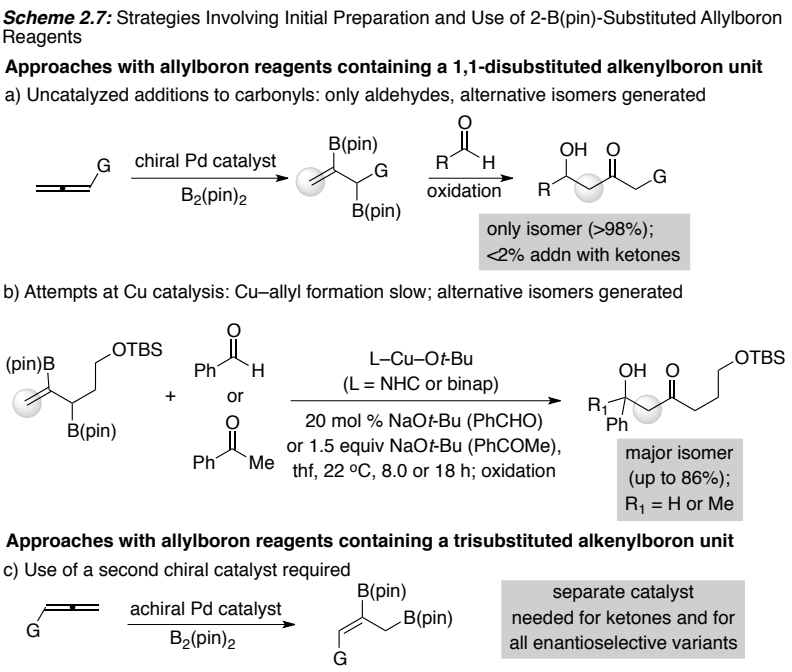
[a–c] See Table 2.1.

Several distinguishing advantages of the multicomponent protocol over the corresponding two-component alternative regarding efficiency and selectivity are noteworthy. Pd-catalyzed diboron additions to allenes afford 2-boron-substituted allylborons, which react with aldehydes to deliver acetate aldol products after oxidation (Scheme 2.7a).[16] Related ketone additions have not been reported and might need an additional catalyst. We have also attempted to use the same allylboron reagents as precursors to allylcopper intermediates, as shown in Scheme 2.7b. Reactions of benzaldehyde or acetophenone with the 2-boron-substituted allylboron species lead predominately to the same mode of addition as mentioned above (see Scheme 2.7a). This is likely due to the fact that the corresponding 2-boron-substituted allylcopper complex cannot be generated efficiently through transmetallation of C–B to C–Cu, and therefore both the uncatalyzed allyl addition with the aldehyde as well as the NaO*t*-Bu-promoted addition to the ketone become competitive. A different type of 2-boron-substituted

(16) Woodward, A. R.; Burks, H. E.; Chan, L. M.; Morken, J. P. *Org. Lett.* **2005**, *7*, 5505–5507.

allylboron reagents that contain a trisubstituted alkene moiety can be accessed through Pd-catalyzed diboron addition to allenes.[17] The efficiency of transmetallation might be problematic, as the γ-position of the allylboron entities is more sterically hindered.[18] Also enantioselective transformations of the allylboron reagents with aldehydes or ketones would require the use of a second catalyst.

Scheme 2.7: Strategies Involving Initial Preparation and Use of 2-B(pin)-Substituted Allylboron Reagents

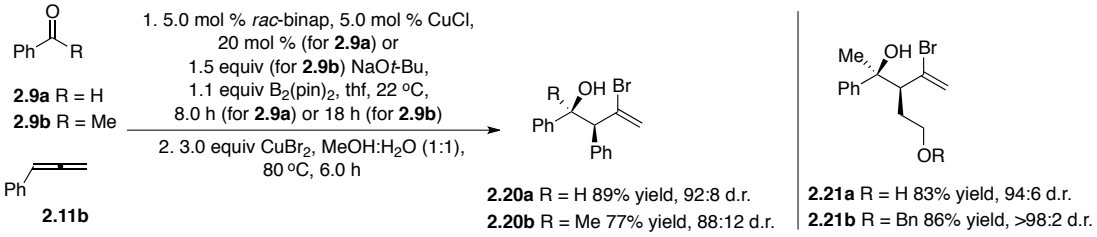


Alkenyl halides are another synthetically useful class of building blocks. Hydroxyl-containing alkenyl bromides **2.20a** (89% yield and 92:8 d.r.) and **2.20b** (77% yield and 88:12 d.r.) can be accessed by subjection of the initial organoboron product mixtures to $CuBr_2$ in a 1:1 mixture of MeOH and water at 80 °C, originating from the reaction of phenyl-substituted allene **2.11b** (Scheme 3.8). Reactions of **2.11a** and benzyl

(17) (a) Yang, F.-Y.; Cheng, C.-H. *J. Am. Chem. Soc.* **2001**, *123*, 761–762. For reactions with (pin)B–$SiMe_2Ph$ and diastereoselective addition of 2-silyl-substituted allylborons to aldehydes, see: (b) Chang, K.-J.; Rayabarapu, D. K.; Yang, F.-Y.; Cheng, C.-H. *J. Am. Chem. Soc.* **2005**, *127*, 126–131. For related studies, see: (c) Suginome, M.; Nakamura, H.; Matsuda, T.; Ito, Y. *J. Am. Chem. Soc.* **1998**, *120*, 4248–4249. (d) Zbieg, J. R.; Moran, J.; Krische, M. J. *J. Am. Chem. Soc.* **2011**, *133*, 10582–10586.
(18) Ardolino, M. J.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, *136*, 7092–7100.

derivative of **2.11a** with acetophenone **2.9b** followed by bromination deliver alkenyl bromides **2.21a** and **2.21b** in 83% and 86% yield with 94:6 and >98:2 d.r., respectively. As far as we know, there is no precedence regarding stereoselective synthesis of alkenyl halide-containing tertiary homoallylic alcohols through direct allyl additions to ketones.[19]

Scheme 2.8: Access to Alkenyl Halides from Alkenylborons through Cu-Catalyzed Multicomponent Reactions



2.4 Identification of the Optimal Catalysts and Scopes for Cu–B Additions to Allenes Followed by Enantioselective Allyl Additions

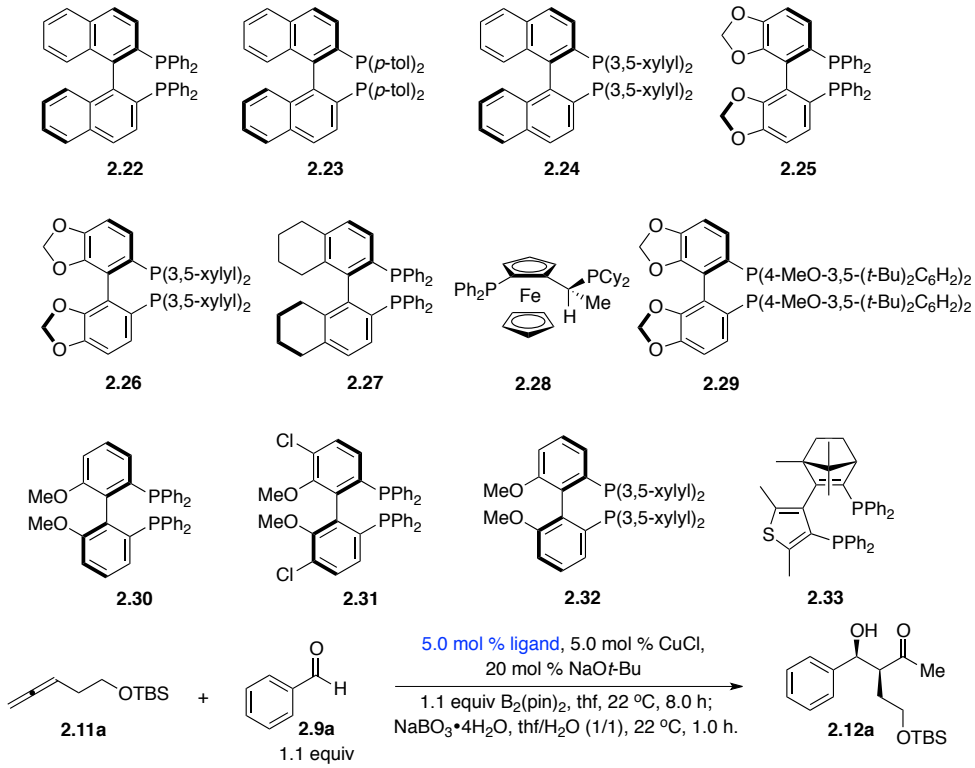
We next investigated numerous chiral ligands for the sequential Cu–B additions to an allene/aldehyde addition. Chiral bisphosphine ligands are essential for not only high chemoselectivity but also enantioselectivity. As illustrated in Table 2.3, change of substituents on phosphorus from Ph to 3,5-$Me_2C_6H_3$ improves the enantioselectivity slightly (entry 1 vs. 3; entry 4 vs. 5; entry 9 vs. 11). Reactions promoted by C_2-symmetric ligands with different dihedral angles lead to **2.12a** in 84–89% yield with 94:6–95:5 d.r. and 87:13–90:10 d.r. (entries 1, 4, 6 and 9). Transformation in the presence of ferrocene-

(19) For catalytic diastereoselective allyl additions to ketones (not 2-B(pin)-substituted), see: (a) Ren, H.; Dunet, G.; Mayer, P.; Knochel, P. *J. Am. Chem. Soc.* **2007**, *129*, 5376–5377. (b) Peng, Z.; Blümke, T. D.; Mayer, P.; Knochel, P. *Angew. Chem., Int. Ed.* **2010**, *49*, 8516–8519. (c) Takeda, T.; Yamamoto, M.; Yoshida, S.; Tsubouchi, A. *Angew. Chem., Int. Ed.* **2012**, *51*, 7263–7266. For reactions of ketones and stoichiometric amounts of allylboronic acids (not 2-boron-substituted), isolated from allylic alcohols by a Pd-catalyzed process, see: (d) Raducan, M.; Alam, R.; Szabó, K. J. *Angew. Chem., Int. Ed.* **2012**, *51*, 13050–13053.

containing C_1-symmetric phosphine ligand **2.28** provide **2.12a** in 91% yield with 97:3 d.r. and 35:65 d.r.. An electronically modified phosphine ligand does not alter the selectivity significantly (entry 10). A C_1-symmetric bisphosphine ligand **2.33** with a camphor backbone delivers the optimal diastereo- and enantioselectivity (entry 11).[20]

(20) Kadyrov, R.; Ilaldinov, I. Z.; Almena, J.; Monsees, A.; Riermeier, T. H. *Tetrahedron Lett*. **2005**, *46*, 7397–7400.

Table 2.3: Ligand Screen for Chiral Phosphine Ligands[a]



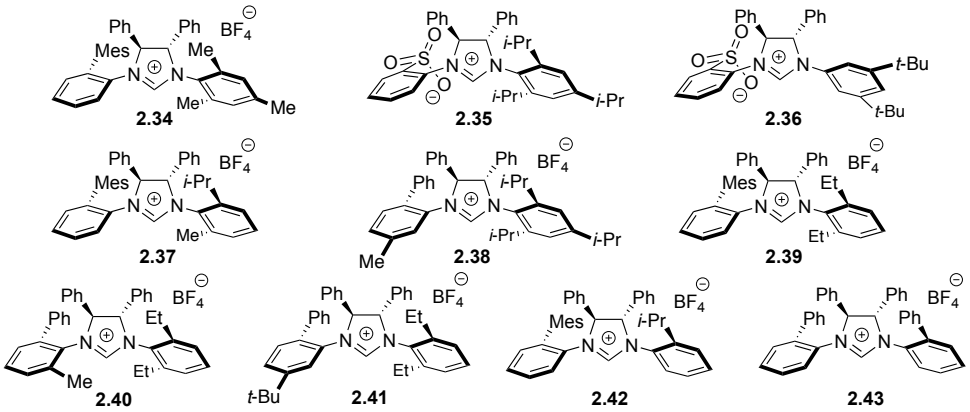
Entry	Ligand	Conv (%)[b]	Yield (%)[c]	d.r.[b]	e.r.[d]
1	**2.22**	>98	84	95:5	87:13
2	**2.23**	>98	86	94:6	87:13
3	**2.24**	>98	91	91:9	89:11
4	**2.25**	>98	89	95:5	88:12
5	**2.26**	>98	87	95:5	90:10
6	**2.27**	>98	85	94:6	88:12
7	**2.28**	>98	91	97:3	35:65
8	**2.29**	58	55	84:16	72:28
9	**2.30**	>98	87	95:5	90:10
10	**2.31**	>98	85	96:4	90:10
11	**2.32**	>98	87	95:5	93:7
12	**2.33**	>98	88	96:4	94:6

[a] Performed under N_2 atm. [b] Determined by analysis of 400 MHz ^{1}H NMR spetra of unpurified mixtures (±2%). [c] Yields of isolated/purified products (±5%; both isomers). [d] Enantiomeric ratio (er) determined by HPLC analysis (±2%).

We then turned our attention to identification of the most selective ligand for multicomponent reaction of allenes and ketones, a more challenging class of electrophiles with $B_2(pin)_2$. Both NHC and phosphine ligands were investigated. Regardless of the

identity of the imidazolinium salt, monodentate or bidentate, C_1-symmetric or C_2-symmetric, is used, the enantioselectivity does not exceed 60:40 e.r. (Table 2.4).

Table 2.4: Investigation of Various Chiral Mono- and Bidentate NHCs[a]

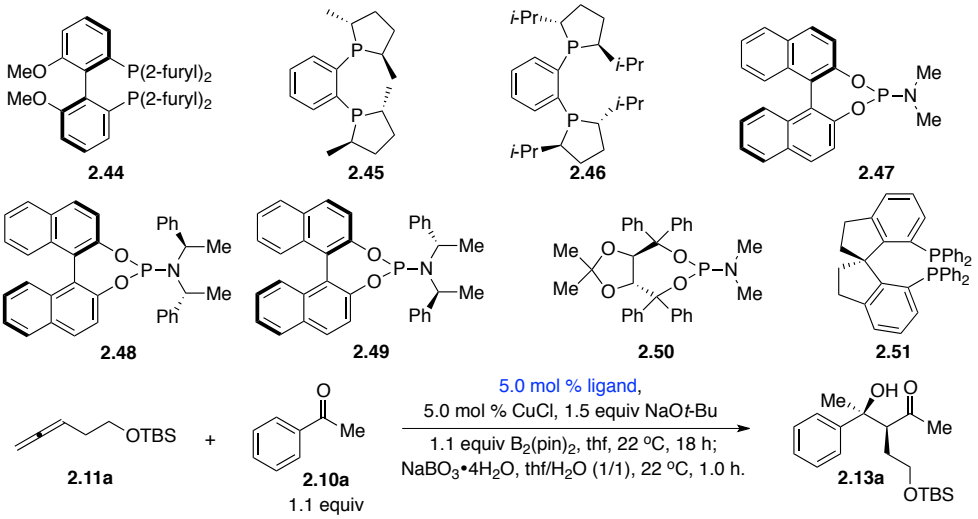


Entry	Imidazolinium salt	Conv (%)[b]	Yield (%)[c]	d.r.[b]	e.r.[d]
1	**2.34**	>98	75	85:15	57:43
2	**2.35**	>98	72	89:11	60:40
3	**2.36**	>98	62	88:12	56:44
4	**2.37**	>98	73	84:16	57:43
5	**2.38**	>98	76	87:13	57:43
6	**2.39**	>98	73	83:17	56:44
7	**2.40**	>98	78	82:18	51:49
8	**2.41**	>98	76	81:19	53:47
9	**2.42**	>98	70	82:18	54:46
10	**2.43**	>98	74	80:20	52:48

[a–d] See Table 2.3.

The performance of a variety of P-based ligands has been explored (Table 2.5). Notably, high diastereoselectivities are generally observed in most cases. Bisphosphines with biaryl backbones provide higher enantioselectivity (entries 1, 5, 6 and 10). Transformations with Duphos and phosphoramidite ligands deliver low enantioselectivies albeit high diastereoselectivities (entries 13 and 14; entries 15–18).

Table 2.5: Investigation of Various Chiral Mono- and Bidentate P-Based Ligands[a]



Entry	Ligand	Conv (%)[b]	Yield (%)[c]	d.r.[b]	e.r.[d]
1	**2.22**	>98	86	94:6	90:10
2	**2.23**	>98	83	92:8	77:23
3	**2.24**	>98	84	90:10	64:36
4	**2.25**	>98	86	91:9	76:24
5	**2.26**	>98	84	90:10	84:16
6	**2.27**	>98	80	96:4	80:20
7	**2.28**	>98	88	97:3	53:47
8	**2.29**	15	nd[e]	nd[e]	nd[e]
9	**2.30**	>98	79	91:9	66:34
10	**2.31**	>98	84	96:4	89:11
11	**2.32**	>98	77	92:8	80:20
12	**2.44**	>98	82	98:2	36:64
13	**2.45**	>98	86	96:4	61:39
14	**2.46**	>98	87	>98:2	48:52
15[f]	**2.47**	>98	87	97:3	55:45
16[f]	**2.48**	>98	88	96:4	41:59
17[f]	**2.49**	>98	89	94:6	57:43
18[f]	**2.50**	>98	88	95:5	53:47
19	**2.51**	20	nd[e]	nd[e]	nd[e]
20	**2.33**	>98	82	92:8	76:24

[a–d] See Table 2.3. [e] Not determined. [f] The reactions were run in the presence of 2.0 mol % $(CuOTf)_2$•toluene, 8.0 mol % ligand and 1.5 equiv NaO*t*-Bu.

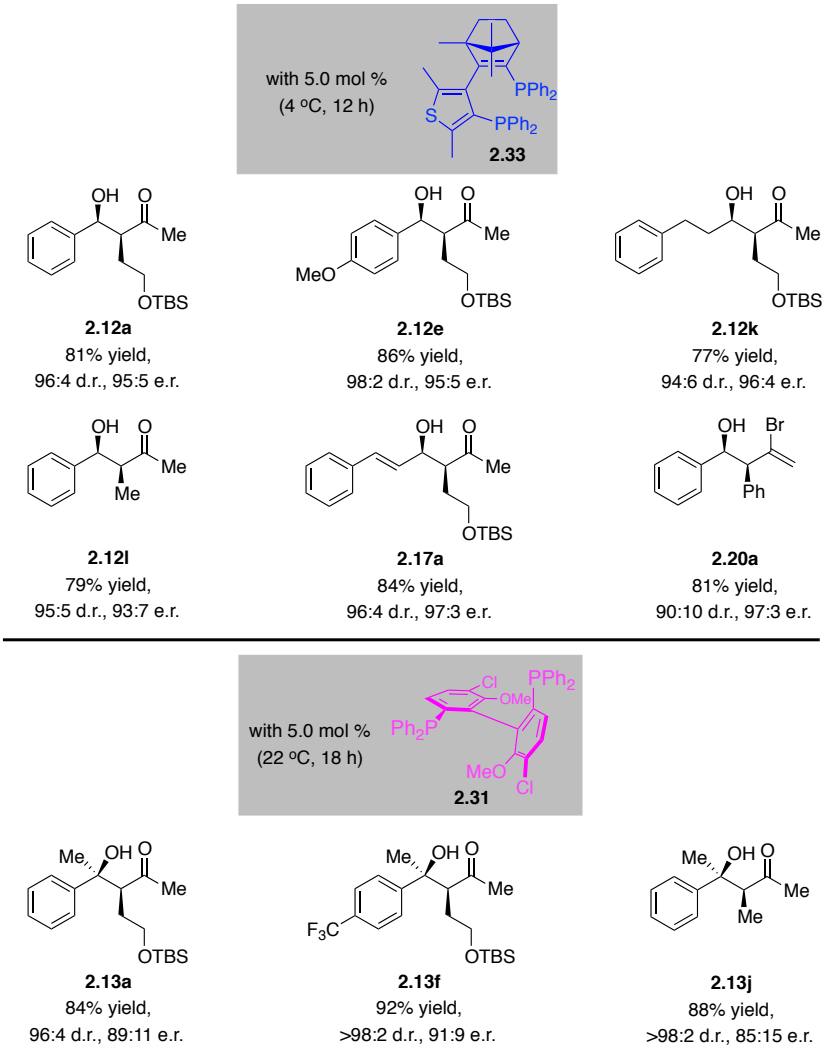
Transformations with a range of aryl-, alkyl- and alkenyl-substituted aldehydes in the presence of chiral phosphine **2.33** at 4 °C deliver up to 97:3 e.r. (cf. **2.12a**, **2.12e**,

2.12k and **2.17a**, Scheme 2.9).[21] Methyl- and phenyl-substituted allenes are also well tolerated, reactions of which provide 93:7 e.r. and 97:3 e.r. (cf. **2.12i** and **2.20a**, Scheme 2.9). With C_2-symmetric bisphosphine **2.31**, a variety of β-hydroxyketones can be introduced in 84–92% yield with up to 91:9 e.r. (cf. **2.13a**, **2.13f** and **2.13j**, Scheme 2.9).[22]

(21) Direct enantioselective catalytic aldol additions with aldehydes have been reported (none wih ketones). Reactions with cyclic ketones (enol precursors) are more common and the large majority of acyclic cases involve transformations with strongly electron-deficient aryl aldehydes and generate products that bear a methyl or an alkoxy unit adjacent to the carbonyl (higher reactivity of the enol); low to moderate site selectivity is typically observed (propionate vs. acetate aldol). For example, see: (a) Luo, S.; Xu, H.; Li, J.; Zhang, L.; Cheng, J.-P. *J. Am. Chem. Soc.* **2007**, *129*, 3074–3074. (b) Aratake, S.; Itoh, T.; Okano, T.; Nagae, N.; Sumiya, T.; Shoji, M.; Hayashi, Y. *Chem. Eur. J.* **2007**, *13*, 10246–10256. Reactions with aliphatic aldehydes are scarce (none with enals); one reported example requires >140 h; see: (c) Ma, G.; Bartoszewicz, A.; Ibrahem, I.; Córdova, A. *Adv. Synth. Catal.* **2011**, *353*, 3114–3122.

(22) For catalytic enantioselective allyl additions to ketones (not 2-B(pin)-substituted), see: (a) Wada, R.; Oisaki, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2004**, *126*, 8910–8911. (b) Wadamoto, M.; Yamamoto, H. *J. Am. Chem. Soc.* **2005**, *127*, 14556–14557. (c) Lou, S.; Moquist, P. N.; Schaus, S. E. *J. Am. Chem. Soc.* **2006**, *128*, 12660–12661. (d) Jiang, X.; Cao, Y.; Wang, Y.; Liu, L.; Shen, F.; Wang, R. *J. Am. Chem. Soc.* **2010**, *132*, 15328–15333.

Scheme 2.9: Scope for Phosphine–Cu-Catalyzed Cu–B Addtions to Allenes Followed by Enantioselective Aldehyde Additions



2.5 Conclusion

In this chapter, we have established a multicomponent protocol involving Cu-catalyzed Cu–B additions to allenes followed by in situ enantioselective additions to carbonyls. A wide range of alkenylboron-containing secondary and tertiary alcohols are obtained in high efficiency and selectivitiy, which can be transformed to a variety of synthetically useful building blocks through conversion of the C–B bond to C–O, C–N

and C–C bonds. Catalysts derived from commercially available chiral ligands and inexpensive abundant copper salt promote the reactions. Moreover, the studies outlined herein open up a new opportunity to engineer an assortment of new multicomponent reactions through in situ reactions of catalytically generated boron-containing organocopper intermediates with other electrophiles to form C–C bonds.

2.6 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). ^{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, br s = broad singlet, m = multiplet, app. = apparent), and coupling constant (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. Enantiomer ratios were determined by high-performance liquid chromatography (HPLC) with a Shimadzu chromatograph (Chiral Technologies Chiralpak AD–H (4.6 x 250 mm), Chiralcel OD–H (4.6 x 250 mm) and Chiralcel OJ–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. Solvents were purified under a positive pressure of dry argon by a modified Innovative Technologies purification system: toluene, benzene and hexanes were purified through a copper oxide and alumina column; CH_2Cl_2 and Et_2O were purged with Ar and purified by passage through two alumina columns. Tetrahydrofuran (Aldrich Chemical Co.) was purified by distillation from sodium benzophenone ketyl immediately prior to use unless otherwise specified. Methanol (Aldrich Chemical Co.) was distilled over CaH_2. All work-up and purification procedures were carried out with reagent grade solvents (purchased from Fisher Scientific) in air.

2.6.1 Reagents and Ligands:

Allenes (2.11a-b): prepared according to previously reported procedures.[23]

Methyl allene (25% by wt in toluene): purchased from ChemSamp. Co. and used as received.

Aldehydes and aryl ketones: purchased from Aldrich Chemical Co. and purified by distillation over CaH_2 (for liquids) or column chromatography prior to use (for solids).

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(23) (a) Crabbé, P.; Fillion, H.; André, D.; Luche, J-L. *J. Chem. Soc., Chem. Commun.* **1979**, 859–860. (b) Searles, S.; Li, Y.; Nassim, B.; Lopes, M-T. R.; Tran, P. T.; Crabbé, P. *J. Chem. Soc., Perkin Trans. 1*, **1984**, 747–751. (c) Inoue, A.; Kondo, J.; Shinokubo, H.; Oshima, K. *Chem. Eur. J.* **2002**, *8*, 1730–1740. (d) Baird, M. S.; Nizovtsev, A. V.; Bolesov, I. G. *Tetrahedron* **2002**, *58*, 1581–1593.

Bis(pinacolato)diboron: purchased from Frontier Scientific, Inc. and recrystallized from pentane.

Copper (II) bromide: purchased from Strem Chemicals Inc. and used as received.

Copper (I) chloride: purchased from Strem Chemicals Inc. and used as received.

Imidazolinium or imidazolium salts (2.14a-b, 2.15a-b, 2.34-2.43[24]): purchased from Aldrich Chemical Co. and used as received.

β–Ionone (2.18c): purchased from Aldrich Chemical Co. and purified by distillation over CaH_2 prior to use.

4-Methylmorpholine *N*-oxide (NMO): purchased from Aldrich Chemical Co. and used as received.

(*E*)-Non-3-en-2-one (2.18b): purchased from Aldrich Chemical Co. and purified by distillation over CaH_2 prior to use.

(*E*)-4-Phenylbut-3-en-2-one (2.18a): purchased from Aldrich Chemical Co. and purified by column chromatography prior to use.

Phosphines (2.22-2.33, 2.44-2.51): purchased from Strem Chemicals Inc. and used as received.

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

Sodium methoxide: purchased from Strem Chemicals Inc. and used as received.

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(24) (a) Lee, K-s.; Hoveyda, A. H. *J. Org. Chem.* **2009**, *74*, 4455–4462. (b) Lee, K-s.; Brown, M. K.; Hird, A. W.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2006**, *128*, 7182–7184. (c) Brown, M. K.; May, T. L.; Baxter, C. A.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 1097–1100. (d) May, T. L.; Brown, M. K.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2008**, *47*, 7468–7472.

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

Tetrabutylammonium fluoride solution (1.0 M in thf): purchased from Aldrich Chemical Co. and used as received.

Tetrapropylammonium perruthenate (TPAP): purchased from TCI Chemical Co. and used as received.

2.8.2 Experimental Procedures and Characterization Data for Cu–Catalyzed Cu–B Addition/Addition to Carbonyls

■ **Representative Experimental Procedure for Cu-Catalyzed Cu–B Addition/ Addition to Aldehydes Followed by *Oxidative Work-up*:** In a N_2-filled glove box, an oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with *rac*-binap (2.5 mg, 0.0040 mmol, 4.0 mol %), CuCl (0.4 mg, 0.004 mmol, 4.0 mol %), NaO*t*-Bu (1.5 mg, 0.016 mmol, 16 mol %) and tetrahydrofuran (thf, 0.5 mL). The vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the solution was allowed to stir at 22 °C for one hour. Bis(pinacolato)diboron (27.9 mg, 0.110 mmol, 1.1 equiv.) was added to the solution, causing it to turn dark brown immediately. The vial was re-sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and removed from the glove box. The mixture was allowed to stir at 22 °C for 30 min under an atmosphere of N_2. Allene **2.11a** (19.8 mg, 0.100 mmol, 1.0 equiv.) and benzaldehyde (**2.9a**; 11.2 μL, 0.110 mmol, 1.1 equiv.) were added through a syringe. The resulting solution was allowed to stir at 22 °C for eight hours before the reaction was quenched by passing the mixture through a short plug of Celite

and silica gel and eluted with Et_2O (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide yellow oil, which was dissolved in thf (0.5 mL). Next, $NaBO_3$•$4H_2O$ (76.9 mg, 0.500 mmol, 5.0 equiv.) and H_2O (0.5 mL) were added. The resulting mixture was allowed to stir at 22 °C for one hour. The reaction was quenched by passing the mixture through a short plug of silica gel and anhydrous $MgSO_4$ and eluted with Et_2O (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide colorless oil, which was purified by silica gel chromatography (hexanes:ethyl acetate = 10:1) to afford the **2.12a** as colorless oil (25.7 mg, 0.080 mmol of **2.12a**, 80% yield).

5-((*tert*-Butyldimethylsilyl)oxy)-3-(hydroxy(phenyl)methyl)pentan-2-one (2.12a). IR (neat): 3431 (br), 2954 (m), 2928 (m), 2856 (m), 1703 (m), 1493 (w), 1254 (m), 1090 (s), 1007 (w), 834 (s), 776 (s), 701 (s), 662 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.33–7.31 (4H, m), 7.27–7.24 (1H, m), 4.93 (1H, d, *J* = 6.0 Hz), 3.59–3.52 (3H, m), 3.03 (1H, app. dd, *J* = 11.6, 6.0 Hz), 2.00 (3H, s), 1.93–1.87 (2H, m), 0.87 (9H, s), 0.02 (3H, s), 0.002 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 212.7, 142.1, 128.5, 127.7, 126.3, 73.8, 61.7, 57.3, 31.3, 30.6, 26.0, 18.4, –5.4; HRMS (ESI^+): Calcd for $C_{18}H_{31}O_3Si_1$ $[M+H]^+$: 323.20425; Found: 323.20456.

5-((*tert*-Butyldimethylsilyl)oxy)-3-(hydroxy(naphthalen-1-yl)methyl)pentan-2-one (2.12b). IR (neat): 3448 (br), 2954 (m), 2928 (m), 2856 (m), 1701 (m), 1511 (w), 1255 (m), 1084 (s), 1032 (m), 939 (w), 833 (s), 776 (s), 732 (m), 660 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.01 (1H, d, *J* = 8.4 Hz), 7.88–7.86 (1H, m), 7.78 (1H, d, *J* = 8.0 Hz), 7.69 (1H, d, *J* = 7.2 Hz), 7.54–7.46 (3H, m), 5.77 (1H, dd, *J* = 4.0, 2.4 Hz), 3.64 (1H, d, *J* = 2.4 Hz), 3.52–3.47 (1H, m), 3.34–3.26 (2H, m), 2.14 (3H, s), 1.96–1.83 (2H, m), 0.76 (9H, s), –0.10 (3H, s), –0.20 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 213.5, 136.9,

134.0, 130.1, 129.2, 128.3, 126.3, 125.6, 125.5, 124.6, 122.9, 70.4, 61.5, 54.6, 31.0, 29.7, 18.2, –5.5, –5.7; HRMS (ESI$^+$): Calcd for $C_{22}H_{31}O_2Si_1$ [M+H–H_2O]$^+$: 355.20933; Found: 355.21032.

5-((*tert*-Butyldimethylsilyl)oxy)-3-((2-chlorophenyl)(hydroxy)methyl)pentan-2-one (2.12c). IR (neat): 3458 (br), 2954 (m), 2928 (m), 2856 (m), 1702 (m), 1471 (w), 1254 (m), 1170 (m), 1093 (s), 1006 (w), 832 (s), 775 (s), 704 (m), 680 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.61 (1H, dd, *J* = 7.6, 1.6 Hz), 7.34–7.28 (2H, m), 7.24–7.19 (1H, m), 5.37 (1H, app. t, *J* = 2.4 Hz), 3.59 (1H, d, *J* = 2.4 Hz), 3.51–3.45 (1H, m), 3.37–3.32 (1H, m), 3.28–3.24 (1H, m), 2.31 (3H, s), 1.92–1.83 (1H, m), 1.70–1.62 (1H, m), 0.82 (9H, s), –0.04 (3H, s), –0.09 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 214.0, 138.7, 131.4, 129.6, 128.7, 128.5, 127.0, 69.7, 61.4, 51.9, 30.8, 28.3, 25.9, 18.3, –5.4, –5.5; HRMS (ESI$^+$): Calcd for $C_{18}H_{30}Cl_1O_3Si_1$ [M+H]$^+$: 357.16527; Found: 357.16429.

5-((*tert*-Butyldimethylsilyl)oxy)-3-(hydroxy(*o*-tolyl)methyl)pentan-2-one (2.12d). IR (neat): 3421 (br), 2955 (s), 2929 (s), 2857 (m), 1709 (m), 1471 (w), 1256 (m), 1166 (w), 1094 (s), 1026 (m), 940 (w), 835 (s), 776 (s), 759 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.50 (1H, d, *J* = 7.6 Hz), 7.22 (1H, t, *J* = 7.2 Hz), 7.16 (1H, td, *J* = 7.2, 1.2 Hz), 7.11 (1H, d, *J* = 7.6 Hz), 5.14 (1H, dd, *J* = 5.6, 2.4 Hz), 3.59–3.55 (1H, m), 3.53–3.49 (1H, m), 3.34 (1H, d, *J* = 2.4 Hz), 3.09–3.05 (1H, m), 2.31 (3H, s), 2.03 (3H, s), 2.01–1.86 (2H, m), 0.86 (9H, s), 0.002 (3H, s), –0.02 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 212.7, 139.9, 134.4, 130.7, 127.6, 126.5, 126.3, 70.1, 61.7, 55.1, 31.2, 30.3, 26.0, 19.3, 18.3, –5.4; HRMS (ESI$^+$): Calcd for $C_{19}H_{31}O_2Si_1$ [M+H–H_2O]$^+$: 319.20933; Found: 319.21078.

5-((*tert*-Butyldimethylsilyl)oxy)-3-(hydroxy(4-methoxyphenyl)methyl)pentan-2-one (2.12e). IR (neat): 3432 (br), 2953 (m), 2929 (m), 2856 (m), 1707 (m), 1512 (s), 1388 (w), 1247 (s), 1173 (m), 1091 (s), 1032 (s), 938 (w), 830 (s), 775 (s), 728 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.24 (2H, d, *J* = 8.8 Hz), 6.86 (2H, d, *J* = 8.8 Hz), 4.84 (1H, app. d, *J* = 6.4 Hz), 3.79 (3H, s), 3.59 (2H, app. t, *J* = 5.6 Hz), 3.41 (1H, s), 2.99 (1H, app. dd, *J* = 12.0, 6.4 Hz), 1.96 (3H, s), 1.93–1.88 (2H, m), 0.87 (9H, s), 0.02 (3H, s), 0.01 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 212.6, 159.2, 134.3, 127.6, 113.9, 73.7, 61.8, 57.7, 55.4, 31.5, 31.0, 26.0, 18.4, –5.4; HRMS (ESI^+): Calcd for $C_{19}H_{31}O_3Si_1$ $[M+H–H_2O]^+$: 335.20425; Found: 335.20411.

5-((*tert*-Butyldimethylsilyl)oxy)-3-((4-chlorophenyl)(hydroxy)methyl)pentan-2-one (2.12f). IR (neat): 3445 (br), 2955 (m), 2928 (m), 2857 (m), 1706 (m), 1492 (w), 1256 (m), 1092 (s), 1033 (m), 939 (w), 834 (s), 777 (s), 731 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.32–7.27 (4H, m), 4.93 (1H, dd, *J* = 5.6, 1.6 Hz), 3.70 (1H, d, *J* = 1.6 Hz), 3.59–3.56 (2H, m), 3.00–2.96 (1H, m), 2.04 (3H, s), 1.94–1.81 (2H, m), 0.87 (9H, s), 0.03 (3H, s), 0.02 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 212.5, 140.6, 133.4, 128.7, 127.8, 73.1, 61.6, 57.2, 31.4, 30.5, 26.0, 18.4, –5.4; HRMS (ESI^+): Calcd for $C_{18}H_{30}Cl_1O_3Si_1$ $[M+H]^+$: 357.16527; Found: 357.16585.

3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-4-hydroxydodecan-2-one (2.12g). IR (neat): 3458 (br), 2954 (m), 2925 (s), 2855 (m), 1703 (m), 1464 (w), 1254 (m), 1093 (s), 938 (w), 833 (s), 775 (s), 721 (w), 662 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 3.89–3.82 (1H, m), 3.72–3.68 (1H, m), 3.64–3.59 (1H, m), 2.89 (1H, d, *J* = 2.8 Hz), 2.75–2.71 (1H, m), 2.22 (3H, s), 1.94–1.87 (1H, m), 1.84–1.79 (1H, m), 1.48–1.43 (1H, m), 1.40–1.20 (16H, m), 0.89 (9H, s), 0.04 (6H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 213.1, 71.3, 61.5,

54.7, 34.9, 32.0, 31.0, 29.7, 29.5, 29.4, 26.2, 26.1, 26.0, 22.8, 18.4, 14.3, –5.3, –5.4; HRMS (ESI^+): Calcd for $C_{20}H_{43}O_3Si_1$ $[M+H]^+$: 359.29815; Found: 359.29876.

4-Hydroxy-3-methyl-4-(4-(trifluoromethyl)phenyl)butan-2-one (2.12h). IR (neat): 3445 (br), 2917 (w), 2849 (w), 1702 (m), 1459 (w), 1322 (s), 1162 (m), 1118 (s), 1066 (s), 1017 (m), 889 (m), 660 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.60 (2H, d, *J* = 8.4 Hz), 7.45 (2H, d, *J* = 8.4 Hz), 5.21 (1H, d, *J* = 2.8 Hz), 3.28 (1H, s), 2.82 (1H, qd, *J* = 7.2, 3.2 Hz), 2.21 (3H, s), 1.06 (3H, d, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 213.7, 145.8 (app. d, *J* = 1.5 Hz), 129.7 (q, *J* = 32.0 Hz), 126.4, 125.3 (q, *J* = 3.7 Hz), 124.3 (q, *J* = 270.8 Hz), 72.1, 52.8, 29.3, 9.7; HRMS (ESI^+): Calcd for $C_{12}H_{14}F_3O_2$ $[M+H]^+$: 247.09459; Found: 247.09474.

4-(3-Bromophenyl)-4-hydroxy-3-methylbutan-2-one (2.12i). IR (neat): 3449 (br), 2963 (w), 2925 (m), 1703 (m), 1569 (w), 1474 (w), 1260 (m), 1070 (m), 1022 (m), 906 (s), 789 (m), 728 (s), 648 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.50–7.49 (1H, m), 7.41–7.37 (1H, m), 7.23–7.20 (2H, m), 5.12–5.10 (1H, m), 3.19 (1H, s), 2.80 (1H, qd, *J* = 7.2, 3.2 Hz), 2.20 (3H, s), 1.06 (3H, d, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 213.7, 144.2, 130.5, 130.0, 129.1, 124.6, 122.7, 72.0, 52.9, 29.4, 9.8; HRMS (ESI^+): Calcd for $C_{11}H_{17}Br_1N_1O_2$ $[M+NH_4]^+$: 274.04427; Found: 274.04551.

4-Cyclohexyl-4-hydroxy-3-methylbutan-2-one (2.12j). IR (neat): 3470 (br), 2922 (s), 2851 (m), 1699 (s), 1449 (m), 1357 (m), 1178 (m), 1087 (w), 977 (m), 921 (w), 866 (w), 682 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 3.63 (1H, d, *J* = 7.2 Hz), 2.70 (1H, qd, *J* = 5.6, 2.0 Hz), 2.56 (1H, s), 2.20 (3H, s), 2.09–2.06 (1H, m), 1.77–1.72 (2H, m), 1.68–1.65 (1H, m), 1.57–1.54 (1H, m), 1.38–1.31 (1H, m), 1.26–1.15 (3H, m), 1.13 (3H, d, *J* = 5.6

Hz), 1.00–0.88 (2H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 214.1, 75.1, 48.0, 40.2, 29.6, 29.1, 29.0, 26.5, 26.2, 26.0, 9.2; HRMS (ESI^+): Calcd for $C_{11}H_{21}O_2$ $[M+H]^+$: 185.15415; Found: 185.15362.

(*E*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-4-hydroxy-6-phenylhex-5-en-2-one (2.17a). IR (neat): 3439 (br), 2954 (m), 2928 (m), 2856 (m), 1705 (m), 1360 (m), 1254 (m), 1169 (w), 1090 (s), 967 (m), 832 (s), 775 (s), 693 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38–7.36 (2H, m), 7.34–7.28 (2H, m), 7.27–7.21 (1H, m), 6.63 (1H, d, *J* = 16.0 Hz), 6.18 (1H, dd, *J* = 16.0, 6.4 Hz), 4.57–4.54 (1H, m), 3.73–3.62 (2H, m), 3.17 (1H, s), 2.95–2.91 (1H, m), 2.24 (3H, s), 1.98–1.84 (2H, m), 0.89 (9H, s), 0.05 (6H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 212.3, 136.7, 131.5, 129.3, 128.7, 127.9, 126.7, 72.6, 61.6, 55.3, 31.4, 30.5, 26.0, 18.4, –5.3, –5.4; HRMS (ESI^+): Calcd for $C_{20}H_{31}O_2Si_1$ $[M+H–H_2O]^+$: 331.20933; Found: 331.20889.

(*E*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-4-hydroxynon-5-en-2-one (2.17b). IR (neat): 3454 (br), 2956 (m), 2927 (m), 2857 (m), 1706 (m), 1463 (w), 1254 (m), 1091 (s), 969 (m), 832 (s), 775 (s), 662 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.72–5.65 (1H, m), 5.44 (1H, dd, *J* = 15.6, 7.2 Hz), 4.29–4.26 (1H, m), 3.71–3.57 (2H, m), 2.82–2.78 (2H, m), 2.20 (3H, s), 2.04–1.98 (2H, m), 1.93–1.78 (2H, m), 1.39 (2H, q, *J* = 7.2 Hz), 0.90–0.87 (12H, m), 0.04 (6H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 212.2, 133.6, 129.9, 73.0, 61.7, 55.6, 34.5, 31.5, 30.6, 26.0, 22.4, 18.4, 13.8, –5.3, –5.4; HRMS (ESI^+): Calcd for $C_{17}H_{33}O_2Si_1$ $[M+H–H_2O]^+$: 297.22498; Found: 297.22540.

■ **Representative Experimental Procedure for Cu-Catalyzed Cu–B Addition/Addition to Ketones Followed by *Oxidative Work-up*:** In a N_2-filled glove

box, an oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with imidazolium salt **2.15b** (2.1 mg, 0.0050 mmol, 5.0 mol %) or *rac*-binap (3.1 mg, 0.0050 mmol, 5.0 mol %), CuCl (0.5 mg, 0.005 mmol, 5.0 mol %), NaO*t*-Bu (14.4 mg, 0.150 mmol, 1.5 equiv.) and tetrahydrofuran (thf, 0.5 mL). The vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the solution was allowed to stir at 22 °C for one hour. Bis(pinacolato)diboron (27.9 mg, 0.110 mmol, 1.1 equiv.) was added to the solution, causing it to turn dark brown immediately. The vial was re-sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and removed from the glove box. The mixture was allowed to stir at 22 °C for 30 min under an atmosphere of N_2. Allene **2.11a** (19.8 mg, 0.100 mmol, 1.0 equiv.) and acetophenone (**2.10a**; 12.8 μL, 0.110 mmol, 1.1 equiv.) were added. The mixture was allowed to stir at 22 °C for 18 h before the reaction was quenched by passing the mixture through a short plug of celite and silica gel and eluted with Et_2O (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide yellow oil, which was dissolved in tetrahydrofuran (thf, 0.5 mL). $NaBO_3$•$4H_2O$ (76.9 mg, 0.500 mmol, 5.0 equiv.) and H_2O (0.5 mL) were added. The resulting mixture was allowed to stir at 22 °C for one hour. The reaction was quenched by passing the mixture through a short plug of silica gel and anhydrous $MgSO_4$ and eluted with Et_2O (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide colorless oil, which was purified by silica gel chromatography (hexanes:Et_2O = 18:1) to afford the desired product **2.13a** as colorless oil (27.9 mg, 0.083 mmol, 83% yield with **2.13**; 28.6 mg, 0.085 mmol, 85% yield with *rac*-binap).

3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-4-hydroxy-4-phenylpentan-2-one (2.13a). IR (neat): 3482 (br), 2954 (m), 2929 (s), 1697 (s), 1447 (m), 1256 (s), 1202 (w), 1172 (m),

1170 (w), 1099 (s), 939 (w), 834 (s), 777 (m), 730 (s), 657 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.44–7.41 (2H, m), 7.35–7.31 (2H, m), 7.25–7.21 (1H, m), 4.04 (1H, s), 3.43–3.37 (1H, m), 3.34–3.29 (1H, m), 3.20 (1H, dd, *J* = 9.6, 4.0 Hz), 2.30 (3H, s), 1.82–1.75 (1H, m), 1.52 (3H, s), 1.50–1.44 (1H, m), 0.85 (9H, s), –0.04 (3H, s), –0.07 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 217.0, 146.0, 128.3, 126.8, 125.0, 75.1, 61.6, 57.9, 33.9, 32.0, 29.7, 26.0, 18.4, –5.41, –5.42; HRMS (ESI^+): Calcd for $C_{19}H_{33}O_3Si_1$ $[M+H–H_2O]^+$: 337.21990; Found: 337.22030.

3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-4-hydroxy-4-(2-(trifluoromethyl)phenyl)pentan-2-one (2.13b). IR (neat): 3466 (br), 2955 (m), 2929 (m), 1698 (m), 1463 (w), 1383 (m), 1303 (s), 1165 (m), 1099 (s), 1034 (s), 960 (w), 833 (s), 670 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.79–7.75 (2H, m), 7.52–7.48 (1H, m), 7.37–7.33 (1H, m), 4.22 (1H, s), 3.58 (1H, dd, *J* = 10.0, 3.6 Hz), 3.46–3.36 (2H, m), 2.24 (3H, s), 1.92–1.84 (1H, m), 1.64 (3H, s), 1.49–1.41 (1H, m), 0.84 (9H, s), –0.04 (3H, s), –0.07 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 216.3, 144.7, 131.7, 129.3, 128.2 (q, *J* = 6.5 Hz), 127.3, 127.0 (q, *J* = 30.5 Hz), 124.9 (q, *J* = 272.3 Hz), 76.0, 61.5, 56.4, 34.0, 32.2, 29.3, 25.9, 18.3, –5.50, –5.51; HRMS (ESI^+): Calcd for $C_{20}H_{32}F_3O_3Si_1$ $[M+H]^+$: 405.20728; Found: 405.20693.

3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-4-hydroxy-4-(2-methoxyphenyl)pentan-2-one (2.13c). IR (neat): 3470 (br), 2954 (m), 2856 (m), 1694 (m), 1583 (w), 1488 (m), 1236 (s), 1096 (s), 1027 (m), 938 (w), 832 (s), 755 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.46 (1H, dd, *J* = 8.0, 1.6 Hz), 7.26–7.22 (1H, m), 6.95 (1H, td, *J* = 7.6, 1.2 Hz), 6.91–6.89 (1H, m), 4.51 (1H, s), 3.89 (3H, s), 3.77 (1H, dd, *J* = 10.4, 3.2 Hz), 3.45–3.39 (2H, m), 2.04 (3H, s), 1.88–1.79 (1H, m), 1.65–1.58 (1H, m), 1.57 (3H, s), 0.85 (9H, s), –

0.037 (3H, s), –0.044 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 215.8, 156.2, 133.4, 128.5, 127.7, 121.1, 111.2, 75.2, 61.8, 55.4, 55.2, 33.6, 31.8, 26.0, 25.5, 18.3, –5.40, –5.42; HRMS (ESI$^+$): Calcd for $C_{20}H_{33}O_3Si_1$ $[M+H–H_2O]^+$: 349.21990; Found: 349.22066.

3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-4-hydroxy-4-(naphthalen-2-yl)pentan-2-one (2.13d). IR (neat): 3483 (br), 2954 (m), 2926 (s), 2855 (m), 1697 (m), 1507 (w), 1360 (m), 1256 (m), 1171 (w), 1097 (s), 939 (w), 834 (s), 777 (s), 748 (m), 663 (w), 477 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.99 (1H, s), 7.87–7.81 (3H, m), 7.50–7.46 (3H, m), 4.24 (1H, s), 3.40–3.30 (3H, m), 2.36 (3H, s), 1.88–1.77 (1H, m), 1.61 (3H, s), 1.52–1.46 (1H, m), 0.84 (9H, s), –0.06 (3H, s), –0.10 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 217.1, 143.2, 133.3, 132.4, 128.4, 128.0, 127.6, 126.2, 125.9, 123.9, 123.2, 75.4, 61.5, 57.5, 34.1, 32.1, 29.9, 26.0, 18.3, –5.5; HRMS (ESI$^+$): Calcd for $C_{23}H_{33}O_2Si_1$ $[M+H–H_2O]^+$: 369.22520; Found: 369.22498.

4-(4-Bromophenyl)-3-(2-((*tert*-butyldimethylsilyl)oxy)ethyl)-4-hydroxypentan-2-one (2.13e). IR (neat): 3479 (br), 2955 (m), 2927 (m), 2856 (m), 1697 (m), 1462 (w), 1256 (m), 1169 (w), 1096 (s), 1007 (w), 833 (s), 777 (s), 696 (m), 611 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.46–7.42 (2H, m), 7.32–7.29 (2H, m), 4.13 (1H, s), 3.43–3.31 (2H, m), 3.15 (1H, dd, J = 9.6, 3.6 Hz), 2.32 (3H, s), 1.80–1.72 (1H, m), 1.49 (3H, s), 1.44–1.25 (1H, m), 0.85 (9H, s), –0.04 (3H, s), –0.06 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 216.8, 145.1, 131.4, 127.0, 120.8, 75.0, 61.4, 57.7, 34.1, 32.0, 29.7, 26.0, 18.4, –5.4; HRMS (ESI$^+$): Calcd for $C_{19}H_{30}Br_1O_2Si_1$ $[M+H–H_2O]^+$: 397.11984; Found: 397.11814.

3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-4-hydroxy-4-(4-(trifluoromethyl)phenyl)pentan-2-one (2.13f). IR (neat): 3467 (br), 2955 (m), 2927 (m),

1697 (m), 1462 (w), 1256 (m), 1169 (w), 1094 (s), 938 (w), 831 (s), 775 (s), 695 (s), 661 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.61–7.55 (4H, m), 4.24 (1H, s), 3.47–3.37 (1H, m), 3.34–3.29 (1H, m), 3.22 (1H, dd, *J* = 9.6, 3.6 Hz), 2.35 (3H, s), 1.81–1.74 (1H, m), 1.48 (3H, s), 1.40–1.33 (1H, m), 0.85 (9H, s), –0.04 (3H, s), –0.08 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 216.8, 150.0 (app. d, *J* = 1.2 Hz), 129.2 (q, *J* = 32.3 Hz), 125.5, 125.3 (q, *J* = 3.8 Hz), 124.3 (q, *J* = 270.5 Hz), 75.1, 61.3, 57.3, 34.1, 32.0, 29.8, 26.0, 18.3, –5.4, –5.5; HRMS (ESI^+): Calcd for $C_{20}H_{32}F_3O_3Si_1$ $[M+H]^+$: 405.20728; Found: 405.20831.

3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-4-hydroxy-4-phenylhexan-2-one (2.13g). IR (neat): 3476 (br), 2955 (m), 2928 (m), 2857 (m), 1694 (m), 1495 (w), 1388 (w), 1334 (m), 1093 (m), 1005 (w), 972 (w), 832 (s), 776 (s), 701 (s), 582 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.39–7.36 (2H, m), 7.34–7.30 (2H, m), 7.24–7.19 (1H, m), 3.87 (1H, s), 3.39–3.34 (1H, m), 3.31–3.26 (1H, m), 3.23 (1H, dd, *J* = 10.0, 3.6 Hz), 2.36 (3H, s), 1.94–1.85 (1H, m), 1.81–1.72 (1H, m), 1.71–1.64 (1H, m), 1.45–1.40 (1H, m), 0.85 (9H, s), 0.62 (3H, t, *J* = 7.2 Hz), –0.06 (3H, s), –0.09 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 217.9, 143.2, 128.2, 126.6, 125.7, 78.5, 61.5, 57.5, 34.5, 34.3, 32.1, 26.0, 18.3, 7.9, –5.42, –5.43; HRMS (ESI^+): Calcd for $C_{20}H_{33}O_2Si_1$ $[M+H–H_2O]^+$: 333.22498; Found: 333.22639.

3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-4-hydroxy-4-(thiophen-2-yl)pentan-2-one (2.13h). IR (neat): 3479 (br), 2954 (m), 2927 (m), 2856 (m), 1697 (m), 1462 (w), 1256 (m), 1169 (m), 1096 (s), 1023 (w), 938 (w), 833 (s), 777 (m), 696 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.18 (1H, dd, *J* = 5.2, 1.6 Hz), 6.95 (1H, dd, *J* = 5.2, 3.6 Hz), 6.84 (1H, dd, *J* = 3.6, 1.6 Hz), 4.13 (1H, s), 3.51–3.39 (2H, m), 3.14 (1H, dd, *J* = 9.2, 3.6 Hz),

2.22 (3H, s), 1.89–1.81 (1H, m), 1.76–1.68 (1H, m), 1.60 (3H, s), 0.86 (9H, s), –0.02 (3H, s), –0.04 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 215.8, 151.3, 126.9, 123.9, 122.4, 75.0, 61.7, 59.5, 33.5, 32.1, 30.1, 26.0, 18.4, –5.38, –5.40; HRMS (ESI$^+$): Calcd for $C_{17}H_{29}O_2S_1Si_1$ [M+H–H_2O]$^+$: 325.16575; Found: 325.16551.

5-((*tert*-Butyldimethylsilyl)oxy)-3-(5-hydroxy-6,7,8,9-tetrahydro-5*H*-benzo[7]annulen-5-yl)pentan-2-one (2.13i). IR (neat): 3470 (br), 2926 (m), 2856 (m), 1694 (m), 1360 (w), 1255 (m), 1164 (w), 1087 (s), 964 (w), 833 (s), 776 (s), 567 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.81 (1H, dd, *J* = 8.0, 1.2 Hz), 7.20 (1H, td, *J* = 7.6, 1.2 Hz), 7.12 (1H, td, *J* = 7.6, 1.6 Hz), 7.05–7.03 (1H, m), 4.52 (1H, s), 3.76–3.73 (1H, m), 3.32–3.27 (1H, m), 3.04–2.92 (2H, m), 2.75 (1H, dd, *J* = 14.0, 4.4 Hz), 2.37 (3H, s), 2.09–2.03 (1H, m), 1.94–1.74 (4H, m), 1.65–1.55 (2H, m), 1.48–1.42 (1H, m), 0.84 (9H, s), –0.08 (3H, s), –0.11 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 217.1, 143.9, 138.7, 131.0, 127.6, 127.2, 126.3, 78.7, 61.1, 41.0, 37.4, 32.6, 31.8, 30.5, 29.8, 28.0, 26.0, 18.3, –5.47, –5.48; HRMS (ESI$^+$): Calcd for $C_{22}H_{35}O_2Si_1$ [M+H–H_2O]$^+$: 359.24063; Found: 359.24132.

4-Hydroxy-3-methyl-4-phenylpentan-2-one (2.13j). IR (neat): 3482 (br), 2974 (w), 2877 (w), 1692 (s), 1495(m), 1373 (m), 1236 (m), 1085 (m), 1024 (m), 911 (m), 866 (w), 786 (m), 701 (s), 657 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.43–7.39 (2H, m), 7.36–7.32 (2H, m), 7.26–7.22 (1H, m), 4.15 (1H, s), 2.99 (1H, q, *J* = 7.2 Hz), 2.27 (3H, s), 1.55 (3H, s), 0.90 (3H, d, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 216.6, 145.8, 128.3, 126.7, 124.9, 75.0, 55.0, 31.6, 29.7, 12.6; HRMS (ESI$^+$): Calcd for $C_{12}H_{15}O_2$ [M+H–H_2O]$^+$: 175.11229; Found: 175.11255.

(*E*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-4-hydroxy-4-methyl-6-phenylhex-5-en-2-one (2.19a). IR (neat): 3387 (br), 3027 (m), 2976 (m), 1709 (w), 1601 (w), 1449 (s), 1372 (s), 1146 (s), 1008 (m), 952 (w), 851 (m), 750 (m), 674 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.39–7.36 (2H, m), 7.33–7.29 (2H, m), 7.26–7.21 (1H, m), 6.67 (1H, d, *J* = 16.4 Hz), 6.08 (1H, d, *J* = 16.4 Hz), 3.62–3.54 (3H, m), 2.95–2.92 (1H, m), 2.32 (3H, s), 1.90–1.85 (2H, m), 1.38 (3H, s), 0.87 (9H, s), –0.02 (6H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 216.0, 137.0, 134.0, 128.7, 128.5, 127.6, 126.6, 74.1, 61.8, 57.0, 33.8, 32.1, 28.1, 26.0, 18.4, –5.33, –5.55; HRMS (ESI^+): Calcd for $C_{21}H_{33}O_2Si_1$ $[M+H–H_2O]^+$: 345.22498; Found: 345.22596.

(*E*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-4-hydroxy-4-methylundec-5-en-2-one (2.19b). IR (neat): 3489 (br), 2955 (m), 2926 (s), 2855 (m), 1698 (m), 1461 (w), 1360 (m), 1169 (w), 1097 (s), 1007 (w), 834 (s), 776 (s), 732 (m), 679 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 5.68 (1H, dt, *J* = 15.6, 6.8 Hz), 5.35 (1H, d, *J* = 15.6 Hz), 3.64–3.52 (2H, m), 3.21 (1H, s), 2.79 (1H, app. t, *J* = 6.8 Hz), 2.28 (3H, s), 2.21–2.15 (1H, m), 2.05–2.00 (2H, m), 1.84–1.80 (2H, m), 1.43–1.33 (3H, m), 1.32–1.28 (2H, m), 1.28–1.19 (6H, m), 0.88 (9H, s), 0.030 (3H, s), 0.026 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 215.9, 134.3, 129.8, 73.6, 61.9, 57.3, 33.8, 32.4, 31.9, 31.5, 29.1, 28.0, 26.0, 22.6, 18.4, 14.2, –5.31, –5.34; HRMS (ESI^+): Calcd for $C_{20}H_{39}O_2Si_1$ $[M+H–H_2O]^+$: 339.27193; Found: 339.27239.

(*E*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-4-hydroxy-4-methyl-6-(2,6,6-trimethylcyclohex-1-en-1-yl)hex-5-en-2-one (2.19c). IR (neat): 3474 (br), 2955 (m), 2927 (m), 2857 (m), 1697 (m), 1461 (w), 1359 (m), 1255 (m), 1169 (w), 1098 (s), 975 (m), 834 (s), 776 (m), 661 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 6.11 (1H, d, *J* = 16.0

Hz), 5.31 (1H, d, J = 16.0 Hz), 3.64–3.52 (2H, m), 3.25 (1H, s), 2.86 (1H, dd, J = 9.2, 4.4 Hz), 2.31 (3H, s), 1.98–1.95 (2H, m), 1.92–1.87 (2H, m), 1.76 (3H, s), 1.66–1.57 (2H, m), 1.46–1.43 (2H, m), 1.27 (3H, s), 0.99 (3H, s), 0.98 (3H, s), 0.87 (9H, s), 0.02 (6H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 216.2, 137.8, 137.2, 128.3, 126.6, 74.3, 61.8, 57.2, 39.6, 34.2, 33.9, 32.9, 32.4, 29.0, 28.9, 28.5, 26.0, 21.6, 19.4, 18.4, –5.4; HRMS (ESI^+): Calcd for $C_{24}H_{43}O_2Si_1$ $[M+H–H_2O]^+$: 391.30323; Found: 391.30360.

■ **Representative Experimental Procedure for Cu-Catalyzed Cu–B Addition/Addition to Carbonyls Followed by *Conversion to Vinylbromide*:** In a N_2-filled glove box, an oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with *rac*-binap (3.1 mg, 0.0050 mmol, 5.0 mol %), CuCl (0.5 mg, 0.005 mmol, 5.0 mol %), NaO*t*Bu (1.9 mg, 0.020 mmol, 20 mol %) and tetrahydrofuran (thf, 0.5 mL). The reaction vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the solution was allowed to stir at 22 °C for one hour. Bis(pinacolato)diboron (27.9 mg, 0.110 mmol, 1.1 equiv.) was added to the solution, causing it to turn dark brown immediately. The vial was re-sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and removed from the glove box. The resulting solution was allowed to stir at 22 °C for 30 min under an atmosphere of N_2. Allene **2.11b** (11.6 mg, 0.100 mmol, 1.0 equiv.) and benzaldehyde (**2.9a**; 11.2 μL, 0.110 mmol, 1.1 equiv.) were added through syringes. The resulting mixture was allowed to stir at 22 °C for eight hours before the reaction was quenched by passing the mixture through a short plug of Celite and silica gel and eluted with Et_2O (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide yellow oil, which was used in the next step without further purification. In a N_2-filled glove-box, an oven-dried vial (4 mL, 17 × 38 mm) with

a magnetic stir bar was charged with $CuBr_2$ (67.0 mg, 0.300 mmol, 3.0 equiv.), the solution of unpurified product obtained above in MeOH (1.0 mL) and H_2O (0.5 mL). The vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the solution was allowed to stir at 80 °C for 6 h. The reaction mixture was washed with Et_2O (3 × 2 mL) after cooling to 22 °C. The combined organic layer was dried over $MgSO_4$ and was concentrated *in vacuo* to provide yellow oil, which was purified by silica gel chromatography (hexanes:ethyl acetate = 10:1) to afford the desired product **2.20a** as a colorless oil (26.9 mg, 0.089 mmol, 89% yield).

3-Bromo-1,2-diphenylbut-3-en-1-ol (2.20a). IR (neat): 3399 (br), 2917 (w), 2849 (w), 1622 (w), 1494 (m), 1452 (m), 1187 (w), 1076 (m), 893 (m), 844 (w), 753 (s), 696 (s), 598 (s), 539 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.40–7.28 (9H, m), 7.19–7.14 (1H, m), 5.70 (1H, d, *J* = 1.6 Hz), 5.40 (1H, d, *J* = 1.6 Hz), 5.37 (1H, dd, *J* = 8.0, 2.8 Hz), 3.95 (1H, d, *J* = 8.0 Hz), 1.97 (1H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 141.7, 137.2, 134.2, 129.3, 128.7, 128.4, 128.1, 127.9, 126.9, 119.4, 74.8, 63.5; HRMS (ESI^+): Calcd for $C_{16}H_{14}Br_1$ $[M+H–H_2O]^+$: 285.02789; Found: 285.02730.

4-Bromo-2,3-diphenylpent-4-en-2-ol (2.20b). IR (neat): 3561 (br), 3060 (w), 3027 (w), 2919 (m), 2850 (w), 1492 (m), 1447 (m), 1336 (w), 1279 (w), 1135 (m), 947 (m), 793 (s), 698 (s), 632 (s), 602 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.56–7.51 (1H, m), 7.42–7.36 (2H, m), 7.20–7.18 (3H, m), 7.13–7.11 (4H, m), 6.36 (1H, d, *J* = 2.0 Hz), 5.83 (1H, d, *J* = 2.0 Hz), 4.08 (1H, s), 2.27 (1H, s), 1.85 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.6, 137.2, 132.5, 129.7, 128.6, 128.0, 127.2, 126.8, 124.9, 121.2, 77.5, 66.7, 29.5; HRMS (ESI^+): Calcd for $C_{17}H_{16}Br_1$ $[M+H–H_2O]^+$: 299.04354; Found: 299.04351.

3-(1-Bromovinyl)-4-phenylpentane-1,4-diol (2.21a). IR (neat): 3386 (br), 2977 (m), 1492 (m), 1260 (w), 1145 (m), 1028 (m), 948 (m), 850 (w), 762 (m), 732 (m), 700 (s), 672 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.46–7.42 (2H, m), 7.36–7.32 (2H, m), 7.26–7.22 (1H, m), 5.83 (1H, d, *J* = 1.6 Hz), 5.71 (1H, d, *J* = 1.6 Hz), 3.62–3.57 (1H, m), 3.45–3.39 (1H, m), 2.92 (1H, dd, *J* = 10.8, 3.2 Hz), 1.88–1.80 (1H, m), 1.62 (3H, s), 1.50–1.46 (1H, m), 1.26 (1H, s), 1.23 (3H, s), 1.17 (1H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.0, 133.7, 128.2, 126.8, 125.0, 121.9, 76.1, 60.5, 55.9, 30.7, 25.0; HRMS (ESI^+): Calcd for $C_{13}H_{16}Br_1O_1$ $[M+H–H_2O]^+$: 267.03845; Found: 267.03963.

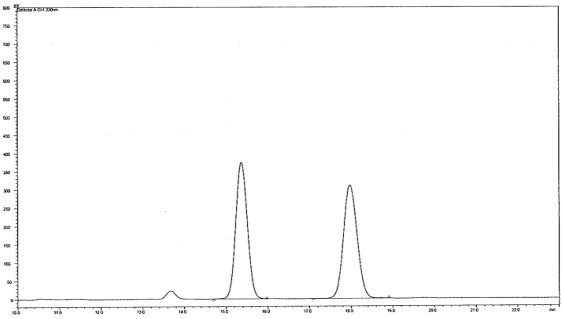
3-(2-(Benzyloxy)ethyl)-4-bromo-2-phenylpent-4-en-2-ol (2.21b). IR (neat): 3472 (br), 2967 (w), 2929 (w), 2855 (m), 1446 (m), 1261 (w), 1098 (m), 1068 (m), 1027 (m), 904 (m), 845 (w), 762 (m), 734 (s), 698 (s), 651 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.48–7.45 (2H, m), 7.37–7.29 (4H, m), 7.29–7.23 (4H, m), 5.79 (1H, d, *J* = 1.6 Hz), 5.69 (1H, d, *J* = 1.6 Hz), 4.35–4.27 (2H, m), 3.44–3.39 (1H, m), 3.37–3.31 (1H, m), 2.96 (1H, dd, *J* = 10.8, 3.2 Hz), 2.56 (1H, s), 1.88–1.80 (1H, m), 1.69–1.63 (1H, m), 1.62 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.0, 138.5, 133.7, 128.4, 128.2, 127.7, 127.6, 126.8, 125.1, 121.9, 76.0, 72.6, 67.6, 56.1, 30.1, 27.6; HRMS (ESI^+): Calcd for $C_{20}H_{22}Br_1O_1$ $[M+H–H_2O]^+$: 357.08540; Found: 357.08525.

■ **Representative Experimental Procedure for Enantioselective Cu-Catalyzed Cu–B Addition/Addition to Aldehydes Followed by Oxidative Work-up:** In a N_2-filled glove box, an oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with phosphine **2.33** (3.1 mg, 0.0050 mmol, 5.0 mol %), CuCl (0.5 mg, 0.005 mmol, 5.0 mol %), NaO*t*Bu (1.9 mg, 0.020 mmol, 20 mol %) and tetrahydrofuran (thf, 0.5 mL). The vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum)

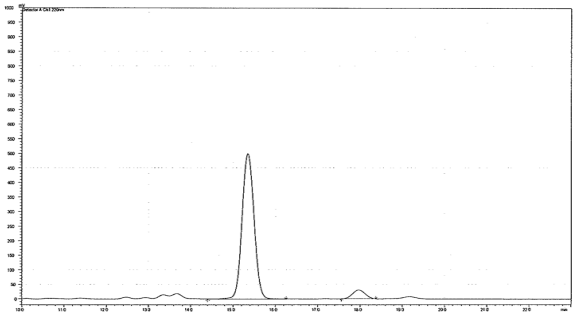
and the solution was allowed to stir at 22 °C for one hour. Bis(pinacolato)diboron (27.9 mg, 0.110 mmol, 1.1 equiv.) was added to the solution, causing it to turn dark brown immediately. The vial was re-sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and removed from the glove-box. The mixture was allowed to stir at 22 °C for 30 min under an atmosphere of N_2. At this time, the mixture was allowed to cool to –78 °C (dry ice/acetone bath) and allene **2.11a** (19.8 mg, 0.100 mmol, 1.0 equiv.) and benzaldehyde (**2.9a**; 11.2 μL, 0.110 mmol, 1.1 equiv.) were added. The vial was placed in a 4 °C cold room. After 12 hours, the solution was allowed to cool to –78 °C and the reaction was quenched by passing the mixture through a short plug of celite and silica gel and eluted with Et_2O (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide yellow oil, which was dissolved in tetrahydrofuran (thf, 0.5 mL). $NaBO_3$•$4H_2O$ (76.9 mg, 0.500 mmol, 5.0 equiv.) and H_2O (0.5 mL) were added. The resulting mixture was allowed to stir at 22 °C for one hour. The reaction was quenched by passing the mixture through a short plug of silica gel and anhydrous $MgSO_4$ and eluted with Et_2O (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide a yellow oil, which was purified by silica gel chromatography (hexanes:ethyl acetate = 10:1) to afford the desired product **2.12a** as a colorless oil (26.3 mg, 0.081 mmol, 81% yield).

The characterization of **2.12a** has been described above. Specific rotation: $[\alpha]_D^{20}$ +4.0 (*c* 1.62, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.

Enantiomeric purity of **2.12a** was determined by HPLC analysis in comparison with authentic racemic material (95:5 e.r. shown; Chiralcel OD–H column, 98:2 hexanes/ *i*PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.359	7175821	373453	50.169	54.518
2	17.969	7127558	311554	49.831	45.482

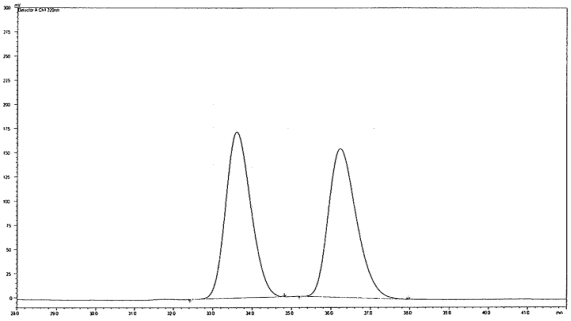


Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.341	9933670	499544	95.071	94.783
2	17.968	515053	27498	4.929	5.217

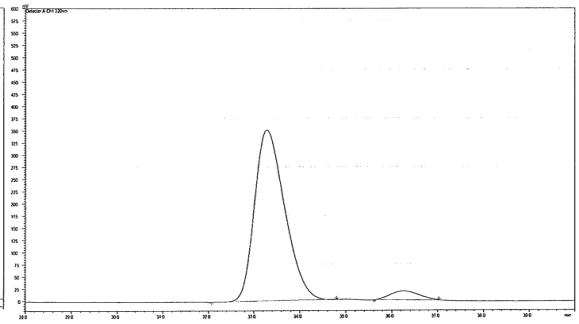
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	15.359	50.169	1	15.341	95.071
2	17.969	49.831	2	17.968	4.929

The characterization of **2.12e** has been described above. Specific rotation: $[\alpha]_D^{20}$ +2.0 (*c* 0.77, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.

Enantiomeric purity of **2.12e** was determined by HPLC analysis in comparison with authentic racemic material (95:5 e.r. shown; Chiralcel OD–H column, 98:2 hexanes/*i*PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	33.600	7658327	171961	50.024	52.729
2	36.224	7650881	154159	49.976	47.271



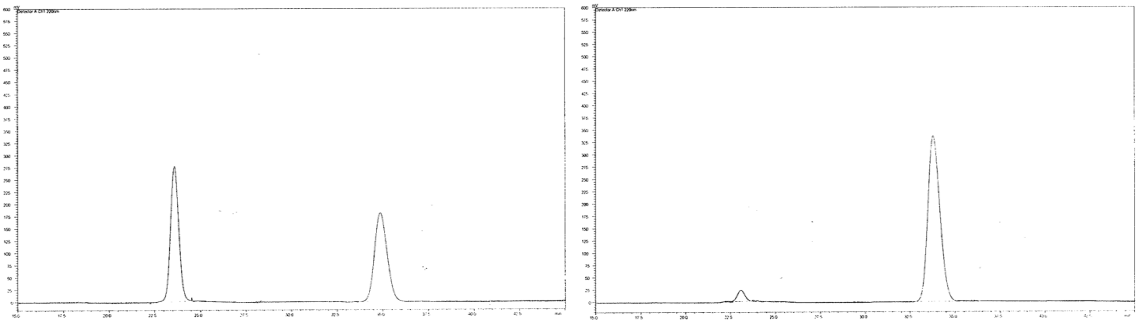
Peak#	Ret. Time	Area	Height	Area %	Height %
1	33.279	16015194	351034	95.390	95.131
2	36.246	773990	17965	4.610	4.869

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	33.600	50.024	1	33.279	95.390
2	36.224	49.976	2	36.246	4.610

(3*S*,4*R*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-4-hydroxy-6-phenylhexan-2-one (2.12k). IR (neat): 3442 (br), 3027 (m), 2952 (m), 2856 (m), 1703 (m), 1496 (w), 1254

(m), 1167 (w), 1088 (s), 937 (w), 832 (s), 776 (s), 699 (s), 662 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.30–7.27 (2H, m), 7.21–7.17 (3H, m), 3.92–3.86 (1H, m), 3.73–3.59 (2H, m), 3.08 (1H, d, J = 3.6 Hz), 2.89–2.82 (1H, m), 2.75–2.70 (1H, m), 2.69–2.65 (1H, m), 2.19 (3H, s), 1.98–1.91 (1H, m), 1.89–1.78 (2H, m), 1.71–1.63 (1H, m), 0.89 (9H, s), 0.05 (6H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 212.8, 142.0, 128.6, 128.5, 126.0, 70.5, 61.5, 55.0, 36.7, 32.5, 30.9, 29.8, 26.0, 18.4, –5.4; HRMS (ESI^+): Calcd for $C_{20}H_{35}O_3Si_1$ $[M+H]^+$: 351.23555; Found: 351.23401; Specific rotation: $[\alpha]_D^{20}$ +6.7 (*c* 1.26, $CHCl_3$) for an enantiomerically enriched sample of 96:4 e.r.

Enantiomeric purity of **2.12k** was determined by HPLC analysis in comparison with authentic racemic material (96:4 e.r. shown; Chiralcel OD–H column, 98:2 hexanes/*i*PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.578	8755495	276747	50.098	60.353
2	34.859	8721384	181797	49.902	39.647

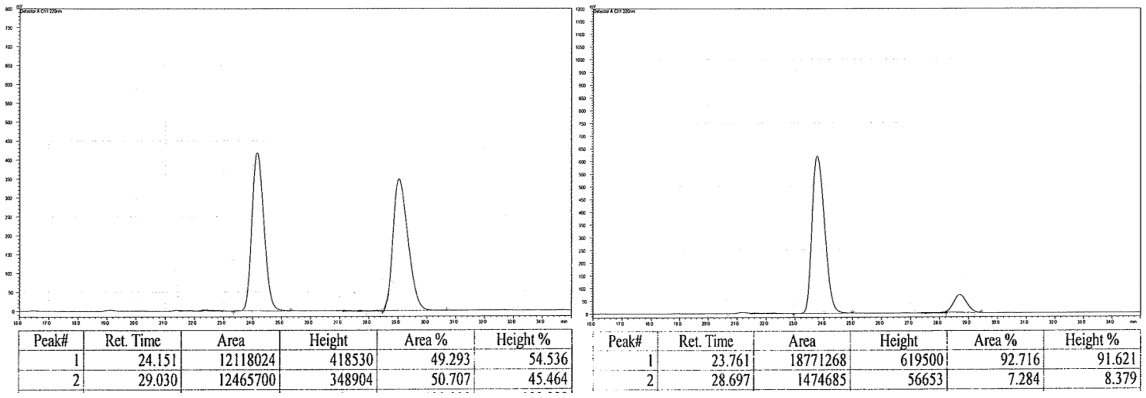
Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.074	635885	22354	3.839	6.215
2	33.775	15929584	337339	96.161	93.785

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	23.578	50.098	1	23.074	3.839
2	34.859	49.902	2	33.775	96.161

(3*S*,4*S*)-4-Hydroxy-3-methyl-4-phenylbutan-2-one (2.12l). IR (neat): 3437 (br), 3030 (w), 2976 (m), 2850 (w), 1701 (s), 1493 (m), 1357 (m), 1234 (m), 1176 (m), 1025 (m), 890 (w), 764 (m), 701 (s), 635 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.37–7.24 (5H, m), 5.12–5.08 (1H, m), 3.02 (1H, s), 2.83 (1H, qd, J = 7.2, 3.6 Hz), 2.15 (3H, s), 1.09 (3H,

d, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 213.7, 141.9, 128.4, 127.5, 126.0, 73.1, 53.3, 29.5, 10.2; HRMS (ESI^+): Calcd for $C_{11}H_{13}O_1$ $[M+H–H_2O]^+$: 161.09664; Found: 161.09619; Specific rotation: $[\alpha]_D^{20}$ –13.6 (*c* 0.96, $CHCl_3$) for an enantiomerically enriched sample of 93:7 e.r.

Enantiomeric purity of **2.12l** was determined by HPLC analysis in comparison with authentic racemic material (93:7 e.r. shown; Chiralcel OD–H column, 99:1 hexanes/*i*PrOH, 0.6 mL/min, 220 nm).



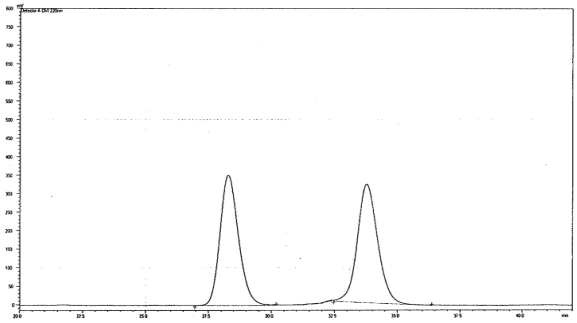
Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.151	12118024	418530	49.293	54.536
2	29.030	12465700	348904	50.707	45.464

Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.761	18771268	619500	92.716	91.621
2	28.697	1474685	56653	7.284	8.379

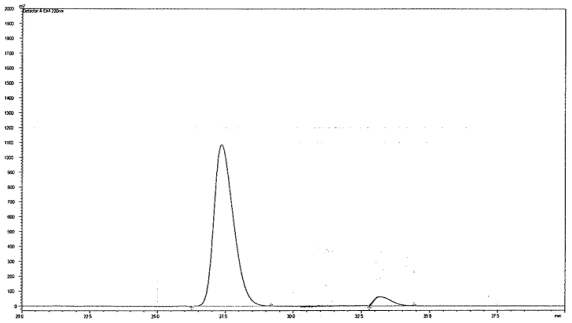
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	24.151	49.293	1	23.761	92.716
2	29.030	50.707	2	28.697	7.284

The characterization of **2.17a** has been described above. Specific rotation: $[\alpha]_D^{20}$ +7.4 (*c* 0.91, $CHCl_3$) for an enantiomerically enriched sample of 97:3 er.

Enantiomeric purity of **2.17a** was determined by HPLC analysis in comparison with authentic racemic material (97:3 er shown; Chiralcel OJ–H column, 98:2 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	28.265	18199451	352420	50.165	52.407
2	33.765	18079595	320053	49.835	47.593



Peak#	Ret. Time	Area	Height	Area %	Height %
1	27.598	59295888	1158328	96.846	96.287
2	33.602	1931081	44663	3.154	3.713

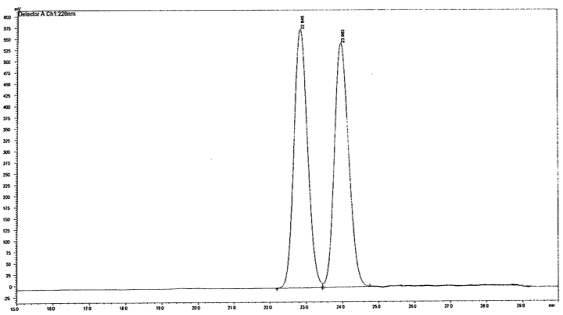
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	28.265	50.165	1	27.598	96.846
2	33.765	49.835	2	33.602	3.154

■ **Representative Experimental Procedure for Enantioselective Cu-Catalyzed Cu–B Addition/Addition to Ketones Followed by Oxidative Work-up:** In a N_2-filled glove box, an oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with phosphine **2.31** (3.2 mg, 0.0050 mmol, 5.0 mol %), CuCl (0.5 mg, 0.005 mmol, 5.0 mol%), NaO*t*Bu (14.4 mg, 0.150 mmol, 1.5 equiv.) and tetrahydrofuran (thf, 0.5 mL). The vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the solution was allowed to stir at 22 °C for one hour. Bis(pinacolato)diboron (27.9 mg, 0.110 mmol, 1.1 equiv.) was added to the solution, causing it to turn dark brown immediately. The vial was re-sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and removed from the glovebox. The mixture was allowed to stir at 22 °C for 30 min under an atmosphere of N_2. Allene **2.11a** (19.8 mg, 0.100 mmol, 1.0 equiv.) and acetophenone (**2.10a**; 12.8 μL, 0.110 mmol, 1.1 equiv.) were added. The mixture was allowed to stir at 22 °C for 18 h before the reaction was quenched by passing the mixture through a short plug of celite and silica gel and eluted with Et_2O (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide yellow oil,

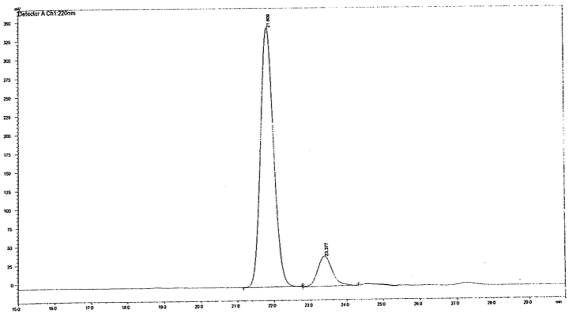
which was dissolved in tetrahydrofuran (thf, 0.5 mL). $NaBO_3 \bullet 4H_2O$ (76.9 mg, 0.500 mmol, 5.0 equiv.) and H_2O (0.5 mL) were added. The resulting mixture was allowed to stir at 22 °C for one hour. The reaction was quenched by passing the mixture through a short plug of silica gel and anhydrous $MgSO_4$ and eluted with Et_2O (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide colorless oil, which was purified by silica gel chromatography (hexanes:Et_2O = 18:1) to afford the desired product **2.13a** as a colorless oil (28.2 mg, 0.084 mmol, 83% yield).

The characterization of **2.13a** has been described above. Specific rotation: $[\alpha]_D^{20}$ +8.7 (*c* 0.64, $CHCl_3$) for an enantiomerically enriched sample of 89:11 e.r.

Enantiomeric purity of **2.13a** was determined by HPLC analysis in comparison with authentic racemic material (89:11 e.r. shown; Chiralcel OD–H column, 99:1 hexanes/*i*PrOH, 0.3 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.845	14953055	576768	50.088	51.417
2	23.963	14900443	544968	49.912	48.583

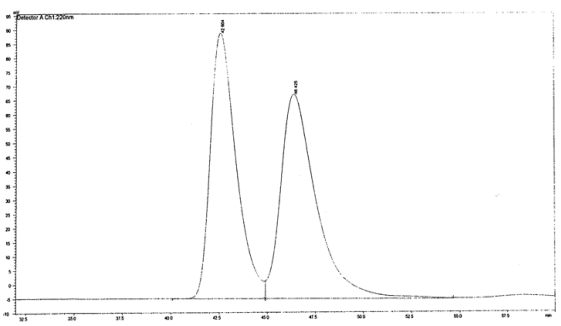


Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.809	8741300	347416	88.787	89.631
2	23.377	1103945	40191	11.213	10.369

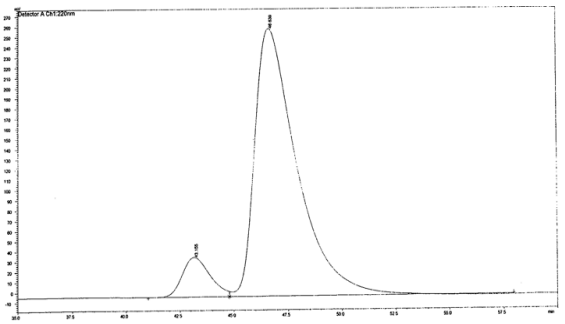
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	22.845	50.088	1	21.809	88.787
2	23.963	49.912	2	23.377	11.213

The characterization of **2.13f** has been described above. Specific rotation: $[\alpha]_D^{20}$ +8.1 (*c* 1.73, $CHCl_3$) for an enantiomerically enriched sample of 91:9 e.r.

Enantiomeric purity of **2.13f** was determined by HPLC analysis in comparison with authentic racemic material (91:9 e.r. shown; Chiralpak AD–H column, 100 % hexanes, 0.2 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	42.604	8988465	93980	49.754	56.542
2	46.425	9077199	72233	50.246	43.458

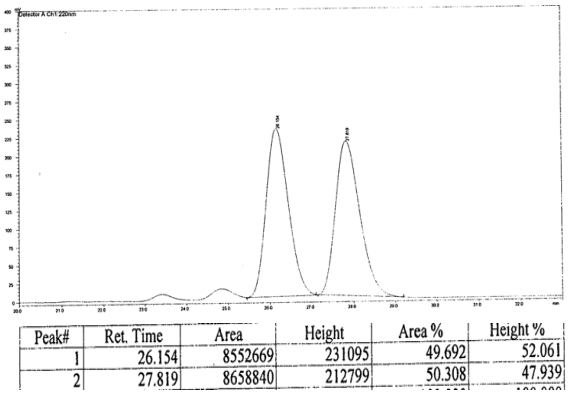


Peak#	Ret. Time	Area	Height	Area %	Height %
1	43.155	3448087	38632	8.896	12.844
2	46.639	35311091	262146	91.104	87.156

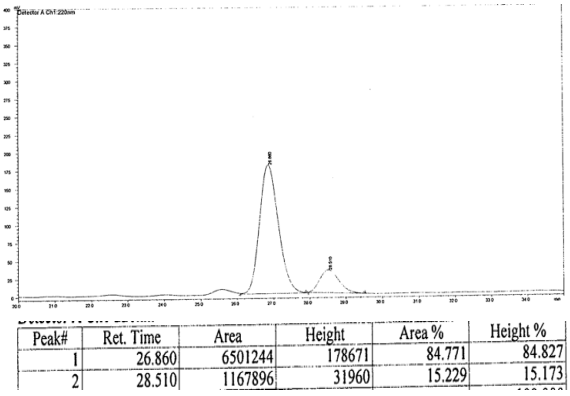
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	42.604	49.754	1	43.155	8.896
2	46.425	50.246	2	46.639	91.104

The characterization of **2.13j** has been described above. Optical rotation: $[\alpha]_D^{20}$ +9.1 (*c* 0.87, $CHCl_3$) for an enantiomerically enriched sample of 85:15 e.r.

Enantiomeric purity of **2.13j** was determined by HPLC analysis in comparison with authentic racemic material (85:15 e.r. shown; Chiralpak AD–H column, 99.5:0.5 hexanes/*i*PrOH, 0.6 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.154	8552669	231095	49.692	52.061
2	27.819	8658840	212799	50.308	47.939



Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.860	6501244	178671	84.771	84.827
2	28.510	1167896	31960	15.229	15.173

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)

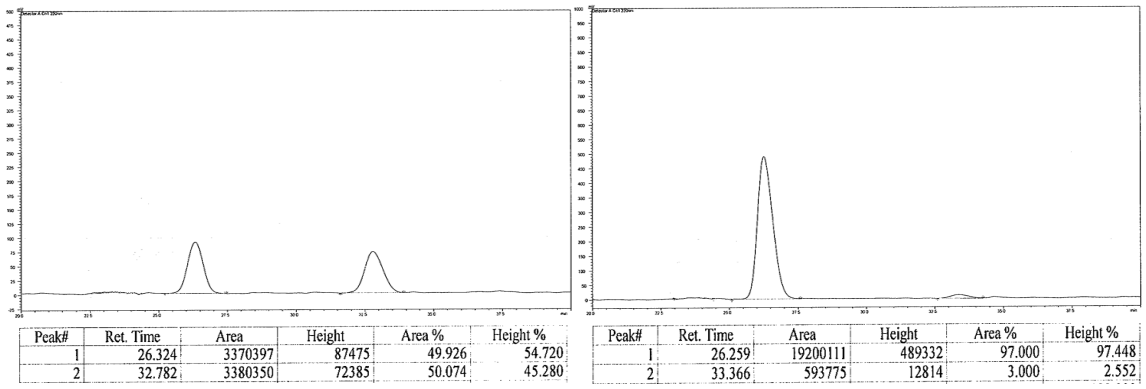
1	26.154	49.692	1	26.860	84.771
2	27.819	50.308	2	28.510	15.229

■ **Representative Experimental Procedure for Enantioselective Cu-Catalyzed Cu–B Addition/Addition to Carbonyls Followed by *Conversion to Vinylbromide*:** In a N_2-filled glove box, an oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with phosphine **2.33** (3.1 mg, 0.0050 mmol, 5.0 mol %), CuCl (0.5 mg, 0.005 mmol, 5.0 mol %), NaO*t*Bu (1.9 mg, 0.020 mmol, 20 mol %) and tetrahydrofuran (thf, 0.5 mL). The reaction vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the solution was allowed to stir at 22 °C for one hour. Bis(pinacolato)diboron (27.9 mg, 0.110 mmol, 1.1 equiv.) was added to the solution, causing it to turn dark brown immediately. The vial was re-sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and removed from the glove box. The resulting solution was allowed to stir at 22 °C for 30 min under an atmosphere of N_2. Allene **2.11b** (11.6 mg, 0.100 mmol, 1.0 equiv.) and benzaldehyde (**2.9a**; 11.2 μL, 0.110 mmol, 1.1 equiv.) were added through syringes. The resulting mixture was allowed to stir at 22 °C for eight hours before the reaction was quenched by passing the mixture through a short plug of Celite and silica gel and eluted with Et_2O (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide yellow oil, which was used in the next step without further purification. In a N_2-filled glove-box, an oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with $CuBr_2$ (67.0 mg, 0.300 mmol, 3.0 equiv.), the solution of unpurified product obtained above in MeOH (1.0 mL) and H_2O (0.5 mL). The vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the solution was allowed to stir at 80 °C for 6 h. The reaction mixture was washed with Et_2O (3 × 2 mL) after cooled to 22 °C. The combined organic layer was dried over

$MgSO_4$ and was concentrated *in vacuo* to provide yellow oil, which was purified by silica gel chromatography (hexanes:ethyl acetate = 10:1) to afford the desired product **2.20a** as a colorless oil (24.5 mg, 0.081 mmol, 81% yield).

The characterization of **2.20a** has been described above. Optical rotation: $[\alpha]_D^{20}$ –11.2 (*c* 0.83, $CHCl_3$) for an enantiomerically enriched sample of 97:3 e.r.

Enantiomeric purity of **2.20a** was determined by HPLC analysis in comparison with authentic racemic material (97:3 e.r. shown; Chiralpak OD–H column, 98:2 hexanes/*i*PrOH, 0.8 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.324	3370397	87475	49.926	54.720
2	32.782	3380350	72385	50.074	45.280

Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.259	19200111	489332	97.000	97.448
2	33.366	593775	12814	3.000	2.552

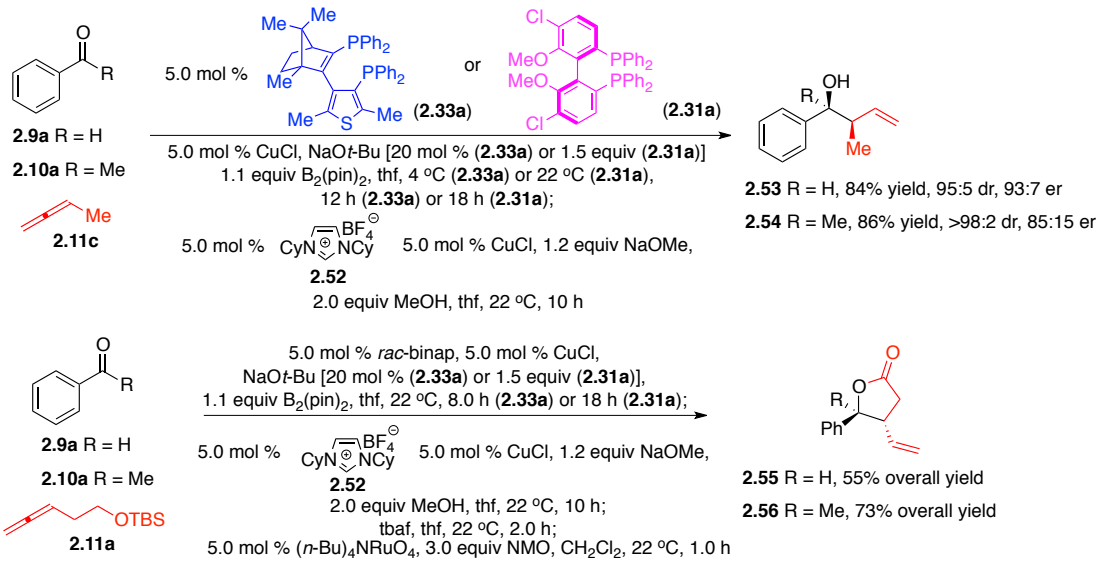
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	26.324	49.926	1	26.259	97.000
2	32.782	50.074	2	33.366	3.000

■ **Proof of Relative and Absolute Stereochemistry:** The relative stereochemistry was determined through comparison ^1H and ^{13}C NMR spectra of **2.53** and **2.54** with the literature[25,26] and NOE study of compound **2.55** and **2.56**. The literature value[24a,b] for compound **2.53** ($[\alpha]_D^{20}$ –15.0 (*c* 0.93, $CHCl_3$), 55% *ee* and $[\alpha]_D^{20}$ –25.9 (*c* 0.80, $CHCl_3$),

(25) (a) Roush, W. R.; Ando, K.; Powers, D. B.; Palkowitz, A. D.; Halterman, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 6339–6348. (b) Hackman, B. M.; Lombardi, P. J.; Leighton, J. L. *Org. Lett.* **2004**, *6*, 4375–4377. (c) Thadani, A. N.; Batey, R. A. *Org. Lett.* **2002**, *4*, 3827–3830; d) Reilly, M. K.; Rychnovsky, S. D. *Org. Lett.* **2010**, *12*, 4892–4895.
(26)Wada, R.; Oisaki, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2004**, *126*, 8910–8911.

95% *ee*) is assigned to the (1*S*, 2*R*) enantiomer. The literature value[25] for compound **2.54** ($[\alpha]_D^{20}$ +4.4 (*c* 1.09, $CHCl_3$), 83% *ee*) is assigned to the (2*S*, 3*R*) enantiomer.

Scheme 2.10: Cu–Catalyzed Cu–B Addition to Allene/Allylation of Carbonyls Followed by Protodeboration



Part I. Representative Experimental Procedure for Cu-Catalyzed Cu–B Addition/Allylation of Aldehyde *Followed by Cu-Catalyzed Protodeboration*: In a N_2-filled glove-box, an oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with phosphine **2.33** (3.1 mg, 0.0050 mmol, 5.0 mol %), CuCl (0.5 mg, 0.005 mmol, 5.0 mol %), NaO*t*-Bu (1.9 mg, 0.020 mmol, 20 mol %) and tetrahydrofuran (thf, 0.5 mL). The vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the solution was allowed to stir at 22 °C for one hour. Bis(pinacolato)diboron (27.9 mg, 0.110 mmol, 1.1 equiv.) was added to the solution, causing it to turn dark brown immediately. The vial was re-sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and removed from the glove box. The mixture was allowed to stir at 22 °C for 30 min under an atmosphere of N_2. At this time, the mixture was allowed to cool to –78 °C (dry ice/acetone bath) and solution of methyl

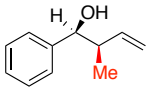
allene [27] (43.3 μL, 0.200 mmol, 2.0 equiv.) and benzaldehyde (**2.9a**; 10.2 μL, 0.100 mmol, 1.0 equiv.) were added through syringes. The vial was placed in a 4 °C cold room. After 12 h, the solution was allowed to cool to –78 °C and the reaction was quenched by passing the mixture through a short plug of celite and silica gel and eluted with Et_2O (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide yellow oil, which was used in the next step without further purification. In a N_2-filled glove-box, an oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with imidazolium salt **2.52** (1.6 mg, 0.0050 mmol, 5.0 mol %), CuCl (0.5 mg, 0.005 mmol, 5.0 mol %), NaOMe (6.5 mg, 0.12 mmol, 1.2 equiv.) and tetrahydrofuran (thf, 0.5 mL). The vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the solution was allowed to stir at 22 °C for one hour. The unpurified yellow oil obtained from the sequential reaction was added to the NHC–Cu complex solution. MeOH (8.2 μL, 0.20 mmol, 2.0 equiv.) was added through a syringe. The vial was re-sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and removed from the glove box. The solution was allowed to stir at 22 °C for ten hours. The reaction was quenched by passing the mixture through a short plug of silica gel and eluted with Et_2O (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide a yellow oil, which was purified by silica gel chromatography (hexanes:ethyl acetate = 18:1) to afford the desired product **2.53** as a colorless oil (13.6 mg, 0.084 mmol, 84% yield).

(1*S*,2*R*)-2-Methyl-1-phenylbut-3-en-1-ol (2.53). The title compound has been previously reported and spectra data match those described.[24] ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36–7.24 (5H, m), 5.81–5.72 (1H, m), 5.09–5.03 (2H, m), 4.62 (1H, d, J = 5.2

(27) Excess amount of methylallene (2.0 equiv.) was used due to its volatility.

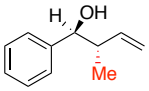
Hz), 2.63–2.52 (1H, m), 1.94 (1H, s), 1.01 (3H, d, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 142.7, 140.4, 128.2, 127.5, 126.6, 115.7, 77.4, 44.8, 14.1. Specific rotation: $[\alpha]_D^{20}$ –20.2 (*c* 0.81, $CHCl_3$) for an enantiomerically enriched sample of 93:7 er.

Enantiomeric purity of **2.53** was determined by HPLC analysis as shown above. Comparison of compounds **2.53** with literature value are shown below:



Reported optical rotation: $[\alpha]_D$ = –15.0 (*c* 0.93, $CHCl_3$) (ref 24a)
Reported ^{1}H NMR data (ref 24):
^{1}H NMR: ($CDCl_3$, 400 MHz) δ 7.37–7.26 (5H, m), 5.81–5.71 (1H, m), 5.07–5.00 (2H, m), 4.58 (1H, dd, J = 5.5, 3.0 Hz), 2.63–2.53 (1H, m), 2.20 (1H, d, J = 3.0 Hz), 1.01 (3H, d, J = 7.0 Hz)

Optical rotation of 3.53 (Scheme S1): $[\alpha]_D$ = –20.2 (*c* 0.81, $CHCl_3$)
^{1}H NMR data for Compound 3.53 (Scheme 3.10)
^{1}H NMR: ($CDCl_3$, 400 MHz): δ 7.36–7.24 (5H, m), 5.81–5.72 (1H, m), 5.09–5.03 (2H, m), 4.62 (1H, d, J = 5.2 Hz), 2.63–2.52 (1H, m), 1.94 (1H, s), 1.01 (3H, d, J = 6.8 Hz)



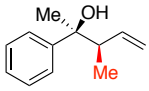
Reported optical rotation: $[\alpha]_D$ = –73.4 (*c* 2.00, $CHCl_3$) (ref 24a)
Reported ^{1}H NMR data (ref 24):
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.37–7.24 (5H, m), 5.81 (1H, ddd, J = 17.0, 10.5, 8.0 Hz), 5.23–5.16 (2H, m), 4.34 (1H, d, J = 8.0 Hz), 2.48 (1H, sextet, J = 7.0 Hz), 2.29 (1H, br s), 0.87 (1H, d, J = 7.0 Hz)

Part II. Representative Experimental Procedure for Cu-Catalyzed Cu–B Addition/Addition to Ketones Followed by *Cu-Catalyzed Protodeboration*: In a N_2-filled glove-box, an oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with phosphine **2.31** (3.2 mg, 0.0050 mmol, 5.0 mol %), CuCl (0.5 mg, 0.005 mmol, 5.0 mol %), NaO*t*-Bu (14.4 mg, 0.150 mmol, 1.5 equiv.) and tetrahydrofuran (thf, 0.5 mL). The vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the solution was allowed to stir at 22 °C for one hour. Bis(pinacolato)diboron (27.9 mg, 0.110 mmol, 1.1 equiv.) was added to the solution,

causing it to turn dark brown immediately. The vial was re-sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and removed from the glove-box. The mixture was allowed to stir at 22 °C for 30 min under an atmosphere of N_2. Methyl allene solution (43.3 μL, 0.200 mmol, 2.0 equiv.) and acetophenone (**2.10a**; 11.7 μL, 0.100 mmol, 1.0 equiv.) were added through syringes. The mixture was allowed to stir at 22 °C for 18 h before the reaction was quenched by passing the mixture through a short plug of celite and silica gel and eluted with Et_2O (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide a yellow oil, which was used in the next step without further purification. In a N_2-filled glove-box, an oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with imidazolium salt **2.52** (1.6 mg, 0.0050 mmol, 5.0 mol %), CuCl (0.5 mg, 0.005 mmol, 5.0 mol %), NaOMe (6.5 mg, 0.12 mmol, 1.2 equiv.) and tetrahydrofuran (thf, 0.5 mL). The reaction vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the solution was allowed to stir at 22 °C for one hour. The unpurified yellow oil obtained from the sequential reaction was added to the NHC–Cu complex solution. MeOH (8.2 μL, 0.20 mmol, 2.0 equiv.) was added through a syringe. The vial was re-sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and removed from the glove-box. The solution was allowed to stir at 22 °C for ten hours. The reaction was quenched by passing the mixture through a short plug of silica gel and eluted with Et_2O (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide a yellow oil, which was purified by silica gel chromatography (hexanes:Et_2O = 18:1) to afford the desired product **2.54** as a colorless oil (15.2 mg, 0.086 mmol, 86% yield).

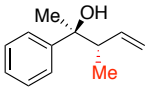
(2*S*,3*R*)-3-Methyl-2-phenylpent-4-en-2-ol (2.54). The title compound has been previously reported and spectra data match those described.[25] ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.42–7.39 (2H, m), 7.36–7.32 (2H, m), 7.26–7.22 (1H, m), 5.82 (1H, q, *J* = 6.8 Hz), 5.14–5.08 (2H, m), 2.55 (1H, q, *J* = 6.8 Hz), 1.86 (1H, s), 1.54 (3H, s), 0.87 (3H, d, *J* = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.1, 140.0, 128.0, 126.6, 125.4, 116.5, 75.9, 49.1, 28.7, 14.9. Optical rotation: $[\alpha]_D^{20}$ +5.7 (*c* 0.87, $CHCl_3$) for an enantiomerically enriched sample of 85:15 er.

Enantiomeric purity of **2.54** was determined by HPLC analysis as shown above. Comparison of compounds **2.54** with literature value are shown below:



Reported optical rotation: $[\alpha]_D$ = +4.4 (*c* 1.09, $CHCl_3$) (ref 25)
Reported ^{1}H NMR data (ref 25):
^{1}H NMR: ($CDCl_3$, 400 MHz) δ 7.41 (2H, m), 7.34 (2H, t, *J* = 7.5 Hz), 7.24 (1H, m), 5.82 (1H, m), 5.12 (2H, m), 2.55 (1H, quintet, *J* = 7.4 Hz), 1.89 (1H, s), 1.54 (3H, s), 0.87 (3H, d, *J* = 7.4 Hz)

Optical rotation of 3.54 (Scheme 3.10): $[\alpha]_D$ = +5.7 (*c* 0.87, $CHCl_3$)
^{1}H NMR data for Compound 3.54 (Scheme 3.10)
^{1}H NMR: ($CDCl_3$, 400 MHz): δ 7.42–7.39 (2H, m), 7.36–7.32 (2H, m), 7.26–7.22 (1H, m), 5.82 (1H, q, *J* = 6.8 Hz), 5.14–5.08 (2H, m), 2.55 (1H, q, *J* = 6.8 Hz), 1.86 (1H, s), 1.54 (3H, s), 0.87 (3H, d, *J* = 6.8 Hz)



Reported optical rotation: $[\alpha]_D$ = –72.8 (*c* 1.05, $CHCl_3$) (ref 25)
Reported ^{1}H NMR data (ref 25):
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.42 (2H, m), 7.33 (2H, t, *J* = 7.5 Hz), 7.23 (1H, m), 5.70 (1H, m), 5.10 (2H, m), 2.59 (1H, quintet, *J* = 6.9 Hz), 1.99 (1H, s), 1.52 (3H, s), 0.96 (3H, d, *J* = 6.9 Hz)

Part III. Representative Experimental Procedure for One-Pot Silyl Ether Removal and Oxidative Lactonization. The unpurified product prepared following the procedures for Cu-catalyzed Cu–B addition to allene/addition to carbonyls shown above was dissolved in thf (1.0 mL). To this latter solution, tbaf (1.0 M in thf, 0.2 mL, 0.20 mmol,

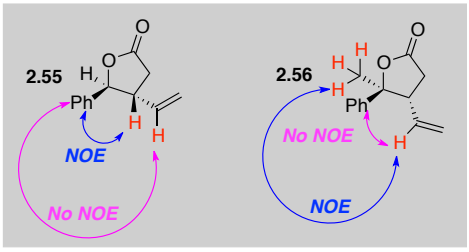
2.0 equiv.) was added through a syringe at 22 °C and the resulting solution was allowed to stir at 22 °C for two hours. The reaction was quenched by passing the reaction mixture through a short plug of silica gel and eluted with Et_2O (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide yellow oil, which was dissolved in CH_2Cl_2 (1.0 mL). NMO (35.1 mg, 0.300 mmol, 3.0 equiv.) and TPAP (1.8 mg, 0.0050 mmol, 5.0 mol %) were added at 22 °C. The mixture was allowed to stir at 22 °C for one hour. The reaction was quenched by passing the mixture through a short plug of silica gel and eluted with Et_2O (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide a yellow oil, which was purified by silica gel chromatography (hexanes:diethyl ether = 20:1) to afford the corresponding lactone as a colorless oil (**2.55**, 10.3 mg, 0.055 mmol, 55% yield; **2.56**, 14.7 mg, 0.073 mmol, 73% yield).

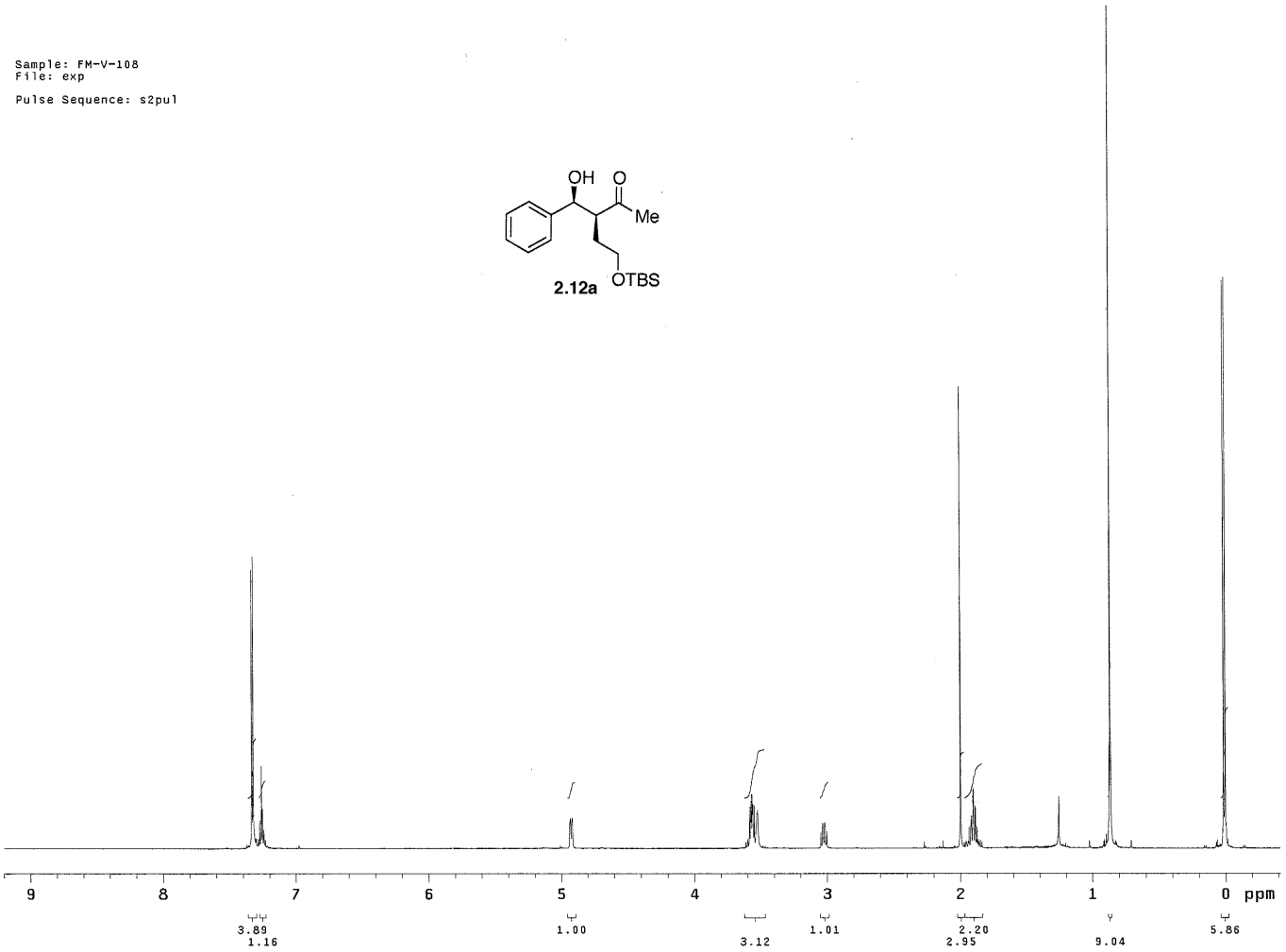
5-Phenyl-4-vinyldihydrofuran-2(3*H*)-one (2.55). IR (neat): 3065 (w), 2926 (w), 1776 (s), 1497 (w), 1264 (m), 1205 (s), 1145 (s), 1078 (w), 993 (s), 862 (w), 760 (s), 699 (s), 528 (m), 489 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.41–7.32 (5H, m), 5.87–5.78 (1H, m), 5.18 (1H, app. d, J = 10.0 Hz), 5.13–5.06 (2H, m), 3.11–3.03 (1H, m), 2.83 (1H, dd, J = 19.2, 8.0 Hz), 2.61 (1H, dd, J = 19.2, 10.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 175.5, 137.6, 134.7, 128.8, 128.7, 125.9, 118.8, 85.6, 49.3, 35.5; HRMS (ESI^+): Calcd for $C_{12}H_{13}O_2$ $[M+H]^+$: 189.09155; Found: 189.09147.

5-Methyl-5-phenyl-4-vinyldihydrofuran-2(3*H*)-one (2.56). IR (neat): 3060 (w), 2919 (m), 2850 (w), 1771 (s), 1497 (m), 1380 (m), 1227 (s), 1091 (m), 1042 (m), 932 (s), 865 (w), 765 (s), 700 (s), 651 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.42–7.35 (4H, m), 7.33–7.29 (1H, m), 5.91 (1H, ddd, J = 19.2, 10.0, 8.4 Hz), 5.28 (1H, d, J = 10.0 Hz), 5.17 (1H, d, J = 19.2 Hz), 3.18 (1H, dd, J = 19.6, 8.4 Hz), 2.70 (1H, dd, J = 19.6, 8.4 Hz), 2.60

(1H, dd, J = 19.6, 9.6 Hz), 1.60 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 175.2, 144.3, 134.1, 128.7, 127.9, 124.2, 119.3, 88.5, 51.2, 34.8, 23.6; HRMS (ESI^+): Calcd for $C_{13}H_{15}O_2$ $[M+H]^+$: 203.10720; Found: 203.10660.

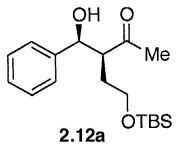
Results of NOE study of lactone **2.55** and **2.56** are as illustrated below:




Sample: FM-V-108
File: exp
Pulse Sequence: s2pul
OH
O
Me
OTBS
2.12a
9
8
7
6
5
4
3
2
1
0 ppm
3.89
1.16
1.00
3.12
1.01
2.20
2.95
9.04
5.86

Sample: FM-V-108
File: /home/ahh/Fanke/FM-V-108-CNMR.fid

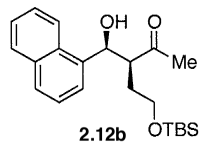
Pulse Sequence: s2pul



2.12a

Sample: FM-V-193
File: exp

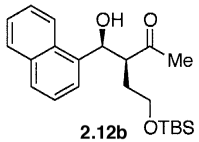
Pulse Sequence: s2pul



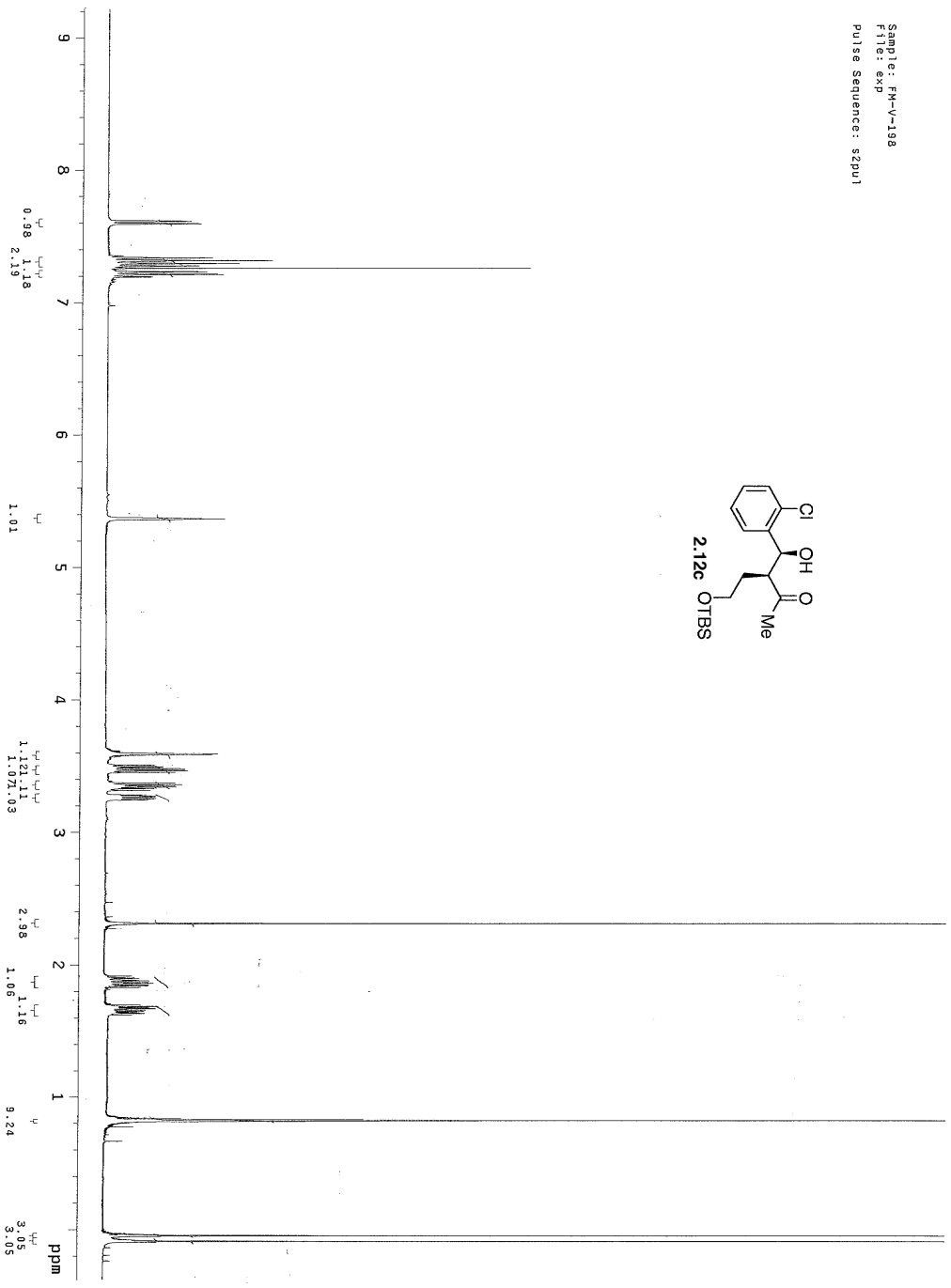
2.12b

Sample: FM-V-193
File: exp

Pulse Sequence: s2pul

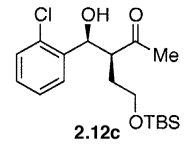


2.12b

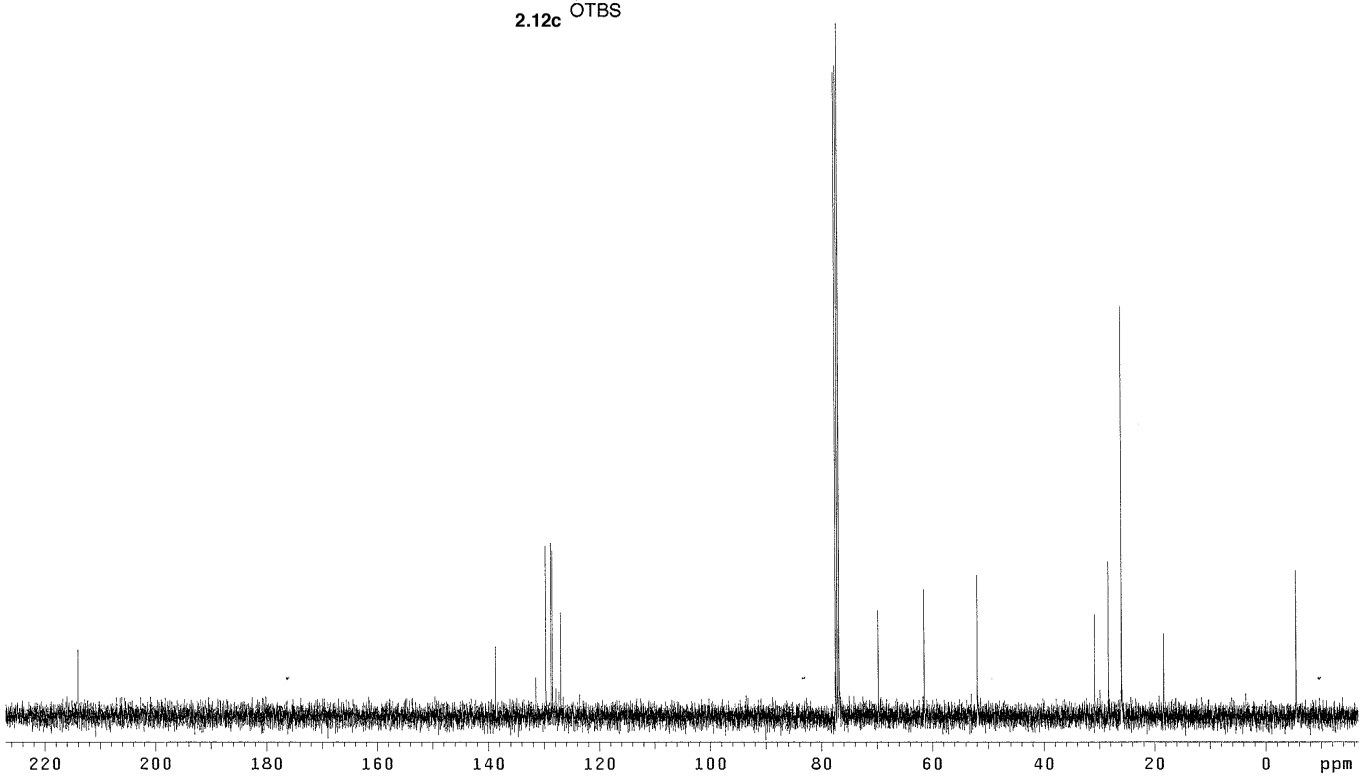

Sample: FM-V-198
File: exp
Pulse Sequence: s2pul
Cl
OH
O
Me
2.12c OTBS
ppm

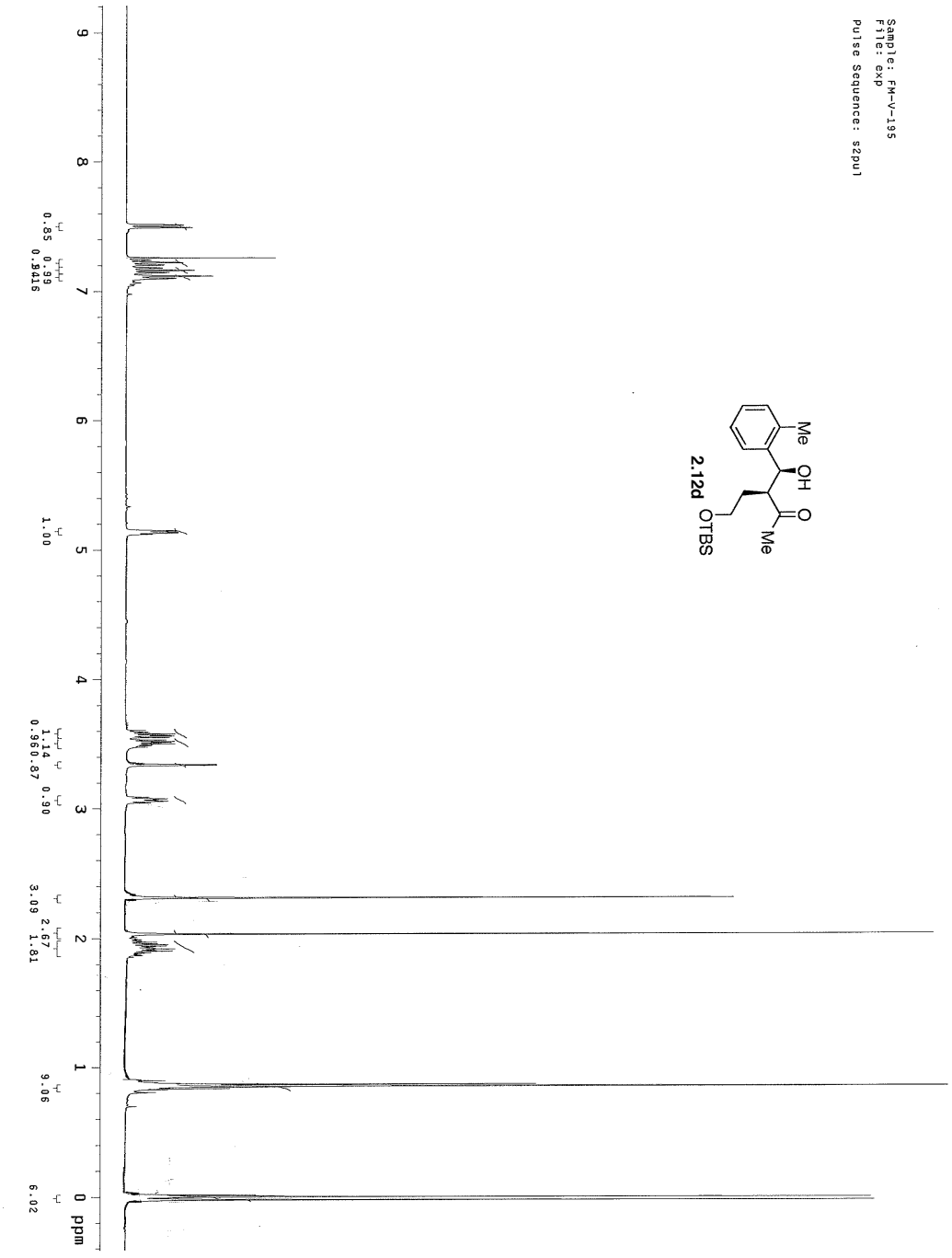
Sample: FM-V-199
File: exp

Pulse Sequence: s2pul



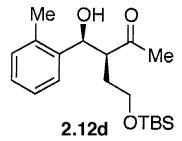
2.12c



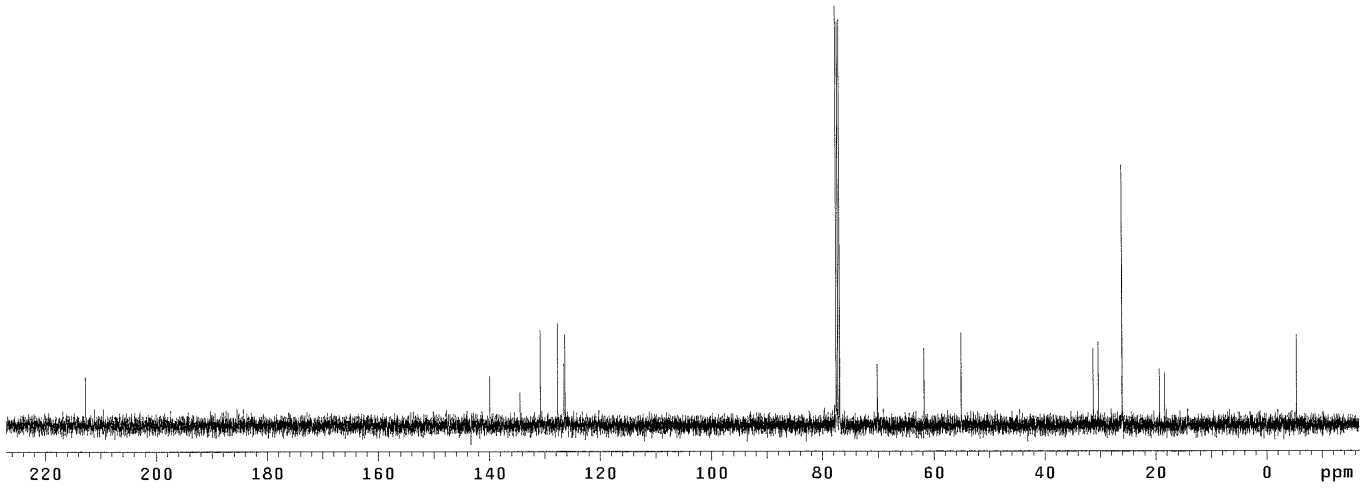

Sample: FM-V-195
File: exp
Pulse Sequence: s2pul
Me
OH
O
Me
2.12d
OTBS
9
8
7
6
5
4
3
2
1
0 ppm
0.85
0.99
0.80
1.00
1.14
0.96
0.87
0.90
3.09
2.67
1.81
9.06
6.02

Sample: FM-V-195
File: exp

Pulse Sequence: s2pul

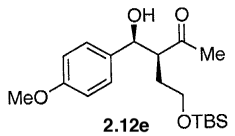


2.12d



Sample: FM-V-174
File: exp

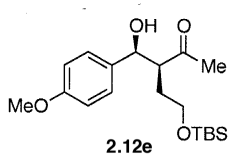
Pulse Sequence: s2pul



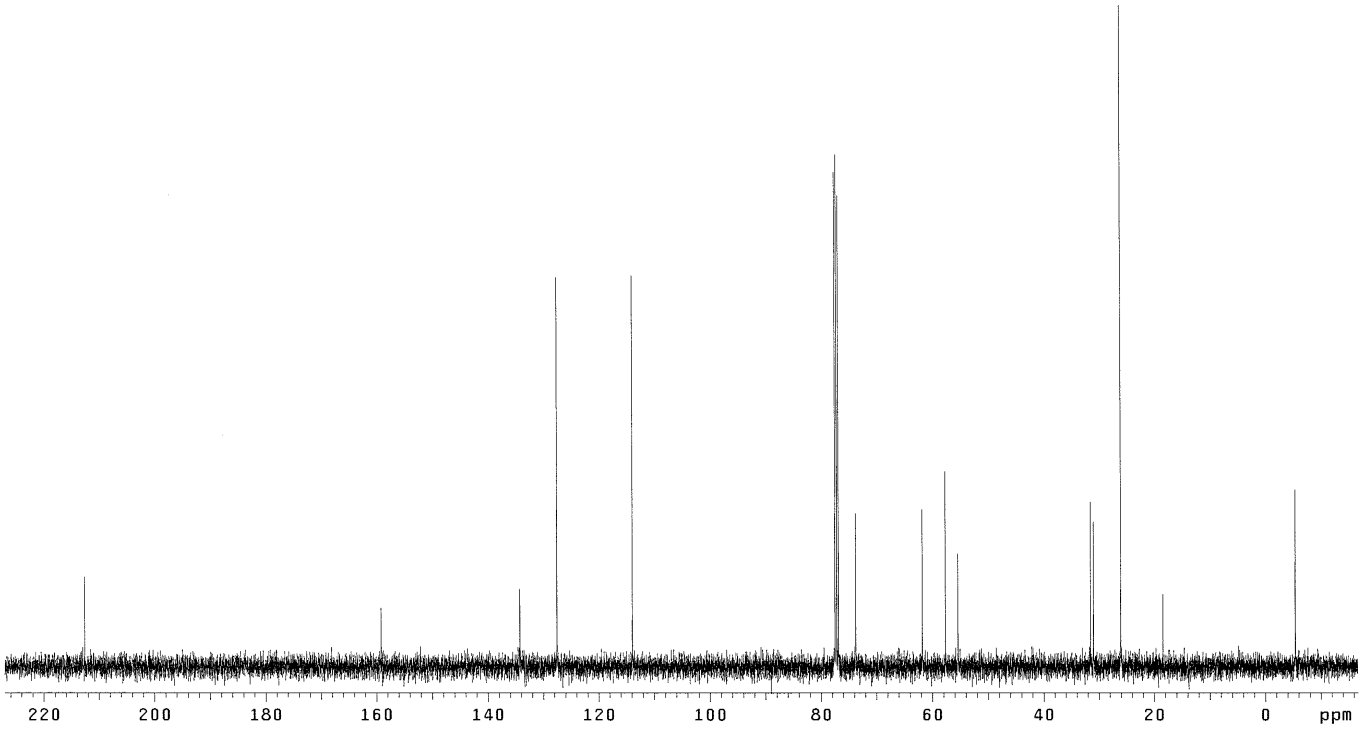
2.12e

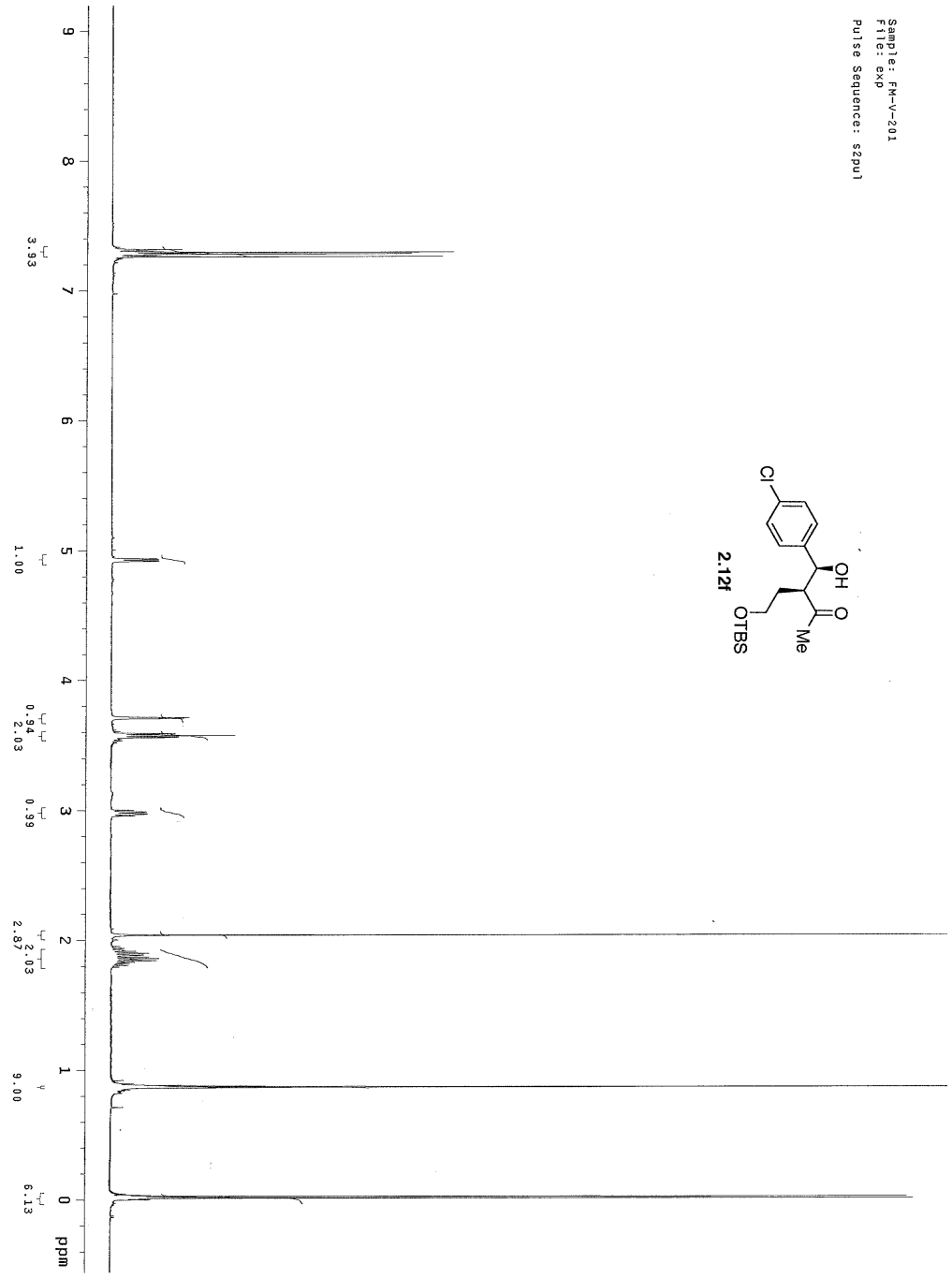
Sample: FM-V-174
File: exp

Pulse Sequence: s2pul



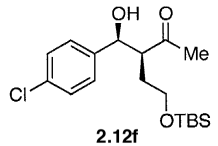
2.12e



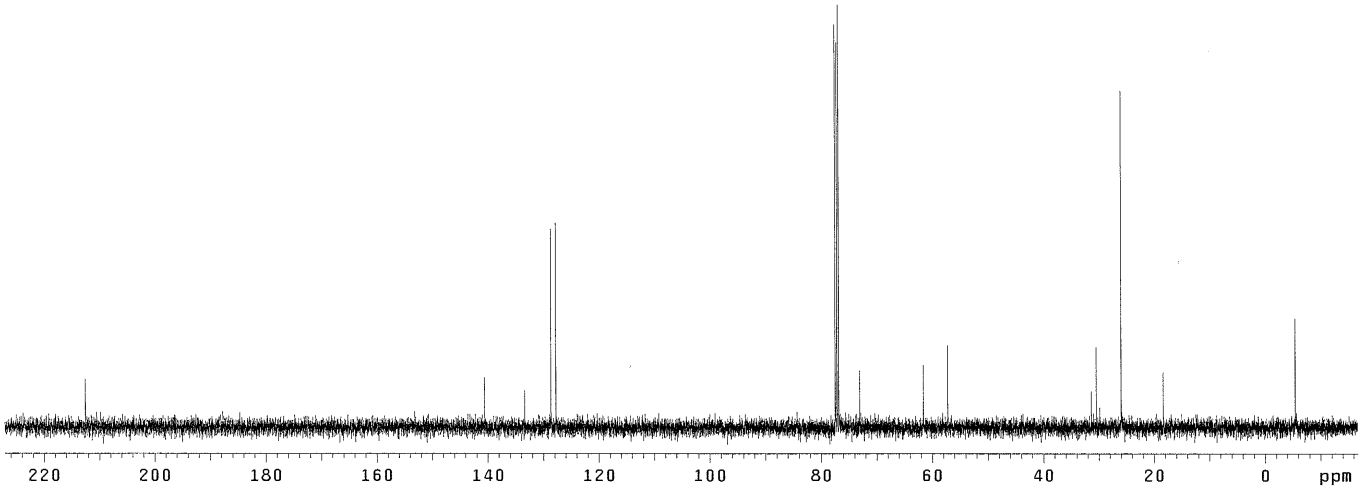

Sample: FM-V-201
File: exp
Pulse Sequence: s2pul
Cl
OH
O
Me
OTBS
2.12f
9
8
7
6
5
4
3
2
1
0
ppm
3.93
1.00
0.94
2.03
0.99
2.87
2.03
9.00
6.13

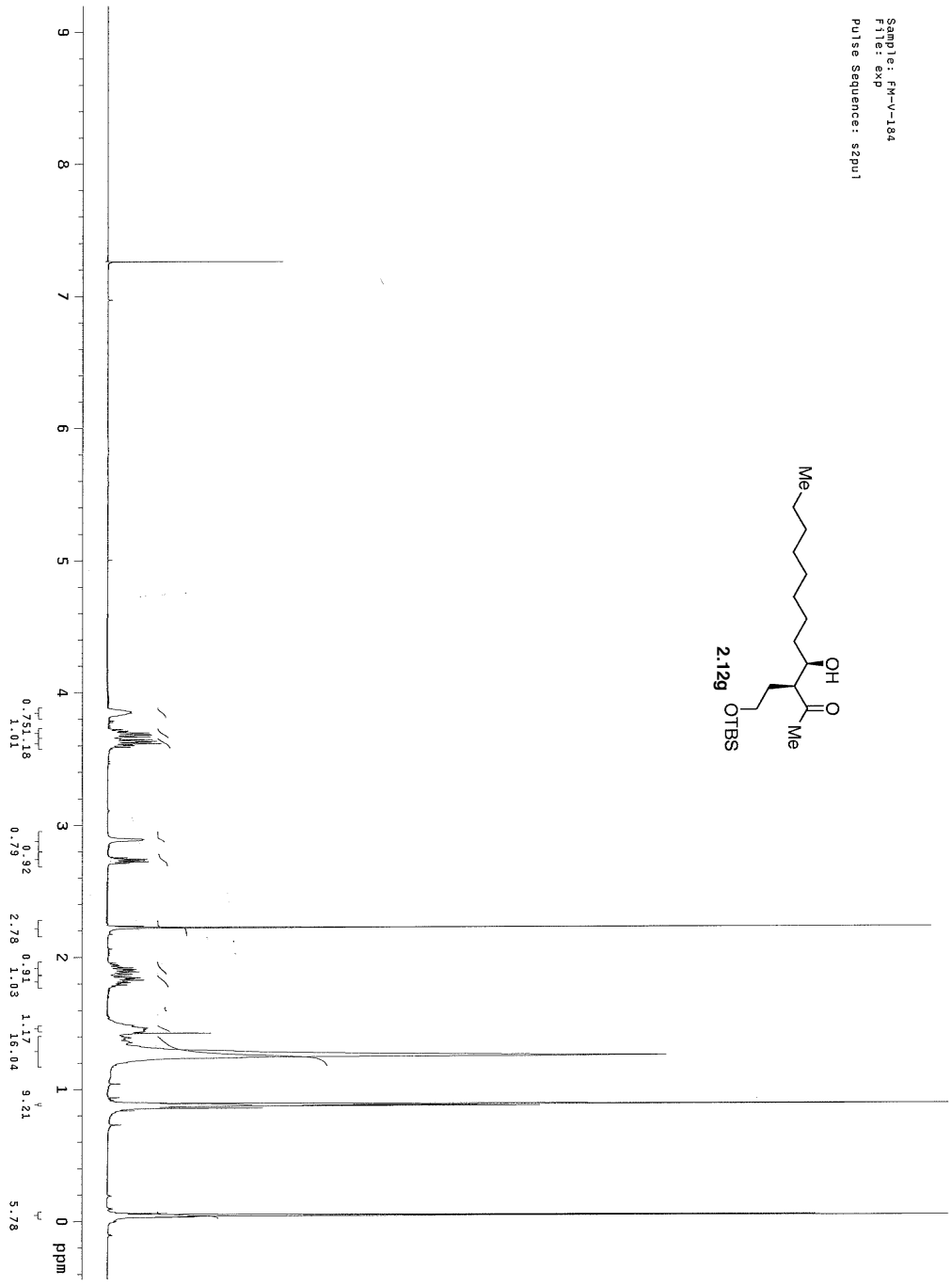
Sample: FM-V-201
File: exp

Pulse Sequence: s2pul



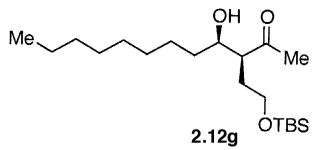
2.12f



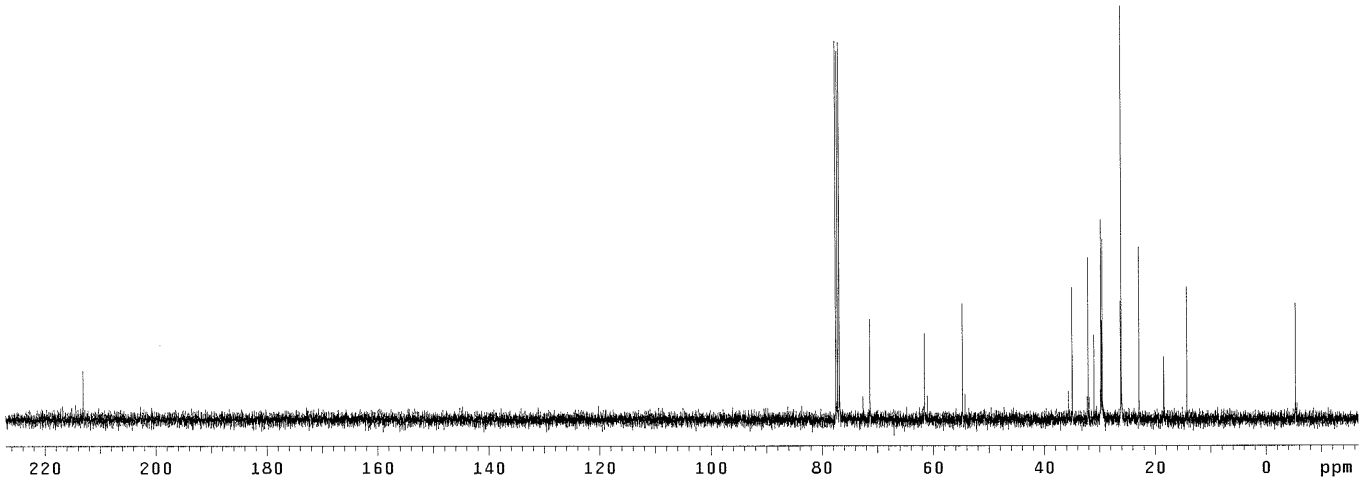

Sample: FM-V-184
File: exp
Pulse Sequence: s2pul
Me
OH
O
Me
2.12g
OTBS
9
8
7
6
5
4
3
2
1
0 ppm
0.751.18
1.01
0.92
0.79
2.78
0.91
1.03
1.17
16.04
9.21
5.78

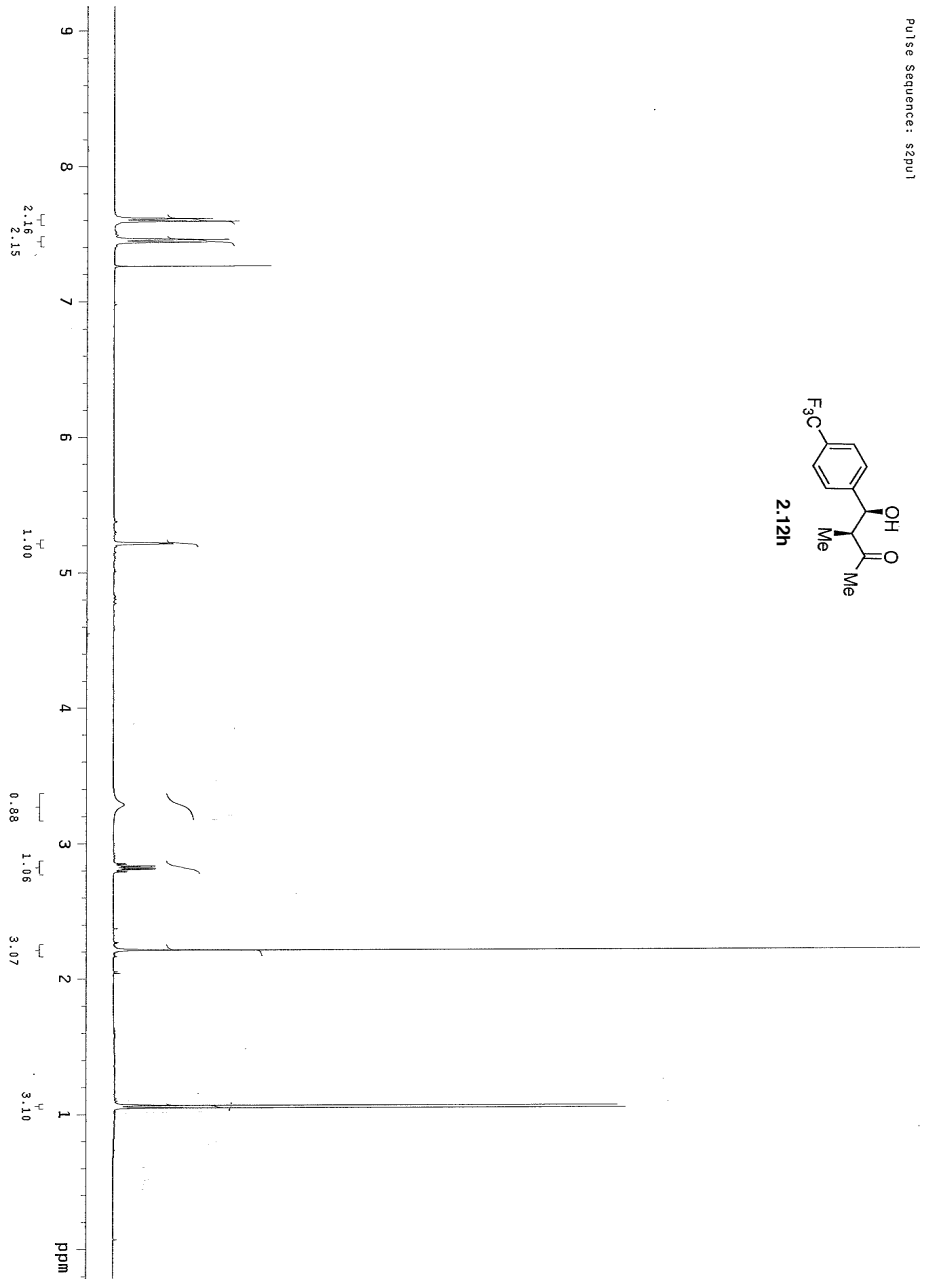
Sample: FM-V-184
File: exp

Pulse Sequence: s2pul



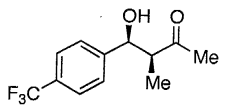
2.12g



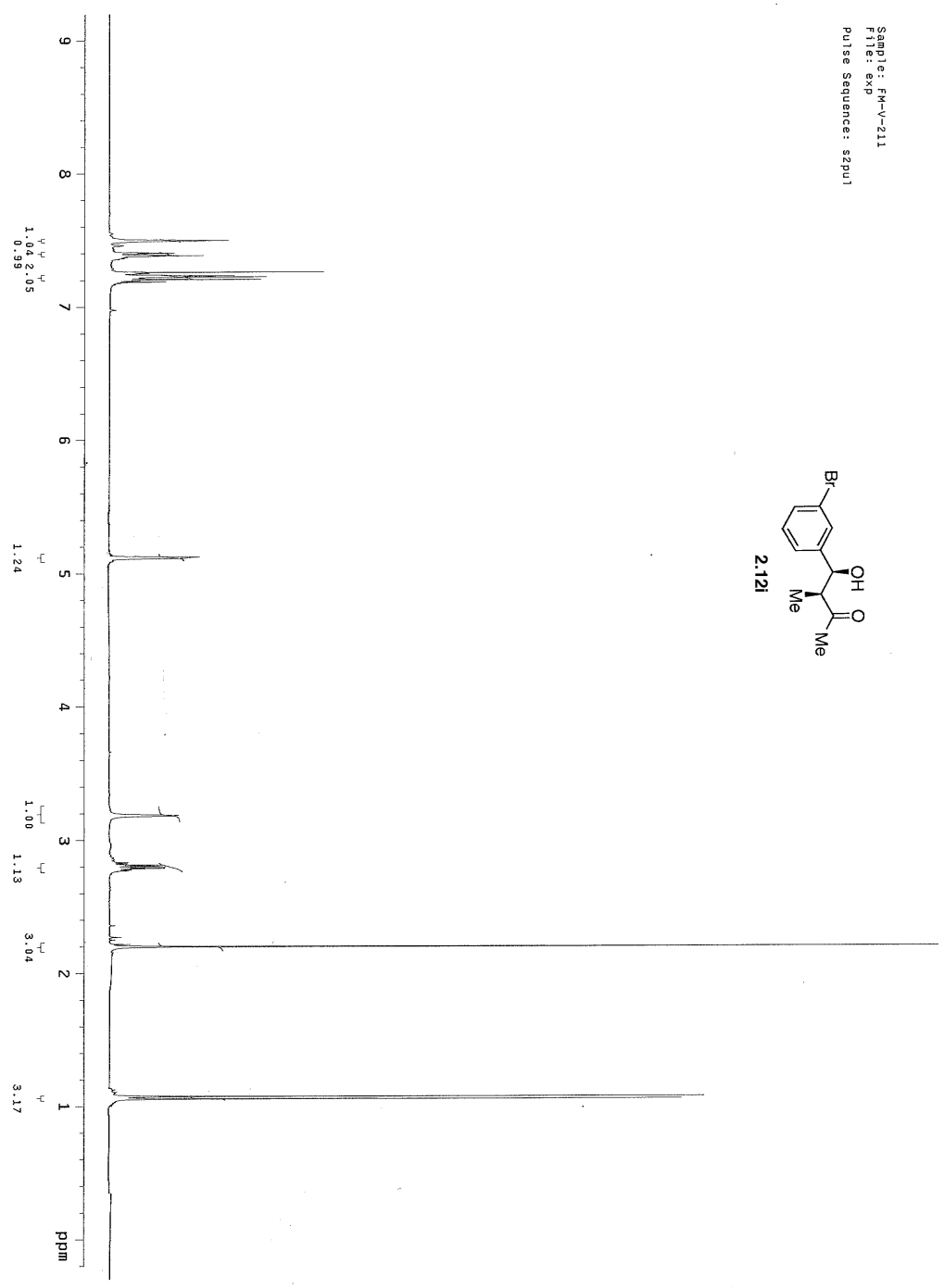

Sample: FM-V-213
File: exp
Pulse Sequence: s2pul
F3C
OH
O
Me
Me
2.12h
9
8
7
6
5
4
3
2
1
ppm
2.16
2.15
1.00
0.88
1.06
3.07
3.10

Sample: FM-V-213
File: /home/ahh/Fanke/FM-V-213-CNMR.fid

Pulse Sequence: s2pul

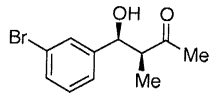


2.12h

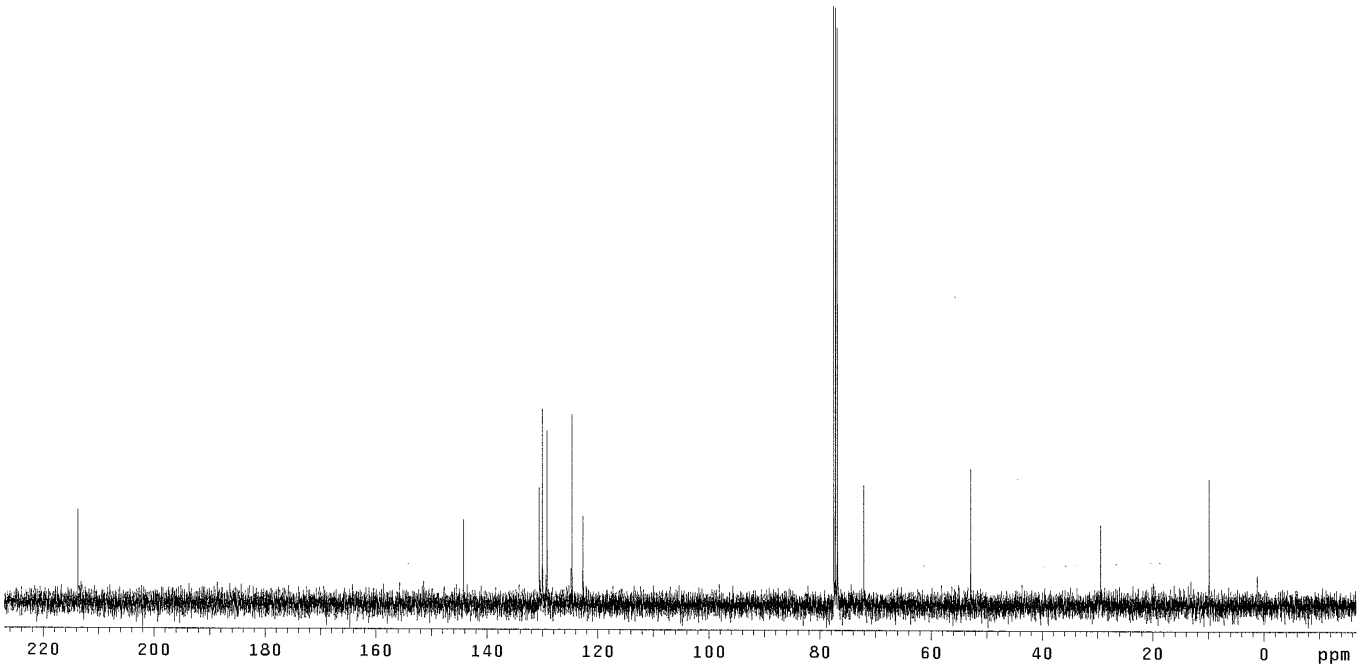

Sample: FM-V-211
File: exp
Pulse Sequence: s2pul
Br
OH
O
Me
Me
2.12i
ppm
1.24
1.04
2.05
0.99
1.00
1.13
3.04
3.17

Sample: FM-V-211
File: exp

Pulse Sequence: s2pul

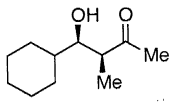


2.12i



Sample: FM-V-249A
File: exp

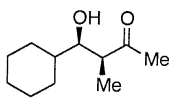
Pulse Sequence: s2pul



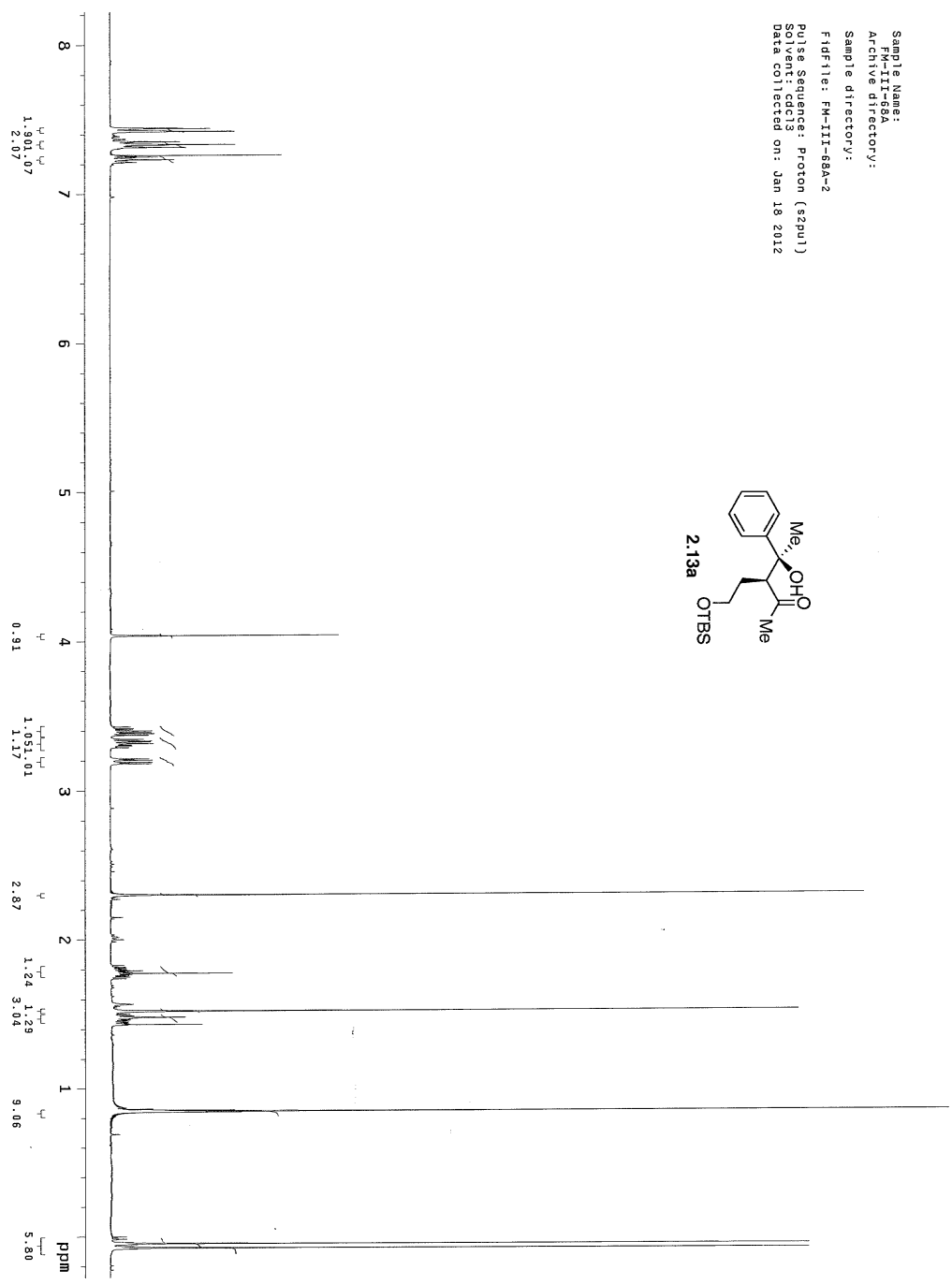
2.12j

Sample: FM-V-249A
File: exp

Pulse Sequence: s2pul



2.12j

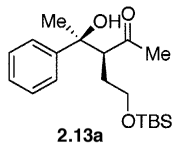

Sample Name:
FM-III-68A
Archive directory:
Sample directory:
FidFile: FM-III-68A-2
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Jan 18 2012
2.13a
Me
OH
O
Me
OTBS
ppm

Sample Name:
FM-III-68A
Archive directory:

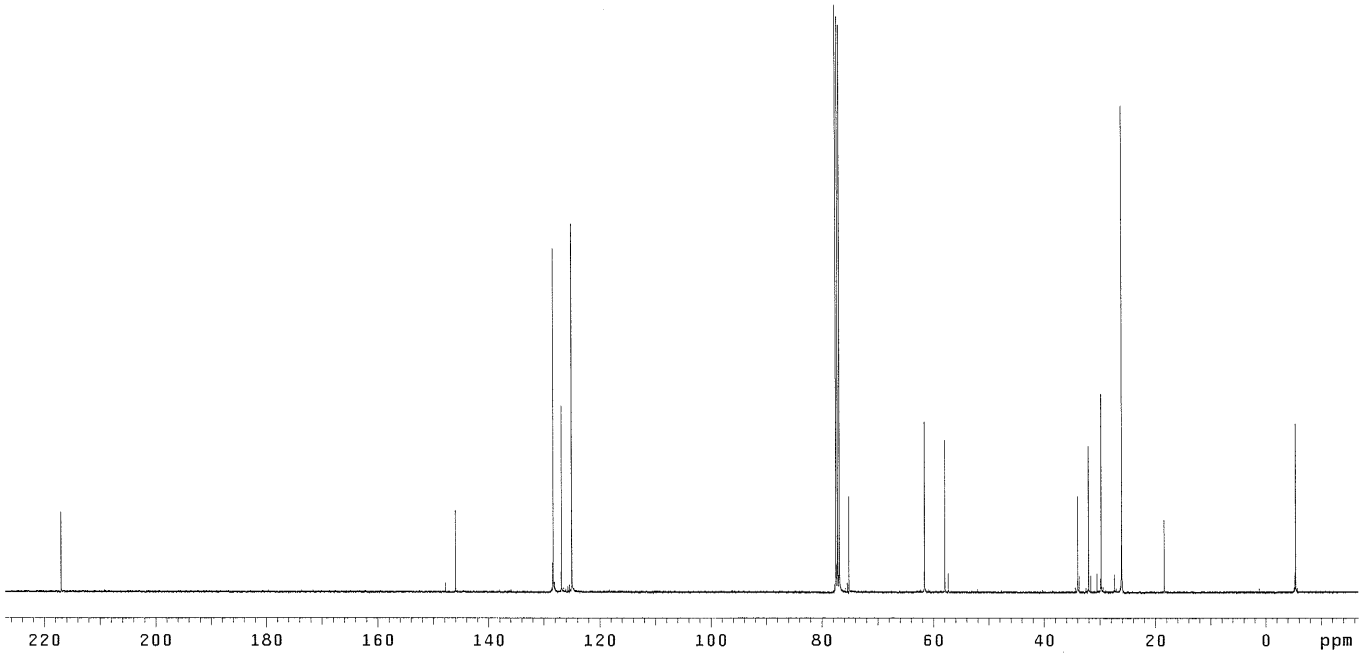
Sample directory:

FidFile: FM-III-68A-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Jan 18 2012



2.13a

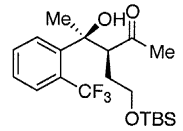


Sample Name:
FM-III-161
Archive directory:

Sample directory:

FidFile: FM-III-161

Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Feb 11 2012



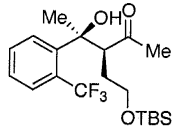
2.13b

Sample Name:
FM-III-161-CNMR
Archive directory:

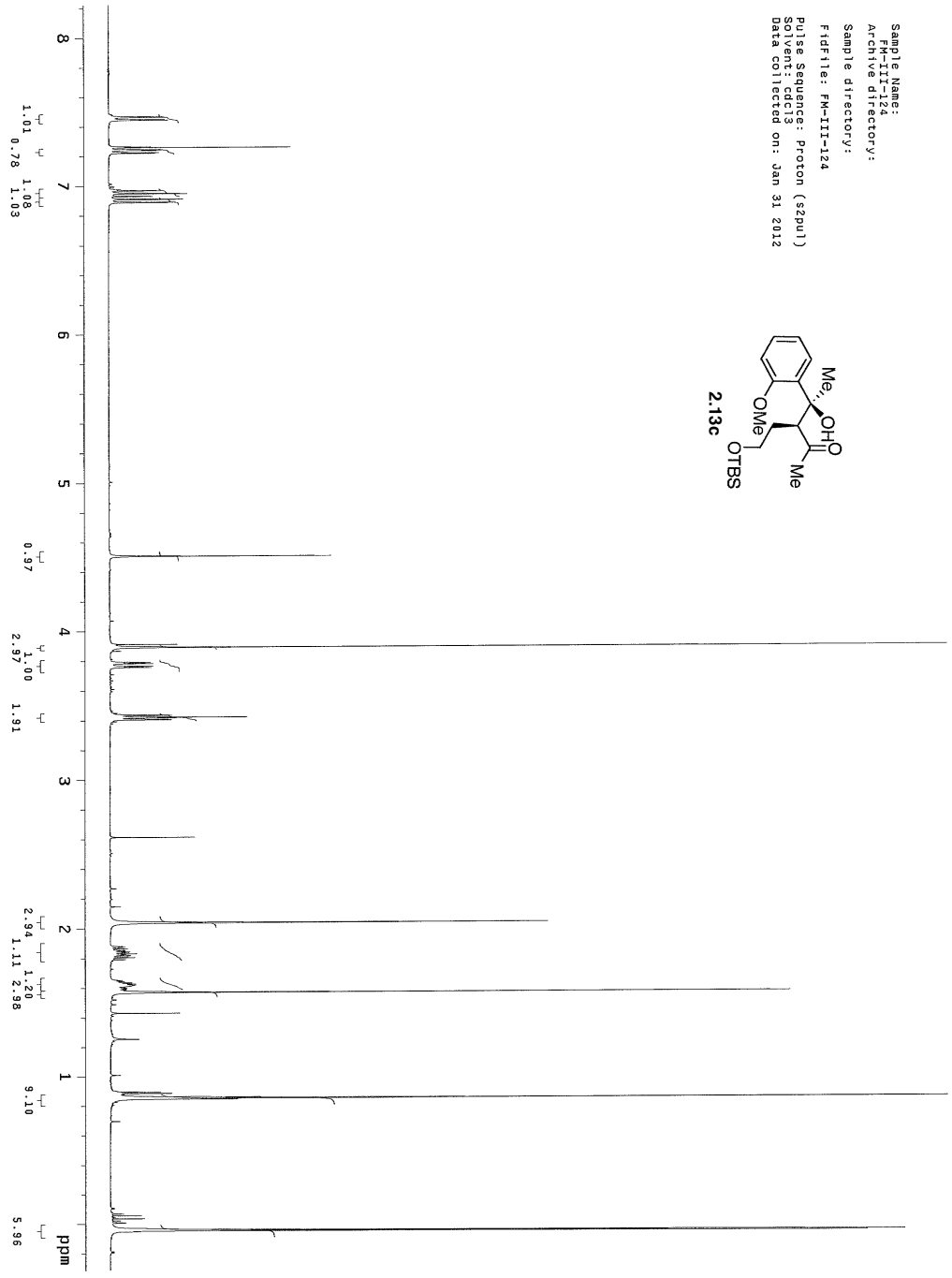
Sample directory:

FidFile: FM-III-161-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Feb 13 2012



2.13b

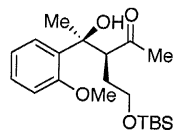

Sample Name:
FM-III-124
Archive directory:
Sample directory:
FidFile: FM-III-124
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Jan 31 2012
Me
OH
O
Me
OMe
OTBS
2.13c
8
7
6
5
4
3
2
1
ppm
1.01
0.78
1.08
1.03
0.97
2.97
1.00
1.91
2.94
1.11
1.20
2.98
9.10
5.96

Sample Name:
FM-III-125-CNMR
Archive directory:

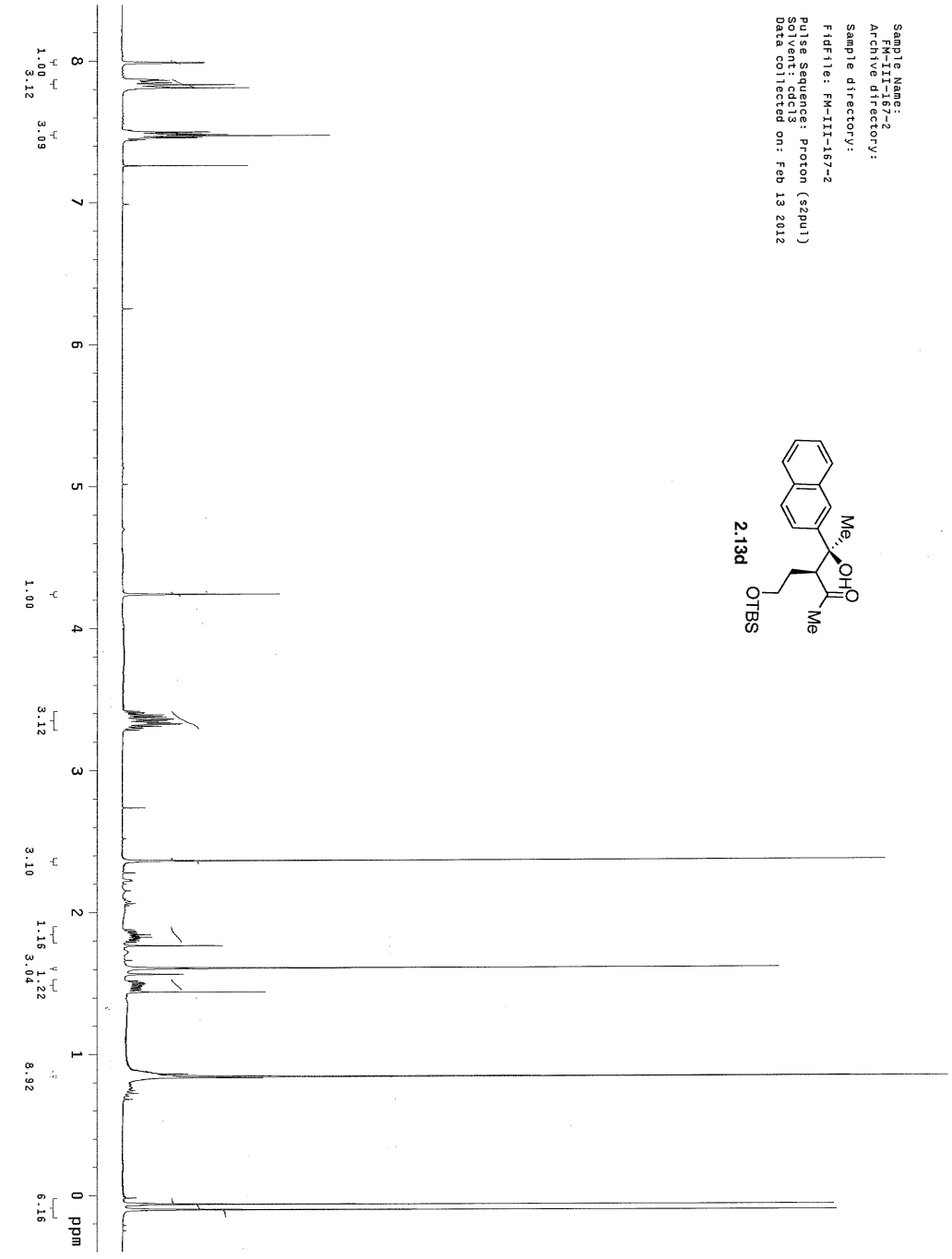
Sample directory:

FidFile: FM-III-125-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Feb 1 2012



2.13c

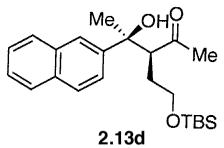

Sample Name:
FM-III-167-2
Archive directory:
Sample directory:
FidFile: FM-III-167-2
Pulse Sequence: Proton (szpul)
Solvent: cdcl3
Data collected on: Feb 13 2012
2.13d
Me
OH
Me
OTBS
8
7
6
5
4
3
2
1
0 ppm
1.00
3.12
3.09
1.00
3.12
3.10
1.16
1.22
3.04
8.92
6.16

Sample Name:
FM-III-167-2
Archive directory:

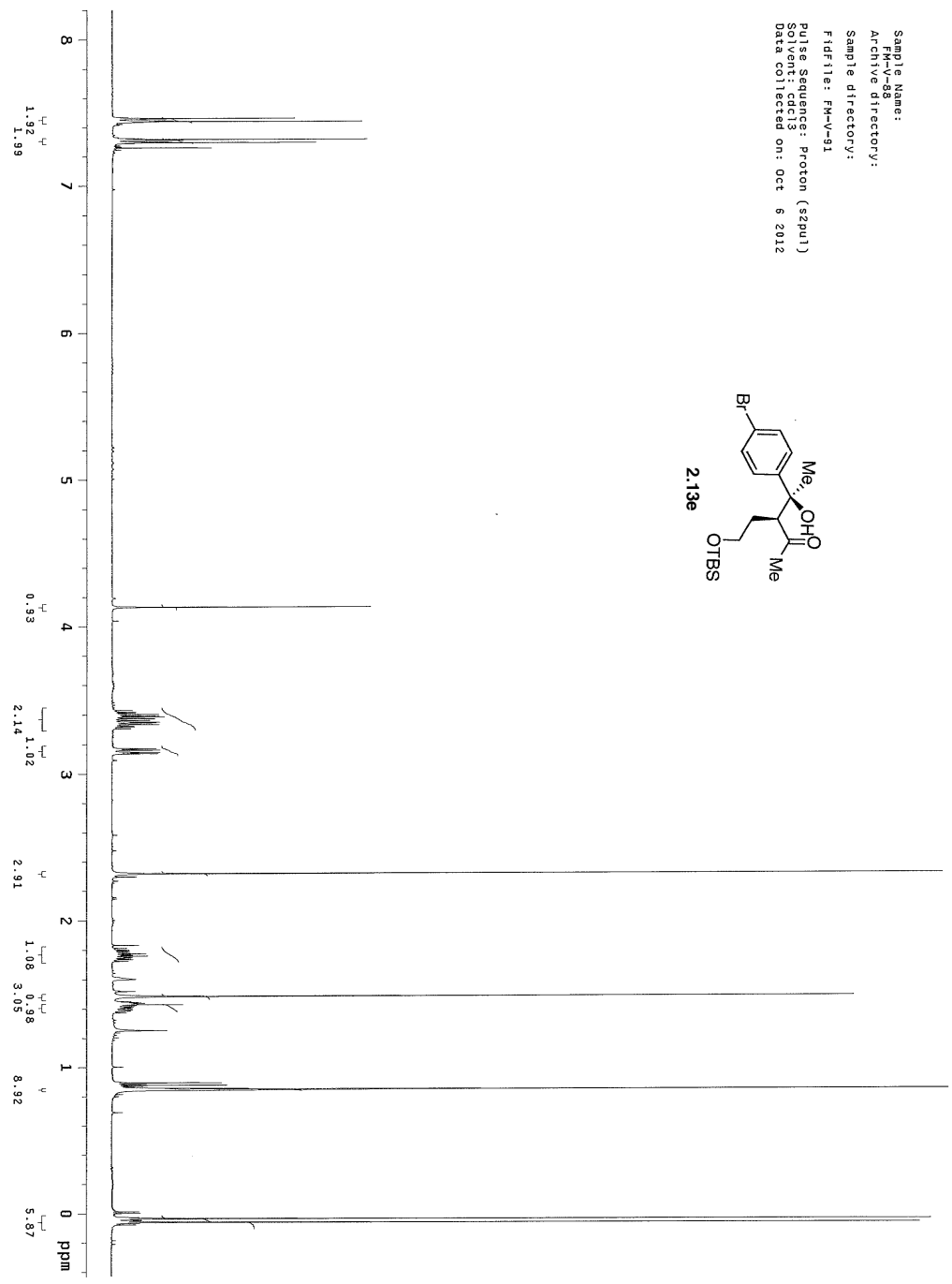
Sample directory:

FidFile: FM-III-167-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Feb 13 2012



2.13d

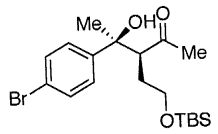

Sample Name:
ppp-v-88
Archive directory:
Sample directory:
FidFile: FM-V-91
Pulse Sequence: Proton (szpul)
Solvent: cdcl3
Data collected on: Oct 6 2012
Br
Me
OH
O
Me
OTBS
2.13e
8
7
6
5
4
3
2
1
0 ppm
1.92
1.99
0.93
2.14
1.02
2.91
1.08
3.05
0.98
8.92
5.87

Sample Name:
FM-V-91
Archive directory:

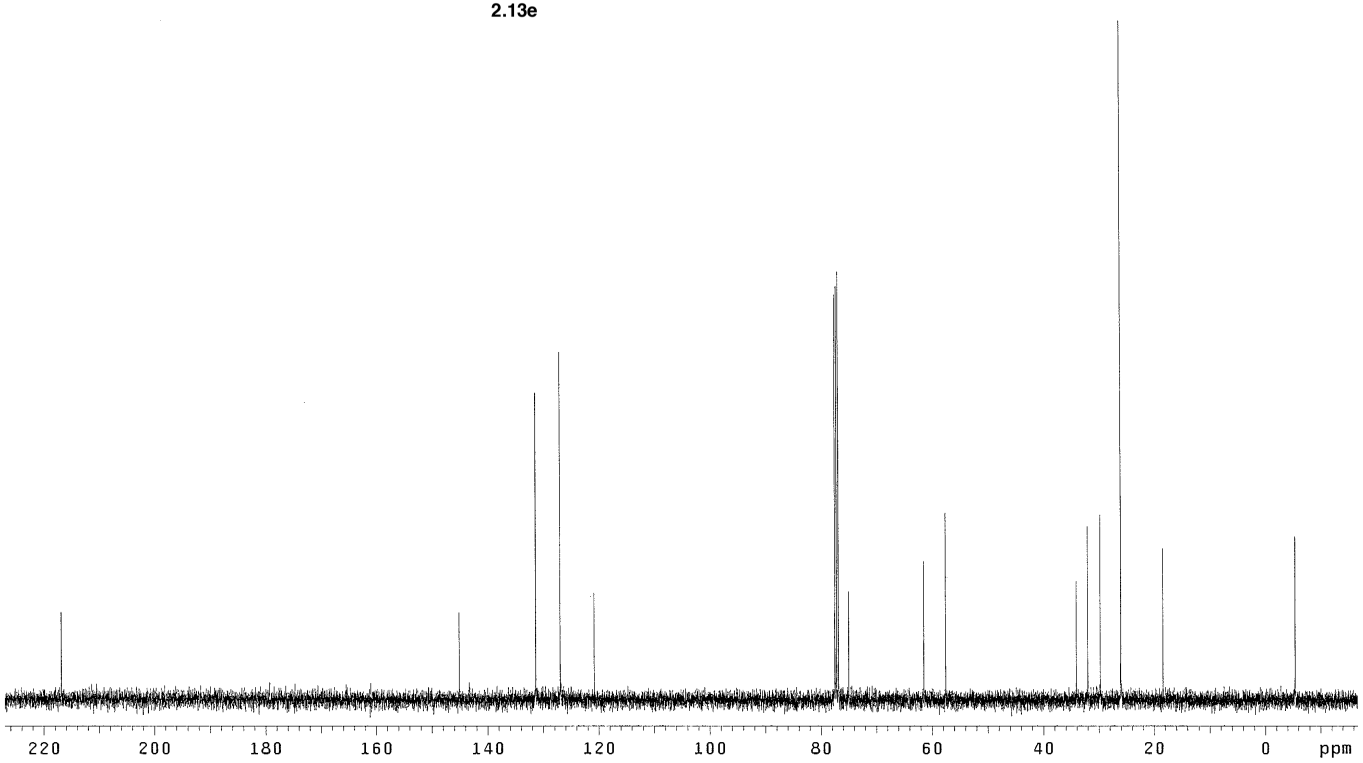
Sample directory:

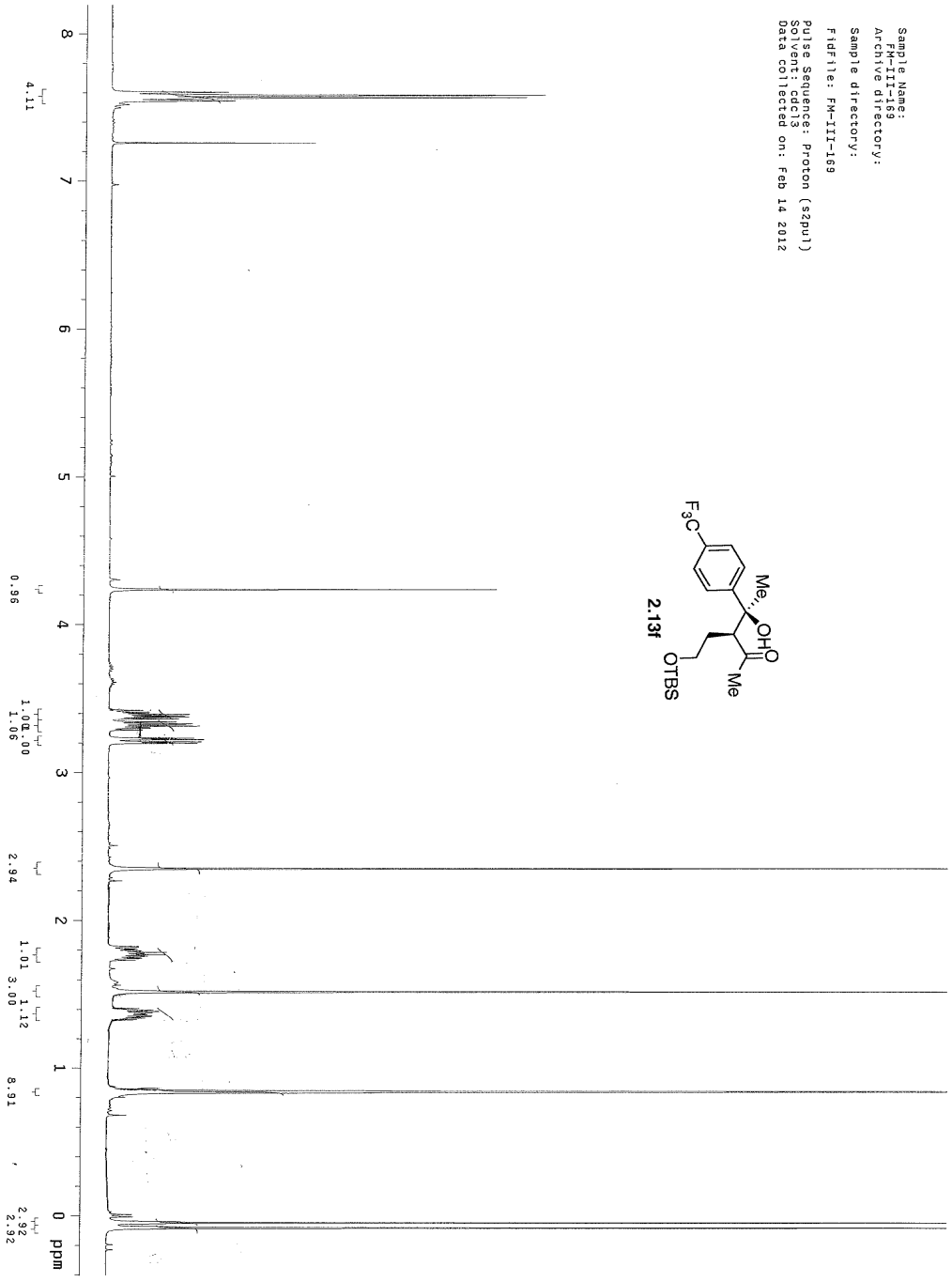
FidFile: FM-V-91-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Oct 6 2012



2.13e



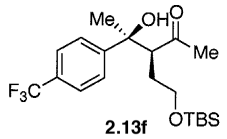

Sample Name:
FM-III-169
Archive directory:
Sample directory:
FidFile: FM-III-169
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Feb 14 2012
F3C
Me
OH
O
Me
OTBS
2.13f
8
7
6
5
4
3
2
1
0 ppm
4.11
0.96
1.06
1.00
1.00
2.94
1.01
3.00
1.12
8.91
2.92
2.92

Sample Name:
FM-III-169-CNMR
Archive directory:

Sample directory:

FidFile: FM-III-169-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Feb 15 2012



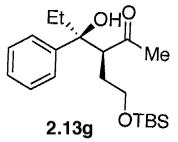
2.13f

Sample Name:
FM-III-201
Archive directory:

Sample directory:

FidFile: FM-III-201

Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Feb 24 2012



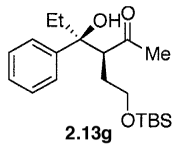
2.13g

Sample Name:
FM-III-202-CNMR
Archive directory:

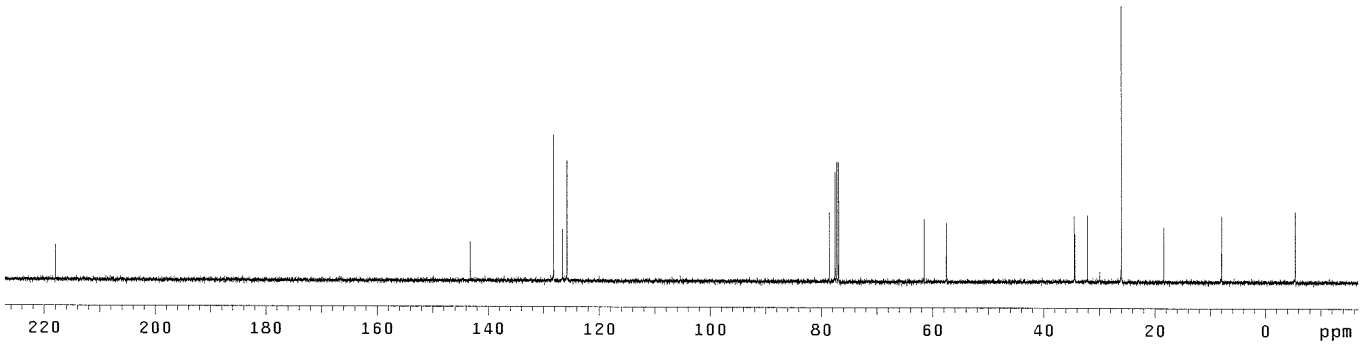
Sample directory:

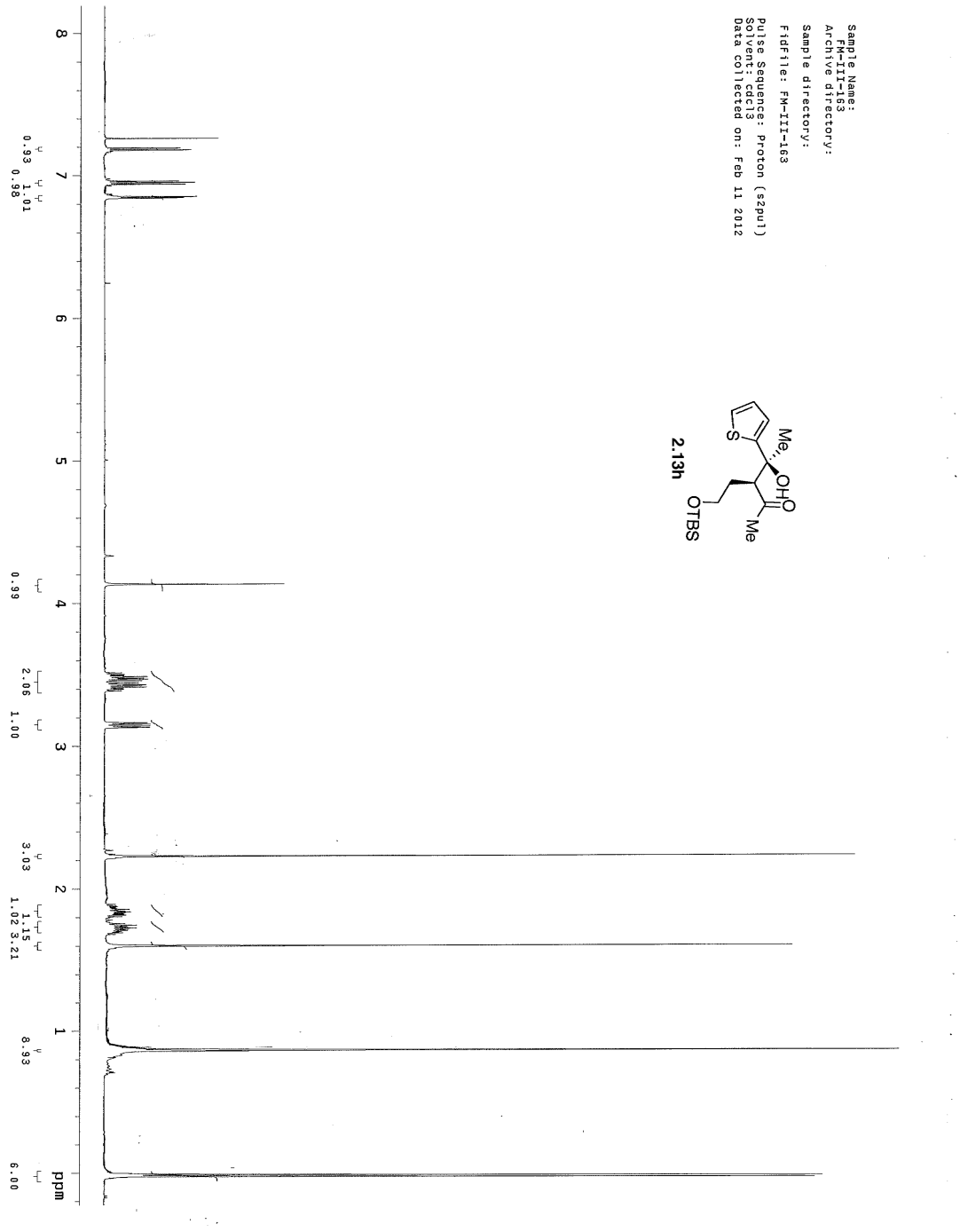
FidFile: FM-III-202-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Feb 24 2012



2.13g



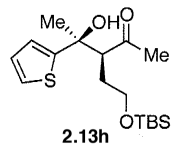

Sample Name:
FM-III-163
Archive directory:
Sample directory:
Fidfile: FM-III-163
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Feb 11 2012
2.13h
Me
OH
O
Me
S
OTBS
8
7
6
5
4
3
2
1
ppm
0.93
1.01
0.98
0.99
2.06
1.00
3.03
1.15
1.02
3.21
8.93
6.00

Sample Name:
FM-III-163-2
Archive directory:

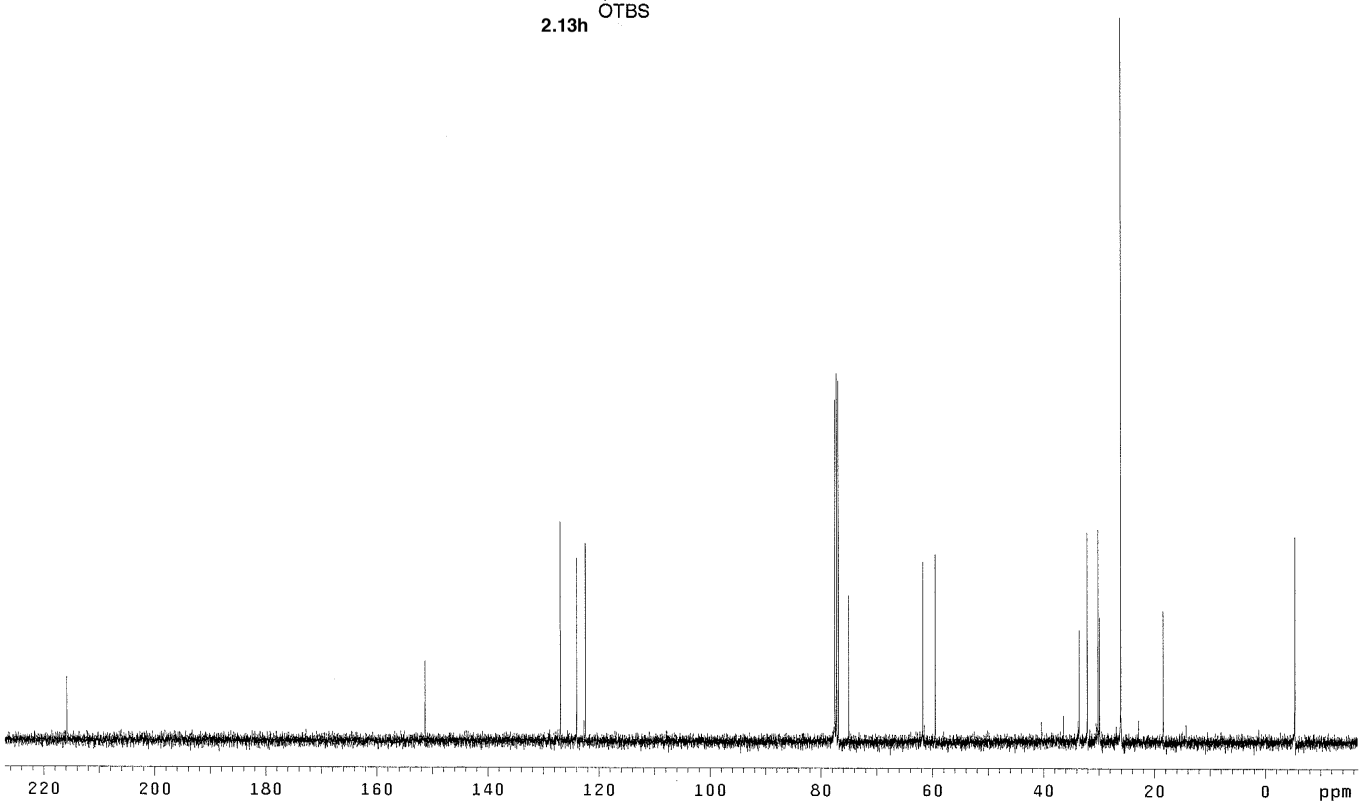
Sample directory:

FidFile: FM-III-163-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Feb 13 2012



2.13h

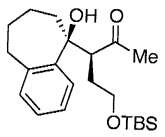


Sample Name:
FM-III-192
Archive directory:

Sample directory:

FidFile: FM-III-191

Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Feb 24 2012



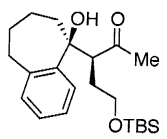
2.13i

Sample Name:
FM-III-192-CNMR
Archive directory:

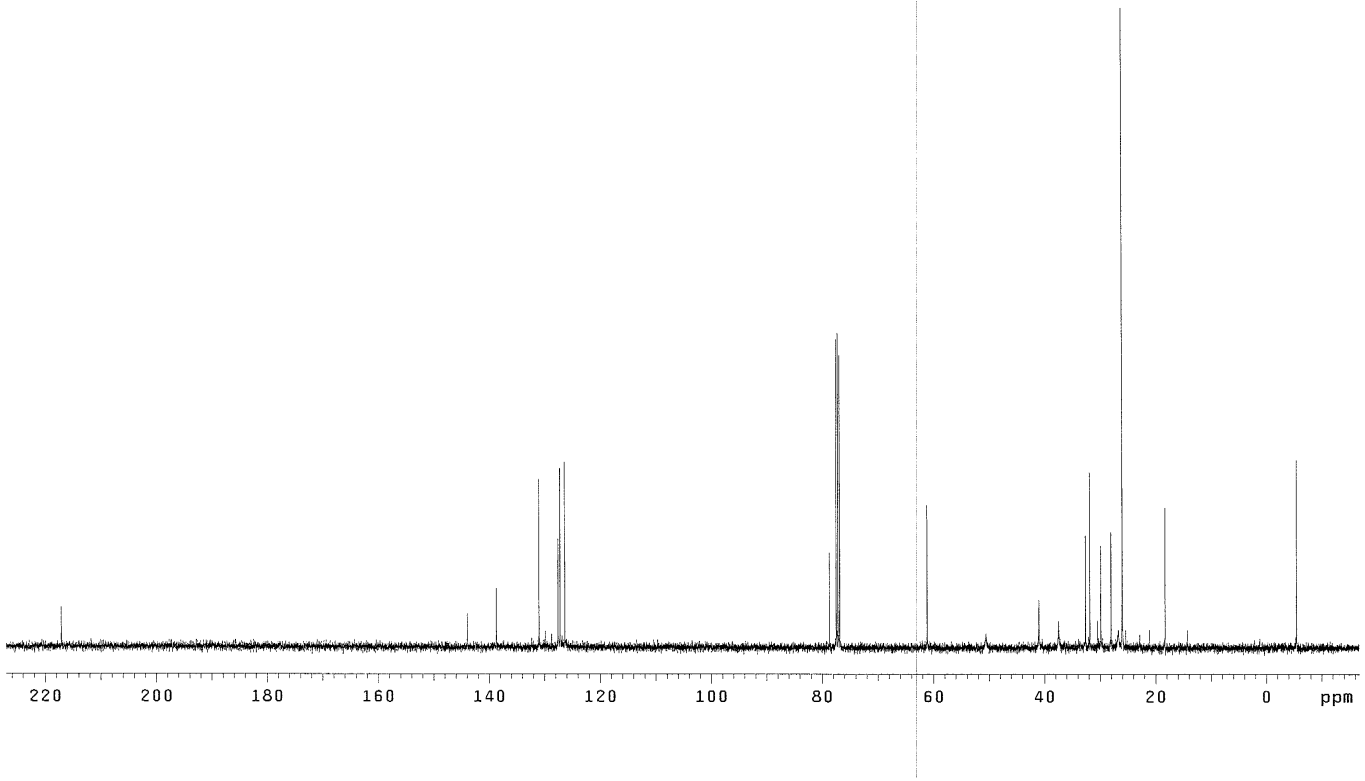
Sample directory:

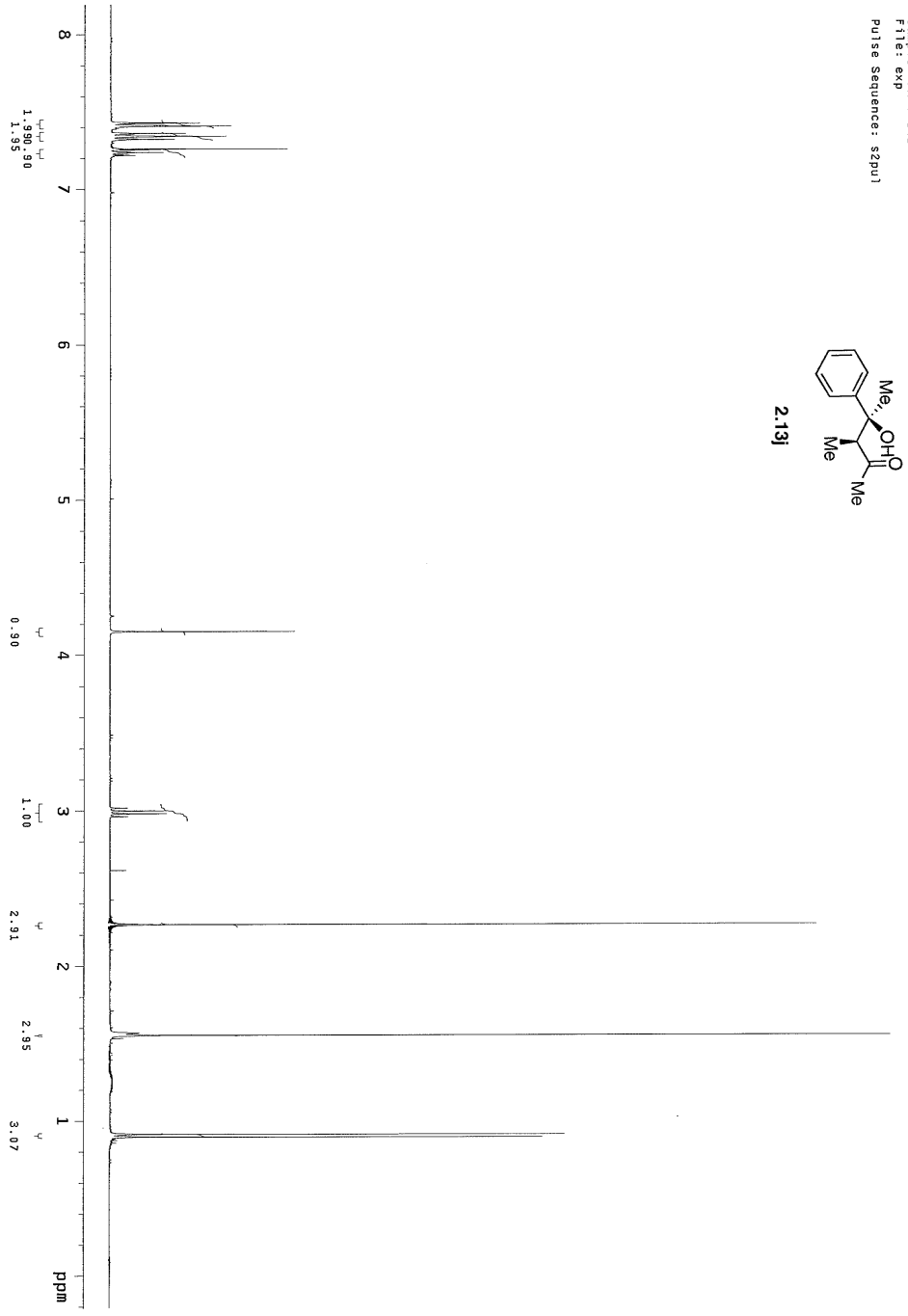
FidFile: FM-III-192-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Feb 24 2012



2.13i



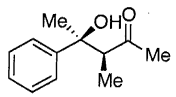

Sample: FM-V-84B
File: exp
Pulse Sequence: s2pul
Me
OH
O
Me
Me
2.13j
8
7
6
5
4
3
2
1
ppm
1.99
1.95
0.90
1.00
2.91
2.95
3.07

Sample Name:
FM-V-84A
Archive directory:

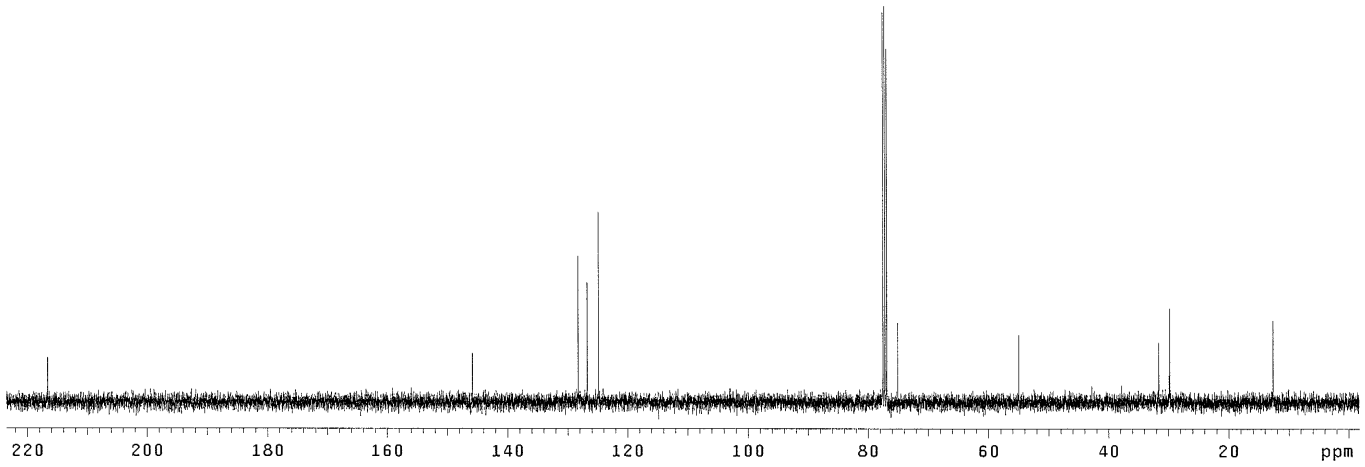
Sample directory:

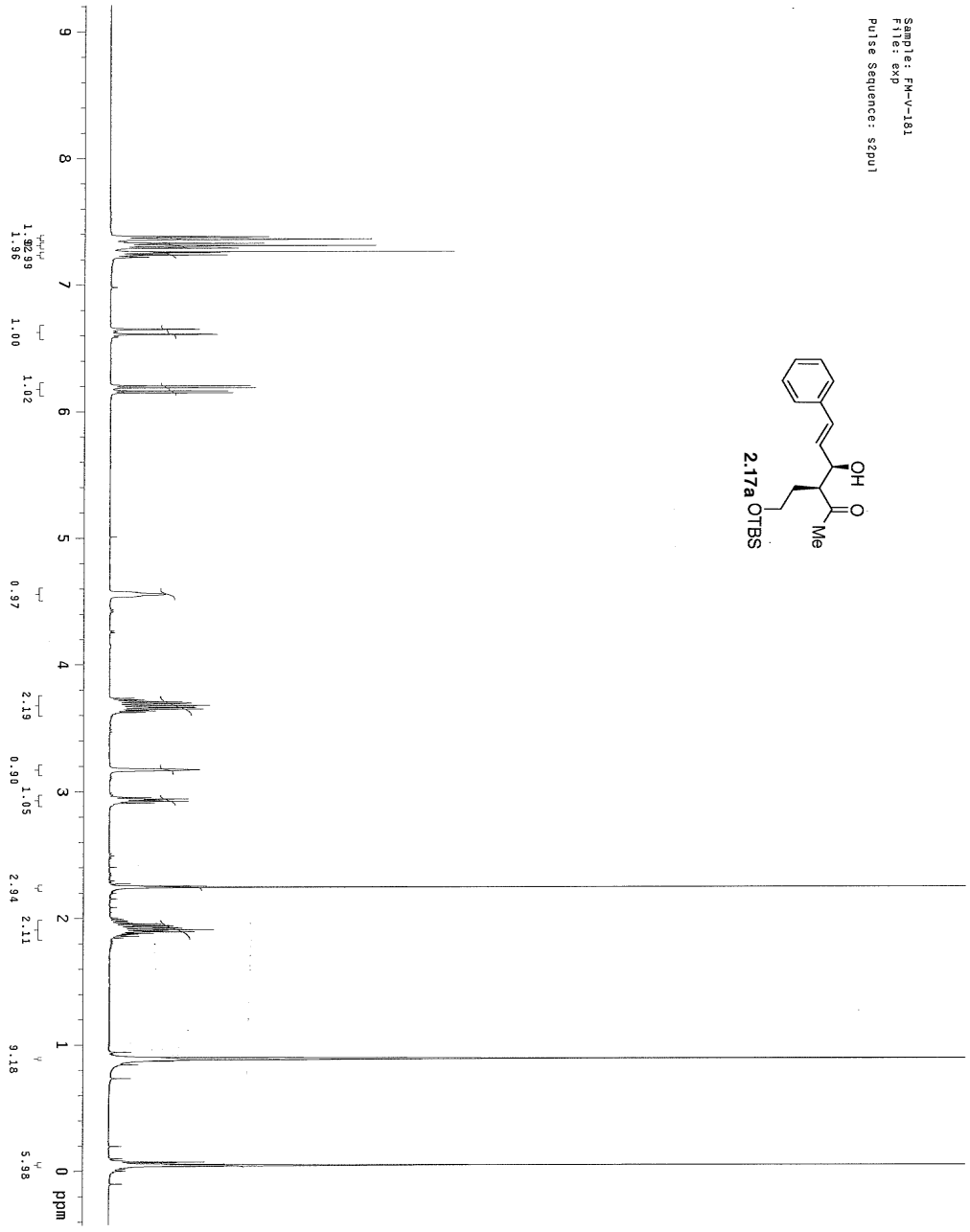
FidFile: FM-V-84A-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Oct 8 2012



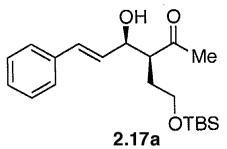
2.13j



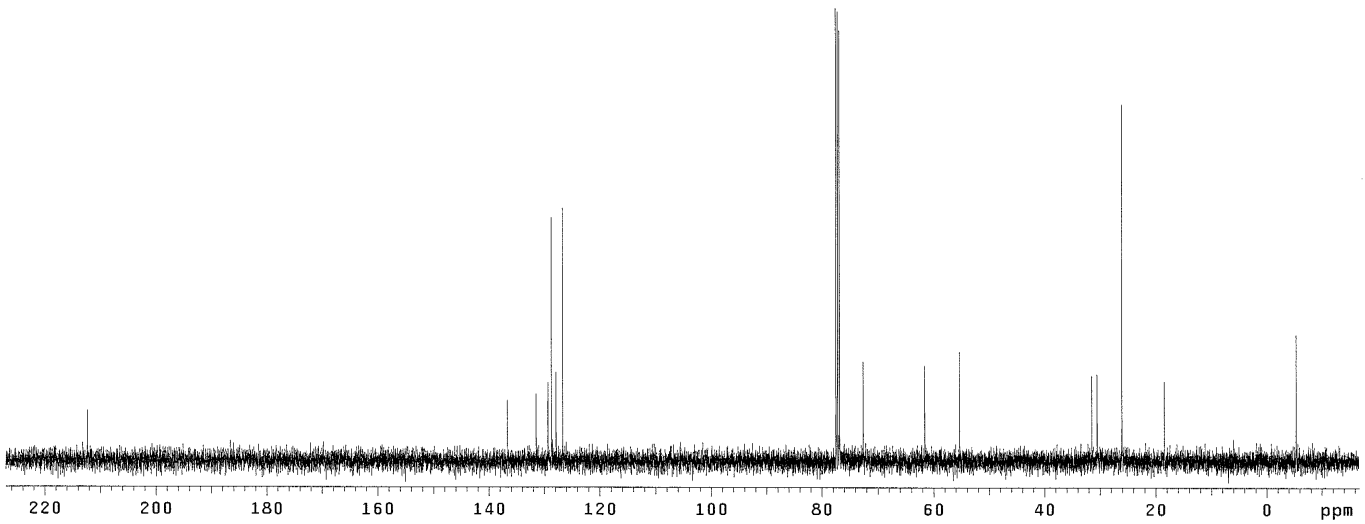

Sample: FM-V-181
File: exp
Pulse Sequence: s2pul
OH
O
Me
2.17a OTBS
9
8
7
6
5
4
3
2
1
0 ppm
1.96
2.99
1.00
1.02
0.97
2.19
0.90
1.05
2.94
2.11
9.18
5.98

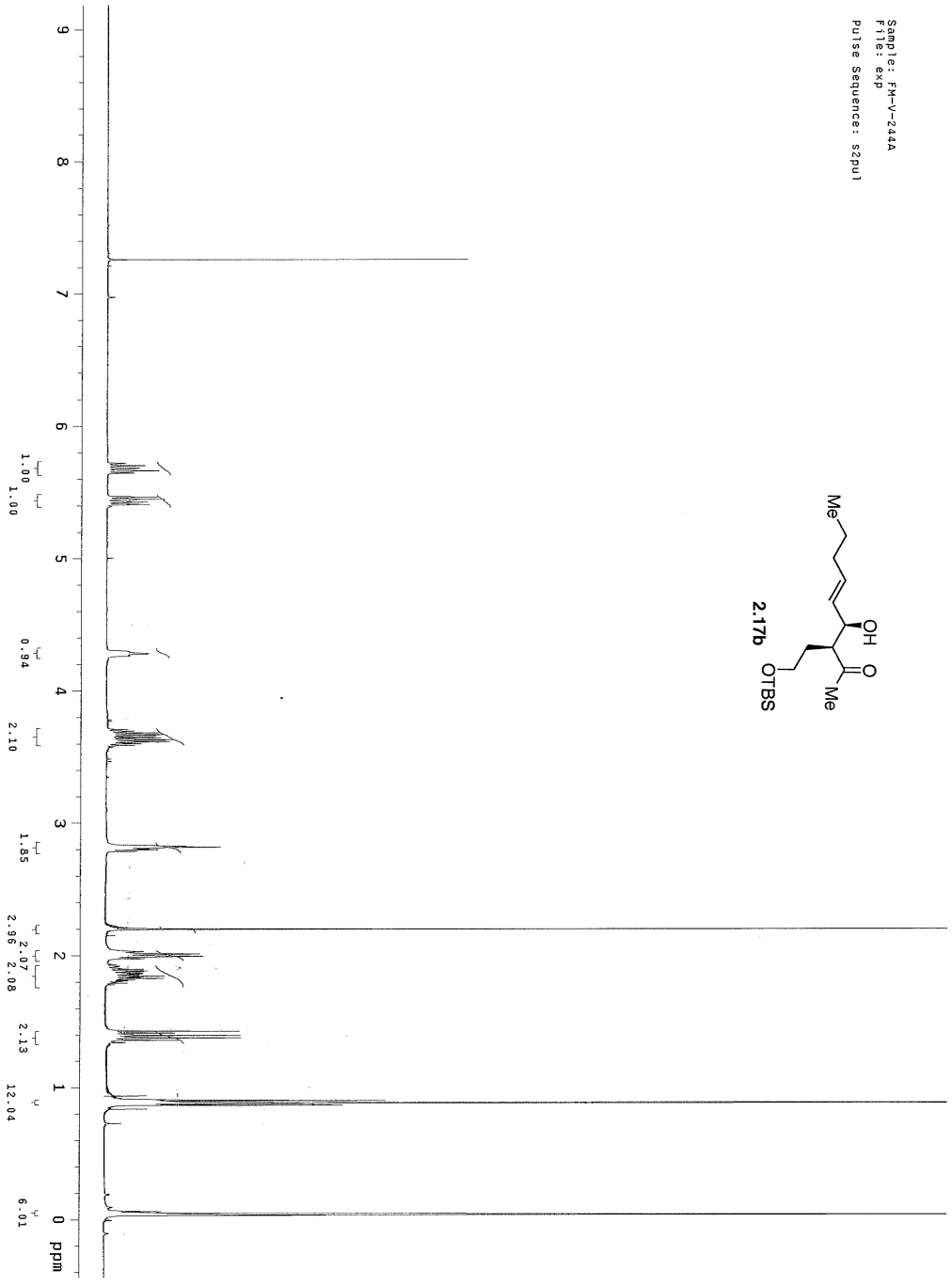
Sample: FM-V-181
File: exp

Pulse Sequence: s2pul



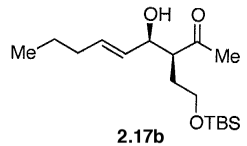
2.17a



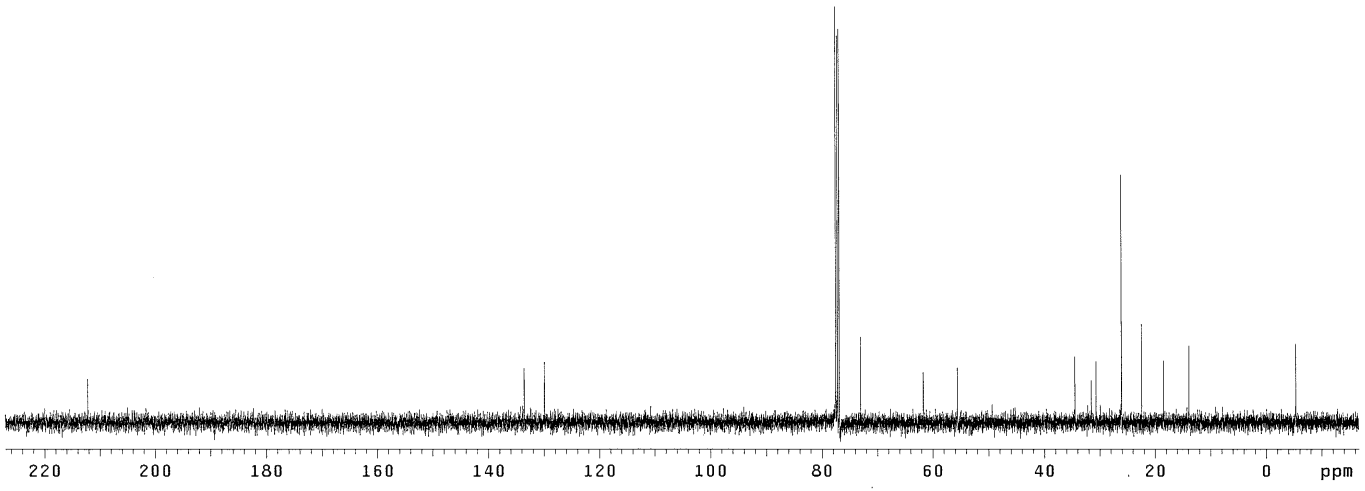

Sample: FM-V-244A
File: exp
Pulse Sequence: s2pul
Me
OH
O
Me
2.17b
OTBS
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.00
0.94
2.10
1.85
2.96
2.08
2.07
2.13
12.04
6.01

Sample: FM-V-244A
File: exp

Pulse Sequence: s2pul



2.17b

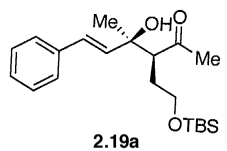


Sample Name:
FM-III-291-1
Archive directory:

Sample directory:

FidFile: FM-III-291-1

Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Apr 6 2012



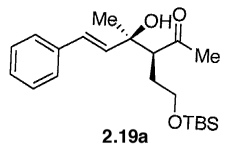
2.19a

Sample Name:
FM-III-291-1-CNMR
Archive directory:

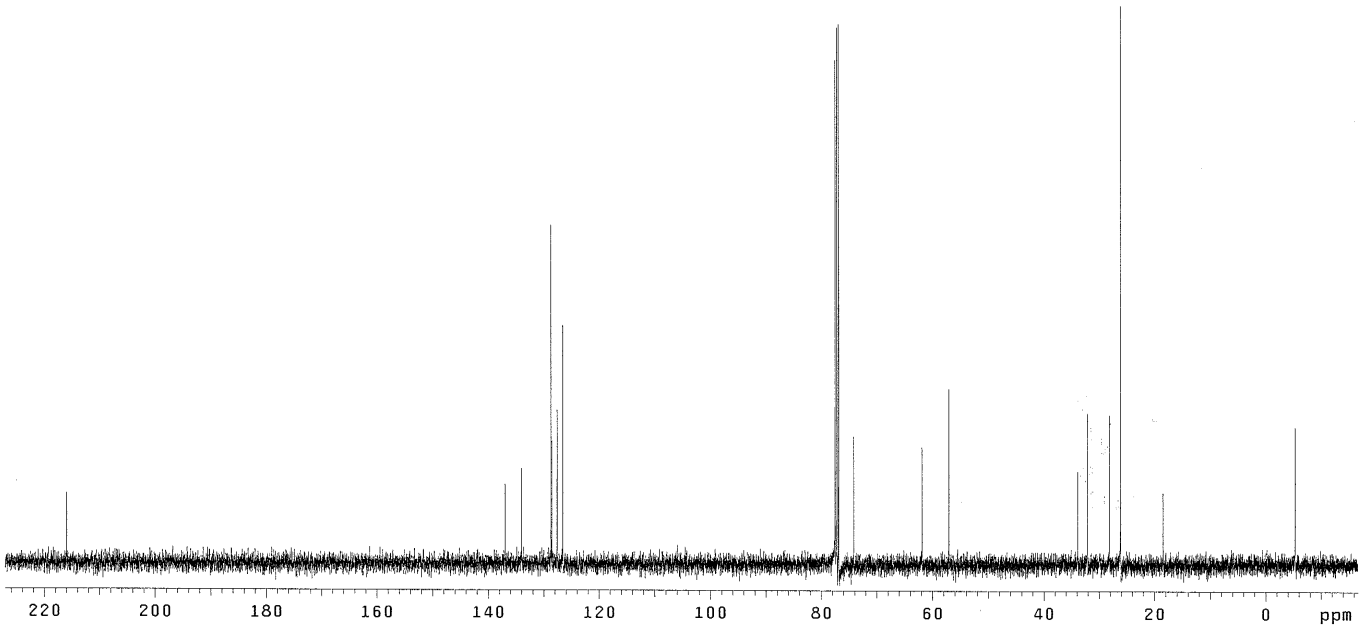
Sample directory:

FidFile: FM-III-291-1-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Apr 6 2012



2.19a

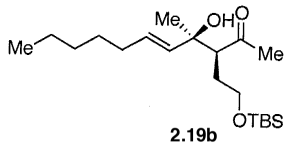


Sample Name:
FM-IV-92
Archive directory:

Sample directory:

FidFile: FM-IV-92

Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Jun 12 2012



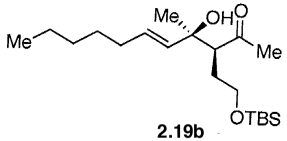
2.19b

Sample Name:
FM-IV-92-CNMR
Archive directory:

Sample directory:

FidFile: FM-IV-92-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Jun 12 2012



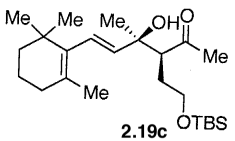
2.19b

Sample Name:
FM-IV-45
Archive directory:

Sample directory:

FidFile: FM-IV-45

Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Apr 30 2012



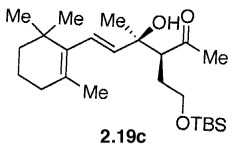
2.19c

Sample Name:
FM-IV-45
Archive directory:

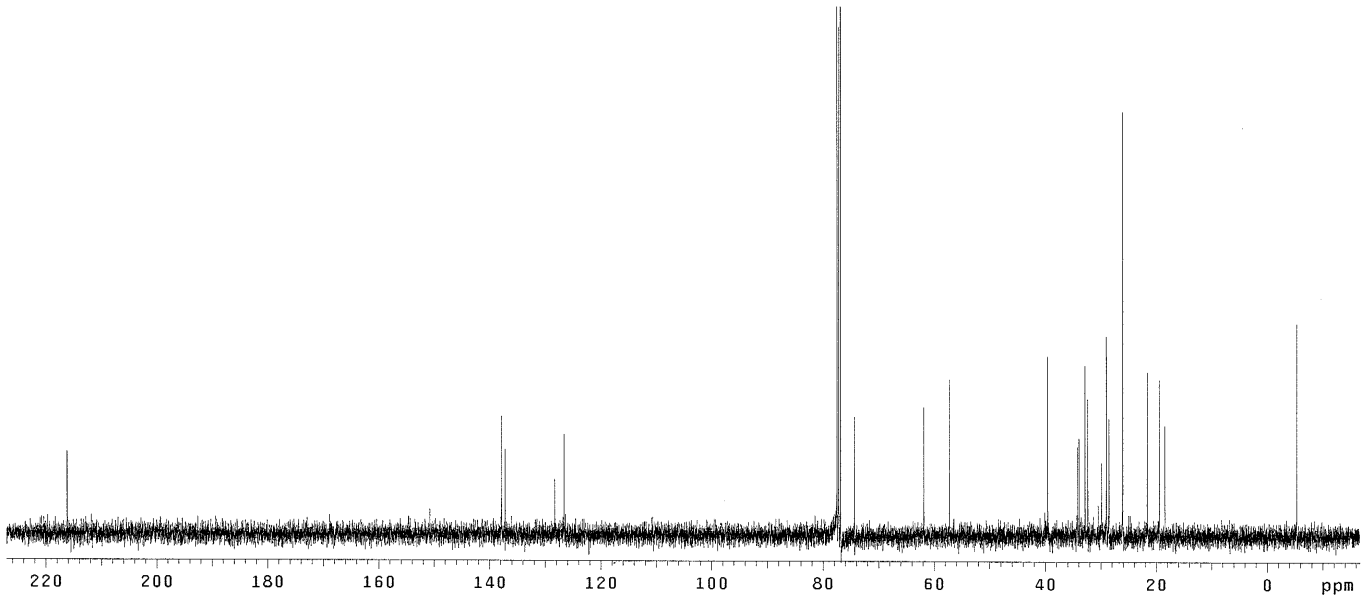
Sample directory:

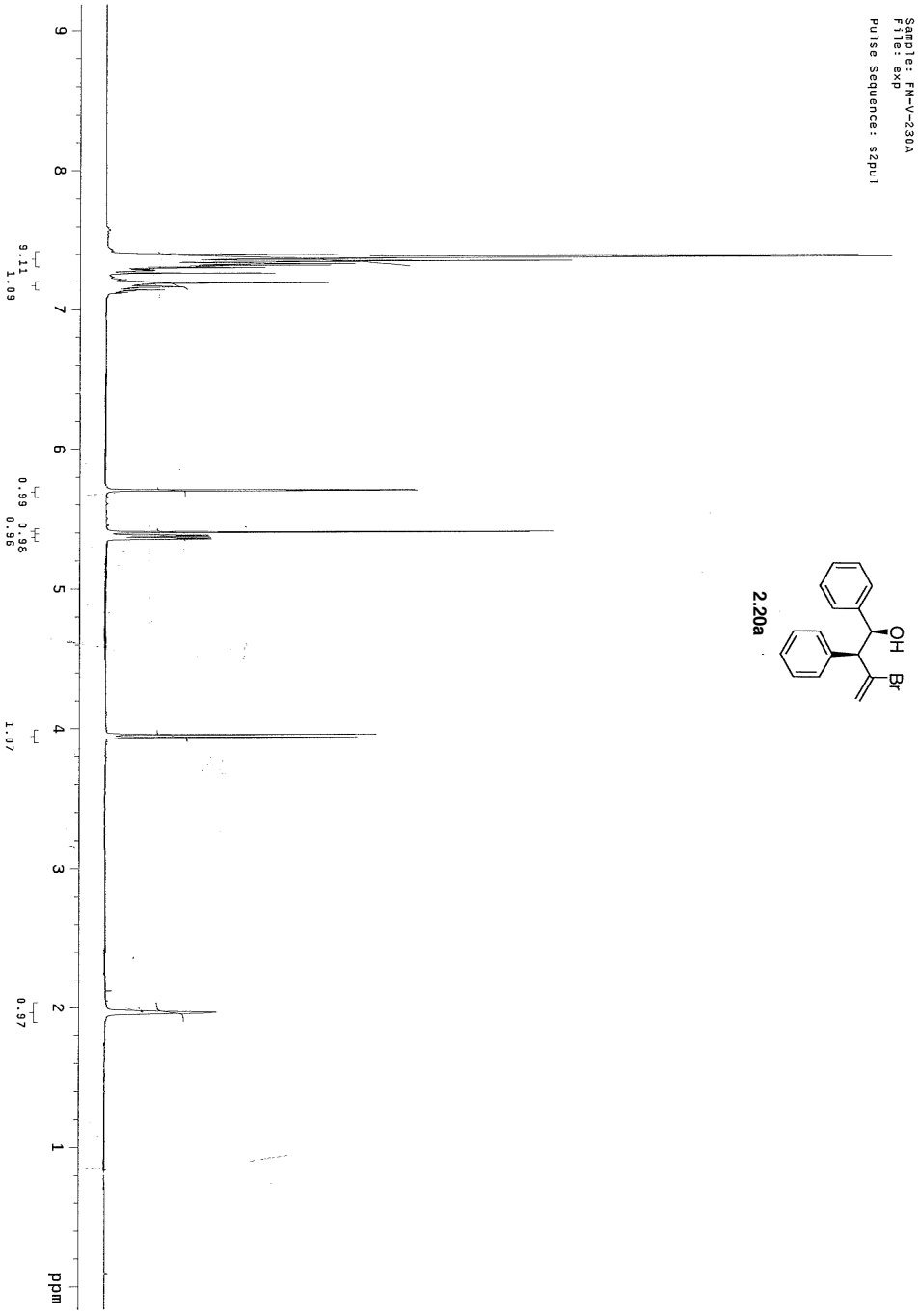
FidFile: FM-IV-45-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Apr 30 2012



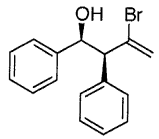
2.19c



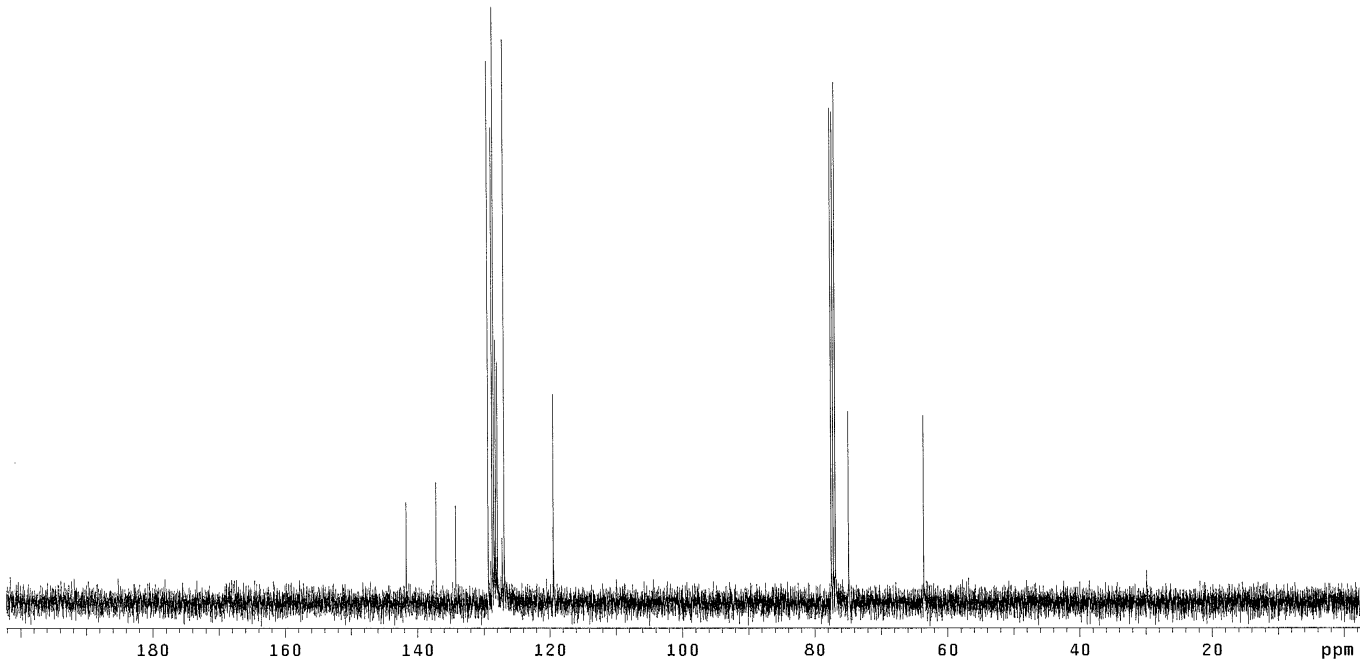

Sample: FM-V-230A
File: exp
Pulse Sequence: s2pul
OH
Br
2.20a
9.11
1.09
0.99
0.98
0.96
1.07
0.97
ppm

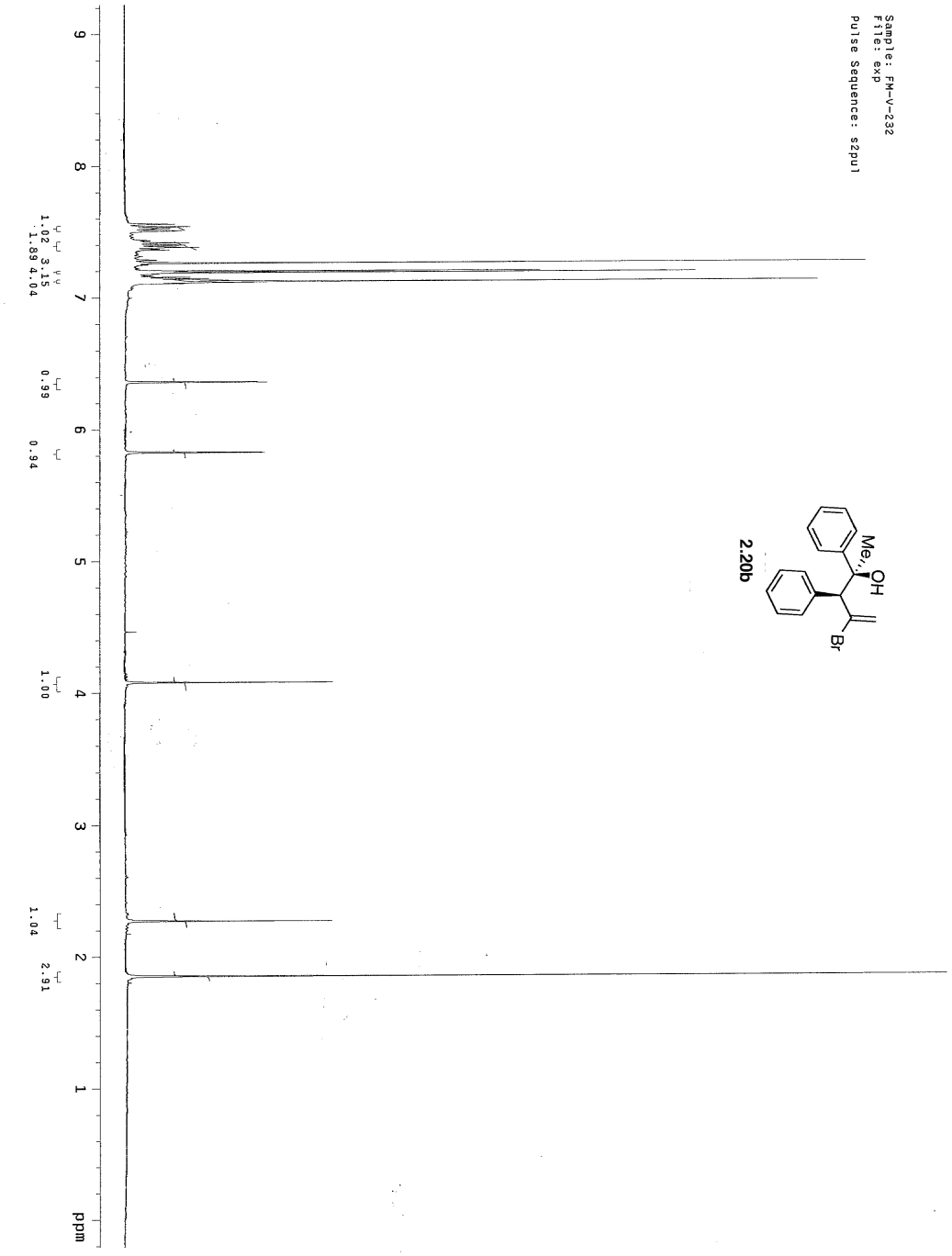
Sample: FM-V-230A
File: exp

Pulse Sequence: s2pul



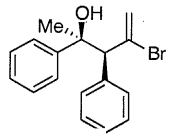
2.20a




Sample: FM-V-232
File: exp
Pulse Sequence: s2pul
Me
OH
Br
2.20b
ppm

Sample: FM-V-232
File: exp

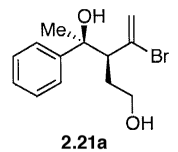
Pulse Sequence: s2pul



2.20b

Sample: FM-V-168
File: exp

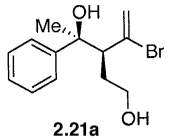
Pulse Sequence: s2pul



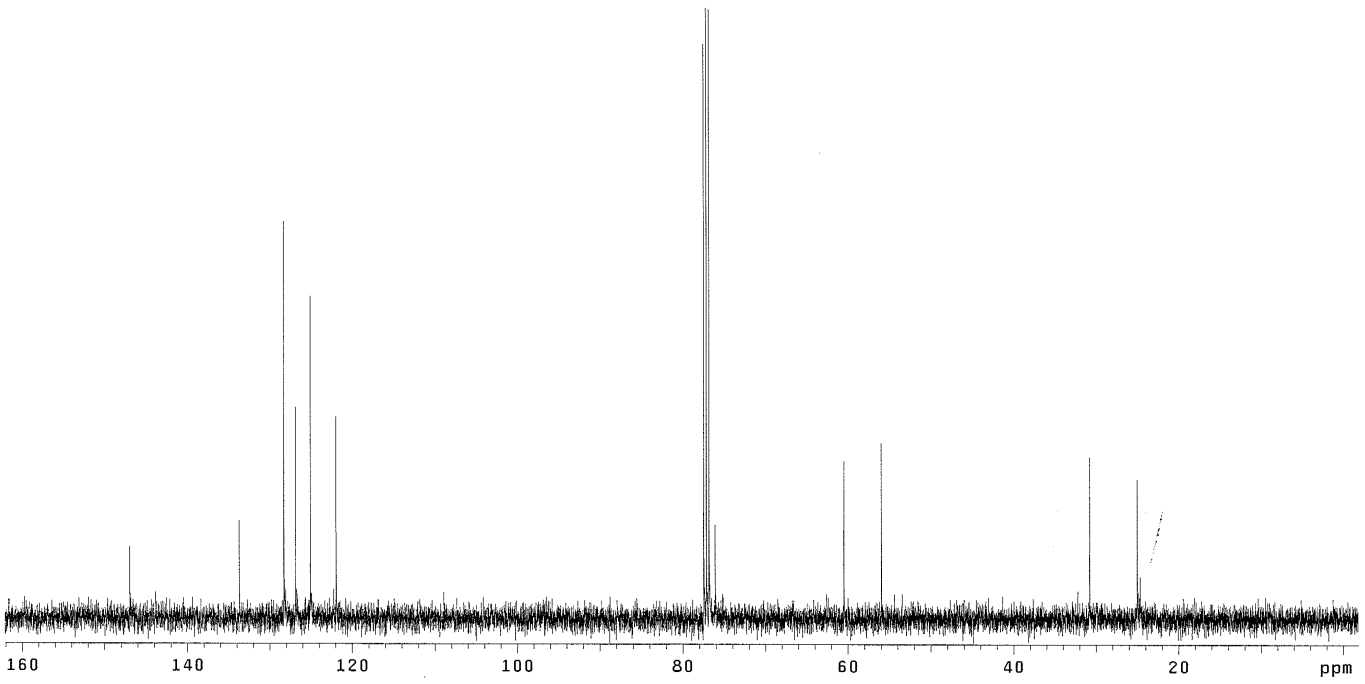
2.21a

Sample: FM-V-168
File: exp

Pulse Sequence: s2pul

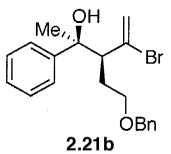


2.21a



Sample: FM-V-207
File: exp

Pulse Sequence: s2pul



2.21b

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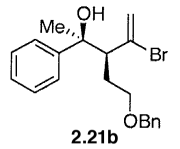
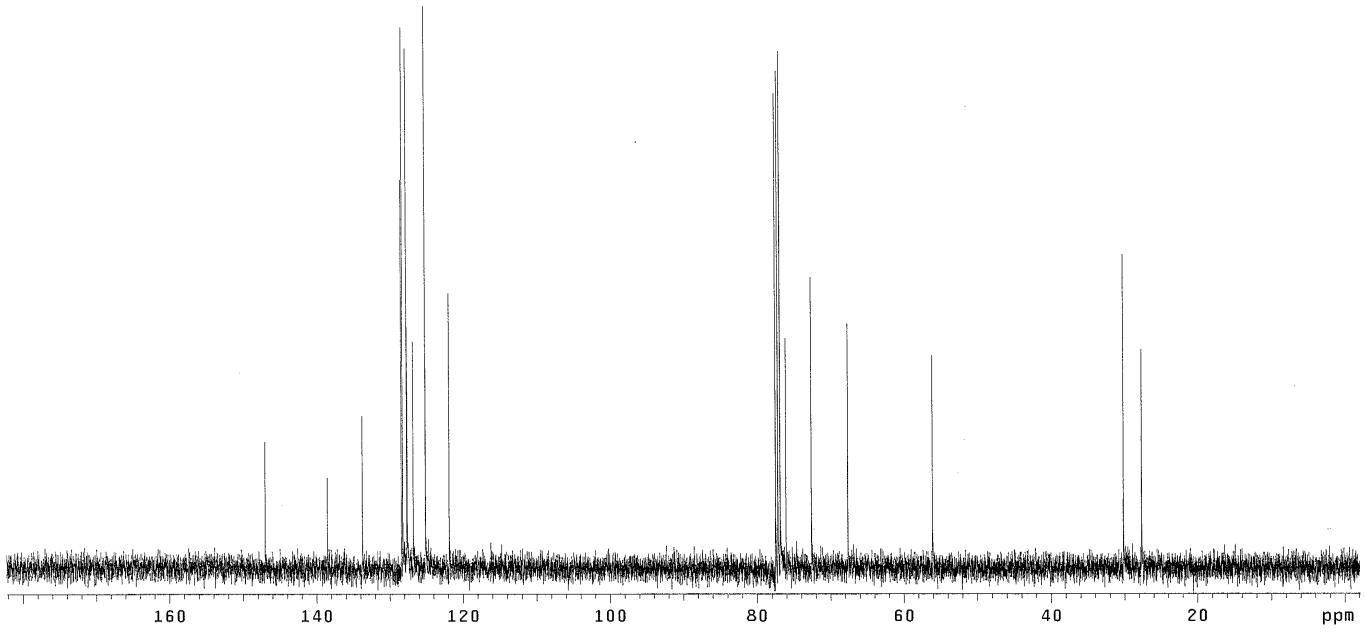
File: exp

Pulse Sequence: s2pul



2.21b



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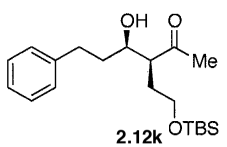
Pulse Sequence: s2pul



2.12k

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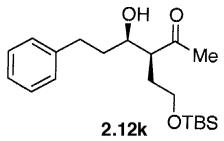
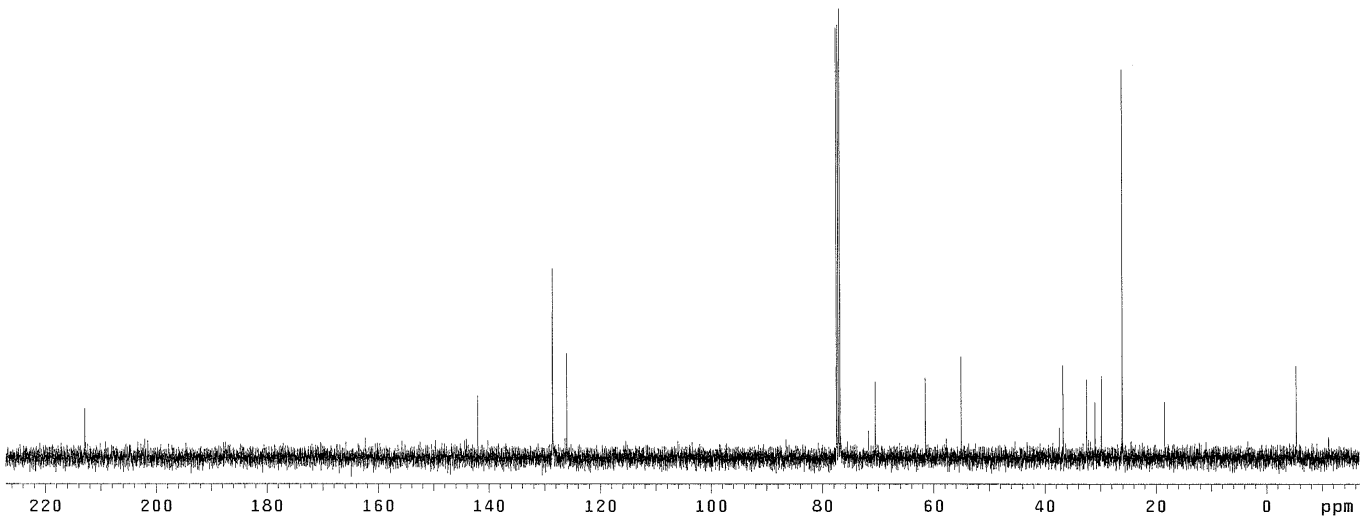
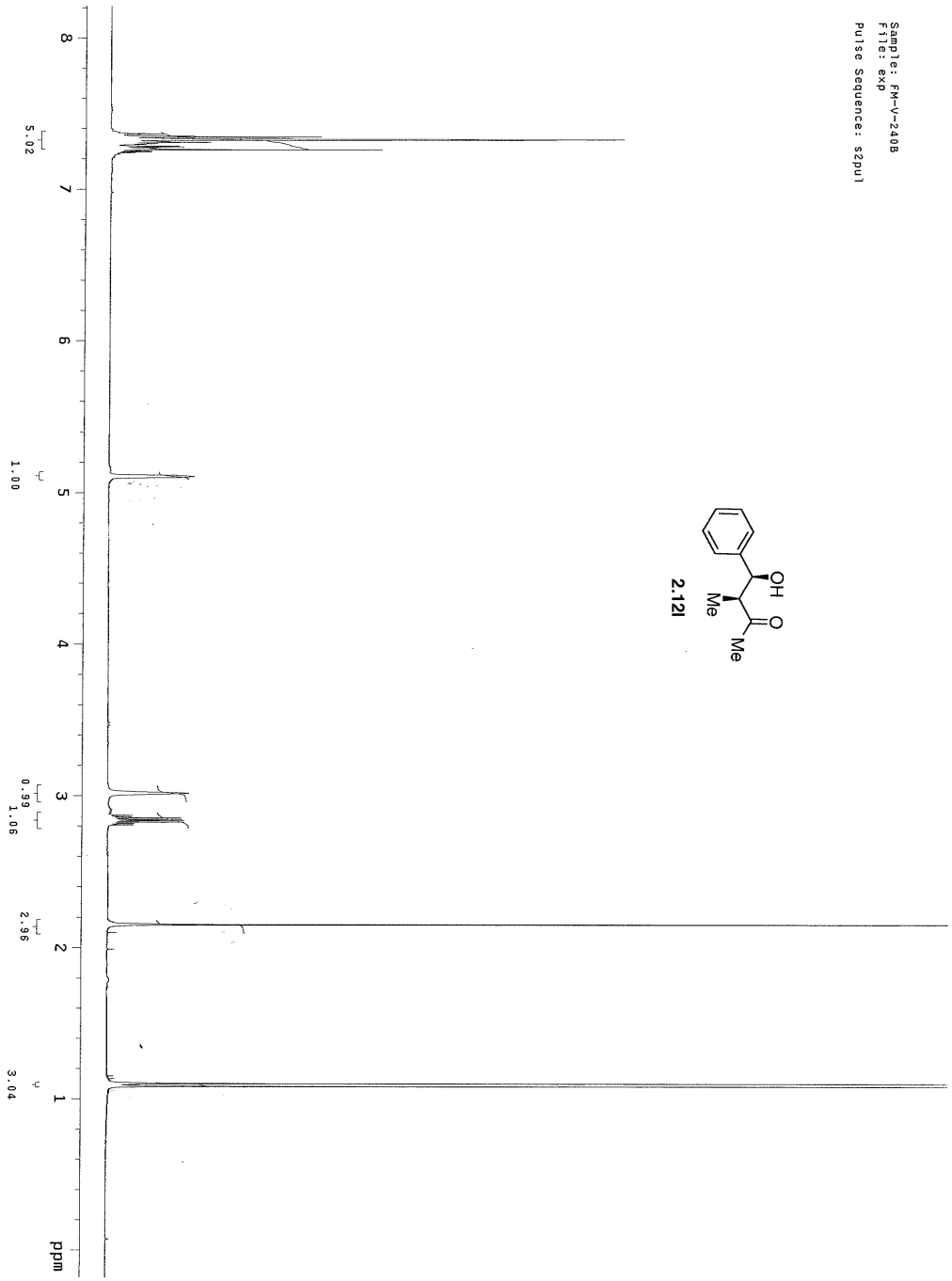
File: exp

Pulse Sequence: s2pul



2.12k

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File: exp
Pulse Sequence: s2pul
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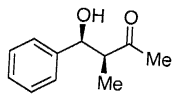
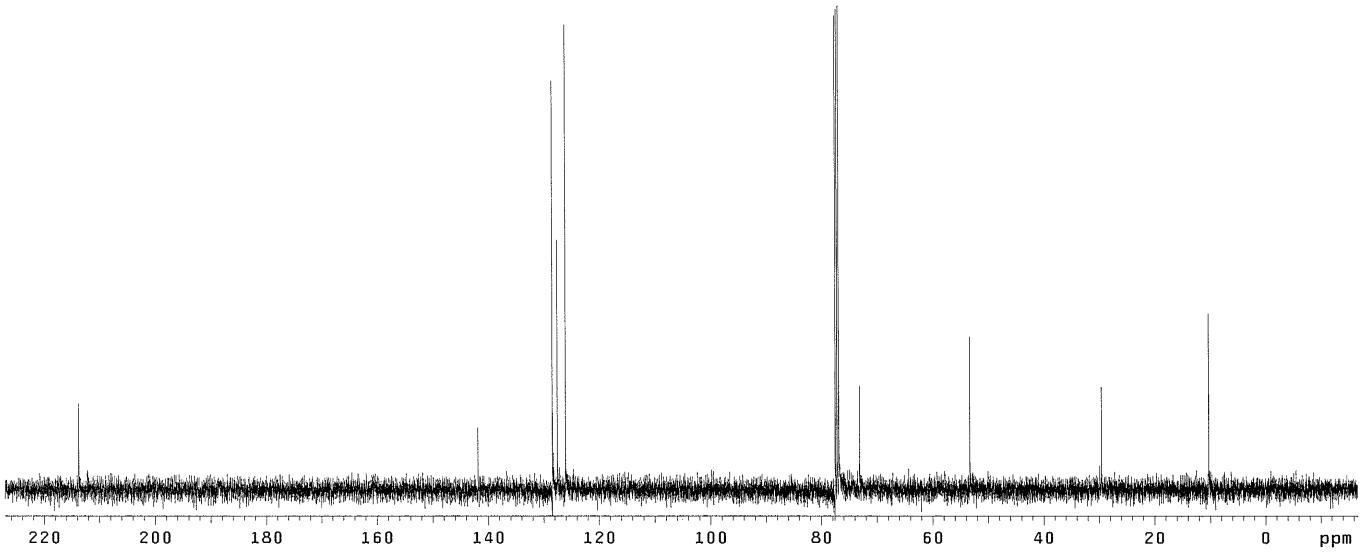
O
Me
Me
2.12l
8
7
6
5
4
3
2
1
ppm
5.02
1.00
0.99
1.06
2.96
3.04

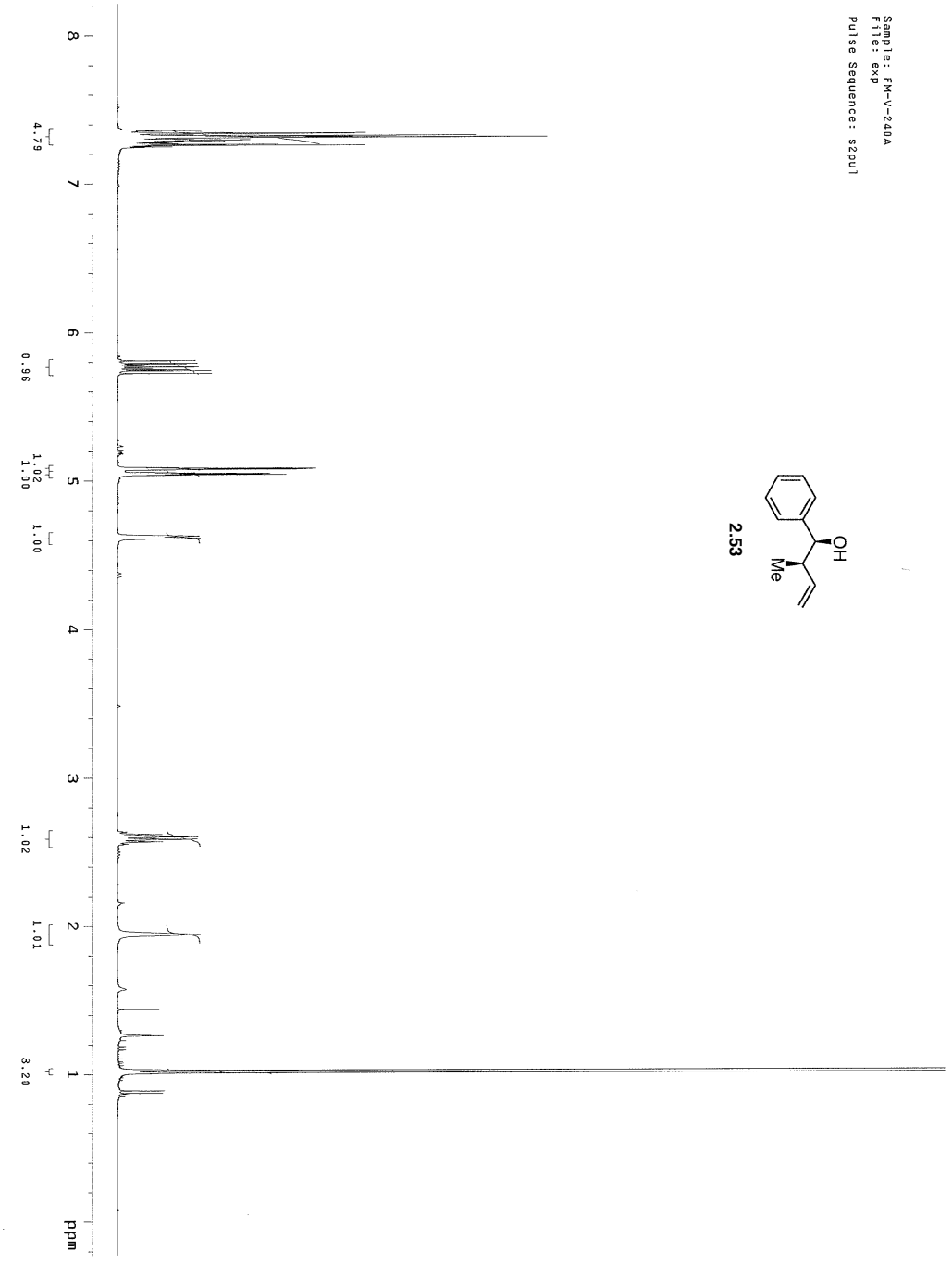
Sample: FM-V-240B
File: exp

Pulse Sequence: s2pul



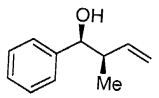
2.12l




Sample: FM-V-240A
File: exp
Pulse Sequence: s2pul
OH
Me
2.53
ppm

Sample: FM-V-240A
File: exp

Pulse Sequence: s2pul



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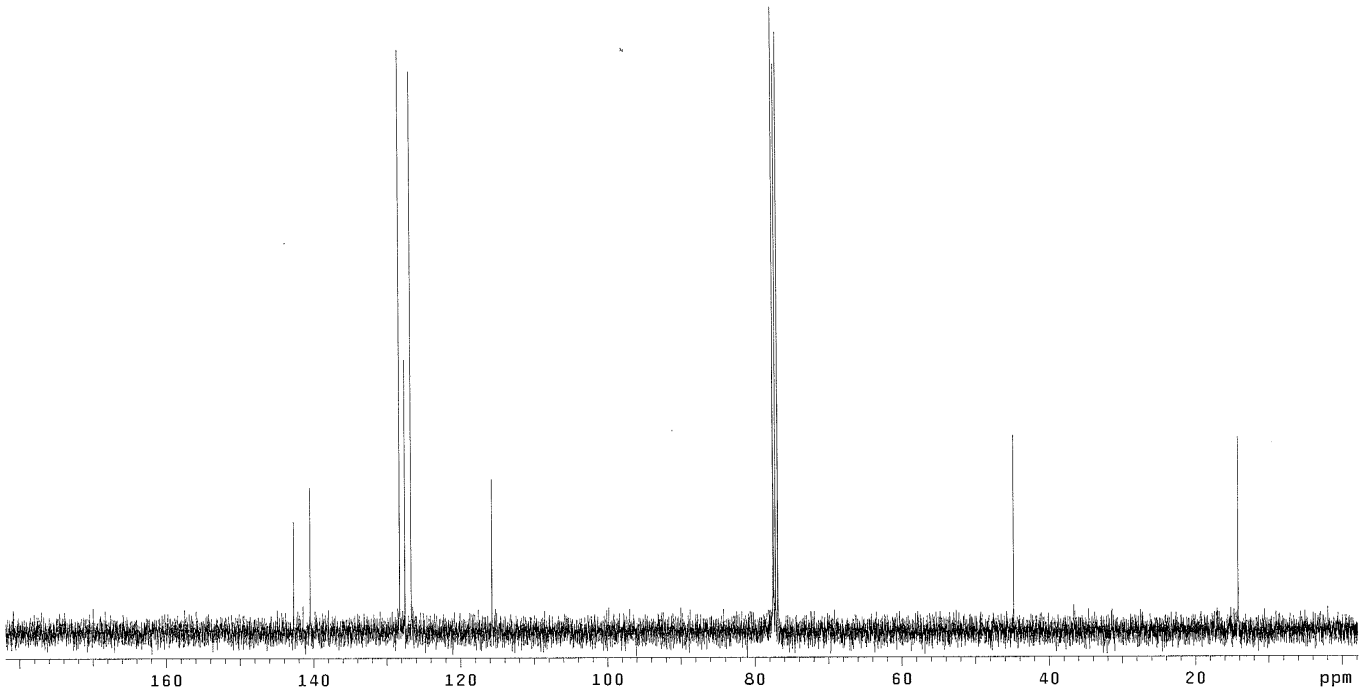

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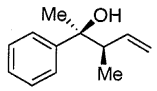


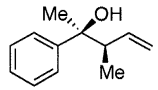
2.54

Sample Name:
FM-V-75
Archive directory:

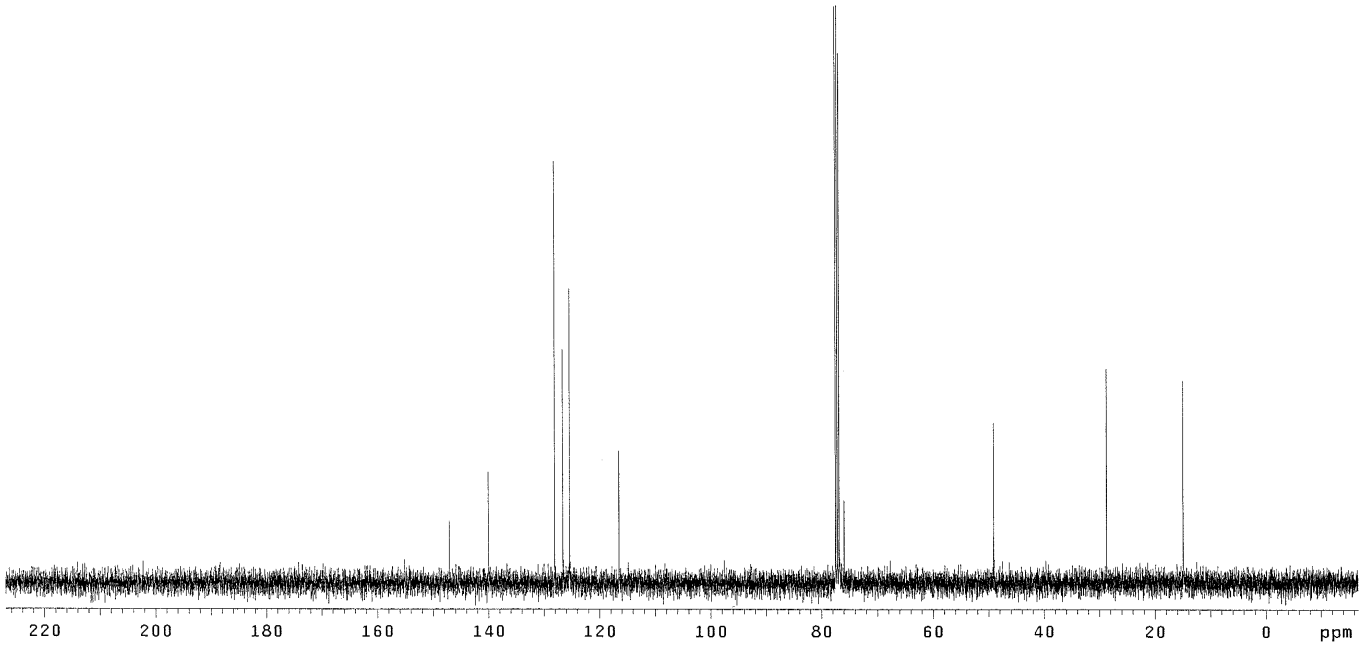
Sample directory:

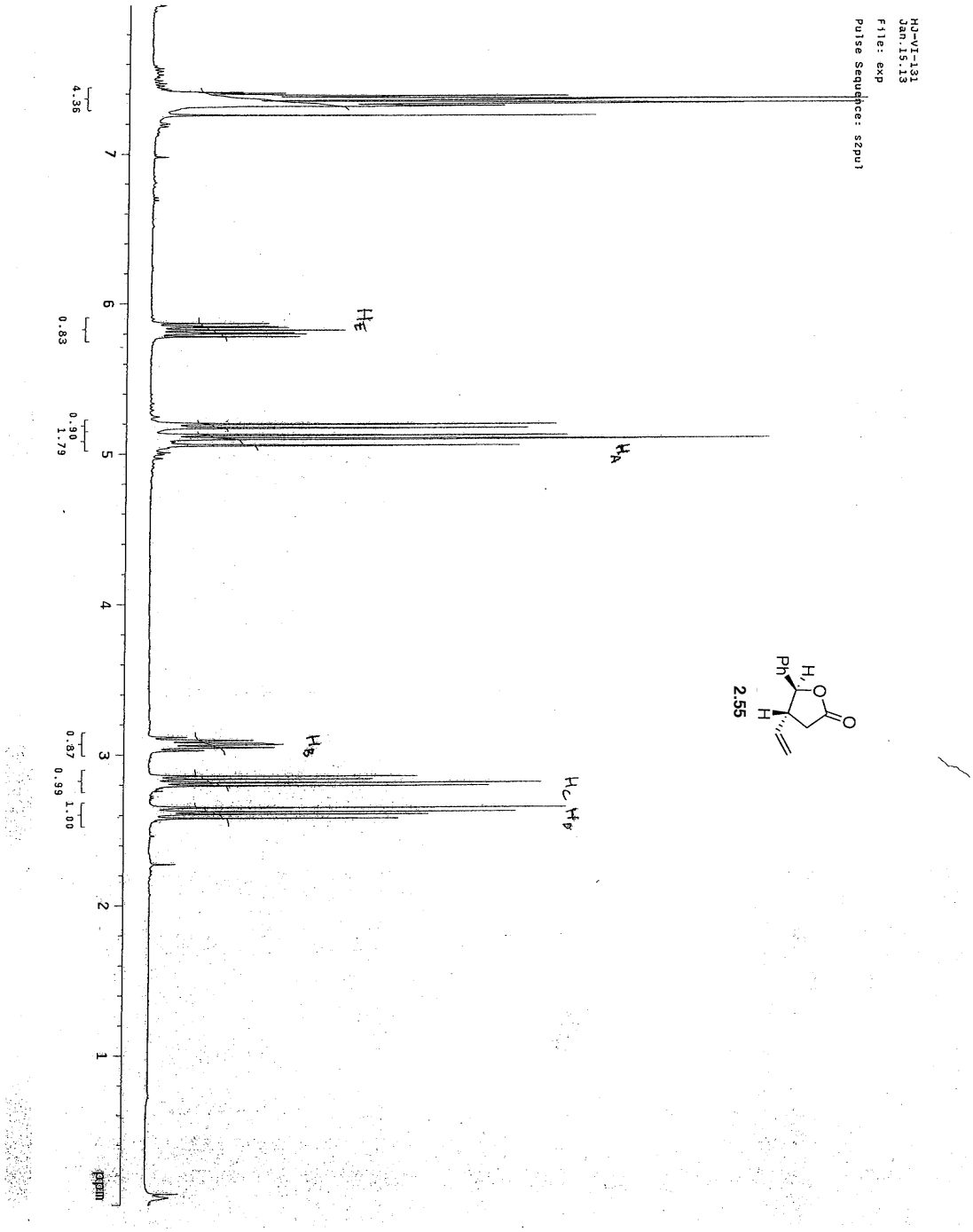
FidFile: FM-V-75-CNMR

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Oct 6 2012



2.54

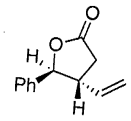



HJ-VI-131
Jan.15.13
File: exp
Pulse Sequence: s2pul
Ph
H
H
O
O
2.55
HE
HA
HB
HC HD
4.36
0.83
0.90
1.79
0.87
0.99
1.00
ppm

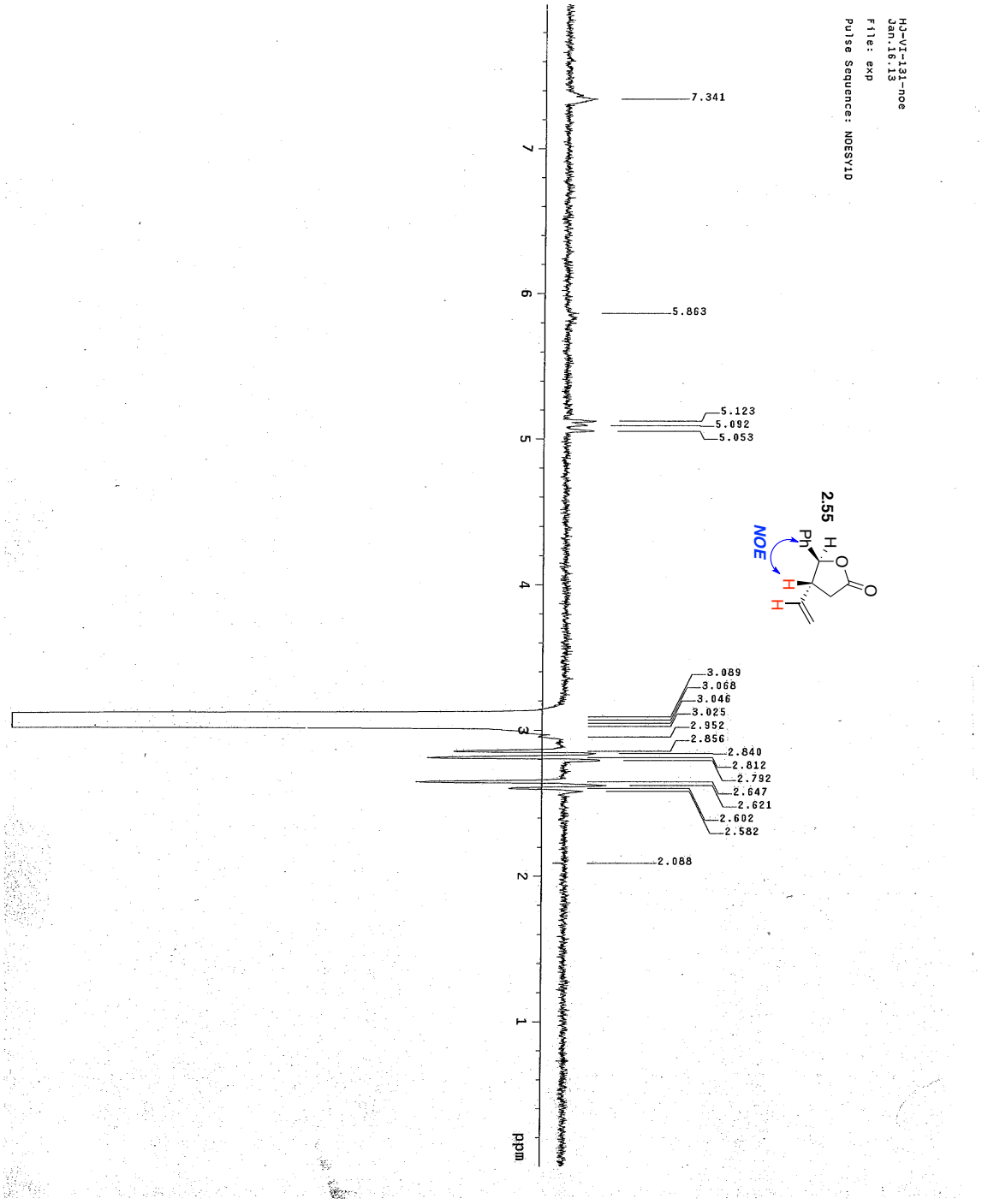
HJ-VI-131-13C
Jan.15.13

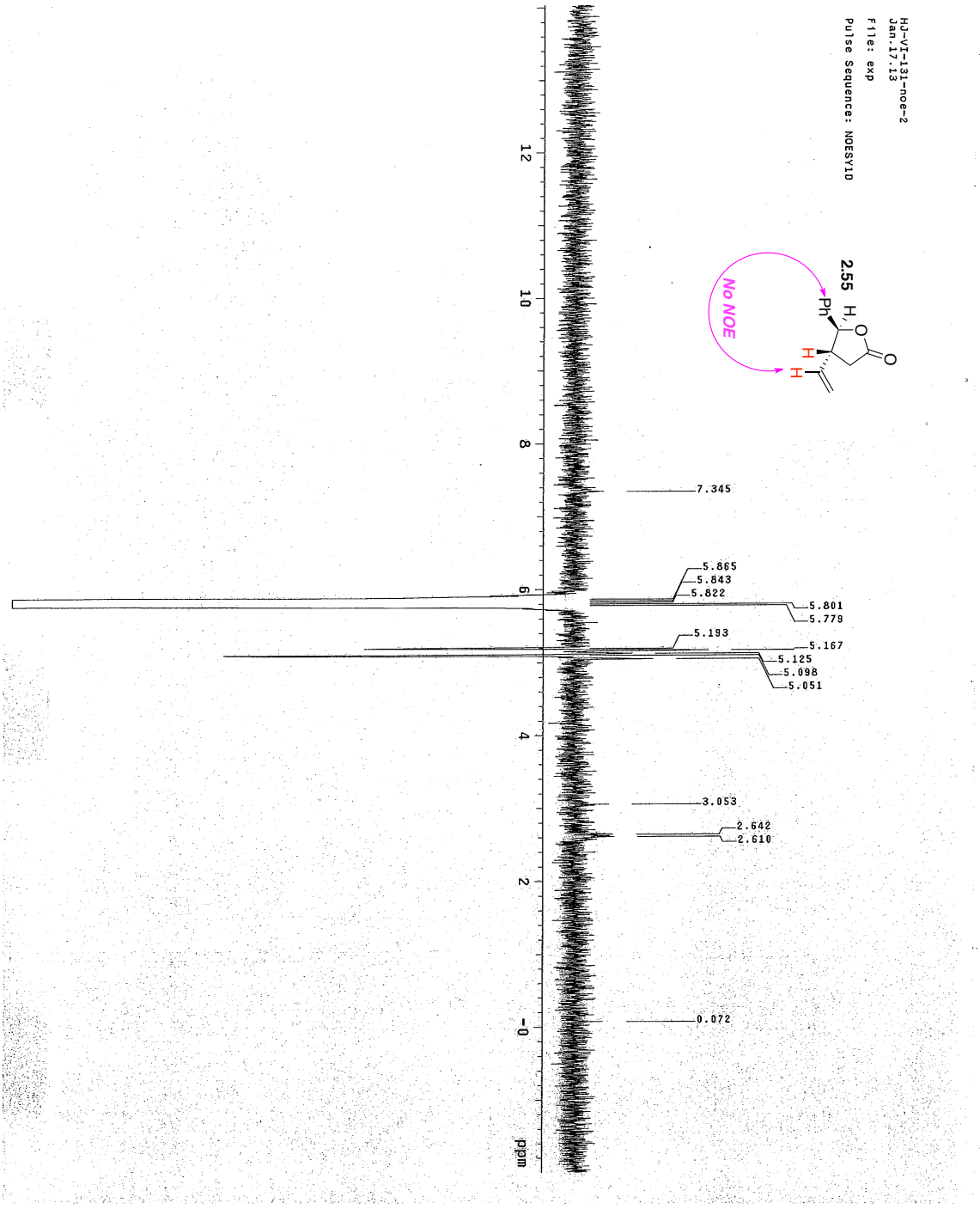
File: /home/ahh/janghw/HJ-VI/HJ-VI-131-13C.fid

Pulse Sequence: s2pul



2.55


HJ-VI-131-noe
Jan.16.13
File: exp
Pulse Sequence: NOESY1D
7.341
5.863
5.123
5.092
5.053
3.089
3.068
3.046
3.025
2.952
2.856
2.840
2.812
2.792
2.647
2.621
2.602
2.582
2.088
2.55
NOE
H
Ph
O
O
H
H
7
6
5
4
3
2
1
ppm


HJ-VT-131-noe-2
Jan.17.13
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Pulse Sequence: NOESY1D
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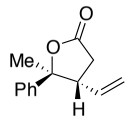
Ph
H
O
O
H
H
No NOE
12
10
8
6
4
2
0
ppm
7.345
5.865
5.843
5.822
5.801
5.779
5.193
5.167
5.125
5.098
5.051
3.053
2.642
2.610
0.072

Sample: FM-III-308
File: exp

Pulse Sequence: s2pul



2.56

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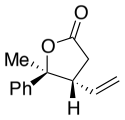
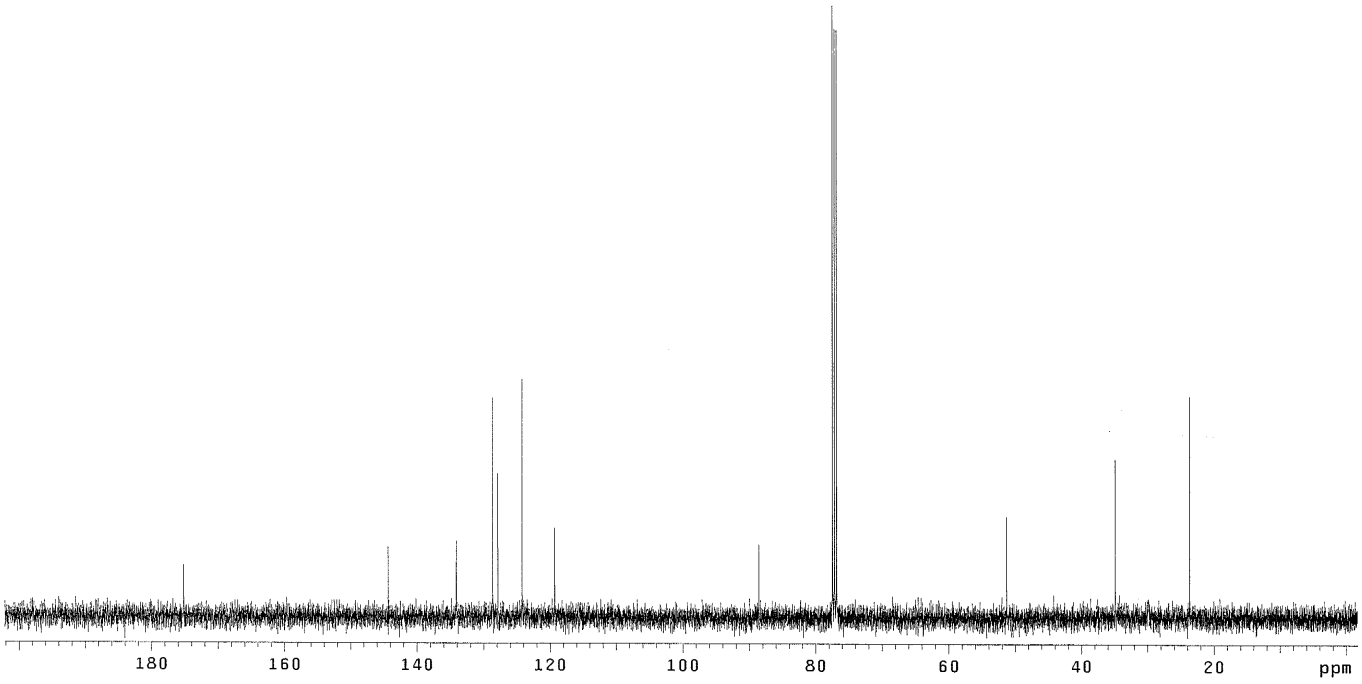
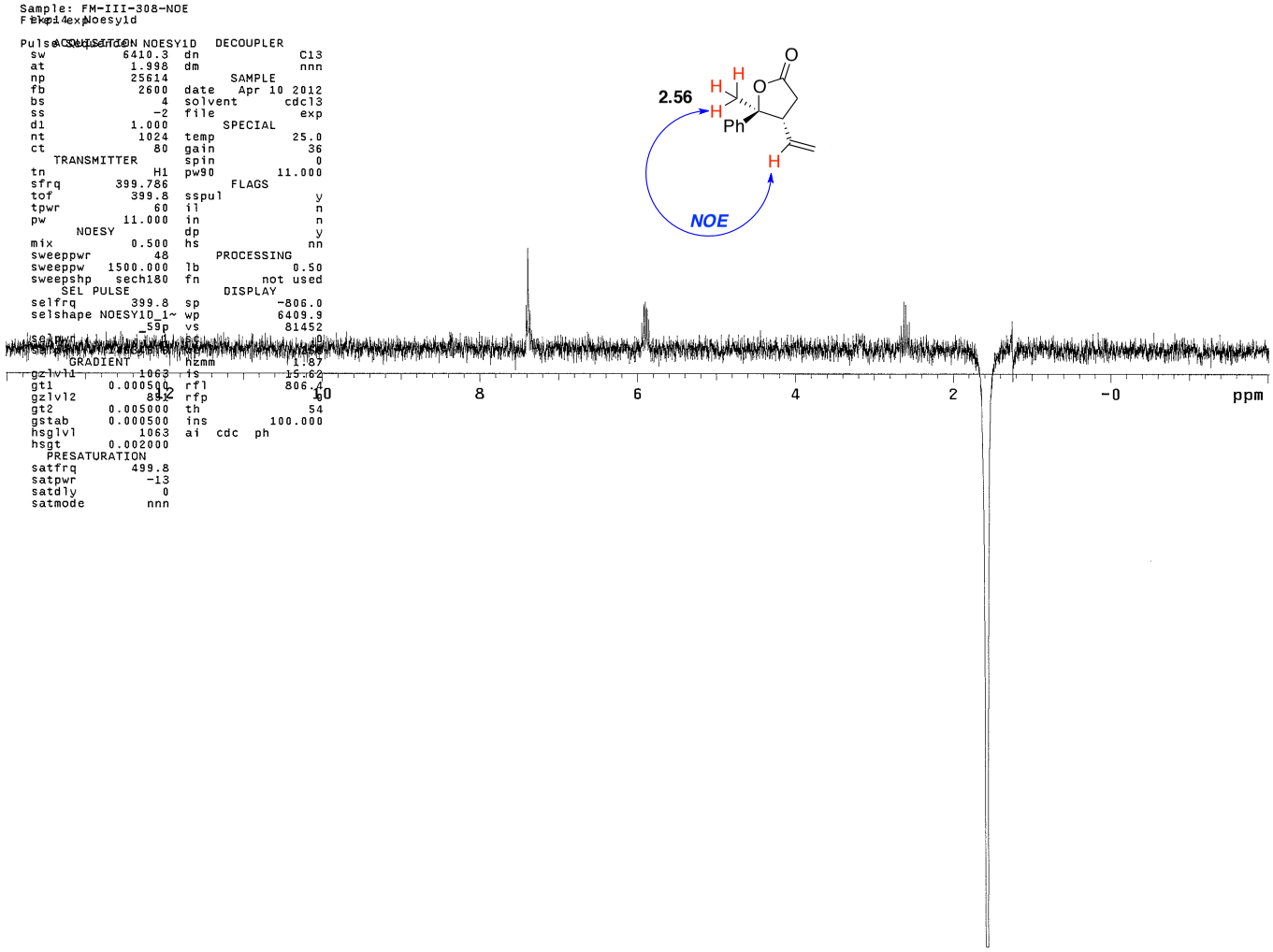
File: /home/ahh/Fanke/FM-III-308-CNMR.fid

Pulse Sequence: s2pul



2.56




Sample: FM-III-308-NOE
Exp14exp4Noesy1d
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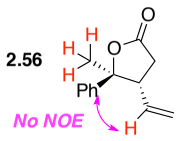
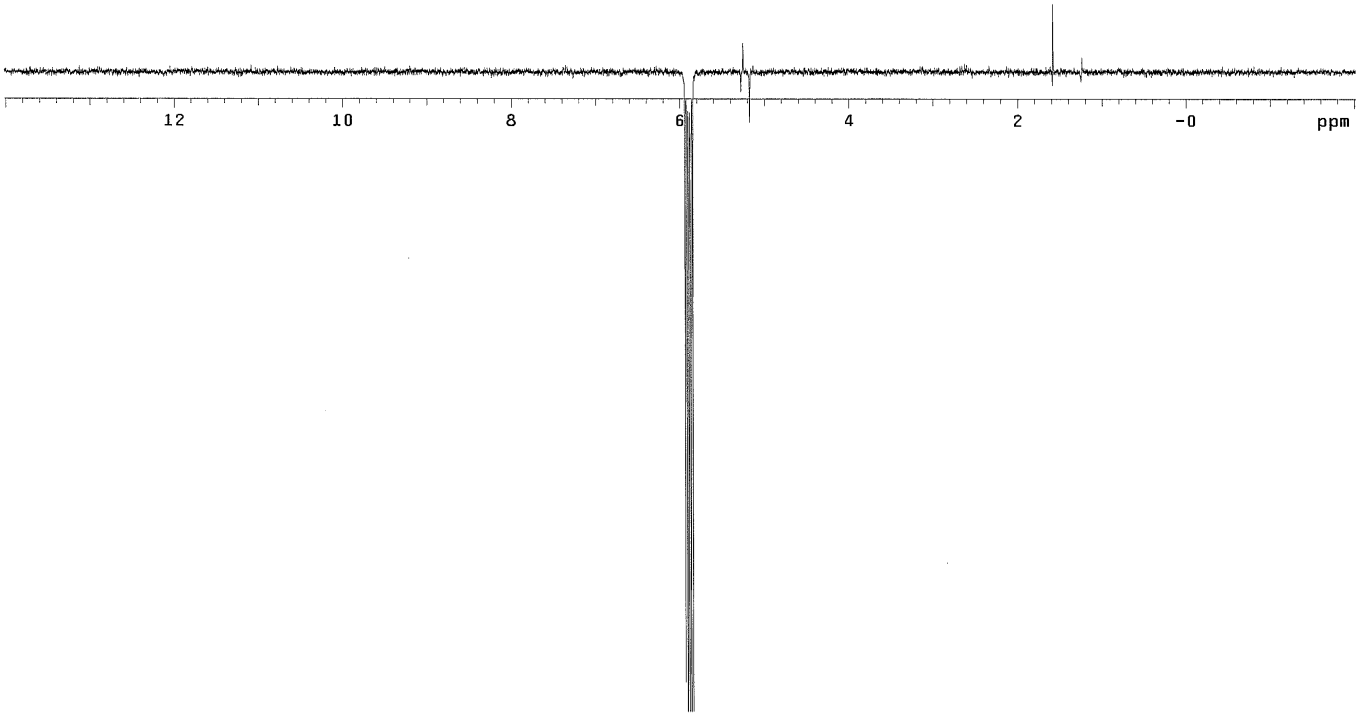
at 1.998
np 25614
fb 2600
bs 4
ss -2
d1 1.000
nt 1024
ct 80
TRANSMITTER
tn H1
sfrq 399.786
tof 399.8
tpwr 60
pw 11.000
NOESY
mix 0.500
sweeppwr 48
sweeppw 1500.000
sweepshp sech180
SEL PULSE
selfrq 399.8
selshape NOESY1D_1~
_59p
GRADIENT
gzlvl1 1063
gt1 0.000500
gzlvl2 852
gt2 0.005000
gstab 0.000500
hsglvl 1063
hsgt 0.002000
PRESATURATION
satfrq 499.8
satpwr -13
satdly 0
satmode nnn
DECOUPLER
dn C13
dm nnn
SAMPLE
date Apr 10 2012
solvent cdcl3
file exp
SPECIAL
temp 25.0
gain 36
spin 0
pw90 11.000
FLAGS
sspul y
il n
in n
dp y
hs nn
PROCESSING
lb 0.50
fn not used
DISPLAY
sp -806.0
wp 6409.9
vs 81452
nzmm 1187
ts 15.62
rfl 806.4
rfp 0
th 54
ins 100.000
ai cdc ph
2.56
H
H
O
O
H
Ph
H
NOE
10
8
6
4
2
-0
ppm

```
Sample: FM-III-308-NOE-2
File: exp

Pulse Sequence: NOESY1D
 Solvent: cdcl3
 Temp. 25.0 C / 298.1 K
Operator: janghw
VNMRS-400  "vnmr13"

 Relax. delay 1.000 sec
 Pulse 90.0 degrees
 Mixing 0.500 sec
 Acq. time 1.998 sec
 Width 6410.3 Hz
 48 repetitions
OBSERVE   H1, 399.7832141 MHz
DATA PROCESSING
 Line broadening 0.5 Hz
FT size 32768
Total time 3 min, 56 sec
```





Chapter 3

Chemo-, Site- and Enantioselective Copper–Boron Additions to 1,3-Enynes Followed by Site- and Diastereoselective Additions of the Resulting Allenylcopper Complexes to Aldehydes

3.1 Introduction

Designing strategies that involve catalytic generation of reactive organometallic reagents and their in situ use for C–C bond forming reactions provides opportunities for invention of new transformations that deliver otherwise difficult-to-access products.[1] Particularly development of such processes requires identification of multitasking catalysts that can address all the issues in each stage of the transformations. Hoveyda and co-workers described a family of multicomponent reactions that involve 2-boron-substituted allylcopper complexes generated from catalytic Cu–B additions to monosubstituted allenes.[1] Another important class of unsaturated hydrocarbons that can serve as precursors for nucleophile is 1,3-enynes. We envisioned that a chiral allenylcopper species **ii**, formed from a site- and enantioselective Cu–B addition[2] to 1,3-

(1) (a) Meng, F.; Jang, H.; Jung, B.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2013**, *52*, 5046–5051. (b) Meng, F.; McGrath, K. P.; Hoveyda, A. H. *Nature* **2014**, *513*, 367–374.

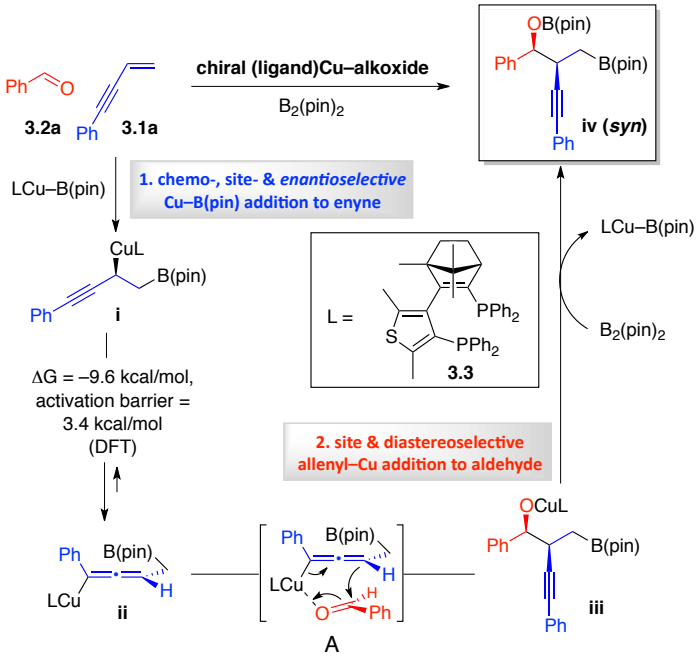
(2) For NHC–Cu-catalyzed enantioselective Cu–B(pin) additions to disubstituted alkenes followed by protonation of the C–Cu bond, see: (a) Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 3160–3161. (b) Lee, Y.; Jang, H.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 18234–18235. (c) Corberán, R.; Mszar, N. W.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2011**, *50*, 7079–7082. (d) Meng, F.; Jang, H.; Hoveyda, A. H. *Chem., Eur. J.* **2013**, *19*, 3204–3214. For bis-phosphine–Cu-catalyzed enantioselective Cu–B(pin) additions to β-alkylstyrenes, see: (e) Matsuda, N.; Hirano, K.; Satoh, T.; Miura, M. *J. Am. Chem. Soc.* **2013**, *135*, 4934–4937.

enyne[3] followed by facile isomerization of the resulting propargylcopper complex **i**, might react with an aldehyde diastereoselectively via transition state **A** (Scheme 3.1). Supported by DFT calculations, the propargylcopper species **i** would collapse to the more energetically favored allenylcopper complex **ii** readily with a low activation barrier (~3.4 kcal/mol). The products of such processes would be boron-containing homopropargyl alcohols that are difficult to introduced otherwise. The resulting multifunctional alkylboron products are versatile building blocks; the alkyne, secondary alcohol and alkylboron moiety can be functionalized selectively. The main challenge of the proposal sequence is that the initial Cu–B addition must be enantioselective, since monosubstituted alkenes are among the most difficult substrates for enantioselective catalysis[4], especially with a small alkyne substituent. We expect to identify an enantiomerically pure catalyst that can promote each stage of the transformation efficiently and selectively.

(3) For phosphine–Cu-catalyzed Cu–B(pin) addition/Cu–C protonation (non-enantioselective) of 1,3-enynes, see: Sasaki, Y.; Horita, Y.; Zhong, C.; Sawamura, M.; Ito, H. *Angew. Chem., Int. Ed.* **2011**, *50*, 2778–2782.

(4) (a) Uozumi, Y.; Hayashi, T. *J. Am. Chem. Soc.* **1991**, *113*, 9887–9888. (b) Becker, H.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **1996**, *35*, 448–451. (c) Kondakov, D. Y.; Negishi, E.-i. *J. Am. Chem. Soc.* **1996**, *118*, 1577–1578. (d) Lo, M. M.-C.; Fu, G. C. *J. Am. Chem. Soc.* **1998**, *120*, 10270–10271. (e) Subbarayan, V.; Ruppel, J. V.; Zhu, S.; Perman, J. A.; Zhang, X. P. *Chem. Commun.* **2009**, 4266–4268. (f) Noonan, G. M.; Fuentes, J. A.; Cobley, C. J.; Clarke, M. L. *Angew. Chem., Int. Ed.* **2012**, *51*, 2477–2480. (g) Mlynarski, S. N.; Schuster, C. H.; Morken, J. P. *Nature* **2013**, *505*, 386–390.

Scheme 3.1: Multicomponent Reaction Design Involving 1,3-Enyne



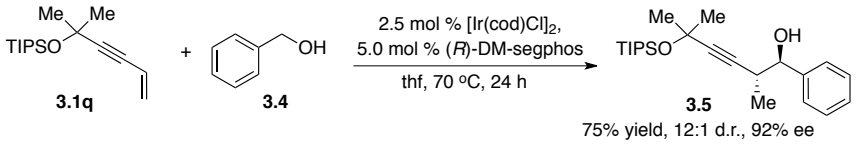
3.2 Background

Homopropargyl alcohols are of significant importance in organic synthesis; catalytic enantioselective access to such entities through C–C bond forming reactions plays a critical role in chemical synthesis. One strategy is additions of enantiomerically pure allenylmetal species (Sn-, Zn-, B-, Si-, or In-based) to aldehydes.[5] Catalytic enantioselective propargyl additions of Sn-, Cr-, or B-based allenyl reagents to aldehydes

(5) For representative reports, see: (a) Haruta, R.; Ishiguro, M.; Ikeda, N.; Yamamoto, H. *J. Am. Chem. Soc.* **1982**, *104*, 7667–7669. (b) Minowa, N.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 3697–3704. (c) Corey, E. J.; Yu, C. M.; Lee, D. H. *J. Am. Chem. Soc.* **1990**, *112*, 878–879. (d) Marshall, J. A.; Wang, X.-J. *J. Org. Chem.* **1991**, *56*, 3211–3213. (e) Marino, J. P.; McClure, M. S.; Holub, D. P.; Comasseto, J. V.; Tucci, F. C. *J. Am. Chem. Soc.* **2002**, *124*, 1664–1668. (f) Lee, K.-C.; Lin, M.-J.; Loh, T.-P. *Chem. Commun.* **2004**, 2456–2457. (g) Hernandez, E.; Burgos, C. H.; Allcea, E.; Soderquist, J. A. *Org. Lett.* **2006**, *8*, 4089–4091. (h) Brawn, R. A.; Panek, J. S. *Org. Lett.* **2007**, *9*, 2689–2692. (i) Francais, A.; Leyva, A.; Etxebarria-Jardi, G.; Ley, S. V. *Org. Lett.* **2010**, *12*, 340–343.

have also been investigated.[6] The majority of such processes leads to products that contain a single stereogenic center; only a limited number of protocols provide access to generation of two stereogenic centers. In 2012, Krische and co-workers described a pioneering work that a range of enantiomerically enriched homopropargyl alcohols can be generated through reaction of an allenyliridium complex formed from in situ addition of Ir–hydride to 1,3-enynes with aldehydes.[7] As shown in Scheme 3.2, coupling of 1,3-enyne **3.1q** and primary alcohol **3.4** in the presence of 5.0 mol % (*R*)-DM-segphos–Ir complex provides homopropargyl alcohol **3.5** in 75% yield with 12:1 dr and 96:4 er. Both aldehydes (in the presence of HCOOH as external hydride source) and primary alcohols are suitable substrates. One limitation of such process is that the scope of enyne partner is restricted to **3.1q** and only methyl-substituted stereogenic center can be introduced.

Scheme 3.2: Phosphine–Ir-Catalyzed Reductive Fusion Involving 1,3-Enynes



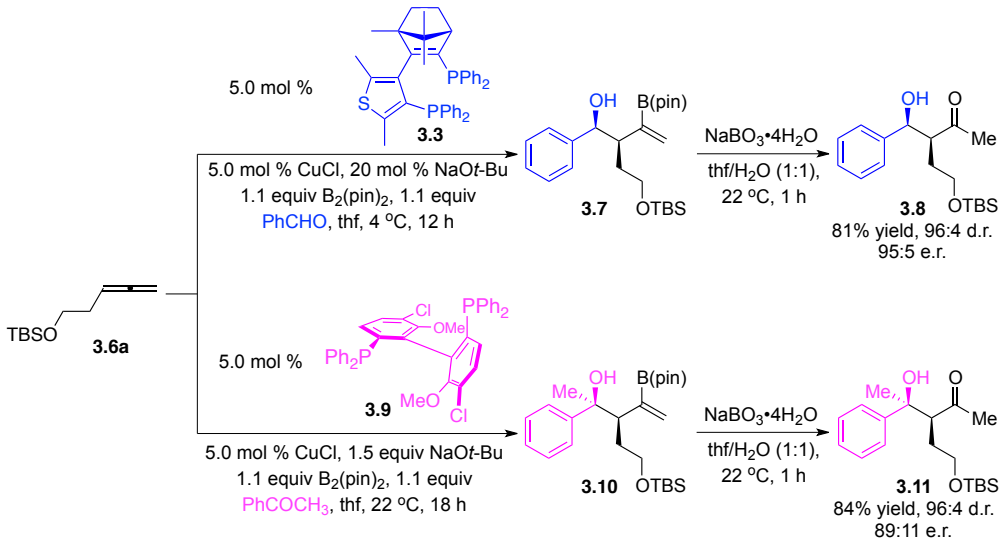
Hoveyda and co-workers developed the first examples of catalytic enantioselective multicomponent reactions involving in situ generation of 2-boron-substituted allylcopper species formed from Cu–B additions to monosubstituted allenes.[1] As illustrated in

(6) For representative reports, see: (a) Keck, G. E.; Krishnamurthy, D.; Chen, X. *Tetrahedron Lett*. **1994**, *35*, 8323–8324. (b) Yu, C.-M.; Yoon, S.-K.; Baek, K.; Lee, J.-Y. *Angew. Chem., Int. Ed*. **1998**, *37*, 2392–2395. (c) Denmark, S. E.; Wynn, T. *J. Am. Chem. Soc*. **2001**, *123*, 6199–6200. (d) Bandini, M.; Cozzi, P. G.; Melchiorre, P.; Tino, R.; Umani-Ronchi, A. *Tetrahedron: Asymmetry* **2001**, *12*, 1063–1069. (e) Inoue, M.; Nakada, M. *Org. Lett*. **2004**, *6*, 2997–2999. (f) Naodovic, M.; Xia, G.; Yamamoto, H. *Org. Lett*. **2008**, *10*, 4053–4055. (g) Liu, S.; Kim, J. T.; Dong, C.-G.; Kishi, Y. *Org. Lett*. **2009**, *11*, 4520–4523. (h) Shi, S.-L.; Xu, L.-W.; Oisaki, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc*. **2010**, *132*, 6638–6639. (i) Fandrick, K. R.; Fandrick, D. R.; Reeves, J. T.; Gao, J.; Ma, S.; Li, W.; Lee, H.; Grinberg, N.; Lu, B.; Senanayake, C. H. *J. Am. Chem. Soc*. **2011**, *133*, 10332–10335. (j) Barnett, D. S.; Schaus, S. E. *Org. Lett*. **2011**, *13*, 4020–4023. (k) Jain, P.; Wang, H.; Houk, K. N.; Antilla, J. C. *Angew. Chem., Int. Ed*. **2012**, *51*, 1391–1394. (l) Harper, K. C.; Sigman, M. S. *Science* **2011**, *133*, 1875–1878.

(7) Geary, L. M.; Woo, S. K.; Leung, J. C.; Krische, M. J. *Angew. Chem., Int. Ed*. **2012**, *51*, 2972–2976.

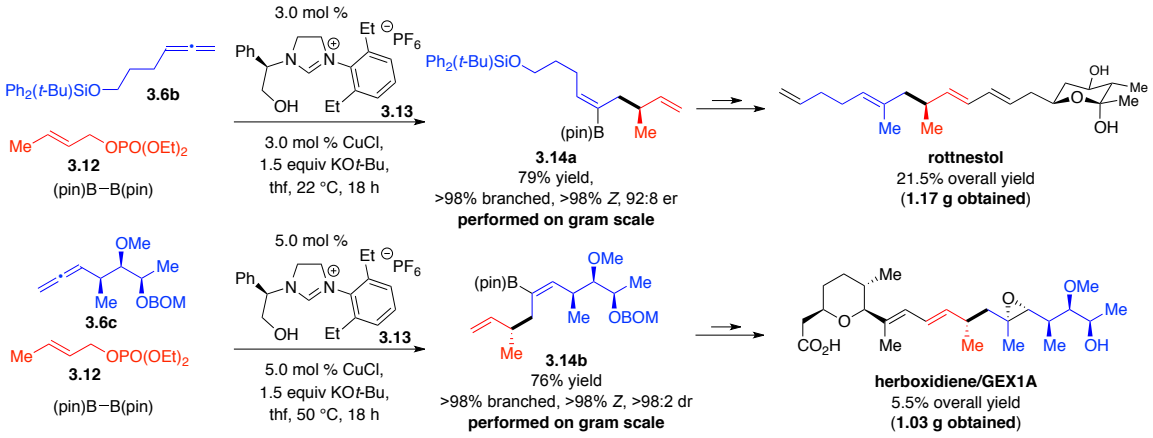
Scheme 3.3, an assortment of β-hydroxyketones can be accessed through additions of the 2-boron-substituted allylcopper complexes to carbonyls promoted by copper catalysts derived from either a C_1-symmetric bisphosphine **3.3** or a C_2-symmetric bisphosphine ligand **3.9**.[1a]

Scheme 3.3: Catalytic Cu–B Addition to Allene Followed by Enantioselective Allyl Addition to Carbonyls



Subsequently the same group found that allylic phosphates can serve as an appropriate class of electrophiles as well.[1b] The catalytic Cu–B addition to allene/enantioselective allylic substitution sequence promoted by an NHC–Cu complex derived from an easily accessible imidazolinium salt **3.13** and inexpensive abundant copper salt provides access to a variety of 1,5-diene compounds (Scheme 3.4). Applications of such protocols are highlighted in scalable syntheses of rottnestol and herboxidiene.

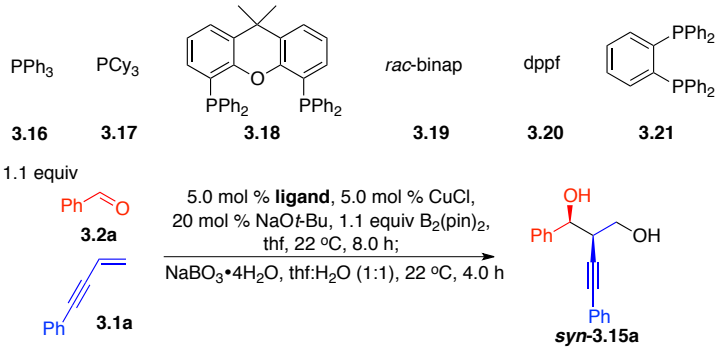
Scheme 3.4: Catalytic Cu–B Addition to Allene Followed by Enantioselective Allylic Substitution



3.3 Identification of the Optimal Catalyst for Catalytic Multicomponent Reactions of 1,3-Enynes and $B_2(pin)_2$ with Aldehydes

Our investigations commenced with examination of a variety of different types of ligands with representative substrates **3.1a** and **3.2a**. Achiral monodentate phosphine–Cu complexes promote the multicomponent transformation efficiently, delivering a mixture of homopropargyl alcohols **3.15a** with *syn*-diastereomer as major product albeit selectivity is low (60:40 and 80:20 dr respectively, entries 1 and 2, Table 3.1). Reactions promoted by Cu catalysts derived from bisphosphine ligands also afford **3.15a** in high efficiency but low diastereoselectivity (entries 3–6, Table 3.1). In all the cases, minimal competitive Cu–B addition to aldehyde **3.2a** is observed (<2%), which is similar to the transformations involving monosubstituted allenes.[1a] Phosphine–Cu complexes promote the sequence chemoselectively.

Table 3.1: Screen of Achiral and Racemic Phosphine Ligands[a]



Entry	Ligand	Conv (%)[b]	Yield (%)[c]	syn:anti (dr)[d]
1	**3.16**	>98	77	60:40
2	**3.17**	>98	81	80:20
3	**3.18**	>98	74	71:29
4	**3.19**	>98	83	54:46
5	**3.20**	69	57	60:40
6	**3.21**	>98	86	57:43

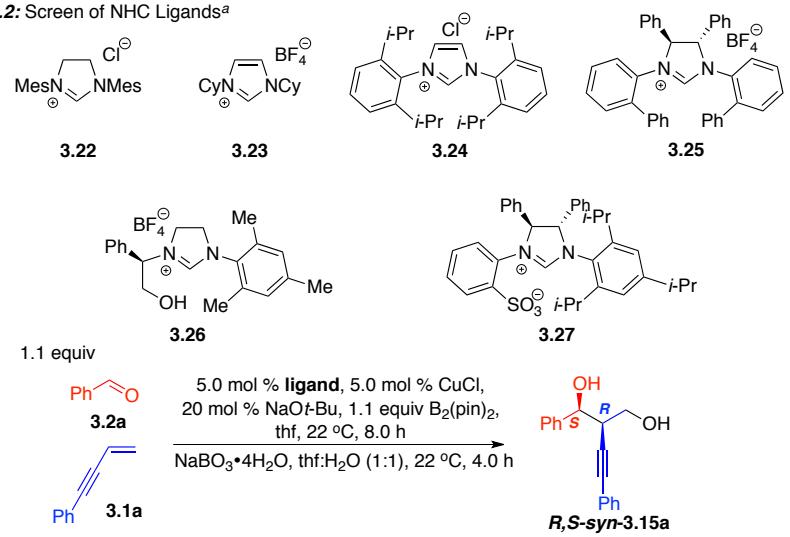
[a] Performed under N_2 atm. [b] Determined by analysis of 400 MHz ^{1}H NMR spectra of unpurified mixtures (±2%). [c] Yields of isolated/purified products (±5%; both isomers). [d] dr was determined by HPLC analysis (±1%). na = not applicable.

rac-binap: (±)-2,2'-bis(diphenylphosphino)-1,1'-binaphthalene
dppf: 1,1'-ferrocenediyl-bis(diphenylphosphine)

We next examine a number of Cu catalysts derived from NHC ligands. Reactions of 1,3-enyne **3.1a** and aldehyde **3.2a** in the presence of NHC–Cu complexes derived from commercially available precursors **3.22** or **3.23** afford **3.15a** in 63% and 66% yield with 81:19 and 80:20 dr, respectively (entries 1 and 2, Table 3.2); Cu–B(pin) addition to aldehyde is a competitive pathway. With Cu catalyst in situ generated from imidazolium salt **3.24** bearing sterically congested N–aryl group, the efficiency of the transformation is significantly diminished. Exposure of 1,3-enyne **3.1a** and aldehyde **3.2a** to enantiomerically pure NHC–Cu complexes derived from **3.25** or **3.26** leads to low diastereoselectivities (73:27 and 81:19 dr respectively, entries 4 and 5, Table 3.2). Similar

to **3.24**, an NHC–Cu catalyst that contains a large aryl unit cannot promote the multicomponent reaction efficiently (cf. **3.27**, entry 6, Table 3.2).

Table 3.2: Screen of NHC Ligands[a]

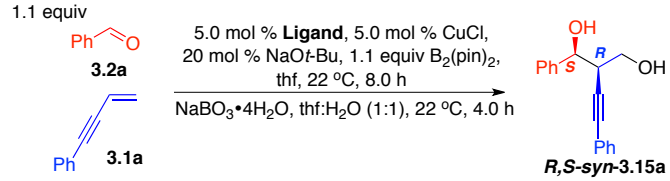


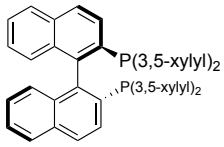
Entry	Ligand	Conv. (%)[b]	Yield (%)[c]	syn:anti[d]	er (syn)[d]	er (anti)[d]
1	**3.22**	81	63	81:19	na	na
2	**3.23**	86	66	80:20	na	na
3	**3.24**	28	nd	nd	na	na
4	**3.25**	>98	81	73:27	19:81	95:5
5	**3.26**	90	72	81:19	57:43	56:44
6	**3.27**	<2	na	na	na	na

[a] Performed under N_2 atm. [b] Determined by analysis of 400 MHz ^{1}H NMR spectra of unpurified mixtures (±2%). [c] Yields of isolated/purified products (±5%; both isomers). [d] dr and er were determined by HPLC analysis (±1%). nd = not determined. na = not applicable.

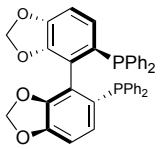
We then turned our attention to chiral phosphine ligands. Cu complexes derived from C_2-symmetric bisphosphines deliver low diastereo- and enantioselectivies (51:49–60:40 syn:anti, 18:82–51:49 er, Scheme 3.5) albeit high efficiencies (70–87% yield), except the phosphine–Cu catalyst generated from sterically congested **3.34** which provides desired product in 70% yield with 94% syn-selectivity and 91:9 er.

Scheme 3.5: Screen of Chiral C_2-Symmetric Bisphosphines with Biaryl Backbones

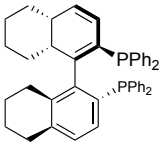




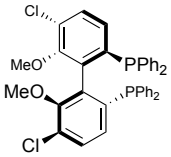
3.28
>98% conv, 87% yield,
52:48 syn:anti,
18:82 er (syn); 81:19 er (anti)



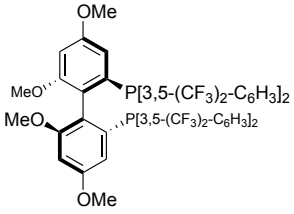
3.29
>98% conv, 82% yield,
59:41 syn:anti,
51:49 er (syn); 51:49 er (anti)



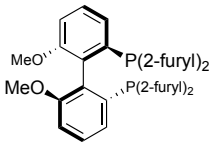
3.30
>98% conv, 70% yield,
60:40 syn:anti,
76:24 er (syn); 61:39 er (anti)



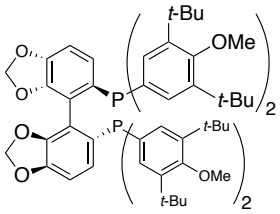
3.31
>98% conv, 86% yield,
56:44 syn:anti,
73:27 er (syn); 57:43 er (anti)



3.32
>98% conv, 72% yield,
58:42 syn:anti,
41:59 er (syn); 83:17 er (anti)



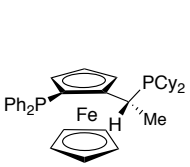
3.33
>98% conv, 72% yield,
51:49 syn:anti,
34:66 er (syn); 67:33 er (anti)



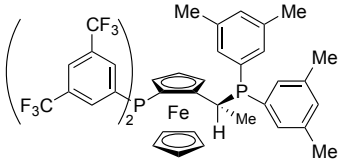
3.34
77% conv, 70% yield,
94:6 syn:anti,
91:9 er (syn); 50:50 er (anti)

As shown in Scheme 3.6, catalysts bearing ferrocene-containing phosphines do not lead to any improvement on diastereoselectivity (cf. **3.35** and **3.36**). Similarly, other C_2-symmetric ligands with different frameworks provide no higher than 75:25 syn:anti ratio although high enantioselectivities are observed in one of the diastereomers (cf. **3.40**, 98:2 er for anti-**3.15a**; **3.43**, 94:6 for anti-**3.15a**).

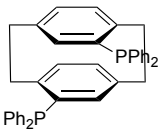
Scheme 3.6: Screen of Ferrocene-Containing and Other Chiral C_2-Symmetric Bisphosphines[a]



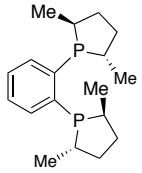
3.35
>98% conv, 79% yield,
40:60 syn:anti,
86:14 er (syn); 95:5 er (anti)



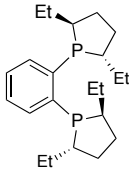
3.36
>98% conv, 79% yield,
46:54 syn:anti,
76:24 er (syn); 63:37 er (anti)



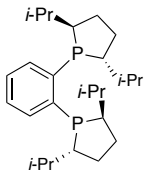
3.37
>98% conv, 91% yield,
57:43 syn:anti,
80:20 er (syn); 74:26 er (anti)



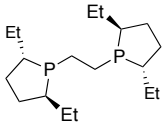
3.38
>98% conv, 82% yield,
64:36 syn:anti,
51:49 er (syn); 53:47 er (anti)



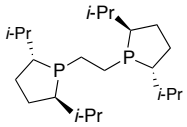
3.39
>98% conv, 80% yield,
59:41 syn:anti,
58:42 er (syn); 65:35 er (anti)



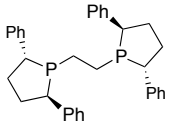
3.40
>98% conv, 78% yield,
28:72 syn:anti,
59:41 er (syn); 98:2 er (anti)



3.41
>98% conv, 79% yield,
71:29 (syn:anti),
44:56 er (syn); 55:45 er (anti)



3.42
>98% conv, 75% yield,
75:25 (syn:anti),
56:44 er (syn); 52:48 er (anti)



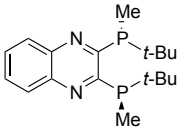
3.43
>98% conv, 84% yield,
43:57 (syn:anti),
19:81 er (syn); 94:6 er (anti)

[a] Same conditions and analytical methods as Scheme 3.5

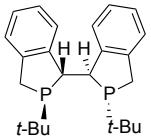
Other C_2-symmetric phosphines that carry P-stereogenic centers with a *t*-Bu group are tested as well, none of which deliver high diastereo- and enantioselectivities. It is the unique C_1-symmetric phosphine **3.3** with camphor backbone that promotes the multicomponent transformation not only efficiently but also diastereo- and enantioselectively (92:8 syn:anti; 95:5 er (syn)).[8] Modification of the PPh_2 unit attached to the camphor backbone to $P(3,5\text{-}C_6H_3)_2$ leads to significant loss of efficiency and stereoselectivity (cf. **3.47**, Scheme 3.7). Cu complexes derived from phosphoramidites are not selective either (**3.48** and **3.49**, Scheme 3.7).

(8) Kadyrov, R.; Iladinov, I. Z.; Almena, J.; Monsees, A.; Riermeier, T. H. *Tetrahedron Lett*. **2005**, *46*, 7397–7400.

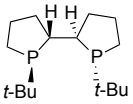
Scheme 3.7: Screen of Phosphines Carrying *t*-Bu-Containing P-Stereogenic Center and Other C_1-Symmetric Ligands[a]



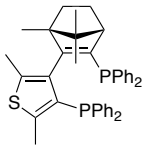
3.44
>98% conv, 65% yield,
54:46 syn:anti,
44:56 er (syn); 58:42 er (anti)



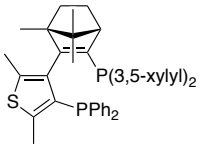
3.45
>98% conv, 76% yield,
52:48 syn:anti,
48:52 er (syn); 83.5:16.5 er (anti)



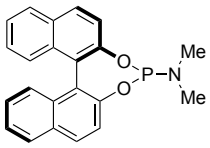
3.46
>98% conv, 74% yield,
61:39 syn:anti,
44:56 er (syn); 75:25 er (anti)



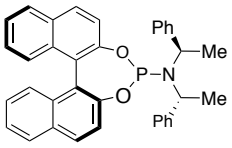
3.3
>98% conv, 76% yield,
92:8 syn:anti,
95:5 er (syn); 56:44 er (anti)



3.47
>98% conv, 41% yield,
84:16 syn:anti,
87:13 er (syn); 62:38 er (anti)



3.48
>98% conv, 73% yield,
71:29 syn:anti,
50:50 er (syn); 63:37 er (anti)



3.49
>98% conv, 71% yield,
71:29 (syn:anti),
15.5:84.5 er (syn); 94:6 er (anti)

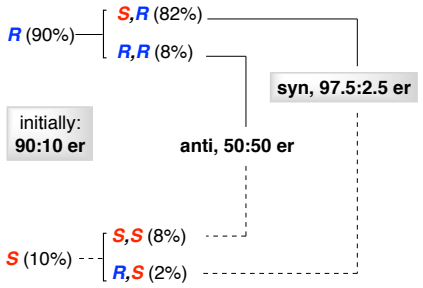
[a] Same conditions and analytical methods as Scheme 3.5

It is noteworthy that the data described above indicate that aldehyde addition is not merely substrate control. The structure of phosphine–Cu complex has a great impact on selectivity. Moreover, The variations in er and dr values in the presence of different Cu complexes imply that selectivity preferences alter in the stereochemistry-generating steps. Formation of one diastereomer in higher er indicates that the other diastereomeric allenylcopper complex has a different preference for selectivity of aldehyde addition, which results in refinement of enantioselectivity of the final product.[9] Namely the enantioselectivity of the final product reflects an improvement on the enantioselectivity of the initial Cu–B(pin) addition. For instance, reactions promoted by **3.34** or **3.3** provide high enantioselectivity for syn isomer albeit nearly racemic anti isomer. As showcased in Scheme 3.8, the small amount of *R,R-anti*-**3.15a** originated from the major allenylcopper species is similar to the quantity of *S,S-anti*-**3.15a** formed from the major product of addition of the minor allenylcopper complex to aldehyde, leading to low

(9) (a) Zhang, W.; Lee, N. H.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1994**, *116*, 425–.426 (b) Ozawa, F.; Kubo, A.; Hayashi, T. *J. Am. Chem. Soc.* **1991**, *113*, 1417–1419.

enantioselectivity of anti diastereomer. As the majority of the minor allenylcopper species produces anti diastereomer after aldehyde addition, only a small amount of such intermediate delivers enantiomeric component of *S*,*R*-*syn*-**3.15a**, causing refinement of enantioselectivity in the initial Cu–B(pin) addition step.

Scheme 3.8: An Illustration for Enantioselectivity Refinement

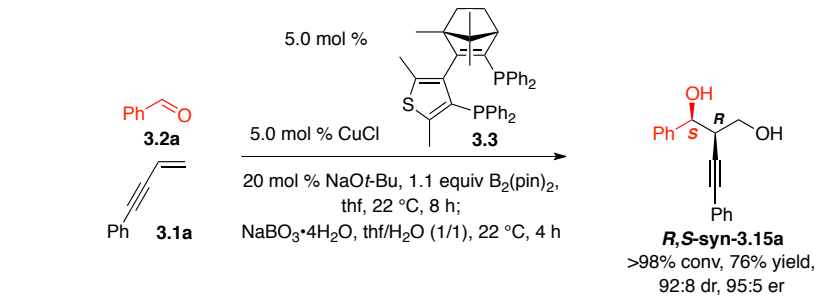


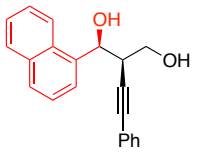
3.4 Scope for Catalytic Multicomponent Reactions of 1,3-Enynes and $B_2(pin)_2$ with Aldehydes

With the optimal conditions in hand, we examined a variety of 1,3-enynes and aldehydes. As shown in Scheme 3.9, a range of aryl- and heteroaryl-substituted aldehydes are well tolerated (**3.15b–f**, Scheme 3.9), including those carrying sterically hindered *ortho* substituents (**3.15b–c**). Oxidation of the alkylboron products provides the 1,3-diols in 66–94% yield and 92.5:7.5–99:1 er. α,β-Unsaturated aldehydes can be used as well. Although lower chemoselectivity is observed with cinnamaldehyde due to competitive Cu–B(pin) addition to the aldehyde (**3.15g**, 66% yield, 96:4 dr, 96:4 er), α,β-unsaturated aldehydes that contain trisubstituted alkenes deliver high efficiency and chemo-, diastereo- and enantioselectivities (**3.15h–i**). Aliphatic aldehydes are also effective substrates (**3.15j–l**). Compound **3.15j** can be generated in 80% yield with 92.5:7.5 er.

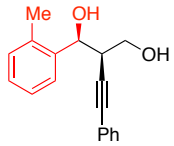
Simple recrystallization can produce further enrichment of major isomer in certain cases (**3.15j**, >98:2 dr and 98:2 er after recrystallization). Reactions of two commercially available enantiomerically pure alkyl-substituted aldehydes deliver either isomer in high efficiency and diastereoselectivity, demonstrating that catalyst can effectively control the stereoselectivity in spite of the presence of a stereogenic center in the substrate. It is noteworthy that although the same allenylcopper species is involved in the transformation, the changes in dr and er imply that the structures of aldehydes have impact on the selectivity in the aldehyde addition step.

Scheme 3.9: Scope of Aldehyde Component

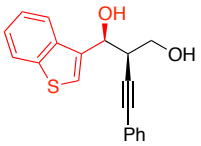




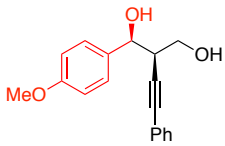
3.15b
>98% conv., 94% yield,
98:2 dr, 97:3 er



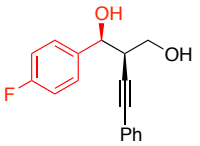
3.15c
>98% conv., 83% yield,
92:8 dr, 97:3 er



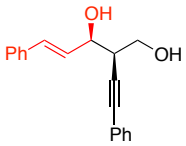
3.15d
>98% conv., 84% yield,
94:6 dr, 95:5 er



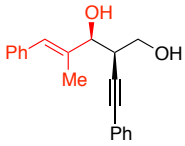
3.15e
>98% conv., 70% yield,
90:10 dr, 94:6 er



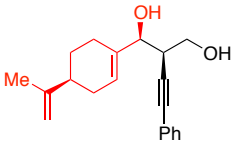
3.15f
>98% conv., 87% yield,
92:8 dr, 94:6 er



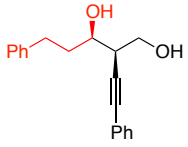
3.15g
75% conv., 66% yield,
96:4 dr, 96:4 er



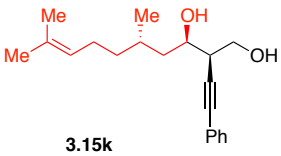
3.15h
>98% conv., 86% yield,
94:6 dr, 93:7 er



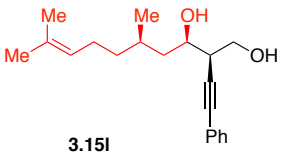
3.15i
>98% conv., 79% yield,
>98:2 dr, 99:1 er



3.15j
>98% conv., 80% yield,
98:2 dr, 92.5:7.5 er
(>98:2 dr, 98:2 er
after recrystallization)



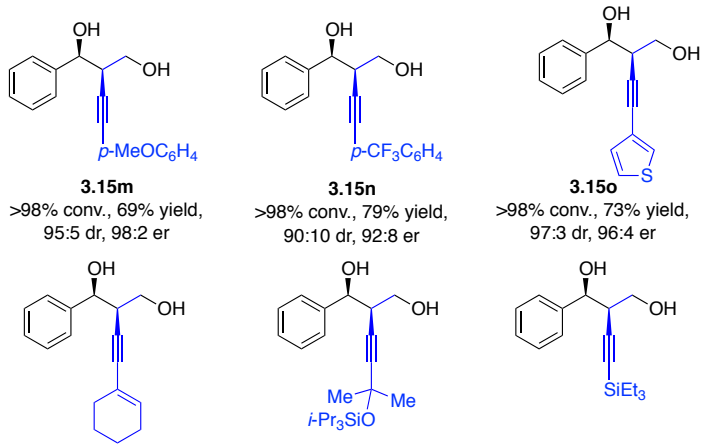
3.15k
>98% conv., 76% yield,
>98:2 dr (>98:2 er)



3.15l
>98% conv., 74% yield,
>98:2 dr (>98:2 er)

Scope of 1,3-enynes was also investigated (Scheme 3.10). A range of 1,3-enynes can be prepared in 80–96% yield through a single Pd-catalyzed cross-coupling of terminal alkynes with vinyl bromide. Reactions with 1,3-enynes bearing electron-donating or eletron-withdrawing aryl group proceed with high selectivity (**3.15m**–**n**). Heteroaryl- and alkenyl-substituted substrates undergo the transformation selectively (**3.15o**–**p**). Enynes with different removable units are also effective (**3.15q**–**r**); the product that contains more sterically congested tertiary alkyl group (**3.15q**) is formed with higher enantioselectivity (94:6 er vs. 85:15 er).

Scheme 3.10: Scope of Enyne Component[a]



3.15m
>98% conv., 69% yield,
95:5 dr, 98:2 er

3.15n
>98% conv., 79% yield,
90:10 dr, 92:8 er

3.15o
>98% conv., 73% yield,
97:3 dr, 96:4 er

3.15p
>98% conv., 70% yield,
96:4 dr, 97:3 er

3.15q
>98% conv., 74% yield,
94:6 dr, 94:6 er

3.15r
>98% conv., 83% yield,
94:6 dr, 85:15 er

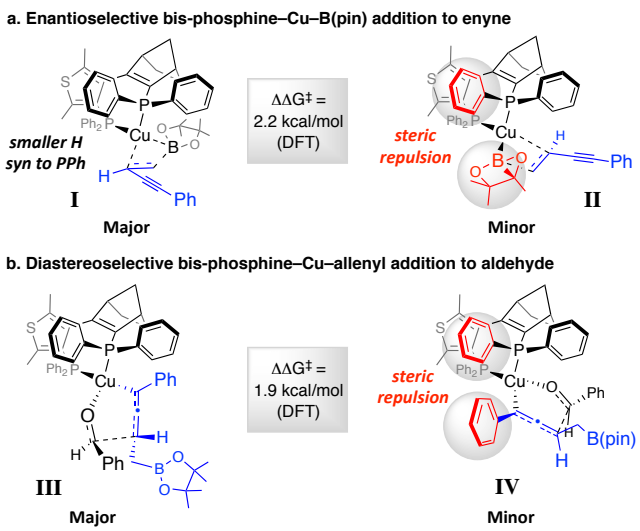
[a] Same conditions and analytical methods as Scheme 3.9

3.5 Stereochemical Models for Catalytic Multicomponent Reactions of 1,3-Enynes and $B_2(pin)_2$ with Aldehydes

To gain further insight into the origins of high selectivities and the uniqueness of the ligand, DFT calculations are investigated. The ligand has only one spacious binding pocket underneath the right phenyl group on phosphorus attached to the camphor

backbone that can accommodate large group. In the Cu–B(pin) addition step, the sterically congested B(pin) unit prefers to locate in the large pocket (transiton state **I**, Scheme 3.11a). Otherwise, as shown in transition state **II** (Scheme 3.11a), steric repulsion between the protruding phenyl group on phosphorus and B(pin) unit results in energetically disfavor. Similarly, in the aldehyde addition step, transition state **III** with the large allenyl group occupying the spacious pocket is preferred. Otherwise, substituents on allenyl group and phosphorus will cause steric repulsion (transition state **IV**).

Scheme 3.11: Stereochemical Models Based on DFT Calculations

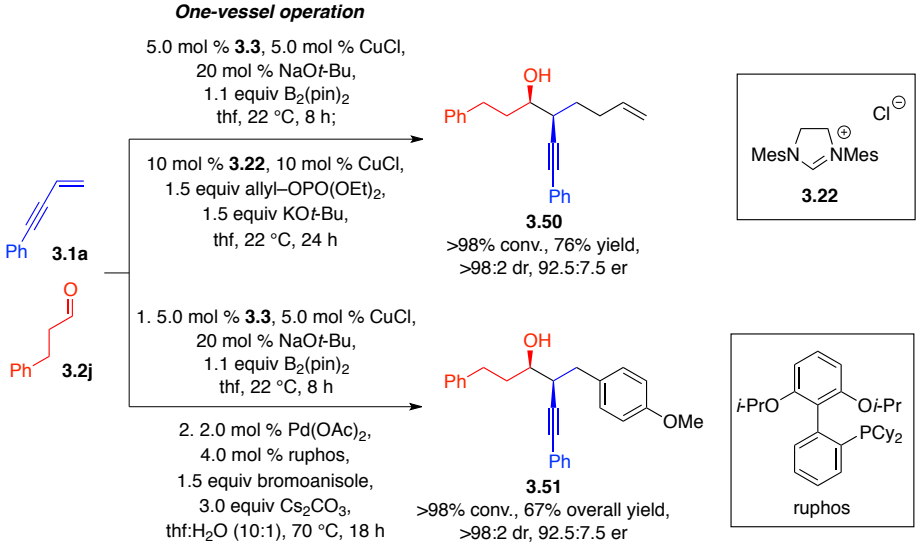


3.6 Functionalization and Applications to Natural Product Fragments Synthesis

The multifunctional alkylboron compounds generated from the multicomponent protocol can be converted to a variety of valuable and otherwise difficult-to-access enantiomerically enriched building blocks. Taking advantage of the intramolecular

chelation of the hydroxyl group to the boronic ester unit, we expected that activation of the alkyl–B(pin) bond by transition metal is more facile. As illustrated in Scheme 3.12, enyne **3.50** is delivered in 76% yield with complete diastereoselectivity and 92.5:7.5 er through the catalytic multicomponent reaction followed by an NHC–Cu catalyzed alkylation of the resulting alkylboron compound. A Pd-catalyzed cross-coupling[10] is combined with the multicomponent process to provide **3.51** in 67% overall yield with >98% dr and 92.5:7.5 er.

Scheme 3.12: Selective Functionalization of the Alkyl–B(pin) Bond



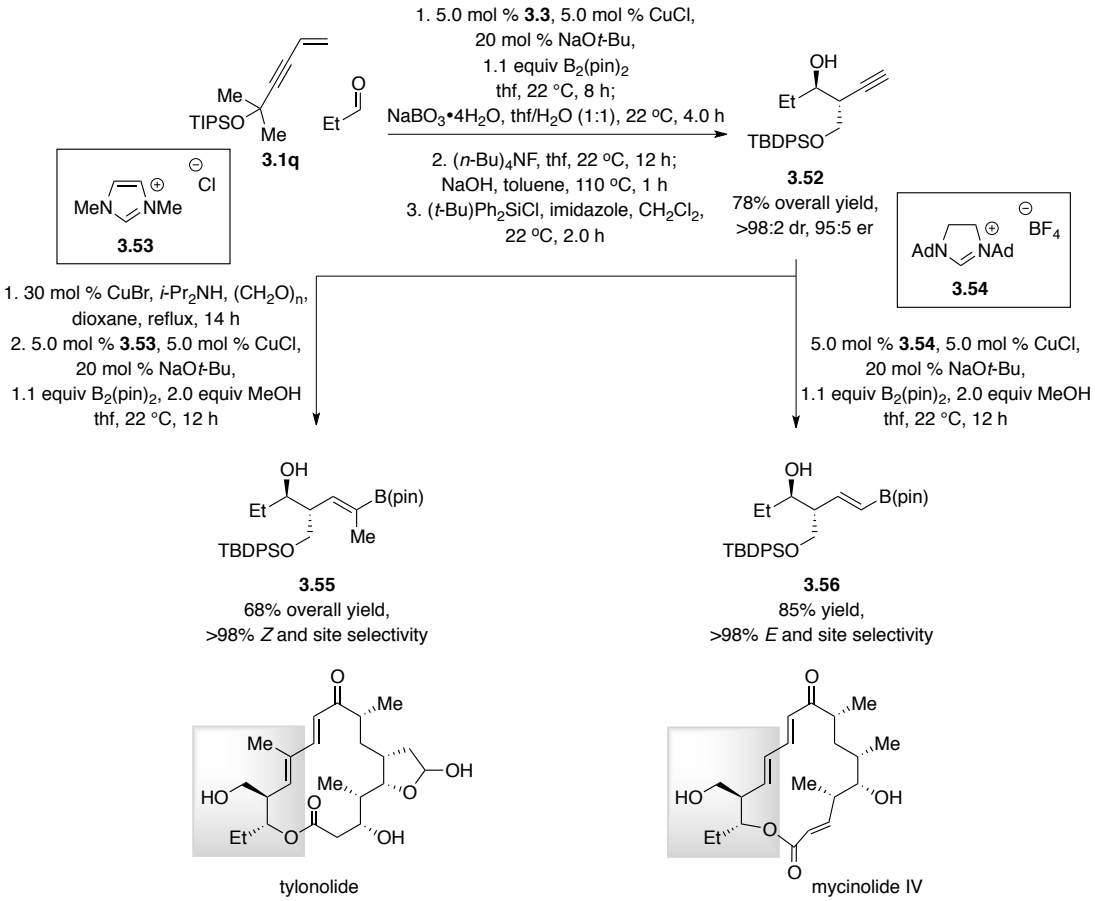
To further demonstrate the utility of the method, we applied the multicomponent protocol to synthesis of fragments of macrolide antibiotic natural products tylonolide[11] and mycinolide IV[12]. As showcased in Scheme 3.13, Cu-catalyzed multicomponent

(10) Doucet, H. *Eur. J. Org. Chem.* **2008**, 2013–2030.
(11) For previous total syntheses of tylonolide, see: (a) Nicolaou, K. C.; Pavia, M. R.; Seitz, S. P. *J. Am. Chem. Soc.* **1982**, *104*, 2027–2029. (b) Masamune, S.; Lu, L. D. L.; Jackson, W. P.; Kaiho, T.; Toyoda, T. *J. Am. Chem. Soc.* **1982**, *104*, 5523–5526. (c) Grieco, P. A.; Inanaga, J.; Lin, N. H.; Yanami, T. *J. Am. Chem. Soc.* **1982**, *104*, 5781–5784.
(12) For a total synthesis of mycinolide IV (via mycinamycin VII), see: Matsumoto, T.; Maeta, H.; Suzuki, K.; Tsuchihashi, G. *Tetrahedron Lett.* **1988**, *29*, 3575–3578.

transformation of 1,3-enyne **3.1q** and $B_2(pin)_2$ with propionaldehyde followed by oxidative work-up, alkyne deprotection and selective protection of the primary alcohol as silyl ether affords **3.52** in 78% overall yield with >98:2 dr and 95:5 er. Cu-catalyzed homologation leads to the corresponding monosubstituted allene, which undergoes a site-selective and diastereoselective protoboration promoted by an NHC–Cu complex derived from commercially available imidazolium salt **3.53** to deliver trisubstituted alkenylboron **3.55** in 68% overall yield and >98% site- and *Z*-selectivity.[13] The trisubstituted alkenylboron can be used in catalytic cross-coupling with an alkenyl halide[14] in a route to the synthesis of tylonolide. Alternatively, in the presence of NHC–Cu catalyst in situ generated from imidazolinium salt **3.54**, *E*-alkenylboron **3.56** is afforded through a site-selective protoboration of terminal alkyne.[15] This fragment might be used for enantioselective synthesis of mycinolide IV.

(13) Meng, F.; Jung, B.; Haeffner, F.; Hoveyda, A. H. *Org. Lett.* **2013**, *15*, 1414–1417.
(14) Kotha, S.; Lahiri, K.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633–9695.
(15) Jang, H.; Zhugralin, A. R.; Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 7859–7871.

Scheme 3.13: Application to Synthesis of Fragments of Tylonolide and Mycinolide IV



3.7 Conclusion

In this chapter, we have described a Cu-catalyzed multicomponent protocol involving 1,3-enynes as precursors for in situ generation of nucleophilic organometallic reagents through copper–boron addition.[16] A wide range of aldehydes and 1,3-enynes can be fused with $B_2(pin)_2$ to furnish a variety of multifunctional alkylboron compounds. The process is promoted by a phosphine–Cu complex derived from a commercially available bisphosphine ligand and inexpensive abundant CuCl. DFT calculations are performed to

(16) Meng, F.; Haeffner, F.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2014**, *136*, 11304–11307.

provide further insights into the origin of high selectivity. The utility of such process is demonstrated by applications to synthesis of fragments of macrolide antibiotic natural products tylonolide and mycinolide IV. Moreover, this study offers an evidence that other unsaturated hydrocarbons can be used in catalytic Cu–B addition to generate boron-containing organocopper species and their in situ use in C–C bond forming reactions.

3.8 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). ^{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, br s = broad singlet, m = multiplet, app. = apparent), and coupling constant (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. Enantiomer ratios were determined by high-performance liquid chromatography (HPLC) with a Shimadzu chromatograph (Chiral Technologies Chiralcel OD-H (4.6 x 250 mm), Chiralcel OJ-H (4.6 x 250 mm), Chiralcel OZ-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. Solvents were purified under a positive pressure of dry argon by a modified Innovative Technologies purification system: toluene, benzene and hexanes were purified through a copper oxide and alumina column; CH_2Cl_2 and Et_2O were purged with Ar and purified by passage through two alumina columns. Tetrahydrofuran (Aldrich Chemical Co.) was purified by distillation from sodium benzophenone ketyl immediately prior to use unless otherwise specified. Methanol (Aldrich Chemical Co.) was distilled over CaH_2. All work-up and purification procedures were carried out with reagent grade solvents (purchased from Fisher Scientific) in air.

3.8.1 Reagents and Ligands

Aldehydes: purchased from Aldrich Chemical Co. and purified by distillation over CaH_2 (for liquids) or column chromatography (for solids) prior to use.

Bis(pinacolato)diboron: purchased from Frontier Scientific, Inc. and recrystallized from pentane.

4-Bromoanisole: purchased from Aldrich Chemical Co. and used as received.

***tert*-Butyl(chloro)diphenylsilane:** purchased from Aldrich Chemical Co. and used as received.

Cesium carbonate: purchased from Strem Chemicals Inc. and used as received.

Copper(I) bromide: purchased from Strem Chemicals Inc. and used as received.

Copper(I) chloride: purchased from Strem Chemicals Inc. and used as received.

Enynes (3.1m-q): prepared according to a previous reported procedure.[17]

Imidazole: purchased from Aldrich Chemical Co. and used as received.

Imidazolinium salt 3.22 and imidazolium salts 3.23 and 3.54: purchased from Aldrich Chemical Co. and used as received.

Imidazolinium salt 3.53: purchased from TCI Chemicals Co. and used as received.

***N*,*N*-Diisopropylamine:** purchased from Aldrich Chemical Co. and used as received.

Palladium(II) acetate: purchased from Strem Chemicals Inc. and used as received.

Paraformaldehyde: purchased from Aldrich Chemical Co. and used as received.

Phosphine ligands 3.3, 3.16–3.21, 3.28–3.49: purchased from Strem Chemicals Inc. and used as received.

Potassium *tert*-butoxide: purchased from Strem Chemicals Inc. and used as received.

RuPhos: purchased from Strem Chemicals Inc. and used as received.

Sodium *tert*-butoxide: purchased from Strem Chemicals Inc. and used as received.

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

Tetrabutylammonium fluoride solution (1.0 M in thf): purchased from Aldrich Chemical Co. and used as received.

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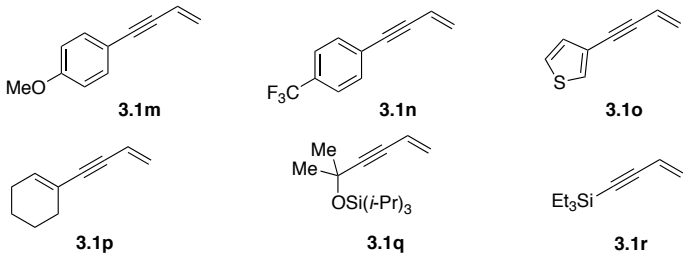
(17) Kang, B.; Kim, D.; Do, Y.; Chang, S. *Org. Lett.* **2003**, *5*, 3041–3043.

3.8.2 Characterization Data of Enynes

Chart S1. Enyne Precursors for **3.15m-r**



3.1a is a known compound and prepared according to a previous procedure.[18]

1-(But-3-en-1-yn-1-yl)-4-methoxybenzene (3.1m). IR (neat): 3041 (w), 3006 (m), 2958 (m), 2909 (m), 2836 (m), 1600 (s), 1507 (s), 1464 (m), 1441 (m), 1290 (s), 1245 (s), 1172 (s), 1106 (m), 1079 (m), 1031 (s), 970 (m), 917 (m), 830 (s), 674 (w), 533 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38 (2H, d, J = 8.4 Hz), 6.84 (2H, d, J = 8.4 Hz), 6.00 (1H, dd, J = 17.6, 11.2 Hz), 5.69 (1H, dd, J = 17.6, 1.6 Hz), 5.50 (1H, dd, J = 11.2, 1.6 Hz), 3.81 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.8, 133.2, 126.2, 117.5, 115.4, 114.1, 90.1, 87.0, 55.4; HRMS (ESI^+) $[M+H]^+$ Calcd for $C_{11}H_{11}O_1$: 159.08099 m/z, Found: 159.08151 m/z.

1-(But-3-en-1-yn-1-yl)-4-(trifluoromethyl)benzene (3.1n). IR (neat): 1616 (m), 1405 (w), 1318 (s), 1166 (m), 1123 (s), 1064 (s), 1017 (m), 969 (m), 925 (m), 839 (s), 704(w), 674 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.59–7.53 (4H, m), 6.02 (1H, dd, J = 17.6, 11.2 Hz), 5.79 (1H, dd, J = 17.6, 1.6 Hz), 5.61 (1H, dd, J = 11.2, 1.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 133.0, 131.9, 130.1 (q, J = 31.8 Hz), 128.3, 125.4 (q, J = 3.8 Hz),

(18) Waser, J.; González-Gómez, J. C.; Nambu, H.; Huber, P.; Carreira, E. M. *Org. Lett.* **2005**, *7*, 4249–4252.

124.1 (q, J = 270.9 Hz), 116.9, 90.5, 88.6; HRMS (ESI$^+$) [M+H]$^+$ Calcd for $C_{11}H_8F_3$: 197.05781 m/z, Found: 197.05815 m/z.

3-(But-3-en-1-yn-1-yl)thiophene (3.1o). IR (neat): 3106 (m), 3007 (w), 1603 (m), 1517 (w), 1356 (m), 1290 (w), 1236 (m), 1185 (m), 1074 (m), 1031 (s), 970 (m), 917 (m), 853 (s), 777 (s), 689 (m), 623 (m), 555 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.45 (1H, dd, J = 2.8, 1.2 Hz), 7.27 (1H, dd, J = 5.2, 2.8 Hz), 7.12 (1H, dd, J = 5.2, 1.2 Hz), 6.00 (1H, dd, J = 17.6, 11.6 Hz), 5.72 (1H, dd, J = 17.6, 2.0 Hz), 5.54 (1H, dd, J = 11.6, 2.0 Hz), 3.81 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 129.9, 128.8, 126.9, 125.5, 122.3, 117.2, 87.8, 85.2; HRMS (ESI$^+$) [M+H]$^+$ Calcd for $C_8H_7S_1$: 135.02685 m/z, Found: 135.02676 m/z.

1-(But-3-en-1-yn-1-yl)cyclohex-1-ene (3.1p). IR (neat): 3026 (w), 2928 (s), 2909 (m), 2858 (m), 1601 (m), 1435 (m), 1347 (m), 1291 (w), 1239 (m), 1174 (w), 1074 (m), 969 (s), 916 (s), 842 (s), 798 (m), 674 (w), 526 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.13–6.11 (1H, m), 5.91 (1H, dd, J = 17.6, 11.6 Hz), 5.58 (1H, dd, J = 17.6, 2.4 Hz), 5.50 (1H, dd, J = 11.6, 2.4 Hz), 2.16–2.09 (4H, m), 1.66–1.54 (4H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 135.4, 125.9, 120.8, 117.6, 92.1, 85.7, 29.3, 25.9, 22.4, 21.6; HRMS (ESI$^+$) [M+H]$^+$ Calcd for $C_{10}H_{13}$: 133.10173 m/z, Found: 133.10184 m/z.

Triisopropyl((2-methylhex-5-en-3-yn-2-yl)oxy)silane (3.1q). The spectral data were identical to those previously reported.[19] ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.78 (1H, dd, J = 17.2, 10.8 Hz), 5.55 (1H, dd, J = 17.2, 2.0 Hz), 5.54 (1H, dd, J = 10.8, 2.0 Hz), 1.53 (6H, s), 1.18–1.11 (3H, m), 1.09–1.06 (18H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 126.4, 117.2,

(19) Geary, L. M.; Woo, S. K.; Leung, J. C.; Krische, M. J. *Angew. Chem., Int. Ed.* **2012**, *51*, 2972–2976.

95.8, 81.1, 66.6, 33.2, 18.5, 13.1.

But-3-en-1-yn-1-yltriethylsilane (3.1r). IR (neat): 3082 (w), 3002 (m), 2962 (m), 2988 (m), 1607 (m), 1502 (m), 1437 (m), 1289 (m), 1169 (m), 1089 (m), 972 (s), 919 (m), 831 (s), 670 (w), 532 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.83 (1H, dd, *J* = 17.6, 11.2 Hz), 5.71 (1H, dd, *J* = 17.6, 2.4 Hz), 5.49 (1H, dd, *J* = 11.2, 2.4 Hz), 1.00 (9H, t, *J* = 8.0 Hz), 0.62 (6H, q, *J* = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 128.0, 117.5, 105.0, 92.7, 7.6, 4.5; HRMS (ESI^+) $[M+H]^+$ Calcd for $C_{11}H_{11}O_1$: 167.12560 m/z, Found: 167.12523 m/z.

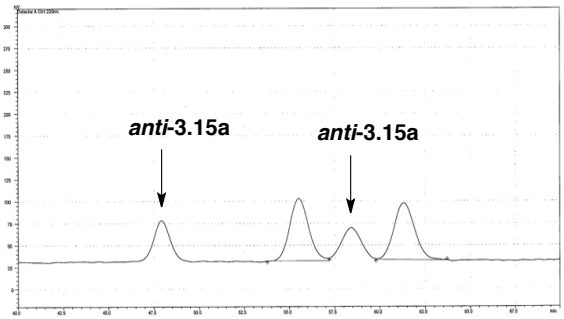
3.8.3 Experimental Procedures and Characterization Data for Bisphosphine–Cu-Catalyzed Reactions of $B_2(pin)_2$, Enynes and Aldehydes

■ **Representative Experimental Procedure for Bisphosphine–Cu-Catalyzed Reactions of $B_2(pin)_2$, Enynes and Aldehydes Followed by *Oxidative Work-up*:** In a N_2-filled glove-box, an oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with bisphosphine **3.3** (3.1 mg, 0.005 mmol, 5.0 mol %), CuCl (0.5 mg, 0.005 mmol, 5.0 mol%), NaO*t*-Bu (1.9 mg, 0.020 mmol, 1.5 equiv) and tetrahydrofuran (thf, 0.5 mL). The vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the solution was allowed to stir at 22 °C for one hour. Bis(pinacolato)diboron (27.9 mg, 0.110 mmol, 1.1 equiv) was added to the solution, causing it to turn dark brown immediately. The vial was re-sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and removed from the glove-box. The mixture was allowed to stir at 22 °C for 30 min under an atmosphere of N_2. Enyne

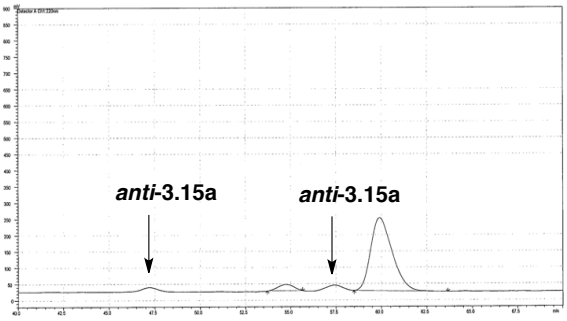
3.1a (12.8 mg, 0.100 mmol, 1.0 equiv) and benzaldehyde **3.2a** (11.2 μL, 0.110 mmol, 1.1 equiv) were added through syringes. The resulting solution was allowed to stir at 22 °C for 8 h before the reaction was quenched by passing the mixture through a short plug of celite and silica gel and eluted with Et_2O (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide yellow oil, which was dissolved in thf (0.5 mL). $NaBO_3$•$4H_2O$ (76.9 mg, 0.500 mmol, 5.0 equiv) and H_2O (0.5mL) were added. The resulting mixture was allowed to stir at 22 °C for three hours. The aqueous layer was washed with Et_2O (3 × 2 mL). The combined organic layers were concentrated *in vacuo* to provide colorless oil, which was purified by silica gel chromatography (hexanes:ethyl acetate = 2.5:1) to afford **3.15a** as white solid (19.2 mg, 0.076 mmol, 76% yield).

(1*S*,2*R*)-1-Phenyl-2-(phenylethynyl)propane-1,3-diol (3.15a). IR (neat): 3354 (br), 3061 (w), 2925 (m), 2889 (m), 1490 (m), 1442 (m), 1120 (m), 1027 (s), 969 (m), 915 (m), 873 (w), 755 (s), 692 (s), 570 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.48–7.45 (2H, m), 7.42–7.37 (4H, m), 7.34–7.26 (4H, m), 5.00 (1H, d, *J* = 4.8 Hz), 3.86 (1H, dd, *J* = 10.8, 6.0 Hz), 3.79 (1H, dd, *J* = 10.8, 4.8 Hz), 3.18–3.14 (1H, m), 2.92 (1H, br s), 2.80 (1H, br s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 141.6, 131.9, 128.5, 128.43, 128.42, 128.1, 126.5, 122.9, 86.0, 74.2, 63.6, 44.2; HRMS (ESI^+) $[M+H-H_2O]^+$ Calcd for $C_{17}H_{15}O_1$: 235.11229 m/z, Found: 235.11251 m/z; Specific rotation: $[\alpha]_D^{20}$ –42.4 (*c* 0.79, $CHCl_3$) for an enantiomerically enriched sample of 95:5 er.

Enantiomeric purity of **3.15a** was determined by HPLC analysis in comparison with authentic racemic material (95:5 er shown; Chiralcel OJ–H column, 93:7 hexanes/ *i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	55.517	5182208	70955	50.349	52.380
2	61.316	5110366	64508	49.651	47.620

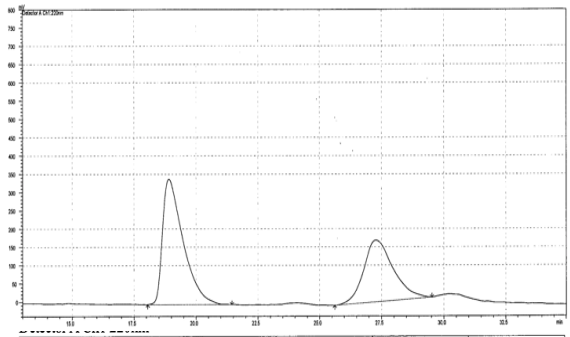


Peak#	Ret. Time	Area	Height	Area %	Height %
1	54.733	1026889	18109	5.253	7.439
2	59.896	18522684	225334	94.747	92.561

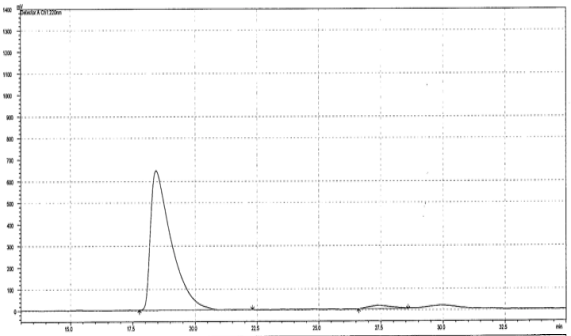
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	55.517	50.349	1	54.733	5.253
2	61.316	49.651	2	59.896	94.747

(1*S*,2*R*)-1-(Naphthalen-1-yl)-2-(phenylethynyl)propane-1,3-diol (3.15b). IR (neat): 3378 (br), 3053 (m), 2929 (m), 2887 (m), 1489 (m), 1442 (w), 1164 (m), 1057 (s), 916 (w), 799 (s), 781 (s), 756 (s), 691 (s), 626 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.11–8.08 (2H, m), 7.91–7.88 (1H, m), 7.84–7.80 (2H, m), 7.54–7.47 (3H, m), 7.39–7.34 (2H, m), 7.31–7.25 (3H, m), 5.84 (1H, d, *J* = 4.8 Hz), 4.01 (1H, dd, *J* = 10.4, 6.4 Hz), 3.79 (1H, dd, *J* = 10.4, 4.8 Hz), 3.43–3.40 (1H, m), 3.04 (1H, br s), 2.42 (1H, br s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 137.4, 133.9, 131.9, 130.3, 129.2, 128.5, 128.4, 126.4, 125.7, 125.4, 124.0, 122.9, 122.8, 86.5, 85.6, 69.8, 63.9, 43.5; HRMS (ESI^+) $[M+H-H_2O]^+$ Calcd for $C_{21}H_{17}O_1$: 285.12794 m/z, Found: 285.12810 m/z; Specific rotation: $[\alpha]_D^{20}$ –38.0 (*c* 1.42, $CHCl_3$) for an enantiomerically enriched sample of 97:3 er.

Enantiomeric purity of **3.15b** was determined by HPLC analysis in comparison with authentic racemic material (97:3 er shown; Chiralcel OD–H column, 90:10 hexanes/ *i*-PrOH, 0.8 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.905	19960563	344402	50.245	65.898
2	27.276	19765948	178229	49.755	34.102

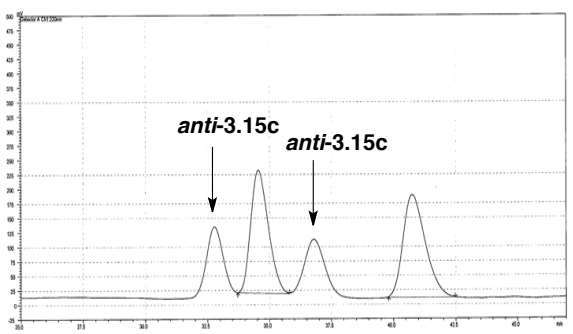


Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.430	37164085	645841	97.361	97.634
2	27.416	1007239	15653	2.639	2.366

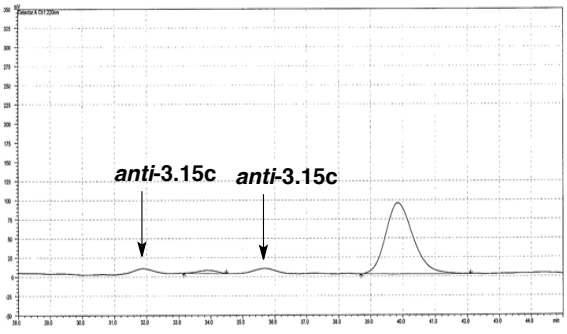
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	18.905	50.245	1	18.430	97.361
2	27.276	49.755	2	27.416	2.639

(1*S*,2*R*)-2-(Phenylethynyl)-1-(*o*-tolyl)propane-1,3-diol (3.15c). IR (neat): 3362 (br), 3061 (m), 2929 (m), 2887 (m), 1489 (m), 1442 (m), 1116 (w), 1028 (s), 912 (m), 867 (w), 753 (s), 691 (s), 528 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.62 (1H, d, *J* = 8.0 Hz), 7.43–7.40 (2H, m), 7.32–7.27 (3H, m), 7.25–7.23 (1H, m), 7.22–7.17 (1H, m), 7.16 (1H, d, *J* = 8.0 Hz), 5.25 (1H, d, *J* = 4.8 Hz), 3.91 (1H, dd, *J* = 11.2, 6.4 Hz), 3.83 (1H, dd, *J* = 11.2, 4.8 Hz), 3.15–3.11 (1H, m), 2.38 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 139.8, 134.8, 131.9, 131.7, 130.5, 128.4, 127.8, 126.2, 126.1, 122.9, 86.0, 85.9, 69.9, 63.8, 43.2, 19.2; HRMS (ESI^+) $[M+H]^+$ Calcd for $C_{18}H_{19}O_2$: 267.13850 m/z, Found: 267.13762 m/z; Specific rotation: $[\alpha]_D^{20}$ –40.9 (*c* 1.14, $CHCl_3$) for an enantiomerically enriched sample of 97:3 er.

Enantiomeric purity of **3.15c** was determined by HPLC analysis in comparison with authentic racemic material (97:3 er shown; Chiralcel OJ–H column, 93:7 hexanes/ *i*-PrOH, 0.6 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	34.544	10985895	216172	50.001	54.923
2	40.754	10985484	177420	49.999	45.077

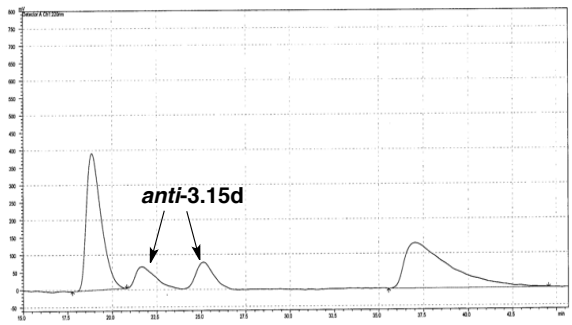


Peak#	Ret. Time	Area	Height	Area %	Height %
1	33.886	175424	4119	3.096	4.247
2	39.843	5490947	92873	96.904	95.753

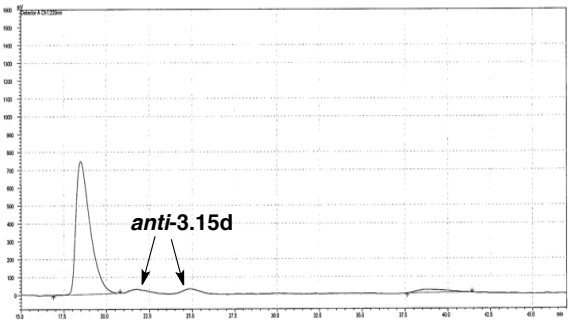
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	34.544	50.001	1	33.886	3.096
2	40.754	49.999	2	39.843	96.904

(1*S*,2*R*)-1-(Benzo[*b*]thiophen-3-yl)-2-(phenylethynyl)propane-1,3-diol (3.15d). IR (neat): 3363 (br), 3058 (m), 2927 (m), 2887 (m), 1489 (m), 1442 (m), 1428 (m), 1308 (m), 1157 (m), 1099 (s), 1051 (s), 910 (m), 872 (w), 756 (s), 732 (s), 691 (s), 460 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.93–7.87 (2H, m), 7.60 (1H, s), 7.41–7.34 (4H, m), 7.31–7.20 (3H, m), 5.42 (1H, d, *J* = 4.4 Hz), 3.99 (1H, dd, *J* = 11.2, 6.4 Hz), 3.92 (1H, dd, *J* = 11.2, 4.8 Hz), 3.42–3.38 (1H, m), 2.94 (1H, br s), 2.39 (1H, br s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 140.8, 137.4, 136.9, 131.9, 128.5, 128.4, 124.6, 124.3, 123.7, 123.1, 122.7, 122.2, 86.4, 85.7, 69.2, 63.7, 42.7; HRMS (ESI^+) $[M+H-H_2O]^+$ Calcd for $C_{19}H_{15}O_1S_1$: 291.08436 m/z, Found: 291.08549 m/z; Specific rotation: $[\alpha]_D^{20}$ –47.6 (*c* 1.30, $CHCl_3$) for an enantiomerically enriched sample of 95:5 er.

Enantiomeric purity of **3.15d** was determined by HPLC analysis in comparison with authentic racemic material (95:5 er. shown; Chiralcel OD–H column, 90:10 hexanes/ *i*-PrOH, 0.8 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.863	22698759	391337	49.595	74.985
2	37.023	23069069	130552	50.405	25.015

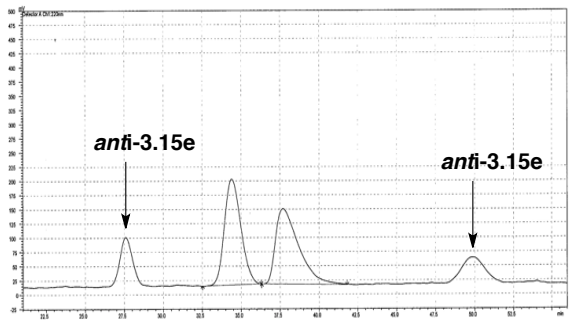


Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.497	43194630	744846	95.345	97.672
2	38.740	2108741	17752	4.655	2.328

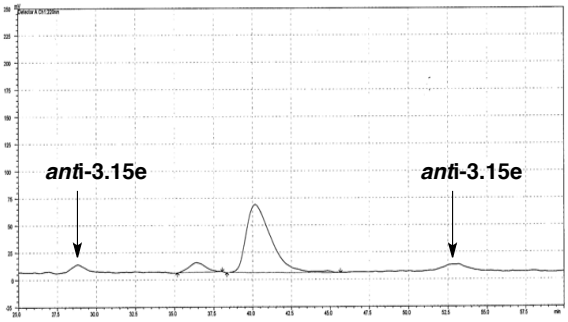
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	18.863	49.595	1	18.497	95.345
2	37.023	50.405	2	38.740	4.655

(1*S*,2*R*)-1-(4-Methoxyphenyl)-2-(phenylethynyl)propane-1,3-diol (3.15e). IR (neat): 3368 (br), 3058 (w), 2933 (m), 2893 (m), 1612 (m), 1512 (s), 1490 (m), 1442 (m), 1302 (m), 1246 (s), 1175 (s), 1029 (s), 916 (w), 876 (m), 757 (s), 732 (s), 692 (s), 579 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.44–7.38 (4H, m), 7.32–7.26 (3H, m), 6.92–6.90 (2H, m), 4.95 (1H, d, *J* = 4.8 Hz), 3.83 (1H, dd, *J* = 10.4, 5.6 Hz), 3.81 (3H, s), 3.76 (1H, dd, *J* = 10.4, 4.8 Hz), 3.15–3.11 (1H, m), 2.79 (1H, br s), 2.20 (1H, br s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.5, 133.7, 131.9, 128.4, 127.9, 127.7, 122.9, 113.9, 86.3, 85.9, 74.0, 63.6, 55.4, 44.3; HRMS (ESI^+) $[M+H-H_2O]^+$ Calcd for $C_{18}H_{17}O_2$: 265.12285 m/z, Found: 265.12378 m/z; Specific rotation: $[\alpha]_D^{20}$ –39.2 (*c* 1.26, $CHCl_3$) for an enantiomerically enriched sample of 94:6 er.

Enantiomeric purity of **3.15e** was determined by HPLC analysis in comparison with authentic racemic material (94:6 er shown; Chiralcel OZ–H column, 93:7 hexanes/ *i*-PrOH, 0.8 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	34.398	13640859	186113	49.966	58.376
2	37.686	13659305	132704	50.034	41.624

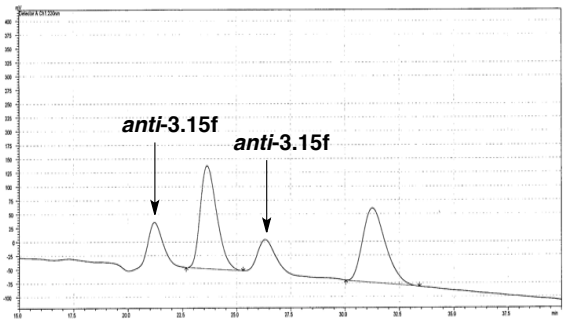


Peak#	Ret. Time	Area	Height	Area %	Height %
1	36.378	479962	7618	6.450	10.825
2	40.163	6961428	62757	93.550	89.175

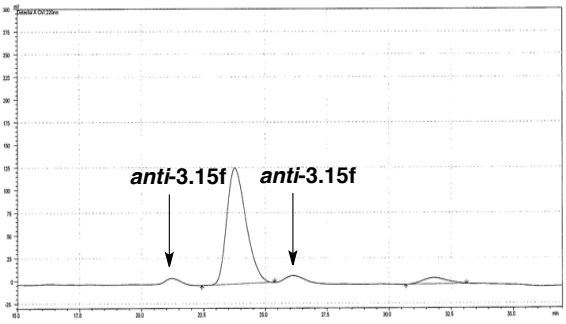
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	34.398	49.966	1	36.378	6.450
2	37.686	50.034	2	40.163	93.550

(1*S*,2*R*)-1-(4-Fluorophenyl)-2-(phenylethynyl)propane-1,3-diol (3.15f). IR (neat): 3363 (br), 3058 (w), 2928 (m), 2890 (m), 1604 (m), 1509 (s), 1490 (m), 1442 (m), 1326 (m), 1223 (s), 1158 (m), 1030 (m), 917 (w), 837 (m), 757 (s), 692 (s), 544 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.46–7.41 (2H, m), 7.41–7.37 (2H, m), 7.32–7.26 (3H, m), 7.09–7.03 (2H, m), 5.01 (1H, d, *J* = 4.8 Hz), 3.87 (1H, dd, *J* = 11.2, 6.4 Hz), 3.79 (1H, dd, *J* = 11.2, 4.8 Hz), 3.13–3.09 (1H, m), 3.03 (1H, br s), 2.33 (1H, br s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 162.6 (d, *J* = 244.4 Hz), 137.3 (d, *J* = 3.0 Hz), 131.7, 128.5, 128.4, 128.1 (d, *J* = 8.4 Hz), 115.3 (d, *J* = 21.3 Hz), 86.1, 85.7, 73.6, 63.6, 44.1; HRMS (ESI^+) $[M+H-H_2O]^+$ Calcd for $C_{17}H_{14}F_1O_1$: 253.10287 m/z, Found: 253.10182 m/z; Specific rotation: $[\alpha]_D^{20}$ –38.2 (*c* 0.83, $CHCl_3$) for an enantiomerically enriched sample of 94:6 er.

Enantiomeric purity of **3.15f** was determined by HPLC analysis in comparison with authentic racemic material (94:6 er shown; Chiralcel OD–H column, 93:7 hexanes/ *i*-PrOH, 0.6 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.639	9900440	186174	50.254	58.012
2	31.261	9800296	134751	49.746	41.988

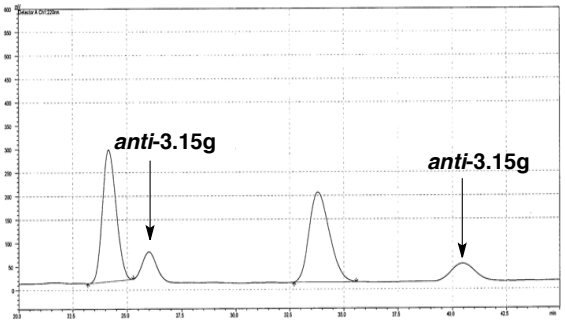


Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.766	6952619	128002	93.739	94.934
2	31.803	464363	6831	6.261	5.066

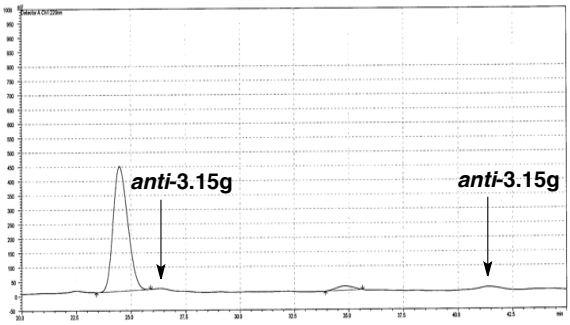
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	23.639	50.254	1	23.766	93.739
2	31.261	49.746	2	31.803	6.261

(2*R*,3*R*,*E*)-5-Phenyl-2-(phenylethynyl)pent-4-ene-1,3-diol (3.15g). IR (neat): 3385 (br), 3057 (m), 2926 (m), 2886 (m), 1577 (s), 1490 (m), 1443 (m), 1157 (w), 1108 (m), 1050 (m), 802 (w), 755 (s), 692 (s), 563 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.45–7.38 (4H, m), 7.35–7.24 (6H, m), 6.74 (1H, d, *J* = 16.0 Hz), 6.41 (1H, dd, *J* = 16.0, 6.4), 4.63–4.61 (1H, m), 3.98 (1H, dd, *J* = 10.8, 6.8 Hz), 3.93 (1H, dd, *J* = 10.8, 4.8 Hz), 3.13–3.09 (1H, m), 2.56 (2H, br s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 136.6, 132.1, 132.0, 129.4, 128.8, 128.5, 128.4, 128.0, 126.8, 122.9, 85.8, 85.7, 73.0, 63.6, 42.4; HRMS (ESI^+) $[M+H-H_2O]^+$ Calcd for $C_{19}H_{17}O_1$: 261.12794 m/z, Found: 261.12886 m/z; Specific rotation: $[\alpha]_D^{20}$ –30.6 (*c* 0.88, $CHCl_3$) for an enantiomerically enriched sample of 96:4 er.

Enantiomeric purity of **3.15g** was determined by HPLC analysis in comparison with authentic racemic material (96:4 er shown; Chiralcel OZ–H column, 93:7 hexanes/ *i*-PrOH, 0.6 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.147	12350241	281033	50.036	59.634
2	33.800	12332689	190231	49.964	40.366

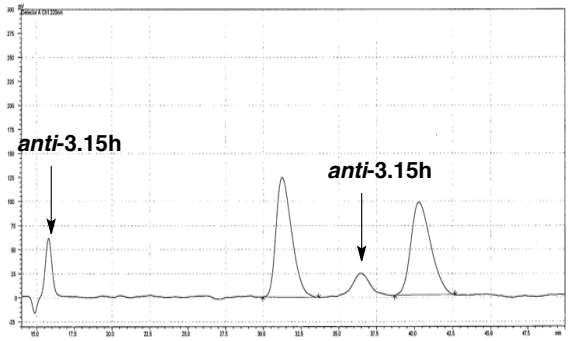


Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.476	20106058	434287	96.179	96.702
2	34.811	798677	14809	3.821	3.298

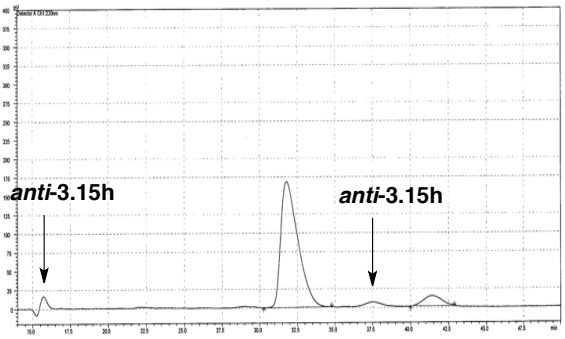
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	24.147	50.036	1	24.476	96.179
2	33.800	49.964	2	34.811	3.821

(2*R*,3*S*,*E*)-4-Methyl-5-phenyl-2-(phenylethynyl)pent-4-ene-1,3-diol (3.15h). IR (neat): 3364 (br), 3054 (m), 2926 (m), 2887 (m), 1577 (s), 1490 (m), 1442 (m), 1179 (w), 1068 (m), 1029 (m), 918 (m), 870 (w), 813 (w), 754 (s), 691 (s), 513 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.44–7.41 (2H, m), 7.36–7.27 (7H, m), 7.26–7.21 (1H, m), 6.67 (1H, s), 4.43 (1H, d, *J* = 5.2 Hz), 3.93 (1H, dd, *J* = 10.8, 6.0 Hz), 3.88 (1H, dd, *J* = 10.8, 5.2 Hz), 3.21–3.17 (1H, m), 2.63 (1H, br s), 2.33 (1H, br s), 1.95 (3H, d, *J* = 1.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 137.7, 137.5, 132.0, 131.8, 129.2, 128.4, 128.3, 128.2, 127.1, 126.7, 122.8, 86.0, 76.7, 63.8, 41.2, 14.4; HRMS (ESI^+) $[M+H-H_2O]^+$ Calcd for $C_{20}H_{19}O_1$: 275.14329 m/z, Found: 275.14359 m/z; Specific rotation: $[\alpha]_D^{20}$ –21.6 (*c* 1.25, $CHCl_3$) for an enantiomerically enriched sample of 93:7 er.

Enantiomeric purity of **3.15h** was determined by HPLC analysis in comparison with authentic racemic material (93:7 er shown; Chiralcel OZ–H column, 94:6 hexanes/ *i*-PrOH, 0.8 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	31.237	8869588	123792	50.308	56.174
2	40.286	8760829	96582	49.692	43.826

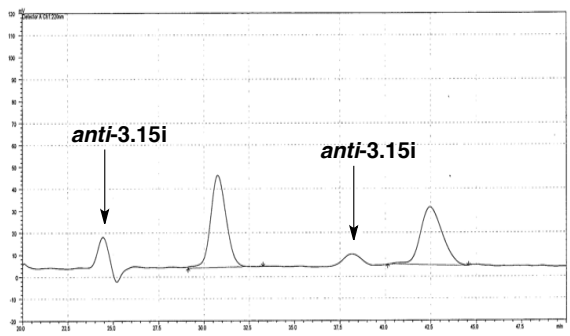


Peak#	Ret. Time	Area	Height	Area %	Height %
1	31.785	13429667	168130	93.329	93.149
2	41.437	959902	12365	6.671	6.851

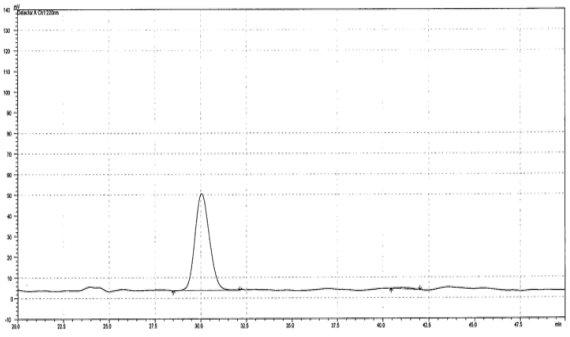
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	31.237	50.308	1	31.785	93.329
2	40.286	49.692	2	41.437	6.671

(1*S*,2*R*)-2-(Phenylethynyl)-1-((*S*)-4-(prop-1-en-2-yl)cyclohex-1-en-1-yl)propane-1,3-diol (3.15i). IR (neat): 3374 (br), 2918 (m), 2837 (m), 1490 (m), 1435 (m), 1374 (m), 1199 (w), 1052 (m), 1029 (m), 965 (m), 916 (m), 887 (m), 828 (w), 755 (s), 691 (s), 541 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.43–7.40 (2H, m), 7.32–7.28 (3H, m), 5.84 (1H, s), 4.75–4.71 (2H, m), 4.23 (1H, d, *J* = 5.2 Hz), 3.84 (1H, dd, *J* = 10.8, 6.0 Hz), 3.79 (1H, dd, *J* = 10.8, 5.2 Hz), 3.10–3.06 (1H, m), 2.33 (1H, br s), 2.29–2.16 (4H, m), 2.10–1.97 (2H, m), 1.91–1.84 (1H, m), 1.75 (3H, s), 1.55–1.45 (1H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 149.7, 137.2, 131.9, 128.4, 128.3, 123.7, 123.0, 108.9, 86.3, 85.7, 75.4, 63.7, 41.1, 41.0, 30.5, 27.5, 25.1, 20.9; HRMS (ESI^+) $[M+H-H_2O]^+$ Calcd for $C_{20}H_{23}O_1$: 279.17489 m/z, Found: 279.17605 m/z; Specific rotation: $[\alpha]_D^{20}$ –38.8 (*c* 1.23, $CHCl_3$) for an enantiomerically enriched sample of 99:1 dr.

Enantiomeric purity of **3.15i** was determined by HPLC analysis in comparison with authentic racemic material (99:1 dr shown; Chiralcel OZ–H column, 95:5 hexanes/ *i*-PrOH, 0.8 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	30.756	2200043	39979	49.994	60.182
2	42.462	2200532	26451	50.006	39.818

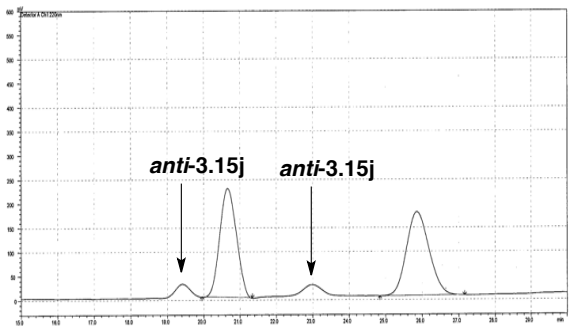


Peak#	Ret. Time	Area	Height	Area %	Height %
1	30.045	2563909	46799	98.609	98.799
2	41.026	36172	569	1.391	1.201

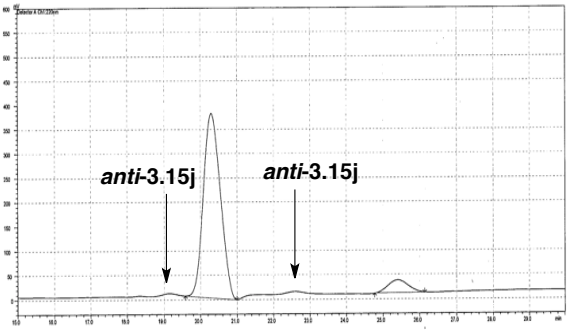
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	30.756	49.994	1	30.045	98.609
2	42.462	50.006	2	41.026	1.391

(2*R*,3*R*)-5-Phenyl-2-(phenylethynyl)pentane-1,3-diol (3.15j). IR (neat): 3358 (br), 3060 (m), 2940 (m), 1599 (w), 1490 (m), 1442 (m), 1411 (m), 1333 (m), 1156 (w), 1029 (m), 916 (m), 755 (s), 692 (s), 527 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.45–7.39 (2H, m), 7.33–7.28 (4H, m), 7.26–7.18 (4H, m), 3.97–3.87 (3H, m), 2.95–2.91 (1H, m), 2.89–2.84 (1H, m), 2.79–2.71 (1H, m), 2.31 (2H, br s), 2.11–1.92 (2H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 175.3, 141.8, 132.0, 128.60, 128.59, 128.4, 126.1, 122.9, 85.7, 85.6, 71.2, 64.1, 41.9, 37.6, 32.2; HRMS (ESI^+) $[M+H]^+$ Calcd for $C_{19}H_{21}O_2$: 281.15415 m/z, Found: 281.15444 m/z; Specific rotation: $[\alpha]_D^{20}$ –14.3 (*c* 1.12, $CHCl_3$) for an enantiomerically enriched sample of 98:2 er.

Enantiomeric purity of **3.15j** was determined by HPLC analysis in comparison with authentic racemic material *before recrystallization* (92.5:7.5 er shown; Chiralcel OZ–H column, 93:7 hexanes/ *i*-PrOH, 0.5 mL/min, 220 nm).



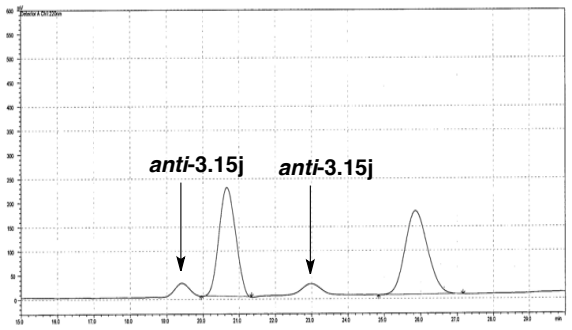
Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.658	7331443	226740	49.903	56.806
2	25.852	7360086	172408	50.097	43.194



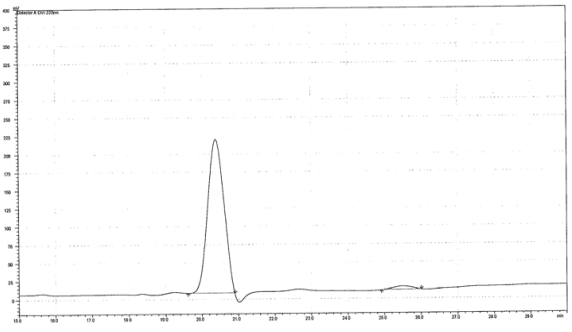
Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.289	12278284	379471	92.495	93.603
2	25.401	996314	25935	7.505	6.397

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	20.658	49.903	1	20.289	92.495
2	25.852	50.097	2	25.401	7.505

Enantiomeric purity of **3.15j** was determined by HPLC analysis in comparison with authentic racemic material *after recrystallization* (98:2 er shown; Chiralcel OZ–H column, 93:7 hexanes/ *i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.658	7331443	226740	49.903	56.806
2	25.852	7360086	172408	50.097	43.194



Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.382	6994292	217956	98.034	98.157
2	25.492	140291	4093	1.966	1.843

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	20.658	49.903	1	20.382	98.034
2	25.852	50.097	2	25.492	1.966

(2*R*,3*R*,5*S*)-5,9-Dimethyl-2-(phenylethynyl)dec-8-ene-1,3-diol (3.15k). IR (neat): 3381 (br), 2959 (m), 2913 (m), 1490 (m), 1442 (m), 1377 (m), 1336 (m), 1048 (m), 961 (w), 837 (w), 755 (s), 690 (s), 542 (m), 527 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.45–7.39 (2H, m), 7.32–7.27 (3H, m), 5.13–5.08 (1H, m), 4.01–3.88 (3H, m), 2.89–2.86 (1H, m), 2.27 (1H, br s), 2.08–1.93 (2H, m), 1.83–1.70 (2H, m), 1.68 (3H, s), 1.58 (3H, s),

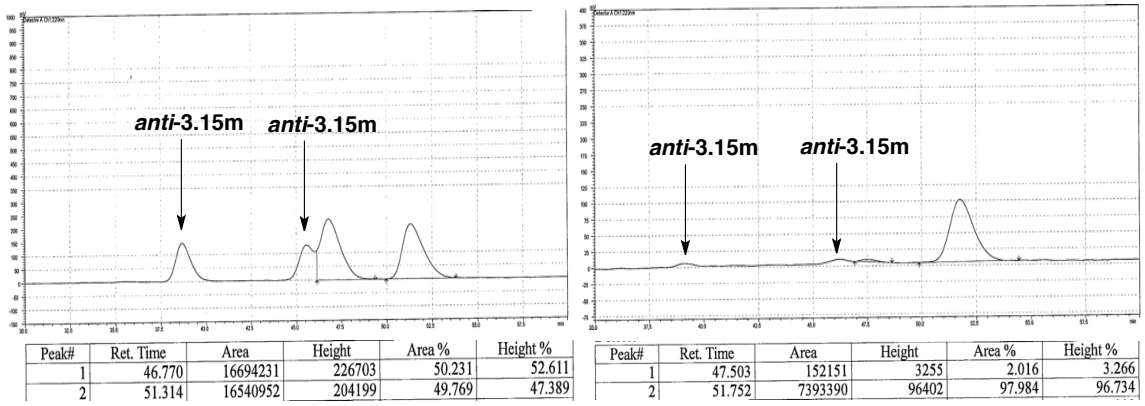
1.39–1.35 (2H, m), 1.34–1.19 (2H, m), 0.96 (3H, d, J = 6.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 131.9, 131.4, 128.4, 128.3, 124.8, 123.0, 86.0, 85.6, 69.6, 64.1, 43.2, 42.4, 37.9, 28.9, 25.8, 25.6, 19.3, 17.8; HRMS (ESI$^+$) $[M+H]^+$ Calcd for $C_{20}H_{29}O_2$: 301.21675 m/z, Found: 301.21730 m/z; Specific rotation: $[\alpha]_D^{20}$ –3.5 (*c* 0.60, $CHCl_3$) for an enantiomerically enriched sample of >98:2 dr.

(2*R*,3*R*,5*R*)-5,9-Dimethyl-2-(phenylethynyl)dec-8-ene-1,3-diol (3.15l). IR (neat): 3373 (br), 2957 (m), 2923 (m), 1490 (m), 1442 (m), 1337 (m), 1049 (m), 962 (w), 835 (w), 755 (s), 691 (s), 542 (m), 526 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.44–7.41 (2H, m), 7.32–7.26 (3H, m), 5.13–5.09 (1H, m), 4.00–3.88 (3H, m), 2.91–2.88 (1H, m), 2.33 (1H, br s), 2.09–1.93 (3H, m), 1.68 (3H, s), 1.67 (1H, br s), 1.64–1.61 (1H, m), 1.58 (3H, s), 1.57–1.52 (1H, m), 1.48–1.40 (1H, m), 1.24–1.13 (1H, m), 0.96 (3H, d, J = 5.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 132.0, 131.5, 128.4, 128.3, 124.8, 123.0, 85.8, 85.6, 70.1, 64.2, 43.3, 41.7, 36.9, 29.4, 25.8, 25.5, 20.3, 17.8; HRMS (ESI$^+$) $[M+H]^+$ Calcd for $C_{20}H_{29}O_2$: 301.21675 m/z, Found: 301.21661 m/z; Specific rotation: $[\alpha]_D^{20}$ –11.7 (*c* 1.12, $CHCl_3$) for an enantiomerically enriched sample of >98:2 dr.

(1*S*,2*R*)-2-((4-Methoxyphenyl)ethynyl)-1-phenylpropane-1,3-diol (3.15m). IR (neat): 3319 (br), 2933 (m), 2838 (m), 1605 (m), 1509 (s), 1465 (m), 1394 (m), 1324 (w), 1288 (m), 1247 (s), 1172 (m), 1104 (m), 1027 (s), 913 (m), 834 (m), 735 (m), 700 (m), 536 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.47–7.44 (2H, m), 7.40–7.29 (5H, m), 6.84–6.79 (2H, m), 4.98 (1H, d, J = 4.8 Hz), 3.83 (1H, dd, J = 10.8, 6.0 Hz), 3.80 (3H, s), 3.76 (1H, dd, J = 10.8, 4.8 Hz), 3.17–3.12 (1H, m), 2.89 (1H, br s), 2.23 (1H, br s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 141.6, 133.3, 128.5, 128.1, 126.5, 115.0, 114.0, 86.0, 84.4, 74.2, 63.6, 55.4, 44.4, 34.9; HRMS (ESI$^+$) $[M+H]^+$ Calcd for $C_{18}H_{19}O_3$: 283.13342 m/z, Found:

283.13394 m/z; Specific rotation: $[\alpha]_D^{20}$ –59.1 (*c* 0.77, $CHCl_3$) for an enantiomerically enriched sample of 98:2 er.

Enantiomeric purity of **3.15m** was determined by HPLC analysis in comparison with authentic racemic material (98:2 er shown; Chiralcel OJ–H column, 87:13 hexanes/ *i*-PrOH, 0.6 mL/min, 220 nm).



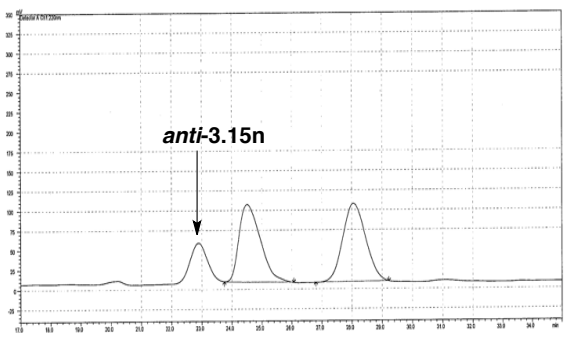
Peak#	Ret. Time	Area	Height	Area %	Height %
1	46.770	16694231	226703	50.231	52.611
2	51.314	16540952	204199	49.769	47.389

Peak#	Ret. Time	Area	Height	Area %	Height %
1	47.503	152151	3255	2.016	3.266
2	51.752	7393390	96402	97.984	96.734

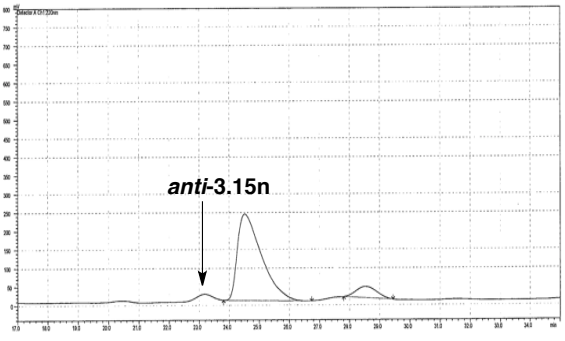
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	46.770	50.231	1	47.503	2.016
2	51.314	49.769	2	51.752	97.984

(1*S*,2*R*)-1-Phenyl-2-((4-(trifluoromethyl)phenyl)ethynyl)propane-1,3-diol (3.15n). IR (neat): 3345 (br), 2933 (w), 2891 (w), 1614 (m), 1405 (m), 1320 (s), 1165 (m), 1121 (m), 1065 (s), 1017 (m), 841 (m), 746 (m), 700 (m), 597 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.55–7.51 (2H, m), 7.49–7.45 (4H, m), 7.41–7.37 (2H, m), 7.35–7.32 (1H, m), 5.05 (1H, d, *J* = 4.8 Hz), 3.90 (1H, dd, *J* = 10.8, 6.0 Hz), 3.84 (1H, dd, *J* = 10.8, 4.8 Hz), 3.19–3.15 (1H, m), 2.91 (1H, br s), 2.33 (1H, br s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 141.5, 132.1, 131.9, 131.1 (q, *J* = 32.6 Hz), 128.5, 128.2, 126.4, 125.3 (q, *J* = 3.8 Hz), 124.0 (q, *J* = 270.2 Hz), 89.0, 84.5, 74.2, 63.6, 43.9; HRMS (ESI^+) $[M+H–H_2O]^+$ Calcd for $C_{18}H_{14}F_3O_1$: 303.09967 m/z, Found: 303.10081 m/z; Specific rotation: $[\alpha]_D^{20}$ –33.9 (*c* 1.38, $CHCl_3$) for an enantiomerically enriched sample of 92:8 er.

Enantiomeric purity of **3.15n** was determined by HPLC analysis in comparison with authentic racemic material (92:8 er shown; Chiralcel OZ–H column, 95:5 hexanes/ *i*-PrOH, 0.6 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.510	4847503	97937	50.367	50.831
2	28.050	4776869	94737	49.633	49.169

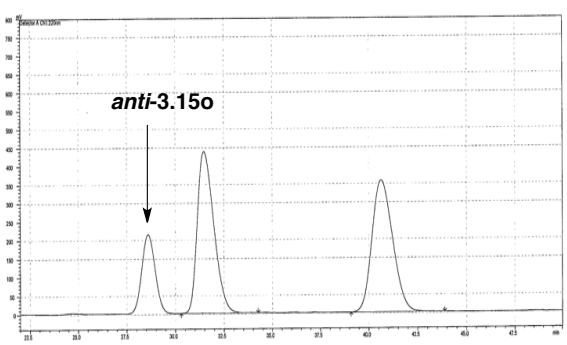


Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.514	13027482	233023	92.203	89.811
2	28.528	1101635	26435	7.797	10.189

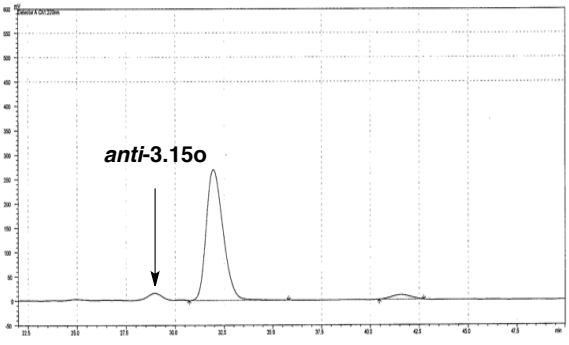
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	24.510	50.367	1	24.514	92.203
2	28.050	49.633	2	28.528	7.797

(1*S*,2*R*)-1-Phenyl-2-(thiophen-3-ylethynyl)propane-1,3-diol (3.15o). IR (neat): 3360 (br), 2930 (m), 2886 (m), 1493 (m), 1453 (m), 1357 (m), 1228 (m), 1053 (s), 1025 (s), 909 (w), 848 (w), 782 (s), 701 (s), 626 (s), 570 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.47–7.44 (2H, m), 7.41–7.35 (3H, m), 7.34–7.29 (1H, m), 7.24 (1H, dd, *J* = 4.8, 2.8 Hz), 7.07 (1H, dd, *J* = 5.2, 1.2 Hz), 4.99 (1H, d, *J* = 4.8 Hz), 3.84 (1H, dd, *J* = 10.8, 6.0 Hz), 3.77 (1H, dd, *J* = 10.8, 4.8 Hz), 3.16–3.12 (1H, m), 2.86 (1H, br s), 2.23 (1H, br s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 141.6, 130.1, 129.0, 128.5, 128.2, 126.5, 125.4, 121.9, 85.7, 81.1, 74.2, 63.6, 44.3; HRMS (ESI^+) $[M+H]^+$ Calcd for $C_{15}H_{15}O_2S_1$: 259.07927 m/z, Found: 259.07976 m/z; Specific rotation: $[\alpha]_D^{20}$ –56.8 (*c* 0.99, $CHCl_3$) for an enantiomerically enriched sample of 96:4 er.

Enantiomeric purity of **3.15o** was determined by HPLC analysis in comparison with authentic racemic material (96:4 er shown; Chiralcel OZ–H column, 93:7 hexanes/ *i*-PrOH, 0.6 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	31.474	25891949	436827	49.619	55.050
2	40.636	26289637	356689	50.381	44.950

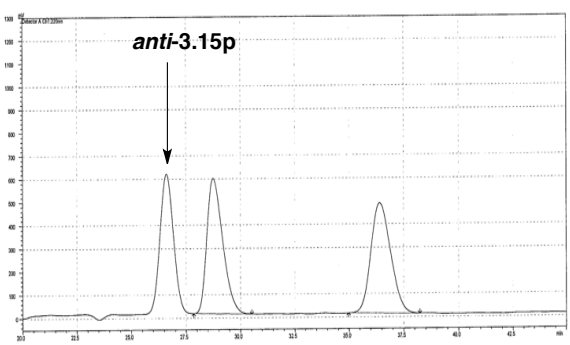


Peak#	Ret. Time	Area	Height	Area %	Height %
1	31.948	16227767	269102	96.160	96.677
2	41.591	648068	9250	3.840	3.323

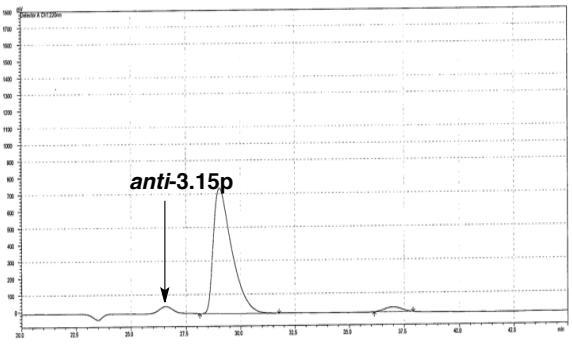
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	31.474	49.619	1	31.948	96.160
2	40.636	50.381	2	41.591	3.840

(1*S*,2*R*)-2-(Cyclohex-1-en-1-ylethynyl)-1-phenylpropane-1,3-diol (3.15p). IR (neat): 3361 (br), 2927 (s), 2885 (m), 1494 (m), 1450 (m), 1347 (m), 1269 (m), 1199 (m), 1046 (s), 1026 (s), 918 (m), 842 (w), 750 (m), 700 (s), 580 (m), 535 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.42–7.39 (2H, m), 7.38–7.34 (2H, m), 7.32–7.27 (1H, m), 6.09–6.07 (1H, m), 4.89 (1H, d, *J* = 5.2 Hz), 3.73 (1H, dd, *J* = 10.8, 6.0 Hz), 3.67 (1H, dd, *J* = 10.8, 5.2 Hz), 3.06–3.02 (1H, m), 2.86 (1H, br s), 2.11–2.04 (4H, m), 1.65–1.53 (5H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 141.6, 135.3, 128.4, 128.0, 126.5, 120.3, 88.1, 82.8, 74.0, 63.5, 44.3, 29.5, 25.7, 22.4, 21.6; HRMS (ESI^+) $[M+H]^+$ Calcd for $C_{17}H_{21}O_2$: 257.15415 m/z, Found: 257.15430 m/z; Specific rotation: $[\alpha]_D^{20}$ –22.6 (*c* 0.90, $CHCl_3$) for an enantiomerically enriched sample of 97:3 er.

Enantiomeric purity of **3.15p** was determined by HPLC analysis in comparison with authentic racemic material (97:3 er shown; Chiralcel OZ–H column, 95:5 hexanes/ *i*-PrOH, 0.6 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	28.746	29826206	582777	50.026	55.060
2	36.407	29795749	475654	49.974	44.940

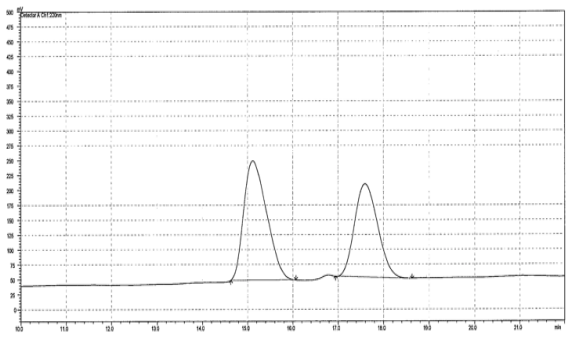


Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.028	44047873	749138	96.768	96.457
2	36.992	1471012	27513	3.232	3.543

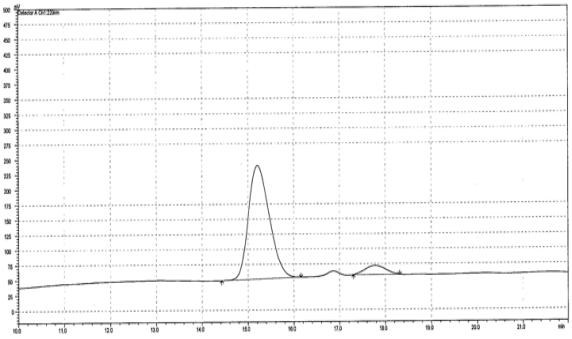
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	28.746	50.026	1	29.028	96.768
2	36.407	49.974	2	36.992	3.232

(1*S*,2*R*)-2-(3-Methyl-3-((triisopropylsilyl)oxy)but-1-yn-1-yl)-1-phenylpropane-1,3-diol (3.15q). IR (neat): 3379 (br), 2942 (m), 2865 (m), 1463 (m), 1450 (m), 1377 (m), 1358 (m), 1239 (m), 1161 (s), 1043 (s), 918 (m), 831 (w), 753 (m), 699 (s), 679 (s), 555 (m), 505 (m), 468 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.41–7.32 (5H, m), 7.31–7.27 (1H, m), 4.89 (1H, d, *J* = 4.8 Hz), 3.73 (1H, dd, *J* = 10.8, 6.4 Hz), 3.68 (1H, dd, *J* = 10.8, 4.8 Hz), 2.97–2.93 (1H, m), 2.69 (1H, br s), 2.06 (1H, br s), 1.50 (3H, s), 1.48 (3H, s), 1.09–0.99 (21H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 141.5, 128.4, 128.0, 126.4, 91.8, 78.3, 73.8, 66.4, 63.3, 43.6, 33.6, 33.5, 18.41, 18.39, 13.14, 13.10; HRMS (ESI^+) $[M+H–H_2O]^+$ Calcd for $C_{23}H_{37}O_2Si_1$: 373.25628 m/z, Found: 373.25456 m/z; Specific rotation: $[\alpha]_D^{20}$ –13.6 (*c* 1.13, $CHCl_3$) for an enantiomerically enriched sample of 94:6 er.

Enantiomeric purity of **3.15q** was determined by HPLC analysis in comparison with authentic racemic material (94:6 er shown; Chiralcel OZ–H column, 97:3 hexanes/ *i*-PrOH, 0.6 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.112	5591719	179205	50.400	53.381
2	17.590	5502914	156504	49.600	46.619

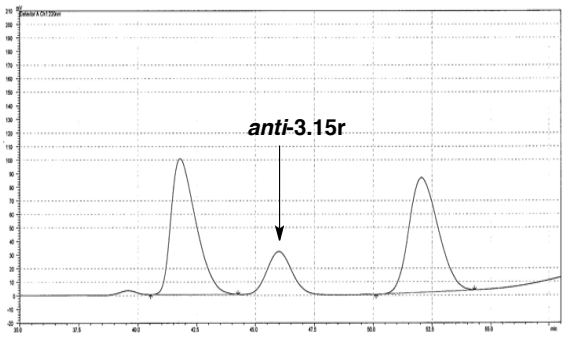


Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.202	5932104	187941	93.711	93.223
2	17.774	398128	13663	6.289	6.777

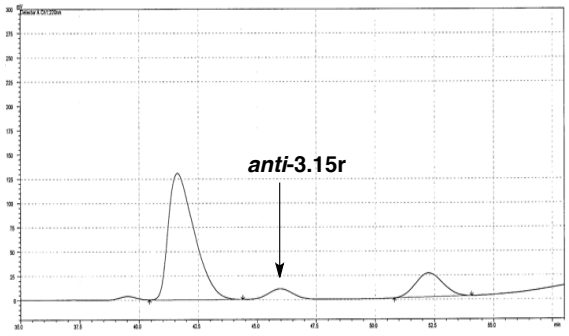
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	15.112	50.400	1	15.202	93.711
2	17.590	49.600	2	17.774	6.289

(1*S*,2*R*)-1-Phenyl-2-(*o*-tolylethynyl)propane-1,3-diol (3.15r). IR (neat): 3375 (br), 2954 (m), 2874 (m), 1496 (m), 1455 (m), 1377 (m), 1178 (m), 1018 (s), 973 (m), 915 (w), 825 (w), 722 (s), 697 (s), 534 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.42–7.39 (2H, m), 7.37–7.32 (2H, m), 7.31–7.27 (1H, m), 4.88 (1H, d, *J* = 5.2 Hz), 3.74 (1H, dd, *J* = 10.8, 6.4 Hz), 3.68 (1H, dd, *J* = 10.8, 5.2 Hz), 3.01–2.97 (1H, m), 2.80 (1H, br s), 2.17 (1H, br s), 0.97 (9H, t, *J* = 8.0 Hz), 0.59 (6H, q, *J* = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 141.4, 128.3, 128.0, 126.4, 103.9, 88.5, 73.7, 63.4, 44.9, 7.6, 4.5; HRMS (ESI^+) $[M+H–H_2O]^+$ Calcd for $C_{17}H_{25}O_1Si_1$: 273.16747 m/z, Found: 273.16680 m/z; Specific rotation: $[\alpha]_D^{20}$ –28.8 (*c* 0.99, $CHCl_3$) for an enantiomerically enriched sample of 85:15 er.

Enantiomeric purity of **3.15r** was determined by HPLC analysis in comparison with authentic racemic material (85:15 er shown; Chiralcel OZ–H column, 98:2 hexanes/ *i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	41.780	7351873	100111	50.220	54.175
2	52.038	7287548	84680	49.780	45.825



Peak#	Ret. Time	Area	Height	Area %	Height %
1	41.607	9944612	130523	84.638	84.758
2	52.250	1804984	23471	15.362	15.242

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	41.780	50.220	1	41.607	84.638
2	52.038	49.780	2	52.250	15.362

■ **Representative Experimental Procedure for Bisphosphine–Cu Catalyzed Reaction of $B_2(pin)_2$, an Enyne and an Aldehyde Followed by *NHC–Cu-Catalyzed Addition to Allylic Phosphate*:** In a N_2-filled glove-box, an oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with bisphosphine **3.3** (3.1 mg, 0.005 mmol, 5.0 mol %), CuCl (0.5 mg, 0.005 mmol, 5.0 mol%), NaO*t*-Bu (1.9 mg, 0.020 mmol, 20 mol %) and thf (0.5 mL). The reaction vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the solution was allowed to stir at 22 °C for one hour. Bis(pinacolato)diboron (27.9 mg, 0.11 mmol, 1.1 equiv) was added to the solution, causing it to turn dark brown immediately. The vial was re-sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and removed from the glove-box. The resulting solution was allowed to stir at 22 °C for 30 min under an atmosphere of N_2. Enyne **3.1a** (12.8 mg, 0.10 mmol, 1.0 equiv) and aldehyde **3.2j** (14.5 μL, 0.11 mmol, 1.1 equiv) were added through syringes. The resulting mixture was allowed to stir at 22 °C for eight hours. After this time, an NHC–Cu complex solution [prepared from mixing imidazolinium salt **3.22** (3.4 mg, 0.010 mmol, 10 mol %), CuCl

(1.0 mg, 0.010 mmol, 10 mol %), KO*t*-Bu (16.8 mg, 0.15 mmol, 1.5 equiv) in thf (0.5 mL) for one hour] and allyl–$OPO(OEt)_2$ (29.1 mg, 0.15 mmol, 1.5 equiv) were transferred into the reaction mixture through syringes. The resulting mixture was allowed to stir at 22 °C for 24 h before the reaction was quenched by passing the mixture through a short plug of celite and silica gel and eluted with Et_2O (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide yellow oil, which was purified by silica gel chromatography (hexanes:ethyl acetate = 10:1) to afford the desired product **3.50** as colorless oil (23.3 mg, 0.076 mmol, 76% yield).

(3*R*,4*S*)-1-Phenyl-4-(phenylethynyl)oct-7-en-3-ol (3.50). IR (neat): 3439 (br), 3026 (w), 2927 (m), 2859 (m), 1640 (m), 1599 (m), 1490 (m), 1453 (m), 1442 (m), 1387 (w), 1155 (w), 1069 (m), 1029 (m), 996 (m), 912 (m), 754 (s), 691 (s), 552 (m), 526 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.45–7.41 (2H, m), 7.33–7.29 (5H, m), 7.26–7.19 (3H, m), 5.90–5.80 (1H, m), 5.11–5.00 (2H, m), 3.64–3.58 (1H, m), 2.92–2.85 (1H, m), 2.80–2.69 (2H, m), 2.41–2.33 (1H, m), 2.28–2.19 (1H, m), 2.00–1.94 (2H, m), 1.86–1.76 (2H, m), 1.73–1.65 (1H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 142.0, 138.1, 131.9, 128.6, 128.5, 128.4, 128.1, 126.0, 123.4, 115.4, 88.7, 85.1, 72.7, 39.5, 37.6, 32.3, 31.9, 31.1; HRMS (ESI^+) $[M+H]^+$ Calcd for $C_{22}H_{25}O_1$: 305.19054 m/z; Found: 305.19122 m/z; Specific rotation: $[\alpha]_D^{20}$ –9.3 (*c* 1.16, $CHCl_3$) for an enantiomerically enriched sample of 92.5:7.5 er. The enantiomeric ratio was shown in **3.15j**.

■ **Representative Experimental Procedure for Bisphosphine–Cu Catalyzed Reaction of $B_2(pin)_2$, an Enyne and an Aldehyde Followed by *Pd-Catalyzed Suzuki***

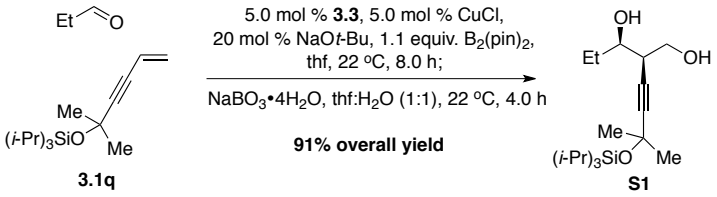
***Coupling of Arylbromide*:** In a N_2-filled glove-box, an oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with phosphine **3.3** (3.1 mg, 0.005 mmol, 5.0 mol %), CuCl (0.5 mg, 0.005 mmol, 5.0 mol%), NaO*t*-Bu (1.9 mg, 0.020 mmol, 20 mol %) and thf (0.5 mL). The reaction vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the solution was allowed to stir at 22 °C for one hour. Bis(pinacolato)diboron (27.9 mg, 0.11 mmol, 1.1 equiv) was added to the solution, causing it to turn dark brown immediately. The vial was re-sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and removed from the glove-box. The resulting solution was allowed to stir at 22 °C for 30 min under an atmosphere of N_2. Enyne **3.1a** (12.8 mg, 0.10 mmol, 1.0 equiv) and aldehyde **3.2j** (14.5 μL, 0.11 mmol, 1.1 equiv) were added through syringes. The resulting mixture was allowed to stir at 22 °C for eight hours before the reaction was quenched by passing the mixture through a short plug of celite and silica gel and eluted with Et_2O (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide yellow oil, which was used in the next step without further purification. In a N_2-filled glove-box, $Pd(OAc)_2$ (0.4 mg, 0.002 mmol, 2.0 mol %), RuPhos (1.9 mg, 0.004 mmol, 4.0 mol %), Cs_2CO_3 (97.7 mg, 0.300 mmol, 3.0 equiv), 4-bromoanisole (18.8 μL, 0.150 mmol, 1.5 equiv) were added to a solution of unpurifed the product obtained from previous step in thf (1.0 mL) and water (0.1 mL). The reaction vessel was sealed with a cap and removed from the glove-box. The solution was allowed to stir at 70 °C for 18 h. After this time, the reaction was quenched by passing the mixture through a short plug of celite and silica gel and eluted with Et_2O (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide yellow oil, which was purified

by silica gel chromatography (hexanes:ethyl acetate = 10:1) to afford the desired product **3.51** as colorless oil (24.9 mg, 0.067 mmol, 67% yield).

(3*R*,4*S*)-4-(4-Methoxybenzyl)-1,6-diphenylhex-5-yn-3-ol (3.51). IR (neat): 3452 (br), 3027 (w), 2930 (m), 2858 (m), 1611 (m), 1511 (s), 1490 (m), 1456 (m), 1442 (m), 1386 (w), 1300 (m), 1244 (s), 1177 (m), 1033 (m), 917 (w), 820 (m), 756 (m), 693 (s), 552 (m), 526 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.41–7.38 (2H, m), 7.32–7.28 (5H, m), 7.23–7.19 (5H, m), 6.88–6.86 (2H, m), 3.82 (3H, s), 3.68–3.60 (1H, m), 2.97–2.95 (2H, m), 2.92–2.81 (2H, m), 2.77–2.69 (1H, m), 2.07–1.93 (2H, m), 1.82–1.80 (1H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.3, 142.0, 131.8, 131.5, 130.4, 128.6, 128.5, 128.4, 128.1, 126.0, 123.3, 113.9, 88.6, 85.5, 71.6, 55.4, 42.3, 38.0, 37.5, 32.3; HRMS (ESI^+) $[M+H]^+$ Calcd for $C_{26}H_{27}O_2$: 371.20110 m/z; Found: 371.20109 m/z; Specific rotation: $[\alpha]_D^{20}$ – 12.1 (*c* 1.25, $CHCl_3$) for an enantiomerically enriched sample of 92.5:7.5 er. The enantiomeric ratio was shown in **3.51j**.

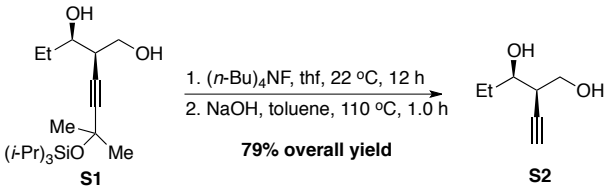
3.8.4 Experimental Procedures and Characterization Data for Synthesis of Fragments of Natural Products

■ **Experimental Procedure for Synthesis of Fragments 3.55–3.56:**



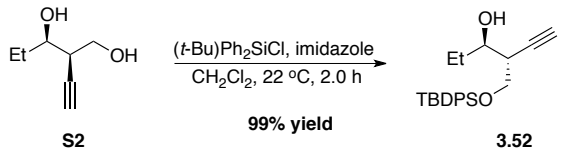
S1 was prepared according to the experimental procedure described above.

(2*R*,3*R*)-2-(3-Methyl-3-((triisopropylsilyl)oxy)but-1-yn-1-yl)pentane-1,3-diol (S1). IR (neat): 3369 (br), 2938 (m), 2867 (m), 1462 (m), 1448 (m), 1374 (m), 1356 (m), 1236 (m), 1160 (s), 1042 (s), 920 (m), 751 (m), 700 (s), 678 (s), 505 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 3.83–3.73 (2H, m), 3.69–3.63 (1H, m), 2.73–2.69 (1H, m), 1.65–1.57 (3H, m), 1.51 (6H, s), 1.16–1.11 (3H, m), 1.11–1.06 (19H, m), 0.97 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 91.3, 78.2, 72.9, 66.4, 63.6, 40.7, 33.7, 28.6, 18.4, 13.1, 10.4; HRMS (ESI^+) $[M+H]^+$ Calcd for $C_{19}H_{39}O_3Si_1$: 343.26685 m/z, Found: 343.26696 m/z; Specific rotation: $[\alpha]_D^{20}$ –7.4 (*c* 1.33, $CHCl_3$).



S2 was prepared according to a previous reported procedure.[19]

(2*R*,3*R*)-2-Ethynylpentane-1,3-diol (S2). The spectral data were identical to those previously reported.[20] ^1H NMR ($CDCl_3$, 400 MHz): δ 3.88–3.80 (2H, m), 3.74–3.66 (1H, m), 2.81 (1H, br s), 2.71–2.66 (1H, m), 2.43 (1H, br s), 2.19–2.16 (1H, m), 1.71–1.58 (2H, m), 0.97 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 80.9, 73.2, 73.0, 63.9, 40.2, 28.6, 10.3. Specific rotation: $[\alpha]_D^{20}$ +1.9 (*c* 1.67, $CHCl_3$).

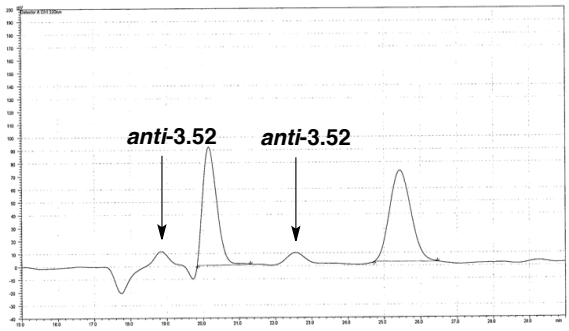


(20) Baker, R.; Head, J. C.; Swain, C. J. *J. Chem. Soc., Perkin Trans. I* **1988**, 85–97.

To a solution of **S2** (180 mg, 1.45 mmol) and imidazole (118.5 mg, 1.74 mmol) in CH_2Cl_2 (3 mL) was added (*t*-Bu)Ph_2SiCl (416 μL, 1.60 mmol) at 22 °C. The resulting mixture was allowed to stir at 22 °C for two hours. The reaction was quenched by addition of water (2 mL) and the aqueous layer was washed with CH_2Cl_2 (3 × 2 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under vacuum. The resulting colorless oil was purified by silica gel chromatography (hexanes:ethyl acetate 20:1) to afford **3.52** as colorless oil (526.4 mg, 1.44 mmol, 99% yield).

(3*R*,4*R*)-4-(((*tert*-Butyldiphenylsilyl)oxy)methyl)hex-5-yn-3-ol (3.52). IR (neat): 3437 (br), 2959 (m), 2931 (m), 2888 (m), 2857 (m), 1472 (m), 1428 (m), 1391 (w), 1112 (s), 998 (w), 822 (m), 740 (m), 701 (s), 608 (m), 505 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.75–7.71 (4H, m), 7.45–7.39 (6H, m), 3.93 (1H, dd, *J* = 10.0, 7.6 Hz), 3.85 (1H, dd, *J* = 10.0, 4.8 Hz), 3.85–3.78 (1H, m), 2.72–2.67 (1H, m), 2.34 (1H, br s), 2.12 (1H, d, *J* = 2.8 Hz), 1.74–1.59 (2H, m), 1.09 (9H, s), 1.00 (3H, t, *J* = 7.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 135.8, 135.7, 133.3, 133.0, 130.0, 129.8, 127.9, 127.8, 81.1, 72.6, 72.2, 64.8, 40.1, 28.5, 26.9, 19.3, 10.5; HRMS (ESI^+) $[M+H]^+$ Calcd for $C_{23}H_{31}O_2Si_1$: 367.20933 m/z, Found: 367.21082 m/z. Specific rotation: $[\alpha]_D^{20}$ +2.3 (*c* 1.56, $CHCl_3$) for an enantiomerically enriched sample of 95:5 er.

Enantiomeric purity of **3.52** was 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 %
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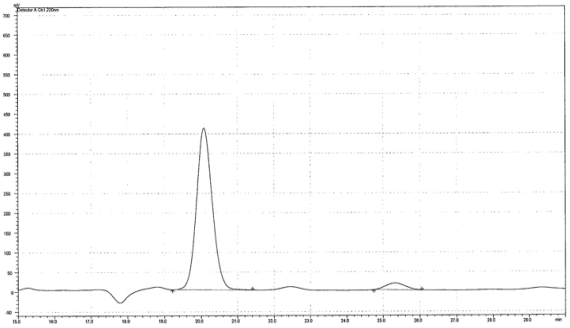
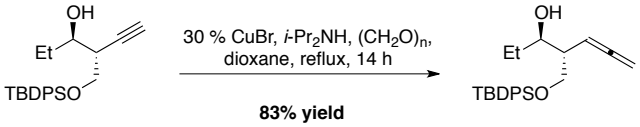
2	25.432	2879385	70693	49.828	41.671



Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.074	12374346	408743	95.180	95.996
2	25.318	626664	17049	4.820	4.004

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	20.153	50.172	1	20.074	95.180
2	25.432	49.828	2	25.318	4.820

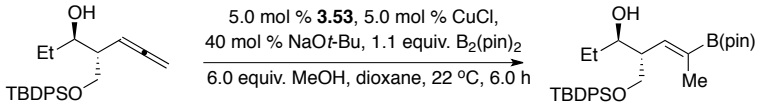


3.52 **S3**

S3 was prepared according to a previous reported procedure.[21]

(3*R*,4*R*)-4-(((*tert*-Butyldiphenylsilyl)oxy)methyl)hepta-5,6-dien-3-ol (S3). IR (neat): 3440 (br), 2959 (m), 2930 (m), 2857 (m), 1471 (m), 1427 (m), 1110 (s), 999 (m), 968 (m), 842 (m), 739 (m), 700 (s), 609 (m), 504 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.73–7.66 (4H, m), 7.46–7.36 (6H, m), 5.27–5.21 (1H, m), 4.68–4.64 (2H, m), 3.87–3.84 (3H, m), 2.67–2.66 (1H, m), 2.39–2.35 (1H, m), 1.63–1.49 (3H, m), 1.08 (9H, s), 0.96 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 209.3, 135.8, 135.7, 133.2, 133.0, 130.0, 129.8, 127.9, 127.8, 86.4, 75.0, 74.7, 66.9, 45.5, 27.7, 27.0, 19.3, 10.5; HRMS (ESI^+) $[M+H]^+$ Calcd for $C_{24}H_{33}O_2Si_1$: 381.22498 m/z, Found: 381.22369 m/z. Specific rotation: $[\alpha]_D^{20}$ +1.6 (*c* 0.97, $CHCl_3$).

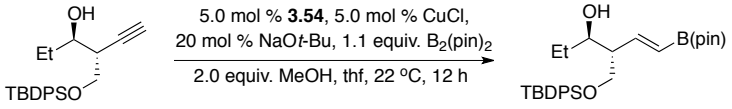
(21) (a) Crabbé, P.; Fillion, H.; André, D.; Luche, J.-L. *J. Chem. Soc., Chem. Commun.* **1979**, 859–860. (b) Searles, S.; Li, Y.; Nassim, B.; Lopes, M.-T. R.; Tran, P. T.; Crabbé, P. *J. Chem. Soc., Perkin Trans. 1*, **1984**, 747–751. (c) Yoshida, M.; Matsuda, K.; Shoji, Y.; Gotou, T.; Ihara, M.; Shishido, K. *Org. Lett.* **2008**, *10*, 5183–5186.



S3 **82% yield** **3.55**

5.55 was prepared according to a previous procedure.[22]

(3*R*,4*R*,*Z*)-4-(((*tert*-Butyldiphenylsilyl)oxy)methyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-5-en-3-ol (3.55). IR (neat): 3505 (br), 2960 (m), 2930 (m), 2856 (m), 1631 (w), 1462 (m), 1368 (s), 1302 (m), 1143 (m), 1109 (s), 1007 (m), 961 (m), 861 (m), 823 (m), 737 (m), 701 (s), 671 (m), 612 (m), 503 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.69–7.64 (4H, m), 7.46–7.36 (6H, m), 6.37 (1H, dd, *J* = 10.0, 2.0 Hz), 3.88–3.83 (1H, m), 3.82 (1H, dd, *J* = 10.0, 7.2 Hz), 3.71 (1H, dd, *J* = 10.0, 4.8 Hz), 2.83–2.77 (1H, m), 2.59–2.58 (1H, m), 1.62 (3H, d, *J* = 2.0 Hz), 1.51–1.42 (2H, m), 1.25 (6H, s), 1.24 (6H, s), 1.06 (9H, s), 0.96 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 141.6, 135.8, 135.7, 133.4, 133.1, 129.9, 127.9, 127.8, 83.3, 74.6, 65.7, 45.1, 27.8, 26.9, 25.2, 25.0, 24.9, 19.3, 14.5, 10.7; HRMS (ESI^+) $[M+H–H_2O]^+$ Calcd for $C_{30}H_{44}B_1O_3Si_1$: 491.31528 m/z, Found: 491.31502 m/z; Specific rotation: $[\alpha]_D^{20}$ +3.0 (*c* 2.09, $CHCl_3$).



3.52 **85% yield** **3.56**

3.56 was prepared according to a previous reported procedure.[23]

(3*R*,4*R*,*E*)-4-(((*tert*-Butyldiphenylsilyl)oxy)methyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hex-5-en-3-ol (3.56). IR (neat): 3520 (br), 2951 (m), 2930 (m), 2857

(22) Meng, F; Jung, B.; Haeffner, F.; Hoveyda, A. H. *Org. Lett.* **2013**, *15*, 1414–1417.
(23) Jang, H.; Zhugralin, A. R.; Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 7859–7871.

(m), 1637 (m), 1471 (m), 1428 (m), 1389 (s), 1214 (m), 1143 (s), 1109 (s), 1003 (m), 969 (m), 849 (m), 823 (m), 740 (m), 701 (s), 613 (m), 504 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.68–7.65 (4H, m), 7.46–7.36 (6H, m), 6.66 (1H, dd, *J* = 18.0, 8.0 Hz), 5.49 (1H, d, *J* = 18.0 Hz), 3.88–3.78 (1H, m), 3.86 (1H, dd, *J* = 10.0, 7.2 Hz), 3.80 (1H, dd, *J* = 10.0, 5.2 Hz), 2.52–2.43 (2H, m), 1.55–1.42 (2H, m), 1.26 (12H, s), 1.06 (9H, s), 0.95 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.4, 135.8, 135.7, 133.3, 133.1, 129.92, 129.90, 127.9, 127.8, 83.2, 74.1, 66.0, 52.0, 27.6, 27.0, 24.9, 19.3, 10.6; HRMS (ESI^+) $[M+H]^+$ Calcd for $C_{29}H_{44}B_1O_4Si_1$: 495.31019 m/z, Found: 495.31020 m/z; Specific rotation: $[\alpha]_D^{20}$ +3.4 (*c* 1.98, $CHCl_3$).

3.8.5 DFT Calculations

All geometries were optimized using the BP86 density functional[24] and the 6-31G* split-valence basis set. Frequency calculations were carried out for all optimized geometries to verify that the structures are minima or 1st order saddle points on the potential energy surface. The normal mode frequencies were used to calculate Gibbs free energy corrections at 298 K and 1 atm. THF solvation was simulated by the Polarizing Continuum Model PCM.[25] All calculations were carried out using the Gaussian 09 program.[26]

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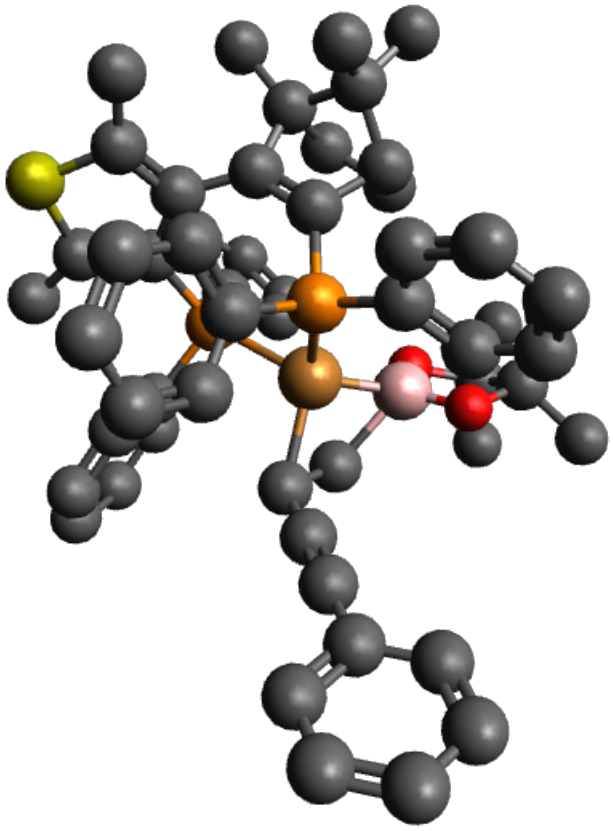
(24) Grimme, S. *J. Comp. Chem.*, **2006,** *27,* 1787–1799.

(25) Tomasi, J.; Mennucci, B.; Cammi, R. *Chem. Rev.* **2005**, *105*, 2999–3094.

(26) Gaussian 09, Revision A.02, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.;

Major Transition State of Cu–B Addition to Enyne (I, Scheme 3.11a)



Cartesian coordinates (Angstroms):

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Iyengar, S.S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford CT, 2009.

C	11.171	1.997	-10.405
C	11.874	0.604	-10.150
C	11.409	2.600	-11.792
C	9.667	1.998	-10.078
C	13.153	0.395	-10.979
C	10.955	-0.614	-10.296
H	13.843	1.249	-10.881
H	12.920	0.250	-12.049
H	13.674	-0.507	-10.614
H	10.097	-0.566	-9.608
H	11.521	-1.535	-10.074
H	10.573	-0.694	-11.330
H	9.468	1.596	-9.070
H	9.093	1.401	-10.808
H	9.292	3.035	-10.111
H	12.481	2.750	-11.994
H	10.907	3.580	-11.863
H	10.990	1.948	-12.578
C	12.146	0.986	-4.674
C	12.375	-1.438	-2.002

C	12.168	-0.103	-4.079
C	12.356	-2.675	-1.346
C	12.159	-1.352	-3.409
C	12.124	-3.864	-2.061
C	11.924	-2.568	-4.119
C	11.908	-3.797	-3.451
C	12.131	2.243	-5.310
C	11.512	2.404	-6.660
H	11.726	-4.716	-4.022
H	11.758	-2.524	-5.200
H	12.110	-4.829	-1.544
H	12.526	-2.711	-0.263
H	12.555	-0.517	-1.437
H	10.957	3.344	-6.786
H	10.894	1.543	-6.957
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C	15.327	-1.976	-8.020
C	15.990	0.227	-7.206

C	16.640	-2.444	-7.857
C	17.309	-0.252	-7.039
C	17.632	-1.577	-7.367
C	18.325	2.535	-3.692
C	17.735	2.500	-4.966
C	16.375	2.157	-5.116
C	17.564	2.223	-2.553
C	16.211	1.875	-2.694
C	15.617	1.844	-3.967
C	16.655	2.558	-9.422
C	16.516	2.965	-7.952
C	16.953	4.258	-7.840
C	15.554	3.376	-10.183
C	16.068	4.837	-10.052
C	17.427	4.691	-9.261
C	18.325	5.916	-9.403
C	17.963	3.315	-9.833
C	18.244	3.324	-11.352
C	19.234	2.768	-9.153
C	16.851	5.198	-6.694

C	17.986	5.769	-6.126
C	15.608	5.729	-6.118
S	17.558	6.983	-4.951
C	15.840	6.754	-5.198
C	19.439	5.432	-6.316
C	14.933	7.692	-4.442
P	13.924	5.100	-6.585
C	12.435	5.301	-2.727
C	13.250	5.069	-3.844
C	11.217	5.992	-2.867
C	12.873	5.549	-5.120
C	10.823	6.446	-4.135
C	11.645	6.228	-5.256
C	11.825	6.858	-9.698
C	12.311	5.947	-8.744
C	12.388	8.139	-9.808
C	13.361	6.318	-7.876
C	13.447	8.508	-8.962
C	13.929	7.605	-8.000
H	13.978	-0.282	-7.852

H	14.548	-2.647	-8.398
H	16.891	-3.481	-8.105
H	18.087	0.407	-6.640
H	18.659	-1.934	-7.233
H	19.382	2.806	-3.590
H	18.334	2.749	-5.847
H	18.026	2.251	-1.559
H	15.612	1.623	-1.812
H	14.561	1.570	-4.072
H	16.637	1.473	-9.615
H	14.557	3.231	-9.734
H	15.496	3.056	-11.239
H	15.368	5.496	-9.513
H	16.252	5.302	-11.038
H	18.431	6.183	-10.470
H	19.339	5.749	-9.002
H	17.898	6.792	-8.882
H	18.426	2.292	-11.707
H	19.157	3.909	-11.568
H	17.429	3.746	-11.959

H	19.492	1.779	-9.575
H	19.117	2.643	-8.064
H	20.098	3.434	-9.335
H	19.556	4.620	-7.050
H	19.892	5.091	-5.366
H	20.028	6.299	-6.667
H	14.651	7.292	-3.452
H	13.999	7.882	-4.993
H	15.436	8.662	-4.282
H	12.748	4.933	-1.743
H	14.187	4.513	-3.727
H	10.579	6.167	-1.994
H	9.874	6.980	-4.258
H	11.330	6.601	-6.236
H	11.010	6.556	-10.365
H	11.896	4.935	-8.707
H	12.012	8.844	-10.558
H	13.903	9.501	-9.049
H	14.763	7.898	-7.354
Cu	13.475	2.732	-6.809

	1	2	3
	A	A	A
Frequencies --	-107.5572	12.2153	14.9263
Red. masses --	7.7896	5.8955	5.7985

Zero-point correction= 0.986546 (Hartree/Particle)

Thermal correction to Energy= 1.050138

Thermal correction to Enthalpy= 1.051082

Thermal correction to Gibbs Free Energy= 0.886715

Sum of electronic and zero-point Energies= -5065.867423

Sum of electronic and thermal Energies= -5065.803831

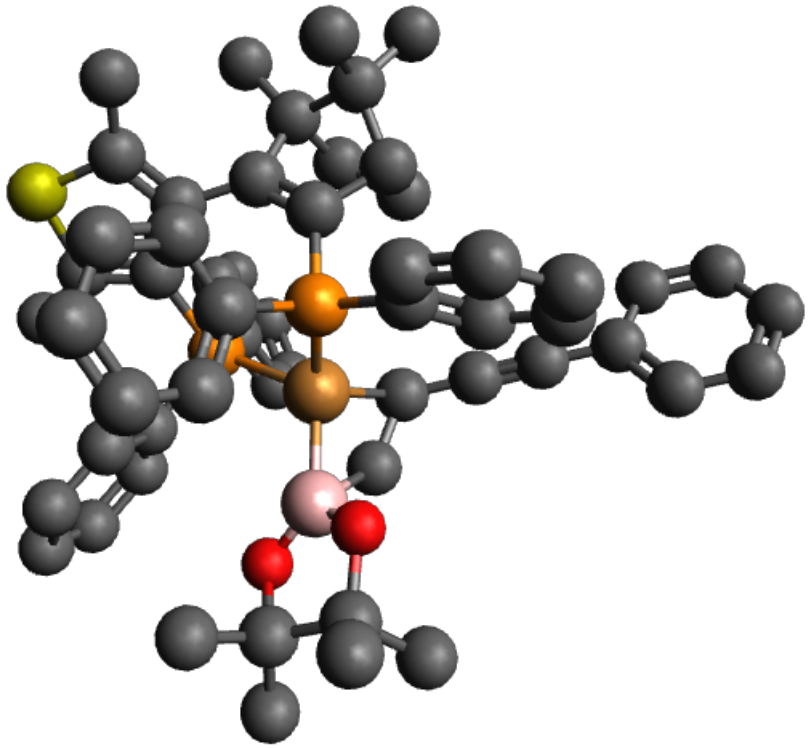
Sum of electronic and thermal Enthalpies= -5065.802887

Sum of electronic and thermal Free Energies= -5065.967254

Item	Value	Threshold	Converged?
Maximum Force	0.000003	0.000450	YES
RMS Force	0.000000	0.000300	YES

SCF = -5066.85396897

Minor Transition State of Cu–B Addition to Enyne (II, Scheme 3.11a)



Cartesian coordinates (Angstroms):

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C	11.847	0.544	-10.148
C	10.252	2.384	-11.143
C	9.476	1.030	-9.173

C	12.761	0.884	-11.337
C	11.366	-0.907	-10.269
H	13.153	1.912	-11.270
H	12.226	0.774	-12.297
H	13.623	0.196	-11.337
H	10.815	-1.233	-9.373
H	12.236	-1.574	-10.396
H	10.711	-1.032	-11.150
H	9.768	0.471	-8.267
H	8.899	0.351	-9.824
H	8.815	1.859	-8.867
H	11.092	2.914	-11.620
H	9.493	3.133	-10.857
H	9.797	1.706	-11.887
C	11.340	3.017	-4.524
C	9.527	4.837	-1.980
C	10.426	3.621	-3.941
C	8.471	5.494	-1.337
C	9.362	4.292	-3.287
C	7.221	5.635	-1.969

C	8.088	4.440	-3.912
C	7.041	5.103	-3.259
C	12.390	2.312	-5.144
C	12.112	1.469	-6.336
H	6.072	5.202	-3.762
H	7.938	4.022	-4.913
H	6.399	6.151	-1.462
H	8.626	5.902	-0.332
H	10.497	4.733	-1.481
H	11.049	1.462	-6.616
H	12.527	0.451	-6.315
H	13.167	1.942	-4.461
P	13.686	4.974	-7.462
C	11.102	5.822	-6.755
C	9.961	6.639	-6.811
C	12.196	6.067	-7.612
C	9.894	7.697	-7.731
C	12.124	7.134	-8.533
C	10.977	7.941	-8.592
C	16.150	6.444	-10.500

C	15.579	6.228	-9.235
C	14.553	5.276	-9.069
C	15.695	5.722	-11.615
C	14.658	4.786	-11.461
C	14.092	4.562	-10.196
C	14.050	6.484	-4.959
C	14.686	5.768	-6.156
C	16.012	5.578	-5.869
C	13.997	5.415	-3.816
C	15.501	5.188	-3.503
C	16.249	6.203	-4.459
C	17.674	6.498	-3.996
C	15.223	7.407	-4.487
C	14.997	8.075	-3.113
C	15.551	8.540	-5.481
C	17.056	4.793	-6.579
C	18.231	5.407	-7.010
C	17.097	3.333	-6.757
S	19.405	4.230	-7.536
C	18.342	2.884	-7.203

C	18.568	6.866	-7.149
C	18.918	1.505	-7.396
P	15.661	2.178	-6.518
C	16.329	0.339	-10.152
C	16.076	1.273	-9.137
C	16.469	-1.026	-9.841
C	15.999	0.862	-7.788
C	16.358	-1.444	-8.507
C	16.133	-0.507	-7.485
C	15.368	-0.282	-3.189
C	15.142	0.344	-4.424
C	16.469	0.088	-2.400
C	16.023	1.345	-4.901
C	17.346	1.085	-2.858
C	17.127	1.706	-4.099
H	11.142	4.993	-6.038
H	9.123	6.439	-6.133
H	9.000	8.329	-7.780
H	12.963	7.334	-9.208
H	10.931	8.765	-9.315

H	16.951	7.184	-10.614
H	15.928	6.802	-8.373
H	16.141	5.892	-12.601
H	14.287	4.228	-12.329
H	13.274	3.842	-10.074
H	13.090	6.983	-5.163
H	13.481	4.502	-4.147
H	13.448	5.811	-2.943
H	15.831	4.153	-3.697
H	15.746	5.410	-2.447
H	17.669	6.778	-2.927
H	18.140	7.328	-4.553
H	18.326	5.613	-4.104
H	14.122	8.750	-3.161
H	15.872	8.693	-2.844
H	14.826	7.366	-2.288
H	14.760	9.311	-5.445
H	15.622	8.188	-6.522
H	16.502	9.038	-5.214
H	17.743	7.493	-6.780

H	18.739	7.130	-8.210
H	19.483	7.141	-6.594
H	18.673	1.086	-8.388
H	18.533	0.806	-6.637
H	20.017	1.533	-7.302
H	16.412	0.679	-11.190
H	15.953	2.332	-9.393
H	16.661	-1.755	-10.636
H	16.463	-2.505	-8.252
H	16.085	-0.850	-6.446
H	14.677	-1.059	-2.842
H	14.277	0.042	-5.026
H	16.642	-0.396	-1.432
H	18.209	1.380	-2.251
H	17.822	2.475	-4.451
Cu	13.433	2.849	-6.872

	1	2	3
	A	A	A
Frequencies --	-86.2770	17.5370	18.8459

Red. masses -- 8.3416 5.8922 5.6257

Zero-point correction= 0.987475 (Hartree/Particle)

Thermal correction to Energy= 1.050576

Thermal correction to Enthalpy= 1.051521

Thermal correction to Gibbs Free Energy= 0.889791

Sum of electronic and zero-point Energies= -5065.866121

Sum of electronic and thermal Energies= -5065.803020

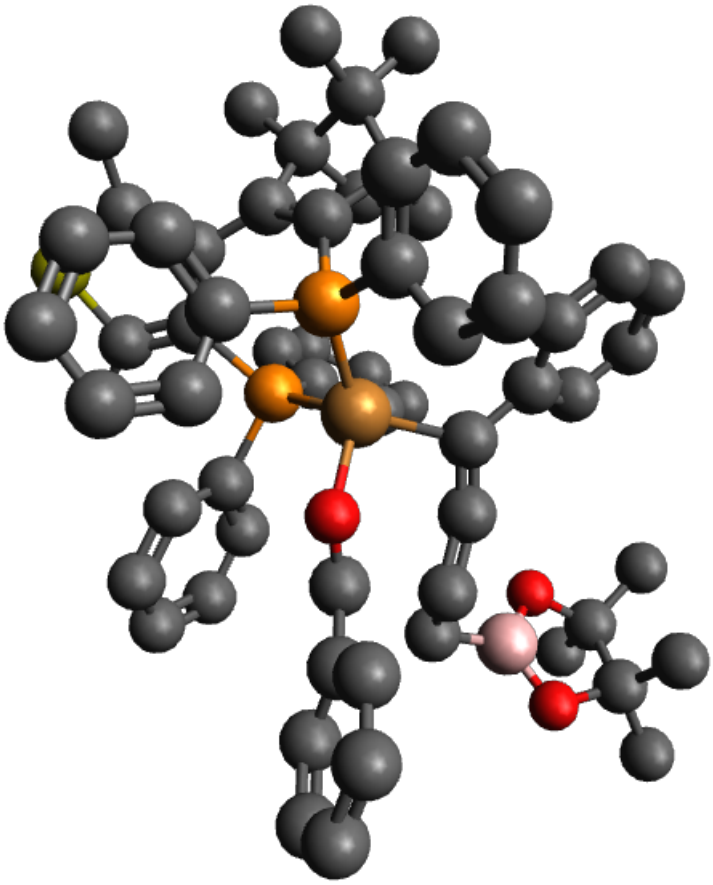
Sum of electronic and thermal Enthalpies= -5065.802076

Sum of electronic and thermal Free Energies= -5065.963805

Item	Value	Threshold	Converged?
Maximum Force	0.000007	0.000450	YES
RMS Force	0.000001	0.000300	YES

SCF = -5066.85359627

Transition State of Allenylcopper Addition to Aldehyde Leading to Major Diastereomer (III, Scheme 3.11b)



Cartesian coordinates (Angstroms):

H	1.228	-6.219	1.501
H	0.565	-5.303	-0.740
C	1.248	-5.139	1.316
C	0.874	-4.624	0.064
C	1.651	-4.252	2.330
H	1.950	-4.640	3.312

C	0.887	-3.240	-0.167
H	0.583	-2.844	-1.141
C	1.685	-2.871	2.093
C	1.299	-2.336	0.838
H	2.025	-2.184	2.876
C	1.385	-0.888	0.581
C	2.331	-0.069	0.877
C	3.170	1.031	0.867
H	4.046	0.920	0.207
C	3.474	1.783	2.175
H	2.524	2.031	2.682
H	3.980	2.734	1.923
B	4.397	0.901	3.108
O	3.904	-0.003	4.036
O	5.780	0.922	3.041
C	5.055	-0.513	4.801
C	6.270	-0.222	3.827
C	4.816	-1.994	5.111
C	5.106	0.302	6.104
C	6.536	-1.359	2.826

C	7.571	0.191	4.522
H	5.611	-1.655	2.300
H	6.956	-2.248	3.325
H	7.262	-1.011	2.071
H	7.435	1.087	5.147
H	8.341	0.415	3.763
H	7.950	-0.628	5.158
H	5.271	1.374	5.902
H	5.909	-0.055	6.773
H	4.144	0.197	6.633
H	4.639	-2.580	4.195
H	3.933	-2.100	5.764
H	5.683	-2.425	5.642
C	3.181	3.002	-1.081
H	3.396	4.550	0.425
C	3.768	4.163	-0.532
H	5.237	5.740	-0.772
C	5.251	4.362	-2.452
H	6.052	4.888	-2.983
H	5.009	2.841	-3.986

C	4.664	3.212	-3.013
H	3.168	1.651	-2.771
C	2.084	2.288	-0.349
C	3.637	2.540	-2.336
C	4.796	4.837	-1.210
O	1.222	1.609	-1.053
H	1.711	2.841	0.537
P	-1.377	-0.469	-1.858
C	0.593	-1.598	-3.503
C	1.099	-2.388	-4.549
C	-0.780	-1.628	-3.180
C	0.239	-3.224	-5.280
C	-1.639	-2.462	-3.929
C	-1.131	-3.260	-4.966
C	-3.768	1.800	-4.427
C	-3.337	0.795	-3.548
C	-2.074	0.879	-2.928
C	-2.938	2.900	-4.703
C	-1.675	2.988	-4.096
C	-1.243	1.986	-3.211

C	-2.783	-2.798	-0.712
C	-2.792	-1.313	-1.088
C	-3.836	-0.736	-0.413
C	-2.346	-2.831	0.798
C	-3.570	-2.208	1.522
C	-4.571	-1.880	0.351
C	-5.998	-1.646	0.836
C	-4.315	-3.107	-0.616
C	-4.642	-4.486	-0.005
C	-5.060	-3.030	-1.962
C	-4.143	0.699	-0.182
C	-5.352	1.250	-0.592
C	-3.344	1.633	0.628
S	-5.560	2.860	0.048
C	-4.022	2.826	0.886
C	-6.395	0.693	-1.520
C	-3.706	4.028	1.739
P	-1.592	1.296	1.162
C	-0.273	5.110	0.268
C	-0.867	3.841	0.205

C	0.326	5.556	1.460
C	-0.882	3.000	1.341
C	0.330	4.719	2.588
C	-0.267	3.447	2.529
C	-0.659	-0.376	4.821
C	-0.618	0.059	3.486
C	-1.816	-0.181	5.593
C	-1.733	0.713	2.915
C	-2.933	0.456	5.028
C	-2.891	0.905	3.698
Cu	-0.036	0.302	-0.258
H	1.269	-0.955	-2.927
H	2.168	-2.354	-4.788
H	0.633	-3.845	-6.091
H	-2.711	-2.486	-3.705
H	-1.808	-3.908	-5.535
H	-4.753	1.723	-4.901
H	-3.990	-0.060	-3.342
H	-3.275	3.684	-5.391
H	-1.020	3.841	-4.308

H	-0.257	2.059	-2.732
H	-2.192	-3.455	-1.369
H	-1.420	-2.258	0.957
H	-2.146	-3.866	1.125
H	-3.317	-1.299	2.090
H	-4.035	-2.914	2.235
H	-6.324	-2.492	1.468
H	-6.719	-1.554	0.006
H	-6.070	-0.728	1.446
H	-4.288	-5.288	-0.681
H	-5.735	-4.610	0.102
H	-4.188	-4.663	0.983
H	-4.771	-3.879	-2.610
H	-4.850	-2.100	-2.513
H	-6.154	-3.098	-1.811
H	-6.119	-0.324	-1.837
H	-6.486	1.314	-2.430
H	-7.395	0.648	-1.050
H	-3.148	4.800	1.179
H	-3.096	3.754	2.612

H	-4.640	4.488	2.109
H	-0.277	5.754	-0.619
H	-1.329	3.502	-0.729
H	0.787	6.549	1.508
H	0.794	5.055	3.522
H	-0.268	2.810	3.420
H	0.214	-0.877	5.253
H	0.280	-0.108	2.881
H	-1.849	-0.530	6.632
H	-3.841	0.606	5.622
H	-3.769	1.392	3.259

	1	2	3
	A	A	A
Frequencies --	-194.5615	11.8185	15.5558
Red. masses --	10.4772	5.1598	5.0928

Zero-point correction= 1.097073 (Hartree/Particle)

Thermal correction to Energy= 1.167748

Thermal correction to Enthalpy= 1.168692

Thermal correction to Gibbs Free Energy= 0.988973

Sum of electronic and zero-point Energies= -5411.375403

Sum of electronic and thermal Energies= -5411.304729

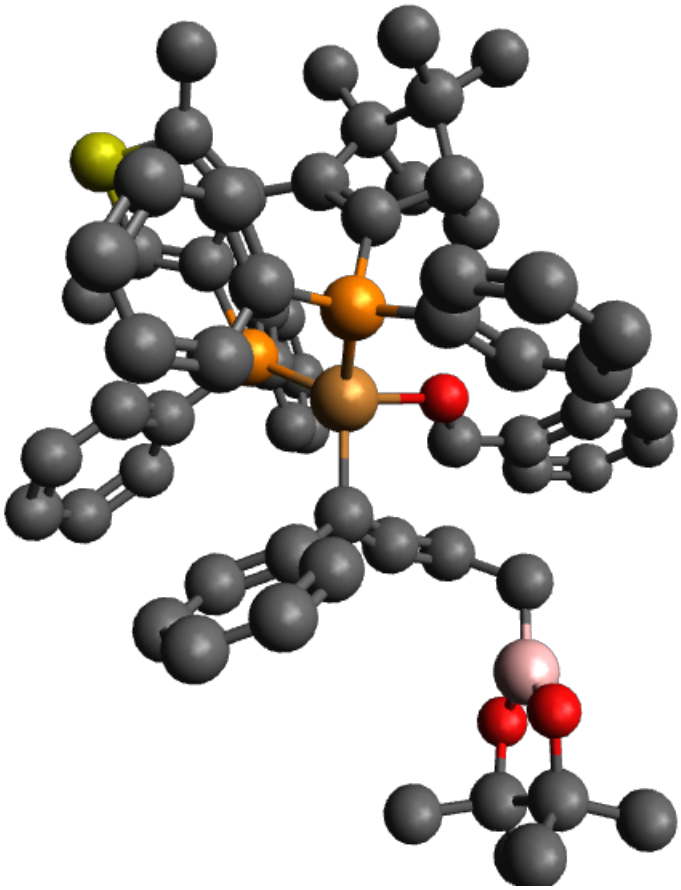
Sum of electronic and thermal Enthalpies= -5411.303785

Sum of electronic and thermal Free Energies= -5411.483504

Item	Value	Threshold	Converged?
Maximum Force	0.000003	0.000450	YES
RMS Force	0.000000	0.000300	YES

SCF= -5412.47247667

Transition State of Allenylcopper Addition to Aldehyde Leading to Minor Diastereomer (IV, Scheme 3.11b)



Cartesian coordinates (Angstroms):

H	3.672	3.273	-5.712
H	8.993	-0.175	-1.730
C	3.251	3.389	-4.706
H	8.319	1.647	-0.471
H	3.751	5.500	-4.563
H	9.527	0.774	0.523

H	2.623	1.316	-4.571
C	3.295	4.639	-4.063
C	8.644	-1.141	-1.332
H	8.455	-1.817	-2.185
C	8.488	1.145	0.498
H	9.453	-1.582	-0.723
C	2.663	2.289	-4.065
H	8.370	1.897	1.298
H	4.472	1.908	-1.778
O	6.345	-0.338	-1.343
C	7.366	-0.987	-0.504
C	2.744	4.778	-2.776
C	7.478	0.007	0.724
C	2.108	2.418	-2.772
H	1.226	0.423	-2.828
B	5.599	0.486	-0.513
H	2.770	5.751	-2.272
H	0.852	-1.601	-5.545
H	8.696	-1.187	2.085
C	4.254	1.186	-0.967

O	6.144	0.630	0.751
C	2.155	3.678	-2.136
H	3.489	-0.301	-2.435
C	1.471	1.240	-2.120
C	7.725	-0.662	2.080
H	7.749	0.105	2.873
H	6.575	-2.929	-1.042
C	6.804	-2.366	-0.121
H	3.827	1.764	-0.127
H	-1.118	-0.949	-6.951
H	7.532	-2.951	0.469
C	3.219	0.173	-1.478
C	-0.119	-1.405	-5.076
H	1.709	3.781	-1.141
C	-1.224	-1.040	-5.864
H	6.933	-1.386	2.327
H	-1.685	4.366	-1.284
H	5.873	-2.272	0.463
H	0.624	-1.776	-3.077
O	0.689	1.420	-1.098

H	-3.689	5.173	-1.353
C	-0.250	-1.511	-3.683
C	2.557	-0.609	-0.554
H	-3.422	3.413	-2.609
H	-0.940	2.755	-1.125
C	-1.880	3.314	-1.010
H	-3.698	5.815	0.310
C	-2.460	-0.788	-5.250
C	-4.134	5.045	-0.354
C	-3.056	2.715	-1.833
H	2.289	4.189	2.286
H	-2.784	1.776	-2.346
H	-3.327	-0.499	-5.855
H	-5.214	5.265	-0.442
H	-1.856	3.820	1.189
C	-1.499	-1.282	-3.055
H	1.001	2.466	0.999
C	1.693	-1.026	0.299
Cu	-0.090	-0.122	-0.097
C	-2.429	3.233	0.454

H	-0.401	-3.791	-2.665
C	1.449	3.669	2.760
C	-2.600	-0.915	-3.857
C	0.729	2.705	2.036
C	-3.927	3.642	0.257
H	-5.752	3.212	-2.046
H	1.673	4.701	4.659
C	-4.188	2.453	-0.755
C	1.104	3.956	4.092
H	0.025	-6.113	-1.919
C	-0.676	-4.082	-1.647
P	-1.606	-1.371	-1.209
H	2.418	-0.273	2.780
C	1.875	-1.912	1.465
C	-2.554	1.737	0.770
C	-5.574	2.345	-1.383
C	-0.357	2.029	2.637
H	-3.573	-0.732	-3.389
C	-0.445	-5.405	-1.228
H	-4.475	4.466	2.200

H	-5.669	1.433	-1.999
P	-1.243	0.773	1.604
H	1.381	-3.759	0.439
C	2.282	-1.357	2.705
C	-4.748	3.606	1.561
C	-3.612	1.247	0.049
C	-1.290	-3.155	-0.781
C	0.032	3.279	4.697
C	1.700	-3.313	1.386
C	-0.698	2.321	3.974
H	-5.831	3.690	1.353
H	-6.385	2.330	-0.636
H	-0.239	3.497	5.736
C	-3.427	-1.248	-0.845
H	-4.576	2.691	2.149
C	-0.832	-5.821	0.056
C	-4.104	-0.145	-0.144
H	-1.532	1.797	4.453
H	-3.355	-3.470	-2.685
C	2.516	-2.176	3.820

C	-1.653	-3.575	0.518
H	-0.662	-6.855	0.376
C	1.937	-4.128	2.504
H	2.837	-1.722	4.765
H	-0.262	-1.457	3.156
C	-1.438	-4.899	0.927
C	-2.078	-0.296	2.857
H	-2.122	-2.866	1.210
C	-4.280	-2.322	-1.103
C	2.345	-3.569	3.727
H	1.799	-5.212	2.415
C	-4.082	-3.604	-1.868
H	-6.022	1.255	1.334
C	-5.412	-0.477	0.207
C	-1.305	-1.312	3.462
H	-4.028	0.655	2.800
H	-5.035	-3.934	-2.316
H	-1.738	-5.207	1.934
C	-3.418	-0.127	3.262
C	-6.414	0.269	1.045

H	-3.712	-4.418	-1.220
H	2.528	-4.210	4.597
H	-7.373	0.421	0.517
S	-5.852	-2.058	-0.388
C	-1.861	-2.135	4.453
H	-6.638	-0.287	1.975
C	-3.975	-0.958	4.248
H	-1.245	-2.916	4.913
C	-3.199	-1.964	4.847
H	-5.019	-0.815	4.551
H	-3.635	-2.611	5.616

	1	2	3
	A	A	A
Frequencies --	-171.3761	9.2816	13.4432
Red. masses --	9.2717	5.4448	4.8186

Zero-point correction= 1.097032 (Hartree/Particle)

Thermal correction to Energy= 1.167751

Thermal correction to Enthalpy= 1.168695

Thermal correction to Gibbs Free Energy= 0.987851

Sum of electronic and zero-point Energies= -5411.371220

Sum of electronic and thermal Energies= -5411.300501

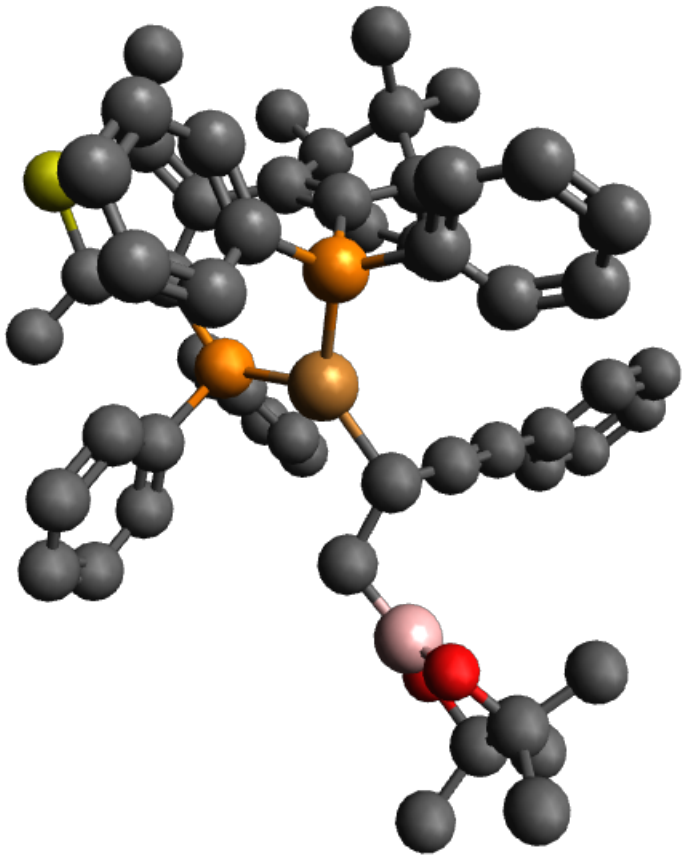
Sum of electronic and thermal Enthalpies= -5411.299557

Sum of electronic and thermal Free Energies= -5411.480401

Item	Value	Threshold	Converged?
Maximum Force	0.000007	0.000450	YES
RMS Force	0.000001	0.000300	YES

SCF= -5412.46825222

Propargylcopper Complex Generated from Cu–B Addition to Enyne (i, Scheme 3.1)



Cartesian coordinates (Angstroms):

H	5.882	2.039	-6.588
H	6.308	0.535	-8.500
H	5.419	0.612	-5.613
C	6.264	1.262	-5.902
C	6.823	-0.211	-7.870
H	6.090	-0.993	-7.603

H	6.647	1.763	-4.996
H	7.624	-0.670	-8.469
C	7.373	0.467	-6.611
O	8.395	1.444	-7.019
H	10.457	3.250	-6.746
H	10.565	1.175	-10.934
H	10.624	0.065	-13.162
B	9.389	1.431	-6.050
H	6.551	-1.673	-4.809
H	6.959	-0.225	-3.836
C	10.620	2.421	-6.034
C	8.181	-0.483	-5.638
C	7.380	-1.034	-4.455
C	11.235	0.325	-11.106
C	11.271	-0.303	-12.357
H	8.208	-2.384	-6.747
O	9.224	0.414	-5.118
H	9.507	-1.238	-7.215
C	8.913	-1.623	-6.368
C	11.981	1.031	-7.641

H	8.035	-1.651	-3.816
C	11.959	1.676	-6.360
C	12.027	0.504	-8.764
C	12.061	-0.127	-10.036
C	12.124	-1.398	-12.587
H	12.149	-1.886	-13.568
H	9.604	-2.115	-5.662
C	12.920	-1.237	-10.287
C	12.946	-1.857	-11.542
H	13.563	-1.602	-9.478
H	13.617	-2.710	-11.706
H	10.719	2.892	-5.037
H	12.134	0.914	-5.572
P	15.572	2.152	-5.671
C	15.016	-0.572	-6.023
C	15.189	-1.953	-5.834
C	15.867	0.350	-5.373
C	16.202	-2.428	-4.984
C	16.880	-0.136	-4.520
C	17.045	-1.516	-4.326

C	18.146	3.995	-2.956
C	17.643	3.424	-4.137
C	16.313	2.958	-4.194
C	17.330	4.099	-1.818
C	16.006	3.629	-1.862
C	15.499	3.065	-3.043
C	16.804	1.525	-8.260
C	16.594	2.537	-7.129
C	16.933	3.773	-7.616
C	15.655	1.824	-9.285
C	16.050	3.227	-9.828
C	17.406	3.557	-9.082
C	18.209	4.663	-9.760
C	18.056	2.119	-8.986
C	18.365	1.465	-10.350
C	19.348	2.035	-8.149
C	16.725	5.119	-7.018
C	17.797	5.945	-6.696
C	15.429	5.779	-6.809
S	17.246	7.523	-6.184

C	15.558	7.103	-6.397
C	19.270	5.649	-6.674
C	14.541	8.181	-6.124
P	13.813	4.898	-6.986
C	12.267	6.208	-3.391
C	13.115	5.703	-4.388
C	11.003	6.722	-3.730
C	12.712	5.715	-5.744
C	10.594	6.727	-5.074
C	11.440	6.224	-6.076
C	11.572	5.005	-10.448
C	12.116	4.650	-9.203
C	12.075	6.114	-11.149
C	13.159	5.416	-8.635
C	13.126	6.868	-10.600
C	13.664	6.524	-9.350
H	14.210	-0.208	-6.673
H	14.523	-2.658	-6.343
H	16.330	-3.505	-4.829
H	17.541	0.567	-4.001

H	17.834	-1.880	-3.658
H	19.180	4.355	-2.925
H	18.283	3.340	-5.020
H	17.724	4.544	-0.898
H	15.365	3.703	-0.977
H	14.464	2.703	-3.074
H	16.876	0.472	-7.946
H	14.662	1.809	-8.803
H	15.634	1.062	-10.083
H	15.292	3.999	-9.617
H	16.208	3.220	-10.922
H	18.376	4.414	-10.823
H	19.197	4.816	-9.293
H	17.670	5.627	-9.725
H	18.623	0.399	-10.206
H	19.241	1.951	-10.818
H	17.535	1.510	-11.073
H	19.699	0.987	-8.098
H	19.209	2.388	-7.115
H	20.159	2.626	-8.614

H	19.458	4.611	-6.990
H	19.685	5.770	-5.656
H	19.842	6.319	-7.342
H	14.212	8.177	-5.068
H	13.643	8.051	-6.746
H	14.965	9.177	-6.340
H	12.596	6.200	-2.346
H	14.102	5.311	-4.116
H	10.341	7.115	-2.951
H	9.611	7.126	-5.348
H	11.110	6.235	-7.121
H	10.762	4.404	-10.876
H	11.745	3.761	-8.678
H	11.657	6.383	-12.125
H	13.530	7.727	-11.147
H	14.493	7.107	-8.934
Cu	13.591	2.792	-6.368

1	2	3
A	A	A

Frequencies -- 9.4944 13.1234 15.7607

Red. masses -- 5.6281 5.1509 5.2287

Zero-point correction= 0.986461 (Hartree/Particle)

Thermal correction to Energy= 1.051366

Thermal correction to Enthalpy= 1.052311

Thermal correction to Gibbs Free Energy= 0.880745

Sum of electronic and zero-point Energies= -5065.900095

Sum of electronic and thermal Energies= -5065.835189

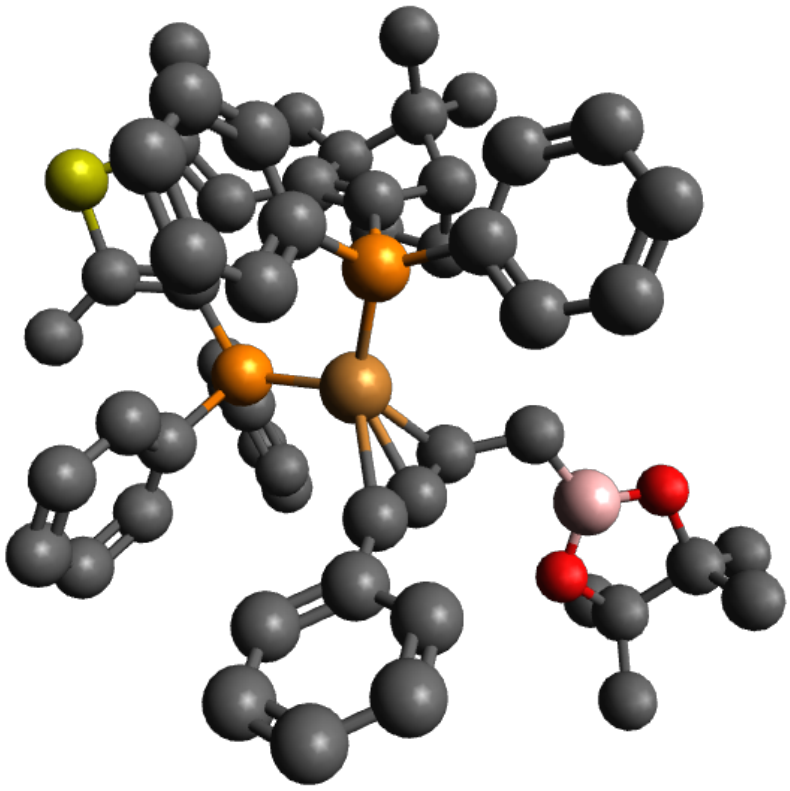
Sum of electronic and thermal Enthalpies= -5065.834245

Sum of electronic and thermal Free Energies= -5066.005811

Item	Value	Threshold	Converged?
Maximum Force	0.000020	0.000450	YES
RMS Force	0.000002	0.000300	YES

SCF = -5066.88655580

Transition State of Isomerization of Propargylcopper Complex to Allenylcopper Complex



Cartesian coordinates (Angstroms):

P	13.836	4.921	-7.470
C	11.111	5.284	-8.013
C	9.933	6.014	-8.246
C	12.311	5.948	-7.685
C	9.943	7.415	-8.149
C	12.316	7.358	-7.606
C	11.137	8.086	-7.829

C	16.264	6.632	-10.414
C	15.673	6.359	-9.169
C	14.736	5.314	-9.040
C	15.917	5.872	-11.544
C	14.978	4.833	-11.424
C	14.395	4.551	-10.178
C	14.034	6.248	-4.859
C	14.747	5.695	-6.098
C	16.061	5.503	-5.759
C	13.977	5.041	-3.856
C	15.472	4.848	-3.477
C	16.217	5.984	-4.286
C	17.614	6.276	-3.746
C	15.148	7.148	-4.230
C	14.828	7.653	-2.807
C	15.492	8.391	-5.076
C	17.143	4.779	-6.478
C	18.307	5.442	-6.857
C	17.226	3.329	-6.716
S	19.516	4.323	-7.432

C	18.483	2.936	-7.177
C	18.611	6.914	-6.888
C	19.076	1.579	-7.453
P	15.817	2.130	-6.560
C	16.447	0.638	-10.356
C	16.233	1.476	-9.252
C	16.552	-0.754	-10.179
C	16.146	0.938	-7.947
C	16.439	-1.297	-8.889
C	16.241	-0.458	-7.778
C	15.505	-0.569	-3.441
C	15.288	0.158	-4.621
C	16.616	-0.281	-2.628
C	16.189	1.173	-5.020
C	17.510	0.733	-3.008
C	17.302	1.452	-4.198
H	11.105	4.190	-8.089
H	9.007	5.487	-8.500
H	9.024	7.985	-8.325
H	13.245	7.889	-7.370

H	11.151	9.179	-7.757
H	16.995	7.444	-10.501
H	15.944	6.956	-8.293
H	16.378	6.088	-12.514
H	14.701	4.237	-12.301
H	13.673	3.730	-10.084
H	13.061	6.730	-5.044
H	13.547	4.149	-4.345
H	13.353	5.287	-2.979
H	15.861	3.853	-3.750
H	15.646	4.976	-2.393
H	17.568	6.464	-2.658
H	18.075	7.160	-4.218
H	18.294	5.419	-3.905
H	13.957	8.334	-2.837
H	15.681	8.232	-2.407
H	14.600	6.854	-2.085
H	14.664	9.123	-5.030
H	15.667	8.150	-6.136
H	16.393	8.898	-4.684

H	17.768	7.491	-6.478
H	18.781	7.263	-7.924
H	19.516	7.167	-6.305
H	18.864	1.235	-8.482
H	18.672	0.823	-6.762
H	20.172	1.604	-7.324
H	16.526	1.074	-11.358
H	16.145	2.558	-9.401
H	16.717	-1.409	-11.041
H	16.516	-2.380	-8.739
H	16.181	-0.898	-6.777
H	14.801	-1.357	-3.152
H	14.411	-0.068	-5.240
H	16.780	-0.842	-1.702
H	18.377	0.966	-2.380
H	18.007	2.237	-4.489
Cu	13.718	2.832	-6.814
H	10.710	-0.794	-12.777
H	12.965	-1.334	-11.812
C	11.028	-0.347	-11.828

C	12.292	-0.646	-11.286
C	10.181	0.539	-11.136
H	9.192	0.782	-11.543
C	12.709	-0.071	-10.079
H	13.698	-0.305	-9.672
C	10.584	1.111	-9.924
C	11.860	0.816	-9.360
H	9.915	1.793	-9.388
C	12.272	1.426	-8.129
C	12.112	1.598	-6.878
C	12.214	2.069	-5.560
H	12.679	1.366	-4.852
C	11.043	2.855	-4.958
H	11.406	3.536	-4.161
H	10.606	3.531	-5.720
B	9.881	1.973	-4.340
O	8.852	2.519	-3.583
O	9.779	0.600	-4.488
C	7.850	1.459	-3.385
C	8.702	0.143	-3.595

C	7.244	1.621	-1.988
C	6.771	1.668	-4.462
C	9.384	-0.356	-2.309
C	7.960	-1.007	-4.282
H	9.930	0.458	-1.802
H	8.651	-0.780	-1.601
H	10.110	-1.145	-2.570
H	7.577	-0.713	-5.272
H	8.643	-1.863	-4.419
H	7.110	-1.346	-3.663
H	7.189	1.559	-5.477
H	5.940	0.950	-4.346
H	6.362	2.688	-4.368
H	8.018	1.621	-1.204
H	6.695	2.577	-1.928
H	6.530	0.806	-1.775

	1	2	3
	A	A	A
Frequencies --	-38.1706	11.3458	14.7750

Red. masses -- 6.9450 4.9845 5.1598

Zero-point correction= 0.986674 (Hartree/Particle)

Thermal correction to Energy= 1.050283

Thermal correction to Enthalpy= 1.051227

Thermal correction to Gibbs Free Energy= 0.885262

Sum of electronic and zero-point Energies= -5065.898844

Sum of electronic and thermal Energies= -5065.835235

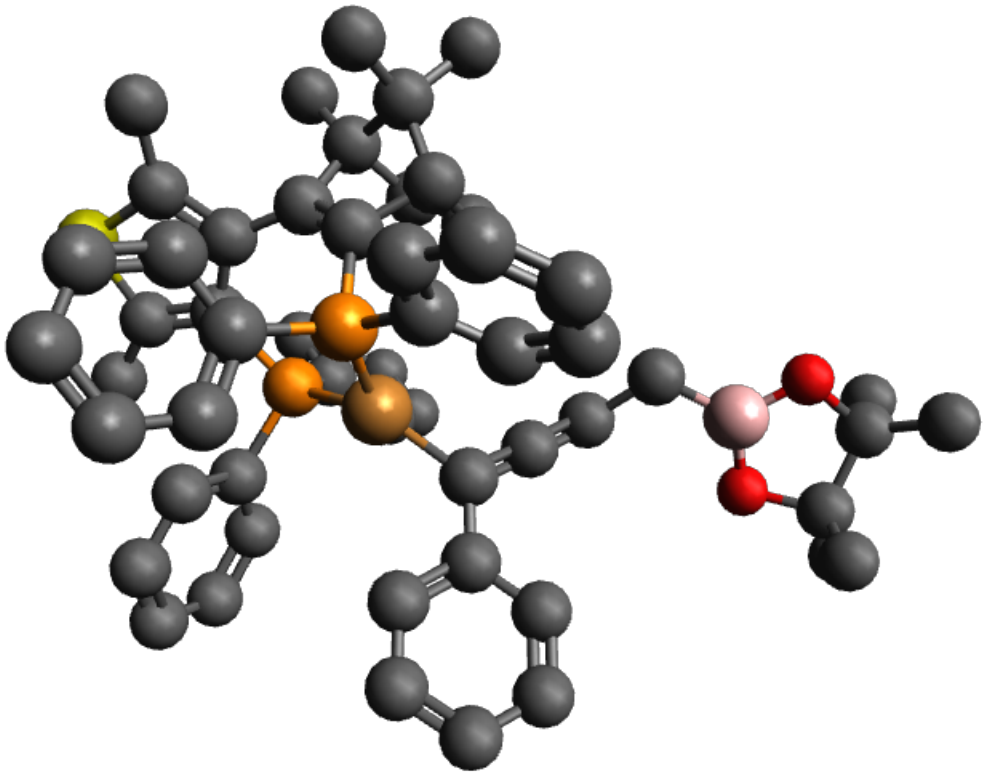
Sum of electronic and thermal Enthalpies= -5065.834291

Sum of electronic and thermal Free Energies= -5066.000256

Item	Value	Threshold	Converged?
Maximum Force	0.000007	0.000450	YES
RMS Force	0.000001	0.000300	YES

SCF = -5066.88551809

Allenylcopper Complex Generated after Isomerization (ii, Scheme 3.1)



Cartesian coordinates (Angstroms):

P	0.012	-5.723	-14.261
C	-2.716	-5.117	-14.505
C	-3.841	-4.447	-15.014
C	-1.426	-4.809	-14.987
C	-3.689	-3.473	-16.014
C	-1.281	-3.831	-15.994
C	-2.407	-3.167	-16.504

C	3.090	-5.046	-16.993
C	2.253	-4.922	-15.872
C	1.192	-5.828	-15.670
C	2.871	-6.071	-17.929
C	1.812	-6.975	-17.739
C	0.979	-6.858	-16.616
C	-0.234	-3.617	-12.241
C	0.684	-4.560	-13.025
C	1.878	-4.627	-12.353
C	-0.617	-4.417	-10.948
C	0.740	-4.495	-10.191
C	1.741	-3.691	-11.117
C	3.006	-3.250	-10.387
C	0.787	-2.568	-11.690
C	0.202	-1.618	-10.622
C	1.406	-1.677	-12.786
C	3.048	-5.524	-12.562
C	4.300	-5.021	-12.900
C	3.076	-6.973	-12.331
S	5.509	-6.285	-12.903

C	4.352	-7.517	-12.443
C	4.712	-3.631	-13.300
C	4.861	-8.919	-12.241
P	1.557	-7.971	-12.027
C	2.376	-10.703	-15.007
C	2.226	-9.520	-14.268
C	2.172	-11.952	-14.395
C	1.882	-9.571	-12.898
C	1.816	-12.007	-13.037
C	1.667	-10.826	-12.292
C	0.379	-9.252	-8.289
C	0.420	-8.938	-9.657
C	1.483	-8.973	-7.466
C	1.581	-8.361	-10.223
C	2.631	-8.379	-8.016
C	2.683	-8.078	-9.387
H	-2.832	-5.891	-13.736
H	-4.839	-4.695	-14.635
H	-4.567	-2.956	-16.417
H	-0.285	-3.592	-16.385

H	-2.284	-2.411	-17.288
H	3.912	-4.336	-17.137
H	2.424	-4.120	-15.148
H	3.525	-6.166	-18.803
H	1.633	-7.775	-18.466
H	0.156	-7.568	-16.470
H	-1.092	-3.216	-12.803
H	-1.036	-5.409	-11.196
H	-1.385	-3.878	-10.366
H	1.091	-5.530	-10.037
H	0.684	-4.022	-9.194
H	2.739	-2.704	-9.464
H	3.636	-2.582	-11.000
H	3.623	-4.118	-10.094
H	-0.607	-1.009	-11.064
H	0.980	-0.918	-10.263
H	-0.211	-2.133	-9.741
H	0.657	-0.951	-13.153
H	1.761	-2.254	-13.655
H	2.256	-1.094	-12.386

H	3.846	-2.953	-13.281
H	5.126	-3.618	-14.326
H	5.487	-3.217	-12.630
H	4.818	-9.508	-13.176
H	4.261	-9.453	-11.488
H	5.910	-8.909	-11.897
H	2.651	-10.647	-16.067
H	2.388	-8.550	-14.754
H	2.287	-12.875	-14.973
H	1.653	-12.976	-12.551
H	1.392	-10.884	-11.234
H	-0.524	-9.704	-7.864
H	-0.457	-9.121	-10.290
H	1.445	-9.209	-6.396
H	3.492	-8.150	-7.378
H	3.579	-7.610	-9.808
H	-4.254	-11.963	-15.782
H	-1.885	-11.191	-16.098
C	-3.822	-11.210	-15.113
C	-2.498	-10.775	-15.289

C	-4.586	-10.665	-14.063
H	-5.622	-10.994	-13.912
C	-1.952	-9.808	-14.430
H	-0.912	-9.483	-14.575
C	-4.035	-9.702	-13.209
C	-2.700	-9.244	-13.368
H	-4.637	-9.283	-12.393
C	-2.087	-8.212	-12.479
C	-2.755	-7.795	-11.412
C	-3.398	-7.352	-10.337
H	-3.254	-7.875	-9.377
C	-4.361	-6.173	-10.306
H	-4.375	-5.676	-11.297
H	-4.000	-5.394	-9.601
Cu	-0.373	-7.428	-12.933
B	-5.857	-6.529	-9.919
O	-6.799	-5.556	-9.620
O	-6.362	-7.816	-9.858
C	-7.997	-6.248	-9.118
C	-7.823	-7.706	-9.708

C	-9.234	-5.490	-9.612
C	-7.919	-6.197	-7.582
C	-8.419	-7.870	-11.117
C	-8.300	-8.839	-8.795
H	-8.074	-7.071	-11.796
H	-9.522	-7.858	-11.094
H	-8.093	-8.838	-11.535
H	-7.787	-8.824	-7.821
H	-8.097	-9.813	-9.274
H	-9.389	-8.767	-8.621
H	-7.029	-6.730	-7.206
H	-8.816	-6.640	-7.116
H	-7.849	-5.143	-7.261
H	-9.240	-5.389	-10.709
H	-9.248	-4.477	-9.174
H	-10.160	-6.007	-9.301

	1	2	3
	A	A	A
Frequencies --	6.9792	9.1920	14.1857

Red. masses -- 5.2501 5.1863 5.3221

Zero-point correction= 0.987212 (Hartree/Particle)

Thermal correction to Energy= 1.051632

Thermal correction to Enthalpy= 1.052576

Thermal correction to Gibbs Free Energy= 0.881621

Sum of electronic and zero-point Energies= -5065.915497

Sum of electronic and thermal Energies= -5065.851078

Sum of electronic and thermal Enthalpies= -5065.850134

Sum of electronic and thermal Free Energies= -5066.021088

Item	Value	Threshold	Converged?
Maximum Force	0.000010	0.000450	YES
RMS Force	0.000002	0.000300	YES

SCF= -5066.90270932

■ **Proof of Stereochemistry: X-ray Characterization Data**

(1*S*,2*R*)-1-Phenyl-2-(phenylethynyl)propane-1,3-diol (3.15a)

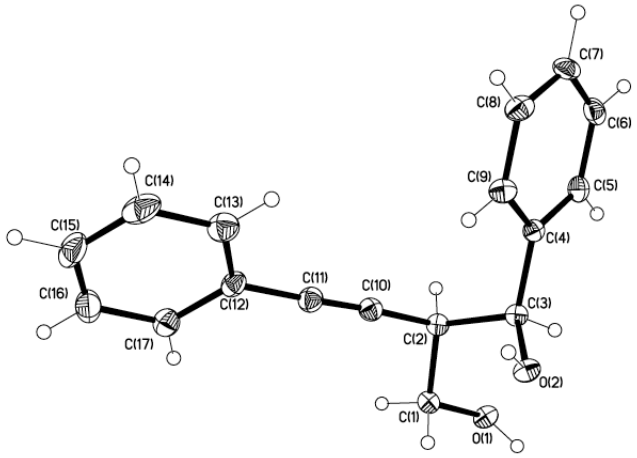


Table 1. Crystal data and structure refinement for $C_{17}H_{16}O_2$.

Identification code	$C_{17}H_{16}O_2$	
Empirical formula	$C_{17}H_{16}O_2$	
Formula weight	252.30	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 21	
Unit cell dimensions	a = 8.3545(6) Å	α= 90°.
	b = 6.0819(4) Å	β= 106.364(3)°.
	c = 13.8786(10) Å	γ = 90°.
Volume	676.62(8) $Å^3$	
Z	2	

Density (calculated)	1.238 Mg/m^3
Absorption coefficient	0.635 mm^{-1}
F(000)	268
Crystal size	0.600 x 0.100 x 0.080 mm^3
Theta range for data collection	3.319 to 66.573°.
Index ranges	-9<=h<=9, -7<=k<=6, -16<=l<=16
Reflections collected	7525
Independent reflections	2298 [R(int) = 0.0368]
Completeness to theta = 66.250°	99.1 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7457 and 0.5842
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2298 / 3 / 180
Goodness-of-fit on F^2	1.046
Final R indices [I>2sigma(I)]	R1 = 0.0283, wR2 = 0.0730
R indices (all data)	R1 = 0.0285, wR2 = 0.0731
Absolute structure parameter	-0.03(6)
Extinction coefficient	na
Largest diff. peak and hole	0.163 and -0.184 e. $Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for $C_{17}H_{16}O_2$. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	925(1)	10676(2)	6124(1)	17(1)
O(2)	1168(1)	5013(2)	5730(1)	16(1)
C(1)	965(2)	9097(3)	6887(1)	16(1)
C(2)	2499(2)	7591(3)	7074(1)	15(1)
C(3)	2588(2)	6398(3)	6105(1)	13(1)
C(4)	4241(2)	5238(3)	6232(1)	14(1)
C(5)	5471(2)	6251(3)	5883(1)	17(1)
C(6)	7005(2)	5242(3)	6003(1)	21(1)
C(7)	7337(2)	3214(3)	6474(1)	21(1)
C(8)	6116(2)	2196(3)	6820(1)	20(1)
C(9)	4588(2)	3195(3)	6704(1)	18(1)
C(10)	2483(2)	6082(3)	7897(1)	17(1)

C(11)	2419(2)	4964(3)	8595(1)	19(1)
C(12)	2419(2)	3695(3)	9471(1)	18(1)
C(13)	3164(2)	1627(3)	9638(1)	24(1)
C(14)	3197(2)	468(4)	10502(2)	30(1)
C(15)	2484(2)	1346(4)	11204(2)	32(1)
C(16)	1731(2)	3382(4)	11041(1)	28(1)
C(17)	1684(2)	4570(3)	10181(1)	22(1)

Table 3. Bond lengths [Å] and angles [°] for $C_{17}H_{16}O_2$.

O(1)-C(1)	1.423(2)
O(1)-H(1O)	0.84(2)
O(2)-C(3)	1.428(2)
O(2)-H(2O)	0.85(2)
C(1)-C(2)	1.536(2)
C(1)-H(1A)	0.9900
C(1)-H(1B)	0.9900
C(2)-C(10)	1.468(2)
C(2)-C(3)	1.549(2)

C(2)-H(2)	1.0000
C(3)-C(4)	1.516(2)
C(3)-H(3)	1.0000
C(4)-C(5)	1.397(2)
C(4)-C(9)	1.397(3)
C(5)-C(6)	1.388(3)
C(5)-H(5)	0.9500
C(6)-C(7)	1.387(3)
C(6)-H(6)	0.9500
C(7)-C(8)	1.390(3)
C(7)-H(7)	0.9500
C(8)-C(9)	1.381(3)
C(8)-H(8)	0.9500
C(9)-H(9)	0.9500
C(10)-C(11)	1.197(3)
C(11)-C(12)	1.439(2)
C(12)-C(13)	1.394(3)
C(12)-C(17)	1.404(3)
C(13)-C(14)	1.385(3)

C(13)-H(13)	0.9500
C(14)-C(15)	1.384(3)
C(14)-H(14)	0.9500
C(15)-C(16)	1.379(3)
C(15)-H(15)	0.9500
C(16)-C(17)	1.386(3)
C(16)-H(16)	0.9500
C(17)-H(17)	0.9500
C(1)-O(1)-H(1O)	111.0(19)
C(3)-O(2)-H(2O)	111.8(16)
O(1)-C(1)-C(2)	111.84(13)
O(1)-C(1)-H(1A)	109.2
C(2)-C(1)-H(1A)	109.2
O(1)-C(1)-H(1B)	109.2
C(2)-C(1)-H(1B)	109.2
H(1A)-C(1)-H(1B)	107.9
C(10)-C(2)-C(1)	108.33(13)
C(10)-C(2)-C(3)	113.34(14)
C(1)-C(2)-C(3)	111.98(13)

C(10)-C(2)-H(2)	107.7
C(1)-C(2)-H(2)	107.7
C(3)-C(2)-H(2)	107.7
O(2)-C(3)-C(4)	113.82(13)
O(2)-C(3)-C(2)	110.73(12)
C(4)-C(3)-C(2)	112.46(13)
O(2)-C(3)-H(3)	106.4
C(4)-C(3)-H(3)	106.4
C(2)-C(3)-H(3)	106.4
C(5)-C(4)-C(9)	118.63(15)
C(5)-C(4)-C(3)	119.33(15)
C(9)-C(4)-C(3)	122.04(15)
C(6)-C(5)-C(4)	120.57(17)
C(6)-C(5)-H(5)	119.7
C(4)-C(5)-H(5)	119.7
C(7)-C(6)-C(5)	120.35(17)
C(7)-C(6)-H(6)	119.8
C(5)-C(6)-H(6)	119.8
C(6)-C(7)-C(8)	119.33(16)

C(6)-C(7)-H(7)	120.3
C(8)-C(7)-H(7)	120.3
C(9)-C(8)-C(7)	120.56(18)
C(9)-C(8)-H(8)	119.7
C(7)-C(8)-H(8)	119.7
C(8)-C(9)-C(4)	120.57(17)
C(8)-C(9)-H(9)	119.7
C(4)-C(9)-H(9)	119.7
C(11)-C(10)-C(2)	175.49(18)
C(10)-C(11)-C(12)	176.69(19)
C(13)-C(12)-C(17)	119.24(17)
C(13)-C(12)-C(11)	121.19(17)
C(17)-C(12)-C(11)	119.56(17)
C(14)-C(13)-C(12)	120.15(19)
C(14)-C(13)-H(13)	119.9
C(12)-C(13)-H(13)	119.9
C(15)-C(14)-C(13)	120.4(2)
C(15)-C(14)-H(14)	119.8
C(13)-C(14)-H(14)	119.8

C(16)-C(15)-C(14)	119.90(18)
C(16)-C(15)-H(15)	120.1
C(14)-C(15)-H(15)	120.1
C(15)-C(16)-C(17)	120.67(18)
C(15)-C(16)-H(16)	119.7
C(17)-C(16)-H(16)	119.7
C(16)-C(17)-C(12)	119.67(18)
C(16)-C(17)-H(17)	120.2
C(12)-C(17)-H(17)	120.2

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for $C_{17}H_{16}O_2$. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	19(1)	10(1)	19(1)	0(1)	2(1)	0(1)

O(2)	17(1)	12(1)	19(1)	2(1)	2(1)	1(1)
C(1)	17(1)	13(1)	18(1)	0(1)	6(1)	0(1)
C(2)	16(1)	13(1)	17(1)	0(1)	5(1)	-1(1)
C(3)	15(1)	8(1)	16(1)	2(1)	4(1)	-1(1)
C(4)	15(1)	12(1)	14(1)	-2(1)	3(1)	0(1)
C(5)	21(1)	15(1)	15(1)	-4(1)	5(1)	-2(1)
C(6)	19(1)	27(1)	18(1)	-8(1)	8(1)	-4(1)
C(7)	15(1)	25(1)	23(1)	-10(1)	3(1)	4(1)
C(8)	22(1)	14(1)	21(1)	-3(1)	1(1)	4(1)
C(9)	17(1)	14(1)	21(1)	0(1)	4(1)	0(1)
C(10)	17(1)	14(1)	18(1)	-1(1)	5(1)	2(1)
C(11)	20(1)	18(1)	18(1)	1(1)	5(1)	2(1)
C(12)	18(1)	18(1)	17(1)	4(1)	2(1)	-2(1)
C(13)	23(1)	22(1)	27(1)	2(1)	6(1)	0(1)
C(14)	25(1)	22(1)	37(1)	13(1)	0(1)	1(1)
C(15)	28(1)	40(1)	24(1)	16(1)	2(1)	-9(1)
C(16)	27(1)	38(1)	20(1)	1(1)	7(1)	-8(1)
C(17)	23(1)	21(1)	21(1)	1(1)	5(1)	-1(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for $C_{17}H_{16}O_2$.

	x	y	z	U(eq)
H(1O)	240(30)	10310(50)	5579(17)	38(7)
H(2O)	1320(30)	3750(30)	5997(17)	26(6)
H(1A)	-60	8190	6686	19
H(1B)	981	9868	7517	19
H(2)	3514	8537	7304	18
H(3)	2517	7567	5587	16
H(5)	5257	7642	5561	21
H(6)	7832	5944	5761	25
H(7)	8389	2526	6558	26
H(8)	6333	802	7139	24
H(9)	3766	2487	6948	21
H(13)	3650	1011	9157	29
H(14)	3713	-937	10614	36
H(15)	2514	547	11797	38

H(16)	1239	3977	11523	34
H(17)	1157	5968	10072	26

Table 6. Torsion angles [°] for $C_{17}H_{16}O_2$.

O(1)-C(1)-C(2)-C(10)	177.57(13)
O(1)-C(1)-C(2)-C(3)	-56.71(18)
C(10)-C(2)-C(3)-O(2)	61.15(17)
C(1)-C(2)-C(3)-O(2)	-61.77(17)
C(10)-C(2)-C(3)-C(4)	-67.43(17)
C(1)-C(2)-C(3)-C(4)	169.64(13)
O(2)-C(3)-C(4)-C(5)	133.92(14)
C(2)-C(3)-C(4)-C(5)	-99.12(17)
O(2)-C(3)-C(4)-C(9)	-47.20(19)
C(2)-C(3)-C(4)-C(9)	79.76(19)
C(9)-C(4)-C(5)-C(6)	0.1(2)
C(3)-C(4)-C(5)-C(6)	179.05(14)
C(4)-C(5)-C(6)-C(7)	-0.2(2)

C(5)-C(6)-C(7)-C(8)	0.3(2)
C(6)-C(7)-C(8)-C(9)	-0.4(3)
C(7)-C(8)-C(9)-C(4)	0.4(3)
C(5)-C(4)-C(9)-C(8)	-0.2(2)
C(3)-C(4)-C(9)-C(8)	-179.13(15)
C(17)-C(12)-C(13)-C(14)	-0.9(3)
C(11)-C(12)-C(13)-C(14)	177.82(18)
C(12)-C(13)-C(14)-C(15)	0.4(3)
C(13)-C(14)-C(15)-C(16)	0.2(3)
C(14)-C(15)-C(16)-C(17)	-0.2(3)
C(15)-C(16)-C(17)-C(12)	-0.3(3)
C(13)-C(12)-C(17)-C(16)	0.9(3)
C(11)-C(12)-C(17)-C(16)	-177.86(16)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for $C_{17}H_{16}O_2$ [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1O)...O(2)#1	0.84(2)	1.88(2)	2.7031(15)	169(3)
O(2)-H(2O)...O(1)#2	0.85(2)	1.91(2)	2.7130(17)	157(2)

Symmetry transformations used to generate equivalent atoms:

#1 -x,y+1/2,-z+1 #2 x,y-1,z

(1*S*,2*R*)-2-(Phenylethynyl)-1-(*o*-tolyl)propane-1,3-diol (3.15c)

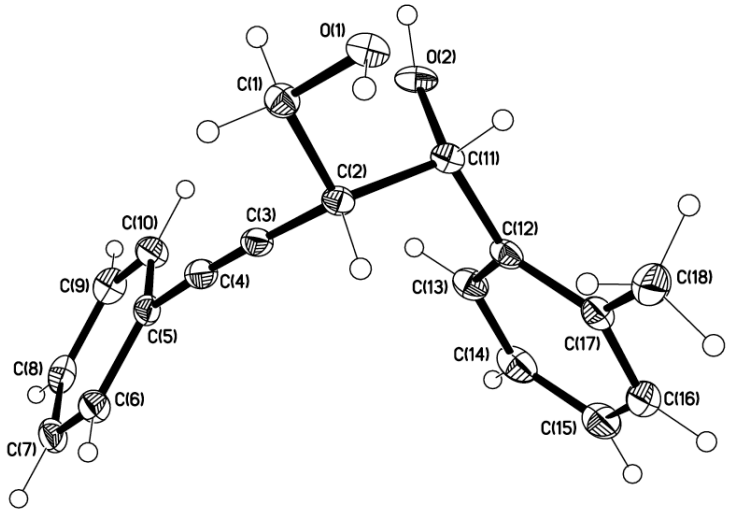


Table 1. Crystal data and structure refinement for $C_{18}H_{18}O_2$.

Identification code	$C_{18}H_{18}O_2$
Empirical formula	$C_{18}H_{18}O_2$

Formula weight	266.32	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 21	
Unit cell dimensions	a = 10.1568(10) Å	α= 90°.
	b = 6.1364(6) Å	β= 110.030(2)°.
	c = 12.3308(12) Å	γ = 90°.
Volume	722.05(12) $Å^3$	
Z	2	
Density (calculated)	1.225 Mg/m^3	
Absorption coefficient	0.620 mm^{-1}	
F(000)	284	
Crystal size	0.500 x 0.060 x 0.050 mm^3	
Theta range for data collection	3.815 to 69.364°.	
Index ranges	-11<=h<=12, -7<=k<=7, -14<=l<=14	
Reflections collected	10529	
Independent reflections	2651 [R(int) = 0.0232]	
Completeness to theta = 67.679°	99.1 %	

Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7533 and 0.6573
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2651 / 3 / 190
Goodness-of-fit on F^2	1.066
Final R indices [I>2sigma(I)]	R1 = 0.0257, wR2 = 0.0650
R indices (all data)	R1 = 0.0258, wR2 = 0.0652
Absolute structure parameter	0.02(3)
Extinction coefficient	na
Largest diff. peak and hole	0.157 and -0.168 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for $C_{18}H_{18}O_2$. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	808(1)	-315(2)	786(1)	15(1)
O(2)	1342(1)	5431(2)	1211(1)	17(1)

C(1)	2020(2)	797(3)	735(1)	15(1)
C(2)	2728(2)	2116(2)	1842(1)	13(1)
C(3)	3967(2)	3265(2)	1778(1)	15(1)
C(4)	4951(2)	4327(3)	1761(1)	16(1)
C(5)	6095(2)	5742(3)	1795(1)	16(1)
C(6)	7486(2)	5136(3)	2392(1)	19(1)
C(7)	8565(2)	6574(3)	2460(1)	21(1)
C(8)	8281(2)	8609(3)	1940(1)	21(1)
C(9)	6908(2)	9214(3)	1343(1)	22(1)
C(10)	5827(2)	7790(3)	1272(1)	20(1)
C(11)	1686(2)	3758(2)	2069(1)	14(1)
C(12)	2296(2)	4772(2)	3256(1)	15(1)
C(13)	3157(2)	6595(3)	3412(1)	18(1)
C(14)	3758(2)	7543(3)	4490(2)	24(1)
C(15)	3499(2)	6653(3)	5433(2)	27(1)
C(16)	2656(2)	4824(3)	5290(1)	25(1)
C(17)	2040(2)	3848(3)	4212(1)	19(1)
C(18)	1121(2)	1871(3)	4104(1)	24(1)

Table 3. Bond lengths [Å] and angles [°] for $C_{18}H_{18}O_2$.

O(1)-C(1)	1.4274(19)
O(1)-H(1O)	0.847(18)
O(2)-C(11)	1.4290(17)
O(2)-H(2O)	0.852(18)
C(1)-C(2)	1.5366(19)
C(1)-H(1A)	0.9900
C(1)-H(1B)	0.9900
C(2)-C(3)	1.469(2)
C(2)-C(11)	1.555(2)
C(2)-H(2)	1.0000
C(3)-C(4)	1.199(2)
C(4)-C(5)	1.439(2)
C(5)-C(10)	1.397(2)
C(5)-C(6)	1.401(2)
C(6)-C(7)	1.387(2)
C(6)-H(6)	0.9500
C(7)-C(8)	1.388(3)

C(7)-H(7)	0.9500
C(8)-C(9)	1.386(2)
C(8)-H(8)	0.9500
C(9)-C(10)	1.382(2)
C(9)-H(9)	0.9500
C(10)-H(10)	0.9500
C(11)-C(12)	1.514(2)
C(11)-H(11)	1.0000
C(12)-C(13)	1.392(2)
C(12)-C(17)	1.410(2)
C(13)-C(14)	1.386(2)
C(13)-H(13)	0.9500
C(14)-C(15)	1.389(3)
C(14)-H(14)	0.9500
C(15)-C(16)	1.386(3)
C(15)-H(15)	0.9500
C(16)-C(17)	1.396(2)
C(16)-H(16)	0.9500
C(17)-C(18)	1.509(2)

C(18)-H(18A)	0.9800
C(18)-H(18B)	0.9800
C(18)-H(18C)	0.9800
C(1)-O(1)-H(1O)	110.6(13)
C(11)-O(2)-H(2O)	109.3(15)
O(1)-C(1)-C(2)	111.20(12)
O(1)-C(1)-H(1A)	109.4
C(2)-C(1)-H(1A)	109.4
O(1)-C(1)-H(1B)	109.4
C(2)-C(1)-H(1B)	109.4
H(1A)-C(1)-H(1B)	108.0
C(3)-C(2)-C(1)	110.76(12)
C(3)-C(2)-C(11)	110.31(12)
C(1)-C(2)-C(11)	111.15(11)
C(3)-C(2)-H(2)	108.2
C(1)-C(2)-H(2)	108.2
C(11)-C(2)-H(2)	108.2
C(4)-C(3)-C(2)	175.42(16)
C(3)-C(4)-C(5)	175.09(16)

C(10)-C(5)-C(6)	118.90(14)
C(10)-C(5)-C(4)	120.14(14)
C(6)-C(5)-C(4)	120.91(15)
C(7)-C(6)-C(5)	119.77(15)
C(7)-C(6)-H(6)	120.1
C(5)-C(6)-H(6)	120.1
C(6)-C(7)-C(8)	120.62(15)
C(6)-C(7)-H(7)	119.7
C(8)-C(7)-H(7)	119.7
C(9)-C(8)-C(7)	119.92(15)
C(9)-C(8)-H(8)	120.0
C(7)-C(8)-H(8)	120.0
C(10)-C(9)-C(8)	119.79(16)
C(10)-C(9)-H(9)	120.1
C(8)-C(9)-H(9)	120.1
C(9)-C(10)-C(5)	121.00(15)
C(9)-C(10)-H(10)	119.5
C(5)-C(10)-H(10)	119.5
O(2)-C(11)-C(12)	109.64(12)

O(2)-C(11)-C(2)	109.90(11)
C(12)-C(11)-C(2)	111.23(11)
O(2)-C(11)-H(11)	108.7
C(12)-C(11)-H(11)	108.7
C(2)-C(11)-H(11)	108.7
C(13)-C(12)-C(17)	119.65(14)
C(13)-C(12)-C(11)	119.59(13)
C(17)-C(12)-C(11)	120.73(14)
C(14)-C(13)-C(12)	121.28(16)
C(14)-C(13)-H(13)	119.4
C(12)-C(13)-H(13)	119.4
C(13)-C(14)-C(15)	119.36(16)
C(13)-C(14)-H(14)	120.3
C(15)-C(14)-H(14)	120.3
C(16)-C(15)-C(14)	119.85(15)
C(16)-C(15)-H(15)	120.1
C(14)-C(15)-H(15)	120.1
C(15)-C(16)-C(17)	121.65(16)
C(15)-C(16)-H(16)	119.2

C(17)-C(16)-H(16)	119.2
C(16)-C(17)-C(12)	118.21(15)
C(16)-C(17)-C(18)	119.40(14)
C(12)-C(17)-C(18)	122.39(14)
C(17)-C(18)-H(18A)	109.5
C(17)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
C(17)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for $C_{18}H_{18}O_2$. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}

O(1)	14(1)	10(1)	18(1)	1(1)	2(1)	-1(1)
O(2)	17(1)	12(1)	17(1)	2(1)	-2(1)	0(1)
C(1)	14(1)	14(1)	16(1)	-1(1)	5(1)	-1(1)
C(2)	12(1)	12(1)	14(1)	2(1)	3(1)	1(1)
C(3)	14(1)	15(1)	13(1)	0(1)	3(1)	3(1)
C(4)	16(1)	17(1)	14(1)	0(1)	4(1)	1(1)
C(5)	14(1)	19(1)	15(1)	-4(1)	6(1)	-1(1)
C(6)	16(1)	21(1)	19(1)	-1(1)	6(1)	0(1)
C(7)	13(1)	28(1)	22(1)	-6(1)	7(1)	-1(1)
C(8)	21(1)	26(1)	21(1)	-10(1)	12(1)	-10(1)
C(9)	27(1)	18(1)	22(1)	0(1)	10(1)	-2(1)
C(10)	16(1)	22(1)	21(1)	0(1)	5(1)	1(1)
C(11)	13(1)	12(1)	16(1)	1(1)	3(1)	0(1)
C(12)	12(1)	14(1)	18(1)	-2(1)	3(1)	3(1)
C(13)	16(1)	15(1)	22(1)	-1(1)	4(1)	2(1)
C(14)	16(1)	20(1)	31(1)	-10(1)	3(1)	0(1)
C(15)	19(1)	38(1)	21(1)	-14(1)	2(1)	4(1)
C(16)	20(1)	38(1)	18(1)	-3(1)	6(1)	4(1)
C(17)	14(1)	23(1)	19(1)	-1(1)	5(1)	4(1)

C(18)	24(1)	28(1)	21(1)	4(1)	10(1)	-2(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for $C_{18}H_{18}O_2$.

	x	y	z	U(eq)
H(1O)	1020(20)	-1570(30)	1080(16)	19(5)
H(2O)	720(20)	4960(40)	597(16)	27(5)
H(1A)	1745	1791	62	18
H(1B)	2693	-277	631	18
H(2)	3042	1076	2506	16
H(6)	7689	3745	2748	22
H(7)	9507	6163	2867	25
H(8)	9026	9584	1992	25
H(9)	6711	10604	984	26
H(10)	4888	8211	860	24
H(11)	808	2962	2021	16
H(13)	3336	7201	2767	22

H(14)	4341	8790	4582	28
H(15)	3900	7296	6174	33
H(16)	2494	4220	5942	30
H(18A)	1168	1390	4875	36
H(18B)	1447	695	3721	36
H(18C)	151	2242	3647	36

Table 6. Torsion angles [°] for $C_{18}H_{18}O_2$.

O(1)-C(1)-C(2)-C(3)	-179.60(12)
O(1)-C(1)-C(2)-C(11)	-56.60(15)
C(10)-C(5)-C(6)-C(7)	0.5(2)
C(4)-C(5)-C(6)-C(7)	-176.79(14)
C(5)-C(6)-C(7)-C(8)	-0.2(2)
C(6)-C(7)-C(8)-C(9)	-0.1(2)
C(7)-C(8)-C(9)-C(10)	0.2(2)
C(8)-C(9)-C(10)-C(5)	0.1(2)
C(6)-C(5)-C(10)-C(9)	-0.5(2)
C(4)-C(5)-C(10)-C(9)	176.85(15)

C(3)-C(2)-C(11)-O(2)	54.92(14)
C(1)-C(2)-C(11)-O(2)	-68.34(15)
C(3)-C(2)-C(11)-C(12)	-66.69(15)
C(1)-C(2)-C(11)-C(12)	170.06(12)
O(2)-C(11)-C(12)-C(13)	-36.51(18)
C(2)-C(11)-C(12)-C(13)	85.25(16)
O(2)-C(11)-C(12)-C(17)	145.64(13)
C(2)-C(11)-C(12)-C(17)	-92.61(16)
C(17)-C(12)-C(13)-C(14)	-0.8(2)
C(11)-C(12)-C(13)-C(14)	-178.70(14)
C(12)-C(13)-C(14)-C(15)	0.2(2)
C(13)-C(14)-C(15)-C(16)	0.5(3)
C(14)-C(15)-C(16)-C(17)	-0.6(3)
C(15)-C(16)-C(17)-C(12)	0.0(2)
C(15)-C(16)-C(17)-C(18)	-179.45(16)
C(13)-C(12)-C(17)-C(16)	0.7(2)
C(11)-C(12)-C(17)-C(16)	178.56(14)
C(13)-C(12)-C(17)-C(18)	-179.86(14)
C(11)-C(12)-C(17)-C(18)	-2.0(2)

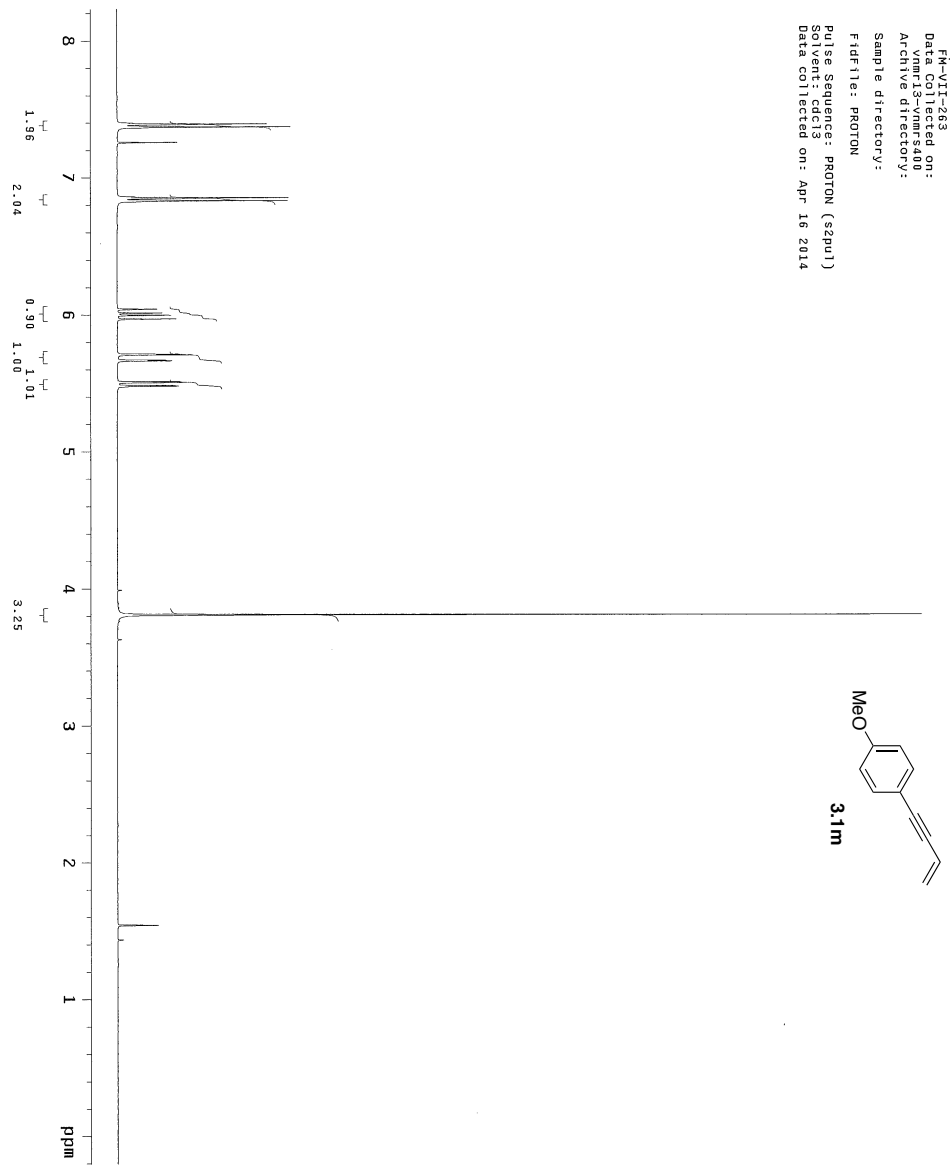
Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for $C_{18}H_{18}O_2$ [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1O)...O(2)#1	0.847(18)	1.867(19)	2.6813(15)	160.9(19)
O(2)-H(2O)...O(1)#2	0.852(18)	1.881(18)	2.7120(15)	165(2)

Symmetry transformations used to generate equivalent atoms:

#1 x,y-1,z #2 -x,y+1/2,-z

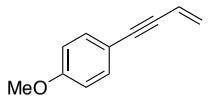

Sample Name:
FM-VII-263
Data collected on:
vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 16 2014
MeO
3.1m
8
7
6
5
4
3
2
1
ppm
1.96
2.04
0.90
1.00
1.01
3.25

Sample Name:
FM-VII-263
Data Collected on:
vnmr13-vnmrs400
Archive directory:

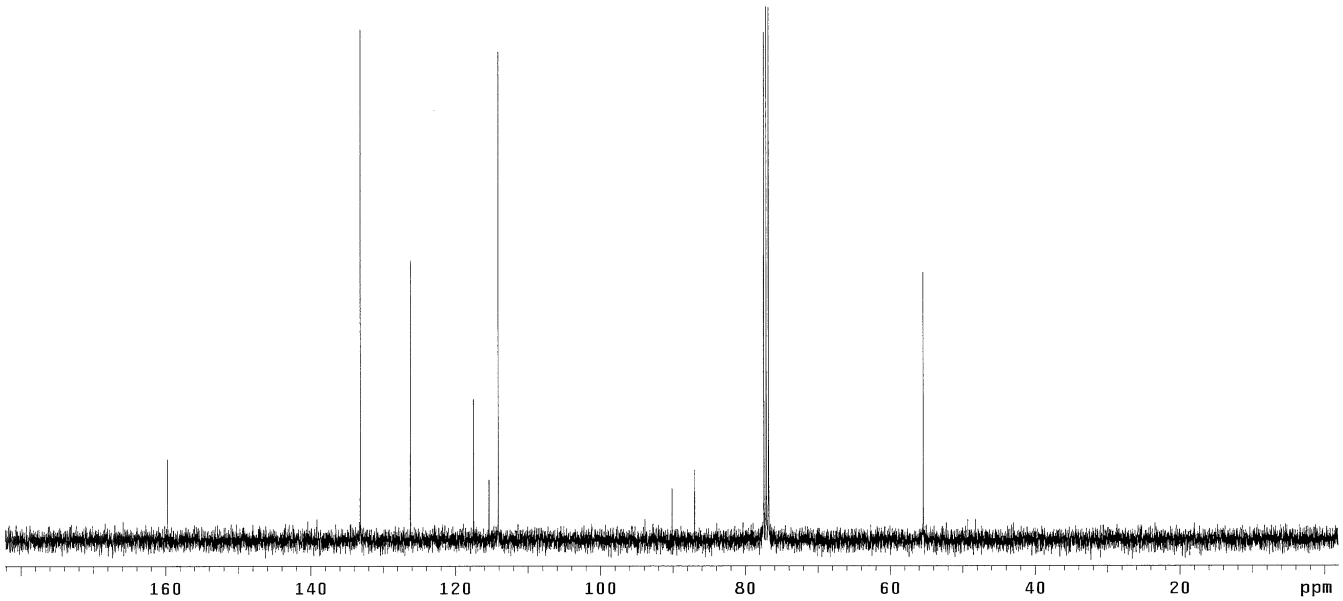
Sample directory:

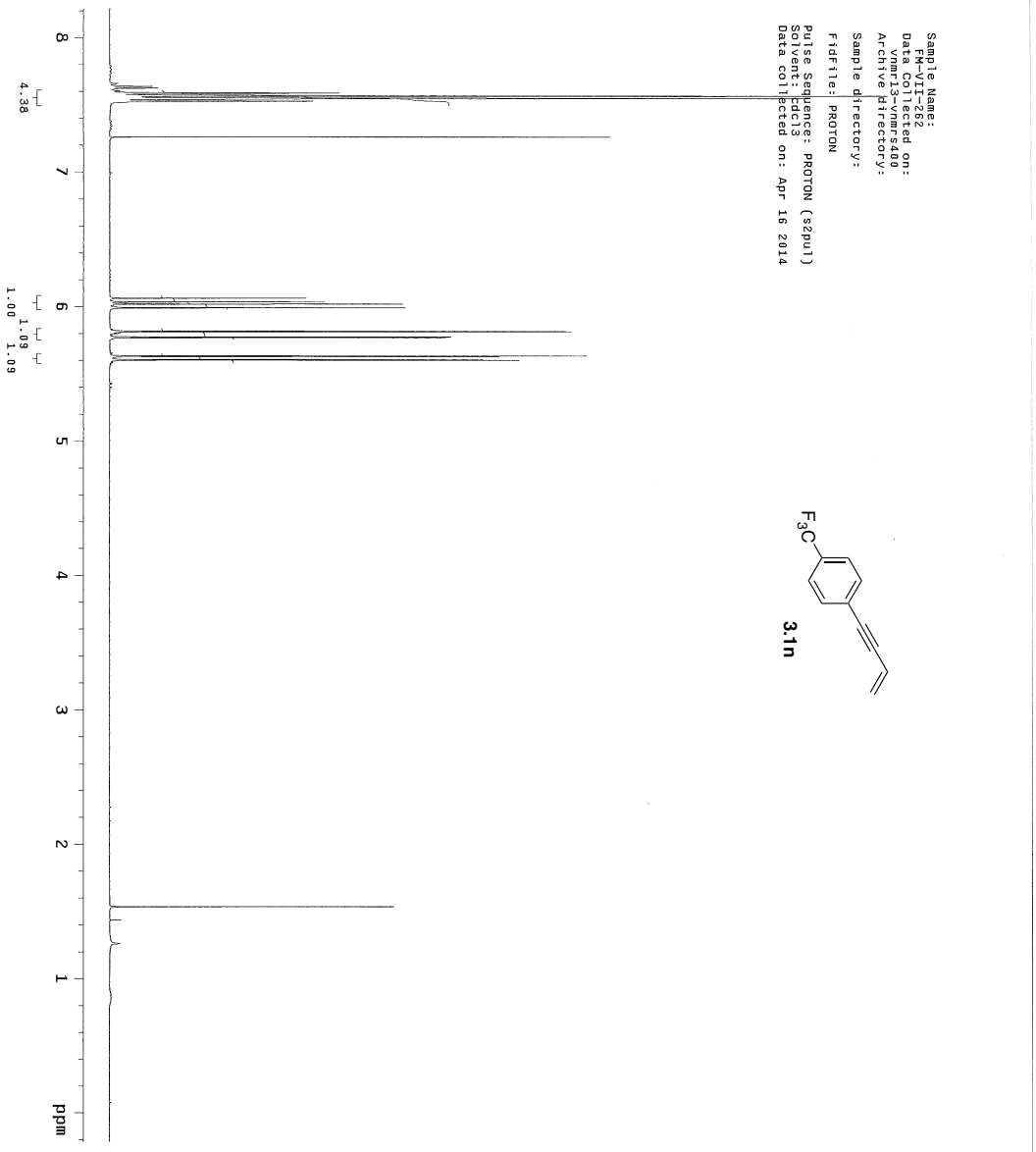
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 16 2014



3.1m



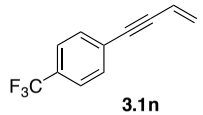

Sample Name:
Data collected on:
FM-01-262
vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 16 2014
F3C
3.1n
8
7
6
5
4
3
2
1
ppm
4.38
1.00
1.09
1.09

Sample Name:
FM-VII-262
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 17 2014



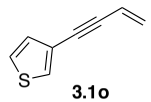
3.1n

Sample Name:
FM-VII-269
Data Collected on:
vnmr13-vnmrs400
Archive directory:

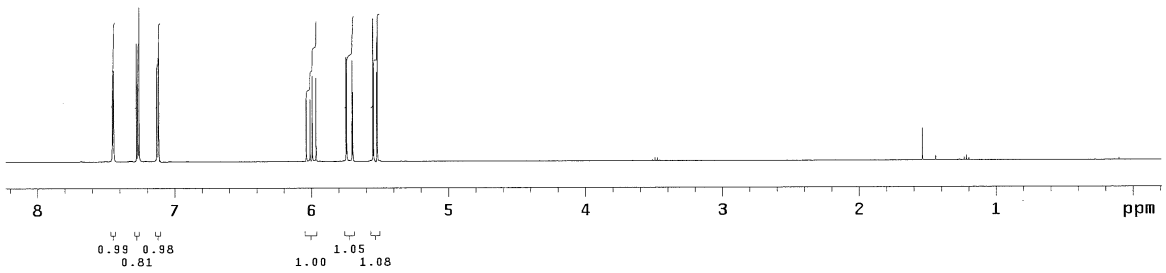
Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 18 2014



3.1o

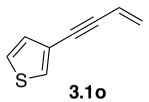


Sample Name:
FM-VII-269
Data Collected on:
vnmr13-vnmrs400
Archive directory:

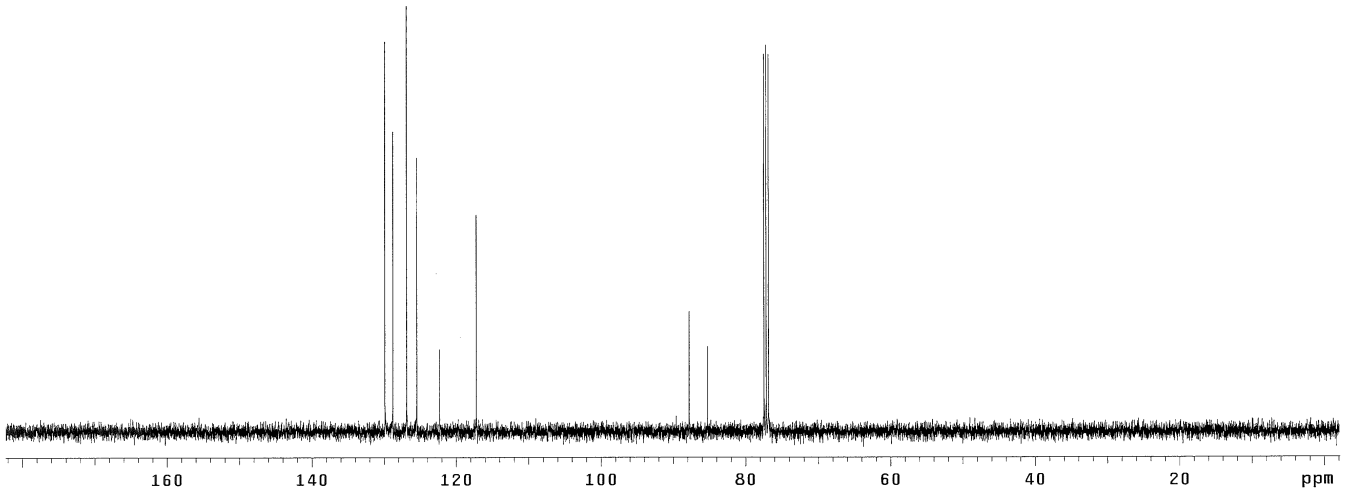
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 18 2014



3.1o

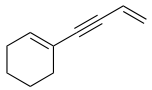


Sample Name:
FM-VII-270
Data Collected on:
vnmr13-vnmrs400
Archive directory:

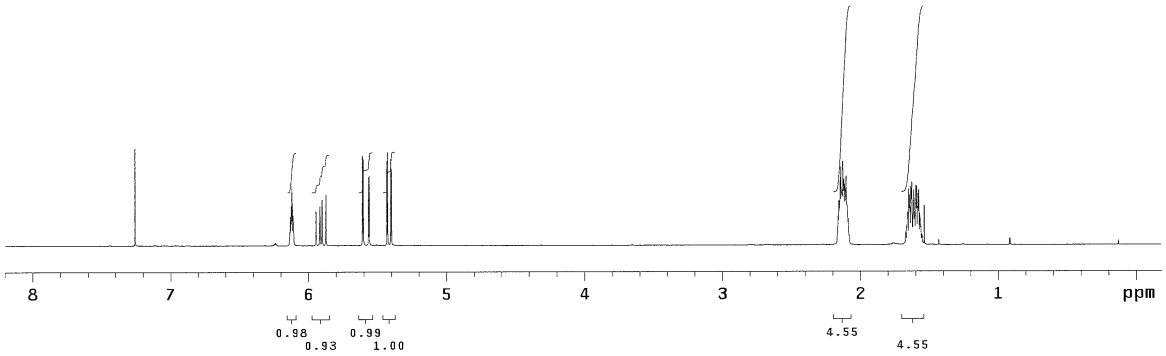
Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 21 2014



3.1p

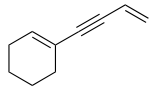


Sample Name:
FM-VII-270
Data Collected on:
vnmr13-vnmrs400
Archive directory:

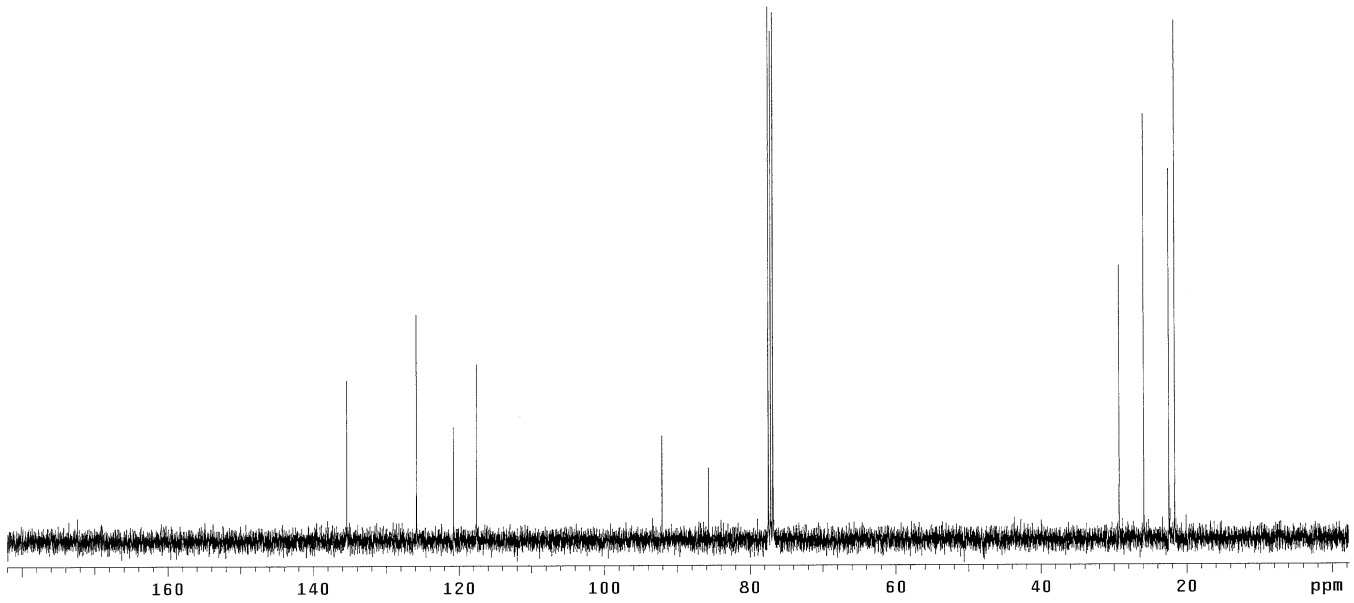
Sample directory:

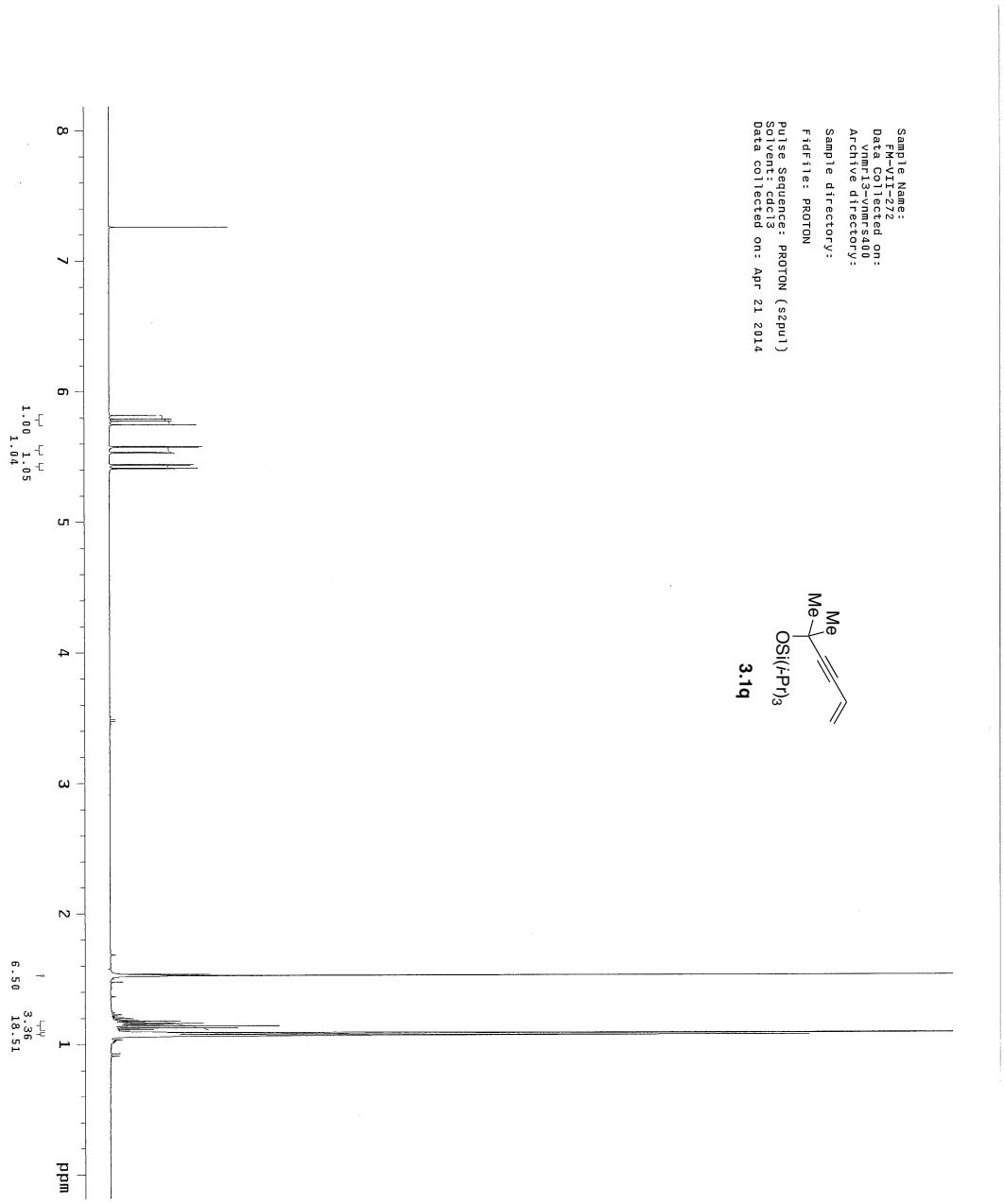
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 21 2014



3.1p



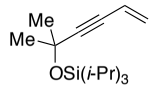

Sample Name:
FM-VII-272
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 21 2014
Me
Me
OSi(i-Pr)3
3.1q
8
7
6
5
4
3
2
1
ppm
1.00
1.05
1.04
6.50
3.36
18.51

Sample Name:
FM-VII-272
Data Collected on:
vnmr13-vnmrs400
Archive directory:

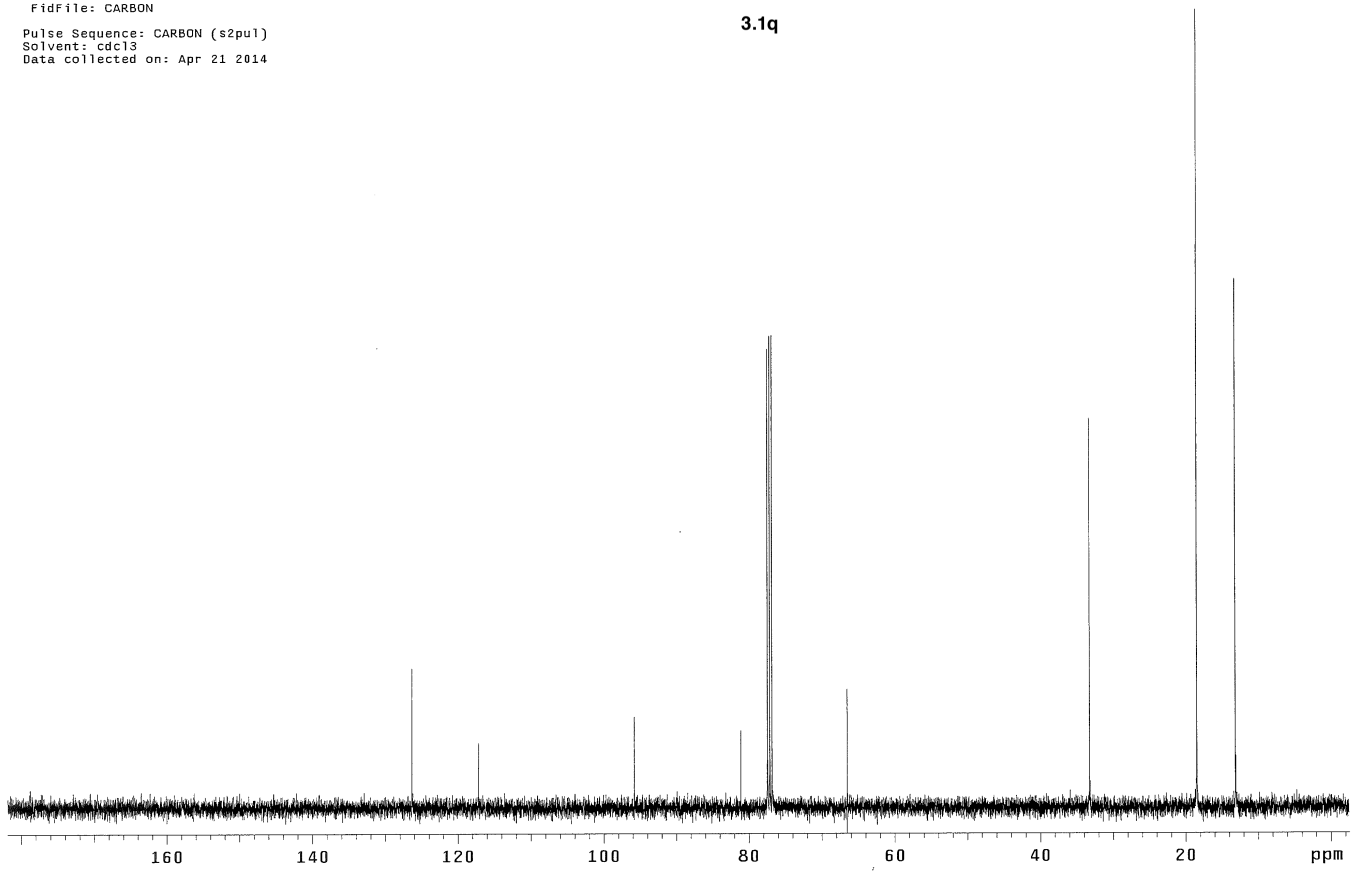
Sample directory:

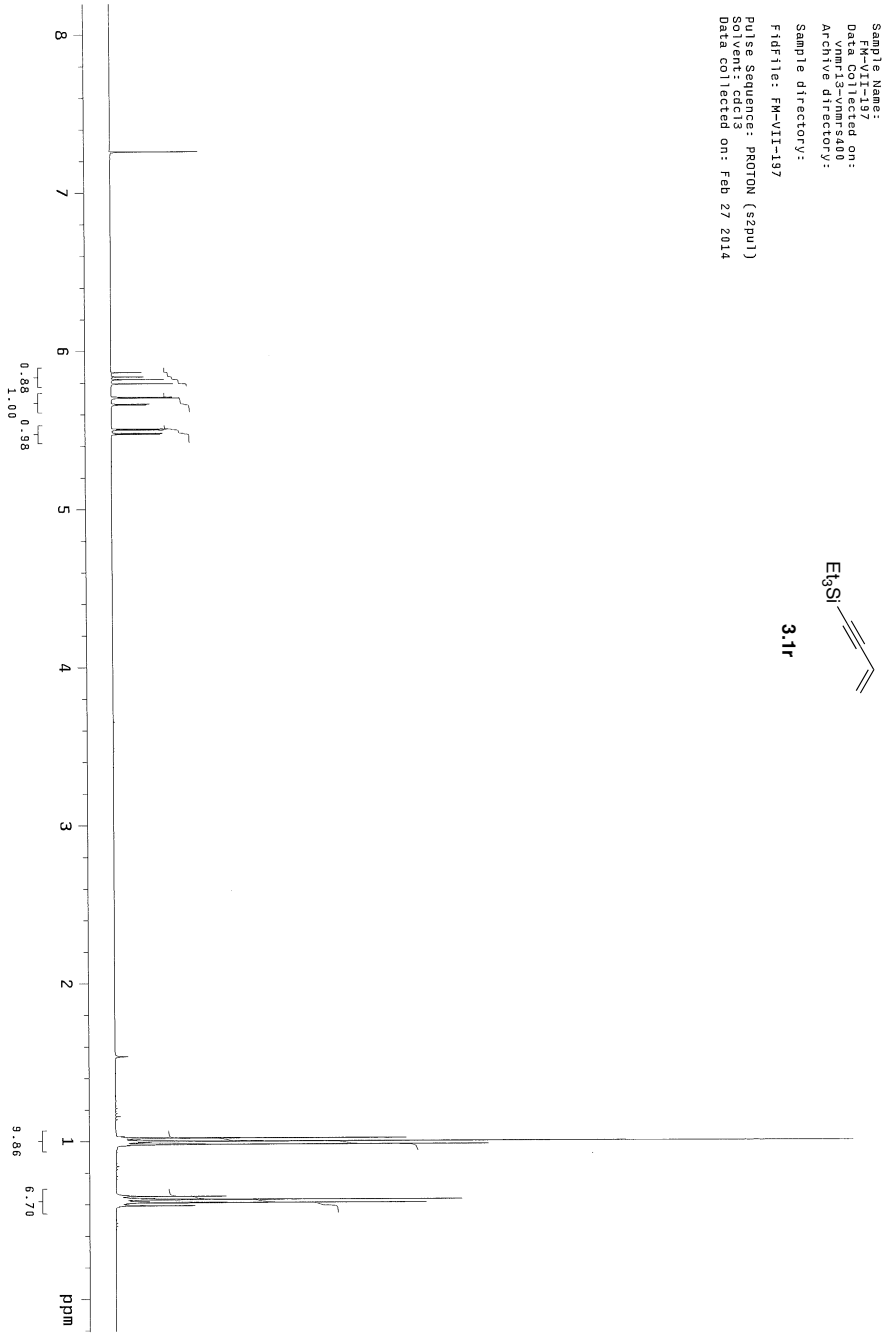
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 21 2014



3.1q



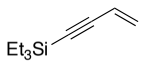

Sample Name:
FM-VII-197
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: FM-VII-197
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Feb 27 2014
Et3Si
3.1r
8
7
6
5
4
3
2
1
ppm
0.88
1.00
0.98
9.86
6.70

Sample Name:
FM-VII-197
Data Collected on:
vnmr13-vnmrs400
Archive directory:

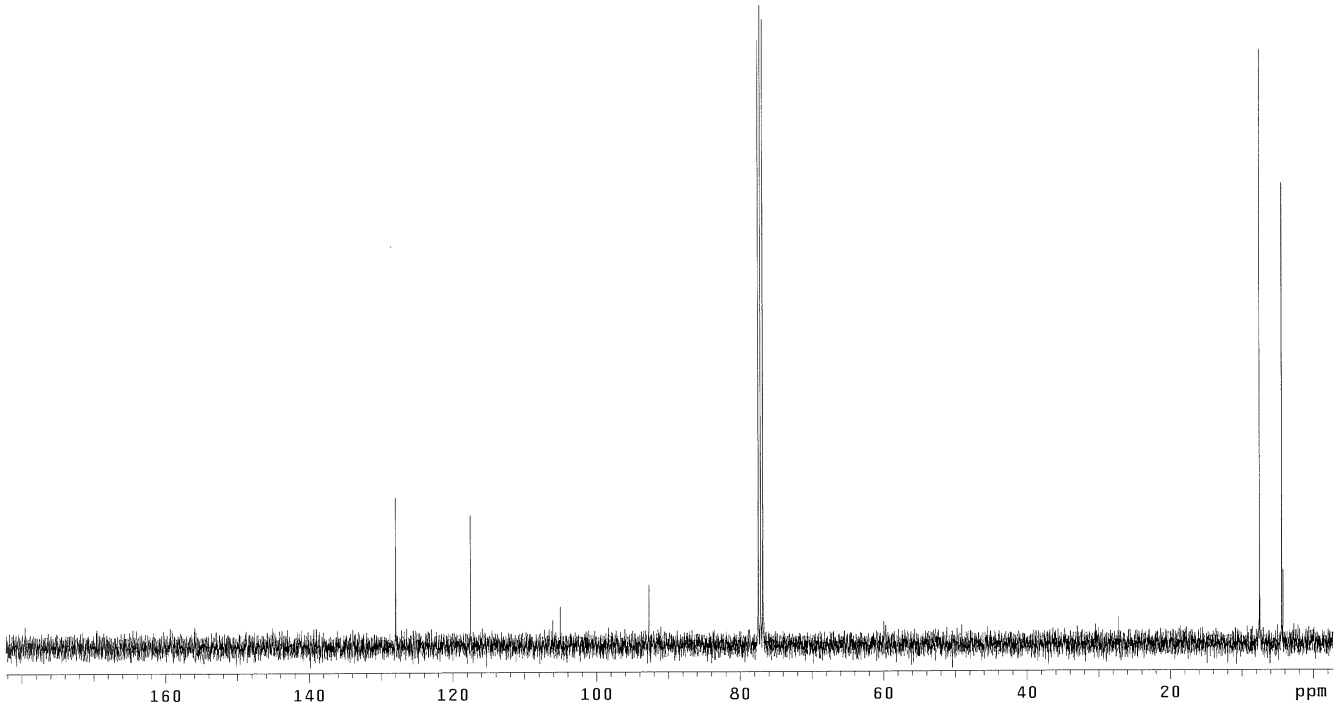
Sample directory:

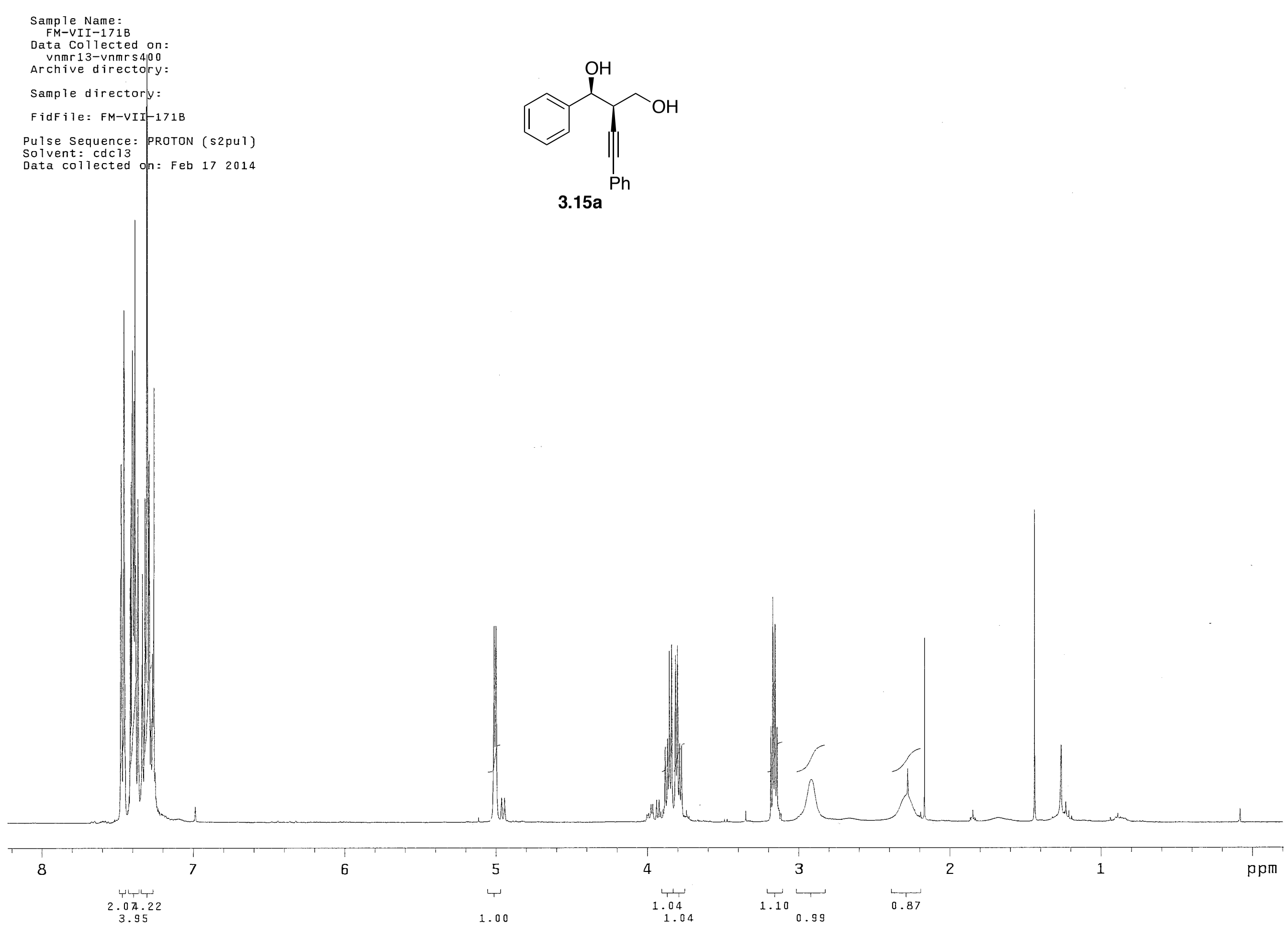
FidFile: FM-VII-197-CNMR

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Feb 27 2014



3.1r



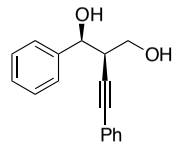

Sample Name:
FM-VII-171B
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: FM-VII-171B
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Feb 17 2014
OH
OH
Ph
3.15a
8
7
6
5
4
3
2
1
ppm
2.07
4.22
3.95
1.00
1.04
1.04
1.10
0.99
0.87

Sample Name:
FM-VII-171B
Data Collected on:
vnmr13-vnmrs400
Archive directory:

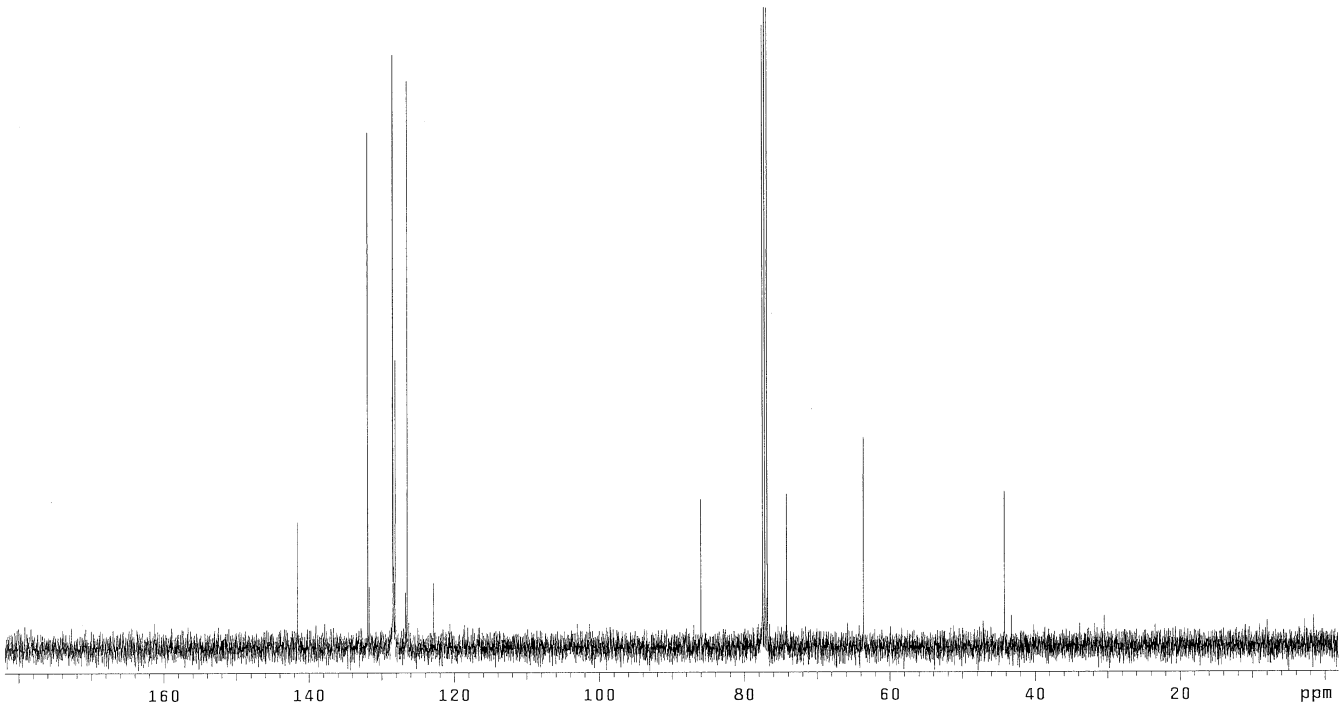
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Feb 17 2014



3.15a

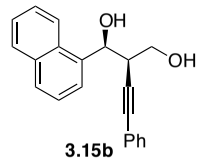


Sample Name:
FM-VII-233-2
Data Collected on:
vnmr13-vnmrs400
Archive directory:

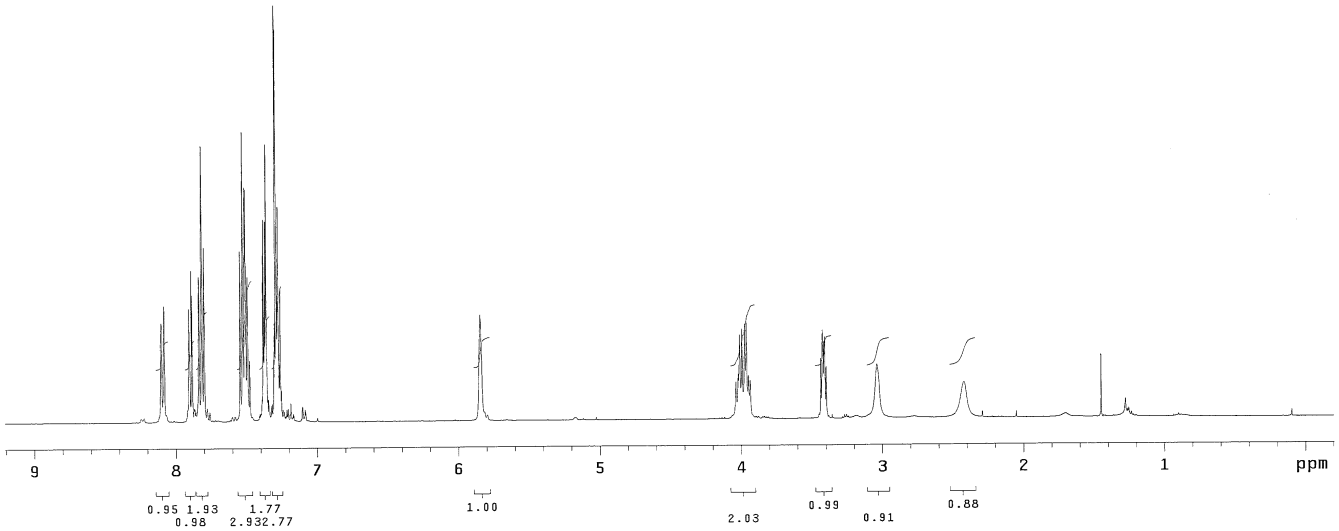
Sample directory:

FidFile: FM-VII-233-2

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 11 2014



3.15b

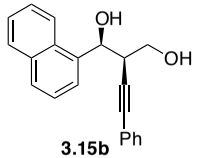


Sample Name:
FM-VII-233-2
Data Collected on:
vnmrl3-vnmrs400
Archive directory:

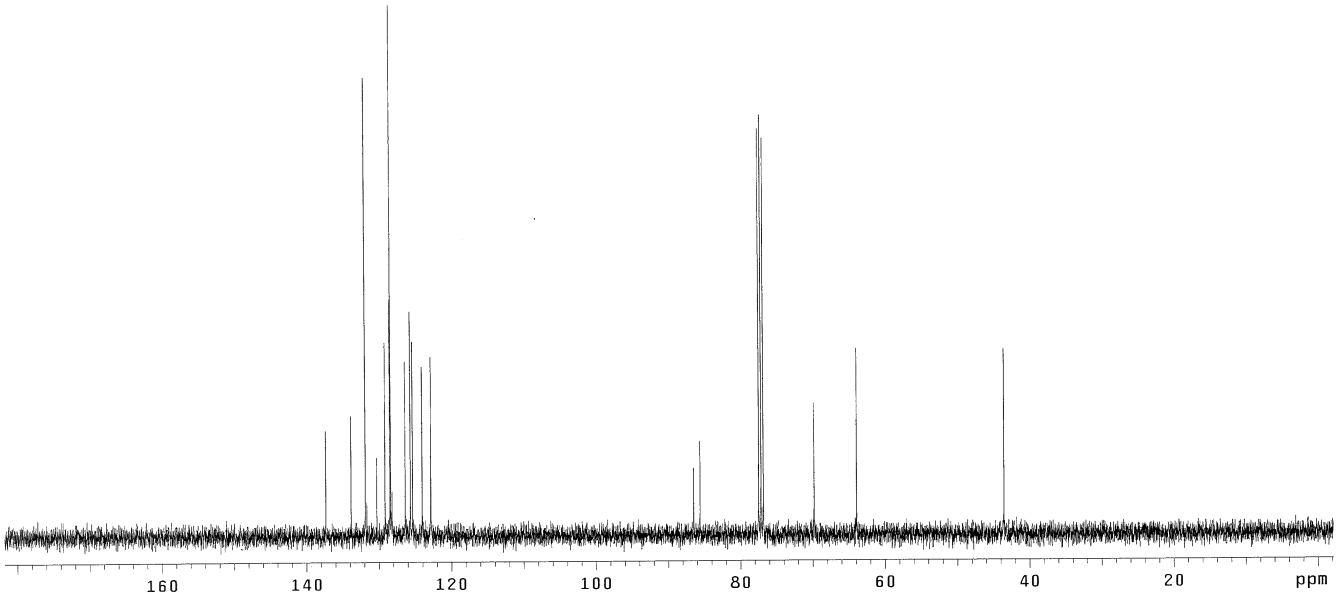
Sample directory:

FidFile: FM-VII-233-CNMR-2

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 11 2014



3.15b

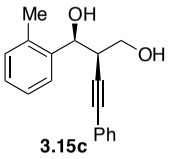


Sample Name:
FM-VII-243
Data Collected on:
vnmr13-vnmrs400
Archive directory:

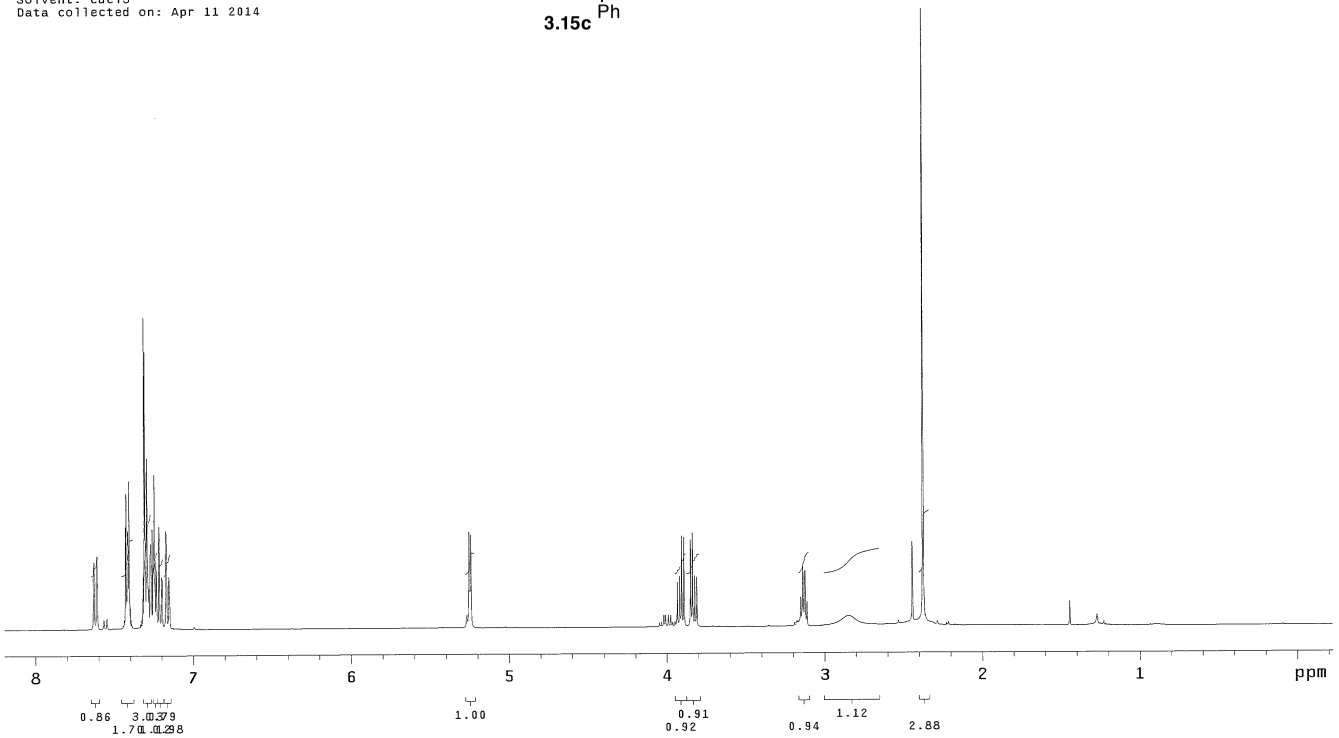
Sample directory:

FidFile: FM-VII-243

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 11 2014



3.15c

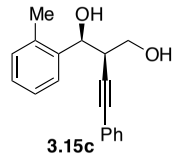


Sample Name:
FM-VII-243
Data Collected on:
vnmr13-vnmrs400
Archive directory:

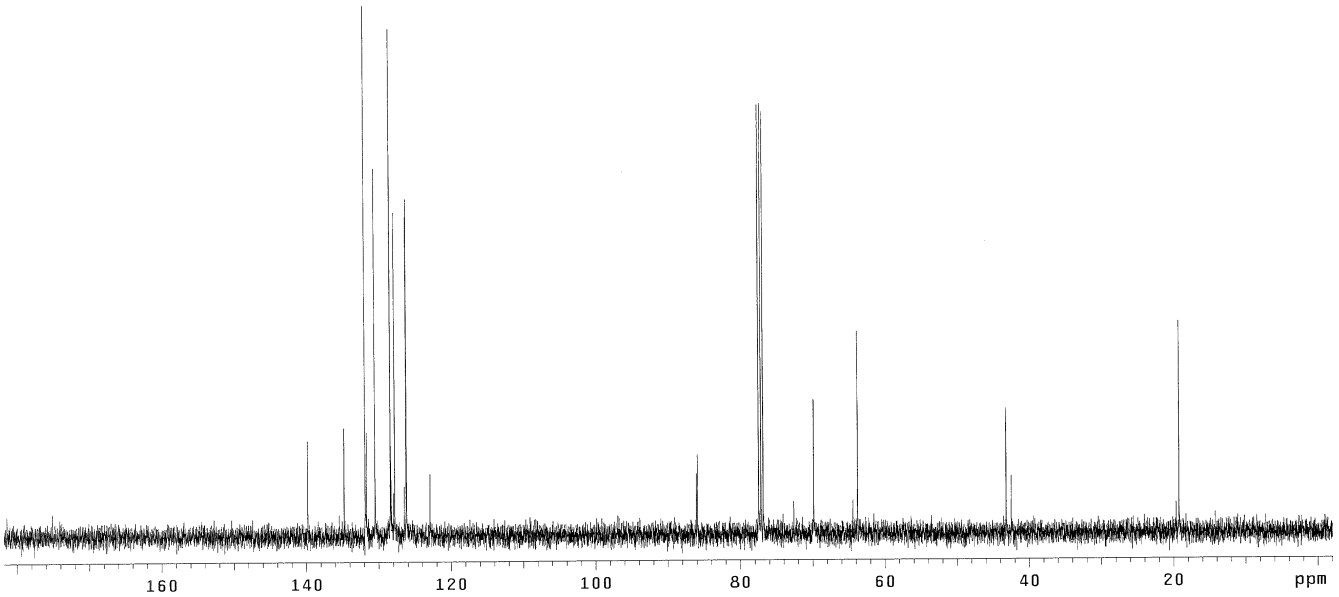
Sample directory:

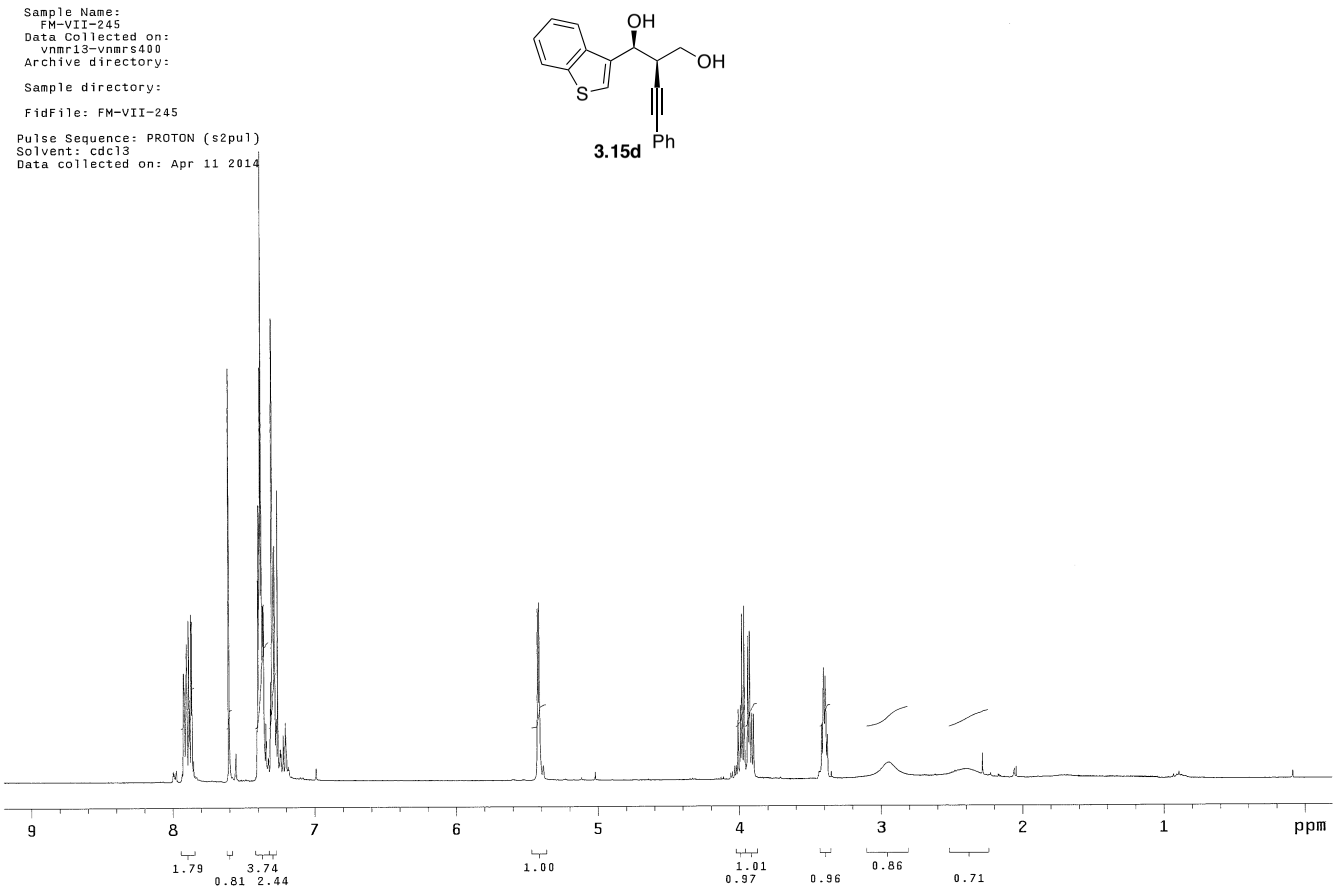
FidFile: FM-VII-243-CNMR

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 11 2014



3.15c



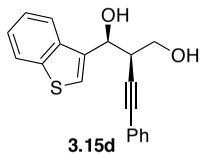

Sample Name:
FM-VII-245
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: FM-VII-245
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 11 2014
OH
OH
S
Ph
3.15d
9
8
7
6
5
4
3
2
1
ppm
1.79
0.81
3.74
2.44
1.00
1.01
0.97
0.96
0.86
0.71

Sample Name:
FM-VII-245
Data Collected on:
vnmr13-vnmrs400
Archive directory:

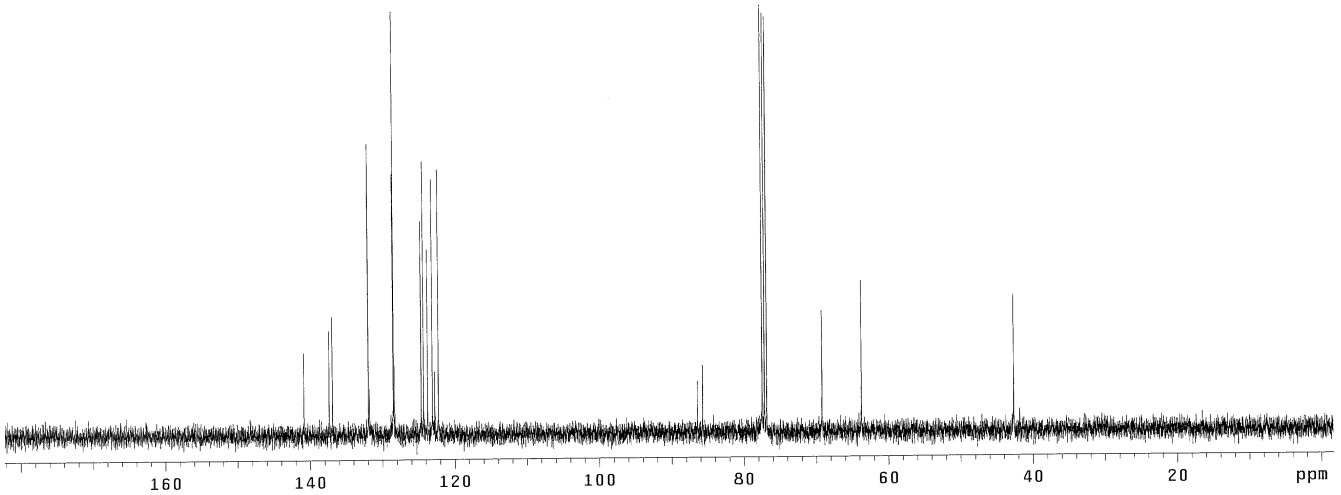
Sample directory:

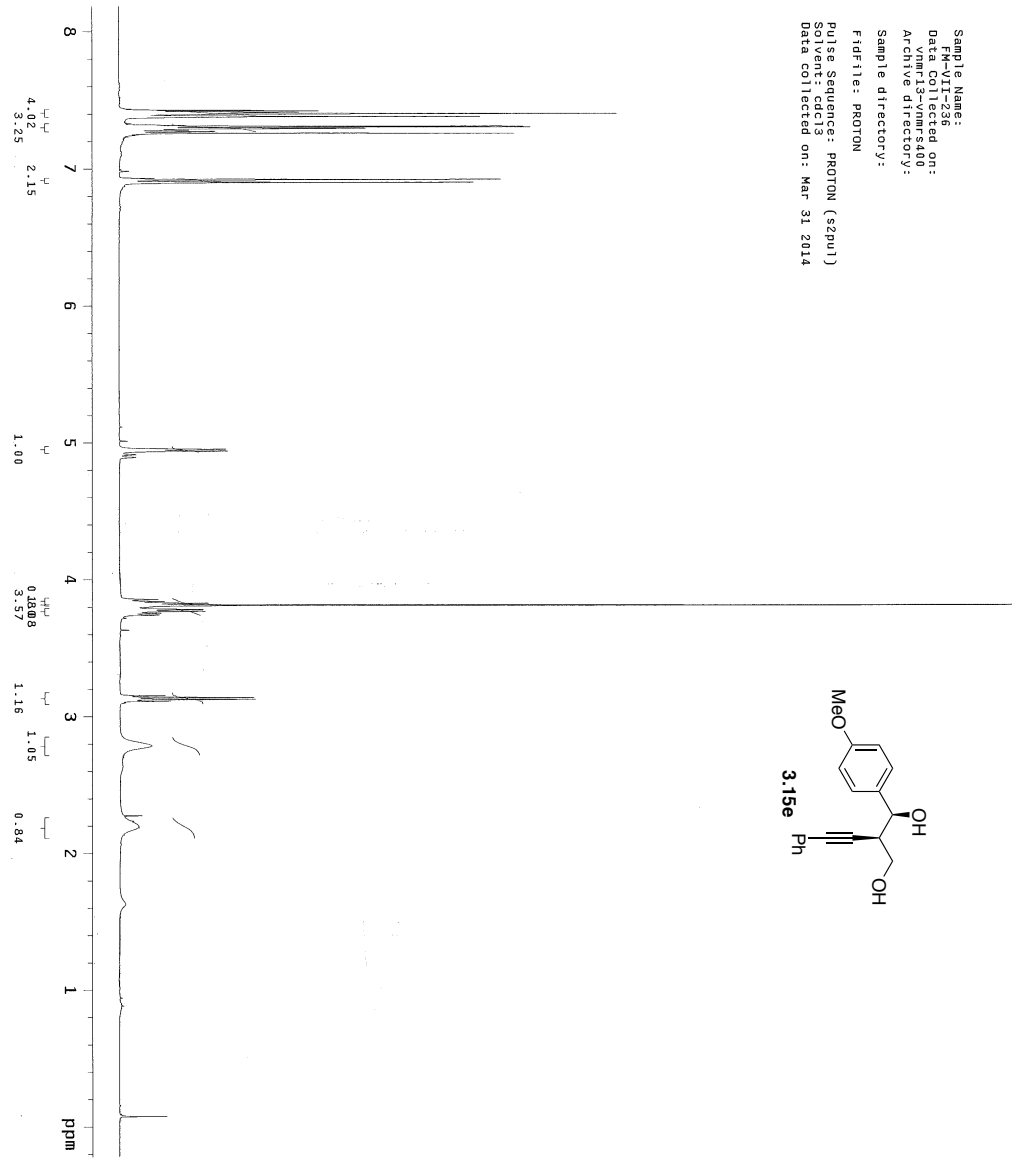
FidFile: FM-VII-245-CNMR

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 11 2014



3.15d



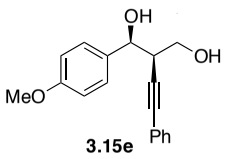

Sample Name:
PM-VII-236
Data Collected on:
vnmrl3-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 31 2014
MeO
OH
OH
Ph
3.15e
8
7
6
5
4
3
2
1
ppm
4.02
2.15
3.25
1.00
0.88
3.57
1.16
1.05
0.84

Sample Name:
FM-VII-236
Data Collected on:
vnmr13-vnmrs400
Archive directory:

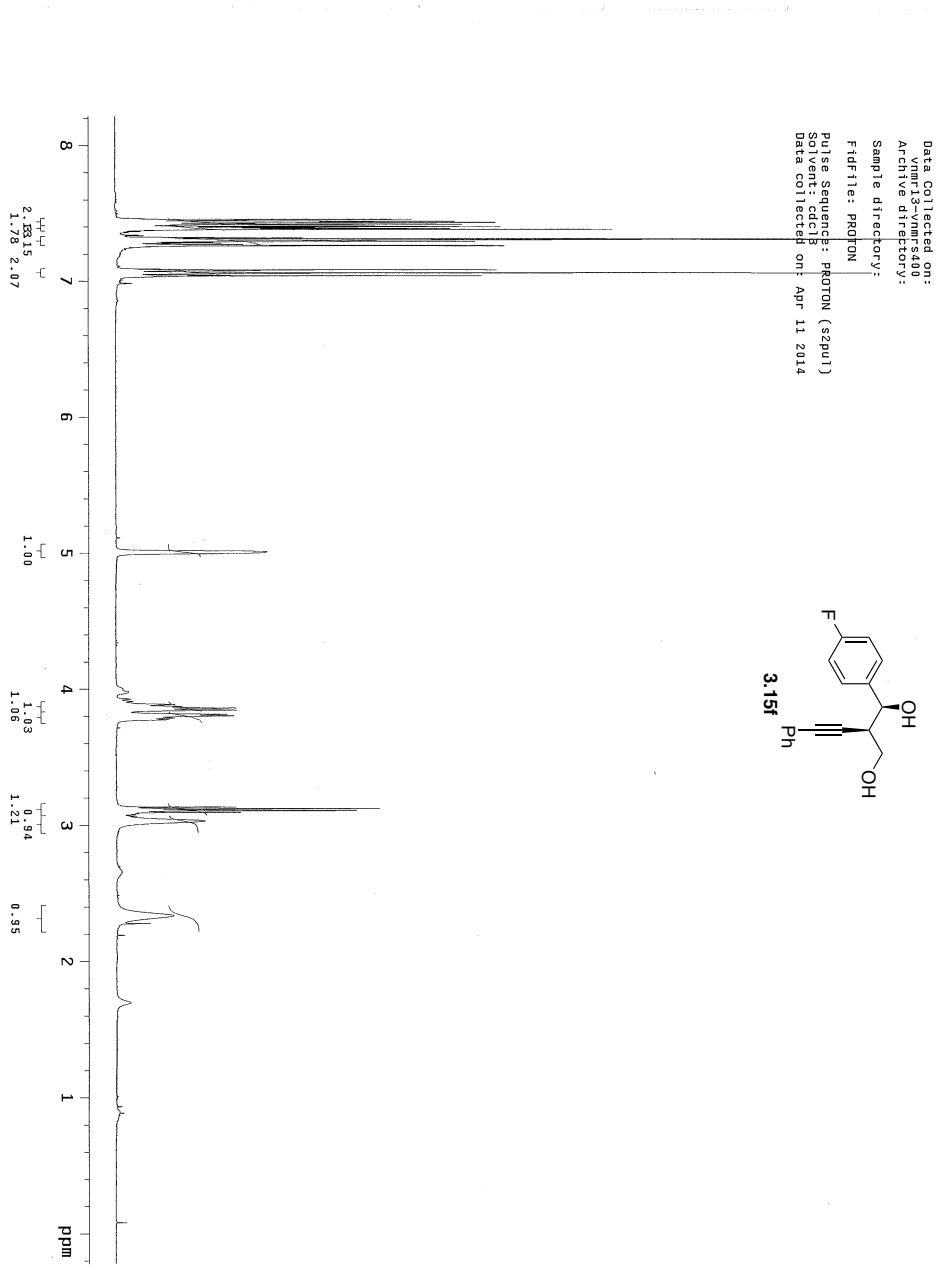
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 31 2014



3.15e

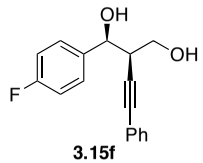

Sample Name:
FM-VII-253
Data Collected on:
vnmrj3-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 11 2014
F
OH
Ph
OH
3.15f
8
7
6
5
4
3
2
1
ppm
2.15
1.78
2.07
1.00
1.03
1.06
0.94
1.21
0.95

Sample Name:
FM-VII-253-CNMR
Data Collected on:
vnmr13-vnmrs400
Archive directory:

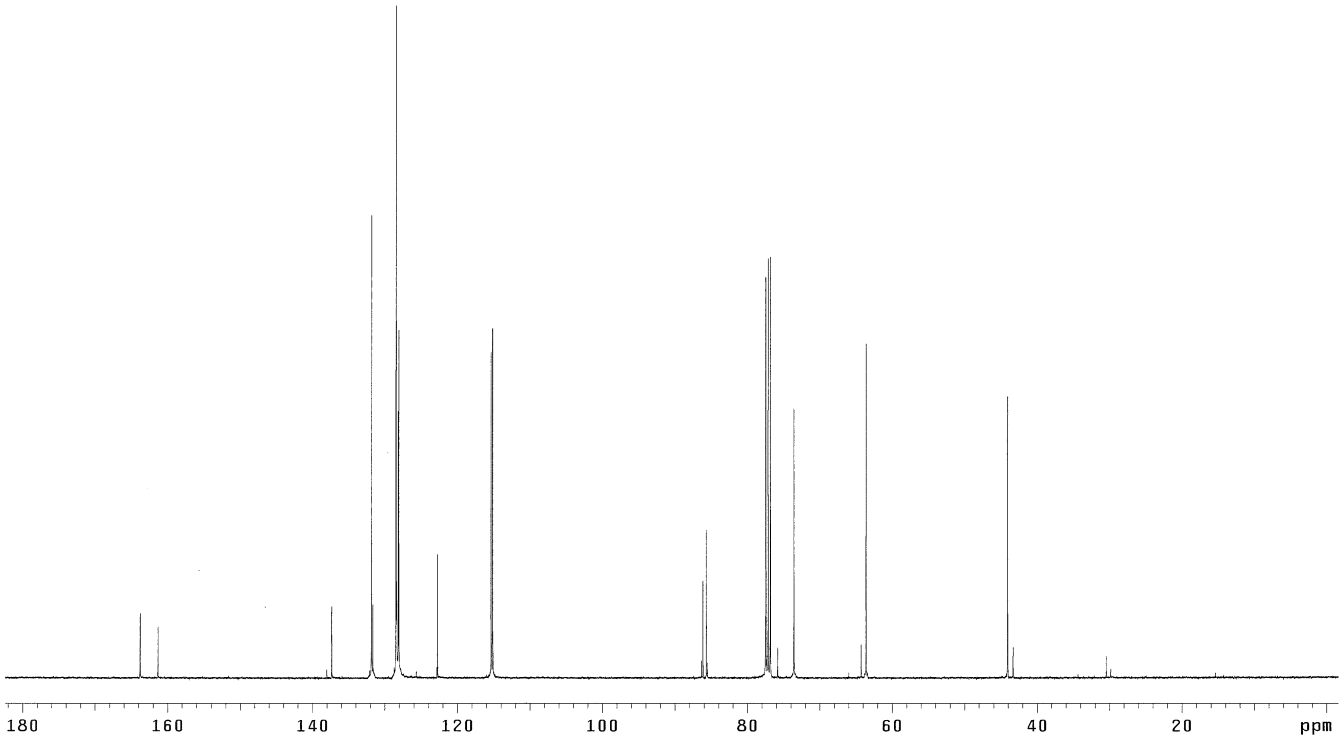
Sample directory:

FidFile: FM-VII-253-CNMR

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 16 2014



3.15f

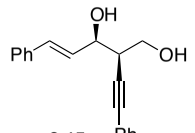


Sample Name:
FM-VII-235
Data Collected on:
vnmr13-vnmrs400
Archive directory:

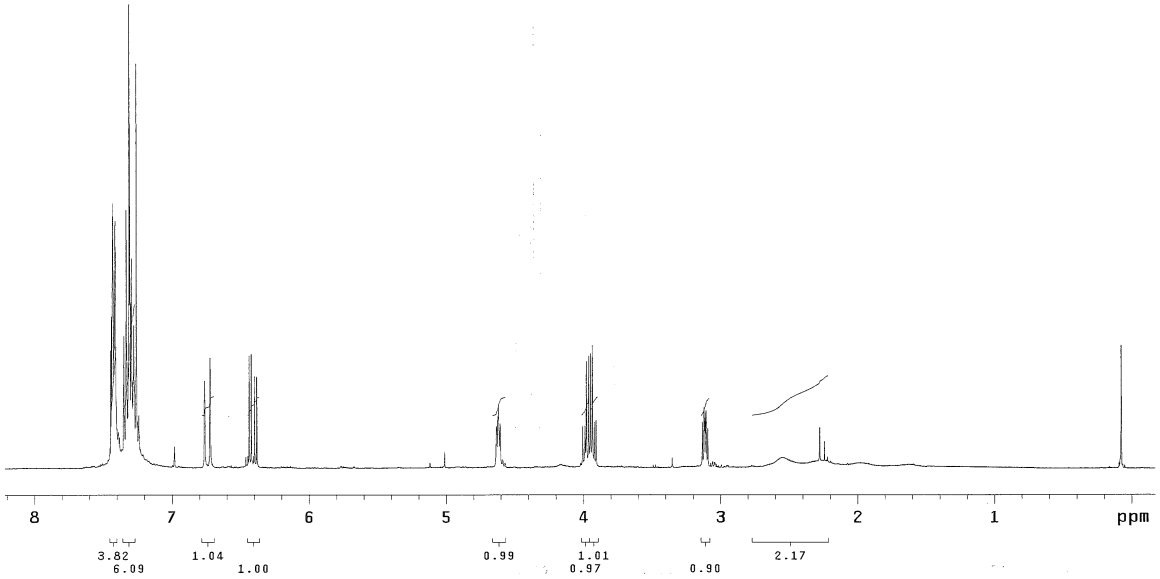
Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 31 2014



3.15g

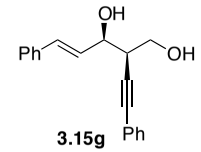


Sample Name:
FM-VII-235
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 31 2014



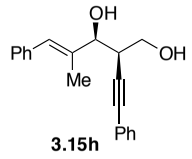
3.15g

Sample Name:
FM-VII-257
Data Collected on:
vnmr13-vnmrs400
Archive directory:

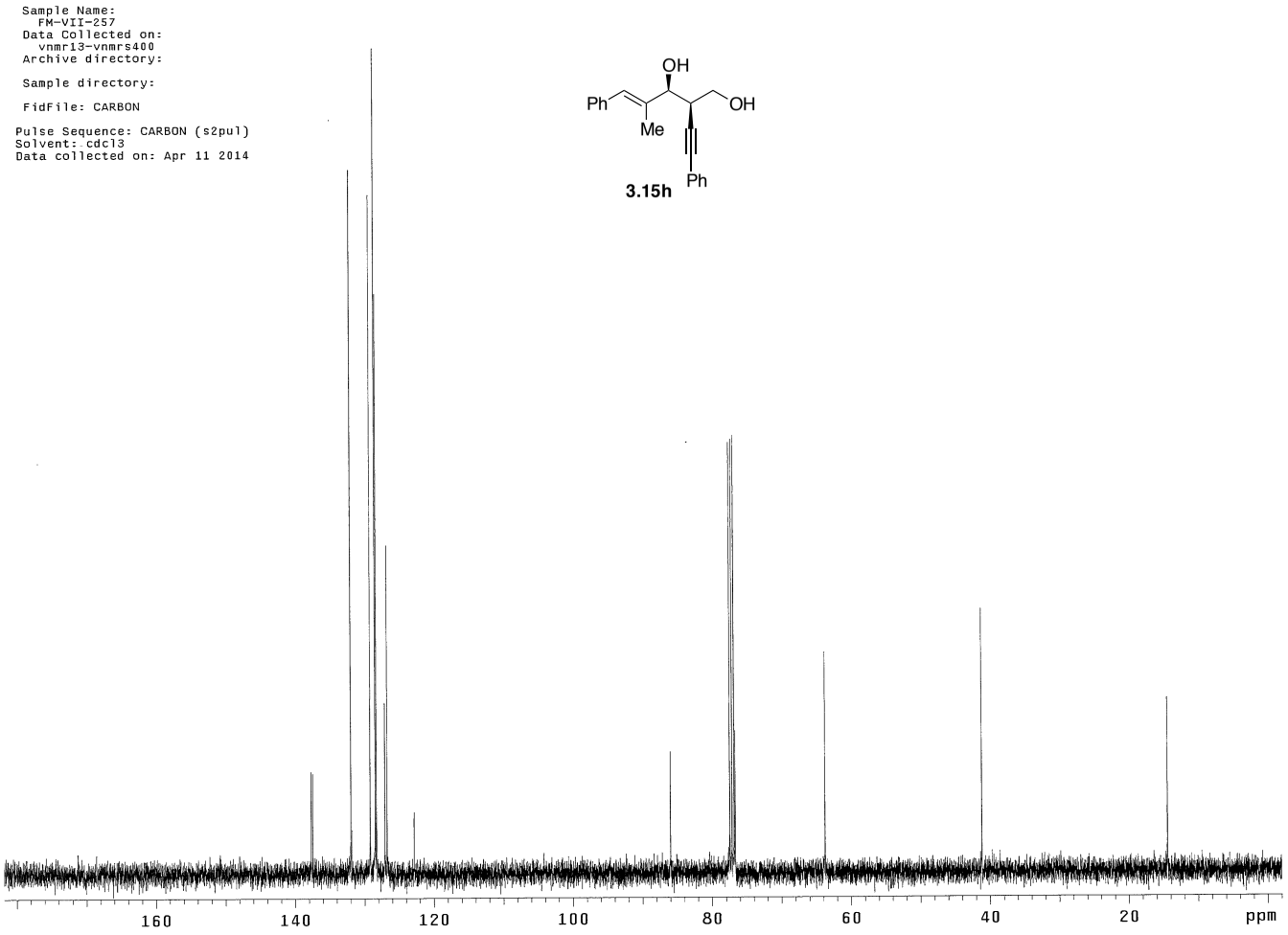
Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 11 2014



3.15h

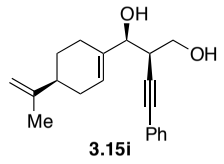

Sample Name:
FM-VII-257
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: CARBON
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 11 2014
OH
Ph
OH
Me
Ph
3.15h
160
140
120
100
80
60
40
20
ppm

Sample Name:
FM-VII-260
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 11 2014



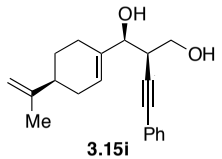
3.15i

Sample Name:
FM-VII-260
Data Collected on:
vnmr13-vnmrs400
Archive directory:

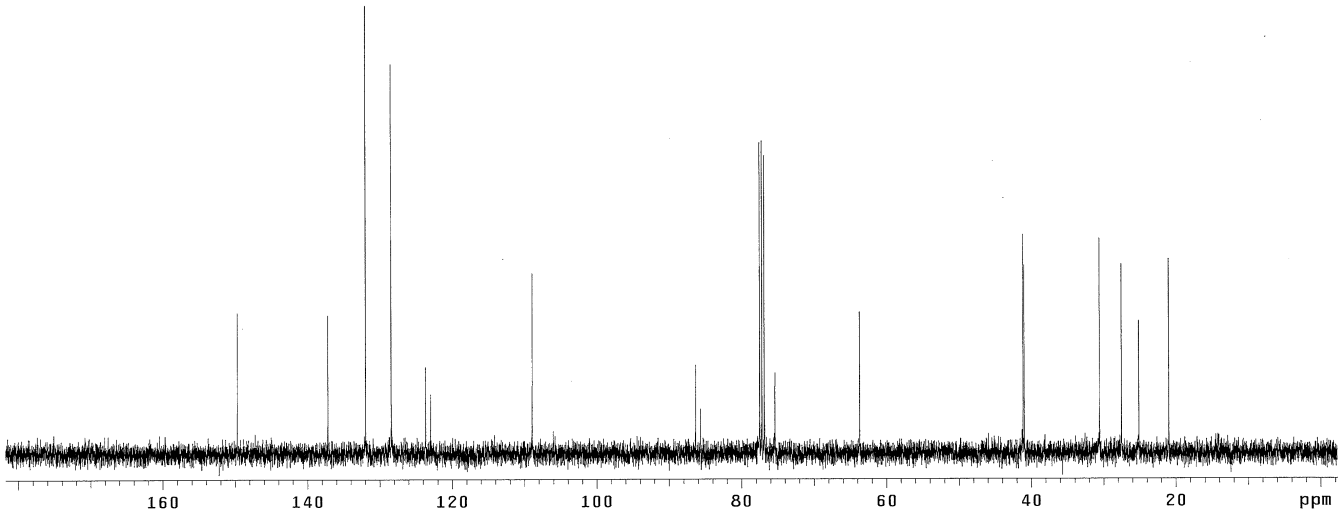
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 11 2014



3.15i

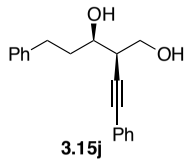


Sample Name:
FM-VII-234
Data Collected on:
vnmr13-vnmrs400
Archive directory:

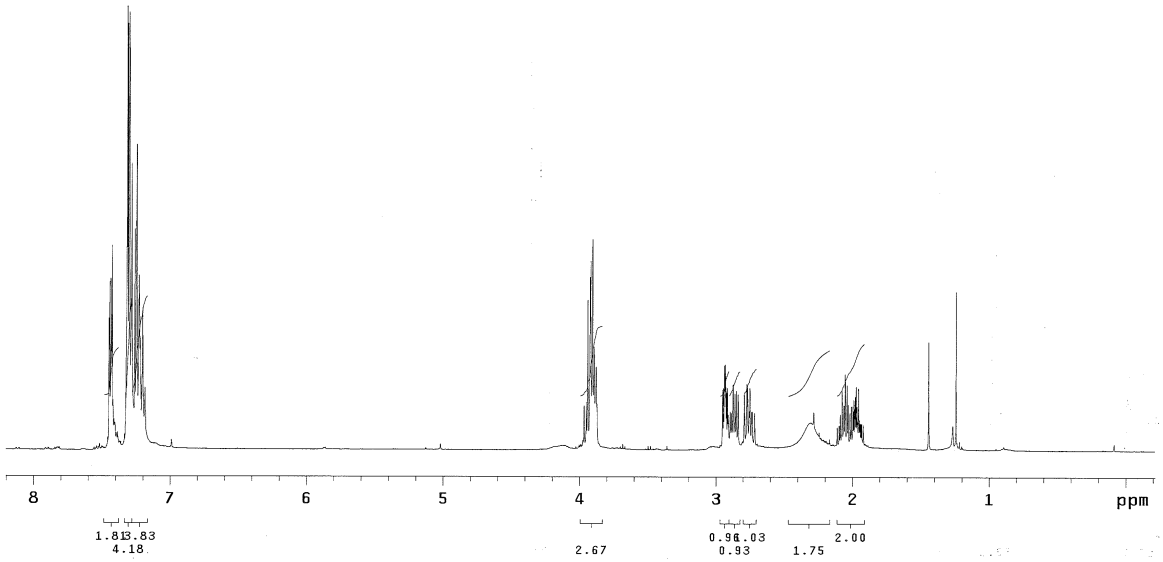
Sample directory:

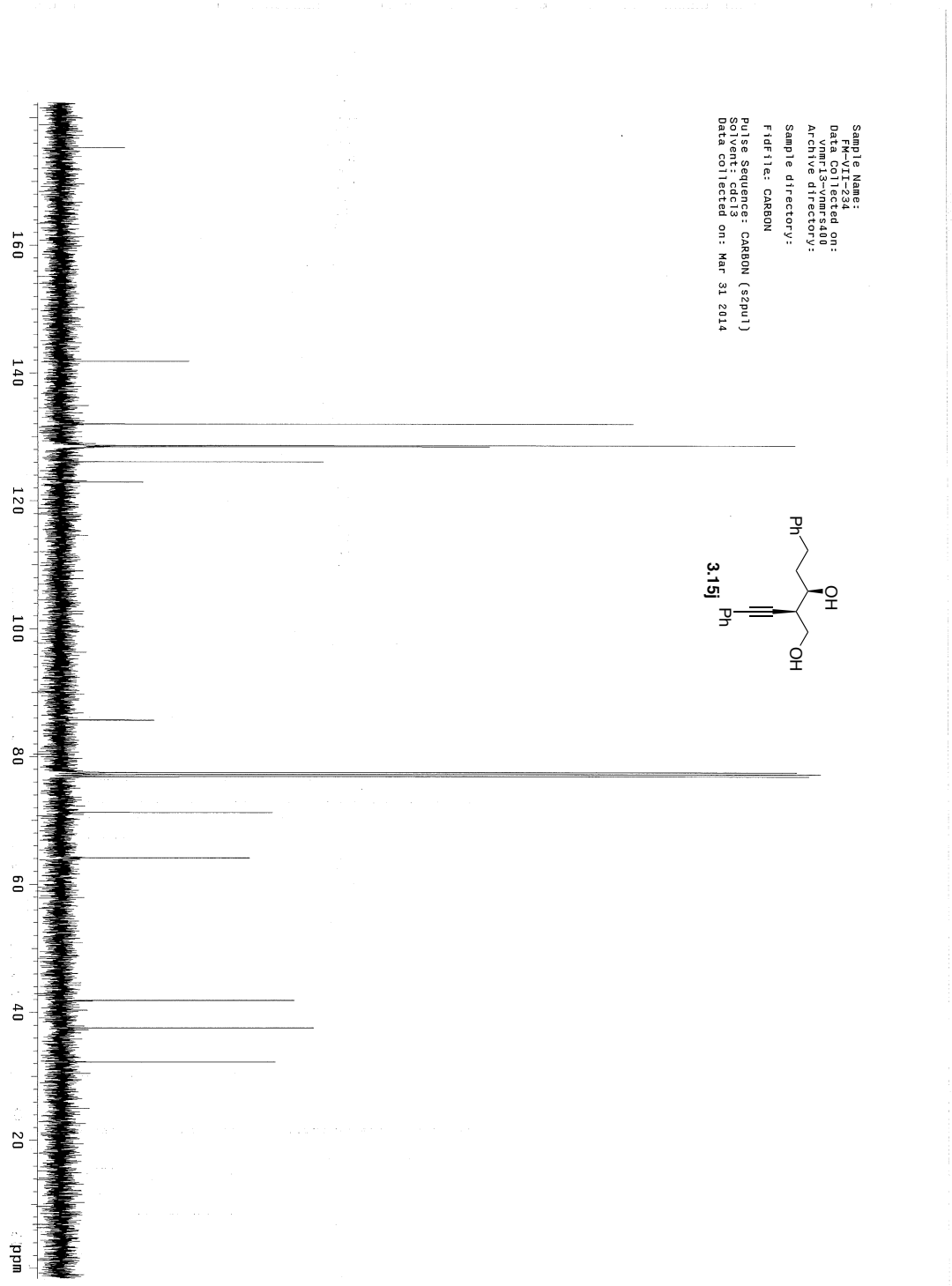
FidFile: PROTON

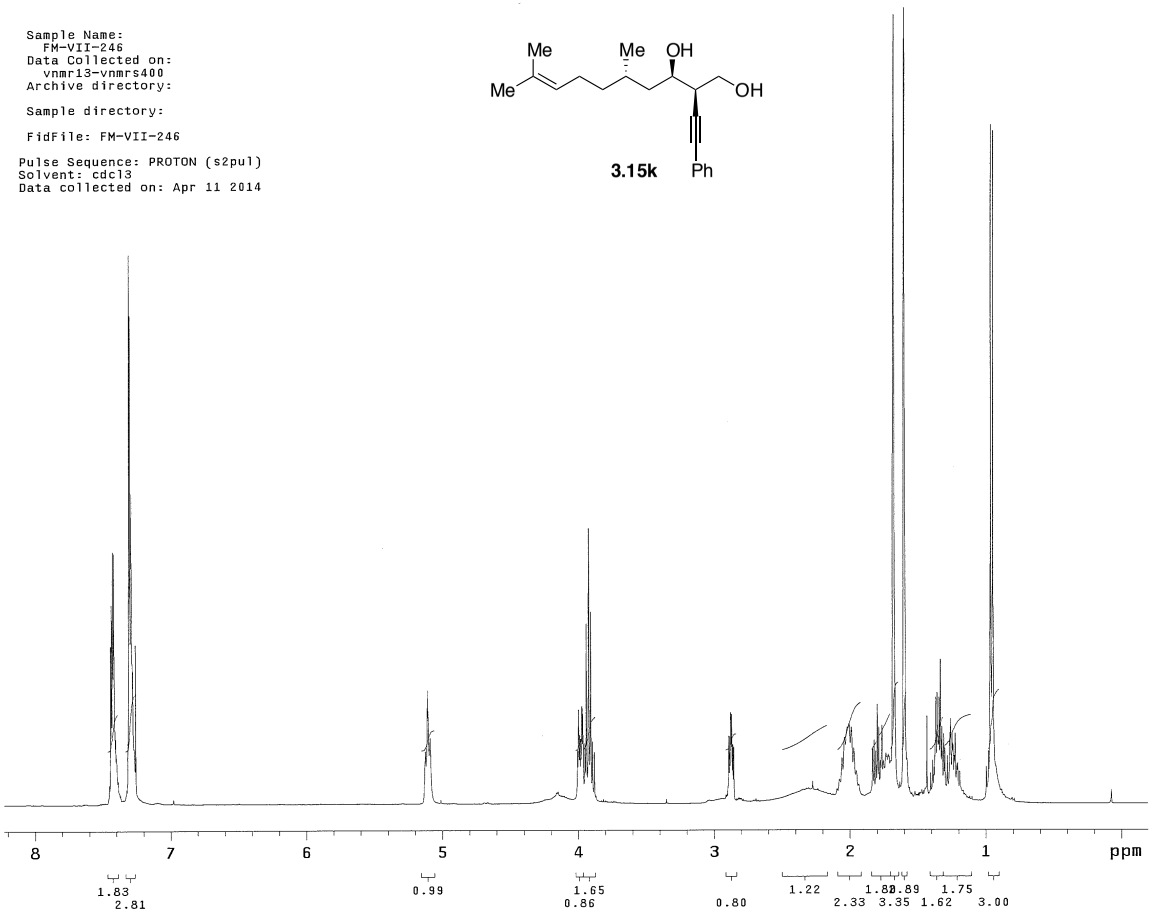
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 31 2014



3.15j




Sample Name:
FM-VII-234
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: CARBON
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 31 2014
Ph
OH
OH
Ph
3.15j
160
140
120
100
80
60
40
20
ppm

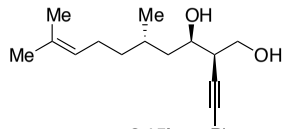

Sample Name:
FM-VII-246
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: FM-VII-246
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 11 2014
Me
Me
OH
Me
OH
3.15k
Ph
8
7
6
5
4
3
2
1
ppm
1.83
2.81
0.99
1.65
0.86
0.80
1.22
2.33
1.88
3.35
1.89
1.62
1.75
3.00

Sample Name:
FM-VII-246
Data Collected on:
vnmr13-vnmrs400
Archive directory:

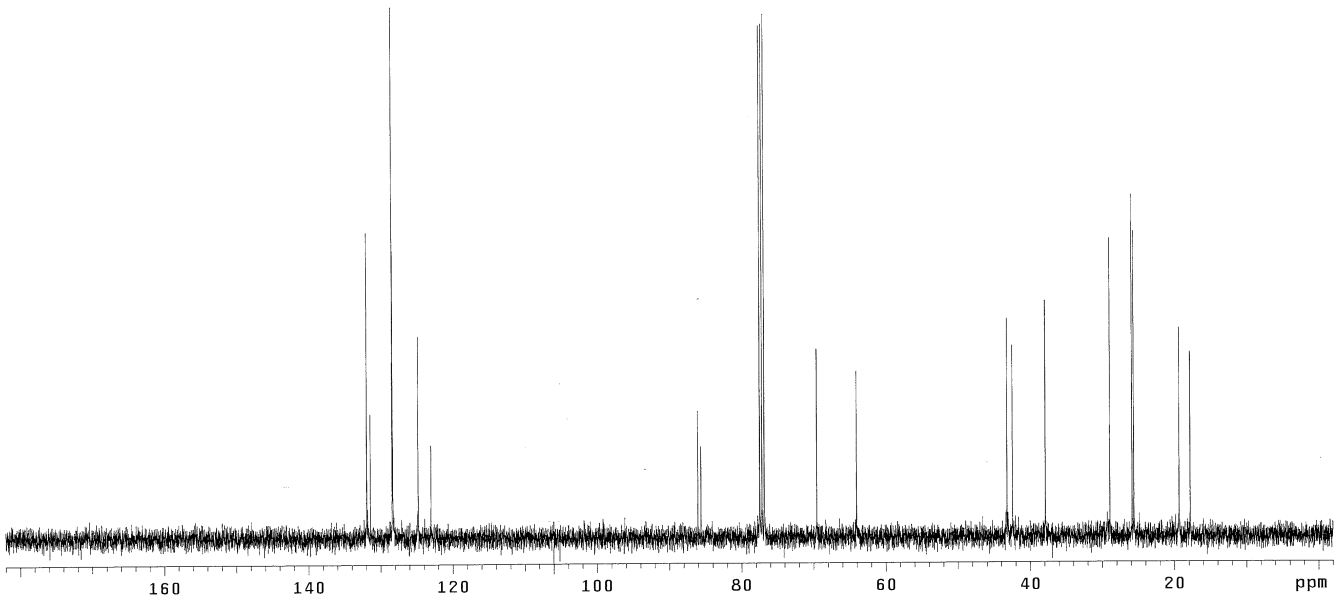
Sample directory:

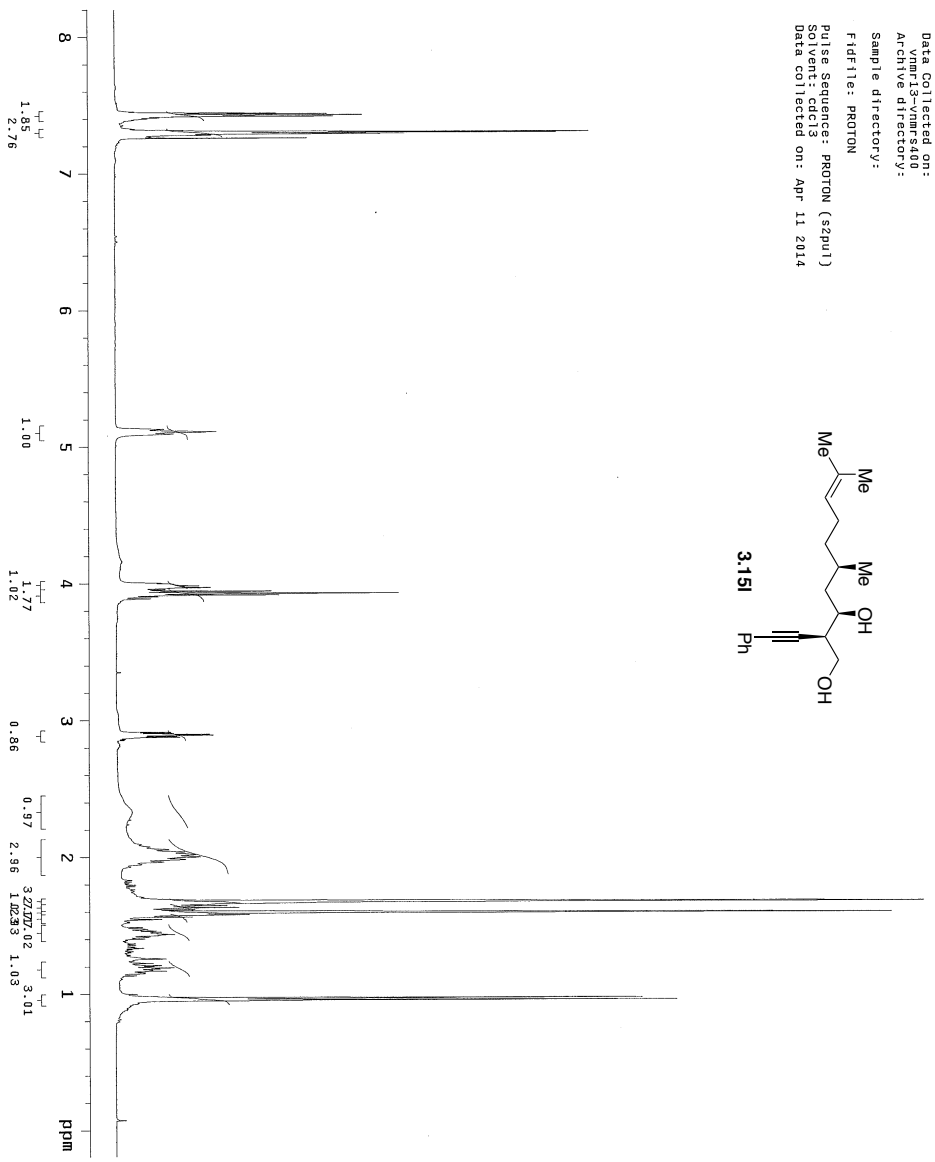
FidFile: FM-VII-246-CNMR

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 11 2014



3.15k



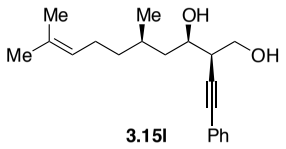

Sample Name:
FM-VII-251
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 11 2014
Me
Me
Me
OH
OH
Ph
3.15l
8
7
6
5
4
3
2
1
ppm
1.85
2.76
1.00
1.77
1.02
0.86
0.97
2.96
3.27
7.02
1.03
3.01
1.03

Sample Name:
FM-VII-251
Data Collected on:
vnmr13-vnmrs400
Archive directory:

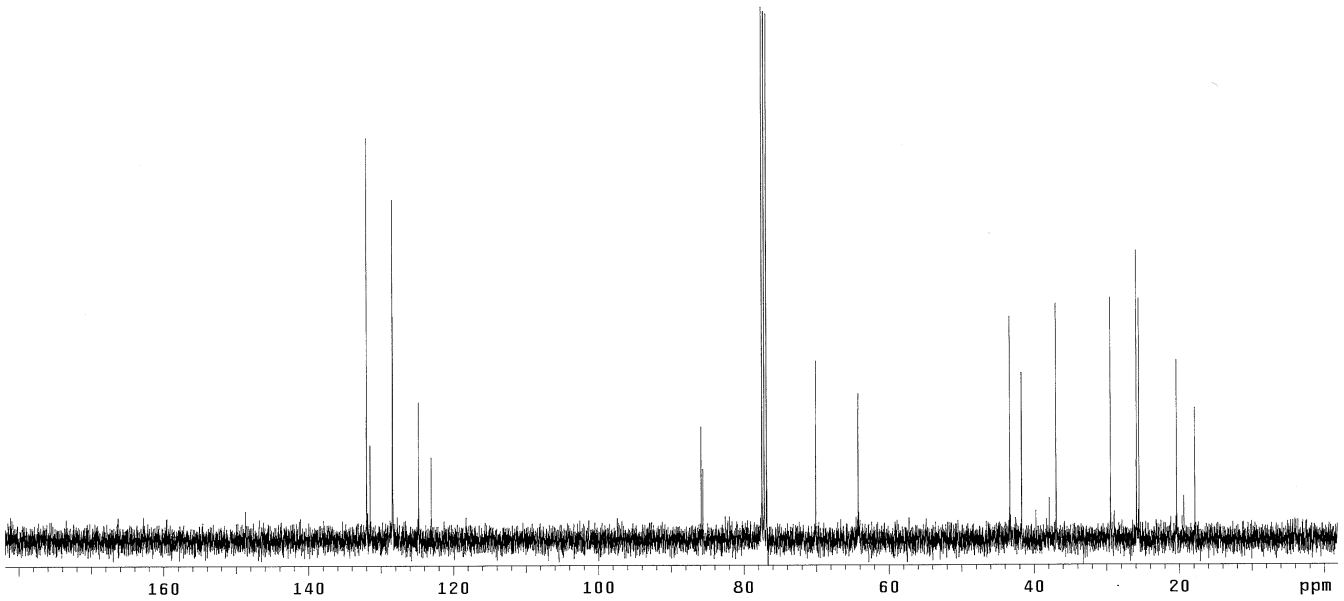
Sample directory:

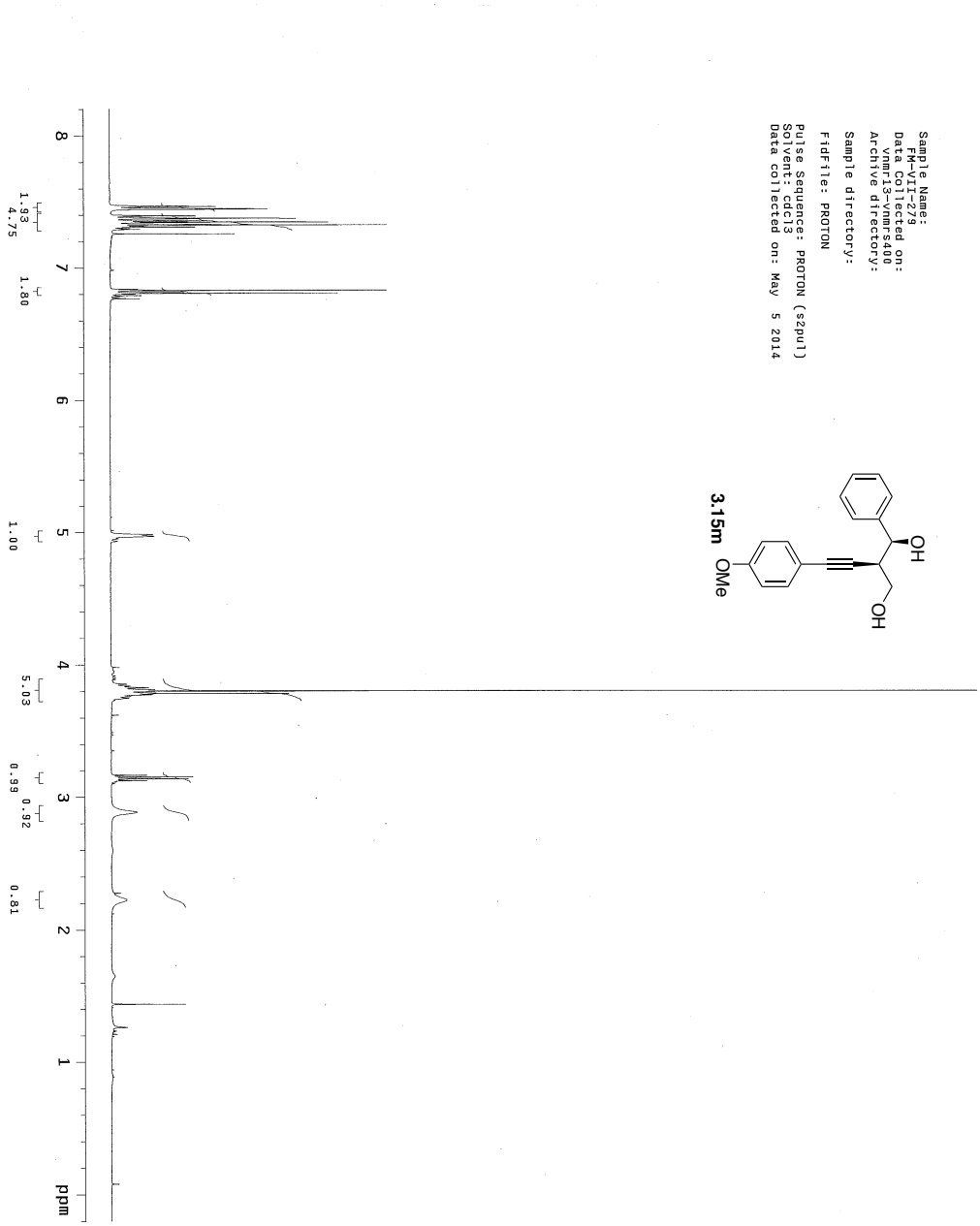
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 11 2014



3.15l



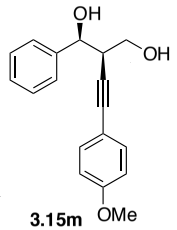

Sample Name:
FM-VII-279
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 5 2014
3.15m
OMe
OH
OH
8
7
6
5
4
3
2
1
ppm
1.93
4.75
1.80
1.00
5.03
0.99
0.92
0.81

Sample Name:
FM-VII-279
Data Collected on:
vnmr13-vnmrs400
Archive directory:

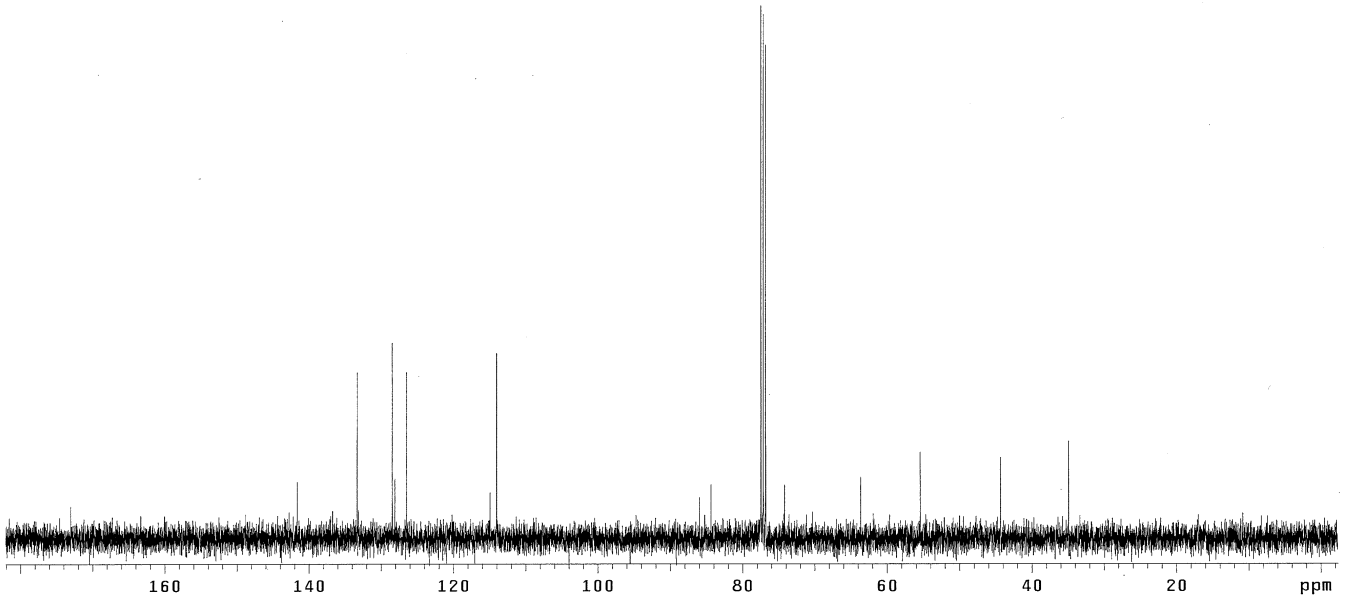
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 5 2014



3.15m

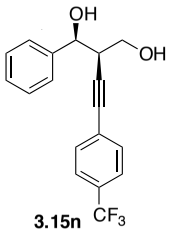


Sample Name:
FM-VII-278
Data Collected on:
vnmr13-vnmrs400
Archive directory:

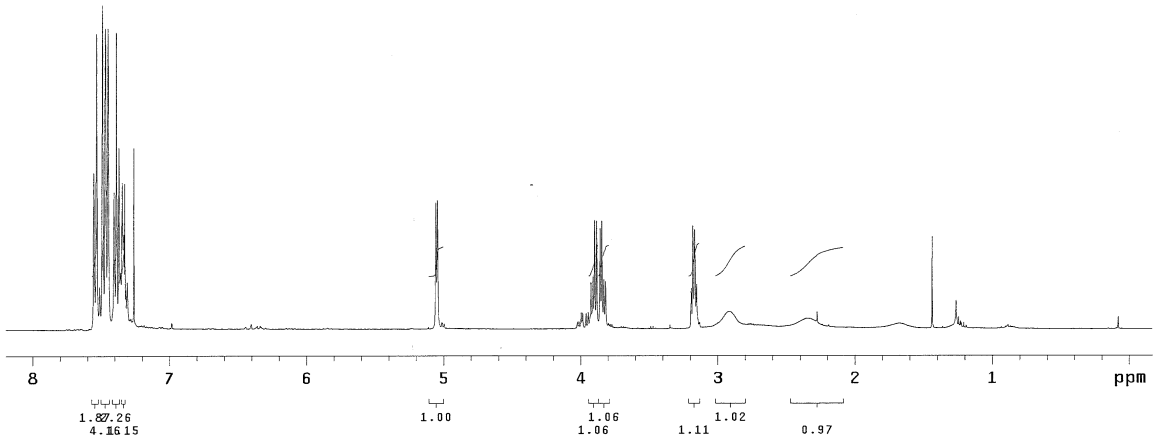
Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 15 2014



3.15n

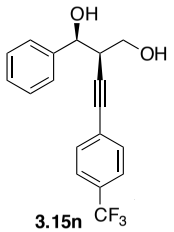


Sample Name:
FM-VII-278
Data Collected on:
vnmri3-vnmrs400
Archive directory:

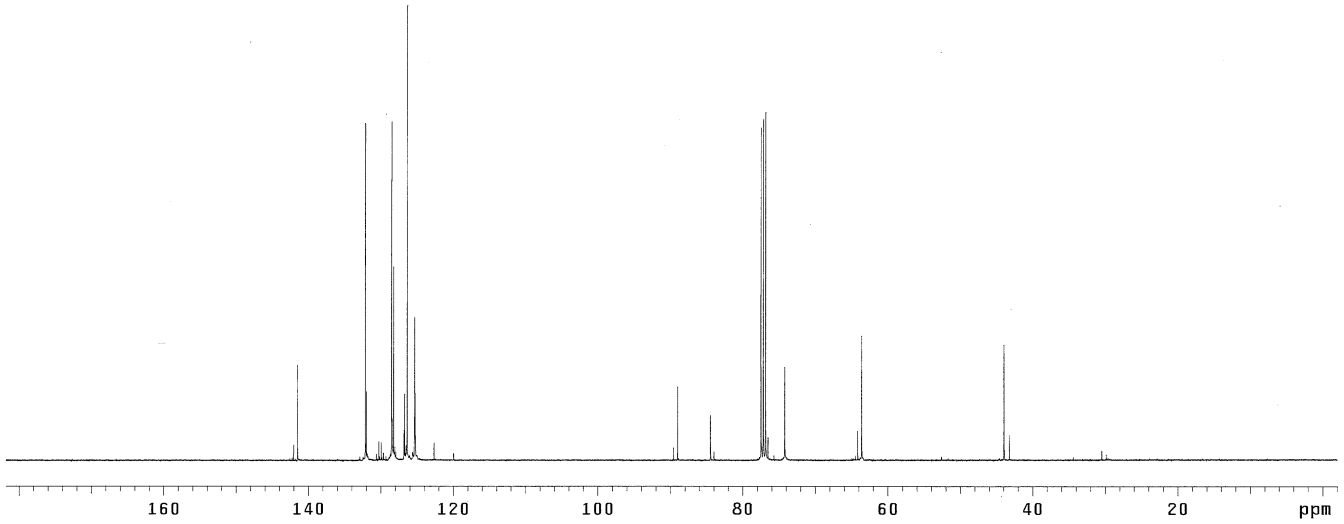
Sample directory:

FidFile: FM-VII-278-CNMR

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 15 2014



3.15n

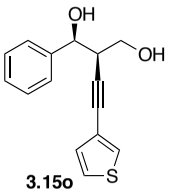


Sample Name:
FM-VII-290
Data Collected on:
vnmr13-vnmrs400
Archive directory:

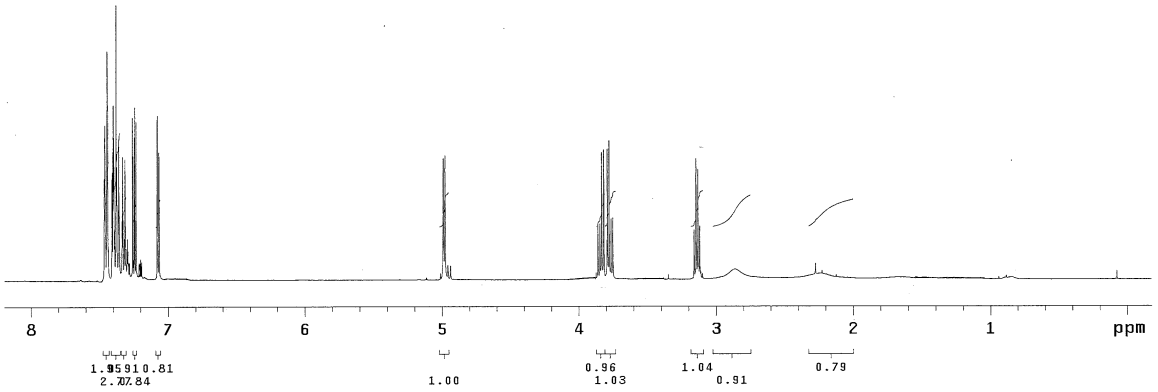
Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 14 2014



3.15o

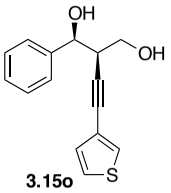


Sample Name:
FM-VII-290
Data Collected on:
vnmr13-vnmrs400
Archive directory:

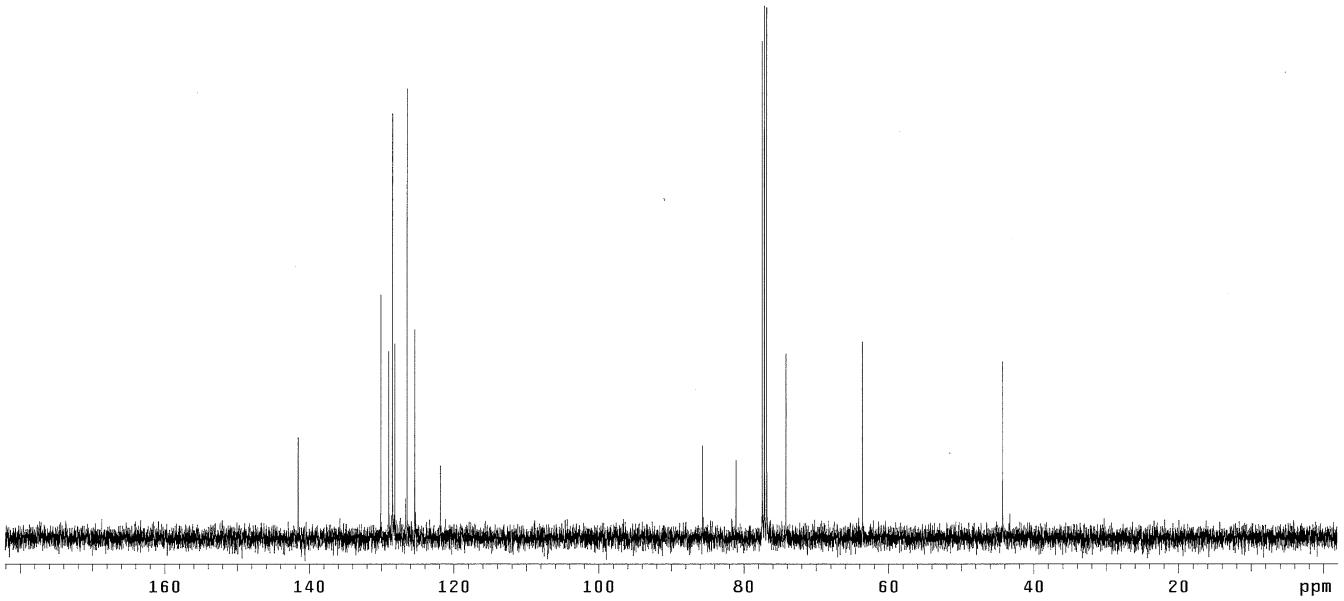
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 14 2014



3.15o

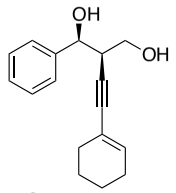


Sample Name:
FM-VII-283
Data Collected on:
vnmr13-vnmrs400
Archive directory:

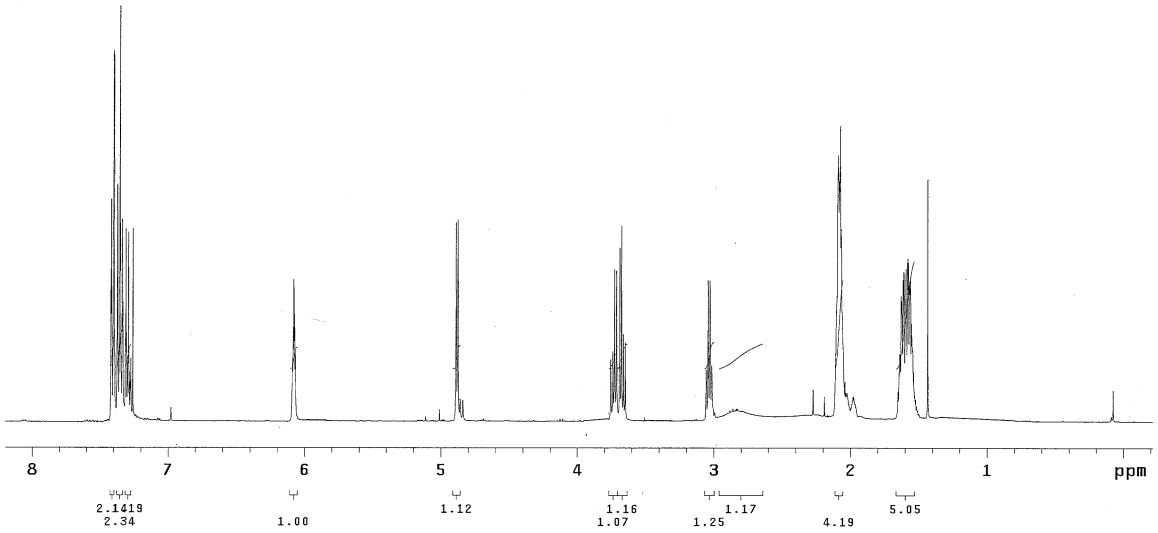
Sample directory:

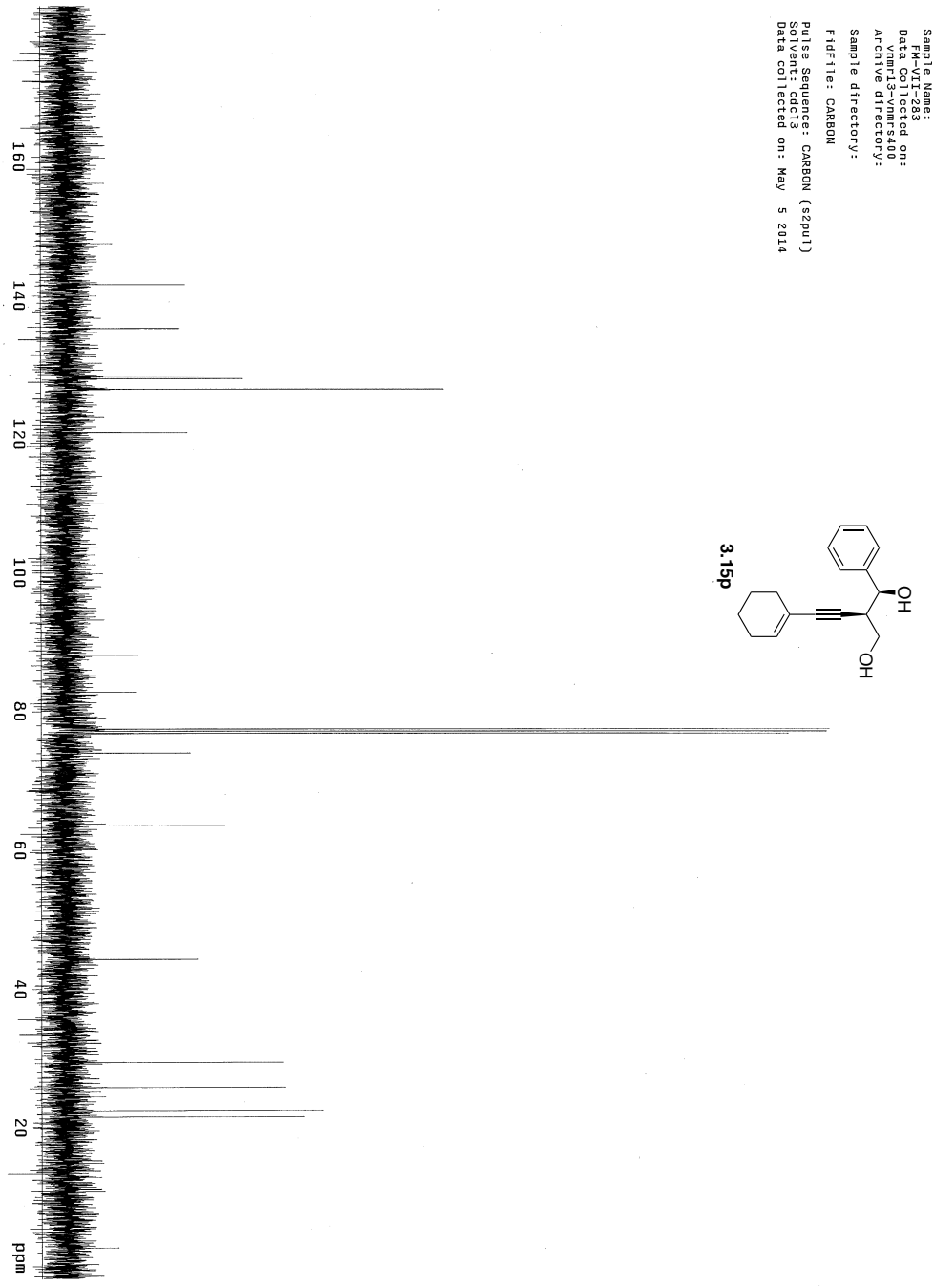
FidFile: PROTON

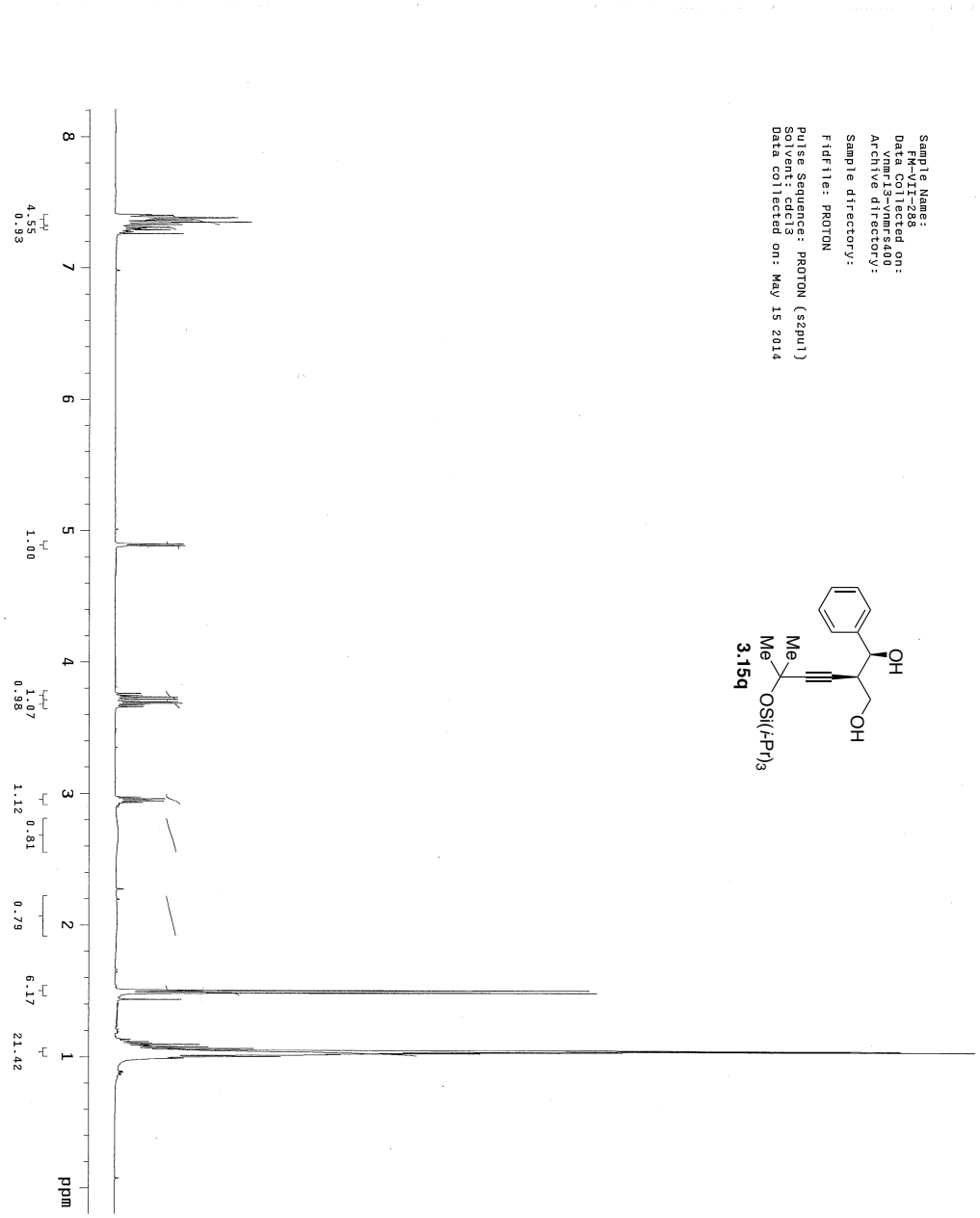
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 5 2014



3.15p




Sample Name:
FM-VII-283
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: CARBON
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 5 2014
3.15p
OH
OH
160
140
120
100
80
60
40
20
ppm

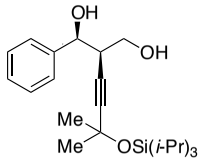

Sample Name:
FM-VII-288
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 15 2014
OH
OH
Me
Me
OSi(i-Pr)3
3.15q
8
7
6
5
4
3
2
1
ppm
4.55
0.93
1.00
1.07
0.98
1.12
0.81
0.79
6.17
21.42

Sample Name:
FM-VII-288
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 15 2014



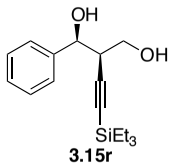
3.15q

Sample Name:
FM-VII-226
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: FM-VII-226

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 24 2014



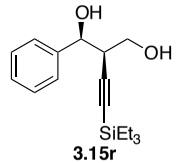
3.15r

Sample Name:
FM-VII-226
Data Collected on:
vnmr13-vnmrs400
Archive directory:

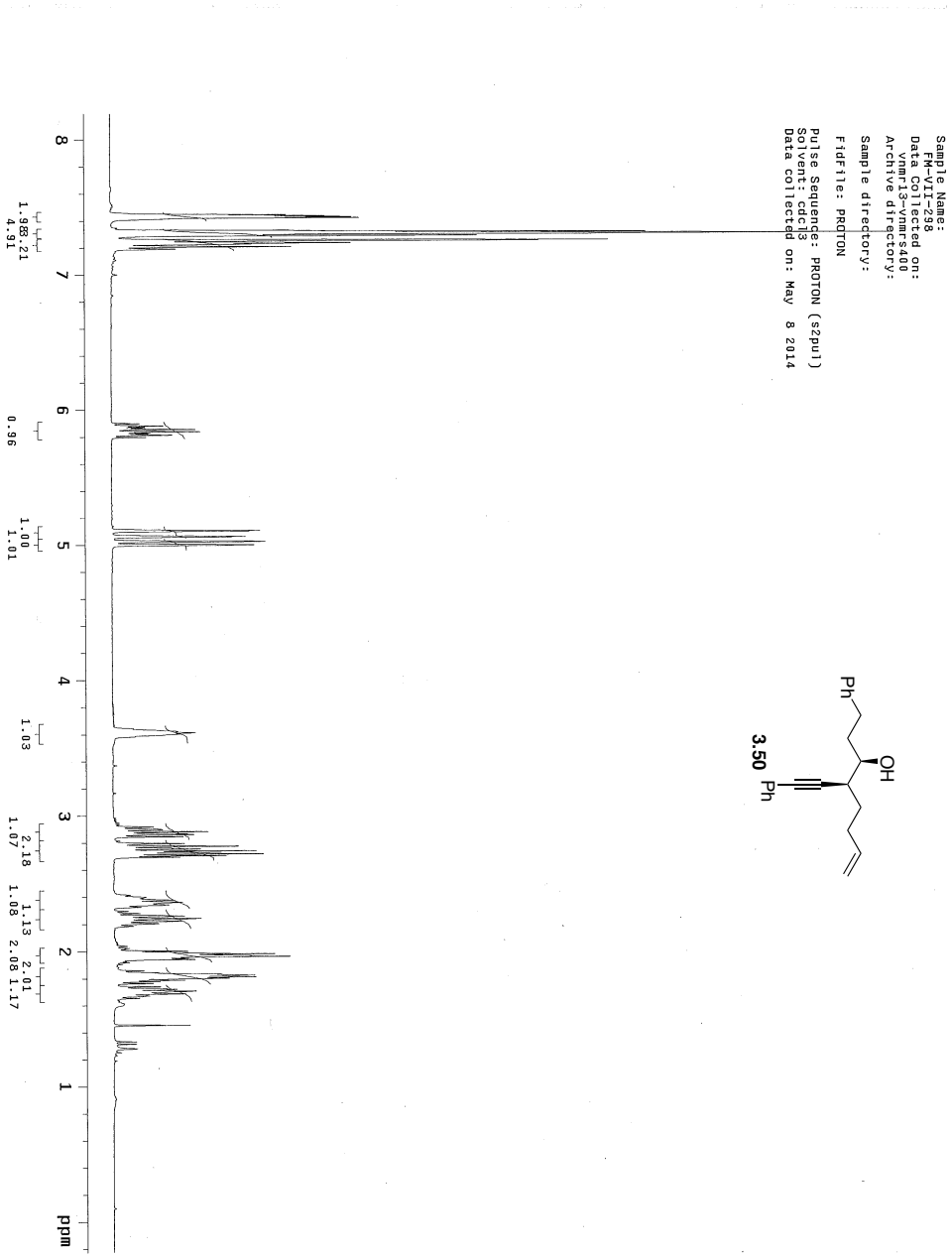
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 24 2014



3.15r

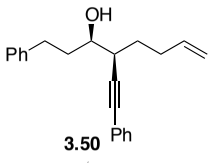

Sample Name:
FM-VII-298
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 8 2014
Ph
OH
3.50
Ph
8
7
6
5
4
3
2
1
ppm
1.98
4.91
21
0.96
1.00
1.01
1.03
2.18
1.07
1.13
1.08
2.01
2.08
1.17

Sample Name:
FM-VII-298
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 8 2014



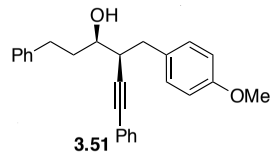
3.50

Sample Name:
FM-VII-297
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 8 2014



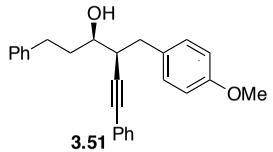
3.51

Sample Name:
FM-VII-297
Data Collected on:
vnmr13-vnmrs400
Archive directory:

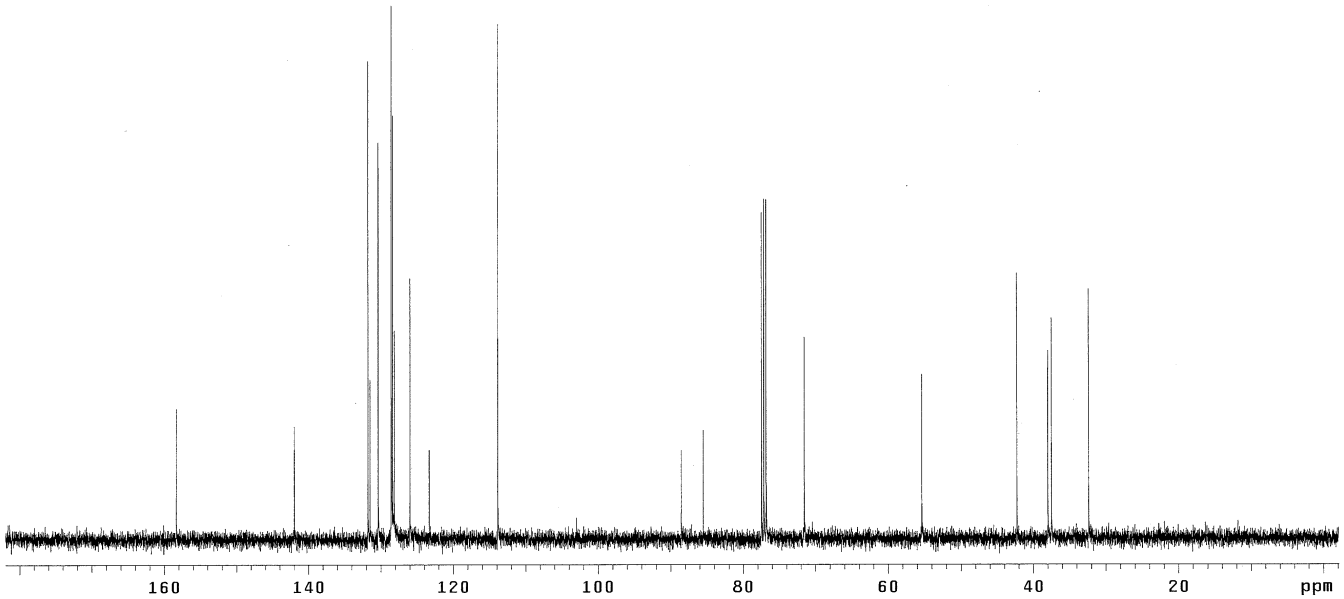
Sample directory:

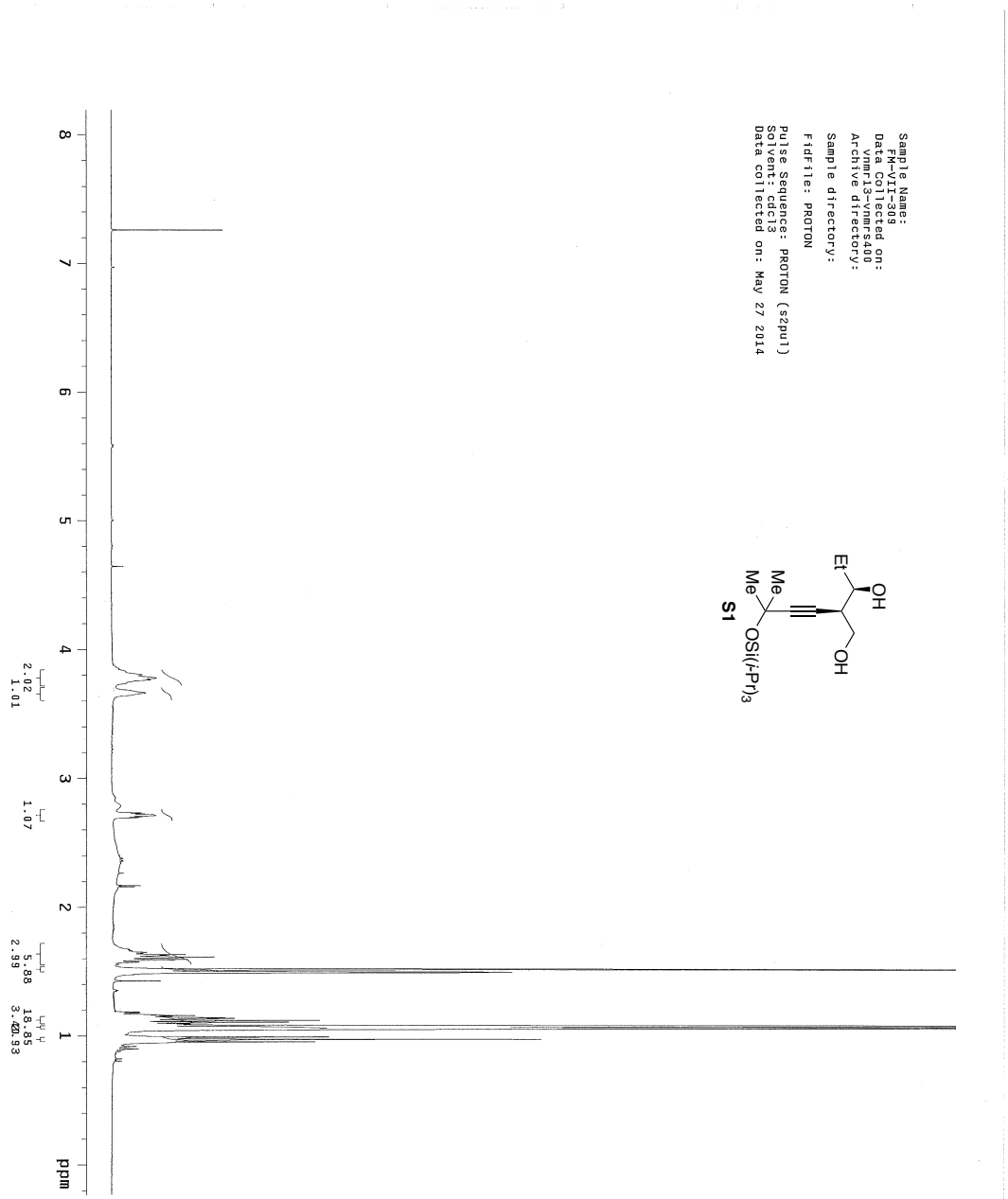
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 8 2014



3.51



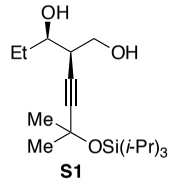

Sample Name:
FM-VII-309
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 27 2014
Et
OH
OH
Me
Me
OSi(iPr)3
S1
8
7
6
5
4
3
2
1
ppm
2.02
1.01
1.07
5.88
2.99
18.85
3.42
10.93

Sample Name:
FM-VII-309
Data Collected on:
vnmr13-vnmrs400
Archive directory:

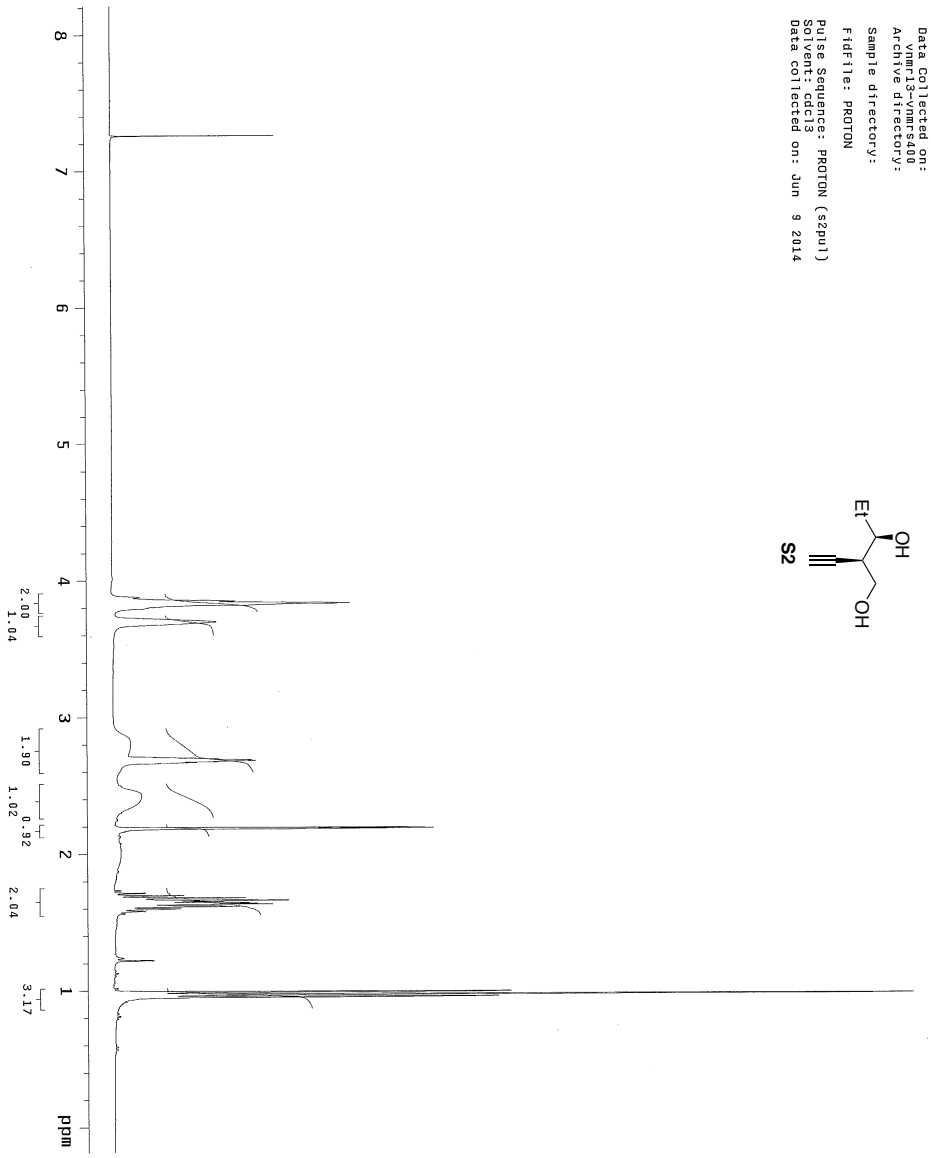
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 27 2014



S1

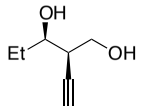

Sample Name:
FM-VII-311-alcohol
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 9 2014
Et
OH
OH
S2
8
7
6
5
4
3
2
1
ppm
2.00
1.04
1.90
1.02
0.92
2.04
3.17

Sample Name:
FM-VII-311-alcohol
Data Collected on:
vnmr13-vnmrs400
Archive directory:

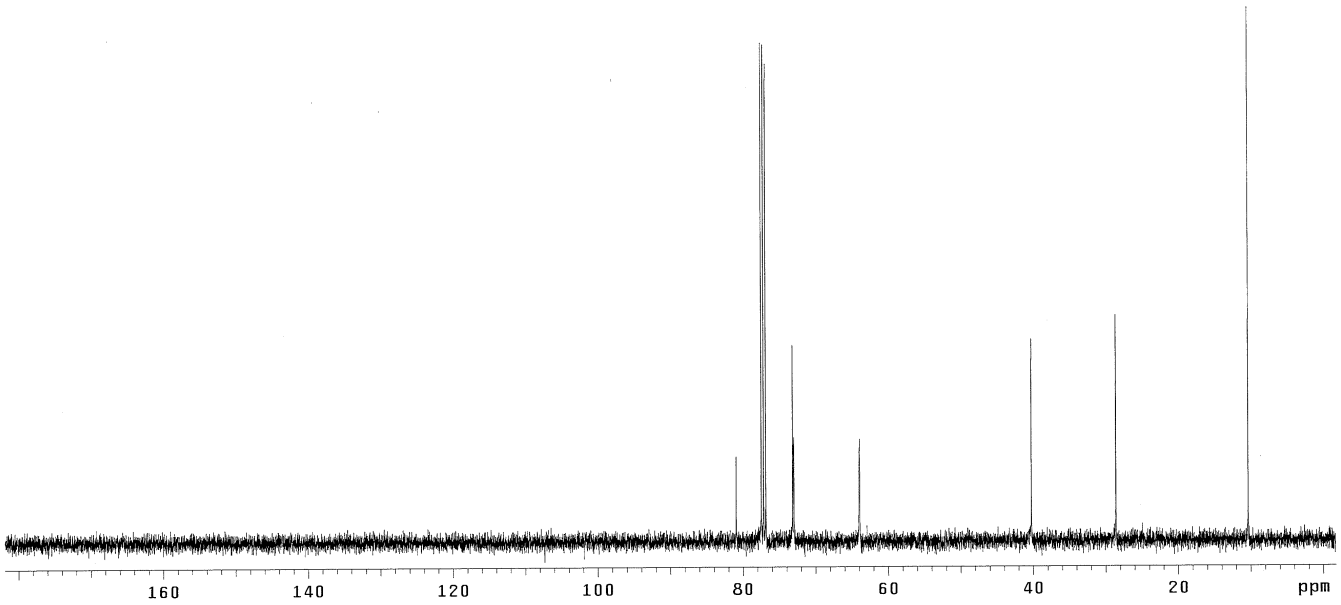
Sample directory:

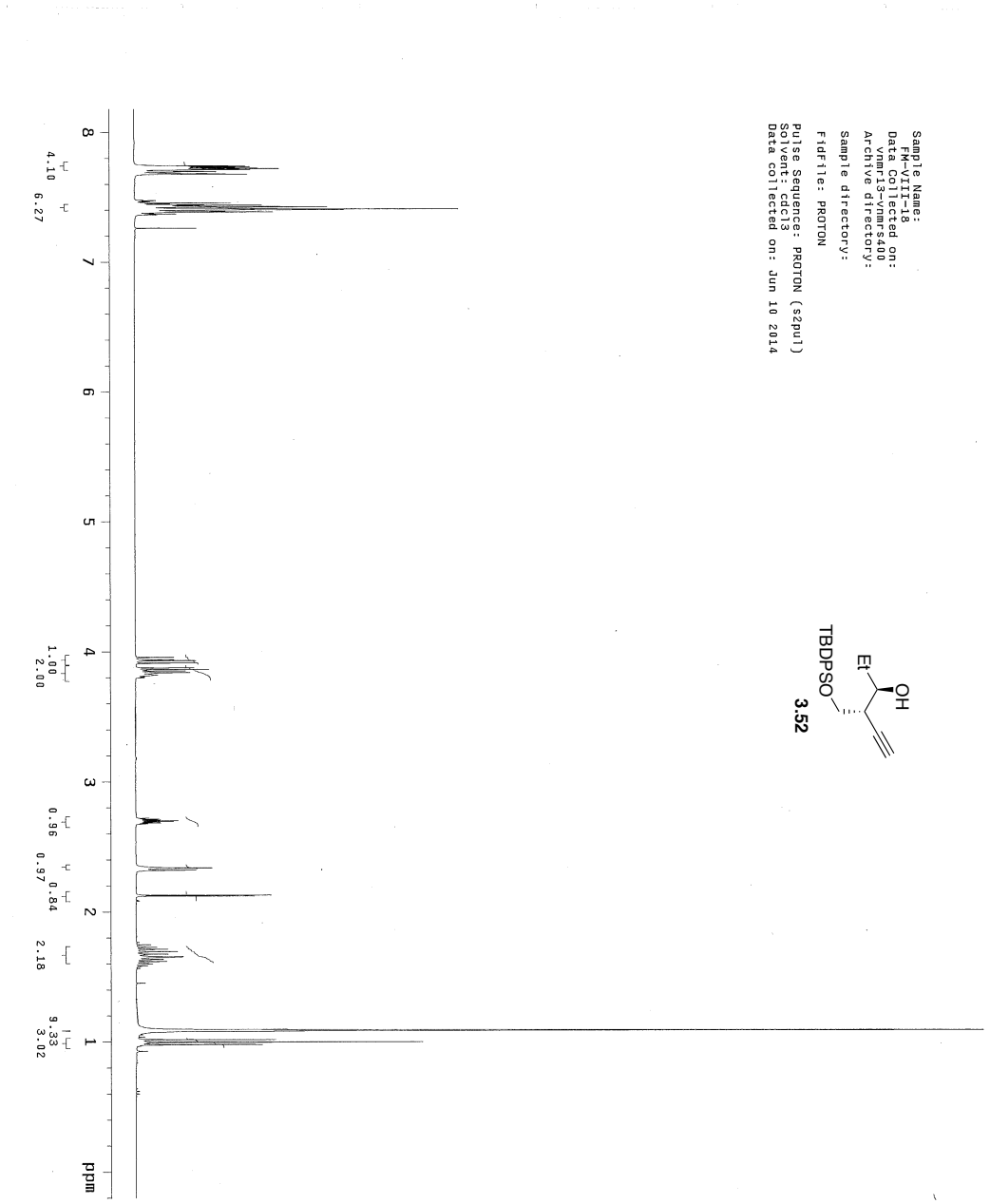
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 9 2014



S2



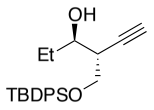

Sample Name:
FM-VII-18
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 10 2014
OH
Et
TBDPSO
3.52
8
7
6
5
4
3
2
1
ppm
4.10
6.27
1.00
2.00
0.96
0.97
0.84
2.18
9.33
3.02

Sample Name:
FM-VIII-18
Data Collected on:
vnmr13-vnmrs400
Archive directory:

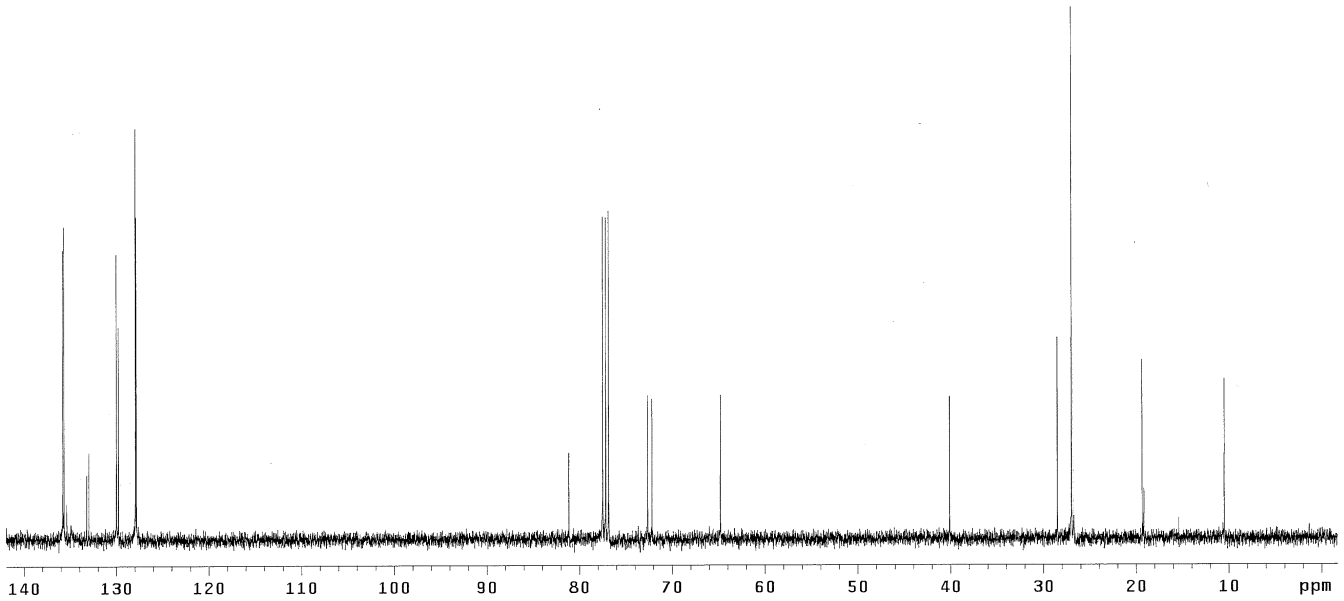
Sample directory:

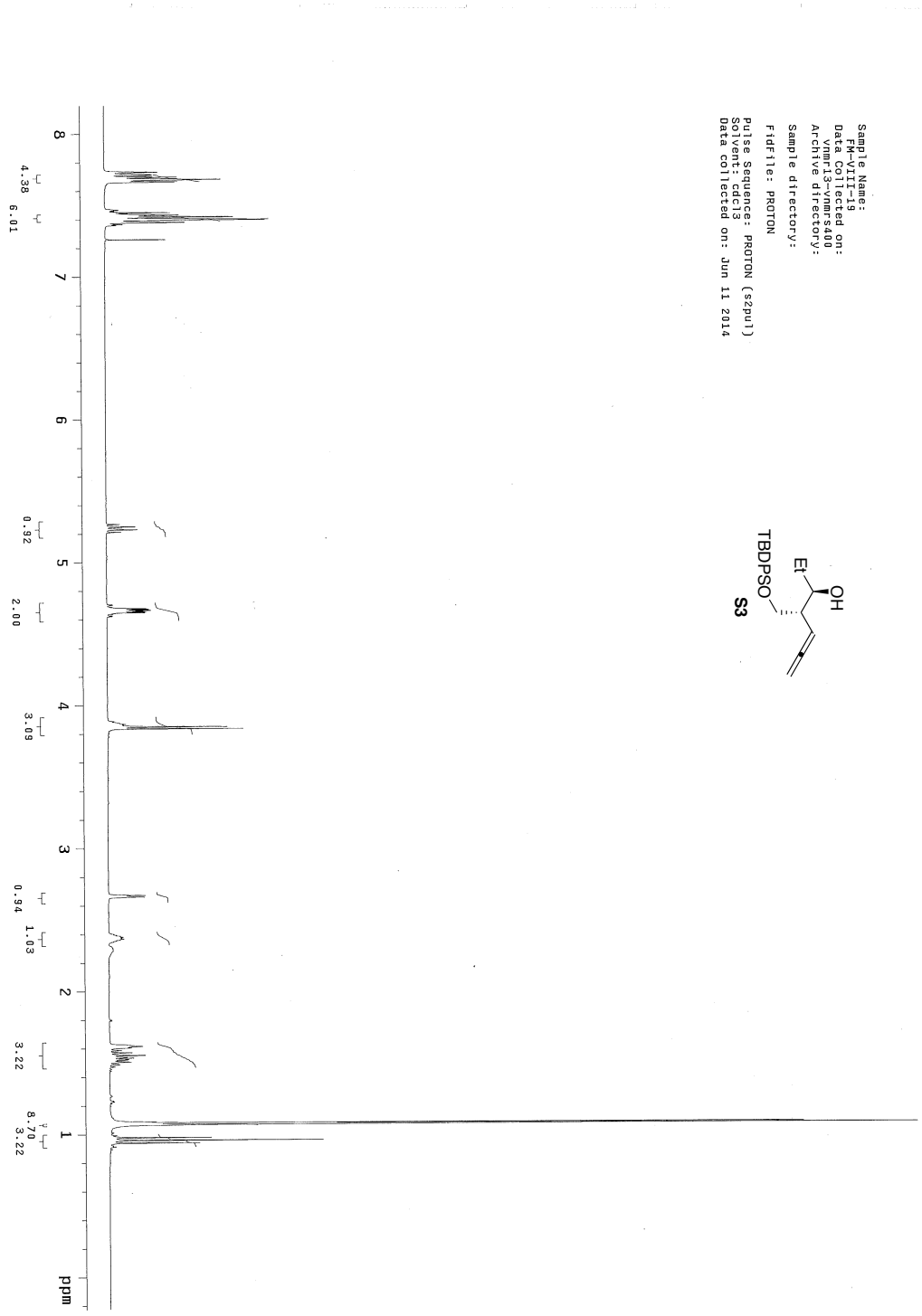
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 10 2014



3.52



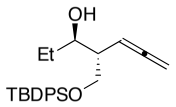

Sample Name:
FM-VII-1g
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 11 2014
OH
Et
TBDPSO
S3
8
7
6
5
4
3
2
1
ppm
4.38
6.01
0.92
2.00
3.09
0.94
1.03
3.22
8.70
3.22

Sample Name:
FM-VIII-19
Data Collected on:
vnmr13-vnmrs400
Archive directory:

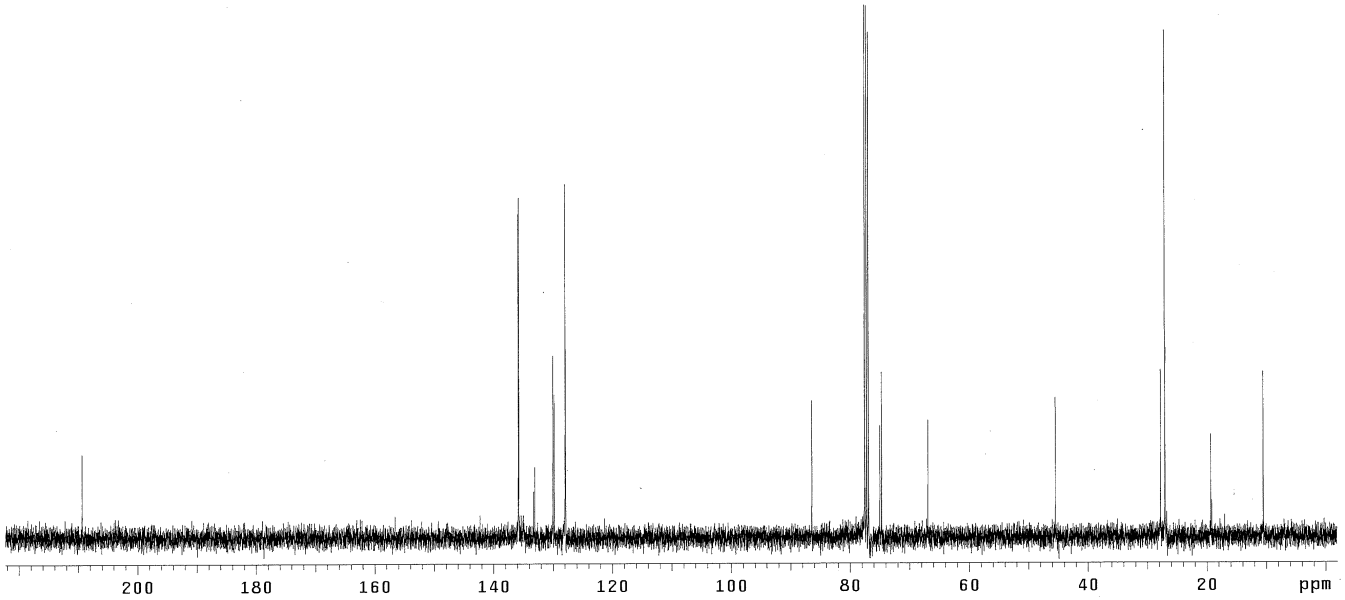
Sample directory:

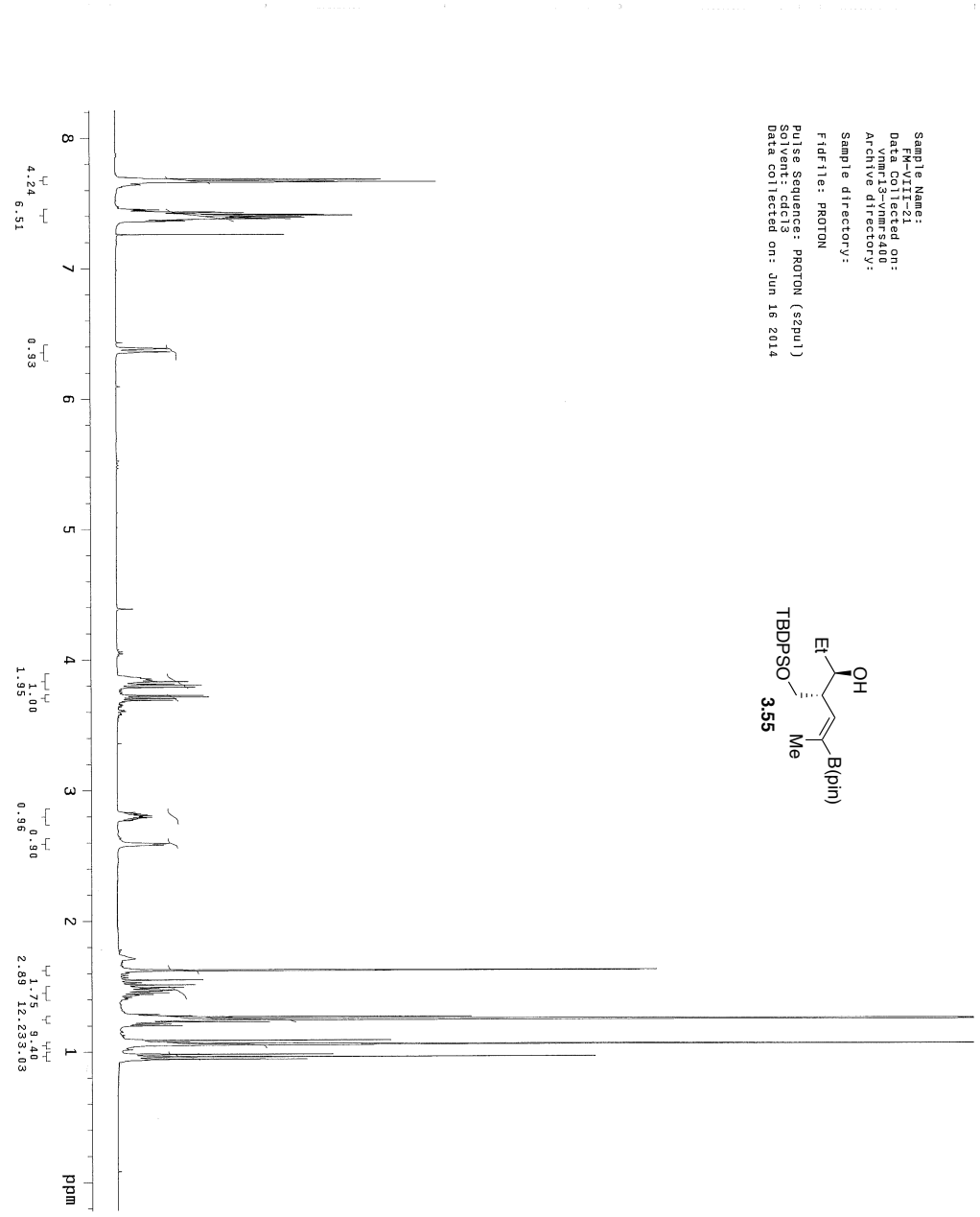
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 11 2014



S3



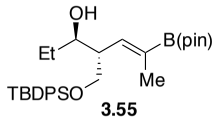

Sample Name:
FM-VII-21
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 16 2014
OH
Et
B(pin)
TBDPSO
Me
3.55
8
7
6
5
4
3
2
1
ppm
4.24
6.51
0.93
1.00
1.95
0.90
0.96
1.75
9.40
2.89
12.23
3.03

Sample Name:
FM-VIII-21
Data Collected on:
vnmr13-vnmrs400
Archive directory:

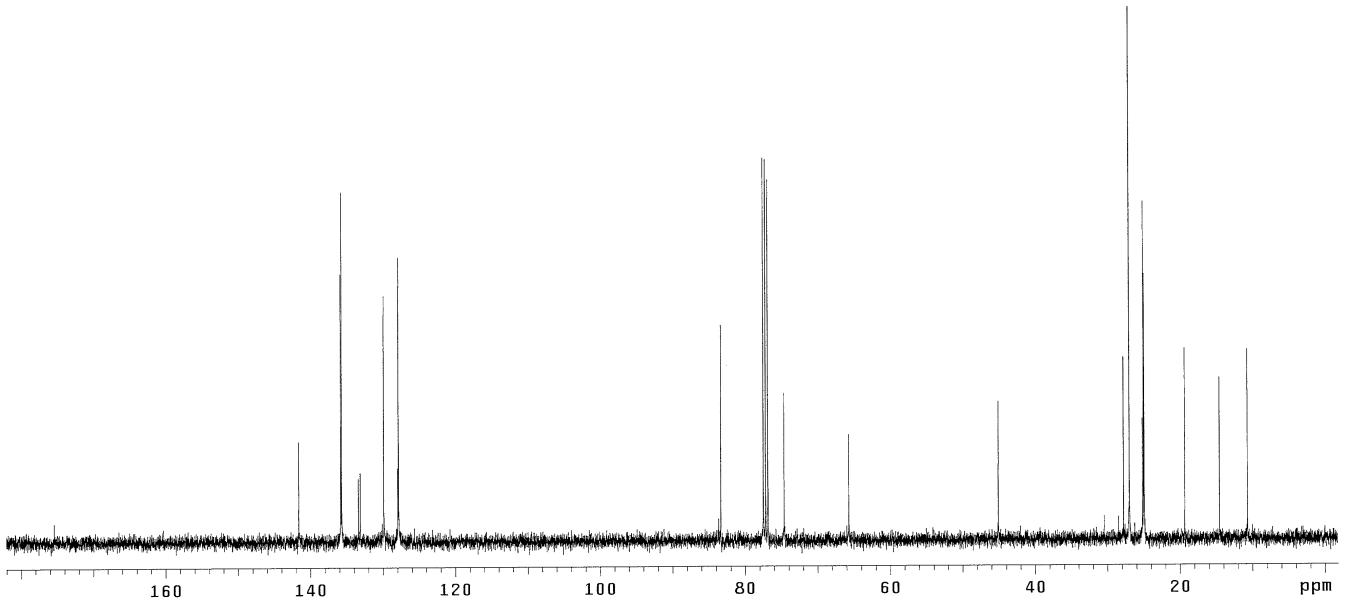
Sample directory:

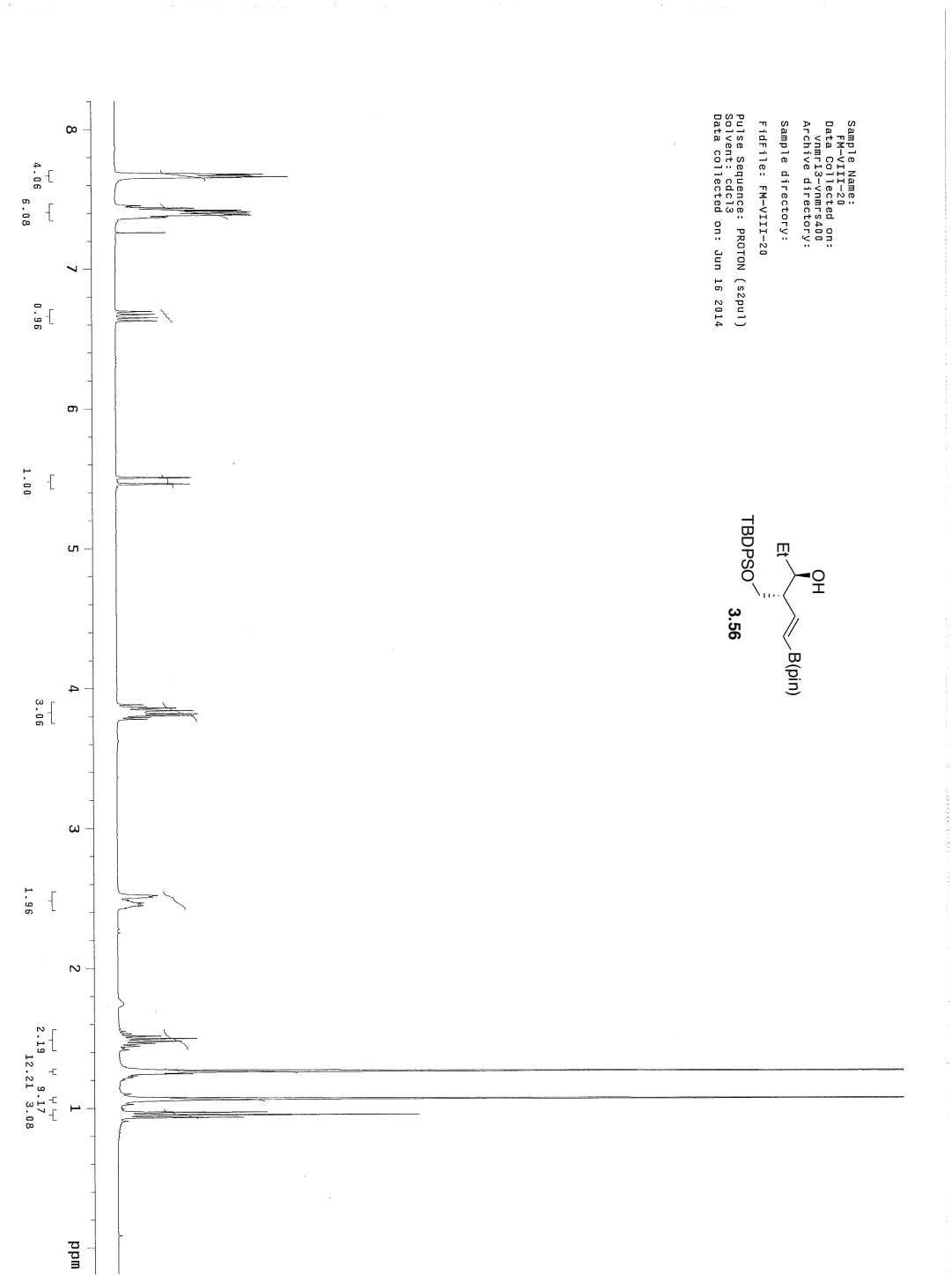
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 13 2014



3.55



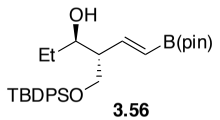

Sample Name:
FM-VIII-20
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: FM-VIII-20
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 16 2014
OH
Et
TBDPSO
B(pin)
3.56
8
7
6
5
4
3
2
1
ppm
4.06
6.08
0.96
1.00
3.06
1.96
2.19
9.17
12.21
3.08

Sample Name:
FM-VIII-20
Data Collected on:
vnmr13-vnmrs400
Archive directory:

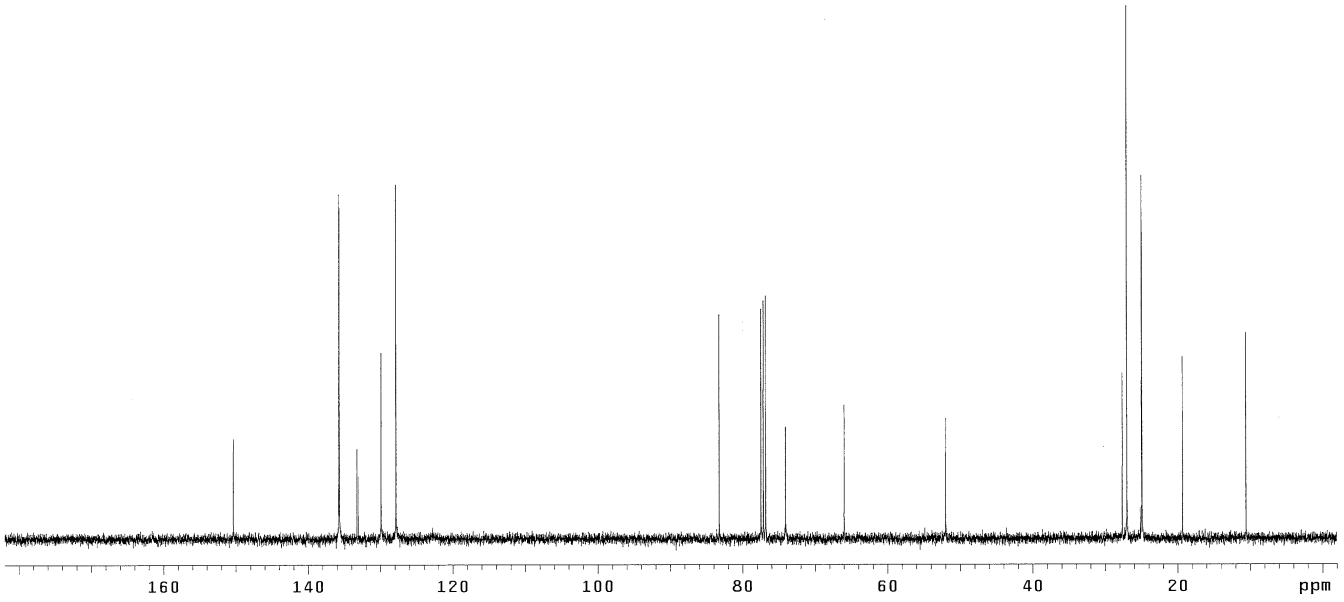
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 16 2014



3.56



Chapter 4

Multifunctional Alkenylboron Compounds through Single-Catalyst-Controlled Multicomponent Reactions and Their Applications in Scalable Natural Product Synthesis

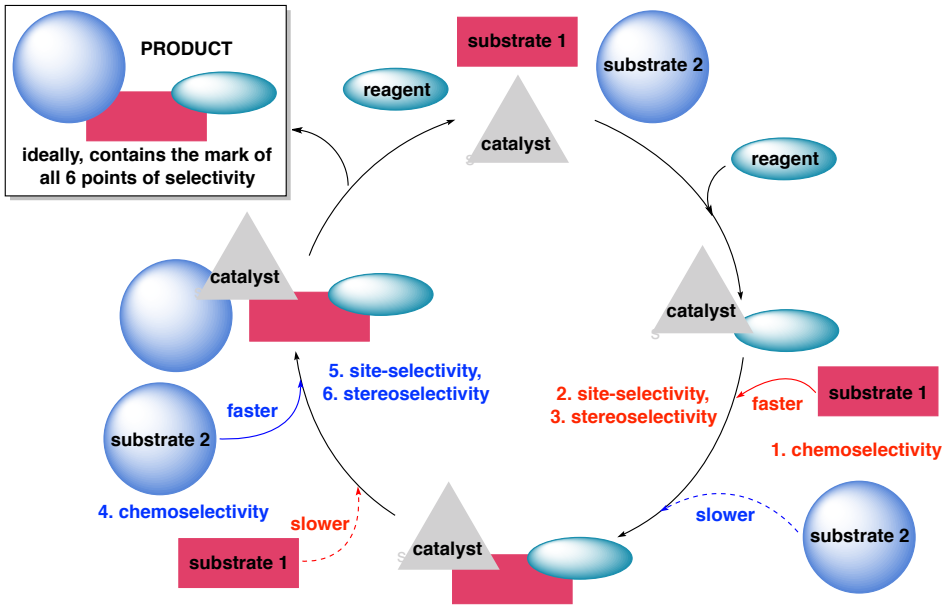
4.1 Introduction

Protocols where a single catalyst unites two substrates and promotes the reaction of the resulting intermediate with a third starting material are sought-after in organic synthesis.[1] Such processes involve intermediates and products that are difficult-to-access otherwise; wasteful and costly isolation and purification of sensitive reagents are avoided.[2] In this way, unprecedented molecular complexity can be built up rapidly if a multitasking catalyst can control all the selectivity issues of each step. These new multicomponent reactions pose unique challenges for catalysis. High chemoselectivity is necessary for each discriminate elementary transformation; the same catalyst has to promote efficient and selective additions in each addition phase. Functionalities of each starting materials are expected to incorporate into the final product (Scheme 4.1). Krische and co-workers have investigated pioneering works for this concept, developing a set of

(1) For reviews on multicomponent reactions, see: (a) Ramón, D. J.; Yus, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 1602–1634. (b) Ruijter, E.; Scheffelaar, R.; Orru, R. V. A. *Angew. Chem., Int. Ed.* **2011**, *50*, 6234–6246.
(2) Bower, J. F.; Kim. I. S.; Patman, R. L.; Krische, M. J. *Angew. Chem., Int. Ed.* **2009**, *48*, 34–46.

reductive multicomponent reactions of hydrogen, unsaturated hydrocarbons and carbonyl or imine compounds in the presence of chiral phosphine–Ir or Ru complexes.[3]

Scheme 4.1: Catalytic Cycle for a Multicomponent Reaction with Each Step Inducing Multiple Selectivities that are Preserved within Product Structure



Alkenylboron compounds are widely used in organic synthesis. Single-catalyst-promoted multicomponent reactions deliver multifunctional alkenylborons are therefore of great interest. In the first phase of our studies, we developed a protocol for the addition of a phosphine–Cu–B(pin) complex, formed through reaction of an in situ generated phosphine–Cu–O*t*-Bu with $B_2(pin)_2$, to a monosubstituted allene, which chemoselectively delivers 2-boron-substituted allylcopper complex **i**. Subsequent reaction with an aldehyde generates hydroxyl-containing alkenylboron compound **iii**. A range of aldol-type building blocks can be accessed after oxidiation of the initial boron-substituted allyl addition products in up to >99:1 diastereomeric ratio (d.r.) and 97:3 enantiomeric ratio (e.r.).[4] For

(3) (a) Ngai, M.-Y.; Barchuk, A.; Krische, M. J. *J. Am. Chem. Soc.* **2007**, *129*, 12644–12645. (b) Hassan, A.; Krische, M. J. *Org. Process Res. Dev.* **2011**, *15*, 1236–1242.
(4) Meng, F.; Jang, H.; Jung, B.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2013**, *52*, 5046–5051.

this transformation, NHC ligands, which are stronger σ-donors compared with phosphines, lead to diminished chemoselectivity and enantioselectivity.

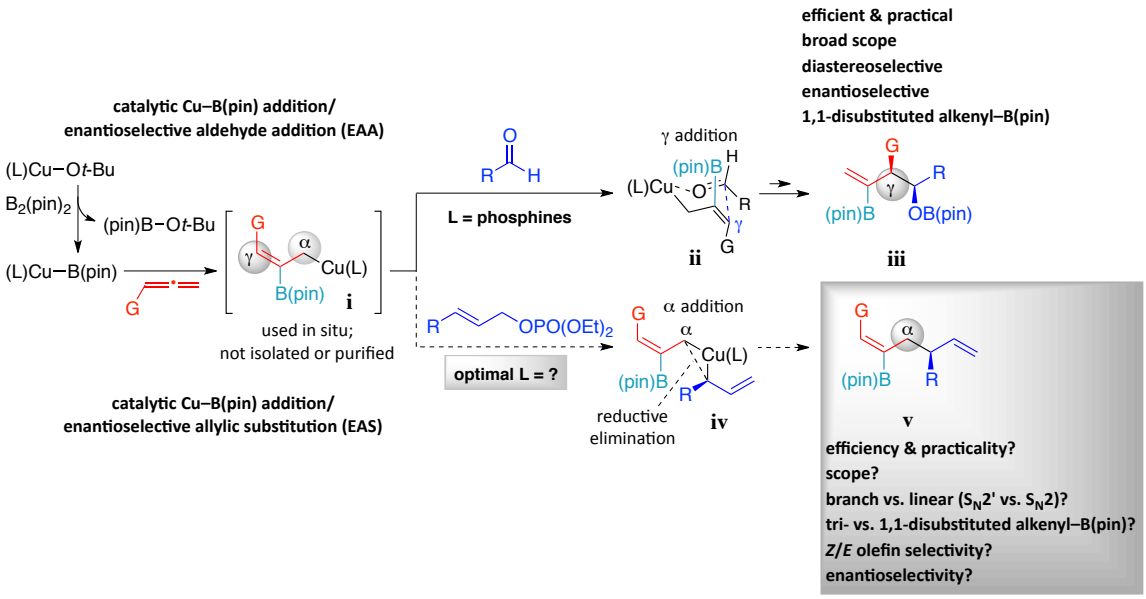
Exclusive formation of 1,1-disubstituted alkenylboron products from the above reaction originates from γ-selective addition of the 2-boron-substituted allylcopper complex to the aldehyde through a six-membered transition state **ii**, which results in loss of the valuable stereochemically defined and modifiable trisubstituted alkenylboron moiety in the initial formed allylcopper intermediate. We hope to design a multicomponent transformation that can preserve this important attribute of the in situ generated organometallic reagent. Besides carbonyl compounds, another valuable class of electrophiles are allylic phosphate. We envisioned that a chemo-, site- and enantioselective transformation of the 2-boron-substituted allylcopper complex generated in situ from a chemo-, site- and stereoselective Cu–B addition to a monosubstituted allene with an allylic phosphate would deliver a multifunctional boron-containing 1,5-diene product **v**. The envisioned catalytic enantioselective allylic substitution (EAS) would be a significant addition to catalytic enantioselective allyl–allyl coupling reactions. The existing strategies require each functional group to be installed individually through extended and less efficient sequence.[5] Also, the state-of-the-art incorporation of allyl groups through EAS is limited to introduction of simple fragments via allylboron,[6] allylmagnesium[7] or allylic alcohol[8] compounds.

---

(5) Takano, D.; Nagamitsu, T.; Ui, H.; Shiomi, K.; Yamaguchi, Y.; Masuma, R.; Kuwajima, I.; Ōmura, S. *Org. Lett.* **2001**, *3*, 2289–2291. (b) Schow, S. R.; Bloom, J. D.; Thompson, A. S.; Winzenberg, K. N.; Smith, A. B. *J. Am. Chem. Soc.* **1986**, *108*, 2662–2674.

(6) (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) Brozek, L. A.; Ardolino, M. J.; Morken, J. P. *J. Am. Chem. Soc.* **2011**, *133*, 16778–16781. (d) Le, H.; Kyne, R. E.; Brozek, L. A.;

Scheme 4.2: Catalytic Multicomponent Methods for Synthesis of Multifunctional Alkenylboron Compounds



The expected products from the proposed multicomponent reaction contain a tertiary stereogenic center, a terminal olefin and a stereochemically defined trisubstituted alkene. The two C–C double bonds can be selectively functionalized. For instance, the boron-containing alkene in **v** can be transformed into a trisubstituted olefin with complete inversion of stereochemistry to generate **vi**. Chemoselective cross metathesis of the terminal olefin in **vi** with vinylB(pin)[9] followed by Pd-catalyzed cross couping of the alkenylboron with alkenylhalide[10] delivers a triene motif **vii** that can be found in a variety of biologically active natural products (Scheme 4.3). A notable case is synthesis of a segment of immunosuppressive agent FK-506.[11] Efficient and stereoselective preparation of such trisubstituted alkene-containing fragments remains a difficult problem. In

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Morken, J. P. *Org. Lett.* **2013**, *15*, 1432–1435. (e) Le, H.; Batten, A.; Morken, J. P. *Org. Lett.* **2014**, *16*, 2096–2099. (f) Ardolino, M. J.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, *136*, 7092–7100.
(7) Hornillos, V.; Pérez, M.; Fañanás-Mastral, M.; Feringa, B. L. *J. Am. Chem. Soc.* **2013**, *135*, 2140–2143.
(8) Hamilton, J. Y.; Sarlah, D.; Carreira, E. M. *J. Am. Chem. Soc.* **2014**, *136*, 3006–3009.
(9) Morrill, C.; Grubbs, R. H. *J. Org. Chem.* **2003**, *68*, 6031–6034.
(10) Kotha, S.; Lahiri, K.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633–9695.
(11) Tanaka, H.; Kuroda, A.; Marusawa, H.; Hatanaka, H.; Kino, T.; Goto, T.; Hashimoto, M. *J. Am. Chem. Soc.* **1987**, *109*, 5031–5033.

previous studies, either the undesired *Z* olefin was separated from a mixture of isomers formed from an unselective Wittig olefination,[12] or modification of a terminal alkyne through a longer sequence involving carboalumination [13] was required. Selective functionalization of the terminal olefin also provides opportunities for numerous types of modifications. One example shown here is the catalytic cross metathesis with vinylB(pin) followed by cross-coupling, which generates an *E*,*E*-diene moiety that is commonly found in natural products. The representative fragments in nafuredin (NADH-fumarate reductase inhibitor[14]), milbemycin β_3 (insecticidal[15]), rottnestol (member of a family of antibiotics[16]), and herboxidiene (phytotoxic, anti-tumor[17]) are highlighted in Scheme 4.3.

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(12) (a) Jones, T. K.; Reamer, R. A.; Desmond, R.; Mills, S. G. *J. Am. Chem. Soc.* **1990**, *112*, 2998–3017. (b) Nakatsuka, M.; Ragan, J. A.; Sammakia, T.; Smith, D. B.; Uehling, D. E.; Schreiber, S. L. *J. Am. Chem. Soc.* **1990**, *112*, 5583–5601.

(13) Ireland, R. E.; Gleason, J. L.; Gegnas, L. D.; Highsmith, T. K. *J. Org. Chem.* **1996**, *61*, 6856–6872.

(14) For isolation, structure determination and biological activity of nafuredin, see: (a) Ōmura, S.; Miyadera, H.; Ui, H.; Shiomi, K.; Yamaguchi, Y.; Masuma, R.; Nagamitsu, T.; Takano, D.; Sunazuka, T.; Harder, A.; Kölbl, H.; Namikoshi, M.; Miyoshi, H.; Sakamoto, K.; Kita, K. *Proc. Natl. Acad. Sci.* **2001**, *98*, 60–62. (b) Ui, H.; Shiomi, K.; Yamaguchi, Y.; Masuma, R.; Nagamitsu, T.; Takano, D.; Sunazuka, T.; Namikoshi, M.; Ōmura, S. *J. Antibiot.* **2001**, *54*, 234–238. (c) Takano, D.; Nagamitsu, T.; Ui, H.; Shiomi, K.; Yamaguchi, Y.; Masuma, R.; Kuwajima, I.; Ōmura, S. *Tetrahedron Lett.* **2001**, *42*, 3017–3020. For total synthesis of nafuredin, see: (d) Takano, D.; Nagamitsu, T.; Ui, H.; Shiomi, K.; Yamaguchi, Y.; Masuma, R.; Kuwajima, I.; Ōmura, S. *Org. Lett.* **2001**, *3*, 2289–2291.

(15) For isolation, structure determination and biological activity of milbemycins, see: (a) Mishima, H.; Kurabayashi, M.; Tamura, C.; Sato, S.; Kuwano, H.; Saito, A. *Tetrahedron Lett.* **1975**, *10*, 711–714. (b) Takiguchi, Y.; Mishima, H.; Okuda, M.; Terao, M. *J. Antibiot.* **1980**, *33*, 1120–1127. (c) Takiguchi, T.; Ono, M.; Muramatsu, S.; Ide, J.; Mishima, H.; Okuda, M.; Terao, M.; Aoki, A.; Fukuda, R. *J. Antibiot.* **1983**, *36*, 502–508. (d) Aoki, A.; Nishida, A.; Ando, M.; Yoshikawa, H. *J. Pesticide Sci.* **1994**, *19*, 245–247. (e) Shoop, W. L.; Mrozik, H.; Fisher, M. H. *Vet. Par.* **1995**, *59*, 139–156. For total synthesis of milbemycin β_3, see: (f) Smith, A. B.; Schow, S. R.; Bloom, J. D.; Thompson, A. S.; Winzenberg, K. N. *J. Am. Chem. Soc.* **1982**, *104*, 4015–4018. (g) Williams, D. R.; Barner, B. A.; Nishitani, K.; Phillips, J. G. *J. Am. Chem. Soc.* **1982**, *104*, 4708–4710. (h) Baker, R.; O'Mahony, M. J.; Swain, C. J. *J. Chem. Soc., Chem. Commun.* **1985**, 1326–1328. (i) Street, S. D. A.; Yeates, C.; Kocieński, P.; Campbell, S. F. *J. Chem. Soc., Chem. Commun.* **1985**, 1386–1388. (j) Yeates, C.; Street, S. D. A.; Kocieński, P.; Campbell, S. F. *J. Chem. Soc., Chem. Commun.* **1985**, 1388–1389. (k) Schow, S. R.; Bloom, J. D.; Thompson, A. S.; Winzenberg, K. N.; Smith, A. B. *J. Am. Chem. Soc.* **1986**, *108*, 2662–2674. (l) Attwood, S. V.; Barrett, A. G. M.; Carr, R. A. E.; Richardson, G. *J. Chem. Soc., Chem. Commun.* **1986**, 479–481. (m) Barrett, A. G. M.; Carr, R. A. E.; Attwood, S. V.; Richardson, G. *J. Org. Chem.* **1986**, *51*, 4840–4856. (n) Kocieński, P. J.; Street, S. D. A.; Yeates, C.; Campbell, S. F. *J. Chem. Soc. Perkin Trans. I* **1987**, 2171–2181. (o) Crimmins, M. T.; Bankaitis-Davis, D. M.; Hollis, W. G. *J. Org. Chem.* **1988**, *53*, 652–657. (p) Li, M.; O'Doherty, G. A. *Org. Lett.* **2006**, *8*, 3987–3990.

(16) For isolation, structure determination and biological activity of rottnestol, see: (a) Erickson, K. L.; Beutler, J. A.; Cardellina, J. H.; Boyd, M. R. *Tetrahedron* **1995**, *51*, 11953–11958. For total synthesis of

Successful execution of the proposed transformations requires a catalyst for high chemoselectivity. Discrimination of two C–C π bonds (allene vs. allylic phosphate) presents a more challenging problem (allene vs. aldehyde in the aldehyde addition case). Both allenes[4] and allylic carbonates[18] can undergo Cu–B additions. Allenes are sterically less hindered and might react with the Cu–B(pin) complex faster, but competitive association of the Lewis basic phosphate with a transition metal may complicate the matter. Another challenge for such process is that reaction of the 2-boron-substituted allylcopper complex with an allylic phosphate must be eliminated rapidly via **iv** (Scheme 4.2). In this way, the trisubstituted alkene moiety can be reserved with formation of a stereogenic center.

4.2 Background

In 2013, Hoveyda and co-workers described an NHC–Cu-catalyzed site-selective protoboration of monosubstituted allenes. 2-Boron-substituted allylcopper complexes are formed through Cu–B addition to monosubstituted allenes, protonation of which

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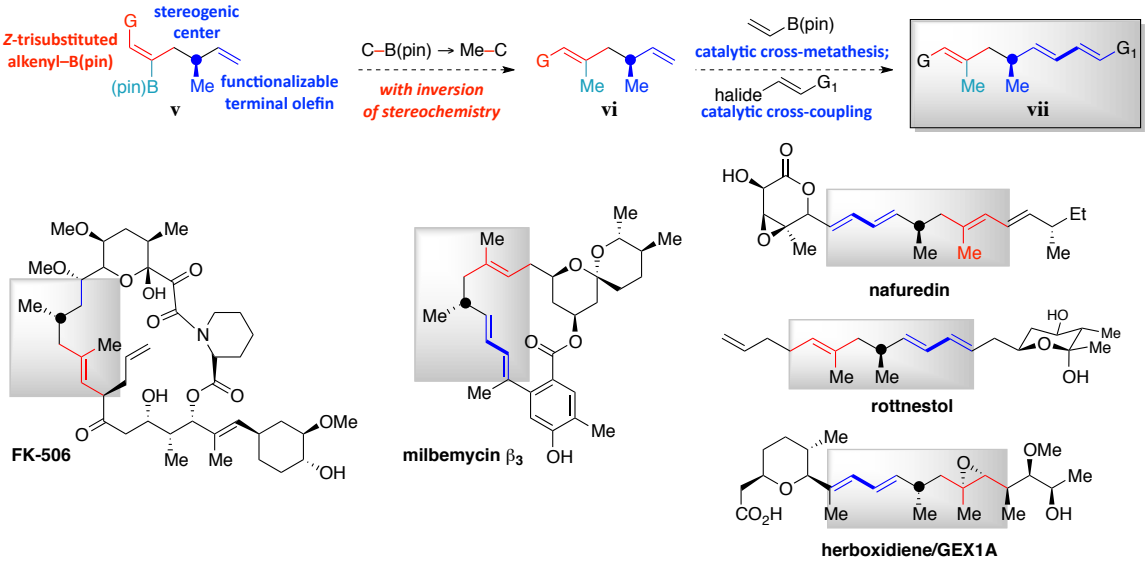
rottnestol, see: (b) Czuba, I. R.; Rizzacasa, M. *Chem. Commun.* **1999**, 1419–1420. (c) Czuba, I. R.; Zammit, S.; Rizzacasa, M. *Org. Biomol. Chem.* **2003**, *1*, 2044–2056.

(17) For isolation, structure determination and biological activity of herboxidiene, see: (a) Isaac, B. G., Ayer, S. W.; Elliott, R. C.; Stonard, R. J. *J. Org. Chem.* **1992**, *57*, 7220–7226. (b) Edmunds, A. J. F.; Trueb, W.; Oppolzer, W.; Cowley, P. *Tetrahedron* **1997**, *53*, 2785–2802. (c) Koguchi, Y.; Nishio, M.; Kotera, J.; Omori, K.; Ohnuki, T.; Komatsubara, S. *J. Antibiot.* **1997**, *50*, 970–971. (d) Sakai, Y.; Yoshida, T.; Ochiai, K.; Uosaki, Y.; Saitoh, Y.; Tanaka, F.; Akiyama, T.; Akinaga, S.; Mizukami, T. *J. Antibiot.* **2002**, *55*, 855–862. (e) Sakai, Y.; Tsujita, T.; Akiyama, T.; Yoshida, T.; Mizukami, T.; Akinaga, S.; Horinouchi, S.; Yoshida, M.; Yoshida, T. *J. Antibiot.* **2002**, *55*, 863–872. (f) Hasegawa, M.; Miura, T.; Kuzuya, K.; Inoue, A.; Ki, S. W.; Horinouchi, S.; Yoshida, T.; Kunoh, T.; Koseki, K.; Mino, K.; Sasaki, R.; Yoshida, M.; Mizukami, T. *ACS Chem. Biol.* **2011**, *6*, 229–233. For total synthesis of herboxidiene, see: (g) Smith, N. D.; Kocieński, P. J.; Street, S. D. A. *Synthesis* **1996**, *5*, 652–666. (h) Blakemore, P. R.; Kocieński, P. J.; Morley, A.; Muir, K. *J. Chem. Soc., Perkin Trans 1* **1999**, 955–968. (i) Banwell, M.; McLeod, M.; Premraj, R.; Simpson, G. *Pure Appl. Chem.* **2000**, *72*, 1631–1634. (j) Premraj, R.; McLeod, M. D.; Simpson, G. W.; Banwell, M. G. *Heterocycles* **2012**, *85*, 2949–2976. (k) Zhang, Y.; Panek, J. S. *Org. Lett.* **2007**, *9*, 3141–3143. (l) Ghosh, A. K.; Li, J. *Org. Lett.* **2011**, *13*, 66–69.

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

generates 1,1-disubstituted or trisubstituted alkenylboron compounds selectively, depending on the size of the NHC ligands.[19]

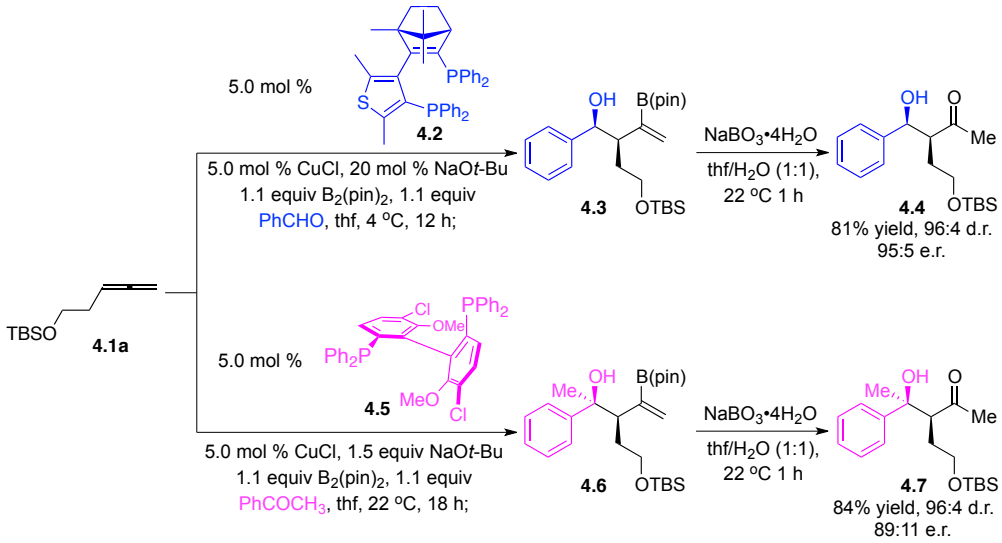
Scheme 4.3: Representative Natural Products that may be Prepared through the New Multicomponent Process



Subsequently, the same group reported the first single-catalyst-controlled multicomponent fusion of monosubstituted allenes, carbonyls and $B_2(pin)_2$ promoted by chiral phosphine–Cu complexes. As illustrated in Scheme 4.4, reactions of allene **4.1** with benzaldehyde or acetophenone in the presence of Cu complexes derived from either C_1-symmetric or C_2-symmetric chiral bisphosphines afford boron-containing secondary or tertiary alcohol **4.3** or **4.6**. After oxidative work-up, β-hydroxyketone **4.4** and **4.7** can be accessed in 81% and 84% yield with 95:5 and 89:11 e.r., respectively.

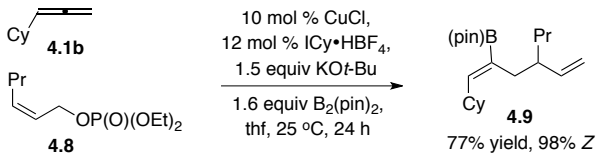
(19) Meng, F.; Jung, B.; Haeffner, F.; Hoveyda, A. H. *Org. Lett.* **2013**, *15*, 1414–1417.

Scheme 4.4: Catalytic Cu–B Addition to Allene Followed by Enantioselective Allyl Addition to Carbonyls



Tsuji and co-worker developed the first sequential Cu–B addition to allene/allylic substitution in 2014.[20] As indicated in Scheme 4.5, with achiral NHC–Cu complex in situ generated from cyclohexyl-containing imidazolium salt, transformation of **4.1b** and *Z*-allylic phosphate **4.8** delivers boron-containing 1,5-diene **4.9** in 77% yield with 98% *Z*-selectivity. The scope is limited to *Z*-allylic phosphates with alkyl substituents. The authors only report reactions with achiral ligands; results with chiral ligands are not disclosed.

Scheme 4.5: Cu–B Addition to Allene/Allylic Substitution Promoted by Achiral NHC–Cu complex



(20) Semba, K.; Bessho, N.; Fujihara, T.; Terao, J.; Tsuji, Y. *Angew. Chem., Int. Ed.* **2014**, *53*, 9007–9011.

4.3 Identification of the Optimal Catalyst for Sequential Cu–B Addition to Allene Followed by Enantioselective Allylic Substitution

We began our study by examining the performance of Cu complexes derived from different types of ligands. Neither monodentate phosphines nor phosphoramidites[21] can catalyze the multicomponent reaction (<2% conv; entries 1–3, Table 4.1). Bisphosphines, which promote sequential catalytic Cu–B additions to monosubstituted allenes followed by aldehyde additions in high efficiency and stereoselectivity, induce complete consumption of allylic phosphate **4.10a** to the boron allylic substitution product. It is unexpected that monodentate NHC–Cu complexes derived from imidazolinium salt **4.17a** or **4.17b** induce multicomponent reactions of monosubstituted allene **4.1a** and allylic phosphate **4.10a** with $B_2(pin)_2$ in a desired sequence, delivering desired product **4.11a** in 81% and 32% yield respectively, with complete branch and *Z* selectivity, because with aldehyde additions, NHC ligands lead to lower chemoselectivity (entries 6–7, Table 4.1).[4] No alternative products (**4.12**, **4.13**, or **4.14**) are detected (<2%). Reactions promoted by chiral bidentate NHC–Cu complexes bearing phenol **4.18**[22] or sulfonate **4.19**[23] substituents either produce **4.11a** in 36% yield with 78:22 e.r., or none at all (entries 8 and 9, Table 4.1). With chiral alternative of **4.17a** that contains a diphenyl backbone (**4.20**), **4.11a** was observed in trace amount (entry 10, Table 4.1). Exposure of monosubstituted allene **4.1a** and allylic phosphate **4.10a** to 5.0 mol % Cu complex generated from monodentate triazolium salt **4.21** or **4.22** results in formation of **4.11a** in 45% and 73% yield albeit 62:38 and 53:47 e.r., respectively (entries 11 and 12, Table

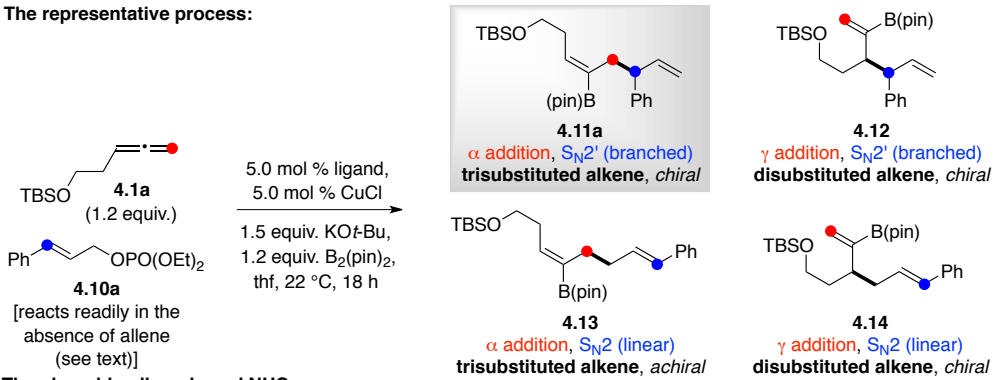
(21) De Vries, A. H. M.; Meetsma, A.; Feringa, B. L. *Angew. Chem., Int. Ed.* **1996**, *35*, 2374–2376.
(22) Van Veldhuizen, J. J.; Campbell, J. E.; Giudici, R. E.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2005**, *127*, 6877–6882.
(23) May, T. L.; Brown, M. K.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2008**, *47*, 7358–7362.

4.1). Reaction with enantiomerically pure NHC precursor bearing an N–aryl and an N–alkyl group provides **4.11a** in 67% yield, >98% S_N2' selectivity and 89:11 e.r. (entry 13, Table 4.1).[24] Further optimization of the aryl moiety and the aminoalcohol substituent leads to imidazolinium salt **4.23d** that delivers not only higher efficiency but also enantioselectivity (80% yield, 94:6 e.r.; entry 16, Table 4.1). Further increasing the size of the substituents at *ortho* position of the N–aryl does not give any improvement (**4.23e**; entry 17, Table 4.1).

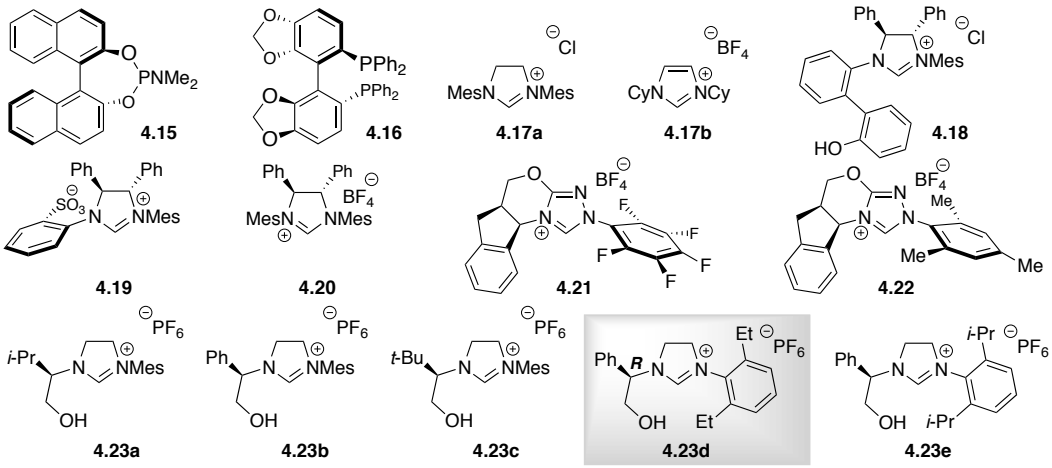
(24) Clavier, H.; Coutable, L.; Toupet, L.; Guillemin, J.-C.; Mauduit, M. *J. Organomet. Chem.* **2005**, *690*, 5237–5254.

Table 4.1: Examination of Cu Complexes as Catalysts for Sequential Cu–B(pin) Addition/EAS[a]

The representative process:



The phosphine ligands and NHC precursors:



Entry number	Ligand or ligand precursor	Conversion (%)[b]; Yield of **4.11a** (%)[c]	Site Selectivity (**4.11a**:**4.12**:**4.13**:**4.14**)[b]	*Z*:*E*[b]	Enantiomeric ratio for **4.11a**[d]
1	PCy_3	<2; NA	NA	NA	NA
2	PPh_3	<2; NA	NA	NA	NA
3	**4.15**	<2; NA	NA	NA	NA
4	*rac*-binap	>98; <2	NA	NA	NA
5	**4.16**	>98; <2	NA	NA	NA
6	**4.17a**	>98; 81	>98:<2:<2:<2	>98:2	NA
7	**4.17b**	>98; 32	>98:<2:<2:<2	>98:2	NA
8	**4.18**	>98; 36	>98:<2:<2:<2	>98:2	22:78 (*R*:*S*)
9	**4.19**	>98; <2	NA	NA	NA
10	**4.20**	40; trace	ND	ND	ND
11	**4.21**	71;45	>98:<2:<2:<2	>98:2	38:62 (*R*:*S*)
12	**4.22**	>98; 73	>98:<2:<2:<2	>98:2	47:53 (*R*:*S*)
13	**4.23a**	>98; 67	>98:<2:<2:<2	>98:2	89:11 (*R*:*S*)
14	**4.23b**	>98; 74	>98:<2:<2:<2	>98:2	93:7 (*R*:*S*)
15	**4.23c**	>98; 72	>98:<2:<2:<2	>98:2	85:15 (*R*:*S*)
16	**4.23d**	>98; 80	>98:<2:<2:<2	>98:2	94:6 (*R*:*S*)
17	**4.23e**	>98; 77	>98:<2:<2:<2	>98:2	92:8 (*R*:*S*)

[a] Performed under N_2 atm. [b] Determined by analysis of 400 MHz ^{1}H NMR spetra of unpurified mixtures (±2%). [c] Yields of isolated/purified products (±5%; both isomers). [d] Enantiomeric ratio (e.r.) determined by HPLC analysis (±2%). NA = Not Available. ND = Not Determined.

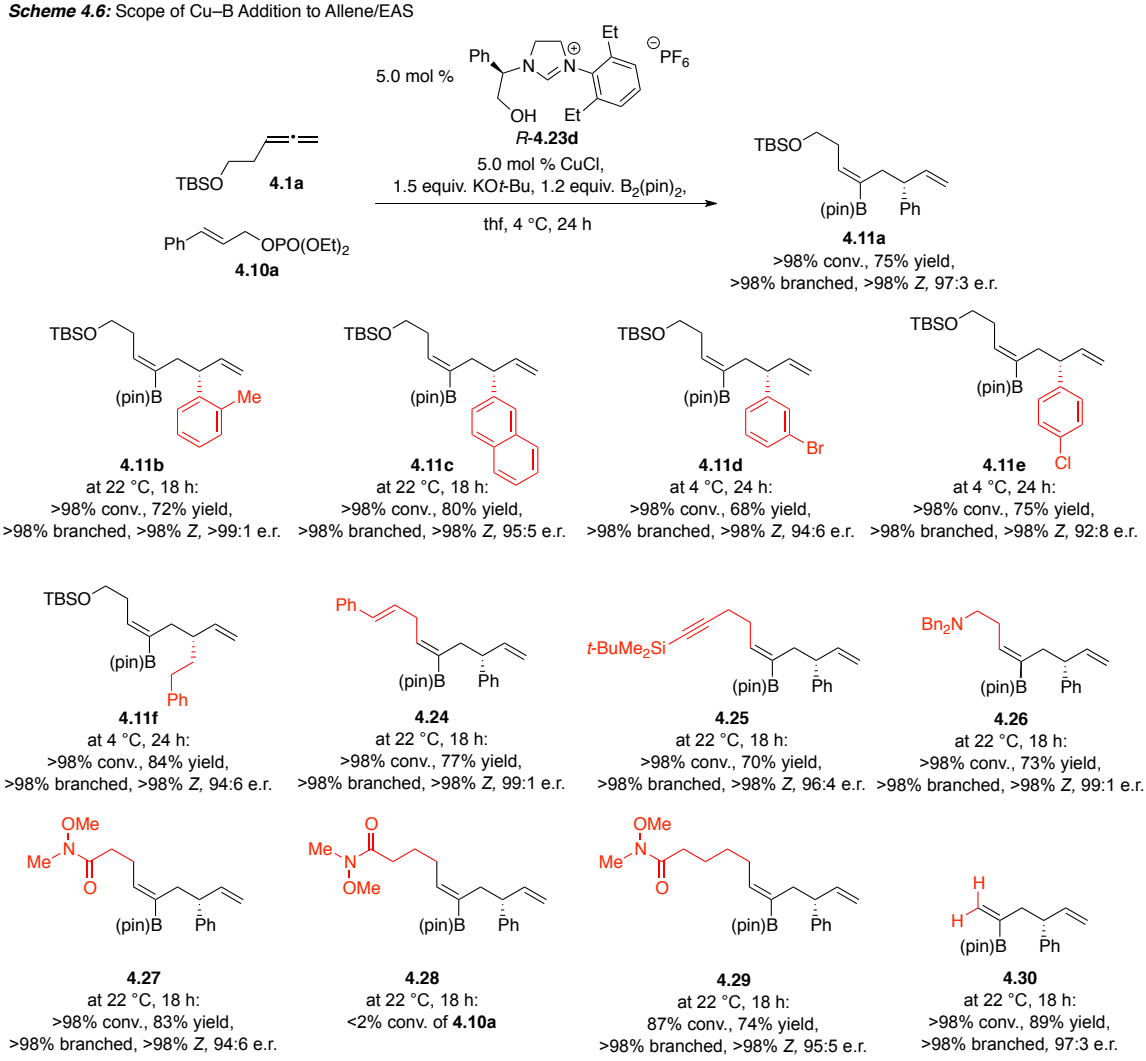
4.4 Scope of Sequential Cu–B Addition to Allene Followed by Enantioselective Allylic Substitution

A range of multifunctional alkenylboron compounds can be prepared through the multicomponent protocol in high selectivity (Scheme 4.6). A notable attribute of the catalytic system is that the imidazolinium salt **4.23d**, an air-stable solid, can be synthesized in multigram quantities through a modified procedure in four steps without any need for wasteful and costly column chromatography purification[24]; the requisite starting materials and reagents, including either form of enantiomeric form of phenylglycinol, can be purchased at low cost. Allylic phosphates that carry sterically congested aryl entities react in high efficiency and enantioselectivity (**4.11b** and **4.11c**, 72% and 80% yield, >99:1 and 95:5 e.r.). Alkyl- (**4.11f**) and halogenated aryl-substituted (**4.11d**, **e**) allylic phosphates are suitable substrates for this transformation. It is noteworthy that the incorporation of a β-alkylstyrene[25] or an internal alkyne[26], which can undergo NHC–Cu–B(pin) additions readily, into the allene does not lead to this undesired pathway, probably due to preferential association of the less sizable allene moiety to the Cu complex (**4.24** and **4.25**). Allenes that contain other modifiable groups, such as an amine (**4.26**) or an amide (**4.27** or **4.29**) are well tolerated. The results of transformations that generate **4.27**–**4.29** indicate the distance between the Lewis basic carbonyl and allene site significantly affect the reaction rate. Reaction of unsubstituted allene provides access

(25) Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 3160–3161.
(26) Jang, H.; Zhugralin, A. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 7859–7871.

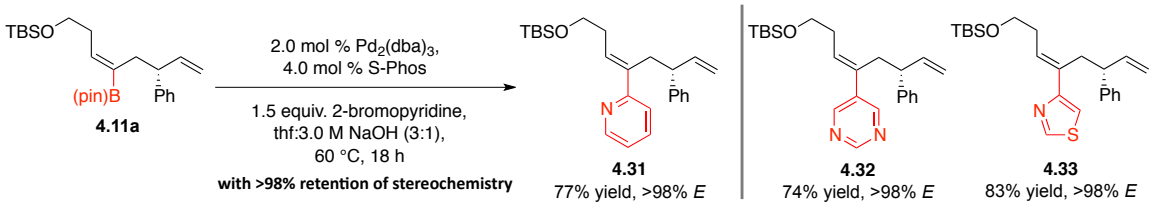
to 1,1-disubstituted alkenylB(pin) **4.30** in 89% yield, >98% branch selectivity and 97:3 e.r..

Scheme 4.6: Scope of Cu–B Addition to Allene/EAS



A variety of trisubstituted alkenes can be delivered through Pd-catalyzed cross-coupling reactions with readily available aryl halides with complete retention of stereochemistry (Scheme 4.7).

Scheme 4.7: Catalytic Cross-Coupling Functionalization of the Trisubstituted Alkenyl–B(pin) Products



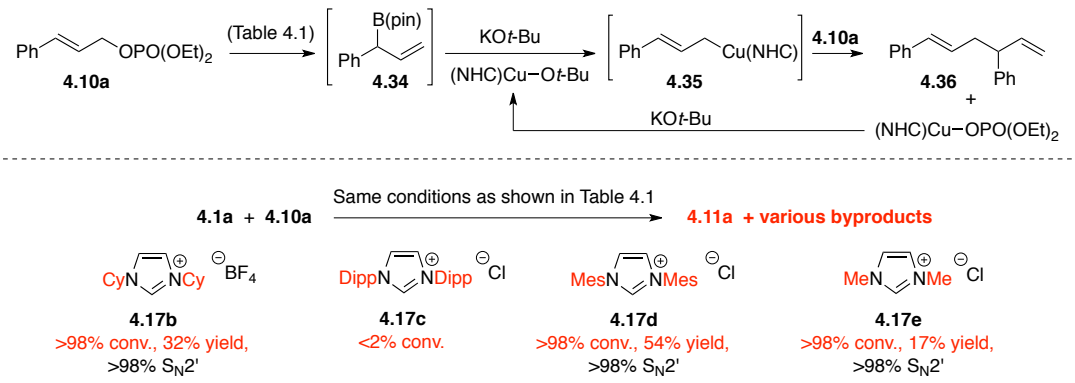
4.5 Explanation for Origin of High Efficiency and Selectivity

The challenge of designing a single-catalyst-controlled multicomponent reaction is to identify a catalyst that can solve all the efficiency and selectivity issues during the whole process. The difference between percentage of conversion of allylic phosphate **4.10a** and yield of **4.11a** indicates a breakdown in chemoselectivity; competitive Cu–B addition to allylic phosphate **4.10a** leads to generation of byproducts. It seems that less Lewis basic and sterically demanding bidentate bisphosphine-based catalysts associate with the allylic phosphate more readily (entries 6 and 7, Table 4.1), distinct from those derived from NHC ligands.[27] It is likely that the HOMO of the bisphosphine–Cu complexes is the $d_{x^2-y^2}$, which could have better interaction with lower-lying π* orbital of allylic phosphate.[28] The competitive side reaction with less effective NHC–Cu complexes results from addition of B(pin) to the allylic phosphate **4.10a** to generate a branched allylboron intermediate **4.34** that can be subsequently transformed to the allylcopper complex **4.35**. Reaction with another molecule of allylic phosphate **4.10a** provides 1,5-diene **4.36** (Scheme 4.8). NHC–Cu complexes promote the formation of **4.36** efficiently in the absence of allene (e.g. 53% yield for **4.17a**, 76% yield for **4.19**, 50% yield for

(27) (a) Díez-González, S.; Nolan, S. P. *Coord. Chem. Rev.* **2007**, *251*, 874–883. (b) Maji, B.; Breugst, M.; Mayr, H. *Angew. Chem., Int. Ed.* **2011**, *50*, 6915–6919.
(28) Yoshikai, N.; Nakamura, E. *Chem. Rev.* **2012**, *112*, 2339–2372.

4.23d). Transmetallation of allylboron **4.34** to the bisphosphine–Cu complex or addition of allylcopper **4.35** to allylic phosphate **4.10a** might be less efficient as a result of the decreased Lewis acidity of the Cu center[29], leading to more complicated side reactions.

Scheme 4.8: Major Side Pathway in NHC–Cu-Catalyzed Reactions and Additonal Findings Relevant to Efficiency



The outcome of transformations performed in the presence of NHC–Cu complexes derived from **4.17b–e** suggest that the appropriate balance between electronic properties and size of the NHC ligand might lead to high efficiency and chemoselectivity. The Cu complex resulting from **4.17c** is too large to promote this reaction, whereas the more nucleophilic ligands **4.17b** and **4.17e** that contain smaller N–alkyl groups (vs. N–aryl) cause lower level of discrimination of allene and allylic phosphate. NHC–Cu complex derived from imidazolinium salt **4.17d** is small enough to promote the desired sequence and not too nucleophilic leading to competitive boron allylic substitution. The Cu catalyst generated from the sulfonate-containing precursor **4.19** is more like the only catalyst which remains a bidentate complex; the cuprate species possesses a higher energy HOMO that has better interaction with the lower-lying π* orbital of the allylic

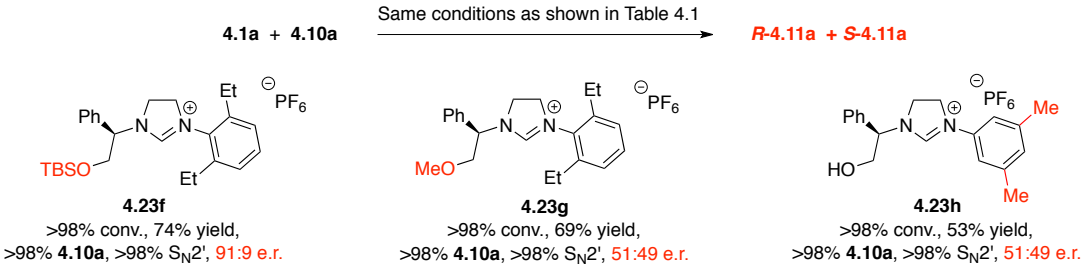
(29) Denmark, S. E.; Beutner, G. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 1560–1638.

phosphate (vs. an allene), leading to more competitive undesired allylic substitution of a B(pin) group (lower chemoselectivity).

In previous cases, chiral NHC ligands that contain a chelating unit commonly serve as precursors to bidentate Cu complexes (cuprate complex), which usually provide exceptional S_N2' selectivity in reactions of organoboron compounds.[30] The selectivity is attributed to facile reductive elimination of the Cu(III) intermediate leading to release of steric hindrance.[29] The less sterically congested monodentate NHC–Cu complexes usually deliver significant amounts of achiral linear S_N2 products.[30] Furthermore, high enantioselectivities have typically been observed with Cu complexes derived from chiral ligands that are either bidentate (e.g. **4.19**, Table 4.1)[24], or monodentate (e.g. **4.20**, Table 4.1) that contains constraining stereogenic centers[31], or both[18, 30]. To further explore the nature of the catalytically active species, we examined the reaction with silyl ether **4.23f**, which proceeds with similar efficiency and selectivity as **4.23d** (Scheme 4.9). In sharp contrast, methyl ether derivative **4.23g** leads to erosion of enantioselectivity (69% yield, 51:49 e.r.). The above data suggest that **4.23d** functions as a monodentate ligand. Cleavage of the Cu–O bond in the NHC–Cu catalyst through reaction with $B_2(pin)_2$ results in a monodentate complex that bears a neutral metal center.[30a] The large B(pin)-substituted chiral appendage is crucial for enantioselectivity, which is emulated by the sizable silyl group in **4.23f**.

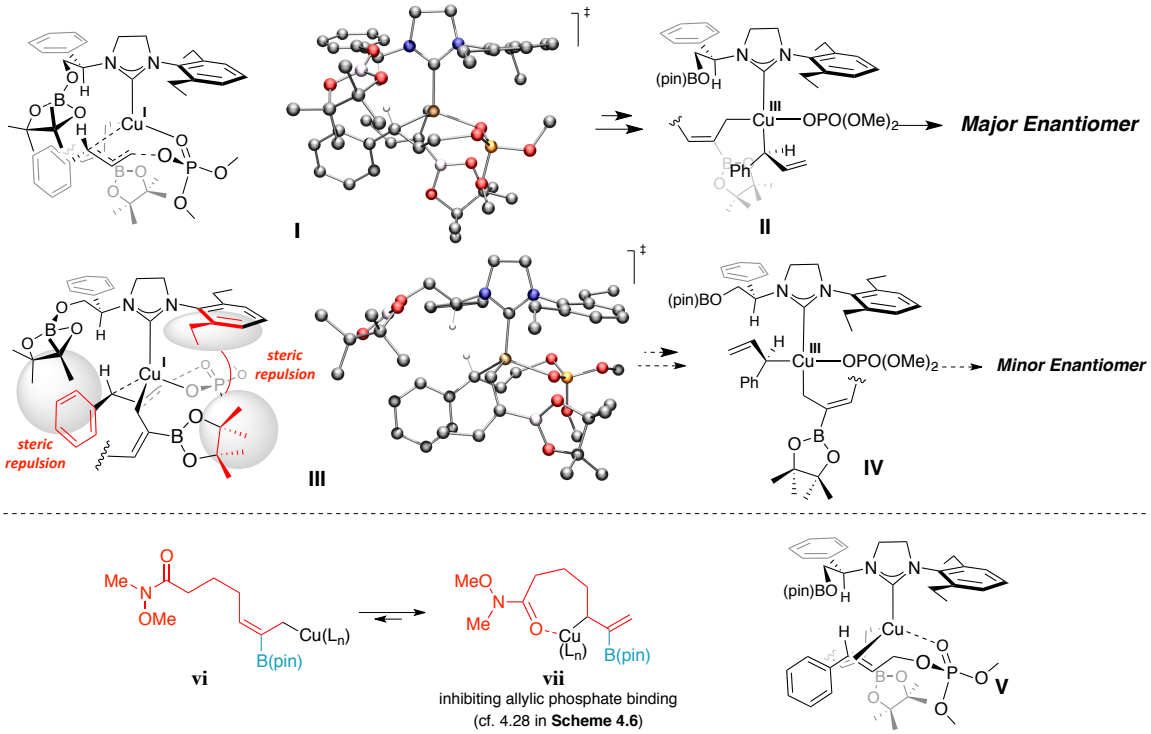
(30) (a) Jung, B.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2012**, *134*, 1490–1493. (b) Gao, F.; Carr, J. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2014**, *136*, 2149–2161.
(31) (a) Park, J. K.; Lackey, H. H.; Ondrusek, B. A.; McQuade, D. T. *J. Am. Chem. Soc.* **2011**, *133*, 2410–2413. (b) Lee, K.-s.; Hoveyda, A. H. *J. Org. Chem.* **2009**, *74*, 4455–4462.

Scheme 4.9: Additional Data Regarding Origin of Enantioselectivity



DFT calculations imply that formation of the major enantiomer proceeds via transition structure **I**. The allylic phosphate occupies two binding sites of the tetrahedral Cu(I) complex to generate a square planar Cu(III) species **II** that undergoes reductive elimination to provide **4.11a** (Scheme 4.10). The association of the Lewis basic phosphate facilitates coordination of the C–C π bond to the sterically hindered metal center. This hypothesis is supported by the different efficiencies observed for transformations delivering **4.27**–**4.29**. In the case of **4.28**, the Lewis basic amide carbonyl is properly located to chelate the copper center, retarding the association of the allylic phosphate. The ring size in the bidentate complex **vii** is similar to that in the oxidative addition precursor **V**.

Scheme 4.10: Stereochemical Models Based on DFT Calculations



The chelation of the allylic phosphate helps to organize the stereochemistry-determining transition state, providing high stereochemistry control via **II**. The minor enantiomer might be generated via **III**, in which the large B(pin) group engenders steric repulsion with the protruding allylic phosphate substituent. The B(pin) unit of the allyl group has to come into contact with the ethyl substituents on the N–aryl moiety or the large B(pin) group on the NHC side chain. *Ortho* substituents on the N–aryl moiety are crucial for high enantioselectivity, forcing the allyl group away from them. This proposal is supported by the fact that complete loss of enantioselectivity is observed when the N–aryl substituents are placed at C3 and C5 position (cf. **4.23h**, Scheme 4.9).

It is unexpected that the multicomponent transformations proceed with complete branch selectivity promoted by a monodentate Cu complex.[30b, 32] The uniqueness of such process is the presence of the sizable B(pin) group of the allyl unit on the Cu(III) complex, leading to an elevation of the ground state energy of the Cu(III) intermediate species **II** (major) and **IV** (minor).[30] As such, the barrier to reductive elimination is smaller, thereby accelerating the rate of reductive elimination versus collapse to the π-allyl species. This hypothesis is supported by DFT calculations.

4.6 Applications to Gram-Scale Natural Product Synthesis

Synthesis of biological active molecules with catalytic multicomponent reactions as key strategies would be a clear demonstration of the utility of such processes, especially if meaningful quantities of a target molecule could be generated in high efficiency and selectivity. Our goal is to design strategies that each issue of stereochemical control would be addressed by a catalytic transformation.

We first designed a route for total synthesis of gram quantities of rottnestol, which was isolated from the sponge *Haliclona* sp. collected in the waters around Rottnest Island off the coast of Western Australia by Boyd and co-workers in 1995.[16a] Rottnestol, featuring a sensitive hemiketal moiety and polyene side chain with a remote stereogenic center in the molecule is a member of a family of marine natural products that show mild antibiotic activities. We envisioned construction of the polyene side chain could be achieved through the NHC–Cu-catalyzed Cu–B addition/EAS protocol, whereas the

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

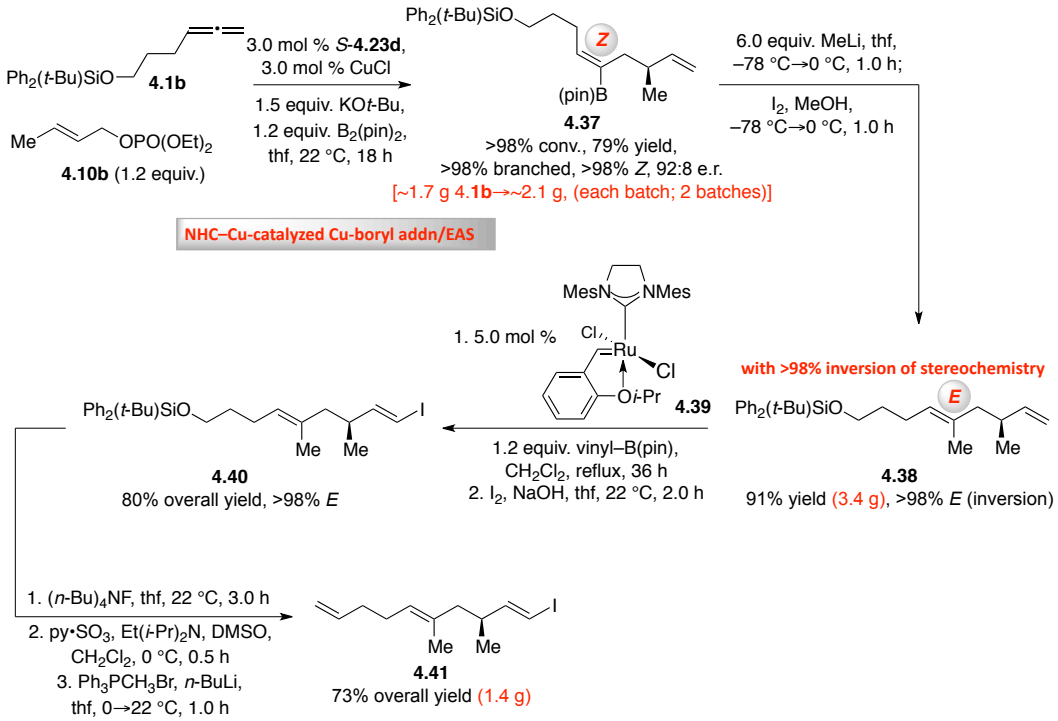
carbohydrate unit could be built up through a catalytic fusion of an allene and an aldehyde with $B_2(pin)_2$.

The synthetic route begins with the catalytic multicomponent reaction with allylic phosphate (Scheme 4.11a). Exposure of monosubstituted allene **4.1b** and methyl-substituted allylic phosphate **4.10b** to 3.0 mol % NHC–Cu complex derived from (*S*)-**4.23d** results in 1,5-diene **4.37** in 79% yield with >98% S_N2' selectivity and 92:8 e.r.; the reaction was performed on multigram scale (1.7 g of **4.1b**), delivering a total of ~4.2 g of **4.37**. Subsequently, the trisubstituted alkenylboron unit is transformed to a trisubstituted olefin with complete inversion of stereochemistry through reaction with methyllithium and iodine[33], generating **4.38** in 91% yield (~3.4 g). Ru-catalyzed cross-metathesis of **4.38** with vinyl–B(pin)[9] promoted by 5.0 mol % Ru carbene **4.39**[34] followed by conversion of the alkenylboron to alkenyliodide[9] leads to formation of **4.40** in 80% overall yield with complete *E* selectivity (~3.6 g). Conversion of the silyl ether moiety in **4.40** to a terminal alkene in three straightforward steps furnishes 1.4 g of triene **4.41** in 73% overall yield.

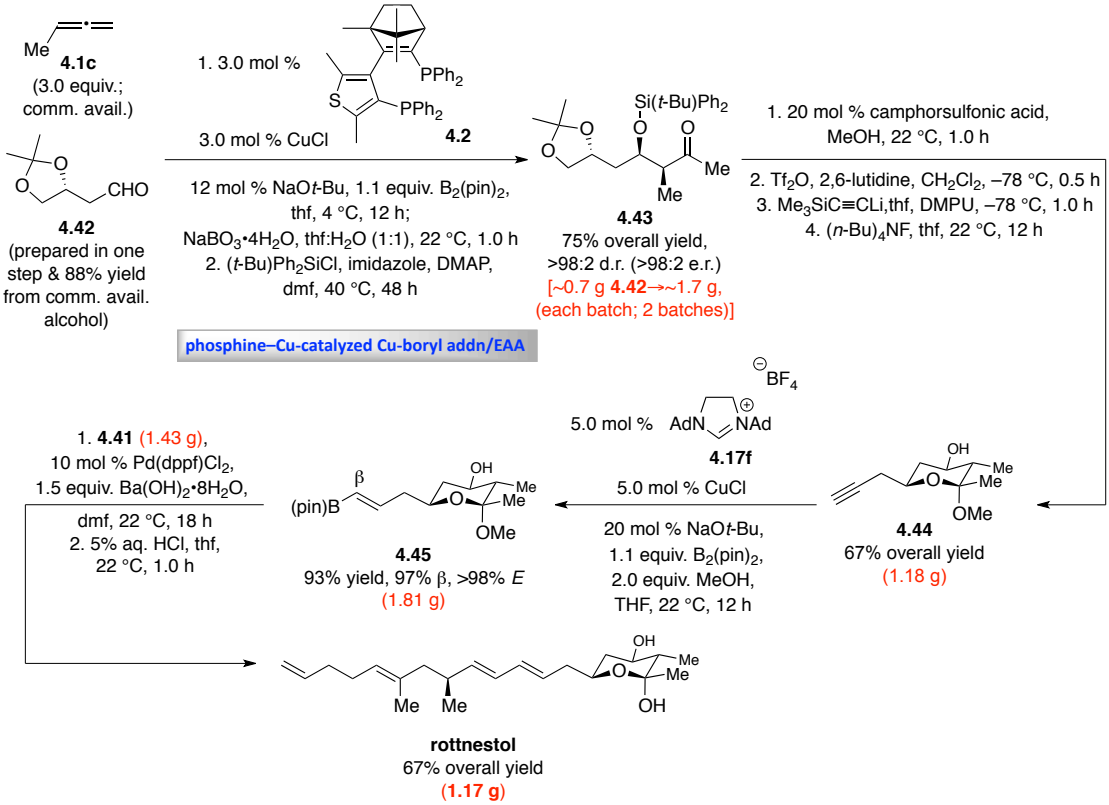
(33) Xu, S.; Lee, C.-T.; Rao, H.; Negishi, E. *Adv. Synth. Catal.* **2011**, *353*, 2981–2987.
(34) Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168–8179.

Scheme 4.11: Gram-Scale Total Synthesis of Rottnestol

a. Enantioselective synthesis of the polyene segment of rottnestol



b. Enantioselective synthesis of the carbohydrate segment of rottnestol and the final fragment coupling



Preparation of the carbohydrate segment commenced with an enantioselective fusion of commercially available methyl-substituted allene **4.1c**, $B_2(pin)_2$ and an enantiomerically pure aldehyde **4.42** which can be accessed in one step from a commercially available alcohol in the presence of a bisphosphine–Cu complex derived from **4.2** (Scheme 4.11b).[4] Subsequent oxidative work-up followed by silyl protection affords β-hydroxyketone **4.43** in 75% overall yield (~3.4 g through two batches) as a single enantiomer (>98:2 d.r. and e.r.). Acid-promoted cleavage of the ketal with simultaneous cyclization followed by selective conversion of the primary alcohol to a triflate with subsequent alkyne substitution and globle deprotection of the silyl groups furnishes terminal alkyne **4.44** in 67% overall yield (~1.18 g). Site selective protoboration of the terminal alkyne in the presence of NHC–Cu complex in situ generated from imidazolinium salt **4.17f** delivers alkenyl–B(pin) **4.45** in 93% yield with 97% β and >98% *E* selectivity (~1.8 g).[26] With the two partners in hand, we investigated Pd-catalyzed cross-coupling of the fragments. It is crucial to perform the reaction at 22 °C; elevated temperatures lead to decomposition of the starting materials and products, probably due to the presence of the sensitive ketal moiety. With 10 mol % $Pd(dppf)Cl_2$ and $Ba(OH)_2•8H_2O$ as a base, coupling of alkenyl–iodide **4.41** and alkenyl–B(pin) **4.45** followed by acidic hydrolysis of the ketal to cyclic hemiketal affords rottnestol in 67% overall yield. The route described above is significantly more efficient than those previously (21.5% vs. 3.7% overall yield)[16b, 16c], wherein only milligram quantities of the target molecule can be accessed.

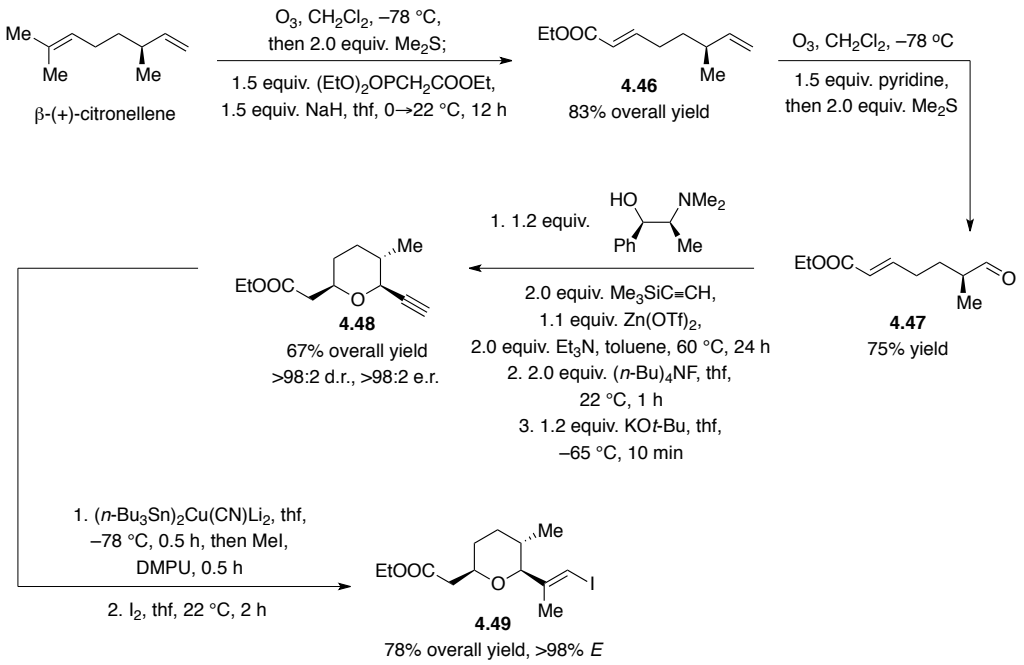
We next targeted herboxidiene to highlight a different aspect of the NHC–Cu-catalyzed multicomponent protocol. In the synthesis of rottnestol, the Cu–B addition/EAS

process was employed in early stage. We would like to investigate the performance of the multicomponent transformation in a later stage of a synthetic sequence, demonstrating the reliability of such process on more complex substrates. Herboxidiene was isolated from *Streptomyces* sp. A7847 by Isaac and co-workers in 1992 at Monsanto and identified as a polyketide metabolite with potent and highly selective phytotoxic properties. It was later shown to affect plasma cholesterol and to be active against several tumor cell lines.[17a-f]

As illustrated in Scheme 4.12, ozone cleavage of the more electron-rich trisubstituted alkene of commercially available β-(+)-citronellene followed by Horner-Wadsworth-Emmons olefination of the resulting aldehyde affords diene **4.46** in 83% overall yield.[35] Chemoselective cleavage of the terminal olefin in the presence of pyridine furnishes aldehyde **4.47** in 75% yield. Zn-mediated alkyne addition[36] followed by desilylation and isomerization[17h] results in tetrahydropyran **4.48** in 67% overall yield with complete stereochemistry control. Cu–Sn addition to the terminal alkyne and subsequent conversion of the C–Sn bond to C–I bond leads to trisubstituted alkenyl–iodide **4.49** in 78% overall yield and >98% *E* selectivity.[37]

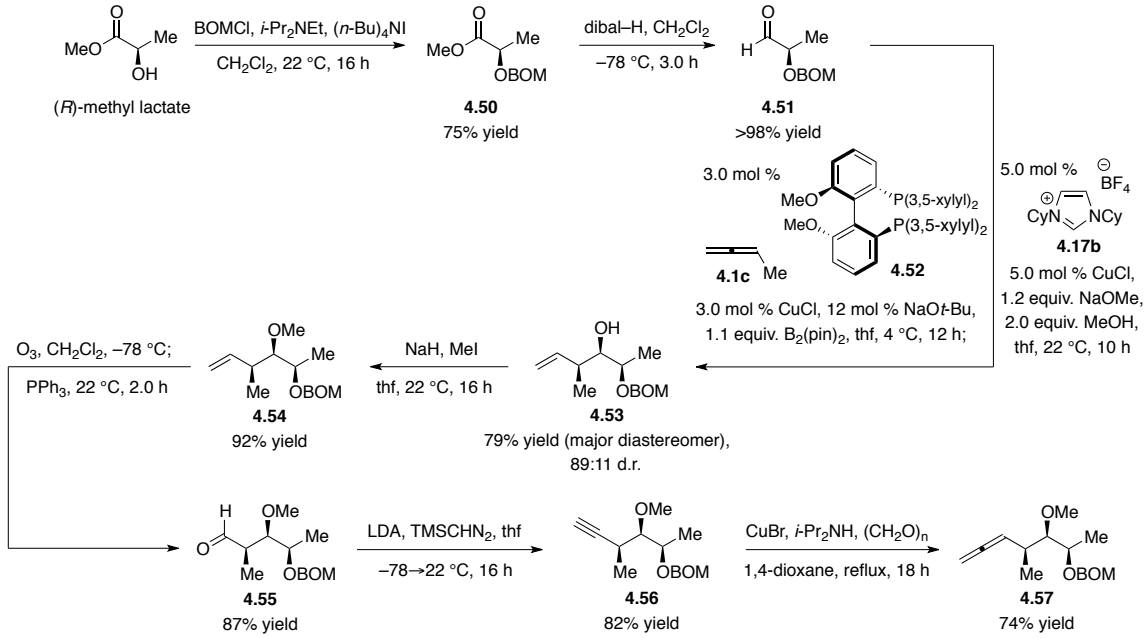
(35) Fürstner, A.; Feyen, F.; Prinz, H.; Waldmann, H. *Tetrahedron* **2004**, *60*, 9543–9558.
(36) Anand, N. K.; Carreira, E. M. *J. Am. Chem. Soc.* **2001**, *123*, 9687–9688.
(37) (a) Lipshutz, B. H.; Ellsworth, E. L.; Dimock, S. H.; Reuter, D. C. *Tetrahedron Lett.* **1989**, *30*, 2065–2068. (b) Liu, P.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2001**, *123*, 10772–10773.

Scheme 4.12:. Preparation of Alkenyliodide **4.49**



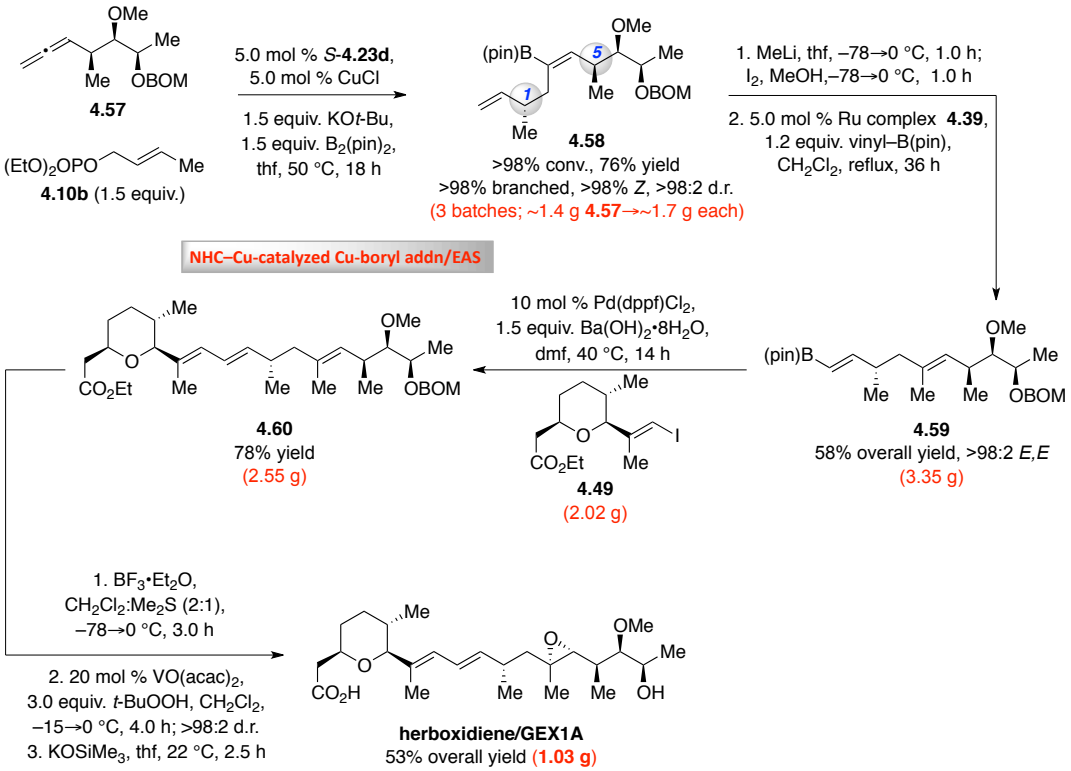
Synthesis of the allene component begins with BOM-protection of commercially available (*R*)-methyl lactate, which is reduced to aldehyde **4.51** by dibal–H in >98% yield (Scheme 4.13). Bisphosphine–Cu-catalyzed fusion of methyl-substituted allene **4.1c**, enantiomerically pure aldehyde **4.51** and $B_2(pin)_2$ followed by NHC–Cu-catalyzed protodeboration delivers homoallylic alcohol in 89:11 d.r..[4] The desired diastereomer **4.53** can be separated in 79% yield. Methylation of the hydroxyl group and cleavage of the terminal alkene followed by conversion of the resulting aldehyde to terminal alkyne affords **4.56** efficiently. Cu-catalyzed homologation of terminal alkyne provides the highly functionalized allene **4.57** in 74% yield.

Scheme 4.13: Preparation of Allene **4.57**



With ~7 g of the complex allene **4.57** prepared in seven steps and 29% overall yield in hand, we turn our attention to examine the key multicomponent transformation involving allylic phosphate **4.10b** (Scheme 4.14). We found that desired 1,5-diene with considerable complexity is generated efficiently when the reaction is performed at 50 ºC; ~5.1 g of **4.58** are obtained in 76% yield with complete site-, *Z*- and diastereoselectivity. Conversion of C–B(pin) to C–Me followed by cross-metathesis with vinyl–B(pin) affords ~3.3 g of trisubstituted olefin **4.59** in 58% yield over 2 steps with complete *E*, *E*-selectivity. Pd-catalyzed cross-coupling of the alkenyl–B(pin) **4.59** and alkenyl–iodide **4.49** leads to ~2.55 g of triene **4.60**, which undergoes deprotection of the BOM group, directed epoxidation and hydrolysis of the ethyl ester, delivering ~1.03 g of the anti-tumor agent herboxidiene in 53% yield over 3 steps. The overall yield of this sequence is almost twice as much as that of the most concise one among those previously reported (5.5% vs. 3.4% overall yield).

Scheme 4.14: Completion of Total Synthesis of Herboxidiene



4.7 Conclusion

In this chapter, we have developed a catalytic enantioselective multicomponent protocol to generate multifunctional alkenylboron compounds. The versatility of such products provides access to a variety of enantiomerically enriched organic molecules. A modifiable stereochemical-defined boron-containing trisubstituted alkene, a stereogenic center and a terminal olefin can be introduced in a single transformation, which leads to highly efficient constructure of complexity. The multitasking NHC–Cu catalyst is derived from an easily accessible air-stable imidazolinium salt and inexpensive abundant copper salt. The starting materials, monosubstituted allenes and allylic phosphates, can be synthesized in high efficiency from cheap reliable methods. The utility of the

multicomponent reactions is demonstrated through applications to gram-scale synthesis of natural products, rottnestol and herboxidiene. Moreover, this study provides mechanistic insights into the origins of chemo-, site- and stereoselectivity, implying the uniqueness of this transformation and paving way for further design of single-catalyst-controlled multicomponent reactions.

4.8 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). ^{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, C_6D_6: d 7.16 ppm, CD_3OD: d 3.31 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br s = broad singlet, m = multiplet, app. = apparent), and coupling constant (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, C_6D_6: d 128.00 ppm, CD_3OD: d 49.00 ppm). High-resolution mass spectrometry was performed on a JEOL AccuTOF DART (positive mode) at the Mass Spectrometry Facility, Boston College. Enantiomer ratios were determined by high-performance liquid chromatography (HPLC) with a Shimadzu chromatograph (Chiral Technologies Chiralpak AD–H (4.6 x 250 mm),

Chiralcel OD–H (4.6 x 250 mm), Chiralcel OJ–H (4.6 x 250 mm) and Chiralcel OZ–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. Solvents were purified under a positive pressure of dry argon by a modified Innovative Technologies purification system: toluene, benzene and hexanes were purified through a copper oxide and alumina column; CH_2Cl_2 and Et_2O were purged with Ar and purified by passage through two alumina columns. 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) in air.

4.8.1 Reagents

Allenes (4.1a-b): prepared according to previously reported procedures.[38]

Barium hydroxide octahydrate: purchased from Aldrich Chemical Co. and used as received.

[1,1'-Bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane: purchased from Strem Chemicals Inc. and used as received.

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(38) (a) Crabbé, P.; Fillion, H.; André, D.; Luche, J.-L. *J. Chem. Soc., Chem. Commun.* **1979**, 859–860. (b) Searles, S.; Li, Y.; Nassim, B.; Lopes, M.-T. R.; Tran, P. T.; Crabbé, P. *J. Chem. Soc., Perkin Trans. 1*, **1984**, 747–751. (c) Yoshida, M.; Matsuda, K.; Shoji, Y.; Gotou, T.; Ihara, M.; Shishido, K. *Org. Lett.* **2008**, *10*, 5183–5186.

Bis(pinacolato)diboron: purchased from Frontier Scientific, Inc. and recrystallized from pentane.

Boron trifluoride: purchased from Aldrich Chemical Co. and used as received.

2-Bromopyridine: purchased from Aldrich Chemical Co. and used as received.

5-Bromopyrimidine: purchased from Aldrich Chemical Co. and used as received.

4-Bromothiazole: purchased from Aldrich Chemical Co. and used as received.

***tert*-Butyl(chloro)diphenylsilane:** purchased from Aldrich Chemical Co. and used as received.

***tert*-Butyl hydroperoxide solution (5.0 M in nonane):** purchased from Aldrich Chemical Co. and used as received.

***n*-Butyllithium solution (15% in hexanes, 1.6 M):** purchased from Strem Chemicals Inc. and used as received.

Camphorsulfonic acid: purchased from Aldrich Chemical Co. and used as received.

CatASium® T1 (4.2): purchased from Strem Chemicals Inc. and used as received.

(+)-β-Citronellene: purchased from Aldrich Chemical Co. and used as received.

Copper (I) chloride: purchased from Strem Chemicals Inc. and used as received.

Copper (I) cyanide: purchased from Strem Chemicals Inc. and used as received.

Diisobutylaluminum hydride: purchased from Aldrich Chemical Co. and used as received.

2,2-Dimethoxypropane: purchased from Alfa Aesar Co. and used as received.

4-(Dimethylamino)pyridine (DMAP): purchased from Oakwood Products Inc. and used as received.

Dimethyl sulfide: purchased from Aldrich Chemical Co. and used as received.

Dimethyl sulfoxide: purchased from Alfa Aesar Co. and used as received.

1,3-Dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (DMPU): purchased from Aldrich Chemical Co. and distilled over CaH_2 prior to use.

Ethynyltrimethylsilane: purchased from Aldrich Chemical Co. and used as received.

Hoveyda-Grubbs Catalyst 2nd Generation (4.39): purchased from Aldrich Chemical Co. and used as received.

Hydrogen peroxide solution (30 wt. % in H_2O): purchased from Aldrich Chemical Co. and used as received.

Imidazole: purchased from Aldrich Chemical Co. and used as received.

Imidazolinium or imidazolium salts (4.17a-f, 4.21, 4.22): purchased from Aldrich Chemical Co. and used as received.

Imidazolinium salts 4.18,[39] 4.19-4.20,[40] 4.23a-c[41]: prepared according to previously reported procedures.

Iodine: purchased from Aldrich Chemical Co. and used as received.

2,6-Lutidine: purchased from Aldrich Chemical Co. and distilled over CaH_2 prior to use.

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(39) Lee, K-s.; Brown, M. K.; Hird, A. W.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2006**, *128*, 7182–7184.

(40) (a) Brown, M. K.; May, T. L.; Baxter, C. A.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 1097–1100. (b) May, T. L.; Brown, M. K.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2008**, *47*, 7468–7472.

(41) Clavier, H.; Coutable, L.; Toupet, L.; Guillemin, J-C.; Mauduit, M. *J. Organomet. Chem.* **2005**, *690*, 5237–5254.

Methanol: purchased from Acros Organics Co. and used as received.

Methyl allene (25% by wt in toluene) (4.1c): purchased from ChemSamp. Co. and used as received.

Methyl (*R*)-lactate: purchased from Aldrich Chemical Co. and used as received.

Methyllithium solution (1.6 M in diethyl ether): purchased from Aldrich Chemical Co. and used as received.

Methyltriphenylphosphonium bromide: purchased from Alfa Aesar Co. and used as received.

(*R*)-MonoPhos® (4.15): purchased from Strem Chemicals Inc. and used as received.

***N*,*N*-Diisopropylethylamine:** purchased from Aldrich Chemical Co. and used as received.

***N*,*N*-Dimethylformamide:** purchased from Aldrich Chemical Co. and used as received.

(1*R*, 2*S*)-(-)-*N*-Methylephedrine: purchased from Aldrich Chemical Co. and used as received.

Potassium *tert*-butoxide (98%)**:** purchased from Strem Chemicals Inc. and used as received.

Potassium trimethylsilanolate: purchased from Aldrich Chemical Co. and used as received.

SPhos: purchased from Strem Chemicals Inc. and used as received.

(*R*)-SEGPHOS® (4.16): purchased from Strem Chemicals Inc. and used as received.

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

Sodium hydride: purchased from Strem Chemicals Inc. and used as received.

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

Sulfur trioxide pyridine complex: purchased from Aldrich Chemical Co. and used as received.

***p*-Toluenesulfonic acid monohydrate:** purchased from Aldrich Chemical Co. and used as received.

Tetrabutylammonium fluoride solution (1.0 M in THF): purchased from Aldrich Chemical Co. and used as received.

Tetrabutylammonium iodide: purchased from Aldrich Chemical Co. and used as received.

Tributyltin hydride: purchased from Aldrich Chemical Co. and used as received.

Triethyl phosphonoacetate: purchased from Aldrich Chemical Co. and used as received.

Trifluoromethanesulfonic anhydride (Tf_2O): purchased from Aldrich Chemical Co. and used as received.

Trimethylsilylacetylene: purchased from Aldrich Chemical Co. and used as received.

Tris(dibenzylideneacetone)dipalladium: purchased from Strem Chemicals Inc. and used as received.

Vanadyl acetylacetonate: purchased from Aldrich Chemical Co. and used as received.

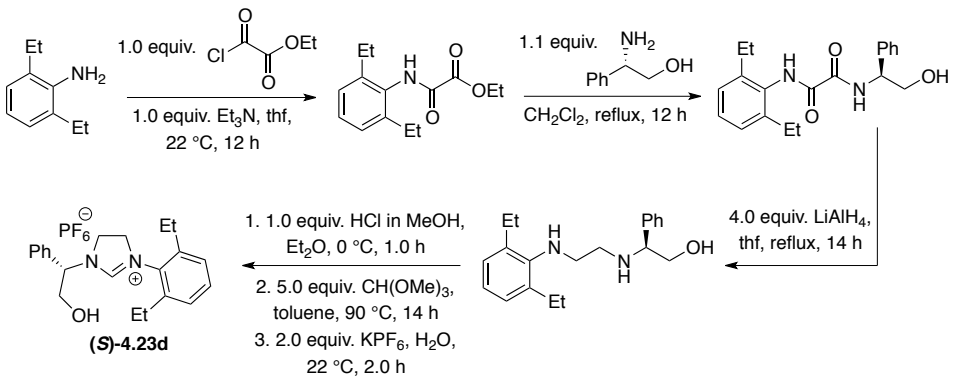
Vinylboronic acid pinacol ester: purchased from Aldrich Chemical Co. and purified by column chromatography followed by distillation over CaH_2 prior to use.

Zinc (II) triflate: purchased from Strem Chemicals Inc. and used as received.

4.8.2 Experimental Procedures and Characterization Data for Synthesis of Imidazolinium Salts and Allenes

■ **Experimental Procedure for Synthesis of Imidazolinium Salts 4.23d-e and 4.23h**

Scheme S1. Synthesis of Chiral Imidazolinium Salts **4.23d-e** and **4.23h**



To a solution of 2,6-diethylaniline (7.16 mL, 43.5 mmol) and triethylamine (6.06 mL, 43.5 mmol) in THF (60 mL) was added ethyl chlorooxoacetate (4.86 mL, 43.5 mmol) slowly at 0 °C. The resulting mixture was allowed to stir at 22 °C for 12 h. The solid was filtered off and the filtrate was washed with 3.0 M aqueous solution of HCl (50 mL). The aqueous layer was washed with ethyl acetate (3 × 40 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The resulting light brown oil was employed in the next step without purification.

The oil obtained from the previous step was dissolved in CH_2Cl_2 (40 mL) and (*S*)-2-phenylglycinol (6.56 g, 47.8 mmol) was added. The mixture was allowed to stir at 50 °C

for 12 h. After this time, the mixture was allowed to cool to 22 °C. The resulting white solid was filtered and washed with cold ethyl acetate (3 × 15 mL).

The solid was dissolved in THF (60 mL). To the solution was added $LiAlH_4$ (6.60 g, 174 mmol) in six portions at 0 °C. The suspension was allowed to stir at 0 °C for 30 min and at 80 °C for 14 h. After this time, the mixture was allowed to cool to 22 °C and added into a mixture of potassium sodium tartrate and ice. The mixture was allowed to stir at 22 °C for 4 h. At this time, the aqueous layer was washed with ethyl acetate (3 × 40 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The resulting yellow oil was used in the next step without further purification.

The oily residue obtained from the previous step was dissolved in Et_2O (50 mL). To this solution was added methanolic solution of HCl (1.0 M, 43.5 mL, 43.5 mmol) at 0 °C. The mixture was allowed to stir at 0 °C for 30 min, after which the volatiles were removed in vacuo. The resulting oil was dissolved in toluene (60 mL) and $CH(OMe)_3$ (23.8 mL, 217 mmol) was added. The mixture was allowed to stir at 90 °C for 14 h. At this time, the mixture was allowed to cool to 22 °C, and the volatiles were removed in vacuo. The resulting yellow oil was dissolved in water (60 mL) and the aqueous layer was washed with ethyl acetate (3 × 20 mL). To the resulting aqueous solution was added KPF_6 (16.0 g, 87.0 mmol) and the mixture was allowed to stir at 22 °C for 2 h. The aqueous solution was washed with CH_2Cl_2 (3 × 40 mL) and the combined organic layers were concentrated in vacuo to afford **(*S*)-4.23d** as light yellow solid (10.2 g, 21.8 mmol, 50% overall yield).

(*S*)-4.23d: IR (neat): 3309 (br), 2972 (w), 2938 (w), 2880 (w), 1632 (s), 1454 (m), 1277 (m), 1196 (w), 1139 (m), 1072 (m), 837 (s), 767 (m), 702 (m), 558 (m), 496 (m) cm^{-1}; ^1H

NMR (400 MHz, $CDCl_3$): δ 8.04 (1H, s), 7.44–7.33 (6H, m), 7.18–7.16 (2H, m), 5.03 (1H, dd, *J* = 9.2, 3.6 Hz), 4.18–4.11 (4H, m), 4.06–3.99 (2H, m), 2.97 (1H, br s), 2.62–2.54 (4H, m), 1.22 (6H, t, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.0, 141.8, 133.0, 131.7, 131.0, 129.8, 129.7, 127.8, 127.5, 64.0, 61.3, 51.9, 47.3, 24.0, 15.1. HRMS (ESI$^+$) $[M–PF_6]^+$ calcd for $C_{21}H_{27}N_2O_1$: 323.21234, found: 323.21312. Specific rotation: $[\alpha]_D^{20}$ +25.4 (*c* 2.64, acetone).

(*R*)-4.23e: IR (neat): 3301 (br), 2967 (w), 2931 (w), 2873 (w), 1632 (s), 1458 (m), 1272 (m), 1196 (w), 1138 (m), 1072 (m), 839 (s), 761 (m), 702 (m), 558 (m), 496 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.02 (1H, s), 7.45–7.41 (4H, m), 7.37–7.35 (2H, m), 7.25–7.23 (2H, m), 5.08 (1H, dd, *J* = 8.4, 4.4 Hz), 4.23–4.08 (6H, m), 2.99 (1H, br s), 2.96–2.87 (2H, m), 1.29 (3H, d, *J* = 7,2 Hz), 1.26 (3H, d, *J* = 6.8 Hz), 1.21 (6H, t, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.0, 146.9, 133.1, 131.5, 129.9, 129.8, 129.7, 127.9, 125.1, 64.0, 61.3, 53.1, 47.5, 28.9, 24.9, 24.1, 23.9. HRMS (ESI$^+$) $[M–PF_6]^+$ calcd for $C_{23}H_{31}N_2O_1$: 351.24364, found: 351.24430. Specific rotation: $[\alpha]_D^{20}$ –18.6 (*c* 1.95, acetone).

(*R*)-4.23h: IR (neat): 3594 (br), 2924 (m), 1631 (s), 1457 (m), 1286 (m), 1151 (m), 1064 (m), 1028 (m), 951 (w), 832 (s), 741 (w), 697 (m), 557 (s), 463 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.72 (1H, s), 7.44–7.37 (3H, m), 7.33–7.31 (2H, m), 6.90–6.88 (3H, m), 5.03 (1H, dd, *J* = 9.2, 3.6 Hz), 4.43–4.35 (1H, m), 4.32–4.26 (1H, m), 4.26–4.17 (1H, m), 4.10–3.99 (2H, m), 3.90–3.82 (1H, m), 3.23 (1H, br s), 2.30 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.7, 140.5, 135.4, 132.6, 129.9, 129.7, 129.6, 127.9, 116.2, 64.6, 61.4, 48.4, 46.8, 21.3. HRMS (ESI$^+$) $[M–PF_6]^+$ calcd for $C_{19}H_{23}N_2O_1$: 295.18104, found: 295.18110. Specific rotation: $[\alpha]_D^{20}$ –10.1 (*c* 0.99, acetone).

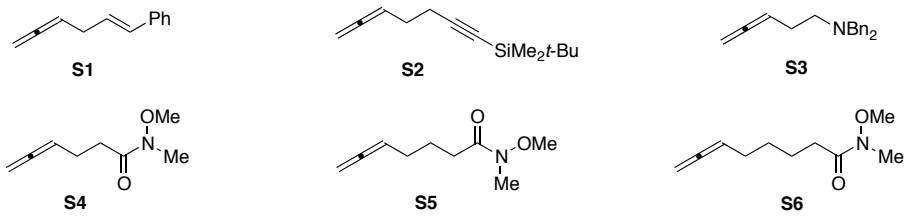
(*R*)-4.23f: IR (neat): 2953 (m), 2930 (m), 2883 (m), 2857 (m), 1632 (s), 1499 (m), 1251 (m), 1102 (m), 912 (w), 827 (s), 779 (s), 610 (w), 556 (s), 468 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.01 (1H, s), 7.45–7.36 (6H, m), 7.21–7.19 (2H, m), 4.96 (1H, dd, *J* = 6.0, 3.2 Hz), 4.26–4.10 (6H, m), 2.65–2.60 (4H, m), 1.29–1.22 (6H, m), 0.82 (9H, s), –0.03 (3H, s), –0.06 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.5, 141.4, 133.6, 131.8, 131.0, 129.6, 129.5, 127.9, 127.3, 64.0, 63.4, 52.0, 48.3, 25.8, 23.8, 18.3, 15.1, –5.7. HRMS (ESI^+) $[M–PF_6]^+$ calcd for $C_{27}H_{41}N_2O_1Si_1$: 437.29827, found: 437.29800. Specific rotation: $[\alpha]_D^{20}$ –26.1 (*c* 1.49, acetone).

(*R*)-4.23g was prepared from **(*R*)-4.23d** according to a previously reported procedure.[42] IR (neat): 2973 (w), 2937 (w), 1632 (s), 1453 (m), 1267 (m), 1155 (m), 1060 (w), 910 (m), 829 (s), 727 (s), 699 (s), 648 (m), 556 (s), 468 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.94 (1H, s), 7.46–7.34 (6H, m), 7.20–7.18 (2H, m), 5.06 (1H, dd, *J* = 8.0, 3.6 Hz), 4.18–4.09 (4H, m), 4.05–4.00 (1H m), 3.93–3.84 (1H, m), 3.43 (3H, s), 2.61 (4H, q, *J* = 7.6 Hz), 1.59 (1H, br s), 1.27–1.22 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.9, 141.9, 133.2, 131.8, 131.0, 129.8, 129.7, 128.1, 127.6, 71.0, 62.0, 59.2, 52.0, 48.0, 23.9, 15.1. HRMS (ESI^+) $[M–PF_6]^+$ calcd for $C_{22}H_{29}N_2O_1$: 337.22799, found: 337.22800. Specific rotation: $[\alpha]_D^{20}$ +3.7 (*c* 1.05, acetone).

■ **Synthesis of Allenes:**

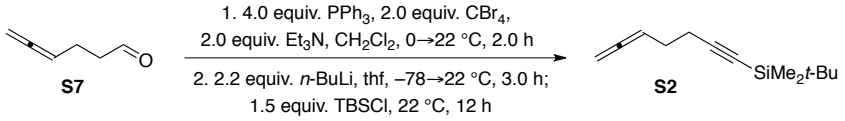
(42) Shintani, R.; Takatsu, K.; Hayashi, T. *Chem. Commun.*, **2010**, *46*, 6822–6824.

Chart S1. Numbering of Allene Precursors for Compounds **4.24-4.29** in Supplementary Information



S1 was prepared according to a formerly reported procedure;[43] **S3, S4-6** were synthesized by Crabbé homologation.[38]

Scheme S2. Preparation of Allene **S2**



***tert*-Butyl(6λ^5-hepta-5,6-dien-1-yn-1-yl)dimethylsilane (S2):** To a solution of CBr_4 (1.33 g, 4.00 mmol) in CH_2Cl_2 (10 mL) was added PPh_3 (2.10 g, 8.00 mmol) at 0 °C. The solution was allowed to stir at 0 °C for 30 min, after which a solution of aldehyde **S7** [44] (192 mg, 2.00 mmol) and Et_3N (557 μL, 4.00 mmol) in CH_2Cl_2 (5 mL) was added at 0 °C. The mixture was allowed to stir at 22 °C for 2 h. At this time, the reaction was quenched by addition of a saturated solution of NH_4Cl (10 mL). The aqueous layer was washed with Et_2O (3 × 10 mL) and the combined organic layers were concentrated in vacuo to afford dark-brown oil, which was passed through a plug of silica gel (eluted with hexanes).

The resulting colorless oil was dissolved in THF (10 mL), and *n*-BuLi (1.6 M, 2.75 mL, 4.40 mmol) was added at –78 °C. The mixture was allowed to warm to 22 °C slowly and stir for 3 h. After this time, TBSCl (452 mg, 3.00 mmol) was added and the mixture was

(43) Meng, F.; Jung, B.; Haeffner, F.; Hoveyda, A. H. *Org. Lett.* **2013**, *15*, 1414–1417.
(44) Tsukamoto, H.; Matsumoto, T.; Kondo, Y. *J. Am. Chem. Soc.* **2008**, *130*, 388–389.

allowed to stir at 22 °C for 12 h. The reaction was quenched by addition of a saturated solution of NH_4Cl (5 mL). The aqueous layer was washed with Et_2O (3 × 5 mL) and the combined organic layers were concentrated in vacuo to provide yellow oil, which was purified by silica gel chromatography (100% hexanes) to afford **S2** as colorless oil (305 mg, 1.48 mmol, 74% overall yield).

IR (neat): 2953 (m), 2928 (m), 2856 (m), 2175 (m), 1958 (w), 1471 (w), 1389 (w), 1250 (m), 1044 (w), 939 (w), 837 (s), 810 (s), 774 (s), 681 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.17 (1H, dt, J = 13.6, 6.8 Hz), 4.72–4.68 (2H, m), 2.36–2.32 (2H, m), 2.26–2.20 (2H, m), 0.93 (9H, s), 0.08 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.7, 107.2, 88.8, 83.2, 75.6, 28.0, 26.2, 20.0, 16.7, –4.3. HRMS (ESI^+) $[M+H]^+$ calcd for $C_{13}H_{23}Si_1$: 207.15690, found: 207.15767.

***N*,*N*-Dibenzyl-4λ^5-penta-3,4-dien-1-amine (S3):** IR (neat): 3084 (w), 2924 (m), 2795 (m), 1954 (m), 1494 (m), 1451 (m), 1366 (m), 1246 (m), 1126 (m), 1074 (m), 975 (w), 841 (m), 732 (s), 696 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.40–7.36 (4H, m), 7.33–7.29 (4H, m), 7.25–7.21 (2H, m), 5.10–5.04 (1H, m), 4.64–4.60 (2H, m), 3.59 (4H, s), 2.55 (2H, t, J = 7.2 Hz), 2.27–2.20 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.8, 139.9, 128.9, 128.3, 126.9, 88.3, 74.7, 58.3, 53.1, 26.4. HRMS (ESI^+) $[M+H]^+$ calcd for $C_{19}H_{22}N_1$: 264.17522, found: 264.17591.

4.8.3 Experimental Procedures and Characterization Data for NHC–Cu-Catalyzed Cu–B Addition to Allenes Followed by Allylic Substitution

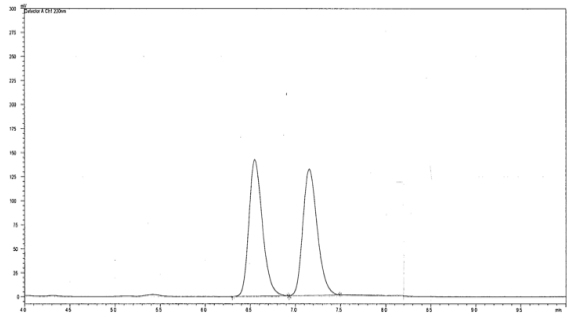
■ **Experimental Procedure for NHC–Cu-Catalyzed Cu–B Addition to Allenes Followed by Allylic Subsititution *at 22 °C*:** An oven-dried vial (4 mL, 17 × 38 mm) equipped with a magnetic stir bar was charged with imidazolinium salt **(*R*)-4.23d** (2.3 mg, 0.0050 mmol, 5.0 mol %), CuCl (0.5 mg, 0.0050 mmol, 5.0 mol %), KO*t*-Bu (16.8 mg, 0.15 mmol, 1.5 equiv.) and THF (0.5 mL) under N_2 atmosphere. The vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the mixture was allowed to stir at 22 °C for 2 h. Bis(pinacolato)diboron (30.5 mg, 0.12 mmol, 1.2 equiv.) was added, causing the mixture to turn dark brown immediately. The solution was allowed to stir at 22 °C for an additional 30 min. Allene **4.1a** (23.8 mg, 0.12 mmol, 1.2 equiv.) and allyl phosphate **4.10a** (27.0 mg, 0.10 mmol, 1.0 equiv.) were added by syringe. After 18 h, the reaction was quenched by passing the mixture through a short plug of Celite and silica gel and eluted with Et_2O (3 × 2 mL). The filtrate was concentrated in vacuo to provide yellow oil, which was purified by silica gel chromatography (75:1 hexanes:diethyl ether) to afford **4.11a** as colorless oil (35.3 mg, 0.080 mmol, 80% yield).

■ **Experimental Procedure for NHC–Cu-Catalyzed Cu–B Addition to Allene Followed by Allylic Subsititution *at 4 °C*:** An oven-dried vial (4 mL, 17 × 38 mm) equipped with a magnetic stir bar was charged with imidazolinium salt **(*R*)-4.23d** (2.3 mg, 0.0050 mmol, 5.0 mol %), CuCl (0.5 mg, 0.0050 mmol, 5.0 mol %), KO*t*-Bu (16.8 mg, 0.15 mmol, 1.5 equiv.) and THF (0.5 mL) under N_2 atmosphere. The vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the solution was allowed to stir at 22 °C for 2 h. Bis(pinacolato)diboron (30.5 mg, 0.12 mmol, 1.2 equiv.) was added to the solution, causing it to turn dark brown immediately. The mixture

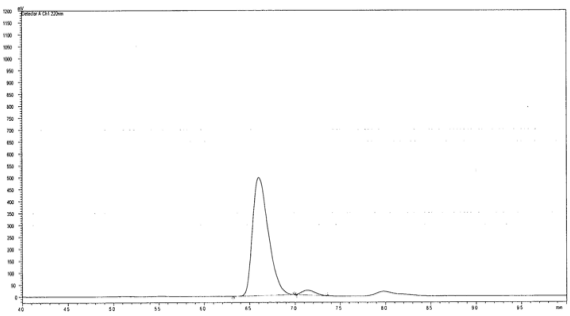
was allowed to stir at 22 °C for 30 min. At this time, the mixture was allowed to cool to –78 °C (dry ice/acetone bath) and allene **4.1a** (23.8 mg, 0.12 mmol, 1.2 equiv.) and allyl phosphate **4.10a** (27.0 mg, 0.10 mmol, 1.0 equiv.) were added by syringe. The vial was placed in a 4 °C cold room. After 24 h the solution was allowed to cool to –78 °C and the reaction was quenched by passing the mixture through a short plug of Celite and silica gel and eluted with Et_2O (3 × 2 mL). The filtrate was concentrated in vacuo to provide yellow oil, which was purified by silica gel chromatography (75:1 hexanes:diethyl ether) to afford **4.11a** as colorless oil (33.2 mg, 0.075 mmol, 75% yield).

(*R*,*Z*)-*tert*-Butyldimethyl((6-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octa-3,7-dien-1-yl)oxy)silane (4.11a). IR (neat): 3027 (m), 2976 (m), 2928 (m), 2856 (m), 1372 (m), 1304 (m), 1214 (m), 1146 (s), 1094 (s), 964 (m), 833 (s), 775 (s), 699 (s), 579 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.28–7.25 (2H, m), 7.21–7.15 (3H, m), 6.27 (1H, t, *J* = 6.0 Hz), 6.00 (1H, ddd, *J* = 14.0, 7.6, 6.0 Hz), 5.01–4.98 (2H, m), 3.60–3.54 (2H, m), 3.41 (1H, app. q, *J* = 6.4 Hz), 2.59 (1H, dd, *J* = 10.8, 6.0 Hz), 2.54 (1H, dd, *J* = 10.8, 6.0 Hz), 2.35–2.23 (2H, m), 1.21 (12H, s), 0.89 (9H, s), 0.04 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.6, 142.9, 142.1, 128.4, 128.0, 126.2, 114.3, 83.2, 62.7, 50.4, 35.0, 32.8, 26.1, 25.0, 24.8, 18.6, –5.1. HRMS (ESI^+) $[M+H]^+$ calcd for $C_{26}H_{44}B_1O_3Si_1$: 443.31528, found: 443.31400. Specific rotation: $[\alpha]_D^{20}$ –3.4 (*c* 1.17, $CHCl_3$) for an enantiomerically enriched sample of 97:3 e.r.

Enantiomeric purity of **4.11a** was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived ketone, which was synthesized by oxidation of the alkenylboron product with $NaBO_3$•$4H_2O$ (97:3 e.r. shown; Chiralpak AD–H column, 99.9:0.1 hexanes/ *i*PrOH, 1.0 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.548	1494806	142164	50.571	51.938
2	7.152	1461079	131556	49.429	48.062



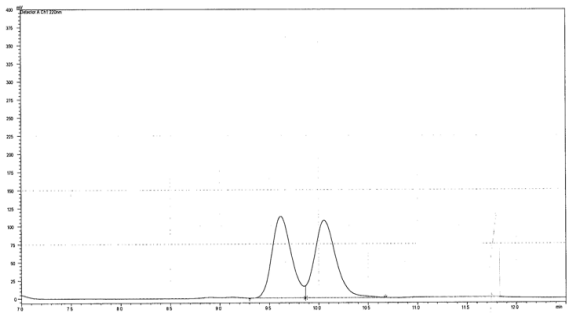
Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.598	6011947	495815	96.689	96.056
2	7.134	205859	20355	3.311	3.944

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	6.548	50.571	1	6.598	96.689
2	7.152	49.429	2	7.134	3.311

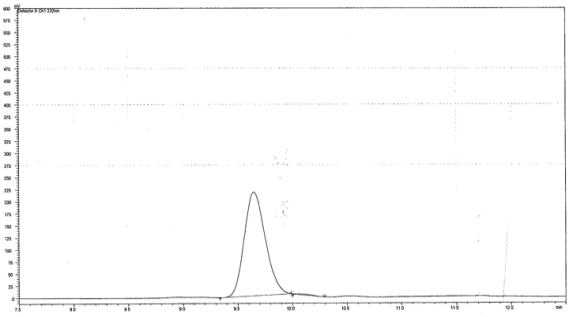
(*R*,*Z*)-*tert*-Butyldimethyl((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6-(*o*-tolyl)octa-3,7-dien-1-yl)oxy)silane (4.11b). IR (neat): 2976 (m), 2954 (m), 2928 (m), 2857 (m), 1632 (w), 1372 (s), 1305 (s), 1255 (m), 1144 (s), 1197 (s), 964 (w), 835 (s), 776 (m), 690 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27–7.25 (1H, m), 7.18–7.05 (3H, m), 6.30 (1H, t, *J* = 7.2 Hz), 5.91 (1H, ddd, *J* = 17.6, 10.0, 7.2 Hz), 4.96–4.93 (1H, m), 4.91–4.86 (1H, m), 3.71 (1H, app. q, *J* = 7.2 Hz), 3.59 (2H, t, *J* = 7.2 Hz), 2.63 (1H, dd, *J* = 12.8, 8.8 Hz), 2.48 (1H, dd, *J* = 12.8, 6.4 Hz), 2.35–2.30 (2H, m), 2.33 (3H, s), 1.23 (6H, s), 1.22 (6H, s), 0.89 (9H, s), 0.04 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.9, 142.8, 141.7, 136.0, 130.3, 127.0, 126.2, 125.9, 114.3, 83.2, 62.7, 45.4, 34.7, 32.8, 26.1, 24.9, 19.8, 18.6, –5.1. HRMS (ESI^+) $[M+H]^+$ calcd for $C_{27}H_{46}B_1O_3Si_1$: 457.33093, found: 457.33025. Specific rotation: $[\alpha]_D^{20}$ –9.9 (*c* 1.58, $CHCl_3$) for an enantiomerically enriched sample of 99.5:0.5 e.r.

Enantiomeric purity of **4.11b** was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived ketone, which was synthesized by

oxidation of the alkenylboron product with $NaBO_3$•$4H_2O$ (99.5:0.5 e.r. shown; Chiralpak AD–H column, 99.9:0.1 hexanes/ *i*PrOH, 0.6 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.613	1554396	112953	49.878	51.329
2	10.051	1562007	107106	50.122	48.671



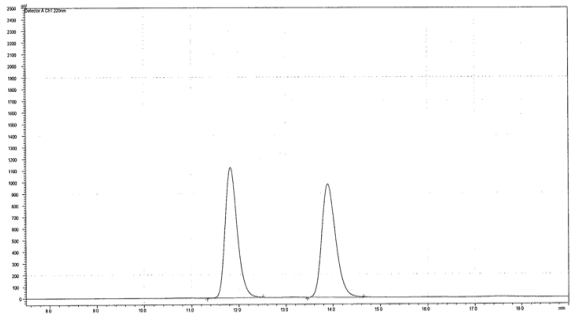
Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.616	2774235	205365	99.501	99.435
2	10.032	13908	1167	0.499	0.565

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	9.613	49.878	1	9.616	99.501
2	10.051	50.122	2	10.032	0.499

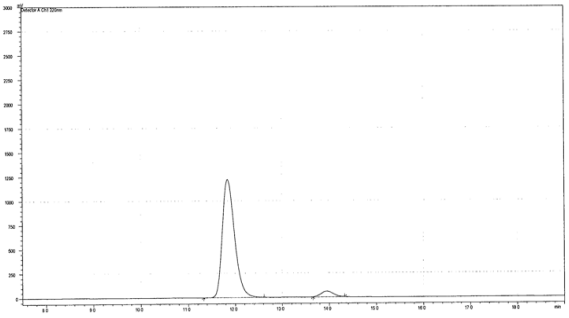
(*R*,*Z*)-*tert*-Butyldimethyl((6-(naphthalen-2-yl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octa-3,7-dien-1-yl)oxy)silane (4.11c). IR (neat): 3055 (m), 2976 (m), 2954 (m), 2928 (m), 2856 (m), 1631 (w), 1371 (m), 1304 (m), 1214 (w), 1094 (m), 1051 (s), 962 (w), 833 (s), 776 (s), 745 (m), 688 (m), 477 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.78–7.74 (3H, m), 7.63–7.62 (1H, m), 7.45–7.37 (3H, m), 6.29 (1H, t, *J* = 7.2 Hz), 6.10 (1H, ddd, *J* = 18.0, 10.0, 7.6 Hz), 5.08–5.03 (2H, m), 3.64–3.55 (3H, m), 2.72–2.63 (2H, m), 2.41–2.27 (2H, m), 1.17 (6H, s), 1.16 (6H, s), 0.88 (9H, s), 0.03 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.0, 142.0, 141.9, 133.7, 132.4, 127.9, 127.8, 127.7, 126.9, 126.2, 125.8, 125.3, 114.6, 83.2, 62.6, 50.5, 34.9, 32.8, 26.1, 24.9, 24.7, 18.6, –5.1. HRMS (ESI^+) $[M+H]^+$ calcd for $C_{30}H_{46}B_1O_3Si_1$: 493.33093, found: 493.33122. Specific rotation: $[\alpha]_D^{20}$ –1.5 (*c* 1.73, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.

Enantiomeric purity of **4.11c** was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived ketone, which was synthesized by

oxidation of the alkenylboron product with $NaBO_3$•$4H_2O$ (95:5 e.r. shown; Chiralpak AD–H column, 99.9:0.1 hexanes/ *i*PrOH, 0.6 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.821	19968753	1124765	49.730	53.521
2	13.889	20185523	976784	50.270	46.479

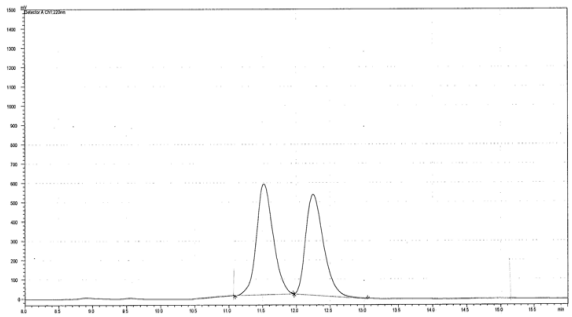


Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.838	22064138	1220575	95.350	95.383
2	13.945	1076028	59088	4.650	4.617

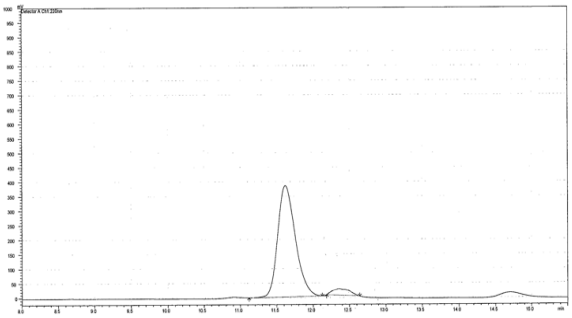
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	11.821	49.730	1	11.838	95.350
2	13.889	50.270	2	13.945	4.650

(*R*,*Z*)-((6-(3-Bromophenyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octa-3,7-dien-1-yl)oxy)(*tert*-butyl)dimethylsilane (4.11d). IR (neat): 2977 (m), 2954 (m), 2928 (m), 2857 (m), 1632 (w), 1472 (m), 1371 (m), 1305 (m), 1255 (m), 1214 (m), 1143 (s), 1094 (s), 964 (m), 833 (s), 775 (s), 678 (m), 579 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.35–7.34 (1H, m), 7.31–7.28 (1H, m), 7.13–7.11 (2H, m), 6.29 (1H, t, *J* = 7.2 Hz), 5.94 (1H, ddd, *J* = 16.8, 10.4, 7.6 Hz), 5.03–4.97 (2H, m), 3.61–3.57 (2H, m), 3.39 (1H, app. q, *J* = 7.6 Hz), 2.57 (1H, dd, *J* = 12.8, 7.6 Hz), 2.52 (1H, dd, *J* = 12.8, 7.6 Hz), 2.36–2.26 (2H, m), 1.20 (12H, s), 0.89 (9H, s), 0.04 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.9, 143.4, 141.4, 131.1, 129.9, 129.3, 126.8, 122.5, 114.9, 83.3, 62.6, 50.0, 34.8, 32.8, 26.1, 24.9, 24.8, 18.6, –5.1. HRMS (ESI^+) $[M+H]^+$ calcd for $C_{26}H_{43}B_1Br_1O_3Si_1$: 521.22579, found: 521.22431. Specific rotation: $[\alpha]_D^{20}$ –2.4 (*c* 1.26, $CHCl_3$) for an enantiomerically enriched sample of 94:6 e.r.

Enantiomeric purity of **4.11d** was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived ketone, which was synthesized by oxidation of the alkenylboron product with $NaBO_3 \bullet 4H_2O$ (94:6 e.r. shown; Chiralpak AD–H column, 99.9:0.1 hexanes/ *i*PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.516	9608905	566854	50.041	52.000
2	12.245	9593100	523254	49.959	48.000

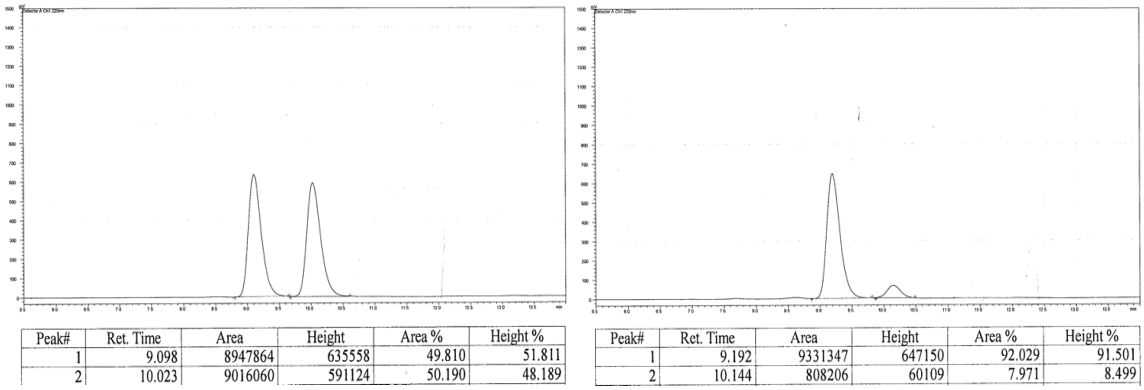


Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.616	6462863	383754	93.789	92.040
2	12.364	428026	33186	6.211	7.960

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	11.516	50.041	1	11.616	93.789
2	12.245	49.959	2	12.364	6.211

(*R*,*Z*)-*tert*-Butyl((6-(4-chlorophenyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octa-3,7-dien-1-yl)oxy)dimethylsilane (4.11e). IR (neat): 2977 (m), 2954 (m), 2928 (m), 2857 (m), 1632 (w), 1371 (m), 1305 (m), 1255 (m), 1214 (m), 1144 (m), 1092 (s), 939 (w), 832 (s), 775 (s), 672 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.22 (2H, d, *J* = 8.8 Hz), 7.12 (2H, d, *J* = 8.8 Hz), 6.28 (1H, t, *J* = 7.2 Hz), 5.96 (1H, ddd, *J* = 17.6, 10.4, 7.2 Hz), 5.03–4.96 (2H, m), 3.60–3.55 (2H, m), 3.40 (1H, app. q, *J* = 7.6 Hz), 2.57 (1H, dd, *J* = 12.8, 7.6 Hz), 2.49 (1H, dd, *J* = 12.8, 7.6 Hz), 2.35–2.23 (2H, m), 1.20 (12H, s), 0.89 (9H, s), 0.04 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.3, 142.9, 141.6, 131.8, 129.5, 128.4, 114.6, 83.3, 62.6, 49.6, 34.8, 32.8, 26.1, 24.9, 24.8, 18.6, –5.1. HRMS (ESI^+) $[M+H]^+$ calcd for $C_{26}H_{43}B_1Cl_1O_3Si_1$: 477.27630, found: 477.27456. Specific rotation: $[\alpha]_D^{20}$ –1.7 (*c* 1.61, $CHCl_3$) for an enantiomerically enriched sample of 92:8 e.r.

Enantiomeric purity of **4.11e** was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived ketone, which was synthesized by oxidation of the alkenylboron product with $NaBO_3 \bullet 4H_2O$ (92:8 e.r. shown; Chiralpak AD–H column, 99.9:0.1 hexanes/ *i*PrOH, 0.8 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.098	8947864	635558	49.810	51.811
2	10.023	9016060	591124	50.190	48.189

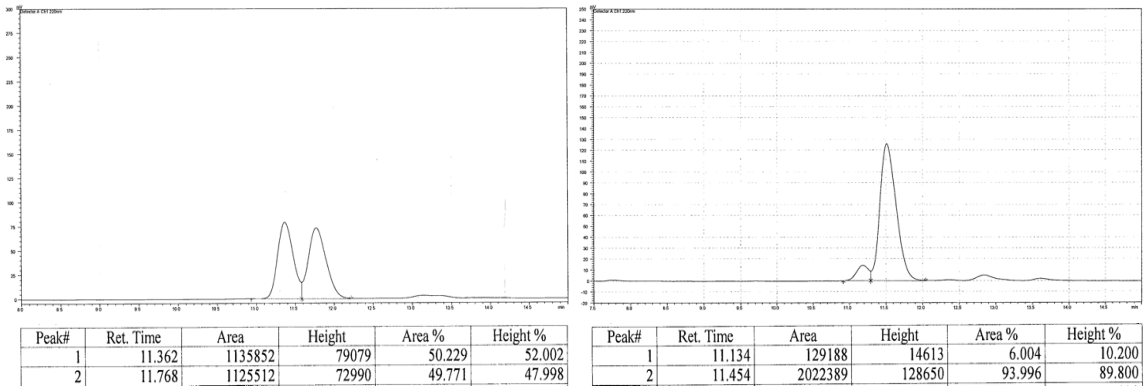
Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.192	9331347	647150	92.029	91.501
2	10.144	808206	60109	7.971	8.499

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	9.098	49.810	1	9.192	92.029
2	10.023	50.190	2	10.144	7.971

(*R*,*Z*)-*tert*-Butyldimethyl((6-phenethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octa-3,7-dien-1-yl)oxy)silane (4.11f). IR (neat): 2977 (m), 2954 (m), 2928 (m), 2857 (m), 1631 (w), 1371 (m), 1304 (m), 1254 (m), 1214 (m), 1144 (s), 1095 (s), 940 (m), 833 (s), 774 (s), 698 (m), 579 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.27–7.23 (2H, m), 7.17–7.13 (3H, m), 6.28 (1H, t, *J* = 7.2 Hz), 5.60 (1H, ddd, *J* = 17.2, 10.4, 8.4 Hz), 4.97 (1H, dd, *J* = 10.4, 2.0 Hz), 4.93 (1H, dd, *J* = 17.2, 2.0 Hz), 3.68–3.59 (3H, m), 2.67 (1H, ddd, *J* = 14.0, 10.0, 4.8 Hz), 2.51 (1H, ddd, *J* = 14.0, 10.0, 6.4 Hz), 2.38 (2H, qd, *J* = 7.2, 2.4 Hz), 2.30–2.20 (2H, m), 1.79–1.68 (1H, m), 1.59–1.52 (1H, m), 1.21 (12H, s), 0.89 (9H, s), 0.05 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.0, 142.9, 142.2, 128.5, 128.3, 125.6, 114.9, 83.2, 62.7, 44.8, 36.6, 34.5, 33.8, 32.9, 26.1, 24.9, 24.8, 18.6, –5.1. HRMS

(ESI$^+$) $[M+H]^+$ calcd for $C_{28}H_{48}B_1O_3Si_1$: 471.34658, found: 471.34827. Specific rotation: $[\alpha]_D^{20}$ –1.1 (*c* 1.67, $CHCl_3$) for an enantiomerically enriched sample of 94:6 e.r.

Enantiomeric purity of **4.11f** was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived ketone, which was synthesized by oxidation of the alkenylboron product with $NaBO_3$•$4H_2O$ (94:6 e.r. shown; Chiralcel OZ–H column, 99.9:0.1 hexanes/ *i*PrOH, 0.6 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.362	1135852	79079	50.229	52.002
2	11.768	1125512	72990	49.771	47.998

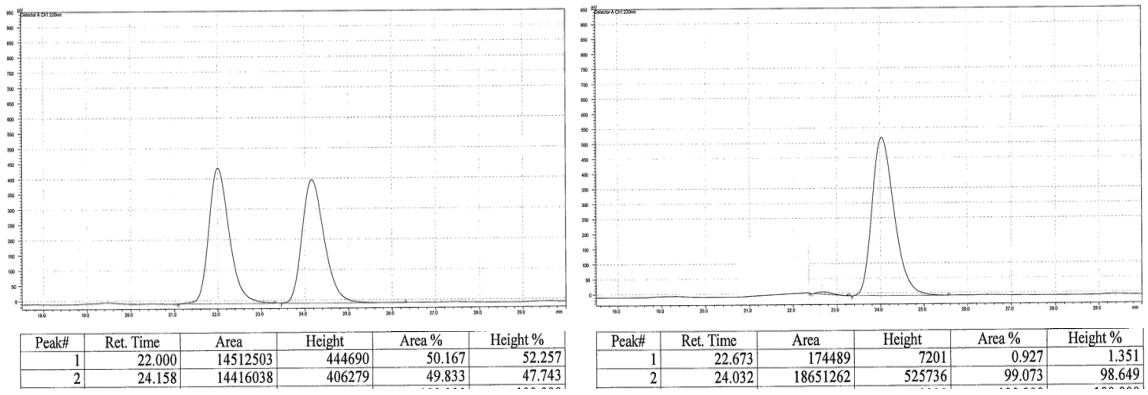
Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.134	129188	14613	6.004	10.200
2	11.454	2022389	128650	93.996	89.800

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	11.362	50.229	1	11.134	6.004
2	11.768	49.771	2	11.454	93.996

2-((*R*,1*E*,4*Z*)-1,7-Diphenylnona-1,4,8-trien-5-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.24). IR (neat): 3060 (w), 3025 (w), 2977 (m), 2929 (m), 1625 (m), 1372 (s), 1345 (m), 1305 (s), 1213 (m), 1143 (s), 1050 (m), 963 (m), 911 (m), 859 (m), 743 (m), 693 (s), 579 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.35–7.27 (6H, m), 7.24–7.16 (4H, m), 6.39–6.33 (2H, m), 6.09–6.00 (2H, m), 5.06–5.02 (2H, m), 3.46 (1H, app. q, *J* = 7.6 Hz), 3.01–2.87 (2H, m), 2.66 (1H, dd, *J* = 12.0, 7.2 Hz), 2.61 (1H, dd, *J* = 12.0, 7.2 Hz), 1.24 (12H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.4, 143.9, 142.1, 137.8, 130.8, 128.6, 128.5, 128.1, 128.0, 127.1, 126.2, 126.1, 114.4, 83.3, 50.4, 34.9, 32.6, 24.9, 24.8.

HRMS (ESI$^+$) $[M+H]^+$ calcd for $C_{27}H_{34}B_1O_2$: 401.26518, found: 401.26632. Specific rotation: $[\alpha]_D^{20}$ –8.3 (*c* 1.63, $CHCl_3$) for an enantiomerically enriched sample of 99:1 e.r.

Enantiomeric purity of **4.24** was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived ketone, which was synthesized by oxidation of the alkenylboron product with $NaBO_3$•$4H_2O$ (99:1 e.r. shown; Chiralpak AD–H column, 99:1 hexanes/ *i*PrOH, 0.4 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.000	14512503	444690	50.167	52.257
2	24.158	14416038	406279	49.833	47.743

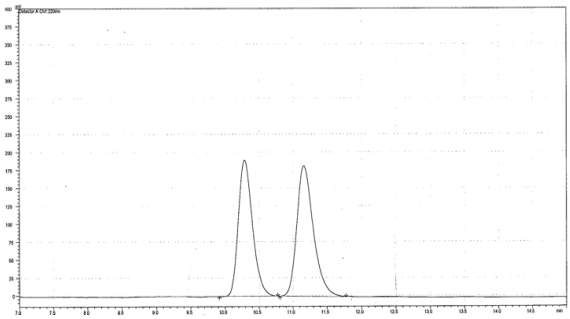
Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.673	174489	7201	0.927	1.351
2	24.032	18651262	525736	99.073	98.649

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	22.000	50.167	1	22.673	0.927
2	24.158	49.833	2	24.032	99.073

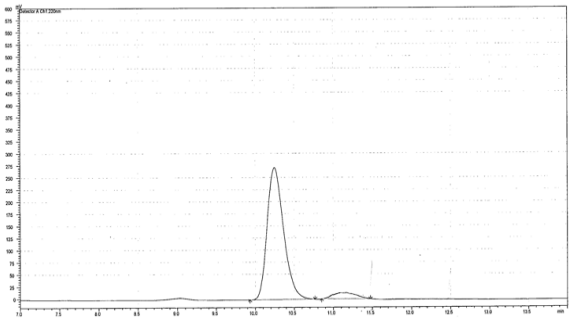
(*R*,*Z*)-*tert*-Butyldimethyl(8-phenyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)deca-5,9-dien-1-yn-1-yl)silane (4.25). IR (neat): 2977 (m), 2954 (m), 2928 (m), 2856 (m), 1632 (m), 1410 (m), 1378 (m), 1348 (m), 1249 (m), 1144 (s), 939 (m), 824 (m), 774 (m), 699 (m), 520 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.29–7.25 (2H, m), 7.20–7.14 (3H, m), 6.31 (1H, t, *J* = 6.8 Hz), 6.01 (1H, ddd, *J* = 17.6, 8.8, 7.2 Hz), 5.03–4.98 (2H, m), 3.40 (1H, app. q, *J* = 7.6 Hz), 2.59 (1H, dd, *J* = 12.8, 7.6 Hz), 2.54 (1H, dd, *J* = 12.8, 7.6 Hz), 2.30–2.13 (4H, m), 1.22 (12H, s), 0.93 (9H, s), 0.08 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.9, 144.4, 142.0, 128.4, 128.0, 126.2, 114.3, 107.5, 83.2, 50.4, 35.0, 28.2, 26.3, 25.0, 24.9, 24.8, 19.6, 16.7, –4.3. HRMS (ESI$^+$) $[M+H]^+$ calcd for

$C_{28}H_{44}B_1O_2Si_1$: 401.26518, found: 401.26632. Specific rotation: $[\alpha]_D^{20}$ –6.5 (*c* 1.33, $CHCl_3$) for an enantiomerically enriched sample of 96:4 e.r.

Enantiomeric purity of **4.25** was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived ketone, which was synthesized by oxidation of the alkenylboron product with $NaBO_3$•$4H_2O$ (96:4 e.r. shown; Chiralpak AD–H column, 99.9:0.1 hexanes/ *i*PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.285	2752967	189796	49.563	51.858
2	11.159	2801471	176198	50.437	48.142



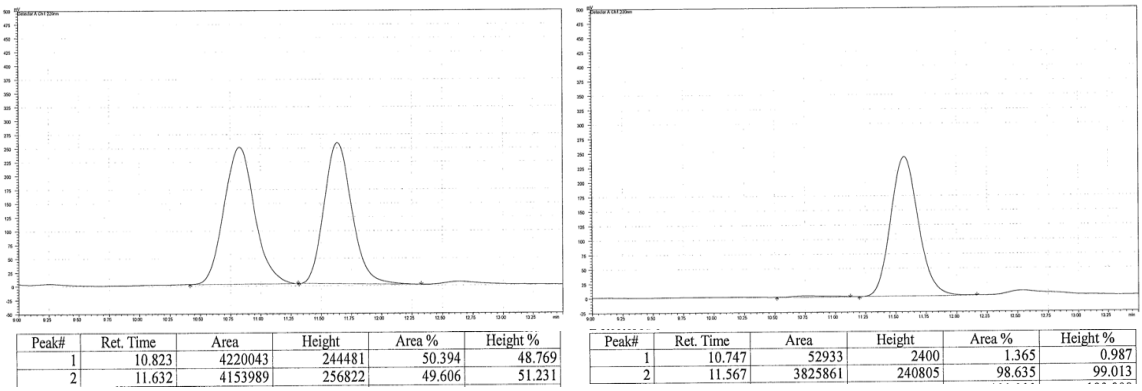
Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.243	4004734	272715	96.348	95.113
2	11.117	151789	14011	3.652	4.887

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	10.285	49.563	1	10.243	96.348
2	11.159	50.437	2	11.117	3.652

(*R*,*Z*)-*N*,*N*-Dibenzyl-6-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octa-3,7-dien-1-amine (4.26). IR (neat): 3027 (w), 2977 (m), 2930 (m), 2797 (m), 1705 (w), 1493 (m), 1410 (m), 1371 (m), 1347 (m), 1303 (m), 1214 (m), 1142 (s), 1028 (m), 908 (s), 859 (m), 730 (s), 697 (s), 579 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.39–7.36 (4H, m), 7.33–7.28 (6H, m), 7.25–7.22 (3H, m), 7.18–7.14 (2H, m), 6.26 (1H, t, *J* = 6.8 Hz), 5.96 (1H, ddd, *J* = 17.6, 10.0, 7.6 Hz), 4.99–4.95 (2H, m), 3.62–3.54 (4H, m), 3.37 (1H, app. q, *J* = 7.6 Hz), 2.56–2.40 (4H, m), 2.31–2.22 (2H, m), 1.23 (12H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.8, 144.4, 142.0, 139.8, 128.7, 128.2, 128.1, 127.9, 126.8, 126.0, 114.2, 83.0, 58.2, 52.4, 50.3, 34.8, 26.4, 24.8, 24.7. HRMS (ESI^+) $[M+H]^+$ calcd

for $C_{34}H_{43}B_1N_1O_2$: 508.33868, found: 508.34028. Specific rotation: $[\alpha]_D^{20}$ –5.7 (*c* 1.95, $CHCl_3$) for an enantiomerically enriched sample of 99:1 e.r.

Enantiomeric purity of **4.26** was determined by HPLC analysis in comparison with authentic racemic material (99:1 e.r. shown; Chiralpak AD column, 99.5:0.5 hexanes/ *i*PrOH, 0.6 mL/min, 220 nm).



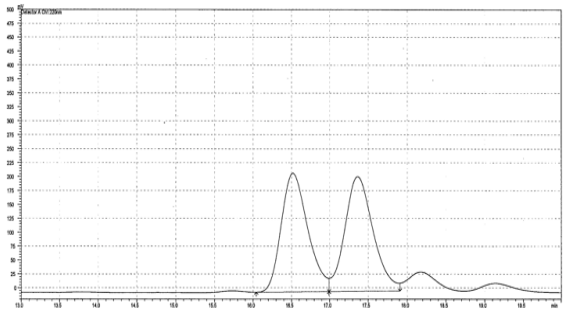
Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.823	4220043	244481	50.394	48.769
2	11.632	4153989	256822	49.606	51.231

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.747	52933	2400	1.365	0.987
2	11.567	3825861	240805	98.635	99.013

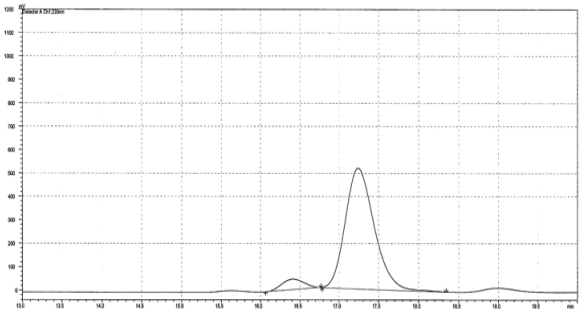
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	10.823	50.394	1	10.747	1.365
2	11.632	49.606	2	11.567	98.635

(*R*,*Z*)-*N*,*O*-Dimethyl-*N*-(8-phenyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)deca-1,5,9-trien-2-yl)hydroxylamine (4.27). IR (neat): 3062 (m), 2977 (m), 2934 (m), 1635 (m), 1472 (m), 1372 (s), 1305 (s), 1143 (s), 965 (m), 912 (m), 852 (m), 746 (m), 700 (m), 674 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.30–7.23 (3H, m), 7.19–7.12 (2H, m), 6.26 (1H, t, *J* = 6.8 Hz), 5.99 (1H, ddd, *J* = 17.6, 10.0, 7.6 Hz), 5.01–4.96 (2H, m), 3.63 (3H, s), 3.41 (1H, app. q, *J* = 7.6 Hz), 3.16 (3H, s), 2.59–2.56 (2H, m), 2.41–2.31 (4H, m), 1.21 (12H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.0, 144.4, 142.1, 128.5, 128.3, 128.0, 126.1, 114.3, 83.2, 75.1, 61.3, 50.3, 34.8, 24.9, 24.7, 24.0; HRMS (ESI^+) $[M+H]^+$ Calcd for $C_{23}H_{35}B_1N_1O_4$: 400.26591, Found: 400.26521; specific rotation: $[\alpha]_D^{20}$ –4.9 (*c* 1.29, $CHCl_3$) for an enantiomerically enriched sample of 94:6 e.r.

Enantiomeric purity of **4.27** was determined by HPLC analysis in comparison with authentic racemic material (94:6 e.r. shown; Chiralpak AD–H column, 97:3 hexanes/ *i*PrOH, 0.3 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.514	5185919	213657	49.766	50.870
2	17.361	5234759	206349	50.234	49.130

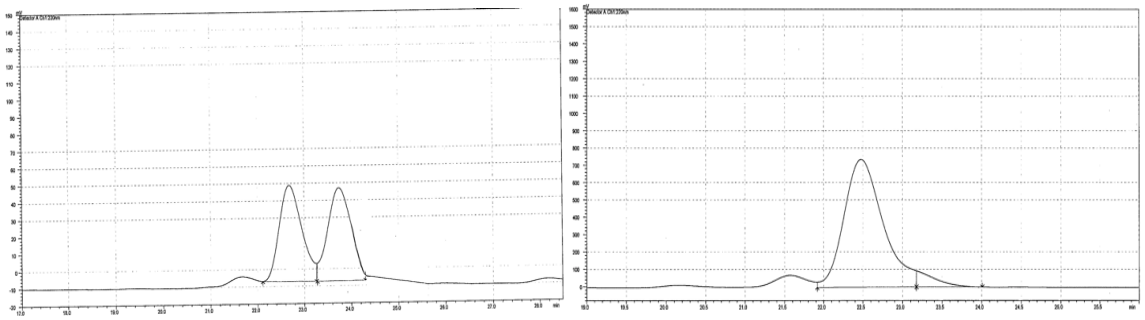


Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.407	857751	44147	6.121	7.877
2	17.236	13155613	516276	93.879	92.123

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	16.514	49.766	1	16.407	6.121
2	17.361	50.234	2	17.236	93.879

(*R*,*Z*)-*N*-Methoxy-*N*-methyl-9-phenyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)undeca-6,10-dienamide (4.29). IR (neat): 2977 (m), 2934 (m), 1638 (m), 1473 (s), 1372 (s), 1305 (s), 1272 (w), 1144 (s), 983 (m), 851 (m), 754 (w), 700 (m), 578 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.28–7.23 (3H, m), 7.19–7.12 (2H, m), 6.28 (1H, t, *J* = 7.2 Hz), 5.99 (1H, ddd, *J* = 17.6, 10.0, 7.6 Hz), 5.00–4.95 (2H, m), 3.66 (3H, s), 3.37 (1H, app. q, *J* = 8.0 Hz), 3.16 (3H, s), 2.56–2.49 (2H, m), 2.42–2.35 (4H, m), 2.05–1.98 (2H, m), 1.63–1.55 (2H, m), 1.25 (12H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.3, 144.5, 142.1, 128.5, 128.3, 128.0, 126.0, 114.2, 83.1, 75.2, 61.3, 50.4, 34.9, 28.9, 28.7, 24.9, 24.7, 24.6; HRMS (ESI^+) $[M+H]^+$ Calcd for $C_{25}H_{39}B_1N_1O_4$: 428.29721; Found: 428.29816; specific rotation: $[\alpha]_D^{20}$ –6.7 (*c* 0.93, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.

Enantiomeric purity of **4.29** was determined by HPLC analysis in comparison with authentic racemic material (95:5 e.r. shown; Chiralpak AD–H column, 97:3 hexanes/ *i*PrOH, 0.3 mL/min, 220 nm).



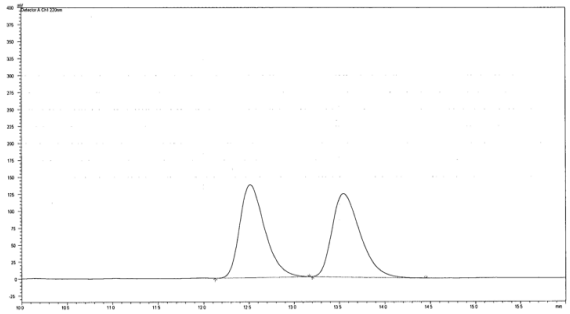
Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.679	2095737	58918	49.380	50.791
2	23.740	2148347	57083	50.620	49.209

Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.471	25357546	737237	94.559	88.859
2	23.175	1459096	92431	5.441	11.141

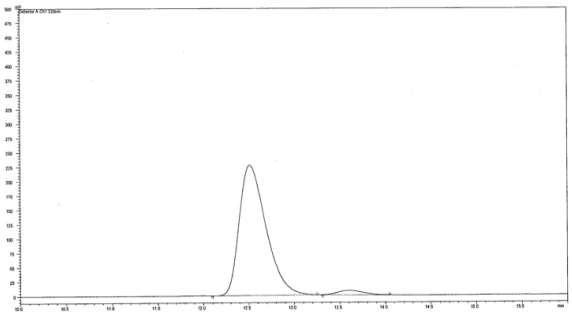
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	22.679	49.380	1	22.471	94.559
2	23.740	50.620	2	23.175	5.441

(*R*)-4,4,5,5-Tetramethyl-2-(4-phenylhexa-1,5-dien-2-yl)-1,3,2-dioxaborolane (4.30). IR (neat): 3061 (w), 3027 (w), 2977 (m), 2929 (w), 1624 (w), 1600 (w), 1492 (w), 1448 (m), 1410 (m), 1367 (s), 1343 (m), 1306 (s), 1272 (m), 1212 (m), 1164 (m), 1139 (s), 1111 (m), 1076 (w), 1029 (w), 992 (w), 961 (w), 942 (m), 912 (m), 860 (s), 834 (m), 755 (m), 698 (s), 670 (s), 578 (m), 520 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.29–7.26 (2H, m), 7.21–7.15 (3H, m), 5.97 (1H, ddd, *J* = 17.4, 10.0, 7.6 Hz), 5.78 (1H, d, *J* = 3.2 Hz), 5.53 (1H, d, *J* = 3.2 Hz), 5.00 (1H, dd, *J* = 10.0, 1.2 Hz), 4.98 (1H, dd, *J* = 17.4, 1.2 Hz), 3.53 (1H, td, *J* = 7.6, 7.0 Hz) 2.58 (2H, dd, *J* = 7.0, 2.8 Hz), 1.24 (12H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 144.4, 142.1, 131.3, 128.6, 128.4, 128.0, 126.1, 114.4, 83.4, 49.9, 41.5, 24.9; HRMS (ESI^+) $[M+H]^+$ Calcd for $C_{18}H_{26}B_1O_2$: 285.2025; Found: 285.2021; specific rotation: $[\alpha]_D^{20}$ –3.8 (*c* 0.85, $CHCl_3$) for an enantiomerically enriched sample of 97:3 e.r.

Enantiomeric purity of **4.30** was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived ketone, which was synthesized by oxidation of the alkenylboron product with $NaBO_3 \bullet 4H_2O$ (97:3 e.r. shown; Chiralpak AD–H column, 99.9:0.1 hexanes/ *i*PrOH, 0.8 mL/min, 220 nm).



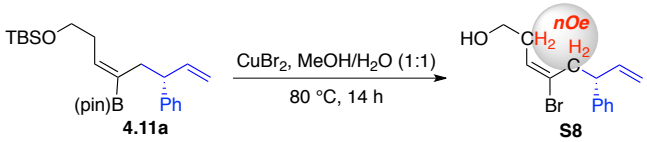
Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.510	2662805	137220	50.042	52.640
2	13.543	2658284	123457	49.958	47.360



Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.511	4660608	227173	96.691	96.593
2	13.594	159498	8013	3.309	3.407

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	12.510	50.042	1	12.511	96.691
2	13.543	49.958	2	13.594	3.309

■ **Proof of stereochemistry:** Literature value ($[\alpha]_D^{20}$ +6.0 (*c* 1.53, $CHCl_3$), 99:1 e.r.) of **(*S*)-4.30** is assigned to the *S* enantiomer.[45] The geometry of the double bond in compound **4.11a** was assigned as *Z* based on nOe experiments with the corresponding bromide **S8**.



(*R*,*E*)-4-Bromo-6-phenylocta-3,7-dien-1-ol (S8). IR (neat): 3331 (br), 3027 (w), 2917 (m), 1638 (m), 1492 (m), 1416 (w), 1300 (w), 1191 (w), 1045 (s), 992 (s), 917 (m), 756 (m), 700 (s), 646 (m), 516 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.35–7.29 (2H, m), 7.25–7.18 (3H, m), 6.04 (1H, ddd, *J* = 17.6, 10.0, 7.2 Hz), 5.84 (1H, t, *J* = 8.0 Hz), 5.15–5.10 (2H, m), 3.78 (1H, app. q, *J* = 7.2 Hz), 3.41–3.32 (2H, m), 2.87–2.79 (2H, m), 2.16–

(45) Le, H.; Kyne, R. E.; Brozek, L. A.; Morken, J. P. *Org. Lett.* **2013**, *15*, 1432–1435.

2.07 (1H, m), 1.97–1.88 (1H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 142.6, 140.2, 130.3, 128.6, 128.1, 126.8, 125.7, 115.3, 61.5, 47.5, 42.0, 33.1; HRMS (ESI$^+$) $[M+NH_4]^+$ Calcd for $C_{14}H_{21}Br_1N_1O_1$: 298.08065; Found: 298.07997; specific rotation: $[\alpha]_D^{20}$ –8.3 (*c* 0.75, $CHCl_3$).

■ **Experimental Procedure for Suzuki Coupling of the Tri-substituted Alkenylboron with Aryl Halide:** In a N_2-filled glove-box, an oven-dried vial (4 mL, 17 × 38 mm) equipped with a magnetic stir bar was charged with alkenylboron compound **4.11a** (44.2 mg, 0.10 mmol), 2-bromopyridine (14.3 μL, 0.15 mmol), $Pd_2(dba)_3$ (1.8 mg, 0.0020 mmol, 2.0 mol %) and S-Phos (1.6 mg, 0.0040 mmol, 4.0 mol %). Tetrahydrofuran (THF, 0.9 mL) and 3M aqueous NaOH solution (0.3 mL) were added by syringe. The vessel was sealed with a cap and removed from the glove-box, and the mixture was allowed to stir at 60 °C for 18 h, after which the mixture was allowed to cool to 22 °C. Water (1 mL) and Et_2O (1 mL) were added to quench the reaction. The aqueous layer was washed with Et_2O (3 × 1 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. The red oil residue was purified by silica gel chromatography (8:1 hexanes:ethyl acetate) to afford **4.31** as colorless oil (30.4 mg, 0.0772 mmol, 77% yield).

(*R*,*E*)-2-(1-((*tert*-Butyldimethylsilyl)oxy)-6-phenylocta-3,7-dien-4-yl)pyridine (4.31). IR (neat): 2953 (m), 2928 (m), 2856 (m), 1622 (m), 1465 (m), 1338 (w), 1253 (m), 1184 (w), 1092 (s), 937 (m), 833 (s), 774 (s), 698 (s), 551 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.75–8.73 (1H, m), 7.62–7.59 (2H, m), 7.45–7.41 (3H, m), 7.34–7.28 (3H, m), 6.25 (1H, t, *J* = 7.2 Hz), 6.19 (1H, ddd, *J* = 17.2, 9.6, 7.2 Hz), 5.19–5.11 (2H, m), 3.74 (2H, app. t, *J* = 7.2 Hz), 3.55 (1H, app. q, *J* = 7.6 Hz), 3.36 (1H, dd, *J* = 10.2, 7.6 Hz),

3.22 (1H, dd, *J* = 10.2, 7.6 Hz), 2.57–2.51 (1H, m), 2.46–2.40 (1H, m), 1.08 (9H, s), 0.23 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.5, 141.5, 134.9, 130.6, 129.1, 128.5, 128.3, 128.0, 126.3, 126.1, 125.6, 121.5, 114.5, 62.8, 48.5, 34.6, 32.7, 26.1, 18.5, –5.1, –5.2. HRMS (ESI$^+$) $[M+H]^+$ calcd for $C_{25}H_{36}N_1O_1Si_1$: 394.25662, found: 394.25556. Specific rotation: $[\alpha]_D^{20}$ –10.4 (*c* 2.25, $CHCl_3$).

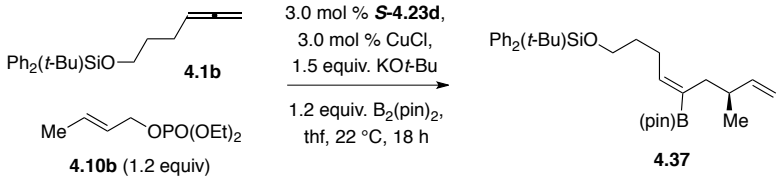
(*R*,*E*)-2-(1-((*tert*-Butyldimethylsilyl)oxy)-6-phenylocta-3,7-dien-4-yl)pyrimidine (4.32). IR (neat): 2953 (m), 2928 (m), 2885 (m), 2856 (m), 1637 (m), 1471 (m), 1341 (w), 1253 (m), 1187 (w), 1094 (s), 1005 (w), 910 (m), 833 (s), 775 (s), 728 (s), 700 (s), 631 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.05 (1H, s), 8.55 (2H, s), 7.29–7.27 (1H, m), 7.25–7.20 (1H, m), 7.17–7.13 (1H, m), 7.06–7.04 (2H, m), 5.96 (1H, ddd, *J* = 17.6, 10.4, 7.2 Hz), 5.70 (1H, t, *J* = 7.2 Hz), 5.03 (1H, dt, *J* = 10.0, 1.2 Hz), 4.96 (1H, dt, *J* = 17.2, 1.2 Hz), 3.61–3.52 (2H, m), 3.24 (1H, app. q, *J* = 7.6 Hz), 2.98 (1H, dd, *J* = 14.0, 7.2 Hz), 2.88 (1H, dd, *J* = 14.0, 7.2 Hz), 2.40–2.33 (1H, m), 2.30–2.23 (1H, m), 0.89 (9H, s), 0.04 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.9, 154.7, 142.7, 140.7, 133.7, 131.3, 128.6, 127.7, 126.8, 126.1, 115.0, 62.4, 48.5, 35.7, 32.6, 26.0, 18.5, –5.1. HRMS (ESI$^+$) $[M+H]^+$ calcd for $C_{24}H_{35}N_2O_1Si_1$: 395.25186, found: 395.25189. Specific rotation: $[\alpha]_D^{20}$ –11.2 (*c* 1.94, $CHCl_3$).

(*R*,*E*)-4-(1-((*tert*-Butyldimethylsilyl)oxy)-6-phenylocta-3,7-dien-4-yl)thiazole (4.33). IR (neat): 2953 (m), 2927 (m), 2855 (m), 1471 (m), 1361 (w), 1252 (m), 1092 (s), 1005 (w), 910 (m), 833 (s), 775 (s), 731 (s), 699 (s), 664 (m), 552 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.74 (1H, d, *J* = 2.0 Hz), 7.29–7.24 (2H, m), 7.19–7.14 (3H, m), 7.00 (1H, d, *J* = 2.0 Hz), 6.37 (1H, t, *J* = 7.2 Hz), 6.07 (1H, ddd, *J* = 17.6, 10.0, 7.2 Hz), 5.06–4.97 (2H, m), 3.58–3.49 (2H, m), 3.46 (1H, app. q, *J* = 7.2 Hz), 3.03 (1H, dd, *J* = 14.0,

7.2 Hz), 2.89 (1H, dd, J = 14.0, 7.2 Hz), 2.35–2.26 (1H, m), 2.21–2.12 (1H, m), 0.90 (9H, s), 0.05 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.4, 152.0, 143.8, 141.3, 132.9, 128.4, 128.0, 126.5, 126.1, 114.6, 111.7, 62.8, 48.7, 35.7, 32.4, 26.1, 18.5, –5.1. HRMS (ESI$^+$) $[M+H]^+$ calcd for $C_{23}H_{34}N_1O_1S_1Si_1$: 400.21304, found: 400.21327. Specific rotation: $[\alpha]_D^{20}$ –15.9 (*c* 2.05, $CHCl_3$).

4.8.4 Experimental Procedures and Characterization Data for Total Synthesis of Rottnestol and Herboxidiene

■ **Total Synthesis of (–)-Rottnestol**

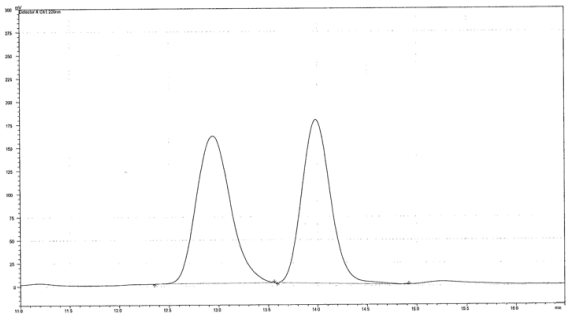


(*S*,*Z*)-*tert*-Butyl((7-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)nona-4,8-dien-1-yl)oxy)diphenylsilane (4.37). An oven-dried 50 mL flask equipped with a magnetic stir bar was charged with imidazolinium salt **(*S*)-4.23d** (70.3 mg, 0.150 mmol, 3.0 mol %), CuCl (14.8 mg, 0.150 mmol, 3.0 mol %), KO*t*-Bu (842 mg, 7.50 mmol, 1.5 equiv.) and THF (20 mL). The flask was sealed with a rubber septum and the solution was allowed to stir at 22 °C for 2 h under N_2 atmosphere. Bis(pinacolato)diboron (1.53 g, 6.00 mmol, 1.2 equiv.) was added to the solution, causing it to turn dark brown immediately. The mixture was allowed to stir at 22 °C for 30 min. Allene **4.1b**[46] (1.68 g, 5.00 mmol, 1.0 equiv.) and allyl phosphate **4.10b** (1.25 g, 6.00 mmol, 1.2 equiv.) were

(46) **1b** was synthesized according to known procedure in 77% overall yield, see ref 1c.

added by syringe. After 18 h, the reaction was quenched by the addition of a saturated solution of NH_4Cl (20 mL). The aqueous layer was washed with Et_2O (3 × 20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the resulting yellow oil by silica gel chromatography (70:1 hexanes:diethyl ether) affords the desired product **4.37** as colorless oil (2.05 g, 3.95 mmol, 79% yield). IR (neat): 3071 (w), 2976 (m), 2930 (m), 2858 (m), 1472 (m), 1371 (m), 1303 (m), 1143 (s), 1109 (s), 908 (w), 863 (m), 702 (s), 614 (m), 505 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.68–7.66 (4H, m), 7.45–7.36 (6H, m), 6.35 (1H, t, *J* = 7.2 Hz), 5.75 (1H, ddd, *J* = 17.2, 10.0, 7.2 Hz), 4.93–4.84 (2H, m), 3.68 (2H, app. t, *J* = 6.4 Hz), 2.28–2.10 (5H, m), 1.69–1.62 (2H, m), 1.26 (12H, s), 1.06 (9H, s), 0.97 (3H, d, *J* = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.5, 144.9, 135.7, 134.2, 129.6, 127.7, 112.3, 83.1, 63.7, 38.7, 35.6, 32.2, 27.0, 25.5, 24.9, 19.9, 19.4. HRMS (ESI^+) $[M+NH_4]^+$ calcd for $C_{32}H_{51}B_1N_1O_3Si_1$: 536.37312, found: 536.37499. Specific rotation: $[a]_D^{20}$ +1.9 (*c* 0.81, $CHCl_3$).

Enantiomeric purity of **4.37** was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived ketone, which was synthesized by oxidation of the alkenylboron product with $NaBO_3$•$4H_2O$ (92:8 e.r. shown; Chiralpak AD column, 99:1 hexanes/ *i*PrOH, 0.3 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
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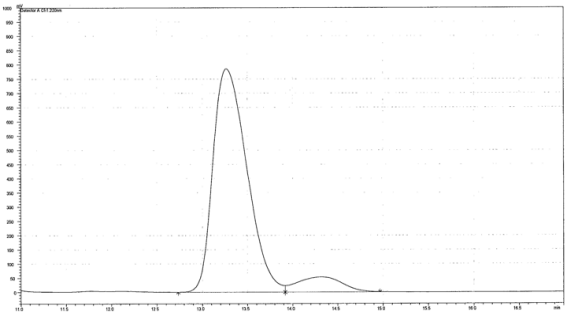
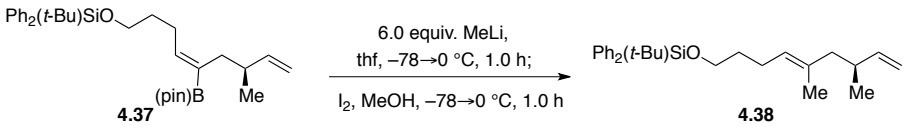
2	13.978	3581455	177024	49.889	53.167



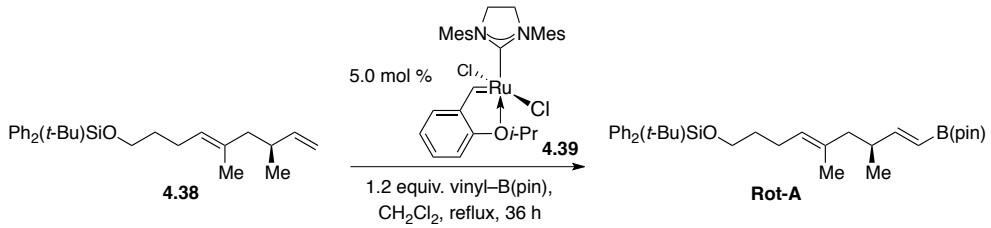
Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.263	20536975	785527	91.788	93.641
2	14.315	1837334	53344	8.212	6.359

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	12.937	50.111	1	13.263	91.788
2	13.978	49.889	2	14.315	8.212



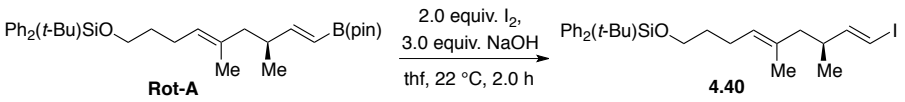
(*S*,*E*)-*tert*-Butyl((5,7-dimethylnona-4,8-dien-1-yl)oxy)diphenylsilane (4.38). A solution of alkenylboron **4.37** (2.65 g, 5.12 mmol) in THF (40 mL) was treated with MeLi (solution in Et_2O; 19.2 mL, 1.6 M, 30.7 mmol) at –78 °C. The mixture was allowed to stir at 0 °C for one hour. Then the mixture was allowed to cool to –78 °C. A solution of I_2 (7.79 g, 30.7 mmol) in MeOH (40 mL) was added and the resulting mixture was allowed to warm to 0 °C and stir at 0 °C for one hour. The reaction was quenched by an addition of a saturated aqueous solution of $Na_2S_2O_3$ (20 mL). The aqueous layer was washed with Et_2O (3 × 20 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Purification of the yellow oil residue by silica gel chromatography (80:1 hexanes:diethyl ether) affords **4.38** as colorless oil (1.89 g, 4.64 mmol, 91% yield). IR (neat): 3071 (w), 2957 (m), 2858 (m), 1428 (m), 1107 (s), 939 (w), 822 (m), 700 (s), 613 (m), 504 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.68–7.66 (4H, m), 7.44–7.36 (6H,

m), 5.71 (1H, ddd, J = 17.2, 10.0, 7.2 Hz), 5.08 (1H, app. t, J = 7.2 Hz), 4.95–4.85 (2H, m), 3.66 (2H, app. t, J = 6.4 Hz), 2.36–2.26 (1H, m), 2.10–2.06 (2H, m), 2.03–1.98 (1H, m), 1.89–1.84 (1H, m), 1.63–1.55 (5H, m), 1.06 (9H, s), 0.91 (3H, d, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.8, 135.7, 134.3, 133.8, 129.7, 127.8, 126.1, 112.1, 63.6, 47.4, 35.6, 32.9, 27.0, 24.3, 19.5, 19.4, 16.0. HRMS (ESI$^+$) $[M+H]^+$ calcd for $C_{27}H_{39}O_1Si_1$: 407.27702, found: 407.27651. Specific rotation: $[\alpha]_D^{20}$ +2.1 (*c* 0.82, $CHCl_3$).



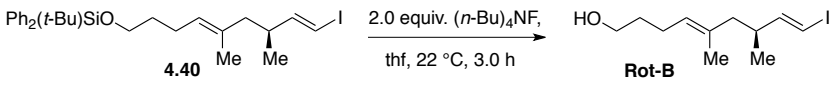
***tert*-Butyl(((*S*,4*E*,8*E*)-5,7-dimethyl-9-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)nona-4,8-dien-1-yl)oxy)diphenylsilane (Rot-A).** To a solution of **4.38** (2.00 g, 4.92 mmol) and vinyl boronic acid pinacol ester (1.00 mL, 5.90 mmol) in CH_2Cl_2 (30 mL) was added Ru-based complex **4.39** (209 mg, 0.25 mmol) at 22 °C. The mixture was allowed to stir at 50 °C for 36 h. The reaction was quenched by passing the mixture through a short plug of silica gel and eluted with hexanes and diethyl ether (1:1, 3 × 30 mL). The filtrate was concentrated in vacuo to provide brown oil, which was purified by silica gel chromatography (50:1 hexanes:diethyl ether) to afford **Rot-A** as colorless oil (2.42 g, 4.55 mmol, 92% yield). IR (neat): 2959 (m), 2858 (m), 1636 (m), 1360 (s), 1321 (s), 1214 (w), 1145 (s), 1109 (s), 998 (m), 823 (m), 702 (s), 579 (m), 505 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68–7.66 (4H, m), 7.44–7.36 (6H, m), 6.56 (1H, dd, J = 18.0, 6.8 Hz), 5.39 (1H, d, J = 18.0 Hz), 5.09 (1H, t, J = 6.8 Hz), 3.66 (2H, app. t, J = 6.4 Hz), 2.41–2.33 (1H, m), 2.12–2.03 (3H, m), 1.87–1.81 (1H, m), 1.63–1.56 (5H, m), 1.26 (12H,

s), 1.06 (9H, s), 0.91 (3H, d, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.1, 135.7, 134.2, 133.5, 129.6, 127.7, 126.3, 83.1, 63.6, 46.7, 37.3, 32.9, 27.0, 24.9, 24.3, 19.4, 18.7, 16.0. HRMS (ESI$^+$) $[M+H]^+$ calcd for $C_{33}H_{50}B_1O_3Si_1$: 533.36223, found: 533.36421. Specific rotation: $[\alpha]_D^{20}$ –0.89 (*c* 2.25, $CHCl_3$).

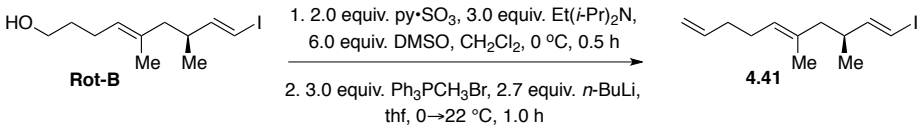


***tert*-Butyl(((*S*,4*E*,8*E*)-9-iodo-5,7-dimethylnona-4,8-dien-1-yl)oxy)diphenylsilane (30).** To a solution of alkenyl boron **Rot-A** (2.42 g, 4.55 mmol) in THF (10 mL) was added 3.0 M NaOH aqueous solution (4.57 mL, 13.7 mmol) at 22 °C. The resulting solution was allowed to stir at 22 °C for 30 min. Then a solution of I_2 (2.31 g, 9.10 mmol) in THF (10 mL) was added, and the mixture was allowed to stir at 22 °C for two hours. The reaction was quenched by the addition of a saturated aqueous solution of $Na_2S_2O_3$ (15 mL). The aqueous layer was washed with Et_2O (3 × 15 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the resulting yellow oil by silica gel chromatography (80:1 hexanes:diethyl ether) affords **4.40** as colorless oil (2.11 g, 3.96 mmol, 87% yield). IR (neat): 3070 (w), 2957 (m), 2857 (m), 1427 (m), 1106 (s), 948 (w), 822 (m), 738 (m), 699 (s), 613 (m), 503 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70–7.66 (4H, m), 7.44–7.36 (6H, m), 6.40 (1H, dd, J = 14.4, 8.0 Hz), 5.92 (1H, d, J = 14.4 Hz), 5.09 (1H, t, J = 6.8 Hz), 3.67 (2H, app. t, J = 6.4 Hz), 2.36–2.29 (1H, m), 2.12–2.07 (2H, m), 2.01 (1H, dd, J = 13.2, 7.6 Hz), 1.88 (1H, dd, J = 13.2, 7.6 Hz), 1.65–1.59 (2H, m), 1.56 (3H, s), 1.07 (9H, s), 0.93 (3H, d, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.1, 135.7, 134.3, 132.9, 129.6, 127.7, 126.9, 73.2, 63.5, 46.8, 38.8, 32.8, 27.0, 24.3, 19.4, 19.1, 16.0. HRMS (ESI$^+$) $[M+H]^+$ calcd for

$C_{27}H_{38}I_1O_1Si_1$: 533.17366, found: 533.17415. Specific rotation: $[\alpha]_D^{20}$ +3.0 (*c* 0.94, $CHCl_3$).



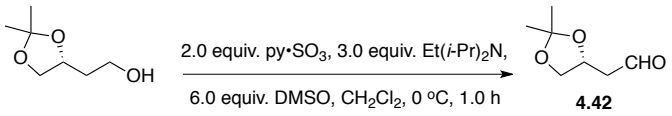
(*S*,4*E*,8*E*)-9-Iodo-5,7-dimethylnona-4,8-dien-1-ol (Rot-B). To a solution of **4.40** (2.11 g, 3.96 mmol) in THF (12 mL) was added tetra(butyl)ammonium fluoride solution (7.92 mL, 1.0 M, 7.92 mmol) at 22 °C. The mixture was allowed to stir at 22 °C for 3 h. The reaction was quenched by addition of water (10 mL). The aqueous layer was washed with Et_2O (3 × 15 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Purification of the resulting yellow oil by silica gel chromatography (4:1 hexanes:ethyl acetate) affords **Rot-B** as colorless oil (1.07 g, 3.64 mmol, 92% yield). IR (neat): 3330 (br), 2956 (s), 2924 (s), 2867 (s), 1453 (s), 1376 (m), 1218 (w), 1167 (w), 1057 (s), 948 (s), 892 (w), 742 (w), 703 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.39 (1H, dd, *J* = 14.4, 7.6 Hz), 5.93 (1H, d, *J* = 14.0 Hz), 5.12 (1H, t, *J* = 7.2 Hz), 3.64 (2H, app. t, *J* = 6.8 Hz), 2.39–2.32 (1H, m), 2.12–2.07 (2H, m), 2.01 (1H, dd, *J* = 12.8, 7.2 Hz), 1.93 (1H, dd, *J* = 12.8, 7.2 Hz), 1.65–1.59 (2H, m), 1.57 (3H, s), 1.49 (1H, br s), 0.95 (3H, d, *J* = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.0, 133.4, 126.5, 73.3, 62.7, 46.8, 38.9, 32.8, 24.3, 19.3, 16.0. HRMS (ESI^+) $[M+H]^+$ calcd for $C_{11}H_{20}I_1O_1$: 295.05588, found: 295.05661. Specific rotation: $[\alpha]_D^{20}$ +3.2 (*c* 0.45, $CHCl_3$).



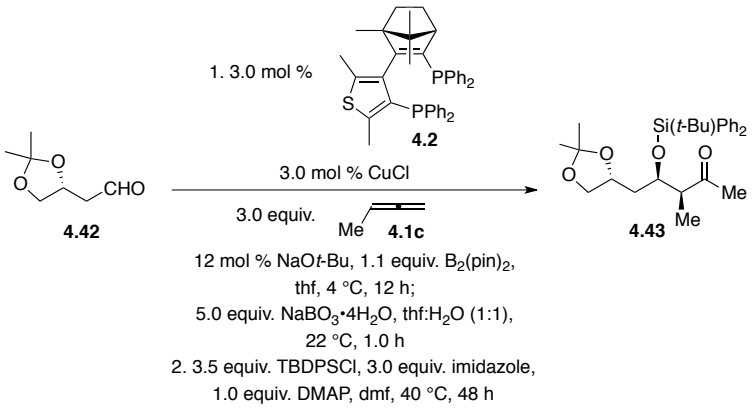
(*S*,1*E*,5*E*)-1-Iodo-3,5-dimethyldeca-1,5,9-triene (4.41). A solution of alcohol **Rot-B** (1.83 g, 6.22 mmol) in CH_2Cl_2 (20 mL) was treated with DMSO (2.65 mL, 37.3 mmol), *i*-Pr_2NEt (3.26 mL, 18.7 mmol) and sulfur trioxide pyridine complex (1.97 g, 12.4 mmol) sequentially at 0 °C. The mixture was allowed to stir at 0 °C for 30 min. Brine (10 mL) was added to quench the reaction. The aqueous layer was washed with Et_2O (3 × 10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The aldehyde was utilized in the next step without purification.

A suspension of Ph_3PCH_3Br (6.68 g, 18.7 mmol) in THF (30 mL) was treated with solution of *n*-BuLi in hexanes (10.5 mL, 1.6 M, 16.8 mmol) at 0 °C. The mixture was allowed to stir at 0 °C for 30 min, after which a solution of unpurified aldehyde in THF (10 mL) was added. The mixture was allowed to stir at 22 °C for 1 h. The reaction was quenched by saturated NH_4Cl solution (20 mL). The aqueous layer was washed with Et_2O (3 × 15 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Purification of the resulting yellow oil by silica gel chromatography (hexanes) affords **4.41** as yellow oil (1.43 g, 4.94 mmol, 79% overall yield). The physical and spectral data were identical to those previously reported.[47] ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.41 (1H, dd, *J* = 14.4, 7.6 Hz), 5.93 (1H, d, *J* = 14.0 Hz), 5.86–5.79 (1H, m), 5.13 (1H, t, *J* = 7.2 Hz), 5.05–4.95 (2H, m), 2.38–2.31 (1H, m), 2.10–2.07 (4H, m), 2.02 (1H, dd, *J* = 13.6, 7.2 Hz), 1.90 (1H, dd, *J* = 13.6, 7.2 Hz), 1.56 (3H, s), 0.95 (3H, d, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.1, 138.8, 133.0, 126.7, 114.7, 73.2, 46.8, 38.8, 34.1, 27.5, 19.1, 16.1. Specific rotation: $[\alpha]_D^{20}$ +10.1 (*c* 1.12, $CHCl_3$).

(47) Czuba, I. R.; Zammit, S.; Rizzacasa, M. A. *Org. Biomol. Chem.* **2003**, *1*, 2044–2056.



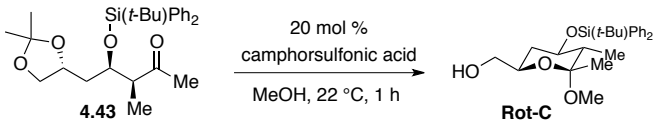
(*R*)-2-(2,2-Dimethyl-1,3-dioxolan-4-yl)acetaldehyde (4.42). To a solution of alcohol (2.00 g, 13.7 mmol) in CH_2Cl_2 (40 mL) was added DMSO (5.8 mL, 82.1 mmol), *i*-Pr_2NEt (7.1 mL, 41.0 mmol), sulfur trioxide pyridine complex (4.35 g, 27.4 mmol) sequentially at 0 °C. The resulting solution was allowed to stir at 0 °C for 1 h. A solution of brine (20 mL) was subsequently added to quench the reaction. The aqueous layer was washed with Et_2O (3 × 20 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The resulting yellow oil was purified by silica gel chromatography (8:1 hexanes:ethyl acetate) to afford **4.42** as colorless oil (1.74 g, 12.0 mmol, 88% yield). The physical and spectral data were identical to those previously reported.[47] ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.80 (1H, s), 4.56–4.49 (1H, m), 4.19 (1H, dd, *J* = 8.0, 6.4 Hz), 3.58 (1H, dd, *J* = 8.0, 6.4 Hz), 2.84 (1H, ddd, *J* = 17.2, 6.8, 2.0 Hz), 2.64 (1H, ddd, *J* = 17.2, 6.0, 1.2 Hz), 1.41 (3H, s), 1.36 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.1, 109.4, 70.8, 69.3, 48.0, 26.9, 25.6. Specific rotation: $[\alpha]_D^{20}$ –15.7 (*c* 0.75, $CHCl_3$).



(3*S*,4*R*)-4-((*tert*-Butyldiphenylsilyl)oxy)-5-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-3-methylpentan-2-one (4.43). An oven-dried 25 mL flask equipped with a magnetic stir bar was charged with phosphine **4.2** (92.2 mg, 0.150 mmol, 3.0 mol %), CuCl (14.8 mg, 0.150 mmol, 3.0 mol %), NaO*t*-Bu (288 mg, 3.00 mmol, 12 mol %) and THF (10 mL) under N_2 atmosphere. The flask was sealed with a rubber septum and the solution was allowed to stir at 22 °C for 1 h. Bis(pinacolato)diboron (1.40 g, 5.50 mmol, 1.1 equiv.) was added to the solution, causing it to turn dark brown immediately. The mixture was allowed to stir at 22 °C for 30 min. At this time, the mixture was allowed to cool to –78 °C and a solution of methyl allene **4.1c** (3.24 mL, 15.0 mmol, 3.0 equiv.) and aldehyde **4.42** (721 mg, 5.00 mmol, 1.0 equiv.) were added by syringe. At this time, the reaction flask was placed in a 4 °C cold room. After 12 h, the mixture was allowed to cool to –78 °C and the reaction was quenched by addition of a saturated aqueous solution of NH_4Cl (20 mL). The aqueous layer was washed with Et_2O (3 × 20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The resulting yellow oil was dissolved in THF (25 mL) and then treated with $NaBO_3$•$4H_2O$ (3.85 g, 25.0 mmol, 5.0 equiv.) and H_2O (25 mL). The resulting mixture was allowed to stir at 22 °C for 1 h, after which the reaction was quenched by the addition of water (20 mL). The aqueous layer was washed with Et_2O (3 × 20 mL). The combined organic layers were dried with $MgSO_4$ and concentrated under reduced pressure.

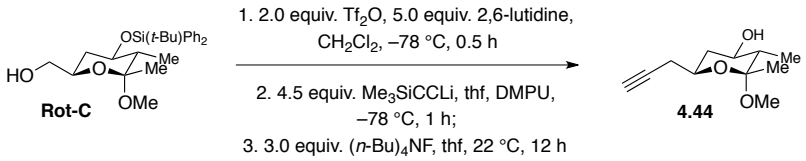
The resulting yellow oil was dissolved in *N*,*N*-dimethylformamide (DMF, 40 mL). To this solution was added imidazole (681 mg, 10.0 mmol), 4-(dimethylamino)pyridine (611 mg, 5.00 mmol) and TBDPSCl (3.25 mL, 12.5 mmol). The mixture was allowed to stir at 40 °C for 24 h. After this time, imidazole (340 mg, 5.00 mmol) and TBDPSCl [*t*-

butyl(diphenyl)silyl chloride; 1.30 mL, 5.00 mmol] were added and the resulting solution was allowed to stir at 40 °C for 24 h. A solution of brine (20 mL) was added to quench the reaction. The aqueous layer was washed with Et_2O (3 × 40 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The yellow oil was purified by silica gel chromatography (15:1 hexanes:ethyl acetate) to afford **4.43** as colorless oil (1.71 g, 3.76 mmol, 75% overall yield). The physical and spectral data were identical to those reported previously.[47] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71–7.67 (4H, m), 7.46–7.36 (6H, m), 4.27 (1H, td, *J* = 6.4, 2.8 Hz), 3.90–3.83 (1H, m), 3.74 (1H, dd, *J* = 7.6, 5.8 Hz), 3.14 (1H, app. t, *J* = 8.0 Hz), 2.64 (1H, qd, *J* = 7.2, 3.2 Hz), 2.06 (3H, s), 1.73 (1H, ddd, *J* = 14.4, 8.8, 6.4 Hz), 1.55 (1H, ddd, *J* = 14.4, 6.8, 4.0 Hz), 1.27 (3H, s), 1.17 (3H, s), 1.07 (3H, d, *J* = 6.8 Hz), 1.04 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.5, 136.1, 136.0, 134.3, 133.4, 130.0, 129.8, 127.8, 127.6, 108.0, 72.8, 72.6, 69.4, 52.1, 38.5, 29.8, 26.9, 25.8, 19.6, 10.5. Specific rotation: $[\alpha]_D^{20}$ +14.8 (*c* 1.20, $CHCl_3$).



((2*R*,4*R*,5*S*,6*R*)-4-((*tert*-Butyldiphenylsilyl)oxy)-6-methoxy-5,6-dimethyltetrahydro-2*H*-pyran-2-yl)methanol (Rot-C). To a solution of ketone **4.43** (1.45g, 3.18 mmol) in MeOH (30 mL) was added (±)-camphor-10-sulfonic acid (148 mg, 0.636 mmol) at 22 °C. The solution was allowed to stir at 22 °C for one hour. The reaction was quenched by saturated $NaHCO_3$ aqueous solution (20 mL). The water layer was washed with diethyl ether (3 × 20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The yellow oil was purified by silica gel

chromatography (4:1 hexanes:ethyl acetate) to afford **Rot-C** as colorless oil (1.34 g, 3.13 mmol, 77% yield). The physical and spectral data were identical to those previously reported.[47] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71–7.66 (4H, m), 7.44–7.34 (6H, m), 3.89 (1H, app. td, *J* = 10.4, 4.8 Hz), 3.42–3.35 (3H, m), 3.07 (3H, s), 1.78 (1H, br t, *J* = 6.8 Hz), 1.64–1.56 (2H, m), 1.42–1.39 (1H, m), 1.31 (3H, s), 1.07 (3H, d, *J* = 7.2 Hz), 1.04 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.1, 135.9, 134.2, 129.7, 129.6, 127.7, 127.6, 102.0, 71.6, 68.8, 65.9, 48.7, 47.6, 36.9, 27.2, 22.0, 19.6, 12.7. Specific rotation: $[\alpha]_D^{20}$ – 74.2 (*c* 1.20, $CHCl_3$).

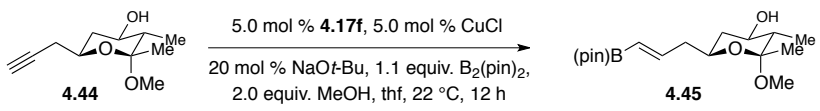


(2*R*,3*S*,4*R*,6*S*)-2-Methoxy-2,3-dimethyl-6-(prop-2-yn-1-yl)tetrahydro-2*H*-pyran-4-ol (4.44). To a solution of alcohol **Rot-C** (2.92 g, 6.81 mmol) in CH_2Cl_2 (30 mL) was added 2,6-lutidine (3.97 mL, 34.1 mmol) and Tf_2O (2.29 mL, 13.6 mmol) at –78 °C. The mixture was allowed to stir at –78 °C for 30 min. The reaction was then quenched by addition of a saturated aqueous solution of $NaHCO_3$ (20 mL). The aqueous layer was washed with diethyl ether (3 × 20 mL), and the combined organic layers were washed with saturated $CuSO_4$ (3 × 30 mL), dried over $MgSO_4$ and concentrated in vacuo.

The triflate derivative was then dissolved in THF (40 mL), and a solution of lithium trimethylsilylacetylide [prepared from trimethylsilyl acetylene (4.82 mL, 34.1 mmol) and *n*-BuLi in hexanes (19.2 mL, 1.6 M, 30.6 mmol)] in THF (40 mL) and 1,3-dimethyl-

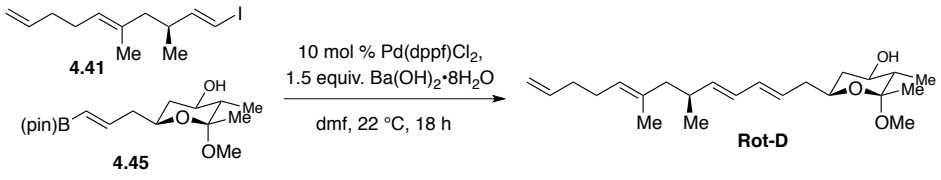
3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (DMPU; 9.0 mL) were added at –78 °C. The mixture was allowed to stir at –78 °C for 1 h. The reaction was then quenched by addition of a saturated aqueous solution of NH_4Cl (40 mL). The aqueous layer was washed with Et_2O (3 × 40 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure.

The resulting dark brown oil was dissolved in THF (30 mL), and the resulting solution was treated with tetrabutylammonium fluoride solution (20.4 mL, 1M, 20.4 mmol) at 22 °C. The mixture was allowed to stir at 22 °C for 12 h. Water was then added and the aqueous layer was washed with diethyl ether (3 × 20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Purification of the resulting dark brown oil by silica gel chromatography (4:1 hexanes:ethyl acetate) afforded **4.44** as yellow oil (1.18 g, 5.94 mmol, 87% overall yield). The physical and spectral data were identical to those previously reported.[47] ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.71–3.64 (2H, m), 3.14 (3H, s), 2.41 (1H, ddd, *J* = 16.8, 6.4, 2.8 Hz), 2.29 (1H, ddd, *J* = 16.8, 6.8, 2.8 Hz), 2.09 (1H, ddd, *J* = 12.0, 4.4, 2.0 Hz), 2.00 (1H, t, *J* = 2.8 Hz), 1.41–1.36 (1H, m), 1.33–1.21 (4H, m), 1.03 (3H, d, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 101.9, 80.9, 70.1, 69.5, 66.9, 47.9, 47.7, 40.0, 25.6, 21.7, 11.8. Specific rotation: $[\alpha]_D^{20}$ –98.4 (*c* 1.00, $CHCl_3$).

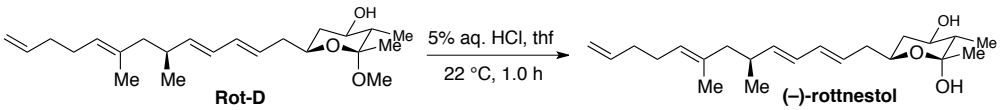


(2*R*,3*S*,4*R*,6*S*)-2-Methoxy-2,3-dimethyl-6-((*E*)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)tetrahydro-2*H*-pyran-4-ol (4.45). An oven-dried 50 mL flask

equipped with a magnetic stir bar was charged with imidazolinium salt **4.17f** (127 mg, 0.297 mmol, 5.0 mol %), CuCl (29.4 mg, 0.297 mmol, 5.0 mol %), NaO*t*-Bu (114 mg, 1.19 mmol, 20 mol %) and THF (25 mL) under N_2 atmosphere. The flask was sealed with a rubber septum and the mixture was allowed to stir at 22 °C for 1 h. Bis(pinacolato)diboron (1.66 g, 6.54 mmol, 1.1 equiv.) was then added, causing the solution to turn immediately dark brown. The mixture was allowed to stir at 22 °C for 30 min. At this time, alkyne **4.44** (1.18 g, 5.94 mmol, 1.0 equiv.) and MeOH (481 μL, 11.9 mmol, 2.0 equiv.) were added by syringe. The resulting mixture was allowed to stir at 22 °C for 12 h, after which the reaction was quenched by addition of a saturated aqueous solution of NH_4Cl (20 mL). The water layer was washed with diethyl ether (3 × 20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The yellow oil residue was purified by silica gel chromatography (3:1 hexanes:ethyl acetate) to afford **4.45** as colorless oil (1.81 g, 5.55 mmol, 93% yield). IR (neat): 3444 (br), 2978 (m), 2940 (m), 1639 (m), 1361 (s), 1321 (s), 1214 (w), 1144 (s), 1047 (m), 967 (m), 891 (w), 849 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.60 (1H, dt, *J* = 18.0, 7.2 Hz), 5.50 (1H, d, *J* = 18.0 Hz), 3.69–3.59 (2H, m), 3.49–3.44 (1H, m), 3.11 (3H, s), 2.46–2.39 (1H, m), 2.30–2.23 (1H, m), 1.98–1.94 (1H, m), 1.42–1.34 (2H, m), 1.29 (3H, s), 1.25 (12H, s), 1.04 (3H, d, *J* = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.0, 101.6, 83.2, 69.8, 67.5, 48.1, 47.7, 42.4, 40.5, 24.9, 21.9, 11.9. HRMS (ESI^+) $[M+Na]^+$ calcd for $C_{17}H_{31}B_1O_5Na_1$: 349.21622, found: 349.21760. Specific rotation: $[\alpha]_D^{20}$ –54.7 (*c* 1.22, $CHCl_3$).



(2*R*,3*S*,4*R*,6*S*)-6-((*S*,2*E*,4*E*,8*E*)-6,8-Dimethyltrideca-2,4,8,12-tetraen-1-yl)-2-methoxy-2,3-dimethyltetrahydro-2*H*-pyran-4-ol (Rot-D). To a solution of alkenylboron **4.45** (1.81 g, 5.55 mmol) and alkenyl iodide **4.41** (1.43 g, 4.93 mmol) in DMF (40 mL) was added $Pd(dppf)Cl_2 \bullet CH_2Cl_2$ (400 mg, 0.49 mmol) and $Ba(OH)_2 \bullet 8H_2O$ (2.33 g, 7.40 mmol) at 22 °C. The resulting mixture was allowed to stir at 22 °C for 18 h. The reaction was quenched through addition of a solution of brine. The aqueous layer was washed with Et_2O (3 × 20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Purification of the resulting yellow oil by silica gel chromatography (6:1 hexanes:ethyl acetate) affords **Rot-D** as yellow oil (1.49 g, 4.11 mmol, 83% yield). The physical and spectral data were identical to those previously reported.[47] ^{1}H NMR (400 MHz, C_6D_6): δ 6.14–6.03 (2H, m), 5.84–5.65 (2H, m), 5.51 (1H, dd, *J* = 14.0, 4.4 Hz), 5.15 (1H, br t, *J* = 6.8 Hz), 5.04 (1H, d, *J* = 16.8 Hz), 4.99 (1H, d, *J* = 10.0 Hz), 3.66 (1H, td, *J* = 10.0, 7.2 Hz), 3.56–3.50 (1H, m), 3.01 (3H, s), 2.38–2.29 (2H, m), 2.20–2.13 (1H, m), 2.09–1.99 (5H, m), 1.91 (1H, dd, *J* = 13.2, 8.0 Hz), 1.79–1.75 (1H, m), 1.50 (3H, s), 1.38–1.32 (1H, m), 1.23 (3H, s), 1.16 (3H, d, *J* = 6.8 Hz), 1.18–1.10 (1H, m), 0.96 (3H, d, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, C_6D_6): δ 139.2, 139.1, 134.2, 133.7, 129.2, 128.0, 126.6, 115.1, 102.0, 70.0, 68.9, 49.0, 48.3, 47.8, 41.5, 39.9, 35.3, 34.7, 28.1, 22.3, 20.4, 16.5, 12.4. Specific rotation: $[\alpha]_D^{20}$ –82.2 (*c* 0.96, CH_2Cl_2).

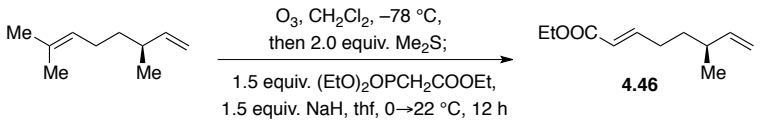


(2*R*,3*S*,4*R*,6*S*)-6-((*S*,2*E*,4*E*,8*E*)-6,8-Dimethyltrideca-2,4,8,12-tetraen-1-yl)-2,3-dimethyltetrahydro-2*H*-pyran-2,4-diol [(–)-rottnestol]. To a solution of mehyl ketal **Rot-D** (1.49 g, 4.11 mmol) in THF (20 mL) was added 5% aqueous HCl solution (4 mL)

at 22 °C. The resulting solution was allowed to stir at 22 °C for 1 h. The reaction was quenched by addition of a saturated aqueous solution of $NaHCO_3$ (20 mL). The aqueous layer was then washed with diethyl ether (3 × 20 mL), and the combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. The resulting yellow oil was purified by silica gel chromatography (3:1 hexanes:ethyl acetate) to afford **(–)-rottnestol** as yellow oil (1.17 g, 3.36 mmol, 81% yield). The physical and spectral data were identical to those previously reported.[47, 48] IR (neat): 3388 (br), 2917 (m), 1701 (w), 1640 (w), 1440 (m), 1379 (m), 1260 (w), 1157 (m), 1077 (m), 1013 (s), 987 (s), 913 (s), 777 (w), 619 (m) cm^{-1}; ^1H NMR (400 MHz, C_6D_6): δ 6.17–6.07 (2H, m), 5.84–5.76 (1H, m), 5.72 (1H, td, *J* = 14.4, 7.2 Hz), 5.53 (1H, dd, *J* = 14.4, 7.2 Hz), 5.17 (1H, br t, *J* = 6.8 Hz), 5.06 (1H, dd, *J* = 17.2, 2.0 Hz), 5.00 (1H, d, *J* = 10.4 Hz), 3.92–3.86 (1H, m), 3.62 (1H, td, *J* = 10.0, 4.4 Hz), 2.41–2.29 (2H, m), 2.24–2.15 (1H, m), 2.09–2.01 (5H, m), 1.92 (1H, dd, *J* = 13.2, 7.6 Hz), 1.79–1.75 (1H, m), 1.51 (3H, s), 1.32–1.26 (1H, m), 1.23 (3H, s), 1.16 (3H, d, *J* = 6.8 Hz), 1.17–1.12 (1H, m), 0.98 (3H, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, C_6D_6): δ 138.8, 138.7, 133.8, 133.2, 128.8, 128.4, 126.2, 114.8, 99.0, 69.8, 68.3, 47.9, 47.2, 41.3, 39.7, 34.9, 34.3, 28.2, 27.8, 20.1, 16.1, 12.3. HRMS (ESI^+) $[M+Na]^+$ calcd for $C_{22}H_{36}O_3Na_1$: 371.25567, found: 371.25700. Specific rotation: $[\alpha]_D^{20}$ –58.3 (*c* 1.25, CH_2Cl_2). In the manuscript that reports the isolation of this natural product, the following optical rotation value is reported: $[\alpha]_D$ +67.4 (*c* 0.43, CH_2Cl_2);[47] in the first total synthesis of (+)-rottnestol, the disclosed optical rotation value is: $[\alpha]_D^{20}$ +58.3 (*c* 0.18, CH_2Cl_2).[48]

■ **Total Synthesis of (+)-Herboxidiene**

(48) Erickson, K. L.; Beutler, J. A.; Cardellina, J. H.; Boyd, M. R. *Tetrahedron* **1995**, *51*, 11953–11958.

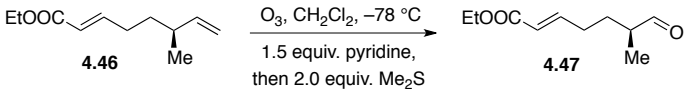


Ethyl (*S*,*E*)-6-methylocta-2,7-dienoate (4.46). Into a solution of (+)-β-citronellene (8.00 g, 57.9 mmol) in CH_2Cl_2 (100 mL) ozone was introduced at –78 °C until TLC analysis indicated complete consumption of the diene substrate. At this time, Me_2S (8.50 mL, 115.8 mmol) was added and the mixture was allowed to stir at 22 °C for 1 h. The volatiles were removed in vacuo and the resulting aldehyde was utilized without purification.

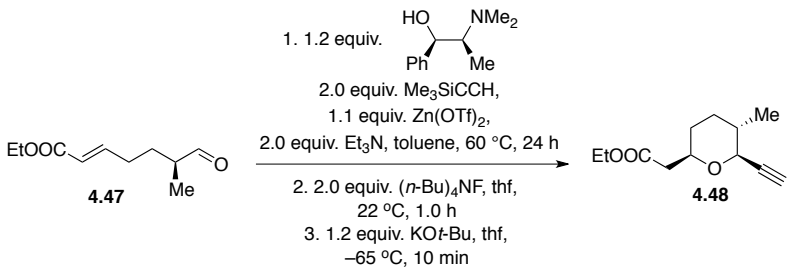
To a solution of triethyl phosphonoacetate (17.2 mL, 86.9 mmol) in THF (120 mL) was added NaH (3.48 g, 60% dispersion in mineral oil, 86.9 mmol) at 0 °C. The mixture was allowed to stir at 0 °C for 1 h. A solution of unpurified aldehyde (see above) in THF (20 mL) was then added. The resulting solution was allowed to stir at 22 °C for 12 h. The reaction was quenched by addition of a saturated aqueous solution of NH_4Cl (60 mL). The aqueous layer was washed with Et_2O (3 × 60 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Purification of the yellow oil residue by silica gel chromatography (10:1 hexanes:diethyl ether) affords **4.46** as colorless oil (8.79 g, 48.2 mmol, 83% overall yield). The physical and spectral data were identical to those previously reported.[49] ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.94 (1H, dt, *J* = 15.6, 6.8 Hz), 5.80 (1H, dt, *J* = 15.6, 1.6 Hz), 5.64 (1H, ddd, *J* = 17.6, 10.0, 7.6 Hz), 4.99–4.92 (2H, m), 4.17 (2H, q, *J* = 7.2 Hz), 2.22–2.11 (3H, m), 1.46–1.41 (2H, m), 1.27 (3H, t, *J* = 7.2 Hz), 0.99 (3H, d, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.9, 149.4, 143.9, 121.4,

(49) Fürstner, A.; Feyen, F.; Prinz, H.; Waldmann, H. *Tetrahedron* **2004**, *60*, 9543–9558.

113.5, 60.3, 37.4, 34.8, 30.0, 20.3, 14.4. Specific rotation: $[\alpha]_D^{20}$ +13.4 (*c* 1.22, $CHCl_3$:MeOH = 9:1).



Ethyl (*S*,*E*)-6-methyl-7-oxohept-2-enoate (4.47). A solution of **4.46** (8.79 g, 48.2 mmol) and pyridine (5.85 mL, 72.3 mmol) in CH_2Cl_2 (120 mL) was treated with O_3 at –78 °C until TLC analysis indicated complete substrate consumption. Subsequently, Me_2S (7.08 mL, 96.4 mmol) was introduced to the solution and the resulting mixture was allowed to stir at 22 °C for 2 h. The volatiles were then removed in vacuo, and the resulting yellow oil was purified by silica gel chromatography (10:1 hexanes:ethyl acetate) to afford **4.47** as colorless oil (6.69 g, 36.3 mmol, 75% yield). IR (neat): 2978 (m), 2876 (m), 1716 (s), 1655 (m), 1459 (m), 1268 (m), 1206 (m), 1174 (m), 1046 (m), 987 (m), 851 (w), 711 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.61 (1H, s), 6.90 (1H, dt, *J* = 15.6, 6.4 Hz), 5.82 (1H, d, *J* = 15.6 Hz), 4.16 (2H, q, *J* = 7.2 Hz), 2.36 (1H, q, *J* = 7.2 Hz), 2.24 (2H, app. q, *J* = 7.2 Hz), 1.93–1.84 (1H, m), 1.53–1.44 (1H, m), 1.26 (3H, t, *J* = 7.2 Hz), 1.11 (3H, d, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.3, 166.5, 147.7, 122.3, 60.4, 45.6, 29.4, 28.7, 14.3, 13.4. HRMS (ESI$^+$) $[M+H]^+$ calcd for $C_{10}H_{17}O_3$: 185.11777, found: 185.11768. Specific rotation: $[\alpha]_D^{20}$ –1.7 (*c* 1.46, $CHCl_3$).



Ethyl 2-((2*R*,5*S*,6*S*)-6-ethynyl-5-methyltetrahydro-2*H*-pyran-2-yl)acetate (4.47). To a solution of $Zn(OTf)_2$ (2.00 g, 5.50 mmol), (1*R*, 2*S*)-(-)-*N*-methylephedrine (1.08 g, 6.00 mmol) in toluene (15 mL) was added Et_3N (1.39 mL, 10.0 mmol) at 22 °C. The mixture was allowed to stir at 22 °C for 1 h and a solution of trimethylsilyl acetylene (1.41 mL, 10.0 mmol) was added. The resulting mixture was allowed to stir at 22 °C for 30 min. At this time, aldehyde **4.47** (921 mg, 5.00 mmol) was introduced into the solution and the mixture was allowed to stir at 60 °C for an additional 24 h. The reaction was quenched by the addition of a saturated solution of aqueous NH_4Cl (15 mL), and the aqueous layer was washed with Et_2O (3 × 10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure.[50]

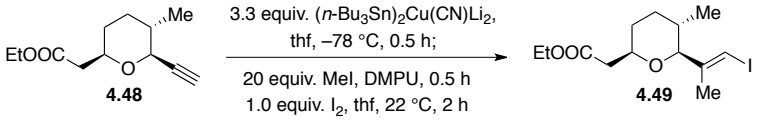
The resulting oil was dissolved in THF (10 mL) and treated with a solution of tetra(butyl)ammonium fluoride (10.0 mL, 1.0 M, 10.0 mmol) in THF at 22 °C, and the mixture was allowed to stir at 22 °C for 1 h. The reaction was quenched by saturated NH_4Cl solution (15 mL). The aqueous layer was washed with Et_2O (3 × 10 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo.

The resulting yellow oil was dissolved in THF (10 mL) and, after cooling the solution to -65 °C, KO*t*-Bu (673 mg, 6.00 mmol) in THF (10 mL) was added; the mixture was allowed to stir at –65 °C for 10 min.[51] The reaction was quenched by the addition of a saturated aqueous solution of NH_4Cl (15 mL). The aqueous layer was washed with Et_2O (3 × 10 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Purification of the resulting yellow oil by silica gel chromatography (10:1

(50) Anand, N. K.; Carreira, E. M. *J. Am. Chem. Soc.* **2001**, *123*, 9687–9688.

(51) Blakemore, P. R.; Kocieński, P. J.; Morley, A.; Muir, K. *J. Chem. Soc., Perkin Trans. I*, **1999**, 955–968.

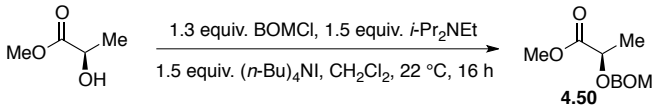
hexanes: ethyl acetate) afforded **4.48** as colorless oil (707 mg, 3.36 mmol, 67% overall yield). IR (neat): 3274 (m), 2957 (m), 2873 (m), 1732 (s), 1458 (m), 1370 (m), 1252 (m), 1193 (s), 1074 (s), 1031 (s), 847 (w), 659 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.12 (2H, q, *J* = 7.2 Hz), 3.77–3.70 (2H, m), 2.62 (1H, dd, *J* = 15.6, 6.4 Hz), 2.44 (1H, d, *J* = 2.0 Hz), 2.38 (1H, dd, *J* = 15.6, 6.4 Hz), 1.84 (1H, dq, *J* = 13.6, 3.6 Hz), 1.73–1.59 (2H, m), 1.40–1.30 (1H, m), 1.23 (3H, t, *J* = 7.2 Hz), 0.96 (3H, d, *J* = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.1, 82.4, 74.7, 74.4, 73.4, 60.6, 41.3, 36.1, 31.9, 31.1, 17.8, 14.3. HRMS (ESI^+) $[M+H]^+$ calcd for $C_{12}H_{19}O_3$: 211.13342, found: 211.13356. Specific rotation: $[\alpha]_D^{20}$ –3.6 (*c* 0.96, $CHCl_3$).



Ethyl 2-((2*R*,5*S*,6*S*)-6-((*E*)-1-iodoprop-1-en-2-yl)-5-methyltetrahydro-2*H*-pyran-2-yl)acetate (4.49). The following procedure for preparation of *n*-Bu_3SnCu(*n*-Bu)$CNLi_2$ is based on a method reported by Lipshutz.[52] To a sample of flame-dried CuCN (1.48 g, 16.5 mmol) placed in a flask was added THF (20 mL) and the slurry was allowed to cool to –78 °C. Then *n*-BuLi (20.6 mL, 1.6 M in hexanes, 33.0 mmol) was added in a dropwise manner. The mixture was allowed to warm slightly, giving rise to a colorless homogenous solution; it was then re-cool to –78 °C. *n*-Bu_3SnH (8.88 mL, 33.0 mmol) was added through a syringe and the resulting solution was allowed to stir at –78 °C for 30 min. To the solution of cuprate was added **4.48** (1.05 g, 5.00 mmol) at –78 °C, and the resulting mixture was allowed to stir at –78 °C for 30 min. At this point, MeI (6.23 mL,

(52) Lipshutz, B. H.; Ellsworth, E. L.; Dimock, S. H.; Reuter, D. C. *Tetrahedron Lett.* **1989**, *30*, 2065–2068.

100 mmol) and 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (DMPU, 2.5 mL) were added. The resulting solution was allowed to warm slowly to 22 °C, after which the reaction was quenched by the addition of a saturated aqueous solution of NH_4Cl (20 mL). The aqueous layer was washed with Et_2O (3 × 20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo.[53] The brown oil was dissolved in Et_2O (25 mL), which was subsequently treated with I_2 (1.27 g, 5.00 mmol) at 0 °C. The mixture was allowed to stir at 22 °C for 2 h. At this time, the reaction was quenched by the addition of a saturated aqueous solution of $Na_2S_2O_3$ (15 mL). The aqueous layer was washed with Et_2O (3 × 15 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Purification of the yellow oil residue by silica gel chromatography (30:1 hexanes: ethyl acetate) afforded **4.49** as yellow oil (1.38 g, 3.92 mmol, 78% overall yield). The physical and spectral data were identical to those previously reported.[54] ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.21–6.19 (1H, m), 4.12 (2H, q, *J* = 7.2 Hz), 3.77 (1H, dtd, *J* = 11.2, 6.4, 2.0 Hz), 3.50 (1H, d, *J* = 10.0 Hz), 2.55 (1H, dd, *J* = 14.8, 6.4 Hz), 2.39 (1H, dd, *J* = 14.8, 6.4 Hz), 1.87–1.80 (1H, m), 1.78 (3H, d, *J* = 1.2 Hz), 1.71–1.64 (1H, m), 1.55–1.47 (1H, m), 1.42–1.31 (1H, m), 1.30–1.18 (1H, m), 1.23 (3H, t, *J* = 7.2 Hz), 0.69 (3H, d, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 147.3, 89.2, 80.4, 74.4, 60.5, 41.6, 32.8, 32.3, 31.6, 19.7, 17.6, 14.3. Specific rotation: $[\alpha]_D^{20}$ +10.6 (*c* 1.33, $CHCl_3$).

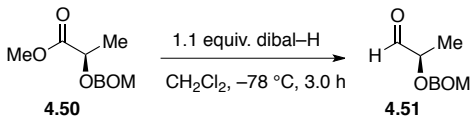


4.50

(53) Liu, P.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2001**, *123*, 10772–10773.

(54) (a) Murray, T. J.; Forsyth, C. J. *Org. Lett.* **2008**, *10*, 3429–3431. (b) Pellicena, M.; Krämer, K.; Romea, P.; Urpí, F. *Org. Lett.* **2011**, *13*, 5350–5353.

Methyl (*R*)-2-((benzyloxy)methoxy)propanoate (4.50). To a solution of methyl-(*R*)-lactate (9.55 mL, 100 mmol) in CH_2Cl_2 (100 mL) was added tetra(butyl)ammonium iodide (55.4 g, 150 mmol), *N*,*N*-diisopropylethylamine (26.1 mL, 150 mmol) and benzyloxymethyl chloride (18.1 mL, 130 mmol) at 22 °C. The mixture was allowed to stir at 22 °C for 16 h. The reaction was then quenched by addition of a 10% aqueous solution of HCl (50 mL). The aqueous layer was washed with Et_2O (3 × 50 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Purification of the yellow oil residue by silica gel chromatography (30:1 hexanes: ethyl acetate) affords **4.50** as yellow oil (16.9 g, 75.4 mmol, 75% yield). The physical and spectral data were identical to those previously reported.[55] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37–7.27 (5H, m), 4.83 (2H, s), 4.68–4.61 (2H, m), 4.30 (1H, q, *J* = 7.2 Hz), 3.71 (3H, s), 1.43 (3H, d, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.6, 137.7, 128.5, 128.0, 127.8, 94.1, 71.8, 70.1, 52.1, 18.6. Specific rotation: $[\alpha]_D^{20}$ +52.3 (*c* 2.00, $CHCl_3$).

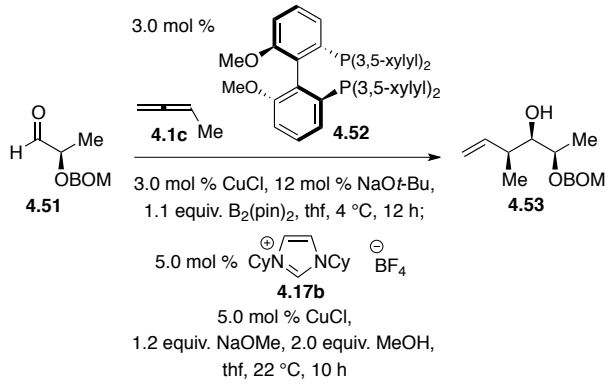


4.50 **4.51**

(*R*)-2-((Benzyloxy)methoxy)propanal (4.51). To a solution of carboxylic ester **4.50** (16.9 g, 75.4 mmol) in CH_2Cl_2 (100 mL) was added diisobutylaluminum hydride (dibal–H; 14.8 mL, 82.9 mmol) in a dropwise manner at –78 °C. The solution was allowed to stir at –78 °C for 3 h, after which MeOH (2.0 mL) was added at –78 °C to quench the reaction. The mixture was subsequently charged with a saturated aqueous solution of potassium-sodium tartrate (100 mL) was added and allowed to stir at 22 °C for 3 h. The

(55) Savage, I.; Thomas, E. J.; Wilson, P. D. *J. Chem. Soc., Perkin Trans. I*, **1999**, 3291–3303.

aqueous layer was washed with Et_2O (3 × 50 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Purification of the colorless oil by silica gel chromatography (10:1 hexanes: ethyl acetate) affords **4.51** as colorless oil (14.6 g, 75.2 mmol, >98% yield). The physical and spectral data were identical to those previously reported.[56] ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.64 (1H, d, *J* = 1.6 Hz), 7.38–7.27 (5H, m), 4.87 (2H, s), 4.72–4.63 (2H, m), 4.11 (1H, qd, *J* = 7.2, 1.6 Hz), 1.33 (3H, d, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.6, 137.5, 128.6, 128.0, 127.9, 94.3, 78.3, 70.2, 15.4. Specific rotation: $[\alpha]_D^{20}$ +57.8 (*c* 1.95, $CHCl_3$).



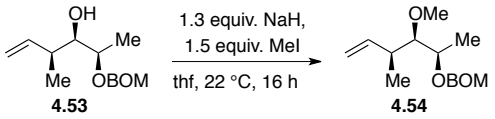
(2*R*,3*R*,4*S*)-2-((Benzyloxy)methoxy)-4-methylhex-5-en-3-ol (4.53). An oven-dried 25 mL flask equipped with a magnetic stir bar was charged with phosphine **4.52** (104 mg, 0.150 mmol, 3.0 mol %), CuCl (14.8 mg, 0.150 mmol, 3.0 mol %), NaO*t*-Bu (288 mg, 3.00 mmol, 12 mol %) and THF (10 mL) under N_2 atmosphere. The flask was sealed with a rubber septum and the solution was allowed to stir at 22 °C for 1 h. Bis(pinacolato)diboron (1.40 g, 5.50 mmol, 1.1 equiv.) was added to the solution, causing it to turn dark brown immediately. The mixture was then allowed to stir at 22 °C for 30 min, after which the solution was allowed to cool to –78 °C (dry ice/acetone bath) and

(56) Hanessian, S.; Chahal, N.; Giroux, S. *J. Org. Chem.* **2006**, *71*, 7403–7411.

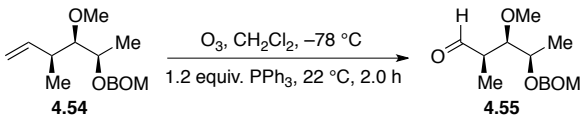
then charged with a solution of methylallene **4.1c** (3.24 mL, 15.0 mmol, 3.0 equiv.) and aldehyde **4.51** (971 mg, 5.00 mmol, 1.0 equiv.) by syringe. The flask was placed in a 4 °C cold room. After 12 h, the solution was allowed to cool to –78 °C, and the reaction was quenched through addition of an aqueous solution of saturated aqueous NH_4Cl (20 mL). The aqueous layer was washed with Et_2O (3 × 20 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vauo to give a yellow oil residue, which was used in the next step without purification.

An oven-dried flask (25 mL) with a magnetic stir bar was charged with imidazolium salt **4.17b** (80.0 mg, 0.250 mmol, 5.0 mol %), CuCl (24.7 mg, 0.250 mmol, 5.0 mol %), NaOMe (324 mg, 6.00 mmol, 1.2 equiv.) and THF (10 mL). The vessel was sealed with a rubber septum and the solution was allowed to stir at 22 °C for 1 h. The unpurified yellow oil obtained from the sequential reaction was added to the NHC–Cu complex solution, and MeOH (402 μL, 10.0 mmol, 2.0 equiv.) was added by syringe. The solution was allowed to stir at 22 °C for 10 h, after which the reaction was then quenched through addition of an aqueous solution of saturated NH_4Cl (20 mL). The aqueous layer was washed with Et_2O (3 × 20 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Purification of the resulting yellow oil by silica gel chromatography (20:1 hexanes: ethyl acetate) afforded **4.53** as colorless oil (994 mg, 3.97 mmol, 79% overall yield). The physical and spectral data were identical to those previously reported.[54a] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.28 (5H, m), 5.84 (1H, ddd, J = 17.6, 10.0, 7.2 Hz), 5.10–5.03 (2H, m), 4.87 (1H, d, J = 7.2 Hz), 4.82 (1H, d, J = 7.2 Hz), 4.65 (2H, s), 3.87–3.79 (1H, m), 3.30–3.26 (1H, m), 2.42–2.36 (2H, m), 1.25 (3H, d, J = 6.4 Hz), 1.07 (3H, d, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.8, 137.7,

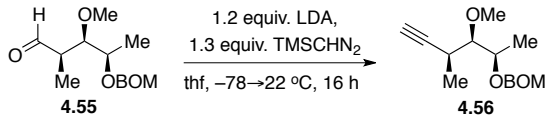
128.6, 128.0, 127.9, 114.8, 93.9, 78.3, 75.3, 69.9, 40.5, 17.5, 14.6. Specific rotation: $[\alpha]_D^{20}$ +12.4 (*c* 1.22, $CHCl_3$).



(((((2*R*,3*R*,4*S*)-3-Methoxy-4-methylhex-5-en-2-yl)oxy)methoxy)methyl)benzene (4.54). To a solution of alcohol **4.53** (10.2 g, 40.7) in THF (100 mL) was added NaH (2.12 g, 60% dispension in mineral oil, 53.0 mmol) at 0 °C. The mixture was allowed to stir at 0 °C for 1 h. At this time, MeI (3.80 mL, 61.0 mmol) was then added by syringe, and the mixture was allowed to stir at 22 °C for 16 h. The reaction was then quenched by the addition of a saturated aqueous solution of NH_4Cl (60 mL). The aqueous layer was washed with Et_2O (3 × 50 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Purification of the resulting yellow oil by silica gel chromatography (20:1 hexanes: ethyl acetate) afforded **4.54** as colorless oil (9.93 g, 37.6 mmol, 92% yield). The physical and spectral data were identical to those previously reported.[54a] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37–7.27 (5H, m), 5.86 (1H, ddd, *J* = 17.6, 10.4, 7.2 Hz), 5.08–4.99 (2H, m), 4.87 (1H, d, *J* = 7.2 Hz), 4.81 (1H, d, *J* = 7.2 Hz), 4.67 (1H, d, *J* = 11.6 Hz), 4.61 (1H, d, *J* = 11.6 Hz), 3.90–3.84 (1H, m), 3.51 (3H, s), 2.91–2.88 (1H, m), 2.56–2.48 (1H, m), 1.25 (3H, d, *J* = 6.4 Hz), 1.07 (3H, d, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.0, 138.2, 128.5, 128.0, 127.7, 114.3, 94.2, 88.7, 74.7, 69.6, 61.4, 39.8, 17.7, 15.3. Specific rotation: $[\alpha]_D^{20}$ +19.1 (*c* 1.35, $CHCl_3$).

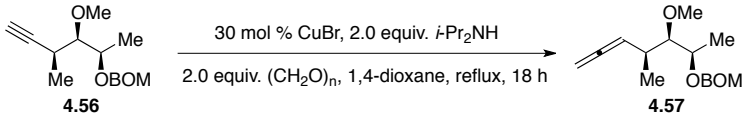


(2*R*,3*R*,4*R*)-4-((Benzyloxy)methoxy)-3-methoxy-2-methylpentanal (4.55). Ozone gas was introduced into a solution of **4.54** (9.93 g, 37.6 mmol) in CH_2Cl_2 (100 mL) at –78 °C until the solution turned blue. Next, PPh_3 (11.8 g, 45.1 mmol) was added and the resulting solution was allowed to stir at 22 °C for 2 h. The volatiles were removed in vacuo, and the resulting yellow oil was purified by silica gel chromatography (10:1 to 3:1 hexanes:ethyl acetate) to afford **4.55** as colorless oil (8.73 g, 32.8 mmol, 87% yield). IR (neat): 3064 (m), 2977 (m), 2829 (m), 1720 (s), 1454 (m), 1382 (m), 1171 (m), 1095 (s), 1037 (s), 938 (m), 847 (w), 739 (s), 699 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.77 (1H, d, *J* = 1.2 Hz), 7.37–7.28 (5H, m), 4.80 (1H, d, *J* = 7.2 Hz), 4.71 (1H, d, *J* = 7.2 Hz), 4.60 (1H, d, *J* = 11.6 Hz), 4.56 (1H, d, *J* = 11.6 Hz), 3.98–3.92 (1H, m), 3.49 (3H, s), 3.47–3.45 (1H, m), 2.71–2.64 (1H, m), 1.26 (3H, d, *J* = 6.8 Hz), 1.13 (3H, d, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.1, 137.9, 128.6, 128.0, 127.9, 93.6, 84.5, 72.8, 70.0, 59.9, 47.2, 16.4, 9.5. HRMS (ESI^+) $[M+Na]^+$ calcd for $C_{15}H_{22}O_4Na_1$: 289.14103, found: 289.14070. Specific rotation: $[\alpha]_D^{20}$ –16.6 (*c* 1.78, $CHCl_3$).



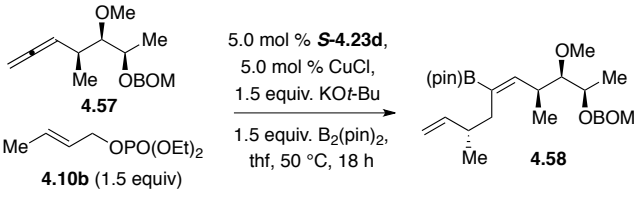
(((((2*R*,3*R*,4*S*)-3-Methoxy-4-methylhex-5-yn-2-yl)oxy)methoxy)methyl)benzene (4.56). To a solution of *i*-Pr_2NH (3.64 mL, 26.0 mmol) in THF (60 mL) was added *n*-BuLi (15.0 mL, 1.6 M in hexanes, 24.0 mmol) at –78 °C. The mixture was allowed to stir at 0 °C for 1 h, after which it was allowed to re-cool to –78 °C. A solution of $TMSCHN_2$ (13.0 mL, 2.0 M in hexanes, 26.0 mmol) was then added, and the mixture was allowed to stir at –78 °C for 1 h. A solution of aldehyde **4.55** (5.33 g, 20.0 mmol) in THF (30 mL)

was added in a dropwise fashion at –78 °C, and the solution was allowed to stir at –78 °C for 3 h; the mixture was then slowly warmed to 22 °C and stir at 22 °C for 16 h. The reaction was quenched through addition of a saturated aqueous solution of NH_4Cl (60 mL). The aqueous layer was washed with Et_2O (3 × 50 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the yellow oil residue by silica gel chromatography (20:1 hexanes: ethyl acetate) afforded **4.56** as colorless oil (4.27 g, 16.3 mmol, 81% yield). IR (neat): 3292 (m), 2974 (m), 2935 (m), 2884 (m), 1455 (m), 1380 (m), 1201 (w), 1097 (s), 1027 (s), 939 (m), 801 (w), 737 (m), 698 (m), 636 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.38–7.27 (5H, m), 4.88 (1H, d, *J* = 7.2 Hz), 4.86 (1H, d, *J* = 7.2 Hz), 4.68 (1H, d, *J* = 11.6 Hz), 4.64 (1H, d, *J* = 11.6 Hz), 4.20 (1H, qd, *J* = 6.8, 2.8 Hz), 3.56 (3H, s), 3.00 (1H, dd, *J* = 8.8, 2.8 Hz), 2.90–2.82 (1H, m), 2.08 (1H, d, *J* = 2.8 Hz), 1.32–1.29 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.2, 128.5, 128.1, 127.7, 94.0, 88.1, 86.7, 73.6, 70.3, 69.7, 62.0, 28.4, 17.4, 17.2. HRMS (ESI^+) $[M+H]^+$ calcd for $C_{16}H_{23}O_3$: 263.16472, found: 263.16323. Specific rotation: $[\alpha]_D^{20}$ +13.6 (*c* 1.67, $CHCl_3$).



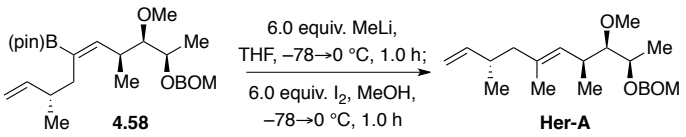
(((((2*R*,3*R*,4*S*)-3-Methoxy-4-methyl-6λ^5-hepta-5,6-dien-2-yl)oxy)methoxy)methyl)benzene (4.57). A flame-dried flask equipped with a magnetic stir bar and a reflux condenser was charged with alkyne **4.56** (4.92 g, 18.7 mmol), CuBr (805 mg, 5.61 mmol) and paraformaldehyde (1.13 g, 37.4 mmol); 1,4-dioxane (60 mL) and *i*-Pr_2NH (5.24 mL, 37.4 mmol) was then added. The resulting mixture was allowed to

stir at 100 °C for 18 h under N_2 atmosphere. After this time, the reaction was allowed to cool to 22 °C, and then the reaction was quenched by passing the mixture through a plug of Celite eluted with Et_2O (3 × 20 mL). The filtrate was concentrated under reduced pressure and the brown oil residue was purified by silica gel chromatography (20:1 hexanes:ethyl acetate) to afford **4.57** as colorless oil (3.81 g, 13.8 mmol, 74% yield). IR (neat): 2971 (m), 2933 (m), 2882 (m), 1955 (m), 1455 (m), 1380 (m), 1149 (m), 1092 (s), 1039 (s), 939 (w), 845 (m), 736 (m), 698 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.37–7.27 (5H, m), 5.23–5.18 (1H, m), 4.85 (1H, d, *J* = 6.8 Hz), 4.81 (1H, d, *J* = 6.8 Hz), 4.72 (1H, d, *J* = 2.0 Hz), 4.70 (1H, d, *J* = 2.0 Hz), 4.66 (1H, d, *J* = 12.0 Hz), 4.62 (1H, d, *J* = 12.0 Hz), 3.97–3.91 (1H, m), 3.52 (3H, s), 2.91 (1H, dd, *J* = 6.4, 4.4 Hz), 2.56–2.50 (1H, m), 1.26 (3H, d, *J* = 6.8 Hz), 1.10 (3H, d, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.2, 138.1, 128.5, 128.0, 127.8, 94.1, 93.7, 88.7, 75.9, 74.4, 69.6, 61.4, 34.9, 17.6, 15.7. HRMS (ESI^+) $[M+Na]^+$ calcd for $C_{17}H_{24}O_3Na_1$: 299.16231, found: 299.16089. Specific rotation: $[\alpha]_D^{20}$ +11.9 (*c* 1.33, $CHCl_3$).



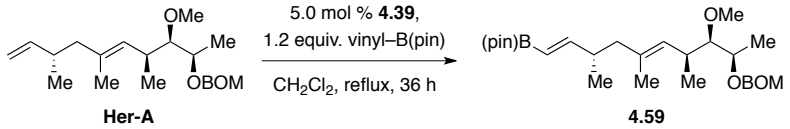
2-((3*S*,7*S*,8*R*,9*R*,*Z*)-9-((Benzyloxy)methoxy)-8-methoxy-3,7-dimethyldeca-1,5-dien-5-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.58). An oven-dried 50 mL flask with a magnetic stir bar was charged with imidazolinium salt **(*S*)-4.23d** (117 mg, 0.250 mmol, 5.0 mol %), CuCl (24.7 mg, 0.250 mmol, 5.0 mol %), KO*t*-Bu (842 mg, 7.50 mmol, 1.5 equiv.) and THF (20 mL) under N_2 atmosphere. The flask was sealed with a rubber

septum and the solution was allowed to stir at 22 °C for 2 h. Bis(pinacolato)diboron (1.90 g, 7.50 mmol, 1.5 equiv.) was added to the solution, causing it to turn dark brown immediately. The mixture was then allowed to stir at 22 °C for 30 min. At this time, allene **4.57** (1.38 g, 5.00 mmol, 1.0 equiv.) and allyl phosphate **4.10b** (1.56 g, 7.50 mmol, 1.5 equiv.) were added by syringe. The mixture was allowed to stir at 50 °C for 18 h under N_2 atmosphere, after which the reaction was quenched through addition of a saturated aqueous solution of NH_4Cl (10 mL). The aqueous layer was then washed with Et_2O (3 × 10 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the resulting yellow oil residue by silica gel chromatography (30:1 hexanes:ethyl acetate) affords **4.58** as colorless oil (1.74 g, 3.80 mmol, 76% yield). IR (neat): 2973 (m), 2931 (m), 2832 (m), 1455 (m), 1371 (m), 1303 (m), 1271 (w), 1144 (s), 1092 (s), 1038 (s), 966 (m), 910 (m), 838 (w), 736 (w), 699 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.36–7.27 (5H, m), 6.34 (1H, d, *J* = 10.0 Hz), 5.75 (1H, ddd, *J* = 17.2, 10.0, 3.6 Hz), 4.95–4.83 (3H, m), 4.74 (1H, d, *J* = 7.2 Hz), 4.69 (1H, d, *J* = 11.6 Hz), 4.54 (1H, d, *J* = 11.6 Hz), 3.77–3.71 (1H, m), 3.51 (3H, s), 2.91–2.83 (2H, m), 2.29–2.20 (1H, m), 2.18–2.07 (2H, m), 1.27 (3H, d, *J* = 6.0 Hz), 1.24 (6H, s), 1.23 (6H, s), 1.04 (3H, d, *J* = 6.4 Hz), 0.95 (3H, d, *J* = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.0, 144.9, 138.2, 128.5, 128.1, 127.7, 112.5, 95.1, 89.0, 83.2, 76.0, 69.6, 61.7, 38.8, 35.0, 25.1, 24.6, 20.0, 18.3, 15.8. HRMS (ESI^+) $[M+Na]^+$ calcd for $C_{27}H_{43}B_1O_5Na_1$: 481.31012, found: 481.31058. Specific rotation: $[\alpha]_D^{20}$ +18.4 (*c* 0.76, $CHCl_3$).

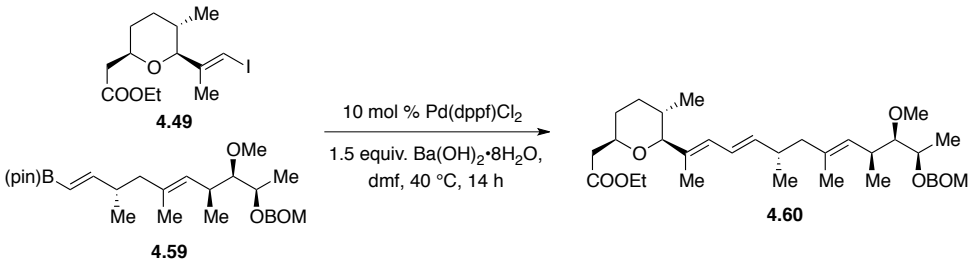


(((((2*R*,3*R*,4*S*,8*S*,*E*)-3-Methoxy-4,6,8-trimethyldeca-5,9-dien-2-yl)oxy)methoxy)methyl)benzene (Her-A). To a solution of alkenylboron **4.58** (5.57 g, 12.1 mmol) in THF (50 mL) cooled to –78 °C, was added a solution of MeLi in Et_2O (45.5 mL, 1.6 M, 72.8 mmol). The mixture was allowed to stir at 0 °C for 1 h, after which it was allowed to cool back to –78 °C. A solution of I_2 (18.5 g, 72.8 mmol) in MeOH (50 mL) was added and the resulting solution was allowed to warm to 0 °C and stir at 0 °C for an additional hour. At this time, the reaction was quenched by addition of an saturated aqueous solution of $Na_2S_2O_3$ (60 mL). The aqueous layer was washed with Et_2O (3 × 40 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Purification of the yellow oil residue by silica gel chromatography (20:1 hexanes:ethyl acetate) affords **Her-A** as colorless oil (2.81 g, 8.50 mmol, 70% yield). IR (neat): 2971 (m), 2930 (m), 2881 (m), 1454 (m), 1380 (m), 1203 (w), 1148 (m), 1097 (s), 1039 (s), 941 (w), 909 (m), 735 (m), 698 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.36–7.27 (5H, m), 5.71 (1H, ddd, *J* = 17.2, 10.4, 3.6 Hz), 5.05 (1H, d, *J* = 9.6 Hz), 4.96–4.87 (2H, m), 4.84 (1H, d, *J* = 7.2 Hz), 4.75 (1H, d, *J* = 7.2 Hz), 4.69 (1H, d, *J* = 12.0 Hz), 4.56 (1H, d, *J* = 12.0 Hz), 3.84–3.78 (1H, m), 3.52 (3H, s), 2.81 (1H, dd, *J* = 6.8, 4.4 Hz), 2.72–2.66 (1H, m), 2.35–2.27 (1H, m), 2.00 (1H, dd, *J* = 13.2, 7.2 Hz), 1.90 (1H, dd, *J* = 13.2, 7.2 Hz), 1.59 (3H, d, *J* = 1.2 Hz), 1.28 (3H, d, *J* = 6.0 Hz), 0.98 (3H, d, *J* = 6.8 Hz), 0.95 (3H, d, *J* = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.5, 138.2, 132.8, 130.2, 128.5, 128.0, 127.7, 112.3, 94.7, 89.5, 75.6, 69.4, 61.6, 47.4, 35.8, 34.7, 19.8, 18.2, 16.5, 16.4. HRMS

(ESI$^+$) $[M+H]^+$ calcd for $C_{22}H_{35}O_3$: 347.25862, found: 347.25992. Specific rotation: $[\alpha]_D^{20}$ +37.1 (*c* 0.83, $CHCl_3$).

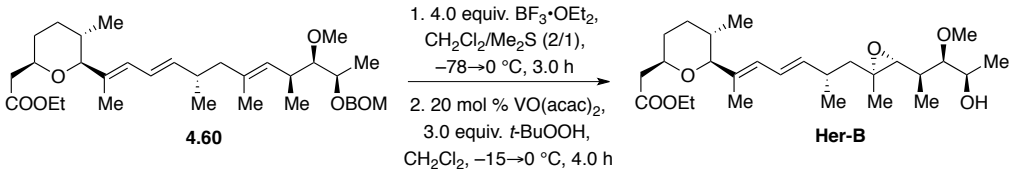


2-((1*E*,3*S*,5*E*,7*S*,8*R*,9*R*)-9-((Benzyloxy)methoxy)-8-methoxy-3,5,7-trimethyldeca-1,5-dien-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.59). To a solution of **Her-A** (2.81 g, 8.50 mmol) and vinyl boronic acid pinacol ester (1.73 mL, 10.2 mmol) in CH_2Cl_2 (60 mL) was added NHC–Ru complex **4.39** (361 mg, 0.43 mmol). The resulting solution was allowed to stir at 50 °C for 36 h. The reaction was quenched by passing the mixture through a short plug of silica gel and eluted with hexanes and diethyl ether (1:1, 3 × 60 mL). The filtrate was concentrated in vacuo to provide a brown oil, which was purified by silica gel chromatography (20:1 hexanes:ethyl acetate) to afford **4.59** as yellow oil (3.35 g, 7.09 mmol, 83% yield). The physical and spectral data were identical to those previously reported.[54a] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.27 (5H, m), 6.49 (1H, dd, *J* = 18.0, 7.2 Hz), 5.35 (1H, d, *J* = 18.0 Hz), 5.03 (1H, d, *J* = 10.0 Hz), 4.83 (1H, d, *J* = 7.2 Hz), 4.74 (1H, d, *J* = 7.2 Hz), 4.68 (1H, d, *J* = 11.6 Hz), 4.55 (1H, d, *J* = 11.6 Hz), 3.82–3.76 (1H, m), 3.50 (3H, s), 2.80 (1H, dd, *J* = 6.8, 4.0 Hz), 2.71–2.64 (1H, m), 2.42–2.35 (1H, m), 2.05–2.01 (1H, m), 1.92–1.84 (1H, m), 1.56 (3H, d, *J* = 1.2 Hz), 1.28–1.24 (15H, m), 0.96 (3H, d, *J* = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.6, 138.2, 132.5, 130.3, 128.5, 128.0, 127.7, 94.6, 89.5, 83.1, 75.6, 69.4, 61.6, 46.9, 37.6, 34.7, 24.9, 19.4, 18.2, 16.5, 16.3. Specific rotation: $[\alpha]_D^{20}$ +36.4 (*c* 1.50, $CHCl_3$).



Ethyl 2-((2*R*,5*S*,6*S*)-6-((2*E*,4*E*,6*S*,8*E*,10*S*,11*R*,12*R*)-12-((benzyloxy)methoxy)-11-methoxy-6,8,10-trimethyltrideca-2,4,8-trien-2-yl)-5-methyltetrahydro-2*H*-pyran-2-yl)acetate (4.60). To a solution of alkenyl iodide **4.49** (2.02 g, 5.74 mmol) and alkenylboron **4.59** (3.35 g, 7.09 mmol) in DMF (60 mL) was added $Pd(dppf)Cl_2•CH_2Cl_2$ (469 mg, 0.57 mmol) and $Ba(OH)_2•8H_2O$ (2.72 g, 8.61 mmol) at 22 °C. The mixture was then allowed to stir at 40 °C for 14 h under N_2 atmosphere, after which the reaction was allowed to cool to 22 °C. A solution of brine (60 mL) was added to quench the reaction. The aqueous layer was subsequently washed with Et_2O (3 × 50 mL), and the combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. Purification of the resulting oil by silica gel chromatography (10:1 hexanes:ethyl acetate) afforded **4.60** as yellow oil (2.55 g, 4.47 mmol, 78% yield). The physical and spectral data were identical to those previously reported.[54a] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.27 (5H, m), 6.16 (1H, dd, *J* = 15.2, 7.6 Hz), 5.89 (1H, d, *J* = 10.0 Hz), 5.51 (1H, dd, *J* = 15.2, 7.6 Hz), 5.02 (1H, d, *J* = 9.6 Hz), 4.83 (1H, d, *J* = 7.2 Hz), 4.74 (1H, d, *J* = 7.2 Hz), 4.68 (1H, d, *J* = 11.6 Hz), 4.55 (1H, d, *J* = 11.6 Hz), 4.11 (2H, q, *J* = 7.2 Hz), 3.81–3.73 (2H, m), 3.50 (3H, s), 3.31 (1H, d, *J* = 10.0 Hz), 2.79 (1H, dd, *J* = 6.8, 4.0 Hz), 2.72–2.64 (1H, m), 2.57 (1H, dd, *J* = 15.2, 6.0 Hz), 2.41–2.31 (2H, m), 2.06–1.82 (3H, m), 1.73–1.66 (1H, m), 1.69 (3H, s), 1.57 (3H, d, *J* = 1.2 Hz), 1.54–1.48 (1H, m), 1.35–1.29 (1H, m), 1.26 (3H, d, *J* = 6.4 Hz), 1.24–1.21 (1H, m), 1.23 (3H, t, *J* = 7.2 Hz), 0.96 (3H, d, *J* = 6.4 Hz), 0.94

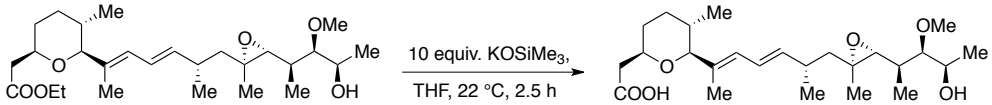
(3H, d, J = 6.4 Hz), 0.67 (3H, d, J = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 140.4, 138.2, 134.4, 132.7, 130.2, 128.5, 127.9, 127.7, 124.1, 94.6, 90.6, 89.4, 75.4, 74.0, 69.4, 61.5, 60.3, 47.7, 41.7, 35.1, 34.7, 32.4, 32.2, 31.7, 20.3, 18.1, 17.7, 16.5, 16.3, 14.3, 12.1. Specific rotation: $[\alpha]_D^{20}$ +32.3 (*c* 1.75, $CHCl_3$).



Ethyl 2-((2*R*,5*S*,6*S*)-6-((*S*,2*E*,4*E*)-7-((2*R*,3*R*)-3-((2*R*,3*R*,4*R*)-4-hydroxy-3-methoxypentan-2-yl)-2-methyloxiran-2-yl)-6-methylhepta-2,4-dien-2-yl)-5-methyltetrahydro-2*H*-pyran-2-yl)acetate (Her-B). To a solution of substrate **4.60** (2.55 g, 4.47 mmol) and Me_2S (20 mL) in CH_2Cl_2 (40 mL) was added BF_3•OEt_2 (2.27 mL, 17.9 mmol) at –78 °C. The resulting solution was allowed to stir at –78 °C for 30 min and warm to 0 °C and stir at 0 °C until TLC analysis indicated complete consumption of starting material. The reaction was then quenched through addition of a saturated aqueous solution of $NaHCO_3$ (20 mL). The aqueous layer was washed with diethyl ether (3 × 20 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The resulting brown residue was purified by silica gel chromatography (6:1 hexanes:ethyl acetate) to afford the desired product contaminated with impurities as yellow oil, which was utilized in the next step without further purification.

To a solution of substrate and $VO(acac)_2$ (356 mg, 1.34 mmol) in CH_2Cl_2 (30 mL) was added *t*-BuOOH (2.68 mL, 5.0 M in nonane, 13.4 mmol) at –15 °C. The mixture was then allowed to warm to 0 °C and stir at 0 °C for 4 h, after which the reaction was

quenched by addition of a solution of brine (20 mL). The aqueous layer was washed with Et_2O (3 × 20 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Purification of the resulting yellow oil by silica gel chromatography (2:1 hexanes:ethyl acetate) affords **Her-B** as colorless oil (1.25 g, 2.68 mmol, 60% overall yield). The physical and spectral data were identical to those previously reported.[54a] ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.21 (1H, dd, *J* = 15.2, 10.8 Hz), 5.87 (1H, d, *J* = 10.8 Hz), 5.42 (1H, dd, *J* = 15.2, 8.8 Hz), 4.10 (2H, q, *J* = 7.2 Hz), 3.87–3.80 (1H, m), 3.76–3.71 (1H, m), 3.52 (3H, s), 3.30 (1H, d, *J* = 9.6 Hz), 2.95 (1H, t, *J* = 5.2 Hz), 2.56 (1H, dd, *J* = 15.2, 6.4 Hz), 2.55 (1H, br s), 2.53 (1H, d, *J* = 10.2 Hz), 2.42–2.34 (1H, m), 2.36 (1H, dd, *J* = 15.2, 6.8 Hz), 1.88 (2H, dd, *J* = 13.6, 4.8 Hz), 1.84–1.80 (1H, m), 1.68 (3H, d, *J* = 1.2 Hz), 1.70–1.65 (1H, m), 1.55–1.47 (2H, m), 1.37–1.27 (1H, m), 1.26 (3H, s), 1.25–1.17 (2H, m), 1.22 (3H, t, *J* = 7.2 Hz), 1.16 (3H, d, *J* = 6.4 Hz), 1.02 (3H, d, *J* = 6.8 Hz), 0.86 (3H, d, *J* = 6.4 Hz), 0.65 (3H, d, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.5, 139.3, 135.4, 128.2, 125.3, 90.7, 87.7, 74.0, 68.4, 66.1, 61.4, 61.3, 60.4, 47.0, 41.7, 35.4, 35.2, 32.4, 32.2, 31.7, 22.1, 19.1, 17.7, 16.6, 14.3, 12.0, 11.9. Specific rotation: $[\alpha]_D^{20}$ +8.8 (*c* 2.32, $CHCl_3$).



Her-B **(+)-herboxidiene**

2-((2*R*,5*S*,6*S*)-6-((*S*,2*E*,4*E*)-7-((2*R*,3*R*)-3-((2*R*,3*R*,4*R*)-4-Hydroxy-3-methoxypentan-2-yl)-2-methyloxiran-2-yl)-6-methylhepta-2,4-dien-2-yl)-5-methyltetrahydro-2*H*-pyran-2-yl)acetic acid [(+)-herboxidiene]. To a solution of ester **Her-B** (1.25 g, 2.68 mmol) in THF (20 mL) was added TMSOK (3.44 g, 26.8 mmol) at 22 °C, and the

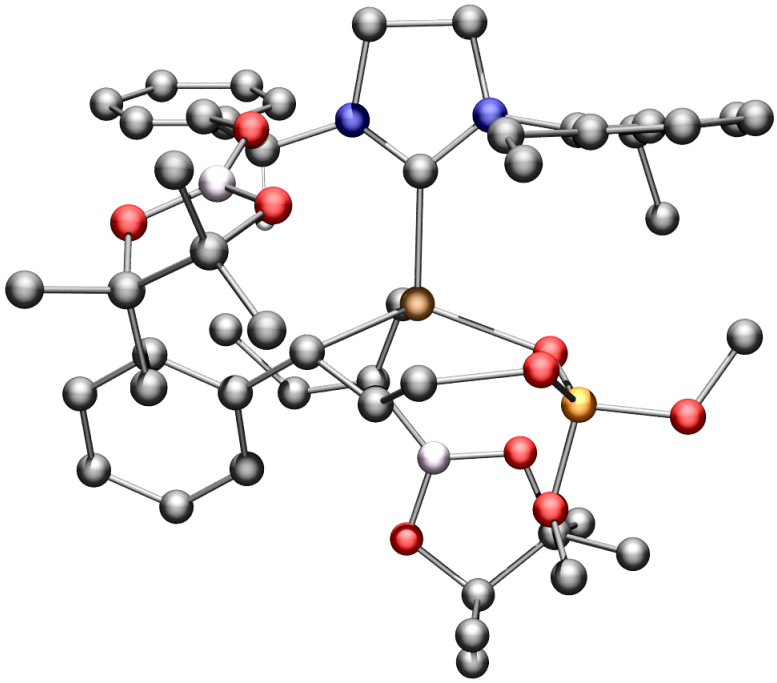
mixture was allowed to stir at 22 °C for 2.5 h. At this time, the reaction was quenched through addition of a 0.5 M aqueous solution of citric acid (20 mL). The aqueous layer (pH = 3–4) was washed with EtOAc (3 × 20 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the yellow oil by silica gel chromatography (95:5 CH_2Cl_2:MeOH) affords **(+)-herboxidiene** as colorless oil (1.03 g, 2.35 mmol, 88% yield). The physical and spectral data were identical to those previously reported.[54] IR (neat): 3467 (br), 2965 (m), 2926 (m), 2852 (m), 1716 (m), 1455 (m), 1382 (m), 1251 (m), 1198 (m), 1154 (m), 1068 (s), 1018 (m), 967 (m), 904 (w), 883 (w) cm^{-1}; ^1H NMR (400 MHz, CD_3OD): δ 6.31 (1H, dd, *J* = 15.2, 10.8 Hz), 5.93 (1H, d, *J* = 10.8 Hz), 5.48 (1H, dd, *J* = 15.2, 9.2 Hz), 3.80–3.74 (2H, m), 3.53 (3H, s), 3.35 (1H, d, *J* = 10.0 Hz), 2.98 (1H, dd, *J* = 6.4, 4.0 Hz), 2.66 (1H, d, *J* = 9.6 Hz), 2.48–2.42 (1H, m), 2.47 (1H, dd, *J* = 15.2, 7.6 Hz), 2.39 (1H, dd, *J* = 15.2, 7.6 Hz), 1.93 (1H, dd, *J* = 13.6, 4.4 Hz), 1.89–1.84 (1H, m), 1.74–1.68 (1H, m), 1.70 (3H, d, *J* = 1.2 Hz), 1.61–1.46 (2H, m), 1.39–1.28 (2H, m), 1.28 (3H, s), 1.27–1.15 (2H, m), 1.11 (3H, d, *J* = 6.8 Hz), 1.05 (3H, d, *J* = 6.8 Hz), 0.84 (3H, d, *J* = 7.2 Hz), 0.69 (3H, d, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, CD_3OD): δ 175.2, 140.8, 136.3, 129.7, 126.6, 92.3, 88.6, 75.6, 70.0, 67.9, 62.7, 62.0, 48.2, 42.4, 36.6, 36.5, 33.6, 33.5, 32.9, 22.9, 20.0, 18.3, 17.0, 12.3, 11.7. HRMS (ESI^+) $[M+H]^+$ calcd for $C_{25}H_{43}O_6$: 439.30596, found: 439.30652. Specific rotation: $[\alpha]_D^{20}$ +6.1 (*c* 1.83, MeOH).

4.8.5 DFT Calculations

Geometry optimizations and frequency calculations were carried out using B97D

functional[57] and 6-31G* basis set. Tetrahydrofuran was simulated by means of the PCM method.[58] The results of harmonic frequency calculations on the optimized geometries showed that all of them are real except for the transition state structures, which have one imaginary frequency. Free energies were computed at 298.15 K and 1.0 atm. by using the unscaled frequencies. All calculations were carried out with the Gaussian09 computer program.[59]

Transition State Leading to the Major Enantiomer



(57) Grimme, S. *J. Comp. Chem.*, **2006,** *27,* 1787–1799.

(58) Tomasi, J.; Mennucci, B.; Cammi, R. *Chem. Rev.* **2005**, *105*, 2999–3094.

(59) Gaussian 09, Revision A.02, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S.S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford CT, 2009.

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 Cartesian coordinates (Angstroms):

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Thermal correction to Gibbs Free Energy= 1.001728

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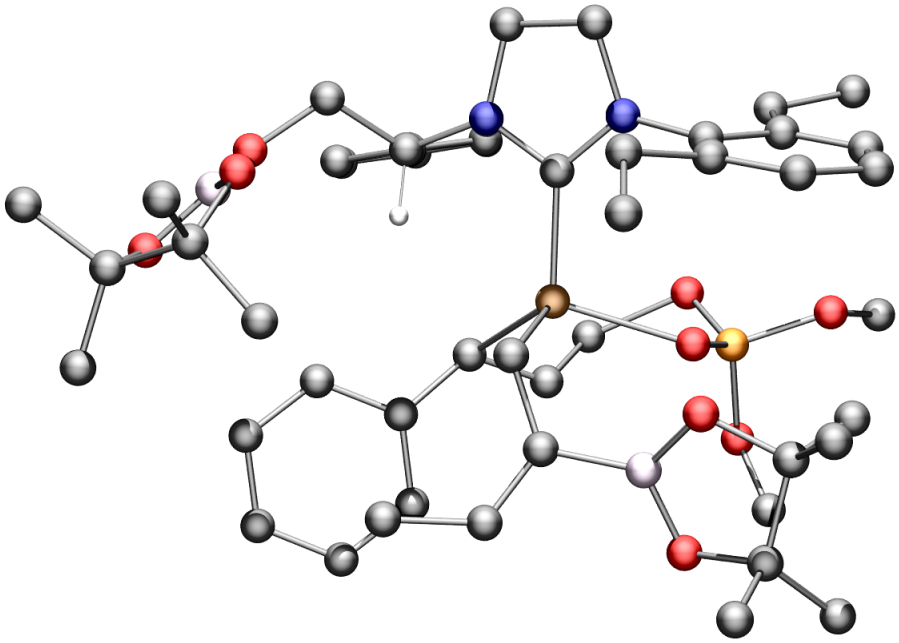
Transition State Leading to the Minor Enantiomer



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C	-1.246	5.099	-1.801
C	-1.247	4.103	-0.811
O	-4.731	1.520	0.642
B	-5.099	0.238	0.969
O	-4.671	-0.441	2.096
O	-5.969	-0.469	0.159
C	-6.335	-1.671	0.921
C	-5.115	-1.832	1.915
C	-3.936	-2.588	1.291
C	-5.474	-2.417	3.281
C	-7.658	-1.357	1.639
C	-6.518	-2.835	-0.054
C	2.106	1.546	2.367
C	2.153	0.360	3.137
C	3.419	-0.107	3.535
C	4.583	0.594	3.198
C	4.506	1.786	2.464

C	3.263	2.291	2.047
Cu	0.223	0.317	-0.365
C	0.874	-0.320	3.609
C	0.984	-1.834	3.868
C	3.122	3.604	1.291
C	4.407	4.436	1.165
C	-0.271	-1.548	0.292
C	0.381	-2.619	-0.471
C	-0.271	-3.607	-1.173
C	-1.752	-3.886	-1.122
B	1.920	-2.858	-0.307
O	2.585	-2.674	0.898
O	2.716	-3.505	-1.256
C	3.966	-3.122	0.725
C	3.852	-4.074	-0.529
C	4.843	-1.891	0.464
C	4.411	-3.814	2.018
C	5.076	-4.088	-1.446
C	3.457	-5.515	-0.156
H	0.026	2.300	3.994

```
H    0.812    3.783    3.368
H   -1.100    4.316    1.972
H   -1.996    3.260    3.109
H   -4.033    3.190    1.606
H   -3.456    1.640    2.300
H   -4.461    3.006   -1.150
H   -4.460    4.757   -2.905
H   -2.400    6.113   -3.333
H   -0.337    5.679   -1.979
H   -0.334    3.908   -0.249
H   -3.695   -2.169    0.306
H   -4.167   -3.657    1.171
H   -3.054   -2.487    1.939
H   -6.213   -1.795    3.804
H   -4.567   -2.487    3.901
H   -5.886   -3.430    3.155
H   -7.529   -0.525    2.347
H   -8.023   -2.236    2.189
H   -8.410   -1.070    0.889
H   -5.625   -2.980   -0.674
```

```
H  -7.377  -2.631  -0.712
H  -6.721  -3.762   0.505
H   3.492  -1.025   4.119
H   5.556   0.213   3.515
H   5.419   2.327   2.220
H   0.075  -0.136   2.878
H   0.543   0.176   4.541
H   1.376  -2.350   2.981
H  -0.011  -2.241   4.108
H   1.649  -2.051   4.719
H   2.351   4.215   1.790
H   2.720   3.390   0.290
H   4.812   4.701   2.155
H   4.200   5.367   0.616
H   5.186   3.884   0.618
H  -1.357  -1.664   0.400
H   0.203  -1.438   1.277
H   0.337  -4.348  -1.702
H  -2.079  -4.493  -1.980
H  -2.012  -4.448  -0.202
```

H	-2.345	-2.965	-1.122
H	4.515	-1.369	-0.439
H	5.898	-2.188	0.357
H	4.749	-1.194	1.306
H	3.720	-4.618	2.303
H	4.445	-3.074	2.831
H	5.420	-4.239	1.892
H	5.310	-3.082	-1.817
H	4.885	-4.747	-2.307
H	5.951	-4.475	-0.900
H	2.573	-5.513	0.500
H	4.281	-6.030	0.360
H	3.213	-6.068	-1.076
C	-3.194	-0.483	-2.128
C	-1.831	-0.552	-2.509
C	-4.132	-1.401	-2.611
C	-3.728	-2.416	-3.498
C	-2.380	-2.503	-3.880
C	-1.436	-1.595	-3.381
C	-0.926	0.525	-2.073

C	0.341	0.751	-2.654
C	0.903	2.055	-2.850
O	2.349	2.414	-1.863
P	3.121	1.093	-1.508
O	4.560	1.520	-0.876
O	3.478	0.479	-2.987
O	2.452	0.099	-0.589
C	5.414	2.397	-1.655
C	4.081	-0.838	-3.058
H	-3.526	0.319	-1.468
H	-5.172	-1.313	-2.296
H	-4.457	-3.129	-3.888
H	-2.056	-3.291	-4.563
H	-0.398	-1.672	-3.701
H	-1.466	1.438	-1.809
H	0.862	-0.085	-3.120
H	0.292	2.897	-2.521
H	1.427	2.215	-3.796
H	4.928	3.372	-1.798
H	5.642	1.945	-2.632

H 6.335 2.516 -1.071

H 3.457 -1.584 -2.549

H 5.086 -0.821 -2.605

H 4.165 -1.076 -4.126

SCF Done: E(RB97D) = -4688.34669575 A.U. after 1 cycles

	1	2	3
	A	A	A
Frequencies --	-333.9068	9.6688	20.0388
Red. masses --	9.6542	4.6757	4.5476

Zero-point correction= 1.102936 (Hartree/Particle)

Thermal correction to Energy= 1.170598

Thermal correction to Enthalpy= 1.171542

Thermal correction to Gibbs Free Energy= 1.002570

Sum of electronic and zero-point Energies= -4687.243760

Sum of electronic and thermal Energies= -4687.176098

Sum of electronic and thermal Enthalpies= -4687.175154

Sum of electronic and thermal Free Energies= -4687.344126

Item	Value	Threshold	Converged?
Maximum Force	0.000020	0.000450	YES
RMS Force	0.000002	0.000300	YES

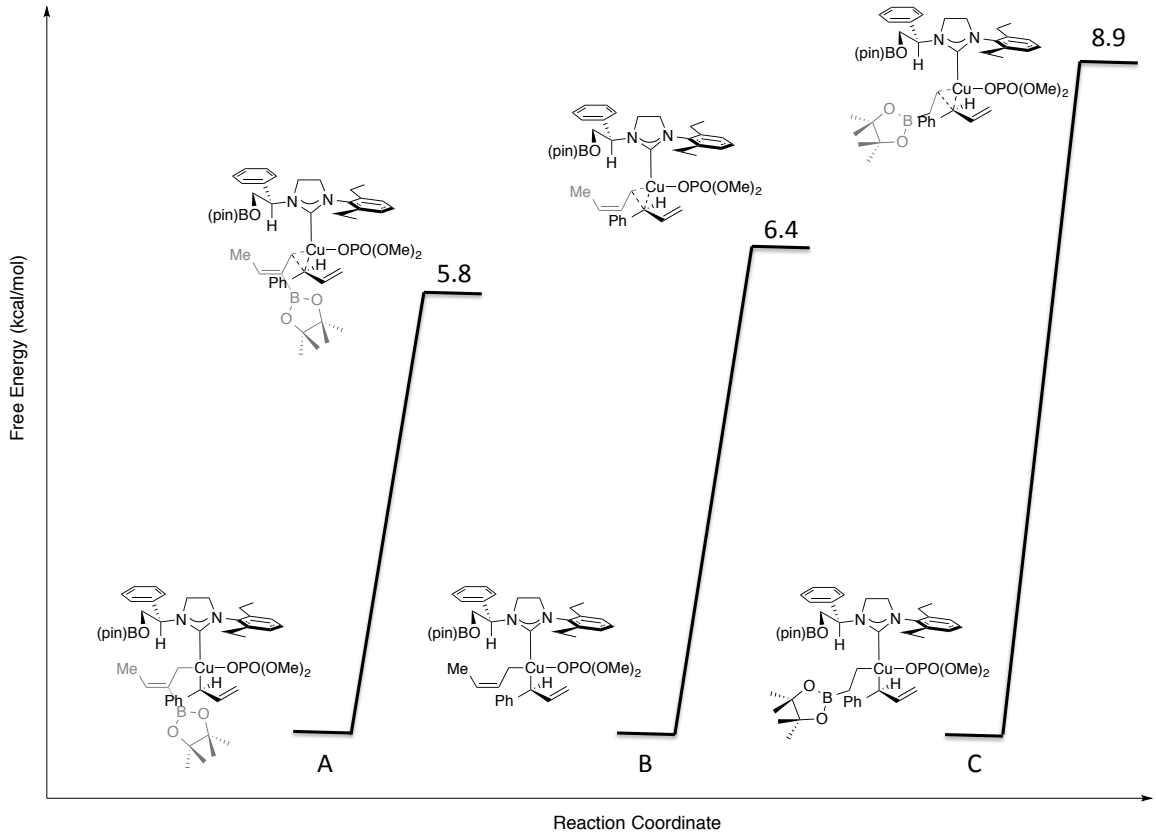

Figure S1. Relative energies for reductive elimination of Cu(III) intermediates. (A) Barrier to reductive elimination of full system. (B) Barrier to reductive elimination of

theoretical system without B(pin) substituent. (C) Barrier to reductive elimination of theoretical system without olefin.

Cu(III) Intermediate of Full System (Path A)

Cartesian coordinates (Angstroms):

C	-2.122243	-0.471735	-1.509106
C	-1.013206	0.003534	-0.673342
C	-1.950643	-0.873871	-2.805371
O	3.484100	-3.997941	-1.191915
P	3.203219	-2.395503	-0.870336
O	4.555858	-1.973323	-0.014625
O	3.094904	-1.686804	-2.196127
C	5.792293	-1.887663	-0.753623
O	2.082941	-2.287023	0.175392
O	1.759254	3.351166	-2.099006
C	2.001644	1.933636	-2.193497
C	2.628377	1.306704	-0.938938
C	1.955125	2.758758	1.070781

N	1.826135	1.504501	0.279492
C	-2.379804	2.934660	3.511552
C	1.101334	2.460367	2.316064
C	-2.075177	1.665539	2.686634
C	4.773527	2.673936	-1.409443
C	1.139511	0.540824	0.920355
C	4.081237	1.703886	-0.663852
N	0.720886	1.041929	2.101271
C	6.108444	2.989275	-1.100342
C	-1.276308	0.638153	3.463498
C	4.739398	1.072645	0.410379
C	0.060198	0.314562	3.141299
C	-1.875613	-0.020761	4.554466
C	6.759292	2.349495	-0.034967
C	6.066737	1.389452	0.723786
C	0.795214	-0.652483	3.871092
C	3.273902	0.031915	3.785550
C	2.209736	-1.047807	3.488396
C	-1.159128	-0.954156	5.312437
C	0.164209	-1.264471	4.967352

C	3.589198	-4.892638	-0.065389
C	-6.800780	-1.963521	-0.703225
C	-6.422919	0.501594	-1.072336
C	-5.795555	-0.817330	-0.590454
O	-4.660233	-1.091962	-1.481443
C	-5.096292	-0.688954	0.816459
C	-5.753951	0.307948	1.771964
C	-4.883240	-2.041000	1.517079
B	-3.532383	-0.576870	-0.858984
O	-3.766142	-0.193249	0.455147
C	-0.643108	-0.998318	-3.530522
O	-0.525356	2.993227	-1.323598
C	-2.333972	3.332238	-2.878140
C	-2.751031	3.393782	-0.402165
C	-1.764275	3.752588	-1.512959
B	0.489444	3.791999	-1.825488
O	0.121173	5.108937	-2.038102
C	-1.233065	5.240600	-1.479895
C	-2.027082	6.218755	-2.345088
C	-1.077345	5.782761	-0.049957

H	-1.377482	0.606649	0.163274
H	-0.294911	0.583840	-1.254735
H	-2.839559	-1.161484	-3.374898
H	6.558764	-1.556024	-0.040805
H	5.706623	-1.153327	-1.568704
H	6.065928	-2.872832	-1.167304
H	1.069162	1.406432	-2.429930
H	2.699323	1.780573	-3.029356
H	2.612826	0.228733	-1.148730
H	1.581668	3.614247	0.499101
H	3.011931	2.933855	1.312921
H	-2.957533	3.654438	2.909539
H	-1.451706	3.426056	3.844991
H	-2.968238	2.685630	4.408710
H	0.201666	3.087985	2.367414
H	1.654511	2.560535	3.260458
H	-3.018787	1.207297	2.360517
H	-1.542275	1.939415	1.768302
H	4.274974	3.200263	-2.222817
H	6.633522	3.743286	-1.690396

```
H    4.205488    0.319846    0.987865
H   -2.912992    0.212376    4.805896
H    7.794937    2.598309    0.205531
H    6.560746    0.885469    1.557245
H    4.279907   -0.363835    3.573341
H    3.237989    0.343494    4.841862
H    3.127341    0.921409    3.157775
H    2.244075   -1.303701    2.419437
H    2.468686   -1.964905    4.041371
H   -1.633794   -1.451657    6.160599
H    0.718358   -2.010655    5.540883
H    3.839464   -5.881816   -0.473154
H    2.633145   -4.947275    0.480238
H    4.382526   -4.562771    0.624957
H   -6.323648   -2.932815   -0.505729
H   -7.230580   -1.981206   -1.716045
H   -7.618250   -1.815988    0.019644
H   -5.703918    1.329667   -0.979684
H   -7.322912    0.746900   -0.488843
H   -6.704547    0.395112   -2.130164
```

```
H  -5.196450   0.333366   2.720475
H  -6.788275  -0.003095   1.986283
H  -5.768085   1.319524   1.344653
H  -4.409690  -2.762662   0.835276
H  -5.838832  -2.458406   1.867806
H  -4.221353  -1.890006   2.382534
H  -0.565560  -2.006873  -3.972138
H   0.222311  -0.850982  -2.869843
H  -0.578637  -0.276339  -4.366075
H  -2.480888   2.241897  -2.873358
H  -1.636131   3.594923  -3.687934
H  -3.299051   3.824150  -3.071103
H  -2.999082   2.324556  -0.455807
H  -3.676766   3.977536  -0.526838
H  -2.335885   3.603091   0.590717
H  -2.026163   5.907220  -3.398148
H  -1.584084   7.223471  -2.272595
H  -3.068223   6.270788  -1.990329
H  -0.523014   5.067947   0.577231
H  -2.060421   5.963604   0.409338
```

```
H  -0.520544   6.730474  -0.084175
C  -2.229510  -4.323825  -3.101159
C  -2.182604  -3.610998  -1.891848
C  -1.075866  -4.945026  -3.600362
C  -0.980420  -3.506417  -1.149974
C   0.120858  -4.874843  -2.858754
C   0.162102  -4.174461  -1.651606
C  -0.943700  -2.731652   0.109267
C  -0.330360  -3.361767   1.289811
C  -0.732379  -3.135810   2.562244
Cu  0.366565  -1.165435  0.197325
H  -3.169928  -4.383627  -3.653851
H  -3.089726  -3.144852  -1.511306
H  -1.107163  -5.488823  -4.547054
H   1.027344  -5.359535  -3.228012
H   1.089801  -4.114829  -1.094382
H  -0.246867  -3.625593   3.406662
H  -1.539162  -2.435892   2.790579
H   0.505052  -4.038882   1.106894
H  -1.918656  -2.296997   0.352851
```

SCF Done: E(RB97D) = -4688.40390726 A.U. after 7 cycles

Reductive Elimination Transition State for Full System (Path A)

Cartesian coordinates (Angstroms):

C	1.595	1.910	-1.507
C	0.470	1.225	-0.906
C	1.469	2.839	-2.514
O	-4.111	3.465	-0.743
P	-3.540	1.906	-0.768
O	-4.928	1.018	-0.613
O	-2.869	1.704	-2.106
C	-5.679	0.740	-1.811
O	-2.789	1.629	0.542
O	-0.531	-2.526	-3.082
C	-1.024	-1.245	-2.635
C	-1.850	-1.287	-1.343
C	-1.021	-3.262	0.073

```
N  -1.110  -1.803  -0.182
C   3.008  -3.151   3.076
C  -0.216  -3.301   1.376
C   2.339  -1.771   2.893
C  -3.648  -2.664  -2.588
C  -0.848  -1.067   0.924
C  -3.211  -1.977  -1.443
N  -0.402  -1.919   1.879
C  -4.921  -3.261  -2.616
C   1.119  -1.589   3.775
C  -4.060  -1.910  -0.321
C  -0.194  -1.609   3.257
C   1.291  -1.351   5.151
C  -5.761  -3.188  -1.494
C  -5.324  -2.511  -0.342
C  -1.323  -1.368   4.078
C  -3.302  -2.718   3.172
C  -2.731  -1.325   3.514
C   0.189  -1.131   5.986
C  -1.106  -1.132   5.446
```

C	-4.742	3.922	0.469
C	6.099	3.139	0.112
C	6.033	1.201	-1.495
C	5.247	1.992	-0.436
O	4.076	2.558	-1.111
C	4.589	1.077	0.666
C	5.392	-0.180	1.004
C	4.233	1.839	1.953
B	3.012	1.698	-0.882
O	3.313	0.700	0.040
C	0.217	3.296	-3.198
O	1.483	-2.271	-1.730
C	3.628	-1.832	-2.727
C	3.449	-2.874	-0.447
C	2.839	-2.813	-1.845
B	0.737	-2.894	-2.720
O	1.372	-3.968	-3.321
C	2.584	-4.213	-2.530
C	3.699	-4.675	-3.468
C	2.240	-5.320	-1.520

```
H   0.726   0.217  -0.580
H  -0.496   1.336  -1.403
H   2.392   3.301  -2.881
H  -6.549   0.146  -1.500
H  -5.072   0.158  -2.520
H  -6.019   1.673  -2.292
H  -0.185  -0.554  -2.492
H  -1.671  -0.851  -3.431
H  -2.035  -0.230  -1.126
H  -0.528  -3.787  -0.749
H  -2.037  -3.669   0.192
H   3.902  -3.234   2.438
H   2.316  -3.966   2.812
H   3.312  -3.294   4.125
H   0.853  -3.482   1.192
H  -0.589  -4.032   2.105
H   3.072  -0.992   3.155
H   2.074  -1.611   1.838
H  -2.997  -2.748  -3.457
H  -5.249  -3.790  -3.513
```

H -3.721 -1.373   0.565

H   2.304 -1.323   5.559

H -6.748 -3.655 -1.516

H -5.971 -2.443   0.535

H -4.337 -2.628   2.806

H -3.301 -3.368   4.061

H -2.710 -3.207   2.387

H -2.745 -0.691   2.614

H -3.387 -0.840   4.254

H   0.337 -0.943   7.051

H -1.967 -0.936   6.089

H -5.100   4.943   0.271

H -4.021   3.937   1.303

H -5.595   3.277   0.737

H   5.508   3.803   0.756

H   6.504   3.729 -0.725

H   6.943   2.737   0.694

H   5.436   0.361 -1.876

H   6.972   0.809 -1.077

H   6.272   1.873 -2.332

```
H    4.857  -0.772   1.760
H    6.370   0.110   1.417
H    5.553  -0.807   0.118
H    3.678   2.760   1.723
H    5.139   2.106   2.517
H    3.599   1.197   2.582
H    0.074   4.376  -3.004
H   -0.687   2.770  -2.867
H    0.318   3.186  -4.294
H    3.569  -0.837  -2.266
H    3.197  -1.782  -3.739
H    4.684  -2.131  -2.806
H    3.490  -1.858  -0.036
H    4.472  -3.281  -0.494
H    2.855  -3.504   0.226
H    3.863  -3.951  -4.277
H    3.432  -5.647  -3.911
H    4.636  -4.796  -2.903
H    1.445  -4.990  -0.835
H    3.122  -5.598  -0.924
```

```
H    1.887  -6.207  -2.067
C    1.214   5.913  -0.967
C    1.373   4.711  -0.258
C   -0.069   6.418  -1.223
C    0.247   4.008   0.237
C   -1.198   5.717  -0.751
C   -1.041   4.533  -0.030
C    0.420   2.770   0.993
C   -0.462   2.511   2.120
C   -0.239   1.461   3.002
Cu  -0.923   0.861   1.071
H    2.097   6.443  -1.334
H    2.373   4.323  -0.069
H   -0.193   7.346  -1.785
H   -2.203   6.085  -0.964
H   -1.916   3.976   0.293
H   -0.904   1.308   3.851
H    0.733   0.967   3.056
H   -1.352   3.133   2.236
H    1.447   2.433   1.133
```

SCF Done: E(RB97D) = -4688.39469068 A.U. after 3 cycles

	1	2	3
	A	A	A
Frequencies --	-159.6341	17.5735	19.9445
Red. masses --	7.7813	5.1029	4.3605

Zero-point correction= 1.104234 (Hartree/Particle)

Thermal correction to Energy= 1.172121

Thermal correction to Enthalpy= 1.173065

Thermal correction to Gibbs Free Energy= 1.002598

Sum of electronic and zero-point Energies= -4687.290457

Sum of electronic and thermal Energies= -4687.222569

Sum of electronic and thermal Enthalpies= -4687.221625

Sum of electronic and thermal Free Energies= -4687.392093

Item	Value	Threshold	Converged?
Maximum Force	0.000030	0.000450	YES
RMS Force	0.000003	0.000300	YES

Cu(III) Intermediate for Theoretical System Lacking B(pin) (Path B)

```
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 Cartesian coordinates (Angstroms):

-----------------------------------


C  -0.508255  -2.228553  -2.421763

C  -0.547540  -1.811720  -0.996061

C  -0.048111  -1.538609  -3.490090

O   4.862728   1.288406  -0.396291

P   3.233466   1.420488  -0.135050

O   3.176550   2.288402   1.277761

O   2.643340   2.153337  -1.307553

C   3.732754   3.621552   1.237385

O   2.708098   0.038929   0.291623

O  -2.908986   2.000459  -1.495620

C  -1.550172   1.714260  -1.874582

C  -0.564249   2.101454  -0.762979

C  -1.805170   1.814929   1.485194

N  -0.828725   1.333125   0.467091

C  -3.535615  -2.623176   2.901988

C  -1.830356   0.648032   2.486420
```

C	-2.268939	-2.611315	2.016911
C	-1.258564	4.567250	-1.112147
C	-0.166818	0.231501	0.857766
C	-0.486653	3.597184	-0.448657
N	-0.661001	-0.155798	2.051218
C	-1.121835	5.928847	-0.790365
C	-1.002334	-2.455618	2.838978
C	0.416411	4.014496	0.549578
C	-0.219474	-1.280326	2.822032
C	-0.597147	-3.514133	3.674087
C	-0.221622	6.335638	0.205331
C	0.547312	5.369946	0.877883
C	0.956032	-1.151977	3.601800
C	1.215120	1.326962	4.242094
C	1.826600	0.088810	3.550203
C	0.545175	-3.401217	4.474052
C	1.314545	-2.230039	4.429123
C	5.649973	0.616805	0.610063
C	0.672879	-0.220976	-3.478262
O	-3.544717	-0.360050	-1.523114

C	-5.329964	-1.111727	-2.962426
C	-4.673102	-2.434937	-0.924241
C	-4.849260	-1.032066	-1.504588
B	-3.811174	0.986279	-1.326814
O	-5.107265	1.257797	-0.921550
C	-5.712212	-0.047010	-0.622785
C	-7.196775	0.001508	-0.983599
C	-5.529247	-0.289332	0.883493
H	-0.806182	-2.665146	-0.352993
H	-1.319625	-1.047595	-0.850518
H	-0.140963	-2.012375	-4.472739
H	3.559310	4.060776	2.229439
H	3.230765	4.228282	0.468774
H	4.814494	3.581488	1.031417
H	-1.428770	0.651480	-2.111648
H	-1.319405	2.301298	-2.776034
H	0.435945	1.795292	-1.105781
H	-2.777112	2.012016	1.020885
H	-1.431723	2.746396	1.933615
H	-4.439845	-2.758590	2.289365

H	-3.635391	-1.681106	3.463726
H	-3.485190	-3.445749	3.631906
H	-2.743985	0.042013	2.405064
H	-1.711208	0.964417	3.530630
H	-2.217521	-3.563845	1.463690
H	-2.335036	-1.818624	1.259352
H	-1.979875	4.271518	-1.872468
H	-1.728576	6.668561	-1.316762
H	1.017267	3.265078	1.063271
H	-1.191828	-4.430360	3.690087
H	-0.120615	7.393295	0.457249
H	1.252800	5.672543	1.654330
H	1.948486	2.148523	4.247566
H	0.928777	1.105140	5.283054
H	0.323905	1.680537	3.705486
H	2.049940	0.342519	2.506370
H	2.787744	-0.149643	4.033658
H	0.846120	-4.229209	5.119054
H	2.219998	-2.146781	5.034366
H	6.696206	0.680350	0.281257

H	5.350920	-0.440017	0.697827
H	5.536545	1.107934	1.590125
H	1.677566	-0.343277	-3.917309
H	0.801221	0.172130	-2.462183
H	0.143807	0.541904	-4.076365
H	-4.567230	-1.633065	-3.558896
H	-5.477998	-0.103583	-3.377721
H	-6.277958	-1.665420	-3.031638
H	-4.036033	-3.031813	-1.593783
H	-5.652708	-2.930111	-0.839707
H	-4.204585	-2.403124	0.066432
H	-7.342504	0.315004	-2.025891
H	-7.714731	0.714299	-0.324403
H	-7.649153	-0.992843	-0.844834
H	-4.460377	-0.354150	1.132857
H	-6.017516	-1.224032	1.194992
H	-5.974183	0.547824	1.440450
C	3.156325	-2.952754	-4.404185
C	2.484888	-3.147098	-3.188438
C	4.213942	-2.032982	-4.486982

```
C    2.850898  -2.429961  -2.023705

C    4.607836  -1.330894  -3.331994

C    3.941095  -1.531582  -2.119568

C    2.092236  -2.637418  -0.767590

C    2.840312  -2.784773   0.495354

C    2.416436  -3.520770   1.547082

Cu   1.053291  -0.970658  -0.156041

H    2.849980  -3.517935  -5.287535

H    1.666242  -3.863629  -3.128996

H    4.732130  -1.871538  -5.434754

H    5.432042  -0.615654  -3.377437

H    4.239424  -0.966342  -1.243515

H    2.997707  -3.587535   2.466765

H    1.458812  -4.046835   1.527050

H    3.781253  -2.238003   0.574601

H    1.348605  -3.432476  -0.881398

H   -0.885773  -3.238635  -2.625468

---------------------------------
```

SCF Done: E(RB97D) = -4277.97456106   A.U. after   7 cycles

Reductive Elimination Transition State for Theoretical System Lacking B(pin) (Path B)

Cartesian coordinates (Angstroms):

C	-0.720	3.294	-0.976
C	-0.642	1.895	-0.668
C	-1.714	3.920	-1.676
O	-4.879	-0.689	-0.660
P	-3.274	-1.083	-0.791
O	-3.323	-2.742	-0.874
O	-2.772	-0.456	-2.068
C	-3.844	-3.311	-2.094
O	-2.576	-0.823	0.550
O	2.509	0.376	-3.067
C	1.071	0.316	-3.004
C	0.575	-0.821	-2.077
C	2.620	-1.705	-0.789
N	1.346	-0.922	-0.810

C	4.531	-0.559	3.663
C	2.844	-1.964	0.709
C	3.089	-0.051	3.440
C	1.350	-2.538	-3.840
C	0.787	-0.798	0.424
C	0.525	-2.193	-2.752
N	1.613	-1.405	1.311
C	1.290	-3.826	-4.395
C	2.040	-1.114	3.706
C	-0.345	-3.161	-2.220
C	1.298	-1.720	2.670
C	1.752	-1.474	5.035
C	0.411	-4.784	-3.866
C	-0.407	-4.447	-2.774
C	0.276	-2.667	2.935
C	0.242	-4.347	0.993
C	-0.544	-3.319	1.836
C	0.747	-2.404	5.325
C	0.016	-2.988	4.279
C	-5.596	-1.192	0.486

C	-2.929	3.280	-2.281
O	2.551	2.207	-1.446
C	3.830	4.221	-1.813
C	3.206	3.481	0.516
C	3.632	3.017	-0.878
B	3.162	1.233	-2.220
O	4.538	1.164	-2.065
C	4.847	2.009	-0.903
C	6.216	2.656	-1.110
C	4.860	1.084	0.323
H	0.389	1.560	-0.578
H	-1.318	1.253	-1.237
H	-1.605	4.996	-1.849
H	-3.837	-4.401	-1.958
H	-3.208	-3.038	-2.950
H	-4.877	-2.968	-2.276
H	0.665	1.277	-2.669
H	0.706	0.120	-4.022
H	-0.454	-0.571	-1.794
H	3.437	-1.131	-1.240

```
H    2.493   -2.635   -1.358
H    5.259    0.241    3.454
H    4.758   -1.415    3.009
H    4.665   -0.888    4.706
H    3.723   -1.433    1.097
H    2.937   -3.029    0.963
H    2.907    0.797    4.121
H    2.979    0.335    2.417
H    2.048   -1.805   -4.244
H    1.935   -4.081   -5.239
H   -0.984   -2.902   -1.377
H    2.310   -0.997    5.844
H    0.364   -5.785   -4.299
H   -1.096   -5.183   -2.355
H   -0.443   -4.882    0.319
H    0.745   -5.085    1.639
H    1.000   -3.859    0.366
H   -0.967   -2.550    1.175
H   -1.399   -3.828    2.308
H    0.525   -2.667    6.361
```

H	-0.776	-3.706	4.502
H	-6.639	-0.865	0.370
H	-5.181	-0.782	1.421
H	-5.554	-2.293	0.523
H	-3.843	3.699	-1.821
H	-2.952	2.190	-2.145
H	-2.986	3.504	-3.362
H	2.877	4.762	-1.903
H	4.143	3.885	-2.812
H	4.592	4.906	-1.414
H	2.353	4.171	0.428
H	4.034	4.013	1.009
H	2.904	2.632	1.144
H	6.257	3.203	-2.062
H	6.996	1.880	-1.114
H	6.427	3.358	-0.288
H	3.860	0.655	0.474
H	5.148	1.631	1.232
H	5.577	0.268	0.155
C	-4.088	4.948	0.630

```
C  -2.896   4.304   1.001

C  -5.252   4.200   0.408

C  -2.857   2.901   1.192

C  -5.221   2.799   0.570

C  -4.044   2.161   0.959

C  -1.621   2.251   1.612

C  -1.686   1.142   2.544

C  -0.555   0.584   3.117

Cu  -0.802   0.198   0.975

H  -4.098   6.032   0.500

H  -1.994   4.888   1.183

H  -6.177   4.698   0.106

H  -6.115   2.204   0.374

H  -4.009   1.077   1.034

H  -0.652  -0.237   3.824

H   0.406   1.103   3.095

H  -2.661   0.693   2.743

H  -0.754   2.904   1.723

H   0.100   3.919  -0.607

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```

SCF Done: E(RB97D) = -4277.96435038 A.U. after 1 cycles

	1	2	3
	A	A	A
Frequencies --	-140.3934	12.5952	19.7957
Red. masses --	8.2110	5.0319	4.7549

Zero-point correction= 0.935066 (Hartree/Particle)

Thermal correction to Energy= 0.993123

Thermal correction to Enthalpy= 0.994067

Thermal correction to Gibbs Free Energy= 0.842585

Sum of electronic and zero-point Energies= -4277.029285

Sum of electronic and thermal Energies= -4276.971227

Sum of electronic and thermal Enthalpies= -4276.970283

Sum of electronic and thermal Free Energies= -4277.121765

Item	Value	Threshold	Converged?
Maximum Force	0.000011	0.000450	YES
RMS Force	0.000001	0.000300	YES

Cu(III) Intermediate for Theoretical System Lacking B(pin) (Path C)

```
C  -2.105360   0.339428  -1.184259
```

C	-1.268204	0.382845	0.109808
O	2.476244	-4.443817	-0.941671
P	2.343771	-2.811789	-0.771276
O	3.845003	-2.411844	-0.183409
O	2.060935	-2.216774	-2.124500
C	4.976633	-2.751861	-1.015018
O	1.413123	-2.500105	0.421461
O	1.147326	3.268538	-2.166939
C	0.986906	1.856582	-2.407124
C	2.077637	1.040757	-1.700162
C	2.761833	2.356250	0.424947
N	2.025530	1.246857	-0.242005
C	-0.638807	3.302080	3.978267
C	2.255014	2.251282	1.875284
C	-0.824510	2.025359	3.128928
C	3.818722	2.150612	-3.254293
C	1.418127	0.429383	0.629989
C	3.501526	1.258701	-2.214449
N	1.600570	0.919530	1.873953
C	5.146309	2.285590	-3.695633

C	-0.051673	0.848839	3.693691
C	4.538234	0.516368	-1.614663
C	1.101929	0.317787	3.076814
C	-0.490241	0.267952	4.897957
C	6.172422	1.540535	-3.095569
C	5.863169	0.655120	-2.048464
C	1.812777	-0.773606	3.634929
C	4.313361	-0.451133	3.165999
C	3.062961	-1.340439	2.990369
C	0.194529	-0.809400	5.470084
C	1.333055	-1.325937	4.836154
C	2.762407	-5.218603	0.240117
C	-6.264458	-2.136044	-2.302240
C	-6.511996	0.346586	-1.939727
C	-5.692043	-0.906812	-1.594707
O	-4.329734	-0.671022	-2.094888
C	-5.455450	-1.084395	-0.045769
C	-6.582834	-0.561980	0.845425
C	-5.086839	-2.525945	0.343692
B	-3.582202	-0.201474	-1.028125

O	-4.257335	-0.263105	0.181159
O	-1.016748	3.458723	-1.048682
C	-2.717380	4.985762	-1.820101
C	-2.688375	4.175323	0.563456
C	-1.828270	4.603651	-0.626495
B	0.185694	3.977937	-1.501751
O	0.365595	5.320779	-1.217493
C	-0.723447	5.688242	-0.302904
C	-1.138841	7.131590	-0.588661
C	-0.168537	5.558966	1.123649
H	-1.884965	0.283411	1.014180
H	-0.743538	1.342063	0.159909
H	5.870642	-2.399328	-0.482539
H	4.906244	-2.249107	-1.991369
H	5.035171	-3.842163	-1.161419
H	0.007754	1.510049	-2.059750
H	1.058361	1.686595	-3.492034
H	1.825016	-0.020033	-1.863086
H	2.523661	3.312909	-0.051760
H	3.843411	2.175686	0.342838

H	-1.229738	4.134324	3.566185
H	0.419135	3.607925	4.005254
H	-0.964355	3.125662	5.015230
H	1.513565	3.026913	2.116910
H	3.056821	2.288763	2.623280
H	-1.895355	1.765436	3.104402
H	-0.532316	2.213984	2.088308
H	3.039478	2.754822	-3.716387
H	5.375471	2.981578	-4.505246
H	4.290604	-0.171704	-0.806714
H	-1.387730	0.665487	5.377265
H	7.203607	1.649721	-3.437673
H	6.652958	0.069509	-1.573431
H	5.198072	-0.964699	2.756453
H	4.501010	-0.227215	4.228776
H	4.201629	0.500640	2.627433
H	2.890368	-1.510761	1.922603
H	3.262375	-2.326137	3.441120
H	-0.162670	-1.253310	6.401634
H	1.868662	-2.171478	5.273781

H 2.790408 -6.270196 -0.075776

H 1.976680 -5.077682 0.997526

H 3.736258 -4.931212 0.669304

H -5.601099 -3.003902 -2.189631

H -6.385483 -1.920937 -3.374655

H -7.252166 -2.385413 -1.884074

H -6.103387 1.230156 -1.426256

H -7.564285 0.220769 -1.643857

H -6.466711 0.515239 -3.025678

H -6.314225 -0.712038 1.902097

H -7.511896 -1.117022 0.642197

H -6.764443 0.507858 0.676061

H -4.287163 -2.915701 -0.302839

H -5.963176 -3.186183 0.260869

H -4.728628 -2.536952 1.383111

H -3.318471 4.111438 -2.110404

H -2.103702 5.296331 -2.679017

H -3.395624 5.810035 -1.554048

H -3.391192 3.391005 0.243983

H -3.267737 5.033533 0.937275

H -2.074374   3.777196   1.380259

H -1.404402   7.267171 -1.645551

H -0.307702   7.809924 -0.343713

H -2.005258   7.404114   0.033746

H   0.096893   4.513975   1.338043

H -0.908753   5.889685   1.866652

H   0.732682   6.181881   1.217304

C -1.827788 -4.284119 -2.770003

C -1.894698 -3.267795 -1.808996

C -1.167731 -5.490763 -2.479201

C -1.304304 -3.423543 -0.529831

C -0.582897 -5.663479 -1.214109

C -0.648120 -4.645180 -0.255401

C -1.431326 -2.327918   0.464202

C -1.226114 -2.593502   1.900831

C -1.996067 -2.053694   2.873197

Cu   0.116882 -1.016827   0.317355

H -2.296058 -4.135053 -3.745769

H -2.428106 -2.347237 -2.041881

H -1.113945 -6.285618 -3.226134

```
H  -0.065855  -6.594898  -0.973095

H  -0.191360  -4.798883   0.719698

H  -1.783158  -2.219803   3.929353

H  -2.839564  -1.405358   2.620400

H  -2.360774  -1.783784   0.314014

H  -2.166957   1.370849  -1.579145

H  -1.602789  -0.231787  -1.984656

H  -0.376849  -3.220880   2.181356

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SCF Done: E(RB97D) = -4611.04748073 A.U. after 7 cycles

Reductive Elimination Transition State for Theoretical System Lacking an Olefin (Path C)

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 Cartesian coordinates (Angstroms):

---------------------------------

C   1.659   1.617  -1.931

C   0.408   1.157  -1.183

O  -4.018   3.502  -1.139
```

P	-3.643	1.889	-0.955
O	-5.094	1.257	-0.461
O	-3.216	1.393	-2.314
C	-6.098	1.039	-1.471
O	-2.744	1.715	0.273
O	-0.663	-2.835	-2.863
C	-1.190	-1.519	-2.602
C	-1.934	-1.364	-1.267
C	-1.069	-3.150	0.363
N	-1.135	-1.736	-0.088
C	2.972	-2.872	3.297
C	-0.213	-3.035	1.629
C	2.426	-1.476	2.927
C	-3.723	-3.043	-2.078
C	-0.787	-0.865	0.885
C	-3.300	-2.042	-1.185
N	-0.321	-1.587	1.933
C	-4.988	-3.637	-1.927
C	1.228	-1.073	3.763
C	-4.151	-1.658	-0.131

C	-0.087	-1.095	3.254
C	1.426	-0.636	5.087
C	-5.834	-3.244	-0.878
C	-5.410	-2.250	0.021
C	-1.196	-0.679	4.033
C	-3.224	-2.085	3.362
C	-2.612	-0.672	3.484
C	0.346	-0.230	5.879
C	-0.953	-0.249	5.348
C	-4.360	4.241	0.050
C	6.042	3.208	-0.194
C	6.074	1.149	-1.644
C	5.241	1.995	-0.668
O	4.067	2.465	-1.413
C	4.589	1.144	0.490
C	5.414	-0.071	0.915
C	4.201	1.983	1.718
B	3.031	1.589	-1.141
O	3.327	0.694	-0.122
O	1.397	-2.367	-1.633

```
C    3.527  -2.028  -2.704
C    3.396  -2.821  -0.326
C    2.757  -2.912  -1.710
B    0.628  -3.123  -2.506
O    1.262  -4.250  -2.996
C    2.504  -4.384  -2.230
C    3.596  -4.927  -3.154
C    2.220  -5.383  -1.095
H    0.552   0.096  -0.972
H   -0.497   1.347  -1.777
H   -6.961   0.590  -0.961
H   -5.728   0.352  -2.247
H   -6.400   1.993  -1.939
H   -0.379  -0.782  -2.642
H   -1.904  -1.294  -3.405
H   -2.102  -0.286  -1.186
H   -0.623  -3.793  -0.400
H   -2.089  -3.508   0.573
H    3.856  -3.116   2.686
H    2.213  -3.654   3.136
```

```
H    3.264  -2.901   4.359
H    0.839  -3.290   1.434
H   -0.583  -3.635   2.469
H    3.226  -0.737   3.096
H    2.175  -1.434   1.859
H   -3.066  -3.366  -2.884
H   -5.307  -4.412  -2.628
H   -3.826  -0.873   0.551
H    2.443  -0.604   5.484
H   -6.816  -3.708  -0.762
H   -6.065  -1.929   0.835
H   -4.261  -2.024   2.999
H   -3.221  -2.596   4.338
H   -2.657  -2.699   2.650
H   -2.629  -0.180   2.500
H   -3.241  -0.065   4.154
H    0.514   0.113   6.902
H   -1.797   0.082   5.957
H   -4.675   5.241  -0.280
H   -3.488   4.329   0.719
```

```
H  -5.187   3.754   0.594
H   5.417   3.899   0.387
H   6.447   3.746  -1.064
H   6.884   2.879   0.435
H   5.503   0.274  -1.987
H   7.003   0.802  -1.169
H   6.332   1.766  -2.518
H   4.895  -0.618   1.713
H   6.389   0.265   1.302
H   5.584  -0.755   0.075
H   3.639   2.880   1.420
H   5.095   2.298   2.276
H   3.566   1.376   2.379
H   3.494  -0.993  -2.339
H   3.068  -2.072  -3.703
H   4.578  -2.344  -2.782
H   3.449  -1.768  -0.026
H   4.417  -3.234  -0.353
H   2.818  -3.375   0.424
H   3.715  -4.292  -4.042
```

H	3.333	-5.944	-3.478
H	4.556	-4.970	-2.616
H	1.440	-4.998	-0.421
H	3.128	-5.578	-0.505
H	1.870	-6.329	-1.533
C	1.508	5.831	-1.667
C	1.599	4.695	-0.847
C	0.261	6.250	-2.158
C	0.442	3.966	-0.503
C	-0.896	5.526	-1.821
C	-0.804	4.397	-0.998
C	0.531	2.789	0.397
C	-0.342	2.844	1.575
C	-0.193	1.973	2.636
Cu	-0.735	1.076	0.702
H	2.414	6.383	-1.925
H	2.572	4.359	-0.489
H	0.192	7.130	-2.801
H	-1.872	5.831	-2.204
H	-1.696	3.831	-0.744

```
H  -0.894    2.000    3.468

H   0.733    1.421    2.801

H   1.549    2.475    0.635

H   1.774    0.909   -2.780

H   1.528    2.604   -2.395

H  -1.211    3.504    1.535

---------------------------------
```

SCF Done: E(RB97D) = -4611.03331812 A.U. after 1 cycles

	1	2	3
	A	A	A
Frequencies --	-223.4210	20.9949	23.2773
Red. masses --	6.8501	5.3150	5.0565

Zero-point correction= 1.071518 (Hartree/Particle)

Thermal correction to Energy= 1.137040

Thermal correction to Enthalpy= 1.137985

Thermal correction to Gibbs Free Energy= 0.972161

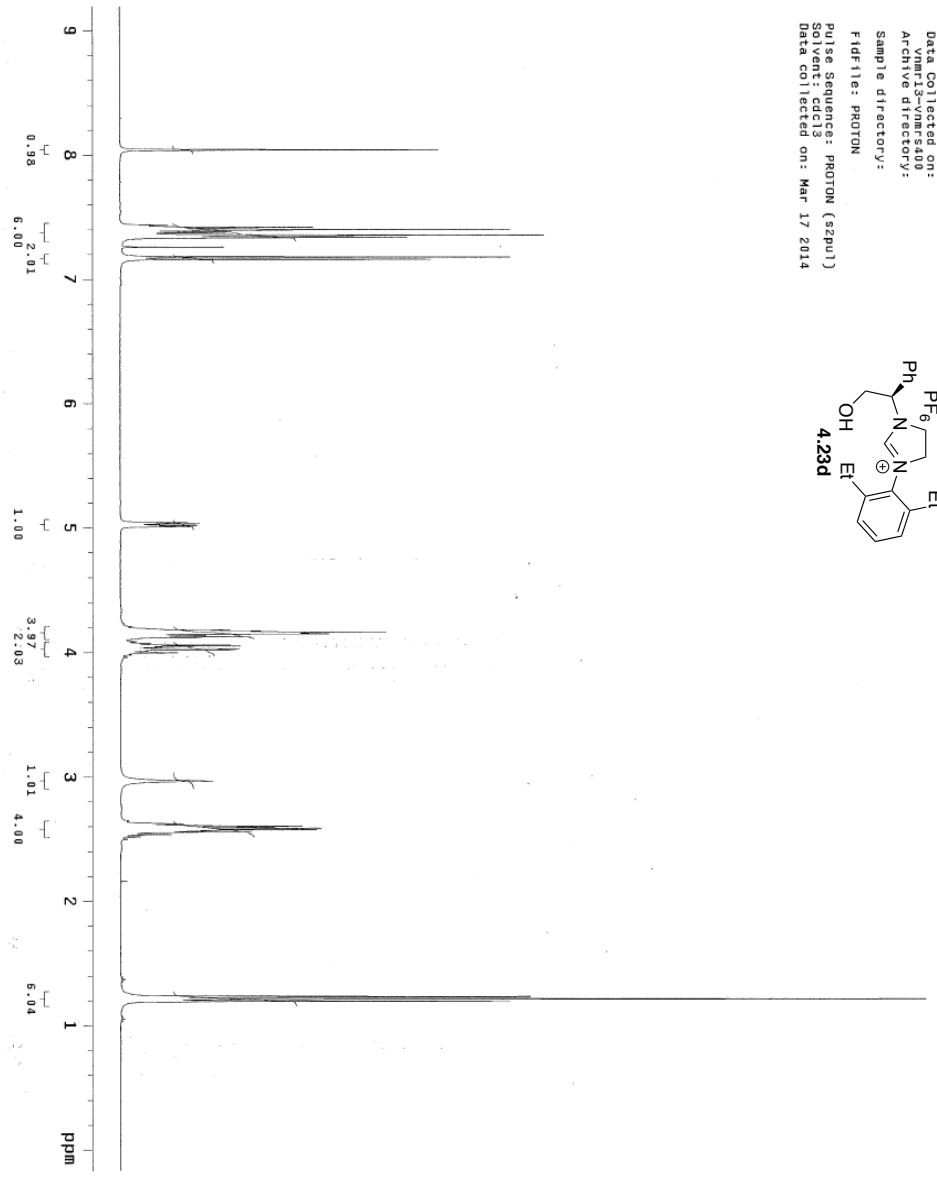
Sum of electronic and zero-point Energies= -4609.961801

Sum of electronic and thermal Energies= -4609.896278

Sum of electronic and thermal Enthalpies= -4609.895333

Sum of electronic and thermal Free Energies= -4610.061157

Item	Value	Threshold	Converged?
Maximum Force	0.000061	0.000450	YES
RMS Force	0.000006	0.000300	YES

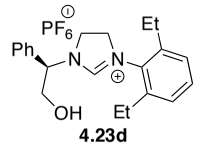

Sample Name:
FM-VI-185
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 17 2014
Ph
PF6
N
OH
Et
N
Et
4.23d
9
8
7
6
5
4
3
2
1
ppm
0.98
6.00
2.01
1.00
3.97
2.03
1.01
4.00
6.04

Sample Name:
FM-VI-185
Data Collected on:
vnmr13-vnmrs400
Archive directory:

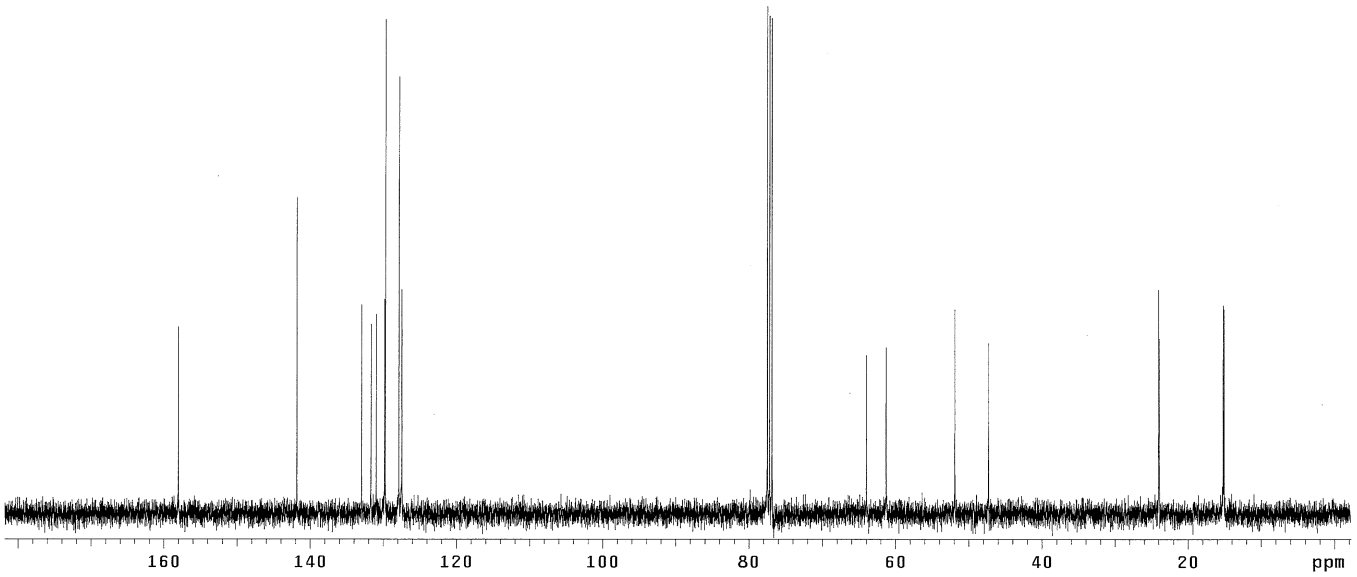
Sample directory:

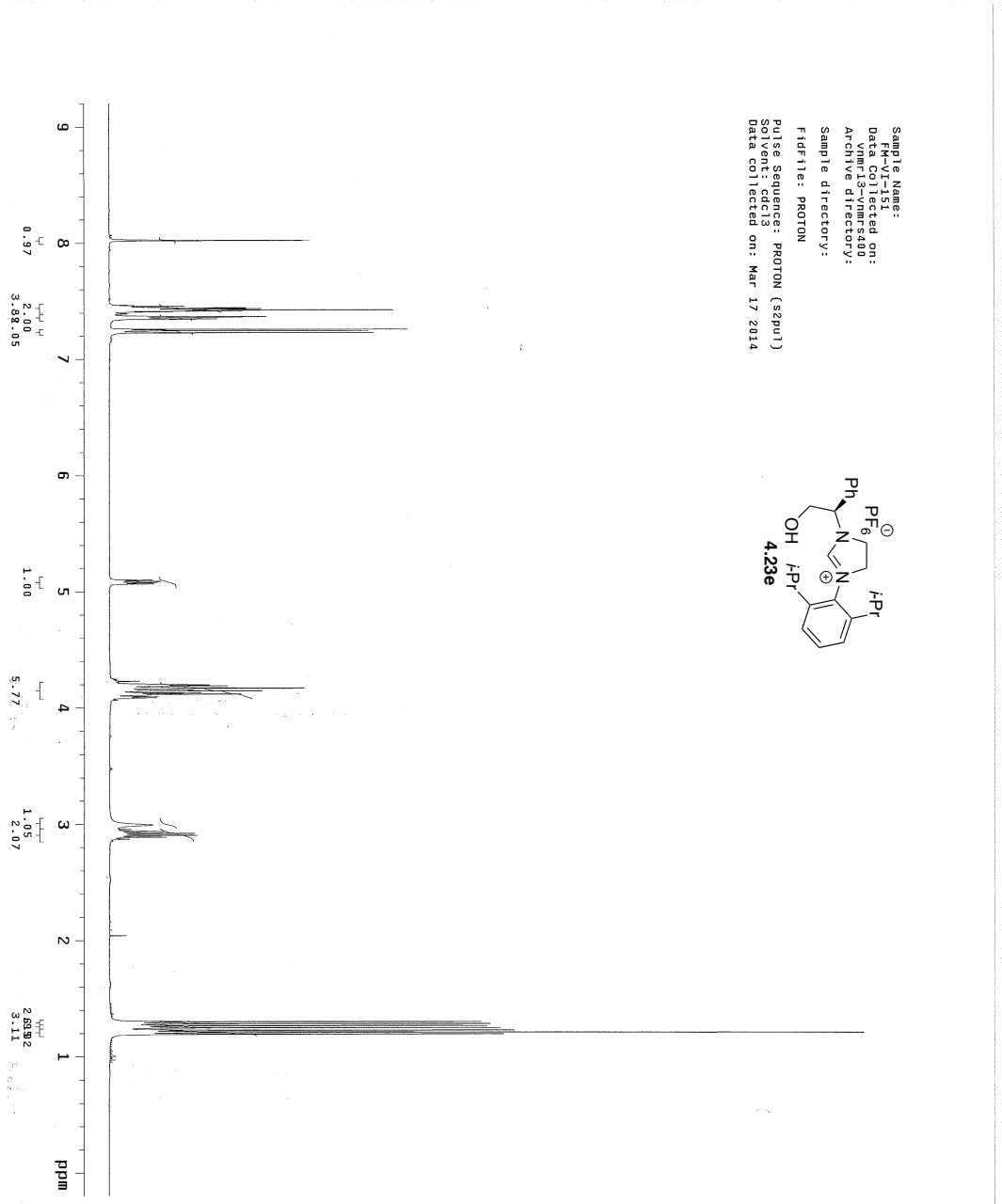
FidFile: FM-VI-185-CNMR

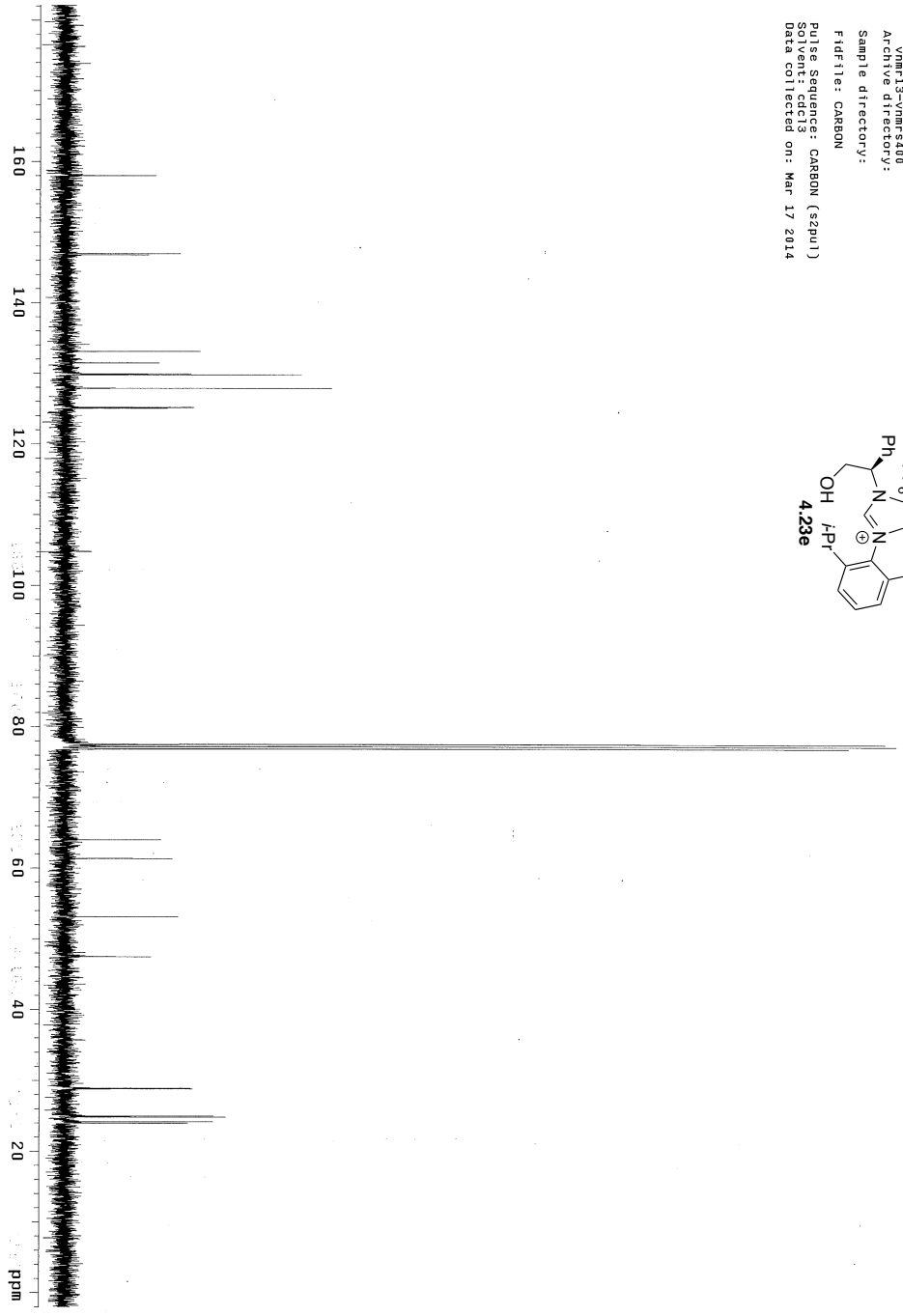
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 17 2014

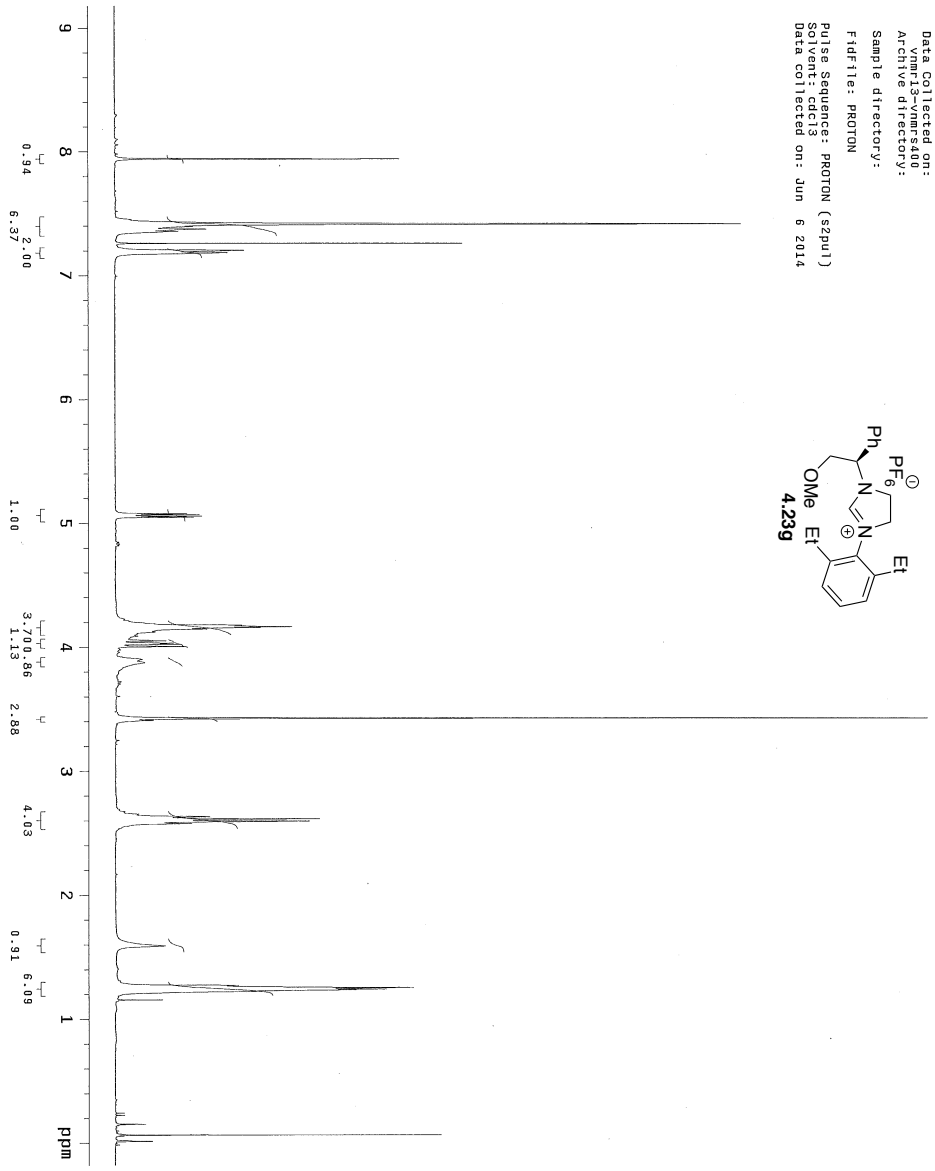


4.23d




Sample Name:
FM-VI-151
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 17 2014
Ph
PF6
N
N
OH
i-Pr
i-Pr
4.23e
9
8
7
6
5
4
3
2
1
ppm
0.97
2.00
3.88.05
1.00
5.77
1.05
2.07
2.69.92
3.11


Sample Name:
FM-VI-151
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: CARBON
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 17 2014
Ph
PF6
N
N
OH
i-Pr
i-Pr
4.23e
160
140
120
100
80
60
40
20
ppm

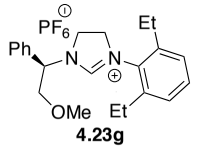

Sample Name:
FM-VII-57
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 6 2014
Ph
PF6
N
N
OMe
Et
Et
4.23g
9
8
7
6
5
4
3
2
1
ppm
0.94
2.00
6.37
1.00
3.70
0.86
1.13
2.88
4.03
0.91
6.09

Sample Name:
FM-VII-57
Data Collected on:
vnmr13-vnmrs400
Archive directory:

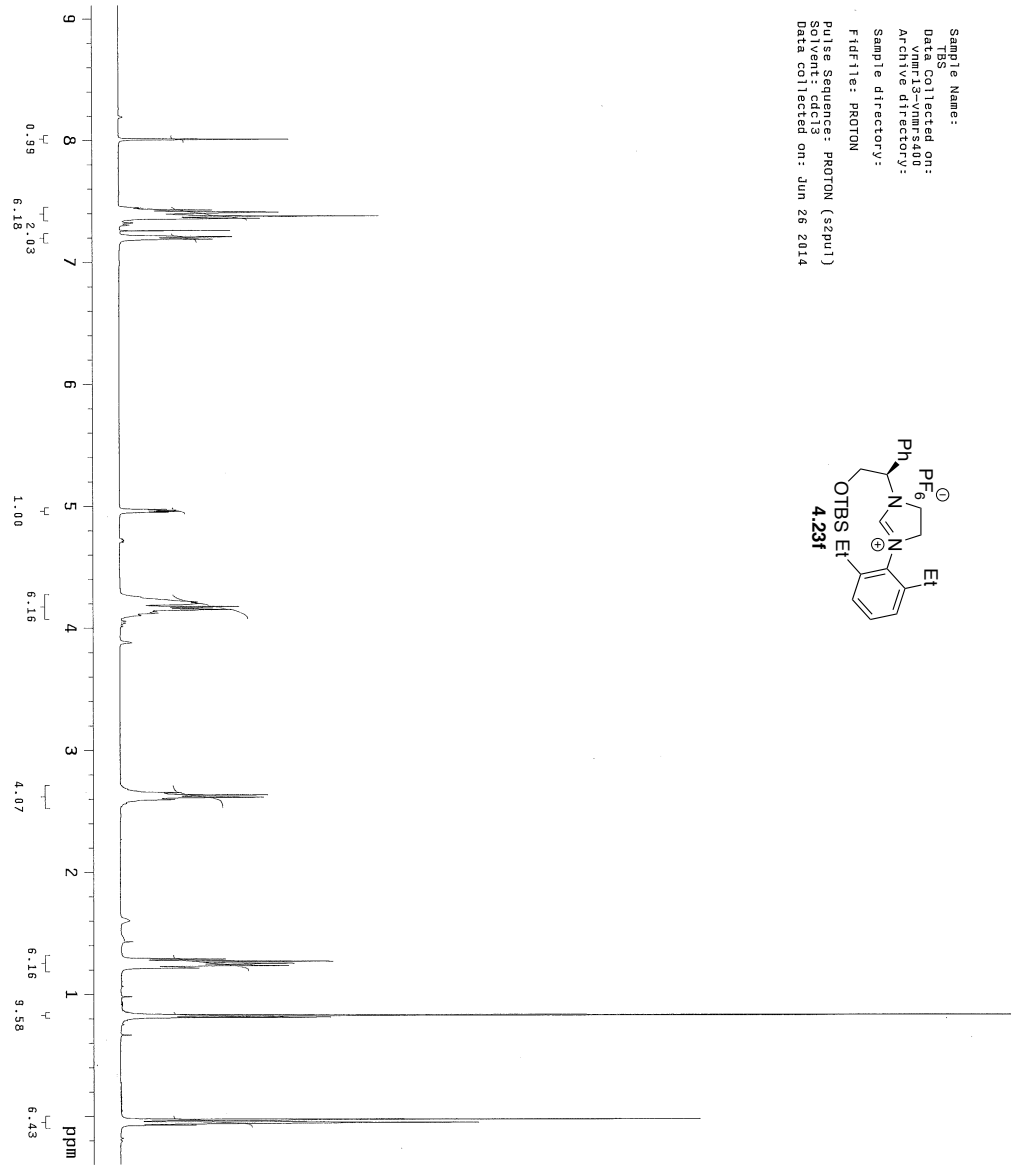
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 6 2014



4.23g

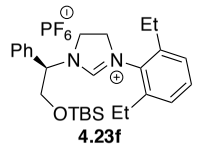

Sample Name:
TBS
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 26 2014
Ph
PF6
N
N
OTBS Et
Et
4.23f
9
8
7
6
5
4
3
2
1
ppm
0.99
2.03
6.18
1.00
6.16
4.07
6.16
9.58
6.43

Sample Name:
TBS
Data Collected on:
vnmr13-vnmrs400
Archive directory:

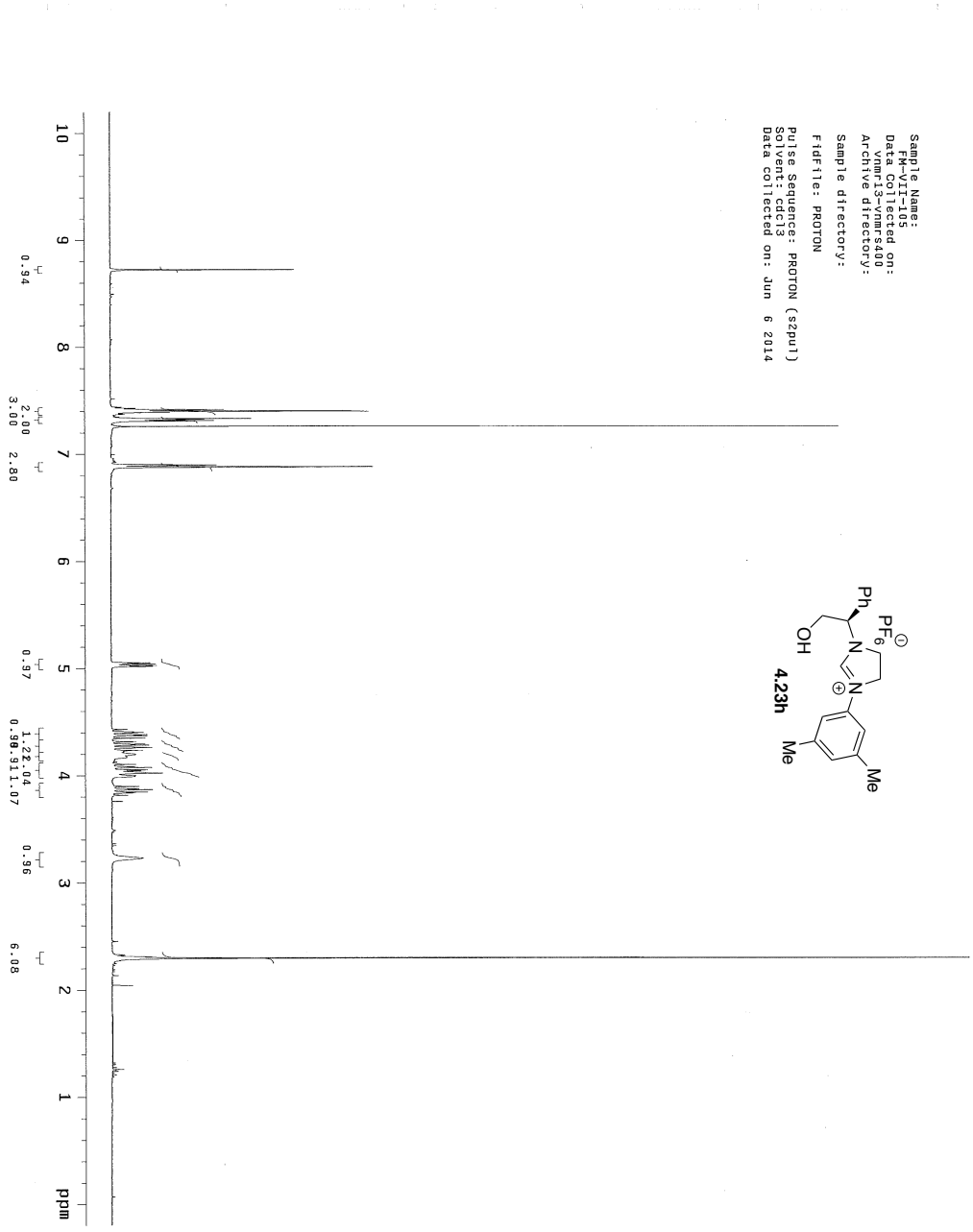
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 26 2014



4.23f

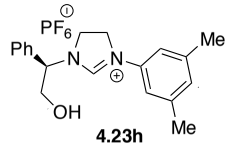

Sample Name:
FM-VII-105
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 6 2014
Ph
PF6
N
OH
N
Me
Me
4.23h
10
9
8
7
6
5
4
3
2
1
ppm
0.94
2.00
3.00
2.80
0.97
1.22
1.04
0.98
1.11
1.07
0.96
6.08

Sample Name:
FM-VII-105
Data Collected on:
vnmr13-vnmrs400
Archive directory:

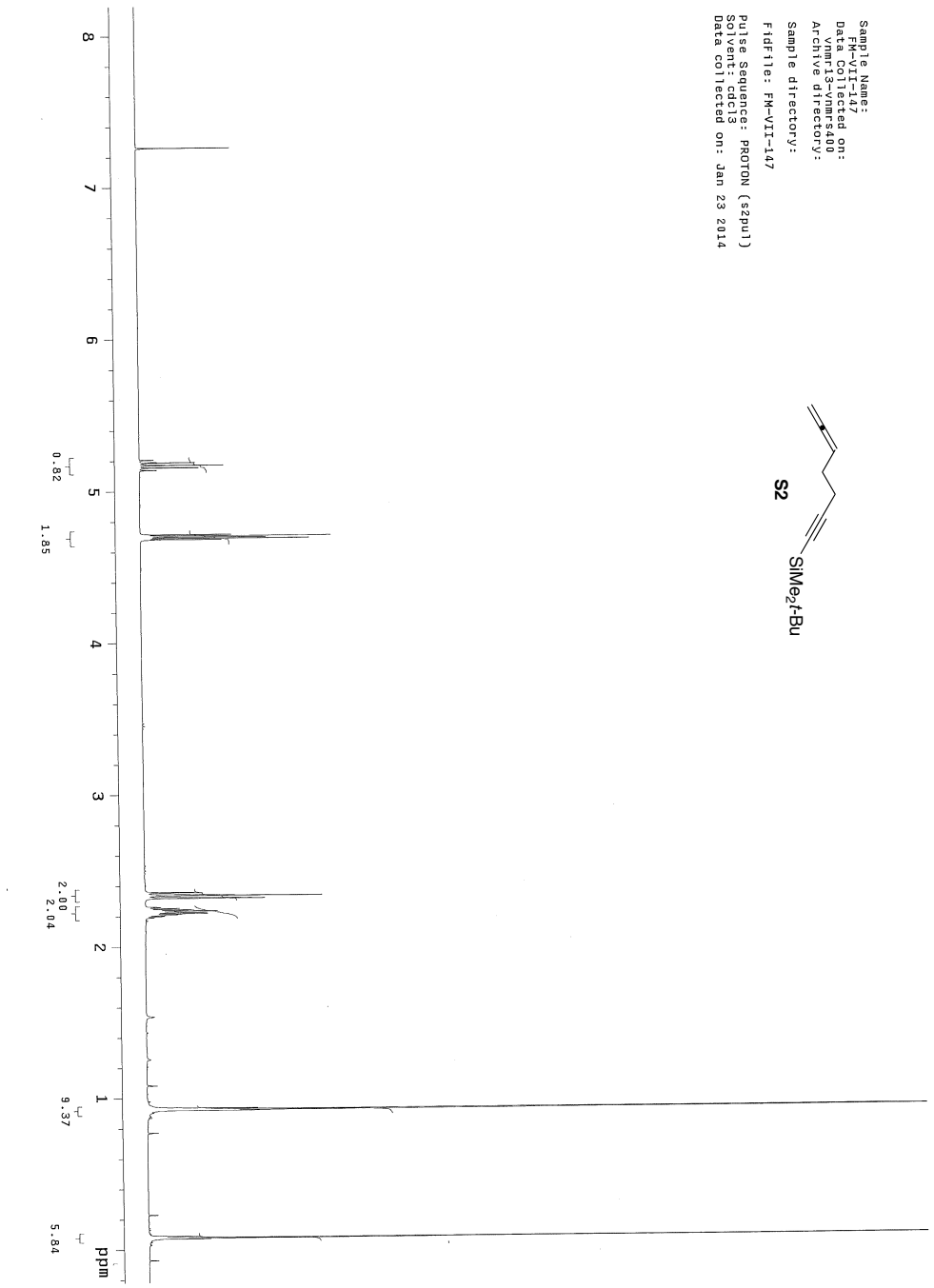
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 6 2014



4.23h

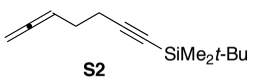

Sample Name:
FM-VII-147
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: FM-VII-147
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 23 2014
S2
SiMe2t-Bu
8
7
6
5
4
3
2
1
ppm
0.82
1.85
2.00
2.04
9.37
5.84

Sample Name:
FM-VII-147
Data Collected on:
vnmr13-vnmrs400
Archive directory:

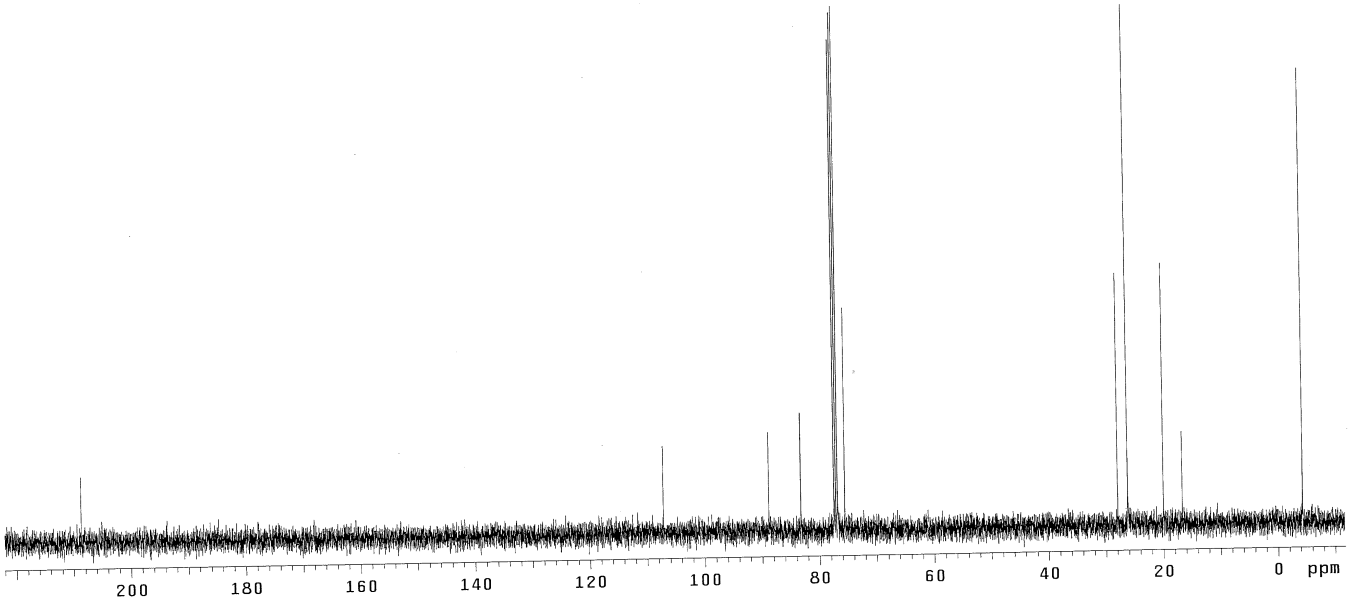
Sample directory:

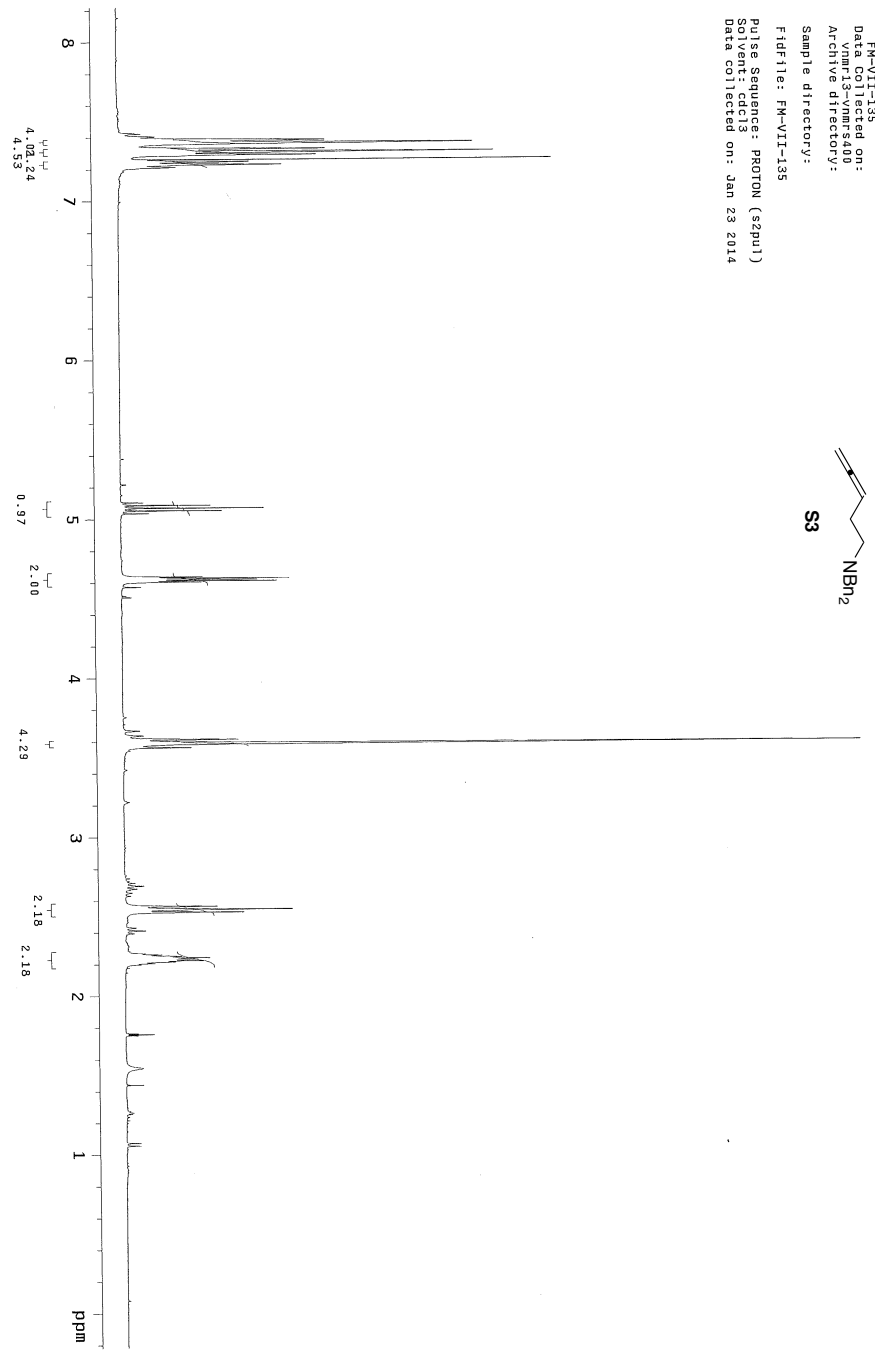
FidFile: FM-VII-147-CNMR

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 23 2014



S2



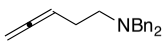

Sample Name:
FM-VII-135
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: FM-VII-135
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 23 2014
S3
NBn2
8
7
6
5
4
3
2
1
ppm
4.02
4.24
4.53
0.97
2.00
4.29
2.18
2.18

Sample Name:
FM-VII-135
Data Collected on:
vnmr13-vnmrs400
Archive directory:

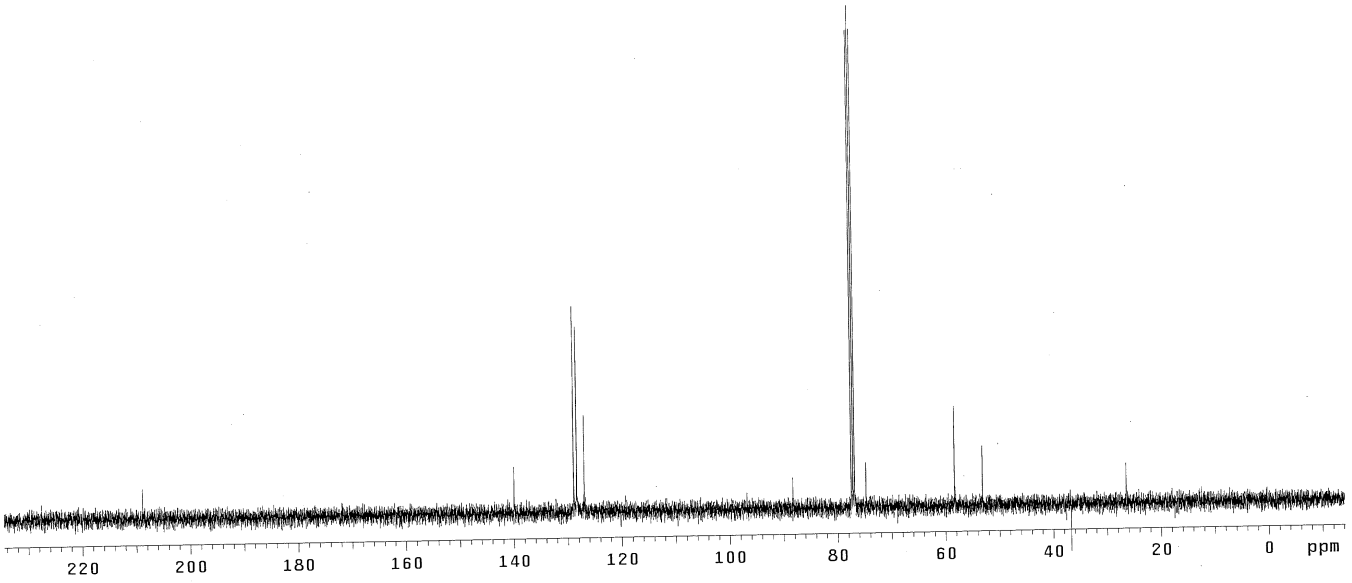
Sample directory:

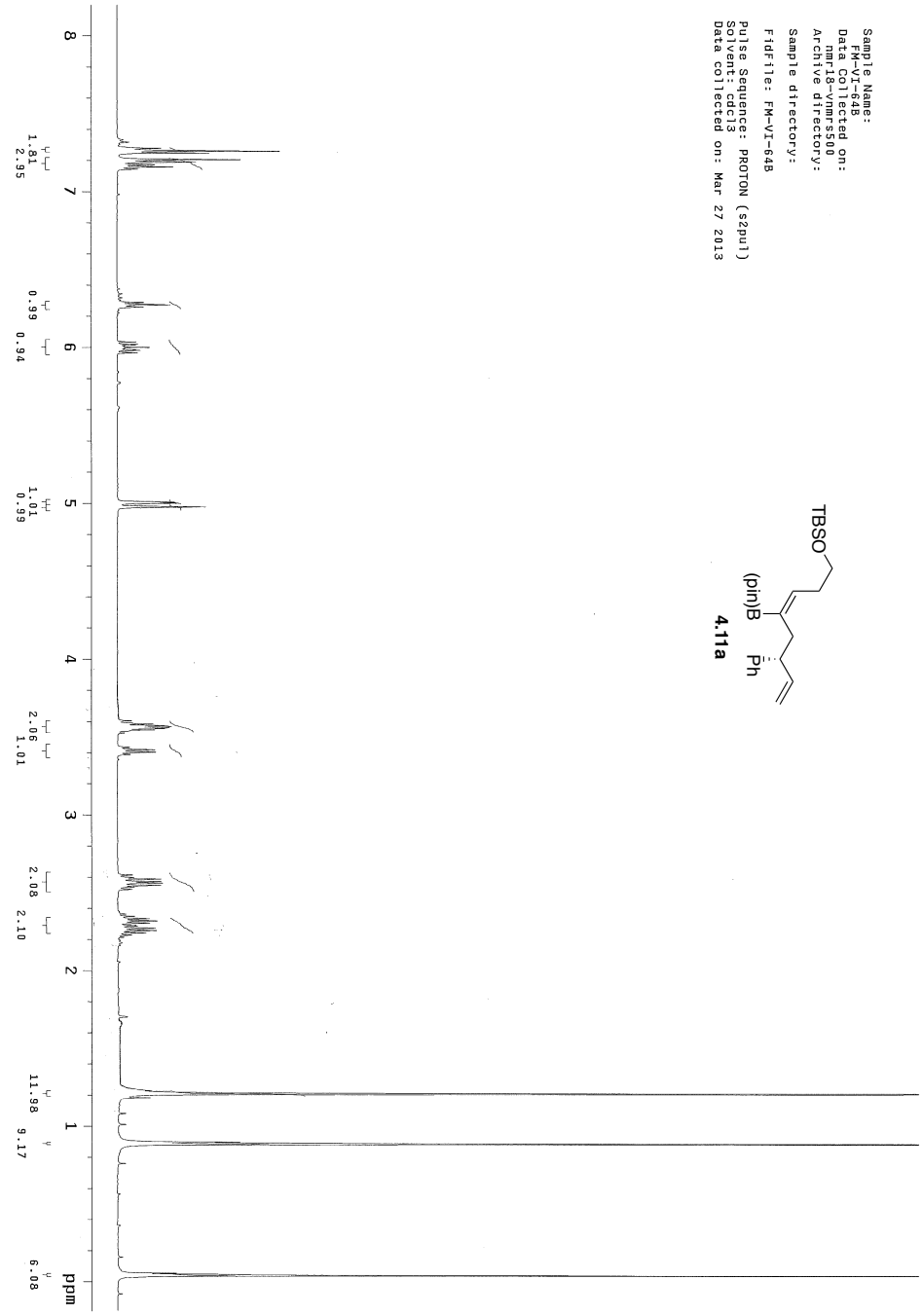
FidFile: FM-VII-135-CNMR

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 23 2014



S3



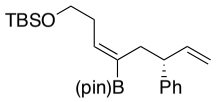

Sample Name:
FM-VI-64B
Data Collected on:
nmr18-vnmrs500
Archive directory:
Sample directory:
FidFile: FM-VI-64B
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 27 2013
TBSO
(pin)B
Ph
4.11a
8
7
6
5
4
3
2
1
ppm
1.81
2.95
0.99
0.94
1.01
0.99
2.06
1.01
2.08
2.10
11.98
9.17
6.08

Sample Name:
FM-VI-64B
Data Collected on:
nmr18-vnmrs500
Archive directory:

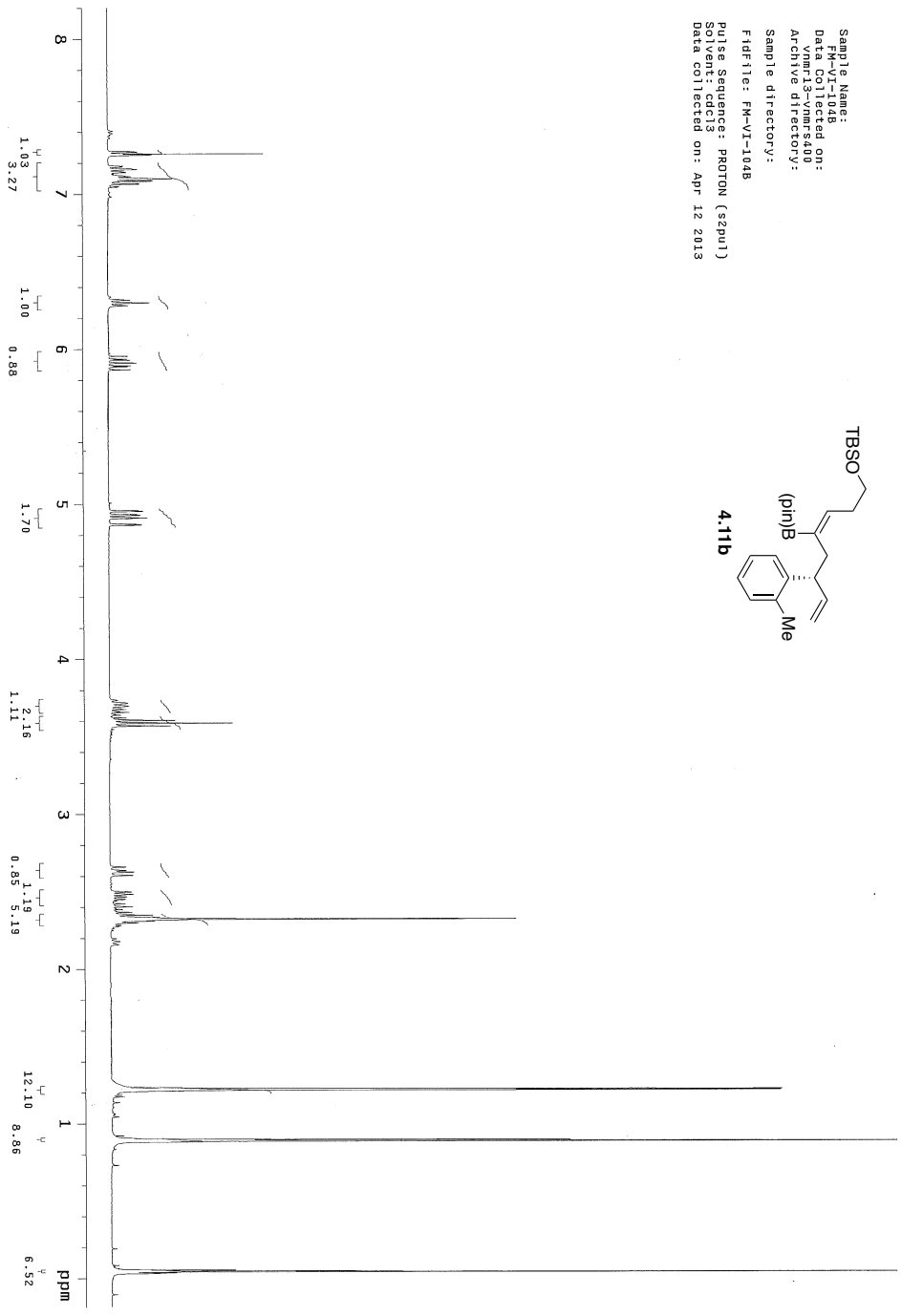
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 27 2013



4.11a

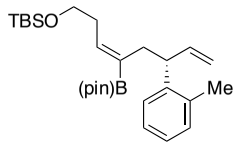

Sample Name:
FM-VI-104B
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: FM-VI-104B
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 12 2013
TBSO
(pin)B
Me
4.11b
ppm

Sample Name:
FM-VI-104B
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 12 2013



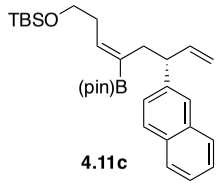
4.11b

Sample Name:
FM-VI-105A
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: FM-VI-105A

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 12 2013



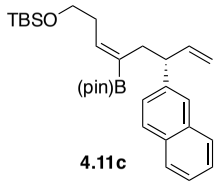
4.11c

Sample Name:
FM-VI-105B
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 12 2013



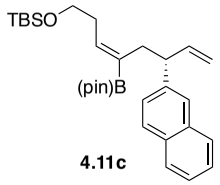
4.11c

Sample Name:
FM-VI-105B
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 12 2013



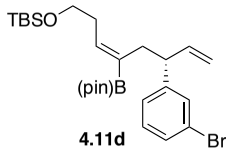
4.11c

Sample Name:
FM-VII-154
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: FM-VII-154A

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 29 2014



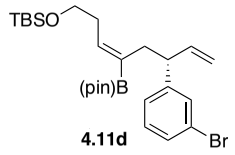
4.11d

Sample Name:
FM-VII-154
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 29 2014



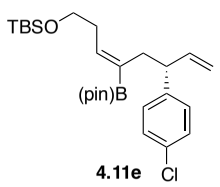
4.11d

Sample Name:
FM-VI-97A
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: FM-VI-97B

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 10 2013



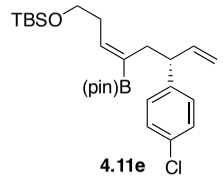
4.11e

Sample Name:
FM-VI-97A
Data Collected on:
vnmr13-vnmrs400
Archive directory:

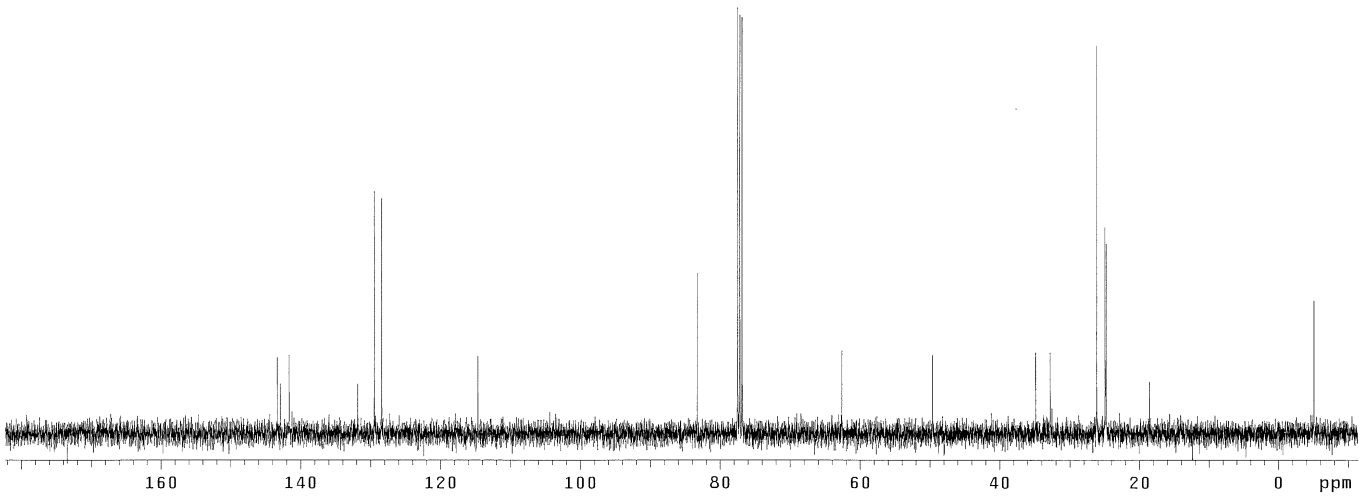
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 10 2013



4.11e

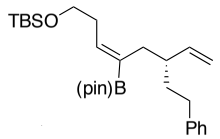


Sample Name:
FM-VI-103A
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: FM-VI-103A

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 12 2013



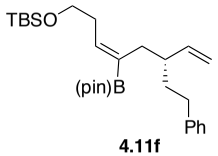
4.11f

Sample Name:
FM-VI-103A
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 12 2013



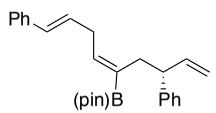
4.11f

Sample Name:
FM-VII-77A
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: FM-VII-77A

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Dec 20 2013



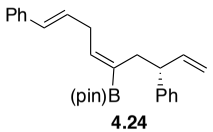
4.24

Sample Name:
FM-VII-77A
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Dec 20 2013



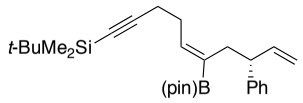
4.24

Sample Name:
FM-VII-149
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: FM-VII-149

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 27 2014



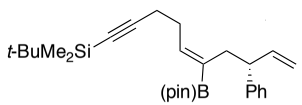
4.25

Sample Name:
FM-VII-149
Data Collected on:
vnmr13-vnmrs400
Archive directory:

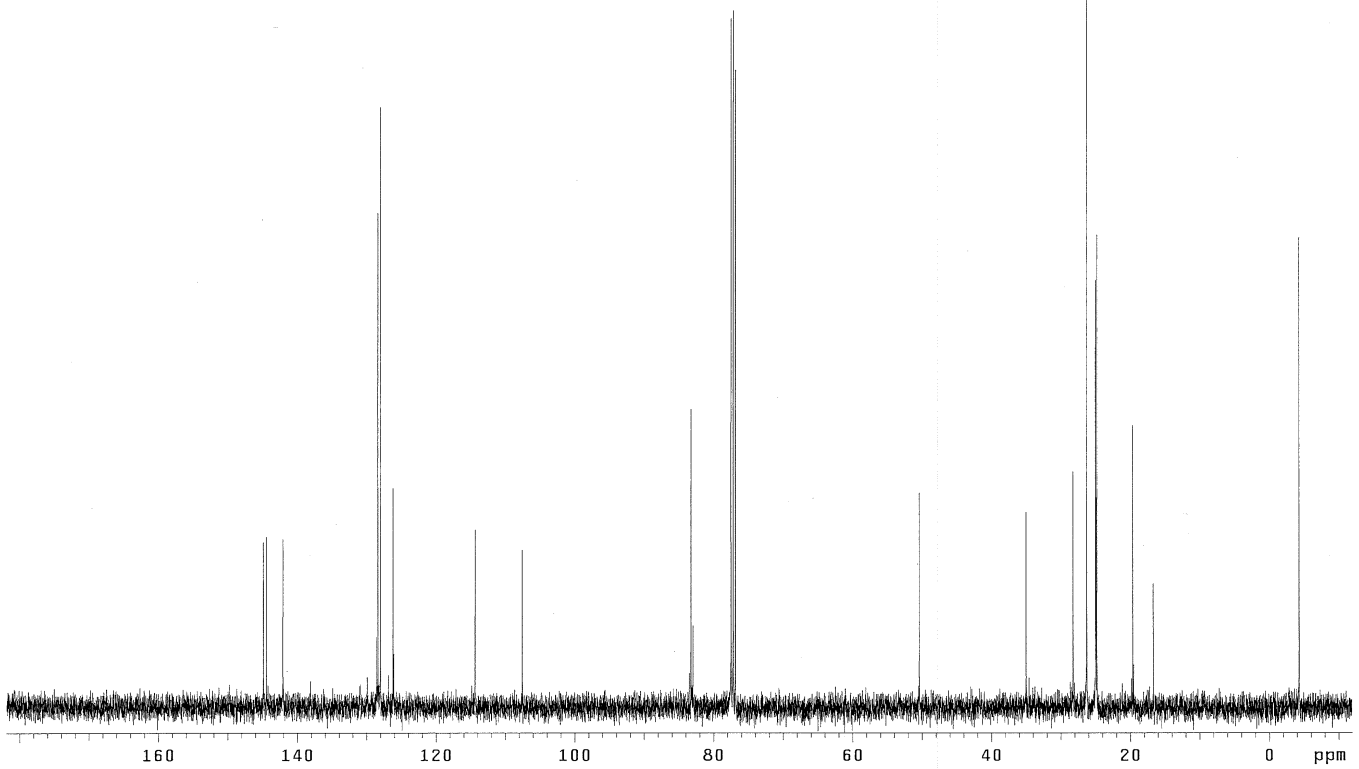
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 27 2014



4.25

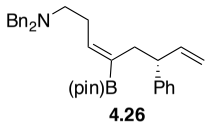


Sample Name:
FM-VII-151
Data Collected on:
vnmr13-vnmrs400
Archive directory:

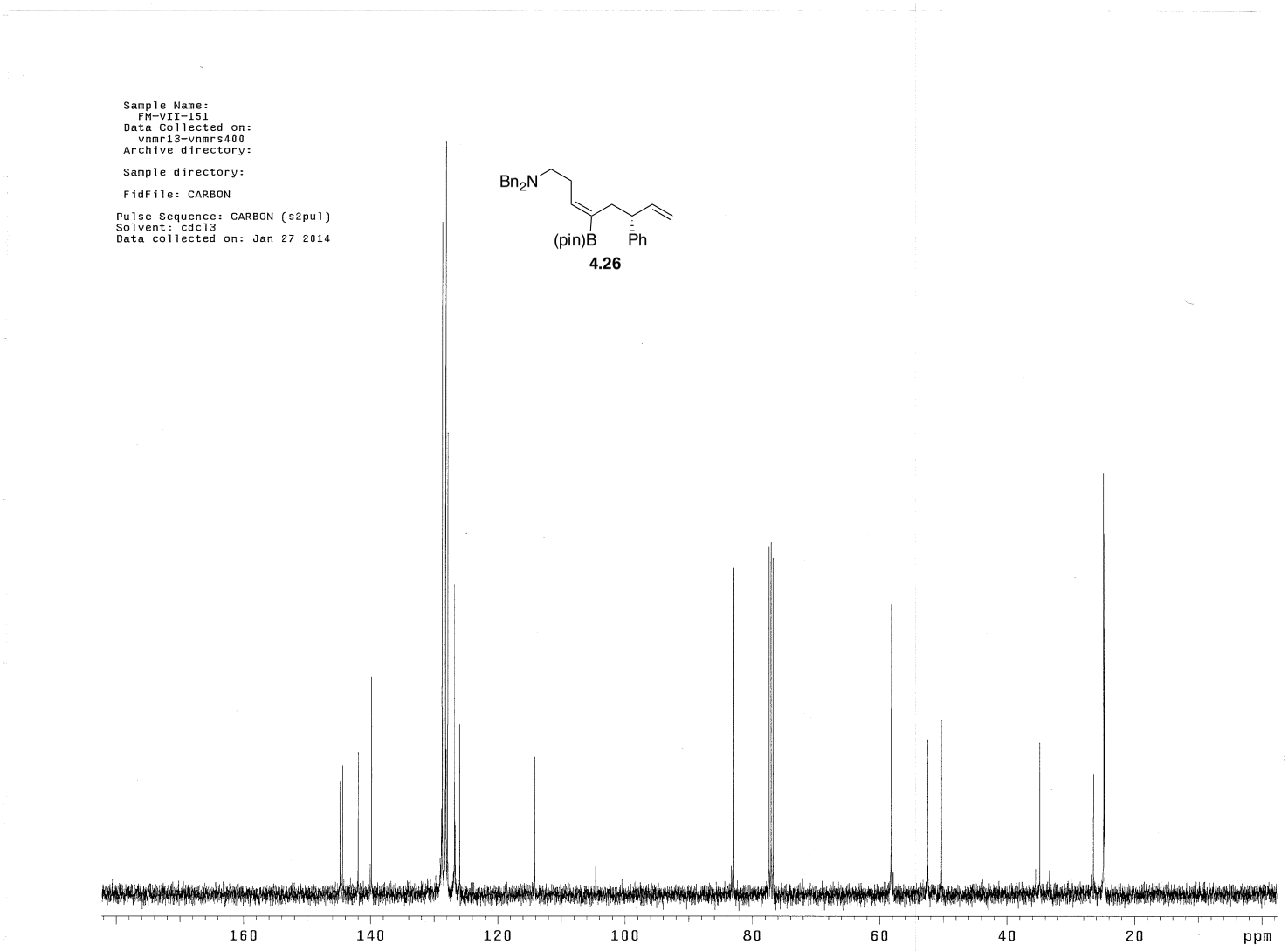
Sample directory:

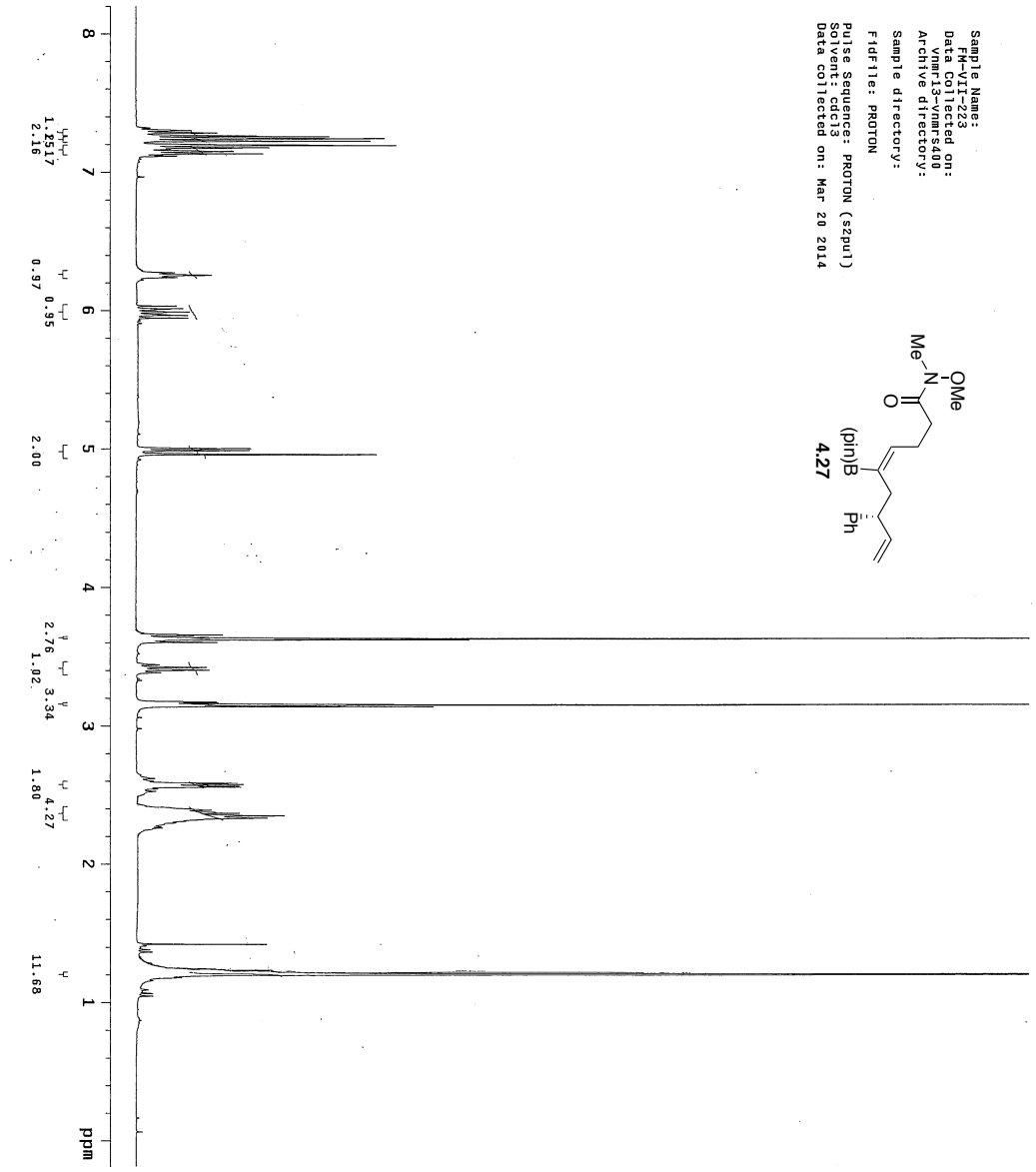
FidFile: FM-VII-151

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 27 2014



4.26


Sample Name:
FM-VII-151
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: CARBON
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 27 2014
Bn2N
(pin)B
Ph
4.26
160
140
120
100
80
60
40
20
ppm

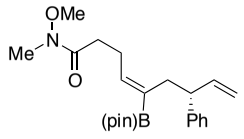

Sample Name:
FM-VII-223
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 20 2014
OMe
Me
N
O
(pin)B
Ph
4.27
8
7
6
5
4
3
2
1
ppm
1.25
2.16
17
0.97
0.95
2.00
2.76
1.02
3.34
1.80
4.27
11.68

Sample Name:
FM-VII-223
Data Collected on:
vnmr13-vnmrs400
Archive directory:

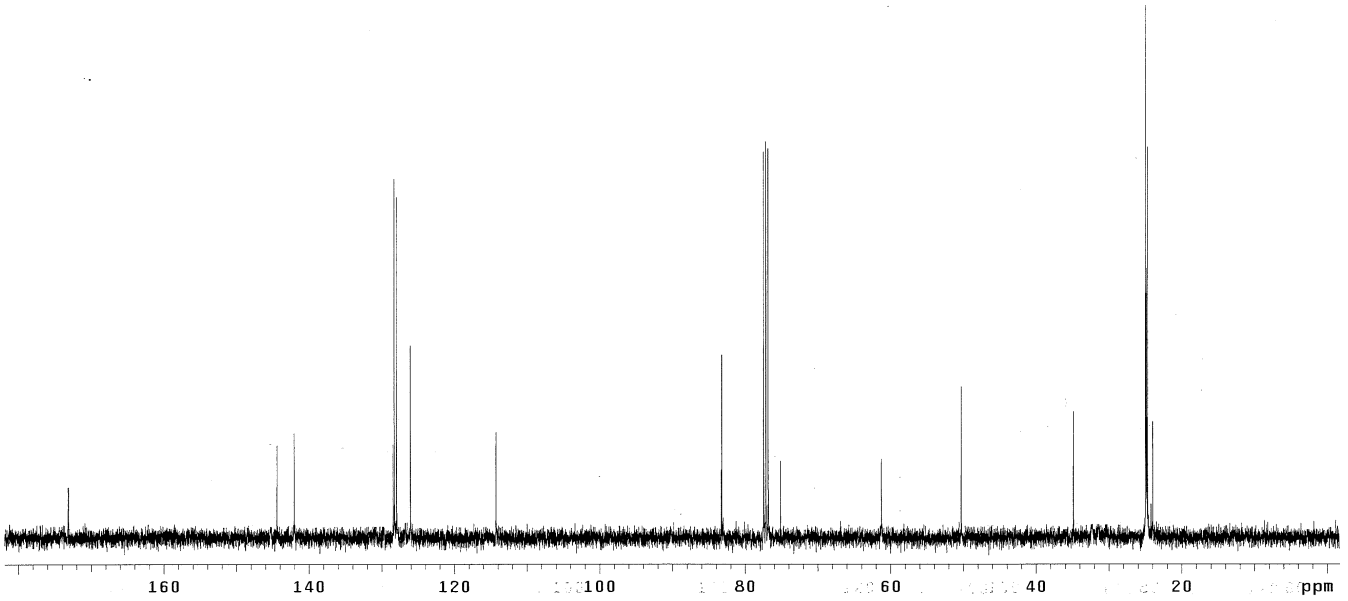
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 20 2014



4.27

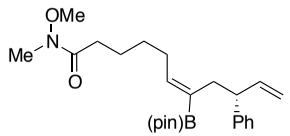


Sample Name:
FM-VII-225
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: FM-VII-225

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 14 2014



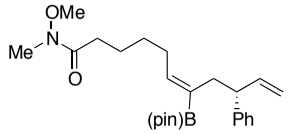
4.29

Sample Name:
FM-VII-225
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 14 2014



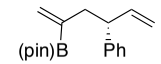
4.29

Sample Name:
FM-VI-176
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 17 2014



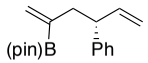
4.30

Sample Name:
FM-VI-176
Data Collected on:
vnmr13-vnmrs400
Archive directory:

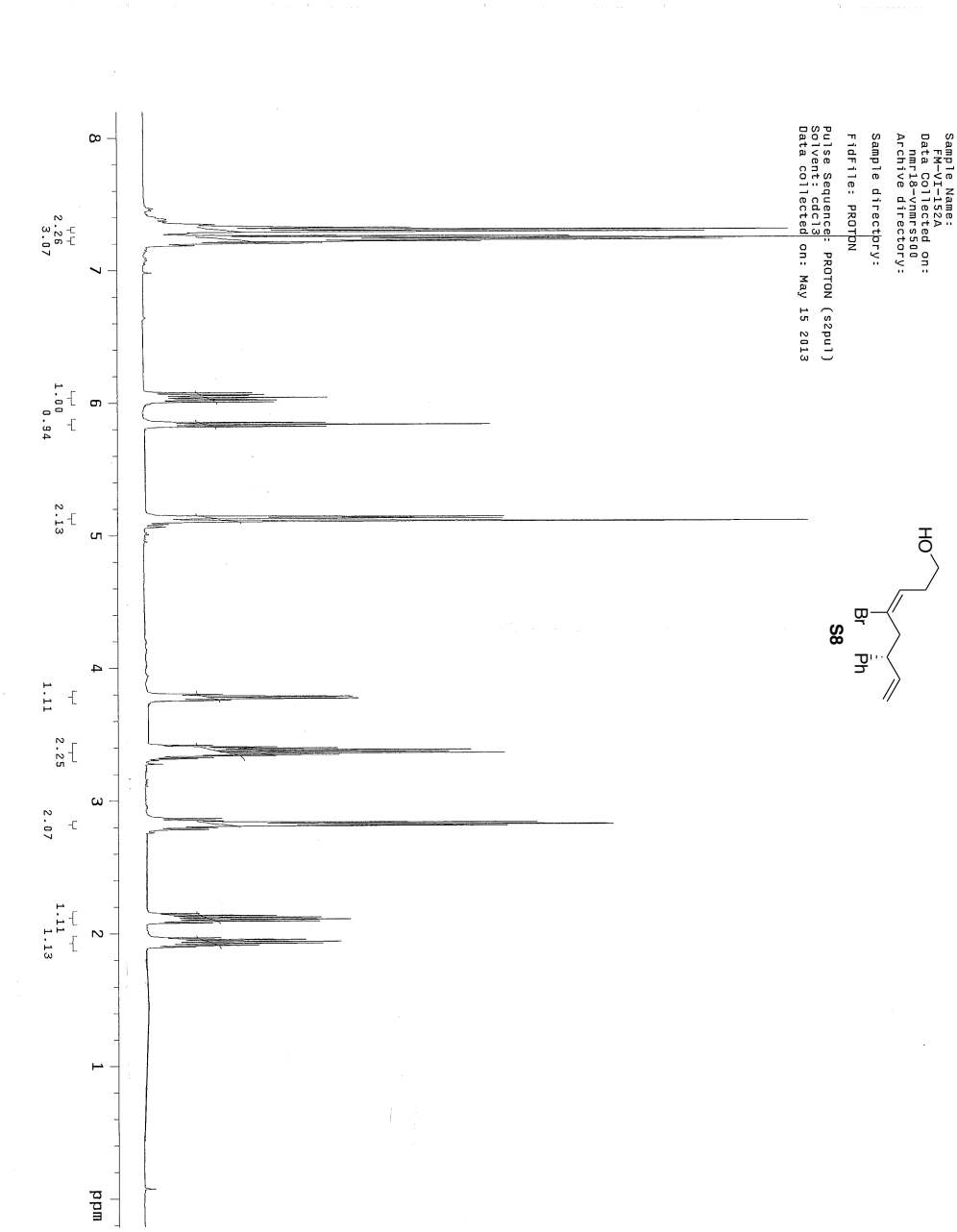
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 17 2014



4.30

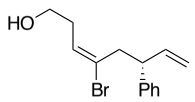

Sample Name:
FM-VI-152A
Data Collected on:
nmr18-vnmrs500
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 15 2013
HO
Br
Ph
S8
8
7
6
5
4
3
2
1
ppm
2.26
3.07
1.00
0.94
2.13
1.11
2.25
2.07
1.11
1.13

Sample Name:
FM-VI-152A
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 15 2013



S8

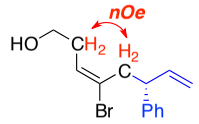
Selective band center: 2.80 (ppm); width: 50.1 (Hz)

Sample Name:
FM-VI-152B-NOE
Data Collected on:
vnmr13-vnmrs400
Archive directory:

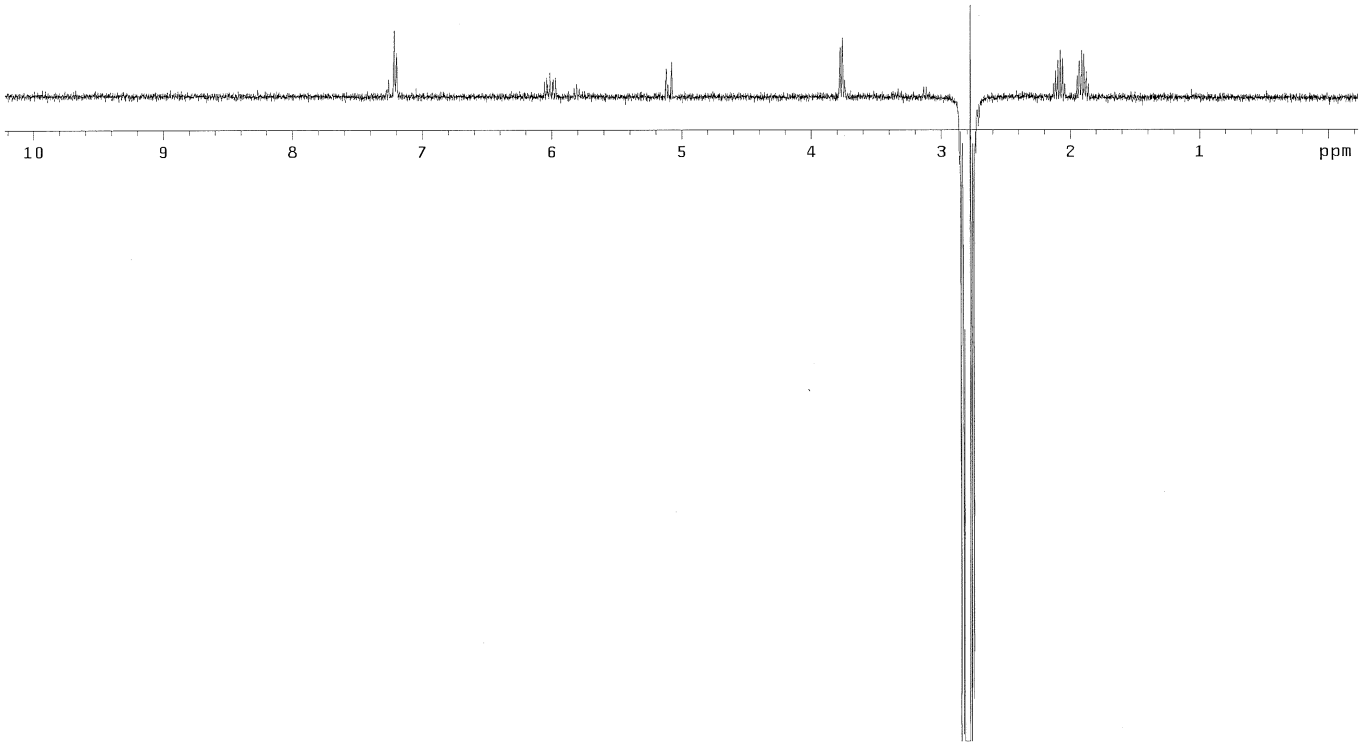
Sample directory:

FidFile: NOESY1D

Pulse Sequence: NOESY1D
Solvent: cdcl3
Data collected on: May 16 2013



S8

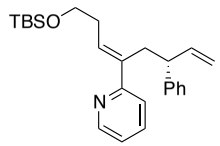


Sample Name:
FM-VII-110
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: FM-VII-110

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 6 2014



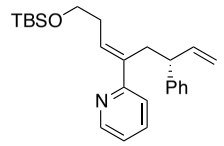
4.31

Sample Name:
FM-VII-110
Data Collected on:
vnmr13-vnmrs400
Archive directory:

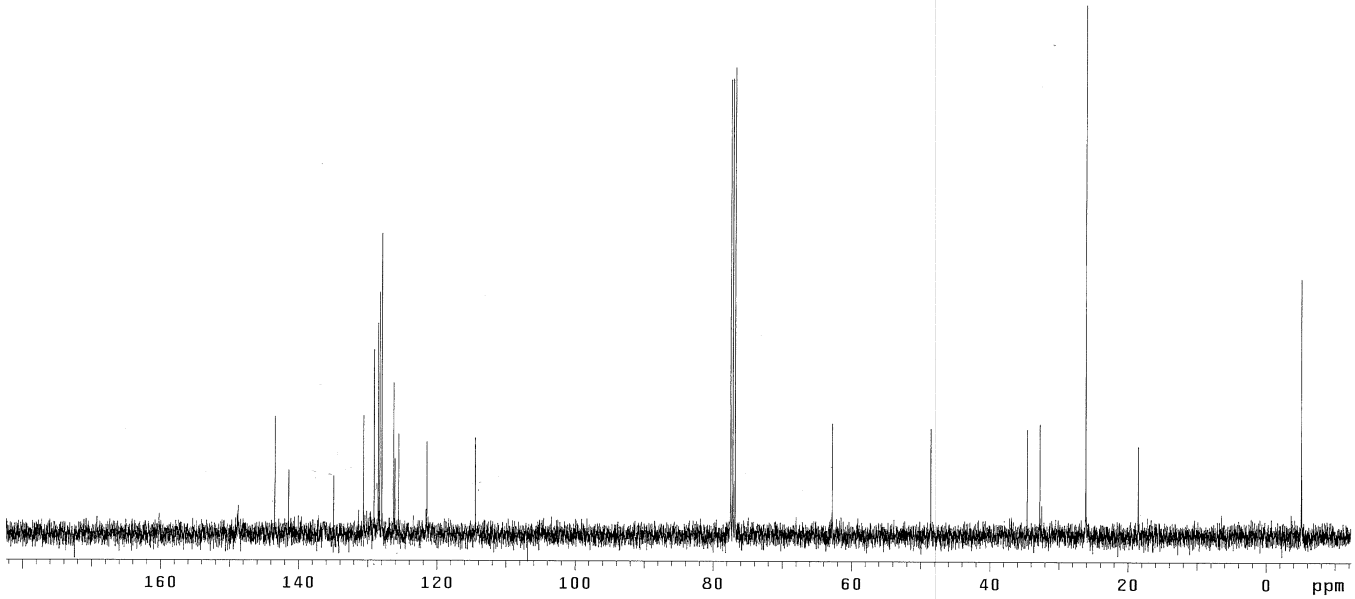
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 6 2014



4.31

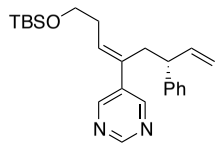


Sample Name:
FM-VII-111
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: FM-VII-111

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 6 2014



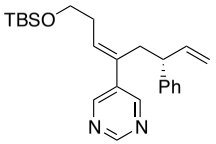
4.32

Sample Name:
FM-VII-111
Data Collected on:
vnmr13-vnmrs400
Archive directory:

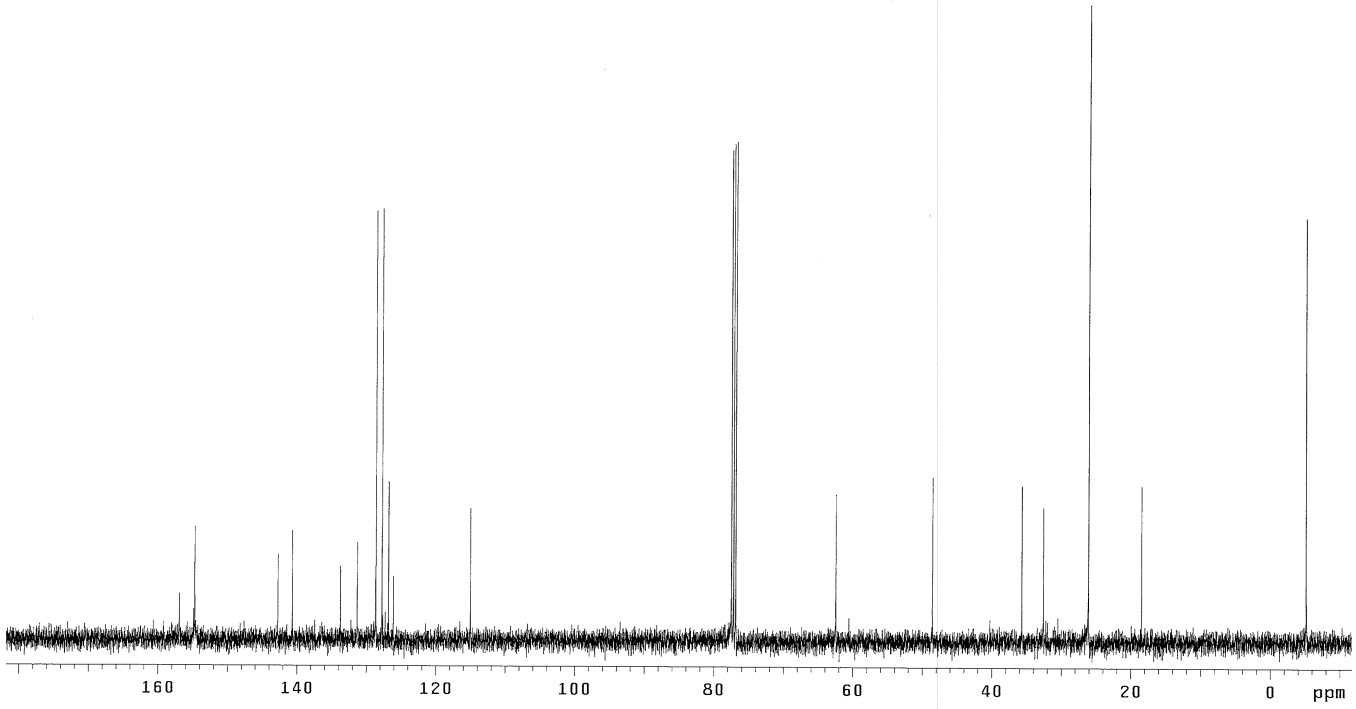
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 6 2014



4.32

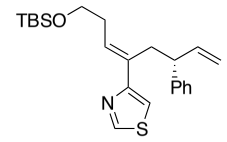


Sample Name:
FM-VII-107
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: FM-VII-107

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 6 2014



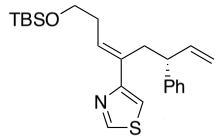
4.33

Sample Name:
FM-VII-107
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 6 2014



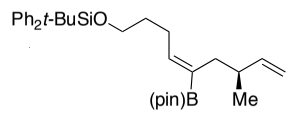
4.33

Sample Name:
FM-VI-173A
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: FM-VI-173A

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 30 2013



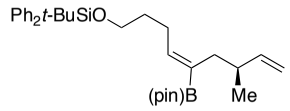
4.37

Sample Name:
FM-VI-173A
Data Collected on:
vnmr13-vnmrs400
Archive directory:

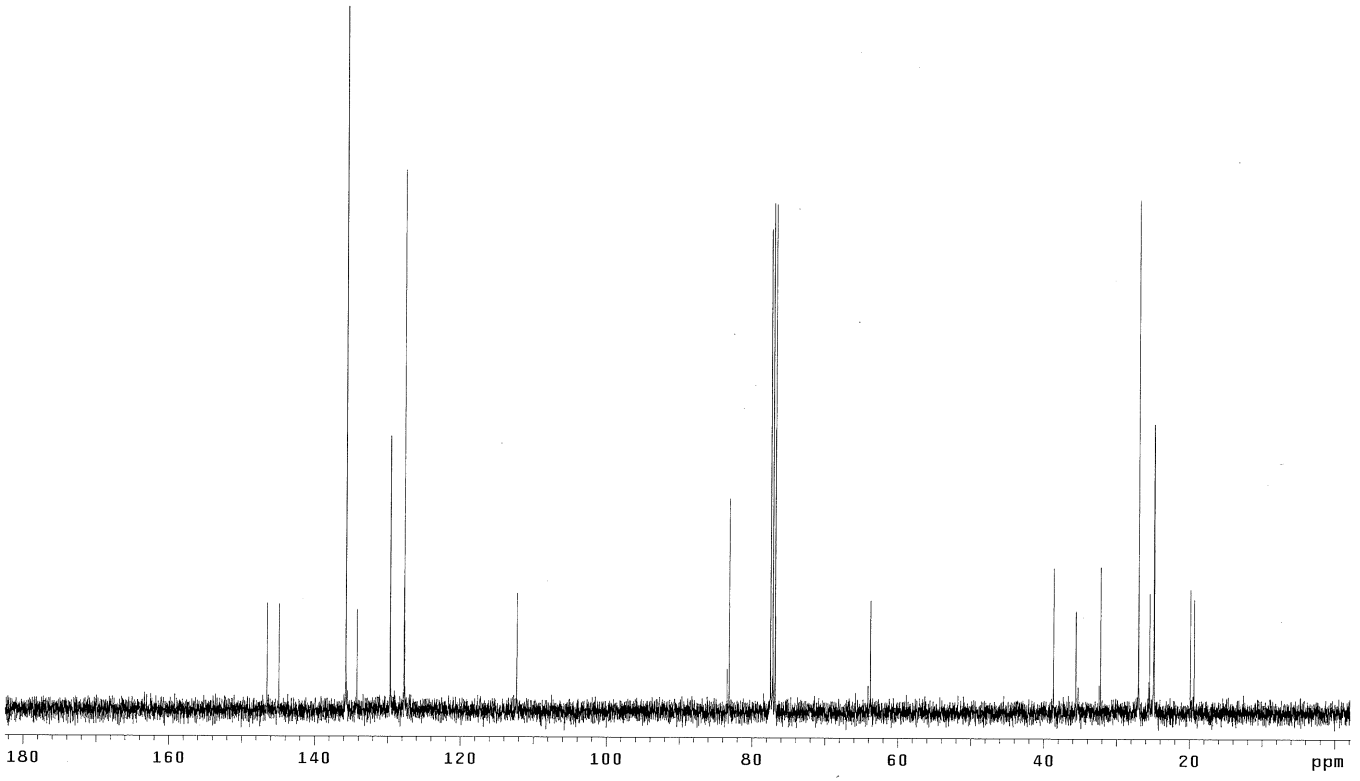
Sample directory:

FidFile: FM-VI-173A-CNMR

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 30 2013



4.37

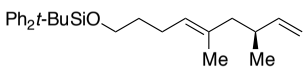


Sample Name:
FM-VI-197
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 27 2013



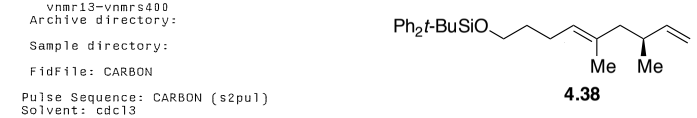
4.38

Sample Name:
FM-VI-197
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 27 2013



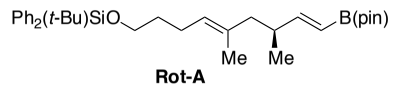
4.38

Sample Name:
FM-VI-209
Data Collected on:
vnmr13-vnmrs400
Archive directory:

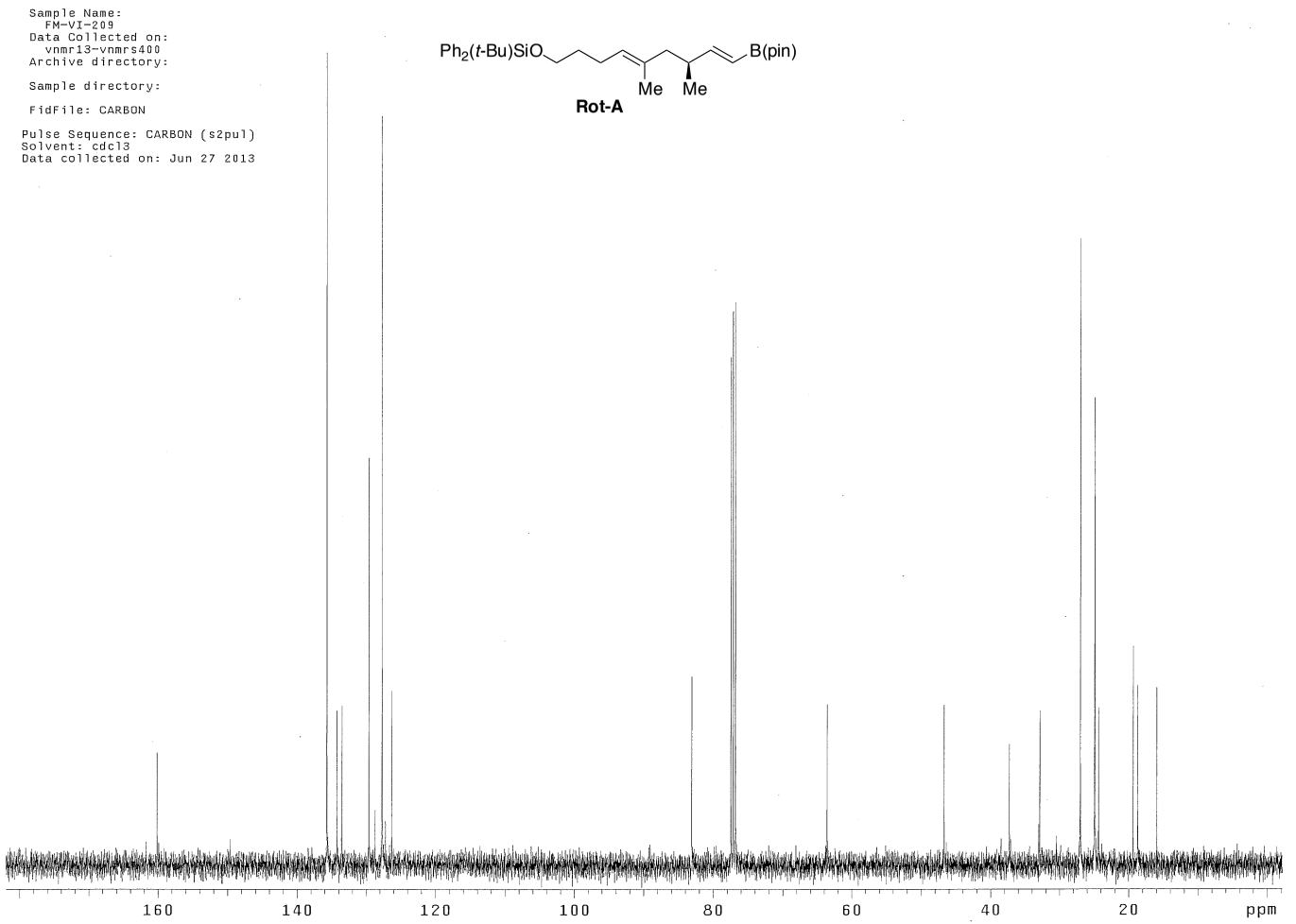
Sample directory:

FidFile: FM-VI-209

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 26 2013



Rot-A

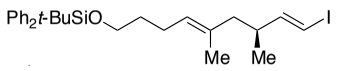

Sample Name:
FM-VI-209
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: CARBON
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 27 2013
Ph2(t-Bu)SiO
B(pin)
Me
Me
Rot-A
160
140
120
100
80
60
40
20
ppm

Sample Name:
FM-VI-239
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: FM-VI-239

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 12 2013



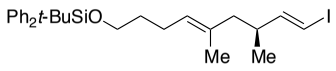
4.40

Sample Name:
FM-VI-239
Data Collected on:
vnmr13-vnmrs400
Archive directory:

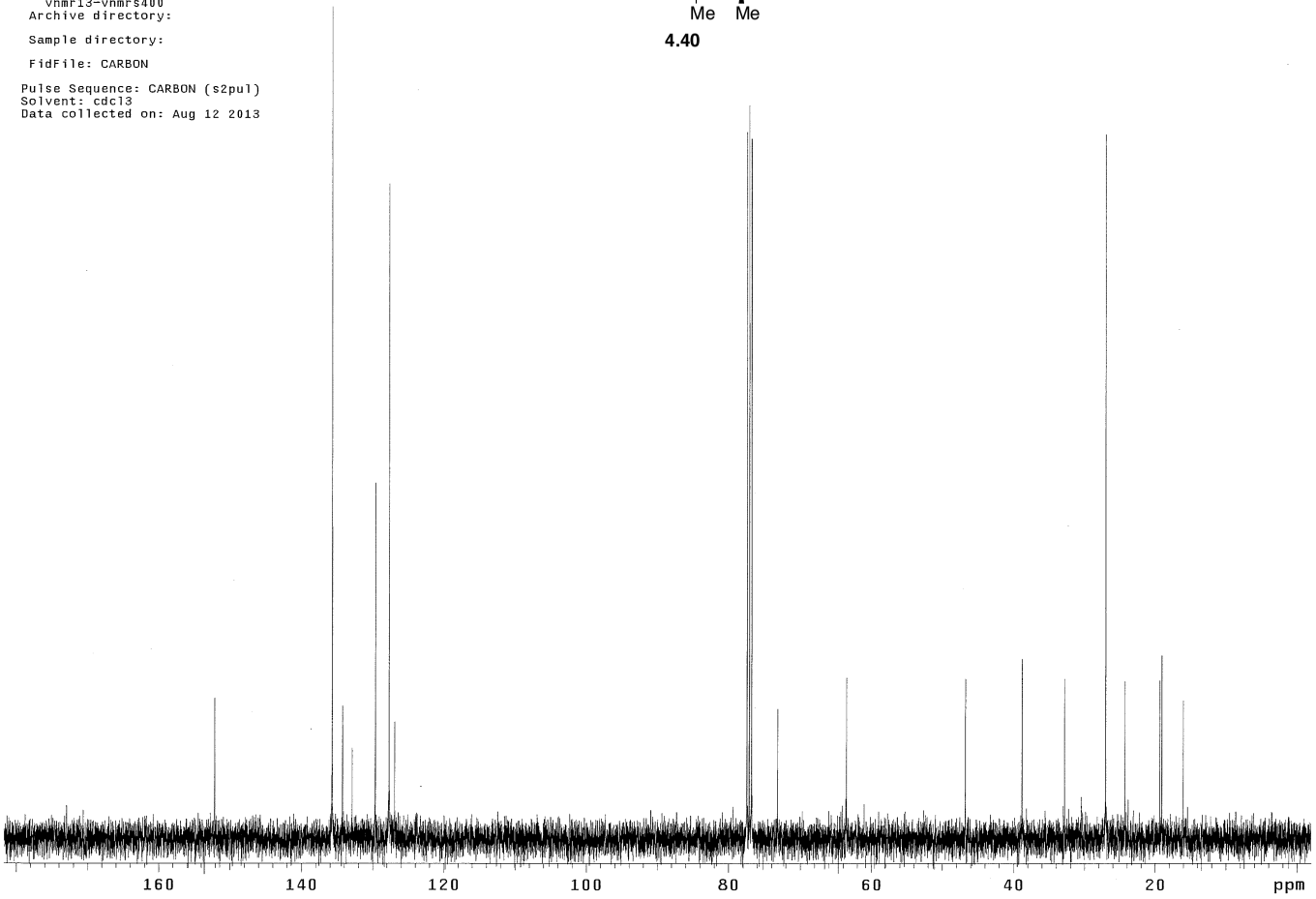
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 12 2013



4.40

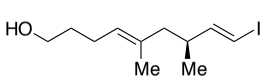


Sample Name:
FM-VI-241
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: FM-VI-241

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 13 2013



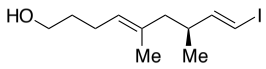
Rot-B

Sample Name:
FM-VI-241
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 13 2013



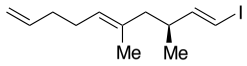
Rot-B

Sample Name:
FM-VI-244
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: FM-VI-244

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 15 2013



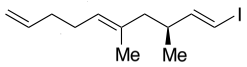
4.41

Sample Name:
FM-VI-244
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 15 2013



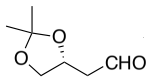
4.41

Sample Name:
FM-VI-214
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jul 2 2013



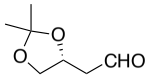
4.42

Sample Name:
FM-VI-214
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jul 2 2013



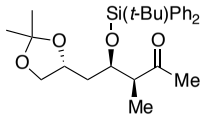
4.42

Sample Name:
FM-VI-236
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: FM-VI-236

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 9 2013



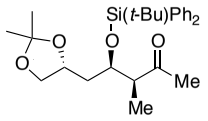
4.43

Sample Name:
FM-VI-236
Data Collected on:
vnmr13-vnmrs400
Archive directory:

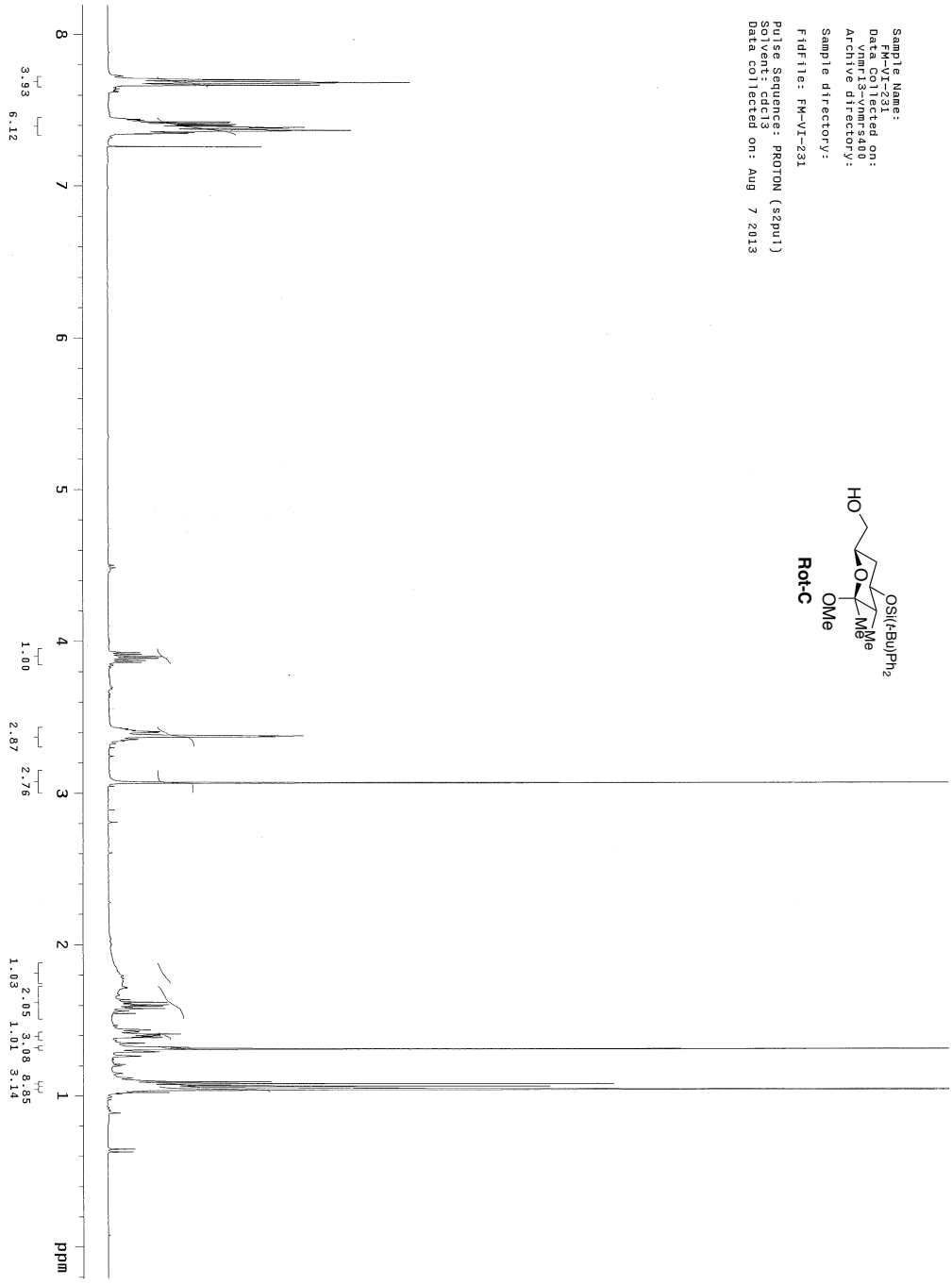
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 9 2013



4.43

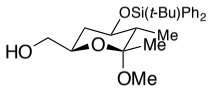

Sample Name:
Experiment:
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: FM-VI-231
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 7 2013
HO
O
OSi(t-Bu)Ph2
Me
Me
OMe
Rot-C
8
7
6
5
4
3
2
1
ppm
3.93
6.12
1.00
2.87
2.76
2.05
3.08
8.85
1.03
1.01
3.14

Sample Name:
FM-VI-231
Data Collected on:
vnmr13-vnmrs400
Archive directory:

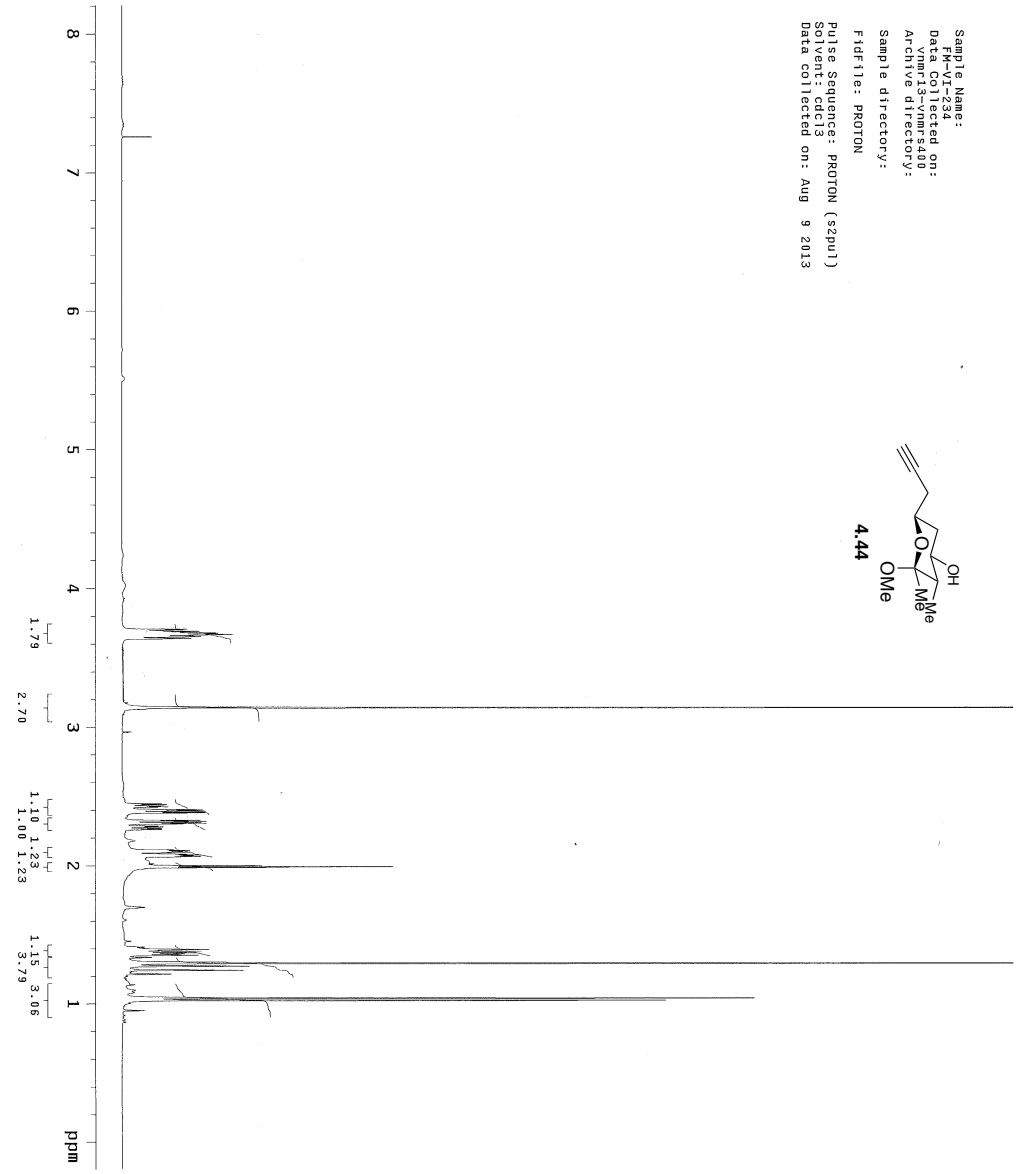
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 7 2013



Rot-C

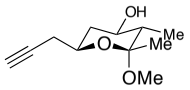

Sample Name:
FM-VI-234
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 9 2013
OH
Me
Me
O
OMe
4.44
8
7
6
5
4
3
2
1
ppm
1.79
2.70
1.10
1.23
1.00
1.23
1.15
3.06
3.79

Sample Name:
FM-VI-234
Data Collected on:
vnmr13-vnmrs400
Archive directory:

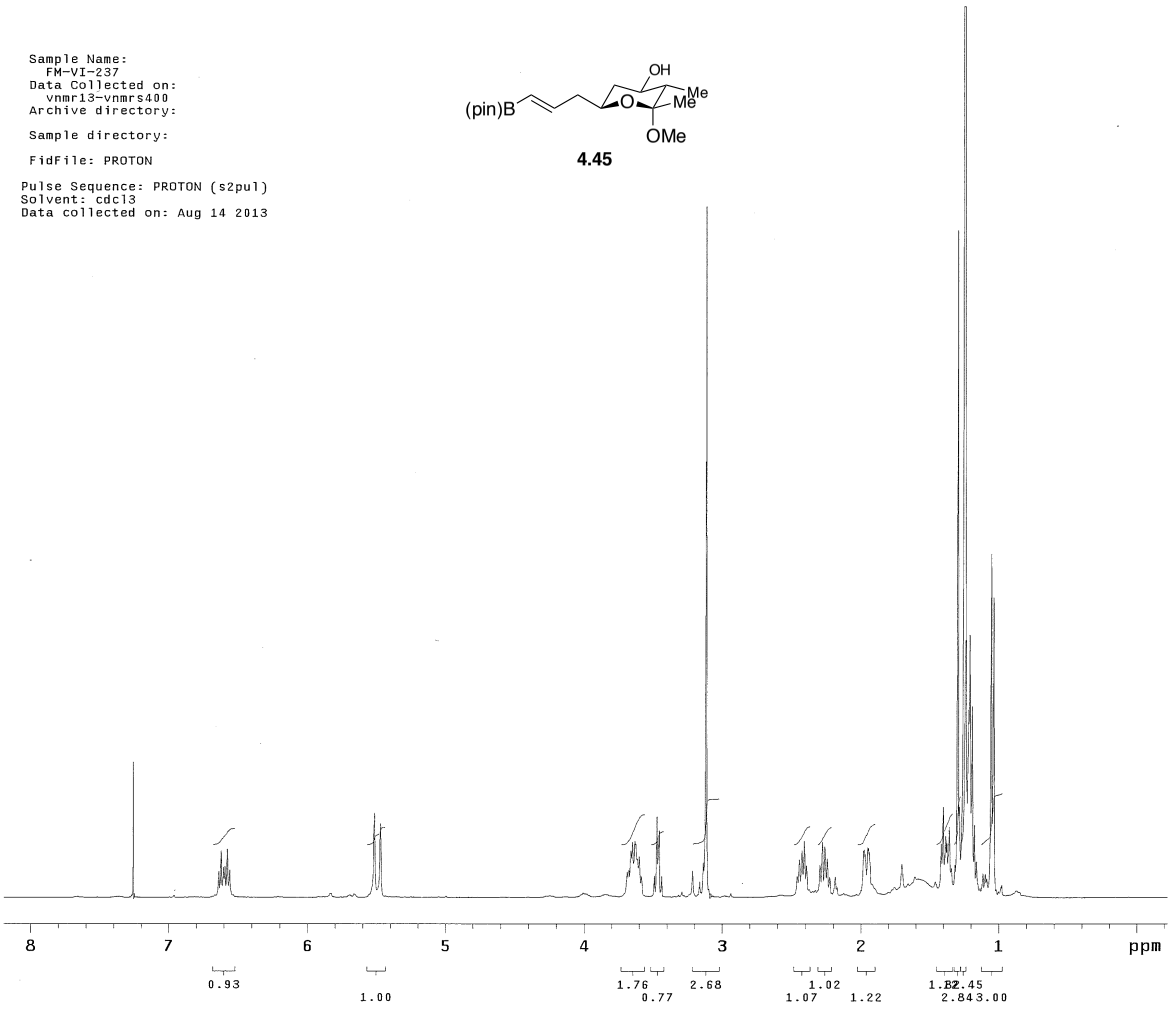
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 9 2013



4.44

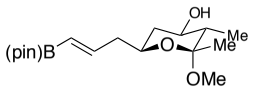

Sample Name:
FM-VI-237
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 14 2013
OH
(pin)B
O
Me
Me
OMe
4.45
8
7
6
5
4
3
2
1
ppm
0.93
1.00
1.76
0.77
2.68
1.02
1.07
1.22
2.45
3.00

Sample Name:
FM-VI-237
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 14 2013



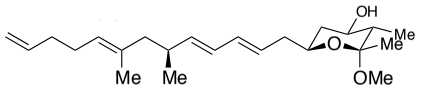
4.45

Sample Name:
FM-VI-248
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: c6d6
Data collected on: Aug 22 2013



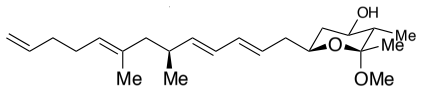
Rot-D

Sample Name:
FM-VI-248
Data Collected on:
vnmr13-vnmrs400
Archive directory:

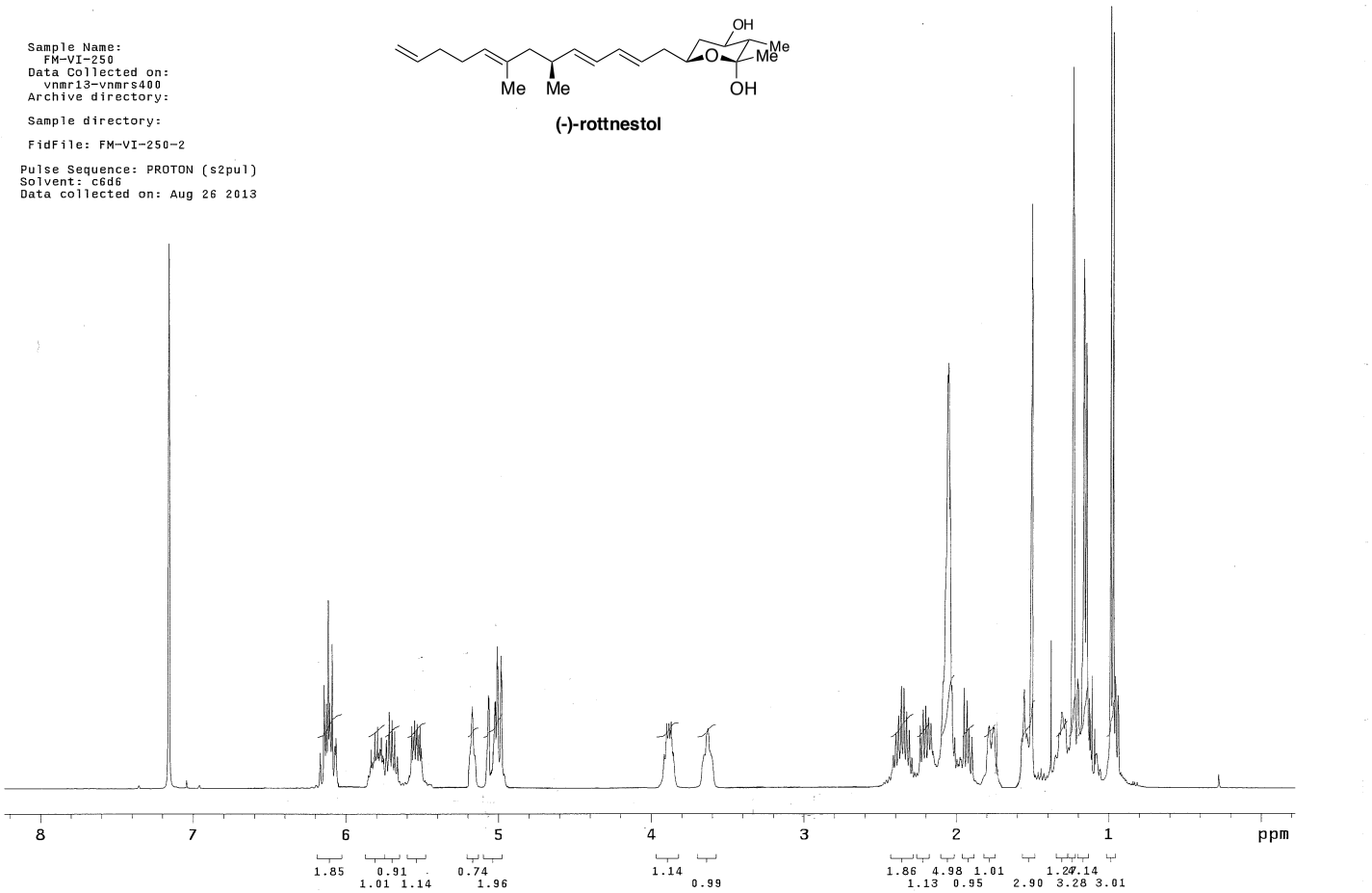
Sample directory:

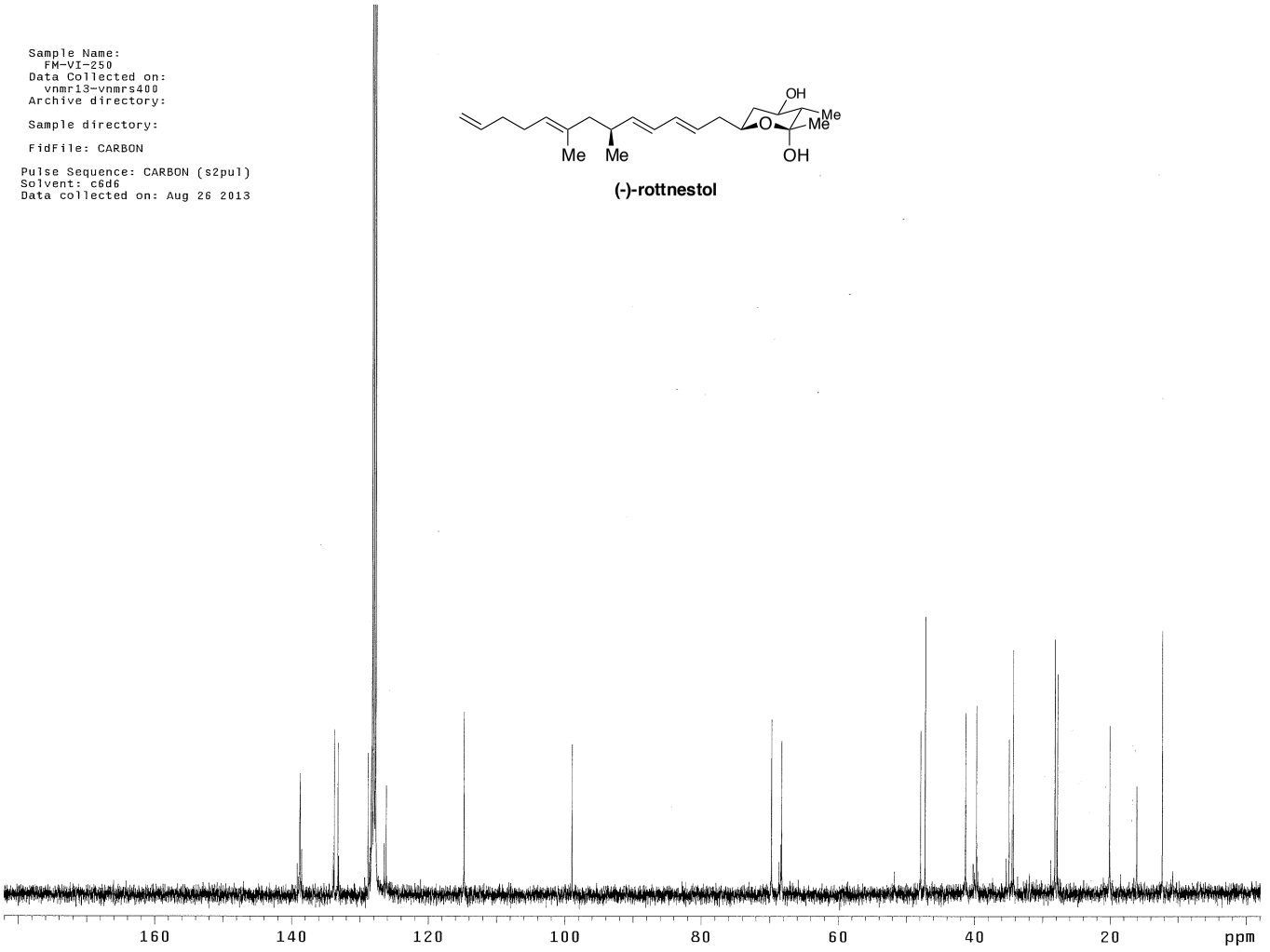
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: c6d6
Data collected on: Aug 22 2013



Rot-D


Sample Name:
FM-VI-250
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: FM-VI-250-2
Pulse Sequence: PROTON (s2pul)
Solvent: c6d6
Data collected on: Aug 26 2013
OH
Me
Me
Me
Me
OH
(-)-rottnestol
8
7
6
5
4
3
2
1
ppm
1.85
0.91
1.01
1.14
0.74
1.96
1.14
0.99
1.86
1.13
4.98
0.95
1.01
2.90
1.24
3.28
7.14
3.01

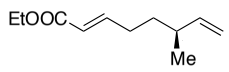

Sample Name:
FM-VI-250
Data Collected on:
vnmr13~vnmrs400
Archive directory:
Sample directory:
FidFile: CARBON
Pulse Sequence: CARBON (s2pul)
Solvent: c6d6
Data collected on: Aug 26 2013
OH
Me
Me
O
Me
Me
OH
(-)-rottnestol
160
140
120
100
80
60
40
20
ppm

Sample Name:
FM-VI-254
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 4 2013



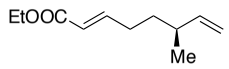
4.46

Sample Name:
FM-VI-254
Data Collected on:
vnmr13-vnmrs400
Archive directory:

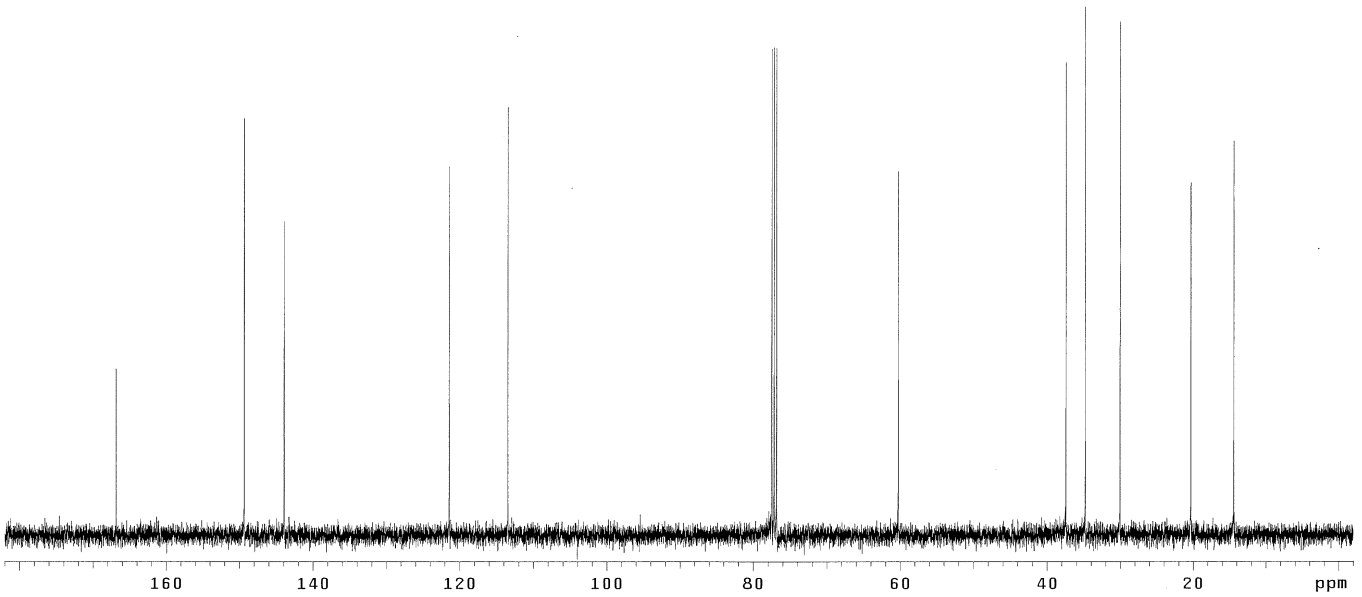
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 4 2013



4.46

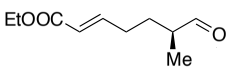


Sample Name:
FM-VI-257
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 10 2013



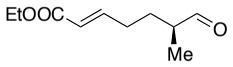
4.47

Sample Name:
FM-VI-257
Data Collected on:
vnmr13-vnmrs400
Archive directory:

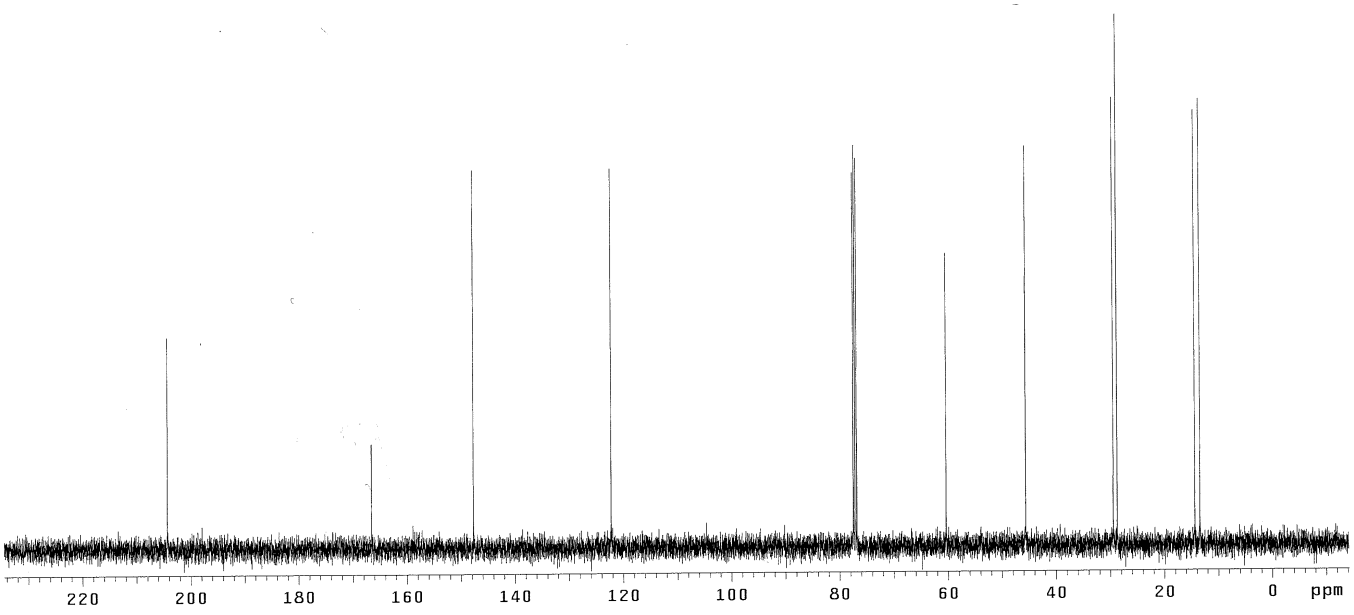
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 10 2013



4.47

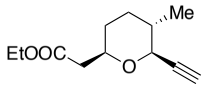


Sample Name:
FM-VI-256
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 10 2013



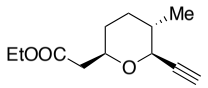
4.48

Sample Name:
FM-VI-256
Data Collected on:
vnmr13-vnmrs400
Archive directory:

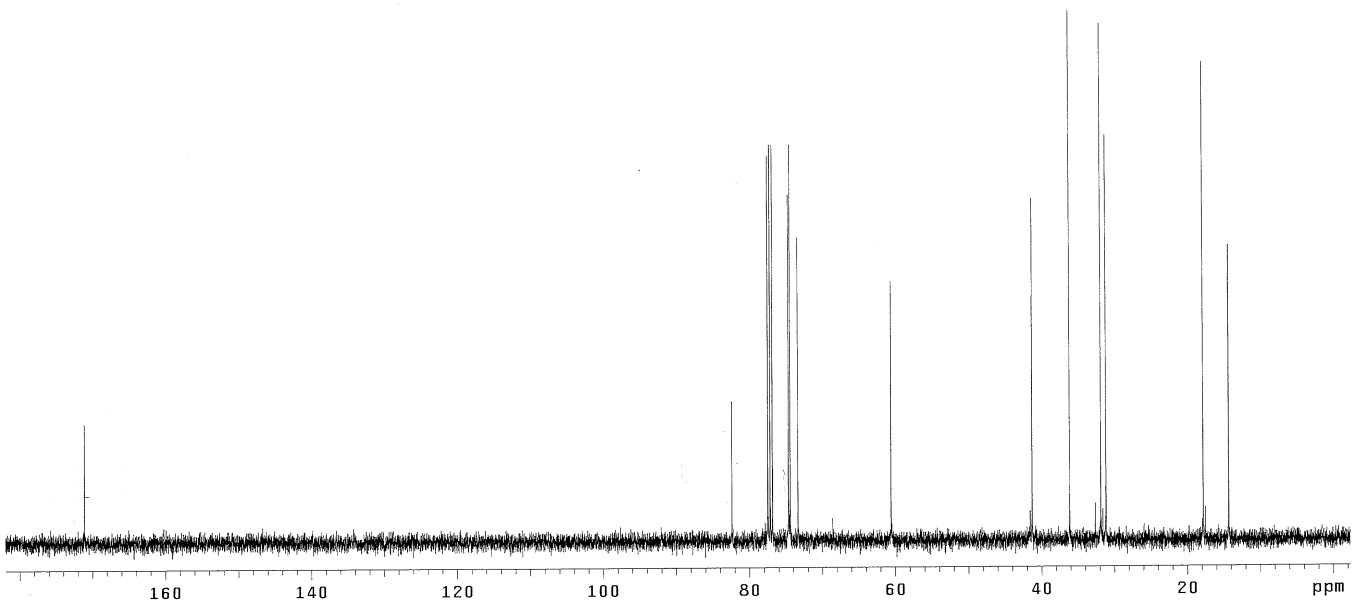
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 10 2013



4.48

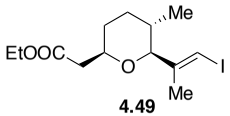


Sample Name:
FM-VI-260
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: FM-VI-260

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 20 2013



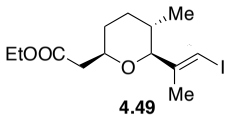
4.49

Sample Name:
FM-VI-260
Data Collected on:
vnmr13-vnmrs400
Archive directory:

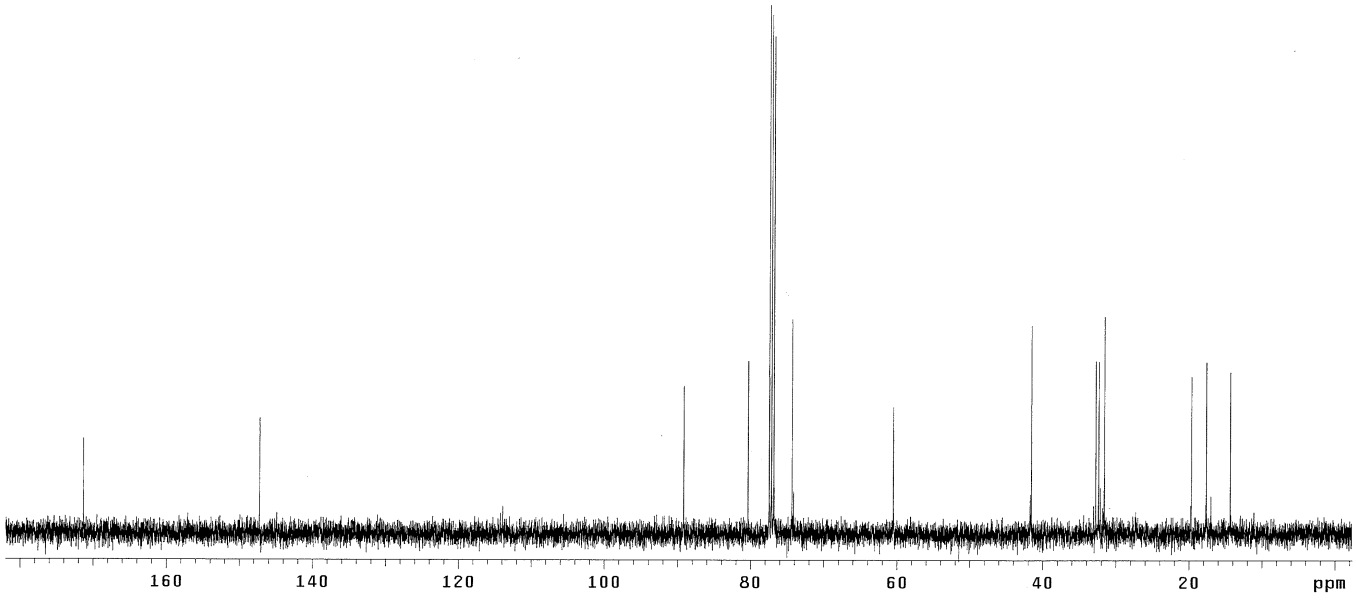
Sample directory:

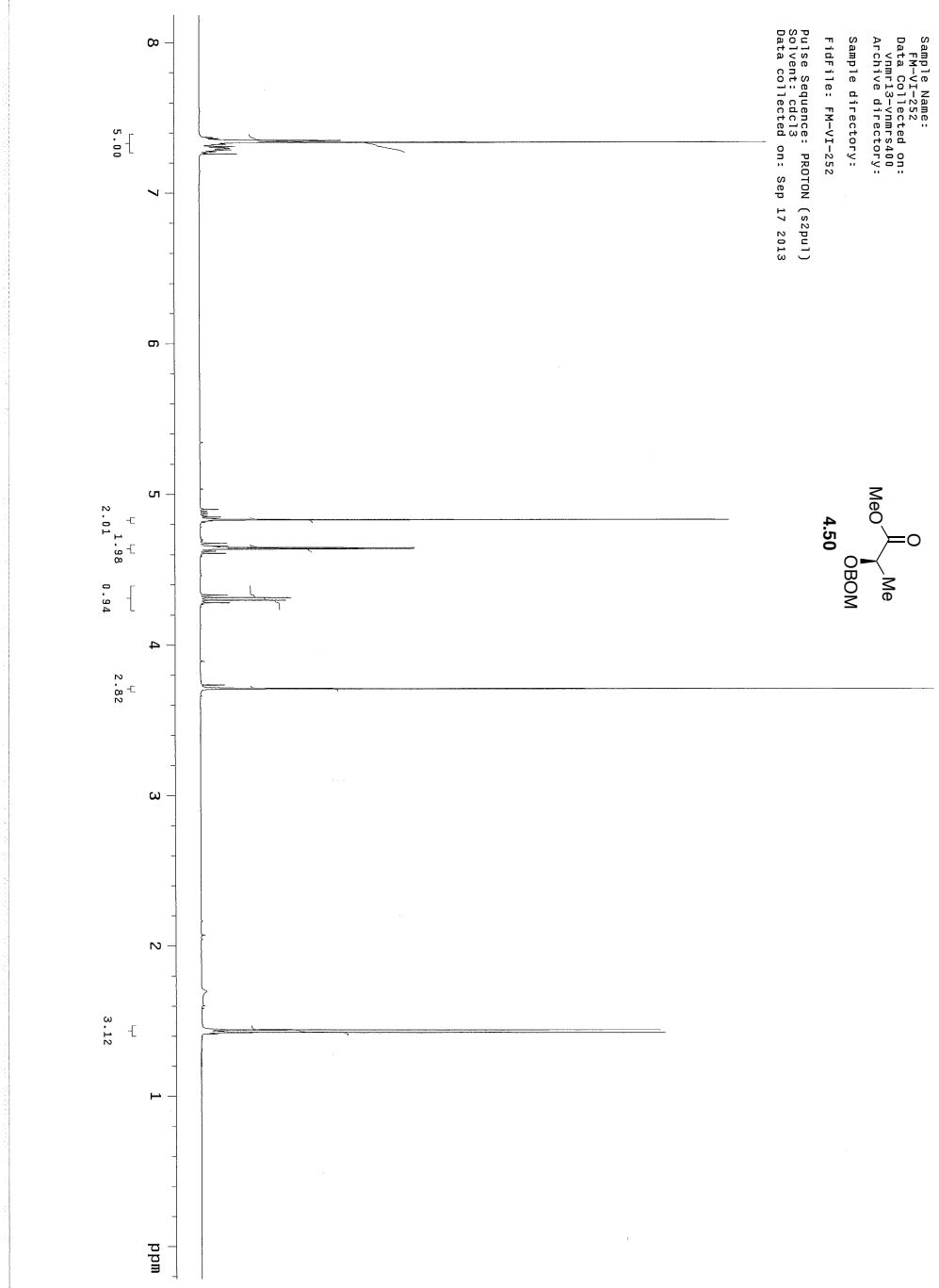
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 20 2013



4.49



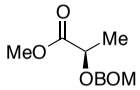

Sample Name:
FM-VI-252
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: FM-VI-252
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 17 2013
MeO
O
Me
OBOM
4.50
8
7
6
5
4
3
2
1
ppm
5.00
2.01
1.98
0.94
2.82
3.12

Sample Name:
FM-VI-252
Data Collected on:
vnmr13-vnmrs400
Archive directory:

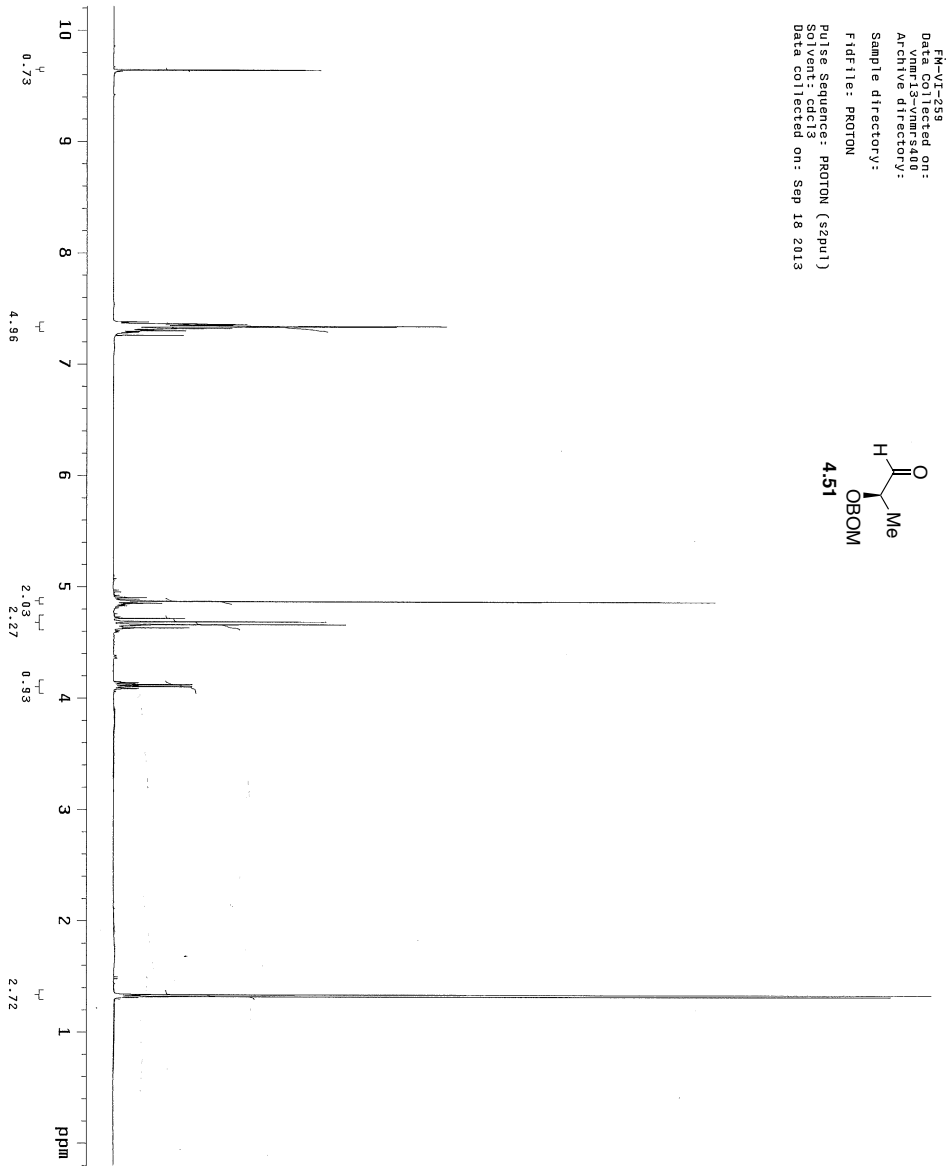
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 17 2013



4.50

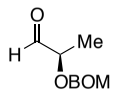

Sample Name:
mayr_zsy
Data Collected on:
vnmrj3-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 18 2013
H
O
Me
OBOM
4.51
ppm
0.73
4.96
2.03
2.27
0.93
2.72

Sample Name:
FM-VI-259
Data Collected on:
vnmr13-vnmrs400
Archive directory:

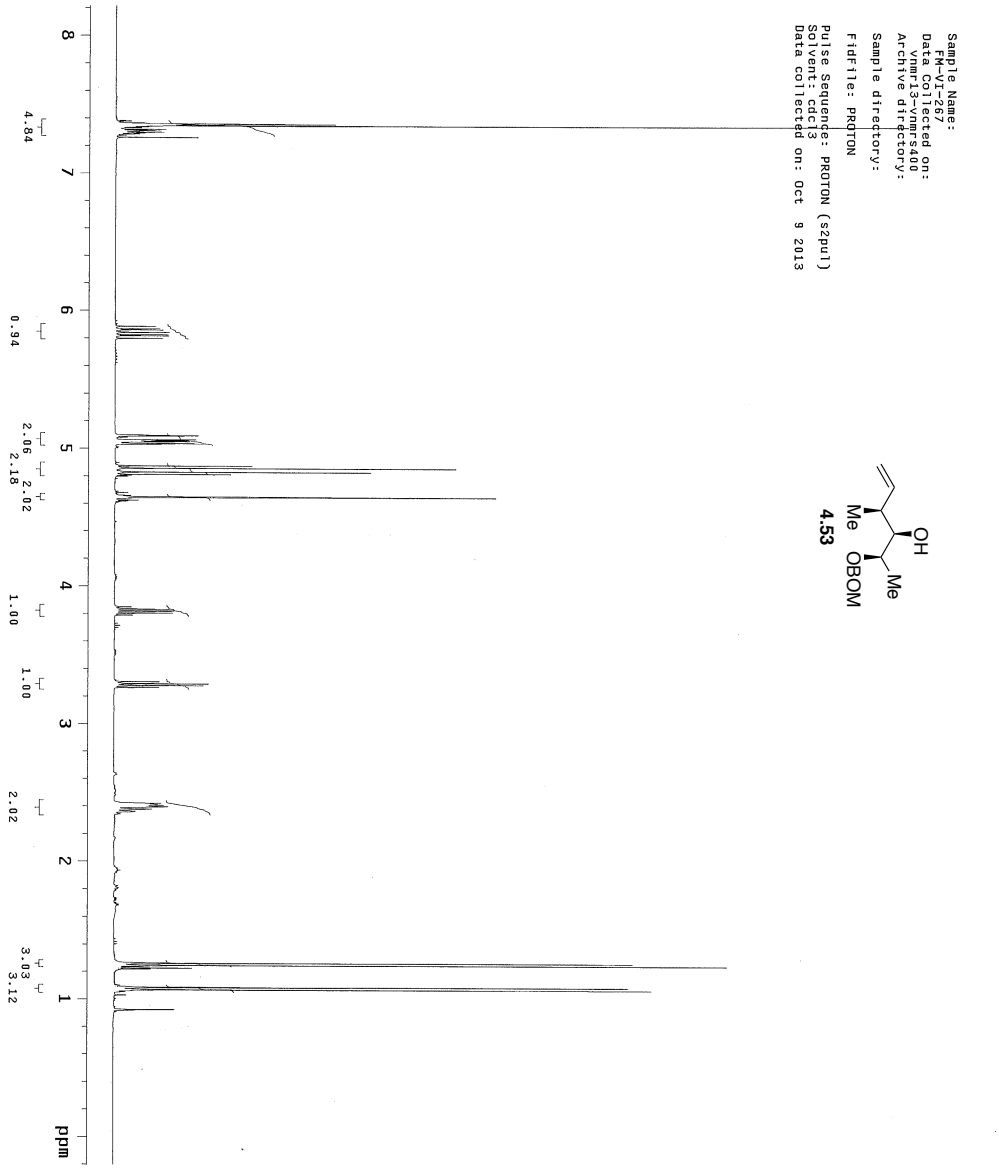
Sample directory:

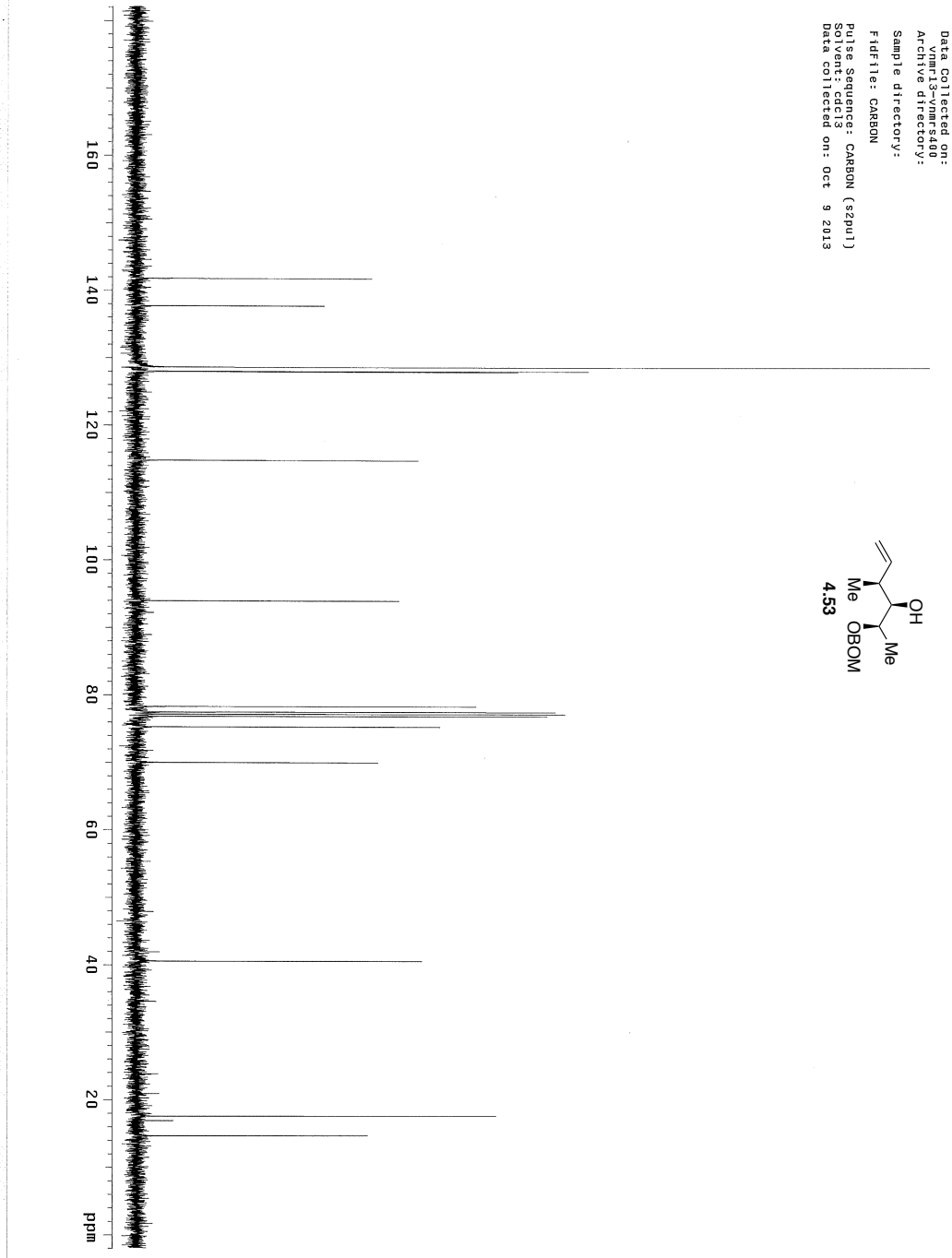
FidFile: CARBON

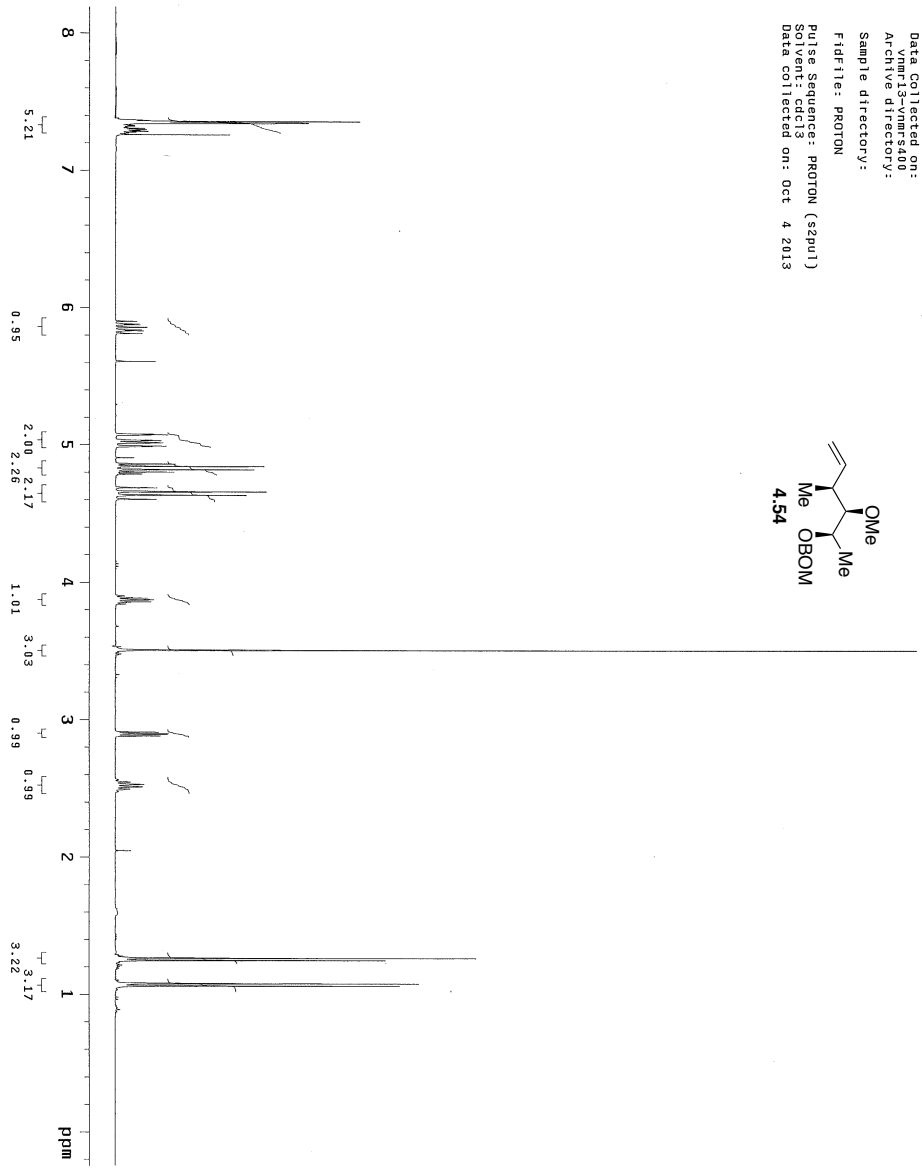
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 18 2013



4.51


Sample Name:
FM-VI-267
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 9 2013
OH
Me
Me
OBOM
4.53
8
7
6
5
4
3
2
1
ppm
4.84
0.94
2.06
2.18
2.02
1.00
1.00
2.02
3.03
3.12


Sample Name:
FM-VI-267
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: CARBON
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 9 2013
OH
Me
Me
OBOM
4.53
160
140
120
100
80
60
40
20
ppm

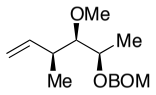

Sample Name:
FM-VI-269
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 4 2013
OMe
Me
Me
OBOM
4.54
8
7
6
5
4
3
2
1
ppm
5.21
0.95
2.00
2.17
2.26
1.01
3.03
0.99
0.99
3.17
3.22

Sample Name:
FM-VI-269
Data Collected on:
vnmr13-vnmrs400
Archive directory:

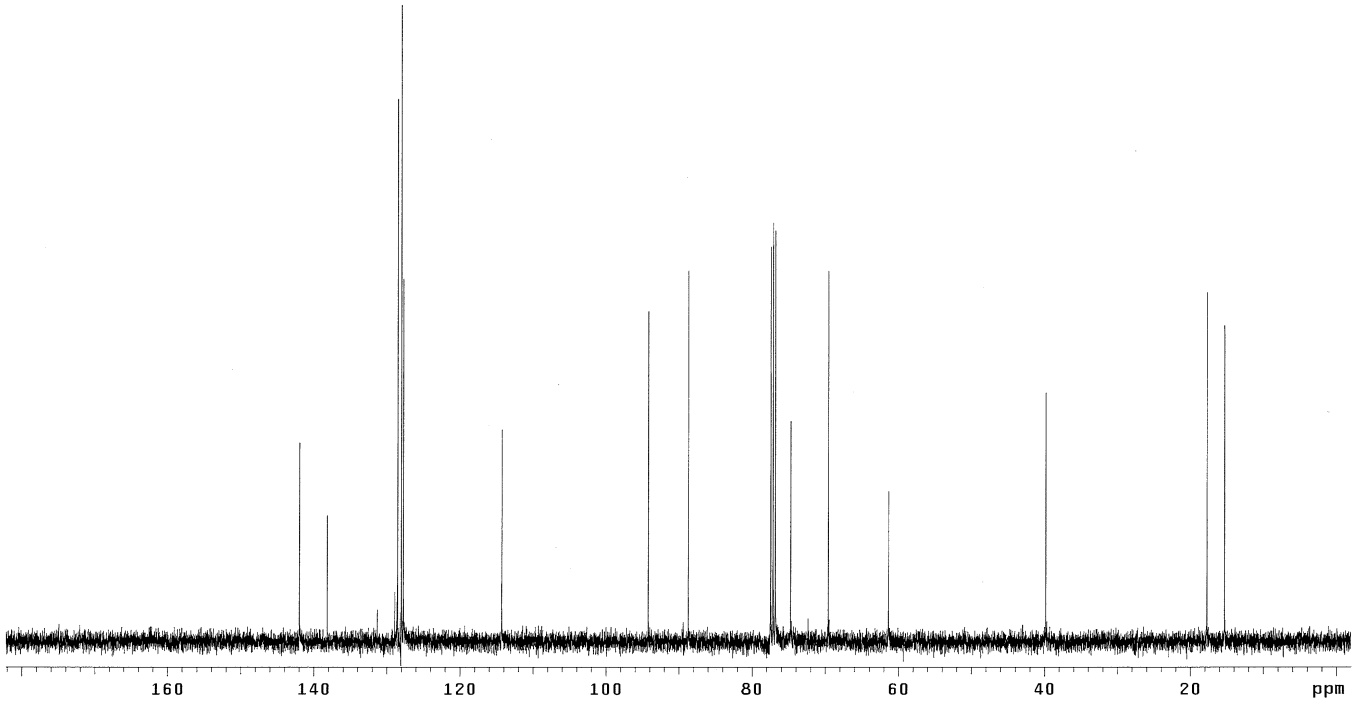
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 4 2013



4.54

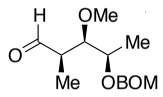


Sample Name:
FM-VI-270
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 11 2013



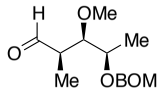
4.55

Sample Name:
FM-VI-270
Data Collected on:
vnmr13-vnmrs400
Archive directory:

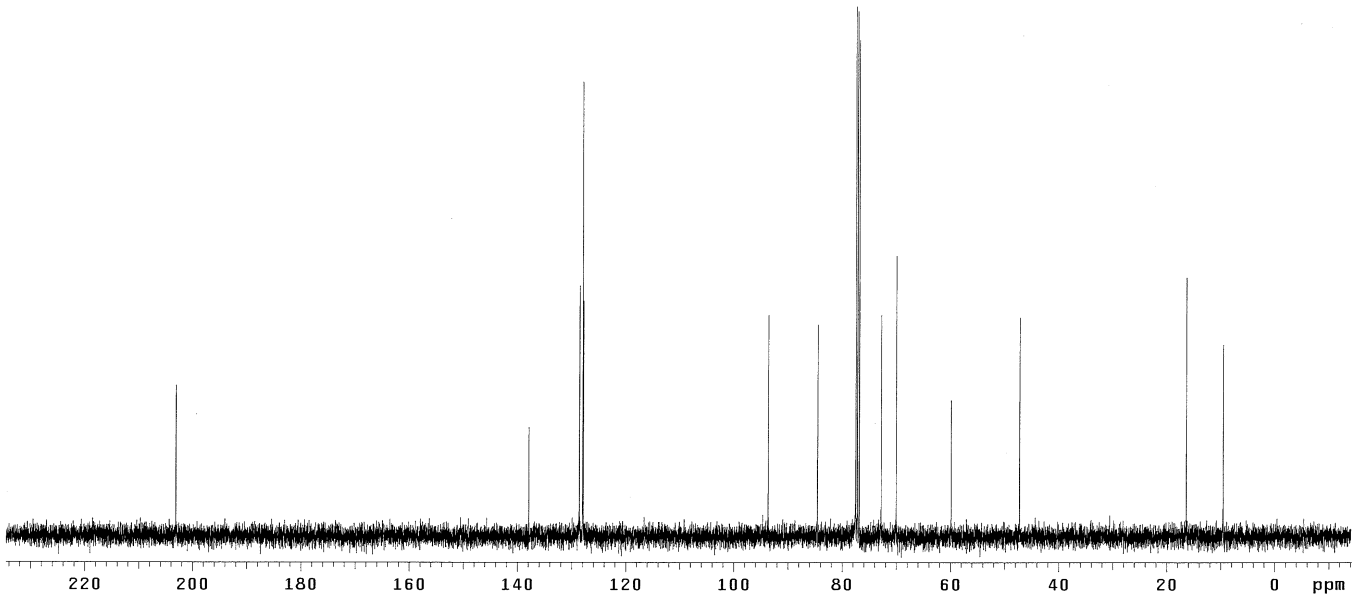
Sample directory:

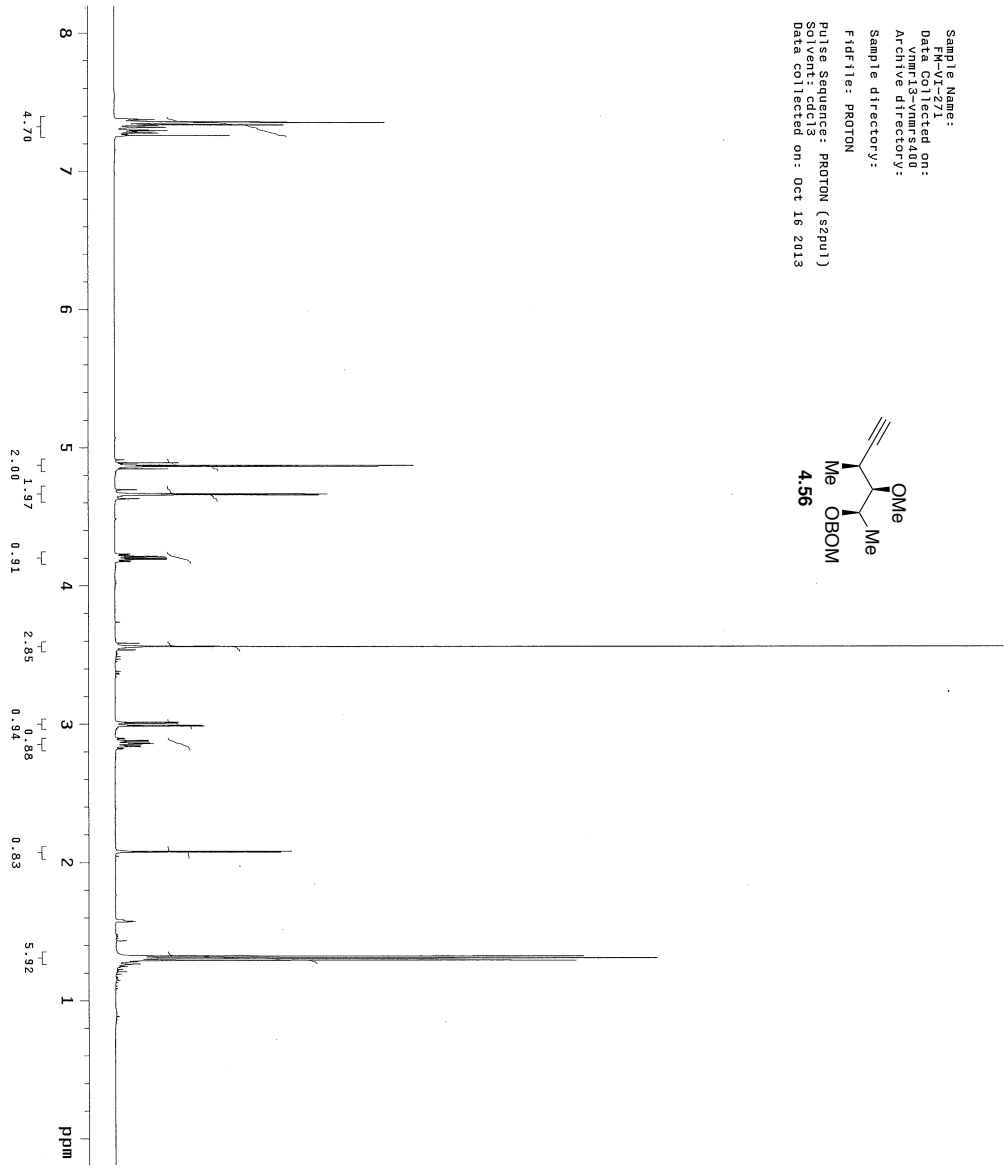
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 11 2013



4.55



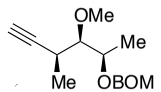

Sample Name:
PM-VI-271
Data Collected on:
vnmrl3-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 16 2013
OMe
Me
Me
OBOM
4.56
8
7
6
5
4
3
2
1
ppm
4.70
2.00
1.97
0.91
2.85
0.94
0.88
0.83
5.92

Sample Name:
FM-VI-271
Data Collected on:
vnmr13-vnmrs400
Archive directory:

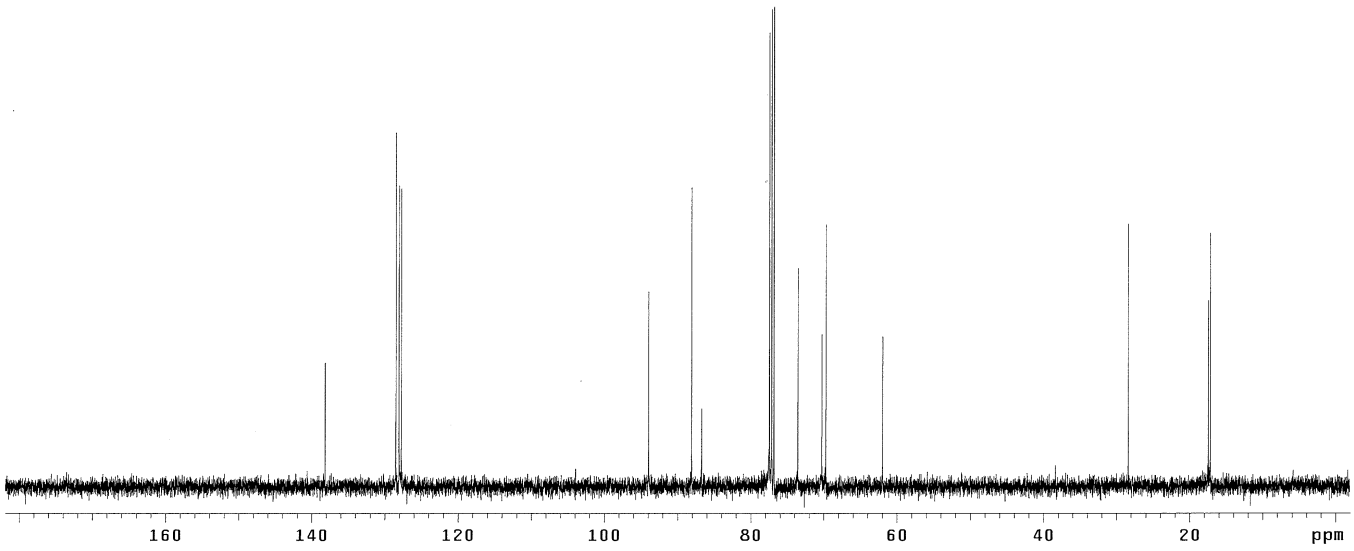
Sample directory:

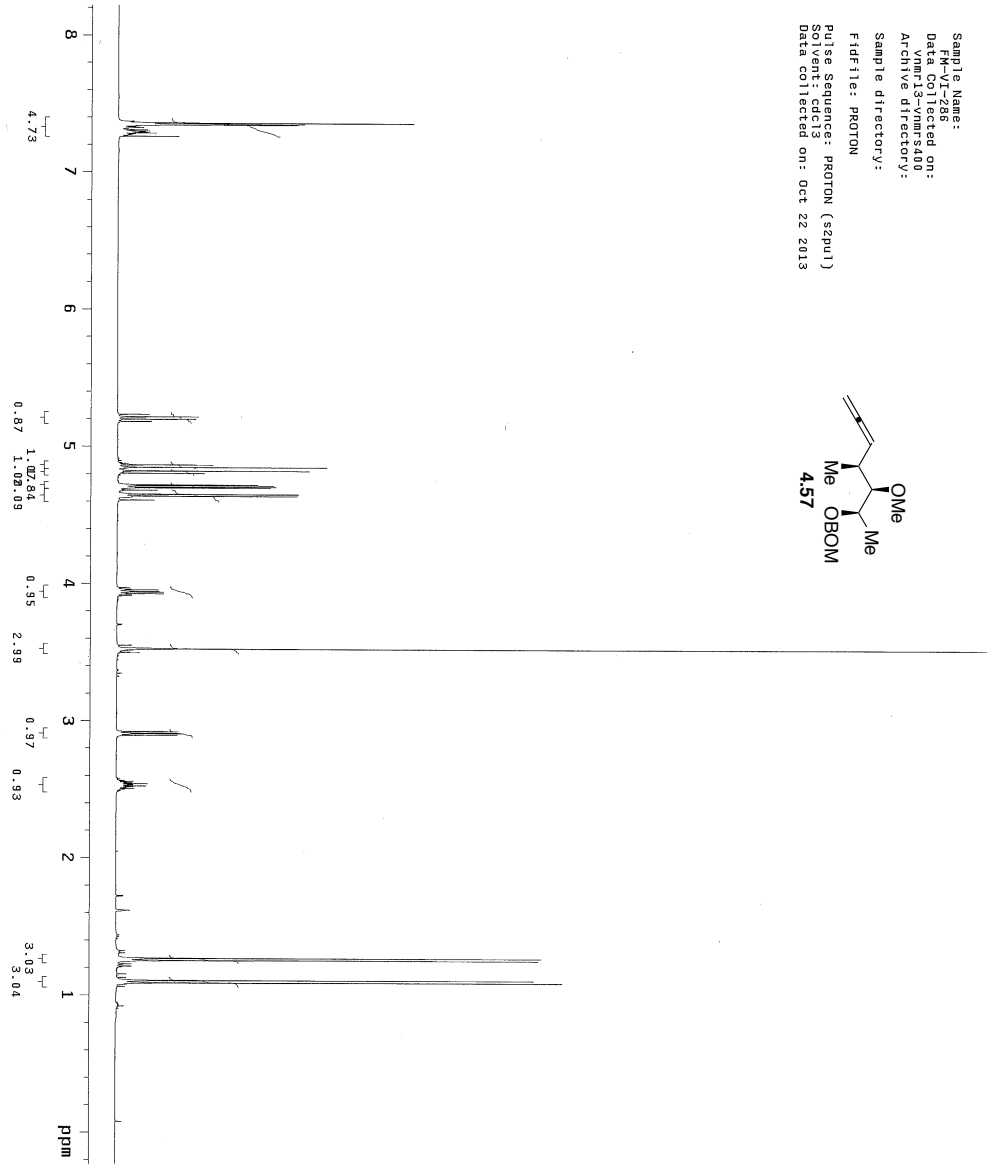
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 16 2013



4.56



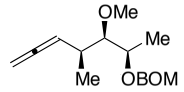

Sample Name:
FM-VI-286
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 22 2013
OMe
Me
Me
OBOM
4.57
ppm

Sample Name:
FM-VI-286
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 22 2013



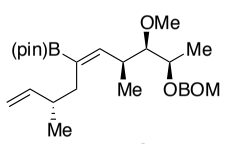
4.57

Sample Name:
FM-VII-9-2
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: FM-VII-9-2

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 25 2013



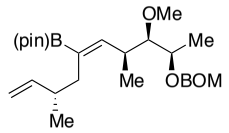
4.58

Sample Name:
FM-VII-9-2
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 25 2013



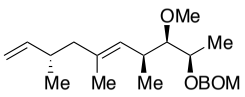
4.58

Sample Name:
FM-VII-27
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Nov 18 2013



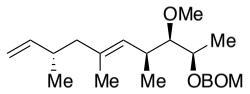
Her-A

Sample Name:
FM-VII-27
Data Collected on:
vnmr13-vnmrs400
Archive directory:

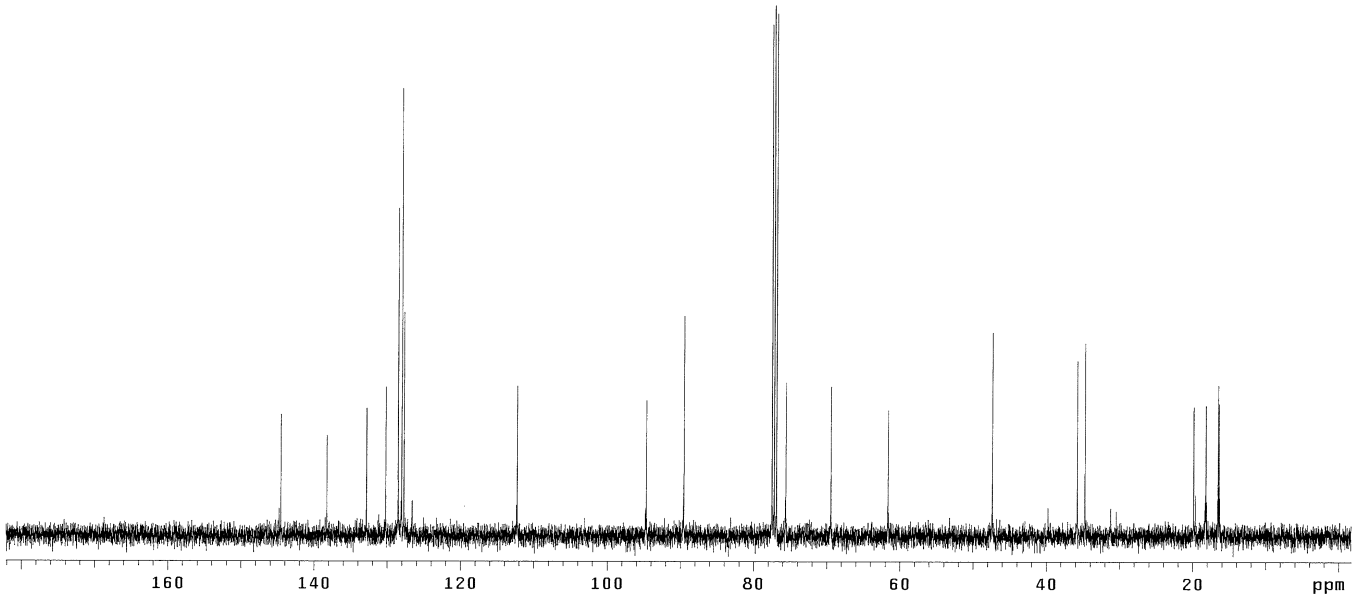
Sample directory:

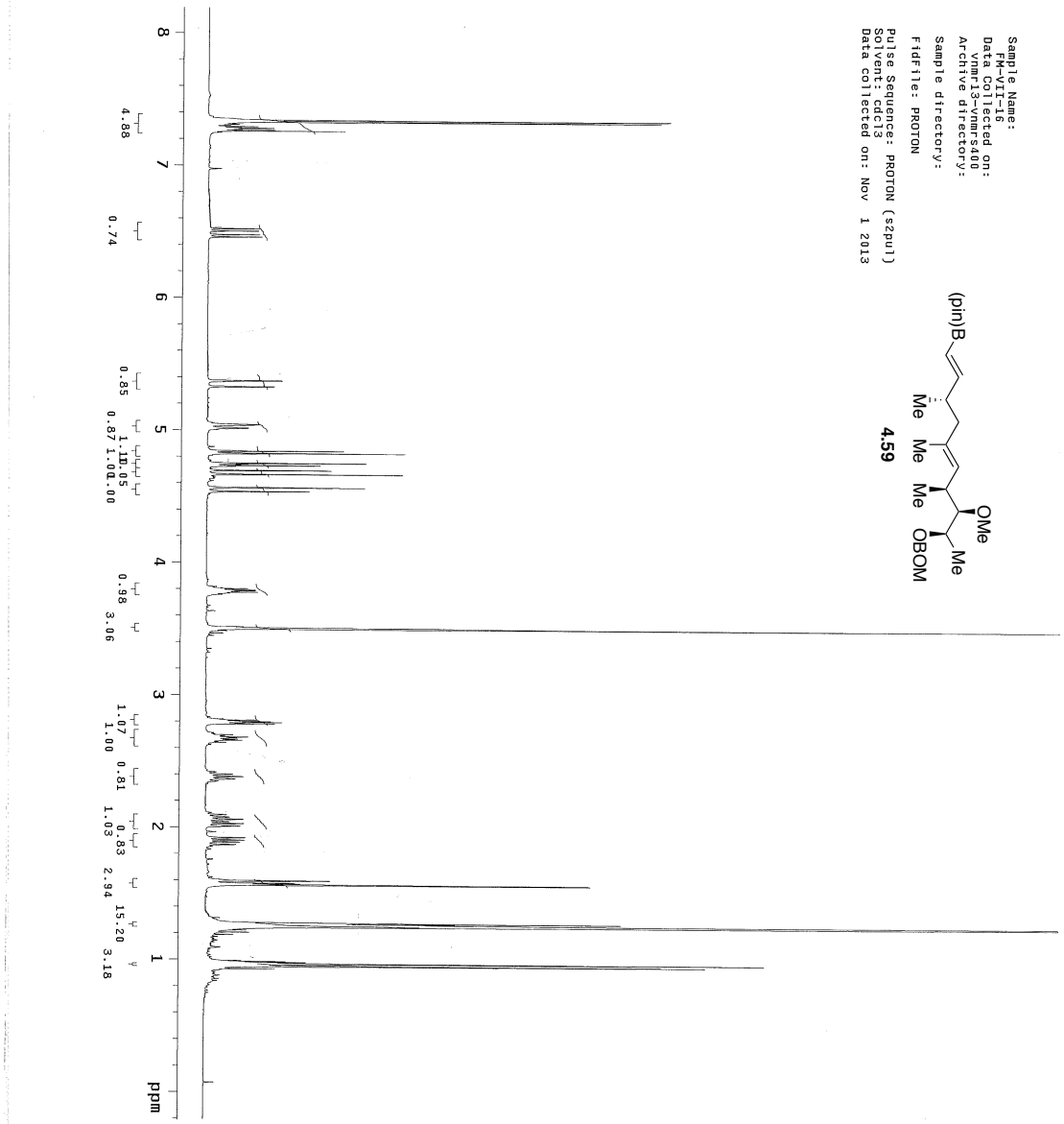
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Nov 18 2013



Her-A



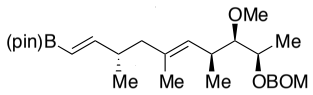

Sample Name:
FM-VII-16
Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Nov 1 2013
(pin)B
Me
Me
Me
OMe
OBOM
Me
4.59
ppm

Sample Name:
FM-VII-16
Data Collected on:
vnmr13-vnmrs400
Archive directory:

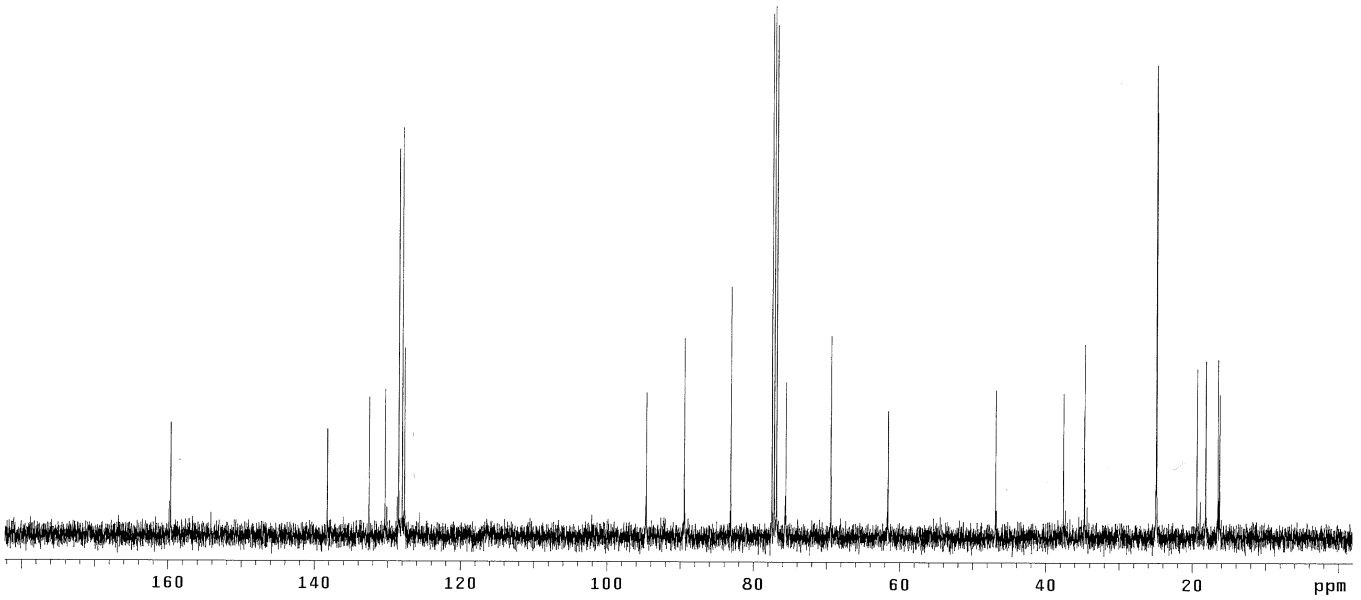
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Nov 1 2013



4.59

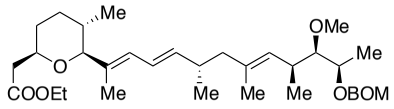


Sample Name:
FM-VII-30
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: FM-VII-30

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Nov 22 2013



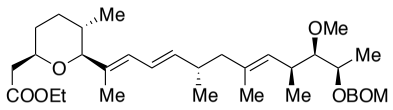
4.60

Sample Name:
FM-VII-30
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Nov 22 2013



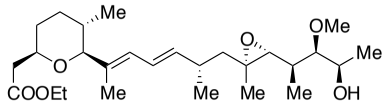
4.60

Sample Name:
FM-VII-34
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Nov 27 2013



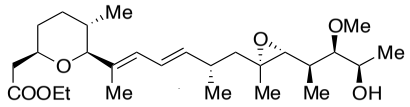
Her-B

Sample Name:
FM-VII-34
Data Collected on:
vnmr13-vnmrs400
Archive directory:

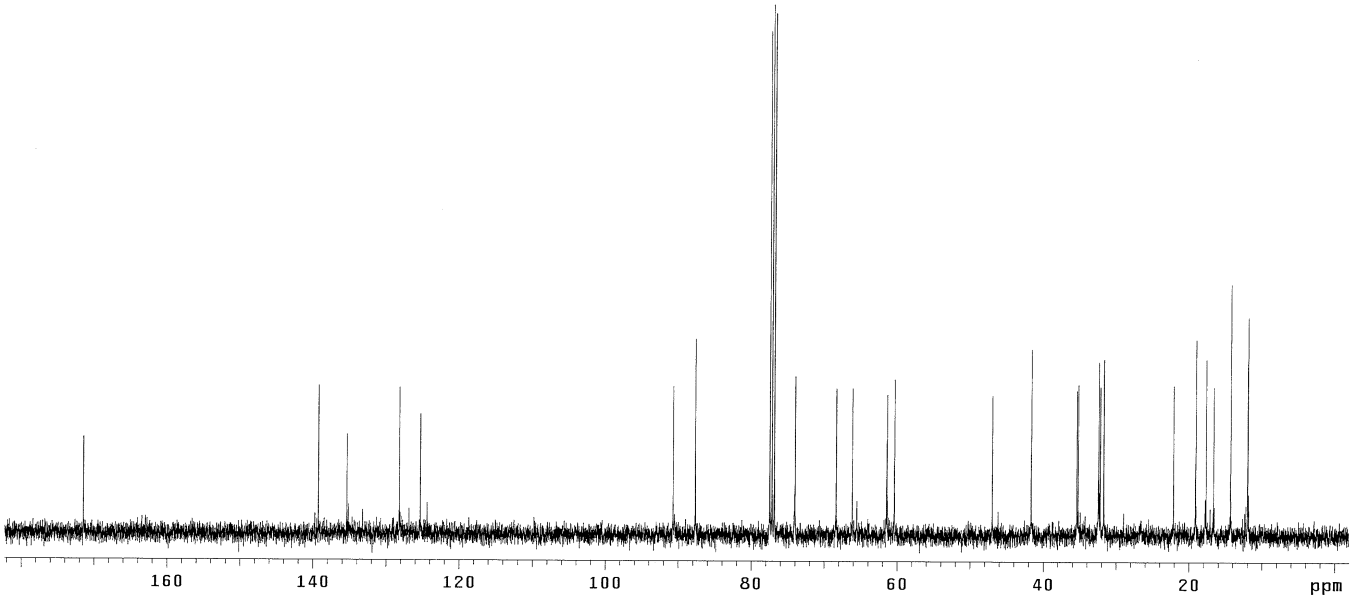
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Nov 27 2013



Her-B



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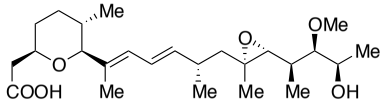
Archive directory:

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cd3od
Data collected on: Nov 27 2013



(+)-herboxidiene

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FM-VII-36
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Archive directory:

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
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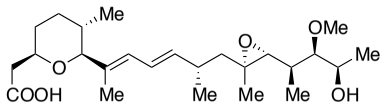
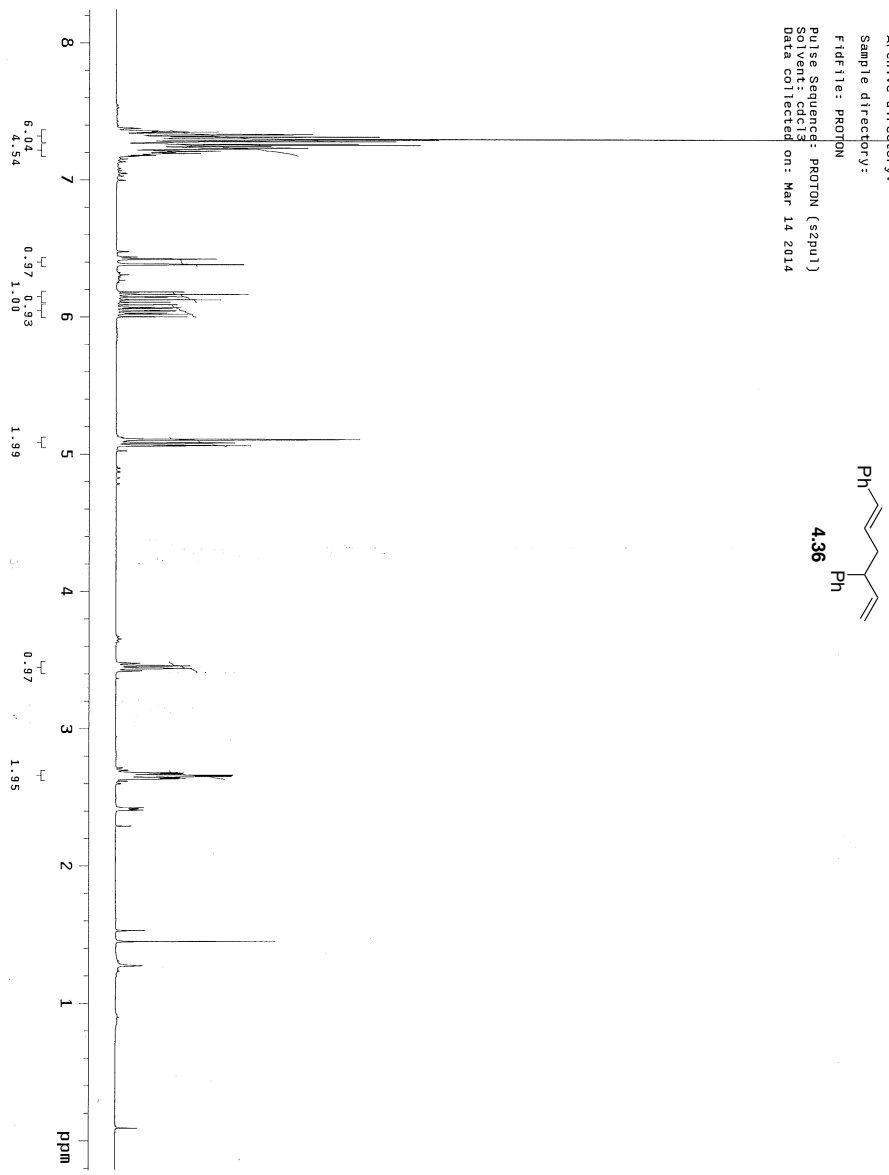
Data collected on: Dec 2 2013



(+)-herboxidiene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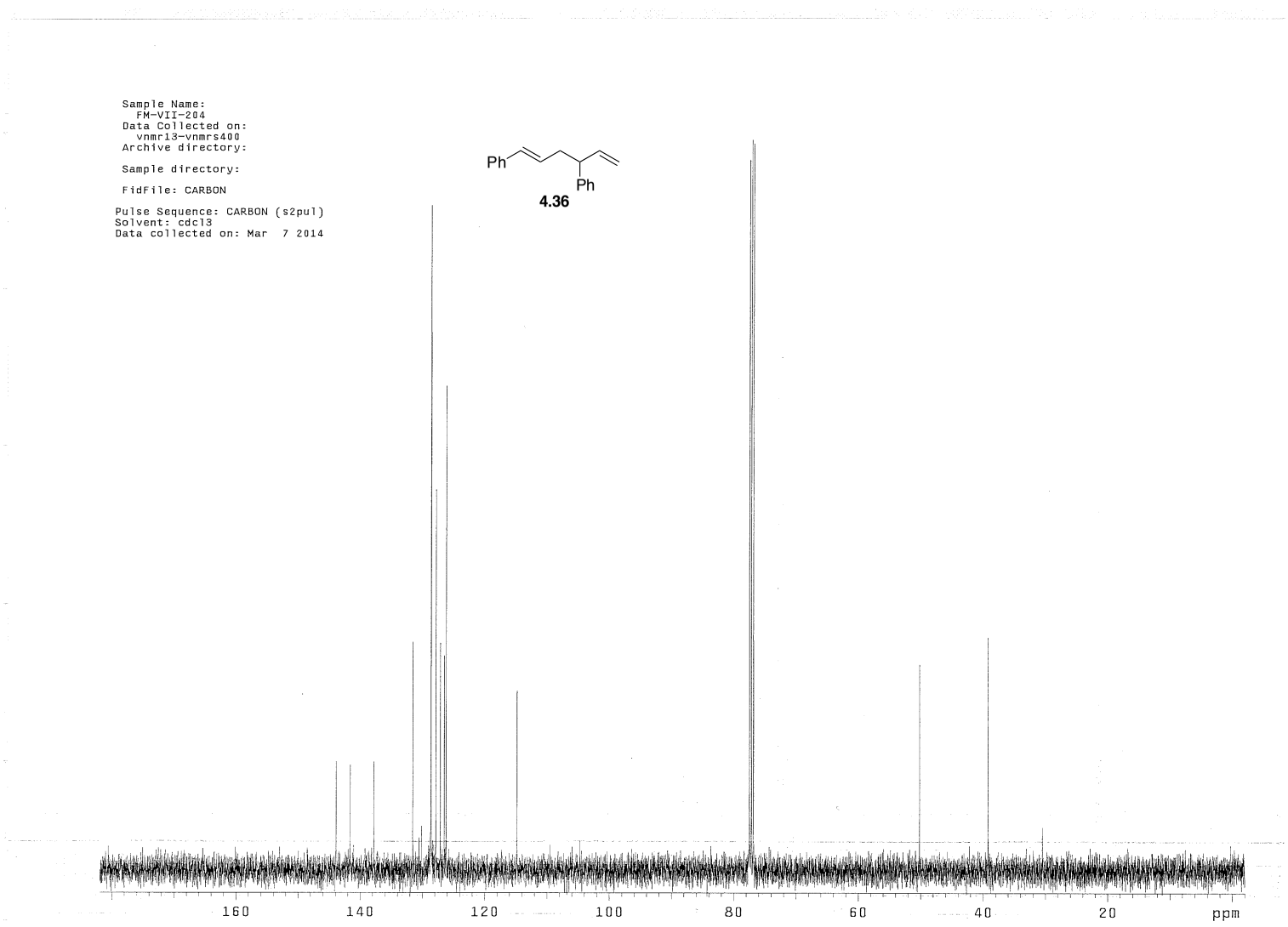
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 14 2014
Ph
Ph
4.36
8
7
6
5
4
3
2
1
ppm
6.04
4.54
0.97
0.93
1.00
1.99
0.97
1.95


Sample Name:
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Data Collected on:
vnmr13-vnmrs400
Archive directory:
Sample directory:
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Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 7 2014
Ph
Ph
4.36
160
140
120
100
80
60
40
20
ppm

Chapter 5

Cu-Catalyzed Enantioselective Allyl and Propargyl 1,6-Conjugate Additions through 3,3'-Reductive Elimination

5.1 Introduction

Catalytic enantioselective conjugate additions constitute an important class of transformations in organic synthesis.[1] A variety of metal-catalyzed conjugate additions employing organometallic reagents, such as Grignard reagent, organoaluminum, organozinc and organoboron reagents have been developed.[1] Aryl, alkenyl and alkyl groups can be transferred in high efficiency and enantioselectivity. However, there are few catalytic enantioselective protocols that incorporate allyl-type group onto α,β-unsaturated carbonyl compounds.[2] This challenging problem originates from formation of stable π-allyl metal complexes that are reluctant to undergo reductive elimination. The small size of allyl-type groups might also raise the barrier of reductive elimination. In addition, the stronger nucleophilicity of allyl metal intermediates might cause significant competitive background reactions.

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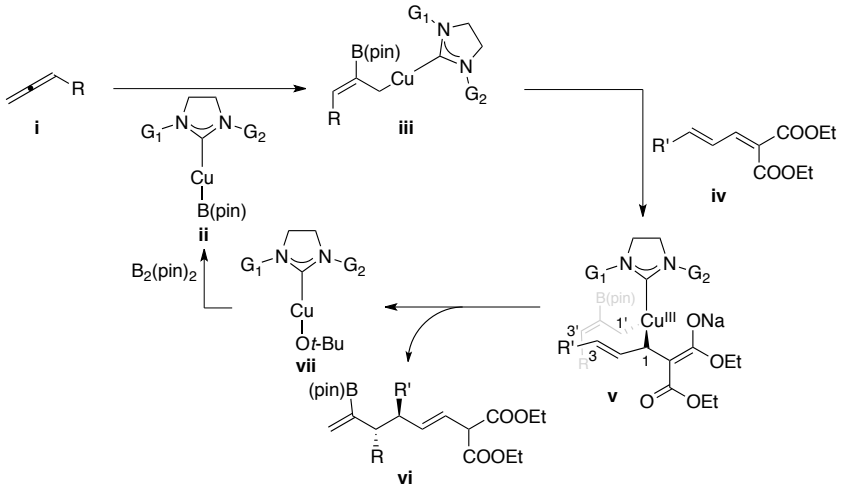
(1) For representative reviews on catalytic enantioselective conjugate addition, see: (a) Harutyunyan, S. R.; den Hartog, T.; Geurts, K.; Minnaard, A. J.; Feringa, B. L. *Chem. Rev.* **2008**, *108*, 2824–2852. (b) Jerphagnon, T.; Pizzuti, M. G.; Minnaard, A. J.; Feringa, B. L. *Chem. Soc. Rev.* **2009**, *38*, 1039–1075. (c) Córdova, A. *Catalytic Asymmetric Conjugate Reactions*; Wiley-VCH: Weinheim, **2010**. (d) Ji, J.-X.; Chan, A. S. C. *Catalyic Asymmetric Synthesis* (Ed.: I. Ojima); Wiley, Hoboken, **2010**, pp. 439–495.

(2) (a) Sieber, J. D.; Liu, S.; Morken, J. P. *J. Am. Chem. Soc.* **2007**, *129*, 2214–2215. (b) Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc.* **2008**, *130*, 4978–4983. (c) Shizuka, M.; Snapper, M. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 5049–5051. (d) Yanagida, Y.; Yazaki, R.; Kumagai, N.; Shibasaki, M. *Angew. Chem., Int. Ed.* **2011**, *50*, 7910–7914. (e) Kuang, Y.; Liu, X.; Chang, L.; Wang, M.; Lin, L.; Feng, X. *Org. Lett.* **2011**, *13*, 3814–3817.

Selective 1,6-conjugate addition is also a challenging problem, as the most electrophilic site of dienoate is at 4-position.[3] Common strategy that has been employed in the literature is to introduce steric hindrance to block the 4-position, leading to 1,6-addition as a major pathway. Another method to achieve addition at 6-position selectively is through chelation of the diene system of the dienoate in *s-cis* conformation to the metal center followed by group transfer from the metal to the 6-position promoted by late transition metal complexes such as Fe-, Rh-, Ir- and Co-based catalysts.[3]

Scheme 5.1: Catalytic Cycle for NHC–Cu-Catalyzed Multicomponent Allyl 1,6-Conjugate Addition



Hoveyda group has recently developed methods of catalytic generation of boron-substituted allylcopper species and their in situ use for C–C bond formations.[4] We design that the 2-boron-substituted allylcopper complex **iii** resulting from catalytic Cu–B addition to allene **i** oxidatively adds to a dienoate **iv**, delivering a Cu(III) intermediate **v** that contains two different allyl groups, which might reductively eliminate in a 3,3'-

(3) For reviews on catalytic 1,6-conjugate additions, see (a) Silva, E. M. P.; Silva, A. M. S. *Synthesis* **2012**, *44*, 3109–3128. (b) Tissot, M.; Li, H.; Alexakis, A. *Copper-Catalyzed Asymmetric Synthesis* (Ed. Alexakis, A.; Krause, N.; Woodward, S.); Wiley-VCH, **2014**, pp. 69–84.
(4) Meng, F.; Jung, B.; Haeffner, F.; Hoveyda, A. H. *Org. Lett.* **2013**, *15*, 1414–1417. (b) Meng, F.; Jang, H.; Jung, B.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2013**, *52*, 5046–5051. (c) Meng, F.; McGrath, K. P.; Hoveyda, A. H. *Nature* **2014**, *513*, 367–374.

fashion to afford 1,6-conjugate addition product **vi**. We envision that 3,3'-reductive elimination pathway might be more facile than 1,1'-reductive elimination pathway if the bisallylcopper intermediate is formed after oxidative addition of the allylcopper complex to a dienoate. Morken group has reported that allyl-allyl coupling can be promoted by phosphine–Pd complexes via bisallyl–Pd intermediate through selective 3,3'-reductive elimination that has lower barrier compared with 1,1'-reductive elimination.[5] Selective allyl 1,6-conjugate addition through Cu-catalyzed 3,3'-reductive elimination is unprecedented.[6] Due to the fundamentally unique mechanistic interest and potential synthetic utilities, we hope to take the advantages of the method that generate the allylcopper species in situ to minimize the background reaction and achieve the multicomponent 1,6-conjugate addition efficienctly and stereoselectively.

5.2 Background

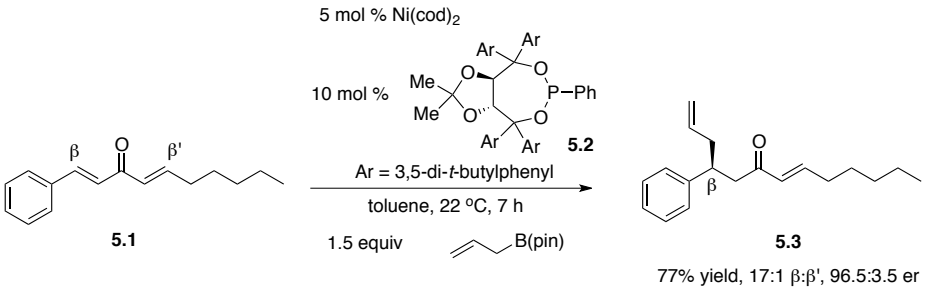
There are few precedents on enantioselective allyl conjugate addition. In 2008, Morken group has developed the first example of Ni-catalyzed allyl conjugate addition to dienone. As shown in Scheme 5.2, reaction of dienone **5.1** with allyl–B(pin) in the presence of a chiral Ni-based catalyst leads to selective addition to styrene to generate **5.2** in 77% yield and 96.5:3.5 enantioselectivity.[2b] The authors proposed the reaction

(5) For Pd-catalyzed allyl–allyl coupling, see: (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) Brozek, L. A.; Ardolino, M. J. Morken, J. P. *J. Am. Chem. Soc.* **2011**, *133*, 16778–16781. (d) Le, H.; Kyne, R. E.; Brozek, L. A.; Morken, J. P. *Org. Lett.* **2013**, *15*, 1432–1435. (e) Le, H.; Batten, A.; Morken, J. P. *Org. Lett.* **2014**, *16*, 2096–2099. (f) Ardolino, M. J.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, *136*, 7092–7100. For Pd-catalyzed allyl–propargyl coupling, see: (g) Ardolino, M. J.; Morken, J. P. *J. Am. Chem. Soc.* **2012**, *134*, 8770–8773.

(6) For Cu-catalyzed allyl–allyl coupling, see: Hornillos, V.; Pérez, M.; Fañanás-Mastral, M.; Feringa, B. L. *J. Am. Chem. Soc.* **2013**, *135*, 2140–2143.

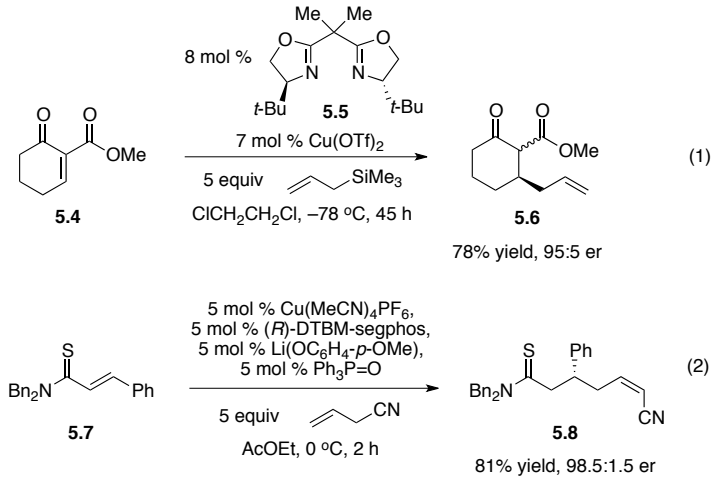
proceeds through a 3,3'-reductive elimination of the bis-allylnickel intermediate mechanism.

Scheme 5.2: Ni-Catalyzed Enantioselective Allyl Conjugate Addition



Subsequently protocols that employ Cu-based catalysts have been reported. As illustrated in Scheme 5.3, with Cu complex derived from $Cu(OTf)_2$ and bisoxazole ligand **5.5**, allyl addition product **5.6** is generated in 78% yield and 95:5 er (eq. 1).[2c] Reaction of allyl cyanide with thioamide 5.7 promoted by phosphine–Cu complex in situ generated from $Cu(MeCN)_4PF_6$ and (*R*)-DTBM-segphos provide 5.8 in 81% yield and 98.5:1.5 er (eq. 2).[2d]

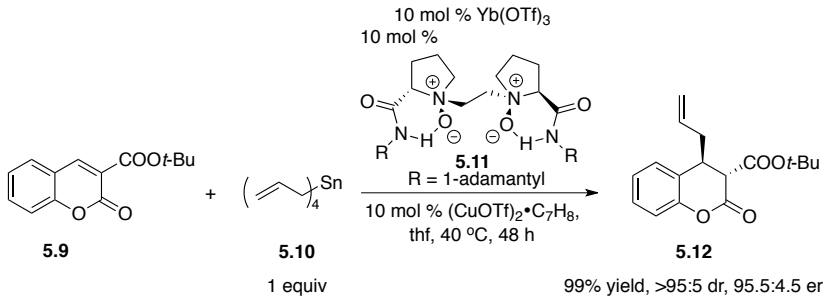
Scheme 5.3: Cu-Catalyzed Enantioselective Allyl Conjugate Addition



In 2011, Feng and co-workers reported a process catalyzed by a chiral rare earth metal complex. Reaction of coumarin **5.9** with allylstannane **5.10** in the presence of Yb-

based complex formed from ligand **5.11** affords **5.12** in 99% yield and 95.5:4.5 with complete diastereoselectivity.[2e]

Scheme 5.4: Yb-Catalyzed Enantioselective Allyl Conjugate Addition

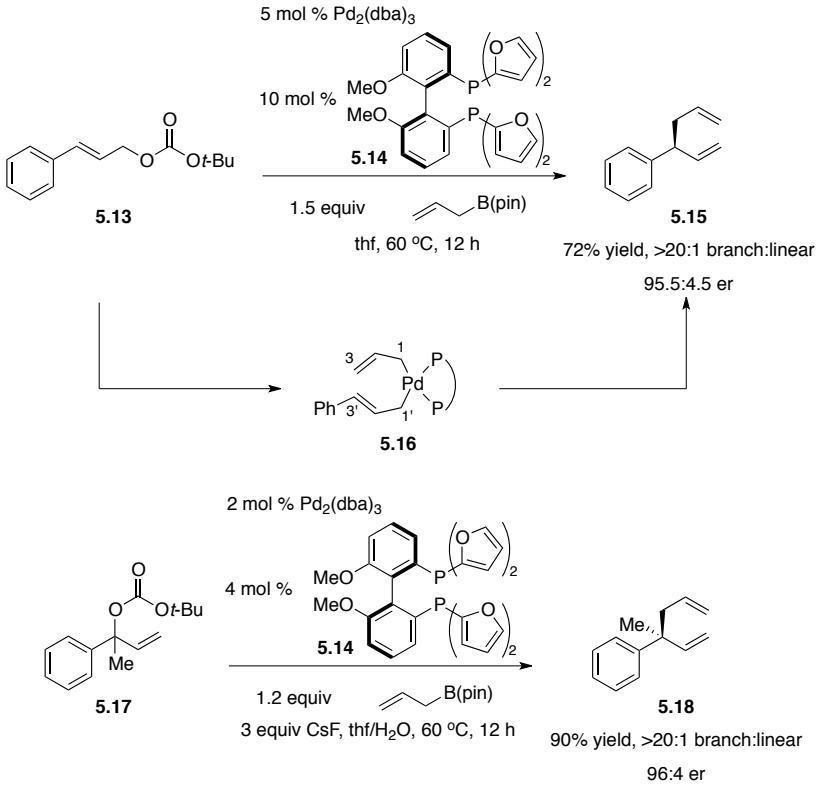


However, although significant progresses have been made, catalytic enantioselective allyl conjugate addition suffers from limited substrate scope, long reaction time and high catalyst loading. Only simple allyl groups can be transferred into the final products. Catalytic enantioselective conjugate additions with functionalized allyl and other allyl-type nucleophiles are unprecedented.

Metal-catalyzed enantioselective allyl–allyl cross-couping reactions through a 3,3'-reductive elimination mechanism have been investigated by Morken and co-workers.[5] They have demonstrated that efficient, branch-selective and enantioselective formation of allyl–allyl product **5.15** from allyl carbonate **5.13** and allyl–B(pin) is promoted by phosphine–Pd complex derived from $Pd_2(dba)_3$ and chiral bisphosphine **5.14** (Scheme 5.5). They proposed that the reaction proceeds via bis(allyl)palladium intermediate **5.16** through 3,3'-reductive elimination.[5a] Subjection of carbonate **5.17** to similar reaction condition leads to product **5.18** that contains a all-carbon quaternary center in 90% yield, >20:1 branch selectivity and 96:4 er.[5b] Subsequently, they also demonstrated that 2- and 3-substituted allyl–B(pin) reagents can be coupled with allyl

chloride and carbonate efficiently and stereoselectively.[5c–f] Propargyl carbonates are also proved to be suitable substrate to access 1,5-enynes.[5g]

Scheme 5.5: Pd-Catalyzed Allyl–Ally Cross-Coupling through 3,3'-Reductive Elimination



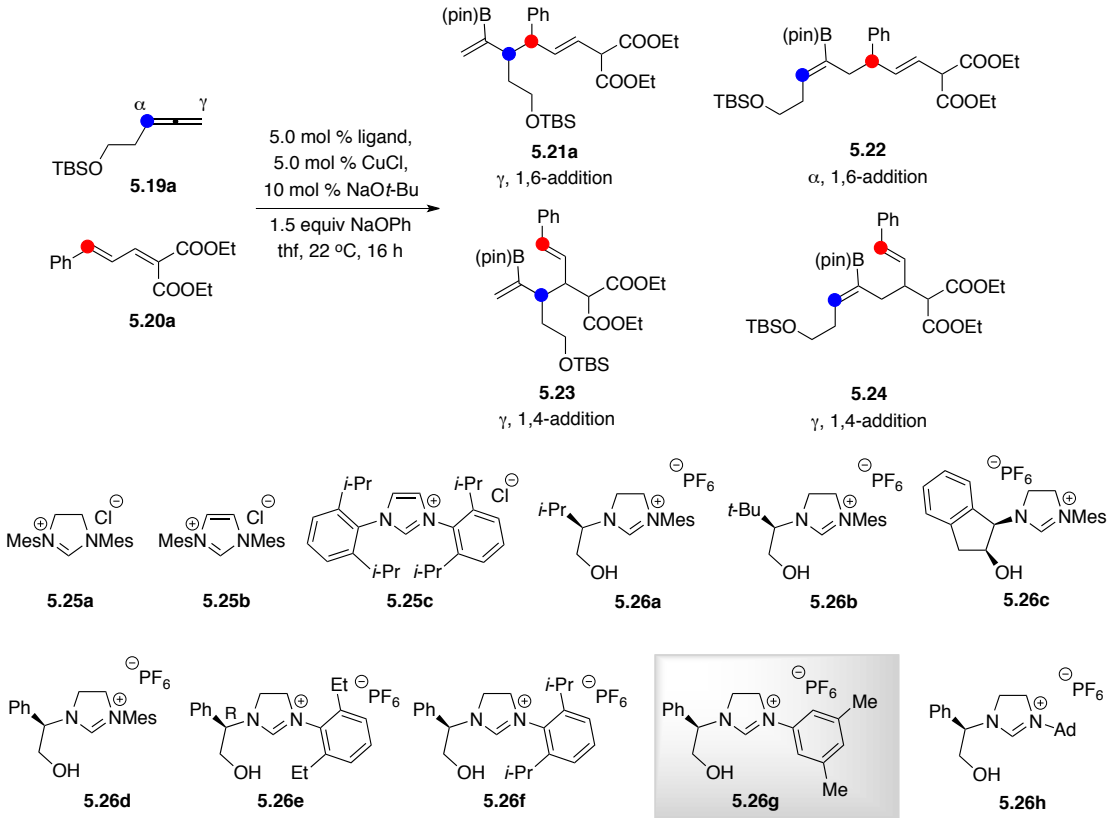
Although significant progress have been made in allyl type cross-coupling reactions through metal-catalyzed 3,3'-reductive elimination, such concept has never been applied to copper catalysis. We hope to design and investigate a set of reactions that might provide otherwise difficult-to-access building blocks based on this conceptually new mechanism.

5.3 Identification of Optimal Catalyst for Cu–B Addition to Allene Followed by 1,6-Conjugate Addition

We began our investigation by examination of a variety of NHC–Cu complexes. As shown in Table 5.1, to our delight, reactions of mono-substituted allene **5.19a** and dienoate **5.20a** in the presence of Cu complexes in situ generated from achiral imidazolinium salts provide desired 1,6-addition product with γ mode of addition exclusively and complete diastereoselectivity albeit in low efficiency (29-40% yield, entries 1-3, Table 5.1). Other possible products **5.22**-**5.24** are not detected, implying that reaction proceeds exclusively through 3,3'-reductive elimination of bis(allyl)copper intermediate (**v**, Scheme 5.1) and possible alternative reaction pathways do not occur. Low yields of the multicomponent process arise from competitive boron 1,4-addition, resulting in diminished chemoselectivity. NHC–Cu complex bearing sterically more congested 2,6-diisopropylphenyl moiety provide higher chemoselectivity (entry 3 vs. entries 1 and 2, Table 5.1), probably because coordination of less hindered allene is more favored with sterically more hindered metal center. Having established that 1,6-conjugate addition product can be formed selectively via a bis(allyl)copper species generated by NHC–Cu-catalyzed Cu–B addition to allene followed by 1,4-oxidative addition to dienoate, we turned our attention to investigation of chiral NHC ligands for enantioselective version of such process. Promising results are obtained with NHC–Cu complexes derived from aminoalcohol-containing imidazolinium salts. As indicated in Table 5.1, although valinol- and *cis*-1-amino-2-indanol-derived catalysts provide 1,6-conjugate addition product **5.21a** in 55% and 49% yield respectively with 81:19 er and complete diastereoselectivity (entries 4 and 6), reactions promoted by Cu complexes in situ generated from imidazolinium salts bearing *tert*-leucinol- and phenylglycinol afford **5.21a** in 63% and 58% yield with 92:8 and 89:11 er respectively as a single diastereomer

(entries 5 and 7). To further improve enantioselectivity, modifications of the aniline moiety on the imidazolinium salts are investigated. Increasing the sterically hindrance of 2,6-substituents leads to erosion of enantioselectivity (entry 9 vs. entries 7 and 8). Moving substituents from *ortho*-positions to *meta*-positions results in improvement of enantioselectivity (62% yield, 96:4 er; entry 10 vs. entry 7).

Table 5.1: Ligand Screen for Cu–B Addition to Allene/1,6-Conjugate Addition



Entry number	Ligand precursor	Conversion (%)[b]; Yield of **5.21a** (%)[c]	Site Selectivity (**5.21a**:**5.22**:**5.23**:**5.24**)[b]	Diastereomeric ratio of **5.21a**[b]	Enantiomeric ratio for **5.21a**[d]
1	**5.25a**	>98; 29	>98:<2:<2:<2	>98:2	NA
2	**5.25b**	>98; 29	>98:<2:<2:<2	>98:2	NA
3	**5.25c**	>98; 40	>98:<2:<2:<2	>98:2	NA
4	**5.26a**	>98; 55	>98:<2:<2:<2	>98:2	81:19
5	**5.26b**	>98; 63	>98:<2:<2:<2	>98:2	92:8
6	**5.26c**	>98; 49	>98:<2:<2:<2	>98:2	81:19
7	**5.26d**	>98; 58	>98:<2:<2:<2	>98:2	89:11
8	**5.26e**	>98; 64	>98:<2:<2:<2	>98:2	90:10
9	**5.26f**	>98; 57	>98:<2:<2:<2	>98:2	75:25
10	**5.26g**	>98; 62	>98:<2:<2:<2	>98:2	96:4
11	**5.26h**	>98; 56	>98:<2:<2:<2	>98:2	80:20

[a] Performed under N_2 atm. [b] Determined by analysis of 400 MHz ^{1}H NMR spetra of unpurified mixtures (±2%). [c] Yields of isolated/purified products (±5%; both isomers). [d] Enantiomeric ratio (e.r.) determined by HPLC analysis (±2%). NA = Not Available.

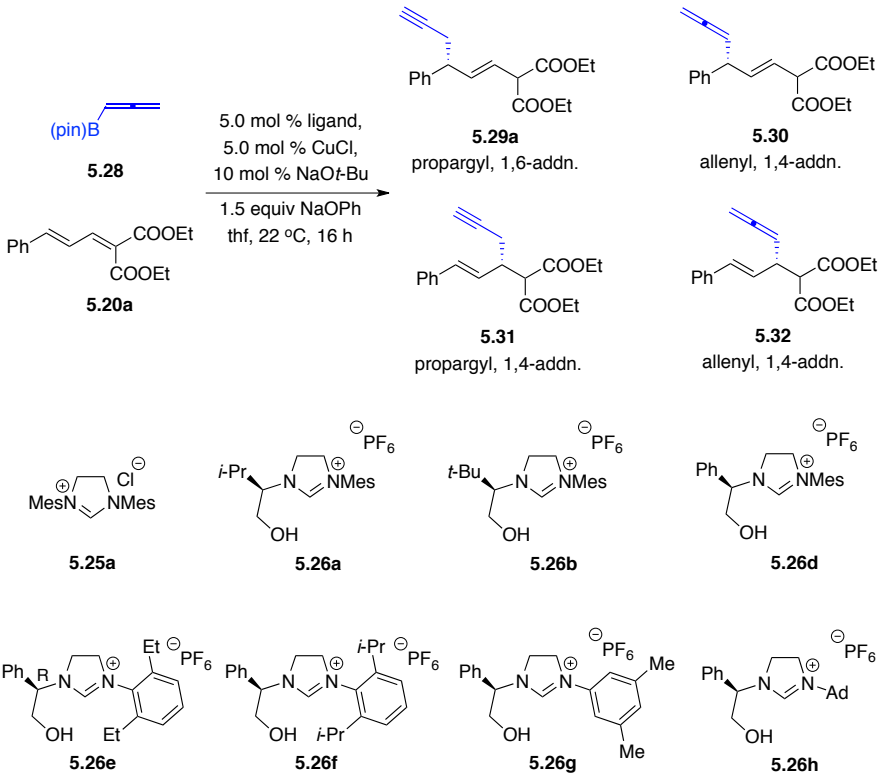
5.4 Identification of Optimal Catalyst for NHC–Cu-Catalyzed Propargyl 1,6-Conjugate Addition with Allenyl–B(pin)

Having identified the optimal catalyst for multicomponent Cu–B addition to allene followed by allyl 1,6-conjugate addition, we are curious whether the bis(allyl)copper intermediate can be generated from corresponding two-component process and undergo 3,3'-reductive elimination selectively, so that a variety of allyl groups with different substituted patterns can be transferred into the products from corresponding substituted allyl–B(pin) reagents. In addition, incorporation of other allyl-type groups such as allenyl and propargyl from proparyl–B(pin) and allenyl–B(pin) into the Cu(III) intermediate (**v**, Scheme 5.1) provide new opportunities to access propargyl and allenyl 1,6-conjugate addition products.

We commenced our study with investigation on reactions with allenyl–B(pin) as the nucleophile. As expected, propargyl 1,6-conjugate addition product **5.29a** is formed in 64% yield exclusively in the presence of NHC–Cu complex derived from imidazolinium salt **5.25a** (Table 5.2, entry 1), implying that the Cu(III) intermediate generated from transmetallation of allenyl–B(pin) reagent **5.28** followed by oxidative addition to the dienoate **5.20a** undergoes 3,3'-reductive elimination selectively. Other possible products **5.30**–**5.32** are not observed. Similar with the multicomponent protocol (Table 5.1), NHC–Cu complexes derived from aminoalcohols provide high enantioselectivity. Reaction with Cu complex in situ generated from imidazolinium salt **5.26d** affords desired product with higher enantioselectivity compared with those derived from imidazolinium salts **5.26a**-**b** bearing valinol and *tert*-leucinol moieties (97.5:2.5 er vs. 91:9 and 93:7 er; entry 4 vs. entries 2 and 3). Increasing the steric hindrance of the *ortho*-substituents leads to erosion of enantioselectivity (entry 6 vs. entries 4 and 5). Reaction in the presence of Cu complex formed from imidazolinium salt **5.26g** that

contains 3,5-substituents delivers **5.29a** in 77% yield and 92:8 er (entry 7), whereas NHC–Cu complex generated from imidazolinium salt **5.26h** bearing an adamantly substituent provides 97.5:2.5 er (entry 8).

Table 5.2: Ligand Screen for NHC–Cu-Catalyzed Propargyl 1,6-Conjugate Addition



Entry number	Ligand precursor	Conversion (%)[b]; Yield of **5.29a** (%)[c]	Site Selectivity (**5.29a**:**5.30**:**5.31**:**5.32**)[b]	Enantiomeric ratio for **5.29a**[d]
1	**5.25a**	>98; 64	>98:<2:<2:<2	NA
2	**5.26a**	>98; 69	>98:<2:<2:<2	91:9
3	**5.26b**	>98; 71	>98:<2:<2:<2	93:7
4	**5.26d**	>98; 74	>98:<2:<2:<2	97.5:2.5
5	**5.26e**	>98; 72	>98:<2:<2:<2	96.5:3.5
6	**5.26f**	>98; 63	>98:<2:<2:<2	67.5:32.5
7	**5.26g**	>98; 77	>98:<2:<2:<2	92:8
8	**5.26h**	>98; 71	>98:<2:<2:<2	97.5:2.5

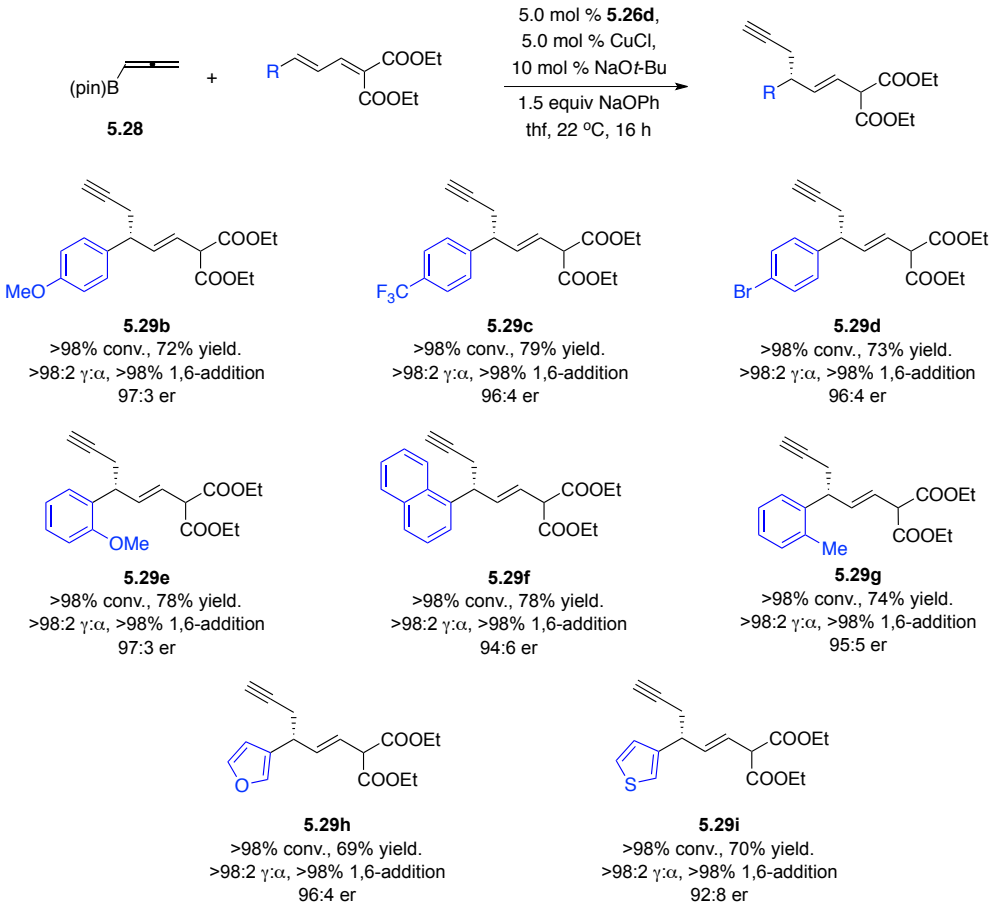
[a] Performed under N_2 atm. [b] Determined by analysis of 400 MHz ^{1}H NMR spetra of unpurified mixtures (±2%). [c] Yields of isolated/purified products (±5%; both isomers). [d] Enantiomeric ratio (e.r.) determined by HPLC analysis (±2%). NA = Not Available.

5.5 Scope for NHC–Cu-Catalyzed Propargyl 1,6-Conjugate Addition with Allenyl–B(pin)

Having identified that NHC–Cu complexes derived from both imidazolinium salts **5.26d** and **5.26h** deliver the best enantioselectivity for propargyl 1,6-conjugate addition, we chose **5.26d** as the optimal ligand due to the lower cost of 2,4,6-trimethylaniline starting material to prepare the ligand compared with 1-adamantylamine and investigated the substrate scope. As indicated in Scheme 5.6, dienoates bearing electron-donating (**5.29b** and **5.29e**) and electron-withdrawing (**5.29c**-**d**) groups are suitable substrates. Halogen substituents are well tolerated (**5.29d**). Reactions of dienoates that contain sterically congested substituents afford desired products in high efficiency and selectivity (**5.29e**-**g**; 74-78% yield, 94:6-97:3 er). Products that contain furyl and thienyl substituents are generated in 69% and 70% yield with 96:4 and 92:8 er respectively (**5.29h**-**i**).

We then turned our attention to reactions with alkyl-substituted dienoates. However, preparation of such class of substrates is not trivial. Employment of the method (Knoevenagel condensation between α,β-unsaturated aldehydes and diethyl malonate) used for synthesis of aryl-substituted dienoates results in either formation of a complex mixture for primary alkyl-substituted α,β-unsaturated aldehydes due to enolization and self-condensation, or <2% conversion of starting materials for α,β-unsaturated aldehydes bearing α-substituents due to steric hindrance and low electrophilicity. The limitation of state-of-the-art synthesis of dienoates prompts us to develop a new way to access this class of building blocks, broadening their scope in organic synthesis.

Scheme 5.6: Substrate Scope for Enantioselective Propargyl 1,6-Conjugate Addition with Aryl-Substituted Dienoates



5.29b
>98% conv., 72% yield.
>98:2 γ:α, >98% 1,6-addition
97:3 er

5.29c
>98% conv., 79% yield.
>98:2 γ:α, >98% 1,6-addition
96:4 er

5.29d
>98% conv., 73% yield.
>98:2 γ:α, >98% 1,6-addition
96:4 er

5.29e
>98% conv., 78% yield.
>98:2 γ:α, >98% 1,6-addition
97:3 er

5.29f
>98% conv., 78% yield.
>98:2 γ:α, >98% 1,6-addition
94:6 er

5.29g
>98% conv., 74% yield.
>98:2 γ:α, >98% 1,6-addition
95:5 er

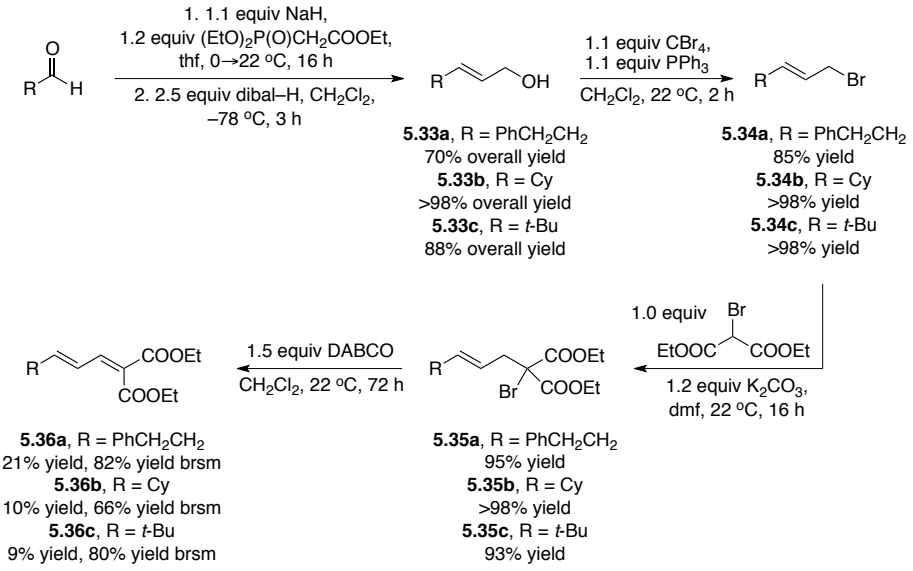
5.29h
>98% conv., 69% yield.
>98:2 γ:α, >98% 1,6-addition
96:4 er

5.29i
>98% conv., 70% yield.
>98:2 γ:α, >98% 1,6-addition
92:8 er

We envisioned that in addition to Knoevenagel condensation, base-mediated elimination of the corresponding diethyl α-bromo-α-allylmalonates might afford the dienoates. The challenge is that the products are sensitive to strong base, which might induce retro-condensation and lead to decomposition of the dienoates. Proper choice of base is essential to achieve product formation without decomposition. Investigation on this strategy is shown in Scheme 5.7. The precursors (**5.35a**-**c**) for elimination are accessed in high efficiency (93%->98% yield) by alkylation of commercially available diethyl bromomalonate with corresponding allyl bromides, which are prepared through Horner-Wadsworth-Emmons reaction and 1,2-reduction with diisobutylaluminum hydride followed by bromination with CBr_4 and PPh_3. Careful screen of bases leads us to

identify DABCO as the optimal choice, which is basic enough to deprotonate the diethyl α-bromo-α-allylmalonates, but not too basic to cause decomposition. Triethylamine is too weak for deprotonation, resulting in no reaction, while DBU is too strong, causing decomposition of the products. Although the elimination process is low yielding (9%-22% yield), especially with sterically congested cyclohexyl- and *tert*-butyl-substituents (**5.36b-c**), the starting materials can be recovered easily in high yield (66%-82% yield). One significant attribute for this route is that all starting materials are commercially available and inexpensive. In addition, each step can be conducted in multi-gram scale.

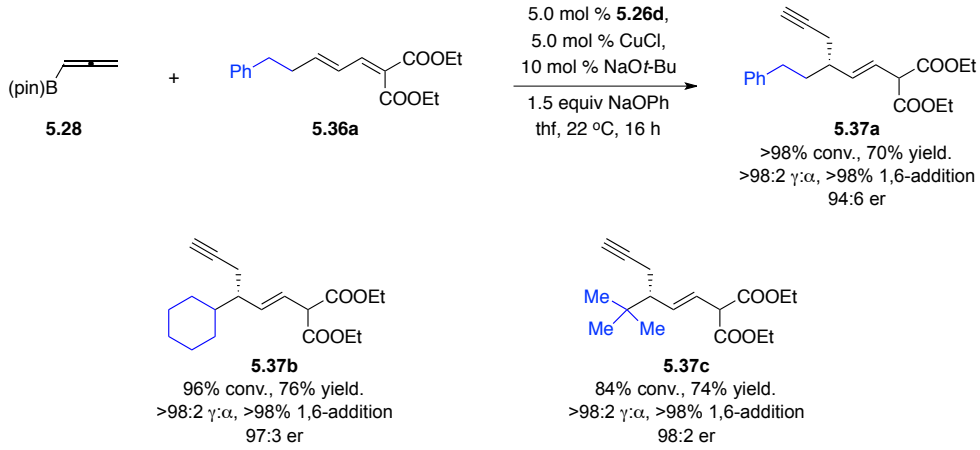
Scheme 5.7: Development of New Synthetic Route for Alkyl-Substituted Dienoates



With alkyl-substituted dienoates in hand, we explored the NHC–Cu-catalyzed enantioselective propargyl 1,6-conjugate addition. Reaction of dienoate **5.36a** in the presence of Cu complex derived from imidazolinium salt **5.26d** affords desired 1,6-addition product **5.37a** in 70% yield and 94:6 er (Scheme 5.8). Sterically more congested cyclohexyl- and *tert*-butyl-substituted dienoates also react in high efficiency and enantioselectivity (**5.37b**, 76% yield, 97:3 er; **5.37c**, 74% yield, 98:2 er). In all cases, only

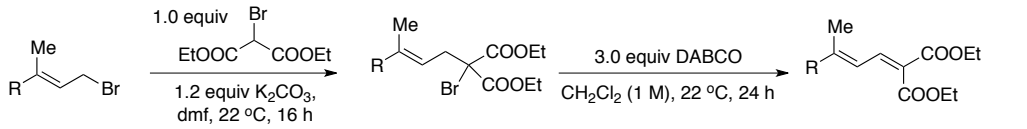
1,6-conjugate addition products are detected, implying 3,3'-reductive elimination pathway is energetically most favored. Even with sterically bulky substrate **5.36c** containing *tert*-butyl group, <2% conversion to 1,1'-reductive elimination product is observed and addition at the congested 6-position occurs exclusively.

Scheme 5.8: Substrate Scope for Enantioselective Propargyl 1,6-Conjugate Addition with Alkyl-Substituted Dienoates



Based on our mechanistic rationale presented in Scheme 5.1, the stereochemical determining step is 1,4-oxidative addition of Cu(I) complex to the dienoate. Thus the enantioselectivity is not sensitive to the substitution patterns at 6-position. We envisioned that similarly high enantioselectivity might be achieved if an additional substituent is incorporated into 6-position of the dienoate, resulting in formation of all-carbon quaternary stereogenic centers. To test this hypothesis, we commenced our investigation with preparation of the substrates. One drawback in the alkyl-substituted dienoates synthesis is low yielding in the elimination step, especially for the sterically congested cyclohexyl- and *tert*-butyl-substituted substrates. We further optimized this step by increasing the reaction concentration and equivalents of base. To our delight, with shorter reaction time, much higher yields of the dienoates are isolated (Scheme 5.9).

Scheme 5.9: Synthesis of Dienoates for Formation of All-Carbon Quaternary Stereogenic Centers

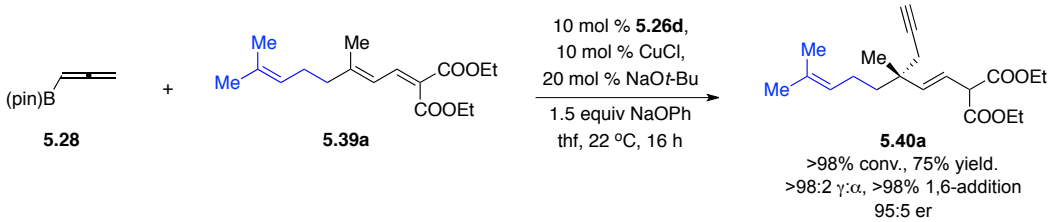


5.38a, R = $Me_2C{=}CHCH_2CH_2$
94% yield
5.38b, R = Ph
99% yield
5.38c, R = 2-naphthyl
97% yield

5.39a, R = $Me_2C{=}CHCH_2CH_2$
65% yield
5.39b, R = Ph
75% yield
5.39c, R = 2-naphthyl
96% yield

With an efficient method to access the substrates in hand, we began to test the Cu-catalyzed enantioselective 1,6-conjugate addition. As illustrated in Scheme 5.10, in the presence of 10 mol % NHC–Cu complex derived from imidazolinium salt **5.26d**, the reactions proceed with high efficiency (73%-80% yield) and enantioselectivity (95:5 er). Alkyl- and aryl-substituted dienoates are suitable substrates. Interestingly even with these sterically congested dienoates, <2% 1,4-reductive elimination products are observed. Another reason for efficient formation of all-carbon quaternary center is that such event occurs intramolecularly via the Cu(III) intermediate (**v**, Scheme 5.1). This conceptually new protocol provides a mechanistically unique way to construct such stereogenic centers.

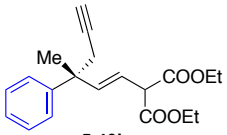
Scheme 5.10: NHC–Cu-Catalyzed Enantioselective 1,6-Conjugate Addition for Formation of All-Carbon Quaternary Centers



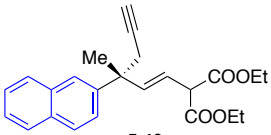
5.28

5.39a

5.40a
>98% conv., 75% yield.
>98:2 γ:α, >98% 1,6-addition
95:5 er



5.40b
>98% conv., 73% yield.
>98:2 γ:α, >98% 1,6-addition
95:5 er



5.40c
>98% conv., 80% yield.
>98:2 γ:α, >98% 1,6-addition
95:5 er

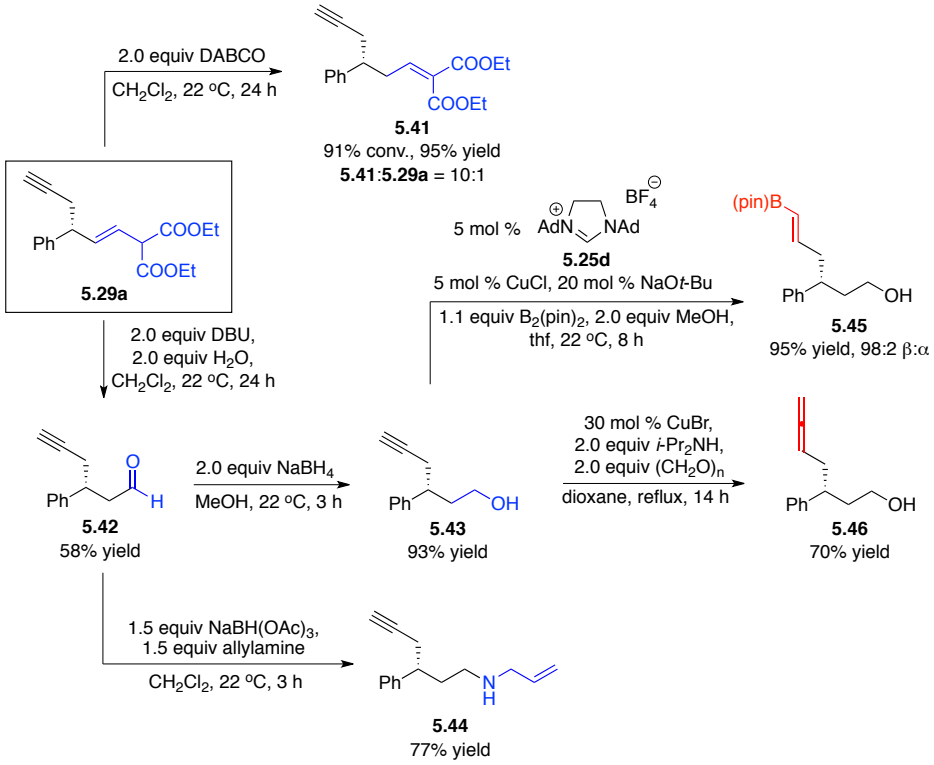
5.6 Functionalization of NHC–Cu-Catalyzed Enantioselective Propargyl 1,6-Conjugate Addition Products

The products generated from NHC–Cu-catalyzed enantioselective propargyl 1,6-conjugate addition contain a terminal alkyne moiety and an alkenylmalonate moiety. Selective functionalization of each functional group provides access to a variety of synthetically useful building blocks that are otherwise difficult-to-access. First we investigated isomerization of the alkene to conjugation. Interestingly we found that treatment of **5.29a** with DBU results in isomerization of the double bond followed by water conjugate addition and retro-aldol reaction, delivering aldehyde **5.42** in 58% overall yield (Scheme 5.9). The aldehyde **5.42** is the product of enantioselective propargyl 1,4-conjugate addition to α,β-unsaturated aldehyde, a process that is so far unprecedented. The screening of a variety of organic bases prompts us to identify DABCO as a suitable base to induce the isomerization without decomposition of the product. Other alternatives are also effective; Subjection of **5.29a** to triethylamine and dimethylaminopyridine (DMAP) in CH_2Cl_2 result in 91% conversion to **5.41** in 95% yield of a 10:1 mixture of **5.41** and **5.29a**. Ratio of **5.41** and **5.29a** keeps unchanged regardless of which base is used, suggesting that a thermodynamic equilibrium between them has been reached. The aldehyde moiety in **5.42** can be converted to alcohol **5.43** and amine **5.44** in high yield.[7] The alkyne moiety of **5.43** can also be transformed to useful functional groups. Treatment of **5.43** with NHC–Cu complex derived from imidazolinium salt **5.25d** affords alkenylboron **5.45** in 95% yield and 98% β-selectivity.[8] In addition,

(7) Graham, T. H.; Jones, C. M.; Jui, N. T.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2008**, *130*, 16494–16495.
(8) Jang, H.; Zhugralin, A. R.; Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 7859–7871.

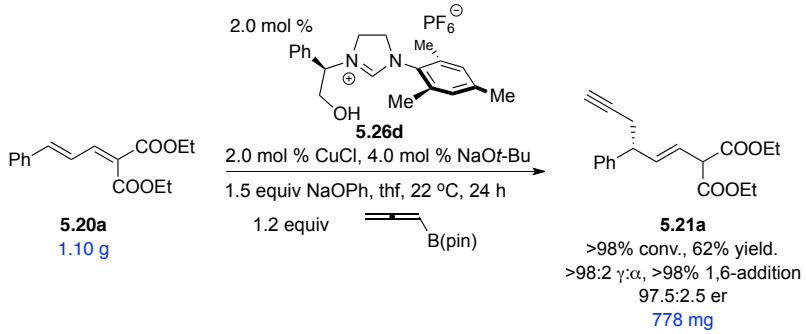
Crabbé homologation of terminal alkyne generates mono-substituted allene **5.46** in 70% yield, which can be further converted to a variety of enantiomerically enriched alkenylboron compounds.[4]

Scheme 5.11: Functionalization of the Enantioselective 1,6-Conjugate Addition Products



The NHC–Cu-catalyzed protocol can be conducted in gram scale, demonstrating the potential utility in organic synthesis. As shown in Scheme 5.10, reaction of 1.10 g dienoate **5.20a** with 1.2 equivalent of allenylboronic acid pinacol ester in the presence of 2.0 mol % NHC–Cu complex in situ generated from imidazolinium salt **5.26d** delivers 778 mg desired product **5.21a** in 62% yield and 97.5:2.5 er.

Scheme 5.12: NHC–Cu-Catalyzed Enantioselective Propargyl 1,6-Conjugate Addition in Gram Scale



5.7 Conclusion

In this chapter, we have described a conceptually new set of NHC–Cu-catalyzed enantioselective 1,6-conjugate addition reactions that incorporate allyl-type groups (such as allyl groups with different substitution patterns, propargyl and allenyl groups). The transformations promoted by NHC–Cu complexes derived from an easily accessible class of imidazolinium salts proceed through 3,3'-reductive elimination of the bis(allyl)copper(III) intermediates. Aryl- and alkyl-substituted dienoates are suitable substrates. The scope of accessible substrates is expended by development of a new route for their preparation. Functionalization of the products results in a variety of synthetically useful building blocks that are otherwise difficult-to-access. Furthermore, identification of this mechanistically unique class of highly selective 1,6-conjugate additions opens up opportunities for further development of such reactions with new allyl-type reagents.

5.8 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). ^{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, br s = broad singlet, m = multiplet, app. = apparent), and coupling constant (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. Enantiomer ratios were determined by high-performance liquid chromatography (HPLC) with a Shimadzu chromatograph (Chiral Technologies Chiralcel OD-H (4.6 x 250 mm), Chiralcel OJ-H (4.6 x 250 mm), Chiralcel OZ-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. Solvents were purified under a positive pressure of dry argon by a modified Innovative Technologies purification system: toluene, benzene and hexanes were purified through a copper oxide and alumina column; CH_2Cl_2 and Et_2O were purged with Ar and purified by passage through two alumina columns. Tetrahydrofuran (Aldrich Chemical Co.) was purified by distillation from sodium benzophenone ketyl immediately prior to use unless otherwise specified. Methanol

(Aldrich Chemical Co.) was distilled over CaH_2. All work-up and purification procedures were carried out with reagent grade solvents (purchased from Fisher Scientific) in air.

5.8.1 Reagents and Ligands

Allenes (5.19a): prepared according to previously reported procedures.[9]

Allenylboronic acid pinacol ester: purchased from Aldrich Chemical Co. and used as received.

Allylamine: purchased from Aldrich Chemical Co. and used as received.

Aryl-substituted dienoates: prepared according to previously reported procedures.[10]

Bis(pinacolato)diboron: purchased from Frontier Scientific, Inc. and recrystallized from pentane.

Copper bromide: purchased from Strem Chemicals Inc. and used as received.

Copper chloride: purchased from Strem Chemicals Inc. and used as received.

Cyclohexanecarboxaldehyde: purchased from Aldrich Chemical Co. and used as received.

1,4-Diazabicyclo[2.2.2]octane (DABCO): purchased from Aldrich Chemical Co. and used as received.

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(9) (a) Crabbé, P.; Fillion, H.; André, D.; Luche, J-L. *J. Chem. Soc., Chem. Commun.* **1979**, 859–860. (b) Searles, S.; Li, Y.; Nassim, B.; Lopes, M-T. R.; Tran, P. T.; Crabbé, P. *J. Chem. Soc., Perkin Trans. 1*, **1984**, 747–751. (c) Inoue, A.; Kondo, J.; Shinokubo, H.; Oshima, K. *Chem. Eur. J.* **2002**, *8*, 1730–1740. (d) Baird, M. S.; Nizovtsev, A. V.; Bolesov, I. G. *Tetrahedron* **2002**, *58*, 1581–1593.
(10) Liu, L.; Sarkisian, R.; Xu, Z.; Wang, H. *J. Org. Chem.* **2012**, *77*, 7693–7699.

1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU): purchased from Aldrich Chemical Co. and used as received.

Diethyl bromomalonate: purchased from Alfa Aesar Co. and used as received.

Diisobutylaluminum hydride (dibal–H): purchased from Aldrich Chemical Co. and used as received.

Hydrocinnamaldehyde: purchased from Aldrich Chemical Co. and used as received.

Imidazolinium salts 5.25a-d: purchased from Aldrich Chemical Co. and used as received.

Imidazolinium salts 5.25a-d: prepared according to previously reported procedures.[4c]

***N*,*N*-Diisopropylamine:** purchased from Aldrich Chemical Co. and used as received.

***N*,*N*-Dimethylformamide:** purchased from Aldrich Chemical Co. and used as received.

Paraformaldehyde: purchased from Aldrich Chemical Co. and used as received.

Potassium carbonate: purchased from Aldrich Chemical Co. and used as received.

Sodium borohydride: purchased from Alfa Aesar Co. and used as received.

Sodium *tert*-butoxide: purchased from Strem Chemicals Inc. and used as received.

Sodium hydride: purchased from Strem Chemicals Inc. and used as received.

Sodium phenoxide: purchased from Alfa Aesar Co. and used as received.

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

Tetrabromomethane: purchased from Aldrich Chemical Co. and used as received.

Triethyl phosphonoacetate: purchased from Aldrich Chemical Co. and used as received.

Trimethylacetaldehyde: purchased from Aldrich Chemical Co. and used as received.

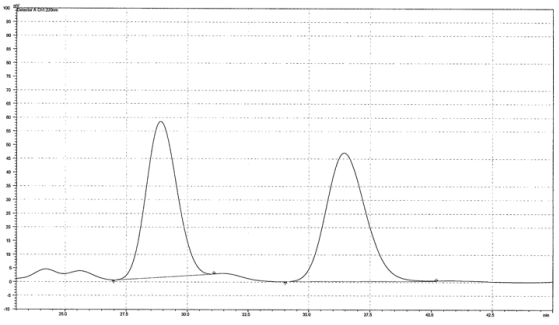
Triphenylphosphine: purchased from Aldrich Chemical Co. and used as received.

5.8.2 Experimental Procedures and Characterization Data for NHC–Cu-Catalyzed Cu–B Addition to Allenes Followed by 1,6-Conjugate Addition

■ **Representative Experimental Procedure for NHC–Cu-Catalyzed Cu–B addition to Allene/1,6-Conjugate Addition.** In a N_2-filled glove box, imidazolinium salt **5.26g** (2.2 mg, 0.0050 mmol), CuCl (0.5 mg, 0.0050 mmol), NaO*t*-Bu (0.9 mg, 0.010 mmol) and NaOPh (17.4 mg, 0.15 mmol) and thf (0.5 mL) are added into an oven-dried vial equipped with a stirring bar. The mixture is allowed to premix for 2 h at 22 ºC. The resulting mixture is then added into a separate oven-dried vial containing bis(pinacolato)diboron (38.1 mg, 0.15 mmol). The vial is sealed with a Teflon screw cap and removed from the glove box. The mixture is allowed to stir at 22 ºC for 30 min. Then allene **5.19a** (29.8 mg, 0.15 mmol) and dienoate **5.20a** (27.4 mg, 0.10 mmol) are added into the solution by syringes. The resulting mixture is allowed to stir at 22 ºC for 16 h. The mixture is filtered through a short plug of Celite and silica gel eluting with diethyl ether. The filtrate is washed with 1M NaOH aqueous solution, dried over $MgSO_4$ and concentrated *in vacuo*. The resulting yellow oil is purified by silica gel chromatography (hexanes:ethyl acetate = 25:1) to obtain 37.4 mg **5.21a** (0.062 mmol, 62% yield) as colorless oil.

(*E*)-Diethyl 2-(4-(2-((*tert*-butyldimethylsilyl)oxy)ethyl)-3-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexa-1,5-dien-1-yl)malonate (5.21a). IR (neat): 3028 (m), 2978 (m), 2955 (m), 2857 (m), 1734 (s), 1417 (m), 1305 (m), 1252 (m), 1141 (s), 1094 (s), 1032 (m), 968 (m), 834 (s), 775 (s), 699 (s), 619 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.21–7.17 (2H, m), 7.10–7.06 (3H, m), 5.80–5.78 (2H, m), 5.63 (1H, d, *J* = 3.2 Hz), 5.32 (1H, d, *J* = 3.6 Hz), 4.21 (2H, q, *J* = 7.2 Hz), 4.13 (2H, q, *J* = 7.2 Hz), 3.99–3.97 (1H, m), 3.63–3.58 (1H, m), 3.55–3.50 (1H, m), 3.44–3.38 (1H, m), 2.60 (1H, td, *J* = 11.2, 2.8 Hz), 1.97–1.88 (1H, m), 1.70–1.61 (1H, m), 1.28 (3H, t, *J* = 7.2 Hz), 1.23 (6H, s), 1.18 (3H, t, *J* = 7.2 Hz), 1.18 (6H, s), 0.88 (9H, s), 0.002 (3H, s), –0.003 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.5, 168.3, 143.7, 139.6, 132.2, 128.5, 128.3, 126.0, 122.4, 83.2, 61.8, 61.7, 61.6, 55.8, 53.5, 48.2, 35.0, 26.1, 25.0, 24.8, 18.4, 14.2, 14.1, –5.12, –5.11; HRMS (ESI+): Calcd for $C_{33}H_{54}B_1O_7Si_1$ $[M+H]^+$: 601.37318 m/z, Found: 601.37467 m/z.

Enantiomeric purity of **5.21a** was determined by HPLC analysis in comparison with authentic racemic material (96:4 e.r. shown; Chiralcel OZ–H column, 99.9:0.1 hexanes/*i*PrOH, 0.8 mL/min, 220 nm). Specific rotation: $[\alpha]_D^{20}$ –10.6 (*c* 1.56, $CHCl_3$).



Peak#	Ret. Time	Area	Height	Area %	Height %
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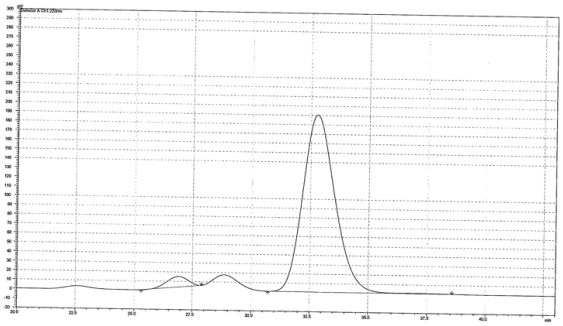
2	36.440	5261123	46901	49.942	44.712



Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.905	693529	11232	3.668	5.584
2	32.781	18213360	189912	96.332	94.416

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)

1	28.882	50.058	1	26.905	3.668
2	36.440	49.942	2	32.781	96.332

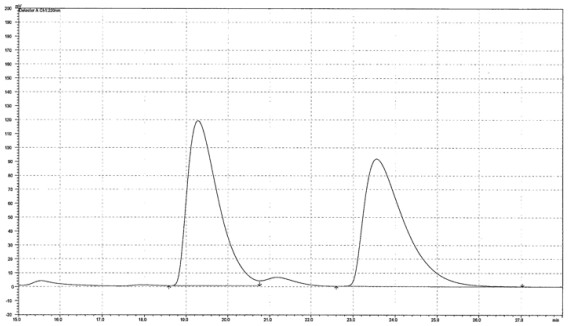
5.8.3 Experimental Procedures and Characterization Data for NHC–Cu-Catalyzed Enantioselective Propargyl 1,6-Conjugate Addition for Formation of Tertiary Centers

■ **Representative Experimental Procedure for NHC–Cu-Catalyzed Enantioselective Propargyl 1,6-Conjugate Addition.** In a N_2-filled glove box, imidazolinium salt **5.26d** (2.3 mg, 0.0050 mmol), CuCl (0.5 mg, 0.0050 mmol), NaO*t*-Bu (0.9 mg, 0.010 mmol) and NaOPh (17.4 mg, 0.15 mmol) and thf (0.5 mL) are added into an oven-dried vial equipped with a stirring bar. The mixture is allowed to premix for 2 h at 22 ºC. The resulting mixture is then added into a separate oven-dried vial containing allenylboronic acid pinacol ester (36.0 μL, 0.20 mmol). The vial is sealed with a Teflon screw cap and removed from the glove box. The mixture is allowed to stir at 22 ºC for 30 min. Then dienoate **5.20a** (27.4 mg, 0.10 mmol) is added into the solution by a syringe. The resulting mixture is allowed to stir at 22 ºC for 16 h. The mixture is filtered through a short plug of Celite and silica gel eluting with diethyl ether. The filtrate is washed with 1M NaOH aqueous solution, dried over $MgSO_4$ and concentrated *in vacuo*. The resulting yellow oil is purified by silica gel chromatography (hexanes:ethyl acetate = 20:1) to obtain 23.3 mg **5.29a** (0.074 mmol, 74% yield) as colorless oil.

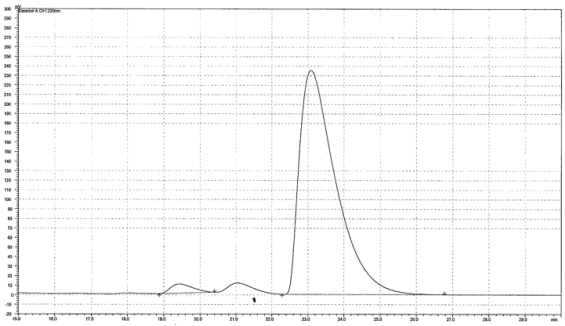
(*R*,*E*)-Diethyl 2-(3-phenylhex-1-en-5-yn-1-yl)malonate (5.29a). IR (neat): 3288 (m), 2982 (m), 2935 (m), 1729 (s), 1601 (w), 1494 (m), 1452 (m), 1368 (m), 1266 (s), 1173 (s), 1030 (s), 970 (m), 863 (m), 700 (s), 637 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.33–7.30 (2H, m), 7.24–7.22 (3H, m), 5.94 (1H, dd, *J* = 15.0, 6.6 Hz), 5.82 (1H, dd, *J* =

15.0, 9.0 Hz), 4.23–4.18 (4H, m), 4.03 (1H, *J* = 9.0 Hz), 3.59 (1H, td, *J* = 7.2, 7.2 Hz), 2.65–2.57 (2H, m), 1.96 (1H, t, *J* = 3.0 Hz), 1.27 (3H, t, *J* = 7.2 Hz), 1.24 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.2, 168.1, 142.1, 137.6, 128.6, 127.8, 127.0, 122.9, 82.1, 70.3, 61.8, 61.7, 55.7, 47.1, 25.4, 14.2, 14.1; HRMS (ESI+): Calcd for $C_{19}H_{23}O_4$ $[M+H]^+$: 315.15963 m/z, Found: 315.16119 m/z. Specific rotation: $[\alpha]_D^{20}$ –4.7 (*c* 0.69, $CHCl_3$).

Enantiomeric purity of **5.29a** was determined by HPLC analysis in comparison with authentic racemic material (97.5:2.5 e.r. shown; Chiralcel OD–H column, 99.5:0.5 hexanes/*i*PrOH, 0.8 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.272	6105575	118616	50.259	56.427
2	23.551	6042610	91594	49.741	43.573



Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.430	410774	9605	2.437	3.928
2	23.078	16447193	234907	97.563	96.072

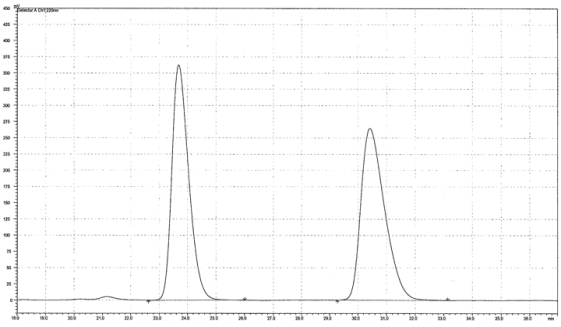
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	19.272	50.259	1	19.430	2.437
2	23.551	49.741	2	23.078	97.563

Proof of Stereochemistry: The corresponding (*R*)-3-phenylhexan-1-ol was obtained after one-pot isomerization and retro-aldol and hydrogenation of the corresponding aldehyde **5.42**. Specific rotation of (*R*)-3-phenylhexan-1-ol: $[\alpha]_D^{20}$ –6.0 (*c* 1.69, $CHCl_3$). Literature value: $[\alpha]_D^{20}$ –6.7 (*c* 2.00, $CHCl_3$).[11]

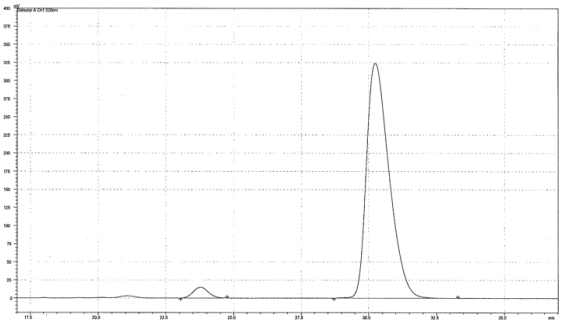
(11) Reyes, E.; Vicario, J. L.; Carrillo, L.; Badía, D.; Uria, U.; Iza, A. *J. Org. Chem.* **2006**, *71*, 7763–7772.

(*R*,*E*)-Diethyl 2-(3-(4-methoxyphenyl)hex-1-en-5-yn-1-yl)malonate (5.29b). IR (neat): 3286 (m), 2982 (m), 2935 (m), 1728 (s), 1610 (m), 1512 (s), 1464 (m), 1246 (s), 1176 (s), 1096 (m), 1030 (s), 971 (m), 830 (m), 640 (m), 545 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.14 (2H, d, *J* = 8.4 Hz), 6.85 (2H, d, *J* = 8.4 Hz), 5.91 (1H, dd, *J* = 15.6, 7.2 Hz), 5.78 (1H, dd, *J* = 15.6, 8.4 Hz), 4.20 (2H, q, *J* = 7.2 Hz), 4.18 (2H, q, *J* = 7.2 Hz), 4.02 (1H, d, *J* = 8.4 Hz), 3.79 (3H, s), 3.55 (1H, td, *J* = 7.2, 6.8 Hz), 2.60–2.56 (2H, m), 1.95 (1H, t, *J* = 2.8 Hz), 1.27 (3H, t, *J* = 7.2 Hz), 1.25 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.3, 168.2, 158.6, 138.0, 134.1, 128.7, 122.6, 114.0, 82.3, 70.3, 61.8, 61.7, 55.7, 55.4, 46.2, 25.5, 14.2, 14.1; HRMS (ESI+): Calcd for $C_{20}H_{25}O_5$ $[M+H]^+$: 345.17020 m/z, Found: 345.17107 m/z. Specific rotation: $[\alpha]_D^{20}$ –10.0 (*c* 1.24, $CHCl_3$).

Enantiomeric purity of **5.29b** was determined by HPLC analysis in comparison with authentic racemic material (97:3 e.r. shown; Chiralcel OZ–H column, 98.5:1.5 hexanes/*i*PrOH, 0.8 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.684	15096524	362409	49.975	57.796
2	30.414	15111662	264640	50.025	42.204



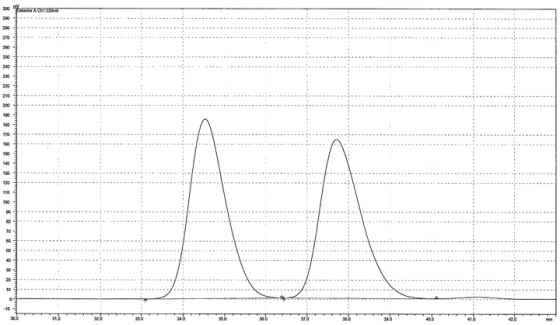
Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.772	574518	14902	2.990	4.399
2	30.233	18642376	323885	97.010	95.601

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	23.684	49.975	1	23.772	2.990
2	30.414	50.025	2	30.233	97.010

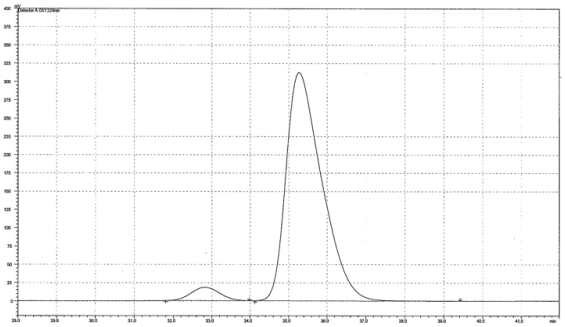
(*R*,*E*)-Diethyl 2-(3-(4-(trifluoromethyl)phenyl)hex-1-en-5-yn-1-yl)malonate (5.29c). IR (neat): 3299 (w), 2984 (w), 2940 (w), 1730 (s), 1619 (w), 1447 (w), 1324 (s), 1269

(m), 1161 (s), 1113 (s), 1067 (s), 1018 (s), 971 (m), 837 (m), 638 (m), 606 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.57 (2H, d, *J* = 8.0 Hz), 7.35 (2H, d, *J* = 8.0 Hz), 5.92 (1H, dd, *J* = 15.6, 6.8 Hz), 5.82 (1H, dd, *J* = 15.6, 8.4 Hz), 4.24–4.16 (4H, m), 4.03 (1H, d, *J* = 8.4 Hz), 2.66 (1H, ddd, *J* = 16.8, 7.2, 2.8 Hz), 1.96 (1H, t, *J* = 2.8 Hz), 1.27 (3H, t, *J* = 6.8 Hz), 1.24 (3H, t, *J* = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.1, 168.0, 146.0, 136.7, 129.3 (q, *J* = 32.6 Hz), 127.9, 125.6 (q, *J* = 3.8 Hz), 124.3 (q, *J* = 270.2 Hz), 123.8, 81.4, 70.9, 61.9, 61.8, 55.6, 46.8, 25.2, 14.2, 14.1; HRMS (ESI+): Calcd for $C_{20}H_{22}F_3O_4$ $[M+H]^+$: 383.14702 m/z, Found: 383.14610 m/z. Specific rotation: $[\alpha]_D^{20}$ –9.5 (*c* 2.16, $CHCl_3$).

Enantiomeric purity of **5.29c** was determined by HPLC analysis in comparison with authentic racemic material (96:4 e.r. shown; Chiralcel OZ–H column, 99.5:0.5 hexanes/*i*PrOH, 0.8 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	34.527	11307932	185229	50.175	53.039
2	37.702	11228926	164005	49.825	46.961



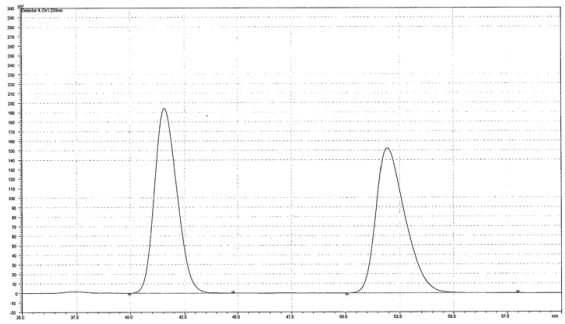
Peak#	Ret. Time	Area	Height	Area %	Height %
1	32.815	874585	17574	4.170	5.334
2	35.266	20098864	311865	95.830	94.666

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	34.527	50.175	1	32.815	4.170
2	37.702	49.825	2	35.266	95.830

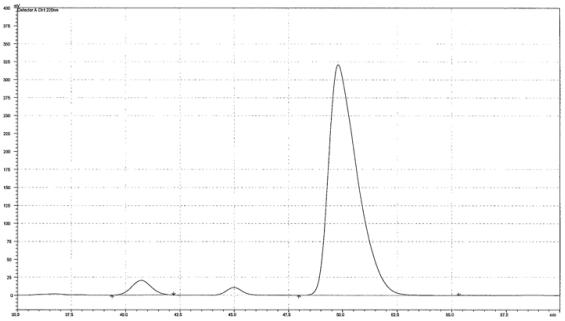
(*R*,*E*)-Diethyl 2-(3-(4-bromophenyl)hex-1-en-5-yn-1-yl)malonate (5.29d). IR (neat): 3297 (w), 2982 (w), 2935 (w), 1728 (s), 1488 (m), 1368 (m), 1264 (m), 1150 (m), 1030 (m), 971 (m), 822 (m), 642 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.43 (2H, d, *J* = 8.4

Hz), 7.11 (2H, d, *J* = 8.4 Hz), 5.89 (1H, dd, *J* = 15.0, 7.2 Hz), 5.79 (1H, dd, *J* = 15.0, 9.0 Hz), 4.21 (2H, q, *J* = 7.2 Hz), 4.18 (2H, q, *J* = 7.2 Hz), 4.02 (1H, d, *J* = 9.0 Hz), 3.55 (1H, td, *J* = 6.6, 7.2 Hz), 2.61 (1H, ddd, *J* = 16.8, 7.2, 2.4 Hz), 1.95 (1H, t, *J* = 2.4 Hz), 1.27 (3H, t, *J* = 7.2 Hz), 1.24 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.1, 168.0, 141.0, 137.1, 131.7, 129.6, 123.4, 120.9, 81.6, 70.7, 61.9, 61.8, 55.6, 46.5, 25.2, 14.2, 14.1; HRMS (ESI+): Calcd for $C_{19}H_{22}Br_1O_4$ $[M+H]^+$: 393.07015 m/z, Found: 393.06864 m/z. Specific rotation: $[\alpha]_D^{20}$ –11.9 (*c* 1.80, $CHCl_3$).

Enantiomeric purity of **5.29d** was determined by HPLC analysis in comparison with authentic racemic material (96:4 e.r. shown; Chiralcel OZ–H column, 99.5:0.5 hexanes/*i*PrOH, 0.8 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	41.563	14035442	194262	49.971	56.045
2	51.939	14051794	152358	50.029	43.955



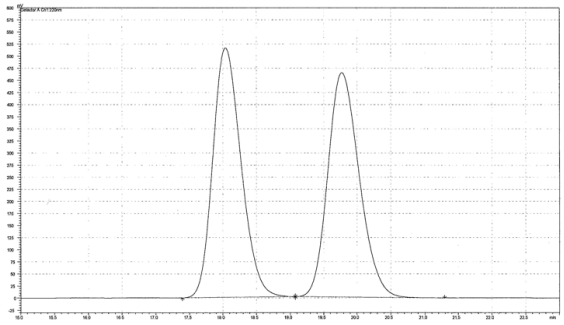
Peak#	Ret. Time	Area	Height	Area %	Height %
1	40.713	1273265	20462	4.156	5.996
2	49.791	29364916	320785	95.844	94.004

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	41.563	49.971	1	40.713	4.156
2	51.939	50.029	2	49.791	95.844

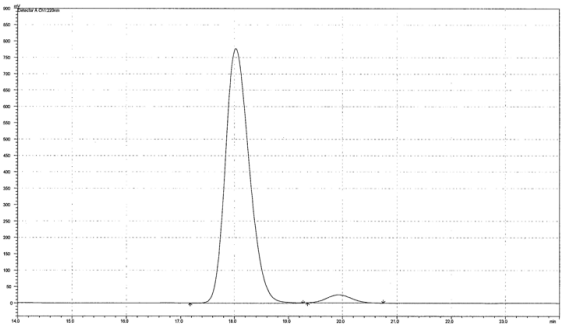
(*R*,*E*)-Diethyl 2-(3-(2-methoxyphenyl)hex-1-en-5-yn-1-yl)malonate (5.29e). IR (neat): 3292 (w), 2982 (w), 2938 (w), 1729 (s), 1599 (w), 1492 (m), 1439 (m), 1240 (s), 1148 (s), 1027 (s), 970 (m), 861 (w), 754 (s), 637 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.21 (1H, td, *J* = 7.8, 1.8 Hz), 7.16 (1H, dd, *J* = 7.8, 1.8 Hz), 6.91 (1H, td, *J* = 7.8, 1.2 Hz), 6.86 (1H, dd, *J* = 7.8, 1.2 Hz), 5.99 (1H, dd, *J* = 15.6, 6.8 Hz), 5.83 (1H, dd, *J* =

15.6, 9.0 Hz), 4.20 (2H, q, *J* = 7.2 Hz), 4.17 (2H, q, *J* = 7.2 Hz), 4.03 (1H, d, *J* = 9.0 Hz), 4.00 (1H, td, *J* = 6.6, 6.6 Hz), 3.82 (3H, s), 2.62–2.60 (2H, m), 1.92 (1H, t, *J* = 3.0 Hz), 1.27 (3H, t, *J* = 7.2 Hz), 1.24 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.3, 168.2, 157.0, 137.0, 130.5, 128.4, 128.0, 122.7, 120.6, 110.8, 82.7, 69.8, 61.7, 61.6, 55.8, 55.5, 40.9, 23.9, 14.2, 14.1; HRMS (ESI+): Calcd for $C_{20}H_{25}O_5$ $[M+H]^+$: 345.17020 m/z, Found: 345.17007 m/z. Specific rotation: $[\alpha]_D^{20}$ –3.9 (*c* 1.69, $CHCl_3$).

Enantiomeric purity of **5.29e** was determined by HPLC analysis in comparison with authentic racemic material (97:3 e.r. shown; Chiralcel OZ–H column, 99:1 hexanes/*i*PrOH, 0.8 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.035	15173222	515519	50.011	52.628
2	19.769	15166318	464026	49.989	47.372



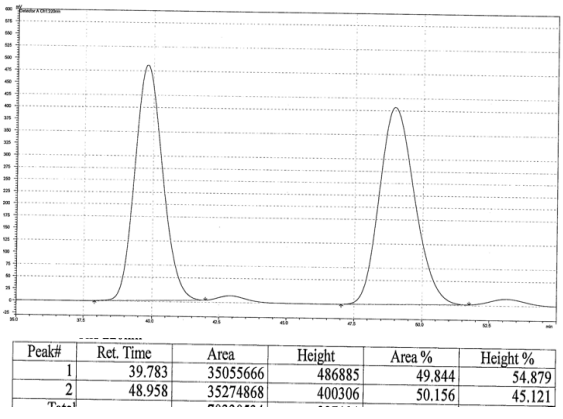
Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.023	23841299	777595	96.791	96.936
2	19.925	790436	24583	3.209	3.064

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	18.035	50.011	1	18.023	96.791
2	19.769	49.989	2	19.925	3.209

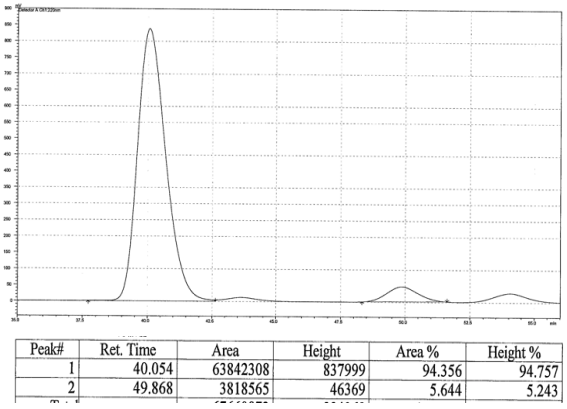
(*R*,*E*)-Diethyl 2-(3-(naphthalen-1-yl)hex-1-en-5-yn-1-yl)malonate (5.29f). IR (neat): 3293 (w), 2982 (w), 2935 (w), 1728 (s), 1368 (m), 1258 (m), 1173 (m), 1095 (m), 1030 (m), 971 (m), 861 (w), 779 (s), 639 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.08 (1H, d, *J* = 8.4 Hz), 7.87 (1H, d, *J* = 8.8 Hz), 7.76 (1H, d, *J* = 8.0 Hz), 7.54–7.39 (4H, m), 6.07 (1H, dd, *J* = 15.6, 6.8 Hz), 5.90 (1H, dd, *J* = 15.6, 8.8 Hz), 4.46 (1H, td, *J* = 6.8, 6.4 Hz), 4.20 (2H, q, *J* = 7.2 Hz), 4.16 (2H, q, *J* = 7.2 Hz), 4.06 (1H, d, *J* = 8.8 Hz), 2.80–2.77

(2H, m), 1.98 (1H, t, *J* = 2.8 Hz), 1.26 (3H, t, *J* = 7.2 Hz), 1.21 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.2, 168.1, 138.0, 137.4, 134.1, 131.4, 129.1, 127.7, 126.2, 125.7, 125.5, 124.5, 123.4, 123.3, 82.3, 70.5, 61.8, 61.7, 55.8, 42.2, 24.8, 14.2, 14.1; HRMS (ESI+): Calcd for $C_{23}H_{25}O_4$ $[M+H]^+$: 365.17528 m/z, Found: 365.17471 m/z. Specific rotation: $[\alpha]_D^{20}$ +23.8 (*c* 1.81, $CHCl_3$).

Enantiomeric purity of **5.29f** was determined by HPLC analysis in comparison with authentic racemic material (94:6 e.r. shown; Chiralcel OZ–H column, 99.5:0.5 hexanes/*i*PrOH, 0.8 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	39.783	35055666	486885	49.844	54.879
2	48.958	35274868	400306	50.156	45.121



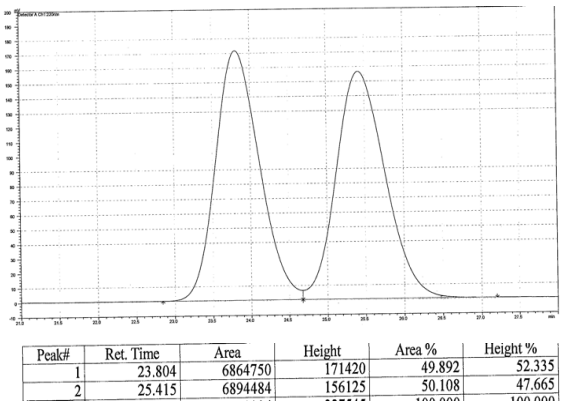
Peak#	Ret. Time	Area	Height	Area %	Height %
1	40.054	63842308	837999	94.356	94.757
2	49.868	3818565	46369	5.644	5.243

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	39.783	49.844	1	40.054	94.356
2	48.958	50.156	2	49.868	5.644

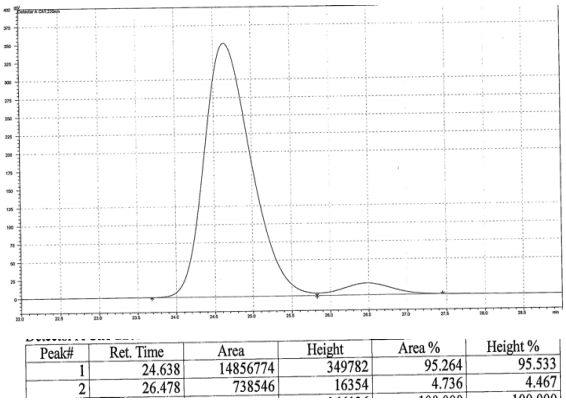
(*R*,*E*)-Diethyl 2-(3-(*o*-tolyl)hex-1-en-5-yn-1-yl)malonate (5.29g). IR (neat): 3288 (m), 2982 (m), 2937 (m), 1729 (s), 1463 (m), 1368 (m), 1265 (s), 1148 (s), 1096 (m), 1029 (s), 970 (m), 863 (m), 757 (m), 638 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.19–7.11 (4H, m), 5.86 (1H, dd, *J* = 15.6, 6.8 Hz), 5.75 (1H, dd, *J* = 15.6, 8.8 Hz), 4.20 (2H, q, *J* = 6.8 Hz), 4.17 (2H, q, *J* = 6.8 Hz), 4.01 (1H, d, *J* = 8.8 Hz), 3.85 (1H, td, *J* = 6.8, 7.2 Hz), 2.63–2.59 (2H, m), 2.35 (3H, s), 1.95 (1H, t, *J* = 2.8 Hz), 1.27 (3H, t, *J* = 6.8 Hz), 1.23 (3H, t, *J* = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.2, 168.1, 140.1, 137.4, 136.2,

130.7, 126.8, 126.5, 126.4, 122.8, 82.3, 70.0, 61.8, 61.7, 55.7, 42.8, 24.5, 19.7, 14.2, 14.1; HRMS (ESI+): Calcd for $C_{20}H_{25}O_4$ $[M+H]^+$: 329.17528 m/z, Found: 329.17450 m/z. Specific rotation: $[\alpha]_D^{20}$ –11.0 (*c* 1.36, $CHCl_3$).

Enantiomeric purity of **5.29g** was determined by HPLC analysis in comparison with authentic racemic material (95:5 e.r. shown; Chiralcel OZ–H column, 99.5:0.5 hexanes/*i*PrOH, 0.8 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.804	6864750	171420	49.892	52.335
2	25.415	6894484	156125	50.108	47.665



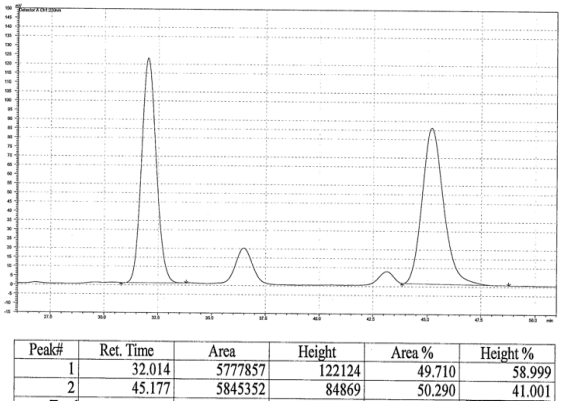
Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.638	14856774	349782	95.264	95.533
2	26.478	738546	16354	4.736	4.467

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	23.804	49.892	1	24.638	95.264
2	25.415	50.108	2	26.478	4.736

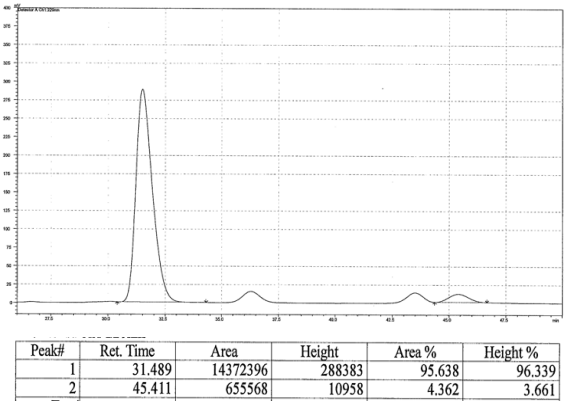
(*R*,*E*)-Diethyl 2-(3-(furan-3-yl)hex-1-en-5-yn-1-yl)malonate (5.29h). IR (neat): 3291 (w), 2982 (w), 2936 (w), 1729 (s), 1465 (w), 1368 (m), 1252 (m), 1174 (m), 1113 (m), 1030 (m), 970 (m), 862 (w), 784 (m), 648 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.28–7.26 (1H, m), 7.08–7.07 (1H, m), 7.00–6.98 (1H, m), 5.90 (1H, dd, *J* = 15.6, 7.2 Hz), 5.82 (1H, dd, *J* = 15.6, 8.4 Hz), 4.21 (2H, q, *J* = 7.2 Hz), 4.20 (2H, q, *J* = 7.2 Hz), 4.03 (1H, d, *J* = 8.4 Hz), 3.69 (1H, td, *J* = 7.2, 6.8 Hz), 2.62–2.59 (2H, m), 1.98 (1H, t, *J* = 2.8 Hz), 1.27 (3H, t, *J* = 7.2 Hz), 1.26 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.21, 168.19, 142.7, 137.3, 127.2, 125.8, 123.1, 121.0, 82.0, 70.5, 61.8, 55.6, 42.7,

25.2, 14.18, 14.16; HRMS (ESI+): Calcd for $C_{17}H_{21}O_5$ $[M+H]^+$: 305.13890 m/z, Found: 305.13793 m/z. Specific rotation: $[\alpha]_D^{20}$ –30.6 (*c* 1.01, $CHCl_3$).

Enantiomeric purity of **5.29h** was determined by HPLC analysis in comparison with authentic racemic material (96:4 e.r. shown; Chiralcel OJ–H column, 98.5:1.5 hexanes/*i*PrOH, 0.8 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	32.014	5777857	122124	49.710	58.999
2	45.177	5845352	84869	50.290	41.001

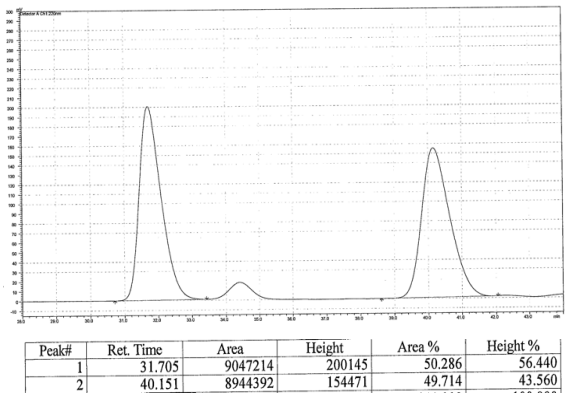


Peak#	Ret. Time	Area	Height	Area %	Height %
1	31.489	14372396	288383	95.638	96.339
2	45.411	655568	10958	4.362	3.661

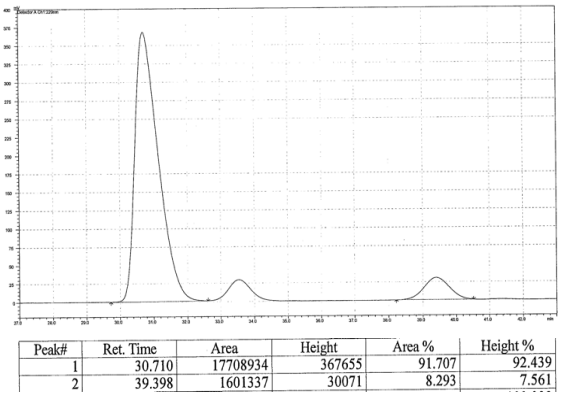
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	32.014	49.710	1	31.489	95.638
2	45.177	50.290	2	45.411	4.362

(*R*,*E*)-Diethyl 2-(3-(thiophen-3-yl)hex-1-en-5-yn-1-yl)malonate (5.29i). IR (neat): 3293 (w), 2983 (w), 2937 (w), 1728 (s), 1505 (w), 1369 (m), 1259 (m), 1152 (s), 1113 (m), 1069 (m), 1026 (s), 969 (m), 876 (m), 790 (m), 731 (m), 639 (m), 600 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.36–7.35 (1H, m), 7.30–7.29 (1H, m), 6.32–6.31 (1H, m), 5.88–5.78 (2H, m), 4.20 (2H, q, *J* = 7.2 Hz), 4.19 (2H, q, *J* = 7.2 Hz), 4.03 (1H, d, *J* = 7.6 Hz), 3.50 (1H, td, *J* = 6.4, 6.4 Hz), 2.54–2.51 (2H, m), 1.98 (1H, t, *J* = 2.8 Hz), 1.27 (3H, t, *J* = 7.2 Hz), 1.26 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.2, 143.1, 139.3, 137.0, 126.1, 123.2, 110.0, 81.9, 70.4, 61.8, 55.5, 38.2, 24.9, 14.2; HRMS (ESI+): Calcd for $C_{17}H_{21}O_4S_1$ $[M+H]^+$: 321.11605 m/z, Found: 321.11658 m/z. Specific rotation: $[\alpha]_D^{20}$ –21.2 (*c* 1.97, $CHCl_3$).

Enantiomeric purity of **5.29i** was determined by HPLC analysis in comparison with authentic racemic material (92:8 e.r. shown; Chiralcel OJ–H column, 99:1 hexanes/*i*PrOH, 0.8 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	31.705	9047214	200145	50.286	56.440
2	40.151	8944392	154471	49.714	43.560

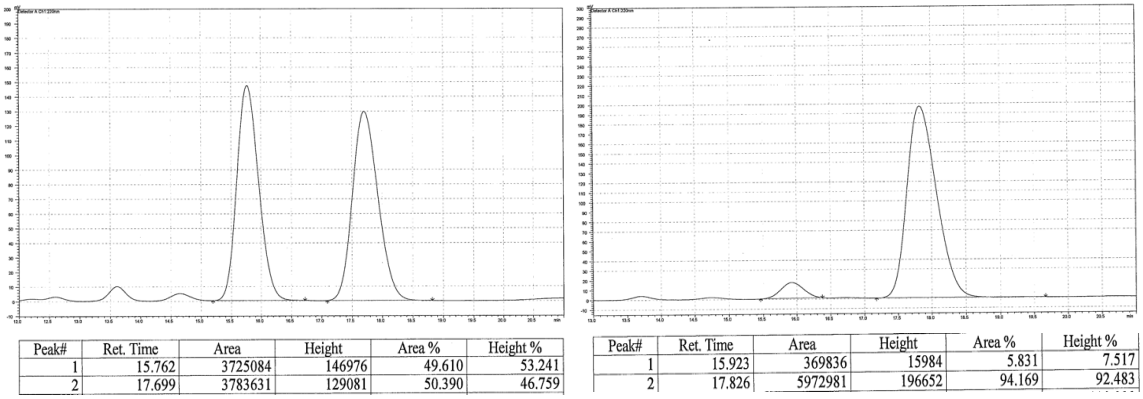


Peak#	Ret. Time	Area	Height	Area %	Height %
1	30.710	17708934	367655	91.707	92.439
2	39.398	1601337	30071	8.293	7.561

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	31.705	50.286	1	30.710	91.707
2	40.151	49.714	2	39.398	8.293

(*R*,*E*)-Diethyl 2-(3-phenethylhex-1-en-5-yn-1-yl)malonate (5.37a). IR (neat): 3286 (w), 2982 (w), 2934 (w), 1730 (s), 1454 (w), 1368 (m), 1262 (m), 1147 (s), 1113 (m), 1030 (s), 971 (m), 862 (w), 748 (m), 700 (m), 639 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.30–7.26 (2H, m), 7.20–7.17 (3H, m), 5.79 (1H, dd, *J* = 15.6, 8.4 Hz), 5.63 (1H, dd, *J* = 15.6, 8.4 Hz), 4.23 (2H, q, *J* = 7.2 Hz), 4.22 (2H, q, *J* = 7.2 Hz), 4.04 (1H, d, *J* = 8.8 Hz), 2.70–2.62 (1H, m), 2.60–2.51 (1H, m), 2.35–2.27 (3H, m), 1.97 (1H, t, *J* = 2.4 Hz), 1.94–1.85 (1H, m), 1.76–1.67 (1H, m), 1.28 (6H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.4, 168.3, 142.1, 138.5, 128.6, 128.5, 125.9, 123.2, 82.0, 70.0, 61.8, 61.7, 55.8, 40.8, 35.3, 33.3, 24.5, 14.21, 14.19; HRMS (ESI+): Calcd for $C_{21}H_{27}O_4$ $[M+H]^+$: 343.19093 m/z, Found: 343.19021 m/z. Specific rotation: $[\alpha]_D^{20}$ +7.8 (*c* 1.26, $CHCl_3$).

Enantiomeric purity of **5.37a** was determined by HPLC analysis in comparison with authentic racemic material (94:6 e.r. shown; Chiralcel OZ–H column, 99.5:0.5 hexanes/*i*PrOH, 0.8 mL/min, 220 nm).



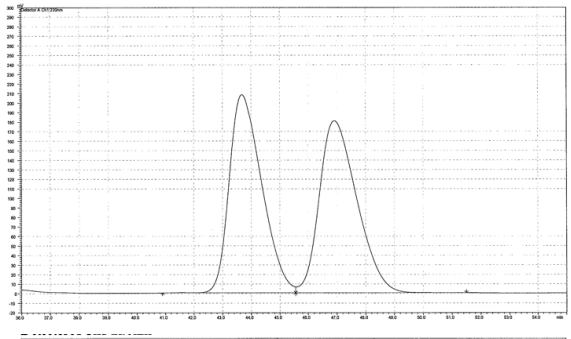
Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.762	3725084	146976	49.610	53.241
2	17.699	3783631	129081	50.390	46.759

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.923	369836	15984	5.831	7.517
2	17.826	5972981	196652	94.169	92.483

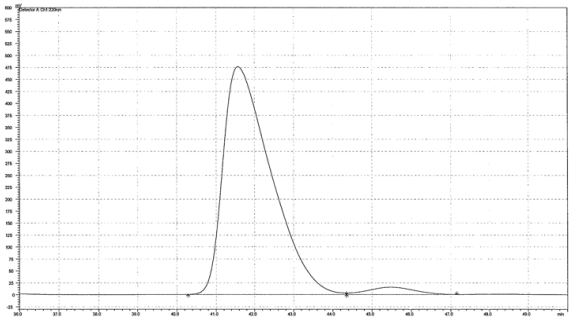
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	15.762	49.610	1	15.923	5.831
2	17.699	50.390	2	17.826	94.169

(*S*,*E*)-Diethyl 2-(3-cyclohexylhex-1-en-5-yn-1-yl)malonate (5.37b). IR (neat): 3288 (w), 2982 (w), 2924 (m), 2852 (m), 1732 (s), 1448 (m), 1368 (m), 1265 (m), 1148 (m), 1032 (m), 972 (m), 862 (w), 630 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 5.70 (1H, dd, *J* = 15.2, 8.4 Hz), 5.59 (1H, dd, *J* = 15.2, 8.8 Hz), 4.19 (4H, q, *J* = 7.6 Hz), 4.00 (1H, d, *J* = 8.8 Hz), 2.30–2.26 (2H, m), 2.09–2.02 (1H, m), 1.93 (1H, t, *J* = 2.8 Hz), 1.76–1.62 (5H, m), 1.49–1.40 (1H, m), 1.26 (3H, t, *J* = 7.2 Hz), 1.25 (3H, t, *J* = 7.2 Hz), 1.22–1.06 (3H, m), 1.00–0.80 (2H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.5, 168.4, 137.7, 123.0, 82.7, 69.7, 61.7, 61.6, 55.8, 47.2, 40.0, 31.0, 29.8, 26.6, 26.53, 26.46, 21.7, 14.2; HRMS (ESI+): Calcd for $C_{19}H_{29}O_4$ $[M+H]^+$: 321.20658 m/z, Found: 321.20727 m/z. Specific rotation: $[\alpha]_D^{20}$ +4.7 (*c* 1.53, $CHCl_3$).

Enantiomeric purity of **5.37b** was determined by HPLC analysis in comparison with authentic racemic material (97:3 e.r. shown; Chiralcel OZ–H column, 99.6:0.4 hexanes/*i*PrOH, 0.8 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	43.676	16409594	207685	50.166	53.523
2	46.912	16301064	180344	49.834	46.477

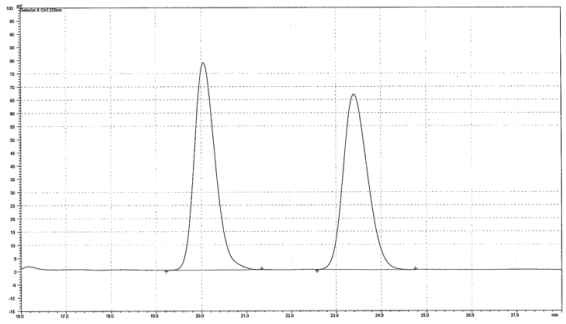


Peak#	Ret. Time	Area	Height	Area %	Height %
1	41.569	41059492	476161	96.996	96.849
2	45.483	1271710	15491	3.004	3.151

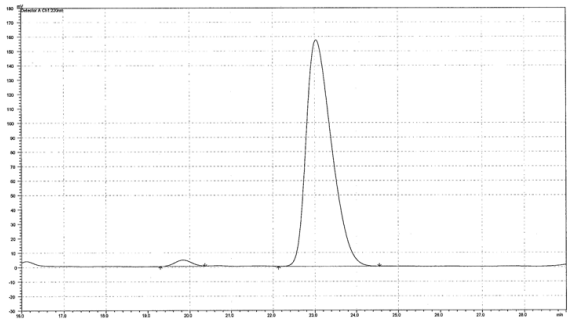
Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	43.676	50.166	1	41.569	96.996
2	46.912	49.834	2	45.483	3.004

(*R*,*E*)-Diethyl 2-(3-(*tert*-butyl)hex-1-en-5-yn-1-yl)malonate (5.37c). IR (neat): 3289 (w), 2962 (m), 2872 (w), 1733 (s), 1468 (w), 1368 (m), 1260 (m), 1148 (m), 1033 (m), 971 (m), 862 (w), 628 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 5.75 (1H, dd, *J* = 15.6, 8.8 Hz), 5.57 (1H, dd, *J* = 15.6, 8.8 Hz), 4.19 (4H, q, *J* =7.2 Hz), 4.03 (1H, d, *J* = 8.8 Hz), 2.41 (1H, dt, *J* = 15.6, 2.8 Hz), 2.13–2.00 (2H, m), 1.89 (1H, t, *J* = 2.8 Hz), 1.26 (3H, t, *J* = 7.2 Hz), 1.25 (3H, t, *J* = 7.2 Hz), 0.88 (9H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.5, 168.4, 136.2, 124.2, 83.7, 69.5, 61.7, 61.6, 55.8, 52.6, 33.3, 27.7, 19.6, 14.2; HRMS (ESI+): Calcd for $C_{17}H_{27}O_4$ $[M+H]^+$: 295.19093 m/z, Found: 295.19175 m/z. Specific rotation: $[\alpha]_D^{20}$ –2.3 (*c* 1.49, $CHCl_3$).

Enantiomeric purity of **5.37c** was determined by HPLC analysis in comparison with authentic racemic material (98:2 e.r. shown; Chiralcel OZ–H column, 99.6:0.4 hexanes/*i*PrOH, 0.8 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.048	2524539	78646	50.148	54.186
2	23.399	2509688	66496	49.852	45.814



Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.832	125019	4329	1.840	2.682
2	23.031	6668277	157079	98.160	97.318

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	20.048	50.148	1	19.832	1.840
2	23.399	49.852	2	23.031	98.160

5.8.4 Experimental Procedures and Characterization Data for Synthesis of Alkyl-Substituted Dienoates

■ **Representative Experimental Procedure for Alkylation of Diethyl Bromomalonate with Allyl Bromide.** To a solution of allyl bromide[12] **5.34a** (4.00 g, 17.8 mmol) and diethyl bromomalonate (2.10 mL, 14.8 mmol) in N,N'-dimethylformamide (dmf, 30 mL) was added K_2CO_3 (2.25 g, 16.3 mmol) at 22 ºC. The resulting mixture was allowed to stir at 22 ºC for 16 h. Water (20 mL) and diethyl ether (30 mL) was added to quench the reaction. The aqueous layer was washed with diethyl ether (2 × 30 mL). The combined organic layers were washed with brine (2 × 30 mL), dried over $MgSO_4$ and concentrated under vacuum. The resulting colorless oil was purified by silica gel column chromatography (hexanes:ethyl acetate = 50:1) to obtain 5.44 g **5.35a** (14.2 mmol, 95% yield) as colorless oil.

(12) Fañanás-Mastral, M.; Pérez, M.; Bos, P. H.; Rudolph, A.; Harutyunyan, S. R.; Feringa, B. L. *Angew. Chem., Int. Ed.* **2012**, *51*, 1922–1925.

(*E*)-Diethyl 2-bromo-2-(5-phenylpent-2-en-1-yl)malonate (5.35a). IR (neat): 2983 (w), 2936 (w), 1739 (s), 1454 (m), 1367 (m), 1233 (s), 1191 (m), 1096 (m), 1030 (m), 969 (m), 857 (m), 746 (m), 698 (m), 650 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.30–7.26 (2H, m), 7.20–7.16 (3H, m), 5.65 (1H, dt, *J* = 15.6, 6.4 Hz), 5.48 (1H, dt, *J* = 15.6, 6.8 Hz), 4.26 (4H, q, *J* = 7.2 Hz), 2.99 (2H, d, *J* = 6.8 Hz), 2.69–2.65 (2H, m), 2.34 (2H, dt, *J* = 7.6, 7.2 Hz), 1.28 (6H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ166.7, 141.7, 135.9, 128.5, 128.4, 125.9, 123.4, 63.0, 62.7, 41.7, 35.8, 34.4, 14.0; HRMS (ESI+): Calcd for $C_{18}H_{24}Br_1O_4$ $[M+H]^+$: 383.08580 m/z, Found: 383.08507 m/z.

(*E*)-Diethyl 2-bromo-2-(3-cyclohexylallyl)malonate (5.35b). IR (neat): 2981 (w), 2923 (m), 2851 (m), 1741 (s), 1447 (m), 1367 (w), 1232 (s), 1187 (m), 1095 (m), 1022 (m), 971 (m), 858 (m), 649 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.52 (1H, dd, *J* = 15.2, 6.4 Hz), 5.37 (1H, dt, *J* = 15.2, 7.2 Hz), 4.24 (4H, q, *J* = 7.2 Hz), 2.94 (2H, d, *J* = 7.2 Hz), 1.97–1.88 (1H, m), 1.72–1.60 (6H, m), 1.27 (6H, t, *J* = 7.2 Hz), 1.25–0.97 (5H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.7, 142.8, 120.2, 63.0, 41.8, 40.9, 32.9, 26.2, 26.0, 14.0; HRMS (ESI+): Calcd for $C_{16}H_{26}Br_1O_4$ $[M+H]^+$: 361.10145 m/z, Found: 361.10139 m/z.

(*E*)-Diethyl 2-bromo-2-(4,4-dimethylpent-2-en-1-yl)malonate (5.35c). IR (neat): 2959 (m), 2867 (w), 1741 (s), 1446 (w), 1365 (m), 1256 (s), 1175 (s), 1095 (m), 1022 (m), 974 (m), 858 (m), 650 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.60 (1H, d, *J* = 15.6 Hz), 5.32 (1H, dt, *J* = 15.6, 7.2 Hz), 4.24 (4H, q, *J* = 7.2 Hz), 2.95 (2H, d, *J* = 7.2 Hz), 1.28 (3H, t, *J* = 7.2 Hz), 0.98 (9H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.7, 147.8, 117.5, 63.00, 62.96, 41.8, 33.3, 29.5, 14.1; HRMS (ESI+): Calcd for $C_{14}H_{24}Br_1O_4$ $[M+H]^+$: 335.08580 m/z, Found: 335.08415 m/z.

■ **Representative Experimental Procedure for Elimination of Bromomalonate.** To a solution of bromomalonate **5.35a** (5.44 g, 14.2 mmol) in CH_2Cl_2 (50 mL) was added DABCO (2.39 g, 21.3 mmol) at 22 ºC. The resulting solution was allowed to stir at 22 ºC for 72 h. Water (30 mL) was added to quench the reaction. The aqueous layer was washed with CH_2Cl_2 (2 × 30 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under vacuum. The resulting yellow oil was purified by silica gel column chromatography (hexanes:ethyl acetate = 30:1 to 10:1) to obtain 885 mg **5.36a** (2.9 mmol, 21% yield) and recover 4.07 g **5.35a** (10.6 mmol, 75% yield) as yellow oil.

(*E*)-Diethyl 2-(5-phenylpent-2-en-1-ylidene)malonate (5.36a). IR (neat): 2983 (w), 2937 (w), 1715 (s), 1636 (m), 1454 (m), 1241 (s), 1211 (s), 1094 (m), 1025 (m), 982 (w), 748 (m), 700 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.32–7.27 (3H, m), 7.22–7.16 (3H, m), 6.54 (1H, dd, *J* = 15.2, 11.6 Hz), 6.32 (1H, dt, *J* = 15.2, 7.2 Hz), 4.31 (2H, q, *J* = 7.2 Hz), 4.25 (2H, q, *J* = 7.2 Hz), 2.78–2.75 (2H, m), 2.57–2.52 (2H, m), 1.33 (3H, t, *J* = 7.2 Hz), 1.30 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 165.5, 164.9, 148.2, 145.2, 141.0, 128.6, 128.5, 126.4, 126.3, 124.3, 61.39, 61.36, 35.1, 35.0, 14.31, 14.29; HRMS (ESI+): Calcd for $C_{18}H_{23}O_4$ $[M+H]^+$: 303.15963 m/z, Found: 303.16021 m/z.

(*E*)-Diethyl 2-(3-cyclohexylallylidene)malonate (5.36b). IR (neat): 2982 (m), 2925 (m), 2852 (m), 1712 (s), 1632 (m), 1448 (m), 1377 (m), 1239 (s), 1122 (m), 1025 (s), 982 (m), 862 (m), 734 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.32 (1H, d, *J* = 11.2 Hz), 6.48 (1H, ddd, *J* = 15.2, 11.2, 1.2 Hz), 6.25 (1H, dd, *J* = 15.2, 6.8 Hz), 4.32 (2H, q, *J* = 7.2 Hz), 4.24 (2H, q, *J* = 7.2 Hz), 2.18–2.11 (1H, m), 1.79–1.62 (5H, m), 1.34 (3H, t, *J* = 7.2 Hz), 1.29 (3H, t, *J* = 7.2 Hz), 1.25–1.08 (6H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 165.6,

165.0, 155.1, 146.1, 123.8, 123.4, 61.31, 61.28, 41.6, 32.2, 26.1, 25.8, 14.35, 14.31; HRMS (ESI+): Calcd for $C_{16}H_{25}O_4$ $[M+H]^+$: 281.17528 m/z, Found: 281.17653 m/z.

(*E*)-Diethyl 2-(4,4-dimethylpent-2-en-1-ylidene)malonate (5.36c). IR (neat): 2962 (m), 2904 (w), 2870 (w), 1715 (s), 1632 (m), 1463 (m), 1366 (m), 1235 (s), 1195 (s), 1144 (m), 1060 (s), 1030 (m), 985 (m), 865 (w), 799 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.34 (1H, d, *J* = 11.2 Hz), 6.46 (1H, dd, *J* = 15.6, 11.6 Hz), 6.31 (1H, d, *J* = 15.2 Hz), 4,33 (2H, q, *J* = 7.2 Hz), 4.24 (2H, q, *J* = 7.2 Hz), 1.34 (3H, t, *J* = 7.2 Hz), 1.30 (3H, t, *J* = 7.2 Hz), 1.07 (9H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 165.6, 165.0, 160.0, 146.3, 124.0, 120.9, 61.3, 34.5, 29.0, 14.35, 14.31; HRMS (ESI+): Calcd for $C_{14}H_{23}O_4$ $[M+H]^+$: 255.15963 m/z, Found: 255.16064 m/z.

5.8.5 Experimental Procedures and Characterization Data for Synthesis of Dienoates For Formation of Quaternary Stereogenic Centers

■ **Representative Experimental Procedure for Alkylation of Diethyl Bromomalonate with Allyl Bromide.** Bromomalonates **5.38a**-**c** were prepared following previously described procedure.

(*E*)-Diethyl 2-bromo-2-(3,7-dimethylocta-2,6-dien-1-yl)malonate (5.38a). IR (neat): 2981 (m), 2926 (m), 1741 (s), 1445 (m), 1367 (m), 1235 (s), 1175 (m), 1096 (m), 1023 (m), 892 (m), 650 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 5.14 (1H, t, *J* = 7.2 Hz), 5.06 (1H, t, *J* = 6.8 Hz), 4.25 (2H, q, *J* = 7.2 Hz), 4.24 (2H, q, *J* = 7.2 Hz), 3.01 (1H, d, *J* = 6.8 Hz), 2.09–1.93 (4H, m), 1.66 (3H, s), 1.63 (3H, s), 1.58 (3H, s), 1.27 (6H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.9, 140.6, 131.7, 124.0, 117.1, 63.1, 63.0, 39.9, 37.1,

26.6, 25.8, 17.8, 16.7, 14.0; HRMS (ESI+): Calcd for $C_{17}H_{28}Br_1O_4$ $[M+H]^+$: 375.11710 m/z, Found: 375.11615 m/z.

(*E*)-Diethyl 2-bromo-2-(3-phenylbut-2-en-1-yl)malonate (5.38b). IR (neat): 2982 (w), 2937 (w), 1739 (s), 1465 (m), 1367 (m), 1257 (s), 1184 (s), 1095 (m), 1036 (m), 972 (w), 858 (m), 756 (m), 698 (m), 651 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.37–7.29 (4H, m), 7.27–7.23 (1H, m), 5.74 (1H, t, *J* = 6.8 Hz), 4.29 (4H, q, *J* = 7.2 Hz), 3.25 (1H, d, *J* = 6.8 Hz), 2.07 (3H, s), 1.29 (6H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.9, 143.5, 139.7, 128.4, 127.3, 126.0, 120.7, 63.2, 62.6, 37.8, 16.7, 14.0; HRMS (ESI+): Calcd for $C_{17}H_{22}Br_1O_4$ $[M+H]^+$: 369.07015 m/z, Found: 369.06938 m/z.

(*E*)-Diethyl 2-bromo-2-(3-(naphthalen-2-yl)but-2-en-1-yl)malonate (5.38c). IR (neat): 3055 (w), 2982 (m), 2938 (w), 1740 (s), 1445 (m), 1367 (m), 1260 (s), 1183 (m), 1095 (m), 1036 (m), 892 (w), 858 (m), 748 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.84–7.77 (4H, m), 7.55 (1H, dd, *J* = 8.4, 2.0 Hz), 7.49–7.42 (2H, m), 5.91 (1H, t, *J* = 7.2 Hz), 4.31 (4H, q, *J* = 7.2 Hz), 2.19 (3H, s), 1.31 (6H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.9, 140.6, 139.5, 133.5, 132.8, 128.2, 127.9, 127.6, 126.2, 125.8, 124.6, 124.5, 121.3, 63.2, 62.6, 37.9, 16.7, 14.0; HRMS (ESI+): Calcd for $C_{21}H_{24}Br_1O_4$ $[M+H]^+$: 419.08580 m/z, Found: 419.08399 m/z.

■ **Representative Experimental Procedure for Elimination of Bromomalonate.** To a solution of bromomalonate **5.38a** (3.54 g, 9.4 mmol) in CH_2Cl_2 (10 mL) was added DABCO (3.18 g, 28.3 mmol) at 22 ºC. The resulting solution was allowed to stir at 22 ºC for 24 h. Water (30 mL) was added to quench the reaction. The aqueous layer was washed with CH_2Cl_2 (2 × 30 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under vacuum. The resulting yellow oil was purified by silica gel

column chromatography (hexanes:ethyl acetate = 12:1) to obtain 1.81 g **5.39a** (6.1 mmol, 65% yield) as yellow oil.

(*E*)-Diethyl 2-(3,7-dimethylocta-2,6-dien-1-ylidene)malonate (5.39a). IR (neat): 2980 (m), 2932 (m), 1715 (s), 1627 (m), 1446 (m), 1380 (m), 1246 (s), 1204 (s), 1143 (m), 1026 (s), 864 (w), 797 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.65 (1H, d, *J* = 12.0 Hz), 6.26 (1H, d, *J* = 12.0 Hz), 5.05 (1H, t, *J* = 6.8 Hz), 4.31 (2H, q, *J* = 7.2 Hz), 4.24 (2H, q, *J* = 7.2 Hz), 2.21–2.10 (4H, m), 1.93 (3H, s), 1.67 (3H, s), 1.58 (3H, s), 1.33 (3H, t, *J* = 7.2 Hz), 1.29 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.0, 165.2, 155.2, 140.4, 132.6, 123.4, 123.2, 120.5, 61.24, 61.21, 40.9, 26.3, 25.8, 17.8, 17.7, 14.31, 14.30; HRMS (ESI+): Calcd for $C_{17}H_{27}O_4$ $[M+H]^+$: 295.19093 m/z, Found: 295.19105 m/z.

(*E*)-Diethyl 2-(3-phenylbut-2-en-1-ylidene)malonate (5.39b). IR (neat): 2982 (w), 2937 (m), 2904 (w), 1711 (s), 1610 (s), 1446 (m), 1378 (m), 1275 (s), 1237 (s), 1170 (s), 1062 (s), 1024 (m), 948 (w), 864 (w), 797 (m), 695 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.83 (1H, d, *J* = 12.4 Hz), 7.51–7.48 (2H, m), 7.39–7.32 (3H, m), 6.89 (1H, d, *J* = 12.4 Hz), 4.35 (2H, q, *J* = 7.2 Hz), 4.29 (2H, q, *J* = 7.2 Hz), 2.35 (3H, d, *J* = 1.6 Hz), 1.35 (3H, t, *J* = 7.2 Hz), 1.33 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 165.9, 165.1, 149.9, 141.9, 140.1, 129.0, 128.7, 126.4, 125.3, 121.8, 61.40, 61.38, 16.8, 14.4, 14.3; HRMS (ESI+): Calcd for $C_{17}H_{21}O_4$ $[M+H]^+$: 289.14398 m/z, Found: 289.14478 m/z.

(*E*)-Diethyl 2-(3-(naphthalen-2-yl)but-2-en-1-ylidene)malonate (5.39c). IR (neat): 3058 (w), 2981 (m), 2937 (w), 1710 (s), 1604 (s), 1466 (m), 1366 (m), 1244 (s), 1164 (s), 1062 (s), 1023 (m), 857 (m), 749 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.95–7.81 (5H, m), 7.64 (1H, dd, *J* = 8.4, 1.6 Hz), 7.52–7.47 (2H, m), 7.06 (1H, d, *J* = 12.0 Hz),

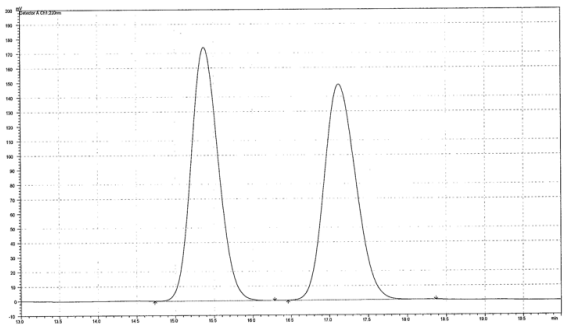
4.38 (2H, q, *J* = 7.2 Hz), 4.31 (2H, q, *J* = 7.2 Hz), 2.46 (3H, d, *J* = 1.6 Hz), 1.39 (3H, t, *J* = 7.2 Hz), 1.35 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 165.9, 165.1, 149.6, 140.1, 139.0, 133.6, 133.3, 128.6, 128.3, 127.7, 126.8, 126.6, 126.0, 125.3, 123.9, 122.2, 61.44, 61.41, 16.8, 14.4, 14.3; HRMS (ESI+): Calcd for $C_{21}H_{23}O_4$ $[M+H]^+$: 339.15963 m/z, Found: 339.15929 m/z.

5.8.6 Experimental Procedures and Characterization Data for NHC–Cu-Catalyzed Enantioselective Propargyl 1,6-Conjugate Addition for Formation of Quaternary Centers

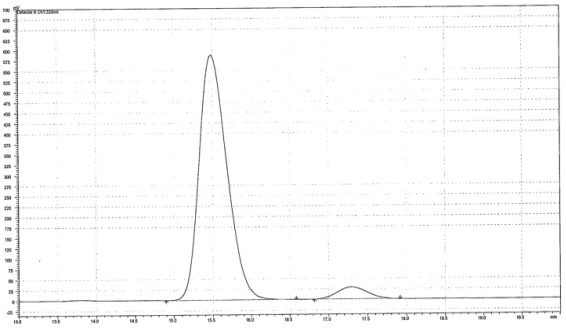
■ **Representative Experimental Procedure for NHC–Cu-Catalyzed Enantioselective Propargyl 1,6-Conjugate Addition.** In a N_2-filled glove box, imidazolinium salt **5.26d** (4.6 mg, 0.010 mmol), CuCl (1.0 mg, 0.010 mmol), NaO*t*-Bu (1.9 mg, 0.020 mmol) and NaOPh (17.4 mg, 0.15 mmol) and thf (0.5 mL) are added into an oven-dried vial equipped with a stirring bar. The mixture is allowed to premix for 2 h at 22 ºC. The resulting mixture is then added into a separate oven-dried vial containing allenylboronic acid pinacol ester (36.0 μL, 0.20 mmol). The vial is sealed with a Teflon screw cap and removed from the glove box. The mixture is allowed to stir at 22 ºC for 30 min. Then dienoate **5.39a** (28.8 mg, 0.10 mmol) is added into the solution by a syringe. The resulting mixture is allowed to stir at 22 ºC for 24 h. The mixture is filtered through a short plug of Celite and silica gel eluting with diethyl ether. The filtrate is washed with 1M NaOH aqueous solution, dried over $MgSO_4$ and concentrated *in vacuo*. The resulting yellow oil is purified by silica gel chromatography (hexanes:ethyl acetate = 20:1) to obtain 24.1 mg **5.40a** (0.073 mmol, 73% yield) as colorless oil.

(*R*,*E*)-Diethyl 2-(3,7-dimethyl-3-(prop-2-yn-1-yl)octa-1,6-dien-1-yl)malonate (5.40a). IR (neat): 3291 (m), 2968 (m), 2918 (m), 1734 (s), 1447 (m), 1369 (m), 1255 (m), 1176 (m), 1149 (m), 1033 (m), 974 (m), 863 (w), 636 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.70–5.61 (2H, m), 5.07 (1H, t, *J* = 7.2 Hz), 4.19 (4H, q, *J* = 7.2 Hz), 3.99 (1H, dd, *J* = 5.6, 2.4 Hz), 2.21–2.20 (2H, m), 1.96 (1H, t, *J* = 2.8 Hz), 1.90–1.82 (2H, m), 1.66 (3H, s), 1.57 (3H, s), 1.51–1.38 (2H, m), 1.26 (3H, t, *J* = 7.2 Hz), 1.25 (3H, t, *J* = 7.2 Hz), 1.11 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.5, 143.2, 131.6, 124.5, 120.1, 81.6, 70.5, 61.7, 55.9, 39.9, 39.2, 30.5, 25.8, 23.6, 23.0, 17.7, 14.2; HRMS (ESI+): Calcd for $C_{20}H_{31}O_4$ $[M+H]^+$: 335.22223 m/z, Found: 335.22233 m/z.

Enantiomeric purity of **5.40a** was determined by HPLC analysis in comparison with authentic racemic material (95:5 e.r. shown; Chiralpak AD–H column, 99.9:0.1 hexanes/*i*PrOH, 0.6 mL/min, 220 nm). Specific rotation: $[\alpha]_D^{20}$ –3.1 (*c* 1.28, $CHCl_3$).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.371	4238862	174308	50.108	54.023
2	17.122	4220548	148345	49.892	45.977



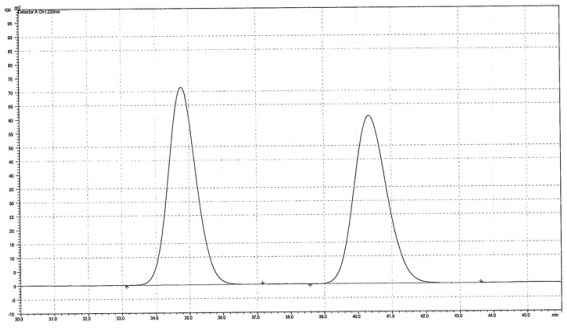
Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.481	14698508	587349	95.067	95.354
2	17.289	762765	28620	4.933	4.646

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	15.371	50.108	1	15.481	95.067
2	17.122	49.892	2	17.289	4.933

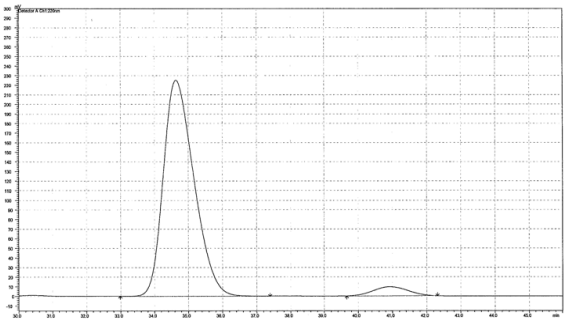
(*R*,*E*)-Diethyl 2-(3-methyl-3-phenylhex-1-en-5-yn-1-yl)malonate (5.40b). IR (neat): 3290 (m), 2980 (m), 2938 (w), 1732 (s), 1464 (m), 1369 (m), 1275 (m), 1177 (m), 1031 (m), 976 (w), 861 (w), 766 (m), 700 (m), 642 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ

7.36–7.29 (4H, m), 7.24–7.19 (1H, m), 5.97 (1H, d, *J* = 16.0 Hz), 5.81 (1H, dd, *J* = 16.0, 8.8 Hz), 4.22 (4H, q, *J* = 7.2 Hz), 4.06 (1H, d, *J* = 8.8 Hz), 2.69 (1H, dd, *J* = 16.4, 2.8 Hz), 2.61 (1H, dd, *J* = 16.4, 2.8 Hz), 1.94 (1H, t, *J* = 2.8 Hz), 1.53 (3H, s), 1.280 (3H, t, *J* = 7.2 Hz), 1.277 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.4, 145.5, 142.9, 128.3, 126.7, 126.6, 120.5, 81.4, 71.0, 61.8, 55.8, 43.9, 31.3, 25.8, 14.2; HRMS (ESI+): Calcd for $C_{20}H_{25}O_4$ $[M+H]^+$: 329.17528 m/z, Found: 329.17620 m/z. Specific rotation: $[\alpha]_D^{20}$ –4.7 (*c* 1.33, $CHCl_3$).

Enantiomeric purity of **5.40b** was determined by HPLC analysis in comparison with authentic racemic material (95:5 e.r. shown; Chiralcel OZ–H column, 99.5:0.5 hexanes/*i*PrOH, 0.6 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	34.770	4117622	71488	50.105	54.051
2	40.336	4100286	60773	49.895	45.949



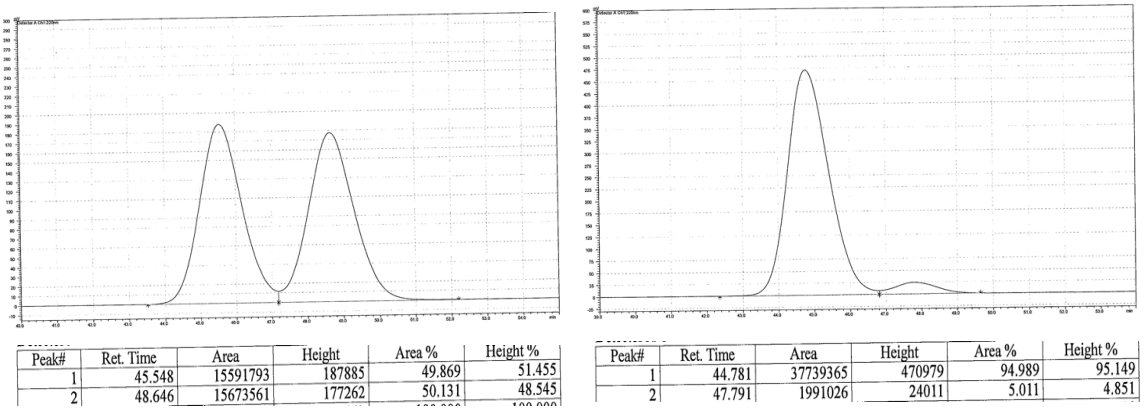
Peak#	Ret. Time	Area	Height	Area %	Height %
1	34.640	14139972	225252	95.429	95.911
2	40.927	677303	9604	4.571	4.089

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	34.770	50.105	1	34.640	95.429
2	40.336	49.895	2	40.927	4.571

(*R*,*E*)-Diethyl 2-(3-methyl-3-(naphthalen-2-yl)hex-1-en-5-yn-1-yl)malonate (5.40c). IR (neat): 3293 (w), 2980 (m), 2937 (w), 1731 (s), 1600 (w), 1463 (w), 1368 (m), 1249 (m), 1175 (m), 1096 (m), 975 (w), 858 (m), 819 (m), 750 (m), 645 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.83–7.78 (4H, m), 7.49–7.43 (3H, m), 6.05 (1H, d, *J* = 16.0 Hz), 5.85 (1H, dd, *J* = 16.0, 8.8 Hz), 4.24 (4H, q, *J* = 7.2 Hz), 4.10 (1H, d, *J* = 8.8 Hz), 2.80

(1H, dd, J = 16.4, 2.8 Hz), 2.73 (1H, dd, J = 16.4, 2.8 Hz), 1.95 (1H, t, J = 2.8 Hz), 1.64 (3H, s), 1.292 (3H, t, J = 7.2 Hz), 1.289 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.3, 142.9, 142.8, 133.3, 132.2, 128.2, 127.9, 127.5, 126.1, 125.9, 125.4, 125.0, 120.9, 81.4, 71.2, 61.8, 55.8, 44.1, 31.3, 25.8, 14.2; HRMS (ESI+): Calcd for $C_{24}H_{27}O_4$ $[M+H]^+$: 379.19093 m/z, Found: 379.19093 m/z. Specific rotation: $[\alpha]_D^{20}$ –9.1 (*c* 2.03, $CHCl_3$).

Enantiomeric purity of **5.40c** was determined by HPLC analysis in comparison with authentic racemic material (95:5 e.r. shown; Chiralcel OZ–H column, 99.5:0.5 hexanes/*i*PrOH, 0.6 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	45.548	15591793	187885	49.869	51.455
2	48.646	15673561	177262	50.131	48.545

Peak#	Ret. Time	Area	Height	Area %	Height %
1	44.781	37739365	470979	94.989	95.149
2	47.791	1991026	24011	5.011	4.851

Peak #	Time (min)	Area (%)	Peak #	Time (min)	Area (%)
1	45.548	49.869	1	44.781	94.989
2	48.646	50.131	2	47.791	5.011

5.8.7 Experimental Procedures and Characterization Data for Functionalization of 1,6-Conjugate Addition Product

■ **Experimental Procedure for Isomerization of 1,6-Conjugate Addition Product.** To a solution of substrate **5.29a** (15.0 mg, 0.049 mmol) in CH_2Cl_2 (1 mL) was added DABCO (11.0 mg, 0.098 mmol) at 22 °C. The resulting solution was allowed to stir at 22

ºC for 16 h. After this time, the solvent was evaporated. The resulting yellow oil was purified by silica gel column chromatography (hexanes:ethyl acetate = 15:1) to obtain 14.2 mg **5.41** (0.045 mmol, 95% yield) as colorless oil.

(*S*)-Diethyl 2-(3-phenylhex-5-yn-1-ylidene)malonate (5.41). IR (neat): 3290 (m), 2982 (m), 2936 (w), 1722 (s), 1453 (m), 1376 (m), 1254 (s), 1224 (s), 1096 (m), 1024 (m), 863 (w), 760 (m), 701 (m), 642 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.34–7.30 (2H, m), 7.26–7.20 (3H, m), 6.87 (1H, t, *J* = 7.6 Hz), 4.29 (2H, q, *J* = 7.2 Hz), 4.19 (2H, q, *J* = 7.2 Hz), 3.03–2.98 (1H, m), 2.92–2.85 (1H, m), 2.74–2.62 (1H, m), 2.53–2.50 (2H, m), 1.98 (1H, t, *J* = 2.8 Hz), 1.32 (3H, t, *J* = 7.2 Hz), 1.25 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 165.4, 163.9, 146.8, 142.3, 130.0, 128.8, 127.5, 127.2, 82.0, 70.6, 61.4, 44.0, 34.9, 26.0, 14.3, 14.2; HRMS (ESI+): Calcd for $C_{19}H_{23}O_4$ $[M+H]^+$: 315.15963 m/z, Found: 315.16105 m/z. Specific rotation: $[\alpha]_D^{20}$ –4.2 (*c* 1.13, $CHCl_3$).

■ **Experimental Procedure for One-Pot Isomerization and Retro-Aldol Reaction.** To a solution of substrate **5.29a** (400 mg, 1.27 mmol) in CH_2Cl_2 (5 mL) was added DBU (380 μL, 2.54 mmol) and water (46 μL, 2.54 mmol) at 22 ºC. The resulting solution was allowed to stir at 22 ºC for 24 h. After this time, the solvent was evaporated under vacuum. The resulting yellow oil was purified by silica gel column chromatography (hexanes:ethyl acetate = 25:1) to obtain 128 mg aldehyde **5.42** (0.74 mmol, 58% overall yield) as yellow oil.

(*R*)-3-Phenylhex-5-ynal (5.42). IR (neat): 3288 (m), 2920 (m), 2832 (m), 2728 (m), 1721 (s), 1495 (m), 1390 (w), 1283 (m), 1181 (m), 1068 (m), 1029 (m), 762 (m), 701 (s), 642 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.73 (1H, t, *J* = 1.6 Hz), 7.34–7.30 (2H, m), 7.26–7.22 (3H, m), 3.50–3.43 (1H, m), 3.04 (1H, ddd, *J* = 17.2, 6.0, 1.6 Hz), 2.84 (1H,

ddd, *J* = 17.2, 8.0, 1.6 Hz), 2.59 (1H, ddd, *J* = 16.8, 6.4, 2.4 Hz), 2.51 (1H, ddd, *J* = 16.8, 7.6, 2.8 Hz), 2.02 (1H, t, *J* = 2.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 201.1, 142.5, 128.8, 127.4, 127.3, 81.8, 71.0, 48.5, 38.6, 26.1; HRMS (ESI+): Calcd for $C_{12}H_{13}O_1$ $[M+H]^+$: 173.09664 m/z, Found: 173.09651 m/z. Specific rotation: $[\alpha]_D^{20}$ –8.3 (*c* 0.60, $CHCl_3$).

■ **Experimental Procedure for Reduction of Aldehyde.** To a solution of aldehyde **5.42** (128 mg, 0.74 mmol) in MeOH (2 mL) was added $NaBH_4$ (56 mg, 1.48 mmol) at 0 ºC. The resulting solution was allowed to stir at 0 ºC for 2 h. The reaction was quenched by addition of water (2 mL) and diethyl ether (4 mL). The aqueous layer was washed by diethyl ether (2 × 4 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under vacuum. The resulting yellow oil was purified by silica gel column chromatography (hexanes:ethyl acetate = 7:1) to obtain 120 mg alcohol **5.43** (0.69 mmol, 93% yield) as light yellow oil.

(*R*)-3-Phenylhex-5-yn-1-ol (5.43). IR (neat): 3320 (br), 3290 (s), 2933 (m), 1602 (m), 1494 (m), 1325 (w), 1045 (s), 762 (m), 701 (s), 640 (s), 548 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35–7.30 (2H, m), 7.26–7.21 (3H, m), 3.62–3.57 (1H, m), 3.54–3.47 (1H, m), 3.03–2.96 (1H, m), 2.52–2.50 (2H, m), 2.20–2.12 (1H, m), 1.98 (1H, t, *J* = 2.8 Hz), 1.95–1.86 (1H, m), 1.38 (1H, br s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 143.6, 128.7, 127.6, 126.9, 82.8, 70.0, 60.9, 41.3, 37.8, 26.4; HRMS (ESI+): Calcd for $C_{12}H_{15}O_1$ $[M+H]^+$: 175.11229 m/z, Found: 175.11283 m/z. Specific rotation: $[\alpha]_D^{20}$ –6.8 (*c* 0.80, $CHCl_3$).

■ **Experimental Procedure for Reductive Amination of Aldehyde.** To a solution of aldehyde **5.42** (30 mg, 0.17 mmol) in CH_2Cl_2 (1 mL) was added allylamine (20 μL, 0.26 mmol) and $NaBH(OAc)_3$ (111 mg, 0.52 mmol) at 22 ºC. The resulting solution was

allowed to stir at 22 ºC for 16 h. After this time, the reaction was quenched by addition of water (1 mL). The aqueous layer was washed with diethyl ether (2 × 2 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under vacuum. The resulting yellow oil was purified by silica gel column chromatography (hexanes:ethyl acetate = 4:1) to obtain 28.6 mg amine **5.44** (0.13 mmol, 77% yield) as yellow oil.

(*R*)-*N*-Allyl-3-phenylhex-5-yn-1-amine (5.44). IR (neat): 3301 (m), 2924 (m), 2812 (m), 1642 (w), 1453 (m), 1297 (m), 1144 (m), 1029 (m), 918 (m), 760 (m), 700 (s), 637 (s), 545 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.33–7.29 (2H, m), 7.25–7.20 (3H, m), 5.92–5.82 (1H, m), 5.19–5.09 (2H, m), 3.80 (1H, br s), 3.25–3.22 (2H, m), 2.92–2.84 (1H, m), 2.63–2.47 (4H, m), 2.19–2.11 (1H, m), 1.96 (1H, t, *J* = 2.8 Hz), 1.98–1.88 (1H, m); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 143.4, 134.9, 128.7, 127.5, 126.9, 117.7, 82.6, 70.1, 51.8, 46.8, 42.7, 34.2, 26.6; HRMS (ESI+): Calcd for $C_{15}H_{20}N_1$ $[M+H]^+$: 214.15957 m/z, Found: 214.15932 m/z. Specific rotation: $[\alpha]_D^{20}$ –9.0 (*c* 1.35, $CHCl_3$).

■ **Experimental Procedure for NHC–Cu-Catalyzed Protoboration of Alkyne.** Alkenylboron **5.45** was prepared according to a previously reported procedure.[10]

(*R*,*E*)-3-Phenyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hex-5-en-1-ol (5.45). IR (neat): 3421 (br), 2977 (m), 2930 (m), 1637 (m), 1453 (m), 1358 (s), 1319 (s), 1141 (s), 1047 (m), 997 (m), 970 (m), 886 (w), 849 (m), 761 (m), 700 (s), 643 (m), 578 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.31–7.26 (2H, m), 7.24–7.16 (3H, m), 6.52 (1H, dt, *J* = 18.0, 6.4 Hz), 5.43 (1H, d, *J* = 18.0 Hz), 3.53–3.39 (2H, m), 2.88–2.81 (1H, m), 2.54–2.41 (2H, m), 2.05–1.96 (1H, m), 1.82–1.72 (1H, m), 1.24 (12H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 152.1, 144.6, 128.6, 127.6, 126.4, 83.2, 61.1, 43.6, 41.8, 38.6, 24.9; HRMS

(ESI+): Calcd for $C_{18}H_{28}B_1O_3$ $[M+H]^+$: 303.21315 m/z, Found: 303.21342 m/z. Specific rotation: $[\alpha]_D^{20}$ +7.1 (*c* 2.56, $CHCl_3$).

■ **Experimental Procedure for Homologation of Alkyne.** Allene **5.46** was prepared according to a previously reported procedure.[11]

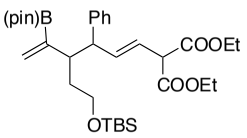
(*R*)-3-Phenylhepta-5,6-dien-1-ol (5.46). IR (neat): 3344 (br), 3027 (w), 2932 (m), 1955 (m), 1602 (w), 1494 (m), 1439 (m), 1364 (w), 1045 (s), 843 (s), 761 (s), 700 (s), 582 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.32–7.27 (2H, m), 7.23–7.17 (3H, m), 4.97–4.89 (1H, m), 4.62–4.52 (2H, m), 3.57–3.43 (2H, m), 2.85–2.78 (1H, m), 2.35–2.30 (2H, m), 2.06–1.98 (1H, m), 1.85–1.76 (1H, m), 1.19 (1H, br s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 209.2, 144.4, 128.6, 127.8, 126.5, 88.1, 74.6, 61.2, 42.6, 38.7, 36.1; HRMS (ESI+): Calcd for $C_{13}H_{17}O_1$ $[M+H]^+$: 189.12794 m/z, Found: 189.12825 m/z. Specific rotation: $[\alpha]_D^{20}$ +21.3 (*c* 0.60, $CHCl_3$).

Sample Name:
FM-VIII-150
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Dec 30 2014



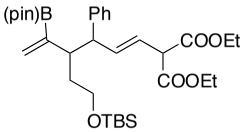
5.21a

Sample Name:
FM-VIII-150
Data Collected on:
vnmr13-vnmrs400
Archive directory:

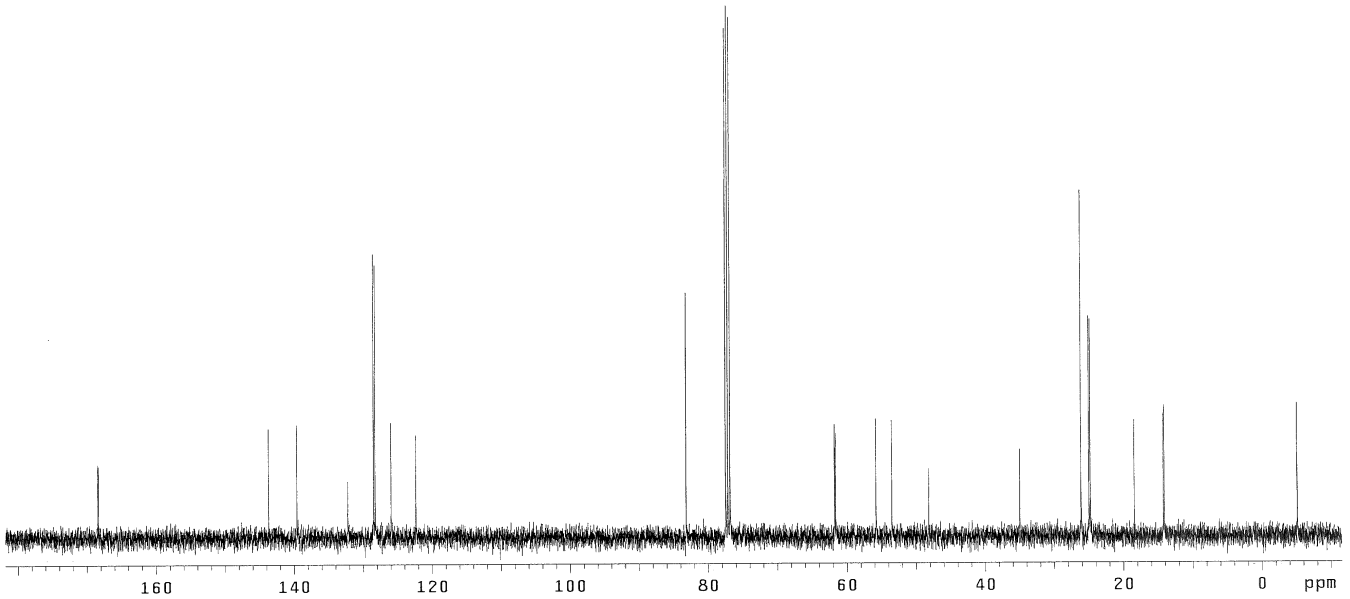
Sample directory:

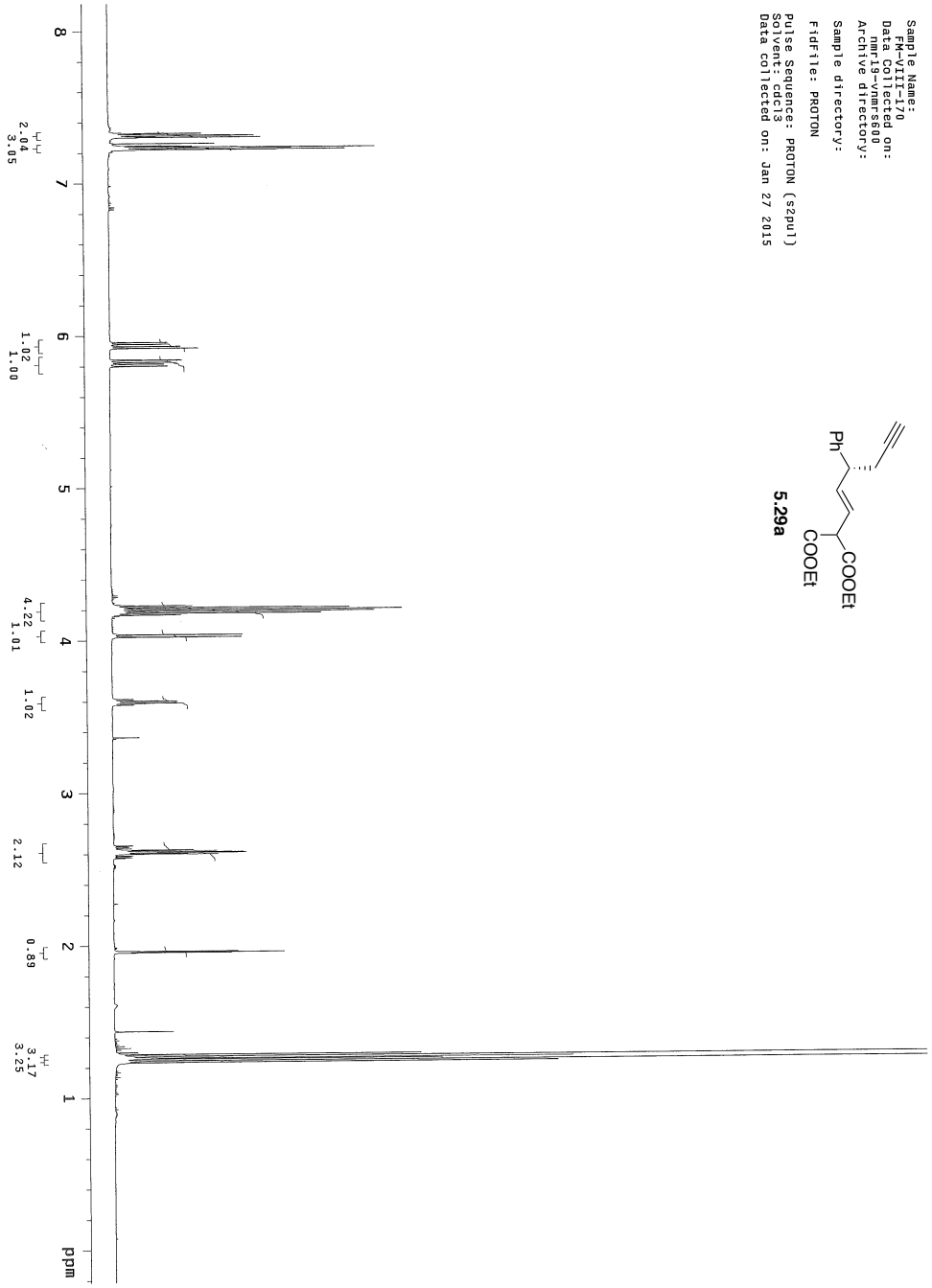
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Dec 30 2014



5.21a



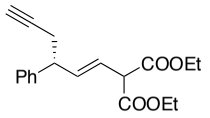

Sample Name:
FM-VIII-170
Data Collected on:
nmr19-vnmrs600
Archive directory:
Sample directory:
F1dFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 27 2015
Ph
COOEt
COOEt
5.29a
8
7
6
5
4
3
2
1
ppm
2.04
3.05
1.02
1.00
4.22
1.01
1.02
2.12
0.89
3.17
3.25

Sample Name:
FM-VIII-170
Data Collected on:
nmr19-vnmrs600
Archive directory:

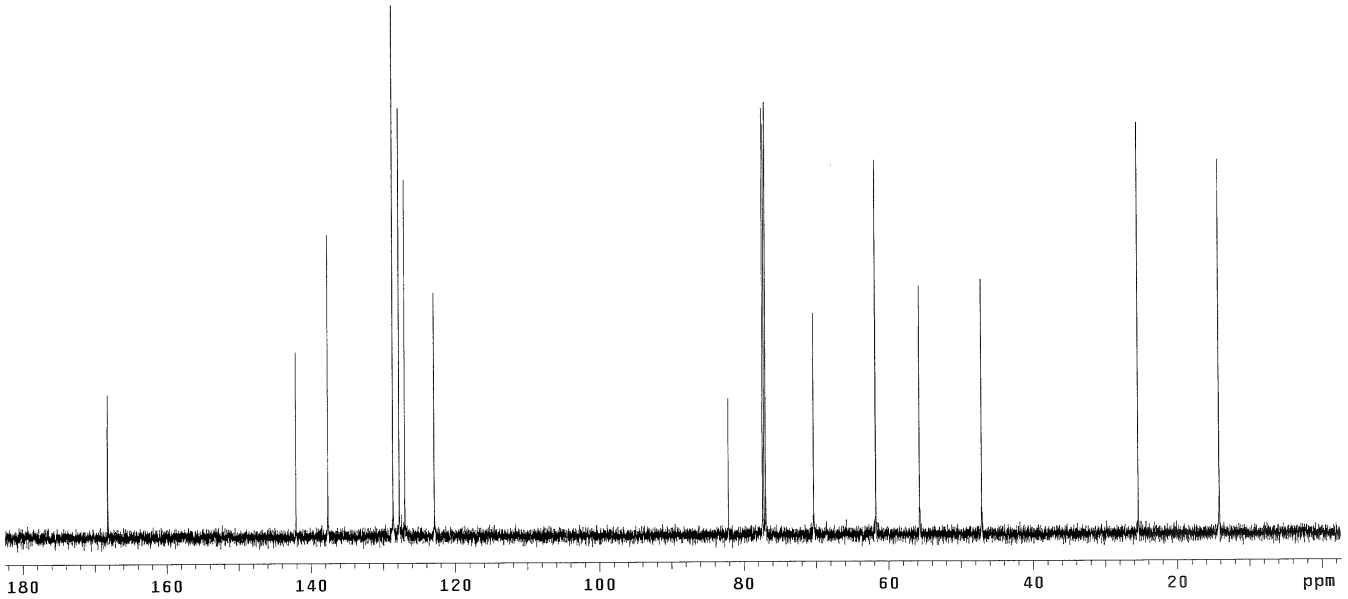
Sample directory:

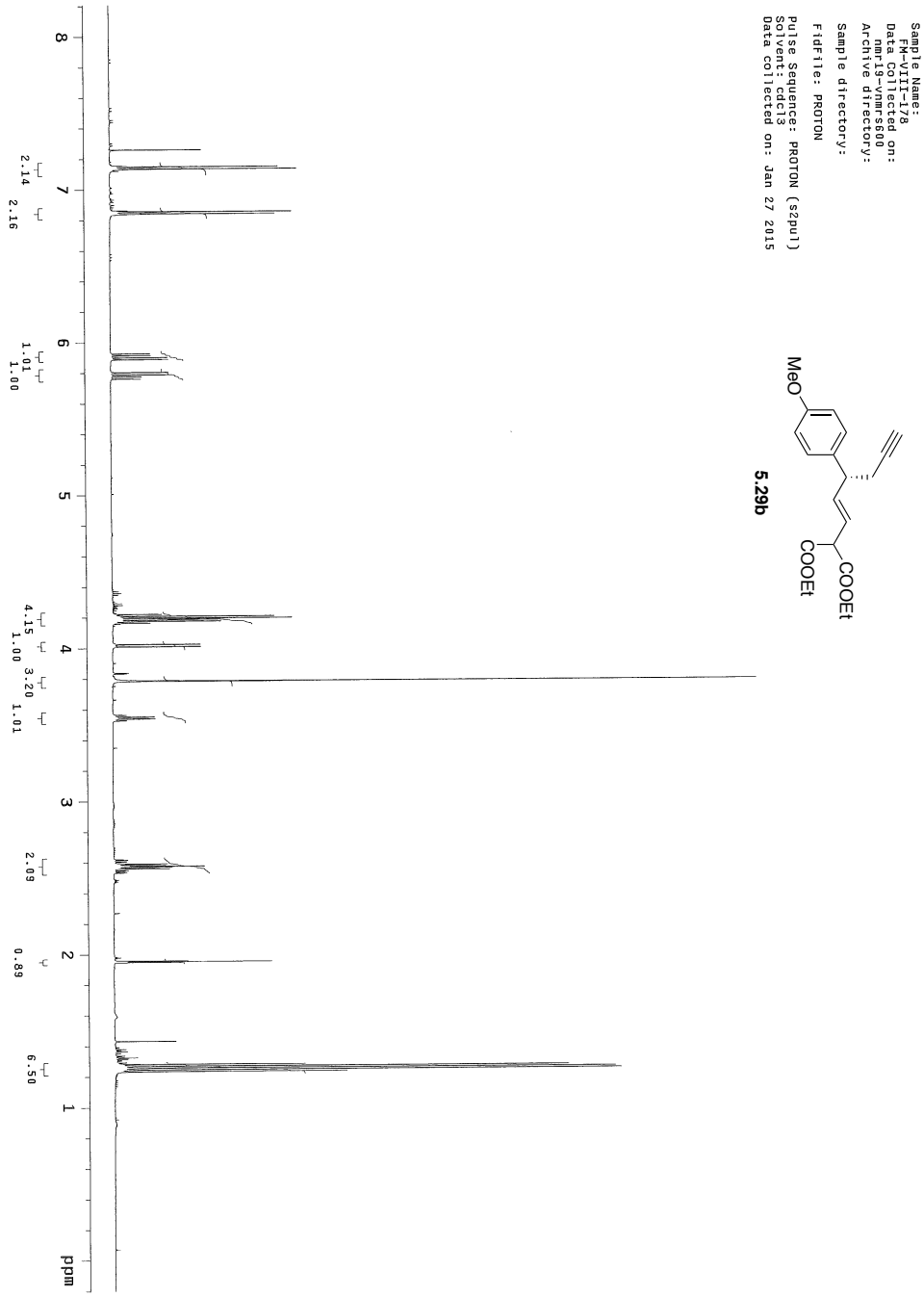
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 27 2015



5.29a



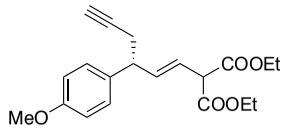

Sample Name:
FM-VIII-178
Data Collected on:
nmr19-vnmrs600
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 27 2015
MeO
COOEt
COOEt
5.29b
8
7
6
5
4
3
2
1
ppm
2.14
2.16
1.01
1.00
4.15
1.00
3.20
1.01
2.09
0.89
6.50

Sample Name:
FM-VIII-178
Data Collected on:
nmr19-vnmrs600
Archive directory:

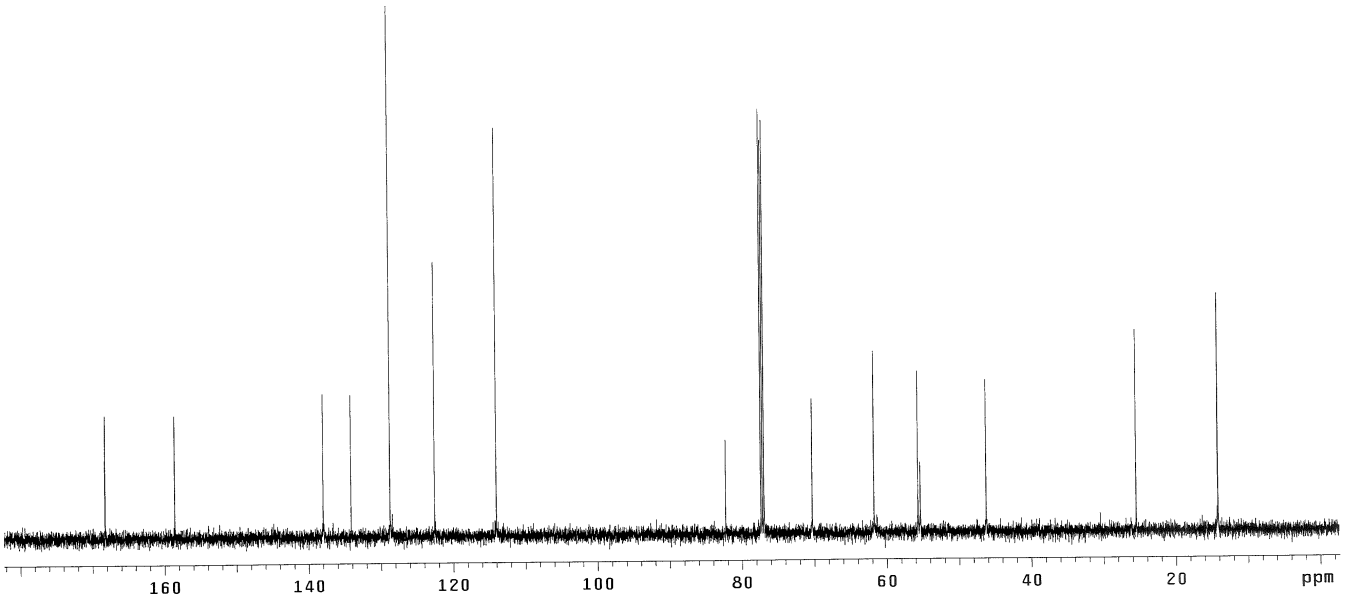
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 27 2015



5.29b

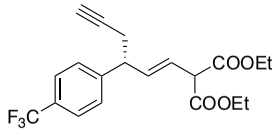


Sample Name:
FM-VIII-187
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Feb 19 2015



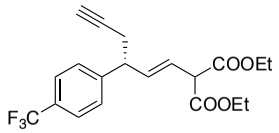
5.29c

Sample Name:
FM-VIII-187-CNMR
Data Collected on:
vnmr13-vnmrs400
Archive directory:

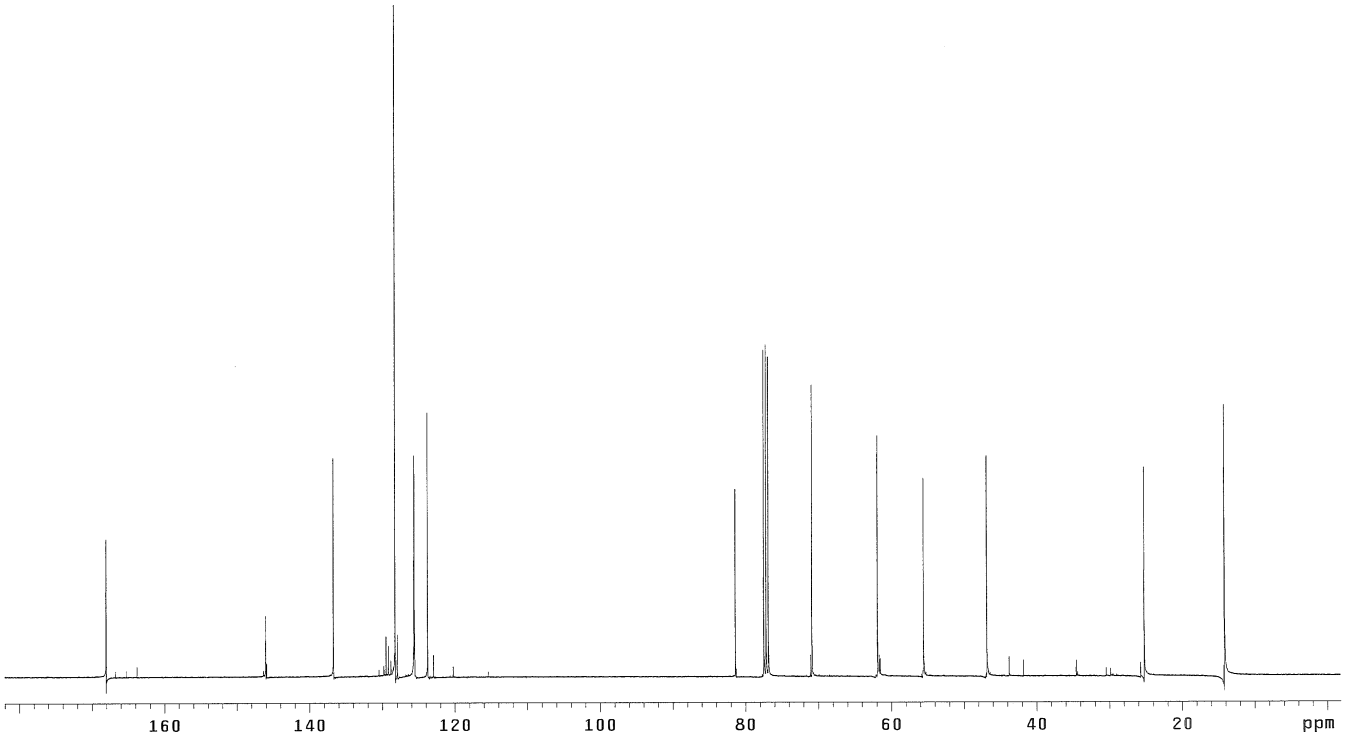
Sample directory:

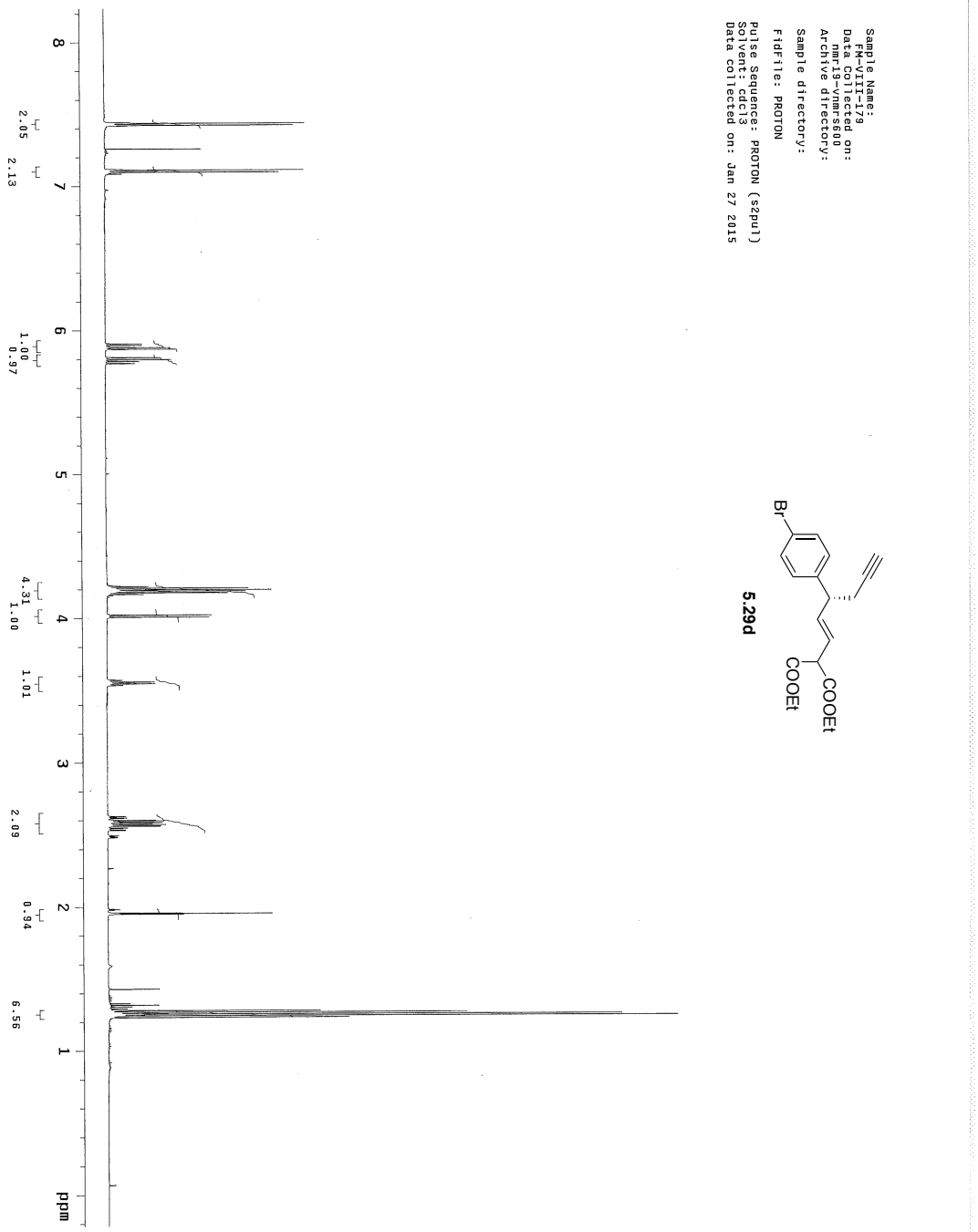
FidFile: FM-VIII-187-CNMR

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Feb 19 2015



5.29c



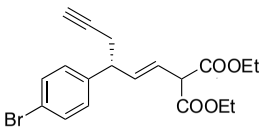

Sample Name:
FM-VIII-179
Data Collected on:
nmr19-vnmrs600
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 27 2015
Br
COOEt
COOEt
5.29d
8
7
6
5
4
3
2
1
ppm
2.05
2.13
1.00
0.97
4.31
1.00
1.01
2.09
0.94
6.56

Sample Name:
FM-VIII-179
Data Collected on:
nmr19-vnmrs600
Archive directory:

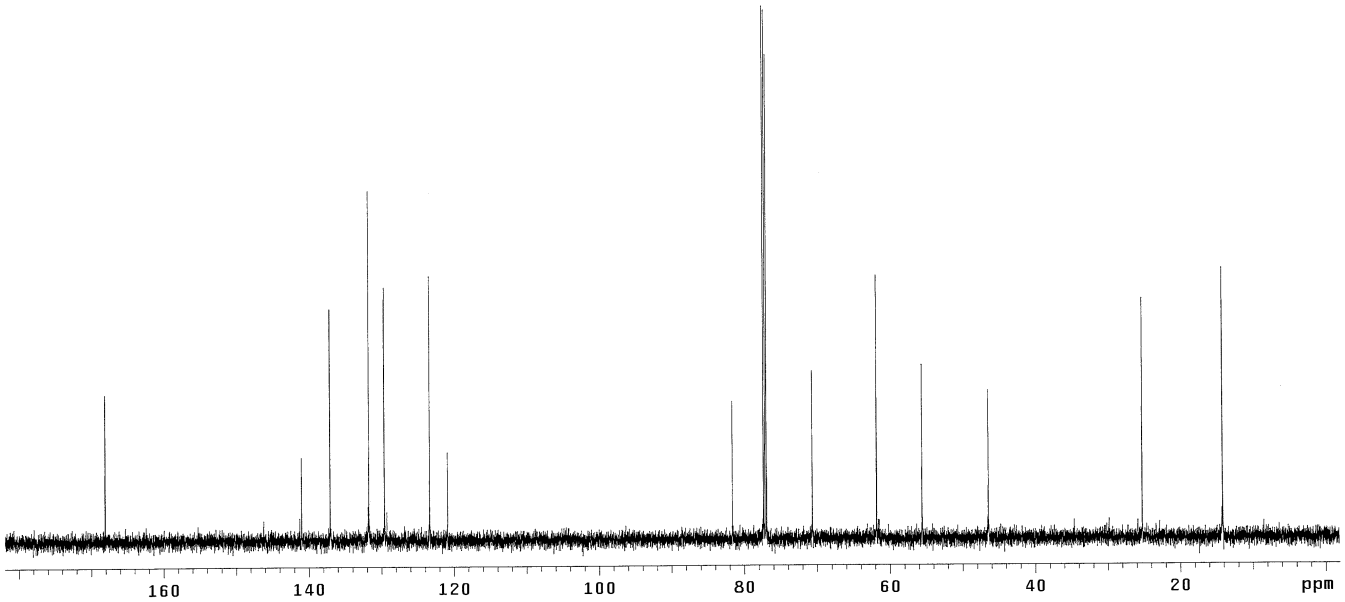
Sample directory:

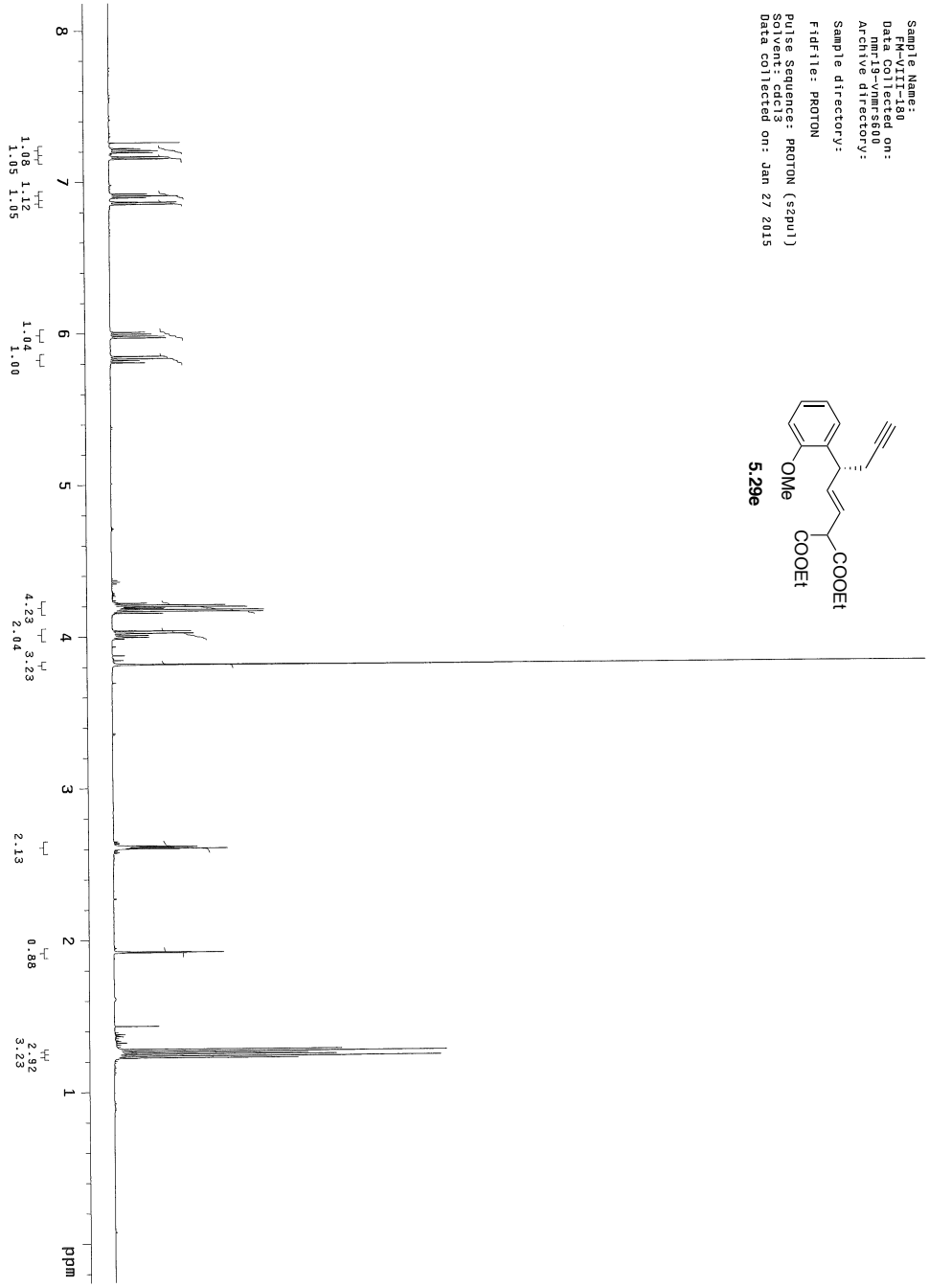
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 27 2015



5.29d



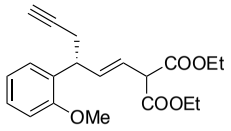

Sample Name:
FM-VIII-180
Data Collected on:
nmr19-vnmrs600
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 27 2015
OMe
COOEt
COOEt
5.29e
ppm

Sample Name:
FM-VIII-180
Data Collected on:
nmr19-vnmrs600
Archive directory:

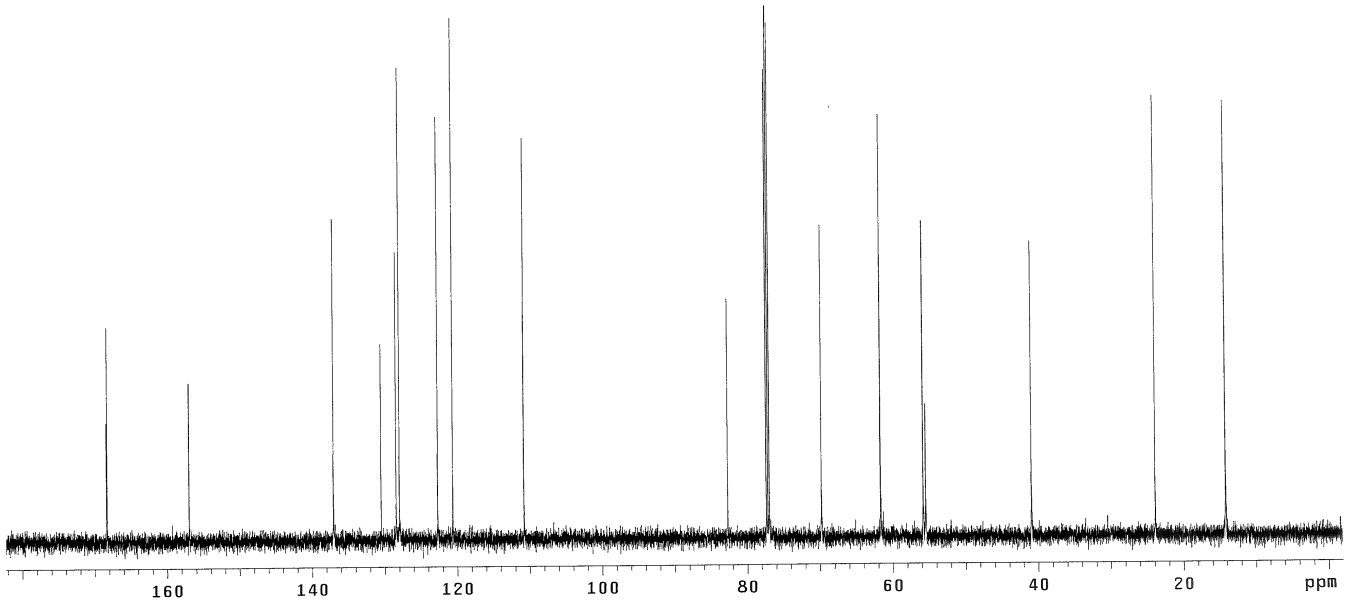
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 27 2015



5.29e

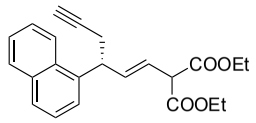


Sample Name:
FM-VIII-210
Data Collected on:
nmr14-vnmrs400
Archive directory:

Sample directory:

FidFile: FM-VIII-210

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 31 2015



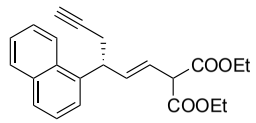
5.29f

Sample Name:
FM-VIII-210-CNMR
Data Collected on:
nmr19-vnmrs600
Archive directory:

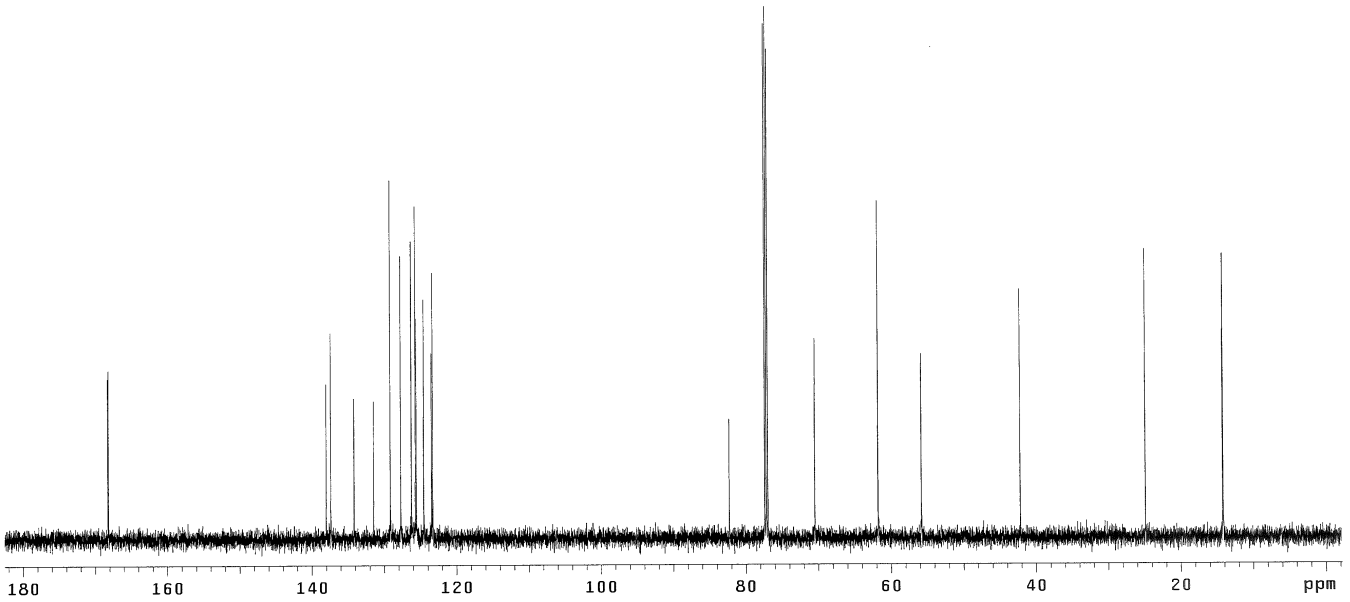
Sample directory:

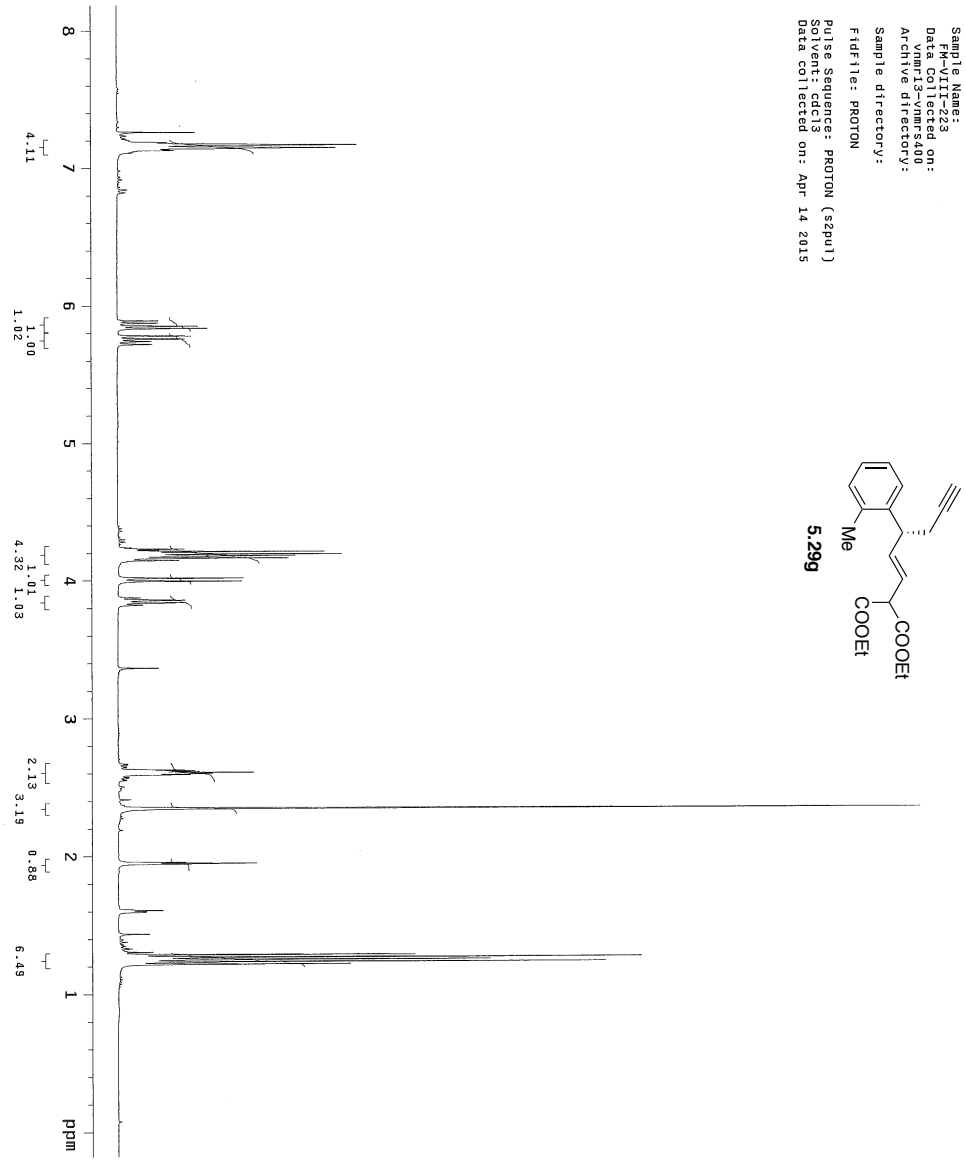
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 31 2015



5.29f



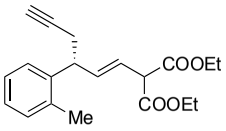

Sample Name:
FM-VII-223
Data Collected on:
vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 14 2015
Me
COOEt
COOEt
5.29g
8
7
6
5
4
3
2
1
ppm
4.11
1.00
1.02
1.01
4.32
1.03
2.13
3.19
0.88
6.49

Sample Name:
FM-VIII-223
Data Collected on:
vnmr13-vnmrs400
Archive directory:

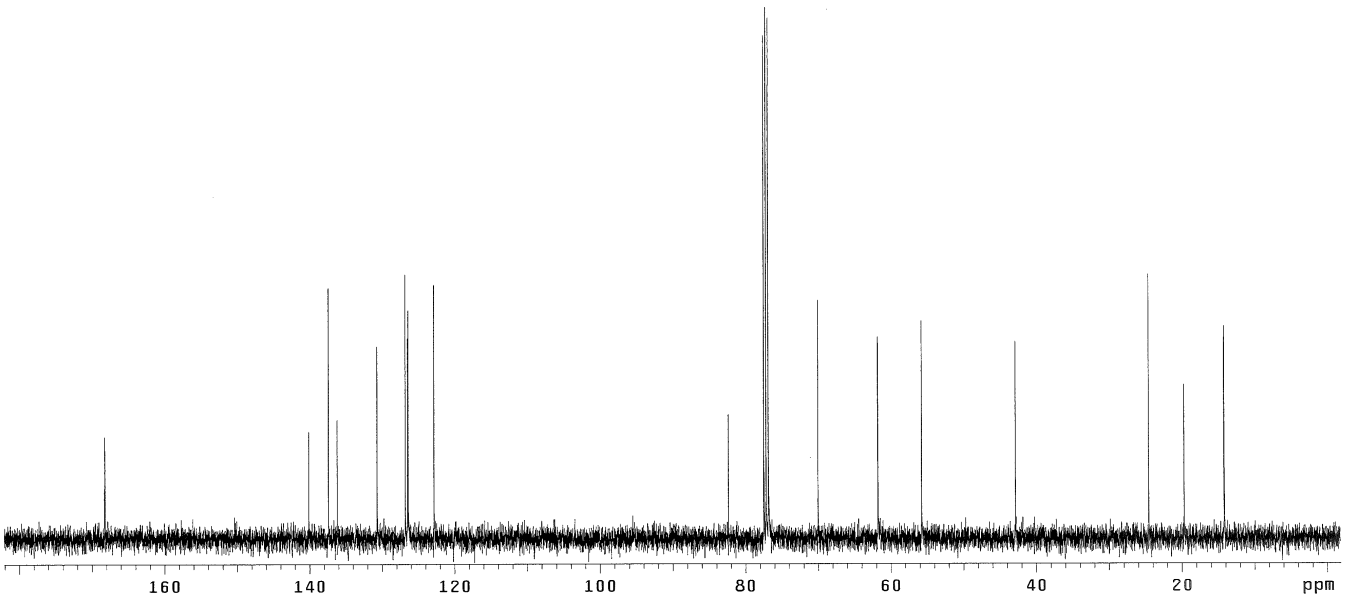
Sample directory:

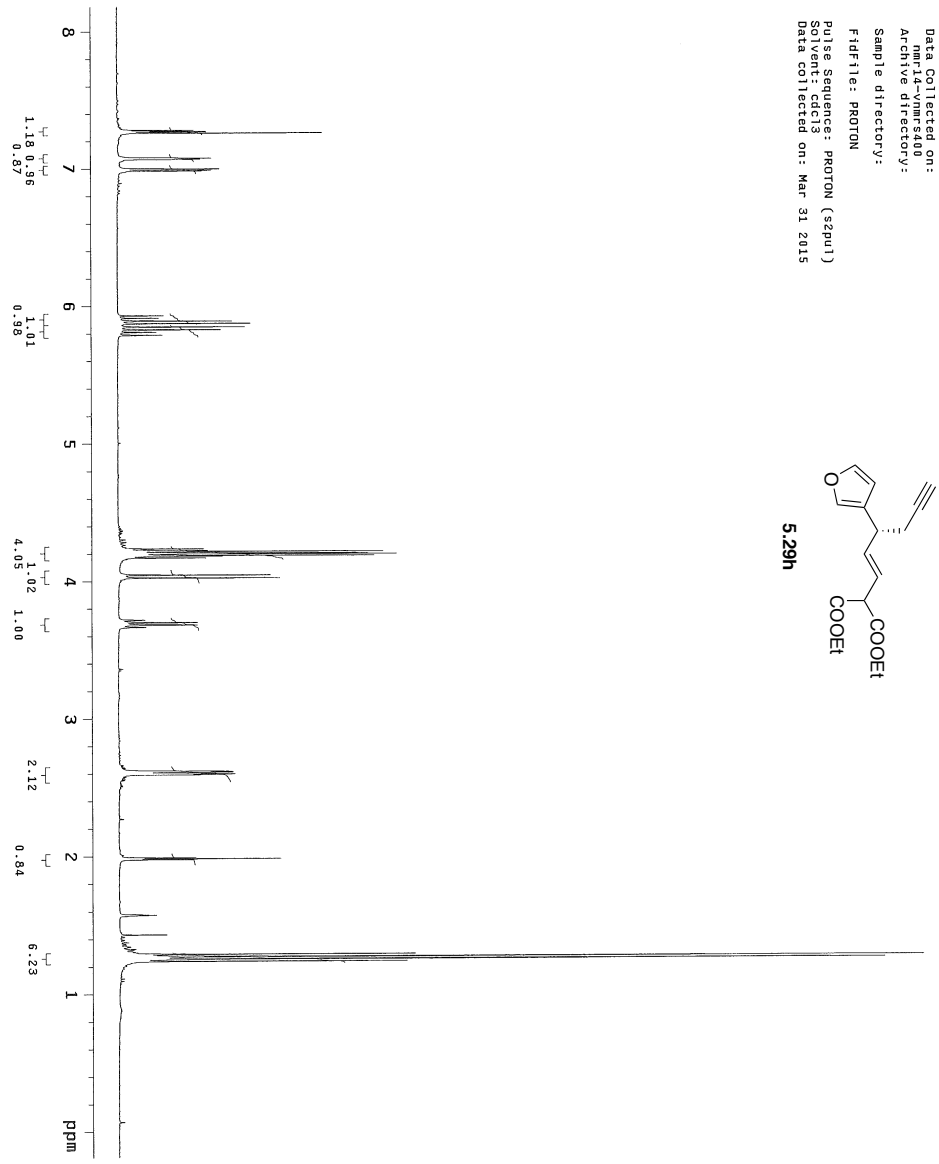
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 14 2015



5.29g



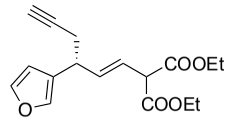

Sample Name:
FM-VIII-212
Data Collected on:
nmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 31 2015
5.29h
COOEt
COOEt
O
8
7
6
5
4
3
2
1
ppm
1.18 0.96
0.87
1.01
0.98
1.02
4.05
1.00
2.12
0.84
6.23

Sample Name:
FM-VIII-212-CNMR
Data Collected on:
nmr19-vnmrs600
Archive directory:

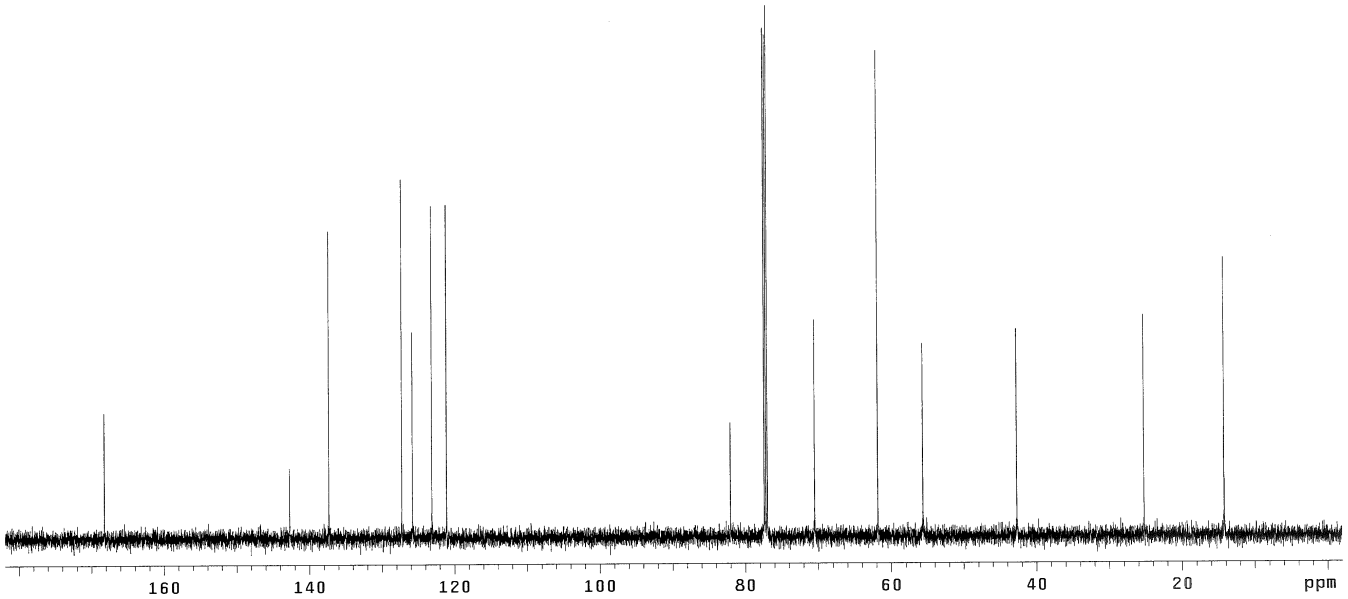
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 31 2015



5.29h

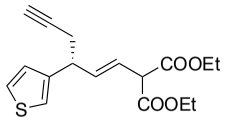


Sample Name:
FM-VIII-204
Data Collected on:
vnmr13-vnmrs400
Archive directory:

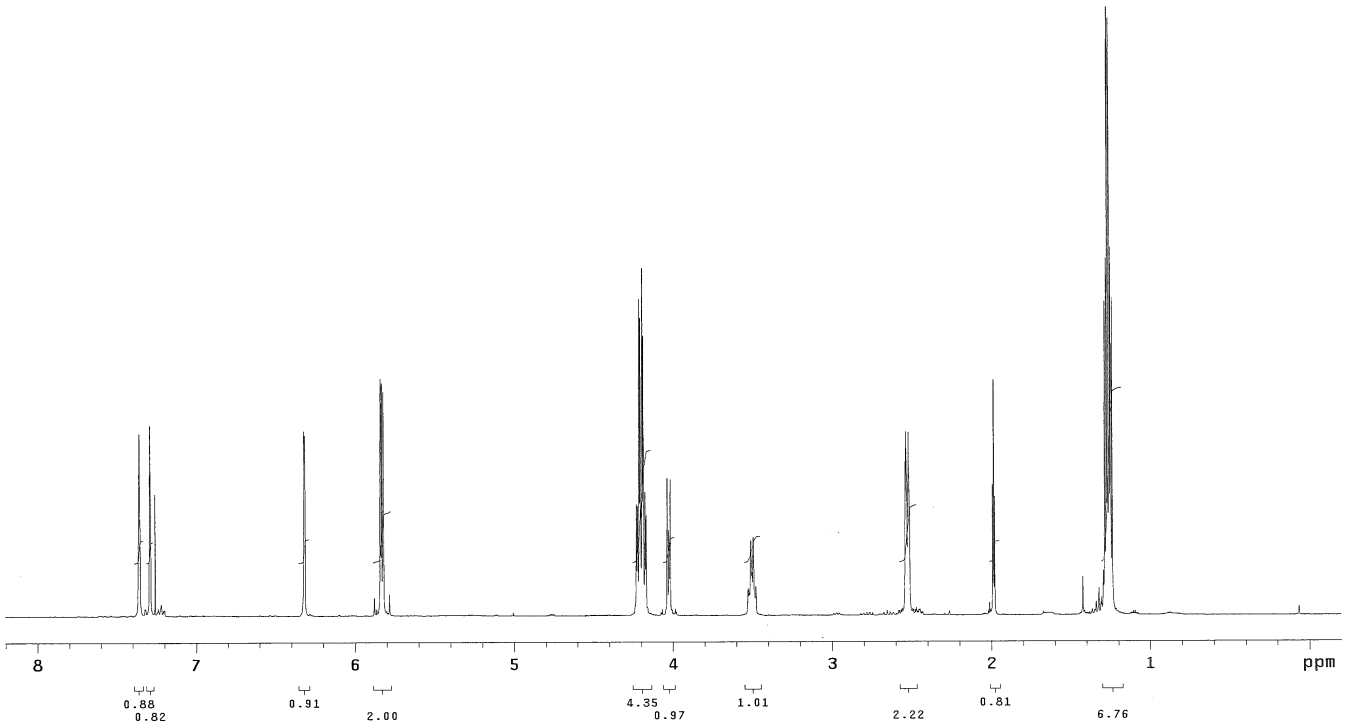
Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 18 2015



5.29i

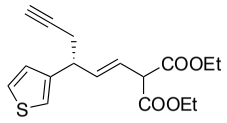


Sample Name:
FM-VIII-204
Data Collected on:
vnmr13-vnmrs400
Archive directory:

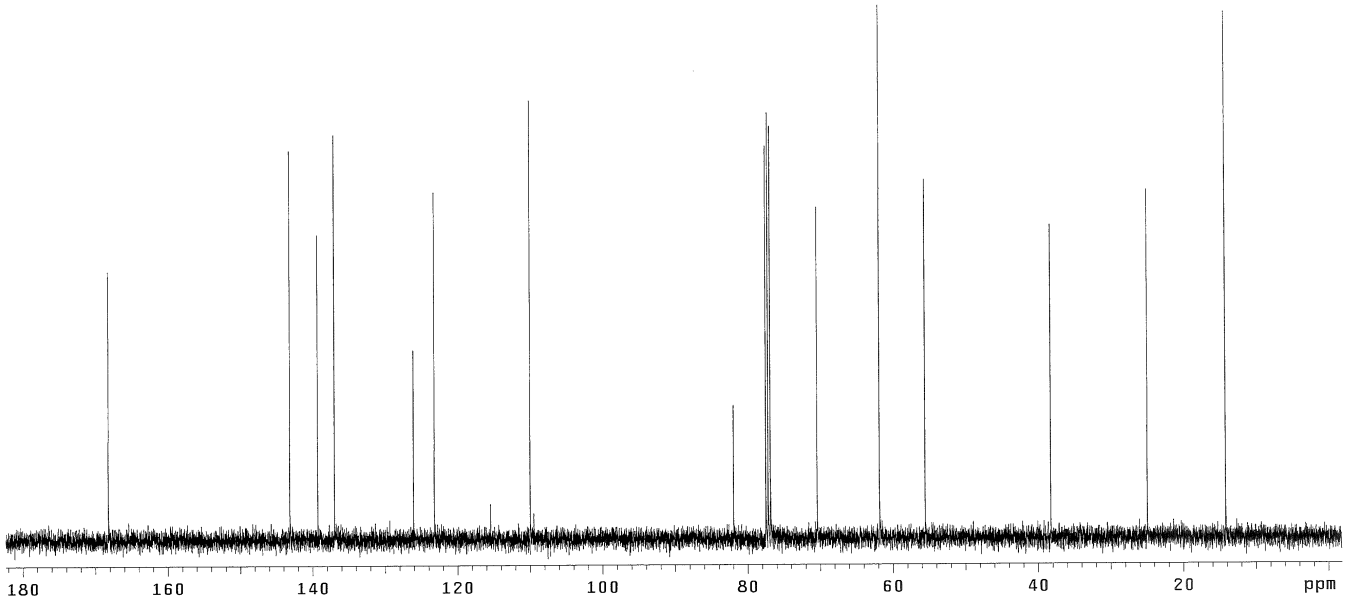
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 18 2015



5.29i

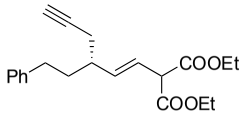


Sample Name:
FM-VIII-288
Data Collected on:
nmr14-vnmrs400
Archive directory:

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jul 27 2015



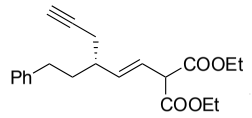
5.37a

Sample Name:
FM-VIII-288
Data Collected on:
nmr14-vnmrs400
Archive directory:

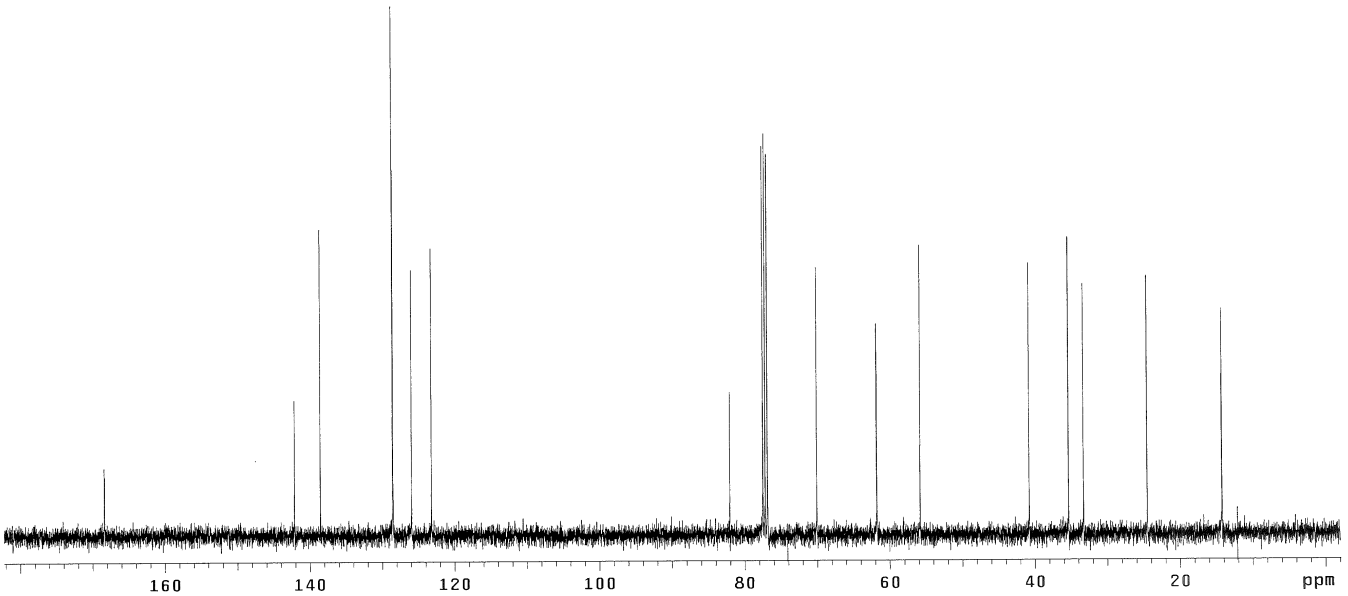
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jul 27 2015



5.37a

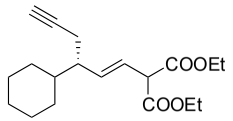


Sample Name:
FM-VIII-290
Data Collected on:
nmr14-vnmrs400
Archive directory:

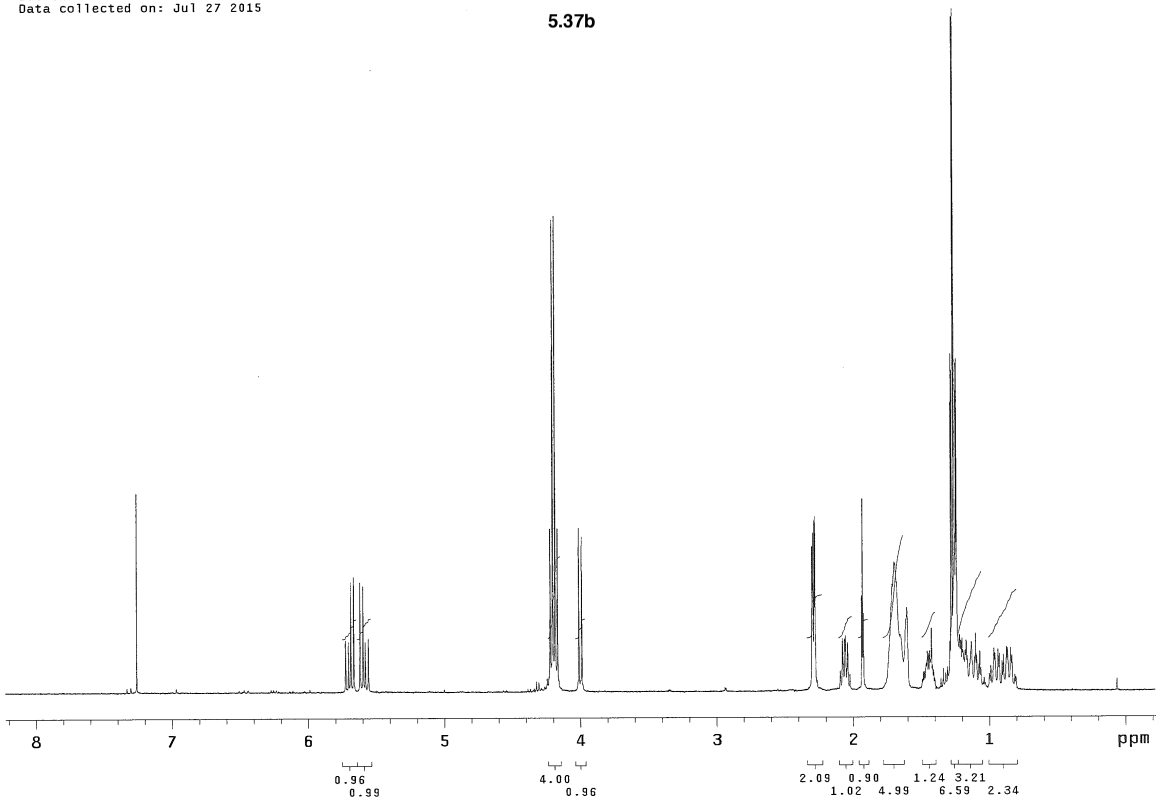
Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jul 27 2015



5.37b

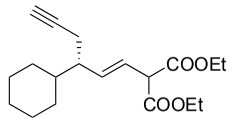


Sample Name:
FM-VIII-290
Data Collected on:
nmr14-vnmrs400
Archive directory:

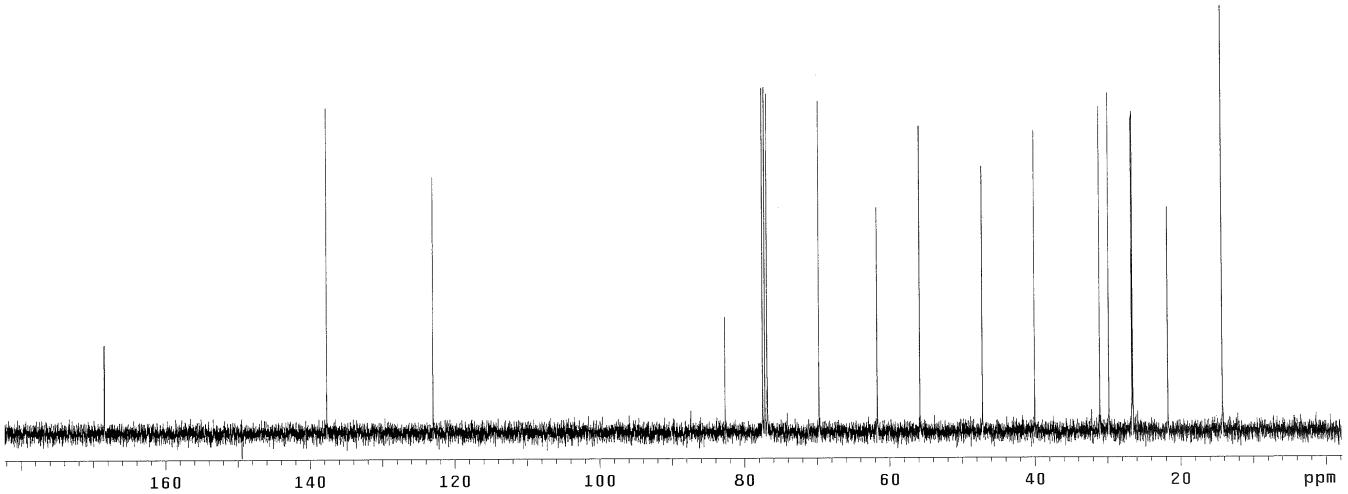
Sample directory:

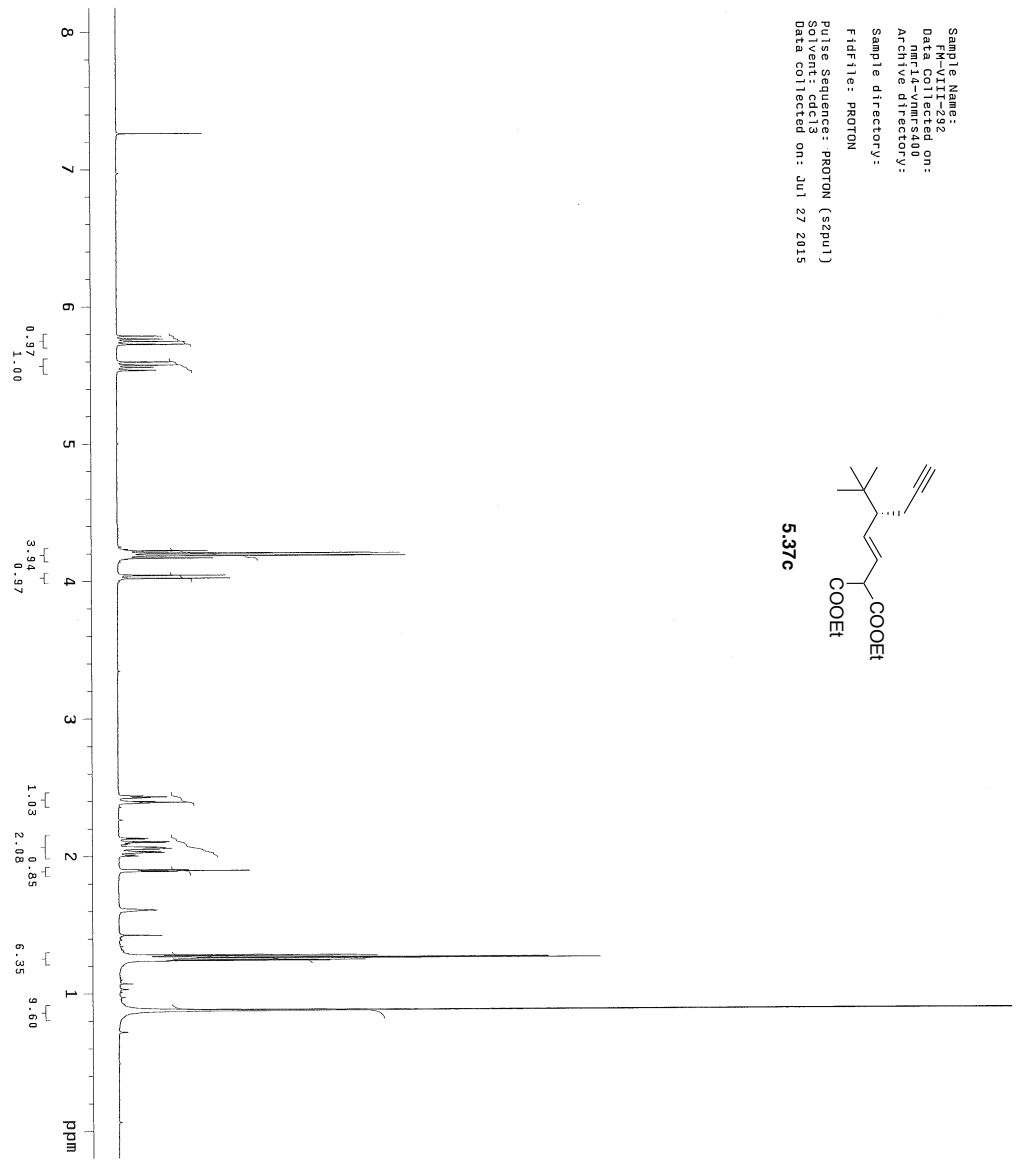
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jul 27 2015



5.37b



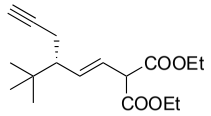

Sample Name:
FM-VIII-292
Data Collected on:
nmr14-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jul 27 2015
5.37c
COOEt
COOEt
8
7
6
5
4
3
2
1
ppm
0.97
1.00
3.94
0.97
1.03
2.08
0.85
6.35
9.60

Sample Name:
FM-VIII-292
Data Collected on:
nmr14-vnmrs400
Archive directory:

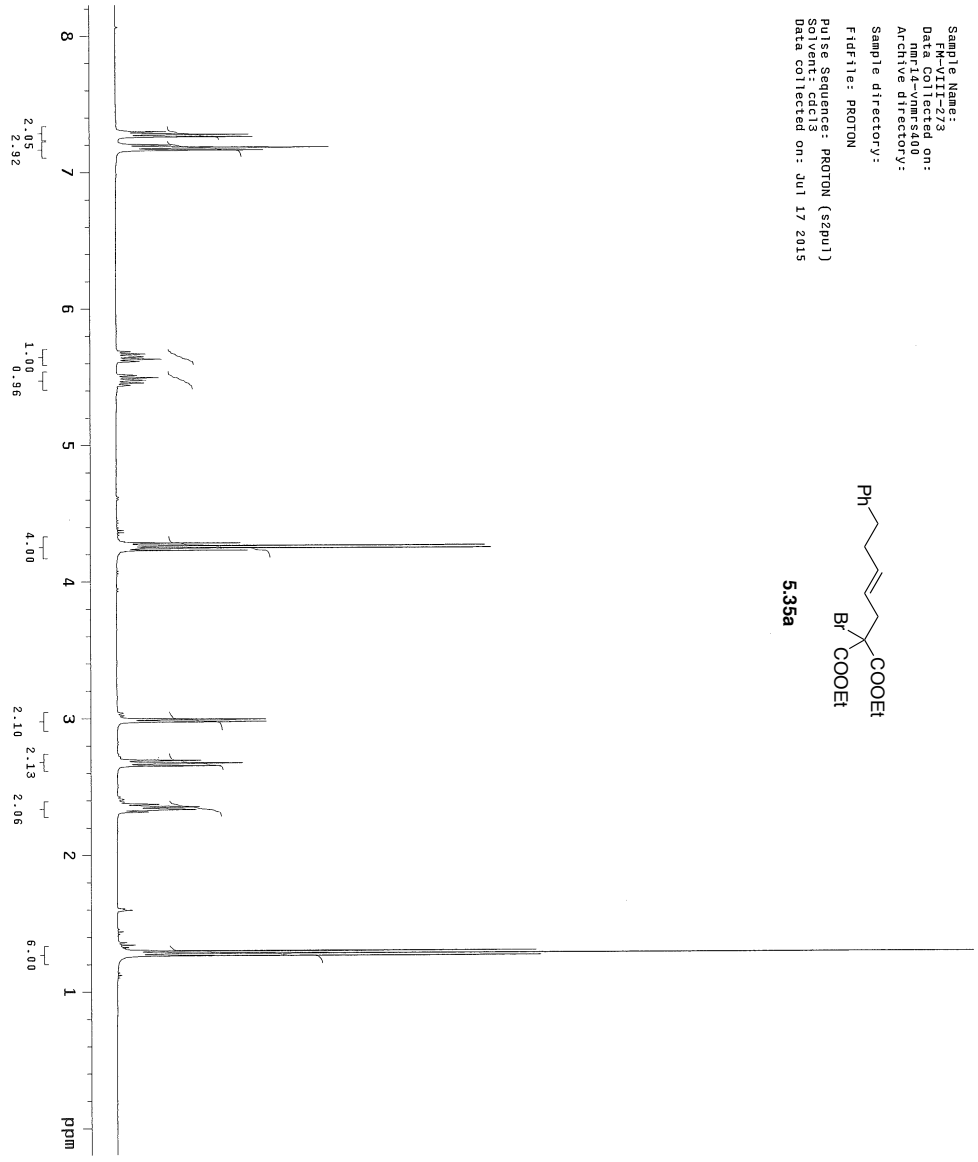
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jul 27 2015



5.37c

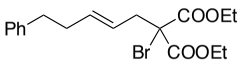

Sample Name:
FM-VIII-273
Data Collected on:
nmr14-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jul 17 2015
Ph
Br
COOEt
COOEt
5.35a
2.05
2.92
1.00
0.96
4.00
2.10
2.13
2.06
6.00
8
7
6
5
4
3
2
1
ppm

Sample Name:
FM-VIII-273
Data Collected on:
nmr14-vnmrs400
Archive directory:

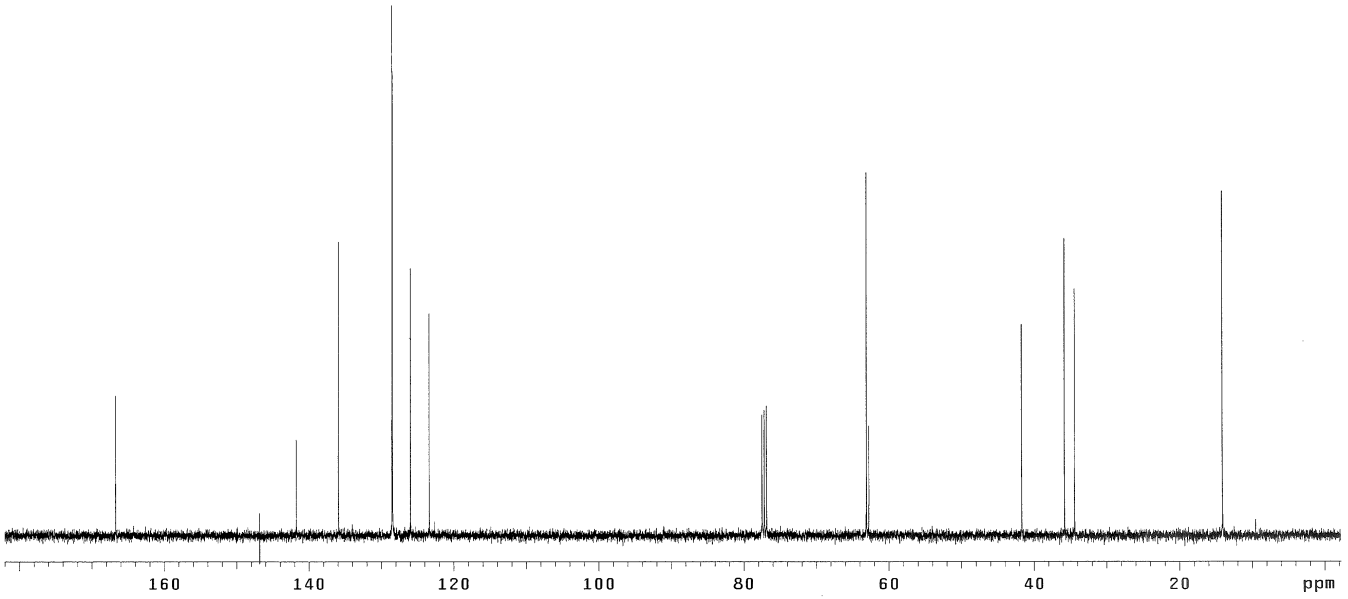
Sample directory:

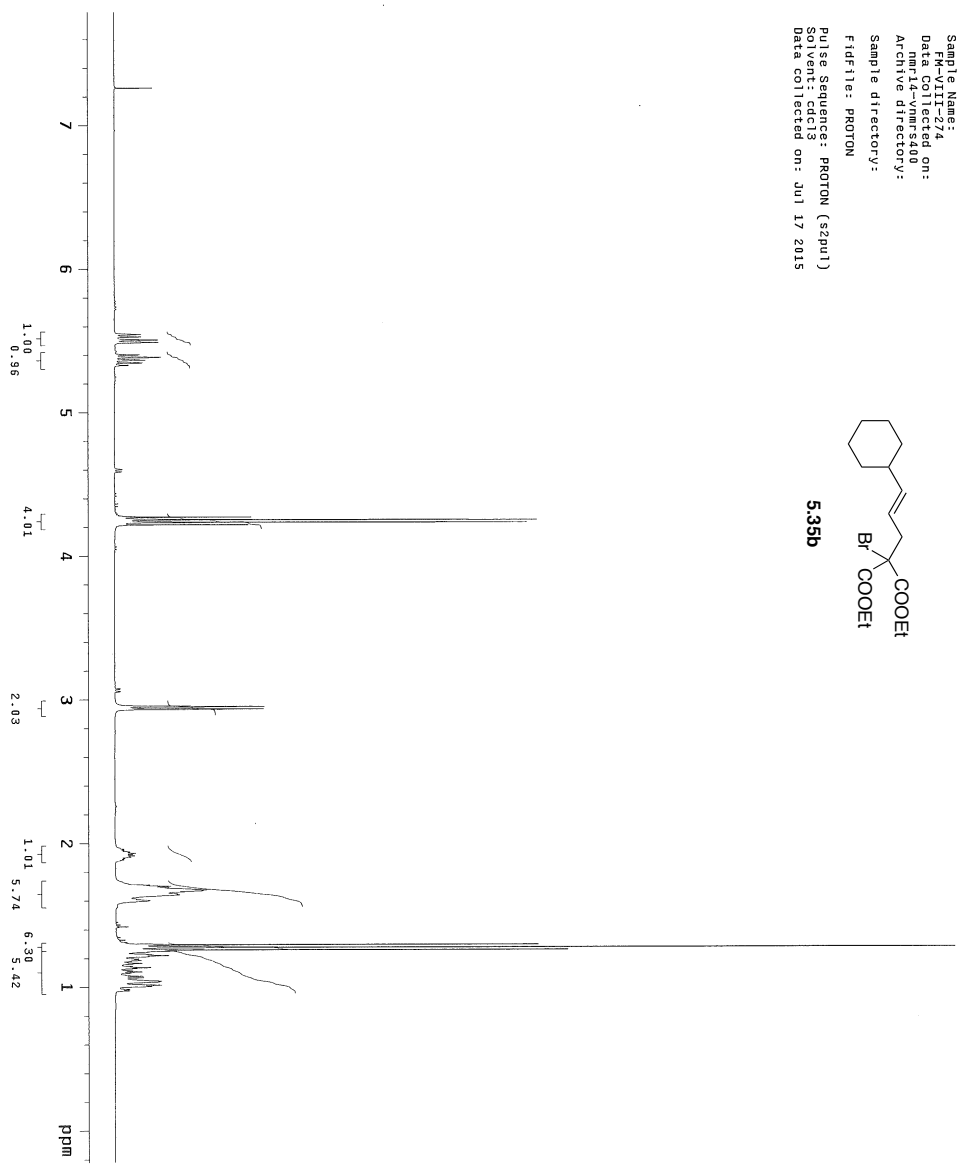
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jul 17 2015



5.35a



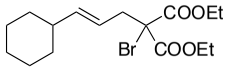

Sample Name:
FM-VIII-274
Data Collected on:
nmr14-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jul 17 2015
Br
COOEt
COOEt
5.35b
7
6
5
4
3
2
1
ppm
1.00
0.96
4.01
2.03
1.01
5.74
6.30
5.42

Sample Name:
FM-VIII-274
Data Collected on:
nmr14-vnmrs400
Archive directory:

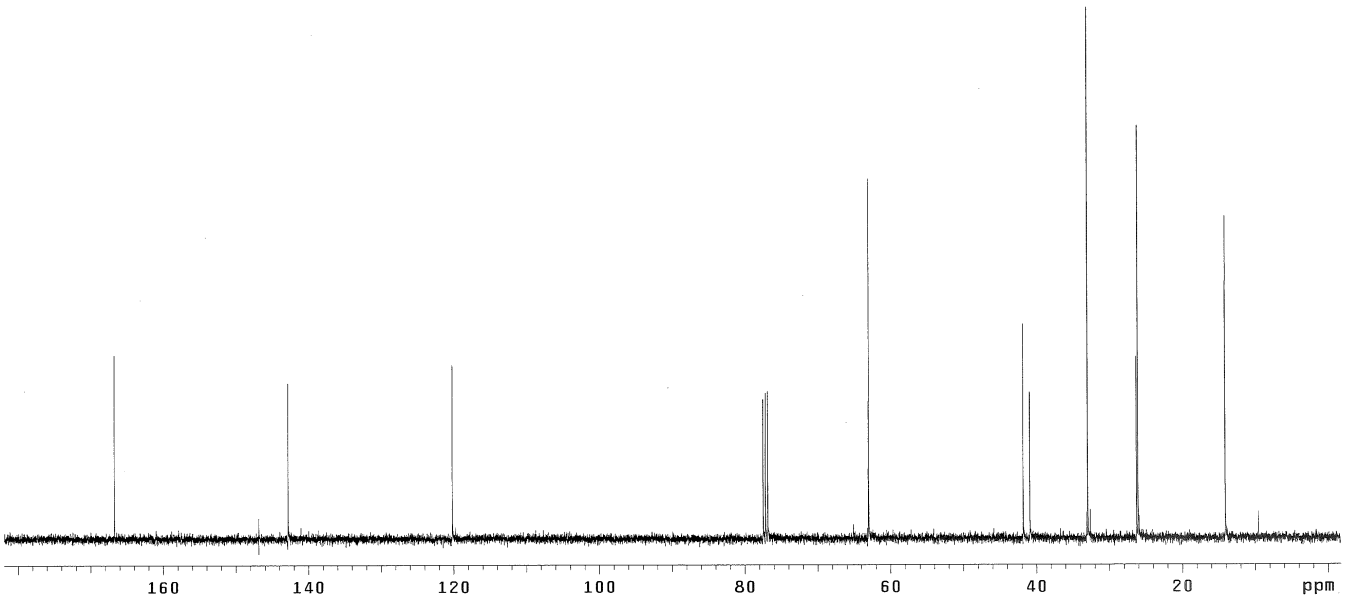
Sample directory:

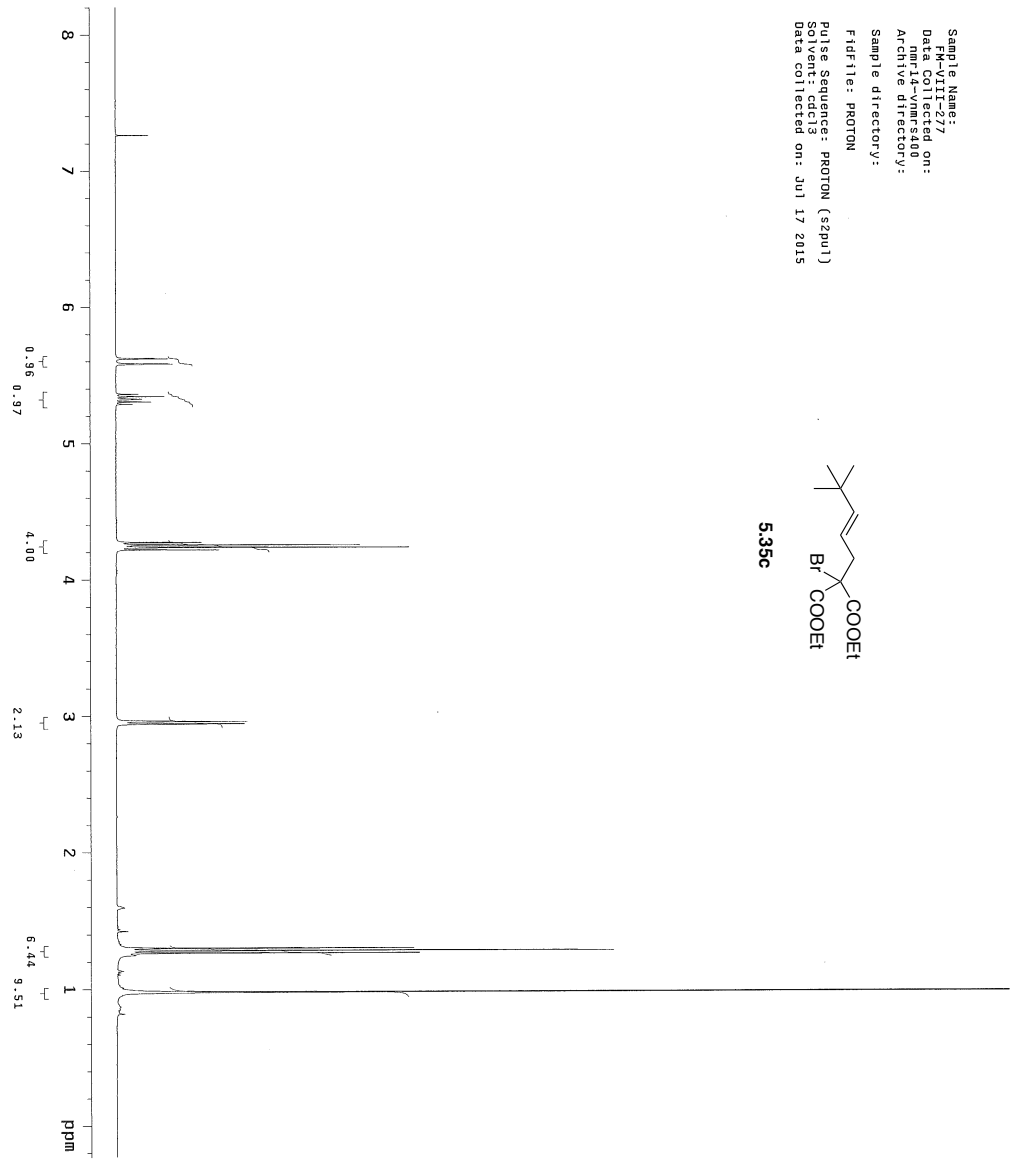
FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jul 17 2015



5.35b



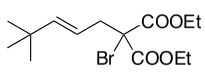

Sample Name:
FM-VIII-277
Data Collected on:
nmr14-vnmrs400
Archive directory:
Sample directory:
FidFile: PROTON
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jul 17 2015
5.35c
Br
COOEt
COOEt
8
7
6
5
4
3
2
1
ppm
0.96
0.97
4.00
2.13
6.44
9.51

Sample Name:
FM-VIII-277
Data Collected on:
nmr14-vnmrs400
Archive directory:

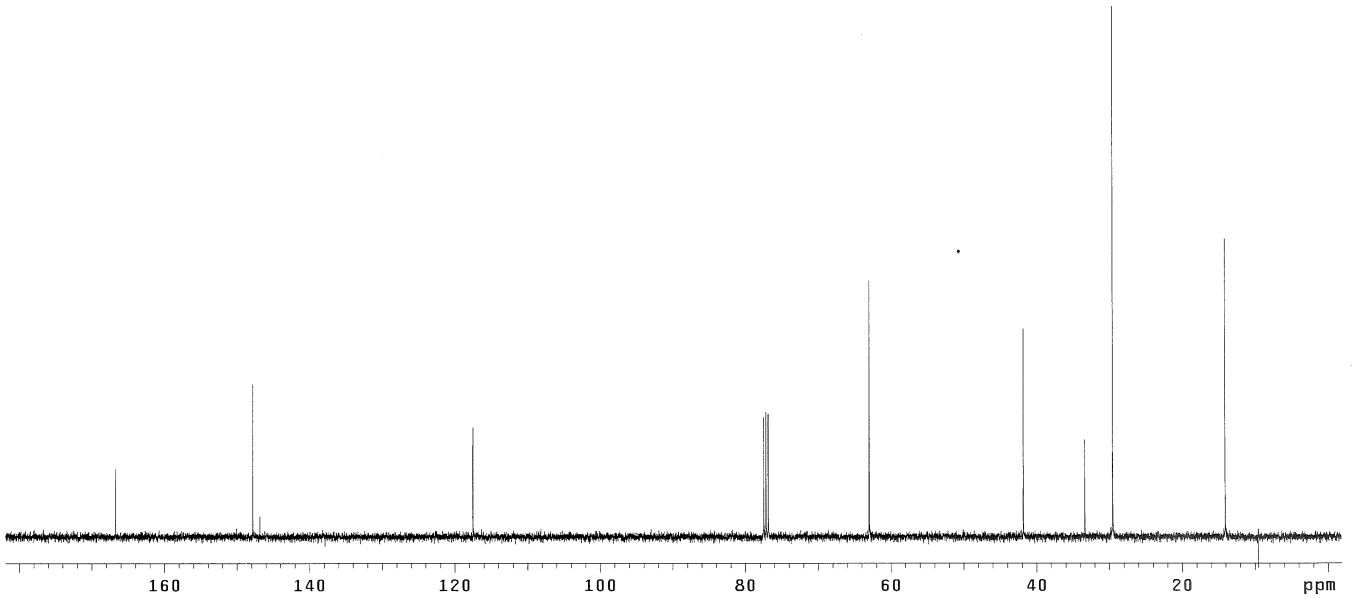
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jul 17 2015



5.35c

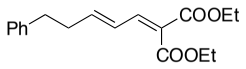


Sample Name:
FM-VIII-282
Data Collected on:
nmr14-vnmrs400
Archive directory:

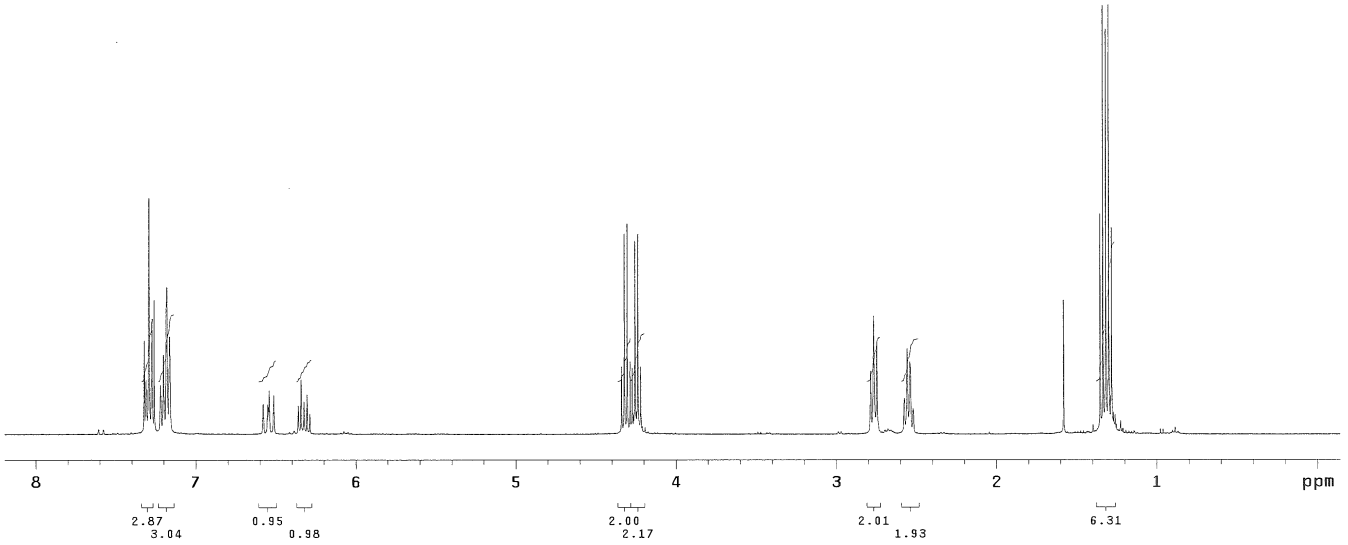
Sample directory:

FidFile: FM-VIII-282

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jul 20 2015



5.36a

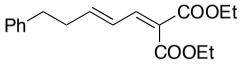


Sample Name:
FM-VIII-282
Data Collected on:
nmr14-vnmrs400
Archive directory:

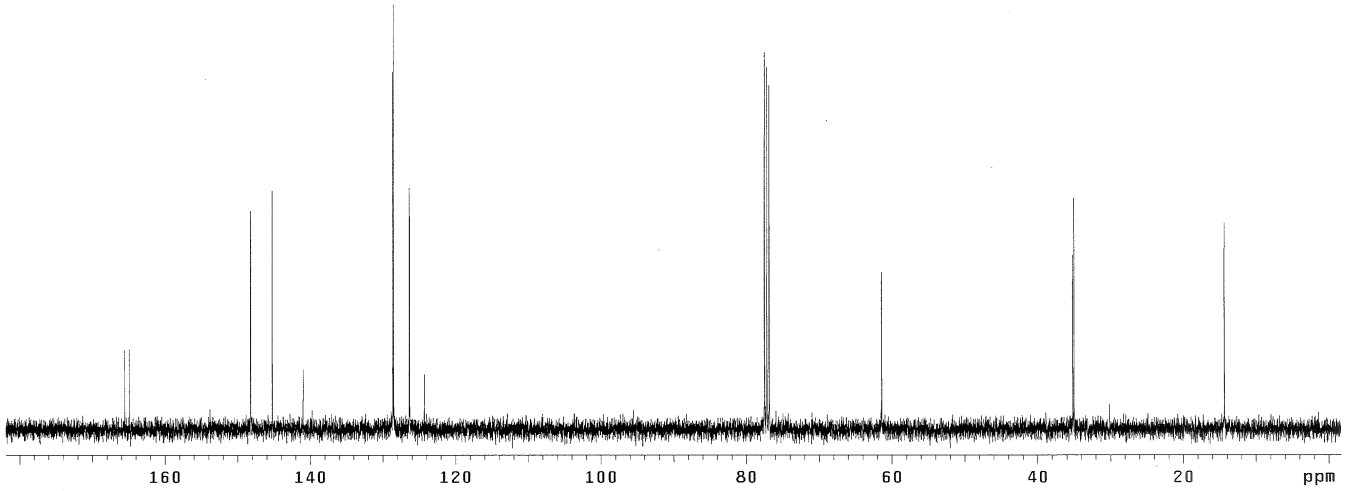
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jul 20 2015



5.36a

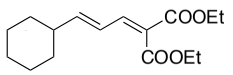


Sample Name:
FM-VIII-283
Data Collected on:
nmr14-vnmrs400
Archive directory:

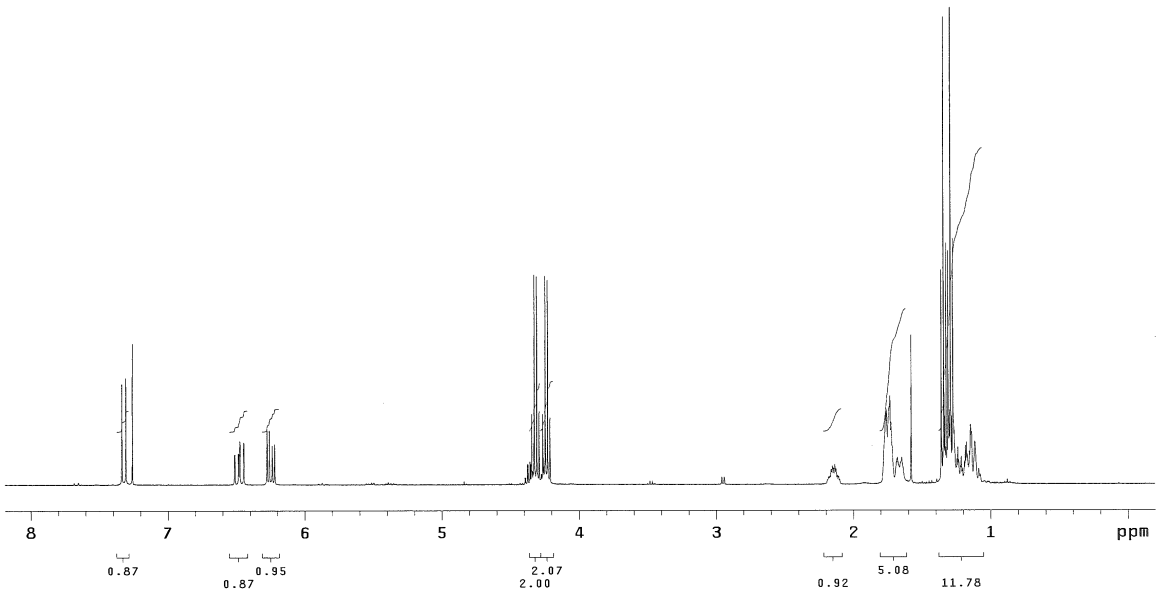
Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jul 20 2015



5.36b

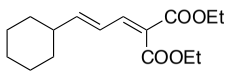


Sample Name:
FM-VIII-283
Data Collected on:
nmr14-vnmrs400
Archive directory:

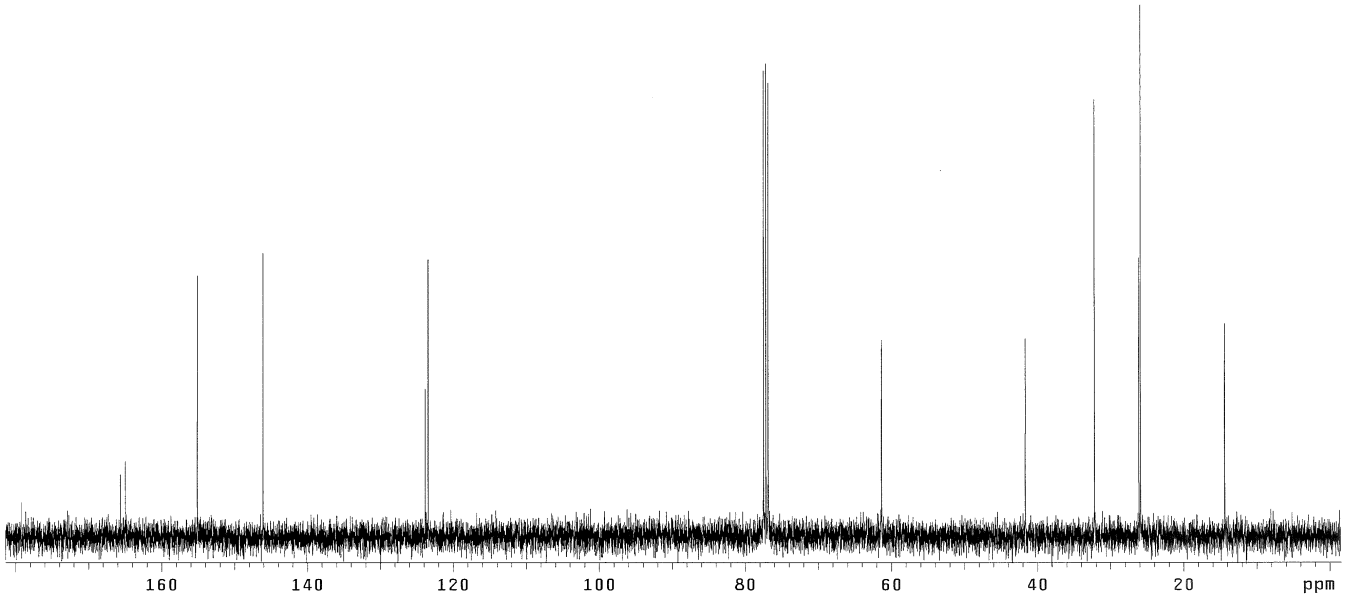
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jul 20 2015



5.36b

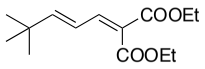


Sample Name:
FM-VIII-284
Data Collected on:
nmr14-vnmrs400
Archive directory:

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jul 20 2015



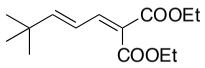
5.36c

Sample Name:
FM-VIII-284
Data Collected on:
nmr14-vnmrs400
Archive directory:

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jul 20 2015



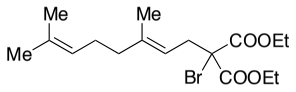
5.36c

Sample Name:
FM-VIII-306
Data Collected on:
nmr14-vnmrs400
Archive directory:

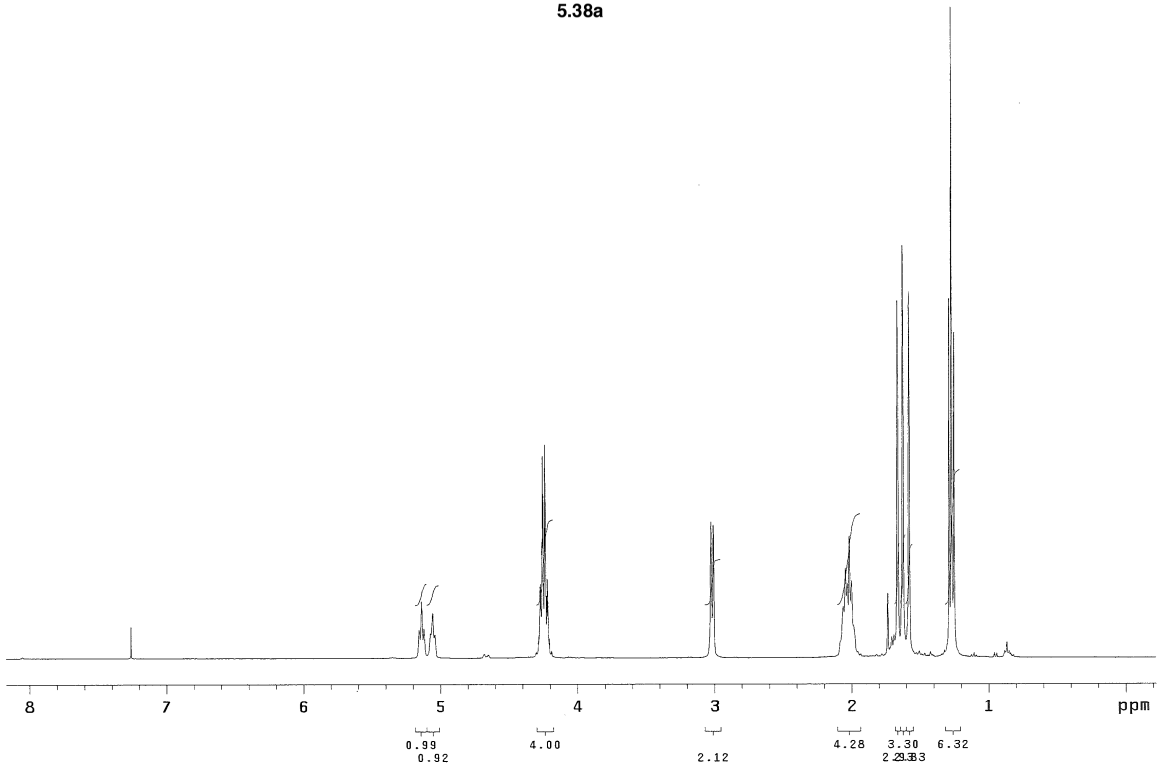
Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 10 2015



5.38a

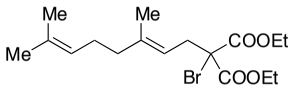


Sample Name:
FM-VIII-306
Data Collected on:
nmr14-vnmrs400
Archive directory:

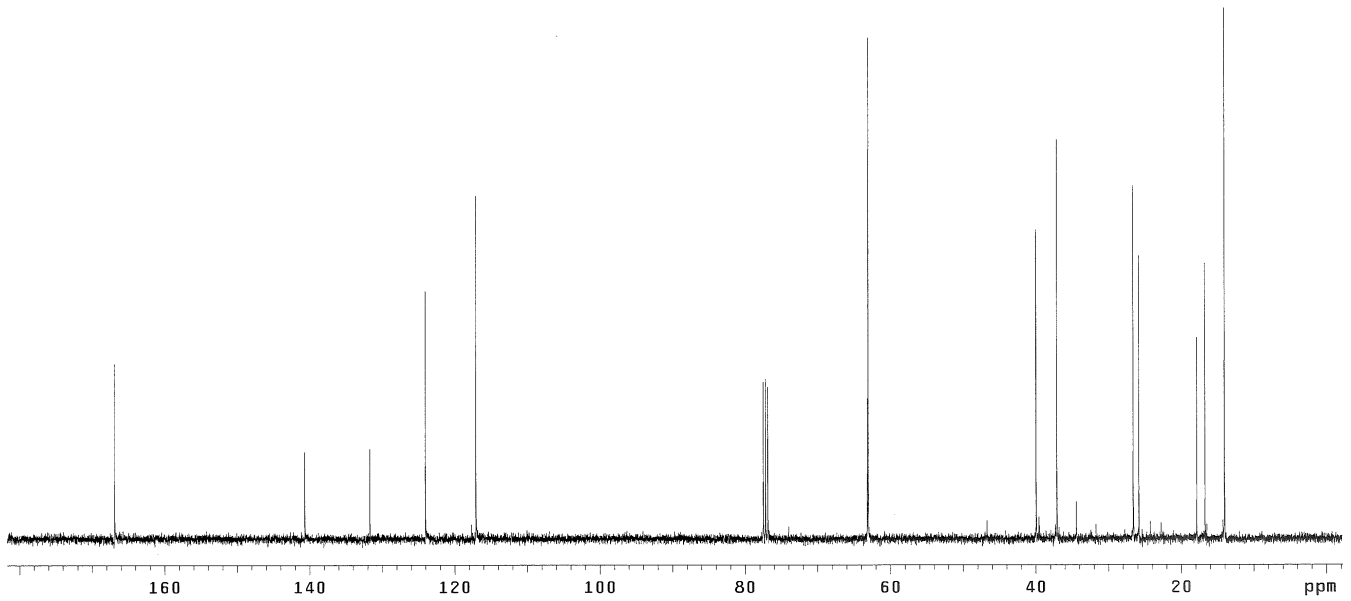
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 10 2015



5.38a



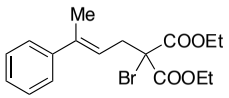
STANDARD FLUORINE PARAMETERS

Sample Name:
FM-VIII-311
Data Collected on:
nmr14-vnmrs400
Archive directory:

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 12 2015



5.38b

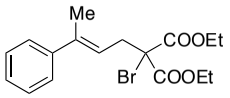
STANDARD FLUORINE PARAMETERS

Sample Name:
FM-VIII-311
Data Collected on:
nmr14-vnmrs400
Archive directory:

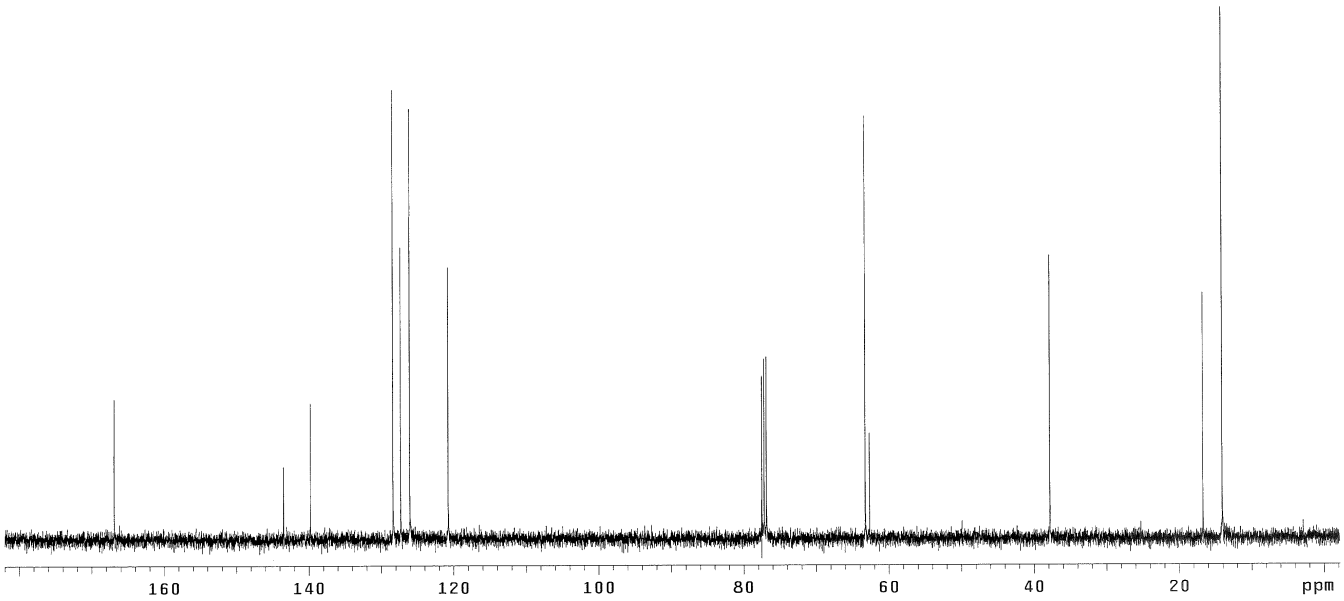
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 12 2015



5.38b

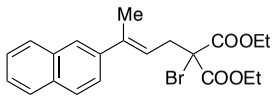


Sample Name:
FM-VIII-312
Data Collected on:
nmr14-vnmrs400
Archive directory:

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 12 2015



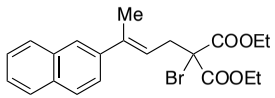
5.38c

Sample Name:
FM-VIII-312
Data Collected on:
nmr14-vnmrs400
Archive directory:

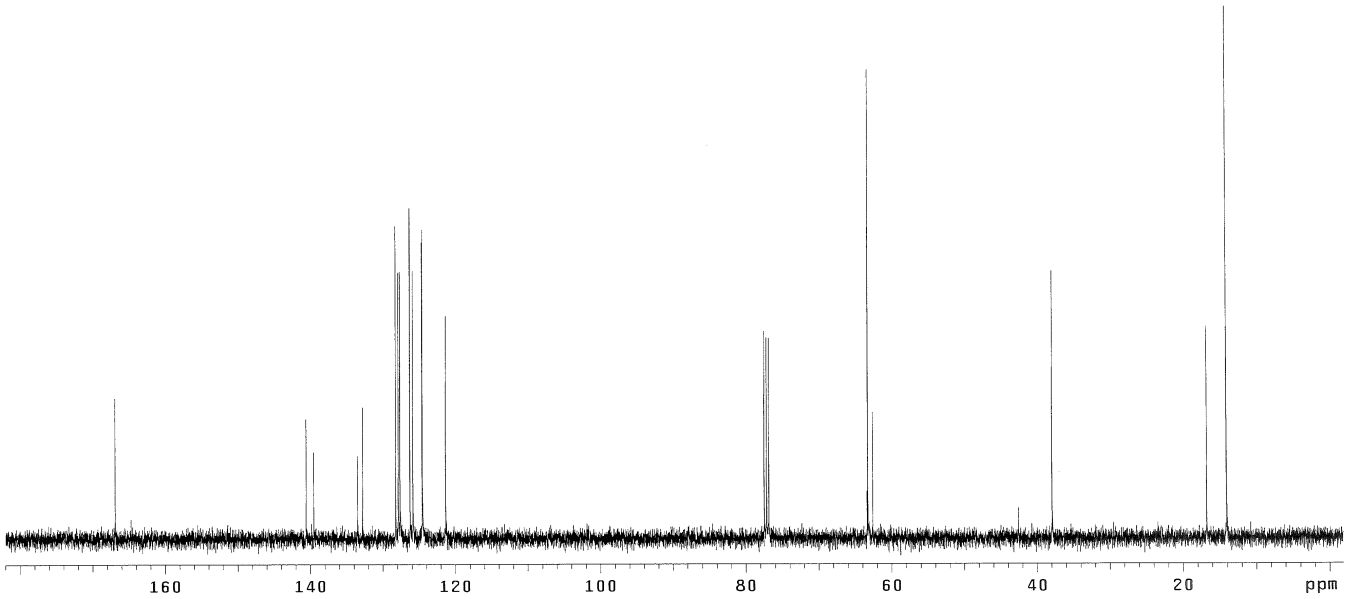
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 12 2015



5.38c

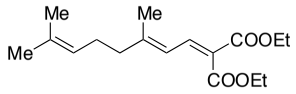


Sample Name:
FM-VIII-307
Data Collected on:
vnmr13-vnmrs400
Archive directory:

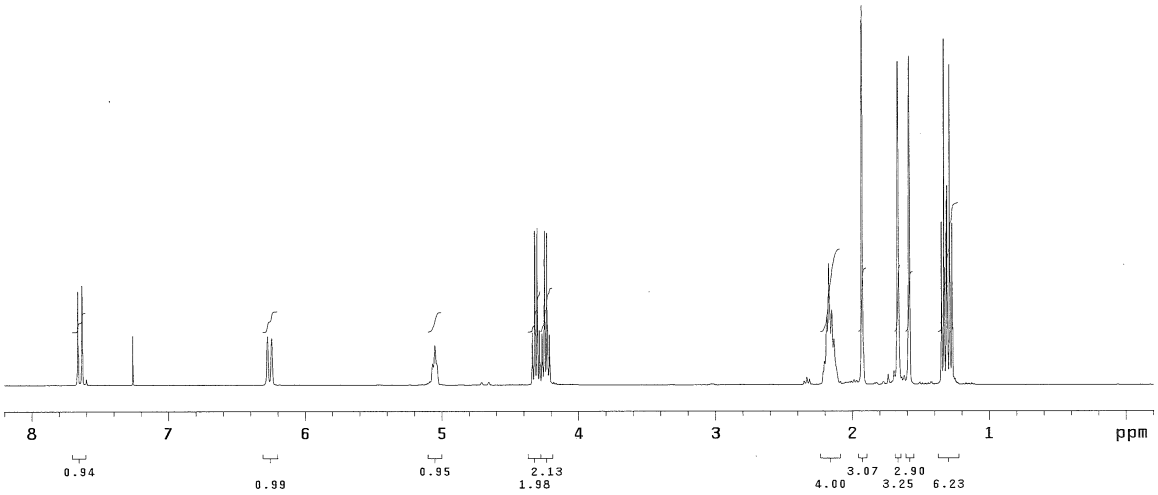
Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 10 2015



5.39a

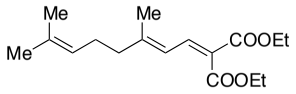


Sample Name:
FM-VIII-307
Data Collected on:
vnmr13-vnmrs400
Archive directory:

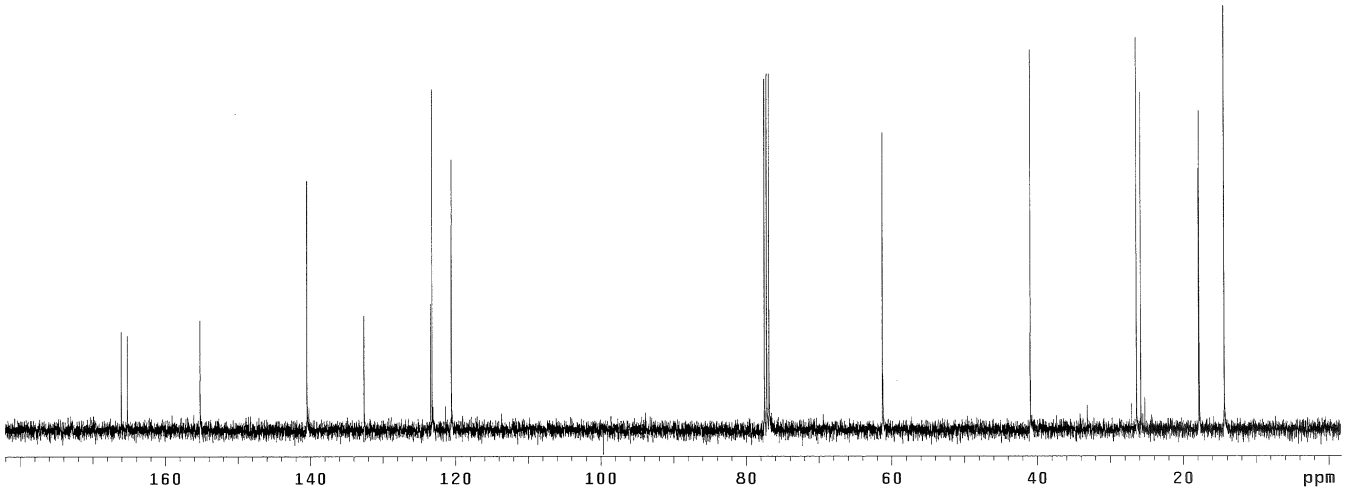
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 10 2015



5.39a

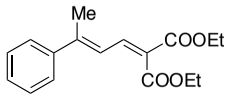


Sample Name:
FM-IX-4
Data Collected on:
vnmr13-vnmrs400
Archive directory:

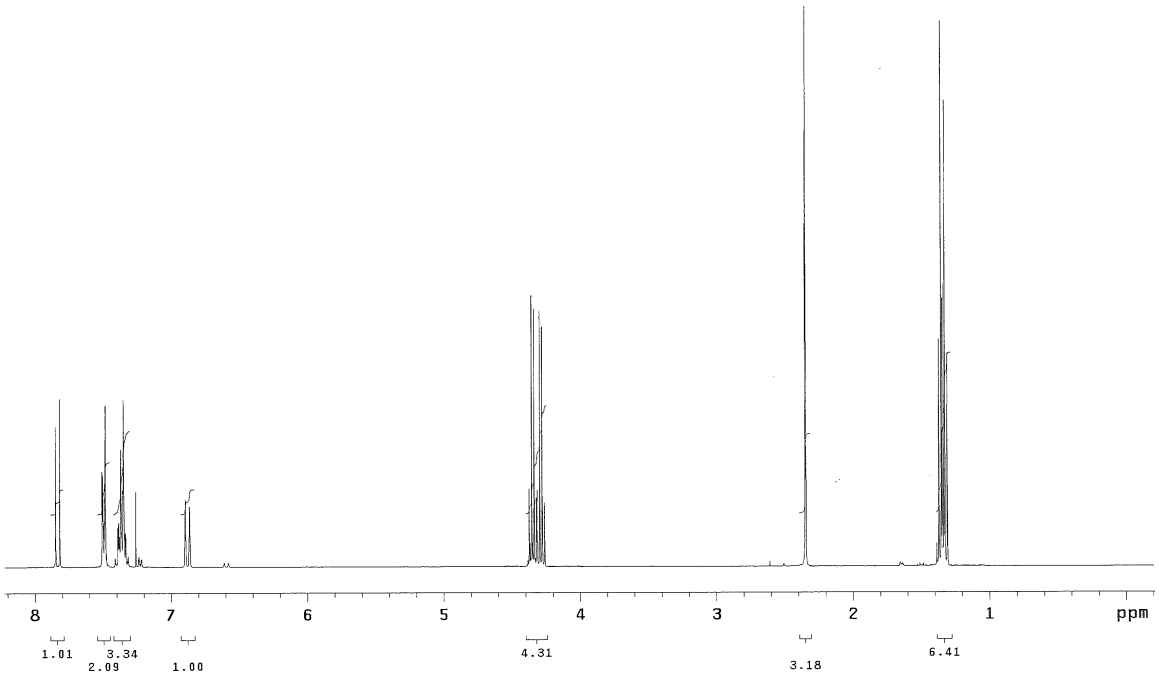
Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 13 2015



5.39b

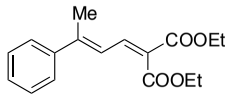


Sample Name:
FM-IX-4
Data Collected on:
vnmr13-vnmrs400
Archive directory:

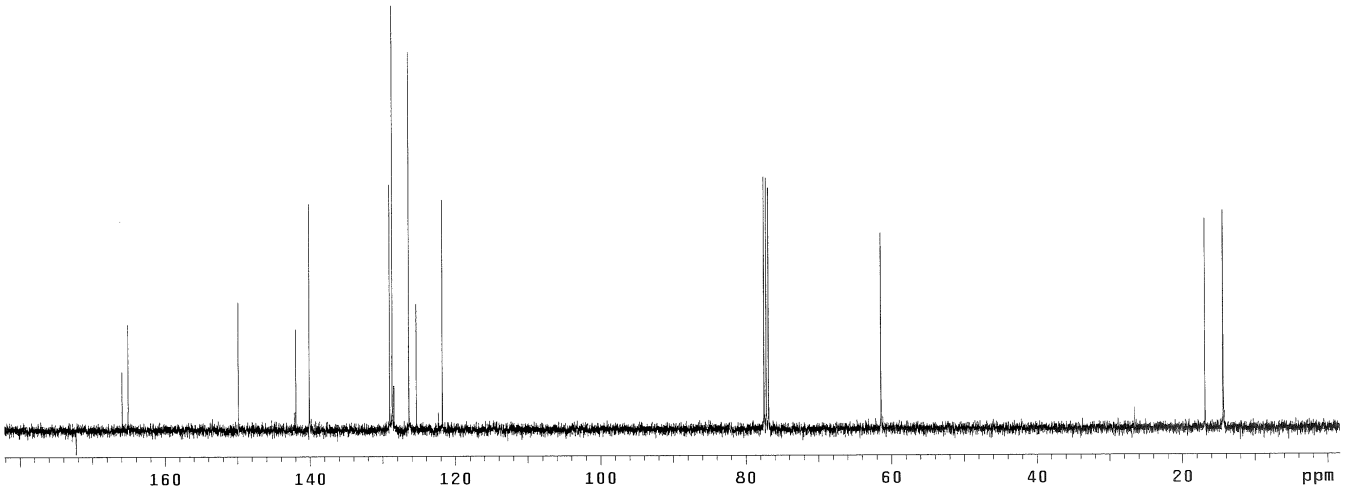
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 13 2015



5.39b

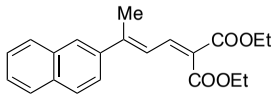


Sample Name:
FM-IX-5
Data Collected on:
vnmr13-vnmrs400
Archive directory:

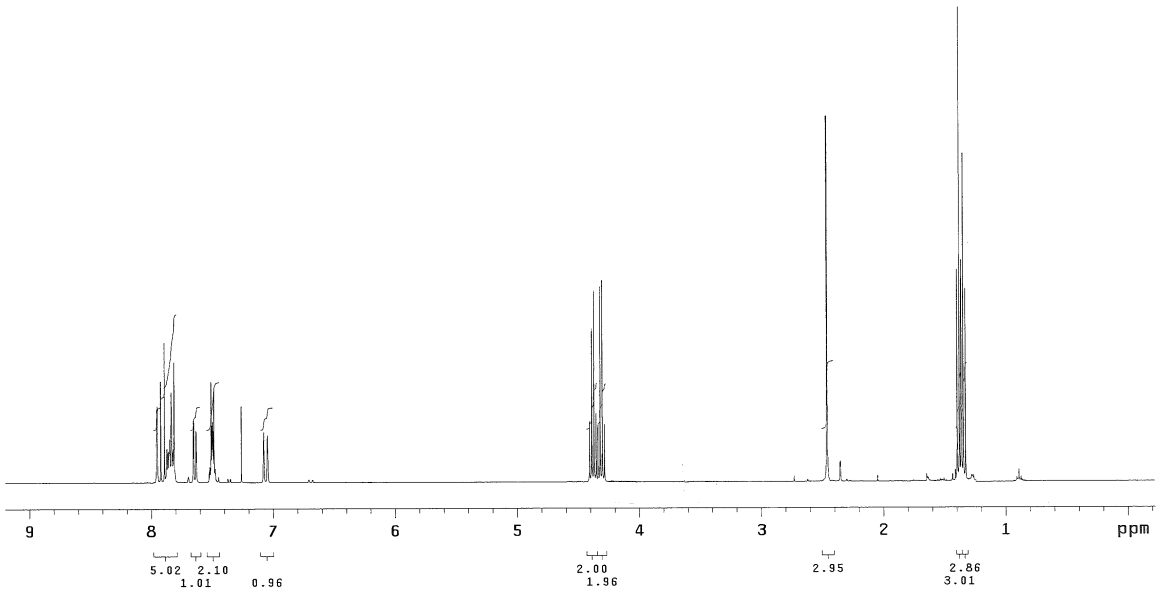
Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 13 2015



5.39c

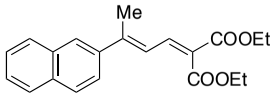


Sample Name:
FM-IX-5
Data Collected on:
vnmr13-vnmrs400
Archive directory:

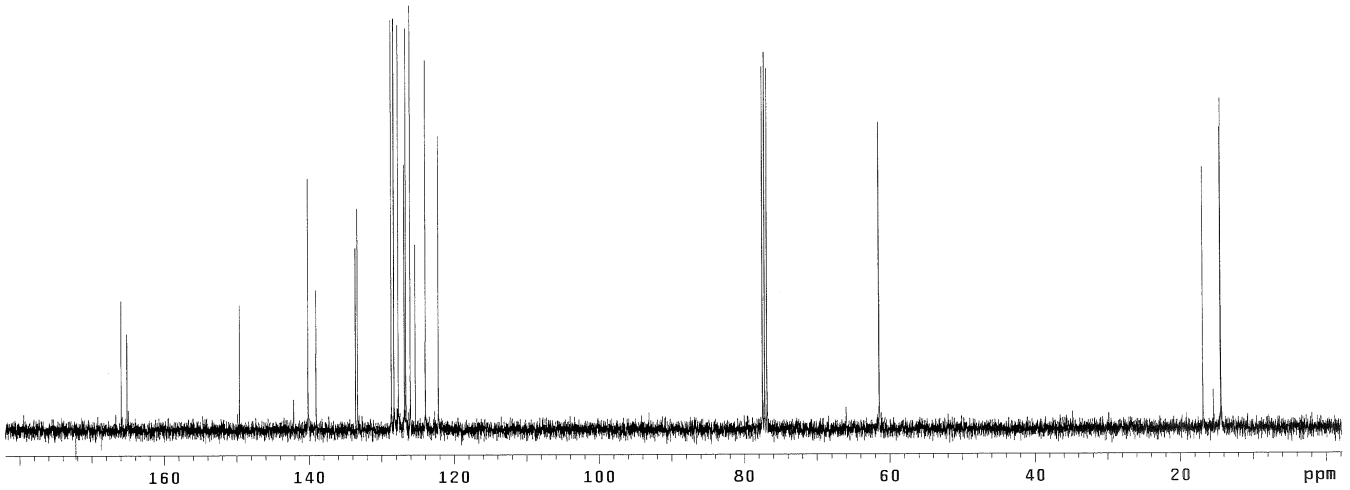
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 13 2015



5.39c

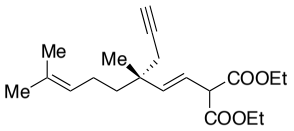


Sample Name:
FM-IX-11
Data Collected on:
vnmr13-vnmrs400
Archive directory:

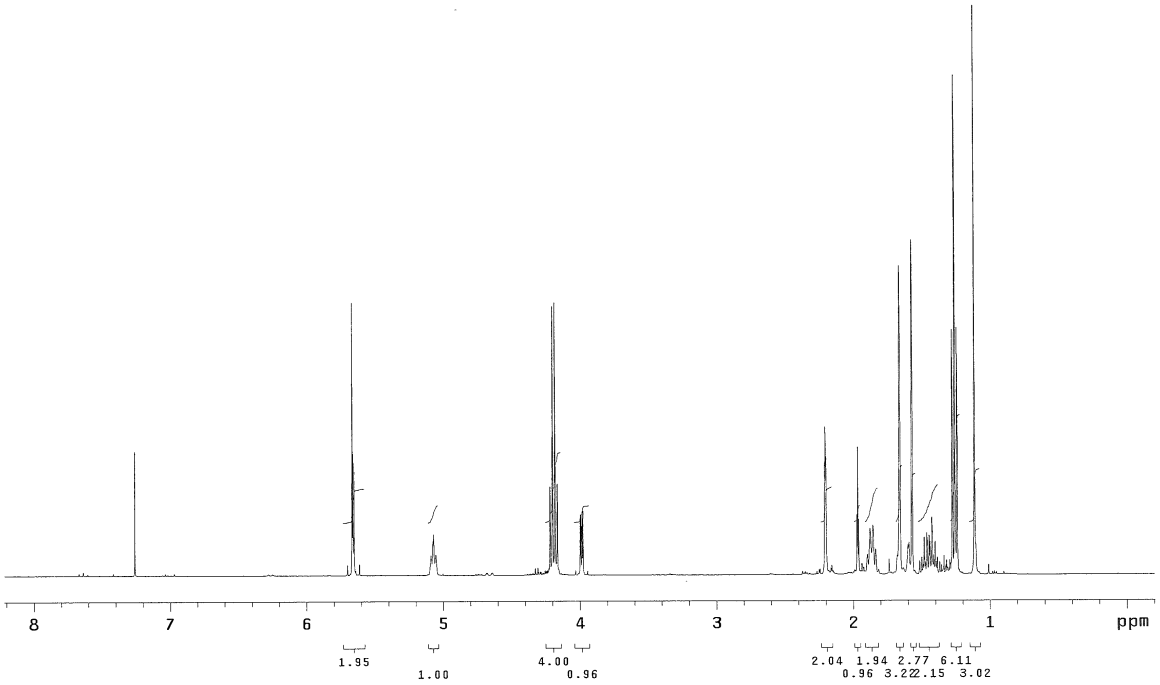
Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 18 2015



5.40a

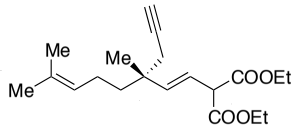


Sample Name:
FM-IX-11
Data Collected on:
vnmr13-vnmrs400
Archive directory:

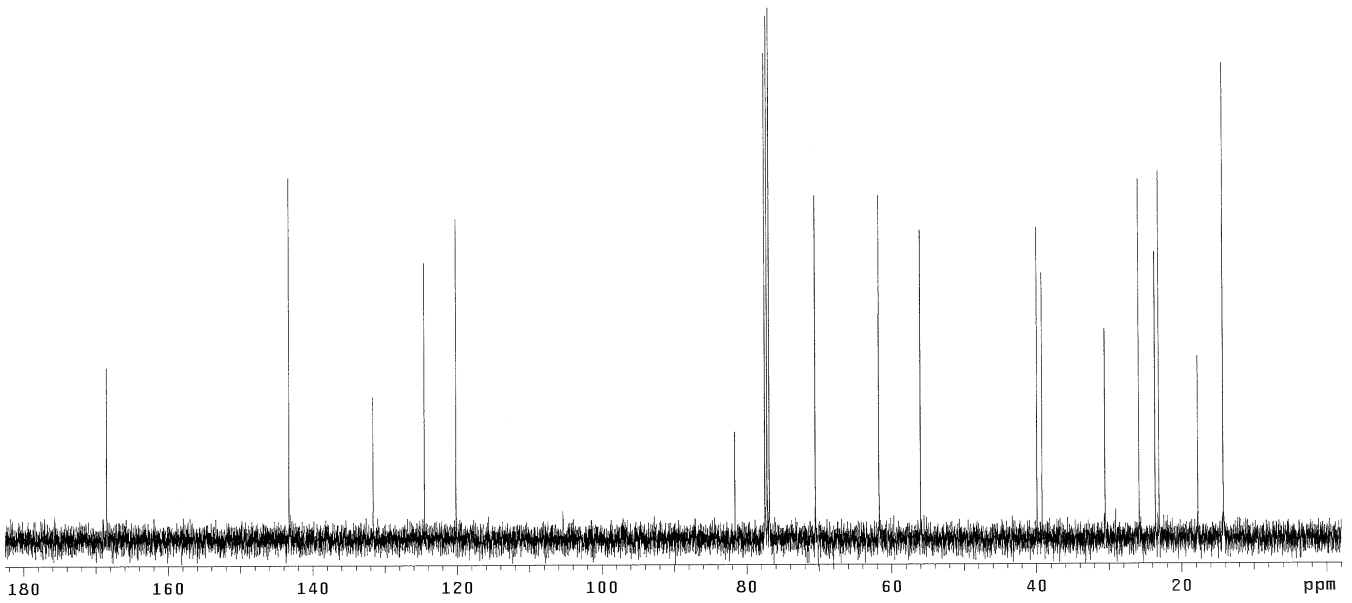
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 18 2015



5.40a

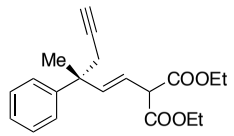


Sample Name:
FM-IX-7
Data Collected on:
vnmr13-vnmrs400
Archive directory:

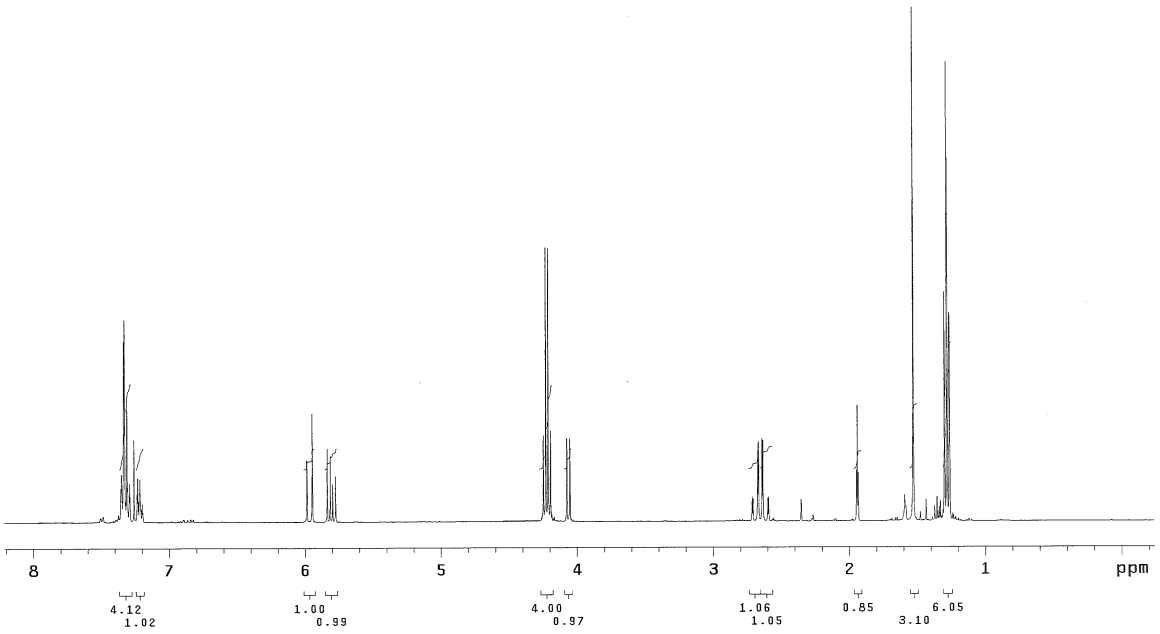
Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 18 2015



5.40b

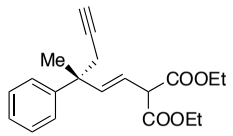


Sample Name:
FM-IX-7
Data Collected on:
vnmr13-vnmrs400
Archive directory:

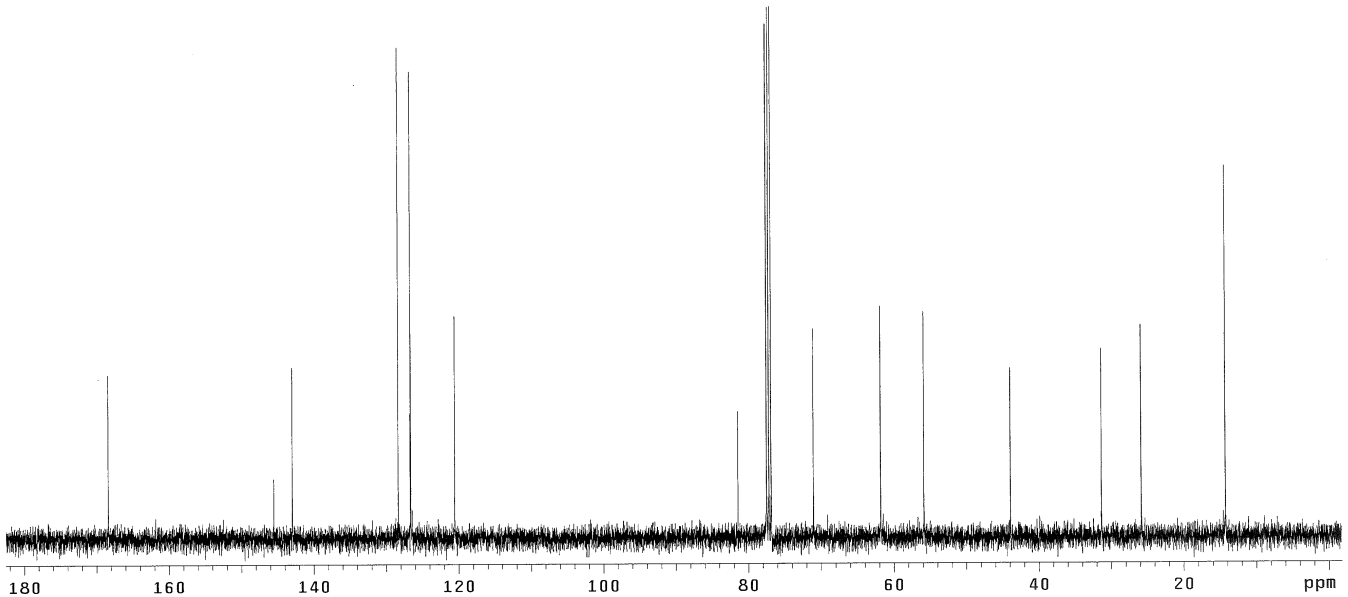
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 18 2015



5.40b

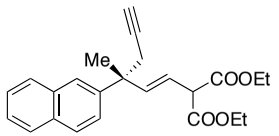


Sample Name:
FM-IX-7
Data Collected on:
vnmr13-vnmrs400
Archive directory:

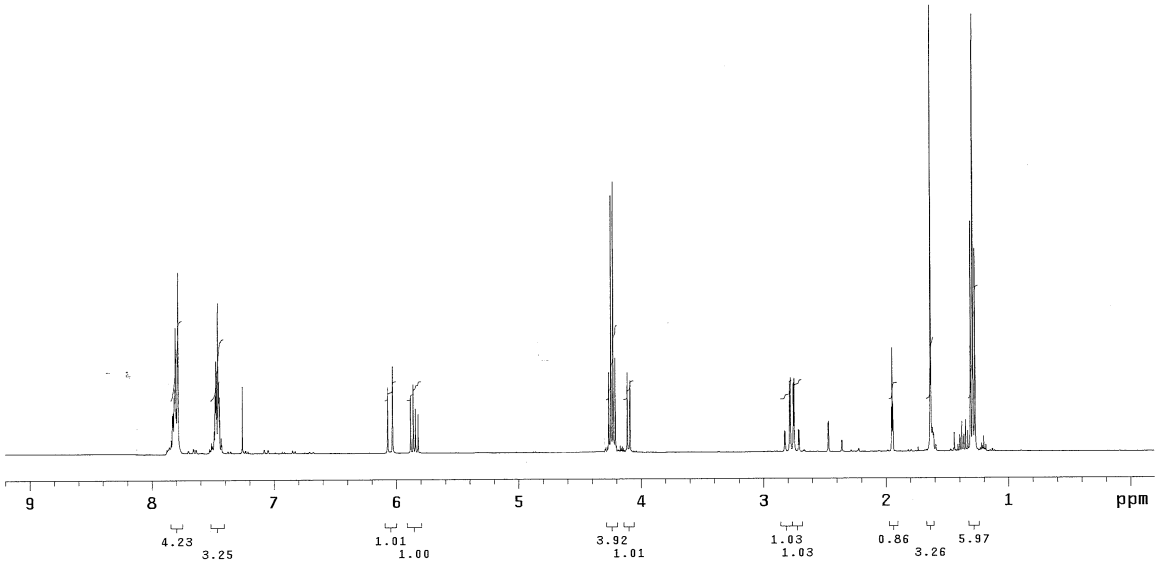
Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 18 2015



5.40c

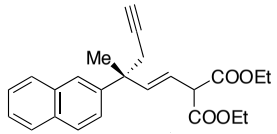


Sample Name:
FM-IX-7
Data Collected on:
vnmr13-vnmrs400
Archive directory:

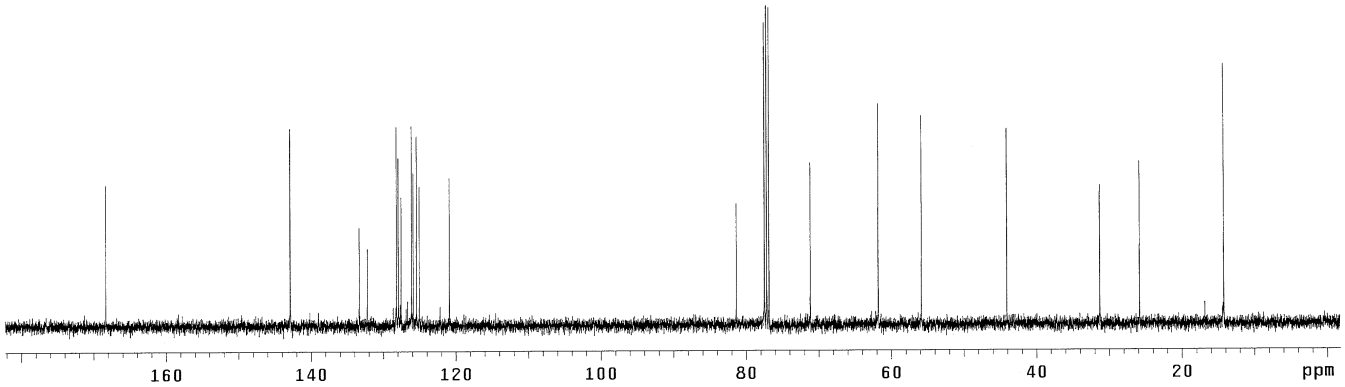
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 18 2015



5.40c

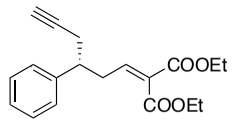


Sample Name:
FM-VIII-252D
Data Collected on:
vnmr13-vnmrs400
Archive directory:

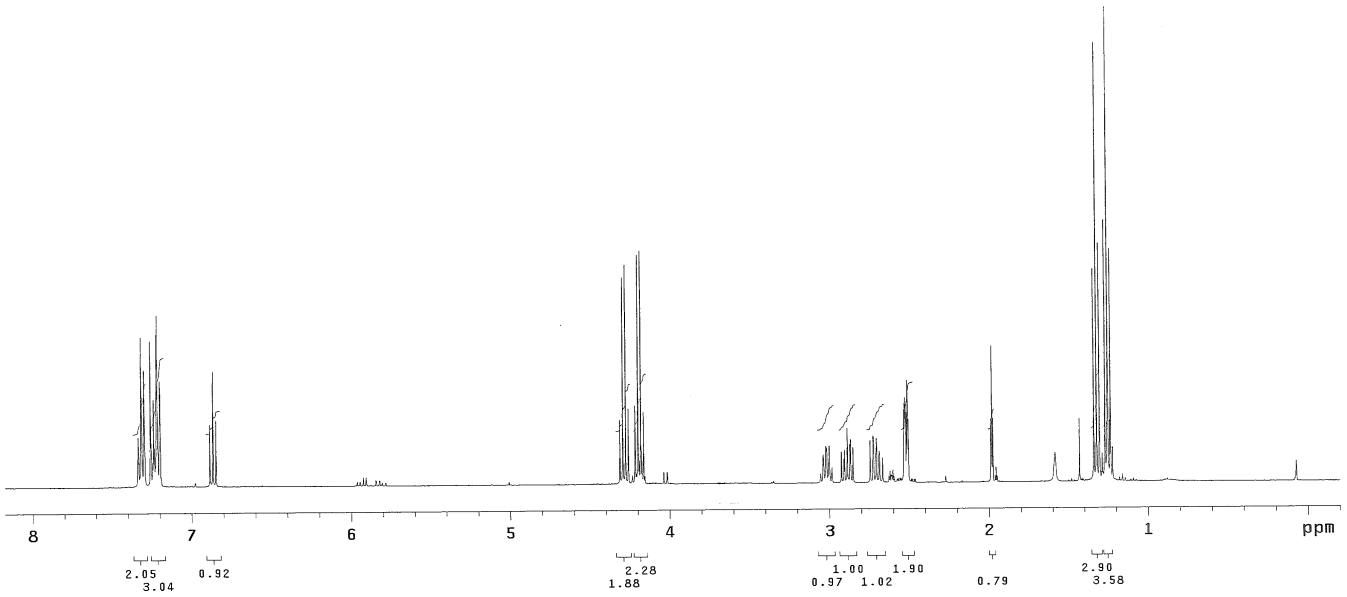
Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jul 1 2015



5.41

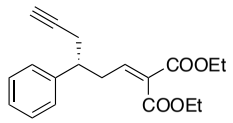


Sample Name:
FM-VIII-252D
Data Collected on:
vnmr13-vnmrs400
Archive directory:

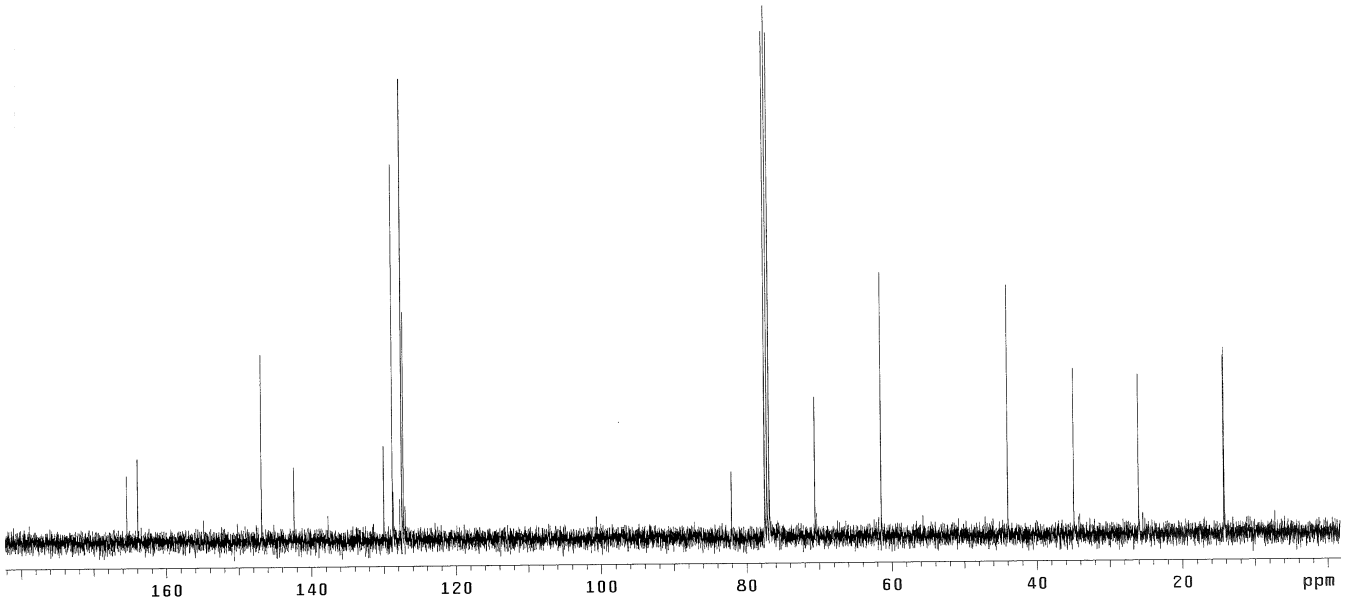
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jul 1 2015



5.41

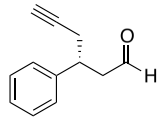


Sample Name:
FM-VIII-238
Data Collected on:
vnmr13-vnmrs400
Archive directory:

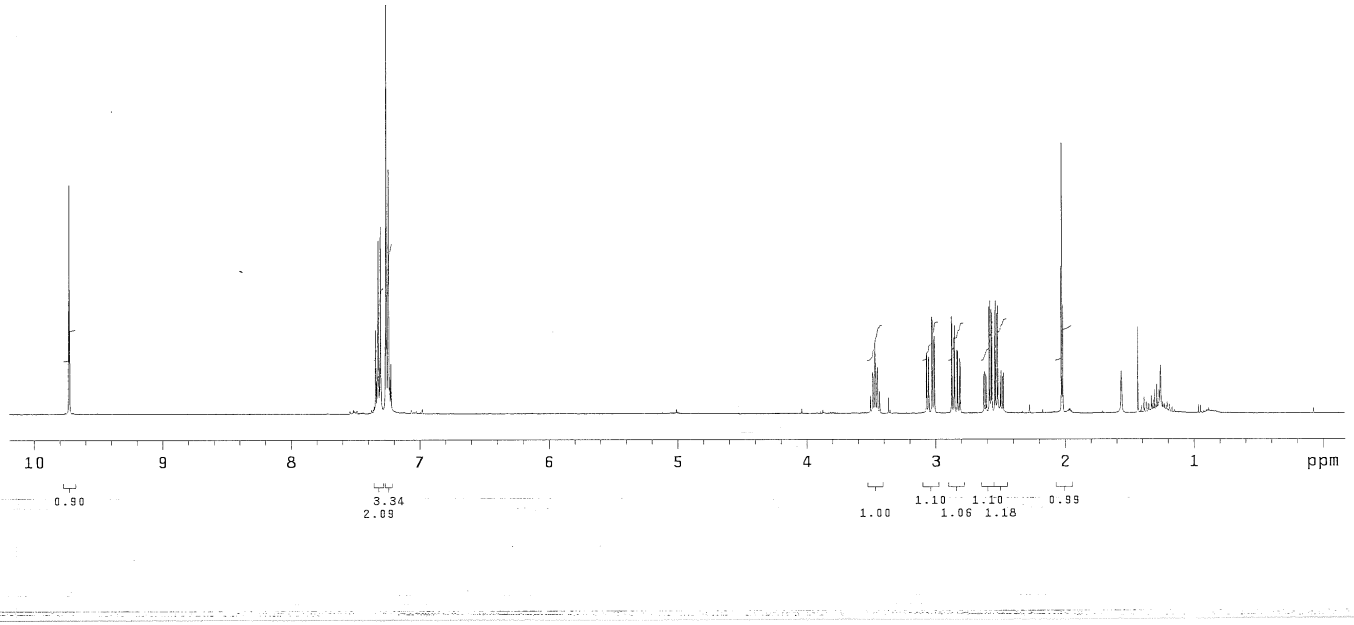
Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 17 2015



5.42

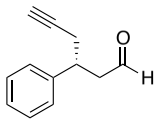


Sample Name:
FM-VIII-238
Data Collected on:
vnmr13-vnmrs400
Archive directory:

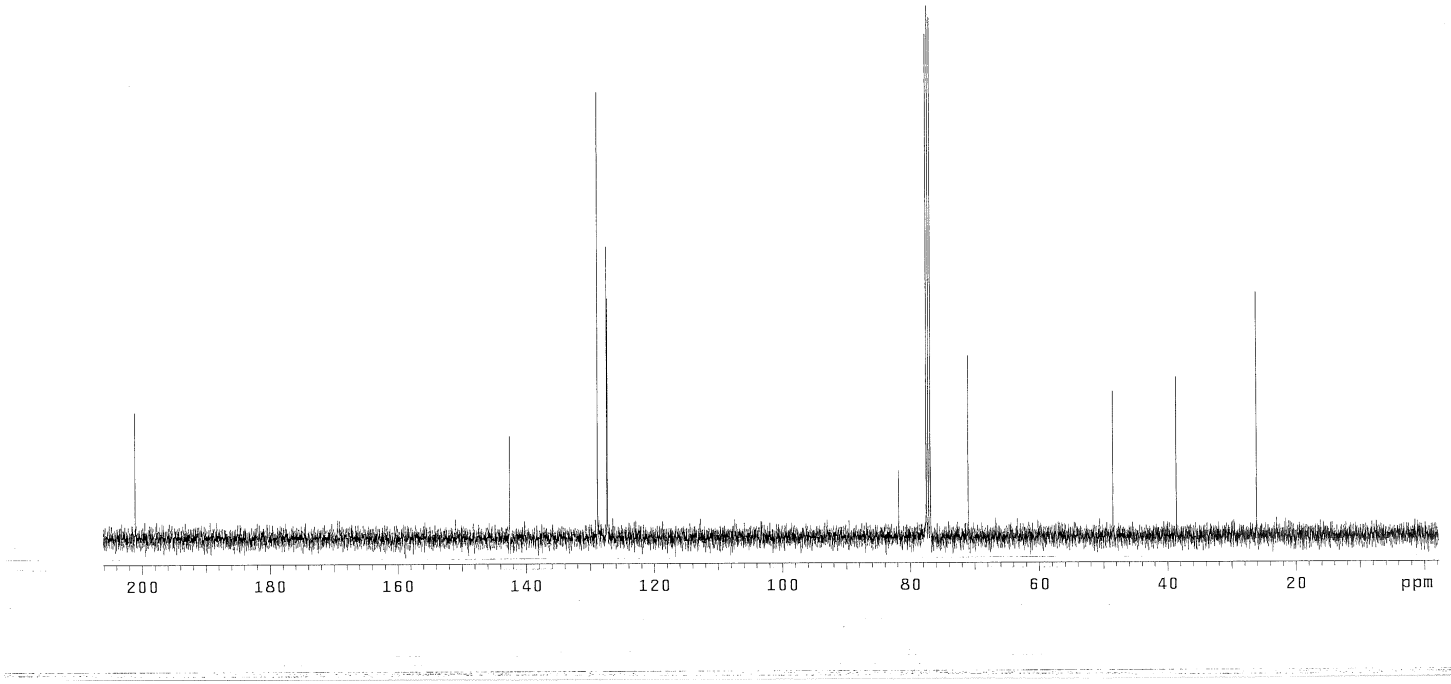
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 17 2015



5.42

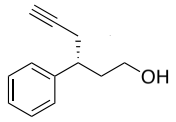


Sample Name:
FM-VIII-241
Data Collected on:
vnmr13-vnmrs400
Archive directory:

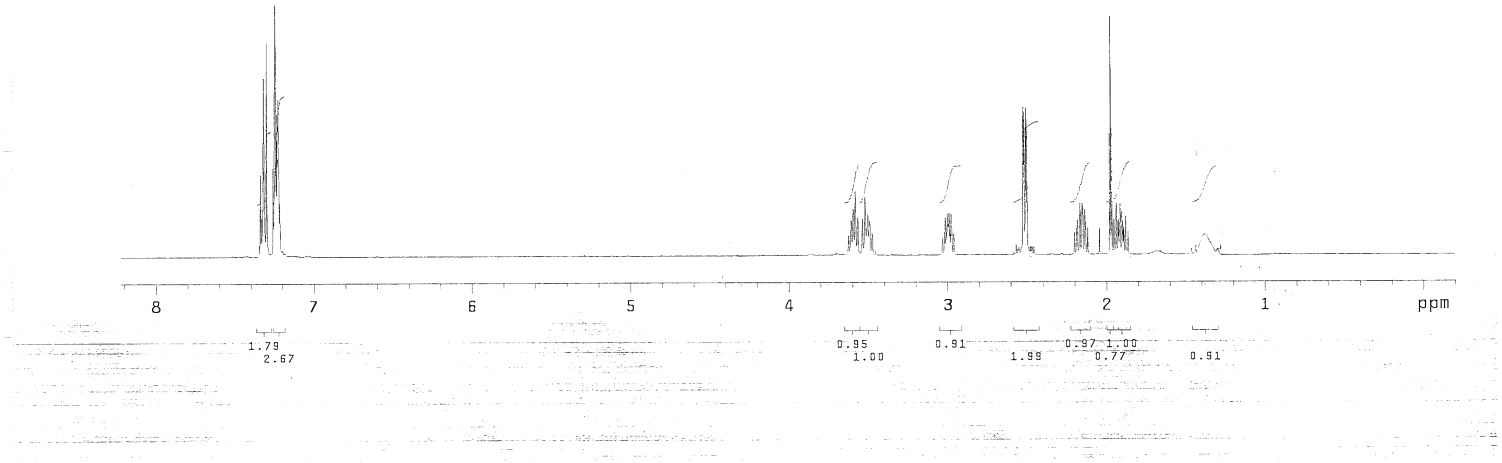
Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 19 2015



5.43

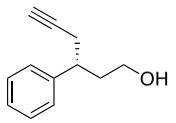


Sample Name:
FM-VIII-241
Data Collected on:
vnmr13-vnmrs400
Archive directory:

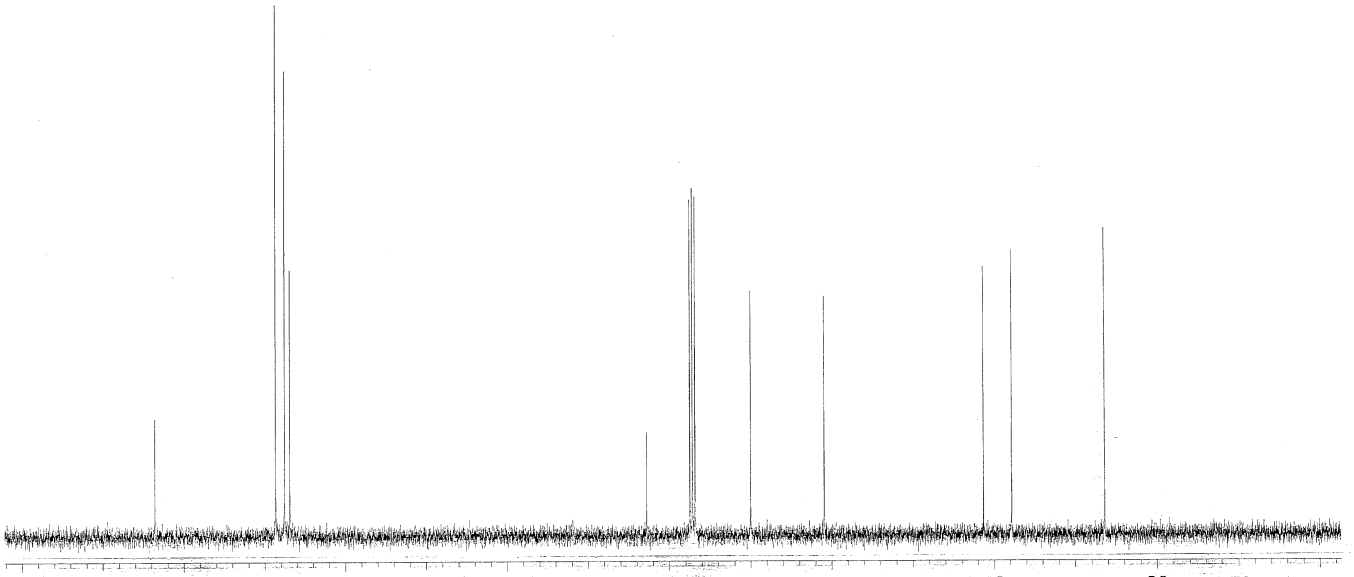
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 19 2015



5.43

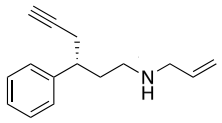


Sample Name:
FM-VIII-245
Data Collected on:
vnmr13-vnmrs400
Archive directory:

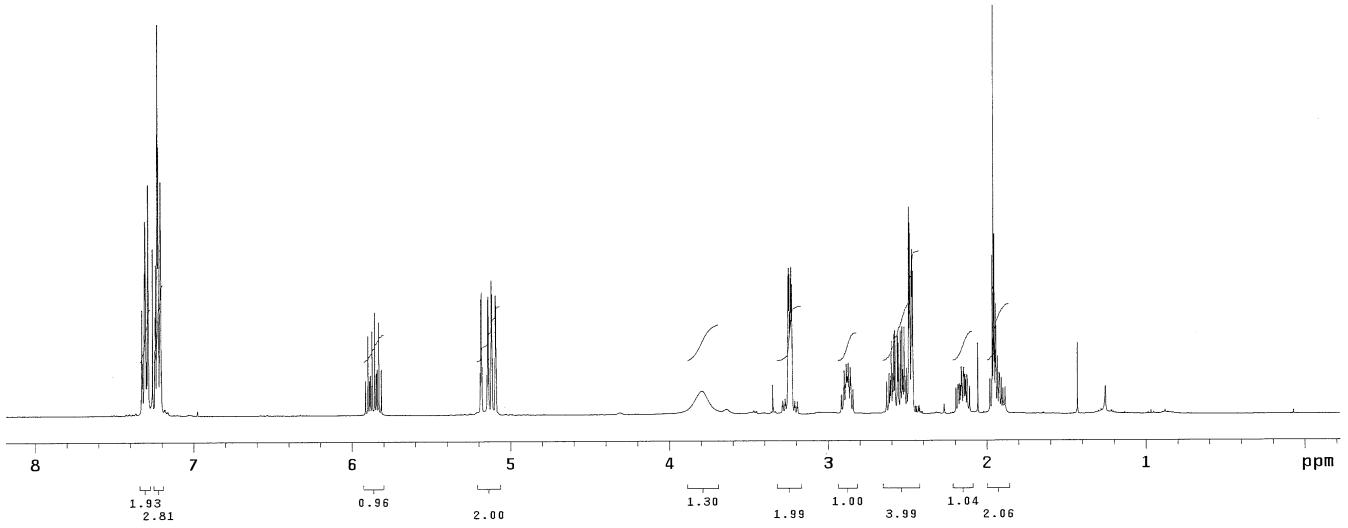
Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 23 2015



5.44

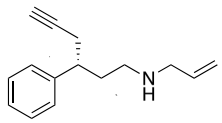


Sample Name:
FM-VIII-245
Data Collected on:
vnmrj3-vnmrs400
Archive directory:

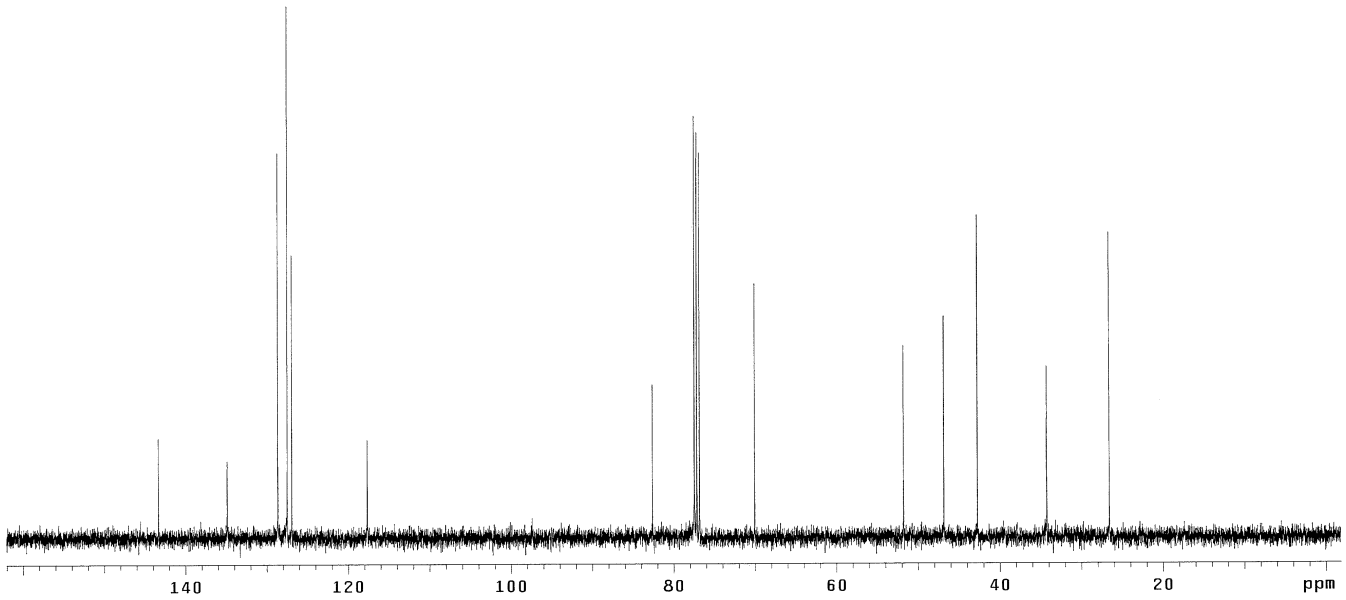
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 23 2015



5.44

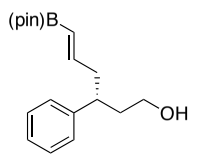


Sample Name:
FM-VIII-246
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 23 2015



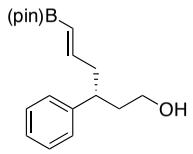
5.45

Sample Name:
FM-VIII-246
Data Collected on:
vnmr13-vnmrs400
Archive directory:

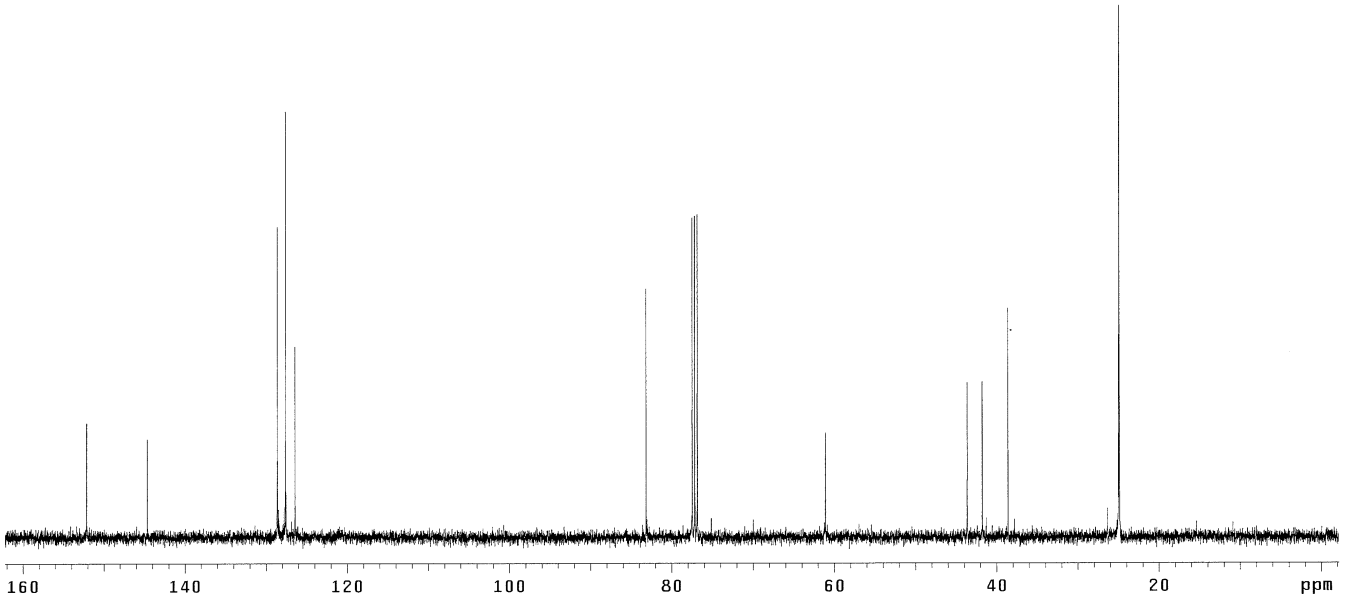
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 23 2015



5.45

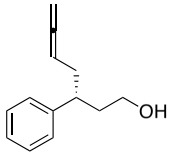


Sample Name:
FM-VIII-242
Data Collected on:
vnmr13-vnmrs400
Archive directory:

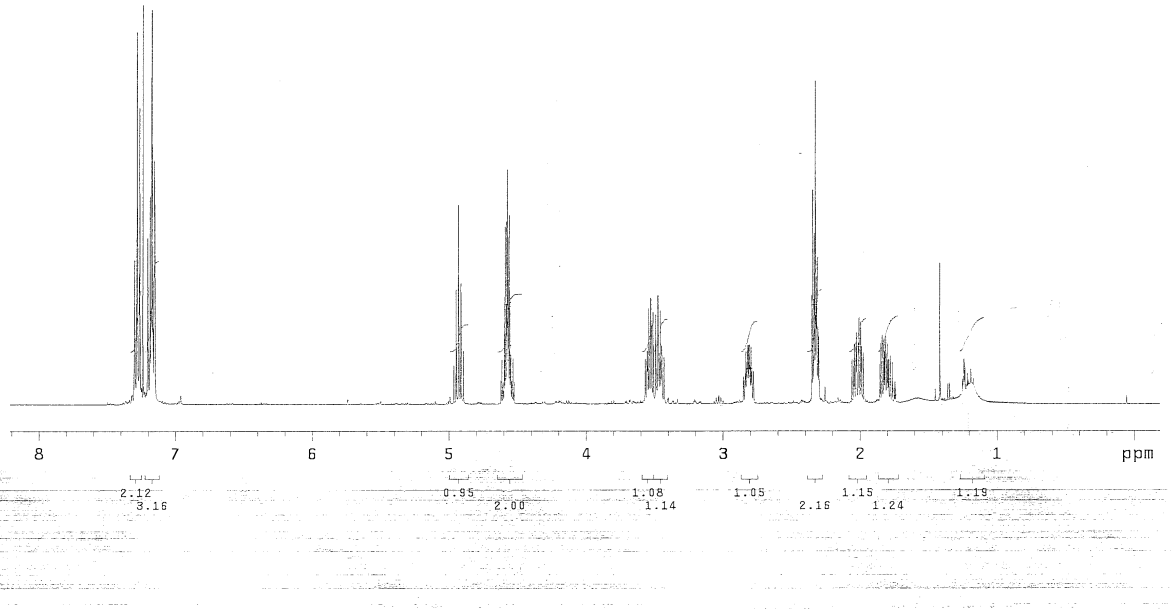
Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 19 2015



5.46

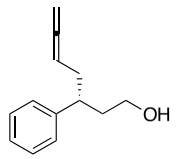


Sample Name:
FM-VIII-242
Data Collected on:
vnmr13-vnmrs400
Archive directory:

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 19 2015



5.46