RACEMIC VINYLALLENES IN CATALYTIC ENANTIOSELECTIVE MULTICOMPONENT PROCESSES

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RACEMIC VINYLALLENES IN CATALYTIC ENANTIOSELECTIVE MULTICOMPONENT PROCESSES

Xinghan Li

Advisor: Professor Amir H. Hoveyda

Dedicated to Prof. Amir H. Hoveyda on the occasion of his 60th birthday

Chapter 1. Development of NHC–Cu Complex Catalyzed Enantioselective Multicomponent Reactions involving Racemic Vinylallene, $B_2(pin)_2$ and *α,β,γ,δ*-Unsaturated Diester

We have developed a broadly applicable protocol for converting a variety of vinylallenes to multifunctional allyl moieties followed by diastereo-, and enantioselective 1,6-conjugate addition to *α,β,γ,δ*-unsaturated diesters. Through just one operation, products bearing vicinal stereogenic centers, a *Z*-trisubstituted alkenyl–B(pin) unit, a vinyl group, a *β,γ*-unsaturated diester moiety were generated in up to 67% yield, 87:13 *Z:E* ratio, >98:2 d.r., and 98:2 e.r. Reactions were readily catalyzed by 5.0 mol % of an amino-alcohol derived NHC–Cu complex at ambient temperature, and involved a vinylallene, $B_2(pin)_2$, an *α,β,γ,δ*-unsaturated diester. Versatility and utility of the products were demonstrated by a variety of chemoselective modifications, involving the *β,γ*-unsaturated diester moiety, vinyl, and alkenyl–B(pin) unit, to access vitamin D_3 side chain. Insights on the dynamic behavior of intermediated Cu–allyl species and accounts for various selectivity profiles were outlined by mechanistic experiments and DFT based stereochemical models.

Chapter 2. Bisphosphine–Cu Complex Promoted Diastereo-, Enantioselective Additions of Boron-Containing Multifunctional Allyl Moieties to Ketones

Racemic vinylallenes are fascinating substrates for catalytic multicomponent processes, due to their ability to form multifunctional allyl moieties. Specifically, an approach for diastereo-, and enantioselective addition to readily available ketones, enones and diennones has been developed. Reactions involving a racemic vinylallene, $B_2(pin)_2$, and ketone were promoted by 3.0-5.0 mol % of a commercially available bisphosphine–Cu complex at ambient temperature, furnishing products that contain an easily functionalizable vinyl moiety, an alkenyl–B(pin) containing *Z*-trisubstituted homoallylic alcohol with vicinal stereogenic centers in up to 83% yield, >98:2 *Z:E* ratio, >98:2 d.r., and 97:3 e.r. Applicability and flexibility of this method is highlighted by chemoselective modifications involving the alkenyl–B(pin) and vinyl unit to obtain a 5-norstemmadenine monoterpenoid indole alkaloid (+)-16-hydroxy-16,22-dihydroappariceine. These studies foreshadow the use of vinylallenes as starting materials to generate structurally unique allyl species in a wide range of multicomponent transformations.

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ACKNOWLEDGMENTS

"Two roads diverged in a yellow wood,
And sorry I could not travel both
And be one traveler, long I stood
And looked down one as far as I could
To where it bent in the undergrowth;"

All endings are beginnings, as well as this Master thesis, which marks the ending of my journey in the United States; while it also represents the beginning of another expedition in *République Française*. The only thing that left unchanged is the architect of my dream of being a chemist — my dear research advisor, Prof. Amir H. Hoveyda, who deserves my deepest appreciation.

First and foremost, I would like to express my sincere gratitude to him for recruiting me as part of his crew both in Boston College and Université de Strasbourg. This erudite gentleman has installed in me the sense of being professional, enthusiastic, innovative, precise and self-critical for research. Without his patient guidance, invaluable suggestions and irreplaceable encouragement, I would not have achieved what I got today. I am also grateful to all the conversations we had and life wisdom he shared with me in his garden. I feel extremely fortunate that my academic career has been and will continue to be illuminated by him.

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Special thanks go to my mentor and collaborator Dr. Youming Huang for his training and insightful discussion about our projects. His intelligence and diligence has impressed and influenced me ever since the first day we worked together. I am looking forward to the reunion of us in Strasbourg soon. My colleagues Dr. Sebastian Torker and Dr. Juan del Pozo del Valle are acknowledged for their contributions to the mechanistic investigations in our project as well as incisive discussion about mechanistic fundamentals. I am always grateful to my talent fellows, Yucheng Mu, Yuebiao Zhou Shaochen Zhang, Dr. Yu Sun, Dr. Felix W. W. Hartrampf, Tobias, Koengeter, Ryan J. Morrison, Diana C. Fager, Chaofan Xu, Dr. Filippo Romiti, Dr. Thach Nguyen, Dr. Farid van der Mei, Dr. Malte S. Mikus, who can always provide practical experimental advice and intellectual perspectives. They are also the people, who together created the wonderful working environment and brought laughter to the laboratory.

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Last but not the least, I want to express the utmost appreciation to my family, especially my dearest parents and my beloved girlfriend Wan-Chen Lee. They are my Polaris in the dark night. Their love and encouragement makes who I am today. I also want to tell you all about how guilty I feel for being not able to accompany you frequently in the future.

"I shall be telling this with a sigh
Somewhere ages and ages hence:
Two roads diverged in a wood, and I—
I took the one less traveled by,
And that has made all the difference."

1.0 DEVELOPMENT OF NHC–Cu COMPLEX CATALYZED ENANTIOSELECTIVE MUTICOMPONENT REACTIONS INVOLVING RACEMIC VINYLALLENE, $B_2(pin)_2$ and *α,β,γ,δ*-UNSATURATED DIESTER

1.1 Introduction

A variety of catalytic methods have recently emerged for enantioselective union of an unsaturated organic molecule with bis(pinacolato)diboron [$B_2(pin)_2$] and an electrophile.[1,2,3,4] Otherwise difficult-to-access multifunctional entities may thus be synthesized by a single catalytic multicomponent operation. Starting materials with multiple unsaturation sites have played a major role in these developments (Scheme 1.1).

(1) For selected reports on enantioselective multicomponent reactions that involve an achiral allene and are catalyzed by a chiral Cu–B(pin) complex, see: with carbonyl- or imine-containing compounds, (a) Meng, F.; Jang, H.; Jung, B.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2013**, *52*, 5046–5051. (b) Yeung, K.; Ruscoe, R. E.; Rae, J.; Pulis, A. P.; Procter, D. J. *Angew. Chem., Int. Ed.* **2016**, *55*, 11912–11916. (c) Jang, H.; Romiti, F.; Torker, S.; Hoveyda, A. H. *Nat. Chem.* **2017**, *9*, 1269–1275. With allylic electrophiles: (d) Meng, F.; McGrath, K. P.; Hoveyda, A. H. *Nature* **2014**, *513*, 367–374. With *α,β*-unsaturated carbonyl compounds: (e) Meng, F.; Li, X.; Torker, S.; Shi, Y.; Shen, X.; Hoveyda, A. H. *Nature* **2016**, *537*, 387–393. For reactions involving 1,1-disubstituted allenes with an alcohol serving as the electrophile, see: (f) Jang, H.; Jung, B.; Hoveyda, A. H. *Org. Lett.* **2014**, *16*, 4658–4661.

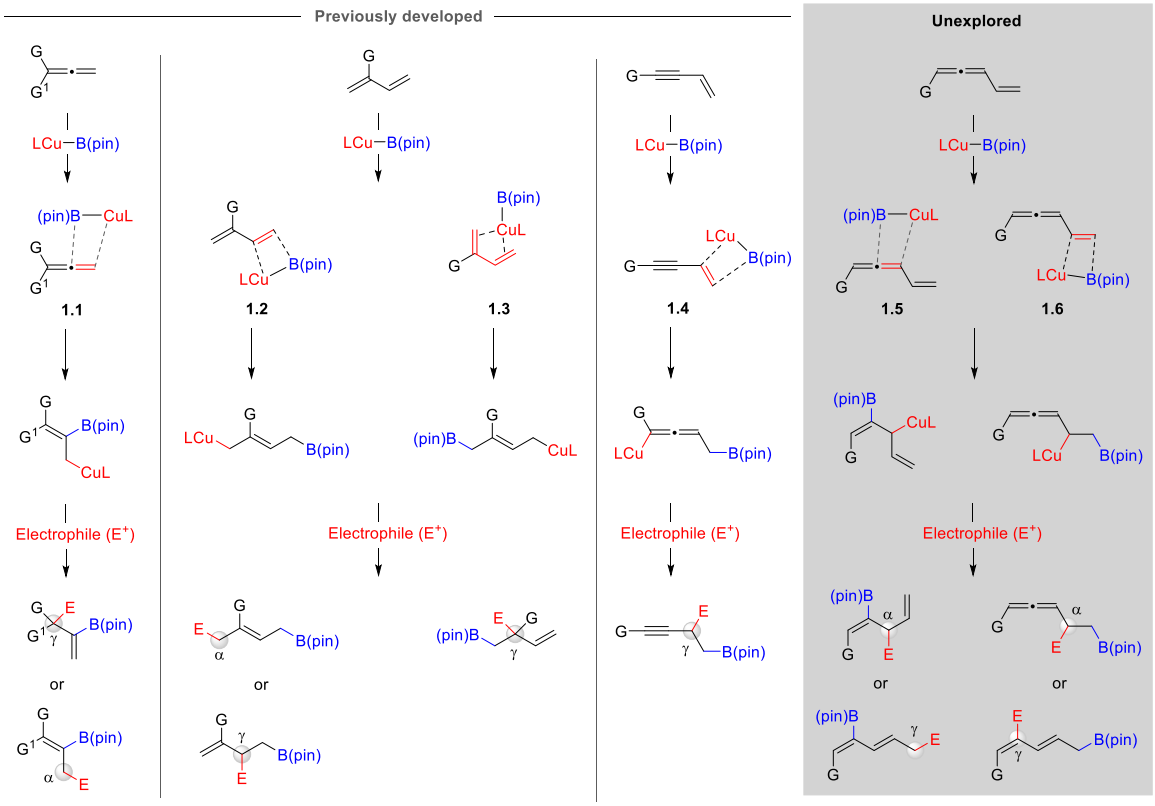
(2) For selected reports on enantioselective multicomponent reactions that involve a 1,3-diene and are catalyzed by a chiral Cu–B(pin) complex, see: (a) Sasaki, Y.; Zhong, C.; Sawamura, M.; Ito, H. *J. Am. Chem. Soc.* **2010**, *132*, 1226–1227. (b) Li, X.; Meng, F.; Torker, S.; Shi, Y.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2016**, *55*, 9997–10002. (c) Jiang, L.; Cao, P.; Wang, M.; Chen, B.; Wang, B.; Liao, J. *Angew. Chem., Int. Ed.* **2016**, *55*, 13854–13858. (d) Jia, T.; He, Q.; Ruscoe, R. E.; Pulis, A. P.; Procter, D. J. *Angew. Chem., Int. Ed.* **2018**, *57*, 11305–11309.

(3) For selected reports on enantioselective multicomponent reactions that involve a 1,3-enyne and are catalyzed by a chiral Cu–B(pin) complex, see: (a) Sasaki, Y.; Horita, Y.; Zhong, C.; Sawamura, M.; Ito, H. *Angew. Chem., Int. Ed.* **2011**, *50*, 2778–2782. (b) Meng, F.; Haeffner, F.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2014**, *136*, 11304–11307. (c) Gan, X.-C.; Zhang, Q.; Jia, X.-S.; Yin, L. *Org. Lett.* **2018**, *20*, 1070–1073.

(4) For recent overviews of this general class of catalytic multicomponent reactions catalyzed by Cu-based complexes, see: (a) Pulis, A. P.; Yeung, K.; Procter, D. J. *Chem. Sci.* **2017**, *8*, 5240–5247. (b) Semba, K.; Fujihara, T.; Terao, J.; Tsuji, Y. *Tetrahedron* **2015**, *71*, 2183–2197. (c) Hemming, D.; Fritzmeier, R.; Westcott, S. A.; Santos, W. L.; Steel, P. G. *Chem. Soc. Rev.* **2018**, *47*, 7477–7494.

Early advances involved regio- and stereoselective addition of an *in situ* generated Cu–B(pin) complex to the less substituted C=C bond (via **1.1**, Scheme 1.1) of achiral monosubstituted or 1,1-disubstituted allenes,[1f] affording a boryl-substituted Cu–allyl species, which was followed by a α- or γ-selective addition to an electrophile. With a 1,3-diene as substrate,[2] the initial Cu–B(pin) addition might occur at the less substituted alkene (**1.2**), or the diene might serve as a bidentate ligand (with monosubstituted phosphine ligands, via **1.3**[1d]), and thus either Cu–allyl regioisomer could be generated. Another reaction class entails additions to 1,3-enynes,[3] where the Cu–B(pin) complex first adds to the less substituted vinyl moiety (via **1.4**); depending on the process, reaction of an electrophile with energetically more favorable Cu–allenyl intermediate [5] (vs. Cu–propargyl) may then furnish the α- or γ-addition isomer.

Scheme 1.1. **Previously Reported Multicomponent Processes Involving Cu–B(pin) Addition to Substrates with Multiple Unsaturation Sites and the Unexplored Strategy with Vinylallene**



(5) Mszar, N. W.; Haeffner, F.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2014**, *136*, 3362–3365.

We envisioned that vinylallenes, readily accessible compounds[6] that have thus far not been examined as substrates for the abovementioned catalytic multicomponent processes, represent an attractive option. The extended vinyl group could lead to products that are structurally distinct and especially versatile (cf. Scheme 1.1), which include a stereochemically defined trisubstituted alkenyl–B(pin) units and vinyl moiety, and thus, such entities represent an attractive possibility for further chemical modifications. Nonetheless, development of such processes poses two key questions: 1) Would Cu–B(pin) selectively add to the allene or the vinyl site? 2) Would enantiomerically enriched vinylallenes be needed for high diastereo- and enantioselectivity?

1.2 Background

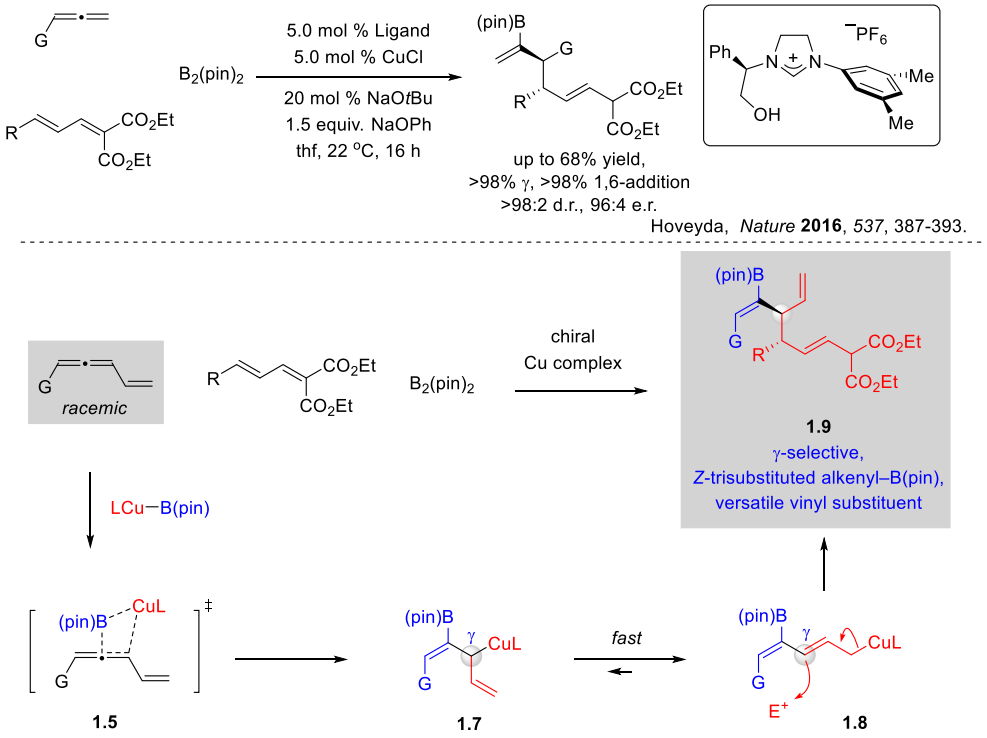
Unlike 1,4-conjugate additions, for which a significant number of catalytic enantioselective variants have been developed,[7] 1,6-conjugate additions involving carbon-based nucleophiles are rare,[8] especially if the C4 site is not fully substituted. Reported instances are due to the pioneering advances by Feringa,[9] Hayashi,[10,11] and Alexakis.[12] These notable advances were however confined to additions of Mg-,[9] Al-, or Zn-based[12] simple alkyl organometallics. Reactions with a silyl-protected alkyne[10] or an

(6) Pu, X.; Ready, J. M. *J. Am. Chem. Soc.* **2008**, *130*, 10874–10875.
(7) Alexakis, A.; Krause, N.; Woodward S. in *Copper-Catalyzed Asymmetric Synthesis* (A. Alexakis, N. Krause, S. Woodward, Eds), Wiley–VCH, Weinheim, **2014**, pp. 33–68.
(8) Tissot, M.; Li, H.; Alexakis, A. in *Copper-Catalyzed Asymmetric Synthesis* (A. Alexakis, N. Krause, S. Woodward, Eds), Wiley–VCH, Weinheim, **2014**, pp. 69–84.
(9) (a) den Hartog, T.; Harutyunyan, S. R.; Font, D.; Minnaard, A. J.; Feringa, B. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 398–401. (b) den Hartog, T.; van Dijken, D. J.; Minnaard, A. J.; Feringa, B. L. *Tetrahedron: Asymmetry* **2010**, *21*, 1574–1584.
(10) Sawano, T.; Ashouri, A.; Nishimura, T.; Hayashi, T. *J. Am. Chem. Soc.* **2012**, *134*, 18936–18939.
(11) (a) Nishimura, T.; Yasuhara, Y.; Sawano, T.; Hayashi, T. *J. Am. Chem. Soc.* **2010**, *132*, 7872–7873. (b) Nishimura, T.; Noishiki, A.; Hayashi, T. *Chem. Commun.* **2010**, *48*, 973–975.
(12) (a) Tissot, M.; Alexakis, A. *Chem. Eur. J.* **2013,** *19*, 11352–11363. (b) Magrez-Chiquet, M.; Morin, M. S. T.; Wencel-Delord, J.; Amraoui, S. D.; Baslé, O.; Alexakis, A.; Crévisy, C.; Mauduit, M. *Chem. Eur. J.* **2013**, *19*, 13663–13667.

aryl entities expanded the scope, although just one Ar group of a $(ArBO)_3$ compound could be transferred.[11] A major issue is that for several reported cases of catalytic enantioselective 1,6-conjugate addition, it is unclear why bond formation at C6 is favored, and, as a result, further rational, mechanism-based development is often not feasible. Controllable 1,6-conjugate addition of multifunctional 2-boryl substituted allyl moiety and propargyl unit to dienoate was reported by Hoveyda in 2016 (Scheme 1.2). DFT calculation based mechanistic insights revealed that the orientation of allylcopper or allenylcopper moiety's Cγ and C6 of dienoate guaranteed the optimal orbital overlap.[1e] Our hope was to build on recent work regarding catalytic 1,6-conjugate additions with monosubstituted allenes, and by using vinylallene as substrates, to help broaden this underdeveloped set of processes.

In a desired transformation, Cu–B(pin) complex would be expected to add regioselectively to a vinylallene to generate Cu–bisallyl **1.7** via **1.5** (Scheme 1.2). Although

Scheme 1.2. **Previously Reported Multicomponent 1,6-Conjugate Addition with Monosubstituted Allene and Anticipant Reaction Sequence with Vinylallene**



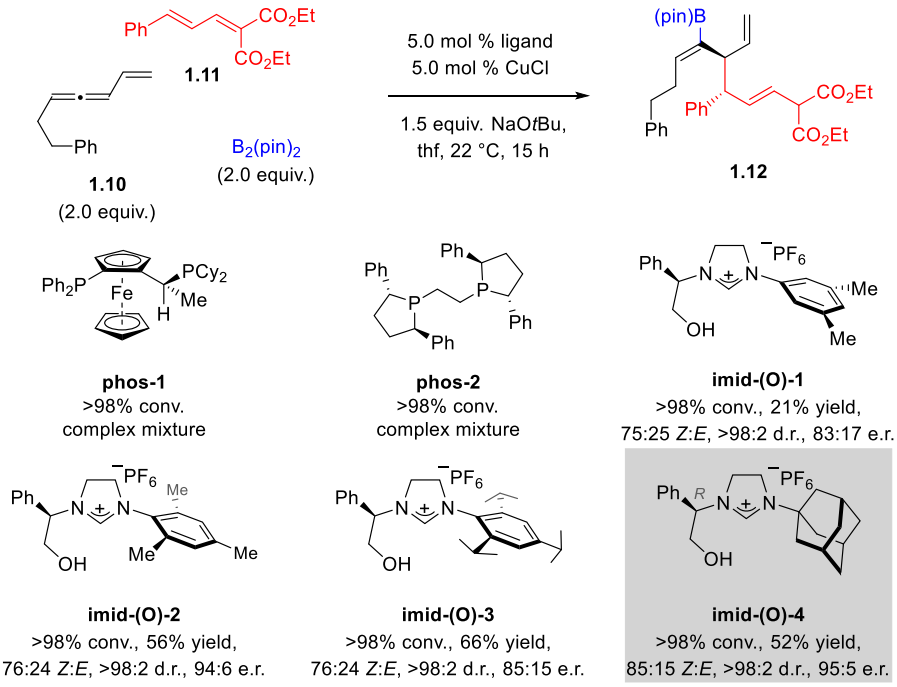
the vinyl site is sterically more accessible, interaction between an allene bond, bearing an sp- and an sp^2-hybridized carbon, where the LUMO presumably resides, and the Cu–B(pin) species, would be preferred. The chiral Cu–bisallyl species **1.7** could isomerize to achiral Cu-allyl **1.8**, the reaction of which with an *α,β,γ,δ*-unsaturated diesters in *γ*-selective fashion would furnish **1.9**. The intermediacy of **1.8** would mean that racemic vinylallene may be used, if the interconversion to **1.8** from **1.7** is expeditious. Otherwise, kinetic resolution or enantiomerically enriched vinylallenes could be utilized to achieve stereoselectivities.

1.3 Identification of Optimal Catalyst for Cu–B(pin) Addition to Vinylallene Followed by Diastereo-, Enantioselective 1,6-Conjugate Addition

To probe feasibility, we examined the process involving vinylallene **1.10**, dienoate **1.11** and $B_2(pin)_2$ (Scheme 1.3). There was complete consumption of **1.11** with chiral phosphine ligands (cf. **phos-1** and **phos-2**, Scheme 1.3), but no **1.12** was detected. When **imid-(O)-1** was used, optimal for reaction with monosubstituted allenes,[1e] **1.12** was obtained in 21% yield, 75:25 *Z:E* selectivity, >98:2 diastereomeric ratio (d.r.), and 83:17 enantiomeric ratio (e.r.); 1,4-conjugate B(pin) addition is likely the main competing pathway. This early finding underscored the distinct nature of the processes with a vinyl-containing 1,3-disubstituted allene compared to previous instances involving monosubstituted allene.[1e]

Other imidazolinium salts were evaluated (Scheme 1.3). With **imid-(O)-2**, d.r. remained high (>98:2), and efficiency (56% yield) and e.r. (94:6) improved considerably,

Scheme 1.3. **Identification of an Effective Ligand**



[a]Conv (±2%; loss of **1.11**), *Z*:*E* ratio, and d.r. (±2%) determined by analysis of ^{1}H NMR spectra of unpurified mixtures. [b]Yield (±5%, average of at least three runs) is for purified product (*Z*/*E* mixture). [c]E.r. determined by HPLC analysis.

but *Z*:*E* ratio remained the same (75:25). With the more sizeable tri(isopropyl)phenyl-substituted **imid-(O)-3**, efficiency further increased (66% yield), but, again, there was hardly any change in *Z*:*E* ratio (76:24), and e.r. returned to the initial level (85:15 e.r.). *N*-adamantyl-substituted **imid-(O)-4**, a less-known member of this class of ligands[13] was then examined, affording the desired product in slightly lower efficiency (52% yield), while *Z*:*E* ratio improved (85:15), and d.r. and e.r. remained high (>98:2 and 95:5, respectively). This observation was out of our expectation, because **imid-(O)-4** resulted in relatively low e.r. (~80:20) when applied in 1,6-conjugate additions of 2-boryl substituted allyl (generated *in situ* from monosubstituted allene) to dienoate (cf. Scheme 1.2). After further optimization,

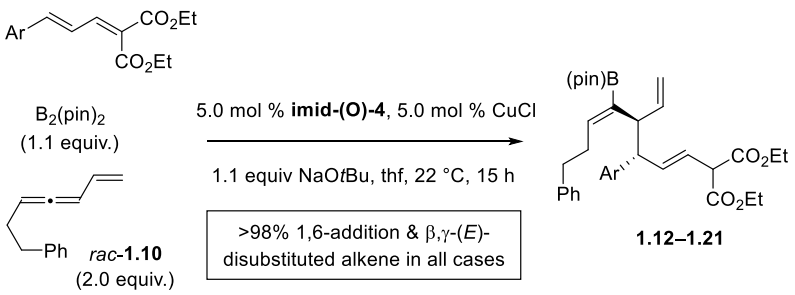
(13) Salt **imid-(O)-4**, although a member of a relatively large class of chiral ligand precursors (ref. 8), to the best of our knowledge, has not been previously identified as optimal for any catalytic enantioselective processes.

1.1 equiv. $B_2(pin)_2$ and NaO*t*Bu were proved to be the most efficient condition, which allowed us to secure **1.12** as single diastereomer in enhanced yield (62% yield vs. 52% yield, Scheme 1.3), same *Z:E* ratio, and enantioselectivity.

1.4 Scope of NHC–Cu Catalyzed Muticomponent Reactions of Vinylallenes, $B_2(pin)_2$ and Dienoates

With the optimal conditions in hand, the scope of aryl-substituted dienoates (Table 1.1) was examined. Single *E*-disubstituted alkene isomer and diastereomer and exclusive 1,6-addition was generated in every case. (>98:2 d.r. and >98% *β,γ*-alkene, respectively). Reactions of sterically encumbered *o*-tolyl-substituted dienoate and 1-naphthyl-containing

Table 1.1. **Multicomponent 1,6-Conjugate Additions involving Racemic Vinylallene 1.10 and Aryl-Substituted Dienoates**



entry	Ar	yield (%)[b]	*Z:E*[c]	d.r.[c]	e.r.[d]
1	C_6H_5 (**1.12**)	62	86:14	>98:2	95:5
2	*o*-MeC_6H_4 (**1.13**)	58	87:13	>98:2	96:4
3	1-naphthyl (**1.14**)	59	87:13	>98:2	95:5
4	*o*-$MeOC_6H_4$ (**1.15**)	64	88:12	>98:2	96:4
5	*m*-MeC_6H_4 (**1.16**)	56	86:14	>98:2	95:5
6	*p*-$MeOC_6H_4$ (**1.17**)	67	87:13	>98:2	95:5
7	*p*-BrC_6H_4 (**1.18**)	53	85:15	>98:2	95:5
8	*p*-$F_3CC_6H_4$ (**1.19**)	63	83:17	>98:2	94:6
9	3-furyl (**1.20**)	65	85:15	>98:2	97:3
10	3-thienyl (**1.21**)	65	86:14	>98:2	97:3

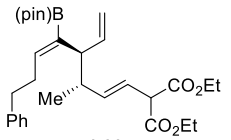
[a]Reactions were performed under N_2 atm. Conversion was >98% in all cases (±2%; loss of allene). [b]Yield (±5%, average of at least three runs) corresponds to purified products (*Z*/*E* mixture). [c]*Z*:*E* ratios and d.r. (±2%) were determined by analysis of ^{1}H NMR spectra of unpurified mixtures. [d]E.r. was determined by HPLC analysis.

dienoate, which furnished **1.13** and **1.14** in 58% and 59% yield, 87:13 *Z*:*E* selectivity, and 96:4 and 95:5 e.r., respectively (entries 2–3). Additions to electron-rich (entries 4–6) or electron-deficient (entry 7–8) dienoates afforded **1.15**–**1.19** in similar efficiency and selectivity, as were the heterocyclic variants **1.20** and **1.21** (entries 9–10). This transformation is applicable to different aryl-substituted dienoates regardless of steric hindrance and electronic properties.

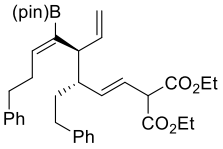
Alkyl-substituted dienoates (Scheme 1.4a) were used to access **1.22**–**1.24** in similar yields and selectivities as the above reactions. 1,6-:1,4-Selectivity and γ-selectivity remained exceptional and none of the *Z*-isomer of the β,γ-unsaturated carbonyl compounds was detected. However, diastereoselectivity varied, depending on the size of the alkyl group: with a smaller methyl group, **1.22** was generated in 81:19 d.r., increasing with a more sizeable alkyl moiety (**1.23**, 87:13 d.r.), and a single diastereomer was obtained as

Scheme 1.4. **Transformations with Different Alkyl-substituted Dienoates and Vinylallenes**

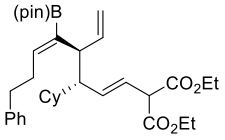
a) Products from reactions with different dienoates:



1.22
>98% conv., 55% yield,
84:16 *Z*:*E*, 81:19 d.r., 97:3 e.r.

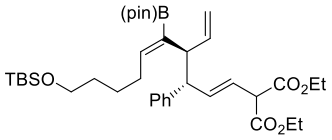


1.23
>98% conv., 60% yield,
85:15 *Z*:*E*, 87:13 d.r., 97:3 e.r.

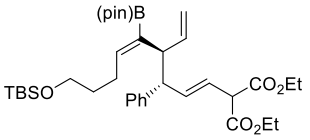


1.24
85% conv., 58% yield,
80:20 *Z*:*E*, >98:2 d.r., 98:2 e.r.

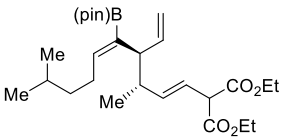
b) Products from reactions with different vinylallenes:



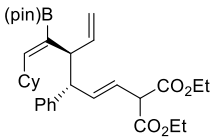
1.25
>98% conv., 50% yield,
86:14 *Z*:*E*, >98:2 d.r., 95:5 e.r.



1.26
>98% conv., 51% yield,
84:16 *Z*:*E*, >98:2 d.r., 96:4 e.r.



1.27
>98% conv., 51% yield,
85:15 *Z*:*E*, 83:17 d.r., 96:4 e.r.



1.28
>98% conv., 55% yield,
86:14 *Z*:*E*, >98:2 d.r., 94:6 e.r.

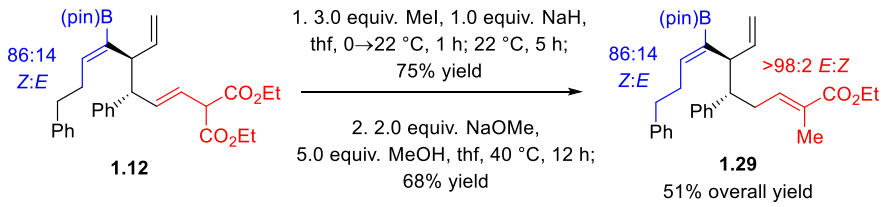
aryl-substituted dienoates cases (cf. Table 1.1) with an even larger cyclohexyl moiety (**1.24**, >98:2 d.r.).

The catalytic method is applicable to a variety of vinylallenes (cf. **1.25**–**1.28**, Scheme 1.4b). In the case of vinylallenes containing a relatively hindered γ-branched substituent (cf. **1.27**) and cyclic α-branched moiety (cf. **1.28**), transformations proceeded with similar efficiency, d.r., *Z*:*E* ratio, and e.r. (**1.27** vs. **1.22** and **1.28** vs. **1.25**, respectively). Conditions that would allow the isolation of the desired product from corresponding reaction with an aryl-substituted vinylallene, could not be identified.

1.5 Functionalization and Applications to Vitamin D_3 Side Chain

To achieve the maximum potential of the present method, it is imperative that the different functional entities within a product structure can be modified with high site-, regio-, and/or stereoselectivity. The transformations in Scheme 1.5 are illustrative. Diester unit in compound **1.12** was converted to *E*-trisubstituted ester **1.29** (<2% *Z*), without any diminution of stereoisomeric purity at the alkenyl boronate in 51% overall yield (Scheme 1.5). In the meanwhile, the isomerization step features a more direct and milder approach compared to a reported two-step sequence, where treatment of the intermediate bearing a quaternary carbon with LiI/2,6-lutidine (145 °C, 4h) is followed by subjection of the isomeric alkene mixture to 1,8-Diazabicyclo[5.4.0]-7-undecene (dbu, 65 °C, 12 h). [14]

Scheme 1.5 **Functionalization of a *β,γ*-Unsaturated Diester to *E*-Trisubstituted Enoate**



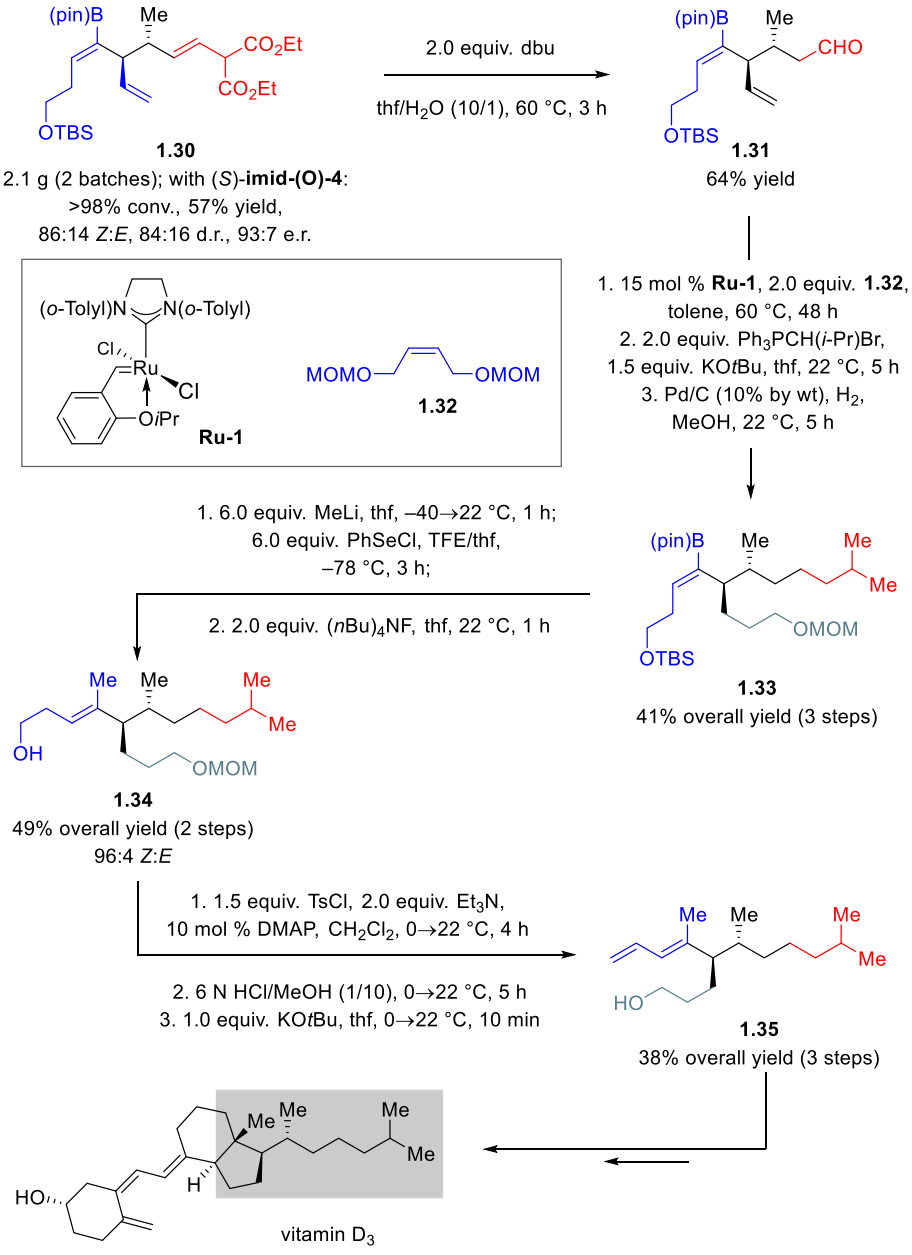
(14) Trost, B. M.; Lee, C. B. *J. Am. Chem. Soc.* **2001**, *123*, 3687–3696.

Repeated attempts to effectuate a catalytic Suzuki-coupling with the sterically hindered trisubstituted alkenyl–B(pin) compounds resulted in <5% conversion to the desired product, which exposes an existing deficiency in the state-of-the-art in this transformation. An alternative Zweifel olefination (non-catalytic) conditions was developed to achieve the same goal. Moreover, sequential "orthogonal" chemo-, regio- and stereoselective transformations leading to **1.35** (Scheme 1.6), formerly reported as precursor to vitamin D_3[15], was carried out. Gram quantities (2.1 g) of **1.30** was prepared in two batches in 57% yield, 86:14 *Z:E* selectivity, 84:16 d.r. and 93:7 e.r. as sole *γ*-selective 1,6-conjuagte addition product (Scheme 1.6). *β,γ*-Unsaturated diester was degraded under mild basic retro-aldol conditions to access **1.31**.[1e] The vinyl moiety was selectively converted to corresponding allylic ether through catalytic stereoretentive cross-metathesis involving the readily available *Z*-alkene **1.32**. Product **1.33** was accessed through a Wittig reaction followed by site-selective reduction of the allylic ether and the newly generated trisubstituted olefin, while the *Z*-trisubstituted alkenyl boronate entity was left untouched. Thus, the inability to effect a stereoretentive catalytic Suzuki coupling to obtain *E*-trisubstituted olefin **1.33**, resulted in a one-vessel Zweifel olefination as surrogate. **1.33** was treated with MeLi, followed by PhSeCl[16] and trifluoroethanol, after removal of the silyl group, furnishing **1.34** with *E*-trisubstituted olefin in 96:4 *Z:E* ratio and 49% overall yield. Formation of the corresponding tosyl ester, acidic cleavage of the methoxymethyl

(15) (a) Clasby, M. C.; Craig, D.; Marsh, A.; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1444–1446. (b) Nemoto, H.; Kurobe, H.; Fukumoto, K.; Kametani, T. *J. Org. Chem.* **1986**, *51*, 5311–5320.
(16) (a) Armstrong, R. J.; García-Ruiz, C.; Myers, E. L.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2017**, *56*, 786–790. (b) Armstrong, R. J.; Aggarwal, V. K. *Synthesis* **2017**, *49*, 3323–3336. When I_2 was used, there was significant loss in alkene stereoisomeric purity; see: (c) Xu, S.; Lee, C.-T.; Rao, H.; Negishi, E.-i. *Adv. Synth. Catal.* **2011**, *353*, 2981–2987.

(MOM) group, and base-induced tosylate elimination settled the diene and hydroxyl moieties of **1.35** in 38% overall yield (for 3 steps).

Scheme 1.6. **Exploration of the Utility of the Catalytic Multicomponent Method in Enantioselective Synthesis of Vitamin D_3 Side Chain**



[a]Yields (±5%) correspond to purified products. For compound **1.30**, the yield is the average of at least three runs and is for *Z*/*E* mixture after silica gel chromatography. [b]*Z*:*E* ratios and d.r. (±2%) were determined by analysis of ^{1}H NMR spectra of unpurified mixtures. [c]E.r. was determined by HPLC analysis.

1.6 Mechanistic Insights of Cu–Allyl Species Generated from Vinylallene and DFT-Based Rationale for Stereoselectivities

Several key mechanistic issues needed to be addressed, including whether achiral Cu–allyl intermediate **1.8** or chiral Cu–allyl intermediate **1.7** is the active species in addition to 1,6-dienoates, precisely how the *E*-trisubstituted alkene isomer formed from intermediate **1.7** and **1.8**, or what other species might lead to the formation of it. We therefore decided to investigate the following specific questions:

1) What is the most thermodynamically stable Cu–allyl intermediate? And which is the kinetically favored species in addition to dienoates?
2) How is the *E*-trisubstituted alkene isomer accessed since the Cu–B(pin) addition is known to occur in a "*syn*" manner?[1f, 17] Why does the catalyst derived from **imid-(O)-4** deliver higher *Z*:*E* selectivity (vs. **imid-(O)-1–3**, Scheme 1.3)?
3) What is the predominant factor to determining d.r and e.r.? Why was lower d.r. obtained with dienoates containing a smaller substituent (cf. Scheme 1.4), while e.r. remained nearly the same?

1.6.1 Rationale for *E*-Isomer Formation and Spectroscopic Analysis of Cu–allyl Intermediates

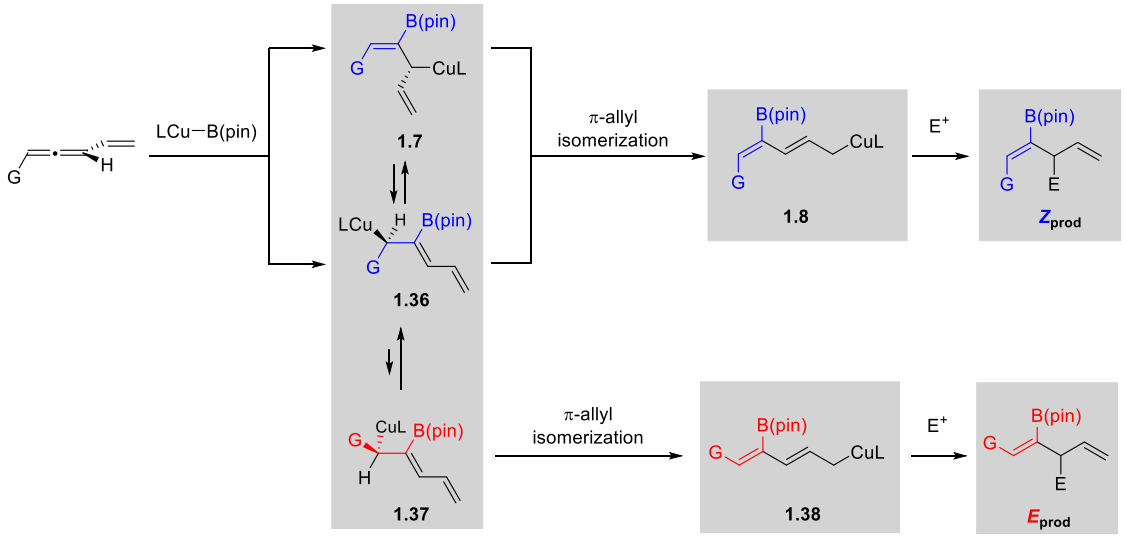
Addition of a Cu–B(pin) to a vinylallene is likely to happen following two different regioseletive pattern, namely, those leading to intermediates **1.7** and **1.36** (Scheme 1.7). These latter organocopper entities could be in equilibrium with a third species **1.37** through π-allyl isomerization and C–C bond rotation. Intermediates **1.7** and **1.36** might then be

(17) Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 3160–3161.

transformed to $\boldsymbol{Z}_{prod}$ via **1.8**, wherein the bulky Cu(NHC) is attached to the least congested primary carbon center, while the formation of higher energy **1.37** involving C–C single bond rotation of **1.36** would deliver $\boldsymbol{E}_{prod}$ via **1.38** (Scheme 1.7). Therefore, there are two ways by which *Z*:*E* selectivity might be influenced. By a relatively slow (vs. addition to dienoates) *Z*-Cu–allyl to *E*-Cu–allyl interconversion; that is, the kinetic selectivity may be established by the initial Cu–B addition, which is maintained and reflected in the final *Z*:*E* ratio. Alternatively, the selectivity may be determined by the relative rates of *Z*-Cu–allyl to *E*-Cu–allyl additions to the dienoate (i.e., Curtin-Hammett kinetics), requiring stereoisomerization to be feasible. To gain mechanistic lucidity, we designed and performed several experiments.

To obtain insight regarding the structure of Cu–allyl intermediates, generated from vinylallenes (cf. Scheme 1.7), we subjected a stoichiometric amount of **NHC–Cu-1**

Scheme 1.7. **Proposed Pathways Leading to Formation of *Z*- and *E*-Alkeneyl–B(pin) Products and Related Cu–Allyl Intermediates**



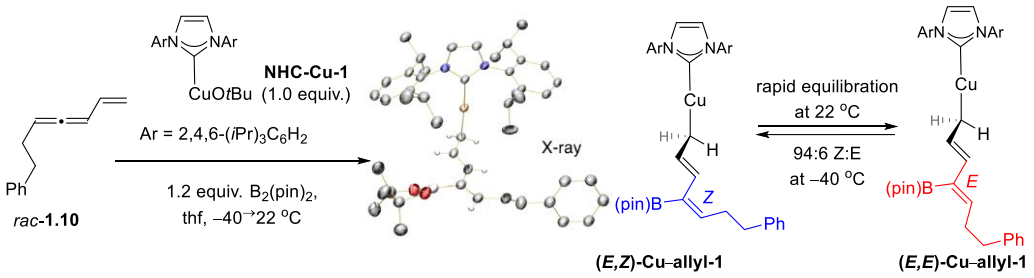
complex (thf-d_8 solution) with $B_2(pin)_2$ and *rac*-**1.10** and monitored the reaction progress by variable temperature NMR (VT NMR) spectroscopy. Two sets of peaks corresponding to **(*E*, *Z*)-Cu–allyl-1** (cf. **1.8**) and **(*E*, *E*)-Cu–allyl-1** (cf. **1.38**) were observed at –40 °C at

94:6 ratio; these signals exchanged rapidly at 22 °C. Moreover, we were able to obtain an X-ray structure for **(*E*, *Z*)-Cu–allyl-1**(Scheme 1.8a).

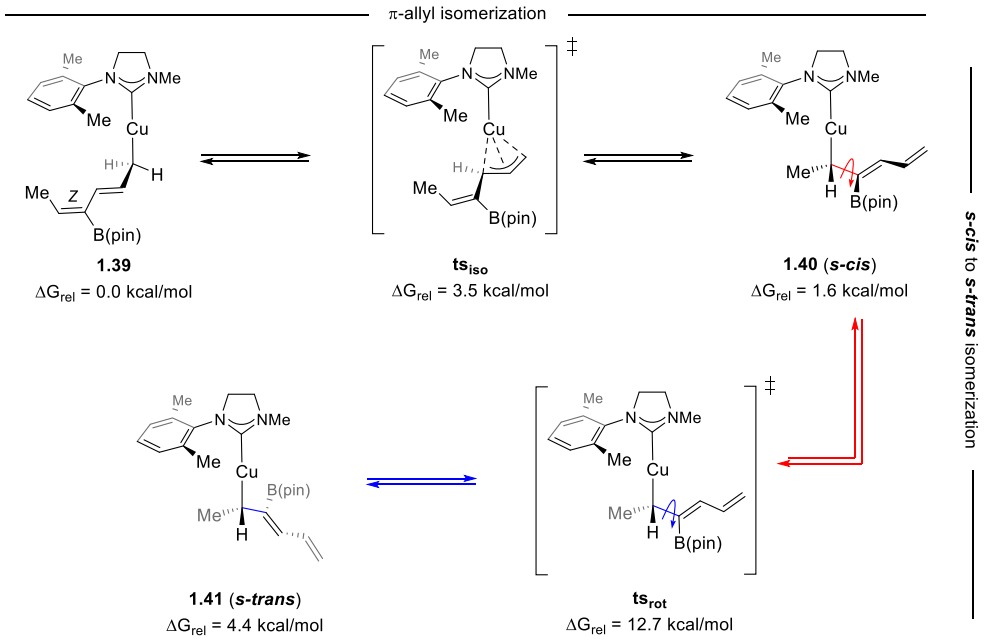
DFT calculations with a simplified model NHC (Scheme 1.8b) indicate that allyl isomerization is facile with an activation barrier of 3.5 kcal/mol (only the highest of two sequential transition states shown).These studies further demonstrated that **1.40** to **1.41**

Scheme 1.8. **Spectroscopic and DFT Calculation Study of Cu–allyl Intermediates and Interconversion**

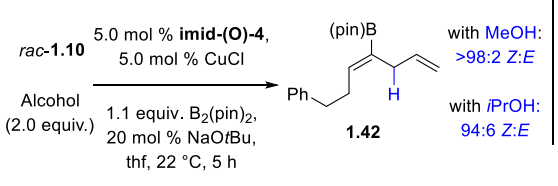
a) Spectroscopic experiment illustrating that Cu–B(pin) addition to vinylallene occurs with high *Z*-kinetic selectivity:



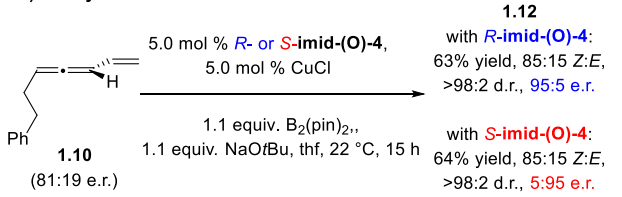
b) Calculated values for arriers of π-allyl isomerization and single bond rotation (*s-cis to s-trans* conversion):



c) *Z*:*E* ratio can vary based on the rate of electrophile trapping:



d) Nearly identical stereocontrol observed with enantio-enriched 1.10:



isomerization is energetically feasible at room temperature with a 12.7 kcal/mol energy penalty, probably due to *s-cis*→*s-trans* single bond rotation.

Proto-boryl additions involving racemic vinylallene **1.10**, $B_2(pin)_2$ and MeOH or *t*BuOH, catalyzed by the NHC–Cu complex derived from **imid-(O)-4**, were carried out in order to shed light on the dynamic behavior of these Cu–allyl species. Diene **1.42** was formed in >98:2 *Z*:*E* ratio with MeOH as the proton source, but selectivity decreased to 94:6 when *t*BuOH was used (Scheme 1.8c). To determine how facile Cu–allyl isomerization is relative to 1,6-conjugate addition, or in other words, whether any chiral Cu–allyl intermediates (e.g. **1.36** and **1.37**, Scheme 1.7) react with dienoate affording desire products directly, control experiments with enantiomerically enriched **1.10** (81:19 e.r.) with NHC–Cu complexes derived from both (*R*)- and (*S*)-**imid-(O)-4** (Scheme 1.8d) were carried out. In both instances, **1.12** was generated with identical *Z*:*E* selectivity (85:15) and with the same level but complete reversal of enantioselectivity. These studies provided a picture of how the *E*-isomer is formed and what is the thermodynamic and kinetic preferences of the Cu–allyl complexes generated from vinylallene.

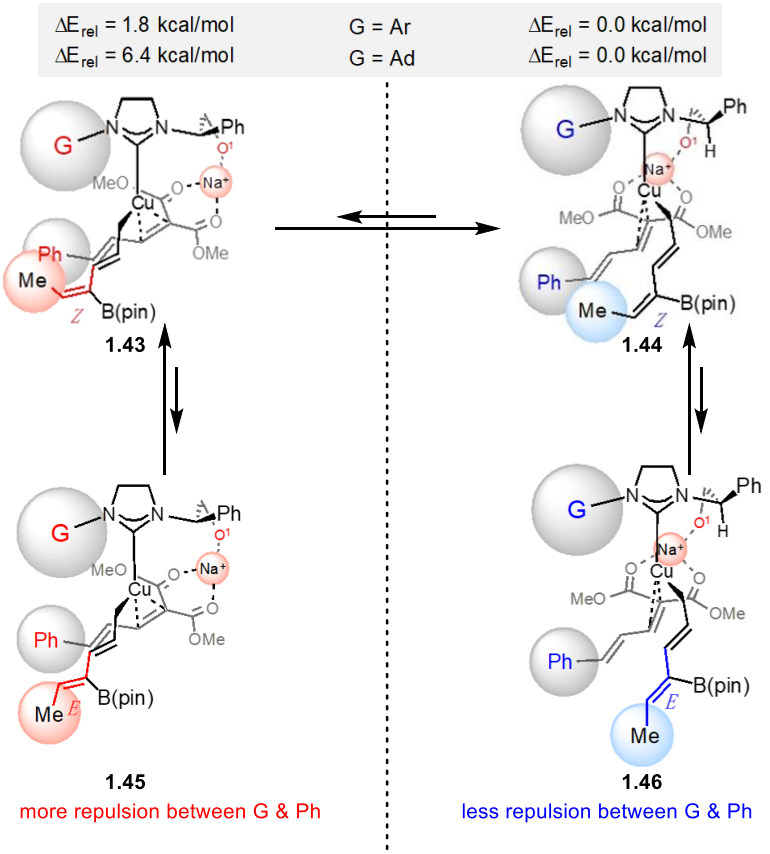
1) Achiral intermediates **1.8** (*Z*-Cu–allyl) and **1.38** (*E*-Cu–allyl) are thermodynamically favored and the species that lead to the corresponding *Z* product isomer ($\boldsymbol{Z}_{prod}$) and *E* product isomer ($\boldsymbol{E}_{prod}$). Otherwise, alteration of enantioselectivity would be observed in the control experiment with enantiomerically enriched vinylallene and the enantiomers of the catalyst derived from **imid-(O)-4** (Scheme 1.8d).
2) The *Z*-Cu–allyl complex (**1.8)** is kinetically preferred and generated by initial Cu–B addition to vinylallenes, as indicated by the fast trapping with MeOH

(>98:2 *Z*:*E*). However, *Z*-to-*E* isomerization can occur, through π-allyl isomerization and C–C bond rotation (Scheme 1.8b), prior to trapping of electrophile when a reaction is more sluggish than isomerization (Curtin-Hammett kinetics). The 1,6-conjugate addition is one such instance.

1.6.2 Rationale for Improved *Z*-Selectivity with Imid-(O)-4

Mechanistic studies described above (section **1.6.1**) had showed us how the *E*-isomer is formed, but the reason for higher *Z*-selectivity with **imid-(O)-4** remained unclear. DFT studies (MN15/def2-TZVPP//M06-L/def2-SVP level) were therefore carried out, indicating that there are two competing coordination geometries associated with the Na^+ bridge (**1.43**-**1.46**, Scheme 1.9); **1.43** and **1.44** lead to the *Z* isomer, whereas **1.45** and **1.46** afford the *E* isomer. When the alkoxide oxygen (O1) points to the right in **1.43** and **1.45**,

Scheme 1.9. **Stereochemical Models Accounting for Improved *Z*-Selectivity with Imid-(O)-4**

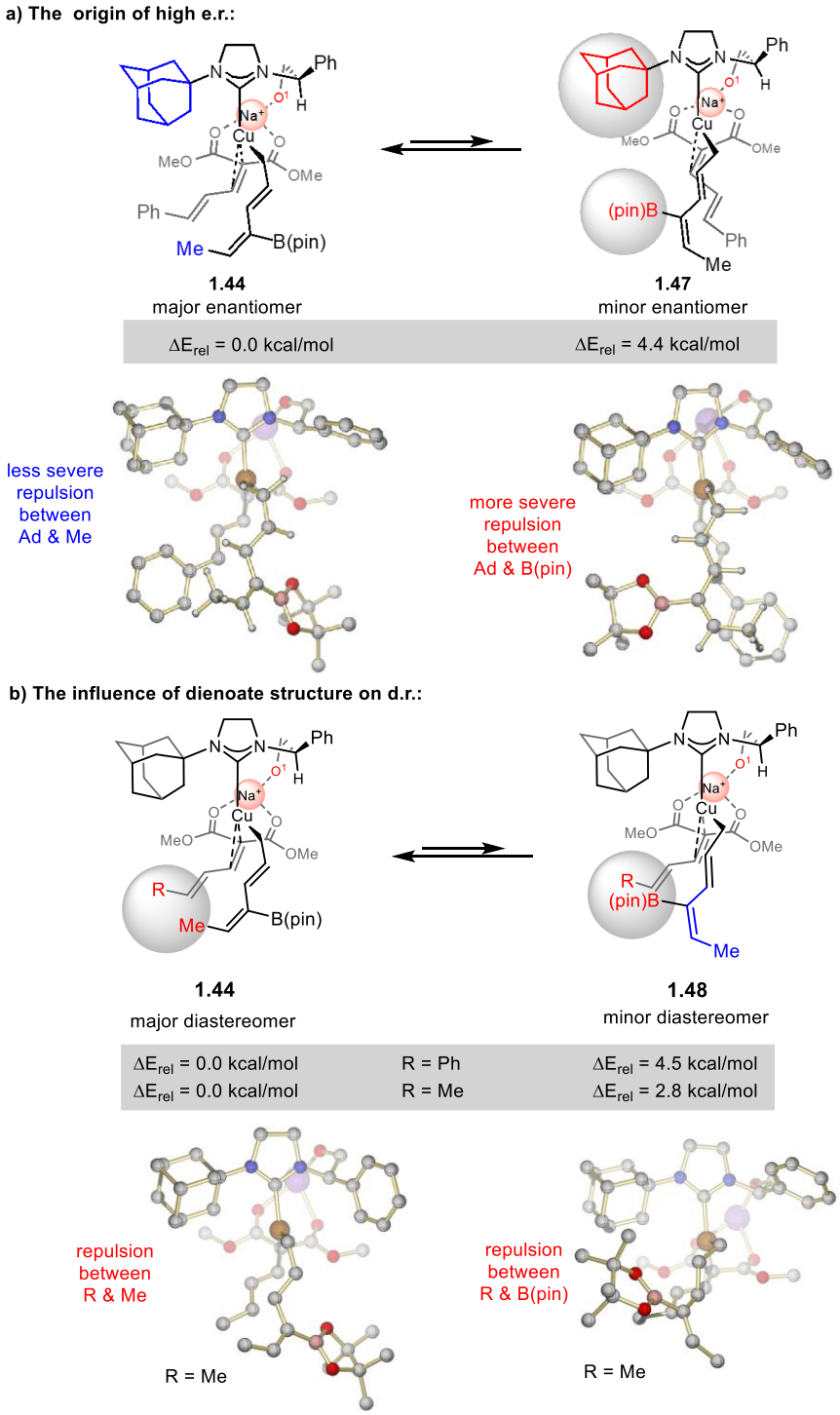


steric repulsion between the bound dienoate and the NHC substituent G results in an increase in energy; no such interaction exists in **1.44** and **1.46**, wherein O1 is oriented in the opposite direction. Reaction via **1.43** and **1.45** would favor an *E*-trisubstituted alkene because of the smaller energy gap separating **1.43** and **1.45** (vs. **1.44** and **1.46**), which probably originates from G and Me groups being more proximal in **1.43** than in **1.44** (i.e., $k_{\mathbf{1.45}}/k_{\mathbf{1.43}} > k_{\mathbf{1.46}}/k_{\mathbf{1.44}}$). To put it another way, if transition states **1.43**/**1.45** were less energetically accessible compared with **1.44**/**1.46**, a higher *Z:E* selectivity would be achieved. In regards to reaction with **imid-(O)-4**, which contains an *N*-Ad moiety, there appears to be a larger energy difference between **1.43**/**1.45** and **1.44**/**1.46**, (ΔE_{rel} between **1.43** and **1.44** = 6.4 ± 2.0 kcal/mol), rendering **1.43**/**1.45** significantly less accessible. In contrast, with a Cu complex that contains a ligand with an *N*-Ar group (e.g. **imid-(O)-1–3**), **1.43**/**1.45** probably contribute more similarly as the energy gap seems to be smaller (ΔE_{rel} = 1.8 ± 2.0 kcal/mol), resulting in preference of formation of the *E* isomer.

1.6.3 Origin of High Enantioselectivity and Diminished Diastereoselectivity with Dienoates Containing Small Alkyl Substituent

Another question is why high enantioselectivity was obtained throughout the scope but lower diastereoselectivity was observed with small alkyl substituted dienoates. The two competing transition states below are **1.44** and **1.47** (Scheme 1.10a); **1.44** would deliver the major enantiomer, whereas **1.47** led to minor enantiomer with 4.4 kcal/mol higher in energy. This energy difference possibly arises from steric repulsion between the *N*-Ad moiety of **imid-(O)-4** and the B(pin) unit of the Cu–allyl complex (Scheme 1.10a). The proposed Na^+–substrate coordination is thus weakened as a result of steric pressure, leading to longer Na·····O distance (2.223 Å in **1.47** vs. 2.204 Å in **1.44**). The diastereoselectivity

Scheme 1.10. **Stereochemical Models Accounting for High e.r. and Variation of d.r. with Different Dienoates**



of the product is likely controlled by the competition between transition states **1.44** (major) and **1.48** (minor). The key interaction is the steric repulsion caused by the substituent of

dienoates and either Me or B(pin) moiety of Cu–allyl complex. With a small alkyl substituent, **1.48** is more accessible (2.8 kcal/mol vs. R = Ph 4.5 kcal/mol over **1.44**) and thus more minor diastereomer is generated (Scheme 1.10b).

1.7 Conclusions

An NHC–Cu-catalyzed multicomponent process involving racemic vinylallenes, $B_2(pin)_2$ and *α,β,γ,δ*-unsaturated diesters has been developed. Reactions afford multifunctional B(pin) containing products and proceed with exclusive 1,6- and *γ*-selectivity. The products feature a stereo-defined trisubstituted alkenyl–B(pin) moiety, a vinyl unit, a *β,γ*-unsaturated diester and vicinal stereogenic centers, functional moieties that can be chemo- and stereoselectively functionalized. Experimental, spectroscopic and computational studies elucidate the thermodynamic and kinetic preference of the key Cu–allyl intermediates. Furthermore, stereochemical models that account for the observed *Z:E*, diastereo- and enantioselectivity level and profile were obtained.

The new catalytic method represents a notable addition to catalytic regio-, diastereo- and enantioselective 1,6-conjugate additions of C-based nucleophiles, especially allyl moiety with multi-functionalizable sites. The findings detailed above foreshadow the use of vinylallenes in a wide range of multicomponent reactions, including processes that involve Cu–H[18] or Cu–B(pin)[4] complexes.

(18) For selected reports involving enantioselective multicomponent reactions catalyzed by a chiral Cu–H complex, see: with mono- and 1,1-disubstituted allenes: (a) Liu, R. Y.; Yang, Y.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2016**, *55*, 14077–14080. (b) Tsai, E. Y.; Liu, R. Y.; Yang, Y.; Buchwald, S. L. *J. Am. Chem. Soc.* **2018**, *140*, 2007–2011. (c) Tan, Y.-X.; Tang, X.-Q.; Liu, P.; Kong, D.-S.; Chen, Y.-L.; Tian, P.; Lin, G.-Q. *Org. Lett.* **2018**, *20*, 248–251. With 1,3-enynes: (d) Yang, Y.; Parry, I. B.; Lu, G.; Liu, P.; Buchwald, S. L. *Science* **2016**, *353*, 144–150. (e) Huang, Y.; del Pozo, J.; Torker, S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2018**, *140*, 2643–2655.

1.8 Experimental

1.8.1 General and Reagents

Infrared (IR) spectra were recorded on a Bruker FT-IR Alpha (ATR mode) spectrophotometer, λ_{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) or Varian Unity INOVA 600 (600 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 = broad, m = multiplet), and coupling constant (Hz). ^{13}C NMR spectra were recorded on a Varian Unity INOVA 400 (101 MHz) or Varian Unity INOVA 600 (151 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. Enantiomeric ratios were determined by HPLC analysis (Chiral Technologies Chiralpak AZ–H (4.6 x 250 mm), Chiralcel OD–H (4.6 x 250 mm), Chiralcel OZ–H (4.6 x 250 mm) and Chiralpak AD–H (4.6 x 250 mm) in comparison with authentic racemic materials. Specific rotations were measured on an ATAGO® AP-300 Automatic Polarimeter or 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 column and an 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, Inc.) in air.

Alkyl-substituted dienoates: prepared according to previously reported procedures.[19]

Aryl-substituted dienoates: prepared according to previously reported procedures.[20]

Vinylallenes: prepared according to previously reported procedures.[6]

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

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

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

1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU): purchased from Aldrich Chemical Co. and used as received.

4-Dimethylaminopyridine (DMAP): purchased from Aldrich Chemical Co. and used as received.

Imidazolinium salts: prepared according to previously reported procedures.[1e, 2b,21]

Isopropyl triphenylphosphonium bromide: purchased from Aldrich Chemical Co. and used as received.

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(19) Singh, R.; Ghosh, S. K. *Tetrahedron* **2010**, *66*, 2284–2292.
(20) Liu, L.; Sarkisian, R.; Xu, Z.; Wang, H. *J. Org. Chem.* **2012**, *77*, 7693–7699.
(21) Clavier, H.; Coutable, L.; Toupet, L.; Guillemin, J-C.; Mauduit, M. *J. Organomet. Chem.* **2005**, *690*, 5237– 5254.

Methoxymethyl chloride (MOMCl): purchased from Aldrich and used after distillation.

Methyl iodide: purchased from Aldrich Chemical Co. and used as received.

Methyl lithium (1.0 M in ether): purchased from Aldrich Chemical Co. and used as received.

Methyl triphenylphosphonium bromide: purchased from Aldrich Chemical Co. and used as received.

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

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

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

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

Ru-based complexes: purchased from Aldrich Chemical Co. and used as received.

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

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

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

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

Tetrabutylammonium fluoride (1.0 M in thf): purchased from Oakwood Products Inc. and used as received.

***p*-Toluenesulfonyl chloride:** purchased from Aldrich Chemical Co. and used as received.

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

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

1.8.2 Representative Procedure for Catalytic Enantioselective 1,6-Conjuagte Addition

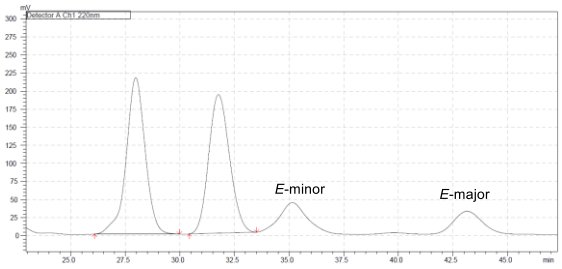
An oven-dried 2-dram vial equipped with a stir bar was charged with **imid-(O)-4** (2.5 mg, 5.0 μmol), CuCl (0.5 mg, 5.0 μmol), NaO*t*-Bu (10.7 mg, 0.11 mmol) and thf (1.0 mL) in a nitrogen-filled glove box. The mixture was allowed to stir for 2 h under N_2 at 22 ℃ , after which $B_2(pin)_2$ (28.0 mg, 0.11 mmol) was added. The resulting solution was allowed to stir for 30 min, after which dienoate **1.11** (27.4 mg, 0.10 mmol) and vinylallene **1.10** (34.0 mg, 0.20 mmol) were added. The mixture was allowed to stir at 22 ℃ for 15 h. Volatiles were then removed in vacuo, affording yellow oil residue, which was purified by silica gel chromatography (30:1 hexanes/ethyl acetate) to afford **1.12** as colorless oil (35.5 mg, 0.062 mmol, 62% yield). This procedure was used in all other cases.

1.8.3 Characterization of Products of Multicomponent Processes

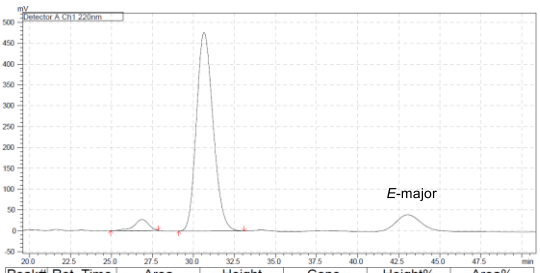
Diethyl 2-((1*E*, 3*S*, 4*S*, 5*Z*)-3,8-diphenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-vinylocta-1,5-dien-1-yl)malonate (1.12)

IR (neat): 2978 (m), 2932 (w), 1732 (s), 1621 (w), 1453 (w), 1370 (m), 1303 (w), 1144 (s), 1030 (m), 700 (s) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.30 – 7.26 (m, 2H), 7.23 – 7.16 (m, 3H), 7.13 – 7.10 (m, 5H), 6.14 (t, J = 6.7 Hz, 1H), 6.01 (ddd, J = 17.0, 10.3, 8.2 Hz, 1H), 5.86 (dd, J = 15.4, 8.2 Hz, 1H), 5.67 (ddd, J = 15.4, 8.7, 0.9 Hz, 1H), 4.96 – 4.88 (m, 2H), 4.17 – 4.11 (m, 4H), 3.96 (dd, J = 8.7, 0.5 Hz, 1H), 3.89 (dd, J = 10.8, 8.4 Hz, 1H), 3.48 (dd, J = 10.9, 8.4 Hz, 1H), 2.53 – 2.44 (m, 1H), 2.39 – 2.27 (m, 2H), 2.25 – 2.16 (m, 1H), 1.28 – 1.18 (m, 18H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 168.5, 168.4, 145.6, 143.2, 142.3, 140.6, 139.7, 128.5, 128.5, 128.4, 128.2, 126.2, 125.9, 122.4, 114.8, 83.1, 61.7, 61.6, 55.8, 51.3, 50.0, 35.2, 31.1, 25.1, 24.7, 14.2, 14.1; **HRMS (DART+):** Calcd for $C_{35}H_{46}BO_6$

[M+H]$^+$: 573.3387. Found: 573.3389. **Specific rotation:** $[\alpha]_D^{20.0}$ –13.2 (*c* 1.76, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.; Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (95:5 e.r. shown; Chiralcel OZ-H column, 99.9:0.1 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	27.967	13072568	216393	50.640	53.025	50.640
2	31.757	12741958	191703	49.360	46.975	49.360
Total		25814527	408096		100.000	100.000



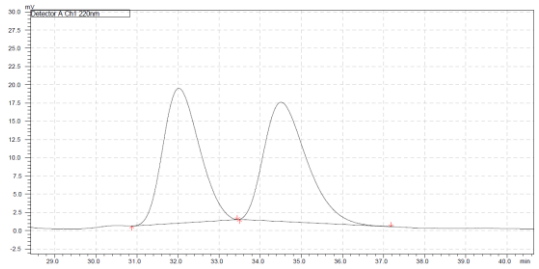
Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	26.847	1624829	26699	4.590	5.303	4.590
2	30.634	33774280	476794	95.410	94.697	95.410
Total		35399109	503493		100.000	100.000

Retention Time	Area	Area%	Retention Time	Area	Area%
27.967	13072568	50.640	26.847	1624829	4.590
31.757	12741958	49.360	30.634	33774280	95.410

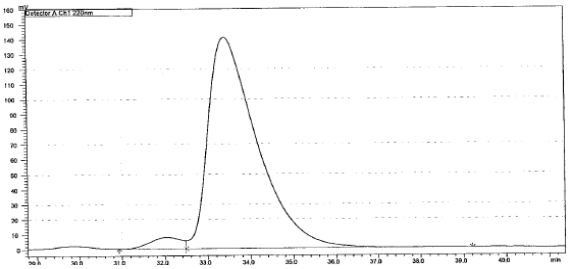
Diethyl 2-((1*E*, 3*S*, 4*S*, 5*Z*)-8-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-(o-tolyl)-4-vinylocta-1,5-dien-1-yl)malonate (1.13)

IR (neat): 2979 (w), 2931 (w), 1734 (s), 1619 (w), 1370 (m), 1347 (m), 1304 (w), 1145 (m), 966 (w) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.32 – 7.26 (m, 2H), 7.22 – 7.13 (m, 3H), 7.09 – 7.00 (m, 4H), 6.25 (t, *J* = 6.7 Hz, 1H), 6.01 (ddd, *J* = 17.0, 10.3, 8.1 Hz, 1H), 5.63 – 5.59 (m, 2H), 4.95 – 4.90 (m, 2H), 4.24 – 4.01 (m, 5H), 3.92 (d, *J* = 7.9 Hz, 1H), 3.61 (dd, *J* = 10.7, 8.4 Hz, 1H), 2.65 – 2.33 (m, 4H), 2.33 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.20 – 1.09 (m, 15H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 168.5, 168.4, 145.9, 142.3, 140.7, 140.5, 139.2, 137.0, 130.3, 128.5, 128.4, 127.6, 126.0, 125.9, 125.8, 122.1, 114.6, 83.1, 61.6, 61.5, 55.8, 48.5, 46.9, 35.2, 31.2, 25.3, 24.2, 19.8, 14.2, 14.1; **HRMS (DART):** Calcd for $C_{36}H_{48}BO_6$ [M+H]$^+$: 587.3544. Found: 587.3544. **Specific rotation:** $[\alpha]_D^{20.0}$ –40.3 (*c* 0.75, $CHCl_3$) for an enantiomerically enriched sample of 96:4 e.r.; Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material after

oxidation of the alkenylboron product with 3.0 equiv sodium perborate tetrahydrate in thf/H_2O (1:1). (96:4 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	Conc.	Height%	Area%
1	32.018	1139833	18486	49.103	53.098	49.103
2	34.504	1181493	16329	50.897	46.902	50.897
Total		2321327	34815		100.000	100.000



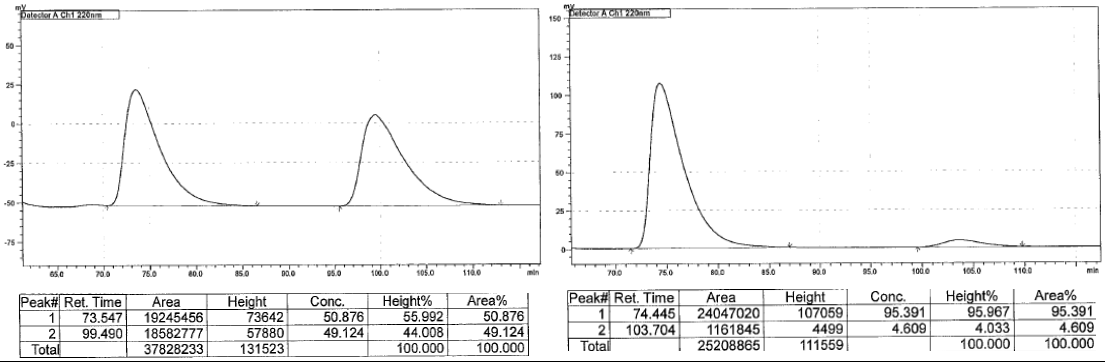
Peak#	Ret. Time	Area	Height	Height%	Area%
1	32.035	385252	7617	5.137	3.347
2	33.407	11126786	140660	94.863	96.653
Total		11512038	148277	100.000	100.000

Retention Time	Area	Area%	Retention Time	Area	Area%
32.018	1139833	49.103	32.035	385252	3.347
34.504	1181493	50.897	33.407	11126786	96.653

Diethyl 2-((1*E*, 3*S*, 4*S*, 5*Z*)-3-(naphthalen-1-yl)-8-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-vinylocta-1,5-dien-1-yl)malonate (1.14)

IR (neat): 2976 (m), 2934 (w), 1733 (s), 1367 (m), 1303 (m), 1144 (w), 1033 (m), 779 (s) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.21 (d, *J* = 9.3 Hz, 1H), 7.77 – 7.73 (m, 1H), 7.63 (d, *J* = 8.1 Hz, 1H), 7.40 – 7.367 (m, 2H), 7.36 – 7.32 (m, 1H), 7.27 – 7.22 (m, 3H), 7.18 (t, *J* = 7.3 Hz, 1H), 7.12 – 7.03 (m, 2H), 6.13 – 6.07 (m, 2H), 5.97 – 5.85 (m, 1H), 5.67 (dd, *J* = 15.5, 8.7 Hz, 1H), 5.00 – 4.94 (m, 2H), 4.77 (t, *J* = 9.4 Hz, 1H), 4.16 – 4.08 (m, 2H), 4.04 – 4.00 (m, 2H), 3.90 (d, *J* = 8.7 Hz, 1H), 3.79 (t, *J* = 9.4 Hz, 1H), 2.53-2.31 (m, 4H), 1.27 – 1.19 (m, 6H), 1.12 – 1.05 (m, 7H). 0.98-0.93 (m, 5H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 168.4, 168.2, 145.6, 142.2, 140.8, 139.0, 134.1, 132.2, 128.7, 128.5, 128.4, 128.3, 128.1, 126.8, 125.9, 125.4, 125.4, 125.2, 124.7, 122.6, 114.9, 83.1, 61.6, 61.5, 55.7, 49.3, 35.1, 31.1, 25.1, 24.2, 14.1, 14.0; **HRMS (DART+):** Calcd for $C_{39}H_{48}BO_6$ $[M+H]^+$: 623.3544. Found: 623.3558. **Specific rotation:** $[\alpha]_D^{20.0}$ –12.6 (*c* 0.67, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.; Enantiomeric purity was determined by

HPLC analysis in comparison with authentic racemic material after oxidation of the alkenylboron product with 3.0 equiv sodium perborate tetrahydrate in thf/H_2O (1:1). (95:5 e.r. shown; Chiralcel OD-H column, 99.5:0.5 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm). mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	73.547	19245456	73642	50.876	55.992	50.876
2	99.490	18582777	57880	49.124	44.008	49.124
Total		37828233	131523		100.000	100.000

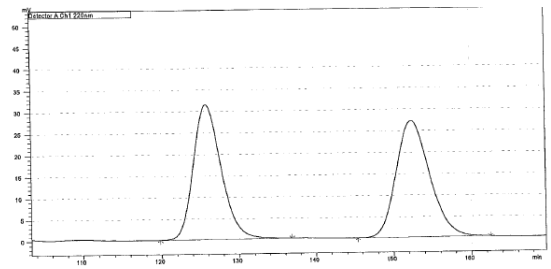
Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	74.445	24047020	107059	95.391	95.967	95.391
2	103.704	1161845	4499	4.609	4.033	4.609
Total		25208865	111559		100.000	100.000

Retention Time	Area	Area%	Retention Time	Area	Area%
73.547	19245456	50.876	74.445	24047020	95.391
99.490	18582777	49.124	103.704	1161845	4.609

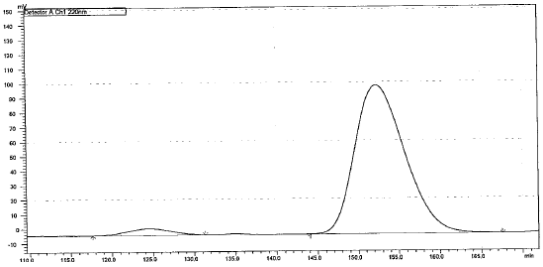
Diethyl 2-((1*E*, 3*S*, 4*S*, 5*Z*)- 3-(2-methoxyphenyl)-8-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-vinylocta-1,5-dien-1-yl)malonate (1.15)

IR (neat): 2978 (w), 2936 (w), 1733 (s), 1493 (w), 1370 (m), 1243 (w), 1145 (m), 1031 (s), 752 (w) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.29 – 7.02 (m, 7H), 6.80 (td, *J* = 7.4, 1.1 Hz, 1H), 6.73 (d, *J* = 8.2 Hz, 1H), 6.15 (t, *J* = 6.8 Hz, 1H), 6.10 – 5.96 (m, 2H), 5.66 (ddd, *J* = 15.4, 8.8, 0.8 Hz, 1H), 4.91 – 4.87 (m, 2H), 4.21 – 4.04 (m, 5H), 3.96 (dd, *J* = 8.8, 0.7 Hz, 1H), 3.82 – 3.78 (m, 1H), 3.70 (s, 3H), 2.53 (dd, *J* = 10.9, 8.2 Hz, 1H), 2.43 – 2.36 (m, 2H), 2.29 – 2.22 (m, 1H), 1.28 – 1.18 (m, 18H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 168.7, 168.5, 157.5, 145.3, 142.5, 141.3, 138.8, 131.0, 128.4, 128.3, 127.3, 125.9, 122.0, 120.3, 114, 110.7, 83.0, 61.6, 61.5, 55.9, 55.1, 47.9, 35.3, 30.7, 25.1, 24.9, 24.7, 14.2, 14.1; **HRMS (DART+):** Calcd. for $C_{36}H_{48}BO_7$ $[M+H]^+$: 603.3493; Found: 603.3467; **Specific rotation:** $[\alpha]_D^{20.0}$ –8.0 (*c* 0.95, $CHCl_3$) for an enantiomerically enriched sample of 96:4 e.r.;

Enantiomeric purity 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, 0.3 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Height%	Area%
1	125.805	7868969	31357	53.646	49.157
2	152.397	8138771	27094	46.354	50.843
Total		16007739	58451	100.000	100.000



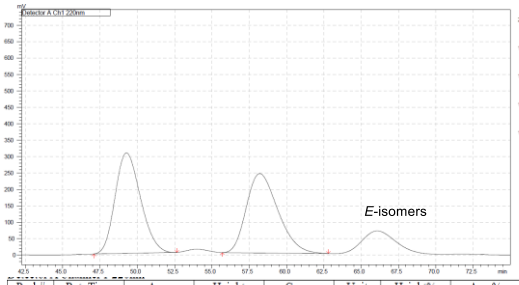
Peak#	Ret. Time	Area	Height	Height%	Area%
1	124.481	1635768	4403	4.126	3.620
2	152.240	43554598	102324	95.874	96.380
Total		45190366	106727	100.000	100.000

Retention Time	Area	Area%	Retention Time	Area	Area%
125.805	7868969	49.157	124.481	1635768	3.620
152.397	8138771	50.843	152.240	43554598	96.380

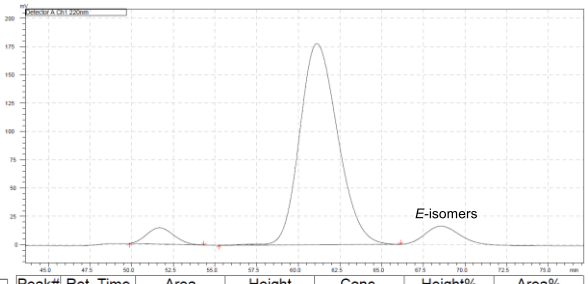
Diethyl 2-((1*E*, 3*S*, 4*S*, 5*Z*)- 8-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-(m-tolyl)-4-vinylocta-1,5-dien-1-yl)malonate (1.16)

IR (neat) 2953 (w), 2927 (w), 2868 (w), 1621 (w), 1467 (m), 1370 (s), 1353 (w), 1299 (s), 1142 (s), 969 (w), 863 (w), 684 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.28 (t, *J* = 7.5 Hz, 2H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.12 (d, *J* = 7.3 Hz, 2H), 7.10 (t, *J* = 7.8 Hz, 1H), 6.93 – 6.90 (m, 3H), 6.14 (t, *J* = 6.7 Hz, 1H), 6.00 (ddd, *J* = 18.0, 10.1, 8.2 Hz, 1H), 5.85 (dd, *J* = 15.4, 8.4 Hz, 1H), 5.68 (dd, *J* = 15.4, 8.8 Hz, 1H), 4.95 – 4.89 (m, *J* = 12.3 Hz, 2H), 4.20 – 4.11 (m, 4H), 3.96 (d, *J* = 8.8 Hz, 1H), 3.85 (dd, *J* = 10.8, 8.6 Hz, 1H), 3.48 (dd, *J* = 10.7, 8.5 Hz, 1H), 2.53 – 2.48 (m, 1H), 2.40 – 2.31 (m, 2H), 2.26 (s, 3H), 2.24 – 2.19 (m, 1H), 1.29 – 1.25 (m, *J* = 6.7 Hz, 9H), 1.22 – 1.19 (m, *J* = 3.5 Hz, 9H); **^{13}C NMR (151 MHz, $CDCl_3$)** δ 168.5, 168.4, 145.5, 143.2, 142.3, 140.7, 139.8, 137.4, 129.4, 128.5, 128.4, 128.1, 127.0, 125.9, 125.4, 122.3, 114.7, 83.1, 61.6, 61.6, 55.8, 51.4, 50.0, 35.2, 31.0, 25.1, 24.7, 21.6, 14.2, 14.1; **HRMS (DART+):** Calcd for $C_{36}H_{48}BO_6$ $[M+H]^+$: 587.3539. Found: 587.3539; **Specific rotation:** $[\alpha]_D^{20.0}$ –6.2 (*c* 1.0, $CHCl_3$) for an enantiomerically enriched

sample of 95:5 e.r.; Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (95:5 e.r. shown; Chiralcel OZ-H column, 99.9:0.1 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Conc.	Unit	Height%	Area%
1	49.264	36326554	306059	50.503		55.876	50.503
2	58.196	35603554	241683	49.497		44.124	49.497
Total		71930108	547742			100.000	100.000



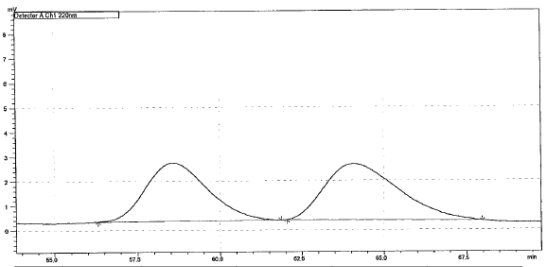
Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	51.668	1629098	14364	5.470	7.479	5.470
2	61.108	28150611	177690	94.530	92.521	94.530
Total		29779709	192053		100.000	100.000

Retention Time	Area	Area%	Retention Time	Area	Area%
49.264	36326554	50.503	51.668	1629098	5.470
58.196	35603554	49.497	61.108	28150611	94.530

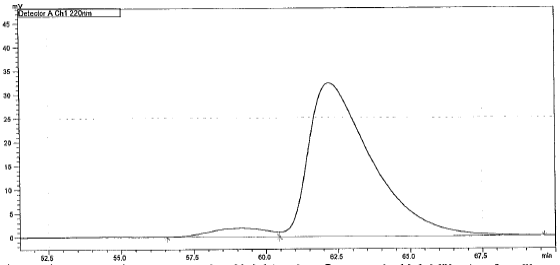
Diethyl 2-((1*E*, 3*S*, 4*S*, 5*Z*)- 3-(4-methoxyphenyl)-8-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-vinylocta-1,5-dien-1-yl)malonate (1.17)

IR (neat): 2979 (w), 2932 (s), 1732 (w), 1610 (m), 1511 (m), 1370 (m), 1301 (s), 1247 (s), 1144 (s), 1033 (m), 700 (w) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.28 (t, *J* = 7.5 Hz, 2H), 7.19 (t, *J* = 7.3 Hz, 1H), 7.13 (d, *J* = 7.2 Hz, 2H), 7.02 (d, *J* = 8.6 Hz, 2H), 6.75 (d, *J* = 8.6 Hz, 2H), 6.16 (t, *J* = 6.7 Hz, 1H), 6.01 (ddd, *J* = 17.1, 10.3, 8.2 Hz, 1H), 5.84 (dd, *J* = 15.4, 8.1 Hz, 1H), 5.64 (dd, *J* = 15.4, 8.8 Hz, 1H), 4.96 – 4.86 (m, 2H), 4.20 – 4.11 (m, 4H), 3.96 (d, *J* = 8.7 Hz, 1H), 3.87 – 3.80 (m, 1H), 3.75 (s, 3H), 3.44 (dd, *J* = 10.9, 8.4 Hz, 1H), 2.57 – 2.48 (m, 1H), 2.40 – 2.29 (m, 2H), 2.28 – 2.16 (m, 1H), 1.28 – 1.19 (m, 18H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 168.5, 168.4, 158.0, 145.5, 142.3, 140.7, 140.0, 135.3, 129.8, 129.3, 128.5, 128.4, 125.9, 122.0, 114.7, 113.6, 83.1, 61.6, 61.6, 55.7, 55.3, 50.4, 50.1, 35.2, 31.0, 25.1, 24.8, 14.2, 14.1; **HRMS (DART+):** Calcd for $C_{36}H_{48}BO_7$ $[M+H]^+$: 603.3493. Found: 603.3467; **Specific rotation:** $[\alpha]_D^{20.0}$ –23.6 (*c* 0.76, $CHCl_3$) for an

enantiomerically enriched sample of 95:5 e.r.; Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material after oxidation of the alkenylboron product with 3.0 equiv sodium perborate tetrahydrate in thf/H_2O (1:1). (95:5 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	Height%	Area%
1	58.565	312618	2392	51.730	48.241
2	64.075	335420	2232	48.270	51.759
Total		648038	4623	100.000	100.000



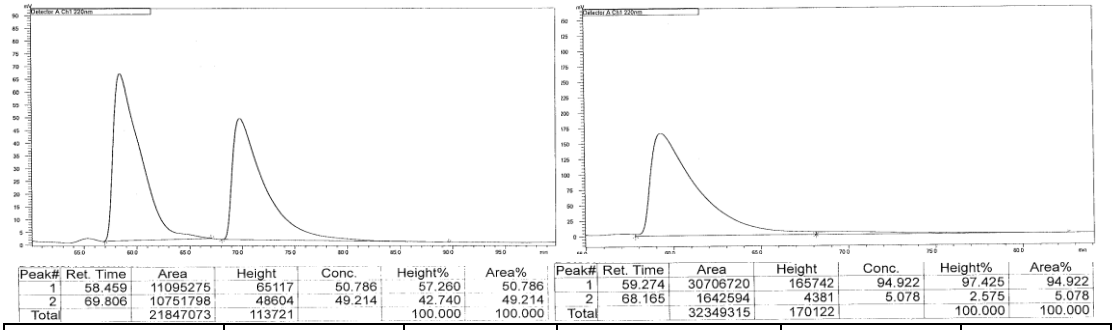
Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	59.132	252238	1837	4.906	5.385	4.906
2	62.206	4889221	32284	95.094	94.615	95.094
Total		5141459	34121		100.000	100.000

Retention Time	Area	Area%	Retention Time	Area	Area%
58.565	312618	48.241	59.132	252238	4.906
64.075	335420	51.759	62.206	4889221	95.094

Diethyl 2-((1*E*, 3*S*, 4*S*, 5*Z*)-3-(4-bromophenyl)-8-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-vinylocta-1,5-dien-1-yl)malonate (1.18)

IR (neat): 2978 (m), 2933 (w), 1732 (s), 1621 (w), 1488 (w), 1372 (m), 1305 (w), 1256 (m), 1224 (w), 1145 (s), 862 (w), 700 (w) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.35 – 7.25 (m, 4H), 7.20 (dd, *J* = 14.6, 7.3 Hz, 1H), 7.12 (d, *J* = 7.2 Hz, 2H), 6.97 (d, *J* = 8.4 Hz, 2H), 6.17 (t, *J* = 6.7 Hz, 1H), 6.02 – 5.90 (m, 1H), 5.81 (dd, *J* = 15.4, 7.9 Hz, 1H), 5.63 (dd, *J* = 15.5, 8.7 Hz, 1H), 4.92 (dd, *J* = 13.0, 11.8 Hz, 2H), 4.21 – 4.07 (m, 4H), 3.95 (d, *J* = 8.7 Hz, 1H), 3.87 (dd, *J* = 10.9, 8.0 Hz, 1H), 3.43 (dd, *J* = 10.9, 8.4 Hz, 1H), 2.59 – 2.47 (m, 1H), 2.45 – 2.29 (m, 2H), 2.25 – 2.10 (m, 1H), 1.30 – 1.15 (m, 18H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 168.2, 168.1, 145.8, 142.1, 141.9, 140.0, 138.9, 131.1, 130.1, 128.4, 128.2, 125.9, 122.7, 119.8, 115.0, 83.0, 61.6, 61.5, 55.5, 50.5, 49.7, 35.0, 30.9, 24.9, 24.6, 14.0, 13.9; **HRMS (DART+):** Calcd $C_{35}H_{45}BBrO_6$ for $[M+H]^+$: 651.2414. Found: 651.2473. **Specific rotation:** $[\alpha]_D^{20.0}$ –11.0 (*c* 0.31, $CHCl_3$) for an enantiomerically

enriched sample of 95:5 e.r.; Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material after oxidation of the alkenylboron product with 3.0 equiv sodium perborate tetrahydrate in thf/H_2O (1:1). (95:5 e.r. shown; Chiralcel OD-H column, 99.5:0.5 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	58.459	11095275	65117	50.786	57.260	50.786
2	69.806	10751798	48604	49.214	42.740	49.214
Total		21847073	113721		100.000	100.000

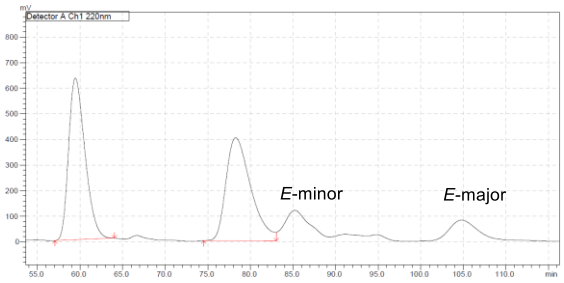
Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	59.274	30706720	165742	94.922	97.425	94.922
2	68.165	1642594	4381	5.078	2.575	5.078
Total		32349315	170122		100.000	100.000

Retention Time	Area	Area%	Retention Time	Area	Area%
58.459	11095275	50.786	59.274	30706720	94.922
69.806	10751798	49.214	68.166	1642594	5.078

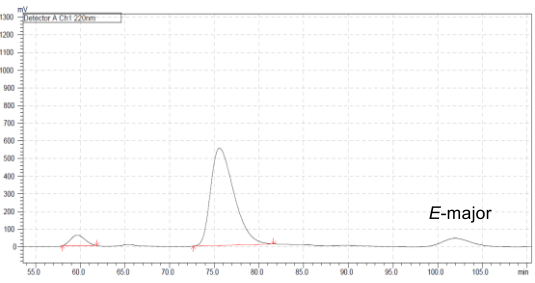
Diethyl 2-((1*E*, 3*S*, 4*S*, 5*Z*)-8-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-(4-(trifluoromethyl)phenyl)-4-vinylocta-1,5-dien-1-yl)malonate (1.19)

IR (neat): 2979 (w), 2929 (w), 1734 (s), 1619 (w), 1371 (w), 1325 (s), 1144 (m), 1123 (s), 1067 (m), 700 (w) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.45 (d, *J* = 8.0 Hz, 2H), 7.28 (t, *J* = 7.4 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 3H), 7.11 (d, *J* = 7.0 Hz, 2H), 6.16 (t, *J* = 6.5 Hz, 1H), 5.98 (ddd, *J* = 17.1, 10.2, 8.1 Hz, 1H), 5.83 (dd, *J* = 15.4, 8.0 Hz, 1H), 5.66 (dd, *J* = 15.5, 8.7 Hz, 1H), 4.95 (dt, *J* = 17.0, 8.4 Hz, 2H), 4.21 – 4.10 (m, 4H), 4.00 – 3.95 (m, 2H), 3.48 (dd, *J* = 10.8, 8.4 Hz, 1H), 2.56 – 2.46 (m, 1H), 2.42 – 2.30 (m, 2H), 2.26 – 2.12 (m, 1H), 1.35 – 1.10 (m, 18H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 168.3, 168.2, 147.5, 146.2, 142.0, 140.0, 138.8, 128.8, 128.7 ($J_{C\text{-}F}$ = 199.8 Hz), 128.5, 128.3, 126.0, 125.2, 125.1, 123.2, 115.3, 83.3, 61.8, 61.7, 55.6, 51.1, 49.8, 35.1, 31.1, 25.1, 24.7, 14.2, 14.1; **^{19}F NMR (376 MHz, $CDCl_3$)** δ –62.3 (s, 3F); **HRMS (DART+):** Calcd for $C_{36}H_{45}BO_6F_3$ $[M+H]^+$: 641.3261. Found: 641.3249; **Specific rotation:** $[\alpha]_D^{20.0}$ –19.6 (*c* 0.46, $CHCl_3$) for an

enantiomerically enriched sample of 94:6 e.r.; Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (94:6 e.r. shown; Chiralcel OZ-H column, 99.9:0.1 hexanes:*i*-PrOH, 0.3 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	59.445	84497683	631457	50.872	61.076	50.872
2	78.270	81602077	402428	49.128	38.924	49.128
Total		166099760	1033885		100.000	100.000



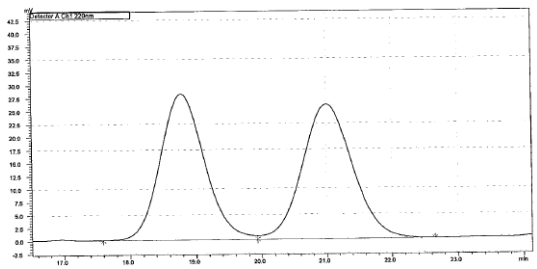
Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	59.672	6716652	59623	6.290	9.764	6.290
2	75.585	100070168	551028	93.710	90.236	93.710
Total		106786820	610650		100.000	100.000

Retention Time	Area	Area%	Retention Time	Area	Area%
59.445	84497683	50.872	59.672	6716652	6.290
78.270	81602077	49.128	75.585	100070168	93.710

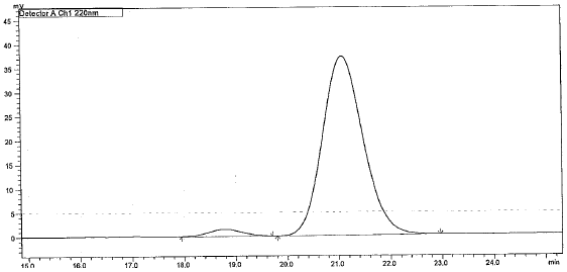
Diethyl 2-((1*E*, 3*S*, 4*S*, 5*Z*)-3-(furan-2-yl)-8-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-vinylocta-1,5-dien-1-yl)malonate (1.20)

IR (neat): 2978 (m), 2930 (w), 1733 (s), 1621 (w), 1370 (m), 1304 (m), 1145 (s), 1031 (m), 700 (w) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.28 (t, *J* = 7.6 Hz, 2H), 7.26 – 7.25 (m, 1H), 7.20 – 7.13 (m, 3H), 6.87 – 6.85 (m, 2H), 6.21 (t, *J* = 6.9 Hz, 1H), 5.97 (ddd, *J* = 17.4, 10.2, 8.2 Hz, 1H), 5.82 (dd, *J* = 15.5, 8.2 Hz, 1H), 5.67 (dd, *J* = 15.5, 8.2 Hz, 1H), 4.93 – 4.88 (m, 2H), 4.19 – 4.14 (m, 4H), 4.06 (dd, *J* = 10.8, 8.2 Hz, 1H), 3.98 (d, *J* = 8.8 Hz, 1H), 3.40 (dd, *J* = 10.8, 8.5 Hz, 1H), 2.55 (ddd, *J* = 13.5, 10.8, 5.6 Hz, 1H), 2.43 (ddd, *J* = 13.5, 10.8, 5.6 Hz, 1H), 2.34 – 2.31 (m, 1H), 2.26 – 2.23 (m, 1H), 1.28 – 1.22 (m, 18H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 168.4, 168.4, 145.6, 143.5, 142.2, 140.4, 139.0, 128.5, 128.4, 127.4, 125.9, 124.9, 122.3, 121.0, 114.8, 83.1, 61.7, 61.6, 55.7, 50.1, 46.6, 35.3, 31.0, 25.1, 24.7, 14.2, 14.1; **HRMS (DART+):** Calcd for $C_{33}H_{44}BO_7$ $[M+H]^+$: 563.3180. Found: 563.3193; **Specific rotation:** $[\alpha]_D^{20.0}$ –18.2 (*c* 1.78, $CHCl_3$) for an enantiomerically enriched sample of 97:3 e.r.; Enantiomeric purity was determined by HPLC analysis in

comparison with authentic racemic material (97:3 e.r. shown; Chiralcel OZ-H column, 99.9:0.1 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	18.782	1313145	28086	48.642	52.058	48.642
2	21.006	1386450	25866	51.358	47.942	51.358
Total		2699595	53952		100.000	100.000



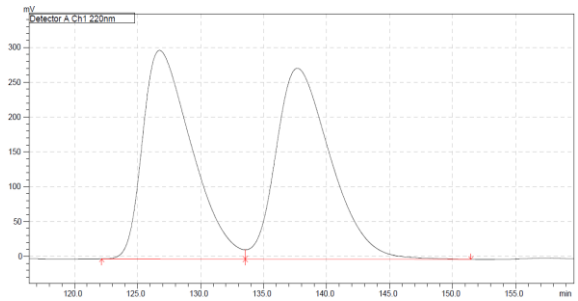
Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	18.763	66743	1441	3.184	3.734	3.184
2	21.072	2029591	37158	96.816	96.266	96.816
Total		2096334	38599		100.000	100.000

Retention Time	Area	Area%	Retention Time	Area	Area%
18.782	1313145	48.642	18.763	66743	3.184
21.006	1386450	51.358	21.072	2029591	96.816

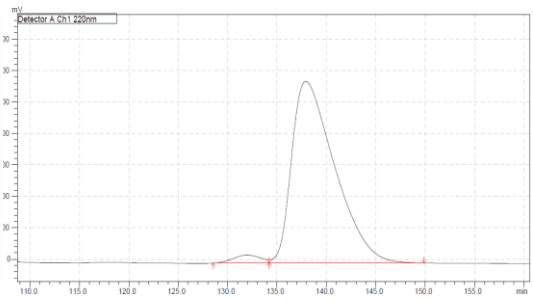
Diethyl 2-((1*E*, 3*S*, 4*S*, 5*Z*)- 8-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-(thiophen-2-yl)-4-vinylocta-1,5-dien-1-yl)malonate (1.21)

IR (neat): 2979 (w), 2932 (w), 1733 (s), 1620 (w), 1371 (w), 1304 (w), 1145 (s), 1027 (m), 700 (w) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.28 – 7.23 (m, 3H), 7.21 – 7.09 (m, 4H), 6.25 (t, *J* = 6.9 Hz, 1H), 6.17 – 6.15 (m, 1H), 5.93 (ddd, *J* = 17.1, 10.2, 8.4 Hz, 1H), 5.76 (dd, *J* = 15.5, 7.5 Hz, 1H), 5.65 (dd, *J* = 15.5, 8.5 Hz, 1H), 4.89 (dt, *J* = 17.1, 7.2 Hz, 2H), 4.19 – 4.13 (m, 4H), 3.96 (d, *J* = 8.5 Hz, 1H), 3.84 (dd, *J* = 10.9, 7.5 Hz, 1H), 3.27 (dd, *J* = 10.7, 8.5 Hz, 1H), 2.62 – 2.46 (m, 2H), 2.41 – 2.24 (m, 2H), 1.26 – 1.18 (m, 18H); **^{13}C NMR (101 MHz, $CDCl_3$):** δ 168.5, 168.4, 145.6, 142.6, 142.2, 140.4, 139.5, 138.8, 128.5, 128.4, 126.2, 126.0, 122.3, 114.9, 110.1, 83.1, 61.7, 61.6, 55.7, 49.8, 41.56, 35.3, 31.0, 25.0, 24.8, 14.2, 14.1; **HRMS (DART):** Calcd for $C_{33}H_{44}BO_6S$ $[M+H]^+$: 579.2952. Found: 579.2946; **Specific rotation:** $[\alpha]_D^{20.0}$ –9.2 (*c* 0.68, $CHCl_3$) for an enantiomerically enriched sample of 97:3 e.r.; Enantiomeric purity was determined by HPLC analysis in

comparison with authentic racemic material (97:3 e.r. shown; Chiralcel OZ-H column, 99.9:0.1 hexanes:*i*-PrOH, 0.3 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	126.743	80787439	299466	49.426	52.211	49.426
2	137.684	82663414	274102	50.574	47.789	50.574
Total		163450854	573568		100.000	100.000



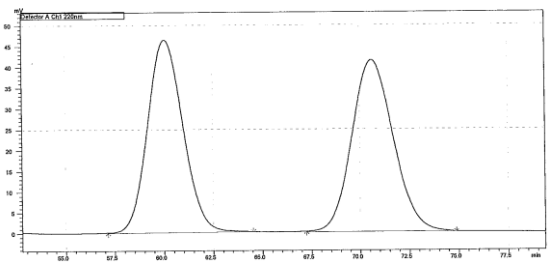
Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	131.974	4968002	25579	2.759	4.235	2.759
2	137.915	175068149	578437	97.241	95.765	97.241
Total		180036151	604016		100.000	100.000

Retention Time	Area	Area%	Retention Time	Area	Area%
126.743	80787439	49.426	131.974	4968002	2.759
137.684	82663414	50.574	137.915	175068149	97.241

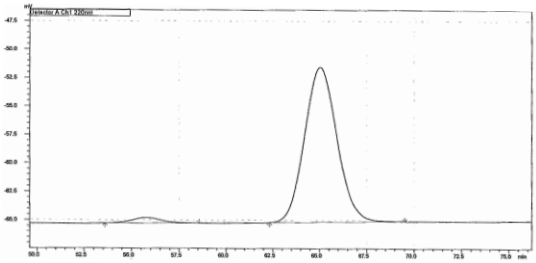
Diethyl 2-((1*E*, 3*S*, 4*S*, 5*Z*)-3-methyl-8-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-vinylocta-1,5-dien-1-yl)malonate (1.22)

IR (neat): 2979 (w), 2932 (w), 1735 (s), 1480 (m), 1301 (w), 1247 (s), 1144 (s), 700 (s) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.30 – 7.22 (m, 2H), 7.20 – 7.13 (m, 3H), 6.42 (t, *J* = 7.0 Hz, 1H), 6.00 – 5.85 (m, 1H), 5.64 (dd, *J* = 15.8, 8.4 Hz, 1H), 5.54 (dd, *J* = 15.6, 7.6 Hz, 1H), 4.90 – 4.75 (m, 2H), 4.21 – 4.11 (m, 4H), 3.94 (d, *J* = 8.3 Hz, 1H), 2.87 – 2.82 (m, 1H), 2.71 – 2.57 (m, 3H), 2.51 – 2.38 (m, 2H), 1.26 – 1.19 (m, 18H), 0.82 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR (101 MHz, $CDCl_3$):** δ 168.7, 168.7, 145.4, 142.2, 142.1, 141.2, 128.5, 128.4, 126.0, 120.6, 114.1, 83.1, 61.6, 55.8, 50.9, 39.1, 35.5, 31.0, 24.9, 24.8, 18.6, 14.2; **HRMS (DART+):** Calcd for $C_{30}H_{44}BO_6$ $[M+H]^+$: 511.3145. Found: 511.3151; **Specific rotation:** $[\alpha]_D^{20.0}$ +30.4 (*c* 1.0, $CHCl_3$) for an enantiomerically enriched sample of 97:3 e.r.; Enantiomeric purity was determined by HPLC analysis in comparison with authentic

racemic material (97:3 e.r. shown; Chiralcel OZ-H column, 99.9:0.1 hexanes:*i*-PrOH, 0.3 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	60.066	5805547	46339	48.881	52.884	48.881
2	70.625	6071260	41285	51.119	47.116	51.119
Total		11876807	87625		100.000	100.000



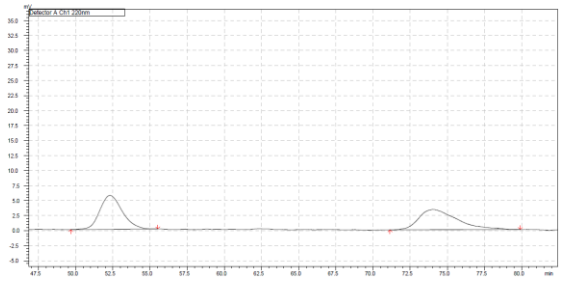
Peak#	Ret. Time	Area	Height	Conc.	Unit	Height%	Area%
1	55.699	50098	481	2.973		3.410	2.973
2	65.042	1634772	13628	97.027		96.590	97.027
Total		1684871	14109			100.000	100.000

Retention Time	Area	Area%	Retention Time	Area	Area%
60.066	5805547	48.881	55.699	50098	2.973
70.625	6071260	51.119	65.042	1634772	97.027

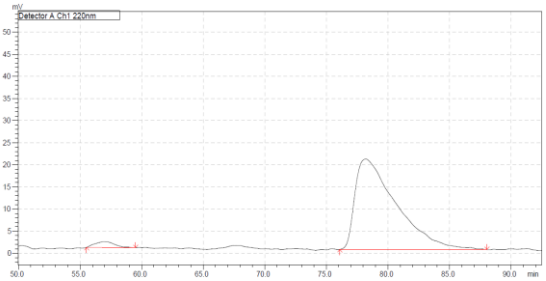
Diethyl 2-((1*E*, 3*S*, 4*S*, 5*Z*)-3-phenethyl-8-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-vinylocta-1,5-dien-1-yl)malonate (1.23)

IR (neat): 2979 (m), 2932 (m), 1749 (w), 1730 (m), 1497 (w), 1453 (w), 1304 (w), 1143 (s), 748 (m), 698 (m) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.25 – 7.07 (m, 10H), 6.42 (t, *J* = 7.0 Hz, 1H), 5.89 – 5.83 (m, 1H), 5.70 (dd, *J* = 15.4, 8.9 Hz, 1H), 5.37 (dd, *J* = 15.4, 9.5 Hz, 1H), 4.90 – 4.73 (m, 2H), 4.21 – 4.12 (m, 4H), 4.02 (d, *J* = 8.9 Hz, 1H), 2.95 (t, *J* = 9.3 Hz, 1H), 2.67 – 2.49 (m, 4H), 2.48 – 2.30 (m, 3H), 1.72 – 1.64 (m, *J* = 14.0, 7.0, 3.5 Hz, 1H), 1.35 – 1.16 (m, 19H); **^{13}C NMR (101 MHz, $CDCl_3$):** δ 168.7, 168.6, 145.8, 142.9, 142.1, 141.1, 140.3, 128.6, 128.5, 128.4, 128.4, 126.0, 125.6, 123.2, 113.8, 83.1, 61.7, 61.6, 55.9, 49.5, 45.1, 35.4, 34.7, 33.7, 31.1, 24.9, 24.8, 14.3, 14.2; **HRMS (DART+):** Calcd for $C_{37}H_{50}BO_6$ $[M+H]^+$: 601.3700. Found: 601.3698; **Specific rotation:** $[\alpha]_D^{20.0}$ +25.8 (*c* 1.1, $CHCl_3$) for an enantiomerically enriched sample of 97:3 e.r.; Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material after oxidation of the alkenylboron product with 3.0 equiv. sodium perborate tetrahydrate in

thf/H_2O (1:1). (97:3 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	Conc.	Unit	Height%	Area%
1	52.309	589523	5637	49.534		62.449	49.534
2	74.022	600609	3390	50.466		37.551	50.466
Total		1190131	9026			100.000	100.000



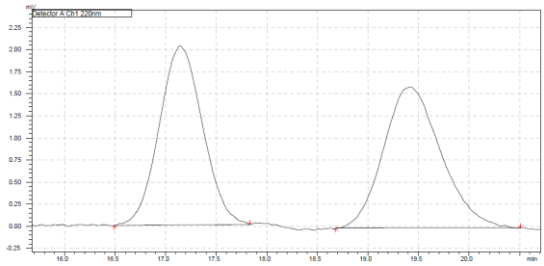
Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	56.965	145027	1287	2.953	5.920	2.953
2	78.212	4765574	20444	97.047	94.080	97.047
Total		4910602	21731		100.000	100.000

Retention Time	Area	Area%	Retention Time	Area	Area%
52.309	589523	49.534	56.965	145027	2.953
74.022	600609	50.466	78.212	4765574	97.047

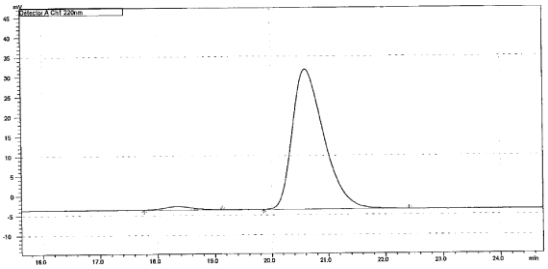
Diethyl 2-((1*E*, 3*S*, 4*S*, 5*Z*)-3-cyclohexyl-8-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-vinylocta-1,5-dien-1-yl)malonate (1.24)

IR (neat): 2979 (w), 2932 (s), 1732 (w), 1610 (m), 1475 (w), 1301 (s), 1201 (w), 1144 (s), 1033 (m), 700 (s) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.31 – 7.15 (m, 5H), 6.42 (t, *J* = 7.0 Hz, 1H), 5.85 – 5.73 (m, 1H), 5.60 (dd, *J* = 15.4, 8.7 Hz, 1H), 5.43 – 5.35 (m, 1H), 4.81 – 4.72 (m, 2H), 4.21 – 4.10 (m, 4H), 3.98 (d, *J* = 8.7 Hz, 1H), 3.18 (dd, *J* = 10.4, 8.6 Hz, 1H), 2.72 – 2.61 (m, 2H), 2.52 – 2.42 (m, 3H), 1.70 – 0.74 (m, 27H); **^{13}C NMR (101 MHz, $CDCl_3$):** δ 168.7, 168.6, 145.5, 142.2, 141.5, 139.3, 137.9, 128.5, 128.4, 126.0, 123.3, 113.3, 83.1, 61.6, 55.9, 50.3, 46.2, 39.7, 35.6, 32.7, 31.2, 26.9, 26.9, 26.8, 26.8, 26.1, 25.0, 24.6, 14.2; **HRMS (DART+):** Calcd for $C_{35}H_{52}BO_6$ $[M+H]^+$: 579.3857. Found: 579.3886; **Specific rotation:** $[\alpha]_D^{20.0}$ +8.2 (*c* 0.37, $CHCl_3$) for an enantiomerically enriched sample of 98:2 e.r.; Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material after oxidation of the alkenylboron product with 3.0 equiv.

sodium perborate tetrahydrate in thf/H_2O (1:1). (98:2 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	Conc.	Height%	Area%
1	17.142	60611	2023	49.044	55.899	49.044
2	19.421	62974	1596	50.956	44.101	50.956
Total		123586	3620		100.000	100.000



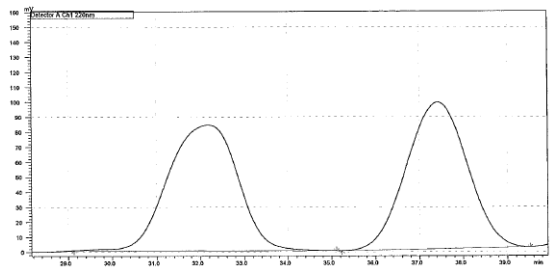
Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	18.372	28430	902	2.030	2.488	2.030
2	20.606	1372353	35353	97.970	97.512	97.970
Total		1400783	36255		100.000	100.000

Retention Time	Area	Area%	Retention Time	Area	Area%
17.142	60611	49.044	18.372	28430	2.030
19.421	62974	50.956	20.606	1372353	97.970

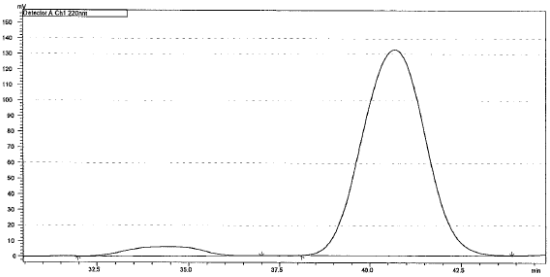
Diethyl 2-((1*E*, 3*S*, 4*S*, 5*Z*)-10-((tert-butyldimethylsilyl)oxy)-3-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-vinyldeca-1,5-dien-1-yl)malonate (1.25)

IR (neat): 2930 (m), 2857 (m), 1735 (s), 1465 (w), 1370 (w), 1253 (w), 1144 (s), 1098 (s), 835 (s), 700 (m) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.19 – 7.16 (m, 2H), 7.10 – 7.07 (m, 3H), 6.05 (t, *J* = 7.0 Hz, 1H), 6.03 – 5.96 (m, 1H), 5.86 (dd, *J* = 15.4, 8.3 Hz, 1H), 5.66 (dd, *J* = 15.4, 8.3 Hz, 1H), 4.94 – 4.90 (m, 2H), 4.22 – 4.11 (m, 4H), 3.97 (d, *J* = 8.8 Hz, 1H), 3.88 (dd, *J* = 10.8, 8.5 Hz, 1H), 3.54 (t, *J* = 6.5 Hz, 2H), 3.46 (dd, *J* = 10.8, 8.5 Hz, 1H), 2.05 (dq, *J* = 8.5, 6.8 Hz, 1H), 1.87 (dq, *J* = 8.5, 6.8 Hz, 1H), 1.44–1.38 (m, 2H), 1.27–1.18 (m, 20H), 0.89 (s, 9H), 0.04 (s, 6H); **^{13}C NMR (101 MHz, $CDCl_3$):** δ 168.5, 168.4, 146.8, 143.2, 140.8, 139.8, 128.5, 128.1, 126.1, 122.2, 114.6, 83.0, 63.2, 61.6, 61.5, 55.8, 51.3, 49.8, 32.9, 26.1, 25.1, 24.7, 18.5, 14.2, 14.1, 13.0, –5.1; **HRMS (DART+):** Calcd for $C_{37}H_{60}BO_7Si$ $[M+H]^+$: 655.4201. Found: 655.4180. **Specific rotation:** $[\alpha]_D^{20.0}$ –4.7 (*c* 1.54, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.; Enantiomeric purity was

determined by HPLC analysis in comparison with authentic racemic material (95:5 e.r. shown; Chiralcel OZ-H column, 99.9:0.1 hexanes:*i*-PrOH, 0.3 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Height%	Area%
1	32.185	9276442	83939	46.190	49.566
2	37.424	9438799	97786	53.810	50.434
Total		18715241	181725	100.000	100.000



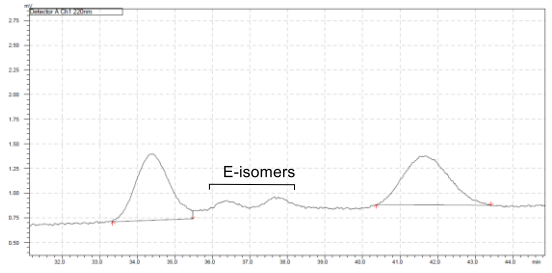
Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	34.510	819876	5907	4.919	4.283	4.919
2	40.696	15847718	132005	95.081	95.717	95.081
Total		16667594	137912		100.000	100.000

Retention Time	Area	Area%	Retention Time	Area	Area%
32.185	9276442	49.566	34.510	819876	4.919
37.424	9438799	50.434	40.696	15847718	95.081

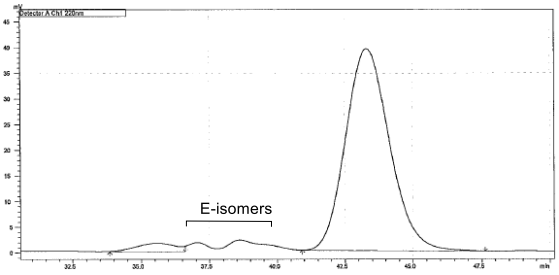
Diethyl 2-((1*E*, 3*S*, 4*S*, 5*Z*)-9-((tert-butyldimethylsilyl)oxy)-3-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-vinylnona-1,5-dien-1-yl)malonate (1.26)

IR (neat): 2954 (m), 2930 (m), 2857 (m), 1737 (s), 1254 (m), 1102 (s), 836 (s), 776 (s) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.19 – 7.16 (m, 2H), 7.10 – 7.07 (m, 3H), 6.06 (t, *J* = 7.1 Hz, 1H), 6.02 – 5.96 (m, 1H), 5.85 (dd, *J* = 15.4, 8.3 Hz, 1H), 5.66 (dd, *J* = 15.4, 8.8 Hz, 1H), 4.95 – 4.91 (m, 22H), 4.22 – 4.11 (m, 4H), 3.96 (d, *J* = 8.8 Hz, 1H), 3.87 (dd, *J* = 11.0, 8.4 Hz, 1H), 3.51 (t, *J* = 6.3 Hz, 2H), 3.48 – 3.42 (m, 1H), 2.15 – 2.07 (m, 1H), 1.97 – 1.87 (m, 1H), 1.48 – 1.30 (m, 2H), 1.30 – 1.18 (m, 18H), 0.90 (s, 9H), 0.04 (s, 6H);**^{13}C NMR (101 MHz, $CDCl_3$):** δ 168.5, 168.4, 146.4, 143.2, 140.7, 139.9, 128.5, 128.1, 126.2, 122.2, 114.6, 83.0, 63.0, 61.7, 61.6, 55.8, 51.4, 49.7, 32.2, 26.1, 25.1, 24.7, 18.5, 14.2, 14.1, –5.1; **HRMS (DART+):** Calcd for $C_{36}H_{58}BO_7Si$ $[M+H]^+$: 641.4045. Found: 641.4033. **Specific rotation:** $[\alpha]_D^{20.0}$ –5.6 (*c* 1.0, $CHCl_3$) for an enantiomerically enriched sample of 96:4 e.r.; Enantiomeric purity 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, 0.3 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Conc.	Unit	Height%	Area%
1	34.401	43238	678	50.399		57.597	50.399
2	41.670	42553	499	49.601		42.403	49.601
Total		85791	1178			100.000	100.000



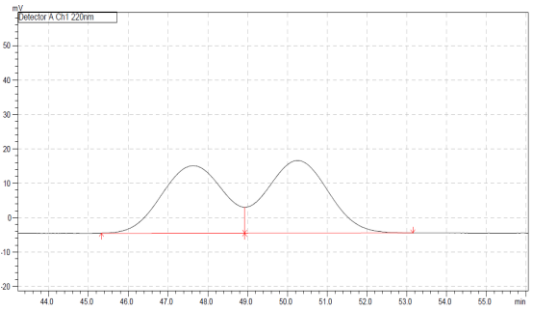
Peak#	Ret. Time	Area	Height	Conc.	Unit	Height%	Area%
1	35.558	169444	1627	3.691		3.975	3.691
2	43.320	4421783	39313	96.309		96.025	96.309
Total		4591227	40940			100.000	100.000

Retention Time	Area	Area%	Retention Time	Area	Area%
34.401	43238	50.399	35.558	169444	3.691
41.670	42553	49.601	43.320	4421783	96.309

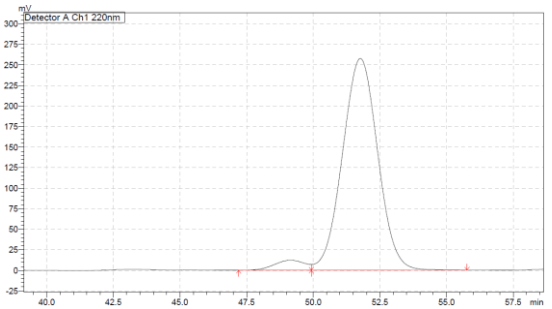
Diethyl 2-((1*E*, 3*S*, 4*S*, 5*Z*)-3,9-dimethyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-vinyldeca-1,5-dien-1-yl)malonate (1.27)

IR (neat): 2976 (w), 2957 (w), 2928 (w), 1736 (s), 1347 (m), 1303 (w), 1143 (s), 1035 (w), 862 (w) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 6.34 (t, *J* = 7.1 Hz, 1H), 5.94 (ddd, *J* = 17.1, 10.3, 8.4 Hz, 1H), 5.66 (dd, *J* = 15.5, 8.4 Hz, 1H), 5.59 (dd, *J* = 15.5, 7.6 Hz, 1H), 4.86 – 4.74 (m, 2H), 4.21 – 4.14 (m, 4H), 3.97 (d, *J* = 8.5 Hz, 1H), 2.88 – 2.83 (m, 1H), 2.67 – 2.61 (m, 1H), 2.17 – 2.07 (m, 2H), 1.58 – 1.52 (m, 1H), 1.29 – 1.19 (m, 21H), 0.90 – 0.83 (m, 8H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 168.8, 168.7, 147.0, 142.2, 141.5, 120.5, 113.9, 83.1, 61.6, 61.5, 55.9, 50.8, 39.1, 38.3, 27.9, 26.7, 24.9, 24.8, 22.7, 222.6, 18.7, 14.2; **HRMS (DART+):** Calcd for $C_{27}H_{46}BO_6$ $[M+H]^+$: 477.3387. Found: 477.3393. **Specific rotation:** $[\alpha]_D^{20.0}$ +22.3 (*c* 1.15, $CHCl_3$) for an enantiomerically enriched sample of 96:4 e.r.; Enantiomeric purity 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, 0.3 mL/min, 220 nm).



Peak#	Ret. Time	Area	Conc.	Height	Height%	Area%
1	47.624	2132852	48.212	19595	48.194	48.212
2	50.255	2291088	51.788	21063	51.806	51.788
Total		4423940		40657	100.000	100.000



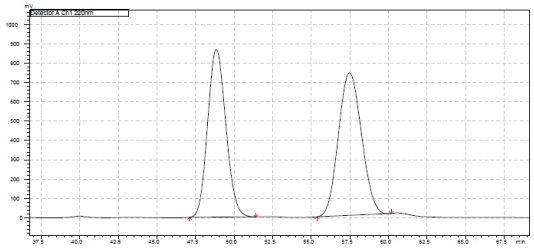
Peak#	Ret. Time	Area	Height	Conc.	Unit	Height%	Area%
1	49.144	973270	12159	3.942		4.509	3.942
2	51.765	23717134	257521	96.058		95.491	96.058
Total		24690404	269681			100.000	100.000

Retention Time	Area	Area%	Retention Time	Area	Area%
47.624	2132852	48.212	49.144	973270	3.942
50.255	2291088	51.788	51.765	23717134	96.058

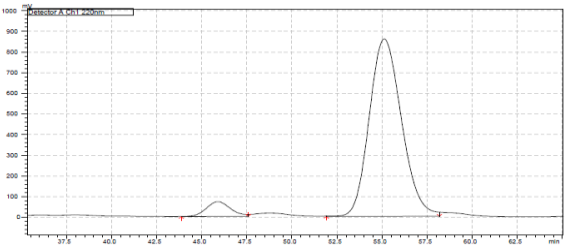
Diethyl 2-((1*E*, 3*S*, 4*S*, 5*Z*)-6-cyclohexyl-3-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-vinylhexa-1,5-dien-1-yl)malonate (1.28)

IR (neat): 2953 (w), 2927 (w), 2868 (w), 1730 (s), 1650 (w), 1351 (m), 1315 (s), 1283 (w), 1195 (s), 1150 (s), 999 (m), 921 (s), 897 (s), 824 (s) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.18 (t, *J* = 7.5 Hz, 2H), 7.10 (d, *J* = 7.5 Hz, 2H), 7.08 (t, *J* = 7.5 Hz, 1H), 6.08 – 6.02 (m, 1H), 5.90 (dd, *J* = 15.3, 8.8 Hz, 1H), 5.83 (d, *J* = 9.8 Hz, 1H), 5.68 (dd, *J* = 15.3, 8.8 Hz, 1H), 4.93 – 4.90 (m, 2H), 4.21 – 4.13 (m, 4H), 3.98 (d, *J* = 8.8 Hz, 1H), 3.86 (dd, *J* = 10.6, 8.8 Hz, 1H), 3.47 (dd, *J* = 10.6, 8.8 Hz, 1H), 2.21 – 2.16 (m, 1H), 1.66 (d, *J* = 13.0 Hz, 1H), 1.60 (t, *J* = 11.6 Hz, 1H), 1.47 (d, *J* = 13.0 Hz, 1H), 1.28 – 1.24 (m, 10H), 1.20 (d, *J* = 6.9 Hz, 9H), 1.17 – 1.04 (m, 3H), 0.95 (ddd, *J* = 19.4, 14.6, 5.5 Hz, 2H), 0.78 (ddd, *J* = 15.8, 12.7, 3.3 Hz, 1H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 168.5, 168.4, 151.9, 143.3, 141.4, 139.9, 128.6, 128.1, 126.1, 122.2, 114.6, 83.0, 61.7, 61.6, 55.8, 51.4, 50.2, 37.9, 32.2, 32.1, 26.2, 26.1, 25.8, 25.1, 24.7, 14.2, 14.1; **HRMS (DART+):** Calcd for $C_{33}H_{48}BO_6$ $[M+H]^+$: 551.3525. Found: 551.3539; **Specific rotation:** $[\alpha]_D^{20.0}$ –2.43 (*c* 0.7, $CHCl_3$) for

an enantiomerically enriched sample of 94:6 e.r.; Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (94:6 e.r. shown; Chiralcel OZ-H column, 99.9:0.1 hexanes:*i*-PrOH, 0.3 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	48.848	70962321	866667	48.116	54.054	48.116
2	57.471	76518372	736676	51.884	45.946	51.884
Total		147480694	1603343		100.000	100.000

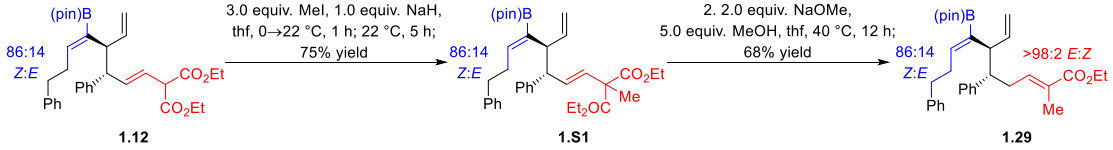


Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	45.888	6648907	71277	5.866	7.669	5.866
2	55.114	106703798	858079	94.134	92.331	94.134
Total		113352705	929355		100.000	100.000

Retention Time	Area	Area%	Retention Time	Area	Area%
48.848	70962321	48.116	45.888	6648907	5.866
57.471	76518372	51.884	55.114	106703798	94.134

1.8.4 Conversion of *β,γ*-Unsaturated Diester to a Trisubstituted Enoate

Scheme S1



1.12 **1.S1** **1.29**

To a solution of compound **1.12** (50.0 mg, 0.087 mmol) in thf (2.0 mL) was added NaH (5.2 mg, 0.131 mmol) at 0 °C. After the mixture was allowed to stir for 1 h (22 °C), it was charged with MeI (37 mg, 0.262 mmol). After 5 h, the reaction was quenched by the addition of a saturated solution of aqueous NH_4Cl (15 mL). The water layer was washed with Et_2O (3 × 20 mL), and the combined organic layers were dried over $MgSO_4$ and the volatiles were removed in vacuo. The resulting yellow oil was purified by silica gel chromatography (10:1 hexanes:Et_2O), affording **S9** as colorless oil (38.4 mg, 0.066 mmol, 75% yield).

Diethyl 2-((1*E*, 3*S*, 4*S*, 5*Z*)-3,8-diphenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-vinylocta-1,5-dien-1-yl)-2-methylmalonate (1.S1)

IR (neat): 3027 (w), 2978 (m), 2927 (m), 2852 (w), 1731 (s), 1602 (w), 1453 (m), 1372 (s), 1260 (s), 1144 (m), 1106 (s), 1023 (m), 863 (w), 700 (s) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.29 – 7.22 (m, 2H), 7.21 – 7.13 (m, 3H), 7.13 – 7.05 (m, *J* = 8.0 Hz, 5H), 6.11 (t, *J* = 6.6 Hz, 1H), 6.03 – 5.93 (m, 1H), 5.89 (d, *J* = 16.4 Hz, 1H), 5.73 (dd, *J* = 15.9, 8.1 Hz, 1H), 4.88 (dd, *J* = 12.7, 10.8 Hz, 2H), 4.18 – 4.06 (m, 4H), 3.85 (dd, *J* = 10.5, 8.6 Hz, 1H), 3.50 – 3.39 (m, 1H), 2.52 – 2.38 (m, 1H), 2.34 – 2.25 (m, 2H), 2.24 – 2.12 (m, 1H), 1.48 (s, 3H), 1.25 (s, 6H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.19 (s, 6H), 1.15 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR (101 MHz, $CDCl_3$):** δ 171.5, 145.6, 143.5, 142.3, 140.8, 135.3, 128.8, 128.5, 128.4, 128.1, 126.1, 125.9, 114.6, 83.1, 61.5, 61.4, 55.5, 51.2, 50.3, 35.2, 31.1, 25.1, 24.7, 20.8, 14.1, 14.0; **HRMS (DART+):** Calcd for $C_{36}H_{48}O_6B$ $[M+H]^+$: 587.3537. Found: 587.3544; **Specific rotation:** $[\alpha]_D^{20.0}$ –23.6 (*c* 1.0, $CHCl_3$).

Methyl (2*E*, 5*S*, 6*S*, 7*Z*)-2-methyl-5,10-diphenyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6-vinyldeca-2,7-dienoate (1.29)

To a solution of compound **1.S1** (20.0 mg, 0.034 mmol) in thf (1.0 mL) was added NaOMe (3.7 mg, 0.068 mmol) and MeOH (5.5 mg, 0.17 mmol), and the resulting mixture was allowed to stir for 15 h at 40 °C. The reaction was then quenched by the addition of a saturated solution of aqueous NH_4Cl (15 mL). The aqueous layer was washed with Et_2O (3 × 20 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated under vacuum, affording yellow oil residue, which was purified by silica gel chromatography (10:1 hexanes: Et_2O) to afford **1.29** as colorless oil (11.6 mg, 0.023 mmol, 68% yield). **IR (neat):** 2953 (m), 2925 (w), 2868 (w), 1622 (m), 1454 (m), 1378 (m), 1301 (m), 1145 (s), 864 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.29 (t, *J* = 7.5 Hz, 2H), 7.23 – 7.15 (m, 3H), 7.15 – 7.08 (m, 3H), 7.06 (d, *J* = 7.4 Hz, 2H), 6.58 (t, *J* = 7.2 Hz, 1H), 6.12

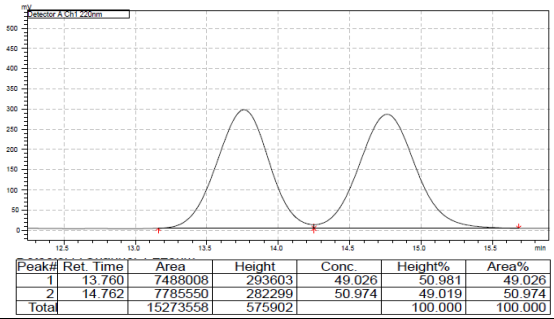
– 6.02 (m, 2H), 5.03 (dd, J = 22.9, 13.5 Hz, 2H), 3.64 (s, 3H), 3.39 (t, J = 10.0 Hz, 1H), 3.22 (dd, J = 10.9, 7.9 Hz, 1H), 2.71 (d, J = 15.3 Hz, 1H), 2.49 (t, J = 9.6 Hz, 1H), 2.36 – 2.28 (m, 3H), 2.25 – 2.15 (m, 1H), 1.66 (s, 3H), 1.27 (s, 6H), 1.21 (s, 6H); **^{13}C NMR (101 MHz, $CDCl_3$):** δ 168.8, 145.2, 143.5, 142.4, 141.5, 141.0, 128.5, 128.5, 128.4, 128.1, 127.9, 126.2, 125.9, 115.3, 102.9, 83.1, 51.9, 47.3, 35.2, 34.3, 31.1, 25.1, 24.8, 12.5; **HRMS (DART+):** Calcd for $C_{32}H_{42}O_4B$ $[M+H]^+$: 501.3186. Found: 501.3176. **Specific rotation:** $[\alpha]_D^{20.0}$ –49.3 (*c* 0.3, $CHCl_3$).

1.8.5 Application to Enantioselective Synthesis of Vitamin D_3

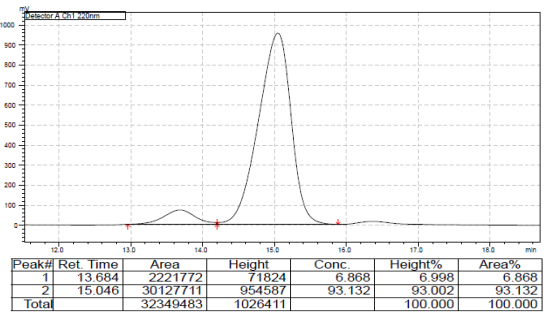
Diethyl 2-((1*E*, 3*S*, 4*S*, 5*Z*)-8-((*tert*-butyldimethylsilyl)oxy)-3-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-vinylocta-1,5-dien-1-yl)malonate (1.30)

IR (neat): 2978 (w), 2957 (w), 2930 (w), 2858 (w), 1733 (s), 1349 (m), 1255 (m), 1143 (s), 1094 (m), 835 (m), 736 (s) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 6.31 (t, J = 7.0 Hz, 1H), 5.98 – 5.87 (m, 1H), 5.65 (dd, J = 15.5, 8.5 Hz, 1H), 5.57 (dt, J = 15.4, 6.7 Hz, 1H), 4.95 – 4.74 (m, 2H), 4.22 – 4.12 (m, 4H), 3.95 (d, J = 8.6 Hz, 1H), 3.64 – 3.57 (m, 2H), 2.86 – 2.81 (m, 1H), 2.67 – 2.51 (m, 1H), 2.42 – 2.33 (m, 2H), 1.29 – 1.13 (m, 18H), 0.92 – 0.78 (m, 12H), 0.05 – 0.01 (m, 6H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 168.7, 168.6, 142.0, 141.9, 141.2, 120.6, 114.1, 83.1, 62.6, 61.6, 55.8, 50.9, 39.1, 32.7, 26.1, 24.9, 24.7, 18.7, 14.2, –5.1; **HRMS (DART+):** Calcd for $C_{30}H_{54}BO_7Si$ $[M+H]^+$: 565.3726; Found: 565.3707; **Specific rotation:** $[\alpha]_D^{20.0}$ –15.1 (*c* 1.10, $CHCl_3$) for an enantiomerically enriched sample of 93:7 e.r.; Enantiomeric purity was determined by HPLC analysis in

comparison with authentic racemic material (93:7 e.r. shown; Chiralcel OZ-H column, 99.9:0.1 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm).



Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	13.760	7488008	293603	49.026	50.981	49.026
2	14.762	7785550	282299	50.974	49.019	50.974
Total		15273558	575902		100.000	100.000



Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	13.684	2221772	71824	6.868	6.998	6.868
2	15.046	30127711	954587	93.132	93.002	93.132
Total		32349483	1026411		100.000	100.000

Retention Time	Area	Area%	Retention Time	Area	Area%
13.760	7488008	49.026	13.684	2221772	6.868
14.762	7785550	50.974	15.046	30127711	93.132

(3*S*, 4*S*, *Z*)-8-((*tert*-Butyldimethylsilyl)oxy)-3-methyl-5-(4,4,5,5-tetramethyl-1,3,2 dioxaborolan-2-yl)-4-vinyloct-5-enal (1.31)

To a solution of **1.30** (1.0 g, 1.77 mmol) in thf/H_2O (15/1.5 mL) was added dbu (539 µL, 3.55 mmol) at 22 °C, and the mixture was allowed to stir at 60 °C for 3 h. The volatiles were then removed in vacuo, and the resulting yellow oil was purified by a silica gel chromatography (20:1 hexanes:EtOAc) to afford **1.35** as yellow oil (481 mg, 1.14 mmol, 64% yield). **IR (neat):** 2976 (w), 2956 (w), 2930 (w), 2857 (w), 1728 (s), 1404 (s), 1371 (w), 1307 (w), 1255 (s), 1139 (s), 1096 (s), 836 (s), 706 (m) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 9.74 (s, 1H), 6.32 (t, *J* = 7.0 Hz, 1H), 5.94 (dt, *J* = 18.1, 9.4 Hz, 1H), 4.98 – 4.93 (m, 2H), 3.66 – 3.60 (m, 2H), 2.84 (t, *J* = 9.9 Hz, 1H), 2.65 (dd, *J* = 16.1, 3.4 Hz, 1H), 2.58 – 2.36 (m, 3H), 2.07 (ddd, *J* = 16.1, 9.4, 3.2 Hz, 1H), 1.24 (s, 12H), 0.88 (s, 9H), 0.81 (d, *J* = 6.7 Hz, 3H), 0.03 (s, 6H); **^{13}C NMR (101 MHz, $CDCl_3$):** δ 203.6, 142.3, 140.9, 115.4, 83.2, 62.5, 52.1, 49.8, 32.7, 30.6, 26.1, 24.9, 24.7, 18.7, –5.1; **HRMS (DART+):** Calcd for $C_{23}H_{44}BO_4Si$ $[M+H]^+$: 423.3096. Found: 423.3084. **Specific rotation:** $[\alpha]_D^{20.0}$ –9.4 (*c* 1.00, $CHCl_3$).

(*R*, 6*E*, 9*Z*)-14,14,15,15-Tetramethyl-8-((*S*, *E*)-6-methylhept-4-en-2-yl)-9-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,4,13-trioxa-14-silahexadeca-6,9-diene (1.S2)

To a solution of compound **1.31** (100.0 mg, 0.24 mmol) in toluene (3.0 mL) was added MOM-protected diol **1.32** (125.0 mg, 0.71 mmol) and the Ru-based complex (20.0 mg, 0.036 mmol) at 22 °C. The mixture was allowed to stir for 48 h at 60 °C, after which the volatiles were removed in vacuo, and the resulting brown residue was used directly in the next step without purification.

To a solution of Ph_3PCH_2Br (357.0 mg, 0.711 mmol) in thf (3 mL) was added KO*t*-Bu (189.0 mg, 0.474 mmol). After the mixture was allowed to stir for 30 min, the solution containing the above residue (in 2 mL thf) was added, and after 5 h the reaction was quenched by the addition of a saturated solution of aqueous 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. The resulting yellow oil was purified by silica gel chromatography (20:1 hexanes:EtOAc) to afford **1.S2** as yellow oil (69.4 mg, 0.13 mmol, 54% overall yield for 2 steps).

IR (neat): 2953 (m), 2926 (m), 2869 (w), 1623 (m), 1465 (w), 1378 (m), 1302 (m), 1146 (s), 863 (w), 837 (w) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 6.25 (t, *J* = 7.1 Hz, 1H), 5.91 (dd, *J* = 15.5, 9.3 Hz, 1H), 5.47 (dt, *J* = 15.3, 6.3 Hz, 1H), 5.24 – 5.17 (m, 2H), 4.63 – 4.59 (m, 2H), 4.01 (dd, *J* = 6.3, 1.1 Hz, 2H), 3.65 (t, *J* = 7.7 Hz, 2H), 3.35 (s, 3H), 2.86 (t, *J* = 9.6 Hz, 1H), 2.57 (dd, *J* = 14.8, 6.5 Hz, 1H), 2.41 (dd, *J* = 14.9, 7.2 Hz, 2H), 2.29 – 2.20 (m, 1H), 1.90 – 1.80 (m, 1H), 1.79 – 1.68 (m, 1H), 1.24 – 1.22 (m, *J* = 3.6 Hz, 12H), 0.93 (dd, *J* = 6.6, 1.2 Hz, 3H), 0.91 – 0.87 (m, 12H), 0.71 (d, *J* = 6.6 Hz, 3H), 0.09 – 0.03 (m, 6H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 141.0, 138.5, 137.8, 126.0, 125.9, 95.4, 83.1, 68.2,

62.7, 55.3, 50.2, 35.7, 32.8, 26.6, 26.2, 24.9, 24.8, 23.3, 23.2, 17.7, –5.1; **HRMS (DART+):** Calcd for $C_{30}H_{61}BNO_5Si$ $[M+NH_4]^+$: 554.4407. Found: 554.4395. **Specific rotation:** $[\alpha]_D^{20.0}$ +8.4 (*c* 0.4, $CHCl_3$).

(*S*, *Z*)-14,14,15,15-Tetramethyl-8-((*S*)-6-methylheptan-2-yl)-9-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,4,13-trioxa-14-silahexadec-9-ene (1.33)

Compound **1.S2** (69.0 mg, 0.13 mmol) and Pd/C (7.0 mg) were placed in MeOH (1.0 mL) under an atmosphere of H_2 (balloon), and the mixture was allowed to stir at 22 °C for 5 h. After which it was filtered through a short column of celite and washed with ethyl acetate. The filtrate was concentrated in vacuo and the resulting yellow oil was purified by silica gel chromatography (20:1 hexanes:EtOAc) to give **1.33** (53.1 mg, 0.098 mmol, 75% yield). **IR (neat):** 2954 (w), 2927 (w), 2857 (w), 1464 (w), 1372 (m), 1299 (w), 1258 (m), 1144 (m), 1101 (s), 1045 (m), 836 (m), 776 (w) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 6.32 (t, *J* = 7.0 Hz, 1H), 4.59 (s, 2H), 3.64 (t, *J* = 7.5 Hz, 2H), 3.46 (ddd, *J* = 8.3, 5.6, 2.4 Hz, 2H), 3.34 (s, 3H), 2.36 (dd, *J* = 14.8, 7.3 Hz, 1H), 2.24 – 2.11 (m, 1H), 1.65 – 1.40 (m, 5H), 1.40 – 1.29 (m, 3H), 1.25 – 1.18 (m, 13H), 1.18 – 1.09 (m, 3H), 1.03 – 0.97 (m, 1H), 0.89 (s, 9H), 0.87 (d, *J* = 2.2 Hz, 3H), 0.86 (d, *J* = 2.2 Hz, 3H), 0.73 (d, *J* = 6.7 Hz, 3H), 0.05 (s, 6H); **^{13}C NMR (101 MHz, $CDCl_3$):** δ 142.0, 96.4, 82.8, 68.4, 62.9, 55.2, 45.2, 39.7, 36.6, 35.1, 33.0, 28.6, 28.1, 28.0, 26.2, 24.8, 24.8, 23.0, 22.7, 18.6, 18.2, –5.1; **HRMS (DART+)**: Calcd for $C_{30}H_{65}BNO_5Si$ $[M+NH_4]^+$: 558.4720. Found: 558.4706. **Specific rotation:** $[\alpha]_D^{20.0}$ +11.2 (*c* 0.5, $CHCl_3$).

(5*R*, 6*R*, *E*)-5-(3-(Methoxymethoxy)propyl)-4,6,10-trimethylundec-3-en-1-ol (1.34)

A solution of alkenyl–B(pin) compound **1.33** (54.0 mg, 0.1 mmol) in thf (3.0 mL) was treated with MeLi (in Et_2O; 375 μL, 1.6 M, 0.6 mmol) at –40 °C. The mixture was

allowed to stir at 0 °C for 30 min and then for another 30 min at 22 °C. The mixture was then allowed to cool to –78 °C, a solution of PhSeCl (38.2 mg, 0.2 mmol) in CF_3CH_2OH/thf (0.5 mL/0.5 mL) was added, and the resulting mixture was allowed to stir at –78 °C for 2 h. At this point, the reaction was quenched by the addition of a saturated solution of aqueous $Na_2S_2O_3$ (2.0 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 residue was used in the next step without further purification. The latter residue was dissolved in thf (2.0 mL) and the solution was charged with (n-Bu)$_4$NF (in thf, 200 μL, 1.0 M, 0.2 mmol); the mixture was allowed to stir for 1 h at 22 °C. The reaction was quenched by addition of a saturated solution of aqueous NH_4Cl (2 mL). The aqueous layer was washed with Et_2O (3 × 10 mL), and the combined organic layers were dried over $MgSO_4$ and the volatiles were removed in vacuo. The resulting yellow oil was purified by silica gel chromatography (10:1 to 2:1 gradient, hexanes:EtOAc) to afford **1.34** as yellow oil (15.4 mg, 0.049 mmol, 49% overall yield for 2 steps).

IR (neat): 2951 (w), 2925 (w), 2869 (w), 1465 (m), 1382 (w), 1150 (w), 1111 (m), 1044 (s), 920 (w) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 5.11 (t, J = 7.3 Hz, 1H), 4.60 (s, 2H), 3.62 (t, J = 6.5 Hz, 2H), 3.48 (dt, J = 9.5, 4.8 Hz, 2H), 3.35 (s, 3H), 2.31 (q, J = 6.7 Hz, 2H), 1.72 – 1.51 (m, 4H), 1.50 (s, 1H), 1.46 – 1.27 (m, 5H), 1.20 – 1.08 (m, 3H), 1.04 – 0.96 (m, 1H), 0.87 (d, J = 1.9 Hz, 3H), 0.86 (d, J = 1.8 Hz, 3H), 0.75 (d, J = 6.7 Hz, 3H); **^{13}C NMR (101 MHz, $CDCl_3$):** δ 139.8, 122.6, 96.5, 68.1, 62.7, 55.3, 54.7, 39.6, 35.2, 34.7, 31.5, 28.3, 28.1, 26.4, 24.8, 23.0, 22.7, 18.2, 12.8; **HRMS (DART+):** Calcd for $C_{19}H_{39}O_3$ $[M+H]^+$: 315.2894. Found: 315.2889. **Specific rotation:** $[\alpha]_D^{20.0}$ +14.2 (*c* 0.23, $CHCl_3$).

(4*R*, 5*R*)-5,9-Dimethyl-4-((*E*)-penta-2,4-dien-2-yl)decan-1-ol (1.35)

To a solution of compound **1.34** (10.0 mg, 0.032 mmol) in CH_2Cl_2 (1.0 mL) was added Et_3N (9.0 μL, 0.064 mmol), DMAP (0.4 mg, 3.2 μmol), and *p*-toluenesulfonyl chloride (9.1 mg, 0.048 mmol). The mixture was allowed to stir at 22 °C for 4 h, after which the reaction was quenched by the addition of a saturated solution of aqueous NH_4Cl (2 mL). The aqueous layer was washed with Et_2O (3 × 10 mL), and the combined organic layers were dried over $MgSO_4$ and the volatiles were removed in vacuo. The resulting yellow oil was used in the next step without purification. The residue was dissolved in MeOH (0.5 mL), 6M HCl (50 μL) was added, and the mixture was allowed to stir for 5 h. The reaction was then quenched by addition of a saturated solution of aqueous $NaHCO_3$. The aqueous layer was washed with Et_2O (3 × 10 mL), and the combined organic layers were dried over $MgSO_4$ and the volatiles were removed under vacuum. The resulting yellow oil was used in the next step without any purification. To a flame-dried 2-dram vial equipped with a magnetic stir bar was added the latter residue in dry thf (0.5 mL) under N_2. The solution was allowed to cool to 0 °C and KO*t*Bu (3.5 mg, 0.032 mmol) was added drop-wise as a solution in thf (0.5 mL). The mixture was allowed to warm to 22 °C and stir for 30 min before the volatiles were removed in vacuo. The resulting yellow oil was purified by silica gel chromatography (10:1 to 2:1 gradient, hexanes:EtOAc) to afford **1.35** as yellow oil (3.1 mg, 0.012 mmol, 38% overall yield for 3 steps).

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.59 (dt, J = 16.8, 10.6 Hz, 1H), 5.81 (d, J = 10.6 Hz, 1H), 5.08 (dd, J = 16.8, 2.0 Hz, 1H), 4.98 (dd, J = 10.6, 2.0 Hz, 1H), 3.67 – 3.56 (m, 2H), 1.78-0.95 (m, 13H), 1.62 (s, 3H), 0.87 (d, J = 6.6 Hz, 6H), 0.76 (d, J = 6.6 Hz, 3H). **HRMS (DART+):** Calcd for $C_{17}H_{33}O$ $[M+H]^+$: 253.2526. Found: 253.2533. **Specific rotation:**

$[\alpha]_D^{20.0}$ +8.9 (*c* 0.1, $CHCl_3$). The characterization data are consistent with those reported previously.[22]

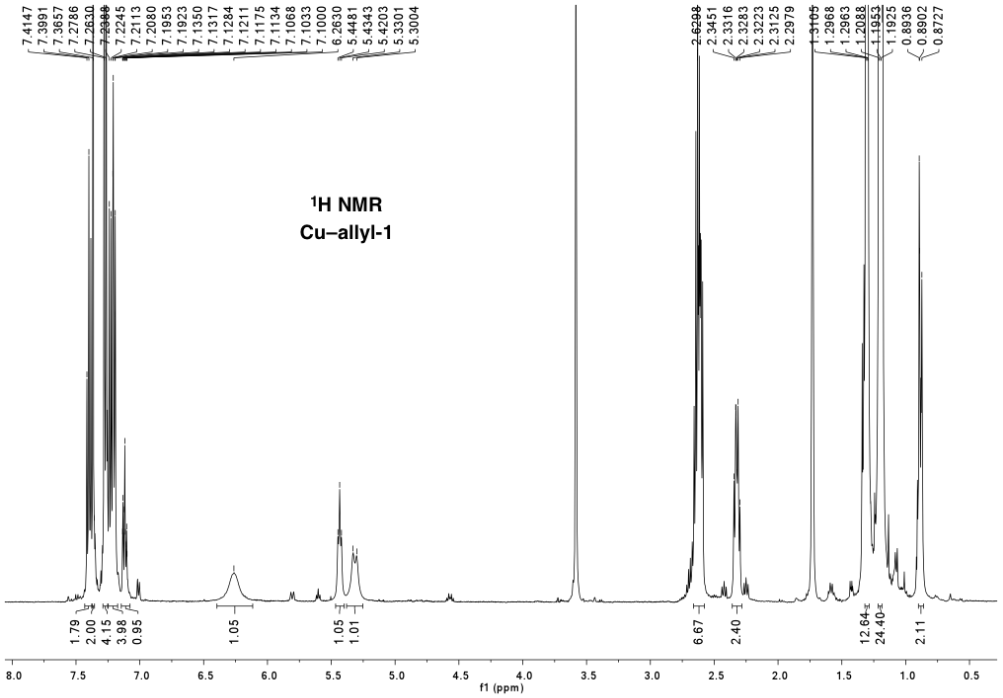
1.8.6 Spectroscopic Investigation of Cu–Allyl Complex

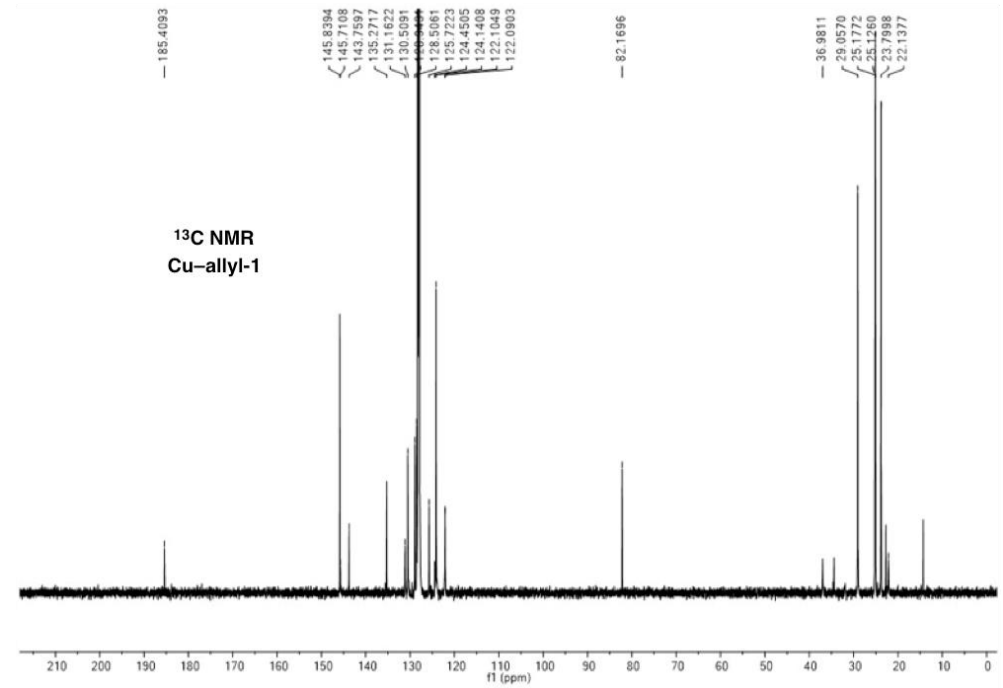
In an N_2-filled glove box, an oven-dried 2-dram vial was charged with [1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene]CuO*t*Bu (20.0 mg, 0.038 mmol) and $B_2(pin)_2$ (11.6 mg, 0.045 mmol), then Et_2O (1.0 mL) was added through a syringe. The vial was manually stirred until most of the solid dissolved and *rac*-**1.10** (7.8 mg, 0.046 mmol) was added by a syringe. The mixture was shaken, which resulted in the formation of a deep yellow homogeneous solution. After 10 min at 22 °C, the volatiles were removed in vacuo. The mixture was redissolved in 0.8 mL of pentane, resulting in a turbid solution, which was kept overnight at –40 °C in a glovebox freezer. This led to formation of light yellow crystals, which were filtered, washed with cold pentane and dried in vacuo to afford **Cu–allyl-1** (25.0 mg, 0.033 mmol, 88% yield). Crystals suitable for X-Ray diffraction were obtained by vapor diffusion of hexanes into a concentrated Et_2O solution at –40 °C. The identity of these crystals was established through NMR spectroscopy (thf-d_8 and C_6D_6 to avoid overlaping of signals in ^{13}C NMR).

^{1}H NMR (500 MHz, thf-d_8): δ 7.40 (t, *J* = 7.8 Hz, 2H), 7.37 (s, 2H), 7.27 (d, *J* = 7.8 Hz, 4H), 7.25 – 7.17 (m, 4H), 7.15 – 7.08 (m, 1H), 6.26 (bs, 1H), 5.43 (bt, *J* = 7.0 Hz, 1H), 5.32 (bd, *J* = 14.9 Hz, 1H), 2.67 – 2.57 (m, 7H), 2.36 – 2.28 (m, 2H), 1.30 (d, *J* = 6.8 Hz, 12H), 1.20 (d, *J* = 8.1 Hz, 24H), 0.88 (m, 2H). **^{13}C NMR (151 MHz, C_6D_6):** δ 185.4, 145.8,

(22) Clasby, M.; Craig, D.; Jaxa-Chamiec, A.; Lai, J.; Marsh, A.; Slawin, A.; White, A. Williams, D. *Tetrahedron*, **1996**, *52*, 4769–4802.

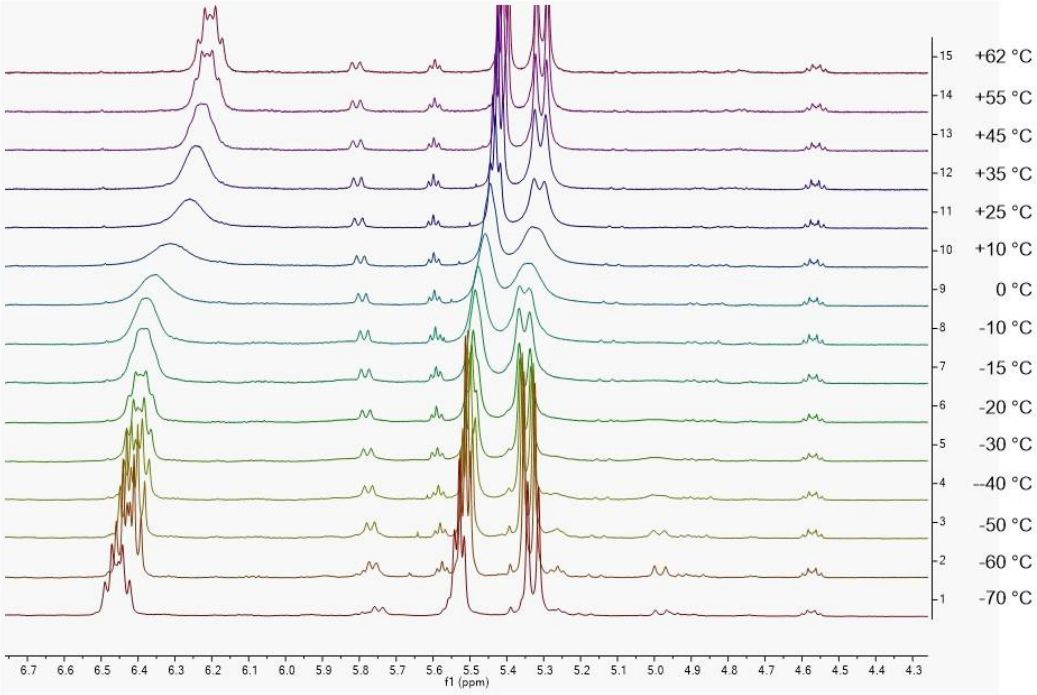
145.7, 143.8, 135.3, 131.2, 130.5, 128.9, 128.5, 125.7, 124.1, 122.1, 82.2, 29.1, 25.2, 25.1, 23.8, 22.1.





A sample of pure **Cu–allyl-1** was prepared, as described above, and dissolved in 0.6 mL of thf-d_8 and transferred to a J-Young NMR tube. This sample was then used in a

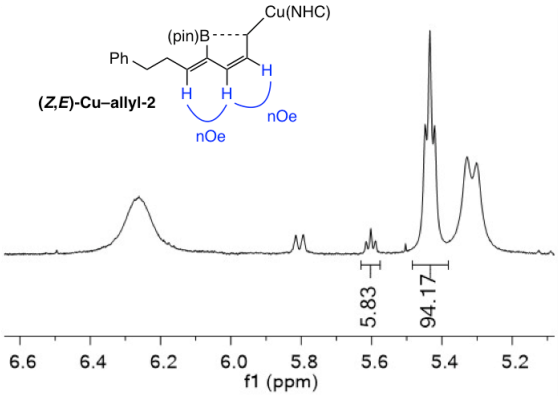
study that was performed with a 500 MHz NMR spectrometer in a probe that was precooled to –70 °C. The sample was warmed in 5–10 °C intervals and after each temperature change a spectrum was acquired. Prior to each acquisition the temperature was allowed to equilibrate for 15 min.



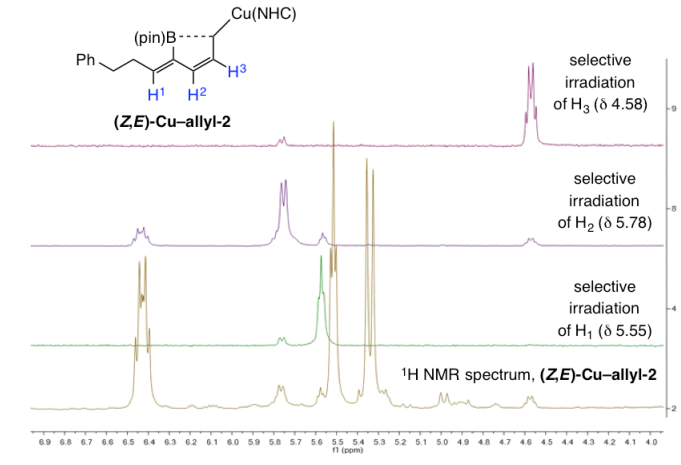
At –50 °C temperature, **Cu–allyl-1** signals resolve into two species in a 94:6 ratio. X-Ray crystallography and nOe analyses indicate that the major species is (***E, Z***)**-Cu–allyl-1**, which is in exchange with a second species. Despite extensive efforts, nOe experiments did not allow definitive assignment of the species which is in exchange with **(*E, Z*)-Cu–allyl-1**. We therefore turned to HCl quenching experiments [23, 24] (fast trapping is hypothesized) and analyzed the stereochemical outcome. These data suggest assignment of this species as (***E, E***)**-Cu–allyl-1**.

(23) Stahl, S. S.; Labinger,J. A.; Bercaw, J. E. *J. Am. Chem. Soc.* **1996**, *118*, 5961–5976.
(24) Roth, K. E.; Blum, S. A. *Organometallics*, **2010**, *29*, 1712–1716.

A third minor species was also detected, the identity of which was established as follows. The chemical shift in the ^{11}B NMR spectrum (shown below) of **(*Z, E*)-NHC–Cu–allyl-2**) is significantly more upfield at 20 ppm (vs. 30 ppm for (***E, Z*)-NHC–Cu–allyl-1**); this indicates that the boryl unit is most likely four-coordinate, probably due to interaction with the electron-rich CH_2–Cu. This species is labeled **(*Z, E*)-Cu–allyl-2**).



Consistent with the above proposal, spectroscopic analysis (i.e., nOe experiments; shown below) revealed correlation between the alkene protons that is characteristic of a *Z*-disubstituted alkene and an *E*-trisubstituted alkene.



We have no indication that **(*Z, E*)-Cu-allyl-2** is involved in dynamic exchange with (***E, Z*)-Cu–allyl-1** between –70 and 62 °C). When a sample of (***E, Z*)-Cu–allyl-1** was

generated *in situ* by the above procedure at –78 °C and allowed to warm up inside the spectrometer precooled at –20 °C, no **Cu-allyl-2** could be detected by ^{1}H NMR spectroscopy. The precise origin of **Cu–allyl-2** is unclear at the present time. Nevertheless, this complex does not seem to play a role in the catalytic process. It is possible that **Cu-allyl-2** is generated at 22 °C without an electrophile or in the course of manipulations required for crystallization.

1.8.7 Proto-boryl Addition to a Vinylallene with MeOH versus *t*BuOH

An oven-dried 2-dram vial equipped with a stir bar was charged with **imid-1d** (2.5 mg, 5.0 μmol), CuCl (0.5 mg, 5.0 μmol), NaO*t*Bu (10.7 mg, 0.02 mmol) and thf (1.0 mL) in a N_2-filled glove box. The mixture was allowed to stir for 2 h under N_2 at 22 ℃ , after which $B_2(pin)_2$ (28.0 mg, 0.11 mmol) was added. The resulting solution was allowed to stir for 30 min, after which vinylallene **1.10** (17.0 mg, 0.10 mmol) and MeOH (8.1 μL, 0.20 mmol) or *t*-BuOH (14.8 mg, 0.20 mmol) were added. The mixture was allowed to stir at 22 ℃ for 5 h. The volatiles were then removed in vacuo, affording yellow oil residue, which was purified by silica gel chromatography (30:1 hexanes/ethyl acetate) to afford **1.42** as colorless oil.

(*Z*)-4,4,5,5-Tetramethyl-2-(7-phenylhepta-1,4-dien-4-yl)-1,3,2-dioxaborolane (1.42)

IR (neat): 2977 (m), 2928 (w), 1407 (w), 1371 (s), 1347 (s), 1304 (s), 1144 (s), 1028 (w), 963 (m), 859 (m), 698 (s) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.28 (dt, *J* = 4.7, 2.7 Hz, 2H), 7.22 – 7.16 (m, 3H), 6.45 (t, *J* = 7.0 Hz, 1H), 5.81 (ddt, *J* = 16.3, 10.1, 6.1 Hz, 1H), 4.92 (ddq, *J* = 17.7, 10.1, 1.7 Hz, 2H), 2.88 (d, *J* = 5.2 Hz, 2H), 2.70 (dd, *J* = 9.6, 6.7 Hz, 2H), 2.44 (dt, *J* = 10.4, 7.2 Hz, 2H), 1.25 (s, 13H); **^{13}C NMR (101 MHz, $CDCl_3$):** δ 146.0,

142.2, 137.4, 128.5, 128.5, 126.0, 114.1, 83.3, 35.5, 32.8, 30.9, 24.9; **HRMS (DART):** Calcd for $C_{19}H_{28}BO_2$ $[M+H]^+$: 299.2177. Found: 299.2183.

1.8.8 Density Functional Theory (DFT) Calculations

DFT computations[25] were performed with the Gaussian 09/Gaussian 16 suite of programs.[26] Geometries were optimized with the M06L[27] functional and the Def2SVP basis set[28] in conjunction with the corresponding Coulomb fitting basis set to speed up calculations.[29] The effect of a polar reaction medium (dichloromethane, DCM) was approximated by means of the SMD solvation model.[30] Stationary points were probed through vibrational analysis and Gibbs free energy corrections were performed under standard conditions (298.15 K, 1.0 atm). Transition states have been verified through Intrinsic Reaction Coordiante calculations (IRC) employing the L(ocal) Q(uadratic)

(25) For reviews on the application of DFT calculations to transition metal chemistry, see: (a) Cramer, C. J.; Truhlar, D. G. *Phys. Chem. Chem. Phys.* **2009**, *11*, 10757–10816. (b) Grimme, S.; Ehrlich, S.; Goerigk, L. *J. Comp. Chem*. **2011**, *32*, 1456–1465. (c) Peverati, R.; Truhlar, D. G. *Phil. Trans. R. Soc. A* **2014**, *372*, 20120476. For comparisons of density functionals in benchmark studies, see: (d) Mardirossian, N.; Head-Gordon, M. *J. Chem. Theory Comput.* **2016**, *12*, 4303–4325. (e) Mardirossian, N.; Head-Gordon, M. *J. Chem. Phys.* **2016**, *144*, 214110. (f) Brauer, B.; Kesharwani, M. K.; Kozuch, S.; Martin, J. M. *Phys. Chem. Chem. Phys.* **2016**, *18*, 20905–20925. (g) Weymuth, T.; Couzijn, E. P. A.; Chen, P.; Reiher, M. *J. Chem. Theory Comput.* **2014**, *10*, 3092–3103. (h) Zhang, W.; Truhlar, D. G.; Tang M. *J. Chem. Theory Comput.* **2013**, *9*, 3965–3977. (i) Yu, H. S.; He, X.; Li, S. L.; Truhlar, D. G. *Chem. Sci.* **2016**, *7*, 5032–5051. (j) Steinmetz, M.; Grimme S. *ChemistryOpen* **2013**, *2*, 115–124. (k) Goerigk, L.; Kruse H.; Grimme, S. *ChemPhysChem* **2011**, *12*, 3421–3433.

(26) 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, Jr., 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, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09, Revision **D.01**,* Gaussian, Inc., Wallingford CT, **2009**.

(27) Zhao, Y.; Truhlar, D. G. *Acc. Chem. Res.* **2008**, *41*, 157–167.

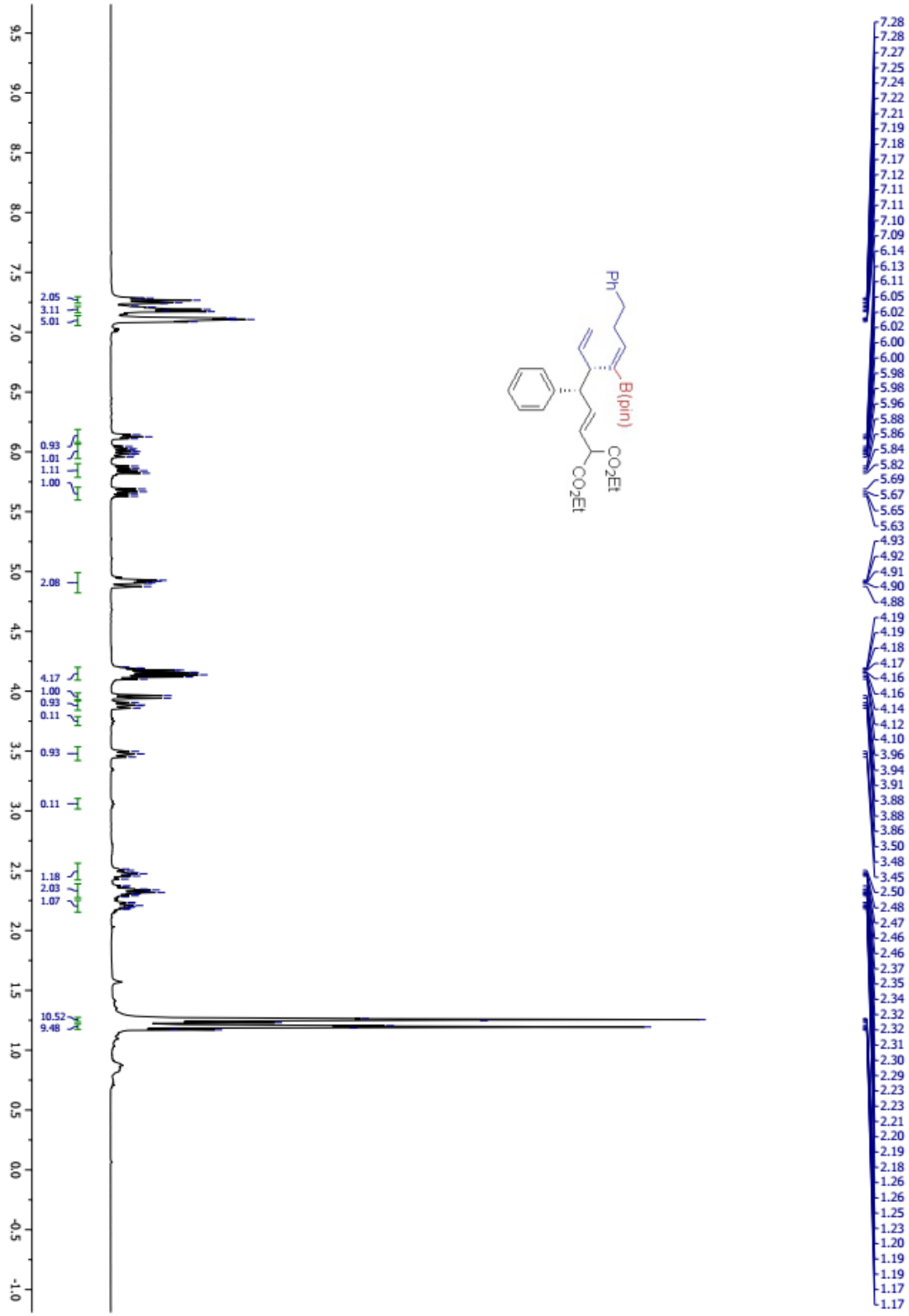
(28) Weigend, F.; Ahlrichs, R. *Phys. Chem. Chem. Phys.* **2005**, *7*, 3297–3305.

(29) Weigend, F. *Phys. Chem. Chem. Phys.* **2006**, *8*, 1057–1065.

(30) Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. *J. Phys. Chem. B* **2009**, *113*, 6378–6396.

A(approximation) method,[31] followed by subsequent optimization of the end points with the above mentioned optimization method. We furthermore probed the performance of various density functionals through single point energy calculations at the geometries optimized with the level described above by means of the SMD solvation model with DCM as solvent and the larger def2-TZVPP[28] basis set. Since the correct density functional is not known we tested several state of the art approaches that have been developed over the past decade:[25,32] MN15,[25i] M06,[27] and B97XD.[33] All functionals provided qualitatively very similar results and we only report the M06L/DF-Def2SVP$_{thf(SMD)}$ along with the MN15/Def2TZVPP$_{thf(SMD)}$//M06L/DF-Def2SVP$_{thf(SMD)}$ energies. For detailed discussion on every possible transition states and parameters for calculation please see the supporting information of the related publication.[34]

(31) (a) Page, M.; McIver Jr., J. W. *J. Chem. Phys.* **1988**, *88*, 922–935. (b) Page, M.; Doubleday Jr., C.; McIver Jr., J. W. *J. Chem. Phys.* **1990**, *93*, 5634–5642.
(32) For selected examples that underscore the importance of including treatment of dispersion interactions in modeling olefin metathesis reactions promoted by Ru carbene complexes, see: (a) Torker, S.; Merki, D.; Chen. P. *J. Am. Chem. Soc.* **2008**, *130*, 4808–4814. (b) Minenkov, Y.; Occhipinti, G.; Singstad, A.; Jensen, V. R. *Dalton Trans.* **2012**, *41*, 5526–5541. (c) Minenkov, Y.; Occhipinti, G.; Jensen, V. R. *Organometallics* **2011**, *32*, 2099–2111. (d) Khan, R. K. M.; Torker, S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2014**, *136*, 14337–14340. (e) Torker, S.; Koh, M. J.; Khan, R. K. M.; Hoveyda, A. H. *Organometallics* **2016**, *35*, 543–562. (f) Mikus, M. S.; Torker, S.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2016**, *55*, 4997–5002.
(33) Chai, J.-D.; Head-Gordon, M. *Phys. Chem. Chem. Phys.* **2008**, *10*, 6615–6620.
(34) Huang, Y.; Torker, S.; Li, X.; del Pozo, J.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2019**, *58*, 2685–2691.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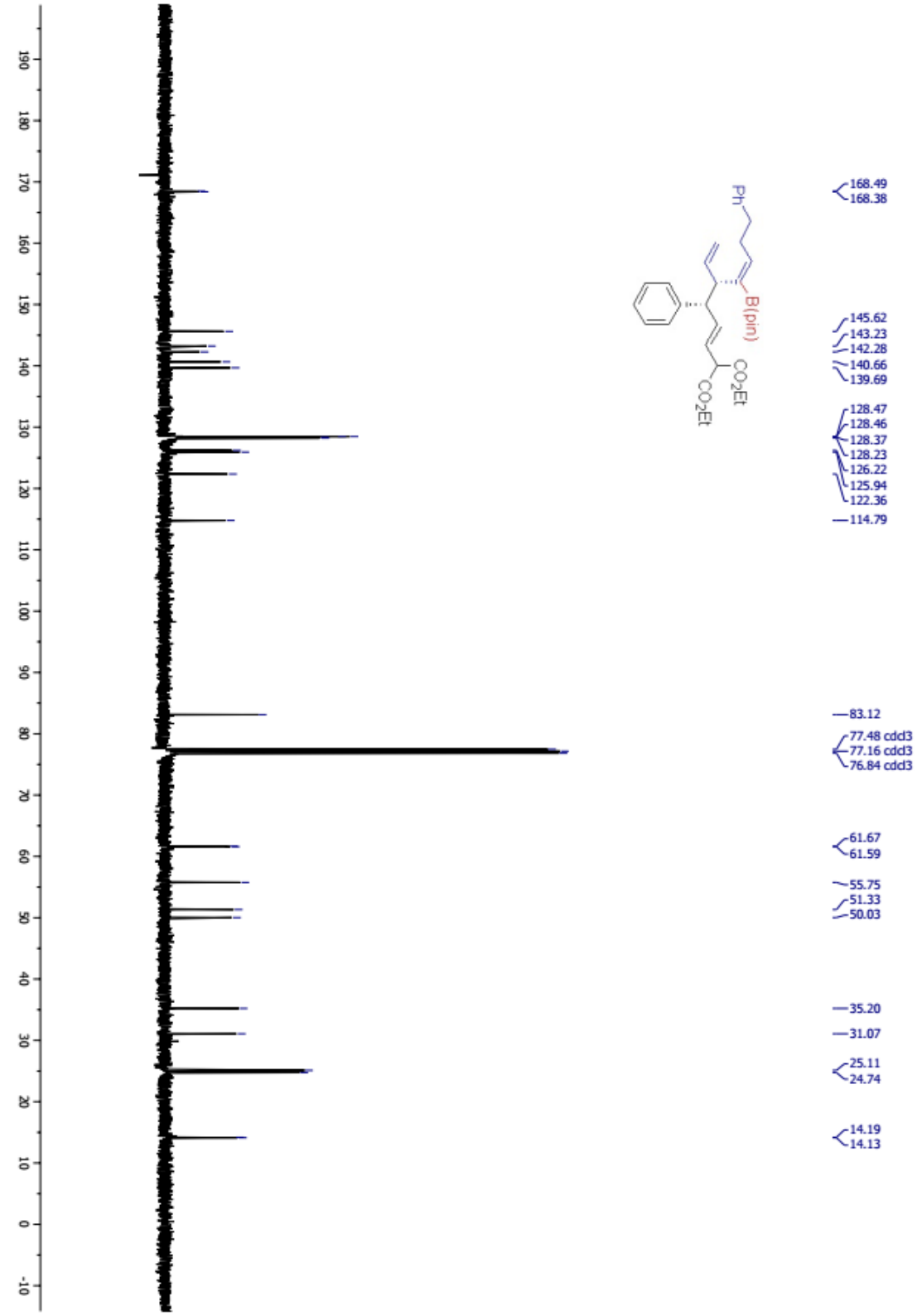
CO2Et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128.46
128.37
128.23
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125.94
122.36
114.79
83.12
77.48 cdcl3
77.16 cdcl3
76.84 cdcl3
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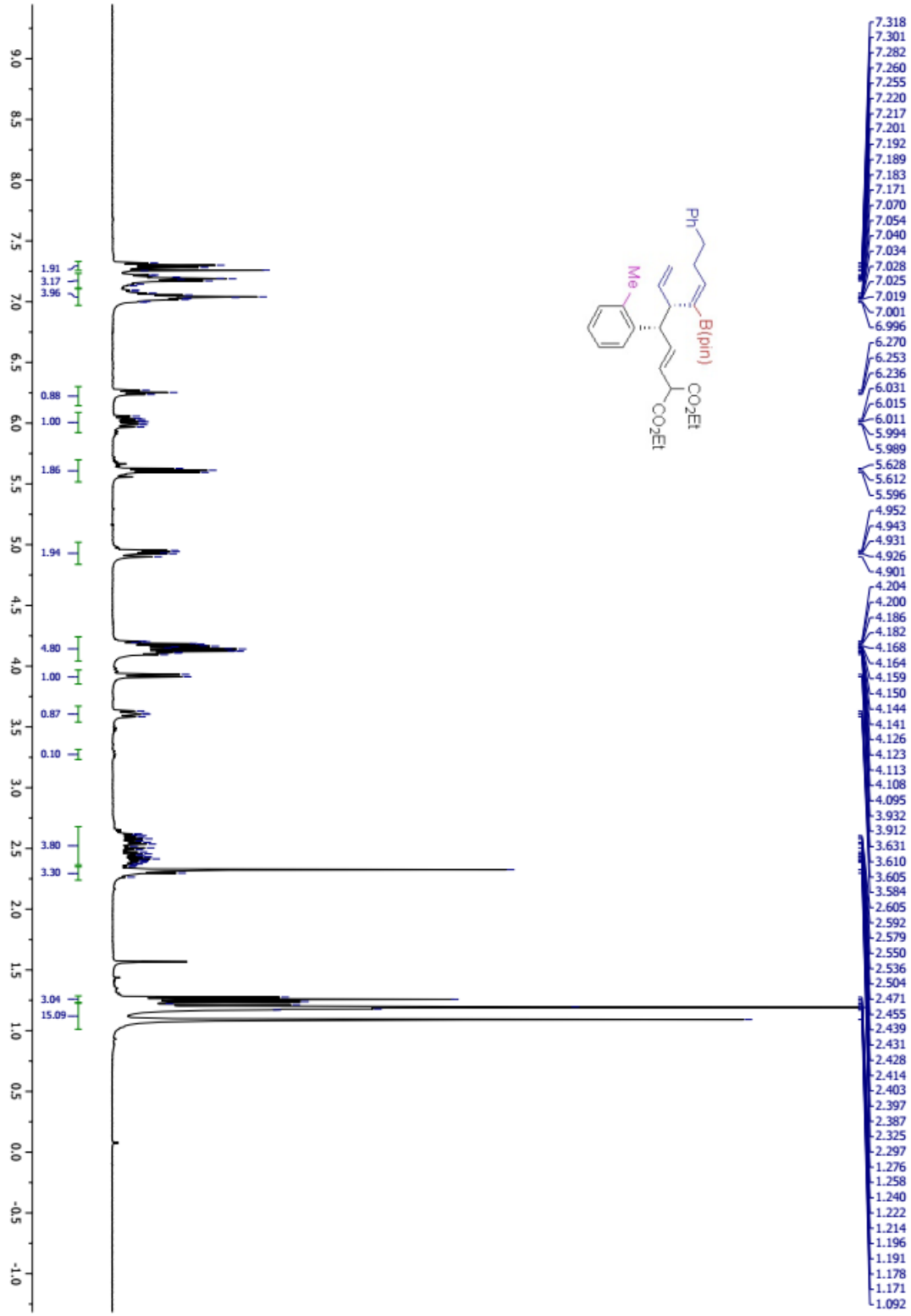
14.13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1.00
0.87
0.10
3.80
3.30
3.04
15.09
7.318
7.301
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7.260
7.255
7.220
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7.201
7.192
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7.183
7.171
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7.040
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6.253
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5.994
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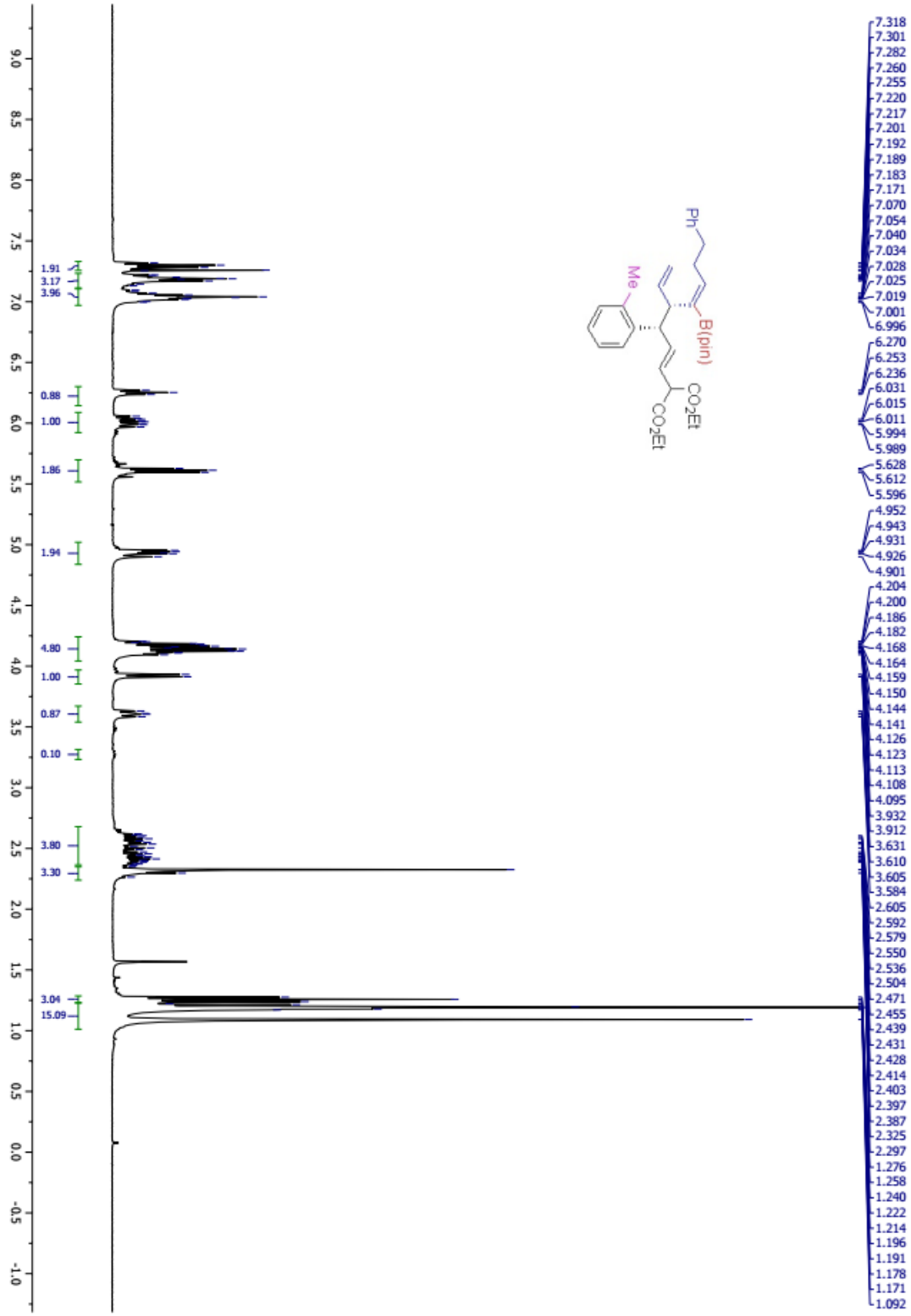
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Me
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CO2Et
CO2Et
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0.88
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4.80
1.00
0.87
0.10
3.80
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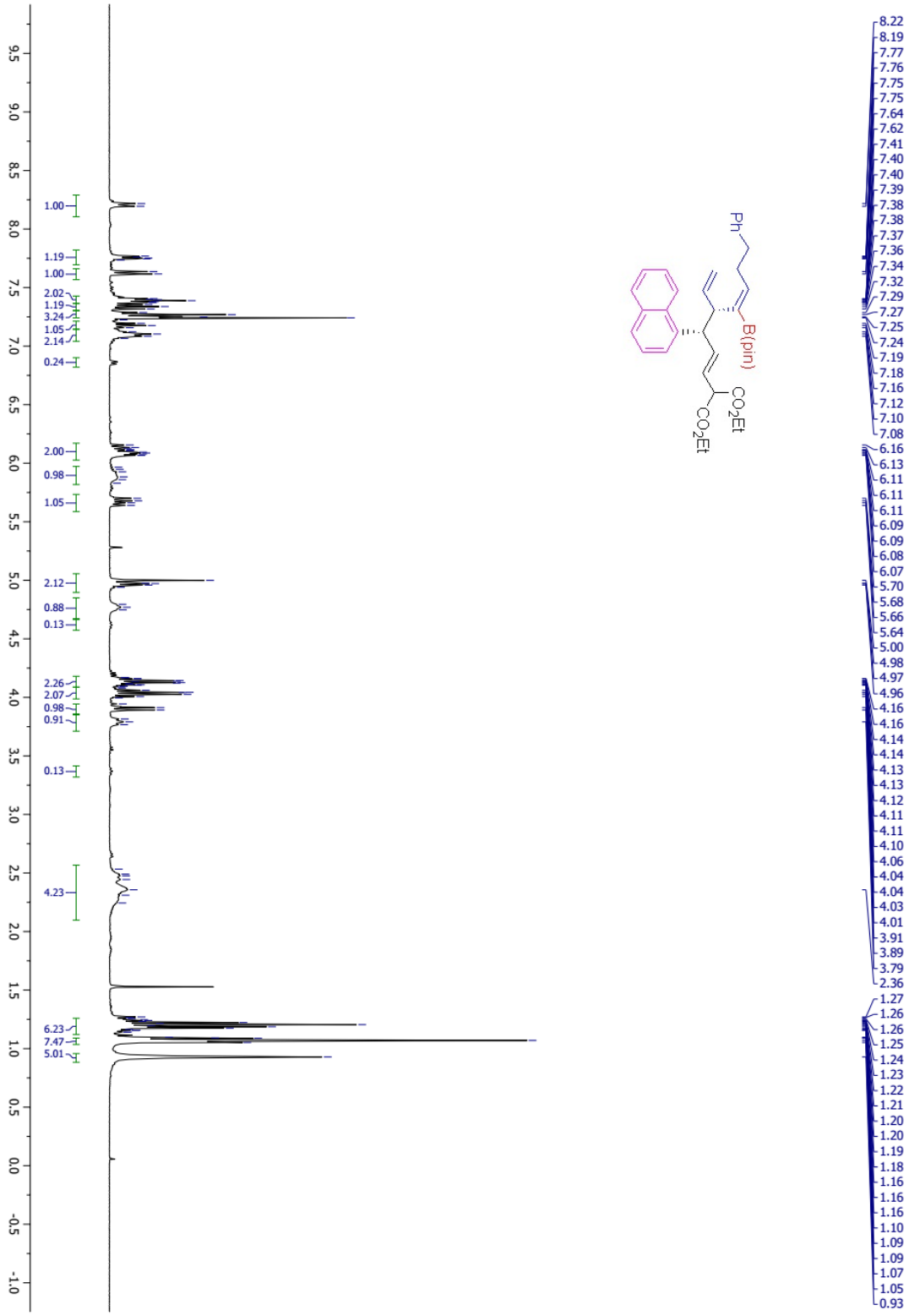
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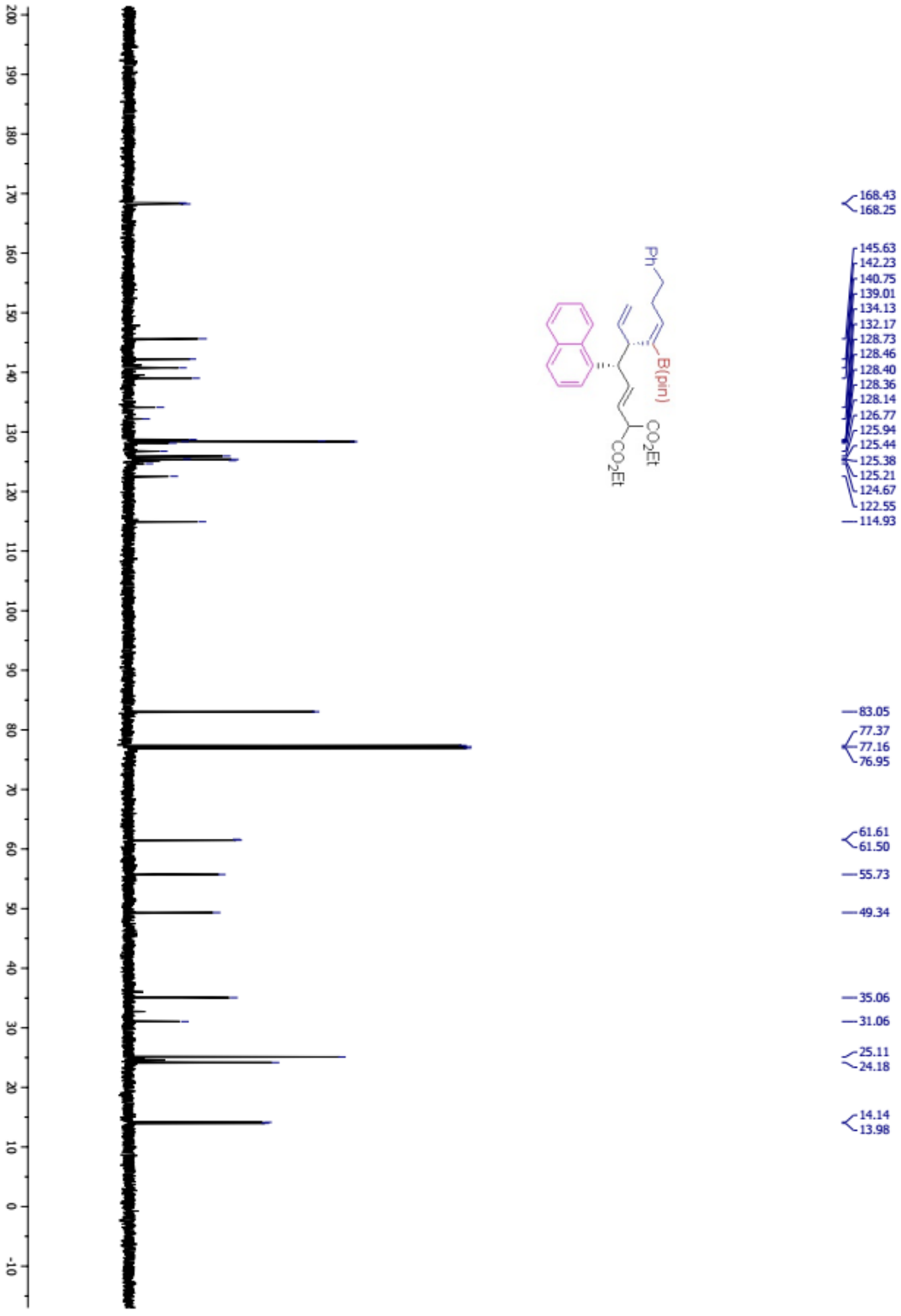
CO2Et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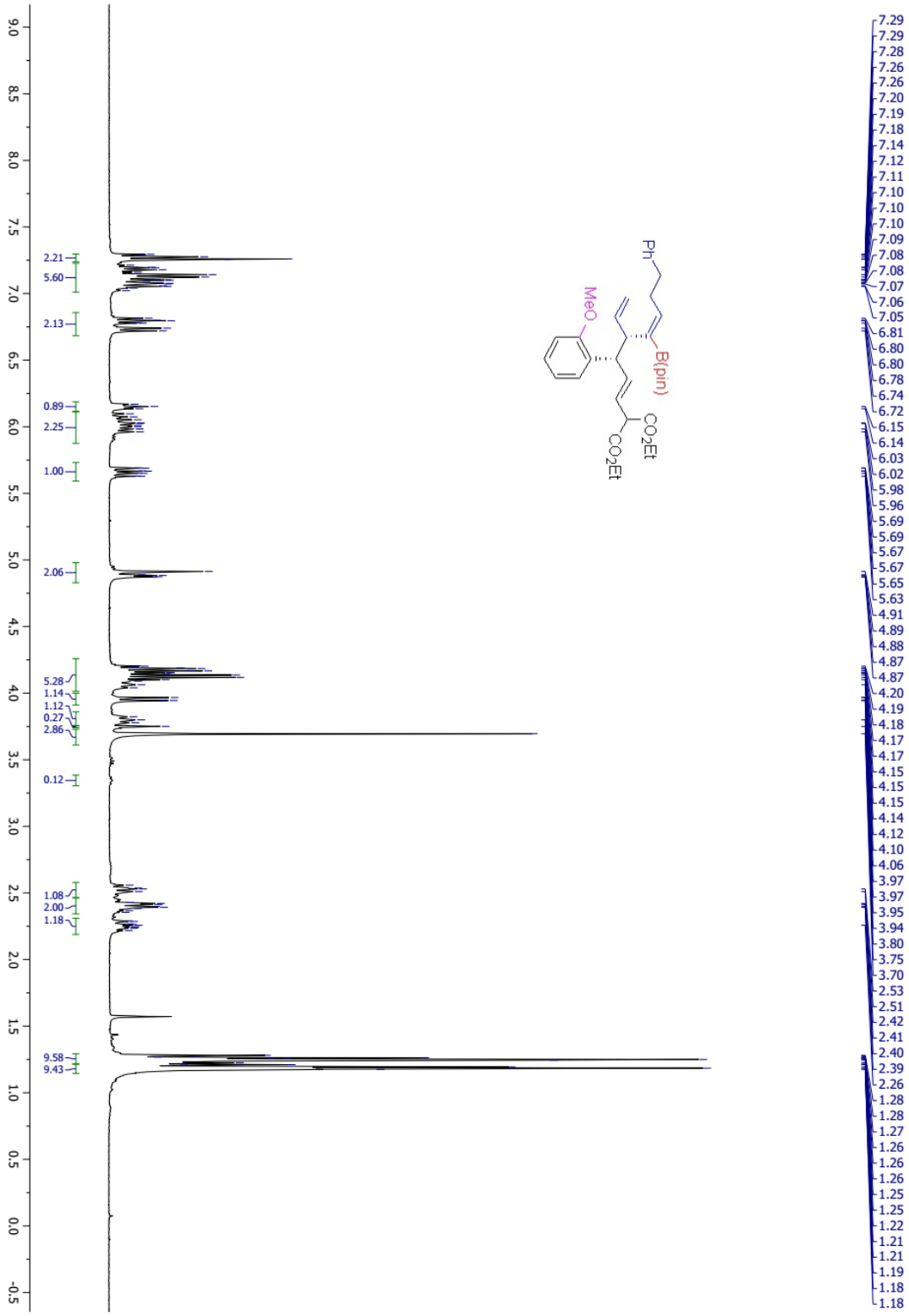
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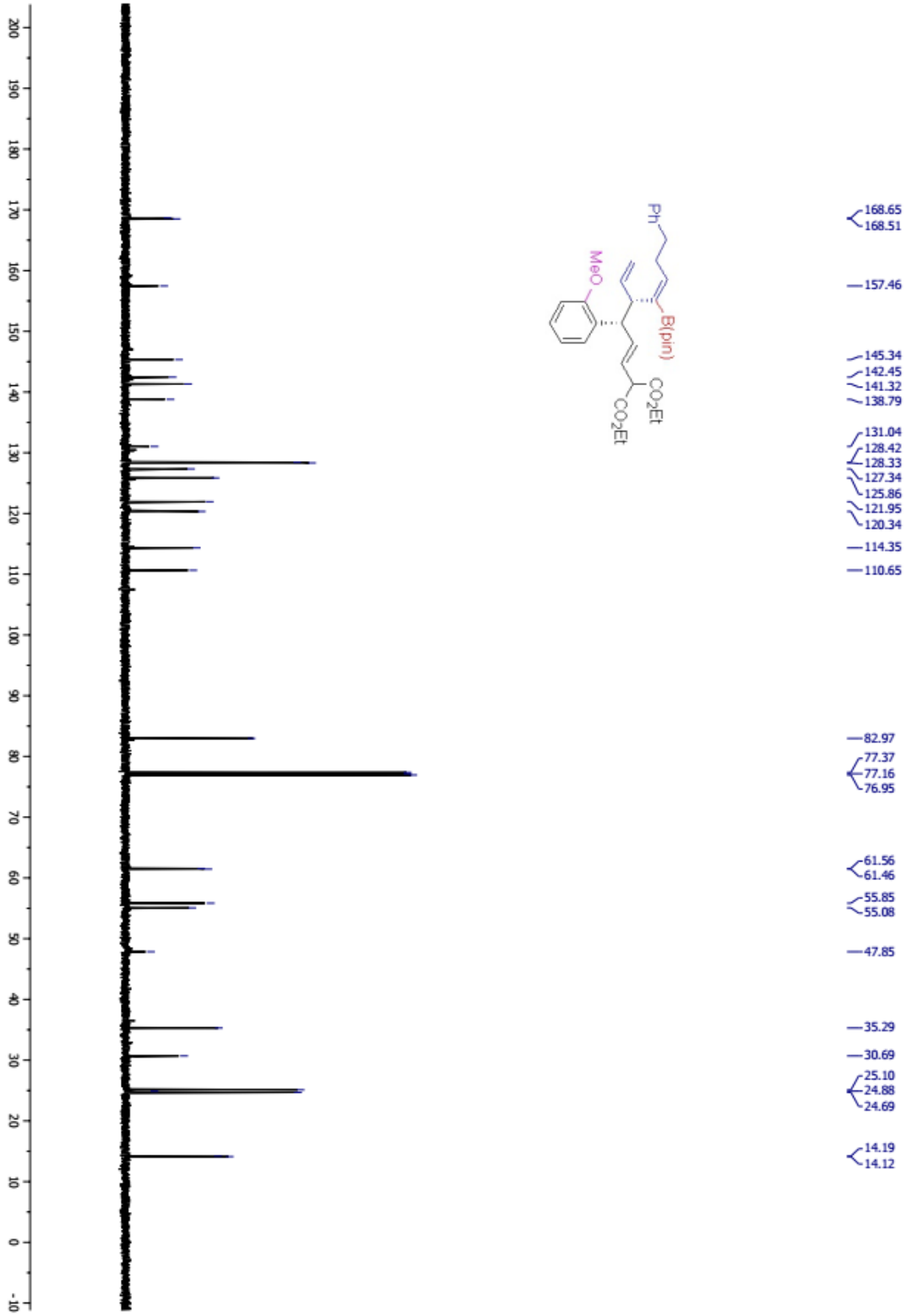
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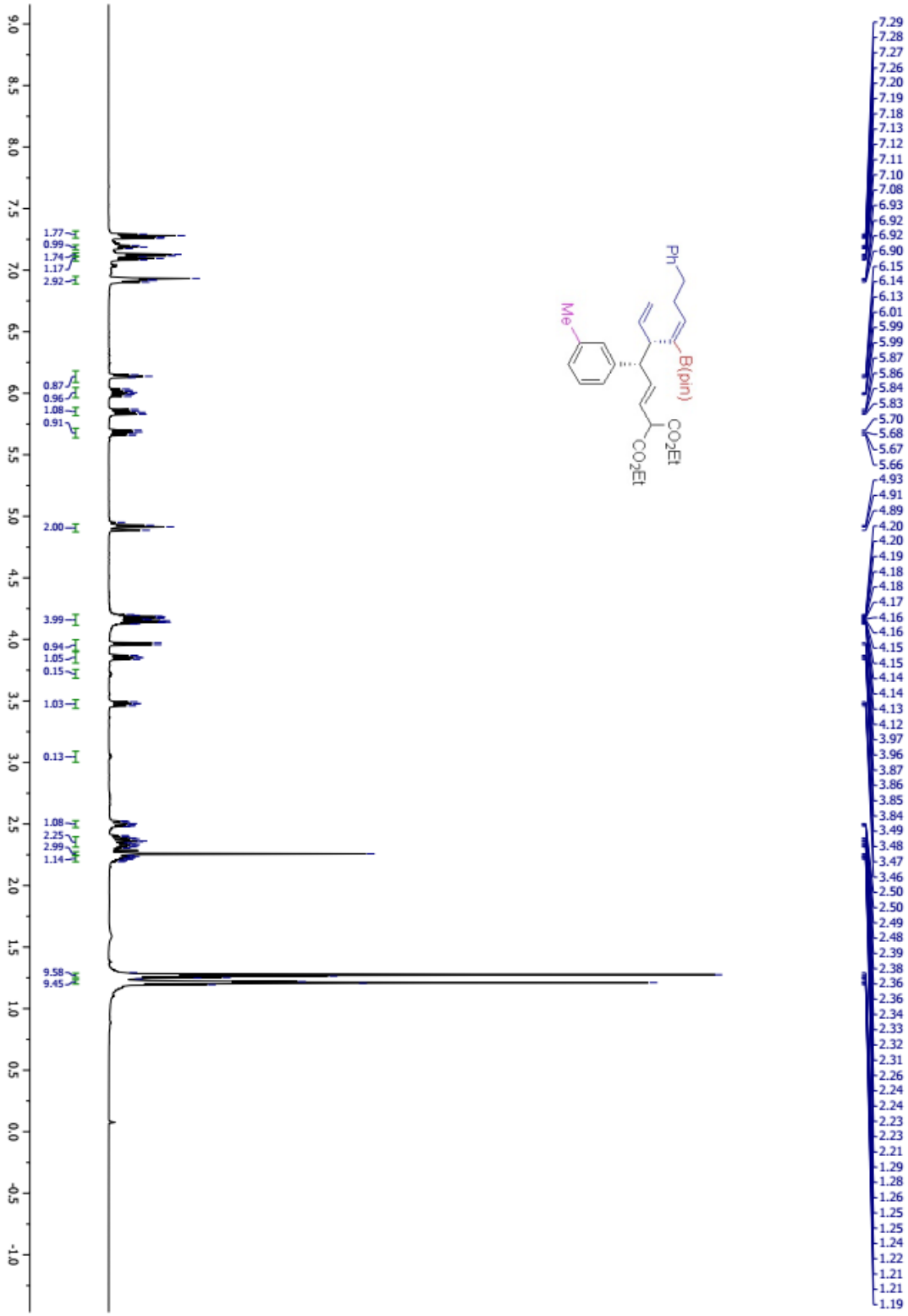
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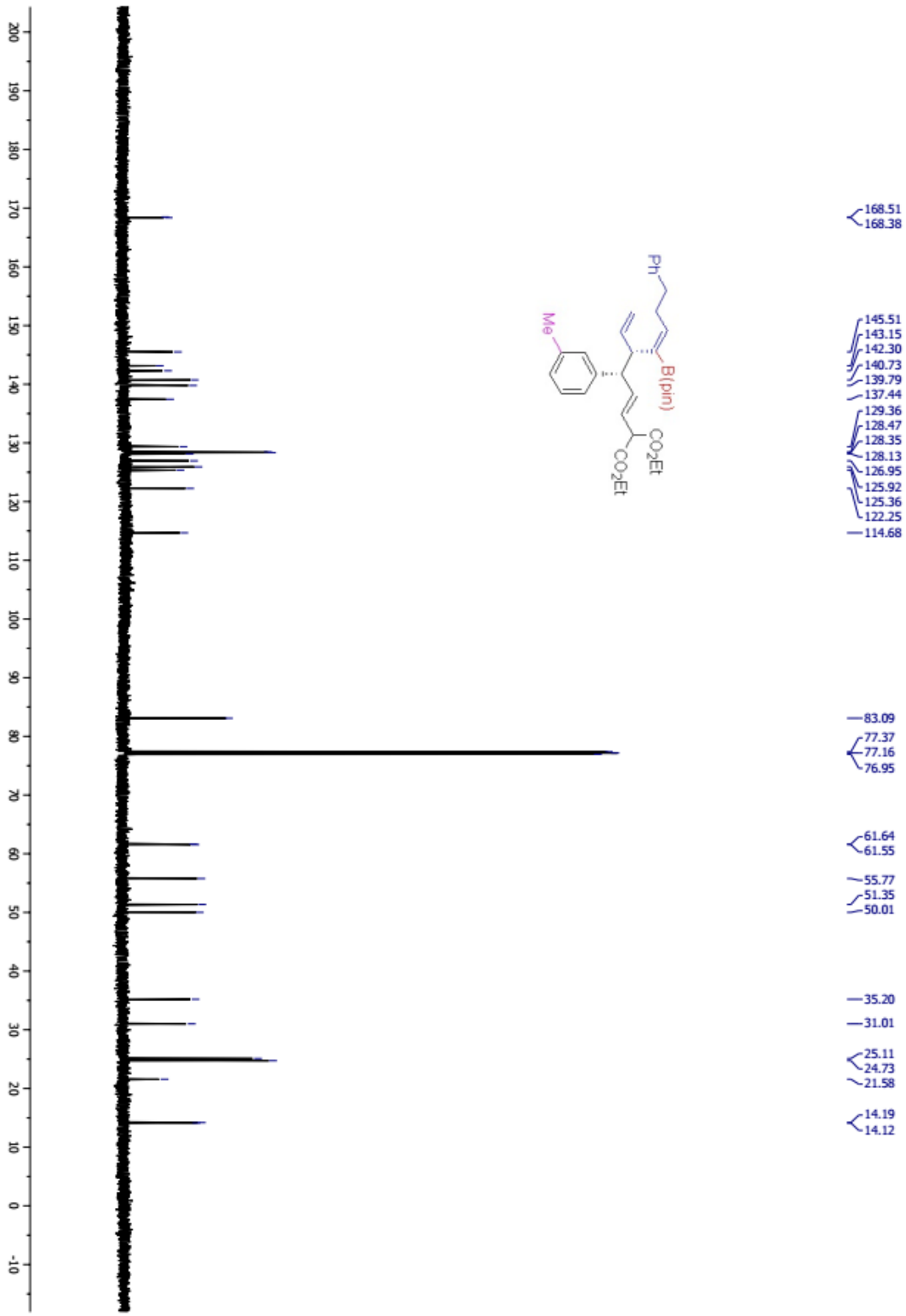
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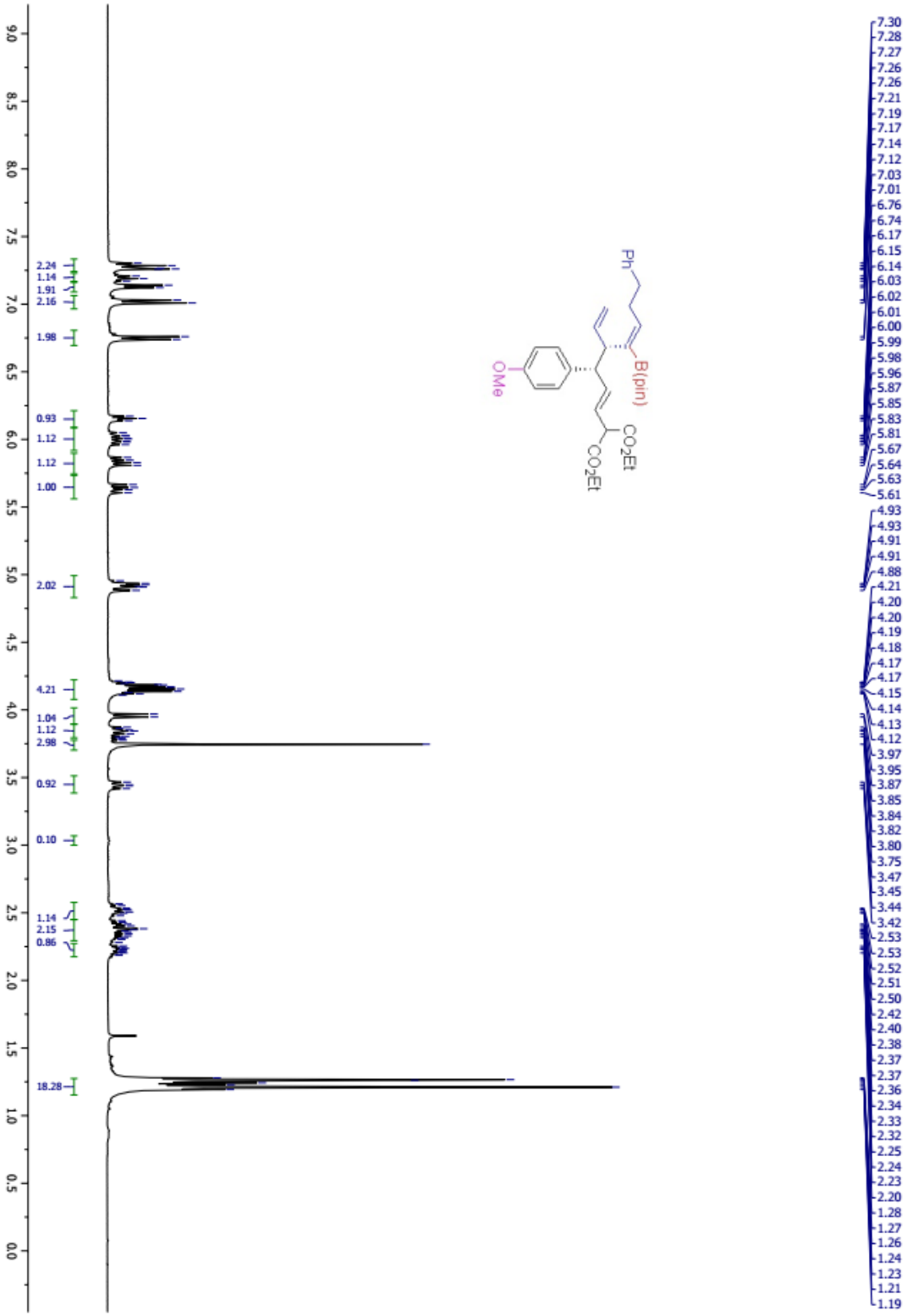
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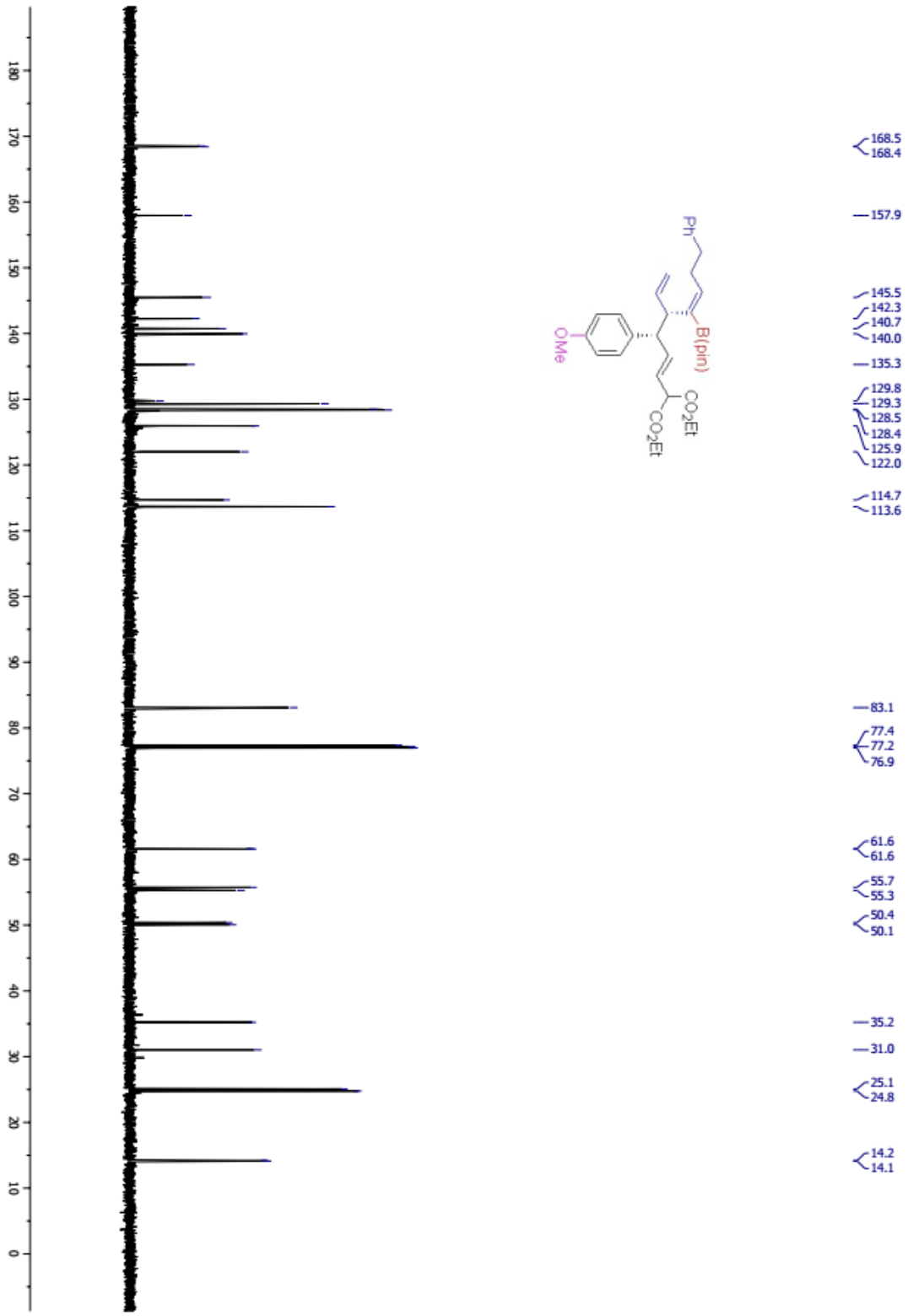
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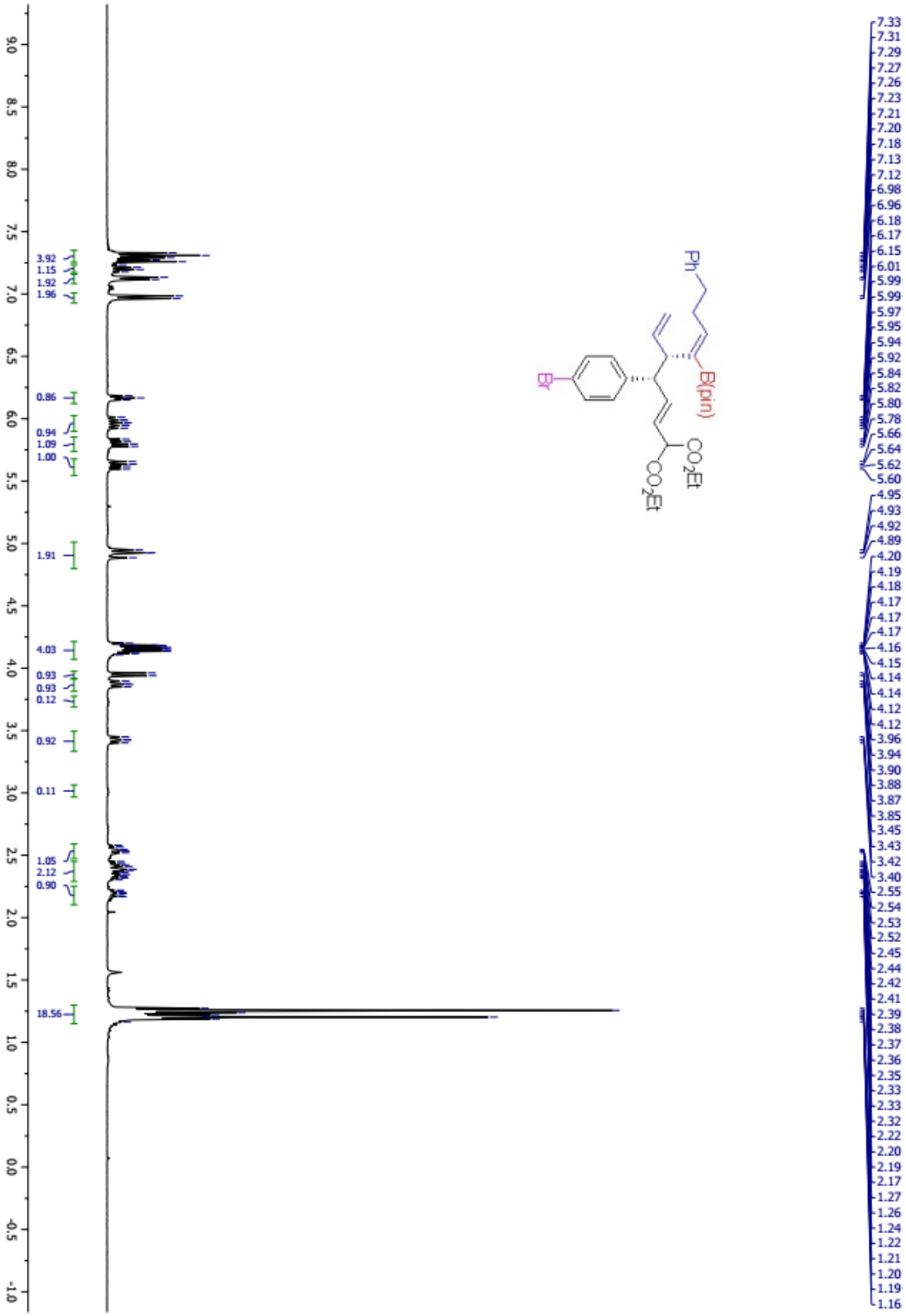
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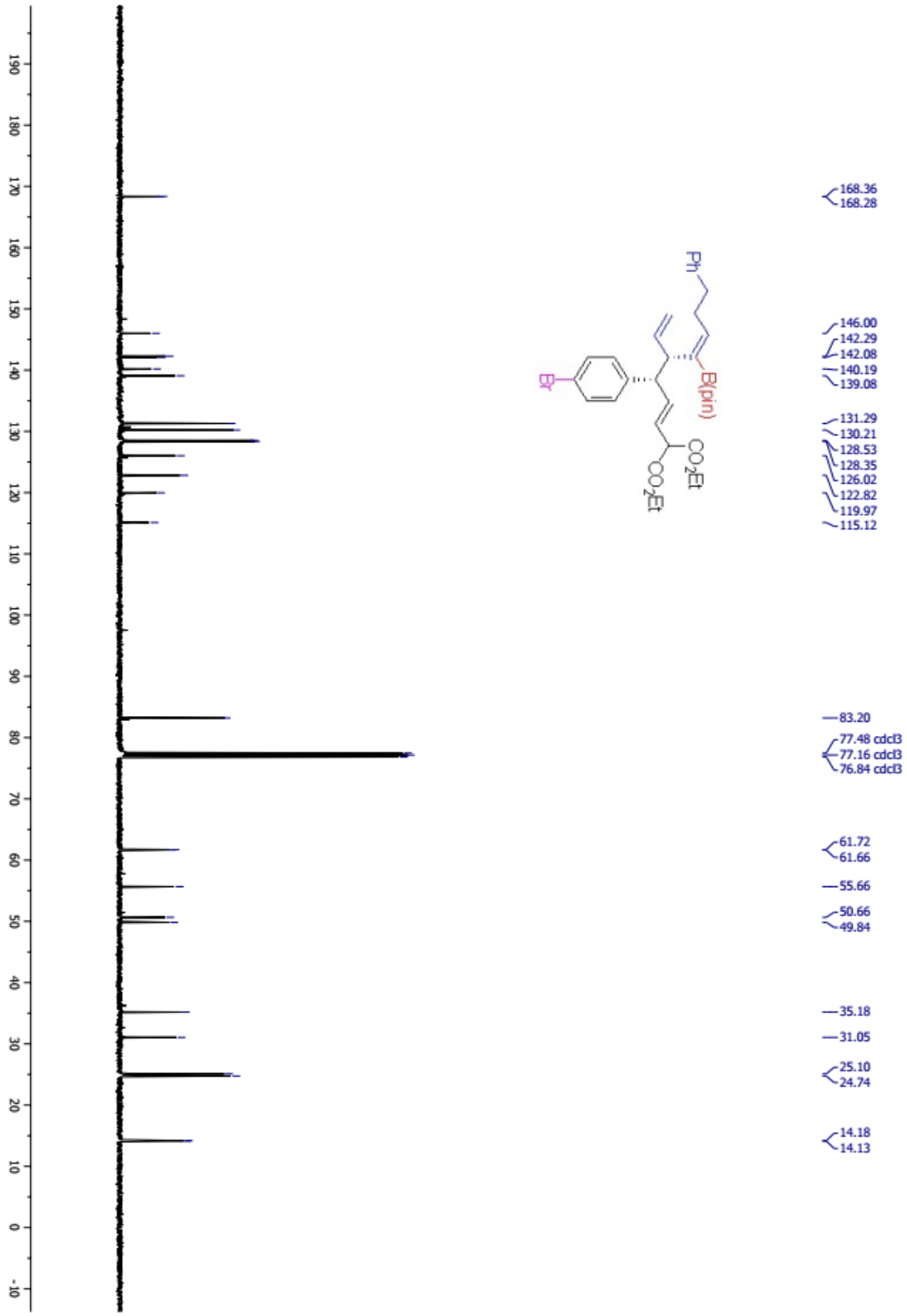
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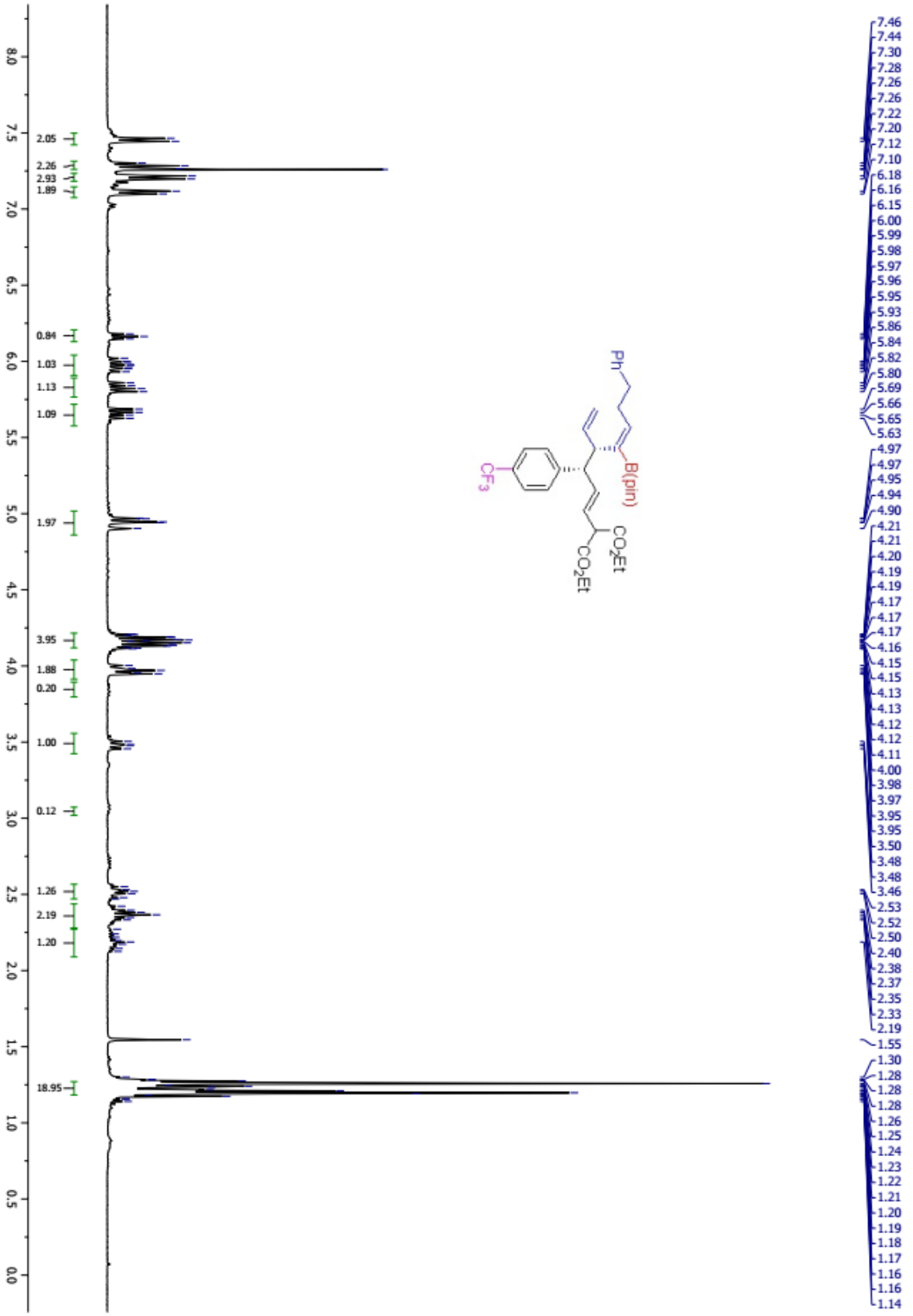
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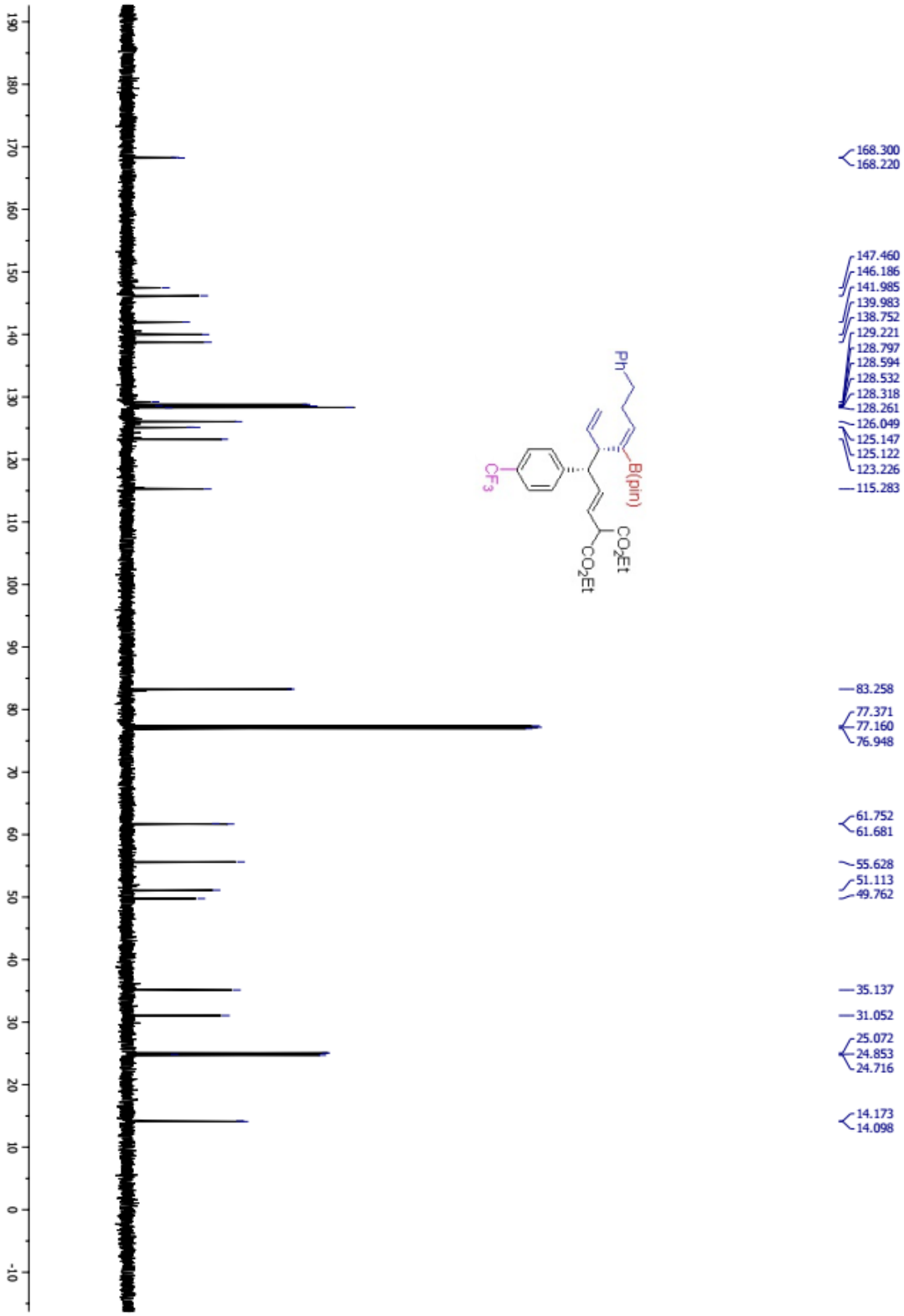
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-10
Ph
B(pin)
CF3
CO2Et
CO2Et
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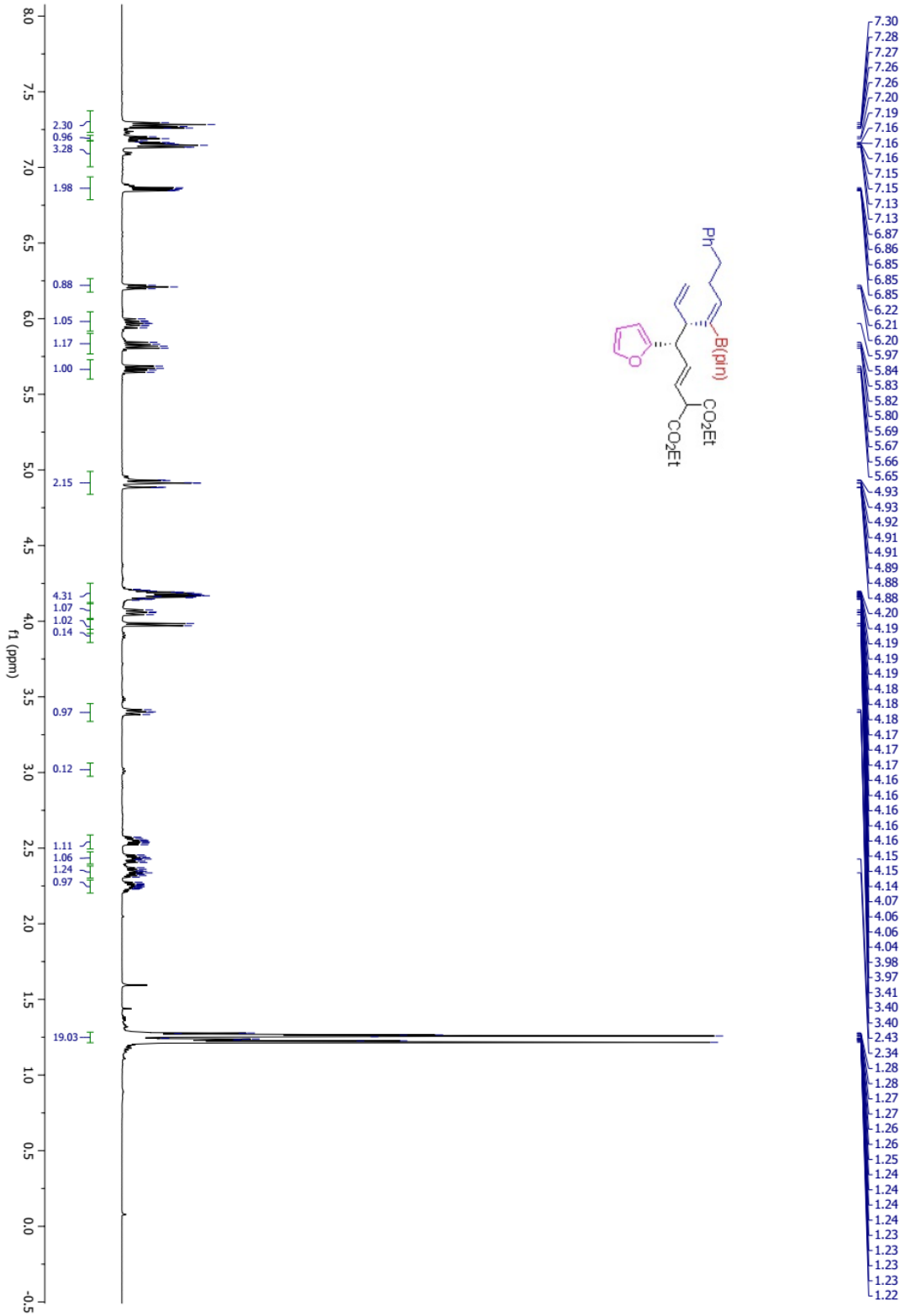
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CO2Et
CO2Et
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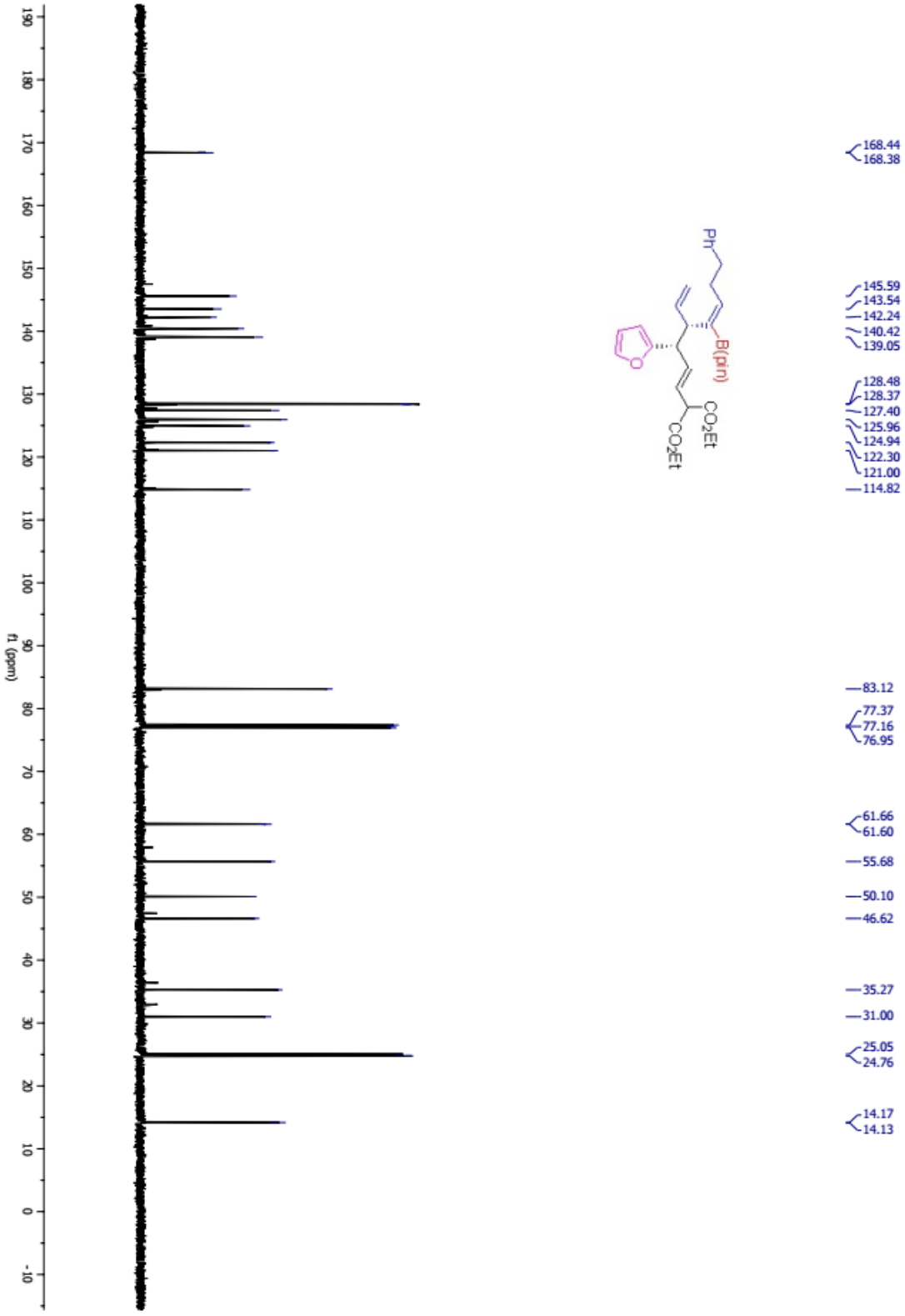
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CO2Et
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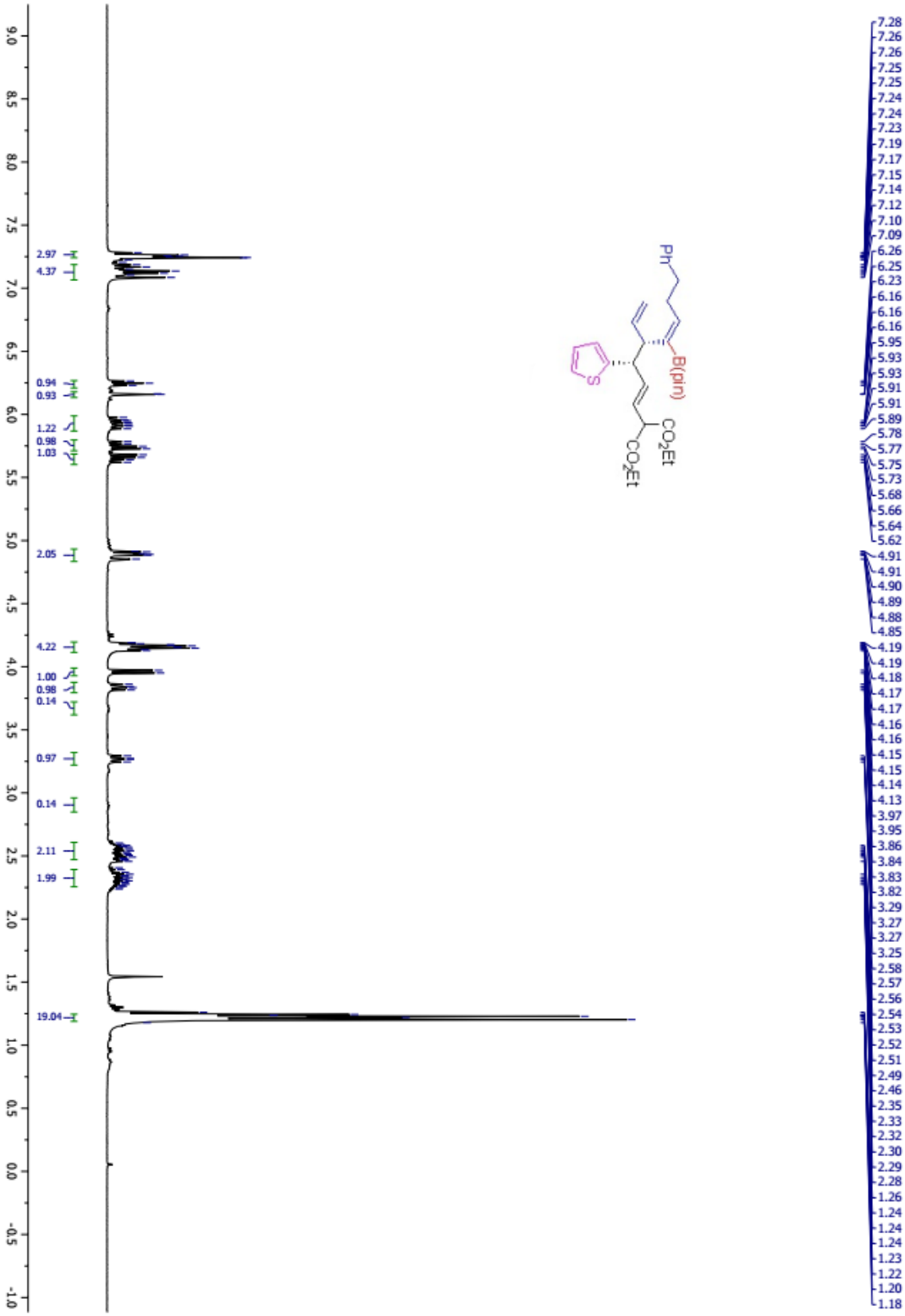
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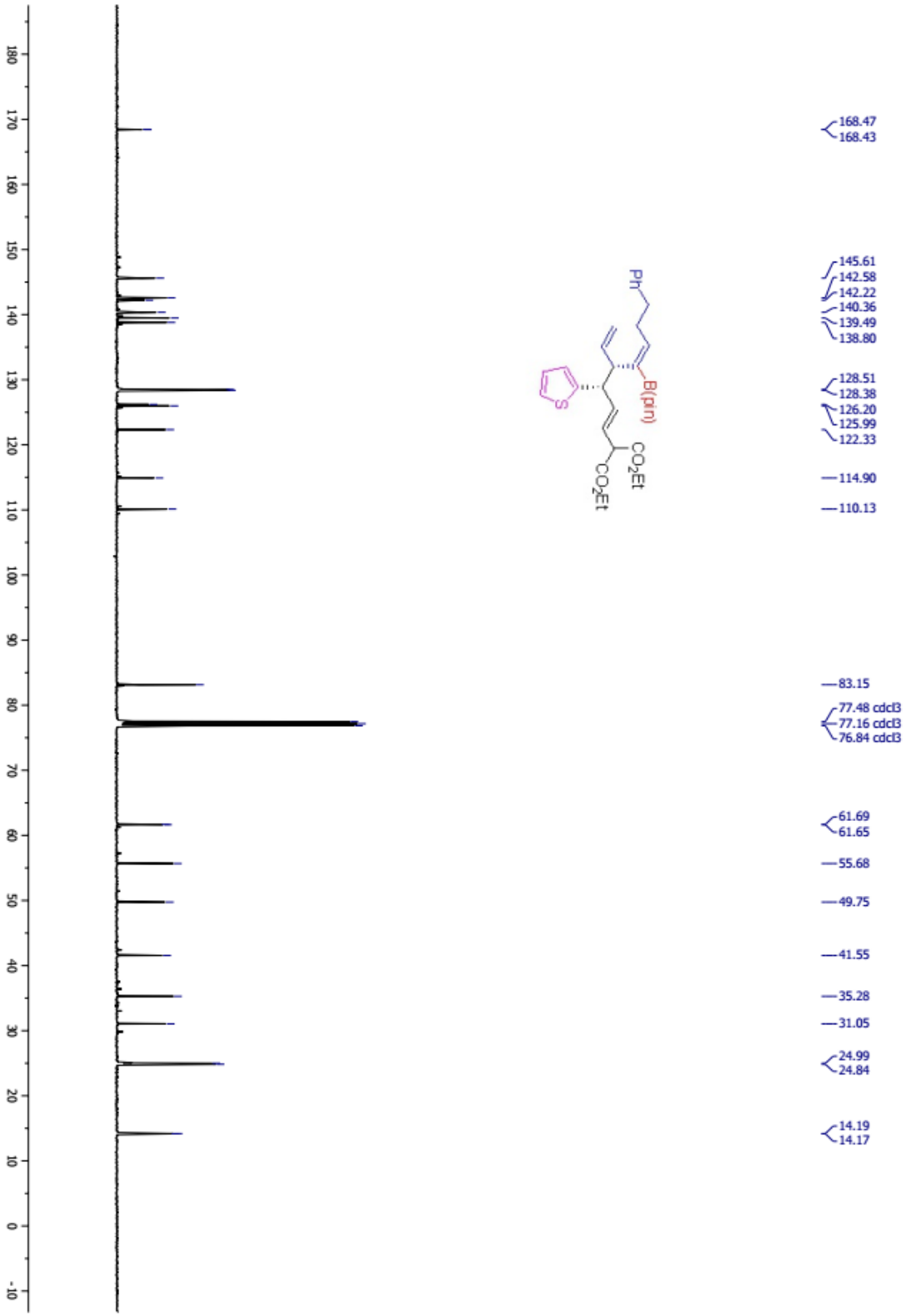
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CO2Et
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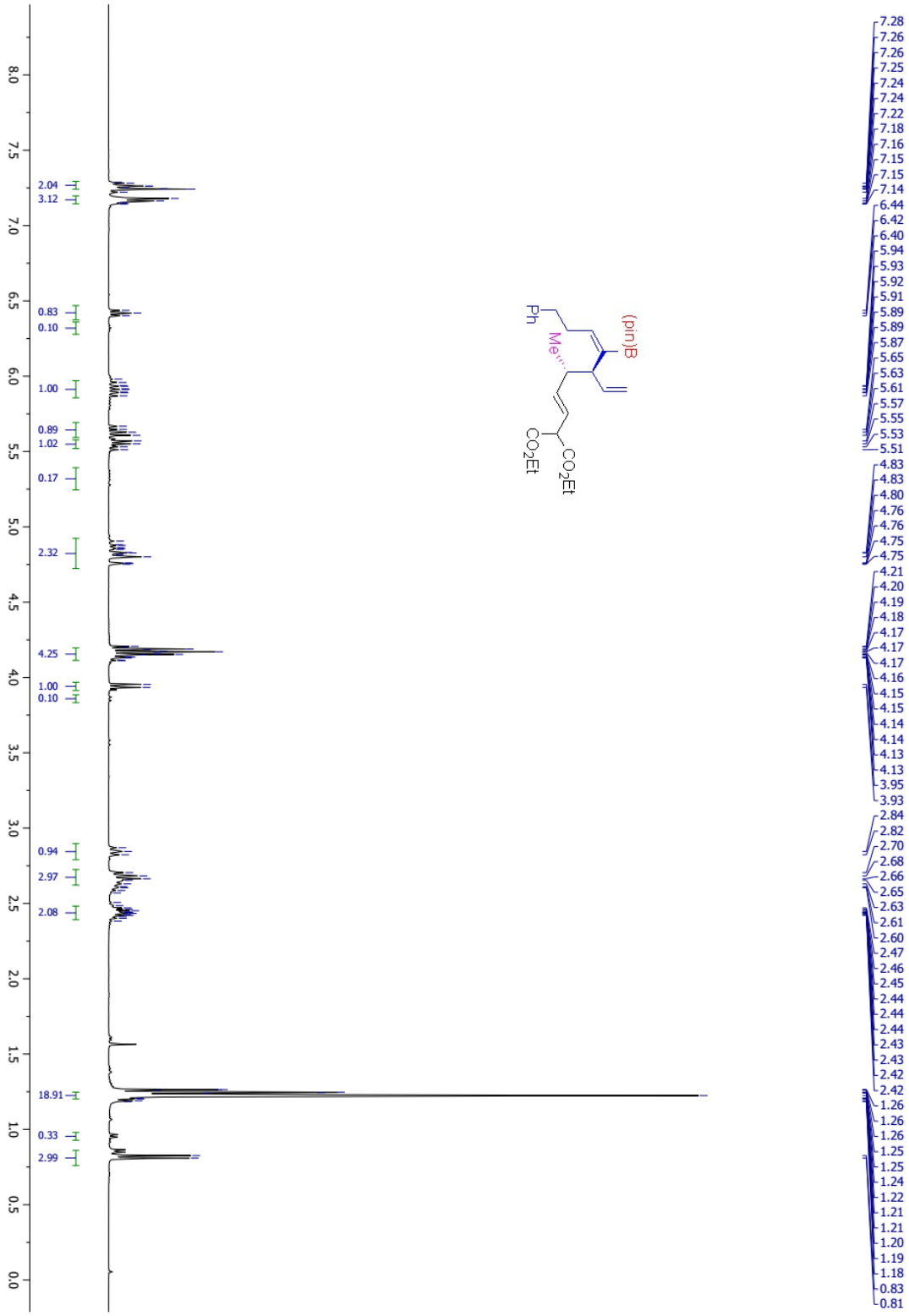
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CO2Et
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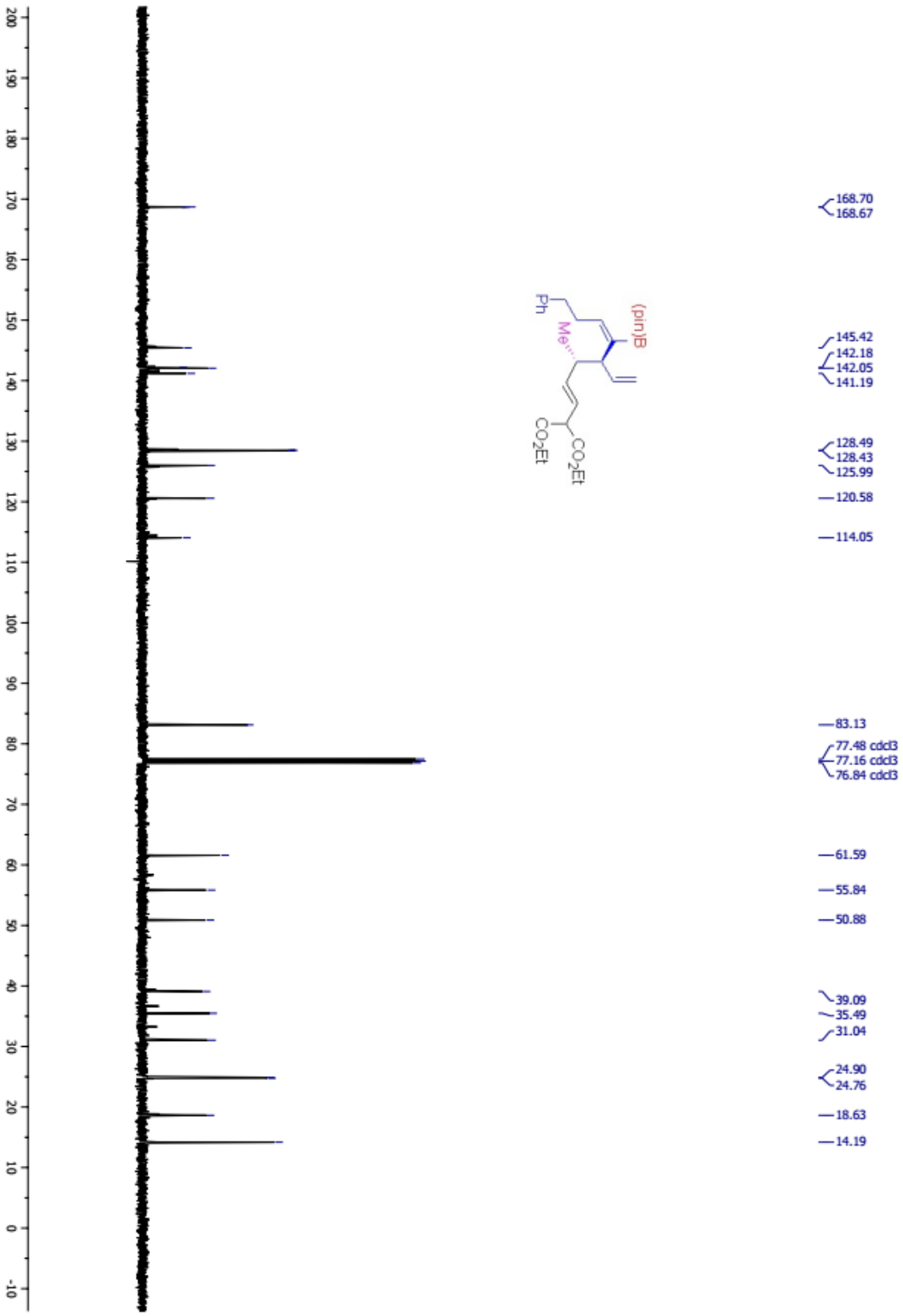
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Mg
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CO2Et
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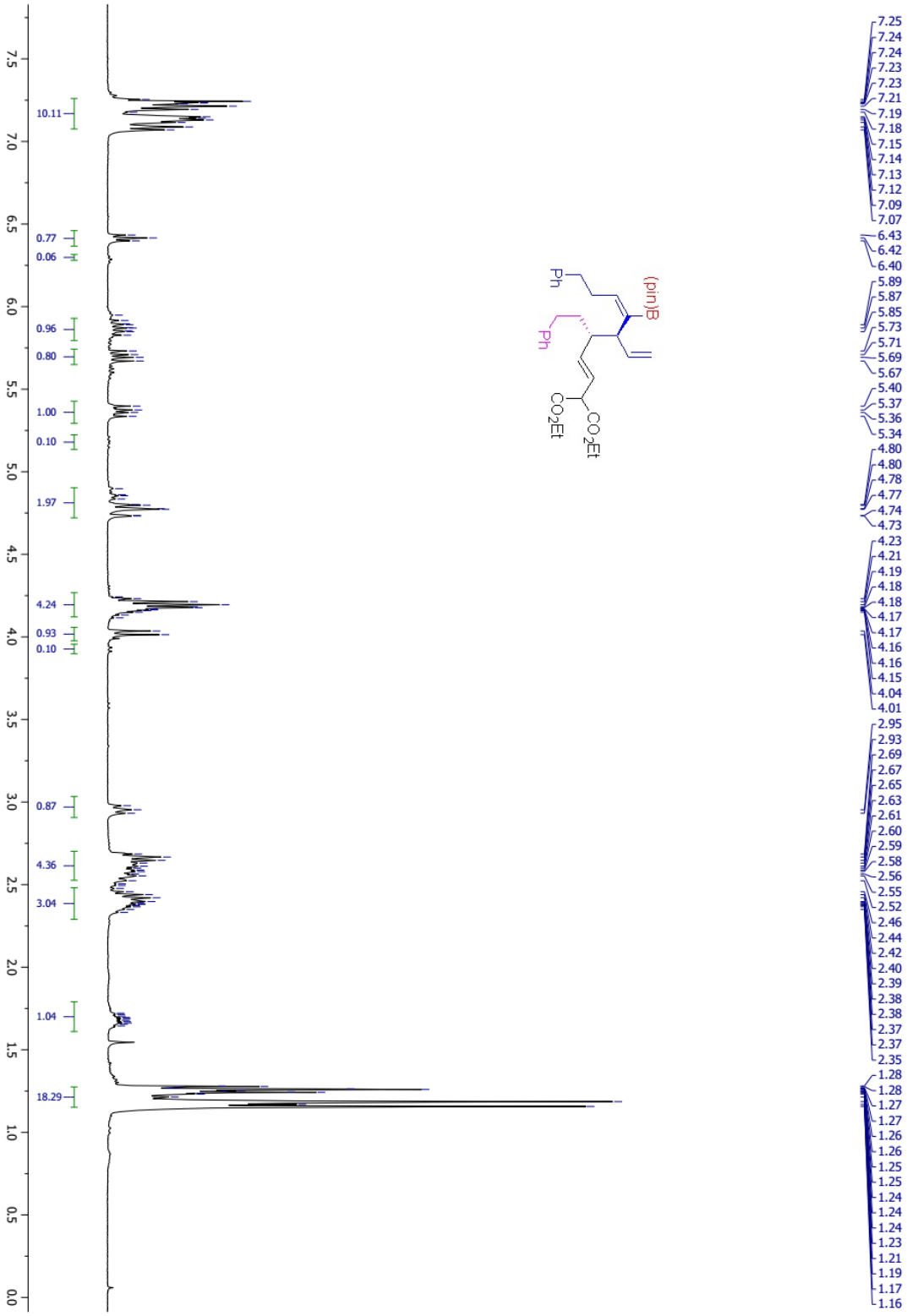
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CO2Et
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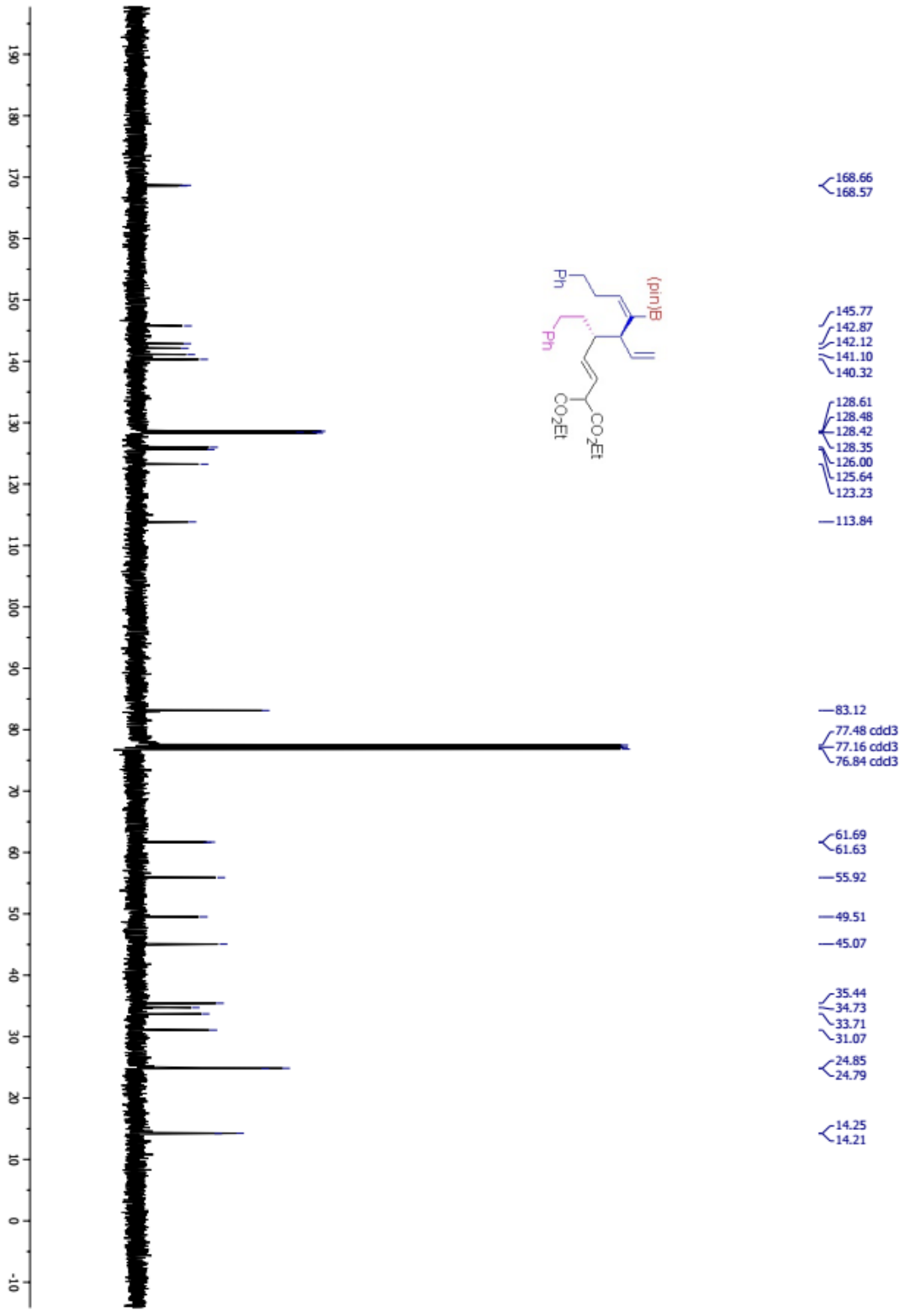
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-10
Ph
Ph
(pin)B
CO2Et
CO2Et
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141.10
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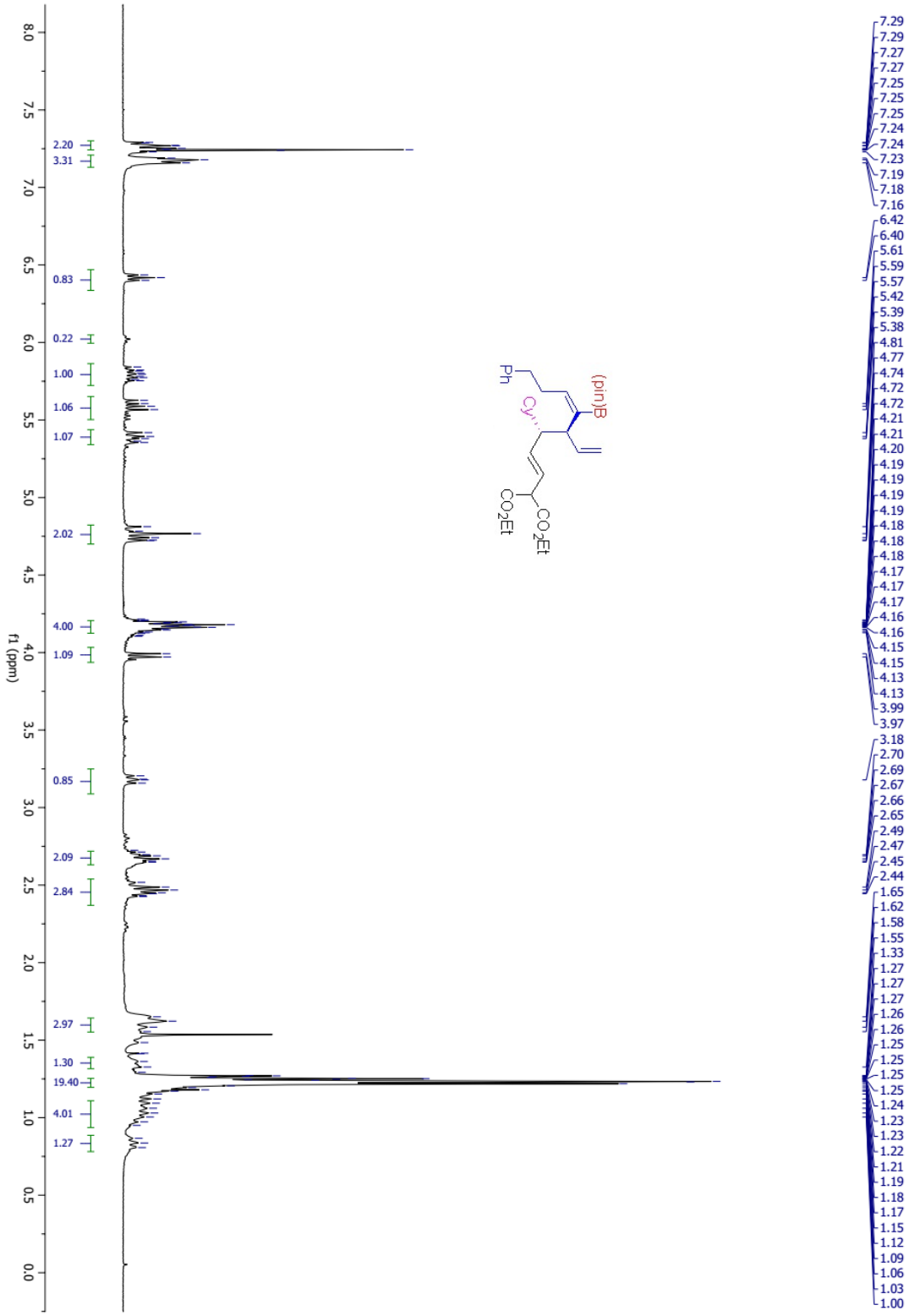
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Ph
Cy
(pin)B
CO2Et
CO2Et
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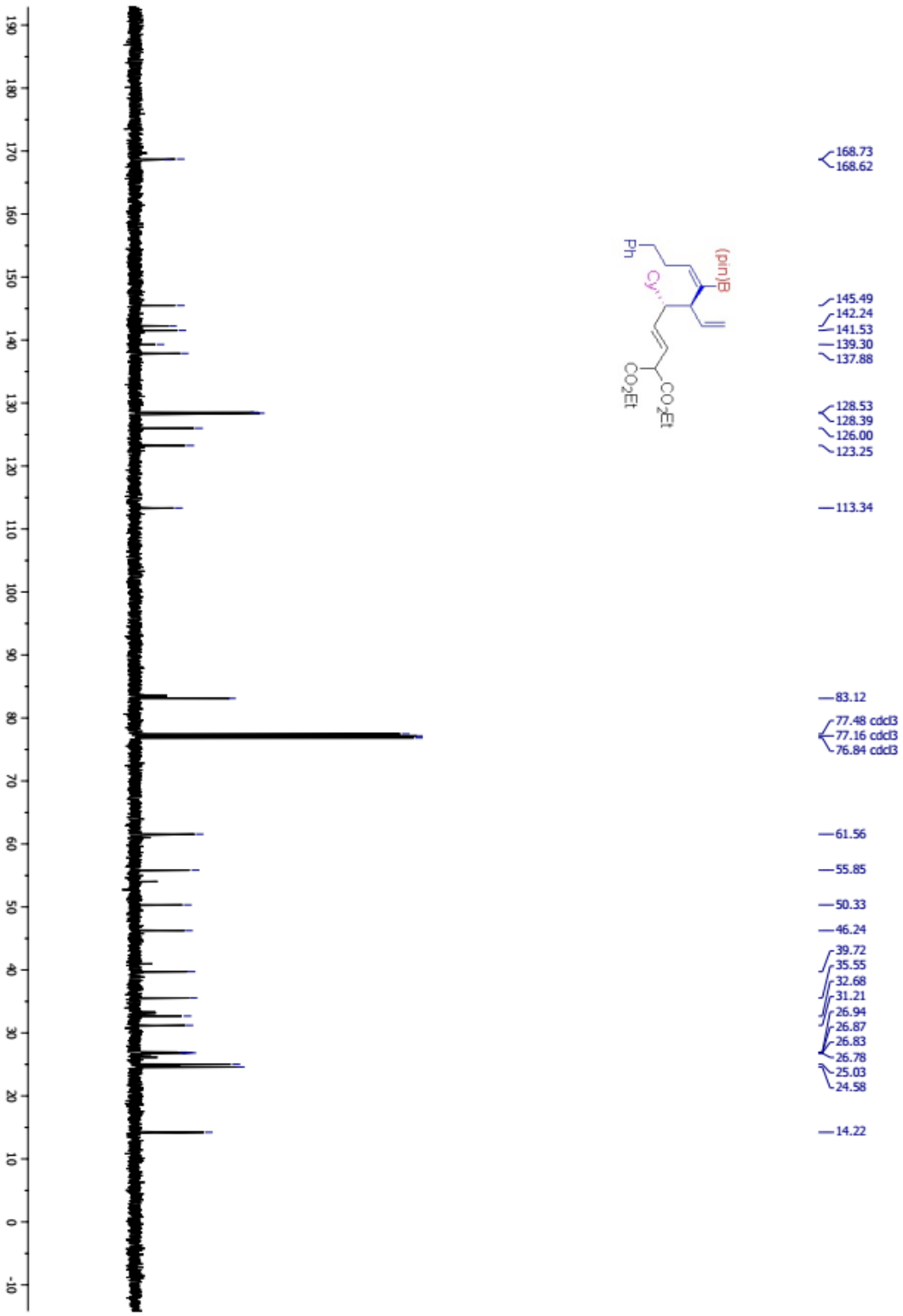
1.03
1.00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-10
(pin)B
Cy
Ph
CO2Et
CO2Et
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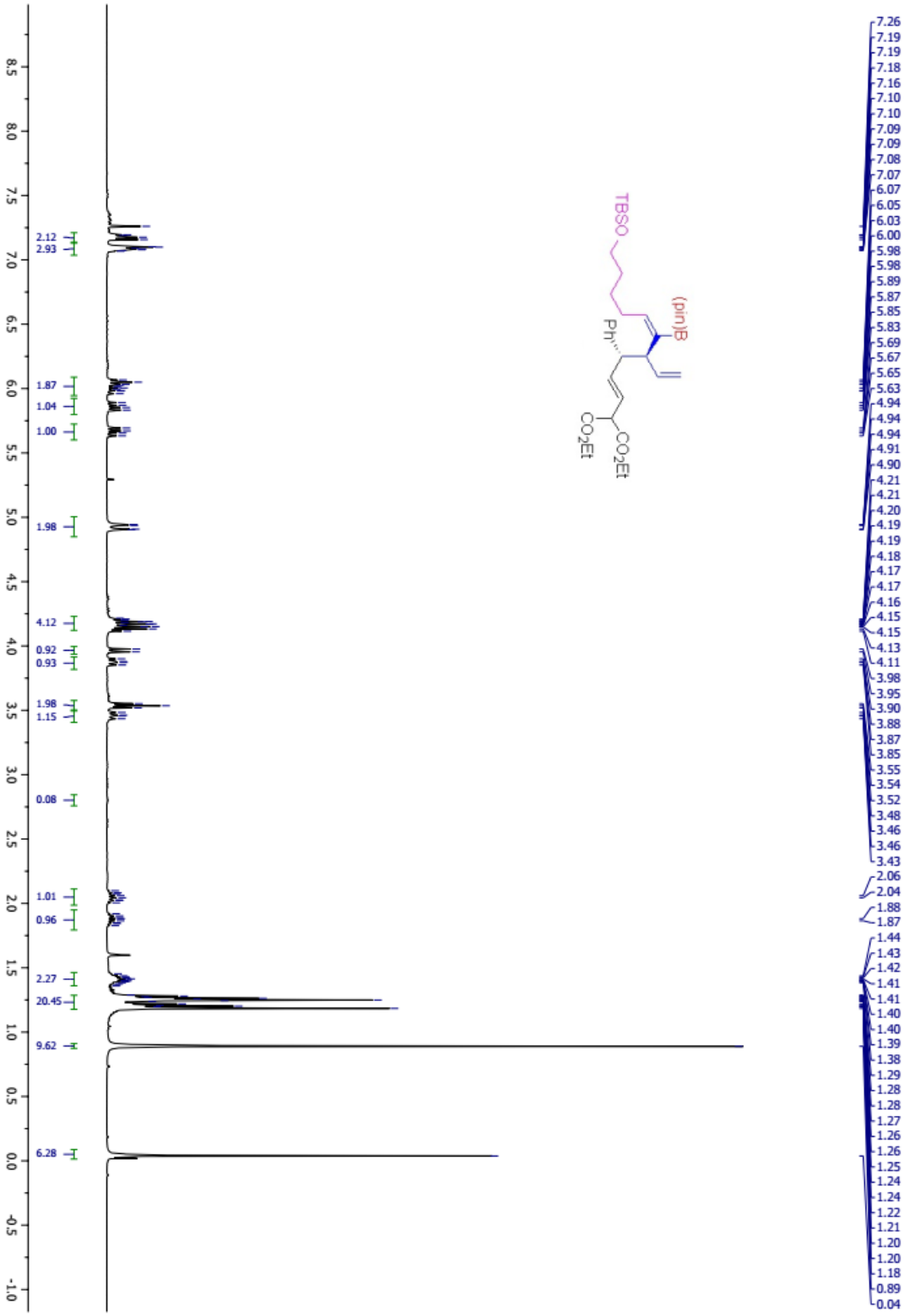
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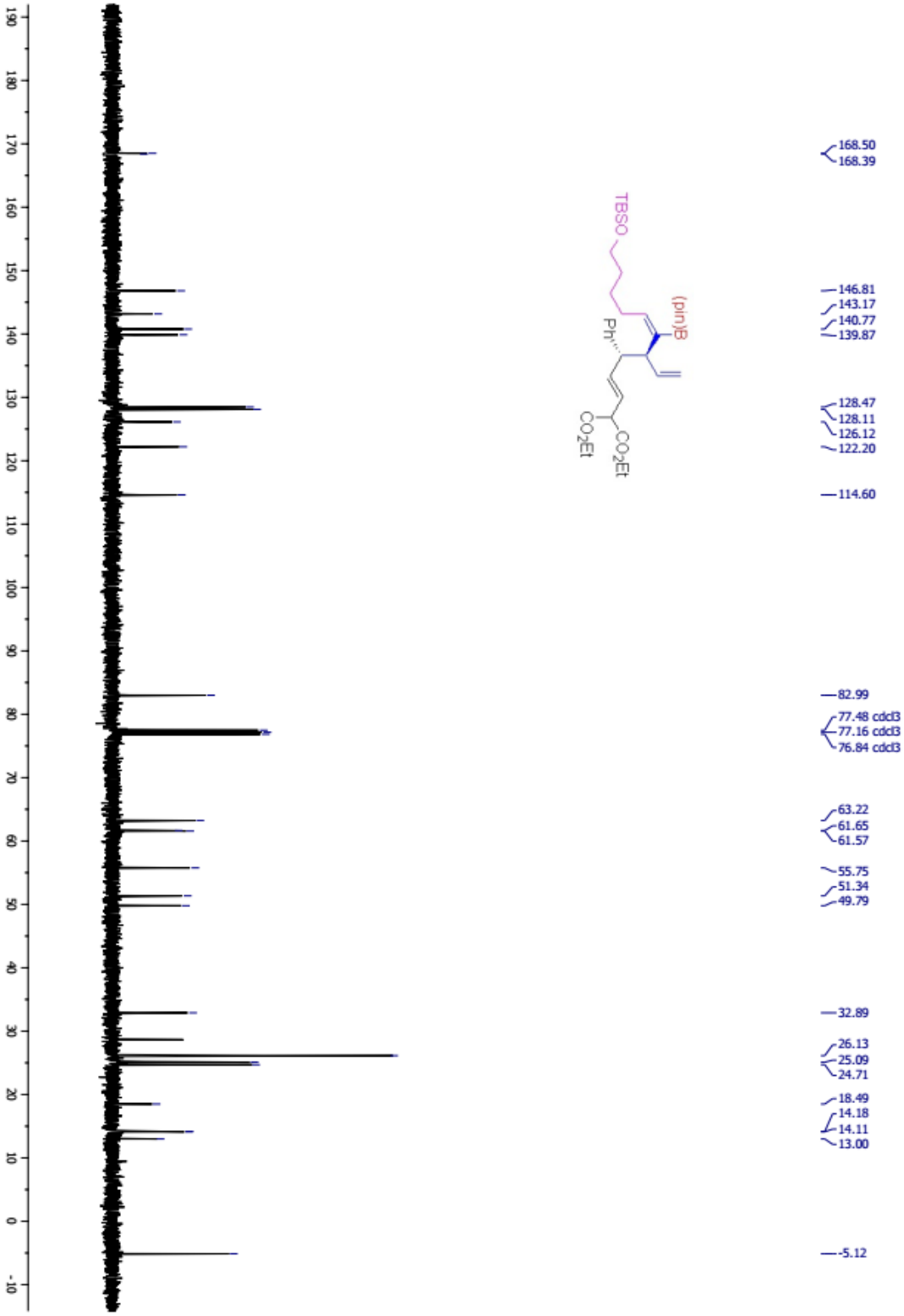
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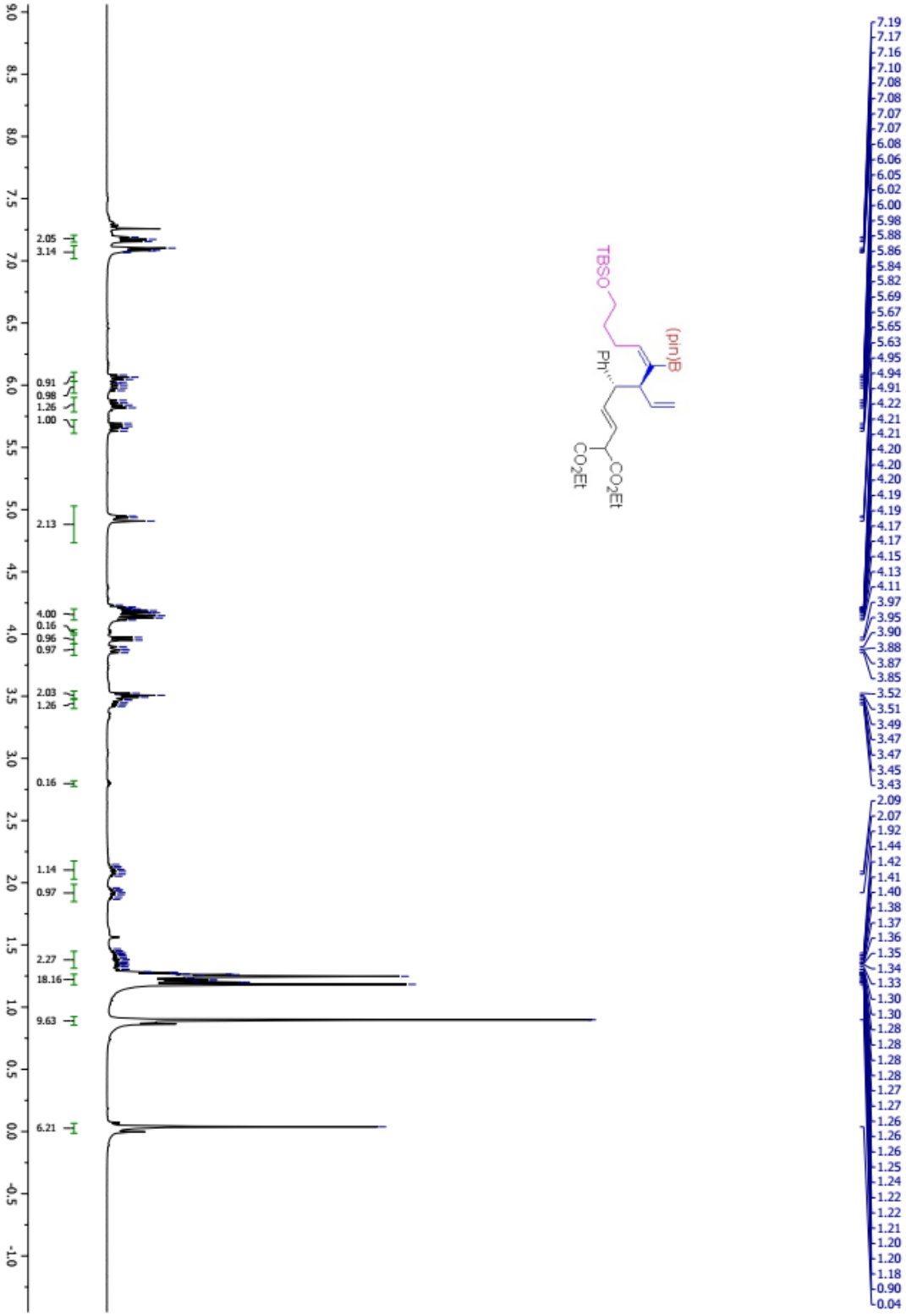
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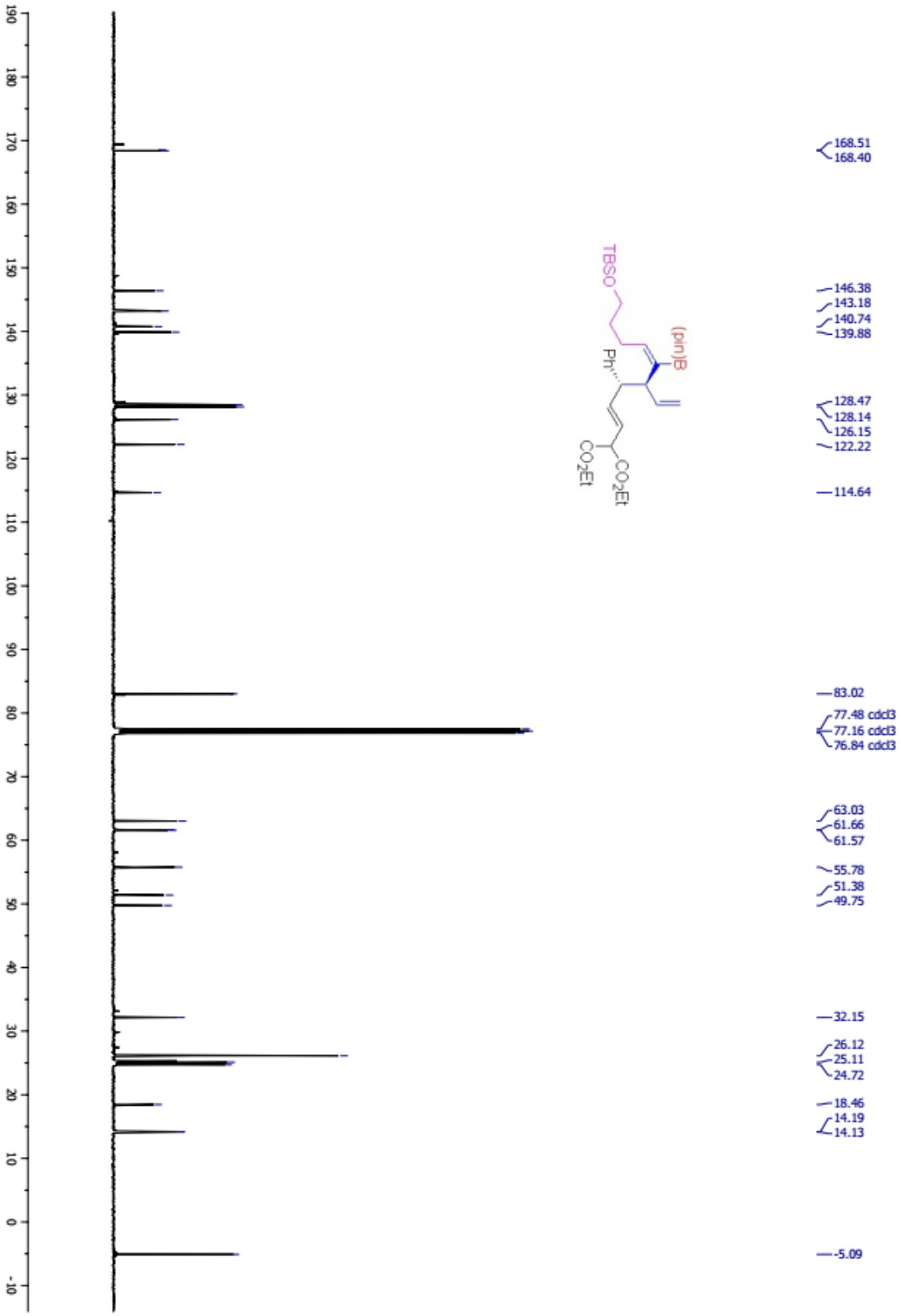
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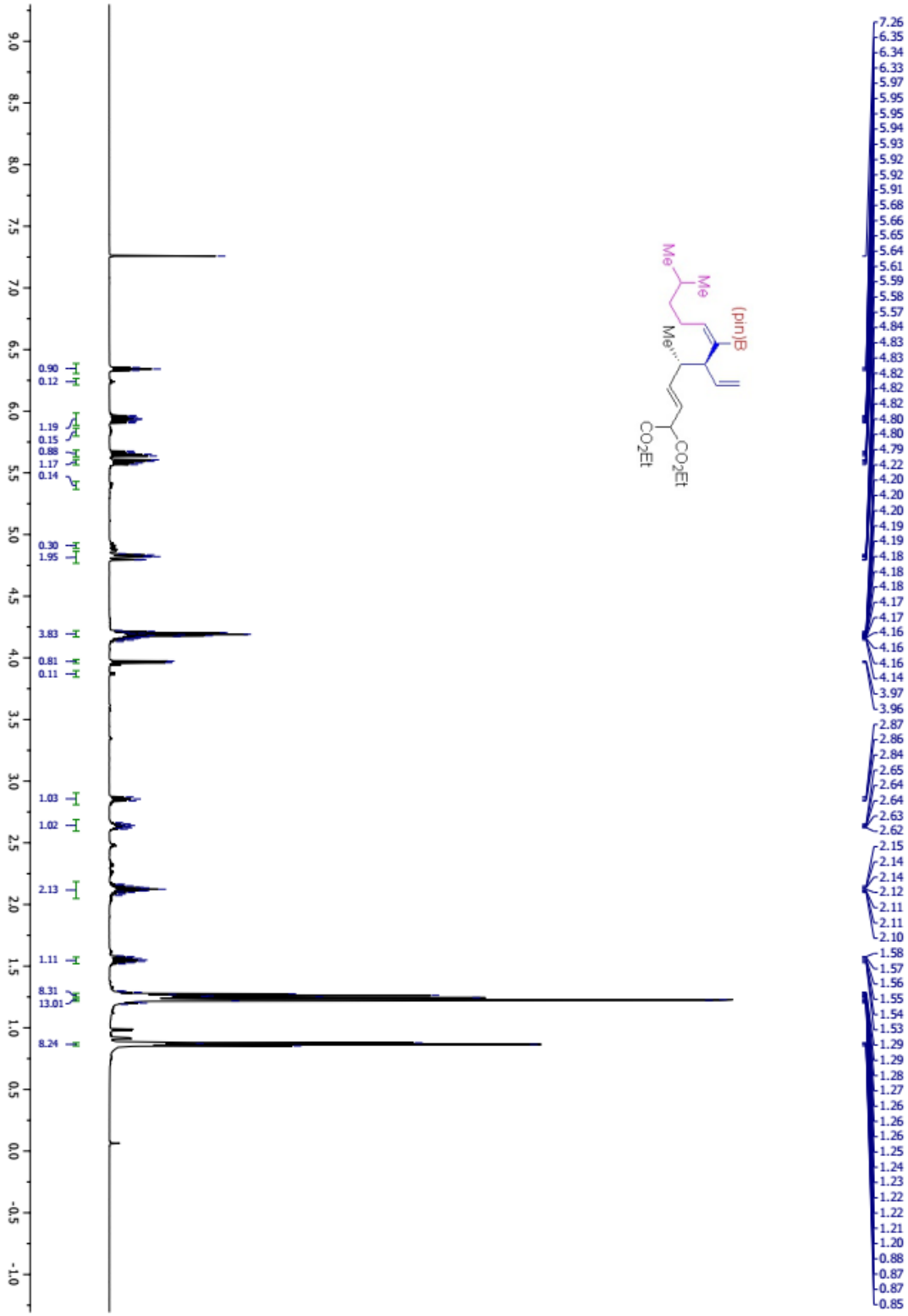
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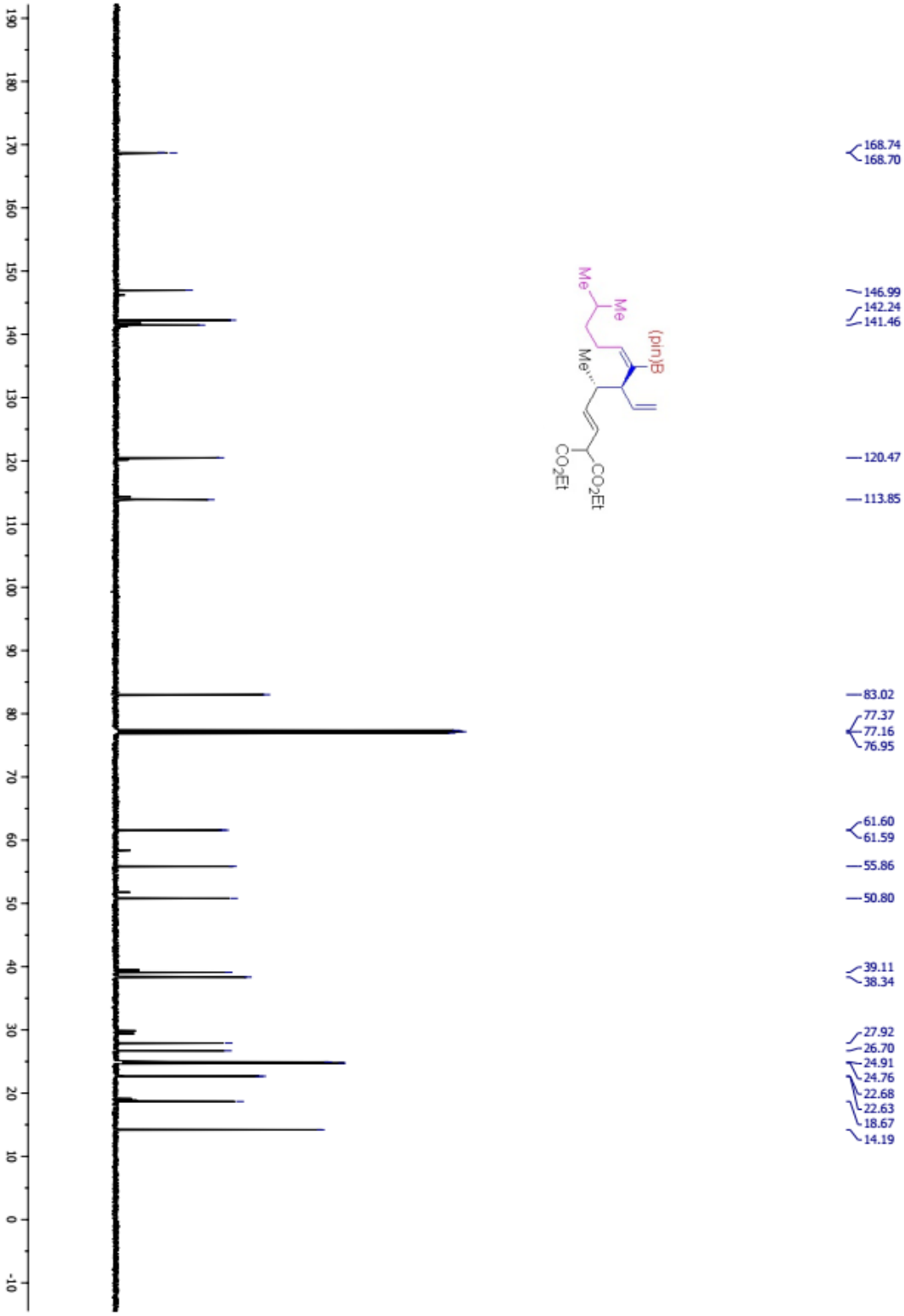
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Me
Me
(pin)B
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CO2Et
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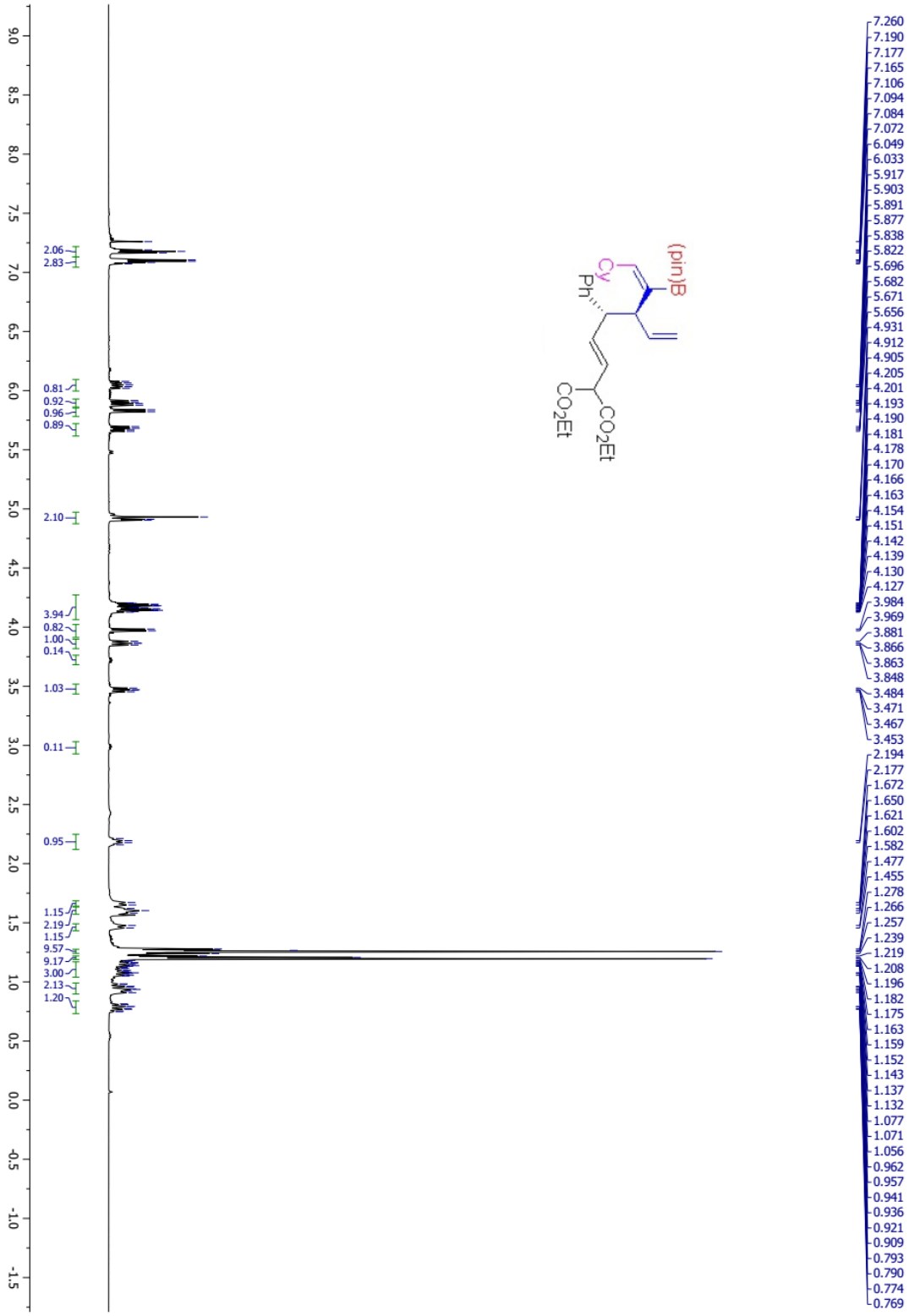
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Ph
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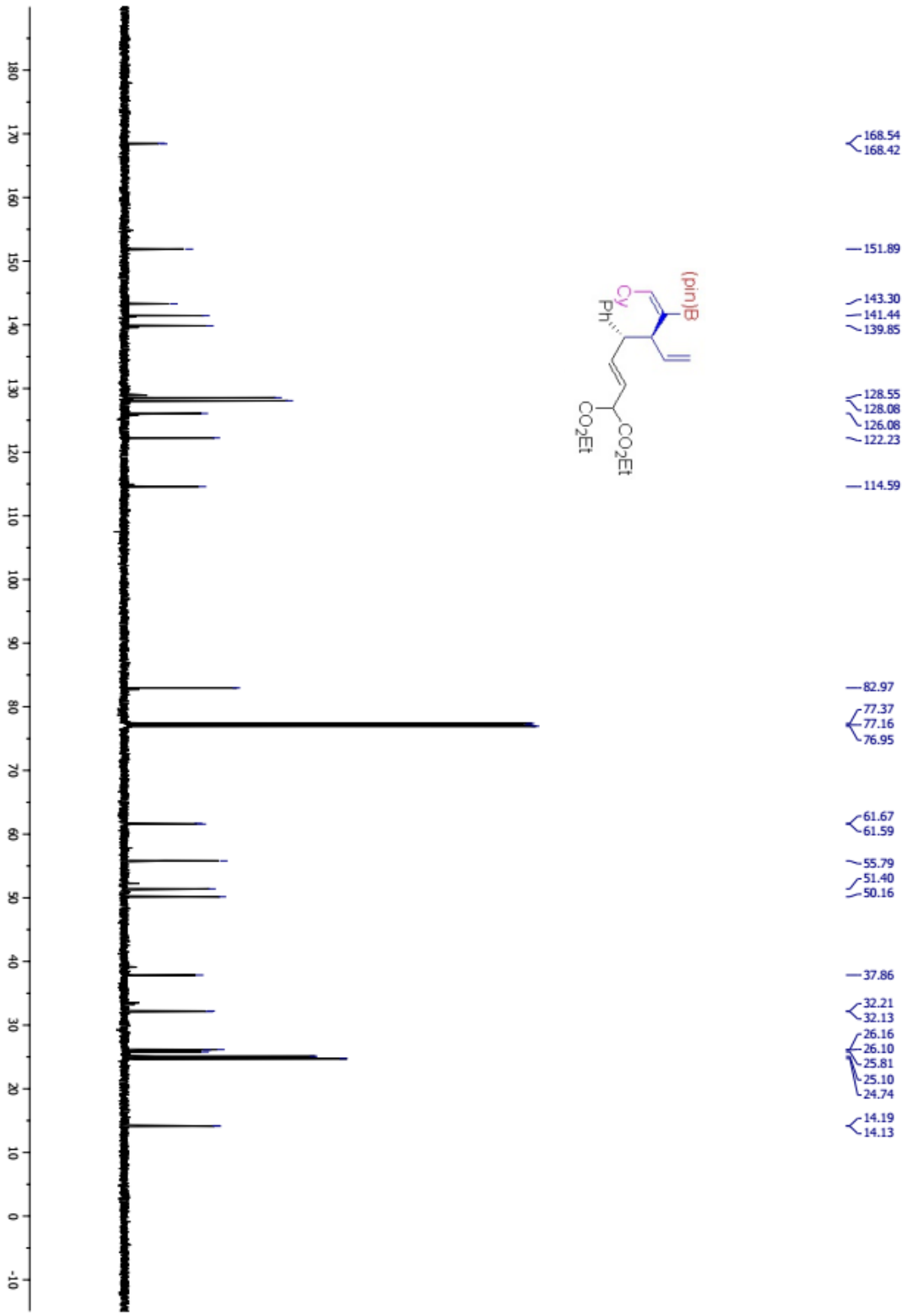
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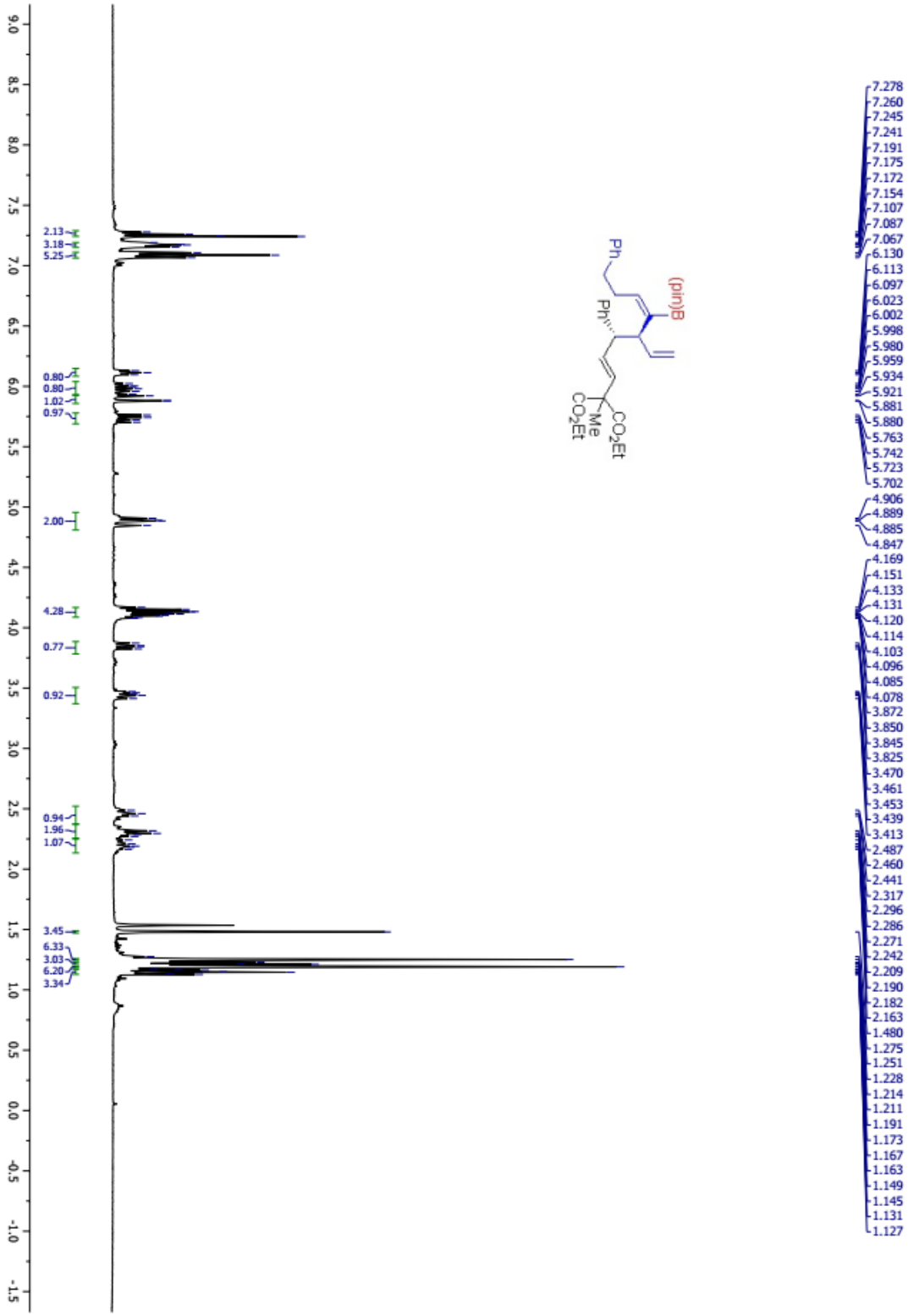
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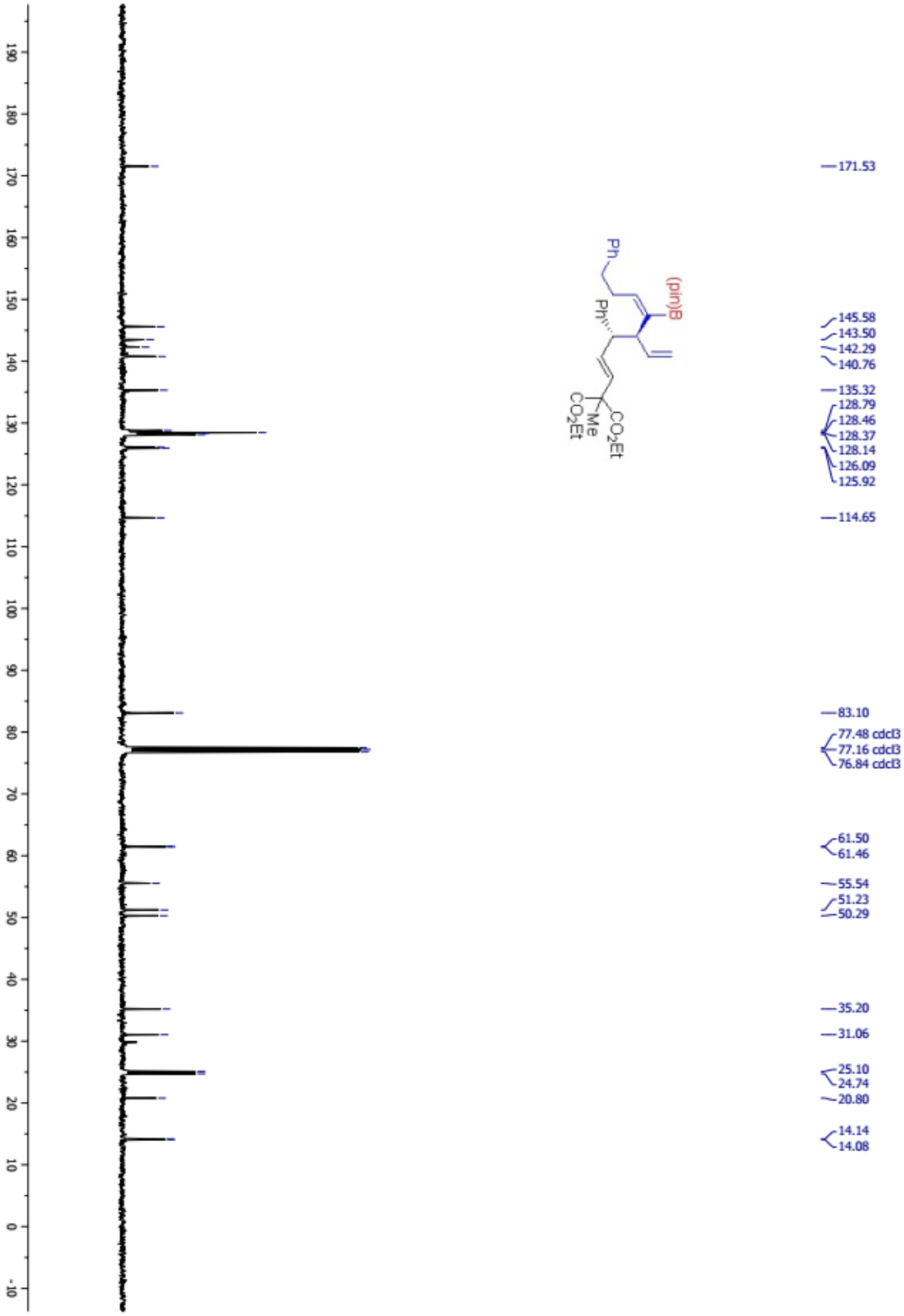
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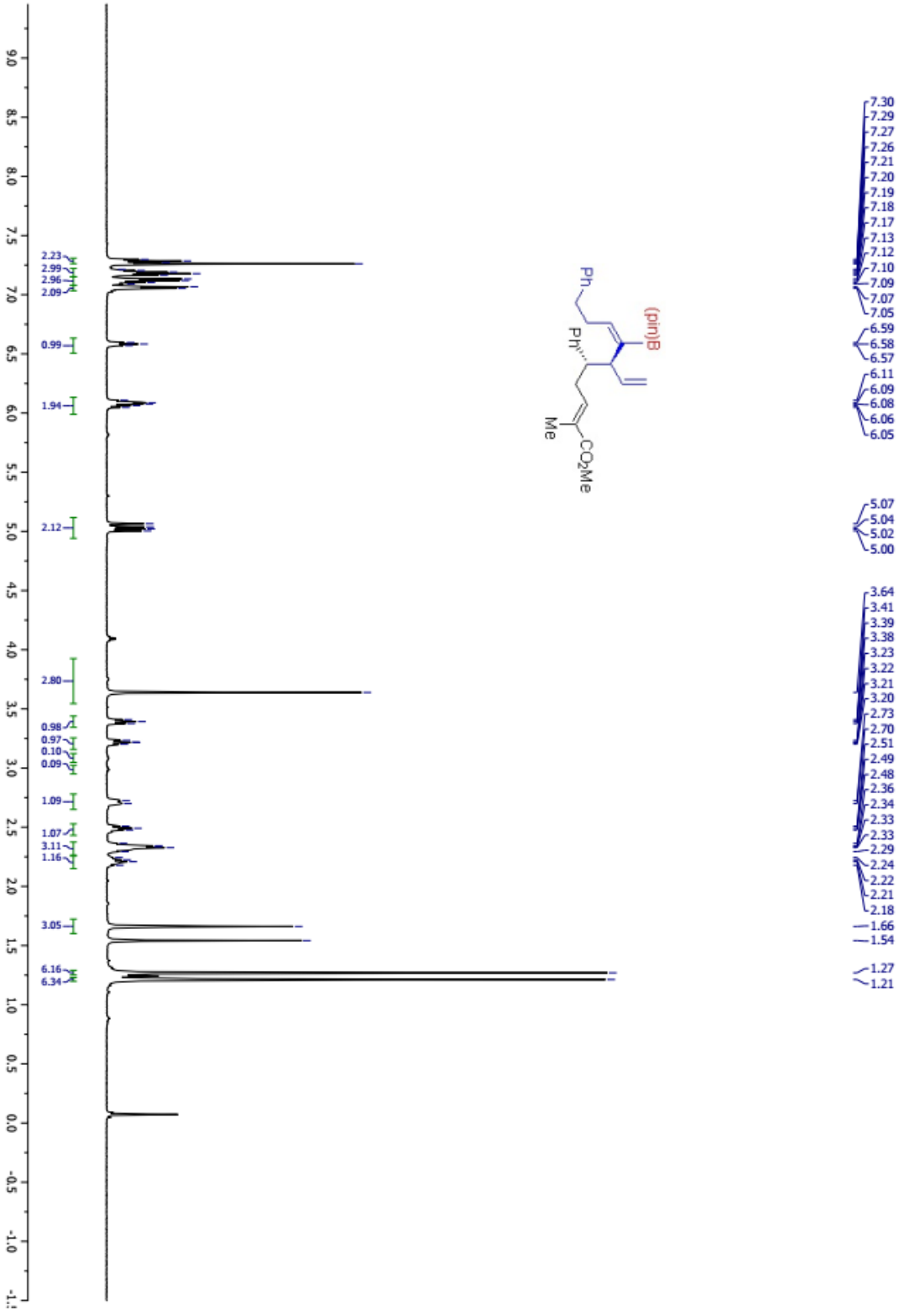
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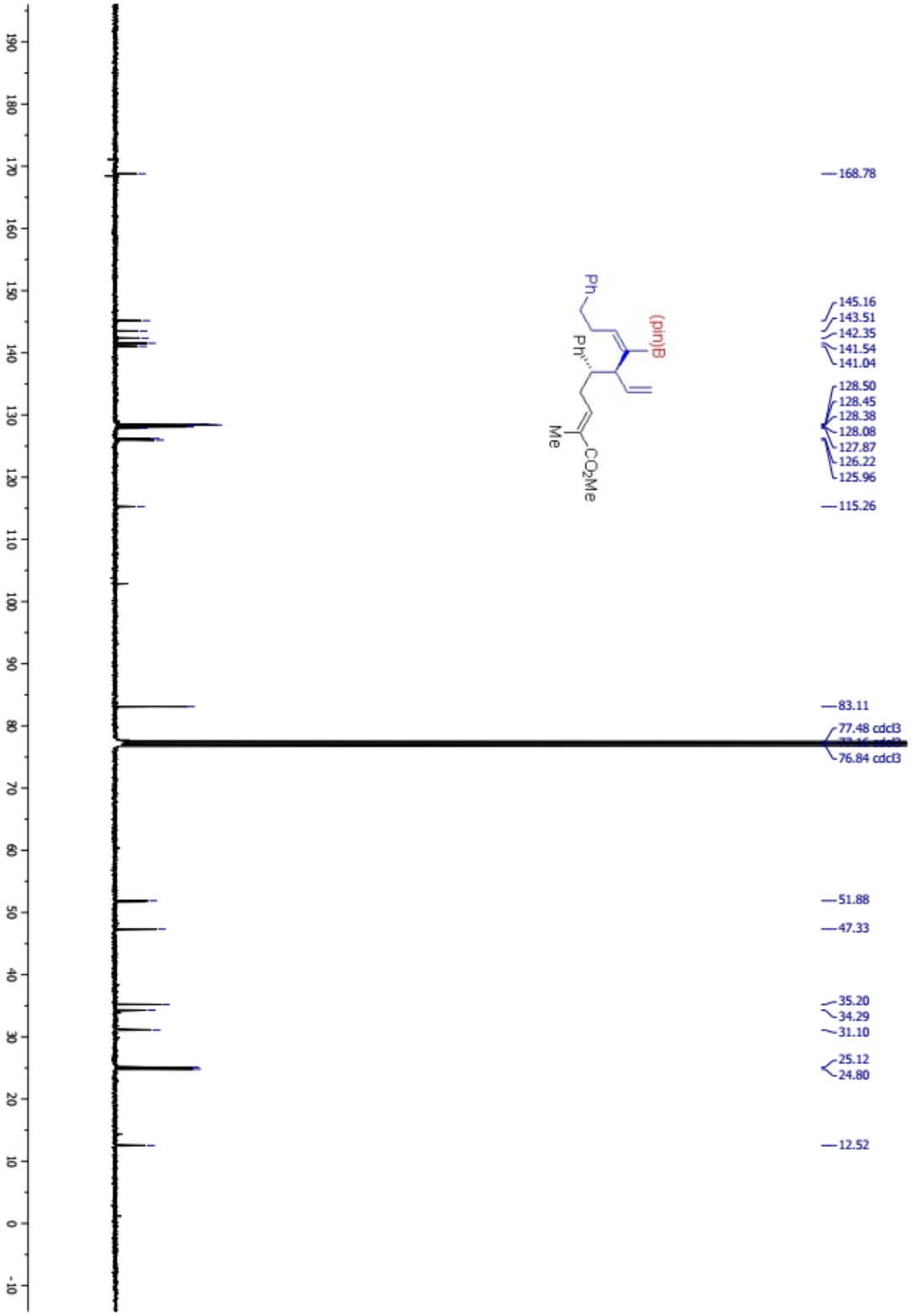
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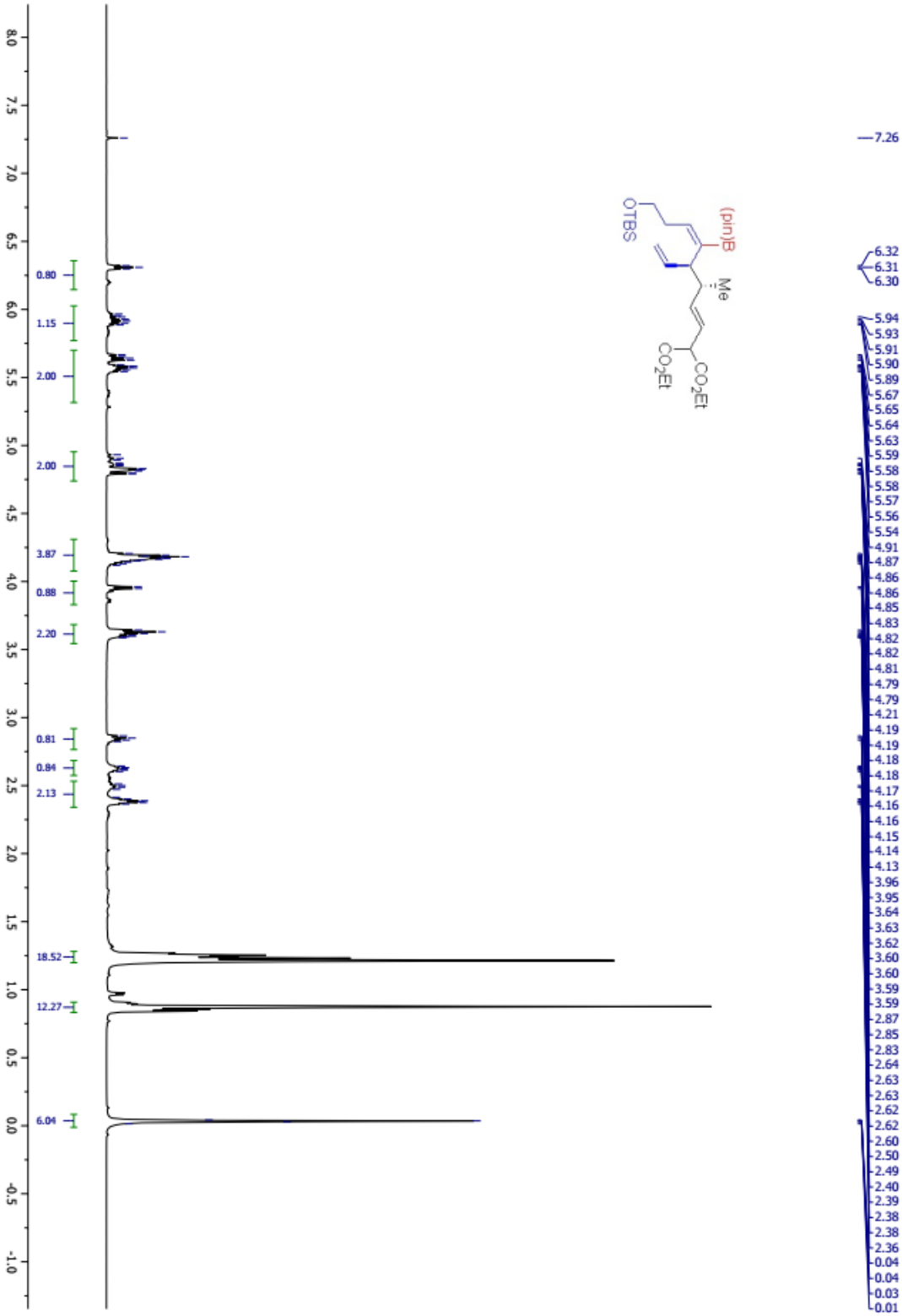
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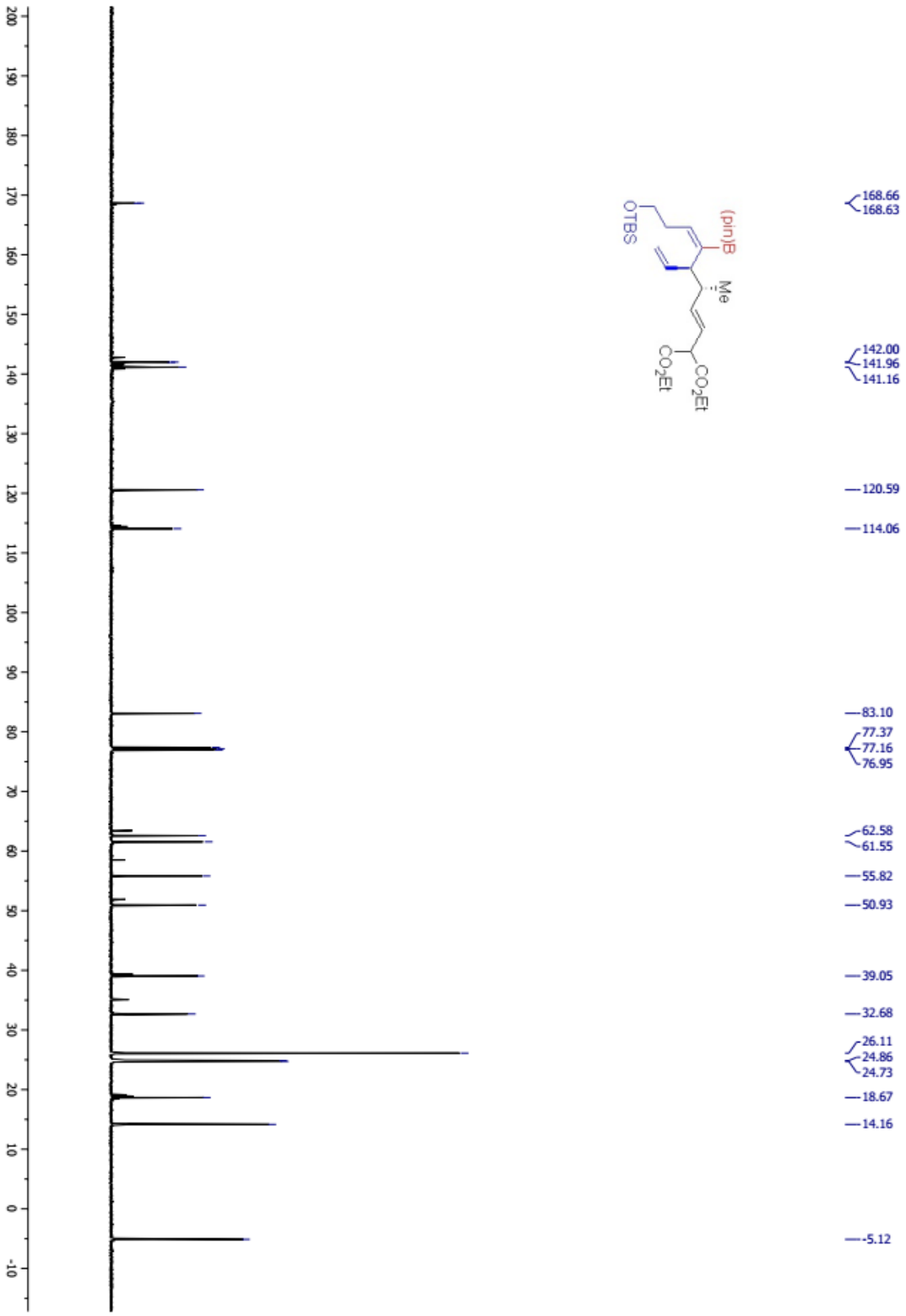
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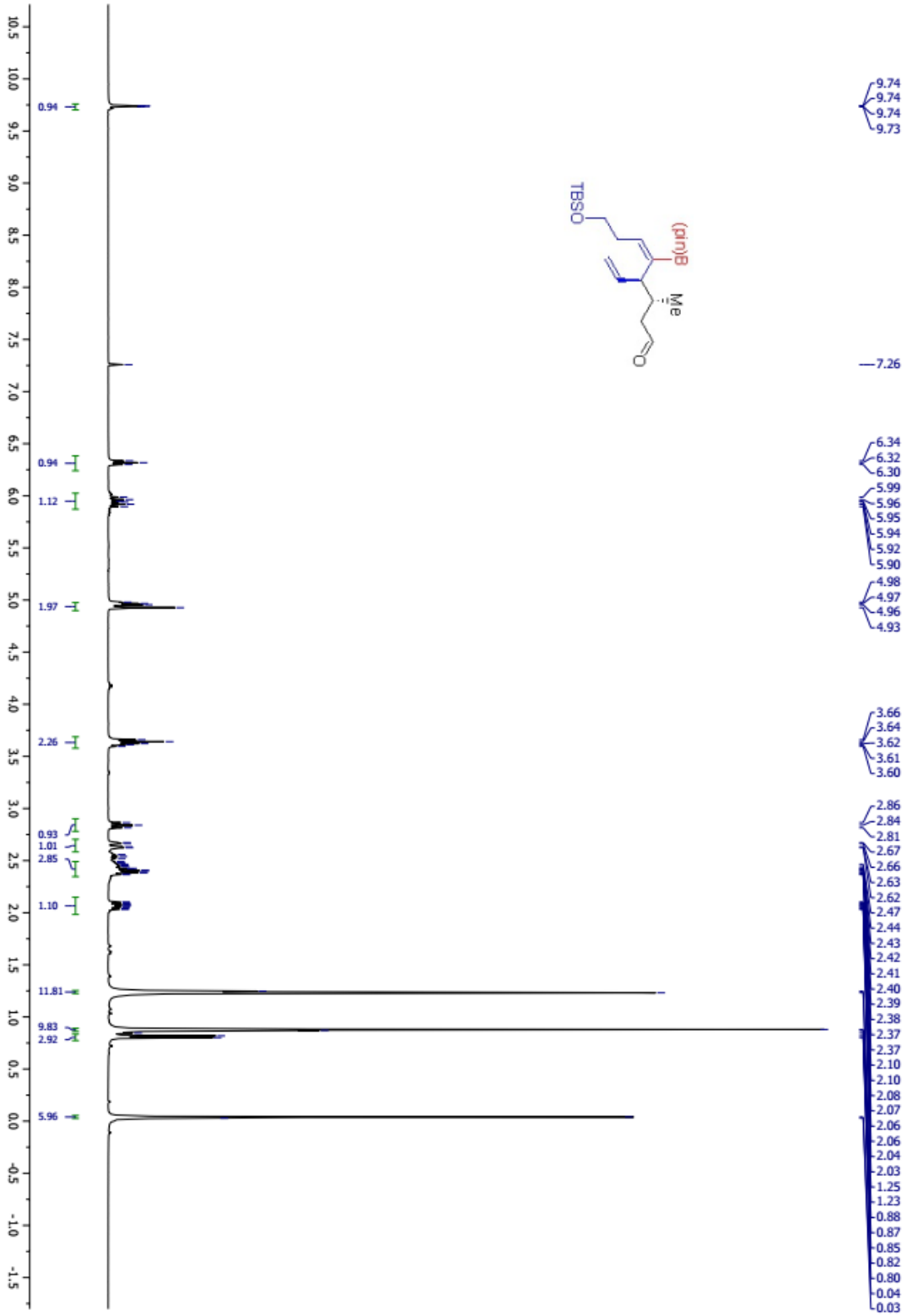
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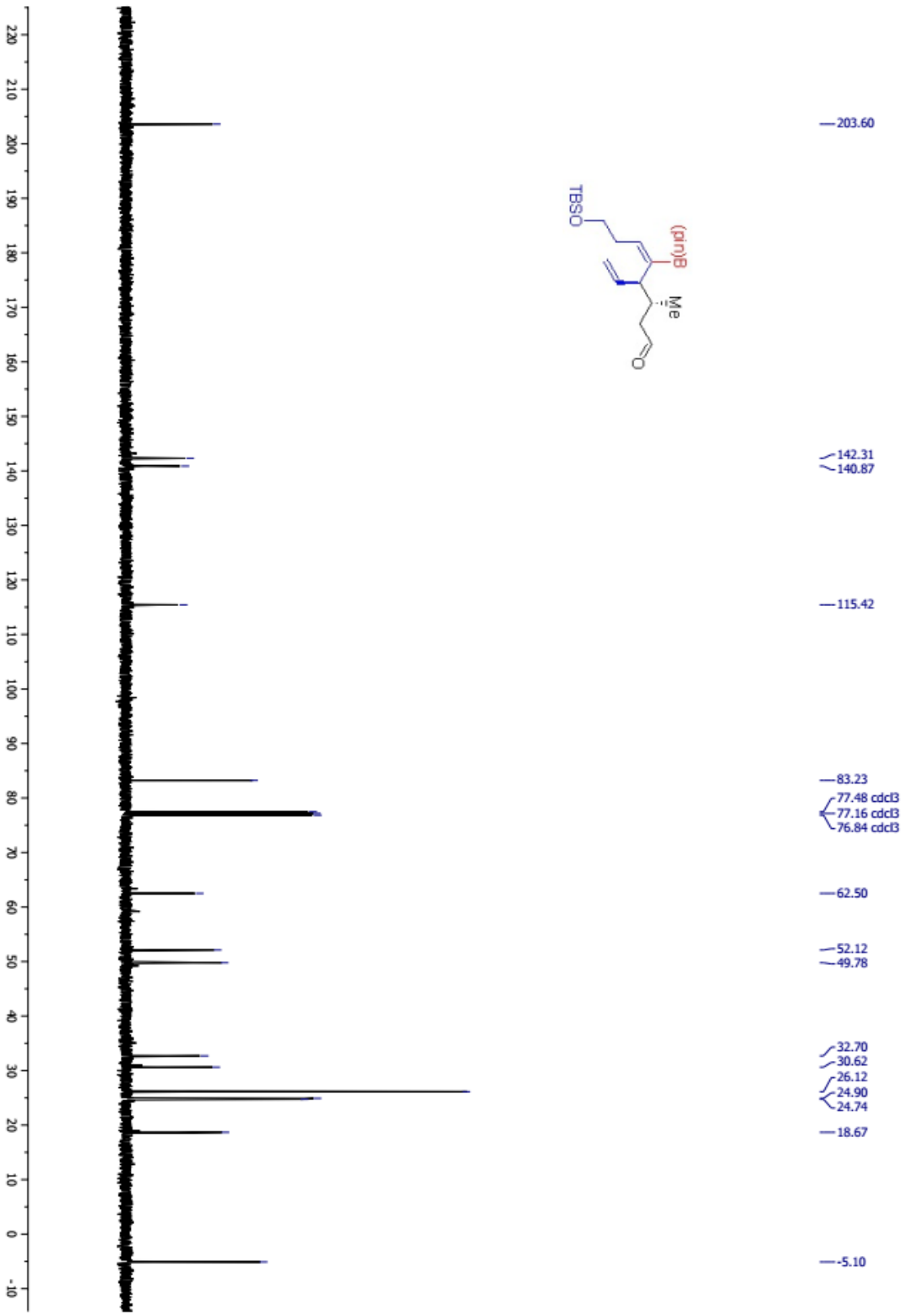
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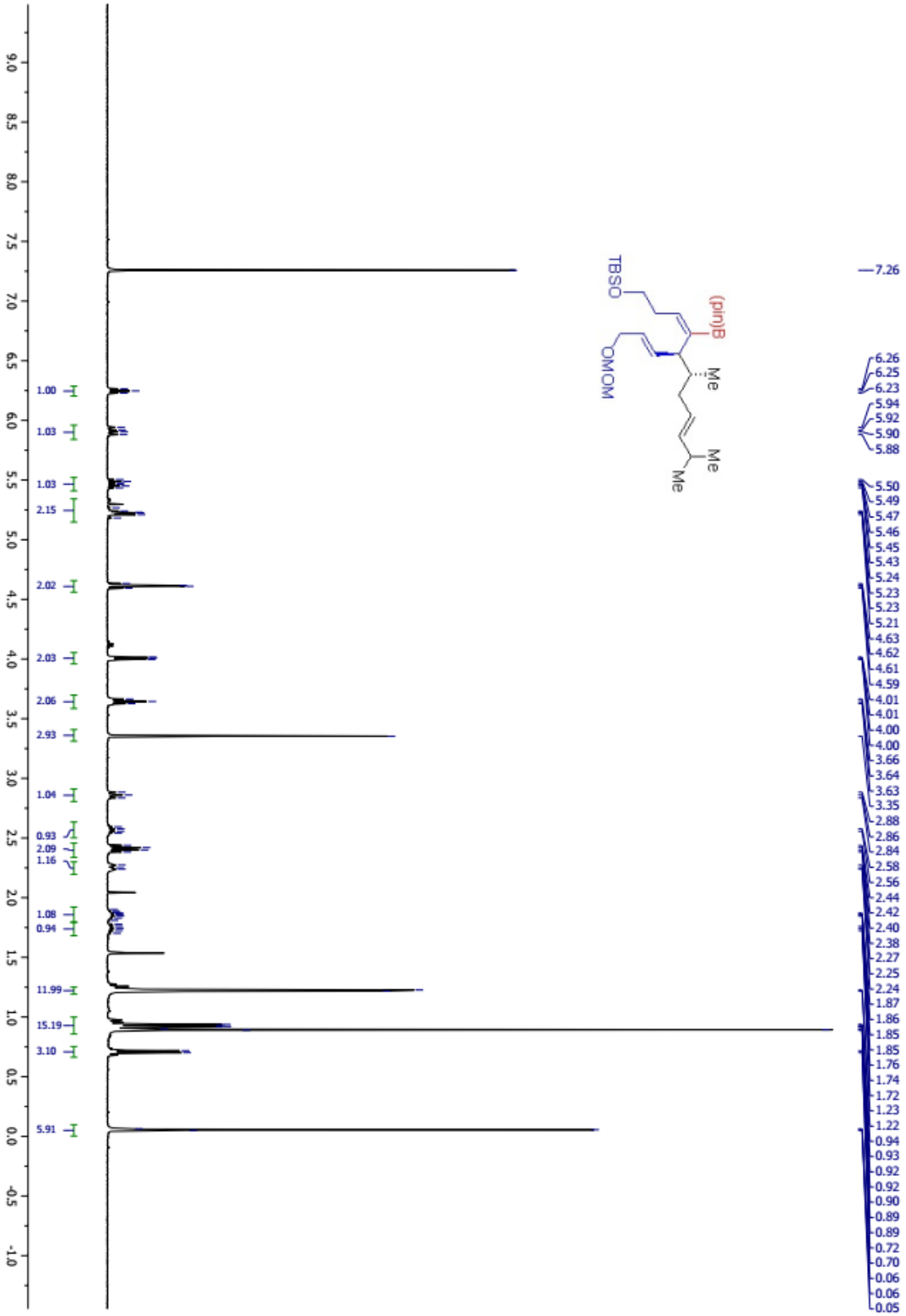
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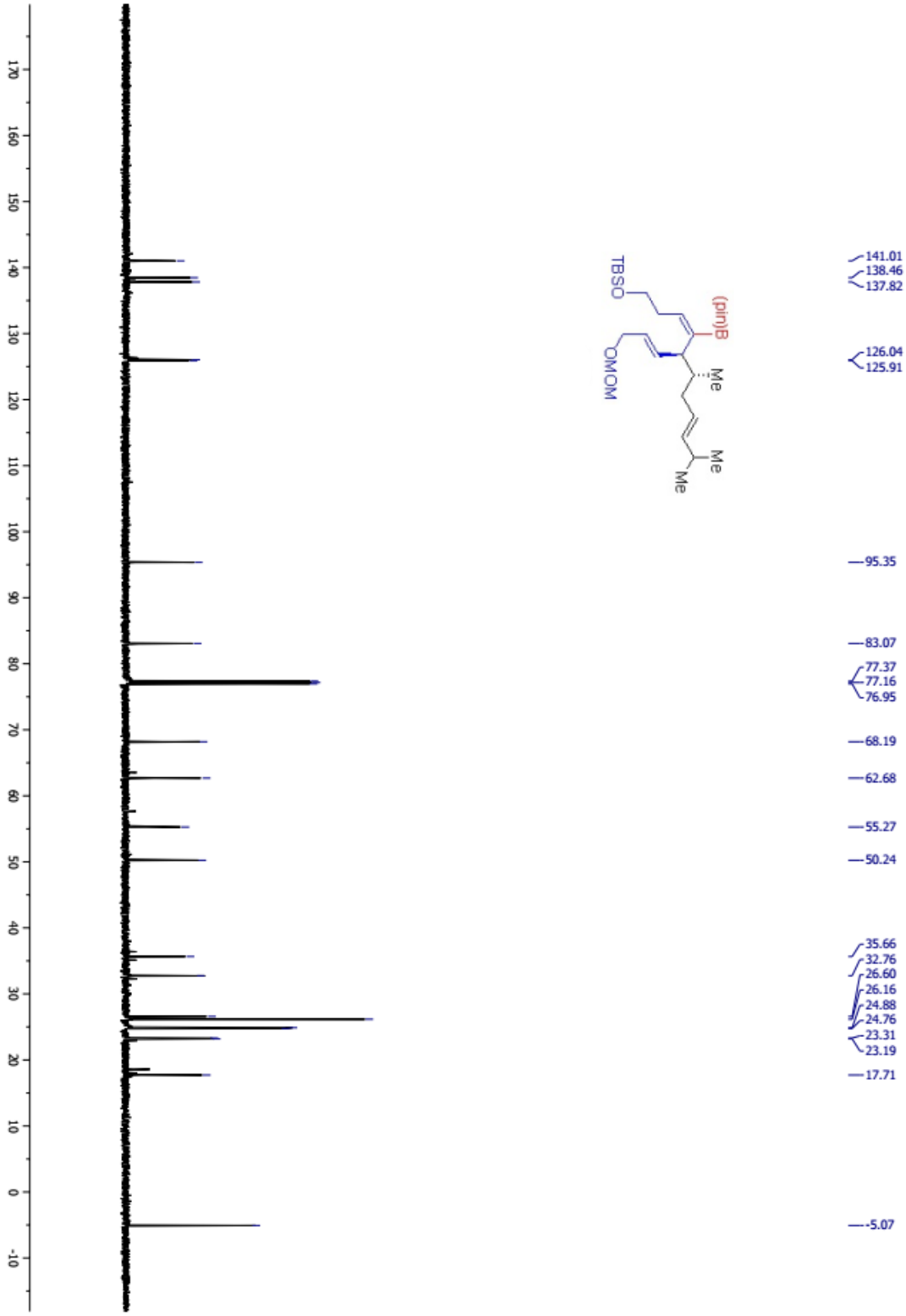
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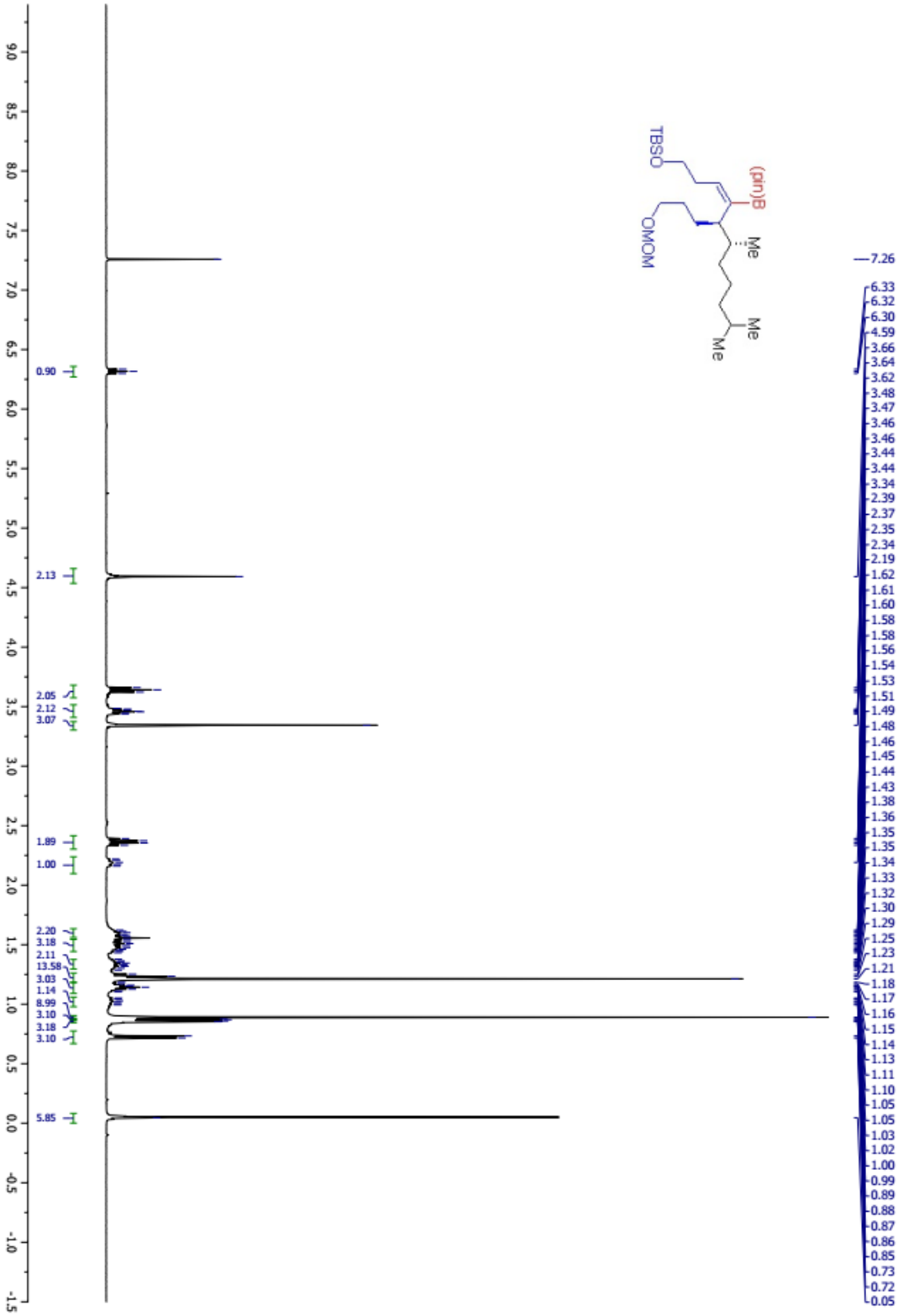
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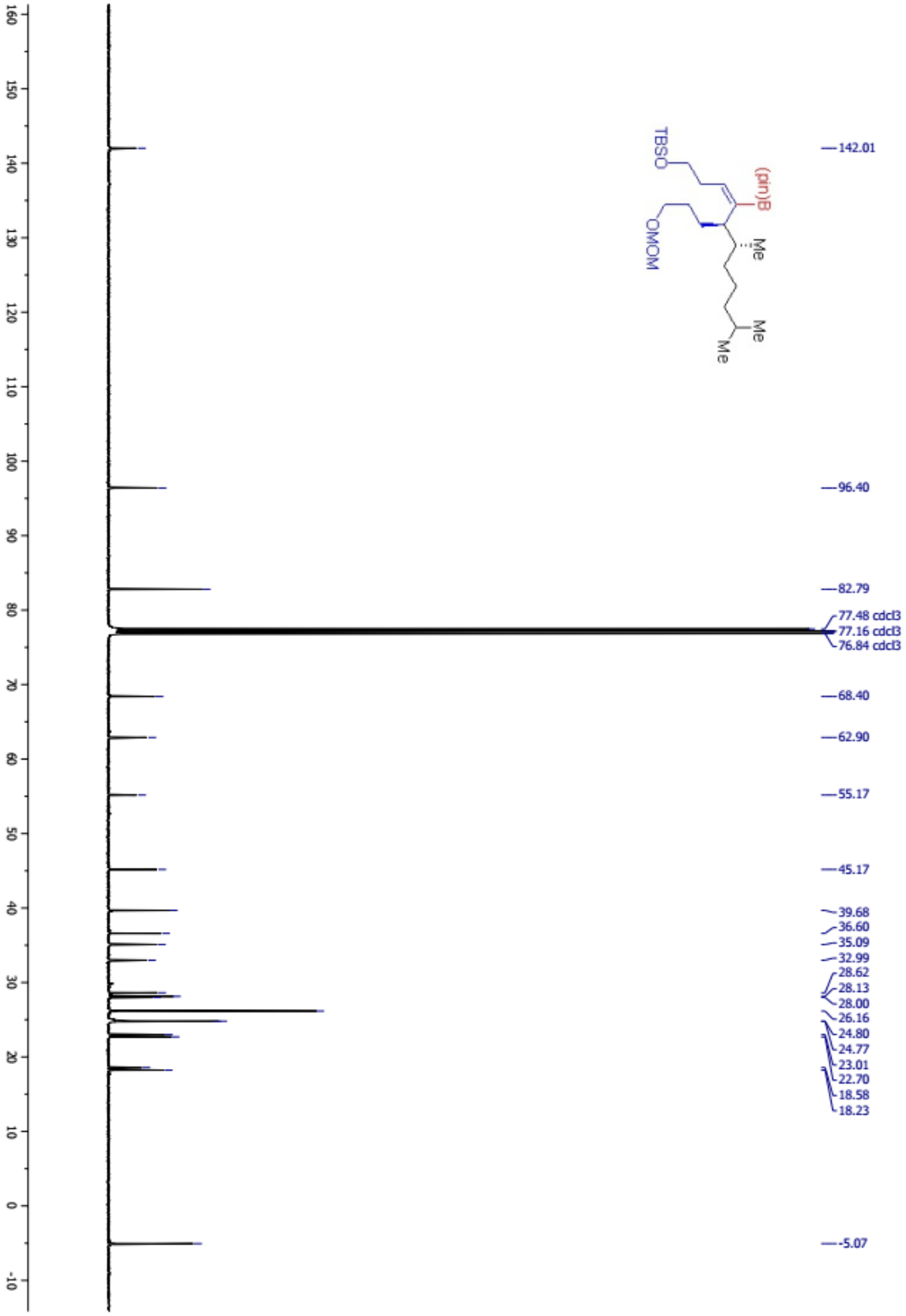
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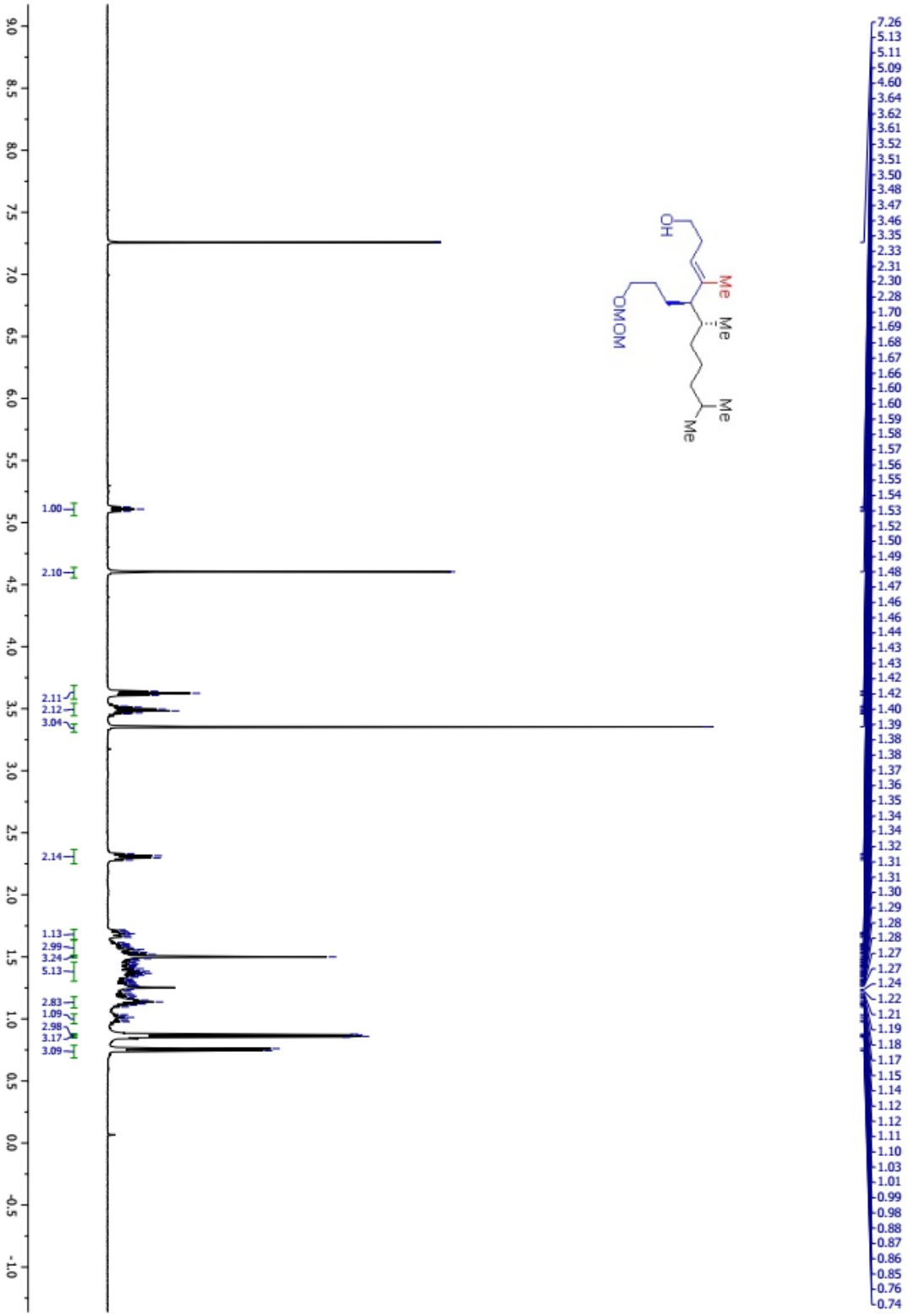
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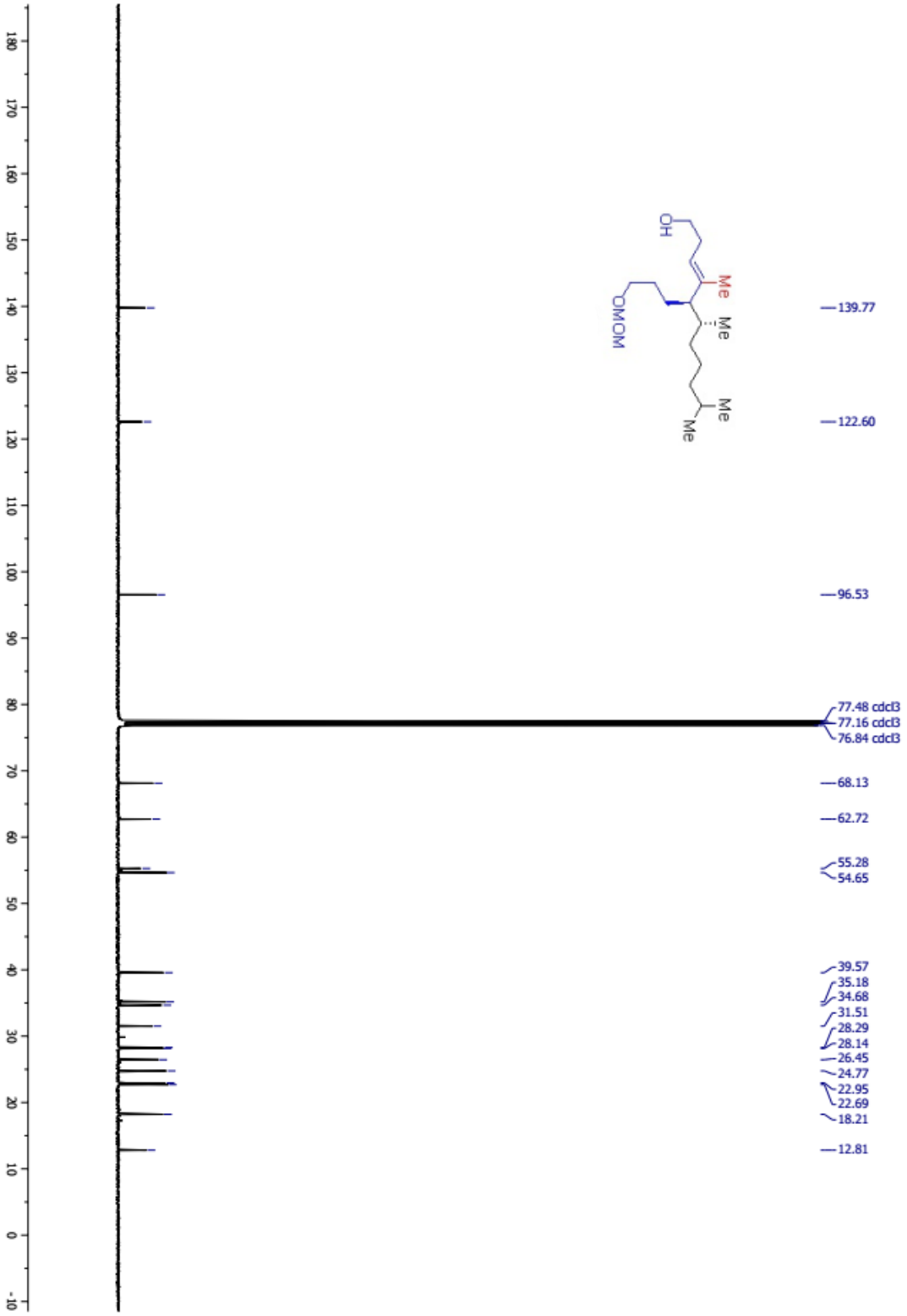
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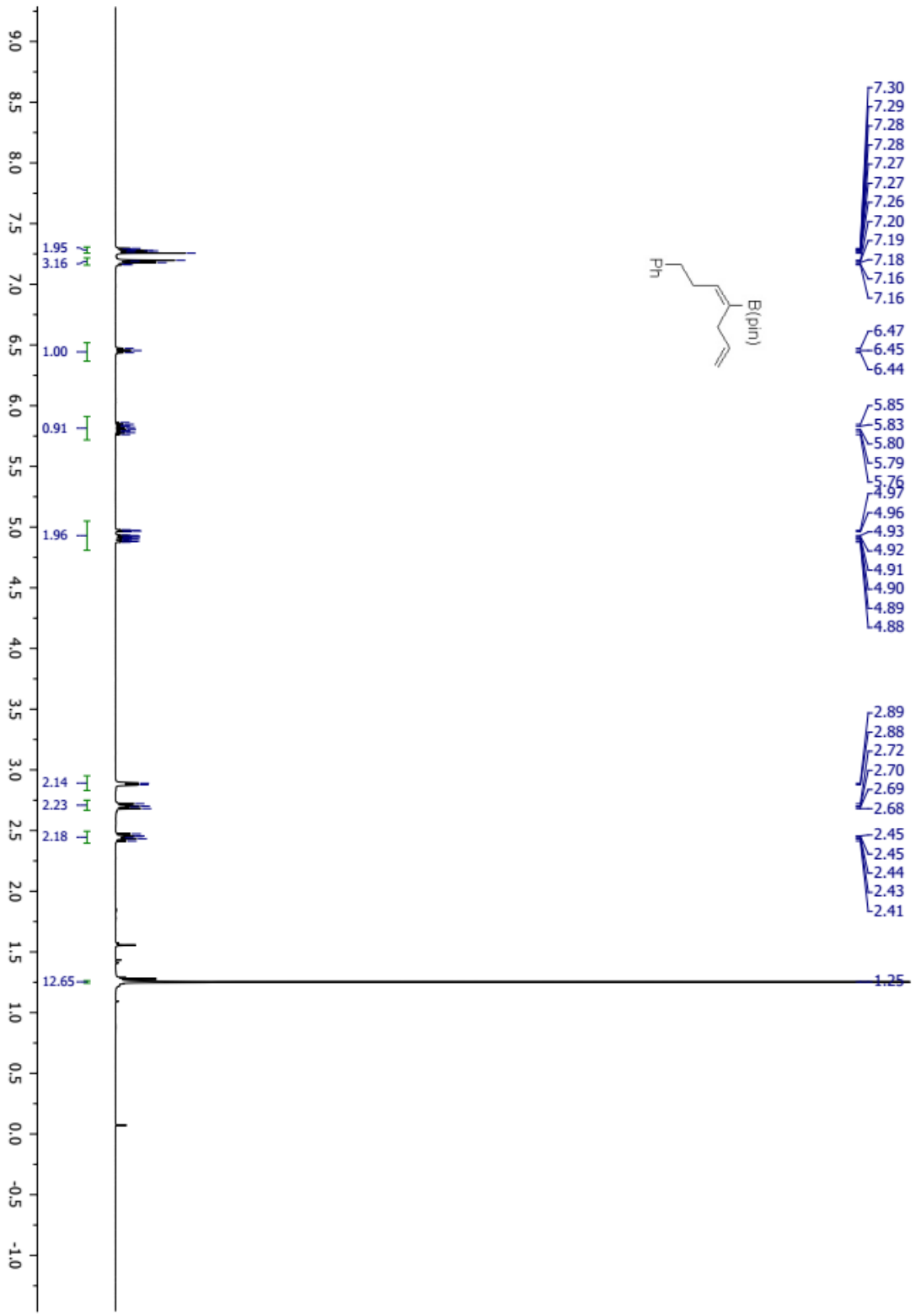
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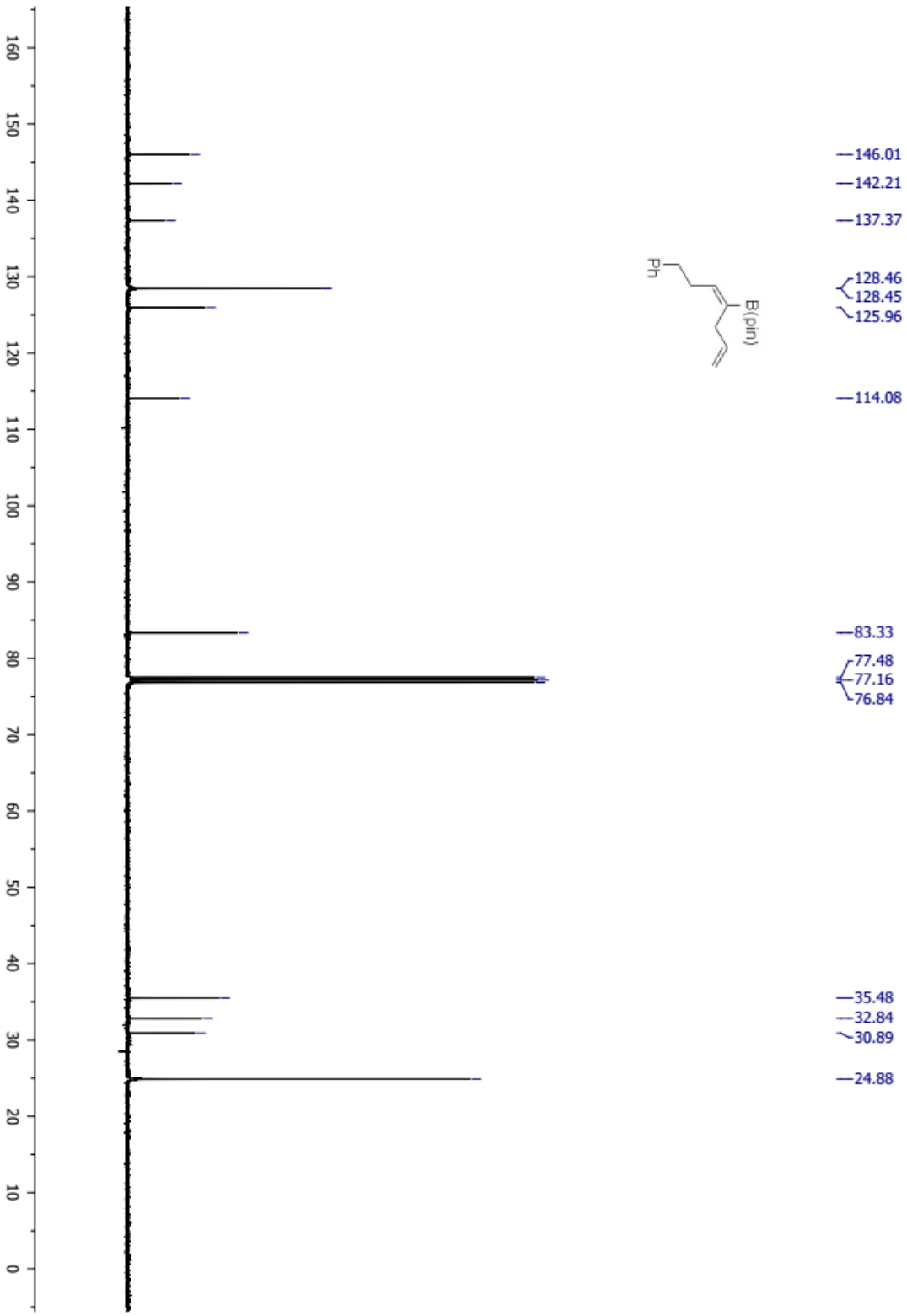
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2.0 BISPHOSPHINE–Cu COMPLEX PROMOTED DIASTEREO-, ENANTIOSELECTIVE ADDITIONS OF BORON CONTAINING MULTIFUNCTIONAL ALLYL MOIETIES TO KETONES

2.1 Introduction

Enantioselective transformations by which a catalyst unites a pair of starting materials and then the *in situ* generated reactive entities reacts with a third substrate are particularly valuable in chemical synthesis.[35] Processes involving difficult-to-access intermediates then become feasible and inefficient and operationally troublesome isolation and/or purification of sensitive reagents can be avoided.[36] Careful orchestration of such multicomponent processes is needed, however, if such processes are to be highly efficient: two starting materials must first be catalytically converted into desired intermediate, which then has to fuse with another substrate to afford corresponding product and regenerate the catalyst. Moreover, when a chiral catalyst structure is incorporated within the intermediate, highly organized enantiomeric control can be achieved from achiral and/or racemic reagents. In multicomponent reactions, complications of reactivity and selectivity need to be addressed at every stage, and proper combination of catalyst and conditions must be resolved to ascertain a successful protocol. An effective multicomponent reaction will

(35) For reviews on catalytic multicomponent reactions, see: (a) Ramón, D. J.; Yus, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 398–401. (b) Ruijter, E.; Schefelaar, R.; Orru, R. V. A. *Angew. Chem., Int. Ed.* **2011**, *50*, 6234–6246. (c) Touré, B. B.; Hall, D. G. *Chem. Rev.* **2009**, *109*, 4439–4486.
(36) For relevant discussions, see: (a) Romiti, F.; del Pozo, J.; Paioti, P. H. S.; Gonsales, S. A.; Li, X.; Hartrampf, F. W. W.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2019**, *141,* 17952–17961. (b) Bower, J. F.; Kim, I. S.; Patman, R. L.; Krische, M. J. *Angew. Chem., Int. Ed.* **2009**, *48*, 34–46.

deliver unprecedented degree of complexity in the final product, where the emblem of every individual catalytic event is present within just one reaction. The resulting multifunctional and versatile entities can be utilized to access various key synthetic intermediates and natural products.[1c-d, 3b, 34, 37, 38] Subsequent to the development of the catalytic multicomponent reactions involving vinylallenes, $B_2(pin)_2$ and dienoates, we decided to investigate other possible electrophiles, that can be merged with the *in situ* generated unique multifunctional Cu–allyl intermediate arising from reaction with vinylallenes.

2.2 Background

Addition of an allylmetal compound to a carbonyl group represents a key transformation in synthetic organic chemistry, especially those can catalytically and enantioselectively provide access to homoallylic alcohols.[39] In comparison with enantioselective allyl addition to aldehydes, generation of enantiomerically enriched tertiary homoallylic alcohols through addition to ketones are more challenging; this is partly because of the lower steric differentiation between the carbonyl substituents and diminished reactivity.[39a, 40] Unlike most reported catalytic enantioselective allyl additions to ketones, where stoichiometric amounts of an allylmetal (including allylboron

(37) Lee, J.; Torker, S,; Hoveyda A. H. *Angew. Chem., Int. Ed.* **2017**, *56*, 821–826.
(38) Zhang, S.; del Pozo, J.; Romiti, F.; Mu, Y.; Torker, S,; Hoveyda A. H. *Science* **2019**, *364*, 45–51.
(39) For reviews on stereoselective allyl addition to carbonyl compounds, see: (a) Yus. M.; Gonzalez-Gomez, J. C.; Foubelo, F. *Chem. Rev.* **2011**, *111*, 7774–7854. (b) Yus. M.; Gonzalez-Gomez, J. C.; Foubelo, F. *Chem. Rev.* **2013**, *113*, 5595–5698. (c) Huo, H.-X.; Duvall, J.R.; Huang, M.-Y.; Hong, R. *Org. Chem. Front.* **2014**, *1*, 303–320. (d) Shibasaki, M.; Kanai, M. *Chem. Rev.* **2008**, *108*, 2853–2873. (e) Hatano, M.; Ishihara, K. *Synthesis* **2008**, *11*, 1647–1675. (f) Denmark, S. E.; Fu, J. *Chem. Rev.* **2003**, *103*, 2763–2793.
(40) Tsai, E. Y.; Liu, R. Y.; Yang, Y.; Buchwald, S. L. *J. Am. Chem. Soc.* **2018**, *140*, 2007–2011.

reagents,[41,42,43] allylsilanes[44] and allylstannanes[45, 46]), an allylic halide,[47] or an allylic acetate[48] is needed, the direct fusion of unsaturated hydrocarbons and ketones via catalytically generated allyl–metal intermediates is rare.[39] Allyl addition methods based on transfer hydrogenation strategy which involve an aldehyde or a primary alcohol have been introduced by Krische.[49] These phosphine–Ru/Ir catalyzed protocols are not generally

(41) For selected reports on enantioselective allyl addition to ketones involving allylboron reagents and catalyzed by a chiral ammonium-boryl catalyst, see: (a) Robins, D. W.; Lee, K.; Silverio, D. L.; Volkov, A.; Torker, S.; Hoveyda A. H. *Angew. Chem., Int. Ed.* **2016**, *55*, 9610–9614. (b) Lee, K.; Silverio, D. L.; Torker, S.; Haeffner, F.; Robbins, D. W.; van der Mei, F. W.; Hoveyda A. H. *Nat. Chem.* **2016**, *8*, 768–777. (c) van der Mei, F. W.; Qin, C.; Morrison, R. J.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2017**, *139*, 9053–9065. (d) Fager, D. C.; Lee, K.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2019**, *141*, 16125–16138.

(42) For selected reports on enantioselective allyl addition to ketones involving allylboron reagents and catalyzed by a chiral diol catalyst, see: (a) Alam, R.; Vollgraff, T.; Eriksson, L.; Szabo, K. J. *J. Am. Chem. Soc.* **2015**, *137*, 11262–11265. (b) Lou, S.; Moquist, P. N.; Schaus, S. E. *J. Am. Chem. Soc.* **2006**, *128*, 12660–12661. (c) Barnett, D. S.; Moquist, P. N.; Schaus, S. E. *Angew. Chem., Int. Ed.* **2009**, *48*, 8679–8682.

(43) For selected reports on enantioselective allyl addition to ketones involving allylboron reagents and catalyzed by a chiral bisphosphine–Cu catalyst, see: (a) Shi, S.-L.; Xu, L.-W.; Oisaki, K,; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2010**, *132*, 6638–6639. (b) Kanai, M.; Wada, R.; Shibuguchi, T.; Shibasaki, M. *Pure Appl. Chem.* **2008**, *80*, 1055–1062. (c) Wada, R.; Oisaki, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2004**, *126*, 8910–8911.

(44) For selected reports on enantioselective Sakurai-Hosomi type allyl addition to ketones involving allylsilanes and catalyzed by a chiral bisphosphine–Ag catalyst, see: (a) Wadamoto M.; Naodovic, M.; Yamamoto, H. *J. Am. Chem. Soc.* **2005**, *127*, 14556–14557. (b) Wadamoto M.; Yamamoto, H. *Eur. J. Org. Chem.* **2009**, 5132–5134.

(45) For selected reports on enantioselective allyl addition to ketones involving allylstannanes and catalyzed by a chiral BINOL–Ti catalyst, see: (a) Casolari, S.; D'Addario, D.; Tagliavini, E. *Org. Lett.* **1999**, *1*, 1061–1063. (b) Kii, S.; Maruoka, K. *Chirality* **2003**, *15*, 68–70. (c) Kim, J. G.; Waltz, K. M.; Garcia, I. F.; Kwiatkowski, D.; Walsh, J. *J. Am. Chem. Soc.* **2004**, *126*, 12580–12585. (d) Wooten, A. J.; Kim, J. G.; Walsh, P. J. *Org. Lett.* **2007**, *9*, 381–384. (e) Kim, J. G.; Camp, E. H.; Walsh, P. J. *Org. Lett.* **2006**, *8*, 4413–4416.

(46) For selected reports on enantioselective allyl addition to ketones involving allylstannanes and catalyzed by a chiral BINOL–In catalyst, see: (a) Teo, Y.-C.; Goh, J.-D.; Loh, T.-P. *Org. Lett.* **2005**, *7*, 2743–2745. For reactions catalyzed by chiral *N,N'*-dioxide–In complex, see: (b) Zhang, X.; Chen, D.; Liu, X.; Feng, X. *J. Org. Chem.* **2007**, *72*, 5227–5233. For reactions catalyzed by chiral PyBOX–In complex, see: (c) Lu, J.; Hong, M.-L.; Ji, S.-J.; Teo, Y.-C.; Loh, T.-P. *Chem. Commun.* **2005**, 4217–4218.

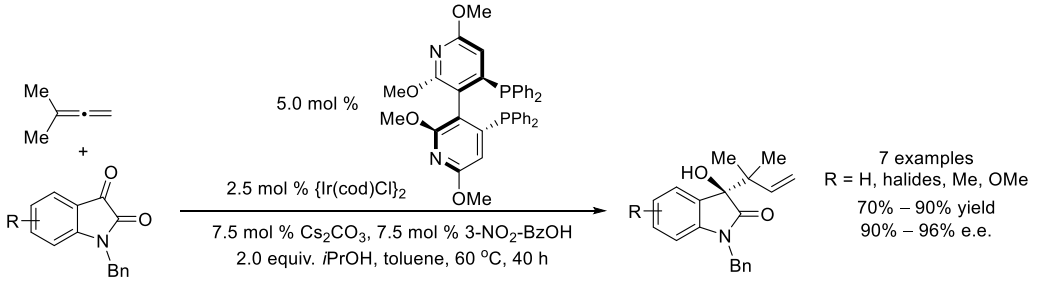
(47) For selected reports on enantioselective Nozaki-Hiyama-Kishi type allyl addition to ketones involving allylic halides and catalyzed by a chiral Cr complex, see: (a) Miller, J. J.; Sigman, M. S. *J. Am. Chem. Soc.* **2007**, *129*, 2752–2753. (b) Chen, R.-Y.; Dhondge, A. P.; Lee, G.-H.; Chen, C. *Adv. Synth. Catal.* **2015**, *357*, 961–966. (b) Huang, X.-R.; Chen, C.; Lee, G.-H.; Peng, S.-M. *Adv. Synth. Catal.* **2009**, *351*, 3089–3095.

(48) For a recent example on enantioselective allyl addition to ketones involving allylic acetate and are catalyzed by a chiral SEGPHOS–Ir complex, see: Brito, G.; Jung, W.-O.; Yoo, M.; Krische, M. J. *Angew. Chem. Int. Ed.* **2019**, *58*, DOI: 10.1002/anie.201908939

(49) For selected reviews on enantioselective reductive coupling of unsaturated hydrocarbons and aldehydes, as well as transfer hydrogenative coupling processes wherein corresponding primary alcohols serve as hydrogen donor and aldehyde proelectrophile, see: (a) Nguyen, K. D.; Park, B. Y.; Luong, T.; Sato, H.; Garza, V. J.; Krische, M. J.; *Science* **2016**, *354*, aah5133. (b) Holmes, M; Schwartz, L. A.; Krische, M. J.; *Chem. Rev.* **2018**, *118*, 6026–6052. (c) Hassan, A.; Krische, M. J.; *Org. Process Res. Dev.* **2011**, *15*, 1236–1242. (d) Ketcham, J. M.; Shin, I.; Montgomery, T. P.; Krische, M. J. *Angew. Chem., Int. Ed.* **2014**, *53*, 9142–9150. (e) Kim, S. W.; Zhang, W.; Krische, M. J.; *Acc. Chem. Res.* **2017**, *50*, 2371–2380.

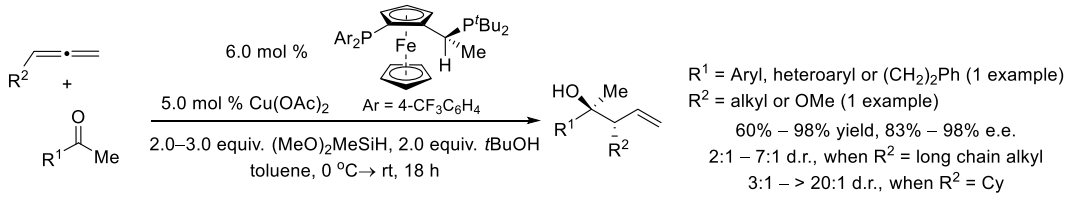
Scheme 2.1. **Review on Previously Reported Catalytic Enantioselective Ketone Allylation Methods Starting from Unsaturated Hydrocarbons**

a) The only enantioselective transfer hydrogenative allylation of actived ketone:



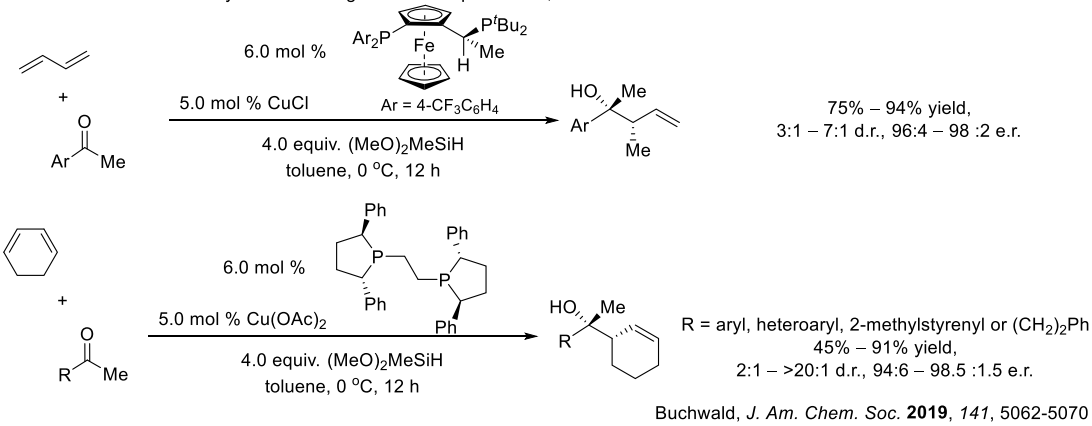
Krische, *Angew. Chem., Int. Ed.* **2009**, *48*, 6313-6316

b) Enantioselective ketone allylation involving a Cu-H complex and allene:



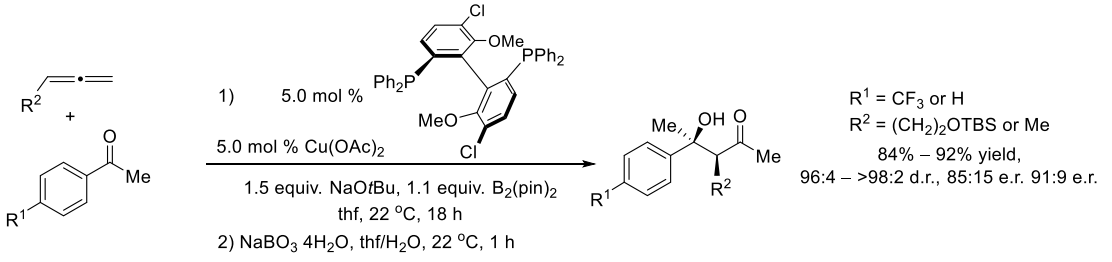
Buchwald, *J. Am. Chem. Soc.* **2018**, *140*, 2007-2011

c) Enantioselective ketone allylation involving a Cu-H complex and 1,3-diene:



Buchwald, *J. Am. Chem. Soc.* **2019**, *141*, 5062-5070

d) Enantioselective ketone allylation involving a Cu-B(pin) complex and allene:



Hoveyda, *Angew. Chem. Int. Ed.* **2013**, *52*, 5046-5051

applicable to ketones or secondary alcohols;[50] the only enantioselective method is limited to reverse prenyl addition to *N*-benzyl isatins (Scheme 2.1a).[50c] A recent development in

(50) Ru/Ir–catalyzed transfer hydrogenative allylation strategy with ketone to generate tertiary homoallylic alcohol represents a persistent challenge, only three instances were reported. For racemic transfer

the context of catalytic enantioselective allyl addition to ketones involving unsaturated hydrocarbons was reported by Buchwald, wherein Cu–H complex was utilized to generate allylcopper species from allenes[40, 51] and 1,3-diene[52] (Scheme 2.1b–c). Nevertheless, methods that allow for highly diastereoselective allyl addition of a wide range of substrates is lacking. It merits note that stereoselective strategies for introducing relatively complex allyl fragments to ketones are scarce. To the best of our knowledge, the only precedence was reported by Hoveyda in 2013,[1a] where a 2-B(pin)-substituted allylcopper was obtained from monosubstituted allene when exposed to *in situ* generated Cu–B(pin) complex, followed by a *γ*-selective addition to ketones. This transformation, which was catalyzed by a chiral BIPHEP–Cu complex at ambient temperature and involved an alkyl-substituted allene and acetophenone. The transformations were highly efficient (84% to 92% yield) and diastereoselective (96:4 d.r. to >98:2 d.r.), but enantioselectivity was moderate ranging from 85:15 e.r. to 91:9 e.r. What is worse, isolation of the product containing 1,1-disubstituted alkenyl boronate entity was problematic at that time.[53] Therefore, it was required that the initial product mixture be subjected to a mild oxidation condition; the methyl ketone was isolated as final product. Thus, the main drawback of the latter approach is the loss of alkenyl–B(pin) functionality. A recent discovery of column chromatography

hydrogenative coupling of 1,3-diene and α-hydroxy ester, see: (a) Leung, J. C.; Geary, L. M.; Chen, T.-Y.; Zbieg, J. R.; Krische, M. J. *J. Am. Chem. Soc.* **2012**, *134*, 15700–15703. For racemic transfer hydrogenative coupling of isoprene and secondary 2-pyridyl carbinols, see: (b) Park, B. Y.; Montgomery, T. P.; Garza, V. J.; Krische, M. J.; *J. Am. Chem. Soc.* **2013**, *135*, 16320–16323. For enantioselective reductive coupling of 1,1-dimethylallene and *N*-benzyl isatin, see: (c) Itoh, J.; Han, S. B.; Krische, M. J. *Angew. Chem., Int. Ed.* **2009**, *48*, 6313–6316.

(51) Mainly monosubstituted allenes were used, including only one example of symmetric 1,1-disubstituted allene.

(52) Li, C.; Liu, R. Y.; Jesikiewicz, L. T.; Yang, Y.; Liu, P.; Buchwald, S. L. *J. Am. Chem. Soc.* **2019**, *141*, 5062–5070.

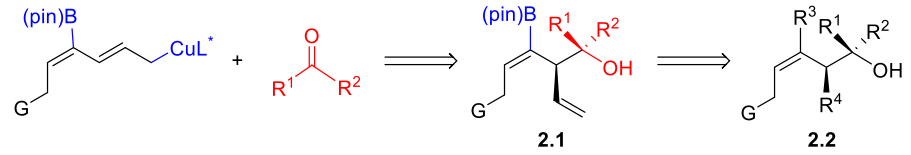
(53) A possible reason could be that the newly formed *β*-hydroxyl group might activate the B(pin) group, leading to partially release of the pinacol group. The complex product mixture contained different boronates along with boronic acid.

condition by us has been able to solve this problem, and the boronates may be converted to boronic acids.

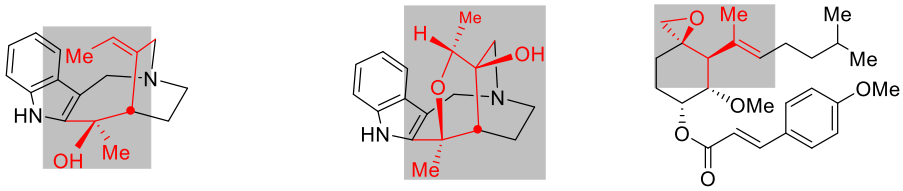
Regarding the challenge of highly diastereo-, and enantioselective and broadly applicable polyfunctional allyl addition to ketone, we considered the possibility of a strategy involving the fusion of vinylallenes, $B_2(pin)_2$ and ketones. For instance, as a case in point, product **2.1** (Scheme 2.2a)**,** which can be accessed through this protocol, features the following distinct attributes: 1) a stereo-defined trisubstituted alkenyl–B(pin) unit, which can be transformed to various of *Z* and/or *E* trisubstituted olefins;[54] 2) a terminal vinyl moiety that can be easily differentiated from trisubstituted alkenyl–B(pin); 3) a tertiary homoallylic alcohol unit; 4) vicinal stereogenic centers at allylic and homoallylic

Scheme 2.2. **Excogitation of Catalytic Enantioselective Multifunctional Allyl Addition to Ketones and Related Natural Products Sharing the Same Structural Hallmarks**

a) Excogitation of multicomponent reactions involving vinylallene, $B_2(pin)_2$, and ketone:



b) Representative natural products sharing the same core structure:



(+)-16-Hydroxy-16,22-dihydroappapicine

Isobrafouedine
(*only isolation reported*)

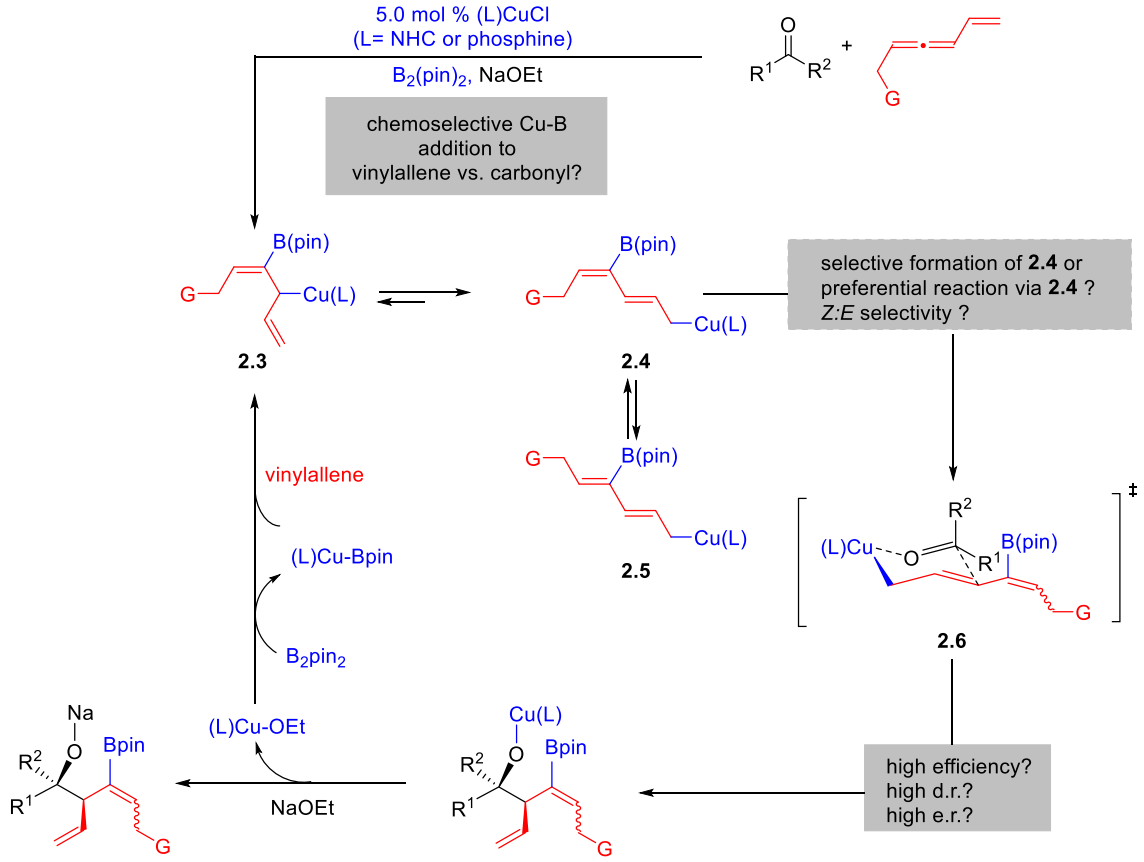
Fumagillin Analogue, CDK-732
(MetAP-2 inhibitor, anti-tumor)

(54) For transformations of C−B bonds, see: (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457−2483. (b) Doucet, H. *Eur. J. Org. Chem.* **2008**, 2013−2030. (c) Brown, H. C.; Singh, S. M.; Rangaishenvi, M. V. *J. Org. Chem.* **1986**, *51*, 3150−3155. (d) Matteson, D. S. *Tetrahedron* **1998**, *54*, 10555−10607. (e) Armstrong R. J.; Aggarwal, V. K. *Synthesis* **2017**, *49*, 3323−3336.

positions. These features render product such as **2.1** particularly suitable for applications to natural product synthesis (Scheme 2.2b).[55, 56, 57]

There are a number of challenges associated with the abovementioned design. 1) We have reported that allylcopper intermediate **2.4** may be generated by site-selective

Scheme 2.3. **Potential Challenges Associated with the Design of Muticomponent Reactions Involving Vinylallenes, $B_2(pin)_2$, and Ketones**



(55) For isolation of 16-hydroxy-16,22-dihydroapparicine, see: (a) Perera, P,; van Beek, T. A.; Verpoorte, R. *J. Nat. Prod.* **1984**, *47*, 835–838. For racemic synthesis and relative chemistry reassignment of 16-hydroxy-16,22-dihydroapparicine, see: (b) Noguchi, Y.; Hirose, T.; Furuya, Y.; Ishiyama, A.; Otoguro, K.; Ōmura, S.; Sunazuka, *Tetrahedron Lett.* **2012**, *53*, 1802–1807. For enantioselective synthesis and structure reassignment of (+)–16-hydroxy-16,22-dihydroapparicine, see: (c) T. Hirose, T.; Noguchi, Y.; Furuya, Y.; Ishiyama, A.; Iwatsuki, M.; Otoguro, K.; Ōmura, S.; Sunazuka, T. *Chem. Eur. J.* **2013,** *19,* 10741–10750.
(56) For isolation of isobrafouedine, see: Michel, S.; Tiliequin, F.; Koch, et M. *J. Nat. Prod.* **1986**, *49*, 452–455
(57) For review on total synthesis of fumagillin and ovalicin analogues, see: Yamaguchi, J.; Hayashi, Y. *Chem. Eur. J.* **2010,** *16,* 3884–3901.

Cu−B(pin) addition to a vinylallene[34] with a dienoate or an alcohol serving as the electrophile. The question here was if Cu−B(pin) addition to vinylallenes would proceed chemoselectively in the presence of ketones, since direct addition of such complexes to ketones has been reported.[58] 2) Based on previous studies (chapter 1.0), in the case of intermediate **2.4** where the Cu center is bound to an NHC ligand, π-allyl isomerization to **2.5** is feasible and the final *Z:E* ratio can thus depend on the kinetic preference for reaction via **2.4**. However, when a different ligand is bound to the Cu center, the thermodynamic and kinetic profile might be entirely different, *Z:E* selectivity might be minimal. 3) Previously reported 2-B(pin)-substituted allyl addition to ketones (Scheme 2.1d), where the sizable B(pin) group resides at pseudo-axial position within the six-membered ring transition state,[1a] and is likely to be important for enough high d.r. and e.r. In contrast, such interactions are basent in transition state **2.6**, and, as a consequence, diastereo- and enantioselectivity might suffer.

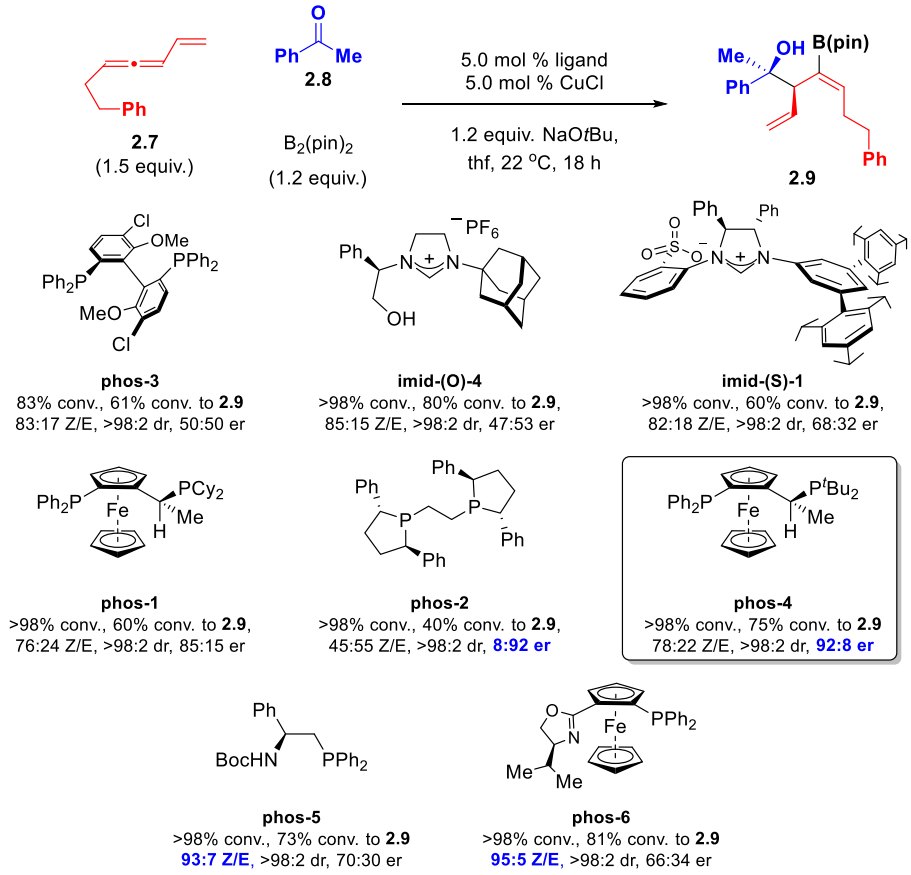
2.3 Identification of Optimal Catalyst and Conditions for Multicomponent Reaction Involving Vinylallenes, $B_2(pin)_2$, and Ketones

We began by studying the Cu-based catalyst derived from **phos-3**, which is the optimal ligand for allyl addition to ketones with a monosubstituted allene; thus we examined the reaction with vinylallene **2.7**, ketone **2.8**, and $B_2(pin)_2$ (Scheme 2.4). There was 83% consumption of **2.8** and 61% conversion to **2.9** (*Z* isomer), 83:17 *Z:E* ratio and

(58) For examples of ketone 1,2-addition with a Cu–B(pin) complex, see: (a) McIntosh, M. L.; Moore, C. M.; Clark, T. B. *Org. Lett.* **2010**, *12*, 1996–1999. (b) Kubota, K.; Osaki, S.; Jin M.; Ito, H.; *Angew. Chem., Int. Ed.* **2017**, *56*, 6646–6650. (c) Kubota, K.; Uesugi, M.; Osaki, S.; Ito, H. *Org. Biomol. Chem.* **2019**, *17*, 5680–5683

>98:2 d.r. Surprisingly, however, there was no enantioselectivity. The above finding emphasized the distinct nature of the processes with a vinyl-containing 1,3-disubstituted allene compared to transformations with monosubstituted allenes.

Scheme 2.4. **Identification of an Effective Ligand**



[a]Conv (±2%; consumption of **2.8**), conv. to prod. (±2%; formation of **2.9** (only *Z* isomer)), *Z*:*E* ratio, and d.r. (±2%) were determined by analysis of ^{1}H NMR spectra of unpurified mixtures with diphenylmethane as internal standard. [b]E.r. were determined by HPLC analysis of corresponding lactone after carbonylation reaction.

Ligand screening study led us to establish that with **imid-(O)-4** optimal for 1,6-conjugate additions involving vinylallenes,[34] while there was improved efficiency (>98% conv. and 80% conv. to **2.9**) negligible enantioselectivity persisted. With a sulfonate-containing imidazolinium salt **imid-(S)-1**,[1c] **2.9** was obtained in 68:32 e.r. and similar efficiency and *Z*:*E* ratio. Reactions with related chiral NHC ligands did not result in any improvement.

The above unsatisfactory results triggered us to examine chiral phosphines as ligands. Screening study led us to identified two categories of effective bisphosphines, namely, Josiphos (**phos-1**) and Ph-BPE (**phos-2**). With **phos-1**, there was 60% conversion to the desired product **2.9** (*Z* isomer), which was formed in 76:24 *Z:E* ratio, >98:2 d.r. and 85:15 e.r. With **phos-2**, there was 40% conv. to **2.9** which was accessed in 92:8 e.r. but *Z:E* selectivity was low (45:55 *Z:E* ratio). Cu-based catalysts derived from other BPE ligands (e.g. Me-BPE, *i*Pr-BPE) and related DuPhos ligands (e.g. Me-Duphos) were ineffective.

Ligand screening led us to recognize **phos-4** as optimal ligand: there was 75% conversion to **2.9**, which was generated in 78:22 *Z:E* selectivity, >98:2 d.r., and 92:8 e.r. It is noteworthy to mention that aminophosphine **phos-5**[59] and phosphine-oxazoline **phos-6** were similarly effective, furnishing **2.9** in high efficiency, *Z:E* selectivity (93:7 *Z:E* ratio, and 95:5 *Z:E* ratio, respectively), and diastereoselectivity (>98:2 d.r.), but no more than 70:30 e.r.[60]

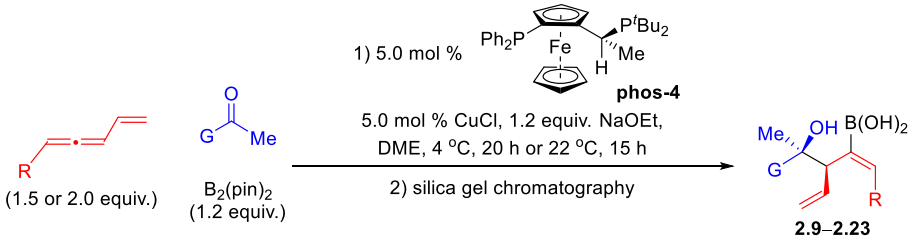
Further optimization led us to determine that 1.2 equivalents NaOEt in dimethoxyethane (DME) at 4 °C (vs. NaO*t*Bu, thf, 22 °C) represented the best combination, affording the boronic acid form of **2.9** in 72% yield, >98:2 d.r., and 94:6 e.r. (Scheme 2.5).

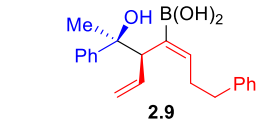
(59) For synthesis of aminophosphines, see: Xiao, H.; Chai, Z.; Zheng C.-W.; Ynag, Y.-Q.; Liu, W.; Zhang, J.-K.; Zhao, G. *Angew. Chem., Int. Ed.* **2010**, *49*, 4467–4470.
(60) Modification on these ligand structures resulted in no improvement on enantioselectivity, however, *Z:E* ratios were generally high.

2.4 Scope of Bisphosphine–Cu Promoted Enantioselective B(pin)-Containing Multifunctional Allyl Addition to Ketones

The catalytic protocol is broadly applicable (**2.9**–**2.23**, Scheme 2.5). Similarly high efficiency and enantioselectivity (72%–83% yield of *Z* isomer, 92:8–94:6 e.r., respectively) were observed for a variety of vinylallenes. Especially noteworthy is the reaction with

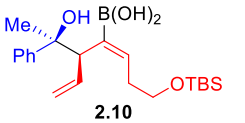
Scheme 2.5. **Transformations with Different Vinylallenes and Aryl/Heteroaryl-Substituted Ketones**





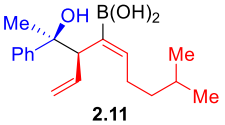
2.9

>98% conv., 72% yield (pure *Z*)
76:24 *Z*:*E*, >98:2 d.r., 94:6 e.r.



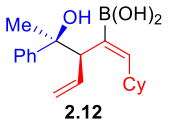
2.10

>98% conv., 77% yield (pure *Z*)
78:22 *Z*:*E*, >98:2 d.r., 93.5:6.5 e.r.



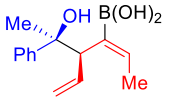
2.11

>98% conv., 80% yield (pure *Z*)
87:13 *Z*:*E*, >98:2 d.r., 93:7 e.r.



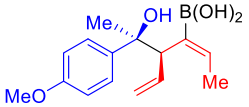
2.12

>98% conv., 83% yield (pure *Z*)
>98:2 *Z*:*E*, >98:2 d.r., 92:8 e.r.



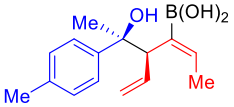
2.13

>98% conv., 73% yield (pure *Z*)
86:14 *Z*:*E*, >98:2 d.r., 95:5 e.r.
11% yield (*E* isomer), >98:2 d.r., 94:6 e.r.



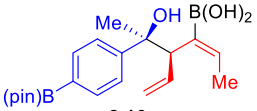
2.14

>98% conv., 73% yield (pure *Z*)
89:11 *Z*:*E*, >98:2 d.r., 94:6 e.r.



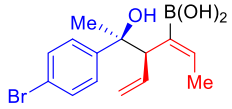
2.15

>98% conv., 78% yield (pure *Z*)
87:13 *Z*:*E*, >98:2 d.r., 92:8 e.r.



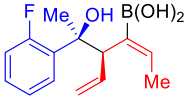
2.16

>98% conv., 70% yield (pure *Z*)
88:12 *Z*:*E*, >98:2 d.r., 92:8 e.r.



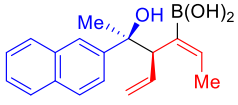
2.17

>98% conv., 70% yield (pure *Z*)
87:13 *Z*:*E*, >98:2 d.r., 90:10 e.r.



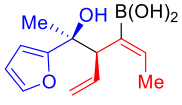
2.18

>98% conv., 74% yield (pure *Z*)
82:18 *Z*:*E*, >98:2 d.r., 92:8 e.r.



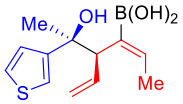
2.19

>98% conv., 68% yield (pure *Z*)
85:15 *Z*:*E*, >98:2 d.r., 90:10 e.r.



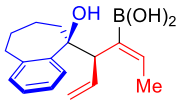
2.20

>98% conv., 72% yield (pure *Z*)
87:13 *Z*:*E*, >98:2 d.r., 94:6 e.r.



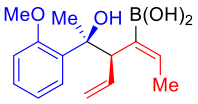
2.21

>98% conv., 69% yield (pure *Z*)
87:13 *Z*:*E*, >98:2 d.r., 94:6 e.r.



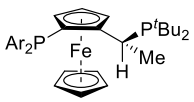
2.22

>98% conv., 81% yield (pure *Z*)
83:17 *Z*:*E*, >98:2 d.r., 92:8 e.r.



2.23

>98% conv., 60% yield (pure *Z*)
ND *Z*:*E*, >98:2 d.r., 97:3 e.r.



Ar = 4-MeO-3,5-$Me_2C_6H_2$
phos-7

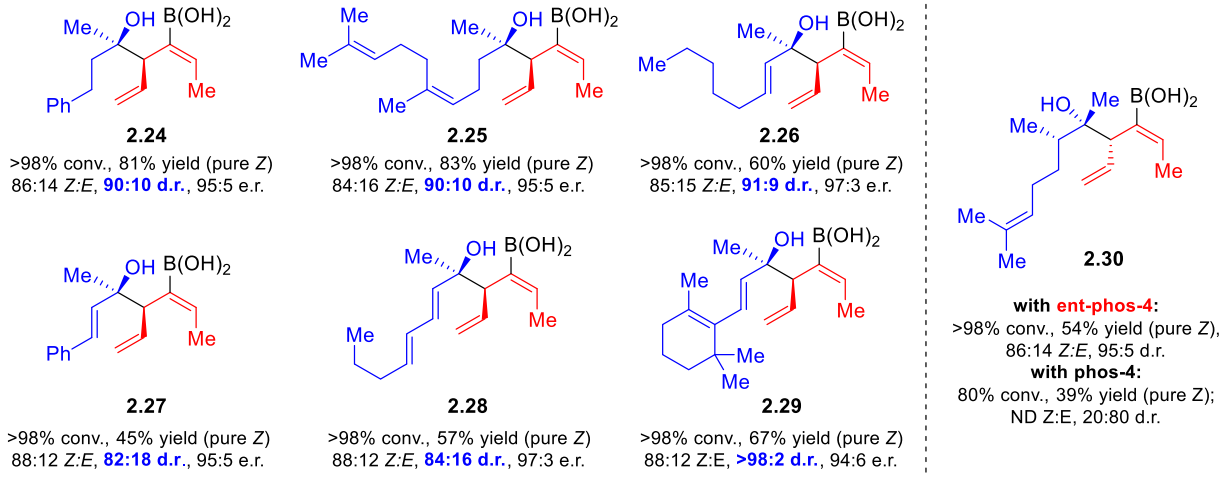
[a]Reactions were performed under N_2 atm. Conv. (±2%; consumption of ketone), *Z*:*E* ratio, and d.r. (±2%) were determined by analysis of ^{1}H NMR spectra of unpurified mixtures and double checked by mass of separated *Z*/*E* isomers. [b]Yield (±5%, average of at least two runs) corresponded purified pure Z isomers. [c]E.r. were determined by HPLC analysis of corresponding lactone after carbonylation reaction.

cyclohexyl-substituted vinylallene, affording **2.12** with >98:2 *Z:E* ratio. Reaction with methyl-substituted vinylallene is equally noteworthy because the reaction was carried out at room temperature, furnishing **2.13** in 73% yield, 86:14 *Z:E* ratio, >98:2 d.r., and 95:5 e.r. The corresponding *E* isomer was isolated in 11% yield, >98:2 d.r. and 94:6 e.r. A variety of aryl-substituted ketones, including those with an electron-donating (**2.14**–**2.15**, Scheme 2.5) or an electron-withdrawing substituent (**2.16**, **2.18**) were suitable substrates; products were obtained in high efficiency (70%–78% yield of *Z* isomer), >98:2 d.r., and 82:18–89:11 *Z:E* ratio, and 92:8–94:6 e.r. Slightly lower enantioselectivities (90:10 vs. 94:6 e.r.) were observed with *para*-bromo-containing **2.17** and 2-naphthyl-containing **2.19** but similar efficiency and diastereoselectivity. Reactions with heterocyclic ketones, 2-acetylfuran and 3-acetothiophene, were effective, affording **2.20** and **2.21** with 87:13 *Z:E* ratio, >98:2 d.r. and 94:6 e.r. A more challenging case corresponded to that of a cyclic ketone, wherein **2.22** was generated in 81% yield (pure *Z* isomer), 83:17 *Z:E* ratio and 92:8 e.r. Addition to more steric demanding *ortho*-methoxyl-substituted ketone suffered from significant loss of enantiomeric purity (85:15 e.r. for **2.23** vs. 94:6 e.r. for **2.13**). To address this issue, we determined that with **phos-7** (Scheme 2.5) instead of **phos-4** as the chiral ligand **2.23** can be obtained as single diastereomer in 60% yield and 97:3 e.r. One limitation of this method is that with aryl-substituted ketones such as propiophenone and indanone, enantioselectivities were lower (85:15 e.r.); efficiency, *Z:E* selectivity and diastereoselectivity still remained high.

The catalytic method is broadly applicable, as various alkyl-substituted ketones (**2.24**–**2.25**, **2.30**), enones (**2.26**–**2.27**) and dienones (**2.28**–**2.29**, Scheme 2.6) may be used. Alkyl-substituted ketone and nerylacetone were converted to **2.24** and **2.25** in 81% and

83% yield, 86:14 and 84:16 *Z:E* ratios, respectively, and 95:5 e.r. Diastereoselectivity was slightly reduced (90:10 d.r.) in comparison with the cases of aryl-substituted ketones. Enone may also be used; thus, **2.26** was prepared in 85:15 *Z:E* ratio, 91:9 d.r. and 97:3 e.r. The somewhat lower yield (60% yield) may be due to competitive Cu–B(pin) conjugate addition.[61] Reaction with aryl-substituted enone, a superior Michael acceptor for Cu–B(pin) complex, afforded **2.27** in similar *Z:E* ratio (88:12) and enantioselectivity (95:5 e.r.) but lower diastereoselectivity (82:18 d.r.) and yield (45% yield). Product **2.28**, generated through reaction with a dienone, was accessed in 57% yield, 88:12 *Z:E* ratio and 84:16 d.r. (vs. 91:9 for **2.26**), and e.r. remained high (97:3 e.r.). In the case of more sterically congested *γ,δ*-substituted dienone, **2.29** was generated in 67% yield (vs. 57% yield for **2.28**), 88:12 *Z:E* ratio, >98:2 d.r., and 94:6 e.r. Reaction with enantiomerically enriched *α*-branced ketone clearly showed that substrate-control is operative: in the "matched" case,

Scheme 2.6. **Protocol is Widely Applicable to Different Alkyl-Substituted Ketones, Enones and Dienones**



[a]Reactions were performed under N_2 atm. Conv. (±2%; loss of ketone), *Z:E* ratio, and d.r. (±2%) were determined by analysis of ^{1}H NMR spectra of unpurified mixtures and double checked by mass of separated *Z/E* isomers. [b]Yield (±5%, average of at least two runs) corresponded purified pure Z isomers (diastereomeric mixtures). [c]E.r. were determined by HPLC analysis of corresponding lactone after carbonylation reaction.

(61) For selected examples of Cu–B(pin) conjugate addition to enones, see: (a) Ito, H.; Yamanaka, H.; Tateiwa, J.-I.; Hosomi, A. *Tetrahedron Lett.* **2000**, *41*, 6821–6825. (b) Mun, S.; Lee J.-E.; Yun, J.; *Org. Lett.* **2006**, *8*, 4887–4889.

2.30 was formed in 54% yield, 86:14 *Z:E* ratio and 95:5 d.r. with the alternative enantiomer of **phos-4**.

2.5 Application to Total Synthesis of Monoterpenoid Indole Alkaloid (+)-16-Hydroxy-16,22-Dihydroappariciné

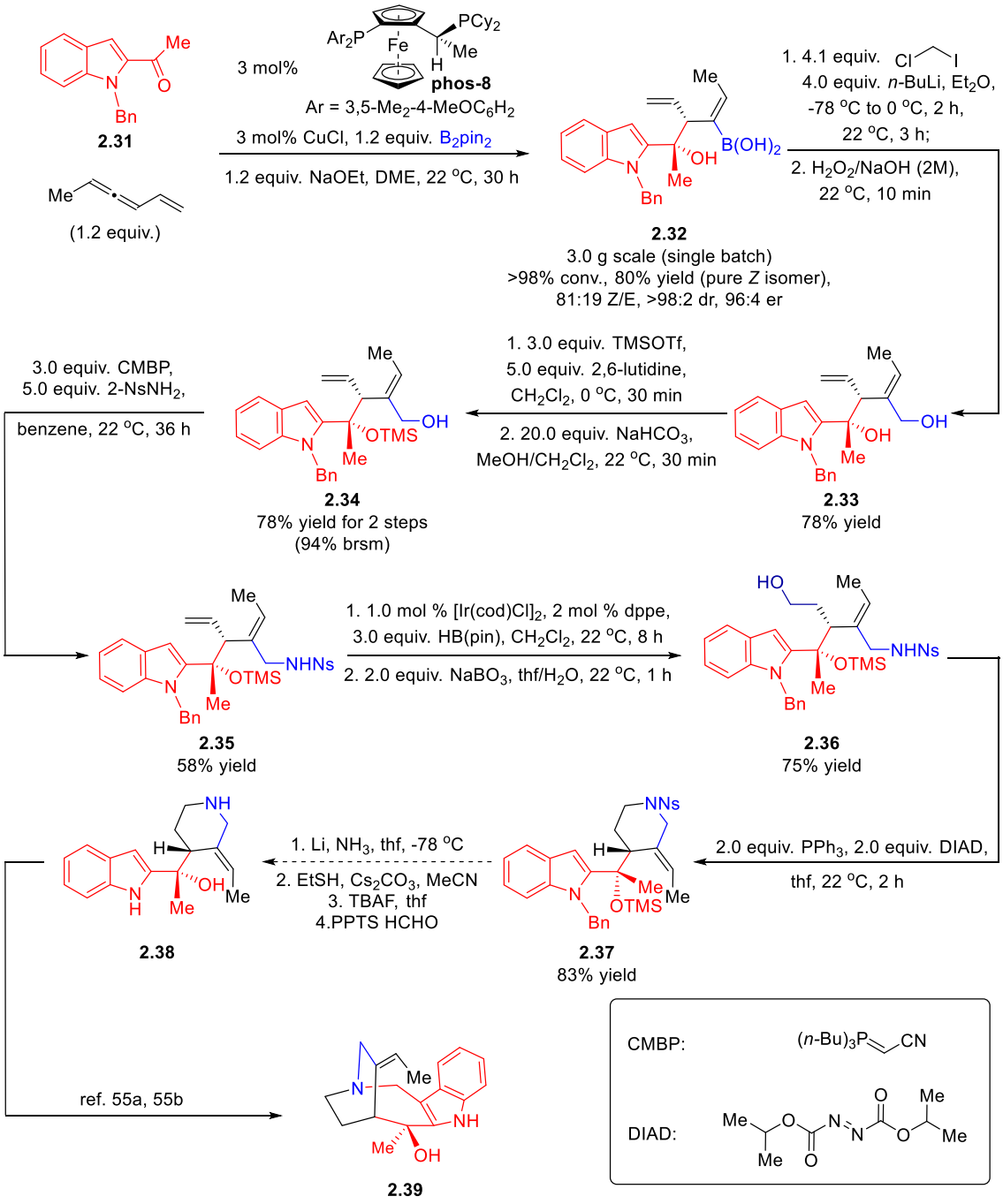
To demonstrate the utility of the new method, it is imperative that the different functionalities within the product can be readily modified with high site-, regio-, and/or stereoselectivity for synthesis of biologically active compounds. Towards this end, we choose to pursue a concise synthesis of 5-norstemmadenine monoterpenoid indole alkaloid (+)-16-Hydroxy-16,22-dihydroapparicine.[55] The same target molecule has previously been synthesized by Sunazuka et al. through a 23-step (longest linear step) route, affording the final product in 4.7% overall yield.[55c]

Our synthesis started from the currently developed multicomponent reaction involving methyl-substituted vinylallene, ketone **2.31**, and $B_2(pin)_2$. With the optimal ligand **phos-4**, **2.32** could be effectively generated in 67% yield, 81:19 *Z:E* ratio, and >98:2 d.r., but, surprisingly, in low enantioselectivity (53:47 e.r.). With **phos-8** as the chiral ligand, enantioselectivity improved significantly (96:4 e.r.). Thus, we were able to prepare three grams of **2.32** (single batch) in 80% yield (pure *Z* isomer), 83:17 *Z:E* ratio, >98:2 d.r. and 96:4 e.r. (Scheme 2.7). It is also noteworthy that only 1.2 equiv. of vinylallene (vs. 1.5–2.0 equiv. for 0.1 mmol scale process) was used in presence of 3.0 mol % **phos-8**–Cu complex (vs. 5.0 mol % for 0.1 mmol scale process) without any diminution in efficiency and selectivity. Allylic alcohol **2.33** was then accessed through Matteson[54d, 62]

(62) Matteson, D. S.; Majumdar, D. *Organomtallics 1983*, **2**, 1529–1535.

homologation stereoretentively and in 78% yield. Site-selective silyl protection of primary alcohol, followed by base-induced silyl transfer furnished **2.34** in 78% overall yield (94%

Scheme 2.7. **Investigation on the Utility of the Multifunctional Allyl Addition to Ketone Method in Enantioselective Synthesis of 16-Hydroxy-16,22-dihydroappariceine**



[a]Yields (±5%) correspond to purified products. [b]*Z*:*E* ratios and d.r. (±2%) were determined by analysis of ^{1}H NMR spectra of unpurified mixtures. [c]E.r. was determined by HPLC analysis.

based on recovery of starting material). Ensuing Mitsunobu reaction with Tsunoda reagent[63] and 2-nitrobenzenesulfonamide afforded **2.35** in 58% yield. The vinyl moiety was then transformed into corresponding primary alcohol (cf. **2.36**) through site-selective catalytic hydroboration[64] and oxidative work up. Importantly, the trisubstituted olefin remained intact. A second Mitsunobu reaction[65] was carried out to generate the piperidine ring, affording **2.37** in 83% yield. After debenzylation,[66] we will be able to access **2.38**, a previously reported intermediate which would be used to prepare **2.39**.[55b, 55c, 67] So far, nosyl and silyl deprotection has been successfully achieved.

2.6 Conclusions

In summary, a bisphosphine–Cu catalyzed multicomponent transformation involving racemic vinylallenes, $B_2(pin)_2$ and ketones has been developed. The method is applicable to a variety of ketones (including aryl/alkyl-substituted ketones, enones and dienones). Catalytic enantioselective addition to ketones with a multifunctional allyl entity

(63) Tsunoda reagent, (tributylphosphoranylidene)acetonitrile (CMBP), was specially designed for Mitsunobu reactions with benzenesulfonamides. For synthesis and related reactions, see: (a) Tsunoda, T.; Ozaki, F.; Ito, S. *Tetrahedron Lett.* **1994**, *35*, 5081–5082. (b) Tsunoda, T.; Yamamoto, H.; Goda, K.; Ito, S. *Tetrahedron Lett.* **1996**, *37*, 2457–2458.

(64) Yamamoto, Y.; Fujikawa, R.; Umemoto, T.; Miyaura, N. Tetrahedron, 2004, 60, 10695–10700.

(65) For the original report by Mitsunobu, see: (a) Mitsunobu, O.; Yamada, M.; *Bull. Chem. Soc. Jpn.* **1967**, *40*, 2380–2382. For selected reviews on Mitsunobu reaction, see: (b) Mitsunobu, O. *Synthesis* **1981**, 1981, 1–28. (c) Swamy, K. C. K.; Kumar, N. N. B.; Balaraman, E.; Kumar, K. V. P. P.; *Chem. Rev.* **2009**, *109*, 2551–2651. (d) Fletcher, S. *Org. Chem. Front.* **2015**, *2*, 739–752. For review on catalytic Mitsunobu reaction, see: (e) Beddoe, R.; Sneddon, H. F.; Denton, R. M. *Org. Biomol. Chem.* **2018**, *16*, 7774–7781.

(66) For selected methods on indole debenzylation, see: (a) Suzuki, H.; Tsukuda, A.; Kondo, M.; Aizawa, M.; Senoo, Y.; Nakajima, M.; Watanabe, T.; Yokoyama, Y.; Murakami, Y. Tetrahedron Lett. 1995, 36, 1671–1672. (b) Hoddach, A. A.; Kelleman, A.; Deaton-Rewolinski, M. V. Tetrahedron Lett. 2002, 43, 399–402. (c) Watanabe, T.; Kobayashi, A.; Nishiura, M.; Takahashi, H.; Usui, T.; Kamiyama, I.; Mochizuki, N.; Noritake, K.; Yokoyama, Y.; Murakami, Y. Chem. Pharm. Bull. 1991, 39, 1152–1156. (d) Rao, T. S.; Pandey, P. S. Synth. Commun. 2004, 34, 3121–3127. (e) Talukdar, S.; Nayak, S. K.; Banerji, A. J. Org. Chem. 1998, 63, 4925–4929.

(67) An X-ray structure of lactone derivative of **2.32** was secured (Scheme 2.7). The route shown will lead to (-)-16-hydroxy-16,22-dihydroapparicine, namely, the enantiomer of reported natural product.

afford versatile products that can be used to access a wide range of complex building blocks. Desired products were obtained effectively and in high stereoselectivity, featuring a stereo-defined trisubstituted alkenyl–B(pin) moiety, a vinyl unit, a tertiary homoallylic alcohol and vicinal stereogenic centers. The considerable utility of the new catalytic protocol will be highlighted by a concise enantioselective synthesis of monoterpenoid indole alkaloid 16-hydroxy-16,22-dihydroappariciné.

2.7 Experimental

2.7.1 General and Reagents

Infrared (IR) spectra were recorded on a Bruker FT-IR Alpha (ATR mode) spectrophotometer, λ_{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 VNMRS 600 (600 MHz), Varian VNMRS 500 (500 MHz), Varian INOVA 500 (500 MHz) or Varian MR-400 (400 MHz) spectrometer. Chemical shifts are reported in ppm 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 = broad, m = multiplet), and coupling constant (Hz). ^{13}C NMR spectra were recorded on a Varian MR-400 (101 MHz), Varian VNMRS 500 (126 MHz), or Varian VNMRS 600 (151 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: δ 77.16 ppm). ^{11}B NMR spectra were recorded on a Varian MR-400 (128 MHz), Varian VNMRS 500 (160 MHz), or Varian VNMRS 600 (192 MHz) spectrometer with complete proton decoupling. Chemical

shifts are reported in ppm with $BF_3 \cdot Et_2O$ as reference. High-resolution mass spectrometry was performed on a JEOL AccuTOF DART (positive mode) at the Mass Spectrometry Facility, Boston College. Enantiomeric ratios were determined by HPLC analysis (Chiral Technologies Chiralpak AZ–H (4.6 x 250 mm), Chiralcel OD–H (4.6 x 250 mm), Chiralcel OZ–H (4.6 x 250 mm), Chiralpak AS–H (4.6 x 250 mm) and Chiralpak AD–H (4.6 x 250 mm) in comparison with authentic racemic materials. Specific rotations were measured on an ATAGO® AP-300 Automatic Polarimeter or 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 column and an alumina column; CH_2Cl_2 and Et_2O were purged with Ar and purified by passage through two alumina columns. Tetrahydrofuran (Aldrich Chemical Co.) and dimethoxyethane (Acros) were 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, Inc.) in air.

Ketones: purchased from Aldrich Chemical Co. or Tokyo Chemical Industry Co., purified by distillation or column chromatography and dried under vacuum prior to use.

(3*E*, 5*E*)-Nona-3,5-dien-2-one: prepared according to previously reported procedure.[68]

(68) Walleser, P.; Brückner. R. *Eur. J. Org. Chem.* **2010**, 4802–4822.

(*S*)-3,7-dimethyloct-6-en-2-one: prepared according to previously reported procedure.[69]

Vinylallenes: prepared according to previously reported procedures.[6]

Methyl vinylallenes: prepared according to a modified procedure, details see below.

Acrolein (3 wt% H_2O, 1000 ppm hydroquinone): purchased from Oakwood Chemicals Inc. and distilled under N_2 prior to use.

Benzoquinone: purchased from Aldrich Chemical Co., recrystallized from hexanes and dried under vacuum prior to use.

***n*-Butyllithium solution (2.5 M in hexanes):** purchased from Aldrich Chemical Co., and titrated prior to use.

Bis(1,5-cyclooctadiene)diiridium(I) dichloride: purchased from Strem Chemicals Inc. and used as received.

Bis(pinacolato)diboron: purchased from Frontier Scientific, Inc., recrystallized from pentane and dried under vacuum prior to use.

Carbon monoxide (compressed gas): purchased from Airgas and used as received.

Chloroiodomethane: purchased from Oakwood Chemicals Inc. and used as received.

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

Diisopropyl azodicarboxylate (DIAD): purchased from Acros and used as received.

Diethylzinc (neat, >52 wt % Zn basis): purchased from Aldrich Chemical Co. and used as received.

Hydrogen Peroxide (30% aqueous): purchased from Fisher Scientific, Inc. and used as received.

Imidazolinium salts: prepared according to previously reported procedures.[1e, 2b, 21]

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(69) Chang, L.; Jiang, H.; Fu, J.; Liu, B.; Li, C.-C.; Yang, Z. *J. Org. Chem.* **2012**, 77, 3609–3614.

2,6-Lutidine: purchased from Aldrich Chemical Co. and used as received.

Methanol (anhydrous, 99.8%): purchased from Aldrich Chemical Co. and used as received.

Methyl lithium (3.1 M in diethoxymethane): purchased from Aldrich Chemical Co. and used as received.

2-Nitrobenzenesulfonamide: purchased from Oakwood Chemicals Inc. and used as received.

Phosphines: purchased from Strem Chemicals Inc. or Solvias AG and used as received.

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

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

Sodium hydroxide: purchased from Fisher Scientific, Inc. and used as received.

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

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

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

Tetrabutylammonium fluoride (1.0 M in thf): purchased from Oakwood Products Inc. and used as received.

4,4,5,5-Tetramethyl-1,3,2-dioxaborolane: purchased from Aldrich Chemical Co. and distilled prior to use.

(Tributylphosphoranylidene)acetonitrile (CMBP): purchased from Tokyo Chemical Industry Co. and used as received.

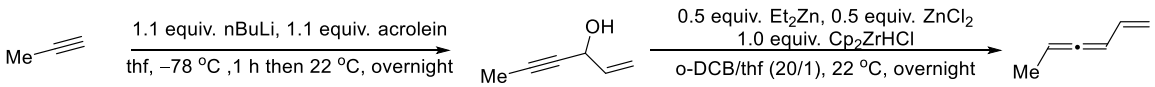
Trimethylsilyl trifluoromethanesulfonate: purchased from Aldrich Chemical Co. and used as received.

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

Zinc chloride (anhydrous, 98%+): purchased from Alfa Aesar and used as received.

Zirconocene chloride hydride (Schwartz's reagent): purchased from Tokyo Chemical Industry Co. and used as received.

2.7.2 Preparation of Methyl Vinylallene[6]



A 500 mL flame-dried flask was with charged anhydrous thf (300 mL) and cooled to –78 ℃ . And then compressed propyne gas (12.0 g, 300 mmol) was bubbled into the pre-cooled thf slowly (allowing for condensation) through a cannula. n-BuLi (11 M in hexanes, 30 mL) was added in 10 min under vigorous stirring followed by addition of acrolein (330 mmol, 22.1 mL) in 5 min, after which the solution was allowed to stir for 1 h at –78 °C, warm to 22 ℃ and stir for overnight. The reaction was then quenched by the addition of a saturated solution of NH_4Cl (50 mL) in ice bath. The aqueous phase was separated and extracted with Et_2O (3 × 150 mL), and the organic layers were combined and dried over Na_2SO_4. The volatiles were removed in vacuo, affording orange oil, which was purified by distillation under vacuum to afford the desired propargylic alcohol as a colorless liquid.

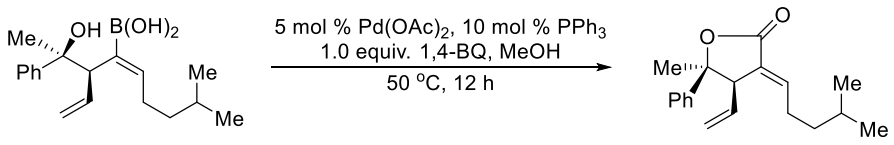
A 150 mL flame-dried flask was charged with $ZnCl_2$ (10.0 mmol, 1.3629 g), followed by the addition of 1.5 mL anhydrous thf, 15 mL 1,2-dichlorobenzene and neat Et_2Zn (10 mmol, 1.2351 g, 1.02 mL) and The mixture was allowed to stir for 40 min at 22 ℃ , after which aforementioned propargylic alcohol (20.0 mmol, 1.9226 g) in 1,2-dichlorobenzene (15 mL) was added. The mixture was allowed to stir for 30 min and then was charged with Schwartz's reagent (5.1574 g, 20.0 mmol) in a single portion. The

mixture was allowed to stir vigorously at 22 °C overnight. Product was purified by vacuum transfer affording the desired methyl vinylallene as a colorless solution in 1,2-dichlorobenzene and thf. Concentration of the solution (usually 30–40 wt %) was determined by integration of related peaks in ^{1}HNMR.

2.7.3 Representative Procedure for Catalytic Enantioselective Multicomponent Ketone Allylation involving Vinylallene and $B_2(pin)_2$

An oven-dried 2-dram vial equipped with a stir bar was charged with **phos-4** (2.7 mg, 5.0 μmol), CuCl (0.5 mg, 5.0 μmol), NaOEt (8.2 mg, 0.12 mmol) and DME (1.0 mL) in a nitrogen-filled glove box. The mixture was allowed to stir for 15 min under N_2 at 22 ℃ , after which $B_2(pin)_2$ (30.5 mg, 0.12 mmol) was added. The resulting solution was allowed to stir for 10 min, after which vinylallene **2.7** (25.5 mg, 0.15 mmol) and ketone **2.8** (12.0 mg, 0.10 mmol) were added. The vessel was removed from glovebox and the mixture was allowed to stir at 4 ℃ for 20 h. Volatiles were then removed in vacuo, affording yellow oil residue, which was purified by silica gel chromatography (30:1 to 5:1 hexanes/ethyl acetate) to afford **2.9** (boronic acid) as colorless oil (24.1 mg, 0.072 mmol, 72% yield). This procedure was used in all other cases.

2.7.4 Representative Procedure for Carbonylation of Product to Access Lactone for Enantiomeric Ratio Determination[70]



2.11 **2.S1**

(70) Yamamoto Y. *Adv. Synth. Catal.* **2010**, *352*, 478–492.

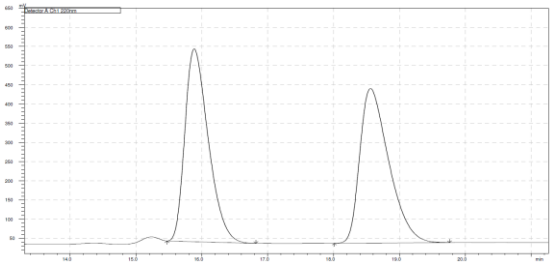
An oven-dried 6-dram vial equipped with a stir bar was charged with **2.11** (30.2 mg, 0.1 mmol), $Pd(OAc)_2$ (1.1 mg, 5.0 μmol), PPh_3 (2.6 mg, 0.01 mmol), 1,4-BQ (10.8 mg, 0.1 mmol) and MeOH (1.0 mL) in a nitrogen-filled glove box. The vessel was sealed with a rubber septum and removed from glovebox. The vessel was purged with CO for 2 times, and the mixture was allowed to stir at 50 ℃ for 12 h with CO balloon. Volatiles were then removed in vacuum, affording dark brown oil residue, which was purified by silica gel chromatography (30:1 to 5:1 hexanes/ethyl acetate) to afford corresponding lactone **2.S1** as colorless oil (24.7 mg, 0.087 mmol, 87% yield). This procedure was used in all other cases.

2.7.5 Characterization of Products of Multicomponent Processes involving Vinylallene, $B_2(pin)_2$, and Ketones

((*R*, *Z*)-3-((*S*)-1-hydroxy-1-phenylethyl)-7-phenylhepta-1,4-dien-4-yl)boronic acid (2.9)

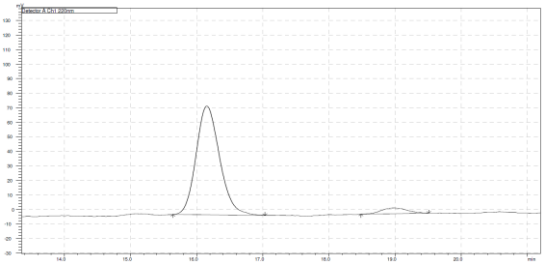
IR (neat): 3371 (w, br), 3024 (w), 2922 (w), 1662 (m), 1412 (s), 1262 (s), 1044 (m), 905 (m), 760 (m), 698 (s) cm^{-1} ; **^{1}H NMR (400 MHz, $CDCl_3/D_2O$, 100:1)** δ: 7.35 – 7.26 (m, 6H), 7.25 – 7.16 (m, 4H), 6.36 (td, *J* = 7.2, 1.8 Hz, 1H), 5.07 (ddd, *J* = 17.2, 9.9, 8.7 Hz, 1H), 4.83 (d, *J* = 17.1 Hz, 1H), 4.72 (dd, *J* = 10.0, 1.8 Hz, 1H), 3.43 (d, *J* = 8.4 Hz, 1H), 2.72 (ddt, *J* = 21.5, 13.8, 7.0 Hz, 2H), 2.47 (q, *J* = 7.6 Hz, 2H), 1.51 (s, 3H); **^{13}C NMR (126 MHz, $CDCl_3/D_2O$, 100:1)** δ: 144.1, 142.0, 141.8, 137.5, 128.6, 128.5, 127.9, 126.6, 126.1, 125.7, 114.6, 86.7, 58.1, 35.0, 32.0, 31.7; **^{11}B NMR (160 MHz, $CDCl_3/D_2O$, 100:1)** δ: 28.41; **HRMS (DART+):** Calcd for $C_{21}H_{24}BO_2$ $[M+H-H_2O]^+$: 319.1864; Found: 319.1868; **Specific rotation:** $[\alpha]_D^{20.0}$ –33.2 (*c* 0.80, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r. Enantiomeric purity was determined by HPLC analysis in

comparison with authentic racemic material after carbonylation (95:5 er shown; Chiralcel OD-H column, 95.0:5.0 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm).



Detector A Channel 1 220nm

Peak#	Ret. Time	Area	Area%
1	15.882	12422882	50.208
2	18.559	12320027	49.792
Total		24742909	100.000

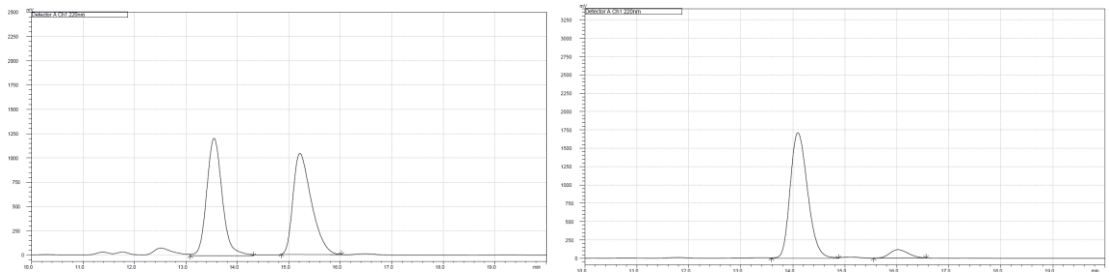


Detector A Channel 1 220nm

Peak#	Ret. Time	Area	Area%
1	16.153	1851626	94.523
2	18.981	107284	5.477
Total		1958910	100.000

((*R*, *Z*)-7-((*tert*-butyldimethylsilyl)oxy)-3-((*S*)-1-hydroxy-1-phenylethyl)hepta-1,4-dien-4-yl)boronic acid (2.10)

IR (neat): 3374 (w, br), 2952 (m), 2854 (m), 1665 (w), 1425 (s), 1255 (s), 1092 (s), 834 (s), 775 (s), 699 (s) cm^{-1} ; **^{1}H NMR (400 MHz, $CDCl_3/D_2O$, 100:1)** δ: 7.35 – 7.28 (m, 4H), 7.25 – 7.18 (m, 1H), 6.34 (td, *J* = 7.1, 1.9 Hz, 1H), 5.08 (ddd, *J* = 17.1, 10.0, 8.5 Hz, 1H), 4.84 (ddd, *J* = 17.0, 2.0, 0.9 Hz, 1H), 4.71 (ddd, *J* = 10.1, 2.0, 0.8 Hz, 1H), 3.68 (ddt, *J* = 10.0, 6.4, 3.0 Hz, 2H), 3.54 (d, *J* = 8.1 Hz, 1H), 2.46 – 2.29 (m, 2H), 1.60 (s, 3H), 0.90 (s, 9H), 0.06 (d, *J* = 1.0 Hz, 6H); **^{13}C NMR (126 MHz, $CDCl_3/D_2O$, 100:1)** δ: 144.2, 139.3, 137.5, 127.9, 126.6, 125.8, 114.7, 86.7, 62.3, 58.2, 34.0, 31.8, 26.1, 18.5, -5.1; **^{11}B NMR (126 MHz, $CDCl_3/D_2O$, 100:1)** δ: 28.47; **HRMS (DART+):** Calcd for $C_{21}H_{34}BO_3Si$ $[M+H-H_2O]^+$: 373.2365; Found: 373.2351; **Specific rotation:** $[\alpha]_D^{20.0}$ +4.4 (*c* 1.05, $CHCl_3$) for an enantiomerically enriched sample of 93.5:6.5 e.r. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material after carbonylation (93.5:6.5 er shown; Chiralcel OD-H column, 99.9:0.1 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm).



Detector A Channel 1 220nm

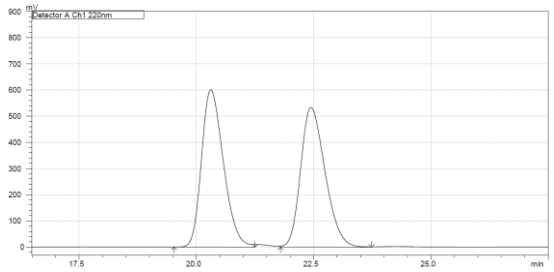
Peak#	Ret. Time	Area	Area%
1	13.545	25285621	49.508
2	15.213	25787992	50.492
Total		51073613	100.000

Detector A Channel 1 220nm

Peak#	Ret. Time	Area	Area%
1	14.096	39749882	93.456
2	16.021	2783600	6.544
Total		42533483	100.000

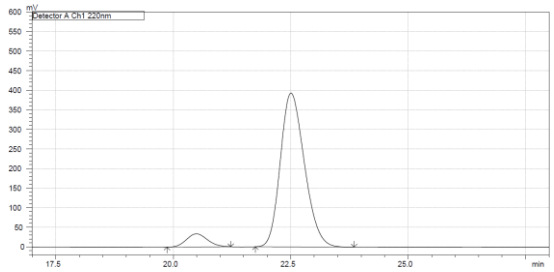
((*R*, *Z*)-3-((*S*)-1-hydroxy-1-phenylethyl)-8-methylnona-1,4-dien-4-yl)boronic acid (2.11)

IR (neat): 3366 (w, b), 2952 (m), 2866 (w), 1662 (m), 1302 (s), 1263 (s), 1029 (m), 904 (m), 760 (m), 699 (s) cm^{-1} ; **^{1}H NMR (400 MHz, $CDCl_3/D_2O$, 100:1)** δ: 7.33 – 7.31 (m, 4H), 7.25 – 7.19 (m, 1H), 6.32 (td, *J* = 7.1, 1.9 Hz, 1H), 5.09 (ddd, *J* = 17.0, 10.0, 8.6 Hz, 1H), 4.84 (dd, *J* = 17.1, 2.2 Hz, 1H), 4.72 (dd, *J* = 10.0, 2.0 Hz, 1H), 3.53 (dd, *J* = 8.6, 1.9 Hz, 1H), 2.13 (q, *J* = 7.2 Hz, 2H), 1.61 (s, 3H), 1.55 (dt, *J* = 13.3, 6.6 Hz, 1H), 1.34 – 1.24 (m, 2H), 0.91 – 0.87 (m, 6H); **^{13}C NMR (101 MHz, $CDCl_3/D_2O$, 100:1)** δ: 144.2, 143.8, 137.6, 127.9, 126.6, 125.8, 114.5, 86.8, 58.1, 37.9, 31.7, 28.1, 27.9, 22.8, 22.4; **^{11}B NMR (160 MHz, $CDCl_3/D_2O$, 100:1)** δ: 28.43; **HRMS (DART+):** Calcd for $C_{18}H_{26}BO_2$ $[M+H-H_2O]^+$: 285.2020. Found: 285.2023. **Specific rotation:** $[\alpha]_D^{20.0}$ +8.9 (*c* 0.83, $CHCl_3$) for an enantiomerically enriched sample of 93:7 e.r. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material after carbonylation (93:7 e.r. shown; Chiralcel OZ-H column, 99.5:0.5 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm).



Detector A Channel 1 220nm

Peak#	Ret. Time	Area	Area%
1	20.310	19542978	50.282
2	22.447	19323986	49.718
Total		38866964	100.000

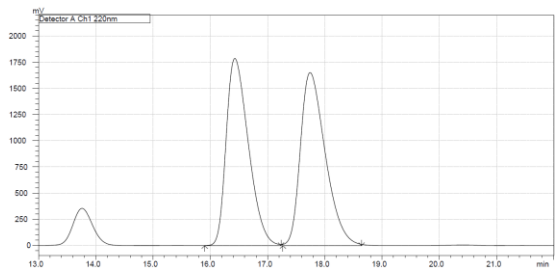


Detector A Channel 1 220nm

Peak#	Ret. Time	Area	Area%
1	20.492	1041478	6.919
2	22.506	14011576	93.081
Total		15053054	100.000

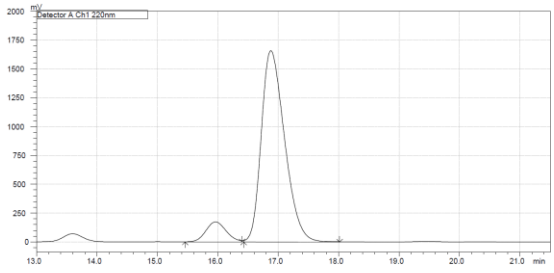
((*R*, *Z*)-1-cyclohexyl-3-((*S*)-1-hydroxy-1-phenylethyl)penta-1,4-dien-2-yl)boronic acid (2.12)

IR (neat): 3372 (w, b), 2920 (s), 2847 (m), 1661 (m), 1412 (s), 1260 (s), 1041 (m), 901 (s), 760 (s), 699 (s) cm^{-1} ; **^{1}H NMR (500 MHz, $CDCl_3/D_2O$, 100:1)** δ: 7.35 – 7.29 (m, 4H), 7.25 – 7.18 (m, 1H), 6.14 (dd, *J* = 9.7, 1.8 Hz, 1H), 5.13 (ddd, *J* = 17.0, 10.1, 8.4 Hz, 1H), 4.86 (ddd, *J* = 17.1, 2.0, 1.0 Hz, 1H), 4.71 (ddd, *J* = 10.1, 2.0, 0.7 Hz, 1H), 3.56 (dd, *J* = 8.4, 1.9 Hz, 1H), 2.28 (tdt, *J* = 11.1, 9.6, 3.7 Hz, 1H), 1.78 – 1.55 (m, 9H), 1.34 – 1.25 (m, 1H), 1.22 – 1.13 (m, 3H), 1.09 – 1.01 (m, 1H); **^{13}C NMR (126 MHz, $CDCl_3/D_2O$, 100:1)** δ: 148.6, 144.2, 138.4, 127.9, 126.6, 125.8, 114.4, 86.7, 58.0, 39.2, 32.6, 31.8, 31.6, 26.1, 25.9, 25.7; **^{11}B NMR (160 MHz, $CDCl_3/D_2O$, 100:1)** δ: 29.03; **HRMS (DART+):** Calcd for $C_{19}H_{26}BO_2$ $[M+H-H_2O]^+$: 297.2020. Found: 297.2014. **Specific rotation:** $[\alpha]_D^{20.0}$ +4.9 (*c* 0.83, $CHCl_3$) for an enantiomerically enriched sample of 92:8 e.r. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material after carbonylation (92:8 e.r. shown; Chiralcel OZ-H column,99.5:0.5 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm).



Detector A Channel 1 220nm

Peak#	Ret. Time	Area	Area%
1	16.427	48243360	49.128
2	17.743	49955185	50.872
Total		98198545	100.000

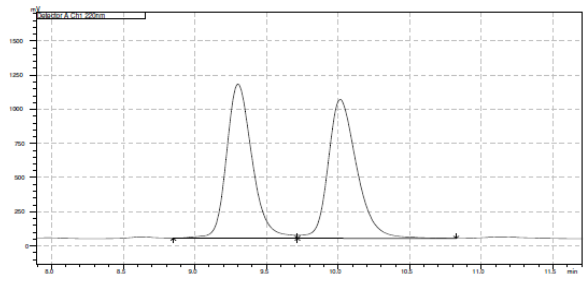


Detector A Channel 1 220nm

Peak#	Ret. Time	Area	Area%
1	15.961	4049972	8.336
2	16.877	44533070	91.664
Total		48583042	100.000

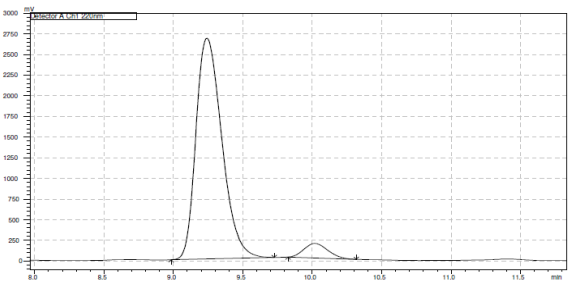
((*R*, *Z*)-4-((*S*)-1-Hydroxy-1-phenylethyl)hexa-2,5-dien-3-yl)boronic acid (2.13)

IR (neat): 3375 (s), 2973 (m), 2923 (w), 1666 (s), 1412 (s), 1314 (s), 1207 (m), 1045 (w), 904 (m), 761 (s), 700 (s) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$/D_2O, 100:1)** δ 7.32 (m, 4H), 7.22 (dq, *J* = 8.7, 4.1 Hz, 1H), 6.42 (q, *J* = 6.4 Hz, 1H), 5.06 (dt, *J* = 17.9, 9.4 Hz, 1H), 4.83 (d, *J* = 17.0 Hz, 1H), 4.72 (d, *J* = 10.1 Hz, 1H), 3.53 (d, *J* = 8.6 Hz, 1H), 1.75 (d, *J* = 6.8 Hz, 3H), 1.60 (s, 3H); **^{13}C NMR (151 MHz, $CDCl_3$/D_2O, 100:1)** δ 144.3, 137.7, 137.1, 127.9, 126.6, 125.8, 114.5, 86.7, 57.9, 31.9, 15.9; **^{11}B NMR (160 MHz, $CDCl_3$/D_2O, 100:1)** δ: 27.44; **HRMS (DART+)**: Calcd for $C_{14}H_{18}BO_2$ $[M+H-H_2O]^+$: 229.1394; Found: 229.1396; **Specific rotation**: $[\alpha]_D^{20.0}$ +29.0 (*c* 1.0, $CHCl_3$) for an enantiomerically enriched sample of 94:6 e.r.; Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (94:6 e.r. shown; Chiralcel OD-H column, 95:5 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm).



Detector A Channel 1 220nm

Peak#	Ret. Time	Area%
1	9.301	49.800
2	10.015	50.200
Total		100.000

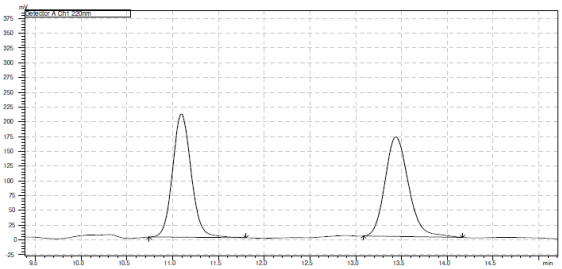


Detector A Channel 1 220nm

Peak#	Ret. Time	Area%
1	9.241	94.312
2	10.017	5.688
Total		100.000

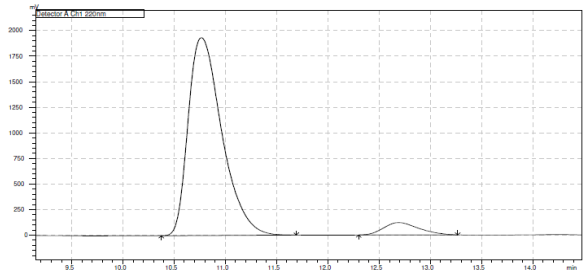
((*R*, *Z*)-4-((*S*)-1-Hydroxy-1-(4-methoxyphenyl)ethyl)hexa-2,5-dien-3-yl)boronic acid (2.14)

IR (neat): 2990 (w), 2914 (m), 1649 (w), 1493 (s), 1380 (s), 1267 (s), 1194 (m), 904 (s), 760 (w), cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3/D_2O$, 100:1)** δ 7.22 (d, *J* = 8.5 Hz, 2H), 6.85 (d, *J* = 8.5 Hz, 2H), 6.41 (q, *J* = 6.6, 5.9 Hz, 1H), 5.07 (dt, *J* = 18.2, 9.4 Hz, 1H), 4.83 (d, *J* = 16.9 Hz, 1H), 4.73 (d, *J* = 10.1 Hz, 1H), 3.80 (s, 3H), 3.49 (d, *J* = 8.4 Hz, 1H), 1.74 (d, *J* = 6.7 Hz, 3H), 1.57 (s, 3H); **^{13}C NMR (126 MHz, $CDCl_3/D_2O$, 100:1)** δ 158.2, 137.6, 137.4, 136.5, 126.9, 114.4, 113.3, 86.5, 58.0, 55.3, 31.9, 15.9; **^{11}B NMR (160 MHz, $CDCl_3/D_2O$, 100:1)** δ: 28.04; **HRMS (DART+)**: Calcd for $C_{15}H_{20}BO_3$ $[M+H-H_2O]^+$: 259.1500; Found: 259.1507; **Specific rotation**: $[\alpha]_D^{20.0}$ +15.6 (*c* 0.3, $CHCl_3$) for an enantiomerically enriched sample of 94:6 e.r.; Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (94:6 e.r. shown; Chiralcel OD-H column, 95:5 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm).



Detector A Channel 1 220nm

Peak#	Ret. Time	Area%
1	11.094	49.409
2	13.437	50.591
Total		100.000



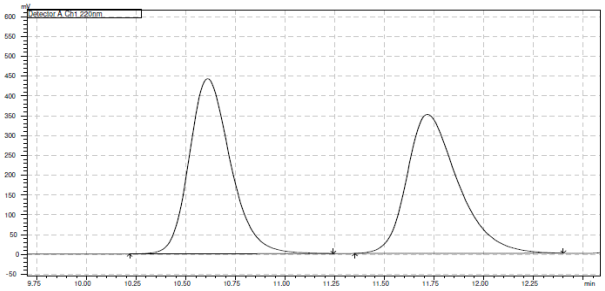
Detector A Channel 1 220nm

Peak#	Ret. Time	Area%
1	10.766	93.872
2	12.692	6.128
Total		100.000

((*R*, *Z*)-4-((*S*)-1-Hydroxy-1-(*p*-tolyl)ethyl)hexa-2,5-dien-3-yl)boronic acid (2.15)

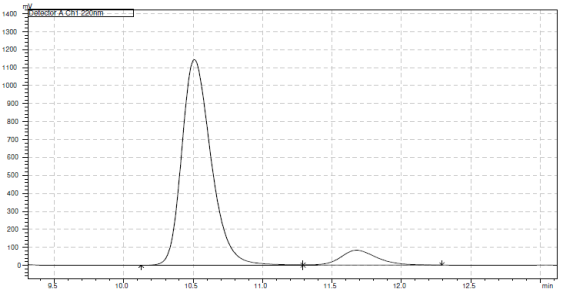
IR (neat): 2971 (w), 2921 (w), 1664 (m), 1512 (w), 1407 (s), 1370 (w), 1262 (s), 1075 (m), 1051 (m), 904 (s), 816 (s), 674 (w) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3/D_2O$, 100:1)** δ 7.20 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 6.41 (qd, *J* = 6.8, 1.8 Hz, 1H), 5.08 (ddd, *J* = 17.1, 10.0, 8.6 Hz, 1H), 4.89 – 4.78 (m, 1H), 4.78 – 4.68 (m, 1H), 3.51 (d, *J* = 8.5 Hz, 1H),

2.33 (s, 3H), 1.75 (d, J = 6.8 Hz, 3H), 1.58 (s, 3H); **^{13}C NMR (126 MHz, $CDCl_3/D_2O$, 100:1)** δ 141.4, 137.5, 137.3, 136.1, 128.6, 125.7, 114.4, 86.6, 57.9, 32.0, 21.2, 15.9; **^{11}B NMR (160 MHz, $CDCl_3/D_2O$, 100:1)** δ: 27.67; **HRMS (DART+)**: Calcd for $C_{15}H_{20}BO_2$ $[M+H-H_2O]^+$: 243.1551; Found: 243.1556; **Specific rotation**: $[\alpha]_D^{20.0}$ +21.6 (*c* 0.5, $CHCl_3$) for an enantiomerically enriched sample of 92:8 e.r.; Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (92:8 e.r. shown; Chiralcel OD-H column, 98:2 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm).



Detector A Channel 1 220nm

Peak#	Ret. Time	Area%
1	10.609	50.407
2	11.716	49.593
Total		100.000



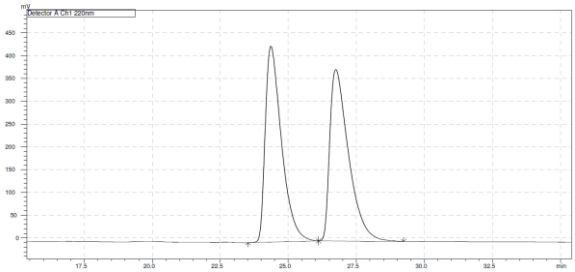
Detector A Channel 1 220nm

Peak#	Ret. Time	Area%
1	10.509	91.809
2	11.678	8.191
Total		100.000

((*R*, *Z*)-4-((*S*)-1-Hydroxy-1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl) ethyl)hexa-2,5-dien-3-yl)boronic acid (2.16)

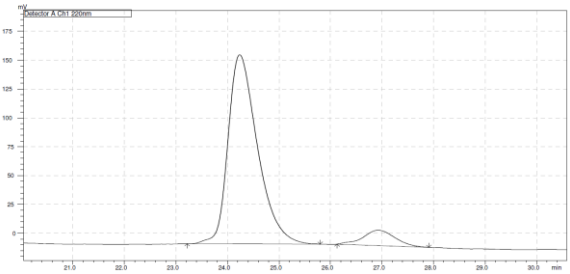
IR (neat): 3364 (m), 2973 (w), 2925 (w), 1666 (s), 1408 (s), 1306 (m), 1208 (m), 913 (m), 785 (m), 697 (m) cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3/D_2O$, 100:1)** δ 7.76 (d, J = 7.2 Hz, 2H), 7.33 (d, J = 7.1 Hz, 2H), 6.41 (q, J = 6.7 Hz, 1H), 5.04 (dt, J = 18.3, 9.3 Hz, 1H), 4.82 (d, J = 16.9 Hz, 1H), 4.70 (d, J = 10.1 Hz, 1H), 3.54 (d, J = 8.5 Hz, 1H), 1.74 (d, J = 6.7 Hz, 3H), 1.57 (s, 3H), 1.34 (s, 12H); **^{13}C NMR (126 MHz, $CDCl_3/D_2O$, 100:1)** δ 147.5, 137.7, 136.9, 134.5, 125.2, 114.6, 86.7, 83.9, 57.8, 31.9, 25.0, 25.0, 15.9; **^{11}B NMR (160 MHz, $CDCl_3/D_2O$, 100:1)** δ: 27.86; **HRMS (DART+)**: Calcd for $C_{20}H_{29}B_2O_4$ $[M+H-H_2O]^+$: 355.2247; Found: 355.2261; **Specific rotation**: $[\alpha]_D^{20.0}$ +6.1 (*c* 1.0, $CHCl_3$) for an enantiomerically enriched sample of 92:8 e.r.; Enantiomeric purity was determined by

HPLC analysis in comparison with authentic racemic material (92:8 e.r. shown; Chiralcel OD-H column, 98:2 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm).



Detector A Channel 1 220nm

Peak#	Ret. Time	Area%
1	24.359	49.763
2	26.745	50.237
Total		100.000

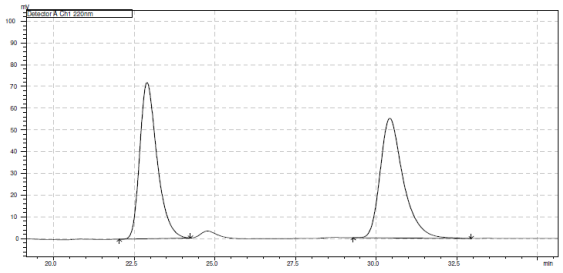


Detector A Channel 1 220nm

Peak#	Ret. Time	Area%
1	24.237	91.936
2	26.924	8.064
Total		100.000

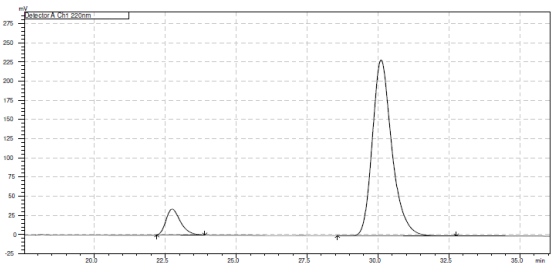
((*R*, *Z*)-4-((*S*)-1-(4-Bromophenyl)-1-hydroxyethyl)hexa-2,5-dien-3-yl)boronic acid (2.17)

IR (neat): 2971 (m), 2923 (w), 1665 (s), 1423 (s), 1305 (m), 1261 (s), 1078 (m), 1008 (s), 909 (m), 827 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3/D_2O$, 100:1)** δ 7.43 (d, *J* = 8.2 Hz, 2H), 7.19 (d, *J* = 8.1 Hz, 2H), 6.42 (q, *J* = 6.7 Hz, 1H), 5.03 (dt, *J* = 17.6, 9.3 Hz, 1H), 4.84 (d, *J* = 16.9 Hz, 1H), 4.75 (d, *J* = 10.1 Hz, 1H), 3.51 (d, *J* = 8.6 Hz, 1H), 1.75 (d, *J* = 6.4 Hz, 3H), 1.56 (s, 3H); **^{13}C NMR (151 MHz, $CDCl_3/D_2O$, 100:1)** δ 143.5, 138.1, 136.9, 131.0, 127.7, 120.5, 114.9, 86.3, 57.8, 31.9, 15.9; **^{11}B NMR (160 MHz, $CDCl_3/D_2O$, 100:1)** δ: 27.70; **HRMS (DART+)**: Calcd for $C_{14}H_{17}BO_2Br$ $[M+H-H_2O]^+$: 307.0500; Found: 307.0490; **Specific rotation**: $[\alpha]_D^{20.0}$ +2.1 (*c* 0.8, $CHCl_3$) for an enantiomerically enriched sample of 90:10 e.r.; Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (90:10 e.r. shown; Chiralcel AD-H column, 99.5:0.5 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm).



Detector A Channel 1 220nm

Peak#	Ret. Time	Area%
1	22.895	49.630
2	30.419	50.370
Total		100.000

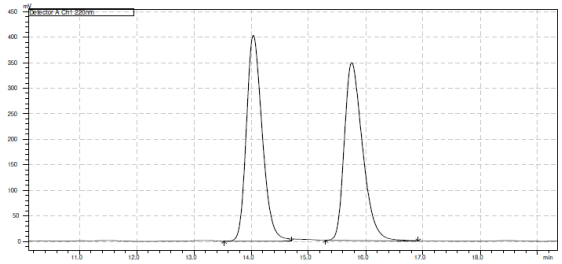


Detector A Channel 1 220nm

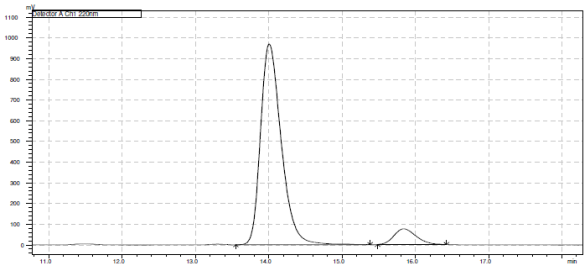
Peak#	Ret. Time	Area%
1	22.742	9.875
2	30.108	90.125
Total		100.000

((*R*, *Z*)-4-((*S*)-1-(2-Fluorophenyl)-1-hydroxyethyl)hexa-2,5-dien-3-yl)boronic acid (2.18)

IR (neat): 2971 (m), 2926 (w), 1665 (s), 1412 (s), 1288 (s), 1210 (m), 1116 (m), 1054 (m), 909 (s), 825 (m), 757 (s) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3/D_2O$, 100:1)** δ 7.60 (td, *J* = 7.8, 1.8 Hz, 1H), 7.25 – 7.18 (m, 1H), 7.11 (td, *J* = 7.6, 1.2 Hz, 1H), 6.97 (ddd, *J* = 11.4, 8.1, 1.1 Hz, 1H), 6.41 (qd, *J* = 6.7, 1.6 Hz, 1H), 5.15 (dt, *J* = 17.0, 9.4 Hz, 1H), 4.94 (d, *J* = 16.9 Hz, 1H), 4.70 (dd, *J* = 10.1, 1.9 Hz, 1H), 3.73 (dd, *J* = 8.8, 3.4 Hz, 1H), 1.77 (d, *J* = 6.7 Hz, 3H), 1.56 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3/D_2O$, 100:1)** δ 159.9, 157.5, 137.9, 136.0, 132.0, 131.9, 128.8, 128.7, 127.0, 127.0, 123.9, 123.9, 115.5, 115.3, 114.4, 85.6, 56.5, 30.0, 15.9; **^{11}B NMR (160 MHz, $CDCl_3/D_2O$, 100:1)** δ: 27.61； **HRMS (DART+)**: Calcd for $C_{14}H_{17}BO_2F$ $[M+H-H_2O]^+$: 247.1300; Found: 247.1299; **Specific rotation**: $[\alpha]_D^{20.0}$ +24.4 (*c* 0.6, $CHCl_3$) for an enantiomerically enriched sample of 92:8 e.r.; Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (92:8 e.r. shown; Chiralcel OD-H column, 99.5:0.5 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm).



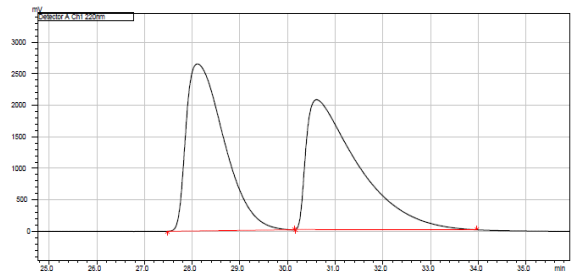
Peak#	Ret. Time	Area%
1	14.036	50.115
2	15.755	49.885
Total		100.000



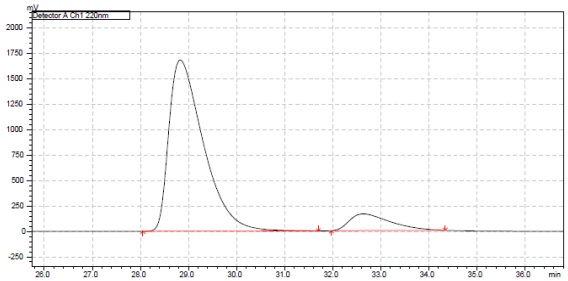
Peak#	Ret. Time	Area%
1	14.007	92.319
2	15.841	7.681
Total		100.000

((*R*,*Z*)-4-((*S*)-1-Hydroxy-1-(naphthalen-2-yl)ethyl)hexa-2,5-dien-3-yl)boronic acid (2.19)

IR (neat): 3387 (m), 3053 (w), 2971 (m), 2923 (w), 1665 (s), 1410 (s), 1269 (m), 1231 (s), 1140 (m), 1056 (m), 816 (s), 746 (s) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3/D_2O$, 100:1)** δ 7.90 (s, 1H), 7.88 – 7.76 (m, 3H), 7.50 – 7.42 (m, 2H), 7.36 (d, *J* = 8.6 Hz, 1H), 6.45 (q, *J* = 6.6 Hz, 1H), 5.10 (dt, *J* = 18.3, 9.3 Hz, 1H), 4.87 (d, *J* = 16.9 Hz, 1H), 4.67 (d, *J* = 10.0 Hz, 1H), 3.65 (d, *J* = 8.6 Hz, 1H), 1.78 (d, *J* = 6.8 Hz, 3H), 1.68 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3/D_2O$, 100:1)** δ 141.8, 137.9, 137.0, 133.3, 132.3, 128.3, 127.6, 127.4, 126.1, 125.8, 124.8, 123.9, 114.7, 86.8, 57.7, 32.0, 16.0; **^{11}B NMR (160 MHz, $CDCl_3/D_2O$, 100:1)** δ: 27.85; **HRMS (DART+)**: Calcd for $C_{18}H_{20}BO_2$ $[M+H-H_2O]^+$: 279.1551; Found: 279.1565; **Specific rotation**: $[\alpha]_D^{20.0}$ -14.6 (*c* 1.0, $CHCl_3$) for an enantiomerically enriched sample of 90:10 e.r.; Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (90:10 e.r. shown; Chiralcel OD-H column, 99.5:0.5 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm).



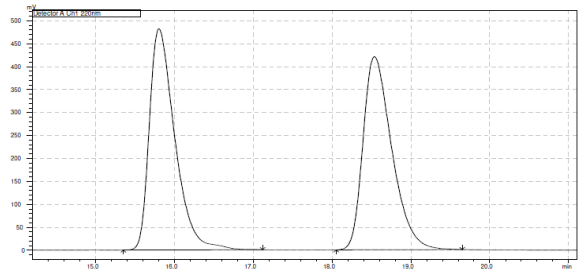
Peak#	Ret. Time	Area	Area%
1	28.109	146565252	48.493
2	30.609	155673463	51.507
Total		302238715	100.000



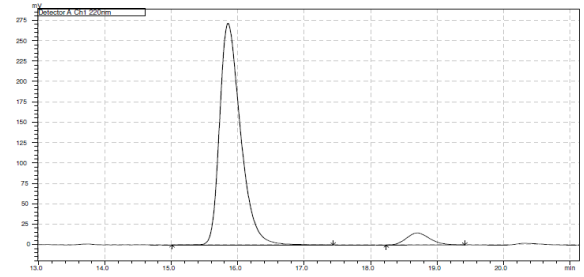
Peak#	Ret. Time	Area	Area%
1	28.829	83787989	89.649
2	32.635	9674119	10.351
Total		93462107	100.000

((*R*, *Z*)-4-((*S*)-1-(Furan-2-yl)-1-hydroxyethyl)hexa-2,5-dien-3-yl)boronic acid (2.20)

IR (neat): 3377 (m), 2975 (m), 2928 (w), 1664 (m), 1416 (s), 1278 (s), 1157 (w), 1002 (m), 730 (s) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$/D_2O, 100:1)** δ 7.34 (s, 1H), 6.41 (qd, *J* = 6.8, 2.0 Hz, 1H), 6.29 (dd, *J* = 3.1, 1.7 Hz, 1H), 6.18 (d, *J* = 3.2 Hz, 1H), 5.27 (dt, *J* = 17.2, 9.3 Hz, 1H), 4.95 (d, *J* = 17.0 Hz, 1H), 4.85 (d, *J* = 10.0 Hz, 1H), 3.45 (d, *J* = 8.6 Hz, 1H), 1.74 (d, *J* = 6.9 Hz, 3H), 1.63 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$/D_2O, 100:1)** δ 156.7, 141.8, 138.2, 136.5, 115.5, 110.1, 106.0, 83.6, 58.5, 27.5, 15.9; **^{11}B NMR (160 MHz, $CDCl_3$/D_2O, 100:1)** δ: 27.86; **HRMS (DART+)**: Calcd for $C_{12}H_{16}BO_3$ $[M+H-H_2O]^+$: 219.1187; Found: 219.1187; **Specific rotation**: $[\alpha]_D^{20.0}$ +4.8 (*c* 0.5, $CHCl_3$) for an enantiomerically enriched sample of 94:6 e.r.; Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (94:6 e.r. shown; Chiralcel OD-H column, 98:2 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm).



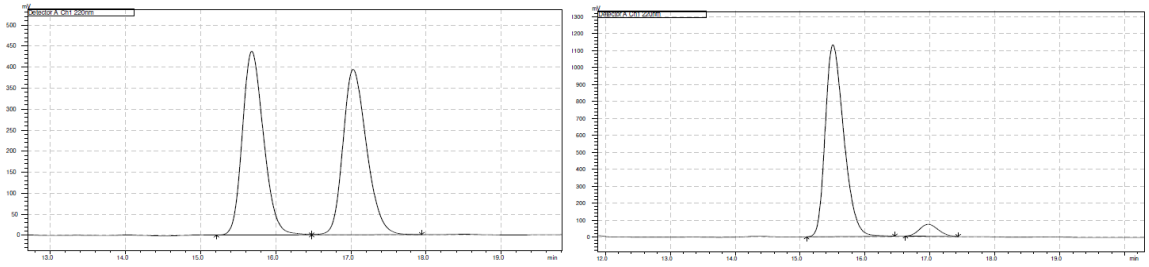
Peak#	Ret. Time	Area%
1	15.801	50.341
2	18.536	49.659
Total		100.000



Peak#	Ret. Time	Area%
1	15.852	94.177
2	18.704	5.823
Total		100.000

((*R*, *Z*)-4-((*S*)-1-Hydroxy-1-(thiophen-3-yl)ethyl)hexa-2,5-dien-3-yl)boronic acid (2.21)

IR (neat): 3363 (s), 2972 (m), 2923 (w), 1664 (s), 1410 (s), 1370 (m), 1284 (s), 1083 (m), 1053 (m), 784 (s), 673 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$/D_2O, 100:1)** δ 7.26 – 7.22 (m, 1H), 7.15 – 7.02 (m, 1H), 6.89 (d, *J* = 4.9 Hz, 1H), 6.42 (q, *J* = 6.4 Hz, 1H), 5.16 (dt, *J* = 18.2, 9.3 Hz, 1H), 4.88 (d, *J* = 17.0 Hz, 1H), 4.79 (d, *J* = 10.1 Hz, 1H), 3.45 (d, *J* = 8.4 Hz, 1H), 1.74 (d, *J* = 6.8 Hz, 3H), 1.60 (s, 3H); **^{13}C NMR (151 MHz, $CDCl_3$/D_2O, 100:1)** δ 145.9, 138.1, 137.1, 126.4, 125.3, 120.1, 114.7, 85.9, 58.2, 31.0, 15.9; **^{11}B NMR (160 MHz, $CDCl_3$/D_2O, 100:1)** δ: 27.74; **HRMS (DART+)**: Calcd for $C_{12}H_{16}BO_2S$ [M+H-H_2O]$^+$: 235.0959; Found: 235.0962; **Specific rotation**: $[\alpha]_D^{20.0}$ +5.2 (*c* 0.9, $CHCl_3$) for an enantiomerically enriched sample of 94:6 e.r.; Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (94:6 e.r. shown; Chiralcel OD-H column, 98:2 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm).



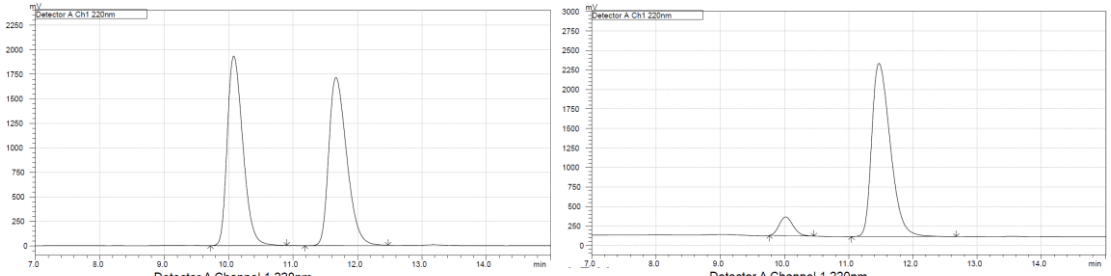
Peak#	Ret. Time	Area%
1	15.680	49.961
2	17.029	50.039
Total		100.000

Peak#	Ret. Time	Area%
1	15.505	94.070
2	16.973	5.930
Total		100.000

((*R*, *Z*)-4-((*S*)-5-hydroxy-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-yl)hexa-2,5-dien-3-yl)boronic acid (2.22)

IR (neat): 3356 (w, br), 2924 (m), 2855 (w), 1665 (m), 1409 (s), 1310 (s), 1275 (m), 987 (m), 907 (m), 744 (s) cm^{-1} ; **^{1}H NMR (400 MHz, $CDCl_3$/D_2O, 100:1)** δ: 7.66 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.18 (td, *J* = 7.6, 1.6 Hz, 1H), 7.13 (td, *J* = 7.3, 1.5 Hz, 1H), 7.03 (dd, *J* = 7.3,

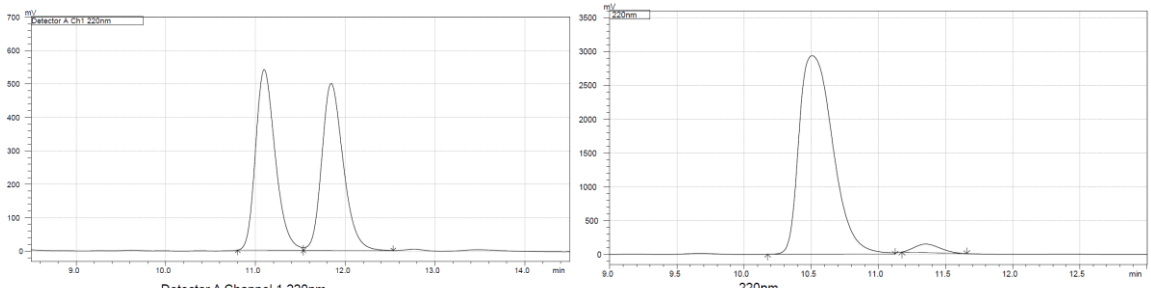
1.6 Hz, 1H), 6.41 (qd, *J* = 6.8, 1.8 Hz, 1H), 5.07 (ddd, *J* = 16.9, 10.0, 8.5 Hz, 1H), 4.91 – 4.85 (m, 1H), 4.65 (dd, *J* = 10.1, 1.9 Hz, 1H), 4.16 (d, *J* = 8.1 Hz, 1H), 2.86 – 2.77 (m, 1H), 2.75 – 2.66 (m, 1H), 2.00 – 1.81 (m, 5H), 1.78 (d, *J* = 6.8 Hz, 3H), 1.45 – 1.34 (m, 1H); **^{13}C NMR (126 MHz, CDCl$_3$/D$_2$O, 100:1)** δ: 143.5, 139.6, 137.5, 135.8, 130.1, 127.1, 126.0, 126.0, 113.5, 90.4, 49.8, 41.5, 37.1, 27.7, 27.3, 15.9; **^{11}B NMR (160 MHz, CDCl$_3$/D$_2$O, 100:1)** δ: 27.75; **HRMS (DART+):** Calcd for $C_{17}H_{22}BO_2$ $[M+H-H_2O]^+$: 269.1707; Found: 269.1717; **Specific rotation:** $[\alpha]_D^{20.0}$ +74.6 (*c* 0.77, $CHCl_3$) for an enantiomerically enriched sample of 92:8 e.r.; Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material after carbonylation (92:8 e.r. shown; Chiralcel OD-H column, 97.5:2.5 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm).



((*R*, *Z*)-4-((*S*)-1-hydroxy-1-(2-methoxyphenyl)ethyl)hexa-2,5-dien-3-yl)boronic acid (2.23)

IR (neat): 3500 (s), 2968 (m), 2925 (m), 1666 (s),1432 (s), 1308 (m), 1252 (w), 1042 (w), 753 (m) cm^{-1}; **^{1}H NMR (400 MHz, CDCl$_3$/D$_2$O, 100:1)** δ 7.59 (d, *J* = 7.5 Hz, 1H), 7.23 (t, *J* = 7.3 Hz, 1H), 6.94 (t, *J* = 7.5 Hz, 1H), 6.82 (d, *J* = 8.2 Hz, 1H), 6.38 (q, *J* = 6.4 Hz, 1H), 5.16 (dt, *J* = 17.6, 9.3 Hz, 1H), 4.82 (dd, *J* = 17.0, 2.1 Hz, 1H), 4.64 (dd, *J* = 10.1, 2.0 Hz, 1H), 3.89 – 3.72 (m, 2H), 3.82 (s, 3H), 1.77 (d, *J* = 6.7 Hz, 3H), 1.56 (s, 3H); **^{13}C NMR (151 MHz, CDCl$_3$/D$_2$O, 100:1)** δ 155.3, 137.0, 136.8, 132.8, 128.1, 126.4, 120.4, 113.4,

110.3, 86.7, 56.0, 54.9, 29.2, 15.9; **^{11}B NMR (160 MHz, $CDCl_3/D_2O$, 100:1)** δ: 27.47; Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material after carbonylation (97:3 e.r. shown; Chiralcel OD-H column, 98:2 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm).



Detector A Channel 1 220nm

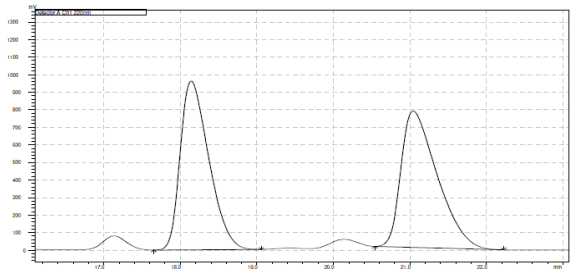
Peak#	Ret. Time	Area	Area%
1	11.095	8239204	49.829
2	11.842	8295729	50.171
Total		16534932	100.000

220nm

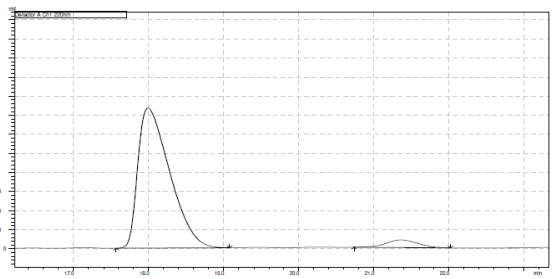
Peak#	Ret. Time	Area	Area%
1	10.507	51370730	96.841
2	11.353	1675495	3.159
Total		53046226	100.000

((4*R*, 5*R*, *Z*)-5-Hydroxy-5-methyl-7-phenyl-4-vinylhept-2-en-3-yl)boronic acid (2.24)

IR (neat): 3334 (m), 2935 (w), 1664 (m), 1422 (s), 1377 (w), 1290 (s), 1024 (s), 745 (w), 698 (s) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3/D_2O$, 100:1)** δ 7.31 – 7.23 (m, 2H), 7.19 (d, *J* = 7.5 Hz, 2H), 6.36 (qd, *J* = 6.7, 2.0 Hz, 1H), 5.80 – 5.64 (m, 1H), 5.14 – 4.99 (m, 2H), 3.24 (d, *J* = 9.2 Hz, 1H), 2.70 (t, *J* = 8.7 Hz, 2H), 1.94 – 1.78 (m, 2H), 1.74 (d, *J* = 6.8 Hz, 3H), 1.33 (s, 3H); **^{13}C NMR (126 MHz, $CDCl_3/D_2O$, 100:1)** δ 142.7, 137.5, 136.6, 128.5, 125.9, 115.8, 85.2, 57.2, 40.8, 30.6, 27.7, 15.8; **^{11}B NMR (160 MHz, $CDCl_3/D_2O$, 100:1)** δ: 27.31; **HRMS (DART$^+$)**: Calcd for $C_{16}H_{22}BO_2$ $[M+H-H_2O]^+$: 257.1707; Found: 257.1710; **Specific rotation**: $[\alpha]_D^{20.0}$ -20.6 (*c* 1.0, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.; Enantiomeric purity 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, 0.8 mL/min, 220 nm).



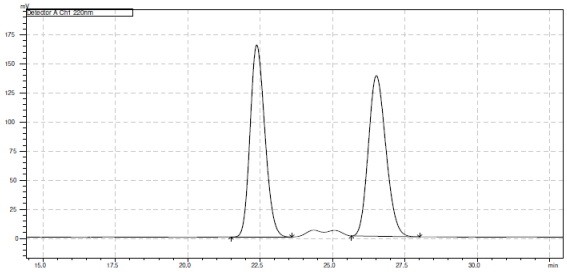
Peak#	Ret. Time	Area	Area%
1	18.141	24968281	49.402
2	21.042	25572698	50.598
Total		50540979	100.000



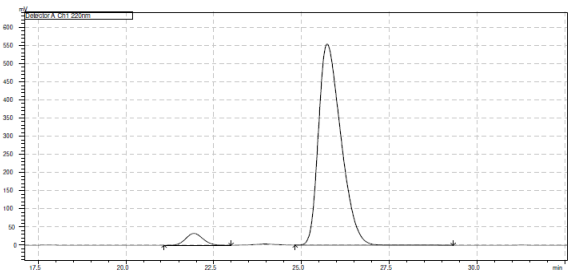
Peak#	Ret. Time	Area	Height	Conc.	Height%	Area%
1	17.991	53937996	1834080	94.763	94.840	94.763
2	21.359	2980596	99792	5.237	5.160	5.237
Total		56918592	1933872		100.000	100.000

((2*Z*, 4*R*, 5*R*, 8*Z*)-5-Hydroxy-5,9,13-trimethyl-4-vinyltetradeca-2,8,12-trien-3-yl)boronic acid (2.25)

IR (neat): 3335 (m), 2971 (m), 2929 (w), 1664 (m), 1432 (s), 1290 (s), 1062 (m), 744 (s) cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3/D_2O$, 100:1)** δ 6.36 (s, 1H), 5.70 (ddt, *J* = 14.9, 9.1, 7.4 Hz, 1H), 5.15 – 4.96 (m, 4H), 3.17 (d, *J* = 9.2 Hz, 1H), 2.05 (q, *J* = 7.5 Hz, 4H), 2.00 – 1.93 (m, 2H), 1.72 (dd, *J* = 6.8, 1.0 Hz, 3H), 1.67 (s, 3H), 1.59 (d, *J* = 2.6 Hz, 6H), 1.58 – 1.49 (m, 2H), 1.24 (s, 3H); **^{13}C NMR (126 MHz, $CDCl_3/D_2O$, 100:1)** δ 137.2, 136.7, 135.2, 131.5, 124.5, 124.3, 115.5, 85.6, 57.1, 39.8, 38.6, 27.6, 26.8, 25.8, 22.8, 17.8, 16.1, 15.8; **^{11}B NMR (160 MHz, $CDCl_3/D_2O$, 100:1)** δ: 26.99; **HRMS (DART^{+})**: Calcd for $C_{19}H_{32}BO_2$ $[M+H-H_2O]^{+}$: 303.2490; Found: 303.2492; **Specific rotation**: $[\alpha]_D^{20.0}$ -6.4 (*c* 1.0, $CHCl_3$) for an enantiomerically enriched sample of 95.5:4.5 e.r.; Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (95.5:4.5 e.r. shown; Chiralcel OZ-H column, 99.5:0.5 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm).



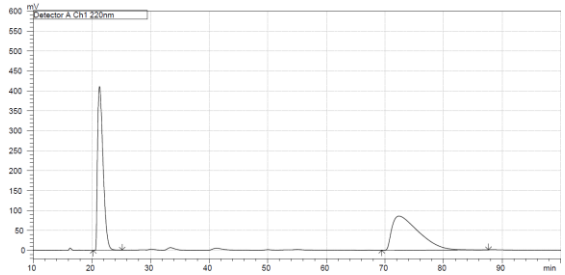
Peak#	Ret. Time	Area%
1	22.385	50.010
2	26.516	49.990
Total		100.000



Peak#	Ret. Time	Area%
1	21.936	4.321
2	25.730	95.679
Total		100.000

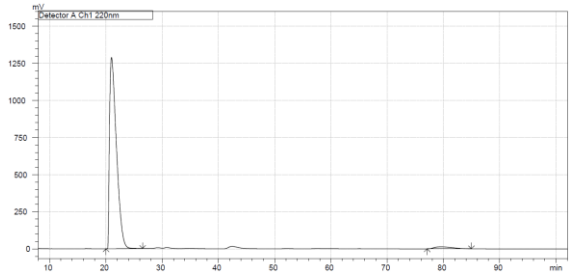
((2*Z*, 4*R*, 5*R*, 6*E*)-5-hydroxy-5-methyl-4-vinyldodeca-2,6-dien-3-yl)boronic acid (2.26)

IR (neat): 3364 (w, br), 2956 (m), 2923 (s), 1664 (m), 1430 (s), 1370 (m), 1284 (s), 973 (m), 908 (w), 660 (w) cm^{-1} ; **^{1}H NMR (600 MHz, $CDCl_3/D_2O$, 100:1)** δ: 6.36 (qd, *J* = 6.8, 2.2 Hz, 1H), 5.62 – 5.54 (m, 2H), 5.41 (d, *J* = 15.5 Hz, 1H), 5.01 – 4.91 (m, 2H), 3.20 (d, *J* = 9.1 Hz, 1H), 2.02 (q, *J* = 7.1 Hz, 2H), 1.72 (d, *J* = 6.8 Hz, 3H), 1.43 – 1.13 (m, 9H), 0.88 (t, *J* = 6.9 Hz, 3H); resolved peaks for minor diastereomer: δ: 5.68 (dt, *J* = 17.0, 9.5 Hz, 1H), 5.51 – 5.48 (m, 2H), 5.07 – 5.02 (m, 2H), 3.24 (d, *J* = 9.3 Hz, 1H); **^{13}C NMR (151 MHz, $CDCl_3/D_2O$, 100:1)** δ: 137.9, 137.8, 137.7, 133.1, 129.0, 114.6, 84.8, 57.8, 32.4, 31.5, 29.1, 28.9, 22.6, 15.8, 14.2; resolved peaks for minor diastereomer: δ: 136.7, 136.6, 127.9, 84.5, 56.4, 32.2, 31.4, 24.4; **^{11}B NMR (160 MHz, $CDCl_3/D_2O$, 100:1)** δ: 29.15; **HRMS (DART+):** Calcd for $C_{15}H_{26}BO_2$ $[M+H-H_2O]^+$: 249.2020; Found: 249.2029; **Specific rotation:** $[\alpha]_D^{20.0}$ +5.1 (*c* 0.53, $CHCl_3$) for an enantiomerically enriched sample of 97:3 e.r.; Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material after carbonylation (97:3 e.r. shown; Chiralpak AS-H column, 99.7:0.3 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm).



Detector A Channel 1 220nm

Peak#	Ret. Time	Area	Area%
1	21.303	26843430	50.024
2	72.370	26817658	49.976
Total		53661088	100.000

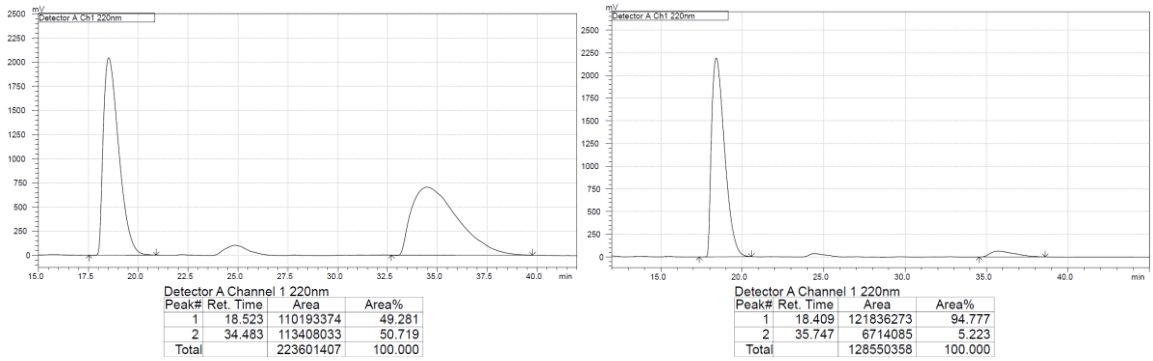


Detector A Channel 1 220nm

Peak#	Ret. Time	Area	Area%
1	20.996	110145089	97.321
2	79.601	3032039	2.679
Total		113177129	100.000

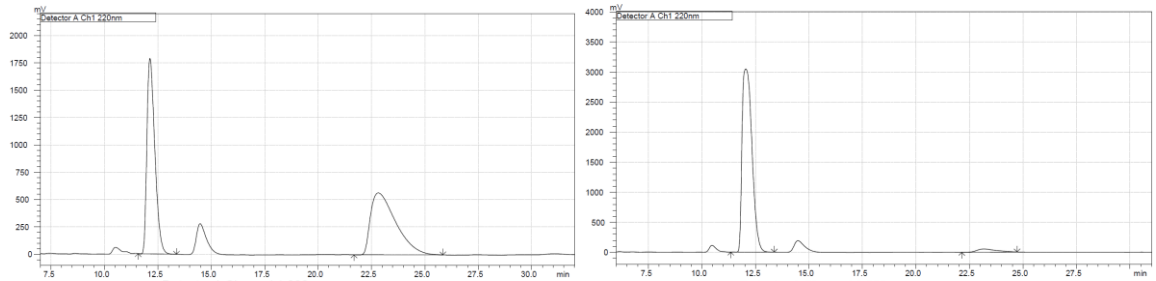
((2*Z*, 4*R*, 5*R*, 6*E*)-5-hydroxy-5-methyl-7-phenyl-4-vinylhepta-2,6-dien-3-yl)boronic acid (2.27)

IR (neat): 3368 (w, b), 3023 (w), 2972 (w), 1664 (m), 1414 (s), 1290 (s), 970 (m), 894 (m), 748 (s), 692 (m) cm^{-1} ; **^{1}H NMR (400 MHz, $CDCl_3/D_2O$, 100:1)** δ: 7.40 – 7.34 (m, 2H), 7.33 – 7.27 (m, 2H), 7.25 – 7.18 (m, 1H), 6.58 (d, *J* = 16.0 Hz, 1H), 6.39 (qd, *J* = 6.8, 2.2 Hz, 1H), 6.19 (d, *J* = 16.0 Hz, 1H), 5.60 (ddd, *J* = 17.0, 10.1, 9.1 Hz, 1H), 5.06 – 4.97 (m, 2H), 3.35 (d, *J* = 9.8 Hz, 1H), 1.75 (dd, *J* = 6.8, 1.3 Hz, 3H), 1.44 (s, 3H). resolved peaks for minor diastereomer: δ: 6.48 (d, *J* = 15.9 Hz, 1H), 6.37 – 6.32 (m, 1H), 6.26 (d, *J* = 15.9 Hz, 1H), 5.74 (ddd, *J* = 16.9, 10.1, 9.0 Hz, 1H), 5.15 – 5.08 (m, 2H), 3.37 (d, *J* = 12.2 Hz, 2H), 1.71 (dd, *J* = 6.8, 1.2 Hz, 3H), 1.39 (s, 3H); **^{13}C NMR (126 MHz, $CDCl_3/D_2O$, 100:1)** δ: 138.1, 137.5, 137.3, 136.5, 133.4, 128.7, 127.5, 127.4, 126.6, 115.0, 85.0, 58.1, 29.3, 15.9; resolved peaks for minor diastereomer: δ: 127.6, 126.7, 116.0, 84.7, 56.4, 30.5; **^{11}B NMR (160 MHz, $CDCl_3/D_2O$, 100:1)** δ: 28.60; **HRMS (DART+):** Calcd for $C_{16}H_{20}BO_2$ $[M+H-H_2O]^+$: 255.1551; Found: 255.1563; Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material after carbonylation (95:5 e.r. shown; Chiralpak AS-H column, 97.5:2.5 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm).



((2*Z*, 4*R*, 5*R*, 6*E*, 8*E*)-5-hydroxy-5-methyl-4-vinyldodeca-2,6,8-trien-3-yl)boronic acid (2.28)

IR (neat): 3361 (w, b), 2958 (m), 2924 (m), 1664 (m), 1414 (s), 1282 (s), 1231 (m), 988 (s), 909 (w), 660 (w) cm^{-1} ; **^{1}H NMR (600 MHz, $CDCl_3/D_2O$, 100:1)** δ: 6.35 (qd, *J* = 6.9, 2.2 Hz, 1H), 6.17 (dd, *J* = 15.3, 10.5 Hz, 1H), 6.06 – 5.99 (m, 1H), 5.68 (dt, *J* = 14.6, 6.9 Hz, 1H), 5.60 – 5.50 (m, 2H), 5.01 – 4.94 (m, 2H), 3.24 (d, *J* = 9.1 Hz, 1H), 2.05 (qd, *J* = 7.0, 1.5 Hz, 2H), 1.72 (dd, *J* = 6.8, 1.3 Hz, 3H), 1.44 – 1.37 (m, 2H), 1.34 (s, 3H), 0.90 (t, *J* = 7.4 Hz, 3H); resolved peaks for minor diastereomer: δ: 6.09 (dd, *J* = 15.3, 10.4 Hz, 1H), 5.09 – 5.01 (m, 2H), 3.28 (d, *J* = 9.3 Hz, 1H), 1.70 (dd, *J* = 6.8, 1.2 Hz, 3H), 1.29 (s, 3H); **^{13}C NMR (151 MHz, $CDCl_3/D_2O$, 100:1)** δ: 137.8, 137.7, 134.8, 134.2, 129.9, 128.3, 114.8, 84.8, 58.0, 34.9, 29.1, 22.6, 15.9, 13.9; resolved peaks for minor diastereomer: δ: 135.3, 56.4, 24.5; **^{11}B NMR (160 MHz, $CDCl_3/D_2O$, 100:1)** δ: 29.82; **HRMS (DART+):** Calcd for $C_{15}H_{24}BO_2$ $[M+H-H_2O]^+$: 247.1864; Found: 247.1866; **Specific rotation:** $[\alpha]_D^{20.0}$ –40.6 (*c* 0.77, $CHCl_3$) for an enantiomerically enriched sample of 97:3 e.r. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material after carbonylation (97:3 e.r. shown; Chiralpak AS-H column, 97.5:2.5 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm).



Detector A Channel 1 220nm

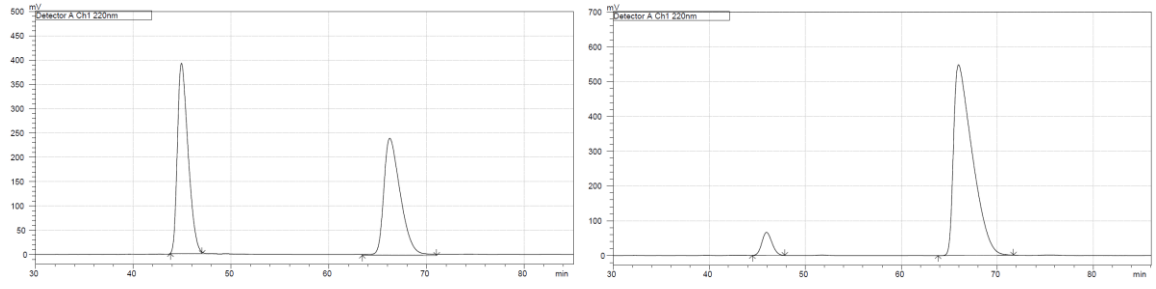
Peak#	Ret. Time	Area	Area%
1	12.131	46203317	49.825
2	22.822	46527760	50.175
Total		92731077	100.000

Detector A Channel 1 220nm

Peak#	Ret. Time	Area	Area%
1	12.046	98041642	96.701
2	23.171	3344837	3.299
Total		101386479	100.000

((2*Z*, 4*R*, 5*R*, 6*E*)-5-hydroxy-5-methyl-7-(2,6,6-trimethylcyclohex-1-en-1-yl)-4-vinylhepta-2,6-dien-3-yl)boronic acid (2.29)

IR (neat): 3348 (w, b), 2960 (m), 2923 (m), 1664 (m), 1437 (s), 1282 (s), 1115 (w), 974 (m), 908 (w), 654 (w) cm^{-1} ; **^{1}H NMR (500 MHz, $CDCl_3/D_2O$, 100:1)** δ: 6.36 (qd, *J* = 6.9, 2.2 Hz, 1H), 6.03 (ddd, *J* = 16.0, 2.7, 1.5 Hz, 1H), 5.71 – 5.56 (m, 1H), 5.38 (d, *J* = 16.1 Hz, 1H), 5.02 – 4.95 (m, 2H), 3.26 (d, *J* = 9.3 Hz, 1H), 1.95 (t, *J* = 6.5 Hz, 2H), 1.73 (dd, *J* = 6.8, 1.2 Hz, 3H), 1.64 (s, 3H), 1.62 – 1.55 (m, 2H), 1.46 – 1.41 (m, 2H), 1.38 (s, 3H), 1.01 – 0.92 (m, 6H); **^{13}C NMR (126 MHz, $CDCl_3/D_2O$, 100:1)** δ: 138.2, 137.7, 137.4, 136.7, 128.1, 125.8, 114.7, 85.5, 58.0, 39.6, 34.2, 32.8, 29.2, 28.8, 21.6, 19.5, 15.8; **^{11}B NMR (160 MHz, $CDCl_3/D_2O$, 100:1)** δ: 28.75; **HRMS (DART+):** Calcd for $C_{19}H_{30}BO_2$ $[M+H-H_2O]^+$: 301.2333. Found: 301.2332. **Specific rotation:** $[\alpha]_D^{20.0}$ –16.3 (*c* 0.80, $CHCl_3$) for an enantiomerically enriched sample of 94:6 e.r.; Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material after carbonylation (94:6 e.r. shown; Chiralcel OZ-H column, 99.7:0.3 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm).



Detector A Channel 1 220nm

Peak#	Ret. Time	Area	Area%
1	44.929	29812817	51.229
2	66.245	28382259	48.771
Total		58195076	100.000

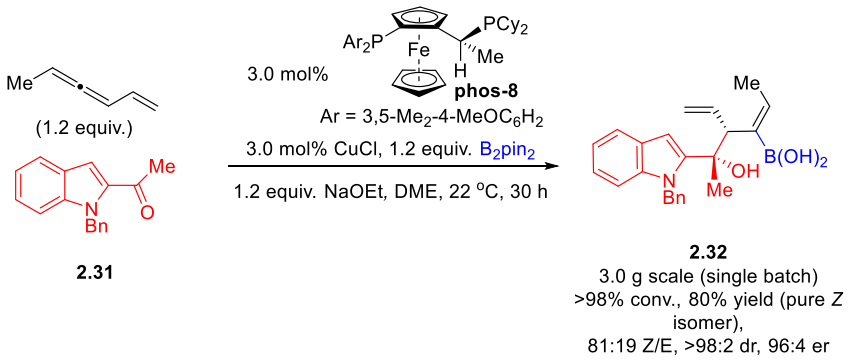
Detector A Channel 1 220nm

Peak#	Ret. Time	Area	Area%
1	45.967	4856171	6.142
2	65.964	74207424	93.858
Total		79063595	100.000

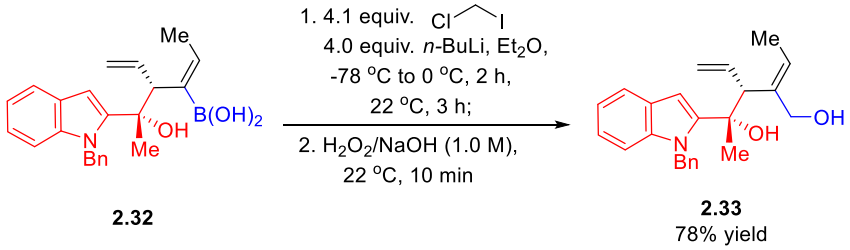
((4*S*, 5*S*, 6*S*, *Z*)-5-hydroxy-5,6,10-trimethyl-4-vinylundeca-2,9-dien-3-yl)boronic acid (2.30)

IR (neat): 3372 (w, br), 2963 (m), 2922 (m), 1668 (m), 1412 (s), 1376 (s), 1272 (m), 1081 (m), 906 (w), 686 (w) cm^{-1} ; **^{1}H NMR (500 MHz, $CDCl_3/D_2O$, 100:1)** δ: 6.28 (qd, *J* = 6.8, 1.7 Hz, 1H), 5.63 (dt, *J* = 16.7, 9.8 Hz, 1H), 5.13 – 5.06 (m, 1H), 5.05 – 4.94 (m, 2H), 3.23 (d, *J* = 9.4 Hz, 1H), 2.10 – 1.99 (m, 1H), 1.86 (dq, *J* = 14.4, 7.5 Hz, 1H), 1.81 – 1.73 (m, 1H), 1.70 (d, *J* = 6.8 Hz, 3H), 1.68 (s, 3H), 1.59 (s, 3H), 1.46 (td, *J* = 11.6, 6.5 Hz, 1H), 1.31 – 1.18 (m, 1H), 1.04 (s, 3H), 1.01 (d, *J* = 6.6 Hz, 3H), 0.94 – 0.84 (m, 1H); **^{13}C NMR (126 MHz, $CDCl_3/D_2O$, 100:1)** δ: 136.3, 135.8, 131.5, 124.8, 114.8, 87.9, 56.4, 38.2, 32.6, 26.4, 25.8, 22.8, 17.7, 15.6, 14.1; **^{11}B NMR (160 MHz, $CDCl_3/D_2O$, 100:1)** δ: 29.20; **HRMS (DART+):** Calcd for $C_{16}H_{28}BO_2$ $[M+H-H_2O]^+$: 263.2177; Found: 263.2185; **Specific rotation:** $[\alpha]_D^{20.0}$ –19.6 (*c* 0.45, $CHCl_3$) for an diastereomerically enriched sample of 95:5 d.r..

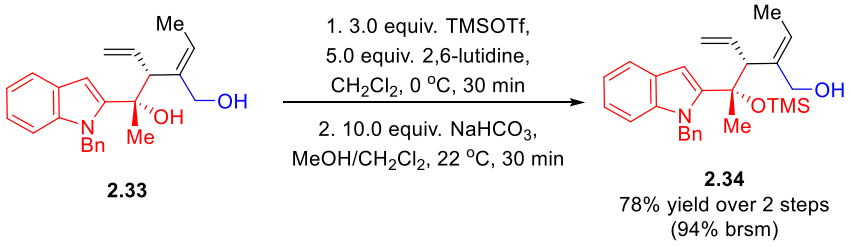
2.7.6 Representative Procedures in Application to Enantioselective Synthesis of (-)-16-Hydroxy-16,22-dihydroappariciné



An oven-dried flask equipped with a stir bar was charged with **phos-8** (213.2 mg, 0.30 mmol), CuCl (29.7 mg, 0.30 mmol), NaOEt (816.6 mg, 12.0 mmol) and DME (80 mL) in a nitrogen-filled glove box. The mixture was allowed to stir for 15 min under N_2 at 22 °C, after which $B_2(pin)_2$ (3.0473 g, 12.0 mmol) was added. The resulting mixture was allowed to stir for 10 min, the solution of methyl-substituted vinylallene in *o*-DCB and thf (methyl vinylallene : *o*-DCB : thf = 1 : 0.58 : 0.42, 2.37 g, 12.0 mmol) and ketone **2.31** (2.4931 g, 10.0 mmol) were added. The flask was removed from glovebox and the mixture was allowed to stir at 22 °C for 30 h. The mixture was filtrated by silica with Et_2O as eluent and concentrated in vacuo, affording yellow oil residue, which was purified by silica gel chromatography (30:1 to 3:1 hexanes/ethyl acetate) to afford **2.32** as a white foam (2.991 g, 8.0 mmol, 80% yield), and ***E*-2.32** as white foam (697.5 mg, 1.8 mmol, 18% yield).

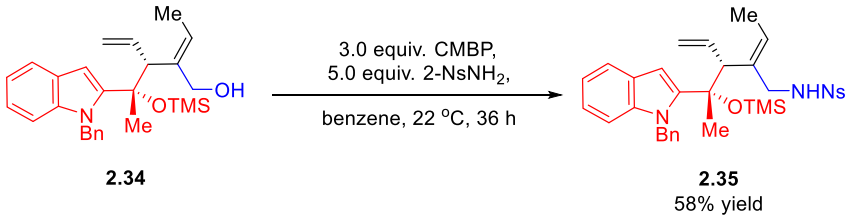


In a flamed-dried 6-drum vial under nitrogen a solution of alkenylboronic acid **2.32** (112.6 mg, 0.30 mmol) and chloroiodomethane (216.9 mg, 1.23 mmol) in anhydrous Et_2O (3.0 mL) was cooled to −78 °C. *n*-Butyllithium (2.6 M in hexanes, 0.45 mL, 1.20 mmol) was added slowly via syringe (around 5 drops per minute). The reaction mixture was stirred for 1h at −78 °C and then slowly warmed to 0 °C in 2h. After a further 3 h at 22 °C, a solution of H_2O_2/NaOH (2.0 M) (1.0 mL/1.0 mL) was added and the resulting mixture was allowed to stir for 10 min. The reaction was quenched by an addition of a saturated aqueous solution of $Na_2S_2O_3$ (3.0 mL). The aqueous layer was washed with Et_2O (3 × 5 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo, affording yellow oil residue, which was purified by silica gel chromatography (10:1 to 3:1 hexanes/ethyl acetate) to afford **2.33** as greenish foam (84.5 mg, 0.23 mmol, 78% yield).



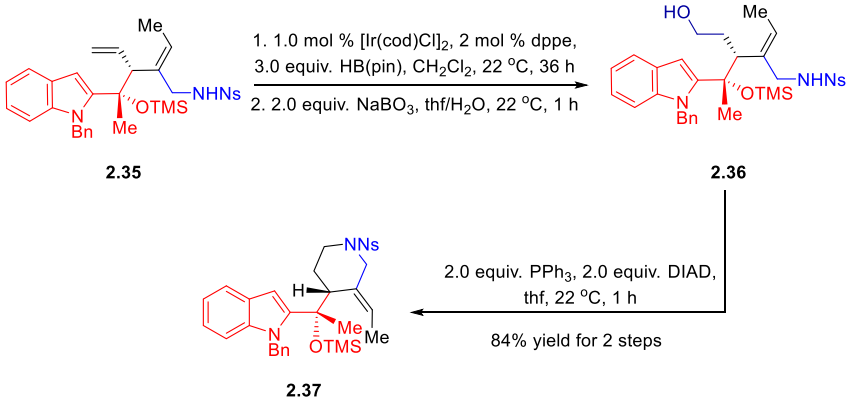
To a solution of diol **2.33** (65.0 mg, 0.18 mmol) in DCM (3.0 mL) was treated with 2,6-lutidine (96.0 mg, 0.90 mmol) and TMSOTf (120 mg, 0.54 mmol) at 0 °C. The mixture was allowed to stir at 0 °C for 30 min. The reaction was quenched by an addition of a saturated aqueous solution of $NaHCO_3$ (2.0 mL). The aqueous layer was washed with DCM (3 × 10 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The resulting yellow oil residue was used in the next step without any further purification. The above obtained product was dissolved in MeOH/DCM (3.0 mL / 3.0 mL), $NaHCO_3$ (151.0 mg, 1.8 mmol) was added and the resulting mixture was allowed to stir at 22 °C for 30 min. The reaction was quenched by an addition of H_2O (2.0 mL). The aqueous

layer was washed with DCM (3 × 10 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo, affording yellow oil residue, which was purified by silica gel chromatography (10:1 to 5:1 hexanes/ethyl acetate) to afford **2.34** as white foam (60.7 mg, 0.14 mmol, 78% yield), and recovery of **2.33**. (10.5 mg, 0.03 mmol, 16% yield).



2.34 **2.35**
58% yield

A flamed-dried flask equipped with a stir bar was charged with **2.34** (50.0 mg, 0.12 mmol), benzene (3.0 mL), *o*-$NsNH_2$ (116.0 mg, 0.58 mmol) and CMBP (83.5 mg, 0.34 mmol) in a nitrogen-filled glove box. The flask was removed from glovebox and the mixture was allowed to stir at 22 °C for 36 h. The mixture was concentrated in vacuo, affording yellow oil residue, which was purified by silica gel chromatography (10:1 to 5:1 hexanes/ethyl acetate) to afford **2.35** as white foam (41.3 mg, 0.07 mmol, 58% yield).



2.35 **2.36**

2.37

In a flamed-dried flask under nitrogen, $[Ir(cod)Cl]_2$ (1.1 mg, 0.0016 mmol), dppe (1.3 mg, 0.0032 mmol) and DCM (5 mL) were added. The mixture was allowed to stir for 10 min at 22 °C, after which HB(pin) (62 mg, 0.486 mmol) and **2.35** (100 mg, 0.162 mmol)

was added. The resulting mixture was allowed to stir for 36 h and quenched by an addition of a saturated aqueous solution of $NaHCO_3$ (2.0 mL). The aqueous layer was washed with DCM (3 × 10 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The resulting yellow oil residue was used in the next step without any further purification. To the above obtained residue was added THF/H_2O (2.0 mL / 2.0 mL), and sodium perborate tetrahydrate (75.0 mg, 0.486 mmol), the resulting mixture was allowed to stir at 22 °C for 1 h. The reaction was quenched by an addition of H_2O (2.0 mL). The aqueous layer was washed with DCM (3 × 10 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo, affording yellow oil residue, which was purified by a short column of silica gel (3:1 hexanes/ethyl acetate) to afford **2.36** with unknown inseparable impurities.

The above obtained mixture was dissolved in THF (5.0 mL), PPh_3 (85.0 mg, 0.324 mmol) and DIAD (65.0 mg, 0.324 mmol) were added and the resulting mixture was allowed to stir at 22 °C for 1 h. The reaction was quenched by an addition of a saturated aqueous solution of NH_4Cl (2.0 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, affording yellow oil residue, which was purified by silica gel chromatography (10:1 to 3:1 hexanes/ethyl acetate) to afford **2.37** as white foam (87.1 mg, 0.141 mmol, 84% yield).

2.7.7 X-Ray Crystallography Determination of Absolute Configuration

Table 1. Crystal data and structure refinement for compound

Identification code	CCDC 1874716
Empirical formula	C24 H23 N O2
Formula weight	357.43
Temperature	100(2) K
Wavelength	1.54178 Å

Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 8.6992(3) Å	= 90°.
	b = 11.0291(4) Å	= 90°.
	c = 20.5630(7) Å	= 90°.
Volume	1972.90(12) $Å^3$	
Z	4	
Density (calculated)	1.203 Mg/m^3	
Absorption coefficient	0.599 mm^{-1}	
F(000)	760	
Crystal size	0.520 x 0.280 x 0.220 mm^3	
Theta range for data collection	4.300 to 66.353°.	
Index ranges	-10<=h<=10, -12<=k<=13, -24<=l<=24	
Reflections collected	39909	
Independent reflections	3437 [R(int) = 0.0221]	
Completeness to theta = 66.353°	98.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7528 and 0.7000	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3437 / 0 / 246	
Goodness-of-fit on F^2	1.043	
Final R indices [I>2sigma(I)]	R1 = 0.0251, wR2 = 0.0659	
R indices (all data)	R1 = 0.0253, wR2 = 0.0663	
Absolute structure parameter	0.01(3)	
Extinction coefficient	0.0157(10)	
Largest diff. peak and hole	0.201 and -0.109 e.$Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for C24H23NO2. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	4552(2)	6818(1)	1640(1)	43(1)
O(2)	3189(1)	5976(1)	2440(1)	38(1)
N(1)	2374(1)	4826(1)	4092(1)	30(1)
C(1)	6732(2)	5273(3)	4025(1)	64(1)
C(2)	5740(2)	5686(2)	3598(1)	40(1)

C(3)	5142(2)	4936(1)	3044(1)	29(1)
C(4)	5742(2)	5435(1)	2410(1)	30(1)
C(5)	4506(2)	6151(2)	2106(1)	33(1)
C(6)	3370(2)	5012(1)	2928(1)	31(1)
C(7)	2433(2)	5440(1)	3502(1)	31(1)
C(8)	1546(2)	6457(2)	3543(1)	38(1)
C(9)	878(2)	6490(1)	4177(1)	37(1)
C(10)	-117(2)	7289(2)	4505(1)	49(1)
C(11)	-539(2)	7033(2)	5133(1)	54(1)
C(12)	-12(2)	5992(2)	5449(1)	50(1)
C(13)	961(2)	5180(2)	5142(1)	40(1)
C(14)	1409(2)	5456(1)	4506(1)	33(1)
C(15)	2967(2)	3629(1)	4250(1)	30(1)
C(16)	1760(2)	2642(1)	4211(1)	28(1)
C(17)	367(2)	2824(2)	3898(1)	35(1)
C(18)	-679(2)	1880(2)	3833(1)	41(1)
C(19)	-338(2)	751(2)	4081(1)	40(1)
C(20)	1031(2)	567(2)	4404(1)	40(1)
C(21)	2071(2)	1512(2)	4472(1)	34(1)
C(22)	7136(2)	5345(2)	2152(1)	35(1)
C(23)	8443(2)	4656(2)	2435(1)	46(1)
C(24)	2775(2)	3852(2)	2617(1)	37(1)

Table 3. Bond lengths [Å] and angles [°] for C24H23NO2.

O(1)-C(5)	1.2084(19)
O(2)-C(5)	1.350(2)
O(2)-C(6)	1.4702(18)
N(1)-C(14)	1.382(2)
N(1)-C(7)	1.390(2)
N(1)-C(15)	1.454(2)
C(1)-C(2)	1.313(3)
C(1)-H(1A)	0.9500
C(1)-H(1B)	0.9500
C(2)-C(3)	1.501(2)

C(2)-H(2A)	0.9500
C(3)-C(4)	1.509(2)
C(3)-C(6)	1.562(2)
C(3)-H(3A)	1.0000
C(4)-C(22)	1.327(2)
C(4)-C(5)	1.472(2)
C(6)-C(7)	1.510(2)
C(6)-C(24)	1.522(2)
C(7)-C(8)	1.364(2)
C(8)-C(9)	1.429(3)
C(8)-H(8A)	0.9500
C(9)-C(14)	1.403(2)
C(9)-C(10)	1.407(2)
C(10)-C(11)	1.372(3)
C(10)-H(10A)	0.9500
C(11)-C(12)	1.397(3)
C(11)-H(11A)	0.9500
C(12)-C(13)	1.385(3)
C(12)-H(12A)	0.9500
C(13)-C(14)	1.399(2)
C(13)-H(13A)	0.9500
C(15)-C(16)	1.515(2)
C(15)-H(15A)	0.9900
C(15)-H(15B)	0.9900
C(16)-C(21)	1.384(2)
C(16)-C(17)	1.388(2)
C(17)-C(18)	1.389(2)
C(17)-H(17A)	0.9500
C(18)-C(19)	1.377(3)
C(18)-H(18A)	0.9500
C(19)-C(20)	1.379(3)
C(19)-H(19A)	0.9500
C(20)-C(21)	1.386(2)
C(20)-H(20A)	0.9500
C(21)-H(21A)	0.9500
C(22)-C(23)	1.486(2)

C(22)-H(22A)	0.9500
C(23)-H(23A)	0.9800
C(23)-H(23B)	0.9800
C(23)-H(23C)	0.9800
C(24)-H(24A)	0.9800
C(24)-H(24B)	0.9800
C(24)-H(24C)	0.9800

C(5)-O(2)-C(6)	111.09(12)
C(14)-N(1)-C(7)	108.37(13)
C(14)-N(1)-C(15)	122.34(13)
C(7)-N(1)-C(15)	128.52(13)
C(2)-C(1)-H(1A)	120.0
C(2)-C(1)-H(1B)	120.0
H(1A)-C(1)-H(1B)	120.0
C(1)-C(2)-C(3)	123.0(2)
C(1)-C(2)-H(2A)	118.5
C(3)-C(2)-H(2A)	118.5
C(2)-C(3)-C(4)	109.61(13)
C(2)-C(3)-C(6)	115.38(14)
C(4)-C(3)-C(6)	100.94(12)
C(2)-C(3)-H(3A)	110.2
C(4)-C(3)-H(3A)	110.2
C(6)-C(3)-H(3A)	110.2
C(22)-C(4)-C(5)	122.53(14)
C(22)-C(4)-C(3)	129.34(14)
C(5)-C(4)-C(3)	108.05(12)
O(1)-C(5)-O(2)	121.22(15)
O(1)-C(5)-C(4)	129.70(15)
O(2)-C(5)-C(4)	109.08(13)
O(2)-C(6)-C(7)	104.43(12)
O(2)-C(6)-C(24)	106.54(12)
C(7)-C(6)-C(24)	114.05(13)
O(2)-C(6)-C(3)	104.37(12)
C(7)-C(6)-C(3)	115.49(13)
C(24)-C(6)-C(3)	110.84(13)

C(8)-C(7)-N(1)	108.97(14)
C(8)-C(7)-C(6)	127.65(15)
N(1)-C(7)-C(6)	123.38(13)
C(7)-C(8)-C(9)	107.92(15)
C(7)-C(8)-H(8A)	126.0
C(9)-C(8)-H(8A)	126.0
C(14)-C(9)-C(10)	118.77(18)
C(14)-C(9)-C(8)	106.53(14)
C(10)-C(9)-C(8)	134.71(18)
C(11)-C(10)-C(9)	119.10(19)
C(11)-C(10)-H(10A)	120.4
C(9)-C(10)-H(10A)	120.4
C(10)-C(11)-C(12)	121.30(17)
C(10)-C(11)-H(11A)	119.4
C(12)-C(11)-H(11A)	119.4
C(13)-C(12)-C(11)	121.29(19)
C(13)-C(12)-H(12A)	119.4
C(11)-C(12)-H(12A)	119.4
C(12)-C(13)-C(14)	117.16(19)
C(12)-C(13)-H(13A)	121.4
C(14)-C(13)-H(13A)	121.4
N(1)-C(14)-C(13)	129.44(16)
N(1)-C(14)-C(9)	108.19(14)
C(13)-C(14)-C(9)	122.36(16)
N(1)-C(15)-C(16)	113.27(12)
N(1)-C(15)-H(15A)	108.9
C(16)-C(15)-H(15A)	108.9
N(1)-C(15)-H(15B)	108.9
C(16)-C(15)-H(15B)	108.9
H(15A)-C(15)-H(15B)	107.7
C(21)-C(16)-C(17)	118.73(15)
C(21)-C(16)-C(15)	119.50(14)
C(17)-C(16)-C(15)	121.72(14)
C(16)-C(17)-C(18)	120.52(15)
C(16)-C(17)-H(17A)	119.7
C(18)-C(17)-H(17A)	119.7

C(19)-C(18)-C(17)	120.11(17)
C(19)-C(18)-H(18A)	119.9
C(17)-C(18)-H(18A)	119.9
C(18)-C(19)-C(20)	119.80(16)
C(18)-C(19)-H(19A)	120.1
C(20)-C(19)-H(19A)	120.1
C(19)-C(20)-C(21)	120.10(16)
C(19)-C(20)-H(20A)	120.0
C(21)-C(20)-H(20A)	120.0
C(16)-C(21)-C(20)	120.71(15)
C(16)-C(21)-H(21A)	119.6
C(20)-C(21)-H(21A)	119.6
C(4)-C(22)-C(23)	125.50(15)
C(4)-C(22)-H(22A)	117.3
C(23)-C(22)-H(22A)	117.3
C(22)-C(23)-H(23A)	109.5
C(22)-C(23)-H(23B)	109.5
H(23A)-C(23)-H(23B)	109.5
C(22)-C(23)-H(23C)	109.5
H(23A)-C(23)-H(23C)	109.5
H(23B)-C(23)-H(23C)	109.5
C(6)-C(24)-H(24A)	109.5
C(6)-C(24)-H(24B)	109.5
H(24A)-C(24)-H(24B)	109.5
C(6)-C(24)-H(24C)	109.5
H(24A)-C(24)-H(24C)	109.5
H(24B)-C(24)-H(24C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for C24H23NO2. The anisotropic displacement factor exponent takes the form: $-2\ ^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	39(1)	49(1)	41(1)	18(1)	-3(1)	1(1)

O(2)	28(1)	45(1)	41(1)	15(1)	-2(1)	4(1)
N(1)	26(1)	28(1)	36(1)	-1(1)	2(1)	-1(1)
C(1)	44(1)	113(2)	37(1)	3(1)	-7(1)	-20(1)
C(2)	36(1)	53(1)	32(1)	-2(1)	2(1)	-13(1)
C(3)	25(1)	31(1)	32(1)	4(1)	-2(1)	0(1)
C(4)	30(1)	30(1)	30(1)	1(1)	-3(1)	-2(1)
C(5)	30(1)	36(1)	33(1)	4(1)	-2(1)	-2(1)
C(6)	26(1)	33(1)	33(1)	6(1)	-2(1)	1(1)
C(7)	25(1)	29(1)	39(1)	3(1)	0(1)	-3(1)
C(8)	32(1)	27(1)	54(1)	4(1)	2(1)	-1(1)
C(9)	28(1)	27(1)	57(1)	-7(1)	3(1)	-5(1)
C(10)	35(1)	29(1)	82(1)	-13(1)	4(1)	0(1)
C(11)	36(1)	52(1)	72(1)	-30(1)	13(1)	-4(1)
C(12)	38(1)	58(1)	54(1)	-22(1)	11(1)	-8(1)
C(13)	32(1)	46(1)	43(1)	-9(1)	5(1)	-6(1)
C(14)	24(1)	30(1)	44(1)	-8(1)	2(1)	-5(1)
C(15)	27(1)	31(1)	32(1)	1(1)	-2(1)	1(1)
C(16)	28(1)	30(1)	24(1)	-1(1)	3(1)	1(1)
C(17)	31(1)	32(1)	42(1)	4(1)	-3(1)	-1(1)
C(18)	31(1)	45(1)	48(1)	-3(1)	-2(1)	-6(1)
C(19)	40(1)	37(1)	44(1)	-6(1)	10(1)	-12(1)
C(20)	52(1)	29(1)	39(1)	4(1)	8(1)	-1(1)
C(21)	37(1)	34(1)	31(1)	4(1)	0(1)	3(1)
C(22)	34(1)	40(1)	31(1)	3(1)	1(1)	-1(1)
C(23)	32(1)	56(1)	50(1)	3(1)	2(1)	8(1)
C(24)	30(1)	43(1)	37(1)	-2(1)	-2(1)	-3(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for C24H23NO2.

	x	y	z	U(eq)
H(1A)	7103	4466	3992	77
H(1B)	7078	5782	4368	77

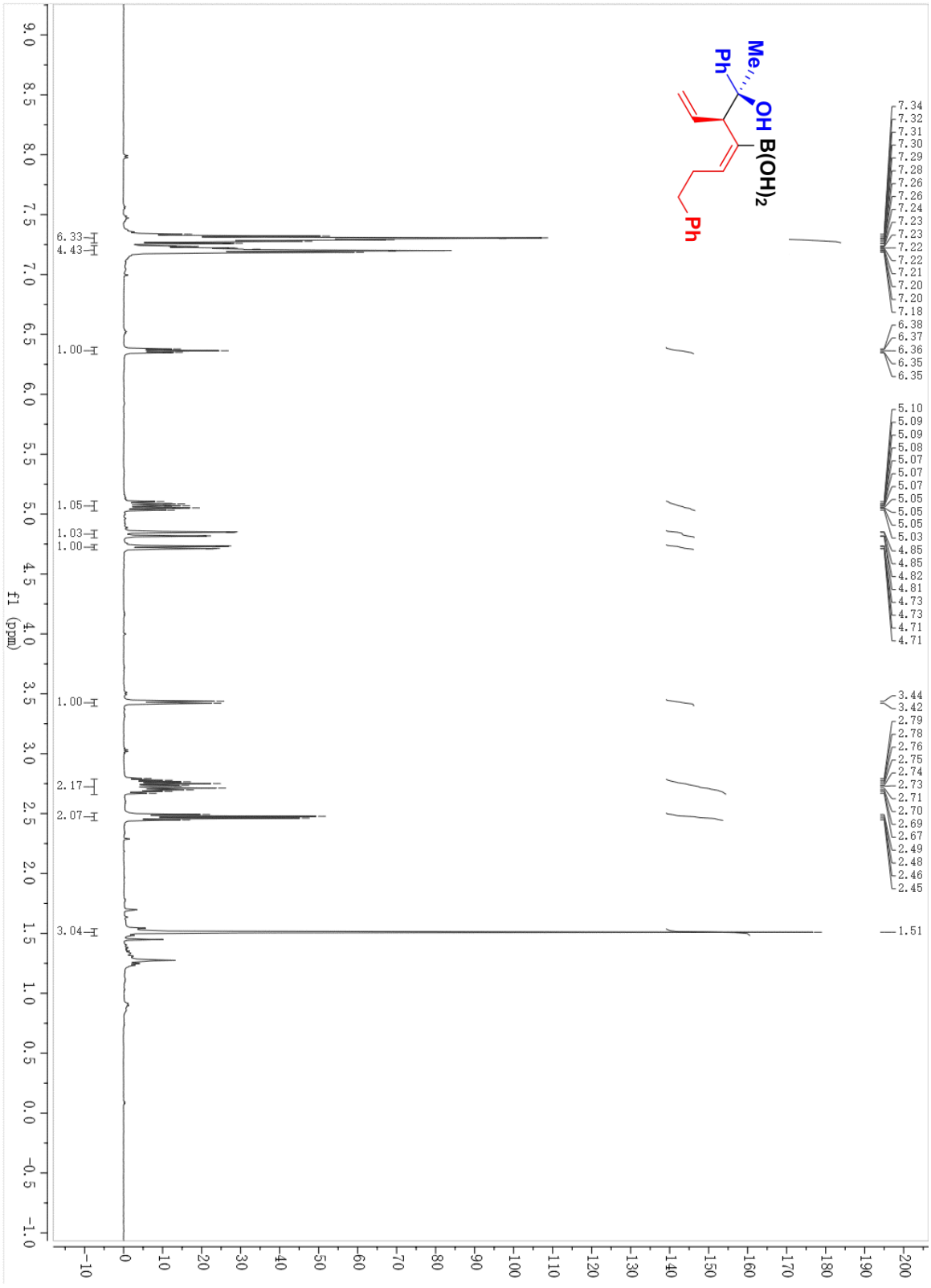
H(2A)	5385	6497	3642	49
H(3A)	5466	4072	3097	35
H(8A)	1399	7040	3209	45
H(10A)	-493	7995	4294	58
H(11A)	-1202	7575	5357	64
H(12A)	-326	5839	5884	60
H(13A)	1308	4465	5354	48
H(15A)	3399	3646	4695	36
H(15B)	3814	3431	3946	36
H(17A)	126	3600	3725	42
H(18A)	-1630	2012	3618	49
H(19A)	-1045	102	4029	48
H(20A)	1263	-208	4580	48
H(21A)	3006	1381	4700	41
H(22A)	7313	5755	1752	42
H(23A)	9158	5221	2645	69
H(23B)	8978	4214	2089	69
H(23C)	8054	4080	2759	69
H(24A)	2873	3180	2926	55
H(24B)	1691	3956	2499	55
H(24C)	3376	3672	2226	55

Table 6. Torsion angles [°] for C24H23NO2.

C(1)-C(2)-C(3)-C(4)	-111.94(18)
C(1)-C(2)-C(3)-C(6)	134.98(18)
C(2)-C(3)-C(4)-C(22)	75.3(2)
C(6)-C(3)-C(4)-C(22)	-162.54(17)
C(2)-C(3)-C(4)-C(5)	-101.29(15)
C(6)-C(3)-C(4)-C(5)	20.86(16)
C(6)-O(2)-C(5)-O(1)	172.50(15)
C(6)-O(2)-C(5)-C(4)	-8.15(18)
C(22)-C(4)-C(5)-O(1)	-6.8(3)
C(3)-C(4)-C(5)-O(1)	170.09(17)
C(22)-C(4)-C(5)-O(2)	173.95(15)

C(3)-C(4)-C(5)-O(2)	-9.18(18)
C(5)-O(2)-C(6)-C(7)	143.05(13)
C(5)-O(2)-C(6)-C(24)	-95.93(15)
C(5)-O(2)-C(6)-C(3)	21.41(17)
C(2)-C(3)-C(6)-O(2)	93.27(15)
C(4)-C(3)-C(6)-O(2)	-24.77(15)
C(2)-C(3)-C(6)-C(7)	-20.8(2)
C(4)-C(3)-C(6)-C(7)	-138.80(13)
C(2)-C(3)-C(6)-C(24)	-152.40(14)
C(4)-C(3)-C(6)-C(24)	89.56(15)
C(14)-N(1)-C(7)-C(8)	1.28(17)
C(15)-N(1)-C(7)-C(8)	171.25(14)
C(14)-N(1)-C(7)-C(6)	-179.60(14)
C(15)-N(1)-C(7)-C(6)	-9.6(2)
O(2)-C(6)-C(7)-C(8)	3.4(2)
C(24)-C(6)-C(7)-C(8)	-112.46(18)
C(3)-C(6)-C(7)-C(8)	117.43(18)
O(2)-C(6)-C(7)-N(1)	-175.51(13)
C(24)-C(6)-C(7)-N(1)	68.59(19)
C(3)-C(6)-C(7)-N(1)	-61.52(19)
N(1)-C(7)-C(8)-C(9)	-0.82(19)
C(6)-C(7)-C(8)-C(9)	-179.90(15)
C(7)-C(8)-C(9)-C(14)	0.07(18)
C(7)-C(8)-C(9)-C(10)	-179.92(18)
C(14)-C(9)-C(10)-C(11)	0.0(2)
C(8)-C(9)-C(10)-C(11)	179.99(19)
C(9)-C(10)-C(11)-C(12)	-0.7(3)
C(10)-C(11)-C(12)-C(13)	0.2(3)
C(11)-C(12)-C(13)-C(14)	0.9(3)
C(7)-N(1)-C(14)-C(13)	178.23(16)
C(15)-N(1)-C(14)-C(13)	7.5(2)
C(7)-N(1)-C(14)-C(9)	-1.22(17)
C(15)-N(1)-C(14)-C(9)	-171.94(13)
C(12)-C(13)-C(14)-N(1)	178.97(16)
C(12)-C(13)-C(14)-C(9)	-1.6(2)
C(10)-C(9)-C(14)-N(1)	-179.30(14)

C(8)-C(9)-C(14)-N(1)	0.71(17)
C(10)-C(9)-C(14)-C(13)	1.2(2)
C(8)-C(9)-C(14)-C(13)	-178.79(15)
C(14)-N(1)-C(15)-C(16)	72.03(18)
C(7)-N(1)-C(15)-C(16)	-96.69(17)
N(1)-C(15)-C(16)-C(21)	-167.01(13)
N(1)-C(15)-C(16)-C(17)	15.6(2)
C(21)-C(16)-C(17)-C(18)	-1.5(2)
C(15)-C(16)-C(17)-C(18)	175.82(15)
C(16)-C(17)-C(18)-C(19)	0.0(3)
C(17)-C(18)-C(19)-C(20)	1.2(3)
C(18)-C(19)-C(20)-C(21)	-0.8(3)
C(17)-C(16)-C(21)-C(20)	2.0(2)
C(15)-C(16)-C(21)-C(20)	-175.45(15)
C(19)-C(20)-C(21)-C(16)	-0.8(2)
C(5)-C(4)-C(22)-C(23)	179.01(17)
C(3)-C(4)-C(22)-C(23)	2.9(3)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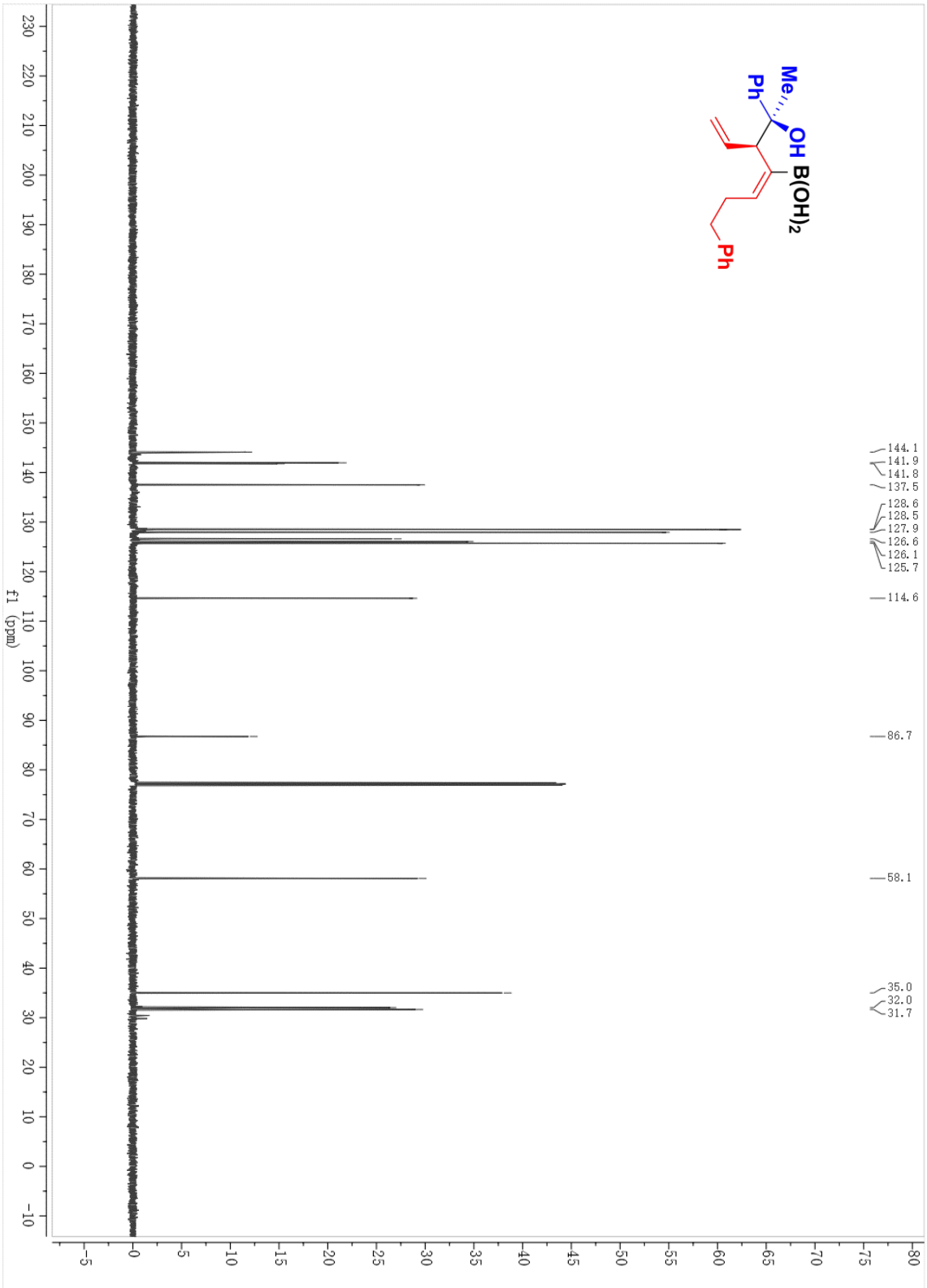
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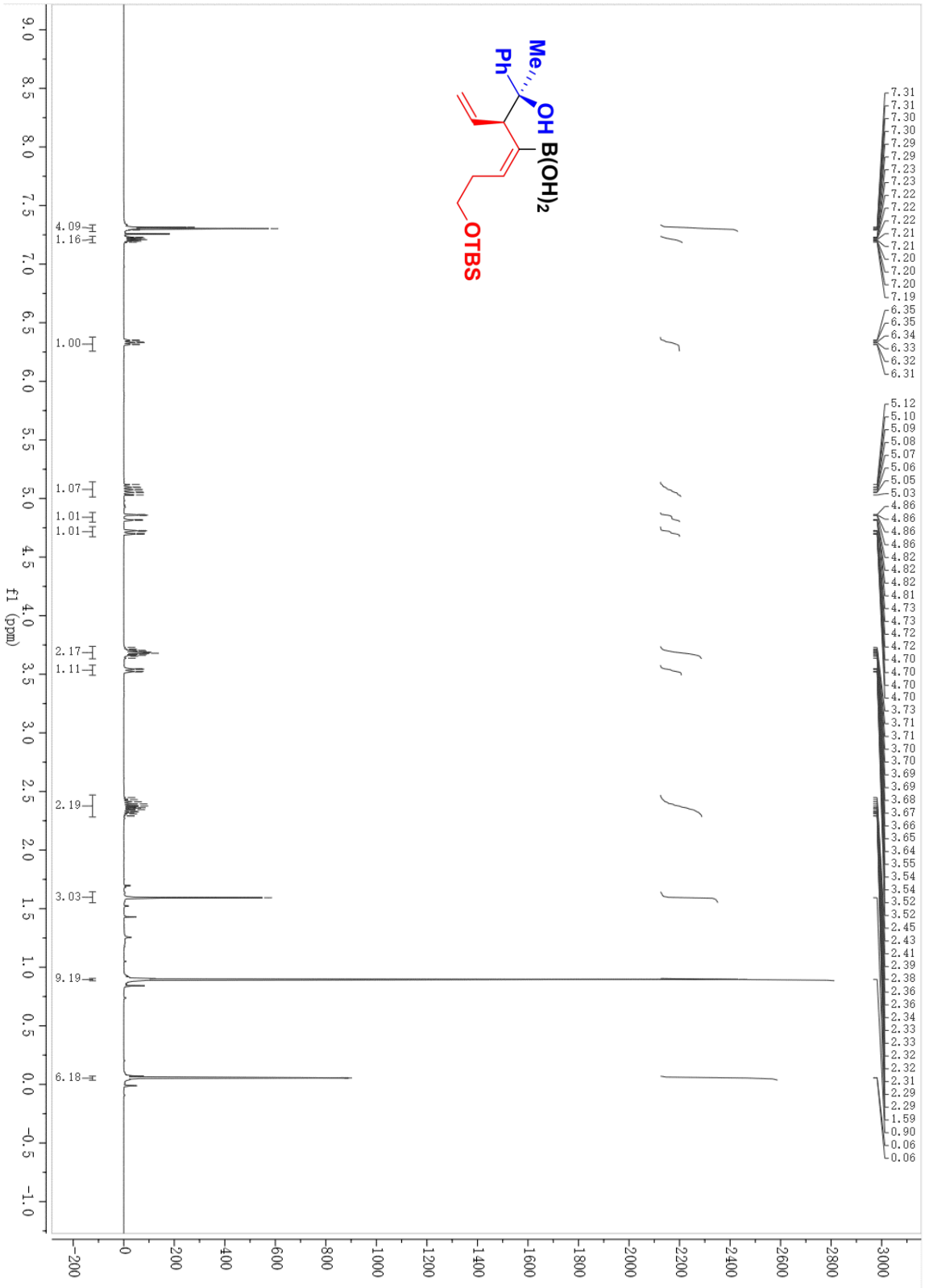
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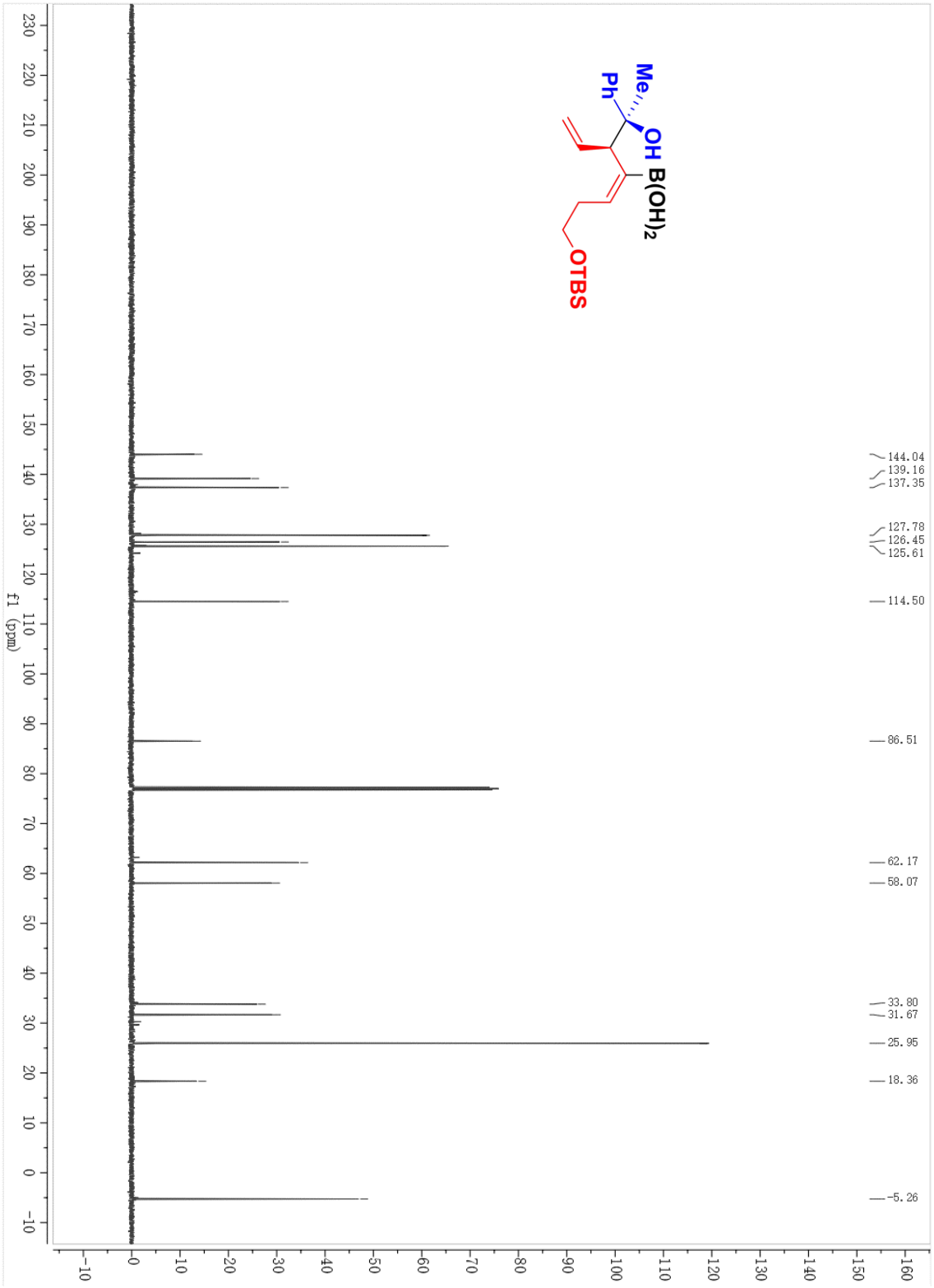
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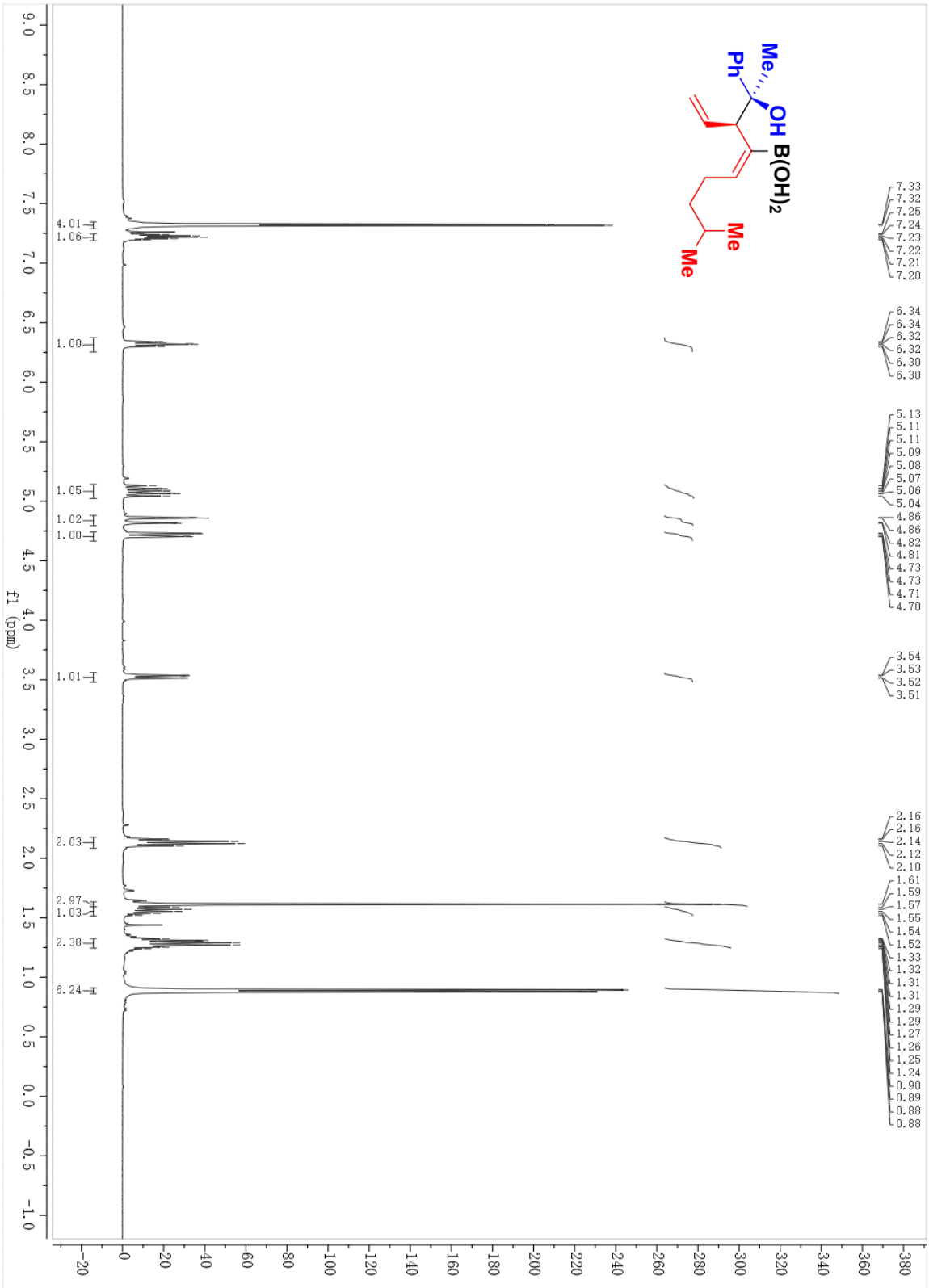
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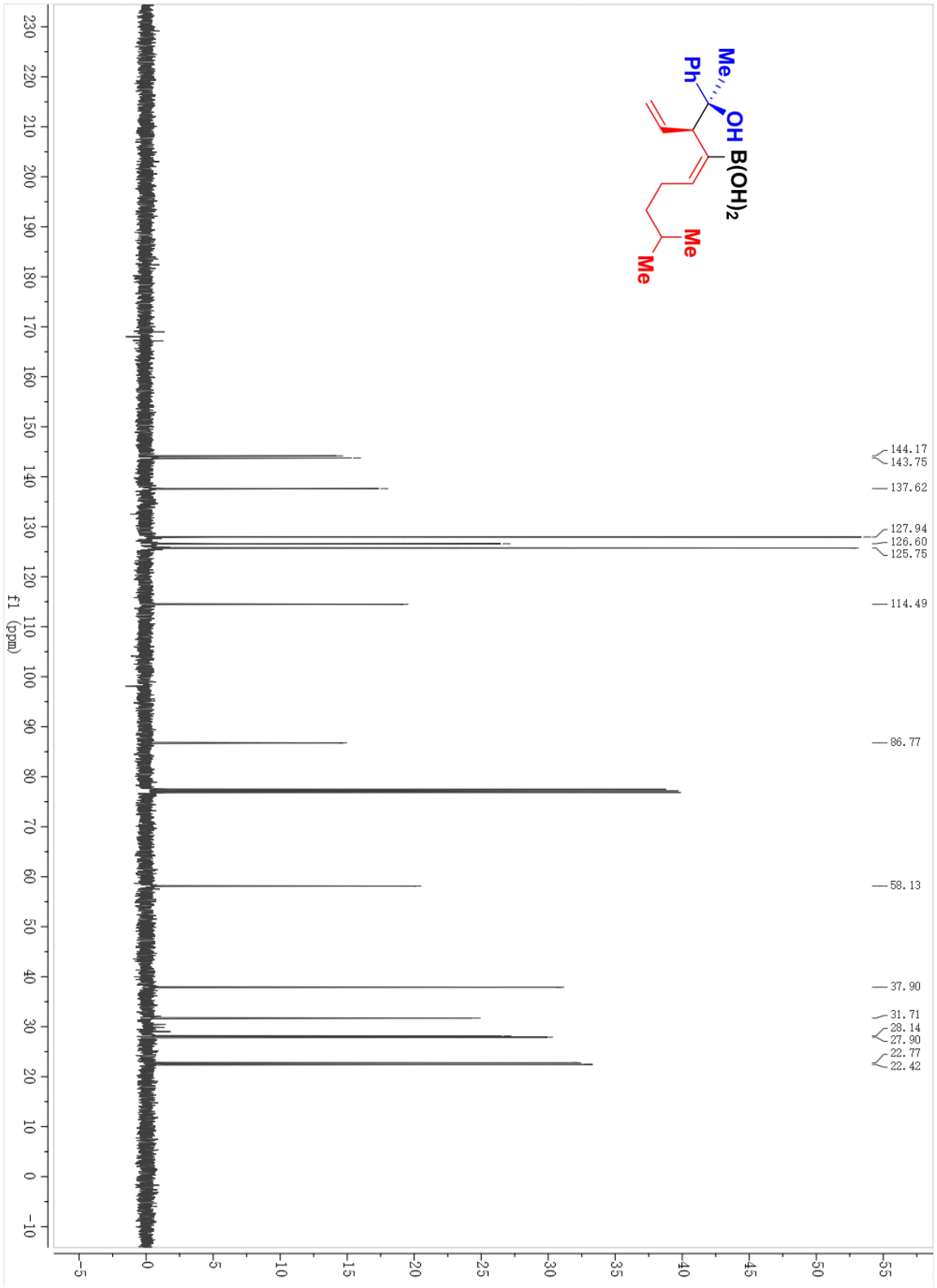
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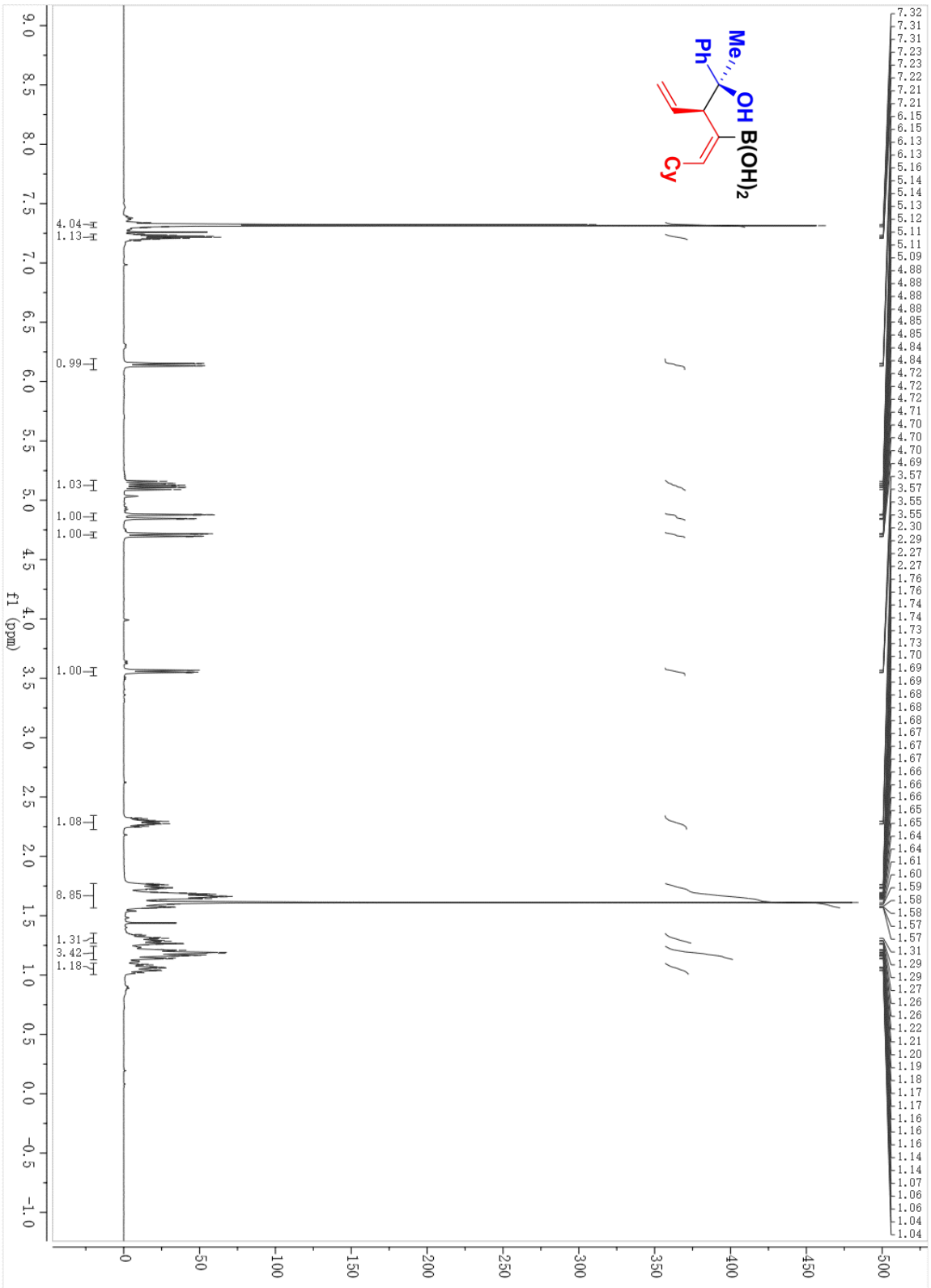
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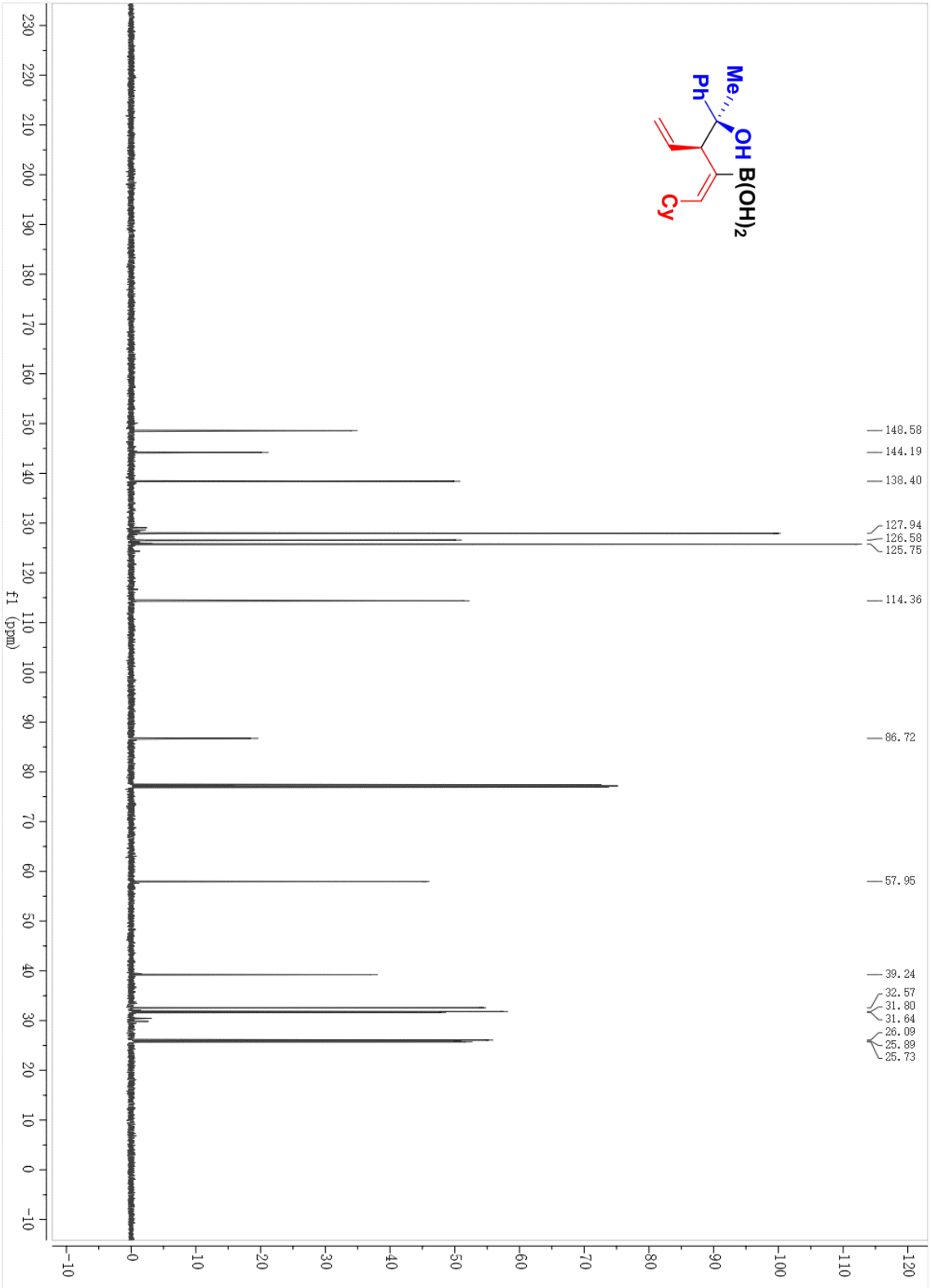
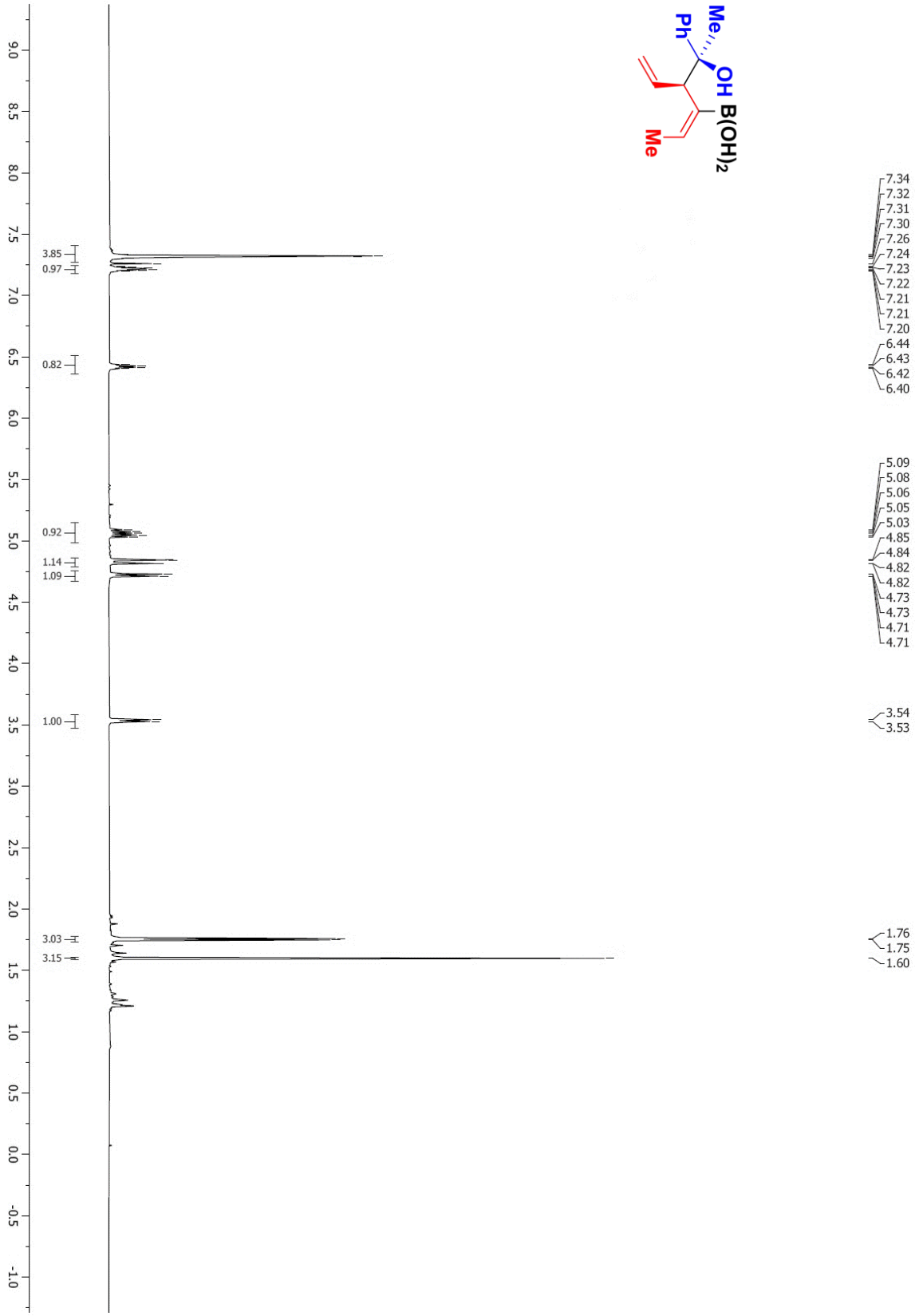
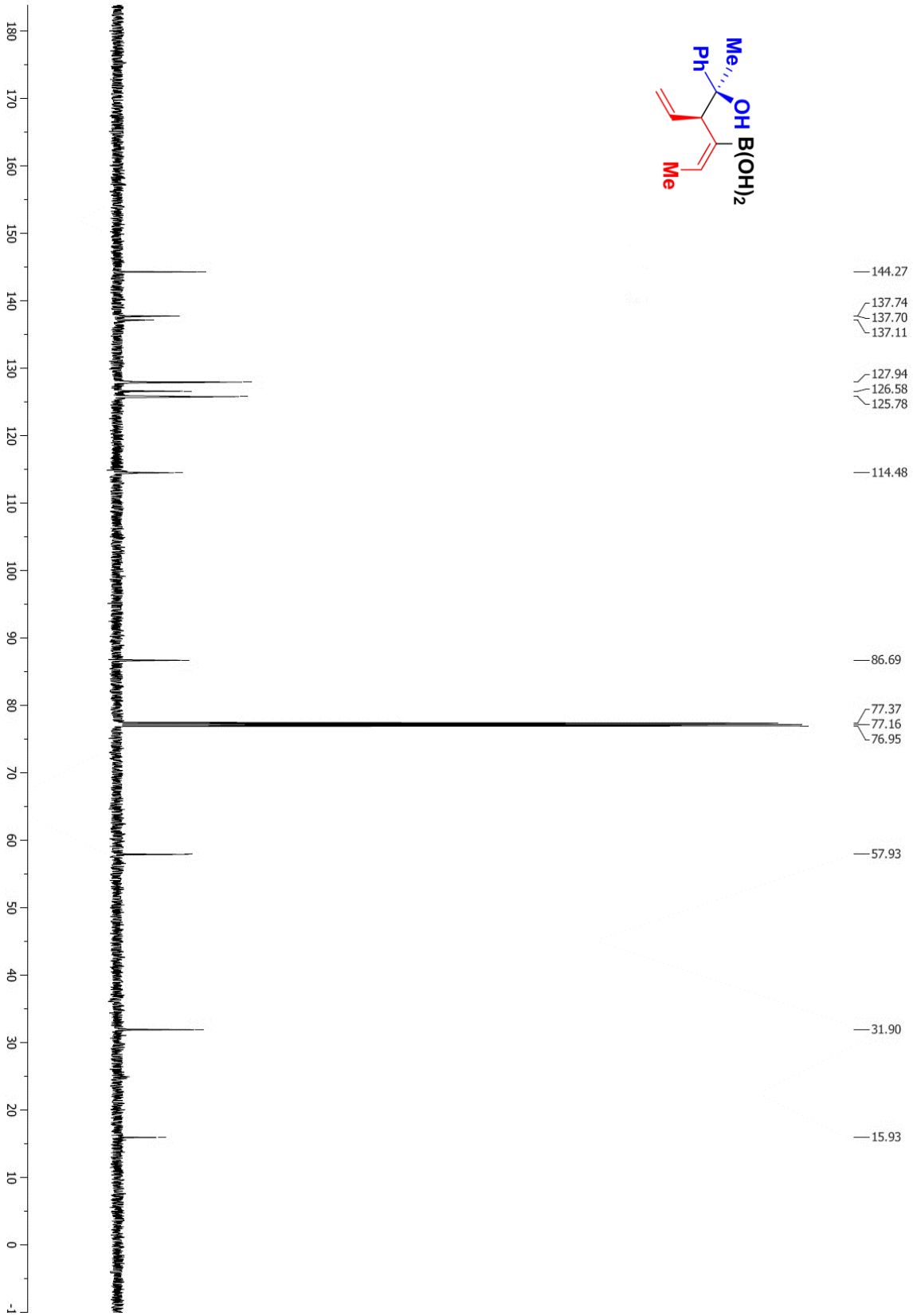
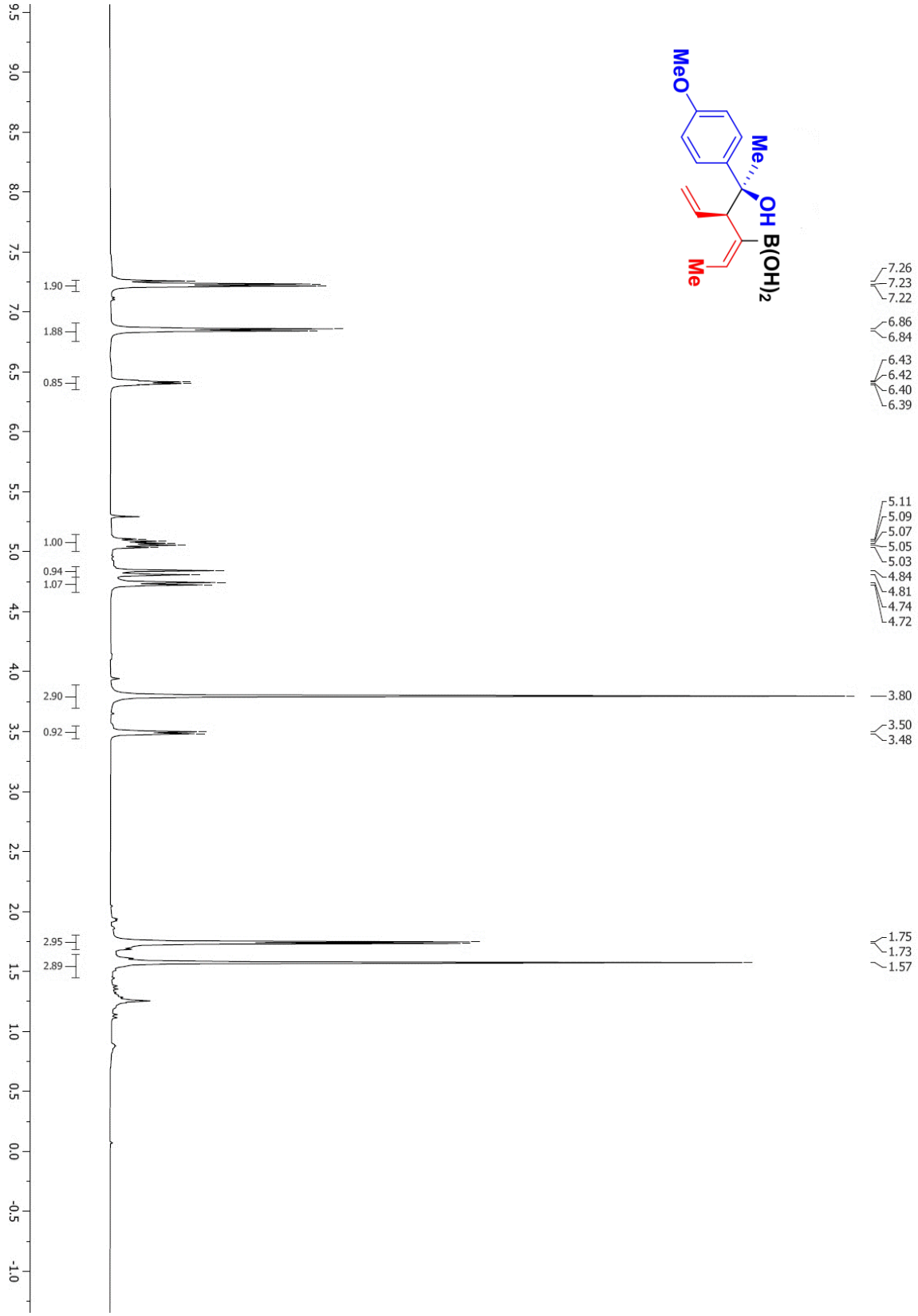
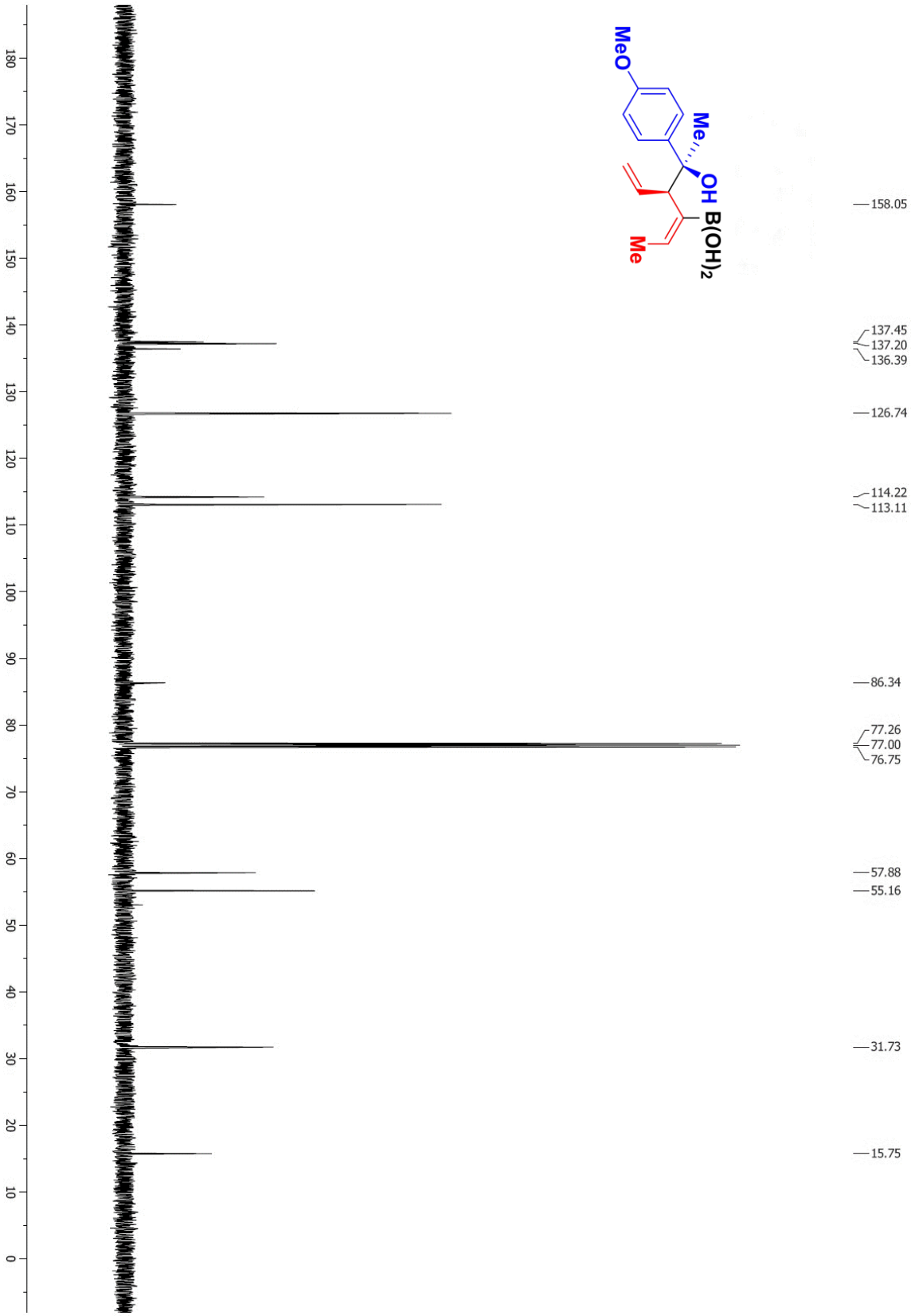
f1 (ppm)

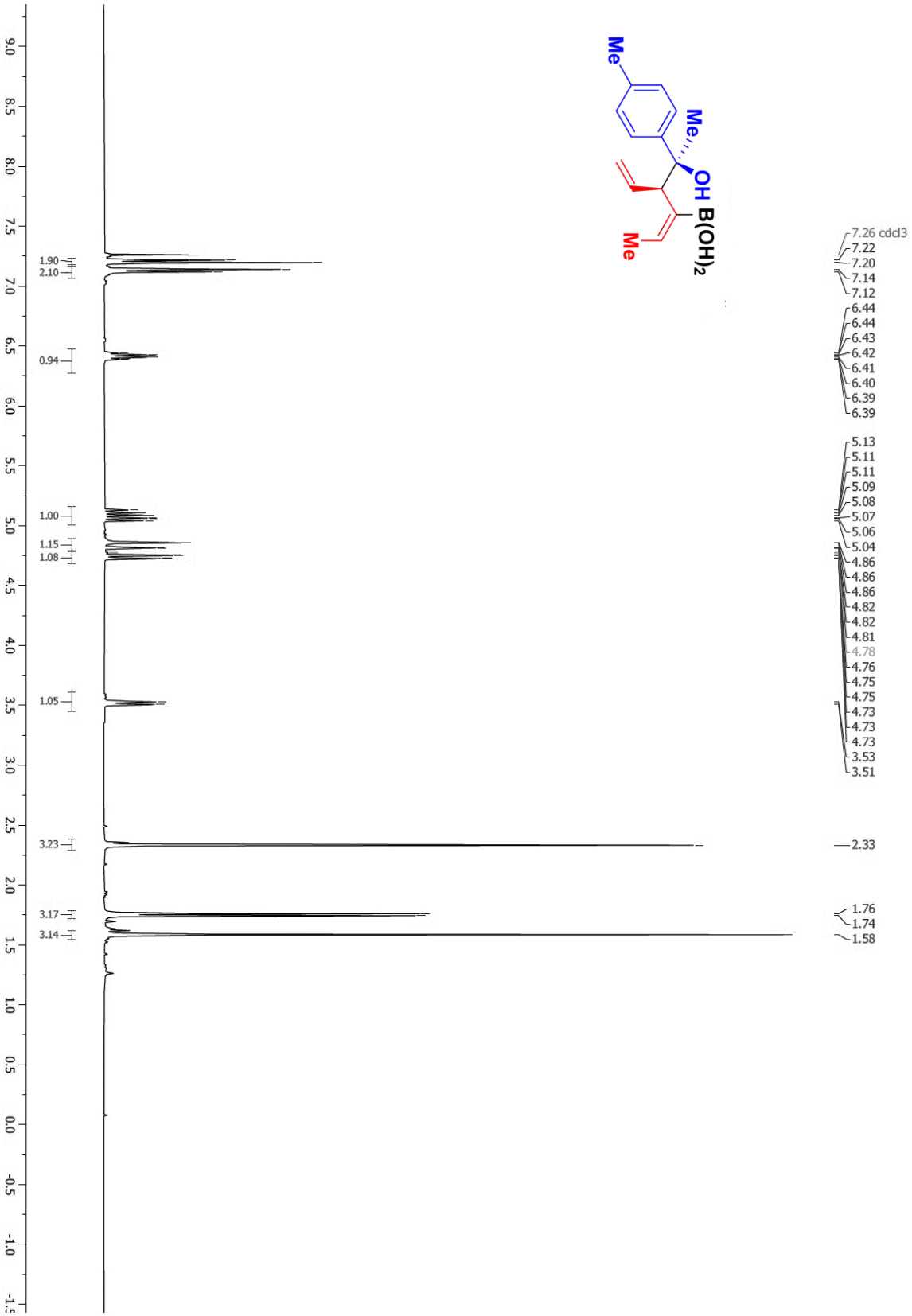

Me
Ph
OH
B(OH)2
Cy
148.58
144.19
138.40
127.94
126.58
125.75
114.36
86.72
57.95
39.24
32.57
31.80
31.64
26.09
25.89
25.73
f1 (ppm)


Me
Ph
OH
B(OH)2
Me
3.85
0.97
0.82
0.92
1.14
1.09
1.00
3.03
3.15
7.34
7.32
7.31
7.30
7.26
7.24
7.23
7.22
7.21
7.21
7.20
6.44
6.43
6.42
6.40
5.09
5.08
5.06
5.05
5.03
4.85
4.84
4.82
4.82
4.73
4.73
4.71
4.71
3.54
3.53
1.76
1.75
1.60


Me
Ph
OH
B(OH)2
Me
144.27
137.74
137.70
137.11
127.94
126.58
125.78
114.48
86.69
77.37
77.16
76.95
57.93
31.90
15.93


MeO
Me
OH
B(OH)2
Me
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
1.90
1.88
0.85
1.00
0.94
1.07
2.90
0.92
2.95
2.89
7.26
7.23
7.22
6.86
6.84
6.43
6.42
6.40
6.39
5.11
5.09
5.07
5.05
5.03
4.84
4.81
4.74
4.72
3.80
3.50
3.48
1.75
1.73
1.57


MeO
Me
OH
B(OH)2
Me
158.05
137.45
137.20
136.39
126.74
114.22
113.11
86.34
77.26
77.00
76.75
57.88
55.16
31.73
15.75


Me
Me
OH
B(OH)2
Me
1.90
2.10
0.94
1.00
1.15
1.08
1.05
3.23
3.17
3.14
7.26 cdcl3
7.22
7.20
7.14
7.12
6.44
6.44
6.43
6.42
6.41
6.40
6.39
6.39
5.13
5.11
5.11
5.09
5.08
5.07
5.06
5.04
4.86
4.86
4.86
4.82
4.82
4.81
4.78
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4.73
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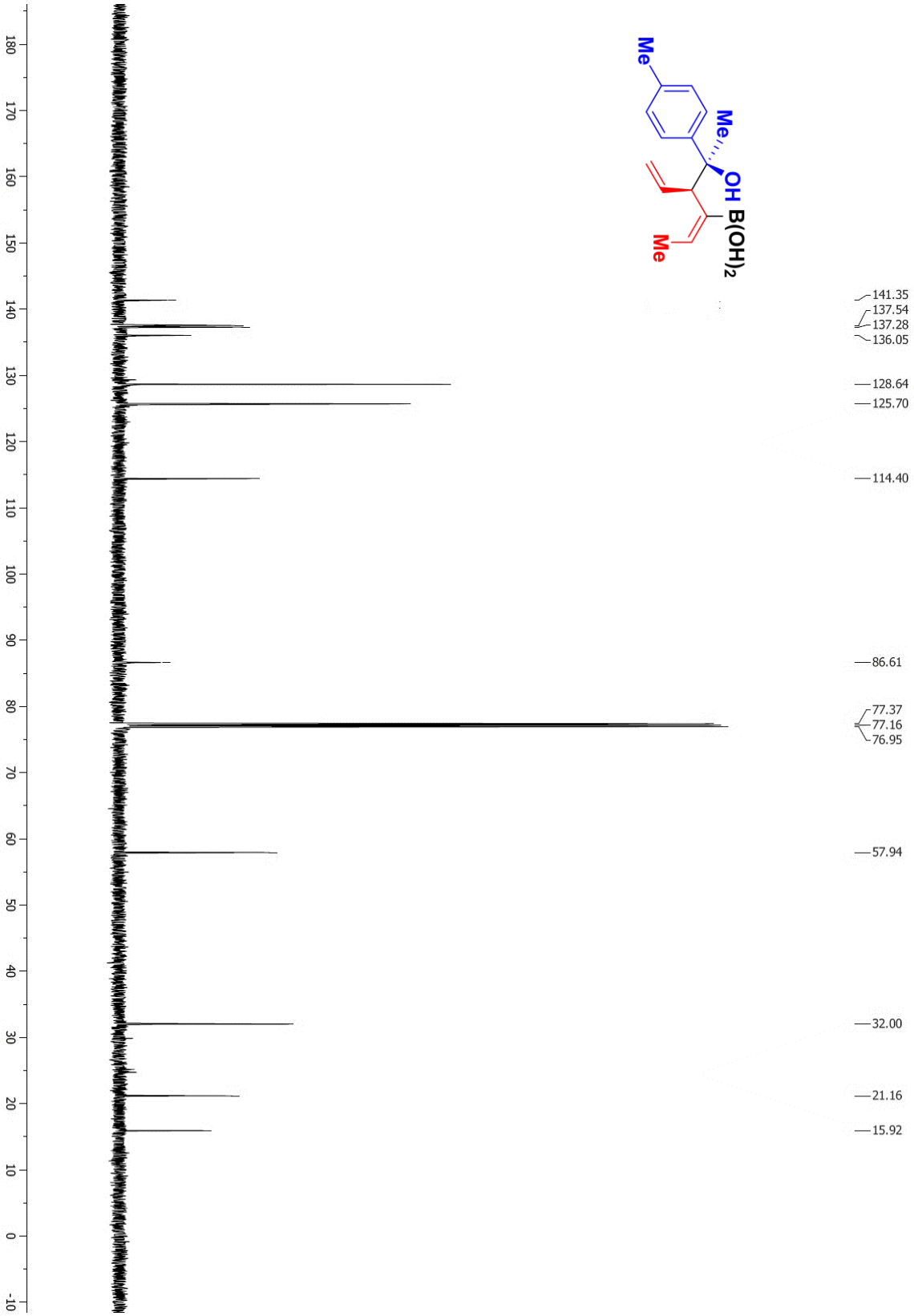
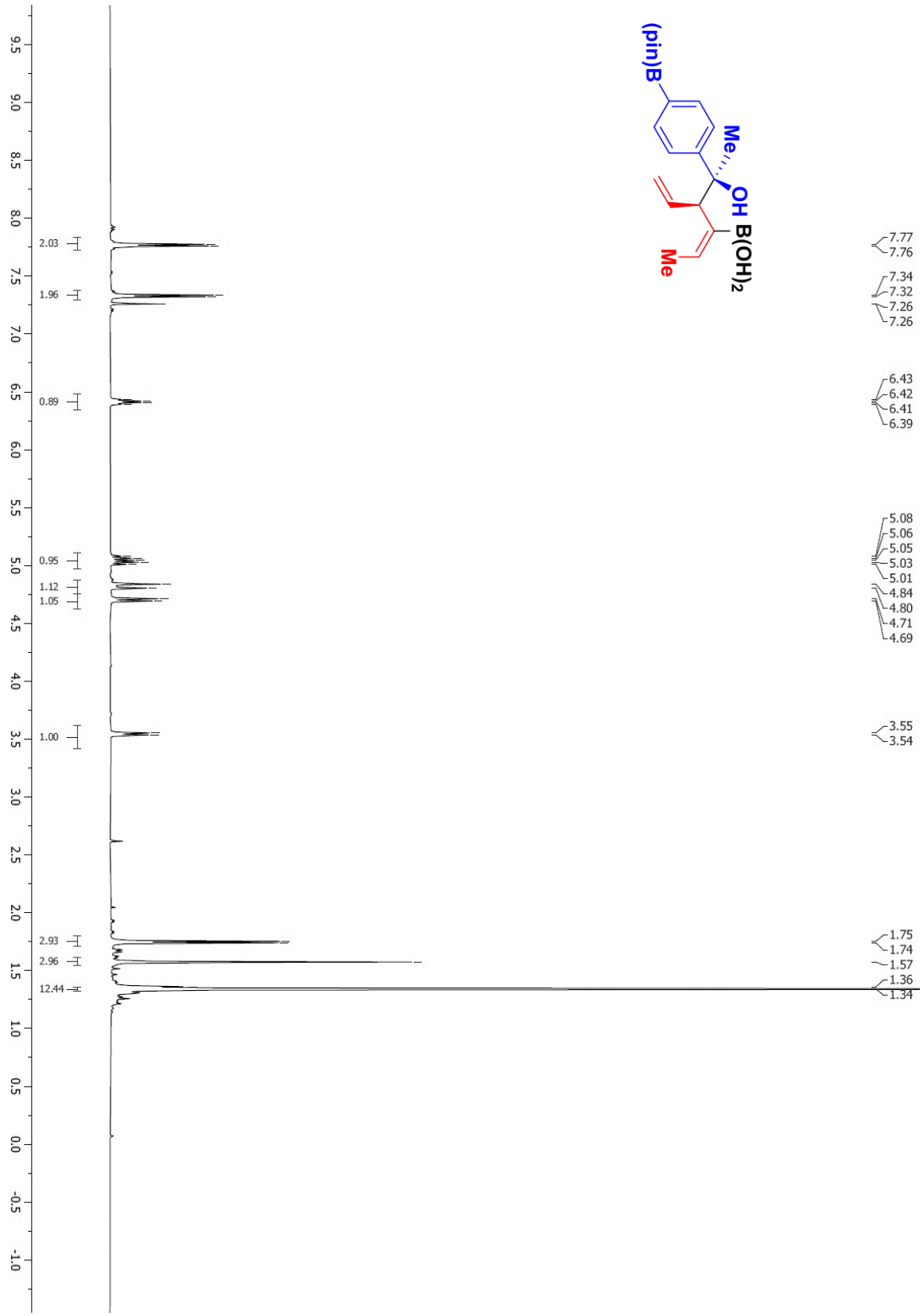
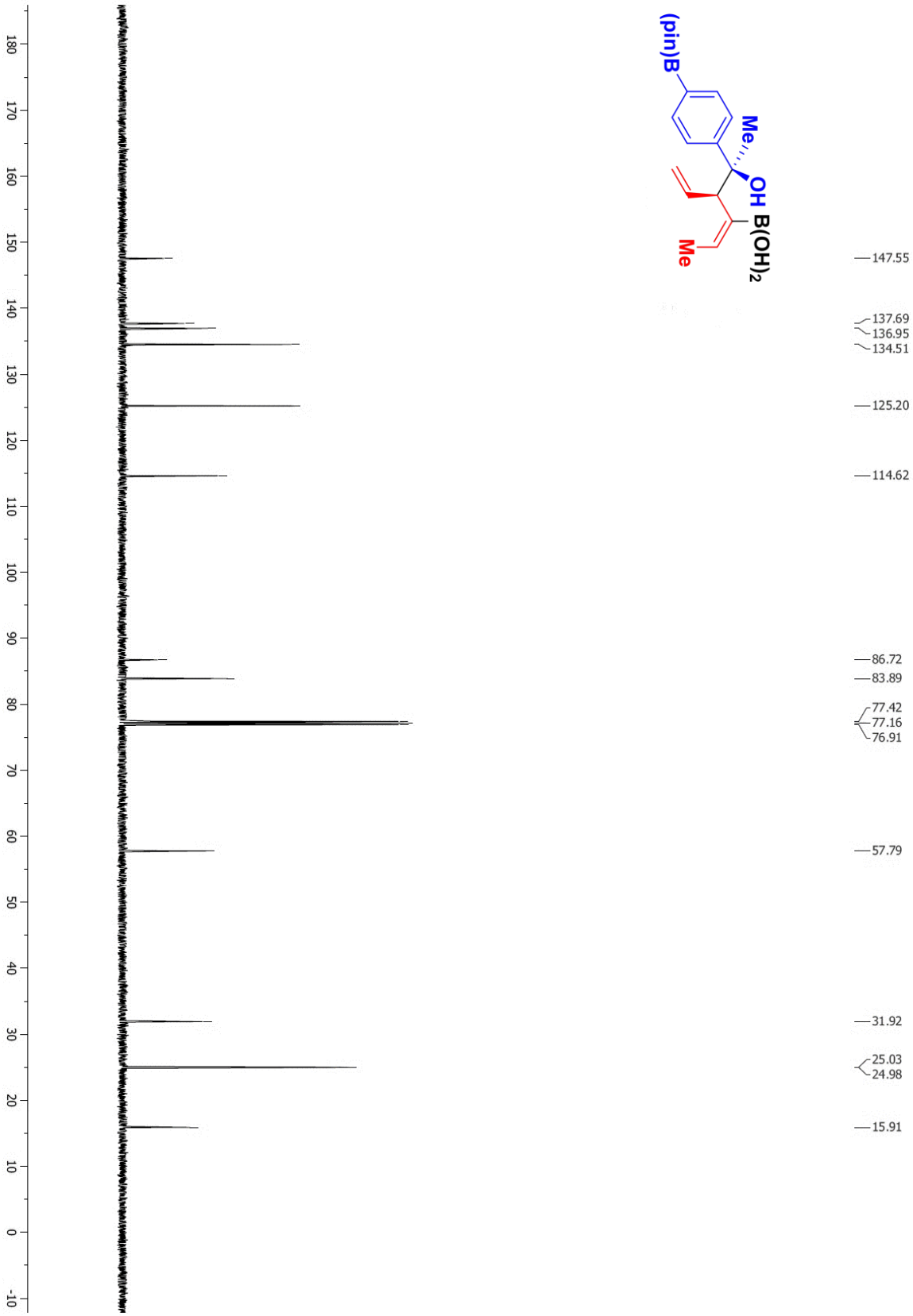
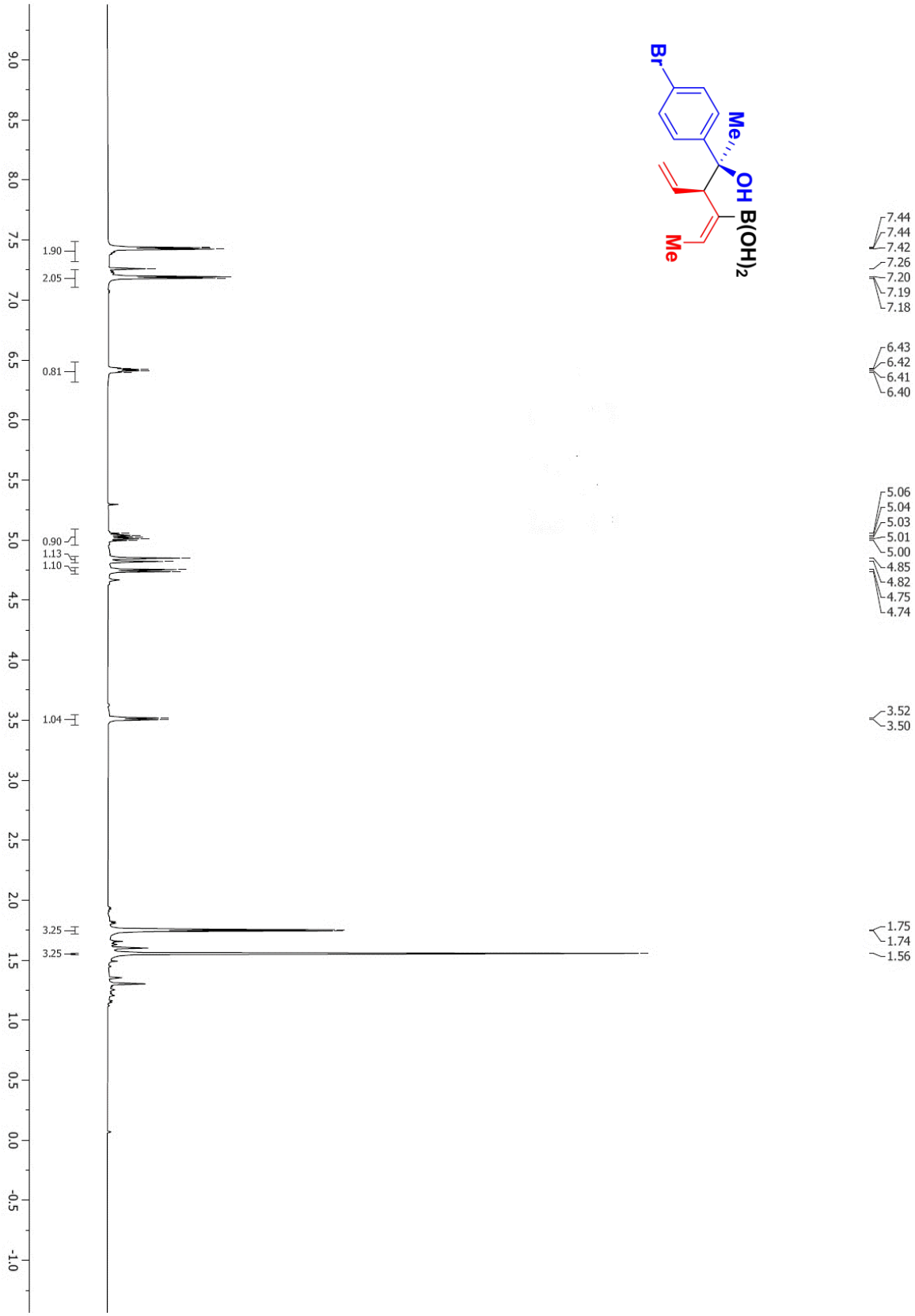
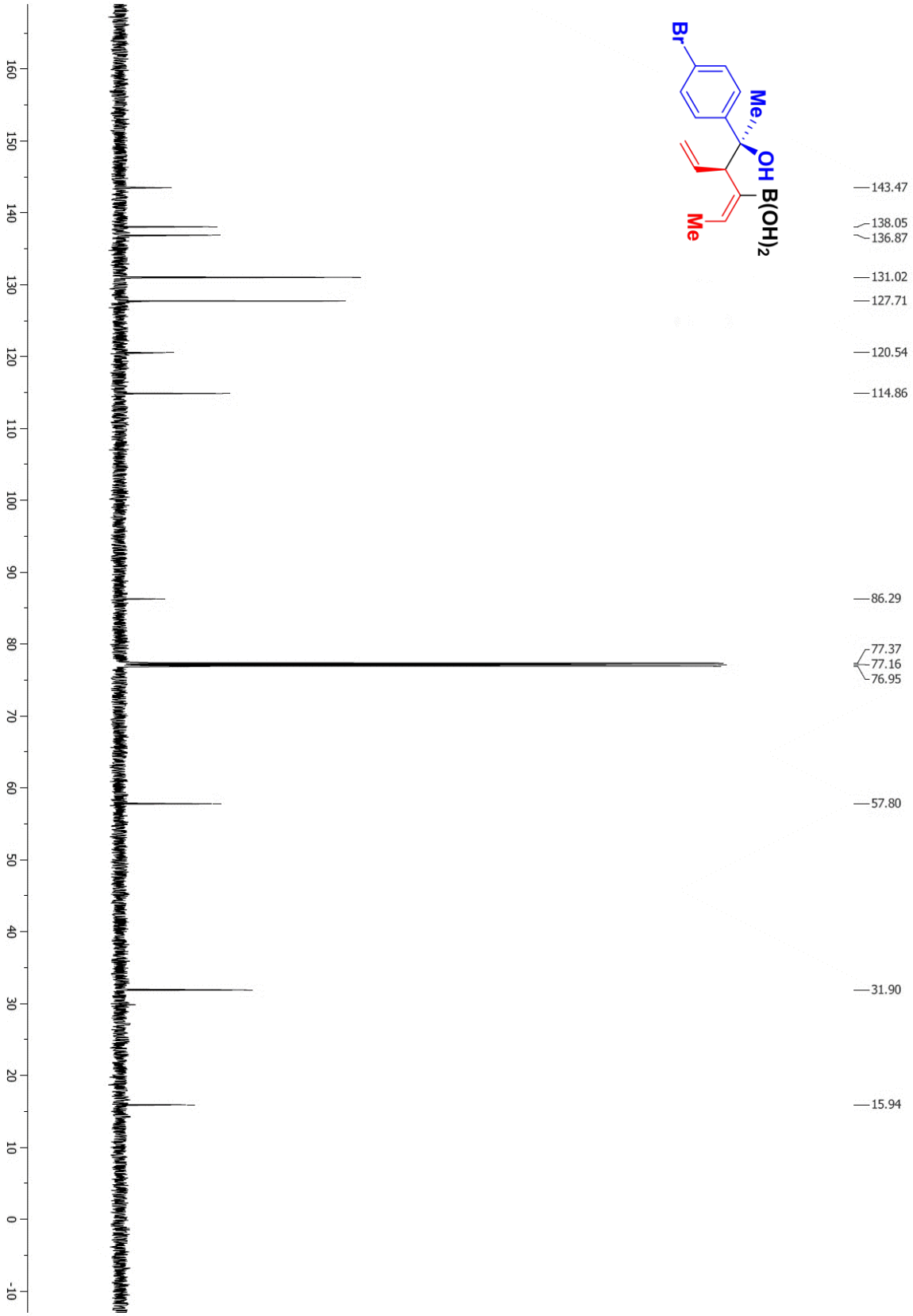
4.73
3.53
3.51
2.33
1.76
1.74
1.58

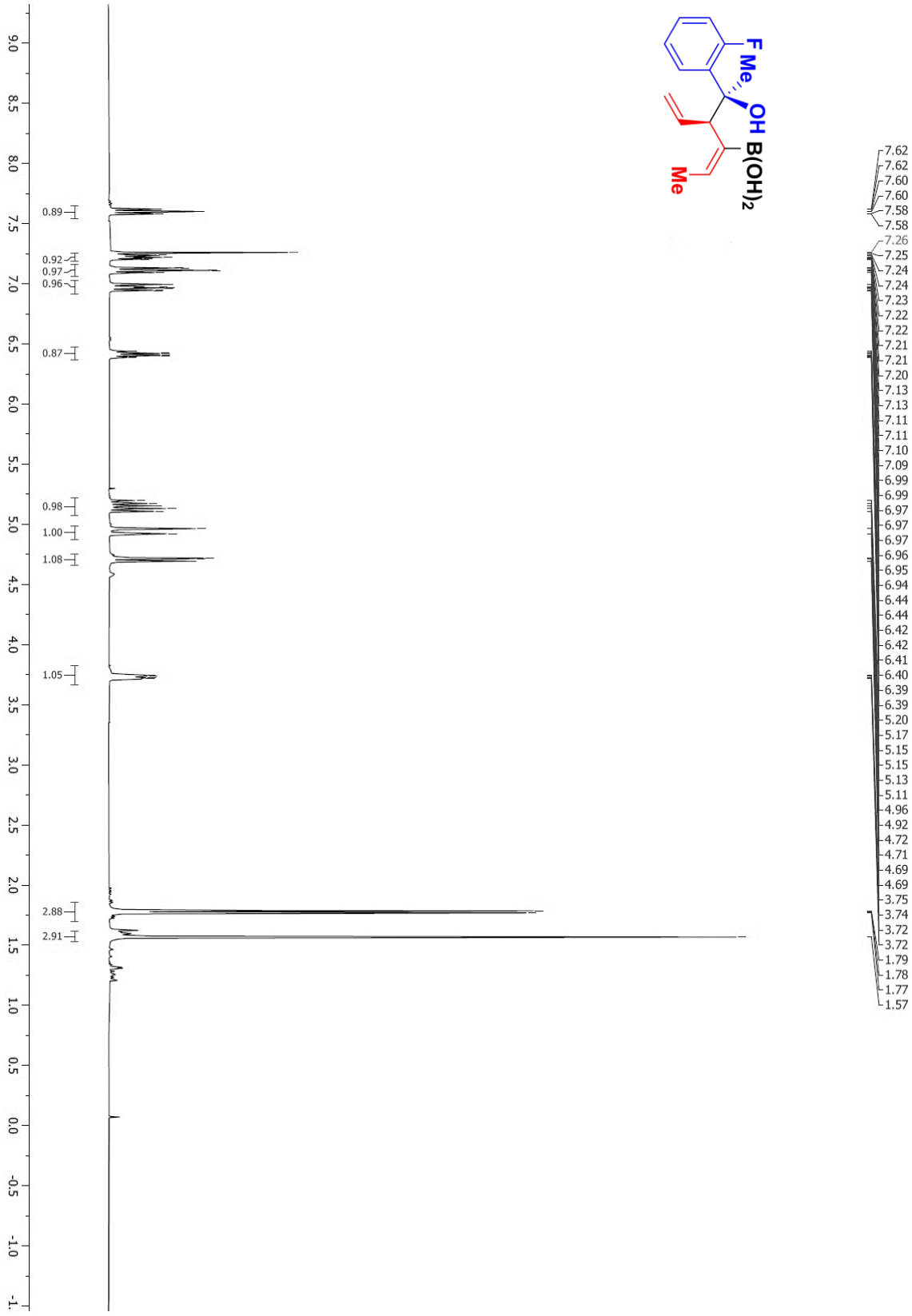

Me
Me
OH
B(OH)2
Me
141.35
137.54
137.28
136.05
128.64
125.70
114.40
86.61
77.37
77.16
76.95
57.94
32.00
21.16
15.92

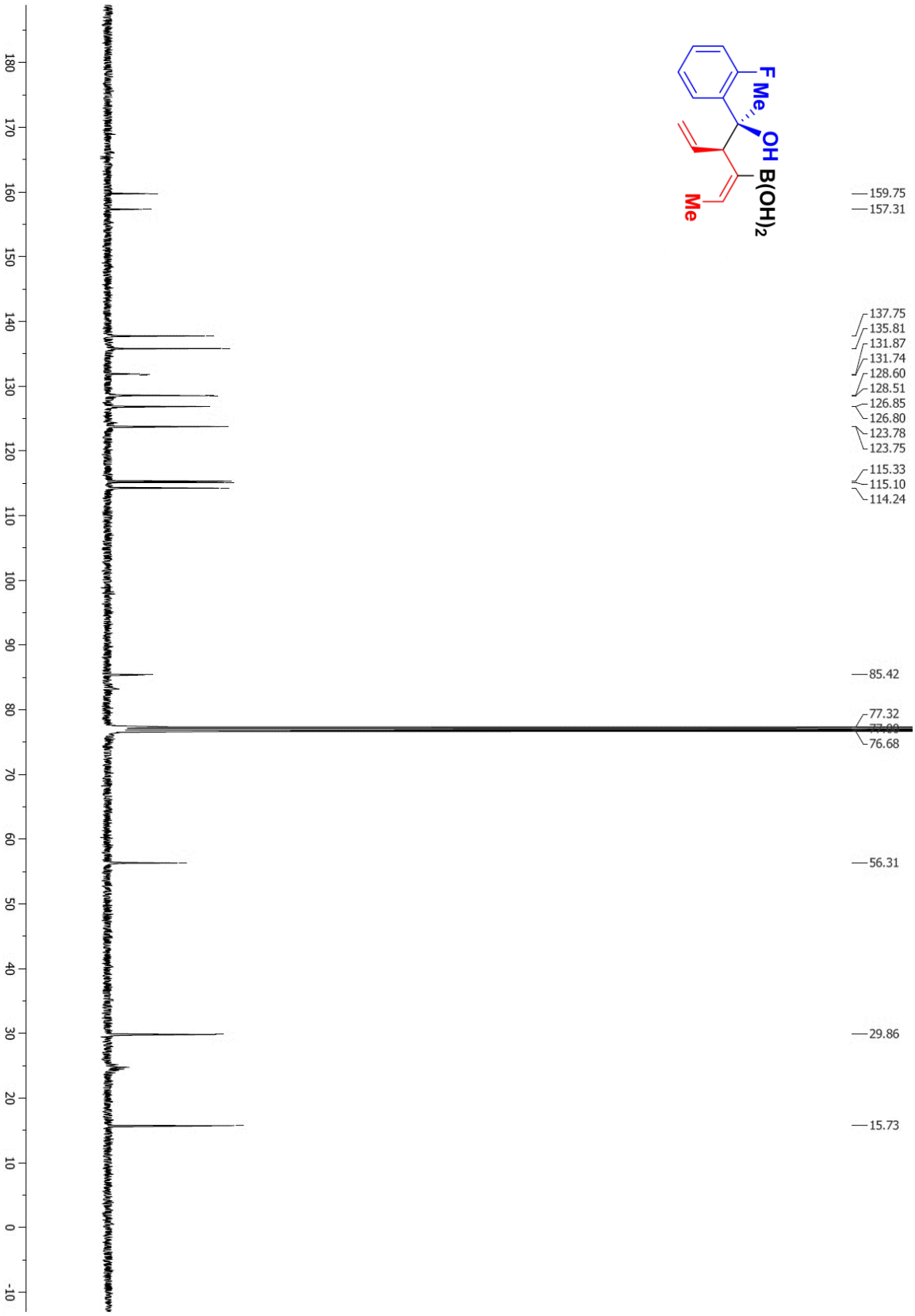

(pin)B
Me
OH
B(OH)2
Me
2.03
1.96
0.89
0.95
1.12
1.05
1.00
2.93
2.96
12.44
7.77
7.76
7.34
7.32
7.26
7.26
6.43
6.42
6.41
6.39
5.08
5.06
5.05
5.03
5.01
4.84
4.80
4.71
4.69
3.55
3.54
1.75
1.74
1.57
1.36
1.34

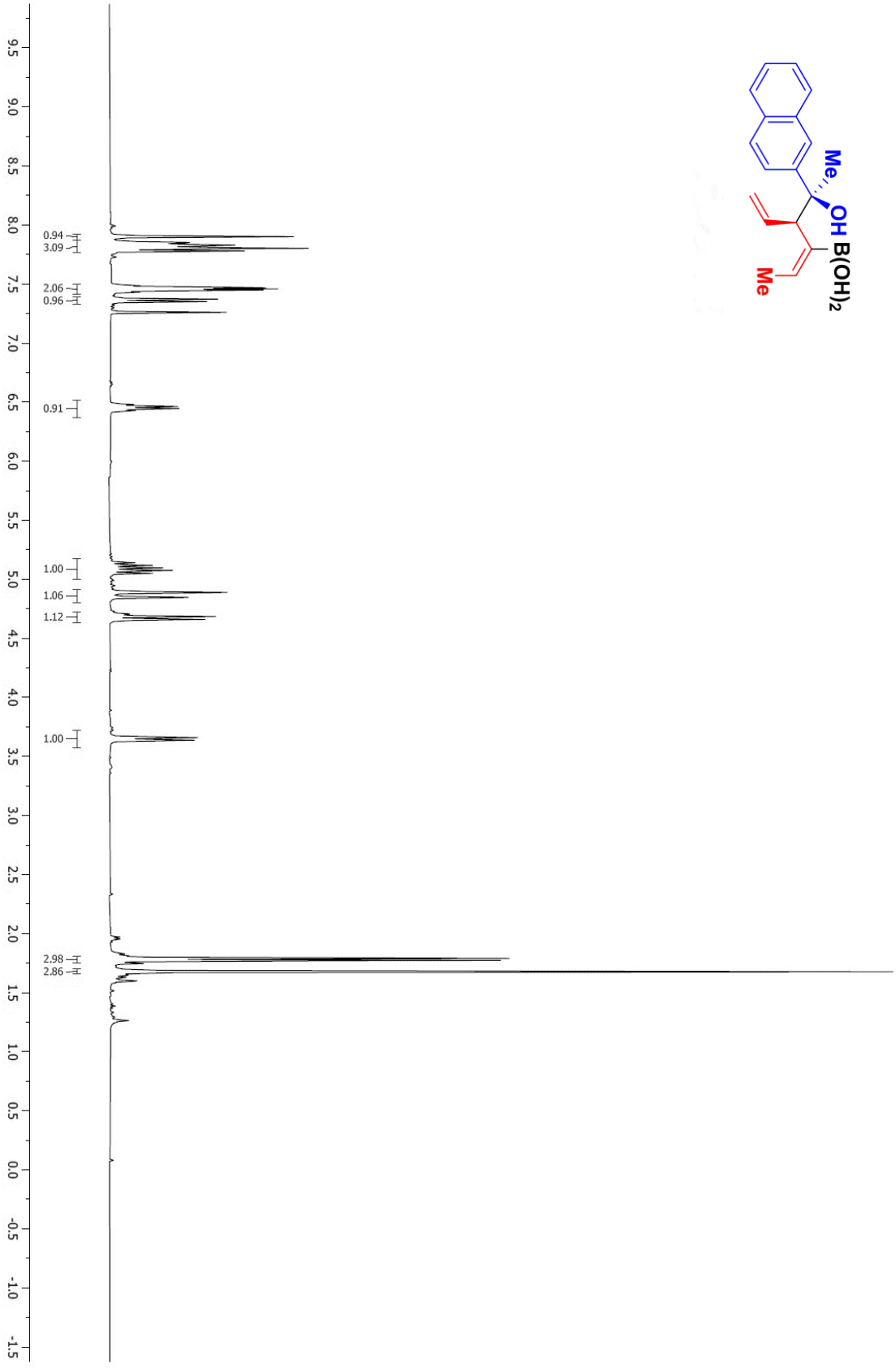

(pin)B
Me
OH
B(OH)2
Me
147.55
137.69
136.95
134.51
125.20
114.62
86.72
83.89
77.42
77.16
76.91
57.79
31.92
25.03
24.98
15.91

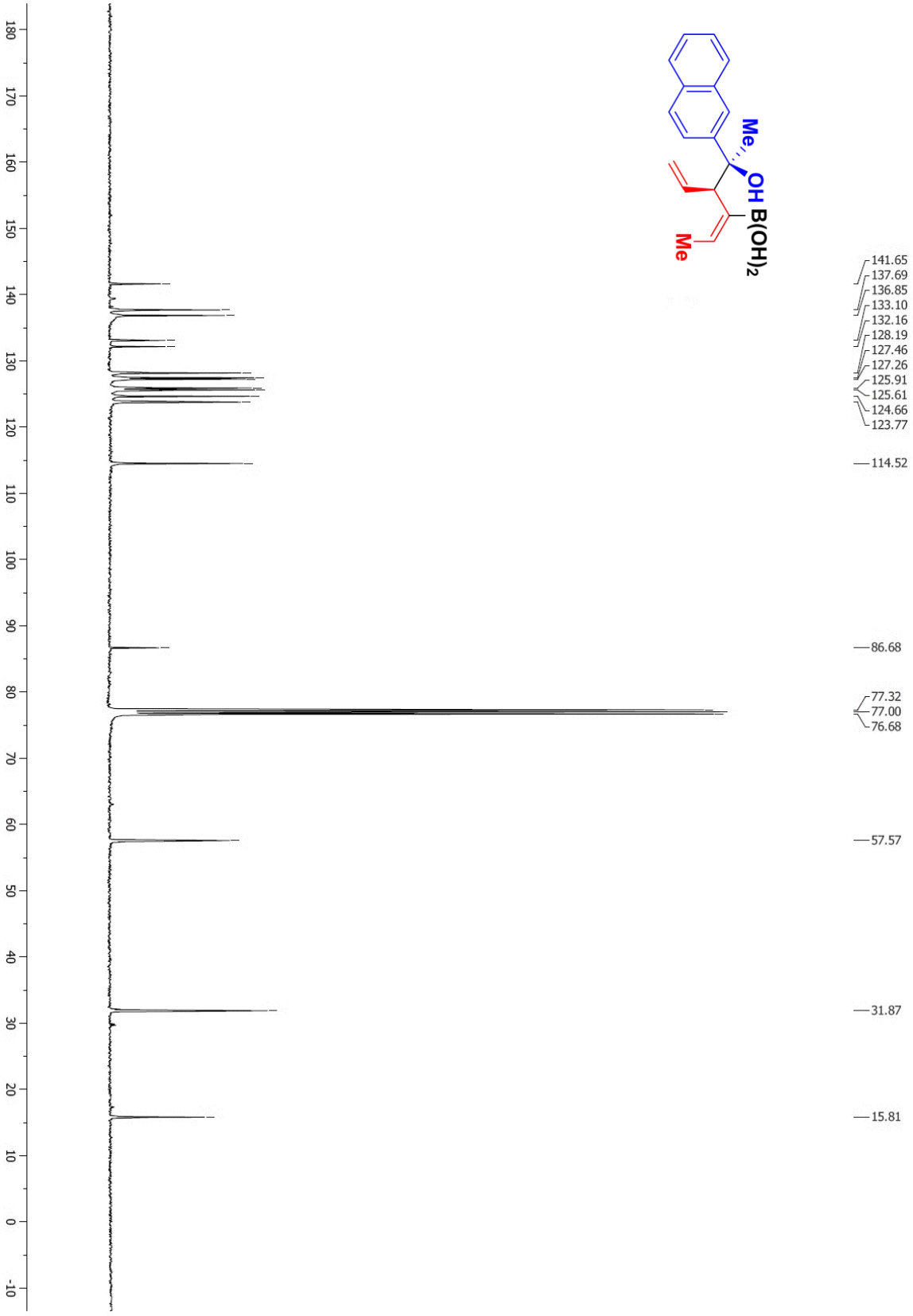

Br
Me
OH
B(OH)2
Me
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
1.90
2.05
0.81
0.90
1.13
1.10
1.04
3.25
3.25
7.44
7.44
7.42
7.26
7.20
7.19
7.18
6.43
6.42
6.41
6.40
5.06
5.04
5.03
5.01
5.00
4.85
4.82
4.75
4.74
3.52
3.50
1.75
1.74
1.56

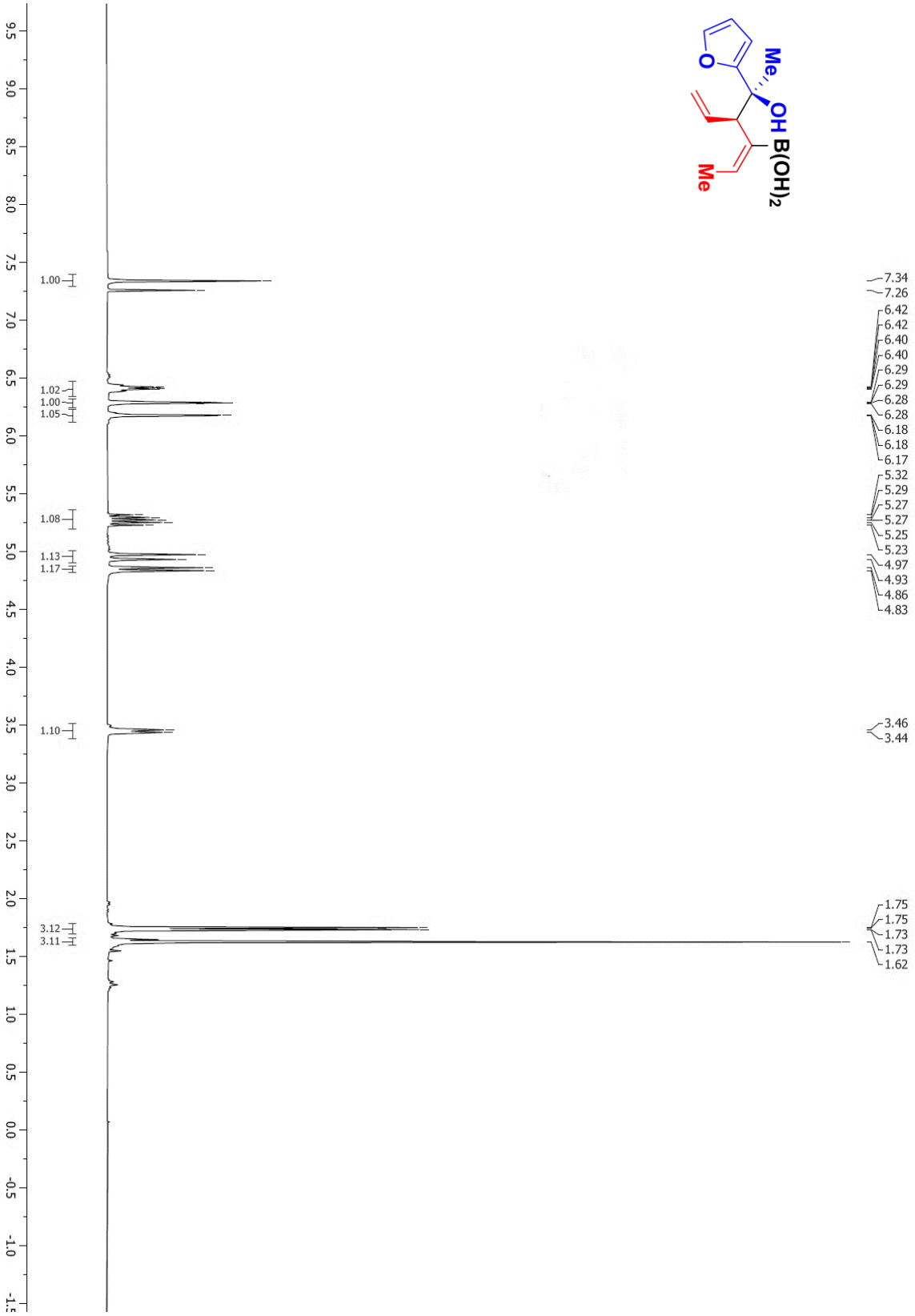

Br
Me
OH
B(OH)2
Me
143.47
138.05
136.87
131.02
127.71
120.54
114.86
86.29
77.37
77.16
76.95
57.80
31.90
15.94
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

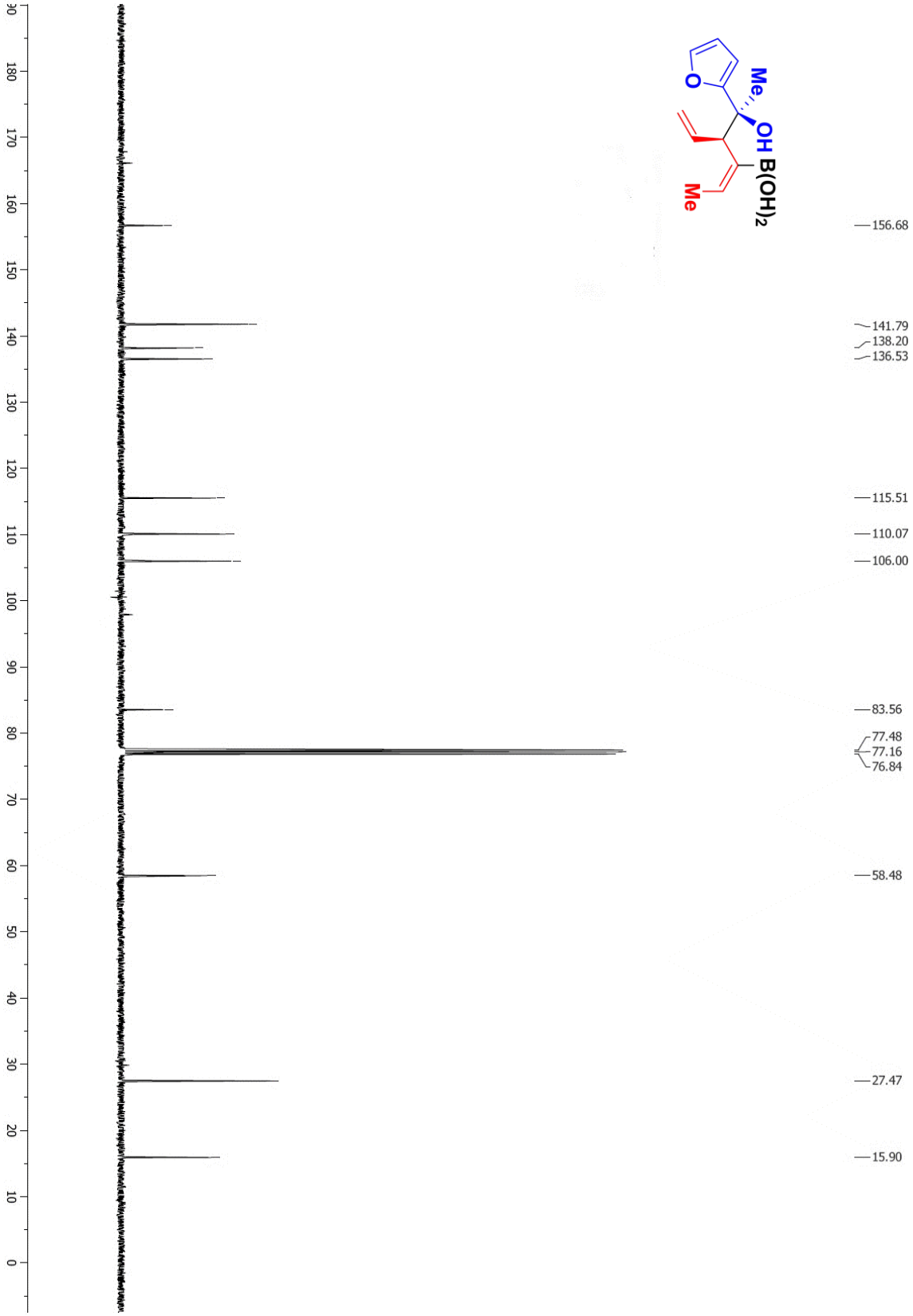

F
Me
OH
B(OH)2
Me
0.89
0.92
0.97
0.96
0.87
0.98
1.00
1.08
1.05
2.88
2.91
7.62
7.62
7.60
7.60
7.58
7.58
7.26
7.25
7.24
7.24
7.23
7.22
7.22
7.21
7.21
7.20
7.13
7.13
7.11
7.11
7.10
7.09
6.99
6.99
6.97
6.97
6.97
6.96
6.95
6.94
6.44
6.44
6.42
6.42
6.41
6.40
6.39
6.39
5.20
5.17
5.15
5.15
5.13
5.11
4.96
4.92
4.72
4.71
4.69
4.69
3.75
3.74
3.72
3.72
1.79
1.78
1.77
1.57

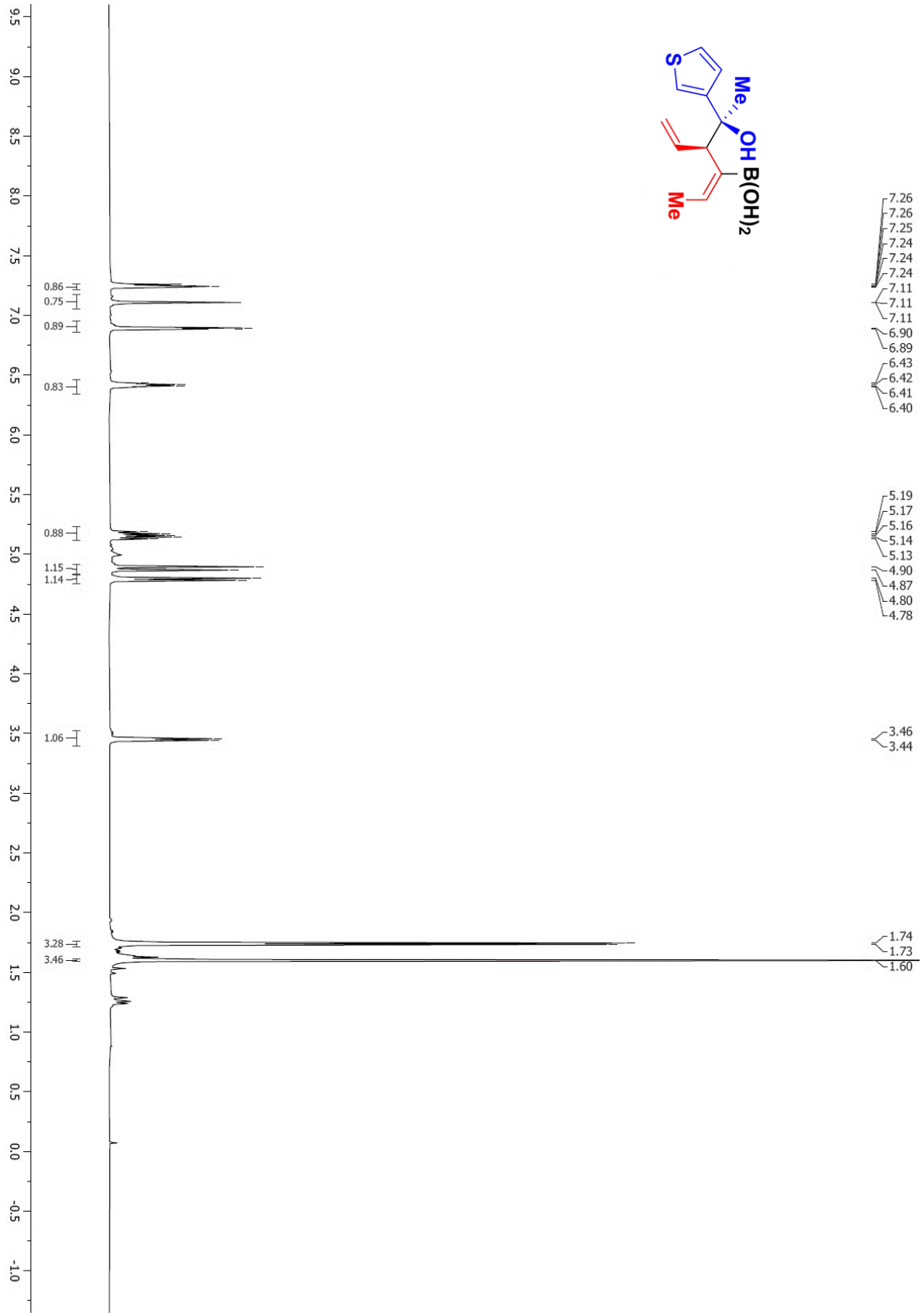

F
Me
OH
B(OH)2
Me
159.75
157.31
137.75
135.81
131.87
131.74
128.60
128.51
126.85
126.80
123.78
123.75
115.33
115.10
114.24
85.42
77.32
76.68
56.31
29.86
15.73

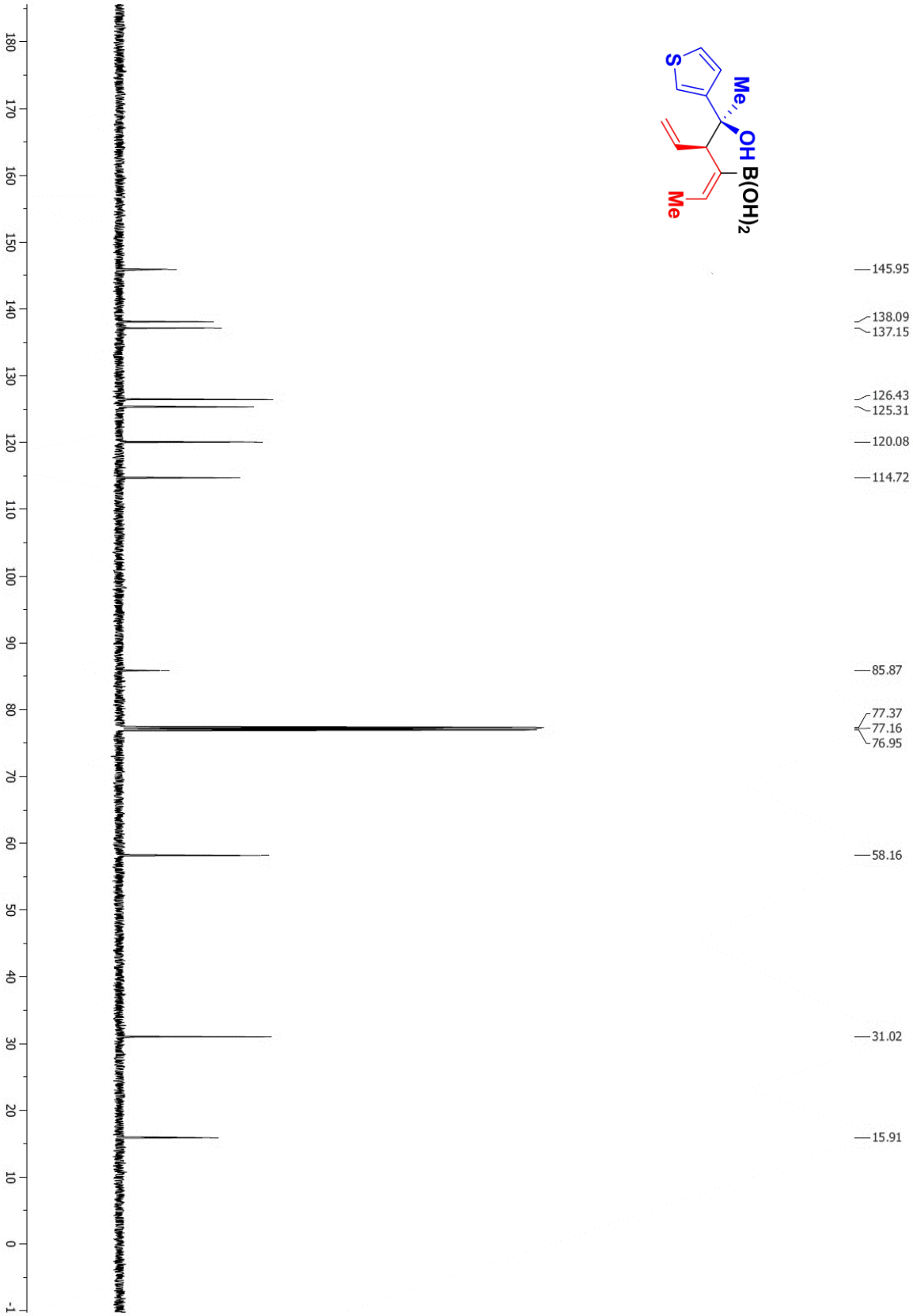

Me
OH B(OH)2
Me
0.94
3.09
2.06
0.96
0.91
1.00
1.06
1.12
1.00
2.98
2.86
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5

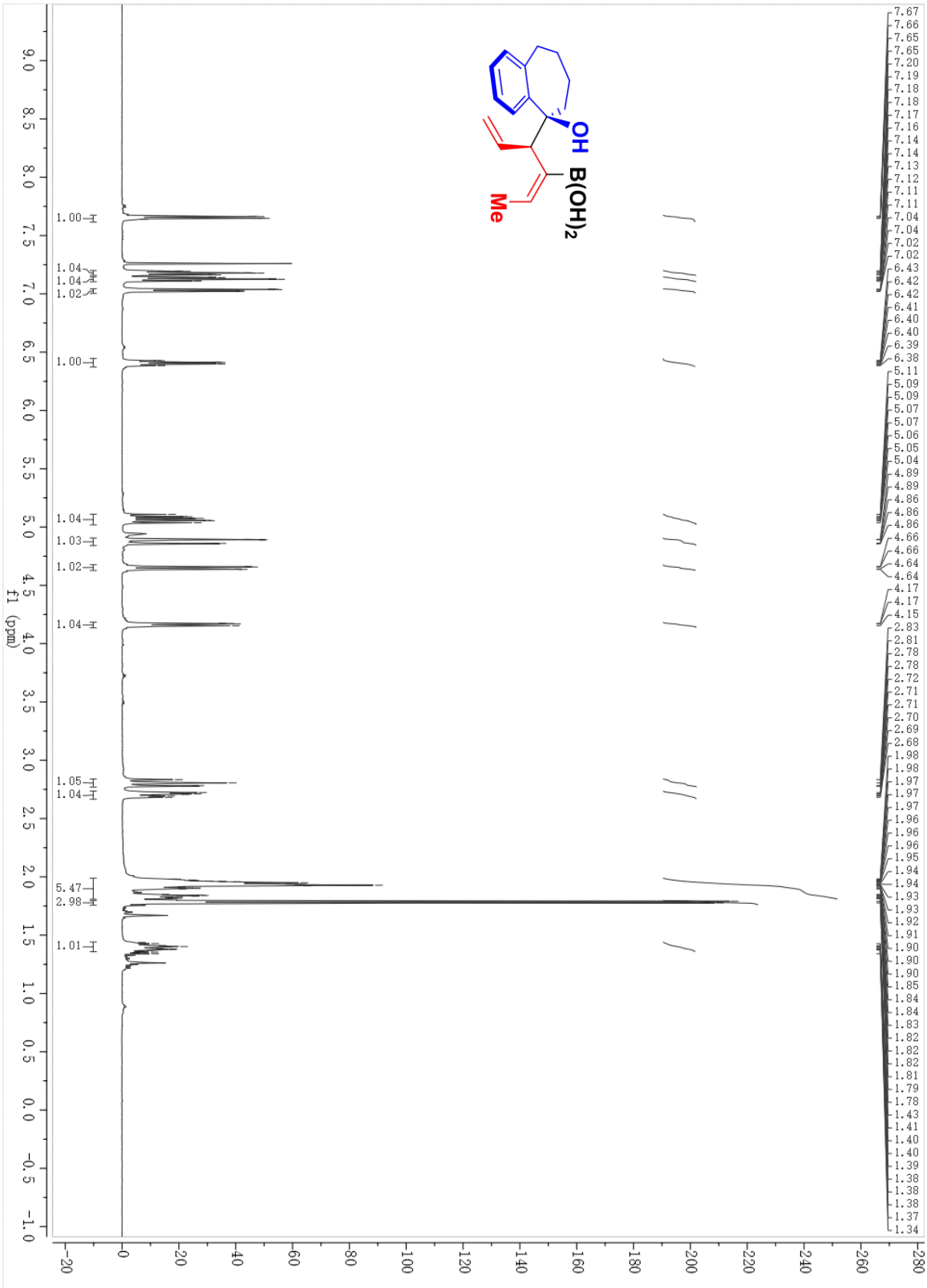

Me
OH
B(OH)2
Me
141.65
137.69
136.85
133.10
132.16
128.19
127.46
127.26
125.91
125.61
124.66
123.77
114.52
86.68
77.32
77.00
76.68
57.57
31.87
15.81

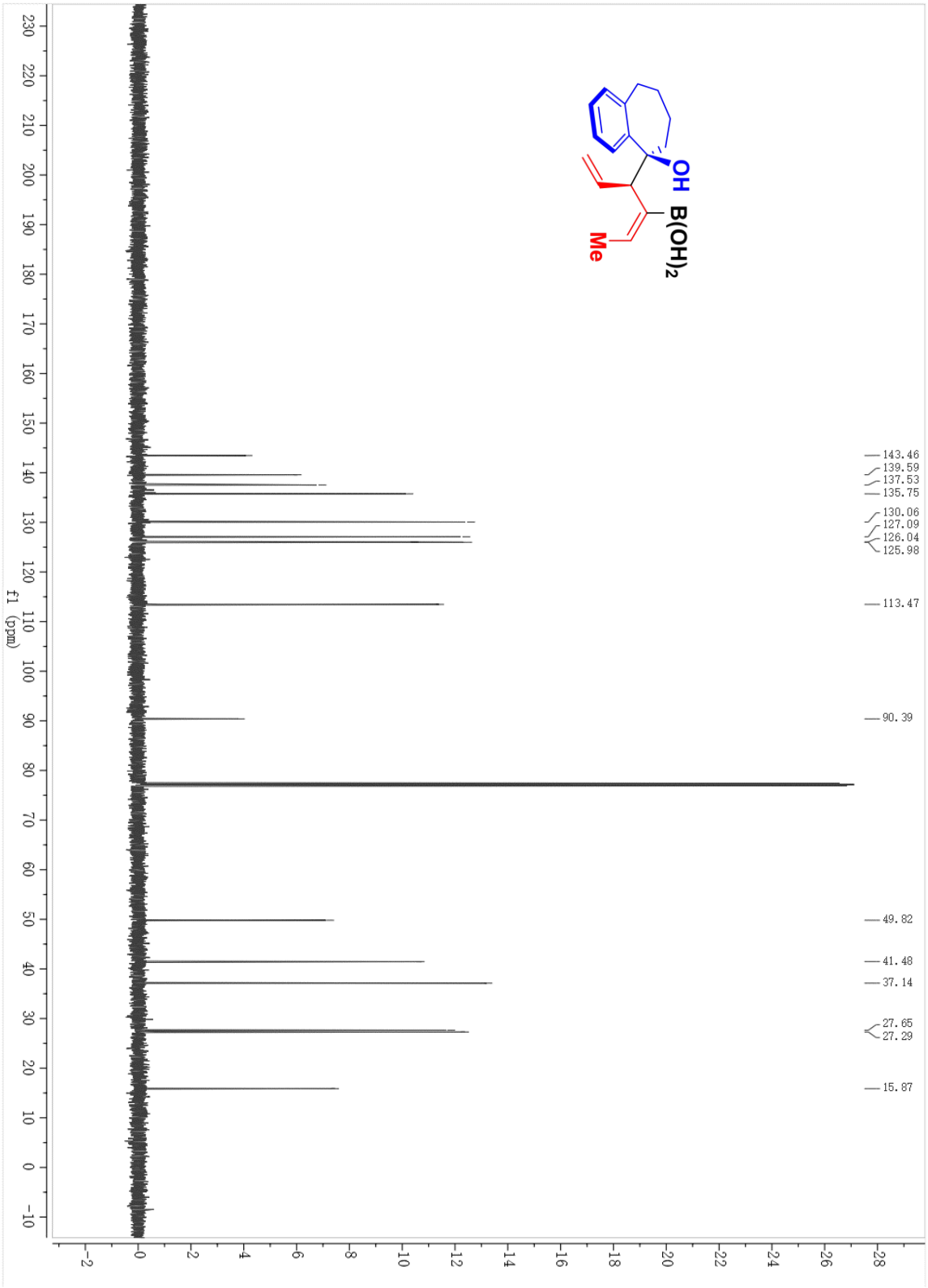

Me
OH
B(OH)2
O
Me
1.00
1.02
1.00
1.05
1.08
1.13
1.17
1.10
3.12
3.11
7.34
7.26
6.42
6.42
6.40
6.40
6.29
6.29
6.28
6.28
6.18
6.18
6.17
5.32
5.29
5.27
5.27
5.25
5.23
4.97
4.93
4.86
4.83
3.46
3.44
1.75
1.75
1.73
1.73
1.62

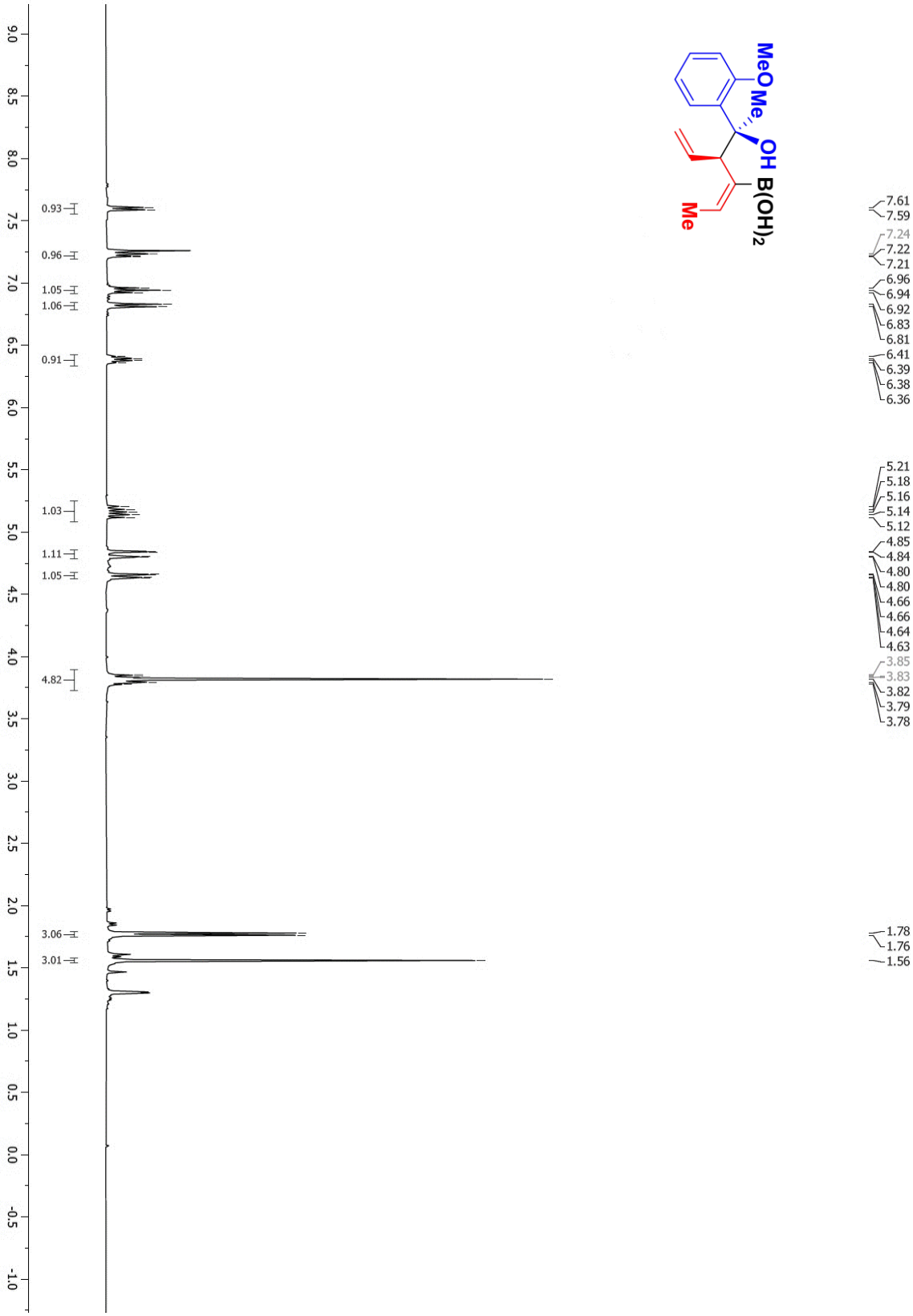

Me
OH
B(OH)2
O
Me
156.68
141.79
138.20
136.53
115.51
110.07
106.00
83.56
77.48
77.16
76.84
58.48
27.47
15.90

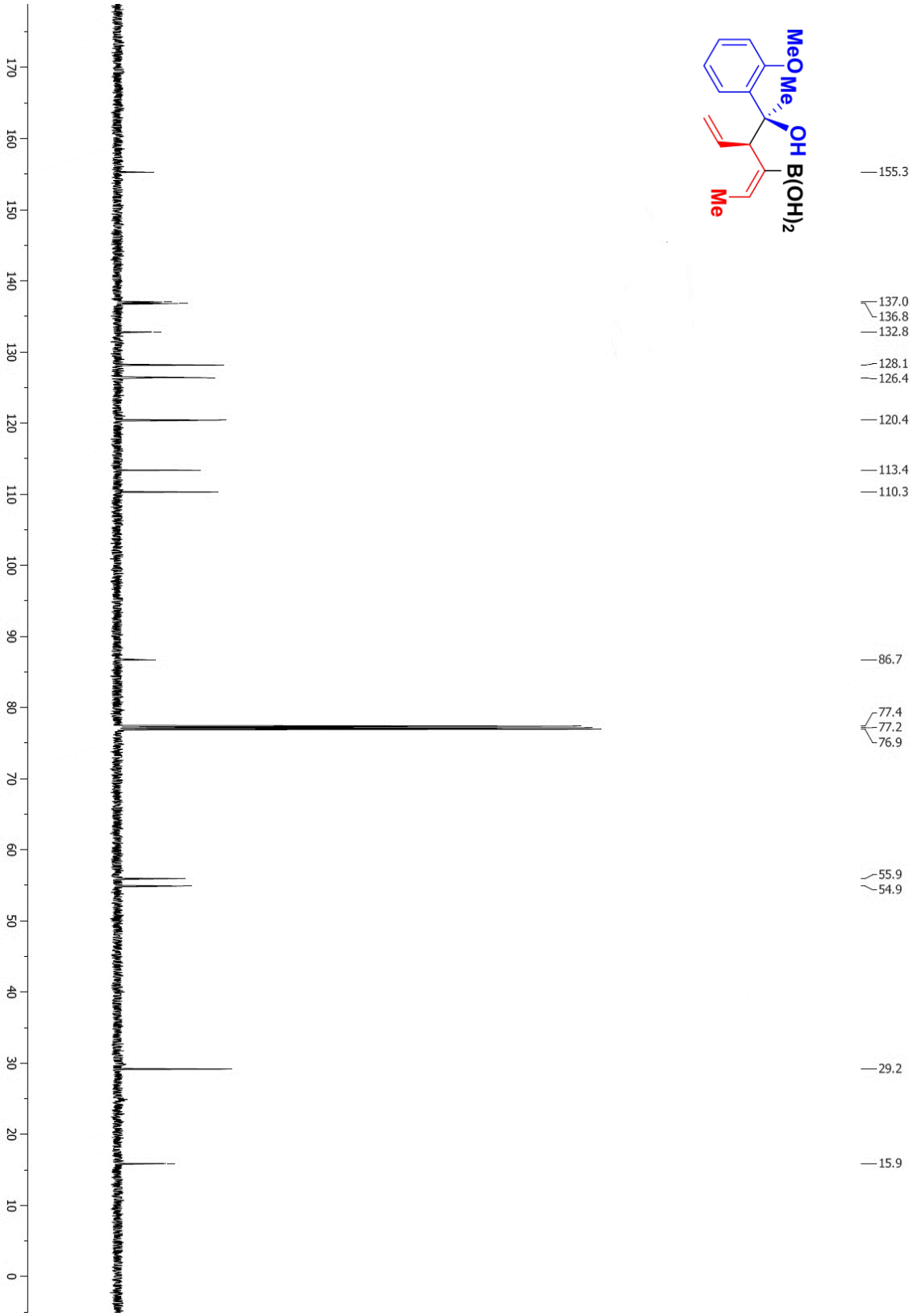

S
Me
OH
B(OH)2
Me
0.86
0.75
0.89
0.83
0.88
1.15
1.14
1.06
3.28
3.46
7.26
7.26
7.25
7.24
7.24
7.24
7.11
7.11
7.11
6.90
6.89
6.43
6.42
6.41
6.40
5.19
5.17
5.16
5.14
5.13
4.90
4.87
4.80
4.78
3.46
3.44
1.74
1.73
1.60

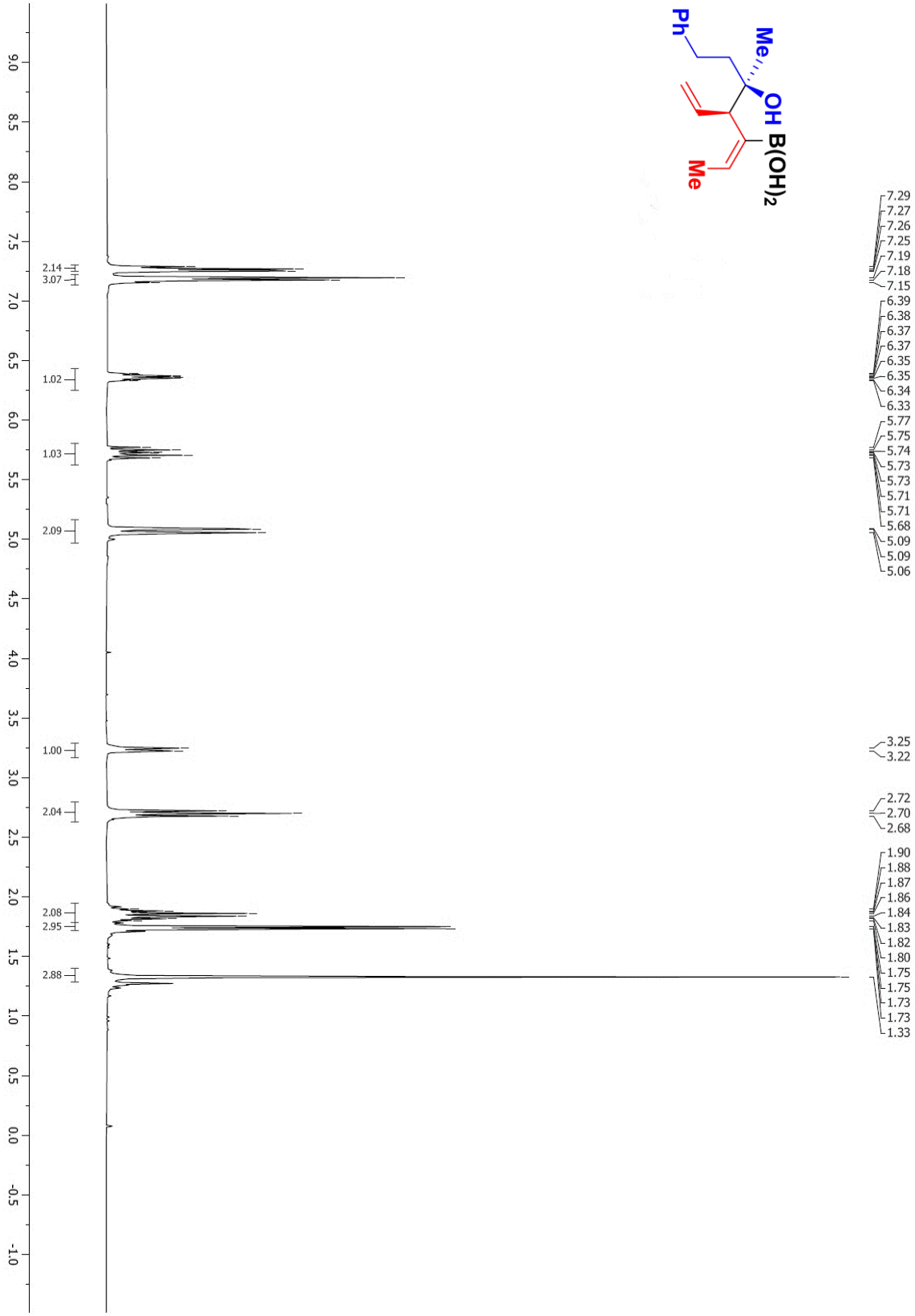

S
Me
OH
B(OH)2
Me
145.95
138.09
137.15
126.43
125.31
120.08
114.72
85.87
77.37
77.16
76.95
58.16
31.02
15.91

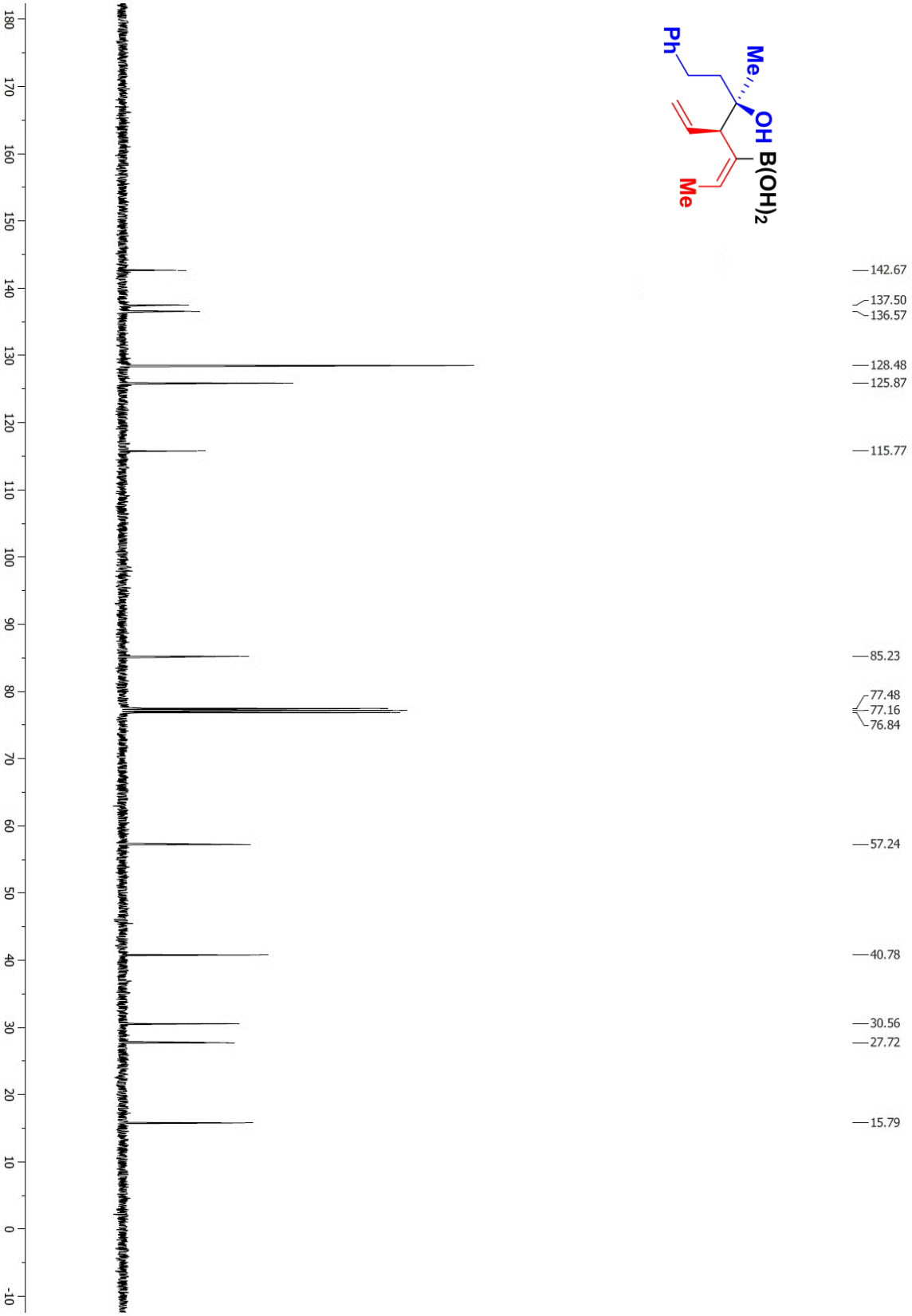

OH
B(OH)2
Me
f1 (ppm)

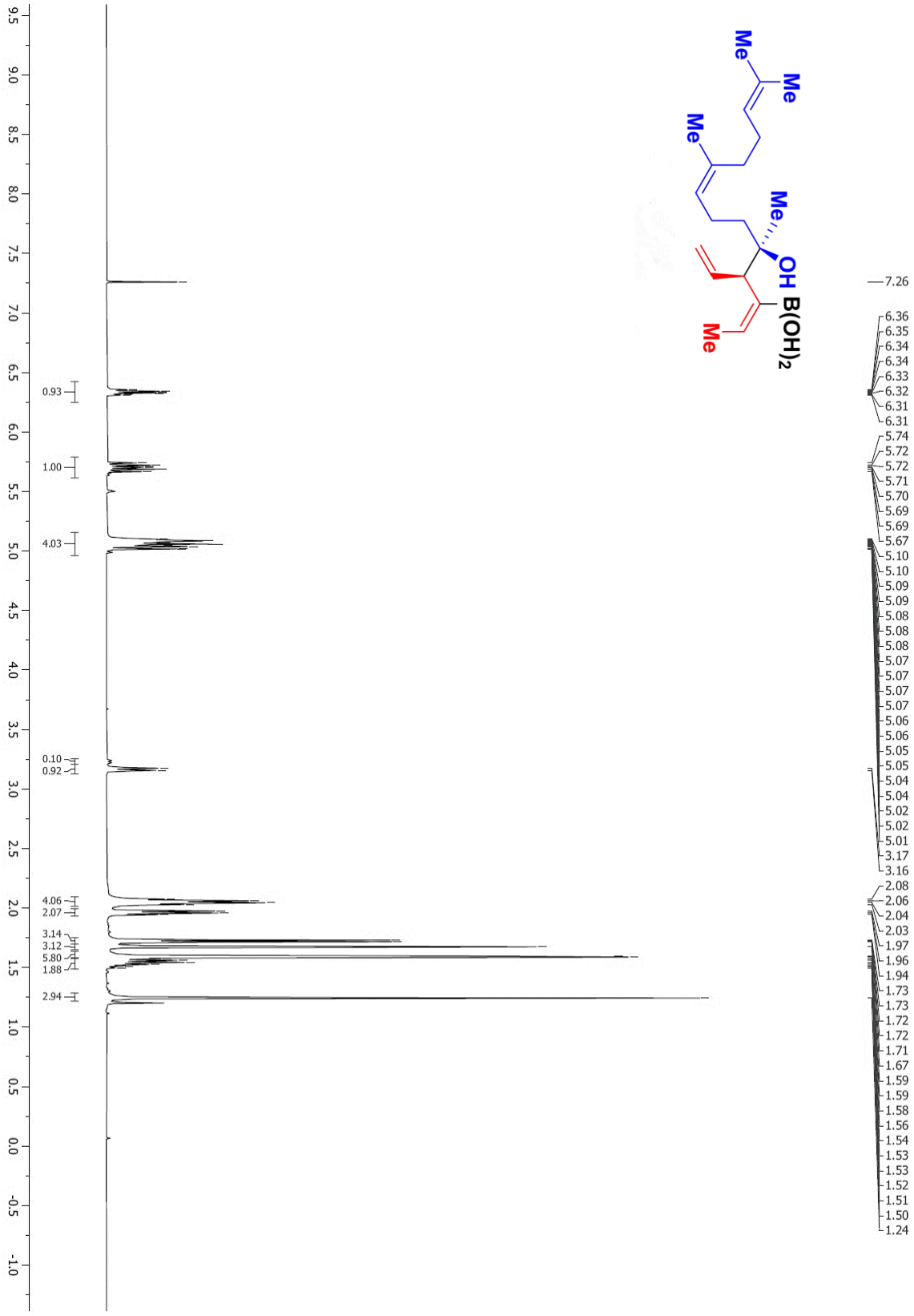

OH
B(OH)2
Me
143.46
139.59
137.53
135.75
130.06
127.09
126.04
125.98
113.47
90.39
49.82
41.48
37.14
27.65
27.29
15.87
f1 (ppm)

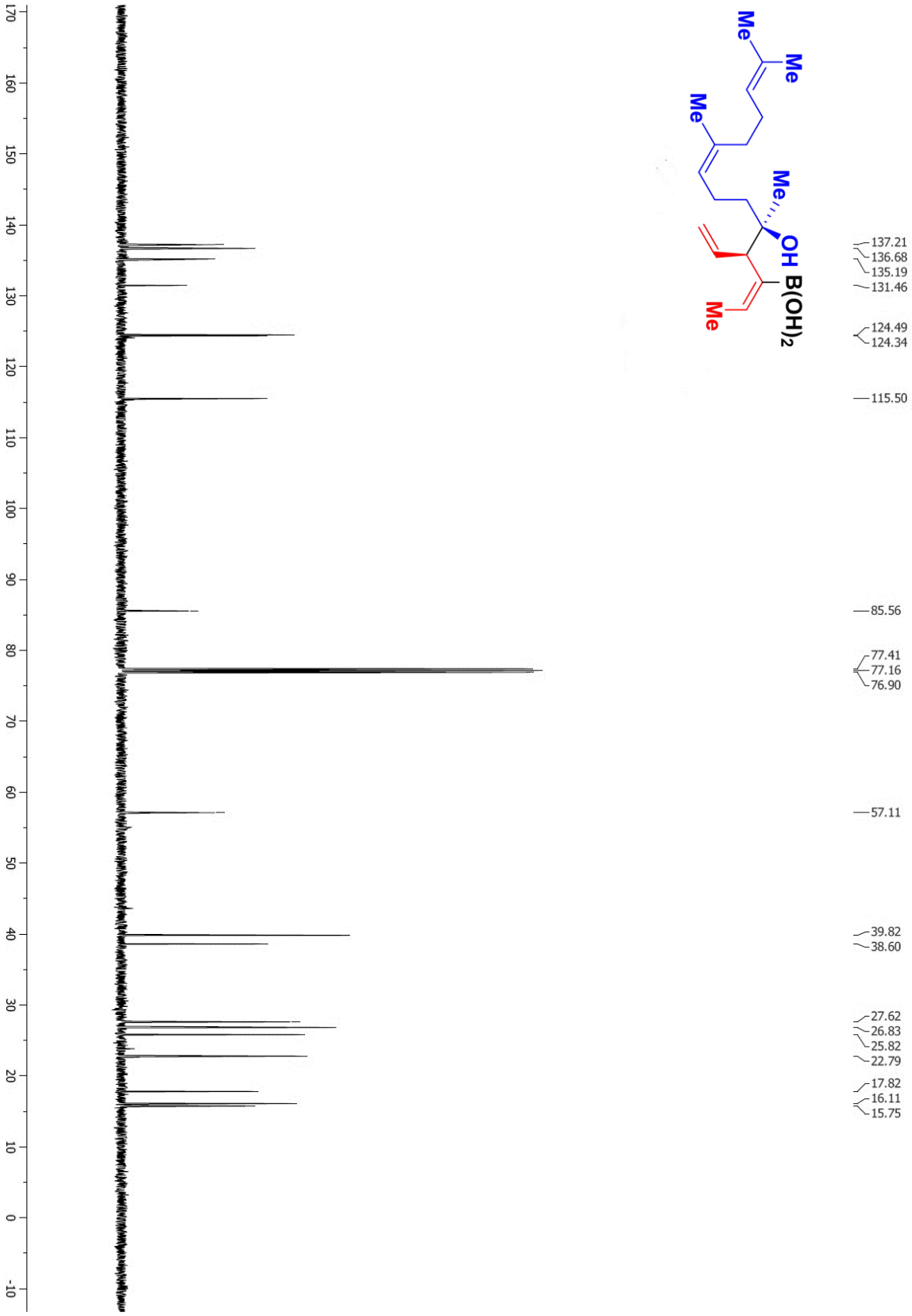

MeO
Me
OH
B(OH)2
Me
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
0.93
0.96
1.05
1.06
0.91
1.03
1.11
1.05
4.82
3.06
3.01
7.61
7.59
7.24
7.22
7.21
6.96
6.94
6.92
6.83
6.81
6.41
6.39
6.38
6.36
5.21
5.18
5.16
5.14
5.12
4.85
4.84
4.80
4.80
4.66
4.66
4.64
4.63
3.85
3.83
3.82
3.79
3.78
1.78
1.76
1.56

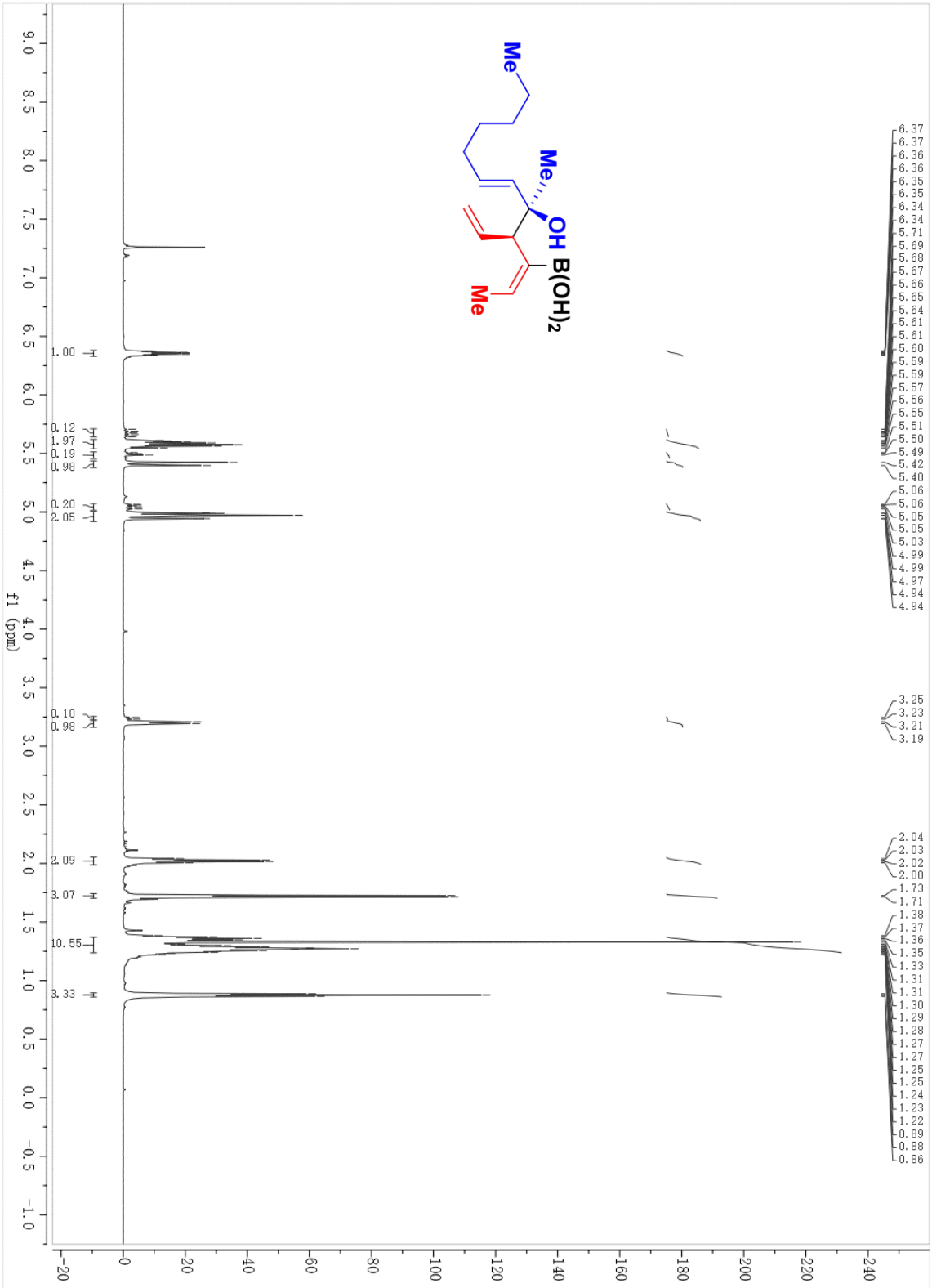

MeO
Me
OH
B(OH)2
Me
155.3
137.0
136.8
132.8
128.1
126.4
120.4
113.4
110.3
86.7
77.4
77.2
76.9
55.9
54.9
29.2
15.9

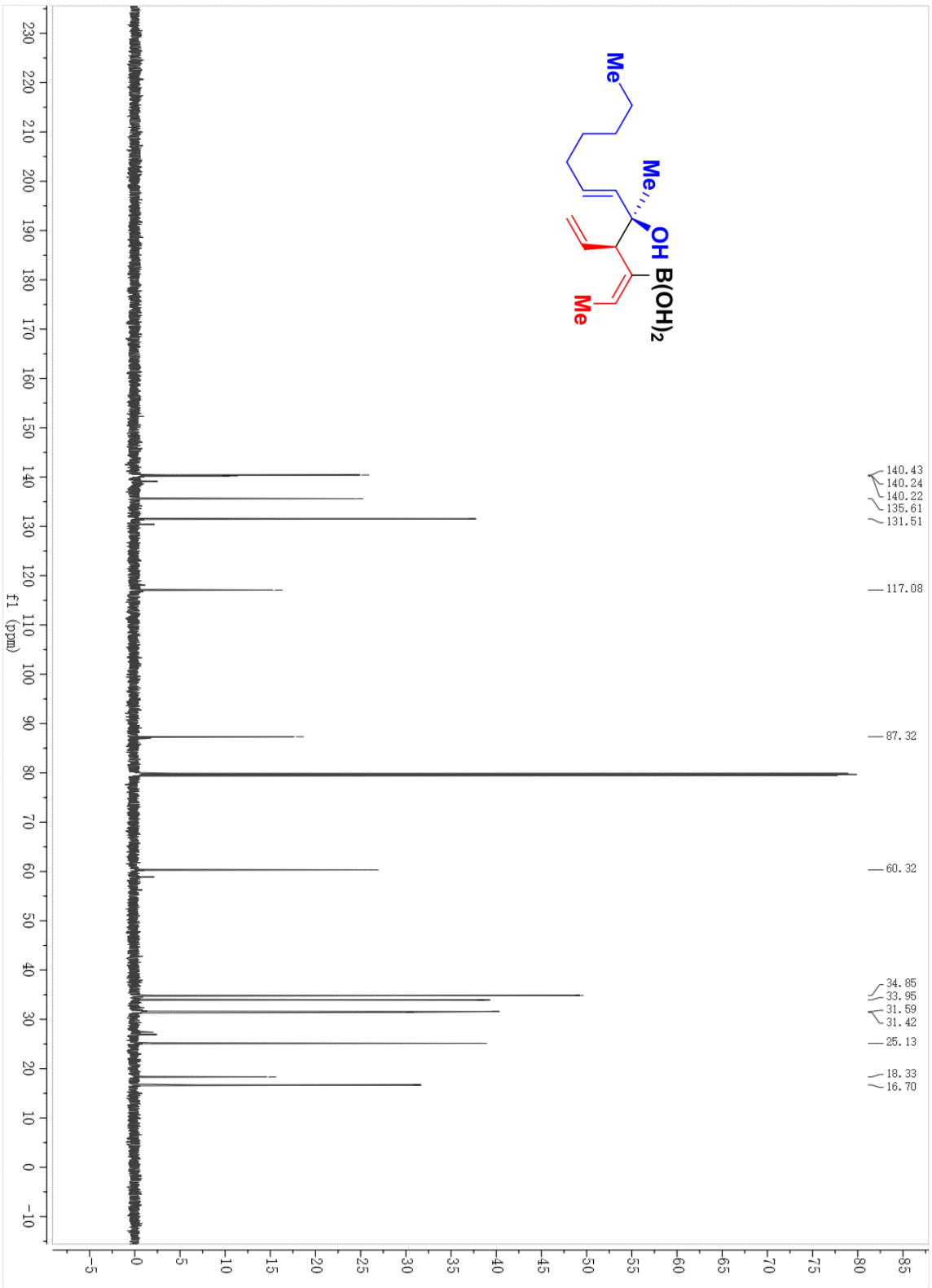

Ph
Me
OH
B(OH)2
Me
2.14
3.07
1.02
1.03
2.09
1.00
2.04
2.08
2.95
2.88
7.29
7.27
7.26
7.25
7.19
7.18
7.15
6.39
6.38
6.37
6.37
6.35
6.35
6.34
6.33
5.77
5.75
5.74
5.73
5.73
5.71
5.71
5.68
5.09
5.09
5.06
3.25
3.22
2.72
2.70
2.68
1.90
1.88
1.87
1.86
1.84
1.83
1.82
1.80
1.75
1.75
1.73
1.73
1.33

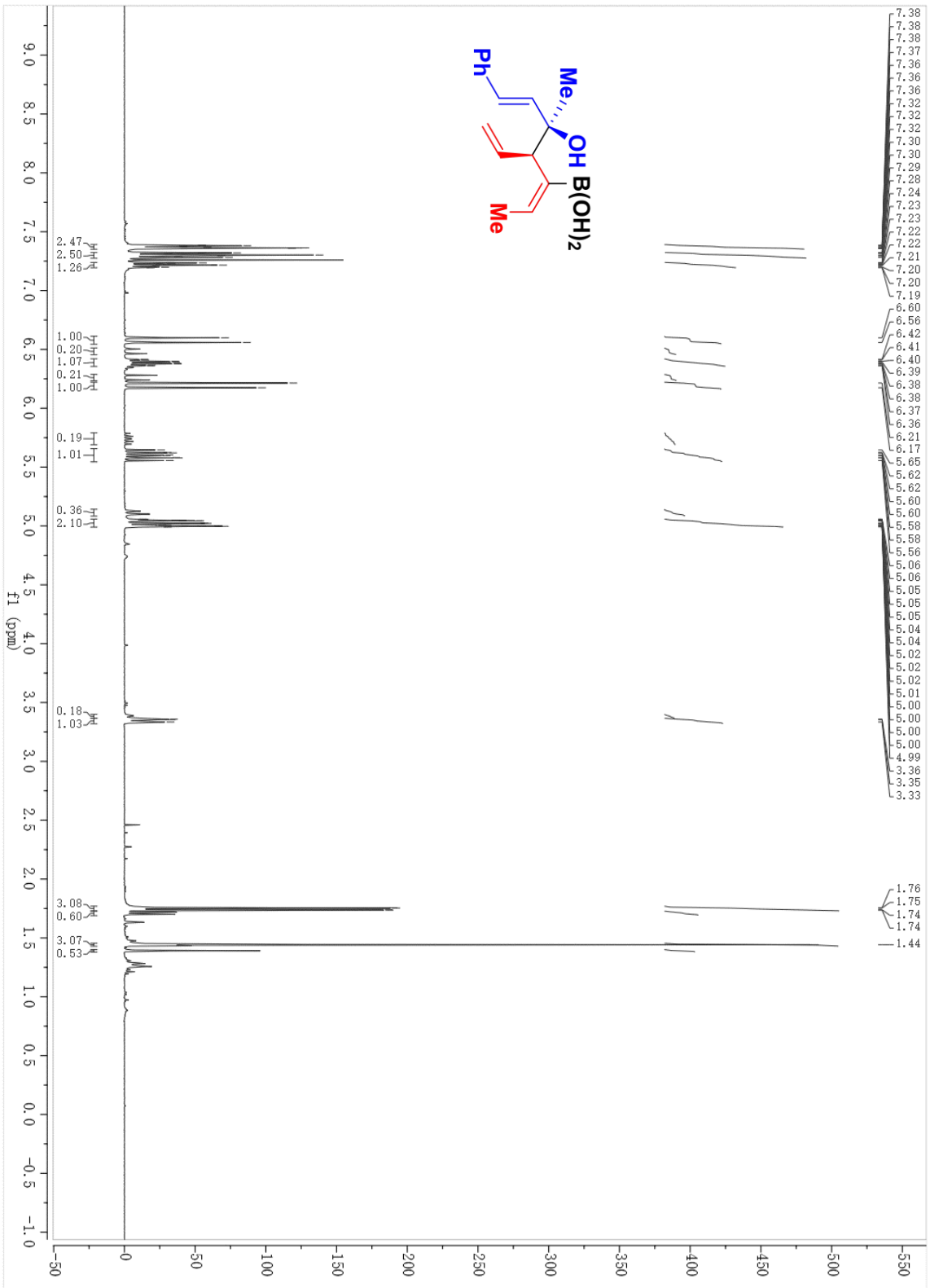

Ph
Me
OH
B(OH)2
Me
142.67
137.50
136.57
128.48
125.87
115.77
85.23
77.48
77.16
76.84
57.24
40.78
30.56
27.72
15.79

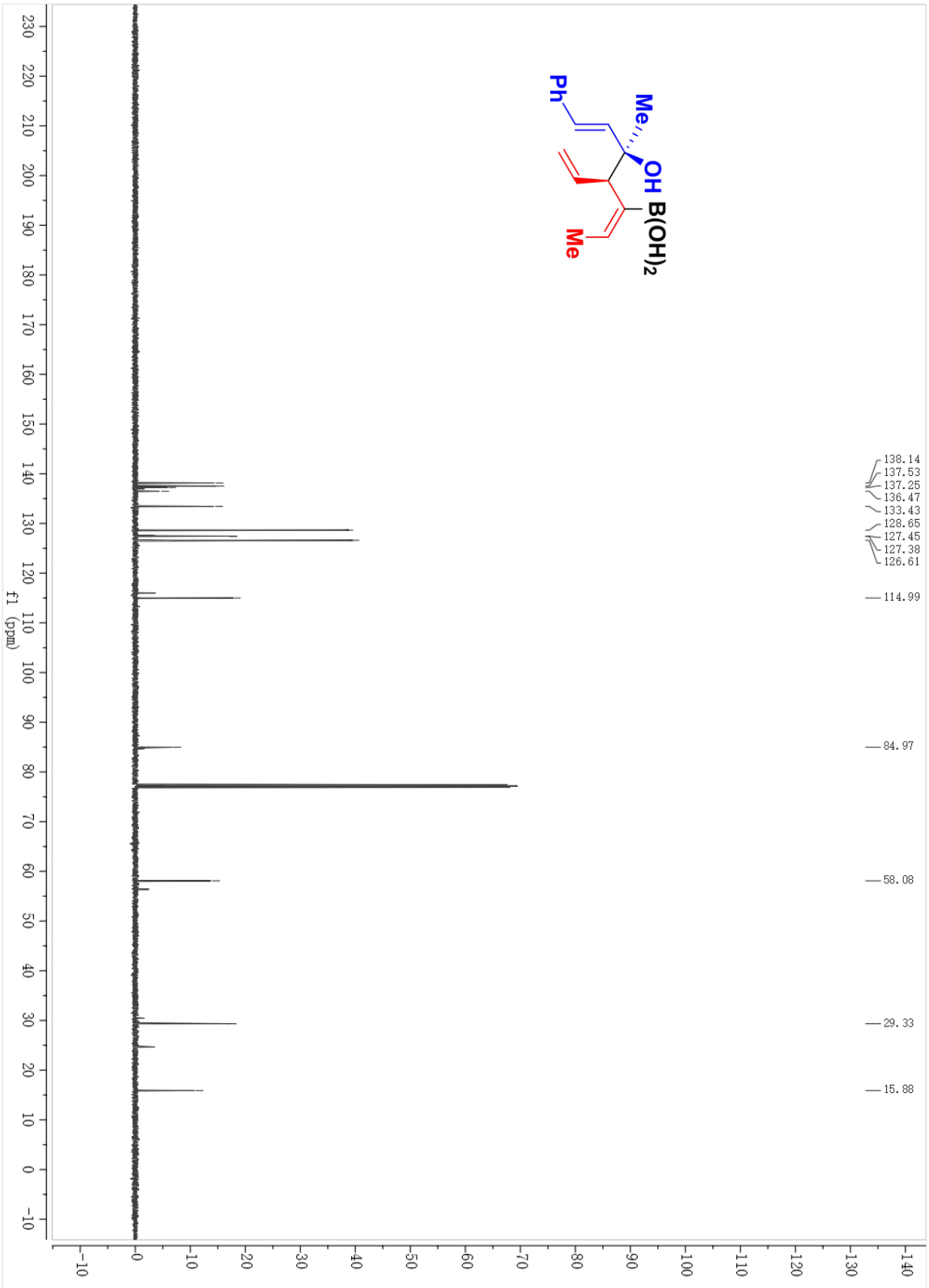

Me
Me
Me
Me
OH
B(OH)2
Me
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
0.93
1.00
4.03
0.10
0.92
4.06
2.07
3.14
3.12
5.80
1.88
2.94
7.26
6.36
6.35
6.34
6.34
6.33
6.32
6.31
6.31
5.74
5.72
5.72
5.71
5.70
5.69
5.69
5.67
5.10
5.10
5.09
5.09
5.08
5.08
5.08
5.07
5.07
5.07
5.07
5.06
5.06
5.05
5.05
5.04
5.04
5.02
5.02
5.01
3.17
3.16
2.08
2.06
2.04
2.03
1.97
1.96
1.94
1.73
1.73
1.72
1.72
1.71
1.67
1.59
1.59
1.58
1.56
1.54
1.53
1.53
1.52
1.51
1.50
1.24

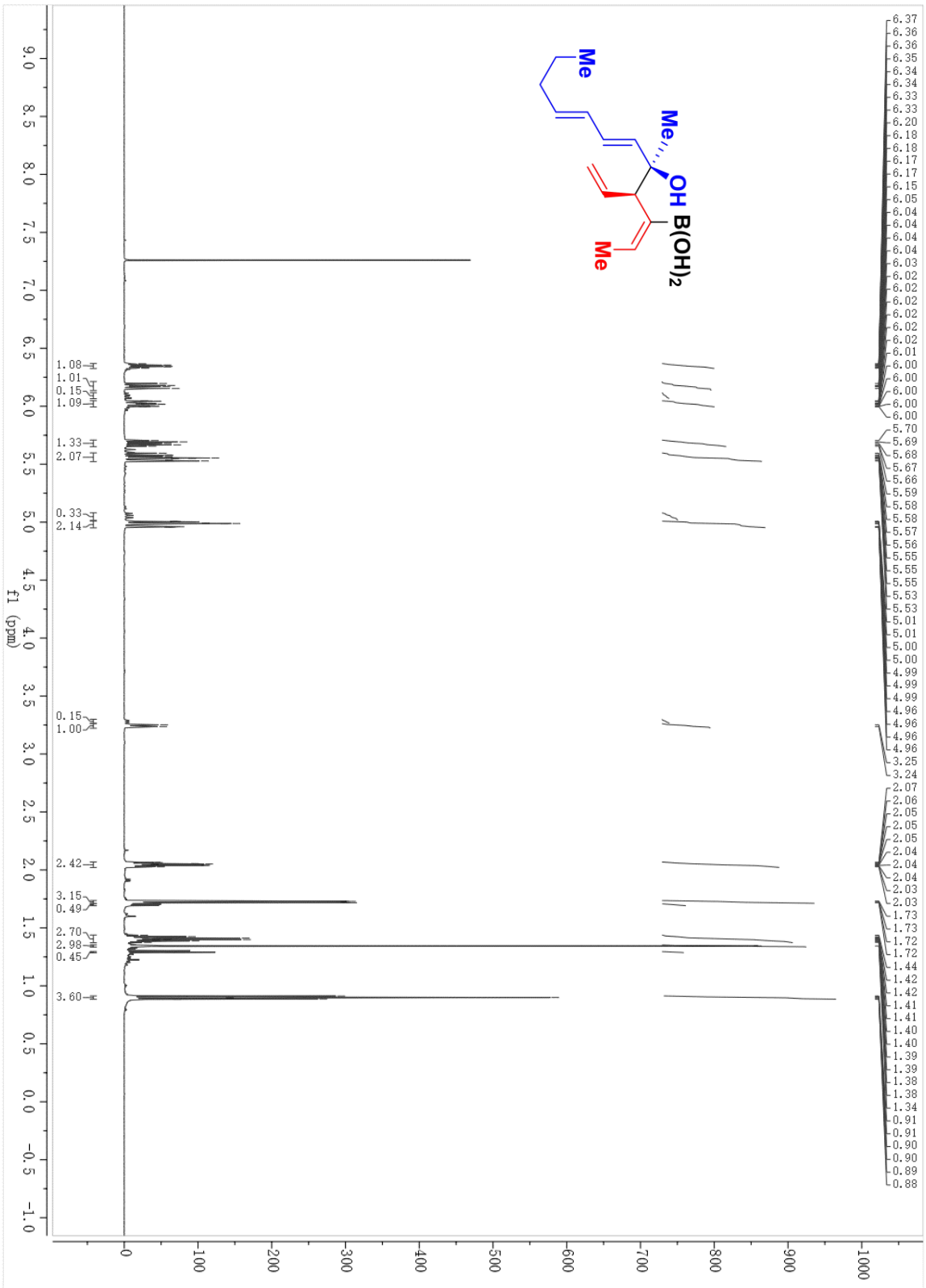

Me
Me
Me
Me
OH
B(OH)2
Me
137.21
136.68
135.19
131.46
124.49
124.34
115.50
85.56
77.41
77.16
76.90
57.11
39.82
38.60
27.62
26.83
25.82
22.79
17.82
16.11
15.75
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

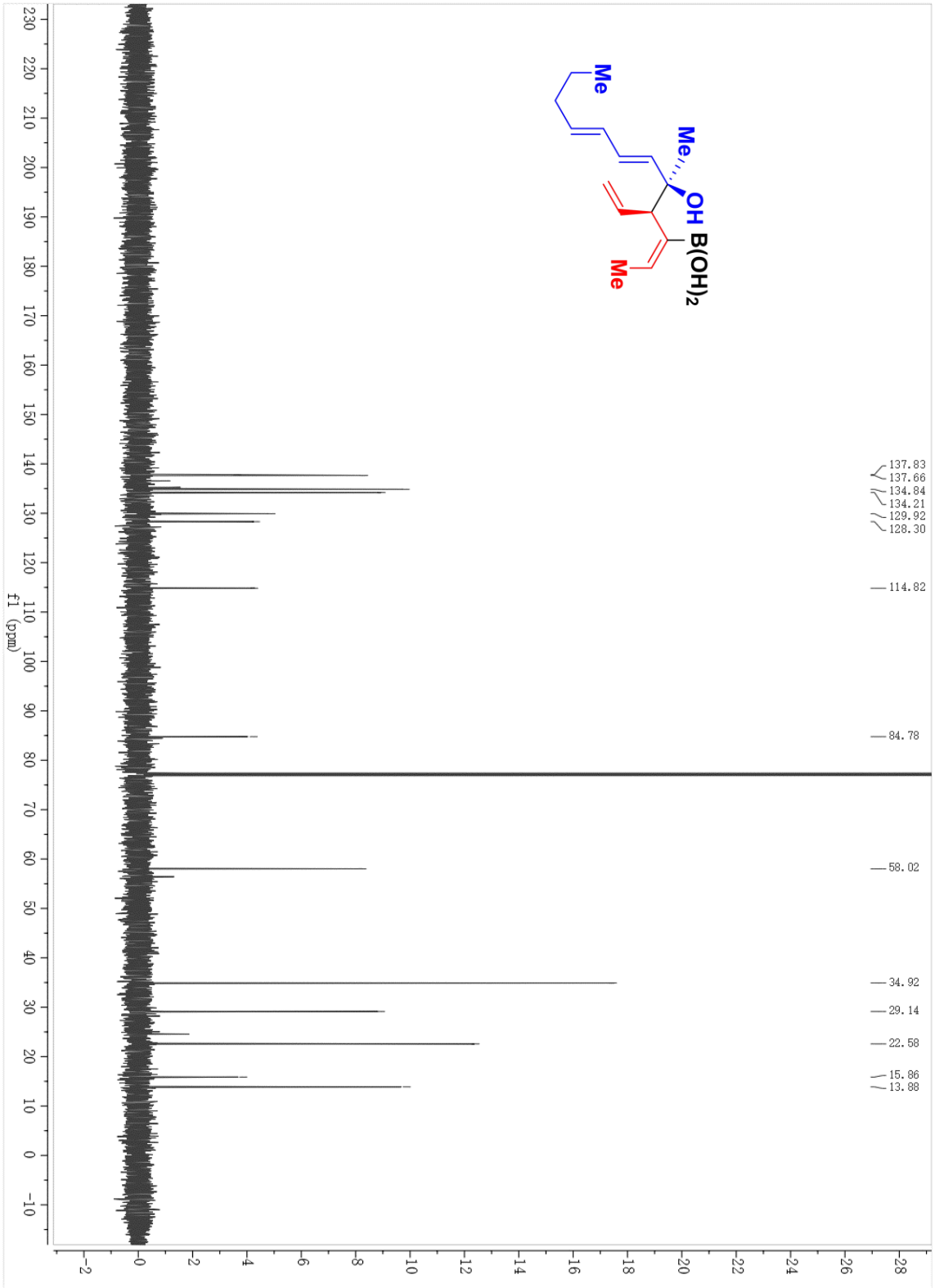

Me
Me
OH B(OH)2
Me
f1 (ppm)

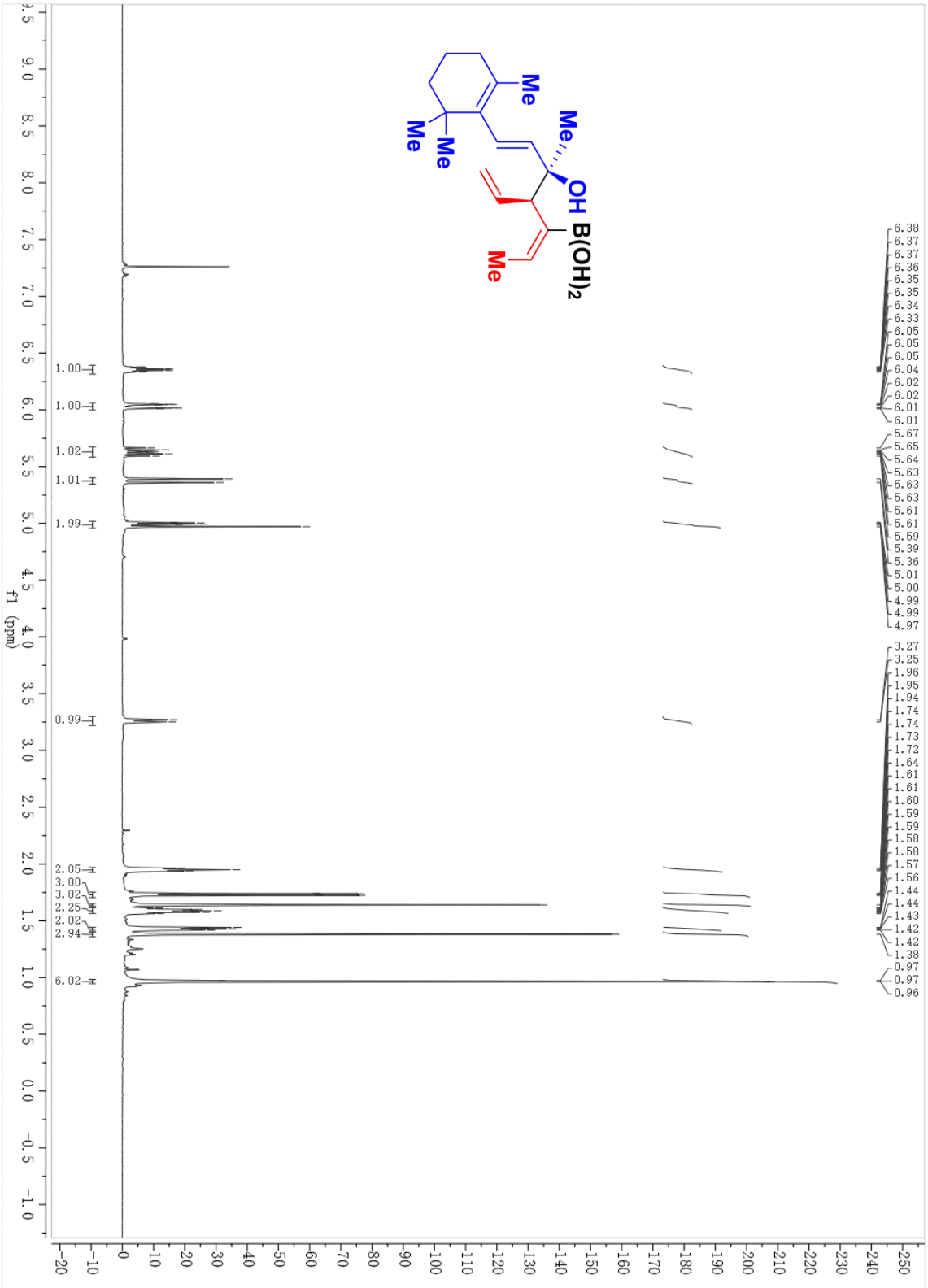

Me
Me
OH
B(OH)2
Me
140.43
140.24
140.22
135.61
131.51
117.08
87.32
60.32
34.85
33.95
31.59
31.42
25.13
18.33
16.70
f1 (ppm)

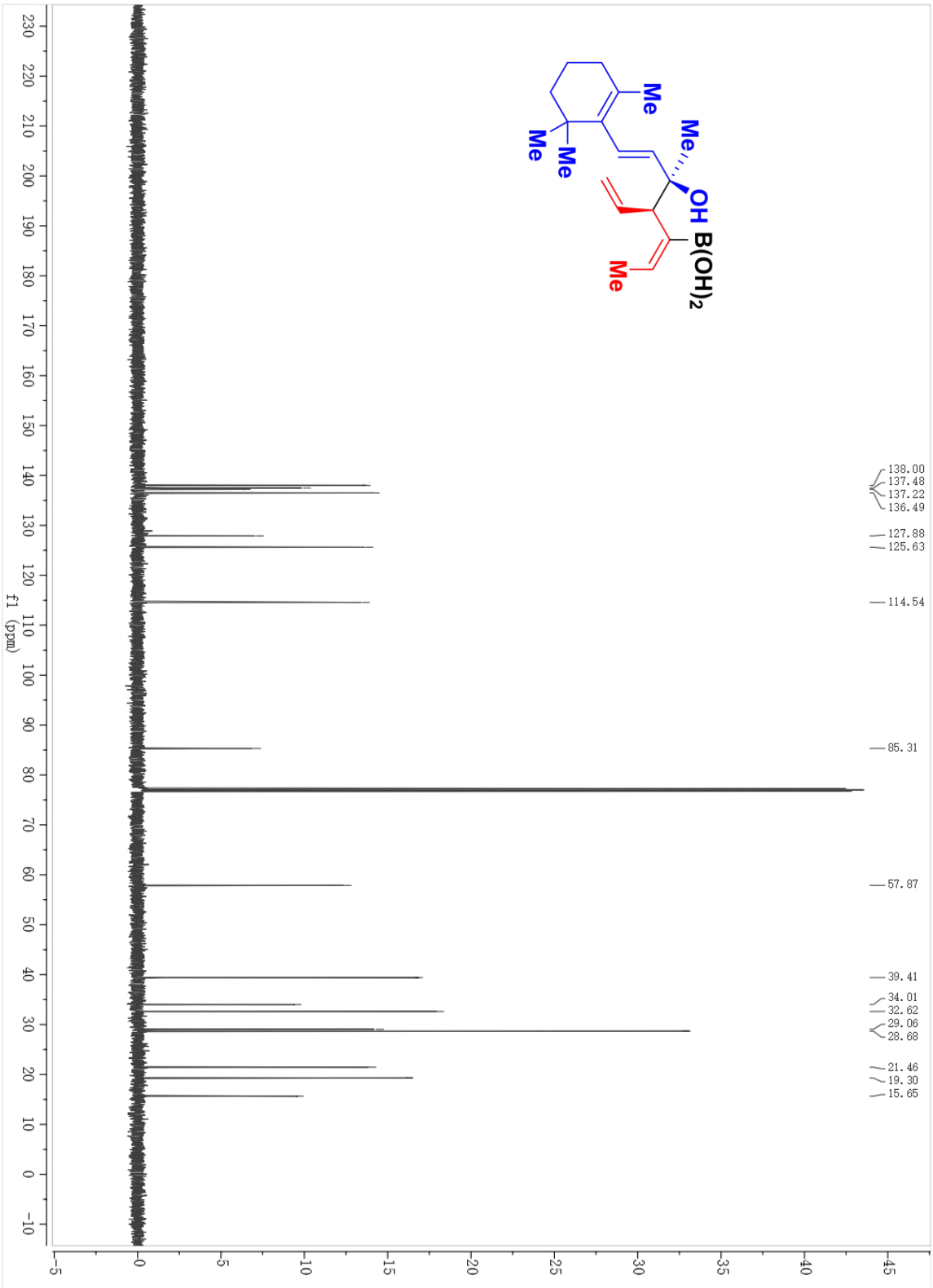

Ph
Me
OH B(OH)2
Me
f1 (ppm)
2.47
2.50
1.26
1.00
0.20
1.07
0.21
1.00
0.19
1.01
0.36
2.10
0.18
1.03
3.08
0.60
3.07
0.53

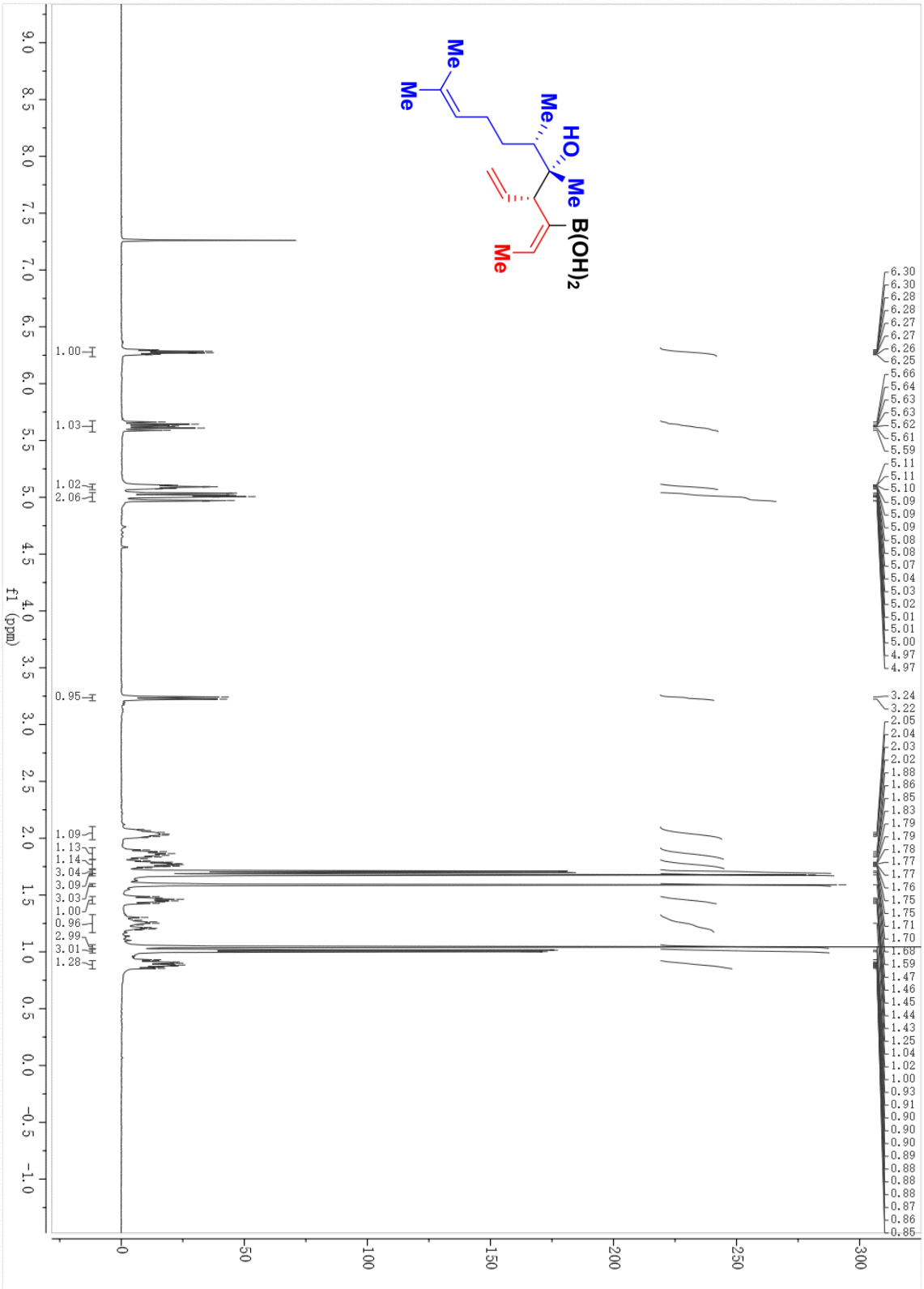

Ph
Me
OH
B(OH)2
Me
138.14
137.53
137.25
136.47
133.43
128.65
127.45
127.38
126.61
114.99
84.97
58.08
29.33
15.88
f1 (ppm)

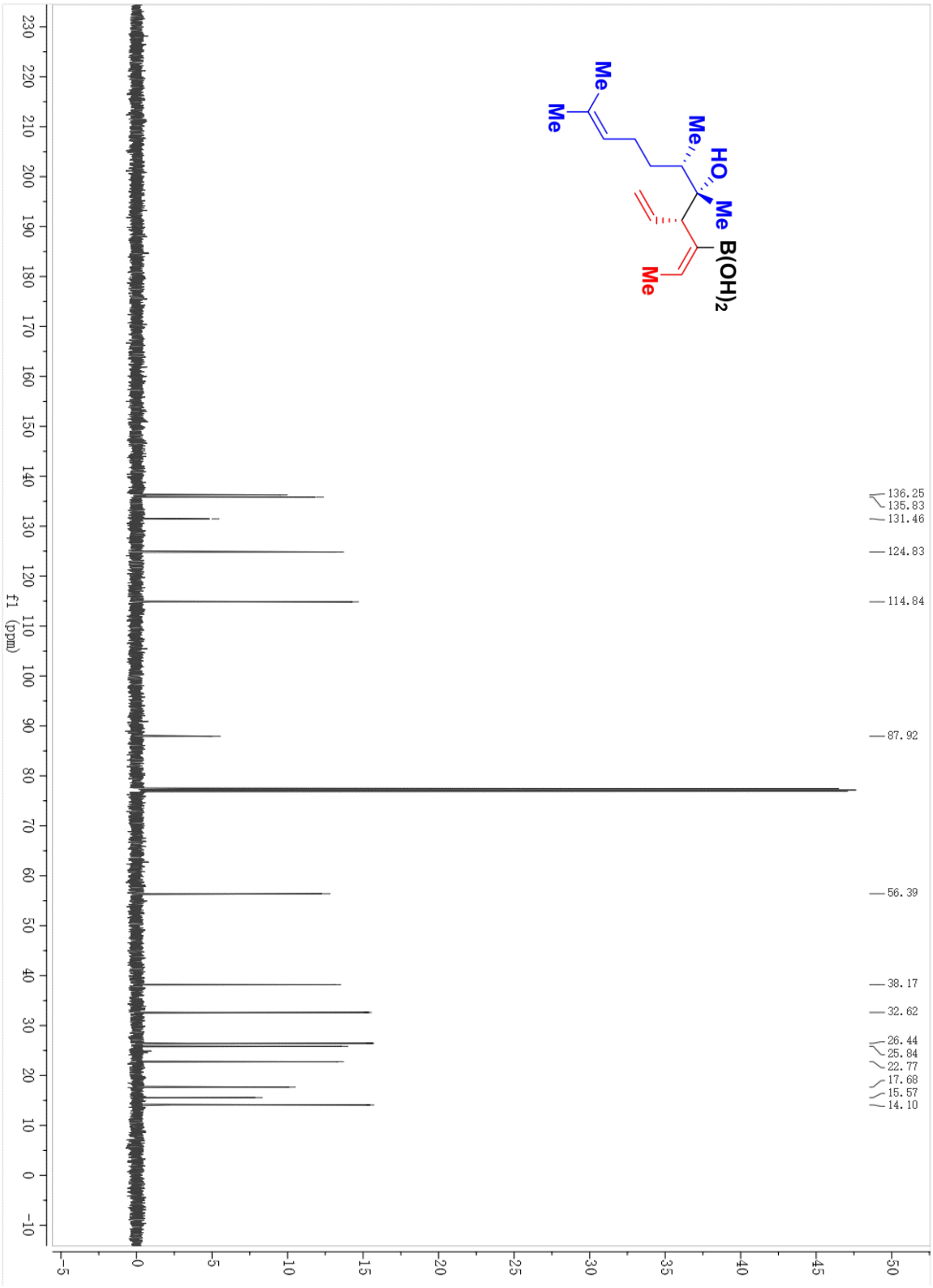

Me
Me
OH
B(OH)2
Me
f1 (ppm)


Me
Me
OH
B(OH)2
Me
137.83
137.66
134.84
134.21
129.92
128.30
114.82
84.78
58.02
34.92
29.14
22.58
15.86
13.88
f1 (ppm)


Me
Me
Me
Me
OH
B(OH)2
Me
f1 (ppm)
1.00
1.00
1.02
1.01
1.99
0.99
2.05
3.00
3.02
2.25
2.02
2.94
6.02


Me
Me
Me
Me
OH
B(OH)2
Me
138.00
137.48
137.22
136.49
127.88
125.63
114.54
85.31
57.87
39.41
34.01
32.62
29.06
28.68
21.46
19.30
15.65
f1 (ppm)


Me
Me
Me
HO
Me
B(OH)2
Me
f1 (ppm)
1.00
1.03
1.02
2.06
0.95
1.09
1.13
1.14
3.04
3.09
3.03
1.00
0.96
2.99
3.01
1.28


Me
Me
Me
HO
Me
B(OH)2
Me
136.25
135.83
131.46
124.83
114.84
87.92
56.39
38.17
32.62
26.44
25.84
22.77
17.68
15.57
14.10
f1 (ppm)