Synthesis of Trisubstituted α,β-Unsaturated Esters through Catalytic Stereoretentive Cross-Metathesis

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Synthesis of Trisubstituted α,β-Unsaturated Esters through Catalytic Stereoretentive Cross-Metathesis

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Abstract

We have devised a broadly applicable catalytic cross-metathesis method for stereoretentive synthesis of *Z*- and *E*-trisubstituted α,β-unsaturated esters. Several new Mo-bisaryloxide complexes were prepared, and they showed superior efficiency in synthesizing the *Z*-trisubstituted enoates (vs. corresponding mono-aryloxide pyrrolide complexes). Synthetic utility of the method was demonstrated through several concise syntheses of bioactive triterpenoids and value-added derivatives of prenyl-containing compounds such as citronellal, citronellol, and geraniol, all of which are isolated from essential oils. This transformation offers a valuable alternative to carbonyl olefination approaches such as Wittig and Horner-Wadsworth-Emmons reactions.

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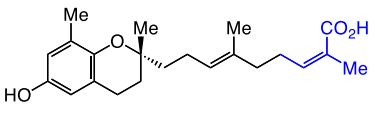
1.0 CHAPTER 1

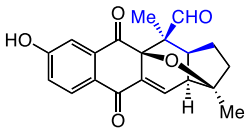
1.1 INTRODUCTION

Trisubstituted α,β-unsaturated carboxylic acids and esters are prevalent in natural products and bioactive molecules (Scheme 1.1.1). Compared to disubstituted enoates, one merit of trisubstituted analogs is their ability to form α-quaternary carbon centers[1,2]. Moreover, derivatizations such as dihydroxylation[3] and sigmatropic rearrangement[4] can lead to various synthetically useful building blocks (Scheme 1.1.2).

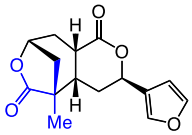
Scheme 1.1.1. Occurence of Trisubstituted Enoates in Natural Products and Bioactive Compounds



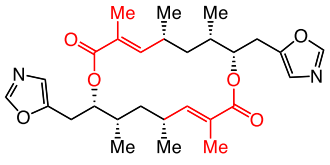
Polycerasoidol
PPAR agonist and anti-inflammatory



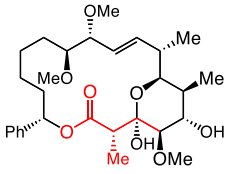
Pinnatal
potent antimalarial



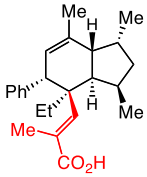
Deoxycollybolidol
Isolated from *collybia peronata*



Conglobatin
Hsp90-inhibitory, anti-leukemia



Soraphen A
ACC-inhibitory, anti-HIV-1



Plakotenin
cytotoxic against human
epidermoid carcinoma KB cell

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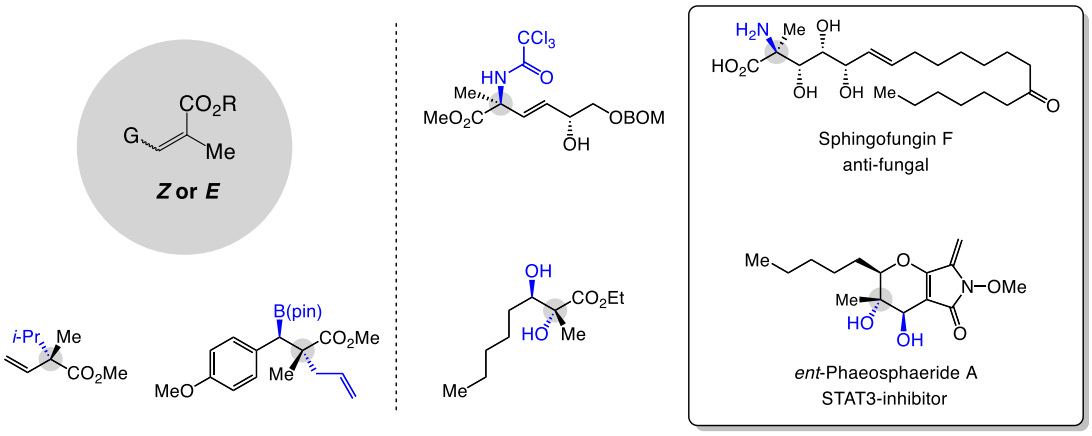
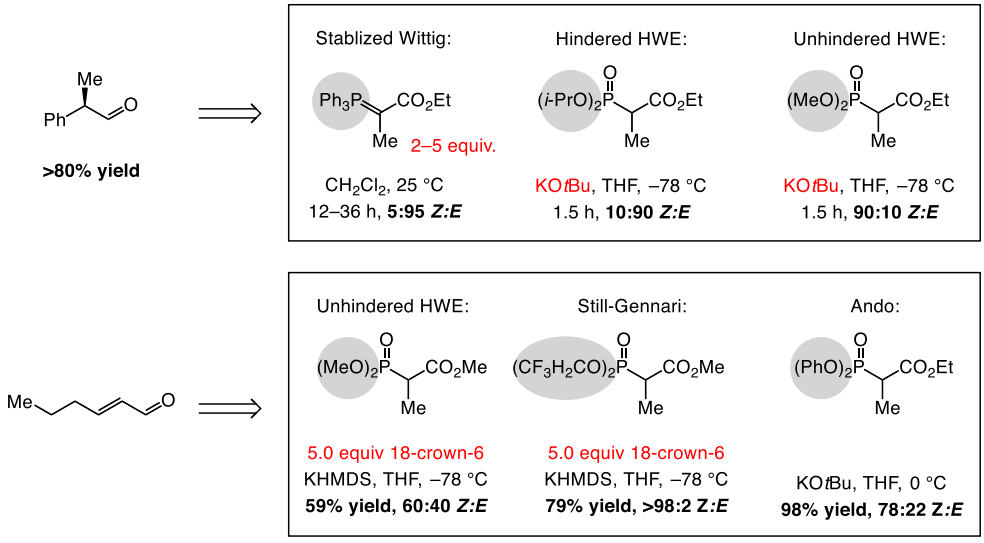
(1) (a) Murphy, K. E.; Hoveyda, A. H. *Org. Lett.* **2005**, *7*, 1255–1258. (b) Lee, Y; Hoveyda, A. H. *J. Am. Chem. Soc.* **2006**, *128*, 15604–15605.
(2) Zuo, Y.-J. *et al. Org. Biomol. Chem.*, **2018**, *16*, 9237–9242.
(3) Kobayashi, K. *et al. J. Org. Chem.* **2015**, *80*, 1243–1248.
(4) Tsuzaki, S. *et al. Org. Lett.* **2015**, *17*, 1704–1707.

Scheme 1.1.2. Trisubstituted Enoates as Useful Building Blocks in Organic Synthesis



A well-established method to synthesize trisubstituted enoates is through carbonyl olefination reactions. Such transformations, however, often require stoichiometric or excess amounts of costly reagents, harsh reaction conditions, and the *Z*:*E* ratio of the products is highly substrate-dependent[5] (Scheme 1.1.3). A case in point is the multi-step sequence in the total synthesis of transtaganolide B that converts diene **1.1** to methyl enoate **1.2**[6] (Scheme 1.1.4). The aldehyde intermediate was obtained by oxidative

Scheme 1.1.3. Synthesizing Trisubstituted Enoates through Carbonyl Olefination Reactions

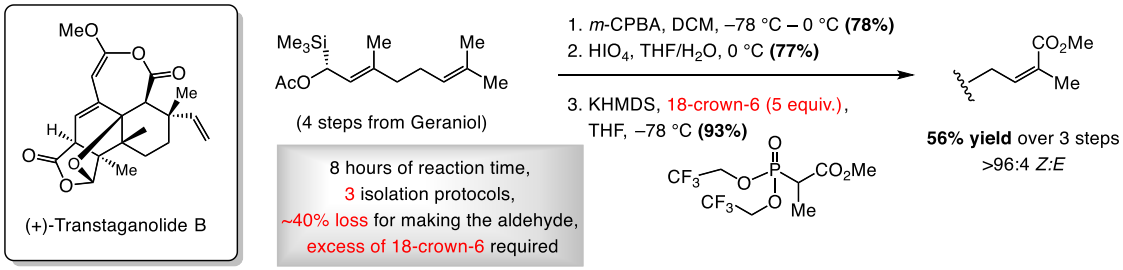


(5) (a) Still, W.C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405–4408. (b) Ando, K. *J. Org. Chem.* **1998**, *63*, 8411–8416.

(6) Nelson, H. M.; Gordon, J. R.; Virgil, S. C.; Stoltz, B. M. *Angew. Chem. Int. Ed.* **2013**, *52*, 6699–6703.

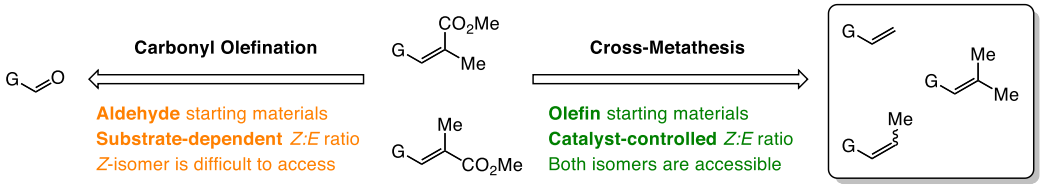
cleavage of the prenyl terminus in **1.1**, resulting in 40% loss of material. The subsequent Still-Gennari reaction requires excess amount of toxic 18-crown-6 and cryogenic conditions to ensure high *Z* selectivity and efficiency to yield the methyl enoate.

Scheme 1.1.4. An Example of The Olefin–Aldehyde–Olefin Sequence



In this regard, the development of a kinetically controlled catalytic cross-metathesis (CM) method that can provide access to stereodefined trisubstituted enoates, especially the higher-energy *Z*-isomer, is of high importance. This transformation would offer a valuable disconnection complementary to Wittig-type reactions, allowing for the direct implementation of an ester functional group, thus avoiding the intermediary of an aldehyde altogether. (Scheme 1.1.5).

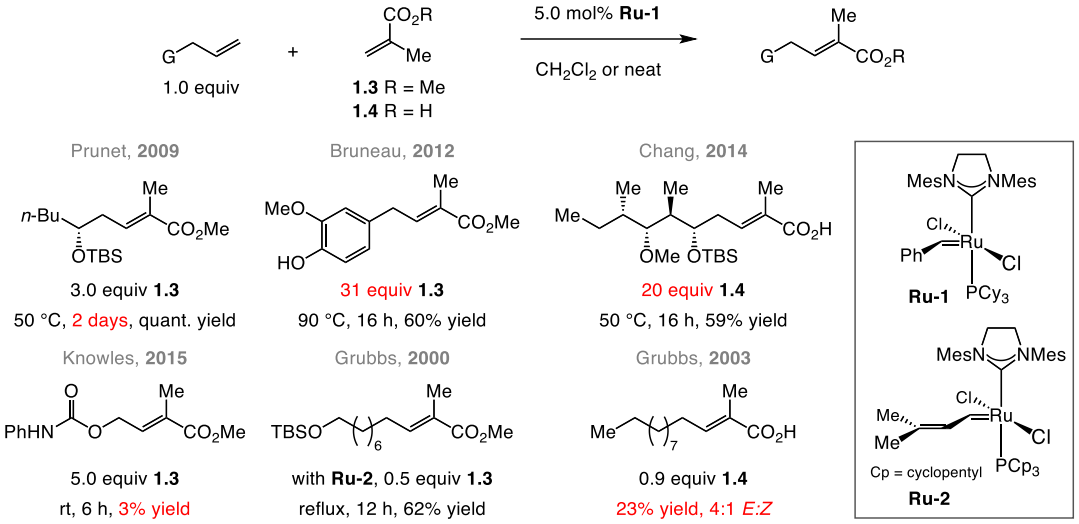
Scheme 1.1.5 Comparisons of Cabonyl Olefination and Cross-Metathesis



1.2 DESIGN PRINCIPLES FOR STEREORETENTIVE CROSS-METATHESIS OF TRISUBSTITUTED ENOATES

Although disubstituted enoic acids and esters have been successfully prepared through catalytic CM[7], the synthesis of trisubstituted variants still poses significant challenges. To date, there are only few reports on the synthesis of such moieties with Ru-based complexes, and only the *E*-isomers are accessible (Scheme 1.2.1)[8].

Scheme 1.2.1. State-of-the-Art in CM Towards Trisubtituted Enoic Acids and Esters

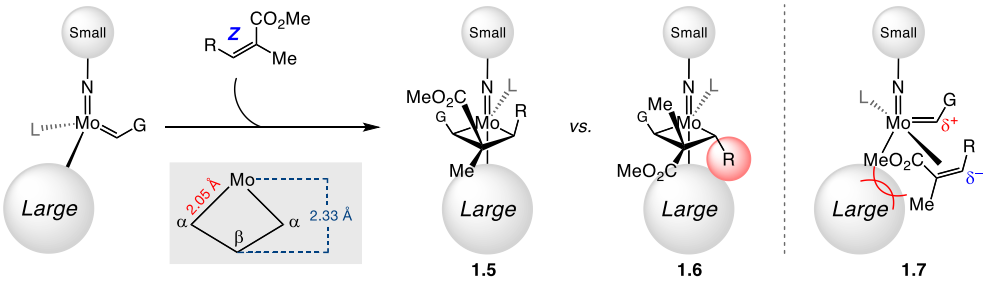


(7) (a) Chatterjee, A. K.; Morgan, J. P.; Scholl, M.; Grubbs, R. H. *J. Am. Chem. Soc.* **2000**, *122*, 3783−3784. (b) Choi, T.-L.; Lee, C. W.; Chatterjee, A. K.; Grubbs, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 10417−10418. (c) Yu, E. C. *et al. Angew. Chem. Int. Ed.* **2016**, *55*, 13210–13214. (d) Liu, Z.; Xu, C.; del Pozo, J.; Torker, S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2019**, *141*, 7137−7146.

(8) (a) Ref. 7a. (b) Chatterjee, A. K.; Choi, T. L.; Sanders, D. P.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 11360–11370. (c) Aouzal, R.; Prunet, J. *Org. Biomol. Chem.* **2009**, *7*, 3594–3598. (d) Bilel, H.; Hamdi, N.; Zagrouba, F.; Fischmeister, C.; Bruneau, C. *RSC Adv.* **2012**, *2*, 9584–9589. (e) Liu, H. M.; Chang, C. Y.; Lai, Y. C.; Yang, M. D.; Chang, C. Y. *Tetrahedron*: *Asymmetry* **2014**, *25*, 187–192. (b) Tarantino, K. T.; Miller, D. C.; Callon, T. A.; Knowles, R. R. *J. Am. Chem. Soc.* **2015**, *137*, 6440–6443.

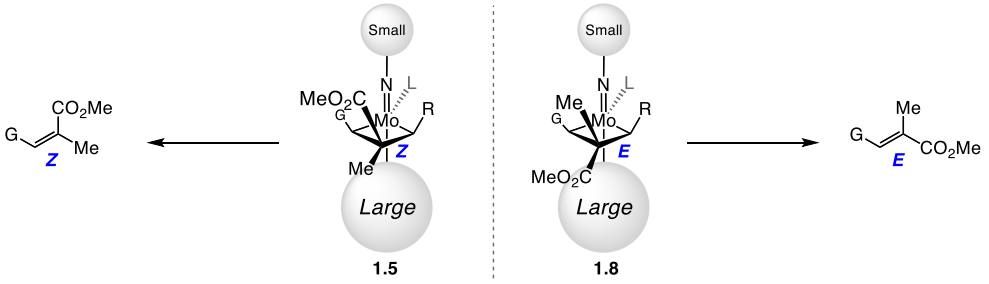
We consider addressing these shortcomings through a Molybdenum-alkylidene-catalyzed, kinetically controlled stereoretentive CM[9], a powerful method that can furnish both *Z*- and *E*-olefins in high isomeric purity. The stereochemical model for the stereoselectivity of trisubstituted olefin metathesis emerges from analysis of the X-ray structure of an unsubstituted molybdacyclobutane[10]: As the Cα of the metallacyclobutane is closer to the Mo-center than Cβ (2.05 vs. 2.33 Å, boxed structure in Scheme 1.2.2), we

Scheme 1.2.2. Design Principle of Stereoselective CM with Trisubstituted Olefins



surmised that the steric repulsion for substituents at the Cα is likely more severe, positioned away from the larger aryloxide ligand to ensure stereoselectivity (**1.5** vs. **1.6**, Scheme 1.2.2). Furthermore, competing **1.7** is destabilized (albeit electronically favored) due to the steric interactions with the closer Cα position in the forming mcb. Since the steric effect at Cβ becomes less consequential, the configuration of the alkene is retained in the CM product (**1.5** and **1.8**, Scheme 1.2.3).

Scheme 1.2.3. Design Principle of Stereoretentive CM

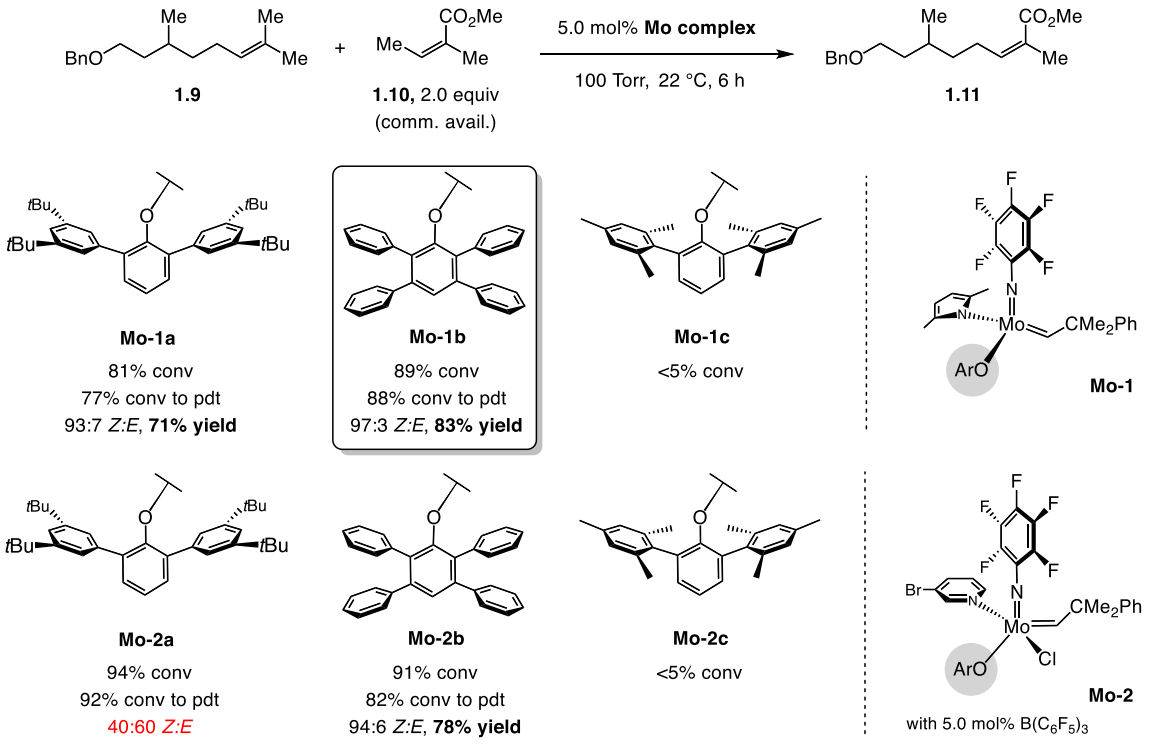


(9) Montgomery, T. P.; Ahmed, T. S.; Grubbs, R. H. *Angew. Chem. Int. Ed.* **2017**, *56*, 11024–11036.
(10) Marinescu, S. C.; Schrock, R. R.; Müller, P.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 10840–10841.

1.3 IDENTIFICATION OF AN OPTIMAL COMPLEX FOR *Z*-SELECTIVE CROSS-METATHESIS

We began by probing the reaction between two trisubstituted olefins in order to diminish the competitive homocoupling pathway[11] as well as methylidene formation, which benefits catalyst longevity[12]. As illustrated in Scheme 1.3.1, reaction between citronellic benzyl ether **1.9** and commercially available methyl angelate **1.10** in the presence of 5.0 mol % **Mo-1a** afforded the desired CM product **1.11** in 71% yield and 93:7 *Z*:*E* ratio. Mild vacuum (100 Torr) was employed to remove 2-methyl-2-butene byproduct and to

Scheme 1.3.1. Identification of an Effective Catalyst

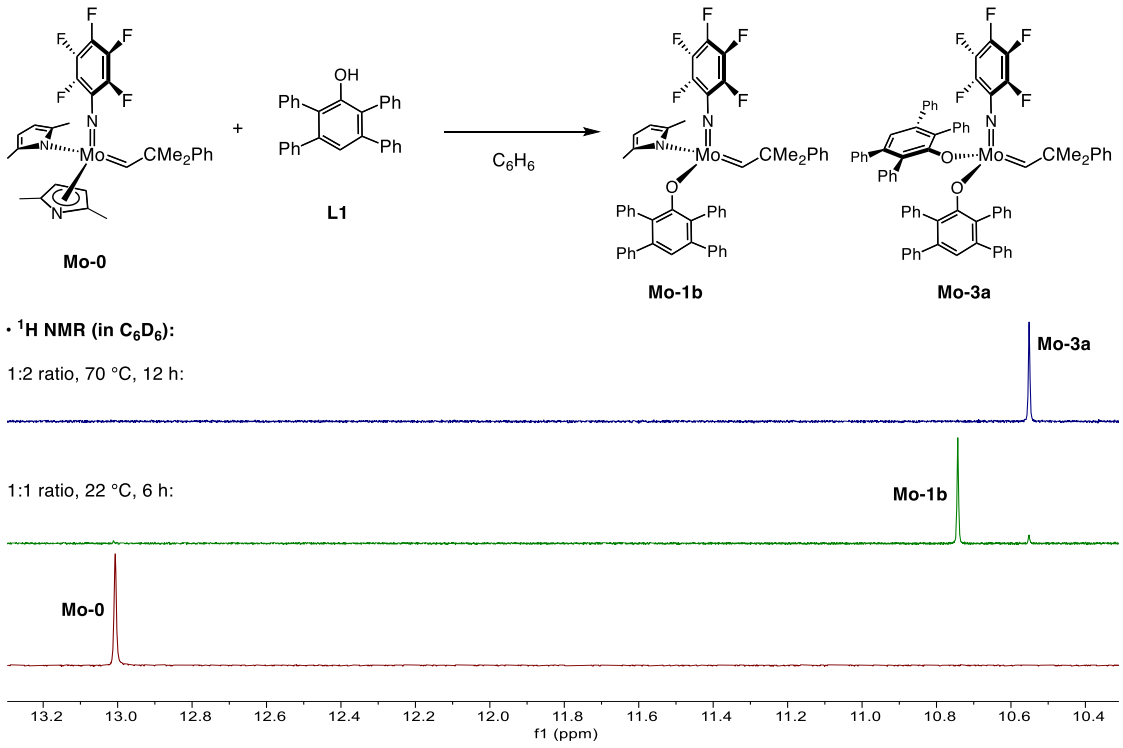


(11) Liu, Q.; Mu, Y.; Koengeter, T.; Schrock, R. R.; Hoveyda, A. H. *manuscript submitted*.

(12) For discussions on decomposition pathways of a methylidene complex, see: Hoveyda, A. H.; Liu, Z.; Qin, C.; Koengeter, T.; Mu, Y. *Angew. Chem. Int. Ed.* **2020**, *59*, 22324–22348.

ensure maximum efficiency. Optimal yield of **1.11** and further improvement in *Z* selectivity were achieved with **Mo-1b** (83% yield, 97:3 *Z*:*E*). The highly reactive but comparatively short-lived Molybdenum monoaryloxide chloride (MAC) complexes[13], however, led to either diminished *Z* selectivity (**Mo-2a**) or lower conversion (**Mo-2b–c**). An unexpected alkylidene NMR signal was observed during the preparation of MAP complex **Mo-1b** (Scheme 1.3.2). Further investigation led to the discovery of a new bisaryloxide complex **Mo-3a**; it may be formed by a second ligand exchange of residual phenol (**L1**) with in-situ generated MAP complex (**Mo-1b**). With 2.0 equivalents of **L1** added, bisaryloxide **Mo-3a** was formed exclusively after 12 hours at 70 °C.

Scheme 1.3.2. Analysis of The Molybdenum Bisaryloxide Formation



(13) (a) Lam, J. K. *et al. J. Am. Chem. Soc.* **2016**, *138*, 15774–15783. (b) Koh, M. *et al. Nature* **2017**, *542*, 80–85.

The 2,6-diisopropylphenyl imido variant of **Mo-3a** was prepared by Schrock et al. in 2014 through a different route[14], although in the homo-metathesis of 1-octene, it showed lower efficiency when compared to the corresponding monoaryloxide pyrrolide complex (13% vs. 67% conversion after 6 hours). In addition, several bisaryloxide complexes with sterically congested (*ortho*-F-substituted) or electron-deficient (2,6-perfluorophenyl) phenol ligands (essential for allowing for the aforementioned second ligand exchange to occur) have been reported and used to address lower reactivity and/or selectivity issues of the MAP complexes in ring-opening metathesis polymerization (ROMP) [15] and macrocyclic ring-closing metathesis (RCM) reactions[16].

Although computations by Eisenstein and co-workers[17] have shown that having two different ligands (one strong σ-donor and one weak σ-donor; such as in **Mo-1** and **Mo-2**) improves the overall performance of the olefin metathesis catalyst, we surmised that the bisaryloxide could be a superior catalyst here as methylidene decomposition pathways and post-metathesis isomerization are less of concerns[16]. Experimental data substantiated this hypothesis (Scheme 1.3.3): reaction with 5.0 mol % **Mo-3a** indeed further increased product formation (from 83% to 91% yield) without compromising selectivity (97:3 vs. 95:5 *Z*:*E*).

---

(14) Townsend E. M. *et al. Organometallics* **2014**, *33*, 5334−5341.

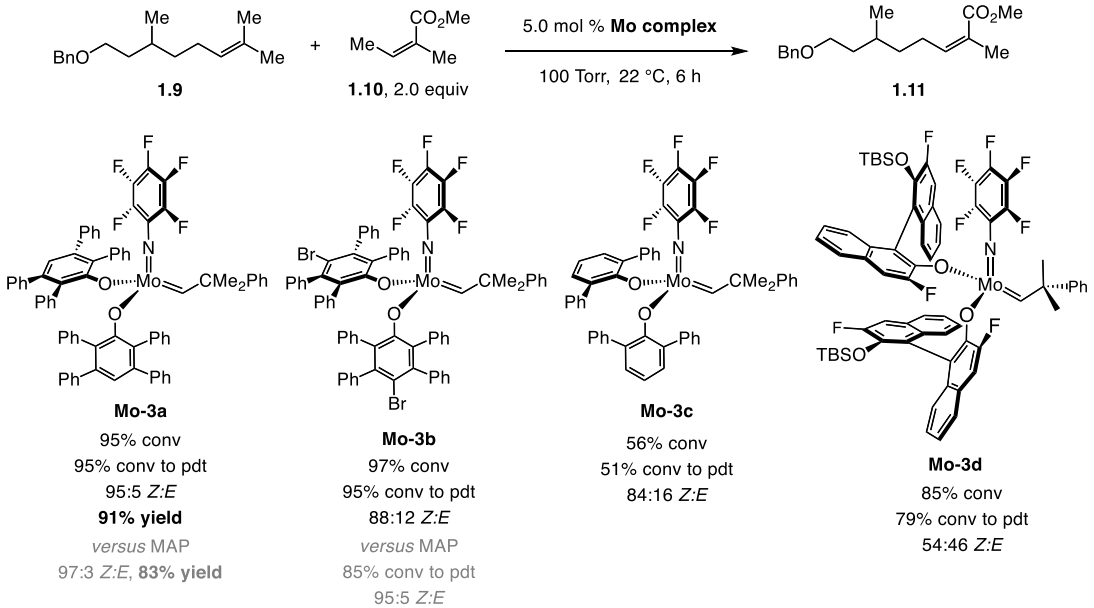
(15) (a) Yuan, J.; Schrock, R. R.; Müller, P.; Axtell, J. C.; Dobereiner, G. E. *Organometallics* **2012**, *31*, 4650–4653. (b) Yuan, J., Schrock, R. R.; Gerber, L. C.; Müller, P.; Smith, S. *Organometallics* **2013**, *32*, 2983–2992.

(16) (a) Wang, C.; Haeffner, F.; Schrock, R. R.; & Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2013**, *52*, 1939–1943. (b) Yu, M.; Schrock, R. R.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2015**, *54*, 215–220.

(17) (a) Solans-Monfort, X.; Clot, E.; Copéret, C.; Eisenstein, O. *J. Am. Chem. Soc.* **2005**, *127*, 14015–14025. (b) Poater, A.; Solans-Monfort, X.; Clot, E.; Copéret, C.; Eisenstein, O. *J. Am. Chem. Soc.* **2007**, *129*, 8207–8216.

Several other bisaryloxide complexes were prepared and subjected to the CM reaction. **Mo-3b** bearing a *para*-Br substituent on the phenoxide ligand proved to be more reactive but less stereoselective. **Mo-3c** is less stable, presumably due to a lack of rigidity, and only 56% of **1.9** was consumed after 6 hours. To our surprise, **Mo-3d**[16a], which was used for *Z*-selective macrocyclic RCM in the synthesis of epothilone D, furnished **1.11** in a 1:1 *Z*:*E* ratio and isomerized methyl enoate **1.10** from >98:2 to 72:28 *Z*:*E* after 6 hours. It became evident that unlike macrocyclic RCM reactions in which geometric constraints force the tethered enoate into the desired orientation through substrate control, in CM, selectivity is solely governed by the size difference of the two ligands occupying the apical positions of the trigonal bipyramidal (TBP) metallacyclobutane (mcb) intermediate, namely the aryl imido group and the aryloxide. Thus, controlling the kinetic selectivity becomes more challenging in CM reactions, and, in this case, a smaller *ortho*-fluorine substituent (vs. a bromide or a phenyl ring) eroded the steric bulkiness of the BINOL-derived phenoxide in **Mo-3d**, resulting in low stereo-control.

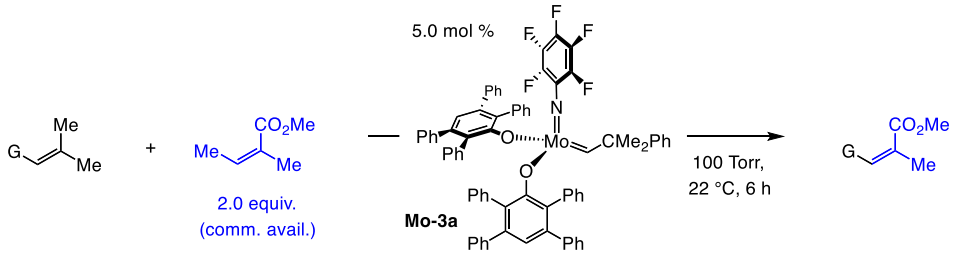
Scheme 1.3.3. CM Promoted by Mo Bisaryloxide Complexes

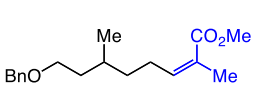


1.4 KINETICALLY CONTROLLED *Z*-SELECTIVE CROSS-METATHESIS TO ACCESS *Z*-ENOATES

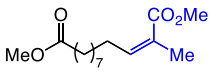
As shown in Scheme 1.4.1, many *n*-alkyl-*Z*-trisubstituted methyl enoates were obtained from naturally abundant or readily available alkyl-substituted *gem*-dimethyl alkenes. These include products bearing an allylic ether (**1.13**), a phthalimide (**1.14**), a B(pin) group (pin, pinacolato; **1.16**), an indole (**1.17**), an acetal (**1.18**), a Boc-protected proline (Boc, *tert*-butoxy carbonyl; **1.19**), a β-aryl-substituted alkene (**1.20**), a tertiary amine

Scheme 1.4.1. Synthesis of *Z*-Enoic Acid Methyl Esters through *Z*-Selective CM

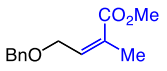




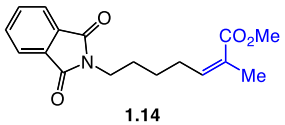
1.11
95% conv, 95:5 *Z*:*E*
91% yield (85% for pure *Z*)



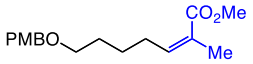
1.12
81% conv, 96:4 *Z*:*E*
82% yield



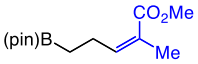
1.13
82% conv, >98:2 *Z*:*E*
79% yield



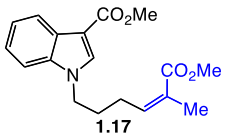
1.14
79% conv, 96:4 *Z*:*E*
77% yield



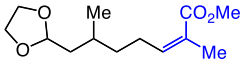
1.15
94% conv, 94:6 *Z*:*E*
87% yield (pure *Z*)



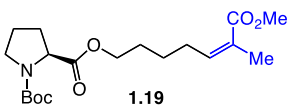
1.16
93% conv, 94:6 *Z*:*E*
72% yield



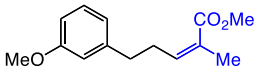
1.17
87% conv, 98:2 *Z*:*E*
81% yield



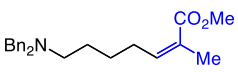
1.18
97% conv, 97:3 *Z*:*E*
91% yield



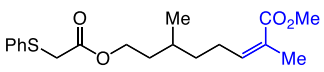
1.19
43% conv, 32% conv to pdt
97:3 *Z*:*E*
with 10 mol % *Z*-3-hexene
89% conv, 97:3 *Z*:*E*
85% yield



1.20
48% conv, 36% conv to pdt
Z:*E* n.d.
with 10 mol % *Z*-3-hexene
69% conv, >98:2 *Z*:*E*
65% yield



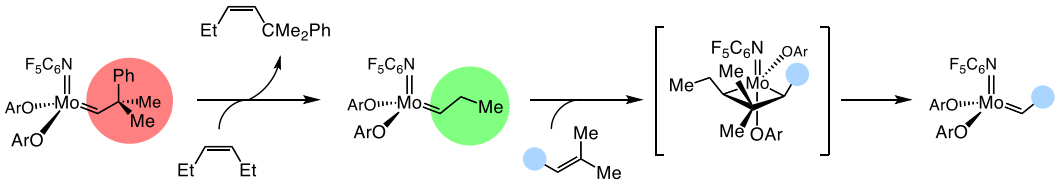
1.21
50% conv, 50% conv to pdt
95:5 *Z*:*E*
with 10 mol % *Z*-3-hexene
89% conv, 96:4 *Z*:*E*
85% yield



1.22
59% conv, 53% conv to pdt
97:3 *Z*:*E*
with 10 mol % *Z*-3-hexene
89% conv, 98:2 *Z*:*E*
86% yield (pure *Z*)

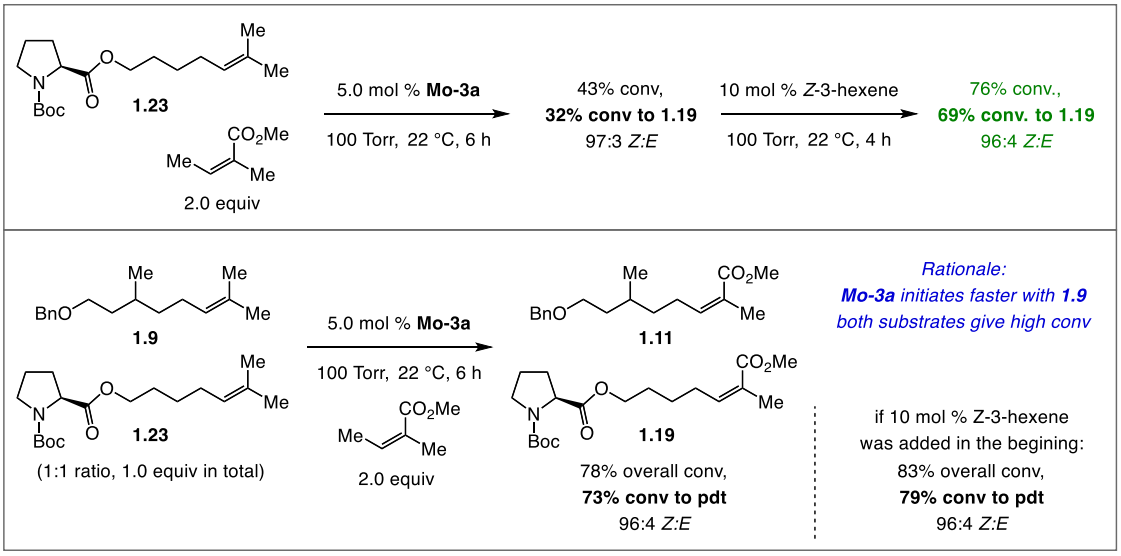
(**1.21**), or a thiol ether (**1.22**). A catalytic amount of *Z*-3-hexene was added whenever initiation of the Mo neophylidene complex was sluggish (i.e., required a long induction period; Scheme 1.4.2) to improve the reaction efficiency[11] (**1.19**–**1.22**).

Scheme 1.4.2. Alkene-Assisted Initiation Promotes CM Between Two Trisubstituted Olefins



The concept of facilitating catalyst initiation proved successful. Addition of 10 mol % *Z*-3-hexene to the reaction of **1.23** after 6 hours (Scheme 1.4.3) resulted in an increase of product formation from 32% to 69%, indicating that a majority of **Mo-3a** remained inert until *Z*-3-hexene was added. In another example, **1.9** and **1.23** were mixed in a 1:1 ratio and subjected to standard reaction conditions. Both CM products **1.11** and **1.19** were formed, and addition of 10 mol % *Z*-3-hexene in the beginning did not drastically change the conversion (73% vs. 79% conversion to products). This is probably because in the first catalytic cycle, most of **Mo-3a** was initiated by the more reactive substrate **1.9**, and

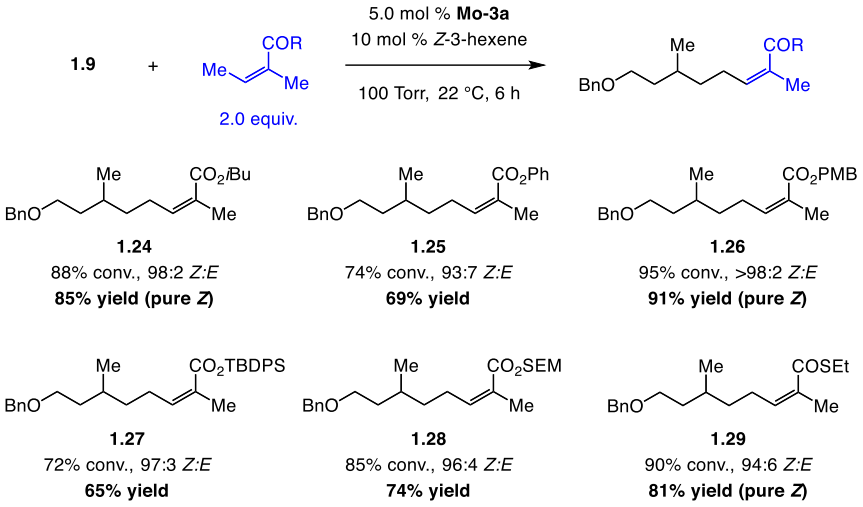
Scheme 1.4.3. Further Proof-of-Principle



subsequent CM with **1.23** generated an ethylidene complex, reacting with both of the remaining substrates. The overall outcome is the same: to provide a less hindered and thus more active alkylidene species (either methyl- or ethyl substituted alkylidene).

We then investigated different carboxylic acid derivatives to extend the scope of this method (Scheme 1.4.4). Neither steric bulkiness nor electronic bias impacted the reaction efficiency. Silyl-containing esters (**1.27** and **1.28**) are amenable to standard conditions, which are known to hydrolyze easily. Phenyl ester (**1.25**) and ethyl thiol ester (**1.29**), precursors to ketones and aldehydes, were also successfully synthesized.

Scheme 1.4.4. *Z*-Selective CM with different Carboxylic Acid Derivatives

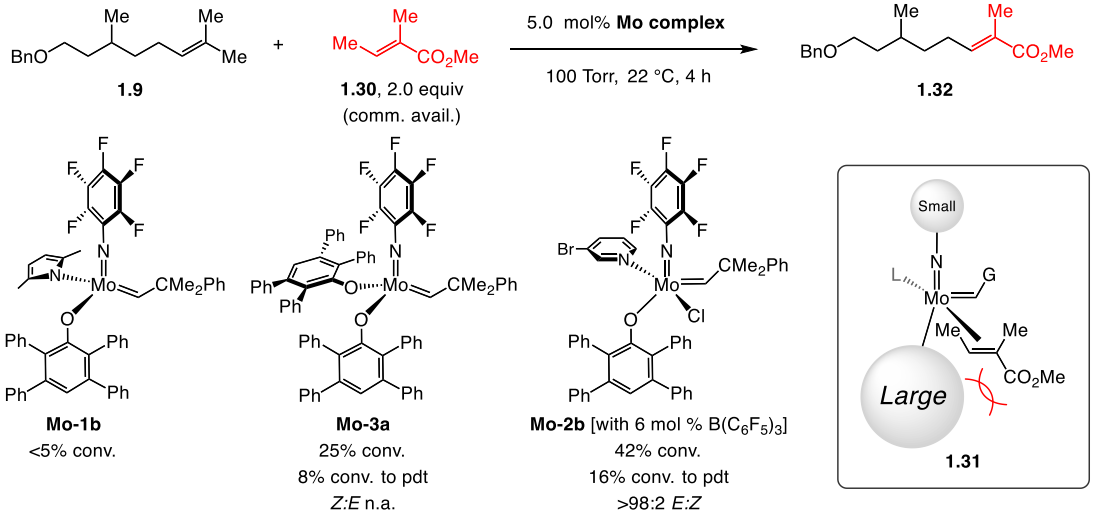


1.5 KINETICALLY CONTROLLED *E*-SELECTIVE CROSS-METATHESIS TO ACCESS *E*-ENOATES

In contrast to what we had predicted in Scheme 1.2.3, CM between **1.9** and the *E*-enoate **1.30** resulted in minimal formation of **1.32** (Scheme 1.5.1). This could be attributed to the increased steric repulsion between the carboxyl group and the aryloxide ligand in **1.31**. Molybdenum MAC complex **Mo-2b**, bearing a smaller chloride ligand, rather than 2,5-dimethyl pyrrolide in **Mo-1b** or aryloxide in **Mo-3a**, indeed promoted the reaction to afford 16% of the desired product with complete stereoretention ($B(C_6F_5)_3$ was added to scavenge the pyridyl ligand; Scheme 1.5.1). Following the same trend, **Mo-2a**, bearing a more spacious tetra-*tert*-butyl terphenyloxide ligand showed higher efficiency, furnishing **1.32** in 85% yield and 97:3 *E*:*Z* ratio (Scheme 1.5.2).

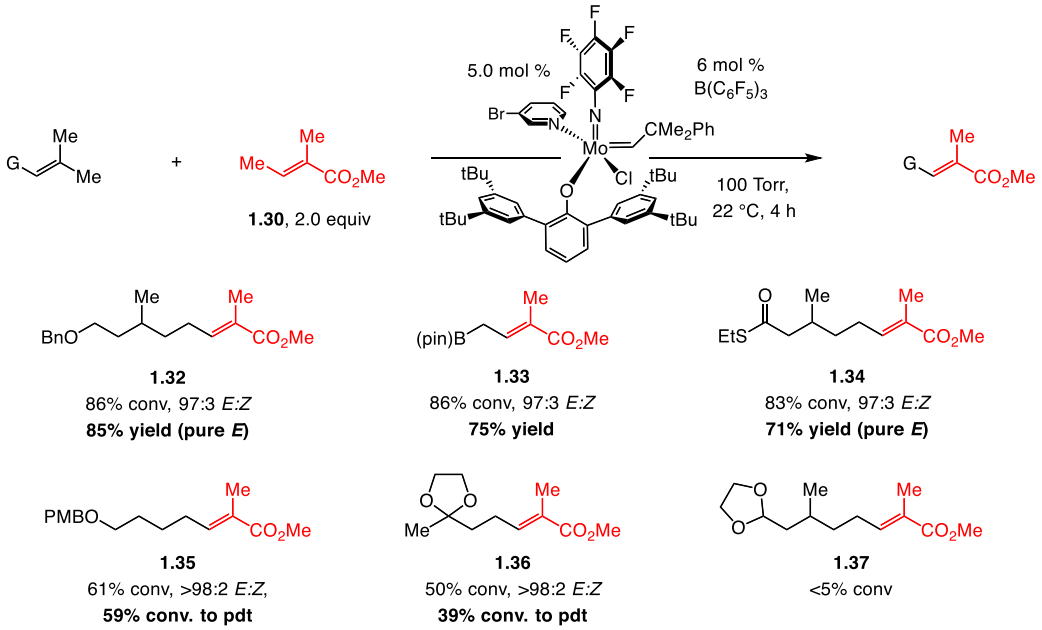
Substrates with an allylic B(pin) (**1.33**) or a thiol ester (**1.34**), functional groups that are not compatible with Wittig-type reaction conditions, showed appreciable yield and

Scheme 1.5.1. Identification of an Effective Catalyst for *E*-Enoates



selectivity. The method, however, owing to the use of a highly reactive and thus short-lived molybdenum chloride complex and a strong Lewis acid such as tris(pentafluorophenyl)borane, is not as broadly applicable as the *Z*-selective variant. Reaction with PMB ether (**1.35**) is less efficient (vs. **1.15**), and acid-sensitive acetals (**1.36** and **1.37**) only afforded minimal to no product formation.

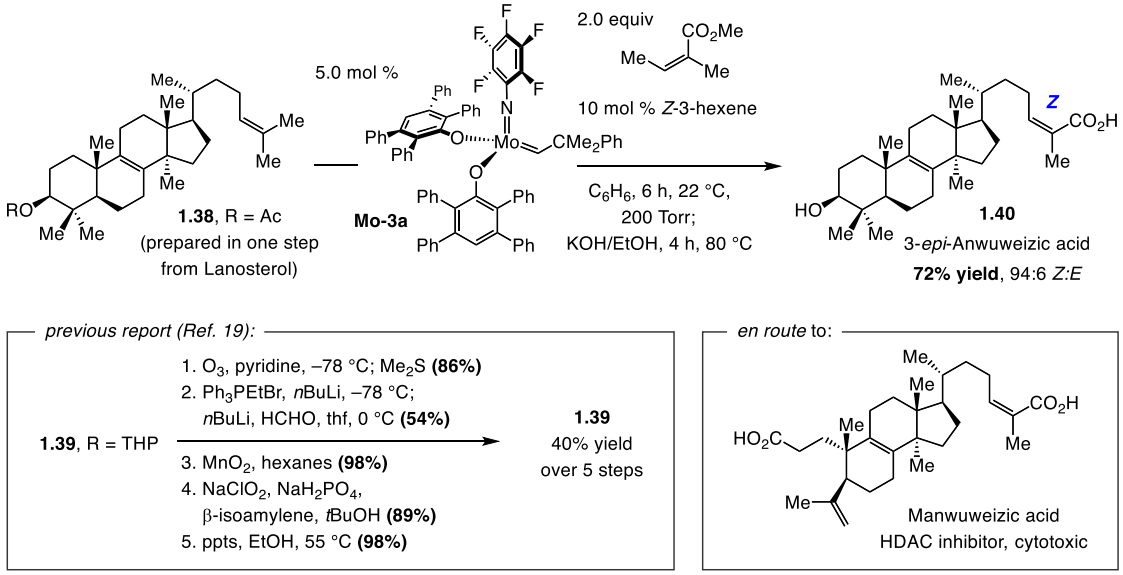
Scheme 1.5.2. Stereorentative Cross-Metathesis with *E*-Methyl Enoate



1.6 APPLICATION TO SYNTHESIS OF BIOACTIVE COMPOUNDS

Concise and stereorententive syntheses of bioactive triterpenoids were demonstrated (Scheme 1.6.1 and 1.6.2). Carboxylic acid **1.40**, a precursor to bioactive anwuweizonic acid and manwuweizic acid[18], was obtained through reaction of lanosterol acetate **1.38** and methyl angelate, followed by a one-pot hydrolysis, in 72% yield and 94:6 *Z*:*E* ratio. Compared to the previous method (from **1.39**, Scheme 1.6.1)[19], synthesizing **1.40** through CM circumvents preparation of the aldehyde intermediate through multi-step oxidations and tedious purifications (72% yield in one step vs. 40% yield over five steps). The corresponding *E*-isomer ganoderic acid Z **1.41**, a bioactive triterpenoid isolated from

Scheme 1.6.1. Formal Synthesis of Manwuweizic acid

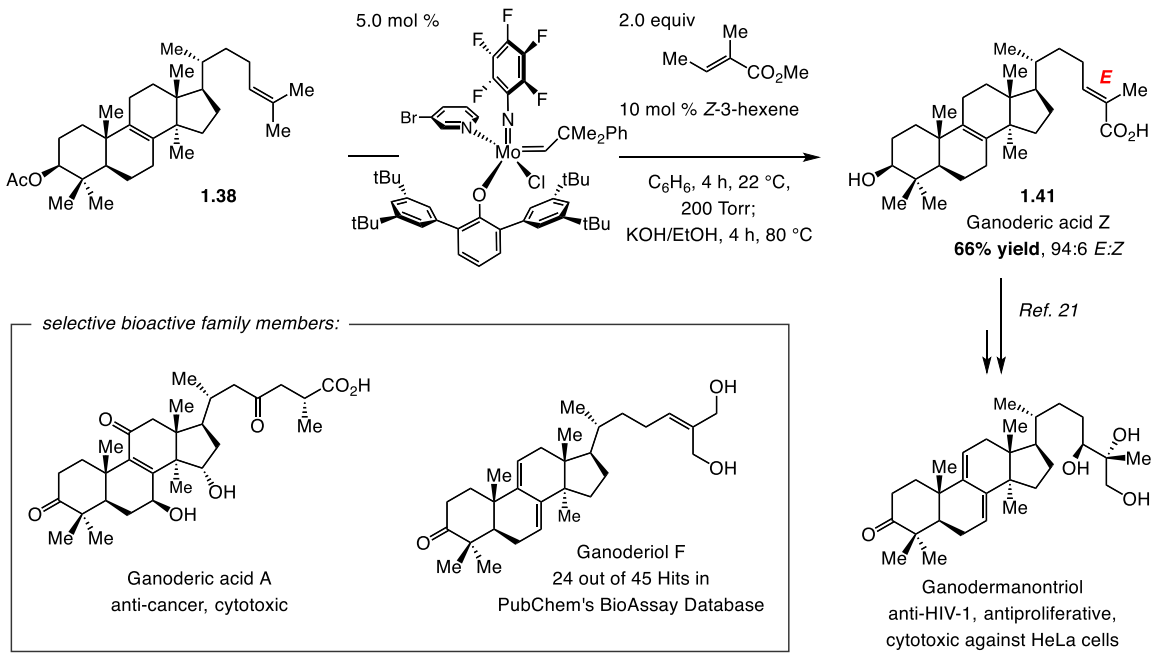


(18) Liu, J-S.; Huang, M-F.; Tao, Y. *Can. J. Chem.* **1988**, *66*, 414–415.
(19) Liu, J-S.; Tao, Y. *Tetrahedron* **1992**, 48, 6793–6798.

Ganoderma lucidum[20], was prepared by CM between **1.38** and methyl tiglate in 66% yield and 94:6 *E*:*Z* ratio (Scheme 1.6.2) and can be derived to ganodermanontriol by a reported procedure[21].

The present advance enables a direct functionalization of naturally occurring prenyl termini. As demonstrated in Scheme 1.6.3, enoate **1.18** was prepared from citronellal in 89% yield and 97:3 *Z*:*E*; synthesizing the *E*-isomer was unsuccessful due to functional group incompatibility. Citronellol furnished both *Z*- and *E*-isomer **1.42** and **1.43** over two steps, which are precursors to important food additives mintlactone and isomintlactone[22] and can be transformed to the bioactive compound menthofuran[23]. Diene **1.44**, an

Scheme 1.6.2. Synthesis of Ganoderic acid Z



(20) Toth, J. O.; Luu, B.; Ourisson, G. *Tetrahedron Lett.* **1983**, *24*, 1081–1084

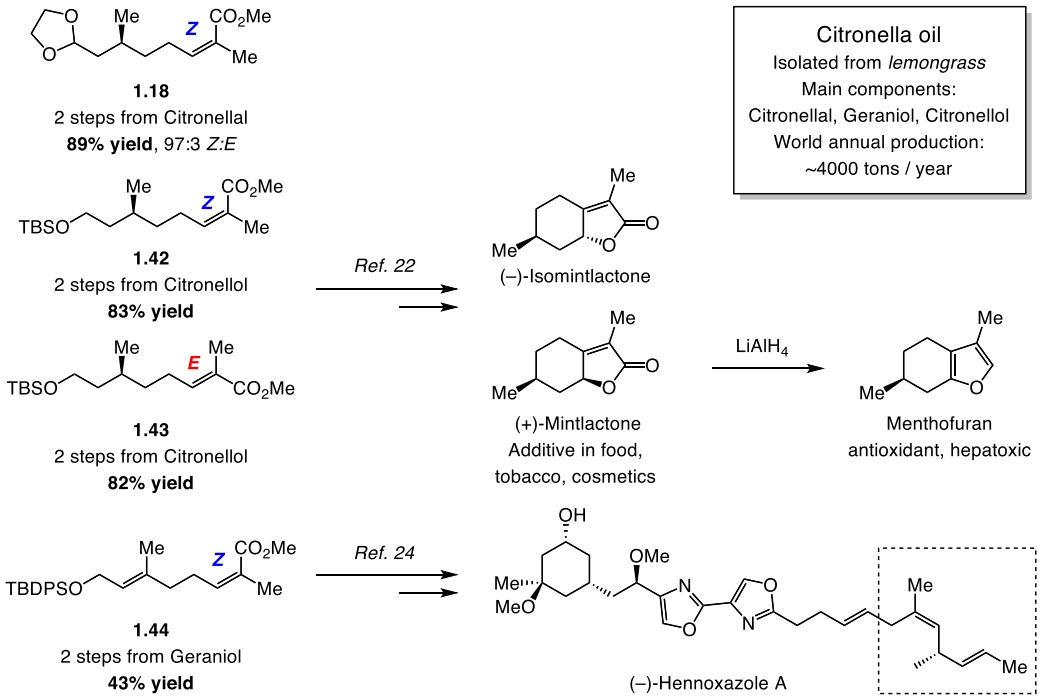
(21) (a) El-Mekkawy, S. *et al. Phytochemistry* **1998**, *49*, 1651–1657. (b) Kennedy, E. M.; P'Pool, S. J.; Jiang, J.; Sliva, D.; Minto, R. E. *J. Nat. Prod.* **2011**, *74*, 2332–2337.

(22) Wang, X. et al. *Synlett* **2017**, *28*, 1660–1662.

(23) Tsuboi, S.; Shimozuma, K.; Takeda, A. *J. Org. Chem.* **1980**, *45*, 1517–1520.

intermediate en route to hennoxazole A[24], was also successfully synthesized from geraniol. The low yield is due to competitive formation of the trisubstituted allylic silyl ether, generated by reaction of the internal trisubstituted double bond with methyl angelate.

Scheme 1.6.3. Exploiting Naturally Occurring Prenyl Termini



(24) Yokokawa, F.; Asano, T.; Shioiri, T. *Tetrahedron* **2001**, *59*, 6311–6327.

1.7 CONCLUSIONS

Trisubstituted enoates exist in various natural products and bioactive molecules and serve as an important scaffold in organic synthesis (Scheme 1.1.1 and 1.1.2). A common approach to this moiety is carbonyl olefination, typically a Horner-Wadsworth-Emmons reaction and *Z*-selective modifications (Scheme 1.1.3). However, these methods require stoichiometric amounts of toxic reagents and harsh reaction conditions. What is more, the use of an aldehyde, which is often obtained from an alkene through multi-step oxidation procedures, as intermediate is inevitable (Scheme 1.1.4) and can be problematic.

To address these issues, herein, we have devised a broadly applicable catalytic cross-metathesis procedure for the stereoretentive synthesis of trisubstituted methyl enoates (Scheme 1.4.1 and 1.5.2). Both *Z*- and *E*-isomers can be furnished from naturally abundant or readily available prenyl groups under mild conditions. In addition, we have prepared a new bisaryloxide complex **Mo-3a**, and it has shown superior efficiency (vs. MAP **Mo-2b**, Scheme 1.3.3) in synthesizing *Z*-trisubstituted enoates. The distinct reactivity of this complex could be attributed to decreased HOMO–LUMO gap in the alkene–alkylidene coordination and increased stability of the metallacyclobutane, resulting in a lower transition state energy[25].

We have demonstrated the synthetic utility of this method through concise syntheses of 3-*epi*-anwuweizic acid **1.40**, a precursor to anwuweizonic acid and manwuweizic acid (Scheme 1.6.1), and ganoderic acid Z **1.41** (Scheme 1.6.2). Compared to previously

(25) For related DFT computations, see Ref. 13b and 16a.

reported syntheses, the CM reactions are carried out under milder conditions and do not require a series of functional group manipulations (Scheme 1.1.4 and 1.6.1). Finally, citronellal, citronellol, and geraniol (main components in various essential oils) were utilized to furnish the corresponding methyl enoates, which serve as valuable building blocks in syntheses of several natural products (Scheme 1.6.3). The approach presented here offers a valuable disconnection that is complementary to Wittig-type reactions, and it enables the direct functionalization of naturally occurring prenyl termini to value-added enoic esters and acids.

1.8 EXPERIMENTAL SECTION

1.8.1 General

Unless otherwise noted, transformations were performed with distilled and degassed solvents under an atmosphere of dry N_2, in oven- (135 °C) or flame-dried glassware with standard glovebox or Schlenk techniques. Infrared (IR) spectra were recorded on a Bruker FTIR Alpha (ATR Mode) spectrometer, ν_{max} in cm^{-1}. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). ^1H NMR spectra were recorded on a Varian Unity INOVA 400 (400 MHz), 500 (500 MHz) or 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, C_6D_6: δ 7.16 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on a Varian Unity INOVA 400 (100 MHz), 500 (125MHz), or 600 (151 MHz) spectrometers with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 77.16 ppm, C_6D_6: δ 128.00 ppm). ^{11}B NMR spectra were recorded on a Varian Unity INOVA 400 (128 MHz), 500 (160 MHz) or 600 (192 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with BF_3•Et_2O (10% in $CDCl_3$) as reference. High-resolution mass spectrometry was performed on a Micromass LCT ESI-MS and JEOL AccuTOF DART (positive mode) at the Boston College Mass

Spectrometry Facility. Values for *E*:*Z* ratios of products were determined by analysis of 1H NMR spectra.

Solvents:

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 argon and purified by passage through two alumina columns. Tetrahydrofuran (THF; Fisher Scientific) was purified by distillation from sodium benzophenone ketyl immediately prior to use. Work-up and purification procedures involved the use of reagent grade solvents (Fisher Scientific) in air.

Reagents:

Methyl (*Z*)-2-methylbut-2-enoate (TCI), isobutyl (*Z*)-2-methylbut-2-enoate, methyl (*E*)-2-methylbut-2-enoate (TCI), 3-methyl-2-butenylboronic acid pinacol ester (Aldrich) were either distilled from CaH_2 under vacuum prior to use.

Citronellol (Aldrich), citronellal (AK Scientific), geraniol (Aldrich), angelic acid (TCI), (2*S*)-1-[(*tert*-butoxy)carbonyl]pyrrolidine-2-carboxylic acid (Synthonix), methyl 1H-Indole-3-carbaldehyde (Oakwood) were used as received.

phenyl (*Z*)-2-methylbut-2-enoate, 4-methoxybenzyl (*Z*)-2-methylbut-2-enoate, *tert*-butyldiphenylsilyl (*Z*)-2-methylbut-2-enoate, (2-(trimethylsilyl)ethoxy)methyl (*Z*)-2-methylbut-2-enoate, *S*-ethyl (Z)-2-methylbut-2-enethioate were prepared from angelic acid (TCI) according to reported procedures[26].

(26) Liu, Z.; Xu, C.; del Pozo, J.; Torker, S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2019**, *141*, 7137–7146.

1.8.2 Preparation of Organometallic Complexes

Mo monoaryloxide pyrrolide (MAP) complexes **Mo-1a–1c**, were prepared according to previously reported procedure[27]. Mo monoaryloxide chloride (MAC) complexes **Mo-2a–2c** were synthesized according to previously reported procedure[28]. Mo bisaryloxide complexes **Mo-3d** were prepared according to previously reported procedure[16]. Mo complexes were manipulated under an atmosphere of N_2 in a glove box.

General procedure for in situ preparation of Mo-3a for NMR analysis: In a N_2-filled Glove box, an oven-dried 1-dram vial equipped with a magnetic stir bar was charged with pentafluorophenylimido Mo bispyrrolide complex **Mo-0** (15.0 mg, 0.0251 mmol), phenol ligand **L1** (20.0 mg, 0.0502 mmol) and C_6D_6 (1 mL), generating a dark-red suspension. The vial was capped and the mixture was allowed to stir for 12 h at 70 °C, after which it was transferred to a screw cap NMR tube by pipette. The NMR tube was capped and sealed with Teflon tape. Diagnostic NMR data for **Mo-3a**: ^{1}H NMR (400 MHz, C_6D_6): δ 10.55 (1H, s). **Mo-3b:** ^{1}H NMR (400 MHz, C_6D_6): δ 10.65 (1H, s). **Mo-3c:** ^{1}H NMR (400 MHz, C_6D_6): δ 10.50 (1H, s).

General procedure for in situ preparation of Mo-3a: In a N_2-filled glove box, an oven-dried 4 mL vial equipped with a magnetic stir bar was charged with pentafluorophenylimido Mo bispyrrolide complex **Mo-0** (59.8 mg, 0.100 mmol), phenol

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(27) (a) Nguyen, T. T.; Koh, M. J.; Shen, X.; Romiti, F.; Schrock, R. R.; Hoveyda, A. H. *Science* **2016**, *352*, 569–575. (b) Koh, M. J.; Thach, T. T.; Zhang, H.; Schrock, R. R.; Hoveyda, A. H. *Nature* **2016**, *531*, 459–465.

(28) (a) Lam, J. K.; Zhu, C.; Bukhryakov, K. V.; Müller, P.; Hoveyda, A. H.; Schrock, R. R. *J. Am. Chem. Soc.* **2016**, *138*, 15774–15783. (b) Mu, Y.; Nguyen, T. T.; Koh, M. J.; Schrock, R. R.; Hoveyda, A. H. *Nat. Chem.* **2019**, *11*, 478–487.

ligand **L1** (79.7 mg, 0.200 mmol) and C_6H_6 (1 mL), resulting in a dark red suspension. The vial was capped and the mixture was allowed to stir for 12 h at 70 °C, after which time the solution was transferred to the reaction mixture by syringe (dried at 65 °C).

1.8.3 Cross-Metathesis with *Z*-Enoates

General CM Procedure: In a N_2-filled glovebox, an oven-dried 1-dram vial containing a magnetic stir bar was charged with alkene substrate (0.10 mmol) and enoate (0.20 mmol). To this mixture was added a solution of **Mo-3a (**0.1 M in benzene, 50.0 μL, 5.0 μmol) through a syringe. The vial was then connected to the vacuum pump through a needle-pierced septum, and the mixture was allowed to stir under 100 torr pressure, at 22 °C for 6 h, after which the solution was exposed to air and the volatiles were removed in vacuo to afford a dark-brown oil residue which was purified by silica gel chromatography. Conversion and the ratio of alkene isomers was determined by analysis of the ^{1}H NMR spectrum of the unpurified mixture.

Methyl (*Z*)-8-(benzyloxy)-2,6-dimethyloct-2-enoate (1.11). Colorless oil; **IR (neat):** 2949 (m), 2922 (m), 2853 (w), 1714 (s), 1453 (m), 1433 (m), 1363 (m), 1221 (m), 1196 (m), 1143 (m), 1096 (s), 1077 (m), 735 (m), 697 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.36–7.31 (m, 4H), 7.31–7.26 (m, 1H), 5.92 (tq, *J* = 7.5, 1.5 Hz, 1H), 4.50 (d, *J* = 1.5 Hz, 2H), 3.73 (s, 3H), 3.56–3.45 (m, 2H), 2.56–2.39 (m, 2H), 1.92–1.85 (m, 3H), 1.73–1.57 (m, 2H), 1.49–1.38 (m, 2H), 1.31–1.18 (m, 1H), 0.90 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 168.6, 143.8, 138.8, 128.5, 127.7, 127.6, 126.8, 73.0, 68.7, 51.3, 36.8, 36.8, 29.8, 27.2, 20.8, 19.6; **HRMS[M+H]$^+$:** Calcd for $C_{18}H_{27}O_3$: 291.1955, found: 291.1959.

Dimethyl (*Z*)-2-methyldodec-2-enedioate (1.12). Yellowish oil; **IR (neat):** 2924 (m), 2852 (m), 1736 (s), 1716 (s), 1455 (w), 1434 (m), 1363 (w), 1227 (m), 1193 (s), 1165 (s), 1124 (m), 1097 (w), 1077 (w) cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 5.92 (tq, *J* = 7.5, 1.5 Hz, 1H), 3.72 (s, 3H), 3.65 (s, 3H), 2.47–2.39 (m, 2H), 2.29 (t, *J* = 7.5 Hz, 2H), 1.90–1.86 (m, 3H), 1.64–1.55 (m, 2H), 1.43–1.34 (m, 2H), 1.28 (s, 8H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 174.4, 168.7, 143.8, 126.8, 51.5, 51.3, 34.2, 34.2, 29.7, 29.5, 29.4, 29.3, 29.2, 25.1, 20.8; **HRMS[M+H]$^+$:** Calcd for $C_{15}H_{27}O_4$: 271.1904, found: 271.1903.

Methyl (*Z*)-4-(benzyloxy)-2-methylbut-2-enoate (1.13). Colorless oil; **IR (neat):** 3027 (w), 2949 (w), 2850 (w), 1714 (s), 1453 (m), 1434 (m), 1356 (w), 1226 (s), 1141 (s), 1106 (m), 1072 (m), 736 (m), 698 (m) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.39–7.26 (m, 5H), 6.18 (tq, *J* = 5.0, 1.6 Hz, 1H), 4.53 (s, 2H), 4.51–4.45 (m, 2H), 3.72 (s, 2H), 1.95–1.90 (m, 3H); **^{13}C NMR (126 MHz, $CDCl_3$):** δ 167.8, 142.2, 138.3, 128.6, 127.9, 127.8, 127.4, 72.9, 69.0, 51.7, 20.0; **HRMS[M+H]$^+$:** Calcd for $C_{13}H_{17}O_3$: 221.1172, found: 221.1183.

Methyl (*Z*)-7-(1,3-dioxoisoindolin-2-yl)-2-methylhept-2-enoate (1.14). Colorless oil; **IR (neat):** 2943 (w), 2856 (w), 1770 (w), 1701 (s), 1434 (w), 1394 (m), 1368 (m), 1220 (m), 1143 (m), 1103 (m), 1037 (m), 876 (w), 719 (m), 529 (w) cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.87–7.80 (m, 2H), 7.74–7.66 (m, 2H), 5.89 (tq, *J* = 7.5, 1.5 Hz, 1H), 3.71 (s, 3H), 3.68 (t, *J* = 7.2 Hz, 1H), 2.55–2.43 (m, 2H), 1.91–1.84 (m, 3H), 1.74–1.65 (m, 2H), 1.51–1.40 (m, 2H); **^{13}C NMR (126 MHz, $CDCl_3$):** δ 168.5, 168.5, 142.6, 134.0, 132.3, 127.5, 123.3, 51.3, 38.0, 29.2, 28.4, 26.8, 20.8; **HRMS[M+H]$^+$:** Calcd for $C_{17}H_{20}NO_4$: 302.1387, found: 302.1383.

Methyl (*Z*)-7-((4-methoxybenzyl)oxy)-2-methylhept-2-enoate (1.15). Colorless oil; **IR (neat):** 2929 (m), 2854 (m), 1714 (s), 1611 (m), 1511 (s), 1455 (m), 1434 (m), 1363 (m), 1300 (m), 1243 (s), 1214 (m), 1194 (m), 1179 (m), 1138 (m), 1097 (s), 1035 (m), 820 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.28–7.23 (m, 2H), 6.91–6.84 (m, 2H), 5.92 (tq, *J* = 7.3, 1.5 Hz, 1H), 4.43 (s, 2H), 3.80 (s, 3H), 3.72 (s, 3H), 3.44 (t, *J* = 6.5 Hz, 2H), 2.51–2.43 (m, 2H), 1.89 (d, *J* = 1.5 Hz, 3H), 1.66–1.60 (m, 2H), 1.53–1.45 (m, 2H); **^{13}C NMR (126 MHz, $CDCl_3$):** δ 168.6, 159.3, 143.4, 130.9, 129.3, 127.1, 113.9, 72.7, 70.0, 55.4, 51.3, 29.5, 29.4, 26.2, 20.8; **HRMS[M+H]$^+$:** Calcd for $C_{17}H_{23}O_4$: 291.1591, found: 291.1597.

Methyl (*Z*)-2-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-2-enoate (1.16). Colorless oil; **IR (neat):** 2975 (m), 2949 (w), 2926 (w), 1716 (s), 1455 (w), 1434 (w), 1405 (w), 1369 (s), 1324 (m), 1234 (s), 1192 (m), 1165 (m), 1143 (s), 1114 (m), 1081 (m), 967 (m), 870 (w), 846 (w) cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 5.93 (tq, *J* = 7.4, 1.6 Hz, 1H), 3.71 (s, 3H), 2.58–2.49 (m, 2H), 1.88–1.85 (m, 3H), 1.22 (s, 12H), 0.95–0.82 (m, 2H); **^{13}C NMR (126 MHz, $CDCl_3$):** δ 168.7, 145.3, 126.1, 83.2, 51.3, 24.9, 24.2, 20.7, 11.4; **^{11}B NMR (160 MHz, $CDCl_3$):** δ 34.70; **HRMS[M+H]$^+$:** Calcd for $C_{13}H_{24}BO_4$: 255.1762, found: 255.1772.

Methyl (*Z*)-1-(6-methoxy-5-methyl-6-oxohex-4-en-1-yl)-1H-indole-3-carboxylate (1.17). Colorless oil; **IR (neat):** 2947 (w), 1700 (s), 1533 (m), 1466 (m), 1434 (m), 1396 (w), 1380 (m), 1224 (m), 1192 (m), 1170 (m), 1136 (m), 1118 (w), 1094 (m), 1032 (m), 776 (w), 750 (m) cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.23–8.14 (m, 1H), 7.82 (s, 1H), 7.39–7.33 (m, 1H), 7.31–7.24 (m, 2H), 5.85 (tq, *J* = 7.8, 1.6 Hz, 1H), 4.16 (t, *J* = 7.2 Hz, 2H), 3.91 (s, 3H), 3.66 (s, 3H), 2.57–2.47 (m, 2H), 2.03–1.95 (m, 2H), 1.90–1.82 (m, 3H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 168.2, 165.6, 140.9, 136.6, 134.3, 128.6, 126.9, 122.8, 121.9, 121.9, 110.1, 107.1, 51.4, 51.0, 46.7, 29.5, 27.0, 20.7; **HRMS[M+H]$^+$:** Calcd for $C_{18}H_{22}NO_4$: 316.1543, found: 316.1531.

Methyl (*Z*)-7-(1,3-dioxolan-2-yl)-2,6-dimethylhept-2-enoate (1.18). Colorless oil; **IR (neat):** 2949 (m), 2923 (m), 2879 (w), 1714 (s), 1455 (w), 1433 (w), 1363 (w), 1222 (m), 1195 (m), 1143 (s), 1074 (w), 1036 (m), 945 (w) cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 5.93 (tq, *J* = 7.5, 1.5 Hz, 1H), 4.90 (dd, *J* = 5.4, 4.6 Hz, 1H), 4.01–3.91 (m, 2H), 3.89–3.78 (m, 2H), 3.73 (s, 3H), 2.55–2.11 (m, 2H), 1.92–1.85 (m, 3H), 1.77–1.62 (m, 2H), 1.55–1.43 (m, 2H), 1.33–1.22 (m, 1H), 0.96 (d, *J* = 6.5 Hz, 3H); **^{13}C NMR (126 MHz, $CDCl_3$):** δ 168.6, 143.5, 126.9, 103.9, 64.9, 64.8, 51.3, 41.0, 37.0, 29.3, 27.1, 20.8, 19.8; **HRMS[M+H]$^+$:** Calcd for $C_{13}H_{23}O_4$: 243.1590, found: 243.1597.

(*Z*)-1-(*tert*-Butyl) 2-(7-methoxy-6-methyl-7-oxohept-5-en-1-yl) (*S*)-pyrrolidine-1,2-dicarboxylate (1.19). Colorless oil; **IR (neat):** 2971 (w), 2951 (w), 2877 (w), 1742 (m), 1695 (s), 1453 (w), 1389 (s), 1363 (m), 1240 (m), 1157 (s), 1120 (m), 1086 (m), 770 (w) cm^{-1}; **^{1}H NMR (400 MHz, DMSO-d_6, 25 °C):** δ 5.98 (t, *J* = 7.4 Hz, 1H), 4.19–4.11 (m, 1H), 4.11–3.94 (m, 2H), 3.65 (s, 3H), 3.42–3.23 (m, 2H), 2.46–2.34 (m, 2H), 2.28–2.09 (m, 1H), 1.93–1.73 (m, 6H), 1.64–1.51 (m, 2H), 1.50–1.28 (m, 11H); **^{1}H NMR (400 MHz, DMSO-d_6, 85 °C):** δ 5.95 (tq, *J* = 7.4, 1.4 Hz, 1H), 4.22–4.13 (m, 1H), 4.07 (t, *J* = 6.5 Hz, 2H), 3.68 (s, 3H), 3.43–3.27 (m, 2H), 2.45–2.34 (m, 2H), 2.29–2.13 (m, 1H), 1.91–1.77 (m, 6H), 1.67–1.55 (m, 2H), 1.50–1.40 (m, 2H), 1.38 (s, 9H); **^{13}C NMR (100 MHz, DMSO-d_6, 85 °C):** δ 172.9, 168.1, 141.8, 127.6, 79.3, 64.5, 59.2, 51.4, 46.7, 30.5, 28.9, 28.5, 28.3, 25.5, 23.8, 20.5; signal for carbonyl carbon on the Boc– group was not

visible at 85 °C, but was found at 25 °C as a pair of rotamers (153.4 and 152.9 ppm in DMSO-d_6); **HRMS[M+H]$^+$:** Calcd for $C_{19}H_{32}NO_6$: 370.2224, found: 370.2218.

Methyl (*Z*)-5-(3-methoxyphenyl)-2-methylpent-2-enoate (1.20). Colorless oil; **IR (neat):** 2947 (m), 2922 (m), 1713 (s), 1599 (m), 1583 (m), 1487 (m), 1453 (m), 1433 (m), 1364 (w), 1256 (s), 1213 (m), 1193 (m), 1164 (m), 1151 (s), 1120 (s), 1051 (w), 1024 (m), 776 (m), 695 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.23–7.18 (m, 1H), 6.83–6.78 (m, 1H), 6.78–6.72 (m, 2H), 5.97 (tq, *J* = 7.3, 1.6 Hz, 1H), 3.80 (s, 3H), 3.73 (s, 3H), 2.83–2.75 (m, 2H), 2.74–2.67 (m, 2H), 1.93–1.85 (m, 3H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 168.5, 159.8, 143.3, 142.2, 129.4, 127.7, 121.0, 114.4, 111.4, 77.4, 77.2, 76.9, 55.3, 51.4, 35.7, 31.2, 20.8; **HRMS[M+H]$^+$:** Calcd for $C_{14}H_{19}O_3$: 235.1329, found: 235.1332.

Methyl (*Z*)-7-(dibenzylamino)-2-methylhept-2-enoate (1.21). Colorless oil; **IR (neat):** 3020 (w), 2925 (m), 2791 (w), 1714 (s), 1492 (m), 1451 (w), 1433 (w), 1364 (m), 1236 (m), 1213 (m), 1193 (m), 1142 (m), 1107 (w), 1071 (w), 743 (m), 697 (s) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.39–7.34 (m, 4H), 7.33–7.28 (m, 4H), 7.25–7.21 (m, 2H), 5.89 (tq, *J* = 7.3, 1.5 Hz, 1H), 3.71 (s, 3H), 3.56 (s, 4H), 2.46–2.36 (m, 4H), 1.92–1.87 (m, 3H), 1.58–1.50 (m, 2H), 1.44–1.36 (m, 2H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 168.6, 143.6, 140.1, 128.9, 128.2, 126.9, 126.8, 58.4, 53.4, 51.3, 29.6, 27.2, 26.9, 20.8; **HRMS[M+H]$^+$:** Calcd for $C_{23}H_{30}NO_2$: 352.2271, found: 352.2268.

Methyl (Z)-2,6-dimethyl-8-(2-(phenylthio)acetoxy)oct-2-enoate (1.22). Colorless oil; **IR (neat):** 2951 (m), 2921 (m), 2849 (w), 1714 (s), 1455 (m), 1436 (m), 1267 (s), 1222 (m), 1196 (m), 1141 (s), 1077 (w), 739 (m), 689 (m) cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.42–7.38 (m, 2H), 7.32–7.27 (m, 2H), 7.25–7.18 (m, 1H), 5.90 (tq, *J* = 7.4, 1.5 Hz, 1H), 4.22–4.02 (m, 2H), 3.73 (s, 3H), 3.63 (s, 2H), 2.56–2.34 (m, 2H), 1.93–1.84 (m, 3H),

1.69–1.57 (m, 1H), 1.56–1.46 (m, 1H), 1.46–1.34 (m, 2H), 1.34–1.16 (m, 3H), 0.88 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR (126 MHz, $CDCl_3$):** δ 169.9, 168.5, 143.4, 135.2, 130.0, 129.2, 129.2, 127.0, 64.1, 51.3, 36.8, 36.5, 35.3, 29.6, 27.1, 20.8, 19.3; **HRMS[M+H]$^+$:** Calcd for $C_{19}H_{27}O_4S$: 351.1627, found: 351.1621.

Isobutyl (*Z*)-8-(benzyloxy)-2,6-dimethyloct-2-enoate (1.24). Colorless oil; **IR (neat):** 3027 (m), 2955(m), 2924 (m), 2869 (m), 1713 (s), 1643 (w), 1453 (m), 1377 (m), 1365 (m), 1220 (m), 1192 (m), 1144 (s), 1097 (s), 1075 (m), 1027 (m), 998 (w), 944 (w), 734 (m), 696 (m) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.38–7.31 (m, 4H), 7.30–7.24 (m, 1H), 5.91 (tq, *J* = 7.4, 1.5 Hz, 1H), 4.50 (s, 2H), 4.50 (d, *J* = 0.7 Hz, 2H), 3.95–3.90 (m, 2H), 3.56–3.46 (m, 2H), 2.59–2.39 (m, 2H), 2.11–1.92 (m, 1H), 1.92–1.88 (m, 3H), 1.77–1.56 (m, 2H), 1.51–1.38 (m, 2H), 1.32–1.19 (m, 1H), 0.96 (d, *J* = 6.7 Hz, 6H), 0.90 (d, *J* = 6.5 Hz, 3H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 168.3, 143.4, 138.8, 128.5, 127.7, 127.6, 127.2, 73.0, 70.5, 68.7, 36.9, 36.8, 29.9, 27.9, 27.3, 20.9, 19.5, 19.4; **HRMS[M+H]$^+$:** Calcd for $C_{21}H_{33}O_3$: 333.2424, found: 333.2429.

Phenyl (*Z*)-8-(benzyloxy)-2,6-dimethyloct-2-enoate (1.25). Colorless oil; **IR (neat):** 3027 (m), 2951 (m), 2922 (m), 2852 (m), 1732 (s), 1642 (w), 1590 (w), 1491 (m), 1453 (m), 1363 (w), 1194 (s), 1161 (m), 1129 (s), 1091 (m), 1070 (m), 1025 (w), 741 (s), 689 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.44–7.37 (m, 2H), 7.37–7.32 (m, 4H), 7.31–7.27 (m, 1H), 7.26–7.22 (m, 1H), 7.16–7.10 (m, 2H), 6.13 (t, *J* = 7.5 Hz, 1H), 6.13 (t, *J* = 7.5, 1.6 Hz, 1H), 4.50 (d, *J* = 1.5 Hz, 2H), 3.58–3.46 (m, 2H), 2.68–2.51 (m, 2H), 2.06 (d, *J* = 1.5 Hz, 3H), 1.76–1.62 (m, 2H), 1.56–1.42 (m, 2H), 1.37–1.25 (m, 1H), 0.91 (d, *J* = 6.5 Hz, 3H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 166.3, 150.9, 146.4, 138.8, 129.5, 128.5,

128.5z, 126.3, 125.8, 121.9, 73.0, 68.7, 36.8, 36.7, 29.8, 27.5, 20.9, 19.6; **HRMS[M+H]$^+$:** Calcd for $C_{23}H_{29}O_3$: 353.2111, found: 353.2094.

4-Methoxybenzyl (*Z*)-8-(benzyloxy)-2,6-dimethyloct-2-enoate (1.26). Colorless oil; **IR (neat):** 2950 (m), 2922 (m), 2856 (m), 1710 (s), 1612 (m), 1513 (s), 1453 (m), 1359 (w), 1301 (w), 1246 (s), 1174 (m), 1141 (s), 1095 (s), 1075 (m), 1033 (m), 824 (m), 735 (m), 697 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.49–7.19 (m, 8H), 6.97–6.81 (m, 2H), 5.92 (t, *J* = 7.6 Hz, 1H), 5.12 (s, 2H), 4.49 (s, 2H), 3.87–3.72 (m, 3H), 3.55–3.43 (m, 2H), 2.55–2.37 (m, 2H), 1.96–1.86 (m, 3H), 1.70–1.52 (m, 2H), 1.50–1.35 (m, 2H), 1.26–1.17 (m, 1H), 0.86 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 168.1, 159.6, 143.8, 138.8, 130.1, 128.5, 128.5, 127.7, 127.6, 126.9, 114.0, 73.0, 68.8, 65.8, 55.4, 36.8, 36.7, 29.8, 27.3, 20.8, 19.5; **HRMS[M+H]$^+$:** Calcd for $C_{25}H_{33}O_4$: 397.2373, found: 397.2369.

***tert*-Butyldiphenylsilyl (*Z*)-8-(benzyloxy)-2,6-dimethyloct-2-enoate (1.27).** Colorless oil; **IR (neat):** 2952 (w), 2926 (w), 2855 (w), 1702 (m), 1453 (w), 1426 (m), 1362 (m), 1220 (m), 1190 (m), 1146 (s), 1112 (s), 1074 (m), 820 (m), 737 (s), 696 (s), 608 (m), 504 (s), 487 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.77–7.66 (m, 3H), 7.47–7.25 (m, 12H), 5.98 (t, *J* = 7.3 Hz, 1H), 4.48 (s, 2H), 3.57–3.43 (m, 2H), 2.51 (d, *J* = 8.2 Hz, 2H), 2.03 (s, 3H), 1.72–1.52 (m, 2H), 1.51–1.36 (m, 2H), 1.32–1.19 (m, 1H), 1.16–1.07 (m, 9H), 0.88–0.80 (m, 3H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 167.0, 144.9, 138.8, 135.4, 134.9, 132.3, 130.1, 129.8, 128.5, 128.0, 127.9, 127.8, 127.7, 127.6, 73.0, 68.7, 36.9, 36.8, 29.8, 27.3, 27.1, 26.7, 21.5, 19.5, 19.3; **HRMS[M+H]$^+$:** Calcd for $C_{33}H_{43}O_3Si$: 515.2976, found: 515.2988.

(2-(Trimethylsilyl)ethoxy)methyl (*Z*)-8-(benzyloxy)-2,6-dimethyloct-2-enoate (1.28). Colorless oil; **IR (neat):** 2950 (m), 2922 (m), 2854 (m), 1715 (s), 1453 (w), 1363 (w),

1247 (s), 1196 (w), 1143 (m), 1111 (s), 1069 (s), 939 (m), 858 (s), 835 (s), 734 (w), 696 (m) cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.37–7.32 (m, 4H), 7.31–7.24 (m, 1H), 5.97 (t, *J* = 7.4 Hz, 1H), 5.36 (s, 2H), 4.50 (s, 2H), 3.78–3.69 (m, 2H), 3.56–3.45 (m, 2H), 2.60–2.40 (m, 2H), 1.95–1.82 (m, 3H), 1.73–1.59 (m, 2H), 1.50–1.39 (m, 2H), 1.32–1.20 (m, 1H), 1.00–0.95 (m, 2H), 0.90 (d, *J* = 6.6 Hz, 3H), 0.09–-0.02 (m, 9H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 167.5, 144.7, 138.8, 128.5, 127.7, 127.6, 126.7, 88.9, 73.0, 68.7, 67.9, 36.8, 36.8, 29.8, 27.3, 20.8, 19.5, 18.2, -1.3; **HRMS[M+NH_4]$^+$:** Calcd for $C_{23}H_{42}ONO_4Si$: 424.2878, found: 424.2879.

S-Ethyl (*Z*)-8-(benzyloxy)-2,6-dimethyloct-2-enethioate (1.29). Colorless oil; **IR (neat):** 2955 (m), 2923 (m), 2852 (m), 1662 (s), 1620 (w), 1451 (m), 1363 (w), 1098 (s), 1040 (w), 1026 (w), 962 (s), 903 (m), 861 (w), 733 (s), 695 (s), 645 (w) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.38–7.31 (m, 4H), 7.31–7.25 (m, 1H), 5.67 (t, *J* = 7.5 Hz, 1H), 4.50 (s, 2H), 3.58–3.44 (m, 2H), 2.92 (qd, *J* = 7.5, 1.0 Hz, 2H), 2.48–2.30 (m, 2H), 2.02–1.93 (m, 3H), 1.72–1.56 (m, 2H), 1.50–1.38 (m, 2H), 1.32–1.19 (m, 4H), 0.89 (d, *J* = 6.5 Hz, 3H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 194.6, 138.9, 138.8, 134.0, 128.5, 127.7, 127.6, 73.0, 68.7, 36.9, 36.8, 29.8, 27.2, 23.3, 20.9, 19.6, 14.8; **HRMS[M+H]$^+$:** Calcd for $C_{19}H_{29}O_2S$: 321.1883, found: 321.1892.

1.8.4 Cross-Metathesis with *E*-Enoates

General CM Procedure: In a N_2-filled glovebox, an oven-dried 1-dram vial containing a magnetic stir bar was charged with alkene substrate (0.10 mmol) and enoate (0.20 mmol). To this mixture was added a solution of **Mo-2a (**0.1 M in benzene, 50.0 µL, 5.0 µmol) and tris(pentafluorophenyl)borane **(**0.1 M in benzene, 60.0 µL, 6.0 µmol) through

syringes. The vial was then connected to the vacuum pump through a needle-pierced septum, and the mixture was allowed to stir under 100 torr pressure, at 22 °C for 4 h, after which the solution was exposed to air and the volatiles were removed in vacuo to afford a dark-brown oil residue, which was purified by silica gel chromatography. Conversion and the ratio of alkene isomers was determined by analysis of the ^{1}H NMR spectrum of the unpurified mixture.

Methyl (*E*)-8-(benzyloxy)-2,6-dimethyloct-2-enoate (1.32). Colorless oil; **IR (neat):** 2948 (m), 2922 (m), 2852 (m), 1711 (s), 1648 (w), 1452 (m), 1433 (m), 1362 (w), 1264 (s), 1194 (m), 1138 (m), 1095 (s), 1026 (w), 737 (m), 697 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.39–7.31 (m, 4H), 7.31–7.26 (m, 1H), 6.75 (tq, *J* = 7.5, 1.4 Hz, 1H), 4.50 (s, 2H), 3.73 (d, *J* = 1.0 Hz, 3H), 3.56–3.45 (m, 2H), 2.26–2.09 (m, 2H), 1.87–1.78 (m, 3H), 1.73–1.55 (m, 2H), 1.53–1.40 (m, 2H), 1.34–1.23 (m, 1H), 0.91 (dd, *J* = 6.7, 1.0 Hz, 3H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 168.8, 142.8, 138.7, 128.5, 127.7, 127.6, 127.5, 73.1, 68.6, 51.8, 36.7, 35.9, 29.8, 26.3, 19.5, 12.5; **HRMS[M+H]$^{+}$:** Calcd for $C_{18}H_{27}O_3$: 291.1955, found: 291.1943.

Methyl (*E*)-2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-2-enoate (1.33). Colorless oil; **IR (neat):** 2985 (m), 2944 (w), 2926 (w), 1710 (s), 1453 (w), 1366 (s), 1324 (m), 1235 (s), 1192 (m), 1165 (m), 1143 (s), 1114 (m), 1072 (m), 855 (w) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 6.92 (tq, *J* = 8.6, 1.8 Hz, 1H), 3.71 (s, 3H), 1.94–1.76 (m, 5H), 1.24 (s, 12H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 168.8, 138.7, 127.4, 83.7, 51.7, 24.9, 14.3, 12.3; **^{11}B NMR (160 MHz, $CDCl_3$):** δ 33.37; **HRMS[M+H]$^{+}$:** Calcd for $C_{12}H_{22}BO_4$: 241.1606, found: 241.1608.

Methyl (*E*)-8-(ethylthio)-2,6-dimethyl-8-oxooct-2-enoate (1.34). Colorless oil; **IR (neat):** 2950 (m), 2927 (m), 2871 (w), 1712 (s), 1685 (s), 1648 (w), 1433 (m), 1379 (w), 1351 (w), 1265 (s), 1191 (m), 1141 (m), 1092 (m), 1059 (m), 1010 (m), 969 (w), 938 (w), 744 (w) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 6.72 (tq, *J* = 7.5, 1.5 Hz, 1H), 3.72 (s, 3H), 2.87 (q, *J* = 7.5 Hz, 2H), 2.52 (dd, *J* = 14.6, 6.1 Hz, 1H), 2.38 (dd, *J* = 14.5, 7.9 Hz, 1H), 2.25–2.11 (m, 2H), 2.10–2.00 (m, 1H), 1.82 (s, 3H), 1.54–1.44 (m, 1H), 1.37–1.28 (m, 1H), 1.24 (td, *J* = 7.4, 1.3 Hz, 3H), 0.96 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 199.0, 168.7, 142.0, 127.9, 51.8, 51.2, 35.3, 30.9, 26.2, 23.5, 19.5, 14.9, 12.5; **HRMS[M+H]$^+$:** Calcd for $C_{13}H_{23}O_3S$: 259.1362, found: 259.1372.

1.8.5 Application to Naturally Occurring Prenyl Termini

(*R*,*Z*)-6-((3*S*,5*R*,10*S*,13*R*,14*R*,17*R*)-3-hydroxy-4,4,10,13,14-pentamethyl-2,3,4,5,6,7,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[a]phenanthren-17-yl)-2-methylhept-2-enoic acid (1.40). In a N_2-filled glovebox, an oven-dried 2-dram vial containing a magnetic stir bar was charged with lanosterol acetate (**1.38**, 46.9 mg, 0.10 mmol), methyl (*Z*)-2-methylbut-2-enoate (25.0 μL, 0.20 mmol), and benzene (0.2 mL). To this mixture was added a solution of **Mo-3a (**0.1 M in benzene, 50.0 μL, 5.0 μmol) through a syringe. The vial was then connected to the vacuum pump through a needle-pierced septum, and the mixture was allowed to stir under 100 torr pressure, 22 °C for 6 h, after which the solution was exposed to air and the volatiles were removed in vacuo to afford a dark-brown solid residue. 5% KOH in EtOH (4 mL) was added and the vial was capped and allowed to stir at 80 °C for 4 hours, after which it was allowed to cool to room temperature. The reaction was quenched by addition of 1 M HCl aqueous solution

(4 mL), extracted by DCM (3x4 mL). The combined organic layers were washed with brine (4 mL), then dried over Na_2SO_4 and concentrated in vacuo to afford yellow solid, which was purified by silica gel chromatography (5% to 20% EtOAc in hexanes) to afford 1.40 (0.330 g, 0.072 mmol, 72% yield) as white solid. The ratio of alkene isomers was determined by analysis of the ^{1}H NMR spectrum (94:6 *Z*:*E*). The spectral data for this compound were identical to those reported previously[19].

(*R*,*E*)-6-((3*S*,5*R*,10*S*,13*R*,14*R*,17*R*)-3-hydroxy-4,4,10,13,14-pentamethyl-2,3,4,5,6,7,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[a]phenanthren-17-yl)-2-methylhept-2-enoic acid (1.41). In a N_2-filled glovebox, an oven-dried 2-dram vial containing a magnetic stir bar was charged with lanosterol acetate (**1.38**, 46.9 mg, 0.10 mmol), methyl (*E*)-2-methylbut-2-enoate (25.0 μL, 0.20 mmol), and benzene (0.2 mL). To this mixture was added a solution of **Mo-2a (**0.1 M in benzene, 50.0 μL, 5.0 μmol) and tris(pentafluorophenyl)borane **(**0.1 M in benzene, 60.0 μL, 6.0 μmol) through syringes. The vial was then connected to the vacuum pump through a needle-pierced septum, and the mixture was allowed to stir under 100 torr pressure, 22 °C for 4 h, after which the solution was exposed to air and the volatiles were removed in vacuo to afford a dark-brown solid residue. 5% KOH in EtOH (4 mL) was added and the vial was capped and allowed to stir at 80 °C for 4 hours, after which it was allowed to cool to room temperature. The reaction was quenched by addition of 1 M HCl aqueous solution (4 mL), extracted by DCM (3x4 mL). The combined organic layers were washed with brine (4 mL), then dried over Na_2SO_4 and concentrated in vacuo to afford yellow solid, which was purified by silica gel chromatography (5% to 20% EtOAc in hexanes) to afford **1.40** (0.301 g, 0.066 mmol, 66% yield) as white solid. The ratio of alkene isomers was

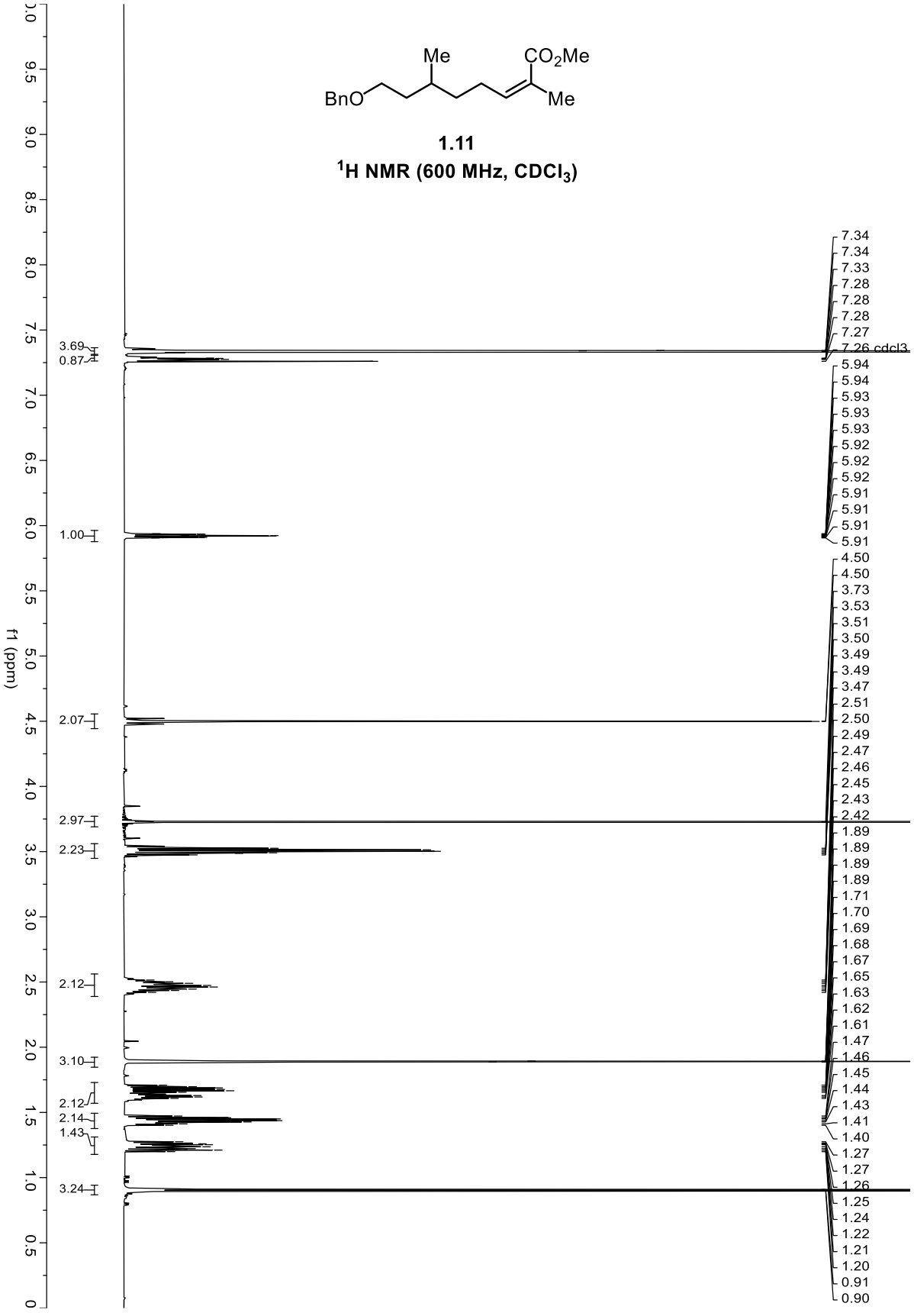
determined by analysis of the ^{1}H NMR spectrum (94:6 *E*:*Z*). The spectral data for this compound were identical to those reported previously[20].

methyl (*S,Z*)-8-((*tert*-butyldimethylsilyl)oxy)-2,6-dimethyloct-2-enoate (1.42). In a N_2-filled glovebox, an oven-dried 5-dram vial containing a magnetic stir bar was charged with TBS-protected citronellol (2.00 g, 7.4 mmol) and methyl (*Z*)-2-methylbut-2-enoate (1.70 g, 14.8 mmol). To this mixture was added a solution of **Mo-3a (**0.1 M in benzene, 740 μL, 0.074 mmol) through a syringe. The vial was then connected to the vacuum pump through a needle-pierced septum, and the mixture was allowed to stir under 100 torr pressure, 22 °C for 8 h, after which the solution was exposed to air and the volatiles were removed in vacuo to afford a dark-brown oil residue which was purified by silica gel chromatography (1% to 3% EtOAc in hexanes) as a single isomer. The spectral data for this compound were identical to those reported previously[22].

methyl (*S,E*)-8-((*tert*-butyldimethylsilyl)oxy)-2,6-dimethyloct-2-enoate (1.43). In a N_2-filled glovebox, an oven-dried 5-dram vial containing a magnetic stir bar was charged with TBS-protected citronellol (273 mg, 1.0 mmol) and methyl (*E*)-2-methylbut-2-enoate (228 mg, 2.0 mmol). To this mixture was added a solution of **Mo-2a (**0.1 M in benzene, 500 μL, 0.05 mmol) and tris(pentafluorophenyl)borane **(**0.1 M in benzene, 600 μL, 0.06 mmol) through syringes. The vial was then connected to the vacuum pump through a needle-pierced septum, and the mixture was allowed to stir under 100 torr pressure, 22 °C for 4 h, after which the solution was exposed to air and the volatiles were removed in vacuo to afford a dark-brown oil residue which was purified by silica gel chromatography (1% to 3% EtOAc in hexanes) as a single isomer. The spectral data for this compound were identical to those reported previously[22].

methyl (2*Z*,6*E*)-8-((tert-butyldiphenylsilyl)oxy)-2,6-dimethylocta-2,6-dienoate (1.44). In a N_2-filled glovebox, an oven-dried 1-dram vial containing a magnetic stir bar was charged with TBDPS-protected geraniol (39.2 mg, 0.1 mmol) and methyl (*Z*)-2-methylbut-2-enoate (25 μL, 0.2 mmol). To this mixture was added a solution of **Mo-3a** **(**0.1 M in benzene, 50 μL, 5.0 μmol) and tris(pentafluorophenyl)borane **(**0.1 M in benzene, 60 μL, 6.0 μmol) through syringes. The vial was then connected to the vacuum pump through a needle-pierced septum, and the mixture was allowed to stir under 100 torr pressure, 22 °C for 6 h, after which the solution was exposed to air and the volatiles were removed in vacuo to afford a dark-brown oil residue which was purified by silica gel chromatography (1% to 3% EtOAc in hexanes) as a single isomer. The spectral data for this compound were identical to those reported previously[24].

1.8.6 NMR Spectra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3.10
2.12
2.14
1.43
3.24
7.34
7.34
7.33
7.28
7.28
7.28
7.27
7.26 cdcl3
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5.93
5.93
5.93
5.92
5.92
5.92
5.91
5.91
5.91
5.91
4.50
4.50
3.73
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3.51
3.50
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3.49
3.47
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2.50
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2.47
2.46
2.45
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2.42
1.89
1.89
1.89
1.89
1.89
1.71
1.70
1.69
1.68
1.67
1.65
1.63
1.62
1.61
1.47
1.46
1.45
1.44
1.43
1.41
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1.26
1.25
1.24
1.22
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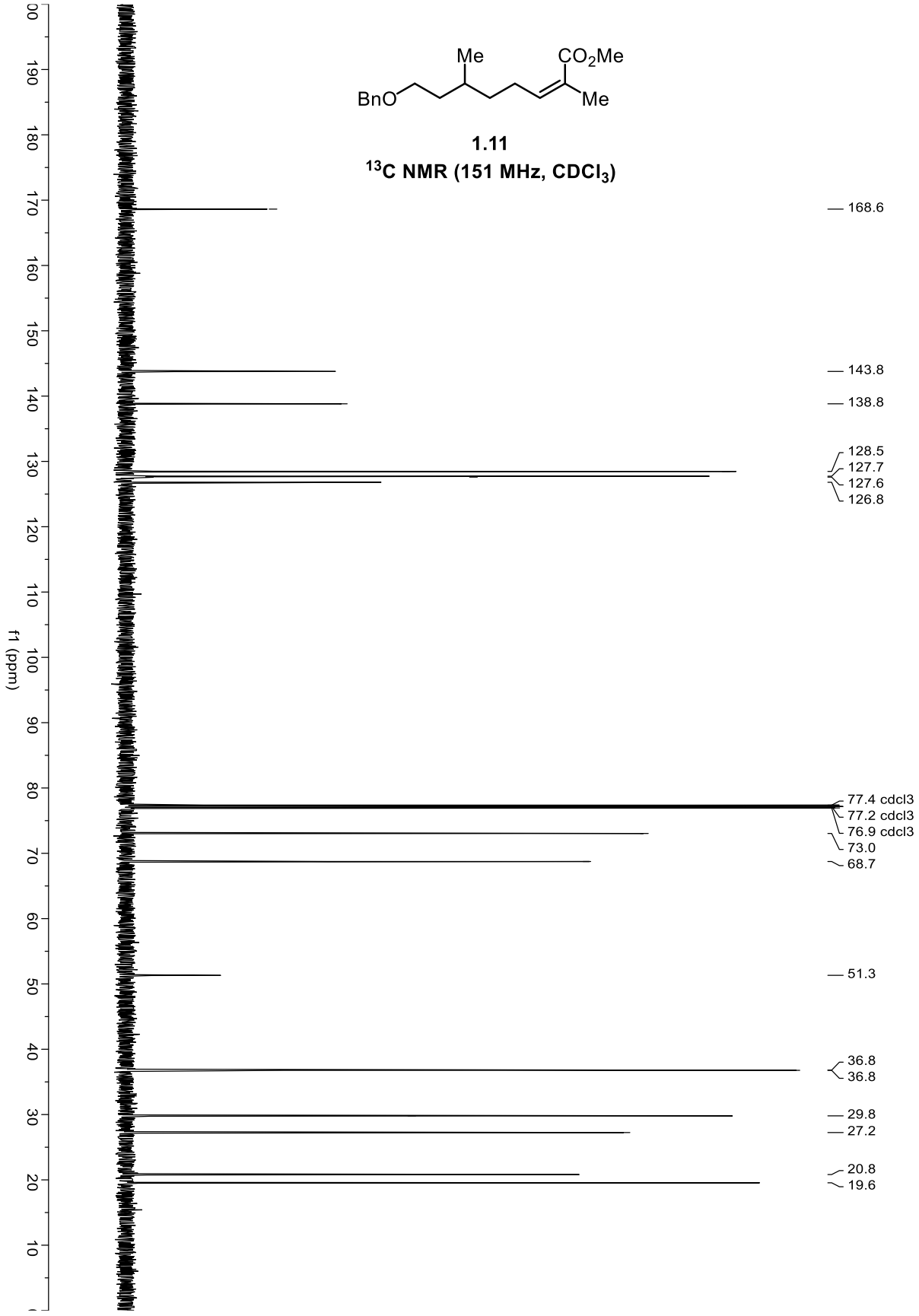
0.91
0.90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BnO
Me
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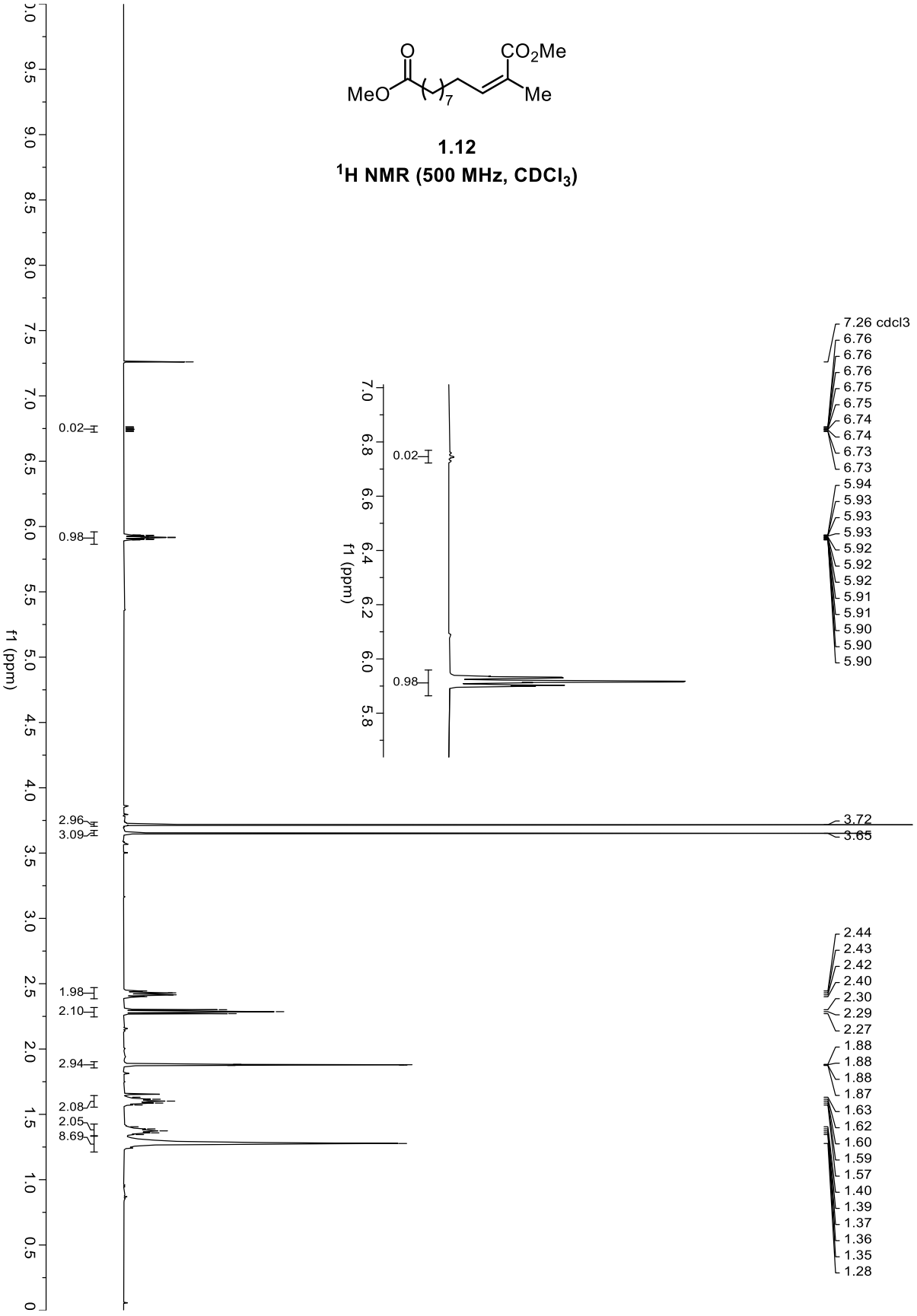
127.7
127.6
126.8
77.4 cdcl3
77.2 cdcl3
76.9 cdcl3
73.0
68.7
51.3
36.8
36.8
29.8
27.2
20.8
19.6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MeO
7
Me
1.12
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f1 (ppm)
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3.09
1.98
2.10
2.94
2.08
2.05
8.69
7.26 cdcl3
6.76
6.76
6.76
6.75
6.75
6.74
6.74
6.73
6.73
5.94
5.93
5.93
5.93
5.92
5.92
5.92
5.91
5.91
5.90
5.90
5.90
3.72
3.65
2.44
2.43
2.42
2.40
2.30
2.29
2.27
1.88
1.88
1.88
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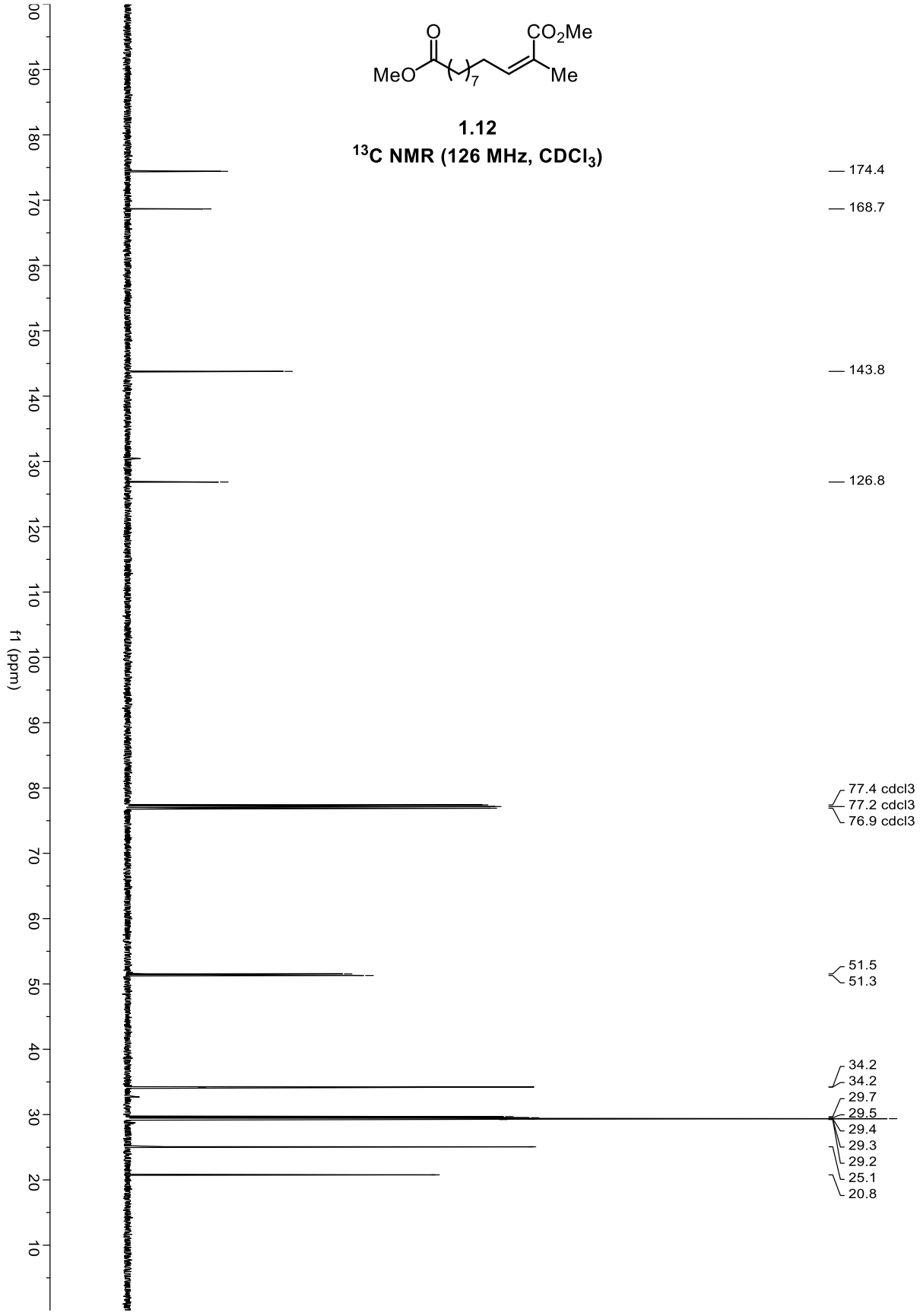
1.28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O
CO2Me
Me
7
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143.8
126.8
77.4 cdcl3
77.2 cdcl3
76.9 cdcl3
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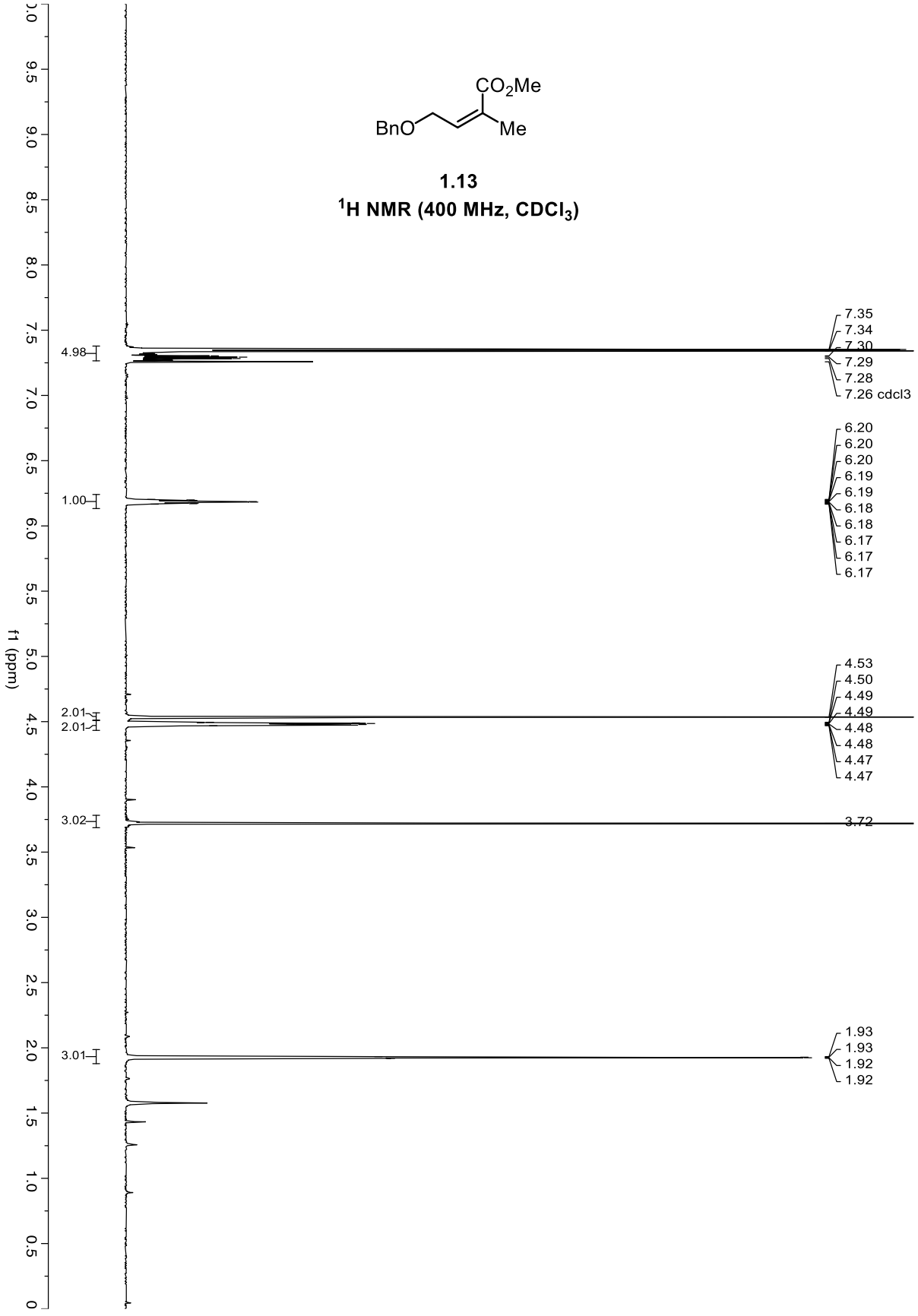
51.3
34.2
34.2
29.7
29.5
29.4
29.3
29.2
25.1
20.8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BnO
Me
1.13
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7.29
7.28
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6.20
6.20
6.20
6.19
6.19
6.18
6.18
6.17
6.17
6.17
4.53
4.50
4.49
4.49
4.48
4.48
4.47
4.47
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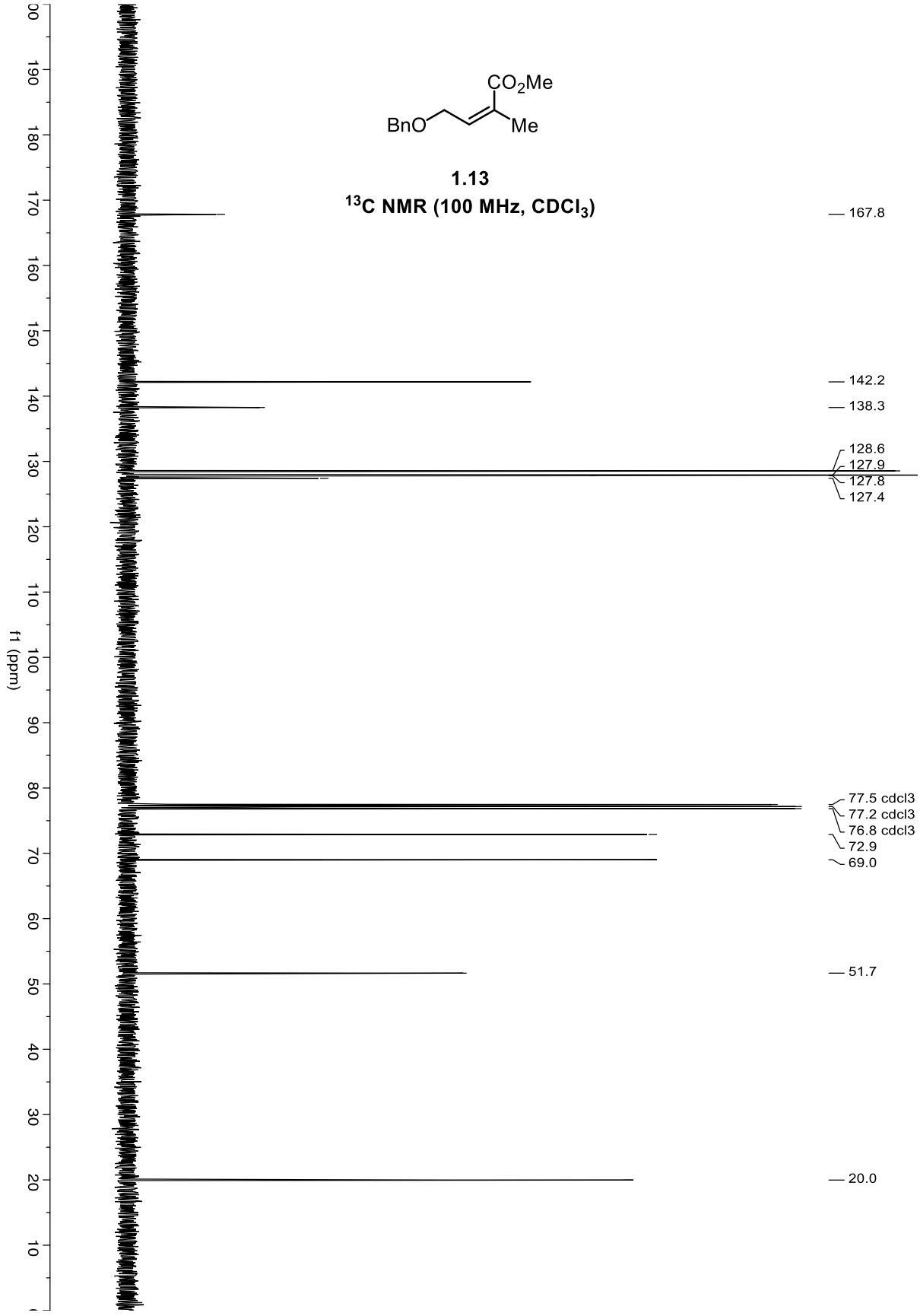
2.01
2.01
3.02
3.01
f1 (ppm)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BnO
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127.9
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127.4
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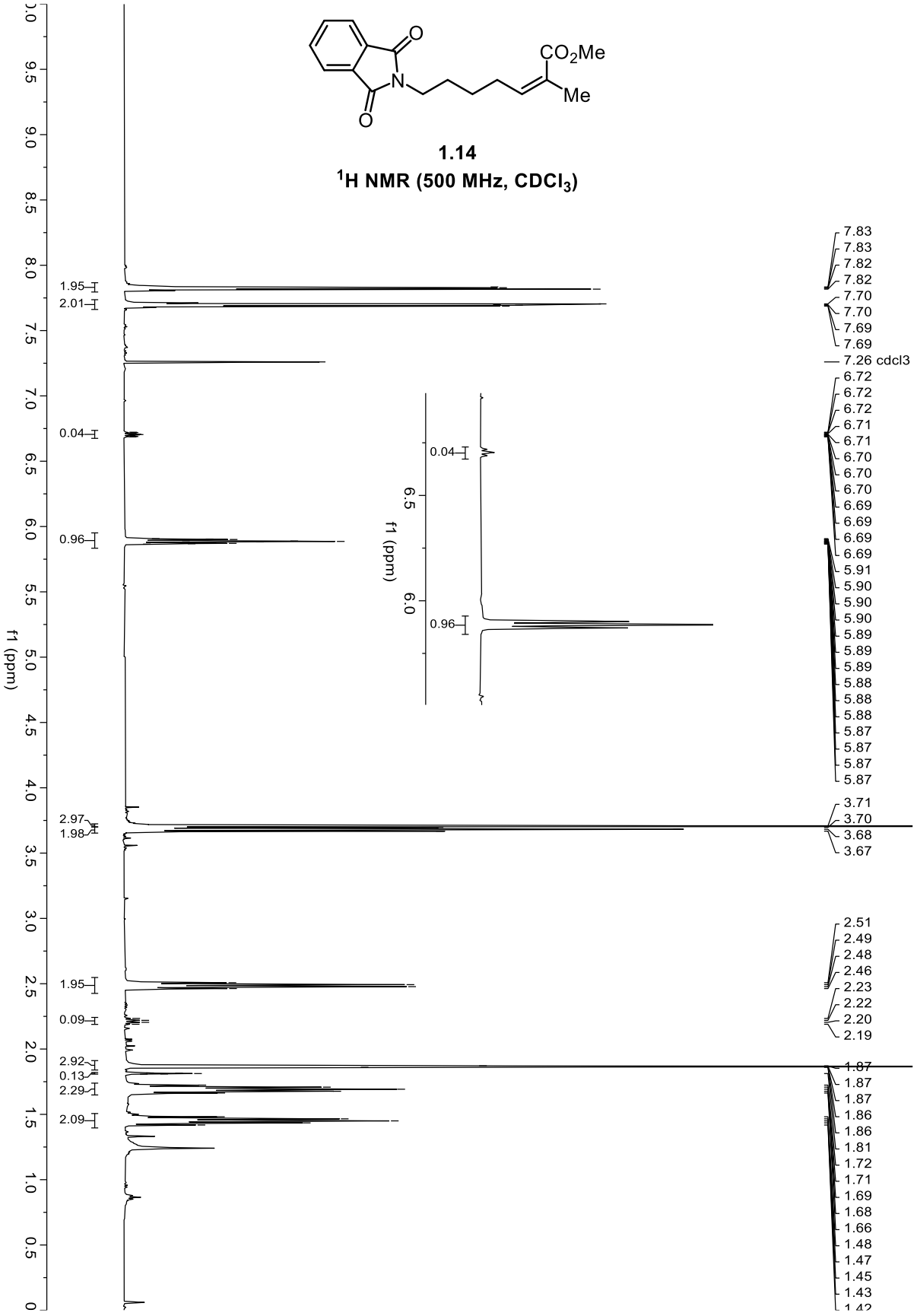
77.2 cdcl3
76.8 cdcl3
72.9
69.0
51.7
20.0
f1 (ppm)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7.82
7.70
7.70
7.69
7.69
7.26 cdcl3
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6.72
6.72
6.71
6.71
6.70
6.70
6.70
6.69
6.69
6.69
6.69
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5.90
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5.89
5.89
5.88
5.88
5.88
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5.87
5.87
5.87
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2.48
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2.23
2.22
2.20
2.19
1.87
1.87
1.87
1.86
1.86
1.81
1.72
1.71
1.69
1.68
1.66
1.48
1.47
1.45
1.43
1.42
1.95
2.01
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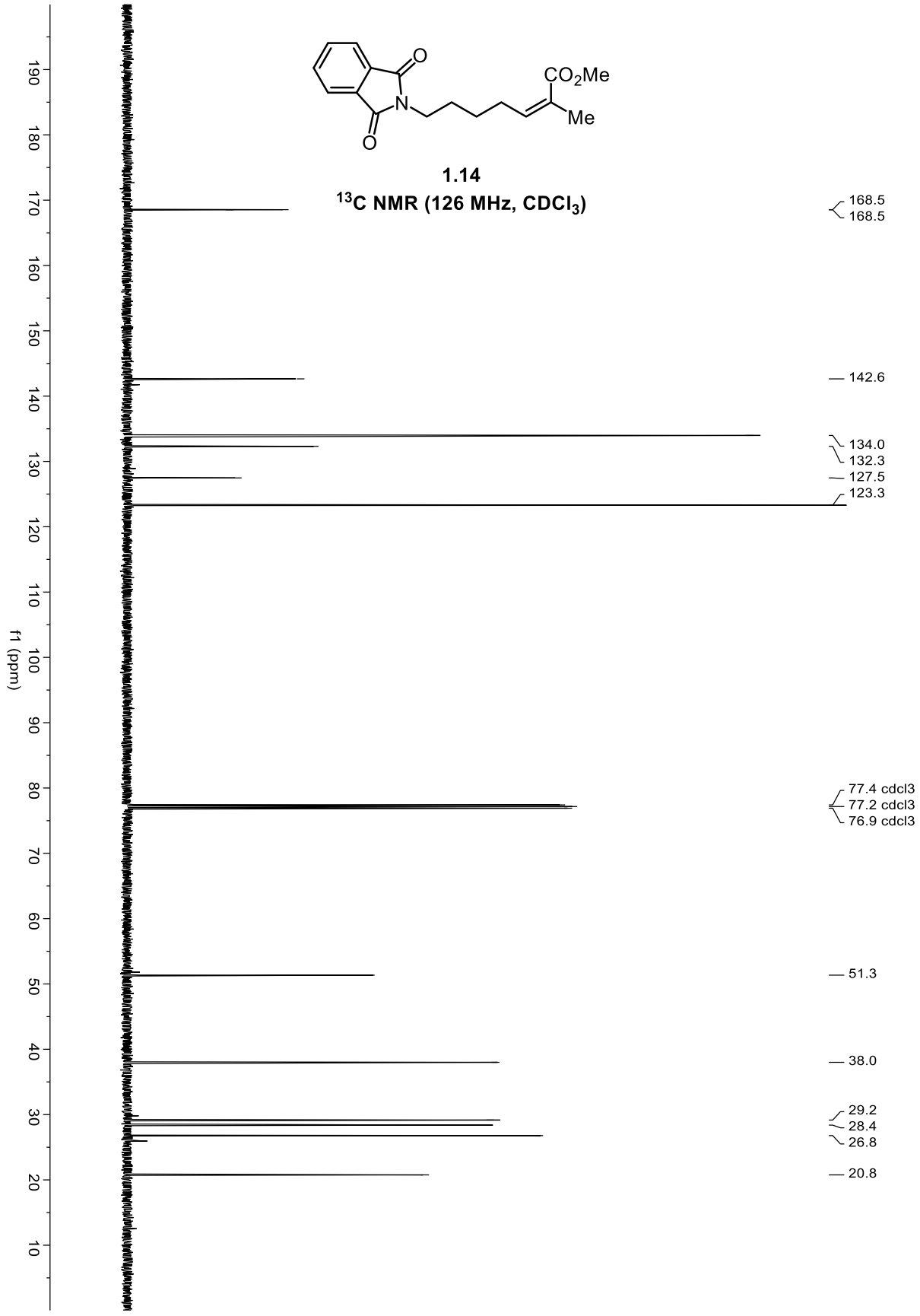
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127.5
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77.4 cdcl3
77.2 cdcl3
76.9 cdcl3
51.3
38.0
29.2
28.4
26.8
20.8
f1 (ppm)
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150
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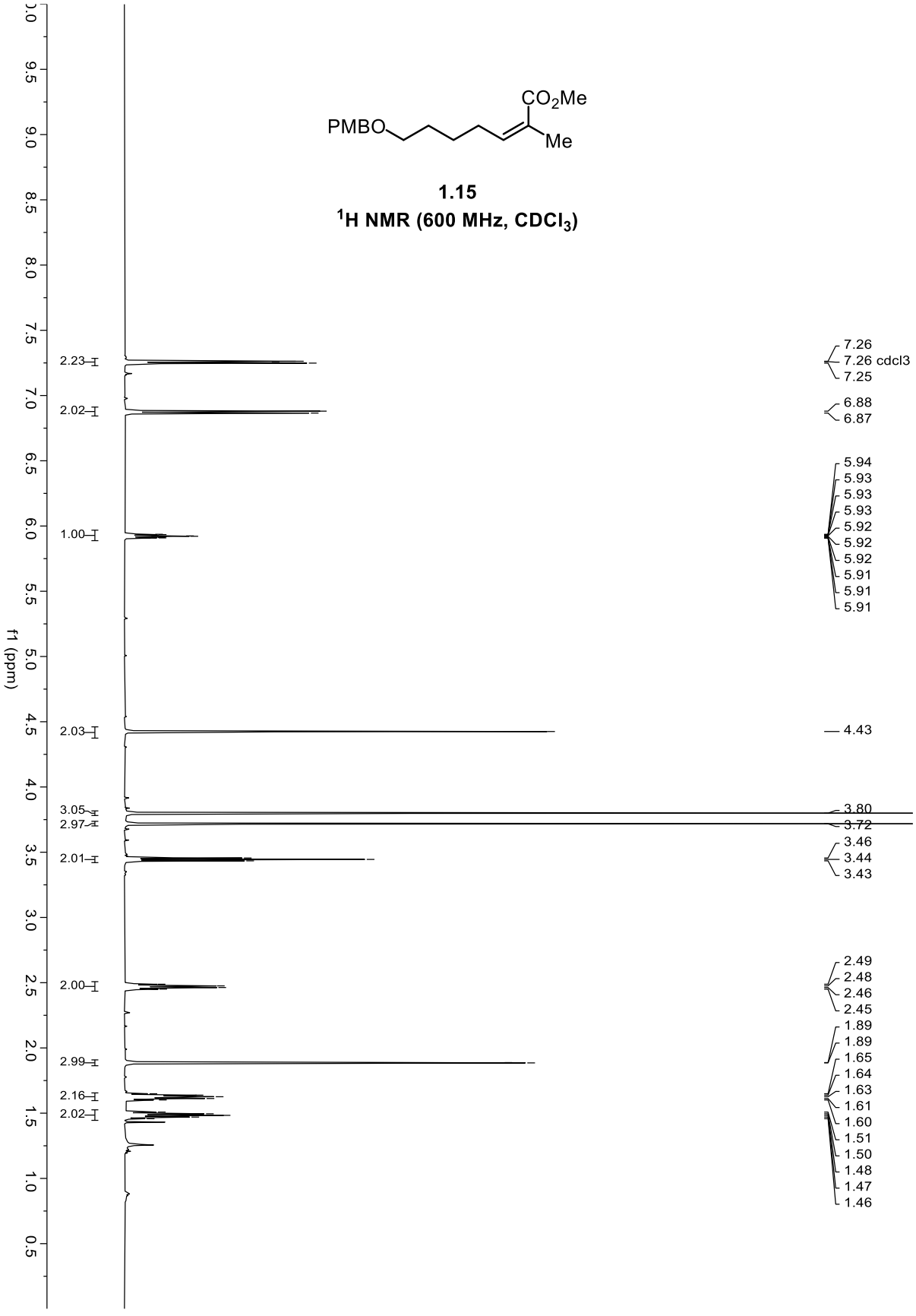
20
10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7.26 cdcl3
7.25
6.88
6.87
5.94
5.93
5.93
5.93
5.92
5.92
5.92
5.91
5.91
5.91
4.43
3.80
3.72
3.46
3.44
3.43
2.49
2.48
2.46
2.45
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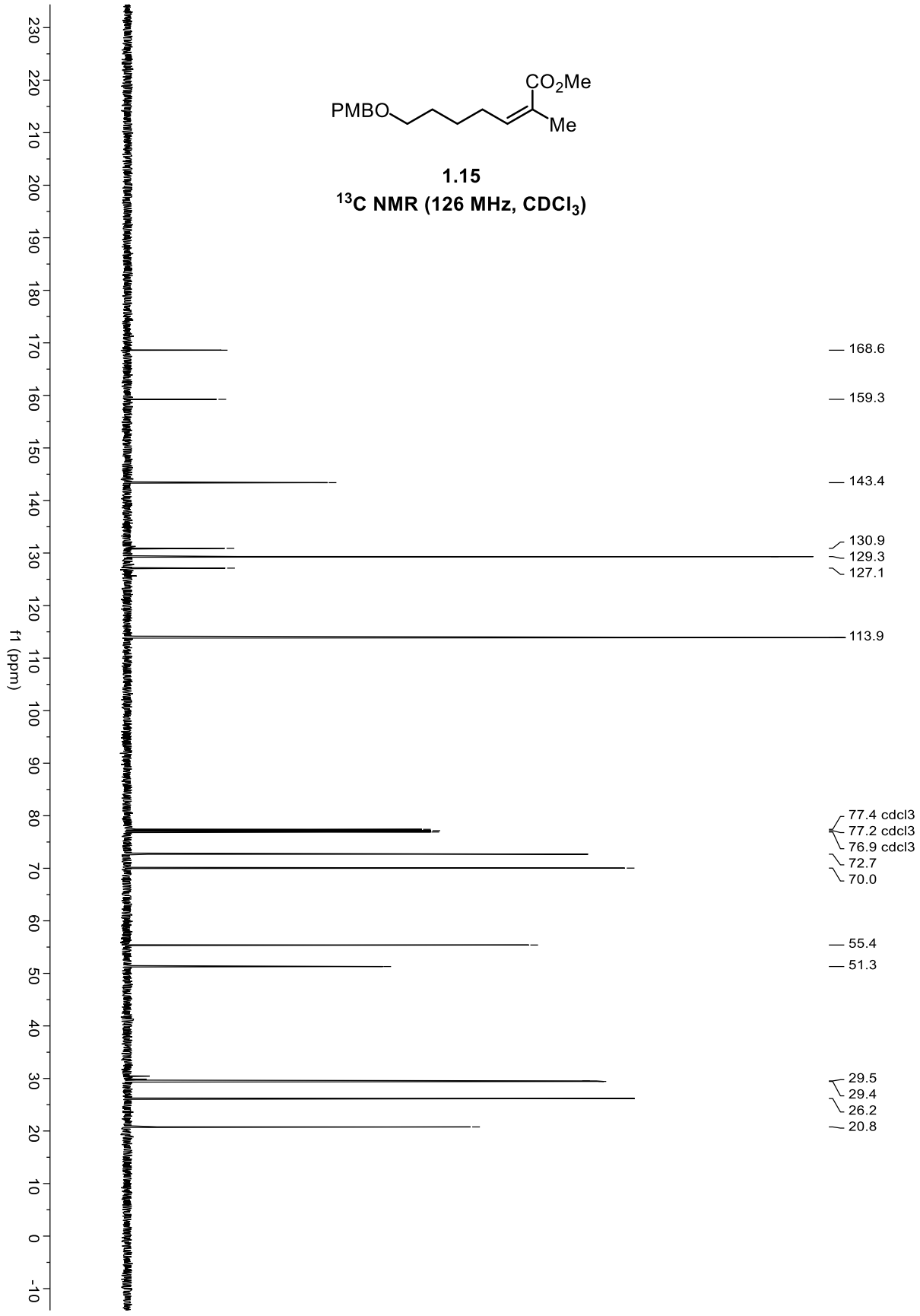
1.46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190
180
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160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
168.6
159.3
143.4
130.9
129.3
127.1
113.9
77.4 cdcl3
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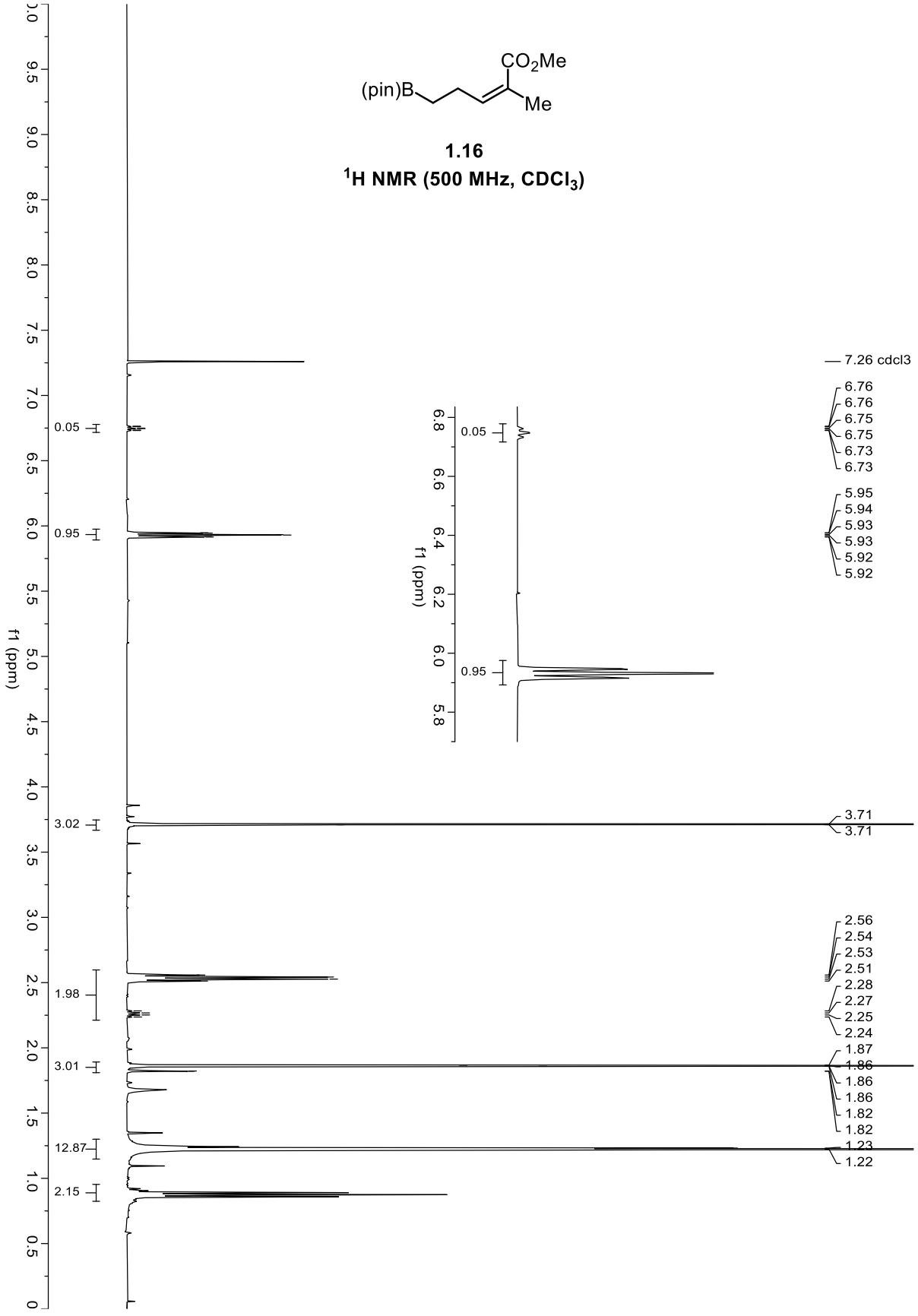
20.8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Me
1.16
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6.75
6.73
6.73
5.95
5.94
5.93
5.93
5.92
5.92
3.71
3.71
2.56
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2.51
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2.27
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1.86
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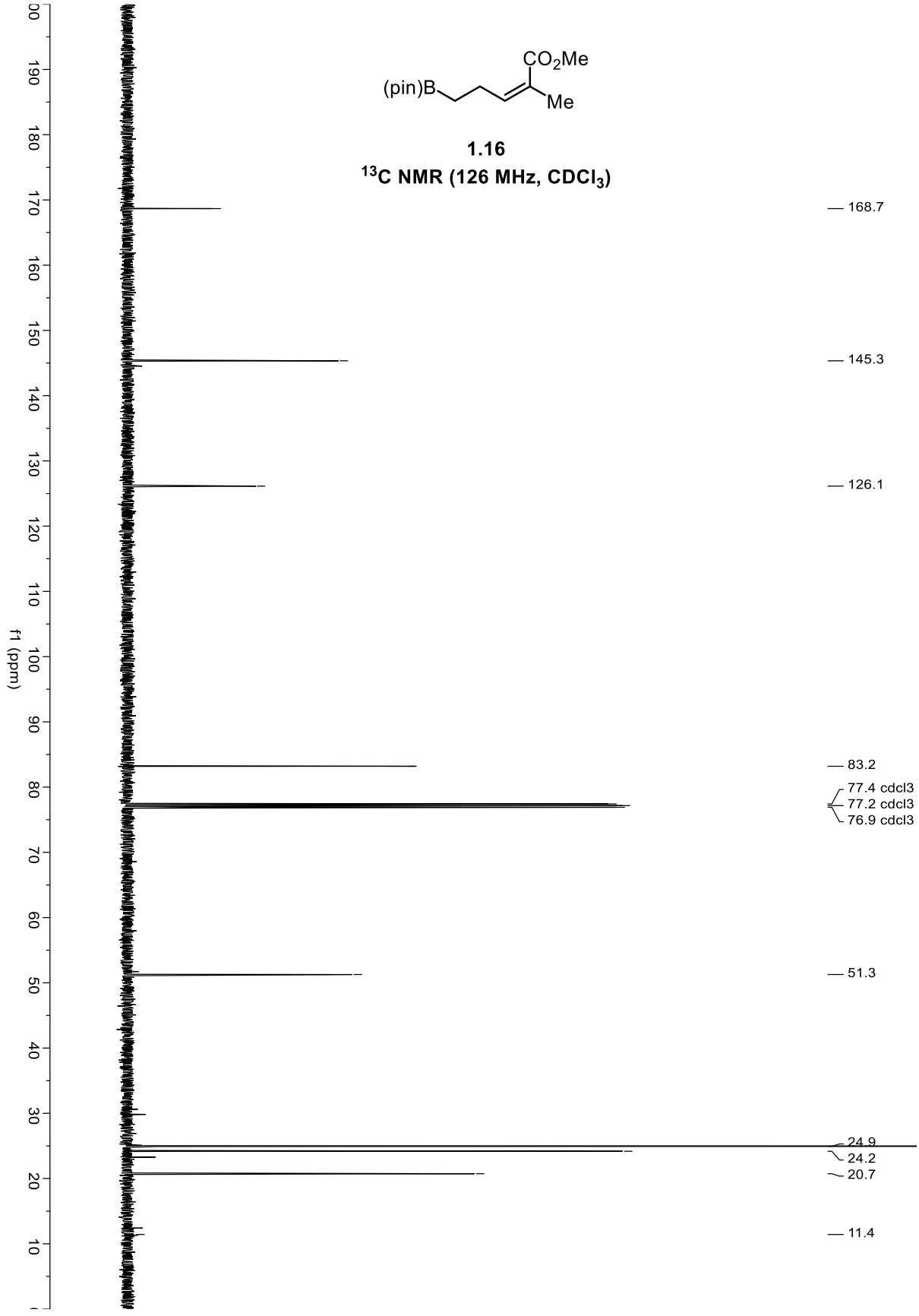
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(pin)B
Me
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f1 (ppm)
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145.3
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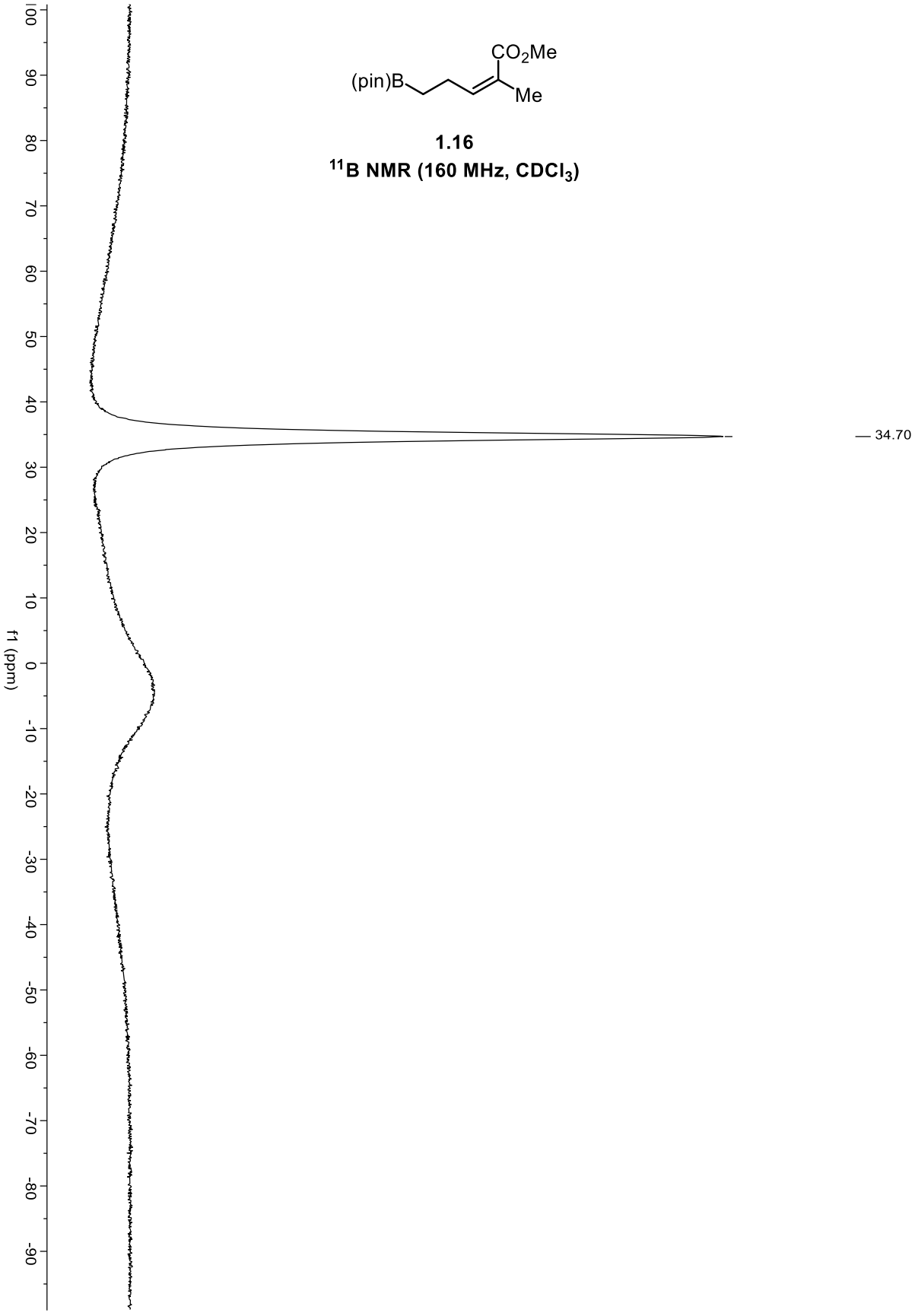
51.3
24.9
24.2
20.7
11.4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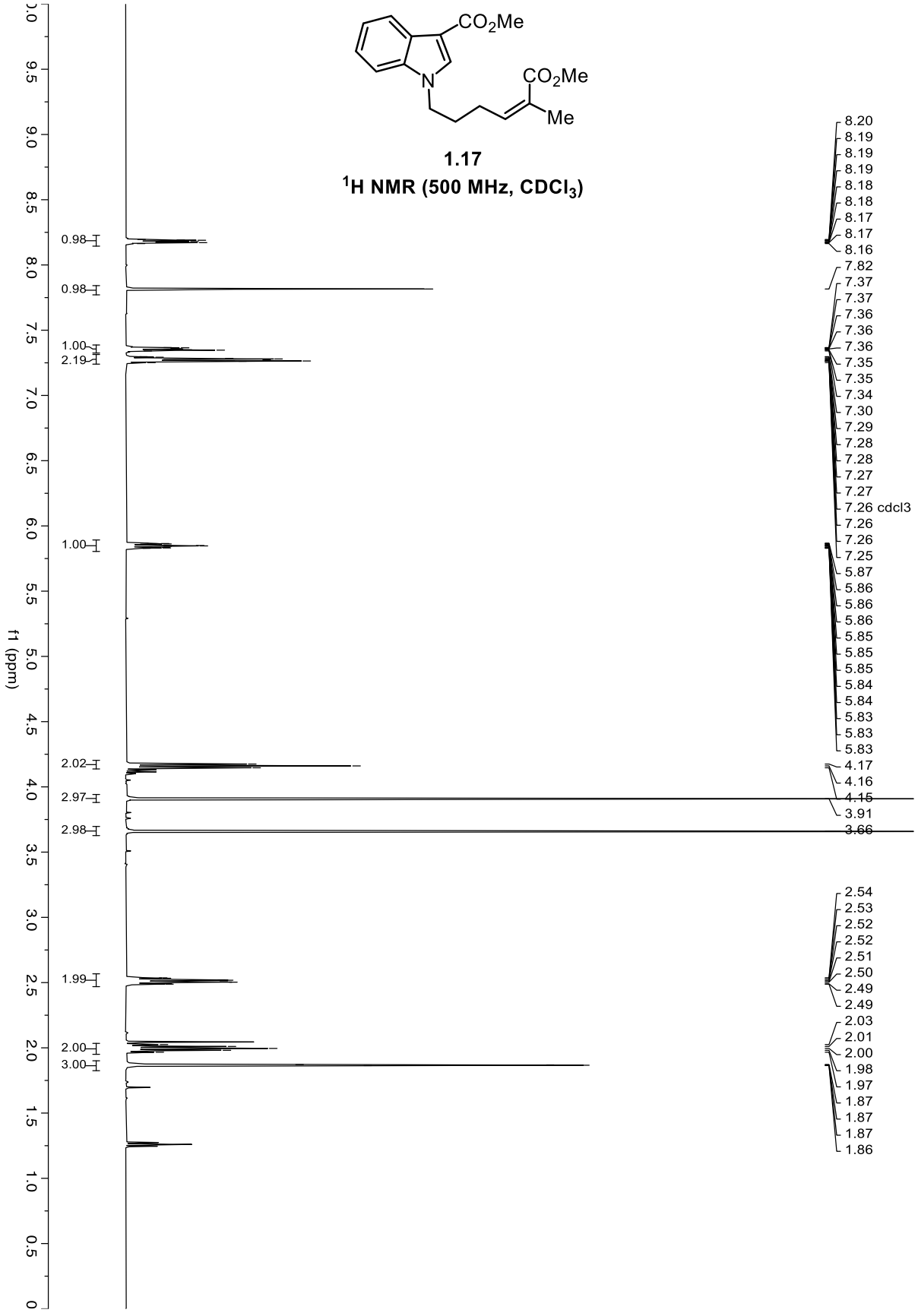
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CO2Me
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2.02
2.97
2.98
1.99
2.00
3.00
8.20
8.19
8.19
8.19
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8.18
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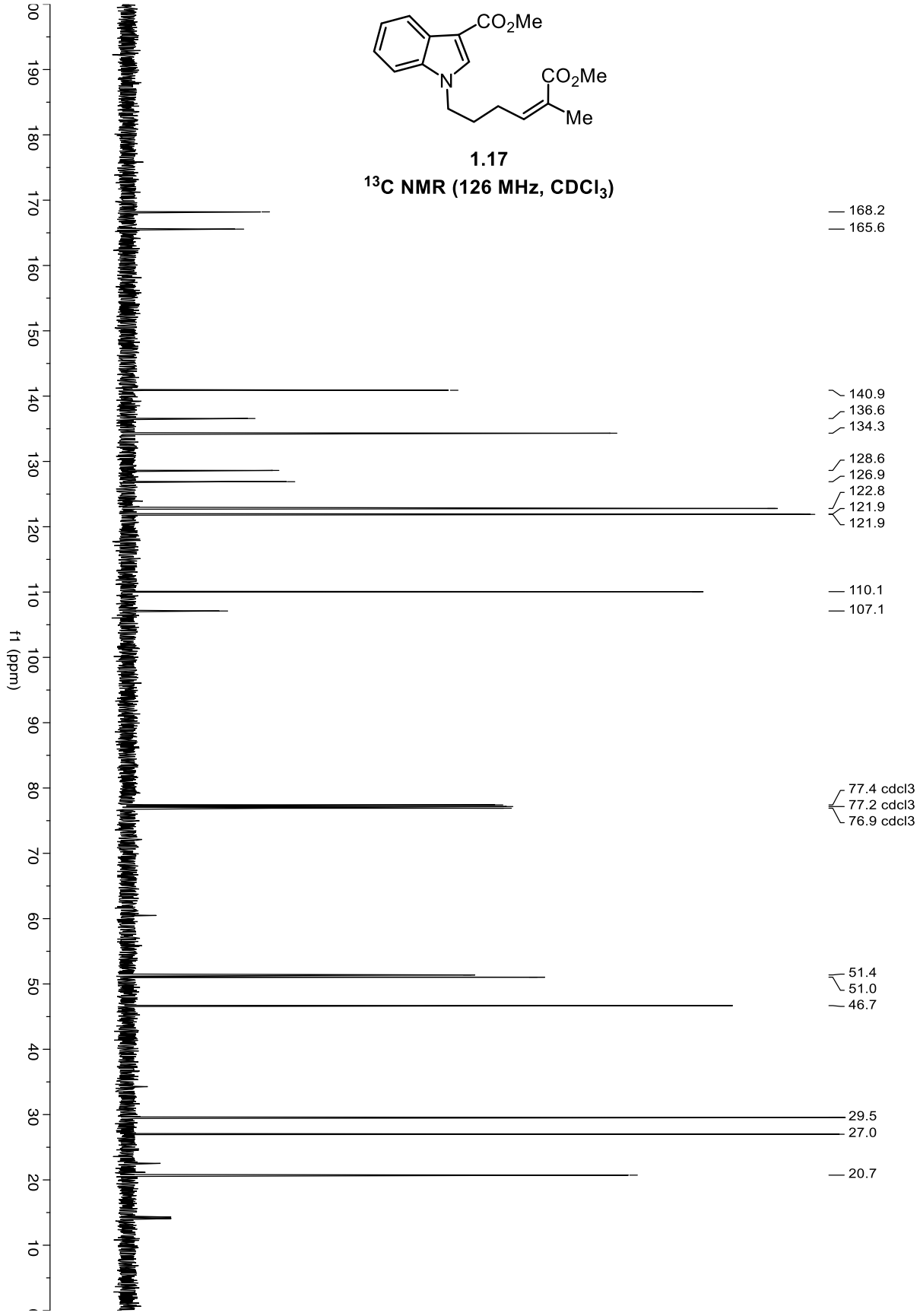
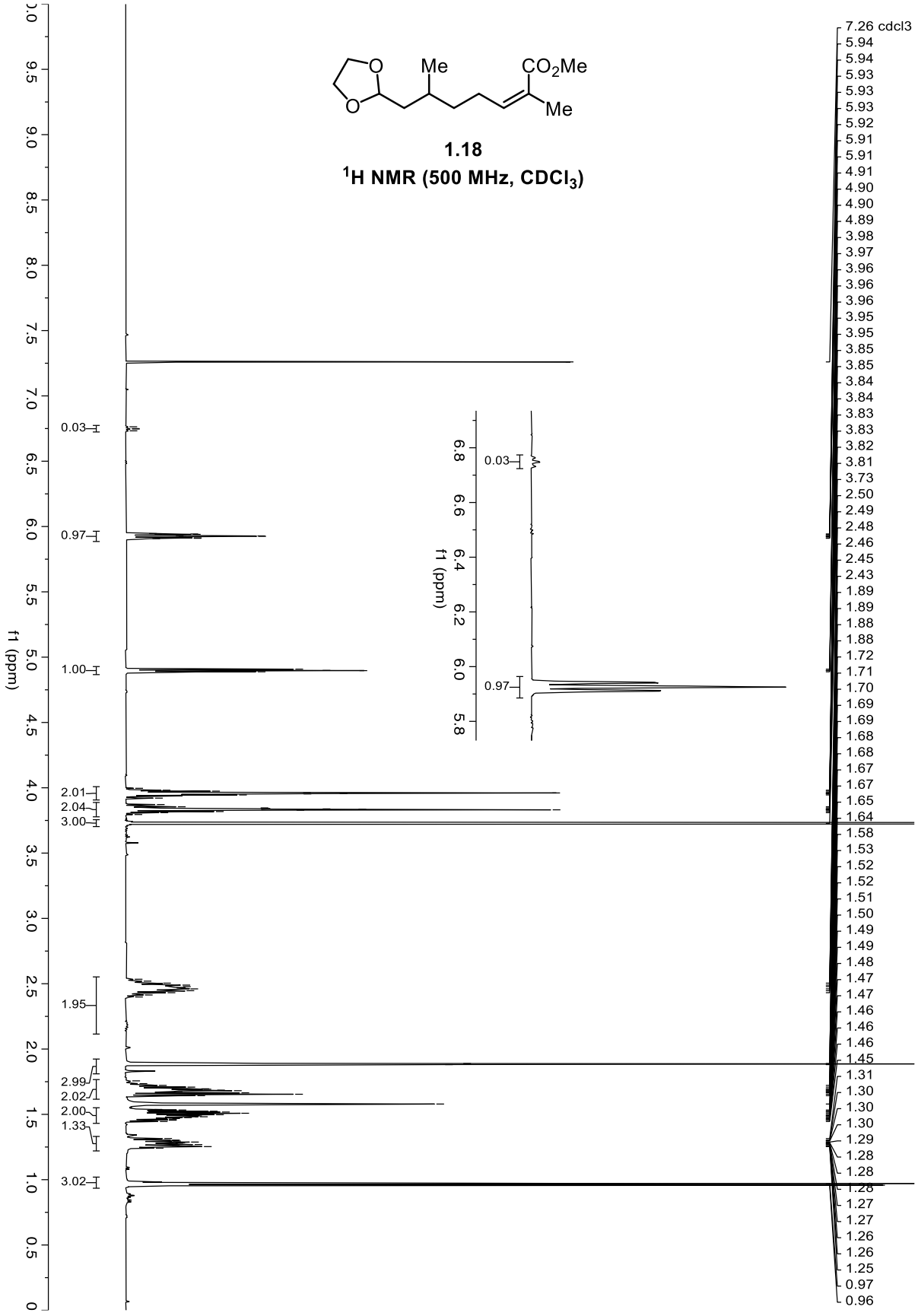
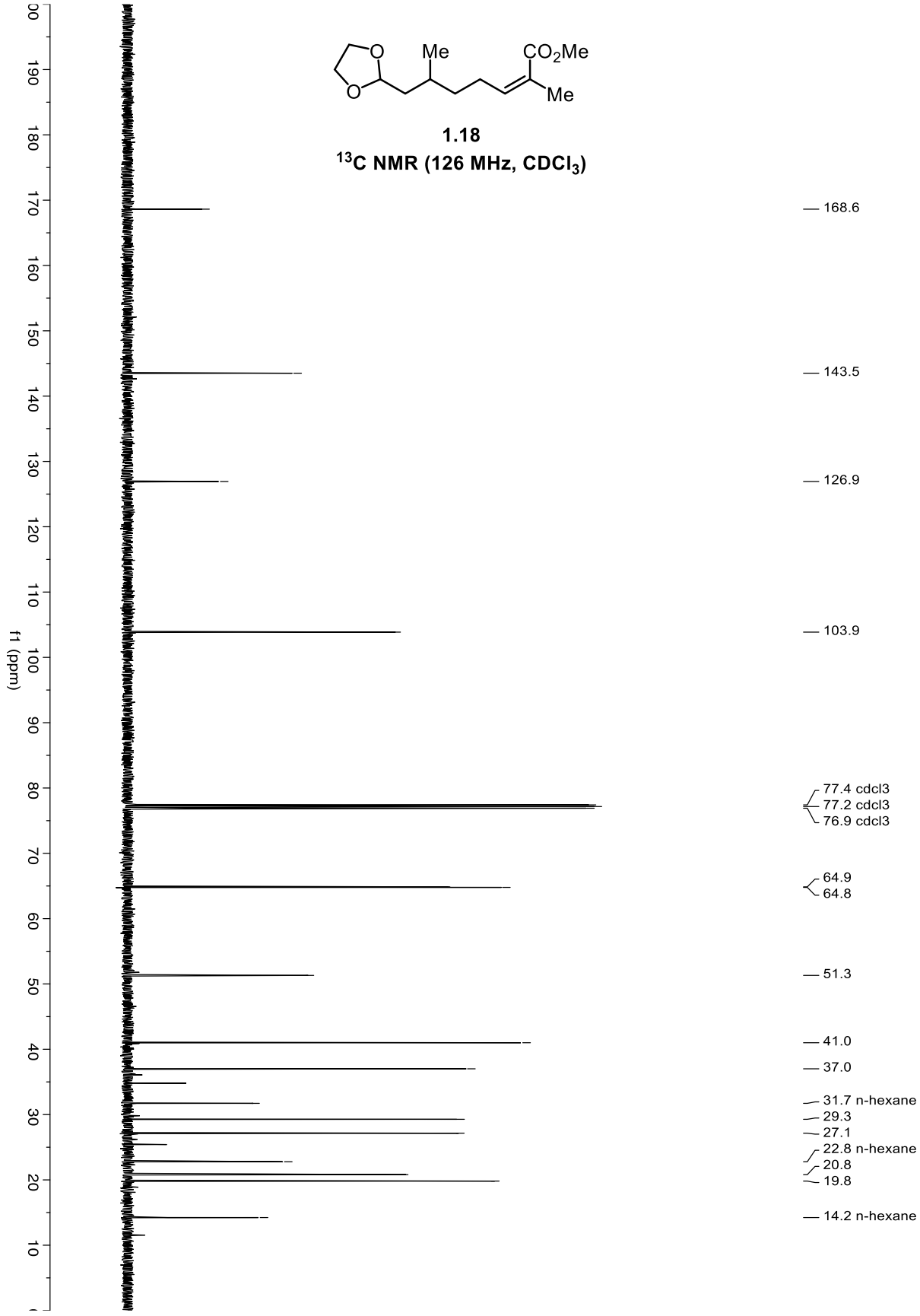
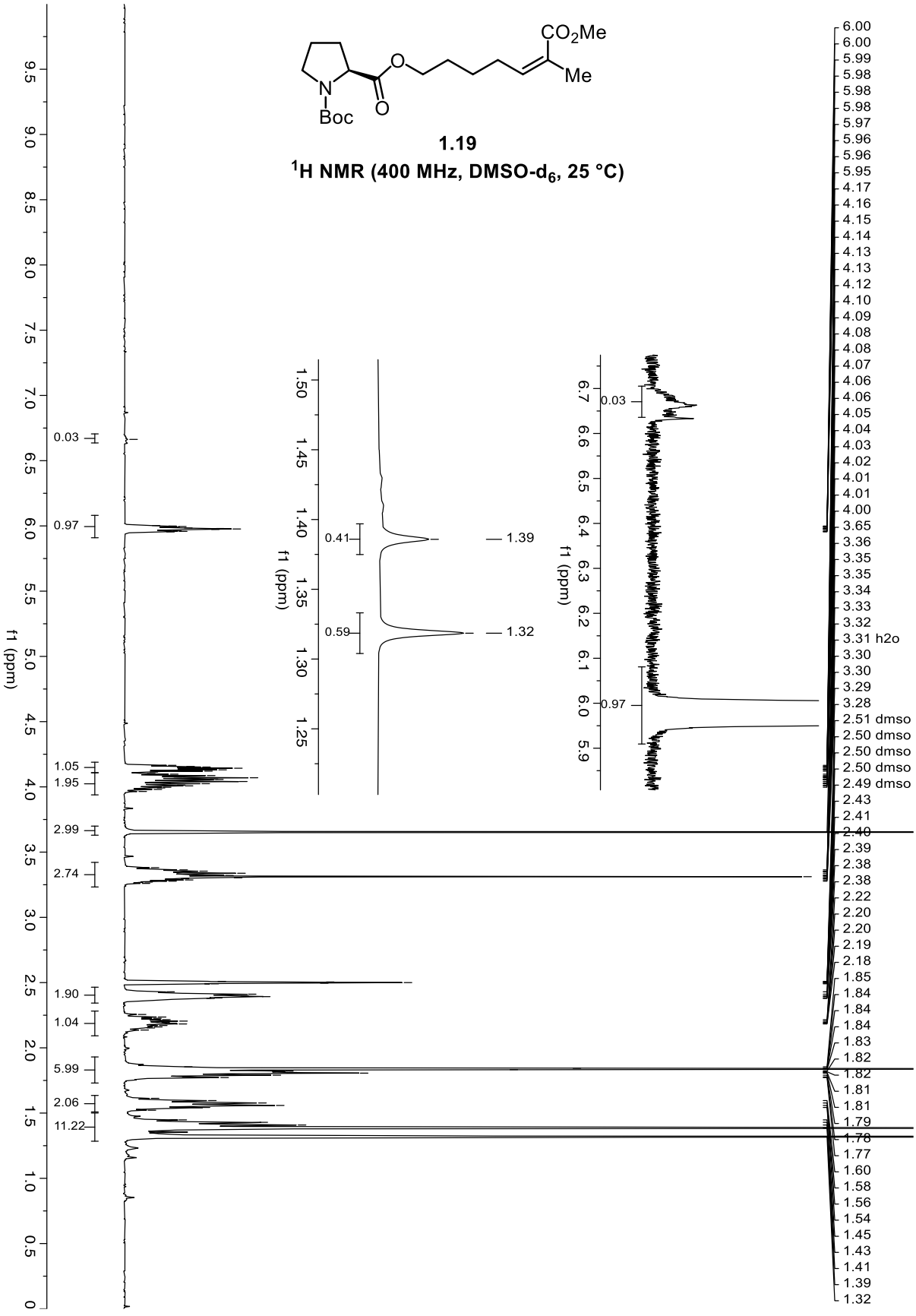
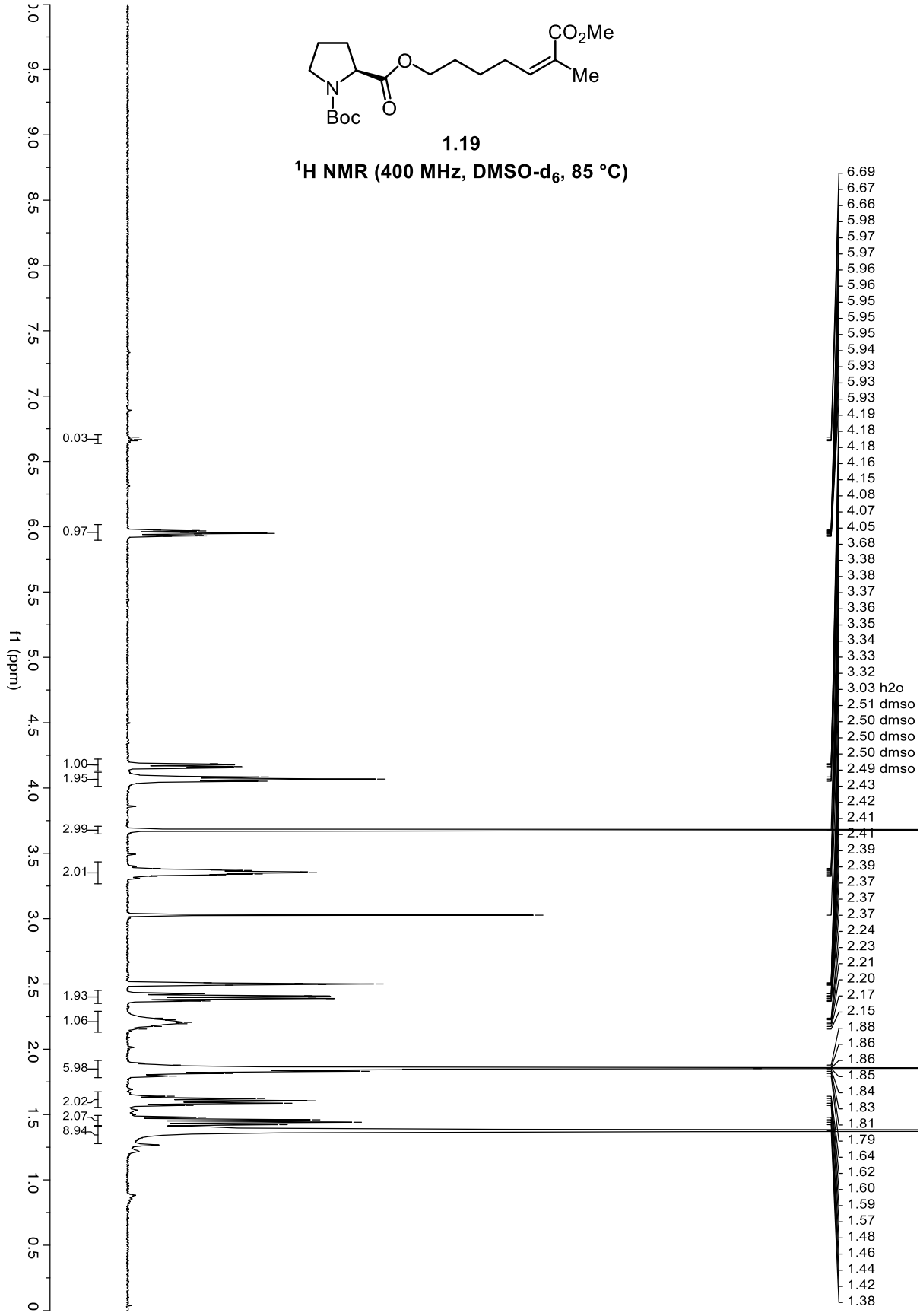
7.26 cdcl3
7.26
7.26
7.25
5.87
5.86
5.86
5.86
5.85
5.85
5.85
5.84
5.84
5.83
5.83
5.83
4.17
4.16
4.15
3.91
3.66
2.54
2.53
2.52
2.52
2.51
2.50
2.49
2.49
2.03
2.01
2.00
1.98
1.97
1.87
1.87
1.87
1.86

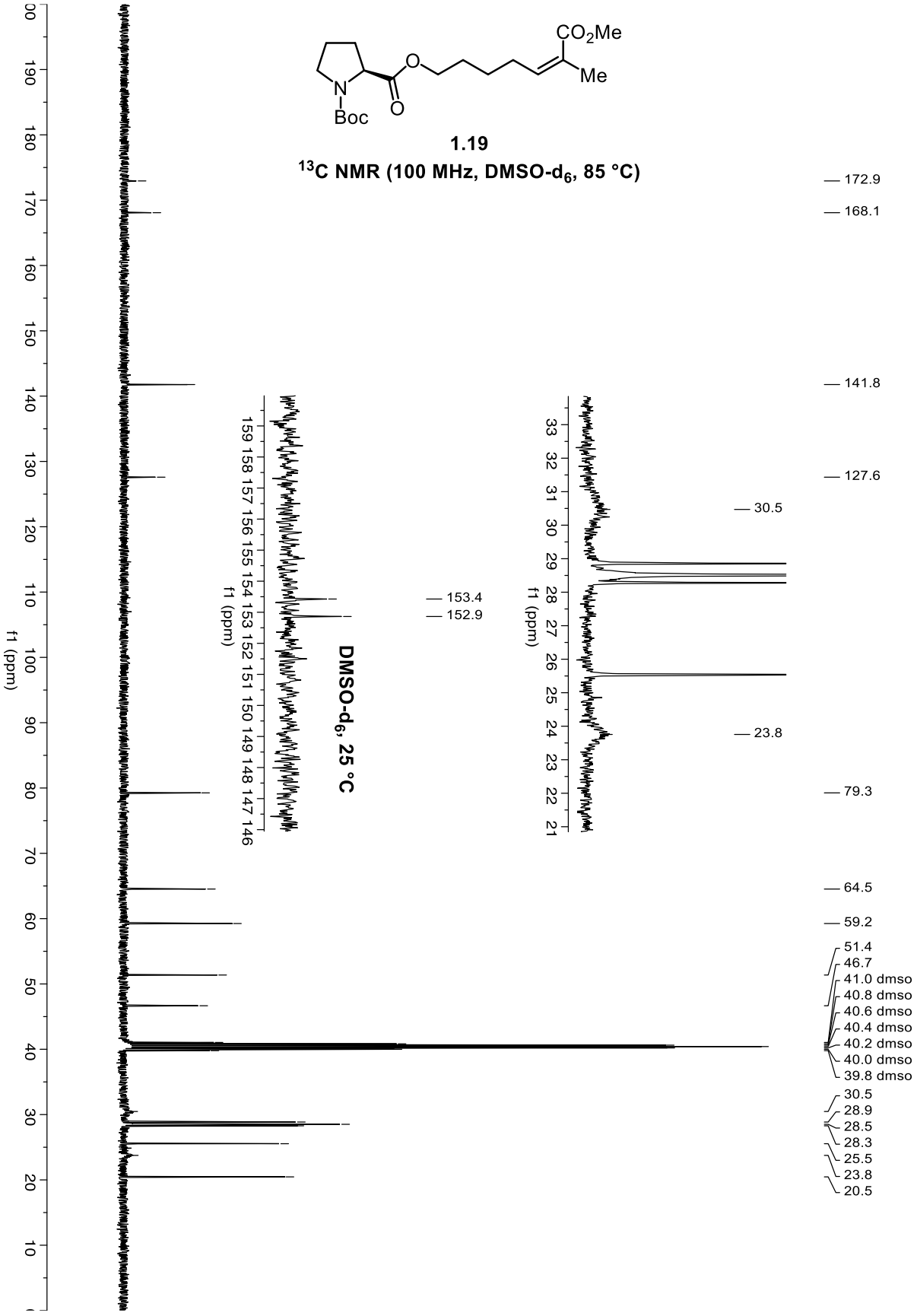

CO2Me
CO2Me
N
Me
1.17
13C NMR (126 MHz, CDCl3)
168.2
165.6
140.9
136.6
134.3
128.6
126.9
122.8
121.9
121.9
110.1
107.1
77.4 cdcl3
77.2 cdcl3
76.9 cdcl3
51.4
51.0
46.7
29.5
27.0
20.7
f1 (ppm)

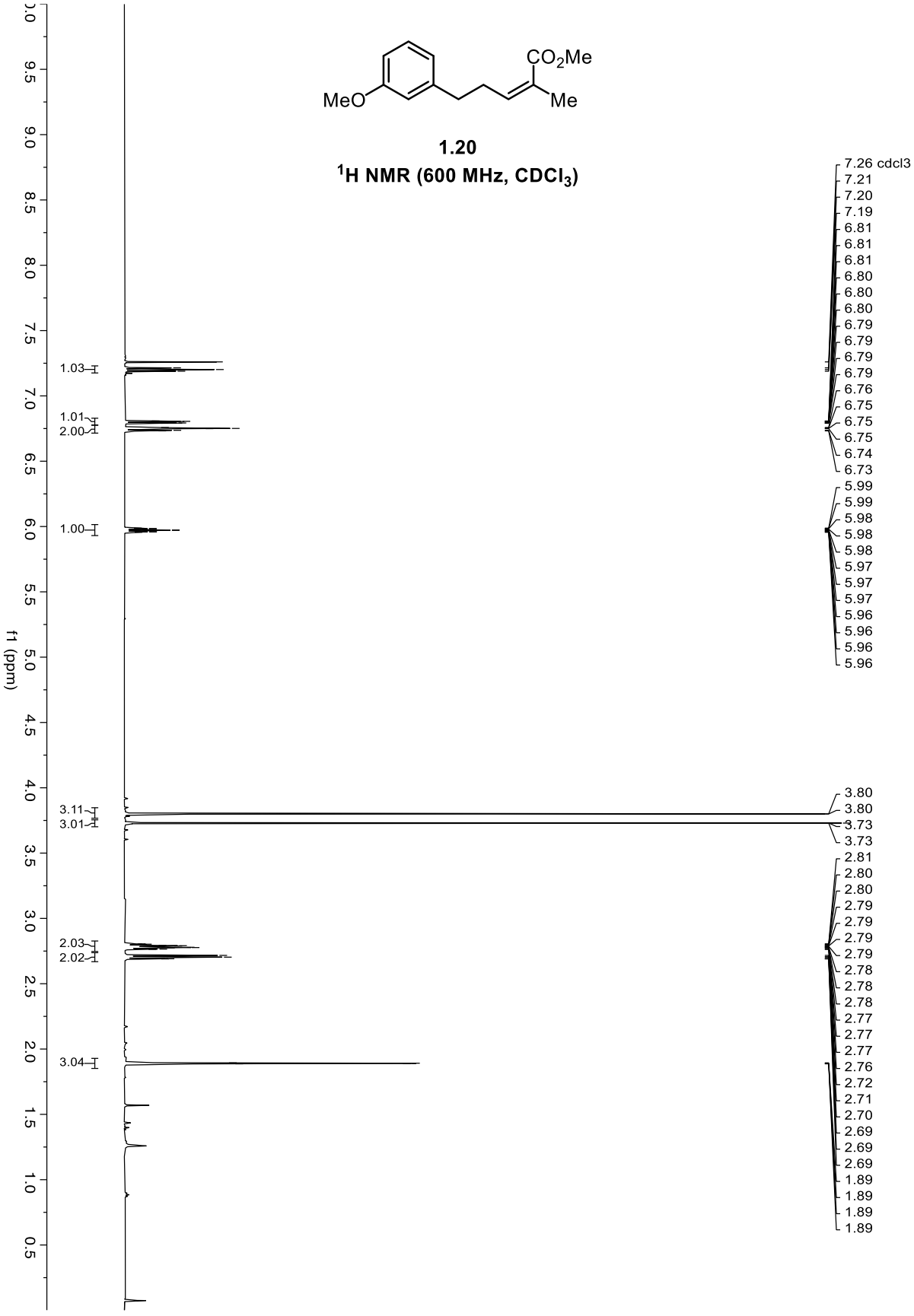

Me
CO2Me
Me
O
O
1.18
1H NMR (500 MHz, CDCl3)
f1 (ppm)
0.03
0.97
1.00
2.01
2.04
3.00
1.95
2.99
2.02
2.00
1.33
3.02
7.26 cdcl3

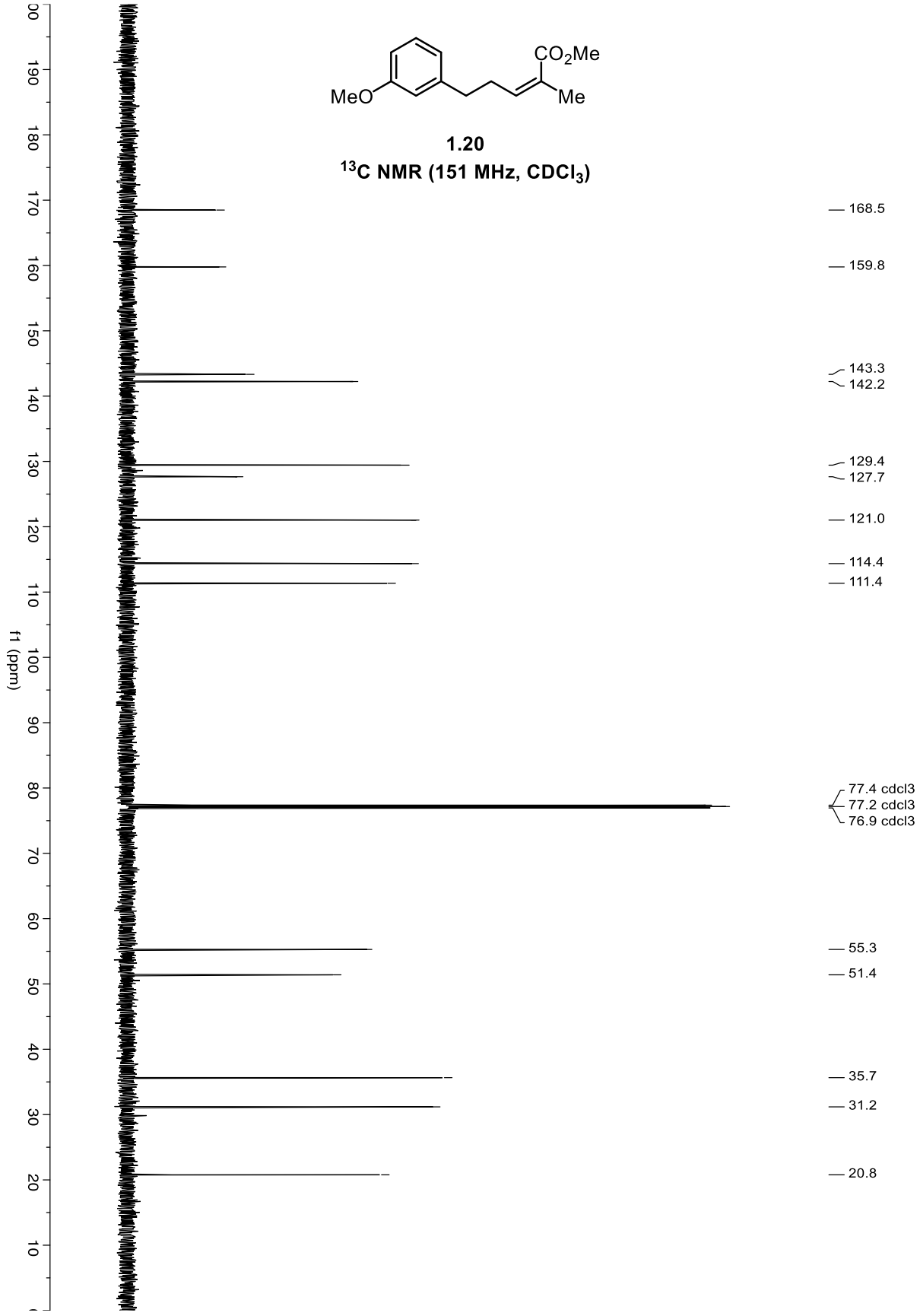

Me
CO_2Me
Me
O
O
1.18
^{13}C NMR (126 MHz, $CDCl_3$)
f1 (ppm)
168.6
143.5
126.9
103.9
77.4 cdcl3
77.2 cdcl3
76.9 cdcl3
64.9
64.8
51.3
41.0
37.0
31.7 n-hexane
29.3
27.1
22.8 n-hexane
20.8
19.8
14.2 n-hexane

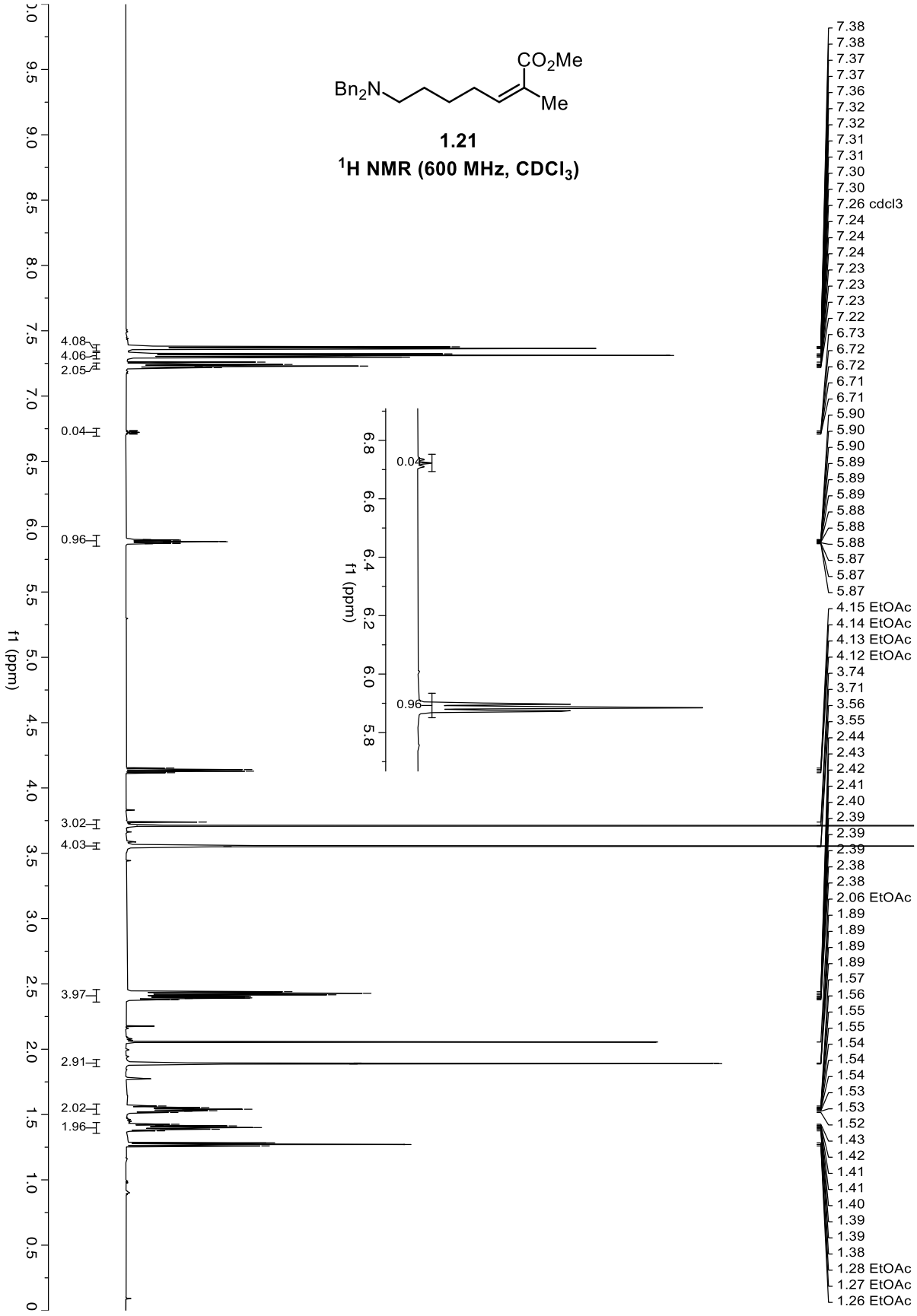

CO2Me
Me
O
N
Boc
O
1.19
1H NMR (400 MHz, DMSO-d6, 25 °C)
f1 (ppm)
0.03
0.97
1.05
1.95
2.99
2.74
1.90
1.04
5.99
2.06
11.22
0.41
0.59
1.39
1.32
2.51 dmso
2.50 dmso
2.49 dmso
3.31 h2o

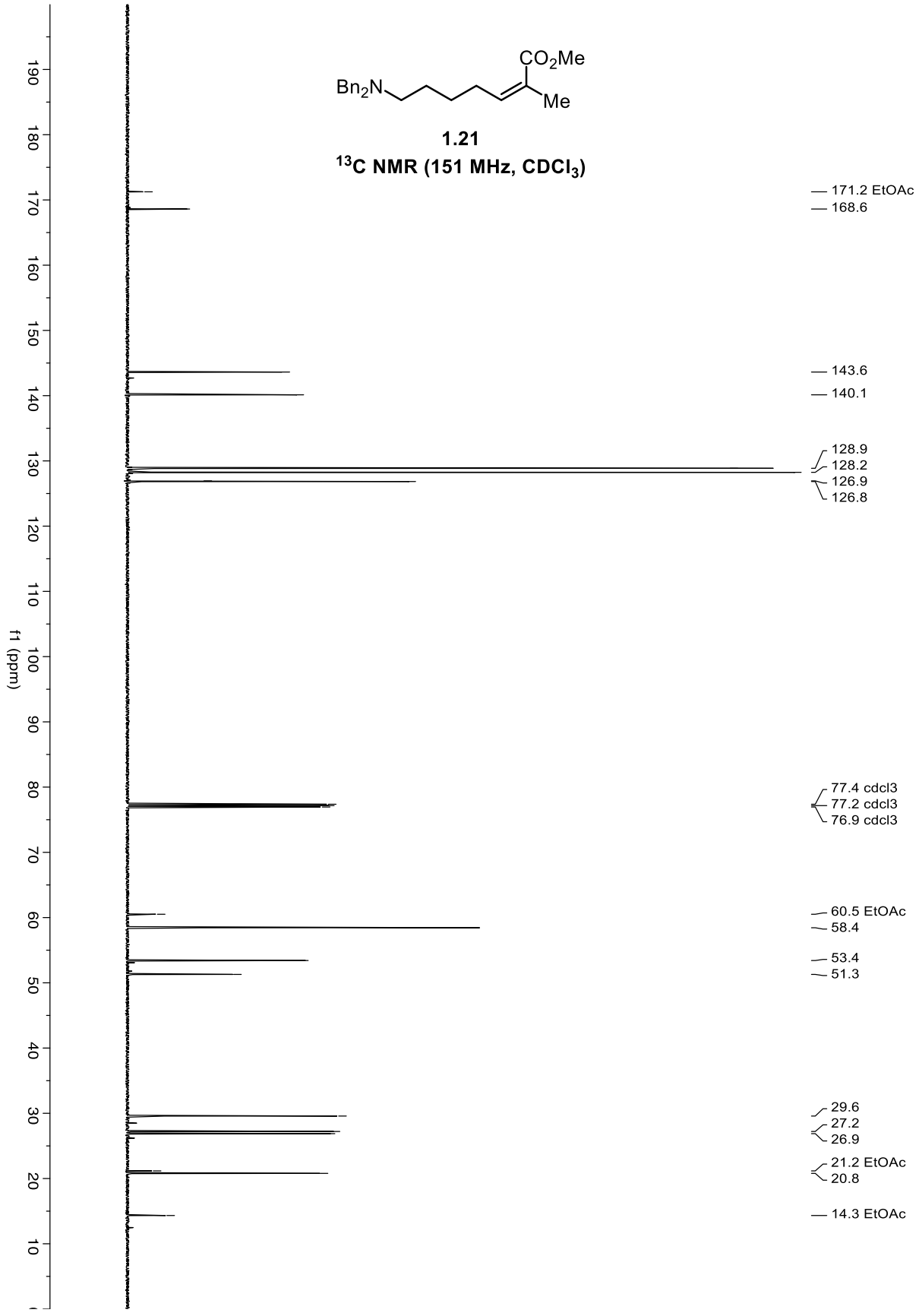

CO2Me
Me
O
N
Boc
O
1.19
1H NMR (400 MHz, DMSO-d6, 85 °C)
f1 (ppm)
0.03
0.97
1.00
1.95
2.99
2.01
1.93
1.06
5.98
2.02
2.07
8.94
6.69
6.67
6.66
5.98
5.97
5.97
5.96
5.96
5.95
5.95
5.95
5.94
5.93
5.93
5.93
4.19
4.18
4.18
4.16
4.15
4.08
4.07
4.05
3.68
3.38
3.38
3.37
3.36
3.35
3.34
3.33
3.32
3.03 h2o
2.51 dmso
2.50 dmso
2.50 dmso
2.50 dmso
2.49 dmso
2.43
2.42
2.41
2.41
2.39
2.39
2.37
2.37
2.37
2.24
2.23
2.21
2.20
2.17
2.15
1.88
1.86
1.86
1.85
1.84
1.83
1.81
1.79
1.64
1.62
1.60
1.59
1.57
1.48
1.46
1.44
1.42
1.38

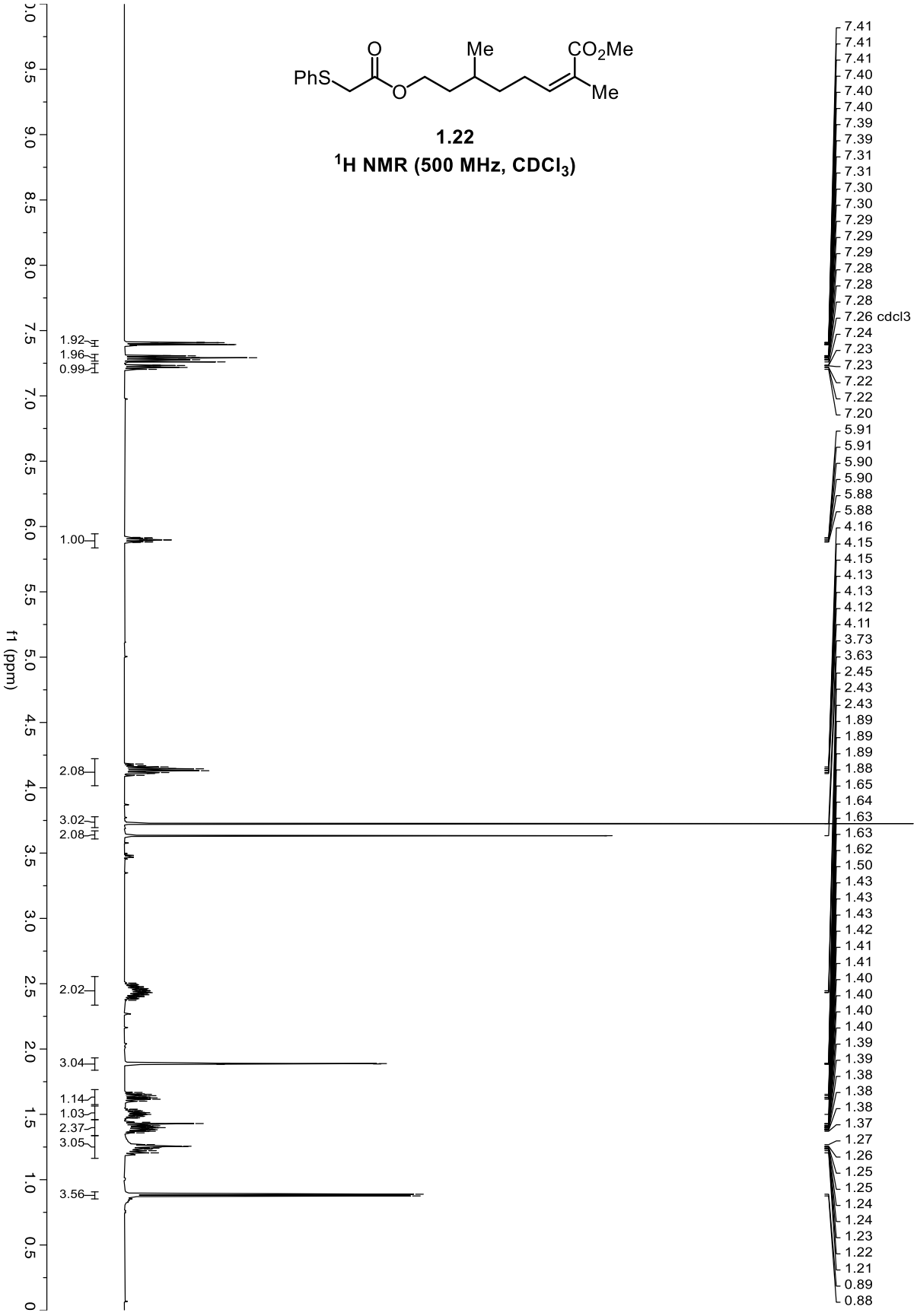

CO2Me
Me
O
N
Boc
O
1.19
13C NMR (100 MHz, DMSO-d6, 85 °C)
172.9
168.1
141.8
127.6
30.5
23.8
79.3
64.5
59.2
51.4
46.7
41.0 dmso
40.8 dmso
40.6 dmso
40.4 dmso
40.2 dmso
40.0 dmso
39.8 dmso
30.5
28.9
28.5
28.3
25.5
23.8
20.5
153.4
152.9
DMSO-d6, 25 °C
f1 (ppm)

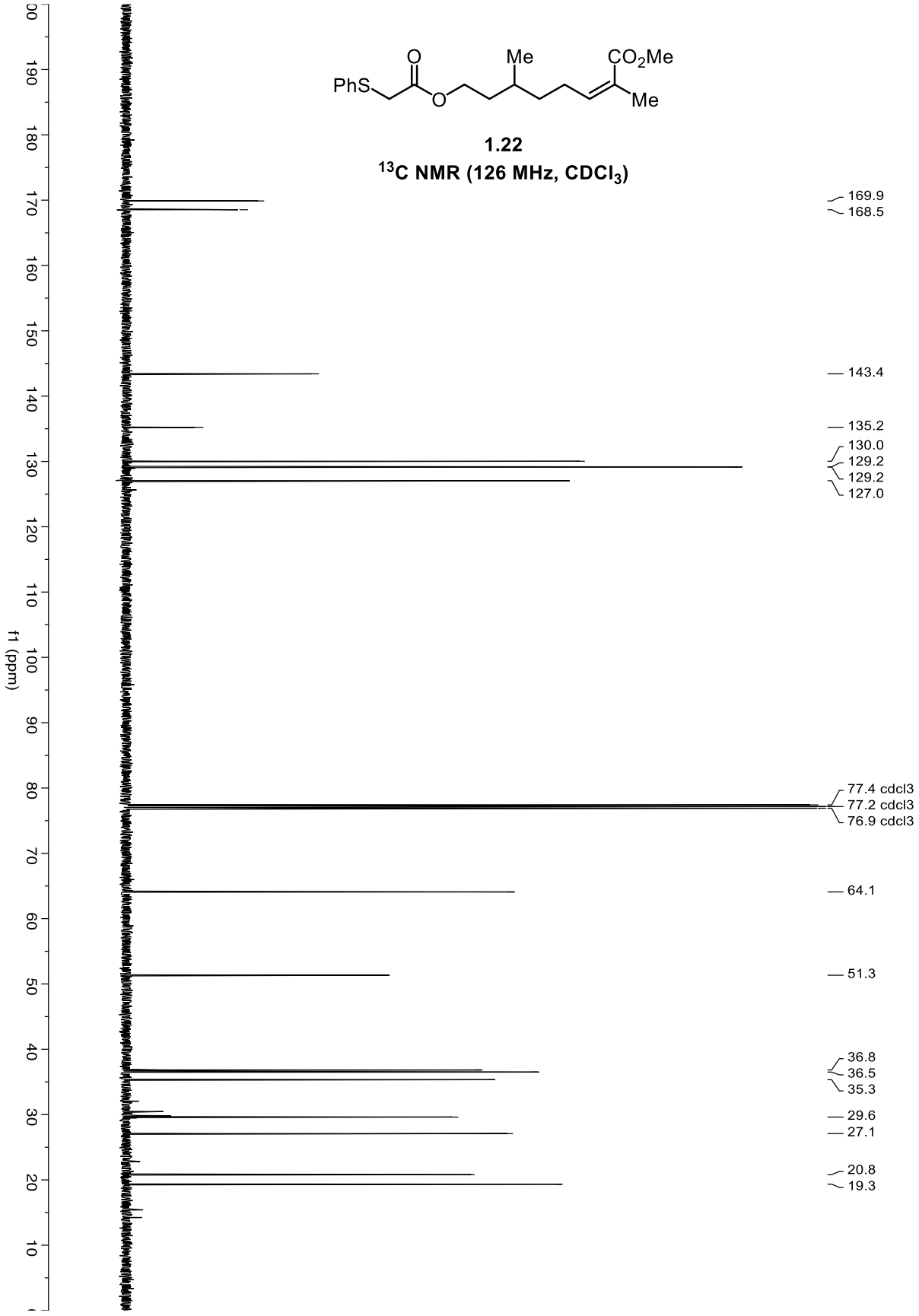

CO2Me
MeO
Me
1.20
1H NMR (600 MHz, CDCl3)
7.26 cdcl3
7.21
7.20
7.19
6.81
6.81
6.81
6.80
6.80
6.80
6.79
6.79
6.79
6.79
6.76
6.75
6.75
6.75
6.74
6.73
5.99
5.99
5.98
5.98
5.98
5.97
5.97
5.97
5.96
5.96
5.96
5.96
3.80
3.80
3.73
3.73
2.81
2.80
2.80
2.79
2.79
2.79
2.79
2.78
2.78
2.78
2.77
2.77
2.77
2.76
2.72
2.71
2.70
2.69
2.69
2.69
1.89
1.89
1.89
1.89
1.03
1.01
2.00
1.00
3.11
3.01
2.03
2.02
3.04
f1 (ppm)


MeO
CO2Me
Me
1.20
13C NMR (151 MHz, CDCl3)
f1 (ppm)
168.5
159.8
143.3
142.2
129.4
127.7
121.0
114.4
111.4
77.4 cdcl3
77.2 cdcl3
76.9 cdcl3
55.3
51.4
35.7
31.2
20.8


CO2Me
Bn2N
Me
1.21
1H NMR (600 MHz, CDCl3)
f1 (ppm)
4.08
4.06
2.05
0.04
0.96
3.02
4.03
3.97
2.91
2.02
1.96
7.38
7.37
7.36
7.32
7.31
7.30
7.26 cdcl3
7.24
7.23
7.22
6.73
6.72
6.71
5.90
5.89
5.88
5.87
4.15 EtOAc
4.14 EtOAc
4.13 EtOAc
4.12 EtOAc
3.74
3.71
3.56
3.55
2.44
2.43
2.42
2.41
2.40
2.39
2.38
2.06 EtOAc
1.89
1.57
1.56
1.55
1.54
1.53
1.52
1.43
1.42
1.41
1.40
1.39
1.38
1.28 EtOAc
1.27 EtOAc
1.26 EtOAc

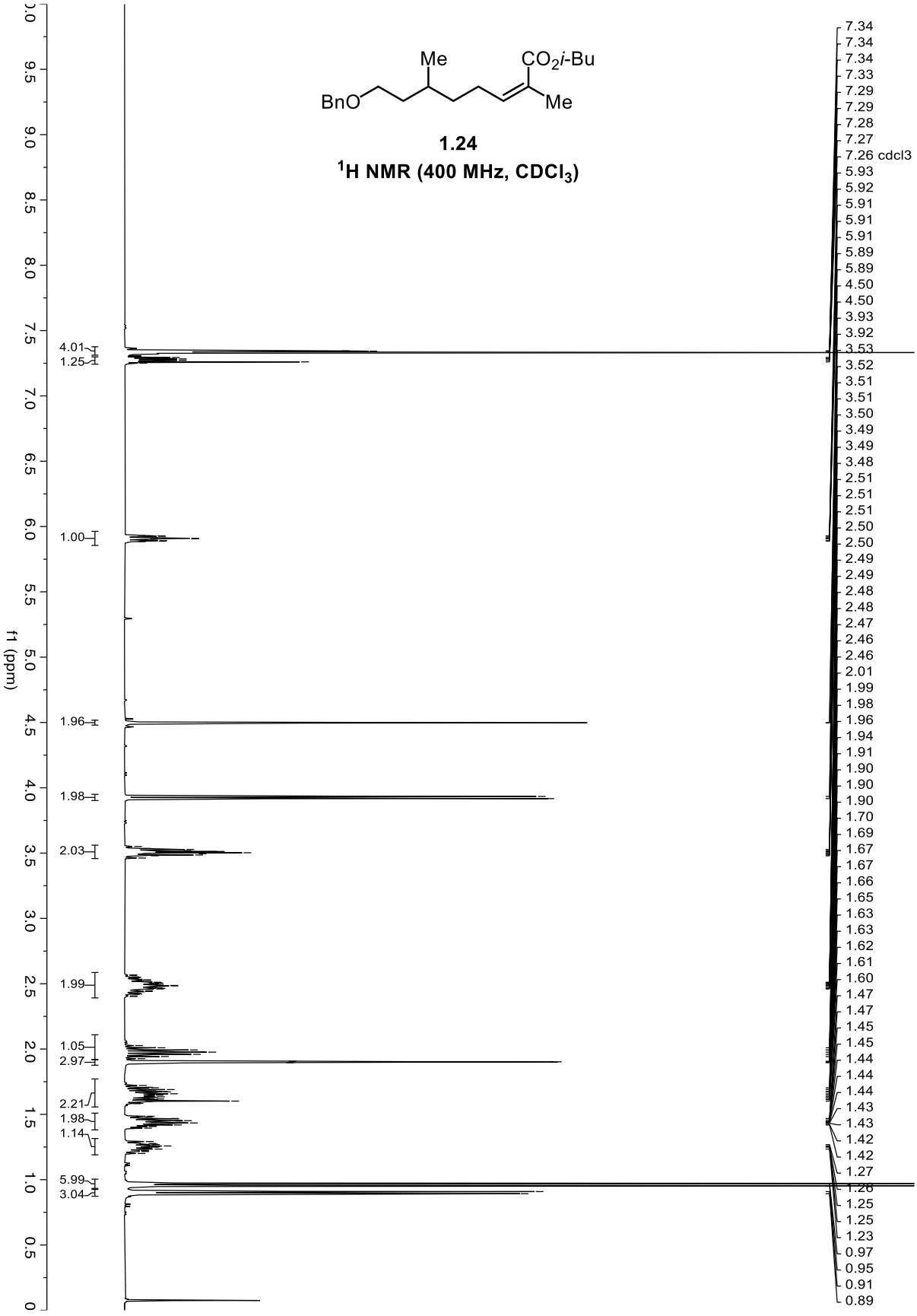

CO2Me
Bn2N
Me
1.21
13C NMR (151 MHz, CDCl3)
171.2 EtOAc
168.6
143.6
140.1
128.9
128.2
126.9
126.8
77.4 cdcl3
77.2 cdcl3
76.9 cdcl3
60.5 EtOAc
58.4
53.4
51.3
29.6
27.2
26.9
21.2 EtOAc
20.8
14.3 EtOAc
f1 (ppm)

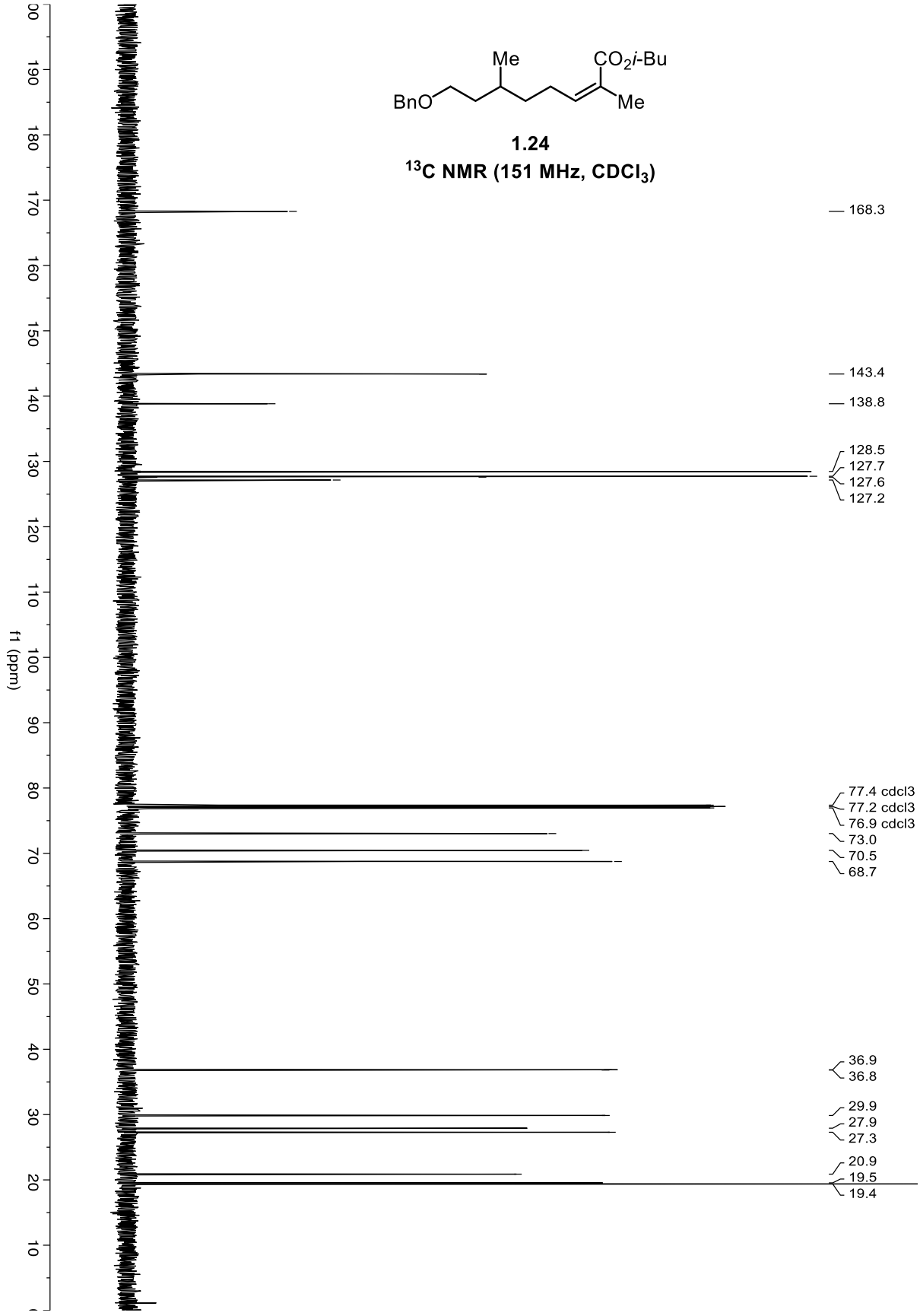

PhS
O
O
Me
CO2Me
Me
1.22
1H NMR (500 MHz, CDCl3)
f1 (ppm)
1.92
1.96
0.99
1.00
2.08
3.02
2.08
2.02
3.04
1.14
1.03
2.37
3.05
3.56
7.41
7.40
7.39
7.31
7.30
7.29
7.28
7.26 cdcl3
7.24
7.23
7.22
7.20
5.91
5.90
5.88
4.16
4.15
4.13
4.12
4.11
3.73
3.63
2.45
2.43
1.89
1.88
1.65
1.64
1.63
1.62
1.50
1.43
1.42
1.41
1.40
1.39
1.38
1.37
1.27
1.26
1.25
1.24
1.23
1.22
1.21
0.89
0.88

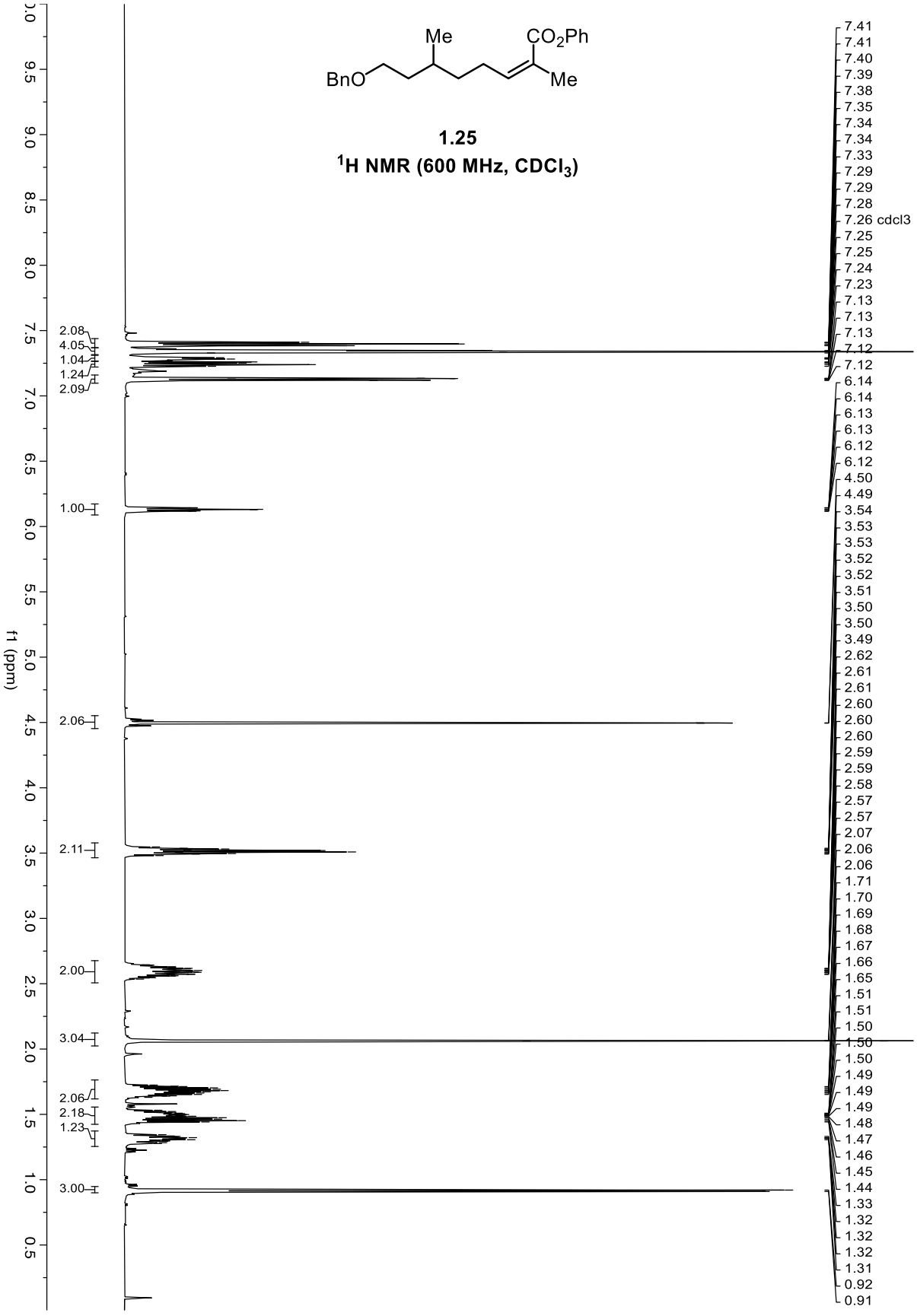


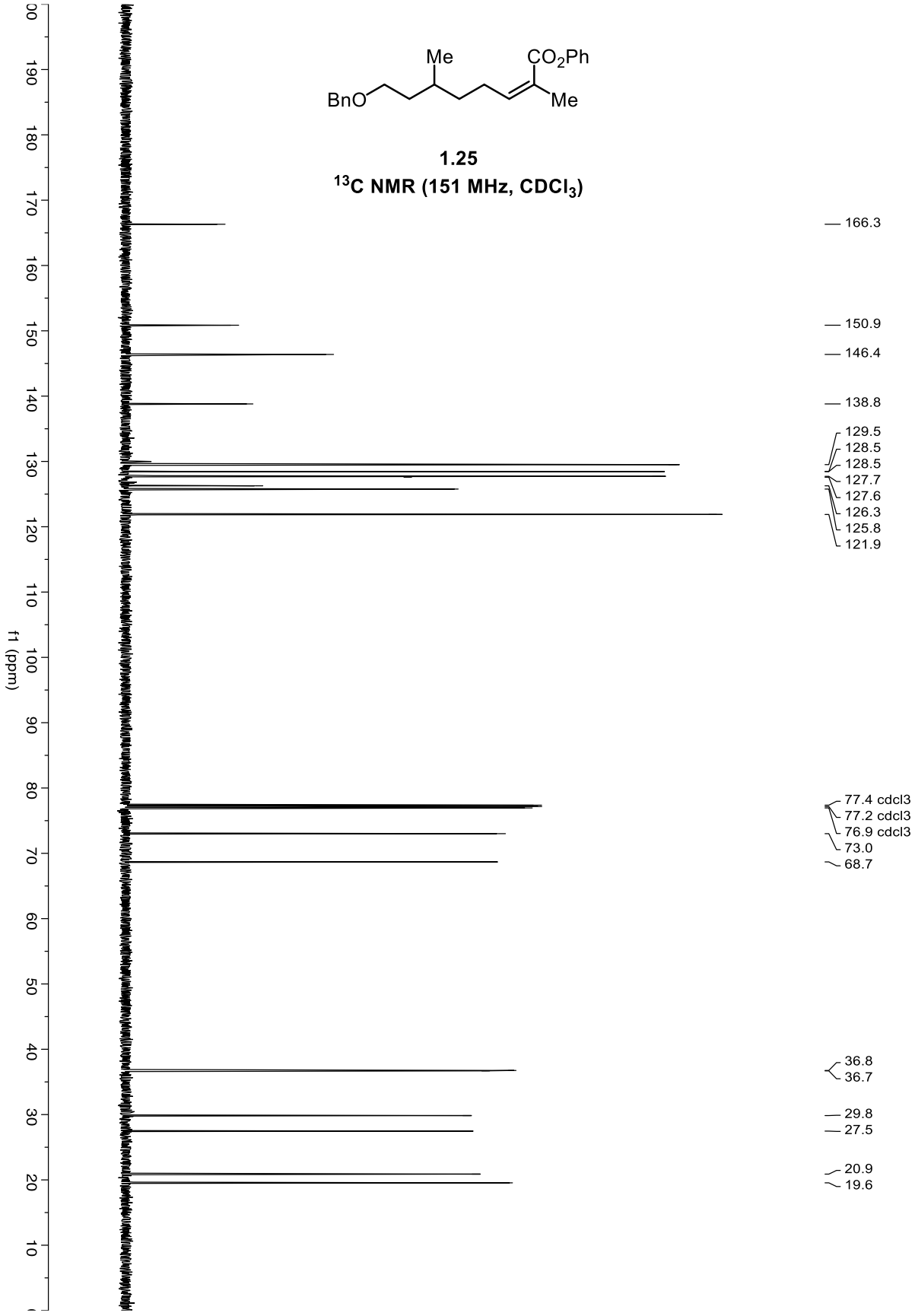
1.22

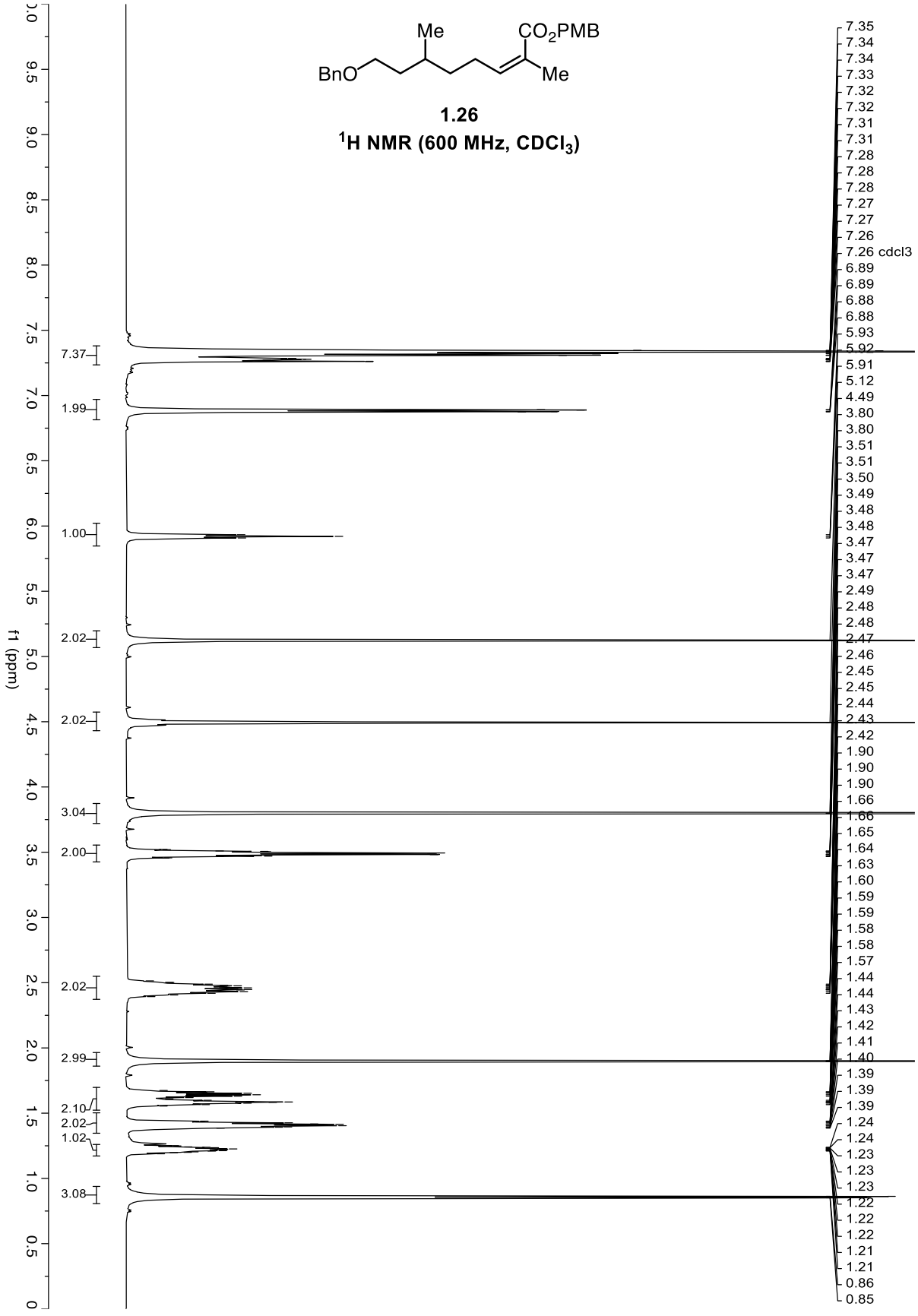
^{13}C NMR (126 MHz, $CDCl_3$)

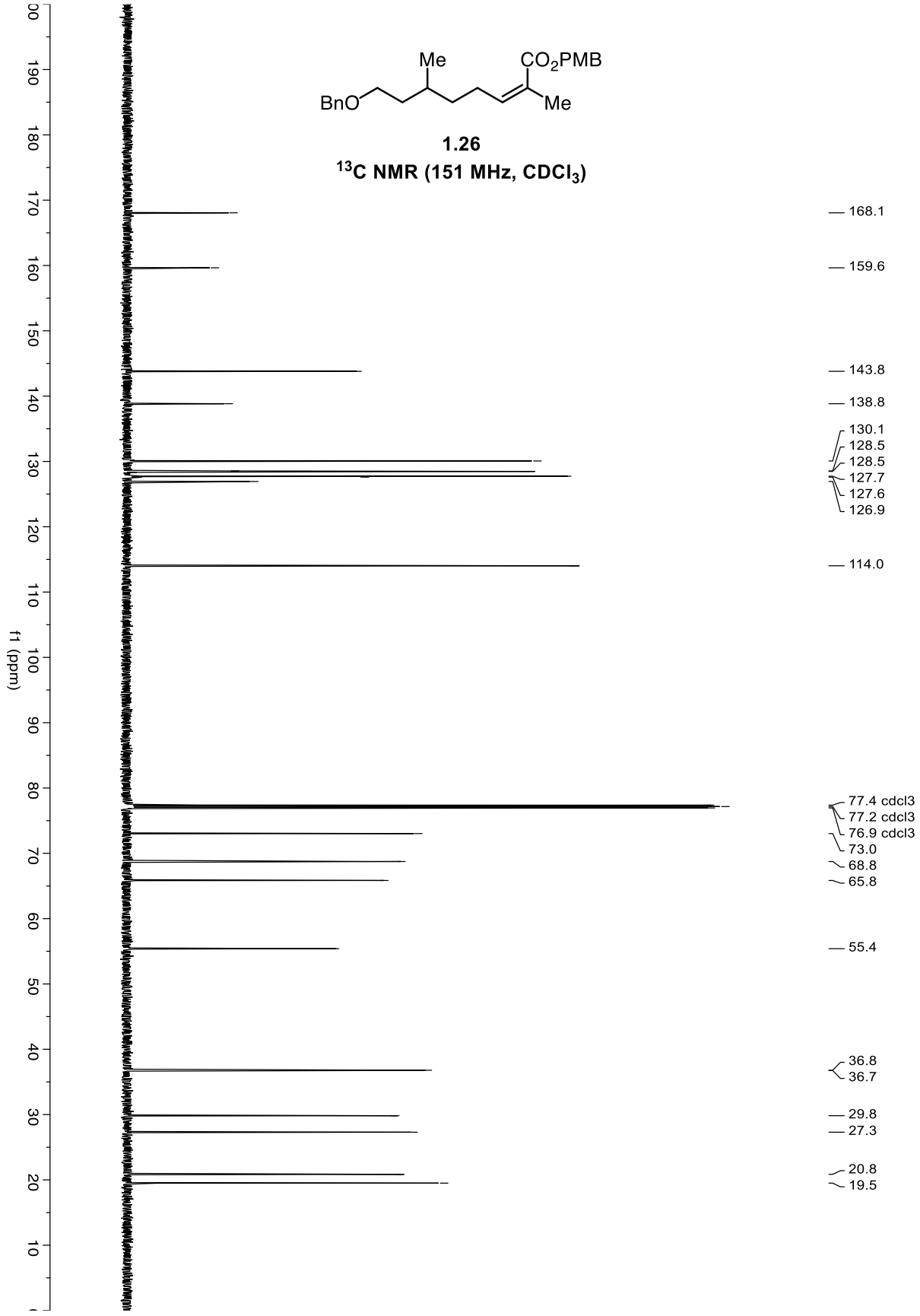

Me
CO2i-Bu
BnO
Me
1.24
1H NMR (400 MHz, CDCl3)
f1 (ppm)
4.01
1.25
1.00
1.96
1.98
2.03
1.99
1.05
2.97
2.21
1.98
1.14
5.99
3.04
7.34
7.34
7.34
7.33
7.29
7.29
7.28
7.27
7.26 cdcl3
5.93
5.92
5.91
5.91
5.91
5.89
5.89
4.50
4.50
3.93
3.92
3.53
3.52
3.51
3.51
3.50
3.49
3.49
3.48
2.51
2.51
2.51
2.50
2.50
2.49
2.49
2.48
2.48
2.47
2.46
2.46
2.01
1.99
1.98
1.96
1.94
1.91
1.90
1.90
1.90
1.70
1.69
1.67
1.67
1.66
1.65
1.63
1.63
1.62
1.61
1.60
1.47
1.47
1.45
1.45
1.44
1.44
1.44
1.43
1.43
1.42
1.42
1.27
1.26
1.25
1.25
1.23
0.97
0.95
0.91
0.89

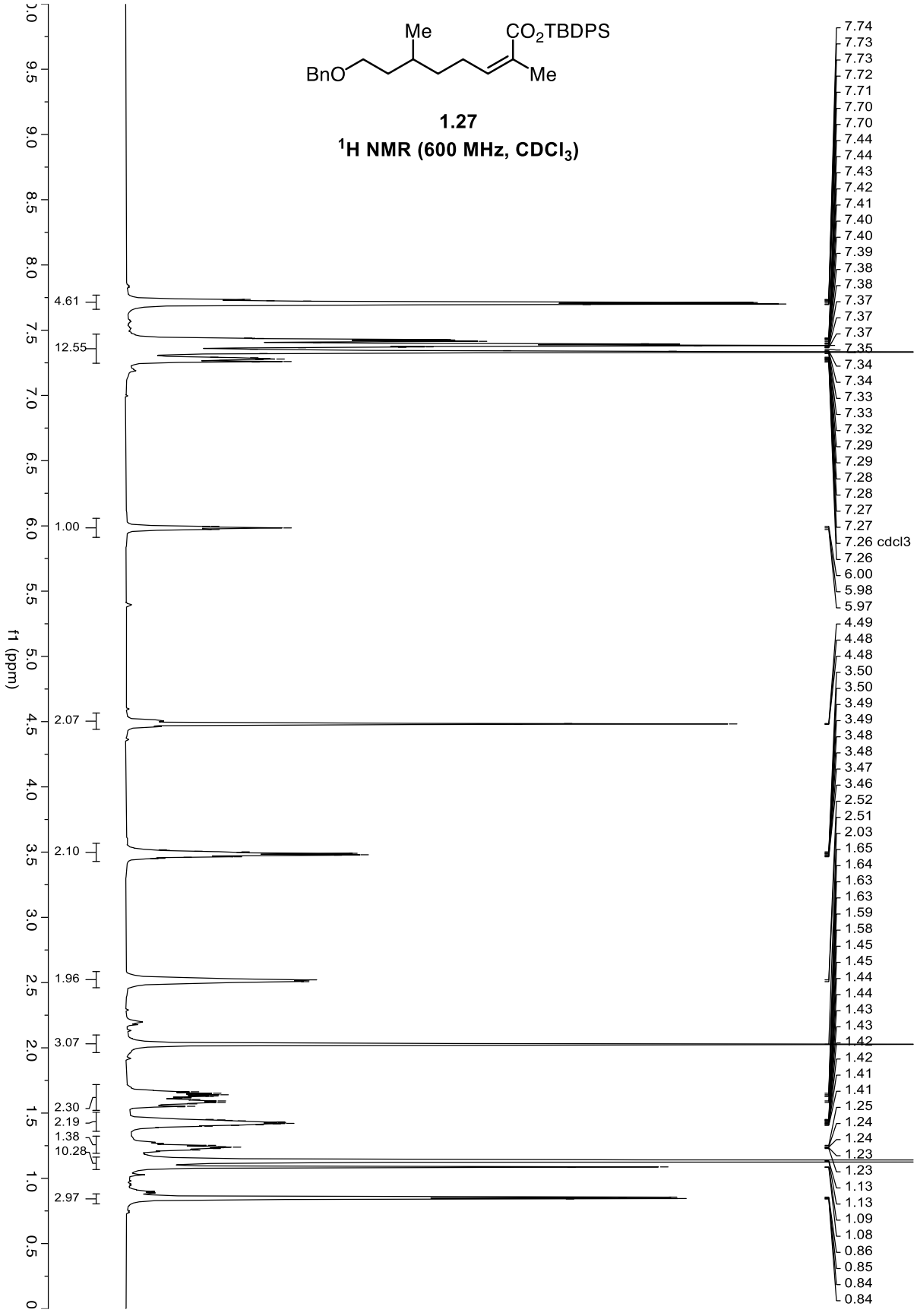

Me
CO2i-Bu
BnO
Me
1.24
13C NMR (151 MHz, CDCl3)
168.3
143.4
138.8
128.5
127.7
127.6
127.2
77.4 cdcl3
77.2 cdcl3
76.9 cdcl3
73.0
70.5
68.7
36.9
36.8
29.9
27.9
27.3
20.9
19.5
19.4
f1 (ppm)

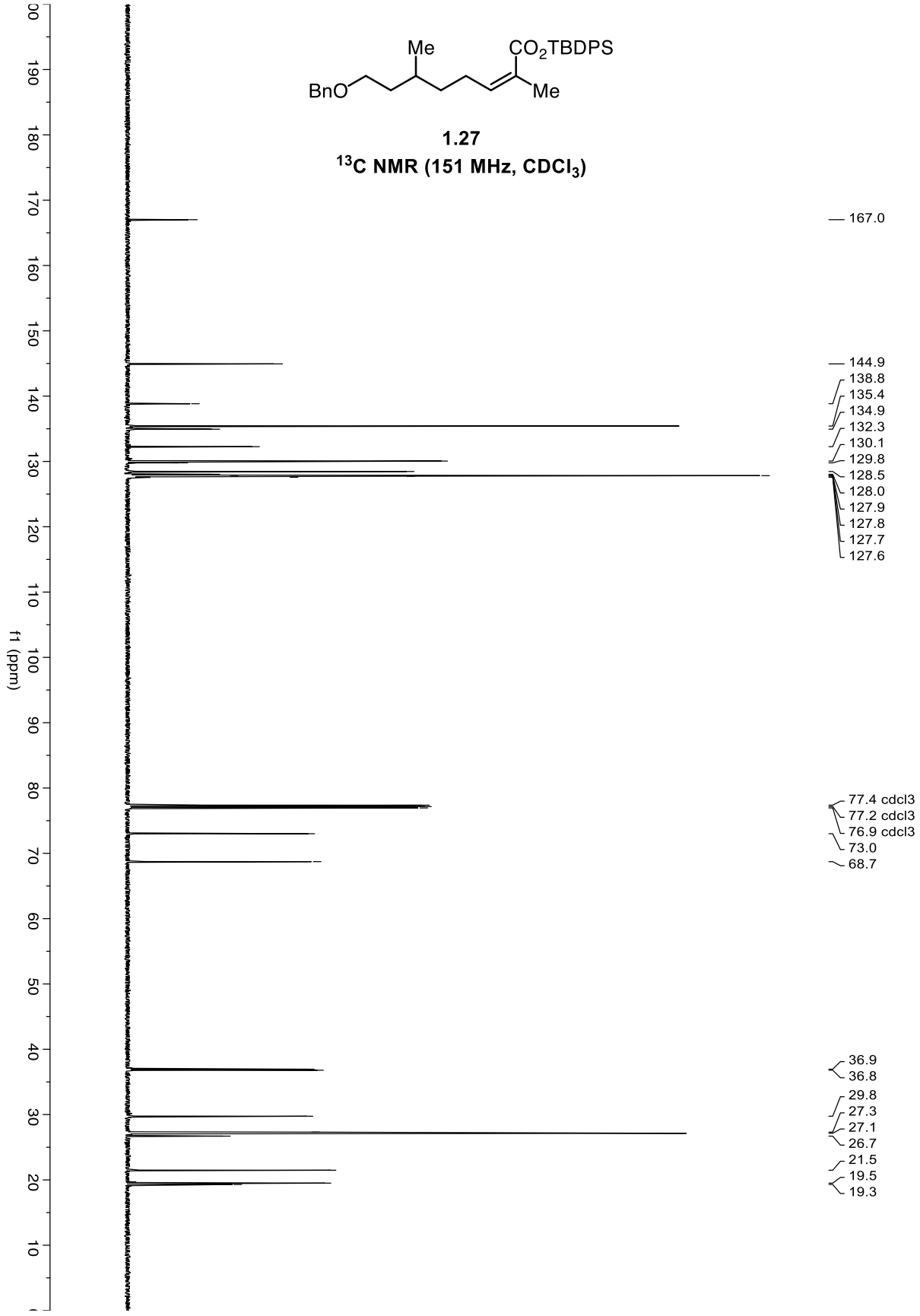

Me
CO2Ph
BnO
Me
1.25
1H NMR (600 MHz, CDCl3)
f1 (ppm)
2.08
4.05
1.04
1.24
2.09
1.00
2.06
2.11
2.00
3.04
2.06
2.18
1.23
3.00
7.41
7.40
7.39
7.38
7.35
7.34
7.33
7.29
7.28
7.26 cdcl3
7.25
7.24
7.23
7.13
7.12
6.14
6.13
6.12
4.50
4.49
3.54
3.53
3.52
3.51
3.50
3.49
2.62
2.61
2.60
2.59
2.58
2.57
2.07
2.06
1.71
1.70
1.69
1.68
1.67
1.66
1.65
1.51
1.50
1.49
1.48
1.47
1.46
1.45
1.44
1.33
1.32
1.31
0.92
0.91

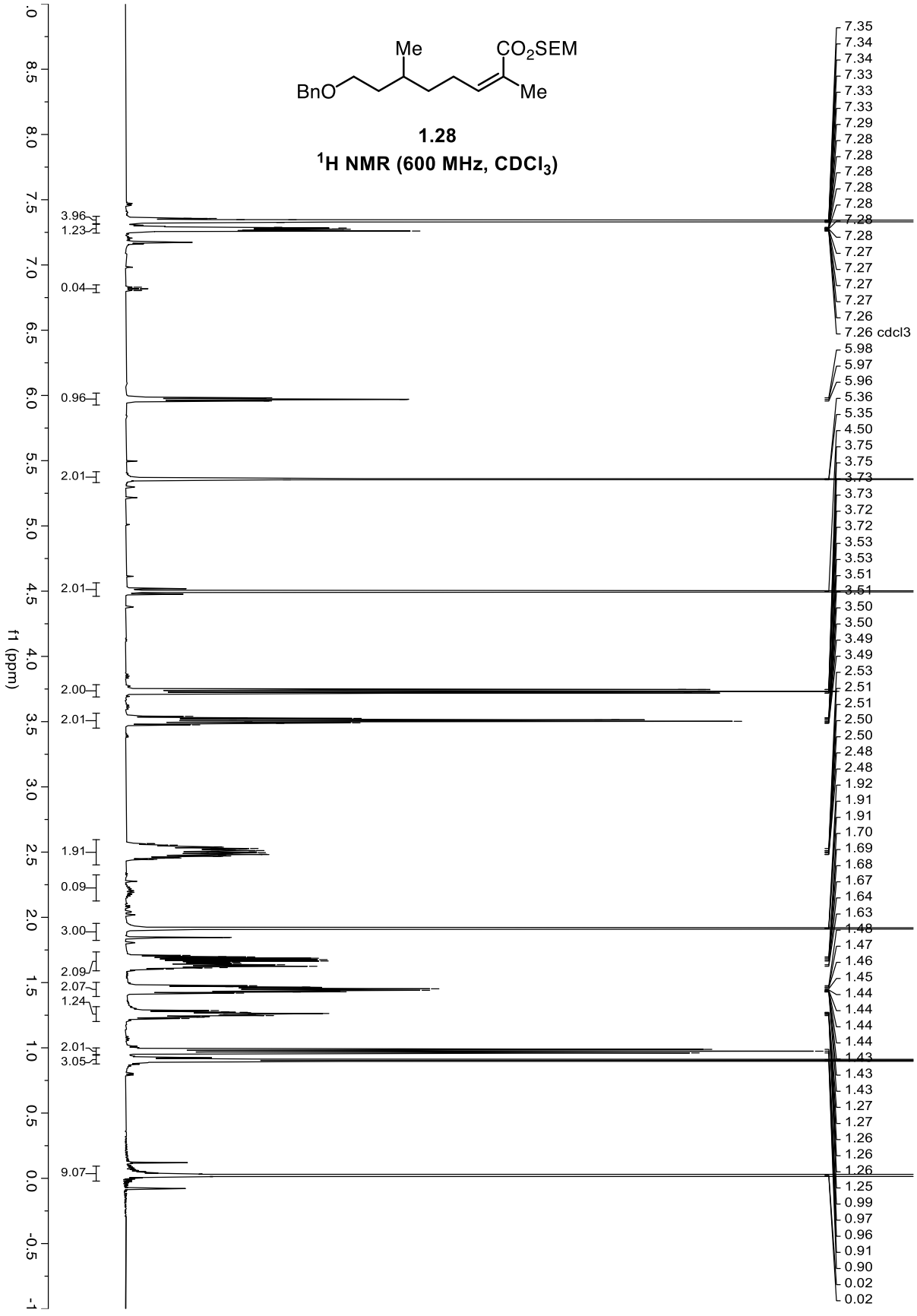

Me
CO2Ph
BnO
Me
1.25
13C NMR (151 MHz, CDCl3)
166.3
150.9
146.4
138.8
129.5
128.5
128.5
127.7
127.6
126.3
125.8
121.9
77.4 cdcl3
77.2 cdcl3
76.9 cdcl3
73.0
68.7
36.8
36.7
29.8
27.5
20.9
19.6
f1 (ppm)

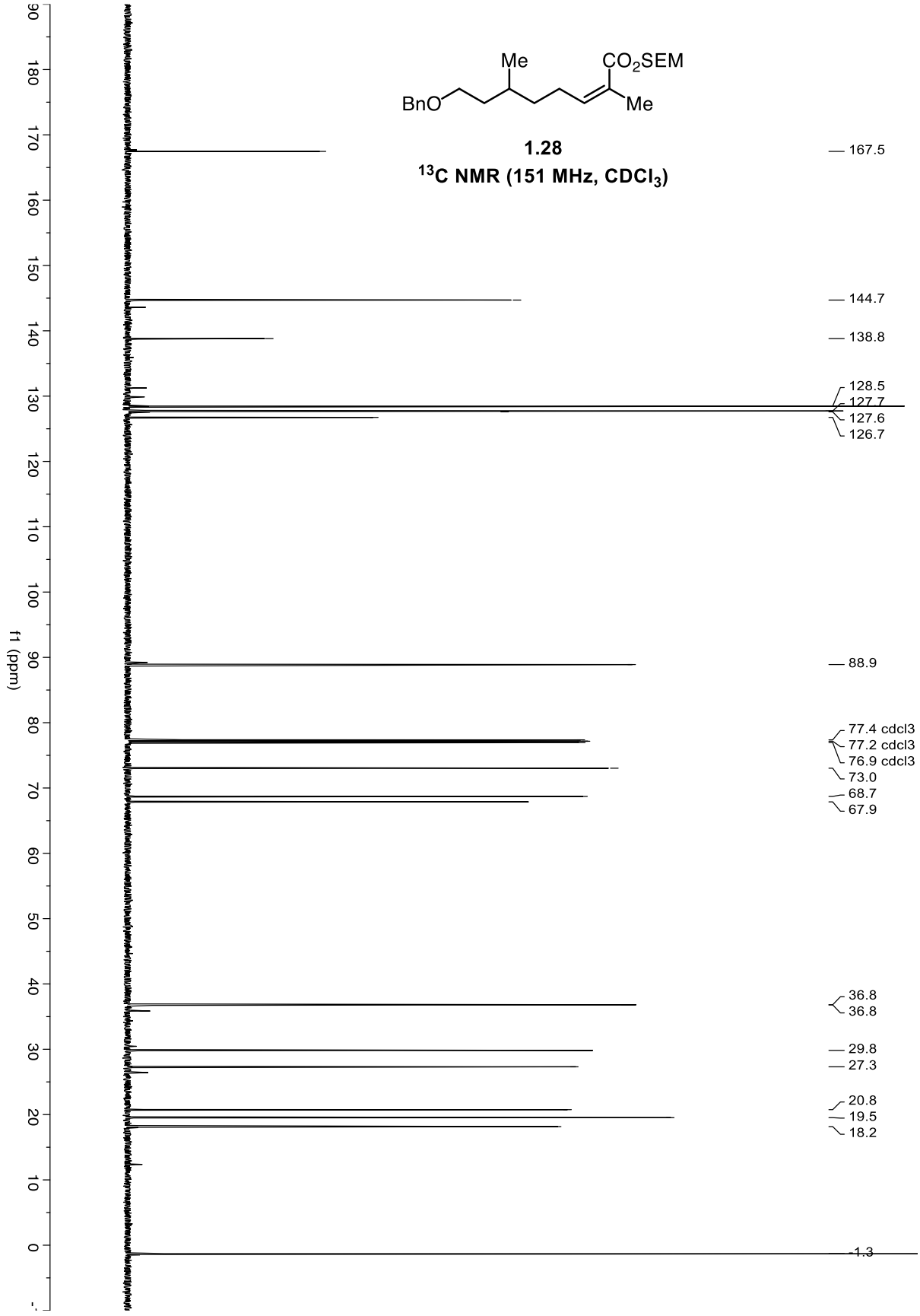

Me
CO2PMB
BnO
Me
1.26
1H NMR (600 MHz, CDCl3)
f1 (ppm)
7.37
1.99
1.00
2.02
2.02
3.04
2.00
2.02
2.99
2.10
2.02
1.02
3.08
7.35
7.34
7.34
7.33
7.32
7.32
7.31
7.31
7.28
7.28
7.28
7.27
7.27
7.26
7.26 cdcl3
6.89
6.89
6.88
6.88
5.93
5.92
5.91
5.12
4.49
3.80
3.80
3.51
3.51
3.50
3.49
3.48
3.48
3.47
3.47
3.47
2.49
2.48
2.48
2.47
2.46
2.45
2.45
2.44
2.43
2.42
1.90
1.90
1.90
1.66
1.66
1.65
1.64
1.63
1.60
1.59
1.59
1.58
1.58
1.57
1.44
1.44
1.43
1.42
1.41
1.40
1.39
1.39
1.39
1.24
1.24
1.23
1.23
1.23
1.22
1.22
1.22
1.21
1.21
0.86
0.85

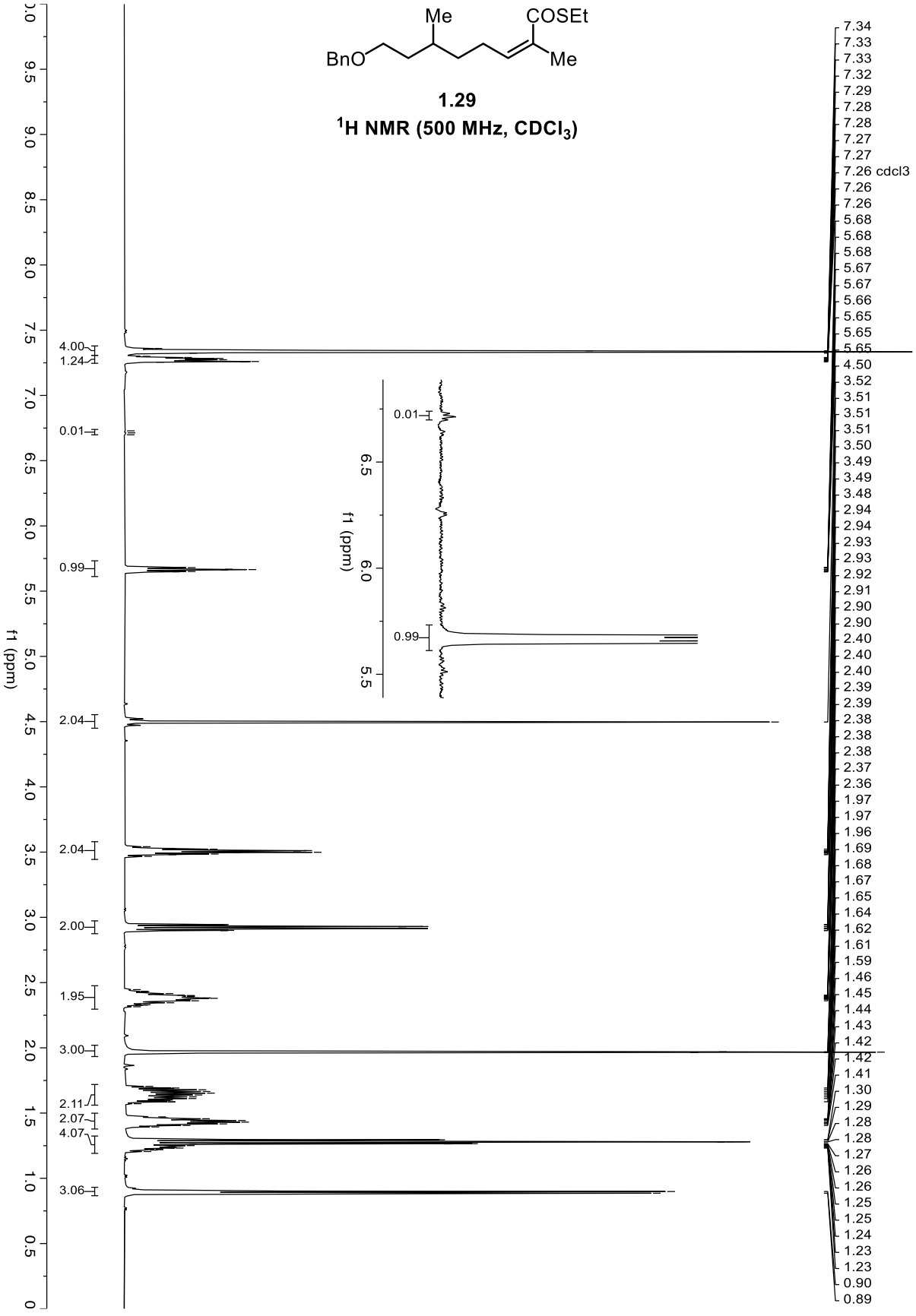

Me
CO2PMB
BnO
Me
1.26
13C NMR (151 MHz, CDCl3)
f1 (ppm)
168.1
159.6
143.8
138.8
130.1
128.5
128.5
127.7
127.6
126.9
114.0
77.4 cdcl3
77.2 cdcl3
76.9 cdcl3
73.0
68.8
65.8
55.4
36.8
36.7
29.8
27.3
20.8
19.5

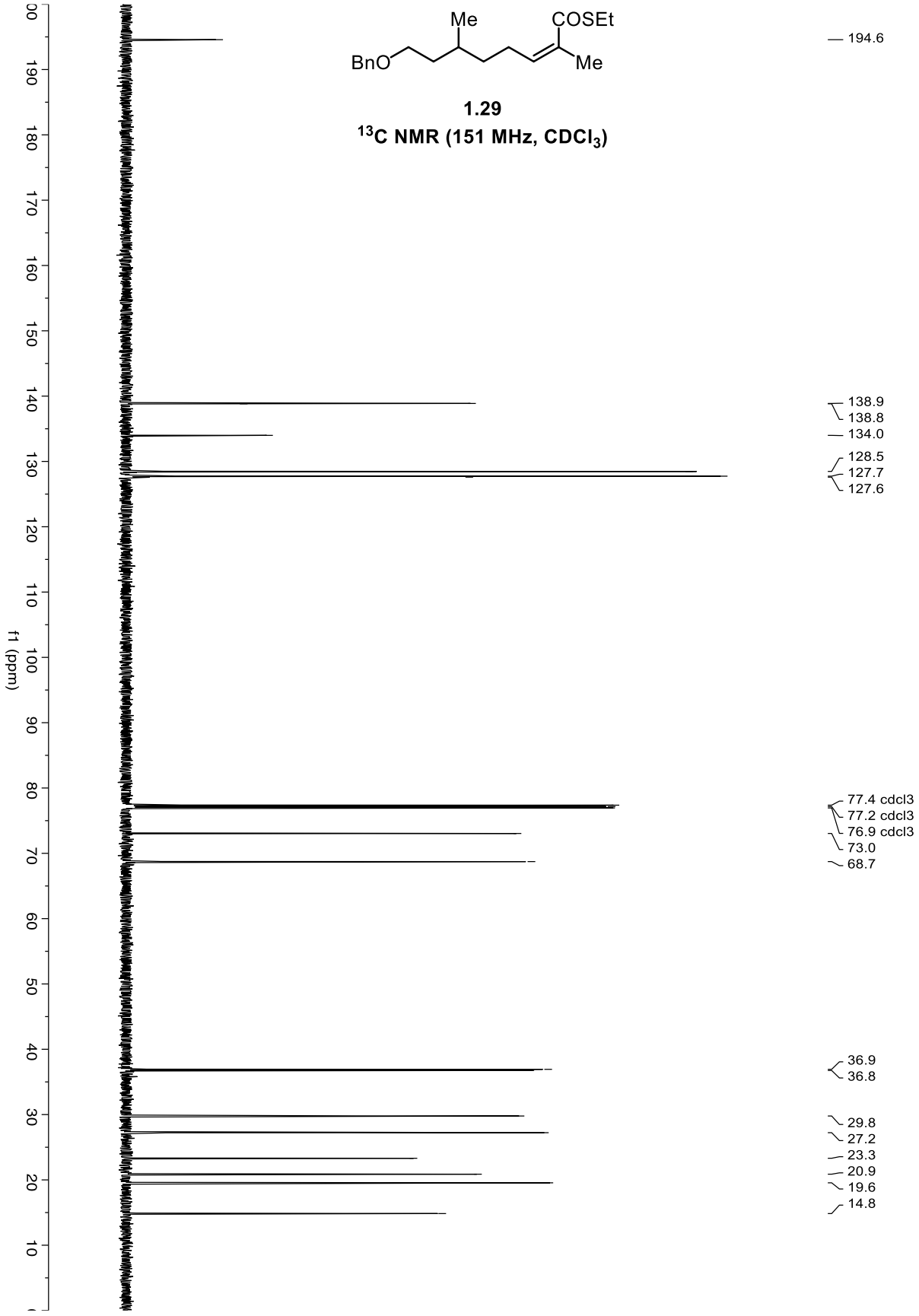

Me
CO_2TBDPS
BnO
Me
1.27
^{1}H NMR (600 MHz, $CDCl_3$)
f1 (ppm)
4.61
12.55
1.00
2.07
2.10
1.96
3.07
2.30
2.19
1.38
10.28
2.97
7.74
7.73
7.73
7.72
7.71
7.70
7.70
7.44
7.44
7.43
7.42
7.41
7.40
7.40
7.39
7.38
7.38
7.37
7.37
7.37
7.35
7.34
7.34
7.33
7.33
7.32
7.29
7.29
7.28
7.28
7.27
7.27
7.26 cdcl3
7.26
6.00
5.98
5.97
4.49
4.48
4.48
3.50
3.50
3.49
3.49
3.48
3.48
3.47
3.46
2.52
2.51
2.03
1.65
1.64
1.63
1.63
1.59
1.58
1.45
1.45
1.44
1.44
1.43
1.43
1.42
1.42
1.41
1.41
1.25
1.24
1.24
1.23
1.23
1.13
1.13
1.09
1.08
0.86
0.85
0.84
0.84


Me
CO_2TBDPS
BnO
Me
1.27
^{13}C NMR (151 MHz, $CDCl_3$)
167.0
144.9
138.8
135.4
134.9
132.3
130.1
129.8
128.5
128.0
127.9
127.8
127.7
127.6
77.4 cdcl3
77.2 cdcl3
76.9 cdcl3
73.0
68.7
36.9
36.8
29.8
27.3
27.1
26.7
21.5
19.5
19.3
f1 (ppm)


Me
CO2SEM
BnO
Me
1.28
1H NMR (600 MHz, CDCl3)
f1 (ppm)
3.96
1.23
0.04
0.96
2.01
2.01
2.00
2.01
1.91
0.09
3.00
2.09
2.07
1.24
2.01
3.05
9.07
7.35
7.34
7.34
7.33
7.33
7.33
7.29
7.28
7.28
7.28
7.28
7.28
7.28
7.28
7.27
7.27
7.27
7.27
7.26
7.26 cdcl3
5.98
5.97
5.96
5.36
5.35
4.50
3.75
3.75
3.73
3.73
3.72
3.72
3.53
3.53
3.51
3.51
3.50
3.50
3.49
3.49
2.53
2.51
2.51
2.50
2.50
2.48
2.48
1.92
1.91
1.91
1.70
1.69
1.68
1.67
1.64
1.63
1.48
1.47
1.46
1.45
1.44
1.44
1.44
1.44
1.43
1.43
1.43
1.27
1.27
1.26
1.26
1.26
1.25
0.99
0.97
0.96
0.91
0.90
0.02
0.02

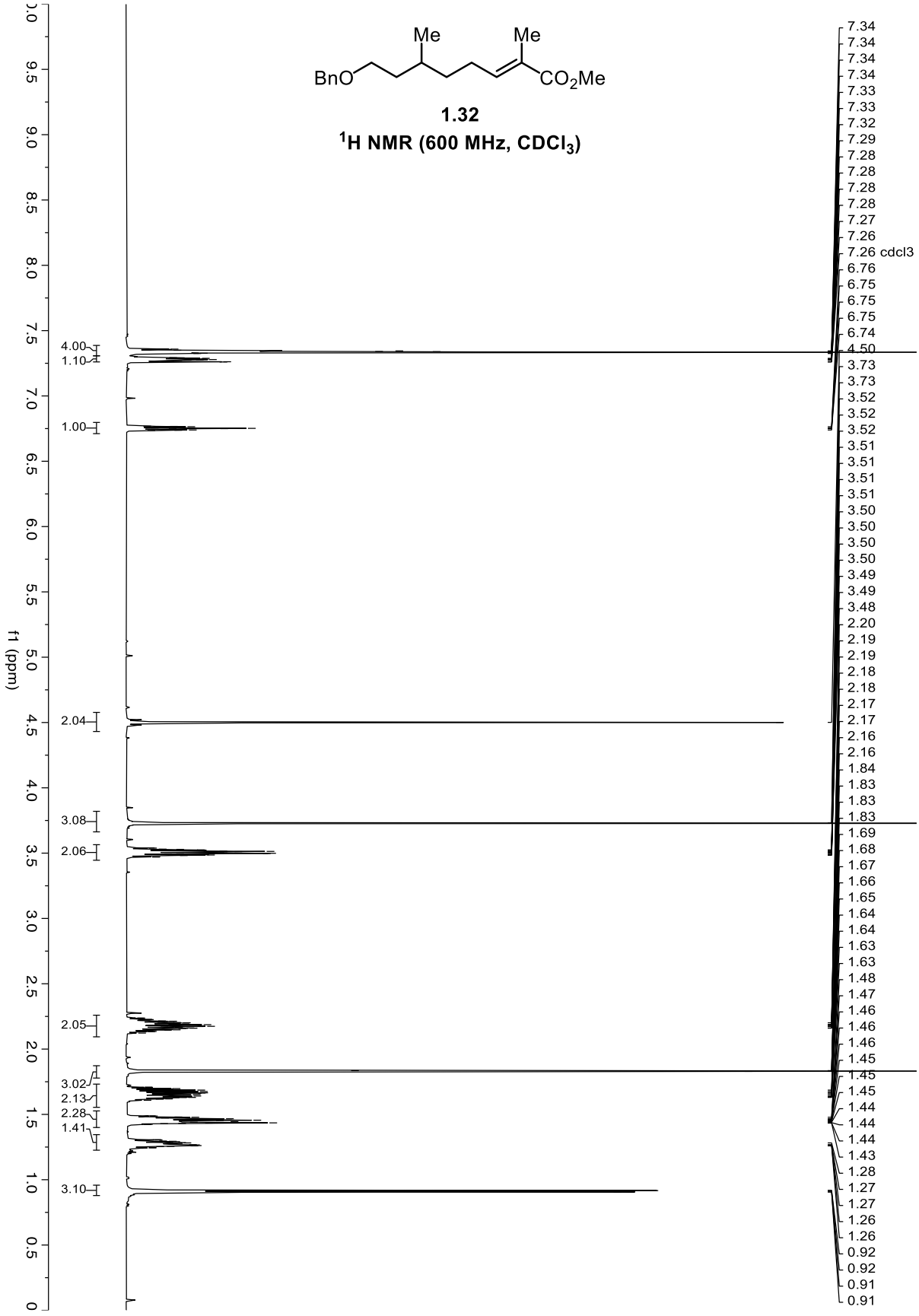

Me
CO2SEM
BnO
Me
1.28
13C NMR (151 MHz, CDCl3)
f1 (ppm)
167.5
144.7
138.8
128.5
127.7
127.6
126.7
88.9
77.4 cdcl3
77.2 cdcl3
76.9 cdcl3
73.0
68.7
67.9
36.8
36.8
29.8
27.3
20.8
19.5
18.2
1.3

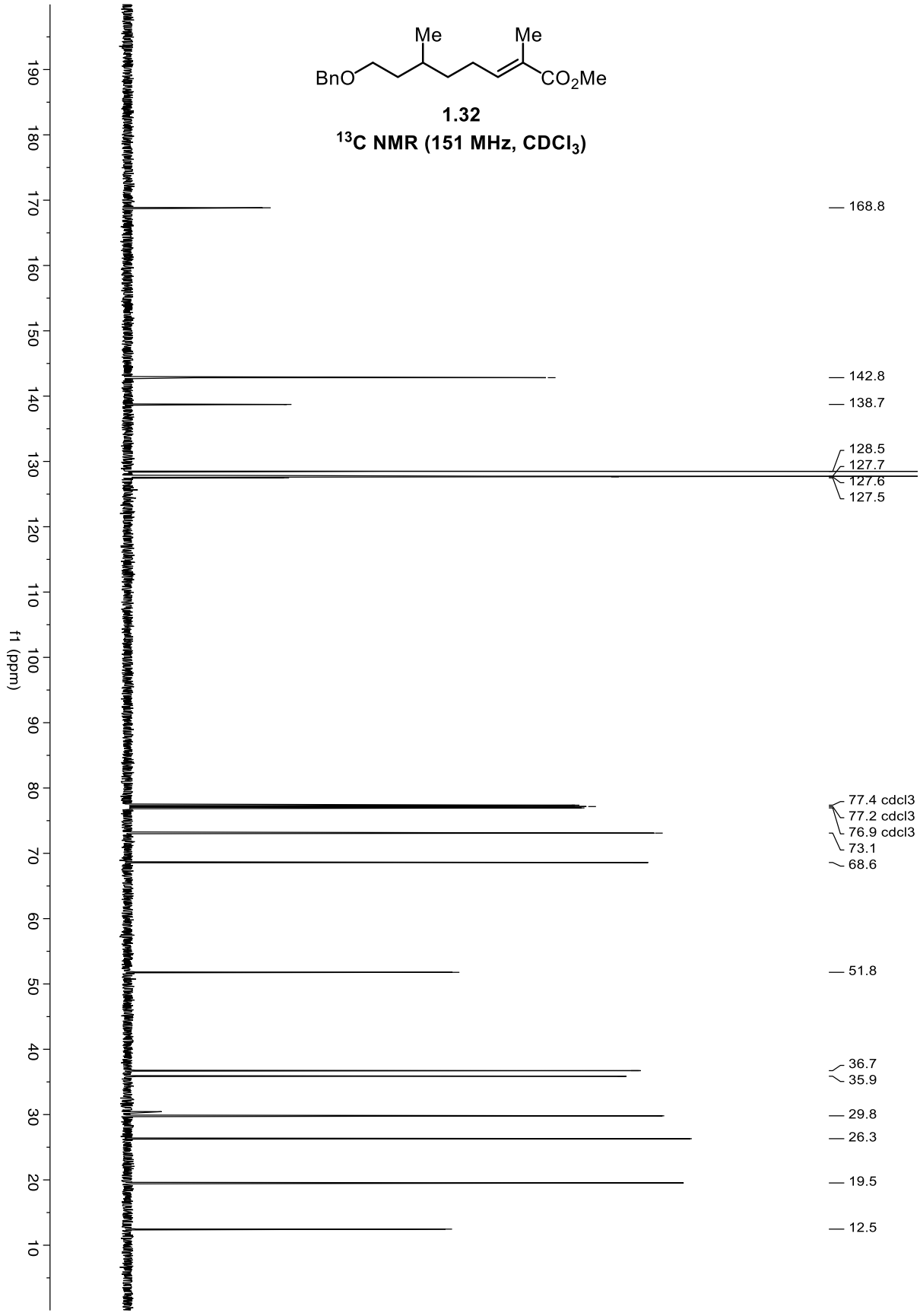

Me
COSEt
BnO
Me
1.29
^{1}H NMR (500 MHz, $CDCl_3$)
f1 (ppm)
4.00
1.24
0.01
0.99
2.04
2.04
2.00
1.95
3.00
2.11
2.07
4.07
3.06
0.01
0.99
6.5
6.0
5.5
7.34
7.33
7.33
7.32
7.29
7.28
7.28
7.27
7.27
7.26 cdcl3
7.26
7.26
5.68
5.68
5.68
5.67
5.67
5.66
5.65
5.65
5.65
4.50
3.52
3.51
3.51
3.51
3.50
3.49
3.49
3.48
2.94
2.94
2.93
2.93
2.92
2.91
2.90
2.90
2.40
2.40
2.40
2.39
2.39
2.38
2.38
2.38
2.37
2.36
1.97
1.97
1.96
1.69
1.68
1.67
1.65
1.64
1.62
1.61
1.59
1.46
1.45
1.44
1.43
1.42
1.42
1.41
1.30
1.29
1.28
1.28
1.27
1.26
1.26
1.25
1.25
1.24
1.23
1.23
0.90
0.89

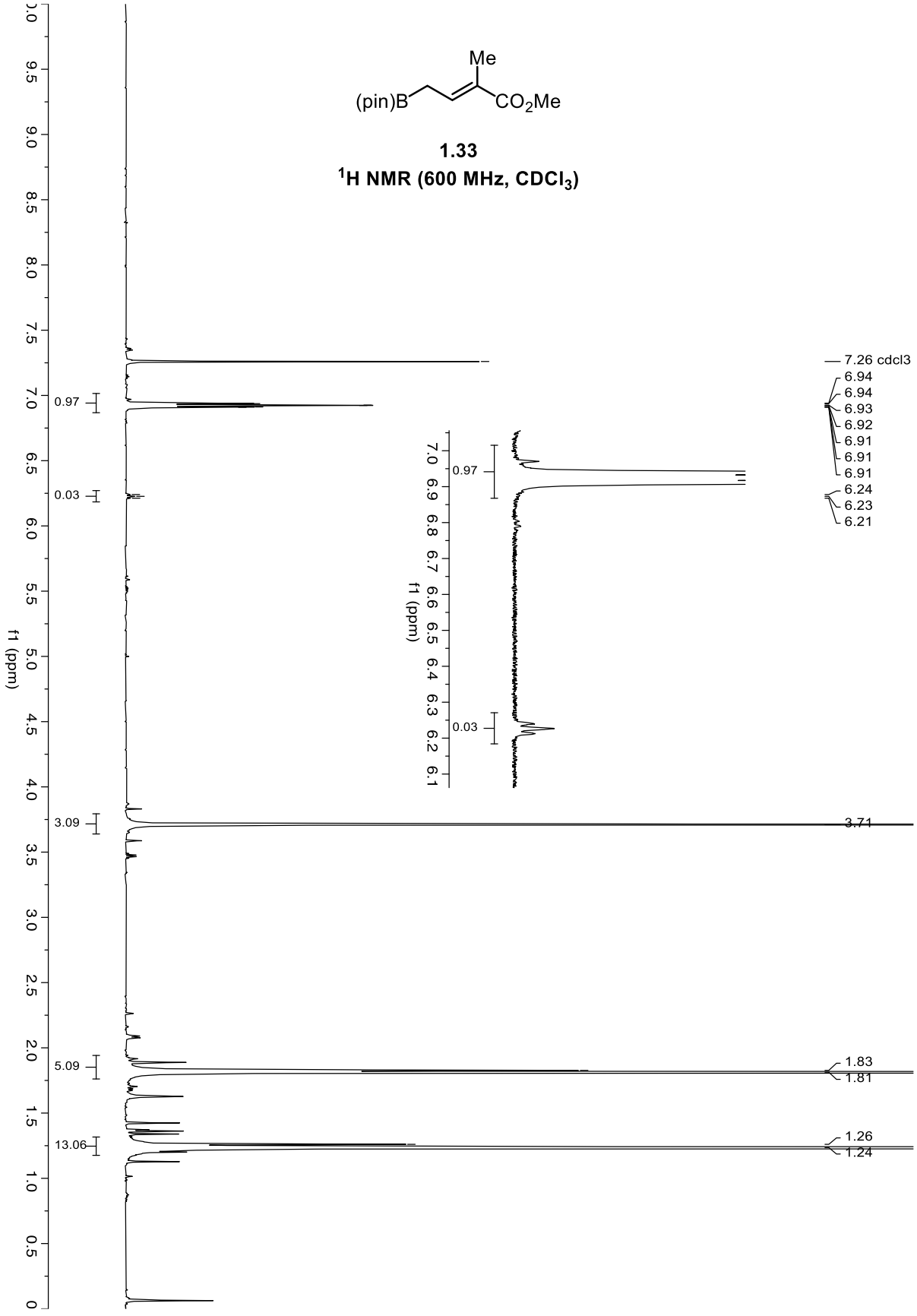


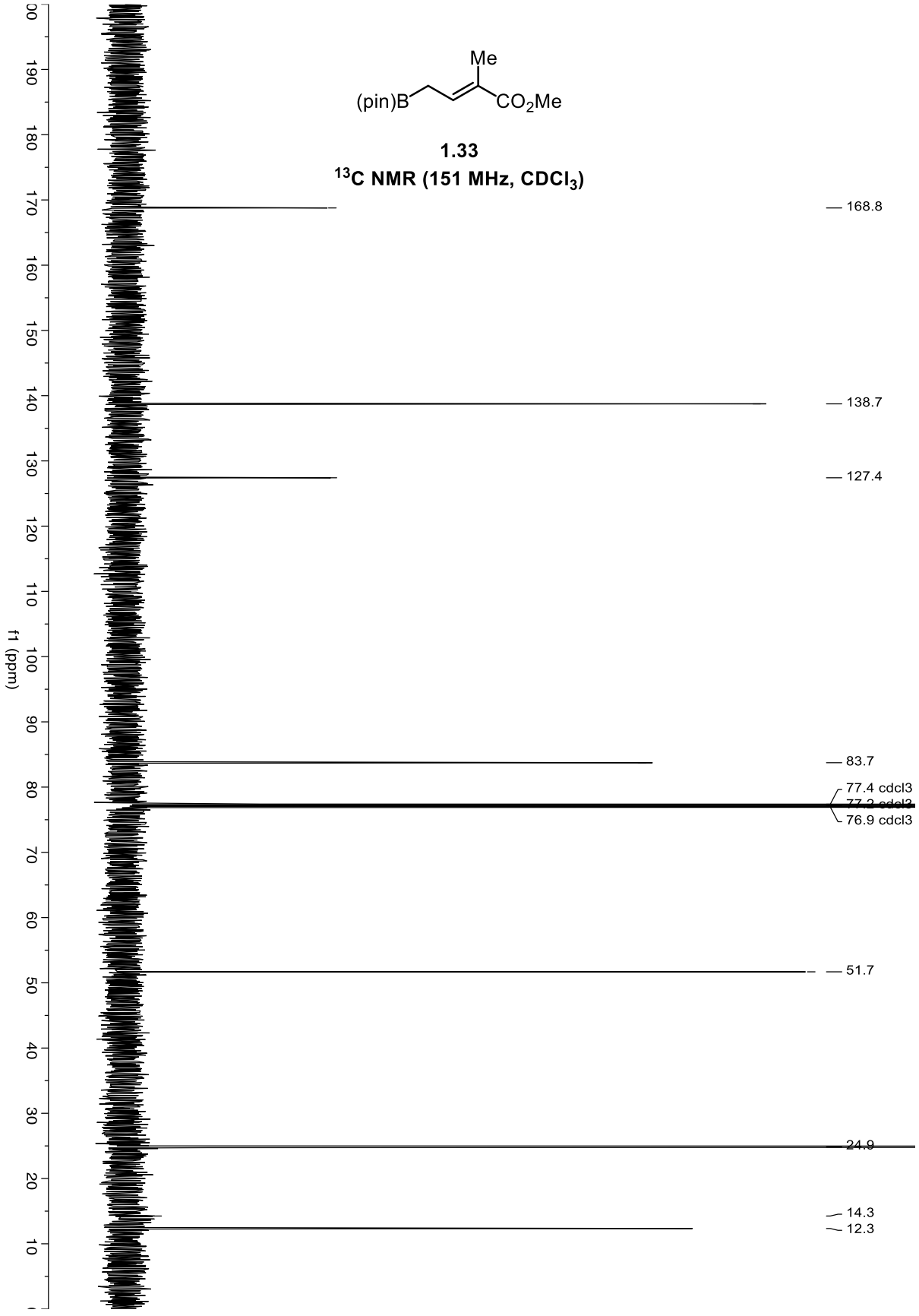
1.29

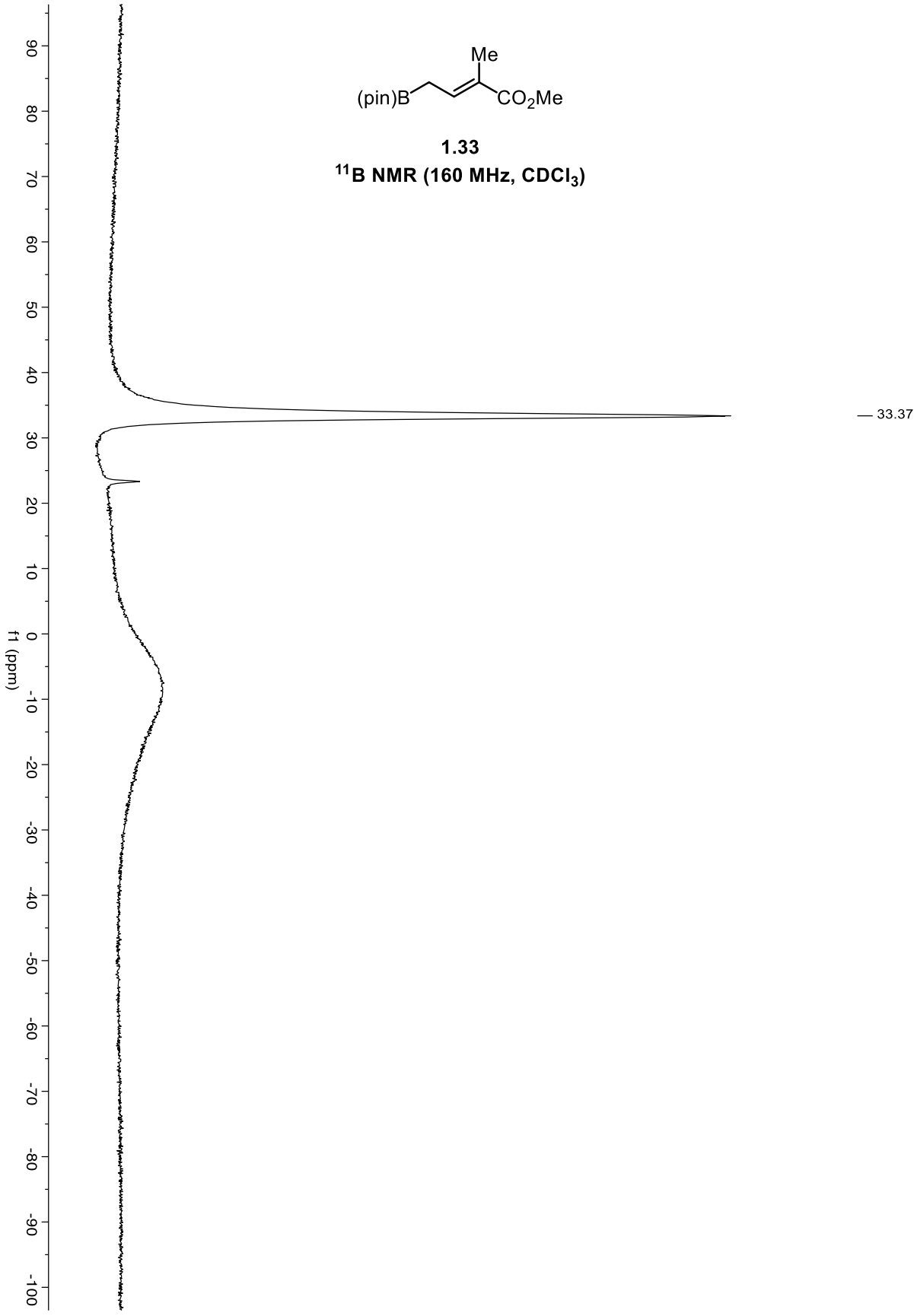
^{13}C NMR (151 MHz, $CDCl_3$)

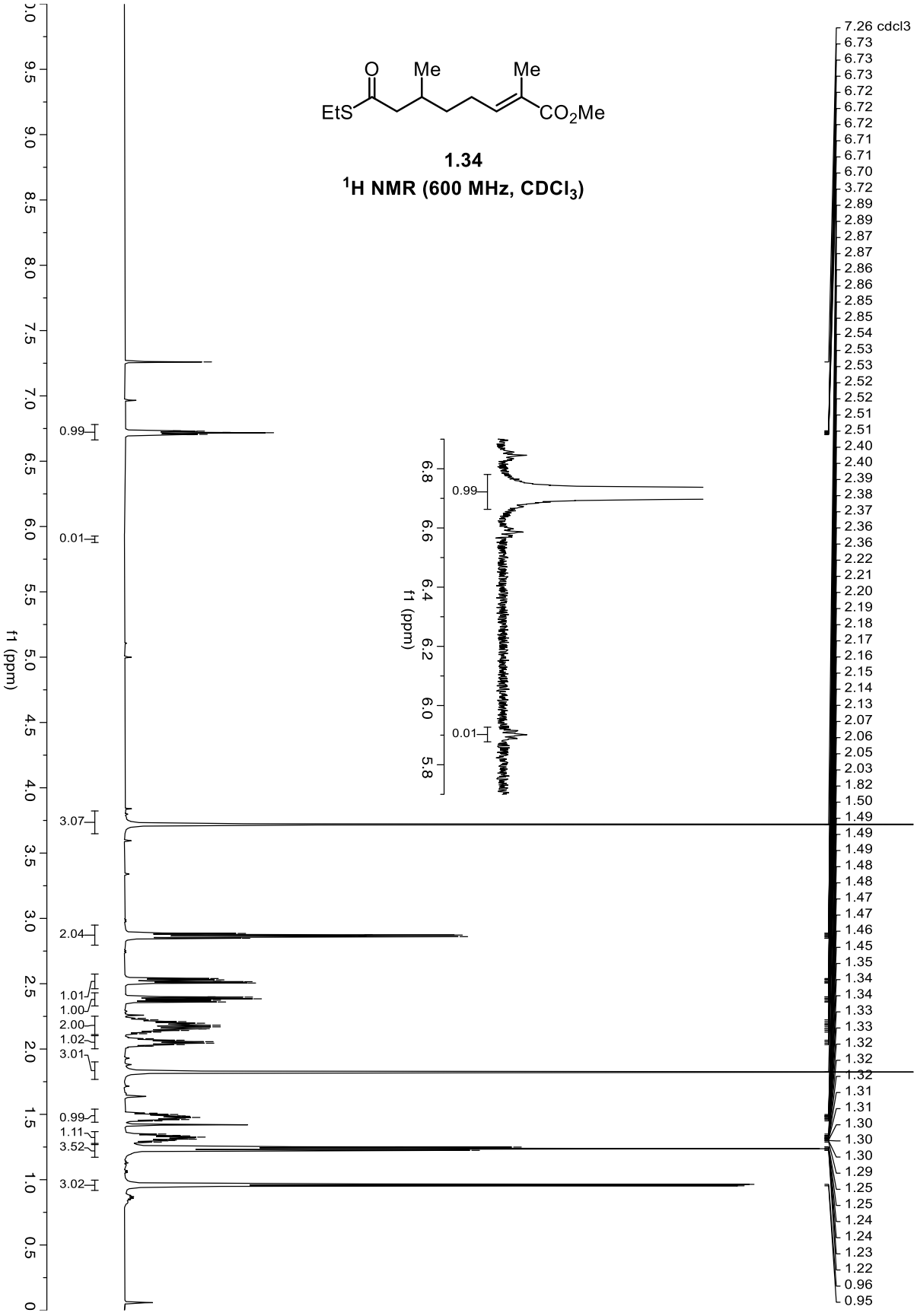

Me
Me
BnO
CO2Me
1.32
1H NMR (600 MHz, CDCl3)
f1 (ppm)
4.00
1.10
1.00
2.04
3.08
2.06
2.05
3.02
2.13
2.28
1.41
3.10
7.34
7.34
7.34
7.34
7.33
7.33
7.32
7.29
7.28
7.28
7.28
7.28
7.27
7.26
7.26 cdcl3
6.76
6.75
6.75
6.75
6.74
4.50
3.73
3.73
3.52
3.52
3.52
3.51
3.51
3.51
3.51
3.50
3.50
3.50
3.50
3.49
3.49
3.48
2.20
2.19
2.19
2.18
2.18
2.17
2.17
2.16
2.16
1.84
1.83
1.83
1.83
1.69
1.68
1.67
1.66
1.65
1.64
1.64
1.63
1.63
1.48
1.47
1.46
1.46
1.46
1.45
1.45
1.45
1.44
1.44
1.44
1.43
1.28
1.27
1.27
1.26
1.26
0.92
0.92
0.91
0.91

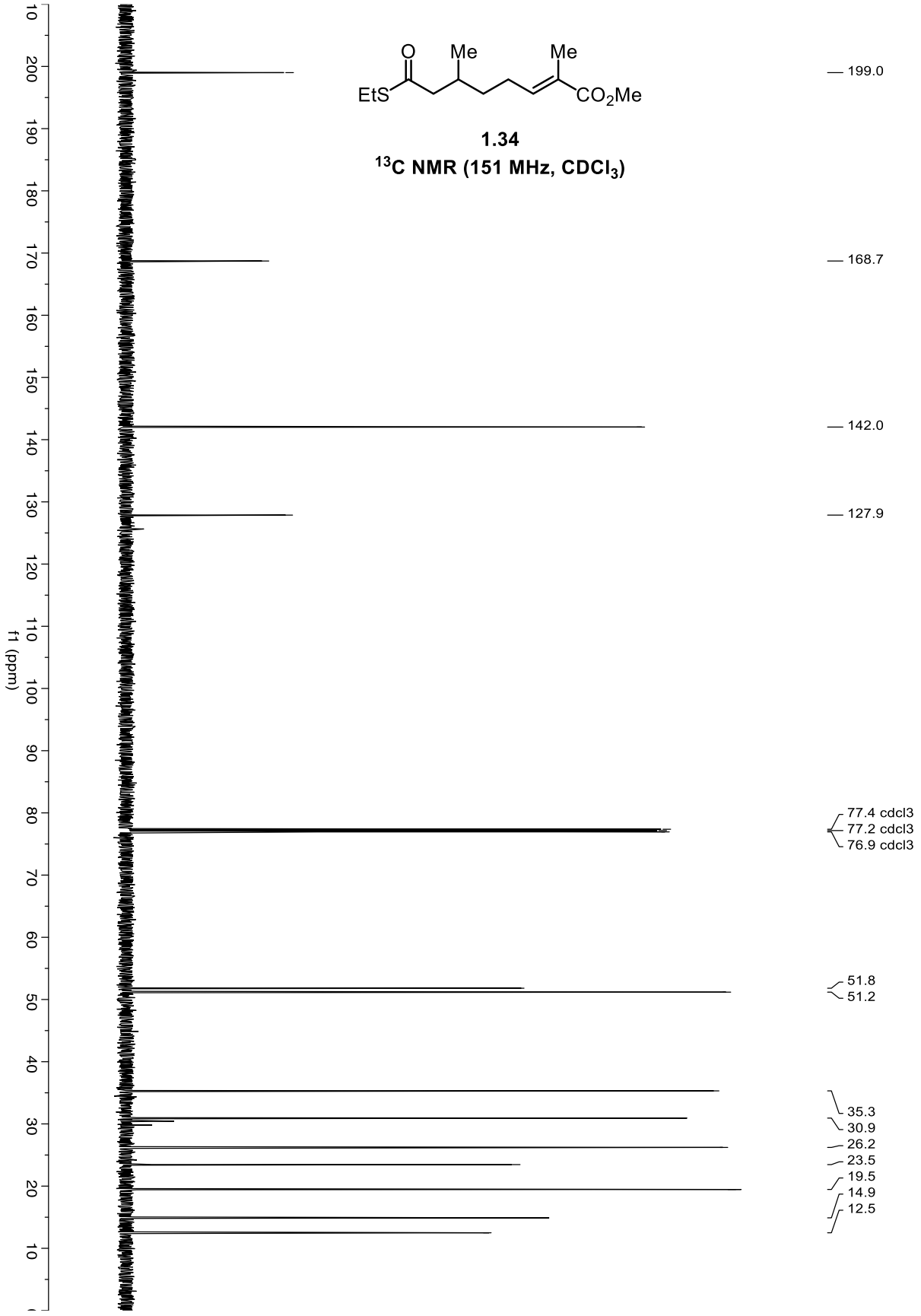

Me
Me
BnO
CO2Me
1.32
13C NMR (151 MHz, CDCl3)
168.8
142.8
138.7
128.5
127.7
127.6
127.5
77.4 cdcl3
77.2 cdcl3
76.9 cdcl3
73.1
68.6
51.8
36.7
35.9
29.8
26.3
19.5
12.5
f1 (ppm)


Me
(pin)B
CO2Me
1.33
1H NMR (600 MHz, CDCl3)
f1 (ppm)
0.97
0.03
3.09
5.09
13.06
7.26 cdcl3
6.94
6.94
6.93
6.92
6.91
6.91
6.91
6.24
6.23
6.21
3.71
1.83
1.81
1.26
1.24


Me
(pin)B
CO2Me
1.33
13C NMR (151 MHz, CDCl3)
168.8
138.7
127.4
83.7
77.4 cdcl3
77.2 cdcl3
76.9 cdcl3
51.7
24.9
14.3
12.3
f1 (ppm)


Me
(pin)B
CO2Me
1.33
11B NMR (160 MHz, CDCl3)
33.37
f1 (ppm)
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100


O
Me
Me
EtS
CO2Me
1.34
1H NMR (600 MHz, CDCl3)
f1 (ppm)
0.99
0.01
3.07
2.04
1.01
1.00
2.00
1.02
3.01
0.99
1.11
3.52
3.02
7.26 cdcl3



1.34

^{13}C NMR (151 MHz, $CDCl_3$)