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A user-friendly approach to sidestep the venerable Grignard addition to unactivated ketones to access tertiary alcohols by reversing the polarity of the disconnection. In this work a ketone instead acts as a nucleophile when adding to simple unactivated olefins to accomplish the same overall transformation. The scope of this coupling is broad as enabled using an electrochemical approach and the reaction is scalable, chemoselective, and requires no precaution to exclude air or water. Multiple applications demonstrate the simplifying nature of the reaction on multi-step synthesis and mechanistic studies point to an intuitive mechanism reminiscent of other chemical reductants such as SmI2 (which cannot accomplish the same reaction).

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Ketyl-Olefin, Ketyl, electrochemical Grignard, electrochemical coupling, reductive coupling.

ABSTRACT: A user-friendly approach to sidestep the venerable Grignard addition to unactivated ketones to access tertiary alcohols by reversing the polarity of the disconnection. In this work a ketone instead acts as a nucleophile when adding to simple unactivated olefins to accomplish the same overall transformation. The scope of this coupling is broad as enabled using an electrochemical approach and the reaction is scalable, chemoselective, and requires no precaution to exclude air or water. Multiple applications demonstrate the simplifying nature of the reaction on multi-step synthesis and mechanistic studies point to an intuitive mechanism reminiscent of other chemical reductants such as SmI_2 (which cannot accomplish the same reaction).

Tertiary alcohols are an abundant functional group with versatile reactivity that are found in natural products,[1] pharmaceuticals,[2] and a multitude of useful materials.[3] Traditionally, perhaps overwhelmingly, the ketone has served as a loyal progenitor of this species (Figure 1A) for good reasons. Every undergraduate organic textbook prescribes a direct nucleophilic addition of a strong nucleophile, such as RMgX or RLi, to these electrophilic species.[4] Although these incredibly robust reactions have been employed countless times, they can indirectly contribute to synthetic inefficiencies as their low chemoselectivity often necessitates the use of protecting groups.[5] This dilemma is nicely illustrated (Figure 1B) by examining the patented route to steroid derivative **2**.[6] Although a Grignard reaction with commercially available ketone **1** is an obvious disconnection, its use introduces several protecting group additions, removals and functional group manipulations throughout the course of a seven-step sequence (only one of which forges a C–C bond).

Within the specific realm of intermolecular alkyl nucleophile additions to unactivated ketones, Grignard and related organometallic additions are fundamentally limited by their 2-electron mechanisms, which render these nucleophiles both strongly nucleophilic and often highly basic.[4,5,7] Efforts to tone down their reactivity have been explored, with the most successful stemming from nucleophiles bearing activated positions (i.e. allylic, benzylic, propargylic, α-carbonyl, Figure 1C).[8,9] Studies employing Zr-,[10] Ti-,[11] Ru-,[12] and Os-[13] based systems, as well as HAT chemistry,[14] have also pointed to the use of olefins as precursors to species capable of adding to carbonyl groups although intermolecular additions into unactivated ketones are without

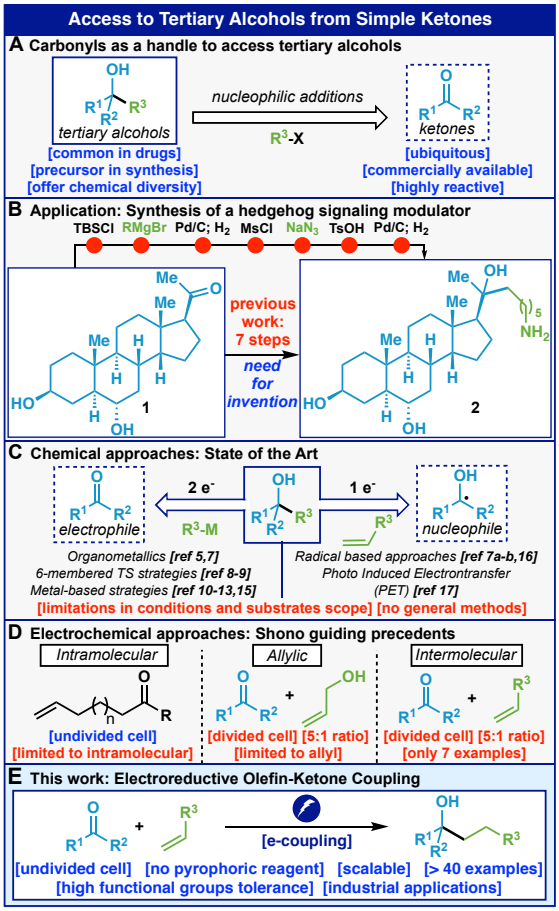


FIGURE 1. Tertiary alcohols from simple ketones remain a challenge for modern synthesis (A). Synthesis of **2** is em-

blematic of the problems with Grignard (B). Recent approaches so far do not address the problem (C). Electrochemical precedent on activated olefins (D) and a summary of this work (E).

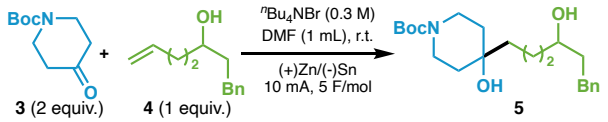
precedent.[15] A less intuitive approach involves an umpolung disconnection, which renders the ketone the nucleophilic group through a reductive 1-electron approach. Thus far, such approaches have relied primarily on Sm(II),[7a-b] Ti(III),[16] or photoinduced electron transfer[17] to couple activated olefins and styrenes to ketones. A general intermolecular reductive coupling of unactivated ketones and olefins is so far absent from the literature. The closest precedent for the desired transformation was disclosed by Shono and co-workers (Figure 1D).[18] These reports focus predominantly on *intra*molecular couplings,[18a-b] with only a few *inter*molecular examples[18c-d] presented. To the best of our knowledge, this chemistry has not been applied in the literature, despite being available for decades, presumably due to the challenges of using a divided cell setup under an argon atmosphere and the need for *at least* a five-fold excess of the ketone. In this Communication, a new protocol for electrochemically driven reductive couplings of unactivated ketones and olefins is presented. This method uses a simple undivided cell tolerating exogenous air and moisture, exhibits a broad scope, and can be easily scaled (Figure 1E).

Explorations began by studying Shono's original conditions[18c] on a medicinally-relevant model substrate pair: homoallylic alcohol **4** and piperidone **3** (Table 1A). In principle, the use of Grignard chemistry to carry out this assembly would necessitate the use of a protecting group on **4** and perhaps other precautions due to the enolizability of **3**, hence, more gentle methodologies were sought. Revisiting the electrochemical method developed by Shono for less *ornate* substrates,[18c] only resulted in low yields (Table 1A, entry 1). This method was pursued with some rigor (see SI for a full listing); however, the yield could not be improved beyond 17%. Chemical reductants such as SmI_2 and LiDBB were examined next, and while these methods have been shown to have success in similar *intramolecular* scenarios, they were found to be unsatisfactory for this purpose (entries 2-5, Table 1a). Developing this chemistry following the guiding principles from our own forays[19,20] into electrochemistry, specifically deeply reductive electrochemistry,[20] allowed us to hone in on the sacrificial anode, electrolyte, current density and concentration needed to facilitate a high yielding olefin-ketone coupling (Table 1A, see the SI for a full listing). As graphically illustrated in Table 1B, these three variables were crucial to the success of this transformation which, after optimization, let to 95% isolated yield of adduct **5** (Table 1A, entry 6). The use of an inexpensive sacrificial anode (Zn) was ideal and, in contrast to prior work, a lower current ensured broad functional group tolerance (10 mA vs. 200 mA). Notably, unlike prior precedent, only 2 equivalents of the ketone are required, inexpensive electrodes are employed, and an operationally simple undivided cell is used. No precautions are taken to exclude air or moisture and in fact the reaction can be run open to the air (cap removed). Finally, the linear *versus* branched selectivity is remarkable (>15:1 in most of the cases).

TABLE 1. Optimization of the reductive ketone olefin coupling. Comparison to known chemical methods (A) and a graphical optimization overview of the newly developed electrochemical protocol (B).

Optimization of the Electroreductive Olefin-Ketone Coupling

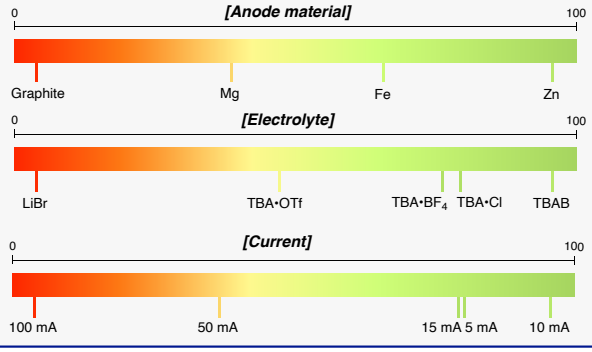
A Comparison with existing procedures



3 (2 equiv.) 4 (1 equiv.) 5

entry	deviation from above conditions	yield (%)[a]
1	**3**/**4** (5/1), (+)C/(-)Pt, divided cell, 0.2 A, 2.5 F/mol (Shono)	<10
2	SmI_2	<10
3	SmI_2 + HMPA	<10
4	SmI_2 + MeOH	<10
5	LiDBB	<5
6	None	95%

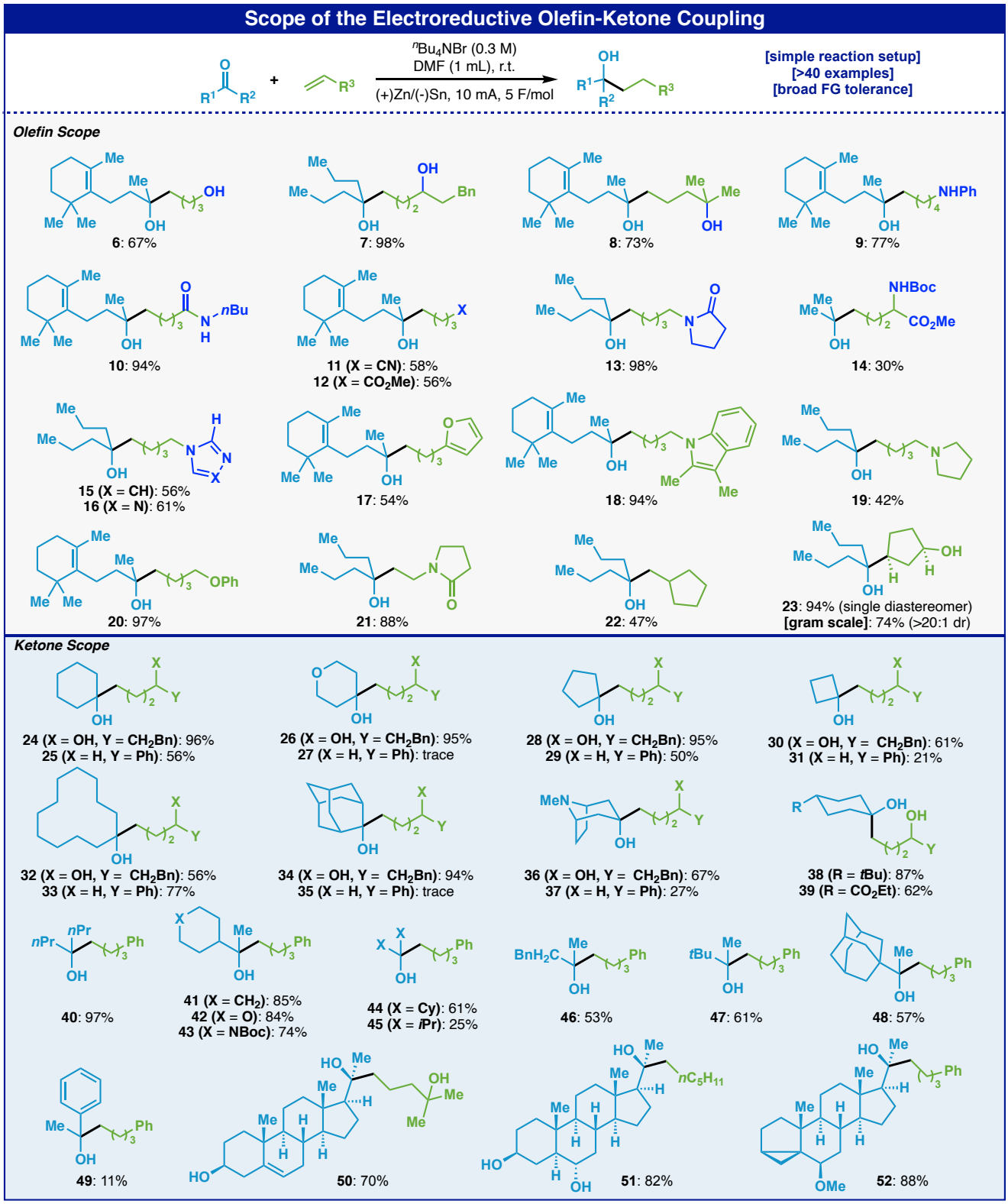
B Importance of Electrochemical Parameters



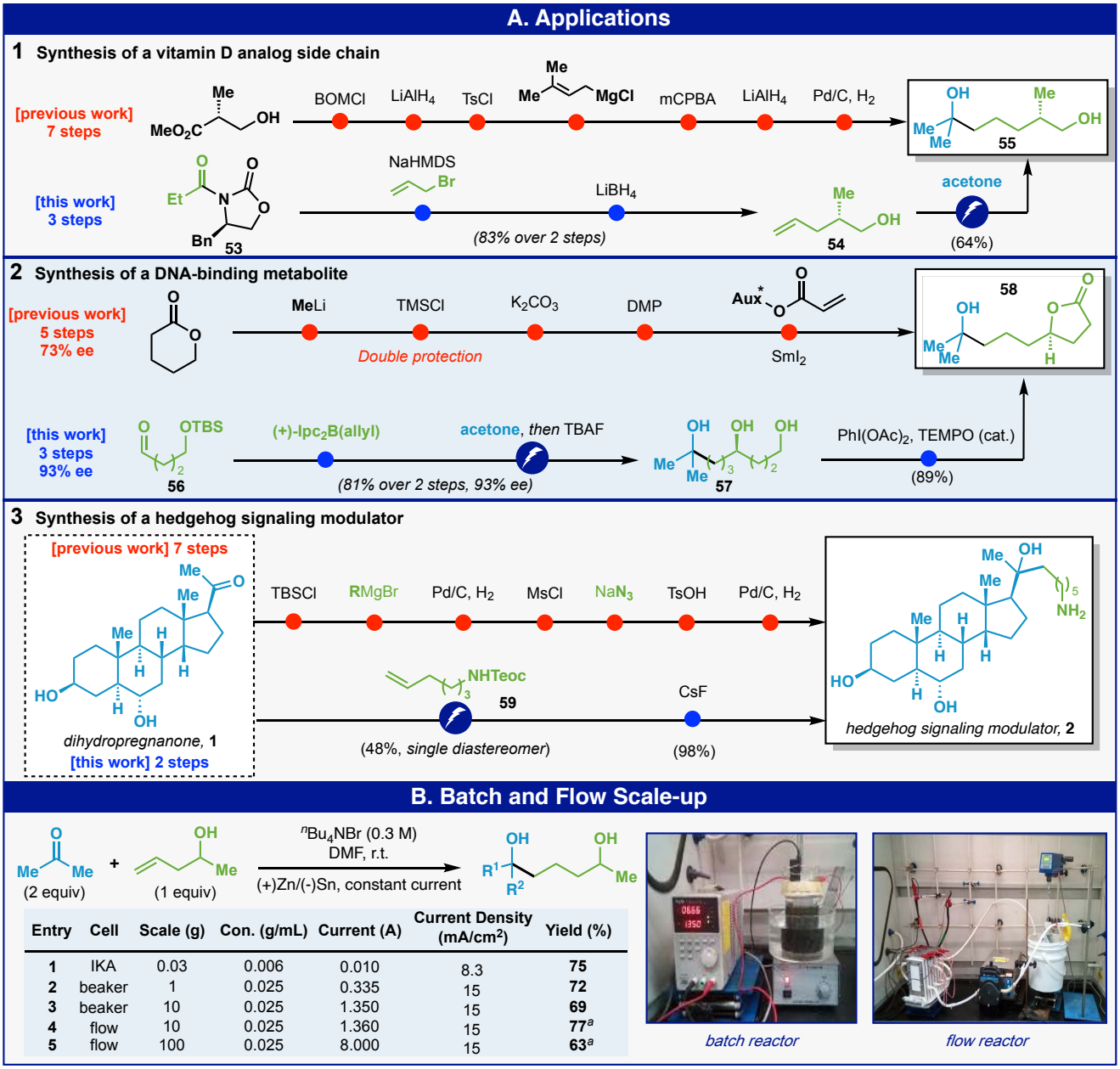
With these results in hand, the scope of the ketone-olefin coupling was investigated (Table 2). Several functionalities on the olefin were tolerated; free alcohols (1°, 2°, and 3°; **6** to **8**), aniline (**9**), amides (**10, 13, 21**), nitrile (**11**), ester (**12**), protected amino acid (**14**), and heterocycles (**15-19**) (moderate to high yields). Most of these functional groups would be challenging to employ using canonical 2e$^-$ tactics such as Grignard. The reaction tolerated mono-substituted olefins well, but performed less successfully with 1,1-di (**22**) and 1,2-di (**23**) substituted olefins – tri- and tetra-substituted olefins were not tolerated, and no reaction was observed in these cases. A plausible reason for this lack of reactivity with more substituted olefins could be due to a slower rate of addition (for steric reasons) compared to the lifetime of the ketyl radical. In the case of cyclopentene-3-ol, an interesting finding was that the reaction took place in high yield with perfect *syn* diastereoselectivity. The analogous TBS-protected olefin did not react, nor did cyclopentene itself. The directing effect of homo-allylic alcohols in this chemistry is notable and perhaps relevant to the mechanism of the reaction (*vide infra*).

In a similar fashion, ketones bearing several different substituents were tolerated (moderate to high yields); ethers (**26**), protected amines (**36-37**), esters (**39**), carbamates (**43**), alcohols (**50-51**), cyclopropanes (**52**). When 4-substituted cyclohexanones were used, single diastereomers were isolated with the selectivity reminiscent of SmI_2 promoted reactions (*anti*, **38-39**).[21] Even cyclic ketones of varying ring sizes (**24-39**) worked well, which are often challenging for other methods; reduction products

TABLE 2. Scope of the electroreductive olefin-ketone coupling.



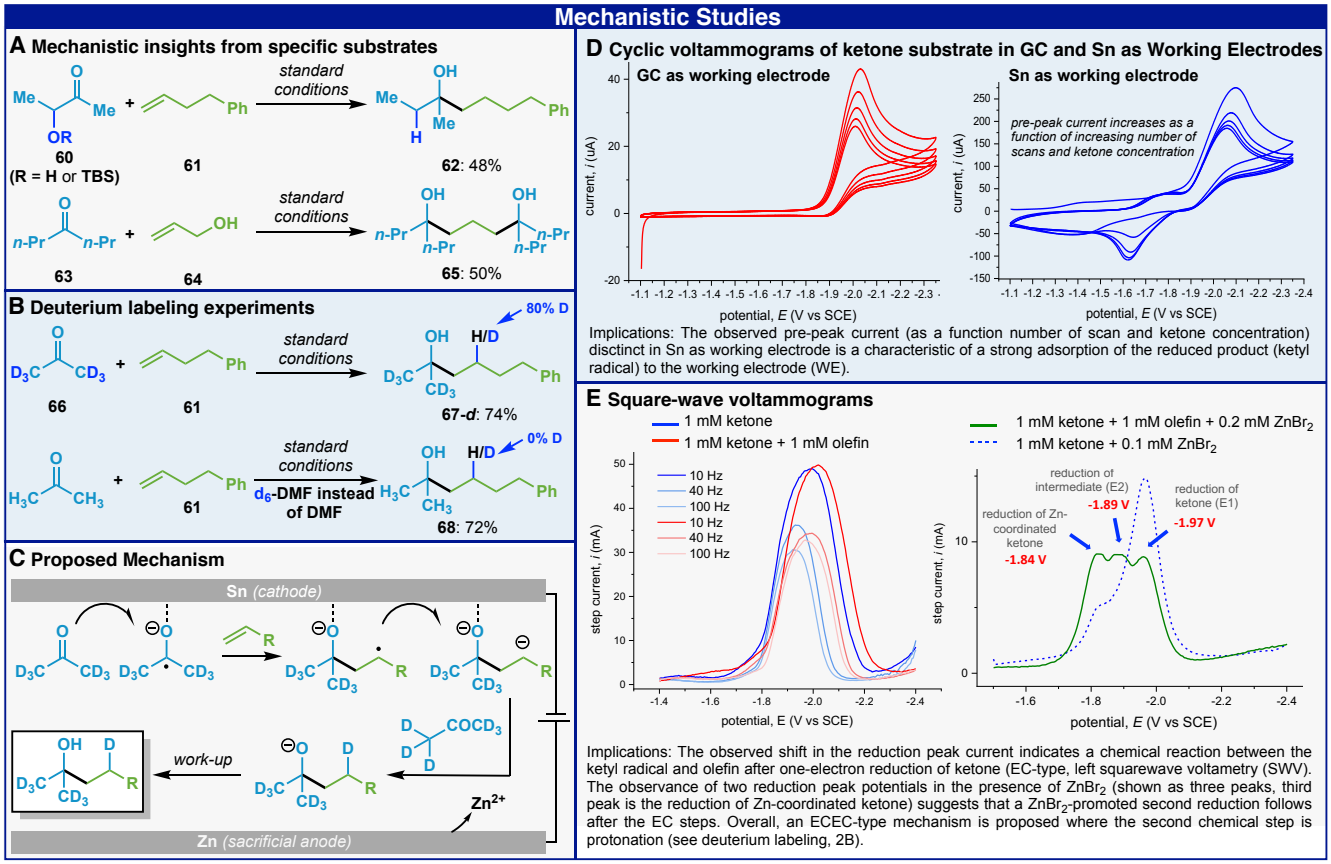
are often observed when sterically hindered ketones react with Grignards. For acyclic ketones, the sterics of the substituents showed a minor impact on the reaction yields (**40**-**48**), although only 25% yield of the desired product was isolated when very hindered diisopropylketone (**45**) was used. Notably, unprotected steroidal substrates **50**-**52** delivered a single diastereomeric product in high yield (see SI for structure confirmation).



Entry	Cell	Scale (g)	Con. (g/mL)	Current (A)	Current Density (mA/cm^2)	Yield (%)
1	IKA	0.03	0.006	0.010	8.3	75
2	beaker	1	0.025	0.335	15	72
3	beaker	10	0.025	1.350	15	69
4	flow	10	0.025	1.360	15	77[a]
5	flow	100	0.025	8.000	15	63[a]

SCHEME 1. (A) Electrochemical ketone-olefin coupling facilitates rapid access to medicinally relevant structures such as a vitamin D sidechain (1), a DNA-binding metabolite (2), and a hedgehog signaling modulator (3). (B) Batch and flow scale-up. [a]Isolated yield

This reductive coupling could also be applied to simplify real-world challenges in medicinal chemistry (Scheme 1). Thus, the synthesis of a simple vitamin D analog sidechain **55** was reported through a seven-step route wherein only one of those steps formed a C–C bond (Scheme 1A).[22] In contrast, commercially available oxazolidinone **53** could be allylated and reduced to yield (*S*)-2 methyl-4-penten-1-ol **54**. Coupling of **54** with acetone under the developed electrochemical conditions then smoothly furnished sidechain **55**. Of the three steps required to access **55**, two forged key C–C bonds. Next, the synthesis of DNA-binding metabolite **58** required a five-step sequence with two protecting groups and air-sensitive SmI_2 to forge a key C–C bond (73% ee, Scheme 1B).[23] Using the electrochemical strategy outlined above, commercially available aldehyde **56** could be converted to the same product in only 3 steps via simple Brown allylation, followed by electrochemical addition of acetone/TBAF work-up and a final oxidative lactonization (72% yield, 93% ee). Finally, the steroidal example[6] mentioned in Figure 1 could be addressed in a similar way from the same starting material (Scheme 1C). Thus, electrochemical addition of **1** to Teoc-protected amine **59** delivered a single diastereomeric tertiary alcohol that, after CsF-induced deprotection delivered **2** in only 2 steps. Clearly, the success of the above applications benefits from the chemoselective (FG tolerant) nature of the electrochemical ketone-olefin coupling.



SCHEME 2. Mechanistic insights from byproducts (A), deuterium labeling (B), proposed reaction mechanism (C), and voltammetry studies (D & E). See SI for details.

In terms of limitations, currently, ketones bearing an α-heteroatom are not tolerated (as they are reduced, *vide infra*) and heterocycles with a higher reductive potential than the ketone are not tolerated, such as thiophenes and simple pyridines (see SI for a full list of failed substrates).

The mechanism of this useful reaction (Scheme 2) was next interrogated through the observation of certain side-products (Scheme 2A), deuterium labeling (Scheme 2B), kinetics, and voltammetric studies (Scheme 2D & 2E). A notable limitation of this chemistry was that ketones bearing alpha-substituents (such as **60**) were not tolerated and elimination of the alpha-substituent was observed (**62**), suggestive of a ketyl radical intermediate. Using allyl alcohol (**64**), the bis addition adduct **65** was observed, perhaps pointing to a carbanion intermediate wherein $ZnBr_2$ generated from anodic oxidation could assist in the departure of the primary alcohol and regeneration of another olefin. Deuterium labeling using acetone-d_6 led to 70% incorporation at the highlighted position (Scheme 2B) further supporting a carbanion intermediate. When regular acetone was used in the same experiment but with deuterated DMF, no deuterated product was observed. Kinetic studies revealed zero-order dependence on all components except current indicating that reduction is purely electrochemical.

Finally, a series of voltammetric studies were performed (Scheme 2D & 2E) to understand how traditionally nucleophilic ketyl radical can serve as competent coupling partners with unactivated olefins, as well as to provide evidence for the overall electrochemical mechanistic sequence as proposed in Scheme 2C. We hypothesized that the change in its electronic property and reactivity can be facilitated by a strong adsorption of the ketyl radical to the Sn electrode. Cyclic voltammetry studies were performed using Sn and glassy carbon (GC) as working electrodes with acetophenone[24] as the source of ketyl radical. Pre-peaks on the CV were observed using Sn as the working electrode but not observed using GC as the working electrode. These pre-peaks are distinct characteristics of an electron transfer where the product (ketyl radical) is strongly adsorbed into the working electrode.[25] Furthermore, the current response observed in the pre-peak in Sn was found to be dependent on the concentration of ketone (see SI).[26] This result also rationalizes the effectiveness of using Sn-cathode over other electrode materials (see SI). Square-wave voltammetry (SWV) studies were performed and the results are summarized in Scheme 2E. The addition of alkene **61** to acetophenone showed an anodic shift in the cathodic peak potential denoting a chemical reaction with the ketyl radical after one-electron reduction. However, even at high frequencies (100 Hz), the expected second reduction peak was not observed. We hypothesized that one crucial role of the sacrificial Zn-anode is to provide Zn^{2+} as a thermodynamic sink for the second electron reduction. SWV analysis in the presence of catalytic amounts of $ZnBr_2$ showed three distinct reduction peaks where the third peak can be the reduction of the $ZnBr_2$-

coordinated ketone (see SI). Taken together, these results suggest an ECEC-type electrochemical mechanism where the ketyl radical formation (E) takes place at the Sn-cathode with strong adsorption characteristic followed by radical addition (C) into the olefin. A second one-electron reduction (second E) of the radical anion to the dianion followed by protonation (second C) and then workup delivers the final product. The enhanced reactivity of homoallylic alcohols may be due to improved binding of the olefin substrate to the cathode surface.

In summary, a chemoselective, scalable method to combine unactivated olefins and ketones has been developed that subverts the issues encountered using Grignard reagents in conventional retrosynthetic analysis. The scope of this reaction is broad and it is operationally simple to perform. A number of applications demonstrate that the utility extends beyond that of a simple tactical change as when strategically employed, it can dramatically reduce overall step count. Mechanistic studies point to an intuitive electrochemically driven reductive pathway that initiates upon the formation of a ketyl radical, addition to the olefin, and further reduction to a stabilized carbanion prior to workup. This work is thus another example of how strongly reducing chemistry can be uniquely facilitated and enabled in complex settings under electrochemical control when classical chemical reagents fail.

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Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

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Electroreductive Olefin-Ketone Coupling

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Supplementary Materials

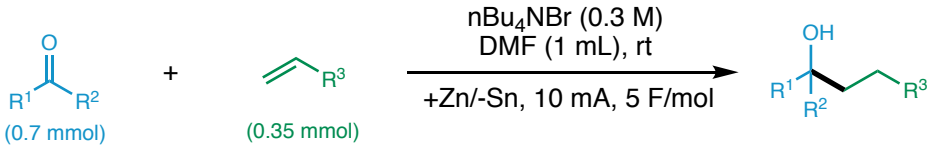
Table of Contents

General Experimental

Tetrahydrofuran (THF), *N*,*N*-dimethylforamide (DMF), acetonitrile (CH_3CN), and dichloromethane (CH_2Cl_2) were obtained by passing the previously degassed solvents through an activated alumina column (*1*). Reagents were purchased at the highest commercial quality grade and used without further purification, unless otherwise stated. Lithium bromide (LiBr) was flamed-dried under high vacuum. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous material, unless otherwise stated. Reactions were monitored by GC/MS, LC/MS, and thin layer chromatography (TLC). TLC was performed using 0.25 mm E. Merck silica plates (60F-254), using short-wave UV light as the visualizing agent, and phosphomolybdic acid and $Ce(SO_4)_2$, acidic ethanolic anisaldehyde, $KMnO_4$, or iodine absorbed on silica gel was used, and heat as developing agents (not for iodine staining). NMR spectra were recorded on Bruker DRX-600, DRX-500, and AMX-400 instruments and are referenced using residual undeuterated solvent ($CHCl_3$ at 7.26 ppm ^{1}H NMR, 77 ppm ^{13}C NMR; acetone at 2.05 ppm ^{1}H NMR, 29.84 ppm ^{13}C NMR; CH_3OH at 3.31 ppm ^{1}H NMR, 49.0 ppm ^{13}C NMR; C_6H_6 at 7.16 ppm ^{1}H NMR, 128.06 ppm ^{13}C NMR; pyridine at 7.22 ppm ^{1}H NMR, 123.87 ppm ^{13}C NMR)(*2*). The following abbreviations were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Column chromatography was performed using E. Merck silica (60, particle size 0.043–0.063 mm), and pTLC was performed on Merck silica plates (60F-254). High-resolution mass spectra (HRMS) were recorded on an Agilent LC/MSD TOF mass spectrometer by electrospray ionization time of flight reflectron experiments. Gas chromatography-mass spectrometry (GCMS) were recorded on an Agilent 5975 MSD Series spectrometer.

General Procedures for Electro-Reductive Ketone-Olefin Coupling

General Procedure A



Setup (see graphical guide):

IKA **Zn** (anode) and **Sn** (cathode) plate electrodes or home-made ones from the corresponding metal wires were connected to an ElectraSyn vial cap. A standard 2-mL ElectraSyn vial was charged a magnetic stirrer bar, $^{n}Bu_4NBr$ (96.7mg, 0.3 mmol), ketone (0.7 mmol), olefin (0.35 mmol) and DMF (1 mL). The cap was installed and the vial was pre-stirred until all solids dissolved. Then, it was fit into the ElectraSyn and the following setup was employed: *New exp.* → *Constant current* → *10 mA* → *No ref. electrode* → *Total charge* → *0.35 mmol, 5 F/mol (see individual compounds)* → *No alternating polarity* → *start*. After completion, the reaction mixture was passed through a short plug of silica gel and washed with EtOAc (20 mL). The solution was further purified via column chromatography to give the desired product. See the graphical representation of the reaction sequence and setup.

General Procedure B

The procedure is the same as procedure A except 0.35 mmol of ketone, 0.7 mmol of olefin and 2.5F/mol were used.

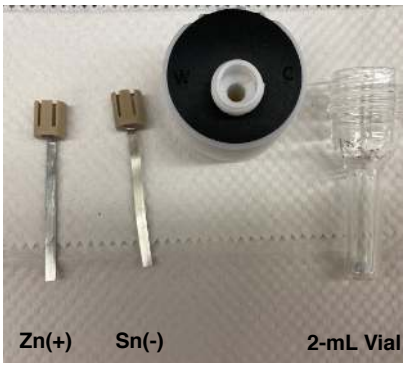
Note: Generally speaking, procedure A gave higher yields than procedure B. However, procedure A would lead to the formation of ~1 equivalent of corresponding secondary alcohol, which came from the reduction of ketone. When a ketone with relatively high molecular weight (e.g. steroids) was used, procedure B led to easier purification.

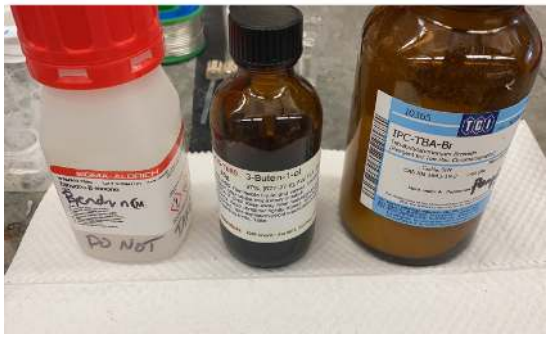
Graphical Guides

Graphical Supporting Information for electrode assembly

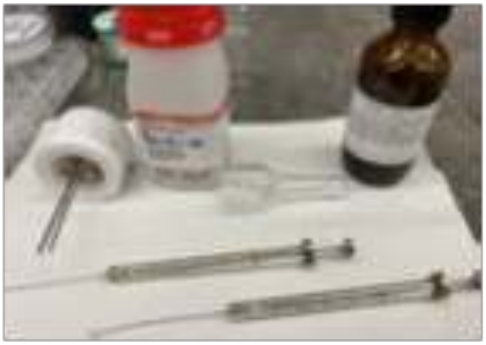
Non-IKA based electrode materials can also be used such as the items shown in the picture. Zinc could also be purchased from Bean Town Chemicals, 2.0 mm diameter (Catalogue no. 141550-1M). Tin can be purchased in the form of solder wire from Amazon (1.5 mm, 98% purity). In order to get these wires to fir into the IKA electrode holders, the ends need to be hammered flat and occasionally filed to ensure a fit; see flattened wire B in picture.

Graphical Supporting Information for setting up Electro-Reductive Ketone-Olefin Coupling

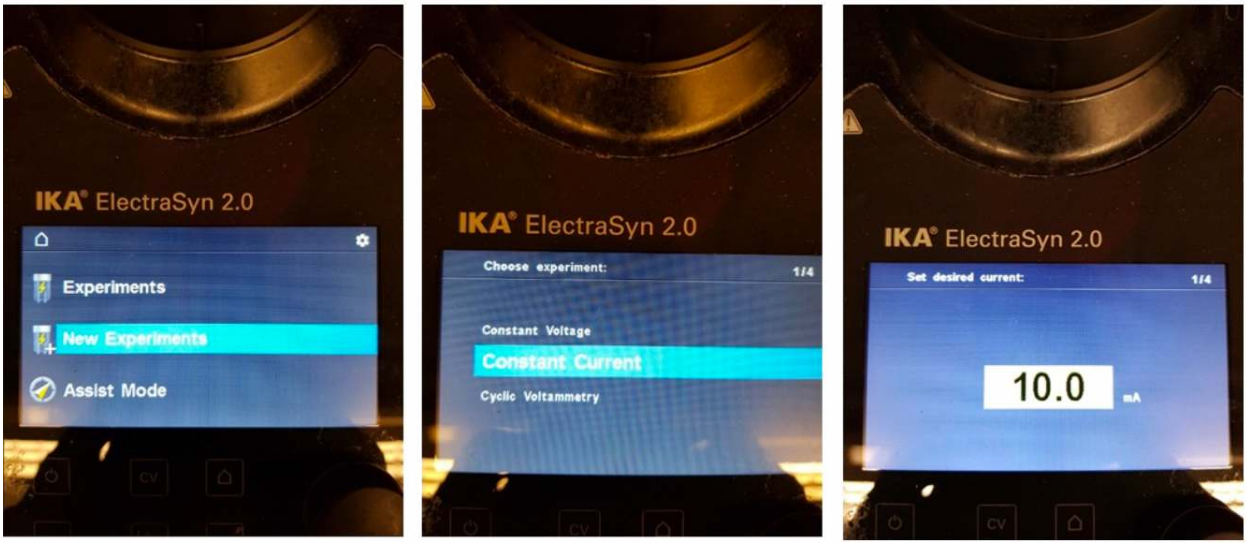




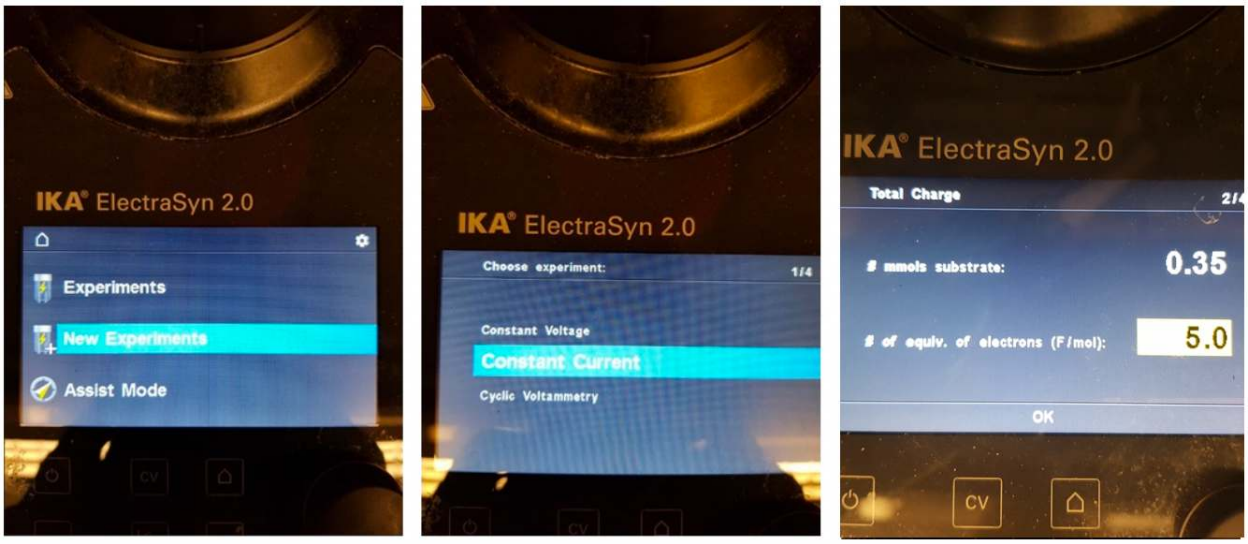
(Left) IKA electrochemical kit needed. **(Right)** Chemicals.



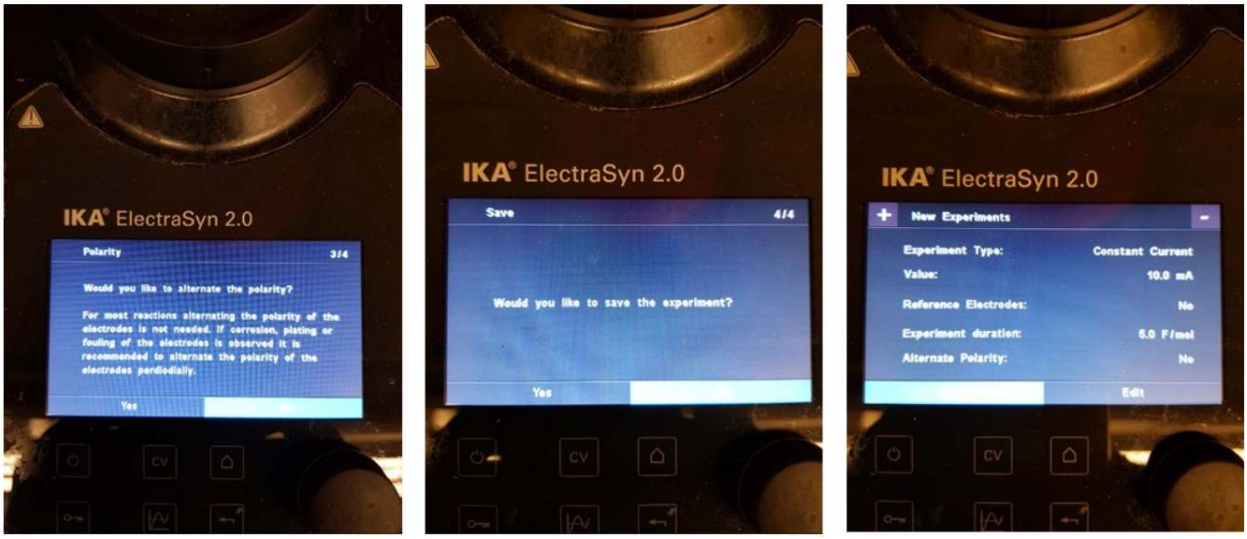
(Left) TBAB added to vial. **(Center)** Liquid reagents added to vial via a micro syringe. **(Right)** Solvent added to vial.



(Left) Selecting a new experiment. **(Center)** Select constant current. **(Right)** Set the current to 10 mA (for a 0.35 mmol scale).



(Left) No need to use a reference electrode, so select *No*. **(Center)** Reactions are run based on how much charge they need. **(Right)** Typically reactions were run on a 0.35 mmol scale and typically current efficiencies are around 50 %, so select double/triple what is needed. *NOTE:* ALL REACTIONS WERE MONITORED AND STOPPED ACCORDING TO TLC ANALYSIS (consumption of starting material), MORE OR LESS CHARGE MAY BE REQUIRED FOR EACH INDIVIDUAL CASE!



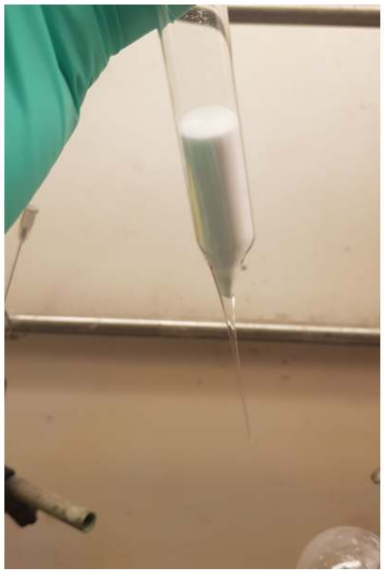
(Left) No need to alternate the polarity, if fact, that will result in NO REACTION. **(Center)** This is up to the individual, but there is really no need to save the experiment. **(Right)** Start when ready!

A typical ongoing reaction.

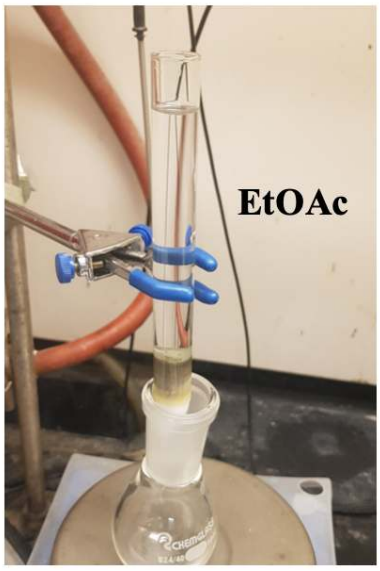
Graphical Supporting Information for Working-Up the Electro-Reductive Ketone-Olefin Coupling



(Left/Center) Heating a tube to fashion a column/filtration utensil. **(Right)** a Kimwipe or piece of cotton can be used as a plug.



(Left) Add ~ 3 cm of silica gel **(Center)** Add the reaction mixture neat onto the dry silica plug. **(Right)** Typical appearance of the setup before rinsing with EtOAc.



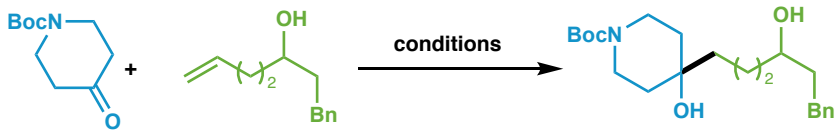
(Left) After sample properly loaded on the silica, ~ 15 mL of EtOAc. **(Right)** Filtered sample ready for removal of the solvent on a Rotavap. Volatiles such as EtOAc are first removed on a Rotavap, and remaining DMF is removed using a high vacuum pump.

Graphical Supporting Information for cleaning the electrodes

(Left) Electrodes after reaction **(Center)** Electrodes can be cleaned with a tissue. **(Right)** Cleaning electrodes with a blade is most efficient but does erode the electrodes.

Attempts to replicate Shono's conditions

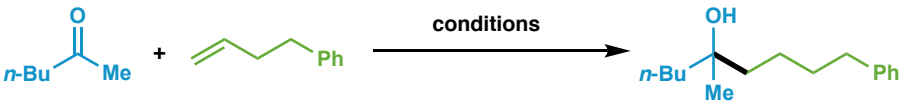
Attempts at applying Shono's conditions on a medicinally-relevant substrate



(2.5 mmol) (0.5 mmol)

Entry	*Anode*	*Cathode*	*Electrolyte*	*Cell*	*Charge*	*Current density/ mA.cm^{-2}*	*Ket:Olefin*	*Conc.of olefin/ M*	*% Yield*
1	Pt	CF	$TBA.BF_4$	divided	2.5	50	5:1	0.14	**8**
2	Pt	CF	$TBA.BF_4$	divided	5	50	5:1	0.14	**10**
3	Pt	CF	$TBA.BF_4$	divided	5	50	2:1	0.14	**8**
4	Pt	CF	$TBA.BF_4$	divided	5	14	2:1	0.35	**17**
5	Pt	CF	$TBA.BF_4$ + $ZnBr_2$	divided	5	50	2:1	0.35	**ND**

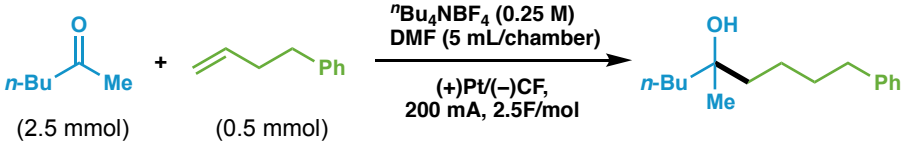
Attempts at repeating Shono's results using a set of simple substrates



(2.5 mmol) (0.5 mmol)

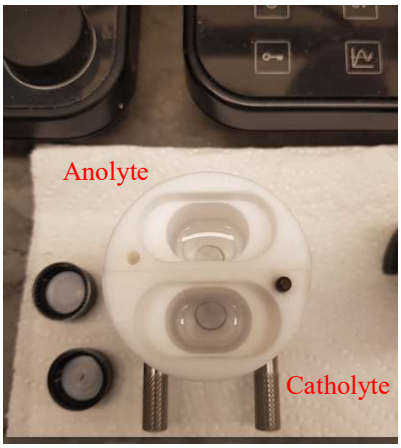
Entry	*Anode*	*Cathode*	*Electrolyte*	*Charge*	*Cell*	*Current density/ mA.cm^{-2}*	*Ket:Olefin*	*Conc.of olefin/ M*	*% Yield*
1	Pt	**CF**	TBA.BF_4	2.5	divided	50	5:1	0.14	**25**
2	Pt	CF	TBA.BF_4	**5**	divided	50	5:1	0.14	**49**
3	Pt	**Sn**	TBA.BF_4	2.5	divided	50	5:1	0.14	**7**
4	Pt	**Zn**	TBA.BF_4	2.5	divided	50	5:1	0.14	**32**

Graphical Supporting Information for reproducing Shono's conditions

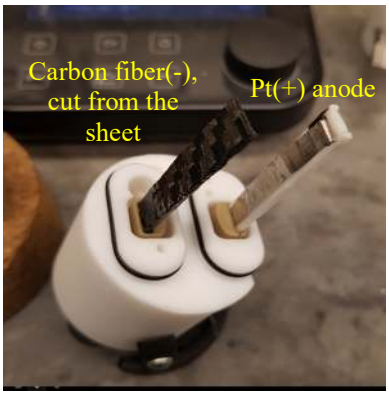


IKA Pt (anode) and 3K Carbon fiber (cathode) purchased from Amazon (cut 8 x5 5 mm, 1 mm thick) plate electrodes were connected to an ElectraSyn vial cap. To the ElectraSyn vial was then added $TBABF_4$ (1.25 mmol) and DMF (5 mL/chamber), followed by olefin (0.5 mmol, 1.0 equiv), and ketone (2.5 mmol, 5.0 equiv) to the cathodic chamber. The ElectraSyn was setup as follows: *New exp. > Constant current > 200 mA > No ref. electrode > Total charge > 0.5 mmol, 2.5 F/mol > No alternating polarity > start*.

Using IKA divided cell



(Left) 3K carbon fiber bought from Amazon **(Center)** IKA divided cell assembly. **(Right)** Reaction setup, with reactants in cathodic chamber.



(Left) Electrode assembly **(Center)** Reaction setup to run -200 mA at cathode, and **(Right)** unable to pass 200 mA when stabilized (85 mA when reaching the voltage limit).

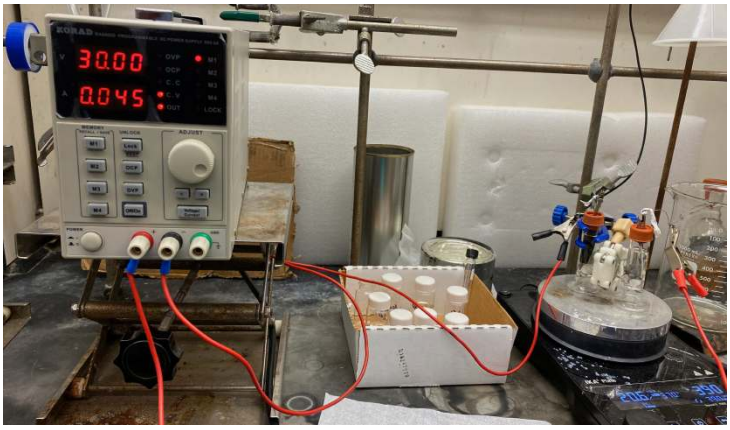


(Left) Reaction after 5 F/mol. **(Center)** Carbon felt/cloth used. **(Right)** Folded carbon cloth cathode secured by rolling and tying it with Teflon tape.

(Left) Reaction after 2.5 F/mol. **(Right)** Reaction after 5 F/mol.

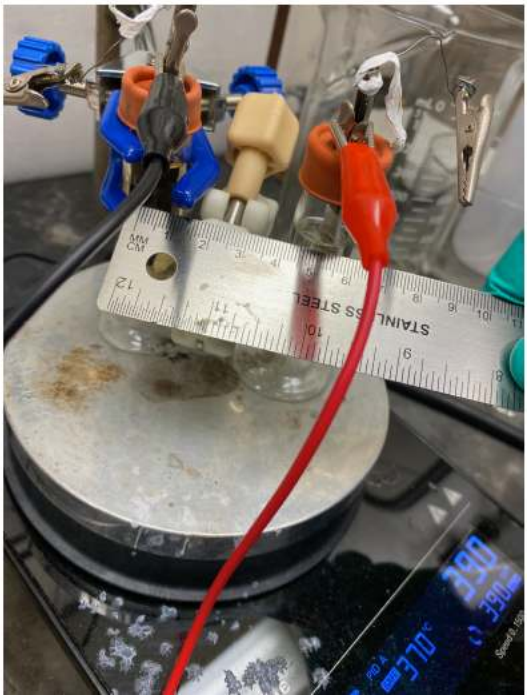
Using a Standard H-cell


(Left) Reaction setup before start. **(Right)** Details of the H-cell.



(Left) unable to pass 200 mA when stabilized (only 45 mA when reaction reached the 30V potential limit of the potential stat.). **(Right)** Reaction after 2.5 F/mol.

Comparison of the electrode distance in IKA divided cell and a standard H-cell



(Left) IKA divided cell's electrode distance is ~2 cm. **(Right)** A standard H-cell we used has an electrode distance of ~5 cm.

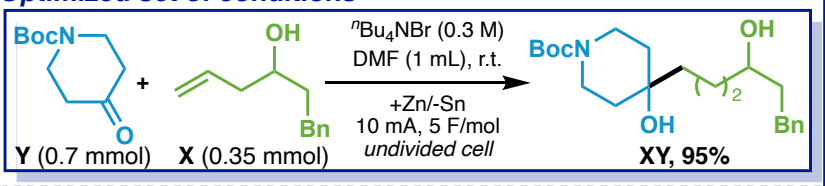
In the case where carbon fiber was used, a yield of 22% was obtained after 2.5 F/mol, and 35% when the reaction was run up to 5 F/mol. When carbon felt was used instead, after 2.5 F/mol, a yield of 19% was obtained, and when this was extended to 5 F/mol the yield was found to be 25%.

Most of the olefin still remained after 5 F/mol (60% in case of the carbon felt). As the reaction proceeds the cell resistance increases significantly, and therefore, after delivery of 5 F/mol, it becomes very difficult to pass current, and comparison of the 2.5 F/mol yield to the 5 F/mol shows that the reaction starts to plateau. The conditions reported in Shono's paper are quite vague, and therefore it is difficult to replicate exactly his reaction conditions. **Nevertheless, in order to reach the 0.2 A current reported in Shono's paper, a customized divided cell is probably required and therefore adds operational difficulties for users.**

Condition Optimization

Optimization of the Reductive Ketone Olefin Coupling

Optimized set of conditions

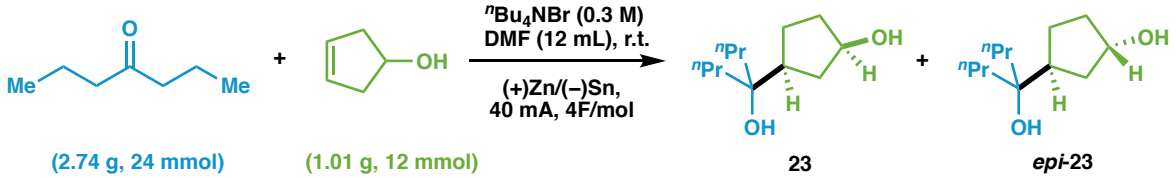


Y (0.7 mmol) **X** (0.35 mmol) **XY, 95%**

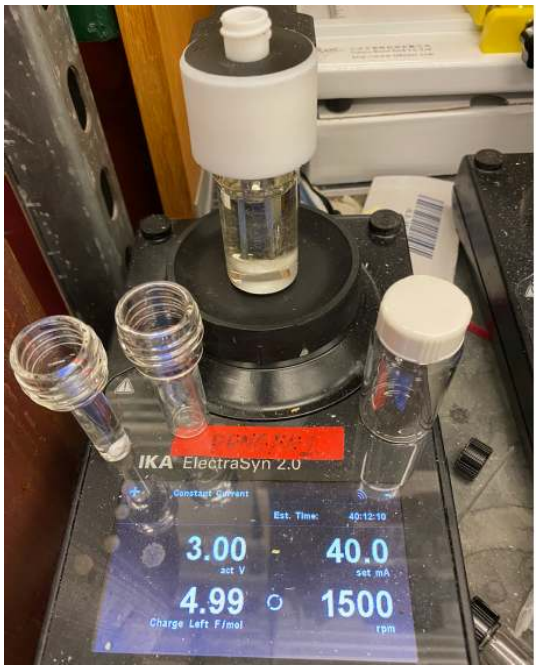
entry	conditions	yield (%)[a]
Comparison with existing procedures		
1	SmI_2	<10
2	SmI_2 + HMPA	<10
3	SmI_2 + MeOH	<10
4	LiDBB	<5
5	**X**/**Y** (5/1), +C/-Pt, divided cell, 0.2 A, 2.5 F/mol (Shono)	<10
Anode Optimization		
6	Fe instead of Zn	64
7	Mg instead of Zn	39
8	Al instead of Zn	64
9	graphite instead of Zn	<5
Electrolyte Optimization		
10	*n*-Bu_4BF_4 instead of *n*-Bu_4Br	75
11	*n*-Bu_4Cl instead of *n*-Bu_4Br	79
12	LiBr instead of *n*-Bu_4Br	<5
13	*n*-Bu_4OTs instead of *n*-Bu_4Br	47
Current Optimization		
14	5 mA instead of 10 mA	80
15	15 mA instead of 10 mA	78
16	50 mA instead of 10 mA	36
17	100 mA instead of 10 mA	<10
Cathode Optimization		
18	Zn instead of Sn	94
19	SS instead of Sn	87
20	graphite instead of Sn	91
21	carbon felt instead of Sn	83
Solvent Optimization		
22	THF instead of DMF	<10
23	THF/TPPA (10:1) instead of DMF	<30
24	CH_3CN instead of DMF	<10
25	CH_2Cl_2 instead of DMF	<10
Substrate Concentration Optimization		
26	0.2 M instead of 0.35 M	78
27	0.3 M instead of 0.35 M	90
28	0.4 M instead of 0.35 M	86
29	0.5 M instead of 0.35 M	69

Scale up experiments

Gram-scale synthesis of compound 23.



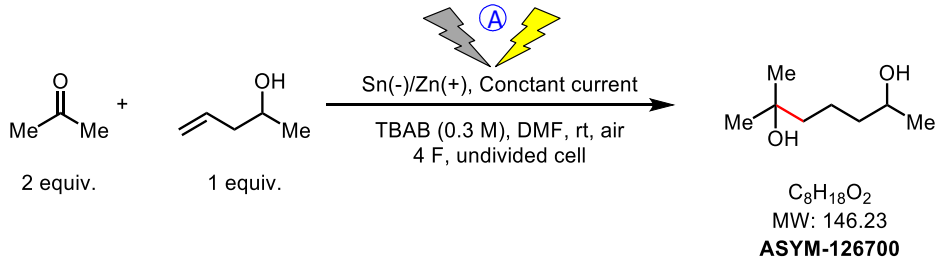
IKA **Zn** (anode) and **Sn** (cathode) plate electrodes were connected to an ElectraSyn vial cap. A standard 20-mL ElectraSyn vial was charged with a magnetic stirrer bar, ^{n}Bu$_4$NBr (1.45 g, 3.6 mmol), ketone (2.74 g, 24 mmol), olefin (1.01 g, 12 mmol) and DMF (12 mL). The cap was installed and the vial was pre-stirred until all solids dissolved. Then, it was fit into the ElectraSyn and the following setup was employed: *New exp.* → *Constant current* → *10 mA* → *No ref. electrode* → *Total charge* → *0.35 mmol, 4 F/mol* → *No alternating polarity* → *start*. After completion, the reaction mixture was directly purified via column chromatography to give product **23** (1.77 g, 74%) and ***epi*-23** (80.4 mg, 3.4%).



<u>*Note:*</u> Due to the high reaction concentration, the reaction mixture solidify after 4F/mol of current was passed and the resistance became very high.

Hundred-gram scale reaction using flow-cell Conducted by Asymchem

A. Reaction scheme



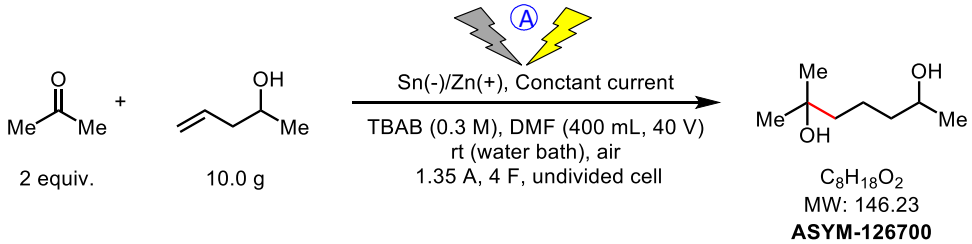
B. Condition optimization:

Entry/Scale (g)	Con. of SM (g/mL)	Acetone/ eq	Anode(+)/ Cathode(-)	Electrolyte	Temperature (^{o}C)	F/mol	Current (mA) /Voltage (V)	CD (mA/cm^2)	NMR/%		Cell
									SM	TP	
2211/**0.03**	0.006	2.0	Zn (+)/Sn (-)	TBAB	rt (24)	4	10/2~5	8.3	0%	75%	IKA
2212/**1.0**	0.025	2.0	Zn (+)/Sn (-)	TBAB	rt (24)	4	335/6~9	15	0%	72%	Beaker
2214/**10.0**	0.025	2.0	Zn (+)/Sn (-)	TBAB	rt (24)	4	1350/6~9	15	0%	69%	Beaker
2215/**10.0**	0.025	2.0	Zn (+)/Sn (-)	TBAB	rt (24)	4	1360/8~32	15	0%	77[a]	Flow cell
2216/**100.0**	0.025	2.0	Zn (+)/Sn (-)	TBAB	rt (24)	4	8000/8~32	15	0%	63[a]	Flow cell

[a]Isolated yield

C. Procedure:

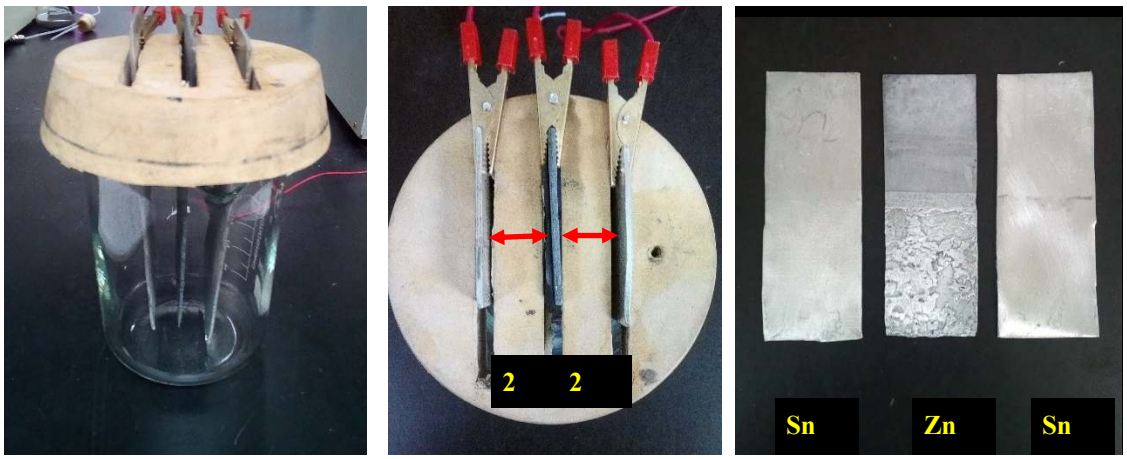
a. 10 g scale-up (in batch)



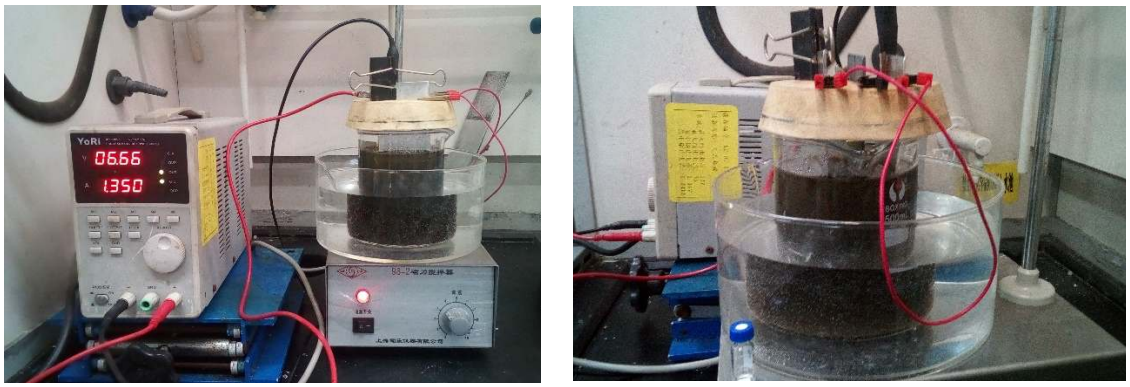
A clean and dry 500 mL beaker equipped with a stir bar was charged with 4-penten-2-ol (10.0 g, 116.3 mmol, 1 equiv.), acetone (13.5 g, 232.6 mmol, 2 equiv.), tetrabutylammonium bromide (TBAB, 38.6 g, 120 mmol, 0.3 M) and DMF (400 mL). A Zn plate and two Sn plates, embedded a rubber cap with a distance of 2.0 cm between them, were inserted into the reaction mixture. The

submerged surface area of electrode was adjusted to 8 cm × 5.5 cm × 2. The undivided cell was put into water bath to release heat produced by electrolysis. Reaction mixture was electrolyzed under a constant current of 1350 mA from DC power for 9 h until the complete consumption of 4-penten-2-ol as judged by TLC.

After reaction, the electrodes were taken out and rinsed with ethyl acetate (EtOAc). The mixture was transferred to a 1.0 L round bottom and volatiles were then removed on the under reduced pressure (~4 mbar, 55 °C oil bath). The remaining oily liquid was eluted with ethyl acetate through a short silica plug. Crude product was delivered after rotary evaporation. 69% yield was obtained through qNMR with maleic acid as internal standard.

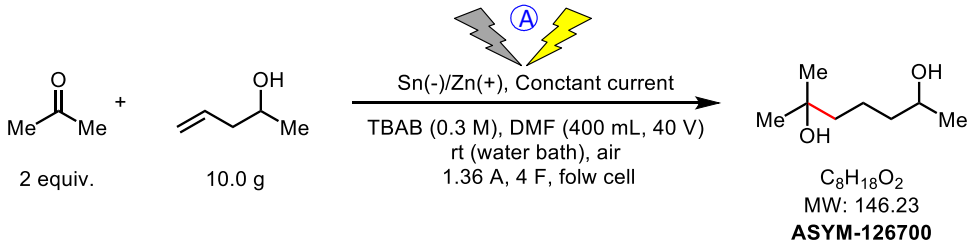


(**Left**) Batch cell. (**Middle**) Top view. (**Right**) electrodes



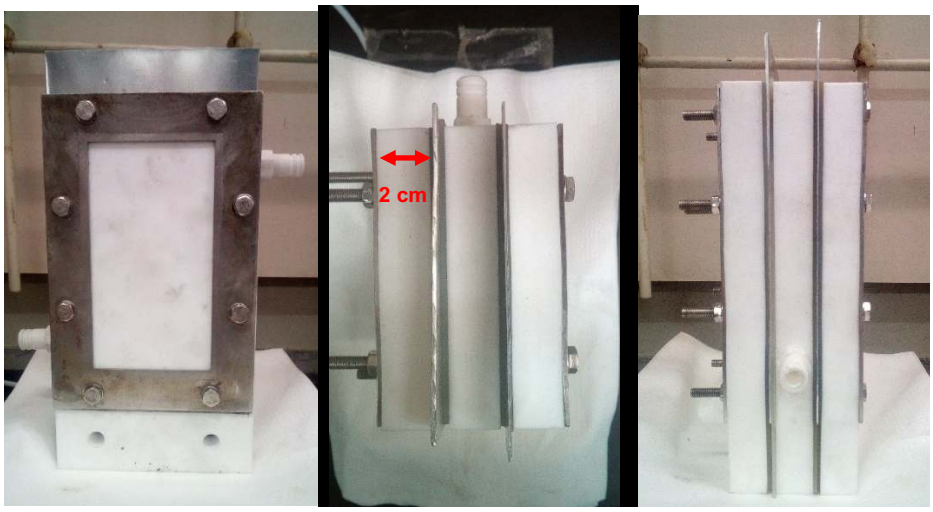
(**Left**) Electrolysis setup. (**Right**) Right view of electrolysis

b. 10 g scale-up (Flow)



Frame Cell Setup: A Sn plate (length: 20.5 cm, width: 12.0 cm, thickness: 2.0 mm) and a Zn plate (length: 20.5 cm, width: 12.0 cm, thickness: 1.5 mm) were used as cathode and anode, respectively. Two silica pads (length: 18.0 cm, width: 12.0 cm, thickness: 2.0 mm) attached on their both sides were inserted between frame (Teflon frame block, length: 18.0 cm, width: 12.0 cm, thickness: 2.0 cm). The two ends of frame cell were attached by two Teflon plates (length: 18.0 cm, width: 12.0 cm, thickness: 2.0 cm) and all components were then threaded through 8 stainless steel screws (length: 10 cm, diameter: 5.0 mm) and locked by nuts above stainless steel gasket. The side of frame was screwed a Teflon joint with which connected rubber tube (6 mm in diameter). The immersion surface area of each electrode in frame cell was 7.0 cm × 13.0 cm (Figure 3 & 4).

Components of frame cell for the flow reactor assembly. (1. Zn plate; 2. Sn plate; 3. Flame cell; 4. Teflon plate; 5. stainless steel sheet ×2; 6. stainless steel screws; 7. silica pads ×2; 8. Teflon plate)

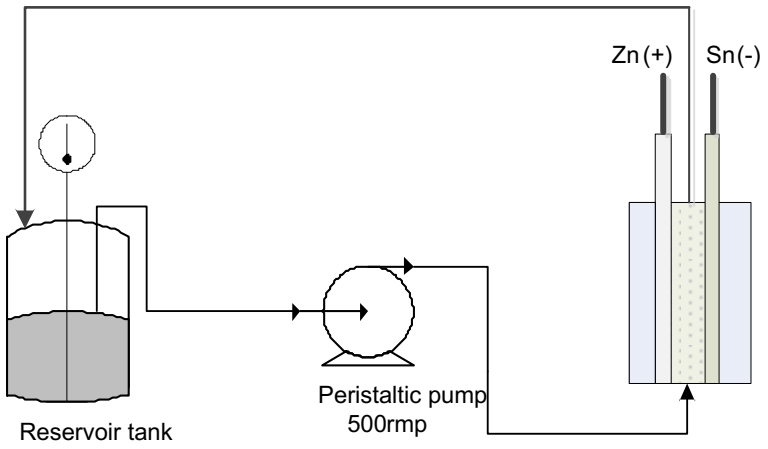


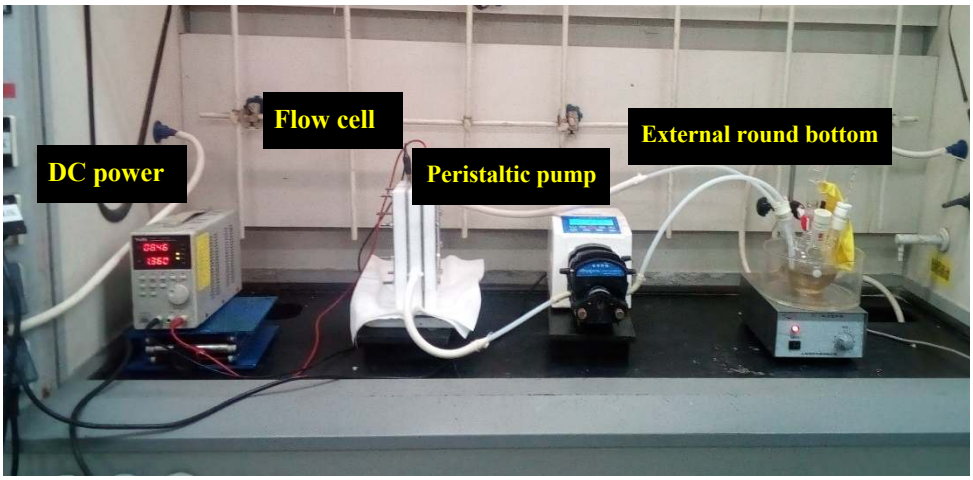
Three views of assembled flow cell

Experimental procedure: A clean and dry 500 mL 4-necked round bottom equipped with a stir bar and used as external container was charged with 4-penten-2-ol (10.0 g, 116.3 mmol, 1 equiv.), acetone (13.5 g, 232.6 mmol, 2 equiv.), tetrabutylammonium bromide (TBAB, 38.6 g, 120 mmol, 0.3 M) and DMF (400 mL). A peristaltic pump was connected with frame cell and external round bottom by rubber tubes (diameter: 6.0 mm) and Teflon tubes (diameter: 6.0 mm) respectively to form a circulatory system. The external round bottom was put into water bath to release heat produced by electrolysis. The mixture was then pumped into frame cell with a speed of 500 rmp in the loop by peristaltic pump. The frame cell with a distance of 2.0 cm between each electrode was then conducted electrolysis (Figure 6) under a constant current of 1.36 A from DC power for 9 h until the complete consumption of 4-penten-2-ol judged by TLC.

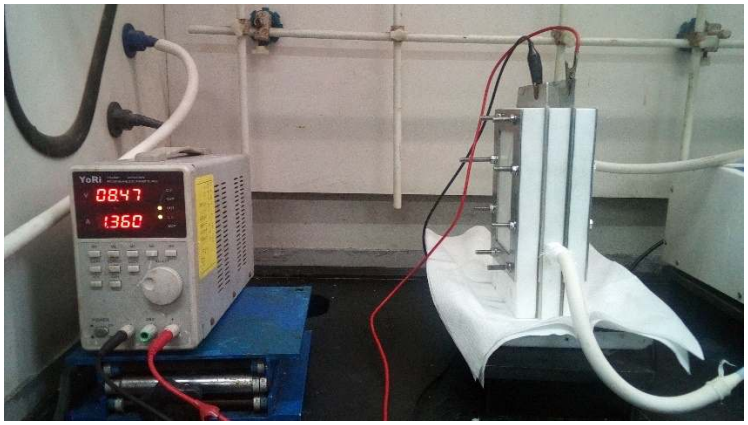
After reaction, the entire mixture was transferred into a 2.0 L round bottom from frame cell and external round bottom by peristaltic pump. 300 mL EtOAc was added and circulated for 5 min to wash frame cell and connecting tube twice (300 mL x 2). The volatiles were then removed on the under reduced pressure (~4 mbar, 55 °C oil bath). The remaining oily liquid was eluted with EtOAc through a short silica plug. Crude product was delivered after rotary evaporation. Crude product was purified by column chromatography (n-Hexane: EA = 1:1) to afford desired product 13.1 g as a colorless oil with 77 % isolated yield.

Figure S1. 10 g scale up flow diagram.



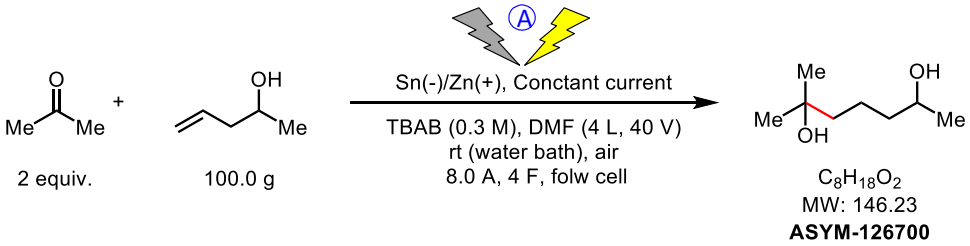


Electrolysis setup in flow cell.



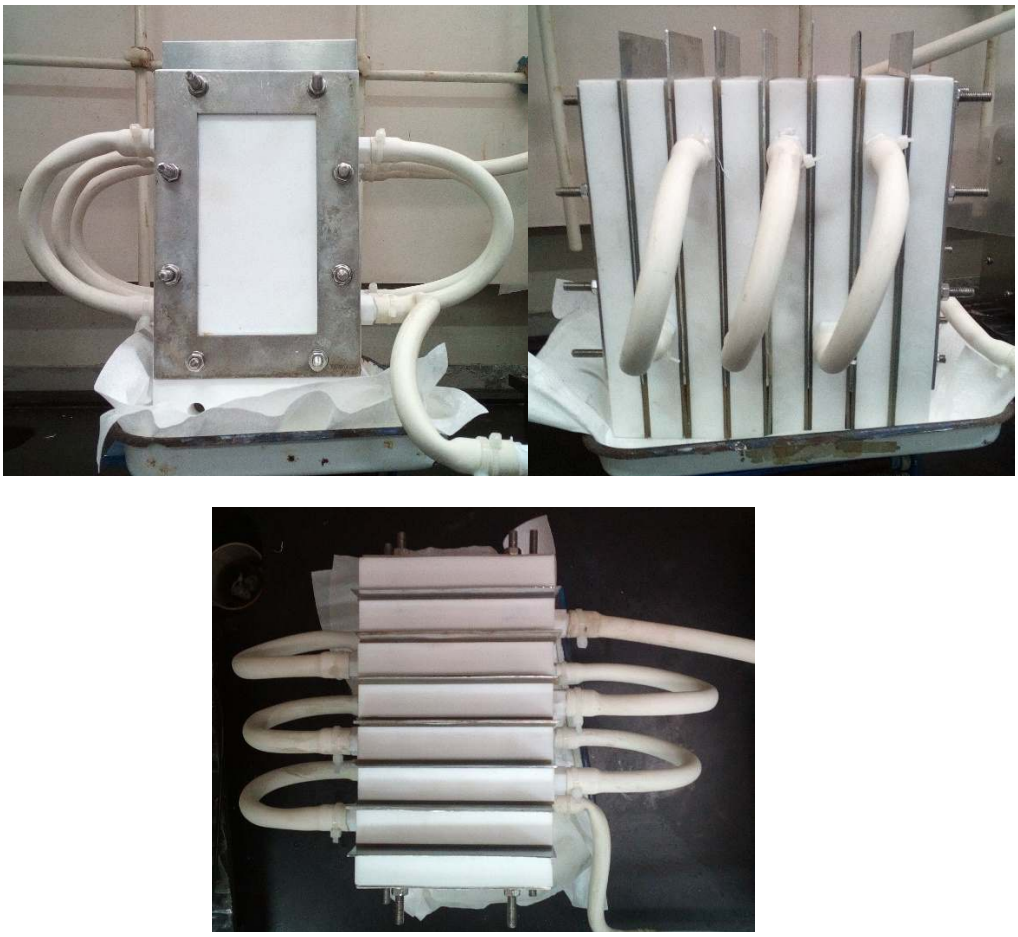
DC power supply and frame cell.

c. 100 g scale-up (Flow)



Frame Cell Setup: Six Teflon frame block (length: 18.0 cm, width: 12.0 cm, thickness: 2.0 cm) were packed in a row, 4 Zn plates (length: 20.5 cm, width: 12.0 cm, thickness: 1.5 mm) as anode and 3 Sn plates (length: 20.5 cm, width: 12.0 cm, thickness: 2.0 mm) as anode which have two silica pads (length: 18.0 cm, width: 12.0 cm, thickness: 2.0 mm) attached on their both sides were inserted between each frame. The two ends of frame cell were attached by two Teflon plates (length: 18.0 cm, width: 12.0 cm, thickness: 2.0 cm) and all components were then threaded through 8 stainless steel screws (length: 25.0 cm, diameter: 5.0 mm) and locked by nuts above stainless steel gasket. The side of each frame was screwed a Teflon joint with which connected rubber tube (6 mm in diameter). The immersion surface area of each electrode in frame cell was 7.0 cm × 13.0 cm (Figure 7).

Components of frame cell for the flow reactor assembly.



Three views of assembled flow cell.

Experimental procedure: A clean and dry 5 L 4-necked round bottom with mechanical stirring and used as an external container was charged with 4-penten-2-ol (100.0 g, 1.16 mol, 1 equiv.), acetone (135 g, 2.32 mol, 2 equiv.), tetrabutylammonium bromide (TBAB, 386 g, 1.2 mol, 0.3 M) and DMF (4 L). A peristaltic pump was connected with frame cell and external round bottom by rubber tubes (diameter: 6.0 mm) and Teflon tubes (diameter: 6.0 mm) respectively to form a circulatory system. The external round bottom was put into water bath to release heat produced by electrolysis. The mixture was then pumped into frame cell with a speed of 200 rmp (~3.5 L/min) in the loop by peristaltic pump. The frame cell with a distance of 2.0 cm between each electrode was then conducted electrolysis under a constant current of 8.0 A from DC power for 15 h until the complete consumption of 4-penten-2-ol judged by TLC.

After reaction, the entire mixture was transferred into a 5.0 L round bottom from frame cell and external round bottom by peristaltic pump. 1 L EtOAc was added and circulated for 5 min to wash frame cell and connecting tube twice (1 L×2). The volatiles were then removed on the under

reduced pressure (~4 mbar, 55 °C oil bath). Rochelle's' salt (2.0 L, 10% aq. solution) was then added followed immediately by the addition of EtOAc (2.0 L) and stirred for 5 min to help precipitate solid and form a liquid-solid biphasic system. The upper organic layer was collected, the under aqueous layer was then washed with EtOAc (5 × 2.0 L). The organic layer was combined and concentrated under reduced pressure. The crude product was purified by column chromatography (*n*-Hexanes: EA = 1:1) to afford desired product (106.8 g) as colorless oil with 63% isolated yield.

Figure S2 100 g scale up flow diagram.

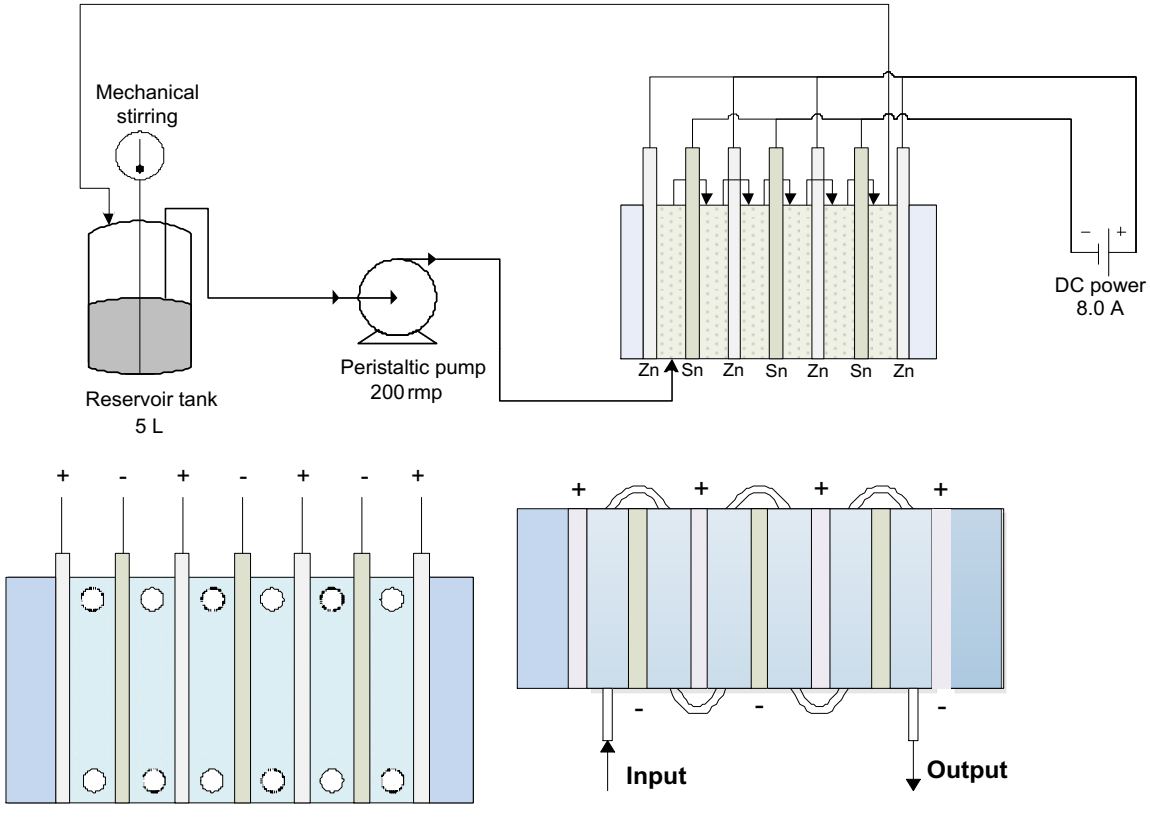
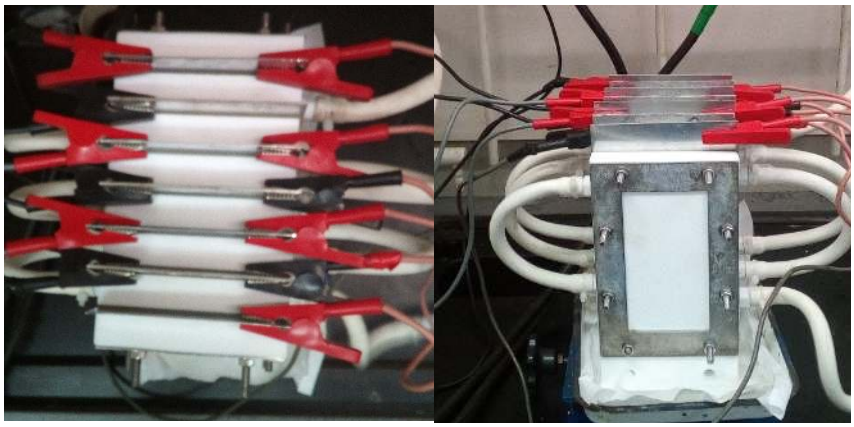


Figure S3. Electrolysis setup in flow cell and local views.



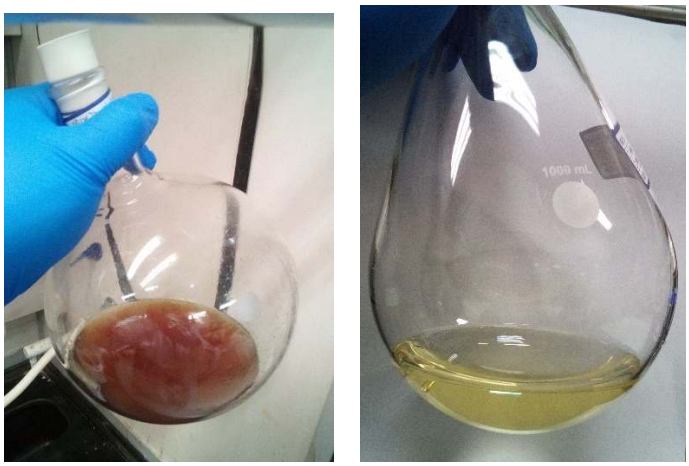
(**Left**) Zn electrode. (**Right**) Sn electrodes.

Figure S4. Workup procedure and local views.

Reduced pressure distillation

The concentrated reaction mixture

Extraction



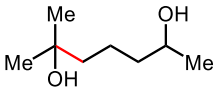
(**Left**) Concentrated crude product. (**Right**) pure product

d. Notes

1. The reaction is not sensitive to air or water, and all reactants were purchased from commercial sources and used without any pretreatment. The purity of zinc and tin electrode is greater than 99.5%.
2. In fact, compared with batch reaction, the voltage of continuous reaction was higher, which might be cause by deposition of generated precipitated solids in the frame cell, leading to poor reaction conductivity. For the electrochemical flow reaction of 10 g and 100 g, the reaction voltages would reach 32 V (maximum range) after electrolysis of 3 F. Through TLC detection, there is basically no starting material left, which means that the reaction didn't need 4 F electric quantity.
3. After the reaction mixture was concentrated, the reaction liquid was very thick. For the post-treatment of 1-10 g scale of reaction, it is relatively easy to be filtered by small silica plug. But for 100 g reaction, the oily substance will block the elution of EtOAc.
4. We have also tried to separate the products directly by vacuum distillation, the products could be obtained under the condition of 4 mbar and 140 °C, but other unknown substances were also obtained at the same time. We speculated that some side reactions might occur at high temperature.
5. In the extraction with pure water or brine, the black substance was mostly in the organic phase and difficult to separate, even although it is also stratified. At present, it was useful to employ Rochelle's' salt to help precipitate solid and form a liquid-solid biphasic system.
6. The under aqueous layer need to be washed with EtOAc (5 x 2.0 L) to separate the product dissolved in aqueous phase. And the times of reverse extraction were determined by TLC results.

7. Based on the literature report (*Org. Lett.* **2016**, *18*, 3826−3829), H of Hydroxyl didn't show up in ^{1}H NMR. But in our experiments, H of Hydroxyl could show up with high concentration of product. Both of NMR data were provided as attachment.

D. Characterization Data

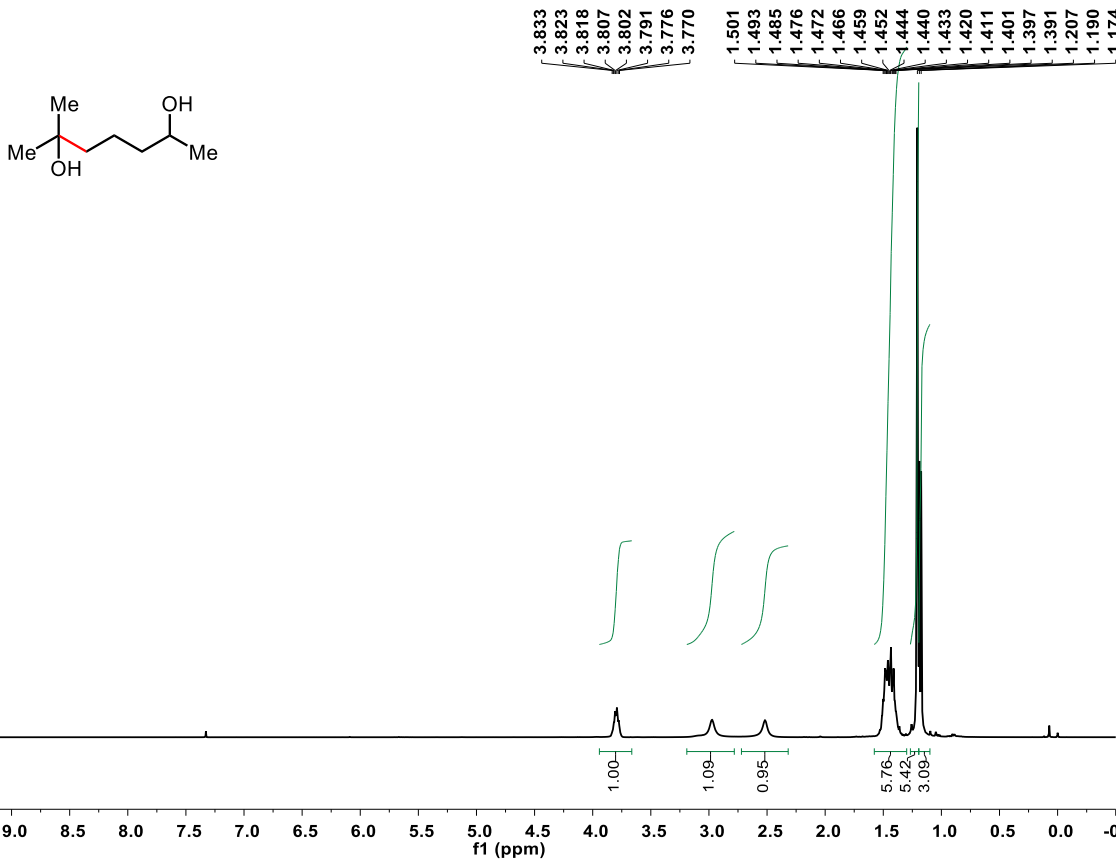


ASYM-126700

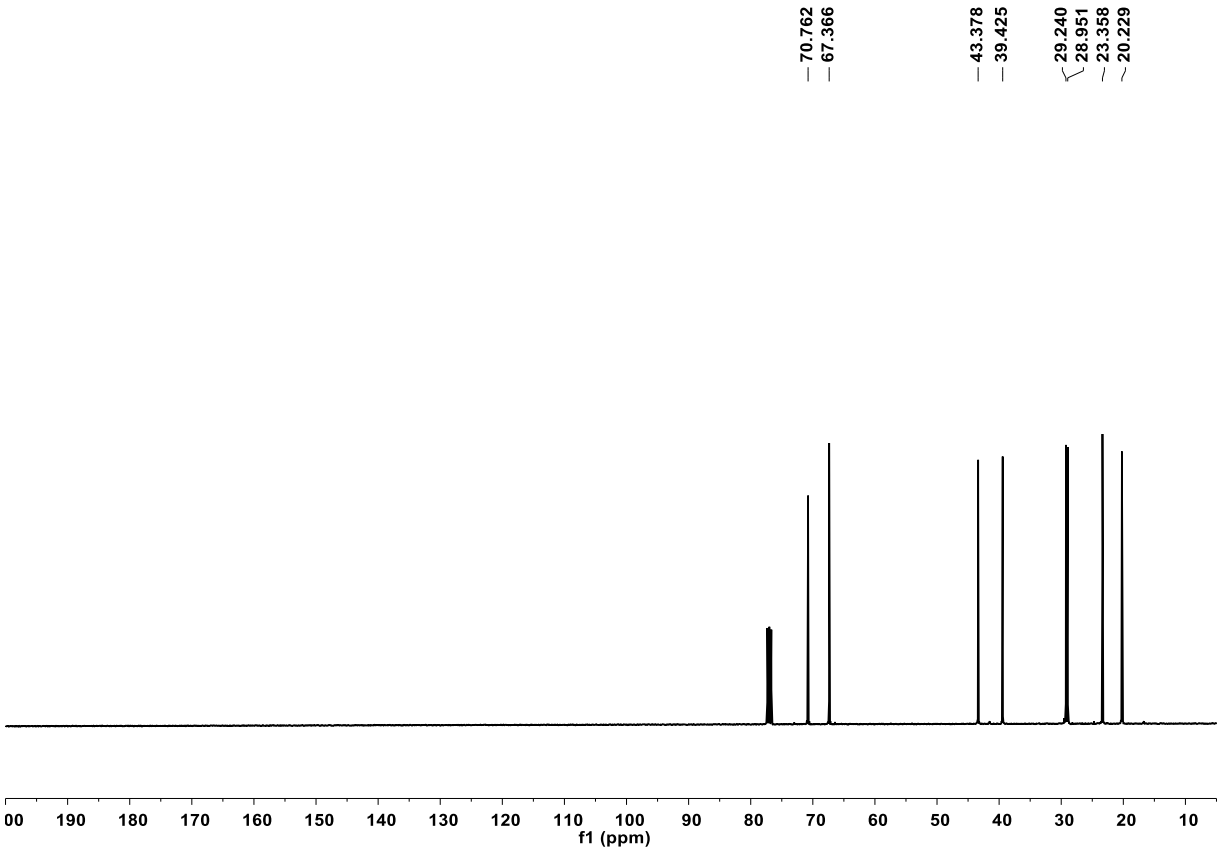
Colorless oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.94 – 3.66 (m, 1H), 2.97 (s, 1H), 2.52 (s, 1H), 1.58 – 1.30 (m, 6H), 1.21 (s, 6H), 1.19 – 1.10 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 70.76, 67.37, 43.38, 39.42, 29.24, 28.95, 23.36, 20.23.

E. NMR and GC-MS spectra

^{1}H NMR



^{13}C NMR


70.762
67.366
43.378
39.425
29.240
28.951
23.358
20.229
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

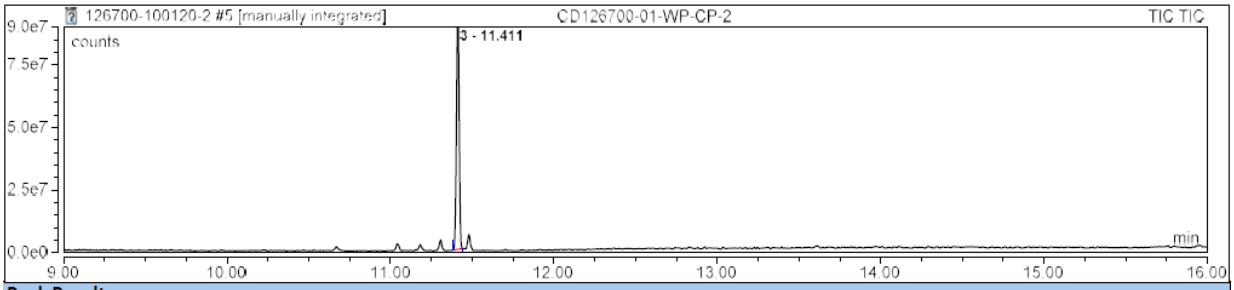
GC-MS

Testing spectra

Injection Details

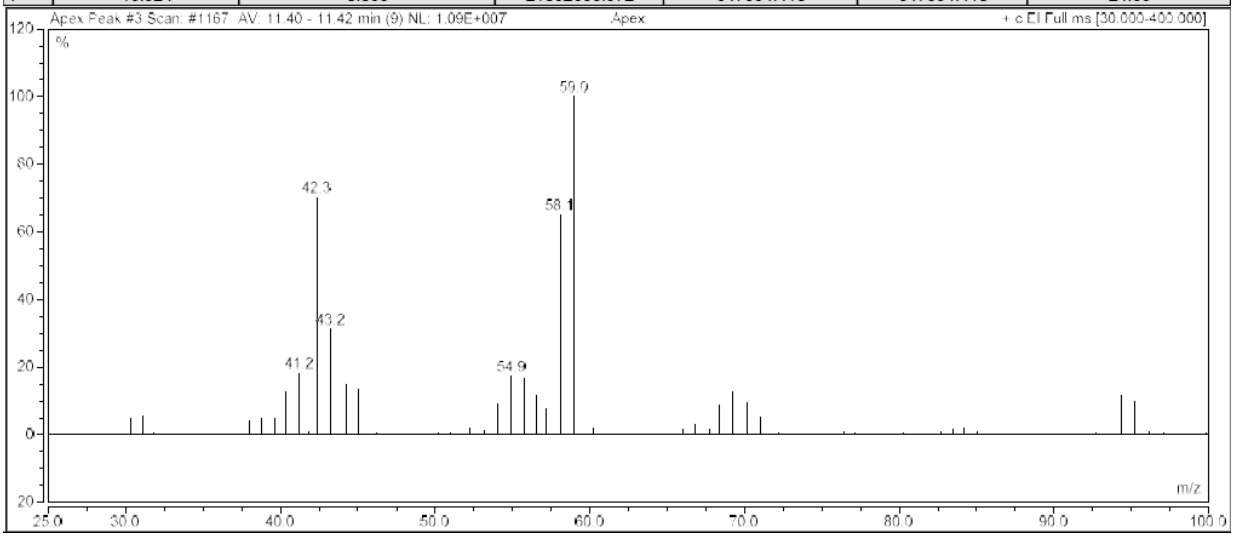
Injection Name:	**CD126700-01-WP-CP-2**	*Run Time (min):*	**11.49**
Vial Number:	**3**	*Injection Date/Time:*	**10/01/2020 13:15:43**
Instrument Method:	**AM-013 for 126700-100120-7.0**	*Processing Method:*	**MS Quantitative**

Chromatogram

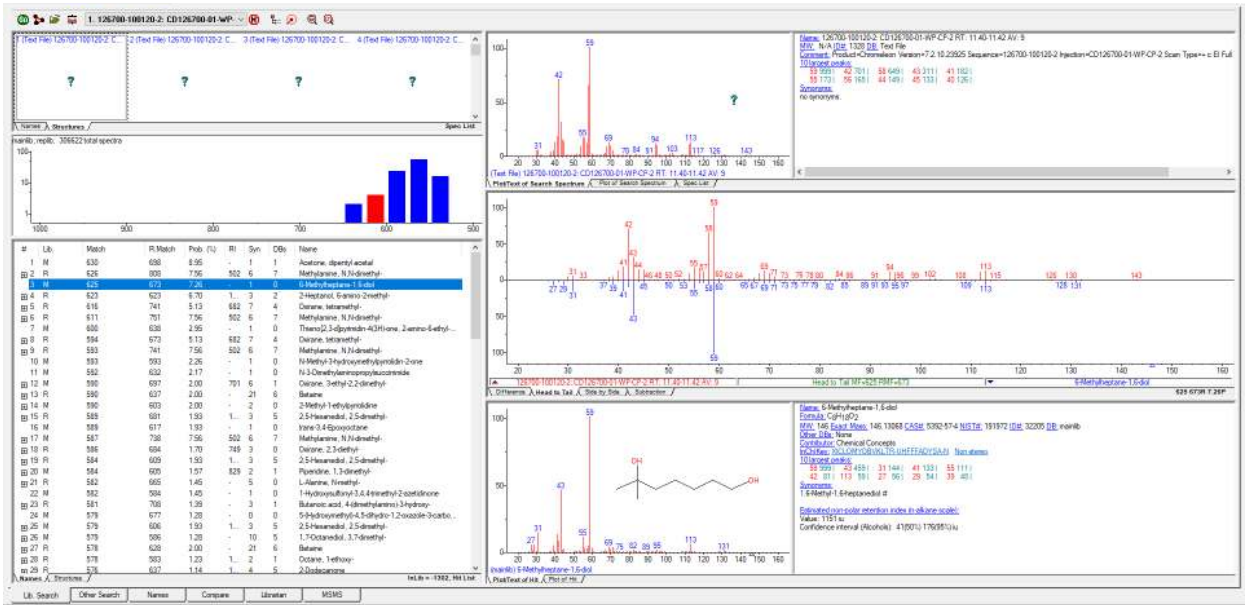


Peak Results

No.	Retention Time min	Width (50%) min	Height counts	Area counts*min	Area counts*min	Rel.Area %
1	8.419	0.023	29545168.706	718459.269	718459.269	21.07
2	8.553	0.021	1396594.173	32340.336	32340.336	0.95
3	11.411	0.018	94897032.913	1812110.367	1812110.367	53.14
4	16.924	0.038	21032688.372	847394.410	847394.410	24.85

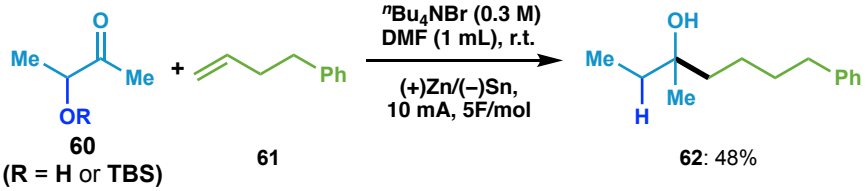


Fitting figure



Mechanistic Studies

Mechanistic insights from specific substrates (compound 62 and 65)



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 50:1 to 20:1) afforded 38.2 mg (53%) of the title compound.

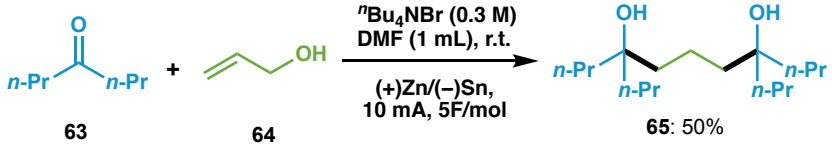
Physical State: colorless oil

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 – 7.23 (m, 2H), 7.21 – 7.14 (m, 3H), 2.63 (t, J = 7.8 Hz, 2H), 1.69 – 1.57 (m, 2H), 1.55 – 1.44 (m, 4H), 1.40 (ddd, J = 10.2, 6.3, 2.8 Hz, 2H), 1.14 (s, 3H), 0.89 (t, J = 7.5 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 142.6, 128.4, 128.2, 125.6, 72.9, 41.1, 35.9, 34.2, 32.1, 26.4, 23.5, 8.2.

HRMS (ESI-TOF): molecular weight peak not found despite extensive efforts.

TLC: R_f = 0.57 (10:1 hexanes/EtOAc).



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 5:1 to 1:1) afforded 53.4 mg (56%) of the title compound XX.

Physical State: white foam.

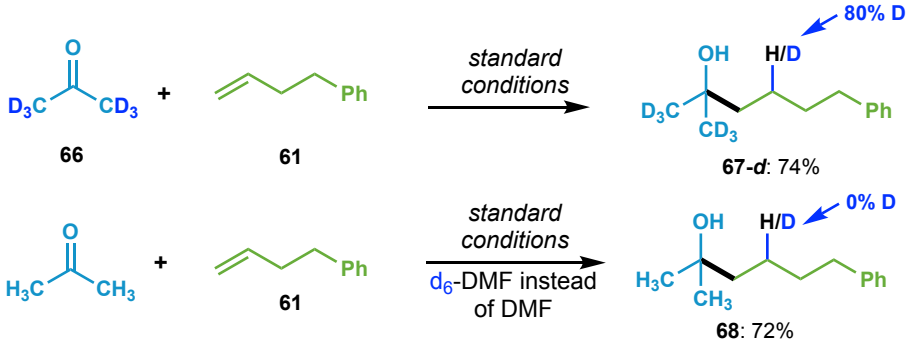
^{1}H NMR (400 MHz, $CDCl_3$):1.45 – 1.35 (m, 12H), 1.34 – 1.23 (m, 10H), 0.90 (t, J = 7.1 Hz, 12H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 74.5, 41.6, 39.9, 17.3, 16.8, 14.7.

HRMS (ESI-TOF): molecular weight peak not found despite extensive efforts.

TLC: R_f = 0.57 (1:1 hexanes/EtOAc).

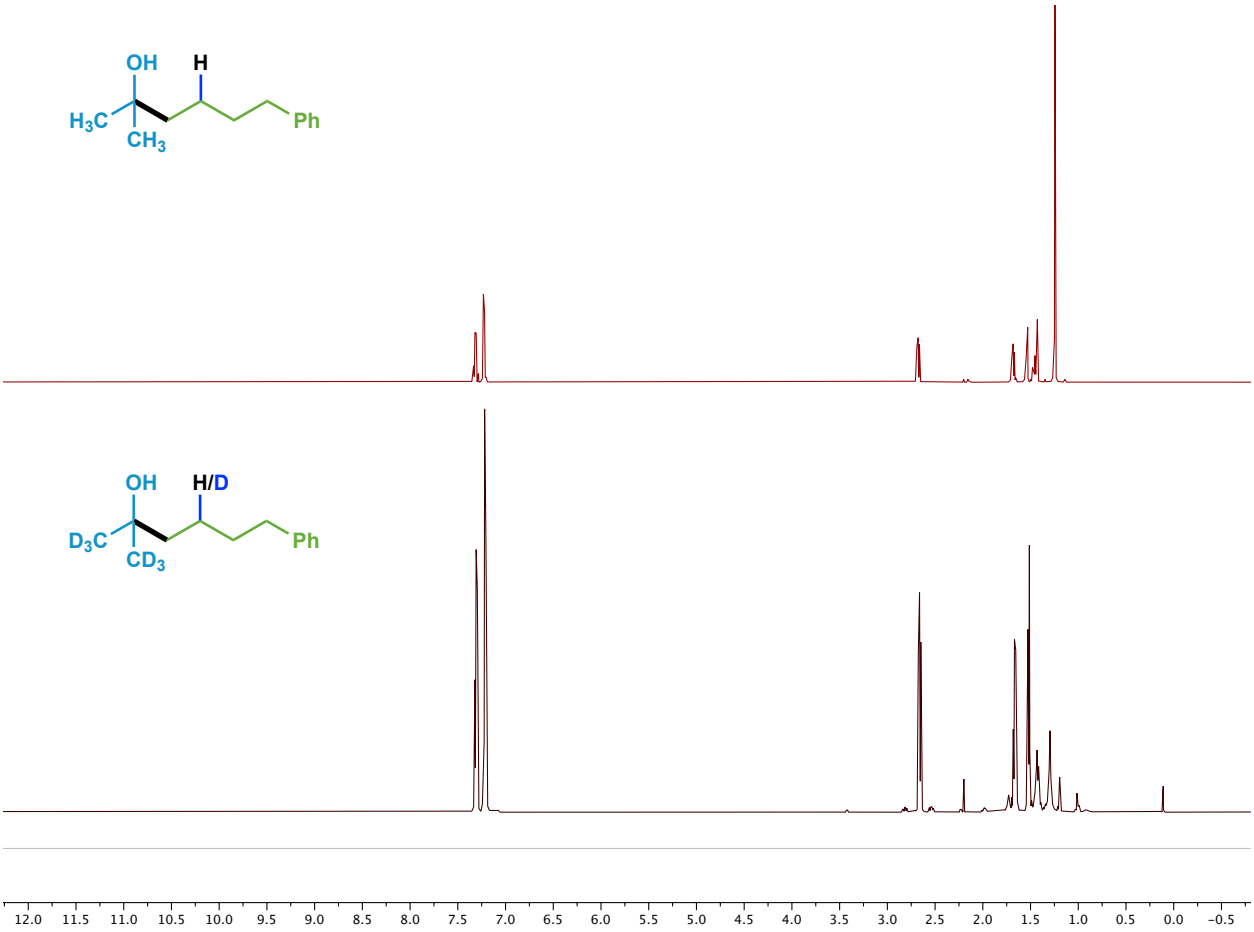
Deuterium Experiments



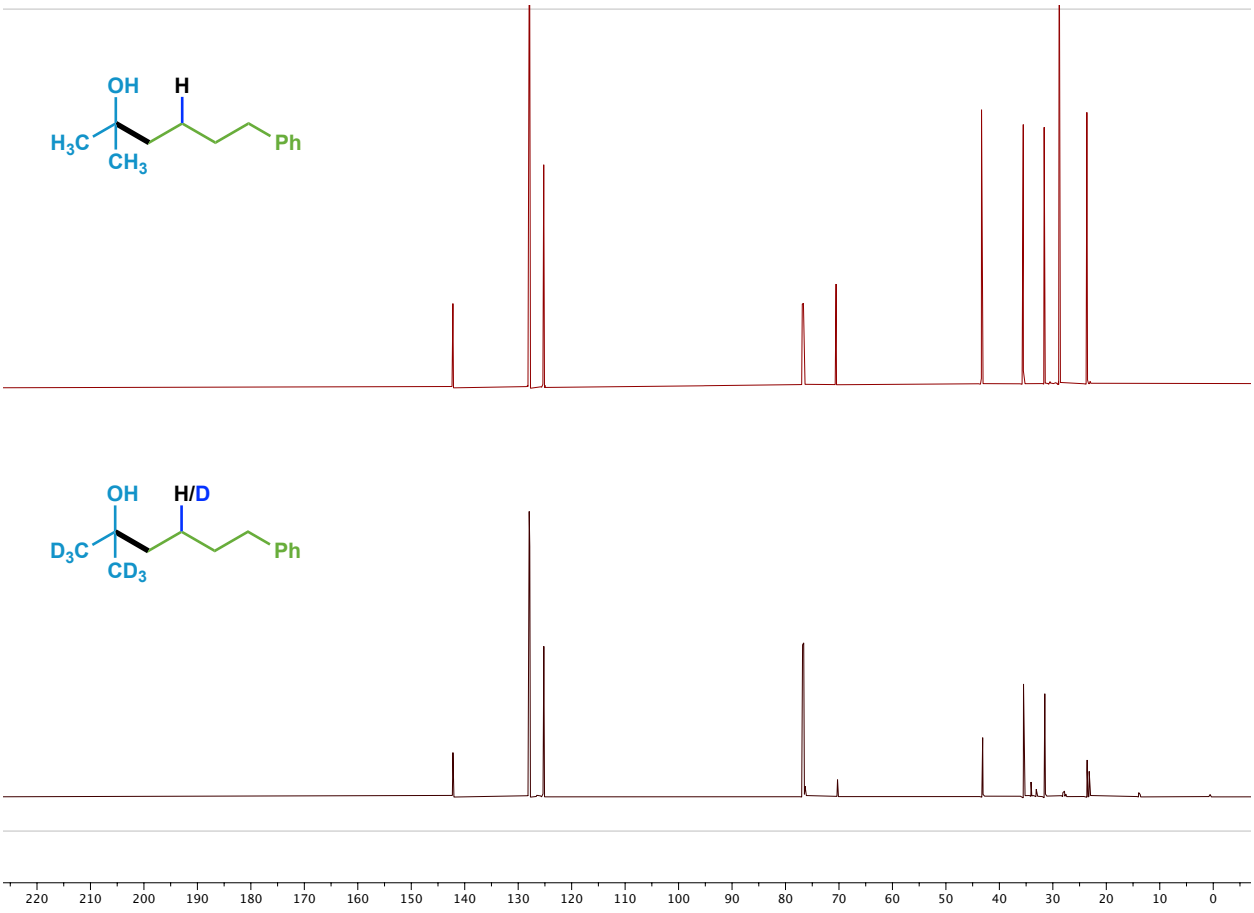
These experiments revealed that the α-proton of the ketone serves as a proton source, rather than the solvent, which indicates the formation of carbanion at the D-incorporated position.

Due to overlapping signals in the ^{1}H NMR (see above spectra), quantitative ^{13}C NMR (NOE decoupled, 60 s relaxation, 15 scans, delayed receiver-gain acquisition sequence) was run to determine the extent of deuterium incorporation. The ratio of 1:3.5, H:D translates to 80% deuterium incorporation where the only source of deuterium is from the d6-acetone. Therefore, it is clear from this data that one equivalent of ketone is consumed as a sacrificial proton source. The 20% β-proton incorporation is suspected to mainly being captured by Zn^{2+} to form alkyl-Zn species, which is protonated to during work-up.

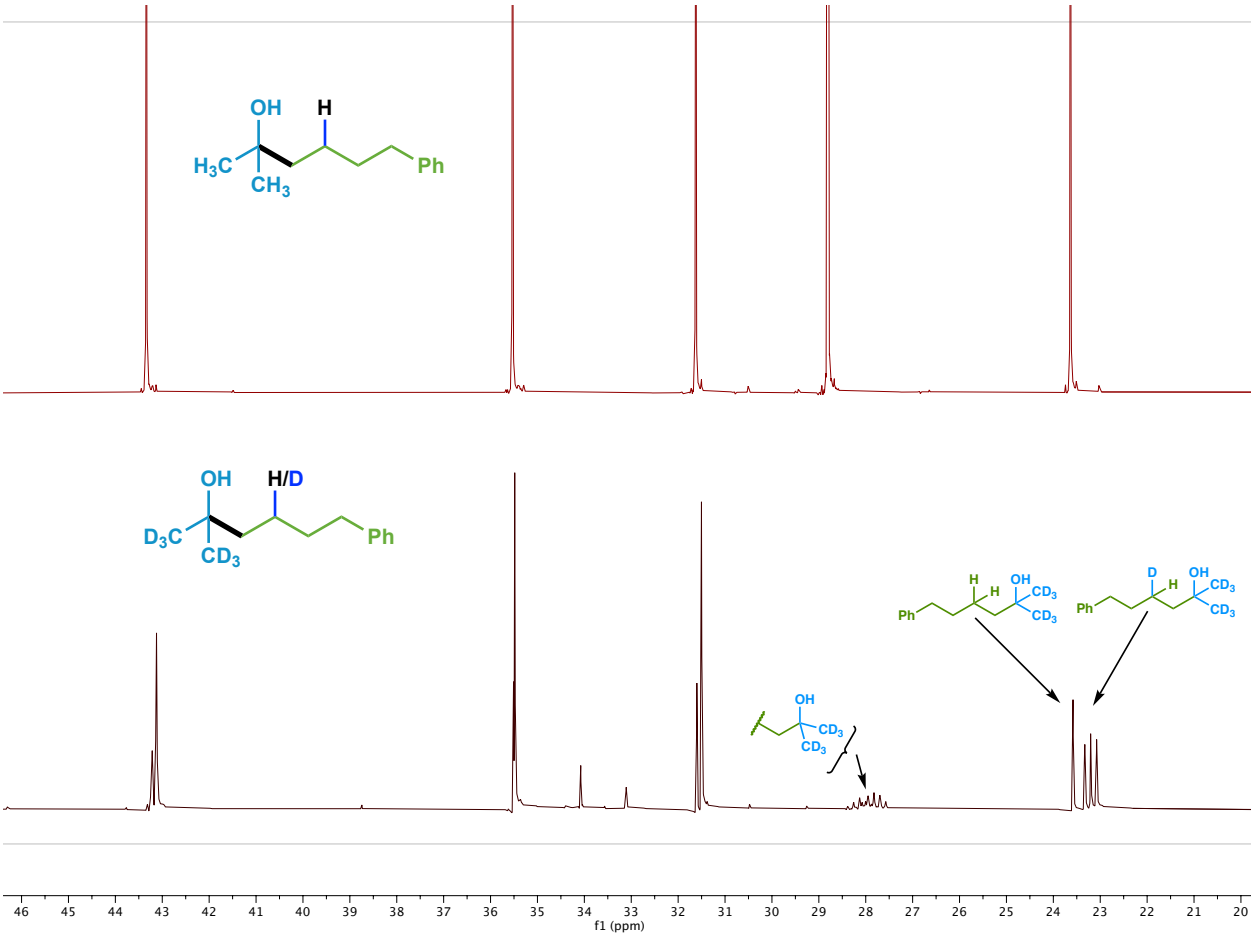
Comparison of the ^{1}H-NMR of authentic sample and deuterium-labeled sample.



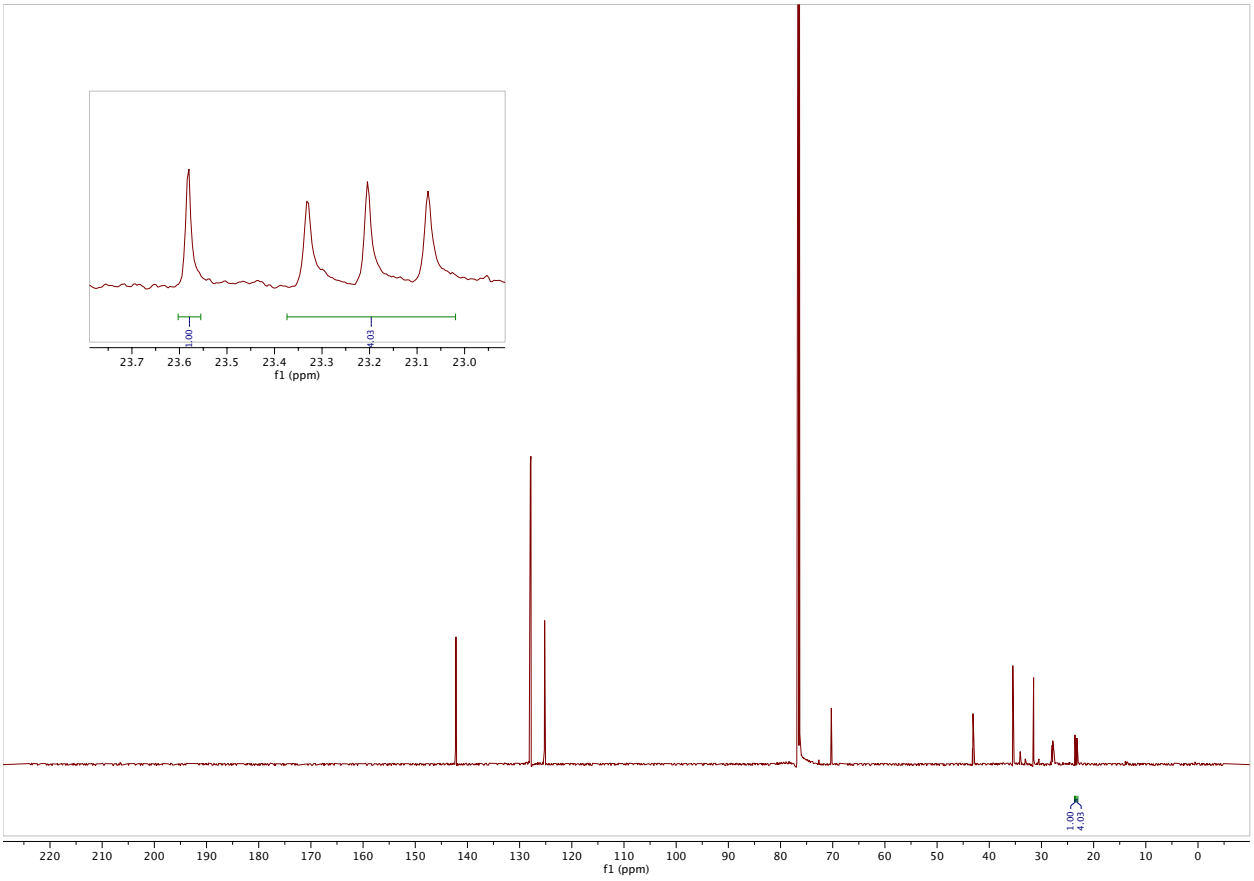
Comparison of the ^{13}C-NMR of authentic sample and deuterium-labeled sample.



Comparison of the ^{13}C-NMR of authentic sample and deuterium-labeled sample (20 to 46 ppm)



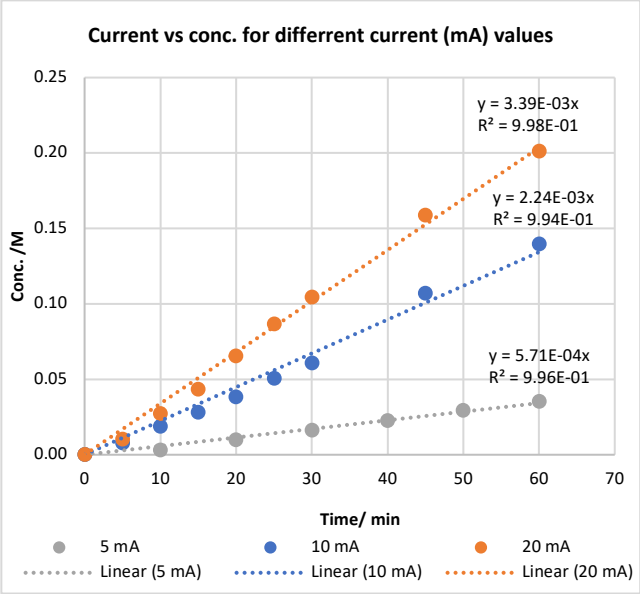
Quantitative ^{13}C-NMR of deuterium-labeled sample

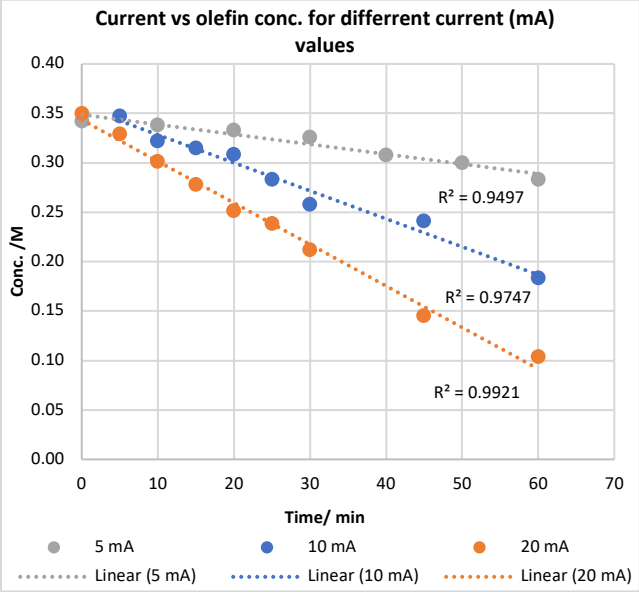


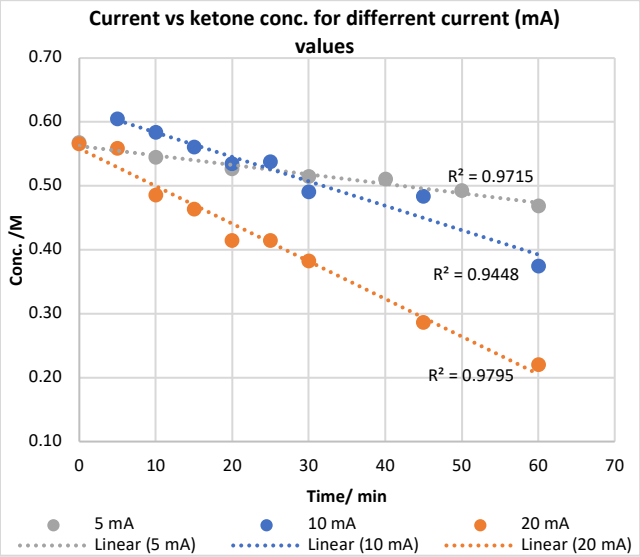
Deuterium vs Non-Deuterium = 4 : 1

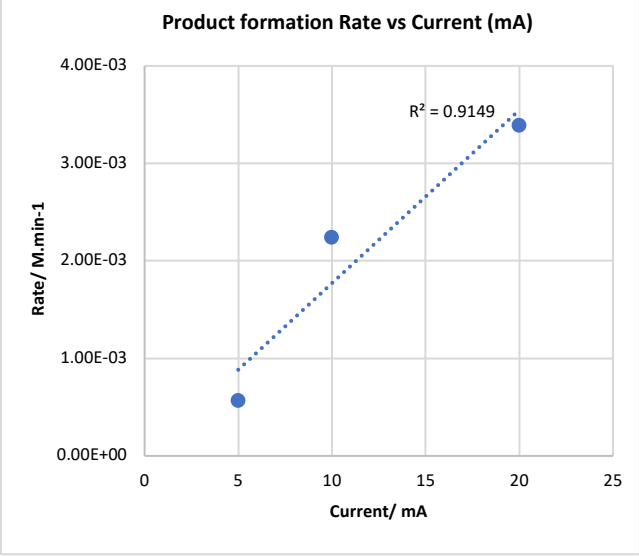
Kinetic Experiments

The kinetics of the reaction were investigated at a number of different currents (5, 10 and 20 mA). The results for the concentration vs time for the product, olefin and ketone are presented in the figure:









Plot **A** is indicative of overall zero-order dependence on product formation. Monitoring the olefin (plot **B**), reveals that there might be an overall zero-order dependence, however, the R^2 values are not significantly high enough to suggest this is certainly the case. The same is true for the ketone (plot **C**), and it is likely that a more complex relationship is at work. Plotting the rate of the product

formation against the current (plot **D**), did not show a good linear fit to suggest an overall first order relationship to current.

Voltametric studies

General Procedure

Mechanistic studies using cyclic voltammetry (CV), square wave voltammetry (SWV), and chronoamperometry (CA) were performed with a Biologic (Model SP-150) with an SCE as reference electrode. A protruding Sn wire (1.5 mm diameter, 2.0 mm length) or glassy carbon (0.0708 cm^2) were used as working electrodes. Platinum gauze was employed as the counter electrode. Experiments were performed using acetophenone (1, 2, or 5 mM) and 4-phenyl-1-butene as coupling substrates. $ZnBr_2$ (0 mM to catalytic amounts) were added in some SWV experiments. Tetrabutylammonium bromide (TBAB) in DMF (100 mM) was used as electrolyte. Total volume of solutions was 2.0 mL unless specified otherwise. All experiments were performed in a drybox under argon.

A. Electrochemical studies on adsorption to Sn electrode

a. CV analysis to observe pre-peak in the voltammogram

Procedure: In a 2 mL vial, 1 mM acetophenone in 100 mM TBAB in DMF were scanned from two different potential windows using Sn and glassy carbon as working electrodes at a scan rate of 100 mV/s. CV analysis of acetophenone in various concentrations (0.5, 1.0, 2.0 mM) were also performed using Sn as working electrode.

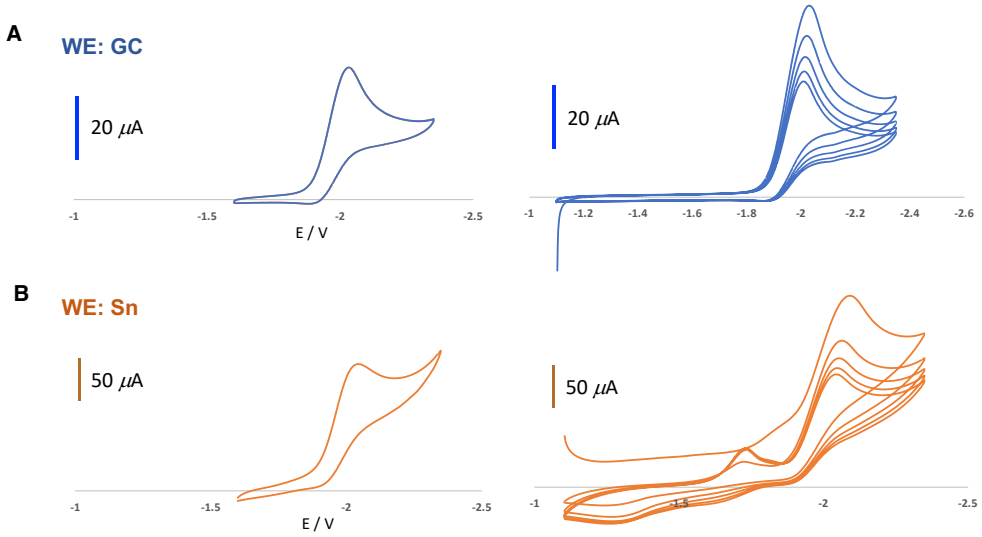


Fig. S5. CV plots of 1 mM acetophenone in (A) glassy carbon and (B) Sn as working electrodes using at two different potential windows, scan rate at 100 mV/s. Potentials are reported vs SCE.

Discussion: Summarized in Fig. S5 are the CV plots obtained from acetophenone in Sn and glassy carbon electrodes in different potential windows. Scanning the potential on less positive value showed a distinct appearance of pre-peaks when Sn electrode was used (but not observed using glassy carbon). Importantly, the pre-peak current increases as function of number of scans and concentration of acetophenone. We hypothesized that change in reactivity can be facilitated by a strong adsorption of the ketyl radical to the Sn electrode. Cyclic voltammetry studies were performed using Sn and glassy carbon (GC) as working electrodes with acetophenone as the source of ketyl radical. Pre-peaks on the CV were observed using Sn as working electrode but not observed using GC. These pre-peaks are distinct characteristics of an electron transfer where the product (ketyl radical) is strongly adsorbed into the working electrode.[3] Furthermore, the current response observed in the pre-peak in Sn was found to be dependent on the concentration of ketone (see Fig. S6). This result also rationalizes for the effectiveness of using Sn-cathode over other electrode materials. From here, additional electrochemical experiments were also performed to support the proposed adsorption (see Sections b and c).

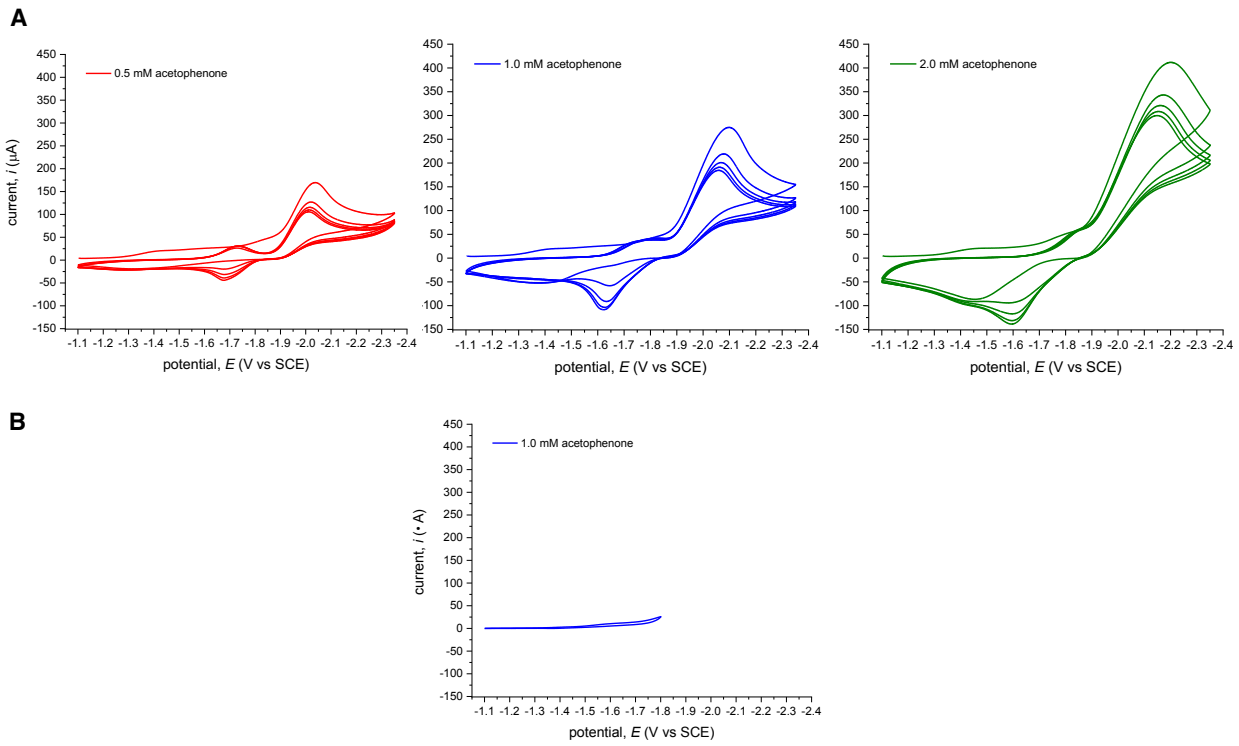


Fig. S6. (A) CV plots of increasing concentration of acetophenone (0.5, 1.0, 2.0 mM) in Sn as working electrodes. (B) A control CV plot of 1 mM acetophenone at potential window where pre-peak was observed. Scan rates were performed at 100 mV/s; currents in mA.

b. CV analysis with various scan rates

Procedure: In a 2 mL vial, 1 mM acetophenone in 100 mM TBAB in DMF were scanned at various scan rates (25, 50, 75, 100, 200, 300, 500, 750, and 100 mV/s) using Sn as working electrode to determine the extent of adsorption. The peak cathodic and peak anodic currents (*ipc* and *ipa*) were plotted versus the square root of the scan rate.

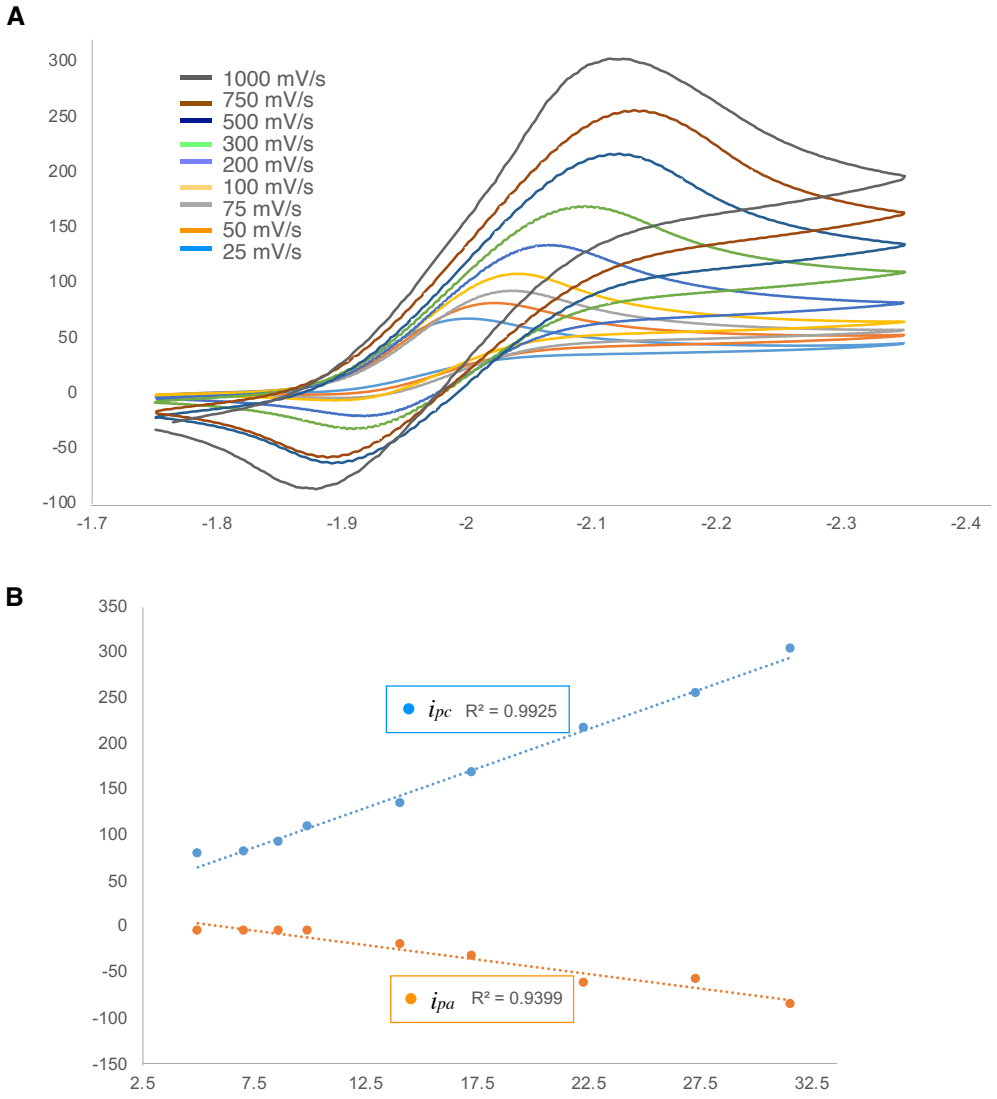


Fig. S7. (A) CV plots of 1 mM acetophenone at various scan rates. (B) Plot of the peak cathodic and peak anodic currents (*ipc* and *ipa*) versus the square root of scan rate.

Discussion: The resulting CV plot (Fig. S7) reveals a quasi-reversible redox couple for which, the distance between the potential at peak cathodic (reductive) current (*Eipc*) and the potential at peak anodic (oxidative) current (*Eipa*) is significantly impacted by scan rate. This behavior is consistent with a homogeneous species exhibiting a reversible electrochemical process with slow heterogeneous electron transfer rates.[4] Furthermore, the peak cathodic and peak anodic currents (*ipc* and *ipa*, Fig. S7) exhibit a linear dependence on the square root of scan rate, however, a deviation on the peak anodic current (*ipa*) was observed. These suggest that acetophenone is not

adsorbed onto the Sn electrode, but the electrochemically reduced species (ketyl radical) is adsorbed onto the electrode surface.[4]

c. Chronoamperometric studies

Procedure: In a 2 mL vial, 2 mM acetophenone in 100 mM TBAB in DMF were electrolyzed for xx min using Sn as working electrode at –2.1 V (vs SCE). Currents were recorded over time. At the end of the electrolysis, a series of electrolysis under similar conditions were performed by reusing the Sn working electrode on a freshly prepared acetophenone solution. The Sn electrode was rinsed in the electrolyte solution for 30 seconds prior to reusing (no electrode polishing was done in between runs).

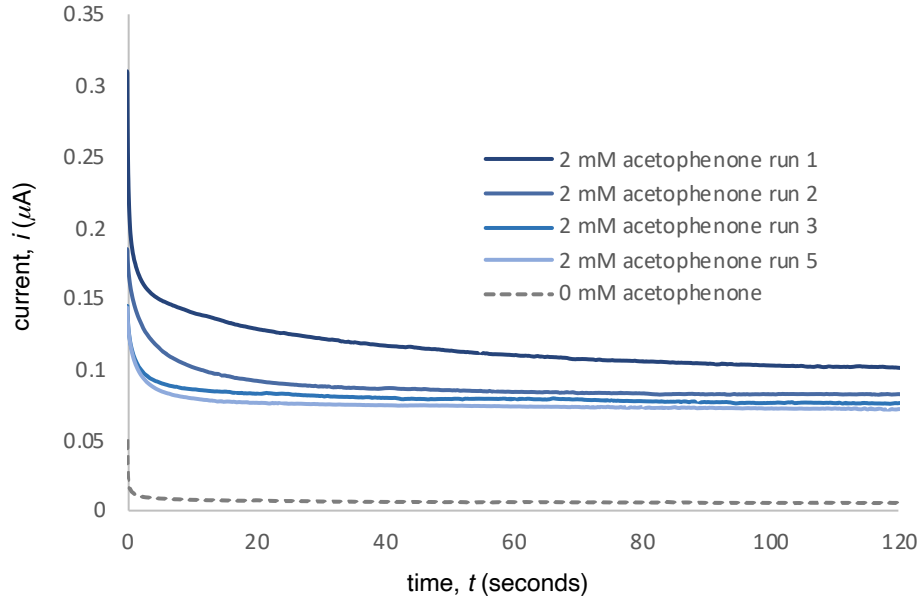


Fig. S8. (A) CA curve of 2 mM acetophenone after several electrolysis and reusing of the Sn electrode. Working electrode potential at –2.1 V (vs SCE).

Discussion: The current vs time plot (Fig. S8) generated in chronoamperometric studies shows a significant decrease in limiting current after each reuse of Sn electrode. This is an indication of an adsorption of the substrate (or the reduced form) to the Sn electrode in every electrolysis.

d. CV analysis of various dialkyl ketones

Procedure: In a 2 mL vial, 5 mM dialkyl ketones in 100 mM TBAB in DMF were scanned using Sn or glassy carbon as working electrodes at a scan rate of 100 mV/s.

Discussion: In our attempt to use dialkyl ketones as model substrates for the electrochemical studies, we found that most of the dialkyl ketones (in general) gave insignificant current responses/peaks under reductive conditions. This is probably due to low interaction of the dialkyl ketones to the electrodes under CV scale.[5] Fig. S9 shows the representative CV plots of various dialkyl ketones in Sn and glassy carbon working electrodes.

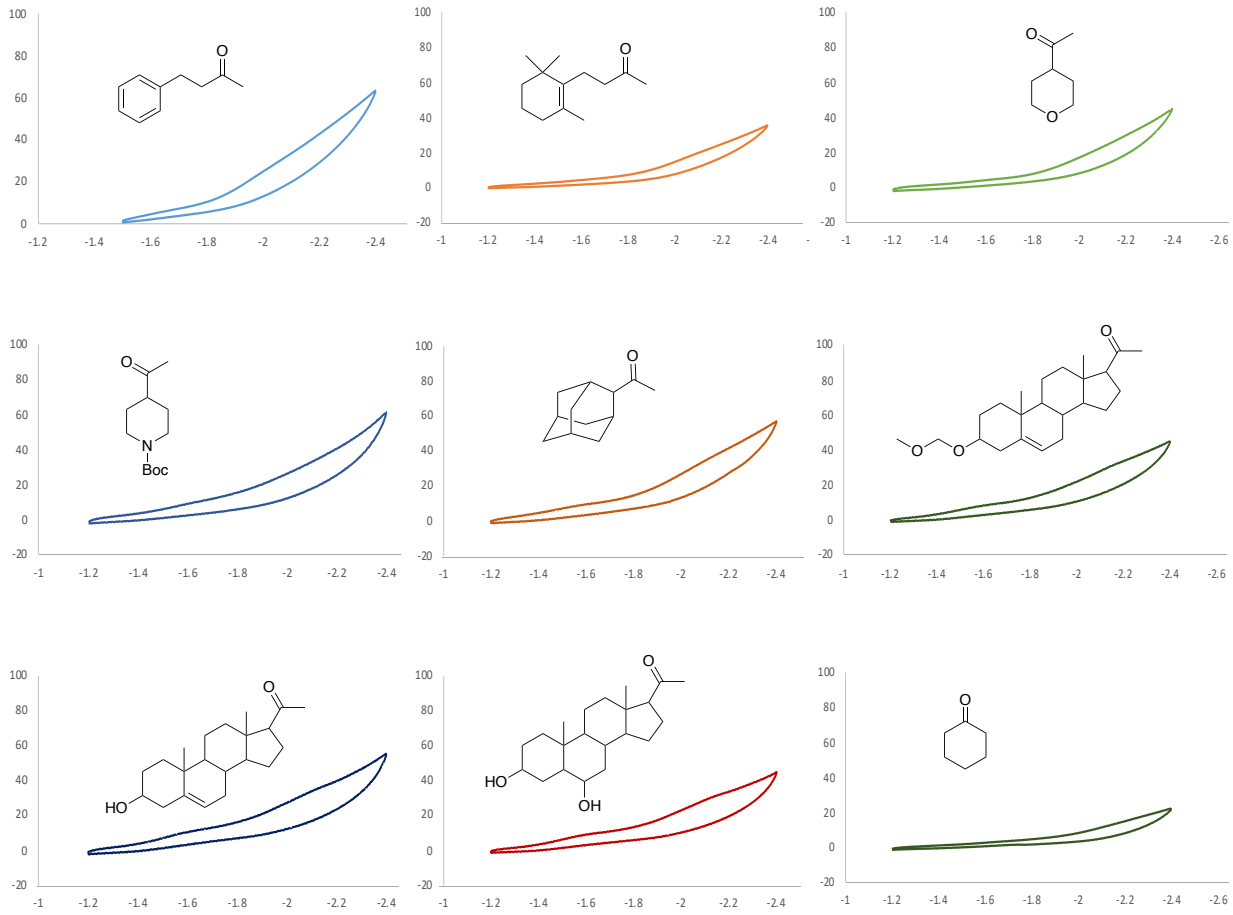


Fig. S9. Representative CV plots of 5 mM dialkyl ketones in Sn working electrode at scan rate of 100 mV/s. Similar CV plots were obtained using glassy carbon electrode. In all cases, no

significant reduction peaks were observed needed for a mechanistic CV analysis. As such, acetophenone was used as the model substrate in all electrochemical mechanistic studies.

B. Electrochemical studies on probing ECEC mechanism

a. SWV studies for the reaction of acetophenone and 4-phenyl-1-butene

Procedure: Variable frequency square wave voltammetry (SWV) was performed on solutions containing 1 mM acetophenone in the presence or absence of 1 mM 4-phenyl-1-butene and catalytic $ZnBr_2$, at a pulse height of 10 mV, step height of 5 mV, and frequencies of 10, 40, and 100 Hz, using a solution of 100 mM TBAB in DMF at 25 °C.

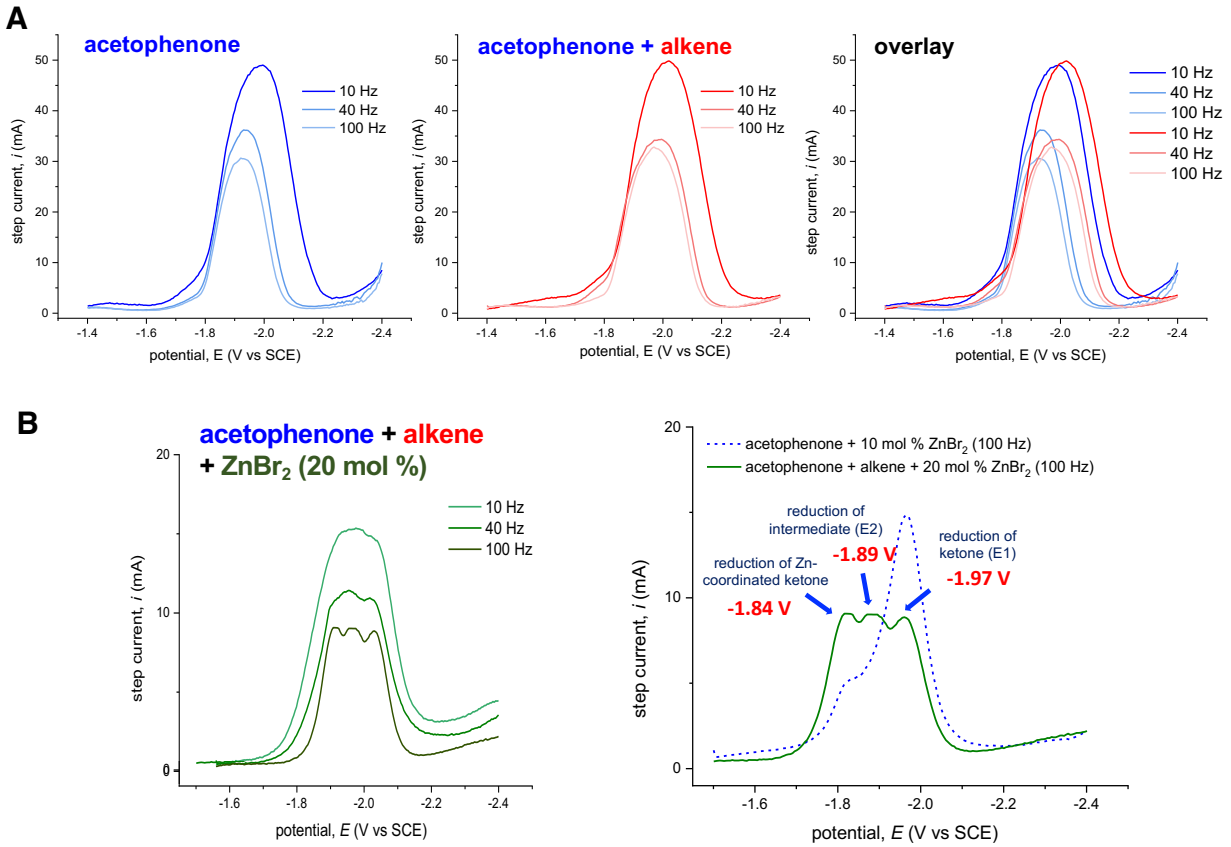


Fig. S10. (A) SWV plots of acetophenone in the absence and presence of alkene. (B) SWV plots of acetophenone, alkene and catalytic amount of $ZnBr_2$. Pulse height of 10 mV, step height of 5 mV, and frequencies of 10, 40, and 100 Hz.

Discussion: Fig. S10 summarized the SWV plots obtained from acetophenone (1 mM) in the absence and presence of alkene (1 mM) (Fig. S10A) and catalytic amount (20 mol %) of $ZnBr_2$

(Fig. S10B). As described in the main text, SWVs of acetophenone in the presence of the alkene gave a cathodic shift on the peak current potential but did not result to the formation of separate peaks even at faster frequencies. The addition of $ZnBr_2$ (Fig. S10B) into this system exhibited a broad peak at low frequencies. However, three separate peaks were resolved at faster frequencies. While the observation of three distinct peaks at low frequencies was unexpected (two peaks were expected from the proposed ECEC mechanism), on a separate control experiment we found that the third (extra) peak at –1.84 V (vs SCE) was due to the reduction of $ZnBr_2$-coordinated acetophenone (see Section b below). These experiments suggest an ECE mechanism, where the final chemical step (protonation of a species resulting from the second electrochemical reduction, see deuteration experiment) would result in an overall ECEC mechanism.

b. Control SWV studies for $ZnBr_2$-coordinated ketone

Procedure: Variable frequency square wave voltammetry (SWV) was performed on solutions containing 1 mM acetophenone in the presence or absence of catalytic $ZnBr_2$ (10, 20 and 40 mol %), at a pulse height of 10 mV, step height of 5 mV, and frequencies of 10, 40, and 100 Hz, using a solution of 100 mM TBAB in DMF at 25 °C.

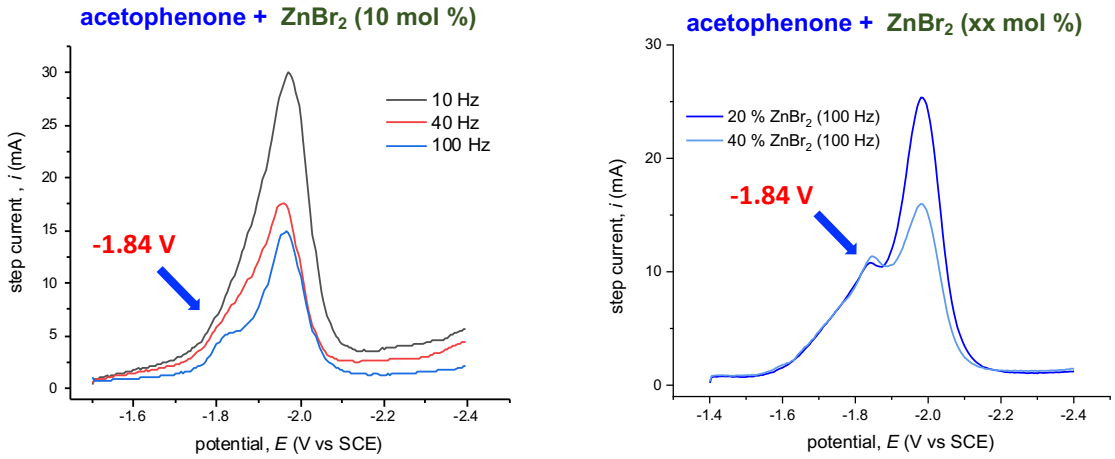


Fig. S11. SWV plots of acetophenone in the presence of catalytic amounts of $ZnBr_2$. Pulse height of 10 mV, step height of 5 mV, and frequencies of 10, 40, and 100 Hz.

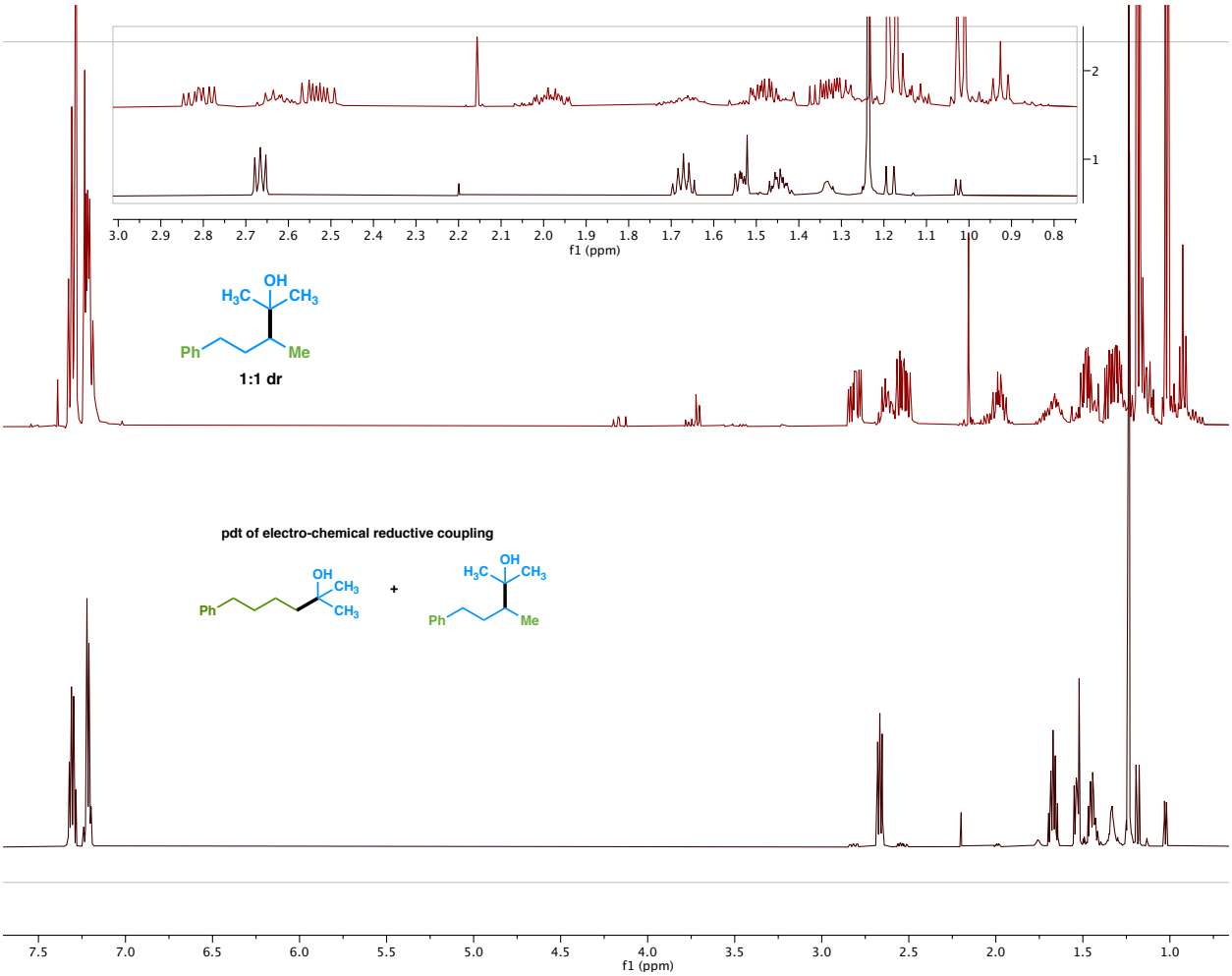
Discussion: The appearance of an additional peak at –1.84 V (vs SCE, Fig. SX) in the presence of $ZnBr_2$ denotes that the observed peak in Section 3.1 is due to the reduction of $ZnBr_2$-coordinated acetophenone. Moreover, the peaks observed for the reduction of $ZnBr_2$-coordinated acetophenone

(–1.84 V vs SCE) and that of free acetophenone (–1.97 V vs SCE), increases and decreases, respectively, as the amount of $ZnBr_2$ is increased.

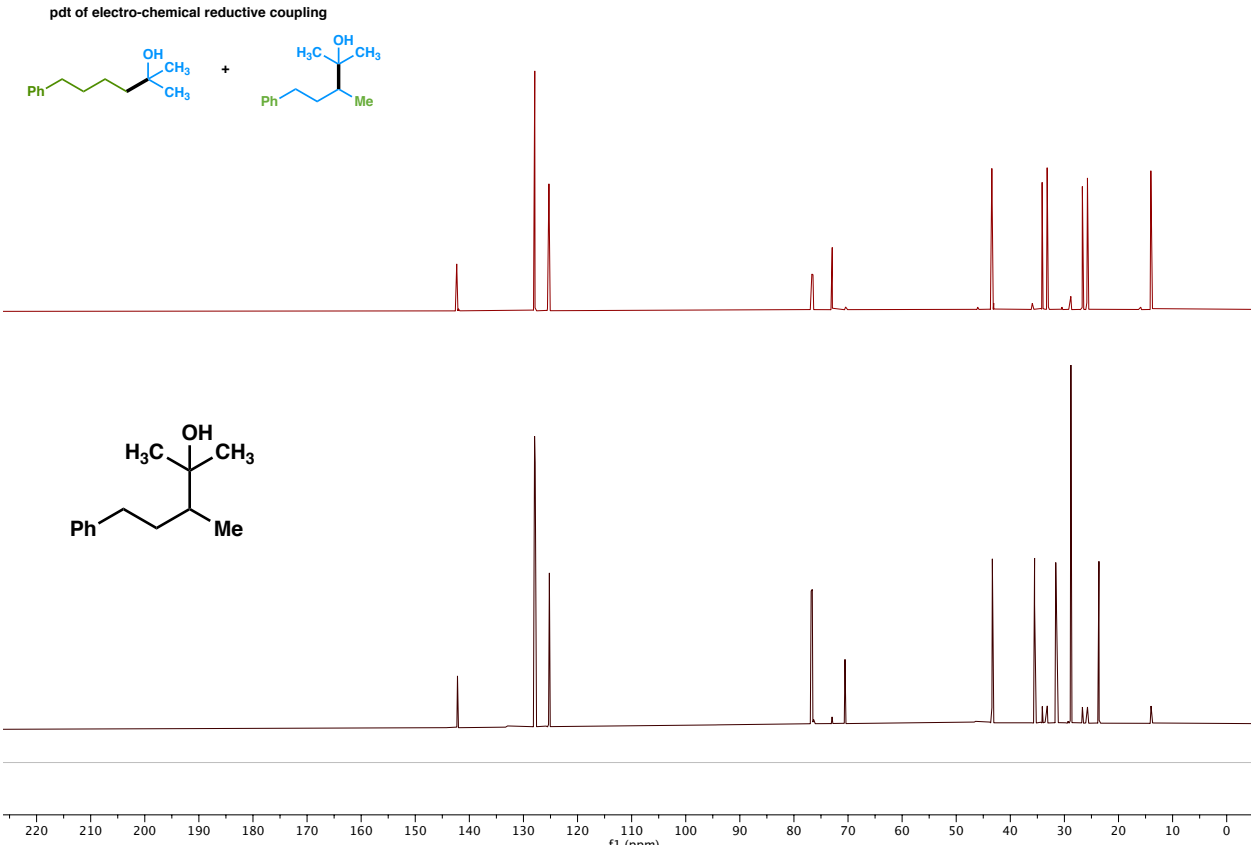
Linear vs Branched Selectivity

The major product of this reaction is the linear product while a small amount of branch-selective minor product can be observed on GC-MS. Typically the selectivity is greater than 15:1. Very often the branch-selective product is hard to be observed due to peak overlapping. In addition, through the course of our investigation, we were not able to isolate a pure sample of the minor product. In order to confirm the structure, we synthesized an authentic sample of the minor regioisomer via an alternative route and verify its ratio via ^{13}C NMR. In following example, the ratio of Branched vs Linear is 1:16.

Comparison of the ^{1}H-NMR of electrochemical ketone-olefin reductive coupling product and authentic branched.

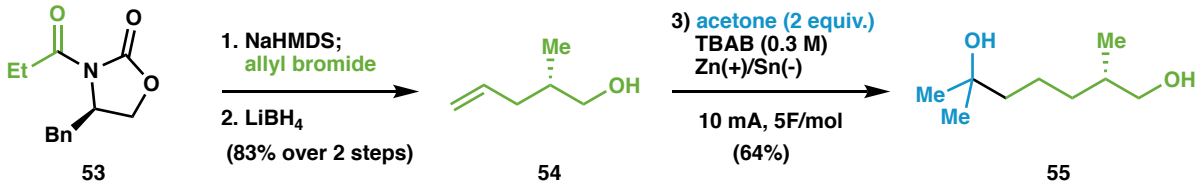


Comparison of the ^{13}C-NMR of electrochemical ketone-olefin reductive coupling product and authentic branched.



Synthetic Applications

Synthesis of a Vitamin D analog side chain 55



53 54 55

The known alcohol **54** was converted to diol **55** following general procedure A on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 5:1 to 1:1) afforded 35.9 mg (64%) of the title compound **55**.

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.51 (dd, *J* = 10.5, 5.9 Hz, 1H), 3.44 (dd, *J* = 10.5, 6.4 Hz, 1H), 1.72 – 1.59 (m, 1H), 1.51 – 1.39 (m, 6H), 1.38 – 1.33 (m, 1H), 1.21 (s, 5H), 1.16 – 1.08 (m, 1H), 0.93 (d, *J* = 6.7 Hz, 3H).

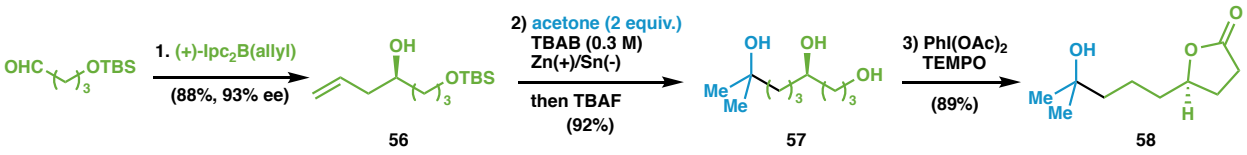
^{13}C NMR (126 MHz, $CDCl_3$): δ 71.0, 68.3, 44.1, 35.7, 33.6, 29.3, 29.2, 21.7, 16.6.

HRMS (ESI-TOF): molecular weight peak not found despite extensive efforts.

TLC: R_f = 0.25 (1:1 hexanes/EtOAc).

$[\alpha]^{20}_D$ = -8.0° (c = 1.0 in $CHCl_3$).

Synthesis of a DNA-binding metabolite 58



56 57 58

The known alcohol **56** (93% ee determined by Mosher ester analysis) was prepared according to literature, Sestelo *et. al. Org. Lett.* **2010**, *12*, 852. It was converted to triol **57** via general procedure A, followed by one-pot deprotection with TBAF (5 equiv) on 0.35 mmol scale. Purification via silica gel column chromatography (EtOAc/MeOH, 20:1) afforded 61.2 mg (92%) of triol **57**.

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.73 – 3.49 (m, 6H), 1.70 – 1.57 (m, 4H), 1.52 – 1.40 (m, 6H), 1.19 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 71.0, 68.3, 44.1, 35.7, 33.6, 29.3, 29.2, 21.7, 16.6.

HRMS (ESI-TOF): molecular weight peak not found despite extensive efforts.

TLC: R_f = 0.44 (20:1 EtOAc/MeOH).

$[\alpha]^{20}_D$ = +1.5° (c = 2.0 in $CHCl_3$).

Synthesis of lactone 58.

To triol **57** (95.0 mg, 0.5 mmol, 1.0 equiv) in CH_2Cl_2 was added $PhI(OAc)_2$ (483.1 mg, 1.5 mmol, 3.0 equiv) and TEMPO (7.8 mg, 0.05 mmol, 0.1 equiv) and the reaction was stirred at room temperature for 2 h. After completion, the reaction mixture was directly purified via column chromatography (hexanes: EtOAc) to give 83.0 mg (89%) of lactone **58**. The characterization data is consistent with literature values (Procter *et. al. Org. Biomol. Chem.* **2004**, *2*, 2476; Thiericke *et. al. J. Antibio.* **1999**, *52*, 1124).

Physical State: colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 4.53 – 4.47 (m, 1H), 2.55 – 2.50 (m, 2H), 2.36 – 2.29 (m, 1H), 1.90 – 1.82 (m, 1H), 1.77 – 1.70 (m, 1H), 1.65 – 1.60 (m, 1H), 1.59 – 1.54 (m, 1H), 1.54 -1.42 (m, 4H), 1.21 (s, 6H).

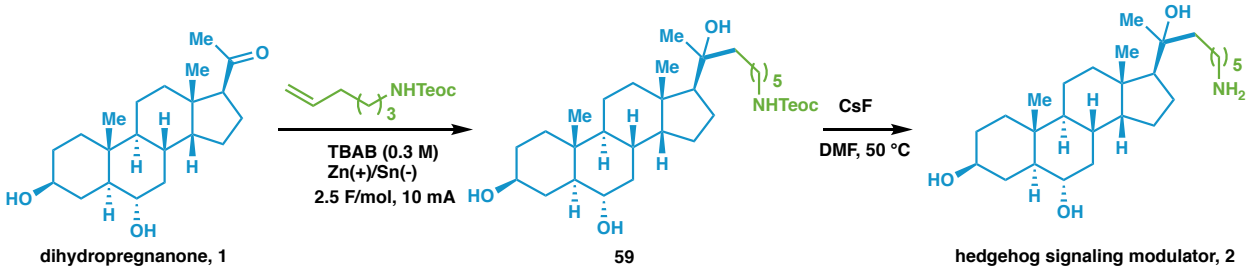
^{13}C NMR (151 MHz, $CDCl_3$): δ 177.2, 80.9, 70.8, 43.4, 36.0, 29.3, 29.2, 28.8, 28.0, 20.2.

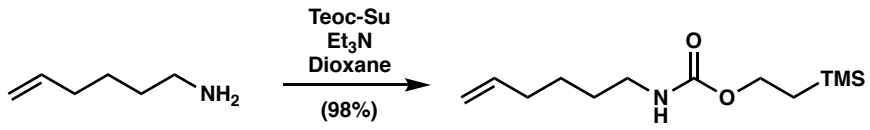
HRMS (ESI-TOF): molecular weight peak not found despite extensive efforts.

TLC: R_f = 0.68 (EtOAc).

$[\alpha]^{20}_D$ = +46.2° (c = 1.0 in MeOH).

Synthesis of a hedgehog signaling modulator 1.





To a solution of 6-amino-1-hexene (1.0 g, 10 mmol, 1.0 equiv.) and Et_3N (2.1 mL, 15 mmol, 1.5 equiv.) in dioxane (20 mL) was added Teoc-Su (2.85 g, 11 mmol, 1.1 equiv.) and the reaction was stirred for 10 h. After reaction completion, the reaction was diluted with EtOAc (50 mL) and H2O

(20 mL). Next, the mixture was transferred to a separatory funnel and the organic phase was separated. The aqueous phase was exacted with EtOAc (3 × 20 mL) and the combined organic layer was washed with H_2O (50 mL), dried over $MgSO_4$, concentrated and further purified via column chromatography (hexanes/EtOAc, 10:1) to give 2.38 g of the desired product (98%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.79 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.03 – 4.93 (m, 2H), 4.58 (brs, 1H), 4.14 (t, *J* = 8.4 Hz, 2H), 3.17 (q, *J* = 6.8 Hz, 2H), 2.13 – 2.00 (m, 2H), 1.54 – 1.46 (m, 2H), 1.46 – 1.37 (m, 2H), 0.97 (t, *J* = 8.5 Hz, 2H), 0.03 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 156.8, 138.4, 114.7, 62.8, 40.8, 33.3, 29.5, 26.0, 17.7, -1.5.

HRMS (ESI-TOF): molecular weight peak not found despite extensive efforts.

TLC: R_f = 0.61 (9:1, Hexanes/EtOAc).

Compound **59** was synthesized following general procedure B on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 1:1 to pure EtOAc) afforded 97.4 mg (48%) of the title compound. The diastereoselectivity can be established via analogy to compound **51**.

Physical State: white foam.

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.61 (s, 1H), 4.16 – 4.09 (m, 1H), 3.56 (tt, *J* = 11.1, 4.7 Hz, 1H), 3.41 (dt, *J* = 10.7, 4.5 Hz, 1H), 3.18 – 3.10 (m, 1H), 2.18 (ddt, *J* = 12.4, 5.0, 2.5 Hz, 1H), 2.04 (dt, *J* = 12.4, 3.6 Hz, 1H), 1.98 (dt, *J* = 12.1, 4.2 Hz, 1H), 1.86 – 1.77 (m, 1H), 1.78 – 1.55 (m, 7H), 1.56 – 1.37 (m, 7H), 1.33 – 1.24 (m, 7H), 1.24 (s, 3H), 1.23 – 1.19 (m, 1H), 1.18 – 1.13 (m, 1H), 1.10 (t, *J* = 5.6 Hz, 0H), 1.07 – 0.93 (m, 5H), 0.90 – 0.83 (m, 1H), 0.82 (s, 3H), 0.80 (s, 3H), 0.65 (ddd, *J* = 12.3, 10.5, 4.1 Hz, 1H), 0.02 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 156.8, 75.1, 71.2, 69.4, 62.8, 57.7, 56.3, 53.7, 51.6, 43.8, 42.9, 41.4, 40.9, 40.1, 37.2, 36.2, 33.6, 32.2, 31.0, 30.0, 29.9, 26.7, 26.3, 24.2, 23.6, 22.3, 21.0, 17.7, 13.7, 13.4, -1.5.

HRMS (ESI-TOF): molecular weight peak not found despite extensive efforts.

TLC: R_f = 0.25 (1:1 hexanes/EtOAc).

$[\alpha]^{20}_D$ = +12.8° (c = 1.0 in $CHCl_3$)

Synthesis of compound 2

To a DMF (5 mL) solution of compound **59** (27.3 mg, 0.047 mmol, 1.0 equiv.) was added

anhydrous CsF (71.0 mg, 0.47 mmol, 10.0 equiv.) and the reaction was stirred at 50 °C for 10h. Next the reaction was diluted with MeOH (10 mL) and the mixture was passed through a syringe filter. The resulted solution was concentrated on a rotavap to give a yellow oil, which was dried on high vacuum overnight under gentle heating to yield a yellow foam. The solid was then subsequently washed with hexanes (5 mL), $CHCl_3$ (5 mL) and toluene (5 mL). Residual solvent was removed under high vacuum to give the 20.0 mg (98%) of compound **2**. No characterization data was given in the patent (WO2012/024584A2) that previously described the title compound.

Physical State: white foam.

^{1}H NMR (600 MHz, d_5-pyr): δ 4.01 – 3.92 (m, 1H), 3.74 (td, *J* = 10.6, 4.5 Hz, 1H), 3.31 – 3.25 (m, 1H), 3.18 – 3.04 (m, 2H), 2.33 (dt, J = 12.2, 4.3 Hz, 1H), 2.29 – 2.16 (m, 2H), 2.15 – 2.08 (m, 2H), 2.07 – 1.98 (m, 1H), 1.87 – 1.70 (m, 5H), 1.70 – 1.64 (m, 1H), 1.61 – 1.52 (m, 5H), 1.48 (s, 3H), 1.46 – 1.35 (m, 5H), 1.34 – 1.20 (m, 6H), 1.14 (s, 3H), 1.14 – 1.06 (m, 2H), 0.93 (s, 3H), 0.81 – 0.74 (m, 1H).

^{13}C NMR (151 MHz, d_5-Pyr): δ 74.4, 71.4, 69.1, 59.0, 57.3, 54.8, 53.2, 45.4, 43.6, 43.2, 43.1, 41.2, 38.5, 36.9, 34.7, 34.5, 34.1, 32.8, 31.1, 27.8, 27.2, 25.2, 24.6, 23.3, 21.9, 14.6, 14.2.

HRMS (ESI-TOF): calc'd for $C_{27}H_{48}NO_2$ $[M+H-H_2O]^+$: 418.3685, found 418.3687.

$[\alpha]^{20}_D$ = +24.4° (c = 1.0 in MeOH).

Troubleshooting: Frequently Asked Questions

Question 1:

How do I monitor the reaction?

Answer:

We use TLC analysis with UV visualization (254 nm) for compounds that contain a chromophore. Staining with iodine (absorbed on silica gel) brings about a strong deep red spot for the product. The product responds well to anisaldehyde or Hanessian's stain. The product is substantially more polar than the two starting materials, and typically even the most greasy products tend to need at least EtOAc/Hex 1:1, to move sufficiently on TLC.

Question 2:

How much can the reaction be scaled up on the ElectraSyn? Does it take longer if you scale up?

Answer:

Reactions ranging from gram scale to hundred-gram scale have been conducted (see SI for details). If the current remains the same, the reaction will take longer. The current can be increased to reduce the reaction time, but the yield may drop.

Question 3:

Why does the reaction start to turn dark brown/black after ~ 2 F/mol?

Answer:

If you look carefully at the cathode, what you will see toward the 2 F/mol mark is the formation of a brown cloud. This is the destruction of the $^{n}Bu_4NBr$ electrolyte to tributyl amine. This is happening constantly throughout the reaction, but as the concentration of the ketone decrease more and more of this Lewis acid coordinated base is formed. We still continue to run the reaction longer as there are still small amounts of product that are formed.

Question 4:

How moisture and oxygen sensitive is the reaction? Is it worthwhile just operating under Schlenk-type conditions to be sure? Are there any signs that moisture has been is a problem?

Answer:

The reaction was found to give the same yield with or without the use of strictly anhydrous conditions. $^{n}Bu_4NBr$ is known to be hygroscopic and this electrolyte we use is a crystalline solid, despite being stored in a reagent bottle on the bench for a long time. Although we have not

examined wet $^{n}Bu_4NBr$, we do recommend using this compound with good quality.

Question 5:

The resistance of the reaction is very high and ElectraSyn can't deliver the set charge, or just registers that the resistance is too high and will not carry out the electrolysis, what could be wrong?

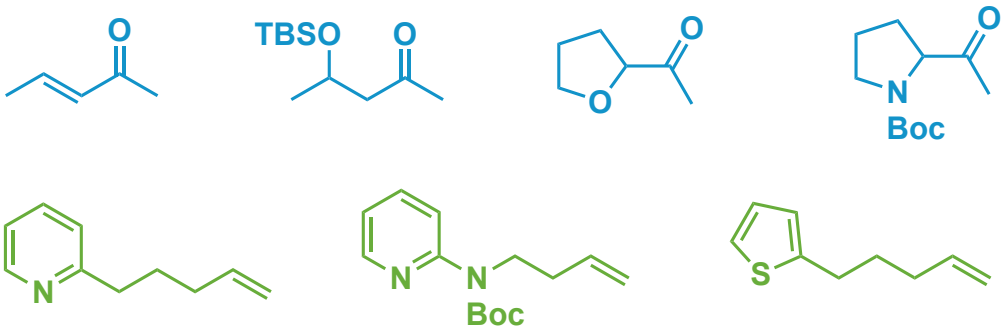
Answer:

Several things could be wrong, so let's go through them step by step:

- The electrode surfaces might be contaminated. Wiping with a cloth vigorously is advised. Sonication can also help.
- The electrode connections to the terminals of the cap might be poor. Make sure the contact is good, otherwise wipe both surfaces with some sand paper until shiny.
- The solution is not mixed well prior to electrolysis. Ensure the TPPA has mixed with the THF, by stirring or sonication.
- The upper Voltage limit on the ElectraSyn might be set too low. To adjust, on the home screen, select the ⚙ *(top right corner)* → *Voltage limit* → *set to 30 V*

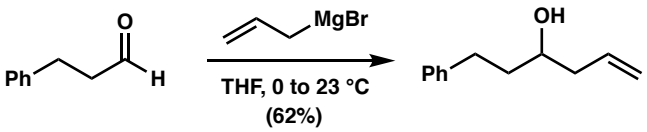
A useful trick is to remove the vial and replace it with a short vial or bowl containing brine. Brine is an excellent conductor, so there are still conductivity issues using brine, it is very likely a connection issue that is occuring either between the electrodes and the cap, or the cap and the ElectraSyn (turning off and unplugging the devices helps occasionally).

Unsuccessful Substrates



Preparation of substrates

Compound S1



To a solution of phenylpropionaldehyde (4.50 g, 30 mmol, 1 equiv.) in THF (30 mL) was added allylmagnesium bromide (40 mmol, 1.0 M in ether, 1.33 equiv.) dropwise at 0 °C over 30 minutes. The reaction was then slowly warmed to 23 °C and monitored via TLC. After 1h, the reaction was quenched with H_2O and then diluted with ether (150 mL) and saturated NH_4Cl (100 mL). The resulted mixture was transferred to a separatory funnel and the aqueous phase was separated. The organic phase was washed with H_2O (3 × 100 mL) and brine (50 mL), dried over $MgSO_4$, concentrated and purified via column chromatography (hexanes/EtOAc, 3:1 to 1:1) to give the 3.28 g of the title compound (62%).

Physical State: colorless oil.

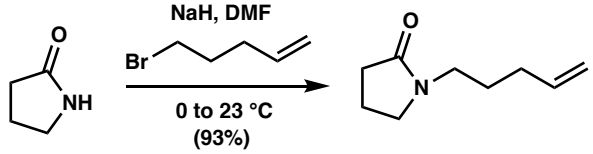
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 – 7.28 (m, 2H), 7.23 – 7.28 (m, 3H), 5.87 – 5.78 (m, 1H), 5.18 – 5.11 (m, 2H), 3.72 – 3.65 (m, 1H), 2.82 (ddd, J = 13.7, 9.0, 6.4 Hz, 1H), 2.70 (ddd, J = 13.7, 9.1, 7.2 Hz, 1H), 2.36 – 2.30 (m, 1H), 2.23 – 2.15 (m, 1H), 1.85 – 1.75 (m, 2H), 1.66 (brs, 1H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 142.0, 134.6, 128.4, 128.4, 125.8, 118.3, 69.9, 42.1, 38.4, 32.0.

HRMS (ESI-TOF): calc'd for $C_{12}H_{15}O$ $[M+H-H_2O]^+$: 159.1174, found 159.1174.

TLC: R_f = 0.39 (1:3 hexanes/EtOAc).

Compound S2



To a solution of 2-pyrrolidinone (0.851 g, 10 mmol, 1.0 equiv.) in DMF (10 mL) was added 60% NaH in mineral oil (100 mg, 25 mmol, 2.5 equiv.) at 0 °C and the reaction was stirred at this temperature for 30 mins. Next, pure 5-bromo-1-pentene (1.4 mL, 12 mmol, 1.2 equiv) was added and the reaction was allowed to warm to 23 °C and stirred for 10 h. After reaction completion, it was quenched with saturated NH_4Cl (10 mL) and diluted with H_2O (20 mL) and EtOAc (20 mL).

The mixture was transferred to a separatory funnel and the organic phase was separated. The aqueous layer was exacted with EtOAc (3 × 20 mL). The organic phase was combined and dried over $MgSO_4$, concentrated and purified via column chromatography (EtOAc) to give the 1.42 g of desired product (93%).

Physical State: colorless oil.

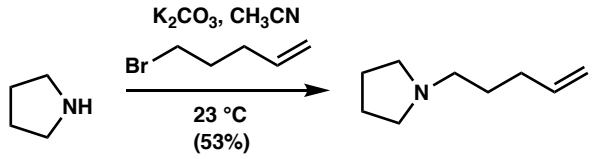
^{1}H NMR (500 MHz, $CDCl_3$): δ 5.78 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.01 (dd, *J* = 17.1, 1.8 Hz, 1H), 4.95 (dt, *J* = 10.2, 1.6 Hz, 1H), 3.35 (t, *J* = 7.1 Hz, 2H), 3.31 – 3.19 (m, 2H), 2.36 (t, *J* = 8.2 Hz, 2H), 2.06 – 2.01 (m, 2H), 2.01 – 1.96 (m, 2H), 1.60 (p, *J* = 7.6 Hz, 2H).

^{13}C NMR (151 MHz, $CDCl_3$): 174.8, 137.6, 115.0, 47.1, 42.0, 31.0, 31.0, 26.5, 17.9.

HRMS (ESI-TOF): calc'd for $C_9H_{16}NO^+$ $[M+H]^+$: 154.1226, found 154.1232.

TLC: R_f = 0.43 (EtOAc)

Compound S3



A suspension of pyrrolidine (1.64 mL, 20 mmol, 1.0 equiv.), K_2CO_3 (4.17 g, 30 mmol) and 5-bromo-1-pentene (2.6 mL, 22 mmol, 1.1 equiv) in CH_3CN (30 mL) was stirred for 10 h. Next, it was diluted with EtOAc (50 mL) and filtered through Celite. The mixture was concentrated and purified via column chromatography (EtOAc) to give the 1.42 g of desired product (93%).

Physical State: colorless oil.

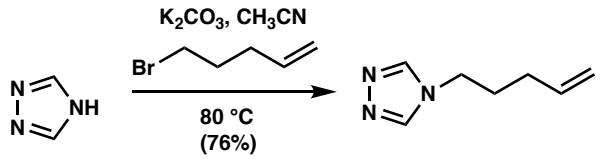
^{1}H NMR (500 MHz, $CDCl_3$): δ 5.83 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.02 (dd, *J* = 17.2, 1.9 Hz, 1H), 4.95 (dt, *J* = 10.3, 1.7 Hz, 1H), 2.48 (ddt, *J* = 8.0, 5.3, 2.7 Hz, 4H), 2.45 – 2.40 (m, 2H), 2.09 (td, *J* = 7.5, 5.9 Hz, 2H), 1.86 – 1.73 (m, 4H), 1.66 – 1.57 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 138.7, 114.5, 56.1, 54.2, 31.9, 28.3, 23.4.

HRMS (ESI-TOF): calc'd for $C_{22}H_{34}NO_4$ $[M+H]^+$: 140.1439, found 140.1432.

TLC: R_f = 0.51 (50:1, EtOAc/Et_3N).

Compound S4



A suspension of 1,2,4-triazole (691 mg, 10 mmol, 1.0 equiv.), K_2CO_3 (3.45 g, 25 mmol) and 5-bromo-1-pentene (1.3 mL, 11 mmol, 1.1 equiv) in CH_3CN (20 mL) was refluxed at 80 °C for 10 h. Next, it was diluted with EtOAc (50 mL) and filtered through Celite. The mixture was concentrated and purified via column chromatography (EtOAc) to give the 1.04 g of desired product (76%).

Physical State: colorless oil.

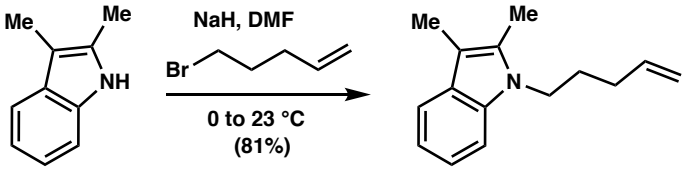
^{1}H NMR (600 MHz, $CDCl_3$): δ 8.02 (s, 1H), 7.91 (s, 1H), 5.74 (ddt, *J* = 16.0, 10.7, 6.5 Hz, 1H), 5.03 (dq, *J* = 7.1, 1.6 Hz, 1H), 5.00 (t, *J* = 1.5 Hz, 1H), 4.15 (t, *J* = 6.9 Hz, 2H), 2.07 – 2.00 (m, 2H), 2.00 – 1.93 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 151.9, 142.9, 136.5, 116.1, 48.7, 30.2, 28.5.

HRMS (ESI-TOF): calc'd for $C_7H_{12}N_3$ $[M+H]^+$: 138.1026, found 138.1030.

TLC: R_f = 0.50 (EtOAc)

Compound S5



To a solution of 2,3-dimethylindole (2.0 g, 13.8 mmol, 1.0 equiv.) in DMF (30 mL) was added 60% NaH in mineral oil (826 mg, 20.7 mmol, 1.5 equiv.) at 0 °C and the reaction was stirred at this temperature for 30 mins. Next, pure 5-bromo-1-pentene (2.4 mL, 20.7 mmol, 1.5 equiv) was added and the reaction was allowed to warm to 23 °C and stirred for 10 h. After reaction completion, it was quenched with saturated NH_4Cl (10 mL) and diluted with H_2O (20 mL) and EtOAc (20 mL). The mixture was transferred to a separatory funnel and the organic phase was separated. The aqueous layer was exacted with EtOAc (3 × 20 mL). The organic phase was combined and dried over $MgSO_4$, concentrated and purified via column chromatography (EtOAc) to give the 2.38 g of desired product (93%).

Physical State: colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, *J* = 7.8 Hz, 1H), 7.25 – 7.22 (m, 1H), 7.13 (ddd, *J* = 8.1, 6.9, 1.3 Hz, 1H), 7.07 (ddd, *J* = 7.9, 7.1, 1.1 Hz, 1H), 5.83 (ddt, *J* = 16.9, 10.2, 6.5 Hz, 1H), 5.24 – 4.98 (m, 2H), 4.13 – 3.98 (m, 2H), 2.35 (s, 3H), 2.25 (s, 3H), 2.17 – 2.07 (m, 2H), 1.91 – 1.75 (m, 2H).

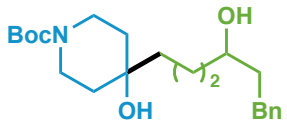
^{13}C NMR (151 MHz, $CDCl_3$): δ 137.6, 135.8, 132.0, 128.5, 120.4, 118.5, 117.9, 115.3, 108.6, 106.4, 42.6, 31.0, 29.3, 10.1, 8.8.

HRMS (ESI-TOF): calc'd for $C_{15}H_{20}N$ $[M+H]^+$: 214.1596, found 214.1600

TLC: R_f = 0.79 (9:1, Hexanes/EtOAc).

Experimental Procedures and Characterization Data

Compound 5



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 3:1 to 1:1) afforded 125.5 mg (95%) of the title compound.

Physical State: amorphous solid.

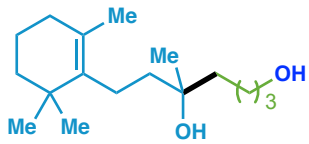
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 – 7.25 (m, 2H), 7.21 – 7.16 (m, 3H), 3.78 – 3.67 (m, 2H), 3.67 – 3.58 (m, 1H), 3.22 – 3.08 (m, 2H), 2.83 – 2.74 (m, 1H), 2.71 – 2.62 (m, 1H), 1.83 – 1.69 (m, 3H), 1.56 – 1.46 (m, 8H), 1.45 (s, 9H), 1.46 – 1.39 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 154.8, 142.0, 128.4, 128.4, 125.8, 79.4, 71.1, 69.7, 42.8, 39.2, 37.7, 36.7, 36.6, 32.1, 28.4, 18.8.

HRMS (ESI-TOF): calc'd for $C_{17}H_{28}NO_2$ $[M+2H–Boc]^+$: 278.2115, found 278.2121.

TLC: R_f = 0.39 (1:3 hexanes/EtOAc).

Compound 6



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 3:1 to 1:1) afforded 62.9 mg (67%) of the title compound.

Physical State: colorless oil.

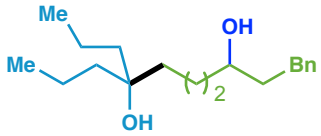
^{1}H NMR (500 MHz, $CDCl_3$): δ 3.66 (t, J = 6.5 Hz, 2H), 2.14 – 1.98 (m, 2H), 1.89 (t, J = 6.3 Hz, 2H), 1.61 – 1.54 (m, 4H), 1.59 (s, 3H), 1.53 – 1.47 (m, 4H), 1.46 – 1.38 (m, 4H), 1.20 (s, 3H), 0.99 (d, J = 1.2 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 136.7, 127.0, 73.1, 62.6, 42.0, 41.2, 39.9, 35.1, 33.1, 32.8, 28.7, 26.4, 22.7, 20.0, 19.8, 19.5.

HRMS (ESI-TOF): calc'd for $C_{17}H_{31}O$ $[M+H-H_2O]^+$:251.2375, found 251.2376.

TLC: R_f = 0.47 (1:1 hexanes/EtOAc).

Compound 7



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 3:1 to 1:1) afforded 100.3 mg (98%) of the title compound.

Physical State: colorless oil.

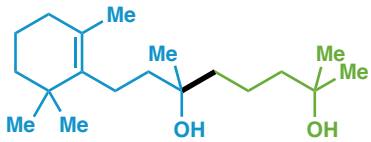
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 – 7.26 (m, 2H), 7.22 – 7.16 (m, 3H), 3.67 – 3.61 (m, 1H), 2.80 (ddd, *J* = 13.8, 9.7, 5.7 Hz, 1H), 2.67 (ddd, *J* = 13.8, 9.6, 6.7 Hz, 1H), 1.83 – 1.70 (m, 2H), 1.49 – 1.42 (m, 4H), 1.42 – 1.36 (m, 5H), 1.36 – 1.24 (m, 5H), 0.91 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 142.2, 128.4, 128.4, 125.8, 74.5, 71.1, 41.7, 41.6, 39.2, 39.1, 38.0, 32.1, 19.5, 16.8, 16.8, 14.7.

HRMS (ESI-TOF): calc'd for $C_{19}H_{31}O$ $[M+H-H_2O]^+$: 275.2375, found 275.2374.

TLC: R_f = 0.56 (1:1 hexanes/EtOAc).

Compound 8



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 3:1 to 1:3) afforded 75.6 mg (73%) of the title compound.

Physical State: colorless sticky oil.

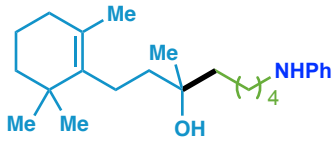
^{1}H NMR (600 MHz, $CDCl_3$): δ 2.05 – 2.00 (m, 2H), 1.91 – 1.87 (m, 2H), 1.59 (s, 3H), 1.58 – 1.50 (m, 5H), 1.49 – 1.43 (m, 6H), 1.42– 1.39 (m, 2H), 1.22 (s, 6H), 1.20 (s, 3H), 0.99 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$): δ 136.7, 127.0, 73.1, 71.0, 44.4, 42.0, 41.9, 39.8, 35.1, 32.8, 29.3, 29.2, 28.6, 26.6, 22.7, 19.8, 19.5, 18.7.

HRMS (ESI-TOF): calc'd for $C_{19}H_{35}O$ $[M+H-H_2O]^+$: 279.2688, found 279.2695.

TLC: R_f = 0.71 (1:3 hexanes/EtOAc).

Compound 9



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 5:1 to 3:1) afforded 92.6 mg (77%) of the title compound.

Physical State: yellow foam.

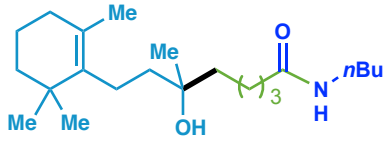
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.20 – 7.11 (m, 2H), 6.70 (t, *J* = 7.3 Hz, 1H), 6.61 (d, *J* = 7.9 Hz, 2H), 3.12 (t, *J* = 7.1 Hz, 2H), 2.24 – 1.98 (m, 2H), 1.92 (t, *J* = 6.3 Hz, 2H), 1.70 – 1.62 (m, 2H), 1.61 (s, 3H), 1.60 – 1.56 (m, 1H), 1.55 – 1.47 (m, 3H), 1.46 – 1.40 (m, 6H), 1.21 (s, 3H), 1.01 (s, 6H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 148.4, 136.7, 129.2, 126.9, 117.1, 112.7, 73.0, 43.9, 41.9, 41.6, 39.8, 35.0, 32.8, 29.5, 28.6, 27.7, 26.5, 23.7, 22.7, 19.7, 19.5.

HRMS (ESI-TOF): calc'd for $C_{24}H_{40}NO$ $[M+H]^+$:358.2104, found 358.2106.

TLC: R_f = 0.77 (1:1 hexanes/EtOAc).

Compound 10



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc 3:1 to pure EtOAc) afforded 115.7 mg (94%) of the title compound.

Physical State: colorless sticky oil.

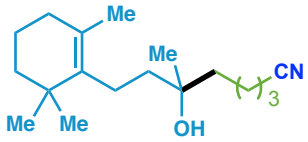
^{1}H NMR (500 MHz, $CDCl_3$): δ 5.45 (s, 1H), 3.27 – 3.21 (m, 2H), 2.18 (t, *J* = 7.5 Hz, 2H), 2.09 – 1.97 (m, 2H), 1.89 (t, *J* = 6.3 Hz, 2H), 1.69 – 1.61 (m, 2H), 1.58 (s, 3H), 1.58 – 1.52 (m, 2H), 1.52 – 1.43 (m, 6H), 1.43 – 1.37 (m, 4H), 1.37 – 1.30 (m, 2H), 1.18 (s, 2H), 0.98 (s, 6H), 0.92 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 172.8, 136.7, 127.0, 72.9, 42.0, 41.3, 39.9, 39.2, 36.8, 35.1, 32.8, 31.7, 28.7, 26.5, 26.3, 23.6, 22.7, 20.1, 19.8, 19.5, 13.7.

HRMS (ESI-TOF): calc'd for $C_{22}H_{40}NO$ $[M+H-H_2O]^+$: 334.3110, found 334.3113.

TLC: R_f = 0.17 (1:3 hexanes/EtOAc).

Compound 11



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 3:1 to 1:1) afforded 50.6 mg (58%) of the title compound.

Physical State: colorless oil.

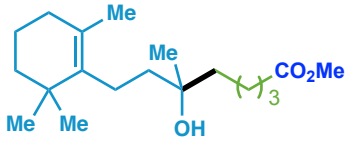
^{1}H NMR (600 MHz, $CDCl_3$): δ 2.39 – 2.34 (m, 2H), 2.05 – 2.00 (m, 2H), 1.72 – 1.65 (m, 2H), 1.59 (s, 3H), 1.58 – 1.54 (m, 3H), 1.54 – 1.46 (m, 6H), 1.43 – 1.38 (m, 2H), 1.21 (s, 3H), 0.99 (s, 6H).

^{13}C NMR (150 MHz, $CDCl_3$): δ 136. 5, 127.1, 119.7, 72.8, 42.0, 40.7, 39.8, 35.1, 32.7, 28.7, 28.6, 26.4, 25.9, 23.1, 22.6, 19.8, 19.5, 17.2.

HRMS (ESI-TOF): calc'd for $C_{18}H_{30}N$ $[M+H-H_2O]^+$: 260.2378, found 260.2379.

TLC: R_f = 0.36 (1:1 hexanes/EtOAc).

Compound 12



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 3:1 to 1:1) afforded 60.9 mg (56%) of the title compound.

Physical State: colorless oil.

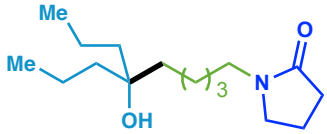
^{1}H NMR (500 MHz, $CDCl_3$): δ 3.65 (s, 3H), 2.31 (t, J = 7.5 Hz, 2H), 2.05 – 1.91 (m, 2H), 1.89 (t, J = 6.4 Hz, 2H), 1.68 – 1.60 (m, 2H), 1.58 (s, 3H), 1.57 – 1.53 (m, 2H), 1.52 – 1.43 (m, 4H), 1.43 – 1.38 (m, 2H), 1.35 – 1.32 (m, 2H), 1.18 (s, 3H), 0.98 (s, 6H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 174.2, 136.7, 126.9, 72.9, 51.4, 41.9, 41.4, 39.8, 35.1, 34.0, 32.8, 29.7, 28.6, 26.5, 24.9, 23.6, 22.7, 19.8, 19.5.

HRMS (ESI-TOF): molecular weight peak not found despite extensive efforts.

TLC: R_f = 0.49 (1:1 hexanes/EtOAc).

Compound 13



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 3:1 to pure EtOAc) afforded 92.4 mg (98%) of the title compound.

Physical State: white foam.

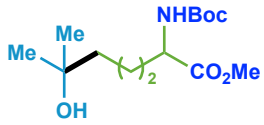
^{1}H NMR (500 MHz, $CDCl_3$): δ 3.36 (t, *J* = 7.1 Hz, 2H), 3.26 (t, *J* = 7.4 Hz, 2H), 2.37 (t, *J* = 8.1 Hz, 2H), 2.05 – 1.96 (m, 2H), 1.56 – 1.47 (m, 2H), 1.44 – 1.34 (m, 6H), 1.34 – 1.22 (m, 10H), 0.90 (t, *J* = 7.2 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 174.8, 74.3, 47.1, 42.5, 41.6, 39.1, 31.1, 27.5, 27.3, 23.1, 17.9, 16.7, 14.7.

HRMS (ESI-TOF): calc'd for $C_{16}H_{30}NO$ $[M+H-H_2O]^+$: 252.2327, found 252.2332.

TLC: R_f = 0.16 (1:3 hexanes/EtOAc).

Compound 14



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 3:1 to 1:1) afforded 30.4 mg (30%) of the title compound.

Physical State: white foam.

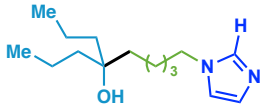
^{1}H NMR (500 MHz, $CDCl_3$): δ 5.08 – 5.00 (m, 1H), 4.36 – 4.27 (m, 1H), 3.73 (s, 3H), 1.83 – 1.74 (m, 1H), 1.67 – 1.57 (m, 2H), 1.55 – 1.49 (m, 1H), 1.46 – 1.39 (m, 3H), 1.44 (s, 9H), 1.20 (s, 3H), 1.19 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 173.4, 155.5, 79.9, 70.7, 53.1, 52.2, 42.9, 33.3, 29.4, 29.1, 28.3, 19.9.

HRMS (ESI-TOF): calc'd for $C_{14}H_{27}NO_5Na$ $[M+Na]^+$: 312.1787, found 312.1789.

TLC: R_f = 0.50 (1:1 hexanes/EtOAc).

Compound 15



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (pure EtOAc, 3:1 to EtOAc:MeOH:Et_3N, 50:1:0.2) afforded 49.5 mg (56%) of the title compound.

Physical State: colorless sticky oil.

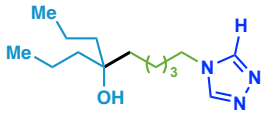
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.49 (s, 1H), 7.06 (s, 1H), 6.90 (s, 1H), 3.93 (t, J = 7.1 Hz, 2H), 1.79 (t, J = 7.3 Hz, 2H), 1.43 – 1.36 (m, 6H), 1.37 – 1.21 (m, 9H), 0.91 (t, J = 7.2 Hz, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 137.0, 129.1, 118.8, 74.3, 47.1, 41.6, 39.0, 31.0, 27.2, 22.9, 16.8, 14.7.

HRMS (ESI-TOF): calc'd for $C_{15}H_{29}N_2O$ $[M+H]^+$: 253.2280, found 253.2287.

TLC: R_f = 0.26 (50:1:0.2 EtOAc/MeOH/Et_3N).

Compound 16



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 3:1 to pure EtOAc) afforded 54.1 mg (61%) of the title compound.

Physical State: colorless sticky oil.

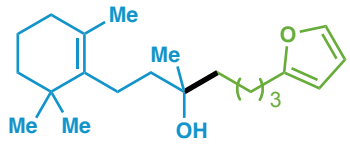
^{1}H NMR (600 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.95 (s, 1H), 4.17 (t, J = 7.1 Hz, 2H), 1.94 – 1.86 (m, 2H), 1.41 – 1.36 (m, 6H), 1.35 – 1.24 (m, 9H), 0.91 (t, J = 7.2 Hz, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 151.6, 142.7, 74.3, 49.7, 41.6, 39.0, 29.8, 27.1, 22.9, 16.8, 14.7.

HRMS (ESI-TOF): calc'd for $C_{14}H_{26}N_3$ $[M+H-H_2O]^+$: 236.2127, found 236.2132.

TLC: R_f = 0.19 (1:3 hexanes/EtOAc).

Compound 17



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 3:1 to pure EtOAc) afforded 60.2 mg (54%) of the title compound.

Physical State: white foam.

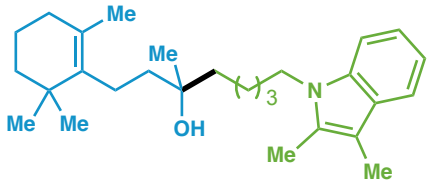
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 (d, *J* = 1.8 Hz, 1H), 6.27 (dd, *J* = 3.1, 1.9 Hz, 1H), 5.97 (d, *J* = 3.0 Hz, 1H), 2.63 (t, *J* = 7.5 Hz, 2H), 2.24 – 1.97 (m, 2H), 1.90 (t, *J* = 6.3 Hz, 2H), 1.70 – 1.62 (m, 2H), 1.59 (s, 3H), 1.59 – 1.54 (m, 2H), 1.53 – 1.44 (m, 4H), 1.43 – 1.40 (m, 2H), 1.38 - 1.35 (m, *2*H), 1.19 (s, 3H), 0.99 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 156.4, 140.6, 136.7, 126.9, 110.0, 104.6, 73.0, 41.9, 41.6, 39.9, 35.1, 32.8, 29.8, 28.9, 28.0, 27.9, 26.6, 23.7, 22.7, 19.8, 19.5.

HRMS (ESI-TOF): calc'd for $C_{21}H_{33}O$ $[M+H-H_2O]^+$: 301.2526, found 301.2525.

TLC: R_f = 0.71 (3:1 hexanes/EtOAc).

Compound 18



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 10:1 to 3:1) afforded 134.8 mg (94%) of the title compound.

Physical State: yellow solid.

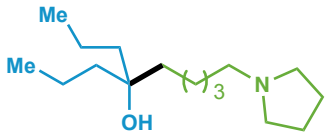
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49 (d, *J* = 7.7 Hz, 1H), 7.25 (d, *J* = 8.1 Hz, 1H), 7.14 (d, *J* = 1.2 Hz, 1H), 7.08 (d, *J* = 6.9 Hz, 1H), 4.06 (t, *J* = 7.4 Hz, 2H), 2.36 (s, 3H), 2.26 (s, 3H), 2.07 – 1.98 (m, 2H), 1.91 (t, *J* = 6.3 Hz, 2H), 1.79 – 1.66 (m, 2H), 1.59 (s, 3H), 1.59 – 1.55 (m, 2H), 1.52 – 1.48 (m, 2H), 1.46 – 1.36 (m, 8H), 1.18 (s, 3H), 1.00 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 136.7, 135.8, 132.0, 128.4, 127.0, 120.3, 118.4, 117.9, 108.6, 106.3, 72.9, 43.2, 42.0, 41.6, 39.8, 35.1, 32.8, 30.4, 28.7, 27.6, 26.5, 23.7, 22.6, 19.8, 19.5, 10.2, 8.8.

HRMS (ESI-TOF): calc'd for $C_{28}H_{42}N$ $[M+H-H_2O]^+$: 392.3317, found 392.3322.

TLC: R_f = 0.65 (3:1 hexanes/EtOAc).

Compound 19



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc/Et3N, 30:10:0.4 to EtOAc:Et_3N, 50:1) afforded 37.6 mg (42%) of the title compound.

Physical State: colorless oil.

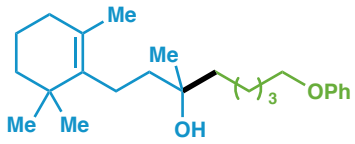
^{1}H NMR (399 MHz, $CDCl_3$): δ 2.56 – 2.48 (m, 4H), 2.47 – 2.41 (m, 2H), 1.81 – 1.70 (m, 4H), 1.60 – 1.48 (m, 2H), 1.43 – 1.35 (m, 6H), 1.34 – 12.4 (m, 6H), 0.90 (t, J = 7.1 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 74.4, 56.5, 54.1, 41.7, 39.2, 28.8, 28.3, 23.4, 23.3, 16.7, 14.7.

HRMS (ESI-TOF): calc'd for $C_{16}H_{33}N$ $[M+H-H_2O]^+$: 239.2613, found 239.2610.

TLC: R_f = 0.24 (50:1 EtOAc/Et_3N).

Compound 20



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 10:1 to 5:1) afforded 121.7 mg (97%) of the title compound.

Physical State: white foam.

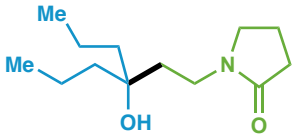
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 – 7.24 (m, 2H), 6.96 – 6.88 (m, 3H), 3.97 (t, J = 6.5 Hz, 1H), 2.07 – 2.01 (m, 2H), 1.93 – 1.88 (m, 2H), 1.85 – 1.79 (m, 2H), 1.60 (s, 3H), 1.59 – 1.56 (m, 2H), 1.56 – 1.45 (m, 7H), 1.44 – 1.40 (m, 3H), 1.21 (s, 3H), 1.00 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 159.0, 136.7, 129.4, 126.9, 120.4, 114.4, 73.0, 67.7, 41.9, 41.6, 39.8, 35.1, 32.8, 29.3, 28.7, 26.7, 26.5, 23.7, 22.7, 19.8, 19.5.

HRMS (ESI-TOF): calc'd for $C_{24}H_{37}O$ $[M+H-H_2O]^+$: 341.2844, found 341.2851.

TLC: R_f = 0.67 (3:1 hexanes/EtOAc).

Compound 21



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 3:1 to pure EtOAc) afforded 70.0 mg (88%) of the title compound.

Physical State: white foam.

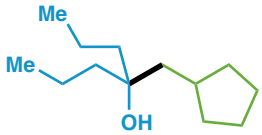
^{1}H NMR (600 MHz, $CDCl_3$): δ 3.38 (t, *J* = 7.1 Hz, 2H), 3.36 – 3.32 (m, 2H), 2.34 (t, *J* = 8.1 Hz, 2H), 2.21 (brs, 1H), 2.03 – 1.93 (m, 2H), 1.69 – 1.58 (m, 2H), 1.47 – 1.37 (m, 4H), 1.34 – 1.21 (m, 4H), 0.89 (t, *J* = 7.3 Hz, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 175.1, 73.2, 47.4, 41.5, 38.1, 36.0, 31.0, 17.8, 16.8, 14.6.

HRMS (ESI-TOF): calc'd for $C_{19}H_{32}NO$ $[M+H-H_2O]^+$:290.2478, found 290.2476.

TLC: R_f = 0.32 (1:3 hexanes/EtOAc).

Compound 22



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 10:1) afforded 32.6 mg (47%) of the title compound.

Physical State: colorless liquid.

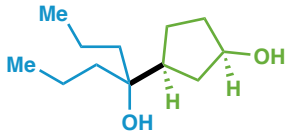
^{1}H NMR (600 MHz, $CDCl_3$): δ 1.88 – 1.75 (m, 3H), 1.65 – 1.56 (m, 2H), 1.51 (m, 4H), 1.46 – 1.39 (m, 4H), 1.35 – 1.25 (m, 4H), 1.11 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 75.0, 45.3, 42.1, 35.8, 34.5, 24.9, 16.9, 14.7.

HRMS (ESI-TOF): molecular weight peak not found despite extensive efforts.

TLC: R_f = 0.54 (10:1 hexanes/EtOAc).

Compound 23



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 3:1 to 1:3) afforded 65.9 mg (94%) of the title compound XX.

Physical State: colorless sticky oil.

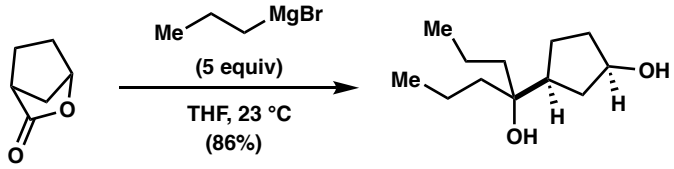
^{1}H NMR (600 MHz, $CDCl_3$): δ 4.25 – 4.19 (m, 1H), 2.73 – 2.52 (m, 2H), 2.20 – 2.10 (m, 1H), 1.87 – 1.80 (m, 1H), 1.80 – 1.63 (m, 3H), 1.60 – 1.53 (m, 1H), 1.53 – 1.44 (m, 2H), 1.44 – 1.36 (m, 2H), 1.33 – 1.22 (m, 4H), 0.96 – 0.88 (m, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 75.2, 73.0, 44.2, 40.5, 39.3, 35.8, 35.5, 23.4, 17.3, 17.1, 14.7, 14.7.

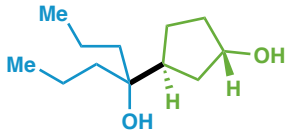
HRMS (ESI-TOF): molecular weight peak not found despite extensive efforts.

TLC: R_f = 0.40 (1:1 hexanes/EtOAc).

The diastereoselectivity was determined by comparing with the same compound made from the following well-established reaction.



Compound *epi*-23 (minor diastereomer observed in the gram-scale reaction)



Physical State: colorless sticky oil.

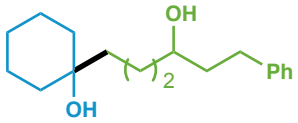
^{1}H NMR (600 MHz, $CDCl_3$): δ 4.42 – 4.34 (m, 1H), 2.41 – 2.39 (m, 1H), 2.00 – 1.90 (m, 1H), 1.83 – 1.75 (m, 1H), 1.75 – 1.54 (m, 4 H), 1.54 – 1.39 (m, 5H), 1.39 – 1.25 (m, 6H), 0.97 – 0.90 (m, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 75.0, 73.7, 44.6, 40.1, 35.9, 35.1, 23.7, 17.0, 16.9, 14.7.

HRMS (ESI-TOF): molecular weight peak not found despite extensive efforts.

TLC: R_f = 0.63 (1:1 hexanes/EtOAc).

Compound 24



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 3:1 to pure EtOAc) afforded 92.9 mg (96%) of the title compound.

Physical State: white foam.

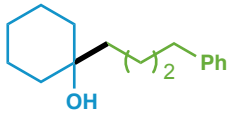
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.30 – 7.26 (m, 2H), 7.22 – 7.16 (m, 3H), 3.67 – 3.62 (m, 1H), 2.80 (ddd, *J* = 13.7, 9.7, 5.8 Hz, 1H), 2.67 (ddd, *J* = 13.8, 9.7, 6.7 Hz, 1H), 1.87 (brs, 1H), 1.82 – 1.70 (m, 2H), 1.61 – 1.36 (m, 15H), 1.30 – 1.22 (m, 1H).

^{13}C NMR (151 MHz, $CDCl_3$): 142.2, 128.4, 128.3, 125.7, 71.4, 71.0, 39.1, 37.9, 37.5, 37.3, 32.1, 25.8, 22.2, 18.8.

HRMS (ESI-TOF): calc'd or $C_{18}H_{27}O$ $[M+H]^+$: 259.2062, found 259.2064.

TLC: R_f = 0.45 (1:1 hexanes/EtOAc).

Compound 25



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 10:1) afforded 45.6 mg (56%) of the title compound.

Physical State: colorless oil.

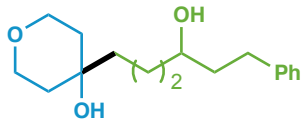
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.29 – 7.24 (m, 2H), 7.20 – 7.15 (m, 3H), 2.65 – 2.60 (m, 2H), 1.66 – 1.60 (m, 2H), 1.60 – 1.54 (m, 2H), 1.53 – 1.44 (m, 7H), 1.44 – 1.38 (m, 4H), 1.29 – 1.22 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 142.7, 128.4, 128.3, 125.6, 71.4, 37.4, 36.0, 32.2, 25.9, 22.6, 22.3.

HRMS (ESI-TOF): calc'd for $C_{16}H_{23}O$ $[M+H]^+$: 215.1800, found 215.1801.

TLC: R_f = 0.42 (10:1 hexanes/EtOAc).

Compound 26



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 3:1 to pure EtOAc) afforded 92.6 mg (95%) of the title compound.

Physical State: white foam.

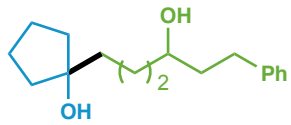
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.32 – 7.25 (m, 2H), 7.22 – 7.16 (m, 3H), 3.79 – 3.71 (m, 4H), 3.68 – 3.62 (m, 1H), 1.83 – 1.72 (m, 2H), 1.71 – 1.64 (m, 2H), 1.58 – 1.40 (m, 10H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 142.0, 128.4, 128.4, 125.8, 71.2, 68.9, 63.8, 43.1, 39.2, 37.7, 37.7, 37.6, 32.1, 18.5.

HRMS (ESI-TOF): calc'd for $C_{17}H_{25}O_2$ $[M+H-H_2O]^+$: 261.1855, found 261.1856.

TLC: R_f = 0.2 (1:3 hexanes/EtOAc).

Compound 28



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 3:1 to 1:1) afforded 87.2 mg (95%) of the title compound XX.

Physical State: white foam.

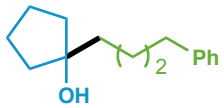
^{1}H NMR (600 MHz, $CDCl_3$): δ δ 7.30 – 7.26 (m, 2H), 7.22 – 7.16 (m, 3H), 3.67 – 3.60 (m, 1H), 2.80 (ddd, J = 13.7, 9.5, 6.0 Hz, 1H), 2.67 (ddd, J = 13.7, 9.5, 6.9 Hz, 1H), 2.44 (brs, 2H), 1.82 – 1.70 (m, 4H), 1.67 – 1.56 (m, 6H), 1.56 – 1.45 (m, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 142.2, 128.4, 128.3, 125.7, 82.4, 70.9, 41.1, 39.7, 39.5, 39.2, 37.8, 32.1, 23.7, 23.7, 20.7.

HRMS (ESI-TOF): calc'd for $C_{17}H_{25}O$ $[M+H-H_2O]^+$: 245.1905, found 245.1907.

TLC: R_f = 0.68 (1:1 hexanes/EtOAc).

Compound 29



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 20:1 to 10:1) afforded 38.2 mg (50%) of the title compound.

Physical State: colorless oil.

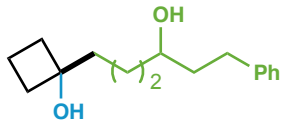
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.30 – 7.26 (m, 2H), 7.20 – 7.16 (m, 3H), 2.65 – 2.61 (m, 2H), 1.85 – 1.72 (m, 2H), 1.69 – 1.58 (m, 8H), 1.58 – 1.51 (m, 2H), 1.50 – 1.43 (m, 2H), 1.33 (brs, 1H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 142.7, 128.4, 128.2, 125.6, 82.5, 41.3, 39.7, 36.0, 32.1, 24.4, 23.8.

HRMS (ESI-TOF): calc'd for $C_{15}H_{21}$ $[M+H-H_2O]^+$: 201.1643, found 201.1636.

TLC: R_f = 0.29 (10:1 hexanes/EtOAc).

Compound 30



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 3:1 to 2:1) afforded 39 mg (45 %) of the title compound.

Physical State: white foam.

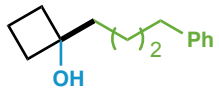
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.31 – 7.26 (m, 2H), 7.23 – 7.16 (m, 3H), 3.69 – 3.64 (m, 1H), 2.80 (ddd, *J* = 13.8, 9.8, 5.8 Hz, 1H), 2.68 (ddd, *J* = 13.7, 9.6, 6.7 Hz, 1H), 2.08 – 2.02 (m, 2H), 2.02 – 1.96 (m, 2H), 1.95 – 1.86 (m, 2H), 1.84 – 1.70 (m, 3H), 1.66 – 1.58 (m, 2H), 1.57 – 1.48 (m, 4H), 1.47 – 1.40 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$): 142.1, 128.4, 125.8, 75.4, 71.3, 39.2, 39.1, 37.7, 36.1, 35.99, 32.1, 19.5, 12.1.

HRMS (ESI-TOF): calc'd for $C_{16}H_{23}O$ $[M+H-H_2O]^+$: 231.1749, found 231.1753.

TLC: R_f = 0.61 (1:1 hexanes/EtOAc).

Compound 31



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 20:1 to 10:1) afforded 15.0 mg (21%) of the title compound.

Physical State: colorless oil.

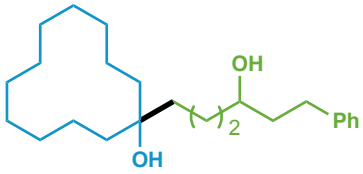
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.30 – 7.25 (m, 2H), 7.21 – 7.16 (m, 3H), 2.67 – 2.62 (m, 2H), 2.07 – 2.02 (m, 2H), 2.02 – 1.95 (m, 2H), 1.78 – 1.71 (m, 1H), 1.71 – 1.65 (m, 2H), 1.65 – 1.60 (m, 3H), 1.56 – 1.48 (m, 1H), 1.48 – 1.40 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$):): δ 142.6, 128.4, 128.2, 125.6, 75.3, 39.3, 36.0, 35.9, 31.9, 23.1, 12.1.

HRMS (ESI-TOF): calc'd for $C_{14}H_{19}$ $[M+H-H_2O]^+$: 187.1481, found 187.1481.

TLC: R_f = 0.33 (10:1 hexanes/EtOAc).

Compound 32



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 5:1 to 1:1) afforded 70.7 mg (56%) of the title compound.

Physical State: white foam.

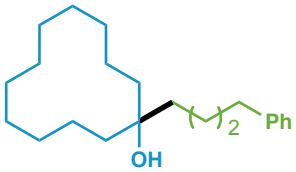
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.30 – 7.25 (m, 2H), 7.22 – 7.16 (m, 3H), 3.67 – 3.62 (m, 1H), 2.80 (ddd, J = 14.9, 9.8, 5.7 Hz, 1H), 2.67 (ddd, J = 13.7, 9.6, 6.6 Hz, 1H), 1.83 – 1.70 (m, 2H), 1.69 – 1.61 (m, 2H), 1.57 – 1.44 (m, 6H), 1.44 – 1.22 (m, 22H).

^{13}C NMR (151 MHz, $CDCl_3$):): δ 142.2, 128.4, 128.3, 125.8, 75.2, 71.1, 40.4, 39.2, 38.0, 34.5, 34.3, 32.1, 26.4, 26.0, 22.5, 22.0, 19.6, 19.5, 18.8.

HRMS (ESI-TOF): calc'd for $C_{24}H_{39}O$ $[M+H]^+$: 343.3001, found 343.2994.

TLC: R_f = 0.73 (1:1 hexanes/EtOAc).

Compound 33



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 5:1 to 3:1) afforded 85.3 mg (77%) of the title compound.

Physical State: white foam.

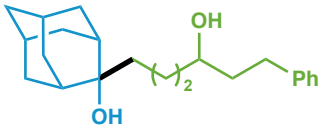
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 – 7.24 (m, 2H), 7.22 – 7.14 (m, 3H), 2.67 – 2.60 (m, 2H), 1.67 – 1.57 (m, 2H), 1.55 – 1.46 (m, 2H), 1.46 – 1.25 (m, 25H).

^{13}C NMR (125 MHz, $CDCl_3$): 142.7, 128.3, 128.2, 125.6, 75.1, 40.7, 36.0, 34.4, 32.2, 26.5, 26.0, 22.6, 22.5, 22.0, 19.6.

HRMS (ESI-TOF): calc'd for $C_{22}H_{35}$ $[M+H-H_2O]^+$: 299.2739, found 299.2742.

TLC: R_f = 0.64 (3:1 hexaness/EtOAc).

Compound 34



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 5:1 to 1:1) afforded 108.1 mg (94%) of the title compound.

Physical State: white solid.

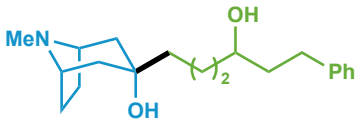
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.31 – 7.24 (m, 2H), 7.22 – 7.16 (m, 3H), 3.69 – 3.63 (m, 1H), 2.80 (ddd, J = 14.9, 9.8, 5.7 Hz, 1H), 2.67 (ddd, J = 13.7, 9.7, 6.7 Hz, 1H), 2.18 – 2.11 (m, 2H), 1.87 – 1.77 (m, 5H), 1.77 – 1.73 (m, 3H), 1.73 – 1.62 (m, 9H), 1.59 – 1.53 (m, 2H), 1.53 – 1.45 (m, 3H), 1.45 – 1.38 (m, 1H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 142.2, 128.4, 128.4, 125.8, 75.1, 71.2, 39.2, 38.3, 38.0, 37.9, 37.0, 36.7, 34.6, 34.6, 32.9, 32.9, 32.1, 27.4, 27.2, 18.1.

HRMS (ESI-TOF): calc'd for $C_{22}H_{31}O$ $[M+H-H_2O]^+$: 311.2375, found 311.2374.

TLC: R_f = 0.73 (1:1 hexanes/EtOAc).

Compound 36



Following **general procedure A** on 0.35 mmol scale. The product was purified by mass-directed prep LC. The crude material was purified on a Waters Autopurification LC with a Waters BEH C18 column (5 um, 19x160 mm) using a 0.1% aqueous formic acid:acetonitrile gradient (30 mL/min, main segment of gradient at 10-25% acetonitrile over 8 minutes) at ambient temperature. Fractionation was triggered by a Waters QDa single quadrupole mass spec (ESI+). The eluent was combined to concentrated to afford 85.2 mg (67%) of the title compound as a formate salt. While it is hard to determine the diastereoselectivity based on the ^{1}H-NMR spectra of the formate salt, the peaks can be well separated in the free base form, which was obtained after washing the Prep-HPLC eluent with K_2CO_3 before concentration. The diastereoselectivity was thus determined to be 3.1:1. The structure of the major diastereomer was determined via analogy to compound **37**.

Physical State: brown solid.

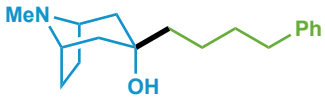
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.49 (s, 1H), 7.26 – 7.21 (m, 2H), 7.19 – 7.11 (m, 3H), 3.81 – 3.55 (m, 3H), 2.98 – 2.92 (m, 0.22), 2.79 – 2.71 (m, 1H), 2.69 – 2.48 (m, 6H), 2.47 – 2.32 (m, 1.78H), 2.10 – 1.98 (m, 2H), 1.96 – 1.79 (m, 2H), 1.75 – 1.65 (m, 2H), 1.55 – 1.32 (m, 5H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 168.0, 142.3, 128.4, 128.4, 128.3, 128.3, 125.7, 70.4, 69.0, 68.6, 62.8, 51.7, 44.6, 41.1, 40.3, 39.9, 39.3, 38.6, 37.8, 37.4, 25.1, 24.1, 20.1, 18.7, 14.1, 13.6, 12.6.

HRMS (ESI-TOF): calc'd for $C_{20}H_{32}NO$ $[M+H]^+$: 318.2433, found 318.2434.

TLC: R_f = 0.45 (1:1 MeOH/Et_3N).

Compound 37



Following **general procedure A** on 0.35 mmol scale. Purification via prep-TLC (50:1:0.5 EtOAc:MeOH:Et_3N) afforded 25.8 mg (27%) of the title compound. Unlike the case of compound **36**, a single diastereomer was isolated. The structure of the product was confirmed by comparing the NMR data with the product obtained from a Grignard reaction, of which the selectivity was well-precedented (Miooque *et. al. Heterocycles* **1985**, *23*, 2173–2175).

Physical State: white foam.

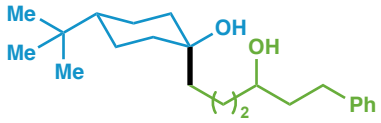
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 – 7.24 (m, 2H), 7.21 – 7.14 (m, 3H), 3.15 – 3.07 (m, 2H), 2.64 – 2.57 (m, 2H), 2.28 (s, 3H), 2.10 – 2.02 (m, 2H), 2.00 – 1.92 (m, 2H), 1.92 – 1.83 (m, 2H), 1.68 – 1.53 (m, 4H), 1.44 – 1.31 (m, 4H), 0.98 (brs, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 142.6, 128.4, 128.3, 125.6, 70.4, 60.4, 46.7, 43.8, 40.3, 35.9, 31.9, 25.4, 22.3.

HRMS (ESI-TOF): calc'd for $C_{18}H_{28}NO$ $[M+H]^+$: 274.2165, found 274.2169.

TLC: R_f = 0.43 (50:1:0.5 EtOAc/MeOH/Et_3N).

Compound 38



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 5:1 to 1:3) afforded 101.2 mg (87%) of the title compound.

Physical State: white solid.

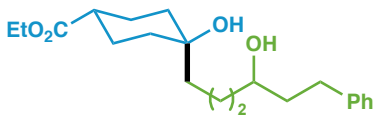
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.30 – 7.25 (m, 2H), 7.22 – 7.16 (m, 3H), 3.69 – 3.63 (m, 1H), 2.81 (ddd, *J* = 13.8, 9.7, 5.8 Hz, 1H), 2.68 (ddd, *J* = 13.7, 9.7, 6.8 Hz, 1H), 1.84 – 1.72 (m, 6H), 1.70 – 1.62 (m, 2H), 1.55 – 1.45 (m, 5H), 1.44 – 1.37 (m, 1H), 1.37 – 1.28 (m, 2H), 1.09 – 0.98 (m, 3H), 0.85 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 142.2, 128.4, 128.3, 125.8, 72.3, 71.1, 47.5, 39.2, 39.1, 38.6, 37.9, 36.0, 32.2, 32.1, 27.6, 24.5, 24.4, 18.7.

HRMS (ESI-TOF): calc'd for $C_{22}H_{35}O$ $[M+H-H_2O]^+$: 315.2688, found 315.2685.

TLC: R_f = 0.59 (1:3 hexanes/EtOAc).

Compound 39



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 5:1 to 1:3) afforded 72.6 mg (62%) of the title compound.

Physical State: white solid.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.31 – 7.26 (m, 2H), 7.22 – 7.16 (m, 3H), 4.14 (d, *J* = 7.1 Hz,

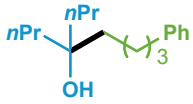
1H), 4.11 (d, J = 7.1 Hz, 1H), 3.68 – 3.62 (m, 1H), 2.79 (ddd, J = 13.7, 9.7, 5.7 Hz, 1H), 2.67 (ddd, J = 13.7, 9.6, 6.7 Hz, 1H), 2.43 – 2.36 (m, 1H), 1.93 – 1.85 (m, 2H), 1.83 – 1.74 (m, 2H), 1.74 – 1.69 (m, 2H), 1.69 – 1.61 (m, 2H), 1.59 – 1.45 (m, 7H), 1.45 – 1.37 (m, 3H), 1.25 (t, J = 7.1 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 175.4, 142.1, 128.4, 125.8, 71.4, 71.2, 60.2, 41.2, 39.2, 37.8, 36.1, 36.0, 32.1, 25.0, 18.8, 14.2.

HRMS (ESI-TOF): calc'd for $C_{21}H_{31}O_3$ $[M+H-_{H2O}]^+$: 331.2273, found 331.2267.

TLC: R_f = 0.47 (1:3 hexanes/EtOAc).

Compound 40



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 5:1 to 3:1) afforded 84.3 mg (97%) of the title compound.

Physical State: colorless oil.

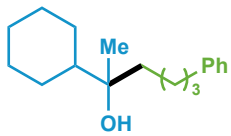
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 – 7.24 (m, 2H), 7.20 – 7.14 (m, 3H), 2.63 (t, J = 7.8 Hz, 2H), 1.67 – 1.58 (m, 2H), 1.48 – 1.42 (m, 2H), 1.42 – 1.26 (m, 10H), 1.12 (brs, 1H), 0.91 (t, J = 7.0 Hz, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): 142.6, 128.3, 128.2, 125.6, 74.4, 41.7, 39.1, 35.9, 32.1, 23.2, 16.7, 14.7.

HRMS (ESI-TOF): calc'd for $C_{17}H_{27}$ $[M+H-H_2O]^+$: 231.2113, found 231.2111.

TLC: R_f = 0.65 (3:1 hexanes/EtOAc).

Compound 41



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 5:1 to 3:1) afforded 77.4 mg (85%) of the title compound.

Physical State: colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 – 7.25 (m, 2H), 7.21 – 7.14 (m, 3H), 2.67 – 2.60 (m, 2H),

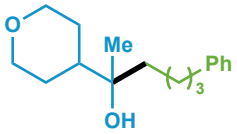
1.85 – 1.75 (m, 3H), 1.75 – 1.66 (m, 2H), 1.66 – 1.59 (m, 2H), 1.50 – 1.45 (m, 2H), 1.44 – 1.35 (m, 2H), 1.34 – 1.25 (m, 1H), 1.27 – 1.20 (m, 2H), 1.20 – 1.10 (m, 2H), 1.09 (s, 3H), 1.07 – 0.94 (m, 2H)

^{13}C NMR (151 MHz, $CDCl_3$): δ 142.7, 128.4, 128.3, 125.6, 74.5, 47.3, 39.7, 36.0, 32.2, 27.6, 26.9, 26.8, 26.8, 26.6, 24.0, 23.0.

HRMS (ESI-TOF): calc'd for $C_{18}H_{34}NO_4$ $[M+H-H_2O]^+$: 231.2107, found 231.2111.

TLC: R_f = 0.63 (3:1 hexanes/EtOAc).

Compound 42



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 5:1 to 3:1) afforded 77.1 mg (84%) of the title compound.

Physical State: colorless oil.

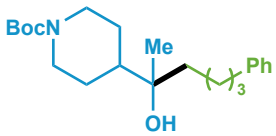
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 – 7.24 (m, 2H), 7.21 – 7.14 (m, 3H), 4.07 – 3.98 (m, 2H), 3.39 – 3.31 (m, 2H), 2.66 – 2.61 (m, 2H), 1.68 – 1.58 (m, 3H), 1.57 – 1.36 (m, 8H), 1.15 (brs, 1H), 1.10 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 142.5, 128.4, 128.3, 125.7, 73.7, 68.4, 68.3, 44.6, 39.4, 35.9, 32.0, 27.5, 26.9, 23.8, 22.9.

HRMS (ESI-TOF): calc'd for $C_{17}H_{25}$ $[M+H-H_2O]^+$: 245.1905, found 245.1905.

TLC: R_f = 0.23 (3:1 hexanes/EtOAc).

Compound 43



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 5:1 to 3:1) afforded 93.6 mg (74%) of the title compound.

Physical State: white solid.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.29 – 7.25 (m, 2H), 7.19 – 7.15 (m, 3H), 4.30 – 4.15 (m, 2H), 2.67 – 2.56 (m, 4H), 1.74 – 1.68 (m, 1H), 1.66 – 1.58 (m, 3H), 1.50 – 1.45 (m, 2H), 1.46 (s, 9H),

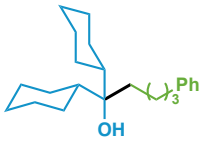
1.44 – 1.36 (m, 4H), 1.29 – 1.17 (m, 2H), 1.09 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 154.8, 142.4, 128.3, 128.2, 125.7, 79.3, 73. 8, 45.7, 39.6, 35.8, 32.0, 28.4, 26.7, 26.0, 23.9, 22.8.

HRMS (ESI-TOF): calc'd for $C_{22}H_{34}NO_2$ $[M+H-H_2O]^+$: 262.2171, found 262.2179.

TLC: R_f = 0.25 (3:1 hexanes/EtOAc).

Compound 44



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 20:1 to 10:1) afforded 70.1 mg (61%) of the title compound.

Physical State: white foam.

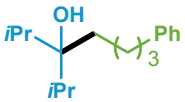
^{1}H NMR (600 MHz, CD_2Cl_2): δ 7.29 – 7.23 (m, 2H), 7.21 – 7.13 (m, 3H), 2.64 – 2.59 (m, 2H), 1.80 – 1.72 (m, 6H), 1.70 – 1.63 (m, 4H), 1.61 – 1.54 (m, 2H), 1.52 – 1.44 (m, 4H), 1.36 – 1.29 (m, 2H), 1.25 – 1.15 (m, 5H), 1.15 – 1.04 (m, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 143.4, 128.9, 128.7, 126.1, 77.4, 45.0, 36.3, 35.1, 33.2, 28.1, 27.8, 27.7, 27.6, 27.4, 24.4.

HRMS (ESI-TOF): calc'd for $C_{23}H_{35}$ $[M+H-H2O]^+$: 311.2739, found 311.2747.

TLC: R_f = 0.63 (10:1 hexanes/EtOAc).

Compound 45



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 20:1 to 10:1) afforded 21.7 mg (25%) of the title compound.

Physical State: colorless oil.

1H NMR (600 MHz, CD_2Cl_2): δ 7.29 – 7.24 (m, 2H), 7.21 – 7.14 (m, 3H), 2.61 – 2.59 (m, 2H), 1.92 – 1.84 (m, 2H), 1.63 – 1.55 (m, 2H), 1.40 – 1.33 (m, 2H), 1.42 – 1.34 (m, 2H), 1.00 (brs, 1H), 0.92 (d, J = 6.9 Hz, 6H), 0.90 (d, J = 6.9 Hz, 6H).

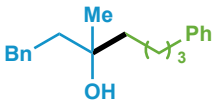
^{13}C NMR (151 MHz, CD_2Cl_2): δ 143.5, 128.9, 128.7, 126.1, 77.5, 36.4, 34.5, 34.5, 33.3, 24.6,

17.9, 17.6.

HRMS (ESI-TOF): calc'd for $C_{22}H_{34}NO_4$ $[M+H]^+$: 231.2113, found 231.2111.

TLC: R_f = 0.66 (3:1 hexanes/EtOAc).

Compound 46



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 20:1 to 5:1) afforded 52.4 mg (53%) of the title compound.

Physical State: colorless oil.

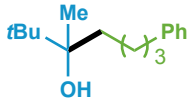
1H NMR (500 MHz, CD_2Cl_2): δ 7.29 – 7.24 (m, 2H), 7.21 – 7.14 (m, 3H), 2.61 – 2.59 (m, 2H), 1.92 – 1.84 (m, 2H), 1.63 – 1.55 (m, 2H), 1.40 – 1.33 (m, 2H), 1.42 – 1.34 (m, 2H), 1.00 (brs, 1H), 0.92 (d, J = 6.9 Hz, 6H), 0.90 (d, J = 6.9 Hz, 6H).

^{13}C NMR (151 MHz, CD_2Cl_2): δ 142.6, 142.5, 128.4, 128.4, 128.3, 128.3, 125.7, 125.7, 72.7, 43.7, 41.8, 35.9, 32.0, 30.3, 27.0, 23.6.

HRMS (ESI-TOF): molecular weight peak not found despite extensive efforts.

TLC: R_f = 0.66 (3:1 hexanes/EtOAc).

Compound 47



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 20:1 to 5:1) afforded 50.0 mg (61%) of the title compound.

Physical State: colorless oil.

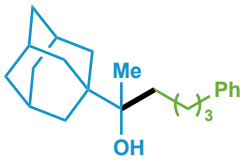
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 – 7.24 (m, 2H), 7.21 – 7.14 (m, 3H), 2.65 (t, J = 7.7 Hz, 2H), 1.69 – 1.60 (m, 2H), 1.57 – 1.38 (m, 4H), 1.11 (s, 3H), 0.94 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 142.7, 128.4, 128.2, 125.6, 76.3, 38.0, 36.1, 35.8, 32.4, 25.3, 23.7, 20.8.

HRMS (ESI-TOF): molecular weight peak not found despite extensive efforts.

TLC: R_f = 0.69 (1:1 hexanes/EtOAc).

Compound 48



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 5:1 to 1:1) afforded 62.3 mg (57%) of the title compound.

Physical State: white solid.

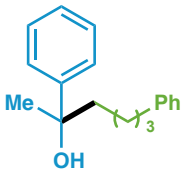
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.30 – 7.25 (m, 2H), 7.21 – 7.14 (m, 3H), 2.64 (t, *J* = 7.8 Hz, 2H), 2.03 – 1.97 (m, 3H), 1.73 – 1.68 (m, 3H), 1.67 – 1.58 (m, 11H), 1.55 – 1.45 (m, 2H), 1.44 – 1.37 (m, 2H), 1.04 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 142.8, 128.4, 128.2, 125.6, 76.0, 39.3, 37.2, 36.1, 36.0, 34.8, 32.4, 28.6, 23.5, 19.8.

HRMS (ESI-TOF): calc'd for $C_{22}H_{31}$ $[M+H-H_2O]^+$: 295.2426, found 295.2419.

TLC: R_f = 0.69 (1:1 hexanes/EtOAc).

Compound 49



Following **general procedure A** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 50:1 to 5:1) afforded 9.8 mg (11%) of the title compound.

Physical State: colorless liquid.

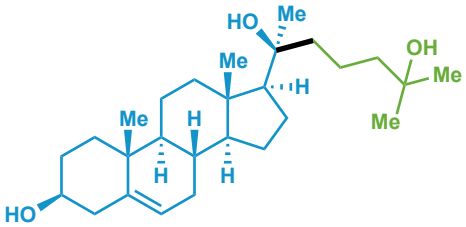
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.45 – 7.41 (m, 2H), 7.37 – 7.32 (m, 2H), 7.28 – 7.22 (m, 3H), 7.20 – 7.14 (m, 1H), 7.14 – 7.10 (m, 2H), 2.59 – 2.50 (m, 2H), 1.92 – 1.75 (m, 2H), 1.70 (brs, 1H), 1.61 – 1.57 (m, 2H), 1.56 (s, 3H), 1.39 – 1.30 (m, 1H), 1.26 – 1.16 (m, 1H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 148.0, 142.6, 128.3, 128.2, 128.1, 126.5, 125.6, 124.7, 74.7, 44.0, 35.8, 31.8, 30.1, 23.7.

HRMS (ESI-TOF): calc'd for $C_{18}H_{21}$ $[M+H-H_2O]^+$: 237.1643, found 237.1645.

TLC: R_f = 0.65 (3:1 hexanes/EtOAc).

Compound 50



Following **general procedure B** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 5:1 to 1:1) afforded 102.6 mg (70%) of the title compound as a single diastereomer. The diastereoselectivity was determined via analogy to compound **51**.

Physical State: white solid.

^{1}H NMR (600 MHz, $CDCl_3$): δ 5.37 – 5.33 (m, 1H), 3.56 – 3.48 (m, 1H), 2.29 (ddd, *J* = 13.0, 5.1, 2.1 Hz, 1H), 2.23 (ddd, *J* = 13.2, 10.8, 2.7 Hz, 1H), 2.09 (dt, *J* = 12.5, 3.5 Hz, 1H), 1.97 (ddt, *J* = 16.9, 5.0, 2.6 Hz, 1H), 1.87 – 1.80 (m, 1H), 1.78 – 1.71 (m, 0H), 1.70 – 1.60 (m, 1H), 1.54 -1.41 (m, 12H), 1.39 – 1.32 (m, 3H), 1.29 (s, 3H), 1.24 – 1.18 (m, 7H), 1.16 – 1.10 (m, 1H), 1.10 -1.04 (m, 1H), 1.04 – 0.96 (m, 4H), 0.92 (dt, *J* = 11.3, 5.2 Hz, 1H), 0.86 (s, 3H).

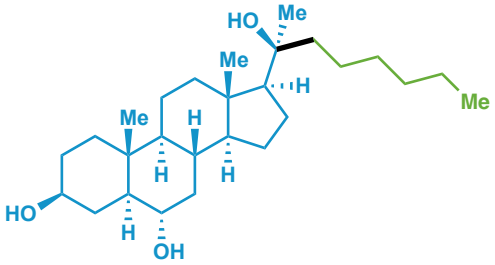
^{13}C NMR (151 MHz, $CDCl_3$): δ 140.8, 121.6, 75.2, 71.7, 71.0, 57.8, 56.8, 50.0, 44.4, 44.2, 42.6, 42.2, 40.1, 37.2, 36.5, 31.8, 31.6, 31.3, 29.5, 29.2, 26.4, 23.8, 22.4, 20.9, 19.4, 18.9, 13.6.

HRMS (ESI-TOF): calc'd for $C_{27}H_{45}O_2$ $[M+H-H_2O]^+$: 401.3420, found 401.3414.

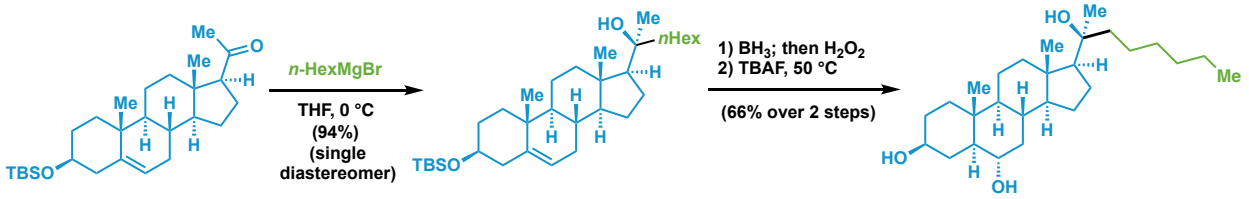
TLC: R_f = 0.21 (1:1 hexanes/EtOAc).

$[\alpha]^{20}_D$ = -51.2° (c = 0.5 in $CHCl_3$)

Compound 51



Following **general procedure B** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 5:1 to pure EtOAc) afforded 120.7 mg (82%) of the title compound as a single diastereomer. The diasterselectivity was determined by comparing with the authentic sample prepared via the following well-established sequence.



Note: Our ^{13}C NMR data matched what is listed in this paper (Stappenbeck et. al. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 5893) but ^{1}H NMR data does not. The ^{1}H NMR data listed in the Stappenbeck's paper clearly does not match the title compound.

Physical State: white solid.

^{1}H NMR (600 MHz, $CDCl_3$): δ 3.64 – 3.57 (m, 1H), 3.45 (dt, *J* = 10.7, 4.6 Hz, 1H), 2.21 (ddt, *J* = 12.2, 5.0, 2.6 Hz, 1H), 2.08 (dt, *J* = 12.6, 3.6 Hz, 1H), 2.02 (dt, *J* = 12.0, 4.2 Hz, 1H), 1.86 – 1.81 (m, 1H), 1.78 – 1.62 (m, 5H), 1.55 – 1.45 (m, 8H), 1.36 – 1.28 (m, 8H), 1.28 (s, 3H), 1.22 – 1.18 (m, 1H), 1.18 – 1.12 (m, 2H), 1.11 – 1.00 (m, 4H), 0.92 – 0.89 (m, 3H), 0.86 (s, 3H), 0.84 (s, 3H), 0.68 (ddd, *J* = 12.4, 10.6, 4.1 Hz, 1H).

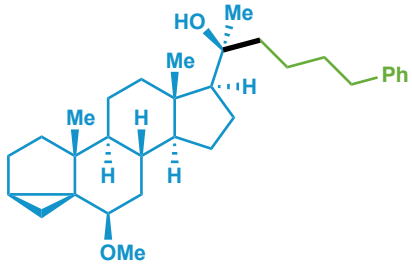
^{13}C NMR (151 MHz, $CDCl_3$): δ 75.1, 71.2, 69.5, 57.6, 56.3, 53.7, 51.7, 44.1, 42.9, 41.5, 40.2, 37.2, 36.2, 33.6, 32.2, 31.9, 31.0, 29.9, 26.4, 24.3, 23.7, 22.6, 22.3, 21.0, 14.1, 13.7, 13.4.

HRMS (ESI-TOF): calc'd for $C_{27}H_{47}O$ $[M+H-H_2O]^+$: 403.3576, found 403.3570.

TLC: R_f = 0.30 (EtOAc).

$[\alpha]^{20}_D$ = +74.8° (c = 1.0 in $CHCl_3$)

Compound 52



Following **general procedure B** on 0.35 mmol scale. Purification via silica gel column chromatography (hexanes/EtOAc, 5:1 to 3:1) afforded 143.1 mg (88%) of the title compound. The diastereoselectivity was determined via analogy to compound **51**.

Physical State: white solid.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.29 – 7.25 (m, 2H), 7.20 – 7.14 (m, 3H), 3.33 (s, 3H), 2.78 (t, *J* = 2.9 Hz, 1H), 2.64 – 2.58 (m, 2H), 2.10 – 2.00 (m, 1H), 1.90 (dt, J = 13.6, 3.2 Hz, 1H), 1.80 –

1.71 (m, 3H), 1.68 – 1.63 (m, 2H), 1.63 – 1.57 (m, 2H), 1.55 – 1.45 (m, 4H), 1.45 – 1.37 (m, 3H), 1.36 – 1.31 (m, 2H), 1.26 (s, 3H), 1.22 – 1.13 (m, 3H), 1.12 – 1.04 (m, 2H), 1.03 (s, 3H), 0.90 (s, 3H), 0.89 – 0.78 (m, 2H), 0.65 (dd, *J* = 5.1, 3.8 Hz, 1H), 0.44 (dd, *J* = 8.1, 5.1 Hz, 1H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 142.6, 128.3, 128.2, 125.6, 82.3, 75.1, 57.8, 56.6, 56.5, 47.9, 43.6, 43.3, 43.0, 40.6, 35.9, 35.2, 34.9, 33.3, 32.1, 29.8, 26.4, 24.9, 23.9, 23.6, 22.6, 22.4, 21.4, 19.2, 14.0, 13.0.

HRMS (ESI-TOF): calc'd for $C_{32}H_{47}O$ $[M+H-H_2O]^+$: 447.3627, found 447.3620.

TLC: R_f = 0.56 (3:1 hexanes/EtOAc).

$[\alpha]^{20}_D$ = +33.6° (c = 1.0 in $CHCl_3$)

X-ray data of compound 38.

Experimental Summary

The single crystal X-ray diffraction studies were carried out on a Bruker APEX II Ultra diffractometer equipped with Mo K_α radiation (λ=0.17073 Å).

Crystals of the subject compound were used as received (grow from $CHCl_3$/Hexane).

A 0.600 x 0.050 x 0.050 mm colorless crystal was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using ϕ and ϖ scans. Crystal-to-detector distance was 40 mm and exposure time was 2.0 seconds (depending on the 2θ range) per frame using a scan width of 0.70°. Data collection was 100.0 % complete to 25.242° in θ. A total of 20286 reflections were collected covering the indices, -7<=h<=7, -12<=k<=12, -20<=l<=20. 3870 reflections were found to be symmetry independent, with a R_{int} of 0.0515. Indexing and unit cell refinement indicated a **P**rimitive, **Monoclinic** lattice. The space group was found to be ***P*-1**. The data were integrated using the Bruker SAINT Software program and scaled using the SADABS software program. Solution by direct methods (SHELXT) produced a complete phasing model consistent with the proposed structure.

All nonhydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All carbon bonded hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014. . Crystallographic data are summarized in Table 1.

Notes: Excellent data and refinement,

Centrosymmetric (racemic) space group

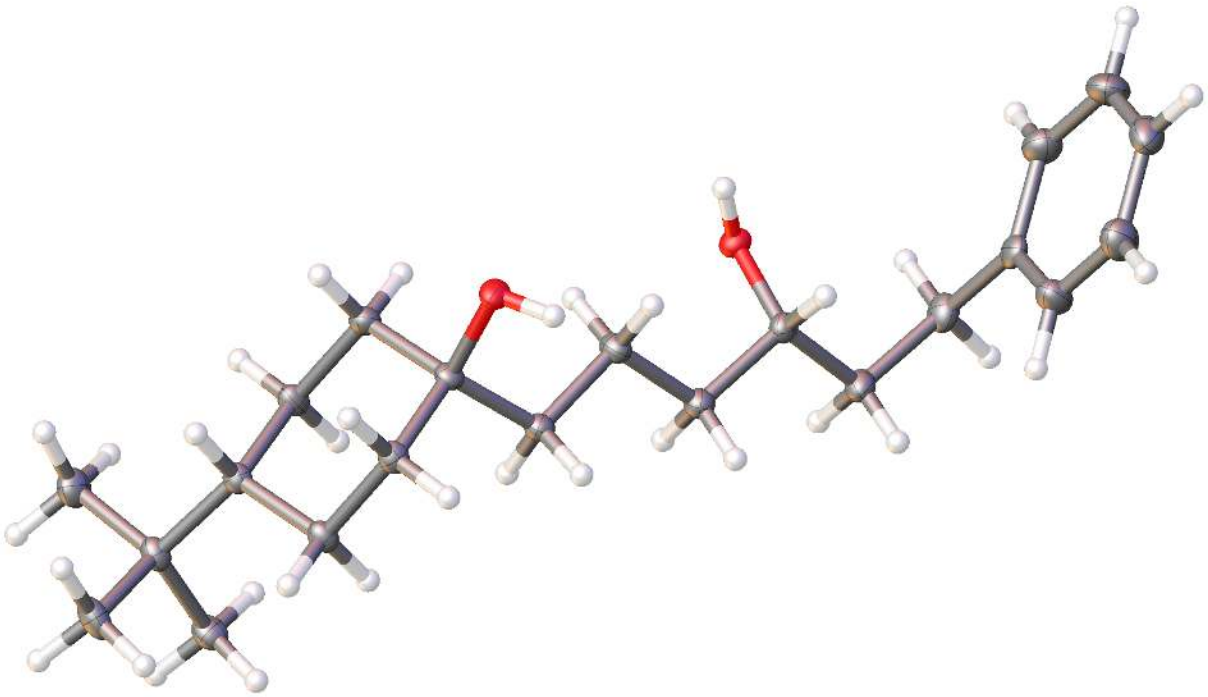


Table S1. Crystal data and structure refinement for Baran771.

Report date	2020-10-16	
Identification code	baran771	
Empirical formula	C22 H36 O2	
Molecular formula	C22 H36 O2	
Formula weight	332.51	
Temperature	100.0 K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 5.8548(3) Å	α= 87.8070(10)°.
	b = 10.1049(5) Å	β= 85.719(2)°.
	c = 16.7631(8) Å	γ = 84.188(2)°.
Volume	983.42(8) $Å^3$	
Z	2	
Density (calculated)	1.123 Mg/m^3	
Absorption coefficient	0.069 mm^{-1}	
F(000)	368	
Crystal size	0.6 x 0.05 x 0.05 mm^3	
Crystal color, habit	colorless needle	
Theta range for data collection	1.219 to 26.017°.	
Index ranges	-7<=h<=7, -12<=k<=12, -20<=l<=20	
Reflections collected	20286	
Independent reflections	3870 [R(int) = 0.0515]	
Completeness to theta = 25.242°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7454 and 0.7030	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3870 / 0 / 224	
Goodness-of-fit on F^2	1.034	
Final R indices [I>2sigma(I)]	R1 = 0.0385, wR2 = 0.0949	
R indices (all data)	R1 = 0.0445, wR2 = 0.0999	
Largest diff. peak and hole	0.328 and -0.180 $e.Å^{-3}$	

Table S2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for Baran771. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	8136(1)	797(1)	4268(1)	18(1)
O(2)	-567(1)	1592(1)	5694(1)	17(1)
C(1)	379(2)	2970(1)	8000(1)	26(1)
C(2)	1402(3)	2347(1)	8650(1)	30(1)
C(3)	557(3)	1225(1)	9011(1)	30(1)
C(4)	-1320(3)	741(1)	8716(1)	35(1)
C(5)	-2334(2)	1365(1)	8062(1)	28(1)
C(6)	-1509(2)	2494(1)	7692(1)	20(1)
C(7)	-2683(2)	3169(1)	6989(1)	22(1)
C(8)	-1073(2)	3695(1)	6316(1)	20(1)
C(9)	681(2)	2631(1)	5952(1)	17(1)
C(10)	2159(2)	3202(1)	5257(1)	18(1)
C(11)	3838(2)	2162(1)	4832(1)	18(1)
C(12)	5467(2)	2781(1)	4199(1)	16(1)
C(13)	7115(2)	1774(1)	3718(1)	15(1)
C(14)	5901(2)	1000(1)	3137(1)	17(1)
C(15)	5114(2)	1857(1)	2412(1)	17(1)
C(16)	7123(2)	2477(1)	1949(1)	15(1)
C(17)	8266(2)	3298(1)	2531(1)	16(1)
C(18)	9058(2)	2439(1)	3249(1)	17(1)
C(19)	6474(2)	3252(1)	1163(1)	17(1)
C(20)	5350(2)	2343(1)	626(1)	24(1)
C(21)	8666(2)	3670(1)	700(1)	24(1)
C(22)	4820(2)	4500(1)	1326(1)	21(1)

Table S3. Bond lengths [Å] and angles [°] for Baran771.

O(1)-H(1)	0.844(16)	C(13)-C(18)	1.5318(15)
O(1)-C(13)	1.4403(13)	C(14)-H(14A)	0.9900
O(2)-H(2)	0.870(16)	C(14)-H(14B)	0.9900
O(2)-C(9)	1.4358(13)	C(14)-C(15)	1.5356(15)
C(1)-H(1A)	0.9500	C(15)-H(15A)	0.9900
C(1)-C(2)	1.3818(19)	C(15)-H(15B)	0.9900
C(1)-C(6)	1.3899(18)	C(15)-C(16)	1.5339(15)
C(2)-H(2A)	0.9500	C(16)-H(16)	1.0000
C(2)-C(3)	1.3832(19)	C(16)-C(17)	1.5359(15)
C(3)-H(3)	0.9500	C(16)-C(19)	1.5590(15)
C(3)-C(4)	1.379(2)	C(17)-H(17A)	0.9900
C(4)-H(4)	0.9500	C(17)-H(17B)	0.9900
C(4)-C(5)	1.385(2)	C(17)-C(18)	1.5290(15)
C(5)-H(5)	0.9500	C(18)-H(18A)	0.9900
C(5)-C(6)	1.3898(17)	C(18)-H(18B)	0.9900
C(6)-C(7)	1.5146(17)	C(19)-C(20)	1.5363(16)
C(7)-H(7A)	0.9900	C(19)-C(21)	1.5377(16)
C(7)-H(7B)	0.9900	C(19)-C(22)	1.5307(17)
C(7)-C(8)	1.5301(16)	C(20)-H(20A)	0.9800
C(8)-H(8A)	0.9900	C(20)-H(20B)	0.9800
C(8)-H(8B)	0.9900	C(20)-H(20C)	0.9800
C(8)-C(9)	1.5213(16)	C(21)-H(21A)	0.9800
C(9)-H(9)	1.0000	C(21)-H(21B)	0.9800
C(9)-C(10)	1.5289(15)	C(21)-H(21C)	0.9800
C(10)-H(10A)	0.9900	C(22)-H(22A)	0.9800
C(10)-H(10B)	0.9900	C(22)-H(22B)	0.9800
C(10)-C(11)	1.5234(16)	C(22)-H(22C)	0.9800
C(11)-H(11A)	0.9900		
C(11)-H(11B)	0.9900	C(13)-O(1)-H(1)	109.5
C(11)-C(12)	1.5318(15)	C(9)-O(2)-H(2)	109.5
C(12)-H(12A)	0.9900	C(2)-C(1)-H(1A)	119.3
C(12)-H(12B)	0.9900	C(2)-C(1)-C(6)	121.38(12)
C(12)-C(13)	1.5382(15)	C(6)-C(1)-H(1A)	119.3
C(13)-C(14)	1.5300(15)	C(1)-C(2)-H(2A)	119.8

C(1)-C(2)-C(3)	120.34(13)	C(11)-C(10)-H(10A)	108.8
C(3)-C(2)-H(2A)	119.8	C(11)-C(10)-H(10B)	108.8
C(2)-C(3)-H(3)	120.5	C(10)-C(11)-H(11A)	109.1
C(4)-C(3)-C(2)	119.09(13)	C(10)-C(11)-H(11B)	109.1
C(4)-C(3)-H(3)	120.5	C(10)-C(11)-C(12)	112.49(9)
C(3)-C(4)-H(4)	119.8	H(11A)-C(11)-H(11B)	107.8
C(3)-C(4)-C(5)	120.41(12)	C(12)-C(11)-H(11A)	109.1
C(5)-C(4)-H(4)	119.8	C(12)-C(11)-H(11B)	109.1
C(4)-C(5)-H(5)	119.4	C(11)-C(12)-H(12A)	108.6
C(4)-C(5)-C(6)	121.26(13)	C(11)-C(12)-H(12B)	108.6
C(6)-C(5)-H(5)	119.4	C(11)-C(12)-C(13)	114.83(9)
C(1)-C(6)-C(7)	122.47(11)	H(12A)-C(12)-H(12B)	107.5
C(5)-C(6)-C(1)	117.53(12)	C(13)-C(12)-H(12A)	108.6
C(5)-C(6)-C(7)	120.00(11)	C(13)-C(12)-H(12B)	108.6
C(6)-C(7)-H(7A)	108.4	O(1)-C(13)-C(12)	108.54(9)
C(6)-C(7)-H(7B)	108.4	O(1)-C(13)-C(14)	106.15(9)
C(6)-C(7)-C(8)	115.41(10)	O(1)-C(13)-C(18)	108.10(9)
H(7A)-C(7)-H(7B)	107.5	C(14)-C(13)-C(12)	113.21(9)
C(8)-C(7)-H(7A)	108.4	C(14)-C(13)-C(18)	108.61(9)
C(8)-C(7)-H(7B)	108.4	C(18)-C(13)-C(12)	111.97(9)
C(7)-C(8)-H(8A)	108.8	C(13)-C(14)-H(14A)	109.0
C(7)-C(8)-H(8B)	108.8	C(13)-C(14)-H(14B)	109.0
H(8A)-C(8)-H(8B)	107.7	C(13)-C(14)-C(15)	112.81(9)
C(9)-C(8)-C(7)	113.88(10)	H(14A)-C(14)-H(14B)	107.8
C(9)-C(8)-H(8A)	108.8	C(15)-C(14)-H(14A)	109.0
C(9)-C(8)-H(8B)	108.8	C(15)-C(14)-H(14B)	109.0
O(2)-C(9)-C(8)	107.43(9)	C(14)-C(15)-H(15A)	109.2
O(2)-C(9)-H(9)	108.9	C(14)-C(15)-H(15B)	109.2
O(2)-C(9)-C(10)	111.22(9)	H(15A)-C(15)-H(15B)	107.9
C(8)-C(9)-H(9)	108.9	C(16)-C(15)-C(14)	111.98(9)
C(8)-C(9)-C(10)	111.47(9)	C(16)-C(15)-H(15A)	109.2
C(10)-C(9)-H(9)	108.9	C(16)-C(15)-H(15B)	109.2
C(9)-C(10)-H(10A)	108.8	C(15)-C(16)-H(16)	106.6
C(9)-C(10)-H(10B)	108.8	C(15)-C(16)-C(17)	108.23(9)
H(10A)-C(10)-H(10B)	107.7	C(15)-C(16)-C(19)	114.35(9)
C(11)-C(10)-C(9)	113.79(9)	C(17)-C(16)-H(16)	106.6

C(17)-C(16)-C(19)	114.02(9)	H(22A)-C(22)-H(22C)	109.5
C(19)-C(16)-H(16)	106.6	H(22B)-C(22)-H(22C)	109.5
C(16)-C(17)-H(17A)	109.4		
C(16)-C(17)-H(17B)	109.4		
H(17A)-C(17)-H(17B)	108.0		
C(18)-C(17)-C(16)	111.02(9)		
C(18)-C(17)-H(17A)	109.4		
C(18)-C(17)-H(17B)	109.4		
C(13)-C(18)-H(18A)	108.8		
C(13)-C(18)-H(18B)	108.8		
C(17)-C(18)-C(13)	113.64(9)		
C(17)-C(18)-H(18A)	108.8		
C(17)-C(18)-H(18B)	108.8		
H(18A)-C(18)-H(18B)	107.7		
C(20)-C(19)-C(16)	109.76(9)		
C(20)-C(19)-C(21)	107.64(10)		
C(21)-C(19)-C(16)	109.56(9)		
C(22)-C(19)-C(16)	112.27(9)		
C(22)-C(19)-C(20)	108.90(10)		
C(22)-C(19)-C(21)	108.59(10)		
C(19)-C(20)-H(20A)	109.5		
C(19)-C(20)-H(20B)	109.5		
C(19)-C(20)-H(20C)	109.5		
H(20A)-C(20)-H(20B)	109.5		
H(20A)-C(20)-H(20C)	109.5		
H(20B)-C(20)-H(20C)	109.5		
C(19)-C(21)-H(21A)	109.5		
C(19)-C(21)-H(21B)	109.5		
C(19)-C(21)-H(21C)	109.5		
H(21A)-C(21)-H(21B)	109.5		
H(21A)-C(21)-H(21C)	109.5		
H(21B)-C(21)-H(21C)	109.5		
C(19)-C(22)-H(22A)	109.5		
C(19)-C(22)-H(22B)	109.5		
C(19)-C(22)-H(22C)	109.5		
H(22A)-C(22)-H(22B)	109.5		

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for Baran771. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	23(1)	15(1)	15(1)	1(1)	-6(1)	2(1)
O(2)	19(1)	14(1)	19(1)	-2(1)	-2(1)	0(1)
C(1)	33(1)	25(1)	22(1)	2(1)	-1(1)	-10(1)
C(2)	35(1)	33(1)	24(1)	-1(1)	-6(1)	-9(1)
C(3)	44(1)	25(1)	20(1)	1(1)	-3(1)	3(1)
C(4)	51(1)	22(1)	32(1)	4(1)	1(1)	-11(1)
C(5)	32(1)	24(1)	30(1)	-2(1)	1(1)	-9(1)
C(6)	23(1)	18(1)	17(1)	-6(1)	5(1)	0(1)
C(7)	22(1)	25(1)	20(1)	-4(1)	1(1)	2(1)
C(8)	26(1)	17(1)	17(1)	-1(1)	-1(1)	3(1)
C(9)	20(1)	16(1)	14(1)	-1(1)	-3(1)	-1(1)
C(10)	22(1)	16(1)	17(1)	0(1)	-1(1)	-1(1)
C(11)	20(1)	16(1)	18(1)	2(1)	1(1)	-1(1)
C(12)	18(1)	14(1)	16(1)	1(1)	-1(1)	-2(1)
C(13)	17(1)	14(1)	14(1)	3(1)	-3(1)	0(1)
C(14)	19(1)	15(1)	17(1)	1(1)	-2(1)	-4(1)
C(15)	17(1)	20(1)	16(1)	1(1)	-3(1)	-6(1)
C(16)	14(1)	17(1)	15(1)	0(1)	-2(1)	-1(1)
C(17)	15(1)	20(1)	16(1)	2(1)	-1(1)	-5(1)
C(18)	15(1)	20(1)	16(1)	0(1)	-3(1)	-3(1)
C(19)	15(1)	22(1)	14(1)	2(1)	-2(1)	-2(1)
C(20)	27(1)	28(1)	18(1)	0(1)	-7(1)	-3(1)
C(21)	18(1)	37(1)	16(1)	6(1)	0(1)	-4(1)
C(22)	20(1)	23(1)	20(1)	4(1)	-3(1)	0(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for Baran771.

	x	y	z	U(eq)
H(1)	8480(20)	1179(8)	4676(9)	27
H(2)	236(18)	828(14)	5757(8)	26
H(1A)	978	3741	7760	32
H(2A)	2693	2690	8849	36
H(3)	1260	794	9457	36
H(4)	-1921	-25	8961	42
H(5)	-3618	1015	7863	34
H(7A)	-3761	3923	7188	27
H(7B)	-3610	2528	6762	27
H(8A)	-2010	4110	5888	25
H(8B)	-243	4396	6528	25
H(9)	1706	2258	6374	20
H(10A)	1134	3646	4863	22
H(10B)	3040	3886	5463	22
H(11A)	2958	1533	4572	22
H(11B)	4758	1650	5233	22
H(12A)	6393	3375	4468	19
H(12B)	4532	3339	3821	19
H(14A)	4543	646	3425	20
H(14B)	6961	234	2945	20
H(15A)	4391	1300	2049	21
H(15B)	3941	2575	2598	21
H(16)	8284	1722	1788	18
H(17A)	9607	3679	2248	20
H(17B)	7157	4045	2721	20
H(18A)	9763	3001	3614	20
H(18B)	10260	1740	3057	20
H(20A)	6325	1501	565	36
H(20B)	5174	2781	100	36
H(20C)	3834	2168	872	36
H(21A)	9352	4311	1010	36
H(21B)	8274	4081	183	36
H(21C)	9769	2884	612	36
H(22A)	3453	4255	1649	32
H(22B)	4359	4914	817	32
H(22C)	5588	5132	1616	32

Table 6. Hydrogen bonds for Baran771 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1)...O(2)#1	0.84	1.91	2.7338(12)	165.6
O(2)-H(2)...O(1)#2	0.87	1.81	2.6771(11)	171.4

Symmetry transformations used to generate equivalent atoms:

#1 x+1,y,z #2 -x+1,-y,-z+1

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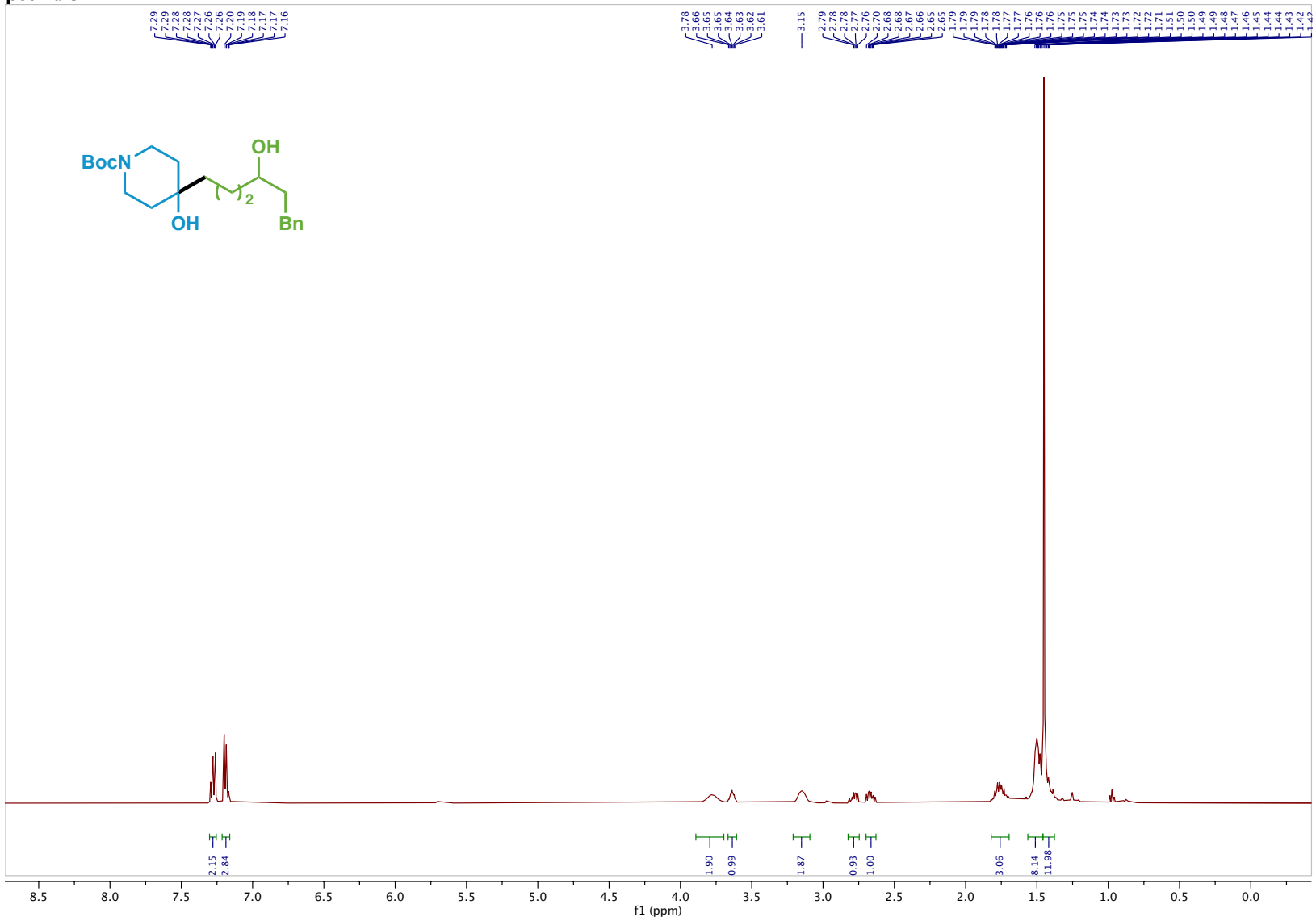
NMR Spectra

Compound 5



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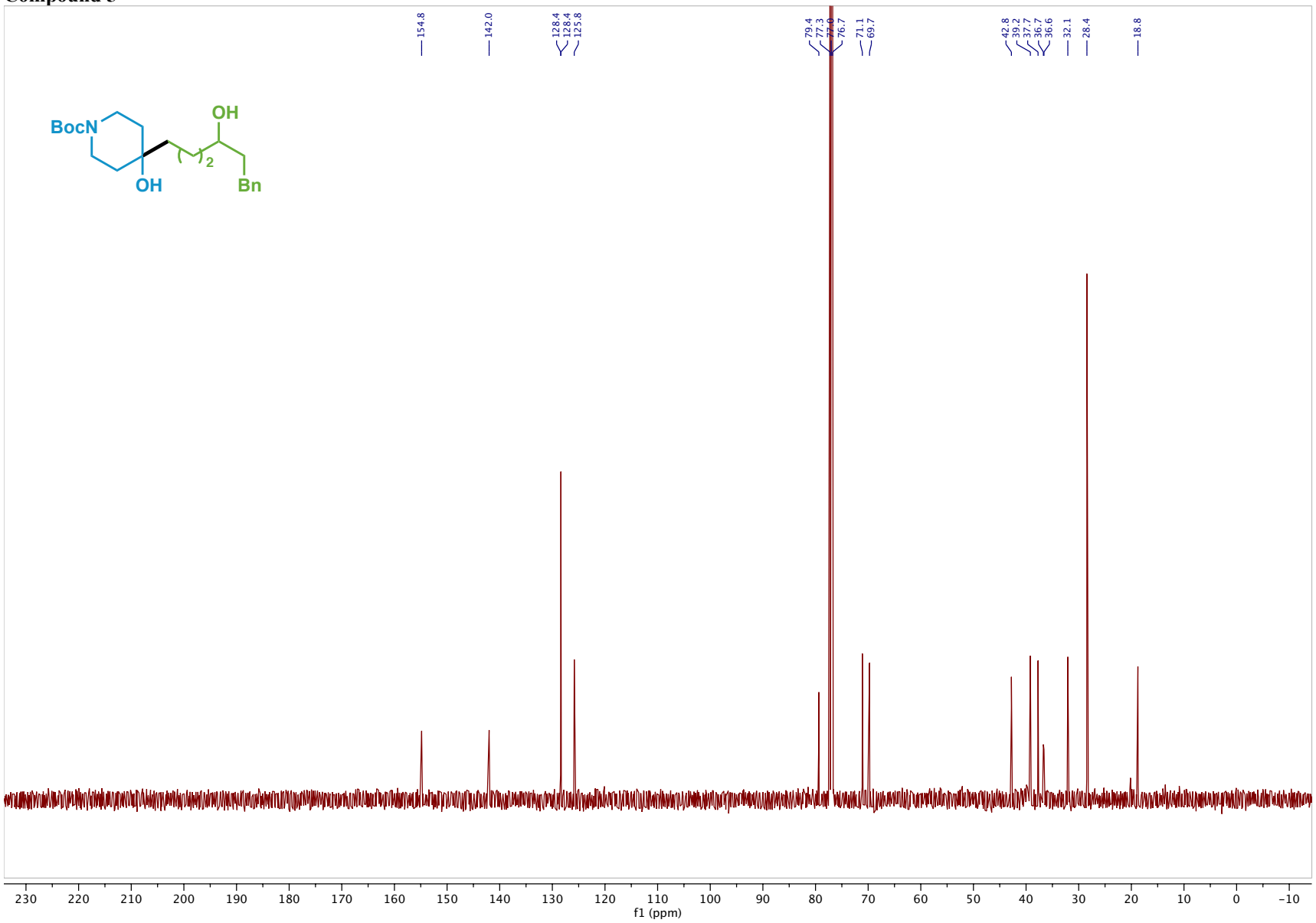
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37.7
36.7
36.6
32.1
28.4
18.8
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OH
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Bn
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210
200
190
180
170
160
150
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20
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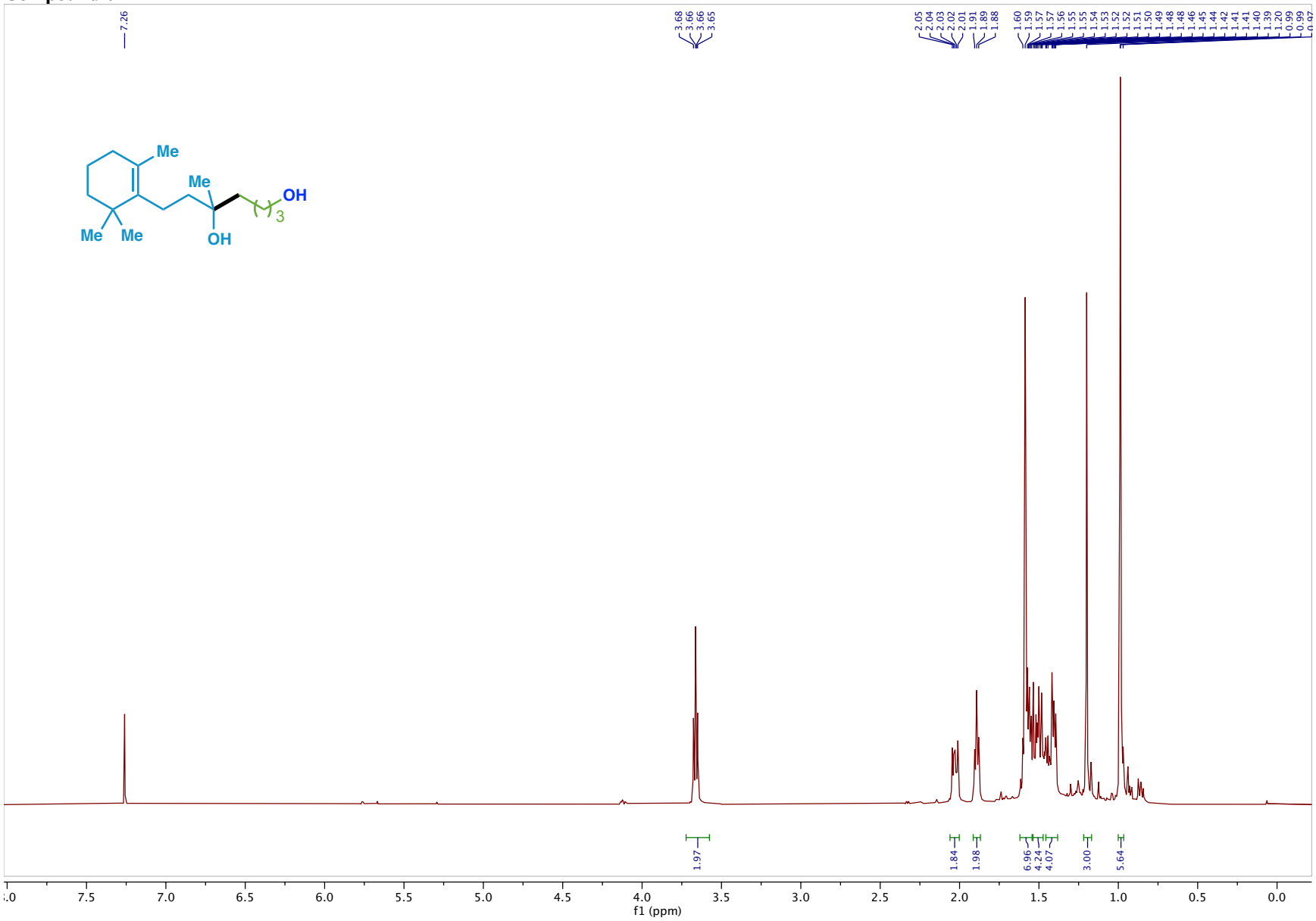
f1 (ppm)

Compound 6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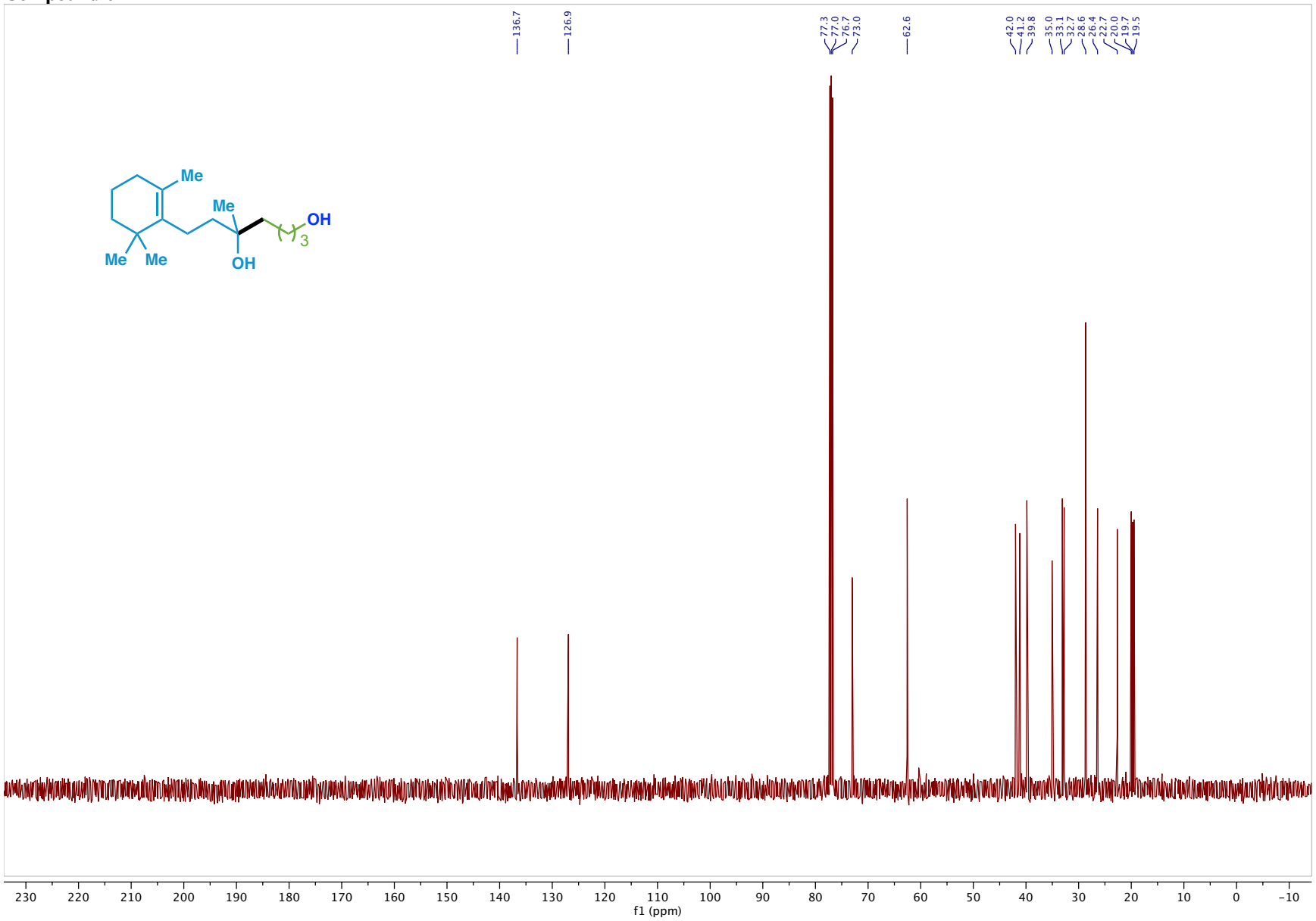
Compound 6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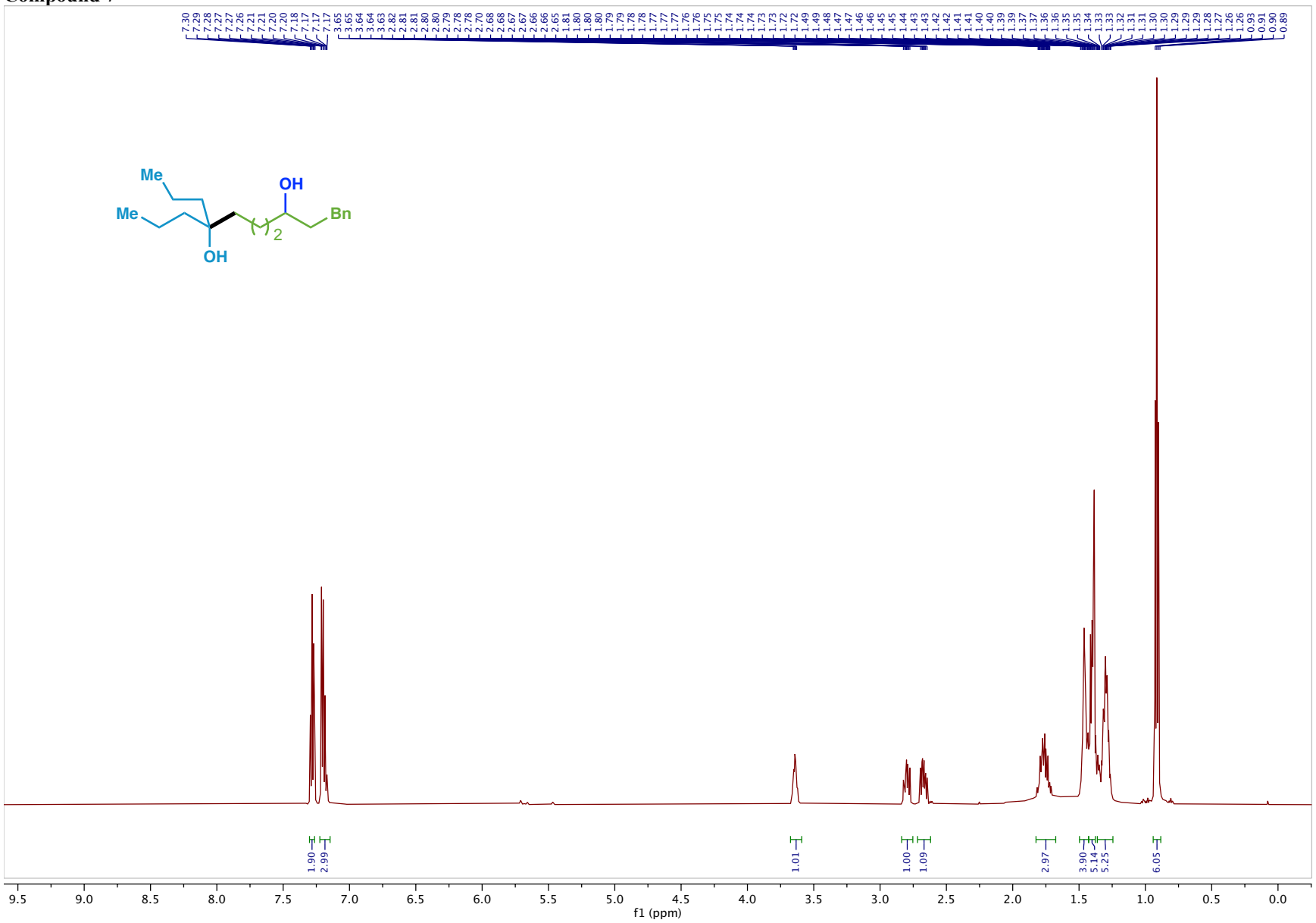

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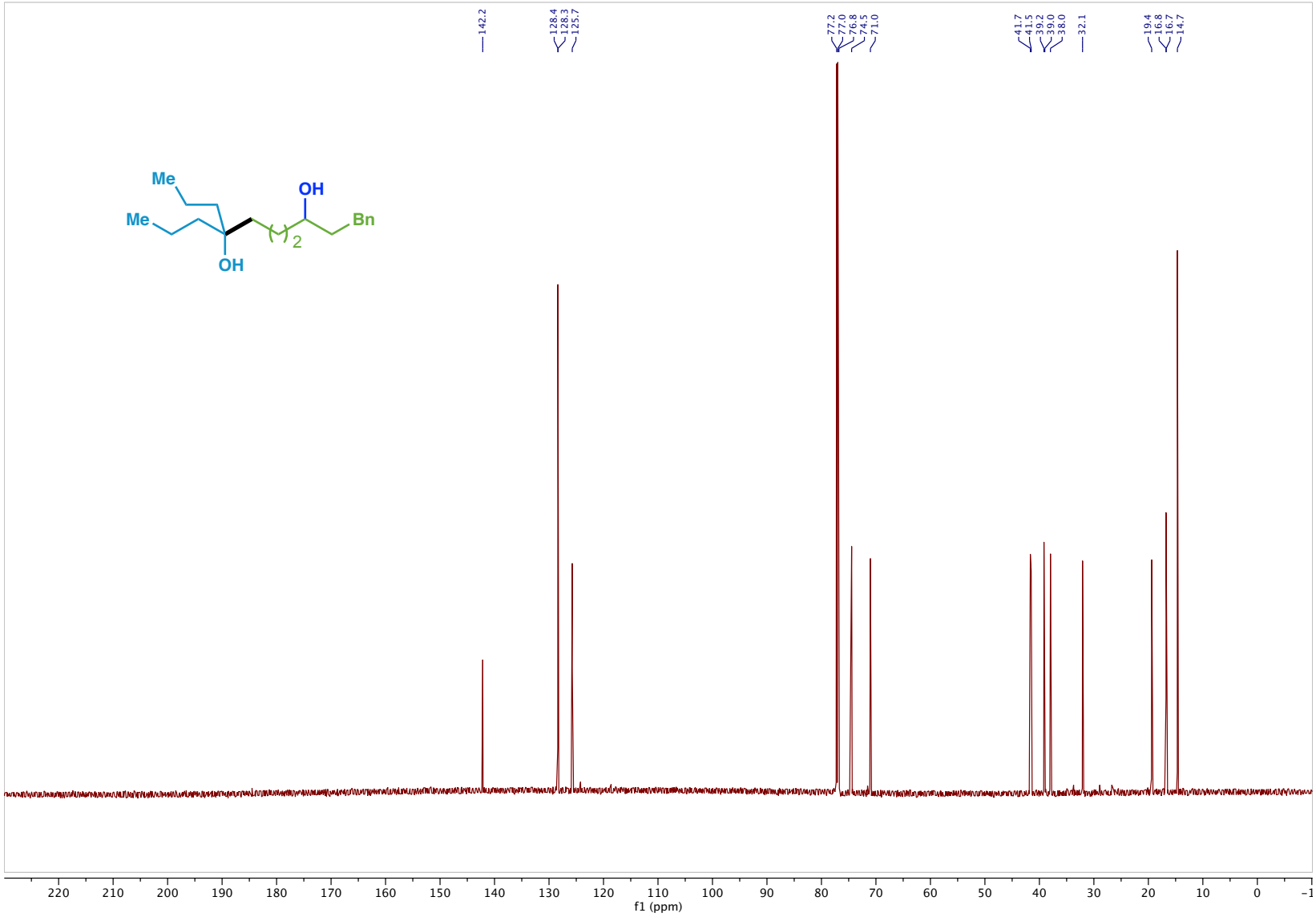
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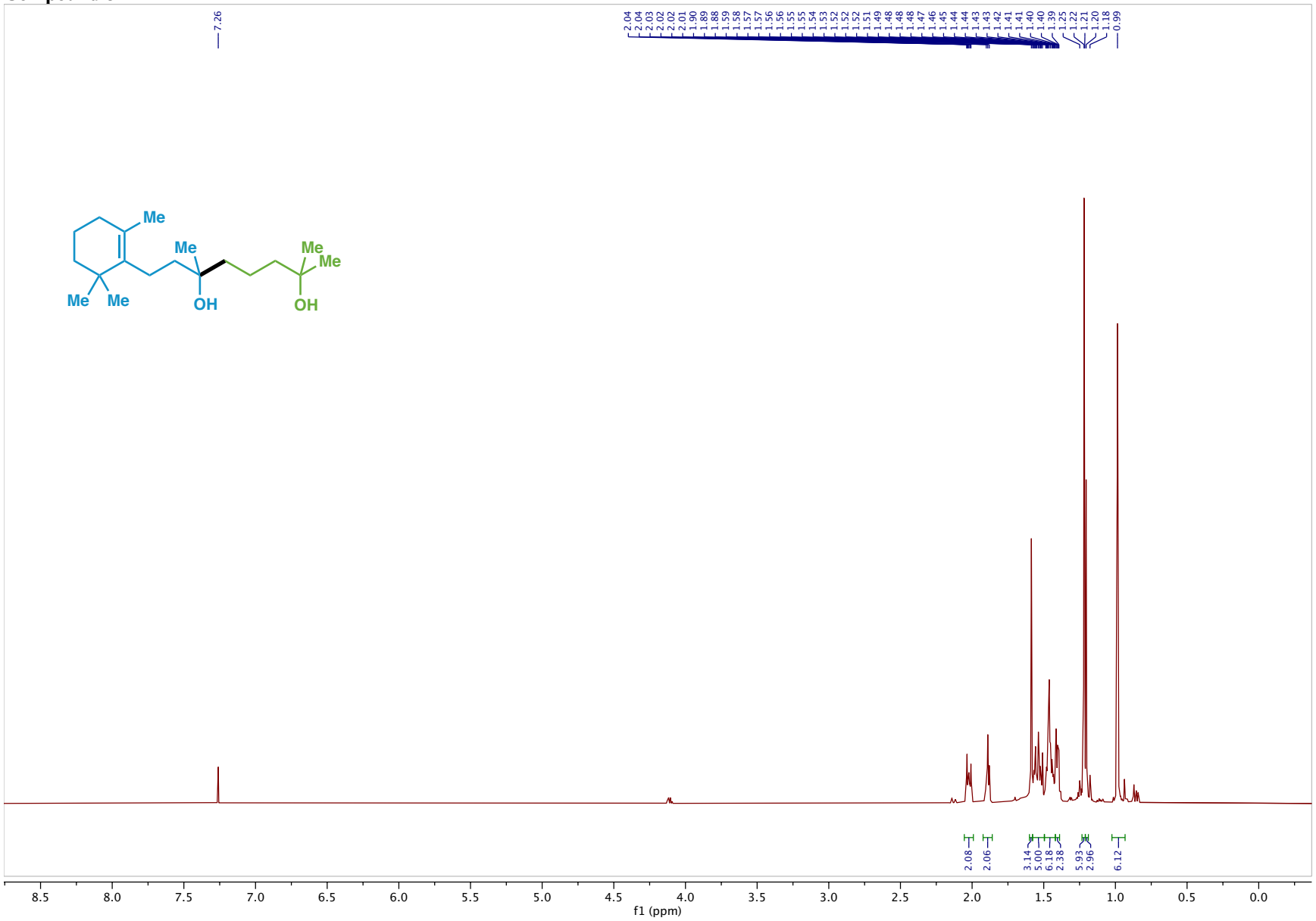
Compound 8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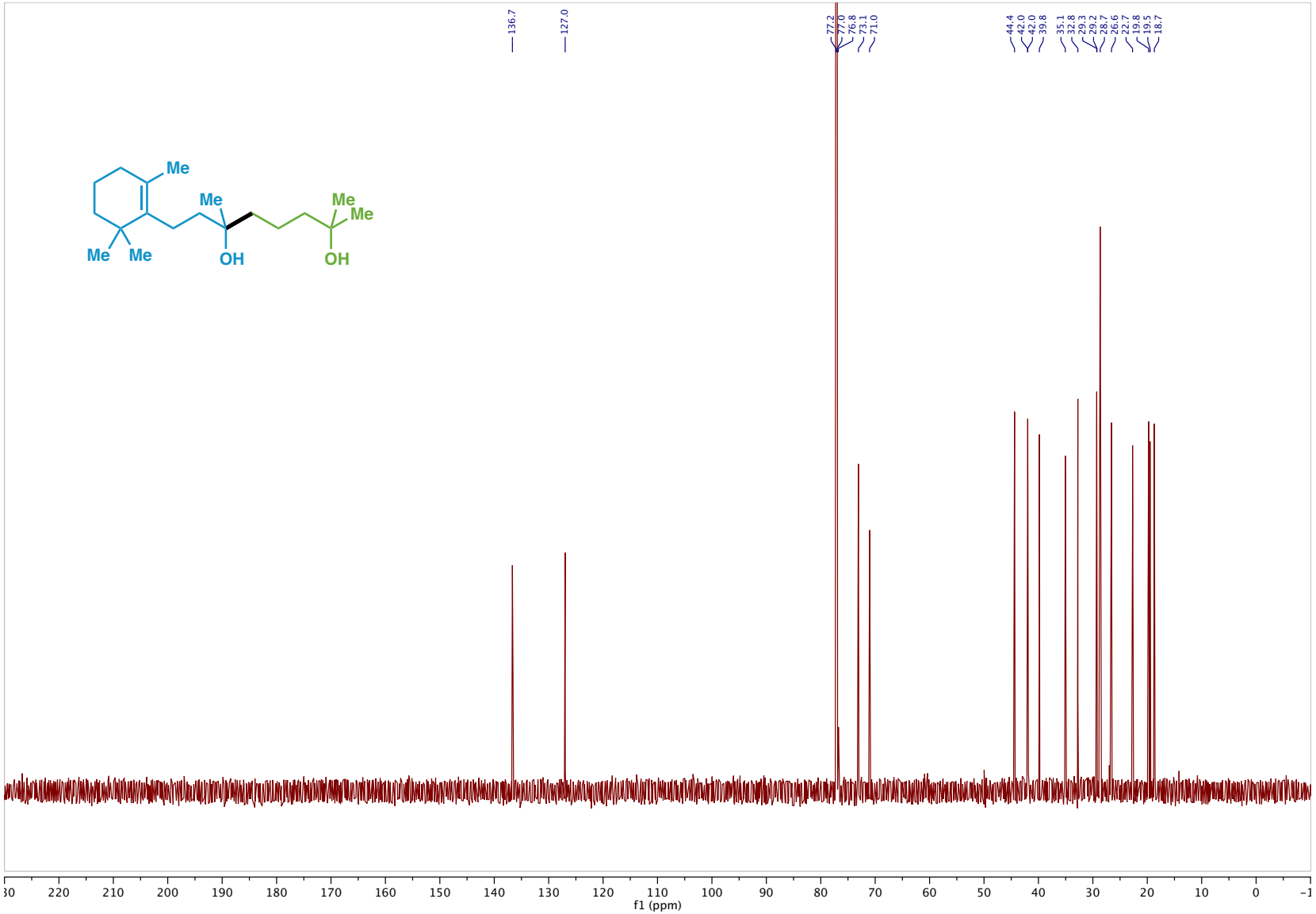
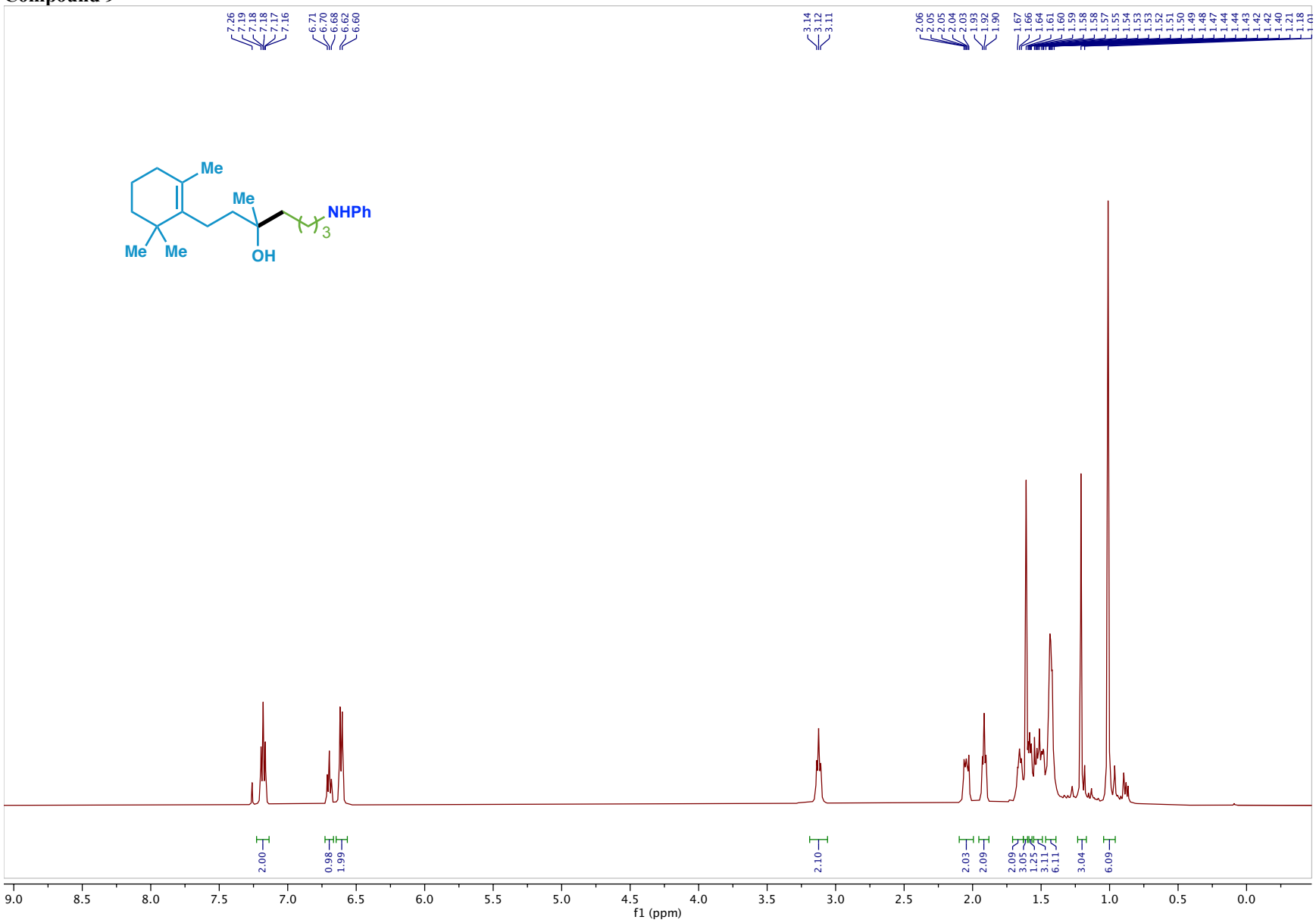
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

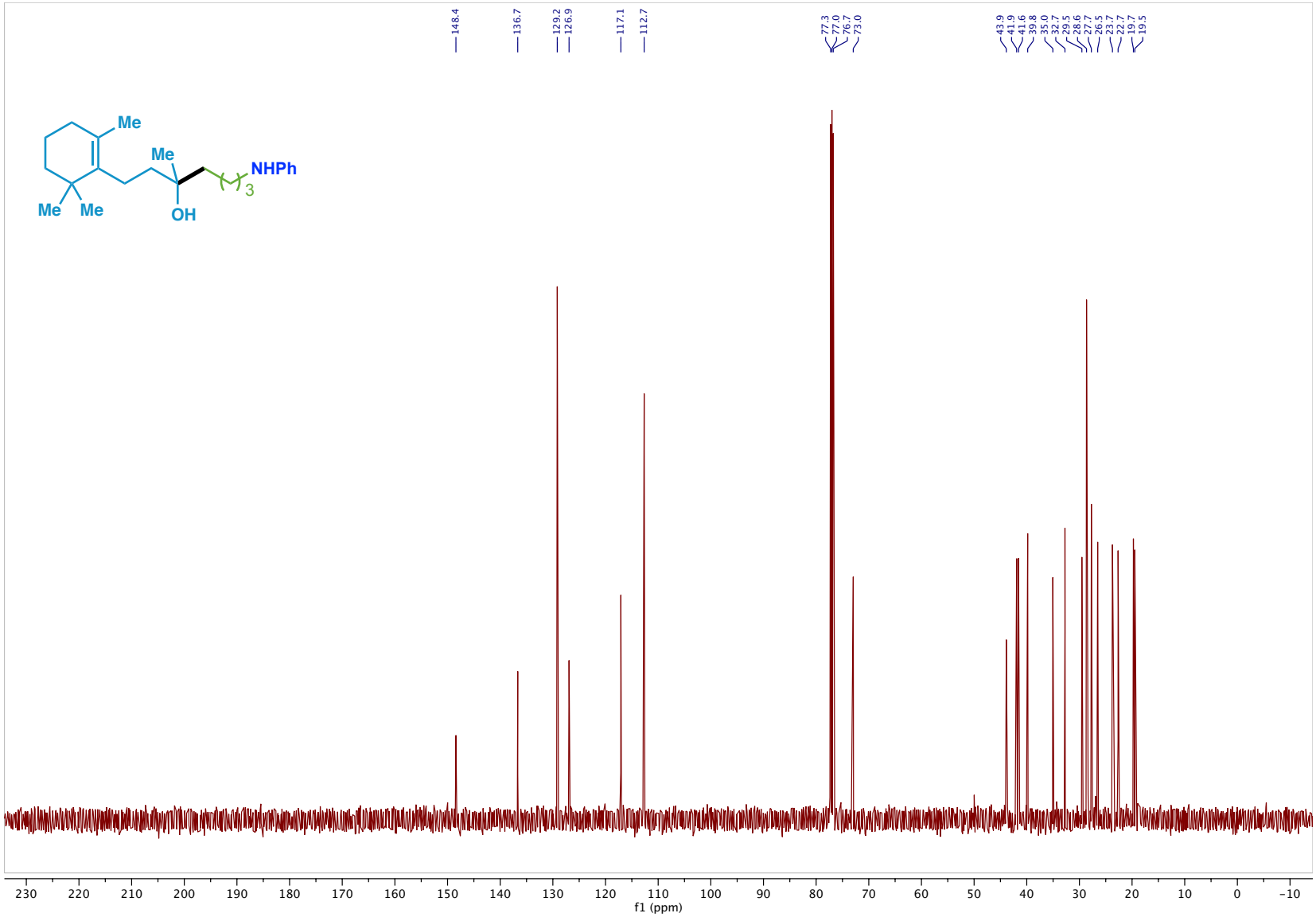
Compound 8


136.7
127.0
77.2
77.0
76.8
73.1
71.0
44.4
42.0
42.0
39.8
35.1
32.8
29.3
29.2
28.7
26.6
22.7
19.8
19.5
18.7
Me
Me
Me
Me
OH
Me
Me
OH
f1 (ppm)

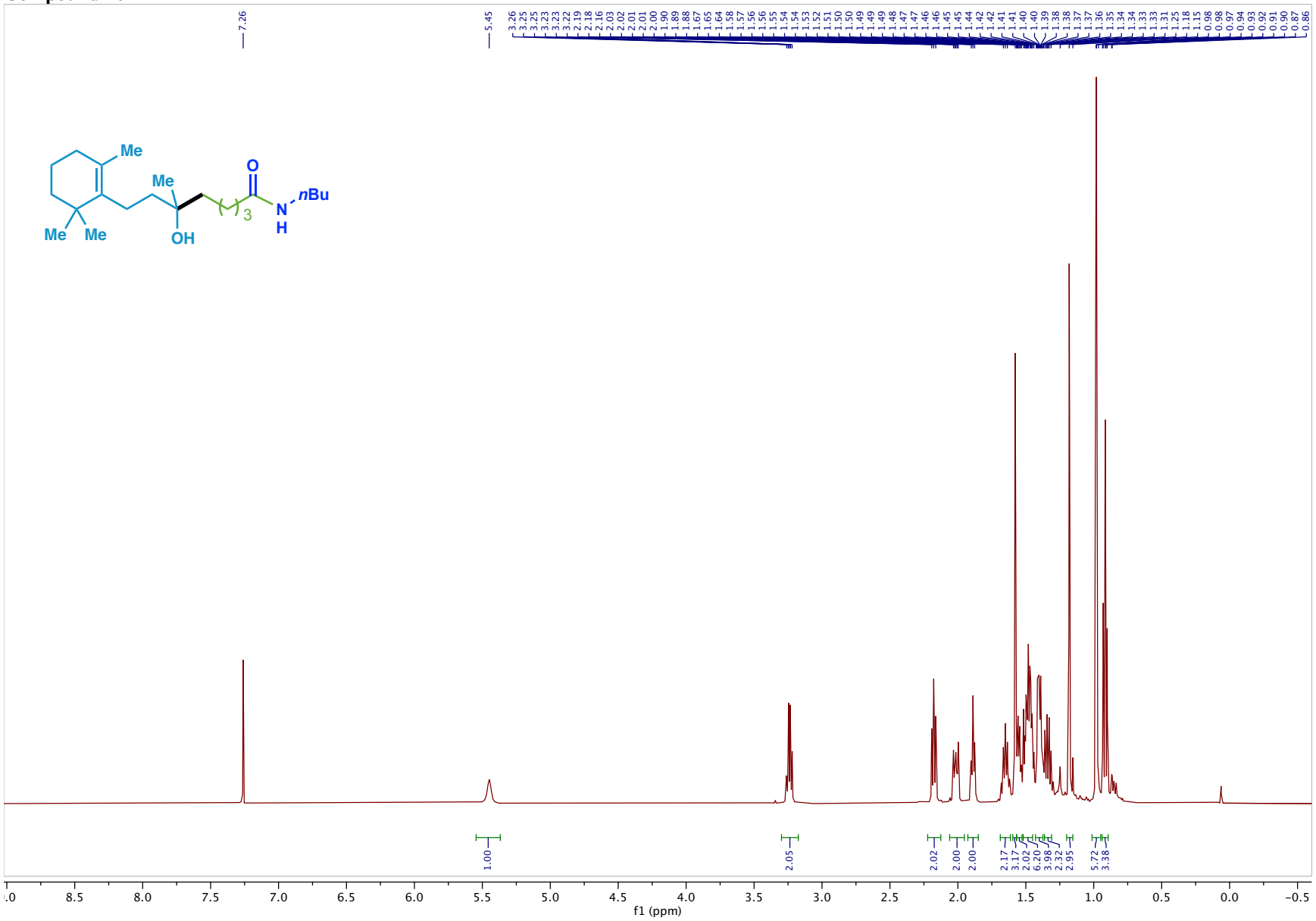
Compound 9


7.26
7.19
7.18
7.18
7.17
7.16
6.71
6.70
6.68
6.62
6.60
3.14
3.12
3.11
2.06
2.05
2.05
2.04
2.03
1.93
1.92
1.90
1.67
1.66
1.64
1.61
1.60
1.59
1.58
1.58
1.57
1.55
1.54
1.53
1.53
1.52
1.51
1.50
1.49
1.48
1.47
1.44
1.44
1.43
1.42
1.42
1.40
1.21
1.18
1.01
Me
Me
Me
Me
OH
NHPh
3
2.00
0.98
1.99
2.10
2.03
2.09
2.09
3.05
1.25
3.11
6.11
3.04
6.09
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
f1 (ppm)

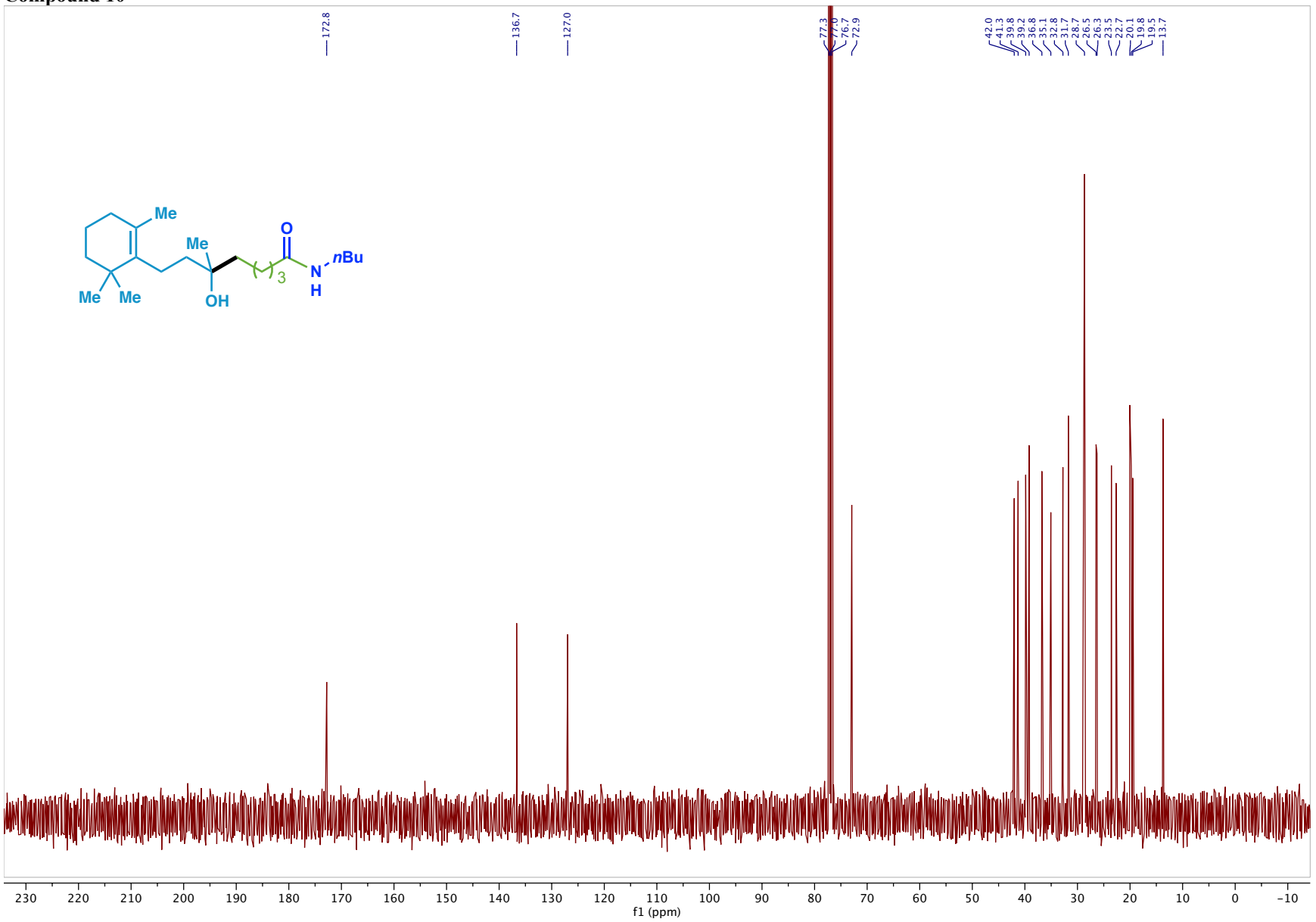
Compound 9


148.4
136.7
129.2
126.9
117.1
112.7
77.3
77.0
76.7
73.0
43.9
41.9
41.6
39.8
35.0
32.7
29.5
28.6
27.7
26.5
23.7
19.7
19.5
Me
Me
Me
Me
OH
NHPh
3
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

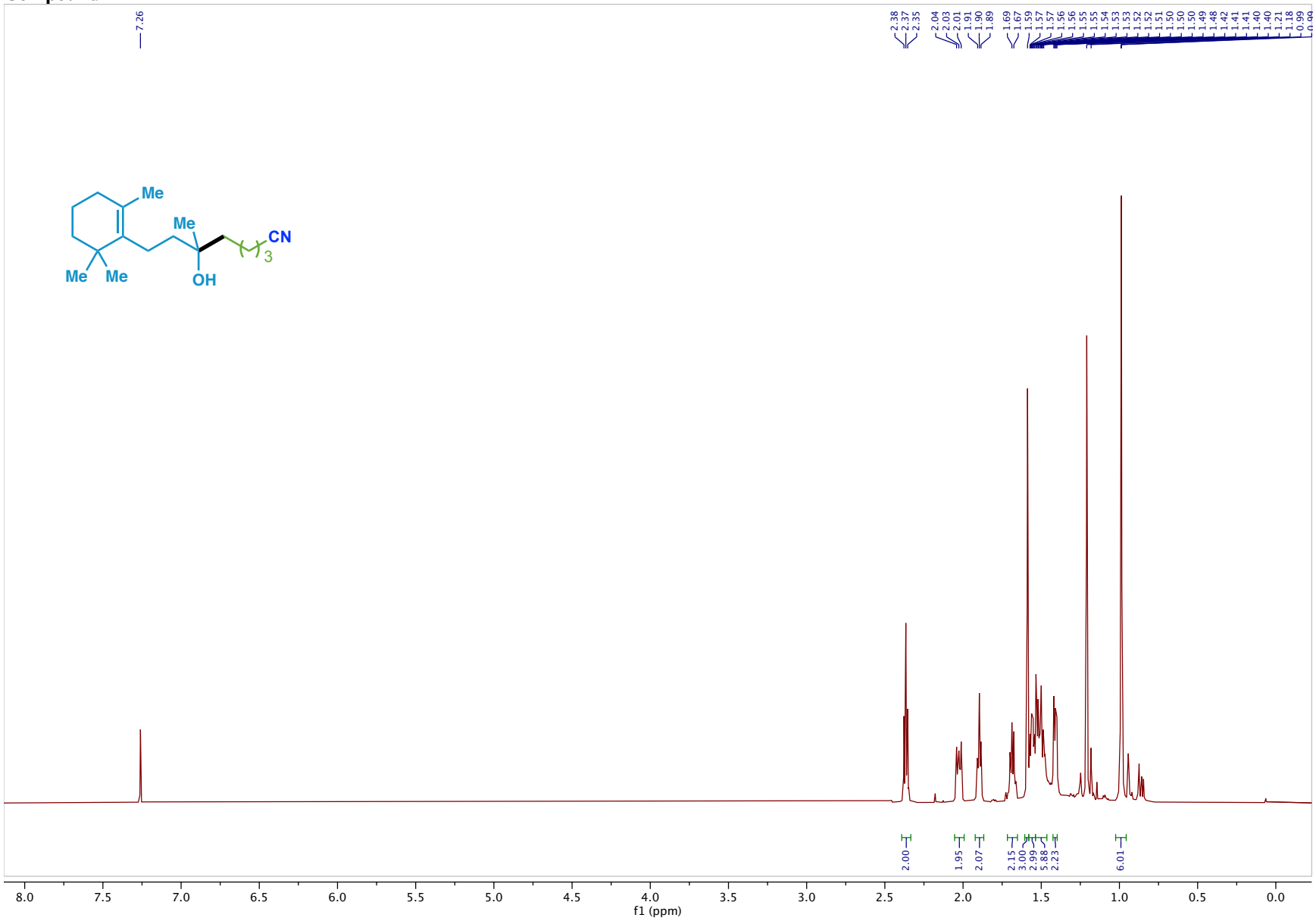
Compound 10


Me
Me
Me
Me
OH
O
3
N
H
nBu
7.26
5.45
1.00
2.05
2.02
2.00
2.00
2.17
3.17
2.02
6.20
3.98
2.32
2.95
5.72
3.38
f1 (ppm)

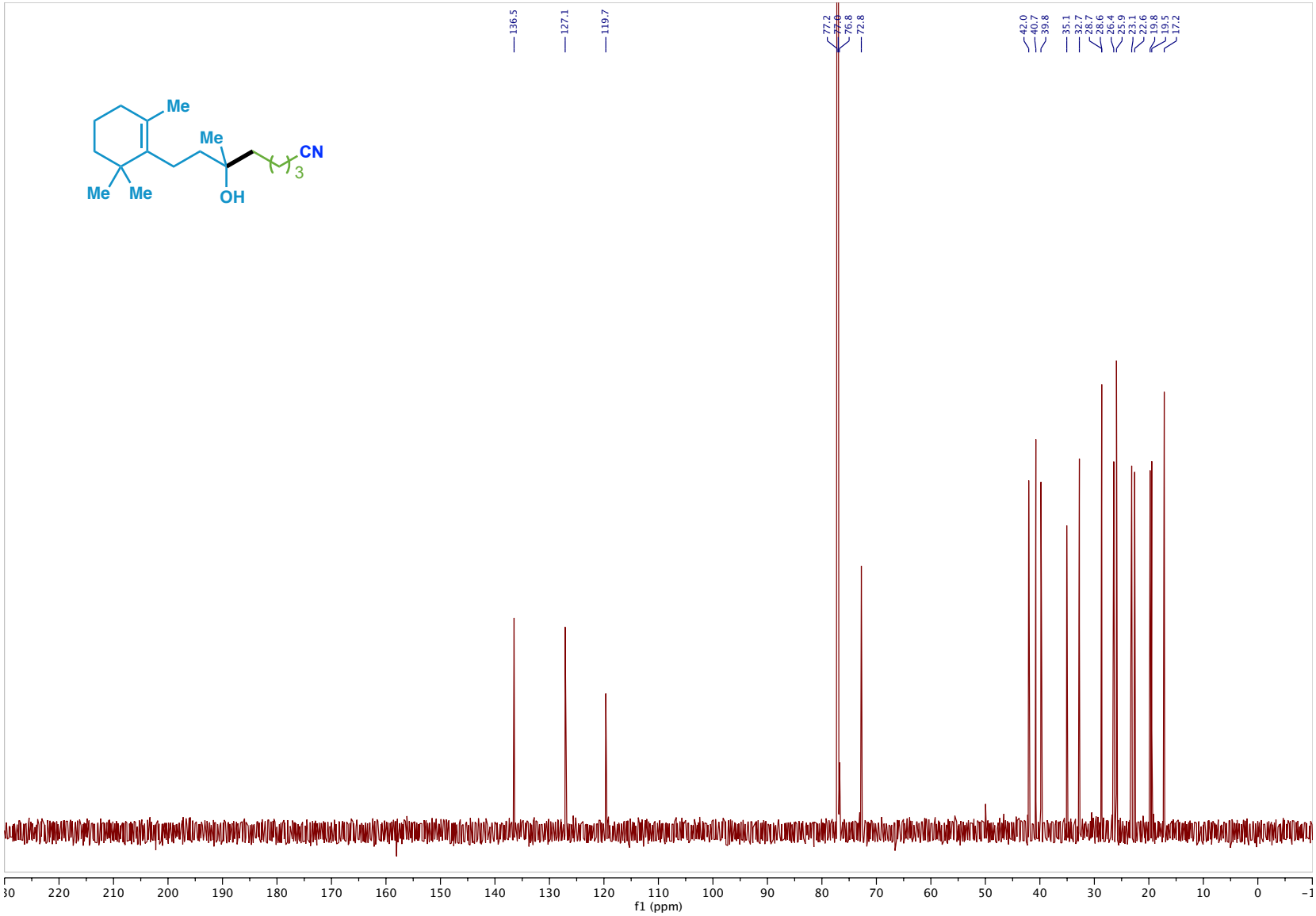
Compound 10


172.8
136.7
127.0
77.3
77.0
76.7
72.9
42.0
41.3
39.8
39.2
36.8
35.1
32.8
31.7
28.7
26.5
26.3
23.5
22.7
20.1
19.8
19.5
13.7
Me
Me
Me
Me
OH
O
3
N
H
nBu
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

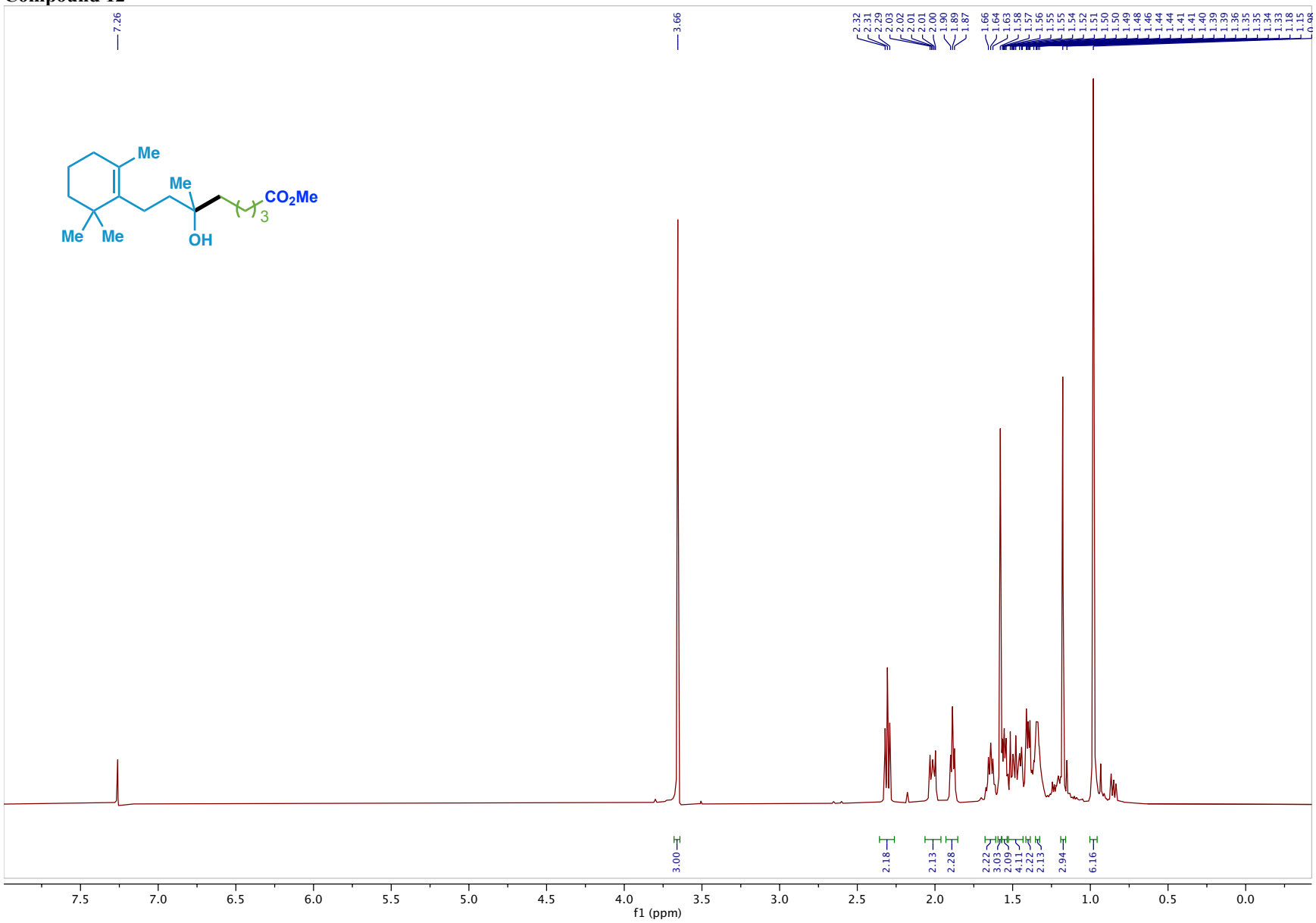
Compound 11


7.26
2.38
2.37
2.35
2.04
2.03
2.01
1.91
1.90
1.89
1.69
1.67
1.59
1.57
1.56
1.55
1.54
1.53
1.52
1.51
1.50
1.49
1.48
1.42
1.41
1.40
1.21
1.18
0.99
Me
Me
Me
Me
OH
CN
3
2.00
1.95
2.07
2.15
3.00
2.99
5.88
2.23
6.01
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
f1 (ppm)

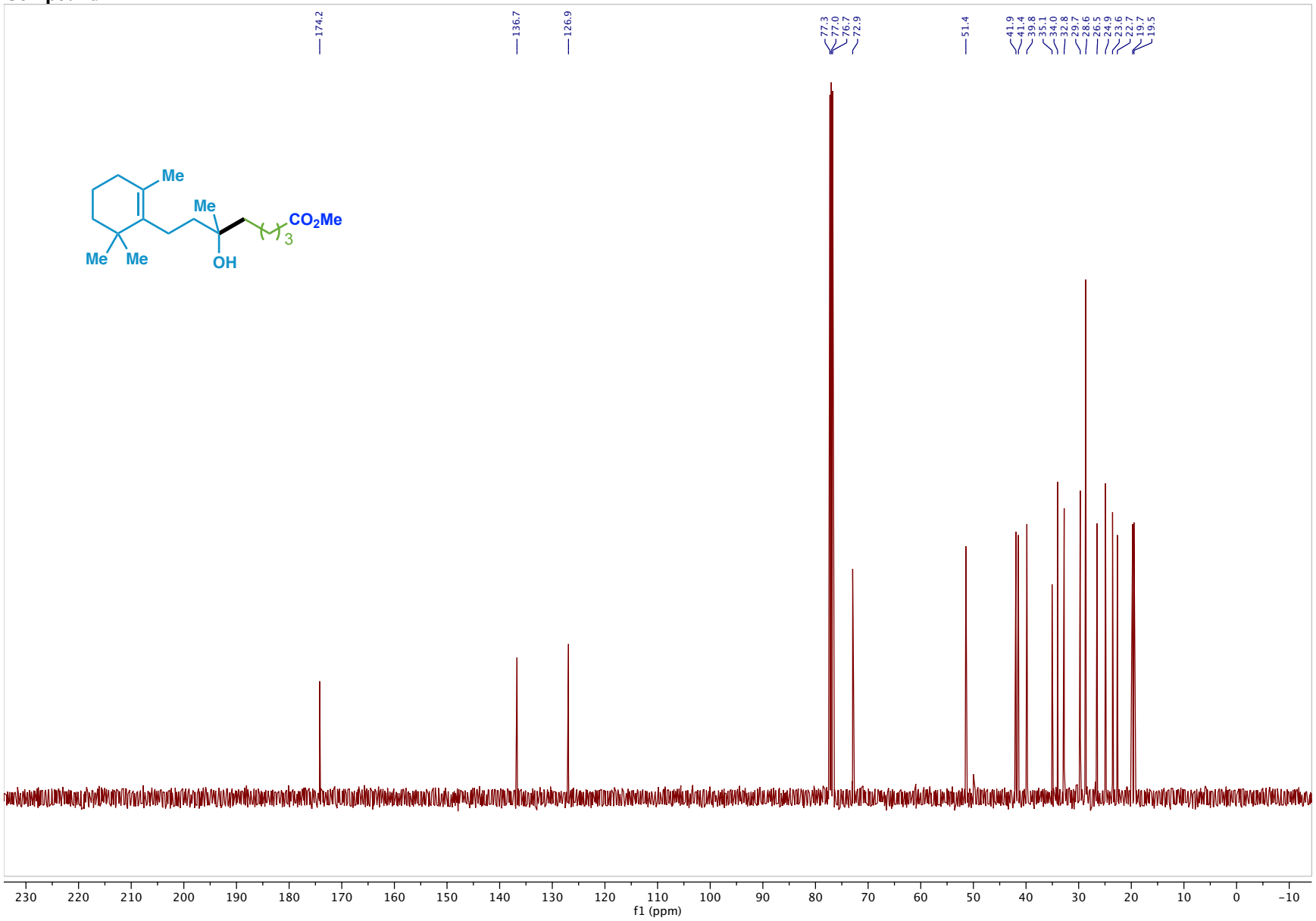
Compound 11


136.5
127.1
119.7
77.2
77.0
76.8
72.8
42.0
40.7
39.8
35.1
32.7
28.7
28.6
26.4
25.9
23.1
22.6
19.8
19.5
17.2
Me
Me
Me
Me
OH
CN
3
f1 (ppm)

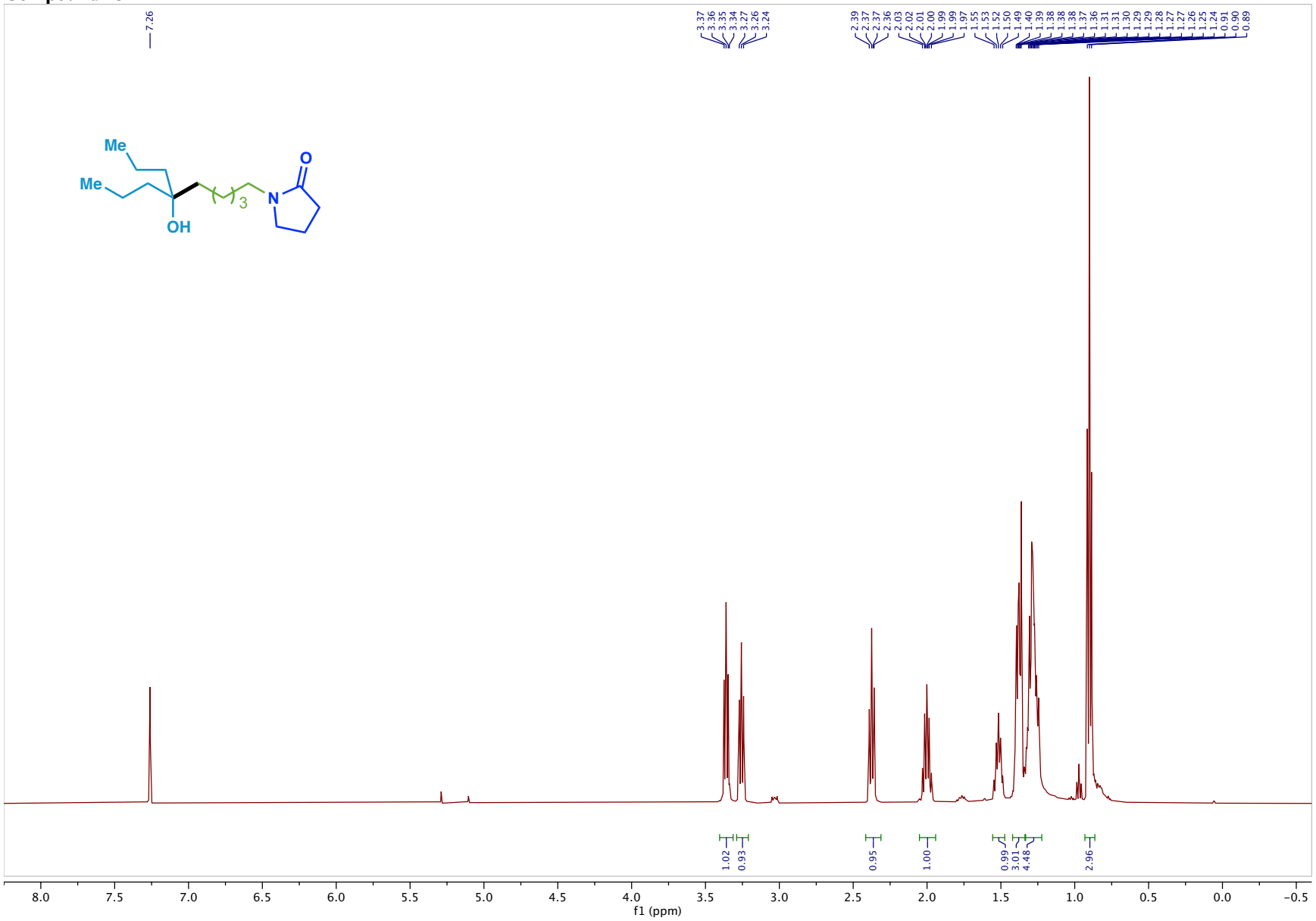
Compound 12


7.26
3.66
2.32
2.31
2.29
2.03
2.02
2.01
2.01
2.00
1.90
1.89
1.87
1.66
1.64
1.63
1.58
1.57
1.56
1.55
1.55
1.54
1.52
1.51
1.50
1.50
1.49
1.48
1.46
1.44
1.44
1.41
1.41
1.40
1.39
1.39
1.36
1.35
1.35
1.34
1.33
1.18
1.15
Me
Me
Me
Me
OH
CO2Me
3
3.00
2.18
2.13
2.28
2.22
3.03
2.09
4.11
2.22
2.13
2.94
6.16
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
f1 (ppm)

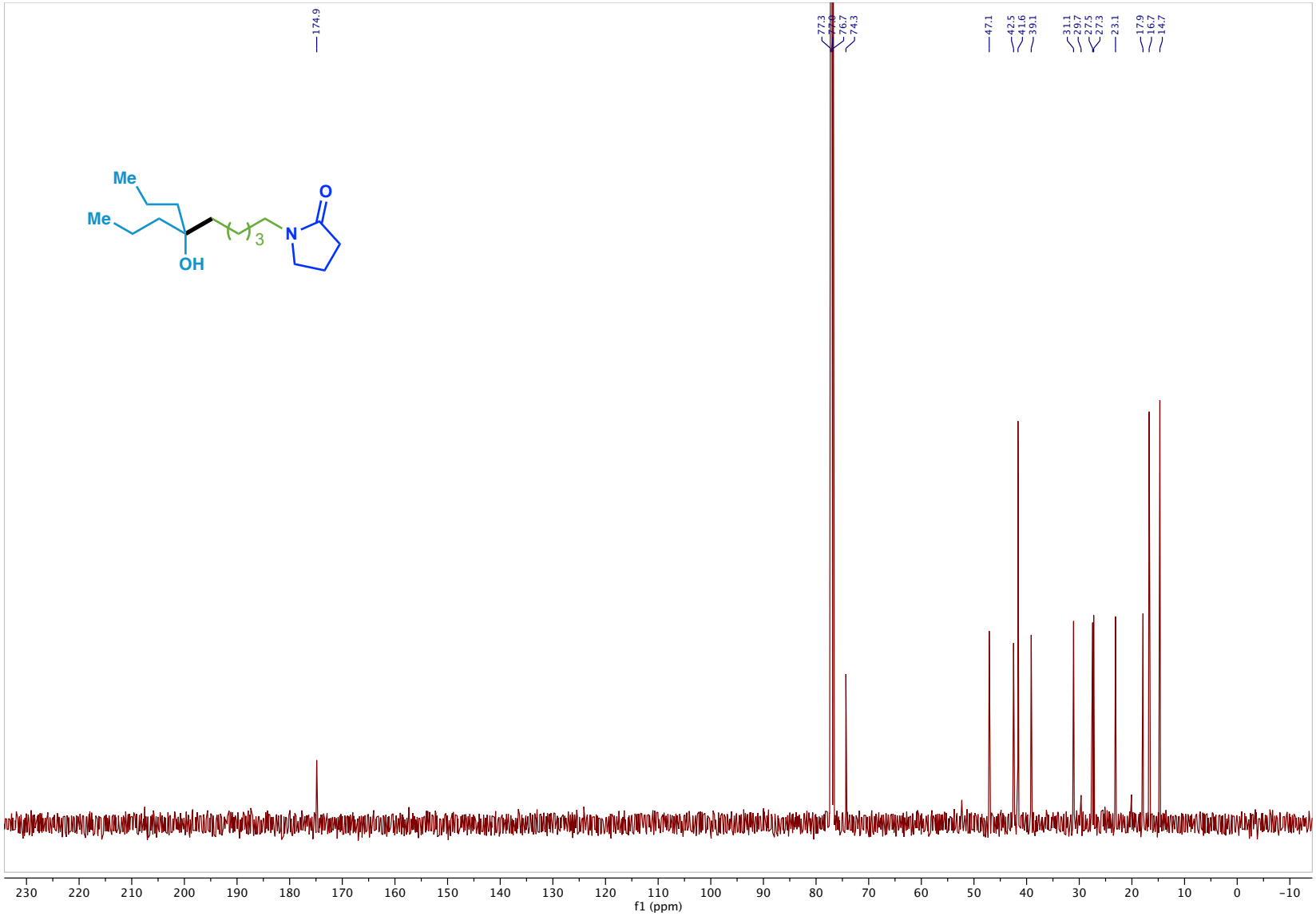
Compound 12


174.2
136.7
126.9
77.3
77.0
76.7
72.9
51.4
41.9
41.4
39.8
35.1
34.0
32.8
29.7
28.6
26.5
24.9
23.6
22.7
19.7
19.5
Me
Me
Me
Me
OH
CO2Me
3
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

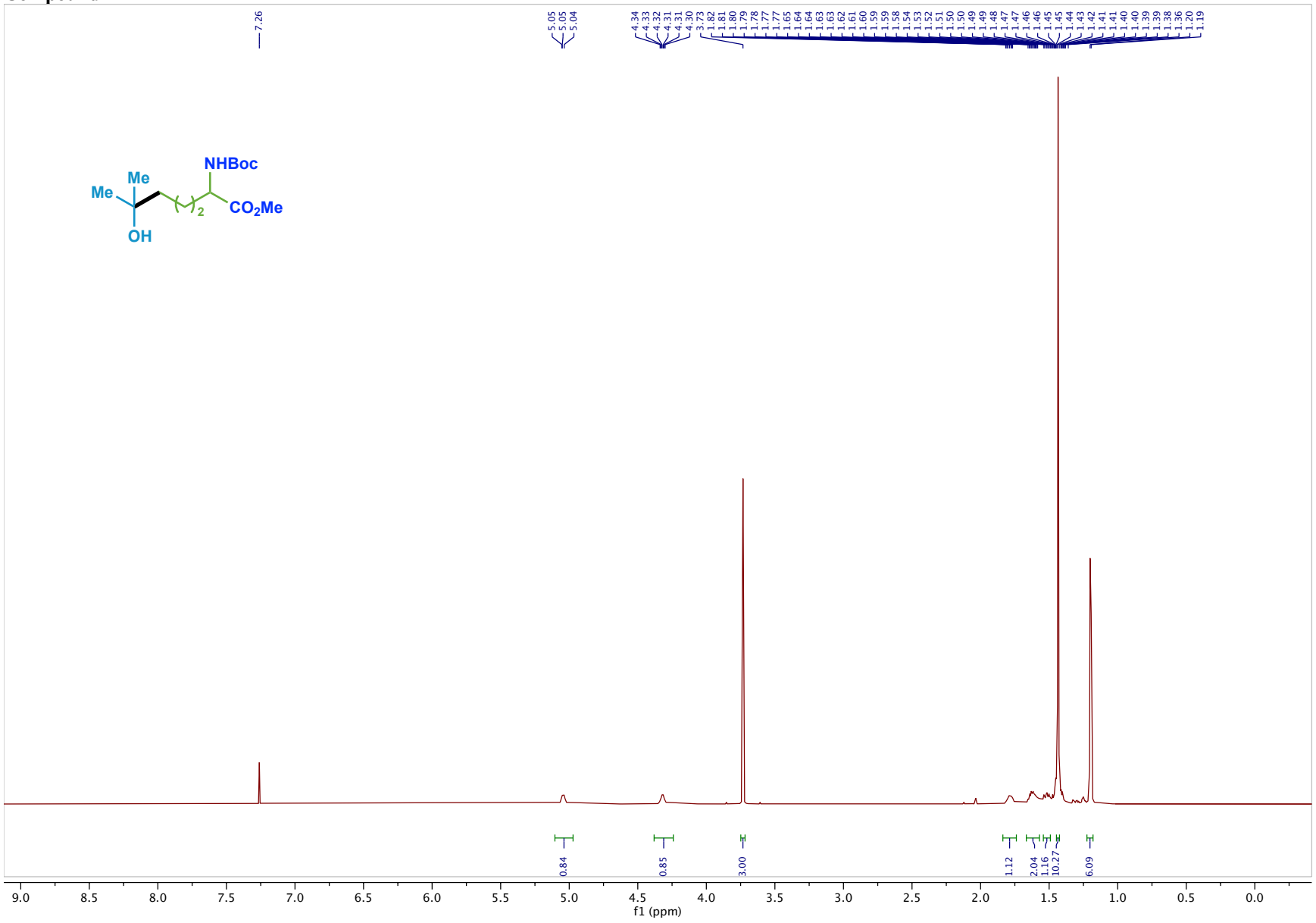
Compound 13


7.26
3.37
3.36
3.35
3.34
3.27
3.26
3.24
2.39
2.37
2.37
2.37
2.36
2.03
2.02
2.01
2.00
1.99
1.99
1.97
1.55
1.53
1.52
1.50
1.49
1.40
1.39
1.38
1.38
1.38
1.37
1.36
1.31
1.31
1.30
1.29
1.29
1.28
1.27
1.27
1.26
1.25
1.24
0.91
0.90
0.89
Me
Me
OH
3
N
O
1.02
0.93
0.95
1.00
0.99
3.01
4.48
2.96
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
f1 (ppm)

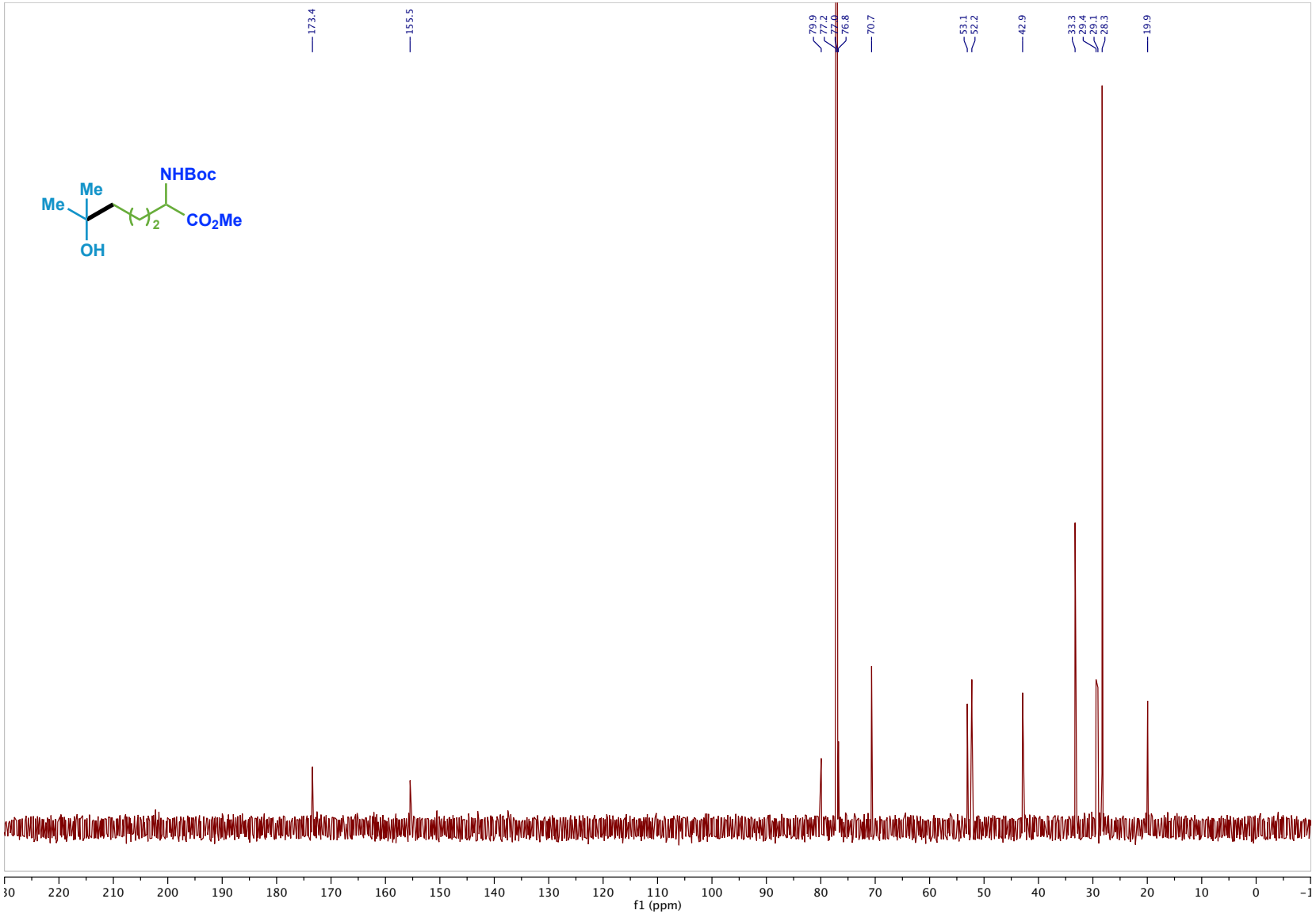
Compound 13


174.9
77.3
77.0
76.7
74.3
47.1
42.5
41.6
39.1
31.1
29.7
27.5
27.3
23.1
17.9
16.7
14.7
Me
Me
OH
3
N
O
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

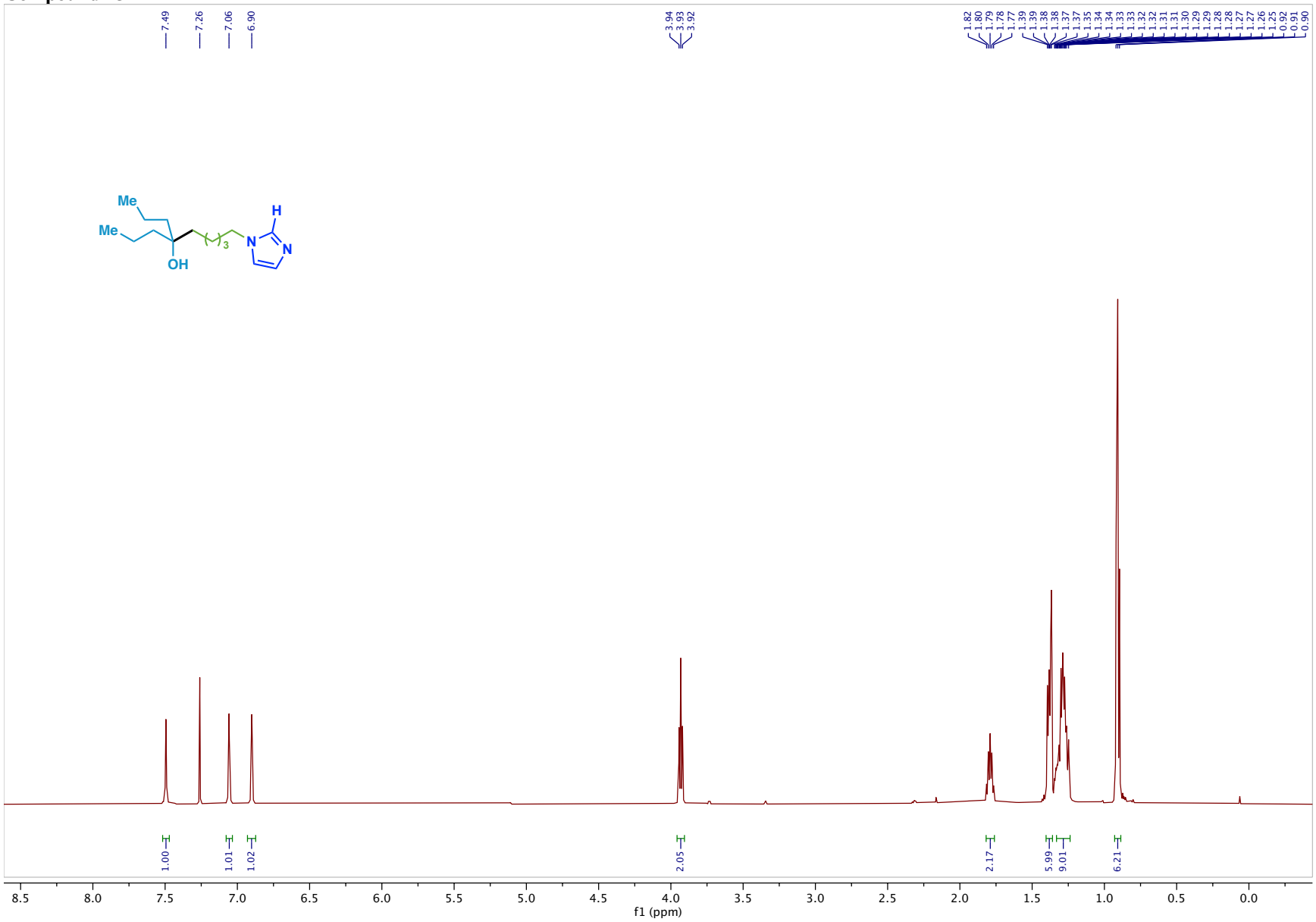
Compound 14


7.26
5.05
5.05
5.04
4.34
4.33
4.32
4.31
4.31
4.30
3.73
1.82
1.81
1.80
1.79
1.78
1.77
1.77
1.65
1.64
1.64
1.63
1.63
1.62
1.61
1.60
1.59
1.59
1.58
1.54
1.53
1.52
1.51
1.50
1.50
1.49
1.49
1.48
1.47
1.47
1.46
1.46
1.45
1.45
1.44
1.43
1.42
1.41
1.41
1.40
1.40
1.39
1.39
1.38
1.36
1.20
1.19
NHBoc
Me
Me
OH
2
CO2Me
0.84
0.85
3.00
1.12
2.04
1.16
10.27
6.09
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
f1 (ppm)

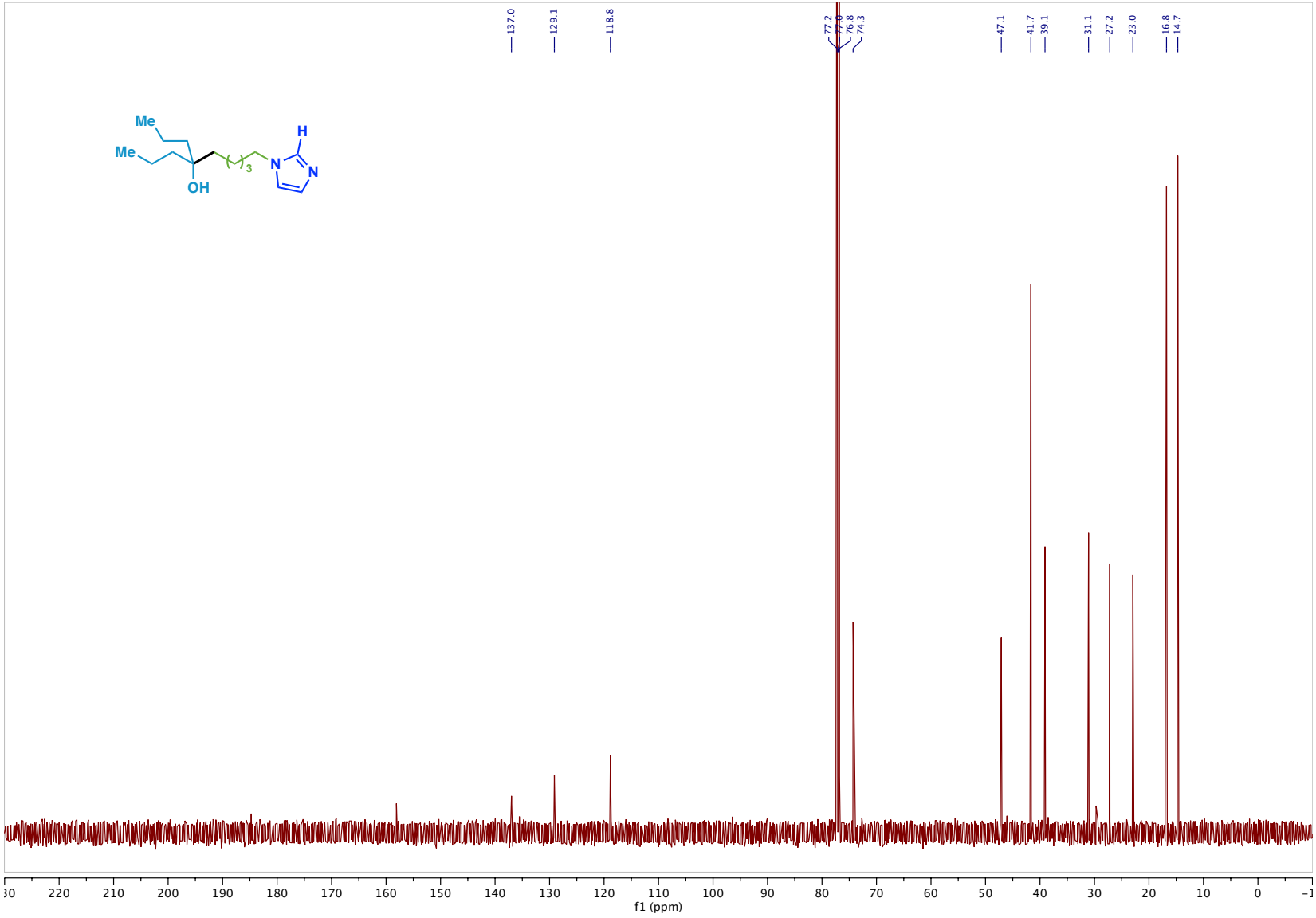
Compound 14


173.4
155.5
79.9
77.2
77.0
76.8
70.7
53.1
52.2
42.9
33.3
29.4
29.1
28.3
19.9
NHBoc
Me
Me
OH
CO2Me
2
f1 (ppm)

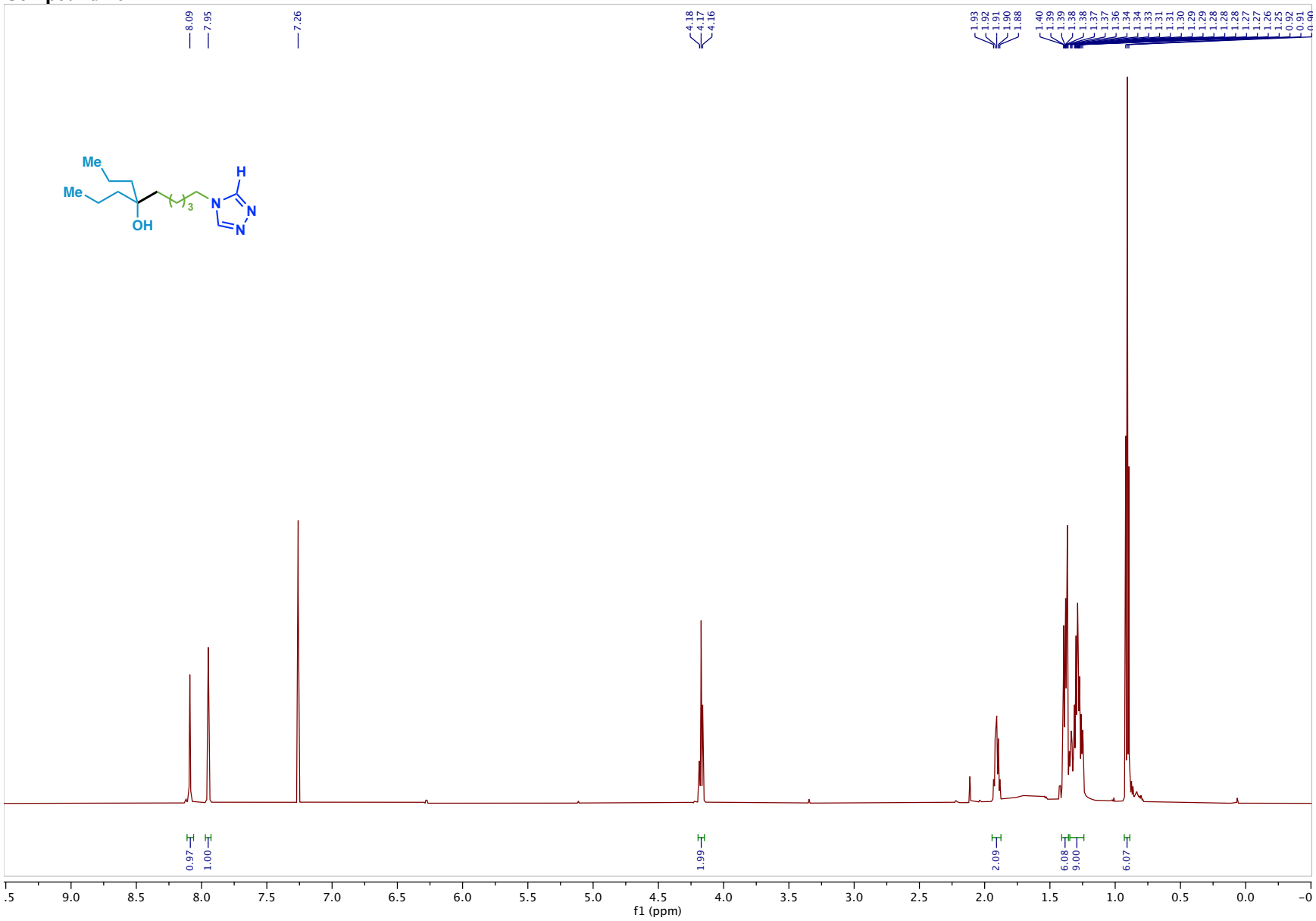
Compound 15


7.49
7.26
7.06
6.90
3.94
3.93
3.92
1.82
1.80
1.79
1.78
1.77
1.39
1.38
1.38
1.37
1.37
1.35
1.34
1.34
1.33
1.33
1.32
1.32
1.31
1.31
1.30
1.29
1.29
1.28
1.28
1.27
1.27
1.26
1.25
0.92
0.91
0.90
Me
Me
OH
3
N
H
N
1.00
1.01
1.02
2.05
2.17
5.99
9.01
6.21
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
f1 (ppm)

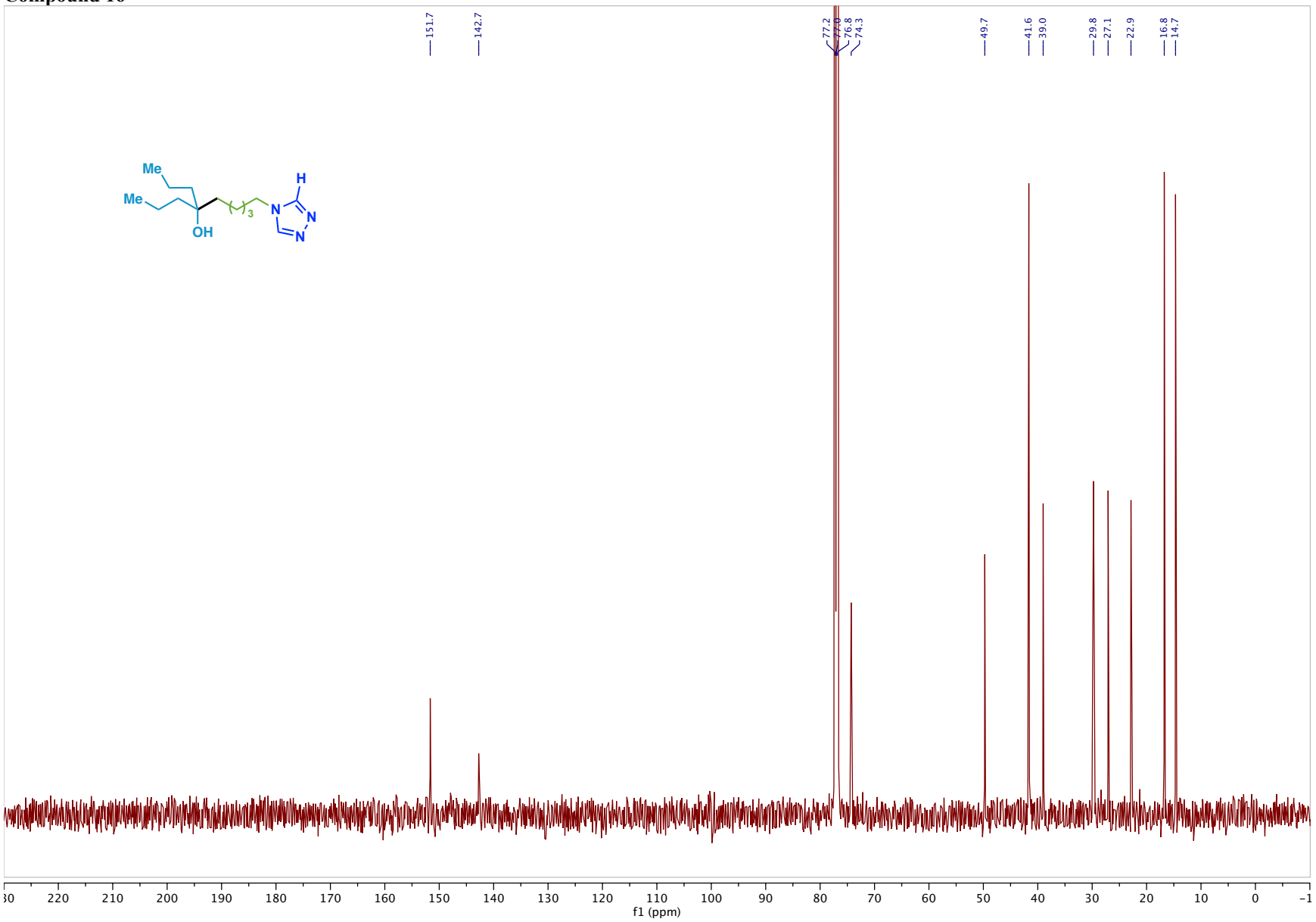
Compound 15


137.0
129.1
118.8
77.2
77.0
76.8
74.3
47.1
41.7
39.1
31.1
27.2
23.0
16.8
14.7
Me
Me
OH
3
N
H
N
f1 (ppm)

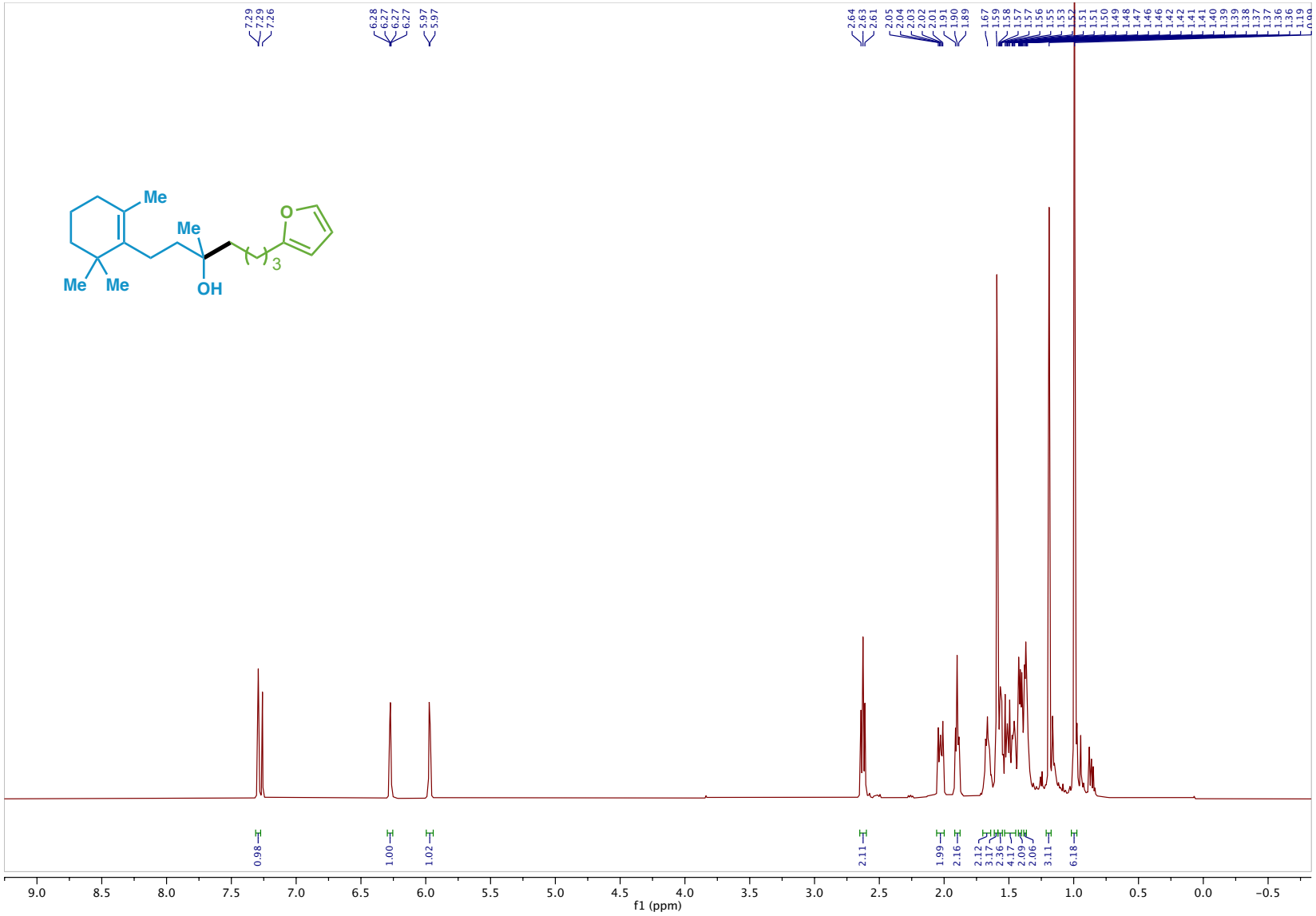
Compound 16


8.09
7.95
7.26
4.18
4.17
4.16
1.93
1.92
1.91
1.90
1.88
1.40
1.39
1.39
1.38
1.38
1.37
1.37
1.36
1.34
1.34
1.33
1.31
1.31
1.30
1.29
1.29
1.28
1.28
1.27
1.27
1.26
1.25
0.92
0.91
Me
Me
OH
H
N
N
N
3
0.97
1.00
1.99
2.09
6.08
9.00
6.07
f1 (ppm)

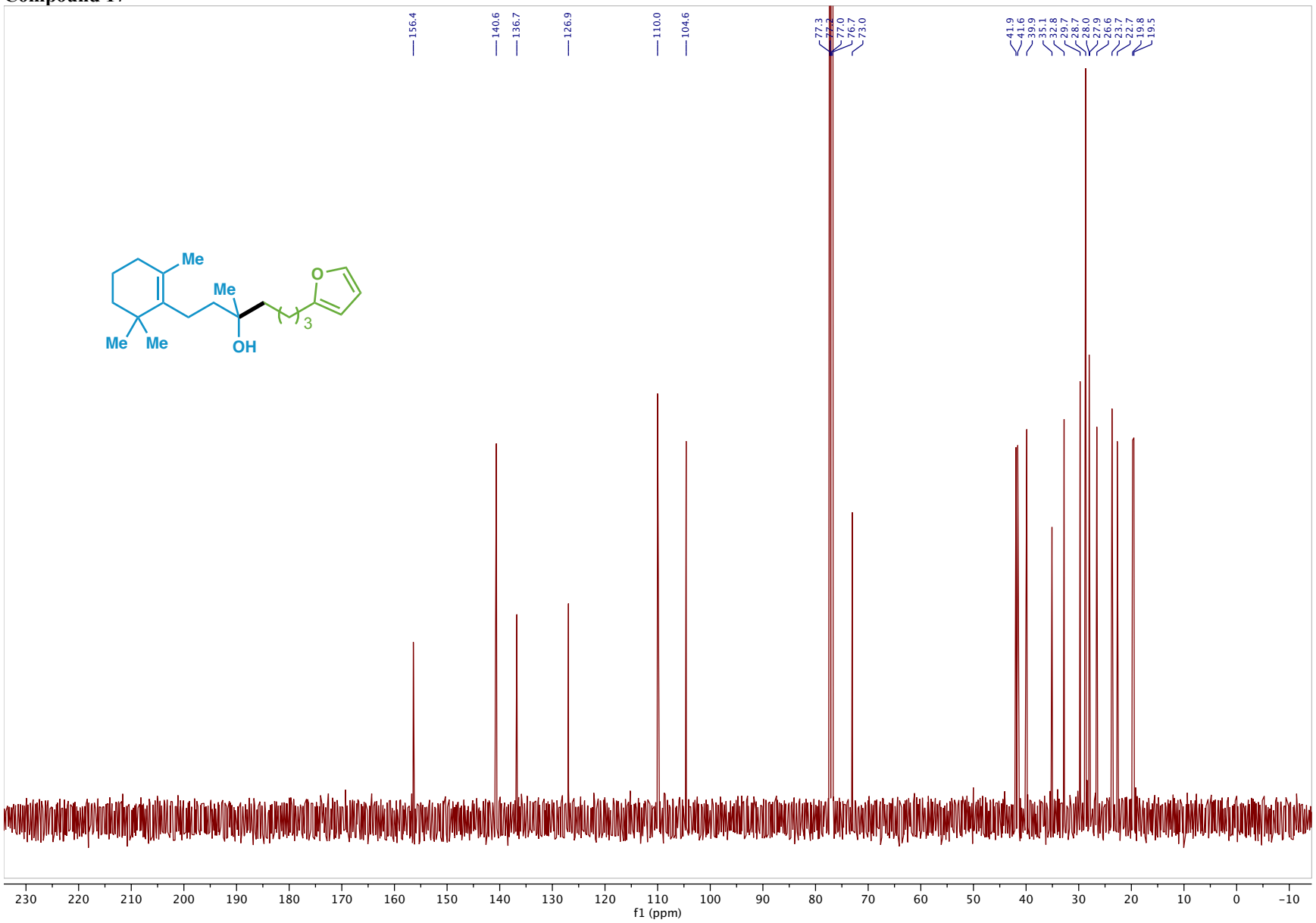
Compound 16


151.7
142.7
77.2
77.0
76.8
74.3
49.7
41.6
39.0
29.8
27.1
22.9
16.8
14.7
Me
Me
OH
3
N
H
N
N
f1 (ppm)

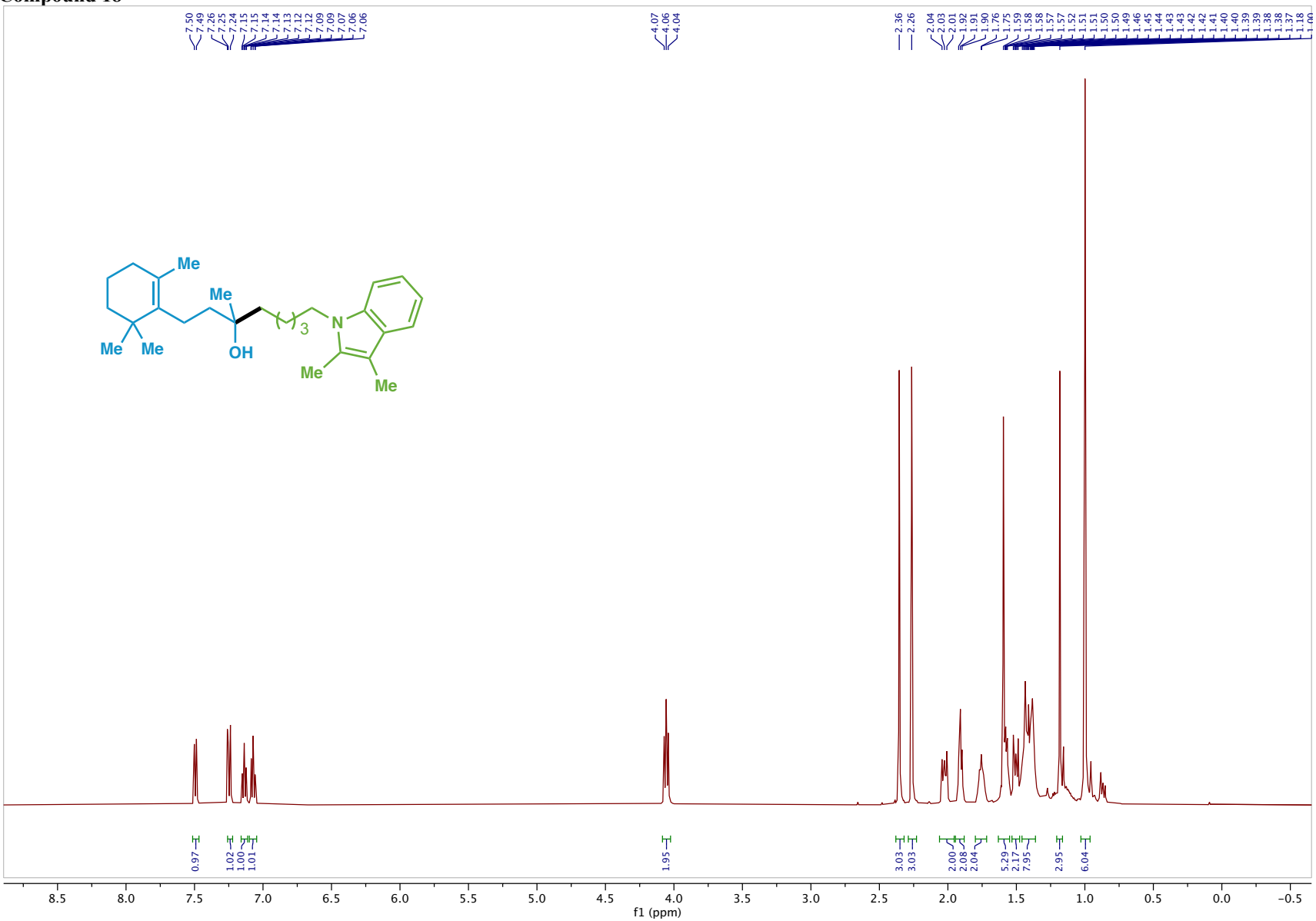
Compound 17



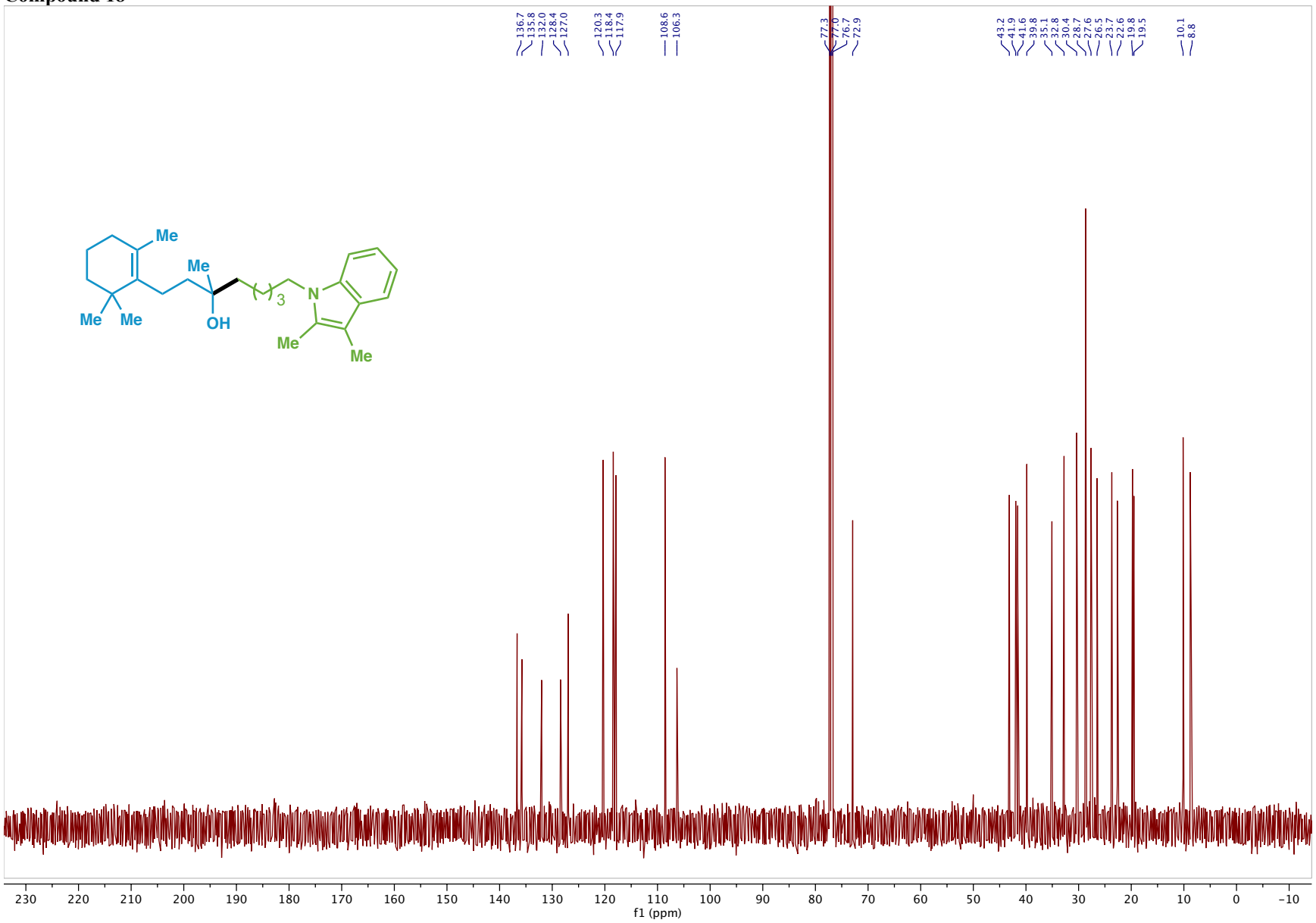
Compound 17


156.4
140.6
136.7
126.9
110.0
104.6
77.3
77.2
77.0
76.7
73.0
41.9
41.6
39.9
35.1
32.8
29.7
28.7
28.0
27.9
26.6
23.7
22.7
19.8
19.5
Me
Me
Me
Me
OH
O
3
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

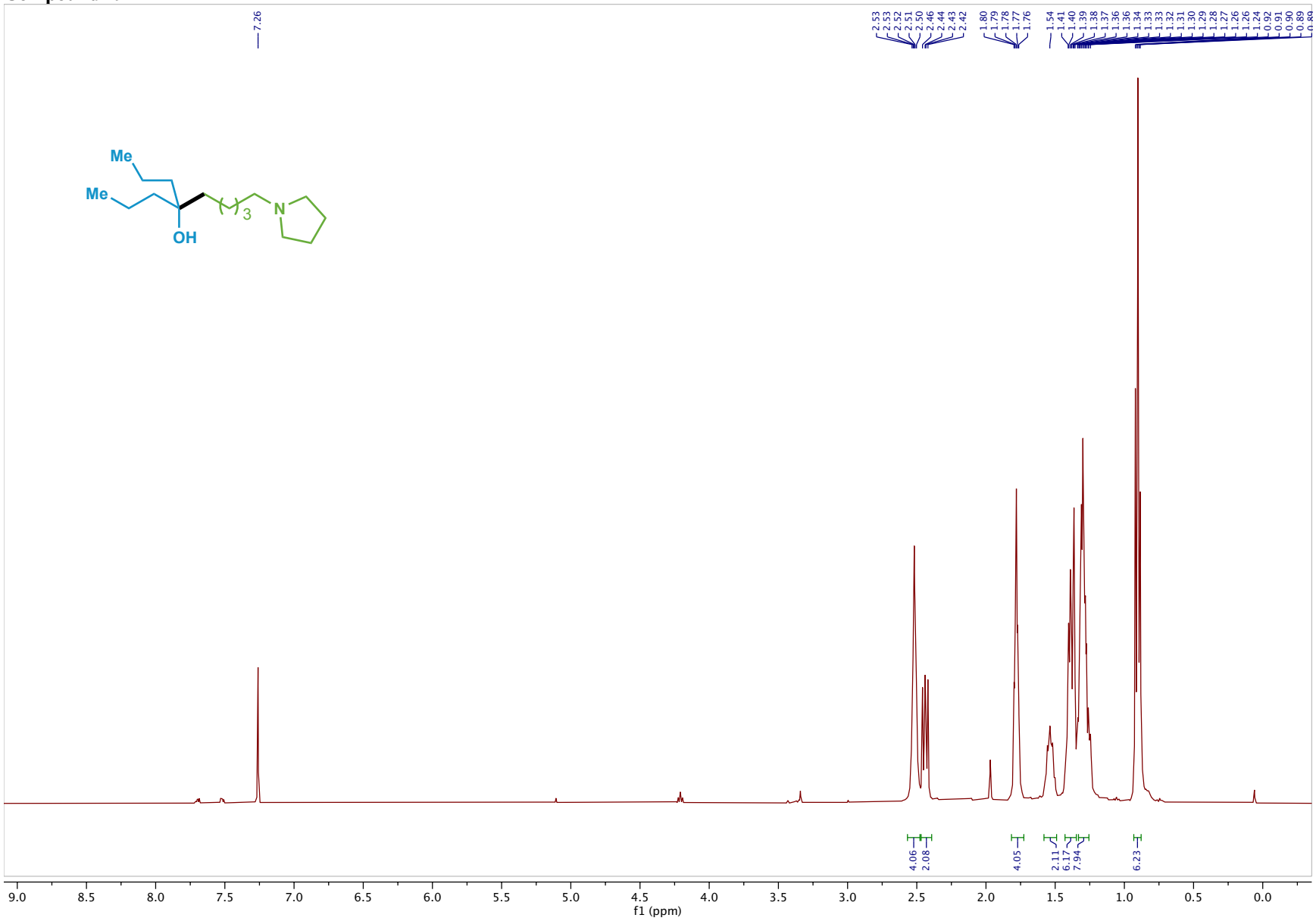
Compound 18



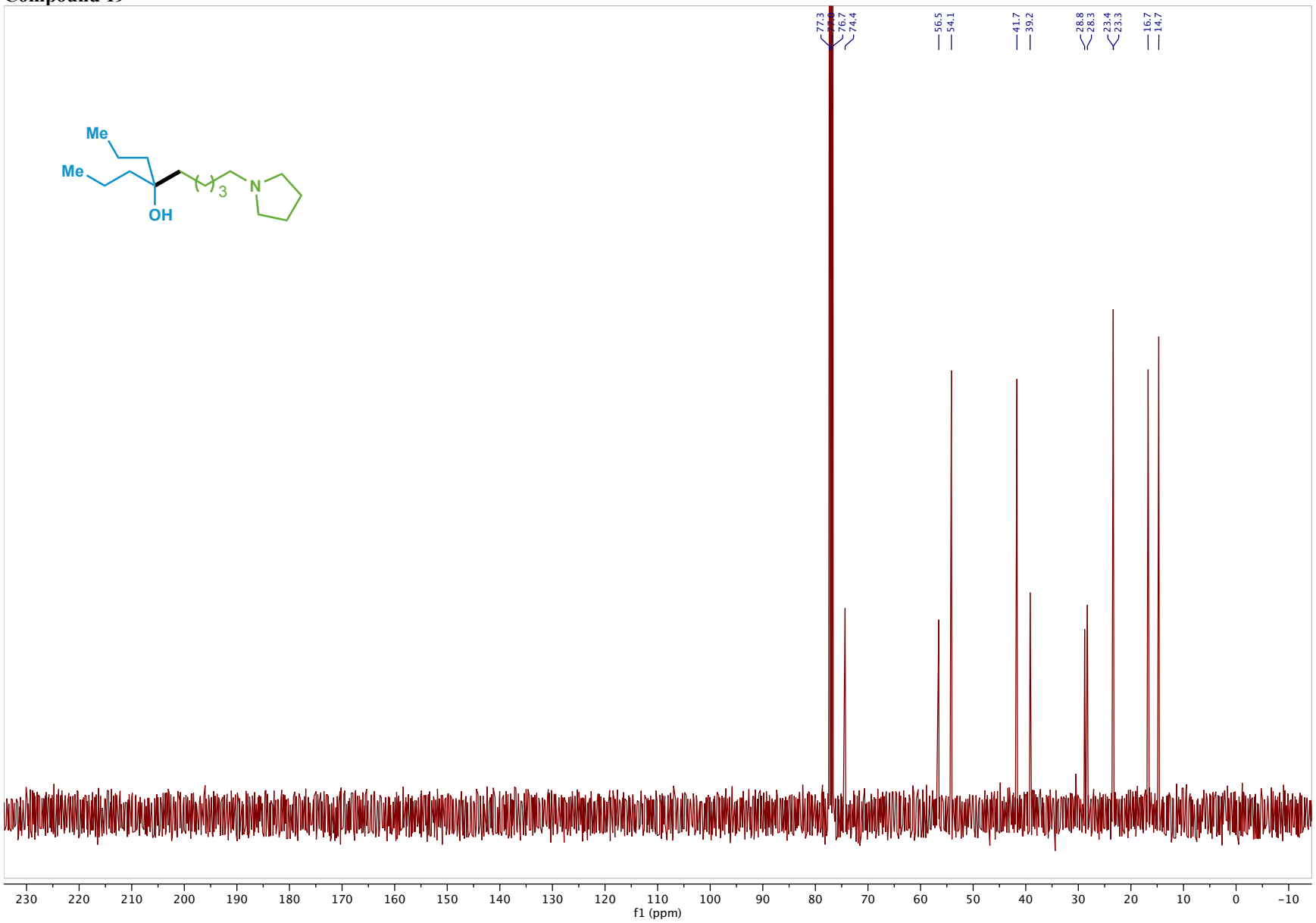
Compound 18


136.7
135.8
132.0
128.4
127.0
120.3
118.4
117.9
108.6
106.3
77.3
77.0
76.7
72.9
43.2
41.9
41.6
39.8
35.1
32.8
30.4
28.7
27.6
26.5
23.7
22.6
19.8
19.5
10.1
8.8
Me
Me
Me
Me
OH
3
N
Me
Me
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

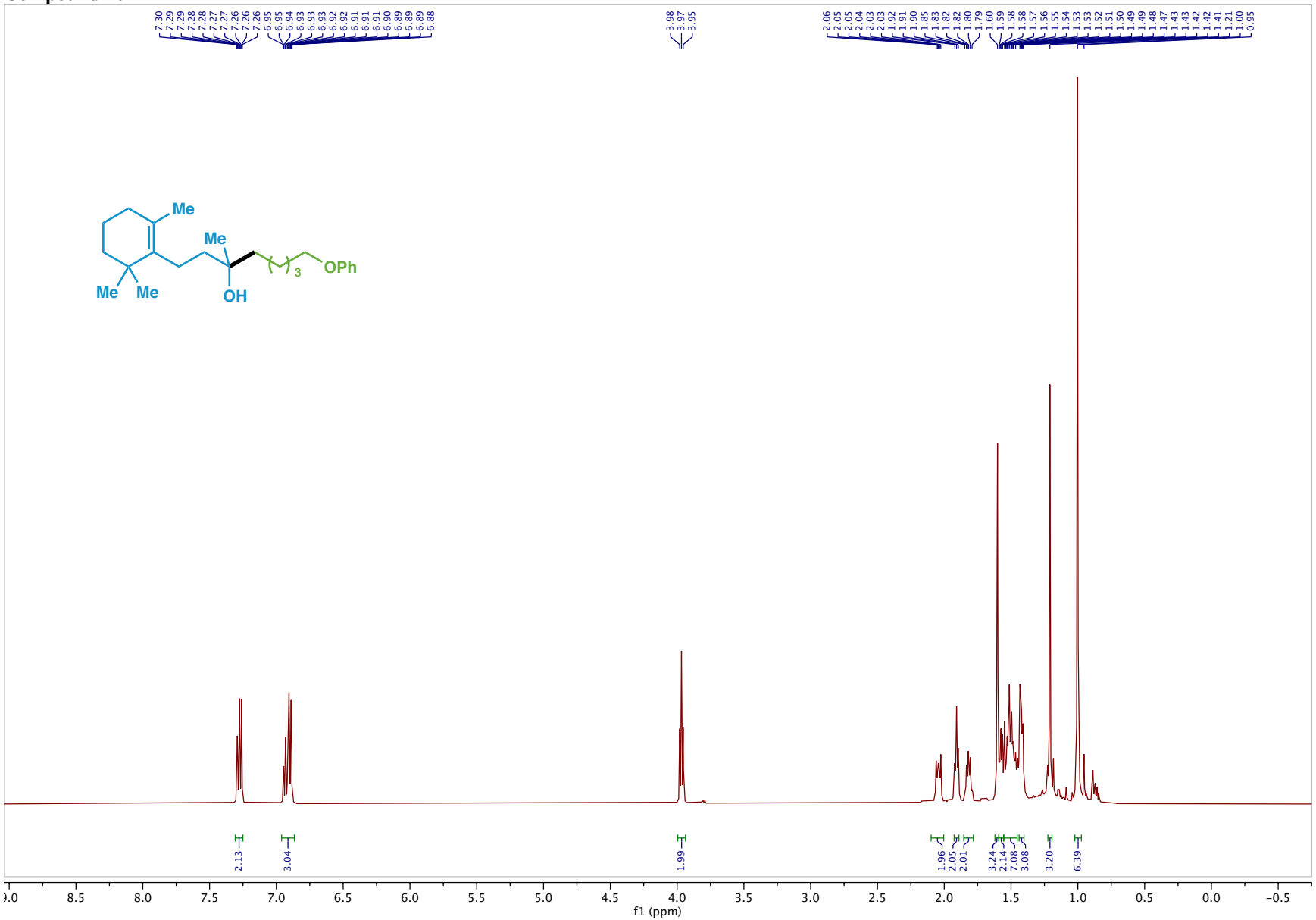
Compound 19


7.26
2.53
2.53
2.52
2.51
2.50
2.46
2.44
2.43
2.42
1.80
1.79
1.78
1.77
1.76
1.54
1.41
1.40
1.39
1.38
1.37
1.36
1.36
1.34
1.33
1.33
1.32
1.31
1.30
1.29
1.28
1.27
1.26
1.26
1.24
0.92
0.91
0.90
0.89
0.84
Me
Me
OH
3
N
4.06
2.08
4.05
2.11
6.17
7.94
6.23
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
f1 (ppm)

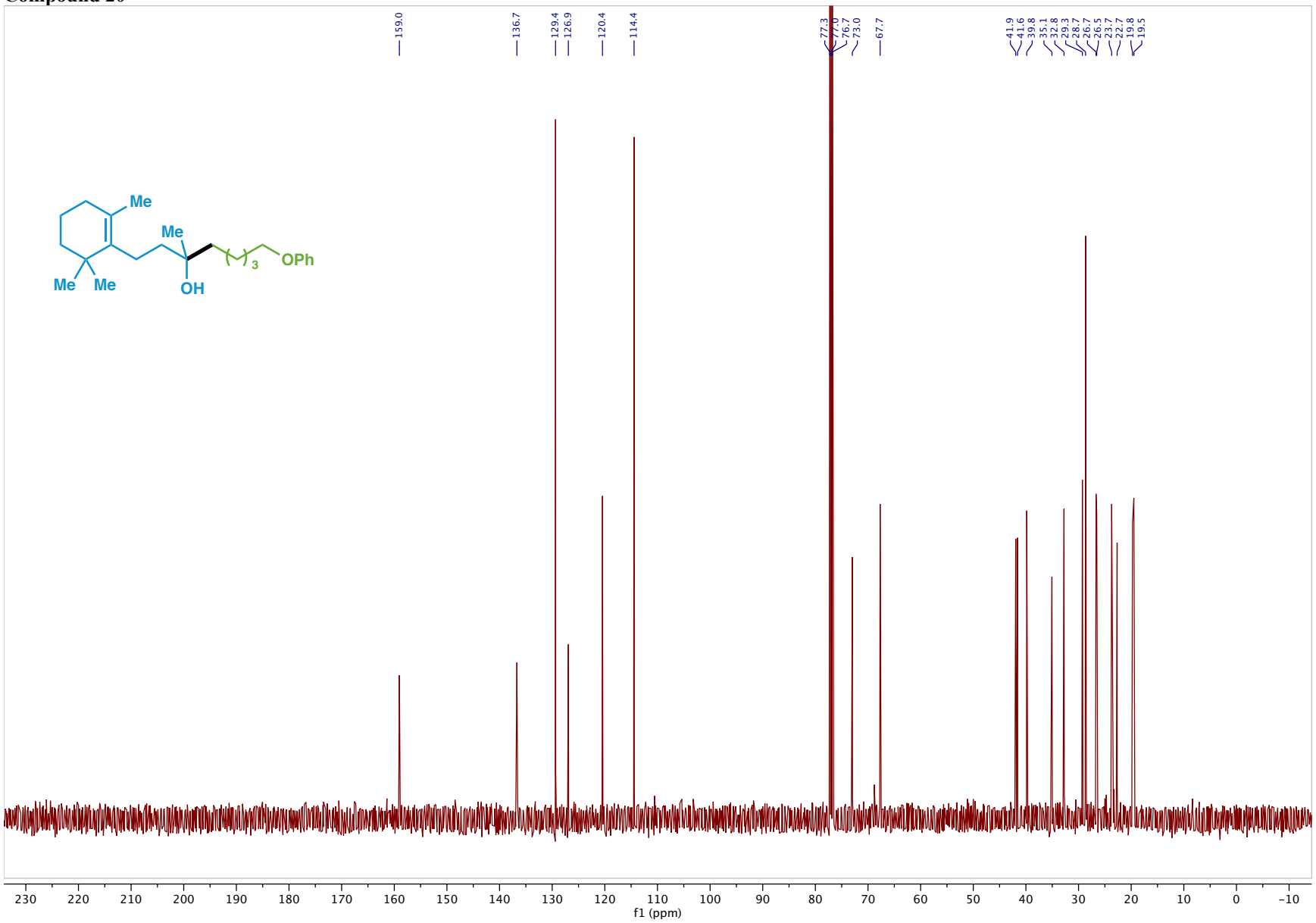
Compound 19


77.3
76.7
74.4
56.5
54.1
41.7
39.2
28.8
28.3
23.4
23.3
16.7
14.7
Me
Me
OH
3
N
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

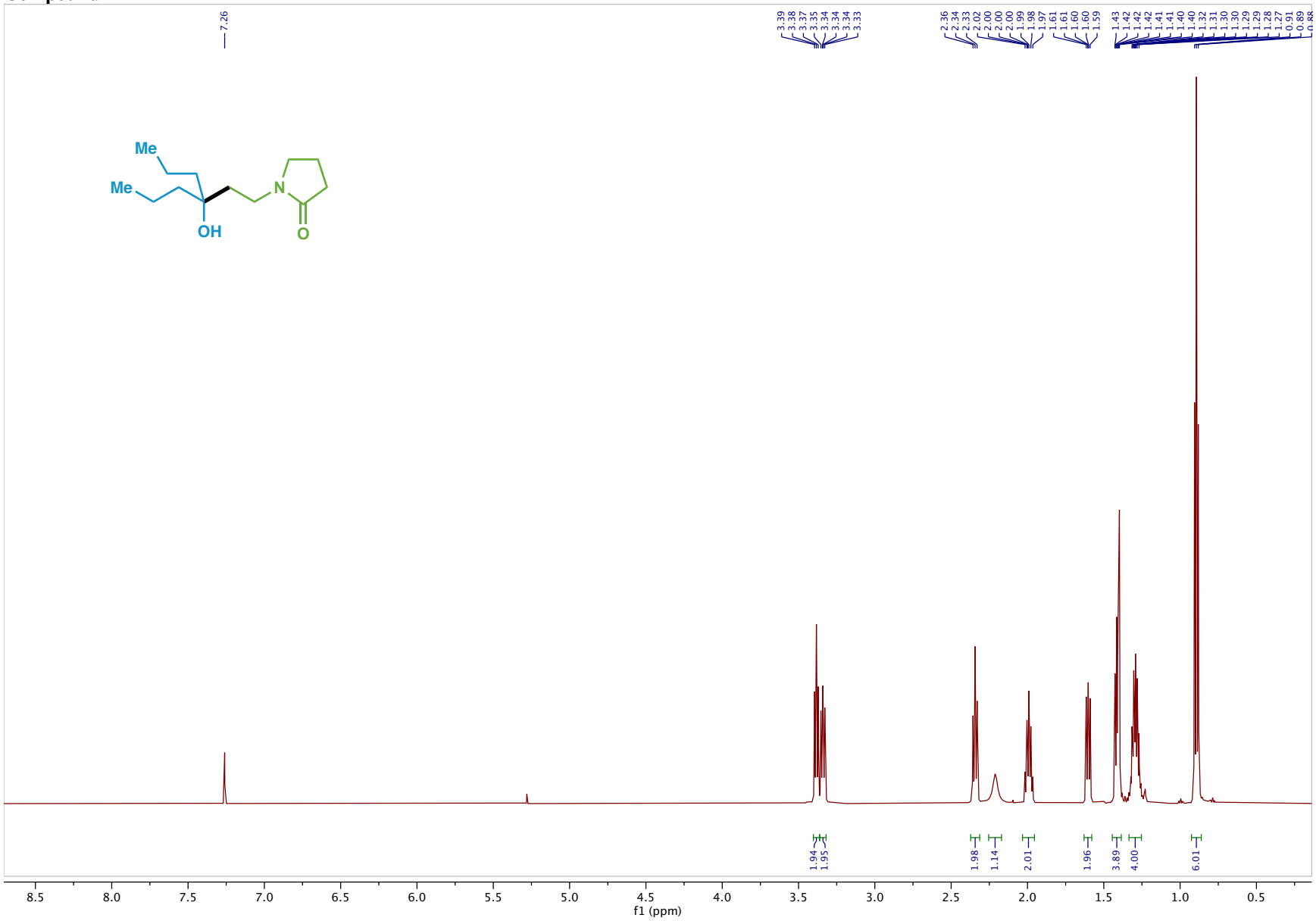
Compound 20



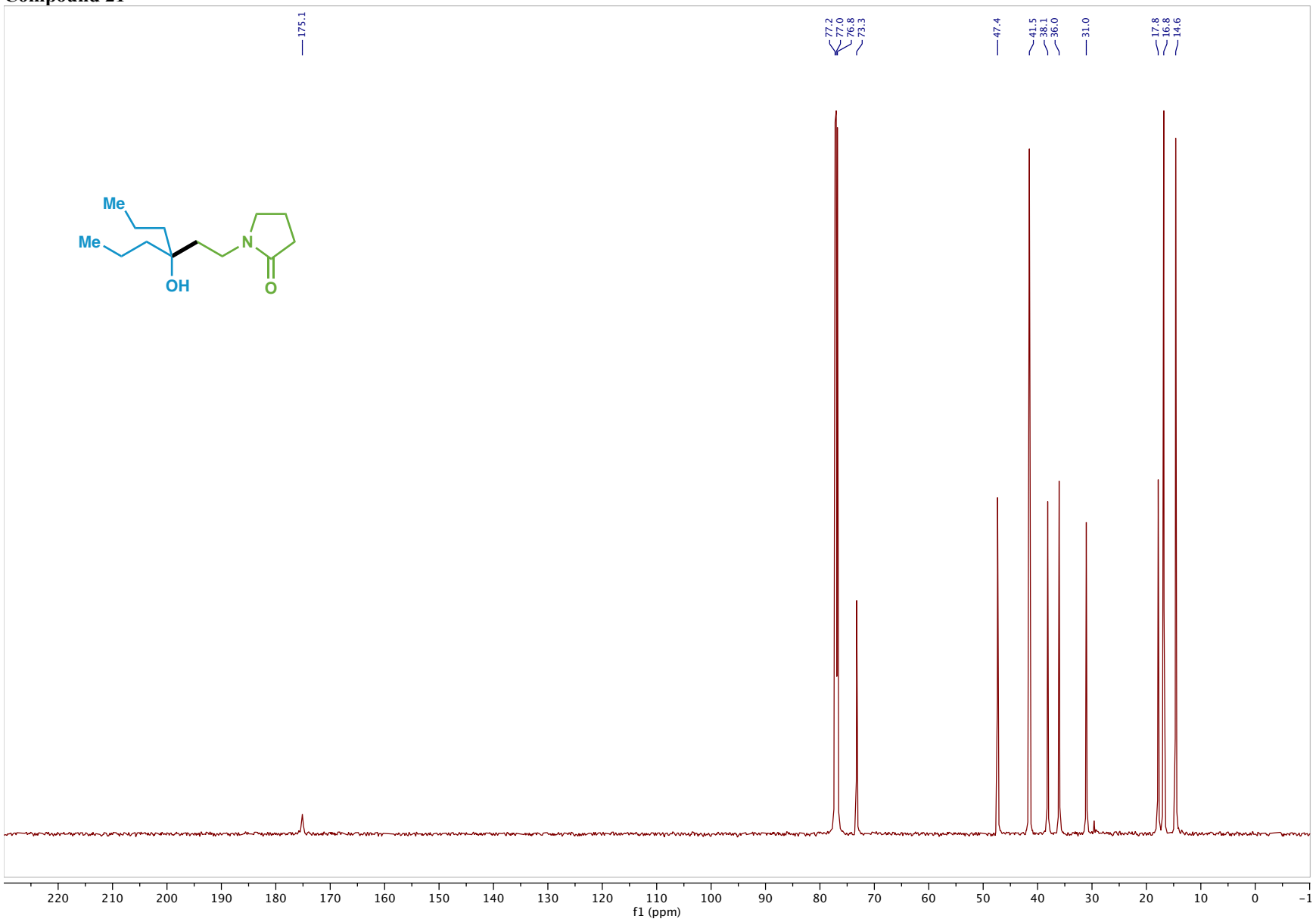
Compound 20


159.0
136.7
129.4
126.9
120.4
114.4
77.3
77.0
76.7
73.0
67.7
41.9
41.6
39.8
35.1
32.8
29.3
28.7
26.7
26.5
23.7
22.7
19.8
19.5
Me
Me
Me
Me
OH
3
OPh
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

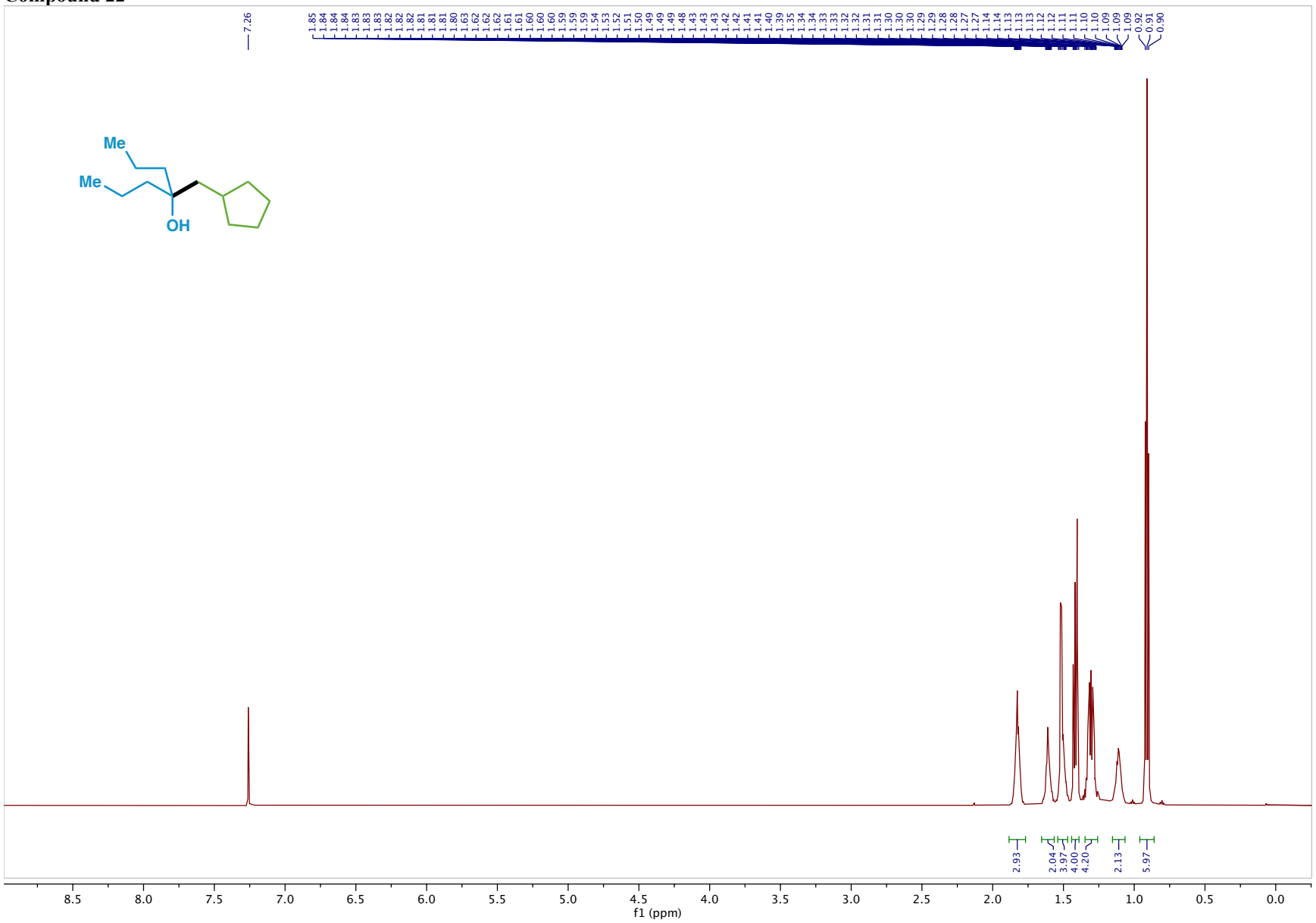
Compound 21


7.26
3.39
3.38
3.37
3.35
3.34
3.34
3.34
3.33
2.36
2.34
2.33
2.02
2.00
2.00
2.00
1.99
1.98
1.97
1.61
1.61
1.60
1.60
1.59
1.43
1.42
1.42
1.42
1.41
1.41
1.40
1.40
1.32
1.31
1.30
1.30
1.29
1.29
1.28
1.27
0.91
0.89
Me
Me
OH
N
O
1.94
1.95
1.98
1.14
2.01
1.96
3.89
4.00
6.01
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
f1 (ppm)

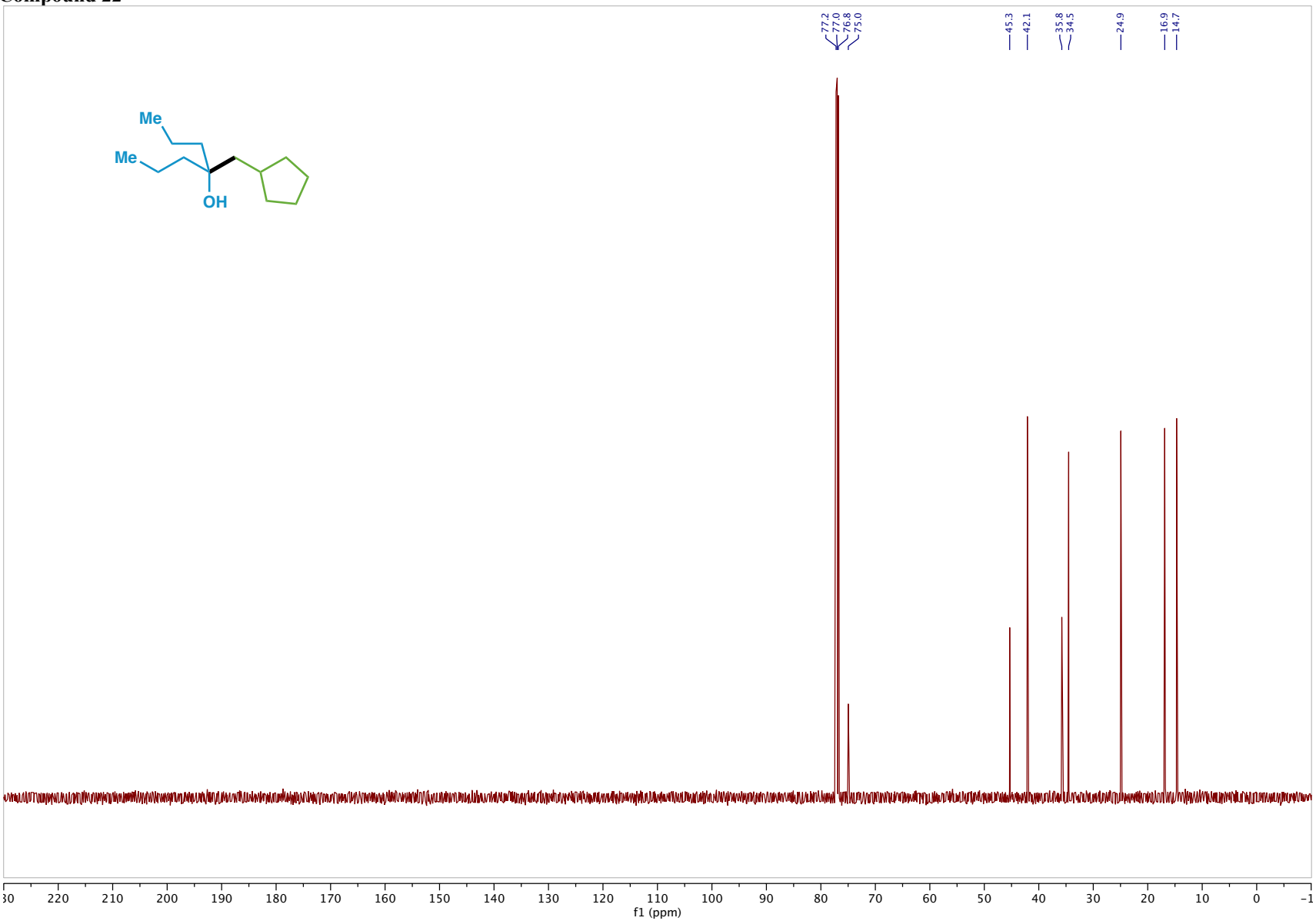
Compound 21


175.1
77.2
77.0
76.8
73.3
47.4
41.5
38.1
36.0
31.0
17.8
16.8
14.6
Me
Me
OH
N
O
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

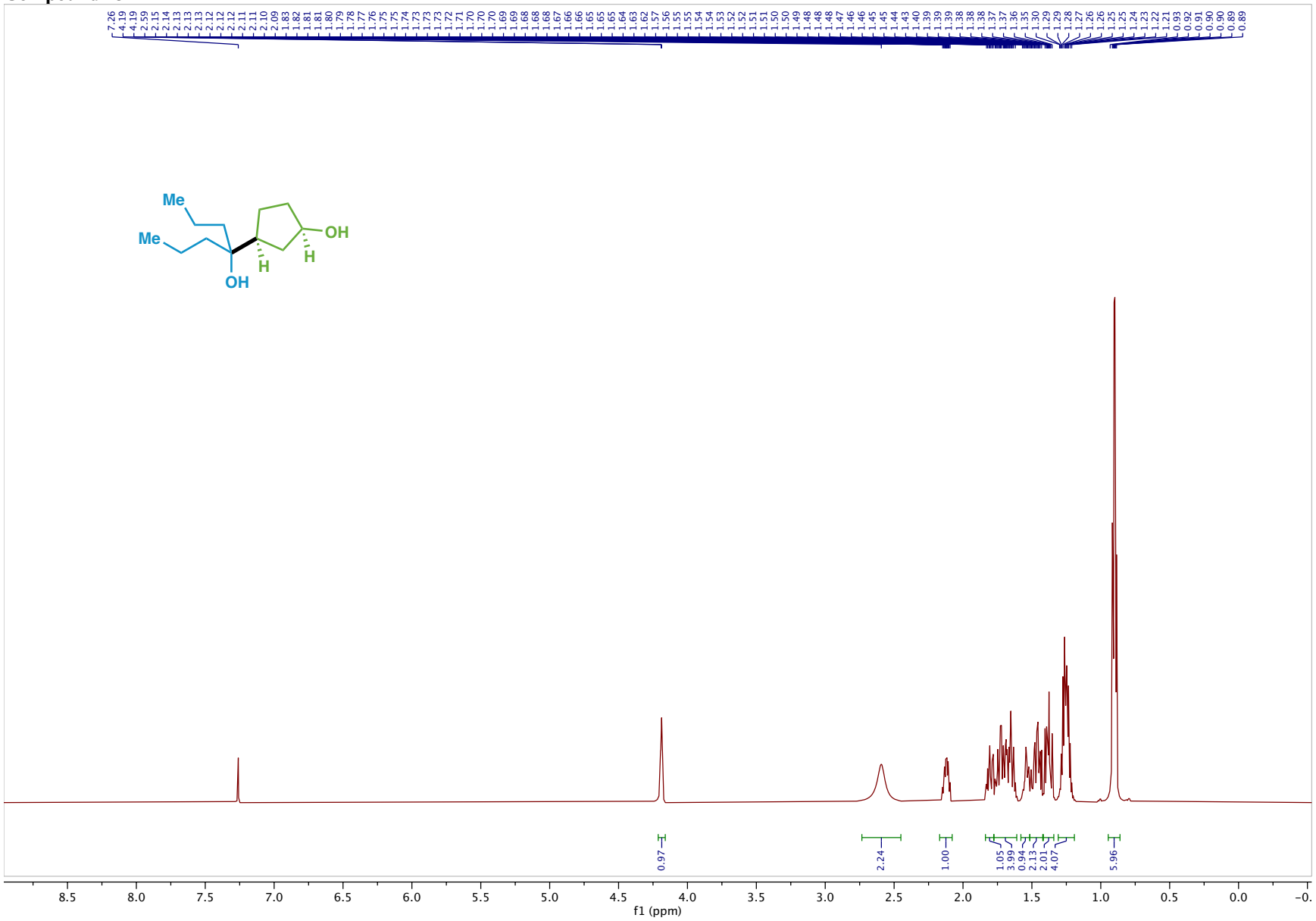
Compound 22


Me
Me
OH
7.26
1.85 1.84 1.84 1.84 1.83 1.83 1.83 1.82 1.82 1.82 1.81 1.81 1.81 1.80 1.63 1.62 1.62 1.62 1.61 1.61 1.60 1.60 1.60 1.59 1.59 1.59 1.54 1.53 1.52 1.51 1.50 1.49 1.49 1.49 1.48 1.43 1.43 1.43 1.42 1.42 1.41 1.41 1.40 1.39 1.35 1.34 1.34 1.33 1.33 1.32 1.32 1.31 1.31 1.30 1.30 1.30 1.29 1.29 1.28 1.28 1.27 1.27 1.14 1.14 1.13 1.13 1.13 1.12 1.12 1.11 1.11 1.10 1.09 1.09 1.09 0.92 0.91 0.90
2.93
2.04
3.97
4.00
4.20
2.13
5.97
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
f1 (ppm)

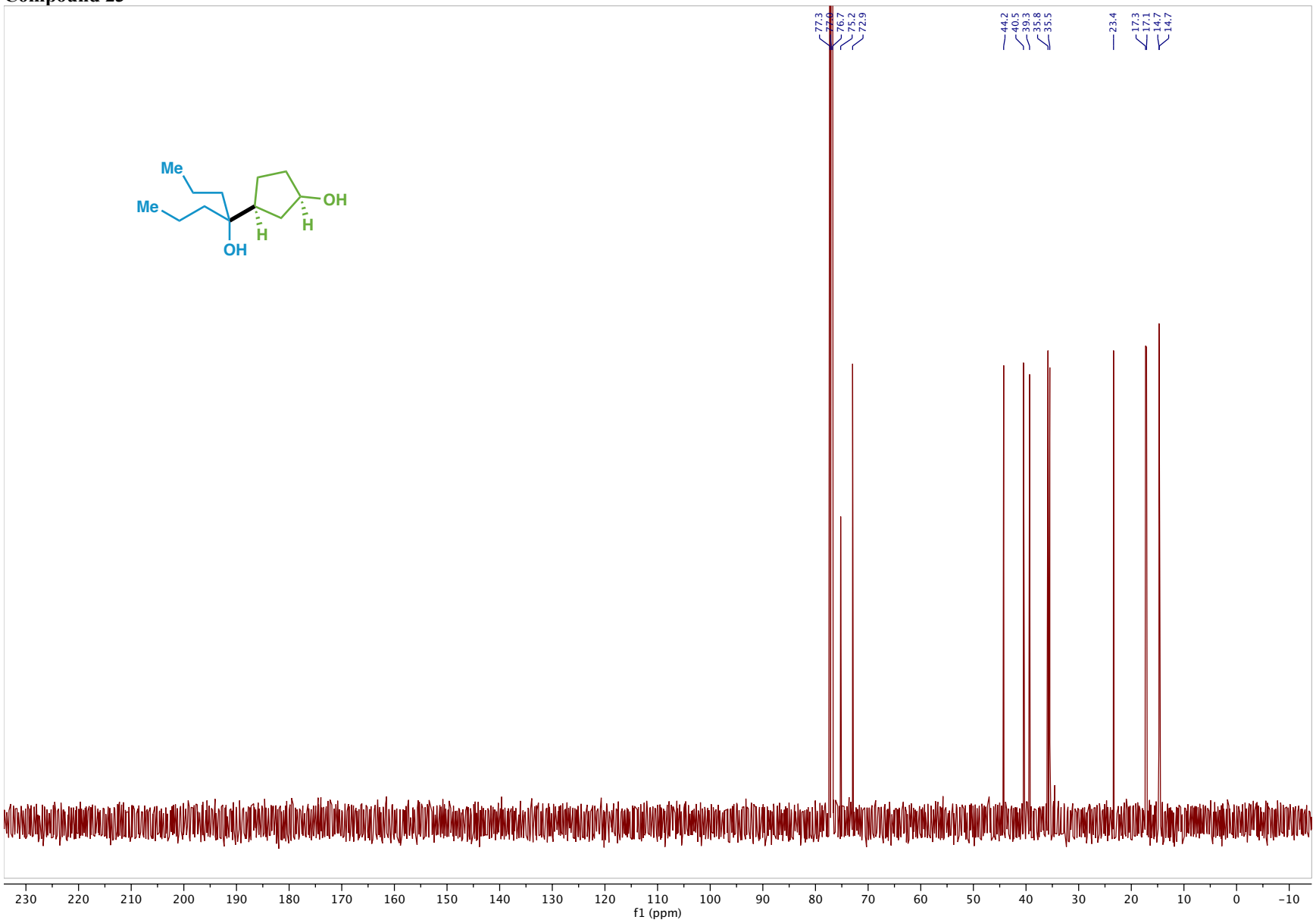
Compound 22



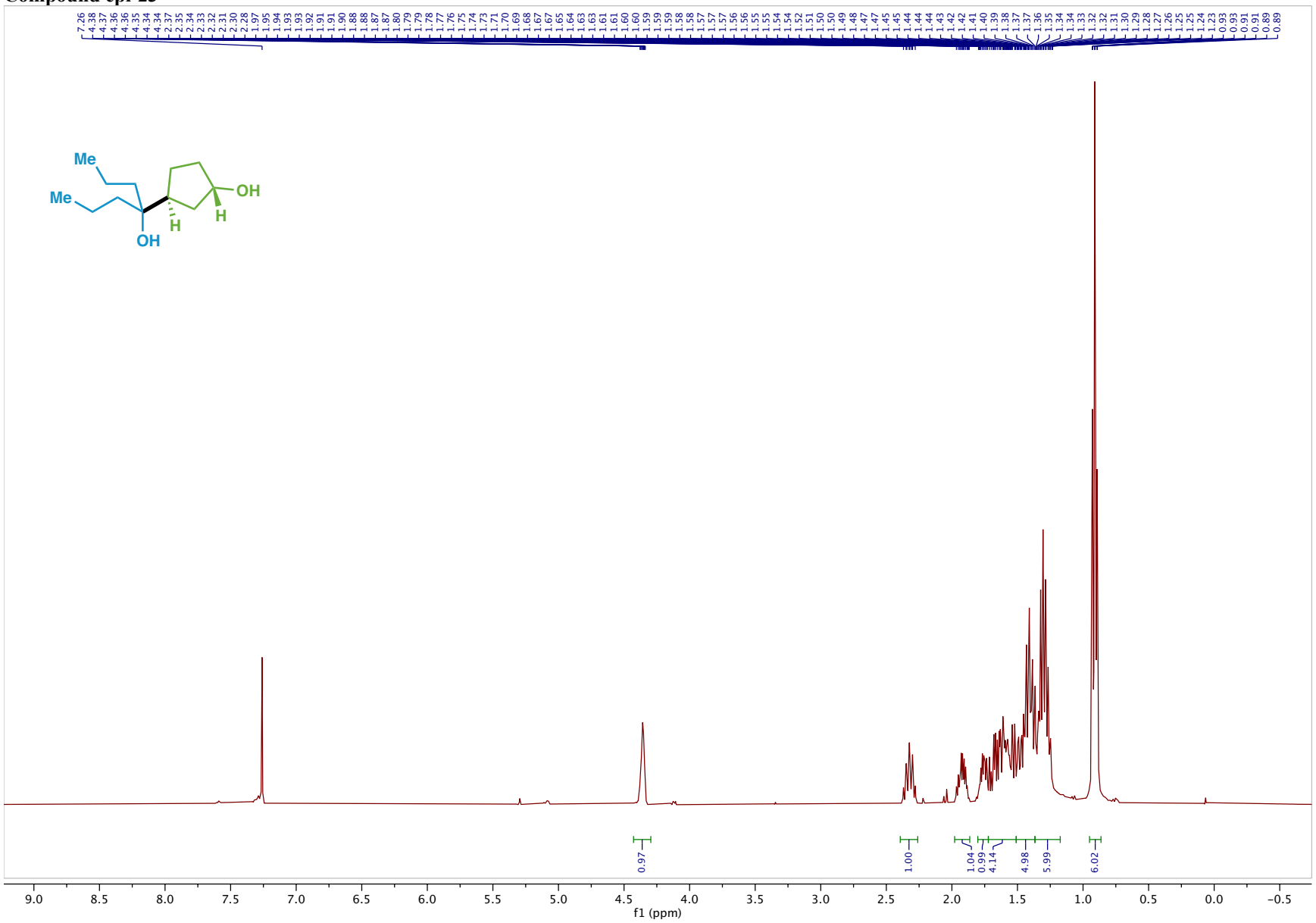
Compound 23



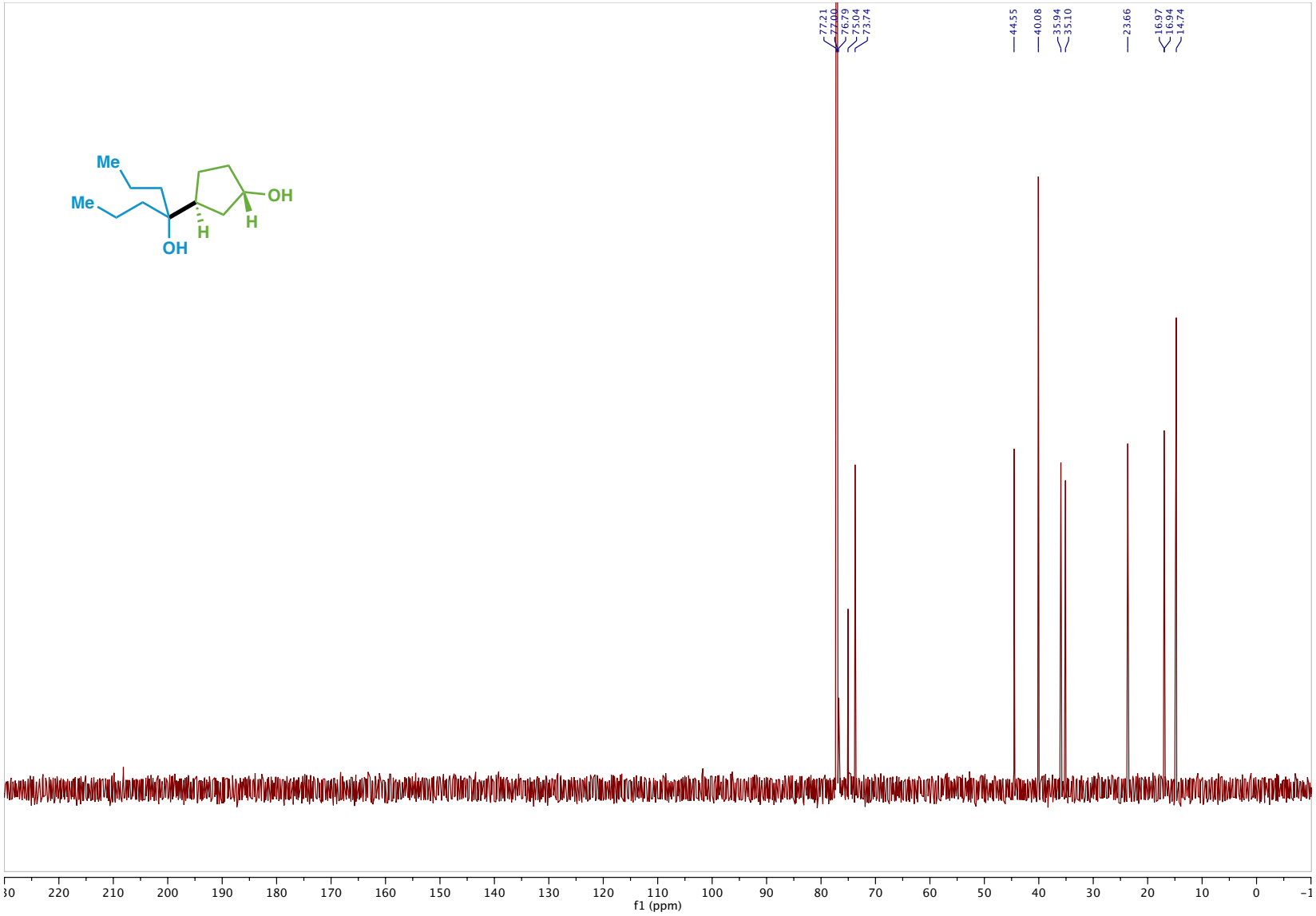
Compound 23


77.3
77.0
76.7
75.2
72.9
44.2
40.5
39.3
35.8
35.5
23.4
17.3
17.1
14.7
14.7
Me
Me
OH
H
H
OH
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

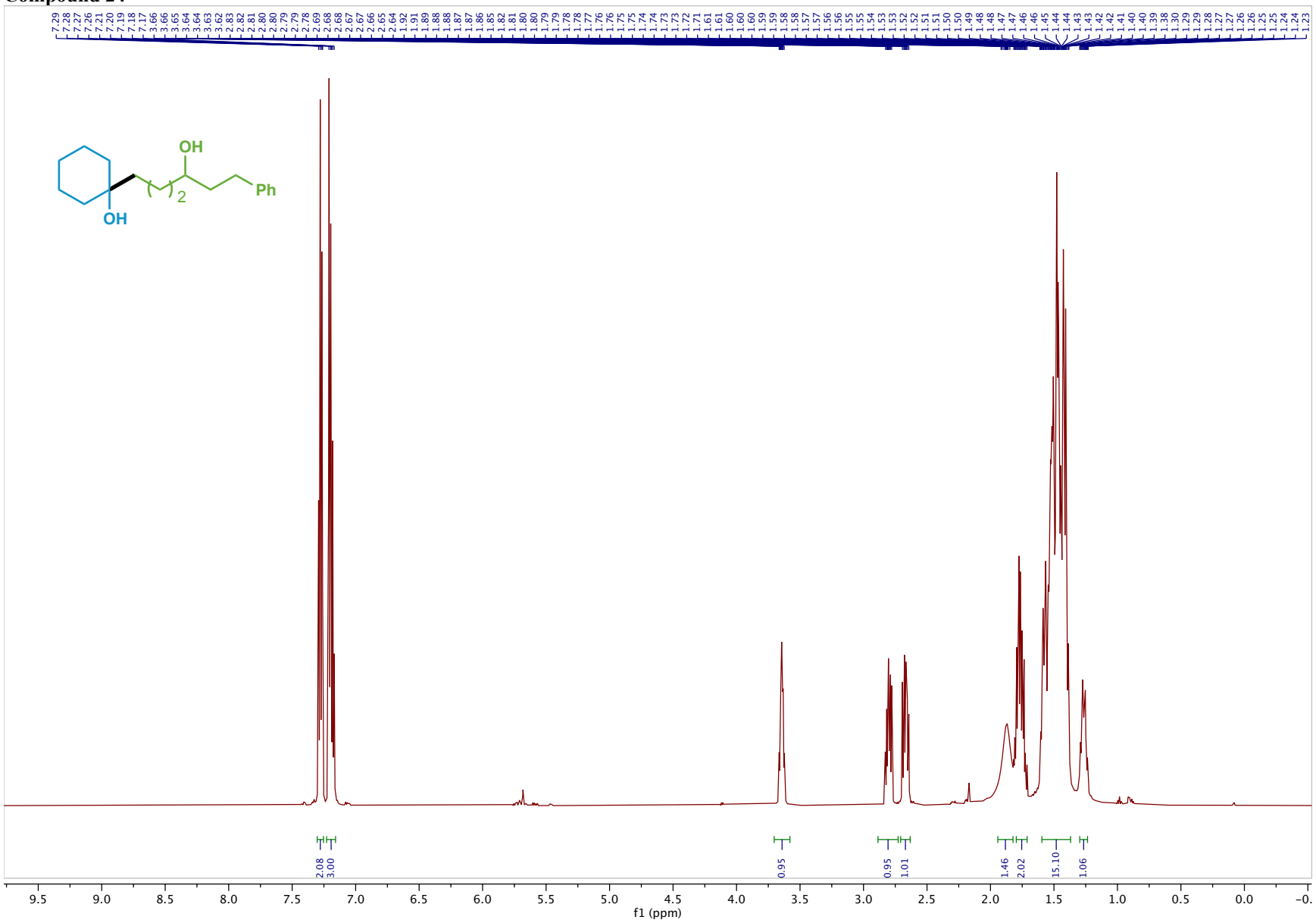
Compound epi-23



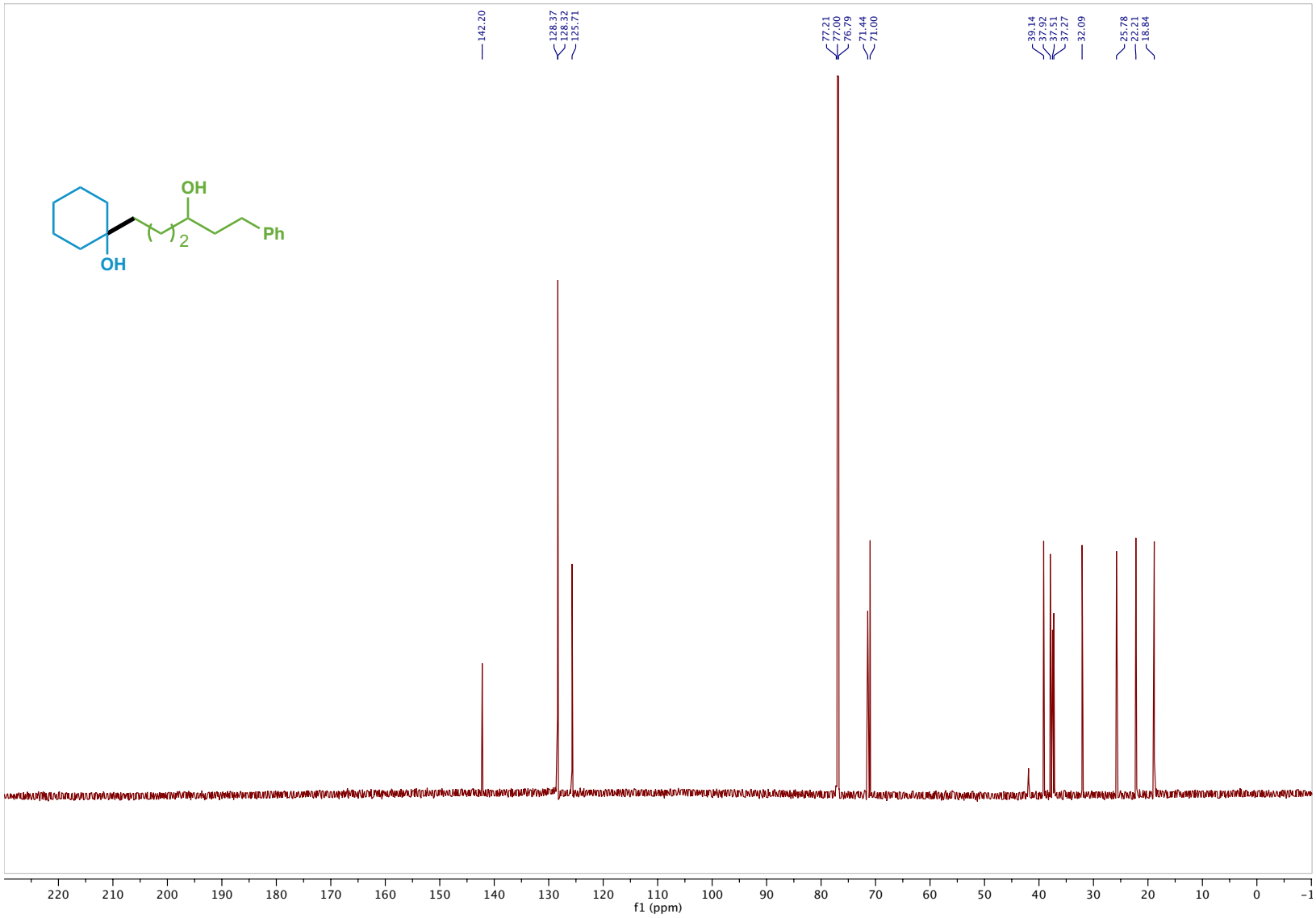
Compound epi-23



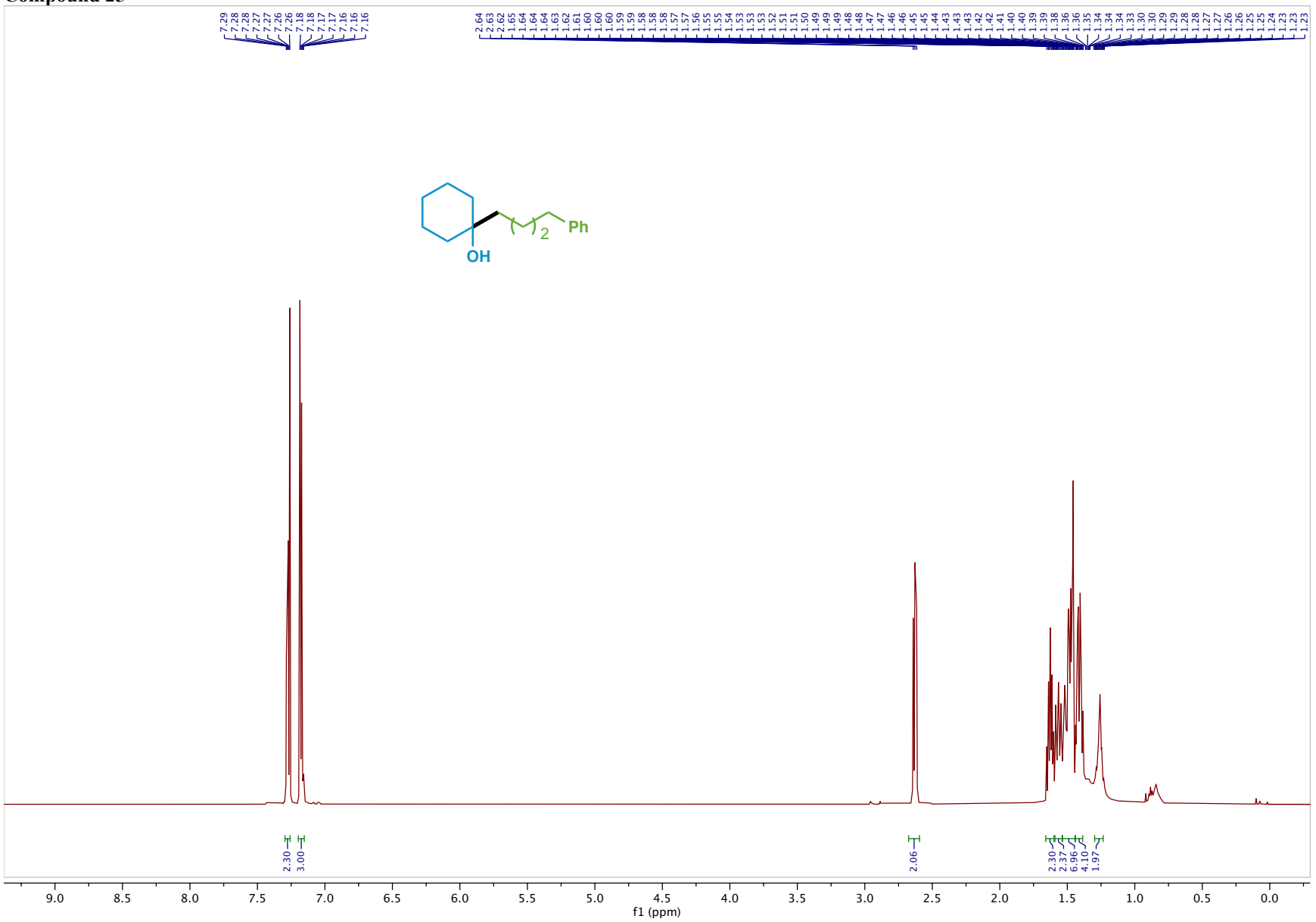
Compound 24



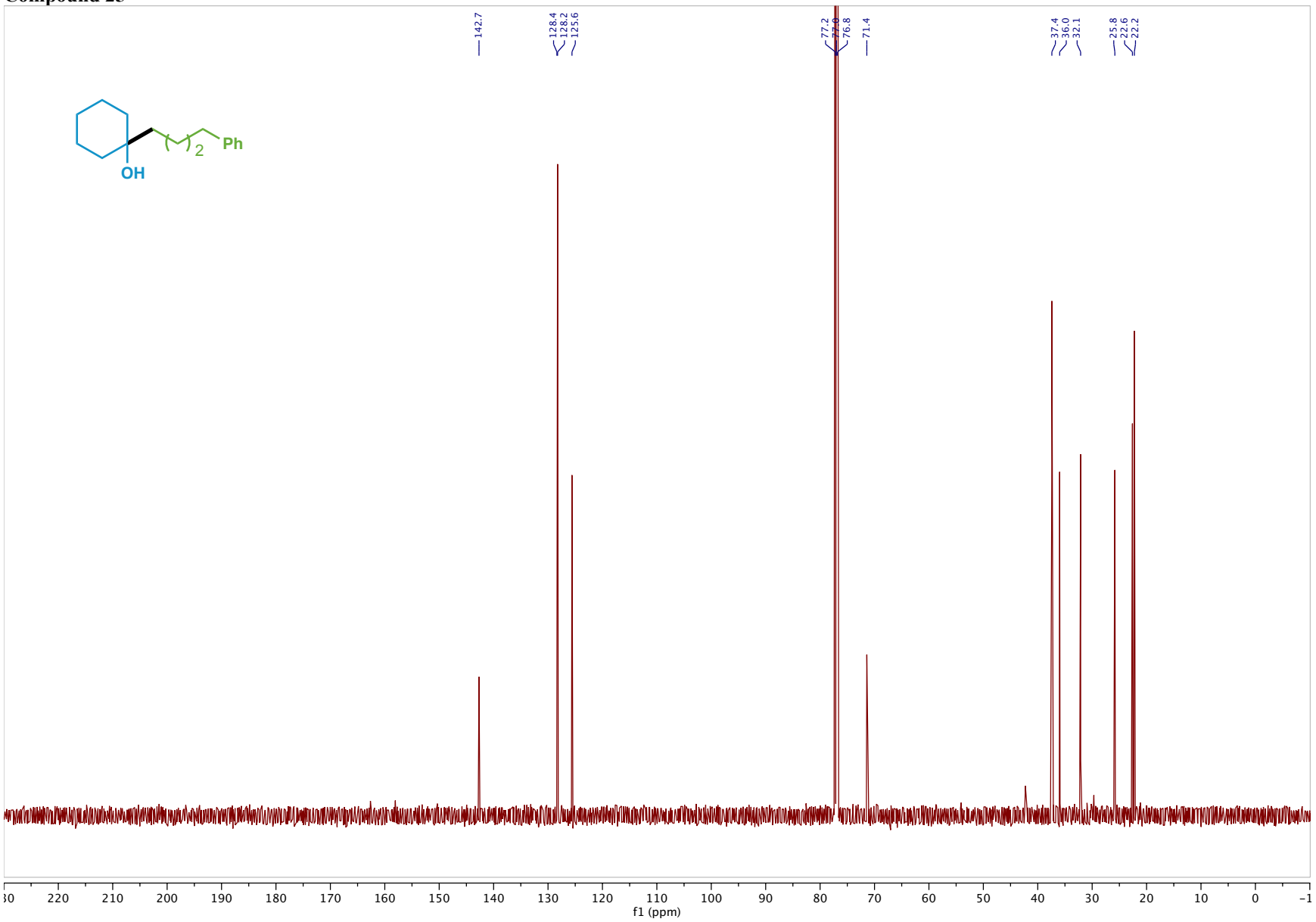
Compound 24


142.20
128.37
128.32
125.71
77.21
77.00
76.79
71.44
71.00
39.14
37.92
37.51
37.27
32.09
25.78
22.21
18.84
OH
OH
2
Ph
f1 (ppm)

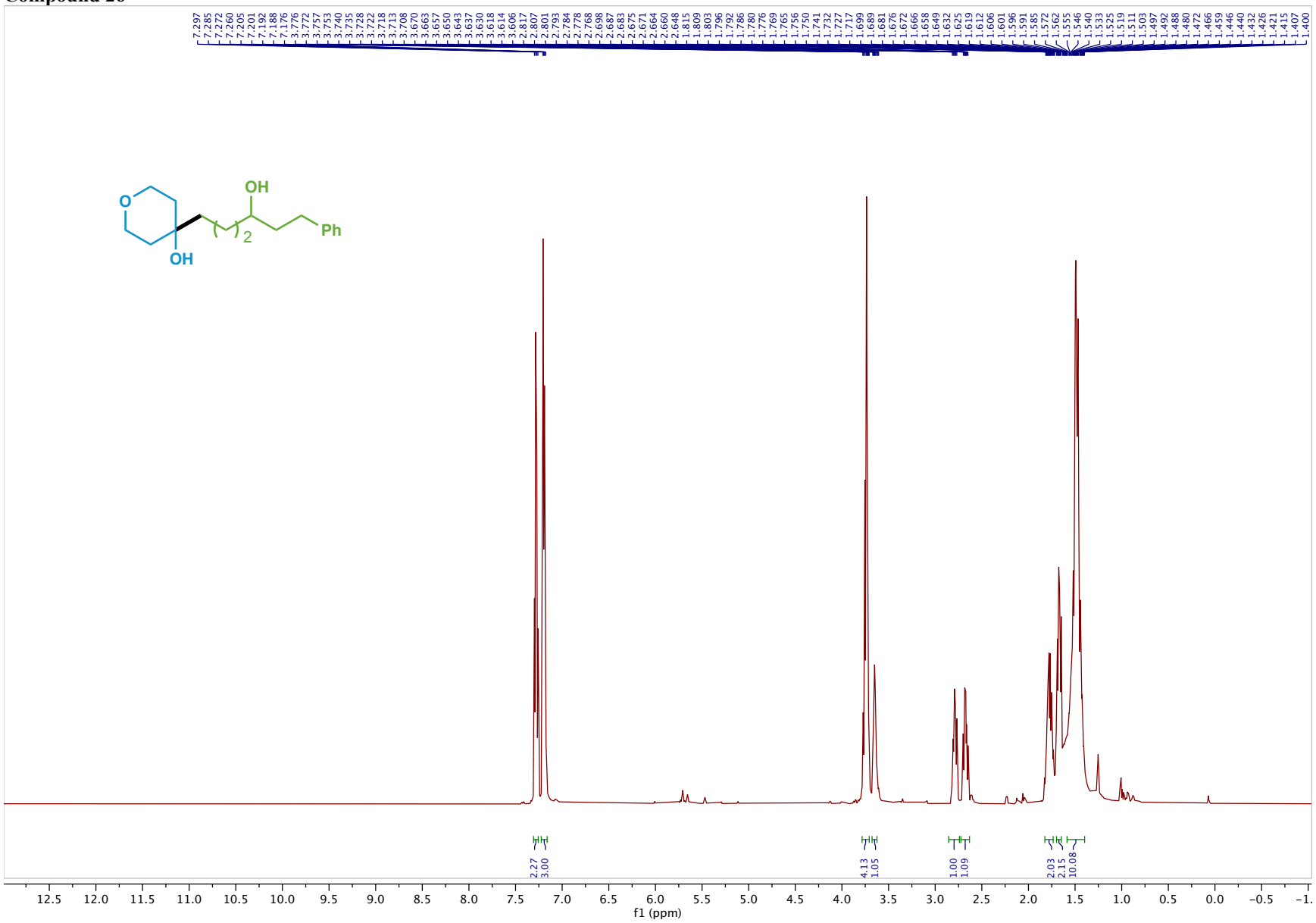
Compound 25



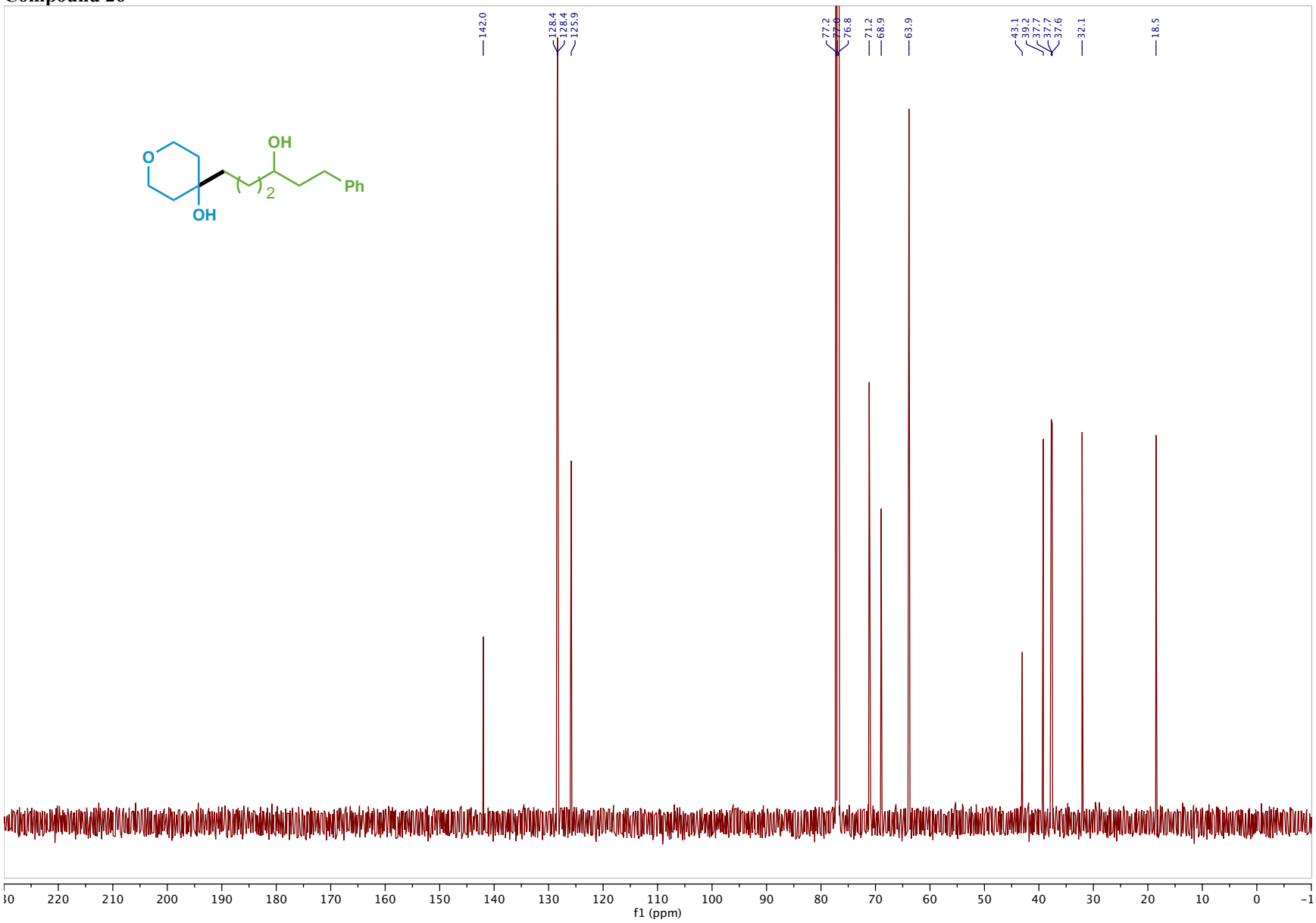
Compound 25


142.7
128.4
128.2
125.6
77.2
76.8
71.4
37.4
36.0
32.1
25.8
22.6
22.2
OH
2
Ph
f1 (ppm)

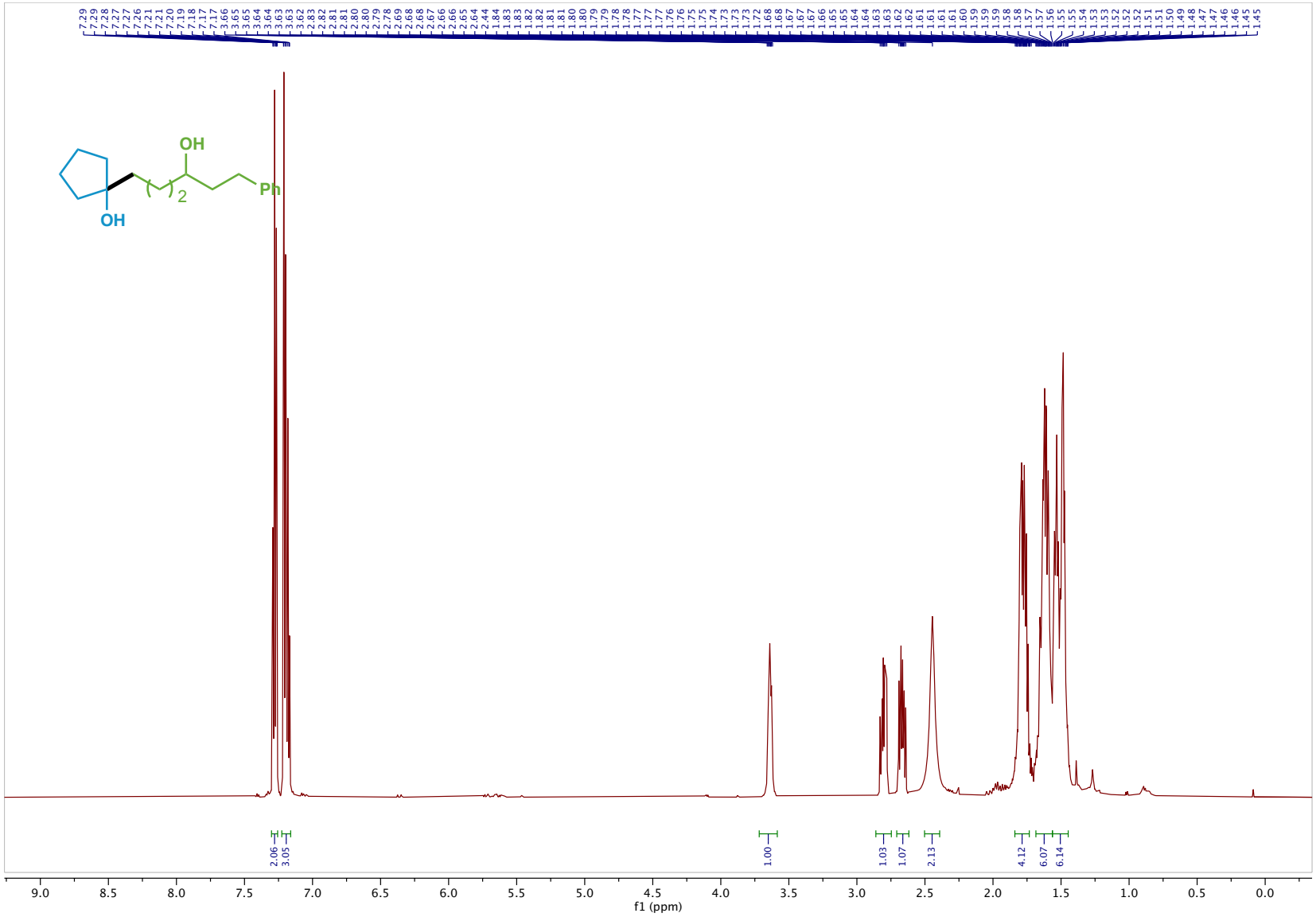
Compound 26



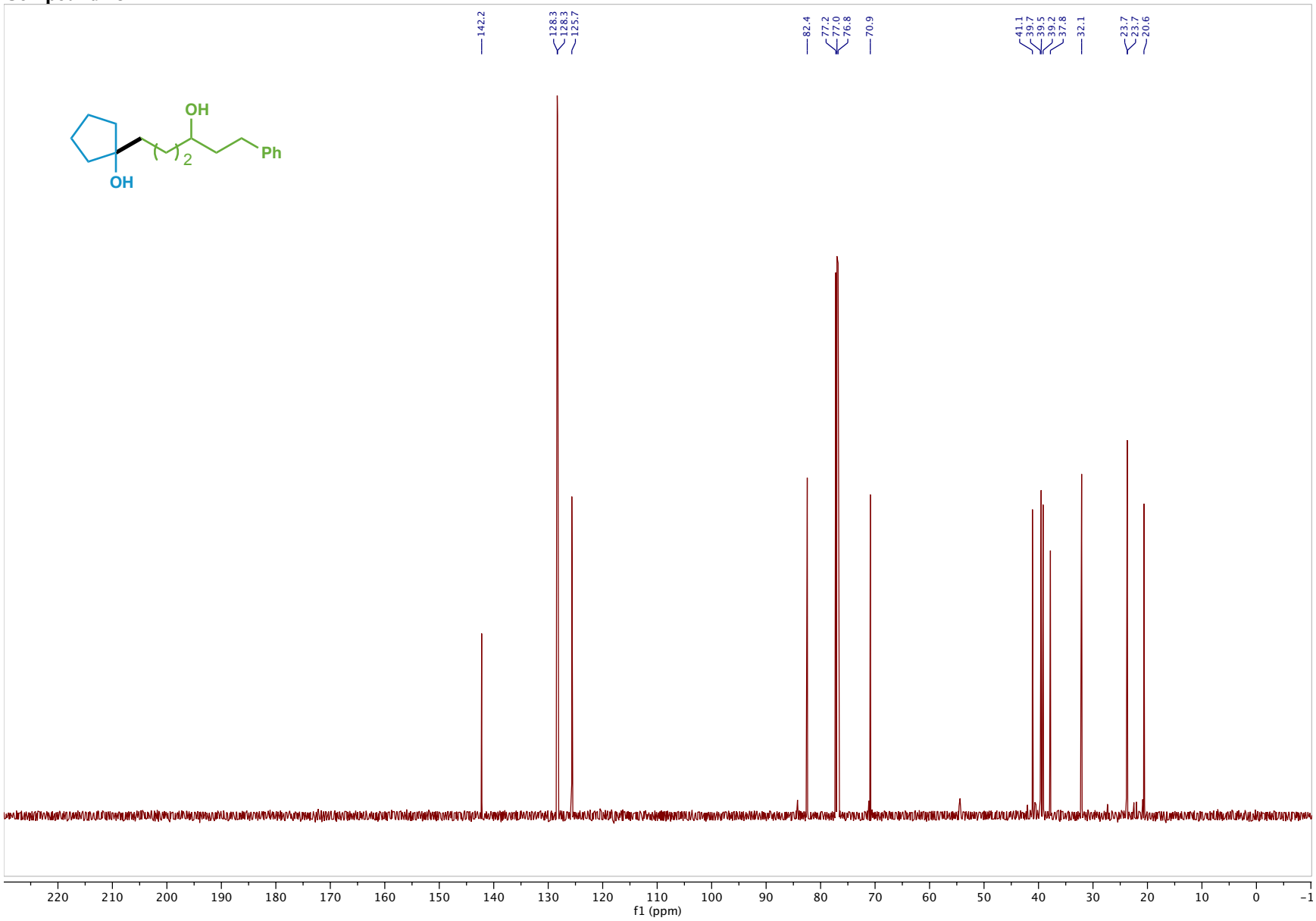
Compound 26


142.0
128.4
128.4
125.9
77.2
76.8
71.2
68.9
63.9
43.1
39.2
37.7
37.7
37.6
32.1
18.5
O
OH
OH
2
Ph
f1 (ppm)

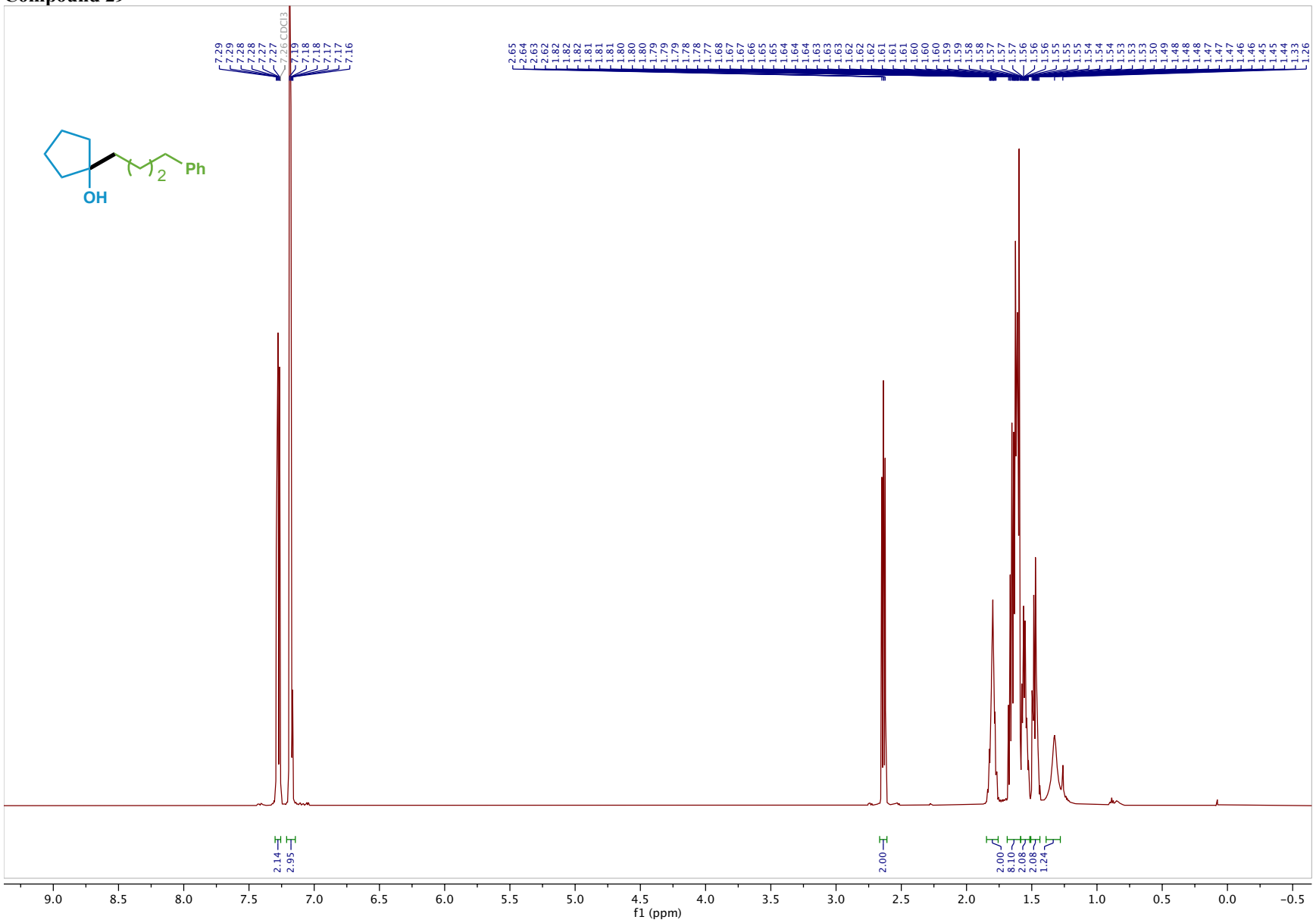
Compound 28



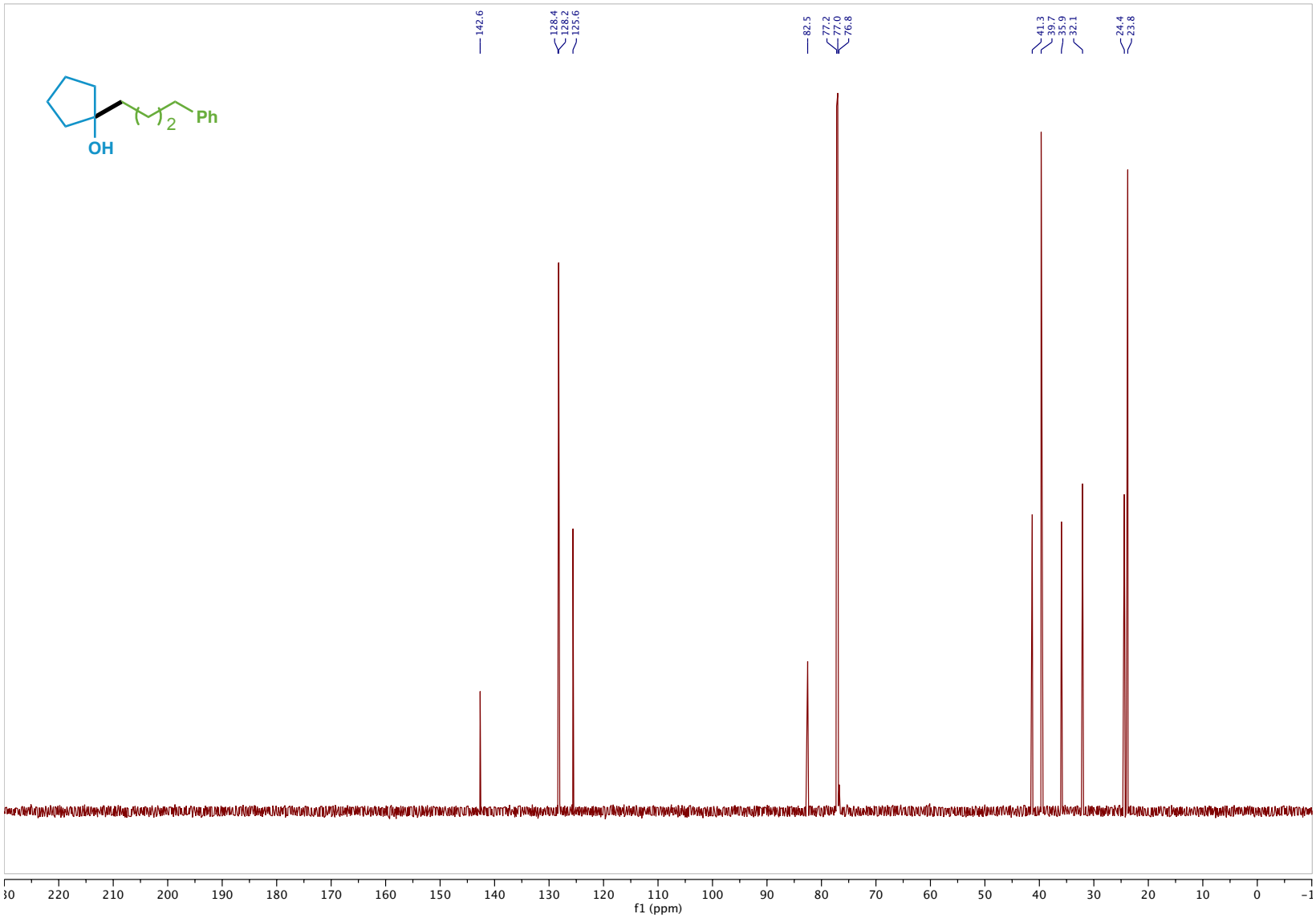
Compound 28


142.2
128.3
128.3
125.7
82.4
77.2
77.0
76.8
70.9
41.1
39.7
39.5
39.2
37.8
32.1
23.7
23.7
20.6
OH
OH
2
Ph
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

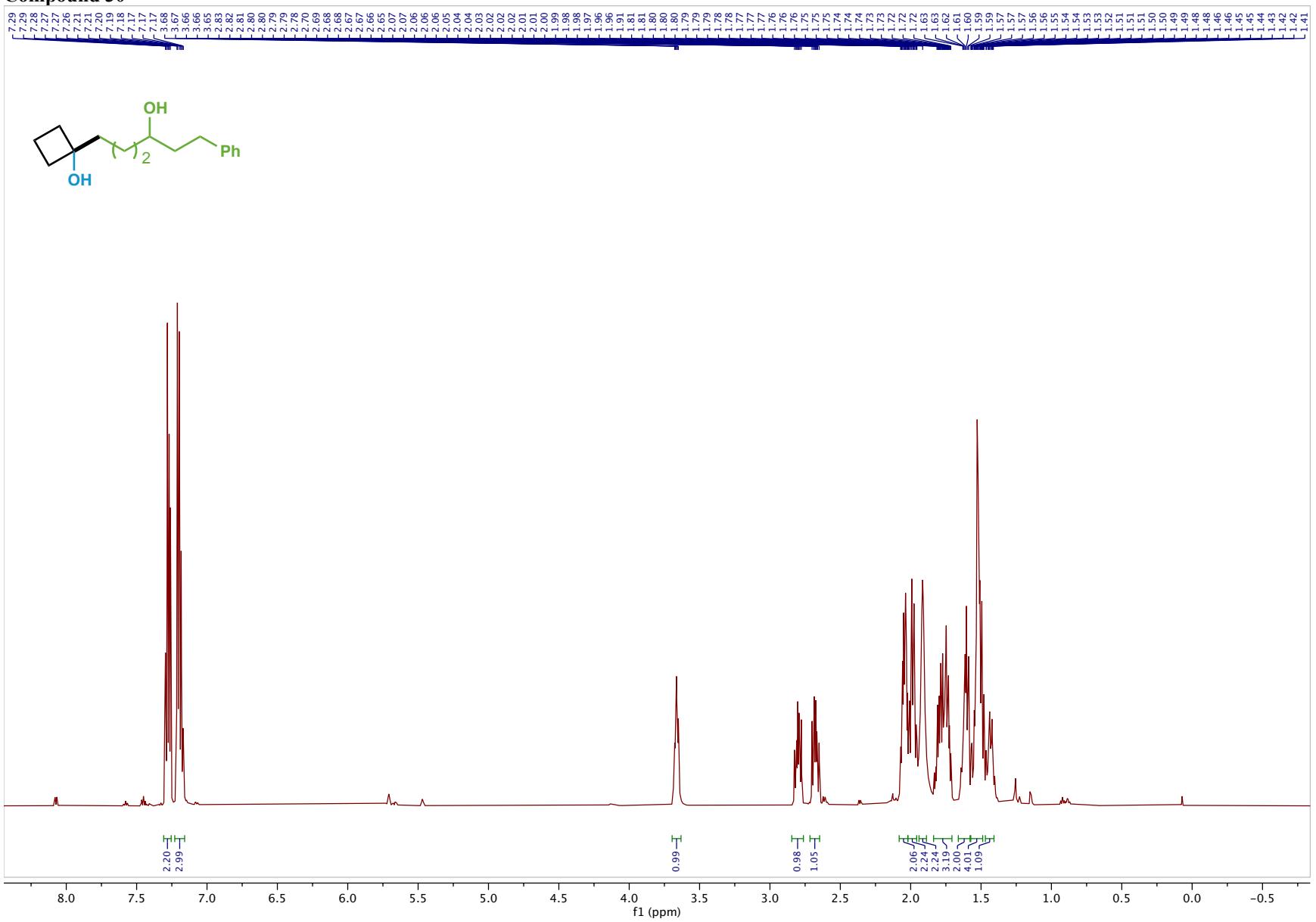
Compound 29



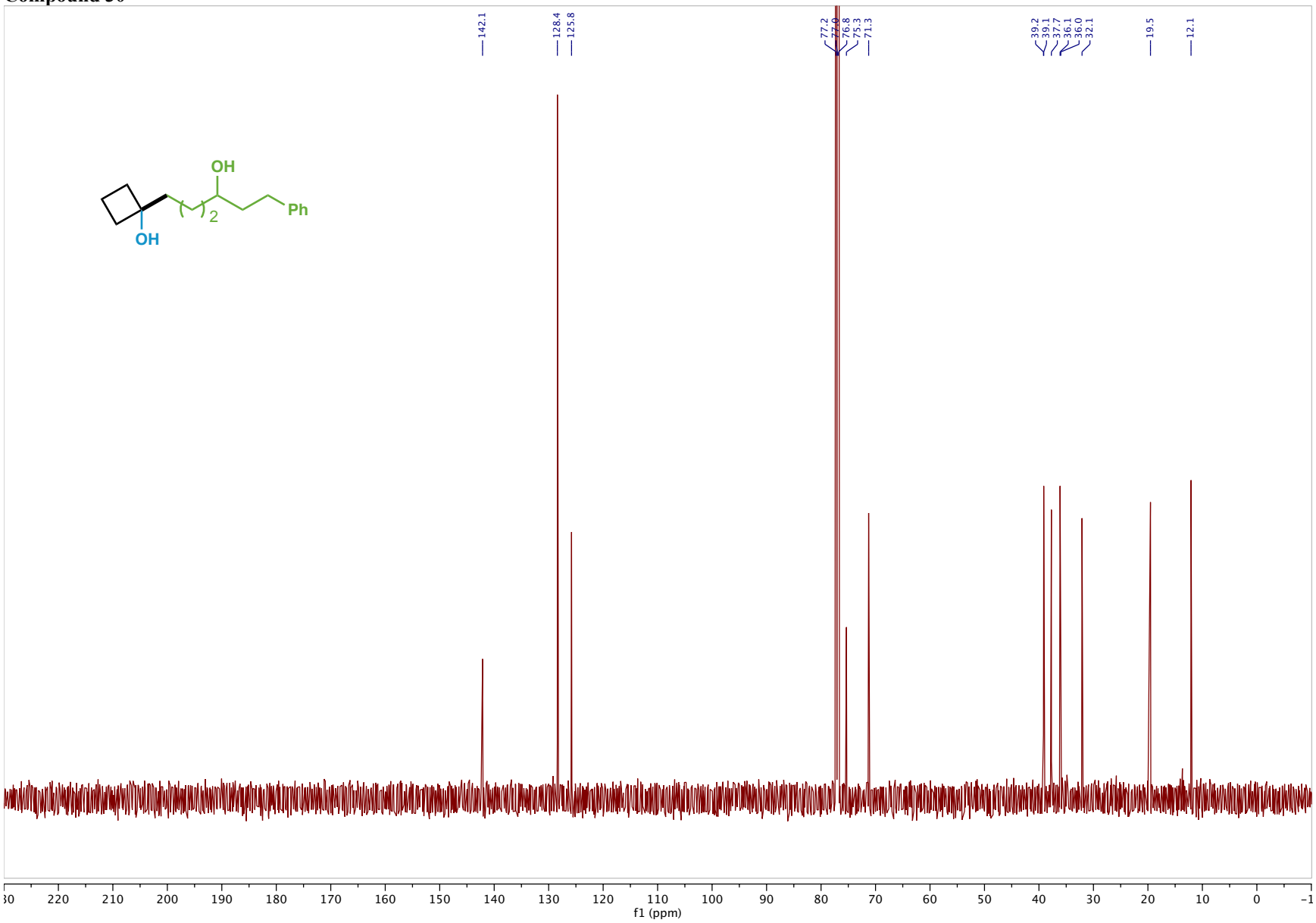
Compound 29


142.6
128.4
128.2
125.6
82.5
77.2
77.0
76.8
41.3
39.7
35.9
32.1
24.4
23.8
OH
2
Ph
f1 (ppm)

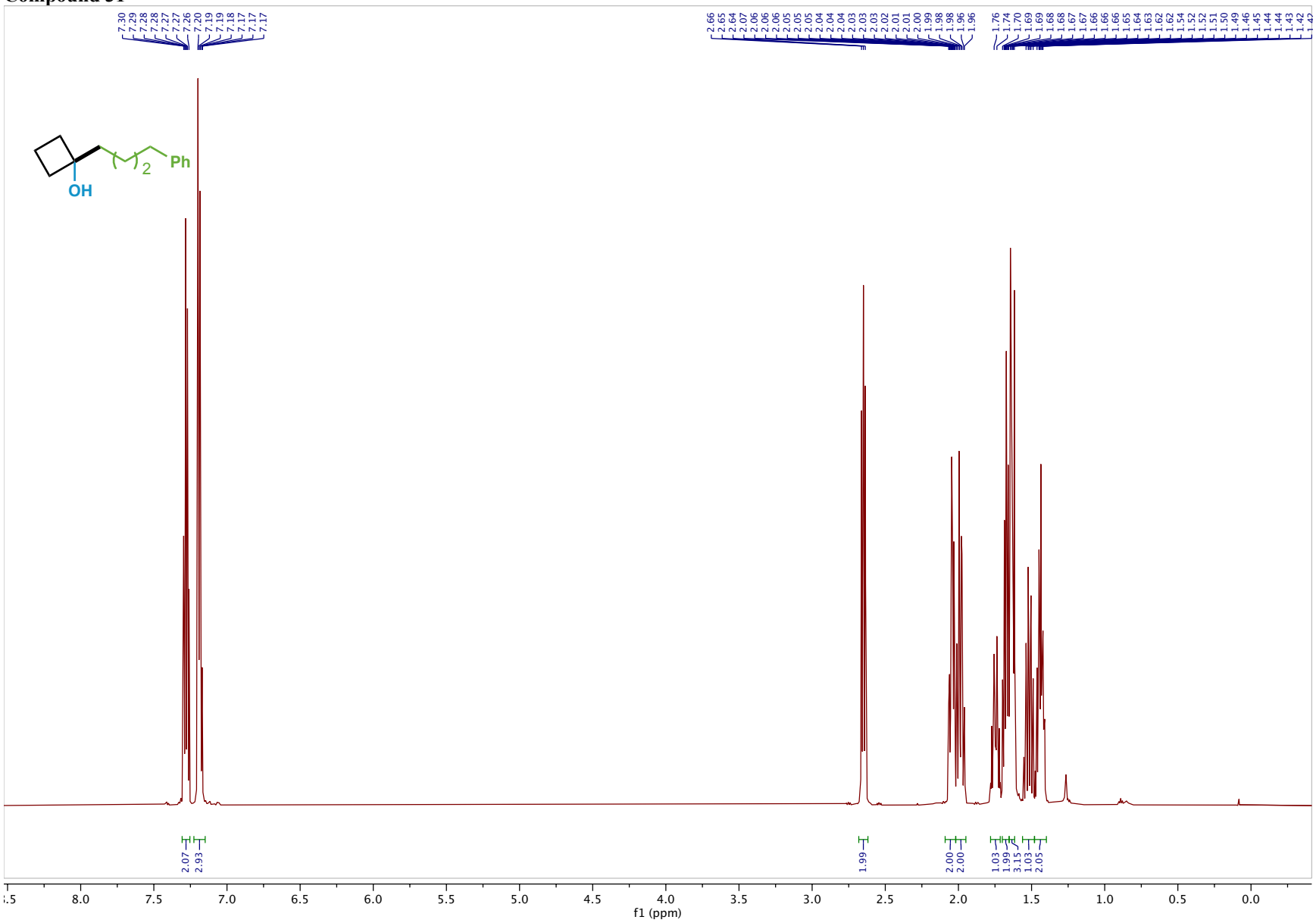
Compound 30



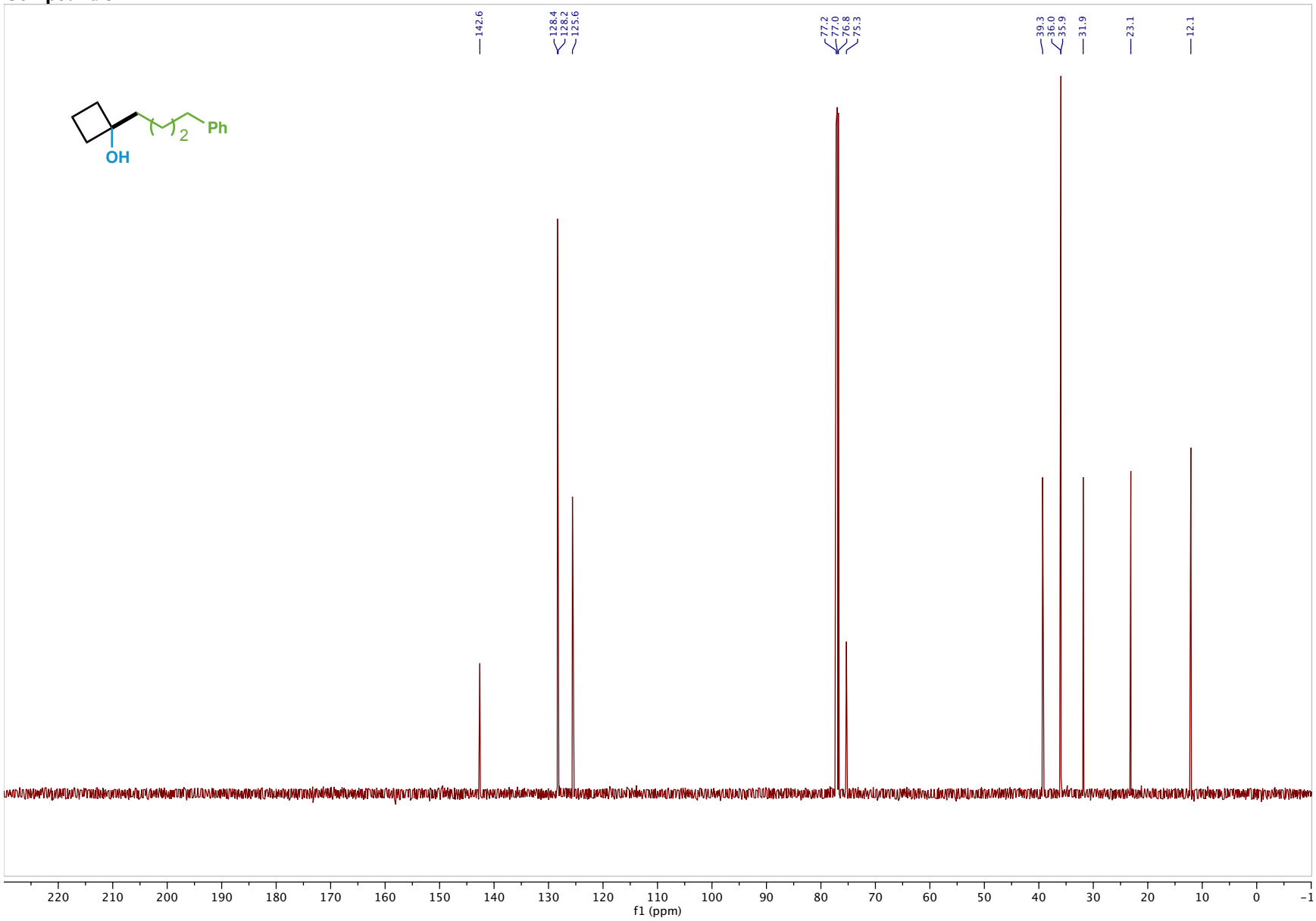
Compound 30


142.1
128.4
125.8
77.2
76.8
75.3
71.3
39.2
39.1
37.7
36.1
36.0
32.1
19.5
12.1
OH
OH
2
Ph
f1 (ppm)

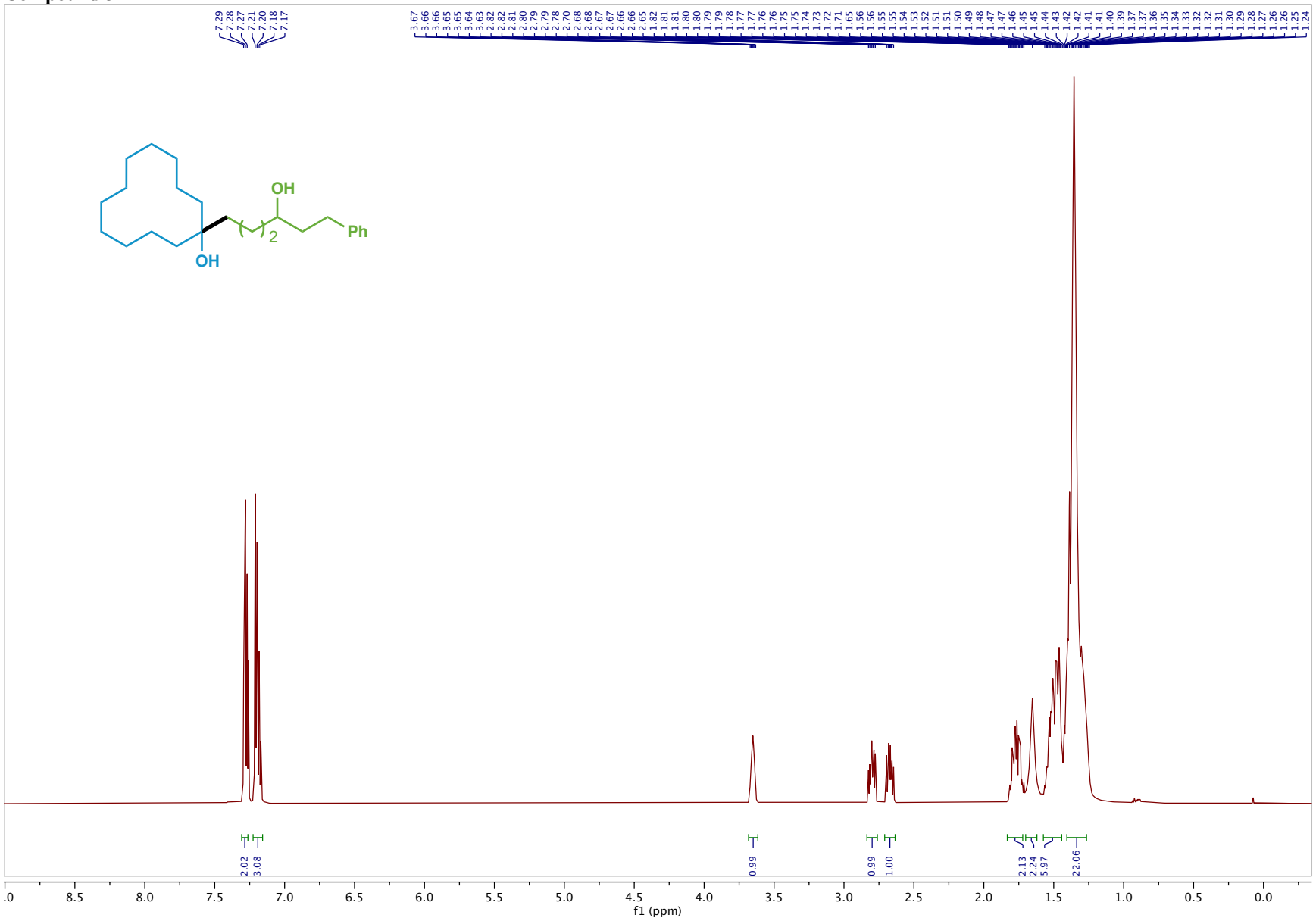
Compound 31



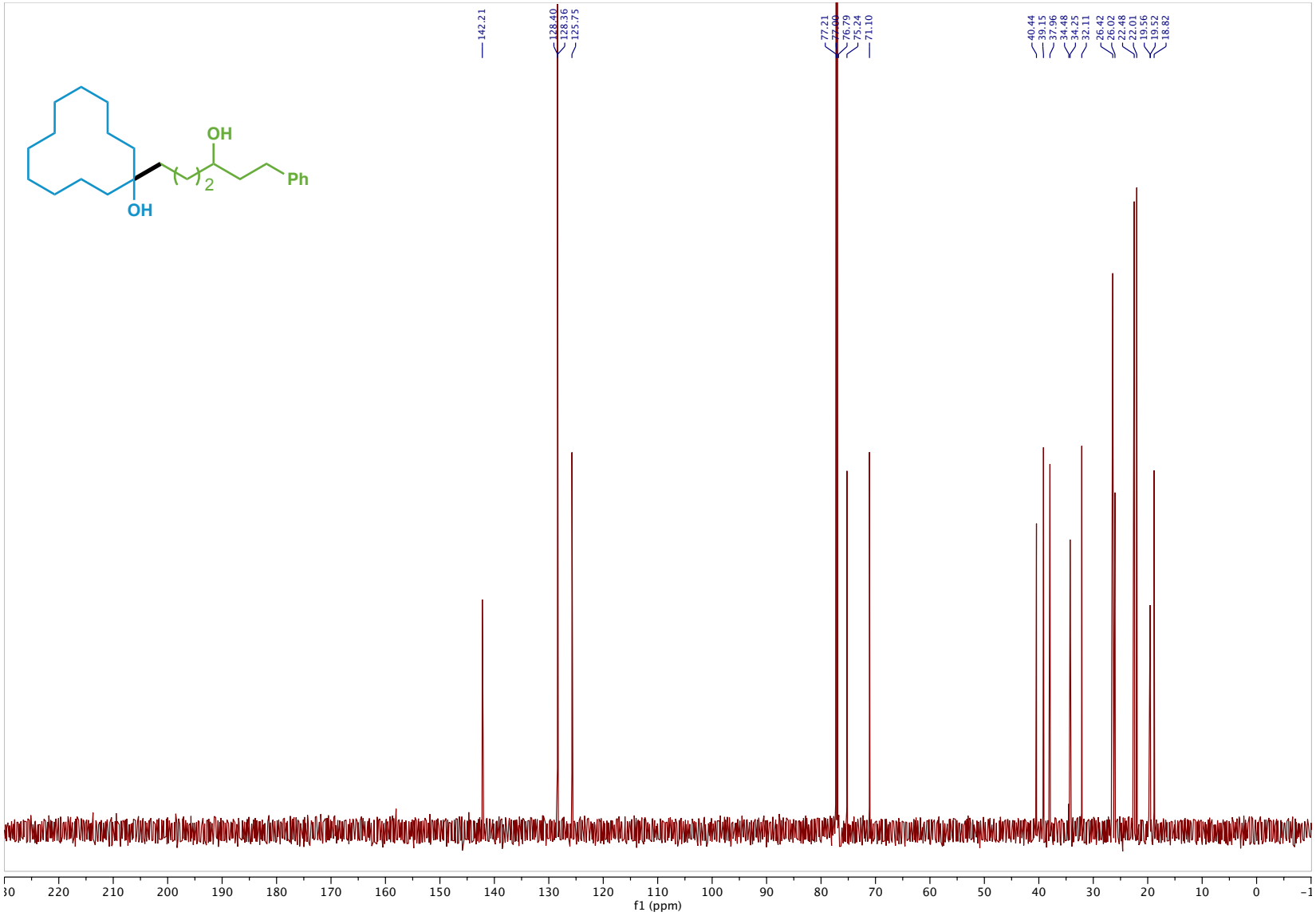
Compound 31


142.6
128.4
128.2
125.6
77.2
77.0
76.8
75.3
39.3
36.0
35.9
31.9
23.1
12.1
OH
2
Ph
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−1
f1 (ppm)

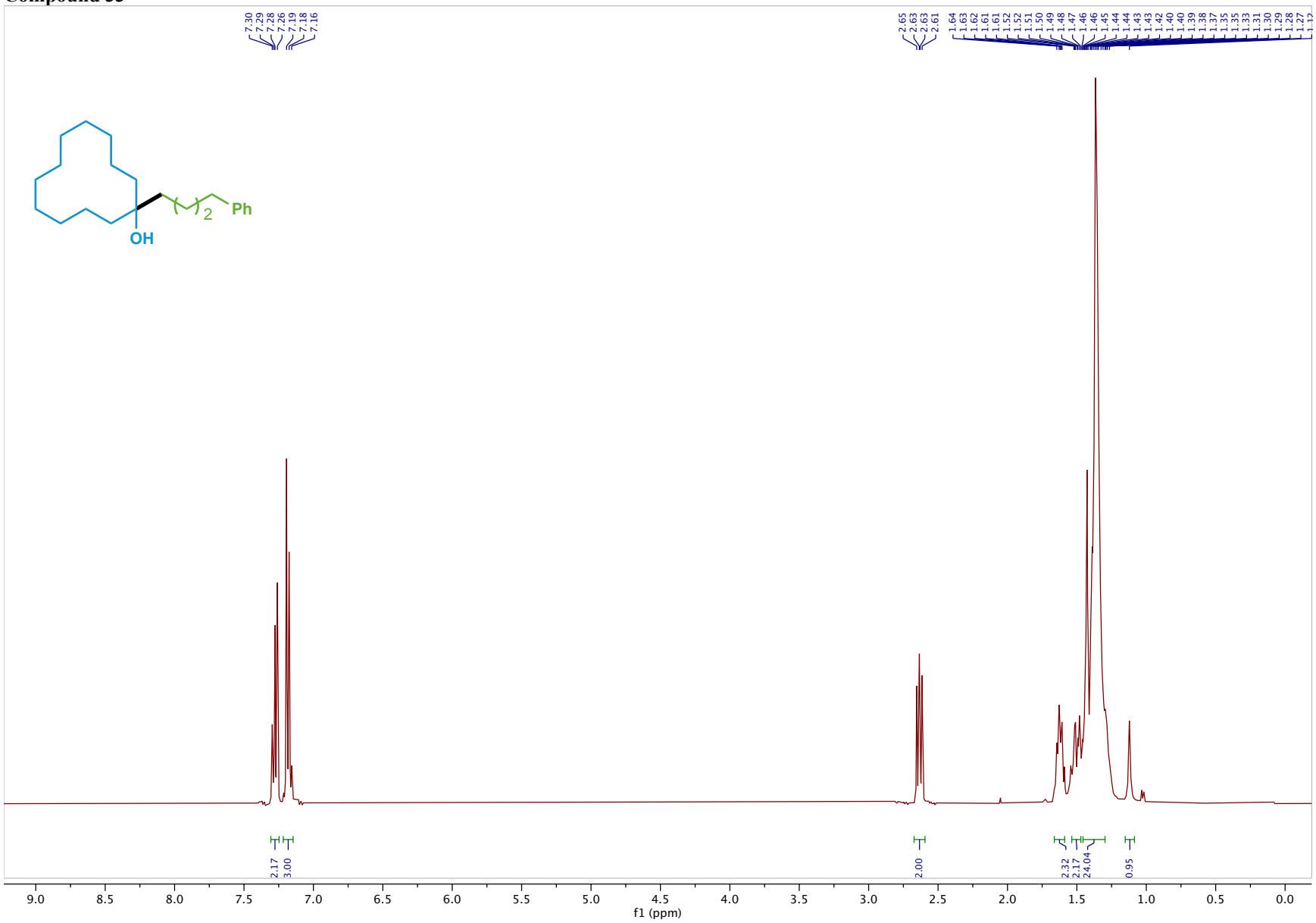
Compound 32


OH
OH
Ph
2
7.29 7.28 7.27 7.21 7.20 7.18 7.17
3.67 3.66 3.66 3.65 3.65 3.64 3.63 2.82 2.82 2.81 2.80 2.79 2.79 2.78 2.70 2.68 2.68 2.67 2.67 2.66 2.66 2.65 1.82 1.81 1.81 1.80 1.80 1.79 1.79 1.78 1.77 1.77 1.76 1.76 1.75 1.75 1.74 1.73 1.72 1.71 1.65 1.56 1.56 1.55 1.55 1.54 1.53 1.52 1.51 1.51 1.50 1.49 1.48 1.47 1.47 1.46 1.45 1.45 1.44 1.43 1.42 1.42 1.41 1.41 1.40 1.39 1.37 1.37 1.36 1.35 1.34 1.33 1.32 1.32 1.31 1.30 1.29 1.28 1.27 1.26 1.26 1.25 1.24
2.02
3.08
0.99
0.99
1.00
2.13
2.24
5.97
22.06
.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
f1 (ppm)

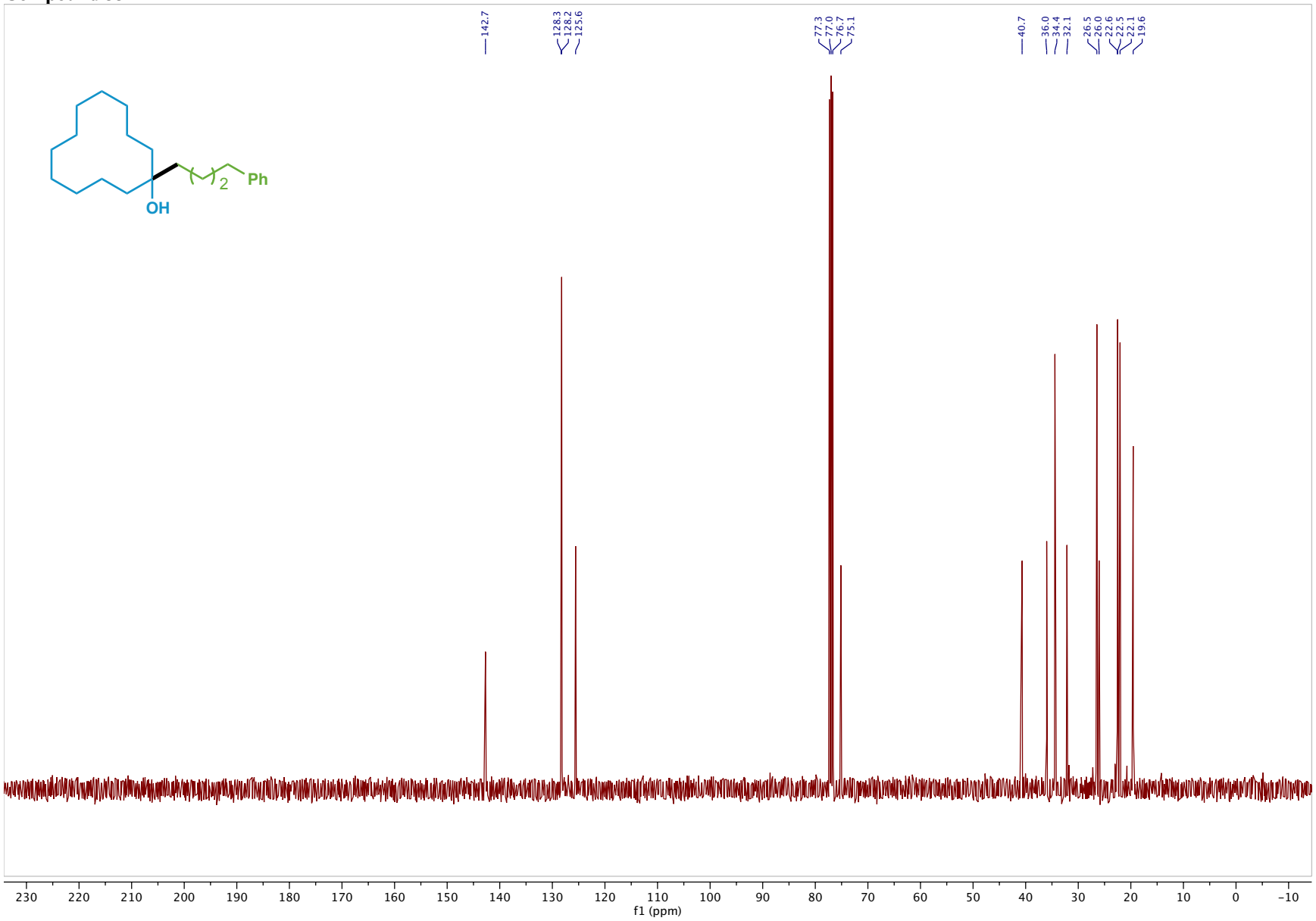
Compound 32


142.21
128.40
128.36
125.75
77.21
77.00
76.79
75.24
71.10
40.44
39.15
37.96
34.48
34.25
32.11
26.42
26.02
22.48
22.01
19.56
19.52
18.82
OH
OH
2
Ph
f1 (ppm)

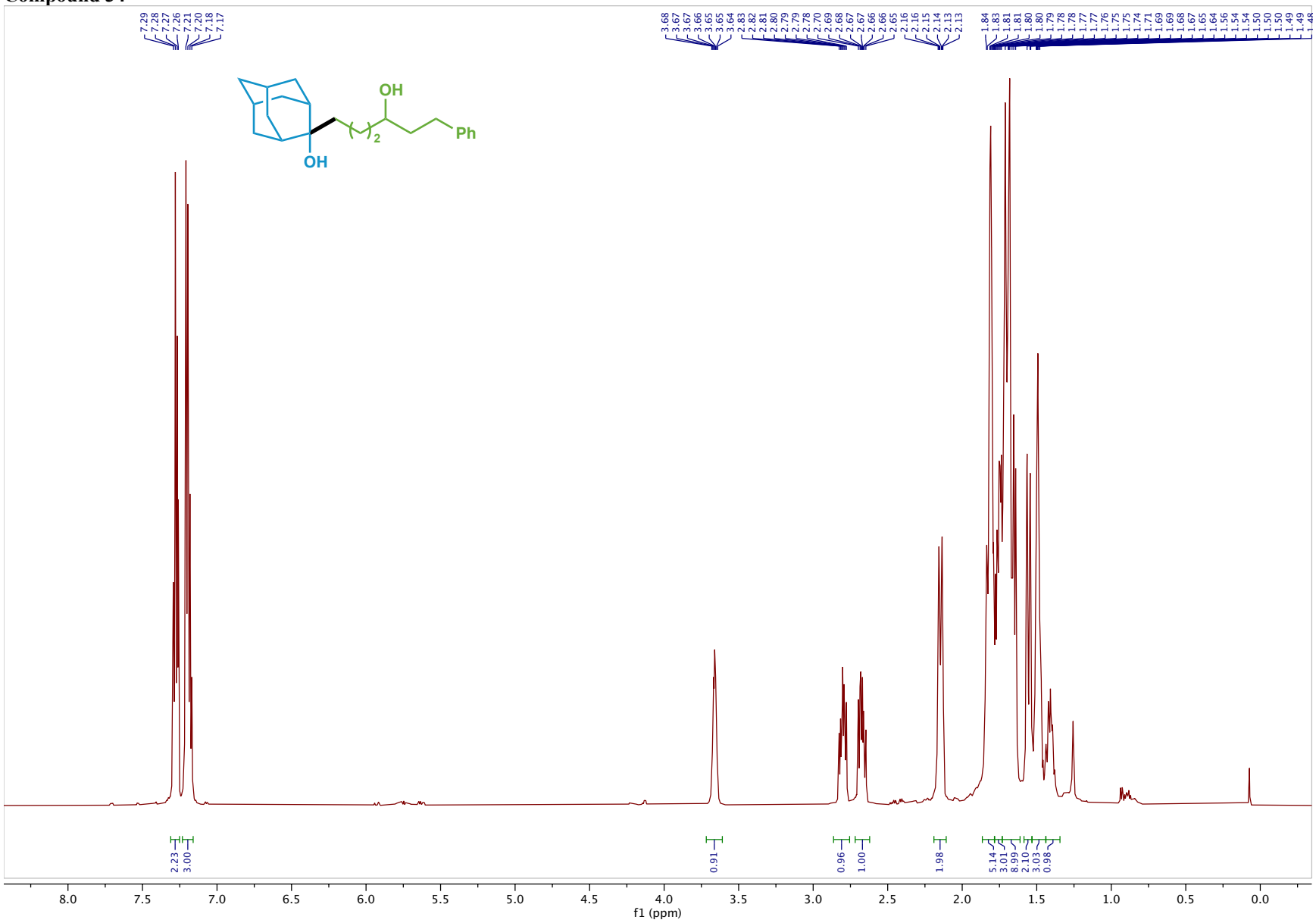
Compound 33


7.30
7.29
7.28
7.26
7.19
7.18
7.16
2.65
2.63
2.63
2.61
1.64
1.63
1.62
1.61
1.61
1.52
1.52
1.51
1.50
1.49
1.48
1.47
1.46
1.46
1.45
1.44
1.44
1.43
1.43
1.42
1.40
1.40
1.39
1.38
1.37
1.35
1.35
1.33
1.31
1.30
1.29
1.28
1.27
OH
2
Ph
2.17
3.00
2.00
2.32
2.17
24.04
0.95
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
f1 (ppm)

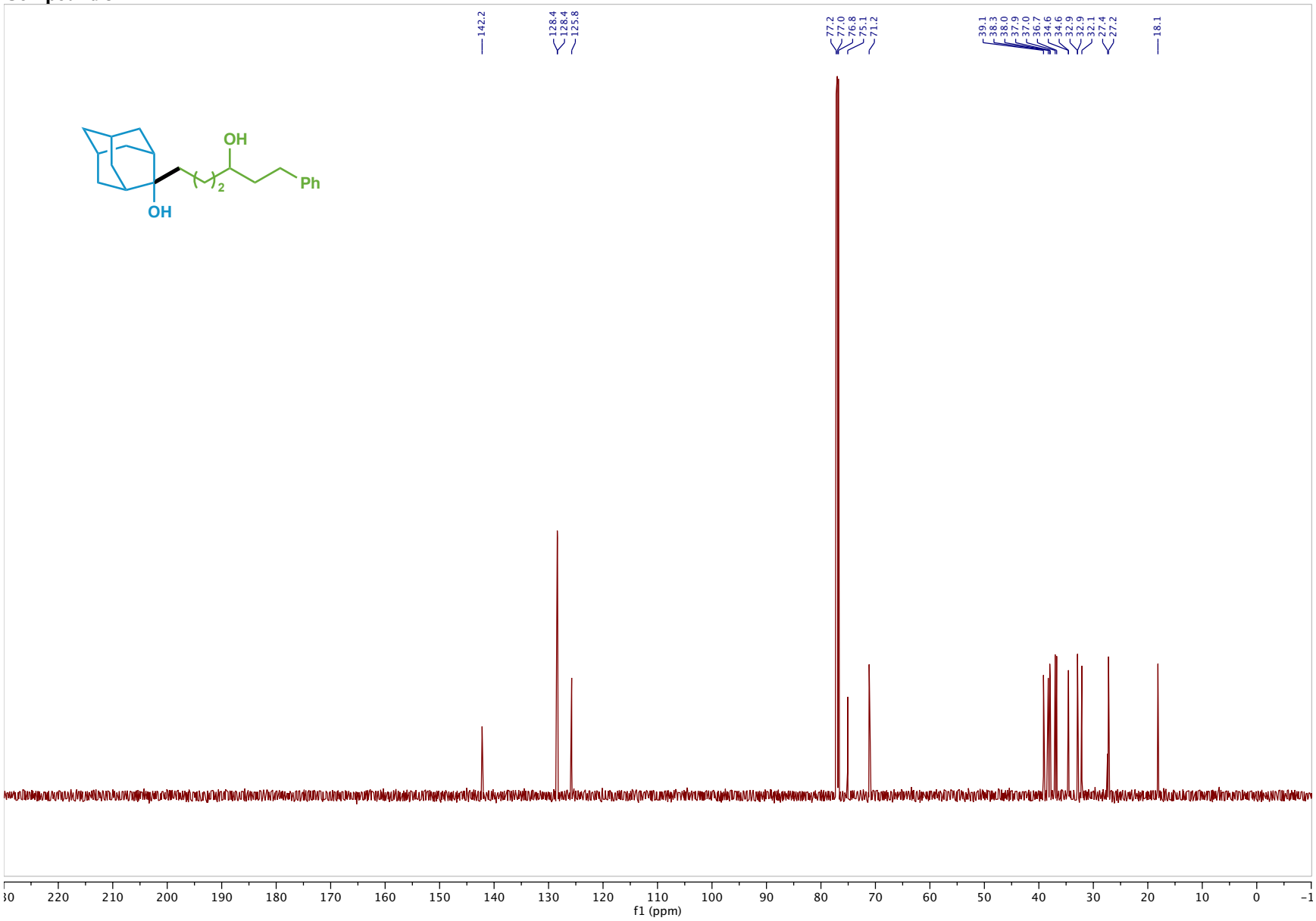
Compound 33


142.7
128.3
128.2
125.6
77.3
77.0
76.7
75.1
40.7
36.0
34.4
32.1
26.5
26.0
22.6
22.5
22.1
19.6
OH
2
Ph
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

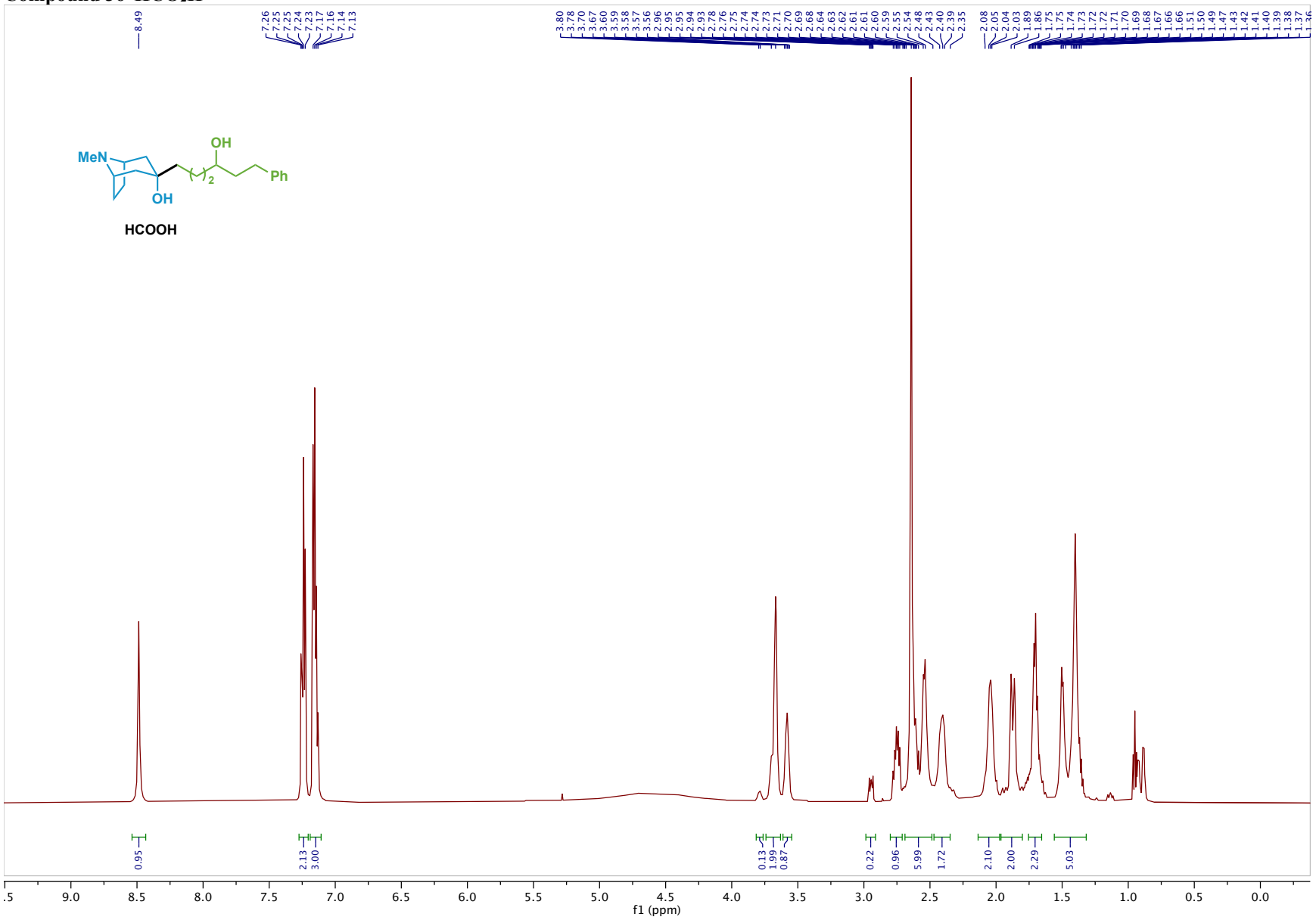
Compound 34



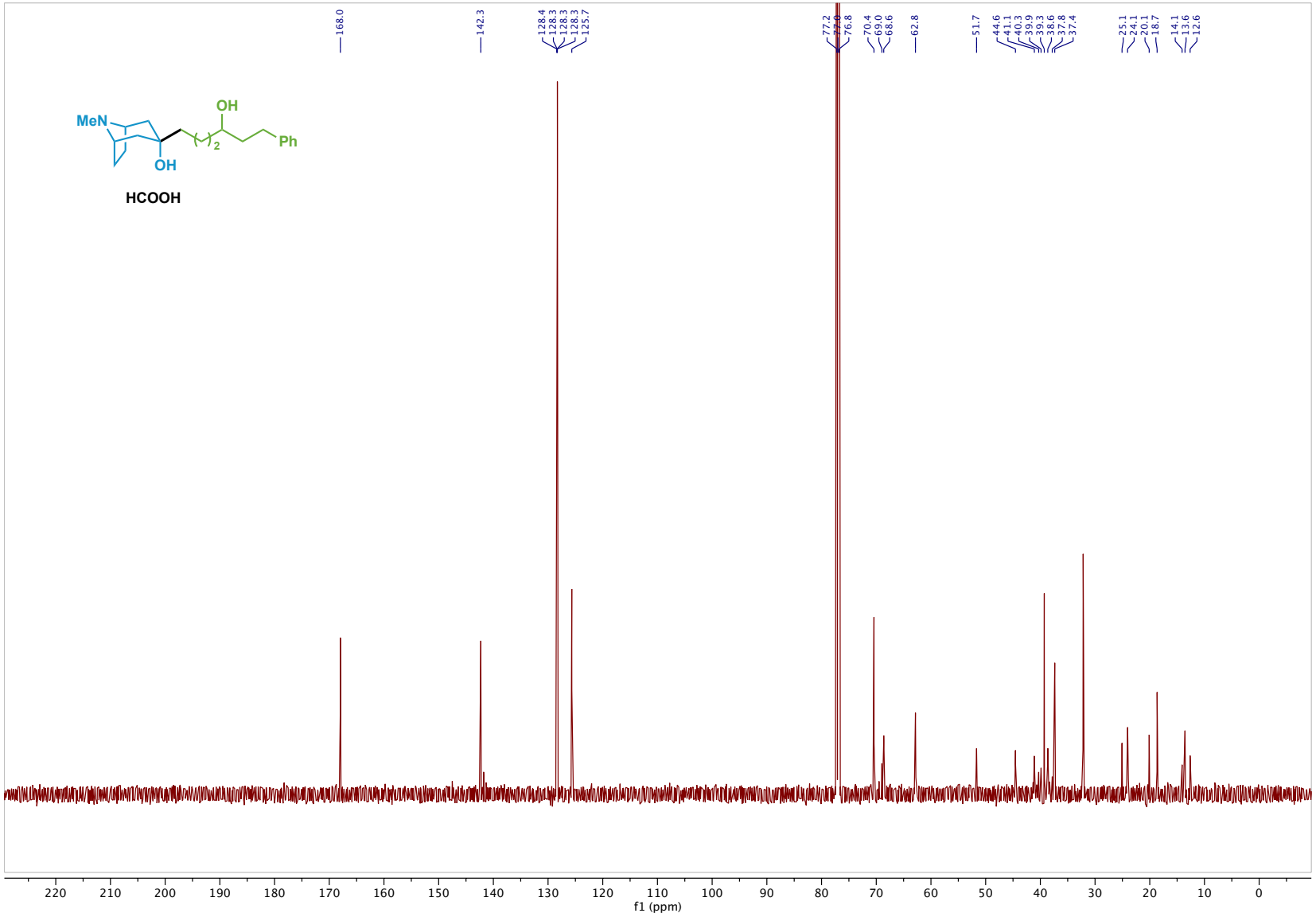
Compound 34


142.2
128.4
128.4
125.8
77.2
77.0
76.8
75.1
71.2
39.1
38.3
38.0
37.9
37.0
36.7
34.6
34.6
32.9
32.9
32.1
27.4
27.2
18.1
OH
OH
Ph
2
f1 (ppm)

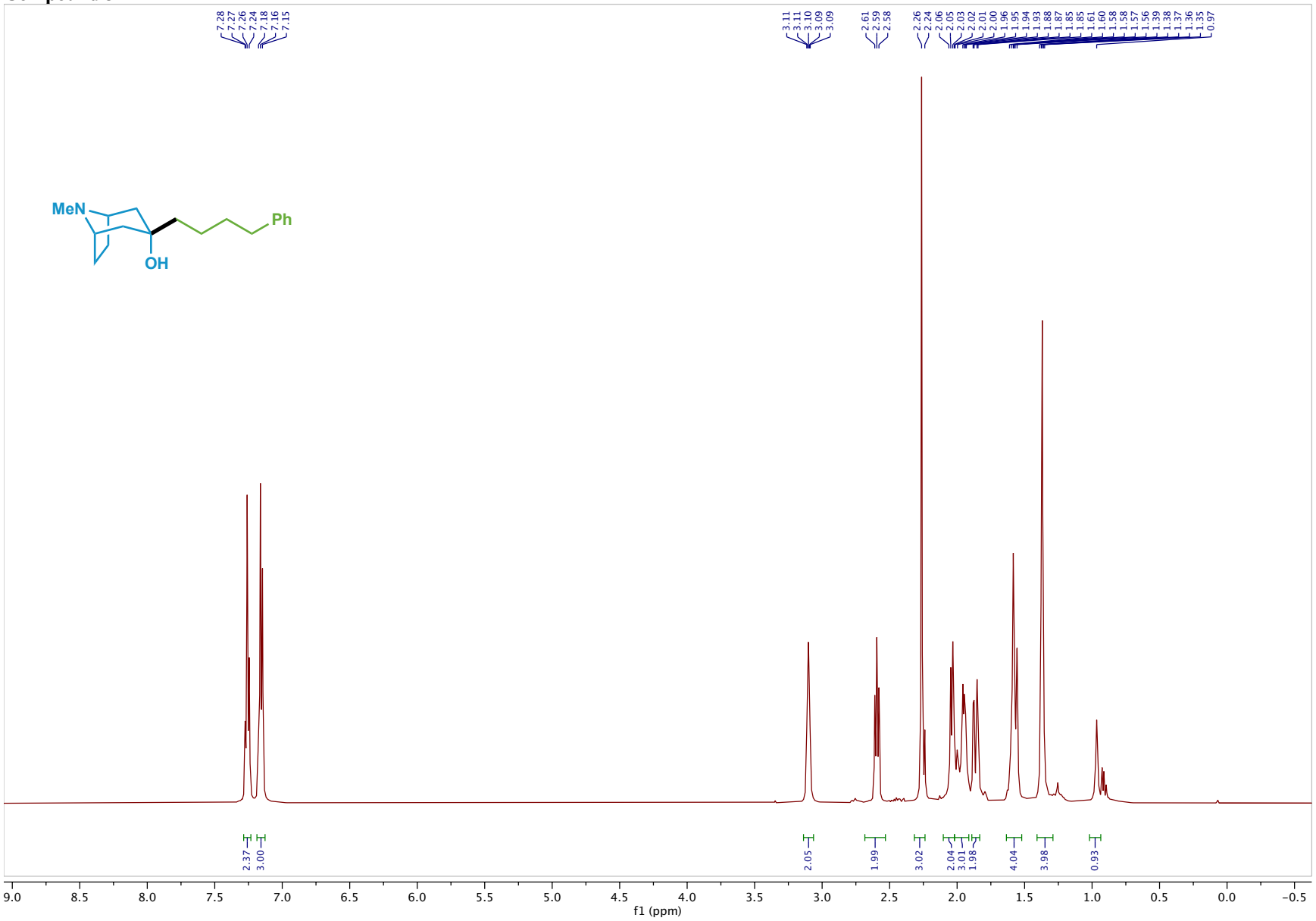
Compound 36•HCO_2H



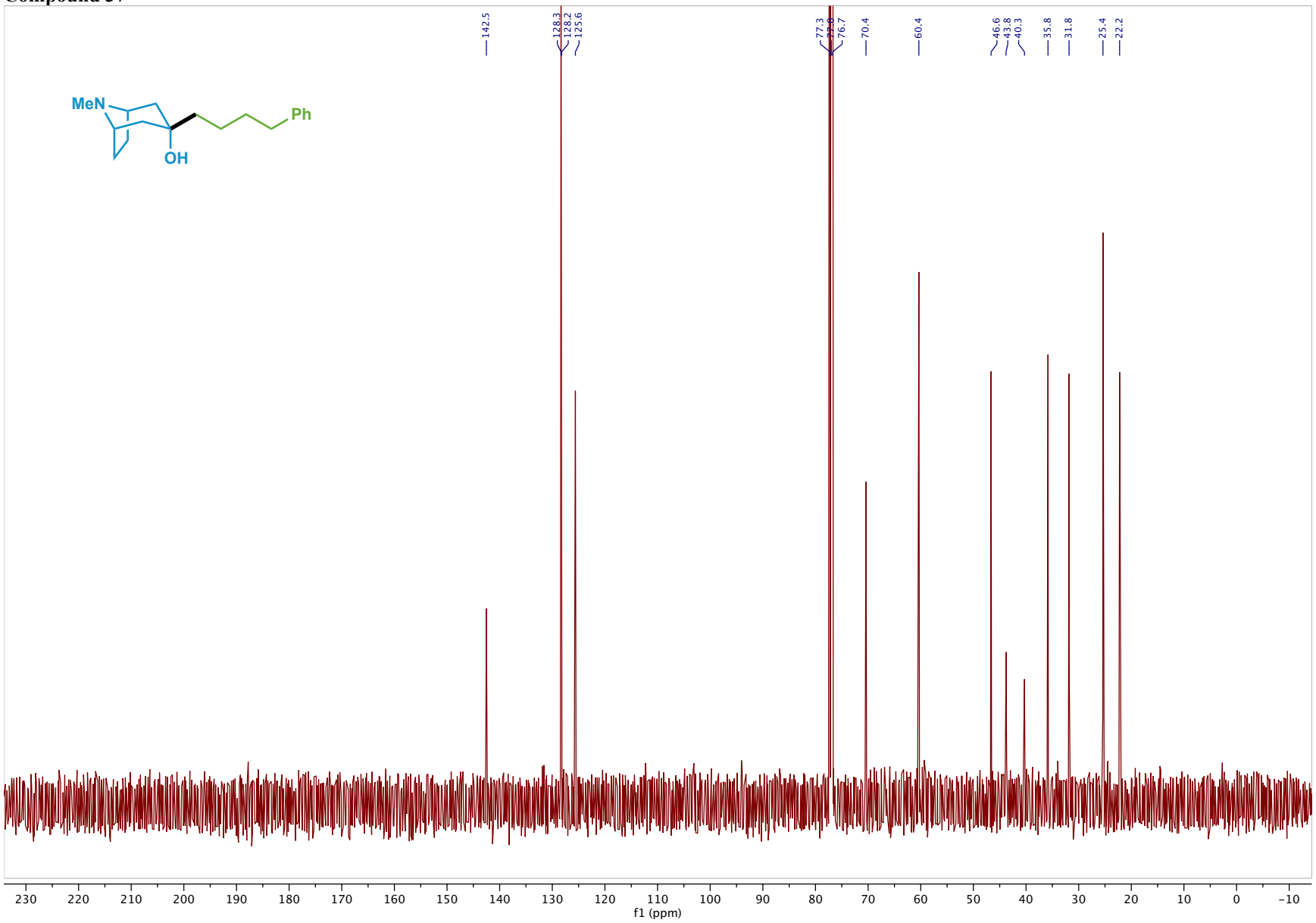
Compound 36•HCO_2H



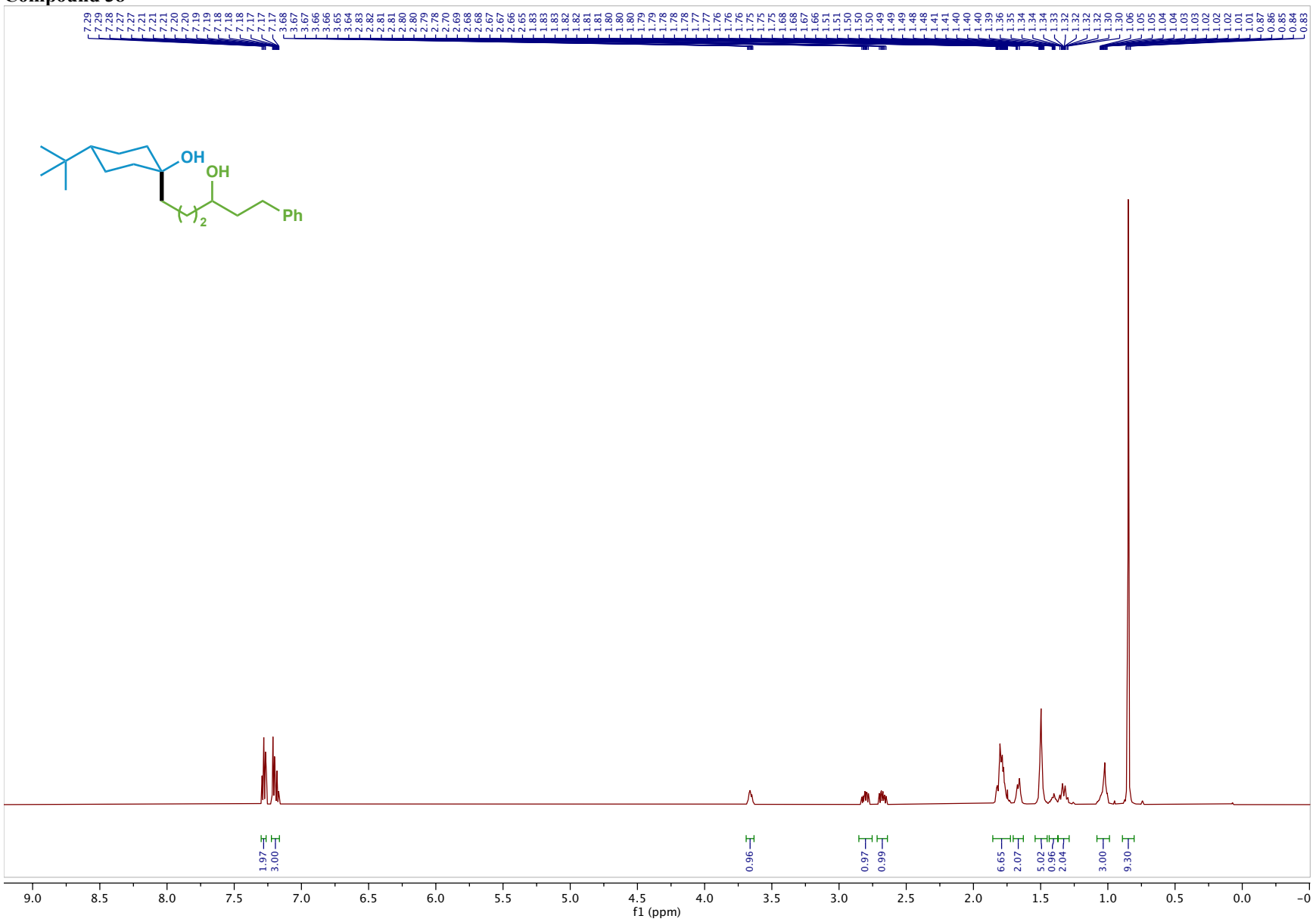
Compound 37


7.28
7.27
7.26
7.24
7.18
7.16
7.15
3.11
3.11
3.10
3.09
3.09
2.61
2.59
2.58
2.26
2.24
2.06
2.05
2.03
2.02
2.01
2.00
1.96
1.95
1.94
1.93
1.88
1.87
1.85
1.85
1.61
1.60
1.58
1.58
1.57
1.56
1.39
1.38
1.37
1.36
1.35
0.97
MeN
Ph
OH
2.37
3.00
2.05
1.99
3.02
2.04
3.01
1.98
4.04
3.98
0.93
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
f1 (ppm)

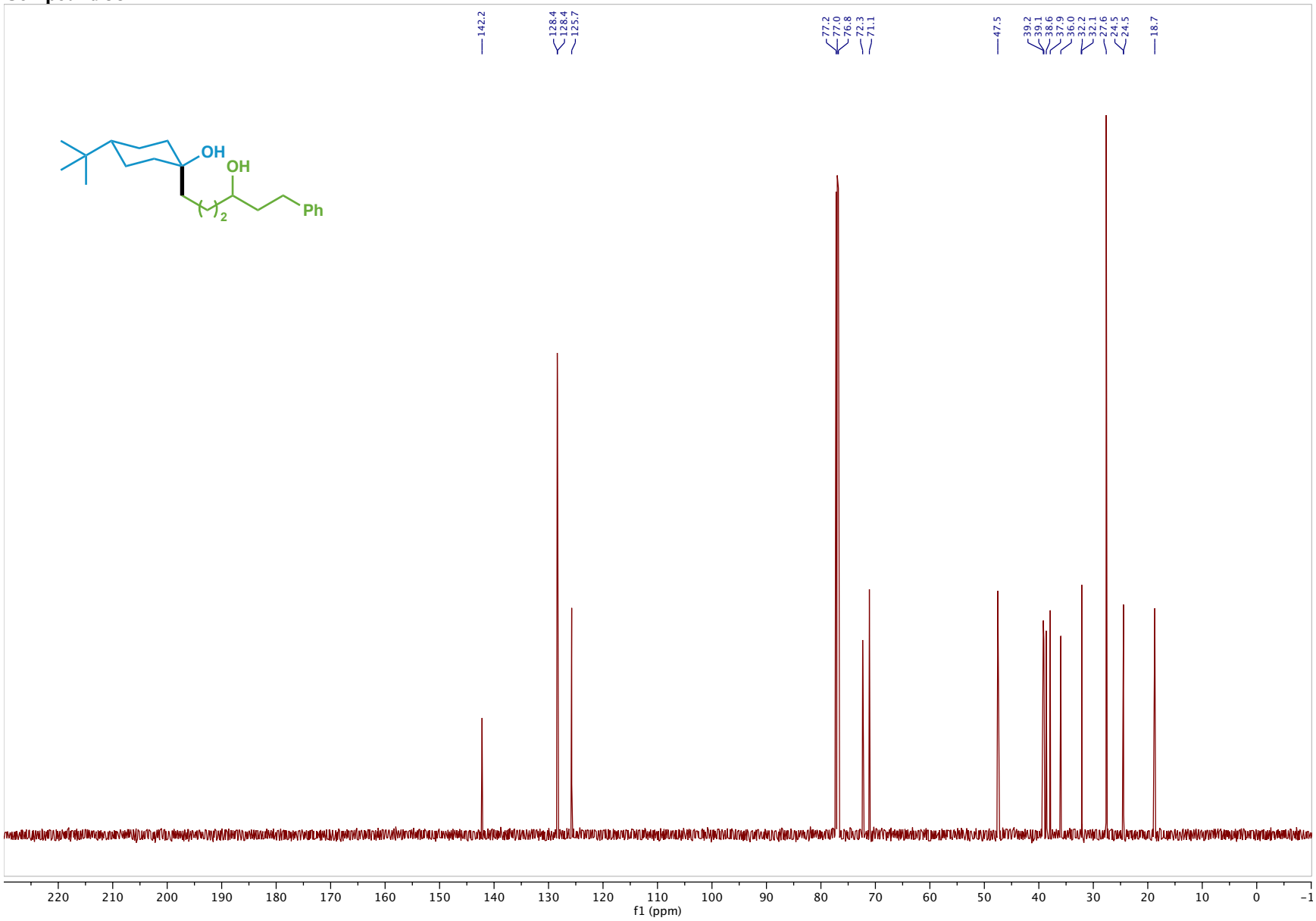
Compound 37


142.5
128.3
128.2
125.6
77.3
77.0
76.7
70.4
60.4
46.6
43.8
40.3
35.8
31.8
25.4
22.2
MeN
Ph
OH
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

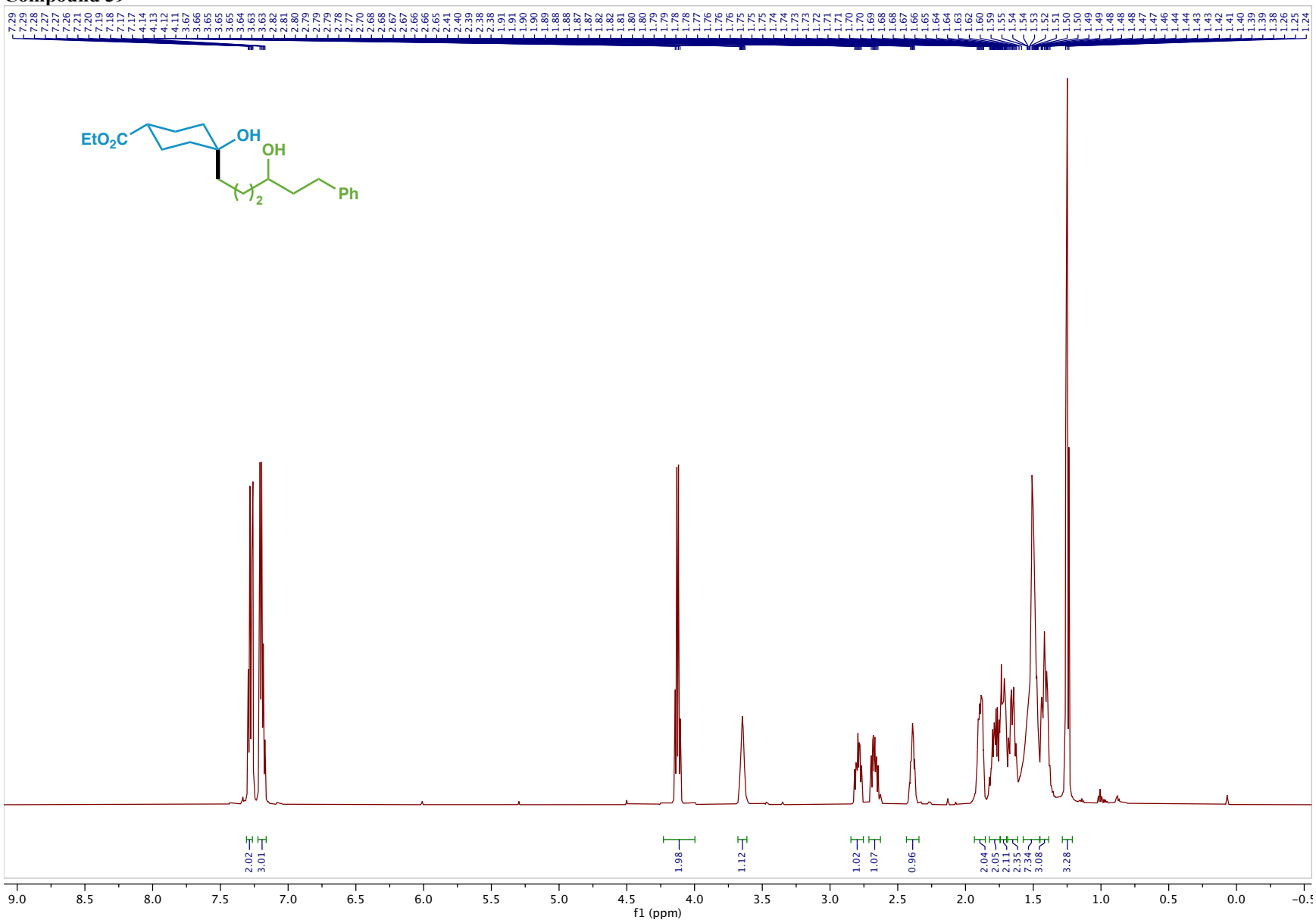
Compound 38



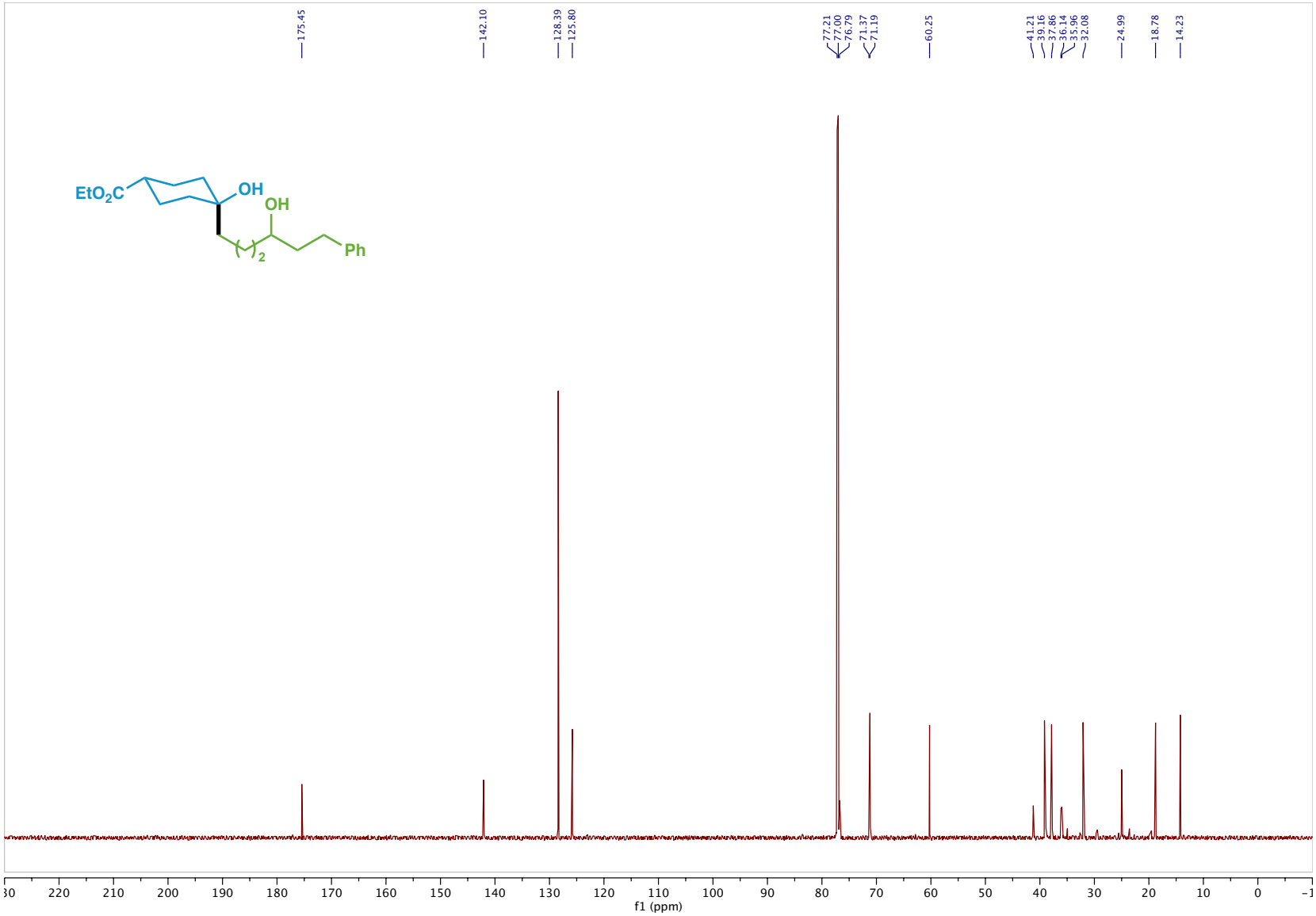
Compound 38


142.2
128.4
128.4
125.7
77.2
77.0
76.8
72.3
71.1
47.5
39.2
39.1
38.6
37.9
36.0
32.2
32.1
27.6
24.5
24.5
18.7
OH
OH
Ph
2
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−1
f1 (ppm)

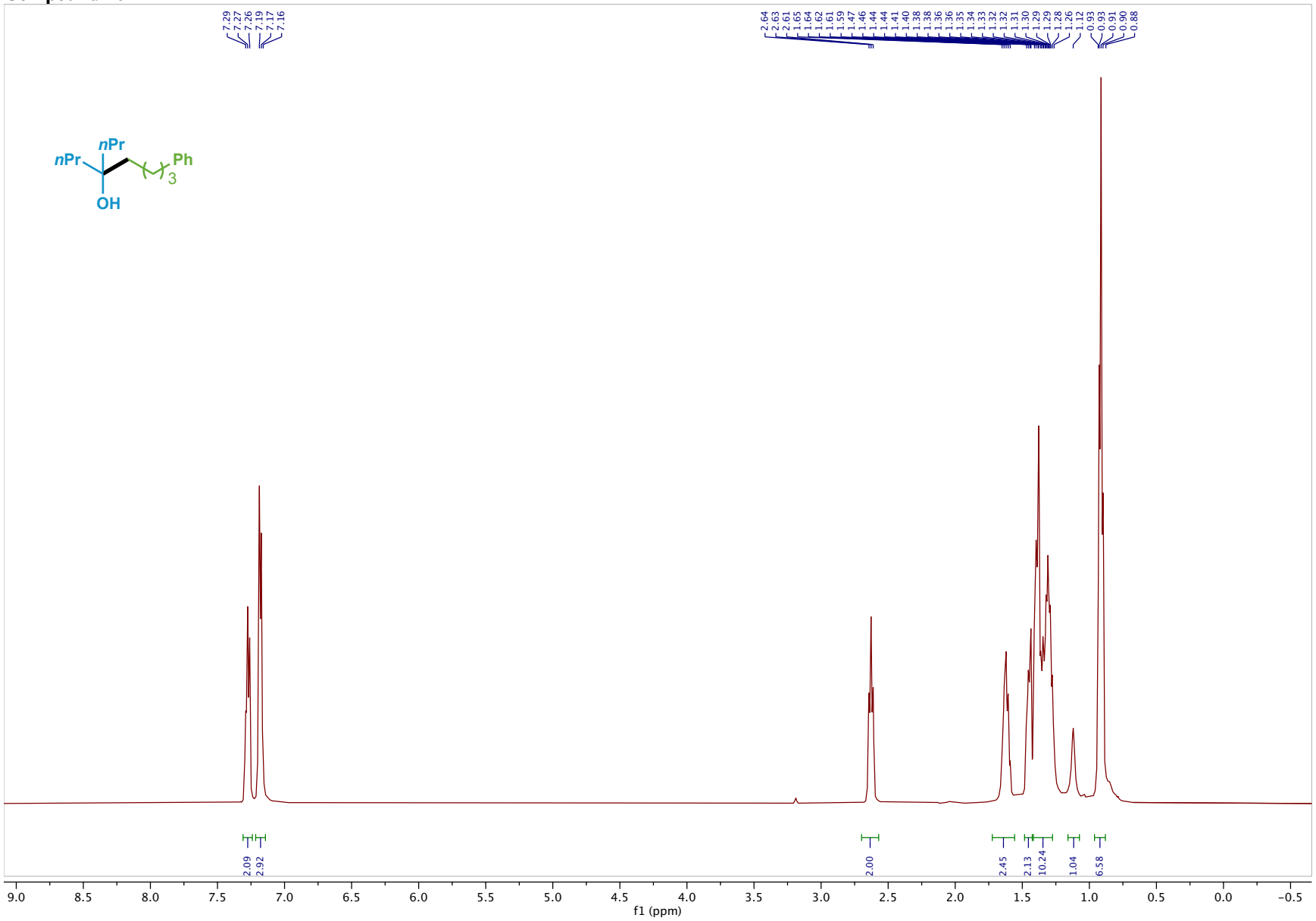
Compound 39


EtO2C
OH
OH
Ph
2
2.02
3.01
1.98
1.12
1.02
1.07
0.96
2.04
2.05
2.11
2.35
7.34
3.08
3.28
f1 (ppm)

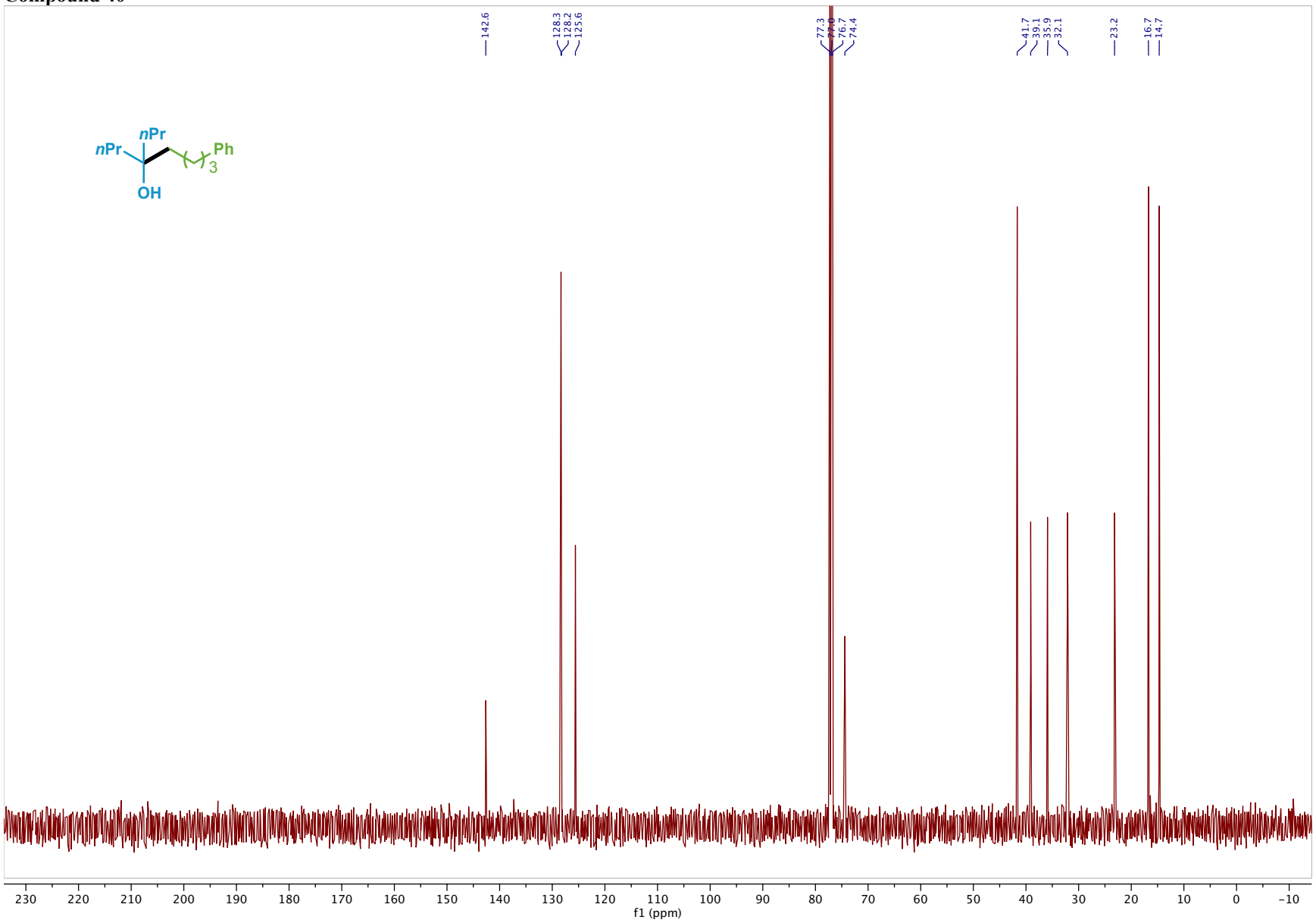
Compound 39


175.45
142.10
128.39
125.80
77.21
77.00
76.79
71.37
71.19
60.25
41.21
39.16
37.86
36.14
35.96
32.08
24.99
18.78
14.23
EtO2C
OH
OH
2
Ph
f1 (ppm)

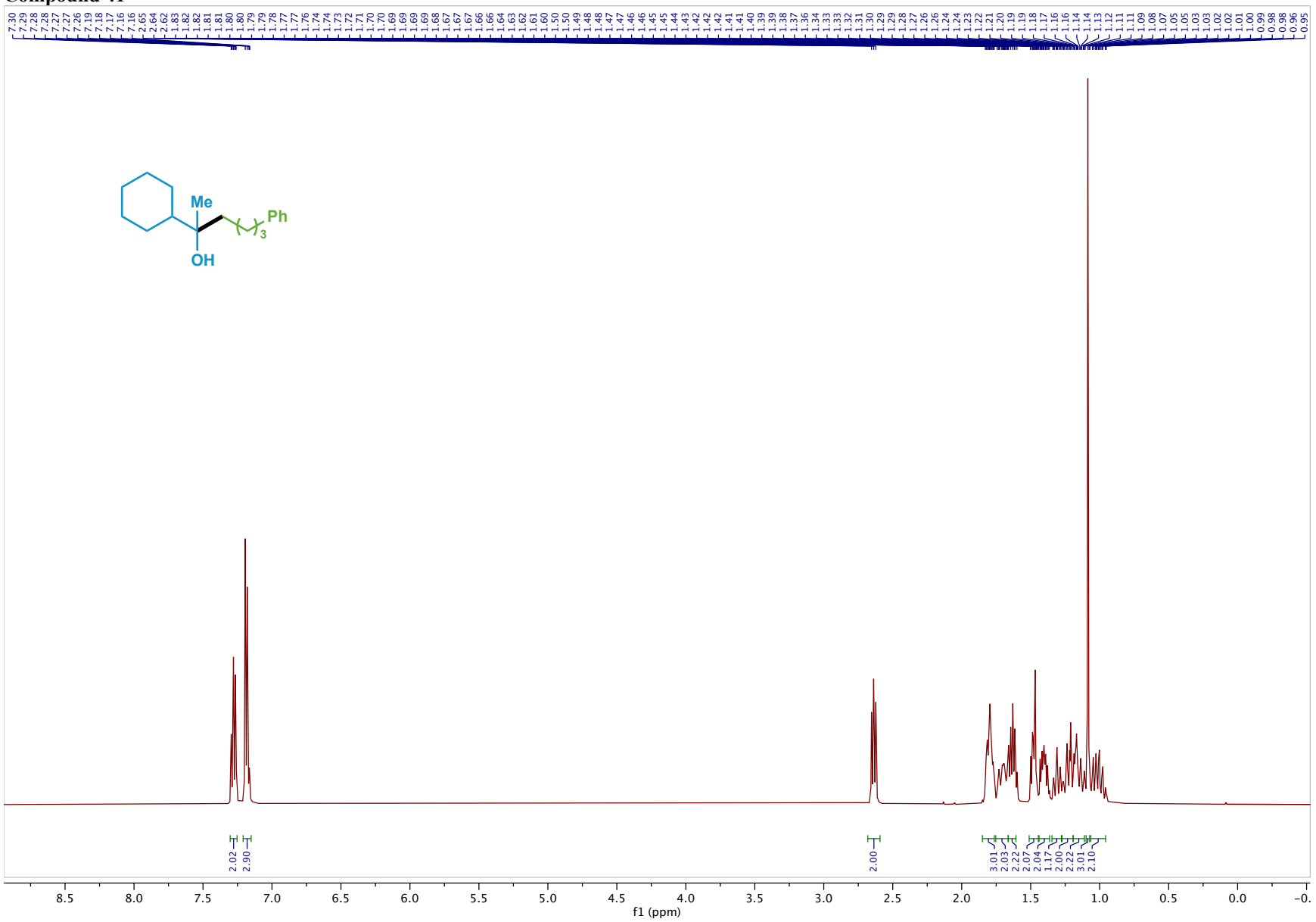
Compound 40


7.29
7.27
7.26
7.19
7.17
7.16
2.64
2.63
2.61
1.65
1.64
1.62
1.61
1.59
1.47
1.46
1.44
1.44
1.41
1.40
1.38
1.38
1.36
1.36
1.35
1.34
1.33
1.32
1.32
1.31
1.30
1.29
1.29
1.28
1.26
1.12
0.93
0.93
0.91
0.90
0.88
nPr
nPr
Ph
3
OH
2.09
2.92
2.00
2.45
2.13
10.24
1.04
6.58
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
f1 (ppm)

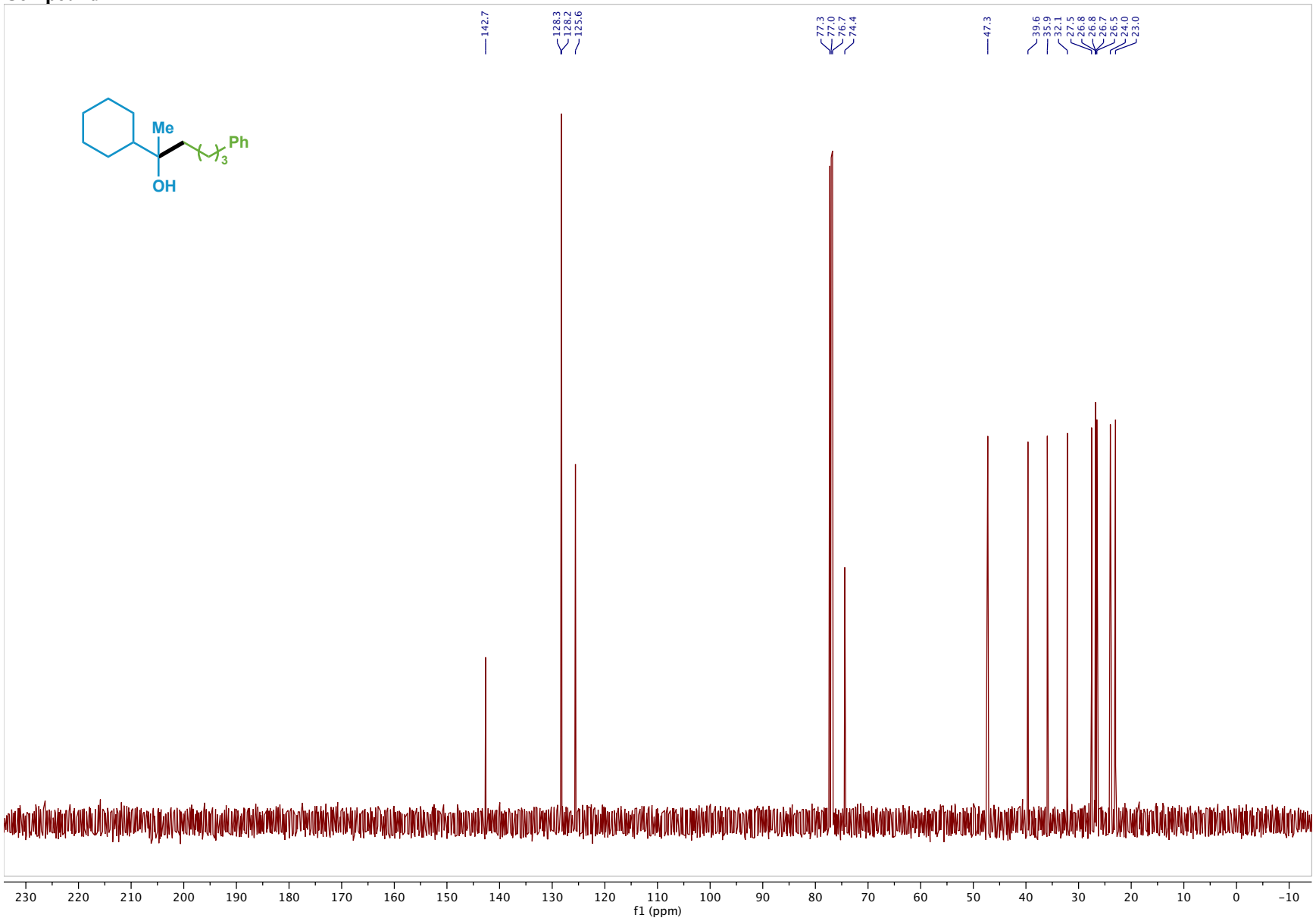
Compound 40


142.6
128.3
128.2
125.6
77.3
77.0
76.7
74.4
41.7
39.1
35.9
32.1
23.2
16.7
14.7
nPr
nPr
OH
Ph
3
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

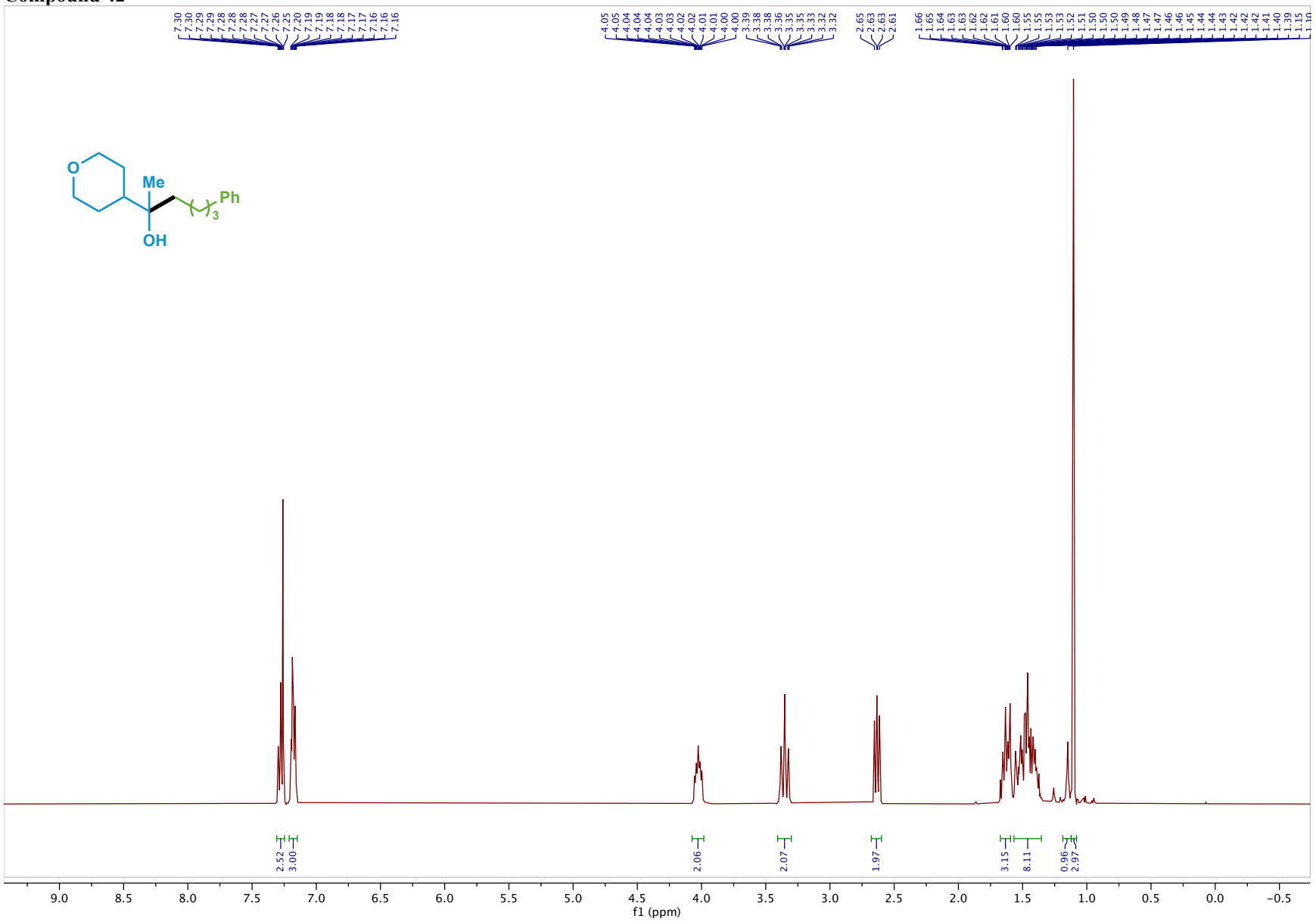
Compound 41


Me
Ph
3
OH
2.02
2.90
2.00
3.01
2.03
2.22
2.07
2.04
1.17
2.00
2.22
3.01
2.10
f1 (ppm)

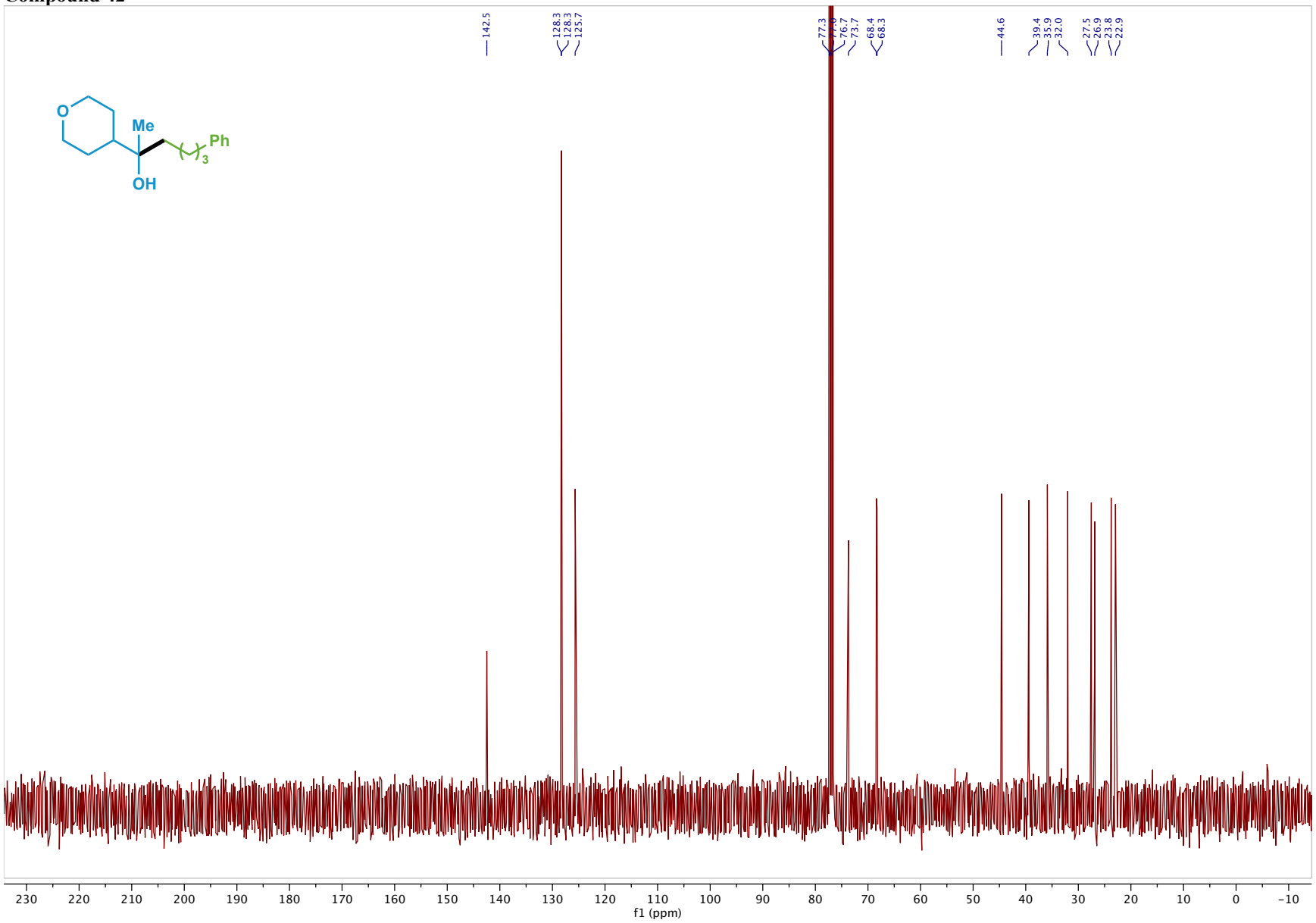
Compound 41


142.7
128.3
128.2
125.6
77.3
77.0
76.7
74.4
47.3
39.6
35.9
32.1
27.5
26.8
26.7
26.5
24.0
23.0
Me
Ph
3
OH
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

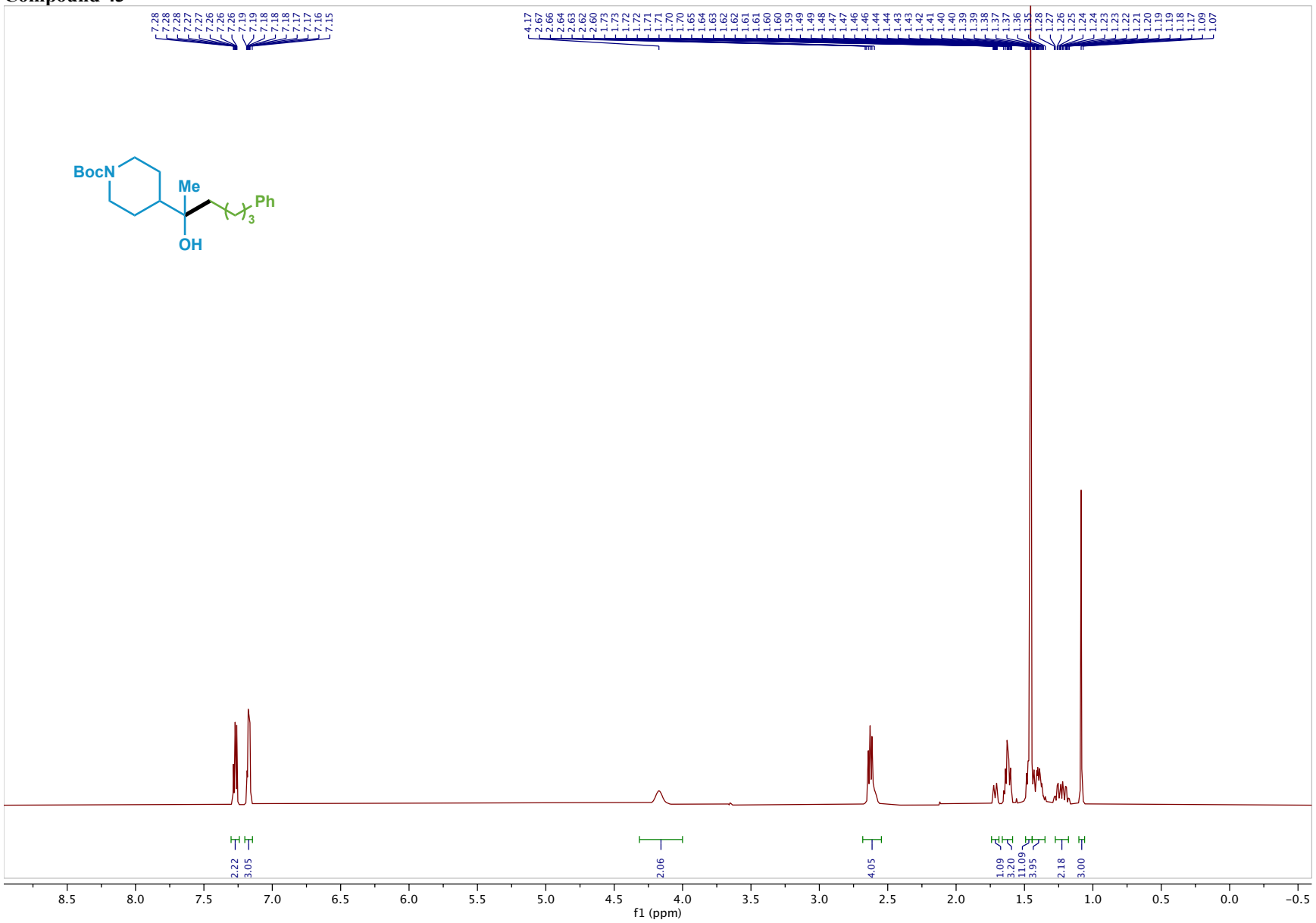
Compound 42



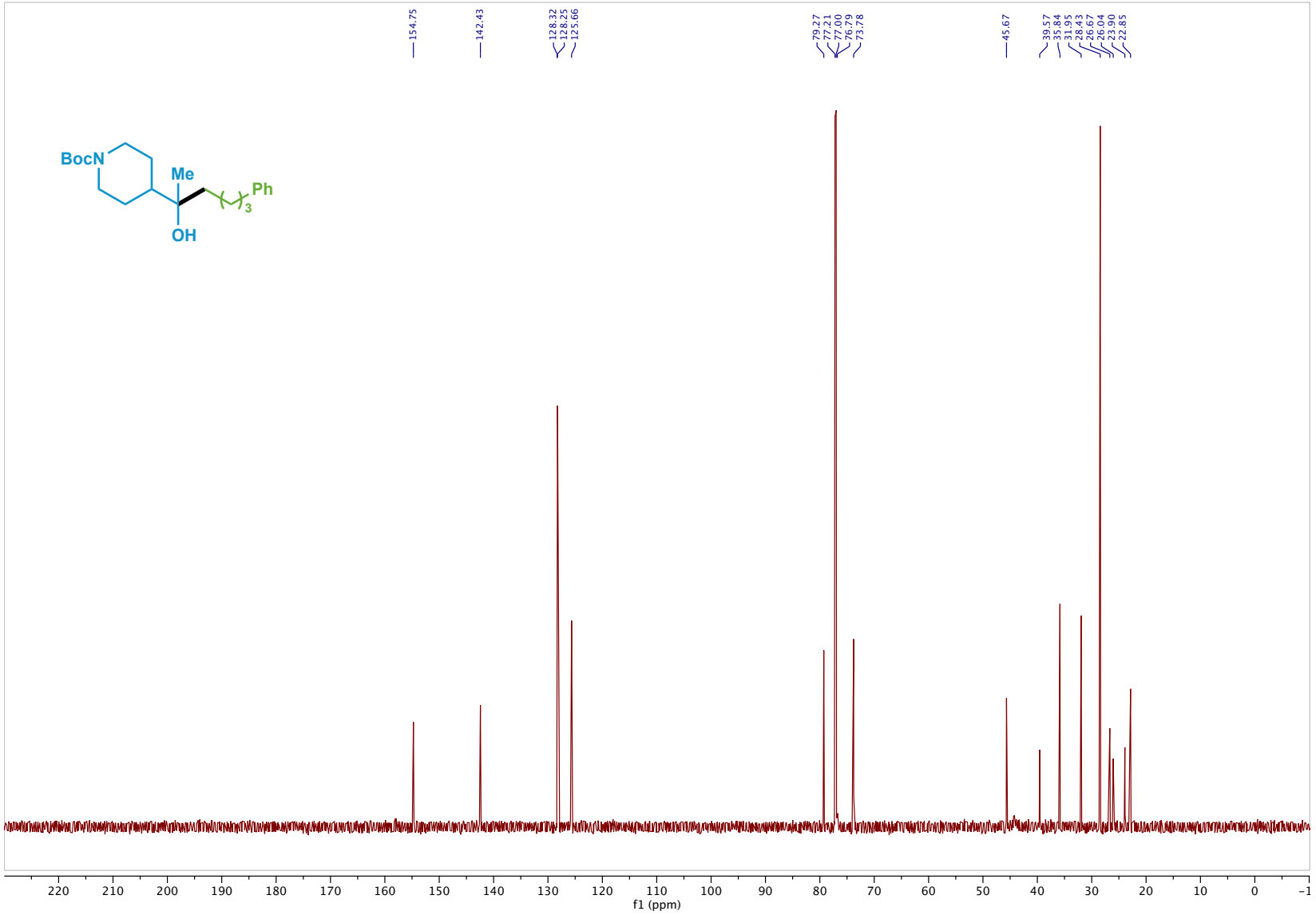
Compound 42


142.5
128.3
128.3
125.7
77.3
76.7
73.7
68.4
68.3
44.6
39.4
35.9
32.0
27.5
26.9
23.8
22.9
O
Me
Ph
3
OH
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

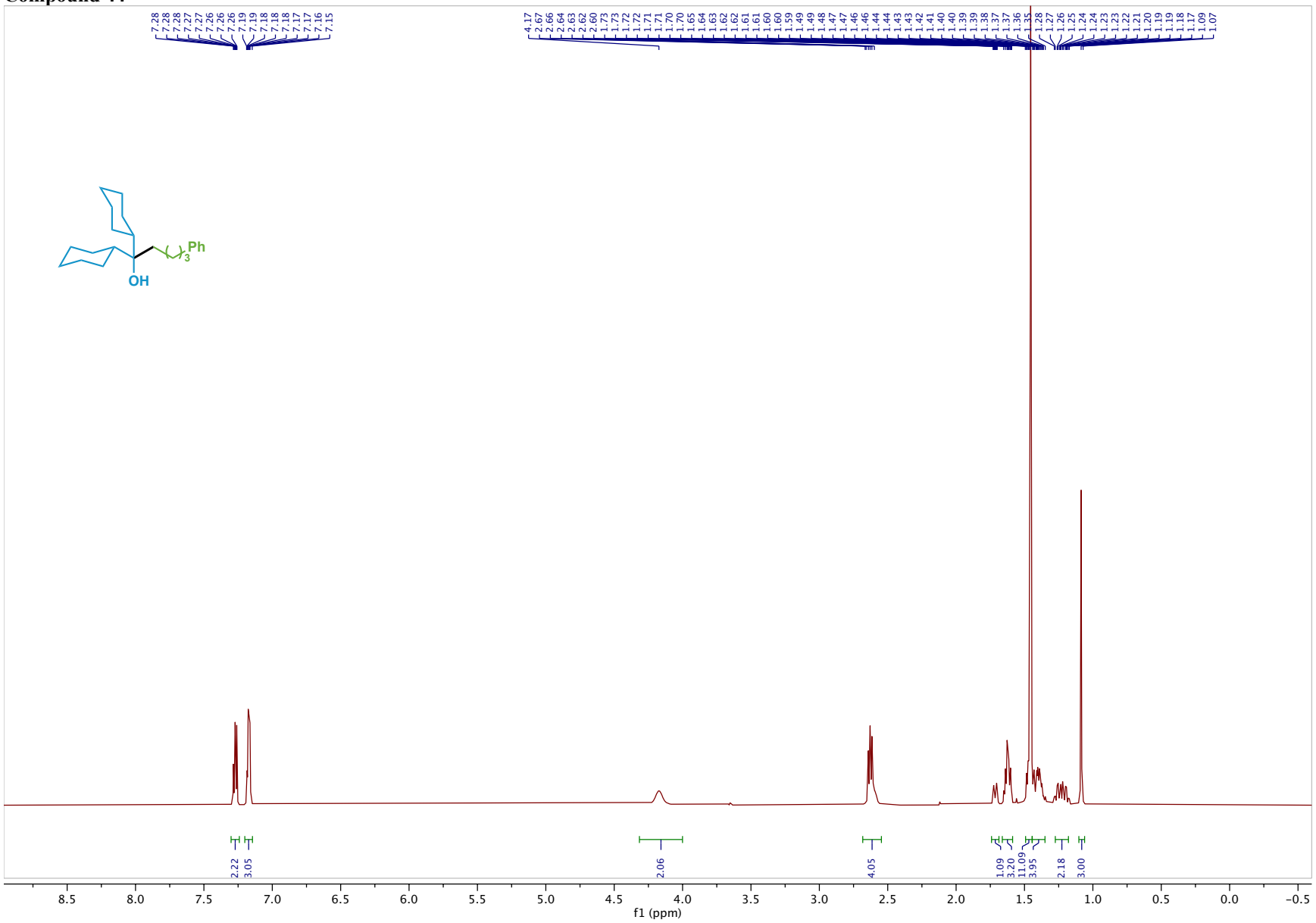
Compound 43



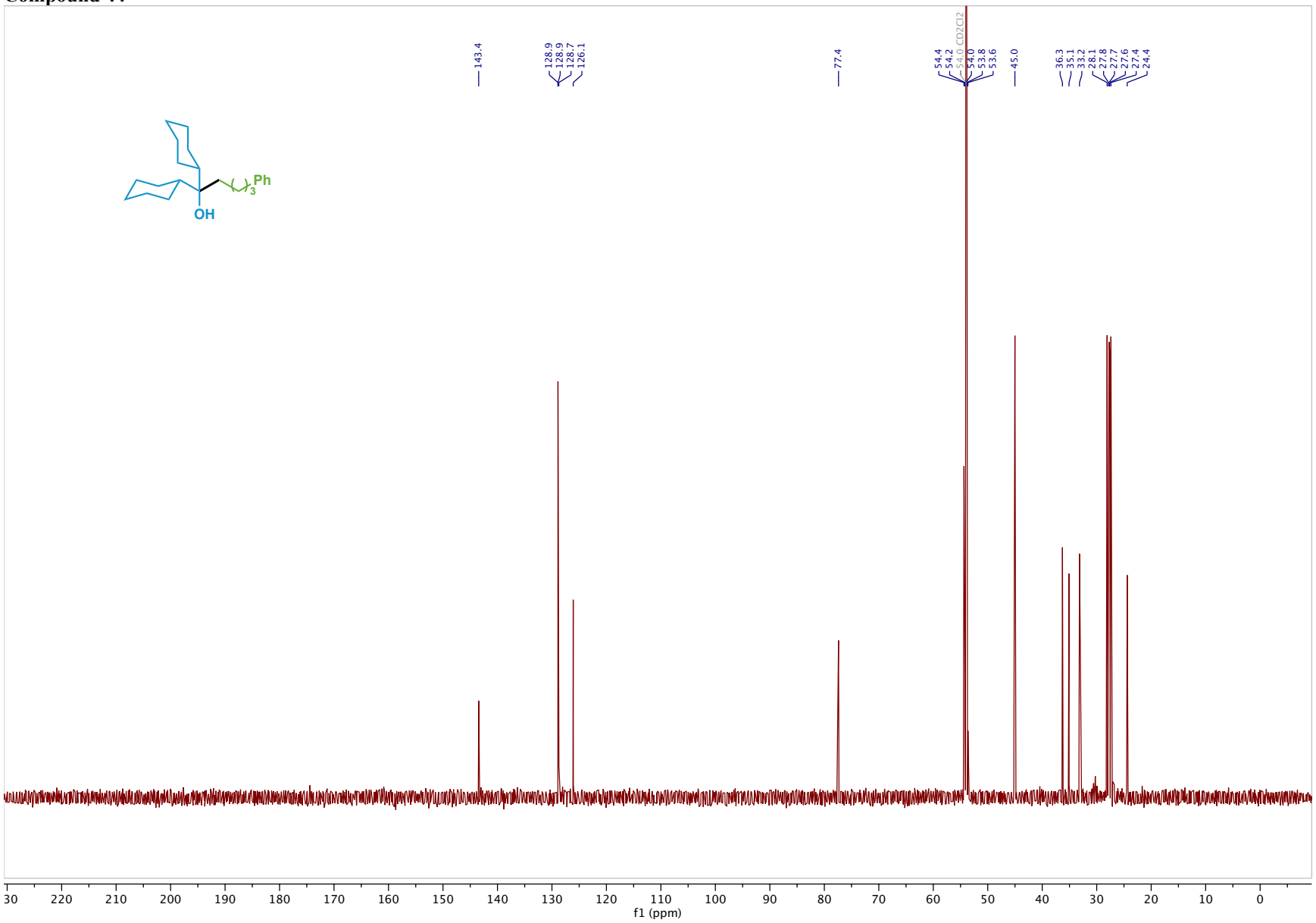
Compound 43


154.75
142.43
128.32
128.25
125.66
79.27
77.21
77.00
76.79
73.78
45.67
39.57
35.84
31.95
28.43
26.67
26.04
23.90
22.85
BocN
Me
Ph
3
OH
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

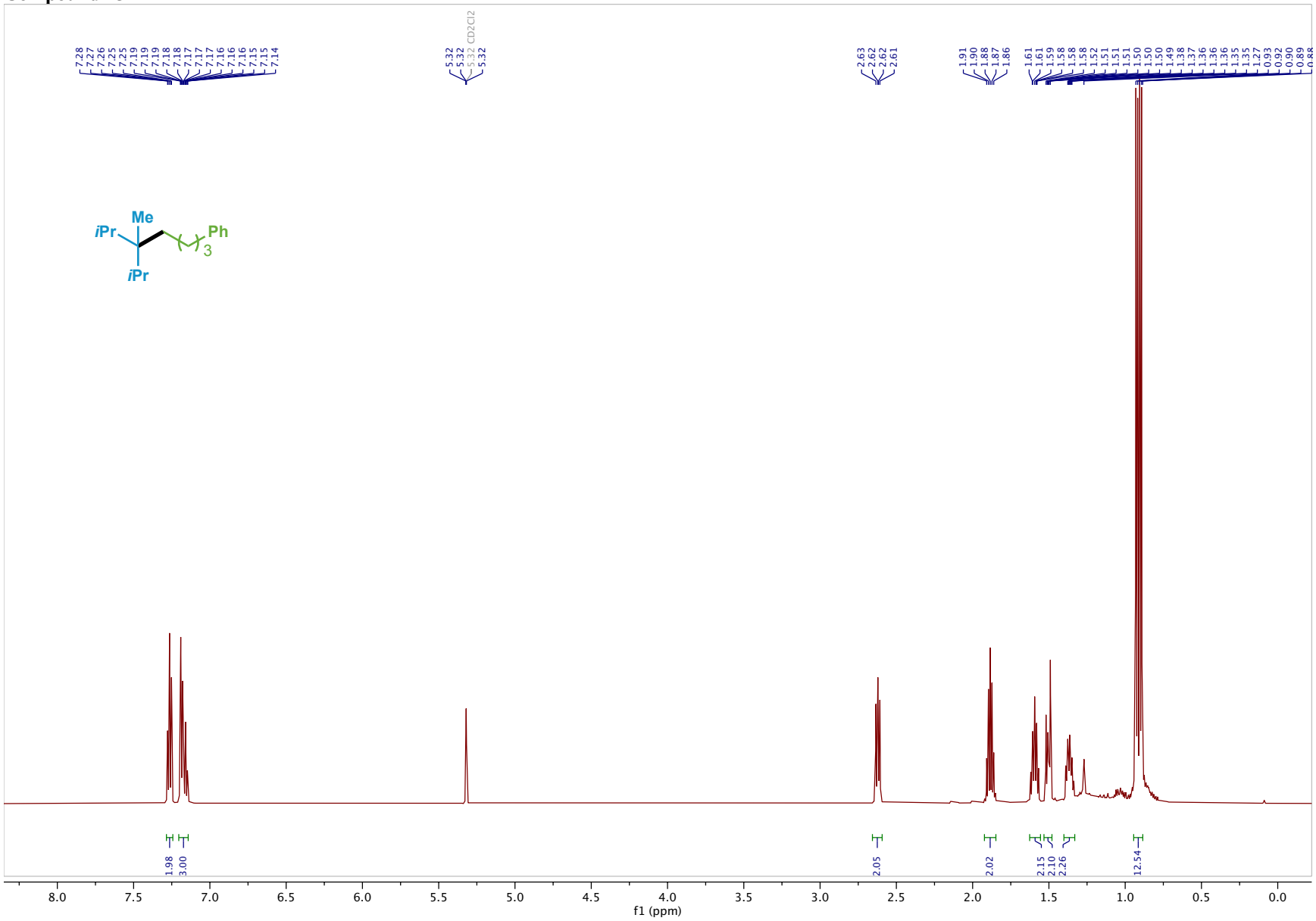
Compound 44


7.28
7.28
7.28
7.27
7.27
7.26
7.26
7.26
7.19
7.19
7.18
7.18
7.18
7.17
7.17
7.16
7.15
4.17
2.67
2.66
2.64
2.63
2.62
2.60
1.73
1.73
1.72
1.72
1.71
1.71
1.70
1.70
1.65
1.64
1.63
1.62
1.62
1.61
1.61
1.60
1.60
1.59
1.49
1.49
1.48
1.47
1.47
1.46
1.46
1.44
1.44
1.43
1.43
1.42
1.41
1.40
1.40
1.39
1.39
1.38
1.37
1.37
1.36
1.35
1.28
1.27
1.26
1.25
1.24
1.24
1.23
1.22
1.21
1.20
1.19
1.19
1.18
1.17
1.09
1.07
Ph
3
OH
2.22
3.05
2.06
4.05
1.09
3.20
11.09
3.95
2.18
3.00
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
f1 (ppm)

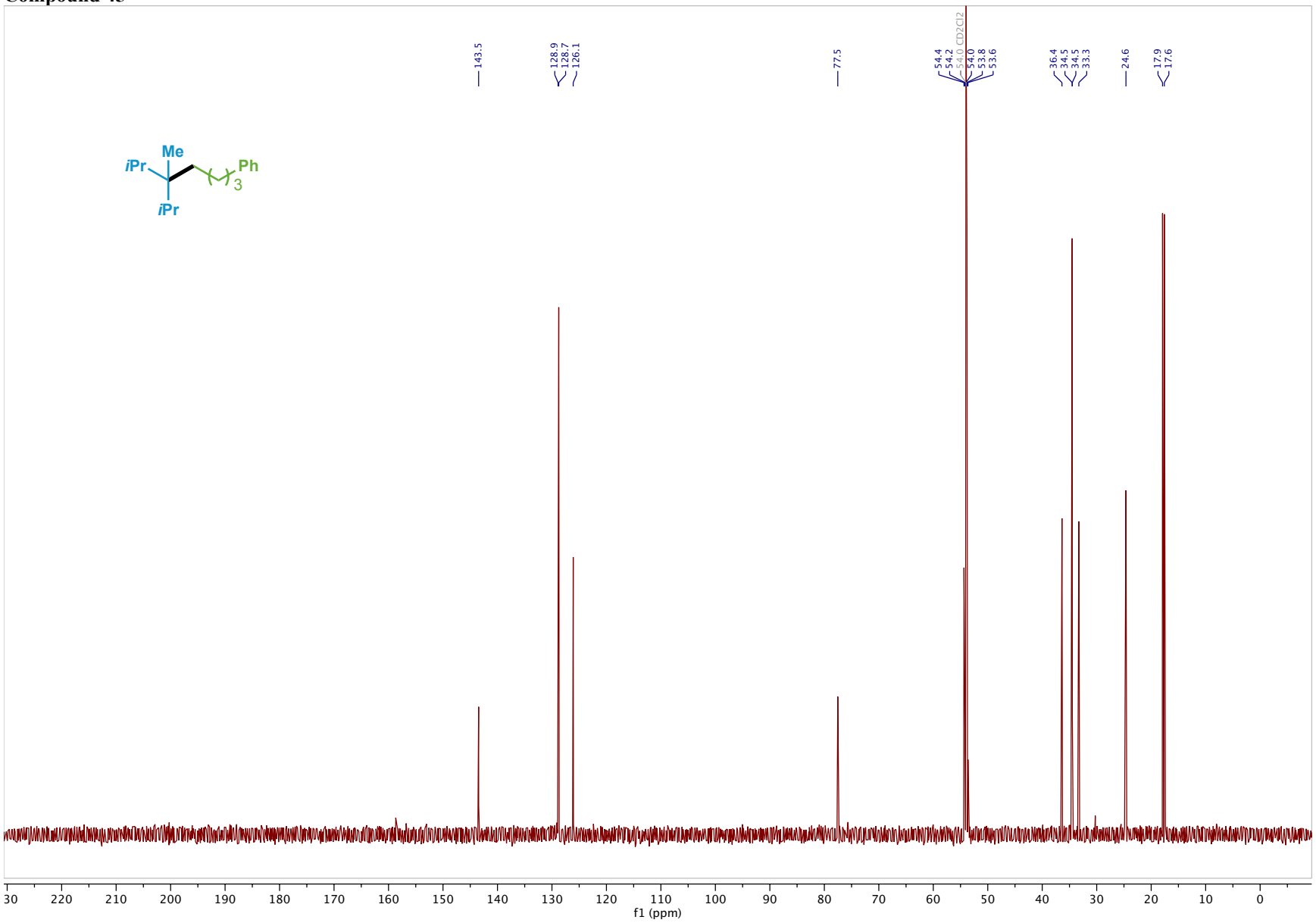
Compound 44


143.4
128.9
128.9
128.7
126.1
77.4
54.4
54.2
54.0 CD2Cl2
54.0
53.8
53.6
45.0
36.3
35.1
33.2
28.1
27.8
27.7
27.6
27.4
24.4
Ph
3
OH
f1 (ppm)

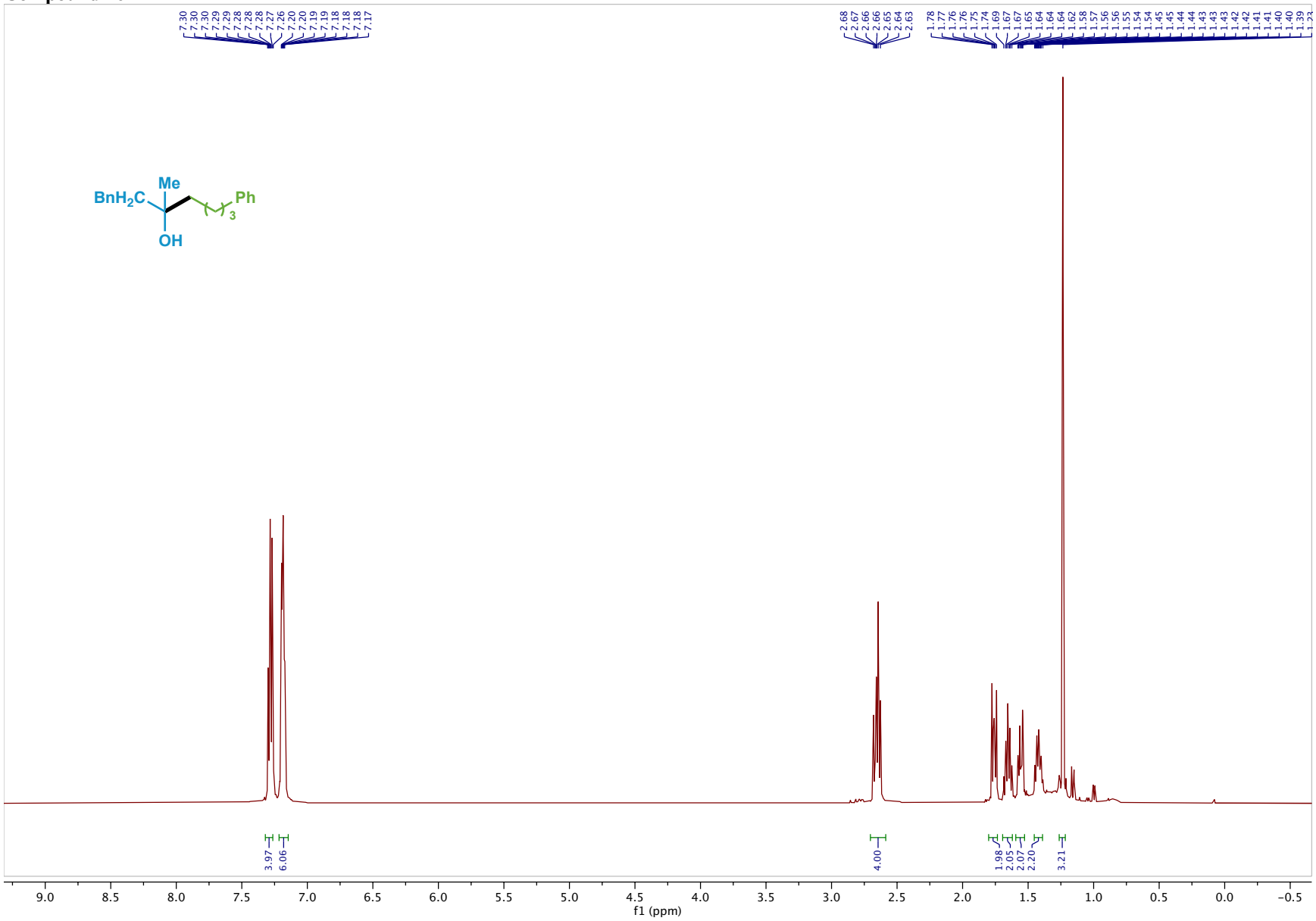
Compound 45



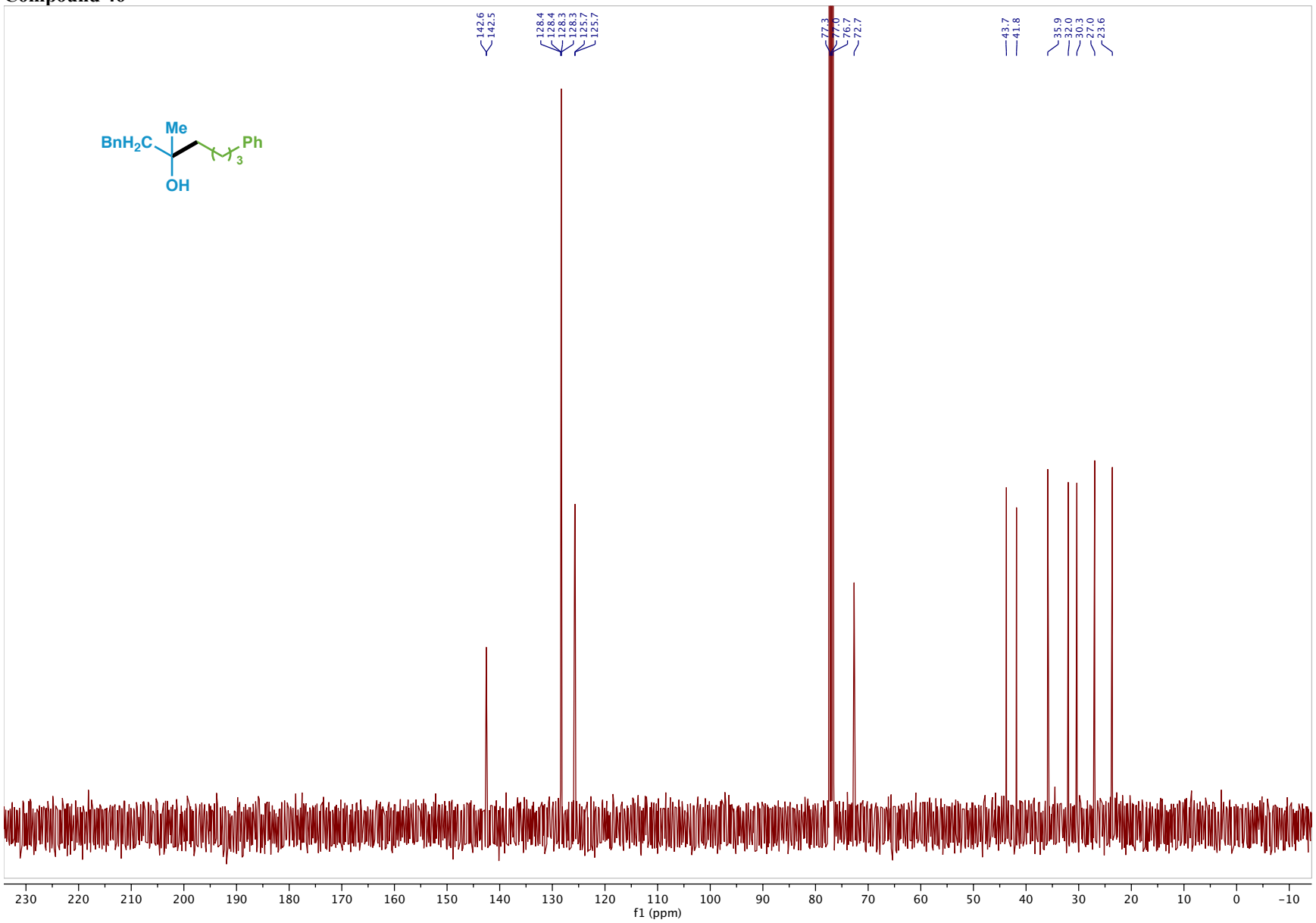
Compound 45


143.5
128.9
128.7
126.1
77.5
54.4
54.2
54.0
53.8
53.6
CD2Cl2
36.4
34.5
34.5
33.3
24.6
17.9
17.6
Me
iPr
Ph
3
iPr
f1 (ppm)

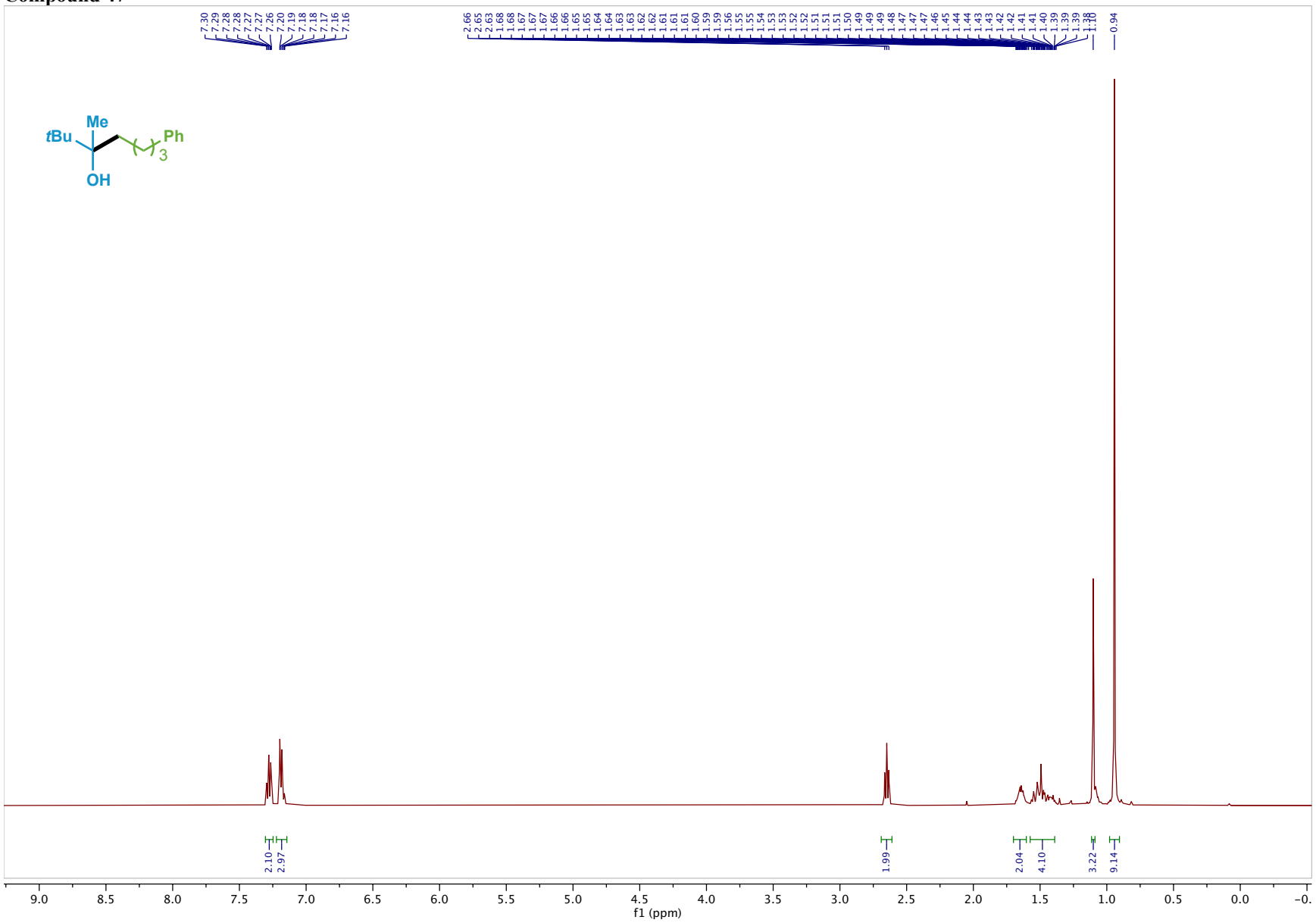
Compound 46


7.30 7.30 7.30 7.29 7.29 7.28 7.28 7.28 7.27 7.26 7.20 7.20 7.19 7.19 7.18 7.18 7.18 7.17
2.68 2.67 2.66 2.66 2.65 2.64 2.63
1.78 1.77 1.76 1.76 1.75 1.74 1.69 1.67 1.67 1.65 1.64 1.64 1.64 1.62 1.58 1.57 1.56 1.56 1.55 1.54 1.54 1.45 1.45 1.44 1.44 1.43 1.43 1.42 1.42 1.41 1.41 1.40 1.40 1.39
Me
BnH2C
Ph
3
OH
3.97
6.06
4.00
1.98
2.05
2.07
2.20
3.21
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
f1 (ppm)

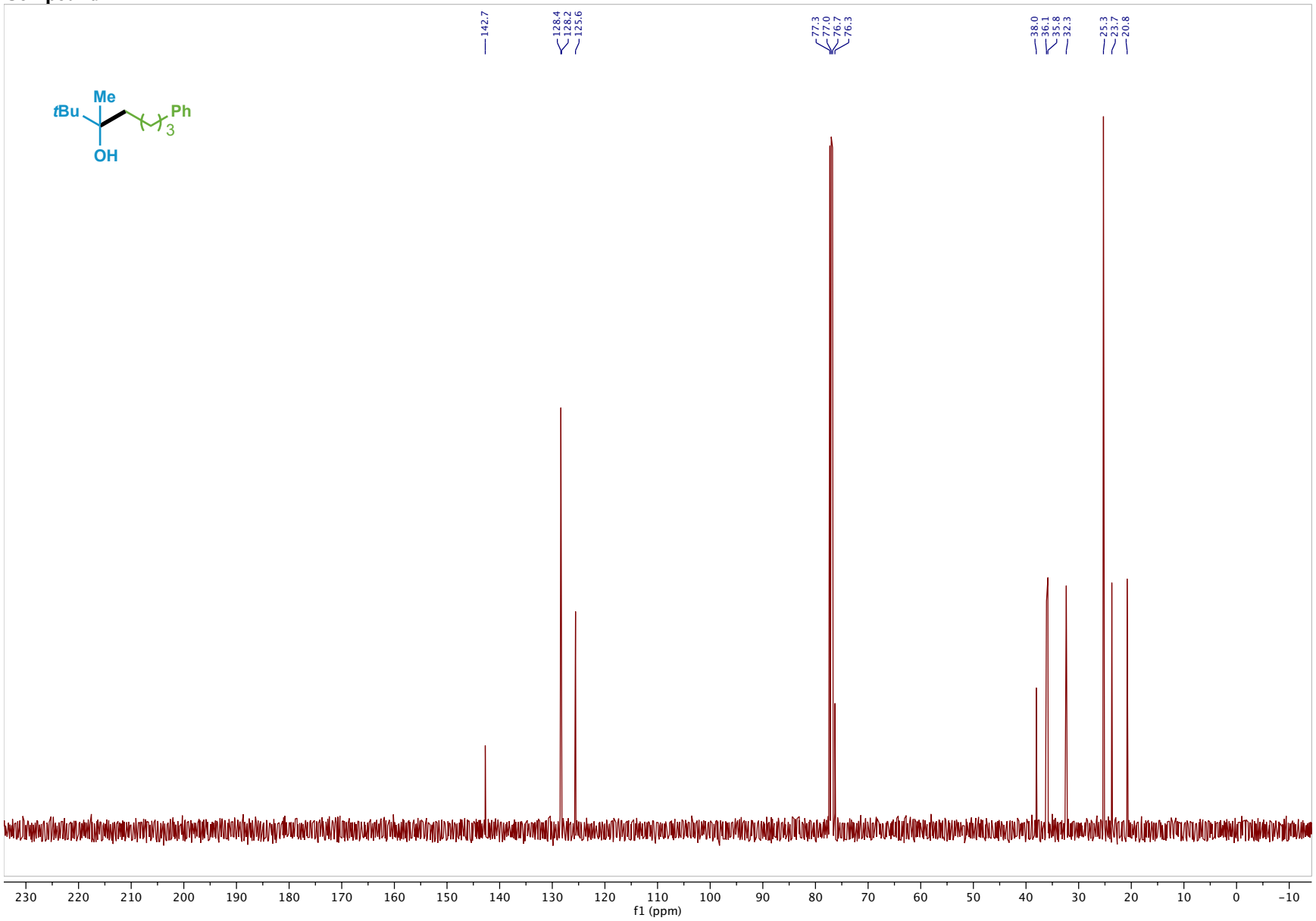
Compound 46


142.6
142.5
128.4
128.4
128.3
128.3
125.7
125.7
77.3
77.0
76.7
72.7
43.7
41.8
35.9
32.0
30.3
27.0
23.6
Me
BnH2C
Ph
3
OH
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

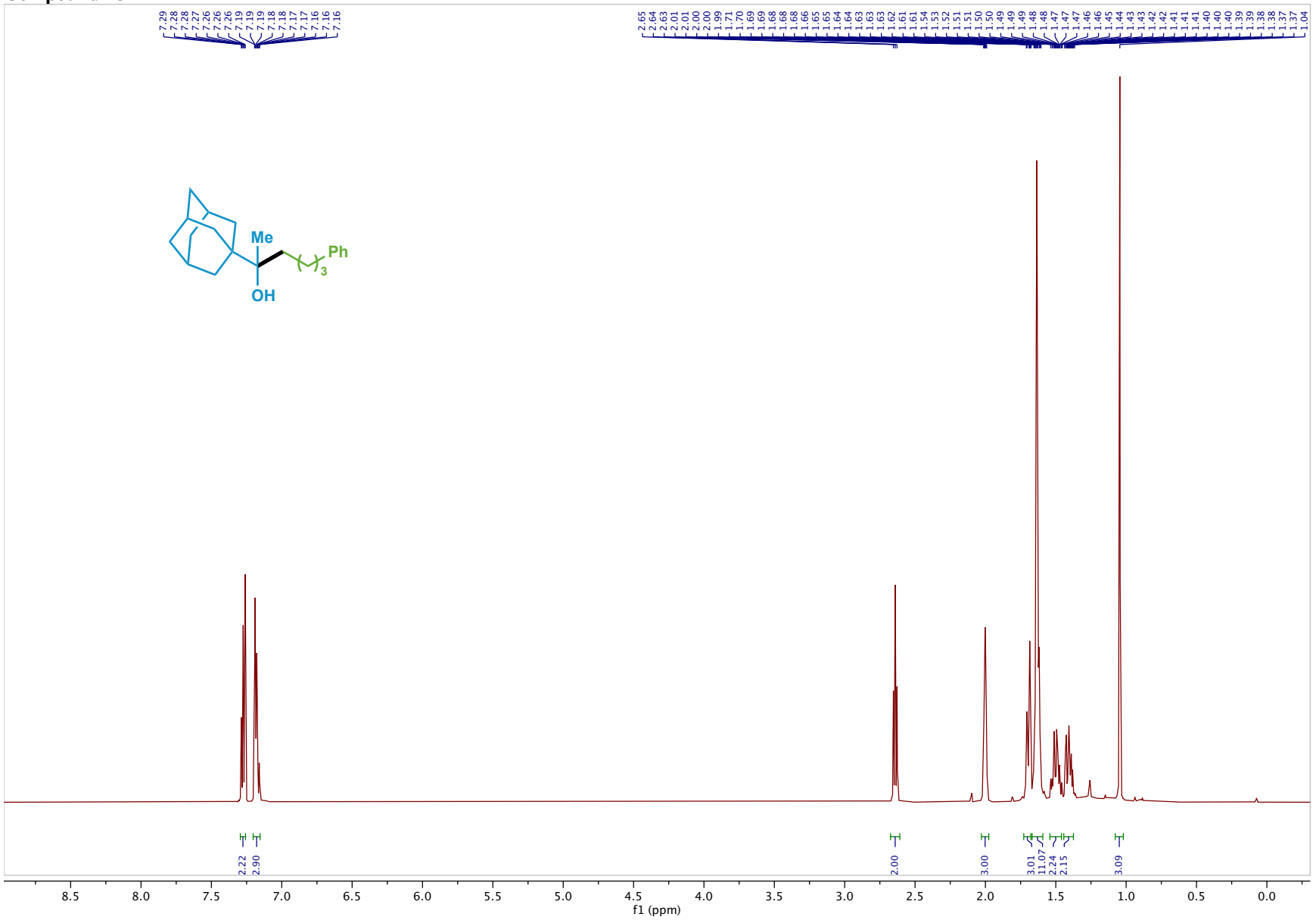
Compound 47



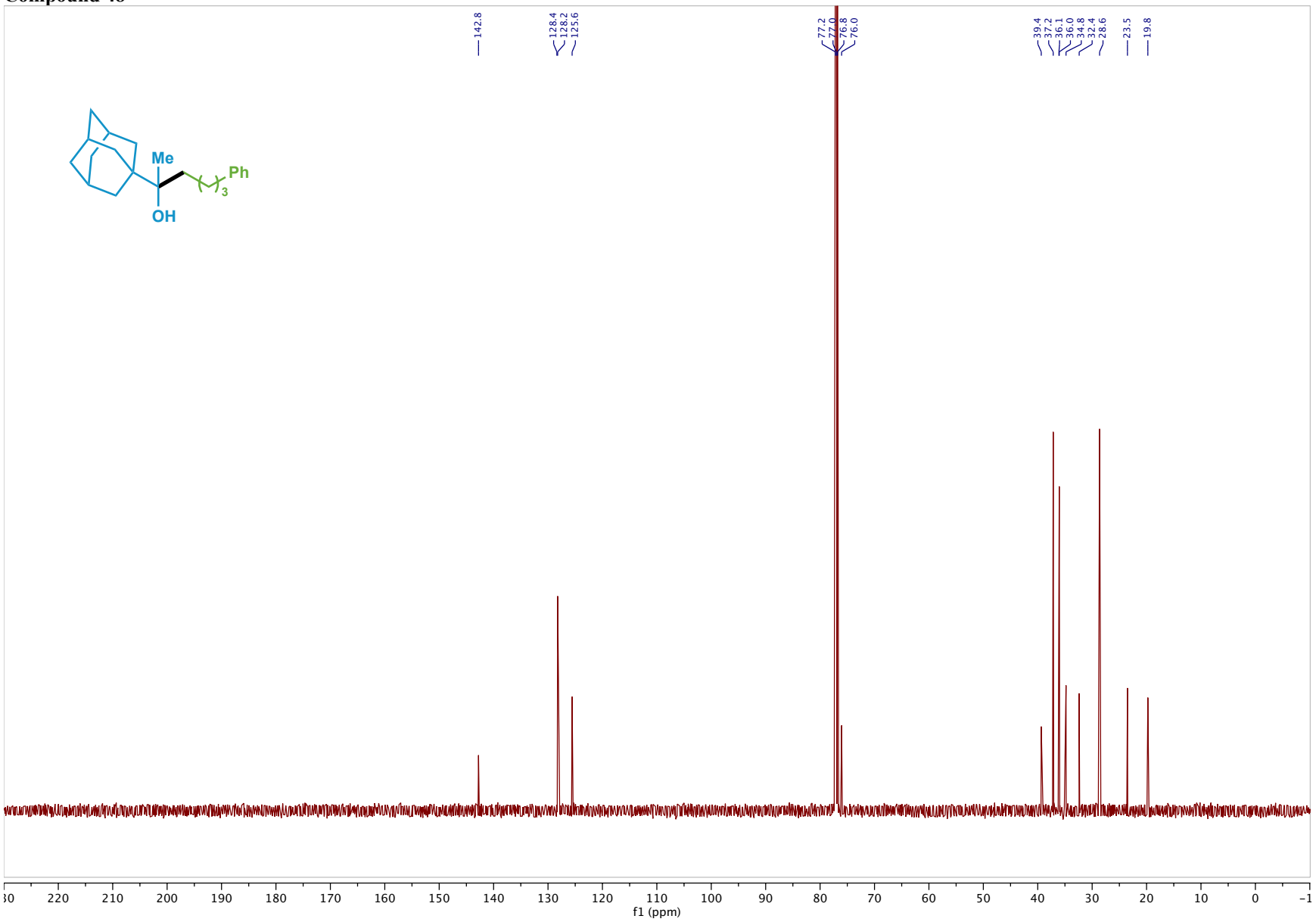
Compound 47


142.7
128.4
128.2
125.6
77.3
77.0
76.7
76.3
38.0
36.1
35.8
32.3
25.3
23.7
20.8
tBu
Me
Ph
3
OH
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

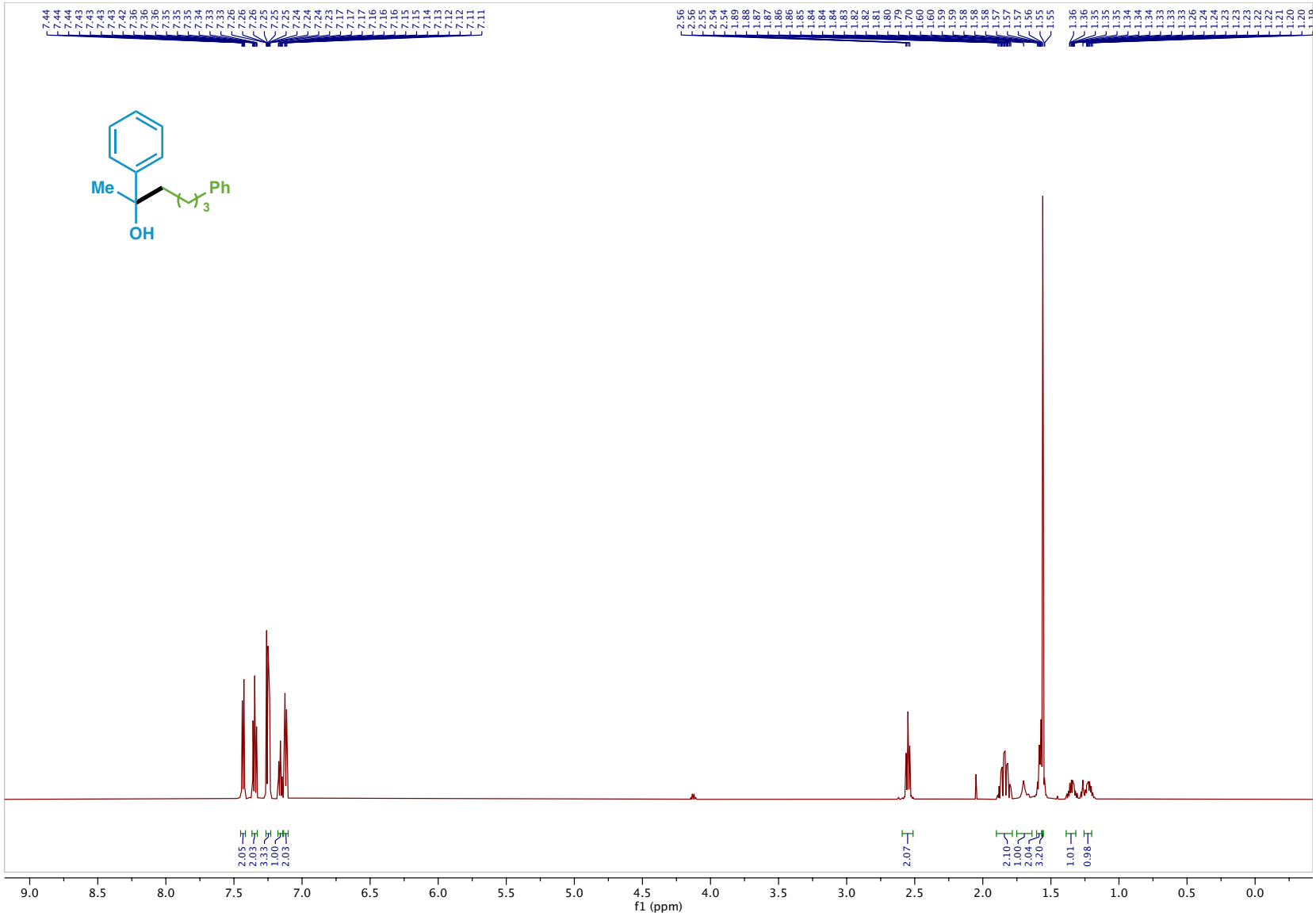
Compound 48



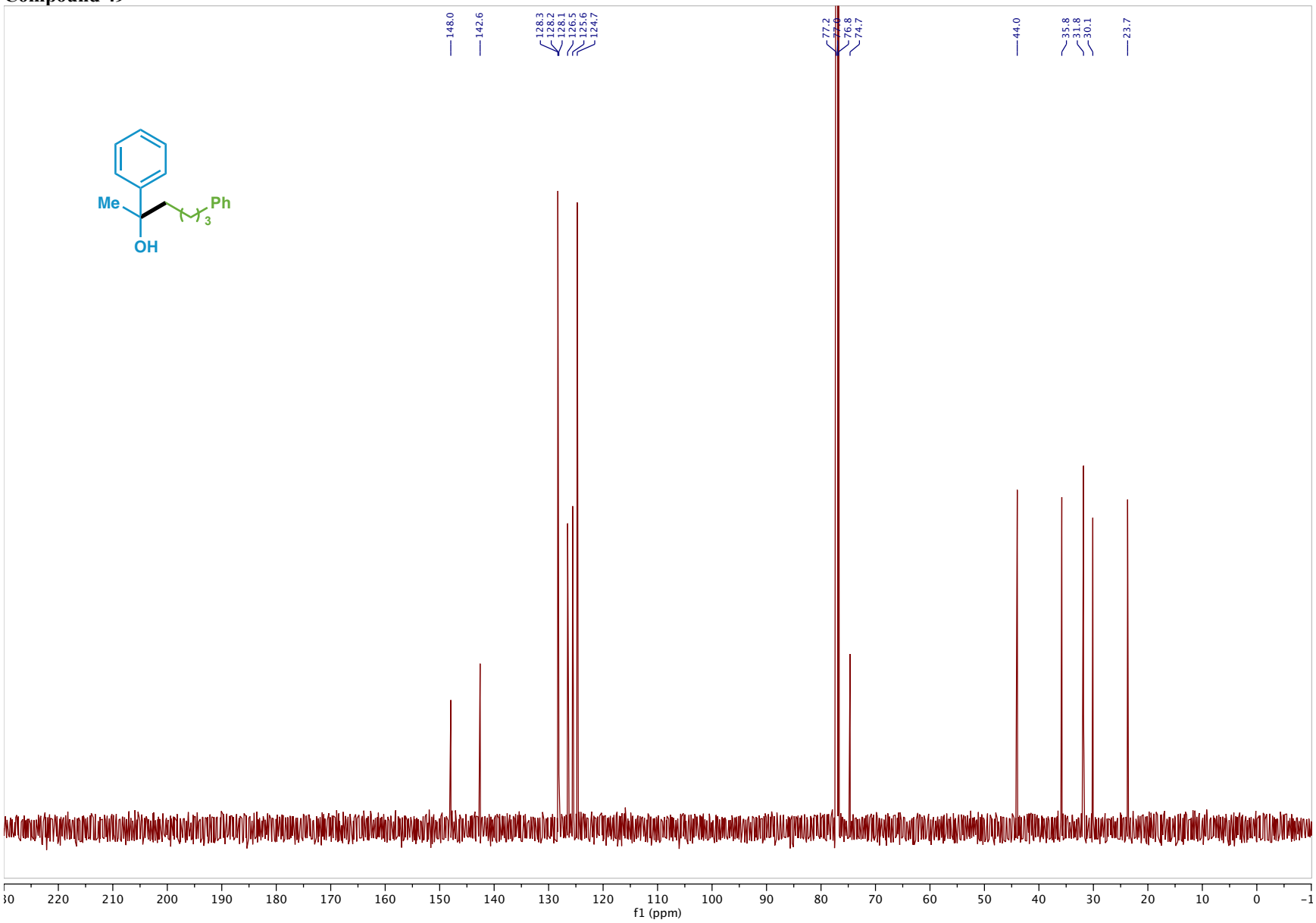
Compound 48


142.8
128.4
128.2
125.6
77.2
77.0
76.8
76.0
39.4
37.2
36.1
36.0
34.8
32.4
28.6
23.5
19.8
Me
Ph
3
OH
f1 (ppm)

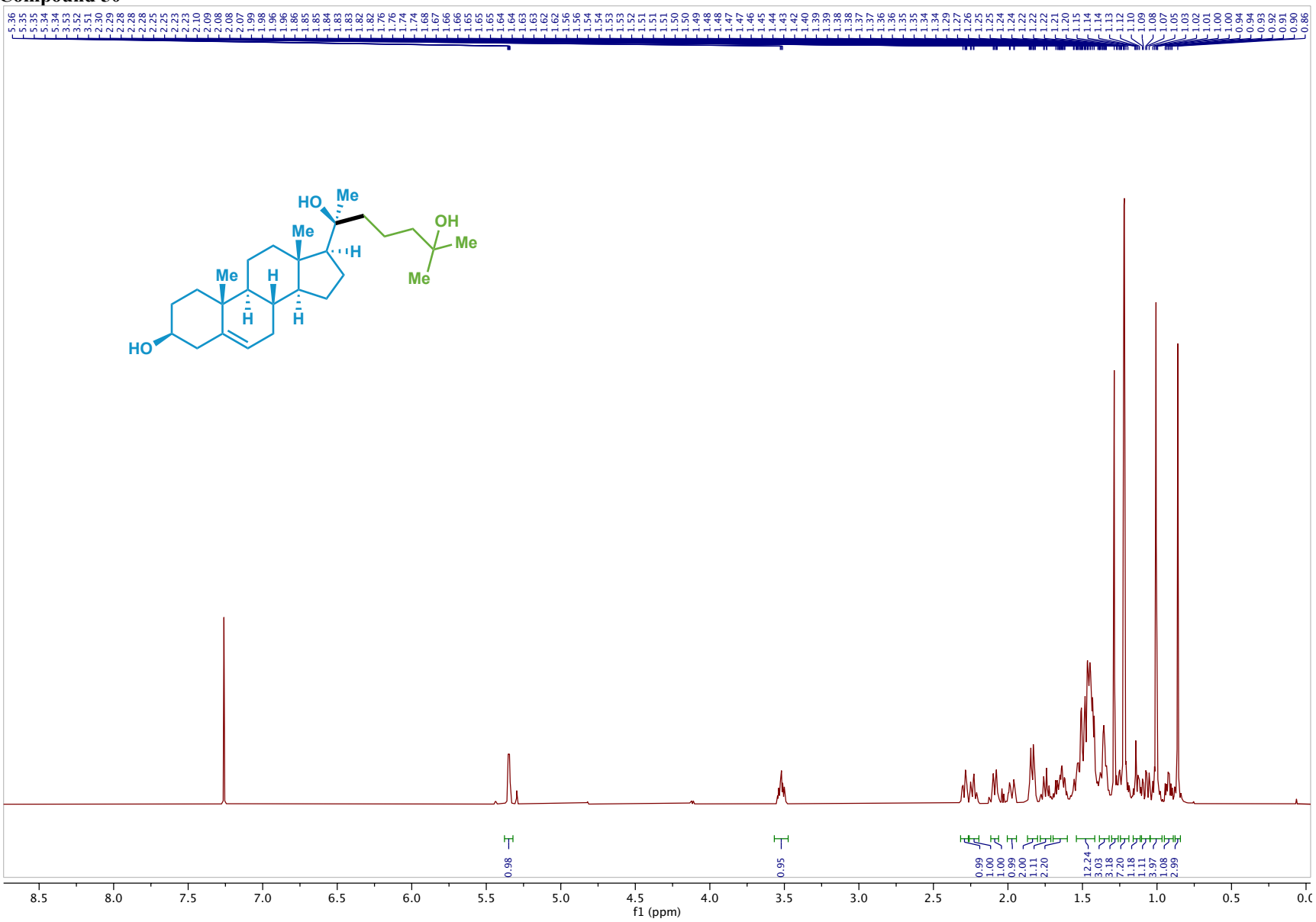
Compound 49



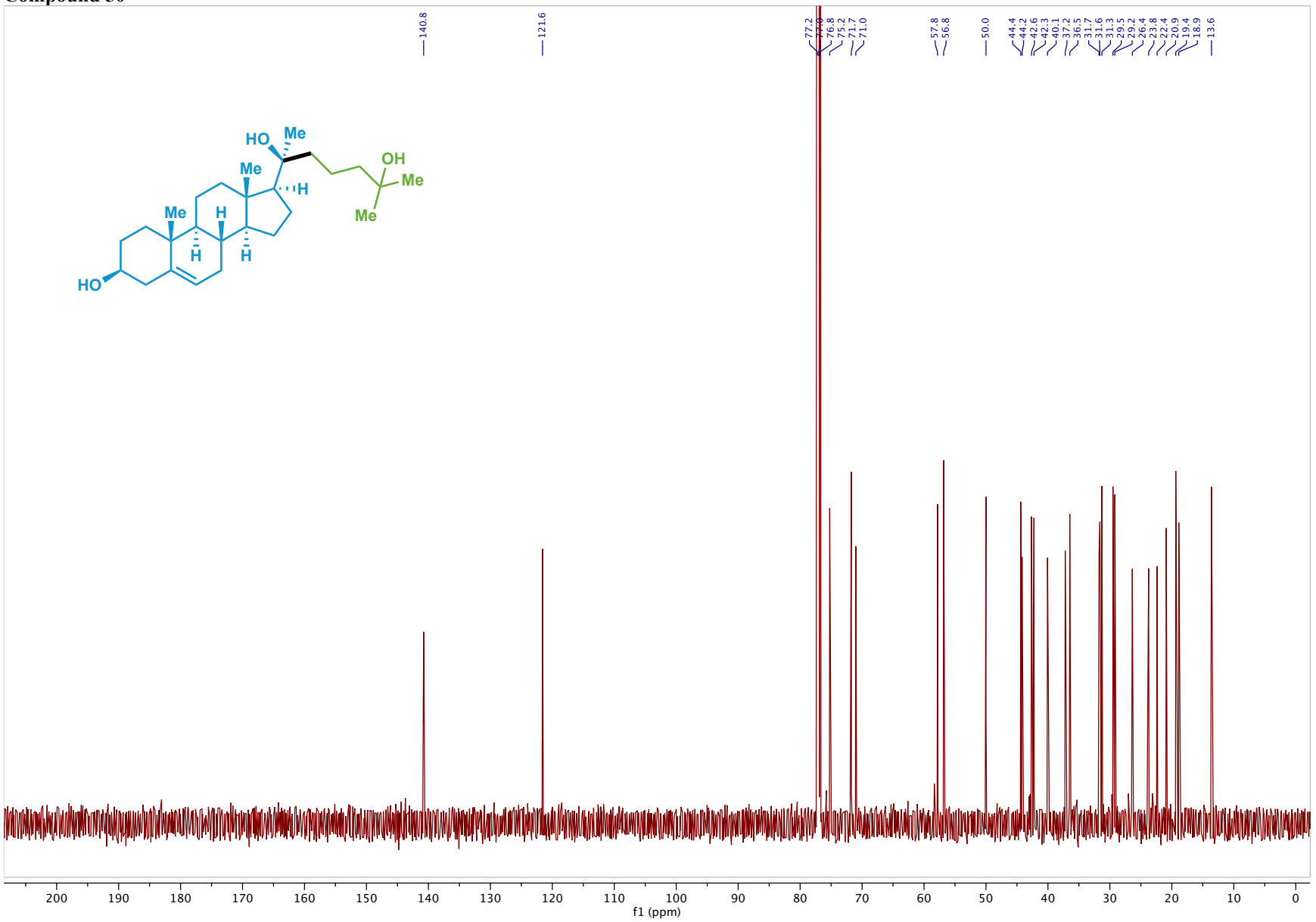
Compound 49


148.0
142.6
128.3
128.2
128.1
126.5
125.6
124.7
77.2
77.0
76.8
74.7
44.0
35.8
31.8
30.1
23.7
Me
Ph
3
OH
f1 (ppm)

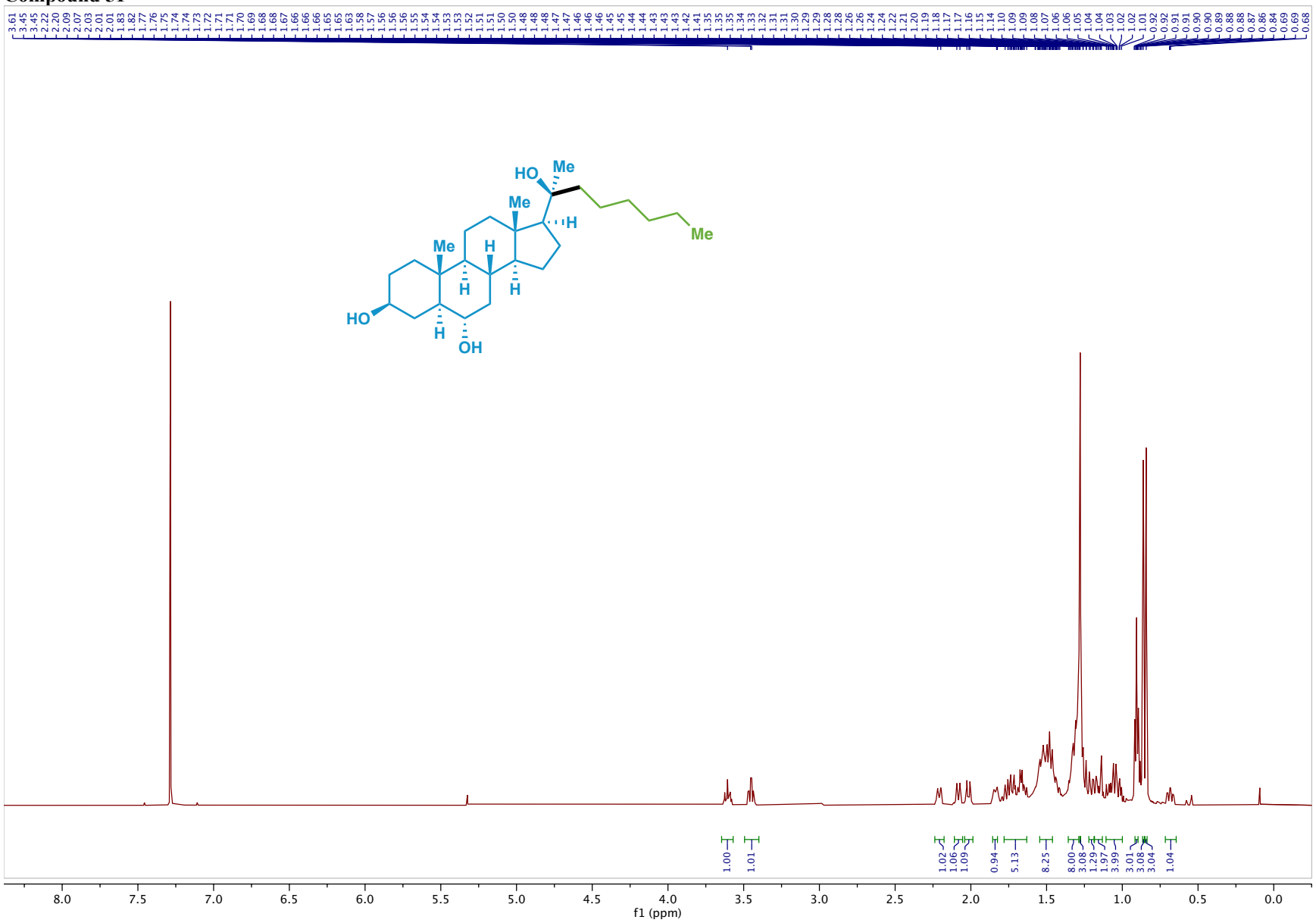
Compound 50



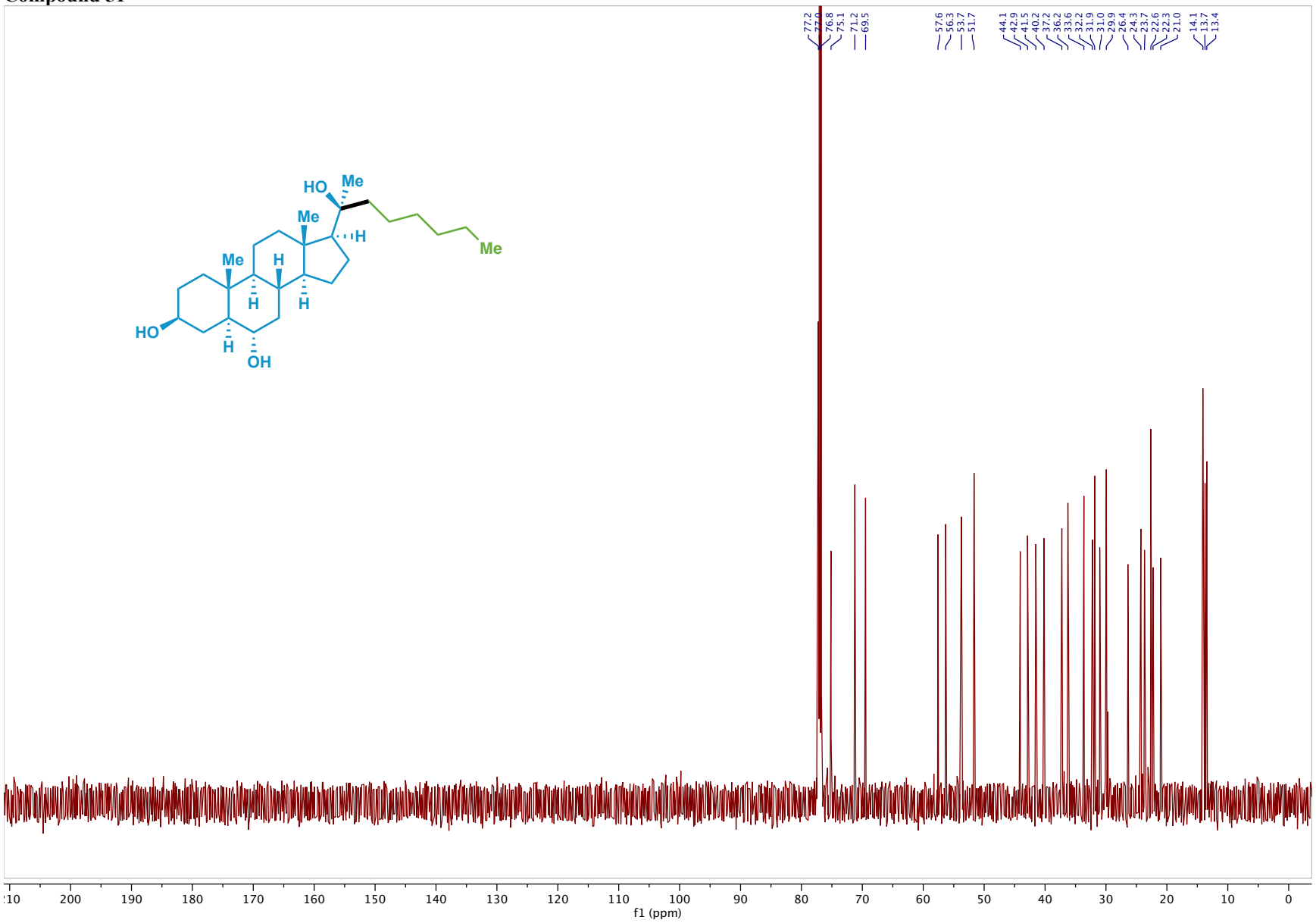
Compound 50


140.8
121.6
77.2
77.0
76.8
75.2
71.7
71.0
57.8
56.8
50.0
44.4
44.2
42.6
42.3
40.1
37.2
36.5
31.7
31.6
31.3
29.5
29.2
26.4
23.8
22.4
20.9
19.4
18.9
13.6
HO
Me
Me
H
OH
Me
Me
Me
H
H
H
HO
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

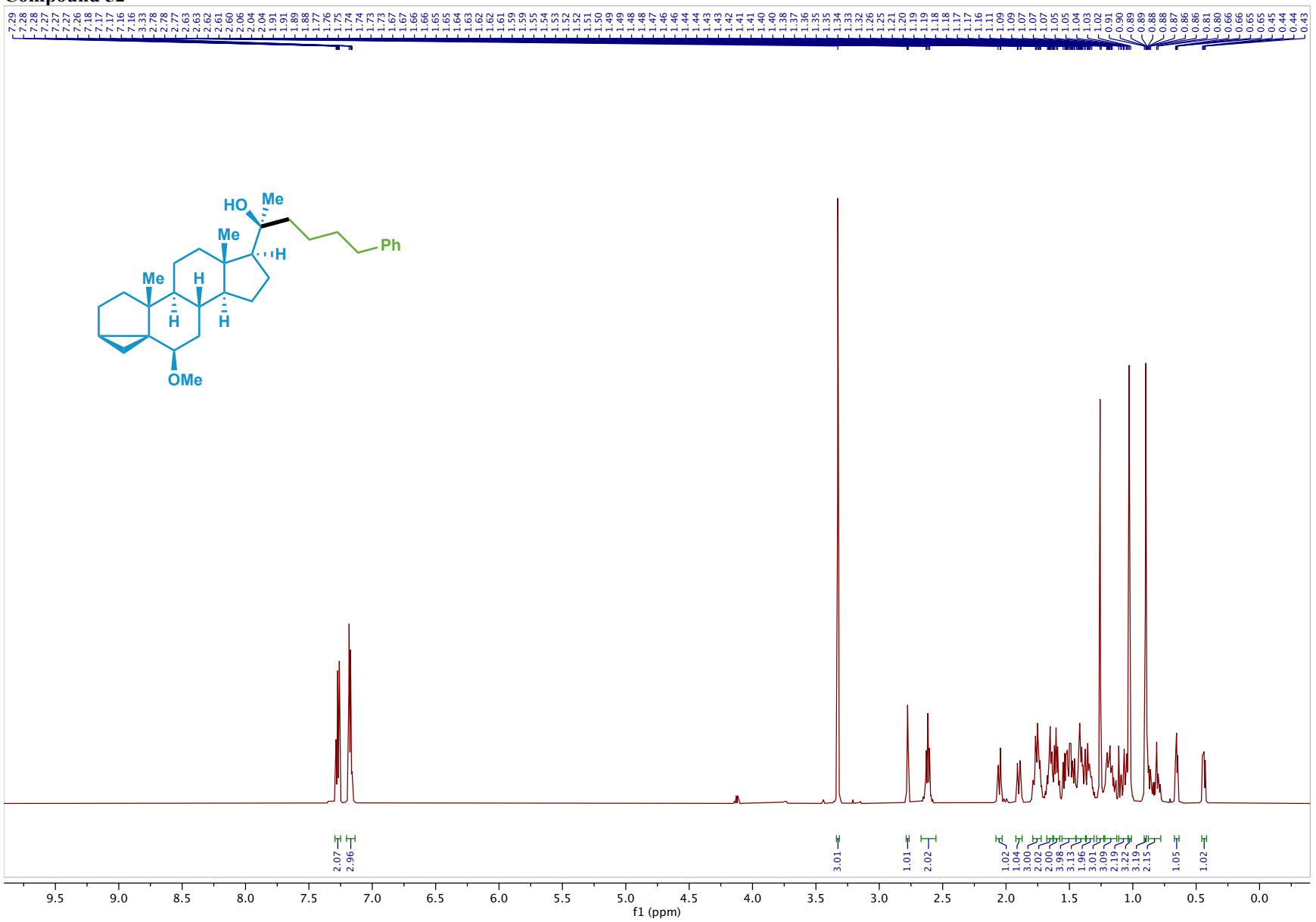
Compound 51



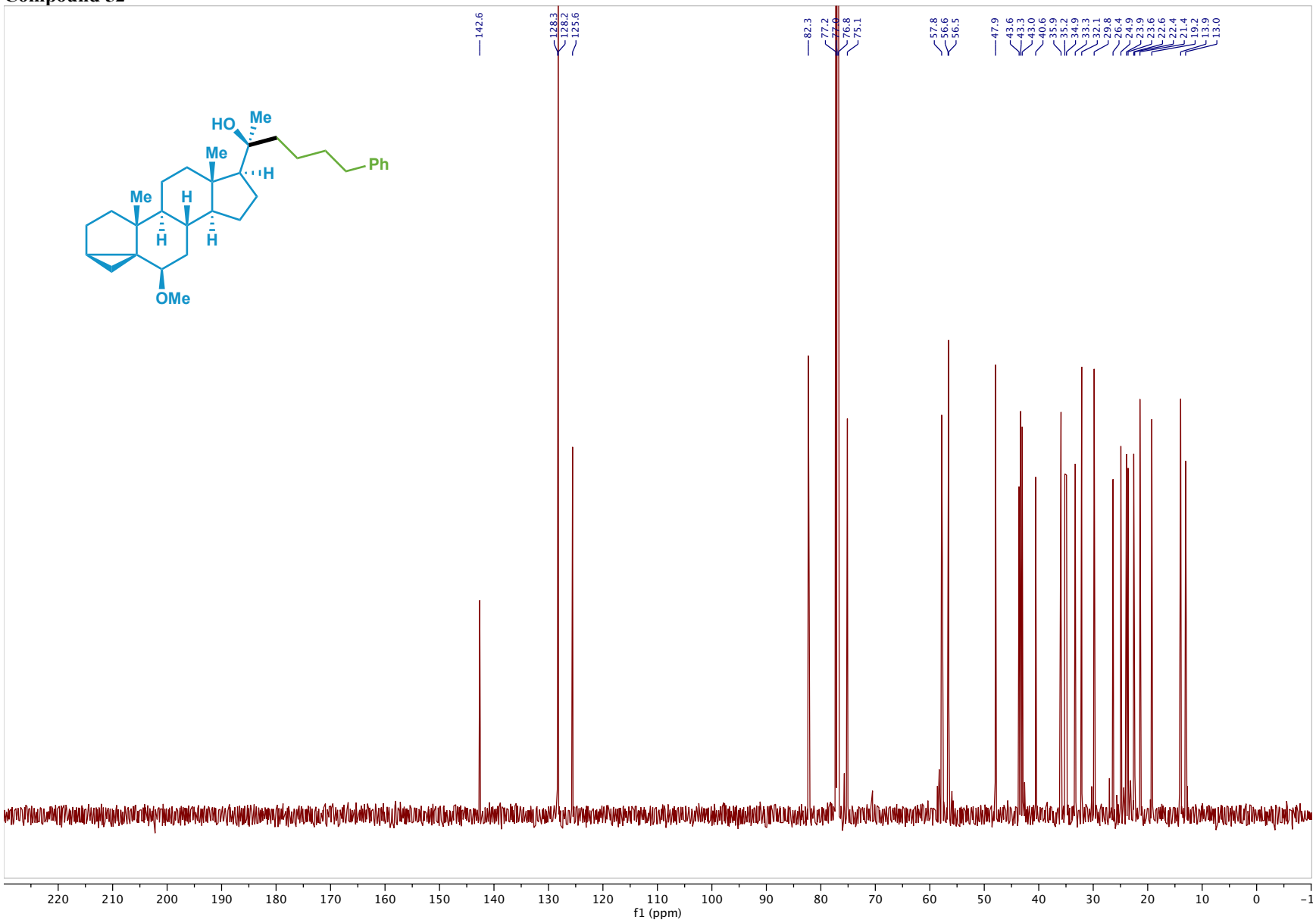
Compound 51


77.2
77.0
76.8
75.1
71.2
69.5
57.6
56.3
53.7
51.7
44.1
42.9
41.5
40.2
37.2
36.2
33.6
32.2
31.9
31.0
29.9
26.4
24.3
23.7
22.6
22.3
21.0
14.1
13.7
13.4
HO
Me
Me
H
Me
H
H
H
HO
H
OH
Me
f1 (ppm)

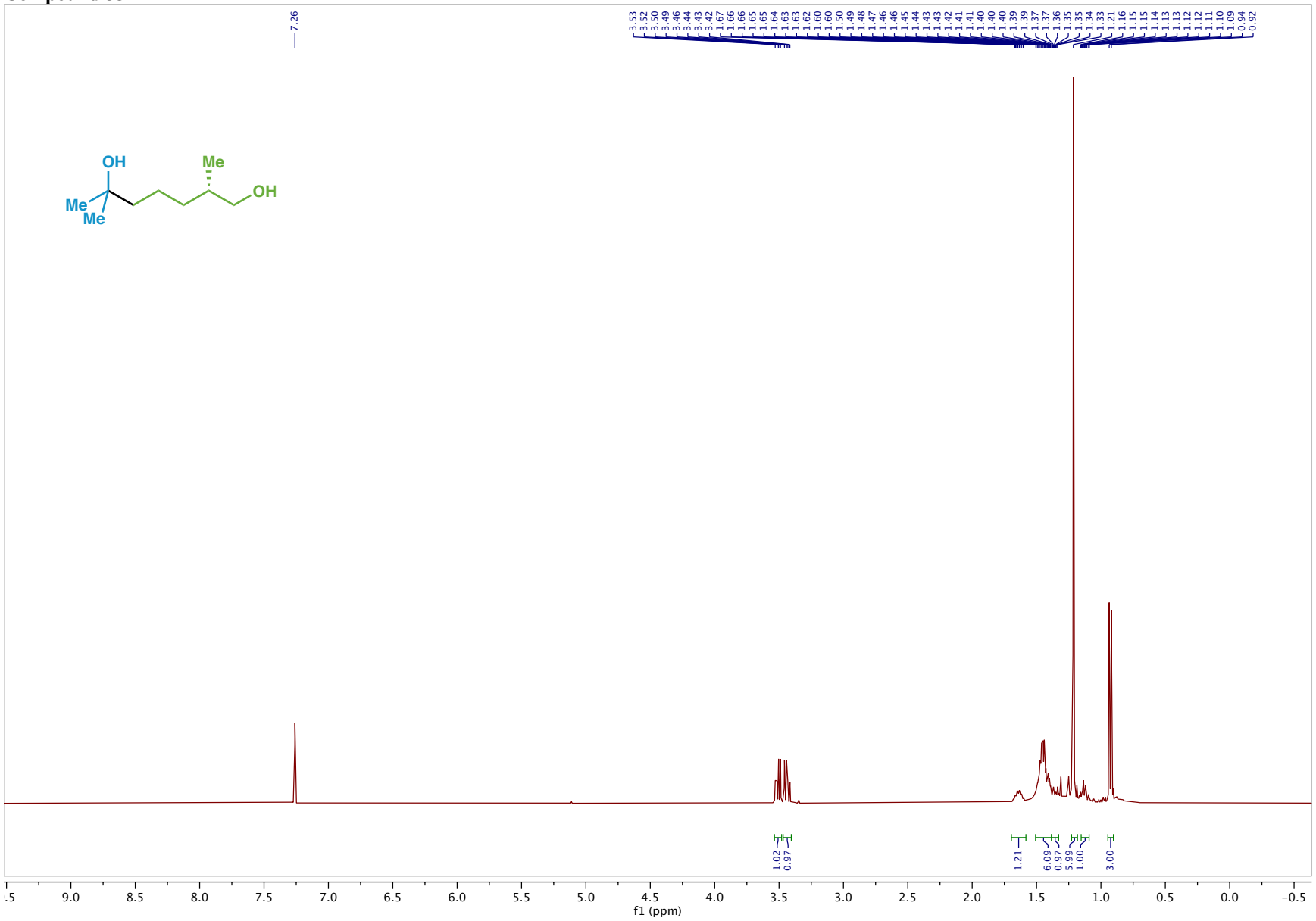
Compound 52


HO
Me
Me
H
Ph
Me
H
H
H
OMe
2.07
2.96
3.01
1.01
2.02
1.02
1.04
3.00
2.02
2.00
3.98
3.13
1.96
3.01
3.09
2.19
3.22
3.19
2.15
1.05
1.02
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
f1 (ppm)

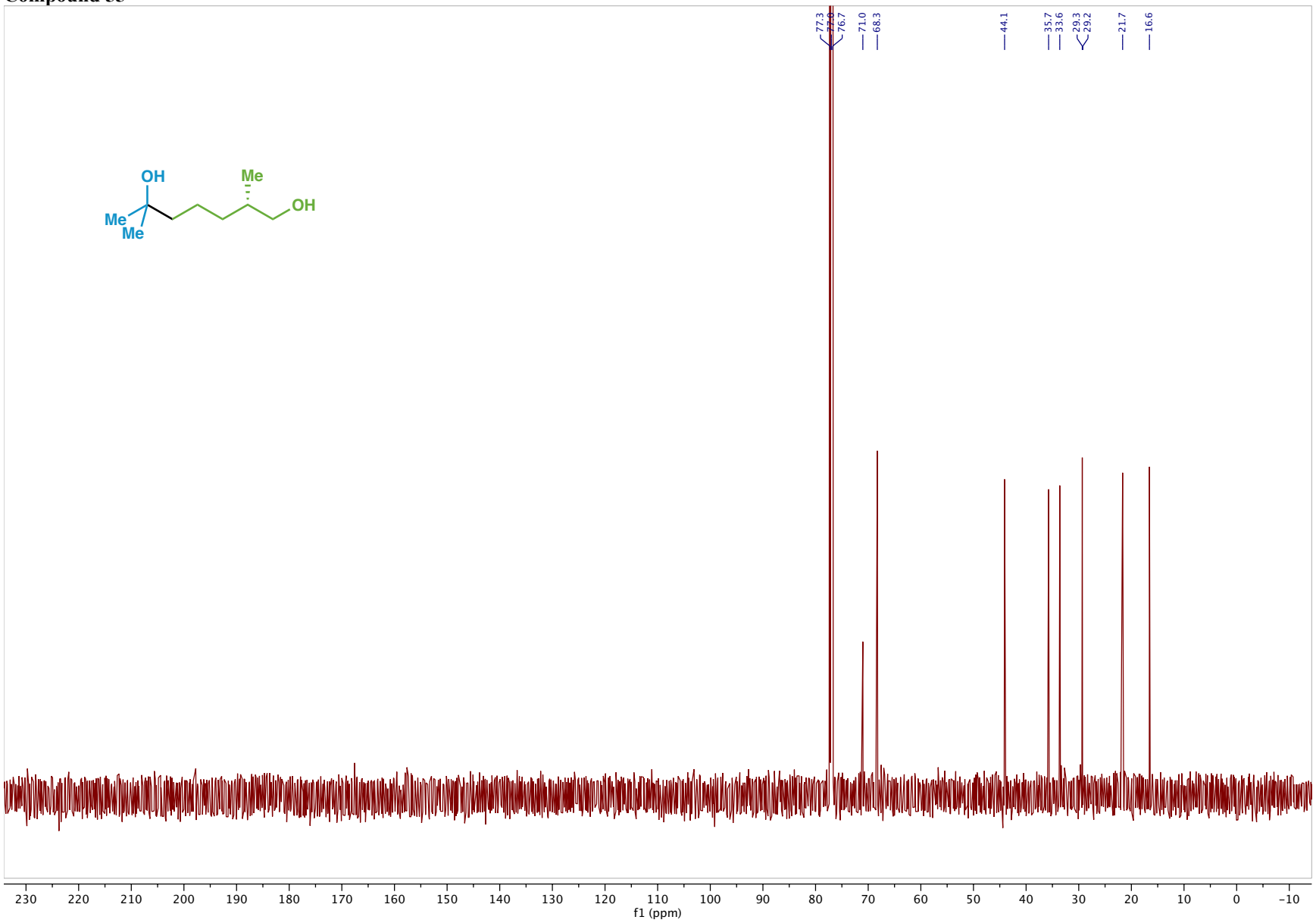
Compound 52


142.6
128.3
128.2
125.6
82.3
77.2
77.0
76.8
75.1
57.8
56.6
56.5
47.9
43.6
43.3
43.0
40.6
35.9
35.2
34.9
33.3
32.1
29.8
26.4
24.9
23.9
23.6
22.6
22.4
21.4
19.2
13.9
13.0
HO
Me
Me
H
Me
H
H
H
Ph
OMe
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−1
f1 (ppm)

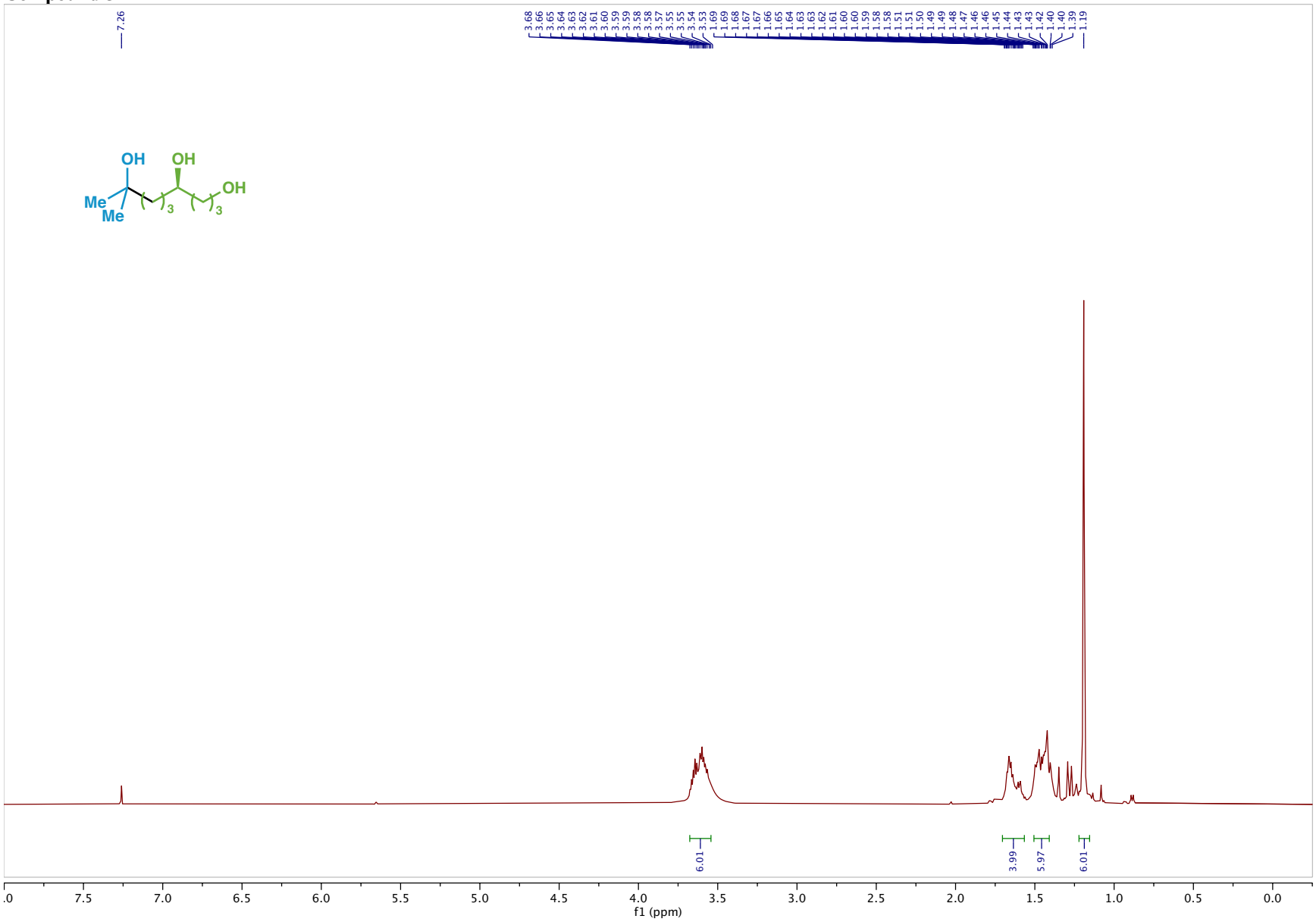
Compound 55


7.26
3.53 3.52 3.50 3.49 3.46 3.44 3.43 3.42 1.67 1.66 1.66 1.65 1.65 1.64 1.63 1.63 1.62 1.60 1.60 1.50 1.49 1.48 1.47 1.46 1.46 1.45 1.44 1.43 1.43 1.42 1.41 1.41 1.40 1.40 1.40 1.39 1.39 1.37 1.37 1.36 1.35 1.35 1.34 1.33 1.21 1.16 1.15 1.15 1.14 1.13 1.12 1.12 1.11 1.10 1.09 0.94 0.92
OH
Me
Me
Me
OH
1.02
0.97
1.21
6.09
0.97
5.99
1.00
3.00
f1 (ppm)

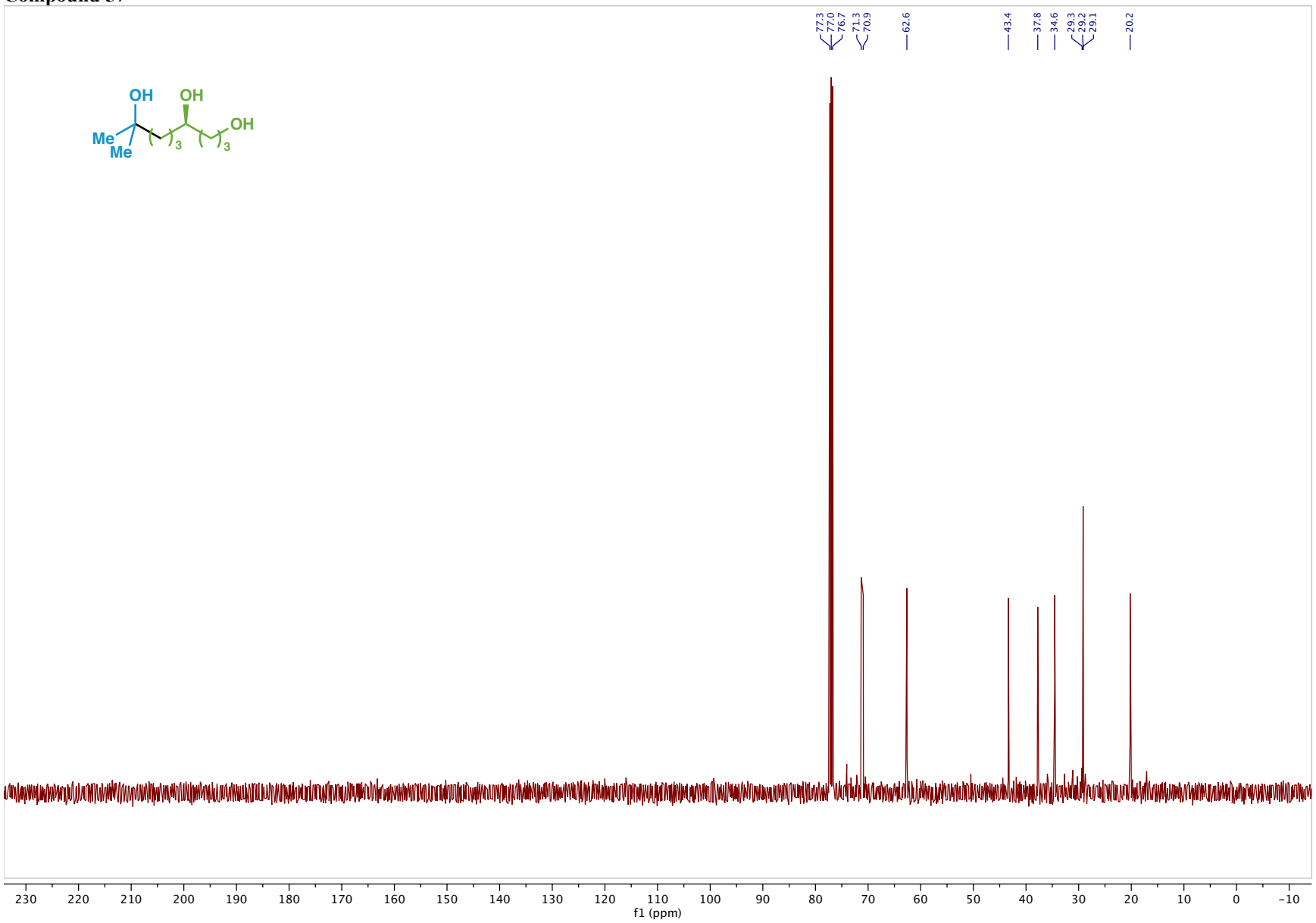
Compound 55


77.3
77.0
76.7
71.0
68.3
44.1
35.7
33.6
29.3
29.2
21.7
16.6
OH
Me
Me
Me
OH
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

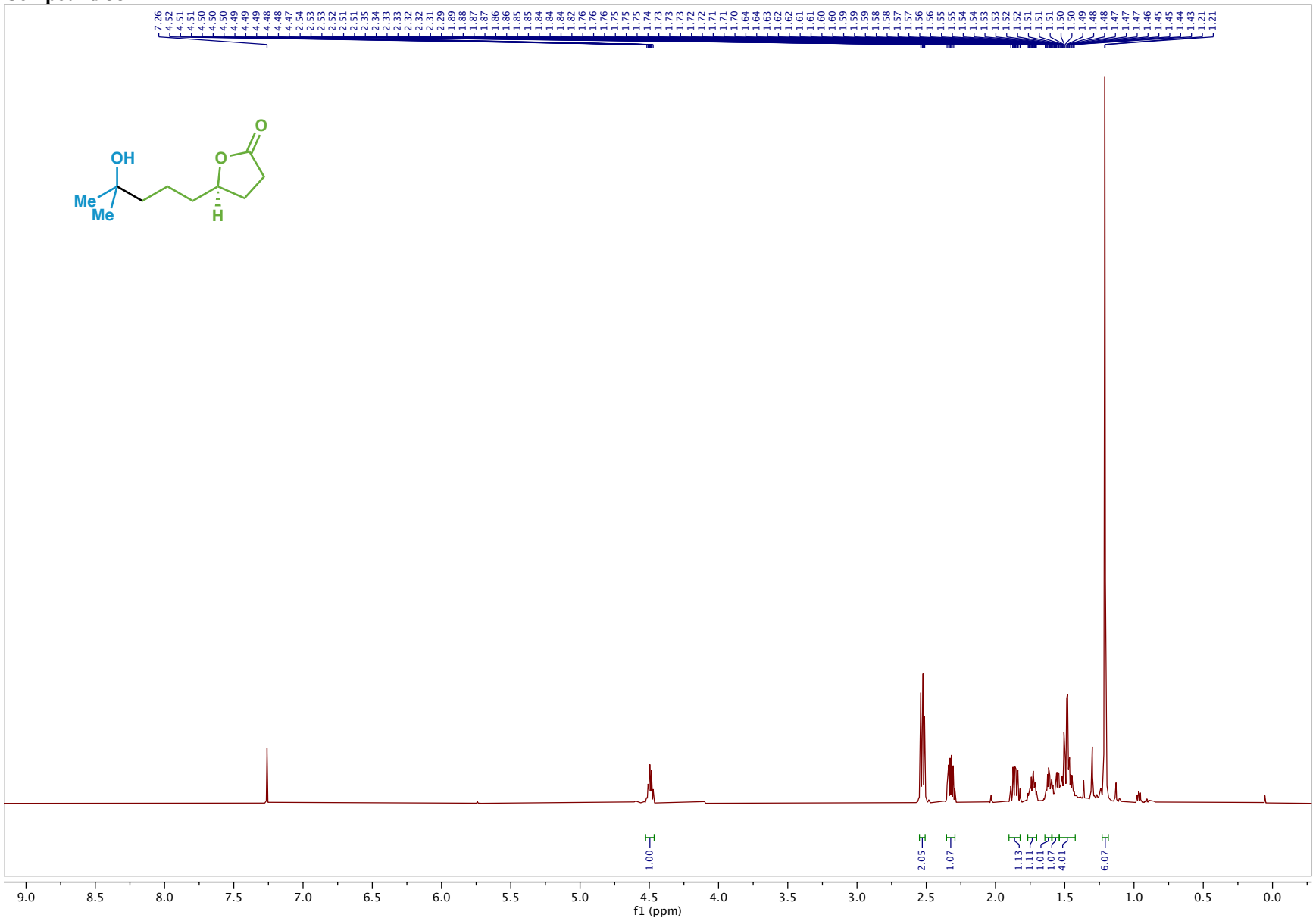
Compound 57


7.26
3.68
3.66
3.65
3.64
3.63
3.62
3.61
3.60
3.59
3.59
3.58
3.58
3.57
3.55
3.55
3.54
3.53
1.69
1.69
1.68
1.67
1.67
1.66
1.65
1.64
1.63
1.63
1.62
1.61
1.60
1.60
1.59
1.58
1.58
1.51
1.51
1.50
1.49
1.49
1.48
1.47
1.46
1.46
1.45
1.44
1.43
1.43
1.42
1.40
1.40
1.39
1.19
OH
OH
OH
Me
Me
3
3
6.01
3.99
5.97
6.01
f1 (ppm)

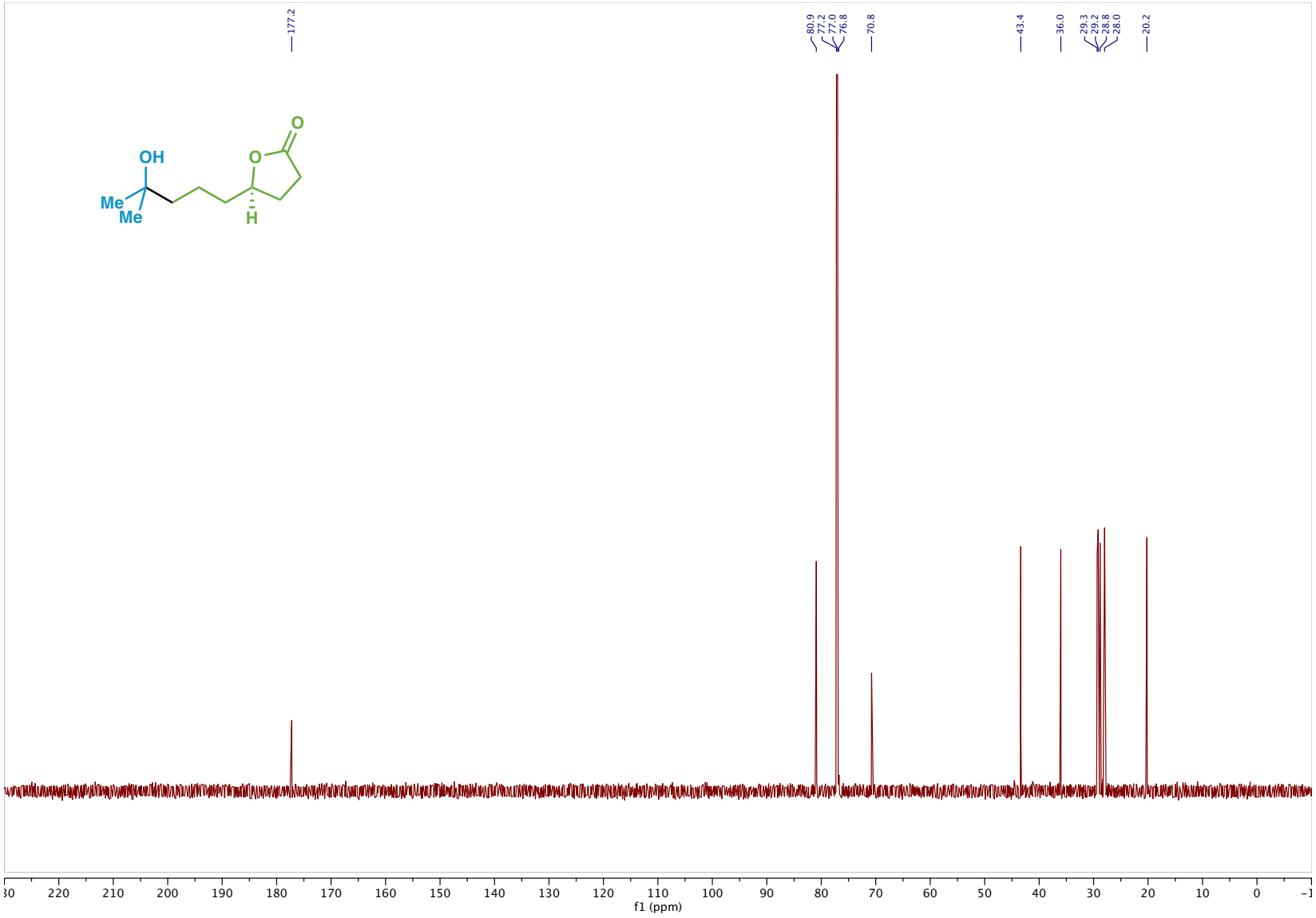
Compound 57


77.3
77.0
76.7
71.3
70.9
62.6
43.4
37.8
34.6
29.3
29.2
29.1
20.2
OH
OH
OH
Me
Me
3
3
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

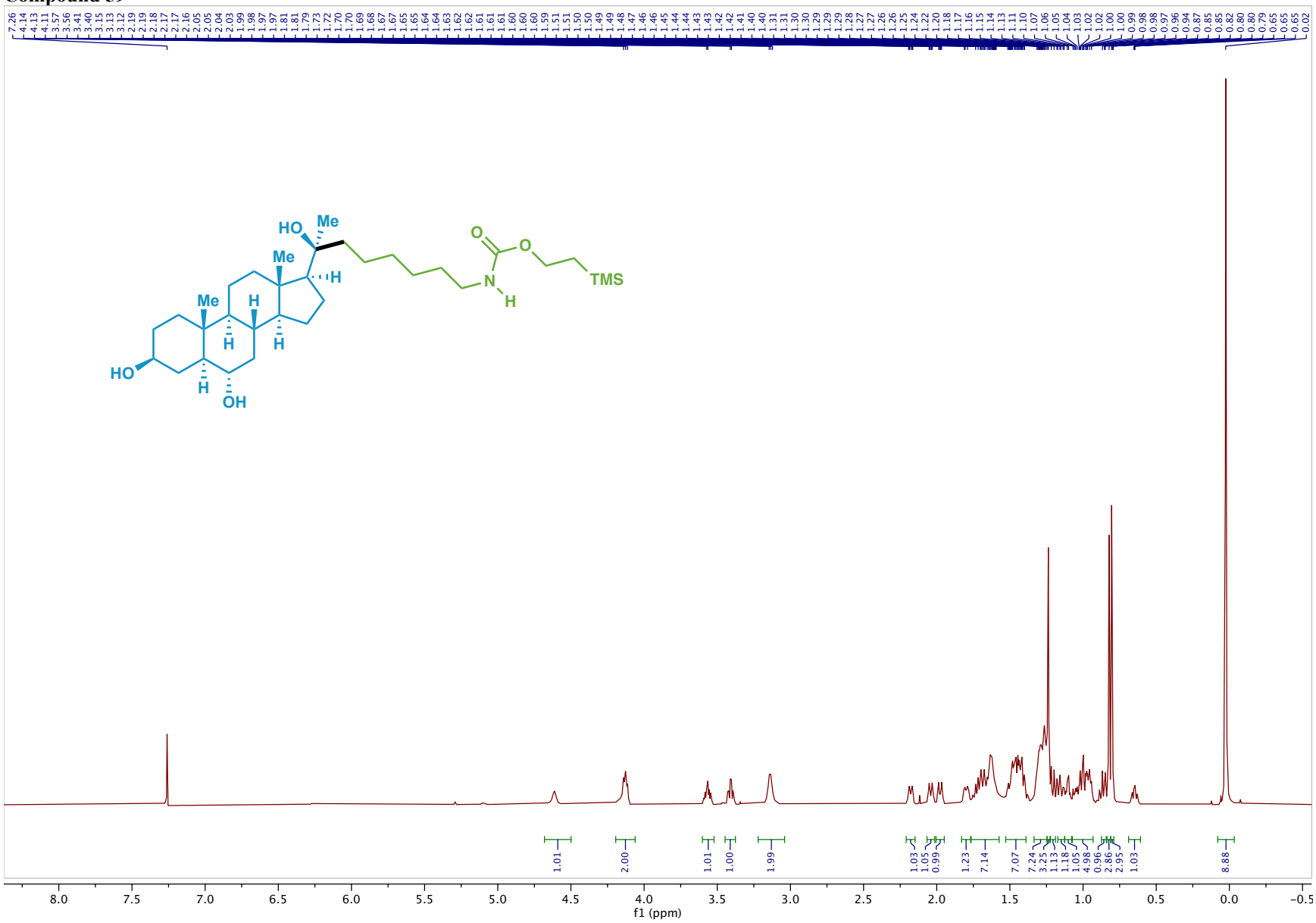
Compound 58


OH
Me
Me
O
O
H
1.00
2.05
1.07
1.13
1.11
1.01
1.07
4.01
6.07
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
f1 (ppm)

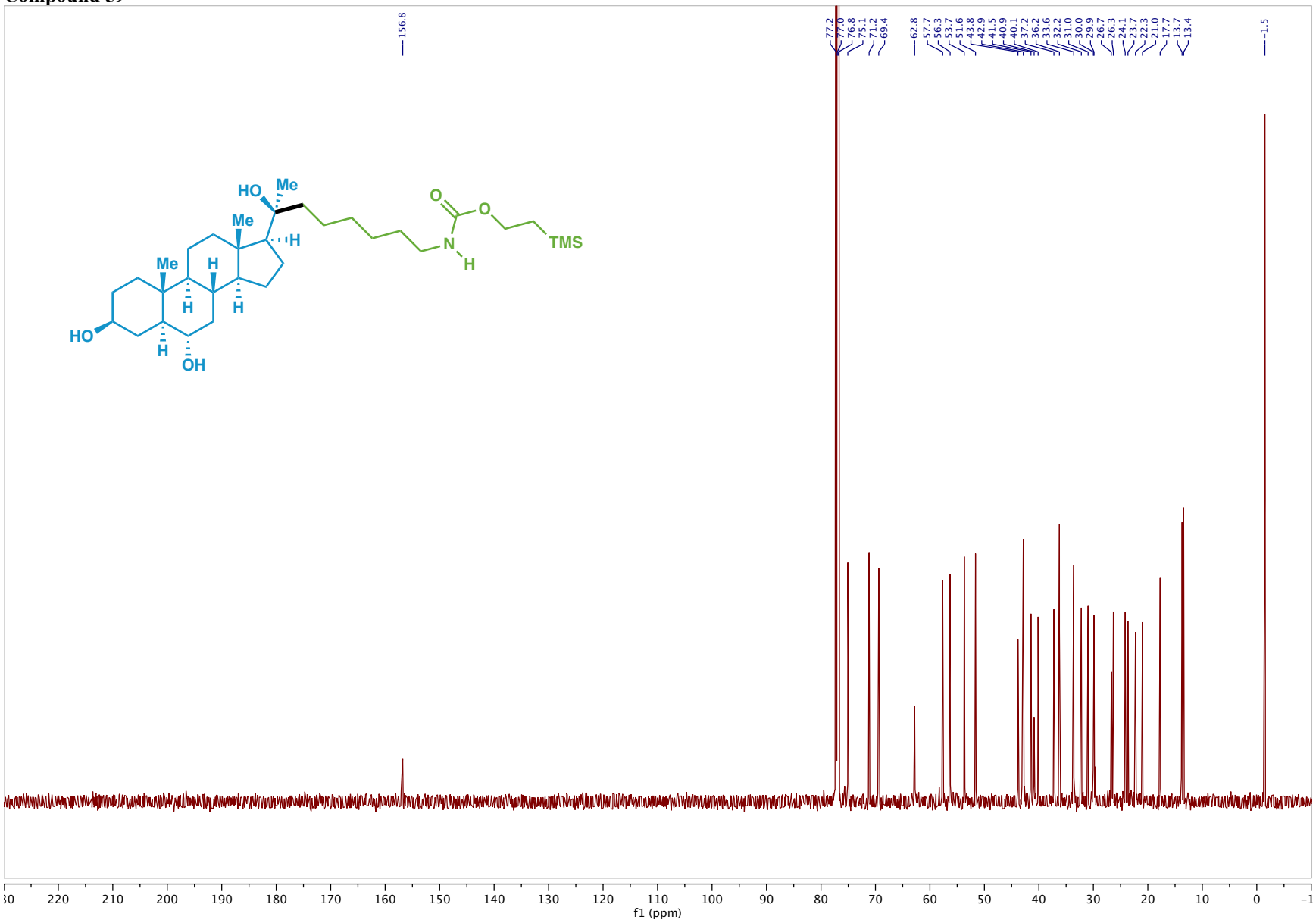
Compound 58


177.2
80.9
77.2
77.0
76.8
70.8
43.4
36.0
29.3
29.2
28.8
28.0
20.2
OH
O
O
Me
Me
H
f1 (ppm)

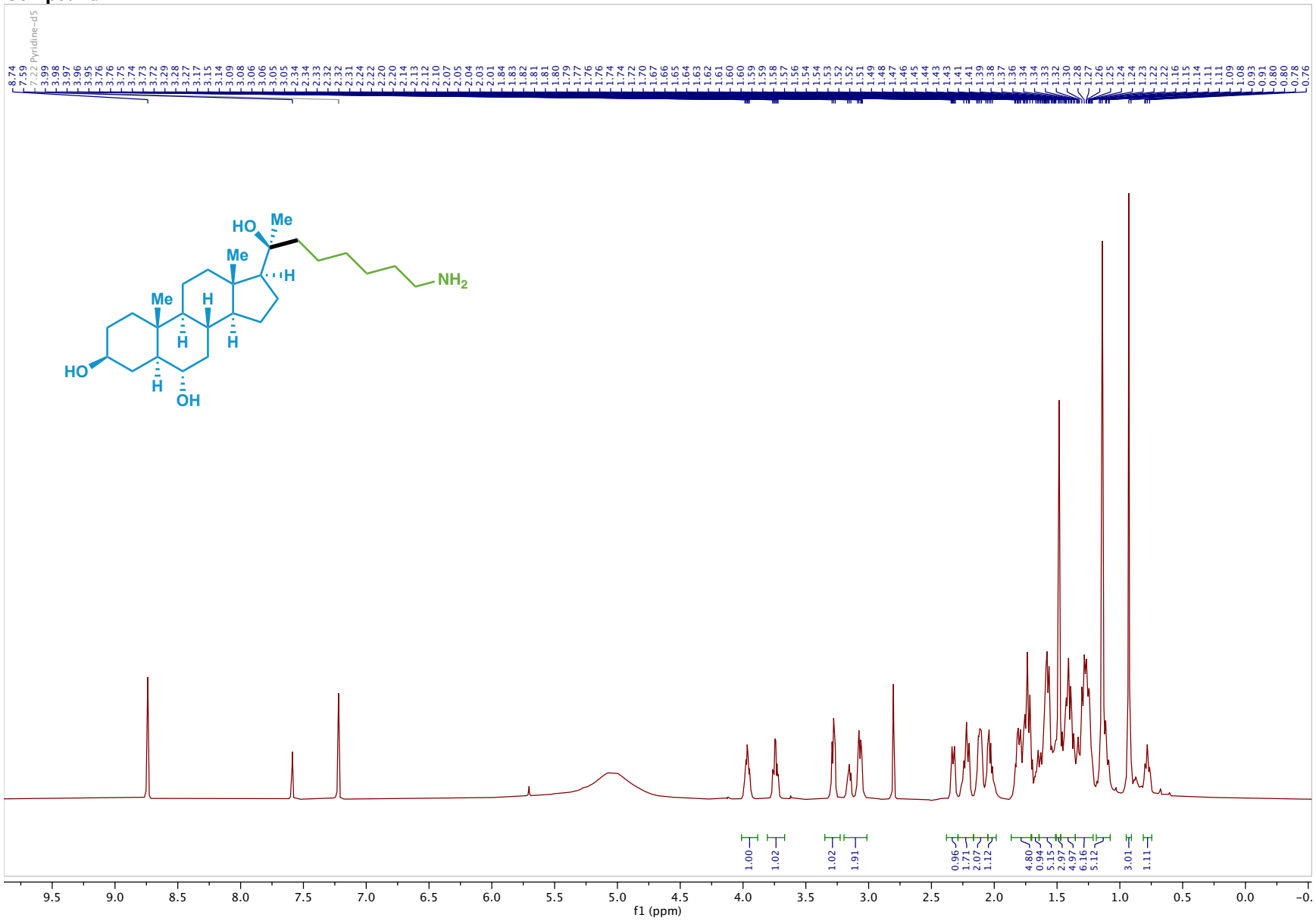
Compound 59



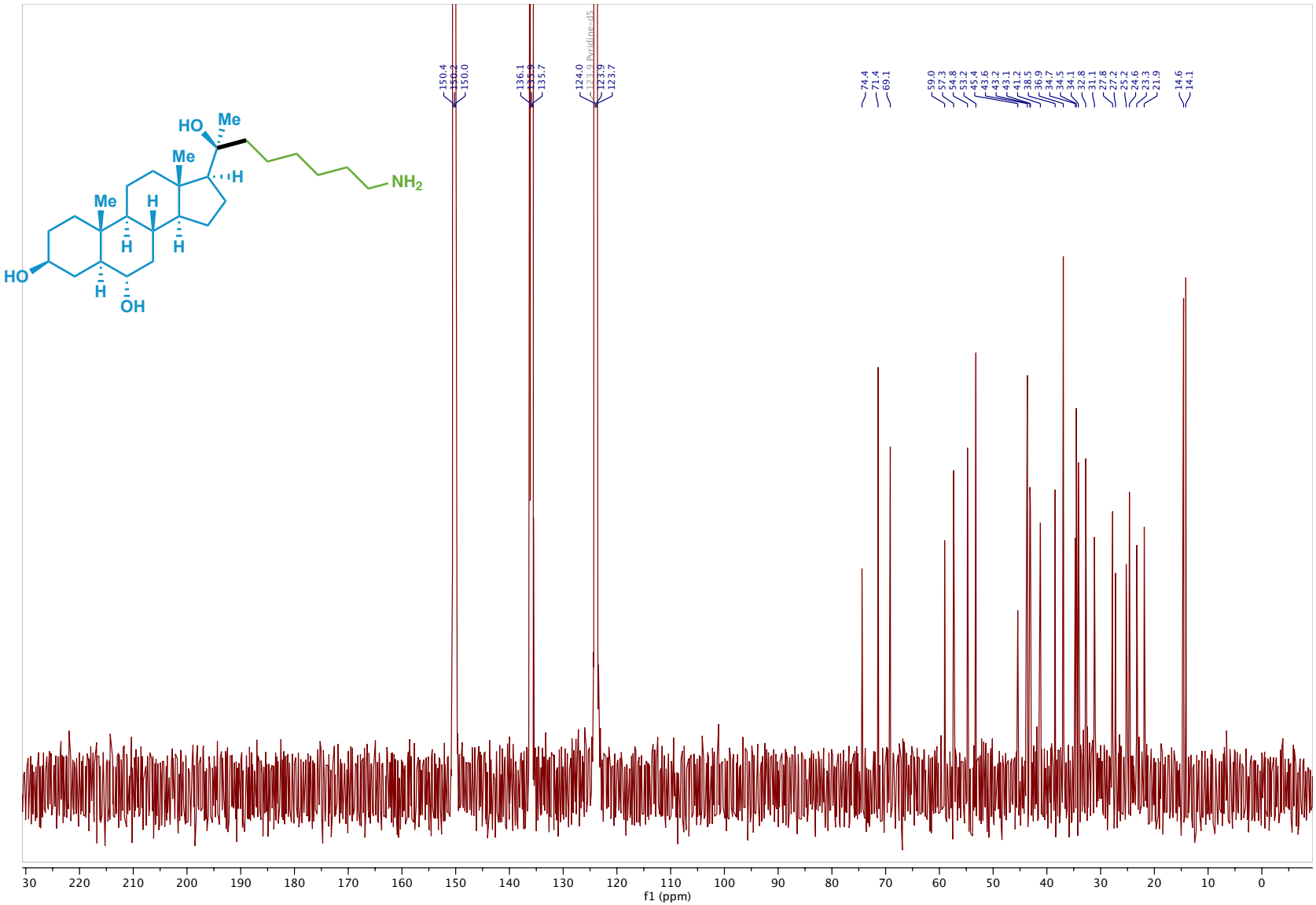
Compound 59


156.8
77.2
77.0
76.8
75.1
71.2
69.4
62.8
57.7
56.3
53.7
51.6
43.8
42.9
41.5
40.9
40.1
37.2
36.2
33.6
32.2
31.0
30.0
29.9
26.7
26.3
24.1
23.7
22.3
21.0
17.7
13.7
13.4
-1.5
HO
Me
Me
H
Me
H
H
H
HO
H
OH
O
O
N
H
TMS
f1 (ppm)

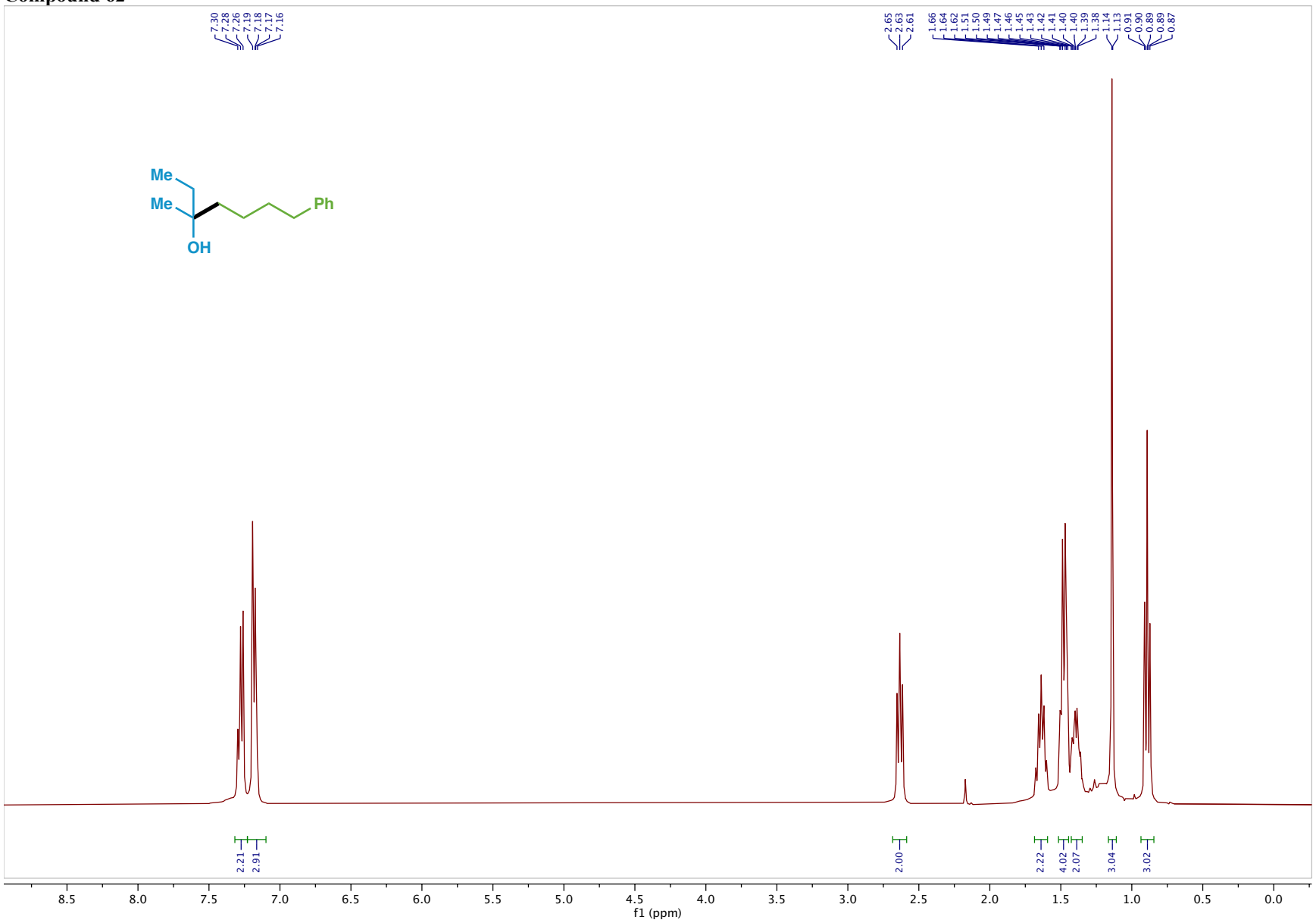
Compound 2



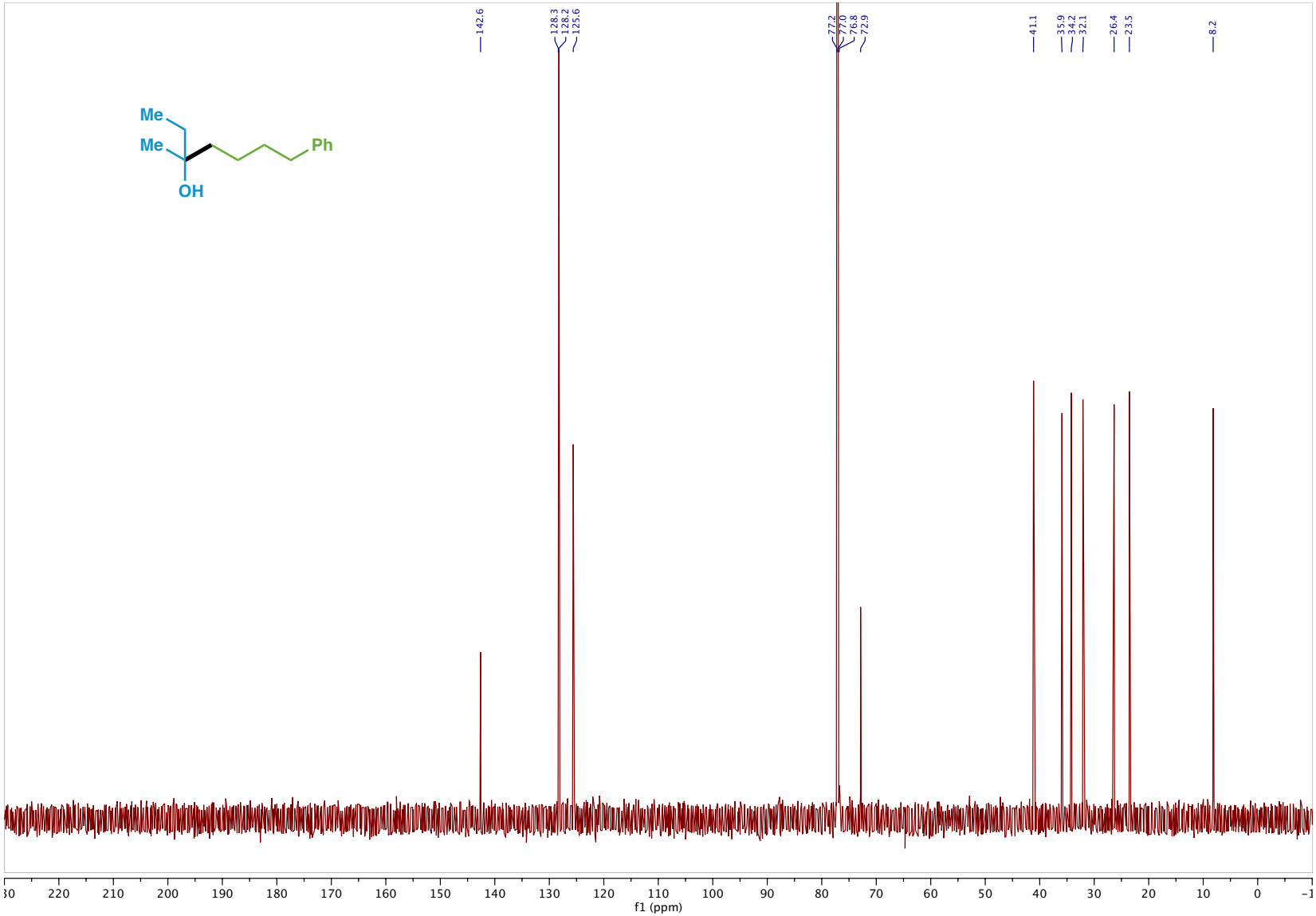
Compound 2


HO
Me
Me
H
NH2
Me
H
H
H
HO
H
OH
150.4
150.2
150.0
136.1
135.8
135.7
124.0
123.9 Pyridine-d5
123.9
123.7
74.4
71.4
69.1
59.0
57.3
54.8
53.2
45.4
43.6
43.2
43.1
41.2
38.5
36.9
34.7
34.5
34.1
32.8
31.1
27.8
27.2
25.2
24.6
23.3
21.9
14.6
14.1
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

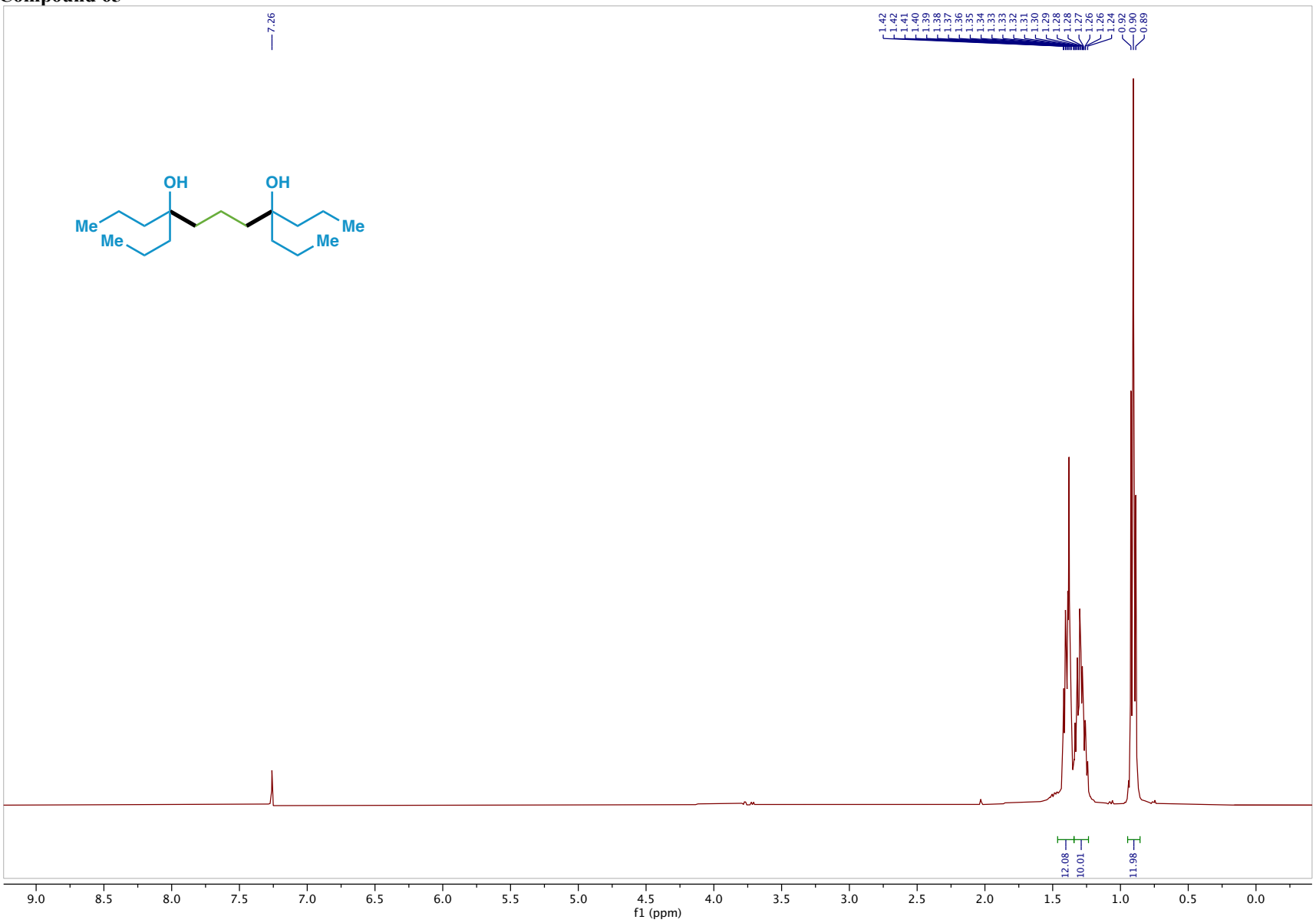
Compound 62


7.30
7.28
7.26
7.19
7.18
7.17
7.16
2.65
2.63
2.61
1.66
1.64
1.62
1.51
1.50
1.49
1.47
1.46
1.45
1.43
1.42
1.41
1.40
1.39
1.38
1.14
1.13
0.91
0.90
0.89
0.89
0.87
Me
Me
Ph
OH
2.21
2.91
2.00
2.22
4.02
2.07
3.04
3.02
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
f1 (ppm)

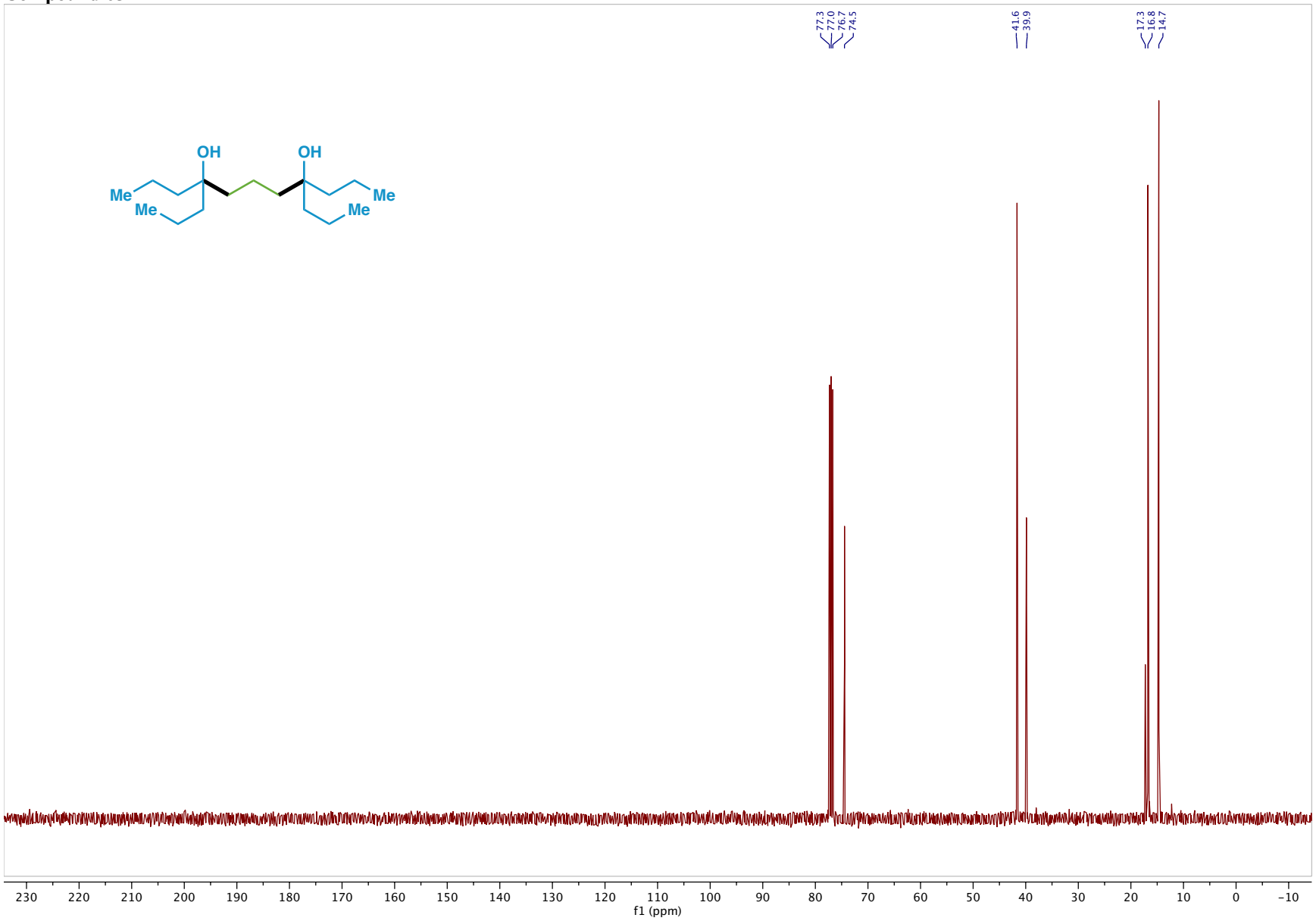
Compound 62


142.6
128.3
128.2
125.6
77.2
77.0
76.8
72.9
41.1
35.9
34.2
32.1
26.4
23.5
8.2
Me
Me
OH
Ph
f1 (ppm)

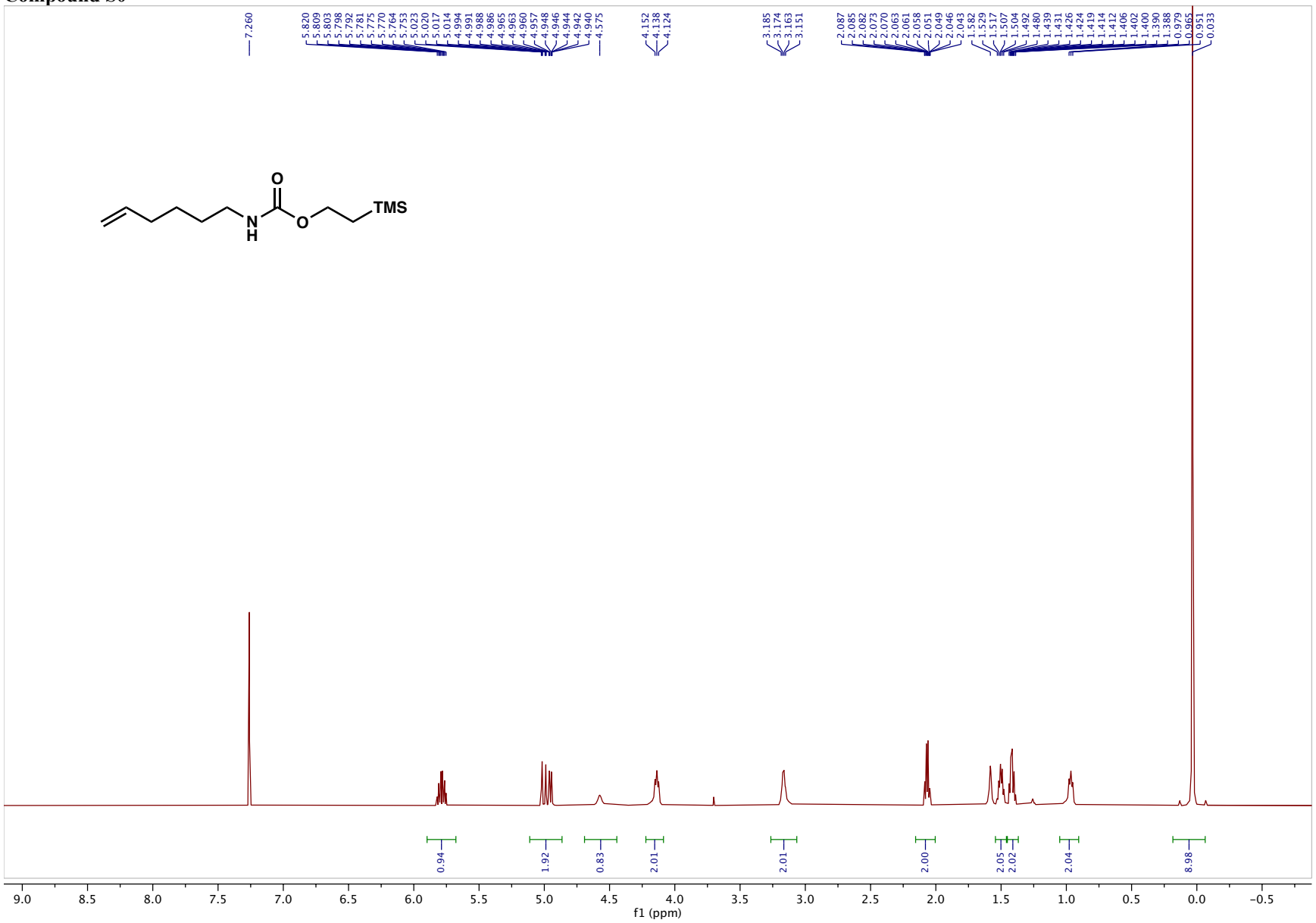
Compound 65


7.26
1.42
1.42
1.41
1.40
1.39
1.38
1.37
1.36
1.35
1.34
1.33
1.33
1.32
1.31
1.30
1.29
1.28
1.28
1.27
1.26
1.26
1.24
0.92
0.90
0.89
OH
OH
Me
Me
Me
Me
12.08
10.01
11.98
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
f1 (ppm)

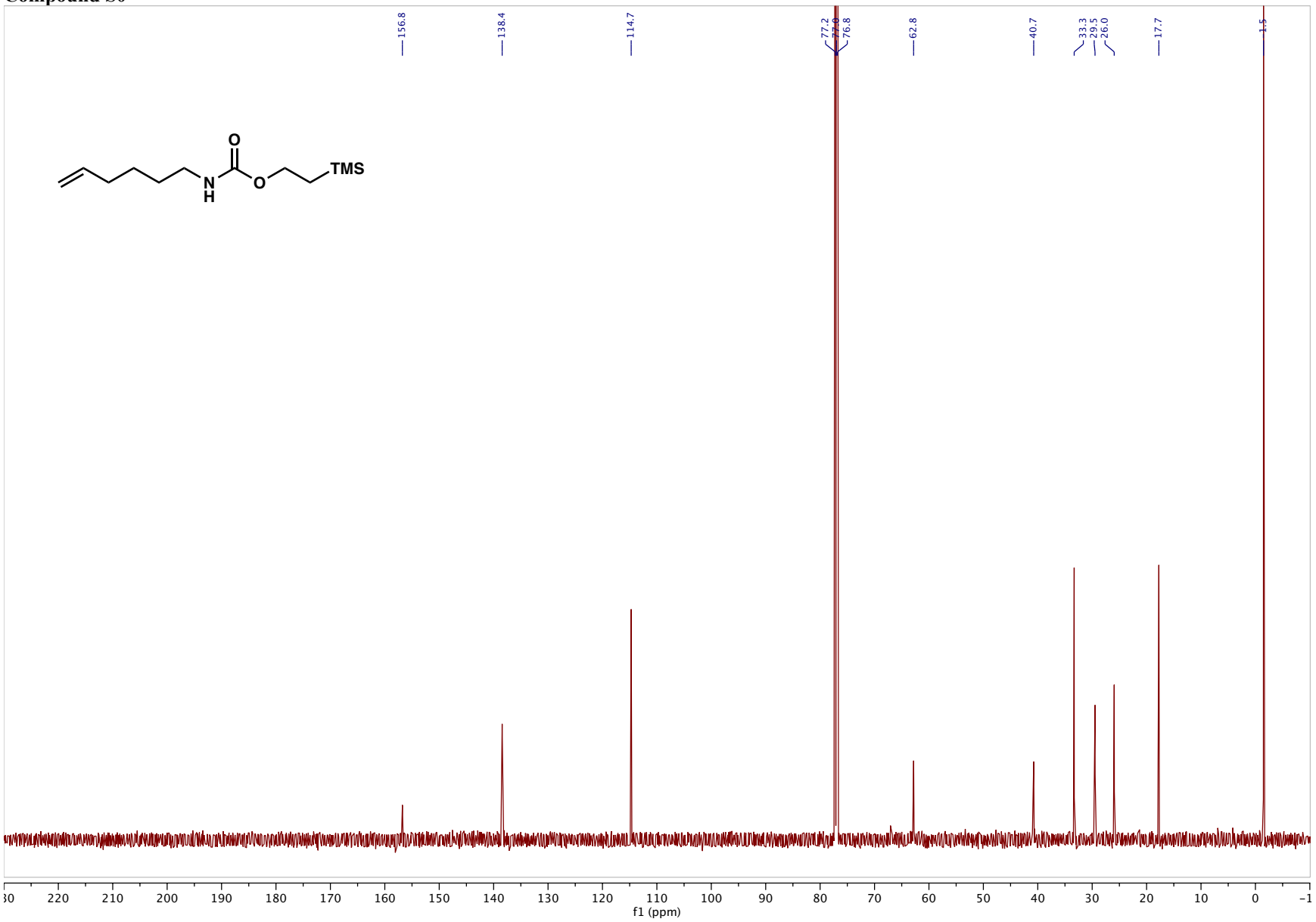
Compound 65


77.3
77.0
76.7
74.5
41.6
39.9
17.3
16.8
14.7
OH
OH
Me
Me
Me
Me
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

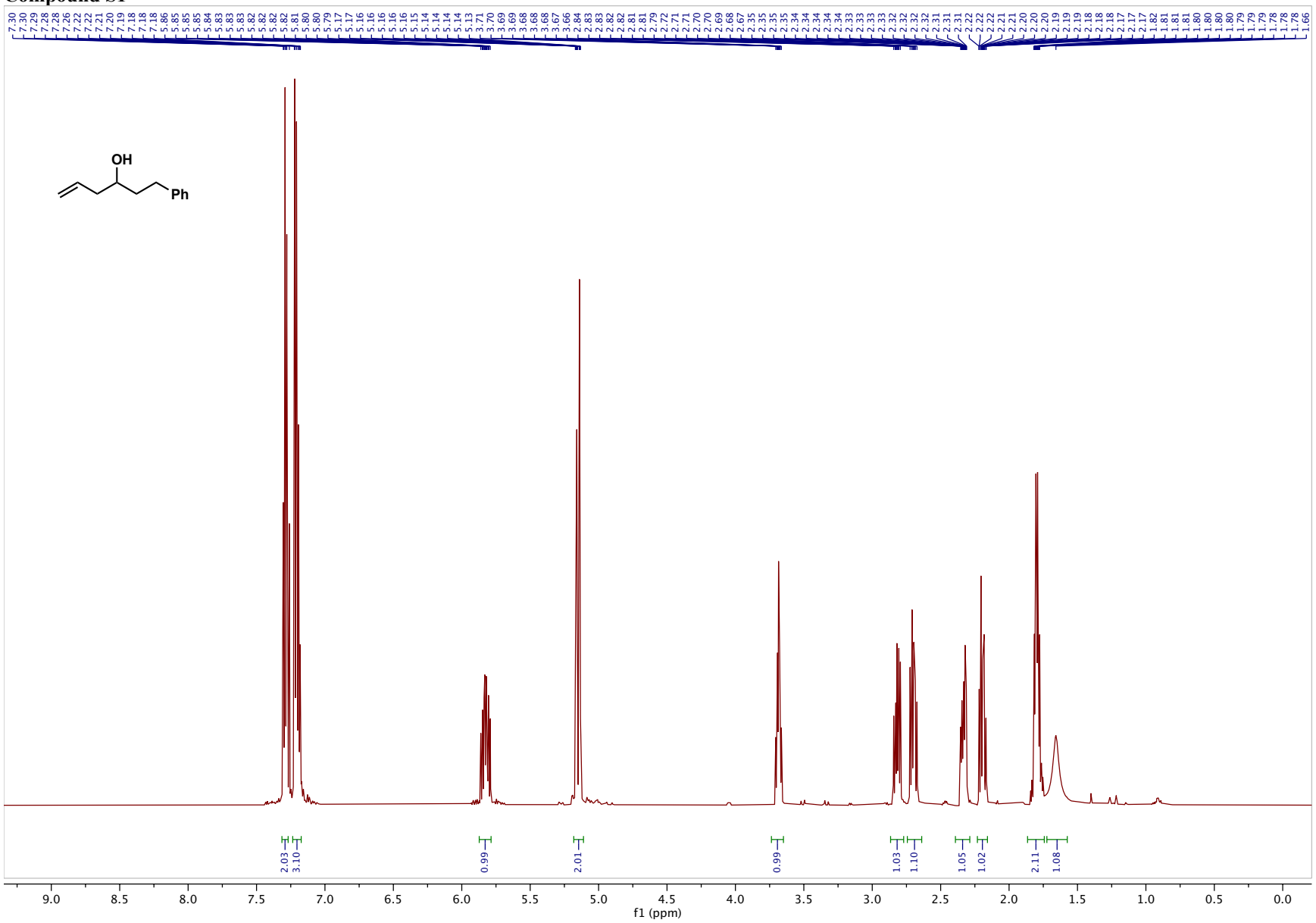
Compound S0


7.260
5.820
5.809
5.803
5.798
5.792
5.781
5.775
5.770
5.764
5.753
5.023
5.020
5.017
5.014
4.994
4.991
4.988
4.986
4.965
4.963
4.960
4.957
4.948
4.946
4.944
4.942
4.940
4.575
4.152
4.138
4.124
3.185
3.174
3.163
3.151
2.087
2.085
2.082
2.073
2.070
2.063
2.061
2.058
2.051
2.049
2.046
2.043
1.582
1.529
1.517
1.507
1.504
1.492
1.480
1.439
1.431
1.426
1.424
1.419
1.414
1.412
1.406
1.402
1.400
1.390
1.388
0.979
0.965
0.951
0.033
O
N
H
O
TMS
0.94
1.92
0.83
2.01
2.01
2.00
2.05
2.02
2.04
8.98
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
f1 (ppm)

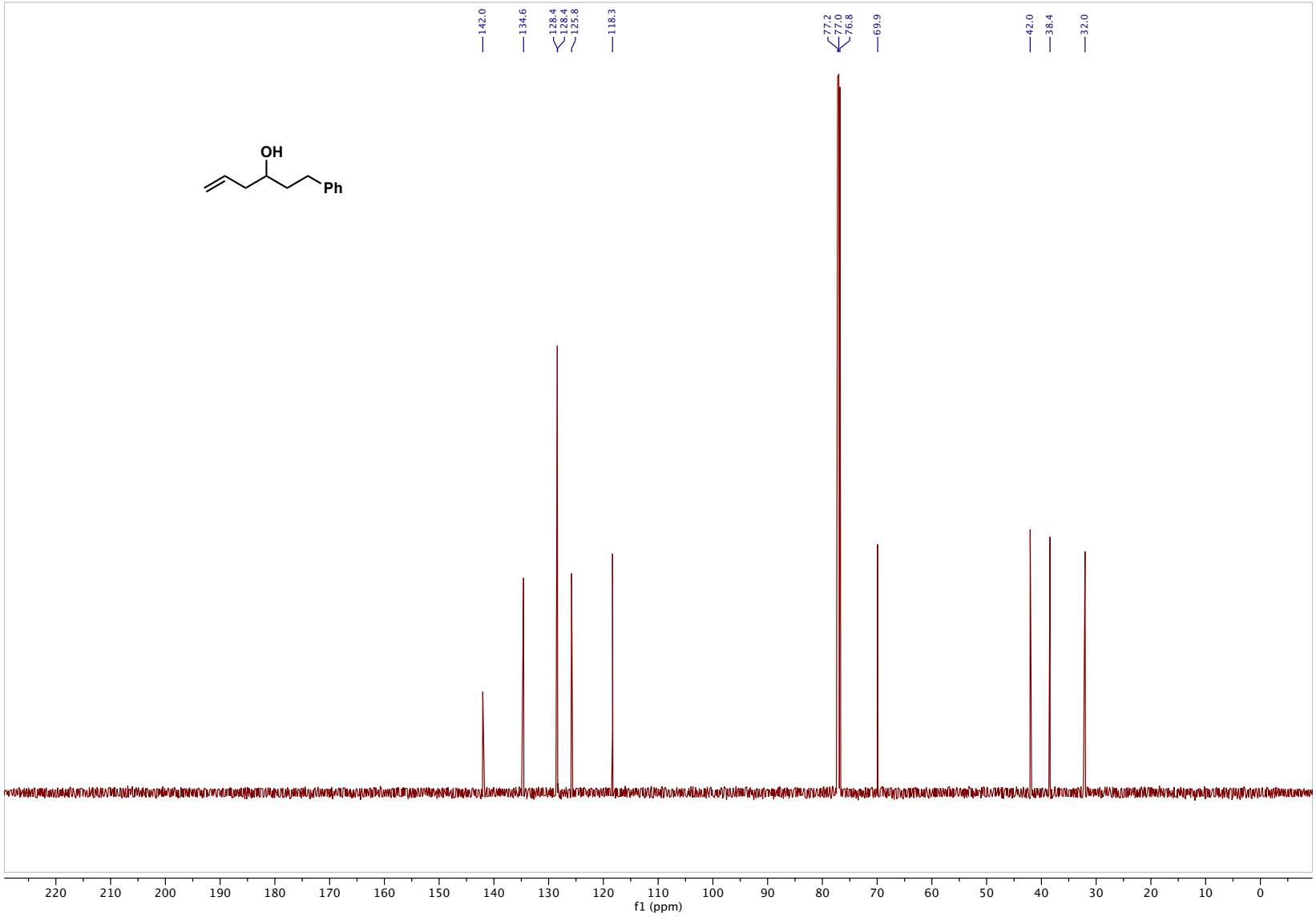
Compound S0


156.8
138.4
114.7
77.2
77.0
76.8
62.8
40.7
33.3
29.5
26.0
17.7
1.5
O
N
H
O
TMS
f1 (ppm)

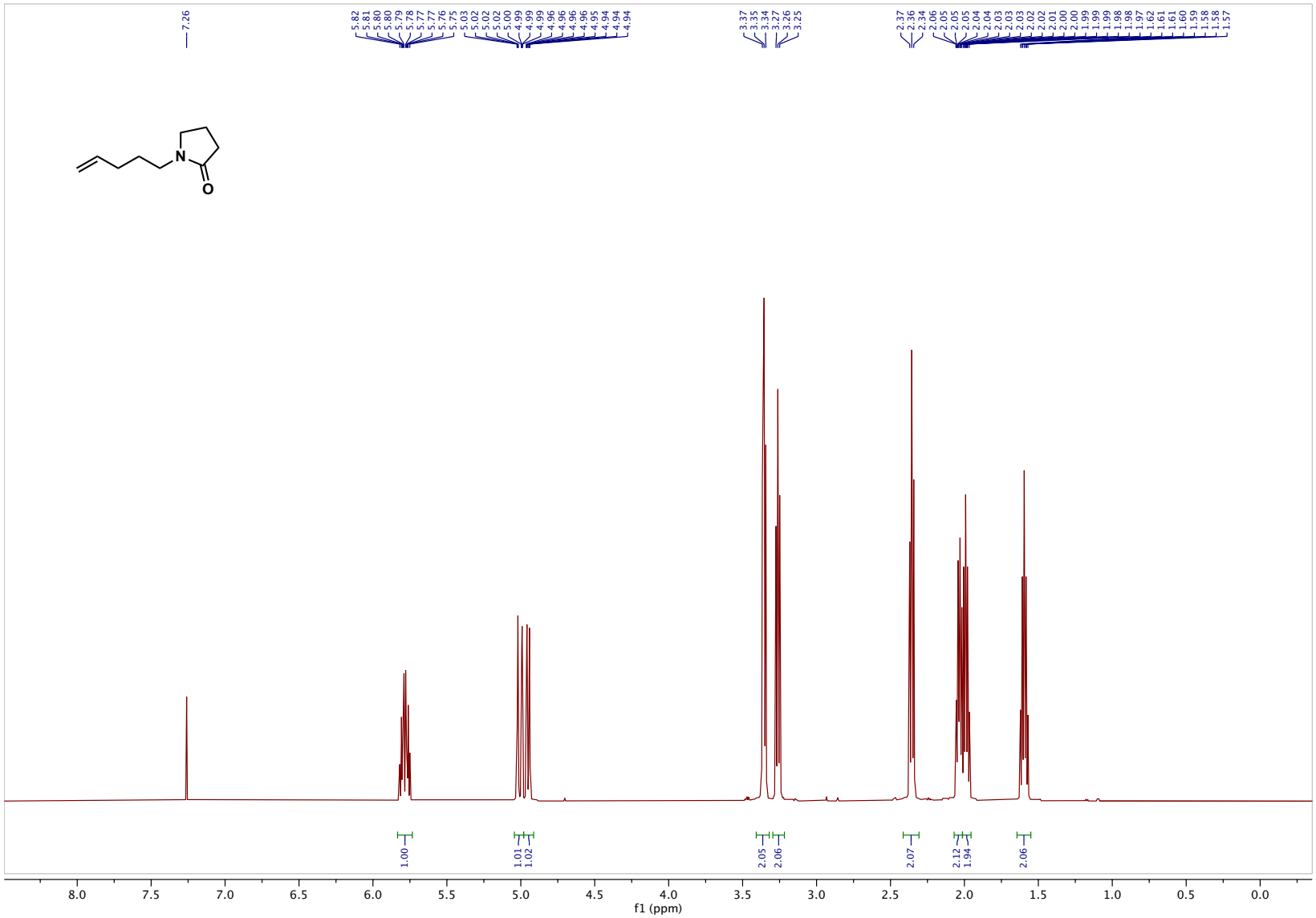
Compound S1



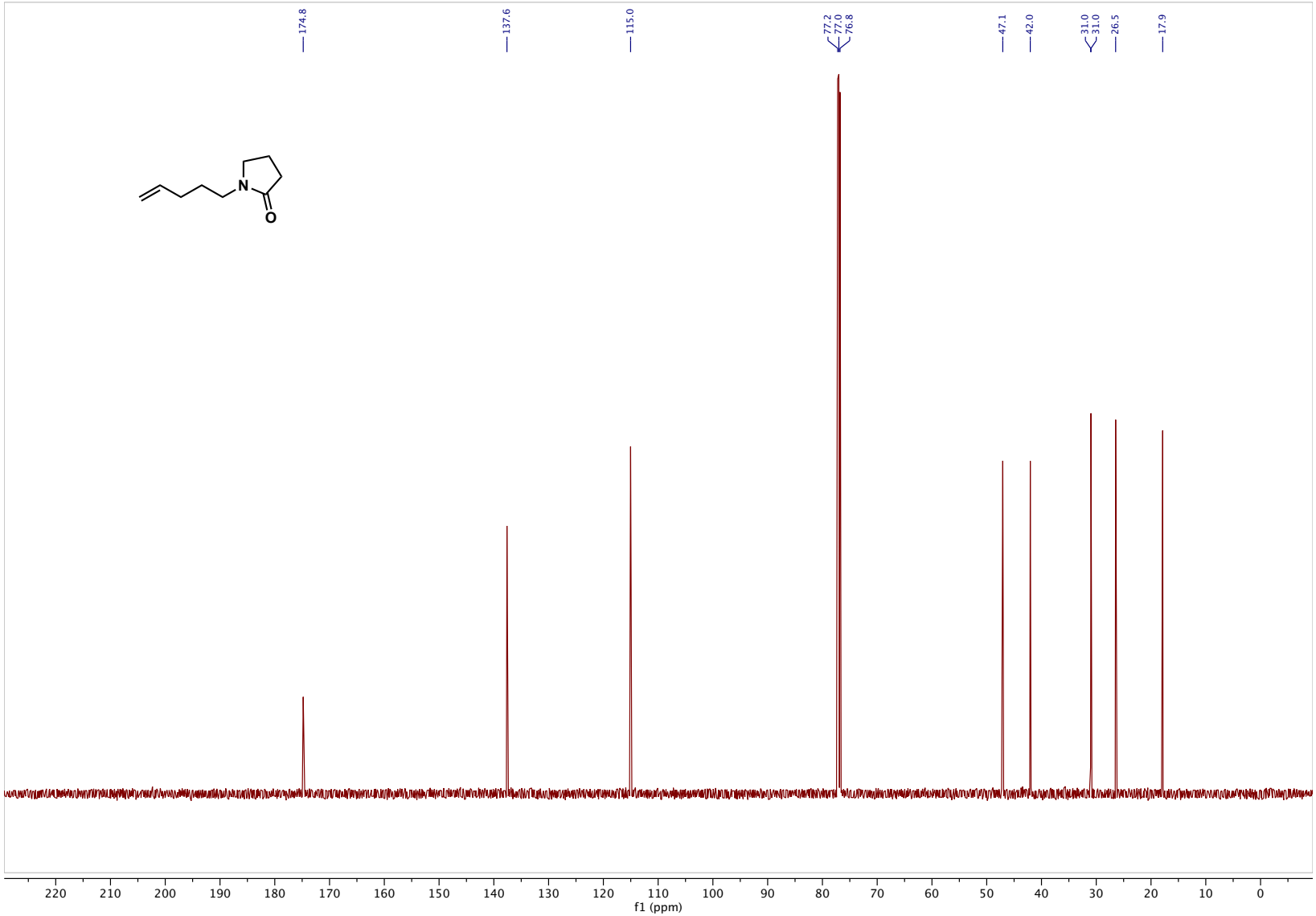
Compound S1


142.0
134.6
128.4
128.4
125.8
118.3
77.2
77.0
76.8
69.9
42.0
38.4
32.0
OH
Ph
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

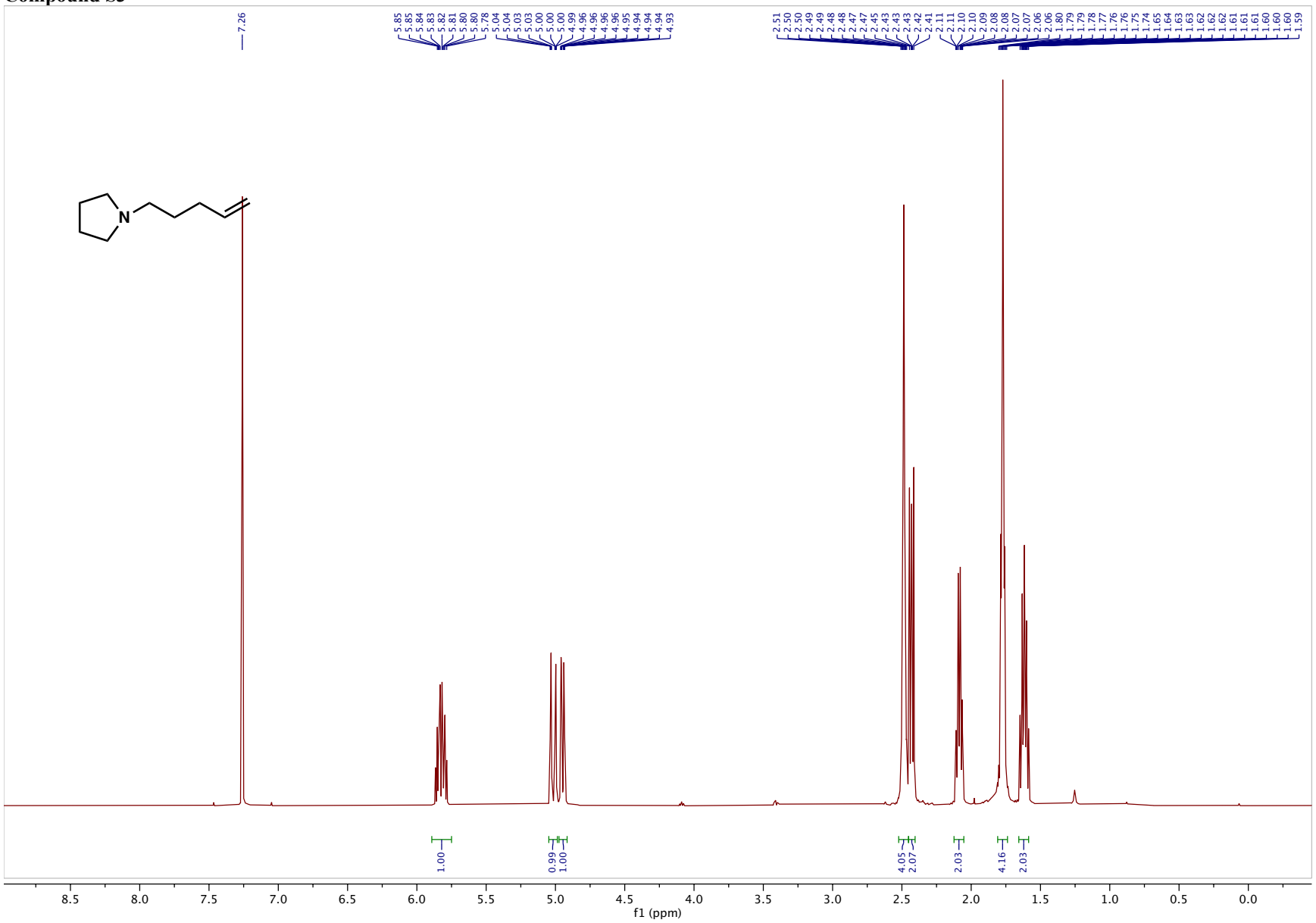
Compound S2


7.26
5.82
5.81
5.80
5.80
5.79
5.78
5.77
5.77
5.76
5.75
5.03
5.02
5.02
5.02
5.00
4.99
4.99
4.96
4.96
4.96
4.96
4.95
4.94
4.94
4.94
3.37
3.35
3.34
3.27
3.26
3.25
2.37
2.36
2.34
2.06
2.05
2.05
2.04
2.04
2.03
2.03
2.02
2.02
2.01
2.00
2.00
1.99
1.99
1.98
1.98
1.97
1.62
1.61
1.61
1.60
1.59
1.58
1.58
1.57
N
O
1.00
1.01
1.02
2.05
2.06
2.07
2.12
1.94
2.06
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
f1 (ppm)

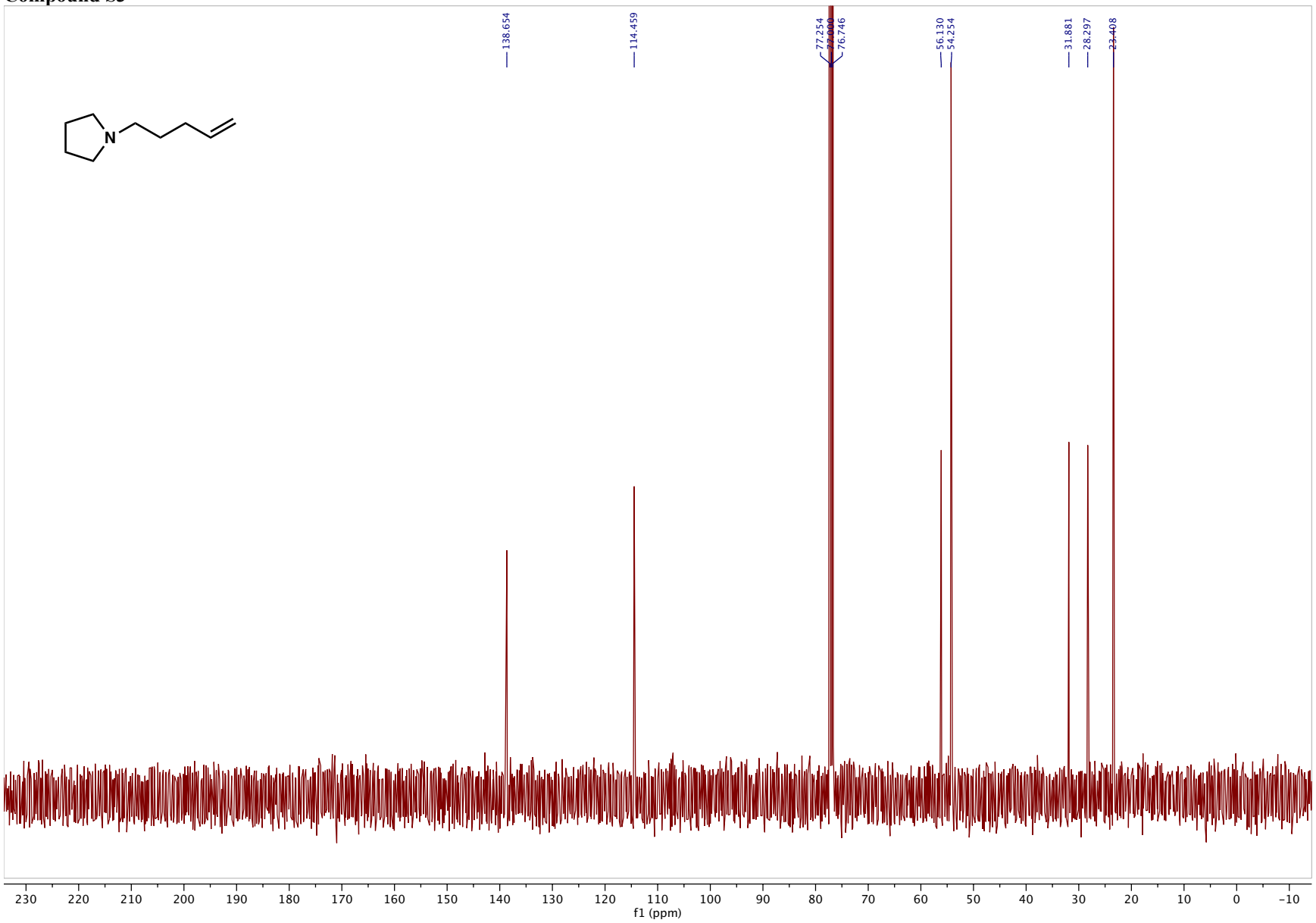
Compound S2


174.8
137.6
115.0
77.2
77.0
76.8
47.1
42.0
31.0
31.0
26.5
17.9
N
O
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

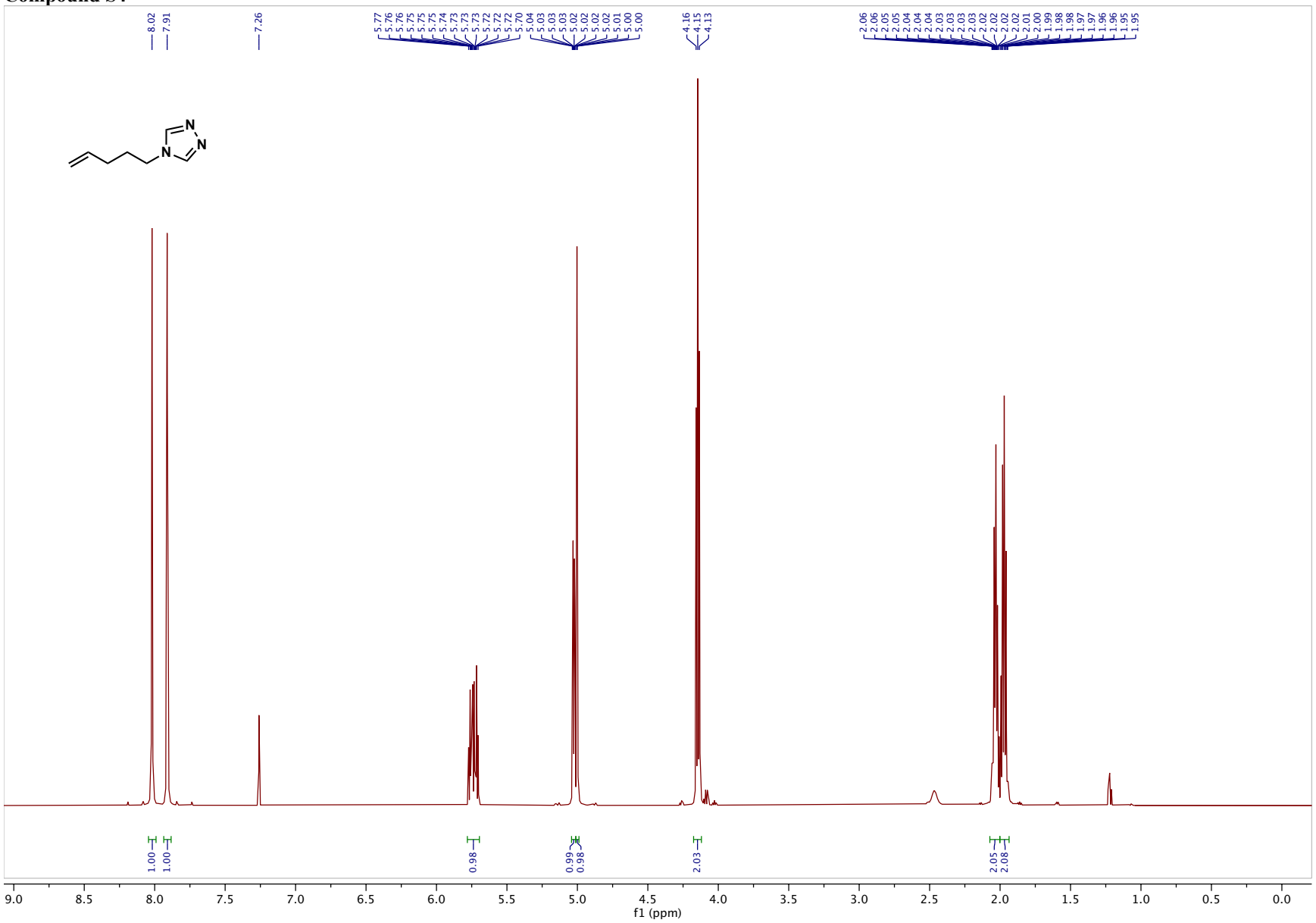
Compound S3


7.26
5.85 5.85 5.84 5.83 5.82 5.81 5.80 5.80 5.78 5.04 5.04 5.03 5.03 5.00 5.00 5.00 4.99 4.96 4.96 4.96 4.96 4.95 4.94 4.94 4.94 4.93
2.51 2.50 2.50 2.49 2.49 2.48 2.48 2.47 2.47 2.45 2.43 2.43 2.42 2.41 2.11 2.11 2.10 2.10 2.09 2.08 2.08 2.07 2.07 2.06 2.06 1.80 1.79 1.79 1.78 1.77 1.76 1.76 1.75 1.74 1.65 1.64 1.63 1.63 1.62 1.62 1.62 1.61 1.61 1.61 1.60 1.60 1.60 1.59
N
1.00
0.99
1.00
4.05
2.07
2.03
4.16
2.03
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
f1 (ppm)

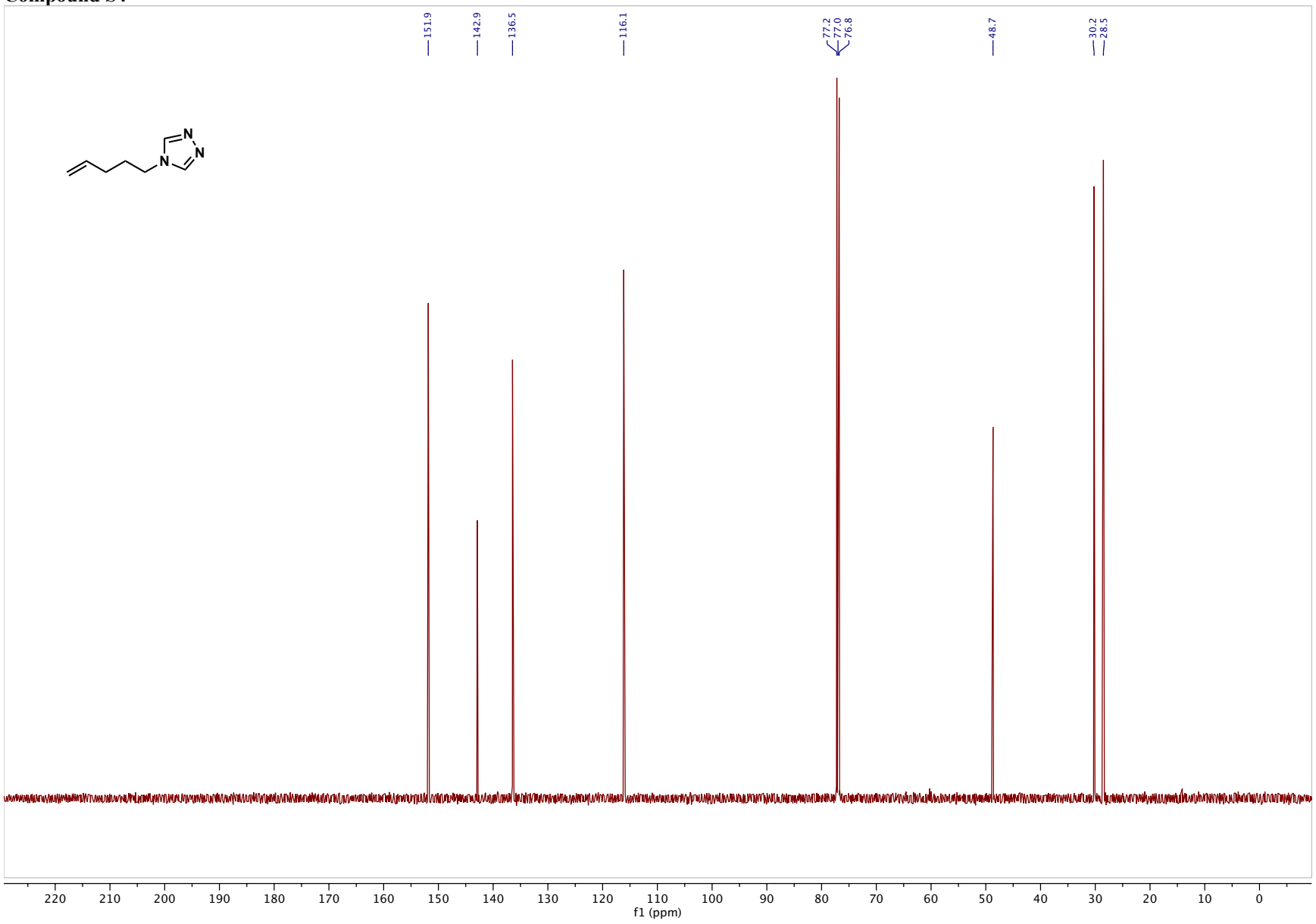
Compound S3


138.654
114.459
77.254
77.000
76.746
56.130
54.254
31.881
28.297
23.408
N
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

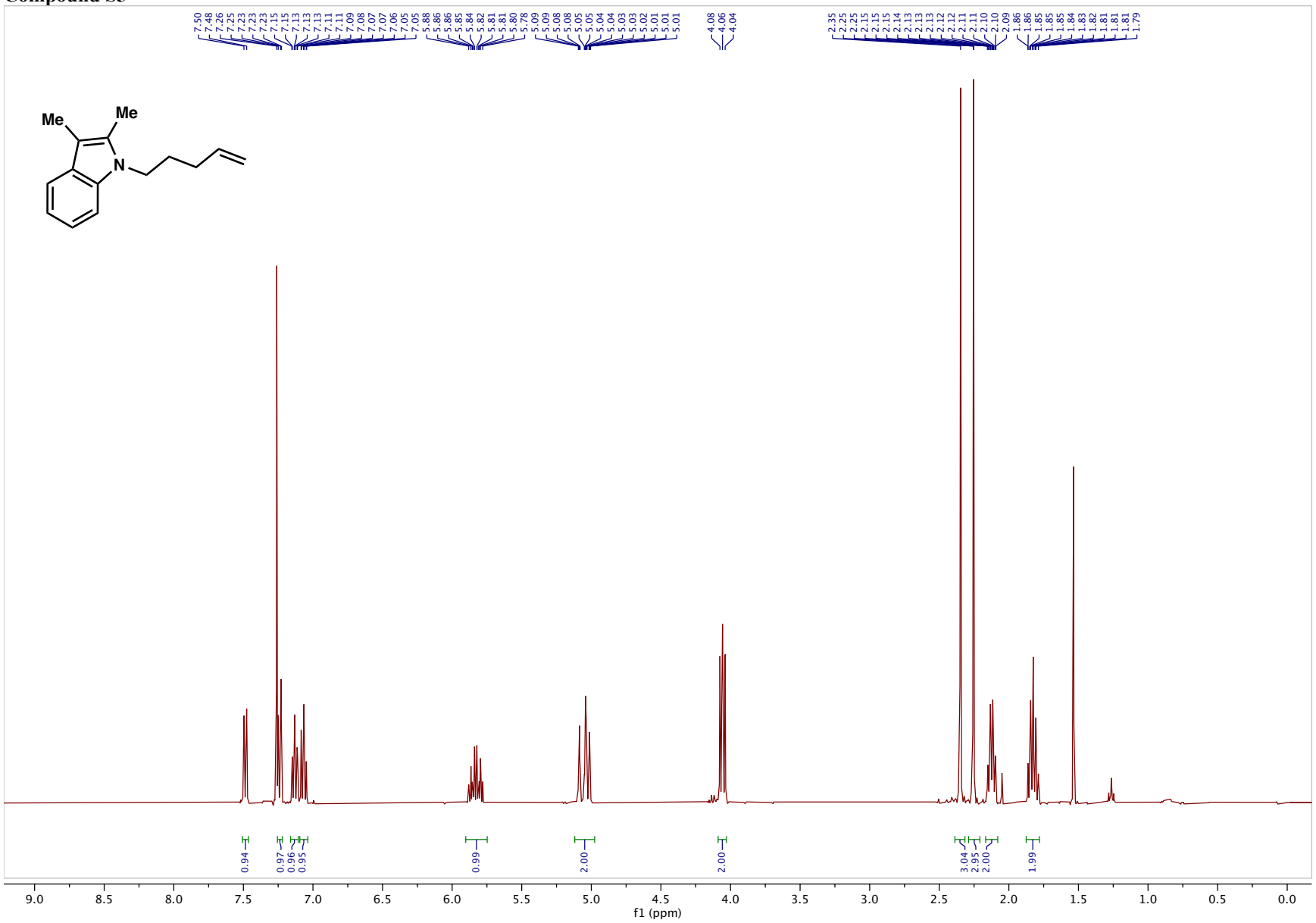
Compound S4


8.02
7.91
7.26
5.77
5.76
5.76
5.75
5.75
5.75
5.74
5.73
5.73
5.72
5.72
5.72
5.70
5.04
5.03
5.03
5.02
5.02
5.02
5.01
5.00
5.00
4.16
4.15
4.13
2.06
2.06
2.05
2.05
2.04
2.04
2.04
2.03
2.03
2.03
2.02
2.02
2.02
2.02
2.01
2.00
1.99
1.98
1.98
1.97
1.97
1.96
1.96
1.95
1.95
N
N
N
1.00
1.00
0.98
0.99
0.98
2.03
2.05
2.08
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
f1 (ppm)

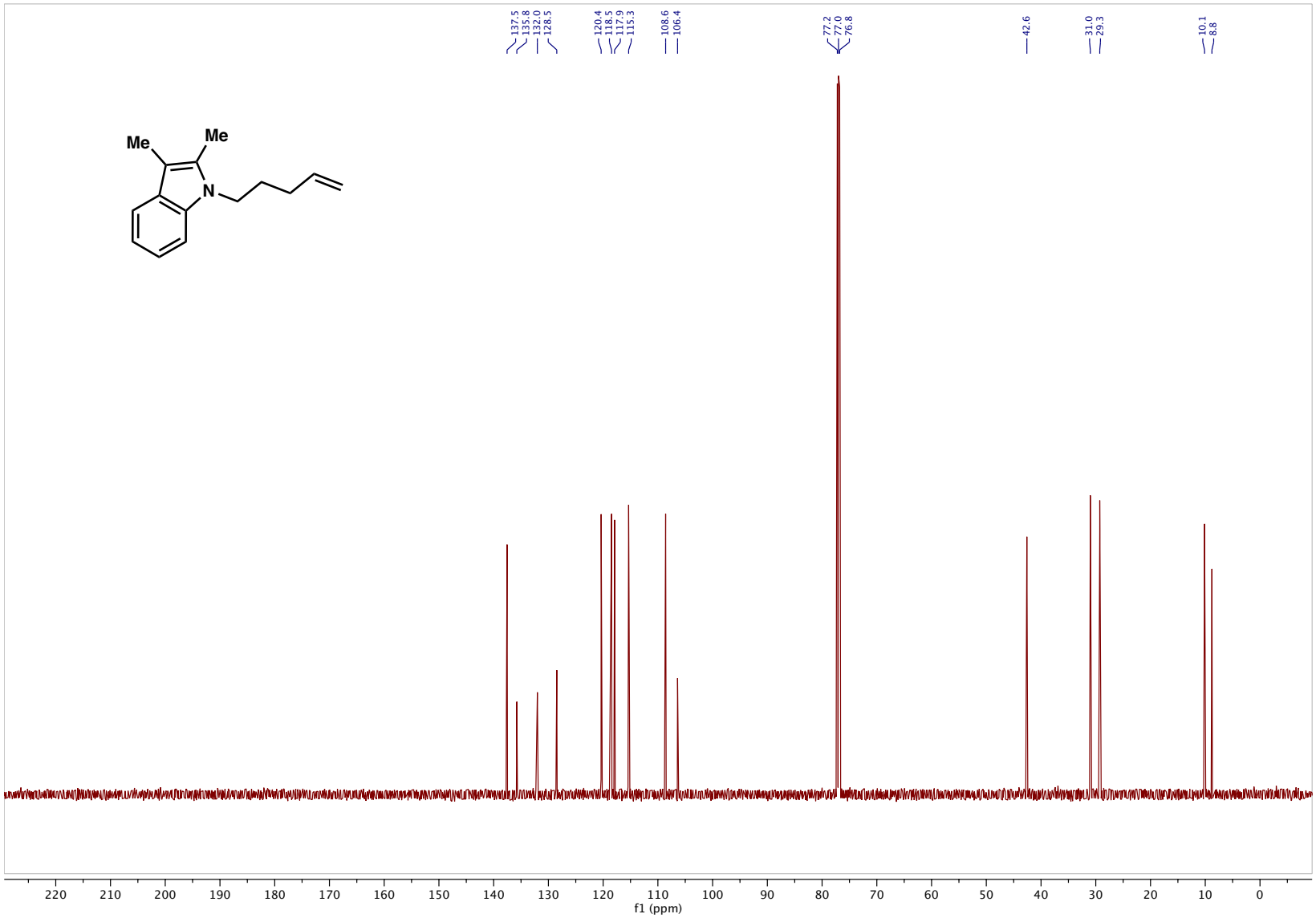
Compound S4


151.9
142.9
136.5
116.1
77.2
77.0
76.8
48.7
30.2
28.5
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

Compound S5



Compound S5


137.5
135.8
132.0
128.5
120.4
118.5
117.9
115.3
108.6
106.4
77.2
77.0
76.8
42.6
31.0
29.3
10.1
8.8
Me
Me
N
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)