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We describe a strategy for the iodane-guided functionalization of sterically congested C-H bonds, which is distinct from electronic, steric or proximity guided C-H functionalization methods. Readily accessible aryl(Mes)iodonium salts serve as the starting materials in these reactions and produce complex 1,2,3,4-substituted arenes via aryne intermediates. This approach is especially powerful when coupled with the innate C-H functionalization reactivity of simple arenes, to replace two C-H bonds with two C-C or C-heteroatom bonds while over-riding steric effects that typically inhibit such reactions. DFT stud-ies reveal a contribution of inductive, resonance, and steric effects on the regioselectivity of C-H cleavage and aryne generatation.

File list (3)

Iodane-Guided C-H Cleavage to Synthesize Densely Functionalized Arenes

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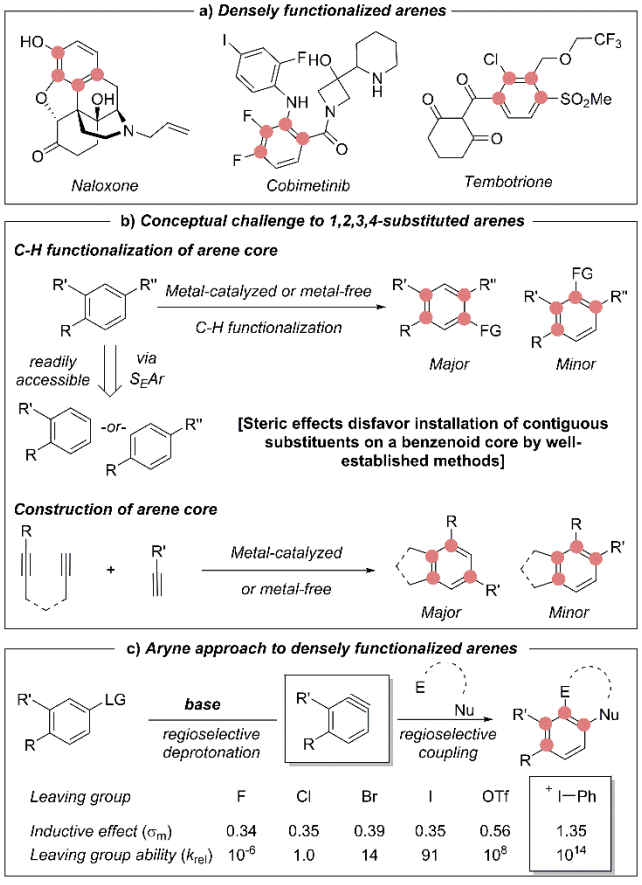
Supporting Information Placeholder

ABSTRACT: Herein, we describe a strategy for the iodane-guided functionalization of sterically congested C-H bonds, which is distinct from electronic, steric or proximity guided C-H functionalization methods. Readily accessible aryl(Mes)iodonium salts serve as the starting materials or intermediates in these reactions and produce complex 1,2,3,4-substituted arenes via aryne intermediates. This approach is especially powerful when coupled with the innate C-H functionalization reactivity of simple arenes, to replace two C-H bonds with two C-C or C-heteroatom bonds while overriding steric effects that typically inhibit such reactions. DFT studies reveal a contribution of inductive, resonance, and steric effects on the regioselectivity of C-H cleavage and aryne generatation.

Densely functionalized arenes with a contiguous arrangement of substituents are found in drugs, agrochemicals, and functional materials. Within this class, 1,2,3,4-substituted benzenoid rings are a component of the active pharmaceutical ingredients Naloxone and Cobimetinib, and the pesticide Tembotrione, among many others (Scheme 1a). Contiguous ring substituents, even two, have a dramatic influence on both structure and reactivity due to steric strain[1] and a so called "buttressing" effect.[2] However, despite both theoretical and applied interest in contiguously substituted arenes there are few general methods to access more highly substituted members of this family. Synthetic strategies to prepare functionalized benzenoid rings are highly sensitive to steric effects and therefore rendered ineffective to install contiguous substituents. For instance, many well-established C-H functionalization reactions that proceed by broadly distinct mechanisms functionalize the most sterically accessible position (Scheme 1b).[3] Additionally, construction of the arene core from unsaturated precursors typically places non-tethered substituents distal to other substituents (Scheme 1b).[4] Collectively, these strategies produce contiguously substituted arenes as the *minor* product, if at all. The development of reactions that overcome inherent substrate steric effects and functionalize hindered positions has not kept pace with these other aforementioned reactions. The consequence of this disparity is that contiguously substituted patterns are difficult to access, and densely functionalized building blocks are rare. Moreover, new synthetic methods that regioselectively functionalized sterically hindered positions have the potential to expand arene chemical space.

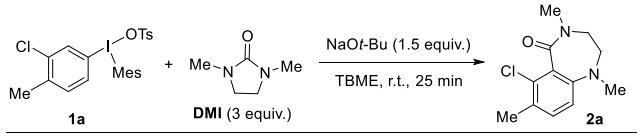
C-H functionalization remains an attractive strategy to functionalization arenes cores due to its intrinsic efficiency. Kinetic depro-

Scheme 1. Approach to densely functionalized arenes.



tonation/trapping of acidic arene C-H bonds is uniquely suited to override inherent steric effects. However, equilibration between kinetic and thermodynamic anions is substrate dependent and therefore limits the generality of this approach. [5] Moreover, the unintended departure of labile *ortho*-leaving groups leads to arynes reducing the yield of the intended product. Yet, *arynes are enticing intermediates to access densely functionalized arenes if they can be strategically used as an element of reaction design* (Scheme 1c). For example, can regioselective C-H deprotonation be coupled with regioselective[6] addition of two new substituents across the transient aryne to access 1,2,3,4-substituted arenes from readily available arene starting materials?[7] With this goal in mind, mono-functional aryne precursors are paramount (Scheme 1c).[8] A resurgence in this approach has focused on (pseudo)halide leaving groups,[9] but aryl carboxylic acids[10] and arylboronic acids[11] have also been used as substrates. Despite the attractive simplicity of mono-functional aryne precursors, three key complications exist. (1) Side reactions are well documented, including thia-Fries rearrangements of *ortho*-metallated aryl triflates,[12] competitive leaving group departure from polyhalo arenes,[9f,13] and competitive nucleophilicity of the base.[9f,g,13,14] (2) In some reactions the regioselectivity of C-H deprotonation remains low or occurs at the most sterically accessible proton, making these methods unsuitable for synthesis of densely functionalized arenes.[9d,e,g,h,11] (3) Many reactions require strong, air-sensitive amide bases,[9b,d,e,g,h] cryogenic temperatures,[9e] or weaker alkoxide bases at high temperatures (>120 °C),[9a,c,d] thus introducing practical limitations. Herein, we describe an approach that draws on the strong inductive withdrawing effect and hypernucleofugality of aryliodonium leaving groups (as estimated by σ_m, Scheme 1c)[15] to address the aforementioned complications of mono-functional aryne precursors. Our approach allows for room temperature C-H deprotonation in a highly regioselective manner with chemoselective ejection of the iodonium leaving group, leading to densely functionalized 1,2,3,4-substituted arenes after aryne capture. Mechanistic investigation by DFT provides a nuanced understanding of the regiocontrol over C-H deprotonation.

Table 1. Influence of reaction conditions.[a]

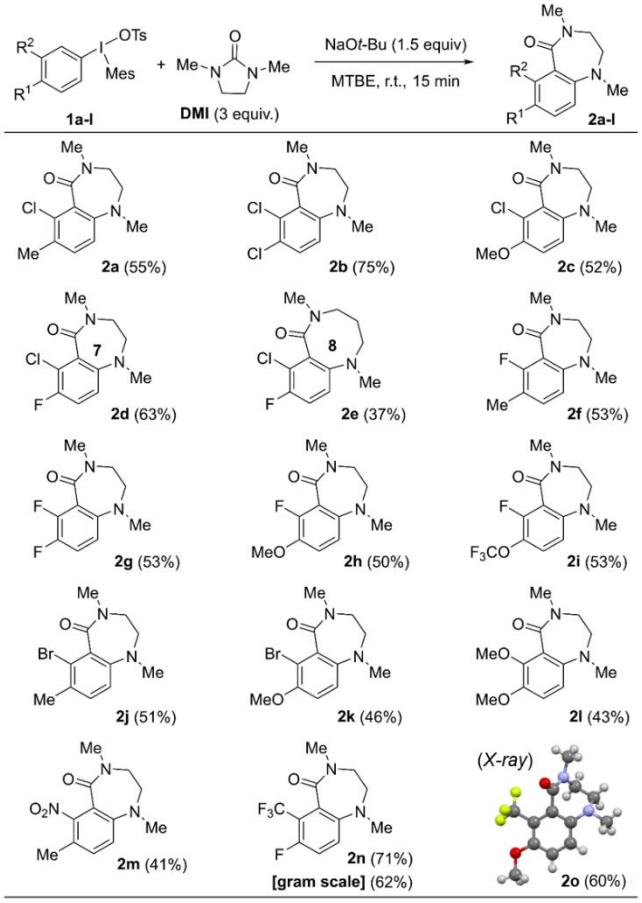


Entry	Deviation from standard conditions	% yield **2a**[b]
1	*none*	**69 (95)**[c]
2	iodide as leaving group	n.d.[d]
3	iodide as leaving group, dioxane as solvent	n.d.[d]
4	iodide as leaving group, dioxane as solvent, 80 °C	n.d.[d]
5	iodide as leaving group, dioxane as solvent, 135 °C	n.d.[d]
6	iodide as leaving group, dioxane as solvent, 135 °C, 24 h	21[e]
7	toluene as reaction solvent	66
8	MeCN as reaction solvent	45
9	1 equiv. of DMI	46
10	50 °C reaction temperature	65
11	15 min reaction time	69
12	5 min reaction time	55

[a]Conditions: **1a** (0.1 mmol, 1 equiv.), **DMI** (0.3 mmol, 3 equiv.), NaO*t*-Bu (0.15 mmol, 1.5 equiv.), TBME (0.5 mL), r.t., 25 min. [b]Determined by ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard. [c]95% consumption of **1a** based on integration of iodomesitylene by-product. [d]n.d. = not detected. [e]Average of two runs (16 and 25% yield) using conditions from ref. 10e

As an entry point to this strategy, we selected compound **1a** as aryne precursor[16] and dimethyl imidazolidone (**DMI**) as arynophile, which leads to medicinally relevant aryl diazepinone **2a** via σ-bond insertion of an aryne into a urea C-N bond. Although aryl diazepinones are desirable targets for medicinal chemistry, only two examples that contain a 1,2,3,4-substituted benzenoid core have been described in the literature.[17] Under our previously reported conditions[18] to generate arynes, with aryl(Mes)iodonium salts and LiHMDS in toluene, we obtained a modest yield of ~ 20%. An extensive survey of bases, solvents, temperature, and reagent stoichiometry provided conditions that vastly improved the yield of **2a**. Employing 1.5 equiv. of NaO*t*-Bu as base in TBME as solvent, we achieved room temperature regioselective C-H deprotonation and trapping of the aryne with 3 equiv. of DMI (Table 1, entry 1; 69% yield). We also assayed the consumption of **1a** at 95% based on the observation of the mesityl iodide by-product (Table 1, entry1). The monovalent iodide leaving group did not lead to any observable quantity of **2a** (Table 1, entry 2), and other solvents (1,4-dioxane) and higher temperatures (80 and 135 °C) did not produce **2a** (Table 1, entry 3-5). When the iodide leaving group was employed in 1,4-dioxane at 135 °C for 24 hours we did observe variable but low quantities of **2a** (Table 1, entry 6). The contrast in conditions required for iodide *vs* iodonium leaving groups is striking: 135 °C for 24 hours (21% yield) *vs* room temperature for 25 minutes (69% yield), and is consistent with the dramatically greater inductive effect of iodonium relative to other (pseudo)halides

Chart 1. Scope of aryl(Mes)iodonium tosylate salts.[a]



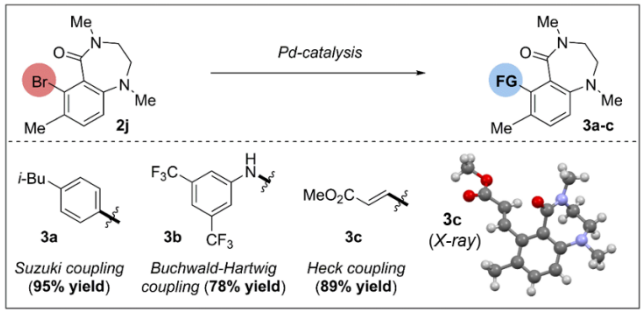
[a]Conditions: **1** (0.5 mmol, 1 equiv.), **DMI** (1.5 mmol, 1-3 equiv.), NaO*t*-Bu (0.75 mmol, 1.5-3 equiv.), MTBE (2.5 mL), r.t., 15-40 min; see SI for variations.

(Scheme 1e). Other relevant aspects of the reaction conditions are presented in Table 1: toluene provides similar yield of product, though acetonitrile resulted in lower yield of **2a** (Table 1, entry 7 and 8). Decreasing the equivalents of urea, resulted in lower yield of **2a** (Table 1, entry 9), and increasing the reaction temperature had a negligible impact on the yield of **2a** (Table 1, entry 10).[19] Finally, we found that similar yield of **2a** was observed after 15 minutes of reaction time and a moderate yield of 55% was observed after only 5 minutes of reaction time (Table 1, entry 11 and 12).

Chart 1 contains examples of selected aryl(Mes)iodonium salts that are compatible under our standard conditions. The isolated yields range from 43-75%, and high regioselectivity was observed for both C-H deprotonation and addition of the C and N atoms of urea across aryne intermediate.[20] Relevant to the regioselectivity of C-H deprotonation, several groups are compatible *meta*- to the iodonium leaving group (Cl: **2a-e**, F: **2f-i**, Br: **2j**,**k**, OMe: **2l**, NO_2: **2m**, and CF_3: **2n**,**o**; Chart 1). Fluoride and fluorinated groups (CF_3, **2n**, **2o**; OCF_3, **2i**) are prevalent in medicinal chemistry and these products represent new building blocks incorporating fluorine. Additionally, the inclusion of chloride (**2a-e**) and bromide (**2j**,**k**) allows for further elaboration of these densely functionalized building blocks by transition metal catalysis. Finally, the X-ray structure of **2o** illustrates the extreme steric congestion present in these products. Closer inspection reveals an out of plane dihedral angle for the benzenoid ring carbons of 6.06 °, which is consistent with dihedral angles observed in highly congested hexasubstituted benzenoid rings.[21]

As highlighted above, the incorporation of chloride and bromide groups in the aryl diazepinone products provides an opportunity for further functionalization of the benzenoid core. The bromide leaving group in **2j** is substituted for an aryl group, an amine, or an alkenyl group via Suzuki, Buchwald-Hartwig, and Heck coupling reactions respectively.[22] Each coupling product is obtained in high yield (**3a-c**, Scheme 2), and the X-ray structure of **3c** shows the E-configuration of the alkene product.

Scheme 2. Derivatization of aryl diazepinone 2b.[a]

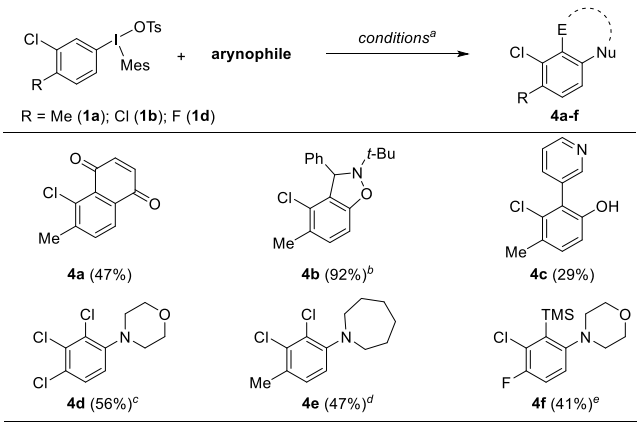


[a]See SI for detailed conditions.

We have also demonstrated that other arynophiles participate in this general strategy to access a range of 1,2,3,4-substituted benzenoid cores (Chart 2). Cycloaddition with 2-(trimethylsiloxy)furan or *N*-*tert*-butylphenylnitrone yielded annulated products **4a** and **4b**, respectively. Reaction with pyridine *N*-oxide led to the heterobiaryl linkage in **4c** with 1,2,3,4-substitution on the benzenoid ring. Regioselective insertion of the aryne intermediate into N-Cl and N-Si σ-bonds yielded **4d-f**. Although in some cases moderate yields were obtained, few other methods of arene C-H functionalization are able to access the 1,2,3,4-substitution pattern with the efficiency obtained by this approach.

The full power of this strategy may be realized by coupling the innate regioselectivity of electron-rich arenes with the iodane guided regioselectivity for dual C-H functionalization of readily available hydrocarbon feedstocks (Scheme 3a). We demonstrate

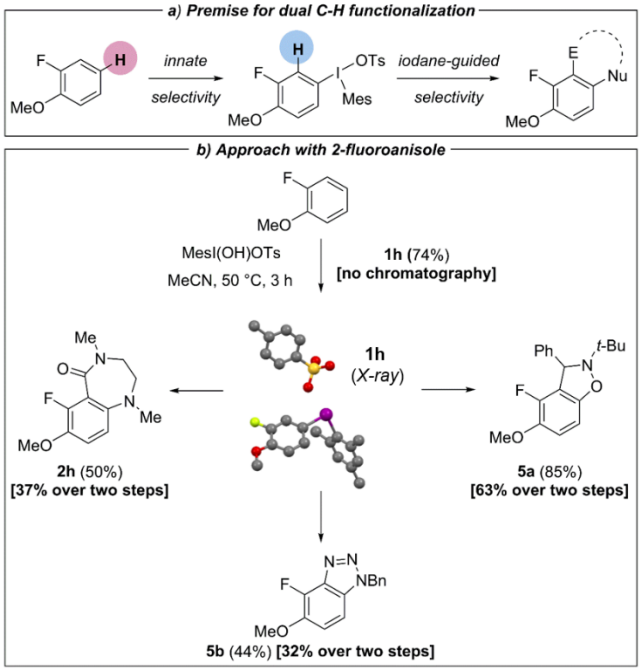
Chart 2. Representative arynophiles.



[a]Conditions: **1a** (0.5 mmol, 1 equiv.), arynophile (1.1-3 equiv.), NaO*t*-Bu (1.5-5 equiv.), MTBE (2.5 mL), r.t., 15-60 min.; see SI for variation. [b]Isolated as a mixture of regioisomers (11:1), see SI. [c]Used **1b** as starting material. [d]Isolated as a mixture of regioisomers (22:1), see SI. [e]Used **1h** as starting material.

this by sequential coupling reactions of 2-fluoroanisole (Scheme 3b). Diaryliodonium **1h** is readily obtained in 74% yield by condensation of 2-fluoroanisole with [hydroxyl(tosyloxy)]iodomesitylene in acetonitrile at 50 °C. The reaction occurs within three hours and the product is isolated by trituration. Treatment of **1h** with NaO*t*-Bu extrudes an aryne intermediate that undergoes annulation with several arynophiles to produce a range of nitrogen heterocycles (Scheme 3b). The total sequence to convert 2-fluoroanisole into **2h**, **5a**, or **5b** by replacing two *ortho* aromatic C-H bonds with C-C, C-N, and C-O bonds requires ~ 4 hours and one chromatographic purification of the final heterocycle. Moreover, this approach to take a 1,2-substituted arene to a 1,2,3,4-substituted arene is virtually unparalleled in efficiency.

Scheme 3. Dual C-H functionalization reactions.[a]



[a]Conditions: **1k**: 2-fluoroanisole (1 mmol, 1 equiv.), MesI(OH)OTs (1 mmol, 1 equiv.), TsOH•H_2O (1 mmol, 1 equiv.),

MeCN (1 mL), 50 °C, 3 hours. **2k**, **5a**, **5b**: **1k** (0.5 mmol, 1 equiv.), arynophile (1.1-3 equiv.), NaO*t*-Bu (1.5-5 equiv.), MTBE (2.5 mL), r.t., 15-60 min.; see SI for variation.

We have previously shown that the selectivity of C-H deprotonation *ortho* to iodonium leaving groups occurs in a contra-steric fashion, although the exact contribution of electronic and steric effects to regioselectivity was unclear.[18a] Here, we use DFT to provide further insight into the structural effects of the iodonium moiety and the transition states that dictate the observed selectivity. All major and minor aryne formation transition structures involving aryl(Mes)iodonium salts (**1a-o**) have been computed using the M06-2X density functional with the PCM solvation model for toluene. The LANL2DZDP basis set and effective core potential was used for iodine and 6-31G* was used for all other elements.[23,24]

Aryne formation occurs via a concerted process in which cleavage of the C-H bond (2- or 6-position) and elimination of the iodo-2,4,6-trimethylbenzene and sodium tosylate of the aryl(Mes)iodonium salt (**1a-o**)[25] by NaO*t*Bu are concurrent (Figure 1). Although not selectivity determining, a cation-π interaction between the mesityl group and the sodium cation (of NaO*t*Bu) brings the base and C-H bond in close proximity in both transition structures. Deprotonation at the more sterically hindered 2-position to form **Major-Aryne-1a** is favored over formation of the **Minor-Aryne-1a** by 4.08 kcal/mol, which corresponds to a product ratio of > 900: 1 at room temperature and is consistent with the experimentally observed exclusive regioselectivity. In fact, this trend is observed for all aryl(Mes)iodonium salts (**1a-o**) in this study with the deprotonation at the 2-position consistently favored by ~ 1–7 kcal/mol.

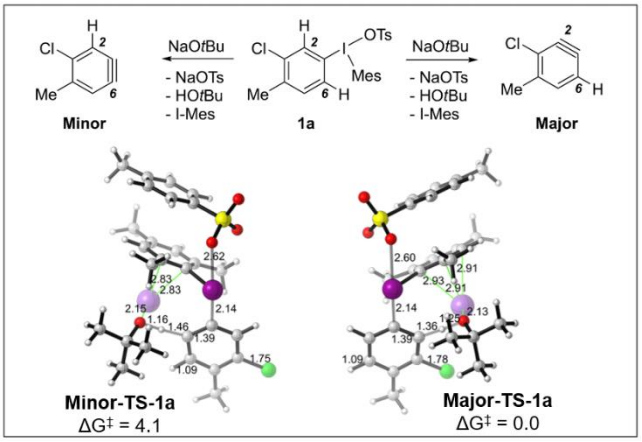


Figure 1. Computed transition structures for formation of **Major** and **Minor-Aryne-1a**. **Major-TS-1a** (right) is the deprotonation at the 2-position for form **Major-TS-1a** is favored over deprotonation at the 6-position, **Minor-TS-1a** (left), to form **Minor-Aryne-1a**. Distances are in Ångströms and energies in kcal/mol.

Regiocontrol appears to stem from differential electronic stabilization of the partial negative charge formed on the aromatic ring during the deprotonation process. The developing anion is better stabilized at the 2-position rather than at the 6-position. This is primarily due to the through-bond inductive electron withdrawing effects of the iodonium moiety and the 3-position moiety rather than resonance effects which is consistent with selectivity for the proximal C-H bond rather than the distal one. Two additional observations support this point: (1) we performed an NBO analysis of the transition structures to quantify the magnitude of orbital interaction between the C-H bond and the substituent in the 3-position (C-Cl in Figure 1). This analysis uniformly showed that the orbital component is not significant. (2) In addition, we have performed a linear free-energy relationship analysis to correlate computed selectivities from major and minor transition structures for substrates **1a-o** with common LFER parameters. We included Hammett constant for *meta* and *para*, σ^+, field inductive effect (F), resonance effect (R), A-values, and ligand repulsive energy (E_R). We have computed every single possible linear regression model containing these terms and their permutations of up to six-term models. The best three-term model in shown in Figure 2.[26] The field inductive effect and the resonance effect[27] from the 3-position substituent (F_3 and R_3), and the σ^+ of the 4-position substituent (σ^+_4) all contribute to the stabilization of the partial negative charge formed during deprotonation (**Eq. 1**). Larger field inductive effects and smaller resonance effects correlate with greater stability for deprotonation at the 2-position relative to the 6-position with the contribution from inductive effects being approximately nine times more significant than those from resonance effects. This is consistent with the moiety at the 3-position being able to stabilize deprotonation at the 2-position by inductive electron withdrawing effects while being able to stabilize deprotonation at the 2- and 6-positions though resonance effects. The significant field inductive effect associated with the iodonium moiety[15] is also required to deprotonate the *ortho* position of the aryl group in substrates **1a-o** and aligns with entries 2-6 in Table 1. There is also a small stabilizing effect correlated with larger steric bulk[28] (as approximated using A-values) at the 4-position.

$$Y = 5.35351 - 17.66168(F_3) + 2.04654(R_3) - 3.20116(\sigma^+_4)$$ **Eq. 1**

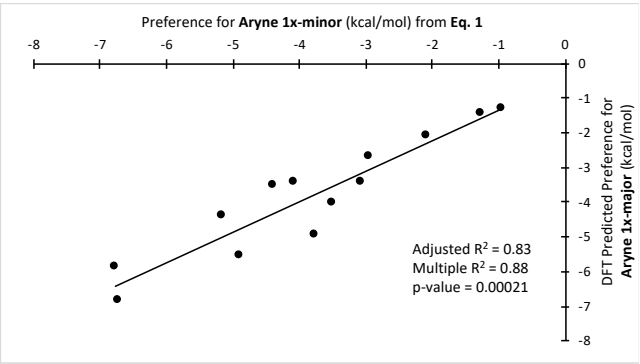


Figure 2. Linear Free Energy Relationship between the DFT-predicted preference for the formation of Major and Minor-1x-Aryne products as given by Eq. 1.

In conclusion, we have described a strategy to functionalize sterically hindered aryl C-H bonds from aryl(Mes)iodonium salts and aryne intermediates. This strategy leads to synthetically challenging and important densely functionalized 1,2,3,4-substituted benzenoid building blocks. Functional group compatibility of aryl bromides allows for downstream derivatization using conventional palladium-catalysis. Arynophiles that undergo annulation or σ-bond insertion with the intermediate aryne introduce new C-C, C-O, C-N, C-Cl, and C-Si bonds. Additionally, dual C-H functionalization elaborates simple arenes via the intermediacy of both aryl(Mes)iodonium salts and aryne intermediates in a regiocontrolled fashion. Finally, insight obtained from DFT calculations highlights a novel cation-π interaction that initiates C-H deprotonation and regioselectivity that includes contributions from field inductive effects, resonance effects, and steric effects. We are continuing to elaborate upon this platform to access other challenging substitution patterns.

ASSOCIATED CONTENT

Supporting Information

Experimental procedures, X-ray and spectral data (PDF), computational data (PDF)

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Notes

The authors declare no competing financial interests.

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REFERENCES

[1] (a) Föster, H.; Vögtle, F. Steric Interactions in Organic Chemistry: Spatial Requirements of Substituents. *Angew. Chem. Int. Ed.* **1977**, *16*, 429-441. (b) March, J. *Advanced Organic Chemistry: Reactions, Mechanism, and Structure* 4th ed.; John Wiley & Sons: New York, 1992; pp 501-568.

[2] (a) Herrmann, R. I.; Rae, I. D. The Effects of Electronic Buttressing on the Conformations of Some *ortho*-Disubstituted Benzenes. *Aust. J. Chem.* **1972**, *25*, 811-815. (b) Orlek, B. S.; Sammes, P. G.; Weller, D. J. Use of Steric Buttresses to Enhance Intramolecular Cycloadditions. *J. Chem. Soc. Chem. Commun.* **1993**, 1412-1413. (c) Decouzon, M.; Ertl, P.; Exner, O.; Gal, J.-F.; Maria, P.-C. Concepts of Sterically Hindered Resonance and Buttressing Effect: Gas-Phase Acidities of Methyl-Substituted Benzoic Acids and Basicities of Their Methyl Esters. *J. Am. Chem. Soc.* **1993**, *115*, 12071-12078. (d) Anderson, J. E.; Bru-Capdeville, V.; Kirsch, P. A.; Lomas, J. S. Attractive Steric Interactions within Molecules. The Masking of Effects in *meta*-Disubstituted Benzenes by Buttressed Repulsive Interactions. *J. Chem. Soc. Chem. Commun.* **1994**, 1077-1078. (e) Heiss, C.; Cottet, F.; Schlosser, M. *meta*- Rather then *ortho*-Directed Metalations: Buttressing Effects Prejudicing the Proton Abstration from (2,6-Dihalophenyl)silanes. *Eur. J. Org. Chem.* **2005**, 5236-5241.

[3] For representative examples of C-H functionalization at the most sterically accessible position, see: (a) Fang, P.; Li, M.; Ge, H. Room Temperature Palladium-Catalyzed Decarbonylative *ortho*-Acylation of Acetanilides with α-Oxocarboxylic Acids. *J. Am. Chem. Soc.* **2010**, *132*, 11898-11899. (b) Giri, R.; Lam, J. K.; Yu, J.-Q. Synthetic Applications of Pd(II)-Catalyzed C-H Carboxylation and Mechanistic Insights: Expedient Routes to Anthrallic Acids, Oxazolinonones, and Quinazolinones. *J. Am. Chem. Soc.* **2010**, *132*, 686-693. (c) Bedford, R. B.; Haddow, M. F.; Mitchell, C. J.; Webster, R. L. Mild C-H Halogenation of Anilides and Isolation of an Unusual Palladium(I)-Palladium(II) Species. *Angew. Chem. Int. Ed.*, **2011**, *50*, 5524-5527. (d) Preshlock, S. M.; Ghaffari, B.; Maligres, P. E.; Krska, S. W.; Maleczka, R. E. Jr.; Smith, M. R. III. High-Throughput Optimization of Ir-Catalyzed C-H Borylation: A Tutorial for Practical Applications. *J. Am. Chem. Soc.* **2013**, *135*, 7572-7582. (e) Rodriguez, R. A.; Pan, C.-M.; Yabe, Y.; Kawamata, Y.; Eastgate, M. D.; Baran, P. S. Palau'chlor: A Practical and Reactive Chlorinating Reagent. *J. Am. Chem. Soc.* **2014**, *136*, 6908-6911. (f) Fernández-Salas, J. A.; Eberhart, A. J.; Procter, D. J. Metal-Free CH-CH Type Cross-Coupling of Arenes and Alkynes Directed by a Multifunctional Sulfoxide Group. *J. Am. Chem. Soc.* **2016**, *138*, 790-793. (g) Yanagi, T.; Otsuka, S.; Kasuga, Y.; Fujimoto, K.; Murakami, K.; Nogi, K.; Yorimitsu, H.; Osuka, A. Metal-Free Approach to Biaryls from Phenols and Aryl Sulfoxides by Temporarily Sulfur-Tethered Regioselective C-H/C-H Coupling. *J. Am. Chem. Soc.* **2016**, *138*, 14582-14585. (h) Davis, H. J.; Mihai, M. T.; Phipps, R. J. Ion Pair-Directed Regiocontrol in Transition-Metal Catalysis: A Meta-Selective C-H Borylation of Aromatic Quaternary Ammonium Salts. *J. Am. Chem. Soc.* **2016**, *138*, 12759-12762. (i) Wang, X-Y.; Dienel, T.; Di Giovannantionio, M.; Barin, G. B.; Karche, N.; Deniz, O.; Urgel, J. I.; Widmer, R.; Stolz, S.; De Lima, L. H.; Muntwiler, M.; Tommasisi, M.; Meuneir, V.; Ruffieux, P.; Feng, X.; Fasel, R.; Müller, K.; Narita, A. Heteroatom-Doped Perihexacene from a Double Helicene Precursor: On-Surface Synthesis and Properties. *J. Am. Chem. Soc.* **2017**, *139*, 4671-4674. (j) Wang, J.; Li, R.; Dong, Z.; Liu, P.; Dong, G. Complementary Site-Selectivity in Arene Functionalization Enabled by Overcoming the *Ortho* Constraint in Palladium/Norbornene Catalysis. *Nat. Chem.* **2018**, *10*, 866-872.

[4] Robinson, J. M.; Sakai, T.; Okano, K.; Kitawaki, T.; Danheiser, R. L. Formal [2+2+2] Cycloaddition Strategy Based on an Intramolecular Propargylic Ene Reaction/Diels-Alder Cycloaddition Cascade. *J. Am. Chem. Soc.* **2010**, *132*, 11039-11041

[5] Mack, K. A.; Collum, D. B. Case for Lithium Tetramethylpiperidide-Mediated Ortholithiations: Reactivity and Mechanisms. *J. Am. Chem. Soc.* **2018**, *140*, 4877-4883.

[6] For leading references, see: (a) Medina, J. M.; Mackey, J. L.; Garg, N. K.; Houk, K. N. The Role of Aryne Distortions, Steric Effects, and Charges in Regioselectivity of Aryne Reactions. *J. Am. Chem. Soc.* **2014**, *136*, 15798-15805. (b) Picazo, E.; Houk, K. N.; Garg, N. K. Computational predictions of substituted benzyne and indolyne regioselectivity. *Tetrahedron Lett.* **2015**, *56*, 3511-3514.

[7] For recent reviews, see: (a) Tadross, P. M.; Stoltz, B. M. A Comprehensive History of Arynes in Natural Product Total Synthesis. *Chem. Rev.* **2012**, *112*, 3550-3577. (b) Gampe, C. M.; Carreira, E. M. Arynes and Cyclohexynes in Natural Product Synthesis. *Angew. Chem. Int. Ed.* **2012**, *51*, 3766-3776. (c) Bhunia, A.; Reddy, S.; Biju, A. T. Recent advances in transition-metal-free carbon-carbon and carbon-heteroatom bond-forming reactions using arynes. *Chem. Soc. Rev.* **2012**, *41*, 3140-3152. (d) Dubrovskiy, A. V.; Markina, N. A.; Larock, R. C. Use of benzyne for the synthesis of heterocycles. *Org. Biomol. Chem.* **2013**, *11*, 191-218. (e) Yoshida, S.; Hosoya, T. The Renaissance and Bright Future of Synthetic Aryne Chemistry. *Chem. Lett.* **2015**, *44*, 1450-1460. (f) Yoshimura, A.; Saito, A.; Zhdankin, V. V. Iodonium Salts as Benzyne Precursors. *Chem. Eur. J.* **2018**, *24*, 15156-15166.

[8] Bifunctional aryne precursors, such as Kobayashi and related reagents are less effective toward this end because of the synthetic inefficiency and challenges of installing the requisite activating (TMS) and leaving (OTf) groups.

[9] Recent examples, see: (a) Yuan, Y.; Thomé, I.; Kim, S. H.; Chen, D.; Beyer, A.; Bonnamour, J.; Zuidema, E.; Chang, S.; Bolm, C. Dimethyl Sulfoxide/Potassium Hydroxide: A Superbase for the Transition Metal-Free Preparation of Cross-Coupling Products. *Adv. Synth. Catal.* **2010**, *352*, 2892-2898. (b) Truong, T.; Daugulis, O. Base-Mediated Intermolecular sp^2 C-H Bond Arylation via Benzyne Intermediates. *J. Am. Chem. Soc.* **2011**, *133*, 4243-4245. (c) Yang, S.; Wu, C.; Ruan, M.; Yang, Y.; Zhao, Y.; Niu, J.; Yang, W.; Xu, J. Metal- and ligand-free Ullman-type C-O and C-N coupling reactions promoted by potassium *tert*-butoxide. *Tetrahedron Lett.* **2012**, *53*, 4288-4292. (d) Truong, T.; Daugulis, O. Divergent reaction pathways for phenol arylation by arynes: synthesis of helicenes and 2-arylphenols. *Chem. Sci.*, **2013**, *4*, 531-535. (e) Truong, T.; Mesgar, M.; Khac, K.; Le, A.; Daugulis, O. General Method for Functionalized Polyaryl Synthesis via Aryne Intermediates. *J. Am. Chem. Soc.* **2014**, *136*, 8568-8576. (f) Dong, Y.; Lipschutz, M. I.; Tilley, T. D. Regioselective, Transition Metal-Free C-O Coupling Reactions Involving Aryne Intermediates. *Org. Lett.* **2016**, *18*, 1530-1533. (g) Mesgar, M.; Nguyen-Le, J.; Daugulis, O. New Hindered Amide Base for Aryne Insertion in Si-P, Si-S, Si-N, and C-C Bonds. *J. Am. Chem. Soc.*, **2018**, *140*, 13703-13710. (h) Cho, S.; Wang, Q. *ortho*-Difunctionalization of arynes by $LiZnEt_2$(TMP)-mediated deprotonative zincation/elimination of aryl triflates. *Tetrahedron* **2018**, *74*, 3325-3328.

[10] Cant, A. A.; Roberts, L.; Greaney, M. F. Generation of benzyne from benzoic acid using C-H activation. *Chem. Commun.* **2010**, *46*, 8671-8673.

[11] Devaraj, K.; Ingner, F. J. L.; Sollert, C.; Gates, P. J.; Orthaber, A.; Pilarski, L. T. Arynes and Their Precursors from Arylboronic Acids via Catalytic C-H Silylation. *J. Org. Chem.* **2019**, *84*, 5863-5871.

[12] Dyke, A. M.; Gill, D. M.; Harvey, J. N.; Hester, A. J.; Lloyd-Jones, G. C.; Munoz, M. P.; Shepperson, I. R. Decoupling Deprotonation from Metallation: Thia-Fries Rearrangement. *Angew. Chem. Int. Ed.* **2008**, *47*, 5067-5070.

[13] Bunnett, J. F.; Kearley, F. J. Jr. Comparative Mobility of Halogens in Reactions of Dihalobenzenes with Potassium Amide in Ammonia. *J. Org. Chem.* **1971**, *36*, 184-186.

[14] (a) Wickham, P. P.; Hazen, K. H.; Guo, H.; Jones, G.; Reuter, K. H.; Scott, W. J. Benzyne Generation from Aryl Triflates. *J. Org. Chem.* **1991**, *56*, 2045-2050. (b) Tripathy, S.; LeBlanc, R.; Durst, T. Formation of 2-Substituted Iodobenzenes from Iodobenzene via Benzyne and Ate Complex Intermediates. *Org. Lett.* **1999**, *1*, 1973-1975.

[15] For σ_m of phenyliodonium, see: (a) Mironova, A. A.; Maletina, I. I.; Iksanova, S. V.; Orda, V. V.; Yagupolskii, L. M. Electronic Nature of Substituents Containing Polyvalent Iodine. *Zh. Org. Chem.* **1989**, *25*, 306-311. For relative leaving group ability of phenyliodonium, see: (b) Okuyama, T.; Takino, T.; Sueda, T.; Ochiai, M. Solvolysis of Cyclohexenyliodonium Salt, a New Precursor for the Vinyl Cation: Remarkable Nucleofugality of the Phenyliodonio Group and Evidence for Internal Return from an Intimate Ion-Molecule Pair. *J. Am. Chem. Soc.* **1995**, *117*, 3360-3367.

[16] The 1,2,4-substitution pattern in **1a** is readily accessible by S_EAr and widely commercially available.

[17] (a) Yoshida, H.; Shirakawa, E.; Honda, Y.; Hiyama, T. Addition of Ureas to Arynes: Straightforward Synthesis of Benzodiazepine and Benzodiazocine Derivatives. *Angew. Chem. Int. Ed.* **2002**, *41*, 3247-3249. (b) Shah, T. K.; Medina, J. M.; Garg, N. K. Expanding the Strained Alkyne Toolbox: Generation and Utility of Oxygen-Containing Strained Alkynes. *J. Am. Chem. Soc.* **2016**, *138*, 4948-4954.

[18] (a) Sundalam, S. K.; Nilova, A.; Seidl, T. L.; Stuart, D. R. A Selective C-H Deprotonation Strategy to Access Functionalized Arynes by Using Hypervalent Iodine. *Angew. Chem. Int. Ed.* **2016**, *55*, 8431-8434. (b) Stuart, D. R. Unsymmetrical Diaryliodonium Salts as Aryne Synthons: Renaissance of a C-H Deprotonative Approach to Arynes. *Synlett* **2017**, *28*, 275-279.

[19] The mass balance appears to be a dual insertion product of aryne into each of the C-N bonds of the urea, which is minimized at the standard conditions with 3 equivalents of urea. Previous methods typically employ > 10 equivalents of urea as the solvent.

[20] Although minor signals in the aromatic region of crude ^{1}H NMR spectrum were difficult to assign, GCMS analysis of crude reaction mixtures did not reveal other regioisomeric products.

[21] Wagen, C. C.; Ingoglia, B. T.; Buchwald, S. L. Unexpected Formation of Hexasubstituted Arenes through a 2-fold Palladium-Mediated Ligand Arylation. *J. Org. Chem.* **2019**, DOI: 10.1021/acs.joc.9b02091.

[22] Suzuki, see: (a) Walker, S. D.; Barder, T. E.; Martinelli, J. R.; Buchwald, S. L. A Rationally Designed Universal Catalyst for Suzuki-Miyaura Coupling Processes. *Angewandte Chemie Int. Ed.* **2004**, *43*, 1871-1876. Buchwald-Hartwig, see: Surry, D. S.; Buchwald, S. L.; Dialkylbiaryl Phosphines in Pd-Catalyzed Amination: A User's Guide. *Chem. Sci*. **2011**, *2*, 27-50.

[23] (a) Y. Zhao and D. G. Truhlar, *Theor. Chem. Acc.*, **2008**, *120*, 215–241; (b) P. C. Hariharan and J. A. Pople, *Theor. Chim. Acta*, **1973**, *28*, 213–222; (c) W. J. Hehre, R. Ditch□eld and J. A. Pople, *J. Chem. Phys.*, **1972**, *56*, 2257–2261; (d) S. Miertu˘s, E. Scrocco and J. Tomasi, *Chem. Phys.*, **1981**, *55*, 117–129.

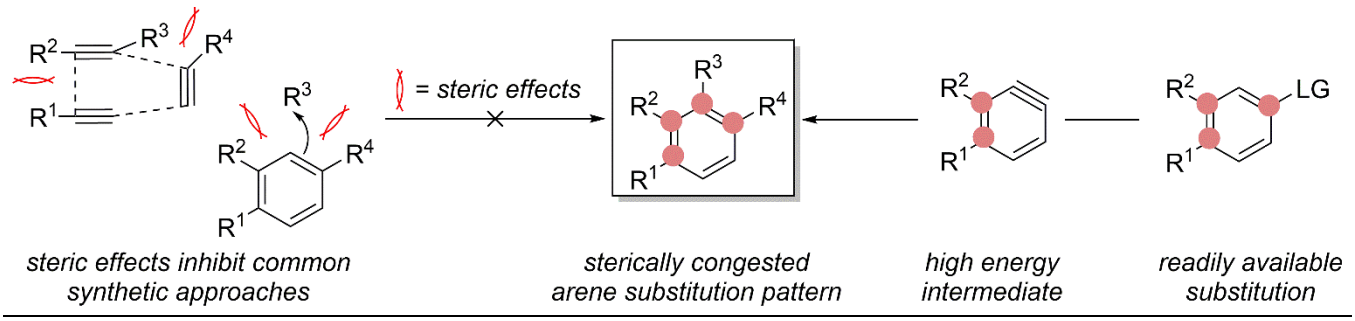
[24] (a) Check, C. E.; Faust, T. O.; Bailey, J. M.; Wright, B. J.; Gilbert, T. M.; Sunderlin, L. S. *J. Phys. Chem. A*, **2001**, *105*, 8111-8116. (b) Wadt, W. R.; Hay, P. J. *J. Chem. Phys.*, **1985**, *82*, 284-298.

[25] Transition structures involving compound **1c** could not be isolated in our hands and have been excluded from the discussion.

[26] Overfitting is a serious problem in cases with many predictors and few measurements. In order to guard against this, we performed the following two things: (1) The selectivity values were scrambled and new linear free energy relationships were computed; the models produced were poor. Even the best five term model only exhibited an R^2 of 0.3922. (2) The selectivity values were scrambled, and the best three-term model found for the real data (Eq. 1) was used to predict the scrambled data; this gave starkly different results from what we observed when we matched to the real selectivity data. See Supporting Information.

[27] Hansch, C.; Leo, A.; Taft, R. W. A Survey of Hammett Substituent Constants and Resonance and Field Parameters. *Chem. Rev.* **1991**, *91*, 165-195.

[28] Anslyn, E. V.; Dougherty, D. A. *Modern Physical Organic Chemistry* **2006**, University Science Books: Sausalito, CA, p. 104.



Supplementary Information – Computational Details

Iodane-Guided C-H Cleavage to Synthesize Densely Functionalized Arenes

Aleksandra Nilova, Paul A. Sibbald, Edward Valente, Gisela A. González-Montiel, H. Camille Richardson, Kevin S. Brown, Paul Ha-Yeon Cheong,* and David R. Stuart*

Table of Contents

1. Complete Authorship of Gaussian 16

Gaussian 16, Revision **A.03**, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, *Gaussian, Inc.*, Wallingford CT, **2016**.

2. General Computation Procedures

Manual conformation searches were performed to locate all transition states. All conformers were optimized using the Gaussian 16 computational package (see above reference) using M06-2X with the LanL2DZDP basis set for I, and 6-31G(d) for all other atoms with PCM solvation model for toluene. Stationary points were confirmed with vibrational frequency computations, with ground state structures having zero imaginary vibrational frequencies and transition states having one imaginary vibrational frequency. Frequencies were computed at 1 atm and 298.15 K (25 ºC) in order to match experimental reaction conditions. All reported energy values are free energies in kcal/mol, and all distances are in Ångströms (Å).

3. Data used to fit Equation 1

Table S1. Descriptors and computed selectivity data used to create linear model shown in Figure 2 and Eq. 1.

	DFT	Substituent at Position 3						Substituent at Position 4					
	$\Delta\Delta G^{\ddagger}$	F	R	Hammett	A	E_R	Sigma+	F	R	Hammett	A	E_R	Sigma+
1a	-4.08	0.42	-0.19	0.23	0.43	1	0.11	0.01	-0.18	-0.17	1.7	18	-0.31
1j	-3.51	0.45	-0.22	0.23	0.38	1.4	0.15	0.01	-0.18	-0.17	1.7	18	-0.31
1e	-5.15	0.45	-0.39	0.06	0.15	0.28	-0.08	0.01	-0.18	-0.17	1.7	18	-0.31
1m	-6.71	0.65	0.13	0.78	1.1	20	0.79	0.01	-0.18	-0.17	1.7	18	-0.31
1n	-0.94	0.38	0.16	0.54	2.1	44	0.612	0.45	-0.39	0.06	0.15	0.28	-0.08
1h=1k	-2.95	0.42	-0.19	0.23	0.43	1	0.11	0.45	-0.39	0.06	0.15	0.28	-0.08
1f	-1.26	0.45	-0.39	0.06	0.15	0.28	-0.08	0.38	0.16	0.54	2.1	44	0.612
1b	-2.07	0.42	-0.19	0.23	0.43	1	0.11	0.42	-0.19	0.23	0.43	1	0.11
1l	-4.89	0.45	-0.22	0.23	0.38	1.4	0.15	0.29	-0.56	-0.27	0.6	67	-0.78
1i	-3.77	0.42	-0.19	0.23	0.43	1	0.11	0.29	-0.56	-0.27	0.6	67	-0.78
1g	-6.78	0.45	-0.39	0.06	0.15	0.28	-0.08	0.29	-0.56	-0.27	0.6	67	-0.78
1o	-4.39	0.38	0.16	0.54	2.1	44	0.612	0.29	-0.56	-0.27	0.6	67	-0.78
1d	-3.07	0.29	-0.56	-0.27	0.6	67	-0.78	0.29	-0.56	-0.27	0.6	67	-0.78

4. Overfit check of Eq. 1 plotted in Figure 2 of the manuscript

The scrambled response data table is shown. The best one, two, three, four, and five term models are also shown.

Table S2. Descriptors and *scrambled* computed selectivity data used to check overfit of model shown in Figure 2 and Eq. 1.

	ΔΔG‡		
	DFT	Scrambled	Predicted by Eq 1
1a	-4.08	-6.78	-3.44
1j	-3.51	-2.07	-4.04
1e	-5.15	-4.89	-4.38
1m	-6.71	-2.95	-6.85
1n	-0.94	-6.71	-1.29
1h=1k	-2.95	-4.08	-2.71
1f	-1.26	-3.77	-1.43
1b	-2.07	-3.51	-2.10
1l	-4.89	-0.94	-5.54
1i	-3.77	-5.15	-4.95
1g	-6.78	-4.39	-5.89
1o	-4.39	-3.07	-3.53
1d	-3.07	-1.26	-3.41

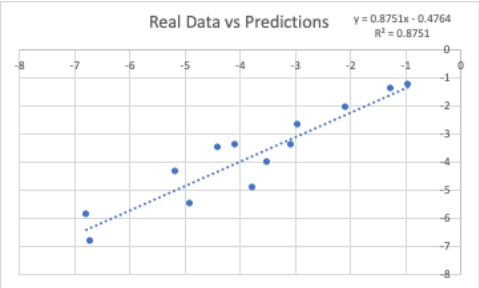


Figure S1. Plot of the DFT selectivity data (ΔΔG‡ DFT) against the selectivity predicted by the linear free energy relationship in Eq 1.

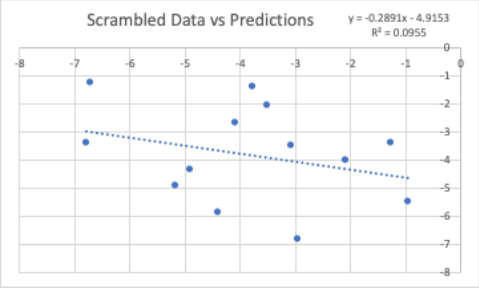


Figure S2. Plot of the scrambled data (ΔΔG‡ Scrambled) and the selectivity predicted by the linear free energy relationship in Eq 1.

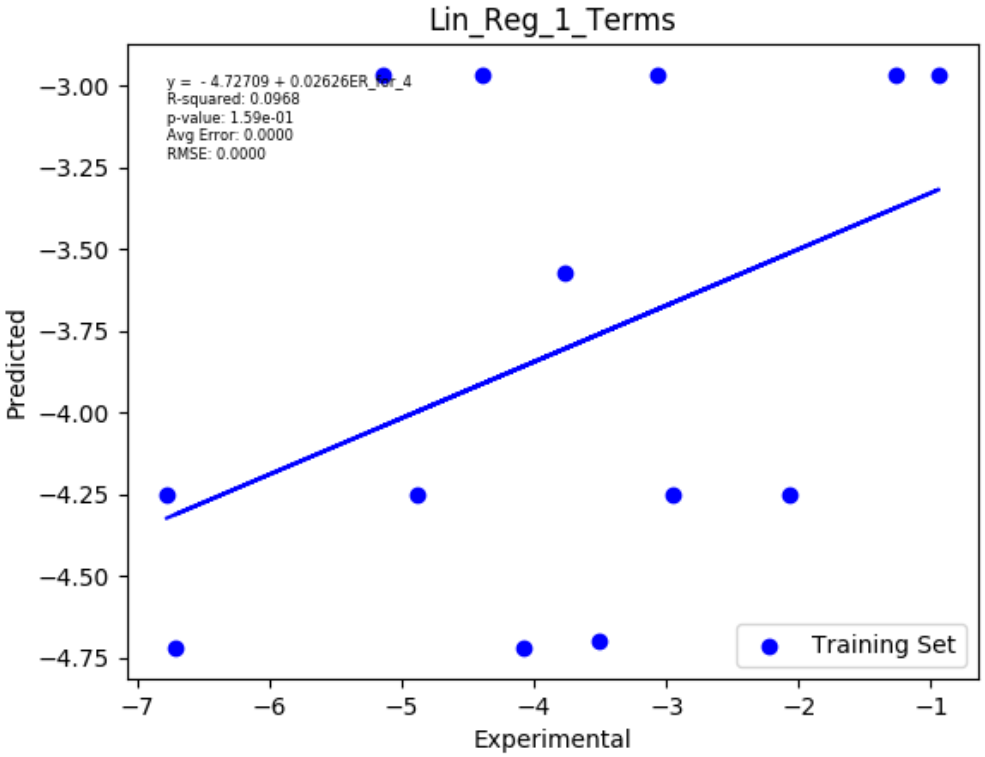


Figure S3. Linear Free Energy Relationship between the DFT-predicted preference for the formation Major and Minor-1x-Aryne products based on an exhaustive one-term model.

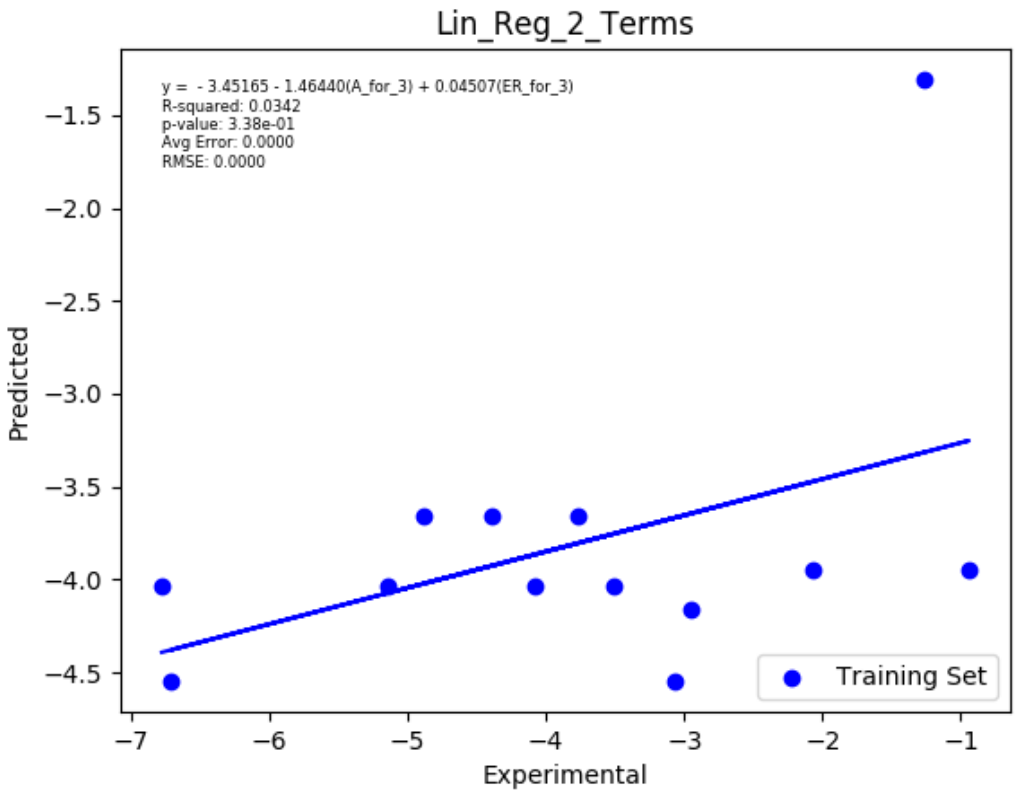


Figure S4. Linear Free Energy Relationship between the DFT-predicted preference for the formation Major and Minor-1x-Aryne products based on an exhaustive two-term model.

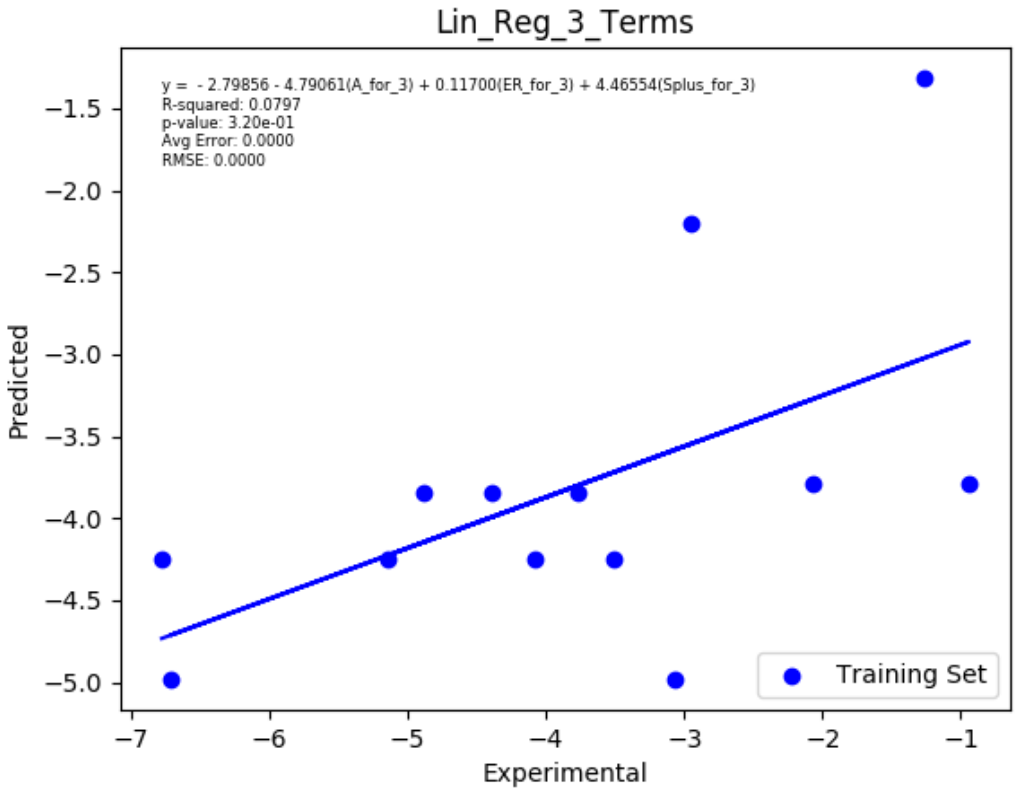


Figure S5. Linear Free Energy Relationship between the DFT-predicted preference for the formation Major and Minor-1x-Aryne products based on an exhaustive three-term model.

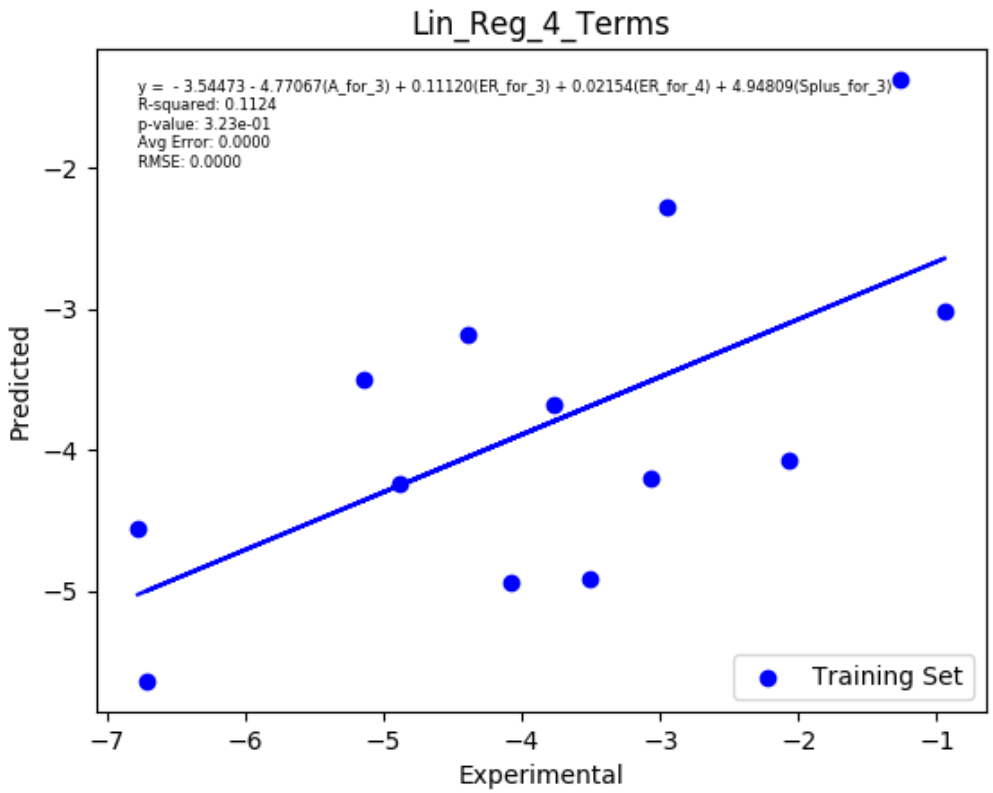


Figure S6. Linear Free Energy Relationship between the DFT-predicted preference for the formation Major and Minor-1x-Aryne products based on an exhaustive four-term model.

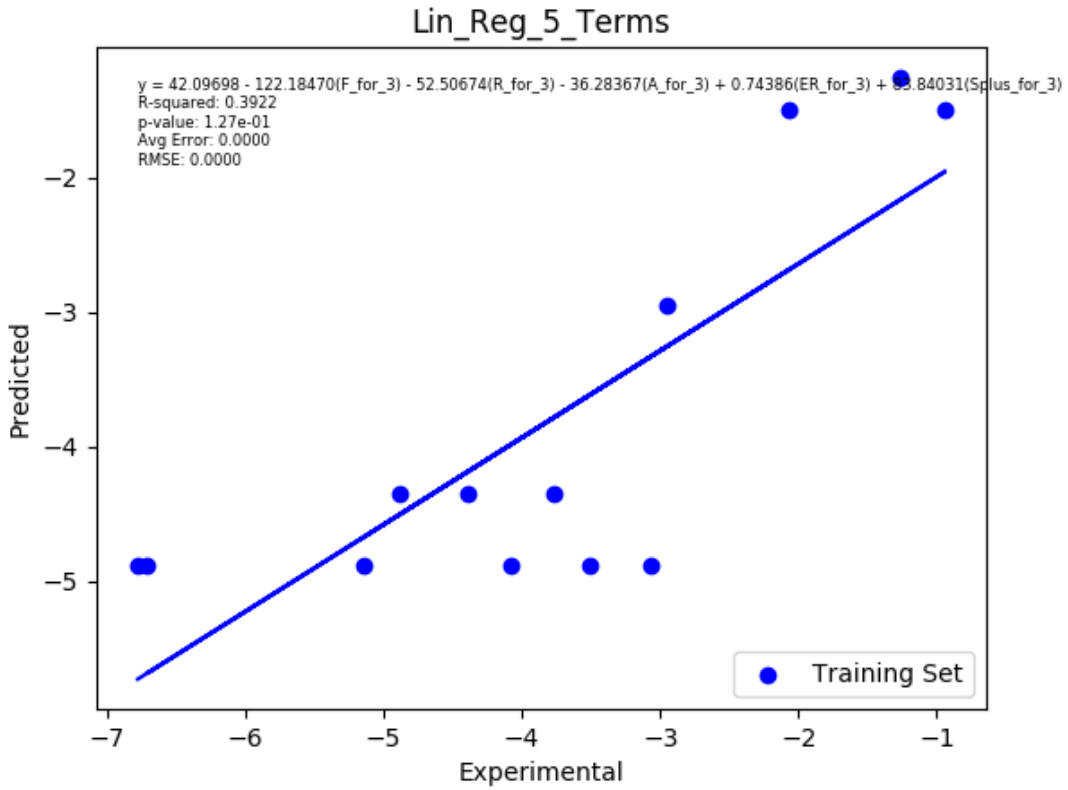


Figure S7. Linear Free Energy Relationship between the DFT-predicted preference for the formation Major and Minor-1x-Aryne products based on an exhaustive five-term model.

5. Computed transition state structures of **1a-o**

Supporting Information: 1a-Major-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current SCRF=(PCM,SOLVENT=Toluene) opt=(maxcycle=250,ts,calcfc,noeigentest) freq=noraman

#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq

---

Pointgroup= C1 Stoichiometry= C27H33ClINaO4S C1[X(C27H33ClINaO4S)] #Atoms= 68

Charge = 0 Multiplicity = 1

SCF Energy= -2380.92766871 Predicted Change= -4.388484D-09

==========

Optimization completed on the basis of negligible forces. {Found 2 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00000	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.01523	0.00180	[NO]	0.01523	0.00180	[NO]

Atomic Type	Coordinates (Angstroms) X	Y	Z
C	0.254384	3.692550	-1.297162
C	-0.240547	2.931217	-2.362650
C	-0.180988	1.543490	-2.350971
C	0.396255	0.969820	-1.226430
C	0.902189	1.606422	-0.119976
C	0.802966	2.993351	-0.215182
H	-0.679880	3.439792	-3.215791
H	-0.574736	0.956248	-3.173099
H	1.286961	0.878335	0.974628
Cl	1.386803	3.960439	1.147770
I	0.454388	-1.183691	-1.231326
C	2.534445	-1.437503	-0.962834
C	3.453609	-0.758904	-1.771178
C	2.916827	-2.330735	0.049828
C	4.809566	-0.977251	-1.508356
C	4.284240	-2.519402	0.247488
C	5.242949	-1.841982	-0.506950
H	5.544097	-0.454877	-2.116560
H	4.606218	-3.210619	1.023161
C	1.922757	-3.062401	0.914487
H	1.316088	-2.334195	1.464899

H	1.257798	-3.704361	0.325592
H	2.443664	-3.697643	1.634438
C	3.064496	0.184230	-2.878917
H	2.235234	-0.208434	-3.476786
H	2.750399	1.153702	-2.478438
H	3.914017	0.350175	-3.544627
C	6.710631	-2.028517	-0.225350
H	7.319693	-1.749733	-1.088618
H	7.019522	-1.401200	0.617997
H	6.934680	-3.066040	0.036760
O	-2.296947	-0.637772	-1.265513
S	-2.702498	-0.348920	0.133621
C	-4.466220	-0.555705	0.207032
C	-4.995175	-1.834226	0.366142
C	-5.295080	0.552234	0.072067
C	-6.374798	-1.997363	0.385078
H	-4.329389	-2.682566	0.488254
C	-6.675169	0.371106	0.093033
H	-4.858613	1.539755	-0.035066
C	-7.232868	-0.900683	0.244817
H	-6.796257	-2.990347	0.517010
H	-7.330116	1.232533	-0.004976
O	-2.413863	1.043598	0.561815
O	-2.114612	-1.315927	1.102493
C	2.468969	0.356763	2.770873
C	2.903394	-0.943110	3.455785
H	2.045291	-1.411611	3.951565
H	3.305086	-1.645366	2.719387
H	3.678545	-0.754183	4.207438
C	2.068049	1.374734	3.847599
H	2.905910	1.624549	4.508630
H	1.712164	2.296178	3.376856
H	1.260499	0.962089	4.466555
C	3.638907	0.906547	1.942371
H	3.878536	0.206481	1.133236
H	3.376807	1.872115	1.496922
H	4.532383	1.044866	2.561994
O	1.368834	0.089701	1.930980
C	-8.727161	-1.096089	0.240740
H	-9.073180	-1.411313	-0.749812
H	-9.026873	-1.868892	0.953983
H	-9.249301	-0.170621	0.496008
Na	-0.802298	0.332205	2.128325
C	0.176757	5.194080	-1.330170
H	-0.424845	5.571650	-0.497520
H	1.171097	5.641411	-1.235640

H -0.272101 5.535948 -2.265195

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -2380.92766871 Predicted Change= -4.388484D-09
Zero-point correction (ZPE)= -2380.3863 0.54133
Internal Energy (U)= -2380.3462 0.58146
Enthalpy (H)= -2380.3452 0.58241
Gibbs Free Energy (G)= -2380.4659 0.46171

Frequencies -- -1046.3741 11.3860 13.0346

Supporting Information: 1a-Minor-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current
SCRF=(PCM,SOLVENT=Toluene) opt=(maxcycle=250,ts,calcfc,noeigentest)
freq=noraman
#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq

---

Pointgroup= C1 Stoichiometry= C27H33ClINaO4S C1[X(C27H33ClINaO4S)] #Atoms= 68
Charge = 0 Multiplicity = 1

SCF Energy= -2380.92229009 Predicted Change= -8.792064D-09

==========

Optimization completed on the basis of negligible forces. {Found 2 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00000	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.00497	0.00180	[NO]	0.00497	0.00180	[YES]

Atomic Type	Coordinates (Angstroms) X	Y	Z
C	0.370149	3.652210	1.214703
C	-0.183984	3.608752	-0.074169
C	-0.152163	2.461592	-0.854306
C	0.463344	1.367017	-0.260802
C	1.021833	1.271477	0.981265
C	0.952424	2.478464	1.702079
H	-0.589964	2.446574	-1.845955
H	1.447792	-0.000657	1.504403
I	0.557775	-0.413349	-1.509646
C	2.645449	-0.713557	-1.376494

C	3.535058	0.323227	-1.682327
C	3.067521	-1.993202	-0.981286
C	4.899938	0.046274	-1.555575
C	4.442512	-2.209507	-0.893311
C	5.371189	-1.203022	-1.161795
H	5.610671	0.837629	-1.781140
H	4.794979	-3.194560	-0.595541
C	2.112428	-3.107936	-0.640338
H	1.506742	-2.812965	0.224023
H	1.444900	-3.352176	-1.473935
H	2.667595	-4.013198	-0.383893
C	3.104732	1.699094	-2.117865
H	2.290715	1.660498	-2.849282
H	2.751708	2.287146	-1.264124
H	3.944608	2.228526	-2.572402
C	6.846434	-1.460350	-1.001319
H	7.135460	-1.377561	0.052260
H	7.111551	-2.466564	-1.336987
H	7.439858	-0.738477	-1.567554
O	-2.215834	-0.013235	-1.242177
S	-2.604728	-0.572001	0.077118
C	-4.352601	-0.883637	0.008754
C	-4.812679	-2.120795	-0.430518
C	-5.239430	0.132516	0.352874
C	-6.183474	-2.337190	-0.526638
H	-4.101874	-2.900190	-0.684859
C	-6.606163	-0.100249	0.250252
H	-4.856502	1.086586	0.700429
C	-7.096763	-1.334540	-0.188327
H	-6.551704	-3.300680	-0.868576
H	-7.305973	0.687498	0.516028
O	-2.379192	0.363977	1.208231
O	-1.944155	-1.878896	0.355809
C	2.654932	-1.189044	2.785665
C	3.144568	-2.637849	2.785028
H	2.318085	-3.314121	3.030637
H	3.523632	-2.901503	1.792017
H	3.947816	-2.788363	3.515039
C	2.213959	-0.787165	4.198890
H	3.043316	-0.820971	4.914144
H	1.812634	0.233413	4.185968
H	1.428007	-1.464548	4.554986
C	3.787917	-0.265035	2.317188
H	4.045025	-0.490220	1.276371
H	3.482291	0.785472	2.372133
H	4.681587	-0.396688	2.937501

O	1.555905	-1.095042	1.903577
C	-8.580700	-1.585940	-0.264547
H	-9.121847	-0.677710	-0.543006
H	-8.813921	-2.364058	-0.995781
H	-8.967910	-1.915856	0.705887
Na	-0.651426	-0.996363	2.083380
C	0.330542	4.909300	2.038721
H	0.810179	4.745797	3.006153
H	0.844671	5.731286	1.530224
H	-0.700487	5.233474	2.211974
H	1.368641	2.515032	2.710160
Cl	-0.931686	5.040694	-0.745617

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -2380.92229009 Predicted Change= -8.792064D-09
Zero-point correction (ZPE)= -2380.3810 0.54121
Internal Energy (U)= -2380.3408 0.58142
Enthalpy (H)= -2380.3399 0.58236
Gibbs Free Energy (G)= -2380.4594 0.46285

Frequencies -- -761.2411 13.8860 16.7128

Supporting Information: 1b-Major-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current
SCRF=(PCM,SOLVENT=Toluene) opt=(maxcycle=250,ts,calcfc,noeigentest)
freq=noraman
#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq

---

Pointgroup= C1 Stoichiometry= C26H30Cl2INaO4S C1[X(C26H30Cl2INaO4S)] #Atoms= 65
Charge = 0 Multiplicity = 1

SCF Energy= -2801.19374184 Predicted Change= -2.494943D-10

==========

Optimization completed. {Found 2 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00000	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.00088	0.00180	[YES]	0.00088	0.00180	[YES]

Atomic Coordinates (Angstroms)

Type	X	Y	Z
C	0.166463	3.616291	-0.884595
C	-0.333695	2.986694	-2.025338
C	-0.239634	1.608364	-2.148501
C	0.365961	0.935683	-1.094412
C	0.869250	1.473172	0.064385
C	0.749514	2.861836	0.137013
H	-0.791064	3.582720	-2.806678
H	-0.632475	1.099726	-3.021764
H	1.263235	0.653523	1.057640
I	0.474611	-1.196128	-1.310285
C	2.564772	-1.417169	-1.090295
C	3.456412	-0.625262	-1.822401
C	2.980617	-2.411372	-0.191094
C	4.820348	-0.834499	-1.594856
C	4.354223	-2.583179	-0.025621
C	5.286805	-1.796200	-0.702964
H	5.534459	-0.225710	-2.144027
H	4.702290	-3.350365	0.662386
C	2.014457	-3.267274	0.586757
H	1.387957	-2.625546	1.216684
H	1.367963	-3.860971	-0.069729
H	2.558610	-3.962318	1.230084
C	3.033980	0.425919	-2.815038
H	2.193759	0.091486	-3.432414
H	2.724888	1.346010	-2.308086
H	3.866355	0.668516	-3.478836
C	6.761624	-1.974335	-0.455740
H	7.354795	-1.561396	-1.275138
H	7.058462	-1.459769	0.464689
H	7.018450	-3.030755	-0.339640
O	-2.263516	-0.718794	-1.275110
S	-2.682343	-0.579746	0.144306
C	-4.451138	-0.740590	0.171300
C	-5.021994	-2.000559	0.318047
C	-5.241670	0.392251	-0.000833
C	-6.407449	-2.122370	0.289218
H	-4.385191	-2.867683	0.459541
C	-6.624545	0.252267	-0.028157
H	-4.773491	1.365812	-0.104342
C	-7.225815	-1.002278	0.117200
H	-6.862149	-3.102548	0.403980
H	-7.249941	1.130792	-0.162230
O	-2.360154	0.749355	0.723999
O	-2.133356	-1.662814	1.006459

C	2.459358	-0.059808	2.799244
C	2.927204	-1.415841	3.338945
H	2.080738	-1.960306	3.773777
H	3.351341	-2.020732	2.532033
H	3.693733	-1.291017	4.112487
C	2.031047	0.821889	3.980936
H	2.862063	1.023304	4.666580
H	1.645702	1.778247	3.614280
H	1.237761	0.320153	4.551084
C	3.618516	0.606722	2.043657
H	3.875074	0.008432	1.161353
H	3.336996	1.610993	1.709407
H	4.507878	0.693831	2.678255
O	1.368760	-0.258178	1.929445
C	-8.726804	-1.136227	0.119242
H	-9.189102	-0.415234	-0.560253
H	-9.035809	-2.140534	-0.181330
H	-9.130353	-0.950450	1.120784
Na	-0.799501	-0.161471	2.230506
Cl	0.027762	5.345563	-0.782121
Cl	1.323060	3.681343	1.574776

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -2801.19374184 Predicted Change= -2.494943D-10
Zero-point correction (ZPE)= -2800.6895 0.50419
Internal Energy (U)= -2800.6502 0.54352
Enthalpy (H)= -2800.6492 0.54447
Gibbs Free Energy (G)= -2800.7655 0.42818

Frequencies -- -1082.2813 17.0992 20.0893

Supporting Information: 1b-Minor-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current
SCRF=(PCM,SOLVENT=Toluene) opt=(maxcycle=250,ts,calcfc,noeigentest)
freq=noraman
#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq

---

Pointgroup= C1 Stoichiometry= C26H30Cl2INaO4S C1[X(C26H30Cl2INaO4S)] #Atoms= 65
Charge = 0 Multiplicity = 1

SCF Energy= -2801.18884116 Predicted Change= -4.719737D-09

==========

Optimization completed on the basis of negligible forces. {Found 2 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00000	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.00497	0.00180	[NO]	0.00497	0.00180	[YES]

Atomic Type	Coordinates (Angstroms) X	Y	Z
C	0.257960	3.578259	0.769944
C	-0.291899	3.429268	-0.510796
C	-0.204429	2.202012	-1.158034
C	0.437080	1.190465	-0.457123
C	0.981665	1.238922	0.797723
C	0.874235	2.501247	1.402478
H	-0.631714	2.072318	-2.146076
H	1.403655	0.055708	1.439121
I	0.584699	-0.698422	-1.500899
C	2.678684	-0.930919	-1.328167
C	3.546607	0.091005	-1.730853
C	3.125969	-2.156307	-0.808395
C	4.916192	-0.140009	-1.568707
C	4.504660	-2.330262	-0.690916
C	5.412342	-1.332985	-1.050165
H	5.610606	0.641521	-1.867460
H	4.876988	-3.273394	-0.297227
C	2.194070	-3.256283	-0.369639
H	1.574230	-2.894341	0.458304
H	1.540700	-3.595977	-1.180789
H	2.767870	-4.119123	-0.023856
C	3.090053	1.406409	-2.304897
H	2.270574	1.279326	-3.019899
H	2.737512	2.077422	-1.514487
H	3.917285	1.897132	-2.821669
C	6.891589	-1.538301	-0.856042
H	7.172937	-1.323987	0.180893
H	7.178840	-2.571582	-1.068291
H	7.473261	-0.876865	-1.502558
O	-2.172960	-0.335093	-1.279788
S	-2.564166	-0.767404	0.086699
C	-4.319966	-1.034207	0.055940
C	-4.818201	-2.273334	-0.334291
C	-5.174382	0.012606	0.388664
C	-6.195198	-2.459188	-0.394828

H	-4.132421	-3.080180	-0.571609
C	-6.548377	-0.190379	0.322370
H	-4.760929	0.964412	0.705663
C	-7.077187	-1.423007	-0.073406
H	-6.593435	-3.425763	-0.691187
H	-7.223215	0.619228	0.586788
O	-2.303144	0.257903	1.129358
O	-1.933631	-2.061482	0.472464
C	2.619691	-1.000255	2.848940
C	3.146170	-2.429693	2.990122
H	2.333092	-3.102982	3.284533
H	3.550266	-2.773931	2.032299
H	3.939645	-2.491093	3.743407
C	2.153044	-0.479965	4.214647
H	2.974827	-0.424027	4.937152
H	1.724903	0.523504	4.103294
H	1.381459	-1.141809	4.627542
C	3.738558	-0.096855	2.310307
H	4.010844	-0.407704	1.295762
H	3.413129	0.948336	2.269984
H	4.628471	-0.154330	2.946982
O	1.530648	-1.014473	1.950623
C	-8.567837	-1.621756	-0.170138
H	-9.094945	-1.043134	0.593154
H	-8.938321	-1.292597	-1.147272
H	-8.836486	-2.674553	-0.051836
Na	-0.664898	-1.075147	2.173034
H	1.269222	2.664721	2.403744
Cl	0.170290	5.107113	1.592540
Cl	-1.075069	4.747674	-1.321776

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -2801.18884116 Predicted Change= -4.719737D-09
Zero-point correction (ZPE)= -2800.6850 0.50377
Internal Energy (U)= -2800.6454 0.54337
Enthalpy (H)= -2800.6445 0.54432
Gibbs Free Energy (G)= -2800.7622 0.42655

Frequencies -- -862.1316 15.2734 23.7152

Supporting Information: 1c-Minor-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

```
=====================================================================
 #M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current
 SCRF=(PCM,SOLVENT=Toluene) opt=(gdiis,maxcycle=250,ts,calcfc,noeigentest)
 freq=noraman
 #N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq
---------------------------------------------------------------------
 Pointgroup= C1   Stoichiometry= C26H30F2INaO4S   C1[X(C26H30F2INaO4S)]  #Atoms= 65
 Charge = 0     Multiplicity = 1
---------------------------------------------------------------------
 SCF Energy= -2080.46202074         Predicted Change= -1.557433D-07
=====================================================================
 Optimization completed.                {Found         1         times}
 Item    Max Val.       Criteria        Pass?   RMS Val.       Criteria          Pass?
 Force          0.00001 ||  0.00045   [ YES ]  0.00000 ||  0.00030   [ YES ]
 Displ  0.02754 ||  0.00180   [ NO ]    0.02754 ||  0.00180   [ NO ]
---------------------------------------------------------------------
         Atomic          Coordinates (Angstroms)
         Type   X       Y       Z
---------------------------------------------------------------------
         C       0.373747        3.808028        0.900785
         C       -0.180289       3.720720        -0.378343
         C       -0.147117       2.529100        -1.075220
         C       0.457708        1.470380        -0.400192
         C       1.006959        1.458424        0.852557
         C       0.950008        2.705715        1.505170
         H       -0.583363       2.461537        -2.065418
         H       1.400258        0.235133        1.468226
         I       0.540051        -0.387335       -1.505659
         C       2.622761        -0.702620       -1.335389
         C       3.528253        0.297745        -1.708580
         C       3.024094        -1.956194       -0.846420
         C       4.888173        0.012784        -1.551698
         C       4.395384        -2.183222       -0.731804
         C       5.339496        -1.210929       -1.064699
         H       5.611289        0.776050        -1.828818
         H       4.732418        -3.148923       -0.361640
         C       2.051520        -3.031680       -0.435961
         H       1.442316        -2.668487       0.399341
         H       1.388231        -3.326999       -1.256335
         H       2.592594        -3.923117       -0.110515
         C       3.119850        1.644254        -2.245285
         H       2.301611        1.565636        -2.968689
         H       2.782391        2.301264        -1.436742
         H       3.966652        2.122814        -2.741437
         C       6.809992        -1.475381       -0.875297
         H       7.095564        -1.309452       0.169326
```

H	7.061415	-2.509737	-1.124840
H	7.416620	-0.811731	-1.496138
O	-2.223236	0.065246	-1.292682
S	-2.627114	-0.377555	0.066142
C	-4.380333	-0.661405	0.016297
C	-4.861440	-1.900779	-0.398189
C	-5.249368	0.367600	0.361516
C	-6.234335	-2.103002	-0.469236
H	-4.163901	-2.694681	-0.644650
C	-6.621601	0.148308	0.284145
H	-4.850219	1.319000	0.697484
C	-7.132105	-1.083156	-0.134060
H	-6.618956	-3.069535	-0.783931
H	-7.307791	0.944817	0.558357
O	-2.387351	0.641853	1.119392
O	-1.991851	-1.670247	0.449718
C	2.576331	-0.883364	2.854274
C	3.049967	-2.334462	2.951903
H	2.214202	-2.984486	3.234176
H	3.433672	-2.666166	1.981370
H	3.846140	-2.445890	3.696559
C	2.135564	-0.384871	4.236404
H	2.962107	-0.380225	4.955669
H	1.745609	0.637025	4.155297
H	1.341306	-1.028981	4.633502
C	3.723239	-0.006136	2.332624
H	3.977194	-0.297964	1.307732
H	3.434557	1.050562	2.323330
H	4.614629	-0.113075	2.960810
O	1.482280	-0.833743	1.963197
C	-8.618210	-1.309888	-0.239382
H	-9.174249	-0.577831	0.351368
H	-8.950290	-1.220715	-1.279538
H	-8.890848	-2.310759	0.106886
Na	-0.719845	-0.699291	2.140907
H	1.350156	2.835477	2.509424
F	-0.729144	4.814069	-0.918946
F	0.323574	4.992664	1.522168

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -2080.46202074 Predicted Change= -1.557433D-07
Zero-point correction (ZPE)= -2079.9553 0.50671
Internal Energy (U)= -2079.9163 0.54567
Enthalpy (H)= -2079.9154 0.54662

Gibbs Free Energy (G)= -2080.0315 0.43042

Frequencies -- -815.9780 16.0144 19.9826

Supporting Information: 1d-Major-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current SCRF=(PCM,SOLVENT=Toluene) opt=(maxcycle=250,ts,calcfc,noeigentest) freq=noraman

#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq

---

Pointgroup= C1 Stoichiometry= C28H36INaO6S C1[X(C28H36INaO6S)] #Atoms= 73

Charge = 0 Multiplicity = 1

SCF Energy= -2111.01239350 Predicted Change= -2.893366D-10

==========

Optimization completed on the basis of negligible forces. {Found 2 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00000	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.00280	0.00180	[NO]	0.00280	0.00180	[YES]

Atomic Type	Coordinates (Angstroms) X	Y	Z
C	0.319872	3.631831	-0.643759
C	-0.200069	3.105567	-1.830786
C	-0.161978	1.731797	-2.061058
C	0.408680	0.959782	-1.063299
C	0.952162	1.390142	0.122210
C	0.897485	2.767775	0.310459
H	-0.647844	3.751617	-2.575966
H	-0.579178	1.310653	-2.969191
H	1.323122	0.493183	1.102288
I	0.401543	-1.170236	-1.399204
C	2.467239	-1.516825	-1.120770
C	3.418506	-0.770966	-1.826197
C	2.808326	-2.524642	-0.204726
C	4.763792	-1.052514	-1.568528
C	4.167264	-2.769892	-0.008804
C	5.156495	-2.038655	-0.667620
H	5.522425	-0.481957	-2.099033
H	4.457974	-3.549942	0.691326
C	1.784729	-3.315364	0.568418

H	1.205438	-2.631790	1.200075
H	1.098615	-3.860501	-0.089301
H	2.281420	-4.047734	1.209082
C	3.070842	0.308522	-2.817118
H	2.252240	0.006177	-3.478668
H	2.755857	1.223855	-2.304836
H	3.939342	0.543691	-3.435934
C	6.613494	-2.295104	-0.384897
H	7.246889	-1.927220	-1.195781
H	6.918624	-1.785132	0.535555
H	6.808623	-3.362369	-0.249472
O	-2.361202	-0.564145	-1.326940
S	-2.732459	-0.401771	0.101179
C	-4.489988	-0.655414	0.199110
C	-4.988946	-1.952242	0.288845
C	-5.345672	0.439569	0.147575
C	-6.364609	-2.147491	0.320744
H	-4.302738	-2.791031	0.347008
C	-6.720646	0.226831	0.180564
H	-4.932709	1.441575	0.095183
C	-7.248378	-1.064399	0.262104
H	-6.762030	-3.156022	0.398104
H	-7.395756	1.077715	0.147673
O	-2.466594	0.956226	0.639395
O	-2.100279	-1.432584	0.970932
C	2.464053	-0.166285	2.828141
C	2.856907	-1.506030	3.455327
H	1.985497	-1.963205	3.937706
H	3.220304	-2.189473	2.680444
H	3.646542	-1.381308	4.205444
C	2.064759	0.828153	3.927184
H	2.893448	1.038722	4.613615
H	1.745087	1.768705	3.464130
H	1.233295	0.420898	4.517061
C	3.655746	0.400702	2.043003
H	3.895850	-0.258778	1.201447
H	3.405693	1.389439	1.644359
H	4.542150	0.497658	2.680554
O	1.374224	-0.378567	1.961315
C	-8.738310	-1.291167	0.267083
H	-9.272560	-0.411091	0.633899
H	-9.100781	-1.501416	-0.745283
H	-9.006896	-2.144423	0.895802
Na	-0.772885	0.135843	2.092418
O	0.294308	4.950092	-0.324616
C	-0.343303	5.831335	-1.227474

H	-0.285957	6.820449	-0.774426
H	0.166743	5.844589	-2.197735
H	-1.393702	5.555235	-1.372490
O	1.352656	3.294260	1.499587
C	2.533232	4.077299	1.389866
H	2.332719	5.027528	0.887585
H	2.877122	4.262968	2.409031
H	3.309442	3.529158	0.842156

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -2111.01239350 Predicted Change= -2.893366D-10
Zero-point correction (ZPE)= -2110.4224 0.58993
Internal Energy (U)= -2110.3802 0.63217
Enthalpy (H)= -2110.3792 0.63311
Gibbs Free Energy (G)= -2110.5016 0.51070

Frequencies -- -968.0036 17.1242 22.2102

Supporting Information: 1d-Minor-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current SCRF=(PCM,SOLVENT=Toluene) opt=(maxcycle=250,ts,calcfc,noeigentest) freq=noraman
#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq

---

Pointgroup= C1 Stoichiometry= C28H36INaO6S C1[X(C28H36INaO6S)] #Atoms= 73
Charge = 0 Multiplicity = 1

SCF Energy= -2111.00483259 Predicted Change= -3.392955D-10

==========

Optimization completed. {Found 2 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00000	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.00107	0.00180	[YES]	0.00107	0.00180	[YES]

Atomic Type	Coordinates (Angstroms) X	Y	Z
C	0.350162	3.560806	0.824516
C	-0.156191	3.458249	-0.487447
C	-0.096039	2.239127	-1.150282

C	0.479752	1.188527	-0.444107
C	1.006163	1.191491	0.816656
C	0.919374	2.450923	1.441158
H	-0.490176	2.156849	-2.157556
H	1.422034	-0.021607	1.474292
I	0.568583	-0.697912	-1.521538
C	2.650038	-1.006550	-1.325634
C	3.555688	-0.015937	-1.724471
C	3.052718	-2.238906	-0.786473
C	4.915288	-0.288046	-1.544038
C	4.424030	-2.455153	-0.650581
C	5.367184	-1.491161	-1.008835
H	5.637749	0.468658	-1.840382
H	4.761642	-3.404951	-0.241739
C	2.081681	-3.302937	-0.343975
H	1.468177	-2.914294	0.476682
H	1.422278	-3.626746	-1.156532
H	2.624445	-4.181254	0.013063
C	3.145784	1.308443	-2.312826
H	2.344951	1.196564	-3.051282
H	2.781303	1.986524	-1.533831
H	3.998894	1.780222	-2.804892
C	6.836815	-1.741027	-0.793808
H	7.447344	-1.096724	-1.431093
H	7.109865	-1.536509	0.247358
H	7.096213	-2.782264	-1.003487
O	-2.215408	-0.249999	-1.319729
S	-2.616251	-0.639927	0.054816
C	-4.357313	-0.994930	0.000197
C	-4.788490	-2.302639	-0.190801
C	-5.267710	0.053858	0.106548
C	-6.153975	-2.559281	-0.277876
H	-4.060006	-3.103563	-0.261987
C	-6.626859	-0.219387	0.016249
H	-4.908062	1.065723	0.264003
C	-7.088916	-1.526538	-0.175710
H	-6.499598	-3.578722	-0.426134
H	-7.344439	0.592764	0.097888
O	-2.431803	0.440208	1.057994
O	-1.938421	-1.885250	0.513574
C	2.602224	-1.071546	2.900654
C	3.087311	-2.515368	3.039318
H	2.256809	-3.162470	3.342561
H	3.469751	-2.871769	2.076977
H	3.886755	-2.599467	3.784132
C	2.154585	-0.537889	4.267377

H	2.979016	-0.509763	4.988618
H	1.761112	0.480009	4.157092
H	1.361916	-1.174735	4.678625
C	3.740791	-0.198382	2.355148
H	4.004819	-0.523064	1.342765
H	3.437352	0.853076	2.306717
H	4.629636	-0.271642	2.991854
O	1.509034	-1.058868	2.007451
C	-8.567411	-1.810926	-0.242052
H	-9.091637	-1.043592	-0.818619
H	-8.764259	-2.782019	-0.702920
H	-9.005423	-1.823075	0.762080
Na	-0.688514	-0.765585	2.127108
H	1.291462	2.594567	2.455632
O	-0.717121	4.531453	-1.127860
C	0.207117	5.573763	-1.427059
H	-0.354368	6.335810	-1.968544
H	0.630255	5.999902	-0.513016
H	1.015166	5.193434	-2.062806
C	-1.004024	5.204111	1.810159
H	-0.885047	6.127196	2.378634
H	-1.583407	5.395463	0.902768
H	-1.521587	4.458337	2.423830
O	0.312362	4.754528	1.496506

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -2111.00483259 Predicted Change= -3.392955D-10
Zero-point correction (ZPE)= -2110.4158 0.58901
Internal Energy (U)= -2110.3730 0.63176
Enthalpy (H)= -2110.3721 0.63270
Gibbs Free Energy (G)= -2110.4967 0.50807

Frequencies -- -755.9157 13.7327 17.5746

Supporting Information: 1e-Major-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current SCRF=(PCM,SOLVENT=Toluene) opt=(maxcycle=250,ts,calcfc,noeigentest) freq=noraman
#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq

---

Pointgroup= C1 Stoichiometry= C27H33FINaO4S C1[X(C27H33FINaO4S)] #Atoms= 68
Charge = 0 Multiplicity = 1

SCF Energy= -2020.56914892 Predicted Change= -5.027838D-10

==========

Optimization completed. {Found 2 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00000	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.00107	0.00180	[YES]	0.00107	0.00180	[YES]

Atomic Type	Coordinates (Angstroms) X	Y	Z
C	0.414226	3.872270	-0.782874
C	-0.133808	3.284236	-1.927322
C	-0.135996	1.902353	-2.101422
C	0.431419	1.163626	-1.071997
C	0.982386	1.630068	0.093519
C	0.942308	3.012680	0.179080
H	-0.561685	3.920516	-2.696778
H	-0.565605	1.445076	-2.985557
H	1.334027	0.797494	1.095950
I	0.470170	-0.977376	-1.335925
C	2.551576	-1.229996	-1.061628
C	3.464377	-0.474390	-1.806917
C	2.943050	-2.183130	-0.107906
C	4.822271	-0.683429	-1.546262
C	4.312567	-2.356683	0.089826
C	5.264123	-1.609109	-0.605169
H	5.551257	-0.103365	-2.106970
H	4.641850	-3.093214	0.819342
C	1.961842	-2.988410	0.703670
H	1.373538	-2.306336	1.328444
H	1.282714	-3.573822	0.074081
H	2.495027	-3.685871	1.353874
C	3.067086	0.542526	-2.844427
H	2.246691	0.184321	-3.474979
H	2.736543	1.474760	-2.374278
H	3.917593	0.769818	-3.490514
C	6.732526	-1.786409	-0.321383
H	7.015972	-1.231345	0.579627
H	6.978485	-2.838022	-0.150744
H	7.344826	-1.416808	-1.147477
O	-2.281878	-0.434417	-1.302435
S	-2.688724	-0.290950	0.118478
C	-4.453614	-0.494270	0.167044

C	-4.992493	-1.768503	0.317780
C	-5.273694	0.618245	0.007096
C	-6.374156	-1.924127	0.305139
H	-4.332998	-2.620029	0.449930
C	-6.653762	0.444806	-0.003873
H	-4.830423	1.602915	-0.100366
C	-7.222222	-0.823626	0.145623
H	-6.803532	-2.915464	0.422843
H	-7.301722	1.308144	-0.128673
O	-2.395141	1.049703	0.686610
O	-2.107684	-1.353876	0.985514
C	2.494139	0.256523	2.859949
C	2.975653	-1.035540	3.524837
H	2.140207	-1.530815	4.032884
H	3.372648	-1.719230	2.766781
H	3.764141	-0.838672	4.260434
C	2.040250	1.257426	3.931892
H	2.856944	1.541473	4.605600
H	1.662886	2.163283	3.444561
H	1.236467	0.819920	4.538065
C	3.646496	0.873374	2.050863
H	3.903624	0.216966	1.211501
H	3.354452	1.849588	1.650301
H	4.536477	1.010579	2.675742
O	1.412376	-0.048444	2.010897
C	-8.718810	-0.999416	0.166505
H	-9.218626	-0.210878	-0.401865
H	-9.009760	-1.965387	-0.254662
H	-9.098964	-0.959407	1.193339
Na	-0.767790	0.169213	2.158129
C	0.434202	5.359985	-0.564127
H	-0.136316	5.629037	0.330058
H	1.456580	5.719407	-0.413040
H	0.003547	5.885406	-1.419219
F	1.449598	3.599391	1.294551

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -2020.56914892 Predicted Change= -5.027838D-10
Zero-point correction (ZPE)= -2020.0258 0.54329
Internal Energy (U)= -2019.9862 0.58287
Enthalpy (H)= -2019.9853 0.58382
Gibbs Free Energy (G)= -2020.1018 0.46732

Frequencies -- -1003.5808 17.7669 19.9243

Supporting Information: 1e-Minor-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current SCRF=(PCM,SOLVENT=Toluene) opt=(gdiis,maxcycle=250,ts,calcfc,noeigentest) freq=noraman

#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq

---

Pointgroup= C1 Stoichiometry= C27H33FINaO4S C1[X(C27H33FINaO4S)] #Atoms= 68

Charge = 0 Multiplicity = 1

SCF Energy= -2020.56009171 Predicted Change= -1.459656D-08

==========

Optimization completed. {Found 1 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00001	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.00920	0.00180	[NO]	0.00920	0.00180	[YES]

Atomic Type	Coordinates (Angstroms) X	Y	Z
C	0.324514	3.858429	0.707885
C	-0.241374	3.639918	-0.551581
C	-0.203212	2.417993	-1.195605
C	0.440837	1.415292	-0.477256
C	1.017127	1.482818	0.757273
C	0.934728	2.769612	1.330505
H	-0.663471	2.286092	-2.167752
H	1.447346	0.292244	1.444243
I	0.542606	-0.508313	-1.494022
C	2.628989	-0.786277	-1.306407
C	3.518836	0.203630	-1.740708
C	3.051071	-2.000038	-0.740673
C	4.883280	-0.049011	-1.567920
C	4.425955	-2.197792	-0.614211
C	5.354375	-1.232961	-1.007234
H	5.593926	0.707642	-1.891640
H	4.778400	-3.133218	-0.185288
C	2.096724	-3.063292	-0.261818
H	1.484243	-2.659496	0.552072
H	1.435949	-3.417859	-1.060348
H	2.652742	-3.924627	0.115566

C	3.088316	1.507486	-2.359142
H	2.280961	1.368352	-3.085655
H	2.725772	2.201845	-1.593867
H	3.930691	1.975288	-2.872891
C	6.828895	-1.461360	-0.802177
H	7.425381	-0.826014	-1.461325
H	7.110569	-1.228792	0.230785
H	7.097729	-2.504450	-0.989518
O	-2.230686	-0.044012	-1.314599
S	-2.632900	-0.349727	0.081712
C	-4.381830	-0.664949	0.053773
C	-4.840681	-1.914749	-0.357370
C	-5.269159	0.345995	0.402672
C	-6.208703	-2.145714	-0.418003
H	-4.129590	-2.692799	-0.616535
C	-6.637883	0.097658	0.336277
H	-4.886338	1.308537	0.725302
C	-7.125380	-1.145504	-0.071911
H	-6.575891	-3.117904	-0.736299
H	-7.338660	0.882410	0.607585
O	-2.411840	0.772041	1.028796
O	-1.981601	-1.589033	0.594137
C	2.617280	-0.723391	2.900990
C	3.101201	-2.163133	3.080526
H	2.268880	-2.802381	3.395250
H	3.490241	-2.544745	2.130611
H	3.895649	-2.227396	3.832615
C	2.162761	-0.153781	4.250790
H	2.983359	-0.106645	4.975393
H	1.769719	0.860797	4.111588
H	1.368036	-0.779668	4.674720
C	3.759166	0.134515	2.338402
H	4.028415	-0.217076	1.336458
H	3.456210	1.184333	2.259806
H	4.644538	0.078310	2.981606
O	1.528637	-0.733086	2.001939
C	-8.606144	-1.421687	-0.118218
H	-9.183799	-0.494671	-0.088786
H	-8.877212	-1.967149	-1.026720
H	-8.913421	-2.035003	0.735882
Na	-0.672215	-0.437468	2.128482
C	0.241338	5.226353	1.326649
H	0.719276	5.232720	2.308674
H	0.733256	5.974280	0.696864
H	-0.800262	5.540083	1.445231
H	1.362473	2.936223	2.320757

F -0.839412 4.677271 -1.166348

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -2020.56009171 Predicted Change= -1.459656D-08
Zero-point correction (ZPE)= -2020.0171 0.54290
Internal Energy (U)= -2019.9774 0.58268
Enthalpy (H)= -2019.9764 0.58363
Gibbs Free Energy (G)= -2020.0936 0.46645

Frequencies -- -766.1663 15.7480 24.2721

Supporting Information: 1f-Major-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current SCRF=(PCM,SOLVENT=Toluene) opt=(gdiis,maxcycle=250,ts,calcfc,noeigentest) freq=noraman
#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq

---

Pointgroup= C1 Stoichiometry= C27H30F4INaO5S C1[X(C27H30F4INaO5S)] #Atoms= 69
Charge = 0 Multiplicity = 1

SCF Energy= -2393.39976071 Predicted Change= -2.022291D-08

==========

Optimization completed. {Found 1 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00001	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.00763	0.00180	[NO]	0.00763	0.00180	[YES]

Atomic Type	Coordinates (Angstroms) X	Y	Z
C	0.126126	3.318147	0.015747
C	-0.382353	2.953133	-1.229761
C	-0.239850	1.636564	-1.661283
C	0.410021	0.761781	-0.803263
C	0.923314	1.046134	0.439277
C	0.756720	2.364729	0.815196
H	-0.878973	3.674031	-1.865885
H	-0.634069	1.330126	-2.623453
H	1.340128	0.086400	1.245297
I	0.631676	-1.262161	-1.472127

C	2.731314	-1.380816	-1.251685
C	3.565173	-0.419442	-1.834795
C	3.215134	-2.466456	-0.504682
C	4.939222	-0.557652	-1.616671
C	4.597162	-2.556625	-0.341455
C	5.471315	-1.607831	-0.873277
H	5.608354	0.180433	-2.052209
H	4.998665	-3.391346	0.228643
C	2.316632	-3.498149	0.126331
H	1.680260	-3.005860	0.870905
H	1.682647	-4.004078	-0.610190
H	2.915255	-4.261913	0.627913
C	3.067539	0.740183	-2.657133
H	2.267592	0.442109	-3.342918
H	2.673146	1.536292	-2.016855
H	3.884567	1.156227	-3.250115
C	6.953446	-1.709254	-0.626561
H	7.520896	-1.160385	-1.382015
H	7.205807	-1.287706	0.352631
H	7.285181	-2.750948	-0.632016
O	-2.132953	-0.981100	-1.345443
S	-2.538402	-1.146808	0.074647
C	-4.295488	-1.408791	0.076588
C	-4.799333	-2.704532	0.033486
C	-5.145207	-0.305808	0.078067
C	-6.177219	-2.892520	-0.011256
H	-4.117322	-3.548437	0.042568
C	-6.518994	-0.511718	0.032059
H	-4.729096	0.695601	0.121397
C	-7.053639	-1.803746	-0.011828
H	-6.579869	-3.901251	-0.044296
H	-7.189913	0.343132	0.032684
O	-2.284263	0.060231	0.902646
O	-1.917499	-2.343093	0.707236
C	2.556988	-0.729185	2.890530
C	3.160619	-2.081706	3.280224
H	2.376566	-2.747706	3.659030
H	3.618894	-2.552350	2.403662
H	3.928832	-1.971490	4.054373
C	2.023323	-0.017953	4.142440
H	2.815234	0.191208	4.870834
H	1.561596	0.932182	3.851603
H	1.265845	-0.641929	4.634567
C	3.645105	0.142809	2.242210
H	3.952411	-0.298201	1.286793
H	3.267559	1.152965	2.052013

H	4.524668	0.223548	2.891090
O	1.502289	-0.945755	1.984421
C	-8.545619	-2.015090	-0.027416
H	-8.945941	-2.022360	0.992465
H	-9.052721	-1.215517	-0.573967
H	-8.806128	-2.969427	-0.492050
Na	-0.674076	-1.038876	2.217347
F	1.205011	2.777418	2.016921
O	0.065168	4.587317	0.564696
C	-0.635175	5.554097	-0.066498
F	-0.120559	5.850352	-1.265235
F	-1.912272	5.215672	-0.254629
F	-0.588760	6.638242	0.688396

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -2393.39976071 Predicted Change= -2.022291D-08
Zero-point correction (ZPE)= -2392.8745 0.52524
Internal Energy (U)= -2392.8322 0.56748
Enthalpy (H)= -2392.8313 0.56842
Gibbs Free Energy (G)= -2392.9549 0.44479

Frequencies -- -1001.4132 10.7595 19.0064

Supporting Information: 1f-Minor-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current
SCRF=(PCM,SOLVENT=Toluene) opt=(maxcycle=250,ts,calcfc,noeigentest)
freq=noraman
#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq

---

Pointgroup= C1 Stoichiometry= C27H30F4INaO5S C1[X(C27H30F4INaO5S)] #Atoms= 69
Charge = 0 Multiplicity = 1

SCF Energy= -2393.39369987 Predicted Change= -3.511925D-09

==========

Optimization completed on the basis of negligible forces. {Found 2 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00000	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.00930	0.00180	[NO]	0.00930	0.00180	[YES]

Atomic Coordinates (Angstroms)

Type	X	Y	Z
C	0.497737	2.884348	1.841394
C	-0.014557	3.147809	0.569142
C	-0.053046	2.148094	-0.386789
C	0.445163	0.916546	0.023149
C	0.944717	0.568869	1.251137
C	0.959088	1.624100	2.181329
H	-0.450787	2.353338	-1.374672
H	1.260778	-0.790510	1.534188
I	0.464045	-0.615851	-1.496482
C	2.538276	-1.017007	-1.415766
C	3.471858	0.021495	-1.517353
C	2.904025	-2.364347	-1.264707
C	4.822443	-0.330852	-1.428600
C	4.267546	-2.649800	-1.202420
C	5.238531	-1.649440	-1.266618
H	5.567090	0.458426	-1.497663
H	4.576546	-3.686810	-1.091647
C	1.900273	-3.483093	-1.154997
H	1.293331	-3.336402	-0.254450
H	1.237346	-3.532572	-2.025892
H	2.414545	-4.443632	-1.075998
C	3.108107	1.471932	-1.703056
H	2.280488	1.601025	-2.408272
H	2.806385	1.927691	-0.753929
H	3.967630	2.025980	-2.085915
C	6.699813	-1.991136	-1.139760
H	6.976589	-2.095333	-0.084822
H	6.929333	-2.938197	-1.635369
H	7.329787	-1.211011	-1.573926
O	-2.262790	-0.128893	-1.188667
S	-2.718812	-0.899750	-0.003541
C	-4.489287	-0.997819	-0.107495
C	-5.083327	-2.091137	-0.728127
C	-5.257637	0.045207	0.403815
C	-6.469976	-2.134138	-0.839464
H	-4.464217	-2.898829	-1.104345
C	-6.640646	-0.013508	0.283170
H	-4.773047	0.880713	0.898662
C	-7.265230	-1.098522	-0.342058
H	-6.943069	-2.988110	-1.316452
H	-7.248782	0.792676	0.684696
O	-2.399018	-0.238121	1.287805
O	-2.202893	-2.297646	-0.002124
C	2.388559	-2.266854	2.577561

C	2.815751	-3.711931	2.315299
H	1.955057	-4.383223	2.413669
H	3.212522	-3.804805	1.298840
H	3.590490	-4.033064	3.020529
C	1.933151	-2.113965	4.034480
H	2.743727	-2.316981	4.743102
H	1.574485	-1.091925	4.206144
H	1.111692	-2.809402	4.247730
C	3.573886	-1.328432	2.308037
H	3.842216	-1.362582	1.246371
H	3.319596	-0.293516	2.561376
H	4.447015	-1.621867	2.901446
O	1.315548	-1.957548	1.712388
C	-8.764507	-1.135047	-0.489245
H	-9.123125	-2.154561	-0.651062
H	-9.258886	-0.732443	0.399131
H	-9.083369	-0.529907	-1.345018
Na	-0.886763	-1.927637	1.896378
H	1.330899	1.479826	3.194083
F	0.528830	3.887462	2.723408
O	-0.490604	4.422453	0.281272
C	0.437904	5.263126	-0.232924
F	1.486084	5.412239	0.578766
F	0.909180	4.825612	-1.406662
F	-0.134636	6.439928	-0.417810

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -2393.39369987 Predicted Change= -3.511925D-09
Zero-point correction (ZPE)= -2392.8691 0.52456
Internal Energy (U)= -2392.8265 0.56715
Enthalpy (H)= -2392.8256 0.56809
Gibbs Free Energy (G)= -2392.9529 0.44076

Frequencies -- -812.0576 12.1516 15.1277

Supporting Information: 1g-Major-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current
SCRF=(PCM,SOLVENT=Toluene) opt=(maxcycle=250,ts,calcfc,noeigentest)
freq=noraman
#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq

---

Pointgroup= C1 Stoichiometry= C27H33FINaO5S C1[X(C27H33FINaO5S)] #Atoms= 69
Charge = 0 Multiplicity = 1

SCF Energy= -2095.74485304 Predicted Change= -1.084450D-09

==========

Optimization completed. {Found 2 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00000	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.00176	0.00180	[YES]	0.00176	0.00180	[YES]

Atomic Type	Coordinates (Angstroms) X	Y	Z
C	0.377027	3.776414	-0.272607
C	-0.152449	3.350938	-1.494670
C	-0.124505	1.998328	-1.835809
C	0.439303	1.134649	-0.912132
C	0.973021	1.463537	0.314239
C	0.920771	2.812141	0.590724
H	-0.586544	4.061985	-2.186908
H	-0.538938	1.659551	-2.778904
H	1.329934	0.524617	1.206562
I	0.483888	-0.943537	-1.435578
C	2.563196	-1.235679	-1.186565
C	3.482511	-0.402279	-1.834763
C	2.945651	-2.293988	-0.347228
C	4.838065	-0.646406	-1.594823
C	4.313806	-2.496369	-0.166441
C	5.271502	-1.678071	-0.766377
H	5.572030	-0.007616	-2.080173
H	4.636765	-3.313842	0.474229
C	1.957301	-3.179205	0.366808
H	1.375088	-2.568088	1.066879
H	1.273004	-3.682615	-0.324868
H	2.484789	-3.951293	0.931742
C	3.092618	0.732065	-2.745438
H	2.278412	0.452170	-3.422044
H	2.756680	1.599941	-2.168216
H	3.948350	1.036548	-3.351573
C	6.738071	-1.892938	-0.499477
H	6.974608	-2.957459	-0.420969
H	7.354077	-1.458253	-1.290431
H	7.026045	-1.420378	0.446058
O	-2.272529	-0.412491	-1.341140
S	-2.670489	-0.429170	0.089522

C	-4.429419	-0.683139	0.124946
C	-4.934184	-1.978771	0.053201
C	-5.279434	0.416500	0.175247
C	-6.310969	-2.167512	0.027901
H	-4.252370	-2.822739	0.026140
C	-6.655268	0.209956	0.148677
H	-4.861606	1.415772	0.239669
C	-7.189140	-1.079428	0.075263
H	-6.713706	-3.175341	-0.027716
H	-7.326488	1.063668	0.186828
O	-2.407846	0.849802	0.797046
O	-2.055573	-1.563970	0.833544
C	2.493413	-0.227598	2.900023
C	2.977566	-1.592628	3.396469
H	2.142709	-2.148934	3.838063
H	3.374918	-2.174895	2.558131
H	3.766459	-1.489377	4.150579
C	2.045907	0.631069	4.091592
H	2.866640	0.829368	4.790639
H	1.665675	1.590569	3.723891
H	1.246093	0.120334	4.643093
C	3.642671	0.485976	2.169470
H	3.898101	-0.061059	1.254296
H	3.348712	1.504167	1.894008
H	4.534854	0.545956	2.803359
O	1.407770	-0.423654	2.025207
C	-8.680139	-1.298697	0.077976
H	-9.042400	-1.485550	1.094983
H	-9.210249	-0.423774	-0.306741
H	-8.953721	-2.163524	-0.532412
Na	-0.765384	-0.159580	2.185755
O	0.406830	5.056616	0.160240
C	-0.176427	6.036296	-0.676206
H	-0.070726	6.983597	-0.149066
H	0.343032	6.094294	-1.639682
H	-1.238661	5.827824	-0.847077
F	1.403042	3.266952	1.769827

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -2095.74485304 Predicted Change= -1.084450D-09
Zero-point correction (ZPE)= -2095.1961 0.54871
Internal Energy (U)= -2095.1556 0.58920
Enthalpy (H)= -2095.1547 0.59015
Gibbs Free Energy (G)= -2095.2745 0.47029

Frequencies -- -1006.9392 11.7699 17.6924

Supporting Information: 1g-Minor-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current SCRF=(PCM,SOLVENT=Toluene) opt=(maxcycle=250,ts,calcfc,noeigentest) freq=noraman

#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq

---

Pointgroup= C1 Stoichiometry= C27H33FINaO5S C1[X(C27H33FINaO5S)] #Atoms= 69

Charge = 0 Multiplicity = 1

SCF Energy= -2095.73375565 Predicted Change= -1.742612D-08

==========

Optimization completed on the basis of negligible forces. {Found 2 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00000	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.01291	0.00180	[NO]	0.01291	0.00180	[YES]

Atomic Type	Coordinates (Angstroms) X	Y	Z
C	0.378805	3.538107	1.302185
C	-0.155231	3.618170	0.007499
C	-0.113418	2.484265	-0.793120
C	0.457456	1.351612	-0.219807
C	0.989167	1.198283	1.030586
C	0.936291	2.375553	1.802478
H	-0.526615	2.521744	-1.795356
H	1.391888	-0.092070	1.517852
I	0.522964	-0.389596	-1.512883
C	2.604403	-0.735213	-1.386350
C	3.515468	0.291748	-1.660331
C	3.000753	-2.033198	-1.025304
C	4.874349	-0.014623	-1.536573
C	4.370931	-2.278358	-0.938516
C	5.319968	-1.282982	-1.175501
H	5.601049	0.768811	-1.737683
H	4.703215	-3.277844	-0.666700
C	2.023362	-3.138243	-0.717544
H	1.423341	-2.856521	0.155185
H	1.351570	-3.344724	-1.557896

H	2.560259	-4.061467	-0.487585
C	3.113783	1.687354	-2.059362
H	2.301772	1.684584	-2.794054
H	2.768601	2.258684	-1.191128
H	3.965921	2.211795	-2.496695
C	6.789204	-1.573699	-1.016881
H	7.071264	-1.545981	0.041415
H	7.039262	-2.567667	-1.397737
H	7.399658	-0.836865	-1.544377
O	-2.239173	0.050766	-1.245250
S	-2.645569	-0.533432	0.057758
C	-4.400764	-0.796883	-0.024005
C	-4.891281	-2.001684	-0.517378
C	-5.261890	0.226136	0.361823
C	-6.266786	-2.178027	-0.625563
H	-4.200270	-2.787908	-0.803585
C	-6.633986	0.033543	0.246408
H	-4.854912	1.153893	0.750627
C	-7.154896	-1.167301	-0.246334
H	-6.658811	-3.115921	-1.009600
H	-7.313998	0.827095	0.544352
O	-2.397983	0.364099	1.214961
O	-2.020678	-1.864875	0.300565
C	2.587609	-1.331702	2.766366
C	3.058640	-2.786202	2.725312
H	2.223639	-3.458187	2.953183
H	3.433408	-3.027396	1.724932
H	3.860537	-2.967235	3.449867
C	2.153874	-0.963115	4.190844
H	2.983940	-1.026439	4.903257
H	1.765062	0.062245	4.206841
H	1.360258	-1.640095	4.529995
C	3.732476	-0.410090	2.322228
H	3.986137	-0.609644	1.275302
H	3.440930	0.642465	2.406900
H	4.624703	-0.570594	2.937807
O	1.488986	-1.199561	1.889040
C	-8.644568	-1.376562	-0.336927
H	-9.161322	-0.442918	-0.574654
H	-8.895366	-2.114234	-1.103455
H	-9.043252	-1.740372	0.616598
Na	-0.716191	-1.067340	2.059376
H	1.317276	2.398456	2.822421
O	-0.725533	4.767478	-0.457260
C	0.198715	5.831253	-0.661301
H	-0.376871	6.665786	-1.062162

H	0.672129	6.129679	0.278018
H	0.968620	5.535829	-1.383705
F	0.329729	4.643903	2.065701

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -2095.73375565 Predicted Change= -1.742612D-08
Zero-point correction (ZPE)= -2095.1858 0.54795
Internal Energy (U)= -2095.1450 0.58872
Enthalpy (H)= -2095.1440 0.58966
Gibbs Free Energy (G)= -2095.2637 0.46997

Frequencies -- -763.3311 16.0178 22.4141

Supporting Information: 1h-Major-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current
SCRF=(PCM,SOLVENT=Toluene) opt=(maxcycle=250,ts,calcfc,noeigentest)
freq=noraman
#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq

---

Pointgroup= C1 Stoichiometry= C26H30ClFINaO4S C1[X(C26H30ClFINaO4S)] #Atoms= 65
Charge = 0 Multiplicity = 1

SCF Energy= -2440.83332663 Predicted Change= -6.165124D-10

==========

Optimization completed on the basis of negligible forces. {Found 2 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00000	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.00243	0.00180	[NO]	0.00243	0.00180	[YES]

Atomic Type	Coordinates (Angstroms) X	Y	Z
C	0.191794	3.629323	-1.283031
C	-0.313907	2.909904	-2.358658
C	-0.226761	1.524105	-2.338704
C	0.374272	0.957159	-1.220486
C	0.880057	1.603434	-0.116147
C	0.770589	2.989181	-0.190434
H	-0.764213	3.443572	-3.187611

H	-0.619575	0.929673	-3.156040
H	1.261429	0.881369	0.959126
I	0.472584	-1.184832	-1.220986
C	2.560788	-1.391616	-0.968898
C	3.458558	-0.687106	-1.778830
C	2.970100	-2.281897	0.036139
C	4.820911	-0.872479	-1.522734
C	4.342454	-2.436620	0.226977
C	5.280487	-1.730482	-0.527533
H	5.539210	-0.329238	-2.131956
H	4.685266	-3.124179	0.996962
C	1.999362	-3.045927	0.899187
H	1.381264	-2.337095	1.461773
H	1.345265	-3.697328	0.308404
H	2.539991	-3.676735	1.608378
C	3.043134	0.249761	-2.882619
H	2.212527	-0.154290	-3.470864
H	2.722109	1.216078	-2.479901
H	3.882444	0.426006	-3.558508
C	6.753398	-1.882633	-0.253053
H	7.044524	-1.275656	0.611169
H	7.008080	-2.921475	-0.026186
H	7.352756	-1.557096	-1.106596
O	-2.271715	-0.698134	-1.243493
S	-2.684068	-0.424484	0.157613
C	-4.453712	-0.573093	0.207335
C	-5.028802	-1.822978	0.415750
C	-5.241051	0.554114	-0.007314
C	-6.414495	-1.939615	0.405600
H	-4.394759	-2.686250	0.590103
C	-6.625185	0.419469	-0.015026
H	-4.769182	1.519378	-0.159211
C	-7.230122	-0.824148	0.191717
H	-6.872232	-2.911622	0.568198
H	-7.248070	1.294062	-0.182315
O	-2.353614	0.950383	0.612468
O	-2.137395	-1.427073	1.114129
C	2.447029	0.374066	2.763255
C	2.918164	-0.907280	3.459013
H	2.073327	-1.398894	3.955535
H	3.343063	-1.601965	2.728148
H	3.684770	-0.690591	4.211903
C	2.004655	1.386688	3.828866
H	2.826800	1.668138	4.496803
H	1.624399	2.293112	3.347576
H	1.203766	0.953624	4.442828

C	3.607301	0.955966	1.942244
H	3.873659	0.261547	1.136665
H	3.322357	1.913090	1.492584
H	4.491401	1.121775	2.568444
O	1.362806	0.068351	1.916634
C	-8.731436	-0.952544	0.214707
H	-9.120782	-0.760053	1.220616
H	-9.200441	-0.234176	-0.462824
H	-9.047869	-1.957698	-0.075442
Na	-0.808098	0.166337	2.205463
F	0.109965	4.962133	-1.308348
Cl	1.333535	4.006771	1.119757

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -2440.83332663 Predicted Change= -6.165124D-10
Zero-point correction (ZPE)= -2440.3278 0.50546
Internal Energy (U)= -2440.2887 0.54459
Enthalpy (H)= -2440.2877 0.54553
Gibbs Free Energy (G)= -2440.4041 0.42921

Frequencies -- -1075.4174 15.1521 20.2251

Supporting Information: 1h-Minor-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current
SCRF=(PCM,SOLVENT=Toluene) opt=(maxcycle=250,ts,calcfc,noeigentest)
freq=noraman
#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq

---

Pointgroup= C1 Stoichiometry= C26H30ClFINaO4S C1[X(C26H30ClFINaO4S)] #Atoms= 65
Charge = 0 Multiplicity = 1

SCF Energy= -2440.82714314 Predicted Change= -6.838556D-10

==========

Optimization completed. {Found 2 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00000	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.00159	0.00180	[YES]	0.00159	0.00180	[YES]

Atomic Coordinates (Angstroms)

Type	X	Y	Z
C	0.298861	3.741292	0.323074
C	-0.292516	3.440150	-0.906166
C	-0.237349	2.159085	-1.425681
C	0.427175	1.231777	-0.631232
C	1.015833	1.419826	0.588814
C	0.933989	2.744547	1.055089
H	-0.707489	1.935325	-2.376391
H	1.428105	0.310238	1.360439
I	0.544476	-0.767150	-1.458477
C	2.633437	-1.011019	-1.249951
C	3.516575	-0.056488	-1.768873
C	3.061745	-2.172126	-0.586800
C	4.882376	-0.286985	-1.578291
C	4.438016	-2.351638	-0.448116
C	5.360500	-1.417997	-0.921892
H	5.588432	0.443262	-1.966281
H	4.796178	-3.246633	0.055618
C	2.114056	-3.195305	-0.015624
H	1.511147	-2.726431	0.770699
H	1.445720	-3.614495	-0.775668
H	2.675725	-4.023101	0.423350
C	3.078454	1.187811	-2.495382
H	2.267158	0.984522	-3.202064
H	2.720495	1.946609	-1.791565
H	3.916062	1.610732	-3.053603
C	6.836678	-1.619784	-0.702085
H	7.125069	-1.265927	0.293914
H	7.105792	-2.677381	-0.766704
H	7.427341	-1.066046	-1.435890
O	-2.213734	-0.330287	-1.313283
S	-2.615925	-0.564197	0.097906
C	-4.374835	-0.811278	0.096304
C	-4.886115	-2.084637	-0.138747
C	-5.217892	0.277099	0.294661
C	-6.264136	-2.261969	-0.179406
H	-4.208661	-2.921864	-0.272165
C	-6.594715	0.081780	0.250191
H	-4.795063	1.256462	0.493307
C	-7.135869	-1.184072	0.008754
H	-6.672637	-3.253658	-0.354482
H	-7.260949	0.924945	0.410866
O	-2.342883	0.591304	0.990048
O	-2.003983	-1.801327	0.660286
C	2.596295	-0.592154	2.907064

C	3.092023	-2.005254	3.219511
H	2.261274	-2.624988	3.575427
H	3.503056	-2.464583	2.314372
H	3.873085	-1.993920	3.988039
C	2.120524	0.089075	4.196783
H	2.933045	0.214164	4.921109
H	1.712066	1.080088	3.964561
H	1.331820	-0.509292	4.669841
C	3.739429	0.223299	2.285871
H	4.015908	-0.204820	1.316117
H	3.435442	1.263198	2.123749
H	4.620817	0.221217	2.936806
O	1.519799	-0.689416	1.998703
C	-8.627608	-1.383434	-0.067474
H	-8.972173	-1.325026	-1.105861
H	-8.916477	-2.364065	0.320086
H	-9.159982	-0.617037	0.501450
Na	-0.685596	-0.612856	2.174771
H	1.364100	3.017254	2.017467
Cl	0.210007	5.373677	0.910697
F	-0.906508	4.403828	-1.597388

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -2440.82714314 Predicted Change= -6.838556D-10
Zero-point correction (ZPE)= -2440.3220 0.50512
Internal Energy (U)= -2440.2826 0.54445
Enthalpy (H)= -2440.2817 0.54540
Gibbs Free Energy (G)= -2440.3994 0.42769

Frequencies -- -844.8705 13.9776 16.7119

Supporting Information: 1i-Major-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current
SCRF=(PCM,SOLVENT=Toluene) opt=(maxcycle=250,ts,calcfc,noeigentest)
freq=noraman
#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq

---

Pointgroup= C1 Stoichiometry= C27H33ClINaO5S C1[X(C27H33ClINaO5S)] #Atoms= 69
Charge = 0 Multiplicity = 1

SCF Energy= -2456.10640040 Predicted Change= -4.236993D-10

Optimization completed. {Found 2 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00000	0.00045	YES	0.00000	0.00030	YES
Displ	0.00107	0.00180	YES	0.00107	0.00180	YES

	Atomic Type	Coordinates (Angstroms) X	Y	Z
	C	0.252796	3.693016	-0.623703
	C	-0.252290	3.139083	-1.806245
	C	-0.181347	1.766450	-2.017421
	C	0.403343	1.006793	-1.016841
	C	0.915185	1.459106	0.180367
	C	0.818940	2.833759	0.336280
	H	-0.701912	3.768665	-2.563869
	H	-0.580143	1.329294	-2.926401
	H	1.307449	0.560501	1.127402
	I	0.467384	-1.103048	-1.376267
	C	2.550431	-1.384657	-1.159555
	C	3.463086	-0.572346	-1.842176
	C	2.940551	-2.430105	-0.308496
	C	4.820931	-0.819538	-1.617643
	C	4.309745	-2.637788	-0.144477
	C	5.262149	-1.835784	-0.774381
	H	5.550716	-0.196211	-2.128750
	H	4.638049	-3.445335	0.506060
	C	1.953061	-3.300762	0.425139
	H	1.346175	-2.676609	1.091611
	H	1.288682	-3.839498	-0.259970
	H	2.480059	-4.044443	1.027179
	C	3.066153	0.538836	-2.778244
	H	2.232480	0.248377	-3.426103
	H	2.755399	1.429708	-2.222527
	H	3.911221	0.811400	-3.413885
	C	6.731658	-2.052784	-0.525872
	H	7.337265	-1.637567	-1.335098
	H	7.036835	-1.562449	0.405085
	H	6.964239	-3.116682	-0.429276
	O	-2.290330	-0.595953	-1.316970
	S	-2.696766	-0.499166	0.108426
	C	-4.456052	-0.748434	0.153871
	C	-4.960823	-2.046311	0.167153
	C	-5.305908	0.351895	0.130455
	C	-6.337289	-2.236409	0.152543

H	-4.279039	-2.890235	0.197030
C	-6.681962	0.143853	0.116167
H	-4.888153	1.353289	0.129383
C	-7.215663	-1.147427	0.127470
H	-6.740077	-3.245749	0.162925
H	-7.353157	0.998203	0.097723
O	-2.434544	0.831701	0.712603
O	-2.088545	-1.572706	0.942823
C	2.476602	-0.255004	2.823914
C	2.916795	-1.649061	3.282952
H	2.057961	-2.201298	3.681509
H	3.332241	-2.212621	2.442252
H	3.682740	-1.585051	4.064534
C	2.058938	0.563140	4.053766
H	2.890600	0.708553	4.752830
H	1.694866	1.546954	3.741450
H	1.254326	0.043195	4.590083
C	3.649206	0.435366	2.112033
H	3.898971	-0.113566	1.196221
H	3.384844	1.462210	1.837764
H	4.537480	0.468953	2.753359
O	1.385058	-0.382638	1.941771
C	-8.706437	-1.367670	0.143062
H	-9.239098	-0.506420	-0.267873
H	-8.981247	-2.252265	-0.437907
H	-9.064468	-1.522453	1.166899
Na	-0.780132	-0.066812	2.165425
O	0.227496	5.010663	-0.339596
C	-0.375008	5.879102	-1.280266
H	-0.304026	6.877753	-0.851713
H	0.155811	5.853605	-2.238534
H	-1.427949	5.620836	-1.437435
Cl	1.393256	3.580215	1.821855

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -2456.10640040 Predicted Change= -4.236993D-10
Zero-point correction (ZPE)= -2455.5589 0.54745
Internal Energy (U)= -2455.5182 0.58812
Enthalpy (H)= -2455.5173 0.58907
Gibbs Free Energy (G)= -2455.6362 0.47016

Frequencies -- -1051.2180 18.1374 22.9779

Supporting Information: 1i-Minor-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current SCRF=(PCM,SOLVENT=Toluene) opt=(gdiis,maxcycle=250,ts,calcfc,noeigentest) freq=noraman

#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq

---

Pointgroup= C1 Stoichiometry= C27H33ClINaO5S C1[X(C27H33ClINaO5S)] #Atoms= 69

Charge = 0 Multiplicity = 1

SCF Energy= -2456.09704654 Predicted Change= -4.024988D-09

==========

Optimization completed on the basis of negligible forces. {Found 2 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00000	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.00467	0.00180	[NO]	0.00467	0.00180	[YES]

	Atomic Type	Coordinates (Angstroms) X	Y	Z
	C	0.451162	3.532925	0.905294
	C	-0.107893	3.477723	-0.381155
	C	-0.103733	2.264368	-1.061902
	C	0.459757	1.187112	-0.390944
	C	1.003985	1.152692	0.863402
	C	0.982661	2.400613	1.512161
	H	-0.539866	2.207263	-2.053736
	H	1.370263	-0.079818	1.472564
	I	0.503748	-0.673610	-1.507571
	C	2.582934	-1.015545	-1.340945
	C	3.501651	-0.024340	-1.706796
	C	2.969265	-2.277662	-0.861772
	C	4.857895	-0.327620	-1.551935
	C	4.337486	-2.523025	-0.748505
	C	5.293879	-1.560324	-1.073872
	H	5.590702	0.428301	-1.823800
	H	4.662143	-3.495785	-0.385846
	C	1.983148	-3.344146	-0.460309
	H	1.378937	-2.980439	0.378374
	H	1.315605	-3.623163	-1.282932
	H	2.512630	-4.245480	-0.143108
	C	3.112507	1.331510	-2.235383
	H	2.287572	1.269972	-2.952824
	H	2.792689	1.991619	-1.421987

H	3.964361	1.796287	-2.736189
C	6.760945	-1.844651	-0.886552
H	7.375858	-1.185473	-1.504060
H	7.049113	-1.688144	0.158811
H	6.998991	-2.880763	-1.141880
O	-2.244856	-0.196879	-1.298273
S	-2.660130	-0.634660	0.058951
C	-4.420354	-0.870720	0.009194
C	-4.936570	-2.100670	-0.386950
C	-5.259540	0.192133	0.329359
C	-6.315828	-2.261666	-0.463320
H	-4.262540	-2.917944	-0.622311
C	-6.636227	0.014130	0.247015
H	-4.832388	1.138911	0.643334
C	-7.182705	-1.211078	-0.147423
H	-6.728018	-3.218920	-0.770806
H	-7.299215	0.838698	0.494788
O	-2.393002	0.374346	1.115367
O	-2.058830	-1.944776	0.438118
C	2.529947	-1.230667	2.848849
C	2.982863	-2.689294	2.933210
H	2.137336	-3.330174	3.207271
H	3.364163	-3.016958	1.960354
H	3.775658	-2.819237	3.678492
C	2.094762	-0.739228	4.235329
H	2.920580	-0.753067	4.955328
H	1.719074	0.288660	4.163691
H	1.291181	-1.375973	4.625561
C	3.690307	-0.365156	2.337284
H	3.940669	-0.649863	1.309467
H	3.417457	0.695775	2.339156
H	4.579508	-0.492020	2.964889
O	1.438169	-1.156801	1.956933
C	-8.676458	-1.403481	-0.199595
H	-8.951905	-2.174025	-0.924240
H	-9.060741	-1.715446	0.777930
H	-9.185616	-0.475382	-0.472527
Na	-0.761147	-0.999256	2.131602
H	1.381442	2.501413	2.520496
O	-0.657809	4.581359	-0.965817
C	0.290273	5.373847	-1.672556
H	-0.258539	6.220214	-2.085619
H	1.075641	5.737464	-1.000917
H	0.744750	4.795491	-2.485899
Cl	0.444850	5.057118	1.752403

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm
==========

SCF Energy= -2456.09704654 Predicted Change= -4.024988D-09
Zero-point correction (ZPE)= -2455.5508 0.54618
Internal Energy (U)= -2455.5096 0.58742
Enthalpy (H)= -2455.5086 0.58836
Gibbs Free Energy (G)= -2455.6302 0.46680

Frequencies -- -827.6676 14.6059 19.1594

Supporting Information: 1j-Major-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016
==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current
SCRF=(PCM,SOLVENT=Toluene) opt=(maxcycle=250,ts,readfc,tight,noeigentest)
freq=noraman geom=check guess=read
#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq
---

Pointgroup= C1 Stoichiometry= C27H33BrINaO4S C1[X(C27H33BrINaO4S)] #Atoms= 68
Charge = 0 Multiplicity = 1

SCF Energy= -4492.24139612 Predicted Change= -4.189529D-12
==========

Optimization completed on the basis of negligible forces. {Found 2 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00000	0.00001	[YES]	0.00000	0.00001	[YES]
Displ	0.00009	0.00006	[NO]	0.00009	0.00006	[YES]

Atomic Type	Coordinates (Angstroms) X	Y	Z
C	0.310625	3.280972	-1.779046
C	-0.222711	2.417574	-2.743804
C	-0.222156	1.040621	-2.563865
C	0.340307	0.580406	-1.381361
C	0.882683	1.325011	-0.361702
C	0.836426	2.692340	-0.622515
H	-0.646977	2.837383	-3.651094
H	-0.647491	0.375934	-3.307607
H	1.254945	0.714394	0.805424
I	0.307315	-1.556240	-1.130391
C	2.377763	-1.866042	-0.851484
C	3.315512	-1.319575	-1.735241

C	2.732961	-2.658531	0.250612
C	4.663792	-1.564468	-1.457428
C	4.093486	-2.882026	0.460019
C	5.071442	-2.331578	-0.369214
H	5.412819	-1.143311	-2.123728
H	4.394706	-3.497230	1.304970
C	1.717005	-3.250039	1.193806
H	1.139185	-2.443376	1.659567
H	1.026412	-3.929805	0.681740
H	2.217737	-3.818823	1.980482
C	2.954580	-0.490785	-2.939892
H	2.101005	-0.910355	-3.482671
H	2.689499	0.531504	-2.650676
H	3.802091	-0.441240	-3.626667
C	6.533162	-2.546380	-0.076789
H	6.880500	-1.828697	0.674549
H	6.714806	-3.549788	0.317455
H	7.142476	-2.410555	-0.973626
O	-2.421239	-0.922332	-1.210890
S	-2.800353	-0.427909	0.137581
C	-4.569053	-0.558766	0.253148
C	-5.140774	-1.706876	0.790483
C	-5.360567	0.477570	-0.235332
C	-6.527556	-1.814866	0.835029
H	-4.503023	-2.496687	1.173600
C	-6.743734	0.353067	-0.184331
H	-4.891957	1.368269	-0.641245
C	-7.345907	-0.790823	0.351160
H	-6.982591	-2.708040	1.254439
H	-7.369357	1.156932	-0.563141
O	-2.461707	1.001295	0.358958
O	-2.233438	-1.266511	1.229875
C	2.415416	0.321648	2.666527
C	2.792780	-0.932662	3.462133
H	1.913562	-1.323148	3.987500
H	3.171475	-1.709812	2.792100
H	3.569988	-0.710879	4.202626
C	2.059197	1.441229	3.654775
H	2.906758	1.706387	4.297243
H	1.745942	2.335686	3.108606
H	1.233478	1.116087	4.301353
C	3.609449	0.746841	1.800326
H	3.819162	-0.030549	1.055801
H	3.389445	1.681316	1.273160
H	4.507602	0.899006	2.409927
O	1.305186	0.034031	1.846894

C	-8.846988	-0.898544	0.430305
H	-9.226794	-0.374253	1.314186
H	-9.322172	-0.450139	-0.446484
H	-9.166703	-1.941259	0.500058
Na	-0.844269	0.458778	1.999845
C	0.290899	4.767698	-2.003177
H	-0.291424	5.271269	-1.225282
H	1.302418	5.183886	-1.964867
H	-0.148281	5.004056	-2.974678
Br	1.515629	3.887045	0.725444

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -4492.24139612 Predicted Change= -4.189529D-12
Zero-point correction (ZPE)= -4491.6999 0.54146
Internal Energy (U)= -4491.6599 0.58148
Enthalpy (H)= -4491.6589 0.58242
Gibbs Free Energy (G)= -4491.7772 0.46419

Frequencies -- -1054.5673 14.6187 18.4022

Supporting Information: 1j-Minor-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current
SCRF=(PCM,SOLVENT=Toluene) opt=(maxcycle=250,ts,calcfc,noeigentest)
freq=noraman
#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq

---

Pointgroup= C1 Stoichiometry= C27H33BrINaO4S C1[X(C27H33BrINaO4S)] #Atoms= 68
Charge = 0 Multiplicity = 1

SCF Energy= -4492.23535809 Predicted Change= -3.589407D-11

==========

Optimization completed. {Found 2 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00000	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.00013	0.00180	[YES]	0.00013	0.00180	[YES]

Atomic Type	Coordinates (Angstroms) X	Y	Z
C	0.174950	3.269148	1.496693

C	-0.391339	3.272380	0.212793
C	-0.269610	2.194207	-0.652374
C	0.447297	1.116401	-0.149516
C	1.029548	0.979325	1.077923
C	0.865874	2.117976	1.888287
H	-0.720135	2.210733	-1.637927
H	1.548978	-0.284738	1.507778
I	0.666718	-0.557318	-1.521912
C	2.770856	-0.713922	-1.404655
C	3.582061	0.404004	-1.633885
C	3.286013	-1.984855	-1.102912
C	4.963839	0.218114	-1.526652
C	4.673511	-2.106914	-1.030175
C	5.525838	-1.019220	-1.224343
H	5.614671	1.072959	-1.694005
H	5.097588	-3.082937	-0.805004
C	2.416129	-3.188010	-0.844909
H	1.792126	-3.000552	0.036094
H	1.766958	-3.421521	-1.695909
H	3.037015	-4.065840	-0.651530
C	3.051428	1.772966	-1.969353
H	2.234875	1.728111	-2.697508
H	2.666656	2.273229	-1.074400
H	3.847271	2.391315	-2.389561
C	7.016521	-1.179403	-1.081419
H	7.306071	-1.125085	-0.026108
H	7.349180	-2.147785	-1.464607
H	7.554203	-0.392029	-1.615225
O	-2.118724	-0.375052	-1.236759
S	-2.468656	-1.013103	0.057759
C	-4.197775	-1.414128	-0.020736
C	-4.593345	-2.683689	-0.423572
C	-5.136527	-0.430711	0.285677
C	-5.953020	-2.969242	-0.522601
H	-3.843343	-3.435396	-0.646337
C	-6.487859	-0.731980	0.180735
H	-4.803960	0.550556	0.608865
C	-6.915115	-2.002449	-0.224946
H	-6.271176	-3.960353	-0.833883
H	-7.227556	0.027604	0.420052
O	-2.288437	-0.115017	1.227250
O	-1.736129	-2.291959	0.277546
C	2.832668	-1.482424	2.711752
C	3.415590	-2.892873	2.611144
H	2.635900	-3.636796	2.809455
H	3.806324	-3.062195	1.602224

H	4.230482	-3.040815	3.328715
C	2.374335	-1.208668	4.150084
H	3.207256	-1.241666	4.861253
H	1.911659	-0.216005	4.209146
H	1.632661	-1.956151	4.457669
C	3.901684	-0.456684	2.308614
H	4.167973	-0.591442	1.254489
H	3.528863	0.565457	2.436681
H	4.804973	-0.572550	2.918066
O	1.725791	-1.398695	1.839178
C	-8.386928	-2.310169	-0.326277
H	-8.886416	-1.612261	-1.005594
H	-8.556128	-3.324344	-0.695603
H	-8.873448	-2.218958	0.650295
Na	-0.482966	-1.411968	2.041393
C	0.040636	4.446251	2.422204
H	0.550614	4.247725	3.367304
H	0.470264	5.349365	1.976714
H	-1.011860	4.661878	2.632183
H	1.291566	2.115051	2.893047
Br	-1.350532	4.795080	-0.395947

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -4492.23535809 Predicted Change= -3.589407D-11
Zero-point correction (ZPE)= -4491.6942 0.54112
Internal Energy (U)= -4491.6540 0.58133
Enthalpy (H)= -4491.6530 0.58227
Gibbs Free Energy (G)= -4491.7716 0.46369

Frequencies -- -809.9740 14.6435 22.1544

Supporting Information: 1k-Major-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current
SCRF=(PCM,SOLVENT=Toluene) opt=(maxcycle=250,ts,calcfc,noeigentest)
freq=noraman
#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq

---

Pointgroup= C1 Stoichiometry= C26H30ClFINaO4S C1[X(C26H30ClFINaO4S)] #Atoms= 65
Charge = 0 Multiplicity = 1

SCF Energy= -2440.83332663 Predicted Change= -5.970007D-11

==========

Optimization completed. {Found 2 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00000	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.00048	0.00180	[YES]	0.00048	0.00180	[YES]

Atomic Type	Coordinates (Angstroms) X	Y	Z
C	0.191791	3.629328	-1.282994
C	-0.313905	2.909921	-2.358629
C	-0.226759	1.524121	-2.338690
C	0.374273	0.957164	-1.220477
C	0.880055	1.603427	-0.116129
C	0.770584	2.989175	-0.190401
H	-0.764209	3.443597	-3.187578
H	-0.619570	0.929697	-3.156033
H	1.261426	0.881352	0.959139
I	0.472592	-1.184826	-1.220999
C	2.560797	-1.391597	-0.968906
C	3.458567	-0.687074	-1.778835
C	2.970112	-2.281883	0.036118
C	4.820916	-0.872445	-1.522743
C	4.342471	-2.436603	0.226955
C	5.280498	-1.730457	-0.527545
H	5.539212	-0.329200	-2.131964
H	4.685282	-3.124171	0.996931
C	1.999381	-3.045933	0.899155
H	1.381277	-2.337115	1.461752
H	1.345290	-3.697332	0.308364
H	2.540015	-3.676745	1.608338
C	3.043136	0.249797	-2.882617
H	2.212543	-0.154263	-3.470877
H	2.722088	1.216104	-2.479893
H	3.882450	0.426066	-3.558496
C	6.753416	-1.882554	-0.253070
H	7.044722	-1.274743	0.610508
H	7.007978	-2.921202	-0.025197
H	7.352729	-1.557944	-1.107000
O	-2.271708	-0.698168	-1.243512
S	-2.684068	-0.424522	0.157592
C	-4.453715	-0.573107	0.207302
C	-5.028826	-1.822965	0.415807
C	-5.241036	0.554098	-0.007431

C	-6.414522	-1.939581	0.405663
H	-4.394797	-2.686235	0.590223
C	-6.625171	0.419478	-0.015135
H	-4.769154	1.519345	-0.159398
C	-7.230128	-0.824115	0.191706
H	-6.872277	-2.911567	0.568336
H	-7.248043	1.294068	-0.182483
O	-2.353600	0.950339	0.612454
O	-2.137415	-1.427120	1.114109
C	2.447017	0.374042	2.763273
C	2.918156	-0.907309	3.459019
H	2.073321	-1.398933	3.955535
H	3.343059	-1.601985	2.728147
H	3.684760	-0.690625	4.211913
C	2.004624	1.386647	3.828894
H	2.826757	1.668088	4.496849
H	1.624373	2.293077	3.347611
H	1.203724	0.953572	4.442834
C	3.607292	0.955960	1.942281
H	3.873673	0.261547	1.136705
H	3.322342	1.913082	1.492620
H	4.491381	1.121779	2.568495
O	1.362802	0.068330	1.916641
C	-8.731443	-0.952463	0.214754
H	-9.120778	-0.759691	1.220613
H	-9.200460	-0.234283	-0.462971
H	-9.047870	-1.957697	-0.075118
Na	-0.808105	0.166271	2.205461
F	0.109963	4.962139	-1.308297
Cl	1.333521	4.006751	1.119805

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -2440.83332663 Predicted Change= -5.970007D-11
Zero-point correction (ZPE)= -2440.3278 0.50546
Internal Energy (U)= -2440.2887 0.54459
Enthalpy (H)= -2440.2877 0.54553
Gibbs Free Energy (G)= -2440.4041 0.42921

Frequencies -- -1075.4172 15.1527 20.2269

Supporting Information: 1k-Minor-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

```
============================================================
 #M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current
 SCRF=(PCM,SOLVENT=Toluene) opt=(gdiis,maxcycle=250,ts,calcfc,noeigentest)
 freq=noraman
 #N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq
------------------------------------------------------------------------
 Pointgroup= C1   Stoichiometry= C26H30ClFINaO4S   C1[X(C26H30ClFINaO4S)]  #Atoms=
65
 Charge = 0     Multiplicity = 1
------------------------------------------------------------------------
 SCF Energy= -2440.82715117         Predicted Change= -1.311522D-08
============================================================
 Optimization completed on the basis of negligible forces.          {Found          2          times}
 Item    Max Val.        Criteria          Pass?   RMS Val.        Criteria          Pass?
 Force           0.00000 ||  0.00045   [ YES ]  0.00000 ||  0.00030   [ YES ]
 Displ  0.01000 ||  0.00180   [ NO ]    0.01000 ||  0.00180   [ YES ]
------------------------------------------------------------------------
          Atomic          Coordinates (Angstroms)
          Type   X         Y         Z
------------------------------------------------------------------------
          C       0.305007        3.739957        0.322164
          C       -0.286883       3.440061        -0.907137
          C       -0.233709       2.159039        -1.427006
          C       0.429649        1.230412        -0.633122
          C       1.018893        1.417447        0.586908
          C       0.938774        2.742035        1.053753
          H       -0.704595       1.936183        -2.377552
          H       1.428726        0.309048        1.359776
          I       0.544350        -0.768158       -1.460897
          C       2.632634        -1.014562       -1.249240
          C       3.517498        -0.061718       -1.768313
          C       3.058650        -2.175007       -0.583447
          C       4.882765        -0.293252       -1.575190
          C       4.434520        -2.355633       -0.442321
          C       5.358683        -1.423666       -0.916181
          H       5.590163        0.435665        -1.963224
          H       4.791016        -3.250135       0.063473
          C       2.108953        -3.196173       -0.012002
          H       1.505550        -2.725407       0.772839
          H       1.441196        -3.615711       -0.772353
          H       2.669050        -4.023970       0.428967
          C       3.081668        1.181863        -2.497419
          H       2.271629        0.978145        -3.205419
          H       2.722851        1.941906        -1.795376
          H       3.920655        1.603463        -3.054561
          C       6.834292        -1.626713       -0.693741
```

H	7.120715	-1.275582	0.303786
H	7.103018	-2.684290	-0.760466
H	7.426786	-1.071436	-1.424890
O	-2.213596	-0.324423	-1.318423
S	-2.617045	-0.554532	0.093015
C	-4.375339	-0.805922	0.091309
C	-4.882863	-2.079537	-0.151013
C	-5.221467	0.280145	0.288597
C	-6.260168	-2.259802	-0.197601
H	-4.202905	-2.913457	-0.292306
C	-6.597768	0.081834	0.238354
H	-4.801440	1.261356	0.484055
C	-7.135094	-1.185471	-0.003361
H	-6.665798	-3.250270	-0.385777
H	-7.266531	0.924475	0.391053
O	-2.347484	0.604202	0.982006
O	-2.003267	-1.788788	0.659750
C	2.591388	-0.594582	2.911655
C	3.084898	-2.008597	3.223660
H	2.252729	-2.627558	3.577558
H	3.496827	-2.467591	2.318759
H	3.864727	-1.998989	3.993469
C	2.114870	0.086109	4.201413
H	2.926523	0.209157	4.927069
H	1.708474	1.078087	3.969579
H	1.324449	-0.511382	4.672694
C	3.736468	0.219896	2.292736
H	4.013325	-0.207475	1.322732
H	3.434234	1.260460	2.131508
H	4.617165	0.215771	2.944592
O	1.516049	-0.689574	2.001859
C	-8.626532	-1.400124	-0.024457
H	-8.905508	-2.166173	-0.752981
H	-8.983477	-1.733037	0.956470
H	-9.156326	-0.477464	-0.274248
Na	-0.689219	-0.595699	2.172031
H	1.369284	3.013664	2.016264
Cl	0.218534	5.372197	0.910428
F	-0.899598	4.404802	-1.597928

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -2440.82715117 Predicted Change= -1.311522D-08
Zero-point correction (ZPE)= -2440.3220 0.50514
Internal Energy (U)= -2440.2826 0.54446

Enthalpy (H)= -2440.2817 0.54540
Gibbs Free Energy (G)= -2440.3993 0.42780

Frequencies -- -848.2979 13.5625 18.4881

Supporting Information: 1l-Major-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016
==========
#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current
SCRF=(PCM,SOLVENT=Toluene) opt=(maxcycle=250,ts,calcfc,noeigentest)
freq=noraman
#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq
---
Pointgroup= C1 Stoichiometry= C27H33BrINaO5S C1[X(C27H33BrINaO5S)] #Atoms= 69
Charge = 0 Multiplicity = 1

SCF Energy= -4567.42022407 Predicted Change= -5.774070D-09
==========
Optimization completed. {Found 1 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00000	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.00581	0.00180	[NO]	0.00581	0.00180	[YES]

Atomic Type	Coordinates (Angstroms) X	Y	Z
C	0.337661	3.371893	-1.255511
C	-0.168256	2.672626	-2.358417
C	-0.157822	1.282584	-2.363434
C	0.370337	0.653254	-1.247130
C	0.880335	1.253616	-0.115357
C	0.844106	2.638303	-0.167415
H	-0.572286	3.202051	-3.212200
H	-0.556649	0.733640	-3.209766
H	1.235874	0.478048	0.958271
I	0.325424	-1.485498	-1.295090
C	2.391821	-1.851309	-1.048223
C	3.342628	-1.195339	-1.838585
C	2.730593	-2.790296	-0.062181
C	4.686262	-1.486039	-1.583911
C	4.087511	-3.050481	0.128053
C	5.077617	-2.398442	-0.607439
H	5.445205	-0.982663	-2.178084
H	4.375704	-3.778596	0.883023

C	1.701719	-3.498328	0.781616
H	1.122796	-2.758562	1.346622
H	1.013858	-4.098539	0.175064
H	2.191592	-4.171326	1.488917
C	2.999832	-0.203935	-2.919215
H	2.146777	-0.534901	-3.520847
H	2.742236	0.770785	-2.492097
H	3.853655	-0.068452	-3.586353
C	6.535002	-2.661172	-0.333159
H	7.151969	-2.427161	-1.204198
H	6.883976	-2.040121	0.499159
H	6.704359	-3.705665	-0.058512
O	-2.410138	-0.837357	-1.279261
S	-2.787031	-0.567641	0.131422
C	-4.554475	-0.730854	0.227118
C	-5.113622	-1.998968	0.363987
C	-5.356980	0.399512	0.121047
C	-6.496700	-2.128833	0.390719
H	-4.467933	-2.866493	0.455618
C	-6.740849	0.251843	0.149722
H	-4.896870	1.377266	0.023643
C	-7.328461	-1.008343	0.284970
H	-6.941585	-3.114590	0.497637
H	-7.375326	1.130113	0.067411
O	-2.457736	0.808177	0.584510
O	-2.211396	-1.570129	1.070876
C	2.396200	-0.170001	2.738208
C	2.779434	-1.519604	3.354576
H	1.901206	-1.983337	3.818692
H	3.163805	-2.195318	2.585153
H	3.553688	-1.397524	4.120875
C	2.029148	0.801167	3.868902
H	2.873653	0.984566	4.543235
H	1.708156	1.758464	3.448143
H	1.206440	0.383479	4.464371
C	3.587918	0.378791	1.941200
H	3.798281	-0.283313	1.092417
H	3.364317	1.378645	1.553810
H	4.486374	0.444840	2.565561
O	1.289536	-0.349343	1.883496
C	-8.826535	-1.160514	0.346366
H	-9.167225	-1.223503	1.385765
H	-9.331078	-0.309144	-0.117241
H	-9.152204	-2.072531	-0.161407
Na	-0.858271	0.027168	2.127195
O	0.364543	4.717409	-1.173506

C	-0.180948	5.458968	-2.247947
H	-0.075627	6.506611	-1.969824
H	0.367610	5.270411	-3.177564
H	-1.240620	5.222119	-2.392885
Br	1.472931	3.653567	1.327577

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -4567.42022407 Predicted Change= -5.774070D-09
Zero-point correction (ZPE)= -4566.8734 0.54681
Internal Energy (U)= -4566.8324 0.58778
Enthalpy (H)= -4566.8314 0.58872
Gibbs Free Energy (G)= -4566.9519 0.46829

Frequencies -- -1047.2129 14.8166 20.2301

Supporting Information: 1l-Minor-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current
SCRF=(PCM,SOLVENT=Toluene) opt=(maxcycle=250,ts,calcfc,noeigentest)
freq=noraman
#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq

---

Pointgroup= C1 Stoichiometry= C27H33BrINaO5S C1[X(C27H33BrINaO5S)] #Atoms= 69
Charge = 0 Multiplicity = 1

SCF Energy= -4567.41044407 Predicted Change= -1.689796D-09

==========

Optimization completed. {Found 2 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00001	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.00055	0.00180	[YES]	0.00055	0.00180	[YES]

Atomic Type	Coordinates (Angstroms) X	Y	Z
C	0.330393	3.308447	0.351284
C	-0.265206	3.053696	-0.892952
C	-0.215802	1.761515	-1.407995
C	0.427559	0.814021	-0.623687

C	1.013971	0.976822	0.600918
C	0.946199	2.297643	1.080133
H	-0.686458	1.547183	-2.361670
H	1.416905	-0.140919	1.367346
I	0.512703	-1.183240	-1.470088
C	2.598885	-1.452068	-1.265747
C	3.492231	-0.505739	-1.782551
C	3.016166	-2.617562	-0.603109
C	4.855667	-0.749617	-1.591986
C	4.390606	-2.810832	-0.464078
C	5.322439	-1.885958	-0.936663
H	5.569122	-0.025906	-1.978745
H	4.739772	-3.709588	0.039344
C	2.057837	-3.630985	-0.032185
H	1.459707	-3.156458	0.754609
H	1.385052	-4.042060	-0.792694
H	2.610857	-4.465079	0.405920
C	3.066597	0.744068	-2.507593
H	2.255863	0.548375	-3.217164
H	2.711638	1.503912	-1.803215
H	3.909789	1.161149	-3.061987
C	6.796480	-2.102780	-0.716472
H	7.056927	-3.161737	-0.793867
H	7.393318	-1.544977	-1.442172
H	7.085877	-1.764099	0.284499
O	-2.233895	-0.709419	-1.312407
S	-2.638189	-0.918230	0.102058
C	-4.397307	-1.166262	0.099607
C	-4.911413	-2.456605	0.030073
C	-5.237914	-0.056407	0.121701
C	-6.290822	-2.632582	-0.020424
H	-4.236041	-3.305815	0.023183
C	-6.613139	-0.250348	0.069446
H	-4.813532	0.940522	0.184615
C	-7.158181	-1.536988	-0.001103
H	-6.701548	-3.637162	-0.074271
H	-7.277089	0.609792	0.085296
O	-2.369930	0.254761	0.972356
O	-2.026650	-2.143057	0.690389
C	2.574054	-1.061578	2.914018
C	3.054831	-2.483148	3.211565
H	2.217957	-3.096200	3.564329
H	3.456928	-2.938469	2.300377
H	3.839008	-2.488257	3.977044
C	2.112322	-0.386548	4.211942
H	2.928668	-0.280545	4.935101

H	1.718640	0.613098	3.990812
H	1.316027	-0.977501	4.681263
C	3.723697	-0.253493	2.295028
H	3.990796	-0.675755	1.319997
H	3.430535	0.791219	2.143923
H	4.608065	-0.271541	2.941726
O	1.492262	-1.138313	2.010783
C	-8.651890	-1.735297	-0.024733
H	-8.918108	-2.687933	-0.489603
H	-9.058346	-1.737138	0.992745
H	-9.148737	-0.932104	-0.575499
Na	-0.708135	-0.920869	2.178863
H	1.370777	2.548755	2.050561
Br	0.255037	5.066734	1.051338
O	-0.901013	4.035350	-1.596345
C	-0.030637	4.767475	-2.452263
H	-0.644200	5.518458	-2.950004
H	0.759435	5.261542	-1.876067
H	0.421405	4.104559	-3.199591

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -4567.41044407 Predicted Change= -1.689796D-09
Zero-point correction (ZPE)= -4566.8646 0.54577
Internal Energy (U)= -4566.8232 0.58716
Enthalpy (H)= -4566.8223 0.58810
Gibbs Free Energy (G)= -4566.9441 0.46630

Frequencies -- -852.9481 15.8242 19.7310

Supporting Information: 1m-Major-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current
SCRF=(PCM,SOLVENT=Toluene) opt=(gdiis,maxcycle=250,ts,calcfc,noeigentest)
freq=noraman
#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq

---

Pointgroup= C1 Stoichiometry= C27H33INNaO6S C1[X(C27H33INNaO6S)] #Atoms= 70
Charge = 0 Multiplicity = 1

SCF Energy= -2125.79093351 Predicted Change= -2.256710D-08

==========

Optimization completed. {Found 1 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00001	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.01976	0.00180	[NO]	0.01976	0.00180	[NO]

Atomic Type	Coordinates (Angstroms) X	Y	Z
C	0.112437	3.172515	-2.111563
C	-0.010983	2.181647	-3.092499
C	0.158426	0.834947	-2.792096
C	0.491600	0.507319	-1.482147
C	0.630557	1.398941	-0.444394
C	0.412620	2.718542	-0.824504
H	-0.269556	2.473100	-4.105619
H	0.024391	0.078064	-3.558269
H	0.985806	1.070885	0.752465
I	0.546082	-1.559892	-0.986627
C	2.614169	-1.752822	-0.606544
C	3.554744	-1.446379	-1.597393
C	2.963145	-2.204744	0.675538
C	4.902240	-1.575685	-1.253204
C	4.325872	-2.330305	0.948444
C	5.305328	-2.007524	0.008800
H	5.654071	-1.335125	-2.000767
H	4.626847	-2.682706	1.932360
C	1.944736	-2.524298	1.740333
H	1.378769	-1.615694	1.987114
H	1.246917	-3.306076	1.420734
H	2.446150	-2.877467	2.644127
C	3.182580	-0.980030	-2.979755
H	2.401249	-1.607790	-3.422039
H	2.810429	0.049805	-2.963150
H	4.053961	-1.011883	-3.636753
C	6.765831	-2.107515	0.362289
H	6.960123	-2.976597	0.996464
H	7.387378	-2.185202	-0.532959
H	7.085677	-1.217937	0.915658
O	-2.145396	-0.946961	-1.140653
S	-2.603630	-0.275365	0.105854
C	-4.334493	-0.654101	0.265767
C	-4.720486	-1.868332	0.829083
C	-5.279858	0.247065	-0.210058
C	-6.072471	-2.177681	0.909048
H	-3.966883	-2.552428	1.206050
C	-6.630800	-0.078267	-0.122765

H	-4.954831	1.190653	-0.635642
C	-7.045268	-1.289410	0.435585
H	-6.382262	-3.122263	1.348478
H	-7.375558	0.621276	-0.492307
O	-2.493637	1.202408	0.065872
O	-1.930279	-0.820968	1.315572
C	2.375985	1.236033	2.577397
C	3.016790	0.191434	3.502402
H	2.270407	-0.178944	4.213954
H	3.390683	-0.655391	2.919473
H	3.857193	0.615089	4.064742
C	2.056402	2.486604	3.411418
H	2.953762	2.896113	3.889893
H	1.613207	3.266583	2.785045
H	1.337105	2.229239	4.198904
C	3.386244	1.606611	1.477917
H	3.574082	0.735548	0.836757
H	3.000764	2.419717	0.849940
H	4.339980	1.937229	1.904710
O	1.207795	0.707027	2.009635
C	-8.508966	-1.628197	0.554234
H	-9.115852	-1.002239	-0.104532
H	-8.693563	-2.675720	0.299569
H	-8.861166	-1.473414	1.579957
Na	-0.942179	1.208608	1.946310
C	-0.111362	4.619385	-2.463193
H	-0.770933	5.112425	-1.743890
H	0.833534	5.168672	-2.463189
H	-0.562581	4.695209	-3.454280
N	0.427112	3.699867	0.274373
O	-0.194412	3.416790	1.290598
O	1.043492	4.735345	0.124690

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -2125.79093351 Predicted Change= -2.256710D-08
Zero-point correction (ZPE)= -2125.2359 0.55502
Internal Energy (U)= -2125.1949 0.59597
Enthalpy (H)= -2125.1940 0.59691
Gibbs Free Energy (G)= -2125.3145 0.47639

Frequencies -- -1022.1178 13.7707 16.9604

Supporting Information: 1m-Minor-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016
==========
#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current
SCRF=(PCM,SOLVENT=Toluene) opt=(maxcycle=250,ts,calcfc,noeigentest)
freq=noraman
#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq
---
Pointgroup= C1 Stoichiometry= C27H33INNaO6S C1[X(C27H33INNaO6S)] #Atoms= 70
Charge = 0 Multiplicity = 1

SCF Energy= -2125.77953451 Predicted Change= -3.806348D-10
==========
Optimization completed. {Found 2 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00000	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.00106	0.00180	[YES]	0.00106	0.00180	[YES]

Atomic Type	Coordinates (Angstroms) X	Y	Z
C	0.145464	3.457940	1.405447
C	-0.395992	3.431612	0.107125
C	-0.258403	2.339459	-0.743740
C	0.431138	1.262424	-0.220922
C	0.987698	1.151049	1.027379
C	0.828835	2.305131	1.811452
H	-0.691150	2.365563	-1.736059
H	1.460540	-0.093233	1.493407
I	0.634297	-0.441402	-1.534264
C	2.735043	-0.623150	-1.390716
C	3.563841	0.475870	-1.646978
C	3.227884	-1.891047	-1.042705
C	4.941117	0.275886	-1.511746
C	4.612341	-2.028235	-0.945014
C	5.481715	-0.957882	-1.159641
H	5.605817	1.115940	-1.698073
H	5.020262	-3.002095	-0.683791
C	2.337865	-3.074443	-0.762871
H	1.707332	-2.853875	0.105792
H	1.695599	-3.322379	-1.615090
H	2.943694	-3.955322	-0.538461
C	3.057233	1.838572	-2.040574
H	2.243521	1.778372	-2.770740
H	2.678740	2.383057	-1.169023
H	3.864980	2.425920	-2.481812

C	6.967710	-1.132360	-0.988350
H	7.523909	-0.371737	-1.541554
H	7.242004	-1.043974	0.068714
H	7.292581	-2.118192	-1.331471
O	-2.129148	-0.194658	-1.261257
S	-2.506686	-0.800641	0.041648
C	-4.254422	-1.108110	-0.023326
C	-4.718922	-2.346741	-0.451622
C	-5.136976	-0.084840	0.313484
C	-6.091371	-2.558535	-0.544031
H	-4.011245	-3.130409	-0.701245
C	-6.503904	-0.313078	0.214264
H	-4.750880	0.870949	0.652835
C	-6.999836	-1.549805	-0.213701
H	-6.463526	-3.523419	-0.877329
H	-7.200498	0.479585	0.473850
O	-2.268862	0.099814	1.199808
O	-1.842117	-2.114272	0.271065
C	2.705323	-1.301244	2.751798
C	3.278037	-2.718199	2.684165
H	2.487812	-3.452709	2.876298
H	3.689439	-2.906050	1.686866
H	4.075838	-2.862746	3.421356
C	2.226199	-1.001405	4.178143
H	3.046907	-1.028026	4.903592
H	1.768343	-0.005388	4.213902
H	1.475111	-1.739606	4.486059
C	3.792512	-0.292804	2.352081
H	4.068972	-0.440696	1.302165
H	3.433294	0.735810	2.467437
H	4.687328	-0.414730	2.972604
O	1.614374	-1.218811	1.860206
C	-8.485431	-1.791100	-0.288636
H	-8.893508	-2.006519	0.705006
H	-9.008893	-0.911842	-0.674205
H	-8.717223	-2.640963	-0.935258
Na	-0.583235	-1.304735	2.063655
C	0.050251	4.624697	2.353730
H	0.693654	4.438972	3.216564
H	0.354034	5.560258	1.878685
H	-0.975903	4.766877	2.699717
H	1.250509	2.315631	2.816981
N	-1.137710	4.572041	-0.442022
O	-1.278539	4.626924	-1.652254
O	-1.580497	5.401171	0.333545

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm
==========

SCF Energy= -2125.77953451 Predicted Change= -3.806348D-10
Zero-point correction (ZPE)= -2125.2250 0.55449
Internal Energy (U)= -2125.1838 0.59566
Enthalpy (H)= -2125.1829 0.59661
Gibbs Free Energy (G)= -2125.3038 0.47573

Frequencies -- -878.4795 16.5659 20.8197

Supporting Information: 1n-Major-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016
==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current
SCRF=(PCM,SOLVENT=Toluene) opt=(maxcycle=250,ts,calcfc,noeigentest)
freq=noraman
#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq
---

Pointgroup= C1 Stoichiometry= C27H30F4INaO4S C1[X(C27H30F4INaO4S)] #Atoms= 68
Charge = 0 Multiplicity = 1

SCF Energy= -2318.20511728 Predicted Change= -3.985231D-09
==========

Optimization completed on the basis of negligible forces. {Found 2 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00000	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.00973	0.00180	[NO]	0.00973	0.00180	[YES]

Atomic Type	Coordinates (Angstroms) X	Y	Z
C	-0.077479	3.087856	-2.056496
C	-0.245373	2.146230	-3.067046
C	-0.008640	0.811399	-2.781687
C	0.433832	0.503726	-1.496341
C	0.636720	1.390728	-0.465470
C	0.333490	2.726283	-0.777578
H	-0.578271	2.473543	-4.044868
H	-0.169023	0.049593	-3.537634
H	1.069704	0.973926	0.728244
I	0.557364	-1.576458	-1.047049
C	2.629280	-1.772528	-0.698810
C	3.565204	-1.330355	-1.640885

C	2.984678	-2.386155	0.511512
C	4.914213	-1.490460	-1.315050
C	4.348160	-2.534770	0.767071
C	5.323496	-2.080907	-0.121118
H	5.662830	-1.147095	-2.024868
H	4.652851	-3.010881	1.696269
C	1.967878	-2.855498	1.521023
H	1.367798	-2.000475	1.856867
H	1.299210	-3.619269	1.107967
H	2.470520	-3.290693	2.387546
C	3.189141	-0.691163	-2.950970
H	2.395917	-1.248987	-3.460940
H	2.829870	0.332423	-2.802650
H	4.055510	-0.652207	-3.614211
C	6.785682	-2.208638	0.216101
H	7.402345	-2.219287	-0.685941
H	7.109849	-1.362457	0.831695
H	6.982706	-3.122671	0.782302
O	-2.185928	-1.053133	-1.165614
S	-2.621762	-0.474166	0.131851
C	-4.361682	-0.809547	0.276077
C	-4.793501	-1.919471	0.991533
C	-5.270451	0.032203	-0.362874
C	-6.158065	-2.190652	1.062997
H	-4.067567	-2.551496	1.492228
C	-6.626836	-0.253058	-0.282634
H	-4.912200	0.902407	-0.903586
C	-7.089734	-1.367410	0.428386
H	-6.504015	-3.054087	1.624414
H	-7.343015	0.400188	-0.774374
O	-2.465139	1.000828	0.204972
O	-1.958491	-1.123568	1.295253
C	2.445663	0.879543	2.543277
C	2.964244	-0.240523	3.453877
H	2.154928	-0.600843	4.099034
H	3.334479	-1.079326	2.858609
H	3.784784	0.113289	4.088874
C	2.137101	2.103036	3.419811
H	3.023360	2.437792	3.971174
H	1.779678	2.934710	2.809710
H	1.360381	1.846983	4.151808
C	3.534708	1.243005	1.522083
H	3.734886	0.384629	0.869296
H	3.209393	2.083712	0.900463
H	4.469441	1.527265	2.019147
O	1.286221	0.441693	1.877009

C	-8.566541	-1.658699	0.502232
H	-8.767671	-2.538969	1.117264
H	-9.111920	-0.811884	0.930750
H	-8.978705	-1.840366	-0.495634
Na	-0.873612	0.843851	1.964631
F	-0.329351	4.364198	-2.363700
C	0.404438	3.723921	0.342901
F	-0.168962	3.211115	1.464007
F	-0.226412	4.871023	0.093624
F	1.667897	4.028322	0.678247

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -2318.20511728 Predicted Change= -3.985231D-09
Zero-point correction (ZPE)= -2317.6840 0.52104
Internal Energy (U)= -2317.6429 0.56217
Enthalpy (H)= -2317.6420 0.56311
Gibbs Free Energy (G)= -2317.7621 0.44301

Frequencies -- -1082.4189 16.7600 21.1806

Supporting Information: 1n-Minor-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current
SCRF=(PCM,SOLVENT=Toluene) opt=(maxcycle=250,ts,calcfc,noeigentest)
freq=noraman
#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq

---

Pointgroup= C1 Stoichiometry= C27H30F4INaO4S C1[X(C27H30F4INaO4S)] #Atoms= 68
Charge = 0 Multiplicity = 1

SCF Energy= -2318.20000688 Predicted Change= -2.322433D-10

==========

Optimization completed. {Found 2 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00000	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.00092	0.00180	[YES]	0.00092	0.00180	[YES]

Atomic Type	Coordinates (Angstroms) X	Y	Z
C	0.125875	3.223640	1.453628

C	-0.451834	3.278371	0.183206
C	-0.293263	2.197420	-0.673220
C	0.442204	1.129836	-0.174312
C	1.017461	1.004463	1.064865
C	0.841551	2.125230	1.895316
H	-0.739138	2.206212	-1.661531
H	1.520346	-0.236996	1.485336
I	0.689781	-0.535545	-1.522199
C	2.795989	-0.659079	-1.393275
C	3.590928	0.471642	-1.615722
C	3.327246	-1.922121	-1.086697
C	4.973918	0.308630	-1.488550
C	4.715220	-2.020843	-0.994097
C	5.551845	-0.918632	-1.175398
H	5.612816	1.173640	-1.649293
H	5.152296	-2.989929	-0.764074
C	2.473083	-3.139893	-0.845651
H	1.834864	-2.965413	0.027898
H	1.840249	-3.380328	-1.707111
H	3.105000	-4.008647	-0.647469
C	3.044412	1.831040	-1.965183
H	2.223858	1.769509	-2.687489
H	2.662578	2.340964	-1.074418
H	3.831590	2.451037	-2.398925
C	7.042684	-1.053598	-1.010582
H	7.315424	-0.994686	0.048909
H	7.397186	-2.016140	-1.388779
H	7.574737	-0.257072	-1.536288
O	-2.084916	-0.357075	-1.252399
S	-2.448643	-1.001992	0.035876
C	-4.185873	-1.361924	-0.042483
C	-4.610616	-2.555924	-0.617653
C	-5.099810	-0.425396	0.430148
C	-5.973921	-2.808800	-0.719920
H	-3.878499	-3.274986	-0.970622
C	-6.459907	-0.694301	0.319388
H	-4.743391	0.494932	0.881131
C	-6.915222	-1.885425	-0.253898
H	-6.315094	-3.738472	-1.167245
H	-7.181275	0.031549	0.684746
O	-2.242047	-0.123942	1.216399
O	-1.744851	-2.300410	0.234383
C	2.778528	-1.463886	2.717042
C	3.384768	-2.864458	2.609668
H	2.609322	-3.622719	2.766625
H	3.812559	-3.009263	1.612040

H	4.176620	-3.015742	3.351914
C	2.275131	-1.223110	4.146267
H	3.086245	-1.258099	4.882053
H	1.796478	-0.238251	4.210145
H	1.535406	-1.986679	4.418071
C	3.846943	-0.418248	2.365252
H	4.136633	-0.522781	1.313704
H	3.464139	0.597632	2.512977
H	4.738119	-0.542181	2.990556
O	1.696778	-1.376164	1.815121
C	-8.390087	-2.182520	-0.339586
H	-8.733847	-2.698262	0.563937
H	-8.974044	-1.263686	-0.437297
H	-8.615209	-2.826985	-1.193308
Na	-0.498462	-1.496356	2.034962
H	1.246931	2.152267	2.904887
C	-1.222380	4.499137	-0.219243
F	-2.275404	4.709357	0.581111
F	-0.462709	5.603430	-0.161743
F	-1.683590	4.396754	-1.473670
F	-0.038174	4.283622	2.256860

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -2318.20000688 Predicted Change= -2.322433D-10
Zero-point correction (ZPE)= -2317.6799 0.52003
Internal Energy (U)= -2317.6382 0.56176
Enthalpy (H)= -2317.6373 0.56270
Gibbs Free Energy (G)= -2317.7606 0.43937

Frequencies -- -865.8441 13.5393 19.7077

Supporting Information: 1o-Major-TS.log

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current
SCRF=(PCM,SOLVENT=Toluene) opt=(gdiis,maxcycle=250,ts,calcfc,noeigentest)
freq=noraman
#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq

---

Pointgroup= C1 Stoichiometry= C28H33F3INaO5S C1[X(C28H33F3INaO5S)] #Atoms= 72
Charge = 0 Multiplicity = 1

SCF Energy= -2333.47727500 Predicted Change= -3.763946D-08

Optimization completed on the basis of negligible forces. {Found 2 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00000	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.01948	0.00180	[NO]	0.01948	0.00180	[NO]

Atomic Type	Coordinates (Angstroms) X	Y	Z
C	0.184126	3.369135	-1.433671
C	0.080359	2.602818	-2.602737
C	0.211484	1.222575	-2.534866
C	0.506279	0.662333	-1.298816
C	0.617898	1.344558	-0.106038
C	0.395459	2.721763	-0.201003
H	-0.117187	3.069590	-3.558971
H	0.095333	0.621481	-3.431395
H	1.016006	0.708845	1.017470
I	0.535194	-1.465379	-1.226998
C	2.594469	-1.820753	-0.919621
C	3.557473	-1.283394	-1.781773
C	2.914973	-2.629048	0.181435
C	4.895777	-1.554009	-1.485929
C	4.268658	-2.877291	0.411175
C	5.269910	-2.338172	-0.396859
H	5.663864	-1.140288	-2.134945
H	4.544925	-3.503529	1.256457
C	1.872137	-3.202545	1.107365
H	1.304299	-2.385730	1.570237
H	1.175144	-3.864390	0.581057
H	2.350357	-3.786024	1.897270
C	3.221237	-0.432784	-2.977480
H	2.408687	-0.869625	-3.568509
H	2.905016	0.570200	-2.672958
H	4.094153	-0.330858	-3.625378
C	6.722376	-2.584480	-0.083729
H	7.346663	-2.464088	-0.972456
H	7.075703	-1.873570	0.671097
H	6.875997	-3.590929	0.314431
O	-2.196137	-0.873299	-1.277920
S	-2.652778	-0.549930	0.098342
C	-4.381911	-0.961588	0.165318
C	-5.333699	0.032493	-0.030400
C	-4.759657	-2.285903	0.373617
C	-6.683012	-0.310137	-0.020200

H	-5.013779	1.058090	-0.181813
C	-6.110314	-2.611350	0.380707
H	-4.000570	-3.044519	0.535840
C	-7.089499	-1.630642	0.185068
H	-7.433150	0.461233	-0.171938
H	-6.413726	-3.642237	0.543178
O	-2.543397	0.888033	0.445599
O	-1.974928	-1.387429	1.126838
C	2.442025	0.318983	2.723991
C	2.974864	-0.941627	3.416189
H	2.184962	-1.391354	4.028602
H	3.301643	-1.676499	2.675761
H	3.828404	-0.708630	4.063342
C	2.190915	1.387405	3.799200
H	3.096553	1.587771	4.383310
H	1.863310	2.324863	3.345845
H	1.410979	1.041330	4.489045
C	3.495328	0.837059	1.732425
H	3.652886	0.099480	0.935825
H	3.159825	1.775268	1.276152
H	4.454239	1.023273	2.229667
O	1.251988	0.004010	2.042335
C	-8.551898	-1.992628	0.225997
H	-8.907039	-2.055025	1.260581
H	-9.160075	-1.245039	-0.289336
H	-8.731690	-2.964710	-0.241483
Na	-0.908367	0.416949	2.144407
O	0.097899	4.714122	-1.428007
C	-0.170442	5.377071	-2.650158
H	-0.217049	6.437570	-2.407694
H	0.629651	5.202362	-3.377709
H	-1.128543	5.053919	-3.070671
C	0.365460	3.504589	1.083710
F	-0.452410	4.558779	1.066122
F	1.578725	3.949015	1.455229
F	-0.074387	2.722115	2.106511

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -2333.47727500 Predicted Change= -3.763946D-08
Zero-point correction (ZPE)= -2332.9149 0.56231
Internal Energy (U)= -2332.8719 0.60529
Enthalpy (H)= -2332.8710 0.60623
Gibbs Free Energy (G)= -2332.9959 0.48136

Frequencies -- -1066.4121 12.6886 17.3608

Supporting Information: **1o-Minor-TS.log**

Using Gaussian 16: ES64L-G16RevA.03 25-Dec-2016

==========

#M062X/gen pseudo=read scf=(maxcycle=300,direct,tight) density=current SCRF=(PCM,SOLVENT=Toluene) opt=(maxcycle=250,ts,calcfc,noeigentest) freq=noraman

#N Geom=AllCheck Guess=TCheck SCRF=Check GenChk RM062X/ChkBas Freq

---

Pointgroup= C1 Stoichiometry= C28H33F3INaO5S C1[X(C28H33F3INaO5S)] #Atoms= 72

Charge = 0 Multiplicity = 1

SCF Energy= -2333.46785507 Predicted Change= -7.295473D-10

==========

Optimization completed on the basis of negligible forces. {Found 2 times}

Item	Max Val.	Criteria	Pass?	RMS Val.	Criteria	Pass?
Force	0.00000	0.00045	[YES]	0.00000	0.00030	[YES]
Displ	0.00197	0.00180	[NO]	0.00197	0.00180	[YES]

Atomic Type	Coordinates (Angstroms) X	Y	Z
C	0.250066	3.336982	0.447282
C	-0.334087	3.082335	-0.802372
C	-0.255432	1.808352	-1.353465
C	0.413119	0.865671	-0.583055
C	0.989157	1.006309	0.646575
C	0.881131	2.316493	1.152273
H	-0.723470	1.591515	-2.307572
H	1.420860	-0.126763	1.385611
I	0.553009	-1.116120	-1.481751
C	2.644967	-1.337902	-1.278073
C	3.515779	-0.353895	-1.761760
C	3.089886	-2.514840	-0.655012
C	4.884546	-0.570937	-1.576142
C	4.468230	-2.679184	-0.518756
C	5.378022	-1.716500	-0.957551
H	5.580691	0.182321	-1.937160
H	4.838293	-3.585847	-0.045396
C	2.155947	-3.572457	-0.126121
H	1.536359	-3.141453	0.668233
H	1.502236	-3.977435	-0.906384
H	2.727977	-4.404228	0.291370

C	3.062233	0.908226	-2.447441
H	2.251916	0.718215	-3.159027
H	2.697113	1.639948	-1.719002
H	3.894428	1.357776	-2.992984
C	6.856411	-1.904541	-0.740533
H	7.441038	-1.310770	-1.447342
H	7.135685	-1.589661	0.271030
H	7.142228	-2.954133	-0.849378
O	-2.209399	-0.703337	-1.322168
S	-2.609163	-0.963007	0.085234
C	-4.369034	-1.204171	0.083910
C	-4.889582	-2.490373	-0.005819
C	-5.204148	-0.090742	0.132773
C	-6.270427	-2.658875	-0.049186
H	-4.218163	-3.342248	-0.032960
C	-6.580371	-0.277135	0.086832
H	-4.774636	0.902795	0.212387
C	-7.132158	-1.559928	-0.003132
H	-6.686372	-3.660347	-0.118015
H	-7.240059	0.585646	0.123791
O	-2.332894	0.177601	0.995555
O	-1.998936	-2.209898	0.626993
C	2.609147	-1.053680	2.898376
C	3.122999	-2.469981	3.162769
H	2.302690	-3.108923	3.508509
H	3.528221	-2.896977	2.239279
H	3.912529	-2.473626	3.922682
C	2.134970	-0.417510	4.211332
H	2.950405	-0.309271	4.935111
H	1.718560	0.577513	4.012625
H	1.352772	-1.035962	4.668825
C	3.737708	-0.205804	2.294341
H	4.013989	-0.602456	1.311295
H	3.418664	0.834050	2.163880
H	4.622915	-0.214760	2.940048
O	1.527207	-1.136466	1.995085
C	-8.627103	-1.749345	-0.018691
H	-9.121075	-0.948968	-0.576243
H	-8.901237	-2.705189	-0.472070
H	-9.029432	-1.736892	1.000325
Na	-0.679003	-1.037067	2.159265
H	1.299757	2.550160	2.129172
O	-0.990420	4.090536	-1.451634
C	-0.292180	4.602373	-2.581022
H	-0.916054	5.393503	-2.996700
H	0.675070	5.014839	-2.276187

H	-0.138607	3.823484	-3.336377
C	0.151531	4.728039	1.004081
F	0.684471	5.638369	0.167761
F	0.806543	4.843725	2.170227
F	-1.115629	5.097352	1.226527

Statistical Thermodynamic Analysis
Temperature= 298.150 Kelvin Pressure= 1.00000 Atm

==========

SCF Energy= -2333.46785507 Predicted Change= -7.295473D-10
Zero-point correction (ZPE)= -2332.9068 0.56098
Internal Energy (U)= -2332.8633 0.60454
Enthalpy (H)= -2332.8623 0.60549
Gibbs Free Energy (G)= -2332.9889 0.47887

Frequencies -- -827.2436 14.2730 17.7667

Supplementary Information – Experimental Details

Iodane-Guided C-H Cleavage to Synthesize Densely Functionalized Arenes

Aleksandra Nilova, Paul A. Sibbald, Edward Valente, Gisela A. González-Montiel, H. Camille Richardson, Kevin S. Brown, Paul Ha-Yeon Cheong,* and David R. Stuart*

Table of Contents

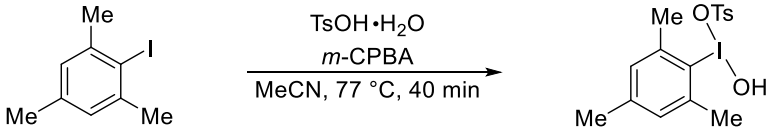
General considerations

Commercially available reagents and solvents were used without further purification. *m*-CPBA was assayed by iodometric titration and determined to contain 72-74% active oxidant. Compounds **1d** and **1j** were prepared according to a literature procedure.[1] *N*-chloroamines **S2** and **S3** were prepared according to a literature procedure[2] using sodium hypochlorite solution (10-15% available chlorine) and the spectral data were consistent with those previously reported.[2,3] All other materials were prepared as described in detail below.

Crude reaction mixtures were analyzed by ^{1}H NMR spectroscopy, GC/MS, and/or thin-layer chromatography (TLC) on silica gel plates (60 Å F-254) or basic alumina plates (F-254) and visualized by UV irradiation or iodine stain. Crude material was purified by flash column chromatography on silica gel unless otherwise stated. ^{1}H, ^{13}C {^{1}H}, ^{19}F {^{1}H} NMR spectra were obtained at 298 K in $CDCl_3$, DMSO-d_6, or $(CD_3)_2CO$ on 400 MHz spectrometer and referenced to residual solvent peaks[4] or tetramethylsilane when applicable. The following notation is used: s – singlet, d – doublet, dd – doublet of doublets, ddd – doublet of doublet of doublets, t – triplet, q – quartet, n – nonet, br – broad signal. High resolution mass spectrometry (HRMS) data were obtained by electron spray ionization (ESI) with an ion trap mass analyzer or electron impact. Infrared spectra were recorded on ATR/FT-IR spectrometer. Melting points (°C) are uncorrected.

Synthesis and characterization of iodonium salts

Preparation of hydroxy(tosyloxy)iodomesitylene S1



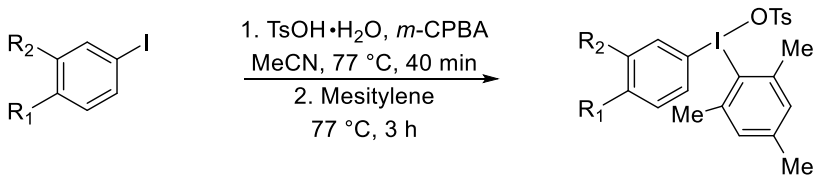
Mesityl iodide (0.7383 g, 3 mmol), acetonitrile (3 mL), and toluenesulfonic acid monohydrate (0.6515 g, 3.03 mmol, 1.01 equiv.) were added to a round bottom flask equipped with a magnetic stir bar. M-CPBA (0.7065 g, 3.03 mmol, 1.01equiv.) was added in one portion at room temperature and the flask was placed into an oil bath set to 77 °C. After 40 min reaction was removed from heat, the contents were allowed to reach ambient room temperature, and the crude residue was triturated with diethyl ether. The precipitate was isolated by vacuum filtration and washed by slurry filtration with diethyl ether to provide analytically pure product in 85% yield (1.1110 g, 2.6 mmol) as white powder. Spectral data are consistent with those previously reported.[5,6]

^{1}H NMR (CD_3OD, 400 MHz) δ 7.61 (d, *J* = 7.9 Hz, 2H), 7.28 (s, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 2.72 (s, 6H), 2.41 (s, 3H), 2.36 (s, 3H).

^{13}C NMR (CD_3OD, 101 MHz) δ 147.4, 144.2, 142.9, 141.9, 130.6, 129.8, 126.9, 26.7, 21.3(4), 21.3(0).

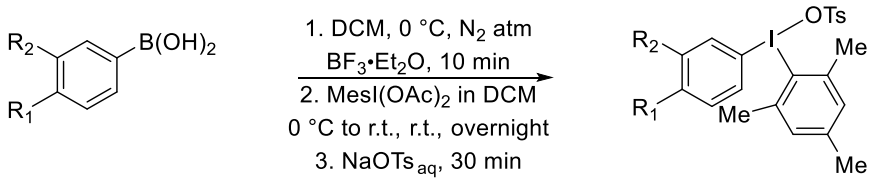
Preparation of aryl(mesityl)iodonium tosylates.

General procedure A[7]



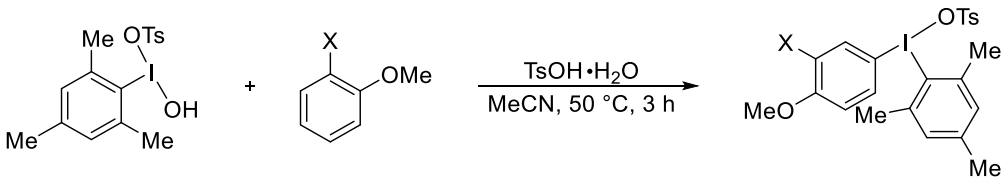
Aryl iodide (1.0 equiv.) and acetonitrile (1 mL/mmol) were added to a round bottom flask, equipped with a magnetic stir bar. Toluenesulfonic acid monohydrate (1.01 equiv.) was added in one portion, followed by one portion of m-CPBA (1.01 equiv.). The flask was lowered into an oil bath set to 77 °C and stirred vigorously. After 30 min 1,3,5-trimethylbenzene (1.01 equiv.) was added in one portion and stirring was continued at 77 °C for 3 hours. The reaction was removed from heat and concentrated under reduced pressure. The resulting crude residue was triturated with diethyl ether. The precipitate was isolated by vacuum filtration and washed by slurry filtration with diethyl ether to give analytically pure aryl(mesityl)iodonium tosylate.

General procedure B[8]



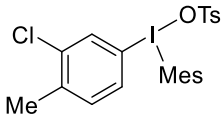
Arylboronic acid (5.0 mmol, 1.0 equiv.) was weighed and transferred to a round bottom flask equipped with a magnetic stir bar. The flask was sealed with a rubber septum, flushed with nitrogen, and left under a static nitrogen atmosphere. DCM (30 mL) was added via syringe to the aryl boronic acid and the solution was cooled to 0 °C in an ice-water bath with stirring. $BF_3 \cdot OEt_2$ (1.1 mL, 9.0 mmol, 3.0 equiv.) was added via syringe to the aryl boronic acid solution and the reaction mixture was stirred for 10 min at 0 °C. Mesitylene iododiacetate (1.20 g, 3.3 mmol, 1.1 equiv.) was weighed and transferred to a separate pear-shaped flask. The flask was sealed with a rubber septum, flushed with nitrogen, and left under a static nitrogen atmosphere. DCM (9 mL) was added to the mesitylene iododiacetate via syringe. The mesitylene iododiacetate solution was added to the aryl boronic acid/$BF_3 \cdot OEt_2$ solution dropwise via syringe at 0 °C. The reaction mixture was allowed to warm to ambient room temperature and stirred overnight. The septum was removed, and an aqueous solution of NaOTs (60 mmol, 20 equiv. in 30 mL of water) was added with vigorous stirring for ~30 min. The biphasic mixture was added to a separatory funnel, and the DCM/water layers were separated. The water layer was extracted with DCM (3 × 30 mL). The combined DCM layers were dried over $MgSO_4$, filtered, and solvent was removed under reduced pressure. The resulting crude residue was triturated with diethyl ether. The precipitate was isolated by vacuum filtration and washed by slurry filtration with diethyl ether to give analytically pure aryl(mesityl)iodonium tosylate. See below for the specific scale of reactions and characterization data of individual compounds.

General procedure C



Hydroxy(tosyloxy)iodomesitylene (0.4343 g, 1mmol), acetonitrile (1 mL), 2-haloanisole (1.01 equiv.), and toluenesulfonic acid monohydrate (0.1902 g., 1 equiv.) were added to a round bottom flask equipped with a magnetic stir bar. The flask was placed into an oil bath set to 50 °C and the mixture was stirred at this temperature for 3 hours. The flask was removed from heat and brought to room temperature. The crude mixture was triturated with diethyl ether. The precipitate was isolated by vacuum filtration and washed by slurry filtration with diethyl ether to give analytically pure aryl(mesityl)iodonium tosylate.

Compound 1a



Prepared according to the general procedure A on 15.0 mmol scale of 2-chloro-4-iodotoluene and obtained in 63% yield (5.1193 g, 9.1 mmol) as white powder.

^{1}H NMR (DMSO-*d*$_6$, 400 MHz) δ 8.13 (s, 1H), δ 7.78 (d, *J* = 8.2 Hz, 1H), δ 7.47-7.45 (m, 3H), δ 7.22 (s, 2H), δ 7.11 (d, *J* = 7.6, 2H), δ 2.60 (s, 6H), δ 2.36 (s, 3H), 2.30-2.29 (m, 6H).

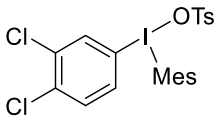
^{13}C NMR (DMSO-*d*$_6$, 101 MHz) δ 145.7, 143.2, 141.6, 140.1, 137.6, 135.3, 134.0, 133.9, 133.0, 129.8, 128.0, 125.5, 122.8, 111.2, 26.3, 20.8, 20.5, 19.5.

FT-IR: 2976, 1574, 1466, 1218, 1150, 1005, 810.

HRMS: Calculated for $C_{16}H_{17}ClI^+$ $[M - OTs]^+$: 371.0058; Found 371.0057.

Melting point: 187 – 189 °C.

Compound 1b



Prepared according to the general procedure B on 5.0 mmol scale of 3,4-dichlorophenyl boronic acid and obtained in 84% yield (2.3628 g, 4.2 mmol) as white powder.

^{1}H NMR (DMSO-*d*$_6$, 400 MHz) δ 8.36 (s, 1H), 7.84 (d, *J* = 8.6 Hz, 1H), 7.75 (d, *J* = 8.6 Hz, 1H), 7.46 (d, *J* = 7.3 Hz, 2H), 7.24 (s, 2H), 7.11 (d, *J* = 7.6 Hz, 2H), 2.60 (s, 6H), 2.31 (s, 3H), 2.29 (s, 3H).

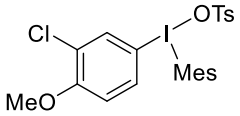
^{13}C NMR (DMSO-*d*$_6$, 101 MHz) δ.145.5, 143.4, 141.8, 137.7, 135.6, 135.3, 134.3, 133.4, 133.3, 129.9, 128.1, 125.5, 122.9, 112.5, 26.3, 20.8, 20.5.

FT-IR: 2982, 1449, 1215, 1170, 1008, 865.

HRMS: Calculated for $C_{15}H_{14}Cl_2I^+$ $[M - OTs]^+$: 390.9512; found 390.9531.

Melting point: 192 – 193 °C.

Compound 1c

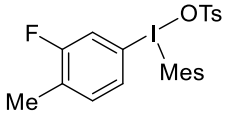


Prepared according to the general procedure A with the following modification: the reaction was conducted on 5.0 mmol scale of mesityl iodide. After 30 min 2-chloroanisole was added in one portion. After standard workup the resulting solid was recrystallized from MeOH/MeCN mixture to provide the product in 45% yield (1.1618 g, 2.3 mmol) as off-white to light brown powder. Spectral data are consistent with those previously reported.[1]

^{1}H NMR (DMSO-*d*$_6$, 400 MHz) δ 8.16 (d, *J* = 2.2Hz, 1H), 7.89 (dd, *J* = 8.9, 2.2 Hz, 1H), 7.45 (d, *J* = 8.0Hz, 2H), 7.23-7.20 (m, 3H), 7.10 (d, *J* = 7.9Hz, 2H), 3.88 (s, 3H), 2.60 (s, 6H), 2.29-2.28 (m, 6H).

^{13}C NMR (DMSO-*d*$_6$, 101 MHz) δ 157.2, 145.7, 143.0, 141.5, 137.6, 135.3, 129.7, 128.0, 125.5, 123.3, 123.1, 115.7, 102.9, 56.7, 26.3, 20.8, 20.5.

Compound 1f



Prepared according to the general procedure A on 5.0 mmol scale of methyl 2-fluoro-4-iodotoluene and obtained in 60% yield (1.5868 g, 3.0 mmol) as white powder.

^{1}H NMR (DMSO-*d*$_6$, 400 MHz) δ 7.93 (m, 1H), 7.68 (m, 1H), 7.48-7.41 (m, 3H), 7.22 (s, 2H), 7.11 (d, *J* = 7.9, 2H), 2.60 (s, 6H), 2.29 (s, 3H), 2.28 (s, 3H), 2.26 (s, 3H).

^{13}C NMR (DMSO-*d*$_6$, 101 MHz) δ 160.6 (d, $J_{C\text{-}F}$ = 251.2), 145.7, 143.1, 141.6, 137.6, 134.5 (d, $J_{C\text{-}F}$ = 4.9), 130.5 (d, $J_{C\text{-}F}$ = 3.7), 129.8, 129.2 (d, $J_{C\text{-}F}$ = 16.9), 128.0, 125.5, 122.9, 121.2 (d, $J_{C\text{-}F}$ = 25.7), 110.5 (d, $J_{C\text{-}F}$ = 8.1), 26.3, 20.8, 20.5, 14.1 (d, $J_{C\text{-}F}$ = 3.0).

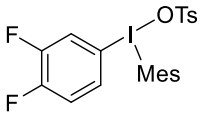
^{19}F{^{1}H} NMR (DMSO-*d*$_6$, 376 MHz) δ -111.6.

FT-IR: 3092, 2921, 1573, 1481, 1212, 1165, 1118, 852.

HRMS: Calculated for $C_{16}H_{17}FI^+$ $[M - OTs]^+$: 355.0356; found 355.0371.

Melting point: 172 – 173 °C.

Compound 1g



Prepared according to the general procedure B on 5.0 mmol scale of 3,4-difluorophenyl boronic acid and obtained in 86% yield (2.2788 g, 4.3 mmol) as white powder.

^{1}H NMR (DMSO-*d*$_6$, 400 MHz) δ 8.26 (m, 1H), 7.82 (m, 1H), 7.61 (m, 1H), 7.46 (d, *J* = 7.2 Hz, 2H),7.23 (s, 2H), 7.11 (d, *J* = 7.5, 2H), 2.61 (s, 6H), 2.31 (s, 3H), 2.29 (s, 3H).

^{13}C NMR (DMSO-*d*$_6$, 101 MHz) δ 151.7 (dd, J_{C-F} = 251.2, 10.5), 150.0 (dd, J_{C-F} = 253.6, 12.6), 145.5, 143.3, 141.7, 137.7, 132.3 (dd, J_{C-F} = 7.2, 4.0), 129.8, 128.1, 125.5, 124.3 (d, J_{C-F} = 20.1), 123.2, 120.8 (d, J_{C-F} = 18.3), 107.7 (dd, J_{C-F} = 5.7, 4.0), 26.3, 20.8, 20.5.

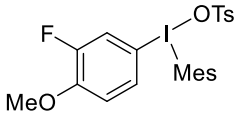
^{19}F{^{1}H} NMR (DMSO-*d*$_6$, 376 MHz) δ -132.19 (d, *J* = 21.8), -132.75 (d, *J* = 21.7).

FT-IR: 2979, 1496, 1272, 1162, 1116, 1030, 812.

HRMS: Calculated for $C_{15}H_{14}F_2I^+$ $[M - OTs]^+$: 359.0103; found 359.0121.

Melting point: 192 – 193 °C.

Compound 1h



Prepared according to the general procedure C on 1.0 mmol scale using 2-fluoroanisole (0.113 mL, 1.01 equiv.) and obtained in 74 %yield (0.4037 g, 0.7 mmol) as white powder.

^{1}H NMR (DMSO-*d*$_6$ with 1% v/v TMS, 400 MHz) δ 8.01 (dd, *J* = 10.2, 2.1, 1H), 7.77-7.76 (m, 1H), 7.46 (d, *J* = 8.0, 2H), 7.27 (dd, appears as triplet, *J* = 8.8 Hz, 1H), 7.20 (s, 2H), 7.10 (d, *J* = 7.9, 2H), 3.87 (s, 3H), 2.60 (s, 6H), 2.29-2.28 (m, 6H).

^{13}C NMR (DMSO-*d*$_6$, 101 MHz) δ 151.56 (d, J_{C-F} = 261.8 Hz), 150.4, 145.4, 143.1, 141.5, 137.9, 132.3 (d, J_{C-F} = 3.7 Hz), 129.8, 128.2, 125.6, 123.3, 122.4 (d, J_{C-F} = 21.3 Hz), 116.6, 101.8 (d, J_{C-F} = 6.9 Hz), 56.5, 26.3, 20.8, 20.6.

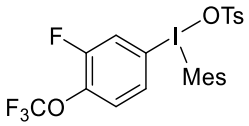
^{19}F{^{1}H} NMR (DMSO-*d*$_6$, 376 MHz) δ -130.2.

FT-IR: 2980, 2842, 1592, 1496, 1208, 1171, 1031, 1009, 815, 680.

HRMS: Calculated for $C_{16}H_{17}FIO^+$ $[M - OTs]^+$: 371.0303; found 371.0295.

Melting point: 179.7 – 180.8 °C.

Compound 1i



Prepared according to the general procedure B on 2.0 mmol scale of 3-fluoro-4-trifluoromethoxyphenyl boronic acid and obtained in 74% yield (0.8794 g, 1.5 mmol) as white powder.

^{1}H NMR (DMSO-*d*$_6$, 400 MHz) δ 8.29 (dd, *J* = 9.2, 2.0 Hz, 1H, 7.86-7.84 (m, 1H), 7.75-7.71 (m, 1H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.25 (s, 2H), 7.10 (d, *J* = 7.9 Hz, 2H), 2.60 (s, 3H), 2.31 (s, 3H), 2.28 (s, 2H).

^{13}C NMR (DMSO-*d*$_6$, 101 MHz) δ 153.7 (d, $J_{C\text{-}F}$ = 258.3 Hz), 145.4, 143.4, 141.8, 137.8-137.7 (m, two overlapping signals), 131.9 (d, $J_{C\text{-}F}$ = 4.1 Hz), 129.8, 128.0, 126.6, 125.4, 124.0 (d, $J_{C\text{-}F}$ = 21.9 Hz), 123.0, 119.8 (q, $J_{C\text{-}F}$ = 259.4 Hz), 112.3 (d, $J_{C\text{-}F}$ = 6.5 Hz), 26.3, 20.7, 20.5.

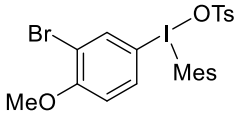
^{19}F{^{1}H} NMR (DMSO-*d*$_6$, 376 MHz) δ -57.8 (d, *J* = 5.2 Hz), -124.3 (q, *J* = 5.2 Hz).

FT-IR: 2981, 1491, 1255, 1164, 1118, 1008, 813.

HRMS: Calculated for $C_{16}H_{14}F_4IO^+$ $[M - OTs]^+$: 425.0020; found 425.0011.

Melting point: 186.3 – 186.7 °C.

Compound 1k



Prepared according to the literature procedure[9] overnight on 1.0 mmol scale of hydroxy(mesityl)iodonium tosylate and 2-bromoanisole and obtained in 52% yield (0.3126 g, 0.52 mmol) as off-white powder.

^{1}H NMR (DMSO-*d*$_6$, 400 MHz) δ 8.29 (d, *J* = 2.1, 1H), 7.93 (d, *J* = 8.9, 2.1, 1H), 7.47 (d, *J* = 8.0, 2H), 7.21-7.18 (m, 3H), 7.11 (d, *J* = 7.8, 2H), 3.89 (s, 3H), 2.61 (s, 6H), 2.30 (m, 6H).

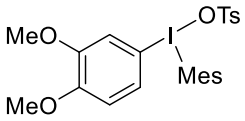
^{13}C NMR (DMSO-*d*$_6$, 101 MHz) δ 158.3, 145.3, 143.3, 141.7, 138.2(2), 138.1(8), 136.0, 130.0, 128.3, 125.7, 123.3, 115.7, 112.9, 103.5, 57.0, 26.4, 21.0, 20.7.

FT-IR: 2978, 2842, 1473, 1439, 1219, 1046, 1030, 814, 679.

HRMS: Calculated for $C_{16}H_{17}BrIO^+$ $[M - OTs]^+$: 430.9502; found 430.9495.

Melting point: 183.8 – 186.4 °C.

Compound 1l



Prepared according to the general procedure B on 3.0 mmol scale of 3,4-dimethoxybenzene boronic acid with the following modification: the reaction was performed with 0.4 mL (1.1 equiv.) of $BF_3 \cdot Et_2O$. and resulted in 65% yield (1.0866 g, 2.0 mmol) as light brown powder.

^{1}H NMR (DMSO-*d*$_6$, 400 MHz) δ 7.58 (d, *J* = 2.0 Hz, 1H), 7.47-7.45 (m, 3H), 7.19 (s, 3H), 7.10 (d, *J* = 7.9 Hz, 2H), 7.02 (d, *J* = 8.7 Hz, 1H), 3.77(5)-3.77(0) (m, 6H), 2.62 (s, 6H), 2.28 (s, 6H).

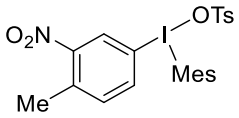
^{13}C NMR (DMSO-*d*$_6$, 101 MHz) δ 151.6, 150.1, 145.6, 142.8, 141.4, 137.6, 129.6, 128.0(3), 128.0(0), 125.5, 123.1, 117.7, 114.2, 102.8, 56.2, 55.8, 26.3, 20.8, 20.5.

FT-IR: 2982, 2920, 1502, 1143, 100, 794, 677.

HRMS: Calculated for $C_{17}H_{20}IO_2^+$ $[M - OTs]^+$: 383.0502; found 383.0493.

Melting point: 186.1 – 187.3°C.

Compound 1m

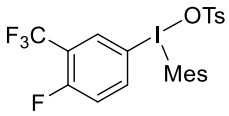


Prepared according to the general procedure A on 3.0 mmol scale of 4-iodo-2-nitrotoluene and obtained in 78% yield (1.2918 g, 2.3 mmol) as off-white powder. Spectral data are consistent with those previously reported.[1]

^{1}H NMR (DMSO-*d*$_6$, 400 MHz) δ 8.60 (d, *J* = 1.7 Hz, 1H), 8.05 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 2H), 7.22 (s, 2H), 7.10 (d, *J* = 7.9, 2H), 2.59 (s, 6H), 2.51 (c, 3H, overlapped with DMSO), 2.30 (s, 3H), 2.28 (s, 3H).

^{13}C NMR (DMSO-*d*$_6$, 101 MHz) δ 149.7, 145.5, 143.4, 141.7, 138.2, 137.7, 136.7, 135.7, 130.0, 129.9,128.1, 125.5, 123.0, 111.0, 26.4, 20.8, 20.6, 19.3.

Compound 1n



Prepared according to the general procedure A on 5.0 mmol scale of 1-fluoro-4-iodo-2-trifluoromethylbenzene and obtained in 67% yield (1.9621 g, 3.4 mmol) as white powder.

^{1}H NMR (DMSO-*d*$_6$, 400 MHz) δ 8.50-8.48 (m, 1H), 8.19-8.15 (m, 1H), 7.64 (dd, appears as triplet, *J*=9.8 Hz, 1H), 7.45 (d, *J*=8.1 Hz, 2H), 7.24 (s, 2H), 7.10 (d, *J*=7.9 Hz, 2H), 2.59 (s, 6H), 2.31 (s, 3H), 2.28 (s, 3H).

^{13}C NMR (DMSO-*d*$_6$, 101 MHz) δ 160.5 (d, J_{C-F} = 260.1 Hz), 145.4, 143.4, 141.8, 141.3 (d, J_{C-F} = 9.7 Hz), 137.8, 133.6 (d, J_{C-F} = 4.0 Hz), 129.9, 128.1, 125.5, 123.0, 121.3 (q, J_{C-F} = 261.0 Hz), 121.0 (d, J_{C-F} = 21.8 Hz), 119.1 (dq, J_{C-F} = 33.3, 13.2 Hz), 108.8 (d, J_{C-F} = 3.6 Hz), 26.3, 20.8, 20.5.

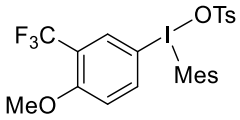
^{19}F{^{1}H} NMR (DMSO-*d*$_6$, 376 MHz) δ -55.53 (d, *J* = 12.3 Hz), -105.51 (q, *J* = 12.5 Hz).

FT-IR: 3059, 1575, 1282, 1127, 1030, 1004, 812, 679.

HRMS: Calculated for $C_{16}H_{14}F_4I^+$ [M – OTs]$^+$: 409.0071; found 409.0072.

Melting point: 178 – 180 °C.

Compound 1o



Prepared according to the general procedure B on 2.0 mmol scale of 4-methoxy-3-trifluoromethylphenyl boronic acid and obtained in 98% yield (1.1618 g, 1.96 mmol) as white powder.

^{1}H NMR (DMSO-*d*$_6$, 400 MHz) δ 8.28 (d, *J* = 1.9 Hz, 1H), 8.11 (dd, *J* = 9.0, 2.1 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 9.0 Hz, 1H), 7.21 (s, 1H), 7.10 (d, *J* = 7.9, 2H), 3.92 (s, 3H), 2.60 (s, 6H), 2.30 (s, 3H), 2.28 (s, 3H).

^{13}C NMR (DMSO-*d*$_6$, 101 MHz) δ 159.4, 145.5, 143.2, 141.6, 140.7, 137.8, 133.1 (q, J_{C-F} = 5.2 Hz), 129.8, 128.1, 125.5, 123.2, 122.6 (q, J_{C-F} = 261.5 Hz), 119.2 (q, J_{C-F} = 31.5 Hz), 116.5, 102.8, 56.9, 26.3, 20.8, 20.5.

^{19}F{^{1}H} NMR (DMSO-*d*$_6$, 376 MHz) δ -61.44.

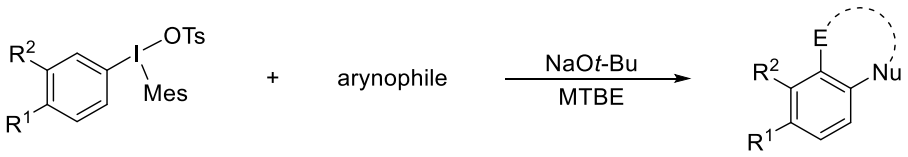
FT-IR: 2979, 1599, 1485, 1119, 1008, 829.

HRMS: Calculated for $C_{17}H_{17}F_3IO^+$ [M – OTs]$^+$: 421.0276; Found 421.0286.

Melting point: 215 – 216 °C.

Aryne coupling

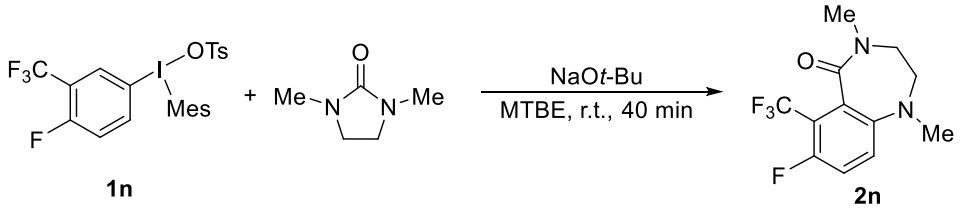
General procedure D



The iodonium salt (0.5 mmol, 1 equiv.) was weighed out and placed in a 12 mL vial containing a magnetic stir bar. MTBE (2.5 mL) and arynophile (1.1 – 3 equiv.) were added sequentially forming slurry. Ground to fine powder NaO*t*-Bu (0.0721g, 0.75 mmol, 1.5 equiv. or as indicated) was

weighed out in air and added to the vial with stirring in one portion. The vial was sealed with a cap, and the reaction mixture was vigorously stirred at the indicated temperature for the indicated period of time. The reaction was quenched with saline solution (7 mL) and extracted with EtOAc (3x3 mL). The combined organic phases were dried with $MgSO_4$, drying agent was removed by vacuum filtration, and solvent was removed on rotary evaporator. The crude residue was purified by column chromatography on silica gel with acetone/hexanes mixture as eluent.

Aryne coupling reaction on 5 mmol scale.



The iodonium salt **1n** (2.9019 g, 5 mmol) was weight out and placed in 100 mL round bottom flask containing a magnetic stir bar. MTBE (25 mL) and 1,2-dimethyl-2-imidazolidinone (DMI, 1.62 mL, 15 mmol, 3 equiv.) were added sequentially forming white slurry (Figure 1, A). Ground to fine powder NaO*t*-Bu (0.7208 g, 7.5 mmol, 1.5 equiv.) was weighed out in air and added to the round bottom flask with stirring in one portion with a powder funnel (Figure 1, B), and the reaction mixture turned yellow within 1 min (Figure 1, C). The contents were vigorously stirred for 40 min. at room temperature without further change in color. The reaction was quenched with saline solution and extracted with EtOAc (3x10 mL). The combined organic phases were dried with $MgSO_4$, drying agent was removed by vacuum filtration, and solvent was removed on rotary evaporator. The crude residue was purified by column chromatography on silica gel with acetone/hexanes mixture as eluent to provide the product in 62% yield (0.8570 g, 3.1 mmol) as white solid.

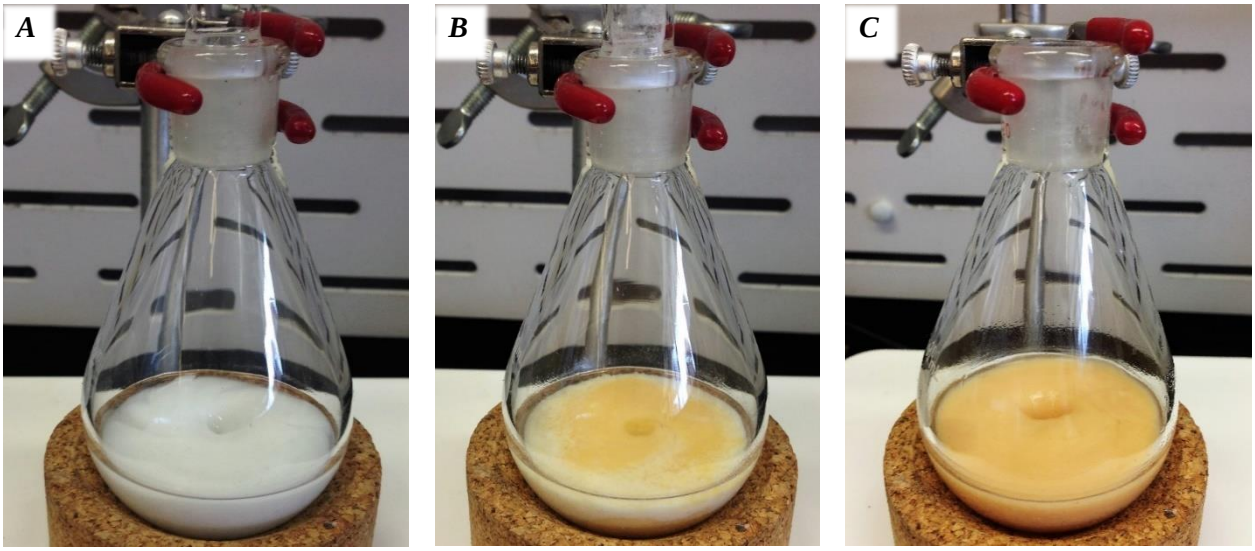
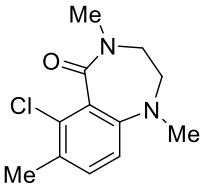


Figure 1. Aryne coupling reaction on 5 mmol scale: A. Slurry of iodonium salt in MTBE and DMI; B. Appearance of the reaction mixture after addition of NaO*t*-Bu; C. Appearance of the reaction mixture after 1 min at stirring.

Compound 2a



Prepared from **1a** and DMI (0.16 mL, 1.5 mmol, 3 equiv.) according to the general procedure A at room temperature for 15 min. and obtained in 55% yield (0.0666 g, 0.28 mmol) as a white solid.

R_f = 0.34 in 35% acetone/hexane.

^{1}H NMR ($CDCl_3$ with 1% v/v TMS, 400 MHz) δ 7.18 (d, *J*=8.1 Hz, 1H), 6.74 (d, *J*=8.1 Hz, 1H), 3.87-3.33 (br, 2H), 3.21 (s, 3H), 2.76 (s, 3H), 2.33 (s, 3H).

Note: two H's of ethelene group are not reported as they appear as broad signals between ~ 4-2 ppm, consistent with previous reports on related compounds.[10]

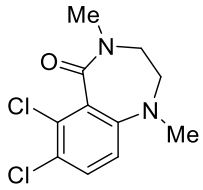
^{13}C NMR ($CDCl_3$ with 1% v/v TMS, 101 MHz) δ 167.7, 145.8, 132.4, 132.2, 131.0, 129.3, 116.0, 57.0, 47.9, 40.1, 33.3, 19.8.

FT-IR: 2944, 1647, 1596, 1482, 1446, 1425, 826.

HRMS (ESI$^+$): calculated for $C_{12}H_{16}ClN_2O^+$ $[M + H]^+$ 239.0948; found 239.0942.

Melting point: 110 – 111°C.

Compound 2b



Prepared from **1b** and DMI (0.16 mL, 1.5 mmol, 3 equiv.) according to the general procedure A at room temperature for 40 min. and obtained in 75% yield (0.0980 g, 0.38 mmol) as an off-white solid.

R_f = 0.22 in 30% acetone/hexane

^{1}H NMR ($(CD_3)_2CO$, 400 MHz) δ 7.51 (d, *J* = 8.8 Hz, 1H), 6.98 (d, *J* = 8.8 Hz, 1H), 3.50 (br, 2H), 3.14 (s, 3H), 2.80 (s, 3H).

Note: two H's of ethelene group are not reported as they appear as a broad signal between ~ 4-2 ppm, consistent with previous reports on related compounds.[10]

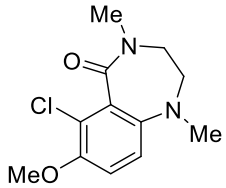
^{13}C NMR ($(CD_3)_2CO$, 101 MHz) δ 166.3, 147.8, 132.2, 132.1, 131.0, 126.5, 118.7, 57.6, 48.0, 40.3, 33.1.

FT-IR: 2942, 2812, 1642, 1579, 1450, 1405, 1255, 1172, 1060, 822, 731.

HRMS (ESI$^+$): calculated for $C_{11}H_{13}Cl_2N_2O^+$ $[M + H]^+$ 259.0399; found 259.0412.

Melting point: 90.6 – 91.6 °C.

Compound 2c



Prepared from **1c** and DMI (0.16 mL, 1.5 mmol, 3 equiv.) according to the general procedure A at room temperature for 40 min. The product was isolated by column chromatography with diethyl ether as eluent and obtained in 52% yield (0.0664 g, 0.26 mmol) as a yellow oil.

R_f = 0.08 in 100% ethyl ether.

^{1}H NMR ($CDCl_3$ with 1% v/v TMS, 400 MHz) δ 6.93 (d, *J* = 8.8 Hz, 1H), 6.80 (d, *J* = 8.8 Hz, 1H), 3.86 (s, 3H), 3.76-3.30 (br, 2H) 3.21 (s, 3H), 2.75 (s, 3H).

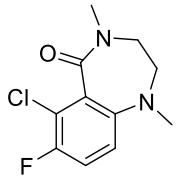
Note: two H's of ethelene group are not reported as they appear as broad signals between ~ 4-2 ppm, consistent with previous reports on related compounds.[10]

^{13}C NMR ($CDCl_3$ with 1% v/v TMS, 101 MHz) δ 167.0, 151.4, 141.0, 130.9, 121.3, 116.5, 113.8, 57.1, 56.7, 48.0, 40.2, 33.3.

FT-IR: 2937, 2843, 1645, 1456, 1433, 1269, 1048, 812, 686.

HRMS (ESI$^+$): calculated for $C_{12}H_{15}ClN_2NaO_2^+$ $[M + Na]^+$ 277.0714; found 277.0708.

Compound 2d



Prepared from **1d** and DMI (0.16 mL, 1.5 mmol, 3 equiv.) according to the general procedure A at room temperature for 25 min. and obtained in 63% yield (0.0761 g, 0.31 mmol) as an off-white solid.

R_f = 0.31 30% acetone/hexanes

^{1}H NMR (CDCl$_3$ with 1% v/v TMS, 400 MHz) δ 7.11 (dd, appears as triplet, *J* = 8.7 Hz, 1H), 6.79 (dd, *J* = 8.9, 4.2 Hz, 1H), 3.53-3.31 (br, 2H), 3.21 (s, 3H), 2.77 (s, 3H).

Note: : two H's of ethelene group are not reported as they appear as broad signals between ~ 4-2 ppm, consistent with previous reports on related compounds.[10]

^{13}C NMR (CDCl$_3$ with 1% v/v TMS, 101 MHz) δ 166.1 (d, $J_{C\text{-}F}$ = 2.6 Hz), 154.3 (d, $J_{C\text{-}F}$ = 243.5 Hz), 143.7 (d, $J_{C\text{-}F}$ = 2.7 Hz), 130.5, 119.9 (d, $J_{C\text{-}F}$ = 19.6 Hz), 117.6 (d, $J_{C\text{-}F}$ = 22.1 Hz), 117.0 (d, $J_{C\text{-}F}$ = 6.8 Hz), 57.1, 47.8, 40.2, 33.4.

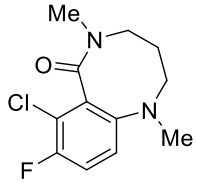
^{19}F{^{1}H} NMR (CDCl$_3$ with 1% v/v TMS, 376 MHz,) δ -121.9.

FT-IR: 2949, 2863, 1650, 1482, 1459,1428, 1258, 826, 759.

HRMS (ESI$^+$): calculated for $C_{11}H_{13}ClFN_2O^+$ $[M + H]^+$ 243.0695; found 243.0706.

Melting point: 113.4 – 113.7 °C

Compound 2e



Obtained in 37% yield (0.0473 g, 0.18 mmol) as an off-white solid from **1d** according to the general procedure A with the following modification: the reaction was conducted at room temperature in toluene (2.5 mL) using *N*,*N*`-dimethylpropylene urea (0.181 mL, 3 equiv.) and LiHMDS (1 M in toluene, 0.5 mL, 1 equiv.) for 40 min.

R_f = 0.18 in 25% Acetone/hexane

^{1}H NMR ($CDCl_3$ with 1% v/v TMS, 400 MHz) δ 7.02 (1H, dd, *J* = 9.2, 8.2 Hz), 6.70 (1H, dd, *J* = 9.3, 4.2 Hz), 3.60-3.52 (1H, m), 3.48-3.41 (1H, m), 3.22-3.16 (1H, m), 3.07 (3H, s), 2.99-2.92 (4H, m), 1.98-1.87 (1H, m), 1.77-1.69 (1H, m).

^{13}C NMR ($CDCl_3$ with 1% v/v TMS,101 MHz) δ 168.8 (d, J_{C-F} = 2.0 Hz), 152.1 (d, J_{C-F} = 240.8 Hz), 146.1 (d, J_{C-F} = 2.4 Hz), 125.9, 119.5 (d, J_{C-F} = 19.1 Hz), 116.9 (d, J_{C-F} = 22.1 Hz), 115.8 (d, J_{C-F} = 6.7 Hz), 50.8, 48.2, 43.1, 33.5, 26.7.

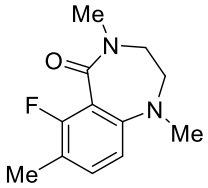
^{19}F{^{1}H} NMR ($CDCl_3$ with 1% v/v TMS, 376 MHz) δ -125.6.

FT-IR: 2961, 2921, 1634, 1496, 1463, 1431,1404, 1267, 1202, 941, 788.

HRMS (ESI$^+$): calculated for $C_{12}H_{14}ClFN_2NaO^+$ $[M + Na]^+$ 279.0671; found 279.0667.

Melting point: 103.6 – 105.4 °C.

Compound 2f



Prepared from **1f** and DMI (0.16 mL, 1.5 mmol, 3 equiv.) according to the general procedure A at room temperature for 40 min. and obtained in 53% yield (0.0587 g, 0.26 mmol) as a white solid.

R_f = 0.13 in 30% acetone/hexane

^{1}H NMR ($CDCl_3$ with 1% v/v TMS, 400 MHz) δ 7.13 (dd, appears as triplet, *J* = 8.3 Hz, 1H), 6.57 (d, *J* = 8.2 Hz, 1H), 3.43 (t, *J* = 5.7 Hz, 2H), 3.19-3.18 (m, 5H), 2.77 (s, 3H), 2.21 (s, 3H).

^{13}C NMR ($CDCl_3$ with 1% v/v TMS, 101 MHz) δ 166.1, 158.8 (d, J_{C-F} = 251.1 Hz), 146.1 (d, J_{C-F} = 5.2 Hz), 133.1 (d, J_{C-F} = 7.5 Hz), 118.8 (d, J_{C-F} = 18.1 Hz), 117.6 (d, J_{C-F} = 14.8 Hz), 112.8 (d, J_{C-F} = 3.4 Hz), 57.4, 47.8, 40.2, 33.5, 14.1 (d, J_{C-F} = 3.8 Hz).

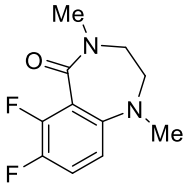
^{19}F{^{1}H} NMR ($CDCl_3$ with 1% v/v TMS, 376 MHz) δ -116.9.

FT-IR: 2945, 2811, 1639, 1491, 1261, 1170, 826.

HRMS (ESI$^+$): calculated for $C_{12}H_{15}FN_2NaO^+$ $[M + Na]^+$ 245.1061; found 245.1055.

Melting point: 107.9 – 109.1 °C.

Compound 2g



Prepared from **1g** and DMI (0.16 mL, 1.5 mmol, 3 equiv.) according to the general procedure A at room temperature for 40 min. and obtained in 53% yield (0.0602 g, 0.27 mmol) as a colorless oil.

R_f = 0.18 in 30% acetone/hexane.

^{1}H NMR (CDCl$_3$ with 1% v/v TMS, 400 MHz) δ 7.13 (m, 1H), 6.61-6.57 (m, 1H), 3.44 (t, *J* = 5.8 Hz, 2H), 3.22-3.20 (m, 5H), 2.78 (s, 3H).

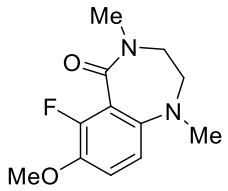
^{13}C NMR (CDCl$_3$ with 1% v/v TMS, 101 MHz) δ 164.7 (d, J_{C-F} = 2.7 Hz), 148.5 (dd, J_{C-F} = 254.6, 14.2 Hz), 146.2 (dd, J_{C-F} = 243.0, 13.2 Hz), 143.5 (m), 119.8 (d, J_{C-F} = 10.7 Hz), 118.6 (dd, J_{C-F} = 17.7, 2.0 Hz), 112.9 (dd, J_{C-F} = 5.9, 3.7 Hz), 57.4, 47.8, 40.3, 33.6.

^{19}F{^{1}H} NMR (CDCl$_3$ with 1% v/v TMS, 376 MHz) δ -137.26 (d, *J* = 21.8 Hz), -145.5 (d, *J* = 21.8 Hz).

FT-IR: 2944, 1645, 1492, 1396, 1262, 1173, 685.

HRMS (ESI$^+$): calculated for $C_{11}H_{13}F_2N_2O^+$ $[M + H]^+$ 227.0991; found 227.1002.

Compound 2h



Prepared from **1h** and DMI (0.16 mL, 1.5 mmol, 3 equiv.) according to the general procedure A at room temperature for 40 min. and obtained in 50% yield (0.0599 g, 0.25 mmol) as a white solid.

R_f = 0.14 in 30% acetone/hexane

^{1}H NMR (CDCl$_3$ with 1% v/v TMS, 400 MHz) δ 6.96 (dd, appears as triplet, *J* = 9.0 Hz, 1H), 6.59 (dd, *J* = 8.8, 1.5 Hz, 1H), 3.85 (s, 3H), 3.41 (t, *J* = 5.8 Hz, 2H), 3.20 (s, 3H), 3.14 (t, *J* = 5.7 Hz, 3H), 2.76 (s, 3H).

^{13}C NMR (CDCl$_3$ with 1% v/v TMS, 101 MHz) δ 165.5, 150.5 (d, J_{C-F} = 253.7 Hz), 143.5 (d, J_{C-F} = 11.2 Hz), 140.9 (d, J_{C-F} = 4.3 Hz), 119.6 (d, J_{C-F} = 11.4 Hz), 115.9 (d, J_{C-F} = 3.6 Hz), 112.6 (d, J_{C-F} = 3.6 Hz), 57.4, 57.0, 47.9, 40.3, 33.5.

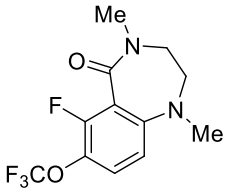
^{19}F{^{1}H} NMR (CDCl$_3$ with 1% v/v TMS, 376 MHz) δ -134.1.

FT-IR: 2953, 2817,1636, 1494,1457, 1267,1059, 814, 695.

HRMS (ESI$^+$): calculated for $C_{12}H_{15}FN_2NaO_2^+$ $[M + Na]^+$ 261.1010; found 261.1005.

Melting point: 106.5 – 108.9 °C.

Compound 2i



Prepared from **1i** and DMI (0.16 mL, 1.5 mmol, 3 equiv.) according to the general procedure A at room temperature for 40 min. and obtained in 53% yield (0.0778 g, 0.27 mmol) as a pale-yellow solid.

R_f = 0.27 in 30% acetone/hexane

^{1}H NMR (CDCl$_3$ with 1% v/v TMS, 400 MHz) δ 7.28-7.23 (m, 1H), 6.64 (dd, *J* = 9.0, 1.6 Hz, 1H), 3.47 (t, *J* = 5.7 Hz, 2H), 3.27 (t, *J* = 5.7 Hz, 2H), 3.20 (s, 3H), 2.81 (s, 3H).

^{13}C NMR (CDCl$_3$ with 1% v/v TMS, 101 MHz) δ 164.5, 152.9 (d, $J_{C\text{-}F}$ = 258.4 Hz), 146.8 (d, $J_{C\text{-}F}$ = 4.7 Hz), 131.1-131.0 (m), 125.6, 120.6 (q, $J_{C\text{-}F}$ = 258.3 Hz), 118.9 (d, $J_{C\text{-}F}$ = 12.0), 113.1 (d, $J_{C\text{-}F}$ = 3.5 Hz), 57.2, 47.6, 40.2, 33.6.

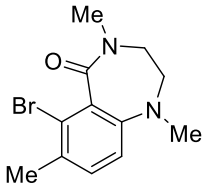
^{19}F{^{1}H} NMR (CDCl$_3$ with 1% v/v TMS, 376 MHz) δ -59.1 (d, *J* = 4.2 Hz), -128.2 (q, *J* = 4.8 Hz).

FT-IR: 3060, 2964, 2821, 1643, 1617, 1495, 1256, 1209, 1158, 827.

HRMS (ESI$^+$): calculated for $C_{12}H_{12}F_4N_2NaO_2^+$ $[M + Na]^+$ 315.0727; found 315.0720.

Melting point: 120.5 – 121.0 °C.

Compound 2j



Prepared from **1j** and DMI (0.16 mL, 1.5 mmol, 3 equiv.) according to the general procedure A under the following conditions: the reaction was conducted using NaO*t*-Bu (0.1441, 1.5 mmol, 3.0 equiv.) on 0.5 mmol scale for 20 min resulting in 51% (0.0720 g, 0.25 mmol) yield; on 2 mmol scale and for 40 min resulting in 55% yield (average of 3 trials) as a white solid.

R_f = 0.22 in 30% acetone/hexane.

^{1}H NMR (CDCl$_3$ with 1% v/v TMS, 400 MHz) δ 7.19 (d, *J* = 8.2 Hz, 1H), 6.79 (d, *J* = 8.2 Hz, 1H), 3.88-3.40 (br, 2H), 3.27-3.02 (br, 1H, overlaps with singlet at 3.21 ppm), 3.21 (s, 3H, overlaps with broad signal), 2.88-2.56 (br, 1H, overlaps with singlet at 2.75 ppm), 2.75 (s, 3H, overlaps with broad signal), 2.37 (s, 3H).

Note: the protons of the ethelene group appear as broad signals at δ 3.88-3.40, 3.27-3.02, and 2.88-2.56 ppm.

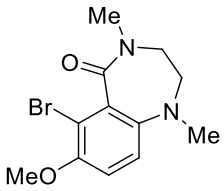
^{13}C NMR ($CDCl_3$ with 1% v/v TMS, 101 MHz) δ 168.5, 145.7, 133.0, 132.0, 131.5, 123.2, 116.7, 56.9, 48.0, 40.1, 33.3, 22.9.

FT-IR: 2942, 1648, 1591, 1415, 1424, 827, 729.

HRMS (ESI$^+$): calculated for $C_{12}H_{16}BrN_2O^+$ $[M + H]^+$ 283.0441; found 283.0452.

Melting point: 119 – 120 °C.

Compound 2k



Prepared from **1k** and DMI (0.16 mL, 1.5 mmol, 3 equiv.) according to the general procedure A at room temperature for 40 min. The product was isolated by column chromatography with diethyl ether as eluent and obtained in 46% yield (0.0684 g, 0.23 mmol) as an off-white solid.

R_f = 0.16 in 30% acetone/hexane

^{1}H NMR ($CDCl_3$ with 1% v/v TMS, 400 MHz) δ 6.90 (d, *J* = 8.8 Hz, 1H), 6.85 (d, *J* = 8.8 Hz, 1H), 3.87 (s, 3H), 3.68-3.40 (br, 2H), 3.25-3.06 (br, 1H, overlaps with singlet at 3.22 ppm), 3.22 (s, 3H, overlaps with broad signal), 2.76 (s, 3H), 2.72-2.50 (br, 1H).

Note: the H's of the ethelene group appear as broad signals between ~ 4-2 ppm.

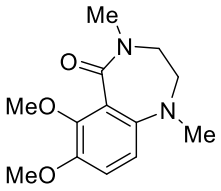
^{13}C NMR ($CDCl_3$ with 1% v/v TMS, 101 MHz) δ 167.8, 152.4, 141.2, 133.2, 117.3, 113.6, 111.1, 57.0, 56.9, 48.1, 40.2, 33.4.

FT-IR: 2937, 2800, 1648, 1436, 1266, 1049, 808, 683.

HRMS (ESI$^+$): calculated for $C_{12}H_{15}BrN_2NaO_2^+$ $[M + Na]^+$ 321.0209; found 321.0203.

Melting point: 143.1 – 143.8 °C.

Compound 2l



Prepared from **1l** and DMI (0.16 mL, 1.5 mmol, 3 equiv.) according to the general procedure A with the following modifications: the reaction was conducted at room temperature using NaO*t*-Bu (0.1441 g, 1.5 mmol, 3 equiv.) for 40 min. The crude mixture was filtered through a pad of celite eluting with EtOAc. The product was obtained in 43% yield (0.0540 g, 0.22 mmol) as an orange solid.

R_f = 0.014 in 30% acetone/hexane

^{1}H NMR ($CDCl_3$ with 1% v/v TMS, 400 MHz) δ 6.90 (d, *J* = 8.8 Hz, 1H), 6.59 (1H, *J* = 8.8 Hz, 1H), 3.96 (s, 3H), 3.84 (s, 3H), 3.53-3.27 (br, 2H), 3.19 (s, 3H), 2.74 (s, 3H).

Note: two H's of ethelene group are not reported as they appear as broad signals between ~ 4-2 ppm, consistent with previous reports on related compounds.[10]

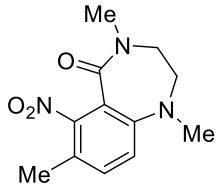
^{13}C NMR ($CDCl_3$ with 1% v/v TMS, 101 MHz) δ 167.6, 148.8, 147.6, 140.6, 125.7, 114.4, 112.5, 61.8, 57.2, 56.2, 48.1, 40.3, 33.4.

FT-IR: 2937, 2810, 1641, 1411, 1432, 1261, 1044, 1011, 827.

HRMS (ESI$^+$): calculated for $C_{13}H_{18}N_2NaO_3^+$ $[M + Na]^+$ 273.1210; found 273.1205.

Melting point: 117.5 – 118.5 °C.

Compound 2m



Prepared from **1m** and DMI (0.16 mL, 1.5 mmol, 3 equiv.) according to the general procedure A at room temperature using NaO*t*-Bu (0.1441 g, 1.5 mmol, 3.0 equiv.) for 25 min. and obtained in 41% yield (0.0517 g, 0.21 mmol) as a yellow solid.

R_f = 0.17 in 30% acetone/hexane.

^{1}H NMR ($CDCl_3$ with 1% v/v TMS, 400 MHz) δ 7.23 (d, *J* = 8.4 Hz, 1H), 6.92 (d, *J* = 8.4 Hz, 1H), 3.54 (t, *J* = 5.7 Hz, 2H), 3.29 (t, *J* = 5.7 Hz, 2H), 3.17 (s, 3H), 2.82 (s, 3H), 2.29 (s, 3H).

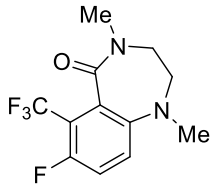
^{13}C NMR ($CDCl_3$ with 1% v/v TMS, 101 MHz) δ 166.3, 150.5, 145.2, 133.8, 123.5, 123.2, 120.2, 57.1, 47.8, 40.1, 33.8, 17.2.

FT-IR: 2942, 1639, 1524, 1493, 1434, 1367, 836.

HRMS (ESI$^+$): calculated for $C_{12}H_{16}N_3O_3^+$ $[M + H]^+$ 250.1186; found 250.1195.

Melting point: 199 °C

Compound 2n



Prepared from **1n** and DMI (0.16 mL, 1.5 mmol, 3 equiv.) according to the general procedure A at room temperature for 40 min. and obtained in 71% yield (0.0983 g, 0.36 mmol) as a white solid.

R_f = 0.22 in 30% acetone/hexane.

^{1}H NMR (CDCl$_3$ with 1% v/v TMS, 400 MHz) δ 7.15 (dd, appears as triplet, *J* = 9.6 Hz, 1H), 7.07-7.04 (m, 1H), 3.67-3.50 (m, 2H), 3.24 (dd, *J* = 14.5, 3.7 Hz, 1H), 3.18 (m, 3H), 2.79-2.73 (m, 4H).

^{13}C NMR (CDCl$_3$ with 1% v/v TMS, 101 MHz) δ 166.9 (d, $J_{C\text{-}F}$ = 2.4 Hz), 155.8 (d, $J_{C\text{-}F}$ = 252.3 Hz), 142.4 (d, $J_{C\text{-}F}$ = 2.7 Hz), 130.8 (d, $J_{C\text{-}F}$ = 2.1 Hz), 122.6 (d, $J_{C\text{-}F}$ = 8.5 Hz), 122.4 (dq, $J_{C\text{-}F}$ = 274.5, 1.8 Hz), 118.7 (d, $J_{C\text{-}F}$ = 23.0 Hz), 116.6 (dq, $J_{C\text{-}F}$ = 32.7, 13.4 Hz), 56.4, 40.1, 40.2, 33.2.

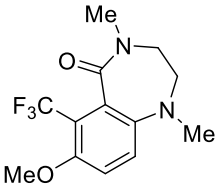
^{19}F{^{1}H} NMR (CDCl$_3$ with 1% v/v TMS, 376 MHz) δ -56.8 (d, *J* = 20.5 Hz), -120.6 (q, *J* = 20.5 Hz).

FT-IR: 2876, 16.48, 1489, 13.94, 1288, 1124, 694.

HRMS (ESI$^+$): calculated for $C_{12}H_{13}F_4N_2O^+$ $[M + H]^+$ 277.0959; found 277.0973.

Melting point: 105 – 106 °C.

Compound 2o



Prepared from **1o** and DMI (0.16 mL, 1.5 mmol, 3 equiv.) according to the general procedure A at room temperature for 40 min. and obtained in 60% yield (0.0867 g, 0.30 mmol) as a white solid.

R_f = 0.11 in 30% acetone/hexane

^{1}H NMR (CDCl$_3$ with 1% v/v TMS, 400 MHz) δ 7.05-7.00 (m, 2H), 3.86 (s, 3H), 3.67-3.58 (m, 1H), 3.53-3.46 (m, 1H), 3.23-3.18 (m, 4H), 2.77 (s, 3H), 2.67-2.64 (m, 1H).

^{13}C NMR (CDCl$_3$ with 1% v/v TMS, 101 MHz) δ 168.1, 154.0 (m), 139.2, 131.7 (q, $J_{C\text{-}F}$ = 2.6 Hz), 123.3 (q, $J_{C\text{-}F}$ = 274.7 Hz), 121.8, 117.0 (q, $J_{C\text{-}F}$ = 30.7 Hz), 114.9, 56.8, 56.4, 48.3, 40.3, 33.1.

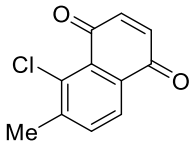
^{19}F{^{1}H} NMR (CDCl$_3$ with 1% v/v TMS, 376 MHz) δ -57.4.

FT-IR: 2937, 2817, 1643, 1485, 1301, 1274, 1120, 1050, 712.

HRMS (ESI$^+$): calculated for $C_{13}H_{16}F_3N_2O_2^+$ $[M + H]^+$ 289.1158; found 289.1167.

Melting point: 197 – 199 °C

Compound 4a



Prepared from **1a** according to the general procedure A with the following modification: the reaction was conducted at room temperature using 2-(trimethylsiloxy)furan (0.126 mL, 1.5 equiv.) and NaO*t*-Bu (0.1442 g, 3 equiv.) for 40 min. The reaction mixture was quenched with 0.1 M HCl, extracted with EtOAc (3x3 mL), and combined organic layers were washed with brine. The product was obtained in 47% yield (0.0489 g, 0.24 mmol) as a yellow to brown solid.

R_f = 0.52 (20% acetone:hexanes)

^{1}H NMR (CDCl$_3$ with 1% v/v TMS, 400 MHz) δ 7.96 (d, *J* = 7.9 Hz, 1H), 7.61 (d, *J* = 7.8 Hz, 1H), 6.95-6.89 (m, 2H), 2.53 (s, 3H).

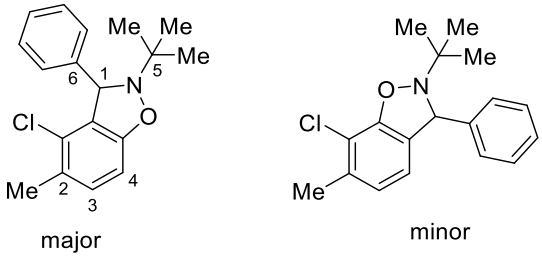
^{13}C NMR (CDCl$_3$ with 1% v/v TMS, 101 MHz) δ 184.0, 183.8, 145.5, 140.4, 136.5, 135.2, 134.3, 132.5, 128.0, 125.3, 21.5.

FT-IR: 3053, 2923, 1661, 1610, 1579, 1310, 1272, 1089, 1067, 845, 818, 802.

HRMS (ESI$^+$): calculated for $C_{11}H_8ClO_2^+$ $[M + H]^+$ 207.0207; found 207.0208.

Melting point: 134.5 – 135.7 °C.

Compound 4b



Prepared from **1a** according to the general procedure A under the following conditions: the reaction was conducted at room temperature using *N*-tert-Butyl-α-phenylnitrone (0.2659 g, 3 equiv.) and NaO*t*-Bu (0.1442 g, 3 equiv.) for 1 hour. The crude product was purified by column chromatography with ethyl acetate/hexanes mixture as eluent and obtained in 92% yield (0.1392 g, 0.46 mmol, mixture of regioisomers, 11.1:1 ratio) as a yellow oil. Characterization for major isomer is provided below.

R_f = 0.71 10% ethyl acetate/hexane

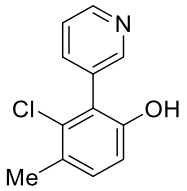
^{1}H NMR (CDCl$_3$ with 1% v/v TMS, 400 MHz) δ 7.32-7.22 (m, 5H, Ph6, overlaps with minor isomer), 7.05 (d, 1H, *J* = 8.2 Hz, H3), 6.66 (d, 1H, *J* = 8.1 Hz, H4, overlaps with minor isomer), 5.57 (s, 1H, H1), 2.22 (s, 3H, $CH_3$2), 1.17 (s, 9H, t-Bu5).

^{13}C NMR (CDCl$_3$ with 1% v/v TMS, 101 MHz) δ 156.7, 141.9, 131.1, 129.2, 128.4, 128.2, 128.0, 127.7, 127.5, 104.8, 67.0, 61.5, 25.3, 18.8.

FT-IR: 2971, 2866, 1601, 1465, 1364, 1298, 804, 695.

HRMS (ESI$^+$): calculated for $C_{18}H_{20}ClNNaO^+$ $[M + Na]^+$ 324.1126; found 324.1118.

Compound 4c



Prepared from **1a** according to the general procedure A under the following conditions: the reaction was conducted at room temperature using pyridine *N*-oxide (0.1427 g, 3 equiv.) and NaO*t*-Bu (0.0721 g, 1.5 equiv.) for 40 min. The product was obtained in 29% yield (0.0324 g, 0.15 mmol) as an orange solid.

R_f = 0.07 20% acetone:hexane

^{1}H NMR (DMSO-*d*$_6$, 400 MHz) δ 9.73 (br, 1H), 8.53 (dd, *J* = 4.8, 1.5 Hz, 1H), 8.41 (d, *J* = 1.6 Hz, 1H), 7.66 (ddd, appears as doublet of triplet, *J* = 7.8, 1.9, 1.9 Hz, 1H), 7.45 (dd, *J* = 7.8, 4.8 Hz, 1H), 7.19 (d, *J* = 8.3 Hz, 1H), 6.86 (d, *J* = 8.3 Hz, 1H), 2.27 (s, 3H).

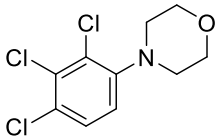
^{13}C NMR (DMSO-*d*$_6$, 101 MHz) δ 154.2, 150.6, 148.1, 138.0, 133.0, 132.2, 130.9, 126.0, 124.4, 123.2, 114.2, 19.7.

FT-IR: 3051, 2922, 2818, 1591, 1394, 1374, 1290, 1183, 1045, 914, 913, 799, 706, 674.

HRMS (ESI$^+$): calculated for $C_{12}H_{11}ClNO^+$ $[M + H]^+$ 220.0524; found 220.0520.

Melting point: decomposed at 233 °C.

Compound 4d



Prepared from **1b** according to the general procedure A under the following conditions: the reaction was conducted using 4-chloromorpholine (0.1824 g, 3 equiv.); NaO*t*-Bu (0.2403 g, 5 equiv.) was added at 0 °C and the mixture was allowed to react at this temperature for 80 min. The crude product was purified by column chromatography with ethyl acetate/hexanes mixture as eluent and obtained in 56% yield (0.0750 g, 0.28 mmol) as a white solid.

R_f = 0.39 20% ethyl acetate:hexane

^{1}H NMR ($CDCl_3$ with 1% v/v TMS, 400 MHz) δ 7.34 (d, *J* = 8.8 Hz, 1H), 6.91 (d, *J* = 8.8 Hz, 1H), 3.88-3.86 (m, 4H), 3.04-3.01 (m, 4H).

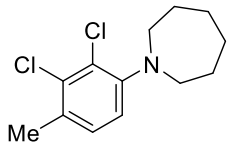
^{13}C NMR ($CDCl_3$ with 1% v/v TMS, 101 MHz) δ 149.4, 132.7, 129.2, 128.3, 128.1, 118.8, 67.0, 51.7.

FT-IR: 2969, 2865, 2824, 1440, 1372, 1236, 1114, 958, 810, 695.

HRMS (ESI$^+$): calculated for $C_{10}H_{11}Cl_3NO^+$ $[M + H]^+$ 265.9901; found 265.9901.

Melting point: 90.1 – 91.9 °C.

Compound 4e



Prepared from **1a** according to the general procedure A under the following conditions: the reaction was conducted using 1-chloroazepane (02004 g, 3 equiv.); NaO*t*-Bu (0.2403 g, 5 equiv.) was added at 0 °C and the mixture was allowed to react at this temperature for 3 h. The crude product was purified by column chromatography with petroleum ether as eluent and obtained in 47% yield (0.0610 g, 0.24 mmol, mixture of regioisomers, 22:1 ratio) as a red oil. Characterization for major isomer is provided below.

R_f = 0.50 in petroleum ether

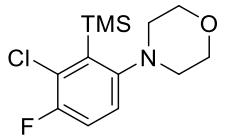
^{1}H NMR ($CDCl_3$ with 1% v/v TMS, 400 MHz) δ 7.02 (d, *J* = 8.3 Hz, 1H), 6.93 (d, *J* = 8.3 Hz, 1H), 3.17-3.14 (m, 4H), 2.34 (s, 3H), 1.85-1.76 (m, 4H), 1.72-1.69 (m, 4H).

^{13}C NMR ($CDCl_3$ with 1% v/v TMS, 101 MHz) δ 151.7, 133.6, 131.1, 128.2, 127.9, 119.8, 55.2, 29.2, 27.1, 20.6.

FT-IR: 2922, 2853, 1592, 1464, 1444, 1032, 808.

HRMS (ESI$^+$): calculated for $C_{13}H_{18}Cl_2N^+$ $[M + H]^+$ 258.0811; found 258.0809.

Compound 4f



Prepared from **1d** according to the general procedure A under the following conditions: the reaction was conducted using 4-(trimethylsilyl)morpholine (0.133 mL, 1.5 equiv.); NaO*t*-Bu (0.1442 g, 3 equiv.) was added at 0 °C and the mixture was allowed to react at this temperature for 40 min. The crude product was purified by column chromatography with ethyl acetate/hexanes mixture as eluent and obtained in 41% yield (0.0584 g, 0.2 mmol) as white solid.

R_f = 0.43 in 16% ethyl acetate/hexane

^{1}H NMR (CDCl$_3$ with 1% v/v TMS, 400 MHz) δ 7.20 (dd, *J* = 8.8, 4.4 Hz, 1H), 7.13 (dd, appears as triplet, *J* = 8.4 Hz, 1H), 3.89-3.86 (m, 2H), 3.81-3.75 (m, 2H), 2.96-2.90 (m, 2H), 2.72-2.69 (m, 2H), 0.45 (s, 9H).

^{13}C NMR (CDCl$_3$ with 1% v/v TMS, 101 MHz) δ 156.1 (d, $J_{C\text{-}F}$ = 3.6 Hz), 156.0 (d, $J_{C\text{-}F}$ = 247.7 Hz), 139.4 (d, $J_{C\text{-}F}$ = 3.4 Hz), 127.2 (d, $J_{C\text{-}F}$ = 16.1 Hz), 122.3 (d, $J_{C\text{-}F}$ = 6.9 Hz), 117.5 (d, $J_{C\text{-}F}$ = 23.3 Hz), 66.7, 54.8, 3.2.

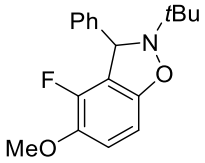
^{19}F{^{1}H} NMR (CDCl$_3$ with 1% v/v TMS, 376 MHz) δ -115.0.

FT-IR: 2952, 2860, 2815, 1436, 1260, 1245, 1111, 839, 820, 729.

HRMS (ESI$^+$): calculated for $C_{13}H_{20}ClFNOSi^+$ $[M + H]^+$ 288.0981; found 288.0978.

Melting point: 91.3 – 92.5 °C.

Compound 5a



Prepared from **1h** according to the general procedure A under the following conditions: the reaction was conducted at room temperature using *N*-tert-Butyl-α-phenylnitrone (0.2659 g, 3 equiv.) and NaO*t*-Bu (0.1442 g, 3 equiv.) for 1 hour. The crude product was purified by column chromatography with ethyl acetate/hexanes mixture as eluent and obtained in 85% yield (0.1282 g, 0.43 mmol) as a red solid.

R_f = 0.47 10% ethyl acetate:hexane

^{1}H NMR (CDCl$_3$ with 1% v/v TMS, 400 MHz) δ 7.41 (d, *J* = 7.5, Hz, 2H), 7.31 (dd, appears as triplet, *J* = 7.5 Hz, 2H), 7.26-7.22 (m, 1H), 6.79 (dd, appears as triplet, *J* = 8.4, 8.4 Hz, 1H), 6.49 (d, *J* = 8.6 Hz, 1H), 5.71 (s, 1H), 3.77 (s, 3H), 1.17 (s, 9H).

^{13}C NMR (CDCl$_3$ with 1% v/v TMS, 101 MHz) δ 152.9 (d, $J_{C\text{-}F}$ = 6.2 Hz), 147.8 (d, $J_{C\text{-}F}$ = 249.3 Hz), 142.1 (d, $J_{C\text{-}F}$ = 10.3 Hz), 142.0, 128.6, 127.6, 127.2, 118.0 (d, $J_{C\text{-}F}$ = 17.4 Hz), 115.1 (d, $J_{C\text{-}F}$ = 1.5 Hz), 101.0 (d, $J_{C\text{-}F}$ = 4.3 Hz), 64.7 (d, $J_{C\text{-}F}$ = 2.1 Hz), 61.4, 57.5, 25.4.

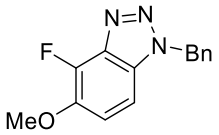
^{19}F{^{1}H} NMR (CDCl$_3$ with 1% v/v TMS, 376 MHz) δ -138.0.

FT-IR: 2972, 2937, 1423, 1364, 1262, 1021, 804, 718, 696.

HRMS (ESI$^+$): calculated for $C_{18}H_{20}FNNaO_2^+$ $[M + Na]^+$ 324.1370; found 324.1366.

Melting point: 77.9 – 79.7 °C.

Compound 5b



Prepared from **1h** according to the general procedure A under the following conditions: the reaction was conducted using benzyl azide (0.069 mL, 1.1 equiv.); NaO*t*-Bu (0.0721 g, 1.5 equiv.) was added at 0 °C and the mixture was allowed to react at this temperature for 40 min. The crude product was purified by column chromatography with ethyl acetate/hexanes mixture as eluent and obtained in 44% yield (0.0560 g, 0.22 mmol) as a white solid.

R_f = 0.29 in 25% ethyl acetate/hexane

^{1}H NMR (CDCl$_3$ with 1% v/v TMS, 400 MHz) δ 7.36-7.25 (m, 5H), 7.19 (dd, *J* = 8.9, 6.9 Hz, 1H), 7.02 (dd, *J* = 8.9, 1.1 Hz, 1H), 5.81 (s, 3H), 3.96 (s, 3H).

^{13}C NMR (CDCl$_3$ with 1% v/v TMS, 101 MHz) δ 142.8 (d, J_{C-F} = 7.4 Hz), 142.5 (d, J_{C-F} = 257.6 Hz), 137.9 (d, J_{C-F} = 16.1 Hz), 134.3, 130.5 (d, J_{C-F} = 5.1 Hz), 129.1, 128.6, 127.6, 119.2, 104.9 (d, J_{C-F} = 5.6 Hz), 59.1 (d, J_{C-F} = 2.0 Hz), 52.5.

^{19}F{^{1}H} NMR (CDCl$_3$ with 1% v/v TMS, 376 MHz) δ -145.8.

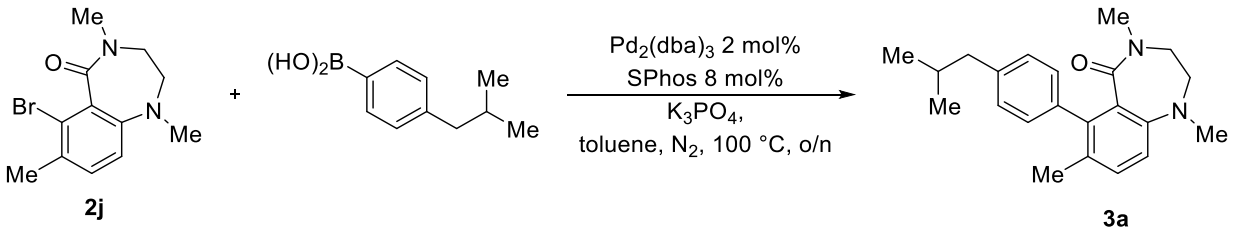
FT-IR: 3021, 2939, 1524, 1455, 1288, 1234, 1089, 1071, 1032, 800, 708, 692, 681.

HRMS (ESI$^+$): calculated for $C_{14}H_{12}FN_3NaO^+$ $[M + Na]^+$ 280.0857; found 280.0850.

Melting point: decomposed at 118.9 °C.

Derivatization of aryne coupling products by transition metal catalysis

Suzuki Coupling



Prepared according to the literature procedure[11]. An oven-dried vial was charged with $Pd_2(dba)_3$ (0.0090 g, 4 mol% Pd), SPhos (0.0164 g, 8 mol%), (4-isobutylphenyl)boronic acid (0.1335 g, 1.5 equiv.), **2j** (0.1416 g, 0.5 mmol, 1 equiv.), and K_3PO_4 (0.3180 g, 3 equiv.) and equipped with a magnetic stir bar. The vial was capped with a rubber septum, flushed with nitrogen and left under static nitrogen atmosphere. Toluene (1 mL) was added via syringe through the septum and the septum was replaced with a screwcap. The resulting mixture was heated at 100 °C under stirring overnight then allowed to cool to room temperature, diluted with diethyl ether, filtered through a thin pad of celite eluting with diethyl ether, and concentrated under reduced pressure. The crude

material was purified by column chromatography on silica gel with acetone/hexane mixture and obtained in 95% yield (0.1605 g, 0.48 mmol) as a white solid.

Compound 3a

R_f = 0.39 (30% acetone/hexane)

^{1}H NMR (CDCl$_3$ with 1% v/v TMS, 400 MHz) δ 7.22-7.20 (m, 1H), 7.17-6.89 (br, 4H), 6.81 (d, *J* = 8.2 Hz, 1H), 3.00 (s, 3H), 2.79 (s, 3H), 2.47 (d, *J* = 7.2 Hz, 2H), 2.06 (s, 3H), 1.89 (n, *J* = 6.7 Hz, 1H), 0.92 (d, *J* = 6.6 Hz, 3H).

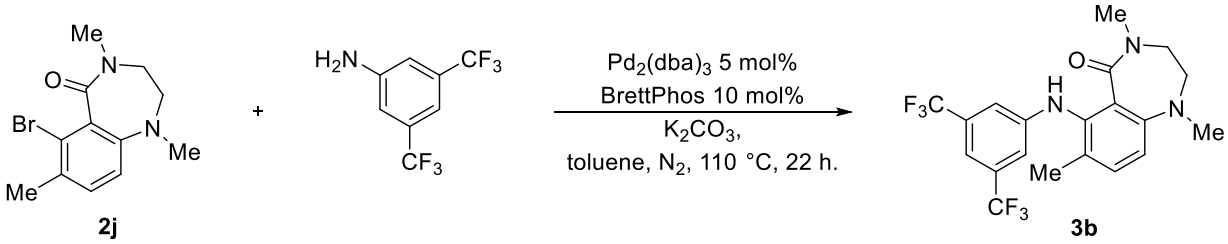
^{13}C NMR (CDCl$_3$ with 1% v/v TMS, 101 MHz) δ 169.7, 144.3, 141.1, 139.9, 137.3, 131.8, 131.0, 130.8, 128.5 (two overlapping signals), 116.2, 57.1, 48.1, 45.4, 40.2, 33.2, 30.1, 22.5, 19.9.

FT-IR: 2953, 2865, 2802, 1651, 1449, 1443, 1384, 1177, 1093, 817.

HRMS (ESI$^+$): calculated for $C_{22}H_{28}N_2NaO^+$ $[M + Na]^+$ 359.2088; found 359.2094.

Melting point: 157.1 – 158.3 °C.

Buckwald-Hartwig coupling



Prepared according to the modified literature procedure.[12] An oven-dried vial was charged with $Pd_2(dba)_3$ (6.9 mg, 5 mol% Pd), BrettPhos (0.0161 g, 5 mol%), **2j** (0.0850 g, 0.3 mmol), and K_2CO_3 (0.0995 g, 0.72 mmol, 2.4 equiv.) and equipped with a magnetic stir bar. The vial was capped with a rubber septum, purged with nitrogen and left under static nitrogen atmosphere. Toluene (0.6 mL) followed by 3,5-bis(trifluoromethyl)aniline (0.056 mL, 0.36 mmol, 1.2 equiv.) were added via syringe. The resulting mixture was heated at 110 °C under stirring for 4.5 hours, then a mixture of $Pd_2(dba)_3$ (6.9 mg, 5 mol% Pd) and BrettPhos (0.0161 g, 5 mol%) was added to the reaction mixture, and the reaction was left at 110 °C under stirring for 17.5 hours. The reaction mixture was cooled to room temperature, diluted with ethyl acetate, filtered through a thin pad celite eluting with ethyl acetate, and concentrated under reduced pressure. The crude material was purified by column chromatography on silica gel with acetone/hexane mixture as eluent and obtained in 78% yield (0.1014 g, 0.24 mmol) as a white solid.

Compound 3b

R_f = 0.30 20% acetone:hexane

^{1}H NMR (CDCl$_3$ with 1% v/v TMS, 400 MHz) δ 8.06 (s, 1H), 7.24 (d, *J* = 8.4 Hz, 1H), 7.20 (s, 1H), 6.91 (s, 2H), 6.77 (d, *J* = 8.3 Hz, 1H), 3.37-3.36 (m, 2H), 2.27-3.16 (br, 2H), 3.11 (s, 3H), 2.82 (s, 3H), 2.05 (s, 3H).

^{13}C NMR (CDCl$_3$ with 1% v/v TMS, 101 MHz) δ 169.2, 146.6, 146.2, 138.0, 133.8, 132.2 (q, $J_{C\text{-}F}$ = 32.8 Hz), 128.1, 124.5, 123.5 (q, $J_{C\text{-}F}$ = 272.7 Hz), 115.3, 114.4 (m), 111.5-111.4 (m), 57.7, 48.2, 40.5, 33.8, 18.1.

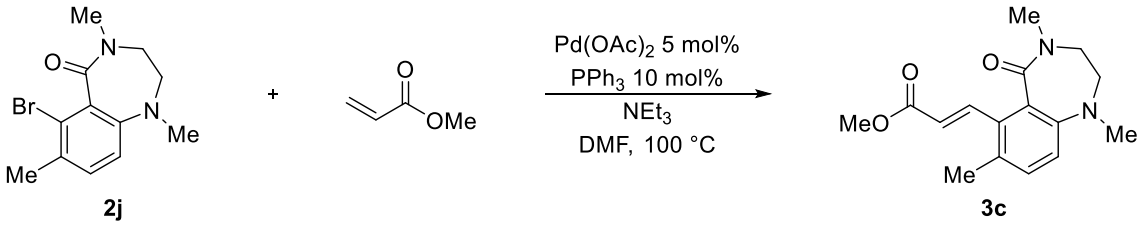
^{19}F{^{1}H} NMR (CDCl$_3$ with 1% v/v TMS, 376 MHz) δ -63.1.

FT-IR: 3231, 3073, 2946, 2805, 1630, 1620, 1480, 1392, 1272, 1161, 1119, 856, 679.

HRMS (ESI$^+$): calculated for $C_{20}H_{19}F_6N_3NaO^+$ $[M + Na]^+$ 454.1324; found 454.1317.

Melting point: 232.1 – 233.9 °C.

Heck coupling



Palladium diacetate (0.0034 g, 5 mol%), triphenylphosphine (0.0079 g, 10 mol%), and **2j** (0.0850 g, 0.3 mmol) were placed into an oven-dried vial equipped with a magnetic stir bar. The vial was capped with a rubber septum, purged with nitrogen and left under static nitrogen atmosphere. DMF (0.6 mL) followed by triethylamine (0.084 mL, 1 mmol, 2 equiv.) and methyl acrylate (0.052 mL, 1 mmol, 2 equiv.) were added via syringe. The resulting mixture was heated at 100 °C under stirring overnight, then cooled to room temperature and subjected to column chromatography on basic alumina with acetone/hexane mixture as eluent. Mixture of *E*/*Z* isomers was isolated in 99% yield (0.0856 g, 0.3 mmol, *E*:*Z* = 9.6:1) as a bright yellow solid. Characterization for *E* isomer is provided below.

Compound 3c

R_f = 0.39 30% acetone:hexane

^{1}H NMR (CDCl$_3$ with 1% v/v TMS, 400 MHz) δ 7.93 (d, *J* = 16.2 Hz, 1H), 7.16 (d, *J* = 8.2 Hz, 1H), 6.80 (d, *J* = 8.2 Hz, 1H), 5.95 (d, *J* = 16.2 Hz, 1H), 3.77 (s, 3H), 3.48-3.45 (m, 2H), 3.18 (s, 3H), 3.16-3.12 (m, 2H), 2.77 (s, 3H), 2.29 (s, 3H).

^{13}C NMR (CDCl$_3$ with 1% v/v TMS, 101 MHz) δ 169.7, 166.7, 144.6, 143.9, 134.1, 132.6, 130.9, 130.3, 122.9, 118.0, 56.8, 51.6, 48.2, 40.1, 33.4, 20.0.

FT-IR: 2947, 2813, 1710, 1634, 1434, 1396, 1300, 1190, 1166, 987, 839.

HRMS (ESI$^+$): calculated for $C_{16}H_{20}N_2NaO_3^+$ $[M + Na]^+$ 311.1366; found 311.1361.

Melting point: 137.4 – 138.9 °C.

Crystal structure

Crystals of **1h** were obtained by the use of vapor diffusion of diethyl ether into methanol solution at room temperature. Crystals of **2o and 3c** were obtained by slow evaporation of acetone solution at room temperature. Single crystals of **1h, 2o, and 3c** were chosen for crystallographic study with Mo Kα radiation (λ = 0.71073 Å) or Cu Kα (λ = 1.5418 Å) radiation. Data were collected on an Oxford Gemini system. Relevant details of the crystallographic experiments are given in Table X. The structures were solved with SHELXS-86 and refined with SHELXL-97.[13] All non-H atoms were found in initial E-maps, and their positions were refined with attendant anisotropic librational parameters. H-atoms on carbons were assigned locations riding on the heavier atoms and given isotropic librational parameters equal to 150% of the equivalent isotropic librational parameter of the attached atom.

Table 1. Selected crystallographic information for structures **1h, 2o, 3c.**

	Compound 1h	**Compound 2o**	**Compound 3c**
Formula	$C_{23}H_{24}FIO_4S$	$C_{13}H_{15}F_3N_2O_2$	$C_{16}H_{20}N_2O_3$
System	monoclinic	monoclinic	triclinic
Space Group	P 2(1)/*n* (#14)	P 2(1)/*n* (#14)	P -1 (#2)
Cell constants			
a (Å)	8.5731(2)	8.6744(3)	9.1953(8)
b (Å)	11.0903(3)	14.6490(4)	10.6663(7)
***c* (Å)**	23.6152(6)	10.4584(3)	15.3224(9)
α (º)	90	90	91.639(5)
β (º)	92.859(2)	103.035(3)	101.895(7)
γ (º)	90	90	90.755(6)
Data, parameters	7372, 271	4263, 181	7253, 380
R_1 (I>4σI)	0.053	0.037	0.052
CCDC	1916592	1916589	1916591

Estimated standard deviations in parentheses.

References

(1) Sundalam, S. K.; Nilova, A.; Seidl, T. L.; Stuart, D. R. A Selective C−H Deprotonation Strategy to Access Functionalized Arynes by Using Hypervalent Iodine. *Angew. Chemie - Int. Ed.* **2016**, *55* (29), 8431–8434. https://doi.org/10.1002/anie.201603222.

(2) Miura, T.; Morimoto, M.; Murakami, M. Copper-Catalyzed Amination of Silyl Ketene Acetals with N-Chloroamines. *Org. Lett.* **2012**, *14* (20), 5214–5217. https://doi.org/10.1021/ol302331k.

(3) Sirois, J. J.; DeBoef, B. Transition-Metal Free Umpolung Carbon–Nitrogen versus Carbon–Chlorine Bond Formation. *Tetrahedron Lett.* **2015**, *56* (41), 5610–5612. https://doi.org/10.1016/J.TETLET.2015.08.053.

(4) Fulmer, G. R.; Miller, A. J. M.; Sherden, N. H.; Gottlieb, H. E.; Nudelman, A.; Stoltz, B. M.; Bercaw, J. E.; Goldberg, K. I. NMR Chemical Shifts of Trace Impurities: Common Laboratory Solvents, Organics, and Gases in Deuterated Solvents Relevant to the Organometallic Chemist. *Organometallics* **2010**, *29* (9), 2176–2179. https://doi.org/10.1021/om100106e.

(5) Sokolovs, I.; Lubriks, D.; Suna, E. Copper-Catalyzed Intermolecular C–H Amination of (Hetero)Arenes via Transient Unsymmetrical Λ3-Iodanes. *J. Am. Chem. Soc.* **2014**, *136* (19), 6920–6928. https://doi.org/10.1021/ja502174d.

(6) A. Merritt, E.; M. T. Carneiro, V.; F. Silva, L.; Olofsson, B. Facile Synthesis of Koser's Reagent and Derivatives from Iodine or Aryl Iodides. *J. Org. Chem.* **2010**, *75* (21), 7416–7419. https://doi.org/10.1021/jo101227j.

(7) Seidl, T. L.; Sundalam, S. K.; McCullough, B.; Stuart, D. R. Unsymmetrical Aryl(2,4,6-Trimethoxyphenyl)Iodonium Salts: One-Pot Synthesis, Scope, Stability, and Synthetic Studies. *J. Org. Chem.* **2016**, *81* (5), 1998–2009. https://doi.org/10.1021/acs.joc.5b02833.

(8) Ochiai, M.; Toyonari, M.; Nagaoka, T.; Chen, D. W.; Kida, M. Stereospecific Synthesis of Vinyl(Phenyl)Iodonium Tetrafluoroborates via Boron-Iodane Exchange of Vinylboronic Acids and Esters with Hypervalent Phenyliodanes. *Tetrahedron Lett.* **1997**, *38* (38), 6709–6712. https://doi.org/10.1016/S0040-4039(97)01571-2.

(9) Dohi, T.; Yamaoka, N.; Kita, Y. Fluoroalcohols: Versatile Solvents in Hypervalent Iodine Chemistry and Syntheses of Diaryliodonium(III) Salts. *Tetrahedron* **2010**, *66* (31), 5775–5785. https://doi.org/10.1016/j.tet.2010.04.116.

(10) Yoshida, H.; Shirakawa, E.; Honda, Y.; Hiyama, T. Addition of Ureas to Arynes: Straightforward Synthesis of Benzodiazepine and Benzodiazepine Derivatives. *Angew. Chemie - Int. Ed.* **2002**, *41* (17), 3247–3249. https://doi.org/10.1002/1521-3773(20020902)41:17<3247::AID-ANIE3247>3.0.CO;2-P.

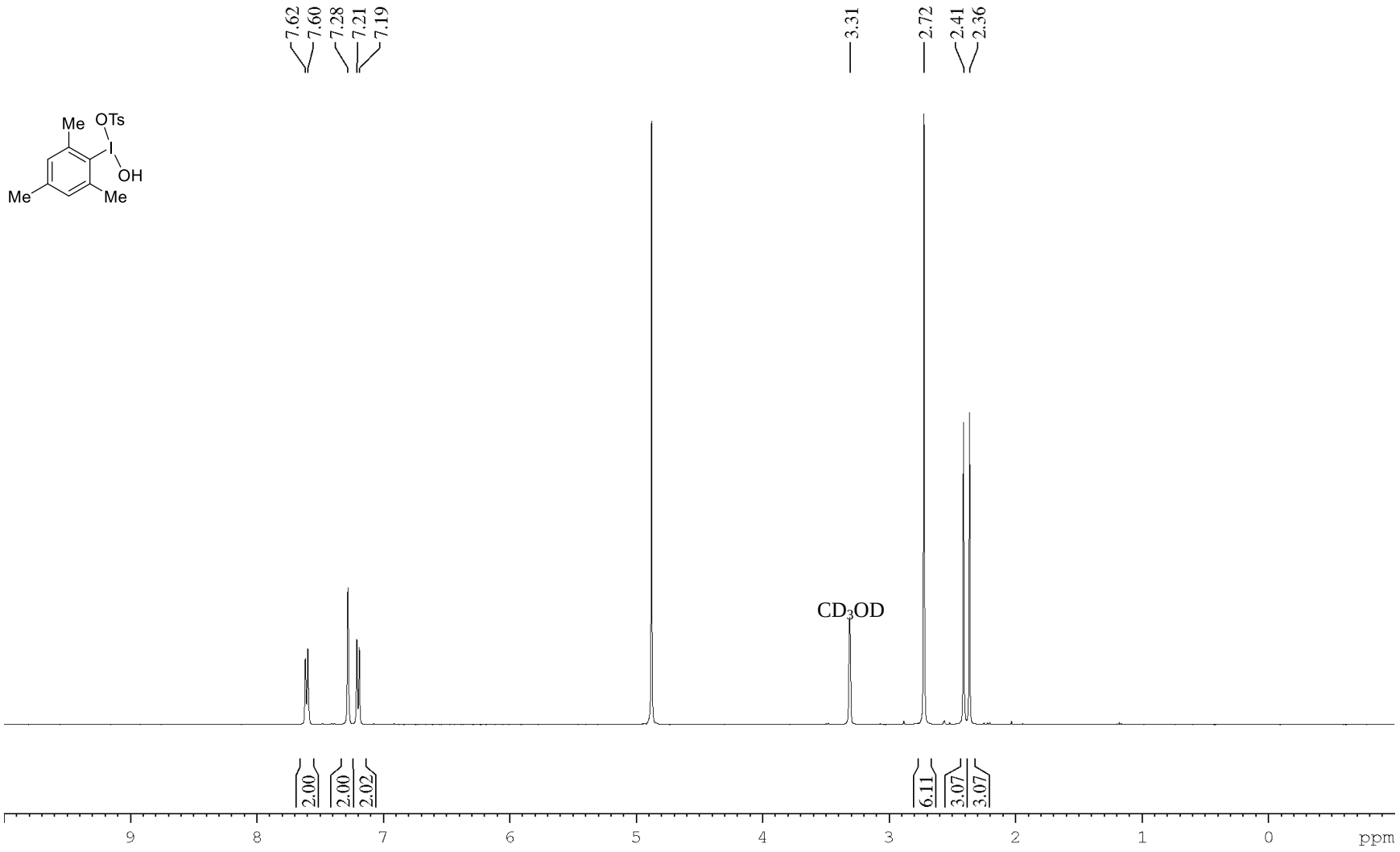
(11) Walker, S. D.; Barder, T. E.; Martinelli, J. R.; Buchwald, S. L. A Rationally Designed Universal Catalyst for Suzuki-Miyaura Coupling Processes. *Angew. Chemie - Int. Ed.* **2004**, *43* (14), 1871–1876. https://doi.org/10.1002/anie.200353615.

(12) Surry, D. S.; Buchwald, S. L. Dialkylbiaryl Phosphines in Pd-Catalyzed Amination: A User's Guide. *Chem. Sci.* **2011**, *2* (1), 27–50. https://doi.org/10.1039/c0sc00331j.

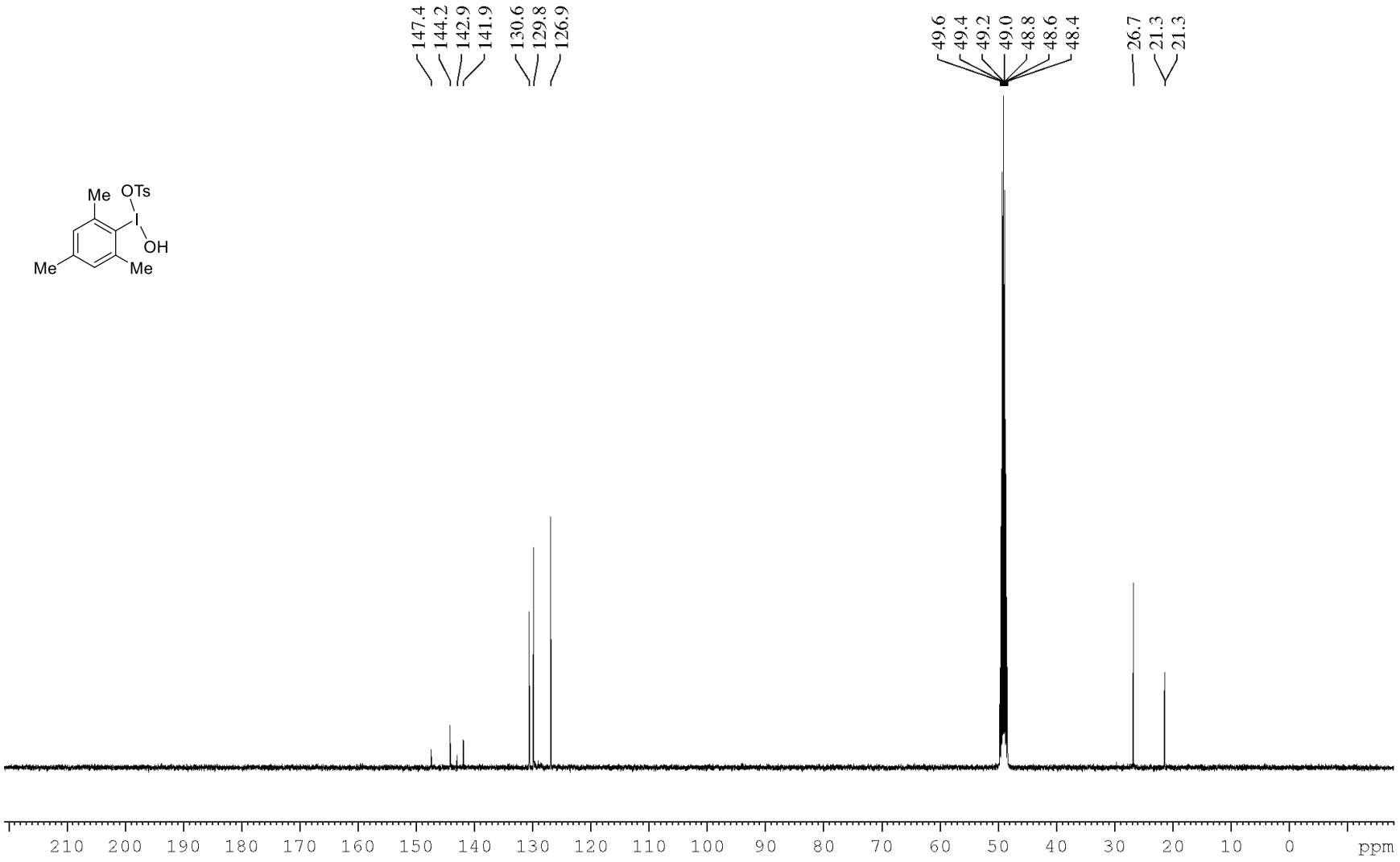
(13) Sheldrick, G. M. A Short History of SHELX. *Acta Crystallogr. Sect. A Found. Crystallogr.* **2008**, *64* (1), 112–122. https://doi.org/10.1107/S0108767307043930.

^{1}H, ^{13}C, and ^{19}F NMR Spectra

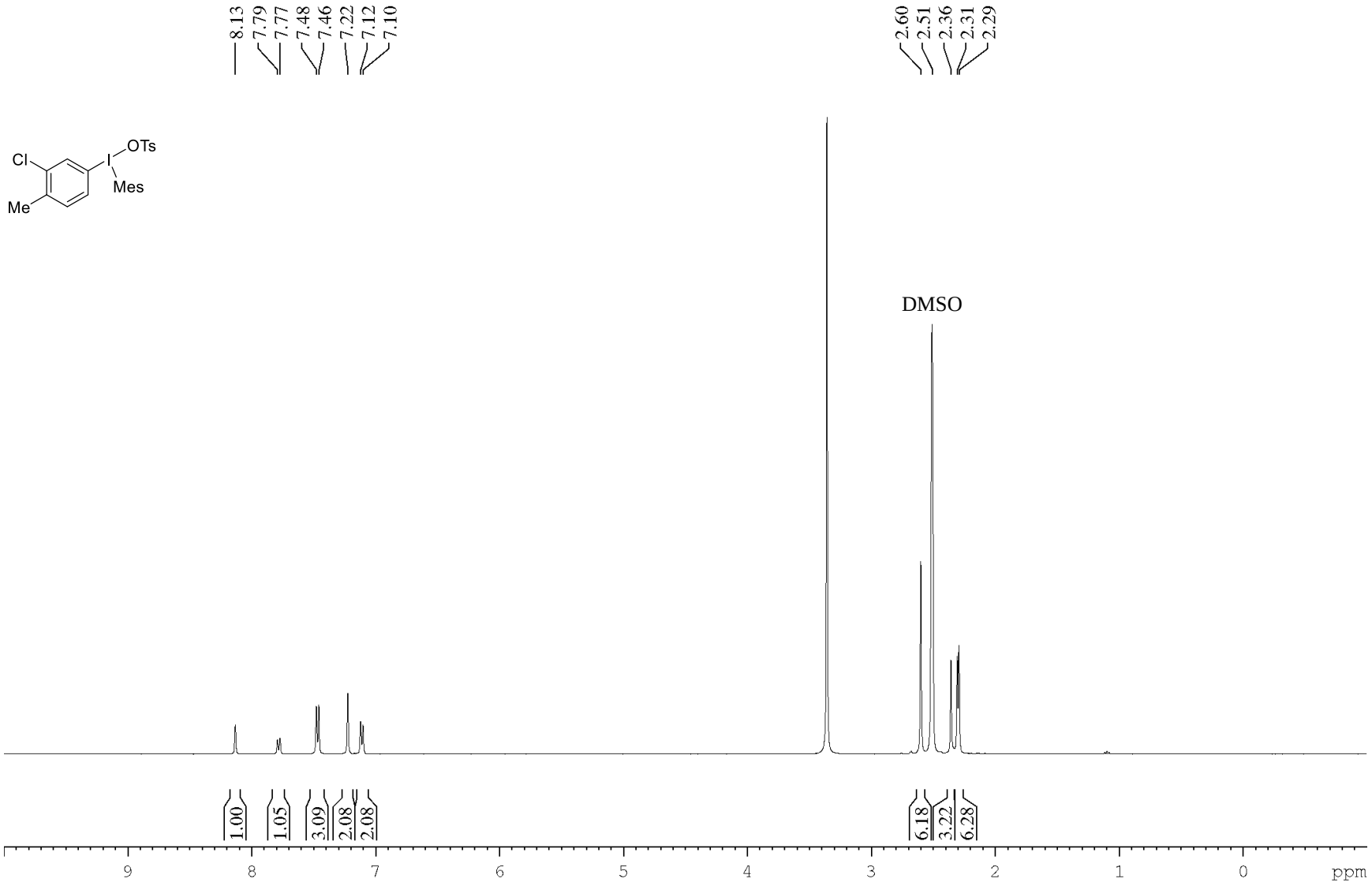
^{1}H NMR of S1 in CD_3OD at 400 MHz



^{13}C {^{1}H} NMR of S1 in CD_3OD at 101 MHz



^{1}H NMR of 1a in DMSO-d_6 at 400 MHz



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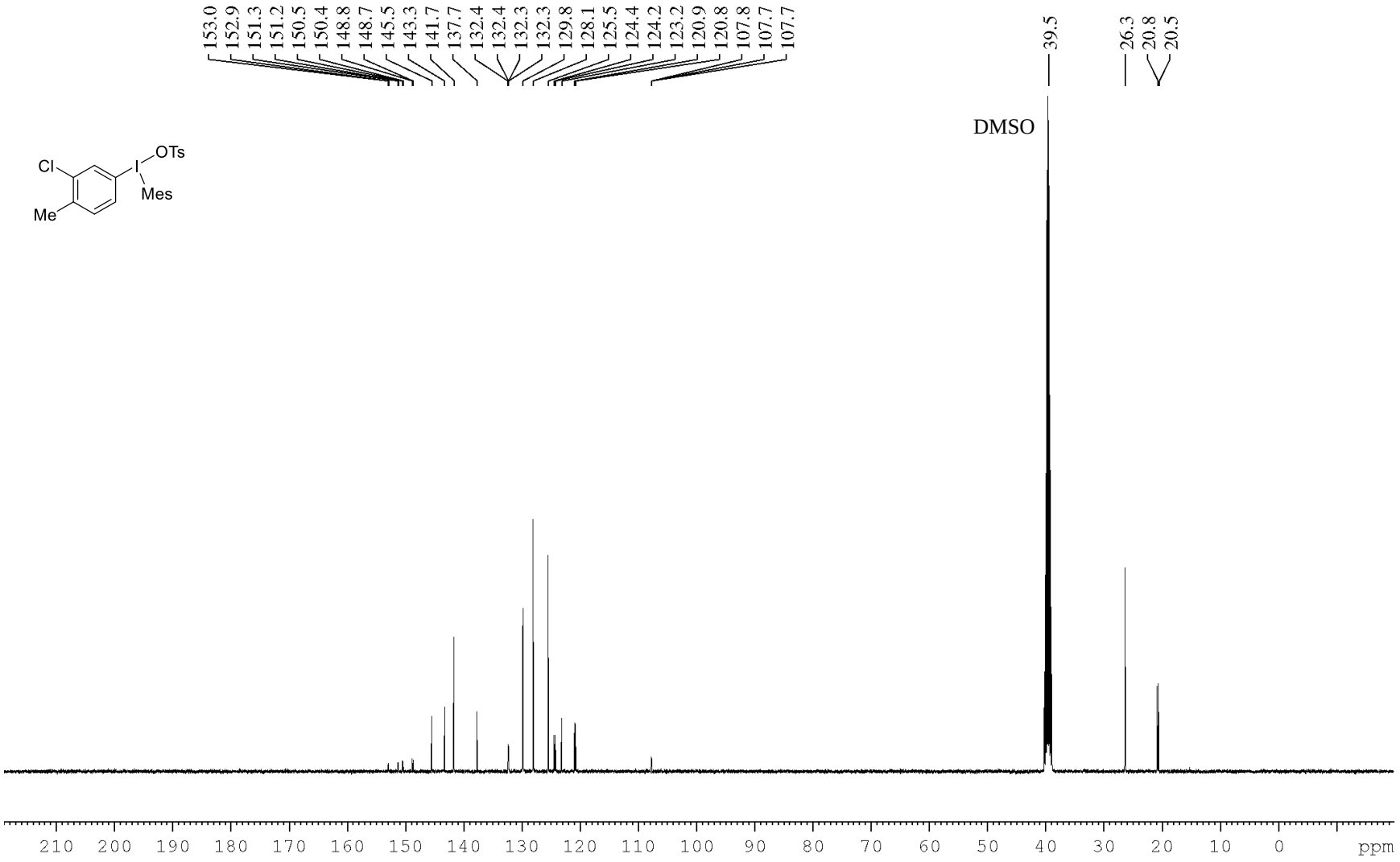
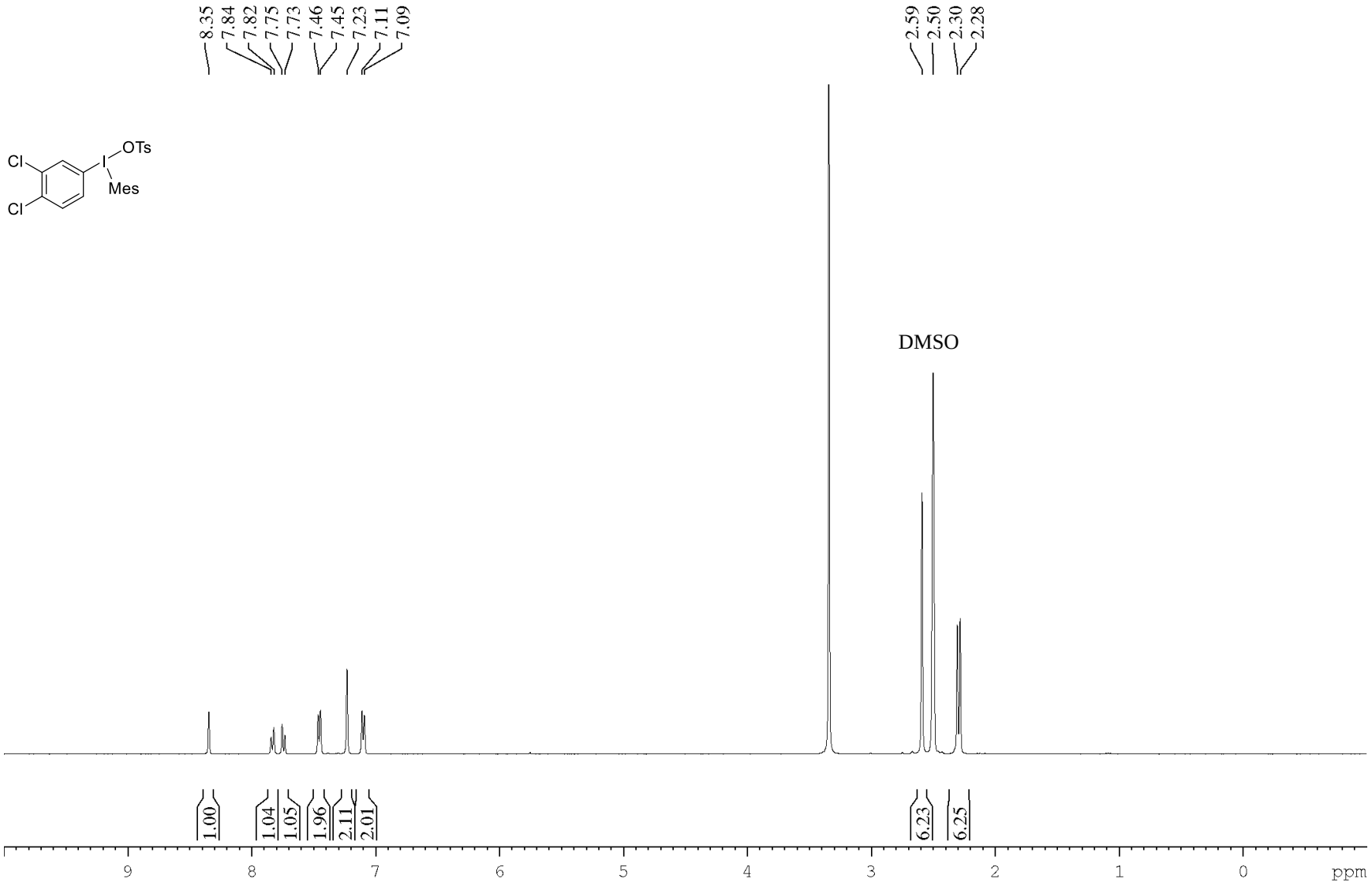
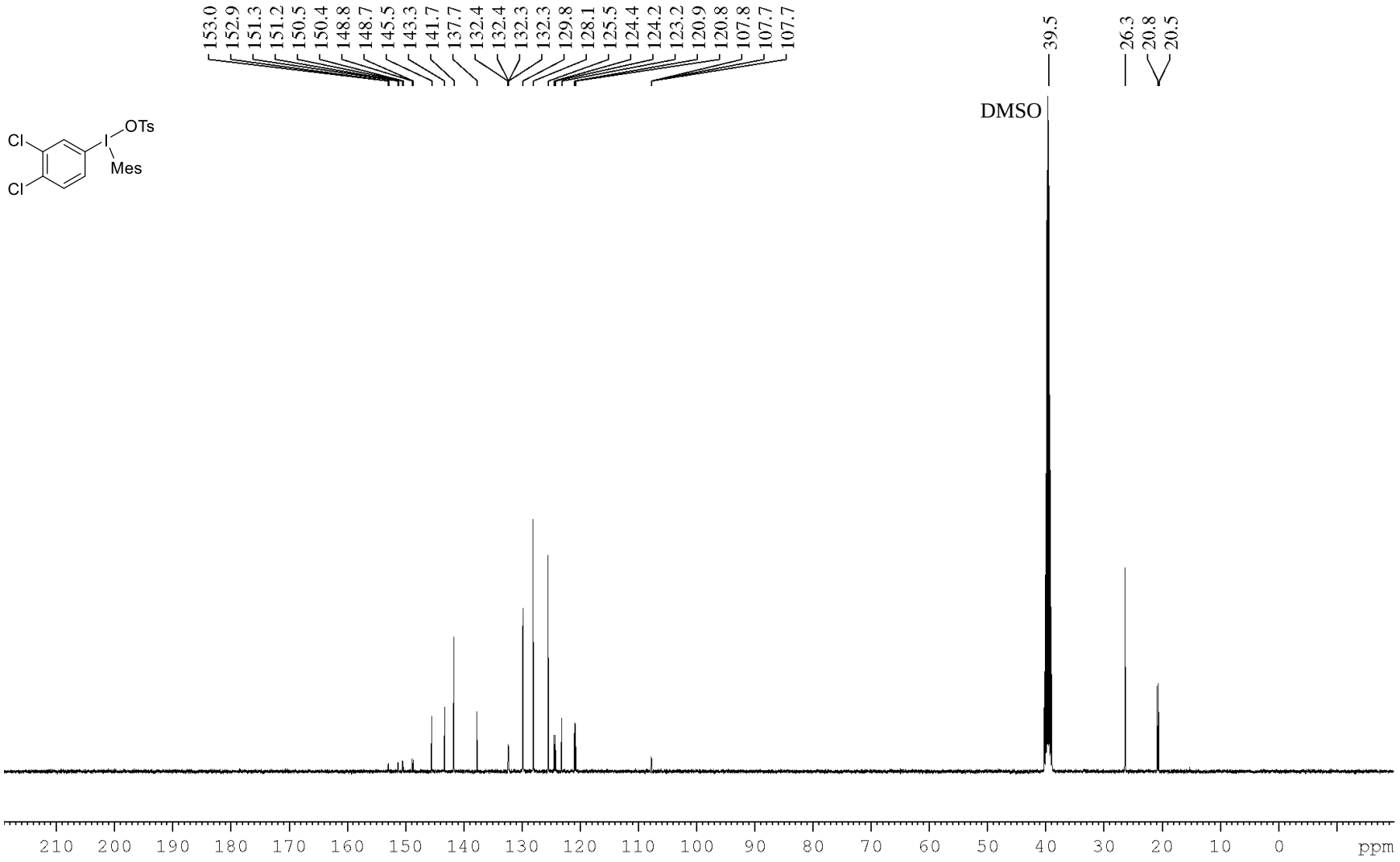


^{1}H NMR of 1b in DMSO-d_6 at 400 MHz



^{13}C {^{1}H} NMR of 1b in DMSO-d_6 at 101 MHz



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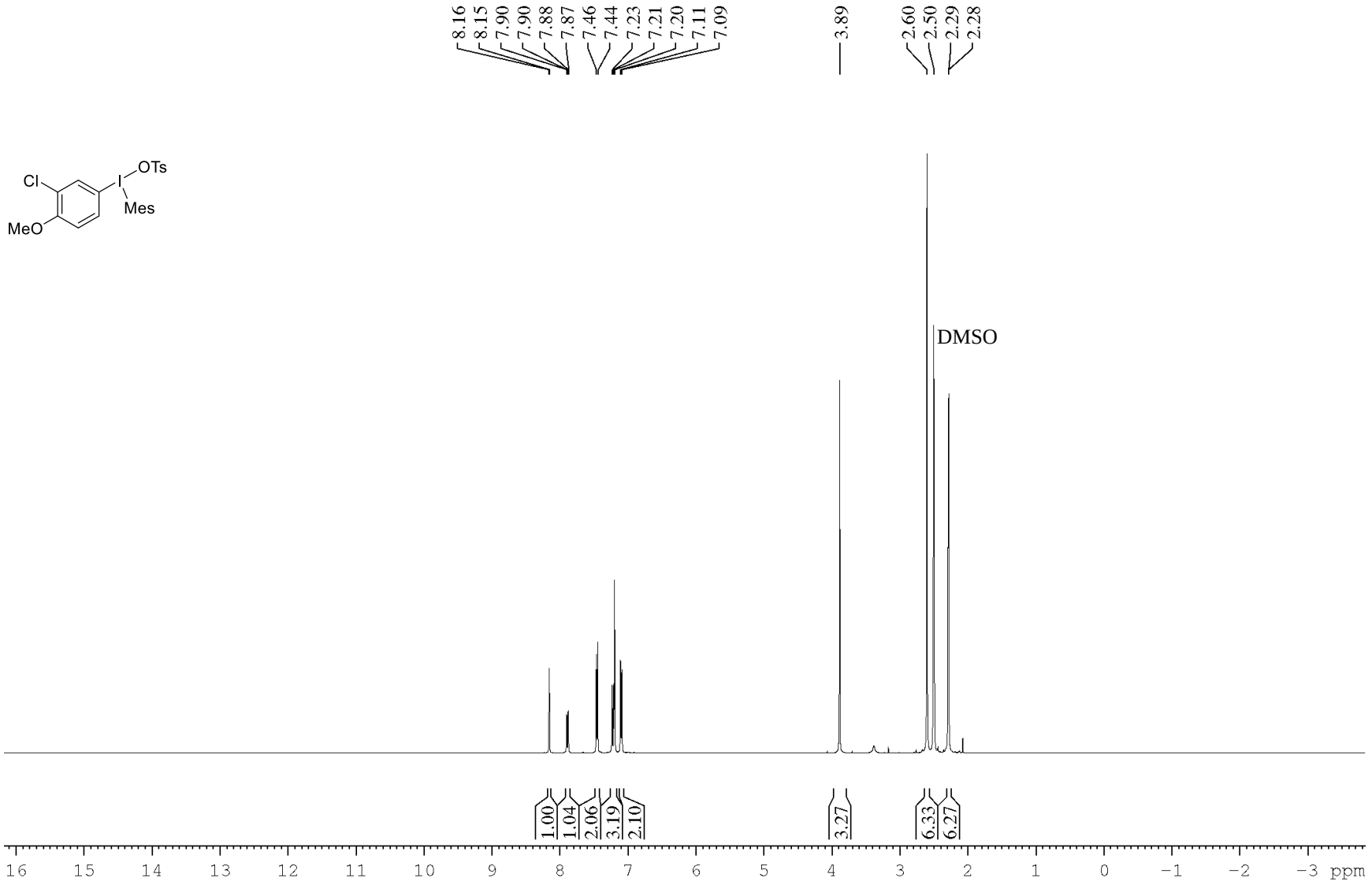

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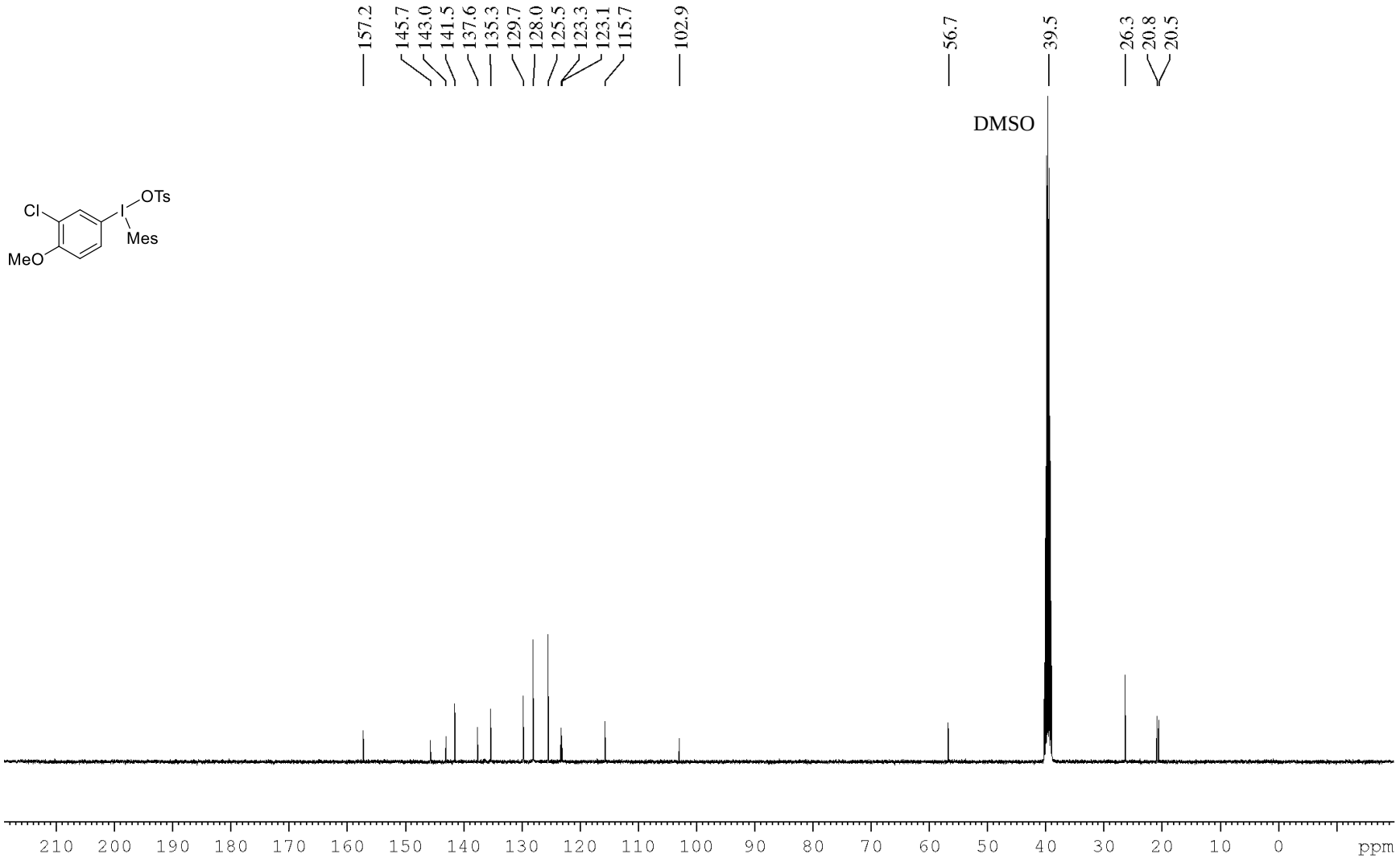

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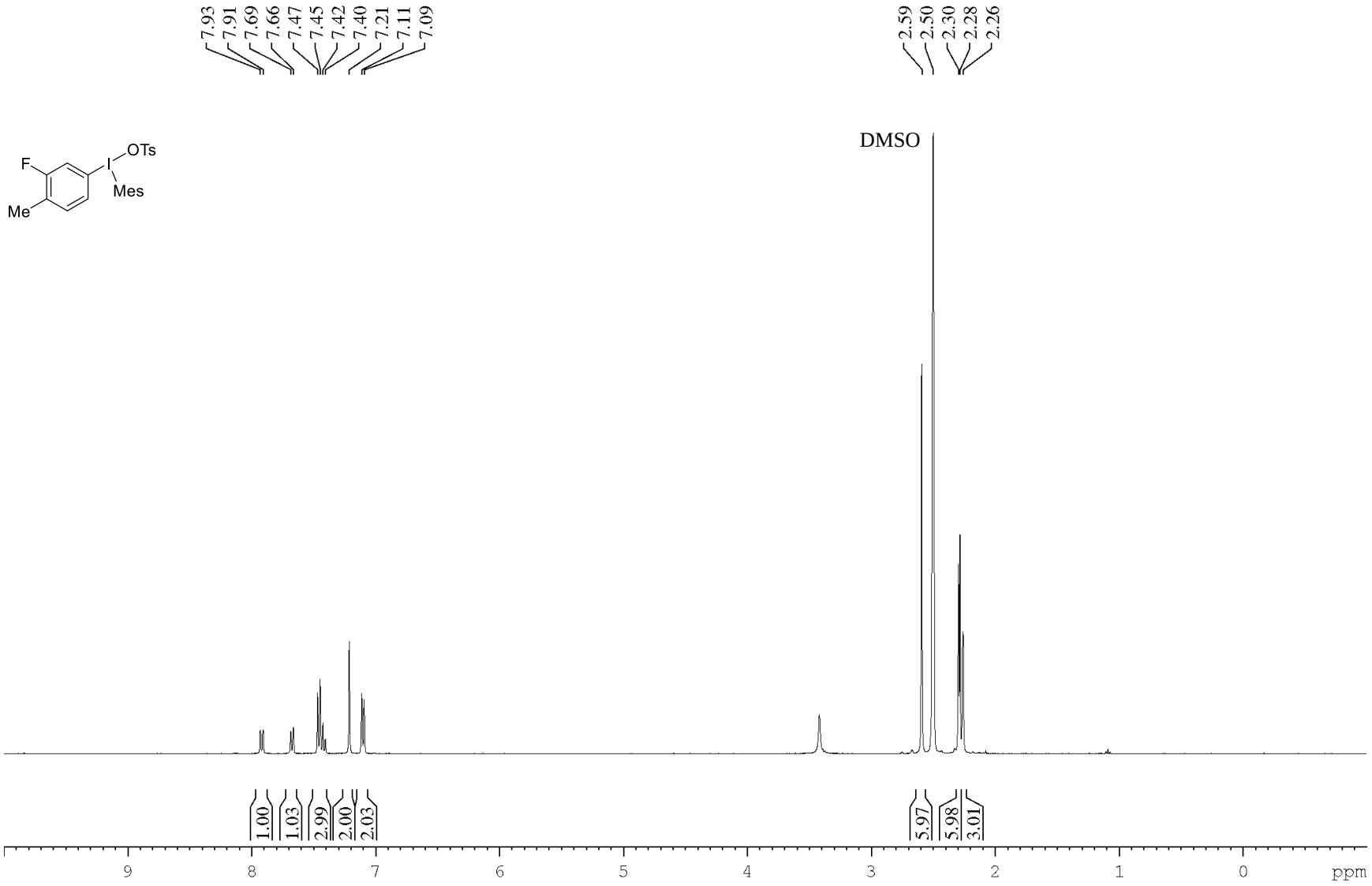

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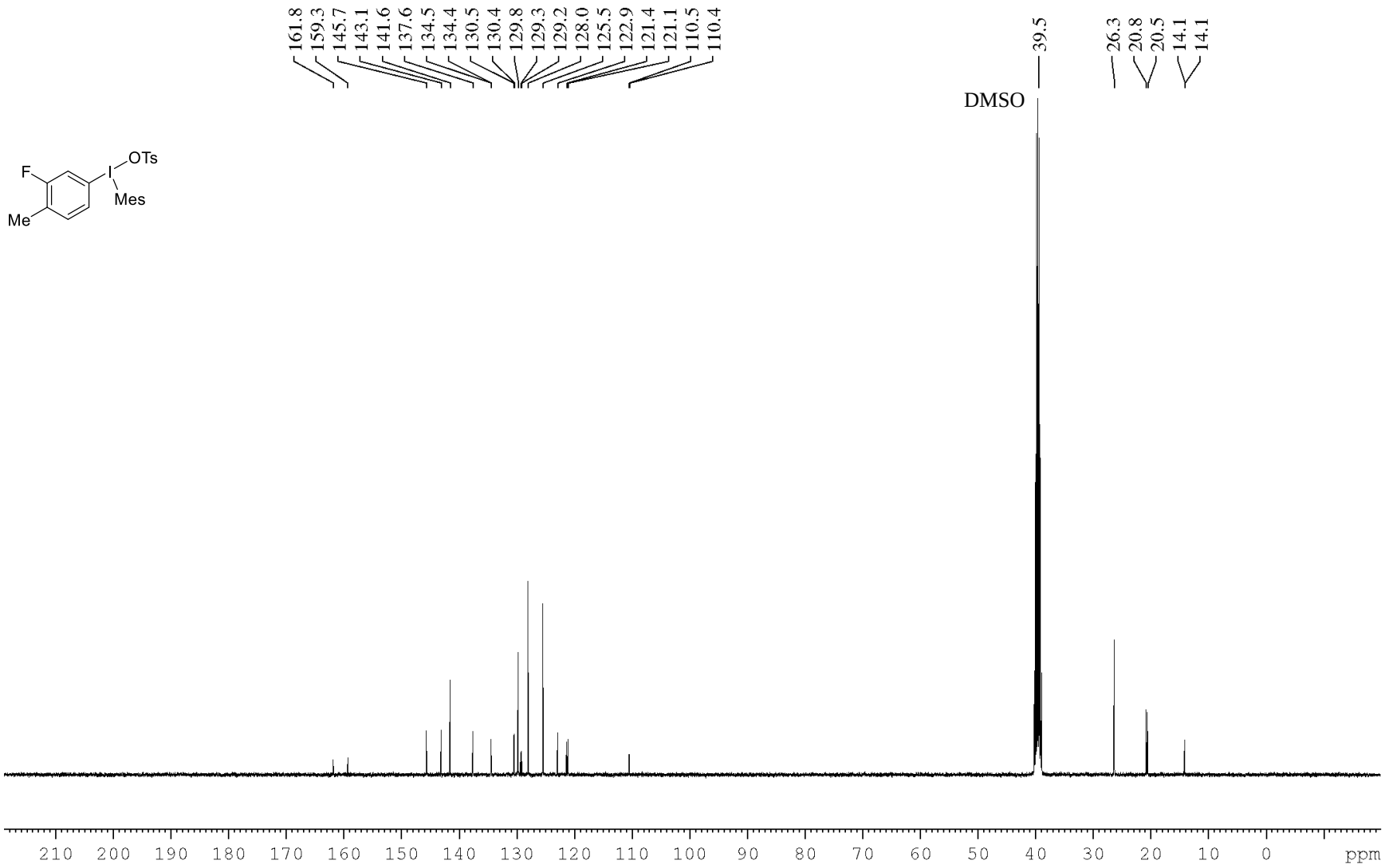
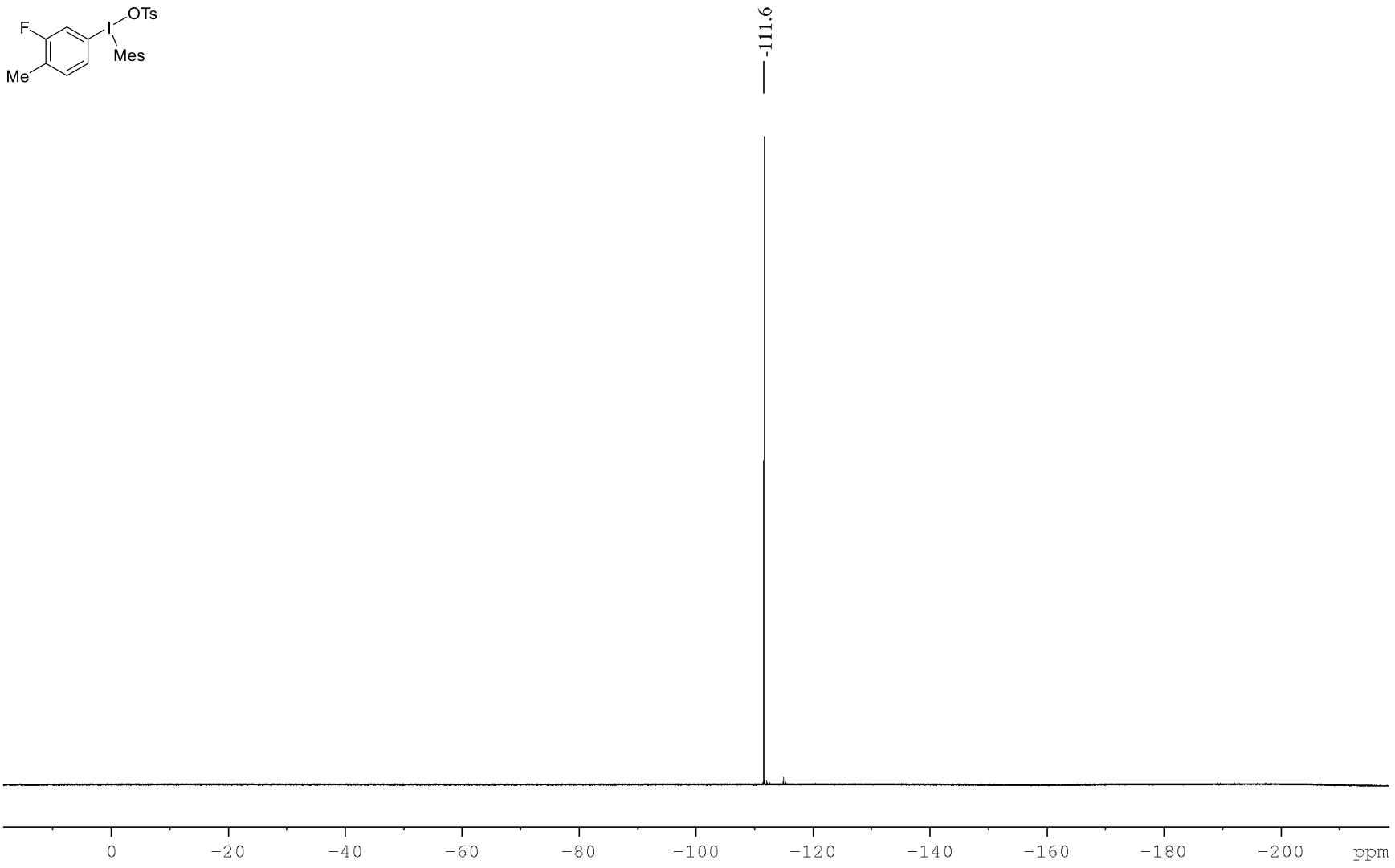
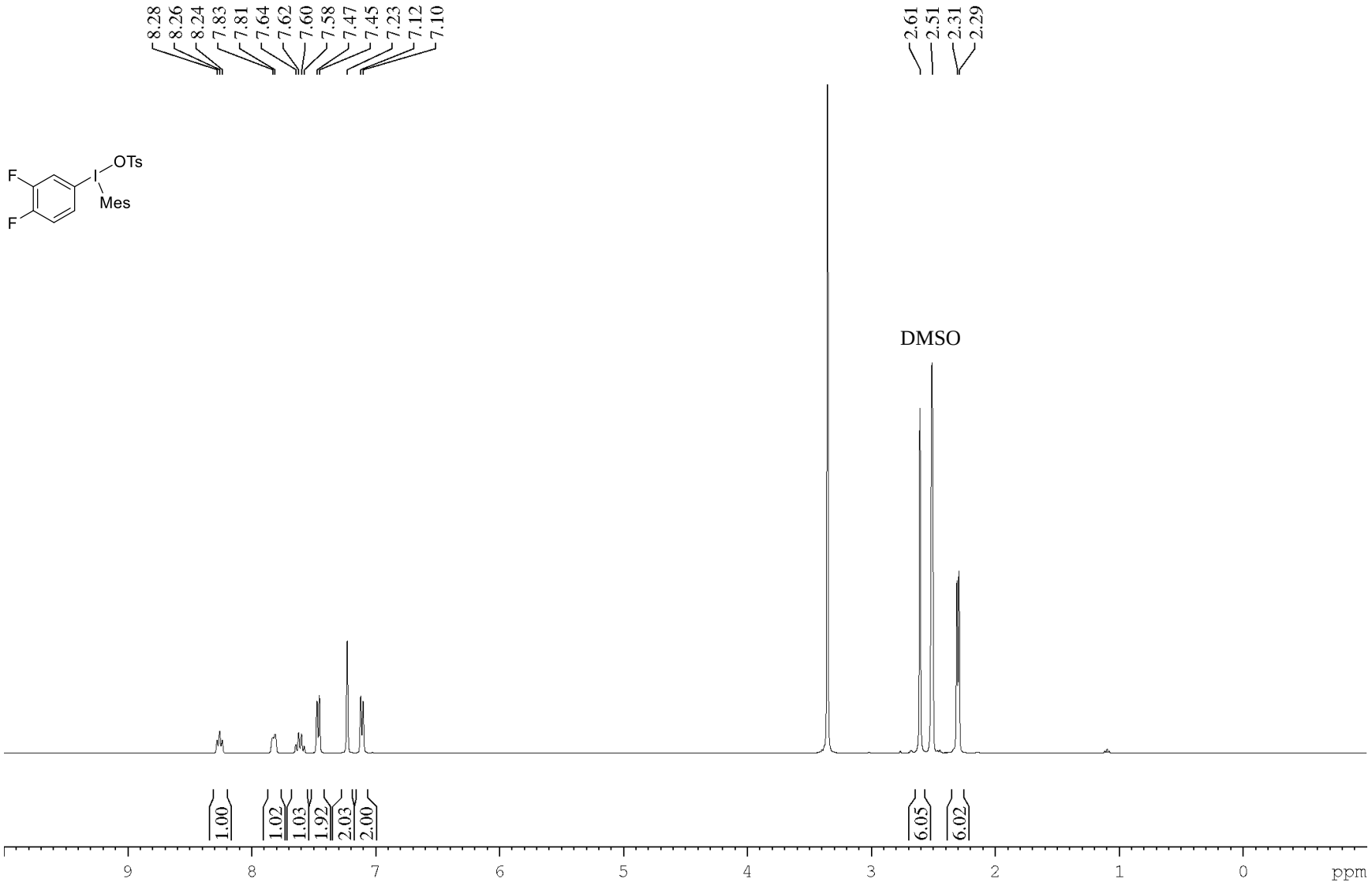


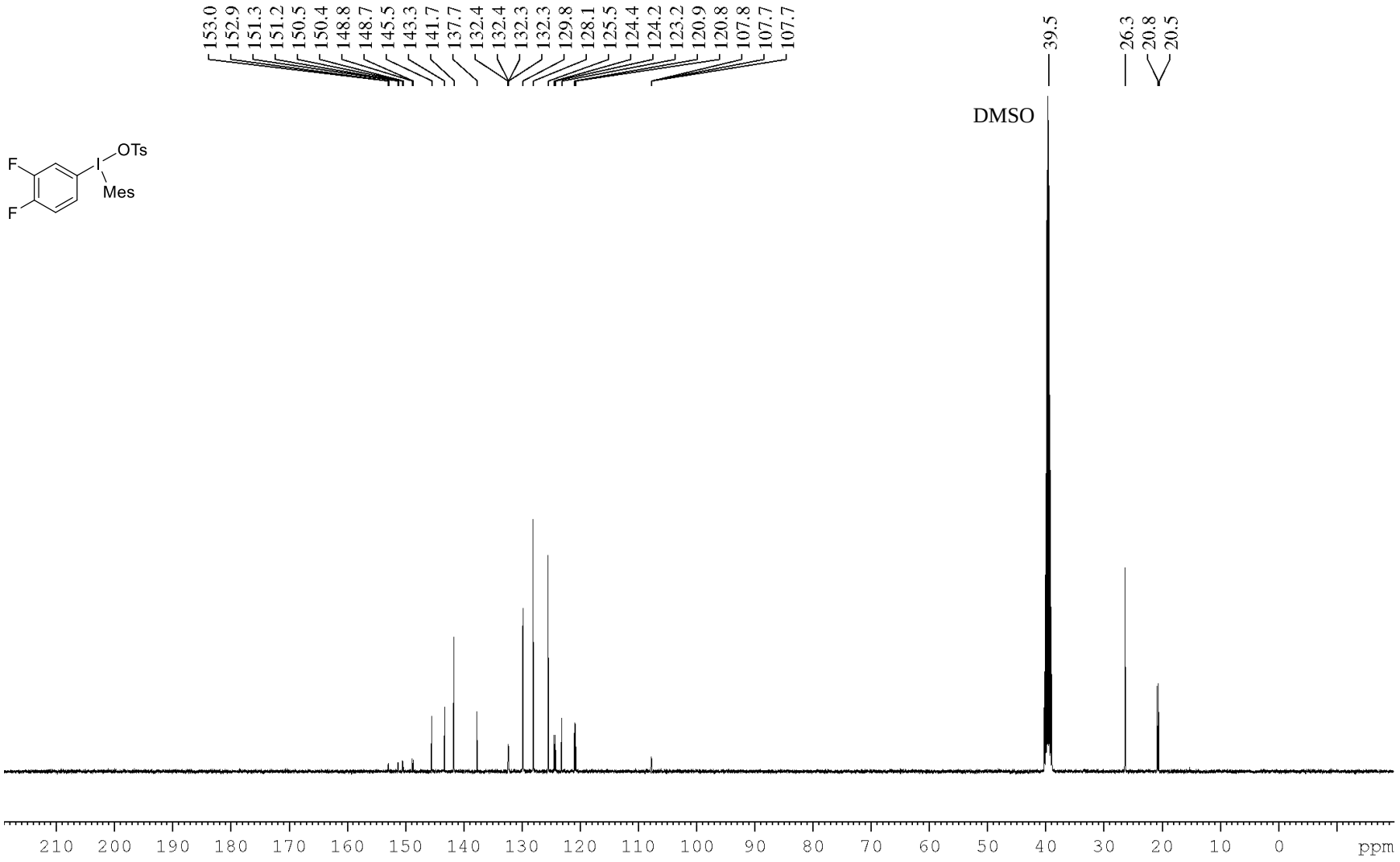
^{19}F {^{1}H} NMR of 1f in DMSO-d_6 at 376 MHz



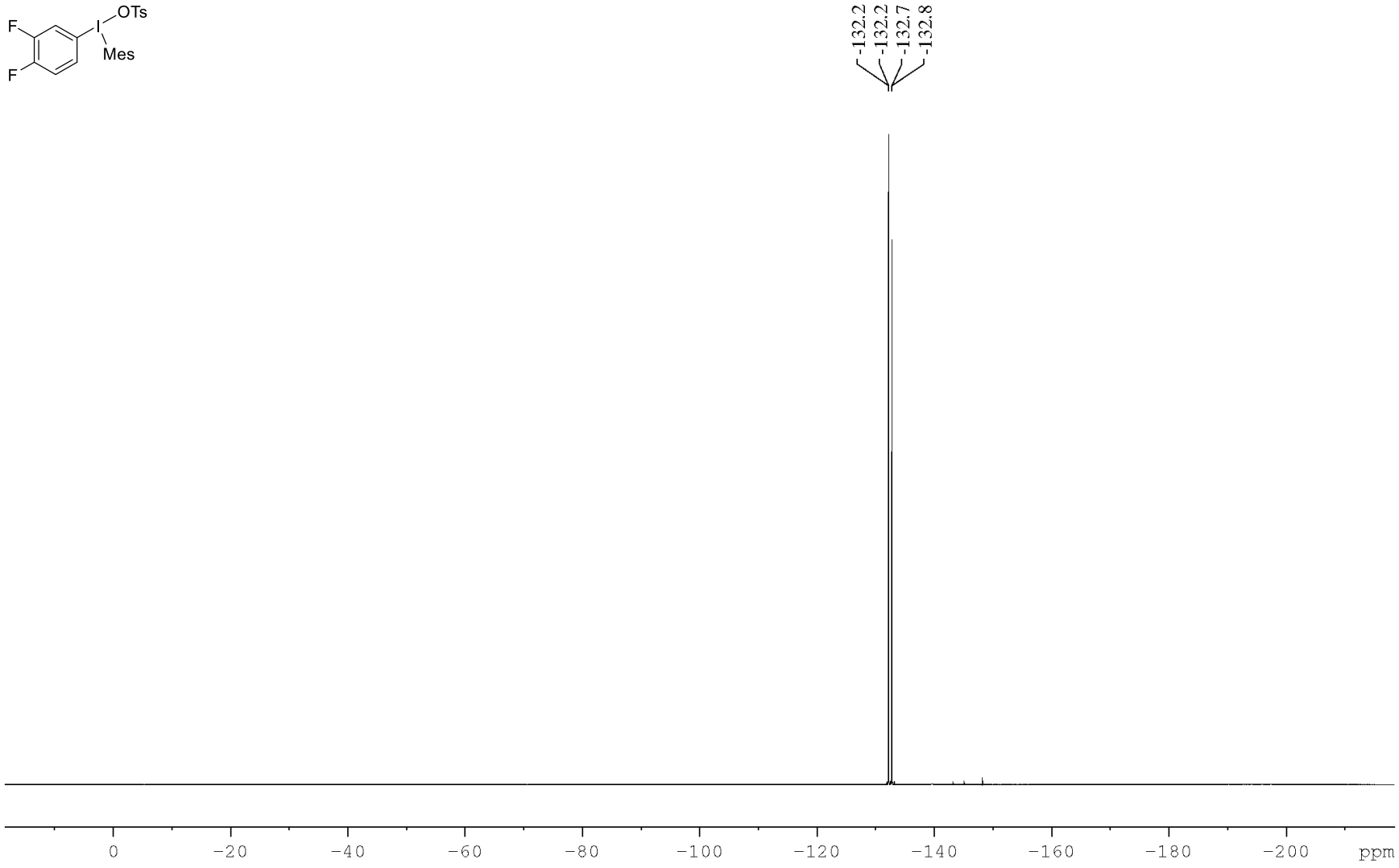
^{1}H NMR of 1g in DMSO-d_6 at 400 MHz



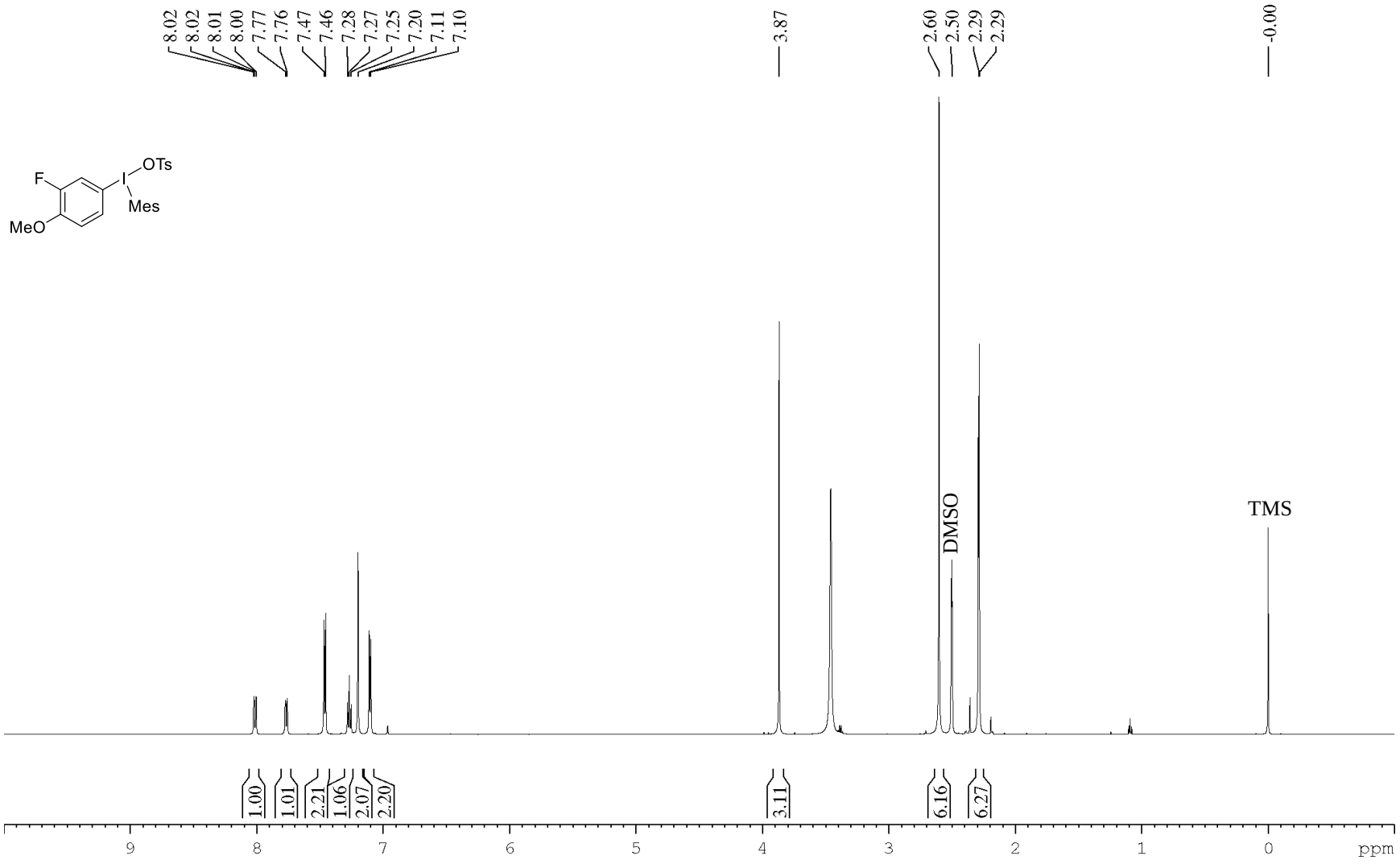
^{13}C {^{1}H} NMR of 1g in DMSO-d_6 at 101 MHz



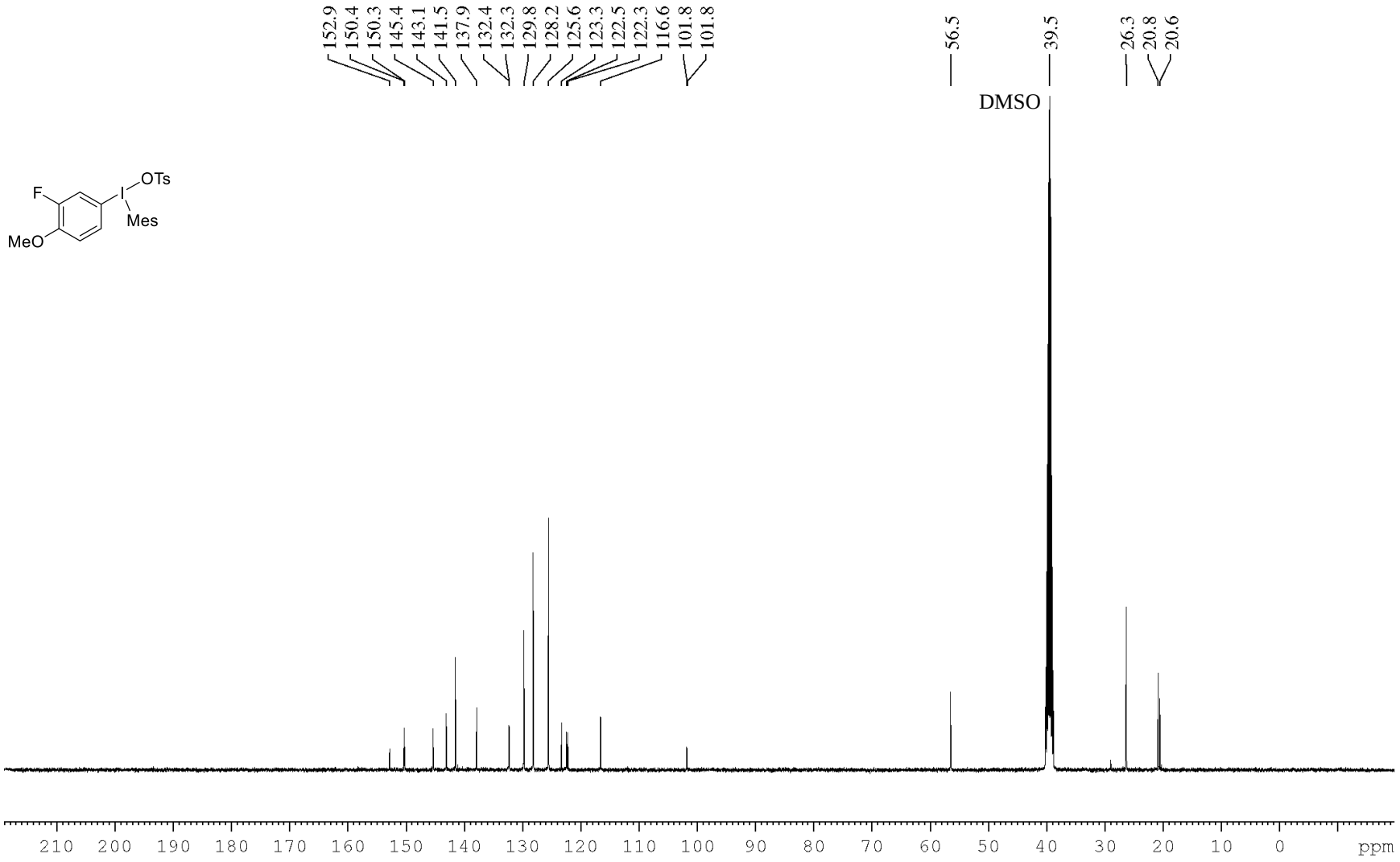
^{19}F {^{1}H} NMR of 1g in DMSO-d_6 at 376 MHz



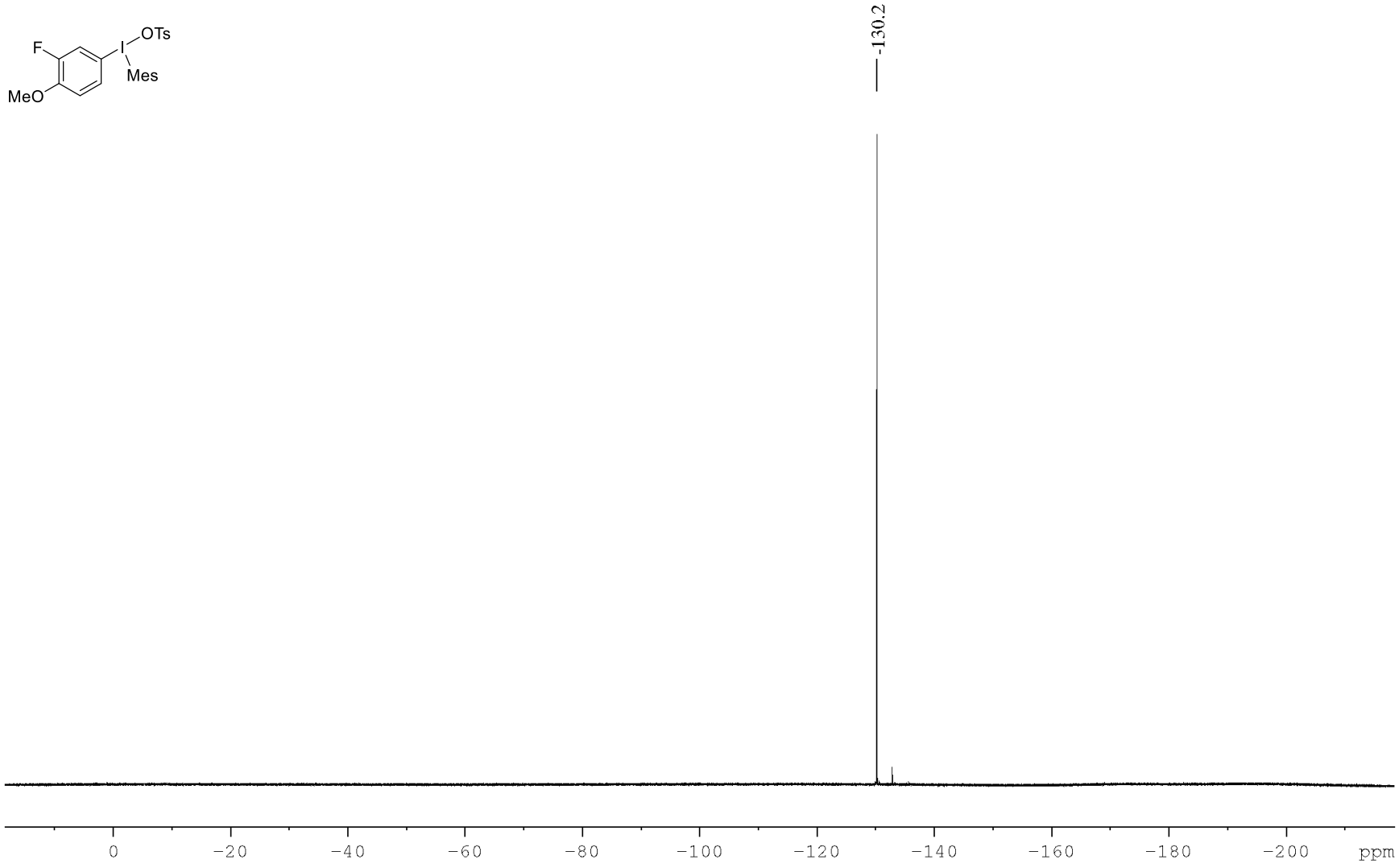
^{1}H NMR of 1h in DMSO-d_6 with 0.05% v/v TMS at 400 MHz



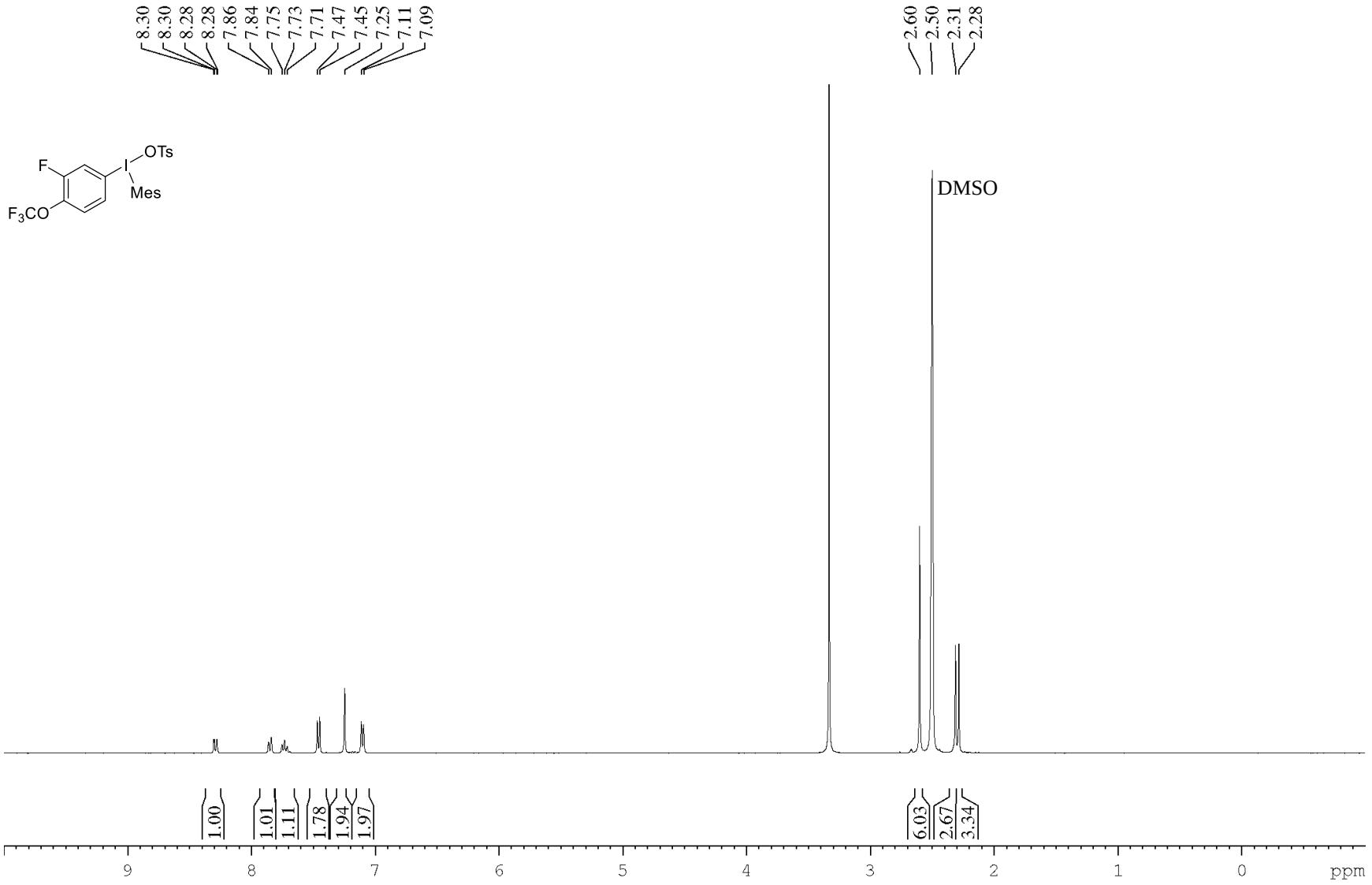
^{13}C {^{1}H} NMR of 1h in DMSO-d_6 with 0.05% v/v TMS at 101 MHz



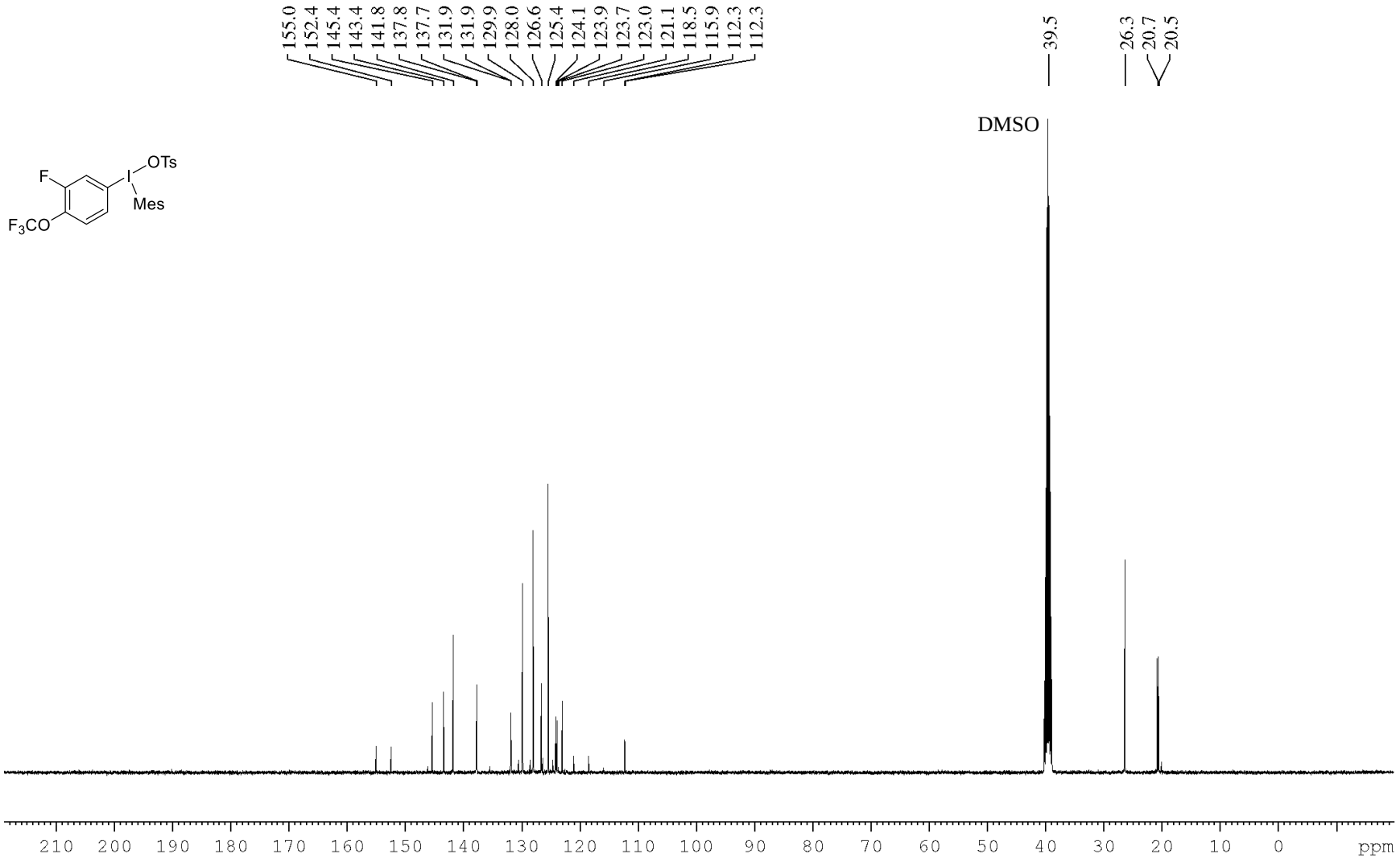
^{19}F {^{1}H} NMR of 1h in DMSO-d_6 with 0.05% v/v TMS at 376 MHz



^{1}H NMR of 1i in DMSO-d_6 at 400 MHz



^{13}C {^{1}H} NMR of 1i in DMSO-d_6 at 101 MHz



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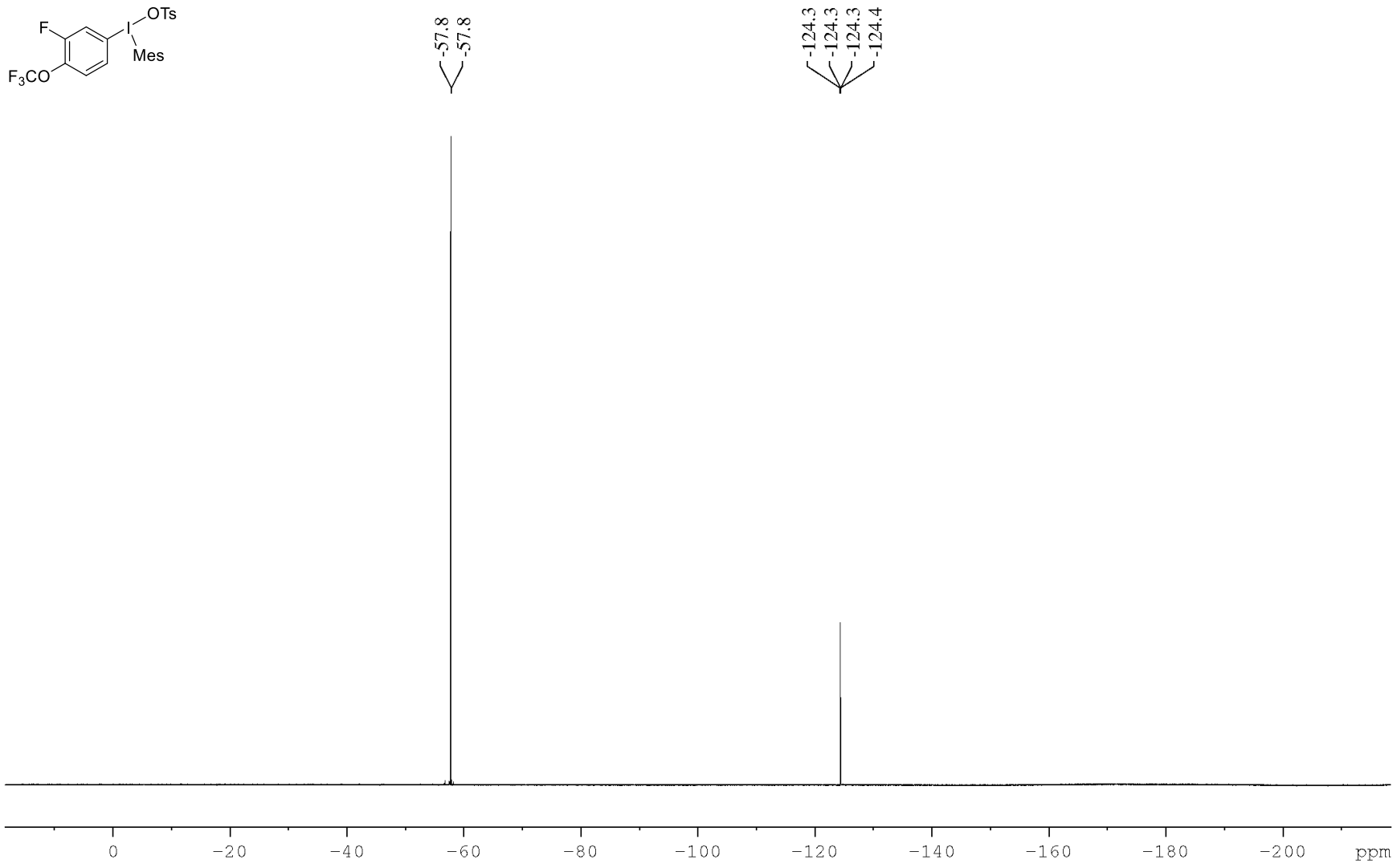

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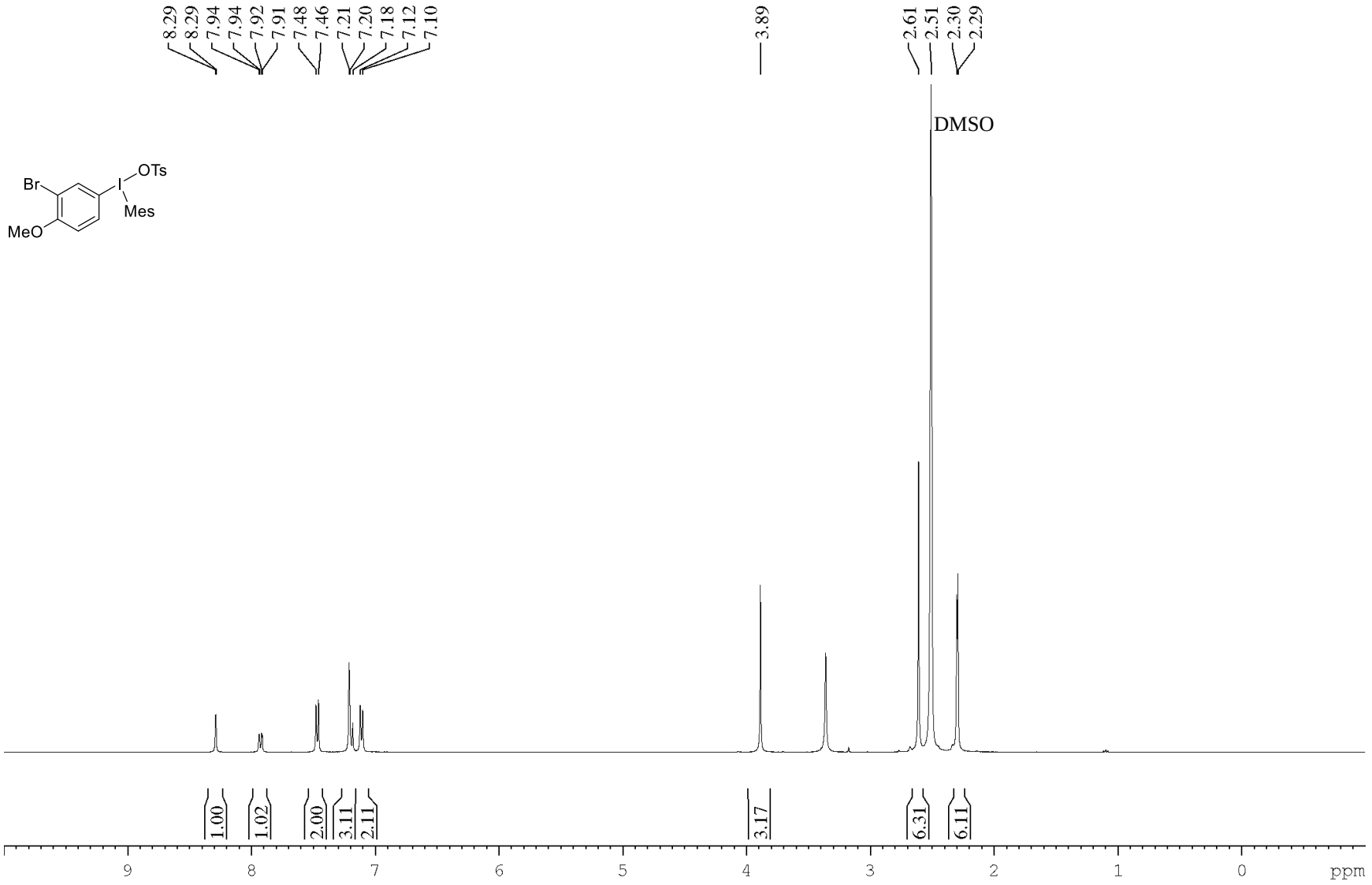

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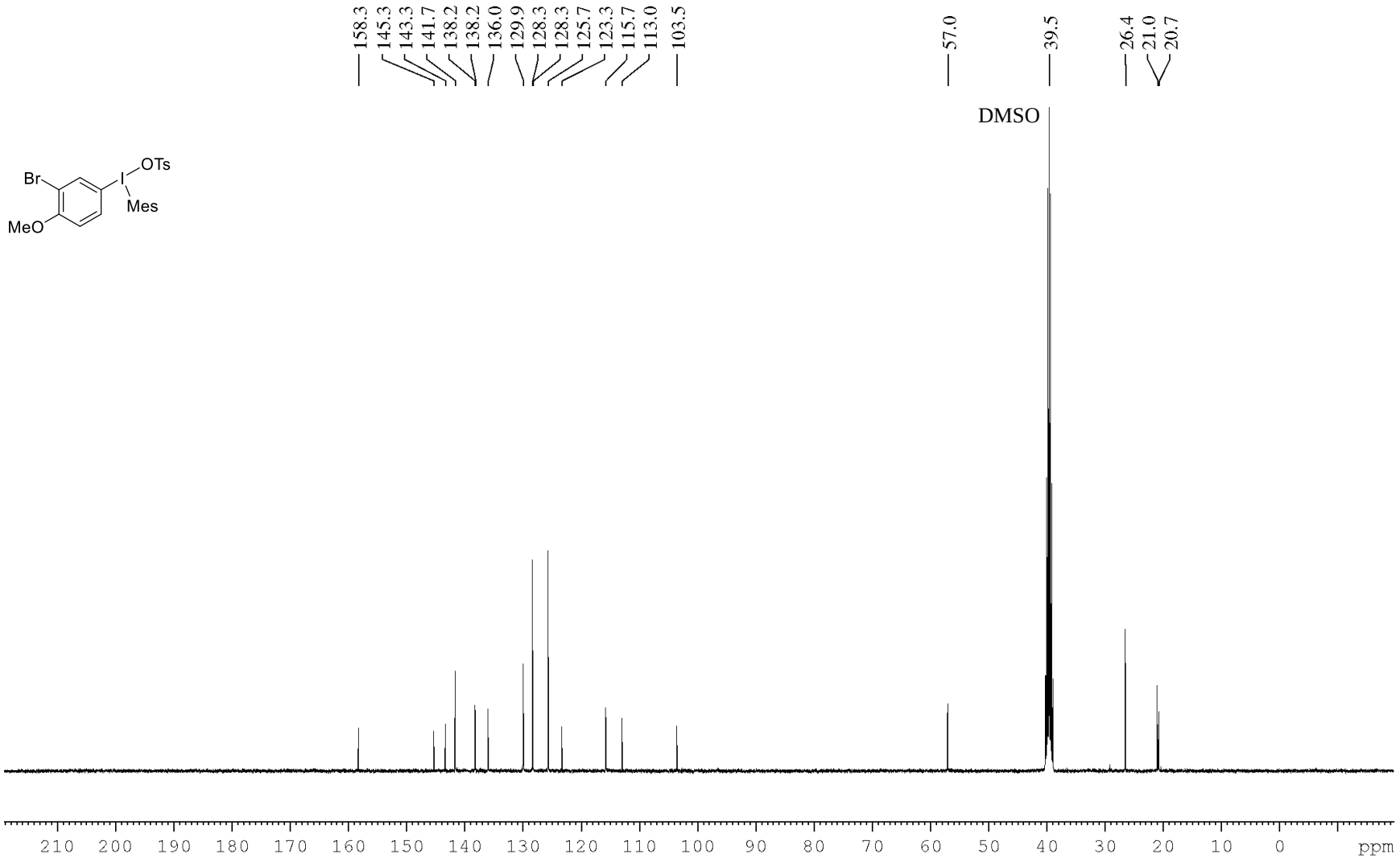

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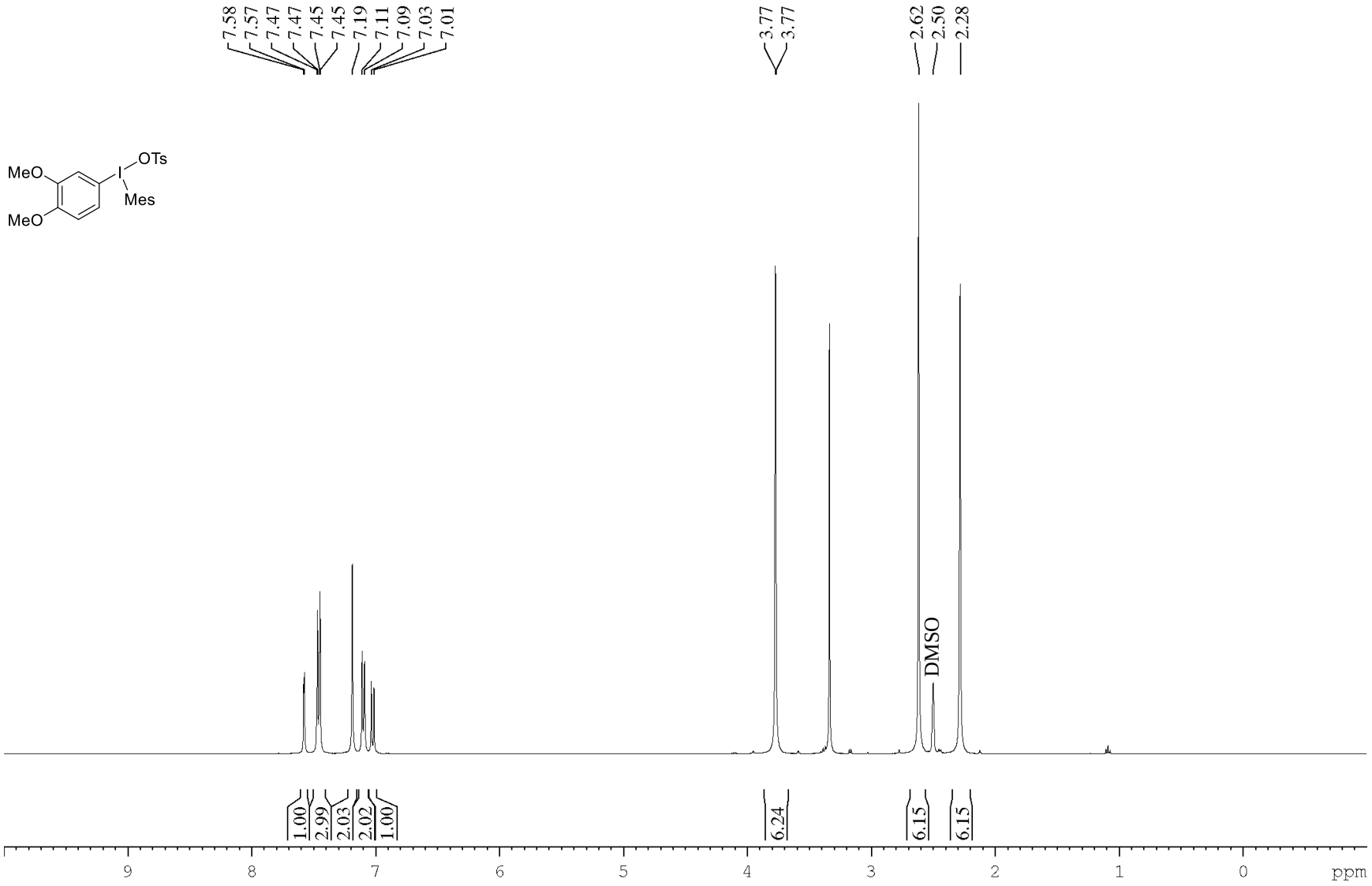

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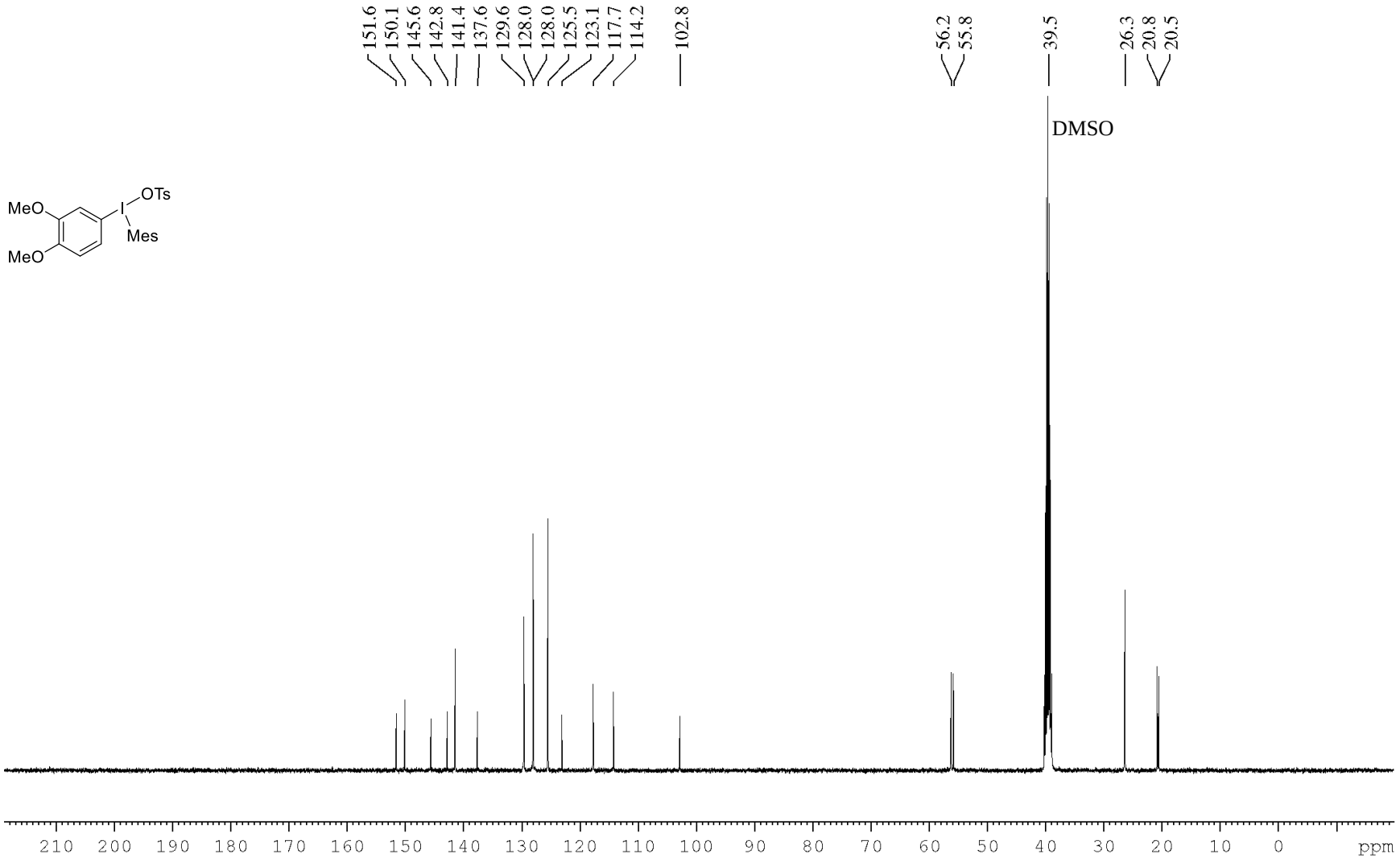

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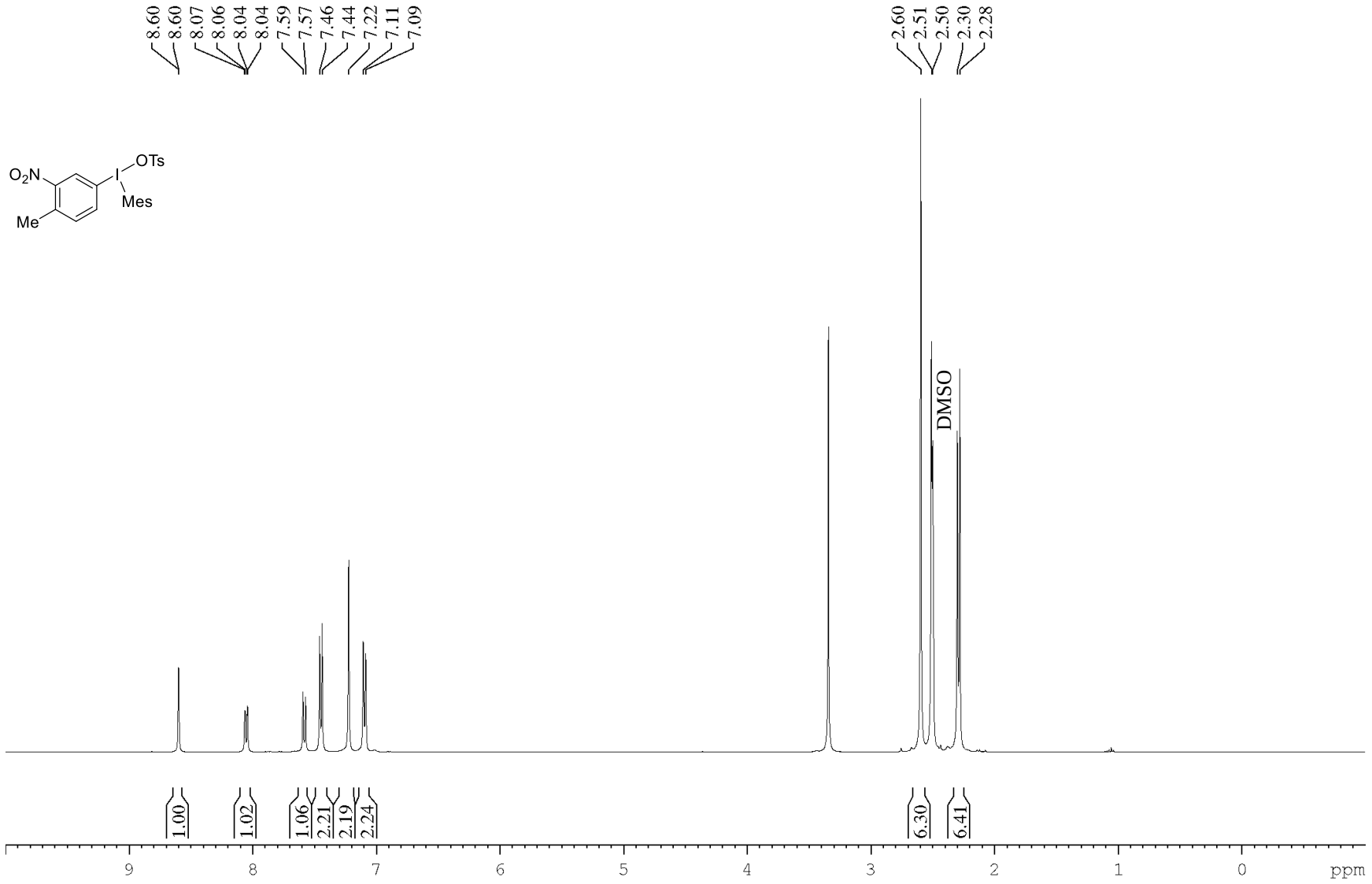

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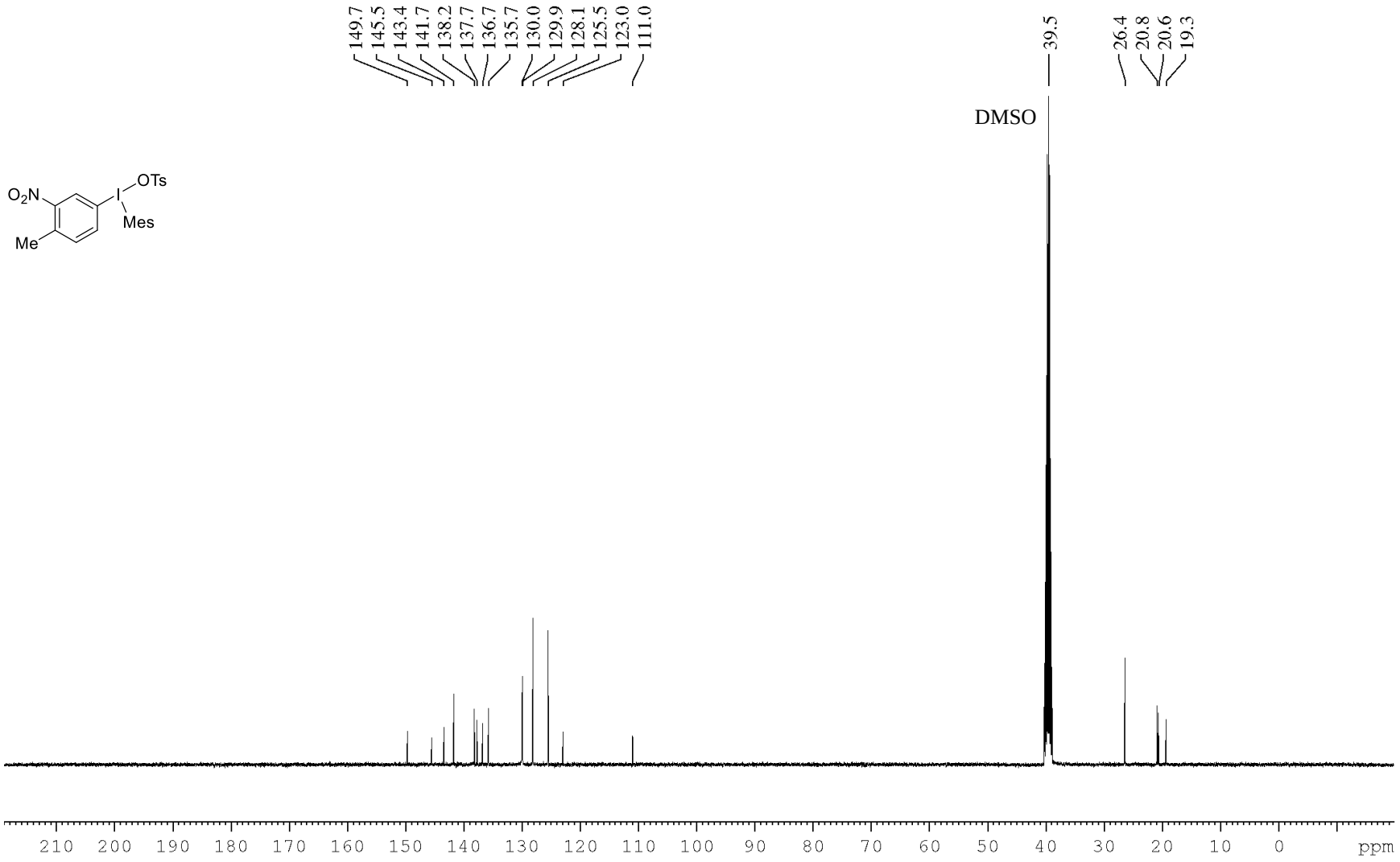

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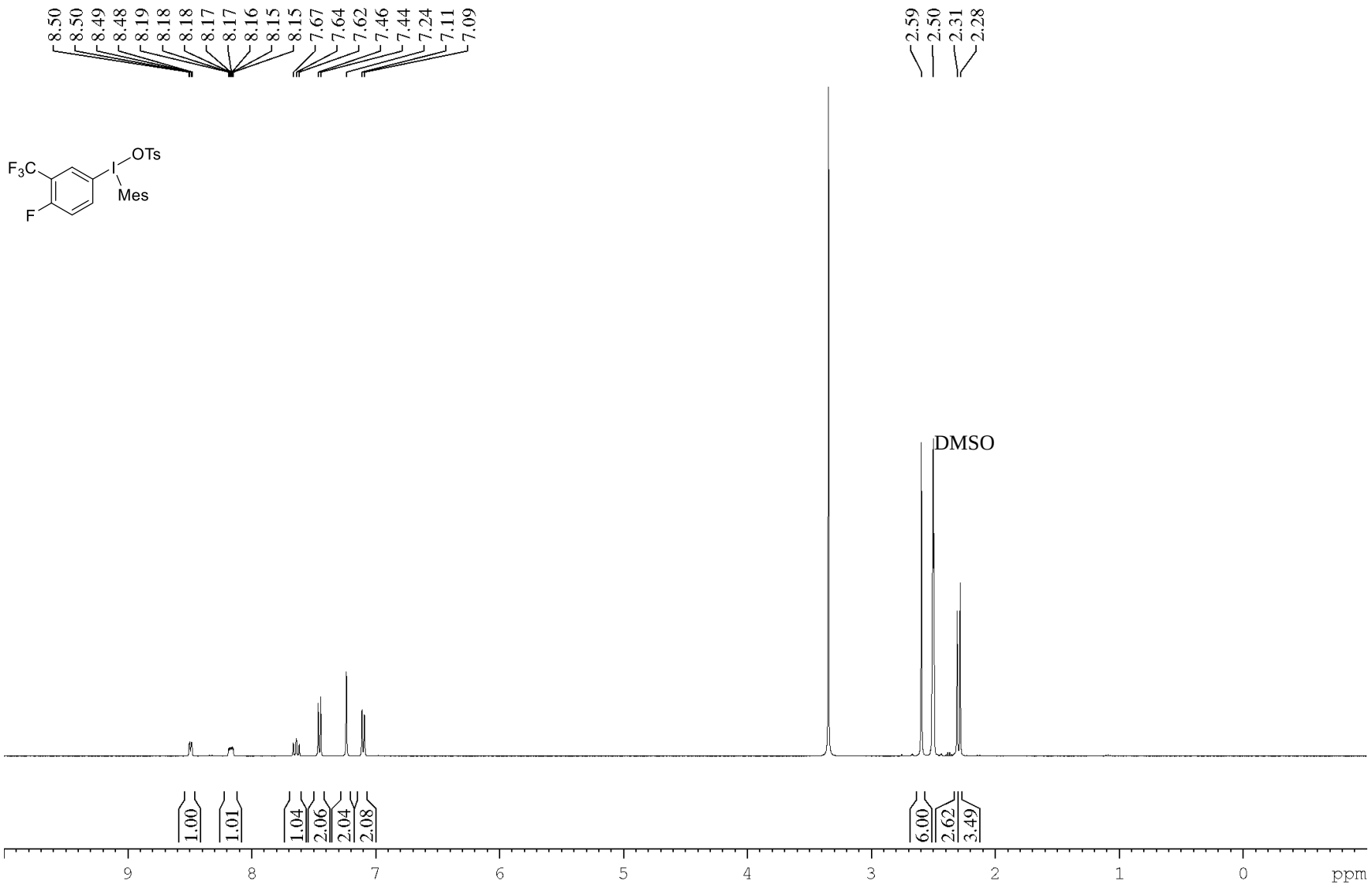

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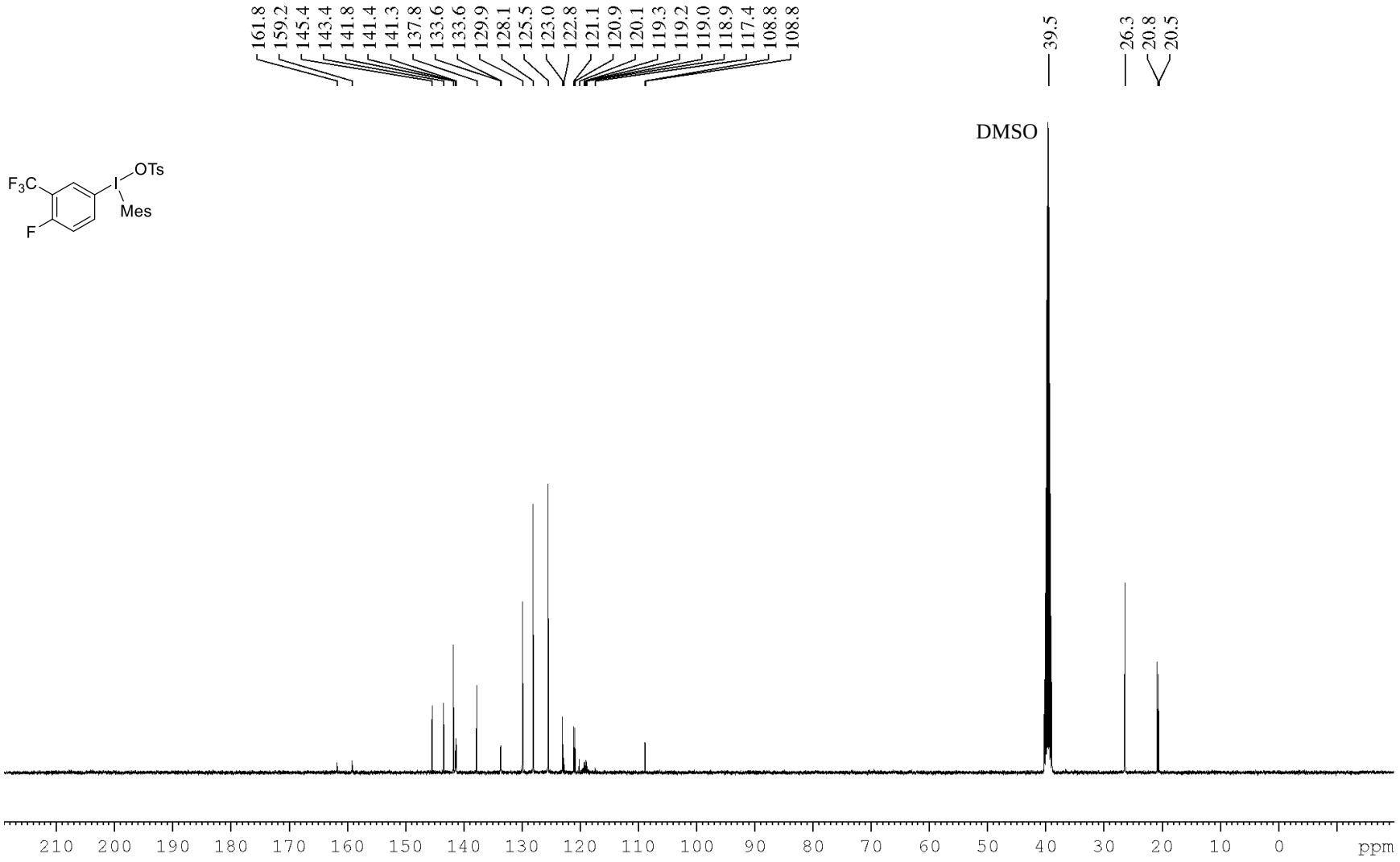
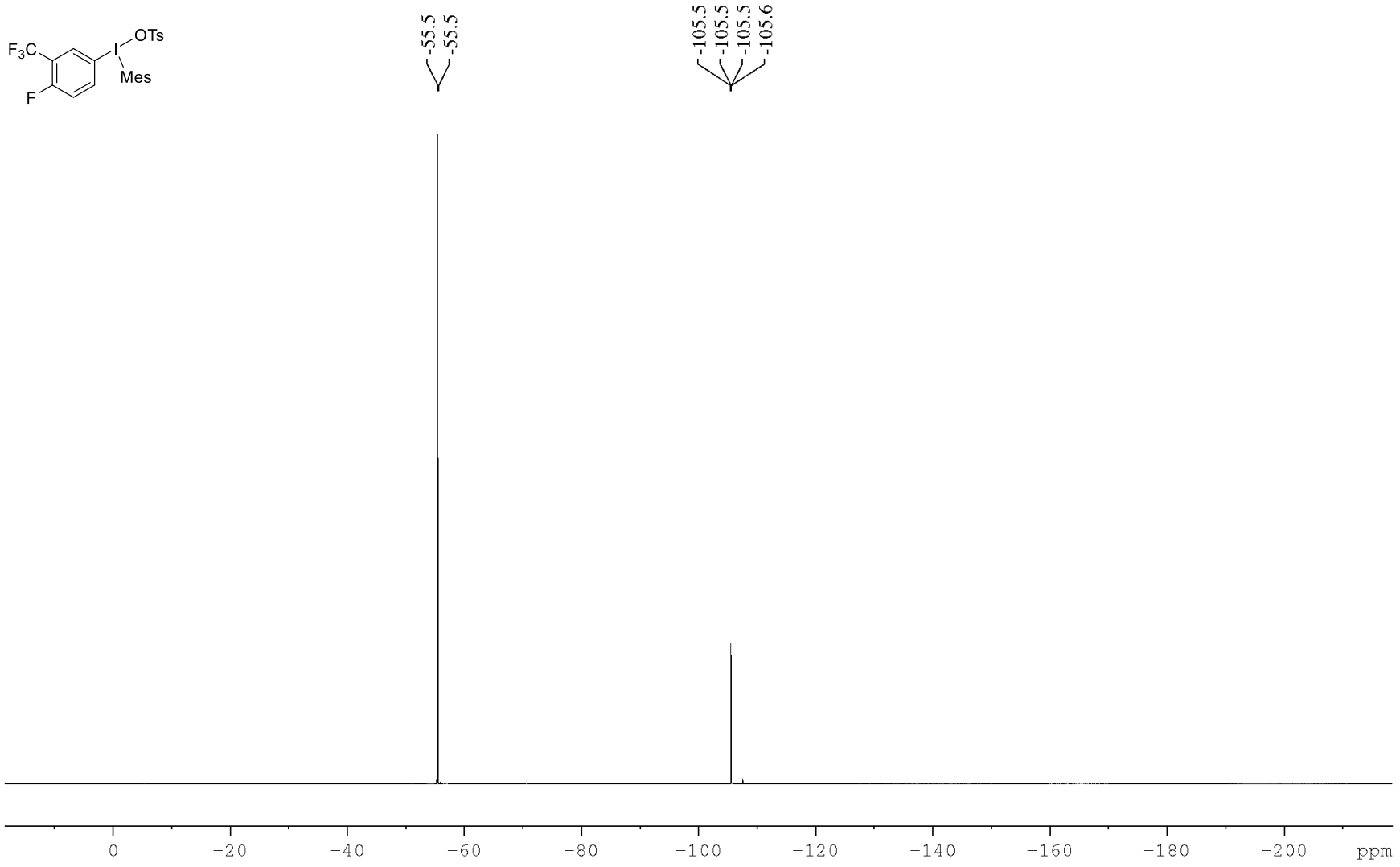
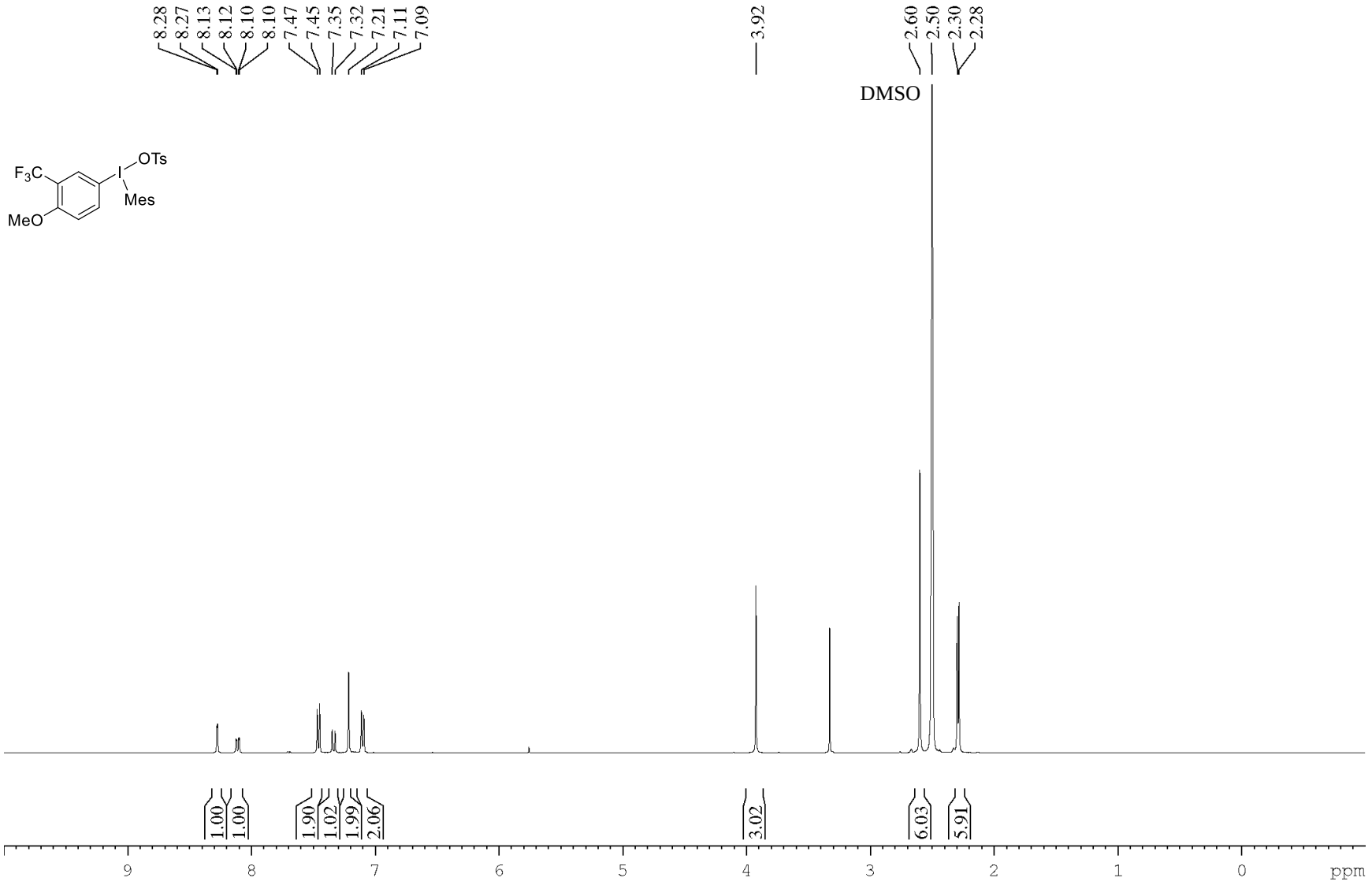


^{19}F {^{1}H} NMR of 1n in DMSO-d_6 at 376 MHz



^{1}H NMR of 1o in DMSO-d_6 at 400 MHz



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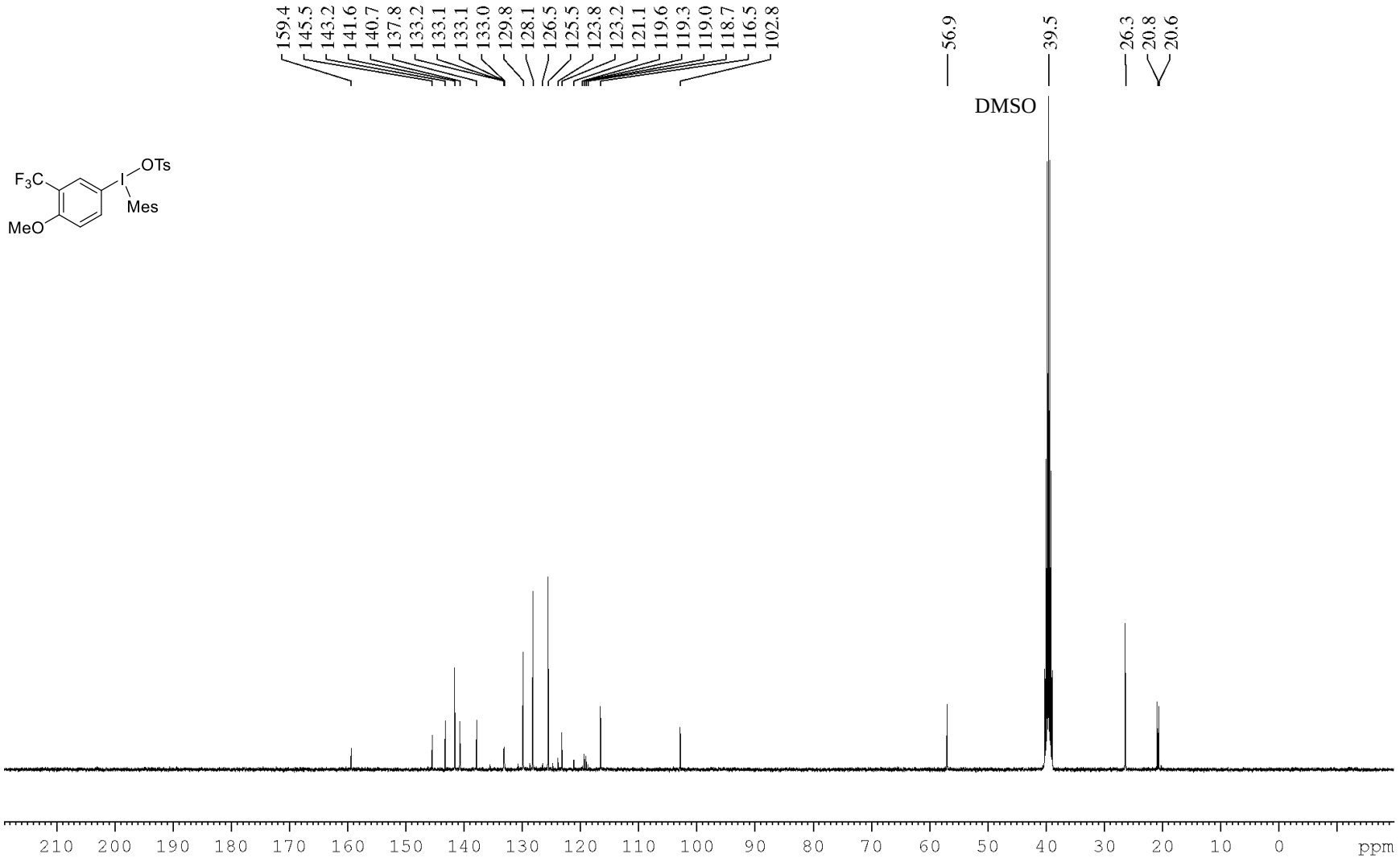

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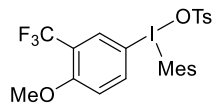
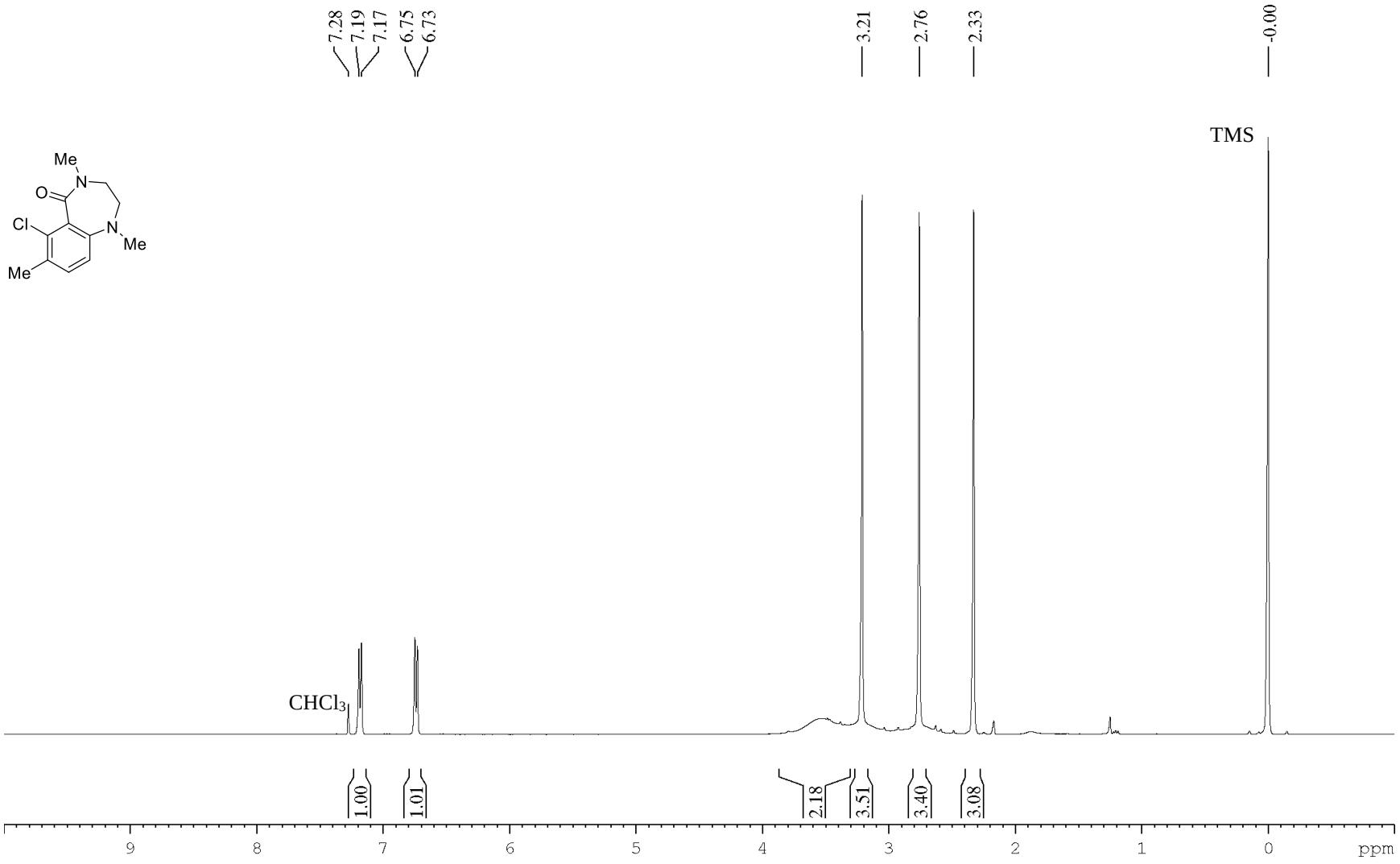
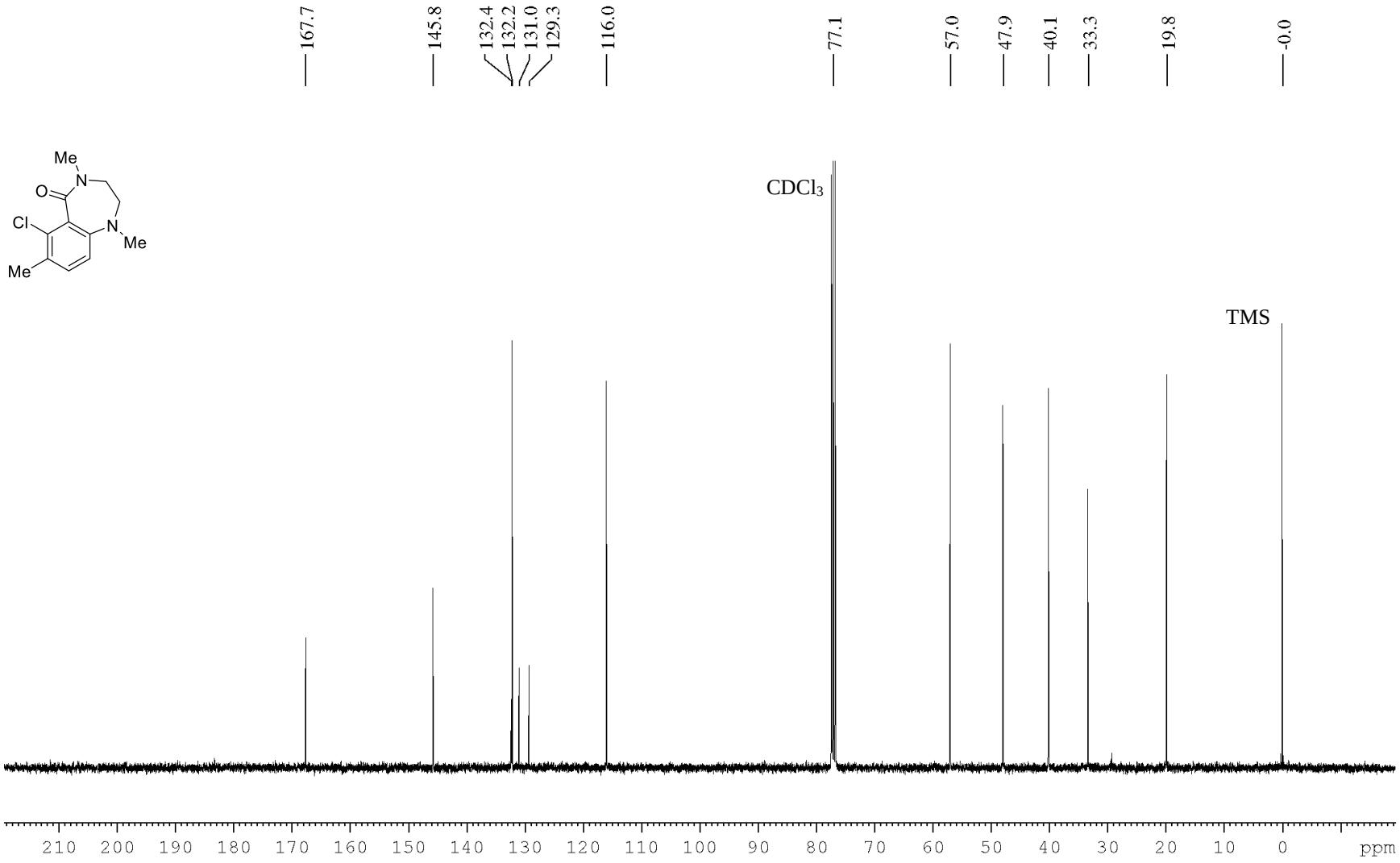


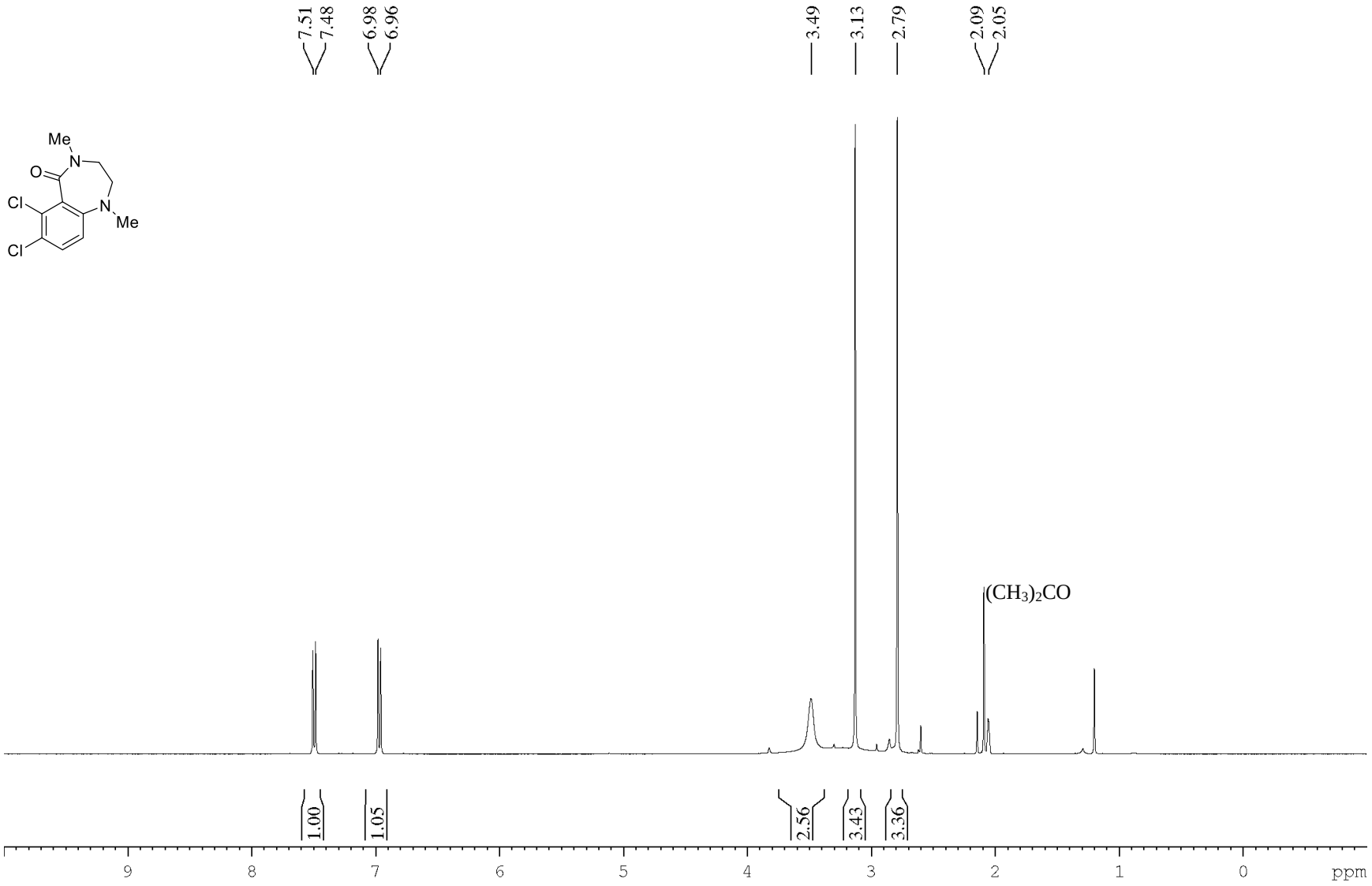
^{1}H NMR of 2a in $CDCl_3$ with 1% v/v TMS at 400 MHz



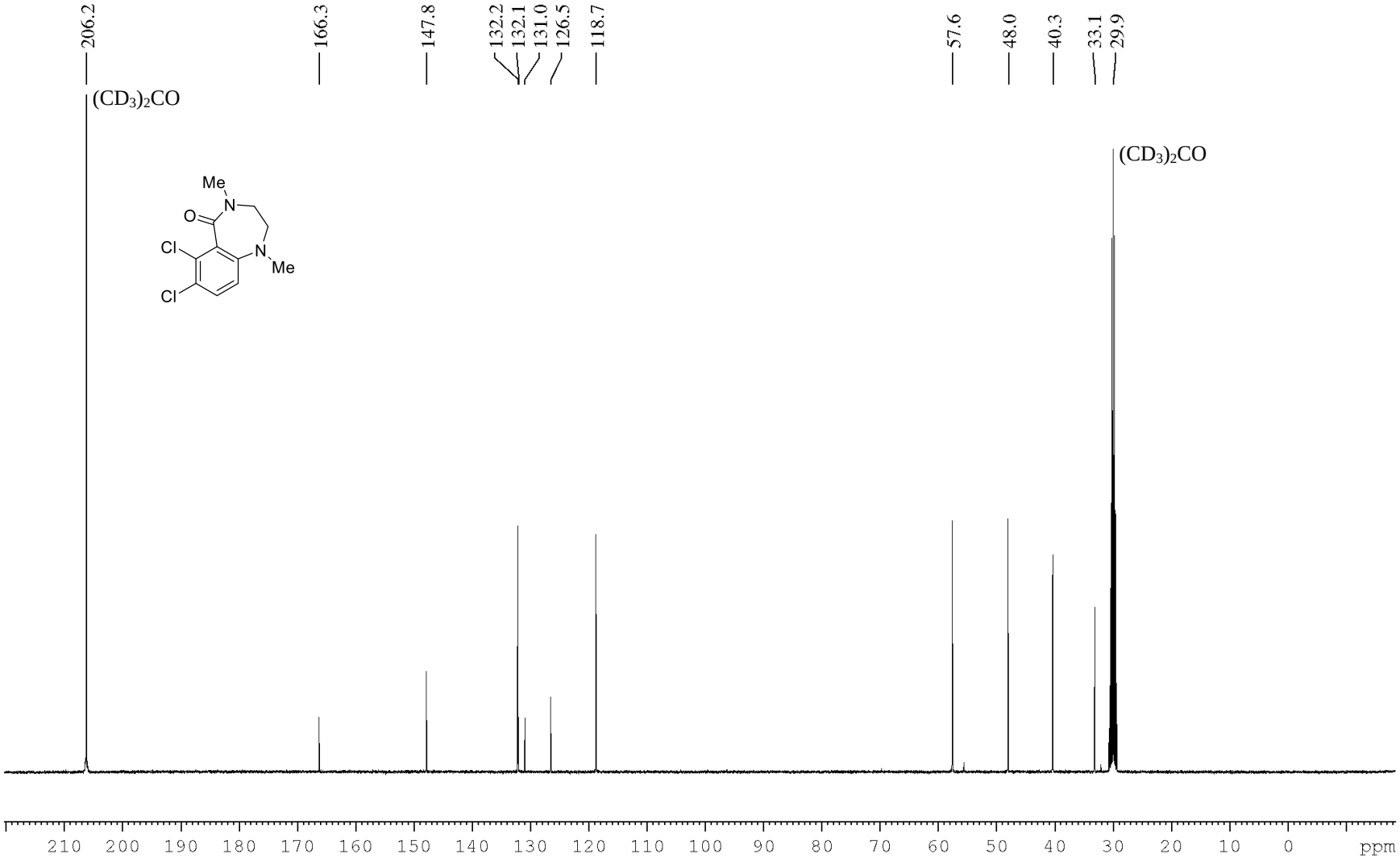
^{13}C {^{1}H} NMR of 2a $CDCl_3$ with 1% v/v TMS at 101 MHz



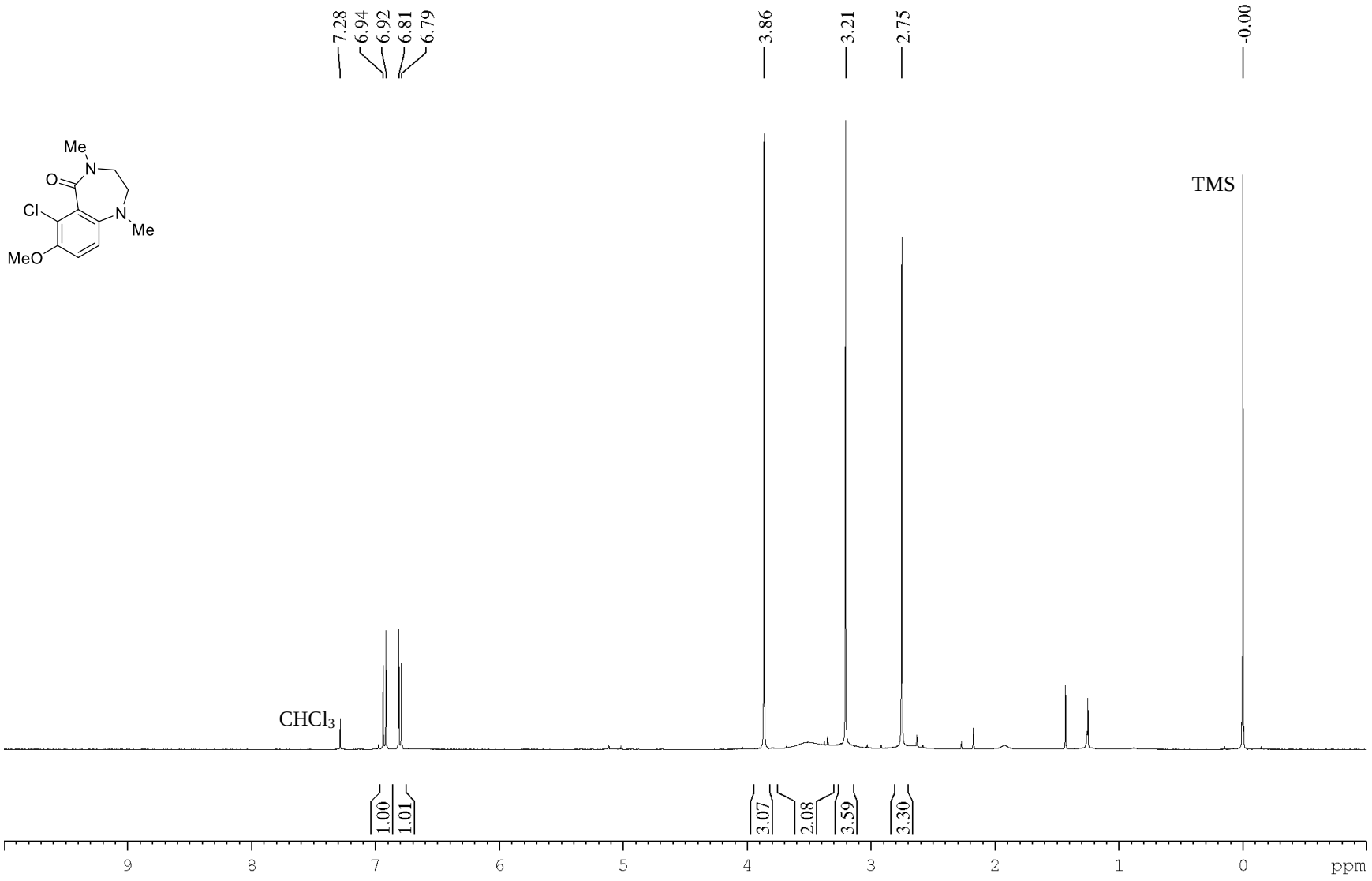
^{1}H NMR of 2b in $(CD_3)_2CO$ at 400 MHz



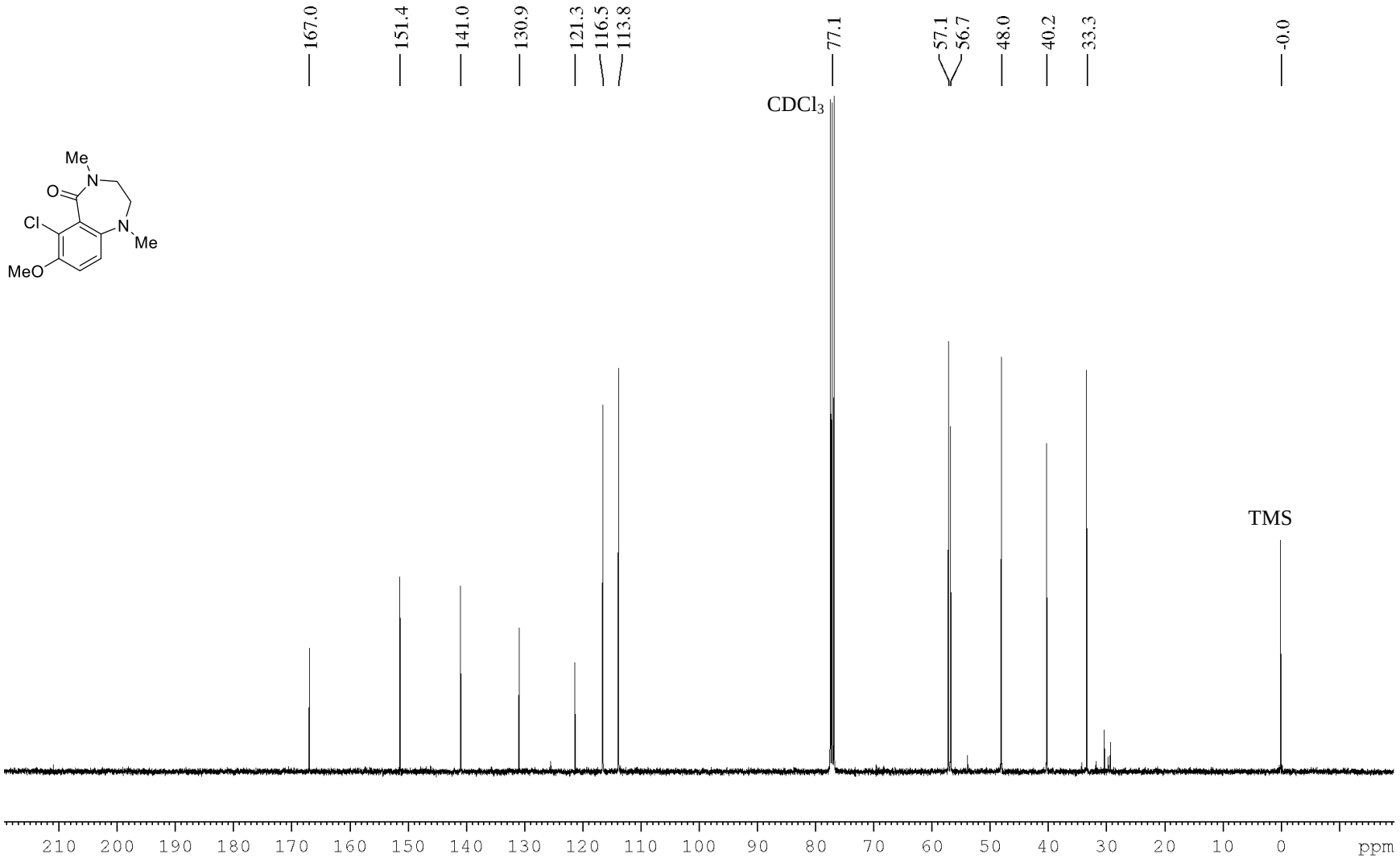
^{13}C {^{1}H} NMR of 2b $(CD_3)_2CO$ at 101 MHz



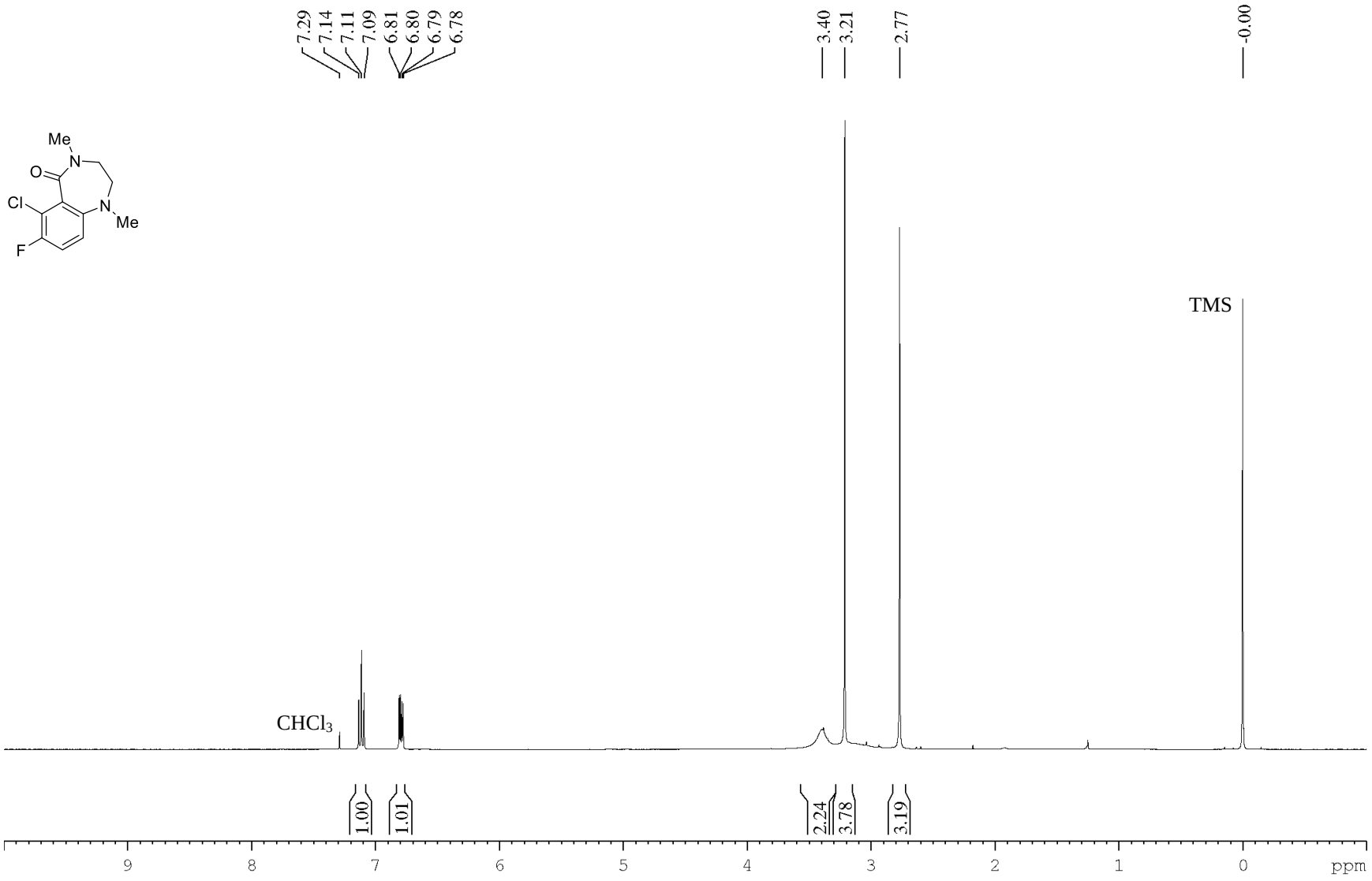
^{1}H NMR of 2c in $CDCl_3$ with 1% v/v TMS at 400 MHz



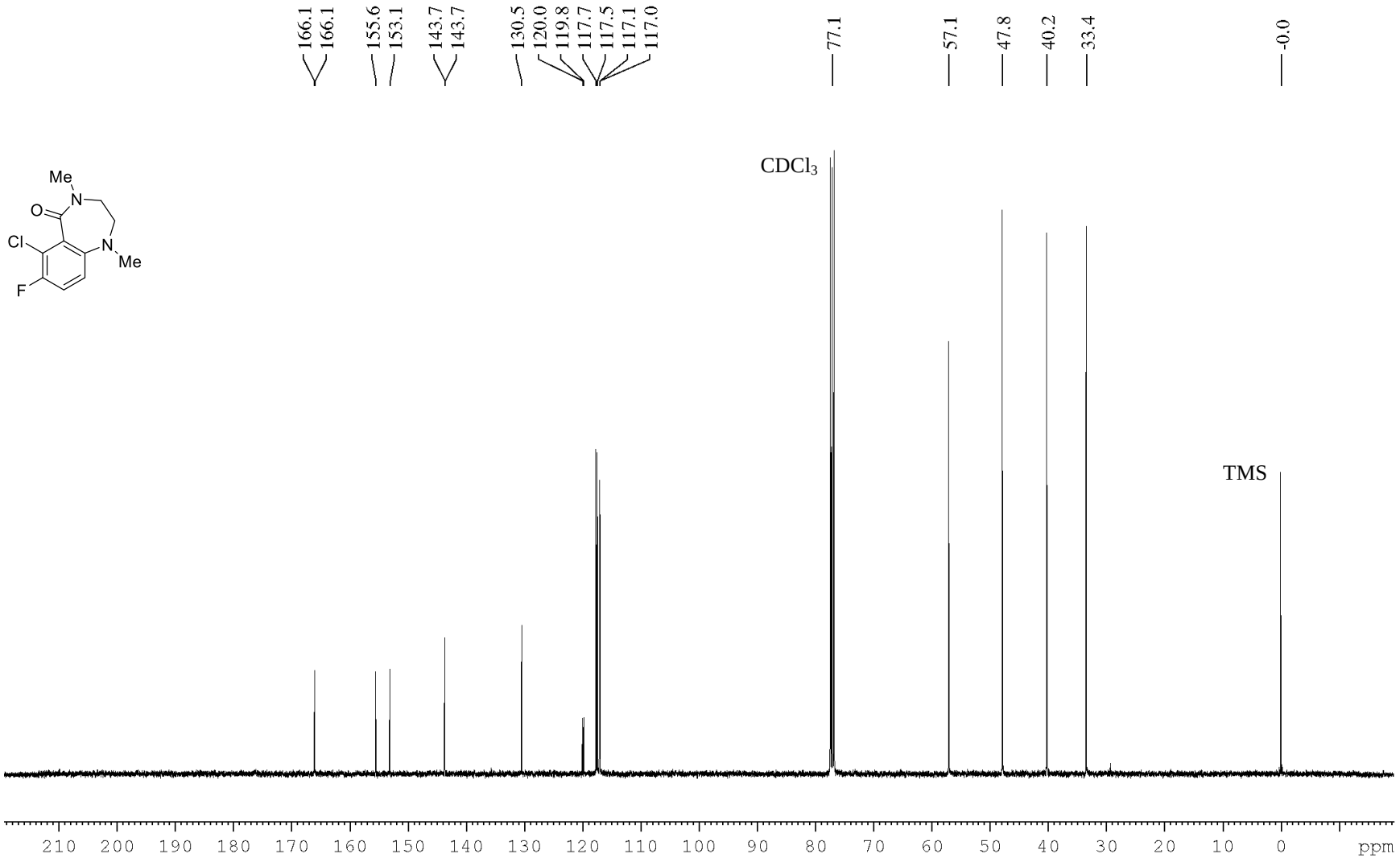
^{13}C {^{1}H} NMR of 2c $CDCl_3$ with 1% v/v TMS at 101 MHz



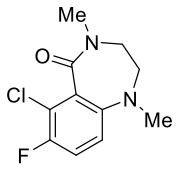
^{1}H NMR of 2d in $CDCl_3$ with 1% v/v TMS at 400 MHz



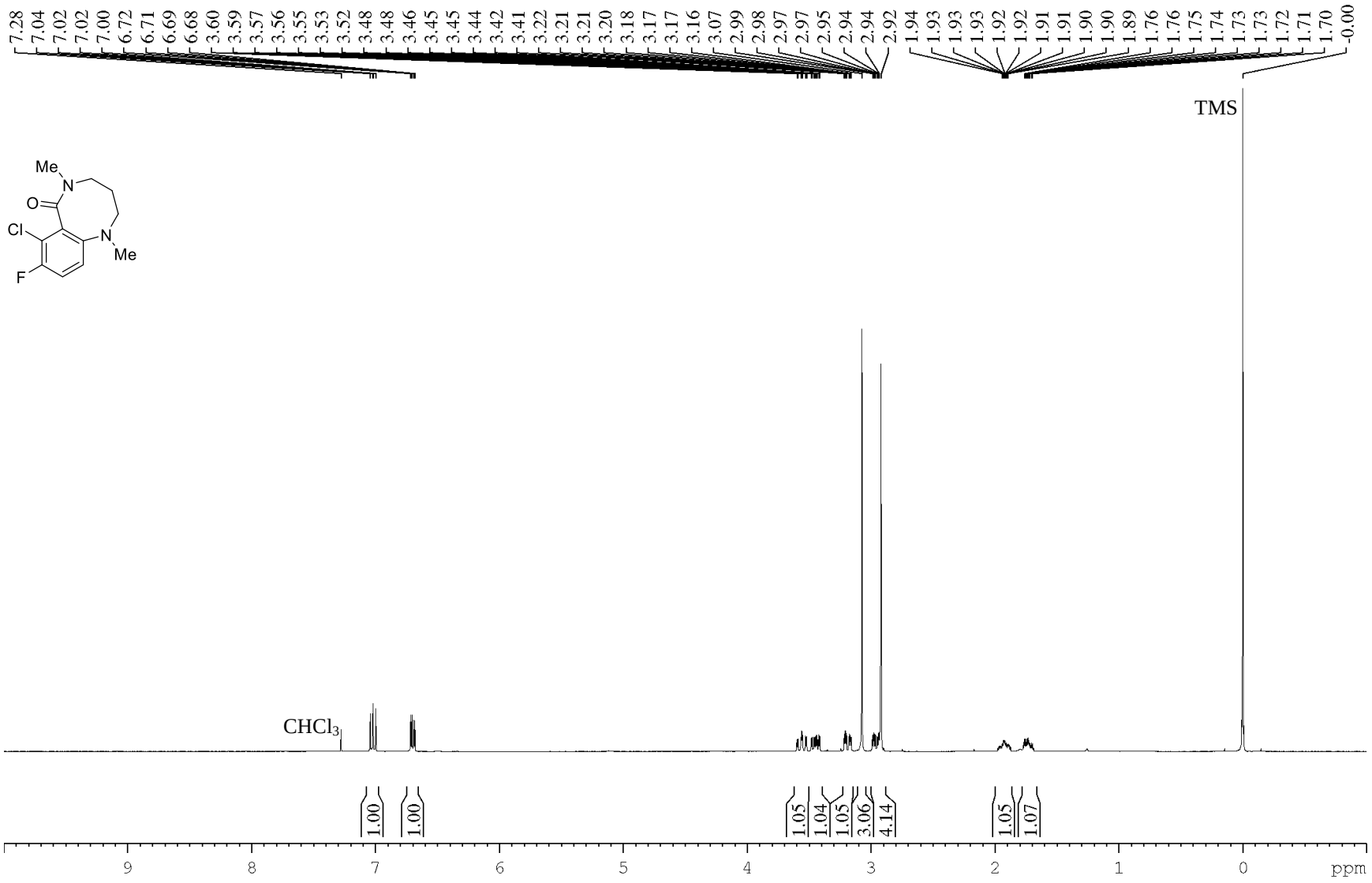
^{13}C {^{1}H} NMR of 2d $CDCl_3$ with 1% v/v TMS at 101 MHz



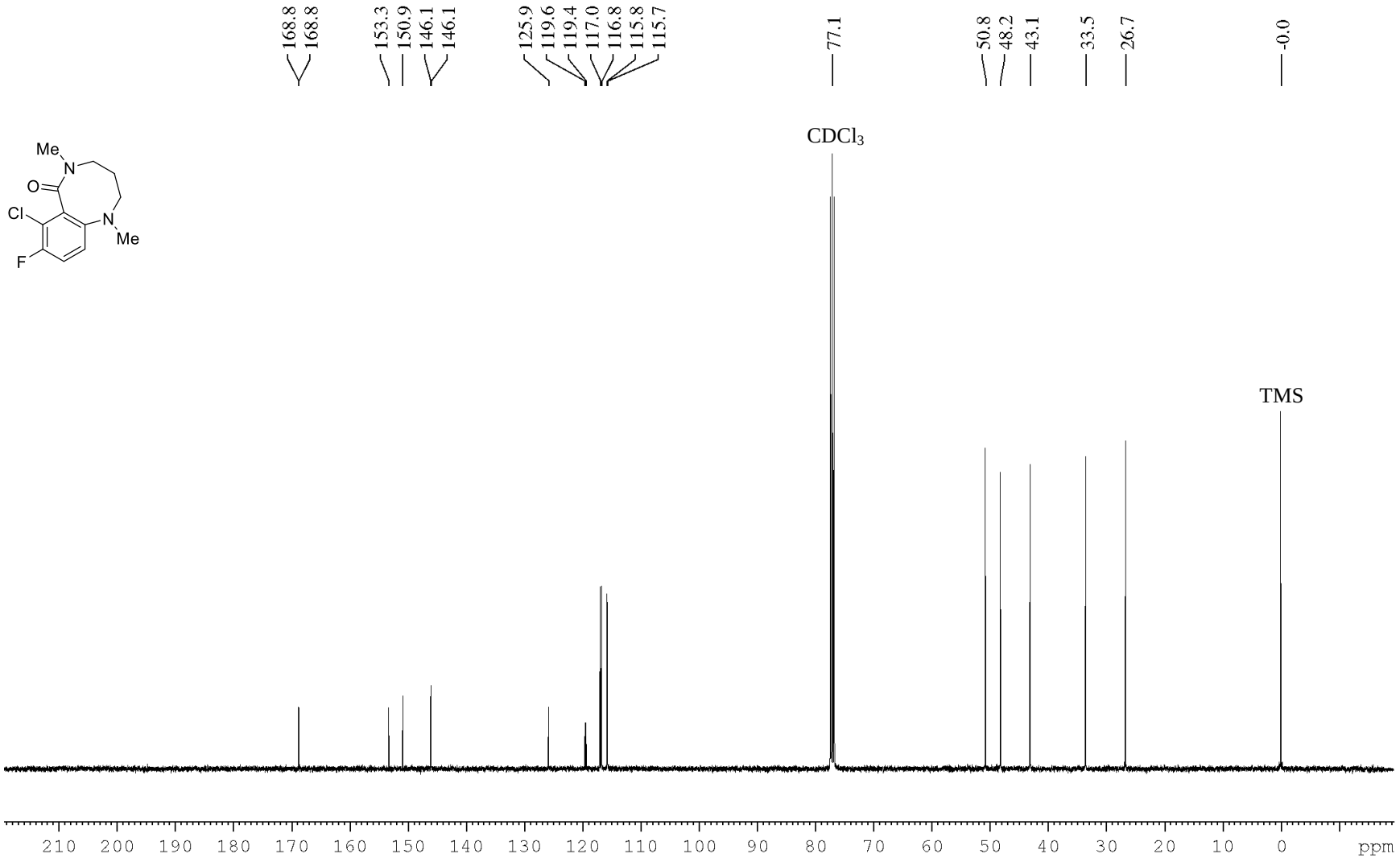
^{19}F {^{1}H} NMR of 2d in $CDCl_3$ with 1% v/v TMS at 376 MHz



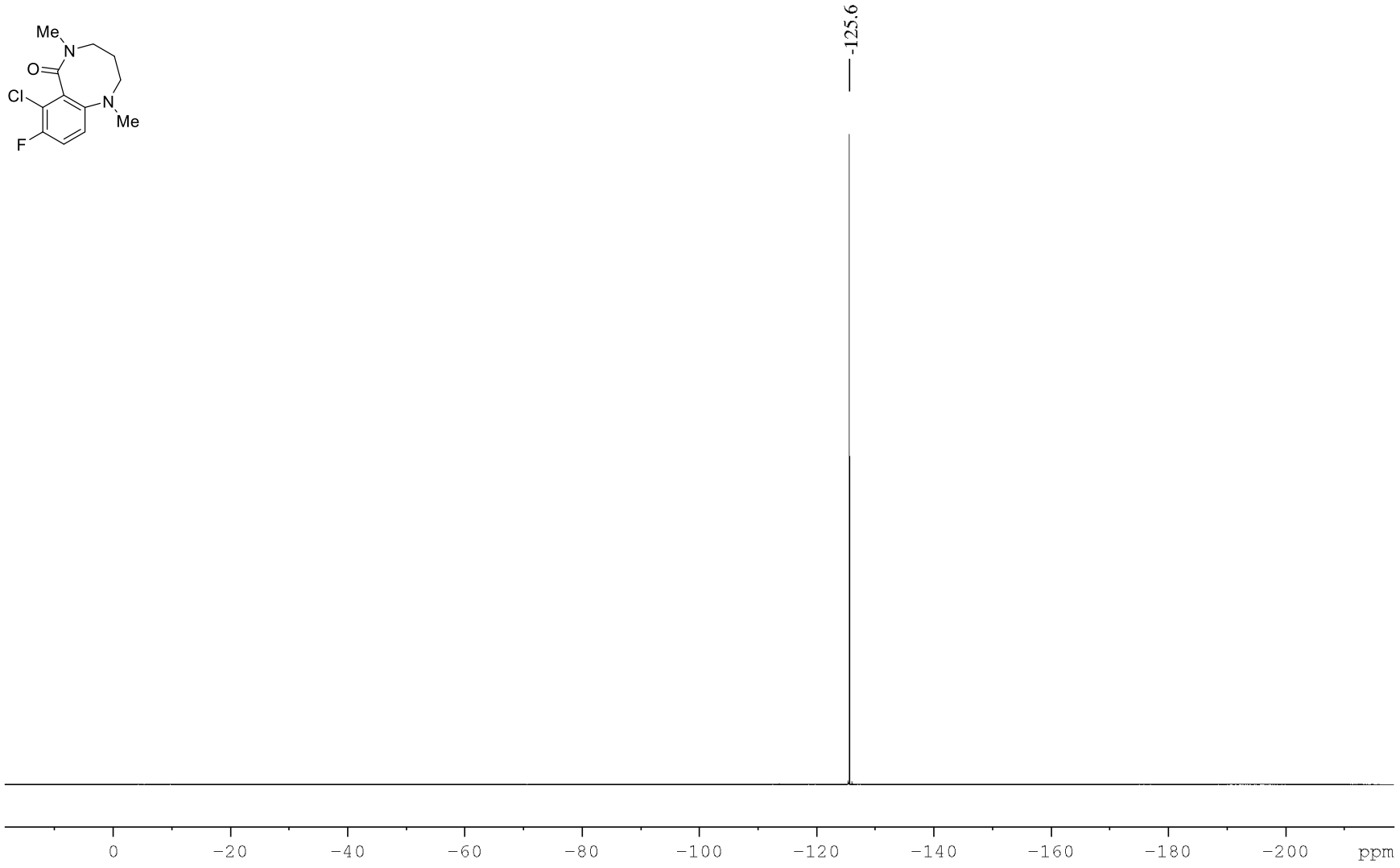
^{1}H NMR of 2e in $CDCl_3$ with 1% v/v TMS at 400 MHz



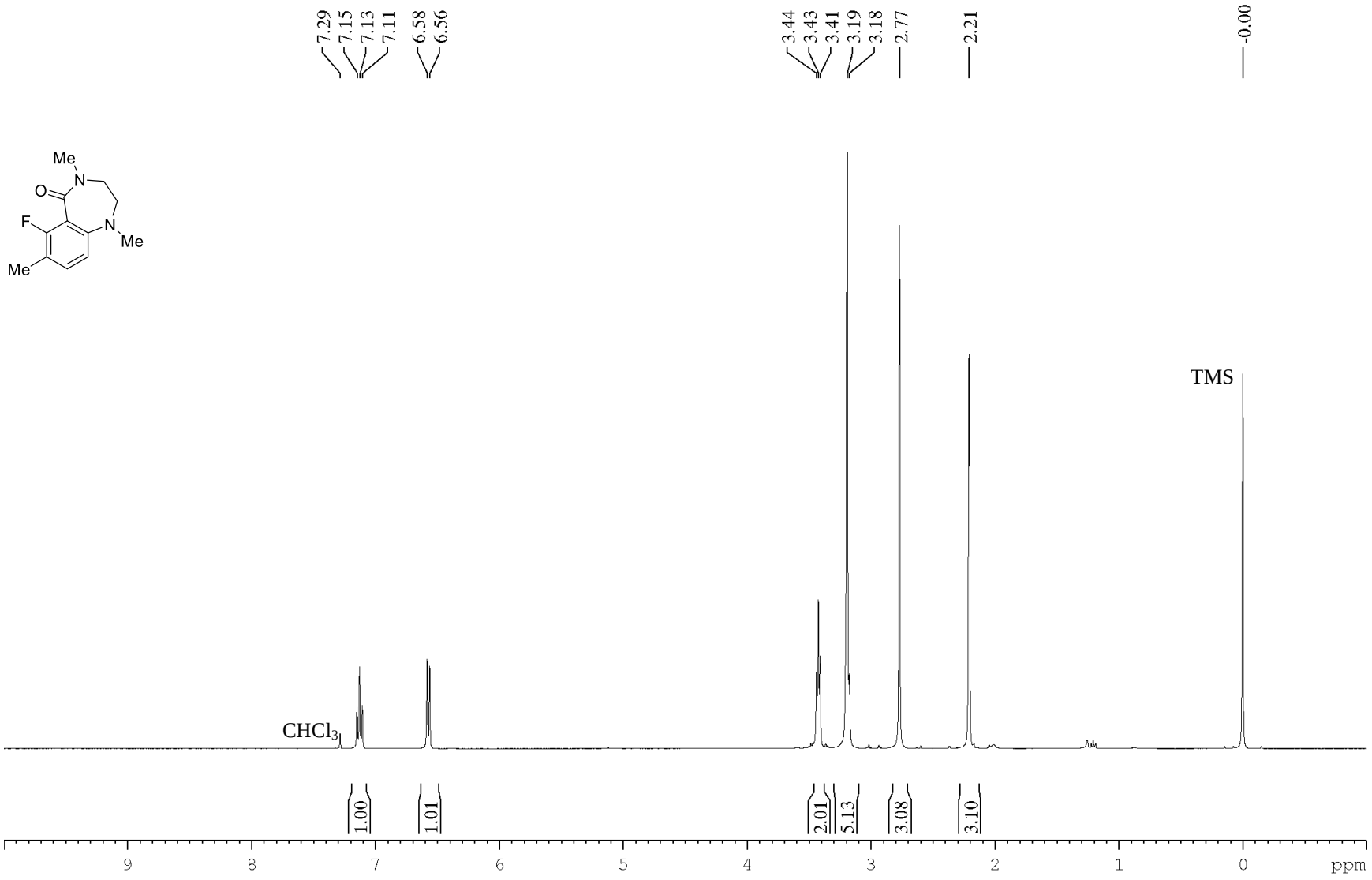
^{13}C {^{1}H} NMR of 2e $CDCl_3$ with 1% v/v TMS at 101 MHz



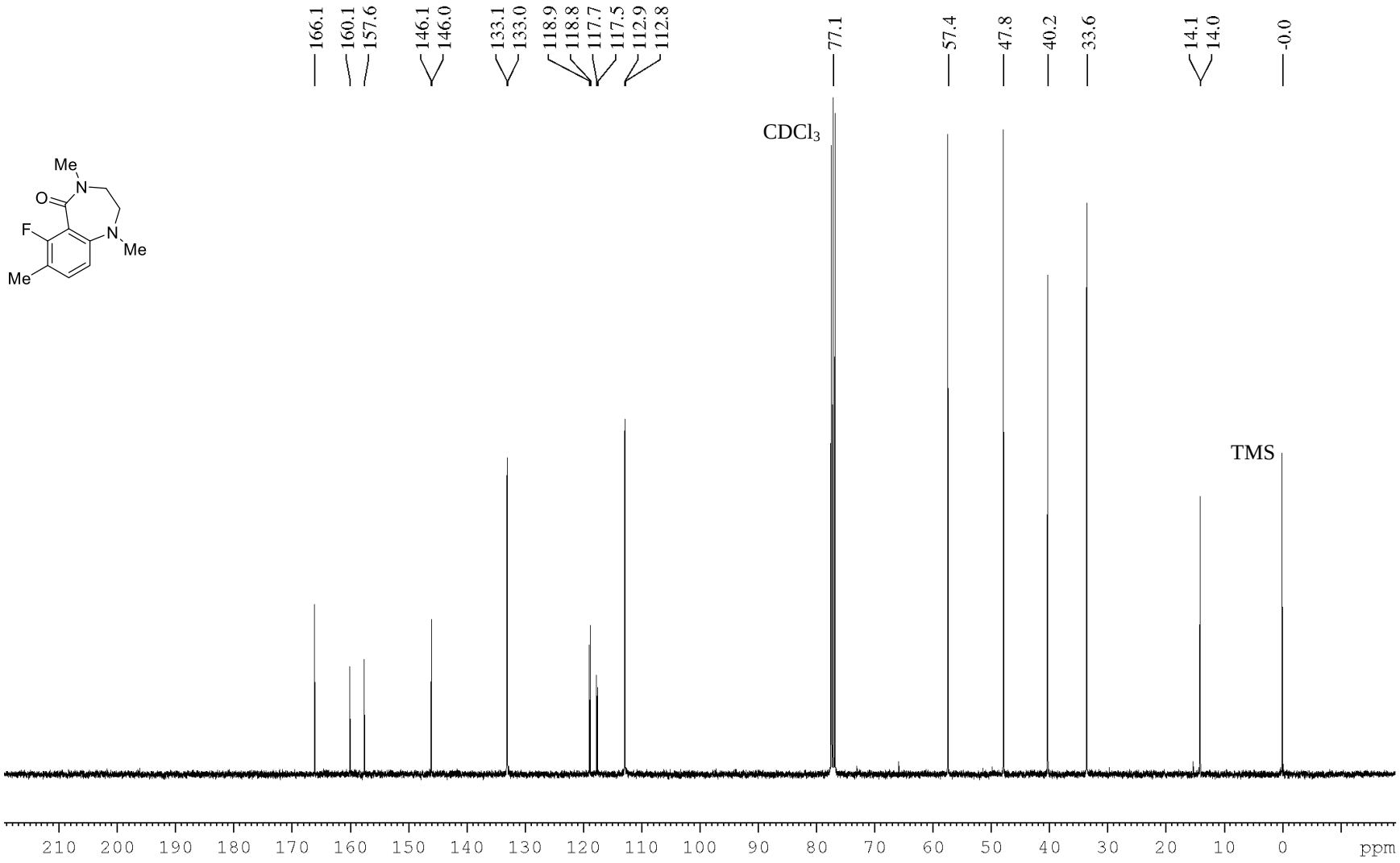
^{19}F {^{1}H} NMR of 2e in $CDCl_3$ with 1% v/v TMS at 376 MHz



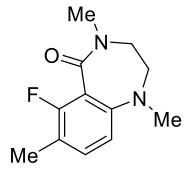
^{1}H NMR of 2f in $CDCl_3$ with 1% v/v TMS at 400 MHz



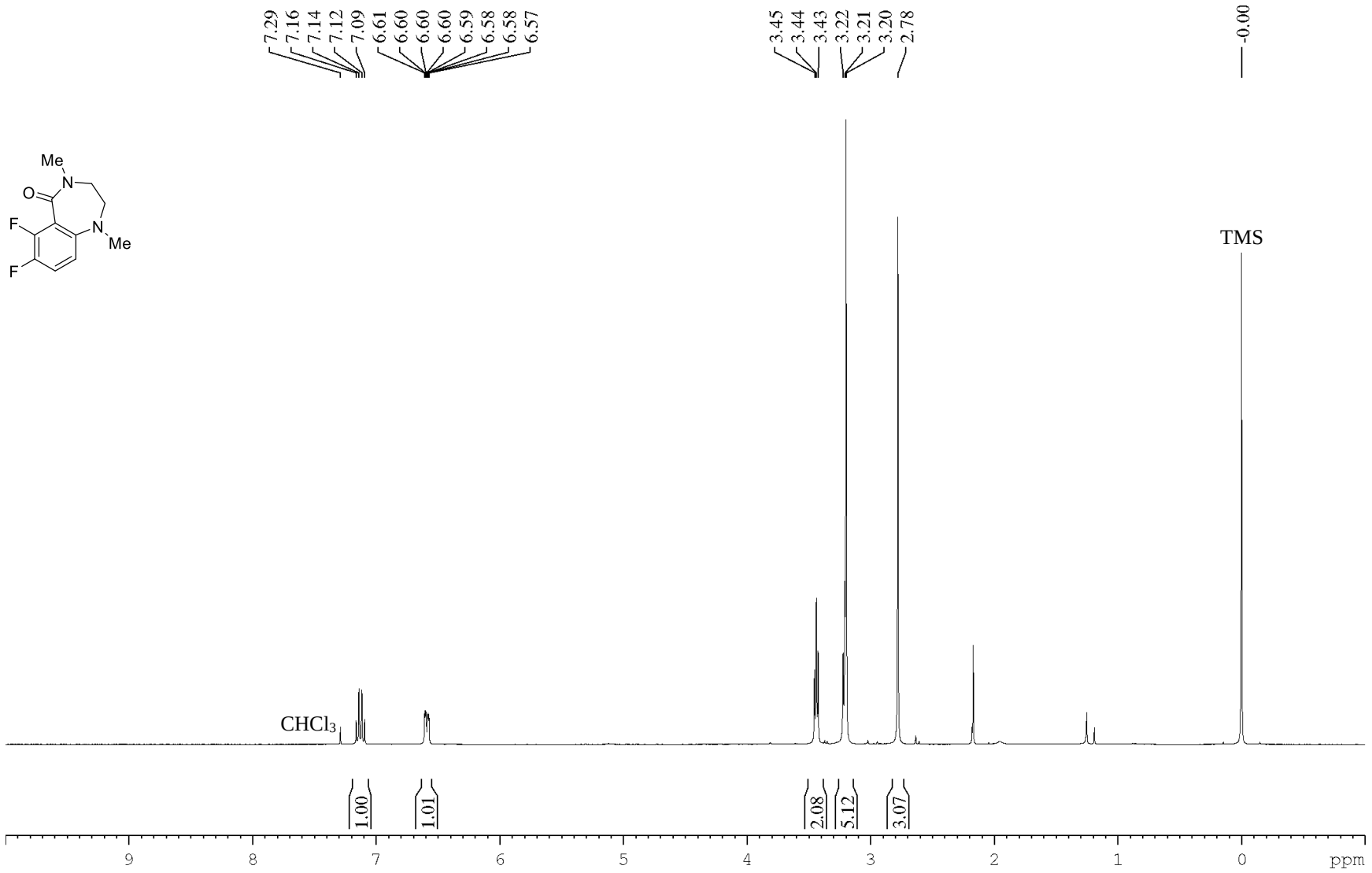
^{13}C {^{1}H} NMR of 2f $CDCl_3$ with 1% v/v TMS at 101 MHz



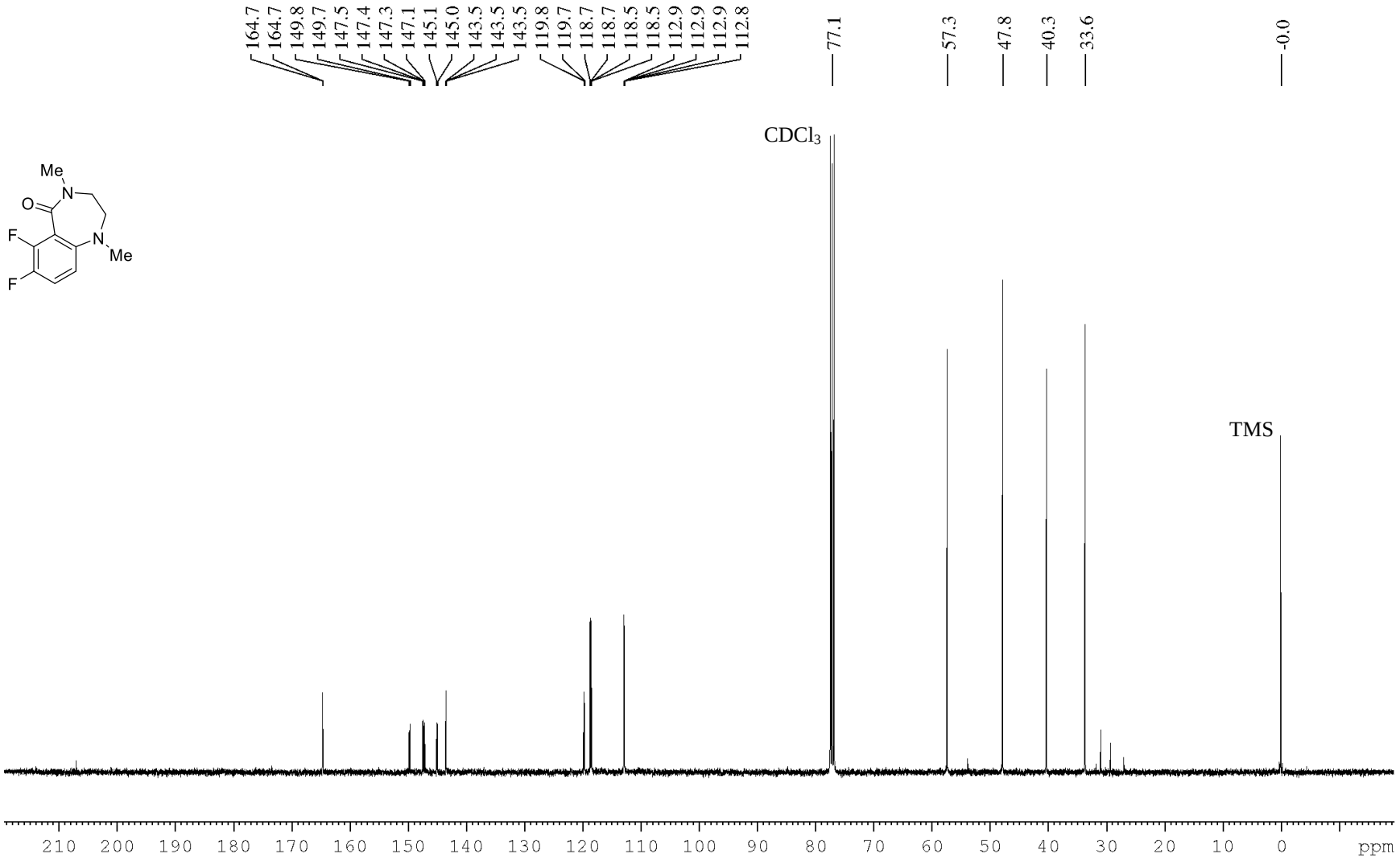
^{19}F {^{1}H} NMR of 2f in $CDCl_3$ with 1% v/v TMS at 376 MHz



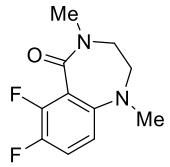
^{1}H NMR of 2g in $CDCl_3$ with 1% v/v TMS at 400 MHz



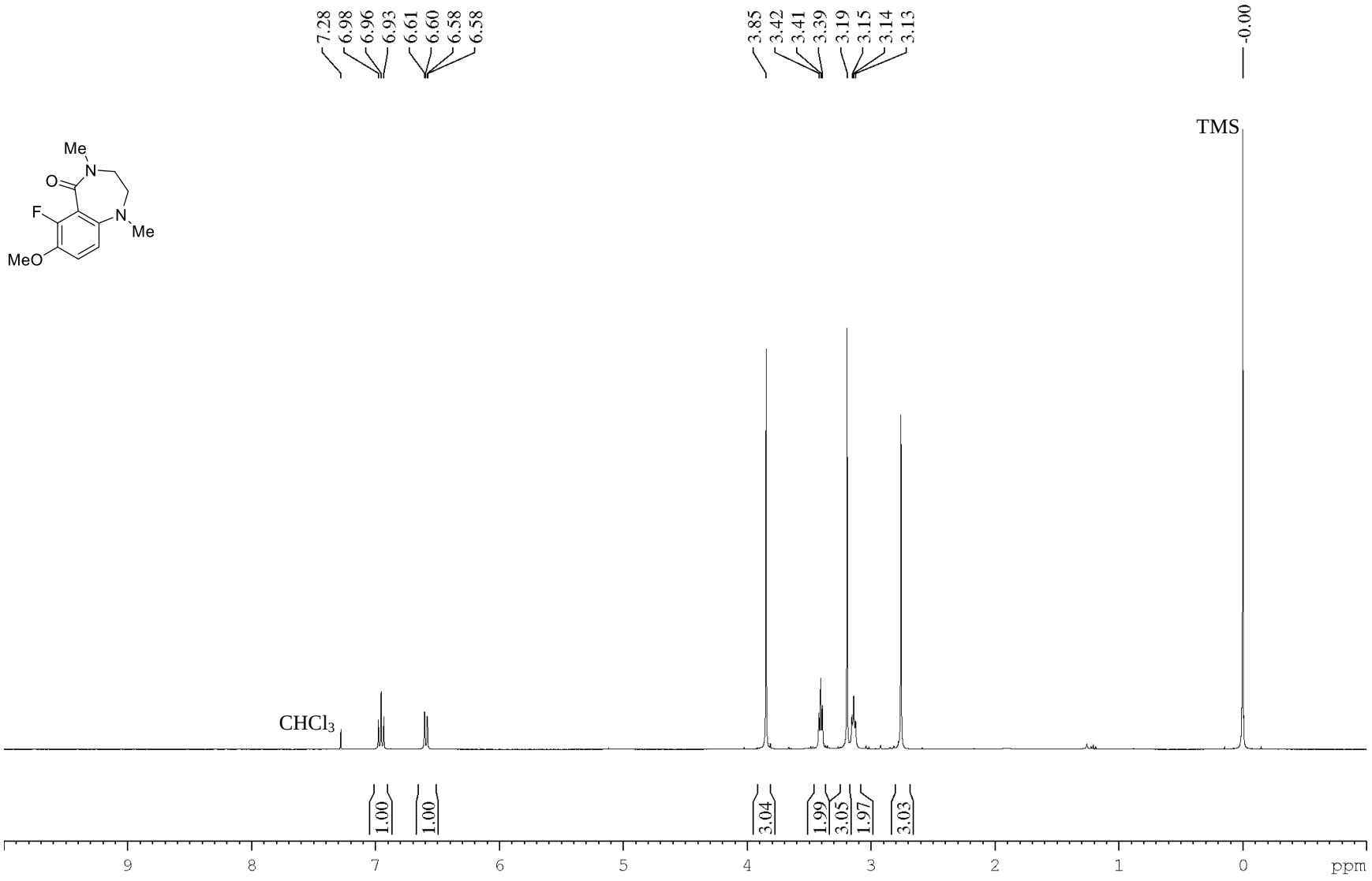
^{13}C {^{1}H} NMR of 2g $CDCl_3$ with 1% v/v TMS at 101 MHz



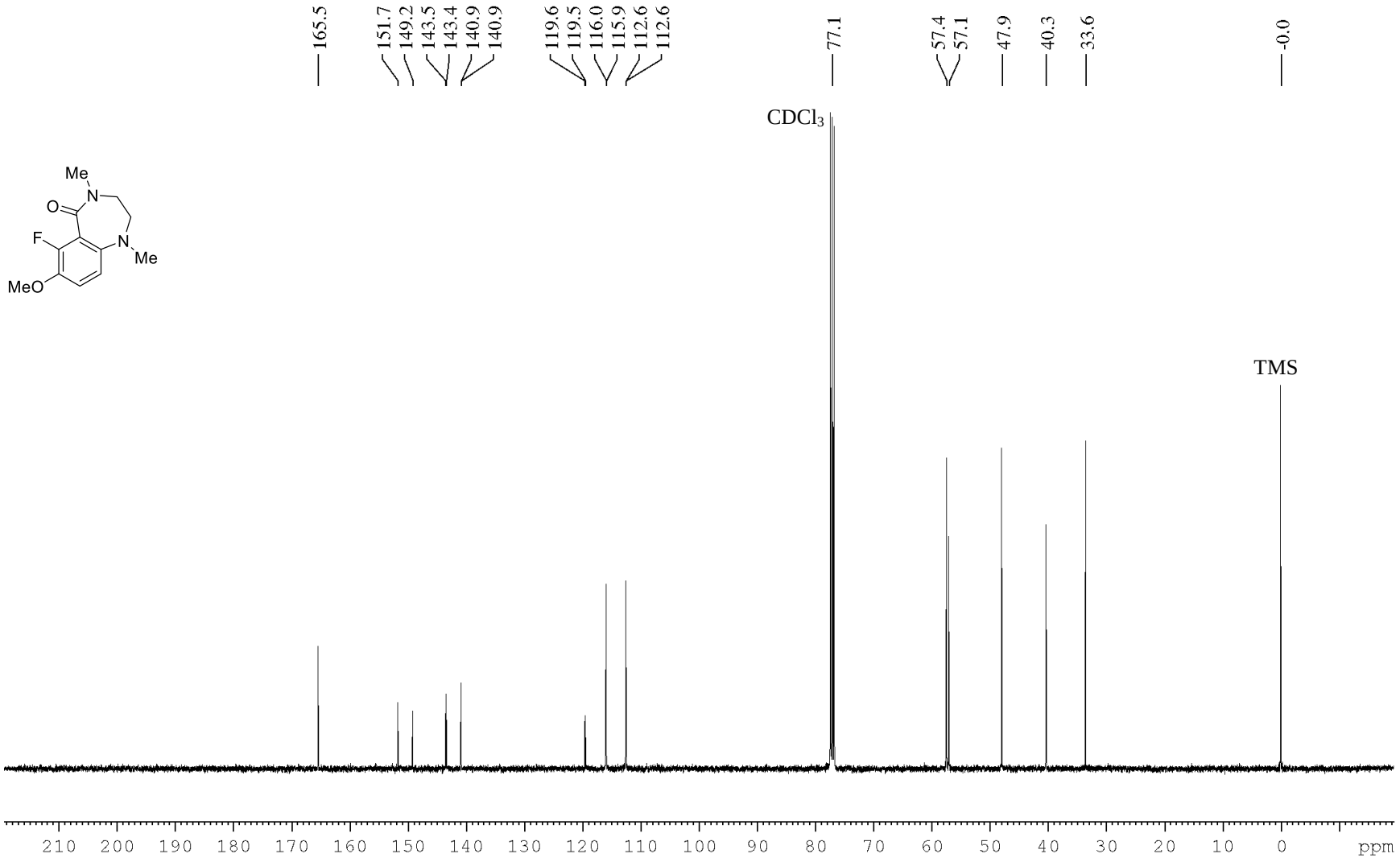
^{19}F {^{1}H} NMR of 2g in $CDCl_3$ with 1% v/v TMS at 376 MHz



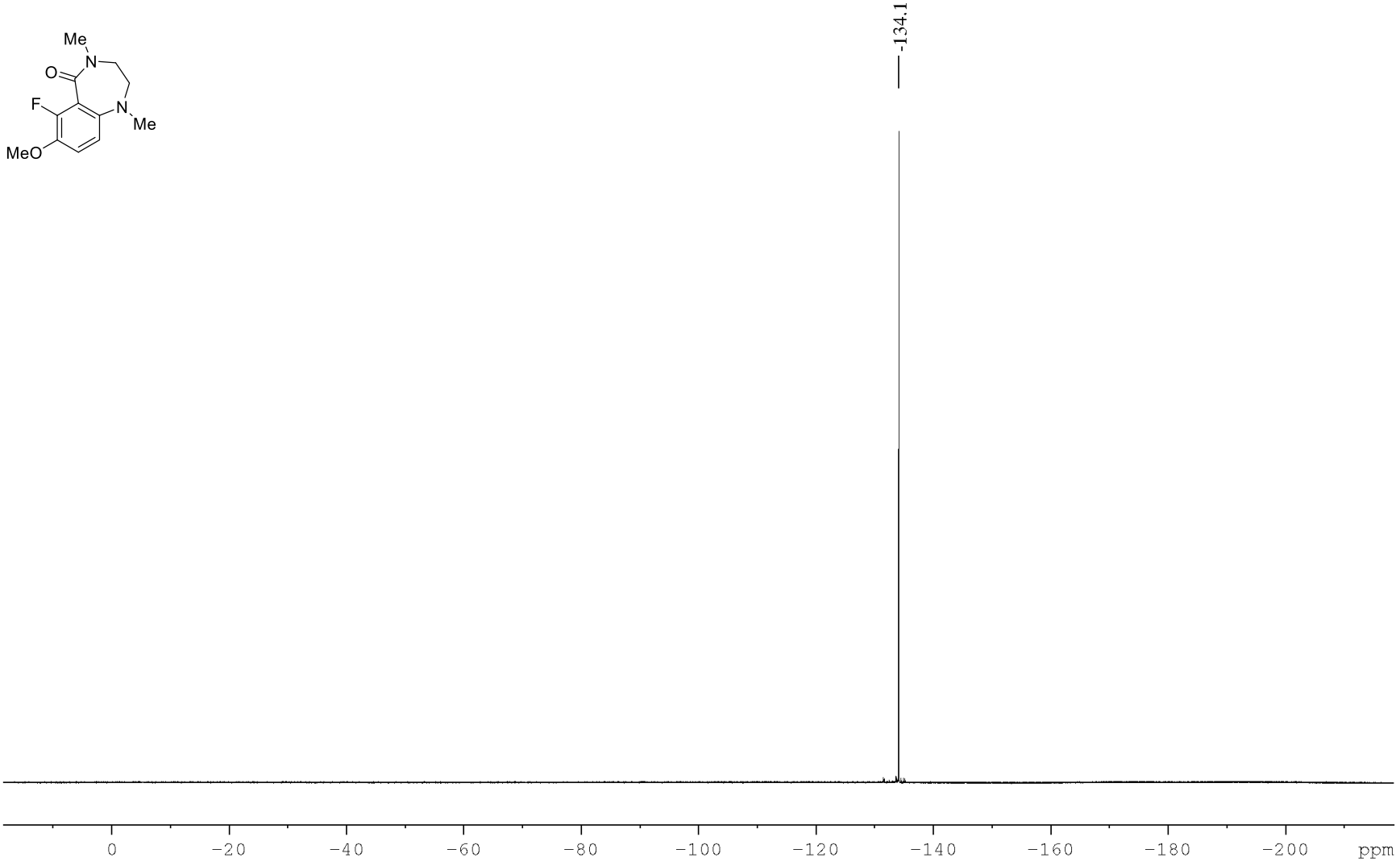
^{1}H NMR of 2h in $CDCl_3$ with 1% v/v TMS at 400 MHz



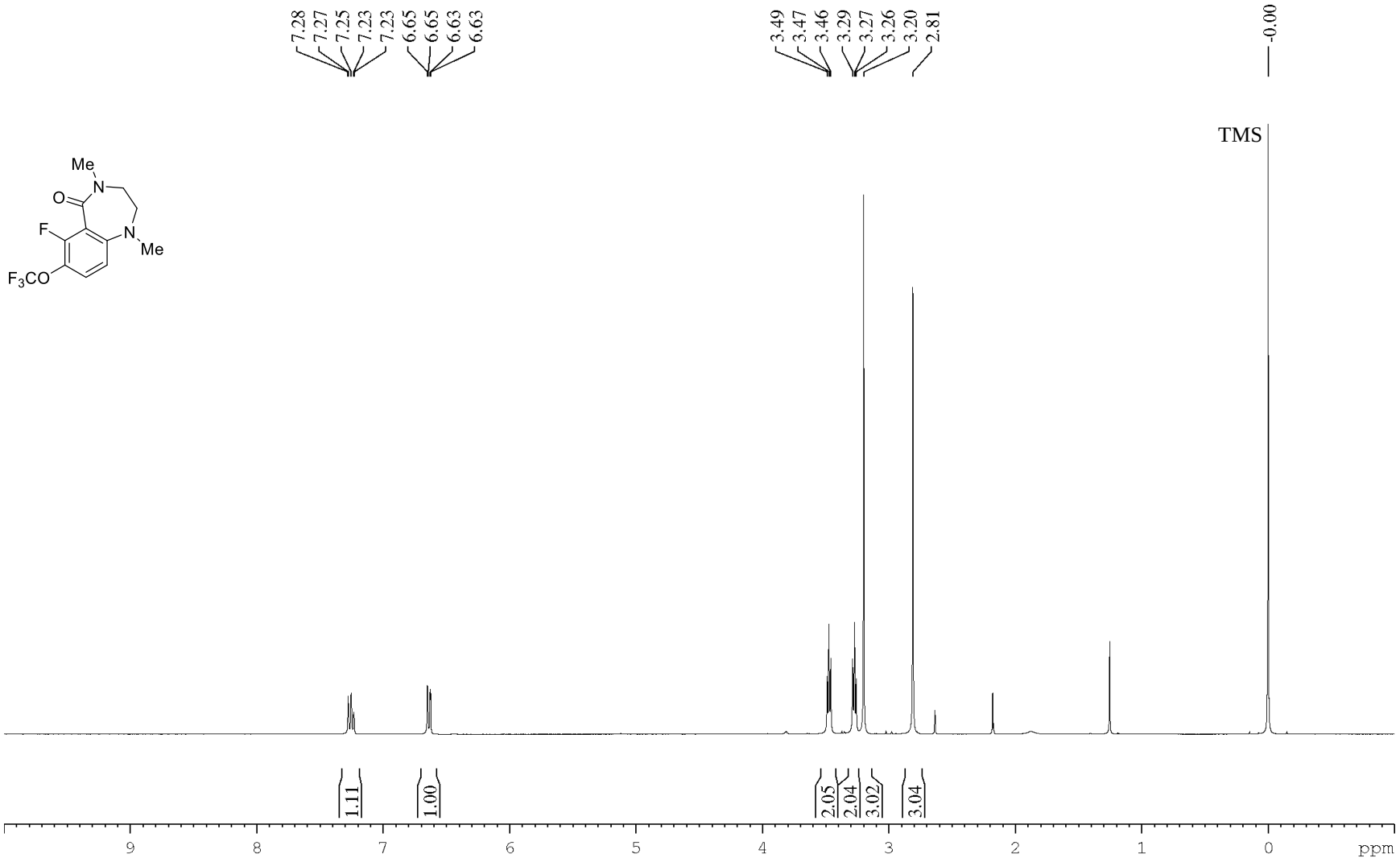
^{13}C {^{1}H} NMR of 2h $CDCl_3$ with 1% v/v TMS at 101 MHz



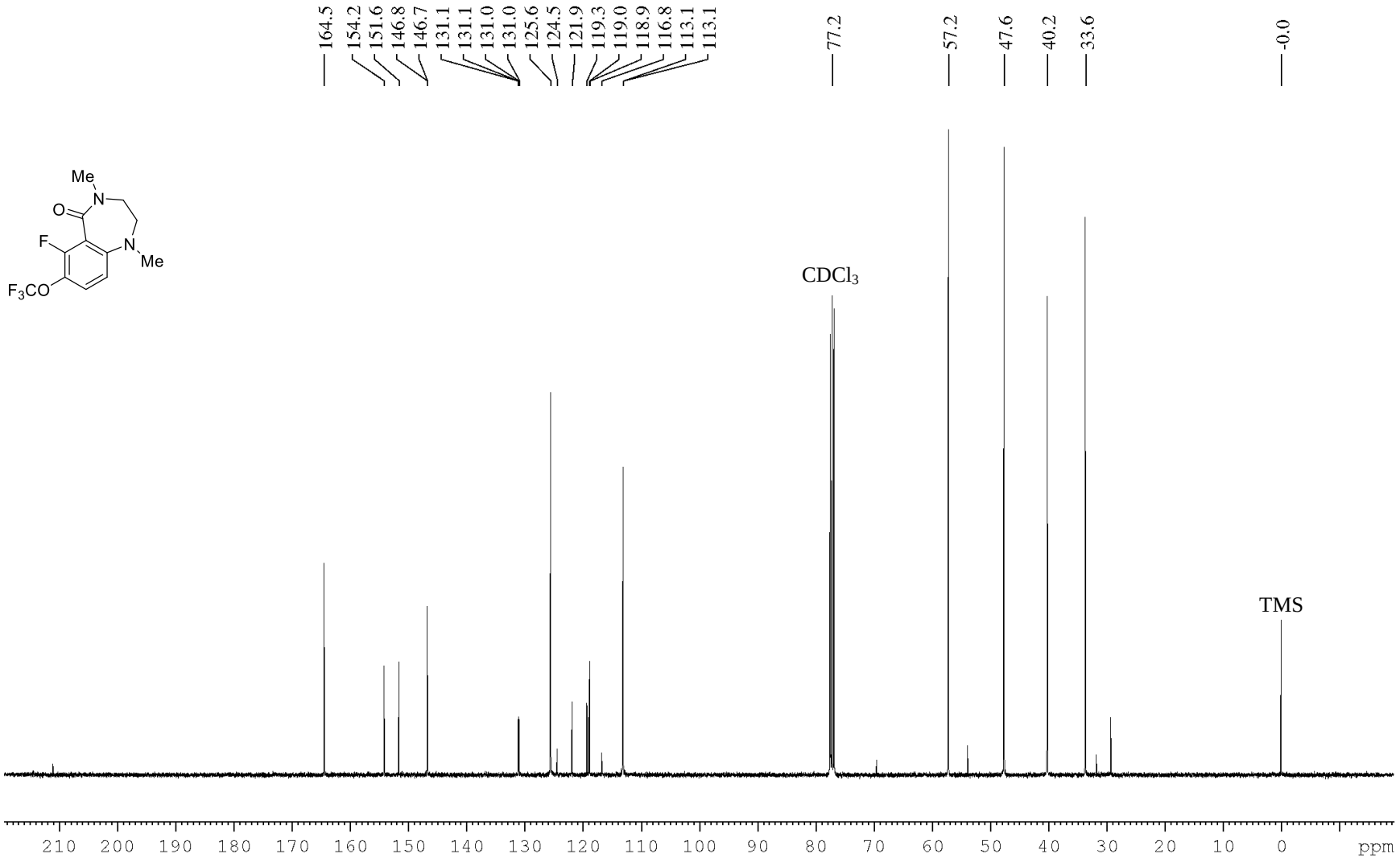
^{19}F {^{1}H} NMR of 2h in $CDCl_3$ with 1% v/v TMS at 376 MHz



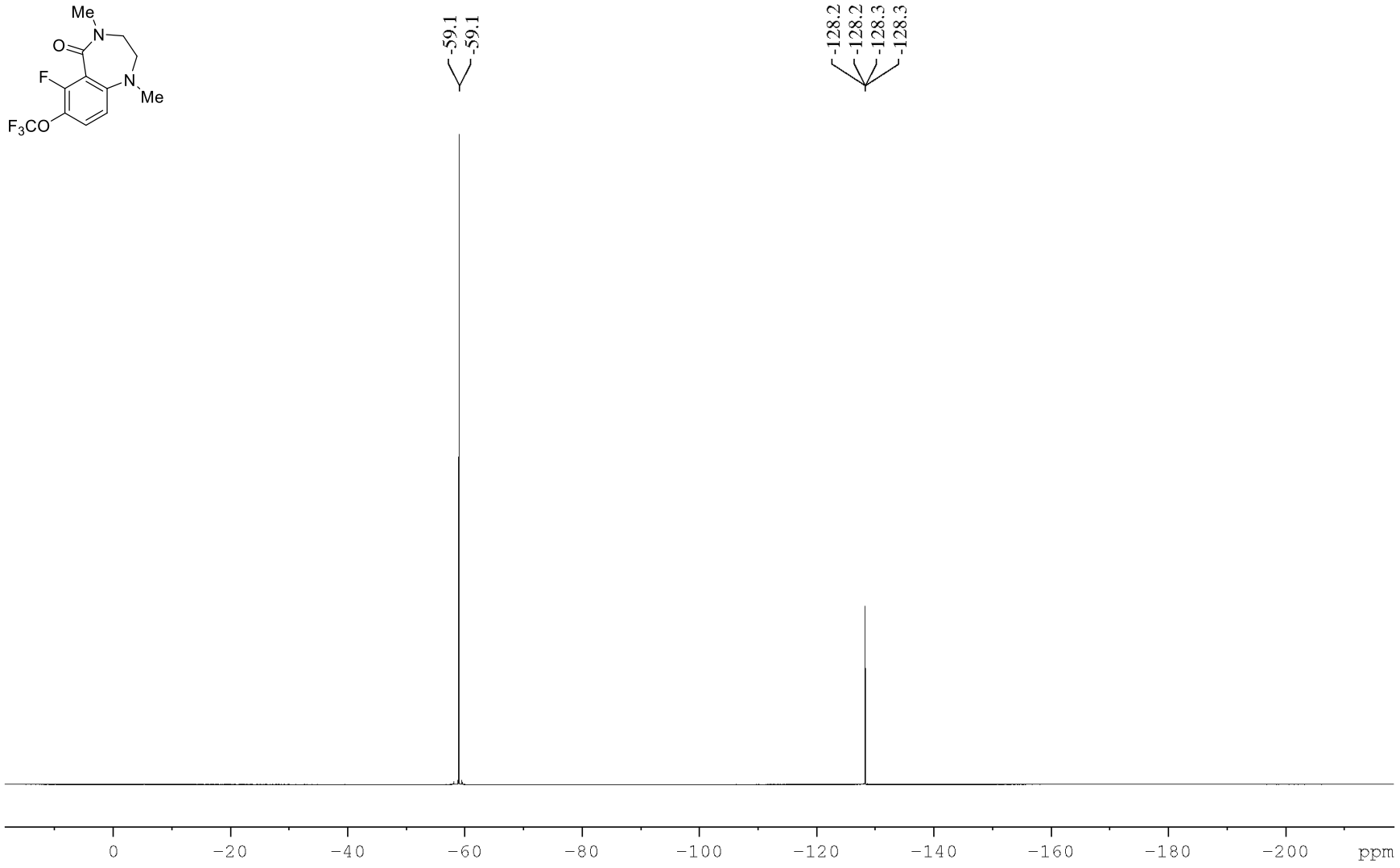
^{1}H NMR of 2i in $CDCl_3$ with 1% v/v TMS at 400 MHz



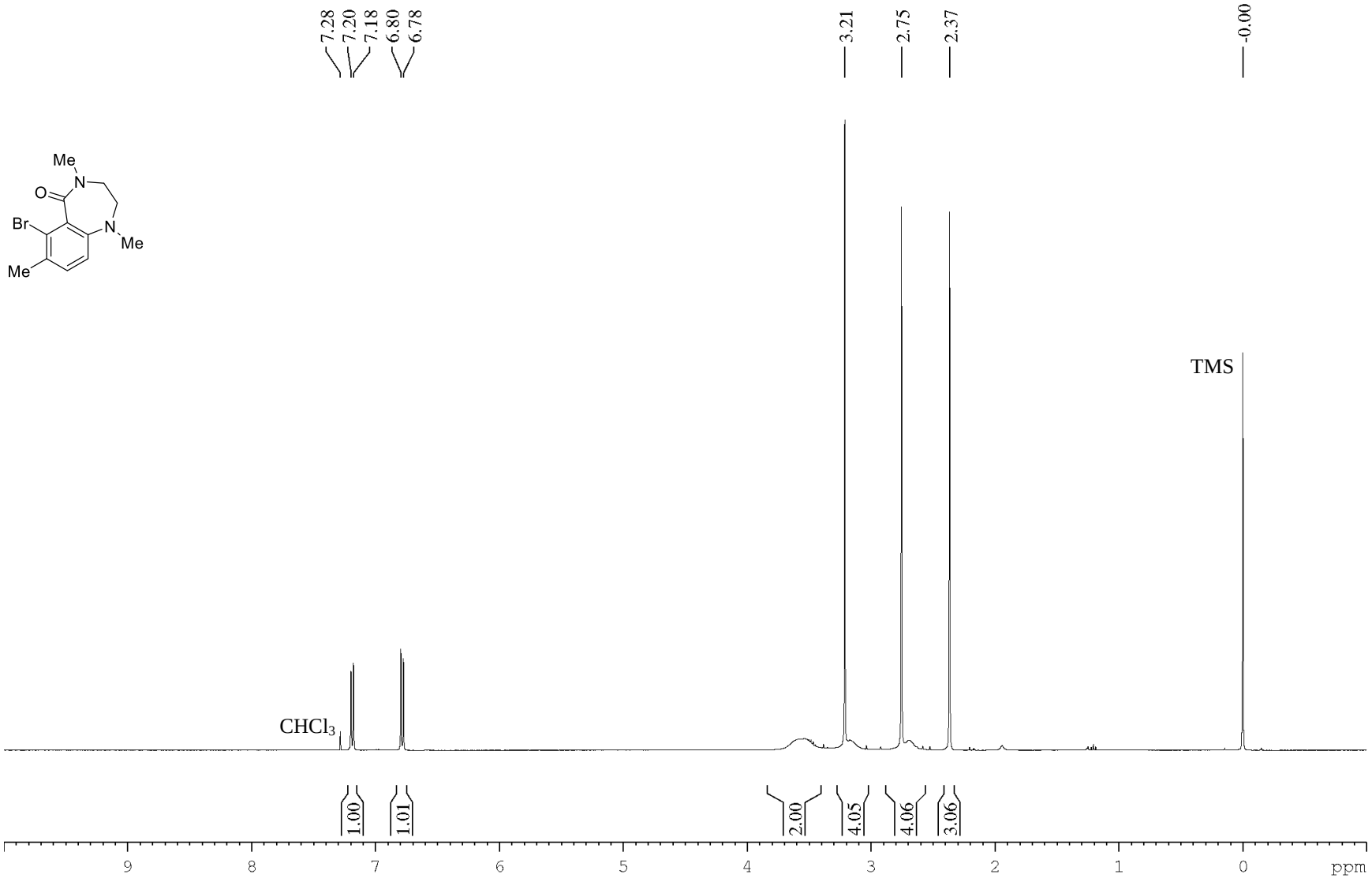
^{13}C {^{1}H} NMR of 2i $CDCl_3$ with 1% v/v TMS at 101 MHz



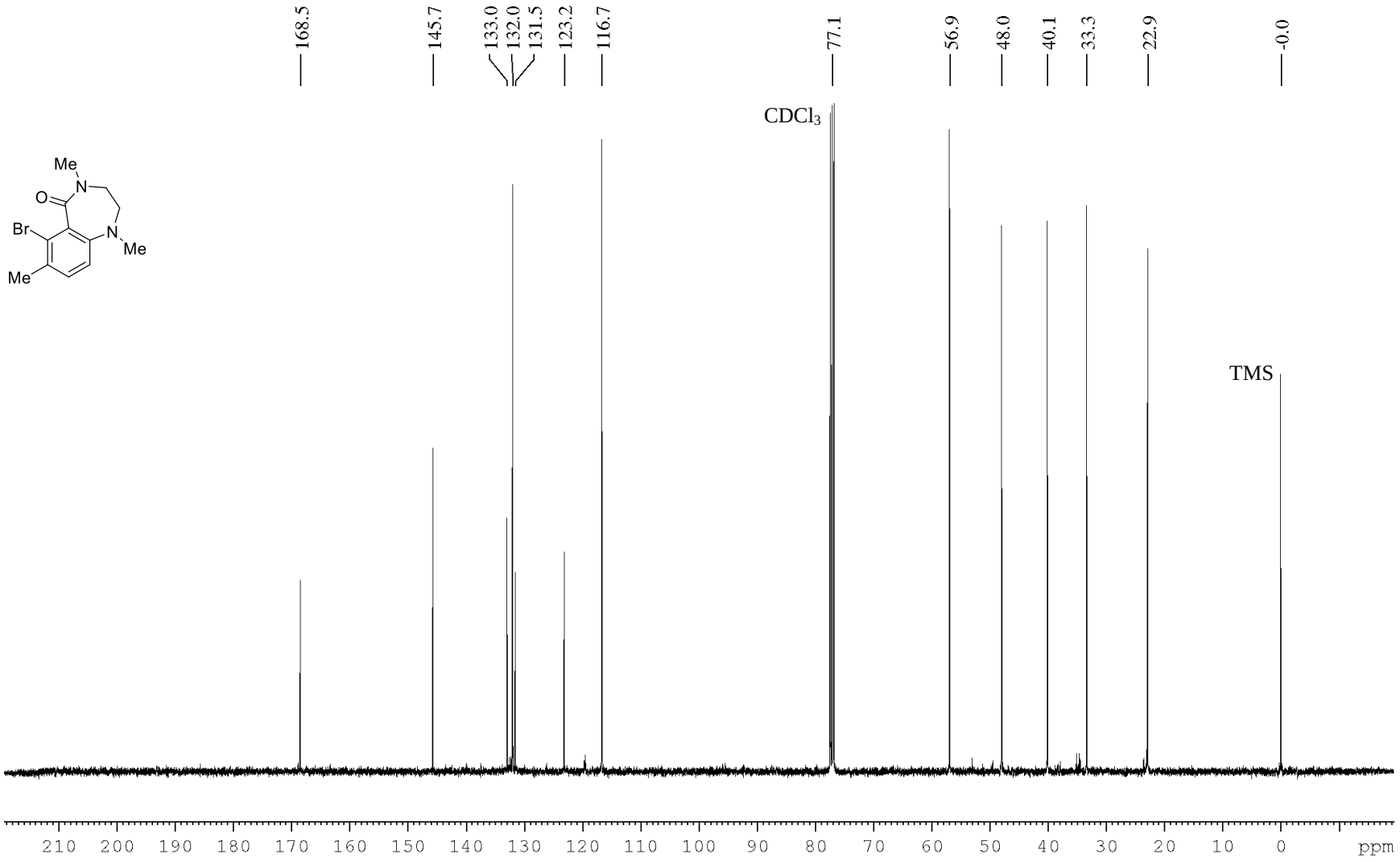
^{19}F {^{1}H} NMR of 2i in $CDCl_3$ with 1% v/v TMS at 376 MHz



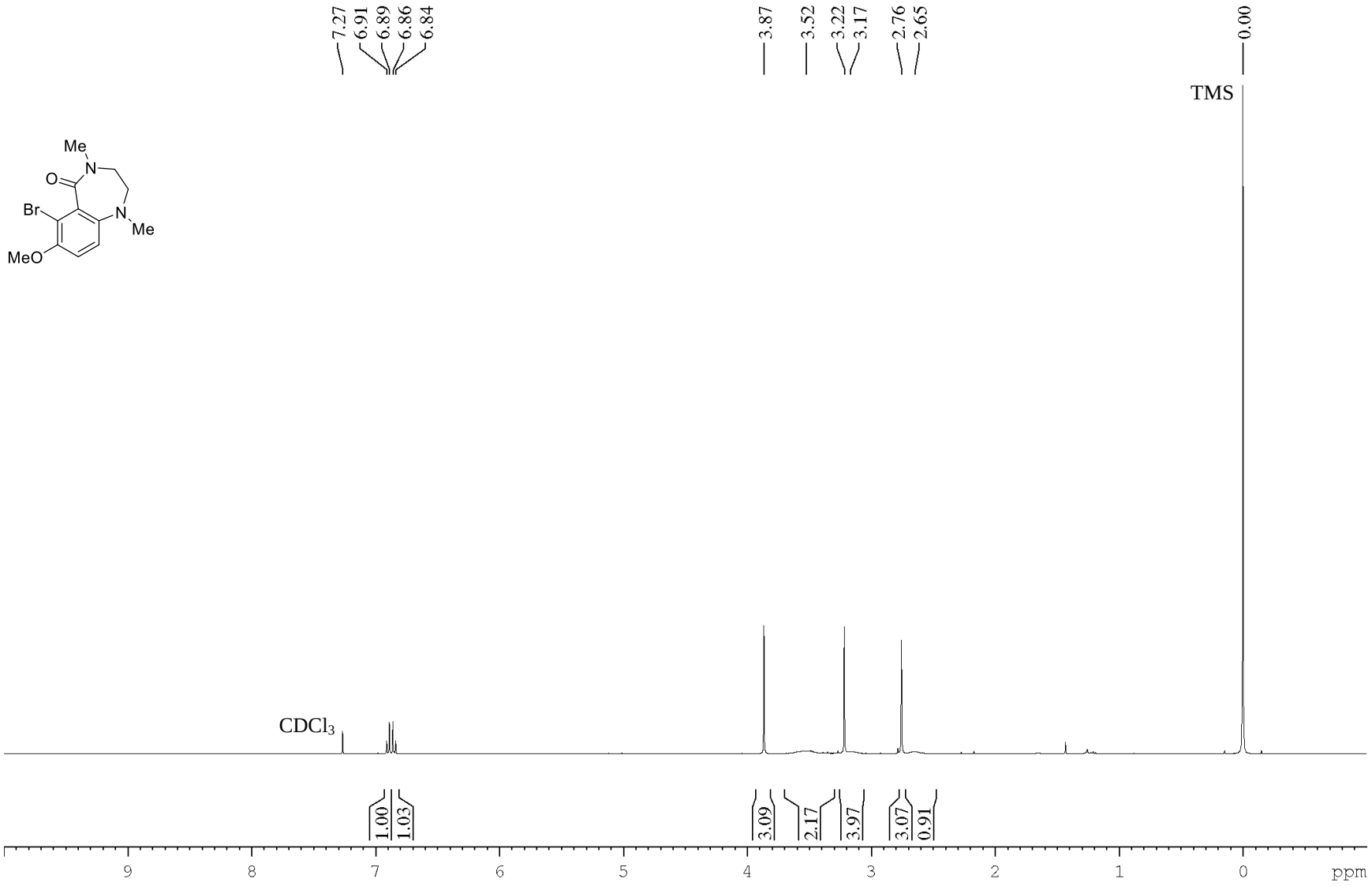
^{1}H NMR of 2j in $CDCl_3$ with 1% v/v TMS at 400 MHz



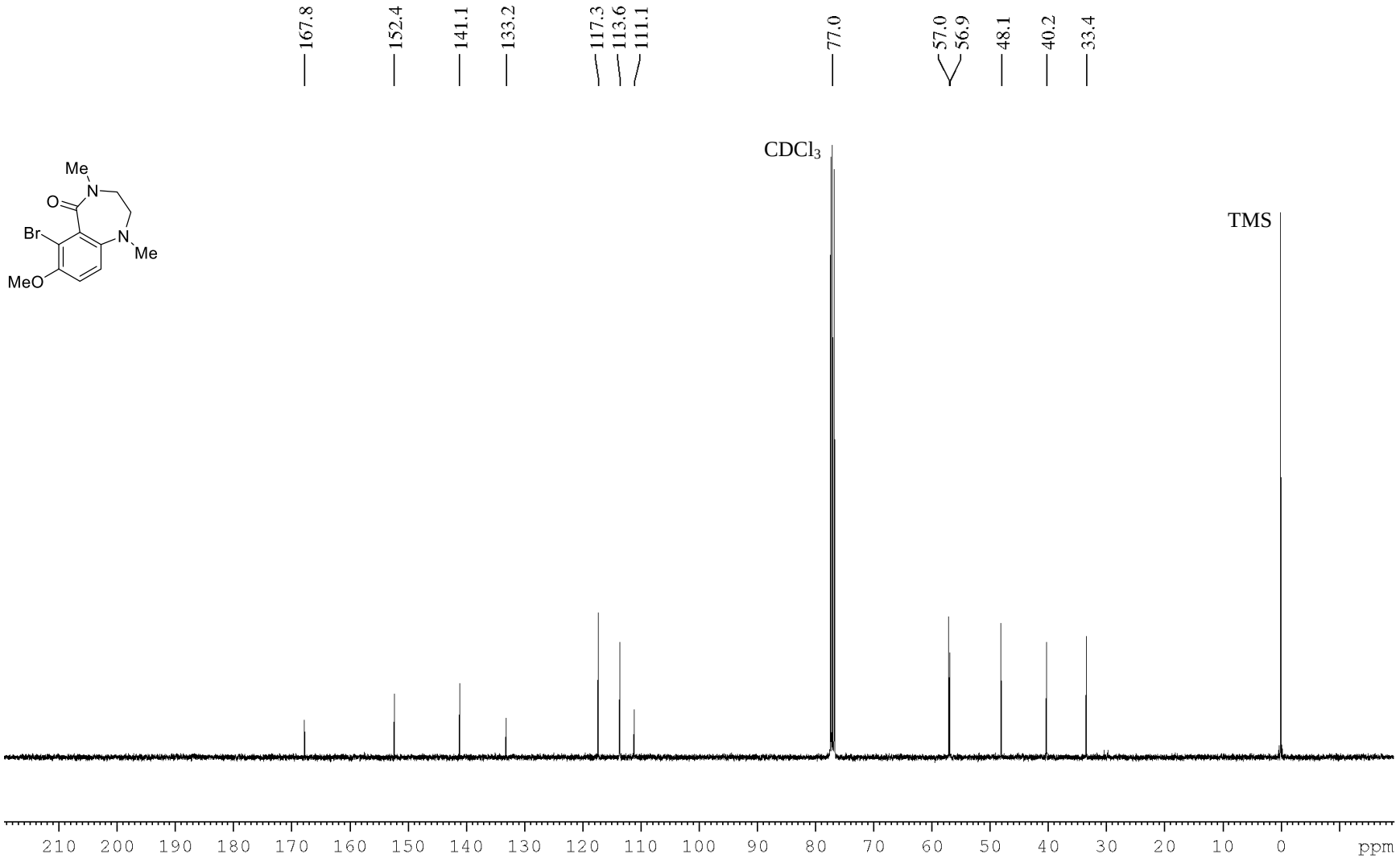
^{13}C {^{1}H} NMR of 2j $CDCl_3$ with 1% v/v TMS at 101 MHz



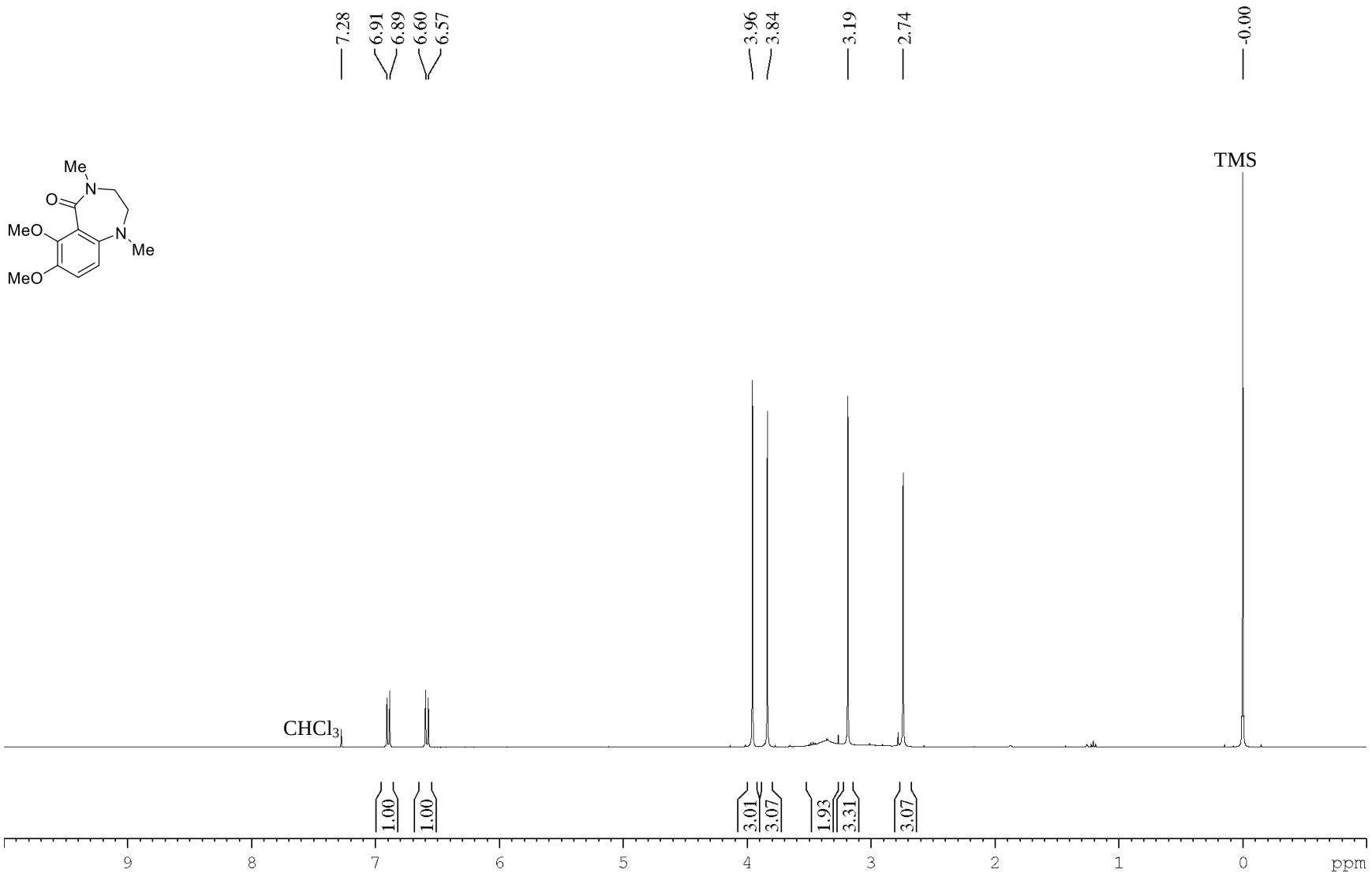
^{1}H NMR of 2k in $CDCl_3$ with 1% v/v TMS at 400 MHz



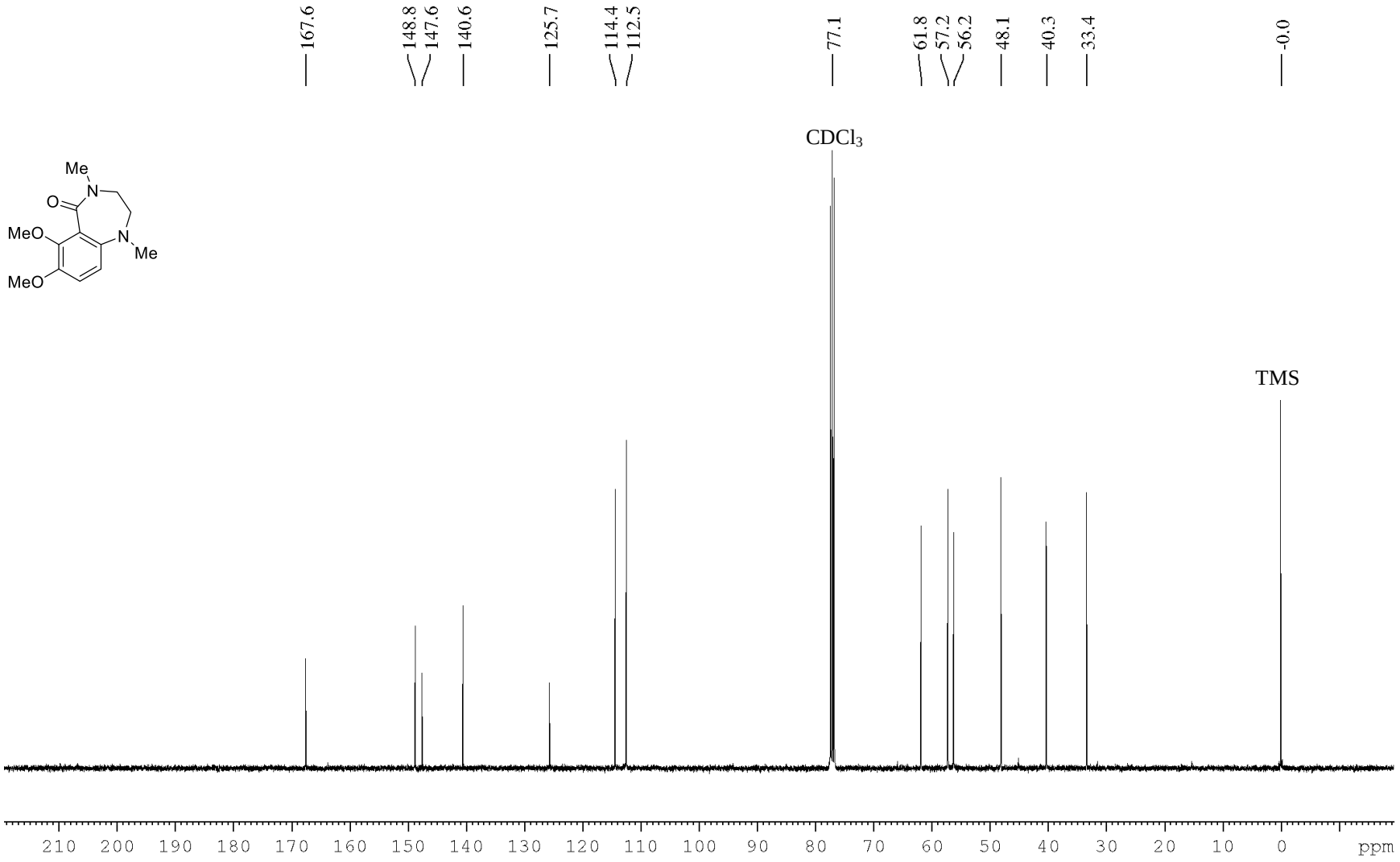
^{13}C {^{1}H} NMR of 2k $CDCl_3$ with 1% v/v TMS at 101 MHz



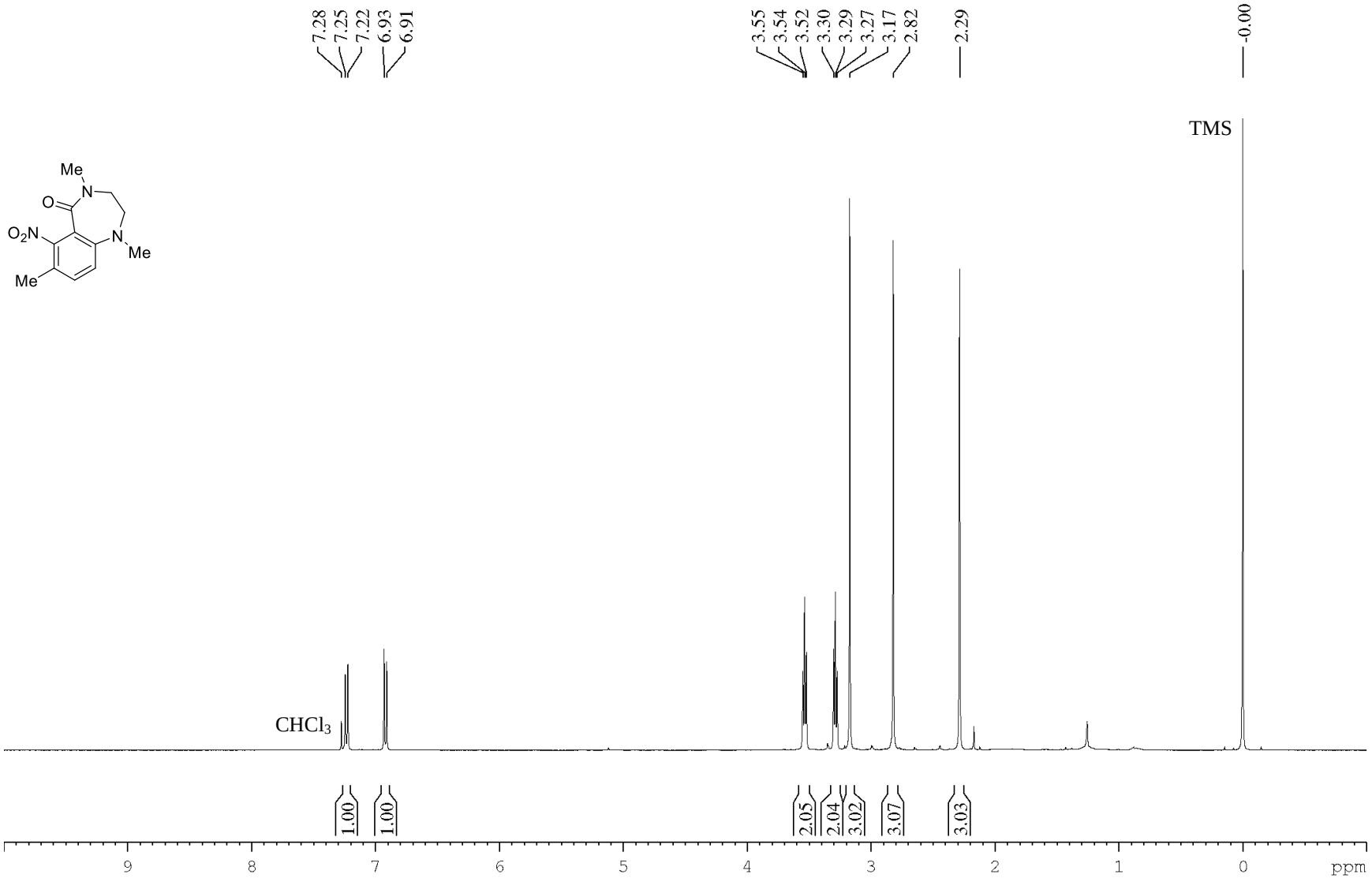
^{1}H NMR of 2l in $CDCl_3$ with 1% v/v TMS at 400 MHz



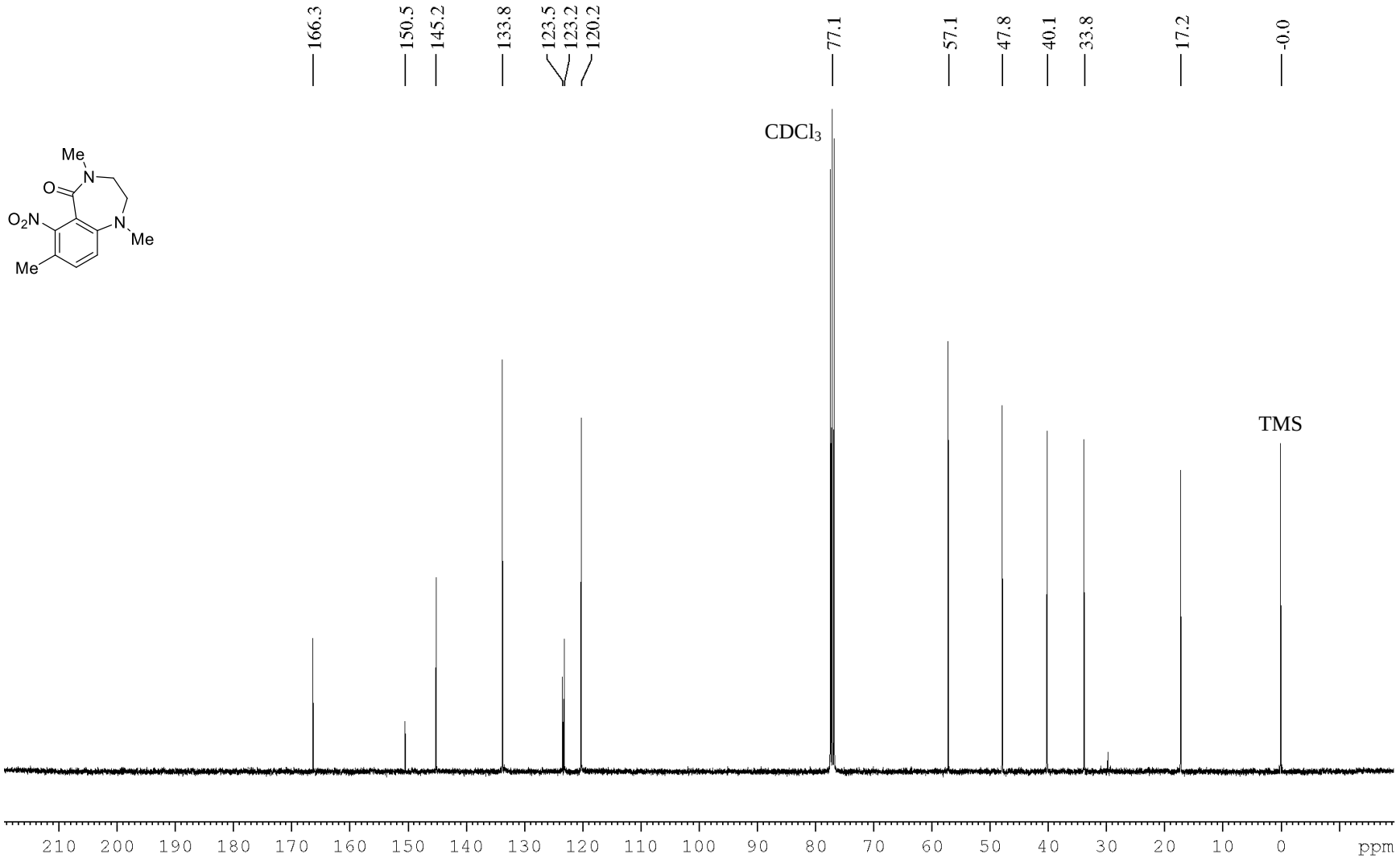
^{13}C {^{1}H} NMR of 2l in $CDCl_3$ with 1% v/v TMS at 101 MHz



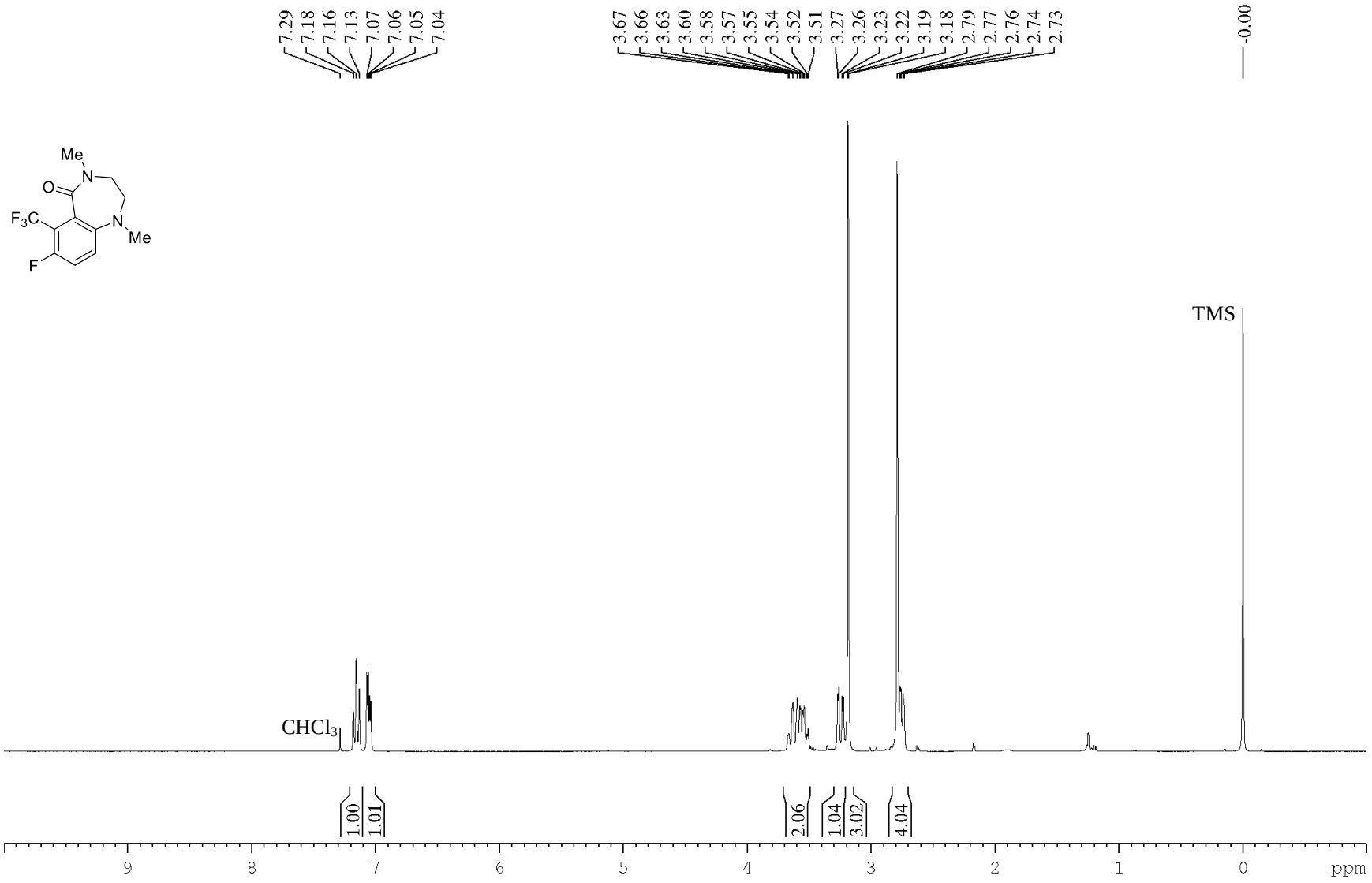
^{1}H NMR of 2m in $CDCl_3$ with 1% v/v TMS at 400 MHz



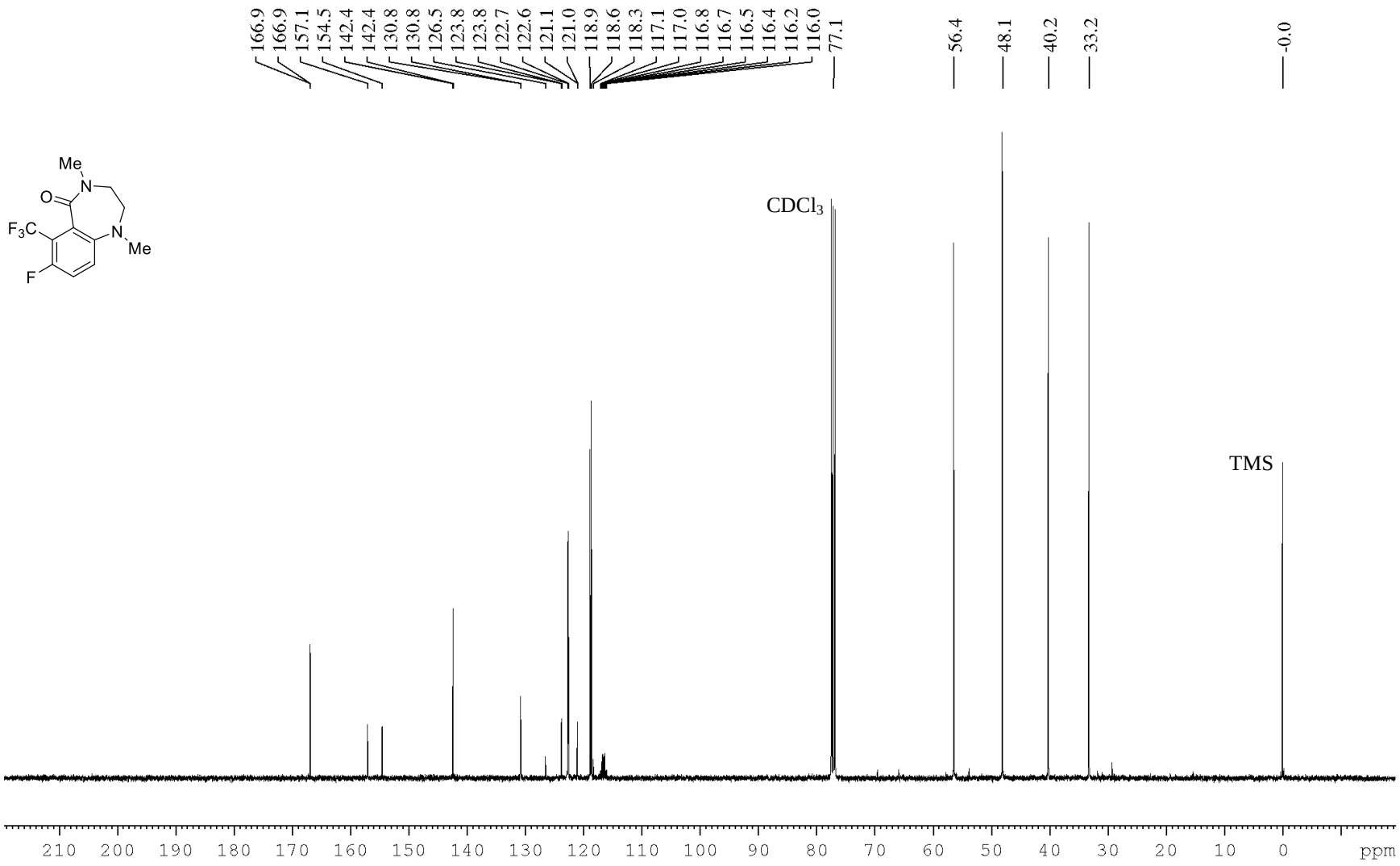
^{13}C {^{1}H} NMR of 2m $CDCl_3$ with 1% v/v TMS at 101 MHz



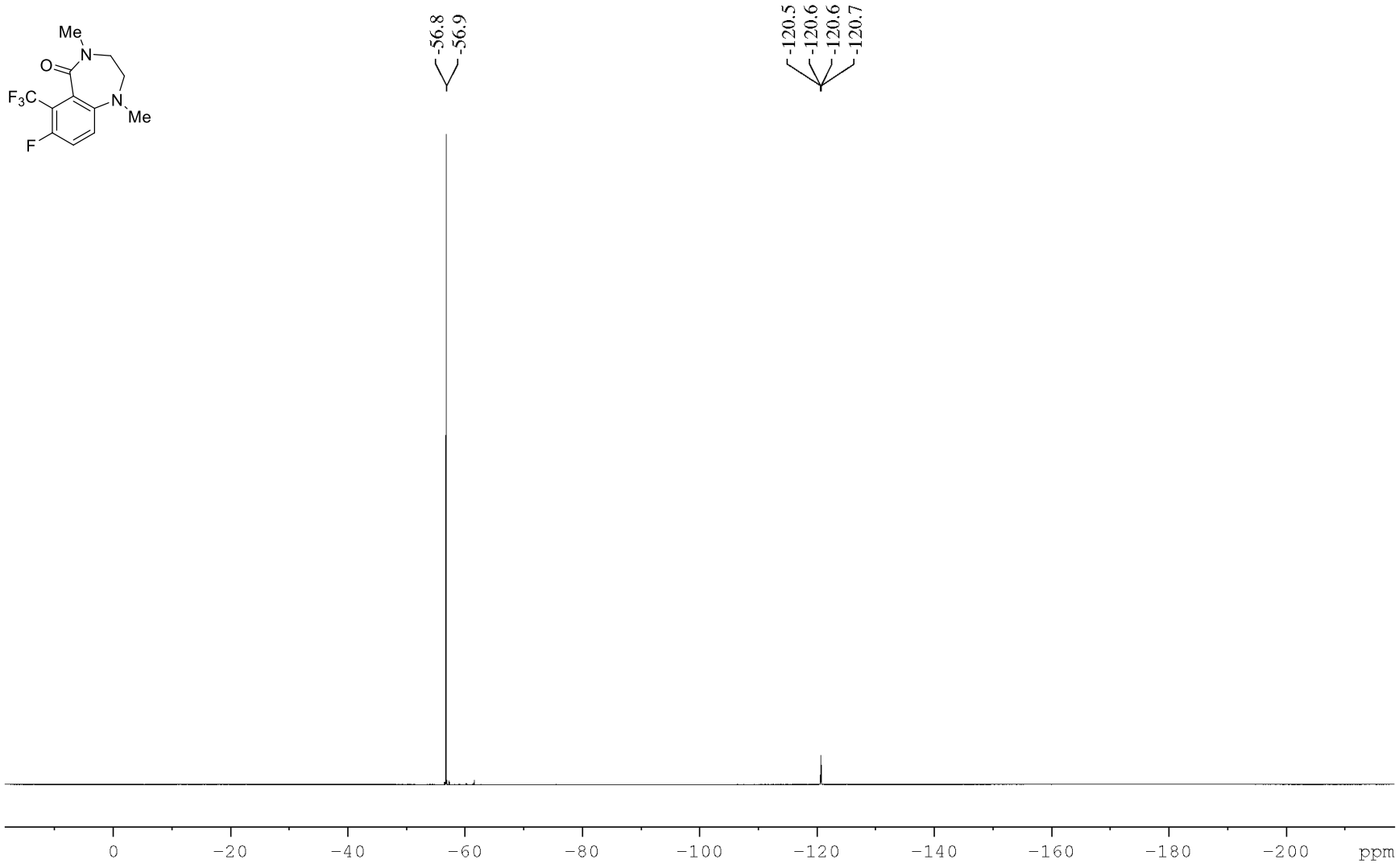
^{1}H NMR of 2n in $CDCl_3$ with 1% v/v TMS at 400 MHz



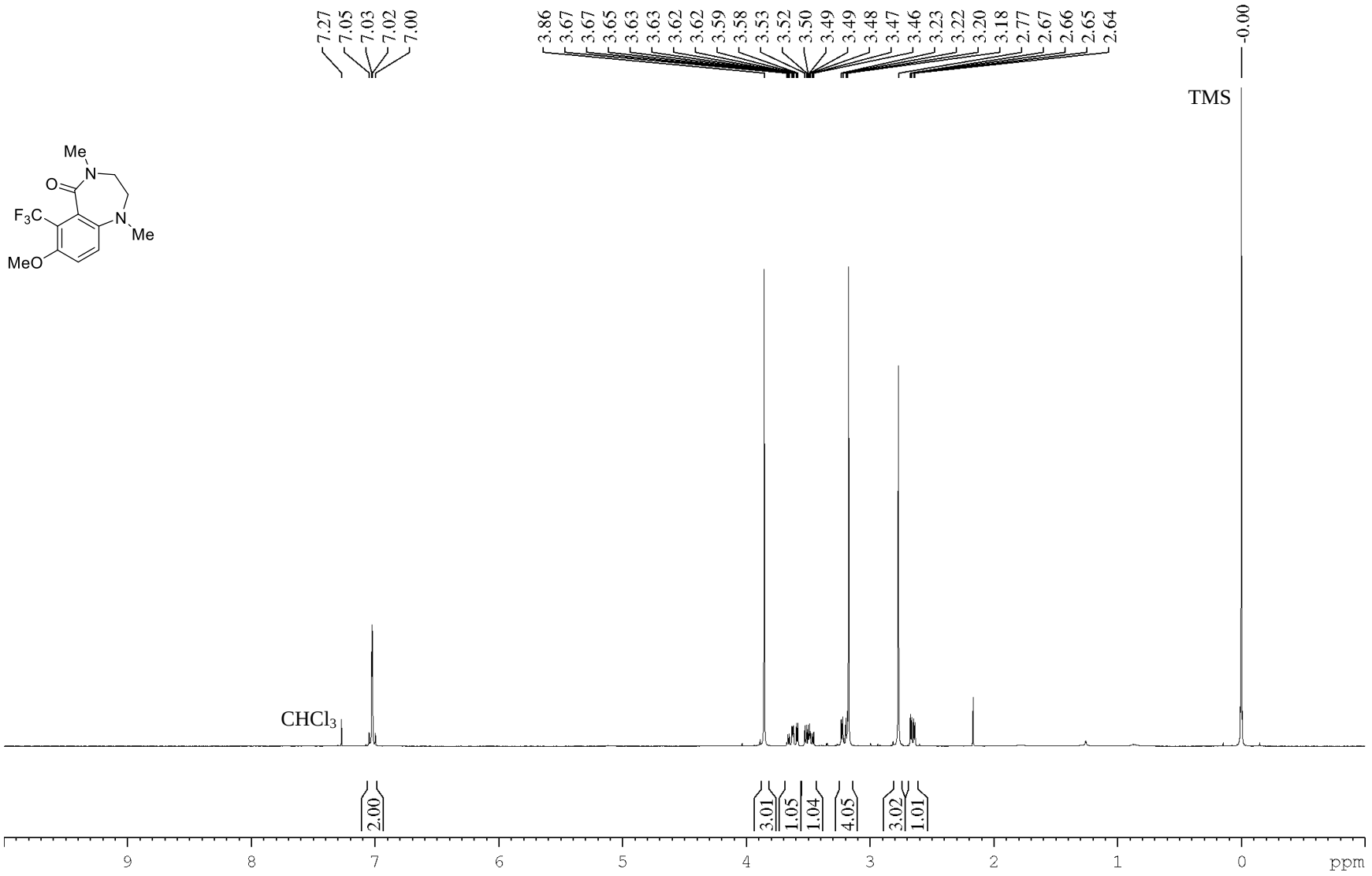
^{13}C {^{1}H} NMR of 2n $CDCl_3$ with 1% v/v TMS at 101 MHz



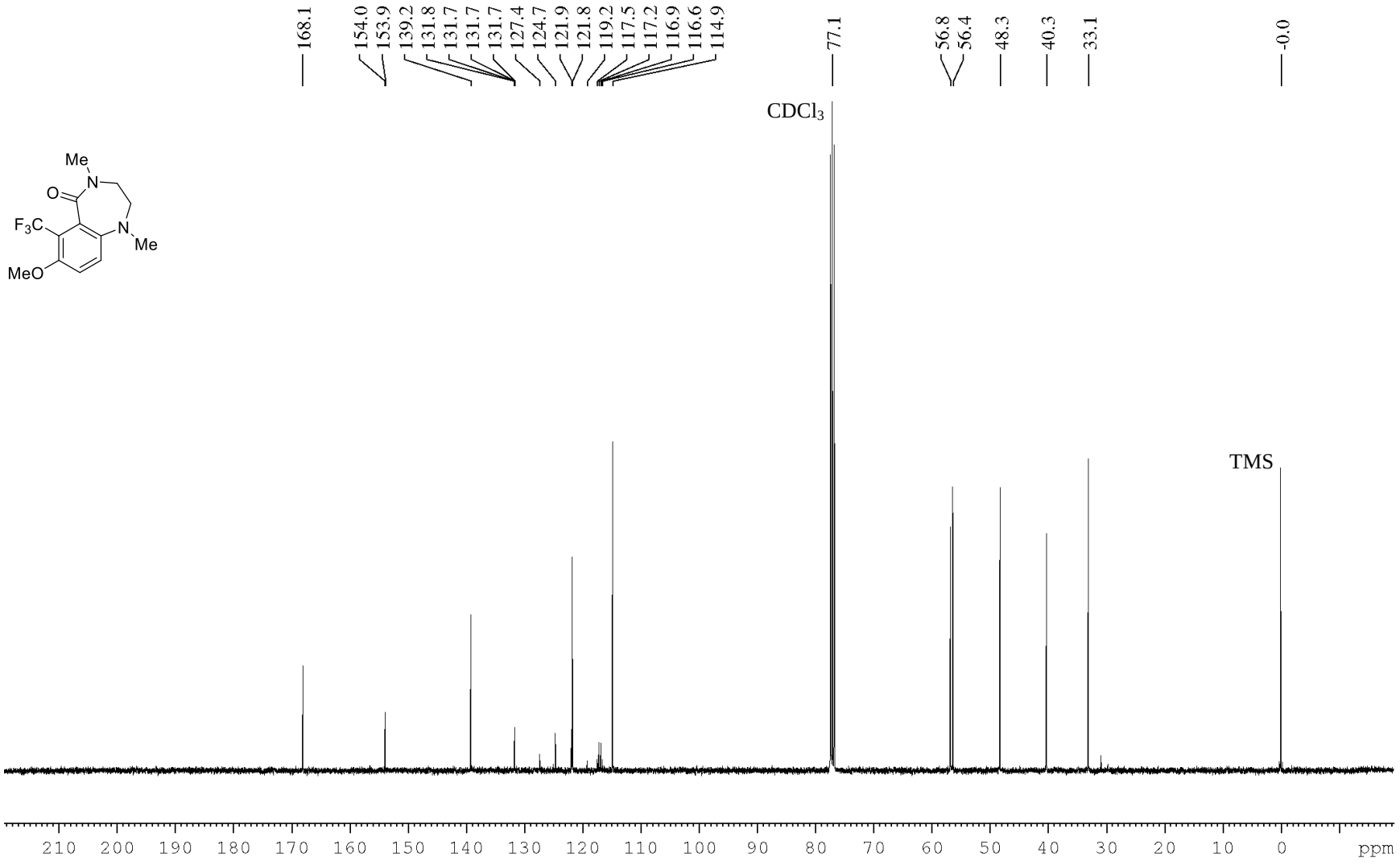
^{19}F {^{1}H} NMR of 2n in $CDCl_3$ with 1% v/v TMS at 376 MHz



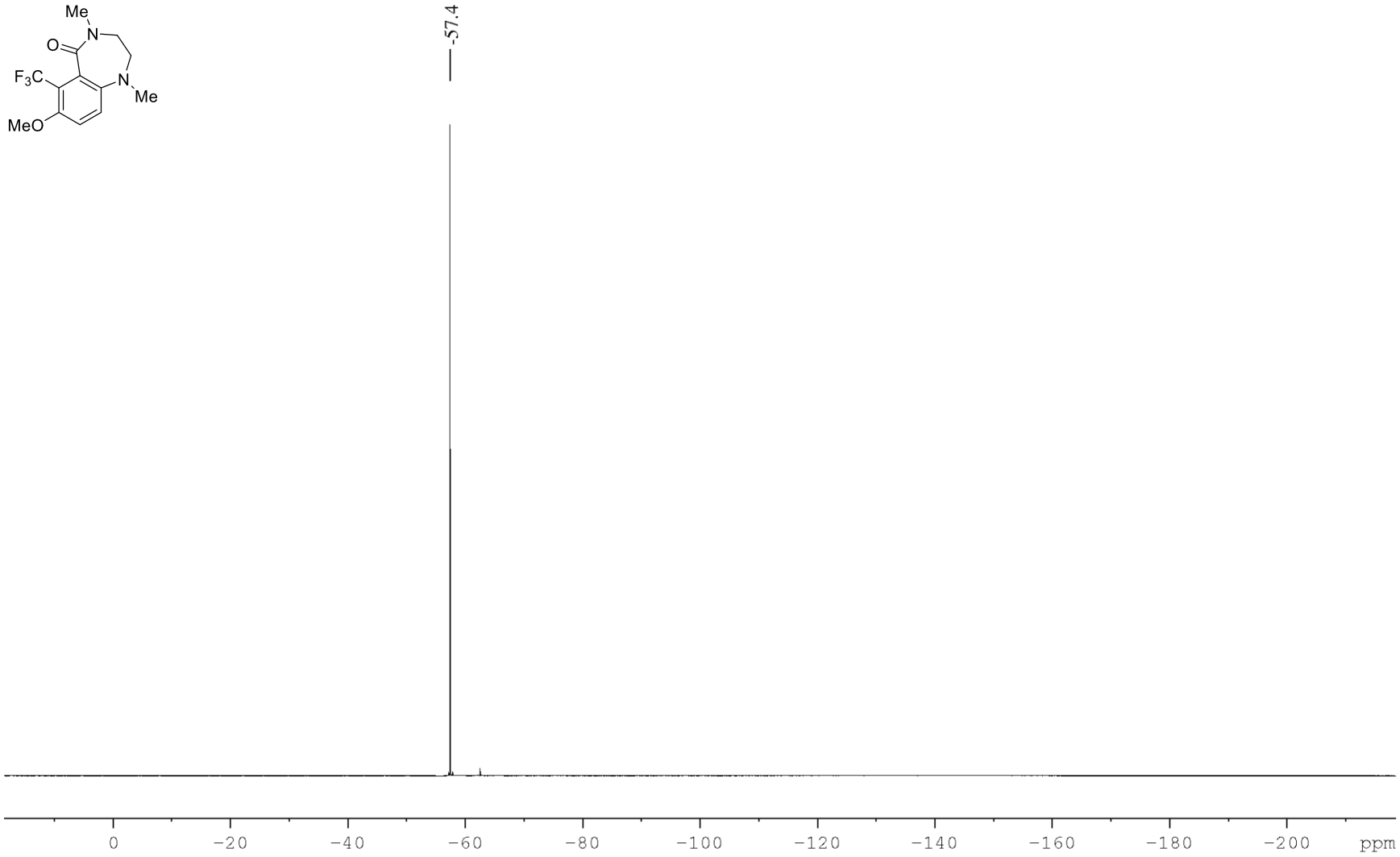
^{1}H NMR of 2o in $CDCl_3$ with 1% v/v TMS at 400 MHz



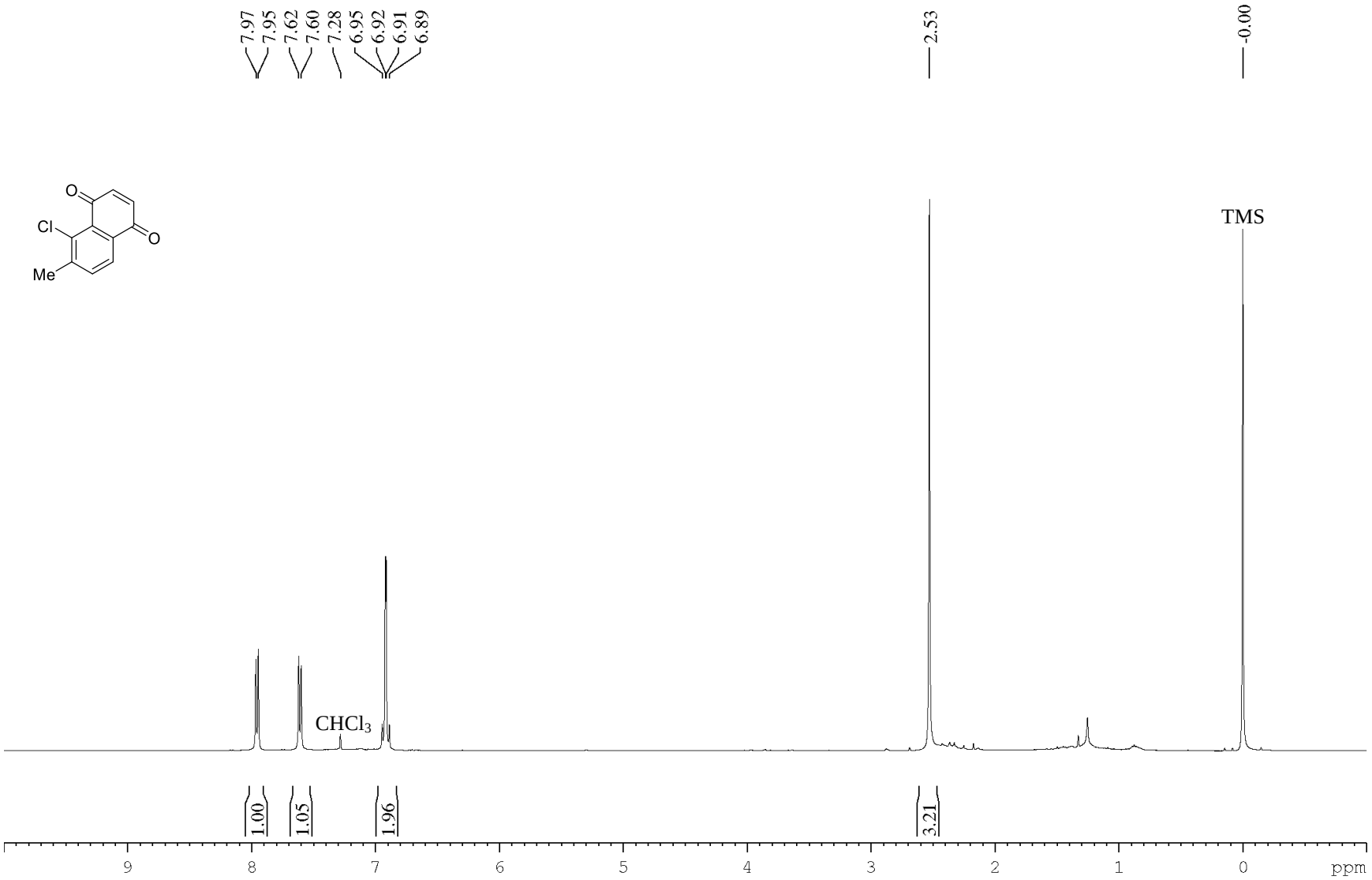
^{13}C {^{1}H} NMR of 2o $CDCl_3$ with 1% v/v TMS at 101 MHz



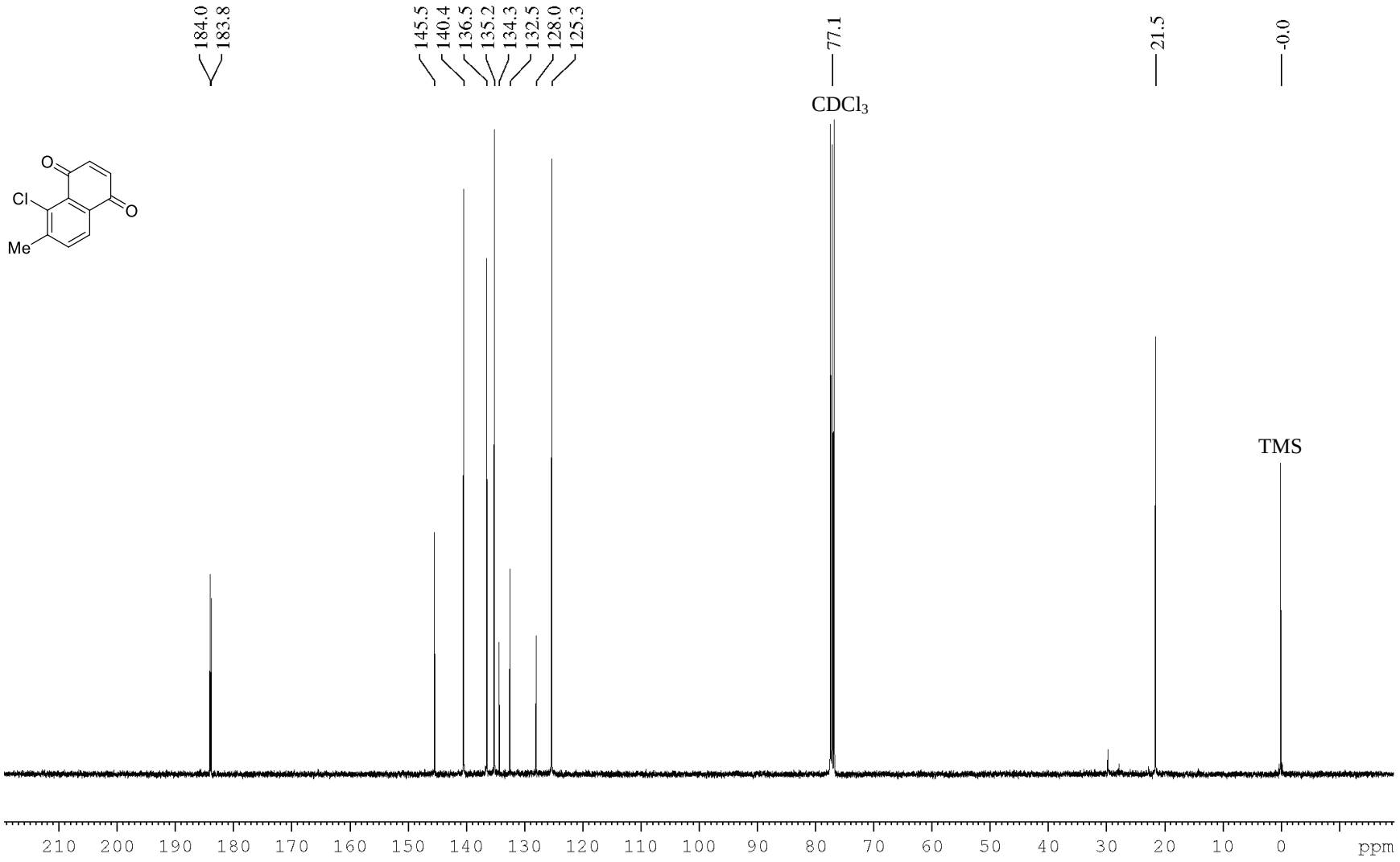
^{19}F {^{1}H} NMR of 2o in $CDCl_3$ with 1% v/v TMS at 376 MHz



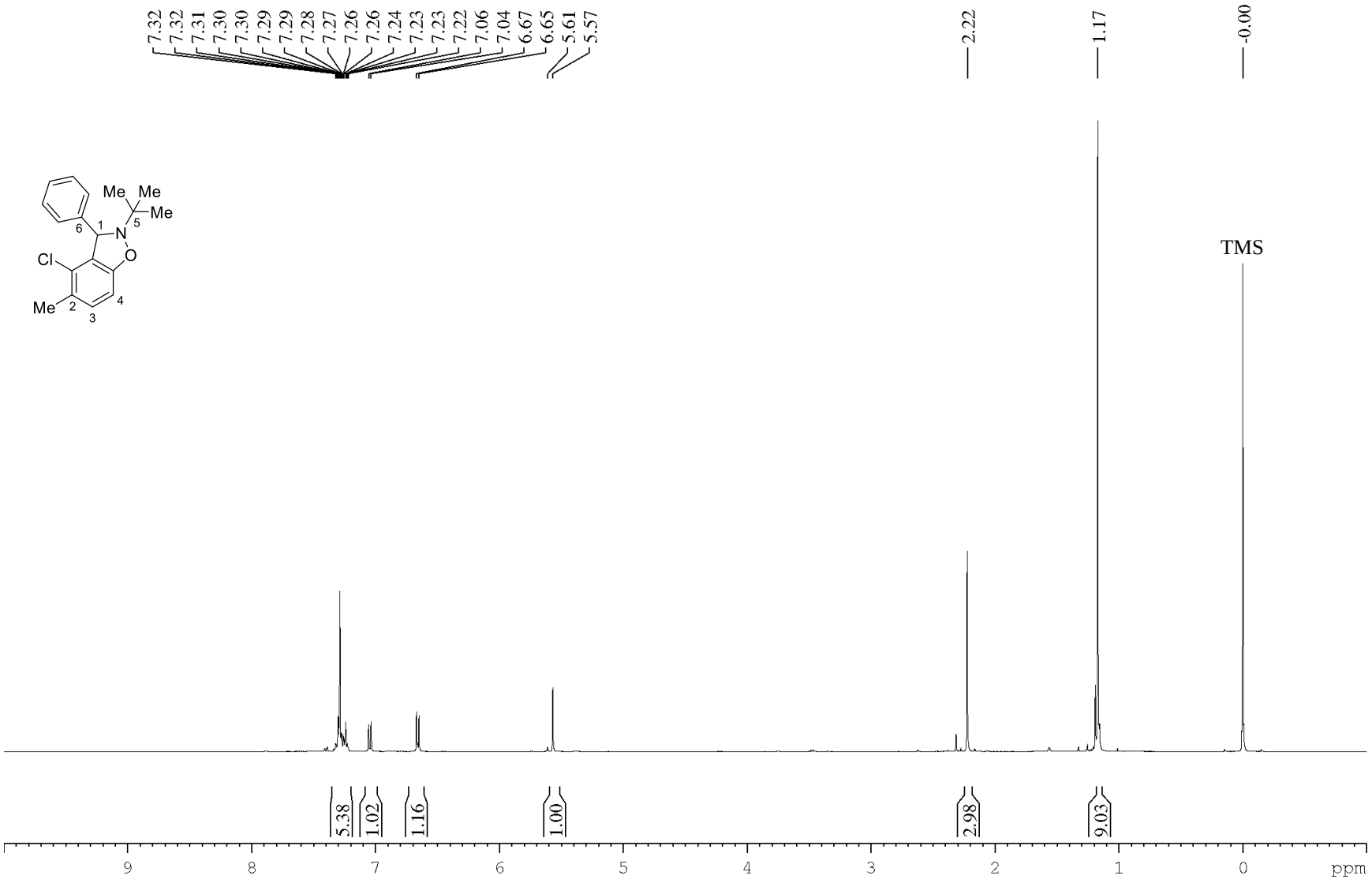
^{1}H NMR of 4a in $CDCl_3$ with 1% v/v TMS at 400 MHz



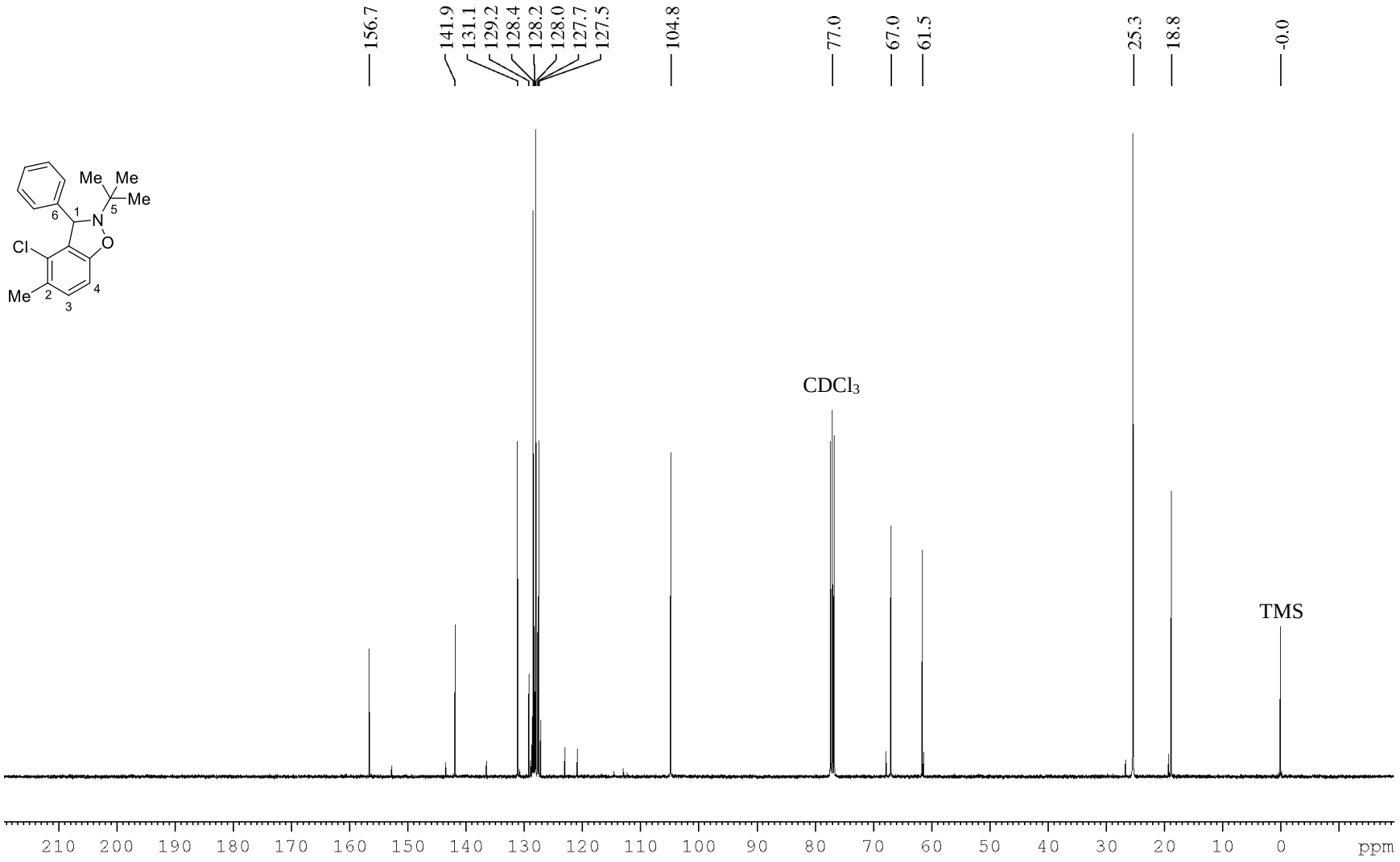
^{13}C {^{1}H} NMR of 4a $CDCl_3$ with 1% v/v TMS at 101 MHz



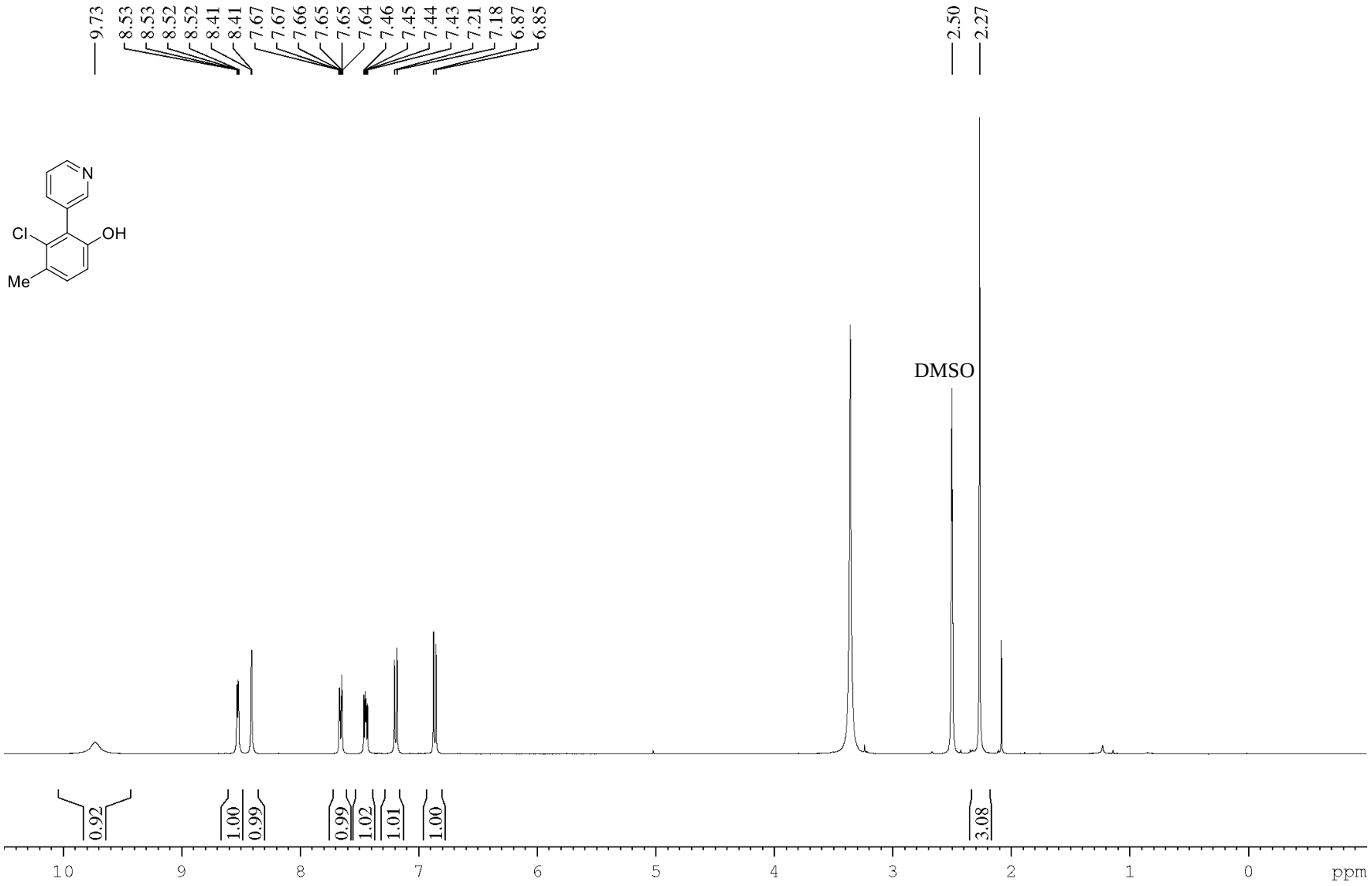
^{1}H NMR of 4b in $CDCl_3$ with 1% v/v TMS at 400 MHz



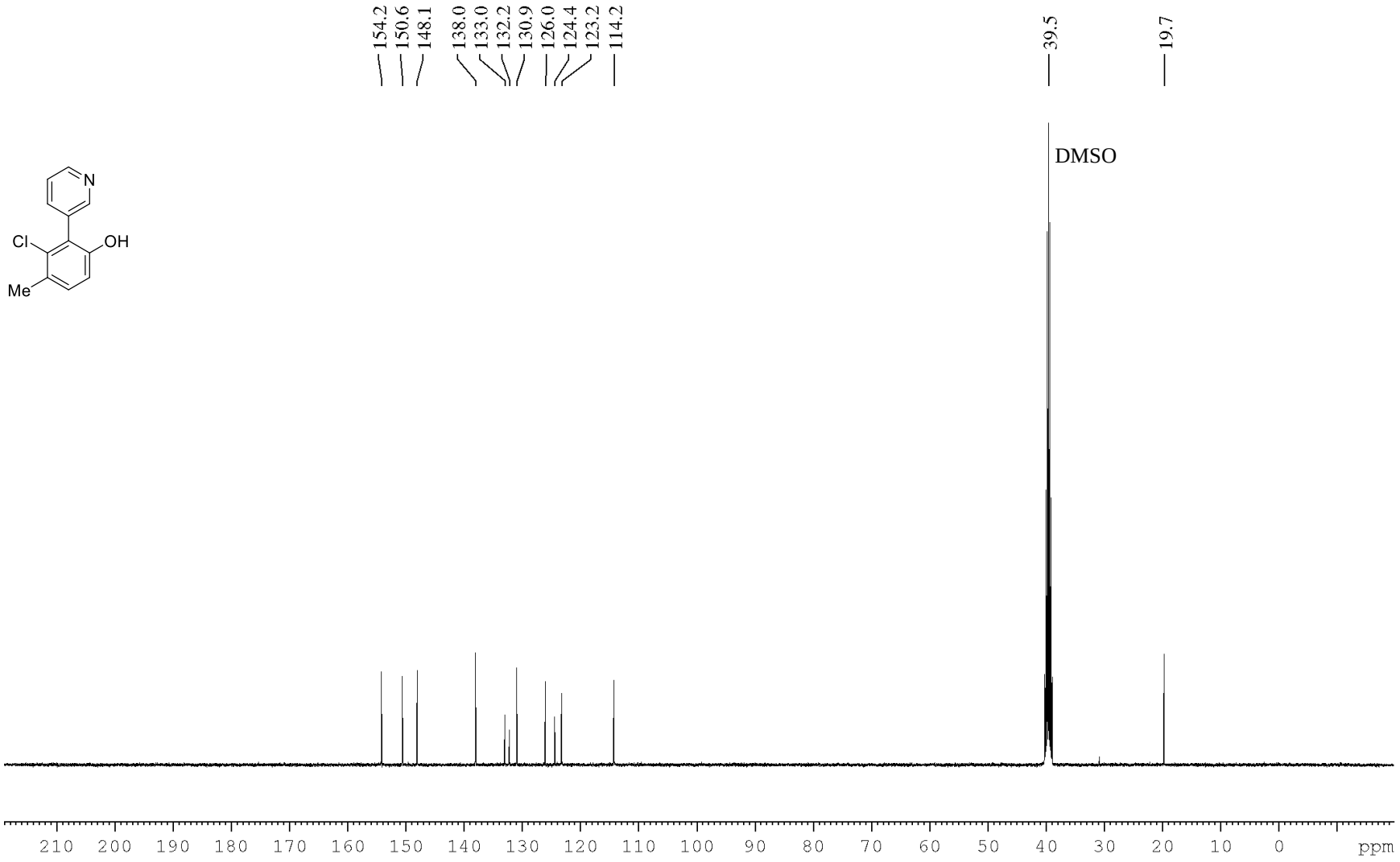
^{13}C {^{1}H} NMR of 4b $CDCl_3$ with 1% v/v TMS at 101 MHz



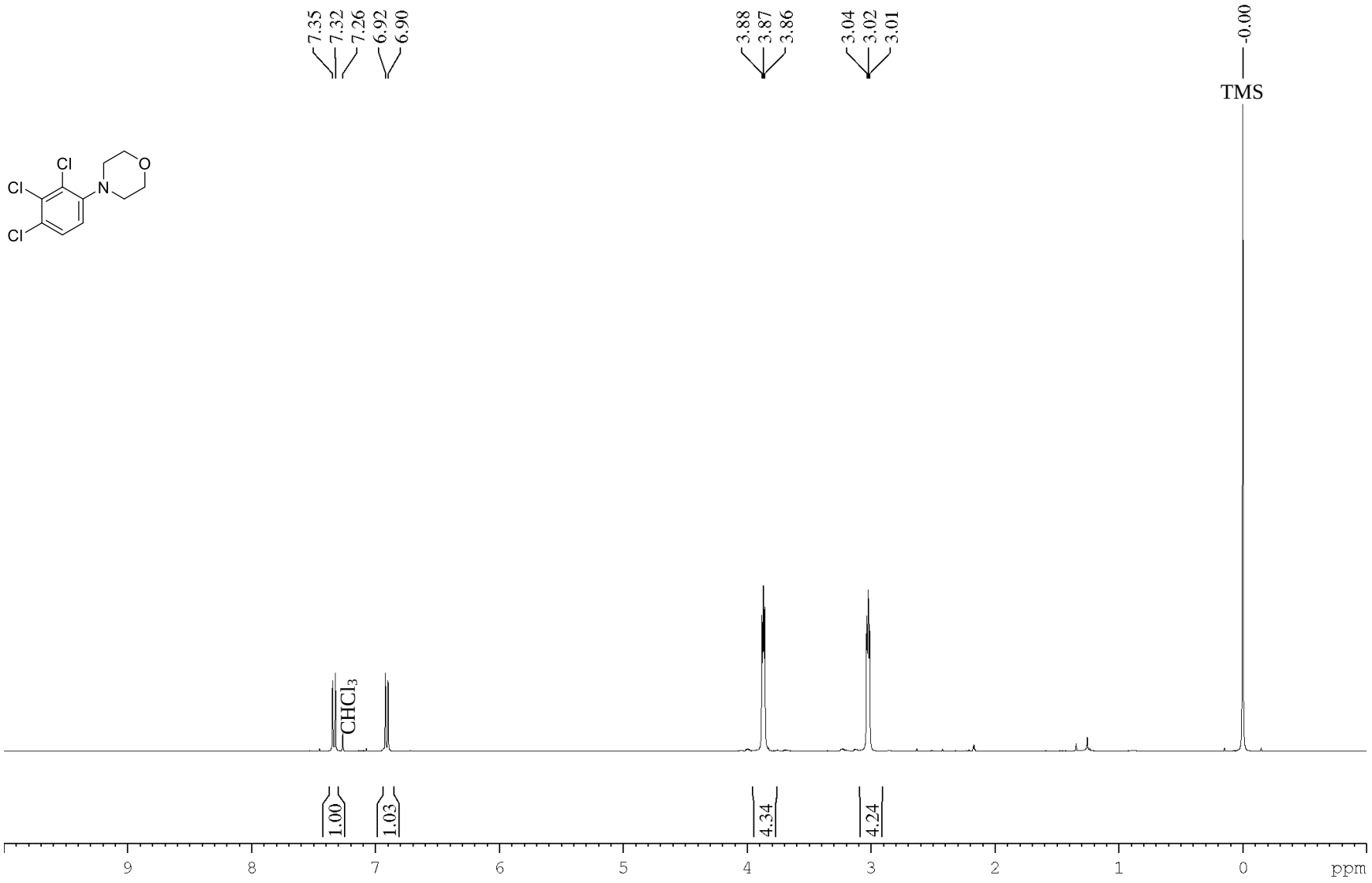
^{1}H NMR of 4c in DMSO-d_6 at 400 MHz



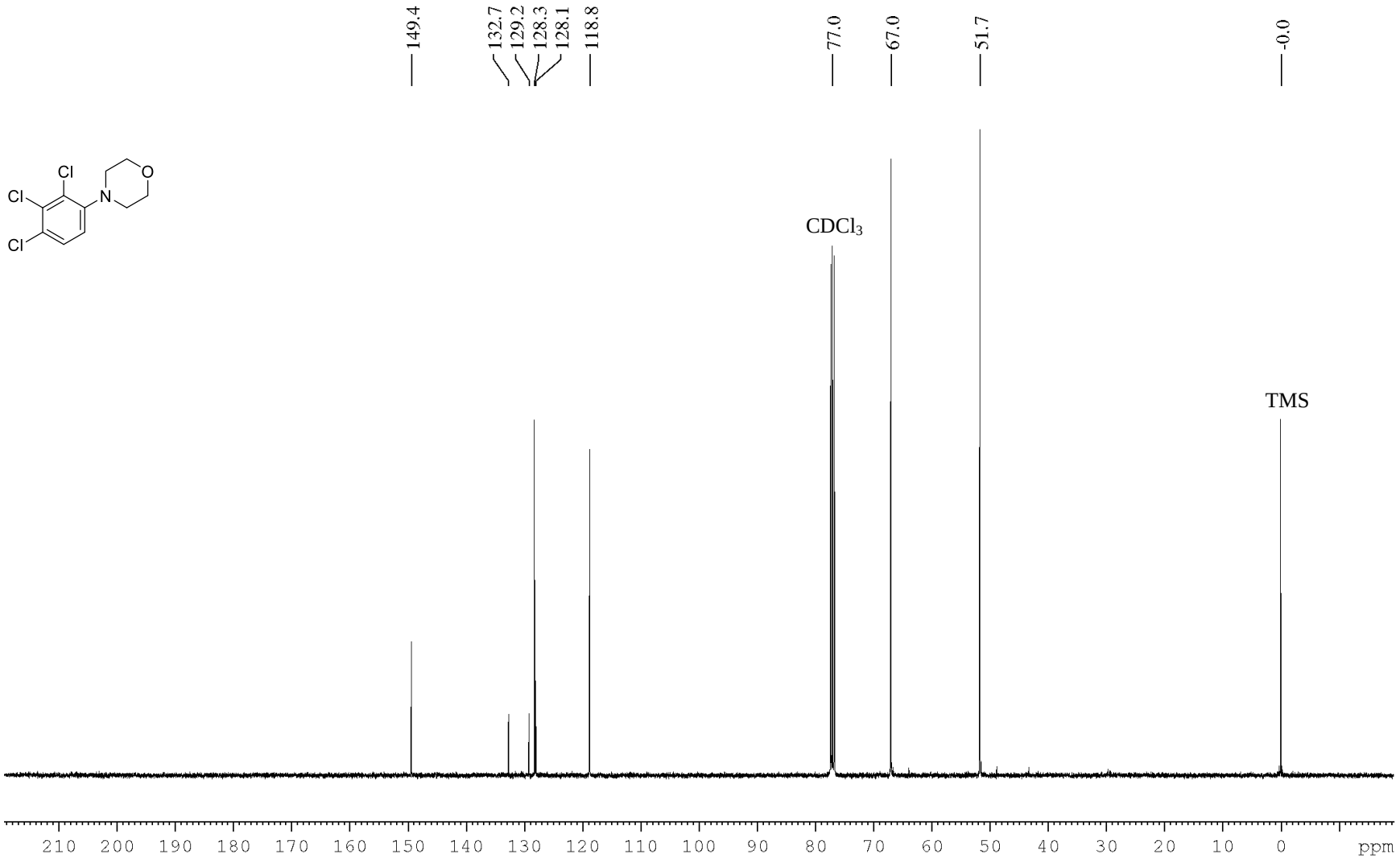
^{13}C {^{1}H} NMR of 4c DMSO-d_6 at 101 MHz



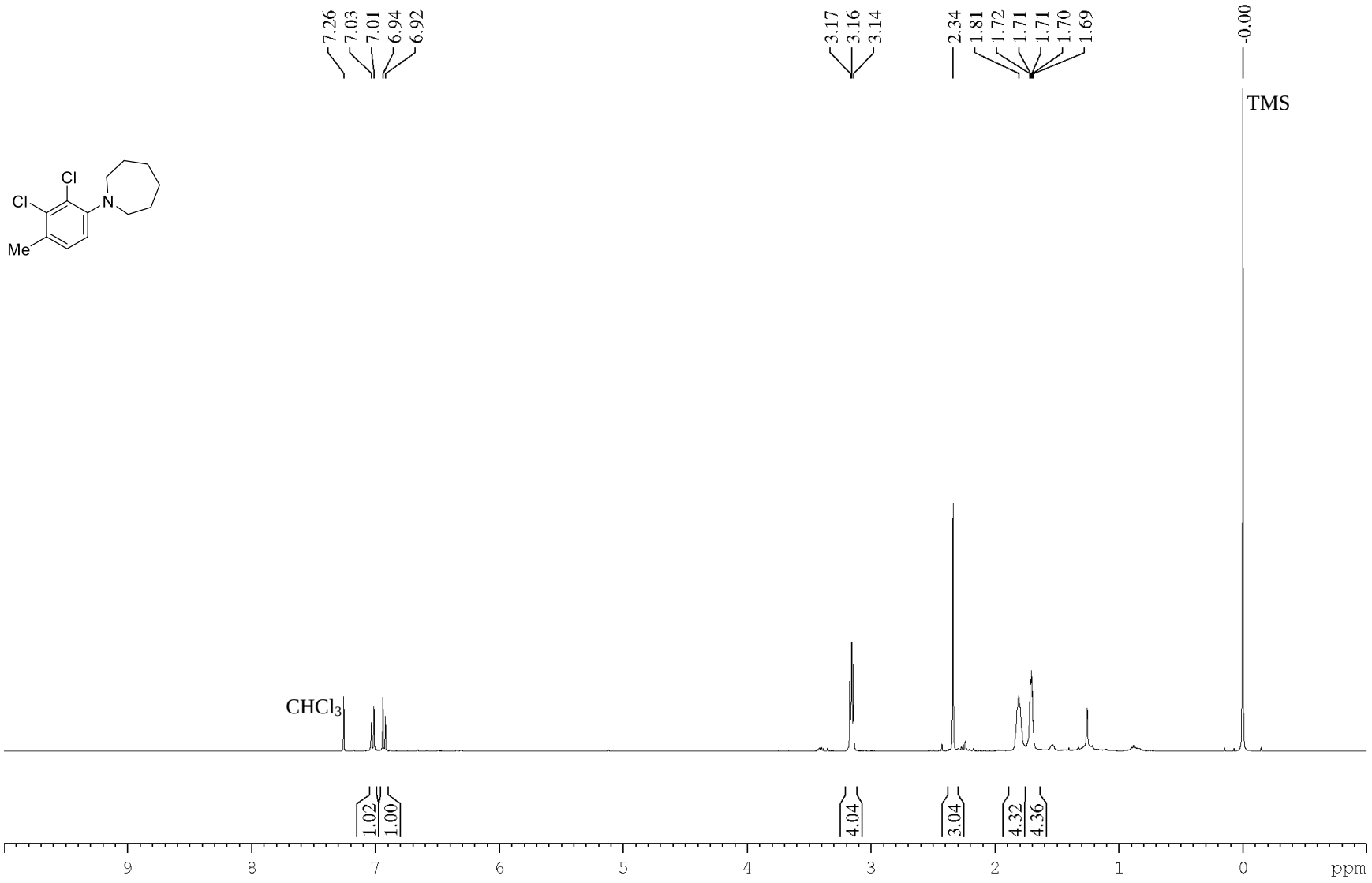
^{1}H NMR of 4d in $CDCl_3$ with 1% v/v TMS at 400 MHz



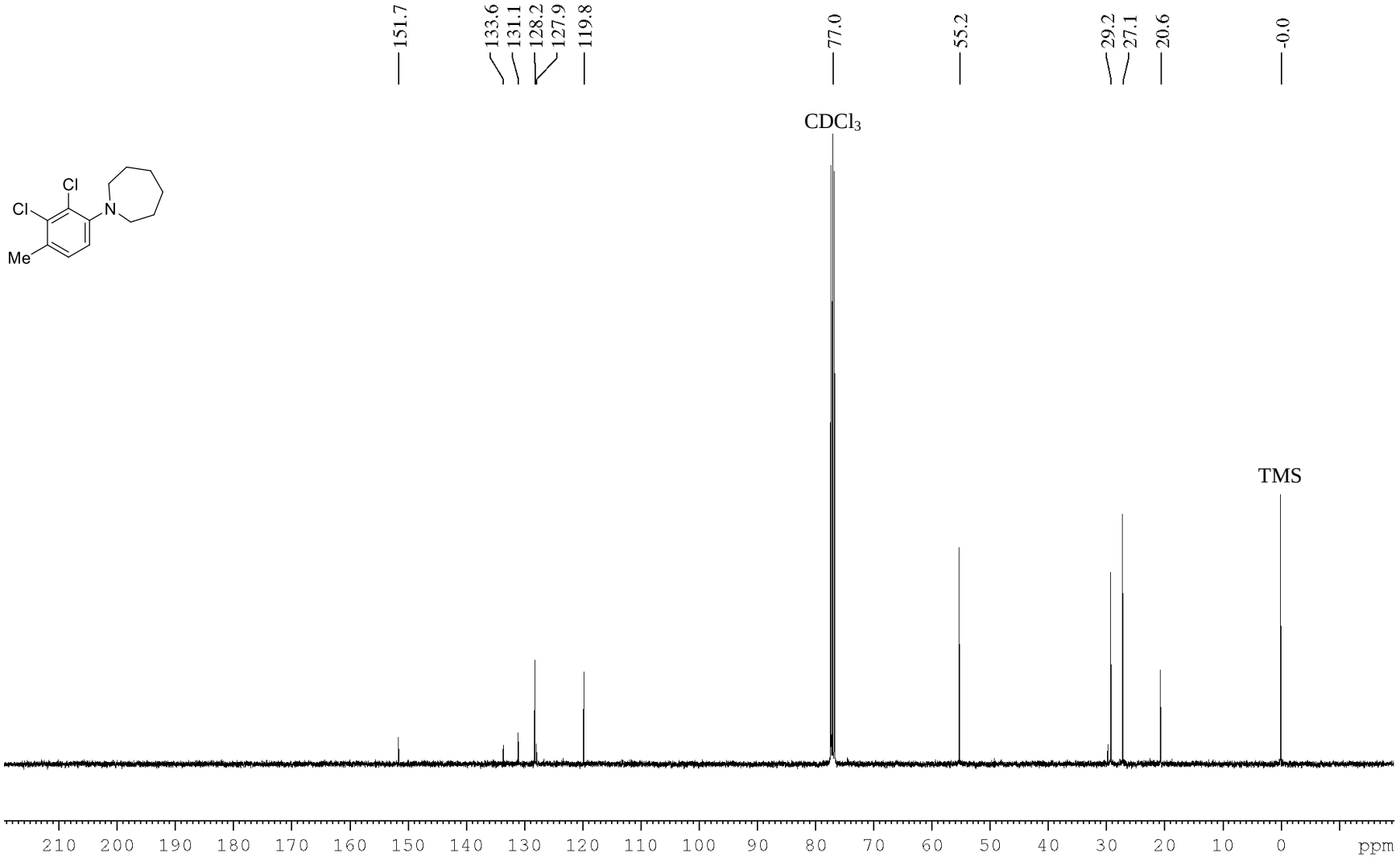
^{13}C {^{1}H} NMR of 4d $CDCl_3$ with 1% v/v TMS at 101 MHz



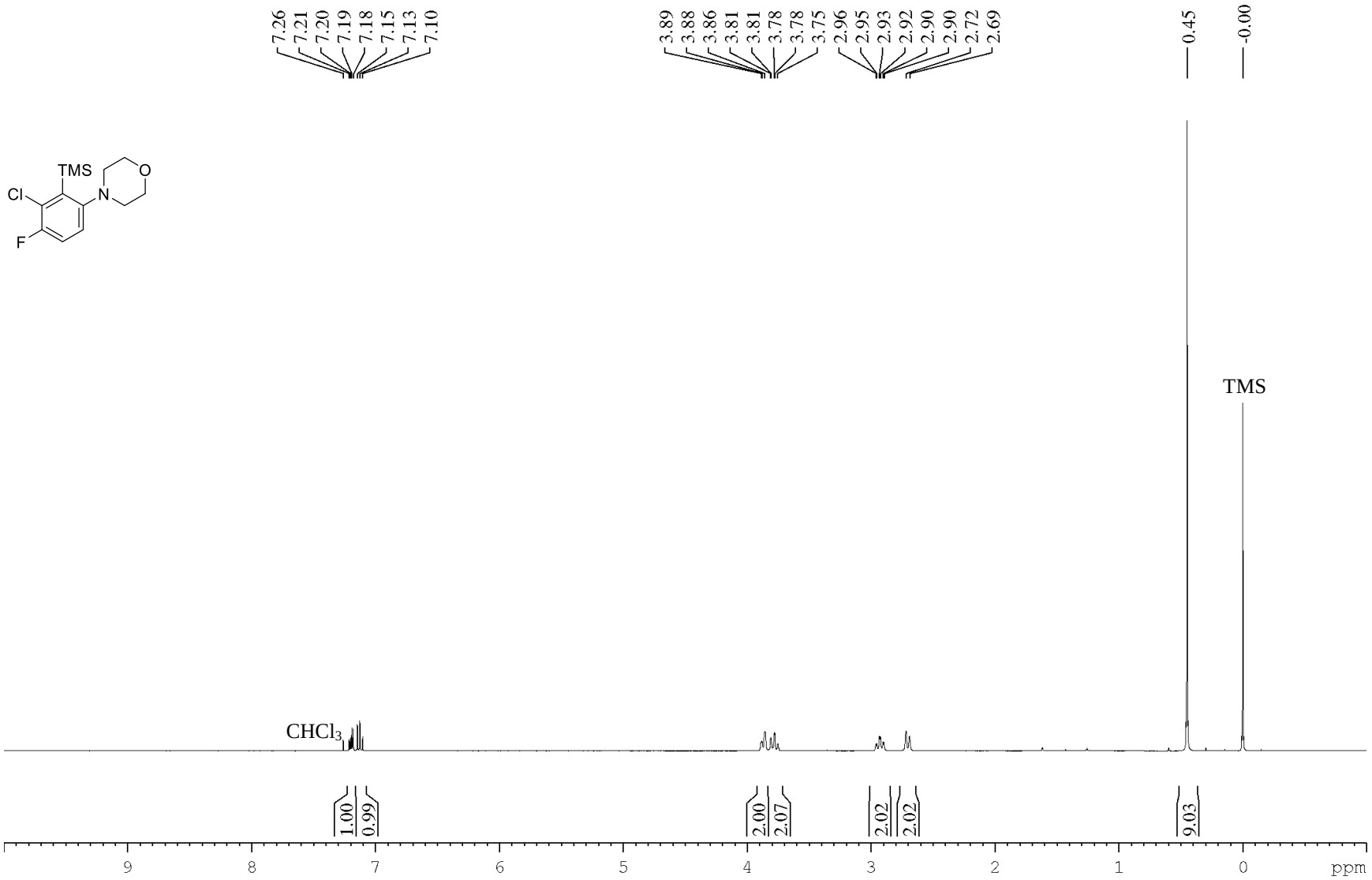
^{1}H NMR of 4e in $CDCl_3$ with 1% v/v TMS at 400 MHz



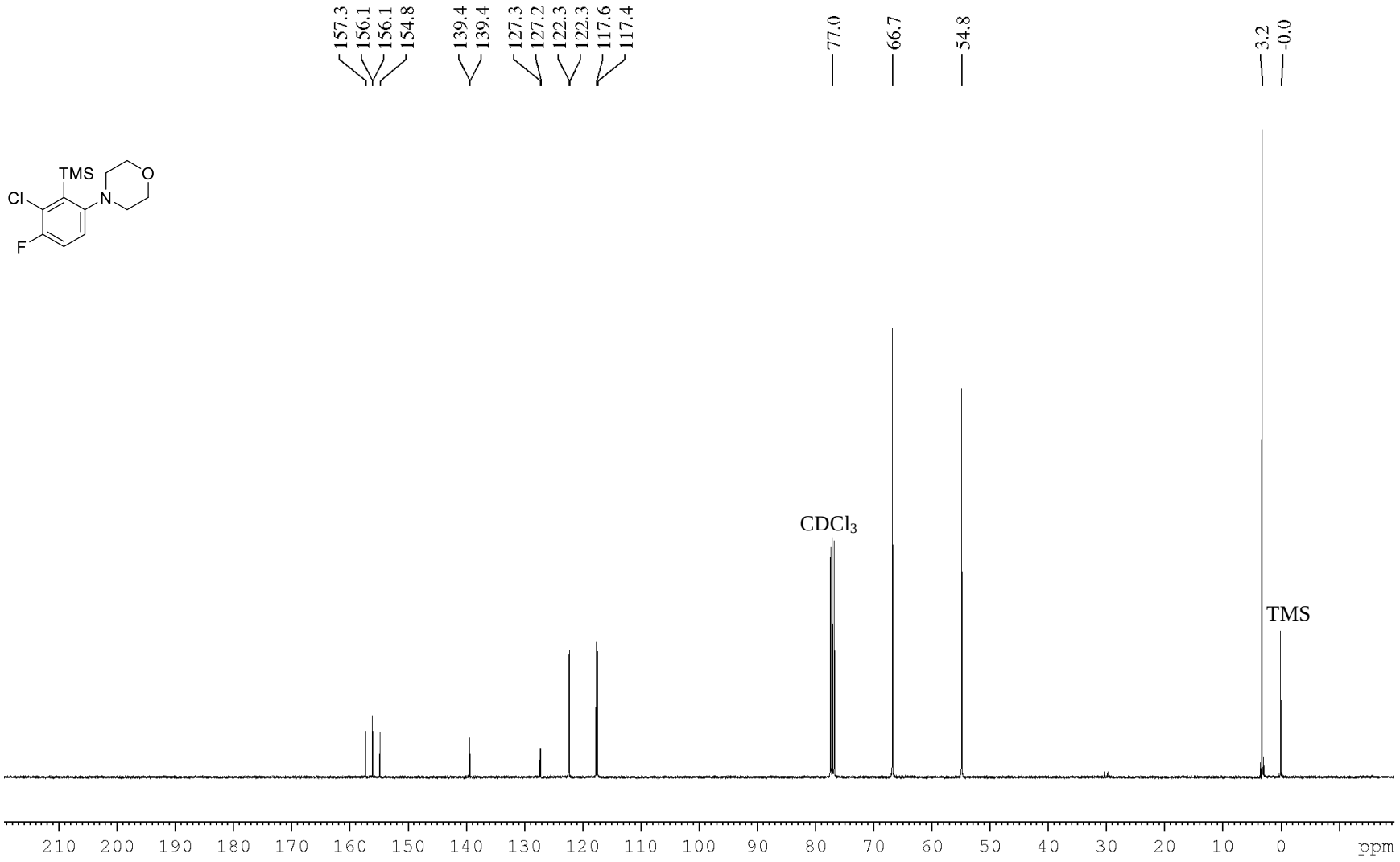
^{13}C {^{1}H} NMR of 4e $CDCl_3$ with 1% v/v TMS at 101 MHz



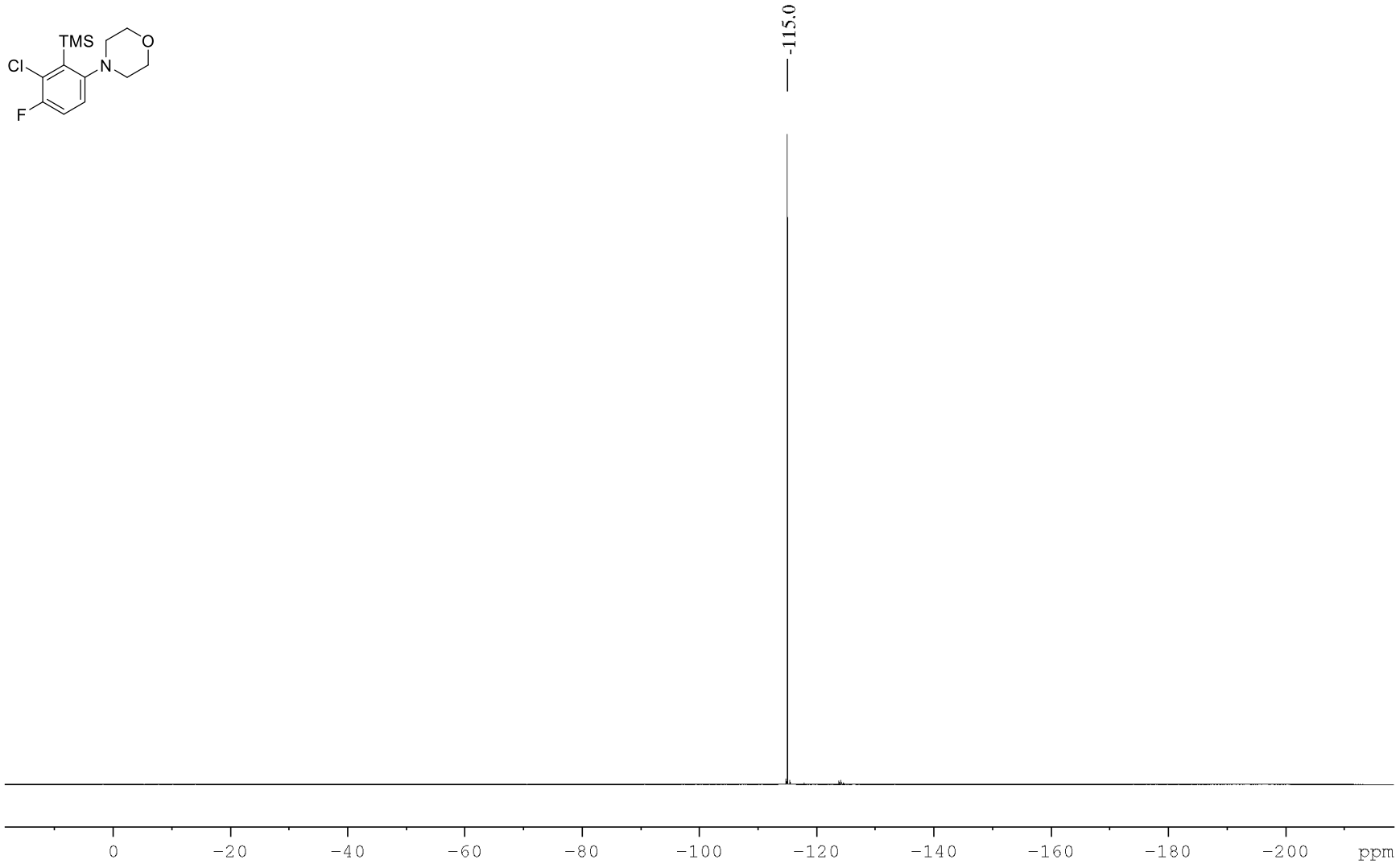
^{1}H NMR of 4f in $CDCl_3$ with 1% v/v TMS at 400 MHz



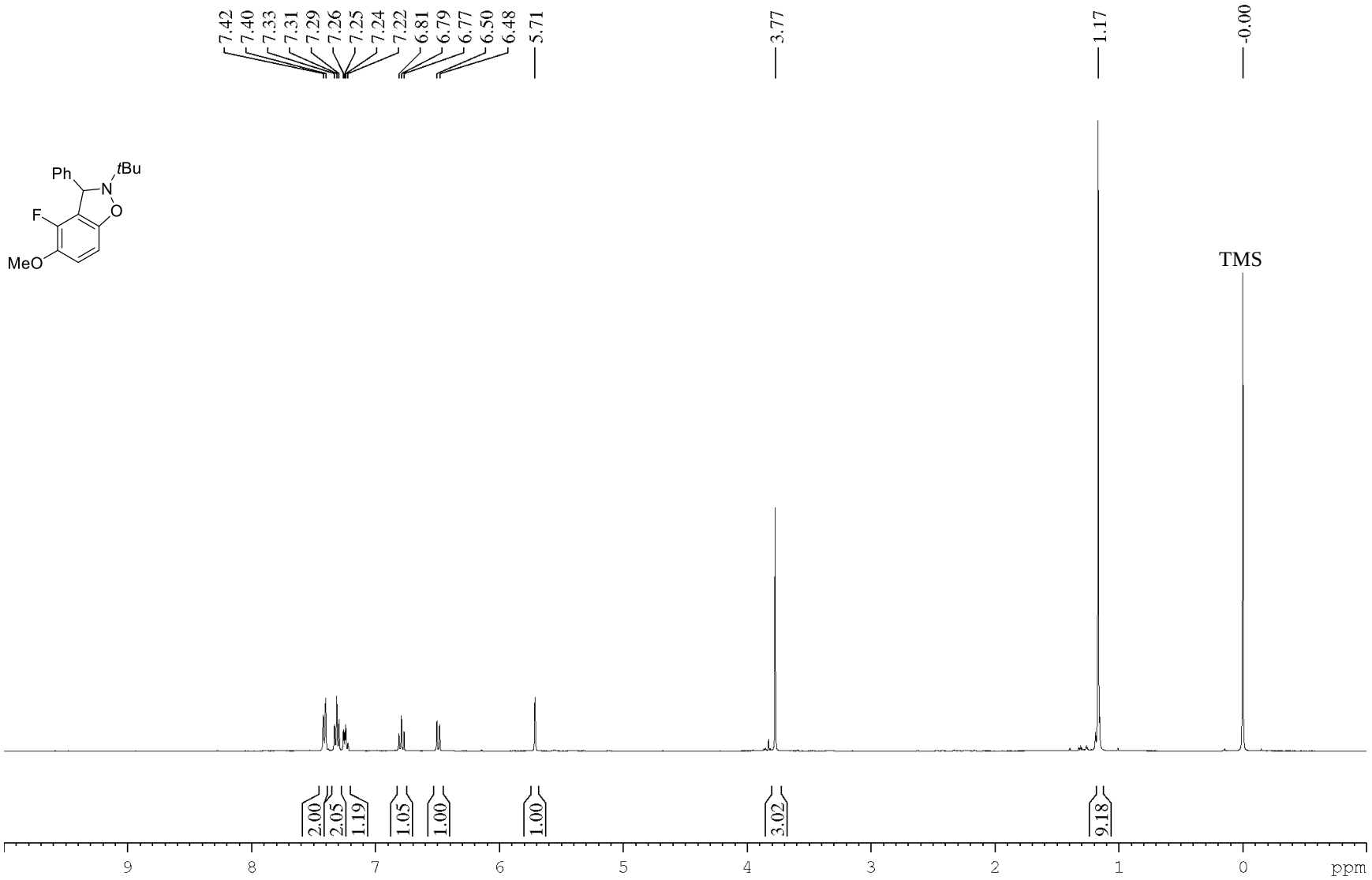
^{13}C {^{1}H} NMR of 4f $CDCl_3$ with 1% v/v TMS at 101 MHz



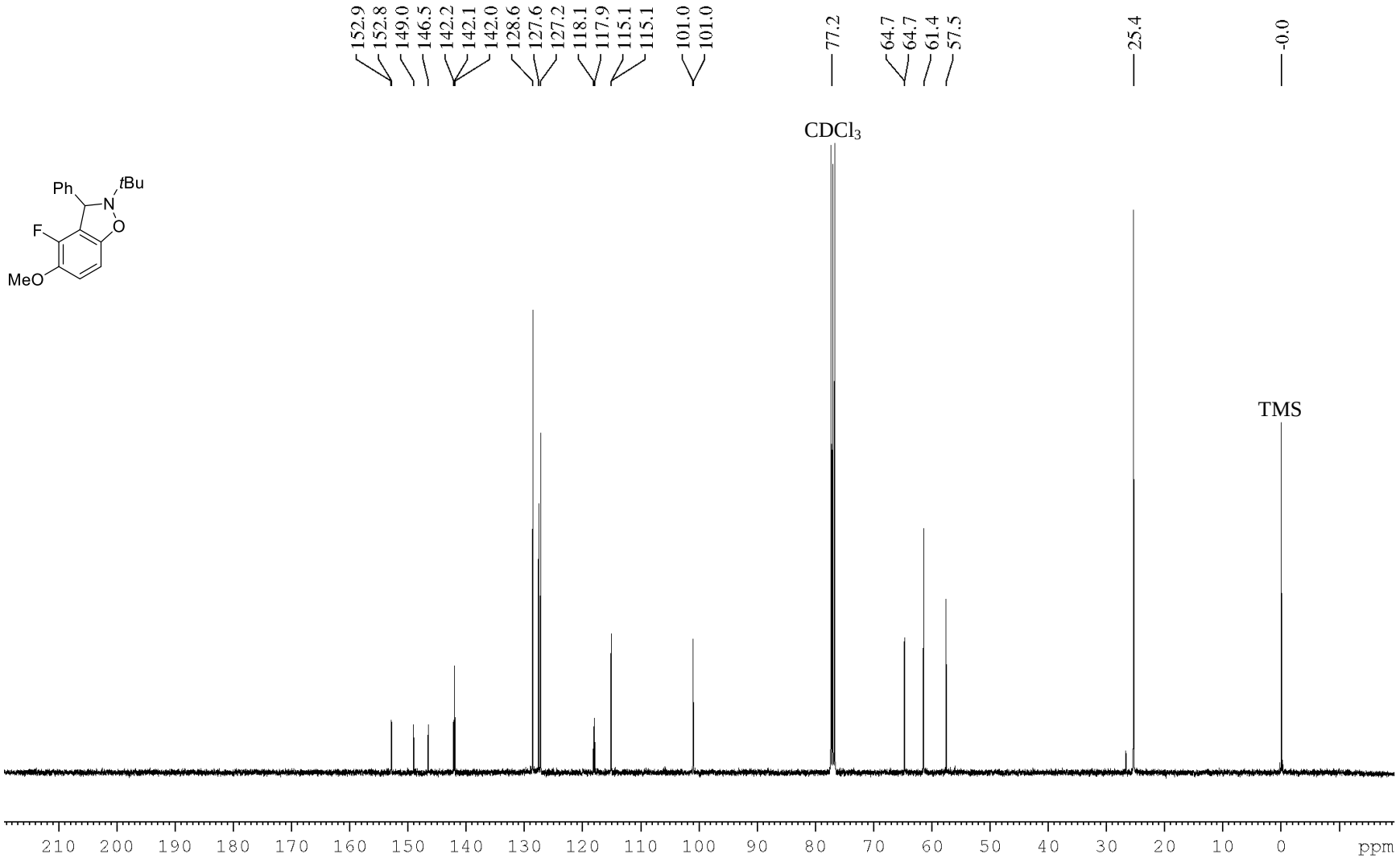
^{19}F {^{1}H} NMR of 4f in $CDCl_3$ with 1% v/v TMS at 376 MHz



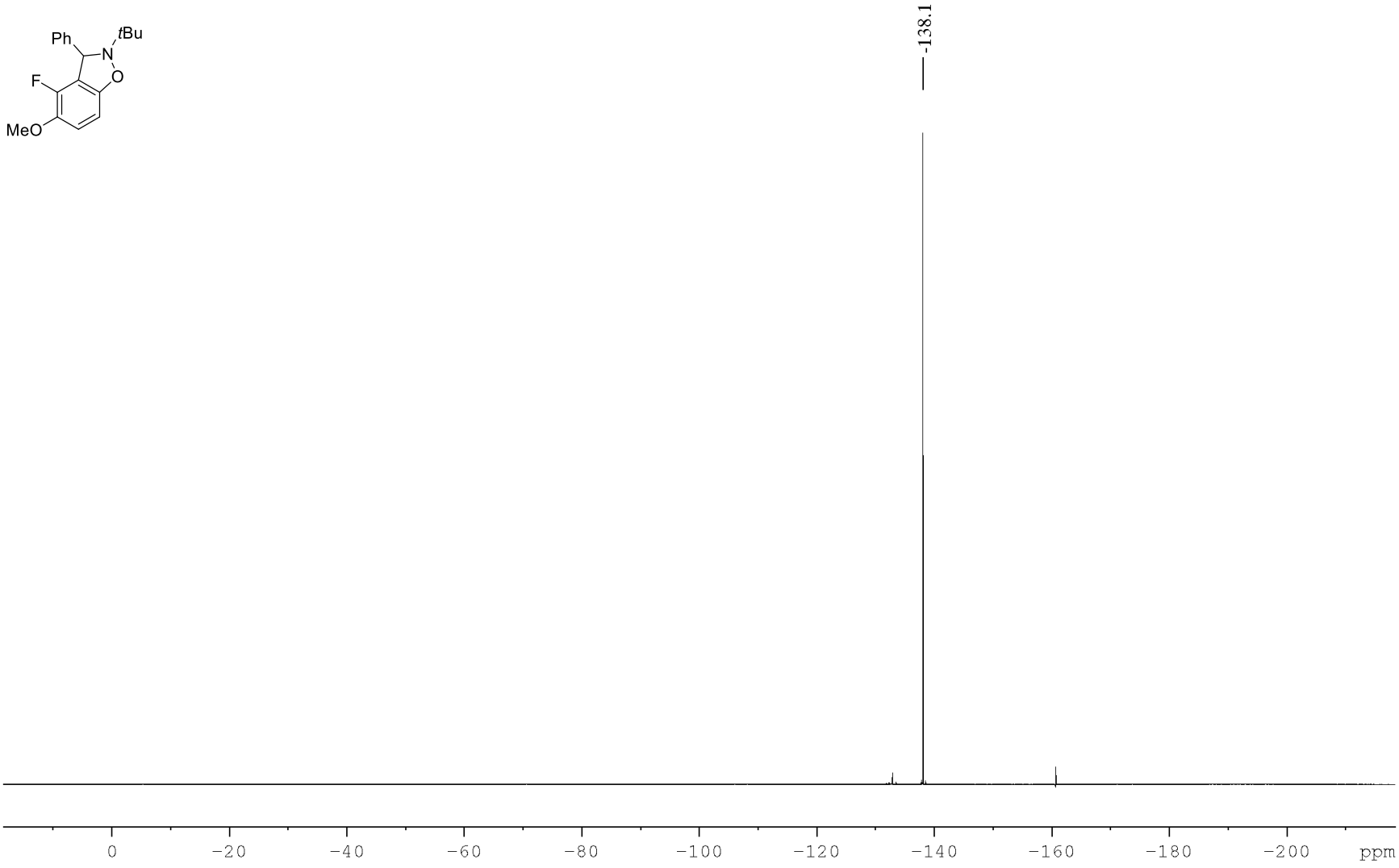
^{1}H NMR of 5a in $CDCl_3$ with 1% v/v TMS at 400 MHz



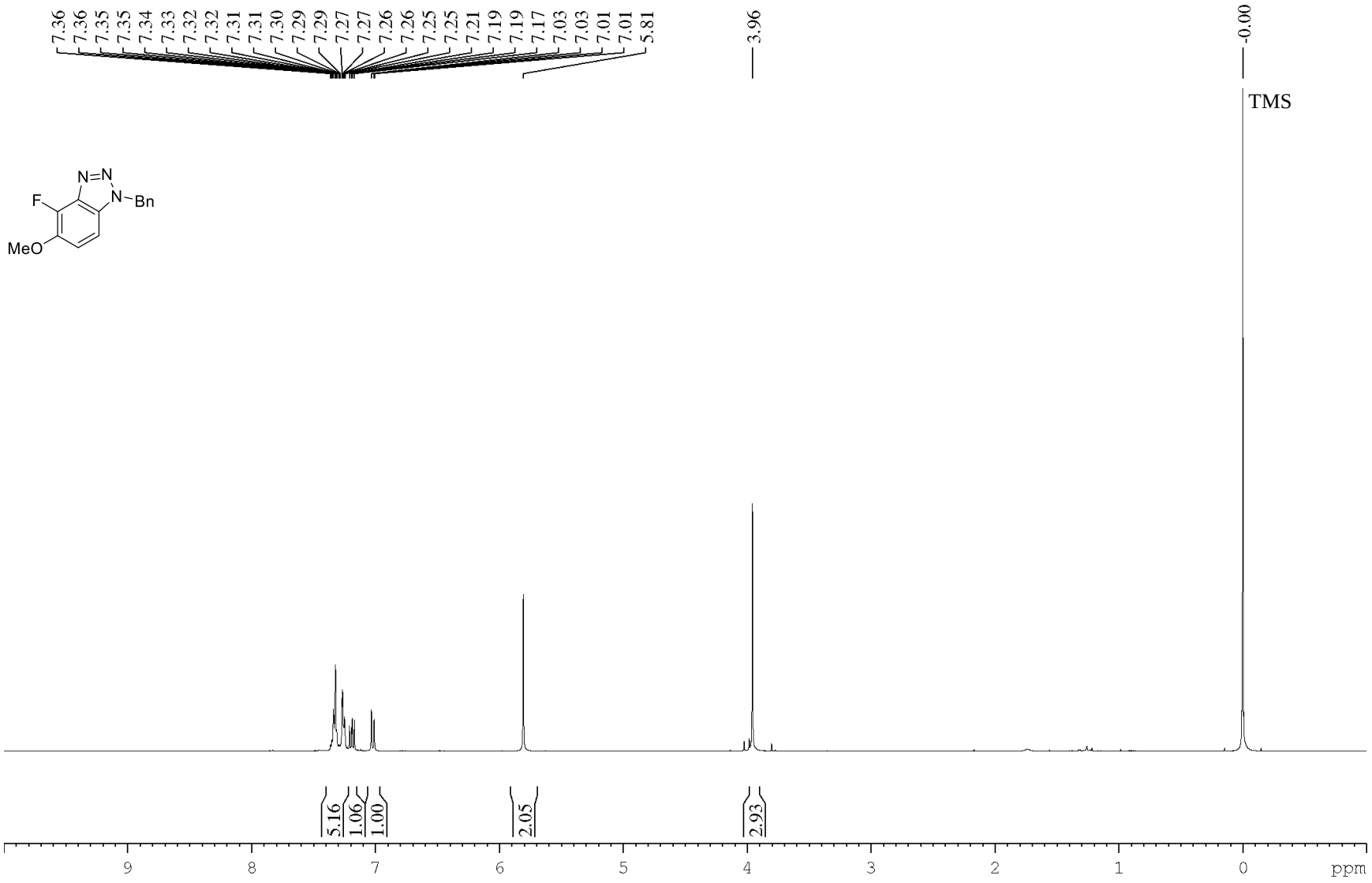
^{13}C {^{1}H} NMR of 5a $CDCl_3$ with 1% v/v TMS at 101 MHz



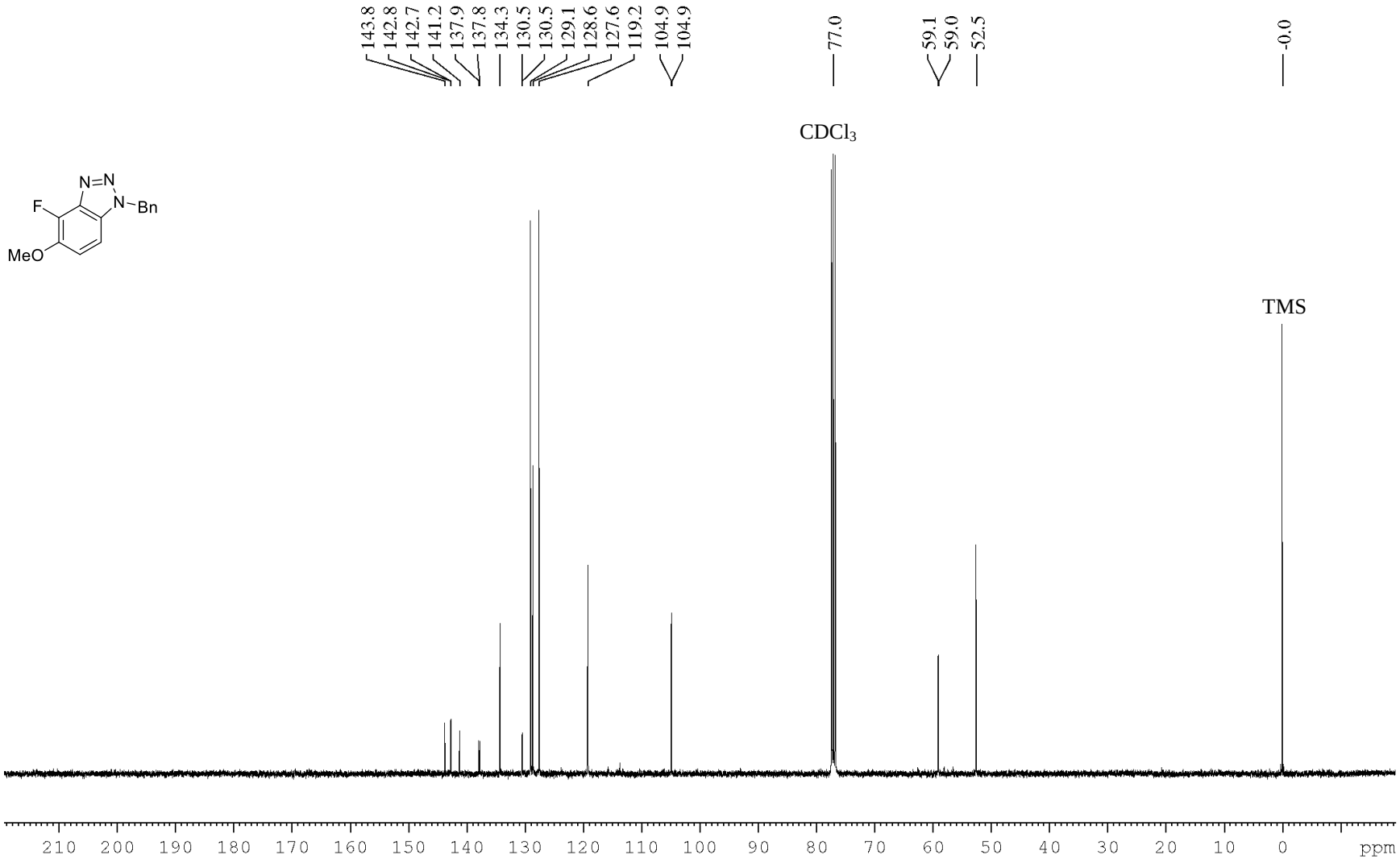
^{19}F {^{1}H} NMR of 5a in $CDCl_3$ with 1% v/v TMS at 376 MHz



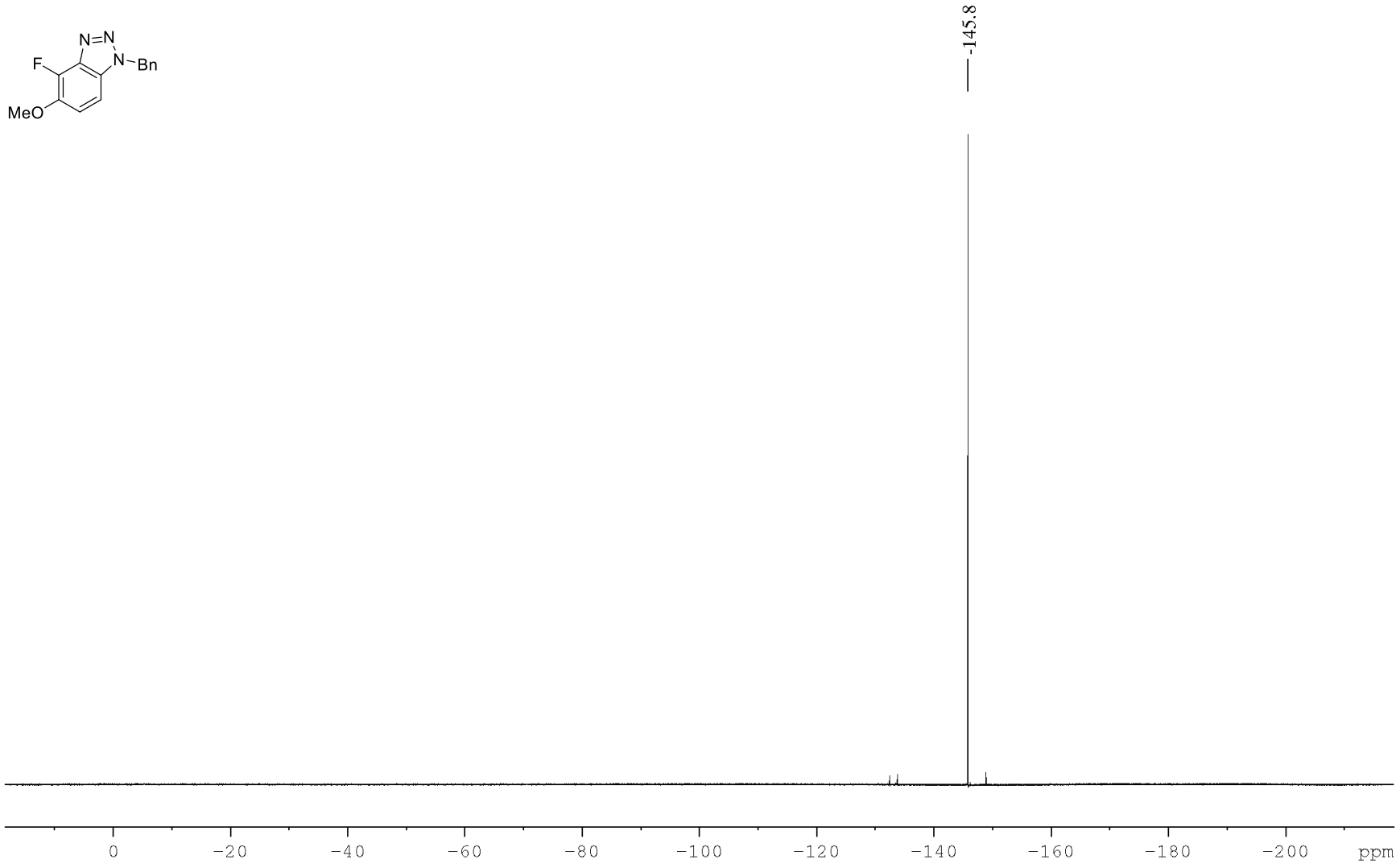
^{1}H NMR of 5b in $CDCl_3$ with 1% v/v TMS at 400 MHz



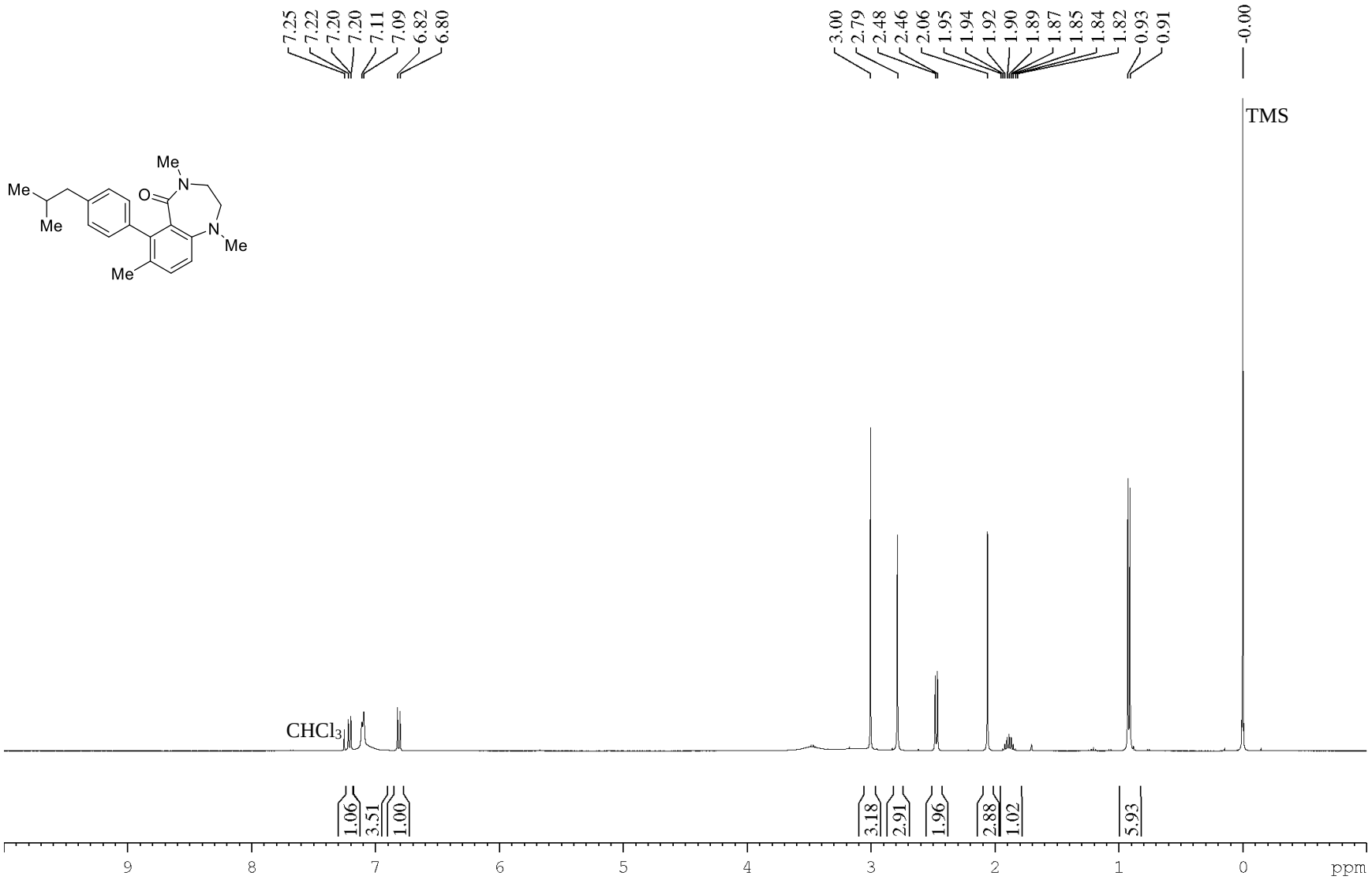
^{13}C {^{1}H} NMR of 5b $CDCl_3$ with 1% v/v TMS at 101 MHz



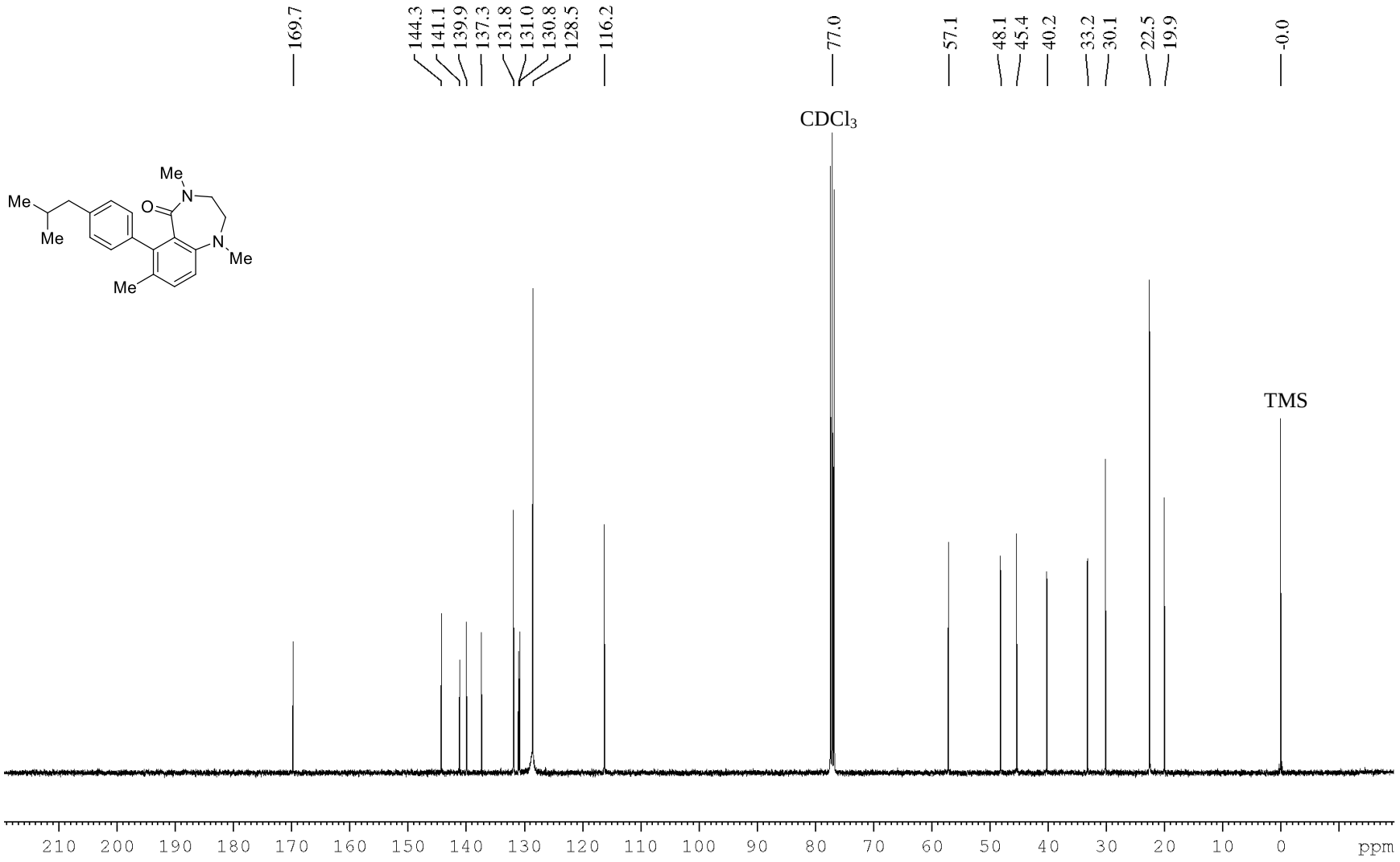
^{19}F {^{1}H} NMR of 5b in $CDCl_3$ with 1% v/v TMS at 376 MHz



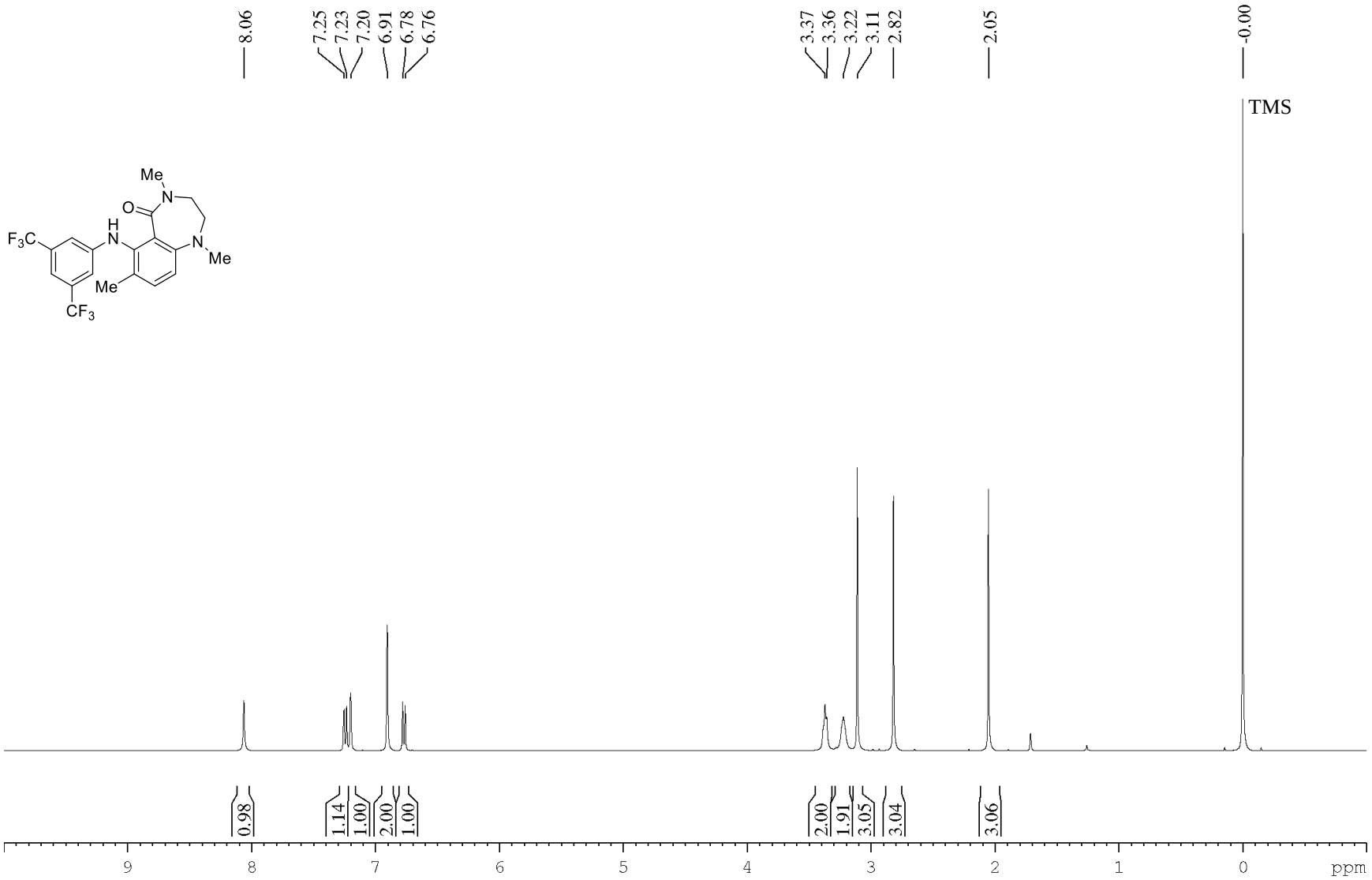
^{1}H NMR of 3a in $CDCl_3$ with 1% v/v TMS at 400 MHz



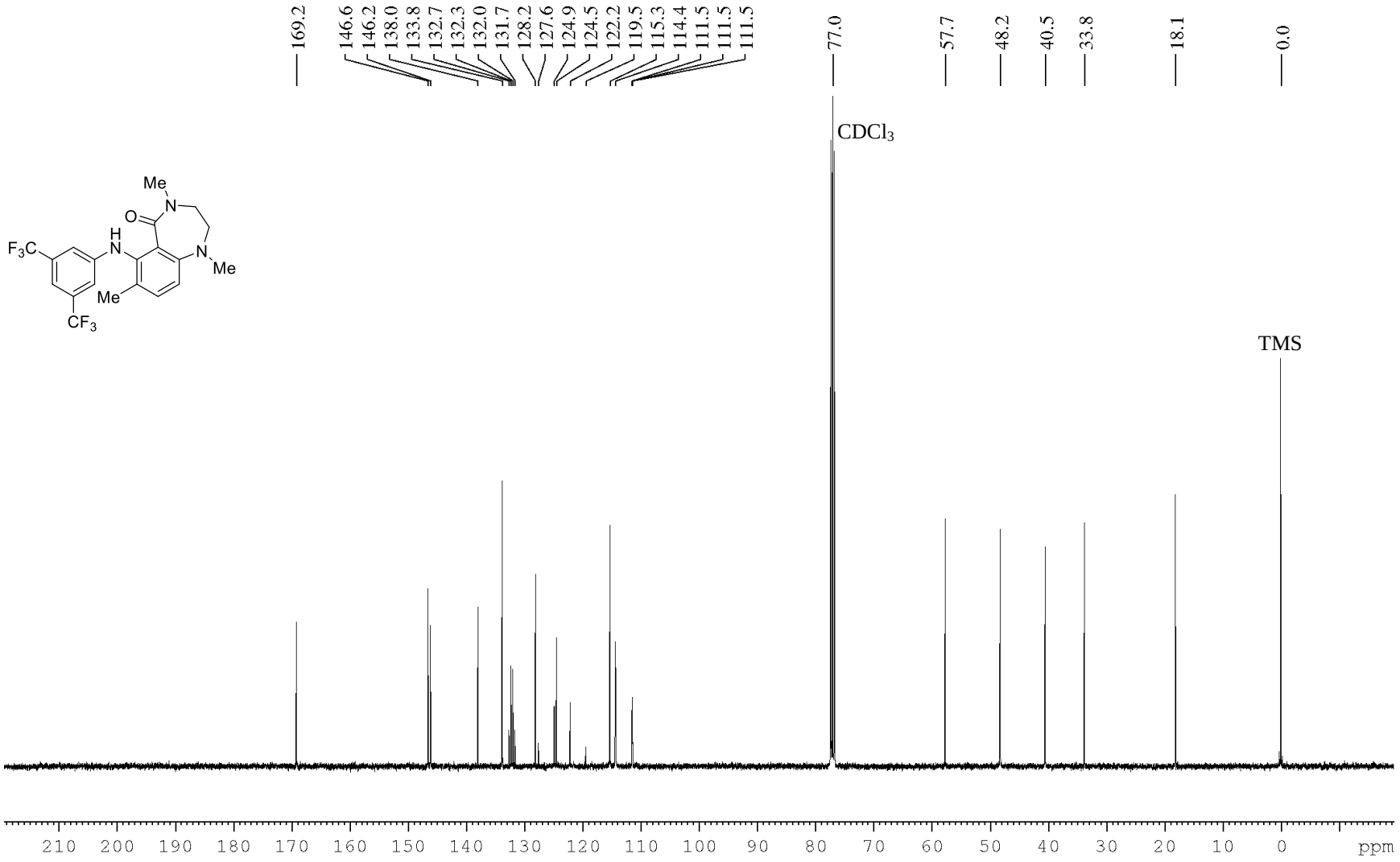
^{13}C {^{1}H} NMR of 3a $CDCl_3$ with 1% v/v TMS at 101 MHz



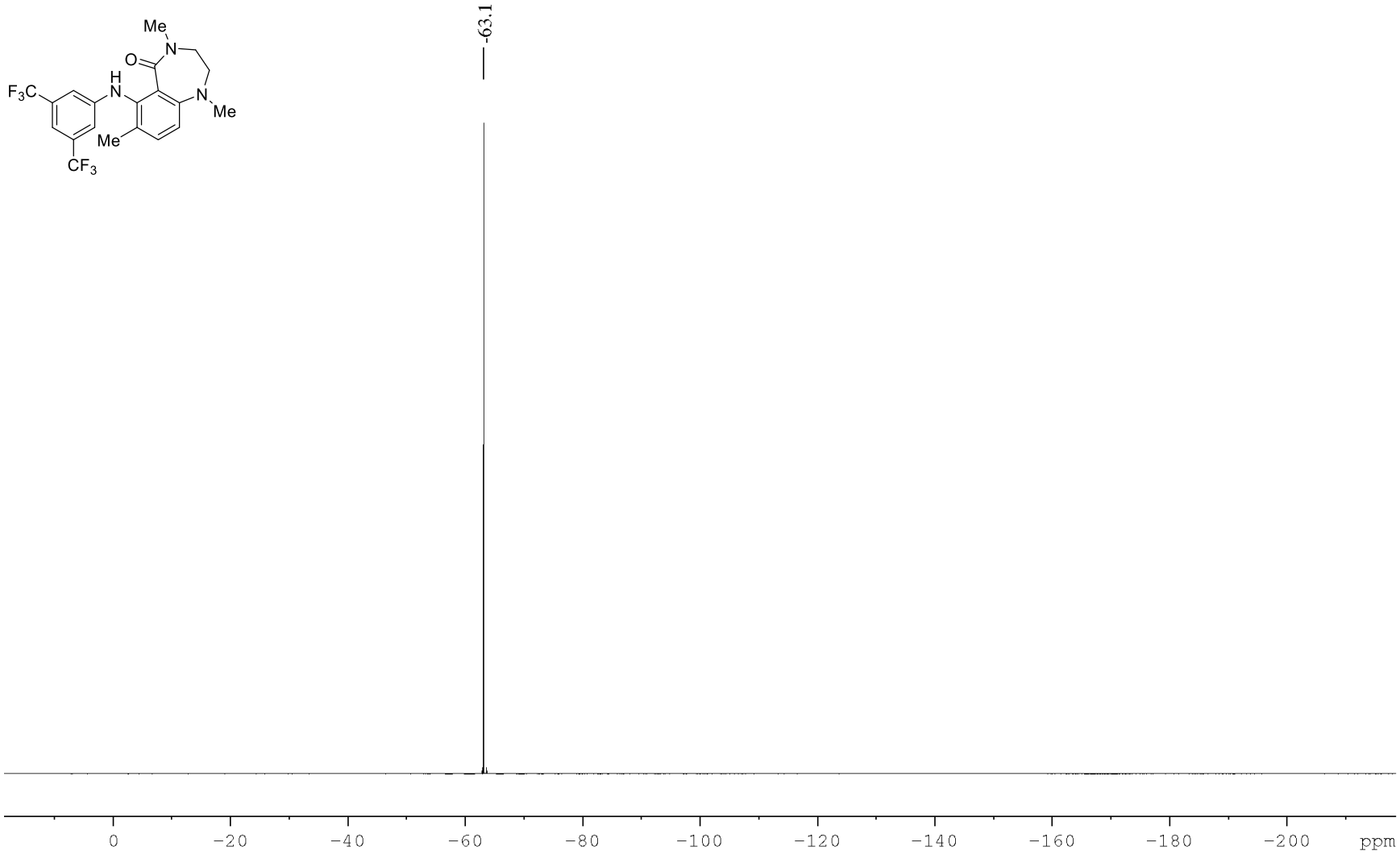
^{1}H NMR of 3b in $CDCl_3$ with 1% v/v TMS at 400 MHz



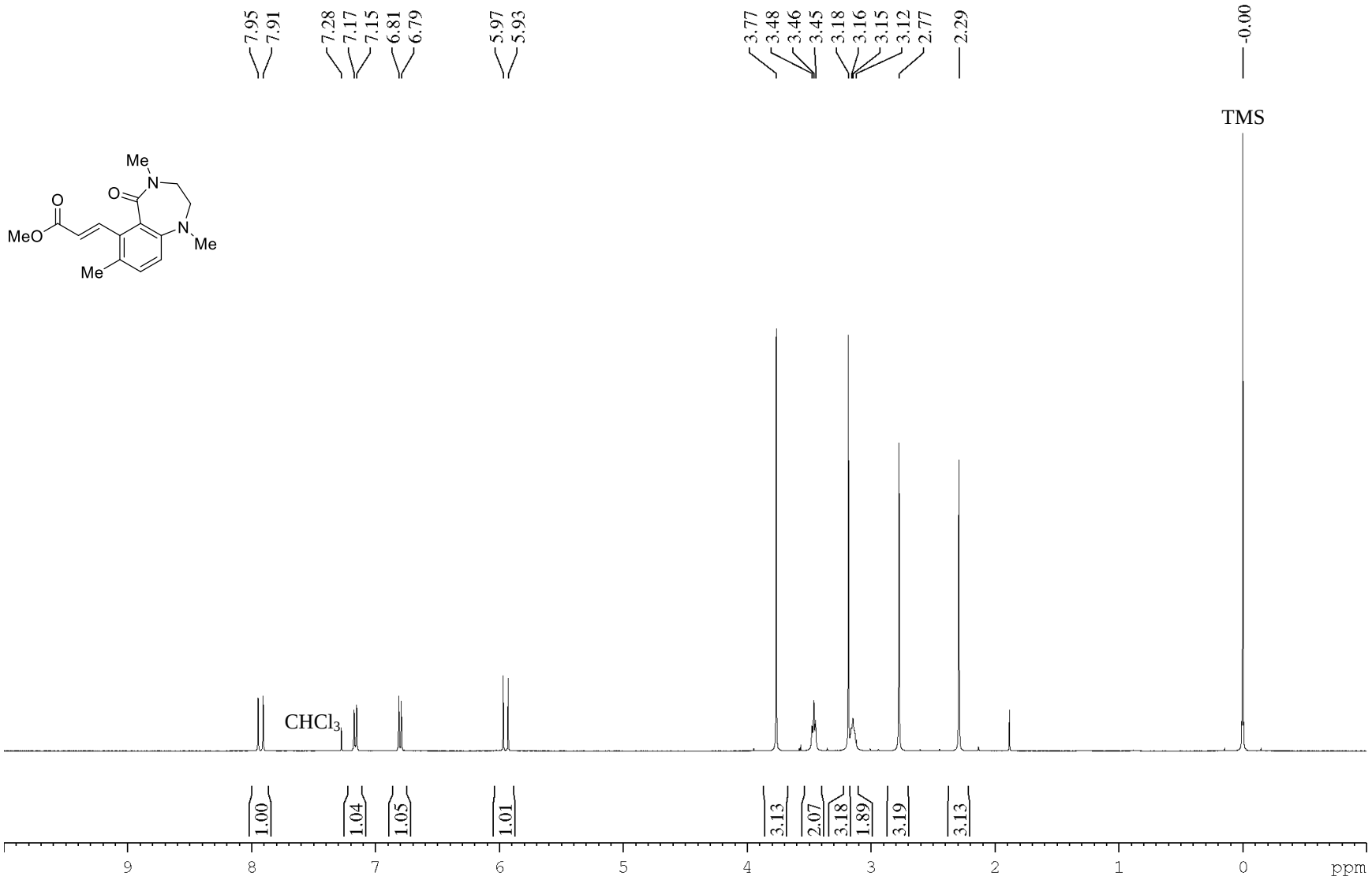
^{13}C {^{1}H} NMR of 3b $CDCl_3$ with 1% v/v TMS at 101 MHz



^{19}F {^{1}H} NMR of 3b in $CDCl_3$ with 1% v/v TMS at 376 MHz



^{1}H NMR of 3c in $CDCl_3$ with 1% v/v TMS at 400 MHz



^{13}C {^{1}H} NMR of 3c $CDCl_3$ with 1% v/v TMS at 101 MHz