Enantioselective Synthesis of Polycyclic Carbocycles via an Alkynylation-Allylation-Cyclization Strategy.

Maria Victoria Vita,[†] Pascal Mieville[‡] and Jerome Waser.*[†]

[†]Laboratory of Catalysis and Organic Synthesis, Ecole Polytechnique Fédérale de Lausanne, EPFL SB ISIC LCSO, BCH 4306, 1015 Lausanne, Switzerland.

[‡]Institute of Chemical Sciences and Engineering (ISIC), Ecole Polytechnique Fédérale de Lausanne (EPFL), 1015 Lausanne, Switzerland

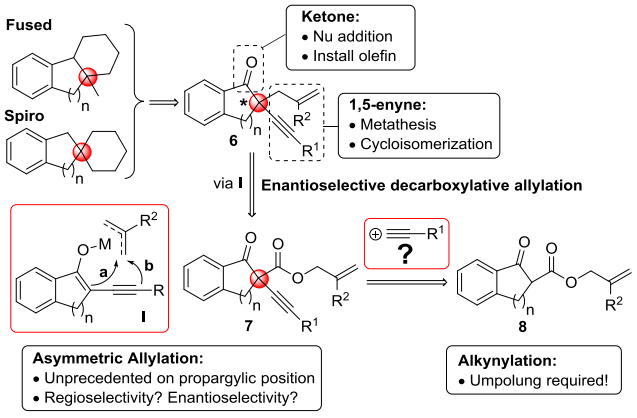
Supporting Information Placeholder

ABSTRACT: A new general three-stage strategy to access polycyclic ring systems bearing all-carbon quaternary centers with high enantioselectivity is reported. The required starting materials were readily accessed in racemic form through the α-alkynylation of ketoesters with EBX (Ethynyl BenziodoXolone) hypervalent iodine reagents. A Pd-catalyzed asymmetric decarboxylation allylation was then achieved in high yields and enantioselectivities with Trost's biphosphine ligands. Finally, transition-metal catalyzed cyclization of the obtained chiral enynes gave access to fused and spiro polycyclic ring systems constituting the core of many bioactive natural products.

The fascinating structure of natural products is the result of millions of years of evolution in interaction with biological targets. Particularly striking is the high occurrence of complex polycyclic ring systems with numerous stereocenters. An interesting substructure present in natural products is constituted by a benzene ring fused to at least two further saturated carbocycles. Both fused and spiro ring systems can be found in important bioactive compounds such as steroids like estradiol or alkaloids like buprenorphine.[1] The presence of all-carbon quaternary centers embedded in the polycyclic core of many of these molecules represents a formidable challenge for synthetic chemistry.[2] In this context, we envisioned that ketone **1** bearing a 1,5 enyne substructure around an all-carbon quaternary center would be an ideal precursor for both fused and spiro ring systems (Scheme 1). Addition of an allyl Grignard reagent, followed by olefin ring-closing metathesis (RCM) would give an easy access to fused ring systems. The 1,5-enyne itself can be used to access spiro or rearranged ring-systems based on transition-metal catalysis.[3] Whereas RCM is now a mature method, cyclisomerization reactions to access spiro ring systems have been much less investigated. Indeed, there are only two examples of such transformations so far, both occurring on unsubstituted alkane rings.[3h,3k]

Nevertheless, the main challenge with the proposed strategy resided in the enantioselective synthesis of enyne **1**. Most synthetic methods known to access 1,5 enynes take advantage of the reactivity of a propargylic cation generated through either catalytic or stoichiometric Lewis acid activation, allowing access only to racemic material.[4] Morken and co-workers showed recently that a Pd-catalyzed enantiospecific cross-coupling reaction gave 1,5-enynes with high enantiomeric excess starting from enantioenriched activated propargylic alcohols and allyl boronic esters.[5a] In this report only one example leading to all-carbon quaternary centers in a non-cyclic product was presented. In 2013, the same group reported a kinetic resolution of racemic propargylic esters using chiral ligands.[5b]

Scheme 1: Our Synthetic Strategy to Access Polycyclic Ring Systems.

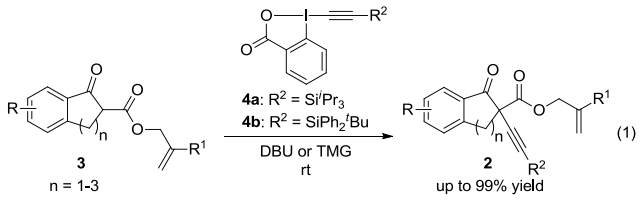


Clearly, none of the reported methods to access 1,5-enynes appeared promising in the context of our synthetic goal, and we decided to developed a new strategy based on the enantioselective decarboxylative allylation of ketoesters (Tsuji-Trost reaction).[6] This very successful approach to access all-carbon quaternary centers on carbocycles was first introduced by Segusa[7] and Tsuji[8] and then further developed into enantioselective methods by Stoltz[9] and Trost.[10,11] Nevertheless, alkynyl substituents in α position of the ketoesters have never been reported. In this class of substrates, the α-alkynyl group would be in conjugation with the formed enolate **I** and will change its electronic properties. It also leads to a major challenge in regioselectivity, as both attack at the α (pathway a) or δ position

(pathway b) would be possible.[12] Moreover, α-alkynyl ketoesters are difficult to access because both enolates and acetylides are nucleophiles, and connecting them requires therefore an Umpolung of the reactivity. To solve the latter synthetic hurdle, our group has used hypervalent iodine reagents for the α-functionalization of carbonyl compounds.[13] We have in particular developed an efficient α-ethynylation of ketoesters under mild conditions using EBX (EthynylBenziodoXolone) reagents.[13a,b]

Herein, we would like to present the successful implementation of the outlined three-stage strategy, including: (1) an improved method for the alkynylation of ketoesters at room temperature in up to quantitative yield, (2) the first example of enantioselective decarboxylative allylation at propargylic position proceeding in up to quantitative yield and with an enantiomeric excess higher than 90% on 5, 6 and 7-membered rings and (3) the use of the obtained enynes to access fused and spiro tricyclic ring systems via a RCM or cycloisomerization strategy, as well as the unanticipated formation of a rearranged [6,6,5,3] ring system.

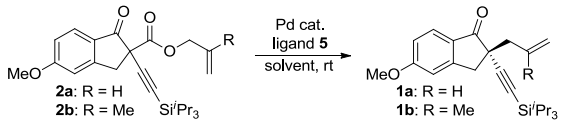
Preliminary studies showed that the decarboxylation-allylation sequence proceeded only in very low yield with ketoesters bearing a free acetylene obtained using our previously published alkynylation method.[13a] We consequently first investigated the possibility to access protected acetylenes in the α-alkynylation of β-keto esters with hypervalent iodine reagents. Using diazabicycloundecene (DBU) or tetramethylguanidine (TMG) as a base, the desired alkynes **2** could be obtained in up to quantitative yield at room temperature using TIPS-EBX (**4a**) and TPDPS-EBX (**4b**) starting from the corresponding ketoesters **3** (eq. 1).[14]



Preliminary studies on the decarboxylative allylation were then conducted using substrate **2a** under the reaction conditions previously reported by Stoltz.[9d] The substrate was converted fully to the desired allylation product **1a**, but no enantiomeric excess was obtained using the PHOX ligand **5a** (Table 1, entry 1). A switch in the Pd source to Pd(cinnamyl)Cp (**6**), an established clean precursor of Pd(0) phosphine complexes,[15] did not improve the result (entry 2). Keeping Pd(cinnamyl)Cp (**6**) as the Pd source, we turned then our attention to Trost ligand **5b** which had been applied previously in the decarboxylation of allyl ketoesters.[10b] Also in this case full conversion to **1a** was observed, but with no enantioselectivity (entry 3). However, changing the solvent to Et_2O gave for the first time a measurable enantioselectivity of 12% (entry 4). A screening of other Trost ligands in Et_2O led to better results with an encouraging 59% *ee* for **5c**, 76% *ee* for **5d** and 74% *ee* for **5e** (entries 5-7). Changing the solvent to MTBE gave the desired product in 70% *ee* with **5d** and 79% *ee* with **5e** (entries 8 and 9). Final optimization of the reaction conditions led to the best results at room temperature with 5 mol % palladium loading and a concentration of 0.1 M in MTBE (entry 10).[16] In the case of ketoester **2b** bearing a sterically more hindered methallyl substituent the enantioselectivity reached a remarkably high 93% *ee* even with only 2 mol % palladium (entry 11).[17] This result is impressive as only moderate enantioselectivity has been reported in the past when using indanone substrates and acyclic allyl groups: 76-84% *ee* with Trost ligands[10] and 71-80% *ee* with phenyloxazoline (PHOX) ligands.[9d]

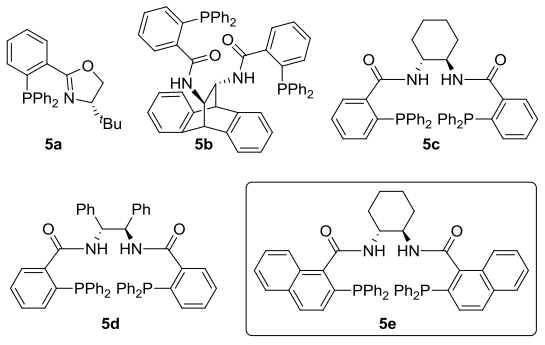
Several indanone derivatives were then subjected to the optimized reaction conditions on a 0.12 mmol scale. 1,5-Enyne **1a** was obtained in 89% *ee* using indanone **2a** (Scheme 2). Compound **2b** yielded product **1b** in 93% *ee* and quantitative yield. A different silyl group (TBDPS) on the acetylene could also be used to give enyne **1c**. Without silyl protecting group, the desired product **1d** was obtained in 41% yield and 87% *ee*.[18] A high tolerance towards the electronic properties and the position of the substituents on the aromatic ring was observed. Neutral indanone **1e** was obtained in quantitative yield and 94% *ee*. Bromo and chloro substituents were also well tolerated (products **1f** and **1g**), but a lower enantiomeric excess was observed in the case of trifluoromethylated product **1h**.

Table 1. Optimization of the Pd-Catalyzed Decarboxylative Allylation.

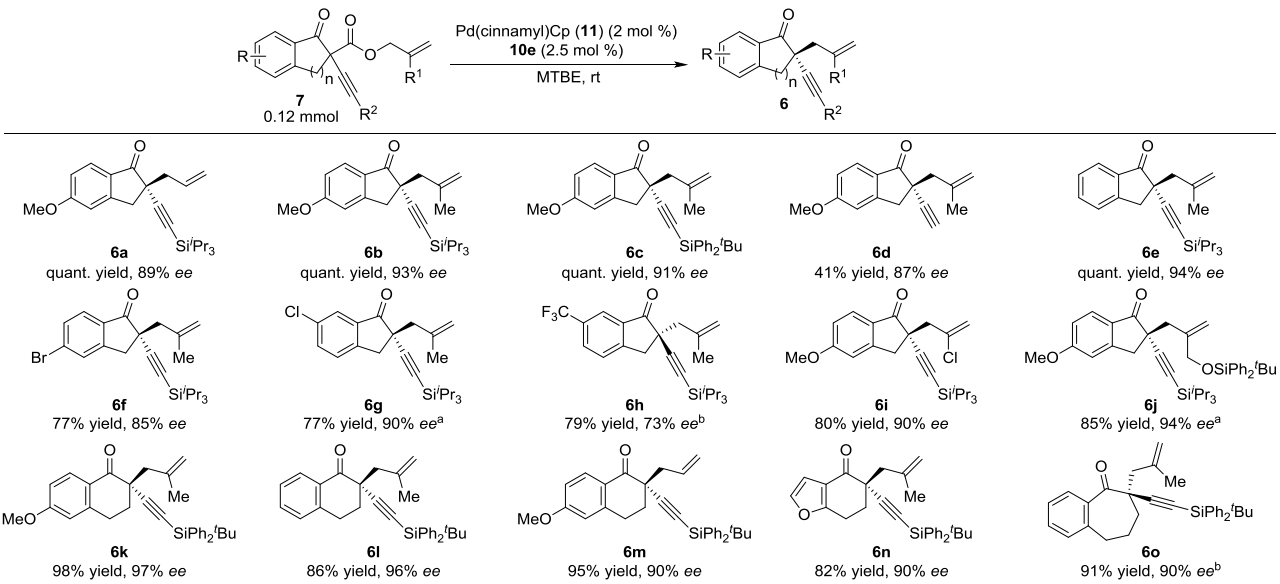


entry	reaction conditions[a]	L	*ee*[b]
1	$[Pd_2(dba)_3]$, THF	**5a**	0
2	Pd(cinnamyl)Cp (**6**), THF	**5a**	0
3	**6**, THF	**5b**	0
4	**6**, Et_2O	**5b**	12
5	**6**, Et_2O	**5c**	59
6	**6**, Et_2O	**5d**	76
7	**6**, Et_2O	**5e**	74
8	**6**, MTBE	**5d**	70
9	**6**, MTBE	**5e**	79
10	5 mol % **6**/ 5 mol % L, MTBE, 0.1 M	**5e**	86
11	2 mol % **6**/ 2.5 mol % L, MTBE, 0.1 M[c]	**5e**	93

[a]All the reaction mixtures were degased three times and stirred at room temperature for 8-12 h using substrate **2a** (0.01 mmol), the indicated solvent (0.033 M), Pd source (20 mol %) and ligand (44 mol %) unless stated otherwise. All the reactions gave full conversion to the desired product **1a** exclusively (yield > 90% by ^1H NMR). [b]The ee was determined by HPLC using Chiralcel columns. [c]Substrate **2b** was used.



Scheme 2: Scope of the Pd-catalyzed Decarboxylative Allylation.

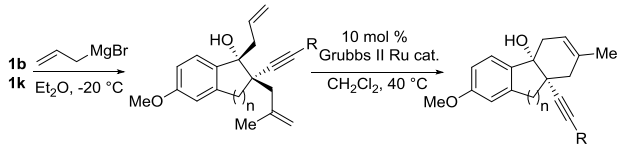


Isolated yields after column chromatography using the conditions of entry 11 in table 1 on 0.12 mmol scale are reported. [a]Using Pd(cinnamyl)Cp (**6**) (5 mol %) and ligand **5e** (6.5 mol %). [b]The (*S*,*S*)-enantiomer of ligand **5e** was used.

Modification of the substituent on the allyl group was also possible: both chloroallyl enyne **1i** and enyne **1j** bearing a protected alcohol were obtained in high enantiomeric excess and yield. When changing to tetralones, *ee* higher than 96% were observed (products **1k-l**). A lower enantioselectivity was obtained for enyne **1m** with a simple allyl substituent. Fused heterocycle **1n** and cycloheptanone **1o** could also be accessed in good yields and 90% *ee*.

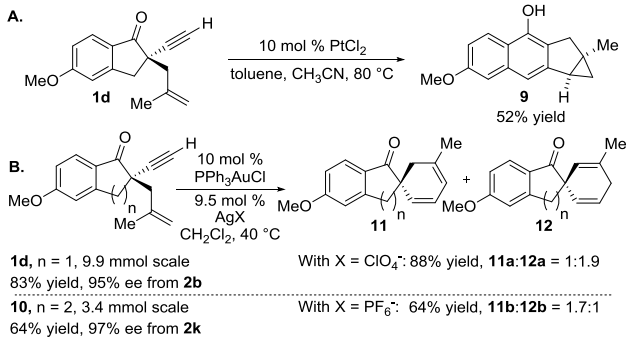
In order to access fused ring systems, allyl Grignard was then added to ketone **1b** and the corresponding alcohol **7b** was obtained in quantitative yield and with 4.5:1 diastereoselectivity (Scheme 3). Fused [6,5,6] tricyclic compound **8b** was then synthesized in 83% yield from the *syn* isomer of **7b** via ring-closing metathesis using Grubbs II ruthenium catalyst. Using the same synthetic sequence, [6,6,6] tricyclic compound **8k** was obtained in 65% overall yield.[19]

Scheme 3: Synthesis of Fused Ring Systems



To study new cycloisomerization reactions, free acetylene **1d** and **10** were synthesized in gram scale (9.9 and 3.4 mmol) in a one-pot asymmetric allylation-silyl deprotection sequence from ketoester **2b** and **2k** in 83% yield/95% *ee* and 64% yield/97% *ee* respectively (Scheme 4). When the synthesis of spiro compound **11a** was attempted using $PtCl_2$ as catalyst with enyne **1d** as reported by Kozmin and co-workers,[3i] cyclopropane product **9** was obtained instead in 52% yield (Scheme 4, **A**).[20] The formation of **9** can be explained by the intermediacy of a platinum-carbenoid, followed by 1,2- shift and re-aromatization. The first two steps of this sequence have been reported by Toste and co-workers, but using a gold catalyst.[3h]

Scheme 4: Au- and Pt-Catalyzed Cycloisomerizations.



Fortunately and somewhat surprisingly, we found that gold catalysis, which usually favours formation of the cyclopropane products, could be used in this case to access the spiro carbocyclic compounds. Diene **11a** and its non-conjugated isomer **12a** were obtained in 88% yield using PPh_3AuClO_4 as catalyst (Scheme 4, **B**) In the case of tetralone **10**, cyclization was much slower and could not be achieved using PPh_3AuClO_4 as catalyst. Higher activity was displayed by PPh_3AuPF_6, which gave the desired spiro tricyclic ring system in 64% yield.

In conclusion, we have reported a new three-stage strategy to access polycyclic ring systems efficiently and in high enantio purity. The first step of our approach was the synthesis of α-alkynylated β-ketoesters in high yields using EBX hypervalent iodine reagents to achieve the Umpolung of acetylide. Cornerstone of the strategy was the second step: the first efficient enantioselective synthesis of 1,5-enynes bearing an all-carbon propargylic quaternary center achieved through a Pd-catalyzed decarboxylative allylation starting from racemic ketoesters. The Pd-catalyzed decarboxylation allylation gave high enantioselectivity by using the DACH-naphthyl Trost

ligand, which had never been used for the allylation of propargylic positions before. In the third stage, the chiral 1,5-enynes obtained were finally converted into the desired tricyclic [6,5,6] and [6,6,6] fused and spiro ring systems using ring-closing metathesis and cycloisomerization reactions respectively. Furthermore, the unanticipated synthesis of a new [6,6,5,3] ring system could also be achieved with a platinum catalyst. The stage is now ready for using the strategy in the synthesis of natural and synthetic bioactive compounds and for extending it to other types of carbocyclic or heterocyclic scaffolds.

ASSOCIATED CONTENT

Supporting Information

Experimental procedures and analytical data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

* jerome.waser@epfl.ch

ACKNOWLEDGMENT

We thank F. Hoffmann-La Roche Ltd for an unrestricted research grant and the Swiss National Science Foundation (SNSF, grant number 200020_134550) for financial support.

REFERENCES

(1) Heel, R. C.; Brogden, R. N.; Speight, T. M.; Avery, G. S. *Drugs* **1979**, *17*, 81.

(2) (a) Douglas, C. J.; Overman, L. E. *Proc. Natl. Acad. Sci. U. S. A.* **2004**, *101*, 5363. (b) Christoffers, J.; Baro, A., *Quaternary Stereocenters: Challenges and Solutions for Organic Synthesis*. John Wiley & Sons: 2006; p 359. (c) Trost, B. M.; Jiang, C. H. *Synthesis* **2006**, 369. (d) Cozzi, P. G.; Hilgraf, R.; Zimmermann, N. *Eur. J. Org. Chem.* **2007**, 5969.

(3) Reviews: (a) Aubert, C.; Buisine, O.; Malacria, M. *Chem. Rev* **2002**, *102*, 813. (b) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271. (c) Jiménez-Núñez, E. s.; Echavarren, A. M. *Chem. Rev* **2008**, *108*, 3326. (d) Michelet, V.; Toullec, P. Y.; Genet, J. P. *Angew. Chem., Int. Ed.* **2008**, *47*, 4268. (e) Watson, I. D. G.; Toste, F. D. *Chem. Sci.* **2012**, *3*, 2899. Selected examples: (f) Mamane, V.; Gress, T.; Krause, H.; Fürstner, A. *J. Am. Chem. Soc.* **2004**, *126*, 8654. (g) Harrak, Y.; Blaszykowski, C.; Bernard, M.; Cariou, K.; Mainetti, E.; Mouriès, V.; Dhimane, A. L.; Fensterbank, L.; Malacria, M. *J. Am. Chem. Soc.* **2004**, *126*, 8656. (h) Luzung, M. R.; Markham, J. P.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 10858. (i) Sun, J.; Conley, M. P.; Zhang, L.; Kozmin, S. A. *J. Am. Chem. Soc.* **2006**, *128*, 9705. (j) Buzas, A.; Gagosz, F. *J. Am. Chem. Soc.* **2006**, *128*, 12614. (k) Fukamizu, K.; Miyake, Y.; Nishibayashi, Y. *Angew. Chem., Int. Ed.* **2009**, *48*, 2534.

(4) Selected examples: (a) Crowe, W. E.; Sammakia, T.; Schreiber, S. L. *J. Am. Chem Soc.* **1986**, *108*, 3128. (b) Mukaiyama, T.; Inubushi, A.; Hayashi, M. *Chem. Lett.* **1987**, 1975. (c) Luzung, M. R.; Toste, F. D. *J. Am. Chem. Soc.* **2003**, *125*, 15760. (d) Georgy, M.; Boucard, V.; Campagne, J. M. *J. Am. Chem. Soc.* **2005**, *127*, 14180. (e) Kabalka, G. W.; Yao, M. L.; Borella, S. *J. Am. Chem. Soc.* **2006**, *128*, 11320. (f) Kuninobu, Y.; Ishii, E.; Takai, K *Angew. Chem., Int. Ed.* **2007**, *46*, 3296. (g) Lepore, A. J.; Pinkerton, D. M.; Ashfeld, B. L. *Adv. Synth. Catal.* **2013**, *355*, 1500.

(5) (a) Ardolino, M. J.; Morken, J. P. *J. Am. Chem. Soc.* **2012**, *134*, 8770. (b) Ardolino, M. J.; Eno, M. S.; Morken, J. P. *Adv. Synth. Catal.* **2013**, *355*, 3413.

(6). Selected reviews: (a) Mohr, J. T.; Stoltz, B. M. *Chem. Asian J.* **2007**, *2*, 1476. (b) Weaver, J. D.; Recio, III A.; Grenning, A. J.; Tunge, J. A. *Chem. Rev.* **2011**, *111*, 1846. (c) Hong, A. Y.; Stoltz, B. M. *Eur. J. Org. Chem.* **2013**, 2745.

(7) Tsuda, T.; Chujo, Y.; Nishi, S.; Tawara, K.; Saegusa, T. *J. Am. Chem. Soc.* **1980**, *102*, 6381.

(8) (a) Shimizu, I.; Yamada, T.; Tsuji, J. *Tetrahedron Lett.* **1980**, *21*, 3199. (b) Shimizu, I.; Tsuji, J. *J. Am. Chem. Soc.* **1982**, *104*, 5844.

(9) (a) Behenna, D. C.; Stoltz, B. M. *J. Am. Chem. Soc.* **2004**, *126*, 15044. (b) Mohr, J. T.; Behenna, D. C.; Harned, A. M.; Stoltz, B. M. *Angew. Chem., Int. Ed.* **2005**, *44*, 6924. (c) Streuff, J.; White, D. E.; Virgil, S. C.; Stoltz, B. M. *Nat Chem* **2010**, *2*, 192. (d) Behenna, D. C.; Mohr, J. T.; Sherden, N. H.; Marinescu, S. C.; Harned, A. M.; Tani, K.; Seto, M.; Ma, S.; Novak, Z.; Krout, M. R.; McFadden, R. M.; Roizen, J. L.; Enquist, J. A.; White, D. E.; Levine, S. R.; Petrova, K. V.; Iwashita, A.; Virgil, S. C.; Stoltz, B. M. *Chem. Eur. J.* **2011**, *17*, 14199. (e) Keith, J. A.; Behenna, D. C.; Sherden, N.; Mohr, J. T.; Ma, S.; Marinescu, S. C.; Nielsen, R. J.; Oxgaard, J.; Stoltz, B. M.; Goddard, W. A. *J. Am. Chem. Soc.* **2012**, *134*, 19050.

(10) (a) Trost, B. M.; Xu, J. *J. Am. Chem. Soc.* **2005**, *127*, 2846. (b) Trost, B. M.; Xu, J.; Schmidt, T. *J. Am. Chem. Soc.* **2009**, *131*, 18343. (c) Trost, B. M.; Schaffner, B.; Osipov, M.; Wilton, D. A. A. *Angew. Chem., Int. Ed.* **2011**, *50*, 3548.

(11) Selected other reports: (a) Fournier, J.; Lozano, O.; Menozzi, C.; Arseniyadis, S.; Cossy, J. *Angew. Chem., Int. Ed.* **2013**, *52*, 1257. (b) Gartshore, C. J.; Lupton, D. W. *Angew. Chem., Int. Ed.* **2013**, *52*, 4113. (c) Li, Z.; Zhang, S.; Wu, S.; Shen, X.; Zou, L.; Wang, F.; Li, X.; Peng, F.; Zhang, H.; Shao, Z. *Angew. Chem., Int. Ed.* **2013**, *52*, 4117.

(12) To the best of our knowledge, this challenging regioselectivity question has never been addressed in the case of α-alkynyl ketoesters. For a related study on the racemic allylation of α-vinyl ketoesters, see: Waetzig, S. R.; Rayabarapu, D. K.; Weaver, J. D.; Tunge, J. A. *Angew. Chem., Int. Ed.* **2006**, *45*, 4977.

(13) (a) Fernández González, D.; Brand, J. P.; Waser, J. *Chem. Eur. J.* **2010**, *16*, 9457. (b) Fernández González, D.; Brand, J. P.; Mondière, R.; Waser, J. *Adv. Synth. Catal.* **2013**, *355*, 1631. (c) Vita, M. V.; Waser, J. *Org. Lett.* **2013**, *15*, 3246.

(14) For some substrates, the use of the more stable TPDPS protecting group was needed to prevent desilylation. Currently, desilylation cannot be prevented in absence of the benzene ring. See Supporting Information for further details.

(15) MacKinnon, A. L.; Baird, M. C. *J. Organomet. Chem.* **2003**, *683*, 114.

(16) See Supporting Information for a full list of tested conditions.

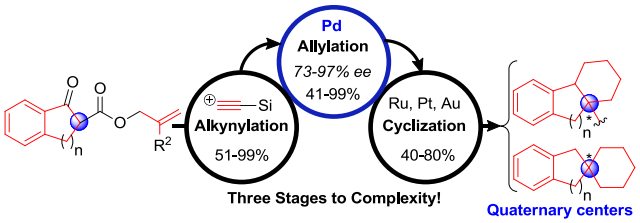
(17) The absolute stereochemistry was determined using Trost's mandelate ester method: (a) Trost, B. M.; Belletire, J. L.; Godleski, S.; McDougal, P. G.; Balkovec, J. M.; Baldwin, J. J.; Christy, M. E.; Ponticello, G. S.; Varga, S. L.; Springer, J. P. *J. Org. Chem* **1986**, *51*, 2370. (b) Trost, B. M.; Schroeder, G. M. *Chem. Eur. J.* **2005**, *11*, 174. The obtained configuration is in accordance with the prediction model developed by Trost and co-workers for this type of ligands (Reference 10, see Figure S1 in Supporting Information).

(18) We speculate that interactions between the free alkyne and the Pd catalyst slow down the reaction in this case. Lower *ee*'s were observed with aryl-substituted alkynes. Alkyl-substituted alkynes cannot be synthesized using EBX reagents.

(19) Overall yield of **8k** from ketone **1k** based on 81% isolated yield of the *cis* isomer of **7k**. In the case of the [6.6.6] ring system, ring closing metathesis of the minor *trans* diastereomer of **7k** was also successful. See Supporting Information.

(20) Interestingly, **9** was optically active. Further studies will be required to determine the enantiomeric excess and absolute configuration of this compound.

Table of Content Graphic



Supporting Information

289 pages

Enantioselective Synthesis of Polycyclic Carbocycles via an Alkynylation-Allylation-Cyclization Strategy.

Maria Victoria Vita, Pascal Miéville and Jérôme Waser

Laboratory of Catalysis and Organic Synthesis, Institute of Chemical Sciences and Engineering, Ecole Polytechnique Fédérale de Lausanne, EPFL SB ISIC LCSO, BCH 4306, 1015 Lausanne, Switzerland.

jerome.waser@epfl.ch

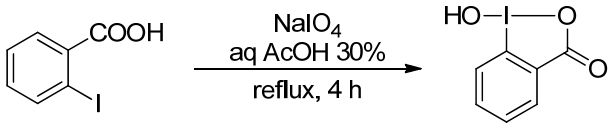
Table of contents

1. General Methods

All reactions were carried out in oven dried glassware under an atmosphere of nitrogen, unless stated otherwise. For quantitative flash chromatography technical grade solvents were used. For flash chromatography for analysis, HPLC grade solvents from Sigma-Aldrich were used. THF, Et_2O, CH_3CN, toluene, hexane and CH_2Cl_2 were dried by passage over activated alumina under nitrogen atmosphere (H_2O content < 10 ppm, *Karl-Fischer* titration). All chemicals were purchased from Acros, Aldrich, Fluka, VWR, Fluorochem, Aplichem or Merck and used without further purification, unless stated otherwise. Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å, using the solvents indicated as eluent with 0.1-0.5 bar pressure. TLC was performed on Merck silica gel 60 F_{254} TLC aluminium plates and visualized with UV light and anisaldehyde stain. Melting points were measured on a calibrated Büchi B-540 melting point apparatus using open glass capillaries. ^{1}H-NMR spectra were recorded on a Bruker DPX-400 400 MHz spectrometer in chloroform-d and/or DMSO-d_6. All signals are reported in ppm with the internal chloroform signal at 7.26 ppm or the internal DMSO signal at 2.50 ppm as standard. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quadruplet, qi = quintet, m = multiplet or unresolved, br = broad signal, app = apparent, coupling constant(s) in Hz, integration, interpretation).^{13}C-NMR spectra were recorded with ^{1}H-decoupling on a Bruker DPX-400 100 MHz spectrometer in chloroform-d and/or DMSO-d_6. All signals are reported in ppm with the internal chloroform signal at 77.0 ppm or the internal DMSO signal at 39.5 ppm as standard. Infrared spectra were recorded on a JASCO FT-IR B4100 spectrophotometer with an ATR PRO410-S and a ZnSe prisma and are reported as cm^{-1} (w = weak, m = medium, s = strong, br = broad). Gas chromatographic and low resolution mass spectrometric measurements were performed on a Perkin-Elmer Clarus 600 gas chromatographer and mass spectrometer using a Perkin-Elmer Elite fused silica column (length: 30 m, diameter: 0.32 mm) and Helium as carrier gas. High resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) Q-TOF Ultima API. All the chiral ligands used in this work are commercially available.

2. Synthesis of Hypervalent iodine Reagents

2.1 Synthesis of 1-Hydroxy-1,2-benziodoxol-3(*1H*)-one (14)



13 **14**

Following a reported procedure,[1] $NaIO_4$ (6.7 g, 31 mmol, 1.0 equiv) and 2-iodobenzoic acid (**13**) (7.4 g, 30 mmol, 1.0 equiv) were suspended in 30% (v:v) aq. AcOH (45 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (120 mL) and allowed to cool to room temperature, protecting it from light. After 1 h, the crude product was collected by filtration, washed on the filter with ice water (3 x 30 mL) and acetone (3 x 30 mL), and air-dried in the dark to give the pure product **14** (7.3 g, 19 mmol, 92%) as a colorless solid.

^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.02 (dd, *J* = 7.7, 1.4, Hz, 1H, Ar*H*), 7.97 (m, 1H, Ar*H*), 7.85 (dd, *J* = 8.2, 0.7 Hz, 1H; Ar*H*), 7.71 (td, *J* = 7.6, 1.2, Hz, 1H, Ar*H*).

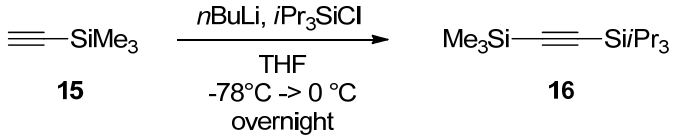
^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 167.7, 134.5, 131.5, 131.1, 130.4, 126.3, 120.4.

IR ν_{max} 3083 (w), 3060 (w), 2867 (w), 2402 (w), 1601 (m), 1585 (m), 1564 (m), 1440 (m), 1338 (s), 1302 (m), 1148 (m), 1018 (w), 834 (m), 798 (w), 740 (s), 694 (s), 674 (m), 649 (m).

The characterization data for compounds **14** corresponded to the reported values.[1]

2.2 Synthesis of 1-[(Tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (4a)

Tri*iso*-propylsilyl trimethylsilylacetylene (16)



15 **16**

Following a reported procedure,[2] *n*-butyllithium (2.5 M in hexanes, 12.0 mL, 29.9 mmol, 0.98 equiv) was added dropwise to a stirred solution of ethynyltrimethylsilane (**15**) (3.0 g, 30 mmol, 1.0 equiv) in THF (48 mL) at –78 °C. The mixture was then warmed to 0 °C and stirred for 5 min. The mixture was then cooled back to –78 °C and chlorotri*iso*-propylsilane (6.4 mL, 30 mmol, 1.0 equiv) was added dropwise. The mixture was then allowed to warm to room temperature and stirred overnight. A saturated solution of ammonium chloride (40 mL) was added, and the reaction mixture was extracted with diethyl ether (2 x 60 mL). The organic layer was washed with water and brine, then dried over $MgSO_4$, filtered and concentrated under

(1) L. Kraszkiewicz, L. Skulski, *Arkivoc*, **2003**, *6*, 120.
(2) C J. Helal, P. A. Magriotis, E. J. Corey, *J. Am. Chem. Soc.* **1996**, *118*, 10938.

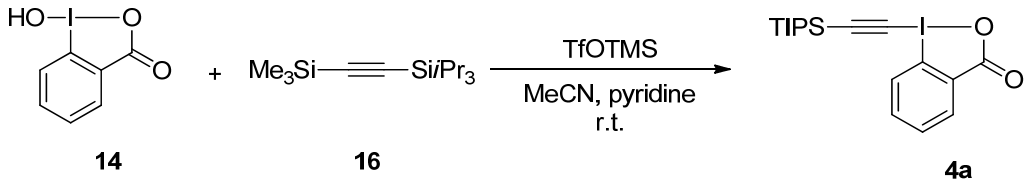
reduced pressure to obtain a colorless liquid which was further purified by Kugelrohr distillation (56-57°C/0.25 mmHg) to yield **16** (7.16 g, 28.0 mmol, 92% yield) as a colorless liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.08 (m, 21H, TIPS), 0.18 (s, 9H, TMS).

IR ν_{max} 2959 (m), 2944 (m), 2896 (w), 2867 (m), 1464 (w), 1385 (w), 1250 (m), 996 (w), 842 (s), 764 (s), 675 (m), 660 (m).

Characterization data of **16** corresponded to the literature values.[2]

1-[(Tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (4a)



14 **16** **4a**

Following a reported procedure,[3] trimethylsilyltriflate (3.6 mL, 20 mmol, 1.1 equiv, freshly distilled) was added dropwise to a stirred solution of 2-iodosylbenzoic acid (**14**) (4.7 g, 18 mmol, 1.0 equiv) in acetonitrile (140 mL). (Trimethylsilyl)(tri*iso*-propylsilyl)acetylene (**16**) (5.0 g, 20 mmol, 1.1 equiv) was then added dropwise, followed, after 15 min, by the addition of pyridine (1.5 mL, 20 mmol, 1.1 equiv). The mixture was stirred 10 min. The solvent was then removed under reduced pressure and the yellow crude oil was dissolved in dichloromethane (50 mL). The organic layer was washed with 1 M HCl (50 mL) and the aqueous layer was extracted with CH_2Cl_2 (50 mL). The organic layers were combined, washed with a saturated solution of $NaHCO_3$ (2 x 50 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (*ca* 35 mL) afforded **4a** (6.3 g, 15 mmol, 83%) as a colorless solid.

Mp (Dec.) 170-176°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (m, 1H, Ar*H*), 8.29 (m, 1H, Ar*H*), 7.77 (m, 2H, Ar*H*), 1.16 (m, 21H, TIPS).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 134.6, 132.3, 131.4, 131.4, 126.1, 115.6, 114.1, 64.6, 18.4, 11.1.

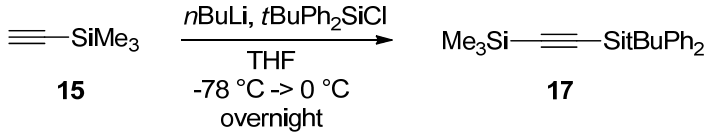
IR ν_{max} 2943 (m), 2865 (m), 1716 (m), 1618 (m), 1604 (s), 1584 (m), 1557 (m), 1465 (m), 1439 (w), 1349 (m), 1291 (m), 1270 (w), 1244 (m), 1140 (m), 1016 (m), 999 (m), 883 (m), 833 (m), 742 (m), 702 (s), 636 (m).

Characterization data of **4a** corresponded to the literature values.[3]

3 V. V.Zhdankin , C. J Kuehl, A. P Krasutsky, J. T. Bolz, A. J. Simonsen, *J. Org. Chem.* **1996**, *61*, 6547.

2.3 Synthesis of 1-[(*tert*Butyldiphenylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (9b)

*tert*Butyldiphenylsilyl trimethylsilylacetylene (17)



15 **17**

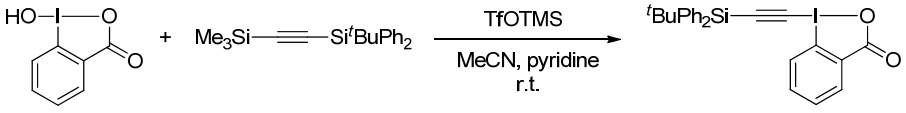
Following a reported procedure,[4] *n*-butyllithium (2.5 M in hexanes, 8.0 mL, 20 mmol, 0.98 equiv) was added dropwise to a stirred solution of ethynyltrimethylsilane (**15**) (2.90 mL, 20.4 mmol, 1.0 equiv) in THF (30 mL) at –78 °C. The mixture was then warmed to 0 °C and stirred for 5 min. The mixture was then cooled back to –78 °C and *tert*-butylchlorodiphenylsilane (6.4 mL, 30 mmol, 1.0 equiv) was added dropwise. The mixture was then allowed to warm to room temperature and stirred overnight. A saturated solution of ammonium chloride (30 mL) was added, and the reaction mixture was extracted with diethyl ether (2 x 50 mL). The organic layer was washed with water and brine, then dried over $MgSO_4$, filtered and concentrated under reduced pressure to obtain a colorless liquid which was further purified by Kugelrohr distillation (bp = 150°C, p = 0.25 mmHg) to yield **17** (2.95 g, 8.76 mmol, 44% yield) as a colorless liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (m, 4H, ArH), 7.38 (m, 6H, ArH), 1.08 (s, 9H, *t*Bu), 0.27 (s, 9H, TMS).

^{13}C NMR (101 MHz, $CDCl_3$) δ 135.6, 133.2, 129.5, 127.7, 119.0, 108.7, 27.0, 18.5, -0.0.

The characterization data for compound **17** corresponded to the reported values.[4]

1-[(*tert*Butyldiphenylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (4b)



14 **17** **4b**

Following a reported procedure,[5] Trimethylsilyltriflate (1.58 mL, 8.70 mmol, 1.1 equiv, freshly distilled) was added dropwise to a stirred solution of 2-iodosylbenzoic acid (**14**) (2.07 g, 7.90 mmol, 1.0 equiv) in acetonitrile (30 mL). Butyldiphenyl((trimethylsilyl)ethynyl)silane (**17**) (2.95 g, 3.70 mmol, 1.1 equiv) was then added dropwise, followed, after 15 min, by the addition of pyridine (710 µL, 3.70 mmol, 1.1 equiv). The mixture was stirred 10 min. The solvent was then removed under reduced pressure and the yellow crude oil was dissolved in dichloromethane. The organic layer was washed with 1 M HCl and the aqueous layer was extracted with CH_2Cl_2. The organic layers were combined, washed with a saturated solution of $NaHCO_3$, dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. The resulting oil was stirred in hexane and ether and then reduced under vacuum to afford a colorless solid. Recrystallization from acetonitrile (*ca* 20 mL) afforded **4b** (2.77 g, 5.42 mmol, 69%) as a colorless solid.

^{1}H NMR (400 MHz, $CDCl_3$) (*ca* 0.12 mmol/mL) δ 8.43 (d, *J* = 6.5 Hz, 1H, ArH), 8.29 (d, *J* = 8.2 Hz, 1H, ArH), 7.82 (d, *J* = 6.6 Hz, 4H, ArH), 7.75 (t, *J* = 7.2 Hz, 1H, ArH), 7.66 (m, 1H, ArH), 7.53-7.41 (m, 6H, ArH), 1.21 (s, 9H, *t*Bu).

(4) P. Cuadrado, A.M. Gonzalez-Nogal, R. Valero, *Tetrahedron* **2002**, *58*, 4975.
(5) J. P Brand, C. Chevalley, R. Scopelliti, J. Waser, *Chem. Eur. J.* **2012**, *18*, 5655.

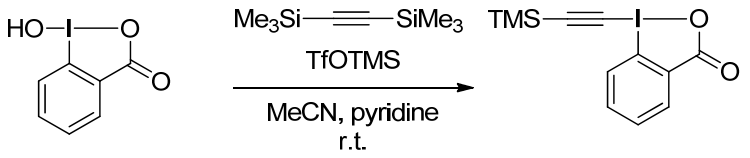
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 135.5, 134.8, 132.4, 131.5, 131.3, 130.2, 128.1, 126.3, 116.0, 112.2, 68.5, 27.0, 18.7. One carbon was not resolved.

IR ν_{max} 3072 (w), 2958 (w), 2932 (w), 2865 (w), 2860 (w), 2248 (w), 1649 (w), 1622 (m), 1561 (w), 1471 (w), 1430 (w), 1336 (w), 1297 (w), 1253 (w), 1113 (w), 1008 (w), 906 (s), 821 (w), 727 (s), 647 (m).

The characterization data for compounds **4b** corresponded to the reported values.[5]

2.4 Synthesis of 1-[(Trimethylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (4c)

1-[(Trimethylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (4c)



14 **4c**

Following a reported procedure,[3] trimethylsiyltriflate (2.8 mL, 15 mmol, 1.4 equiv, freshly distilled) was added dropwise to a stirred solution of 2-iodosylbenzoic acid (**14**) (3.00 g, 11.4 mmol, 1.00 equiv) in acetonitrile (85 mL) until the mixture turned colorless. Bis(trimethylsilyl)acetylene (2.14 g, 12.5 mmol, 1.10 equiv) was then added dropwise, followed, after 20 min, by the addition of pyridine (1.2 mL, 15 mmol, 1.4 equiv). The mixture was stirred 30 min. The solvent was then removed under reduced pressure and the yellow crude oil was dissolved in dichloromethane (80 mL). The organic layer was washed with a large amount of water (130 mL), and the aqueous layer was extracted with CH_2Cl_2 (3 x 65 mL). The organic layer was washed with brine (130 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (2.3 mL) afforded **4c** (2.35 g, 6.84 mmol, 60% yield) as a colorless solid.

Mp: 143-145°C (dec);

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (dd, J = 6.4, 1.9 Hz, 1H, Ar*H*), 8.19 (m, 1H,Ar*H*), 7.78 (m, 2H, Ar*H*), 0.32 (s, 9H, *TMS*)

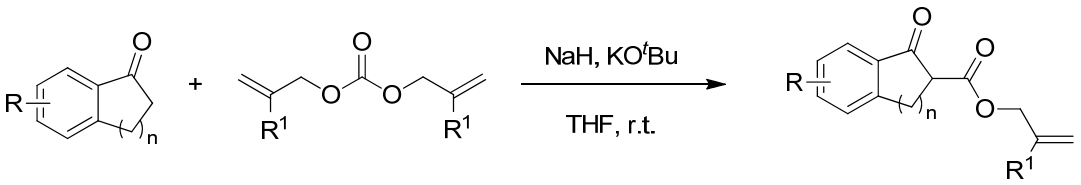
^{13}C NMR (100 MHz, $CDCl_3$) 166.4, 134.9, 132.6, 131.7, 131.4, 126.1, 117.2, 115.4, 64.2, -0.5.

IR ν_{max} 3389 (w), 2967 (w), 1617 (s), 1609 (s), 1562 (m), 1440 (w), 1350 (m), 1304 (w), 1254 (w), 1246 (w), 1112 (w), 1008 (w), 852 (s), 746 (m), 698 (m), 639 (m).

The characterization data for compounds **4c** corresponded to the reported values.[3]

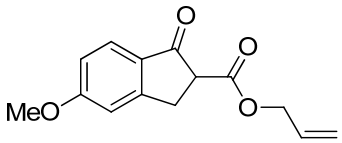
3. Synthesis of starting materials: allyl β-keto esters.

General procedure for the synthesis of β-allyl keto esters.



Following a reported procedure,[6] potassium *tert*-butoxide (0.05 equiv) was added to a suspension of NaH (2.2 equiv) in diallyl carbonate (2.0 equiv). The ketone (1 equiv) was then added dropwise at 0 °C. The reaction was stirred at room temperature and followed by TLC (using the solvent mixture indicated below for the R_f value and UV or *p*-anisaldehyde for visualization). Then 1 M HCl was added until the pH of the solution became neutral or slightly acidic. The organic layers were collected and washed with brine (2 x 20 mL), dried over $MgSO_4$ and concentrated in vacuum. The crude product was purified by column chromatography, using the solvent indicated for the $\mathbf{R_f}$ value.

Allyl 5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (3a)



Starting from 5-methoxy-2,3-dihydro-*1H*-inden-1-one (0.200 g, 1.23 mmol), allyl 5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate **3a** (0.209 g, 0.851 mmol, 69 % yield) was obtained as a brown solid.

R_F 0.3 (pentane:ethyl acetate 3:2).

Mp: 53.5-55.9° C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.70 (d, *J* = 9.2 Hz, 1H, Ar*H*), 6.96 – 6.89 (m, 2H, Ar*H*), 5.94 (ddt, *J* = 17.3, 10.5, 5.6 Hz, 1H, C*H*CH$_2$), 5.37 (dq, *J* = 17.2, 1.5 Hz, 1H, CHC*H$_2$*), 5.25 (dq, *J* = 10.5, 1.3 Hz, 1H, CHC*H$_2$*), 4.69 (tt, *J* = 5.7, 1.4 Hz, 2H, C*H$_2$*CH), 3.90 (s, 3H, O*Me*), 3.74 (dd, *J* = 8.2, 4.0 Hz, 1H, C*H*), 3.52 (dd, *J* = 17.3, 4.0 Hz, 1H, C*H$_2$*), 3.32 (dd, *J* = 17.3, 8.2 Hz, 1H, C*H$_2$*).

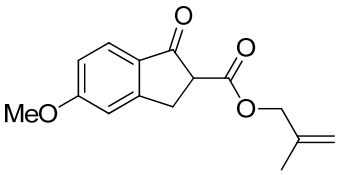
^{13}C NMR (101.00 MHz, Chloroform-*d*) δ 197.4, 169.1, 165.9, 156.7, 131.7, 128.5, 126.4, 118.6, 116.0, 109.6, 66.2, 55.8, 53.5, 30.3.

IR ν_{max} 3021 (w), 3013 (w), 2842 (w), 1738 (m), 1705 (s), 1598 (s), 1491 (w), 1337 (w), 1307 (m), 1259 (s), 1224 (w), 1193 (m), 1156 (m), 1149 (m), 1105 (m), 1089 (m), 1025 (m), 989 (m).

HRMS (ESI) calcd for $C_{14}H_{15}O_4^+$ $[M+H]^+$ 247.0965; found 247.0960.

2-Methylallyl 5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (3b)

(6) M.V. Vita, J. Waser, *Org. Lett.* **2013**, *15*, 3246.



Starting from 5-methoxy-2,3-dihydro-*1H*-inden-1-one (1.76 g, 10.9 mmol), 2-methylallyl 5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate **3b** (2.17 g, 8.34 mmol, 77 % yield) was obtained as a yellowish oil.

R_F 0.6 (pentane:ethyl acetate 7:3).

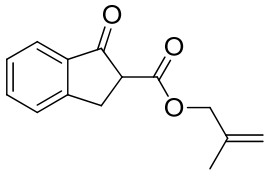
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.70 (d, *J* = 9.1 Hz, 1H, Ar*H*), 6.96-6.92 (m, 2H, Ar*H*), 5.03 (dd, *J* = 1.6, 0.9 Hz, 1H, CMeC*H*$_2$), 4.94 (m, 1H, CMeC*H*$_2$), 4.68 – 4.54 (m, 2H, C*H*$_2$CMe), 3.90 (s, 3H, OC*H*$_3$), 3.78 (dd, 1 H, *J* = 8.2, 4.0 Hz, C*H*), 3.55 (dd, 1 H, *J* = 17.3, 4.0 Hz, C*H*$_2$), 3.35 (dd, 1 H, *J* = 17.3, 8.2 Hz), 1.78 (dd, *J* = 1.6, 0.9 Hz, 3H, CC*H*$_3$).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 197.3, 169.1, 165.9, 156.7, 139.6, 128.6, 126.4, 116.0, 113.3, 109.6, 68.7, 55.8, 53.5, 30.3, 19.5.

IR ν_{max} 2978 (w), 2969 (w), 2942 (w), 1740 (m), 1706 (s), 1600 (s), 1306 (w), 1261 (s), 1156 (m), 1090 (m).

HRMS (ESI) calcd for $C_{15}H_{16}NaO_4^+$ $[M+Na]^+$ 283.0941; found 283.0944.

2-Methylallyl 1-oxo-2,3-dihydro-1H-indene-2-carboxylate (3e)



Starting from 2,3-dihydro-1H-inden-1-one (0.500 g, 3.78 mmol), 2-methylallyl 1-oxo-2,3-dihydro-1H-indene-2-carboxylate **3e** (0.653 g, 2.84 mmol, 75% yield) was obtained as a purple liquid.

R_F 0.3 (pentane:ethyl acetate 3:2).

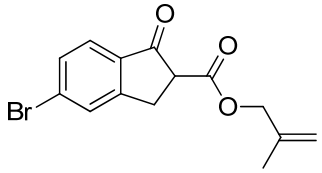
^{1}H NMR (400 MHz, Chloroform-*d*) (ketone/enol 1:0.2) *Ketone:* δ 7.78 (d, *J* = 7.7 Hz, 1H, Ar*H*), 7.63 (dd, *J* = 8.1, 6.8 Hz, 1H, Ar*H*), 7.51 (d, *J* = 7.7 Hz, 1H, Ar*H*), 7.43 – 7.36 (m, 1H, Ar*H*), 5.05 – 4.91 (m, 2H, CMeC*H*$_2$), 4.72 – 4.52 (m, 2H, C*H*$_2$CMe), 3.77 (dd, *J* = 8.3, 4.1 Hz, 1H, C*H*CH$_2$), 3.64 – 3.52 (m, 1H, C*H*$_2$CH), 3.40 (dd, *J* = 17.2, 8.2 Hz, 1H, C*H*$_2$CH), 1.78 (d, *J* = 1.4 Hz, 3H, C*Me*). *Enol:* δ 7.65 (m, 1H, Ar*H*), 7.47 (d, *J* = 1.3 Hz, 1H, Ar*H*), 7.44 (dd, *J* = 7.3, 1.4 Hz, 1H, Ar*H*), 7.39 (m, 1H, Ar*H*), 5.05 (d, *J* = 1.5 Hz, 1H, CMeC*H*$_2$), 4.98 (t, *J* = 1.4 Hz, 1H, CMeC*H*$_2$), 4.69 (s, 2H, C*H*$_2$CMe), 3.56 (s, 2H, C*H*$_2$), 1.82 (s, 3H, C*Me*).

^{13}C NMR (101.00 MHz, Chloroform-*d*) *Ketone:* δ 199.3, 168.8, 153.5, 139.5, 135.4, 135.3, 127.9, 126.6, 124.7, 113.4, 68.8, 53.3, 30.3, 19.5. *Enol:* δ 143.2, 140.0, 136.9, 129.5, 126.9, 124.8, 120.8, 112.8, 102.2, 67.1, 32.5, 29.7. (2C in the enol are missing, one possibly the ester).

IR ν_{max} 1746 (s), 1716 (s), 1464 (w), 1328 (w), 1314 (w), 1300 (w), 1286 (w), 1274 (w), 1248 (w), 1207 (m), 1186 (m), 1155 (m), 1128 (w), 991 (w), 990 (w), 917 (w), 908 (w), 765 (m).

HRMS (ESI) calcd for $C_{14}H_{15}O_3^+$ $[M+H]^+$ 231.1016; found 231.1017.

2-Methylallyl 5-bromo-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (3f)



Starting from 5-bromo-2,3-dihydro-1H-inden-1-one (0.500 g, 2.37 mmol), 2-methylallyl 5-bromo-1-oxo-2,3-dihydro-1H-indene-2-carboxylate **3f** (0.501 g, 1.62 mmol, 68% yield) was obtained as a yellow solid.

R_F 0.3 (pentane:ethyl acetate 3:2).

Mp: 58.2-61.9 °C.

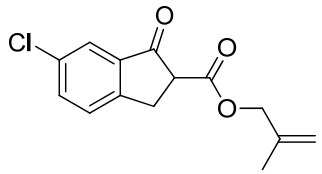
^{1}H NMR (400 MHz, Chloroform-*d*) Keto/enol form (1.5:1) keto: δ 7.69 (d, *J* = 1.6 Hz, 1H, Ar*H*), 7.63 (d, *J* = 8.2 Hz, 1H, Ar*H*), 7.56 – 7.51 (m, 1H, Ar*H*), 5.02 (s, 1H, CCH_2), 4.95 (s, 1H, CCH_2), 4.68 – 4.54 (m, 2H, CH_2C), 3.77 (dd, *J* = 8.3, 4.1 Hz, 1H, C*H*), 3.54 (dd, *J* = 17.4, 4.0 Hz, 1H, CH_2), 3.37 (dd, *J* = 17.5, 8.3 Hz, 1H, CH_2), 1.79 – 1.76 (m, 3H, CCH_3). Enol: δ 10.31 (s, 1H, O*H*), 7.62 (s, 1H, Ar*H*), 7.52 – 7.50 (m, 2H, Ar*H*), 5.05 – 5.03 (m, 1H, CCH_2), 4.98 (t, *J* = 1.4 Hz, 1H, CCH_2), 4.69 (s, 2H, CH_2C), 3.53 (s, 2H, CH_2), 1.82 (t, *J* = 1.1 Hz, 3H, CCH_3).

^{13}C NMR (101.00 MHz, Chloroform-*d*) δ 198.0, 168.3, 155.1, 144.9, 139.9, 139.4, 135.9, 134.1, 131.6, 131.0, 130.2, 129.9, 128.1, 125.8, 124.0, 122.0, 113.5, 113.0, 102.5, 68.9, 67.3, 53.3, 32.4, 30.0, 19.5, 19.5. (2 aromatic C of the enol form are not resolved).

IR ν_{max} 2977 (w), 2940 (w), 2934 (w), 1742 (m), 1717 (s), 1652 (m), 1620 (m), 1597 (m), 1562 (m), 1418 (m), 1316 (m), 1288 (m), 1260 (m), 1211 (s), 1200 (s), 1179 (s), 1159 (m), 1133 (m), 1101 (m), 992 (m), 911 (m).

HRMS (ESI) calcd for $C_{14}H_{13}{}^{79}BrNaO_3^+$ $[M+Na]^+$ 330.9940; found 330.9943.

2-Methylallyl 6-chloro-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (3g)



Starting from 6-chloro-2,3-dihydro-1H-inden-1-one (0.50 g, 3.0 mmol), 2-methylallyl 6-chloro-1-oxo-2,3-dihydro-1H-indene-2-carboxylate **3g** (0.59 g, 2.2 mmol, 74 % yield)was obtained as pink solid.

R_F 0.3 (pentane:ethyl acetate 3:2).

Mp: 71.5-73.7° C.

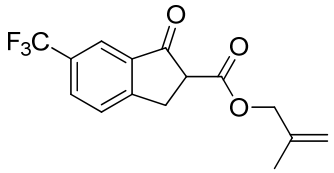
^{1}H NMR (400 MHz, Chloroform-*d*) Keto/enol ratio (1:0.5) *Ketone* δ 7.73 (d, *J* = 2.1 Hz, 1H, Ar*H*), 7.58 (dd, *J* = 8.2, 2.1 Hz, 1H, Ar*H*), 7.39 (d, *J* = 1.3 Hz, 1H, Ar*H*), 5.04 – 5.00 (s, 1H, CCH_2), 4.97 – 4.93 (s, 1H, CCH_2), 4.68 – 4.52 (m, 2H, CH_2C), 3.80 (dd, *J* = 8.2, 4.0 Hz, 1H, C*H*), 3.54 (dd, *J* = 17.3, 4.0, 1H, CH_2), 3.36 (dd, *J* = 17.4, 8.1 Hz, 1H, CH_2), 1.77 (s, 3H, CCH_3). *Enol:* δ 10.25 (s, 1H, O*H*), 7.62 (s, 1H, Ar*H*), 7.45 (d, *J* = 8.1 Hz, 2H, Ar*H*), 5.05 (s, 1H, CCH_2), 4.98 (s, 1H, CCH_2), 4.69 (s, 2H, CH_2C), 3.54 (s, 2H, CH_2), 1.82 (d, *J* = 1.5 Hz, 3H, CCH_3).

^{13}C NMR (101.00 MHz, Chloroform-*d*) δ 198.0, 168.3, 151.6, 141.2, 139.9, 139.4, 138.6, 136.8, 135.5, 134.3, 133.1, 129.4, 127.7, 125.8, 124.4, 120.9, 113.5, 113.0, 103.7, 69.0, 67.3, 53.7, 32.3, 29.9, 19.5, 19.4. (2 aromatic C of the enol form are not resolved).

IR ν_{max} 2975 (w), 2935 (w), 2861 (w), 2860 (w), 1745 (m), 1720 (s), 1652 (m), 1620 (m), 1592 (m), 1568 (m), 1339 (m), 1255 (s), 1201 (s), 1187 (s), 1166 (m), 1131 (m), 1107 (m), 907 (w), 777 (w).

HRMS (ESI) calcd for $C_{14}H_{13}ClNaO_3^+$ $[M+Na]^+$ 287.0445; found 287.0441.

2-Methylallyl 6-trifluoromethyl-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (3h)



Starting from 6-(trifluoromethyl)-2,3-dihydro-1H-inden-1-one (0.23 ml, 1.5 mmol), 2-methylallyl 1-oxo-6-(trifluoromethyl)-2,3-dihydro-1H-indene-2-carboxylate **3h** (0.32 g, 1.1 mmol, 71 % yield) was obtained as pink solid.

R_F 0.25 (pentane:ethyl acetate 9:1).

Mp: 56.7-59.2° C.

^{1}H NMR (400 MHz, Chloroform-*d*) (Ketone/enol 0.5:1) *Ketone* δ 8.05 (d, *J* = 1.7 Hz, 1H, Ar*H*), 7.66 (d, *J* = 8.2 Hz, 2H, Ar*H*), 5.05 – 5.02 (m, 1H, CCH_2), 4.96 (t, *J* = 1.5 Hz, 1H, CCH_2), 4.65 (s, 1H, CH_2CMe), 4.58 (d, *J* = 13.0 Hz, 1H, CH_2CMe), 3.85 (dd, *J* = 8.3, 4.0 Hz, 1H, CH_2), 3.71 – 3.64 (m, 1H, CH_2), 3.46 (dd, *J* = 17.7, 7.9 Hz, 1H, CH_2), 1.81 – 1.76 (m, 3H, CH_2C*Me*). *Enol:* δ 10.29 (s, 1H, OH), 7.93 – 7.90 (m, 1H, Ar*H*), 7.88 (dd, *J* = 8.2, 1.7 Hz, 1H, Ar*H*), 7.59 (d, *J* = 7.9 Hz, 1H, Ar*H*), 5.06 (p, *J* = 1.2 Hz, 1H, CMeCH_2), 5.00 (q, *J* = 1.3 Hz, 1H, CMeCH_2), 4.71 (s, 2H, CH_2CMe), 3.63 (s, 2H, CH_2), 1.86 – 1.80 (m, 3H, CCH_3).

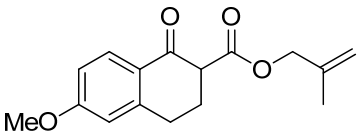
^{13}C NMR (101 MHz, Chloroform-*d*) δ 198.0, 168.6, 168.5, 168.1, 156.6, 146.5, 139.8, 139.3, 137.6, 135.7, 131.9 (q, *J* = 3.6 Hz), 130.7 (t, *J* = 33.1 Hz), 129.7 (d, *J* = 32.4 Hz), 127.4, 126.10 (q, *J* = 3.8 Hz), 125.1, 124.2 (q, *J* = 272.2 Hz), 123.6 (q, *J* = 273 Hz), 122.0 (q, *J* = 4.0 Hz), 117.9 (q, *J* = 3.9 Hz), 113.6, 113.1, 103.7, 69.1, 67.4, 53.5, 32.8, 30.4, 19.5, 19.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.1, -62.6.

IR ν_{max} 2944 (w), 1724 (m), 1657 (m), 1324 (s), 1269 (s), 1254 (m), 1215 (m), 1189 (m), 1164 (s), 1128 (s), 1103 (s), 909 (m).

HRMS (ESI) calcd for $C_{15}H_{13}F_3NaO_3^+$ $[M+Na]^+$ 321.0709; found 321.0695.

2-Methylallyl 6-methoxy-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (3k)



Starting from 6-methoxy-3,4-dihydronaphthalen-1(2H)-one (1.50 g, 8.51 mmol), 2-methylallyl 6-methoxy-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate **3k** (1.55 g, 5.65 mmol, 66 % yield) was obtained as yellow oil.

R_F 0.85 (dichloromethane/pentane 5:1).

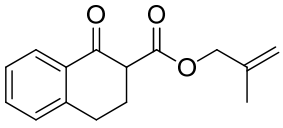
^{1}H NMR (400 MHz, Chloroform-*d*) (keto/enol 1:0.3) *Ketone* δ 8.03 (d, *J* = 8.8 Hz, 1H, Ar*H*), 6.84 (dd, *J* = 8.8, 2.5 Hz, 1H, Ar*H*), 6.70 – 6.68 (m, 1H, Ar*H*), 4.99 (s, 1H, CMeC*H*$_2$), 4.92 (s, 1H, CMeC*H*$_2$), 4.68 (d, *J* = 12.2 Hz, 1H, C*H*$_2$CMe), 4.60 (d, *J* = 13.2 Hz, 1H, C*H*$_2$CMe), 3.86 (s, 3H, O*Me*), 3.61 (dd, *J* = 10.1, 4.7 Hz, 1H, C*H*CH$_2$), 3.09 – 2.90 (m, 2H, CHC*H*$_2$), 2.56 – 2.44 (m, 1H, CH$_2$C*H*$_2$), 2.40 – 2.30 (m, 1H, CH$_2$C*H*$_2$), 1.75 (dd, *J* = 1.5, 0.8 Hz, 3H, C*Me*). *Enol:* δ 12.4 (s, 1H, OH), 7.74 (d, *J* = 8.5 Hz, 1H, Ar*H*), 6.80 (dd, *J* = 8.6, 2.6 Hz, 1H, Ar*H*), 6.71 (d, *J* = 2.6 Hz, 1H, Ar*H*), 5.02 (s, 1H, CMeC*H*$_2$), 4.96 (s, 1H, CMeC*H*$_2$), 4.63 (s, 2H, C*H*$_2$CMe) 3.84 (s, 3H, O*Me*), 2.80 (dd, *J* = 8.9, 6.6 Hz, 2H, CH$_2$C*H*$_2$), 2.64 – 2.57 (m, 2H, CH$_2$C*H*$_2$), 1.80 (dd, *J* = 1.5, 0.8 Hz, 3H, C*Me*).

^{13}C NMR (101.00 MHz, Chloroform-*d*) *Ketone*: δ 191.7, 170.1, 163.9, 146.1, 139.7, 130.3, 125.4, 113.5, 113.2, 112.6, 68.3, 55.5, 54.4, 28.1, 26.5, 19.5. *Enol:* δ 172.4, 165.8, 161.6, 141.8, 140.1, 126.2, 122.8, 113.2, 112.6, 111.7, 94.8, 67.4, 55.4, 28.3, 20.6, 19.5.

IR ν_{max} 2942 (w), 2841 (w), 1739 (m), 1677 (m), 1601 (s), 1277 (s), 1250 (s), 1210 (s), 1151 (m).

HRMS (ESI) calcd for $C_{16}H_{19}O_4^+$ $[M+H]^+$ 275.1278; found 275.1269.

2-Methylallyl-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (3l)



Starting from 3,4-dihydronaphthalen-1(2H)-one (0.50 g, 3.4 mmol), 2-methylallyl 1-oxo-1,2,3,4-tetrahydronaphatane-2-carboxylate **3l** (0.80 g, 3.4 mmol, 99% yield) was obtained as yellow liquid.

R_F 0.4 (pentane:dichloromethane 1:1).

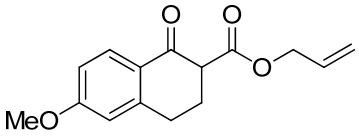
^{1}H NMR (400 MHz, Chloroform-*d*) (ketone/enol 1:1) Ketone δ 7.84 (dd, *J* = 7.5, 1.6 Hz, 1H, Ar*H*), 7.35 (dtd, *J* = 8.5, 4.3, 1.4 Hz, 2H, Ar*H*), 7.32 – 7.27 (m, 1H, Ar*H*), 5.02 (s, 1H, CMeC*H*$_2$), 4.95 (t, *J* = 1.4 Hz, 1H, CMeC*H*$_2$), 4.68 (s, 2H, C*H*$_2$CMe), 3.69 (dd, *J* = 10.3, 4.7 Hz, 1H, C*H*), 3.16 – 2.99 (m, 2H, C*H*$_2$), 2.62 – 2.50 (m, 1H, C*H*$_2$), 2.42 (ddt, *J* = 13.5, 5.9, 4.7 Hz, 1H, C*H*$_2$), 1.79 – 1.76 (m, 3H, CH$_2$C*Me*). Enol: δ 12.42 (s, 1H, O*H*), 8.08 (dd, *J* = 8.0, 1.4 Hz, 1H, Ar*H*), 7.53 (td, *J* = 7.5, 1.5 Hz, 1H, Ar*H*), 7.33 – 7.27 (m, 1H, Ar*H*), 7.23 – 7.19 (m, 1H, Ar*H*), 5.06 (s, 1H, CMeC*H*$_2$), 5.00 (s, 1H, CMeC*H*$_2$), 4.71 – 4.57 (m, 2H, C*H*$_2$CMe), 2.86 (dd, *J* = 8.9, 6.6 Hz, 2H, C*H*$_2$), 2.69 – 2.61 (m, 2H, C*H*$_2$), 1.88 – 1.81 (m, 3H, CH$_2$C*Me*).

^{13}C NMR (101.00 MHz, Chloroform-*d*) (Ketone/enol 1:1) δ 193.1, 172.3, 169.9, 165.4, 143.6, 139.9, 139.6, 139.4, 133.9, 131.8, 130.6, 130.0, 128.8, 127.8, 127.4, 126.9, 126.6, 124.4, 113.4, 112.8, 96.9, 68.4, 67.6, 54.6, 27.8, 27.7, 26.5, 20.5, 19.5, 19.4.

IR ν_{max} 3077 (w), 2975 (w), 2943 (w), 2844 (w), 1742 (m), 1687 (m), 1647 (s), 1619 (m), 1599 (m), 1454 (m), 1386 (m), 1357 (m), 1325 (m), 1307 (m), 1297 (m), 1269 (s), 1212 (s), 1200 (m), 1170 (m), 1156 (m), 1136 (m), 1087 (m), 907 (m), 768 (m), 744 (m).

HRMS (ESI) calcd for $C_{15}H_{17}O_3^+$ $[M+H]^+$ 245.1172; found 245.1166.

<u>Allyl-6-methoxy-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (3m)</u>



Starting from 6-methoxy-3,4-dihydronaphthalen-1(2H)-one(0.50 g, 2.8 mmol), allyl 6-methoxy-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate **3m** (0.50 g, 2.0 mmol, 70% yield) was obtained as a brown oil.

R_F 0.3 (pentane:ethylacetate 8:2).

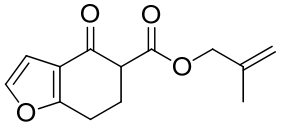
^{1}H NMR (400 MHz, Chloroform-*d*) (ketone/enol 1:0.3) *Ketone:* δ 8.02 (d, *J* = 8.8 Hz, 1H, Ar*H*), 6.84 (dd, *J* = 8.8, 2.5 Hz, 1H, Ar*H*), 6.70 – 6.67 (m, 1H, Ar*H*), 5.99 – 5.89 (m, 1H, C*H*CH$_2$), 5.32 (q, *J* = 1.5 Hz, 1H, CHC*H*$_2$), 5.24 (dq, *J* = 10.5, 1.3 Hz, 1H, CHC*H*$_2$), 4.74 – 4.63 (m, 2H, C*H*$_2$CH), 3.86 (s, 3H, O*Me*), 3.60 (dd, *J* = 10.3, 4.7 Hz, 1H, C*H*), 3.10 – 2.87 (m, 2H, C*H*$_2$), 2.49 (dddd, *J* = 13.4, 10.3, 9.4, 4.9 Hz, 1H, C*H*$_2$), 2.35 (ddt, *J* = 13.4, 5.9, 4.7 Hz, 1H, C*H*$_2$). *Enol*: δ 7.74 (d, *J* = 8.6 Hz, 1H, Ar*H*), 6.80 (dd, *J* = 8.6, 2.6 Hz, 1H, Ar*H*), 6.70 (d, *J* = 2.5 Hz, 1H, Ar*H*), 6.05 – 5.94 (m, 1H, C*H*CH$_2$), 5.40 – 5.33 (m, 1H, CHC*H*$_2$), 5.25 (m, 1H, CHC*H*$_2$), 4.73 – 4.69 (m, 2H, C*H*$_2$CH), 3.83 (s, 3H, O*Me*), 2.79 (dd, *J* = 8.9, 6.6 Hz, 2H, C*H*$_2$), 2.63 – 2.56 (m, 2H, C*H*$_2$).

^{13}C NMR (101.00 MHz, Chloroform-*d*) *Ketone:*δ 191.7, 170.1, 164.0, 146.1, 131.9, 130.3, 125.3, 118.4, 113.49, 112.6, 65.8, 55.5, 54.4, 28.1, 26.5. *Enol*: δ 172.4, 165.8, 161.6, 141.8, 132.4, 126.2, 122.8, 118.0, 113.2, 111.7, 94.8, 64.9, 55.4, 28.3, 20.6.

IR ν_{max} 2942 (w), 2907 (w), 2842 (w), 1738 (m), 1676 (m), 1600 (s), 1306 (m), 1273 (s), 1250 (s), 1210 (s), 1167 (m), 1152 (m), 1092 (m), 914 (m), 733 (s).

HRMS (ESI) calcd for $C_{15}H_{17}O_4^+$ $[M+H]^+$ 261.1121; found 261.1128.

2-Methylallyl 4-oxo-4,5,6,7-tetrahydrobenzofuran-5-carboxylate (3n)



Starting from 6,7-dihydrobenzofuran-4(5H)-one (0.50 g, 3.7 mmol) 2-methylallyl 4-oxo-4,5,6,7-tetrahydrobenzofuran-5-carboxylate **3n** (0.64 g, 2.7 mmol, 75 % yield) was obtained as a green liquid.

R_F 0.33 (pentane/ethy acetate 7:3).

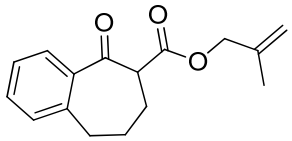
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 (d, *J* = 2.0 Hz, 1H, Ar*H*), 6.69 (dd, *J* = 2.1, 0.9 Hz, 1H, Ar*H*), 5.00 – 4.88 (m, 2H, CMeCH_2), 4.66 – 4.51 (m, 2H, CH_2CMe), 3.54 (dd, *J* = 8.5, 4.7 Hz, 1H, C*H*), 3.06 (dt, *J* = 17.6, 6.0 Hz, 1H, CH_2), 2.90 (ddd, *J* = 17.6, 7.5, 5.5 Hz, 1H, CH_2), 2.58 (ddddd, *J* = 13.9, 8.4, 7.4, 5.4, 0.8 Hz, 1H, CH_2), 2.44 – 2.33 (m, 1H, CH_2), 1.74 (d, *J* = 1.3 Hz, 3H, CH_2C*Me*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 188.6, 169.5, 166.5, 143.1, 139.5, 120.5, 113.3, 106.8, 68.5, 53.3, 25.9, 21.9, 19.4.

IR ν_{max} 2945 (w), 1739 (s), 1682 (s), 1622 (w), 1598 (w), 1518 (w), 1455 (m), 1446 (m), 1363 (w), 1346 (w), 1305 (m), 1270 (w), 1240 (w), 1201 (m), 1173 (w), 1156 (m), 1123 (m), 1027 (w), 982 (w), 942 (w), 910 (w), 875 (w), 738 (w), 717 (w).

HRMS (ESI) calcd for $C_{13}H_{15}O_4^+$ $[M+H]^+$ 235.0965; found 235.0963.

2-Methylallyl 5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-6-carboxylate (3o)



Starting from 5-methoxy-2,3-dihydro-*1H*-inden-1-one (1.00 g, 6.17 mmol), 2-methylallyl 5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate **3o** (0.952 g, 3.66 mmol, 59 % yield) was obtained as colorless liquid.

R_F 0.4 (dichloromethane/pentane 1:1).

^{1}H NMR (400 MHz, Chloroform-*d*) (ketone/enol 0.3:1) *Ketone:*δ 7.67 (dd, *J* = 7.7, 1.5 Hz, 1H, Ar*H*), 7.35 (dd, *J* = 7.5, 1.5 Hz, 1H, Ar*H*), 7.25 – 7.21 (m, 1H, Ar*H*), 7.13 (m, 1H, Ar*H*), 4.91 (t, *J* = 1.3 Hz, 1H, CMeCH_2), 4.87 – 4.84 (m, 1H, CMeCH_2), 4.56 – 4.46 (m, 2H, CH_2CMe), 3.78 (dd, *J* = 10.4, 4.4 Hz, 1H, C*H*), 2.89 (t, *J* = 5.1 Hz, 2H, CH_2), 2.08 (m, 2H, CH_2), 2.00 (m, 1H, CH_2), 1.84 – 1.75 (m, 1H, CH_2), 1.67 (t, *J* = 1.1 Hz, 3H, CH_2C*Me*). *Enol:* δ 12.51 (s, 1H, O*H*), 7.55 (dd, *J* = 7.1, 2.0 Hz, 1H, Ar*H*), 7.29 – 7.24 (m, 2H, Ar*H*), 7.18 – 7.13 (m, 1H, Ar*H*), 4.98 – 4.94 (m, 1H, CMeCH_2), 4.89 (t, *J* = 1.4 Hz, 1H, CMeCH_2), 4.59 (s, 2H, CH_2CMe), 2.57 (t, *J* =

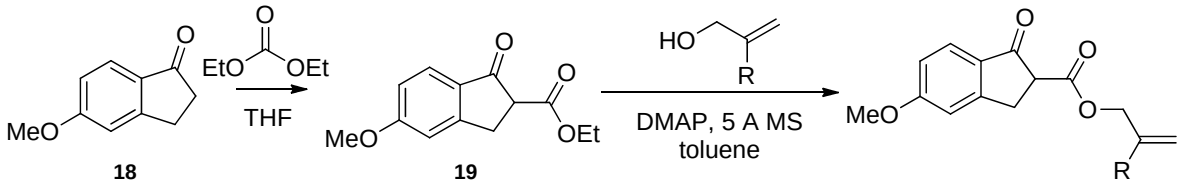
6.9 Hz, 2H, CH_2), 2.10 (td, J = 6.6, 1.6 Hz, 2H, CH_2), 2.07 – 1.99 (m, 2H, CH_2), 1.76 – 1.72 (m, 3H, CMeCH$_2$).

^{13}C NMR (101.00 MHz, Chloroform-*d*) (ketone/enol 0.3:1) *Ketone:* δ 200.5, 172.6, 170.1, 141.2, 139.7, 138.1, 132.4, 129.9, 129.2, 126.8, 68.5, 56.7, 32.8, 25.4, 24.4, 19.5 . *Enol:* δ 170.7, 141.1, 140.0, 135.7, 130.2, 129.0, 127.2, 126.4, 113.4, 112.7, 100.2, 67.6, 33.6, 31.8, 21.9, 19.5

IR ν_{max} 3080 (w), 2976 (w), 2938 (w), 2887 (w), 2882 (w), 2860 (w), 1747 (s), 1681 (w), 1640 (m), 1618 (w), 1592 (w), 1567 (w), 1450 (m), 1383 (w), 1362 (w), 1343 (w), 1298 (m), 1270 (s), 1241 (s), 1202 (m), 1190 (m), 1158 (w), 1127 (m), 1095 (w), 989 (m), 945 (w), 908 (m), 821 (w), 790 (w), 772 (m).

HRMS (ESI) calcd for $C_{16}H_{19}O_3^+$ $[M+H]^+$ 259.1329; found 259.1329.

3.1 Synthesis of substrates 3i and 3j.



18 **19**

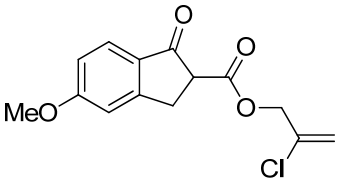
Ethyl 5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (19)

Following a reported procedure,[7] potassium *tert*-butoxyde (6.9 mg, 0.062 mmol, 0.0050 equiv.) was added to a suspension of NaH (1.1 g, 27 mmol, 2.2 equiv.) and diethyl carbonate (7.5 mL, 62 mmol, 5.0 equiv.). 5-Methoxy-2,3-dihydro-1H-inden-1-one (**18**) (2.0 g, 12 mmol) was then added carefully at 0 °C. The reaction was stirred at room temperature and followed by TLC. Then 1 M HCl was added until the pH of the solution became neutral or slightly acidic. The organic layers were collected and washed with brine (2 x 20 mL), dried over $MgSO_4$ and concentrated in vacuum. The crude product was purified by column chromatography (7:3 Pentane/Ethyl acetate) and the pure compound (**19**) was obtained in 96% yield (2.8 g, 12 mmol, 96%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.70 (d, J = 9.1 Hz, 1H, ArH), 6.94 – 6.89 (m, 2H, ArH), 4.29 (dd, 1H, J = 7.2, 0.9 Hz, CH_2CH$_3$), 4.25 (dd, 1H, J = 7.2, 0.8 Hz, CH_2CH$_3$), 3.89 (s, 3H, *OMe*), 3.70 (dd, J = 8.2, 3.9 Hz, 1H, CH), 3.50 (ddt, J = 17.2, 4.0, 1.0 Hz, 1H, CH_2), 3.33 (dd, 1 H, J = 17.3, 8.1 Hz, CH_2), 1.31 (t, J = 7.1 Hz, 3H, CH$_2$CH_3).

The characterization data for compounds **19** corresponded to the reported values.[8]

2-Chloroallyl 5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (3i)



(7) M.V. Vita, J. Waser, *Org. Lett.* **2013**, *15*, 3246-3249.
(8) A. Martinez, M. Fernandez, J. Estevez, J.R. Estevez, L. Castaldo, *Tetrahedron* **2005**, *61*, 1353-1362

Substrate **3i** was synthetized following a reported procedure,[9] in a 2-neck 50 mL flask compound **19** (0.71 g, 3.0 mmol), DMAP (0.37 g, 3.0 mmol, 1.0 equiv.), 2-chloroprop-2-en-1-ol (0.29 g, 3.2 mmol, 1.05 equiv.) and c.a 200-300 mg of activated 5Å MS were heated to reflux till disappearance of the starting material (TLC 9:1, pentane/ethyl acetate). The reaction was quenched with HCl 1 M and water; the aqueous layer was extracted with diethyl ether (2x 30 mL). The organic layers were collected, washed with $NaHCO_3$, brine, dried over $MgSO_4$., filtered and concentrated under reduced pressure. The crude is purified by column chromatography: 1:1 pentane/DCM, 4:1 DCM/penatane and then 100% DCM. The title compound **3i** (0.49 g, 1.8 mmol, 58 % yield) is obtained as yellow oil.

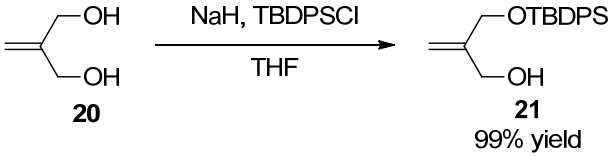
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.69 (d, *J* = 9.2 Hz, 1H, Ar*H*), 6.99 – 6.83 (m, 2H, Ar*H*), 5.58 (q, *J* = 1.5 Hz, 1H, CClCH_2), 5.40 (dt, *J* = 1.9, 0.8 Hz, 1H, CClCH_2), 4.86 – 4.63 (m, 2H, CH_2CCl), 3.89 (s, 3H, O*Me*), 3.77 (dd, *J* = 8.2, 4.0 Hz, 1H, C*H*), 3.52 (dd, *J* = 17.4, 4.0 Hz, 1H, CH_2), 3.33 (dd, *J* = 17.3, 8.2 Hz, 1H, CH_2).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.0, 168.5, 166.0, 156.6, 135.1, 128.3, 126.4, 116.1, 114.8, 109.6, 66.4, 55.8, 53.3, 30.2.

IR ν_{max} 2944 (w), 2843 (w), 1746 (m), 1705 (s), 1599 (s), 1491 (w), 1337 (w), 1306 (m), 1259 (s), 1190 (w), 1144 (m), 1105 (m), 1089 (m), 1026 (w), 987 (w).

HRMS (ESI) calcd for $C_{14}ClH_{14}O_4^+$ $[M+H]^+$ 281.0575; found 281.0568.

2-(((*tert*-Butyldiphenylsilyl)oxy)methyl)prop-2-en-1-ol (21)



20 **21**
99% yield

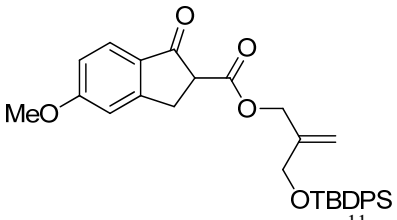
Following a reported procedure,[10] 2-methylenepropane-1,3-diol (**20**) (0.50 mL, 6.1 mmol) was dissolved in THF (15 mL), the solution was cooled at 0 °C before the addition of NaH (0.25 g 60% dispersed in mineral oil, 6.1 mmol, 1.0 equiv.). After 1 h, TBDPSCl (1.6 mL, 6.1 mmol, 1.0 equiv.) was added and the reaction was stirred at room temperature for 18-20 h. The solution was then cooled to 0 °C and quenched with iced water and then extracted with diethyl ether (3 x 50 mL). The organic layers are recombined and washed with a saturated solution of K_2CO_3 (50 mL), brine (50 mL) and dried over Na_2SO_4. Evaporation of the solvent afforded compound **21** (2.0 g, 6.1 mmol, 99% yield) as a colorless oil which was used without further purification for the transesterification.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 – 7.62 (m, 4H, *Ph*), 7.52 – 7.30 (m, 6H, *Ph*), 5.16 (s, 1H, CCH_2), 5.12 (s, 1H, CCH_2), 4.26 (s, 2H, CH_2C), 4.20 – 4.16 (m, 2H, CH_2C), 1.08 (s, 9H, *tBu*).

The characterization data for compounds **21** corresponded to the reported values.[10]

(9) J. Hierold, D.W. Lupton, *Org. Lett.* **2012***, 14,* 3412-3415.
(10) F. Russo, F. Wangsell, J. Saevmarker, M. Jacobsson, M. Larhed, *Tetrahedron* **2009**, *65*, 10047-10059.

2-(((*tert*-Butyldiphenylsilyl)oxy)methyl)allyl 5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (3j)



Substrate **8j** was synthetized following a reported procedure,[11] in a 2 neck 50 mL flask compound **19** (0.30 g, 1.3 mmol) DMAP (0.16 g, 1.3 mmol, 1.0 equiv.), 2-((tert-butyldiphenylsilyl)methyl)prop-2-en-1-ol (**21**) (0.44 g, 1.4 mmol, 1.1 equiv.) and c.a 200-300 mg of activated 5Å MS were heated to reflux till disappearance of the starting material (TLC 8:2, pentane/ethyl acetate). The reaction was quenched with 1M HCl and water; the aqueous layer was extracted with diethyl ether (2 x 30 mL). The organic layers were collected and washed with $NaHCO_3$ and brine and then dried over $MgSO_4$. Filtration and removal of the solvent under reduced pressure afforded the crude product which was purified by column chromatography (8:2 penatane/ethylacetate). The title compound **3j** (0.28 g, 0.53 mmol, 42 % yield) was obtained as a colorless oil

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.71 – 7.64 (m, 4H, *Ph*+ Ar*H*), 7.46 – 7.33 (m, 7H, *Ph*), 6.91 (ddd, *J* = 8.6, 1.9, 1.1 Hz, 1H, Ar*H*), 6.90 – 6.88 (m, 1H, Ar*H*), 5.30 (s, 1H, CMeCH_2), 5.22 (s, 1H, CMeCH_2), 4.77 – 4.67 (m, 2H, CH_2CMe), 4.21 (dt, *J* = 2.2, 1.4 Hz, 2H, CH_2OTBDPS), 3.89 (s, 3H, O*Me*), 3.68 (dd, *J* = 8.2, 4.0 Hz, 1H, C*H*), 3.44 (dd, *J* = 17.3, 4.1 Hz, 1H, CH_2), 3.33 – 3.21 (m, 1H, CH_2), 1.05 (s, 9H, ^{t}*Bu*).

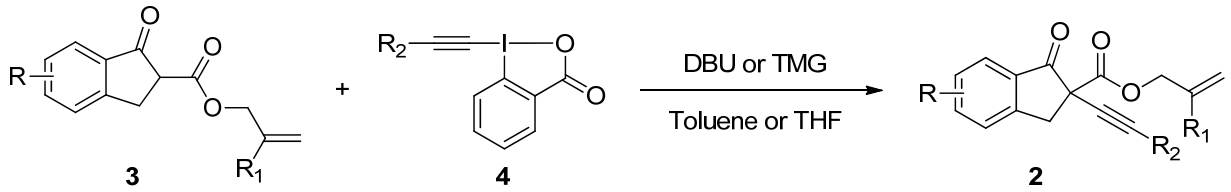
^{13}C NMR (101 MHz, Chloroform-*d*) δ 197.2, 169.0, 165.9, 156.6, 142.3, 135.5, 133.4, 129.7, 128.5, 127.7, 126.4, 115.9, 113.1, 109.6, 65.6, 64.5, 55.8, 53.4, 30.3, 26.8, 19.3.

IR ν_{max} 2956 (w), 2932 (w), 2858 (w), 1744 (w), 1743 (w), 1709 (s), 1600 (s), 1261 (s), 1111 (s), 1090 (m).

HRMS (ESI) calcd for $C_{31}H_{35}O_5Si^+$ $[M+H]^+$ 515.2248; found 515.2248.

(11) J. Hierold, D.W. Lupton , *Org. Lett.* **2012,** *14,* 3412-3415.

4. General procedure for the synthesis of α-alkynyl allyl β-keto esters.



3 4 2

In a 2-neck flask DBU or TMG (1.2 equiv.) was added to a solution of the allyl β-keto ester **3** in toluene (0.08 M). The reaction was stirred for a few minutes followed by the addition in one portion of the hypervalent iodine reagent **4** (1.5 equiv.). The reaction was stirred at room temperature till disappearance of the starting material by TLC. Upon completion the reaction was quenched with water (20 mL) and extracted with diethyl ether (3 x 20 mL). The organic layers were recombined, washed with $NaHCO_3$ (20 mL), brine (20 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The corresponding crude was purified by flash chromatography as indicated by the R_F values for each compound.

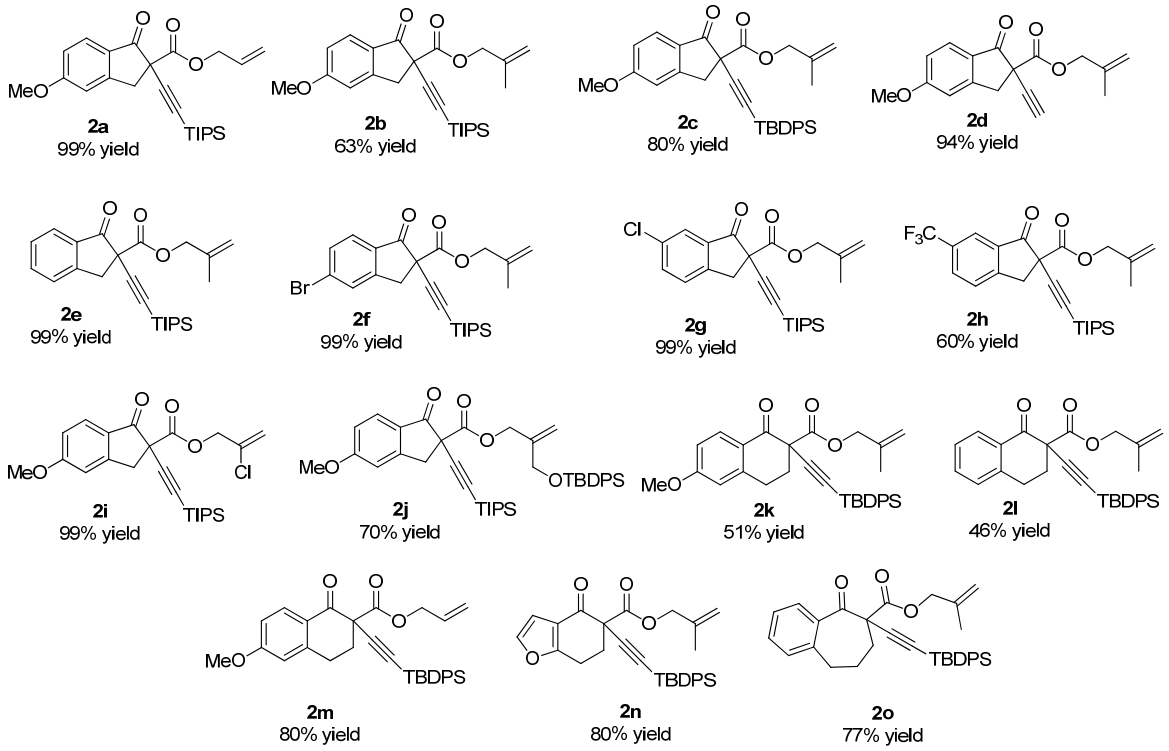
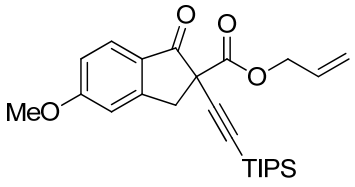


Figure S1. Scope of the α-alkynylation of β-allyl keto esters with hypervalent iodine EBX reagents.

Allyl 5-methoxy-1-oxo-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-indene-2-carboxylate (2a)



Starting from 5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**3a**) (0.300 g, 1.22 mmol), allyl 5-methoxy-1-oxo-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-indene-2-carboxylate (**2a**) (0.518 g, 1.35 mmol, 99 % yield) was obtained as a yellow oil using DBU as the base in the general procedure.

R_F 0.3 (pentane:ethyl acetate 9:1).

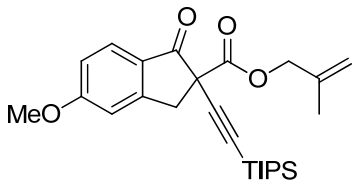
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.74 (d, *J* = 8.5 Hz, 1H, Ar*H*), 6.99 – 6.86 (m, 2H, Ar*H*), 5.89 (ddt, *J* = 16.3, 10.7, 5.5 Hz, 1H, C*H*CH$_2$), 5.34 (dt, *J* = 17.2, 1.7 Hz, 1H, CHC*H$_2$*), 5.21 (dd, *J* = 10.5, 1.5 Hz, 1H, CHC*H$_2$*), 4.66 (m, 2H, C*H$_2$*CH), 3.90 (s, 3H, O*Me*), 3.89 (d, *J* = 16.9 Hz, 1H, C*H$_2$*), 3.43 (d, *J* = 17.1 Hz, 1H, C*H$_2$*), 1.05 (d, *J* = 1.7 Hz, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 193.9, 168.1, 166.1, 155.2, 131.3, 127.5, 126.4, 118.5, 116.3, 109.4, 103.4, 85.2, 66.8, 56.7, 55.8, 41.2, 18.6, 11.2.

IR ν_{max} 2944 (m), 2893 (w), 2866 (m), 2171 (w), 1720 (s), 1599 (s), 1464 (w), 1262 (s), 1210 (m), 1182 (w), 1105 (w), 1092 (m), 884 (m).

HRMS (ESI) calcd for $C_{25}H_{34}NaO_4Si^+$ $[M+Na]^+$ 449.2119; found 449.2110.

2-Methylallyl 5-methoxy-1-oxo-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-indene-2-carboxylate (2b)



Starting from 2-methylallyl 5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**3b**) (1.00 g, 3.84 mmol, 2-methylallyl 5-methoxy-1-oxo-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-indene-2-carboxylate (**2b**) (1.68 g, 3.84 mmol, 99 % yield) was obtained as a yellow solid using DBU as a base in the general procedure.

R_F 0.35 (pentane:ethyl acetate 8:2).

Mp: 37.9-42.7°C.

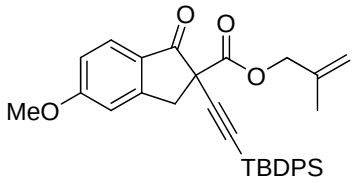
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.74 (d, *J* = 8.5 Hz, 1H, Ar*H*), 6.94 (dd, *J* = 8.6, 2.1 Hz, 1H, Ar*H*), 6.91 – 6.89 (m, 1H, Ar*H*), 5.00 (s, 1H, CC*H$_2$*), 4.90 (s, 1H, CC*H$_2$*), 4.60 (d, *J* = 13.1 Hz, 1H, C*H$_2$*CMe), 4.56 (d, *J* = 13.1 Hz, 1H, C*H$_2$*CMe), 3.90 (m, 1H, C*H$_2$*), 3.90 (s, 3H, O*Me*), 3.44 (dd, *J* = 16.9, 1.0 Hz, 1H, C*H$_2$*), 1.74 (dd, *J* = 1.5, 0.9 Hz, 3H, C*H$_3$*), 1.05 (d, *J* = 1.6 Hz, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 193.9, 168.1, 166.1, 155.2, 139.2, 127.4, 126.5, 116.2, 113.3, 109.4, 103.4, 85.1, 69.5, 56.8, 55.8, 41.2, 19.3, 18.6, 11.2.

IR ν_{max} 2944 (m), 2866 (m), 2172 (w), 1722 (s), 1623 (s), 1602 (s), 1264 (s).

HRMS (ESI) calcd for $C_{26}H_{37}O_4Si^+$ $[M+H]^+$ 441.2456; found 441.2454.

2-Methylallyl 2-((tert-butyldiphenylsilyl)ethynyl)-5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (2c)



Starting from 2-methylallyl 5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**3b**) (0.0600 g, 0.231 mmol), 2-methylallyl 2-((*tert*-butyldiphenylsilyl)ethynyl)-5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**2c**) (0.0960 g, 0.184 mmol, 80 % yield with 92% purity) was obtained as a brown oil using DBU as a base and TBDPS-EBX (**4b**) as the reagent in the general procedure.

R_F 0.33 (pentane:ethyl acetate 9:1).

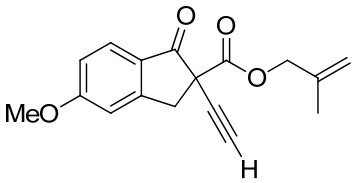
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.90 – 7.69 (m, 5H, *Ph*), 7.43 – 7.29 (m, 6H, *Ph* + Ar*H*), 7.03 – 6.88 (m, 2H, Ar*H*), 5.04 (s, 1H, CCH_2), 4.92 (s, 1H, CCH_2), 4.64 (s, 2H, CH_2C), 3.97 (d, *J* = 17.2 Hz, 1H, CH_2), 3.91 (s, 3H, O*Me*), 3.55 (d, *J* = 17.1 Hz, 1H, CH_2), 1.75 (s, 3H, CH_3), 1.07 (s, 9H, ^{t}*Bu*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 193.5, 167.9, 166.3, 155.3, 139.2, 135.6, 133.1, 133.1, 129.5, 127.7, 126.3, 116.4, 113.6, 109.5, 105.7, 84.4, 72.8, 69.8, 57.0, 55.8, 40.8, 27.0, 19.4.

IR ν_{max} 4488 (w), 3072 (w), 2953 (w), 2933 (w), 2892 (w), 2858 (w), 2174 (w), 1719 (s), 1599 (s), 1262 (s), 1108 (m), 740 (m).

HRMS (ESI) calcd for $C_{33}H_{35}O_4Si^+$ $[M+H]^+$ 523.2299; found 523.2305.

2-Methylallyl 2-ethynyl-5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (2d)



Starting from 2-methylallyl 5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**3b**) (0.517 g, 1.99 mmol), 2-methylallyl 2-ethynyl-5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**2d**) (0.530 g, 1.86 mmol, 94 % yield) was obtained as a yellow oil using TMG as a base and TMS-EBX (**4c**) as the reagent in the general procedure.

R_F 0.31 (pentane:ethyl acetate 7:3).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.75 (d, *J* = 8.6 Hz, 1H, Ar*H*), 6.98 – 6.93 (m, 1H, Ar*H*), 6.93 – 6.89 (m, 1H, Ar*H*), 4.97 (s, 1H, CCH_2), 4.91 (s, 1H, CCH_2), 4.43 (d, *J* = 13.2 Hz, 1H,

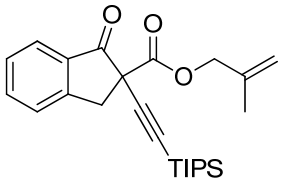
C*H*$_2$CMe), 4.39 (d, *J* = 13.2 Hz, 1H, C*H*$_2$CMe), 3.91 (s, 3H, O*Me*), 3.87 (m, 1H, C*H*$_2$), 3.51 – 3.42 (m, 1H, C*H*$_2$), 2.42 (s, 1H, C*H*), 1.72 (dd, *J* = 1.6, 0.9 Hz, 3H, C*H*$_3$).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 193.8, 167.6, 166.4, 155.3 139.1, 127.5, 126.2, 116.5, 113.3, 109.4, 80.2, 72.2, 69.6, 55.9, 55.8, 40.4, 19.3.

IR ν_{max} 3291 (w), 3275 (w), 2944 (w), 1750 (m), 1717 (s), 1659 (w), 1600 (s), 1493 (w), 1449 (w), 1339 (w), 1306 (w), 1264 (s), 1203 (w), 1183 (w), 1150 (w), 1104 (w), 1093 (m), 1057 (w), 1025 (w), 985 (w), 942 (w), 928 (w), 906 (w), 848 (w), 829 (w), 747 (w), 736 (w), 680 (w), 664 (w), 647 (w), 635 (s), 621 (w), 607 (w).

HRMS (ESI) calcd for $C_{17}H_{17}O_4^+$ $[M+H]^+$ 285.1121; found 285.1124.

2-Methylallyl 1-oxo-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-indene-2-carboxylate (2e)



Starting from 2-methylallyl 1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**3e**) (0.207 g, 0.899 mmol), 2-methylallyl 1-oxo-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-indene-2-carboxylate (**2e**) (0.365 g, 0.889 mmol, 99 % yield) was obtained as a yellow oil using DBU as a base in the general procedure.

R_F 0.3 (pentane:ethyl acetate 95:5).

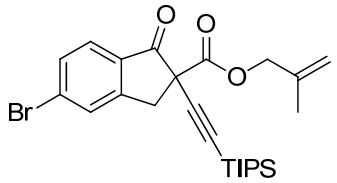
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 (dt, *J* = 7.7, 0.9 Hz, 1H, Ar*H*), 7.65 (td, *J* = 7.5, 1.2 Hz, 1H, Ar*H*), 7.49 (dt, *J* = 7.8, 0.9 Hz, 1H, Ar*H*), 7.42 (ddd, *J* = 7.9, 7.2, 1.0 Hz, 1H, Ar*H*), 5.01 – 4.96 (m, 1H, CMeC*H*$_2$), 4.92 – 4.88 (m, 1H, CMeC*H*$_2$), 4.59 (d, *J* = 13.8 Hz, 1H, C*H*$_2$CMe), 4.56 (d, *J* = 13.9 Hz, 1H, C*H*$_2$CMe), 3.95 (d, *J* = 17.0 Hz, 1H, C*H*$_2$), 3.50 (d, *J* = 17.2 Hz, 1H, C*H*$_2$), 1.73 (t, *J* = 1.1 Hz, 3H, C*Me*), 1.04 (m, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 195.9, 167.8, 152.1, 139.1, 135.7, 133.5, 128.1, 126.4, 125.7, 113.4, 103.0, 85.5, 69.6, 56.5, 41.2, 19.3, 18.6, 11.2.

IR ν_{max} 2943 (m), 2892 (w), 2865 (m), 2171 (w), 1728 (s), 1464 (m), 1245 (m), 1208 (m), 1189 (m), 1176 (m), 918 (m), 883 (m), 751 (m), 736 (m).

HRMS (ESI) calcd for $C_{25}H_{35}O_3Si^+$ $[M+H]^+$ 411.2350; found 411.2356.

2-Methylallyl 5-bromo-1-oxo-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-indene-2-carboxylate (3f)



Starting from 2-methylallyl 5-bromo-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**3f**) (0.20 g, 0.65 mmol), 2-methylallyl 5-bromo-1-oxo-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-indene-2-carboxylate (**2f**) (0.28 g, 0.56 mmol, 87 % yield) was obtained as a yellow solid using DBU as a base in the general procedure.

R_F 0.33 (pentane:ethyl acetate 95:5).

Mp: 42.1-44.4°C.

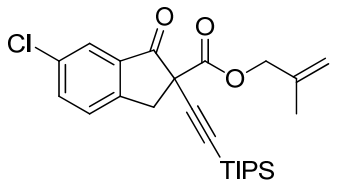
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.65 – 7.55 (m, 2H, Ar*H*), 7.57 – 7.46 (m, 1H, Ar*H*), 4.92 (dt, *J* = 2.6, 1.3 Hz, 1H, C*CH*$_2$), 4.85 (ddd, *J* = 2.7, 1.8, 1.1 Hz, 1H, C*CH*$_2$), 4.59 (d, *J* = 14.7 Hz, 1H, *CH*$_2$CMe), 4.56 (d, *J* = 13.9 Hz, 1H, *CH*$_2$CMe), 3.86 (d, *J* = 17.2 Hz, 1H, *CH*$_2$), 3.46 – 3.34 (m, 1H, *CH*$_2$), 1.73 – 1.61 (m, 3H, C*CH*$_3$), 0.97 (s, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 194.7, 167.5, 153.6, 139.0, 132.3, 131.9, 131.3, 129.7, 126.8, 113.6, 102.4, 86.0, 69.7, 56.5, 40.8, 19.3, 18.6, 11.2.

IR ν_{max} 2943 (m), 2892 (w), 2865 (m), 2172 (w), 1730 (s), 1597 (m), 1582 (w), 1464 (w), 1430 (w), 1289 (w), 1256 (m), 1205 (m), 1180 (m), 1060 (w), 996 (w), 943 (w), 918 (m), 884 (m), 751 (w).

HRMS (ESI) calcd for $C_{25}H_{33}{}^{79}BrNaO_3Si^+$ $[M+Na]^+$ 511.1275; found 511.1273.

2-Methylallyl 6-chloro-1-oxo-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-indene-2-carboxylate (2g)



Starting from 2-methylallyl 6-chloro-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**3g**) (0.300, 1.13 mmol), 2-methylallyl 6-chloro-1-oxo-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-indene-2-carboxylate (**2g**) (0.500 g, 1.12 mmol, 99 % yield) was obtained as a yellow oil using DBU as a base in the general procedure.

R_F 0.37 (dichloromethane:pentane 1:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62 (dd, *J* = 2.1, 0.7 Hz, 1H, Ar*H*), 7.45 (dd, *J* = 8.2, 2.1 Hz, 1H, Ar*H*), 7.28 (dq, *J* = 8.2, 0.9 Hz, 1H, Ar*H*), 4.83 (dq, *J* = 2.0, 1.2 Hz, 1H, CMe*CH*$_2$), 4.76 (ddt, *J* = 2.2, 1.5, 0.8 Hz, 1H, CMe*CH*$_2$), 4.62 (d, *J* = 13.8 Hz, 1H, *CH*$_2$CMe), 4.58 (d, *J* = 13.9

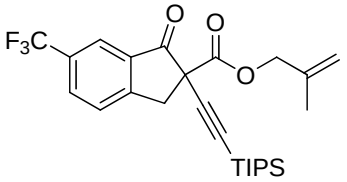
Hz, 1H, CH_2CMe), 3.75 (dt, J = 17.2, 0.7 Hz, 1H, CH_2), 3.37 – 3.24 (m, 1H, CH_2), 1.58 (dd, J = 1.5, 0.9 Hz, 3H, CCH_3), 0.89 (s, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 194.7, 167.5, 150.1, 139.0, 135.8, 135.0, 134.5, 127.6, 125.4, 113.6, 102.3, 86.1, 69.7, 57.0, 40.8, 19.3, 18.6, 11.2.

IR ν_{max} 2943 (m), 2892 (w), 2866 (m), 2173 (w), 1731 (s), 1465 (m), 1262 (m), 1246 (m), 1197 (s), 1186 (s), 884 (m).

HRMS (ESI) calcd for $C_{25}ClH_{34}O_3Si^+$ $[M+H]^+$ 445.1960; found 445.1945.

2-Methylallyl 1-oxo-6-(trifluoromethyl)-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-indene-2-carboxylate (2h)



Starting from 2-methylallyl 1-oxo-6-(trifluoromethyl)-2,3-dihydro-1H-indene-2-carboxylate (**3h**) (0.15 g, 0.50 mmol), 2-methylallyl 1-oxo-6-(trifluoromethyl)-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-indene-2-carboxylate (**2h**) (0.14 g, 0.30 mmol, 60 % yield) was obtained as colorless oil.

R_F 0.35 (pentane:ethyl acetate 9:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.05 – 8.00 (m, 1H, Ar*H*), 7.89 – 7.79 (m, 1H, Ar*H*), 7.63 – 7.53 (m, 1H, Ar*H*), 4.93 (p, J = 1.2 Hz, 1H, CMeCH_2), 4.85 (ddd, J = 2.6, 1.8, 1.0 Hz, 1H, CMeCH_2), 4.61 (d, J = 14.1 Hz, 1H, CH_2CMe), 4.57 (d, J = 14.1 Hz, 1H, CH_2CMe), 3.95 (d, J = 17.5 Hz, 1H, CH_2), 3.48 (d, J = 17.5 Hz, 1H, CH_2), 1.73 – 1.62 (m, 3H, CCH_3), 0.97 (s, 21H, *TIPS*).

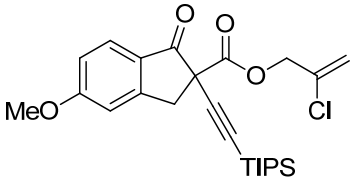
^{13}C NMR (101 MHz, $CDCl_3$) δ 194.7, 167.3, 155.2, 139.0, 134.0 – 132.0 (m), 131.1 (q, J = 33.1 Hz), 127.2, 123.5 (q, J = 272 Hz), 122.9 (q, J = 3.8 Hz). 122.9, 113.7, 102.0, 86.4, 69.9, 56.8, 41.2, 19.3, 18.6, 11.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.6.

IR ν_{max} 2943 (m), 2895 (w), 2866 (m), 2173 (w), 1734 (s), 1332 (s), 1250 (s), 1200 (s), 1186 (s), 1136 (s).

HRMS (ESI) calcd for $C_{26}H_{33}F_3NaO_3Si^+$ $[M+Na]^+$ 501.2043; found 501.2031.

2-Chloroallyl 5-methoxy-1-oxo-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-indene-2-carboxylate (2i)



Starting from 2-chloroallyl 5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**3i**) (0.467 g, 1.66 mmol), 2-chloroallyl 5-methoxy-1-oxo-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-indene-2-carboxylate (**2i**) (0.700 g, 1.52 mmol, 91 % yield) was obtained as a brown oil using DBU as a base in the general procedure.

R_F 0.38 (pentane:ethyl acetate 9:1).

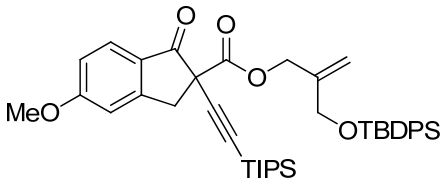
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.74 (d, *J* = 8.5 Hz, 1H, Ar*H*), 6.98 – 6.93 (m, 1H, Ar*H*), 6.91 (q, *J* = 1.1 Hz, 1H, Ar*H*), 5.56 (q, *J* = 1.6 Hz, 1H, CCH_2), 5.38 (dt, *J* = 1.9, 1.0 Hz, 1H, CCH_2), 4.71 (q, *J* = 1.1 Hz, 2H, CH_2C), 3.91 (d, *J* = 17.1, 1.0 Hz, 1H, CH_2), 3.91 (s, 3H, O*Me*), 3.46 (d, *J* = 17.1, 1.0 Hz, 1H, CH_2), 1.05 (m, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 193.5, 167.6, 166.2, 155.2, 134.6, 127.5, 126.3, 116.4, 114.5, 109.5, 102.9, 85.6, 66.9, 56.6, 55.8, 41.1, 18.6, 11.2.

IR ν_{max} 2943 (m), 2893 (w), 2865 (m), 2171 (w), 1721 (s), 1599 (s), 1262 (s), 1203 (m), 1093 (m), 1070 (m), 884 (m).

HRMS (ESI) calcd for $C_{25}H_{33}ClNaO_4Si^+$ $[M+Na]^+$ 483.1729; found 483.1740.

2-(((Tert-butyldiphenylsilyl)oxy)methyl)allyl 5-methoxy-1-oxo-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-indene-2-carboxylate (2j)



Starting from 2-(((*tert*-butyldiphenylsilyl)oxy)methyl)allyl 5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**3j**) (0.152 g, 0.295 mmol), 2-(((*tert*-butyldiphenylsilyl)oxy)methyl)allyl 5-methoxy-1-oxo-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-indene-2-carboxylate (**2j**) (0.180 g, 0.259 mmol, 88 % yield) was obtained as a colorless oil.

R_F 0.3 (pentane:ethyl acetate 9:1).

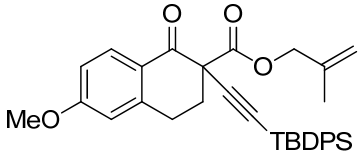
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.70 (d, *J* = 8.6 Hz, 1H, Ar*H*), 7.66 – 7.61 (m, 4H, *Ph*), 7.39 (m, 6H, *Ph*), 6.92 (dd, *J* = 8.6, 2.2 Hz, 1H, Ar*H*), 6.85 (d, *J* = 2.1 Hz, 1H, Ar*H*), 5.23 (t, *J* = 1.5 Hz, 1H, CCH_2), 5.18 (q, *J* = 1.4 Hz, 1H, CCH_2), 4.70 (s, 2H, C(O)OCH_2C), 4.17 (d, *J* = 14.9 Hz,1H, CCH_2OTBDPS), 4.13 (d, *J* = 14.4 Hz, 1H, CCH_2OTBDPS), 3.89 (s, 3H, O*Me*), 3.82 (d, *J* = 17.1 Hz, 1H, CH_2), 3.40 (d, *J* = 17.1 Hz, 1H, CH_2), 1.03 (d, *J* = 2.8 Hz, 30H, *TIPS* +^{t}*Bu*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 193.8, 168.0, 166.1, 155.1, 141.9, 135.5, 133.4, 129.7, 127.7, 127.4, 126.5, 116.2, 112.9, 109.4, 103.4, 85.2, 66.2, 64.6, 56.7, 55.8, 41.2, 26.8, 19.3, 18.6, 11.2.

IR ν_{max} 2941 (m), 2893 (w), 2863 (m), 2171 (w), 1723 (s), 1601 (s), 1464 (m), 1264 (s), 1209 (m), 1111 (s), 1094 (m), 1073 (m), 913 (m), 707 (m).

HRMS (ESI) calcd for $C_{42}H_{54}NaO_5Si_2$ [M+Na] 717.3407; found 717.3408.

2-Methylallyl 2-((tert-butyldiphenylsilyl)ethynyl)-6-methoxy-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (2k)



Starting from 2-methylallyl 6-methoxy-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (**3k**) (1.40 g, 5.10 mmol), 2-methylallyl 2-((tert-butyldiphenylsilyl)ethynyl)-6-methoxy-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (**2k**) (1.37 g, 2.55 mmol, 50% yield) was obtained as a colorless oil using DBU as a base and TBDPS-EBX (**4b**) as the reagent in the general procedure.

R_F 0.3 (dichloromethane:pentane 5:1).

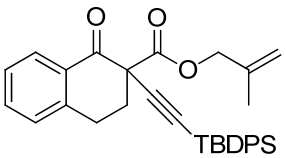
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.07 (d, *J* = 8.8 Hz, 1H, Ar*H*), 7.67 (ddd, *J* = 11.3, 8.1, 1.4 Hz, 3H, Ar*H*), 7.39 – 7.32 (m, 2H, Ar*H*), 7.32 – 7.25 (m, 5H, *Ph*), 6.88 (dd, *J* = 8.8, 2.5 Hz, 1H, Ar*H*), 6.72 (d, *J* = 2.5 Hz, 1H, Ar*H*), 5.09 (s, 1H, CMe*CH$_2$*), 4.96 (s, 1H, CMe*CH$_2$*), 4.77 (d, *J* = 12.9 Hz, 1H, *CH$_2$*CMe), 4.71 (d, *J* = 12.9 Hz, 1H, *CH$_2$*CMe), 3.87 (s, 3H, O*Me*), 3.45 (ddd, *J* = 16.7, 11.7, 4.6 Hz, 1H, *CH$_2$*), 2.99 (dt, *J* = 16.7, 4.2 Hz, 1H, *CH$_2$*), 2.84 (ddd, *J* = 13.3, 11.7, 4.4 Hz, 1H, *CH$_2$*), 2.55 – 2.45 (m, 1H, *CH$_2$*), 1.79 (t, *J* = 1.1 Hz, 3H, C*CH$_3$*), 0.98 (s, 9H, *tBu*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 188.0, 168.7, 164.1, 145.6, 139.4, 135.5, 135.5, 133.0, 133.0, 131.3, 129.5, 127.7, 127.7, 127.6, 123.8, 113.8, 113.7, 112.5, 103.5, 87.7, 69.4, 56.5, 55.6, 32.7, 26.9, 26.4, 19.5, 18.7.

IR ν_{max} 3071 (w), 2955 (w), 2931 (w), 2900 (w), 2892 (w), 2858 (w), 2165 (w), 1741 (w), 1714 (m), 1685 (w), 1600 (s), 1429 (m), 1291 (w), 1260 (s), 1227 (w), 1109 (m), 1090 (m), 821 (w), 741 (m).

HRMS (ESI) calcd for $C_{34}H_{37}O_4Si^+$ $[M+H]^+$ 537.2456; found 537.2452.

2-Methylallyl 2-((tert-butyldiphenylsilyl)ethynyl)-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (2l)



Starting from 2-methylallyl 1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (**3l**) (0.10 g, 0.41 mmol), 2-methylallyl 2-((tert-butyldiphenylsilyl)ethynyl)-1-oxo-1,2,3,4-tetrahydronaphthalene-2-

carboxylate (**2l**) (0.096 g, 0.19 mmol, 46 % yield) was obtained as colorless oil using DBU as a base and TBDPS-EBX (**4b**) as the reagent in the general procedure.

R_F 0.32 (pentane:ethyl acetate 9:1).

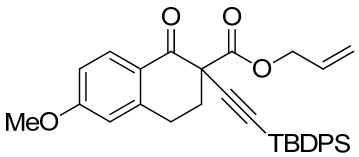
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.10 (dd, *J* = 7.9, 1.4 Hz, 1H, Ar*H*), 7.65 (td, *J* = 8.3, 1.4 Hz, 4H, *Ph*), 7.54 (td, *J* = 7.5, 1.5 Hz, 1H, Ar*H*), 7.39 – 7.33 (m, 3H, Ar*H*), 7.31 – 7.24 (m, 5H, *Ph* + Ar*H*), 5.12 – 5.07 (s, 1H, CMeCH_2), 4.96 (s, 1H, CMeCH_2), 4.75 (d, 1 H, *J* = 12.9 Hz, 1H, CH_2CMe), 4.70 (d, 1 H, *J* = 12.9 Hz, 1H, CH_2CMe), 3.48 (ddd, *J* = 18.0, 11.5, 4.7 Hz, 1H, CH_2), 3.05 (dt, *J* = 17.3, 4.3 Hz, 1H, CH_2), 2.87 (ddd, *J* = 13.4, 11.5, 4.5 Hz, 1H, CH_2), 2.53 (ddd, *J* = 13.4, 4.7, 3.8 Hz, 1H, CH_2), 1.79 (t, *J* = 1.2 Hz, 3H, C*Me*), 0.97 (s, 9H, *tBu*).

^{13}C NMR (101 MHz, $CDCl_3$) δ 189.2, 168.4, 143.1, 139.4, 135.5, 135.4, 134.1, 132.9, 132.9, 130.5, 129.5, 128.8, 128.8, 127.7, 127.1, 113.6, 102.9, 88.2, 69.5, 56.6, 32.5, 26.9, 26.0, 19.5, 18.7. Two carbon of the Ph group are not resolved.

IR ν_{max} 3072 (w), 2932 (w), 2892 (w), 2861 (w), 2255 (w), 2168 (w), 1740 (m), 1697 (m), 1601 (w), 1474 (w), 1464 (w), 1430 (w), 1256 (m), 1225 (m), 1112 (m), 909 (s), 735 (s).

HRMS (ESI) calcd for $C_{33}H_{34}NaO_3Si^+$ $[M+Na]^+$ 529.2169; found 529.2151.

Allyl 2-((tert-butyldiphenylsilyl)ethynyl)-6-methoxy-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (2m)



Starting from allyl 6-methoxy-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (**3m**) (0.103 g, 0.396 mmol), allyl 2-((tert-butyldiphenylsilyl)ethynyl)-6-methoxy-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (**2m**) (0.144 g, 0.275 mmol, 70 % yield) was obtained as colorless oil using DBU as a base and TBDPS-EBX (**4b**) as the reagent in the general procedure.

R_F 0.3 (dichloromethane:pentane 5:1).

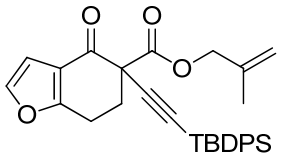
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.06 (d, *J* = 8.8 Hz, 1H, Ar*H*), 7.72 – 7.63 (m, 4H, *Ph*), 7.40 – 7.32 (m, 2H, *Ph*), 7.29 (td, *J* = 6.7, 1.1 Hz, 4H, *Ph*), 6.88 (dd, *J* = 8.8, 2.5 Hz, 1H, Ar*H*), 6.72 (d, *J* = 2.5 Hz, 1H, Ar*H*), 5.99 (ddt, *J* = 17.3, 10.5, 5.6 Hz, 1H, C*H*CH_2), 5.42 (dd, *J* = 17.2, 1.5 Hz, 1H, CHCH_2), 5.26 (dq, *J* = 10.5, 1.3 Hz, 1H, CHCH_2), 4.79 (ddt, *J* = 5.7, 4.2, 1.5 Hz, 2H, CH_2CH), 3.87 (s, 3H, O*Me*), 3.45 (ddd, *J* = 16.7, 11.8, 4.6 Hz, 1H, CH_2), 2.99 (dt, *J* = 17.1, 4.1 Hz, 1H, CH_2), 2.83 (ddd, *J* = 13.4, 11.7, 4.4 Hz, 1H, CH_2), 2.49 (ddd, *J* = 13.3, 4.7, 3.9 Hz, 1H, CH_2), 0.98 (s, 9H, *tBu*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 188.0, 168.7, 164.1, 145.6, 135.5, 135.5, 133.0, 133.0, 131.6, 131.3, 129.5, 127.7, 127.7, 123.8, 118.6, 113.8, 112.5, 103.4, 87.7, 66.7, 56.4, 53.4, 32.6, 26.9, 26.4, 18.7. One carbon of the Ph is not resolved.

IR ν_{max} 2957 (w), 2956 (w), 2934 (w), 2901 (w), 2894 (w), 2859 (w), 2858 (w), 2169 (w), 1744 (m), 1687 (m), 1601 (s), 1256 (s), 1227 (m), 1112 (m), 914 (m), 741 (m).

HRMS (ESI) calcd for $C_{33}H_{34}NaO_4Si^+$ $[M+Na]^+$ 545.2119; found 545.2128.

2-Methylallyl 5-((tert-butyldiphenylsilyl)ethynyl)-4-oxo-4,5,6,7-tetrahydrobenzofuran-5-carboxylate (2n)



Starting from 2-methylallyl 4-oxo-4,5,6,7-tetrahydrobenzofuran-5-carboxylate (**3n**) (0.094 g, 0.40 mmol), 2-methylallyl 5-((tert-butyldiphenylsilyl)ethynyl)-4-oxo-4,5,6,7-tetrahydrobenzofuran-5-carboxylate (**2n**) (0.177 g, 0.321 mmol, 80 % yield with 66% purity) was obtained as a colorless oil using DBU as a base and TBDPS-EBX (**4b**) as the reagent in the general procedure.

R_F 0.4 (pentane:dichloromethyne 1:1).

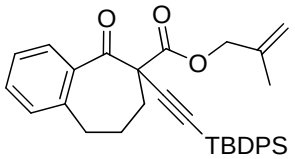
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.72 – 7.67 (m, 6H, *Ph*+Ar*H*), 7.44 – 7.31 (m, 5H, *Ph*), 6.77 (d, *J* = 2.0 Hz, 1H, Ar*H*), 5.10 (s, 1H, CMe*CH$_2$*), 4.97 (s, 1H, CMe*CH$_2$*), 4.73 (d, 1 H, *J* = 12.9 Hz, 1H, *CH$_2$*CMe), 4.67 (d, 1 H, *J* = 12.9 Hz, 1H, *CH$_2$*CMe), 3.33 – 3.17 (m, 1H, *CH$_2$*), 3.07 (dt, *J* = 17.5, 4.6 Hz, 1H, *CH$_2$*), 2.93 (ddd, *J* = 13.4, 10.0, 5.1 Hz, 1H, *CH$_2$*), 2.58 (ddd, *J* = 13.4, 5.1, 3.9 Hz, 1H, *CH$_2$*), 1.85 – 1.76 (m, 3H, C*Me*), 1.03 (s, 9H, *tBu*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 184.9, 168.1, 165.7, 143.3, 139.3, 135.5, 135.5, 134.8, 132.9, 132.8, 129.7, 129.5, 127.7, 118.9, 113.8, 107.5, 103.1, 87.4, 69.6, 56.3, 49.5, 32.9, 26.9, 26.6, 21.3.

IR ν_{max} 3071 (w), 2954 (w), 2931 (m), 2894 (w), 2858 (w), 1742 (w), 1695 (s), 1600 (w), 1471 (w), 1450 (m), 1439 (w), 1429 (s), 1361 (w), 1289 (w), 1258 (w), 1240 (w), 1214 (w), 1201 (w), 1189 (w), 1111 (s), 1010 (w), 939 (w), 925 (w), 911 (w), 877 (w), 821 (w), 741 (s).

HRMS (ESI) calcd for $C_{31}H_{32}O_4SiK^+$ $[M+K]^+$ 519.1932; found 519.1940.

2-Methylallyl 6-((tert-butyldiphenylsilyl)ethynyl)-5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-6-carboxylate (2o)



Starting from 2-methylallyl 5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-6-carboxylate (**3o**)(0.10 g, 0.40 mmol) 2-methylallyl 6-((tert-butyldiphenylsilyl)ethynyl)-5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]annulene-6-carboxylate (**2o**) (0.16 g, 0.31 mmol, 77 % yield) was

obtained as a colorless oil using DBU as a base and TBDPS-EBX (**4b**) as the reagent in the general procedure.

R_F 0.73 (dichloromethane:pentane 1:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.64 (td, *J* = 8.0, 1.5 Hz, 4H, *Ph*), 7.51 (dd, *J* = 7.6, 1.4 Hz, 1H, Ar*H*), 7.40 (dd, *J* = 7.6, 1.5 Hz, 1H, Ar*H*), 7.38 – 7.34 (m, 1H, Ar*H*), 7.34 – 7.28 (m, 6H, *Ph*), 7.21 – 7.16 (m, 1H, Ar*H*), 5.04 (s, 1H, CMe*CH_2*), 4.92 (s, 1H, CMe*CH_2*), 4.69 (d, *J* = 12.9 Hz, 1H, *CH_2*CMe), 4.64 (d, 1 H, *J* = 12.9 Hz, 1H, *CH_2*CMe), 3.16 (ddd, *J* = 15.1, 9.5, 3.6 Hz, 1H, *CH_2*), 2.88 (ddd, *J* = 15.1, 7.5, 4.0 Hz, 1H, *CH_2*), 2.59 – 2.43 (m, 1H, *CH_2*), 2.33 (tdd, *J* = 8.5, 6.9, 4.5 Hz, 2H, *CH_2*), 2.09 – 1.93 (m, 1H, *CH_2*), 1.74 (dd, *J* = 1.7, 0.9 Hz, 3H, C*CH_3*), 0.96 (s, 9H, *tBu*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.6, 168.7, 139.4, 138.8, 138.4, 135.5, 135.5, 133.0, 132.9, 131.8, 129.5, 129.2, 128.9, 127.6, 126.8, 113.7, 104.3, 88.5, 69.5, 60.6, 34.5, 33.8, 26.9, 23.5, 19.5, 18.6. Two carbons of the Ph group are not resolved.

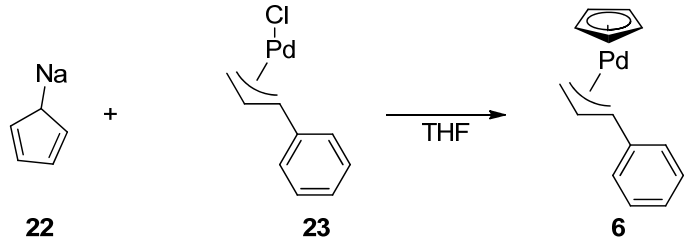
IR ν_{max} 3071 (w), 3049 (w), 2954 (m), 2931 (m), 2893 (w), 2858 (m), 2173 (w), 1749 (s), 1694 (s), 1660 (w), 1599 (w), 1486 (w), 1471 (w), 1461 (w), 1449 (m), 1430 (m), 1390 (w), 1362 (w), 1250 (m), 1213 (s), 1170 (w), 1110 (s), 1031 (w), 1009 (w), 973 (w), 954 (m), 910 (m), 821 (m), 802 (w), 776 (w), 764 (w), 741 (s).

HRMS (ESI) calcd for $C_{34}H_{37}O_3Si^+$ $[M+H]^+$ 521.2506; found 521.2502.

5. Pd-Catalyzed decarboxylation of allyl β-keto esters.

5.1 Synthesis of Pd(cinnamyl)Cp

Pd(cinnamyl)Cp (6)

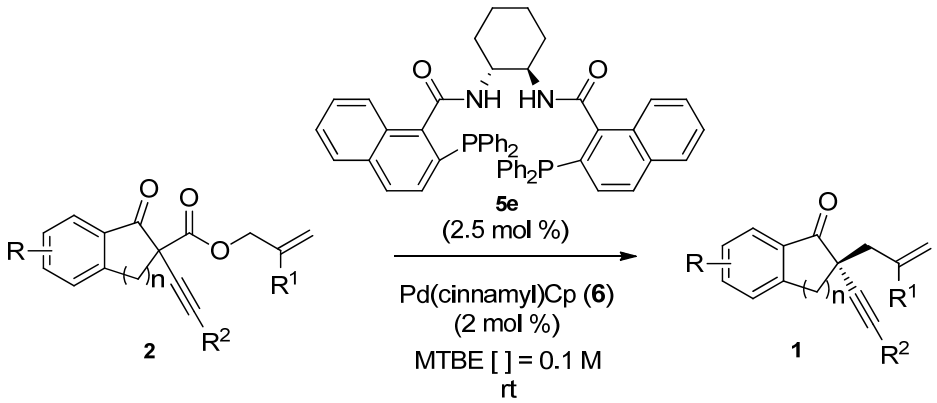


Following a reported procedure,[12] in a 2-neck 25 mL flask cinnamylpalladium(II) chloride (**23**) (0.300 g, 1.15 mmol) was dissolved in THF (10 mL). The solution was cooled to -78 °C. A solution of cyclopenta-2,4-dien-1-ylsodium (**22**) (1.45 mL, 2.90 mmol) in THF (10 ml) was added dropwise. The solution was stirred at -78 °C for 5 min. It was then allowed to warm to room temperature and then cooled again to 0 °C. The solvent was removed from the cooled solution with the high vac. and hexane was added. The dissolved solids were filtered and the filtrated was concentrated in vacuo to obtain an oily purple solid. Upon addition of hexane (1.5 mL) crystallization took place at -40 °C to afford cyclopenta-2,4-dien-1-yl(3-phenylpropyl)palladium (**6**) (0.300 g, 1.04 mmol, 90% yield) as purple cristals.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 (m, 2H, CpC*H*), 7.24 (m, 2H, CpC*H*), 5.65 (s, 5H, *Ph*), 5.49 (ddd, 1 H, *J* = 10.6, 9.9, 6.2 Hz, *CH*), 4.09 (d, 1 H, *J* = 9.8 Hz, *CH*), 3.63 (d, 1 H, *J* = 6.2 Hz, CH_2), 2.38 (dd, 1 H, *J* = 10.6, 0.7 Hz, CH_2).

The characterization data for compounds **11** corresponded to the reported values.[12]

5.2 General procedure for the asymmetric decarboxylation catalyzed by Pd.



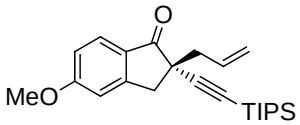
(12) A.W. Fraser, J.E. Besaw, L.E. Hull, M.C. Baird, Organometallics **2012**, *31*, 2470.

Substrate **7** (0.123 mmol), Pd(cinnamyl)Cp (**6**) (2 mol%) and ligand **5e** (2.5 mol%) were placed in a micro wave vial which was sealed. The solvent MTBE (1.2 mL) was added and the reaction was immediately degased three times. The mixture was left stirring at room temperature and monitored by TLC. Upon completeness the reaction was filtered through a plug of silica and the solvent evaporated. Purification by column chromatography yielded the product that was analyzed by chiral HPLC. The procedure used for optimization and scope are the same. (see Table 1 on main manuscript for optimization procedure).

Entry	Reaction conditions[a]	L	*ee*[b]
1	$[Pd_2(dba)_3]$, THF	**5a**	0
2	[Pd(cinnamyl)Cp] (**6**), THF	**5a**	0
3	**6**, THF	**5b**	0
4	**6**, Et_2O	**5b**	12
5	**6**, Et_2O	**5c**	59
6	**6**, Toluene	**5c**	28
7	**6**, CH_2Cl_2	**5c**	3
8	**6**, CH_3CN	**5c**	11
9	**6**, 1,4-dioxane	**5c**	29
10	**6**, Et_2O	**5d**	76
11	**6**, Et_2O	**5e**	74
12	6, MTBE	**5d**	70
13	**6**, MTBE	**5e**	79
14	**6**, MTBE, 0°C	**5e**	77
15	**6**, MTBE, 0.1 M	**5e**	86
16	**6**, MTBE, 0.3 M	**5e**	83
17	5 mol% **6**/ 5 mol% L, MTBE, 0.1 M	**5e**	86
18	5 mol% **6**/ 10 mol% L, MTBE, 0.1 M	**5e**	84
19	2 mol% **6**/ 5 mol% L, MTBE, 0.1 M[c]	**5e**	93

[a]All the reaction mixtures were degased three times and stirred at room temperature for 8-12 h using substrate **2a** (0.01 mmol), the indicated solvent (0.033 M), Pd source (20 mol%) and ligand (44 mol%) unless stated otherwise. All the reactions gave full conversion to the desired product **1a**. [b]The ee was determined by HPLC using Chiralcel columns. [c]Substrate **2b** was used.

(S)-2-Allyl-5-methoxy-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-inden-1-one (1a)



Starting from substrate **2a** (0.052 g, 0.12 mmol), 2-allyl-5-methoxy-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-inden-1-one (**1a**) (0.047 g, 0.12 mmol, 99% yield) was obtained as a yellow oil.

Chiral HPLC conditions: *ee*: 89%.Chiralcel IA 99:1 Hexane/*i*PrOH, 1 mL/min, 15 min t_{R1} = 7.1 min and t_{R2} = 9.3 min. λ = 254 cm^{-1}.

R_F 0.7 (pentane:ethyl acetate 9:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.72 (d, *J* = 8.5 Hz, 1H, Ar*H*), 6.92 (dd, *J* = 8.5, 2.3 Hz, 1H, Ar*H*), 6.84 (d, *J* = 2.3 Hz, 1H, Ar*H*), 5.89 (dddd, *J* = 16.7, 10.1, 7.8, 6.5 Hz, 1H, C*H*CH_2), 5.17 – 5.06 (m, 2H, CHCH_2), 3.88 (s, 3H, OCH_3), 3.30 (d, 1 H, *J* = 17.3 Hz, 1H, CH_2), 3.22 (d, *J* = 17.3 Hz, 1H, CH_2), 2.69 (ddt, *J* = 13.6, 6.5, 1.4 Hz, 1H, CH_2CH), 2.34 (dd, *J* = 13.7, 7.8 Hz, 1H, CH_2CH), 1.04 (s, 21H, *TIPS*).

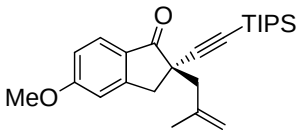
^{13}C NMR (101 MHz, $CDCl_3$) δ 200.9, 165.8, 154.7, 133.6, 127.8, 126.7, 118.7, 115.8, 109.6, 108.6, 82.8, 55.7, 49.0, 42.8, 40.4, 18.6, 11.2.

IR ν_{max} 3071 (w), 3049 (w), 2954 (m), 2931 (m), 2893 (w), 2858 (m), 2173 (w), 1749 (s), 1694 (s), 1660 (w), 1599 (w), 1486 (w), 1471 (w), 1461 (w), 1449 (m), 1430 (m), 1390 (w), 1362 (w), 1250 (m), 1213 (s), 1170 (w), 1110 (s), 1031 (w), 1009 (w), 973 (w), 954 (m), 910 (m), 821 (m), 802 (w), 776 (w), 764 (w), 741 (s).

HRMS (ESI) calcd for $C_{24}H_{35}O_2Si^+$ $[M+H]^+$ 383.2401; found 383.2399.

$[\alpha]_D^{25.0}$ +20.9 (c = 3.78, $CHCl_3$).

<u>(S)-5-Methoxy-2-(2-methylallyl)-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-inden-1-one (1b)</u>



Starting from substrate **2b** (54 mg, 0.12 mmol) (S)-5-methoxy-2-(2-methylallyl)-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-inden-1-one (**1b**) (49 mg, 0.12 mmol, 99% yield) was obtained as a yellow oil.

Chiral HPLC conditions. *ee*: 93%/95%[13]; Chiralcel IA 99:1 Hexane/*i*PrOH, 1 mL/min, 15 min. t_{R1} = 6.4 min and t_{R2} = 9.4 min. λ = 254 cm^{-1}.

R_F 0.88 (pentane:ethyl acetate 9:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 8.5 Hz, 1H, Ar*H*), 6.92 (dd, *J* = 8.5, 2.3 Hz, 1H, Ar*H*), 6.85 (d, *J* = 2.2 Hz, 1H, Ar*H*), 4.86 (s, 1H, CCH_2), 4.80 (s, 1H, CCH_2), 3.89 (s, 3H, OCH_3), 3.37 (d, 1 H, *J* = 17.3 Hz, 1H, CH_2), 3.31 (d, 1 H, *J* = 17.3 Hz, 1H, CH_2). 2.77 – 2.68 (d, *J* = 13.9 Hz, 1H, CH_2CMe), 2.38 – 2.29 (d, *J* = 14.0 Hz, 1H, CH_2CMe), 1.82 (t, *J* = 1.1 Hz, 3H, CCH_3), 1.01 (s, 21H, CTIPS).

^{13}C NMR (101 MHz, $CDCl_3$) δ 201.0, 165.7, 154.8, 142.2, 127.5, 126.9, 115.7, 114.9, 109.6, 109.4, 82.7, 55.7, 48.7, 45.3, 40.6, 23.7, 18.6, 17.7, 12.3, 11.2.

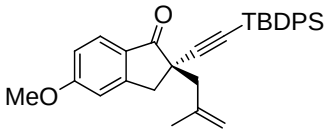
[13] Obtained for the larger scale reaction.

IR ν_{max} 2942 (w), 2923 (w), 2892 (w), 2864 (m), 2161 (w), 1716 (s), 1600 (s), 1491 (w), 1463 (m), 1447 (w), 1382 (w), 1336 (w), 1296 (m), 1209 (w), 1186 (w), 1147 (w), 1103 (m), 1091 (s), 1028 (m), 997 (m), 965 (w), 933 (m), 909 (s), 884 (s), 845 (m), 820 (m), 787 (w), 757 (w), 734 (s).

HRMS (ESI) calcd for $C_{25}H_{37}O_2Si^+$ $[M+H]^+$ 397.2557; found 397.2564.

$[\alpha]_D^{25.0}$ +80.5 (c = 2.75, $CHCl_3$).

(S)-2-((Tert-butyldiphenylsilyl)ethynyl)-5-methoxy-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-one (1c)



Following the general procedure and starting from substrate **2c** (0.070 g, 0.13 mmol) (S)-2-((Tert-butyldiphenylsilyl)ethynyl)-5-methoxy-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-one (**1c**) (0.064 g, 0.12 mmol, quantitative yield) was obtained as a yellow oil.

Chiral HPLC conditions: *ee*: 91%; Chiralcel IA 99:1 Hexane/*i*PrOH, 1 mL/min, 30 min t_{R1} = 5.6 min and t_{R2} = 8.0 min. λ = 280 cm^{-1}.

$\mathbf{R_F}$ 0.4 (pentane:ethylacetate 9:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.85 – 7.69 (m, 5H, Ar*H*), 7.43 – 7.30 (m, 6H, Ar*H*), 7.03 – 6.84 (dd, 2 H, *J* = 8.5, 2.0 Hz, Ar*H*), 4.93 (s, 1H, CCH_2), 4.90 (s, 1H, CCH_2), 3.89 (s, 3H, O CH_3), 3.49 (d, 1 H, *J* = 17.5 Hz, 1H, CH_2), 3.44 (d, 1 H, *J* = 17.5 Hz, 1H, CH_2), 2.91 (d, *J* = 14.1, 1H, CH_2CMe), 2.50 (d, *J* = 14.2 Hz, 1H, CH_2CMe), 1.86 (s, 3H, CCH_3), 1.05 (s, 9H, ^{t}*Bu*).

^{13}C NMR (101 MHz, $CDCl_3$) δ 200.5, 165.9, 154.8, 141.9, 135.6, 133.5, 133.4, 129.4, 127.6, 127.4, 127.0, 115.9, 115.2, 111.8, 109.7, 82.0, 55.7, 49.0, 45.3, 40.4, 27.1, 23.8, 18.7.[14]

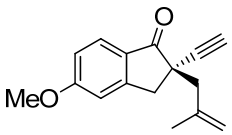
IR ν_{max} 3072 (w), 3052 (w), 2999 (w), 2957 (w), 2929 (w), 2898 (w), 2857 (w), 2162 (w), 1714 (m), 1676 (w), 1646 (w), 1599 (s), 1490 (w), 1470 (w), 1463 (w), 1447 (w), 1429 (m), 1362 (w), 1336 (w), 1293 (w), 1262 (s), 1148 (w), 1106 (m), 1090 (m), 1028 (w), 1011 (w), 1000 (w), 934 (w), 908 (s), 847 (w), 821 (m), 786 (w), 766 (w), 733 (s).

HRMS (ESI) calcd for $C_{32}H_{35}O_2Si^+$ $[M+H]^+$ 479.2401; found 479.2397.

$[\alpha]_D^{25.0}$ +72.9 (c = 3.49, $CHCl_3$).

(S)-2-Ethynyl-5-methoxy-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-one (1d)

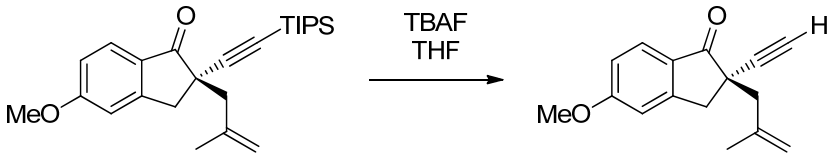
(14) Not all the carbon of the phenyl rings are resolved.



Following the general procedure and starting from .substrate **2d** (0.038 g, 0.13 mmol), 2-ethynyl-5-methoxy-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-one (**1d**) (0.013 g, 0.054 mmol, 41 % yield) was obtained as a yellow oil.

Chiral HPLC conditions: *ee*: 87%; Chiralcel IA 99:1 Hexane/*i*PrOH, 1 mL/min, 30 min.. t_{R1} = 20.7 min and t_{R2} = 25.3 min. λ = 254 cm^{-1}

From Product 1b:



1b **1d** <99% yield 95% *ee*

Following a reported procedure,[15] TBAF (2.54 mL, 2.54 mmol, 1 M in Et_2O, 2.0 equiv.) was added dropwise to a solution of compound **1b** (0.503 g, 1.27 mmol) in THF (16 mL) at room temperature. The reaction was monitored by TLC (8:2 pentane/ethyl acetate). The reaction is quenched with a saturated solution of NH_4Cl (5 mL) and extracted twice with Et_2O (2 x 10 mL). The organic layers were combined, washed with saturated $NaHCO_3$ (10 mL), brine (10 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The crude mixture was purified by flask chromatography (pentane/ethyl acetate 8:2) to afford compound **1d** (0.304 g, 1.27 mmol, <99% yield/95% *ee*) as a yellow oil.

In one pot from 2b:
Starting from substrate **2b** (4.38 g, 9.94 mmol) 2-ethynyl-5-methoxy-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-one (**1d**) (1.98 g, 8.24 mmol, 83% yield/95% *ee*) was obtained as a yellow oil. TBAF (19.8 mL, 19.8 mmol, 2.00 equiv.) was added directly to the reaction mixture after completion of the allylation step.

R_F 0.3 (pentane:ethylacetate 9:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 8.5 Hz, 1H, Ar*H*), 6.92 (ddd, *J* = 8.5, 1.9, 1.0 Hz, 1H, Ar*H*), 6.85 (dt, *J* = 2.1, 1.0 Hz, 1H, Ar*H*), 4.88 (s, 1H, CMeCH_2), 4.81 (s, 1H, CMeCH_2), 3.88 (s, 3H, O*Me*), 3.38 (d, 1 H, *J* = 17.5 Hz, 1H, CH_2), 3.32 (d, 1 H, *J* = 17.5 Hz, 1H, CH_2), 2.72 (dd, *J* = 14.2, 1.1 Hz, 1H, CH_2CMe), 2.36 (dd, *J* = 14.1, 1.1 Hz, 1H, CH_2CMe), 2.22 (s, 1H, CC*H*), 1.79 (dd, *J* = 1.5, 0.8 Hz, 3H, C*Me*).

^{13}C NMR (101 MHz, $CDCl_3$) δ 201.1, 166.0, 154.9, 141.8, 127.2, 126.9, 116.0, 115.2, 109.6, 85.6, 70.5, 55.7, 47.5, 45.1, 39.8, 23.7.

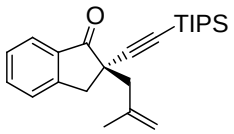
[15] X. Wang, T. Yang, X. Cheng, Q. Shen, *Angew. Chem. Int. Ed.* **2013**, *52*, 12860-12864.

IR ν_{max} 3302 (w), 2945 (w), 2944 (w), 2843 (w), 2253 (w), 1710 (m), 1600 (m), 1264 (m), 907 (s), 730 (s).

HRMS (ESI) calcd for $C_{16}H_{17}O_2^+$ $[M+H]^+$ 241.1223; found 241.1222.

$[\alpha]_D^{25.0}$ +104.1 (c = 2.17, $CHCl_3$).

(S)-2-(2-Methylallyl)-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-inden-1-one (1e)



Following the general procedure and starting from substrate **2e** (51 mg, 0.12 mmol) 2-(2-methylallyl)-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-inden-1-one (**1e**) (0.045 g, 0.13 mmol, quantitative yield) was obtained as a yellow oil.

Chiral HPLC conditions: *ee*: 94%; Chiralcel IF 99.9:0.1 Hexane/*i*PrOH, 1 mL/min, 20 min. t_{R1} = 12.8 min and t_{R2} = 14.7 min. λ = 230 cm^{-1}.

R_F 0.3 (dichloromethane:pentane 5:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.80 (d, *J* = 7.6 Hz, 1H, Ar*H*), 7.62 (td, *J* = 7.5, 1.2 Hz, 1H, Ar*H*), 7.46 – 7.37 (m, 2H, Ar*H*), 4.87 (s, 1H, CMeCH_2), 4.80 (s, 1H, CMeCH_2), 3.42 (d, 1 H, *J* = 17.4 Hz, 1H, CH_2), 3.37 (d, 1 H, *J* = 17.5 Hz, 1H, CH_2), 2.74 (dd, *J* = 14.1, 1.1 Hz, 1H, CH_2CMe), 2.35 (dd, *J* = 14.1, 1.1 Hz, 1H, CH_2CMe), 1.83 (s, 3H, C*Me*CH_2), 1.01 (s, 21H, *TIPS*).

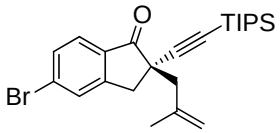
^{13}C NMR (101 MHz, $CDCl_3$) δ 202.8, 151.8, 142.0, 135.2, 134.4, 127.7, 126.5, 125.2, 115.0, 109.0, 83.1, 48.6, 45.1, 40.6, 23.7, 18.6, 11.2.

IR ν_{max} 2943 (s), 2892 (w), 2865 (s), 2161 (w), 1923 (w), 1728 (s), 1686 (w), 1610 (w), 1464 (m), 1436 (w), 1297 (w), 1262 (w), 1017 (w), 997 (w), 928 (w), 886 (m), 784 (w), 737 (s).

HRMS (ESI) calcd for $C_{24}H_{35}OSi^+$ $[M+H]^+$ 367.2452; found 367.2452.

$[\alpha]_D^{25.0}$ +20.0 (c = 2.58, $CHCl_3$).

(S)-5-Bromo-2-(2-methylallyl)-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-inden-1-one (1f)



Following the general procedure and starting from substrate **2f** (60 mg, 0.12 mmol) 5-bromo-2-(2-methylallyl)-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-inden-1-one (**1f**) (0.041 g, 0.092 mmol, 77 % yield) was obtained as a yellow oil.

Chiral HPLC conditions: *ee*: 85%; Chiralcel IF 99:1 Hexane/*i*PrOH, 1 mL/min, 15 min t_{R1} = 12.8 min and t_{R2} = 13.8 min. λ = 254 cm^{-1}.

R_F 0.43 (dichloromethane:pentane 1:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.50 (d, *J* = 8.2 Hz, 1H, Ar*H*), 7.46 (d, *J* = 1.6 Hz, 1H, Ar*H*), 7.38 (dd, *J* = 8.2, 1.6 Hz, 1H, Ar*H*), 4.74 – 4.69 (m, 1H, CCH_2), 4.63 (dd, *J* = 2.2, 1.2 Hz, 1H, CCH_2), 3.39 (d, *J* = 17.4 Hz, 1H, CH_2), 3.34 (d, *J* = 17.4 Hz, 1H, CH_2), 2.57 (dd, *J* = 14.1, 1.1 Hz, 1H, CH_2CMe), 2.20 (dd, *J* = 14.1, 1.1 Hz, 1H, CH_2CMe), 1.69 – 1.62 (m, 3H, CCH_3), 0.85 (s, 21H, C*TIPS*).

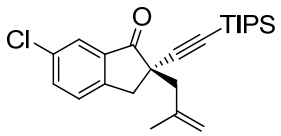
^{13}C NMR (101 MHz, $CDCl_3$) δ. 201.5, 153.4, 141.7, 133.2, 131.4, 130.6, 129.8, 126.3, 115.3, 108.4, 83.6, 48.6, 45.1, 40.2, 23.7, 18.6, 11.2.

IR ν_{max} 2943 (m), 2943 (m), 2891 (w), 2891 (w), 2865 (m), 2865 (m), 2162 (w), 1730 (s), 1597 (s), 1579 (w), 1579 (w), 1464 (w), 1464 (w), 1432 (w), 1415 (w), 1313 (w), 1313 (w), 1261 (w), 1261 (w), 1205 (w), 1205 (w), 1061 (w), 1061 (w), 1017 (w), 997 (w), 997 (w), 885 (m), 885 (m), 863 (w), 817 (w), 817 (w), 779 (w), 745 (w), 733 (w).

HRMS (ESI) calcd for $C_{24}{}^{79}BrH_{34}OSi^+$ $[M+H]^+$ 445.1557; found 445.1570.

$[\alpha]_D^{25.0}$ +68.8 (c = 2.63, $CHCl_3$).

(S)-6-Chloro-2-(2-methylallyl)-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-inden-1-one (6g)



Following the general procedure and starting from substrate **2g** (55 mg, 0.12 mmol) (S)-6-chloro-2-(2-methylallyl)-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-inden-1-one (**1g**) (0.037 g, 0.092 mmol, 77 % yield) was obtained as a yellow oil using 5 mol% Pd and 6.5 mol% of ligand.

Chiral HPLC conditions: *ee*: 90%; Chiralcel IF 99.9:0.1 Hexane/*i*PrOH, 1 mL/min, 20 min t_{R1} = 11.6 min and t_{R2} = 12.4 min. λ = 254 cm^{-1}.

R_F 0.4 (dichloromethane:pentane 1:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.69 (d, *J* = 2.0 Hz, 1H, Ar*H*), 7.50 (dd, *J* = 8.1, 2.1 Hz, 1H, Ar*H*), 7.31 (dd, *J* = 8.1, 0.9 Hz, 1H, Ar*H*), 4.80 (t, *J* = 1.7 Hz, 1H, CCH_2), 4.72 (dd, *J* = 2.2, 1.1 Hz, 1H, CMeCH_2), 3.37 (d, 1 H, *J* = 17.4 Hz, 1H, CH_2), 3.32 (d, 1 H, *J* = 17.4 Hz, 1H, CH_2), 2.65 (dd, *J* = 14.1, 1.1 Hz, 1H, CH_2CMe), 2.29 (dd, *J* = 14.0, 1.1 Hz, 1H, CH_2CMe), 1.74 (t, *J* = 1.1 Hz, 3H, CCH_3), 0.94 (m, 21H, C*TIPS*).

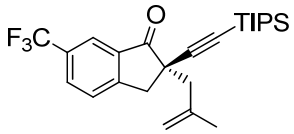
^{13}C NMR (101 MHz, $CDCl_3$) δ. 201.5, 149.8, 141.7, 135.9, 135.3, 134.1, 127.7, 124.9, 115.3, 108.3, 83.6, 49.2, 45.1, 40.2, 23.7, 18.6, 11.2.

IR ν_{max} 2943 (s), 2892 (w), 2865 (s), 2162 (w), 1730 (s), 1466 (m), 1250 (m), 1183 (m), 885 (s), 819 (m).

HRMS (ESI) calcd for $C_{24}ClH_{34}OSi^+$ $[M+H]^+$ 401.2062; found 401.2054.

$[\alpha]_D^{25.0}$ -1.98 (c = 2.82, $CHCl_3$).

(R)-2-(2-Methylallyl)-6-(trifluoromethyl)-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-inden-1-one (1h)



Following the general procedure and starting from substrate **2h** (63 mg, 0.13 mmol), (S)-2-(2-Methylallyl)-6-(trifluoromethyl)-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-inden-1-one (**1h**) (42 mg, 0.097 mmol, 79% yield) was obtained as a yellow oil.[16]

Chiral HPLC conditions: *ee*: 73%; Chiralcel IC 99.9:0.1 Hexane/*i*PrOH, 1 mL/min, 20 min t_{R1} = 5.4 min and t_{R2} = 5.9 min, λ = 280 cm^{-1}.

R_F 0.25 (dichloromethane:pentane 1:5).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.07 (s, 1H, Ar*H*), 7.86 (dd, *J* = 8.0, 1.9 Hz, 1H, Ar*H*), 7.58 (d, *J* = 8.0 Hz, 1H, Ar*H*), 4.89 (s, 1H, CMeCH_2), 4.80 (s, 1H, CMeCH_2), 3.49 (d, 1 H, *J* = 17.8 Hz, 1H, CH_2), 3.42 (d, 1 H, *J* = 17.9 Hz, 1H, CH_2), 2.75 (d, *J* = 14.1 Hz, 1H, CH_2CMe), 2.38 (d, *J* = 14.1 Hz, 1H, CH_2CMe), 1.83 (s, 3H, CCH_3), 1.01 (m, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 201.5, 155.0, 141.6, 134.9, 131.7 (q, *J* = 3.5 Hz), 130.69 (q, *J* = 33.0 Hz), 127.3, 123.7 (q, *J* = 273.0 Hz), 122.4 (q, *J* = 4.2 Hz), 115.4, 108.0, 84.0, 48.93, 45.0, 40.6, 23.7, 18.6, 11.2.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.5.

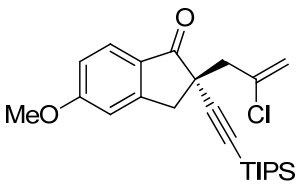
IR ν_{max} 2944 (w), 2893 (w), 2866 (w), 2163 (w), 1733 (m), 1626 (w), 1331 (s), 1251 (m), 1200 (w), 1183 (m), 1170 (m), 1134 (s), 909 (m), 885 (m), 825 (w), 735 (s).

HRMS (ESI) calcd for $C_{25}F_3H_{34}OSi^+$ $[M+H]^+$ 435.2326; found 435.2330.

$[\alpha]_D^{25.0}$ +6.28 (c = 3.42, $CHCl_3$).

(R)-2-(2-Chloroallyl)-5-methoxy-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-inden-1-one (1i)

16 The other enantiomer of the ligand (S enantiomer) was used due to HPLC separation issues



Following the general procedure and starting from substrate **2i** (57 mg, 0.12 mmol) (S)-2-(2-chloroallyl)-5-methoxy-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-inden-1-one (**1i**) (0.041 g, 0.098 mmol, 80 % yield) was obtained as a yellow oil.

Chiral HPLC conditions: *ee*: 90%; Chiralcel IA 95:5 Hexane/*i*PrOH, 1 mL/min, 20 min t_{R1} = 6.0 min and t_{R2} = 6.7 min. λ = 280 cm^{-1}.

R_F 0.45 (pentane:ethylacetate 9:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.58 (d, *J* = 8.5 Hz, 1H, Ar*H*), 6.78 (dd, *J* = 8.6, 2.2 Hz, 1H, Ar*H*), 6.73 (d, *J* = 2.2 Hz, 1H, Ar*H*), 5.24 (s, 1H, CCH_2), 5.17 (s, 1H, CCH_2), 3.74 (s, 3H, OCH_3), 3.44 (d, *J* = 17.4 Hz, 1H, CH_2), 3.28 (d, *J* = 17.4 Hz, 1H, CH_2), 2.92 (d, *J* = 14.8 Hz, 1H, CH_2CMe), 2.50 (dd, *J* = 14.8, 1.0 Hz, 1H, CH_2CMe), 0.85 (m, 21H, C*TIPS*).

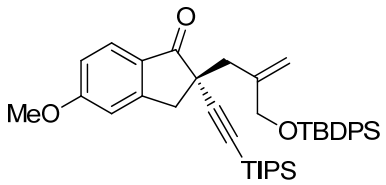
^{13}C NMR (101 MHz, $CDCl_3$) δ 199.8, 165.9, 155.0, 137.8, 127.3, 126.9, 116.7, 115.9, 109.6, 107.6, 83.6, 55.7, 49.2, 45.8, 41.1, 18.6, 11.2.

IR ν_{max} 2944 (m), 2893 (w), 2865 (m), 2163 (w), 1716 (s), 1601 (s), 1464 (m), 1297 (m), 1026 (m), 997 (w), 884 (s), 869 (m), 846 (m), 771 (m).

HRMS (ESI) calcd for $C_{24}H_{33}ClNaO_2Si^+$ $[M+Na]^+$ 439.1831; found 439.1835.

$[\alpha]_D^{25.0}$ +116.9 (c = 3.058, $CHCl_3$).

(R)-2-(2-(((Tert-butyldiphenylsilyl)oxy)methyl)allyl)-5-methoxy-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-inden-1-one (1j)



Following the general procedure and starting from substrate **2j** (78 mg, 0.11 mmol), 2-(2-(((tert-butyldiphenylsilyl)oxy)methyl)allyl)-5-methoxy-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-inden-1-one (**1j**) (0.062 g, 0.095 mmol, 85 % yield) was obtained as a yellow oil using 5 mol% of Pd and 6.5 mol% of ligand.

Chiral HPLC conditions: *ee*: 94%; Chiralcel IF 99:1 Hexane/*i*PrOH, 1 mL/min, 20 min t_{R1} = 7.9 min and t_{R2} = 9.3 min. λ = 254 cm^{-1}.

R_F 0.53 (pentane:ethylacetate 9:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.71 – 7.60 (m, 5H, *Ph*), 7.45 – 7.39 (m, 2H, Ar*H*), 7.35 (tdd, *J* = 6.8, 3.7, 1.6 Hz, 4H, *Ph*), 6.90 (dd, *J* = 8.5, 2.4 Hz, 1H, Ar*H*), 6.79 (d, *J* = 2.2 Hz, 1H, Ar*H*), 5.37 (s, 1H, CCH_2), 5.10 (s, 1H, CCH_2), 4.28 (d, 1 H, *J* = 14.6 Hz, 1H, CH_2OTIPS), 4.10 (d, 1 H, *J* = 14.6 Hz, 1H, CH_2OTIPS), 3.88 (s, 3H, O*Me*), 3.31 (d, 1 H, *J* = 17.3 Hz, 1H, CH_2), 3.21 (d, 1 H, *J* = 17.3 Hz, 1H, CH_2), 2.70 (d, *J* = 14.6 Hz, 1H, CH_2CH$_2$), 2.35 (d, *J* = 14.6 Hz, 1H, CH_2CH$_2$), 1.03 (d, *J* = 2.5 Hz, 9H, *tBu*), 0.93 (m, 21H, *TIPS*).

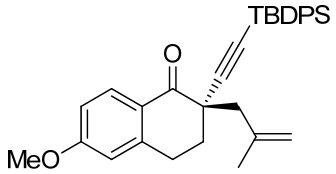
^{13}C NMR (101 MHz, $CDCl_3$) δ 200.9, 165.7, 154.8, 144.0, 135.5, 133.6, 133.5, 129.6, 127.6, 127.4, 126.8, 115.7, 113.3, 109.6, 109.2, 82.8, 66.7, 55.7, 48.7, 40.6, 40.5, 26.8, 19.3, 18.6, 11.1.[13]

IR ν_{max} 2956 (m), 2942 (m), 2892 (w), 2863 (m), 2161 (w), 1718 (s), 1601 (s), 1464 (w), 1293 (w), 1263 (s), 1112 (s), 909 (w), 826 (w), 741 (w), 705 (s).

HRMS (ESI) calcd for $C_{41}H_{54}NaO_3Si_2^+$ $[M+Na]^+$ 673.3504; found 673.3503.

$[\alpha]_D^{25.0}$ +44.3 (c = 1.17, $CHCl_3$).

(R)-2-((Tert-butyldiphenylsilyl)ethynyl)-6-methoxy-2-(2-methylallyl)-3,4-dihydronaphthalen-1(2H)-one (1k)



Following the general procedure and starting from substrate **2k** (69 mg, 0.13 mmol) 2-((tert-butyldiphenylsilyl)ethynyl)-6-methoxy-2-(2-methylallyl)-3,4-dihydronaphthalen-1(2H)-one (**1k**) (0.062 g, 0.13 mmol, 98 % yield) was obtained as a yellow oil.

Chiral HPLC conditions: *ee*: 97%; Chiralcel IF 99:1 Hexane/*i*PrOH, 1 mL/min, 20 min t_{R1} = 9.8 min; t_{R2} = 11.1 min. λ = 280 cm^{-1}.

R_F 0.52 (pentane:ethylacetate 9:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (d, *J* = 8.7 Hz, 1H, Ar*H*), 7.63 (ddt, *J* = 9.9, 6.7, 1.6 Hz, 4H, *Ph*), 7.39 – 7.31 (m, 2H, *Ph*), 7.27 (ddd, *J* = 8.4, 6.6, 5.0 Hz, 4H, *Ph*), 6.88 (dd, *J* = 8.8, 2.6 Hz, 1H, Ar*H*), 6.71 (d, *J* = 2.5 Hz, 1H, Ar*H*), 4.93 (s, 1H, CCH_2), 4.91 – 4.82 (m, 1H, CCH_2), 3.87 (s, 3H, OCH_3), 3.47 (td, *J* = 12.3, 6.1 Hz, 1H, CH_2), 2.99 (d, *J* = 13.8 Hz, 1H, CH_2CMe), 2.96 – 2.87 (m, 1H, CH_2), 2.63 (d, *J* = 13.8 Hz, 1H, CH_2CMe), 2.45 – 2.30 (m, 1H, CH_2), 2.11 – 1.96 (m, 1H, CH_2), 1.92 (s, 3H, CH_3), 0.96 (s, 9H, ^{t}*Bu*).

^{13}C NMR (101 MHz, $CDCl_3$) δ. 192.7, 163.7, 146.0, 142.0, 135.5, 135.4, 133.4, 133.3, 131.1, 129.4, 127.6, 127.6, 124.8, 115.4, 113.5, 112.3, 109.9, 85.2, 55.5, 46.2, 43.5, 32.9, 27.1, 26.9, 24.3, 18.6.[13]

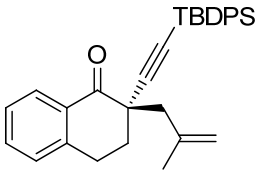
IR ν_{max} 3072 (w), 3050 (w), 3013 (w), 3000 (w), 2956 (w), 2948 (w), 2931 (m), 2894 (w), 2858 (w), 2160 (w), 1713 (w), 1684 (m), 1645 (w), 1600 (s), 1573 (w), 1494 (w), 1463 (w), 1446 (w),

1429 (m), 1360 (w), 1346 (w), 1269 (s), 1255 (s), 1221 (m), 1159 (w), 1158 (w), 1129 (w), 1109 (s), 1031 (w), 1009 (w), 999 (w), 970 (w), 937 (w), 908 (m), 851 (w), 821 (w), 806 (w), 740 (m).

HRMS (ESI) calcd for $C_{33}H_{37}O_2Si^+$ $[M+H]^+$ 493.2557; found 493.2551.

$[\alpha]_D^{25.0}$ -11.2 (c = 2.19, $CHCl_3$).

(R)-2-((Tert-butyldiphenylsilyl)ethynyl)-2-(2-methylallyl)-3,4-dihydronaphthalen-1(2H)-one (1l)



Following the general procedure and starting from substrate **2l** (62 mg, 0.12 mmol) 2-((tert-butyldiphenylsilyl)ethynyl)-2-(2-methylallyl)-3,4-dihydronaphthalen-1(2H)-one (**1l**) (0.049 g, 0.11 mmol, 86 % yield) was obtained as a yellow oil.

Chiral HPLC conditions: *ee*: 96%; Chiralcel IF 99.9:0.1 Hexane/*i*PrOH, 1 mL/min, 20 min t_{R1} = 15.4 min; t_{R2} = 18.7 min. λ = 254 cm^{-1}.

$\mathbf{R_F}$ 0.6 (pentane:ethylacetate 9:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.00 (dd, *J* = 8.0, 1.4 Hz, 1H, Ar*H*), 7.49 (ddd, *J* = 8.2, 6.7, 1.5 Hz, 4H, *Ph*), 7.40 (td, *J* = 7.5, 1.5 Hz, 1H, Ar*H*), 7.29 - 7.23 (m, 3H, *Ph*), 7.19 – 7.10 (d, 5H, *Ph*), 4.83 (s, 1H, CCH_2), 4.76 (s, 1H, CCH_2), 3.38 (td, *J* = 12.2, 6.0 Hz, 1H, CH_2), 2.92 (m, 1H, CH_2CMe), 2.89 (dt, *J* = 17.2, 6.9 Hz, 1H, CH_2), 2.52 (d, *J* = 13.8 Hz, 1H, CH_2CMe), 2.30 (ddd, *J* = 13.5, 4.7, 3.3 Hz, 1H, CH_2), 1.93 (ddd, *J* = 13.4, 12.0, 4.5 Hz, 1H, CH_2), 1.81 (s, 3H, CCH_2), 0.83 (s, 9H, ^{t}*Bu*).

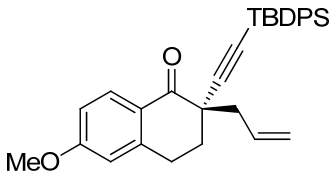
^{13}C NMR (101 MHz, $CDCl_3$) δ. 193.9, 143.5, 141.9, 135.4, 135.4, 133.4, 133.4, 133.2, 131.3, 129.4, 128.7, 128.7, 127.6, 126.8, 115.5, 109.2, 85.8, 46.5, 43.3, 32.8, 26.9, 26.6, 24.3, 18.6.[13]

IR ν_{max} 3071 (w), 3051 (w), 2956 (m), 2930 (m), 2893 (w), 2858 (w), 2161 (w), 1694 (s), 1647 (w), 1600 (w), 1487 (w), 1471 (w), 1455 (m), 1429 (m), 1390 (w), 1378 (w), 1361 (w), 1336 (w), 1292 (w), 1253 (w), 1229 (m), 1195 (w), 1158 (w), 1110 (s), 1031 (w), 1009 (w), 1000 (w), 970 (w), 933 (w), 907 (m), 821 (m), 778 (w), 742 (s).

HRMS (ESI) calcd for $C_{32}H_{35}OSi^+$ $[M+H]^+$ 463.2452; found 463.2446.

$[\alpha]_D^{25.0}$ -68.2 (c = 2.78, $CHCl_3$).

(R)-2-Allyl-2-((tert-butyldiphenylsilyl)ethynyl)-6-methoxy-3,4-dihydronaphthalen-1(2H)-one (1m)



Following the general procedure and starting from substrate **2m** (64 mg, 0.12 mmol) 2-allyl-2-((tert-butyldiphenylsilyl)ethynyl)-6-methoxy-3,4-dihydronaphthalen-1(2H)-one (**1m**) (0.056 g, 0.12 mmol, 95 % yield) was obtained as a yellow oil.

Chiral HPLC conditions: *ee* 90%; Chiralcel IF 95:5 Hexane/*i*PrOH, 1 mL/min, 10 min t_{R1} = 10.1 min; t_{R2} = 11.2 min. λ = 280 cm^{-1}.

R_F 0.47 (pentane:ethylacetate 9:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.08 (d, *J* = 8.8 Hz, 1H, Ar*H*), 7.68 – 7.64 (m, 5H, *Ph*), 7.44 – 7.21 (m, 5H, *Ph*), 6.87 (dd, *J* = 8.8, 2.5 Hz, 1H, Ar*H*), 6.71 (d, *J* = 2.6 Hz, 1H, Ar*H*), 6.13 – 5.95 (m, 1H, C*H*CH_2), 5.27 – 5.14 (m, 2H, CCH_2), 3.87 (s, 3H, OCH_3), 3.46 (ddd, *J* = 16.8, 11.9, 4.6 Hz, 1H, CH_2), 3.02 (dd, *J* = 13.9, 6.6 Hz, 1 H, CH_2CH), 2.95 (dt, 1 H, *J* = 17.1, 3.9 Hz, CH_2), 2.57 (dd, *J* = 13.9, 8.0 Hz, 1H, CH_2CH), 2.38 (dt, *J* = 13.3, 4.1 Hz, 1 H, CH_2), 2.16 – 2.00 (m, 1H, CH_2), 0.98 (s, 9H, ^{t}*Bu*).

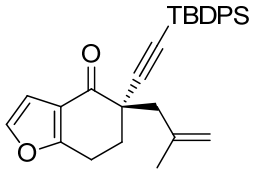
^{13}C NMR (101 MHz, $CDCl_3$) δ. 192.7, 163.7, 146.1, 135.5, 135.5, 134.0, 133.3, 131.0, 129.4, 127.6, 127.6, 124.9, 118.7, 113.5, 112.4, 109.2, 84.8, 55.5, 47.0, 40.5, 33.3, 27.0, 26.9, 18.6.[13]

IR ν_{max} 3071 (w), 3050 (w), 3014 (w), 3009 (w), 3001 (w), 2956 (w), 2931 (w), 2894 (w), 2857 (w), 2161 (w), 1683 (m), 1600 (s), 1494 (w), 1470 (w), 1464 (w), 1429 (m), 1346 (w), 1269 (s), 1253 (s), 1221 (m), 1109 (m), 1031 (w), 998 (w), 910 (m), 820 (m), 738 (s).

HRMS (ESI) calcd for $C_{32}H_{35}O_2Si^+$ $[M+H]^+$ 479.2401; found 479.2408**.**

$[\alpha]_D^{25.0}$ -21.9 (c = 2.69, $CHCl_3$).

(R)-5-((Tert-butyldiphenylsilyl)ethynyl)-5-(2-methylallyl)-6,7-dihydrobenzofuran-4(5H)-one (1n)



Following the general procedure and starting from substrate **2n** (68 mg, 0.14 mmol) (S)-5-((tert-butyldiphenylsilyl)ethynyl)-5-(2-methylallyl)-6,7-dihydrobenzofuran-4(5H)-one (**1n**) (0.051 g, 0.11 mmol, 82 % yield) was obtained as a yellow oil.

Chiral HPLC conditions: *ee*: 90%; Chiralcel IF 99:1 Hexane/*i*PrOH, 1 mL/min, 20 min. t_{R1} = 7.2 min; t_{R2} = 7.9 min. λ = 254 cm^{-1}.

R_F 0.51 (pentane:ethylacetate 9:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.66 (ddt, *J* = 9.4, 6.8, 1.6 Hz, 4H, *Ph*), 7.39 – 7.28 (m, 7H, *Ph*+Ar*H*), 6.75 (d, *J* = 2.1 Hz, 1H, Ar*H*), 4.93 (s, 1H, CCH_2), 4.85 (s, 1H, CCH_2), 3.23 (ddd, *J* = 16.7, 11.0, 5.1 Hz, 1H, CH_2), 3.02 – 2.84 (m, 1H, CH_2), 2.93 (d, *J* = 14.0 Hz, 1H, CH_2CMe), 2.63 (d, *J* = 13.8 Hz, 1H, CH_2CMe), 2.42 (ddd, *J* = 13.5, 5.1, 3.1 Hz, 1H, CH_2), 2.10 (ddd, *J* = 13.5, 11.0, 5.1 Hz, 1H, CH_2), 1.90 (s, 3H, CCH_3), 0.98 (s, 9H, ^{t}*Bu*).

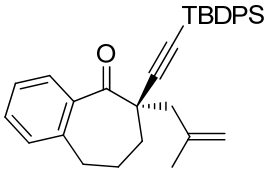
^{13}C NMR (101 MHz, Chloroform-*d*) δ. 189.8, 165.8, 143.1, 141.9, 135.5, 135.4, 133.3, 133.2, 129.4, 127.7, 119.4, 115.6, 109.4, 107.6, 84.9, 46.4, 42.8, 33.0, 26.9, 24.2, 21.7, 18.6.[13]

IR ν_{max} 3072 (w), 2954 (w), 2930 (m), 2893 (w), 2858 (w), 2161 (w), 1692 (s), 1601 (w), 1471 (w), 1449 (w), 1429 (m), 1110 (s), 1026 (w), 1009 (w), 1000 (w), 899 (w), 878 (w), 821 (w), 808 (w), 739 (s).

HRMS (ESI) calcd for $C_{30}H_{33}O_2Si^+$ $[M+H]^+$ 453.2244; found 453.2242.

$[\alpha]_D^{25.0}$ -58.2 (c = 1.34, $CHCl_3$).

(S)-6-((Tert-butyldiphenylsilyl)ethynyl)-6-(2-methylallyl)-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-one (1o)



Following the general procedure and starting from substrate **2o** (65 mg, 0.13 mmol), (S)-6-((tert-butyldiphenylsilyl)ethynyl)-6-(2-methylallyl)-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-one (**1o**) (0.054 g, 0.11 mmol, 91 % yield) was obtained as a yellow oil.[14]

R_F 0.73 (dichloromethane:pentane 1:1).

Chiral HPLC conditions: *ee*: 90%; Chiralcel IF 99:1 Hexane/*i*PrOH, 1 mL/min, 20 min t_{R1} = 6.4 min and t_{R2} = 6.8 min, λ = 254 cm^{-1}.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62 (ddt, *J* = 8.4, 6.6, 1.6 Hz, 4H, *Ph*), 7.45 – 7.23 (m, 9H, *Ph* + Ar*H*), 7.17 (d, *J* = 7.5 Hz, 1H, Ar*H*), 4.88 (s, 1H, CMeCH_2), 4.85 (s, 1H, CMeCH_2), 3.20 (ddd, *J* = 14.3, 9.7, 3.8 Hz, 1H, CH_2), 2.93 (d, *J* = 14.0 Hz, 1H, CH_2CMe), 2.82 (ddd, *J* = 15.1, 7.4, 3.7 Hz, 1H, CH_2), 2.63 (d, *J* = 13.9 Hz, 1H, CH_2CMe), 2.33 (tdd, *J* = 9.9, 4.4, 2.5 Hz, 1H, CH_2), 2.17 (dt, *J* = 13.8, 5.1 Hz, 1H, CH_2), 1.98 – 1.86 (m, 1H, CH_2), 1.85 – 1.78 (m, 1H, CH_2), 1.81 (d, *J* = 1.3 Hz, 3H, CCH_3), 0.95 (s, 9H, ^{t}*Bu*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ. 205.7, 141.7, 140.5, 138.3, 135.5, 135.5, 133.4, 133.4, 130.9, 129.3, 129.3, 129.0, 127.9, 127.6, 126.5, 115.4, 110.4, 86.1, 51.7, 46.5, 37.1, 33.7, 27.0, 24.5, 24.3, 18.5.[13]

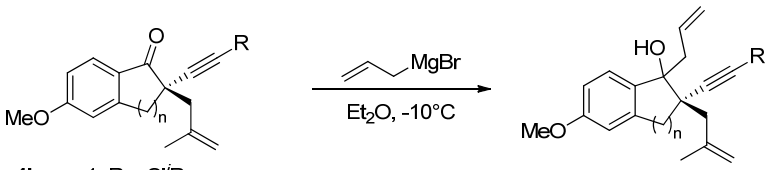
IR ν_{max} 3071 (w), 3051 (w), 2931 (m), 2894 (w), 2893 (w), 2858 (w), 2166 (w), 1693 (m), 1599 (w), 1486 (w), 1471 (w), 1461 (w), 1448 (w), 1429 (m), 1362 (w), 1266 (w), 1250 (w), 1192 (w), 1110 (m), 1032 (w), 1009 (w), 1000 (w), 958 (w), 942 (w), 897 (w), 876 (w), 821 (w), 773 (w), 763 (w), 739 (s).

HRMS (ESI) calcd for $C_{33}H_{37}OSi^+$ $[M+H]^+$ 477.2608; found 477.2603.

$[\alpha]_D^{25.0}$ +39.1 (c = 3.00, $CHCl_3$).

6. Transformation of α-allyl alkynyl ketons.

6.1 Grignard addition to compound 6a and 6b

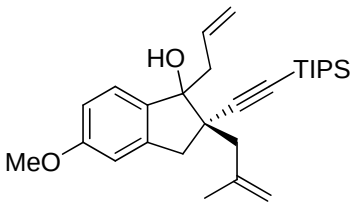


1b, n = 1, R = Si^{i}Pr$_3$
1k, n = 2, R = SiPh$_2$^{t}Bu

7b, quant. yield, 5:1 d.r.
7k, 98% yield, 5:1 d.r

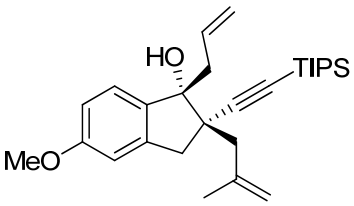
Following a reported procedure,[15] allylmagnesium bromide (2.0 equiv.) was added at -10 °C to a solution of compound **1** in Et_2O (0.05 M). The reaction is monitored by TLC (pentane/ethylacetate 8:2). Upon completion the reaction was quenched with water (5 mL). The organic layer is separated, extracted with Et_2O (3 x 20 mL), washed with $NaHCO_3$ (20 mL), brine (20 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude mixture was purified by flask chromatography (pentane/ethyl acetate 98:2) to afford the two diasteroisomers.

(2S)-1-allyl-5-methoxy-2-(2-methylallyl)-2-((triisopropylsilyl)ethynyl)-2,3-dihydro-1H-inden-1-ol (7b)



Following the general procedure allylmagnesium bromide (160 µL, 0.252 mmol, 2.0 equiv.) was added at -10 °C to a solution of compound **1b** (50.0 mg, 0.126 mmol) in Et_2O (2.5 mL). The reaction is monitored by TLC (pentane/ethylacetate 8:2). After work up the crude mixture was purified by flask chromatography (pentane/ethyl acetate 98:2) to afford the major diasteroisomer (0.045 g, 0.10 mmol, 81 % yield) and the minor diastereoisomer (0.010 g, 0.023 mmol, 18 % yield) as colorless oils. The relative stereochemistry was determined via ROESY NMR analysis (see spectra section).

*Major diastereoisomer (**7b**)*



R_F = 0.33 (pentane:ethylacetate 9:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.18 (d, *J* = 8.3 Hz, 1H, Ar*H*), 6.74 (dd, *J* = 8.3, 2.4 Hz, 1H, Ar*H*), 6.69 (d, *J* = 2.4 Hz, 1H, Ar*H*), 6.00 (dddd, *J* = 17.1, 10.2, 7.7, 6.9 Hz, 1H, C*H*CH$_2$),

5.20 – 5.09 (m, 2H, CHCH_2), 4.85 (s, 1H, CMeCH_2), 4.70 – 4.63 (s, 1H, CMeCH_2), 3.78 (s, 3H, O*Me*), 3.17 (d, *J* = 15.6 Hz, 1H, CH_2), 2.98 (dd, *J* = 13.9, 7.8 Hz, 1H, CH_2CH), 2.96 (d, *J* = 15.6 Hz, 1H, CH_2), 2.61 (dd, 1 H, *J* = 14.0, 7.0 Hz, 1H, CH_2CH), 2.47 (d, 1 H, *J* = 13.5 Hz, 1H, CH_2CMe), 2.19 (dd, *J* = 13.4, 0.8 Hz, 1H, CH_2CMe), 1.97 – 1.91 (m, 3H, C*Me*CH_2), 1.04 (m, 21H, *TIPS*).

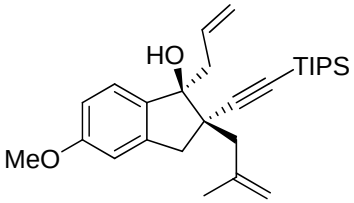
^{13}C NMR (101 MHz, $CDCl_3$) δ 159.9, 143.6, 141.1, 137.6, 134.0, 124.9, 119.1, 114.5, 112.1, 110.2, 85.1, 84.9, 55.4, 51.6, 43.0, 41.8, 41.6, 24.4, 18.6, 11.3.

IR ν_{max} 3019 (w), 2945 (w), 2858 (w), 2154 (w), 1216 (m), 754 (s).

HRMS (ESI) calcd for $C_{28}H_{42}NaO_2Si^+$ $[M+Na]^+$ 461.2846; found 461.2846.

$[\alpha]_D^{25.0}$ -42.6 (c = 2.33, $CHCl_3$).

*Minor diastereoisomer (**7b**)*



R_F = 0.55 (pentane:ethylacetate 9:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.22 (d, *J* = 8.2 Hz, 1H, Ar*H*), 6.73 (d, *J* = 8.2 Hz, 1H, Ar*H*), 6.71 (s, 1H, Ar*H*), 5.93 (dddd, *J* = 15.4, 11.7, 8.0, 6.3 Hz, 1H, C*H*CH_2), 5.11 (t, *J* = 1.1 Hz, 1H, CHCH_2), 5.08 (ddd, *J* = 5.5, 2.7, 1.4 Hz, 1H, CHCH_2), 4.89 (dq, *J* = 2.8, 1.6 Hz, 1H, CMeCH_2), 4.79 (dd, *J* = 2.3, 1.2 Hz, 1H, CMeCH_2), 3.78 (s, 3H, O*Me*), 3.20 – 3.10 (m, 1H, CH_2CH), 2.96 (d, *J* = 15.2 Hz, 1H, CH_2CH), 2.61 – 2.40 (m, 3H, CH_2CMe + CH_2), 2.25 (d, *J* = 13.1 Hz, 1H, CH_2CMe), 1.98 – 1.91 (m, 3H, C*Me*CH_2), 0.93 (s, 21H, *TIPS*).

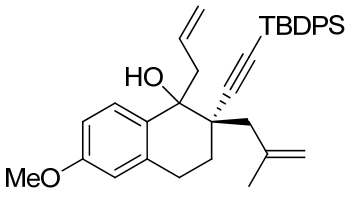
^{13}C NMR (101 MHz, $CDCl_3$) δ 159.7, 142.8, 141.7, 138.0, 133.6, 125.2, 118.3, 114.5, 112.1, 111.6, 110.2, 83.6, 55. 5, 54.8, 42.2, 40.9, 39.7, 34.2, 24.2, 18.5, 11.1.

IR ν_{max} 3532 (w), 2942 (s), 2865 (s), 2158 (w), 1492 (m), 1464 (m), 1259 (s), 1147 (m), 1065 (m), 995 (m), 916 (m), 885 (m), 760 (m).

HRMS (ESI) calcd for $C_{28}H_{42}NaO_2Si^+$ $[M+Na]^+$ 461.2846; found 461.2844.

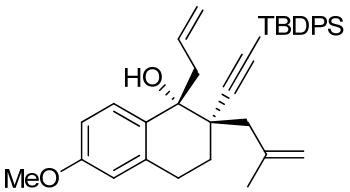
$[\alpha]_D^{25.0}$ -28.8 (c = 0.67, $CHCl_3$).

(2R)-1-allyl-2-((tert-butyldiphenylsilyl)ethynyl)-6-methoxy-2-(2-methylallyl)-1,2,3,4-tetrahydronaphthalen-1-ol (7k)



Following the general procedure allylmagnesium bromide (300 µL, 0.300 mmol, 2.0 equiv.) was added at -10 °C to a solution of compound **1k** (75.0 mg, 0.152 mmol) in Et_2O (3.0 mL). The reaction is monitored by TLC (pentane/ethylacetate 8:2). After work up the crude mixture was purified by flask chromatography (pentane/diethyl ether 98:2) to afford the major diasteroisomer (0.055 g, 0.12 mmol, 80 % yield) and the minor diastereoisomer (0.012 g, 0.028 mmol, 18 % yield) as colorless oils.

*Major diastereoisomer (7**k**)*



R_F = 0.76 (pentane:diethyl ether 9:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.53 (d, *J* = 8.8 Hz, 1H, Ar*H*), 7.51 (dd, *J* = 8.1, 1.4 Hz, 2H, *Ph*), 7.48 – 7.45 (m, 2H, *Ph*), 7.38 – 7.31 (m, 2H, *Ph*), 7.29 – 7.21 (m, 4H, *Ph*), 6.81 (dd, *J* = 8.7, 2.7 Hz, 1H, Ar*H*), 6.65 (d, *J* = 2.7 Hz, 1H, Ar*H*), 5.71 (dddd, *J* = 16.2, 11.1, 8.0, 6.2 Hz, 1H, C*H*CH_2), 5.03 (t, *J* = 1.3 Hz, 1H, CHCH_2), 5.02 – 4.98 (m, 2H, CMeCH_2), 4.93 (dd, *J* = 2.5, 1.2 Hz, 1H, CHCH_2), 3.82 (s, 3H, O*Me*), 3.24 (ddd, *J* = 15.7, 11.7, 7.3 Hz, 1H, CH_2), 2.94 (d, *J* = 12.9 Hz, 1H, CH_2CMe), 2.87 (dd, *J* = 17.7, 6.5 Hz, 1H, CH_2), 2.71 (dd, *J* = 14.0, 6.4 Hz, 1H, CH_2CH), 2.64 (d, *J* = 1.5 Hz, 1H, *OH*), 2.52 (ddd, *J* = 14.0, 7.9, 1.4 Hz, 1H, CH_2CH), 2.35 (d, *J* = 12.8 Hz, 1H, CH_2CMe), 2.33 (m, 1H, CH_2), 2.09 (ddd, *J* = 14.0, 11.8, 6.7 Hz, 1H, CH_2), 2.04 – 1.99 (m, 3H, C*Me*), 0.91 (s, 9H, ^{t}Bu).

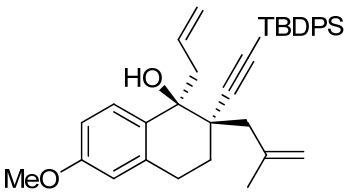
^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6, 142.8, 137.0, 135.4, 134.7, 134.1, 133.3, 133.3, 129.4, 129.3, 129.1, 127.6, 117.3, 115.3, 113.0, 112.4, 112.0, 85.6, 55.9, 46.9, 42.3, 41.8, 29.3, 26.9, 26.8, 25.2, 18.4. Only one Ph of the silyl group is resolved.

IR ν_{max} 3549 (w), 3072 (w), 3052 (w), 2953 (m), 2933 (m), 2858 (m), 2160 (w), 1609 (m), 1498 (m), 1465 (m), 1430 (s), 1327 (m), 1259 (s), 1244 (s), 1109 (s), 1037 (s), 1005 (m), 910 (s).

HRMS (ESI) calcd for $C_{36}H_{42}NaO_2Si^+$ $[M+Na]^+$ 557.2846; found 557.2858.

$[\alpha]_D^{23.0}$ -34.6 (c = 2.25, $CHCl_3$).

*Minor product (7**k**)*



R_F = 0.36 (pentane:diethylether 9:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.81 (dd, *J* = 7.7, 1.8 Hz, 4H, *Ph*), 7.43 – 7.34 (m, 6H, *Ph*), 7.26 (s, 1H, Ar*H*), 6.75 (dd, *J* = 8.7, 2.7 Hz, 1H, Ar*H*), 6.63 (d, *J* = 2.6 Hz, 1H, Ar*H*), 5.71 (dddd, *J* = 16.6, 10.1, 8.3, 6.2 Hz, 1H, C*H*CH_2), 5.08 – 5.00 (m, 1H, CHCH_2), 4.94 (dd, *J* = 17.1,

1.8 Hz, 1H, CHCH_2), 4.87 (s, 1H, CMeCH_2), 4.72 (s, 1H, CMeCH_2), 3.80 (s, 3H, O*Me*), 3.15 (dd, *J* = 13.8, 8.5 Hz, 1H, CH_2CH), 2.95 – 2.85 (m, 2H, CH_2), 2.64 (m, 1H, CH_2CH), 2.62 (dd, *J* = 14.0, 1.6 Hz, 1H, CH_2CMe), 2.37 – 2.30 (m, 1H, CH_2), 2.29 (s, 1H, *OH*), 2.28 – 2.19 (m, 1H, CH_2), 2.13 (d, *J* = 13.9 Hz, 1H, CH_2CMe), 1.95 (s, 3H, C*Me*CH_2), 1.11 (s, 9H, ^{t}Bu).

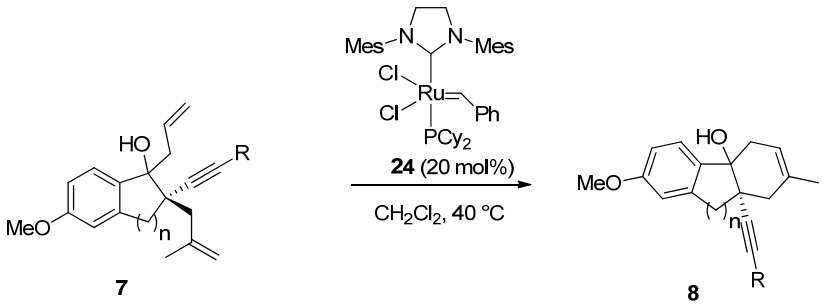
^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4, 143.7, 135.8, 135.7, 135.6, 134.0, 133.6, 131.7, 129.5, 128.0, 127.7, 127.6, 118.6, 115.5, 114.9, 113.2, 111.3, 84.6, 76.3, 55.2, 45.4, 45.1, 40.8, 28.2, 27.2, 27.1, 24.7, 24.7, 18.7. One aliphatic carbon is not resolved.

IR ν_{max} 3549 (w), 3072 (w), 3052 (w), 2953 (m), 2933 (m), 2858 (m), 2160 (w), 1609 (m), 1498 (m), 1465 (m), 1430 (s), 1327 (m), 1259 (s), 1244 (s), 1109 (s), 1037 (s), 1005 (m), 910 (s).

HRMS (ESI) calcd for $C_{36}H_{42}NaO_2Si^+$ $[M+Na]^+$ 557.2846; found 557.2858.

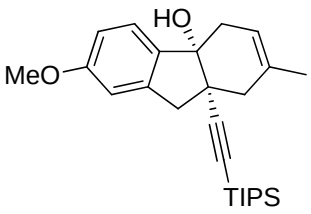
$[\alpha]_D^{23.0}$ -43.5 (c = 1.08, $CHCl_3$).

6.2 Ring closing metathesis with Ru(II) catalyst.



In a microwave vial of 0.5 mL, compound **7b** or **7k** (1 equiv.) was dissolved in CH_2Cl_2 (0.1 M) with catalyst **24** (0.1 equiv.). The vial was then tightly sealed and degased three times, before placing it in an oil bath heated at 40 °C. The reaction was monitored by TLC (8:2 pentane:ethylacetate). Upon completion the reaction was filtered through a plug of celite and purified by flash chromatography to obtain the desired tricyclic compound **8b** or **8k**.

(4aR,9aS)-7-methoxy-2-methyl-9a-((triisopropylsilyl)ethynyl)-4,4a,9,9a-tetrahydro-1H-fluoren-4a-ol (8b)



Compound **7b** (10 mg, 0.023 mmol) was dissolved in CH_2Cl_2 (0.23 mL) with catalyst **24** (1.9 mg, 2.3 μmol, 0.1 equiv.). The desired tricyclic compound **8b** (7.8 mg, 0.019 mmol, 83% yield) was obtained as dark brown oil after column chromatography (pentane/ethyl acetate 9:1).

R_F = 0.45 (pentane:ethyl acetate 9:1).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.26 – 7.17 (m, 1H, Ar*H*), 6.84 (d, *J* = 2.4 Hz, 1H, Ar*H*)), 6.72 (ddd, *J* = 8.2, 2.4, 0.8 Hz, 1H, Ar*H*)), 5.49 (dq, *J* = 4.4, 1.7 Hz, 1H, C*H*CMe), 3.79 (s, 3H,

O*Me*), 3.14 (dt, *J* = 14.3, 1.1 Hz, 1H, CH_2), 3.02 (ddd, *J* = 17.5, 4.4, 2.3 Hz, 1H, CH_2CH), 2.93 (d, *J* = 14.2 Hz, 1H, CH_2), 2.69 – 2.53 (m, 2H, CH_2CH + CH_2CMe) 2.39 – 2.29 (m, 1H, CH_2CMe), 1.80 (dd, *J* = 2.6, 1.4 Hz, 3H, C*Me*), 0.89 – 0.79 (m, 21H, *TIPS*).

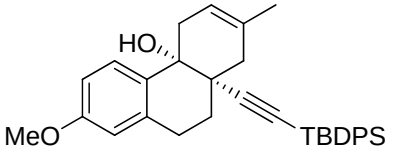
^{13}C NMR (101 MHz, $CDCl_3$) δ 160.2, 145.6, 137.8, 133.6, 122.9, 118.3, 115.1, 112.0, 111.4, 80.5, 78.1, 55.5, 49.7, 42.5, 37.5, 33.5, 24.0, 18.4, 11.1.

IR ν_{max} 3520 (w), 2942 (s), 2894 (m), 2864 (s), 2158 (w), 1610 (m), 1491 (m), 1464 (m), 1258 (s), 1144 (w), 1036 (w), 885 (m).

HRMS (ESI) calcd for $C_{26}H_{38}O_2Si$ [M+] 410.2641; found 410.2637.

$[\alpha]_D^{25.0}$ +3.49 (c = 0.42, $CHCl_3$).

(4aR,10aR)-10a-((tert-butyldiphenylsilyl)ethynyl)-7-methoxy-2-methyl-1,4,4a,9,10,10a-hexahydrophenanthren-4a-ol (8k)



The major diasteroisomer of **7k** (55 mg, 0.10 mmol) was dissolved in CH_2Cl_2 (1.0 mL) with catalyst **24** (9.0 mg, 10.0 μmol, 0.1 equiv.). The desired tricyclic compound **8k** (42 mg, 0.083 mmol, 81% yield) was obtained as brown oil after column chromatography (pentane/diethyl ether 9:1). The relative stereochemistry was determined by ROESY NMR analysis (see spectra section), based on a NOE signal between the OH and the TBDPS group.

R_F = 0.31 (pentane:diethyl ether 9:1).

^{1}H NMR (400 MHz, Benzene-d_6) δ 7.76 (d, *J* = 8.6 Hz, 1H, Ar*H*), 7.74 – 7.69 (m, 4H, *Ph*), 7.20 – 7.13 (m, 6H, *Ph*), 6.79 (s, 1H, Ar*H*), 6.64 (d, *J* = 2.7 Hz, 1H, Ar*H*), 5.13 (m, 1H, C*H*CMe), 3.38 (s, 3H, O*Me*), 3.37 – 3.28 (m, 1H, *CH*$_2$), 3.03 (ddt, *J* = 17.6, 2.9, 1.6 Hz, 1H, *CH*$_2$CMe), 2.57 (dd, *J* = 17.6, 6.8 Hz, 1H, *CH*$_2$), 2.54 – 2.47 (m, 1H, *CH*$_2$CH), 2.44 (app. d, *J* = 2.2 Hz, 1H, *OH*), 2.23 – 2.14 (m, 1H, *CH*$_2$CH), 2.05 – 1.94 (m, , 1H, *CH*$_2$), 2.00 (dd, *J* = 18.9, 1.6 Hz, 1H, *CH*$_2$CMe), 1.69 (ddd, *J* = 13.7, 7.5, 1.4 Hz, 1H, *CH*$_2$), 1.58 (dd, *J* = 2.7, 1.3 Hz, 3H, CHC*Me*), 1.03 (s, 9H, ^{t}Bu).

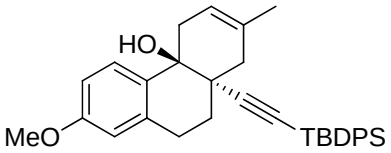
^{13}C NMR (101 MHz, C_6D6) δ 158.9, 137.2, 135.8, 135.5, 133.5, 129.6, 129.4, 127.8, 127.6, 126.6, 117.2, 114.9, 113.3, 112.3, 82.9, 72.2, 54.5, 41.7, 40.2, 39.0, 30.5, 26.8, 26.8, 23.0, 18.3. There are 2 peaks missing for the Ph group.

IR ν_{max} 3555 (w), 3050 (w), 3049 (w), 3009 (w), 3008 (w), 3007 (w), 2931 (m), 2908 (m), 2907 (m), 2906 (m), 2858 (m), 2161 (w), 1605 (m), 1498 (m), 1463 (m), 1431 (m), 1251 (s), 1250 (s), 1109 (s), 1036 (s), 821 (s).

HRMS (ESI) calcd for $C_{34}H_{38}NaO_2Si^+$ $[M+Na]^+$ 529.2533; found 529.2546.

$[\alpha]_D^{25.0}$ +8.71 (c = 3.47, $CHCl_3$).

(4aS,10aR)-10a-((tert-butyldiphenylsilyl)ethynyl)-7-methoxy-2-methyl-1,4,4a,9,10,10a-hexahydrophenanthren-4a-ol (8k)



The minor diasteroisomer of **7k** (13 mg, 0.024 mmol) was dissolved in CH_2Cl_2 (0.25 mL) with catalyst **24** (0.60 mg, 0.70 μmol, 0.1 equiv.). The desired tricyclic compound **8k** (8.0 mg, 0.016 mmol, 65% yield) was obtained as brown oil after column chromatography (pentane/diethyl ether 7:3 and then 6:4).

R_F = 0.31 (pentane:diethyl ether 7:3).

^{1}H NMR (400 MHz, Benzene-d_6) δ 7.81 – 7.68 (m, 4H, *Ph*), 7.30 (d, *J* = 8.7 Hz, 1H, *ArH*), 7.22 – 7.11 (m, 6H, *Ph*), 6.79 (dd, *J* = 8.7, 2.7 Hz, 1H, *ArH*), 6.63 (d, *J* = 2.7 Hz, 1H, *ArH*), 5.42 (m, 1H, C*H*CMe), 3.33 – 3.20 (m, 1H, CH_2), 3.37 (s, 3H, O*Me*), 2.78 (ddd, *J* = 17.4, 4.0, 2.0 Hz, 1H, CH_2CH), 2.51 – 2.37 (m, 2H, CH_2CH + *CH*$_2$), 2.22 – 2.10 (m, 1H, CH_2CMe), 2.03 – 1.87 (m, 2H, CH_2CMe + CH_2), 1.56 – 1.49 (m, 3H, C*Me*), 1.47 (dd, *J* = 12.9, 6.2 Hz, 1H, CH_2), 1.21 (bs, 1H, *OH*), 0.86 (s, 9H, ^{t}Bu).

^{13}C NMR (101 MHz, C_6D6) δ 159.1, 137.9, 135.6, 133.9, 132.7, 131.9, 129.2, 118.8, 115.4, 113.2, 112.8, 100.0, 80.3, 70.0, 54.5, 40.3, 39.9, 36.6, 28.7, 27.4, 26.8, 23.2, 18.5. Not all the aromatic peaks could be resolved.

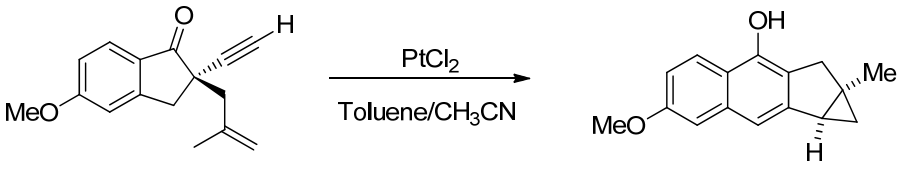
IR ν_{max} 3017 (w), 2936 (w), 1670 (w), 1600 (w), 1255 (w), 1218 (m), 754 (s).

HRMS (ESI) calcd for $C_{34}H_{38}NaO_2Si^+$ $[M+Na]^+$ 529.2533; found 529.2532.

$[\alpha]_D^{25.0}$ -17.99 (c = 0.67, $CHCl_3$).

6.4 Cycloisomerization catalyzed by transition metals

(S)-5'-Methoxy-3-methylspiro[cyclohexa[2,5]diene-1,2'-inden]-1'(3'H)-one (9)



1d **9**

52% yield

Following a reported procedure,[17] $PtCl_2$ (3.4 mg, 0.013 mmol, 0.1 equiv.) and two drops of CH_3CN were added to a solution of compound **1d** (31 mg, 0.13 mmol) in toluene (0.65 mL). The reaction was stirred at room temperature till consumption of the starting material as checked by TLC (pentane:ethylacetate 8:2). The mixture was filtered through a plug of celite and purified on deactivated silica by flash chromatography to obtain compound **9** (16 mg, 0.067 mmol, 52% yield) as colorless oil.

R_F = 0.52 (pentane:ethylacetate 8.2).

(17) J. Sun, P. Conley, L. Zhang, S.A. Kozmin, *J. Am. Chem. Soc.* **2006**, *128*, 9705-9710.

^{1}H NMR (400 MHz, Benzene-d_6) δ 8.32 (d, *J* = 9.1 Hz, 1H, Ar*H*), 7.30 (dd, *J* = 9.1, 2.5 Hz, 1H, Ar*H*), 7.14 (s, 1H, Ar*H*), 7.08 (d, *J* = 2.5 Hz, 1H, Ar*H*), 3.52 (s, 3H, O*Me*), 3.14 – 2.99 (m, 2H, CH_2CMe), 1.61 (dd, *J* = 7.7, 3.3 Hz, 1H, CH_2CH), 1.28 (s, 3H, CH_2C*Me*), 0.84 (dd, *J* = 7.7, 4.2 Hz, 1H, CH_2CH), 0.33 (t, *J* = 3.8 Hz, 1H, CH_2C*H*).

^{13}C NMR (101 MHz, C_6D6) δ 157.6, 146.5, 143.7, 135.7, 125.6, 122.9, 119.1, 116.7, 115.2, 106.0, 54.4, 41.4, 26.1, 24.0, 23.8, 21.4.

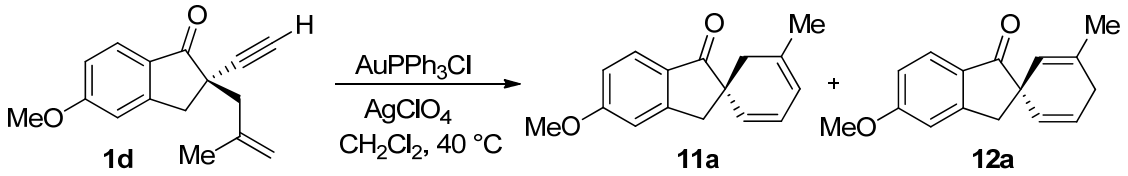
IR ν_{max}3409 (w), 2925 (w), 2864 (w), 1659 (m), 1593 (s), 1421 (w), 1290 (m), 1256 (s), 1223 (s), 760 (s).

HRMS (APPI negative) calcd for $C_{16}H_{15}O_2$ [M+H-1] 239.1072; found 239.1052.

$[\alpha]_D^{25.0}$ -26.3 (c = 0.92, $CHCl_3$).

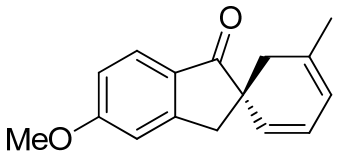
Au-Catalyzed Cyclisomerizations

From 1d



Following a slightly modified procedure,[18] compound **1d** (50 mg, 0.21 mmol) in CH_2Cl_2 (0.50 mL) was added at 40 °C to a pre-stirred solution of PPh_3AuCl (10 mg, 0.021 mmol, 0.1 equiv.) and $AgClO_4$ (4.1 mg, 0.020 mmol, 0.095 equiv.) in CH_2Cl_2 (1.50 mL). After purification by column chromatography (pentane:ethylacetate 8.2) diene **12a** (0.029 g, 0.12 mmol, 58% yield) as a yellowish oil and diene **11a** (0.015 g, 0.062 mmol, 30% yield) as a yellow oil.

(S)-5'-methoxy-5-methylspiro[cyclohexa[2,4]diene-1,2'-inden]-1'(3'H)-one (11a)



R_F = 0.5 (pentane:ethylacetate 8.2).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.72 (d, *J* = 8.5 Hz, 1H, Ar*H*), 6.91 (dd, *J* = 8.5, 2.2 Hz, 1H, Ar*H*), 6.83 (d, *J* = 2.1 Hz, 1H, Ar*H*), 6.03 (dd, *J* = 9.4, 5.4 Hz, 1H, CHC*H*CH), 5.79 – 5.70 (m, 1H, C*H*CH), 5.43 (d, *J* = 9.4 Hz, 1H, CHCHC*H*), 3.88 (s, 3H, O*Me*), 3.16 (d, *J* = 17.3 Hz, 1H, CH_2), 2.97 (d, *J* = 17.3 Hz, 1H, CH_2), 2.80 (dd, *J* = 17.2, 2.7 Hz, 1H, CH_2CMe), 1.95 (d, *J* = 17.2 Hz, 1H, CH_2CMe), 1.81 (s, 3H, CH_2C*Me*).

(18) M.R. Luzung, J.P. Markham, F.D. Toste, *J. Am. Chem. Soc.* **2004**, *126*, 10858.

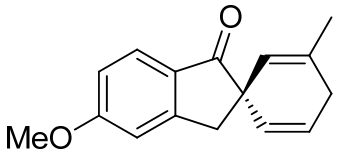
^{13}C NMR (101 MHz, $CDCl_3$) δ 208.4, 165.7, 155.0, 134.1, 128.7, 126.3, 125.5, 125.2, 118.3, 115.5, 109.9, 55.7, 51.6, 42.0, 38.4, 23.6.

IR ν_{max}3019 (w), 1699 (w), 1598 (m), 1265 (w), 1218 (w), 758 (s).

HRMS (ESI) calcd for $C_{16}H_{17}O_2^+$ $[M+H]^+$ 241.1223; found 241.1228.

$[\alpha]_D^{25.0}$ +13.9 (c = 0.29, $CHCl_3$).

(S)-5'-methoxy-3-methylspiro[cyclohexa[2,5]diene-1,2'-inden]-1'(3'H)-one (12a)



R_F = 0.3 (pentane:ethylacetate 8.2).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.70 (d, *J* = 8.5 Hz, 1H, Ar*H*), 6.91 (dd, *J* = 8.4, 2.2 Hz, 1H, Ar*H*), 6.88 – 6.85 (m, 1H, Ar*H*), 6.00 (dt, *J* = 9.9, 3.4 Hz, 1H, C*H*CH_2), 5.49 – 5.42 (m, 1H, C*H*$CHCH_2$), 5.16 (dt, *J* = 3.2, 1.7 Hz, 1H, C*H*CMe), 3.89 (s, 3H, O*Me*), 3.03 (d, *J* = 18.1Hz, CH_2), 2.99 (d, *J* = 18.1 Hz, CH_2), 2.88 – 2.76 (m, 1H, CHCH_2), 2.67 – 2.56 (m, 1H, CHCH_2), 1.76 (d, *J* = 1.5 Hz, 3H, CHC*Me*).

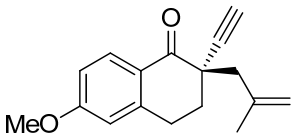
^{13}C NMR (101 MHz, $CDCl_3$) δ 205.3, 165.6, 155.6, 133.7, 128.4, 126.9, 126.6, 126.3, 121.8, 115.7, 109.6, 55.7, 54.3, 43.3, 30.9, 23.3.

IR ν_{max}3019 (w), 1702 (w), 1599 (w), 1261 (w), 1225 (w), 753 (s).

HRMS (ESI) calcd for $C_{16}H_{16}NaO_2^+$ $[M+Na]^+$ 263.1042; found 263.1035.

$[\alpha]_D^{25.0}$ -2.48 (c = 2.42, $CHCl_3$).

(R)-2-ethynyl-6-methoxy-2-(2-methylallyl)-3,4-dihydronaphthalen-1(2H)-one (10)



Following the general procedure and starting from substrate **1k** (1.84 g, 3.43 mmol) (R)-2-ethynyl-6-methoxy-2-(2-methylallyl)-3,4-dihydronaphthalen-1(2H)-one (**10**) (0.560 g, 2.20 mmol, 64 % yield/97% *ee*) [19] was obtained as a yellow oil after deprotection with TBAF (6.86 mL, 6.86 mmol, 2.00 equiv.).

R_F 0.42 (pentane:ethylacetate 8:2).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.04 (d, *J* = 8.8 Hz, 1H, Ar*H*), 6.83 (dd, *J* = 8.8, 2.5 Hz, 1H, Ar*H*), 6.68 (d, *J* = 2.5 Hz, 1H, Ar*H*), 4.90 (dq, *J* = 2.8, 1.6 Hz, 1H, CCH_2), 4.79 (dq, *J* = 1.9,

[19] The ee was measured before TBAF deprotection via the method described for compound **6k.**

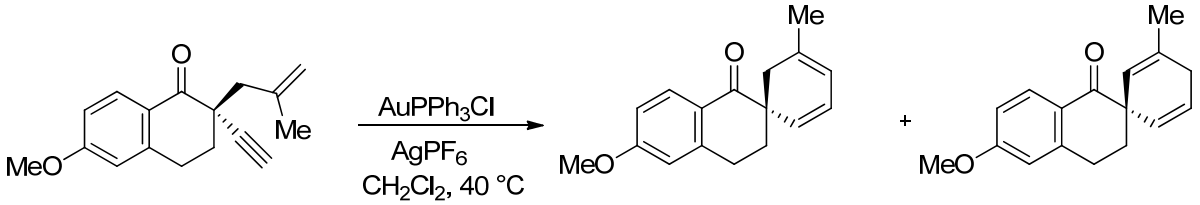
1.0 Hz, 1H, CCH_2), 3.85 (s, 3H, OCH_3), 3.38 – 3.24 (m, 1H, CH_2), 2.88 (dt, *J* = 17.0, 4.3 Hz, 1H, CH_2), 2.81 (dd, *J* = 13.8, 1.1 Hz, 1H, CH_2CMe), 2.60 (dd, *J* = 13.7, 1.0 Hz, 1H, CH_2CMe), 2.25 (dd, *J* = 13.5, 4.5 Hz, 1H, CH_2), 2.22 (s, 1H, CC*H*), 1.99 (ddd, *J* = 13.5, 11.4, 4.2 Hz, 1H, CH_2), 1.84 (s, 3H, C*Me*).

^{13}C NMR (101 MHz, $CDCl_3$) δ. 193.2, 163.8, 146.2, 141.9, 131.3, 124.3, 115.4, 113.5, 112.3, 84.0, 72.6, 55.5, 44.9, 43.7, 32.9, 26.6, 24.2.

IR ν_{max} 3305 (w), 2943 (w), 2252 (w), 1679 (w), 1600 (m), 1264 (w), 908 (s), 732 (s).

HRMS (ESI) calcd for $C_{17}H_{19}O_2^+$ $[M+H]^+$ 255.1380; found 255.1382.

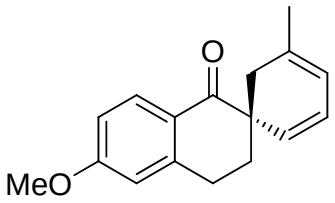
Cycloisomerization of 10



10 **11b** **12b**

Following a slightly modified procedure,[18] compound **10** (50 mg, 0.20 mmol) in CH_2Cl_2 (0.50 mL) was added at 40 °C to a pre-stirred solution of PPh_3AuCl (10 mg, 0.021 mmol, 0.1 equiv.) and $AgPF_6$ (5.0 mg, 0.020 mmol, 0.095 equiv.) in CH_2Cl_2 (1.50 mL). After purification by column chromatography (pentane:ethylacetate 95:5 then 9:1) compound **11b** was obtained (0.020 g, 0.079 mmol, 40% yield) as a colorless oil and diene **12b** (0.012 g, 0.047 mmol, 24 % yield) as a colorless oil.

(R)-6'-methoxy-5-methyl-3',4'-dihydro-1'H-spiro[cyclohexa[2,4]diene-1,2'-naphthalen]-1'-one (11b)



R_F = 0.4 (pentane:ethylacetate 9:1).

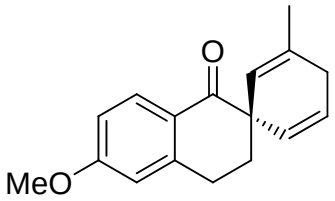
^{1}H NMR (400 MHz, Benzene-d_6) δ 8.36 (d, *J* = 8.7 Hz, 1H, Ar*H*), 6.61 (dd, *J* = 8.7, 2.6 Hz, 1H, Ar*H*), 6.46 (d, *J* = 2.6 Hz, 1H, Ar*H*), 5.88 (dd, *J* = 9.6, 5.3 Hz, 1H, CHC*H*CH), 5.60 – 5.53 (m, 2H, C*H*CHC*H*), 3.33 (dt, *J* = 17.8, 1.6 Hz, 1H, CH_2), 3.21 (s, 3H, O*Me*), 2.83 – 2.73 (m, 1H, CH_2CMe), 2.37 (dt, *J* = 17.3, 4.9 Hz, 1H, CH_2), 2.04 (dt, *J* = 13.0, 5.0 Hz, 1H, CH_2), 1.77 (d, *J* = 17.5 Hz, 1H, CH_2), 1.63 (td, *J* = 1.6, 0.9 Hz, 3H, CH_2C*Me*), 1.56 (ddd, *J* = 13.0, 10.4, 4.9 Hz, 1H, CH_2CMe).
^{13}C NMR (101 MHz, C_6D6) δ 197.5, 163.2, 145.3, 134.6, 130.9, 125.7, 125.3, 124.3, 117.3, 112.9, 112.7, 54.5, 46.4, 35.8, 32.5, 25.3, 23.2.

IR ν_{max} 3019 (w), 2936 (w), 1748 (w), 1600 (w), 1251 (m), 1222 (m), 938 (w), 756 (s).

HRMS (ESI) calcd for $C_{17}H_{18}NaO_2^+$ $[M+Na]^+$ 277.1199; found 277.1204.

$[\alpha]_D^{25.0}$ +86.7 (c = 0.97, $CHCl_3$).

(S)-6'-methoxy-3-methyl-3',4'-dihydro-1'H-spiro[cyclohexa[2,5]diene-1,2'-naphthalen]-1'-one (12b)



R_F = 0.2 (pentane:diethylether 8.2).

NMR (400 MHz, Benzene-d_6) δ 8.32 (d, *J* = 8.7 Hz, 1H, Ar*H*), 6.59 (dd, *J* = 8.7, 2.6 Hz, 1H, Ar*H*), 6.51 – 6.46 (d, *J* = 2.7 Hz, 1H, Ar*H*), 5.79 (d, *J* = 1.4 Hz, 2H, CH_2CHCH+ $CHCH$), 5.55 (dq, *J* = 2.6, 1.5 Hz, 1H, C*H*CMe), 3.21 (s, 3H, O*Me*), 2.71 (dt, *J* = 17.4, 6.7 Hz, 1H, CH_2), 2.60 (dt, *J* = 17.4, 6.1 Hz, 1H, CH_2), 2.44 (m, 1H, CH_2CHCH), 2.37 (m, 1H, CH_2CHCH), 1.90 – 1.85 (m, 2H, CH_2), 1.54 (s, 3H, C*Me*).

^{13}C NMR (101 MHz, C_6D6) δ 195.9, 163.2, 145.1, 133.2, 130.8, 127.4, 126.0, 125.5, 121.5, 113.0, 112.8, 54.5, 49.4, 36.6, 31.3, 25.2, 23.1.

IR ν_{max} 3019 (w), 2938 (w), 2863 (w), 1670 (w), 1600 (w), 1217 (m), 754 (s).

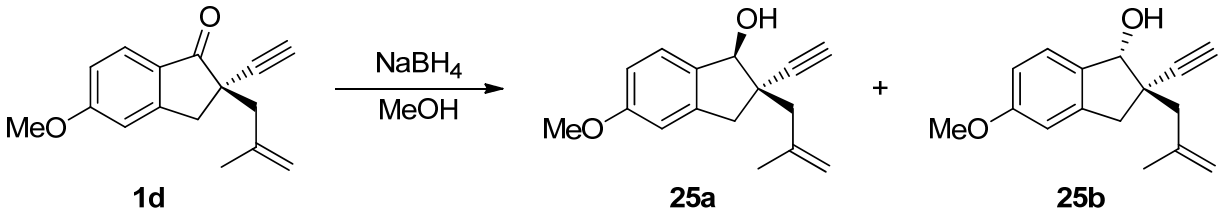
HRMS (ESI) calcd for $C_{17}H_{18}NaO_2^+$ $[M+Na]^+$ 277.1199; found 277.1201.

$[\alpha]_D^{25.0}$ -21.29 (c = 0.90, $CHCl_3$).

7. Absolute stereochemistry

7.1 Determination of the absolute configuration of 6d

(2*S*)-2-ethynyl-5-methoxy-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-ol (30)



1d **25a** **25b**

In a open flask (*S*)-2-ethynyl-5-methoxy-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-one (**1d**) (1.98 g, 8.24 mmol) is dissolved in MeOH (63 mL). The solution is cooled to 0 °C before the addition in one portion of $NaBH_4$ (0.343 g, 9.06 mmol, 1.1 equiv.). The reaction is stirred till consumption of the starting material as shown by TLC (pentane:ethyl acetate, 7:3). Upon completion the reaction is filtered through a plug of silica, wash with ether and ethyl acetate (2 x 50 mL) and the solvent is evaporated. The crude is purified by column chromatography (pentane:ethyl acetate, 95:5 and then pentane: diethyl ether 7:3) to afford the two separated diasteroisomers **25a** and **25b** (1.17 g, 4.84 mmol, 59 % yield, in 1:2 ratio) obtained as colorless oils..

Diasteroisomer (**25a**)

R_F = 0.35 (pentane:ethyl acetate)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 (d, *J* = 8.2 Hz, 1H, Ar*H*), 6.79 (dd, *J* = 8.2, 2.5 Hz, 1H, Ar*H*), 6.76 (d, *J* = 2.3 Hz, 1H, Ar*H*), 5.12 (s, 1H, OHC*H*), 4.93 (t, *J* = 1.8 Hz, 1H, CMe*CH_2*), 4.88 (dt, *J* = 2.2, 1.0 Hz, 1H, CMe*CH_2*), 3.80 (s, 3H, O*Me*), 3.15 (d, *J* = 15.6 Hz, 1H, *CH_2*), 3.03 (d, *J* = 15.6 Hz, 1H, *CH_2*), 2.55 (dd, *J* = 14.0, 1.1 Hz, 1H, *CH_2*CMe), 2.36 – 2.28 (m, 1H, *CH_2*CMe), 2.12 (s, 1H, CC*H*), 1.98 – 1.90 (m, 3H, C*Me*), 1.59 (bs, 1H, *OH*).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.5, 143.4, 142.8, 135.2, 125.7, 114.1, 113.0, 110.3, 89.6, 82.5, 69.9, 55.4, 46.9, 43.0, 40.8, 24.2.

IR ν_{max} 3403 (w), 3296 (m), 3073 (w), 2943 (w), 2836 (w), 1610 (m), 1610 (m), 1493 (s), 1438 (m), 1290 (m), 1257 (s), 1145 (m), 1145 (m), 1117 (s), 1117 (s), 1031 (s), 896 (m).

HRMS (ESI) calcd for $C_{16}H_{18}LiO_2^+$ $[M+Li]^+$ 249.1461; found 249.1465

Diasteroisomer (**25b**)

R_F = 0.3 (pentane:ethyl acetate)

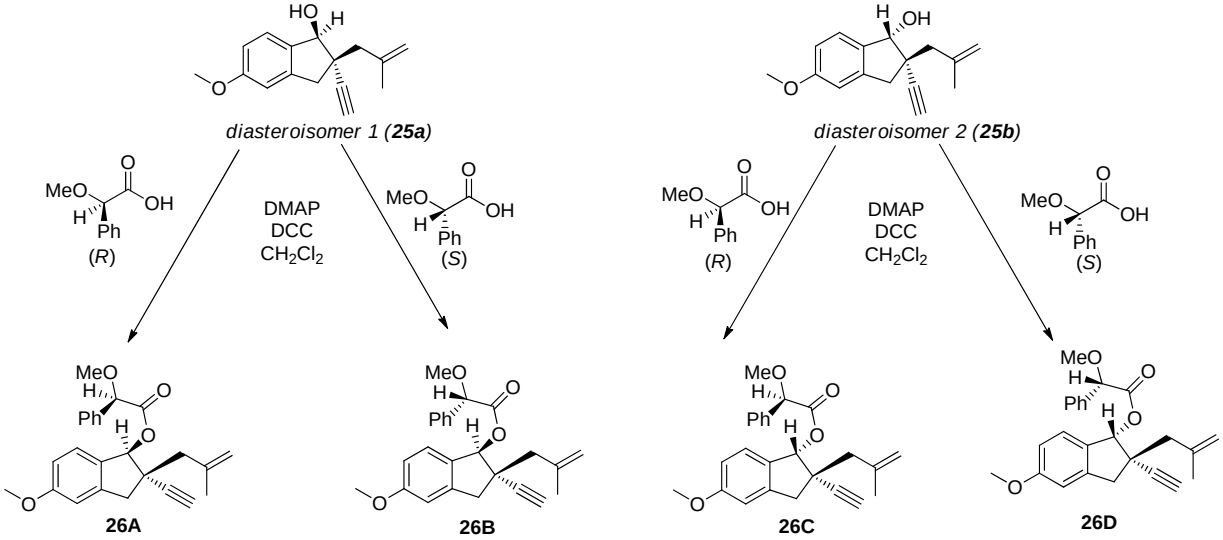
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 (d, *J* = 8.3 Hz, 1H, Ar*H*), 6.79 (dd, *J* = 8.3, 2.4 Hz, 1H, Ar*H*), 6.74 (d, *J* = 2.3 Hz, 1H, Ar*H*), 4.93 (s, 1H, CMe*CH_2*), 4.83 (s, 1H, CMe*CH_2*), 4.78 (s, 1H, OHC*H*), 3.79 (s, 3H, O*Me*), 3.23 (d, *J* = 15.6 Hz, 1H, *CH_2*), 2.94 (d, *J* = 15.6 Hz, 1H, *CH_2*), 2.58 (d, *J* = 13.7 Hz, 1H, *CH_2*CMe), 2.51 – 2.40 (bs, 1H, *OH*), 2.36 (d, *J* = 13.7 Hz, 1H, *CH_2*CMe), 2.26 (s, 1H, C*CH*), 1.96 – 1.88 (m, 3H, C*Me*).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.2, 142.5, 141.7, 135.0, 125.5, 114.6, 112.9, 110.2, 86.2, 81.1, 73.5, 55.4, 50.9, 45.6, 42.8, 24.1.

IR ν_{max} 3528 (w), 3457 (m), 3419 (m), 3394 (m), 3340 (m), 3295 (s), 2922 (w), 1614 (m), 1613 (m), 1493 (m), 1441 (w), 1291 (w), 1256 (s), 1114 (m), 1032 (m), 893 (w).

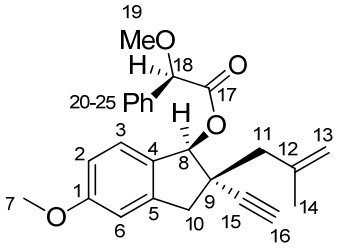
HRMS (ESI) calcd for $C_{16}H_{18}LiO_2^+$ $[M+Li]^+$ 249.1461; found 249.1464.

(*R*/*S*)-(2*S*)-2-ethynyl-5-methoxy-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-yl 2-methoxy-2-phenylacetate (26)



Following a reported procedure,[20] each diasteroisomer of (2*S*)-2-ethynyl-5-methoxy-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-ol (**25**) was placed in a 10 mL microwave vial with DMAP (0.2 equiv.), DCC (1.2 equiv.) and (R/S)-2-methoxy-2-phenylacetic acid (1.2 equiv.). The vial was sealed and flushed three times with vacuo/nitrogen. CH_2Cl_2 (0.03 M) was added and the reaction was stirred at room temperature for 3-4 h till the starting material is consumed as shown by TLC (pentane: ethyl acetate, 8:2).

(*R*)-(1*S*,2*S*)-2-ethynyl-5-methoxy-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-yl 2-methoxy-2-phenylacetate (26A)



A solution of (1*S*,2*S*)-2-ethynyl-5-methoxy-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-ol (**25a**) (21 mg, 0.087 mmol), DMAP (2.1 mg, 0.017 mmol, 0.2 equiv.), DCC (21.5 mg, 0.104 mmol, 1.2 equiv) and (*R*)-2-methoxy-2-phenylacetic acid (17.3 mg, 0.104 mmol, 1.2 equiv.) was stirred at room temperature in DCM (2.9 mL) till consumption of the starting material. (*R*)-(1*R*,2*S*)-2-

[20] Trost, B. M.; Schroeder, G. M. *Chem. Eur. J.* **2005**, *11*, 174.

ethynyl-5-methoxy-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-yl 2-methoxy-2-phenylacetate (**26A**) (11 mg, 0.028 mmol, 33 % yield) was obtained as a colorless oil after column chromatography (pentane:ethyl acetate, 9:1 and then 8:2).

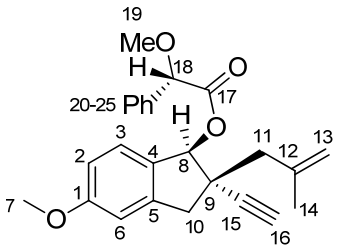
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40-7.31 (m, 6H, Ar H, H20-25 and H3), 6.76 (d, *J* = 7.2 Hz, 1H, Ar*H,* H2), 6.70 (s, 1H, H6) 6.12 (s, 1H, CC*H*OCO, H8), 4.73 (t, *J* = 1.7 Hz, 1H, CMe*CH$_2$,* H13a), 4.68 (s, 1H, Ph*H*OMe, H18), 4.56 (dd, *J* = 2.3, 1.3 Hz, 1H, CMe*CH$_2$*, H13b), 3.80 (s, 3H, Ar O*Me*, H7), 3.36 (s, 3H, *MeO*CHPh, H19), 3.08 (d, *J* = 15.5 Hz, 1H, *CH$_2$,* H10a), 3.01 (d, *J* = 15.5 Hz, 1H, *CH$_2$,* H10b), 2.03 (d, *J* = 14.1 Hz, 1H, *CH$_2$*CMe, H11a), 1.99 (s, 1H, C*CH*, H16), 1.88 (d, *J* = 14.2 Hz, 1H, *CH$_2$*CMe, H11b), 1.61 (d, *J* = 1.4 Hz, 3H, C*Me*¸ H14).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.8, 160.9, 144.6, 142.0, 136.2, 132.3, 128.9, 128.7, 127.5 (2C), 127.4, 113.9, 113.0, 110.1, 87.8, 82.4 (2C), 70.2, 57.2, 55.4, 46.8, 43.9, 40.6, 23.8.

IR ν_{max} 3300 (w), 3299 (w), 3070 (w), 2935 (w), 2835 (w), 1747 (s), 1612 (m), 1493 (m), 1451 (m), 1295 (m), 1257 (s), 1256 (s), 1172 (s), 1112 (s), 911 (m), 734 (s).

HRMS (ESI) calcd for $C_{25}H_{26}NaO_4^+$ $[M+Na]^+$ 413.1723; found 413.1723.

(*S*)-(1*S*,2*S*)-2-ethynyl-5-methoxy-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-yl 2-methoxy-2-phenylacetate (26B)



A solution of (1*S*,2*S*)-2-ethynyl-5-methoxy-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-ol (**25a**) (20 mg, 0.083 mmol), DMAP (2.0 mg, 0.017 mmol, 0.2 equiv.), DCC (20 mg, 0.099 mmol, 1.2 equiv.) and (*S*)-2-methoxy-2-phenylacetic acid (17 mg, 0.099 mmol, 1.2 equiv.) was stirred at room temperature in DCM (2.7 mL) till consumption of the starting material. (*S*)-(1*R*,2*S*)-2-ethynyl-5-methoxy-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-yl 2-methoxy-2-phenylacetate (**26B**) (0.003 g, 8 µmol, 9 % yield) was obtained as a colorless oil after column chromatography (pentane:ethyl acetate, 9:1 and then 8:2).

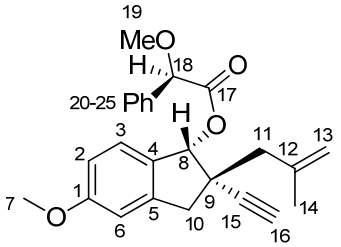
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 (dd, *J* = 6.7, 3.2 Hz, 2H, *Ph*, H20-25), 7.29 – 7.26 (m, 3H, *Ph*, H20-25), 7.04 (d, *J* = 8.3 Hz, 1H, Ar*H*, H3), 6.70 (d, *J* = 2.4 Hz, 1H, Ar*H,* H6), 6.63 (dd, *J* = 8.4, 2.4 Hz, 1H, Ar*H*, H2), 6.16 (s, 1H, CC*H*OCO, H8), 4.88 (t, *J* = 1.7 Hz, 1H, CMe*CH$_2$,* H13a), 4.79 (dd, *J* = 2.2, 1.1 Hz, 1H, CMe*CH$_2$,* H13b), 4.77 (s, 1H, Ph*H*OMe, H18), 3.77 (s, 3H, ArO*Me*, H7), 3.37 (s, 3H, *MeO*CHPh, H19), 3.12 (d, *J* = 15.5 Hz, 1H, *CH$_2$,* H10a), 3.05 (d, *J* = 15.4 Hz, 1H, *CH$_2$,* H10b), 2.44 (d, *J* = 14.0 Hz, 1H, *CH$_2$*CMe, H11a), 2.29 (d, *J* = 13.9 Hz, 1H, *CH$_2$*CMe, H11b), 2.07 (s, 1H, C*CH*, H16), 1.84 (s, 3H, C*Me*, H14).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 160.7, 144.0, 142.2, 135.9, 131.8, 128.6, 128.5, 128.5, 127.0, 126.9, 114.4, 112.8, 110.0, 87.9, 82.9, 82.7, 77.2, 70.4, 57.4, 55.3, 46.5, 43.9, 41.2, 24.1.

IR ν_{max} 3303 (w), 3072 (w), 2932 (w), 2834 (w), 2252 (w), 1745 (m), 1494 (w), 1254 (m), 1195 (m), 1171 (m), 1109 (s), 910 (s), 733 (s).

HRMS (ESI) calcd for $C_{25}H_{26}NaO_4^+$ $[M+Na]^+$ 413.1723; found 413.1715.

(*R*)-(1*R*,2*S*)-2-ethynyl-5-methoxy-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-yl 2-methoxy-2-phenylacetate (26C)



A solution of (1*R*,2*S*)-2-ethynyl-5-methoxy-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-ol (35 mg, 0.14 mmol), DMAP (3.5 mg, 0.029 mmol, 0.2 equiv.), DCC (36 mg, 0.17 mmol, 1.2 equiv) and (*R*)-2-methoxy-2-phenylacetic acid (29 mg, 0.17 mmol, 1.2 equiv.) was stirred at room temperature in DCM (4.8 mL) till consumption of the starting material. (*R*)-(1*R*,2*S*)-2-ethynyl-5-methoxy-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-yl 2-methoxy-2-phenylacetate (**26C**) (18 mg, 0.046 mmol, 32 % yield, contaminated with about 20% of diastereoisomer **26D**) was obtained as a colorless oil after column chromatography (pentane:ethyl acetate, 9:1 and then 8:2).

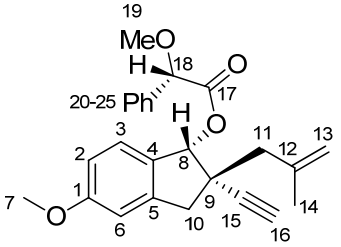
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 – 7.39 (m, 2H, *Ph*, H20-25), 7.34 – 7.27 (m, 3H, *Ph*, H20-25), 6.93 (d, *J* = 8.3 Hz, 1H, Ar*H*, H3), 6.70 (d, *J* = 2.3 Hz, 1H, Ar*H*, H6), 6.67 – 6.60 (m, 1H, Ar*H*, H2), 5.99 (s, 1H, CC*H*OCO, H8), 4.91 – 4.87 (m, 1H, CMe*CH$_2$*, H13a), 4.82 (s, 1H, Ph*H*OMe, H18), 4.68 (m, 1H, CMe*CH$_2$*, H13b), 3.77 (s, 3H, ArO*Me*, H7), 3.44 (s, 3H, *MeO*CHPh, H19), 3.32 (d, *J* = 16.0 Hz, 1H, *CH$_2$*, H10a), 3.02 (d, *J* = 15.9 Hz, 1H, *CH$_2$*, H10b), 2.37 (d, *J* = 13.8 Hz, 1H, *CH$_2$*CMe, H11a), 2.28 (d, *J* = 13.7 Hz, 1H, *CH$_2$*CMe, H11b), 2.12 (s, 1H, C*CH*, H16), 1.90 (dd, *J* = 1.5, 0.8 Hz, 3H, C*Me*, H14).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 160.9, 143.9, 142.0, 136.3, 130.6, 128.5, 128.5, 128.4, 127.8, 127.2, 126.9, 115.3, 113.2, 109.9, 82.7, 82.0, 77.2, 72.3, 57.5, 55.4, 46.2, 45.7, 44.0, 23.9.[21]

IR ν_{max} 3292 (w), 3070 (w), 2934 (w), 2834 (w), 1748 (m), 1613 (w), 1494 (m), 1450 (m), 1334 (w), 1260 (s), 1198 (m), 1170 (s), 1110 (s), 1029 (m), 1001 (m), 969 (m), 904 (m), 815 (w), 733 (m).

HRMS (ESI) calcd for $C_{25}H_{26}NaO_4^+$ $[M+Na]^+$ 413.1723; found 413.1725.

(S)-(1R,2S)-2-ethynyl-5-methoxy-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-yl 2-methoxy-2-phenylacetate (26D)



[21] Two aromatic carbons are overlapping.

A solution of (1*R*,2*S*)-2-ethynyl-5-methoxy-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-ol (**25b**) (28 mg, 0.12 mmol), DMAP (2.8 mg, 0.023 mmol, 0.2 equiv.), DCC (29 mg, 0.14 mmol, 1.2 equiv.) and (*S*-2-methoxy-2-phenylacetic acid (23 mg, 0.14 mmol, 1.2 equiv.) was stirred at room temperature in DCM (3.8 mL) till consumption of the starting material. (*S*)-(1*R*,2*S*)-2-ethynyl-5-methoxy-2-(2-methylallyl)-2,3-dihydro-1H-inden-1-yl 2-methoxy-2-phenylacetate **26d** (32 mg, 0.081 mmol, 70 % yield) was obtained as a colorless oil after column chromatography (pentane:ethyl acetate, 9:1 and then 8:2).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.50 – 7.44 (m, 2H, *Ph*+ Ar*H*, H3 and H20-25), 7.35 – 7.28 (m, 4H, *Ph*, H20-25), 6.77 (dd, *J* = 8.3, 2.5 Hz, 1H, Ar*H*, H2), 6.75 (d, *J* = 2.5 Hz, 1H, Ar*H*, H6), 5.96 (s, 1H, CC*H*OCO, H8), 4.85 – 4.78 (m, 1H, CMe*CH$_2$*, H13a), 4.76 (s, 1H, Ph*H*OMe, H18), 4.58 (dd, *J* = 2.0, 1.0 Hz, 1H, CMe*CH$_2$*, H13b), 3.81 (s, 3H, ArO*Me*, H7), 3.40 (s, 3H, *MeO*CHPh, H19), 3.27 (d, *J* = 15.9 Hz, 1H, *CH$_2$*, H10a), 2.97 (d, *J* = 15.9 Hz, 1H, *CH$_2$*, H10b), 2.19 (d, *J* = 13.9 Hz, 1H, *CH$_2$*CMe, H11a), 2.15 (d, *J* = 14.0 Hz, 1H, *CH$_2$*CMe, H11b), (m, 1H, *CH$_2$*CMe, H11b), 1.79 (dd, *J* = 1.6, 0.8 Hz, 3H, C*Me*, H14), 1.60 (s, 1H, C*CH*, H16).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.3, 161.0, 144.2, 141.9, 136.5, 131.0, 128.5, 128.4, 127.8, 127.3, 115.2, 113.2, 110.1, 84.9, 82.5, 81.6, 77.2, 72.1, 57.3, 55.4, 45.9, 45.4, 43.7, 23.8.

IR ν_{max} 3304 (w), 2937 (w), 2936 (w), 2935 (w), 2834 (w), 2833 (w), 2253 (w), 1745 (w), 1494 (w), 1259 (w), 1193 (w), 1170 (m), 1170 (m), 1111 (m), 1110 (m), 1029 (w), 999 (w), 910 (s), 732 (s).

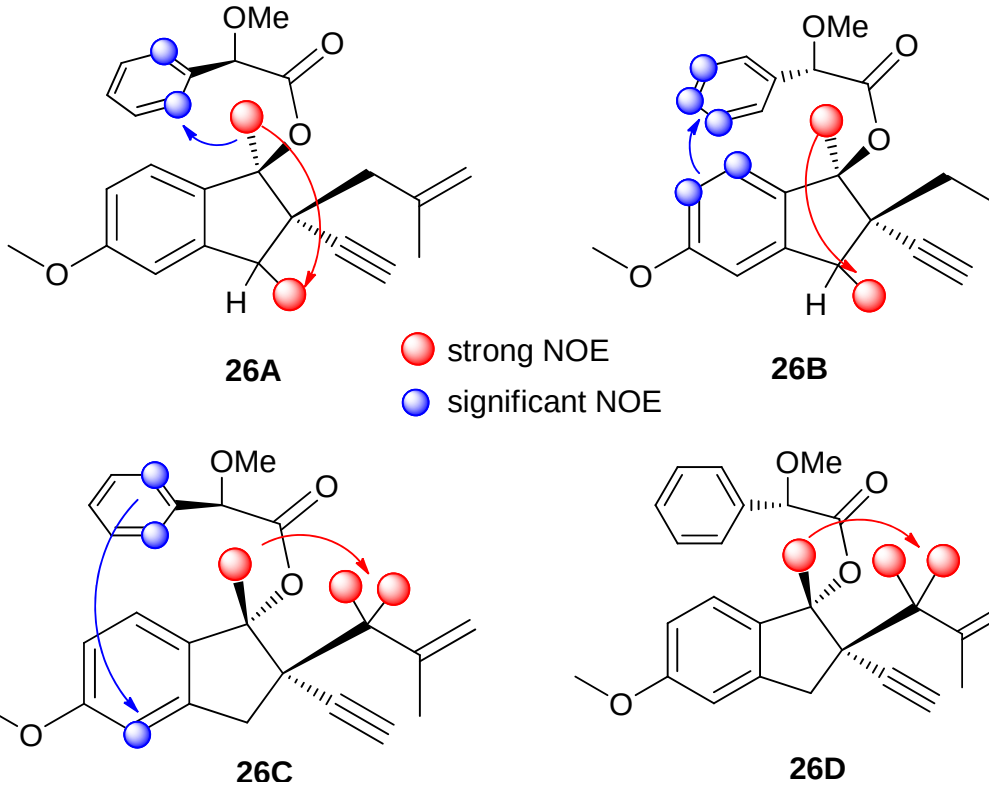
HRMS (ESI) calcd for $C_{25}H_{26}NaO_4^+$ $[M+Na]^+$ 413.1723; found 413.1723.

7.2 Assignment by NMR analysis

1) Assignment of relative configuration at the five-membered ring by ^{1}HNMR NOESY experiment.

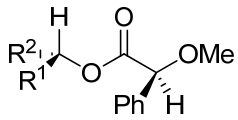
NMR tube preparation. 3.5 mg of each compound (A,B,C,D) were placed in 4 different NMR tubes which were sealed and flashed with vacuo/nitrogen (3 cycles). Dry C6D6 solvent (0.65 mL) was added to each tube.
NOESY experiments were acquired in exactly the same conditions: 8 number of scans, rg 161 and mixing time 1 s.

Proton H8 present a significant NOE with protons H11 in both compound **26C** and **26D**, but no NOE is observed for this interaction in molecules **26A** and **26B**. However, a significant NOE is observed with between protons H8 and H13 in molecules **26A** and **26B**, which is completely absent in compounds **26C** and **26D**. (see spectra in chapter 8). This result allows assigning the *syn* configuration at the stereocenters on the five-membered ring for compounds **26C** and **26D** and the anti one for compounds **26A** and **26B**.



We can conclude by the results obtained from the chemical shift displacement and the NOESY experiments that the absolute configuration of the all-carbon quaternary stereocenter is S (as drawn in the scheme).

2) Assignment of the absolute configuration by ^{1}HNMR chemical shift displacement.

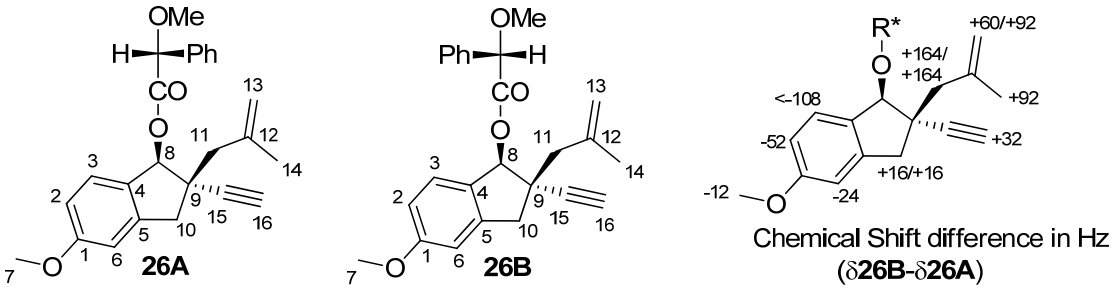


Favored conformation

The analysis of the chemical shift displacement is based on the work of Trost and co-workers, who showed that methyl-mandelic acid esters strongly favor a specific conformation as shown above.[22]

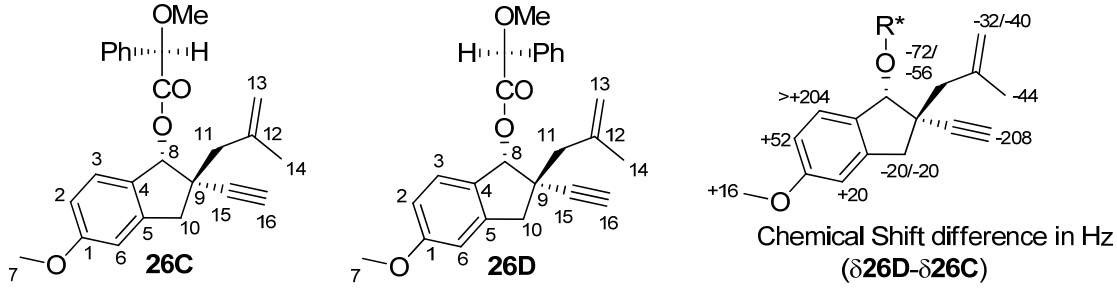
Analysis of the anti-pair: 26A/26B

[22] Trost, B. M.; Belletire, J. L.; Godleski, S.; McDougal, P. G.; Balkovec, J. M.; Baldwin, J. J.; Christy, M. E.; Ponticello, G. S.; Varga, S. L.; Springer, J. P. *J. Org. Chem* **1986**, *51*, 2370.



The chemical shift differences between **26A** and **26B** (measured in Hz for the difference of chemical shift for the signals δ**26B**-δ**26A**) is in full agreement with the drawn configuration. In particular, both protons on C11 are strongly shielded by the phenyl group on **26A** and have a lower chemical shift, whereas the proton on C3 is shielded in **26B**.[23]

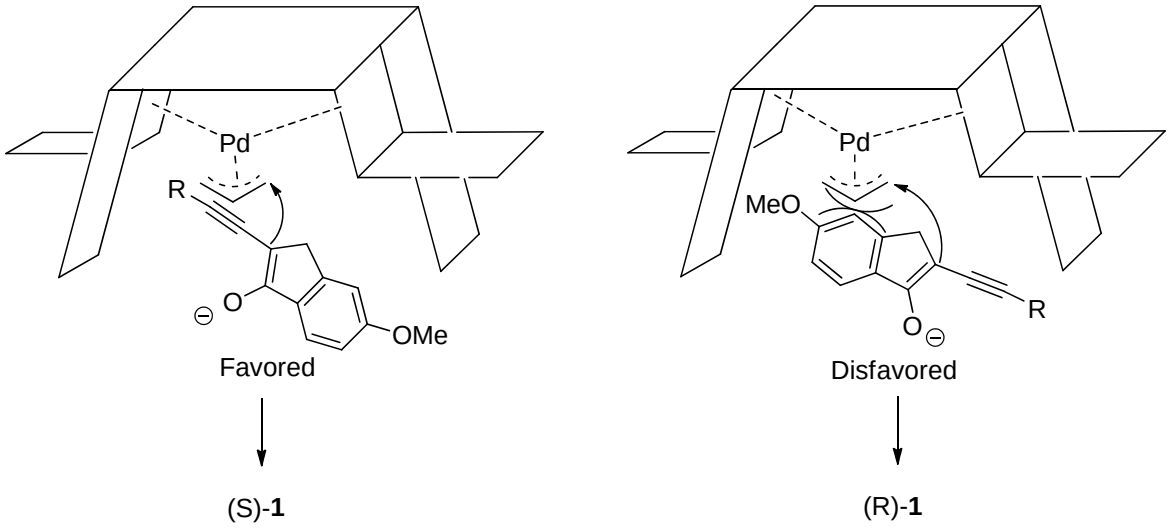
Analysis of the syn-pair: 31C/31D



The chemical shift differences between **26D** and **26C** (measured in Hz for the difference of chemical shift for the signals δ**26D**-δ**26C**) is in full agreement with the drawn configuration. In particular, the proton on C3 is strongly shielded by the phenyl group on **26C** and has a lower chemical shift, whereas the acetylene proton on C16 is shielded in **26D**.[23] Finally, the relative intensity of the anisotropy effect further confirm the assignment of the relative configuration by NOESY.

[23] The exact value of the chemical shift difference at H3 could not be determined due to signal overlap.

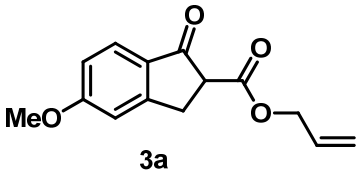
7.2 Model for the absolute stereochemistry



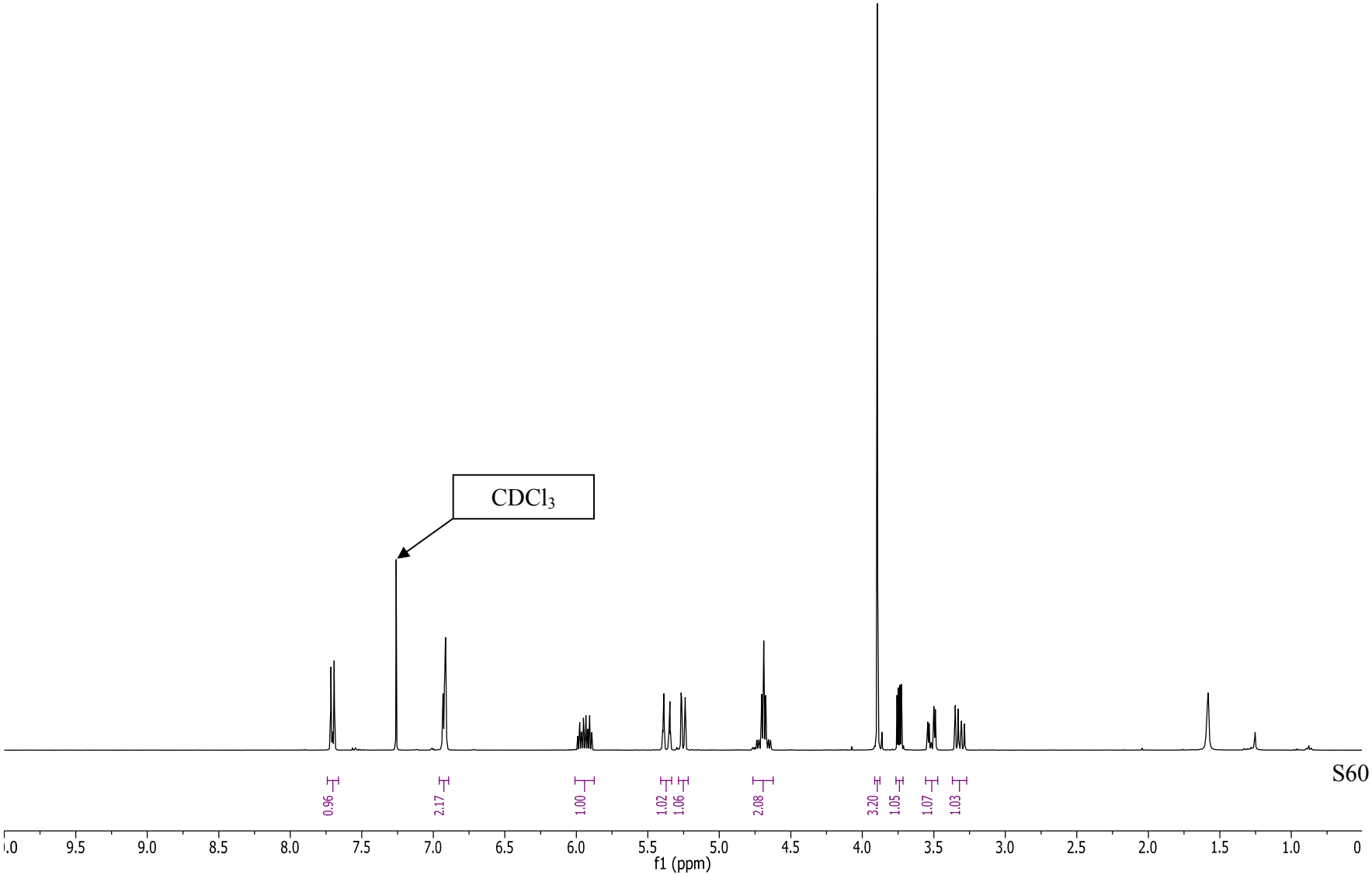
The predictive model of Trost and co-workers can be used in the developed reaction.[24]

[24] Trost, B. M.; Xu, J.; Schmidt, T. *J. Am. Chem. Soc.* **2009**, *131*, 18343.

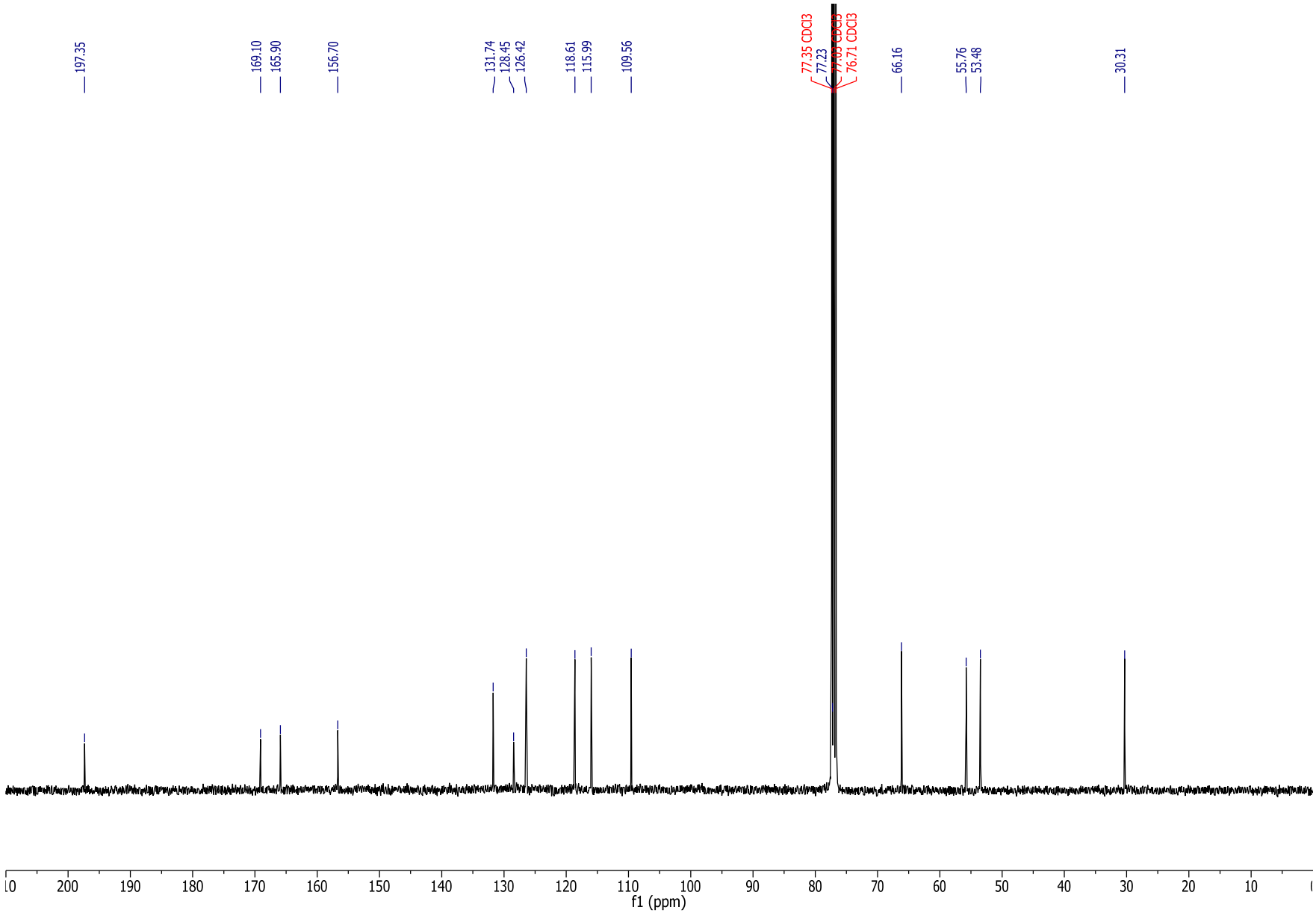
8. Spectra

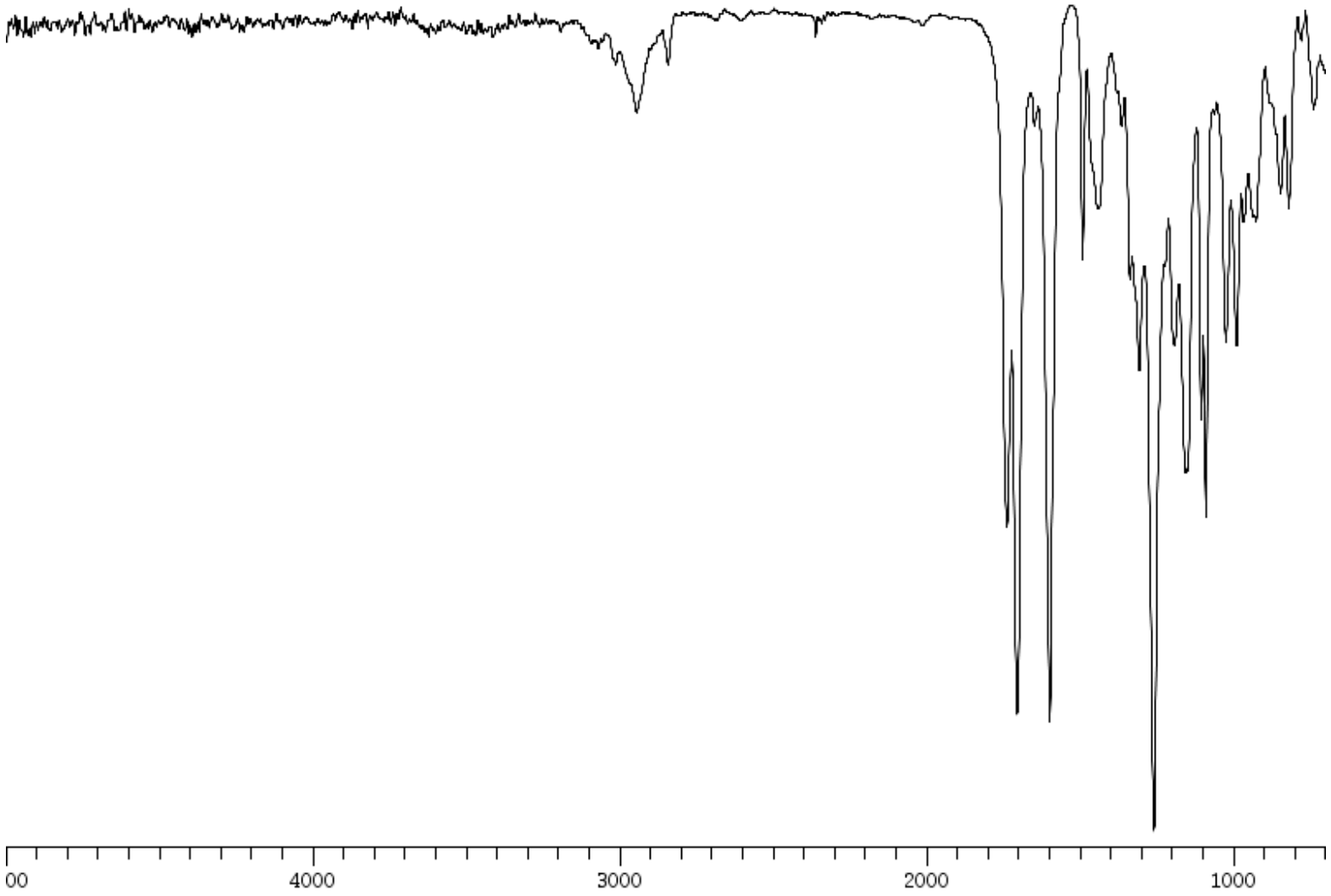


3a

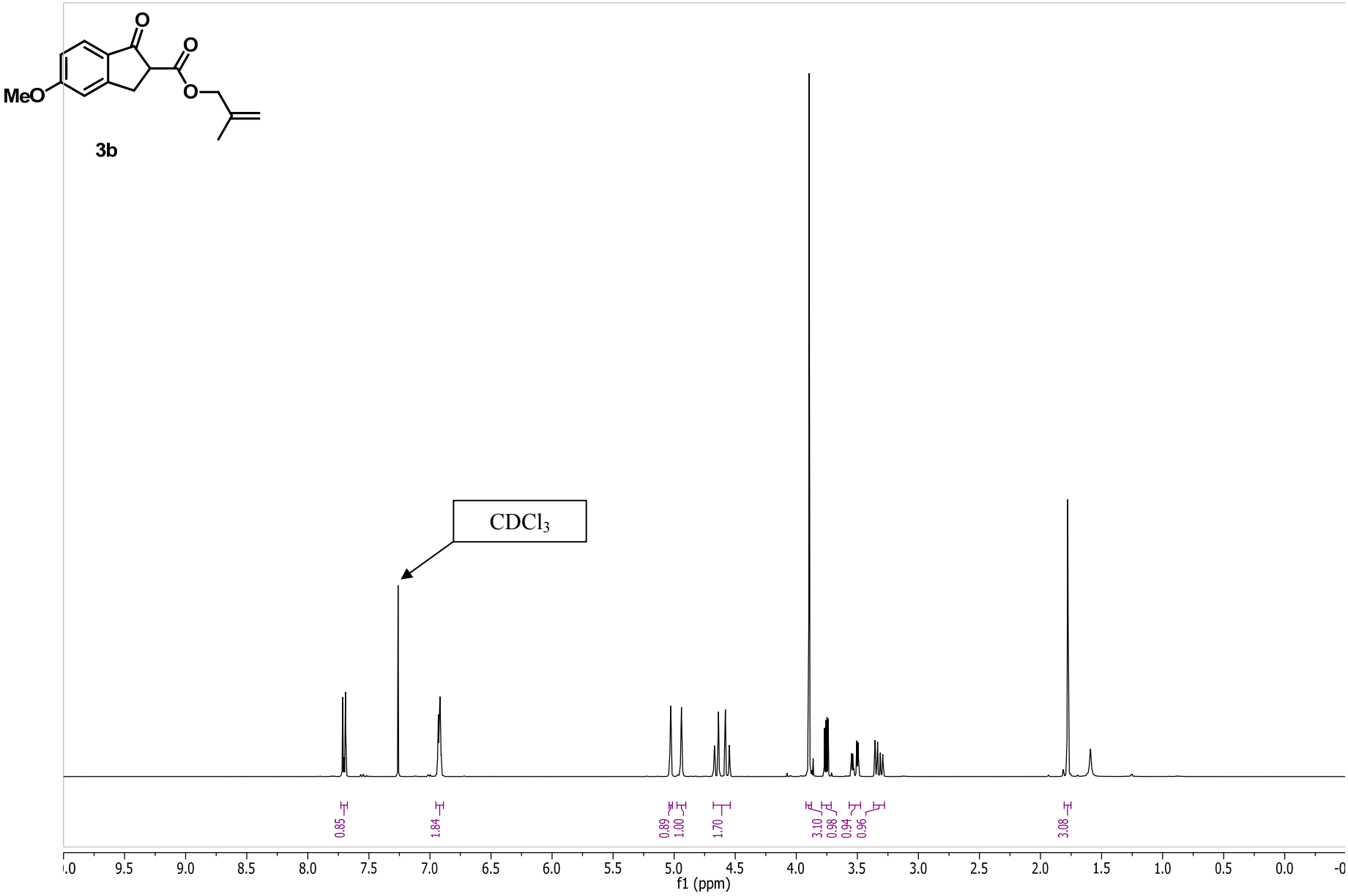


CDCl3
400 MHz

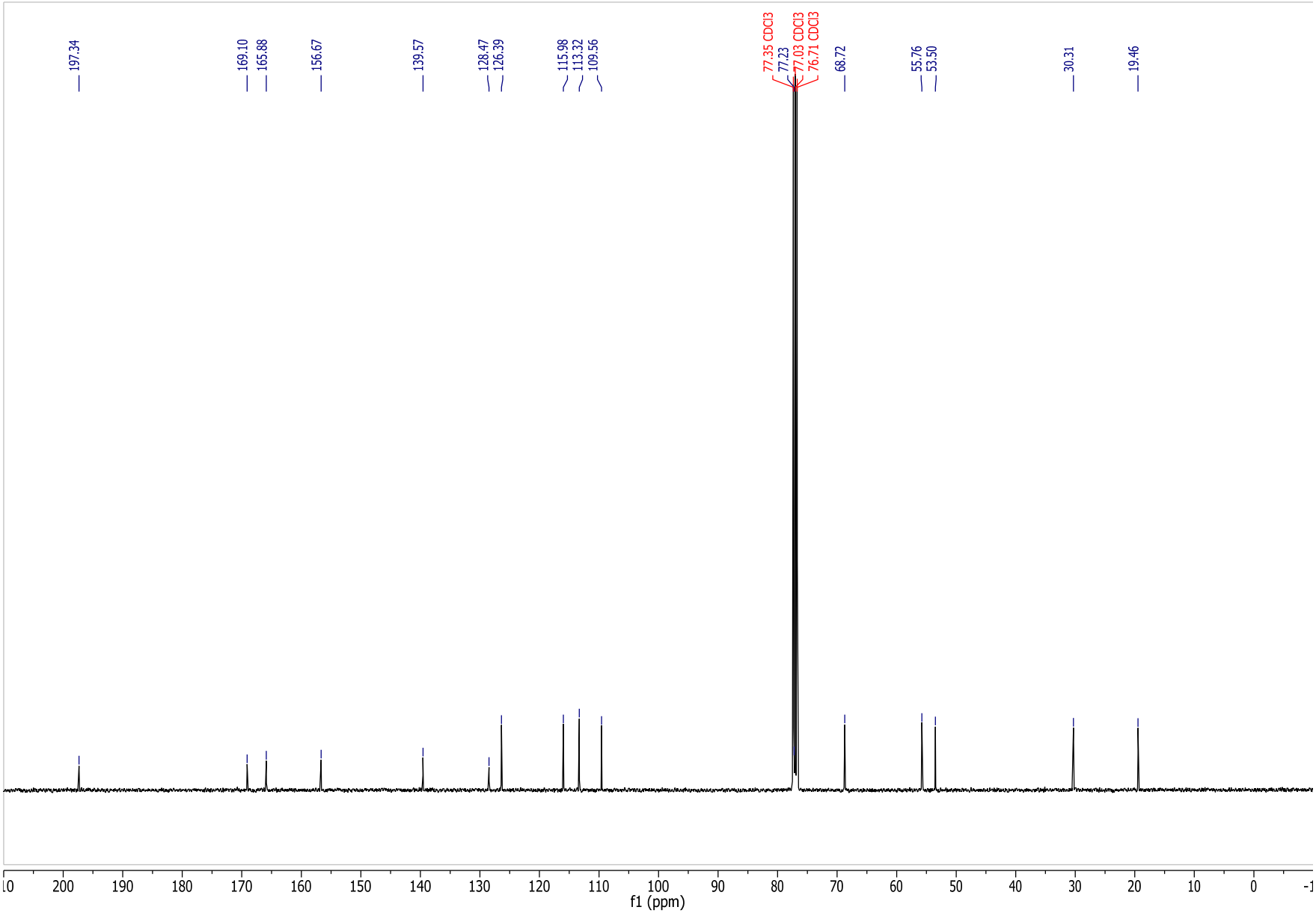

CDCl3
100.1 MHz
197.35
169.10
165.90
156.70
131.74
128.45
126.42
118.61
115.99
109.56
77.35 CDCl3
77.23
76.71 CDCl3
66.16
55.76
53.48
30.31
f1 (ppm)

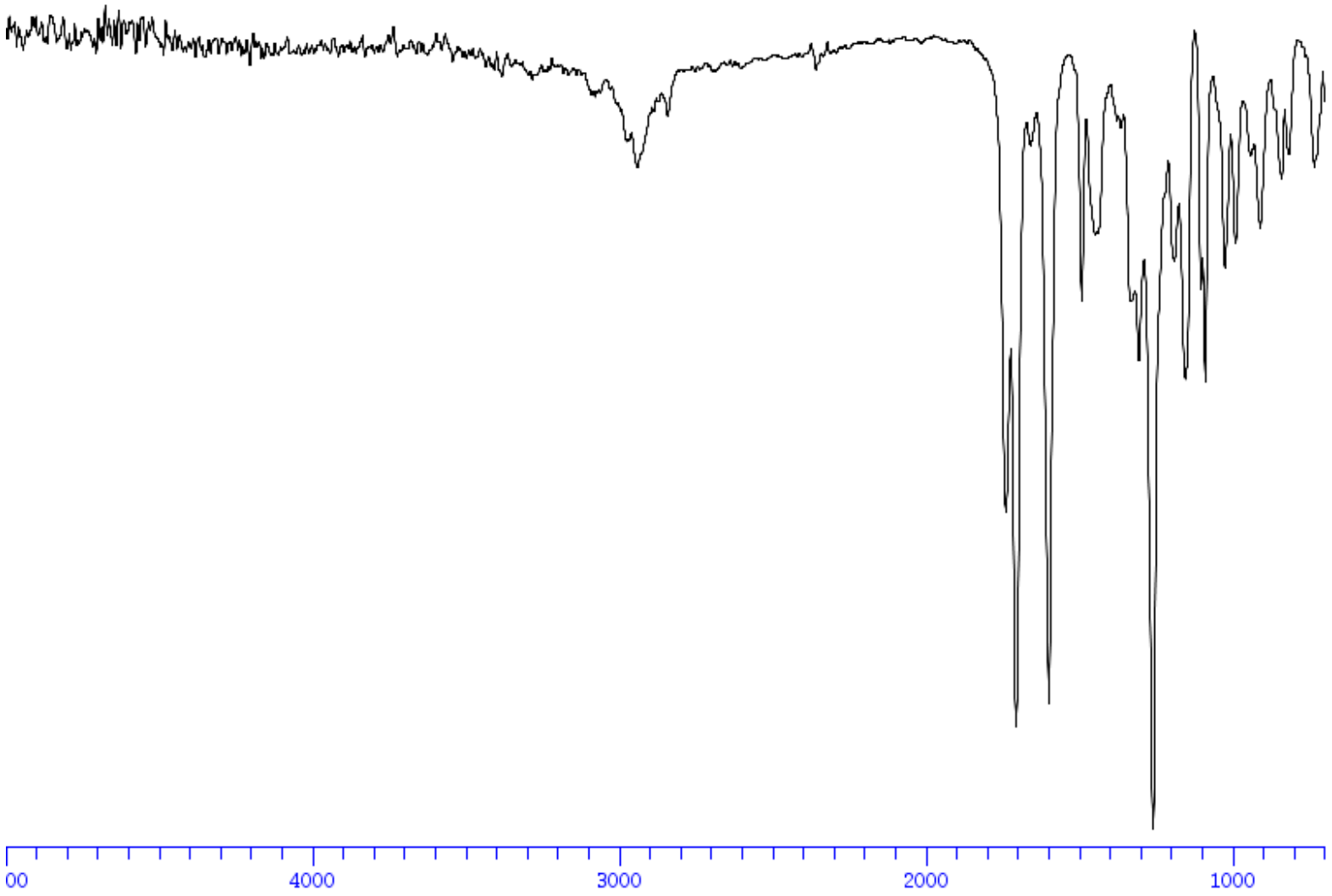

00
4000
3000
2000
1000

$CDCl_3$
400 MHz

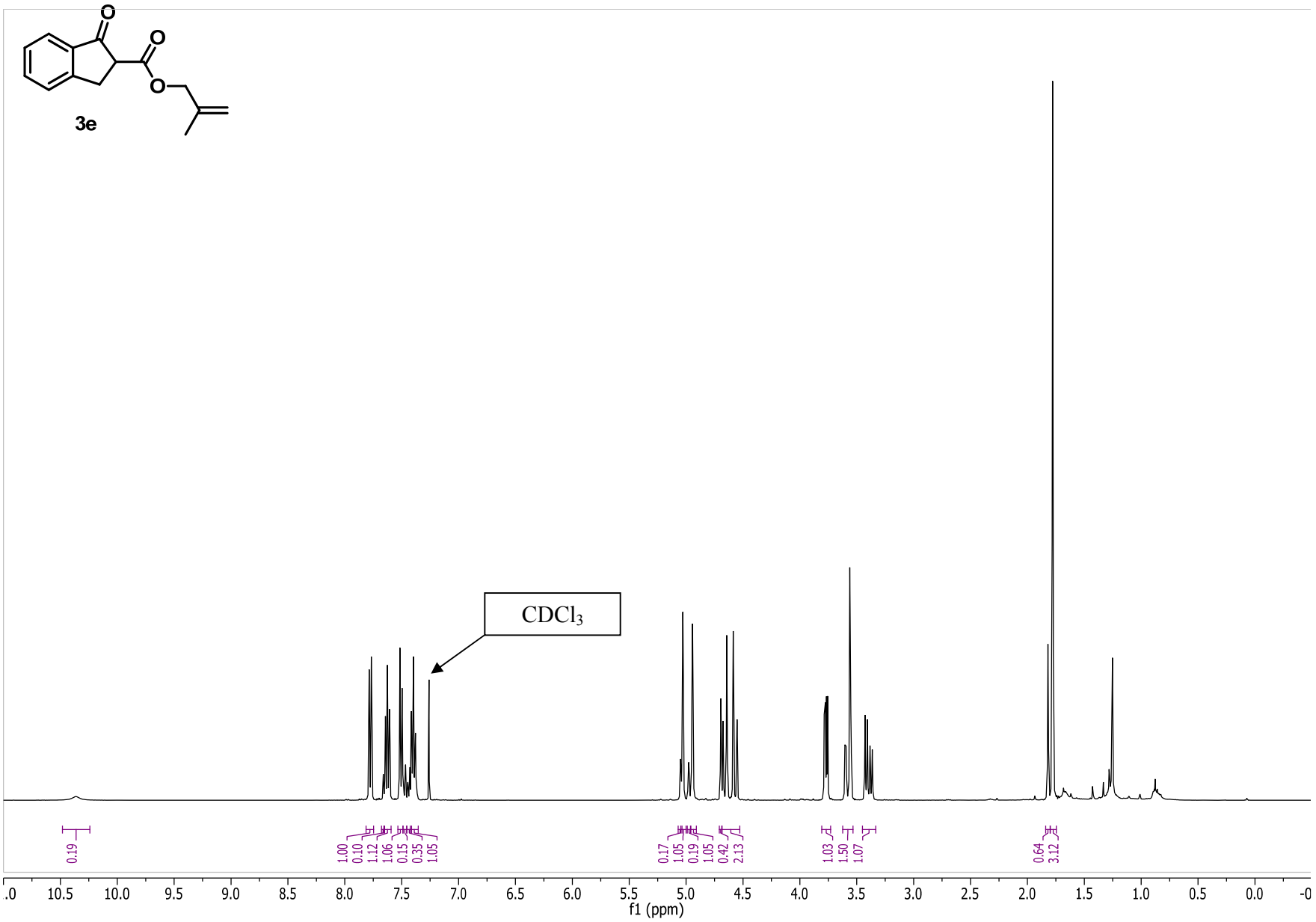


$CDCl_3$
100.1 MHz

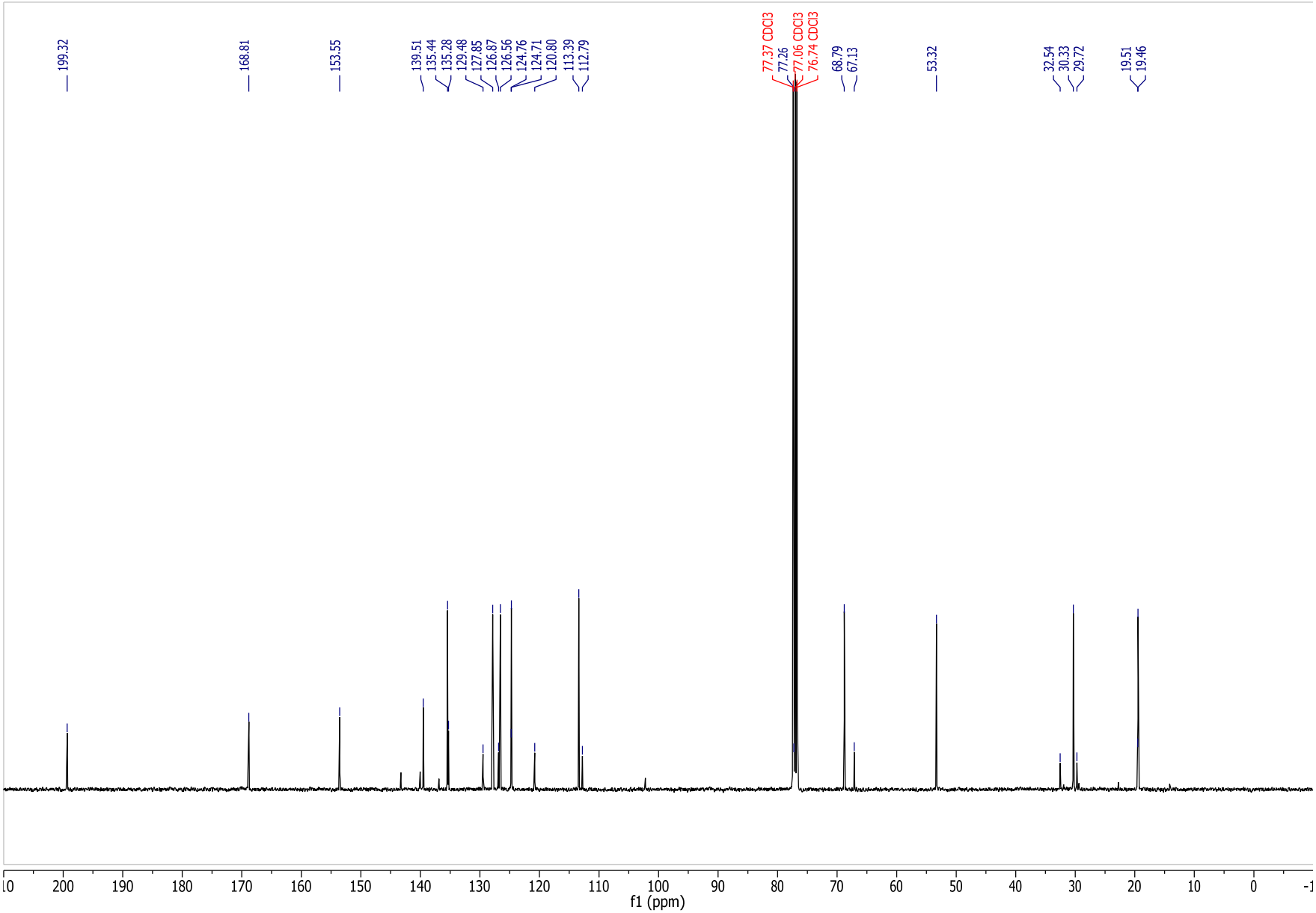


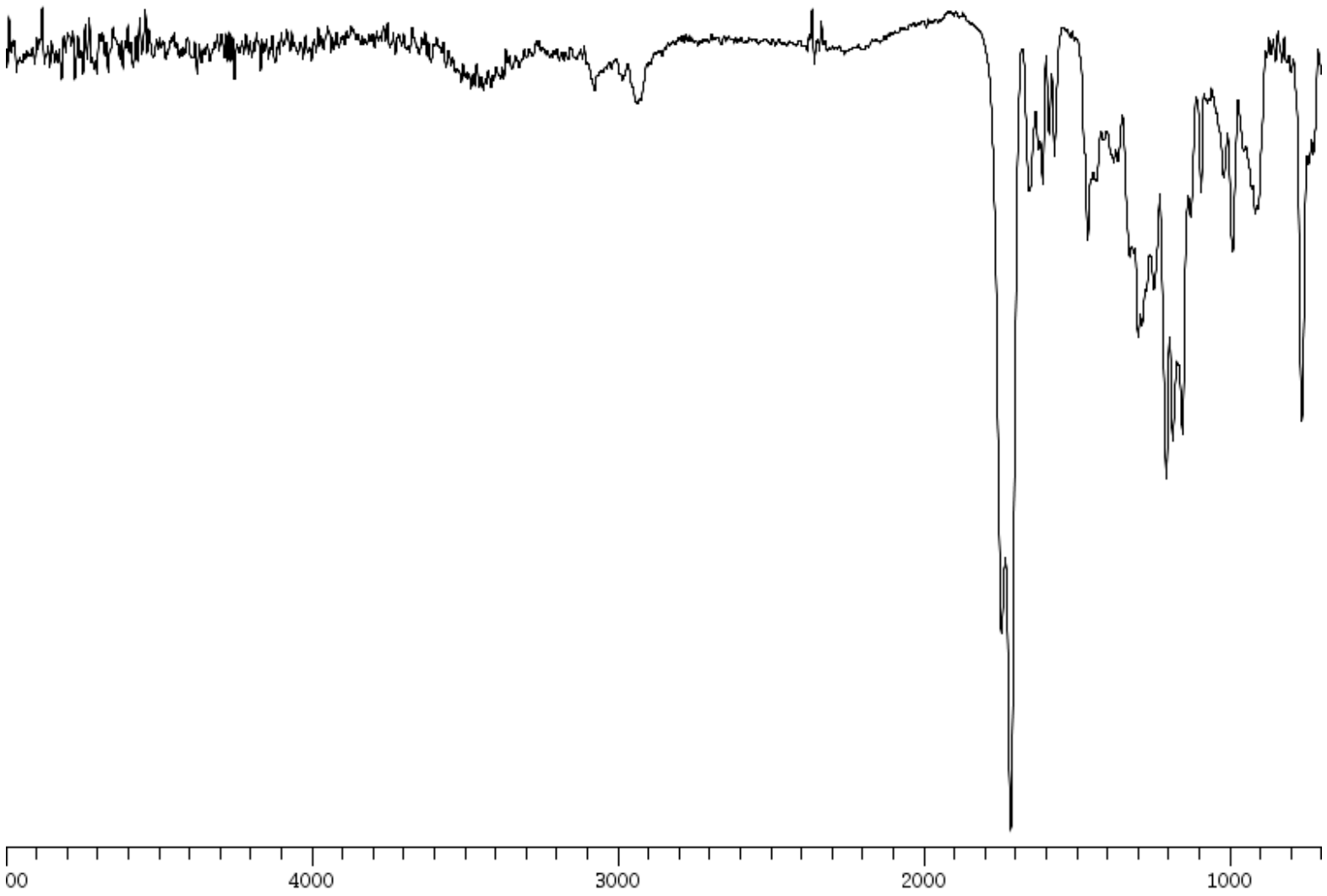

00
4000
3000
2000
1000

$CDCl_3$
400 MHz

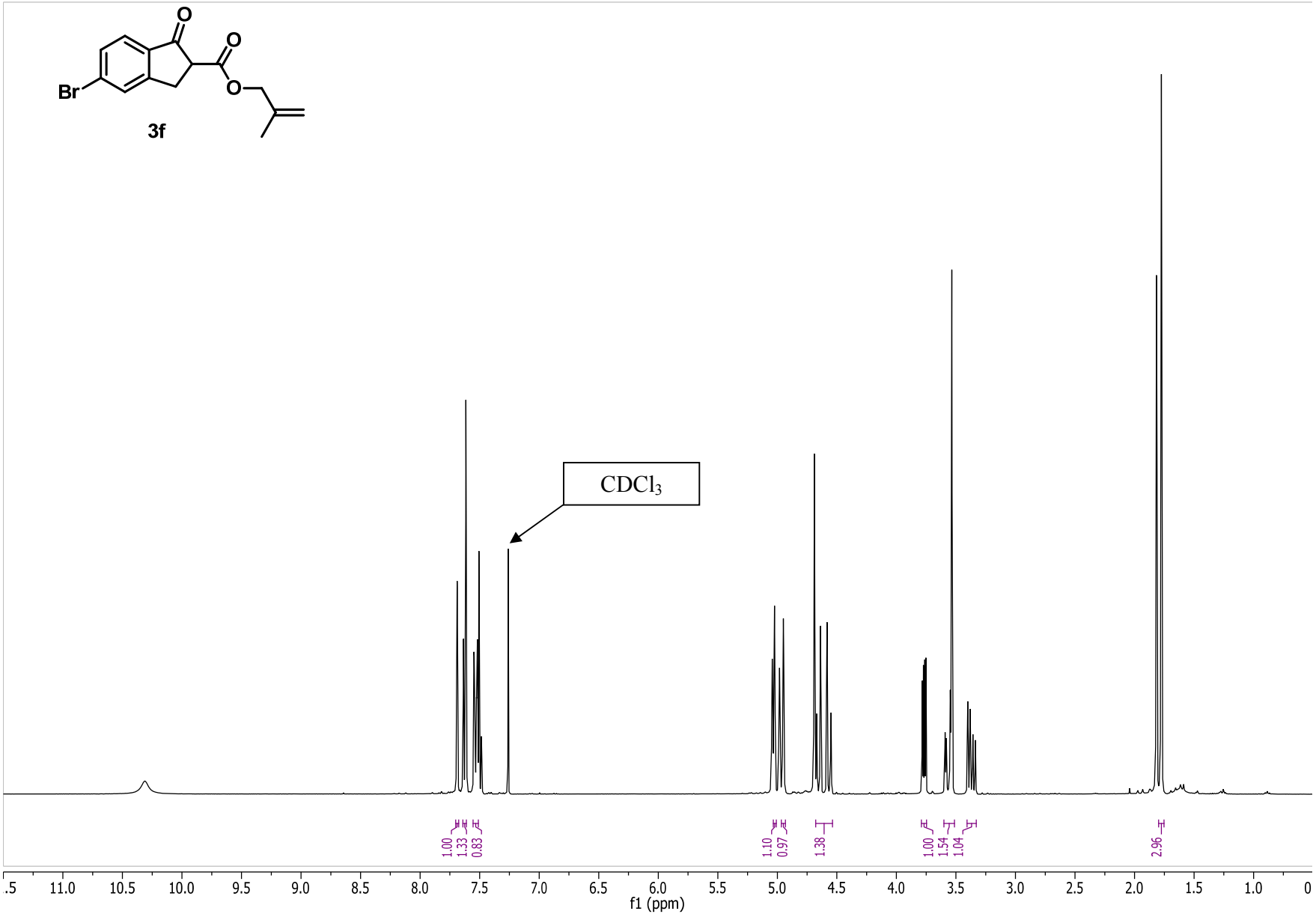


$CDCl_3$
100.1 MHz

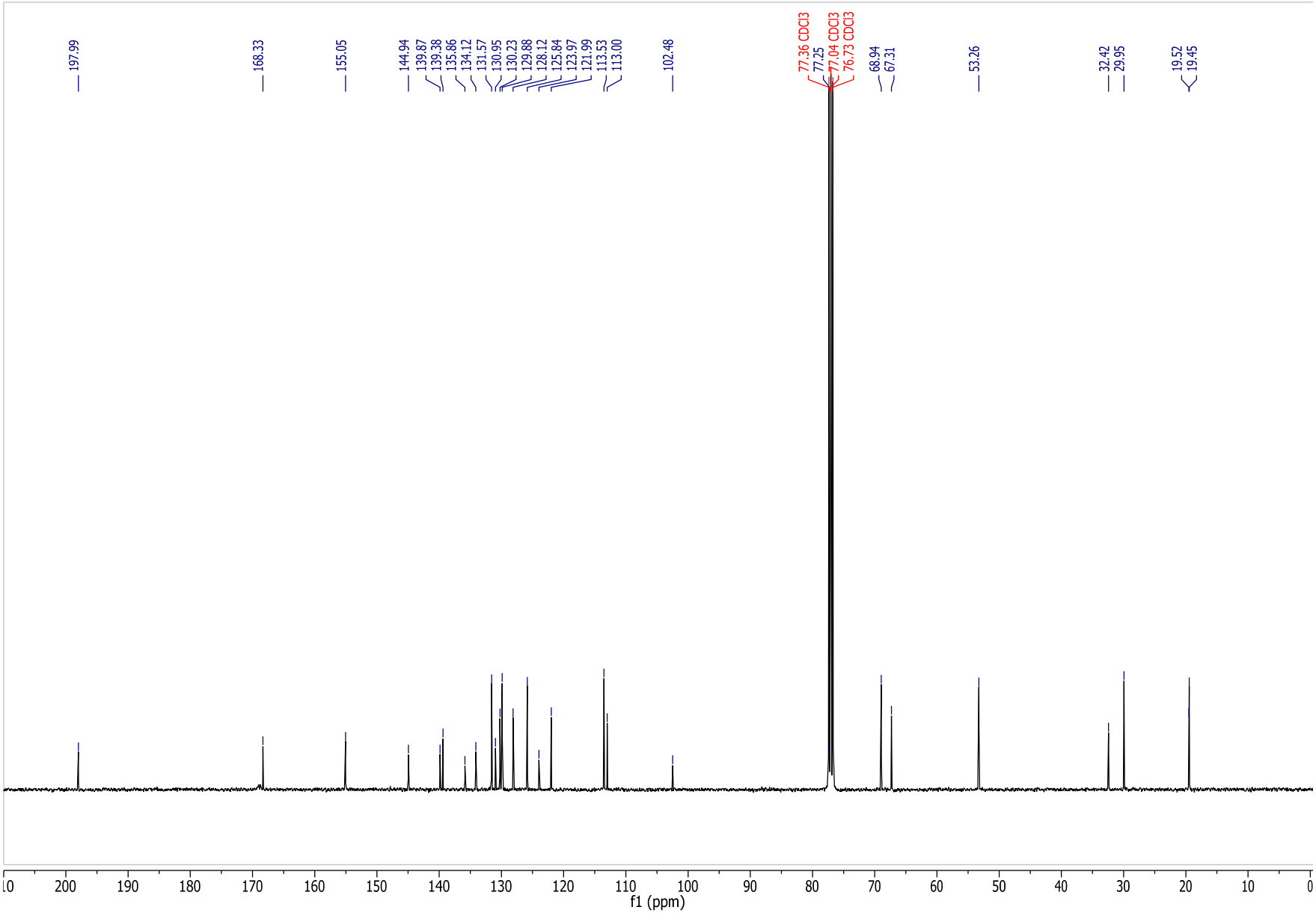


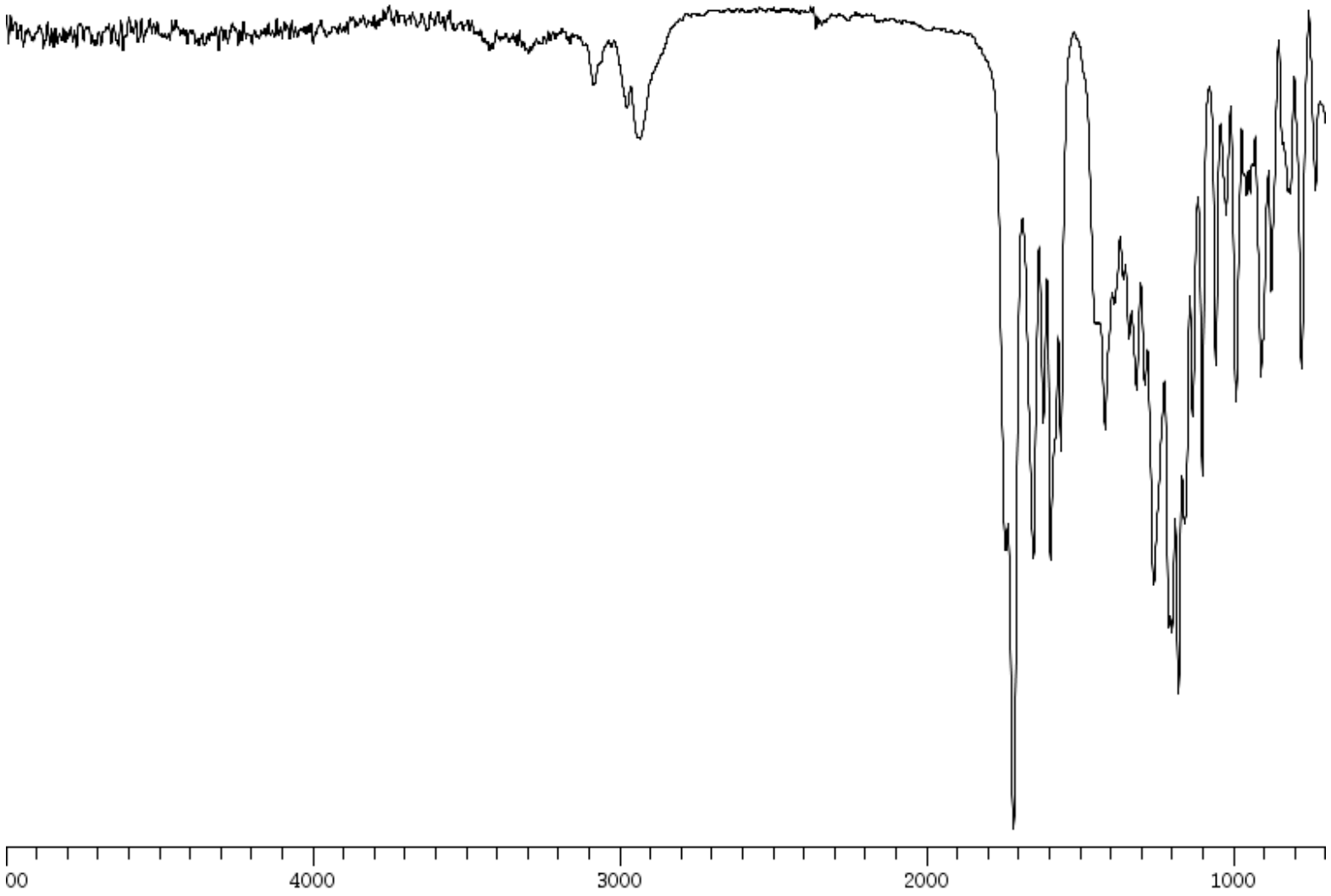

00
4000
3000
2000
1000

$CDCl_3$
400 MHz

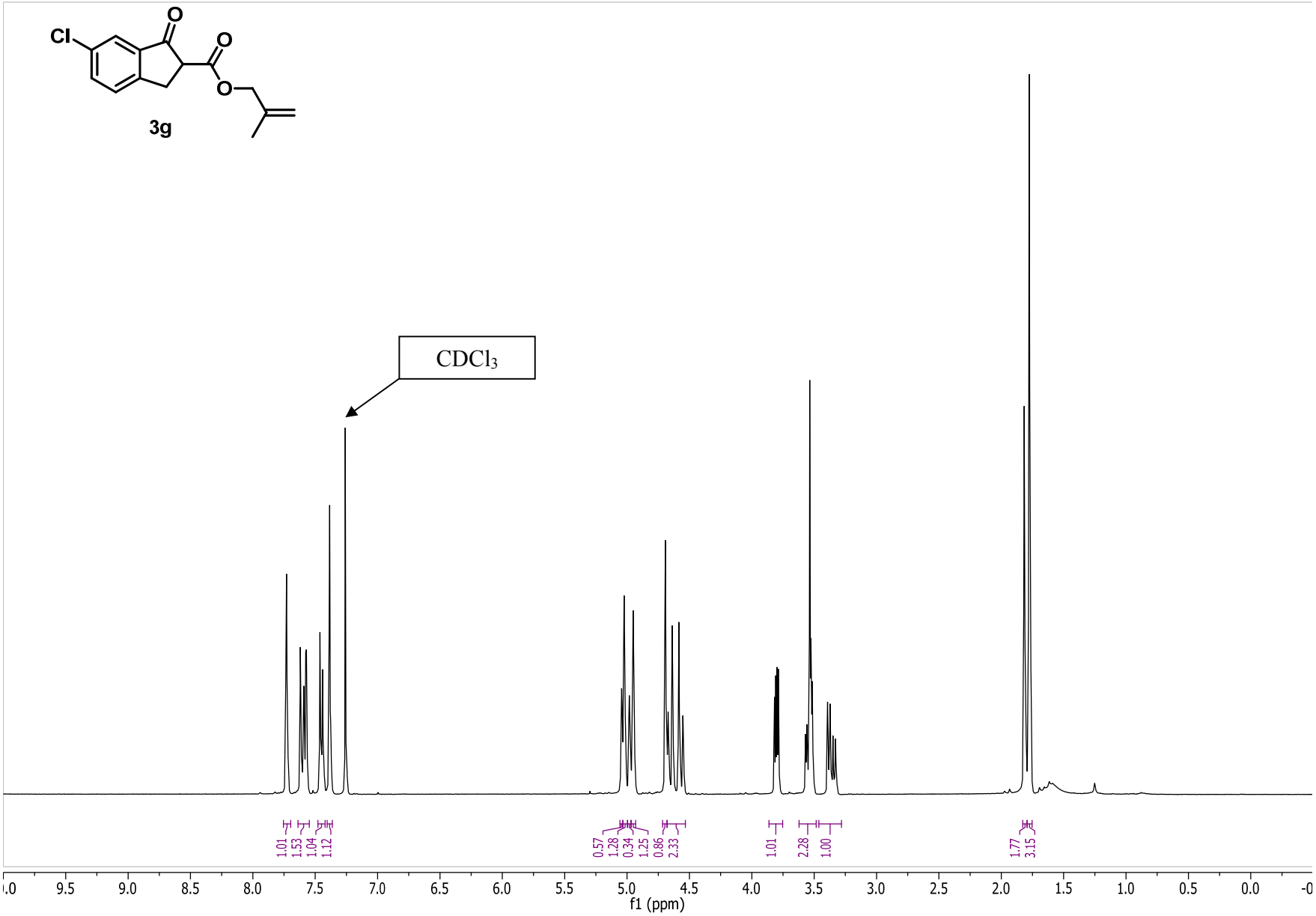


$CDCl_3$
100.1 MHz

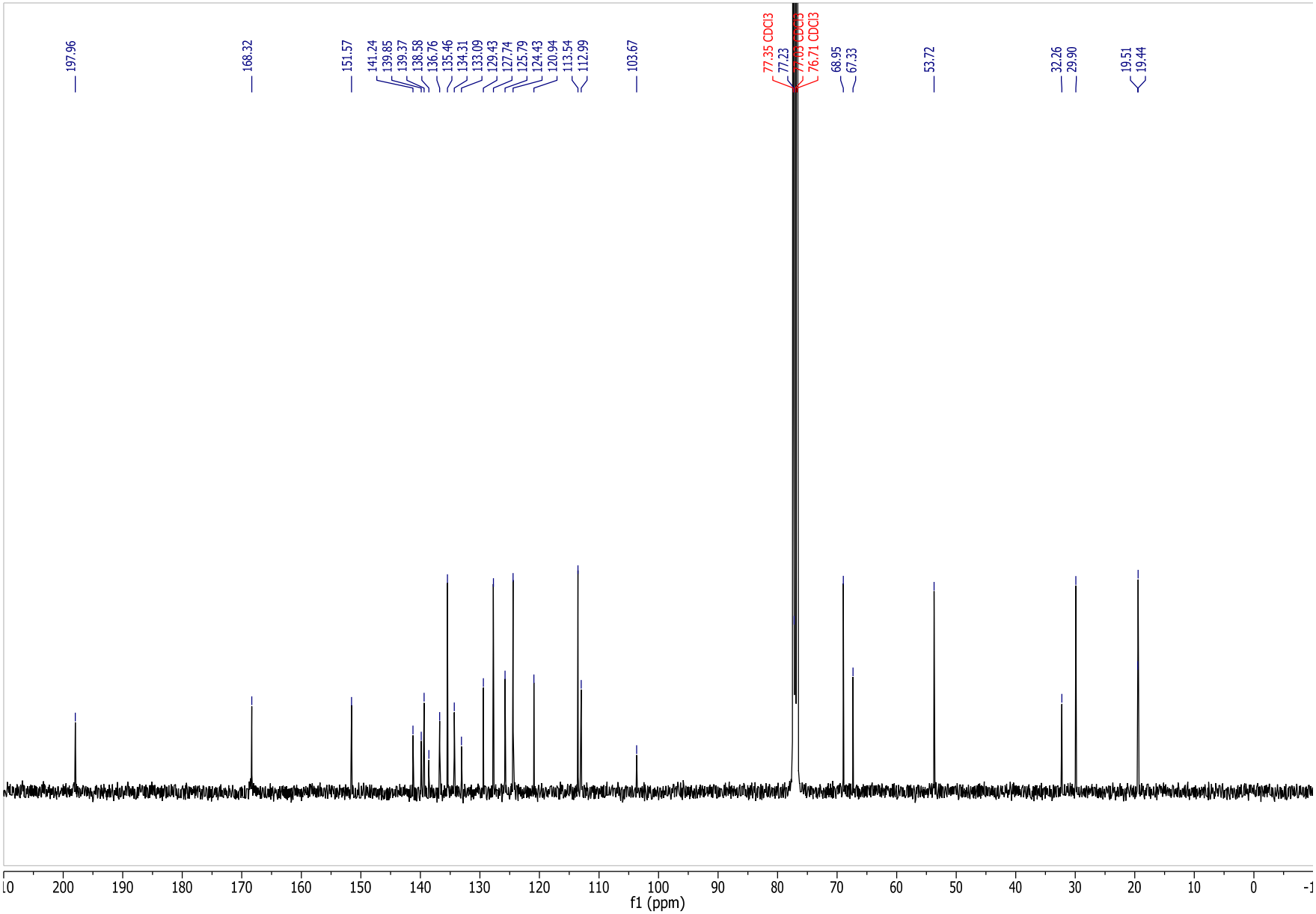


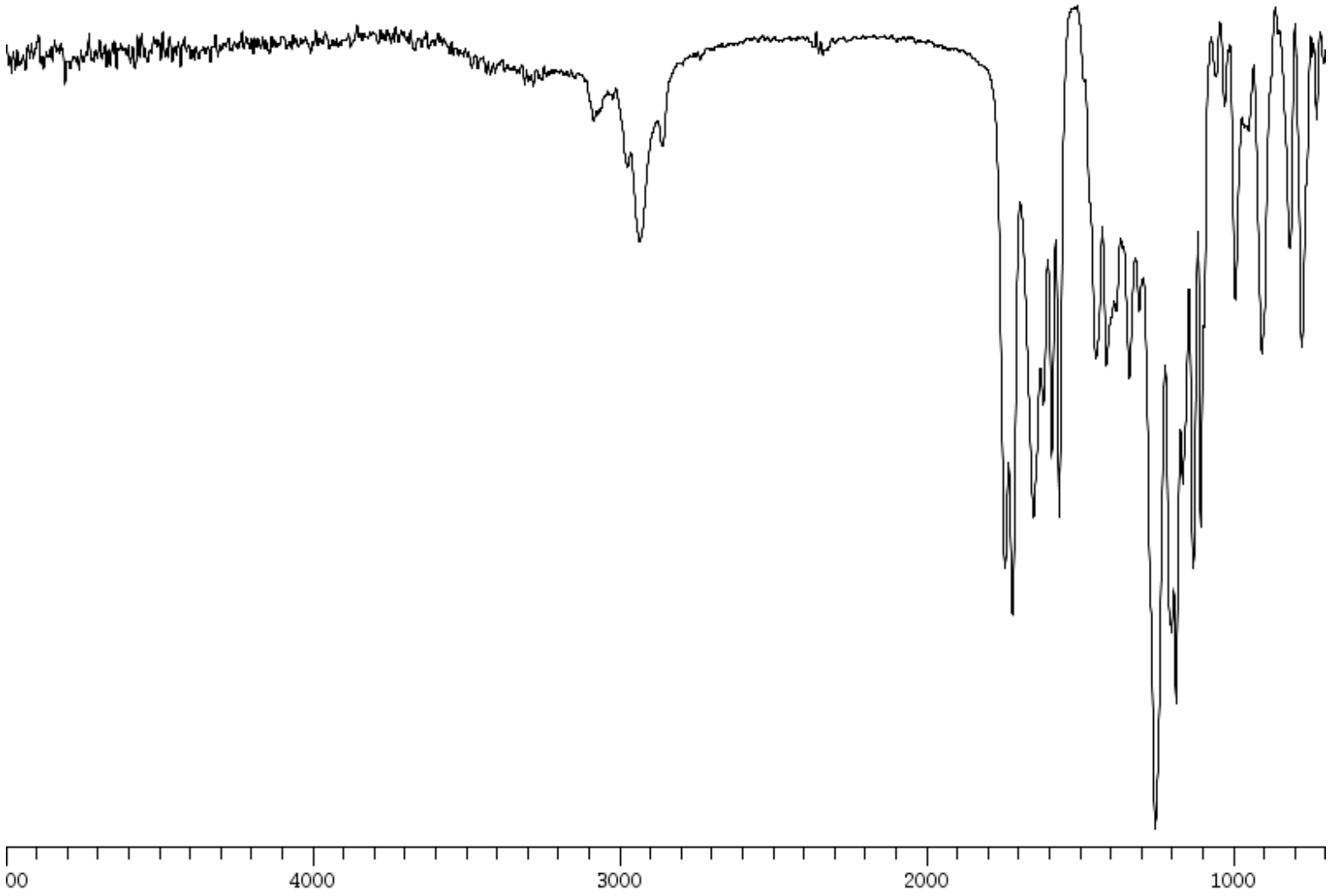

00
4000
3000
2000
1000

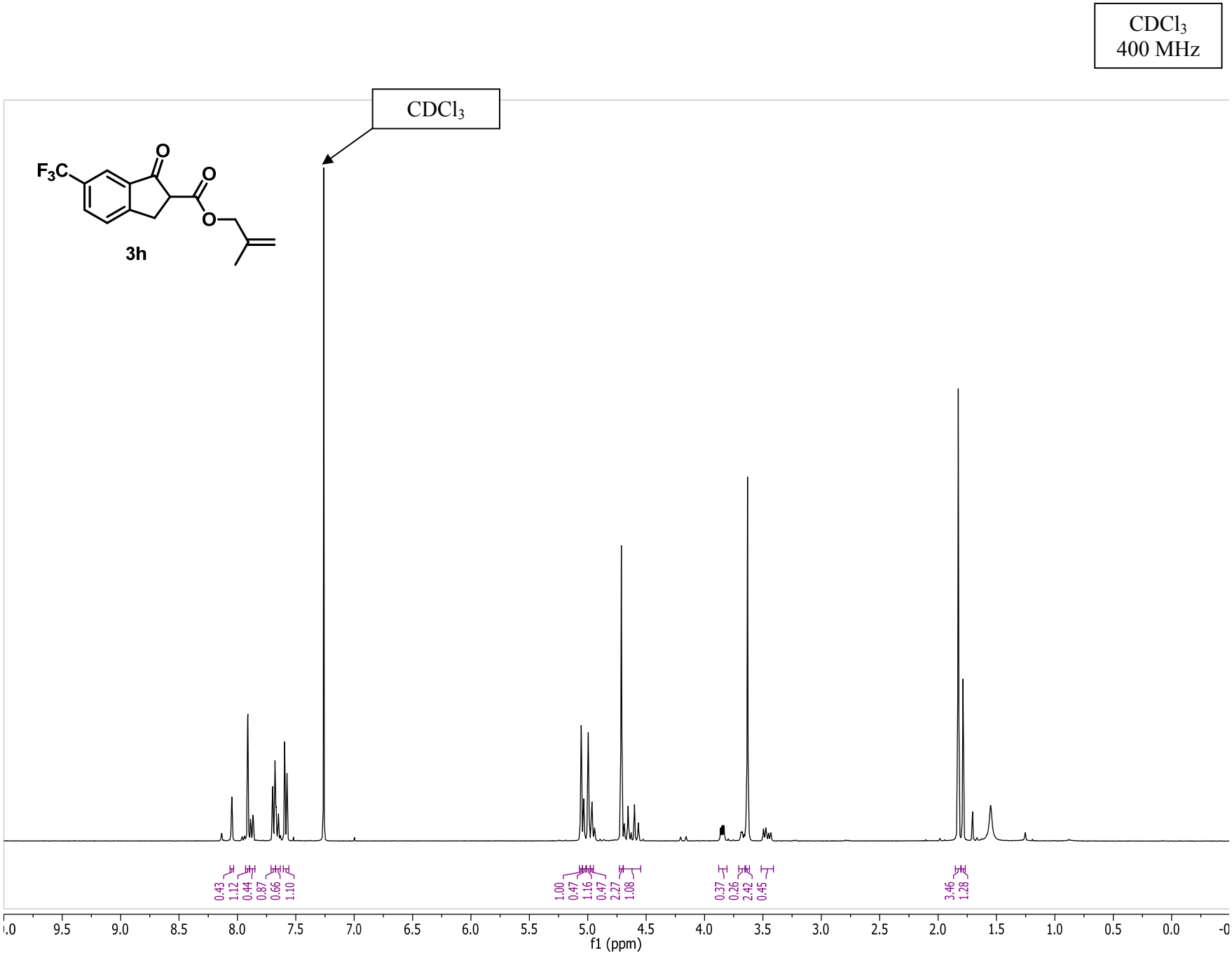
$CDCl_3$
400 MHz



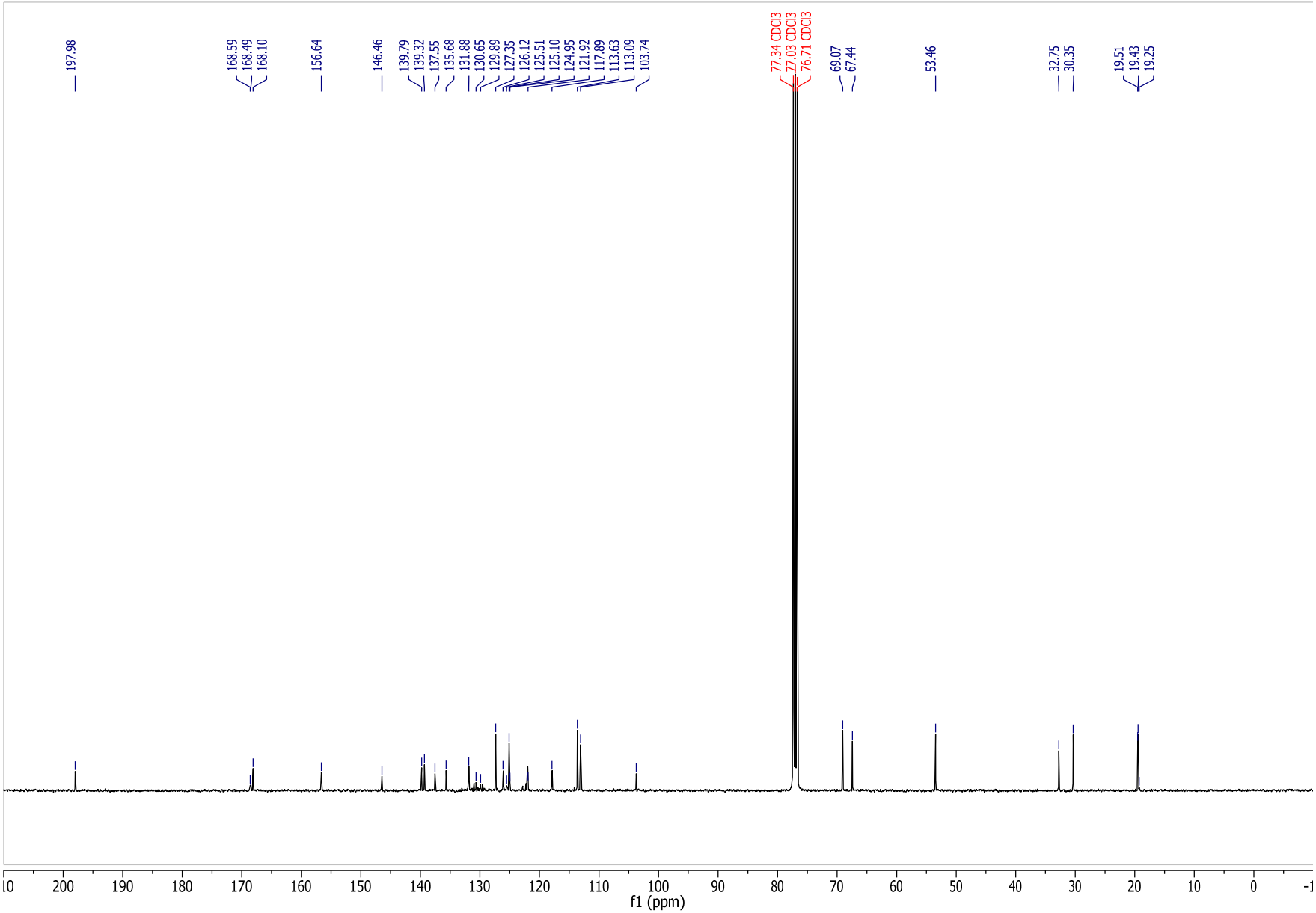
$CDCl_3$
100.1 MHz

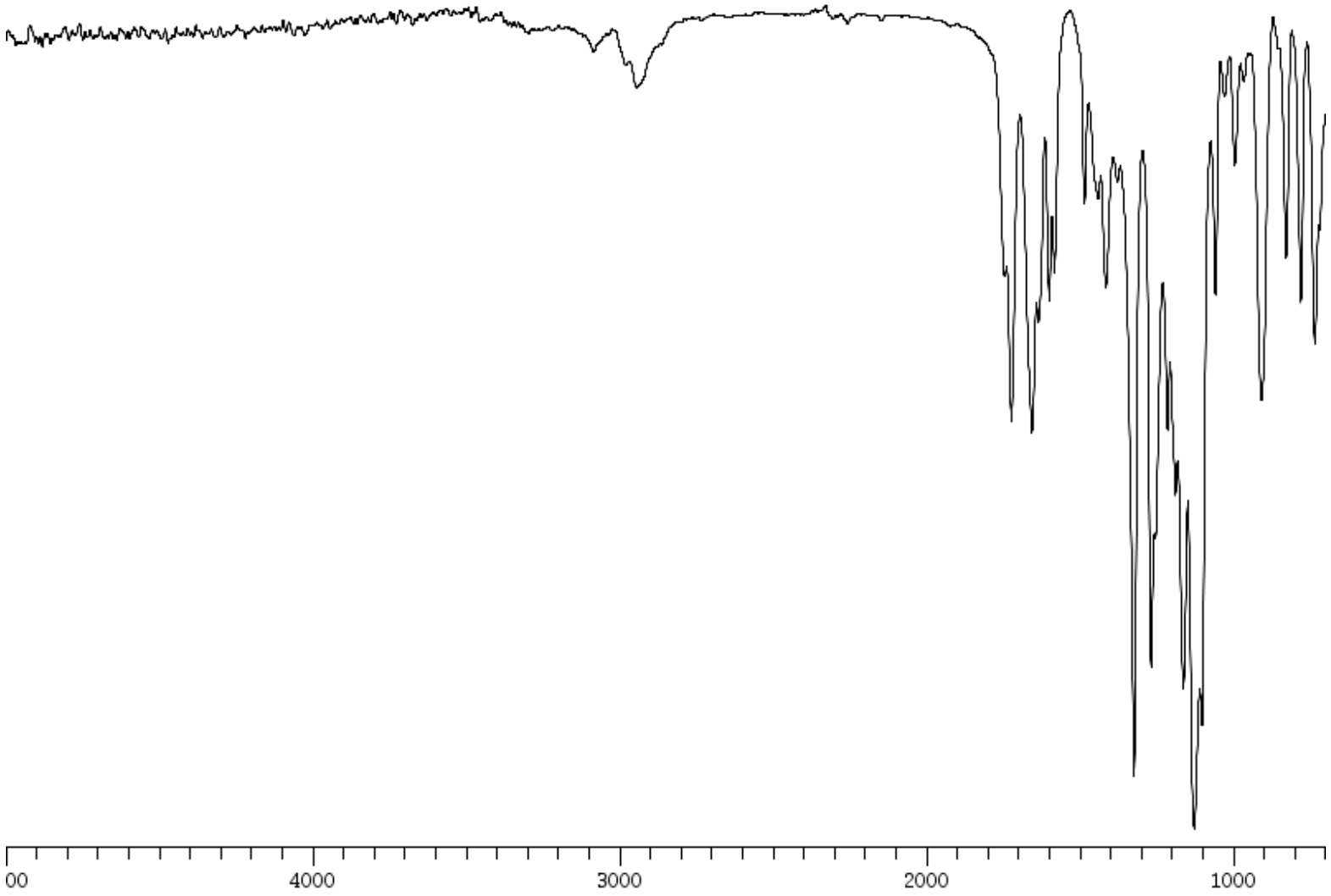


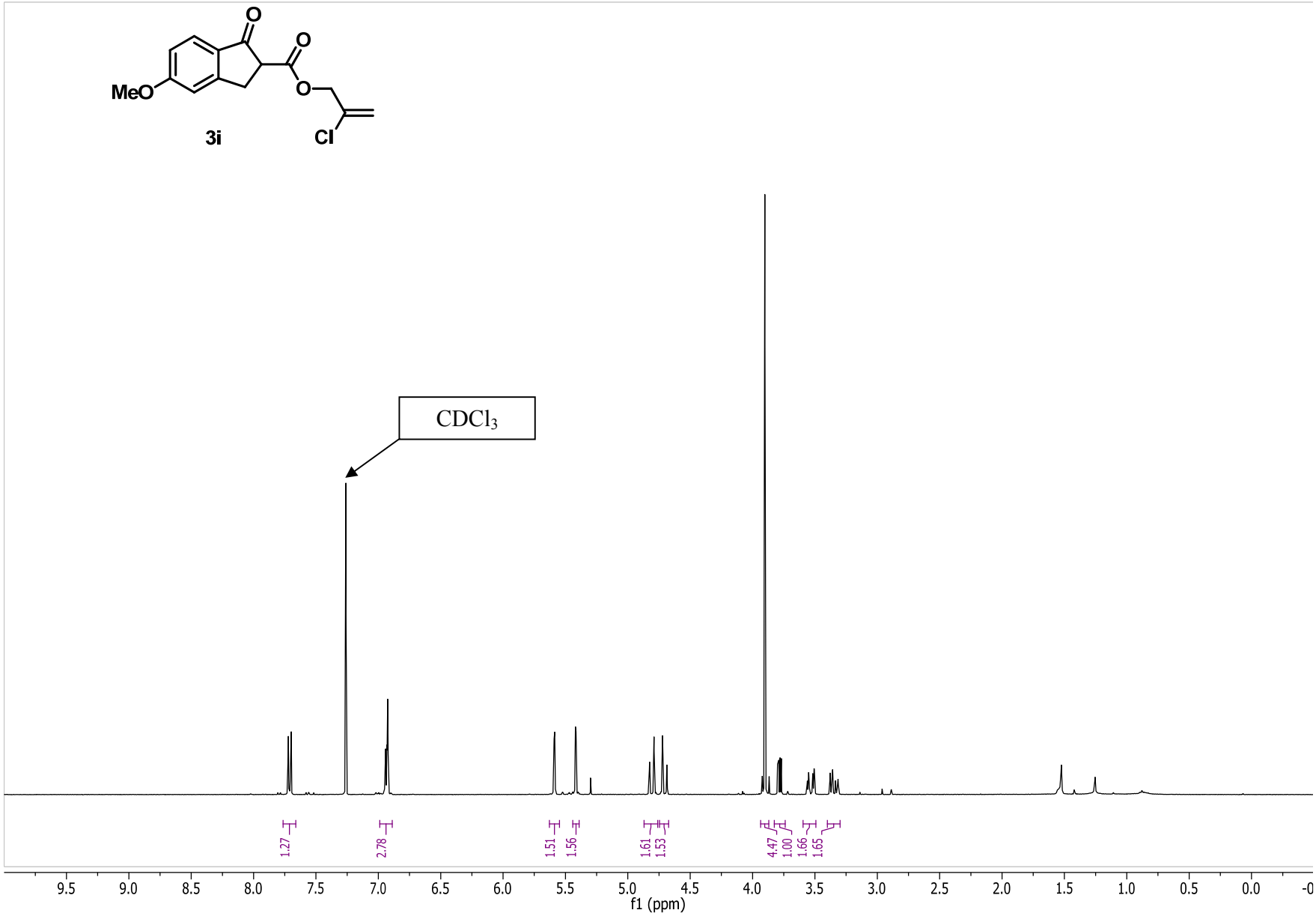

00
4000
3000
2000
1000


CDCl3
400 MHz
CDCl3
F3C
O
O
O
3h
0.43
1.12
0.44
0.87
0.66
1.10
1.00
0.47
1.16
0.47
2.27
1.08
0.37
0.26
2.42
0.45
3.46
1.28
f1 (ppm)

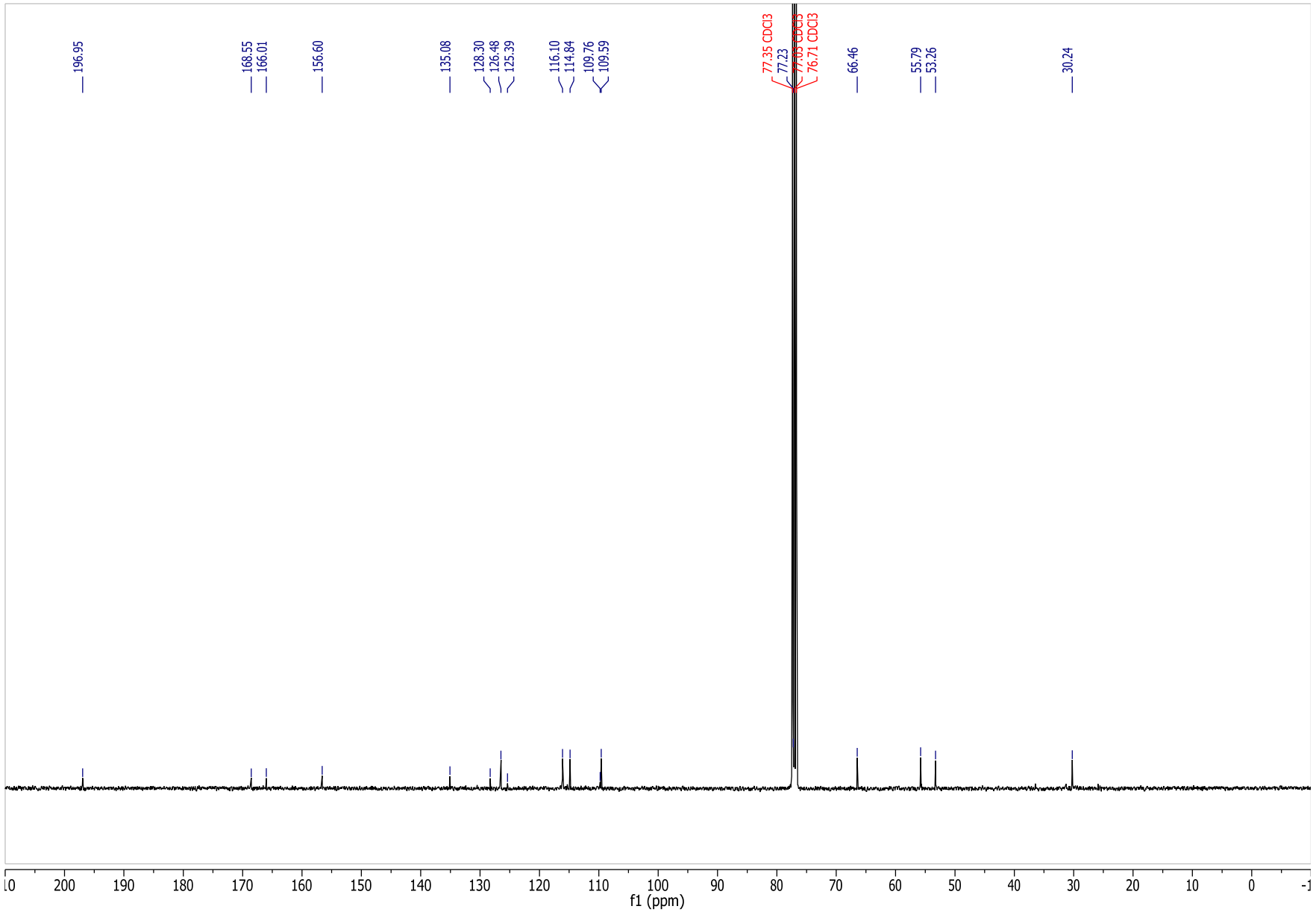
$CDCl_3$
100.1 MHz

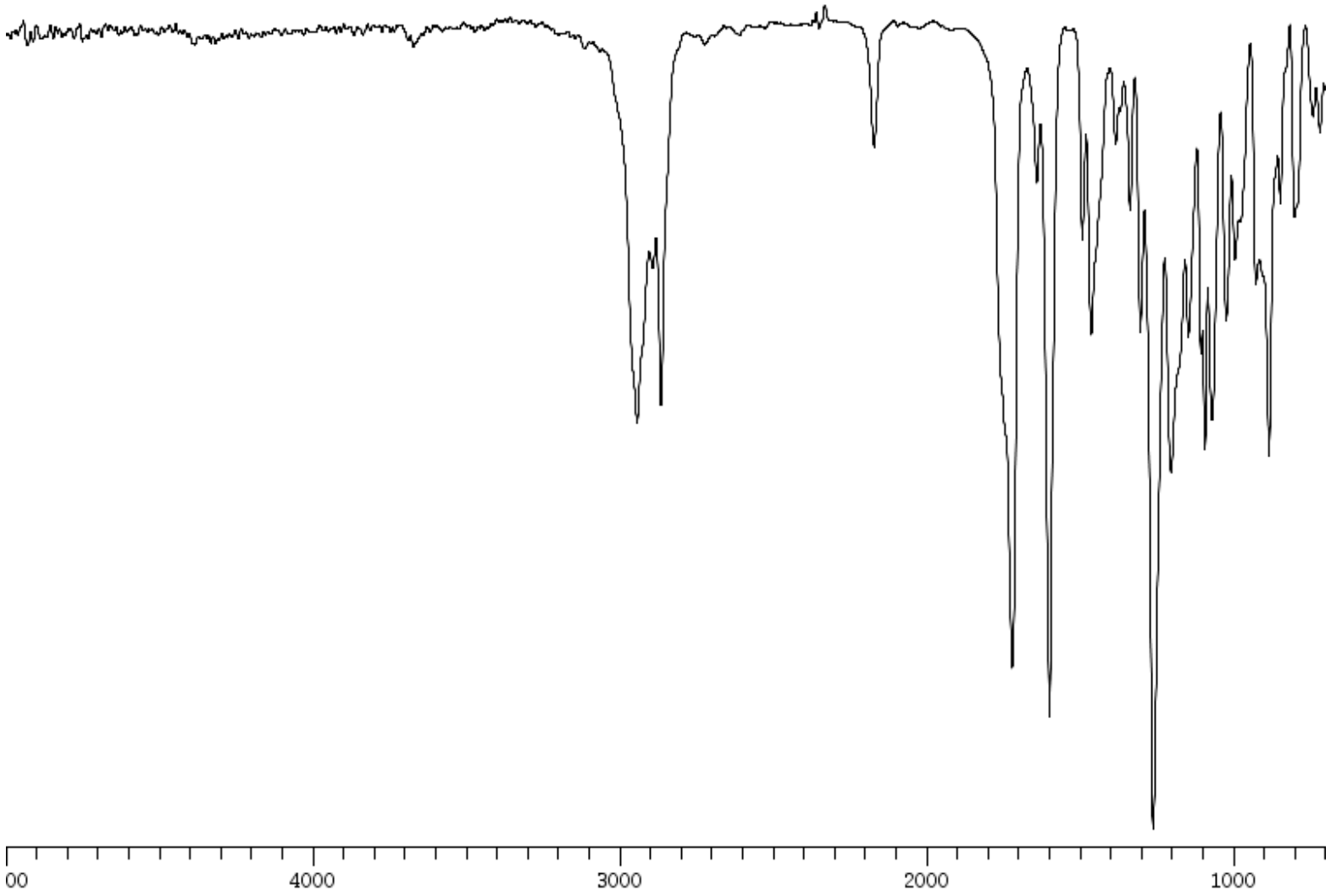



00
4000
3000
2000
1000

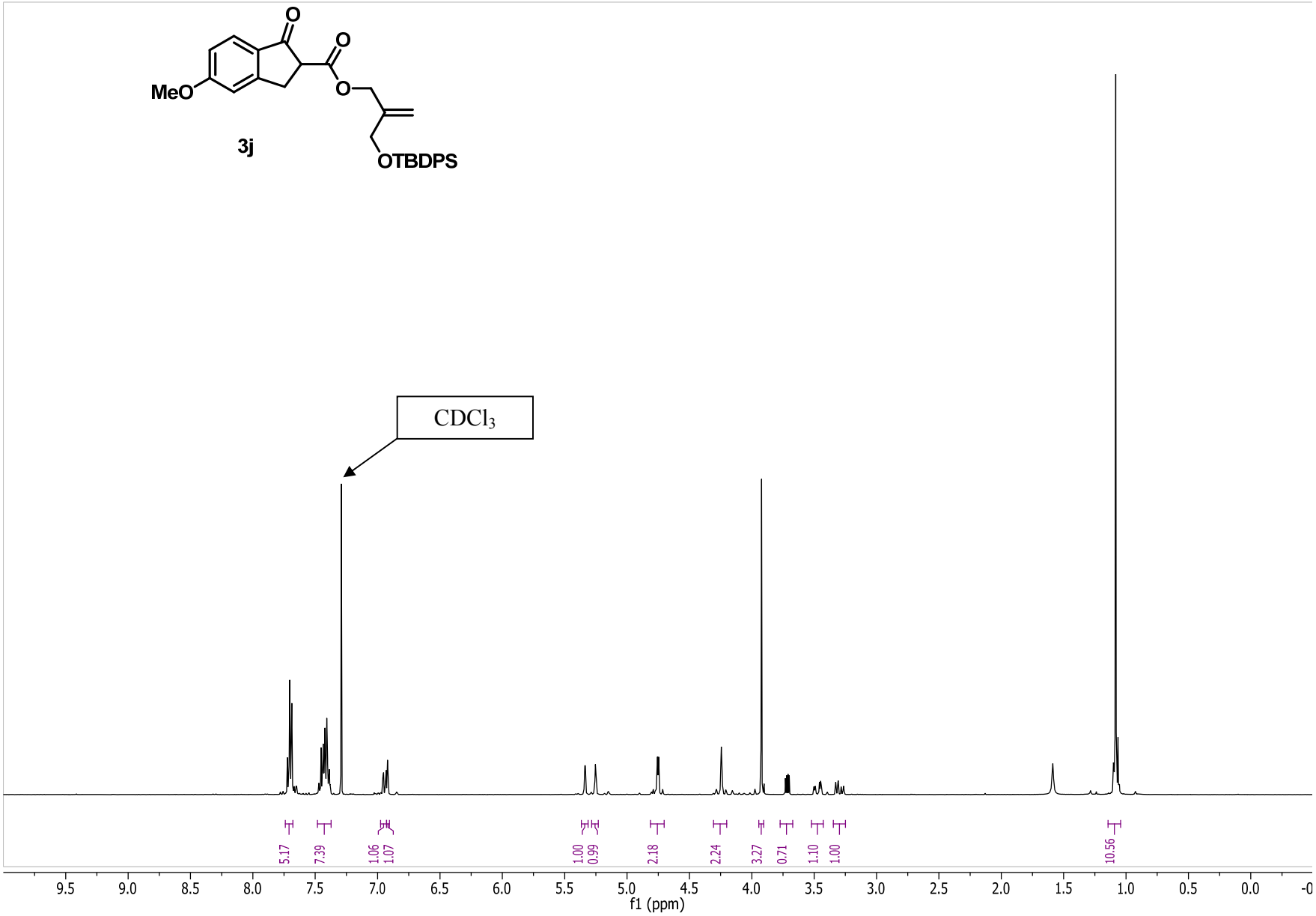

CDCl3
400 MHz
MeO
O
O
O
Cl
3i
CDCl3
1.27
2.78
1.51
1.56
1.61
1.53
4.47
1.00
1.66
1.65
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

$CDCl_3$
100.1 MHz

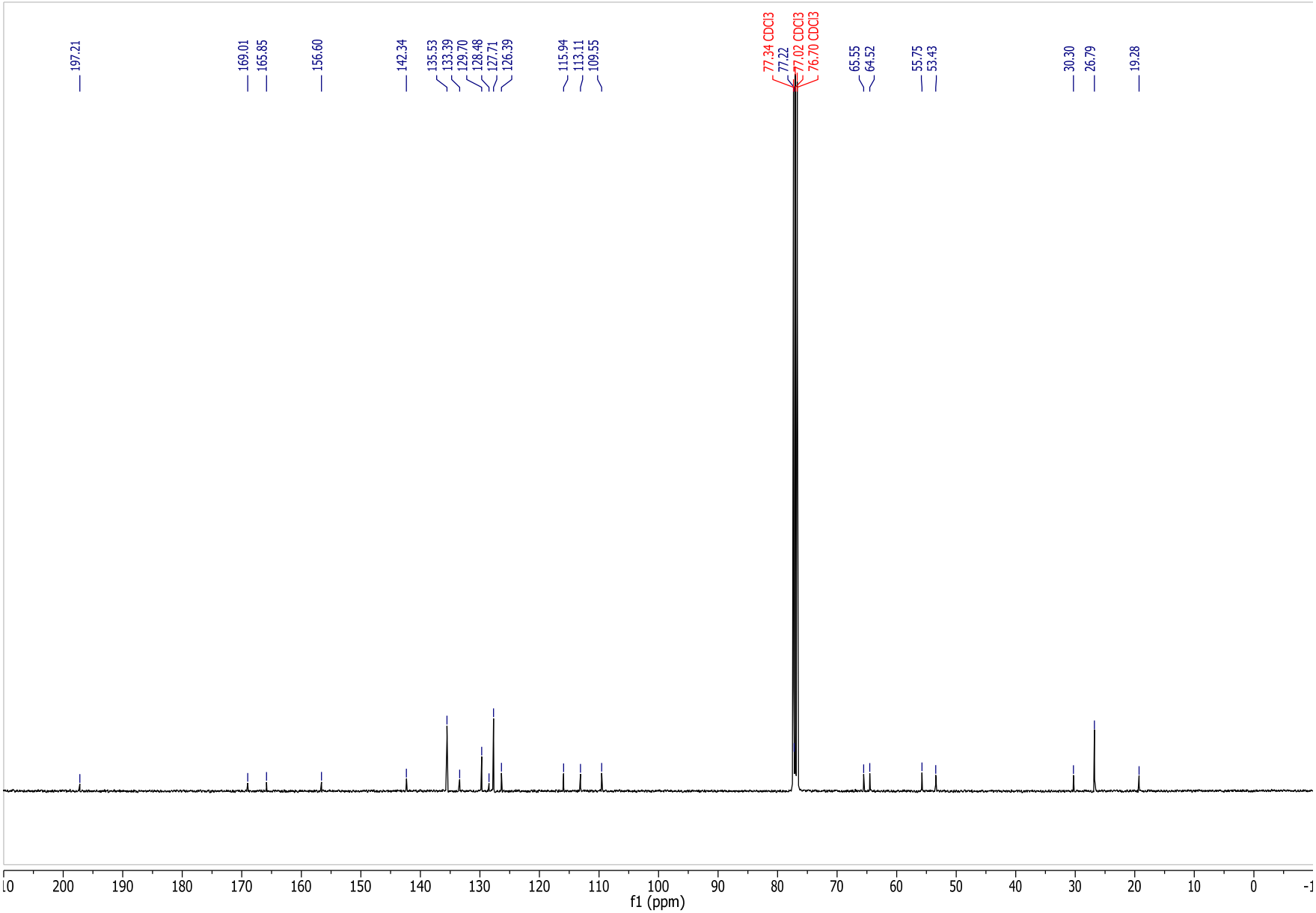


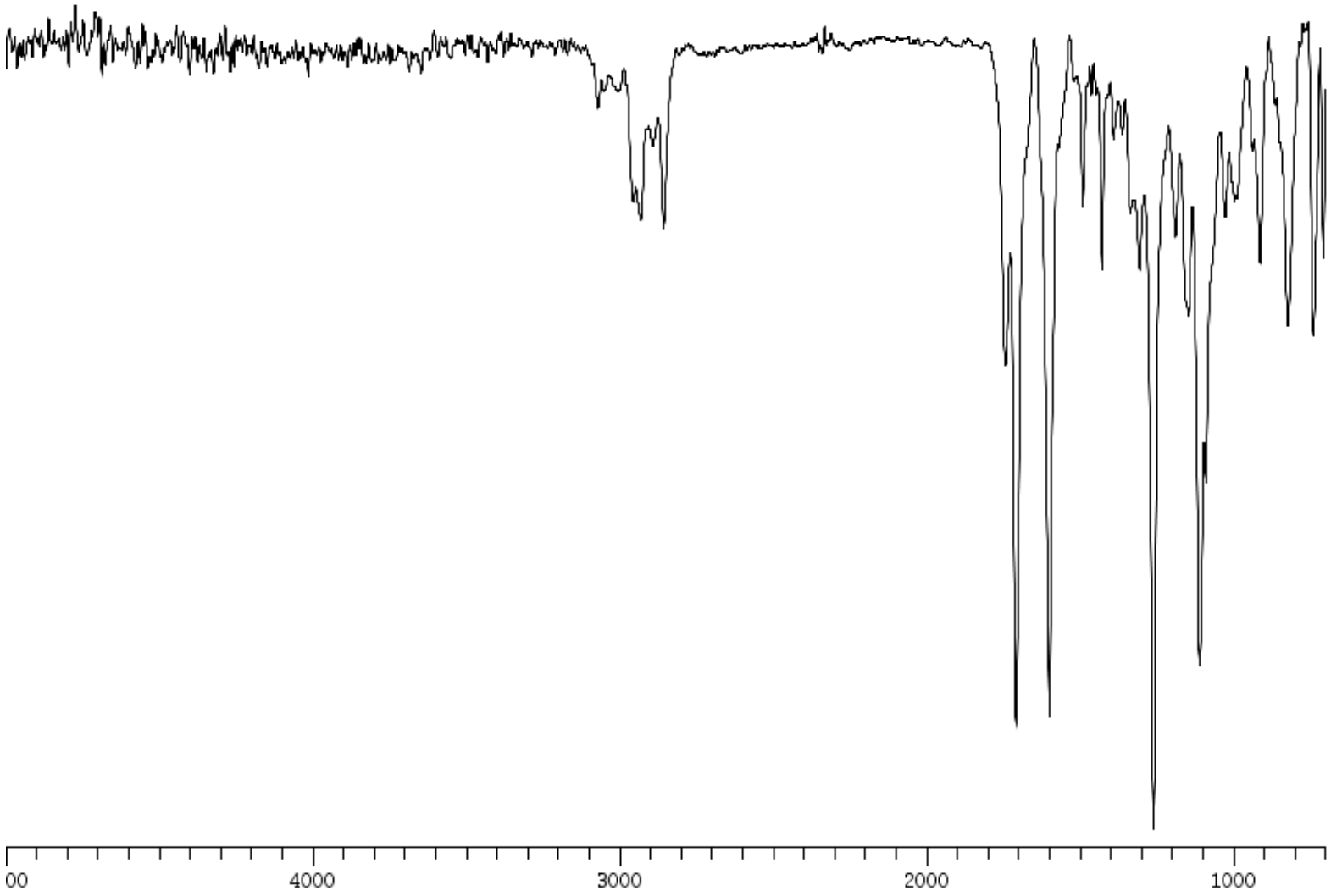

00
4000
3000
2000
1000

$CDCl_3$
400 MHz

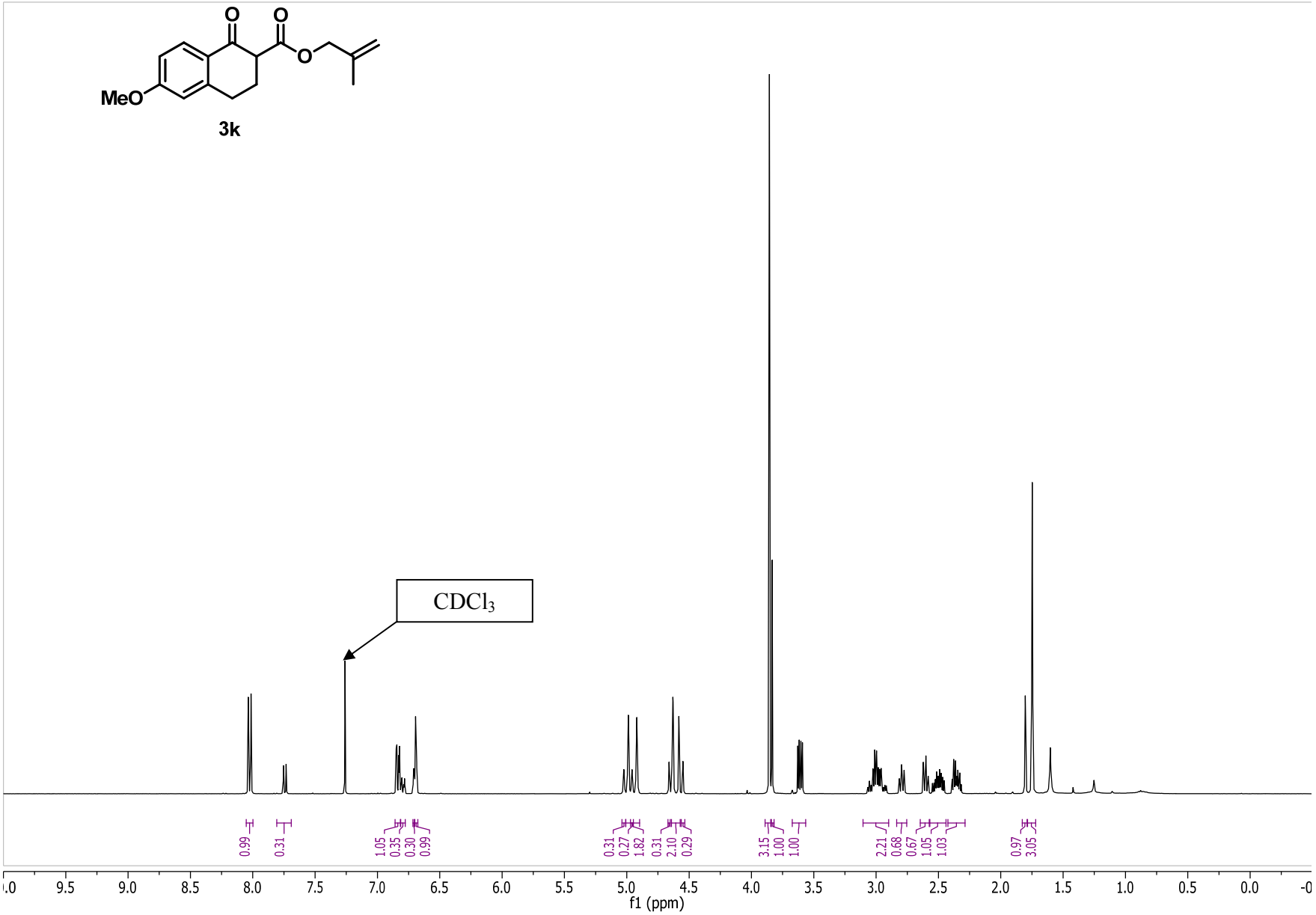


$CDCl_3$
100.1 MHz

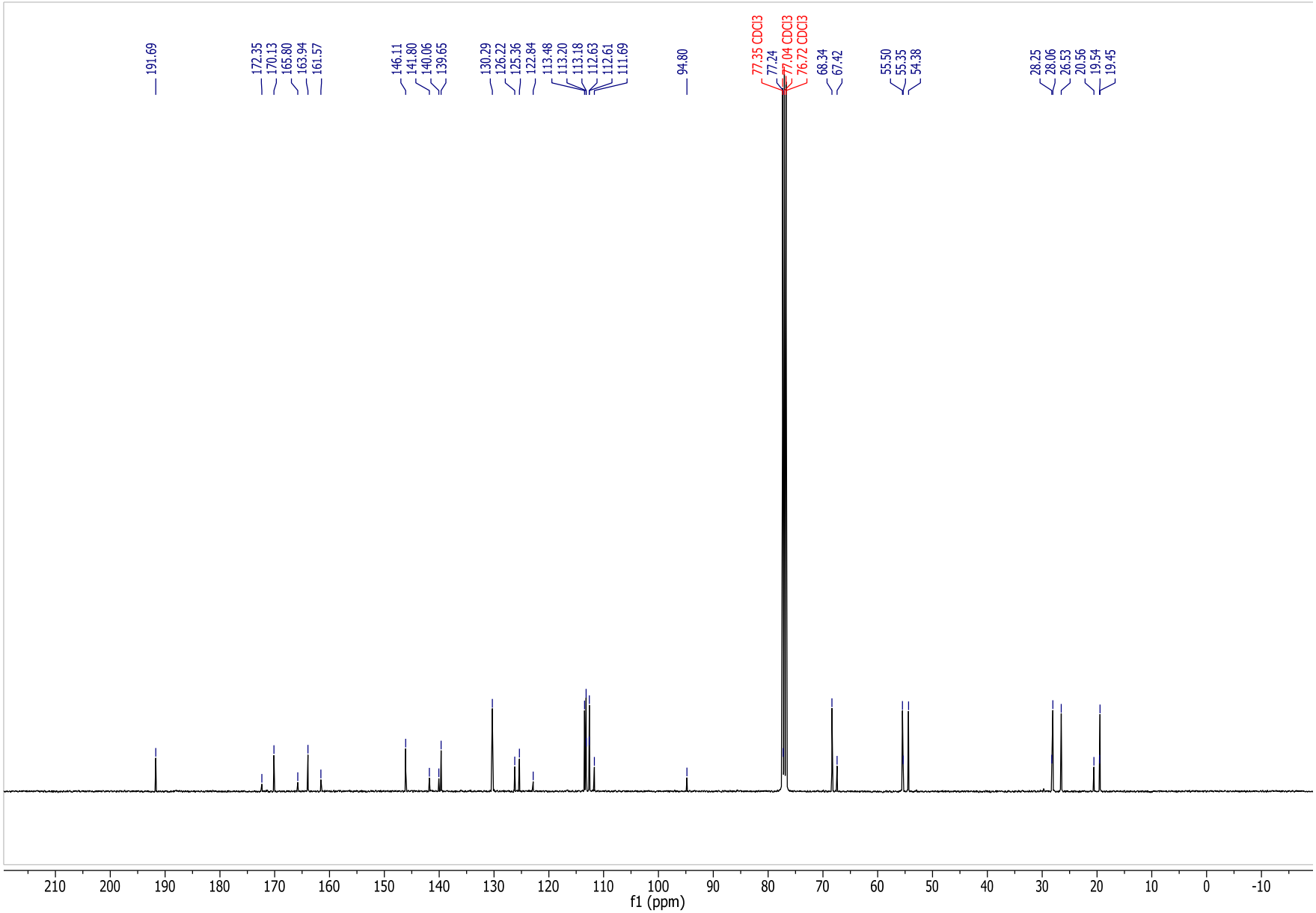


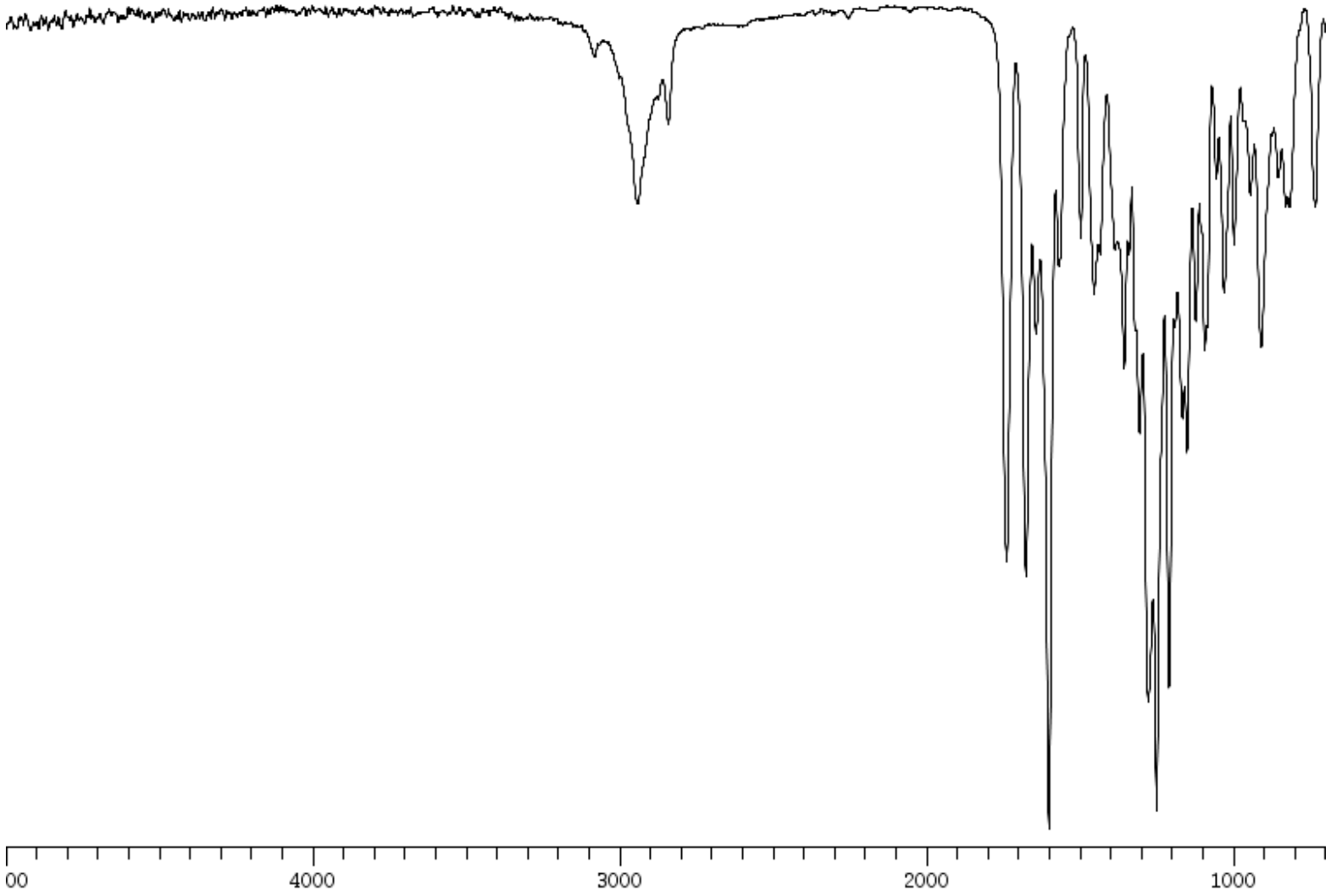

00
4000
3000
2000
1000

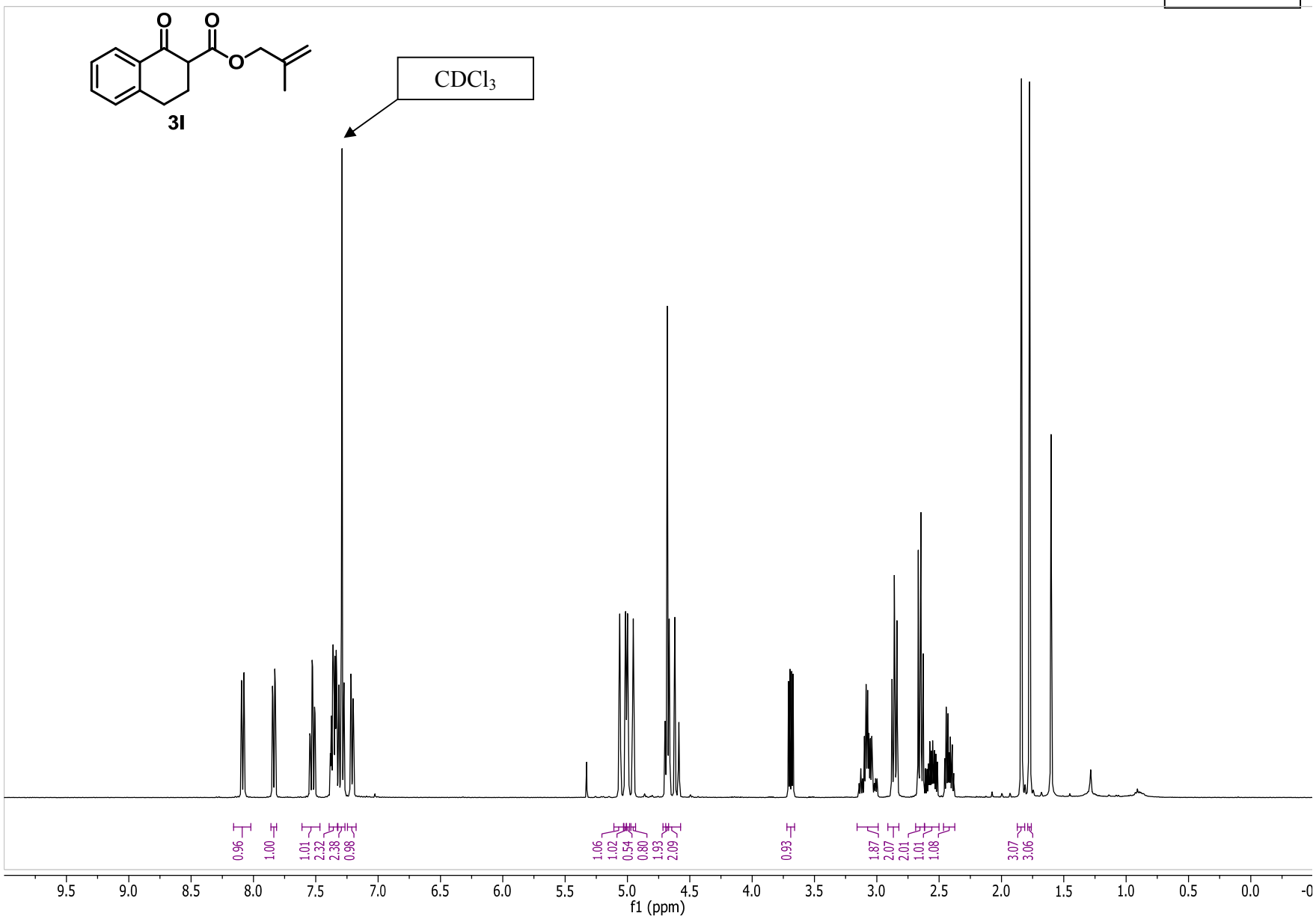
$CDCl_3$
400 MHz



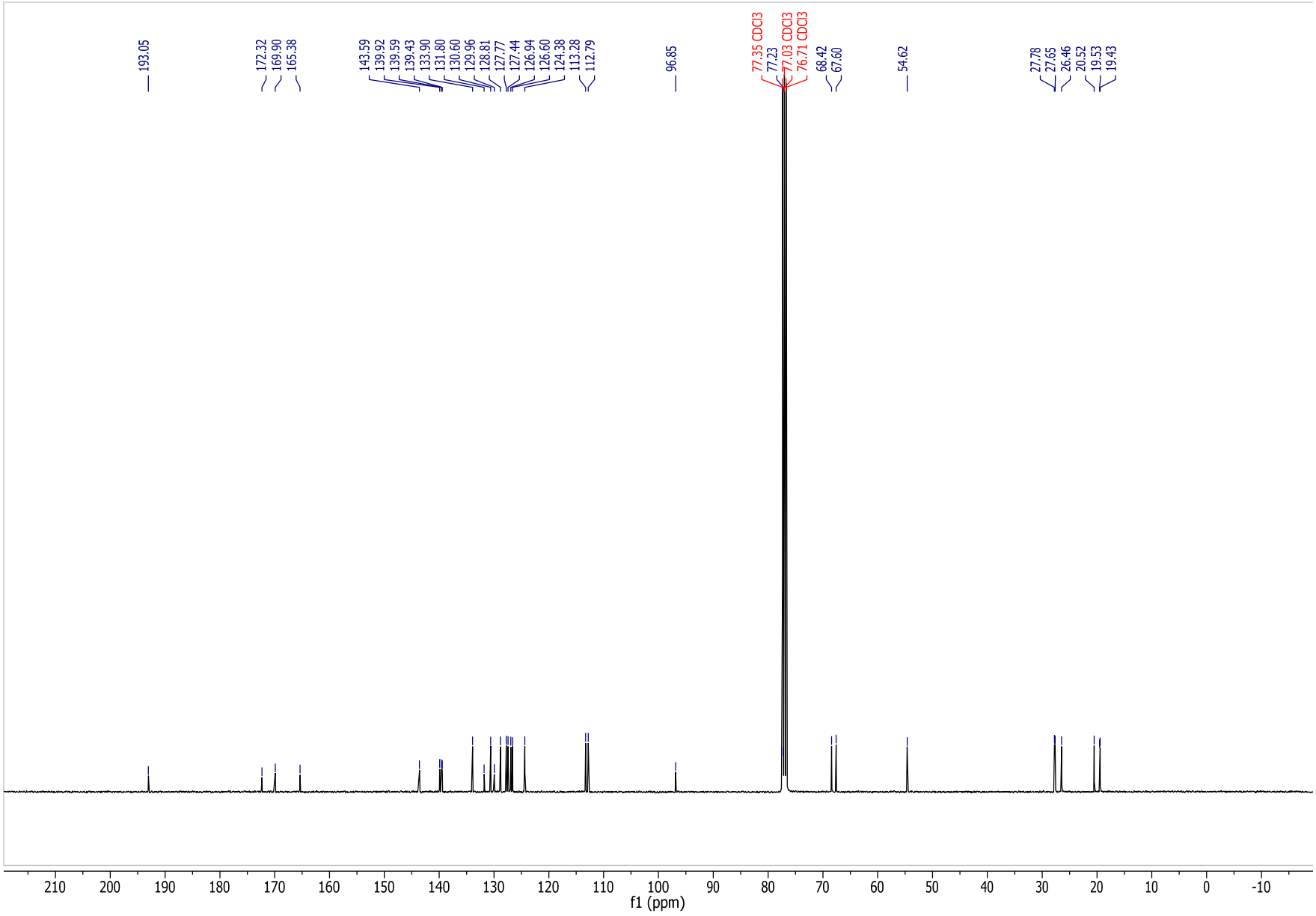
$CDCl_3$
100.1 MHz

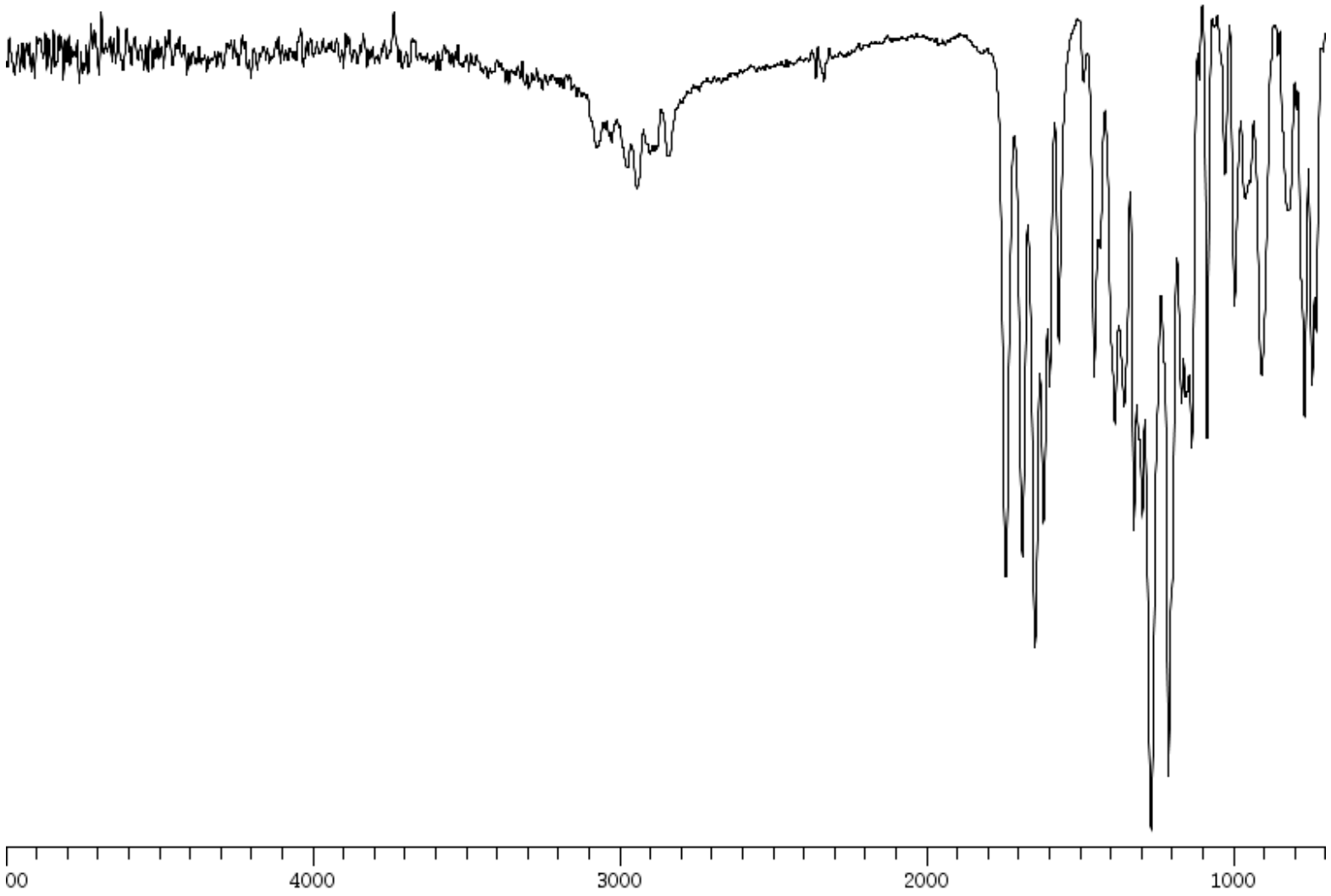


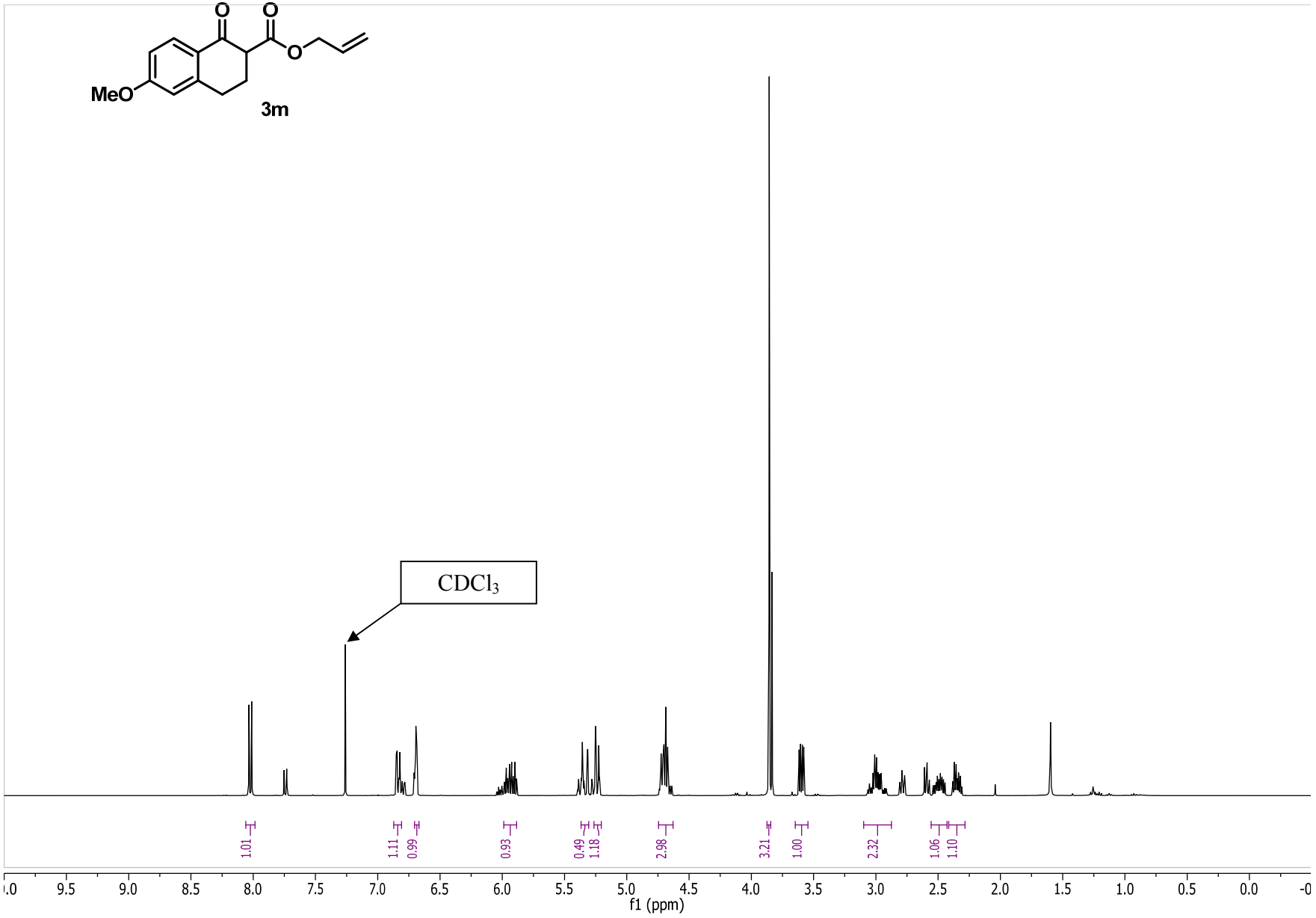

00
4000
3000
2000
1000


CDCl3
400 MHz
3l
CDCl3
0.96
1.00
1.01
2.32
2.38
0.98
1.06
1.02
0.54
0.80
1.93
2.09
0.93
1.87
2.07
2.01
1.01
1.08
3.07
3.06
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

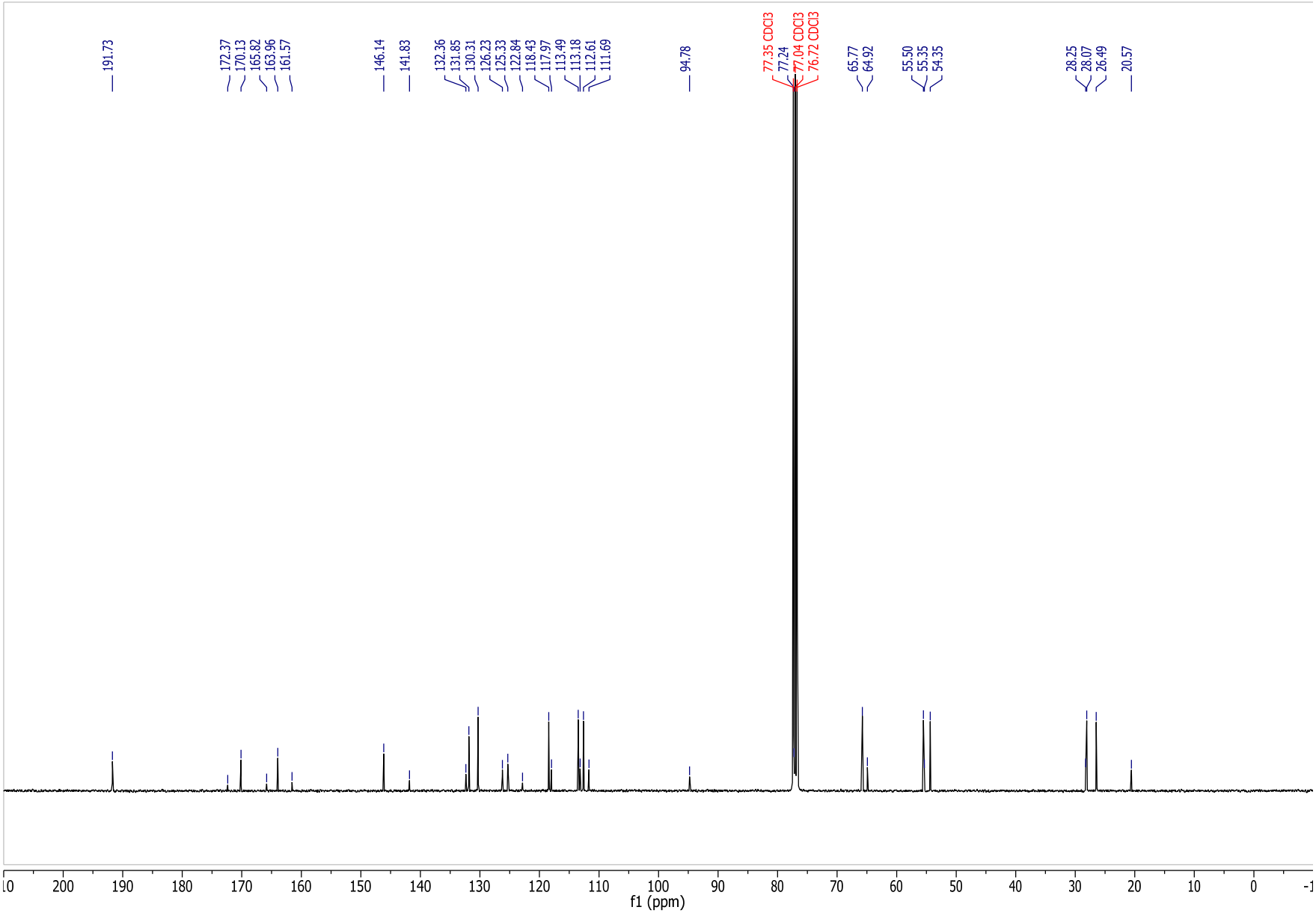
$CDCl_3$
100.1 MHz

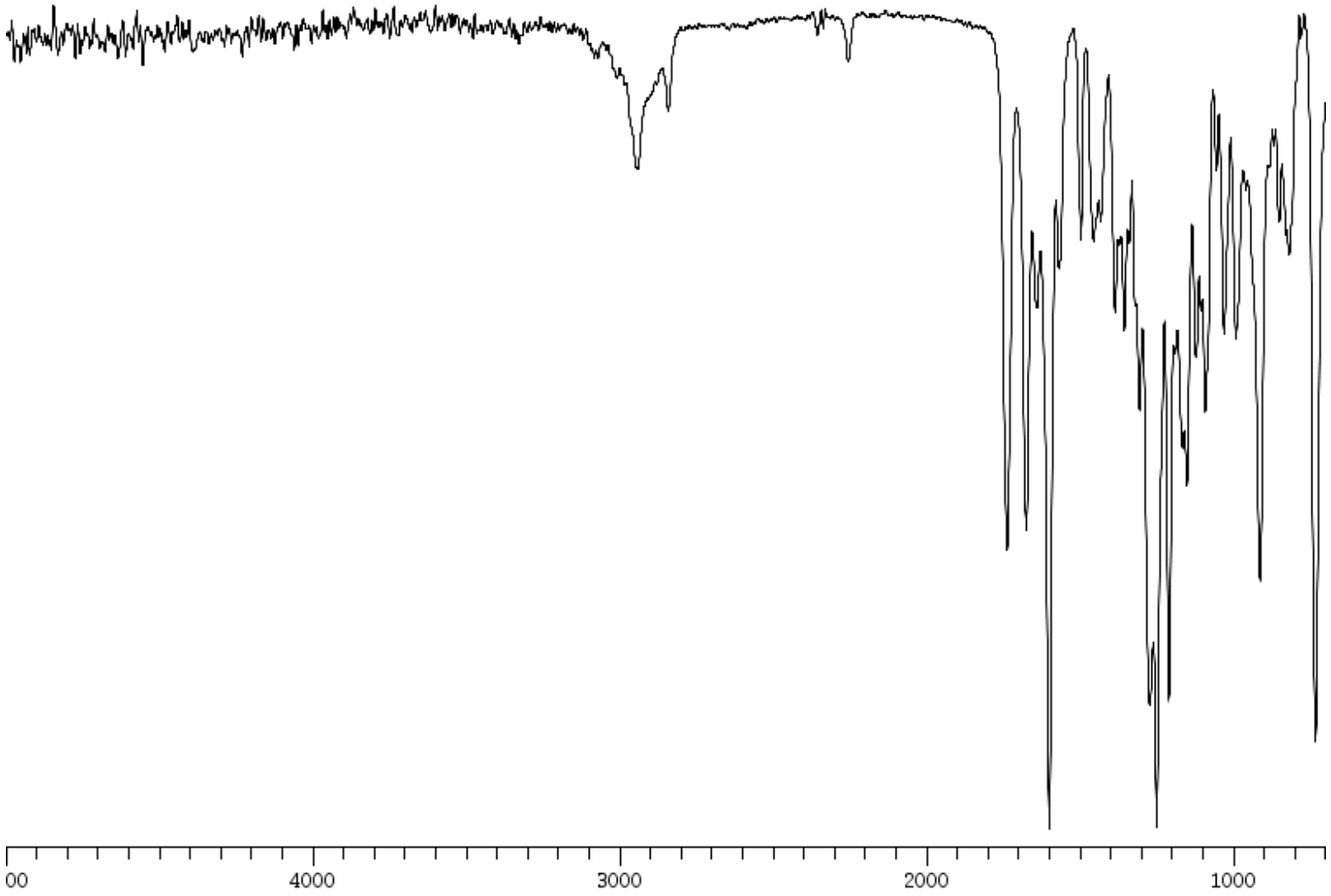



00
4000
3000
2000
1000

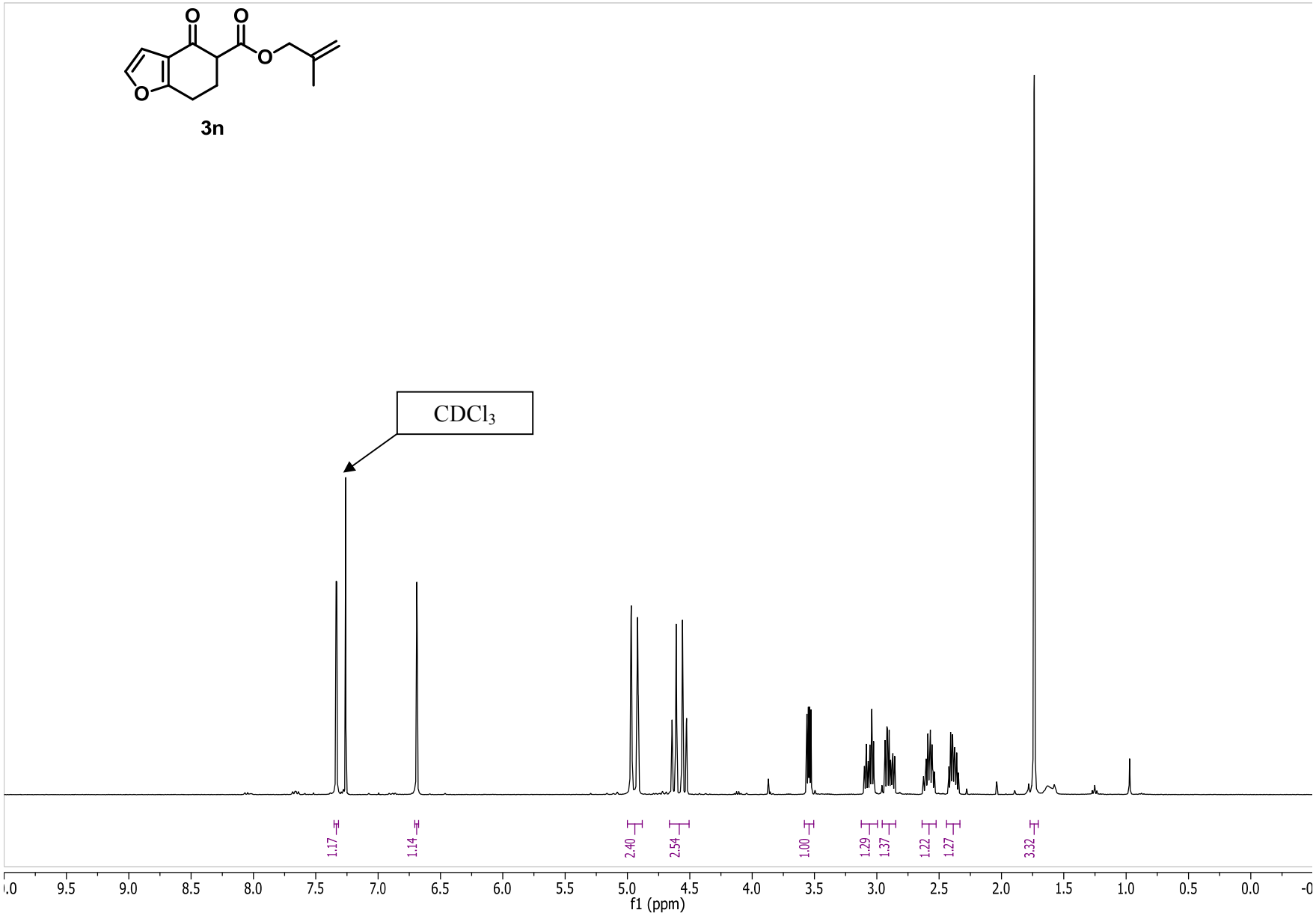

CDCl3
400 MHz
MeO
3m
CDCl3
1.01
1.11
0.99
0.93
0.49
1.18
2.98
3.21
1.00
2.32
1.06
1.10
f1 (ppm)

$CDCl_3$
100.1 MHz

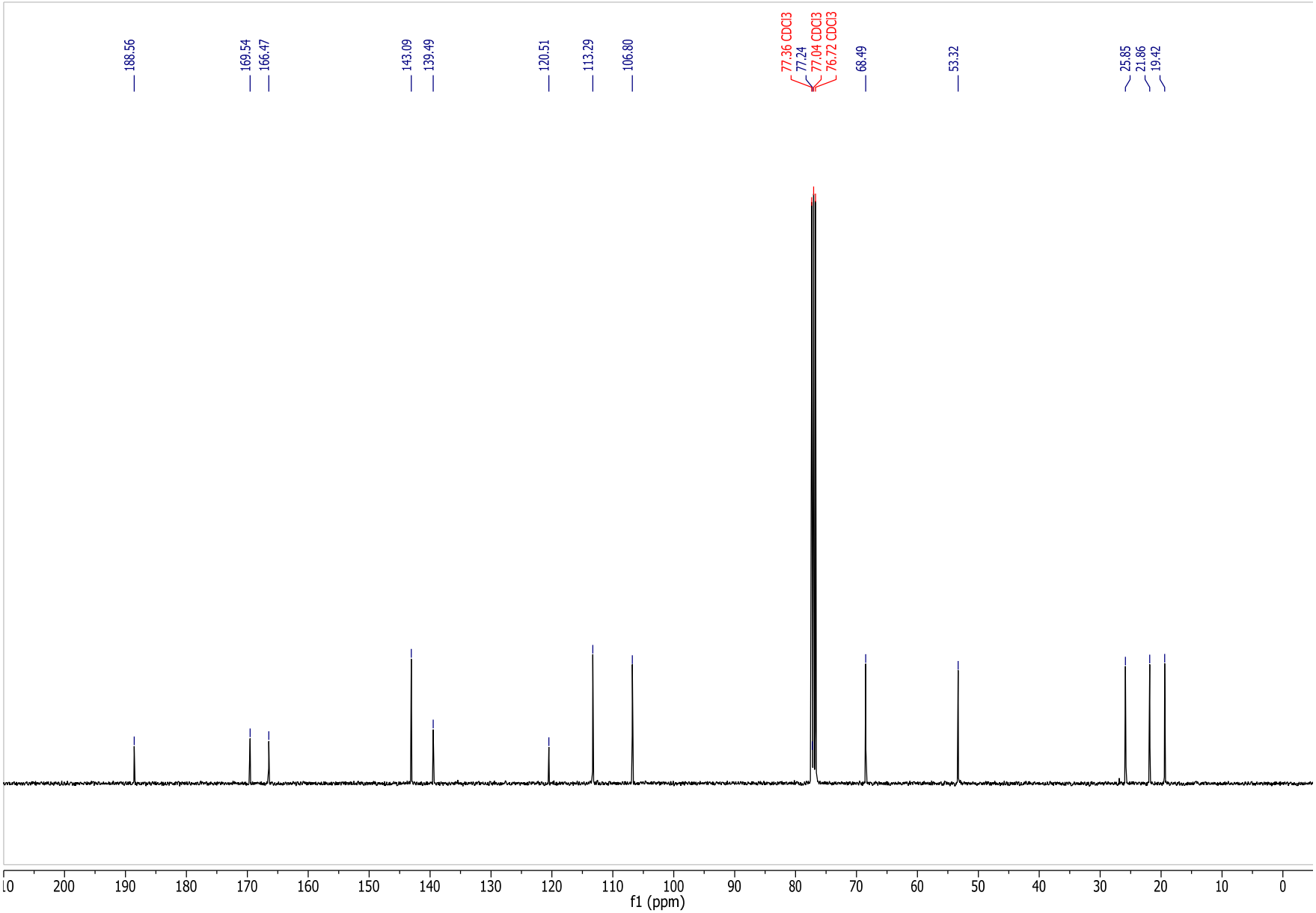


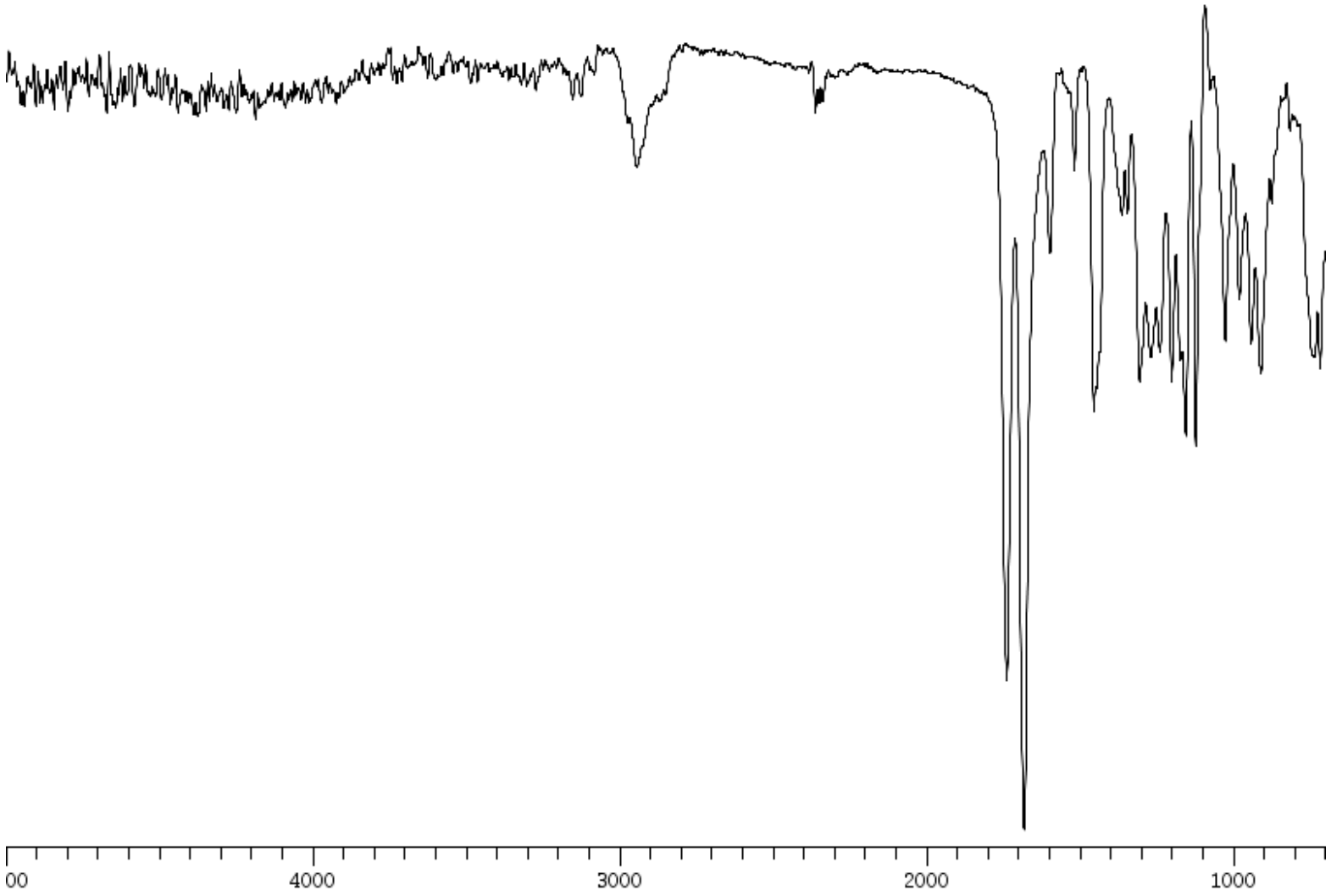

00
4000
3000
2000
1000

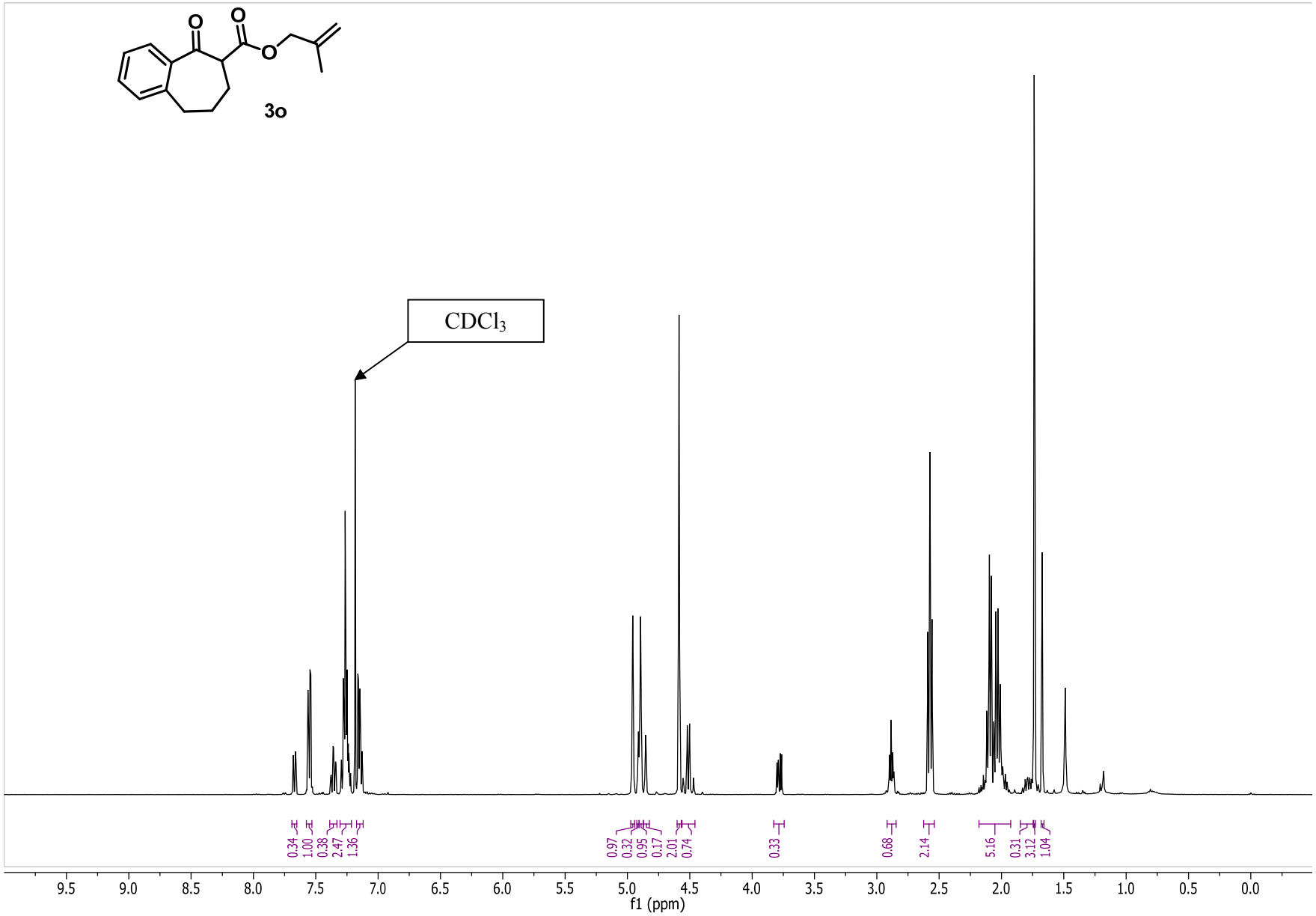
$CDCl_3$
400 MHz



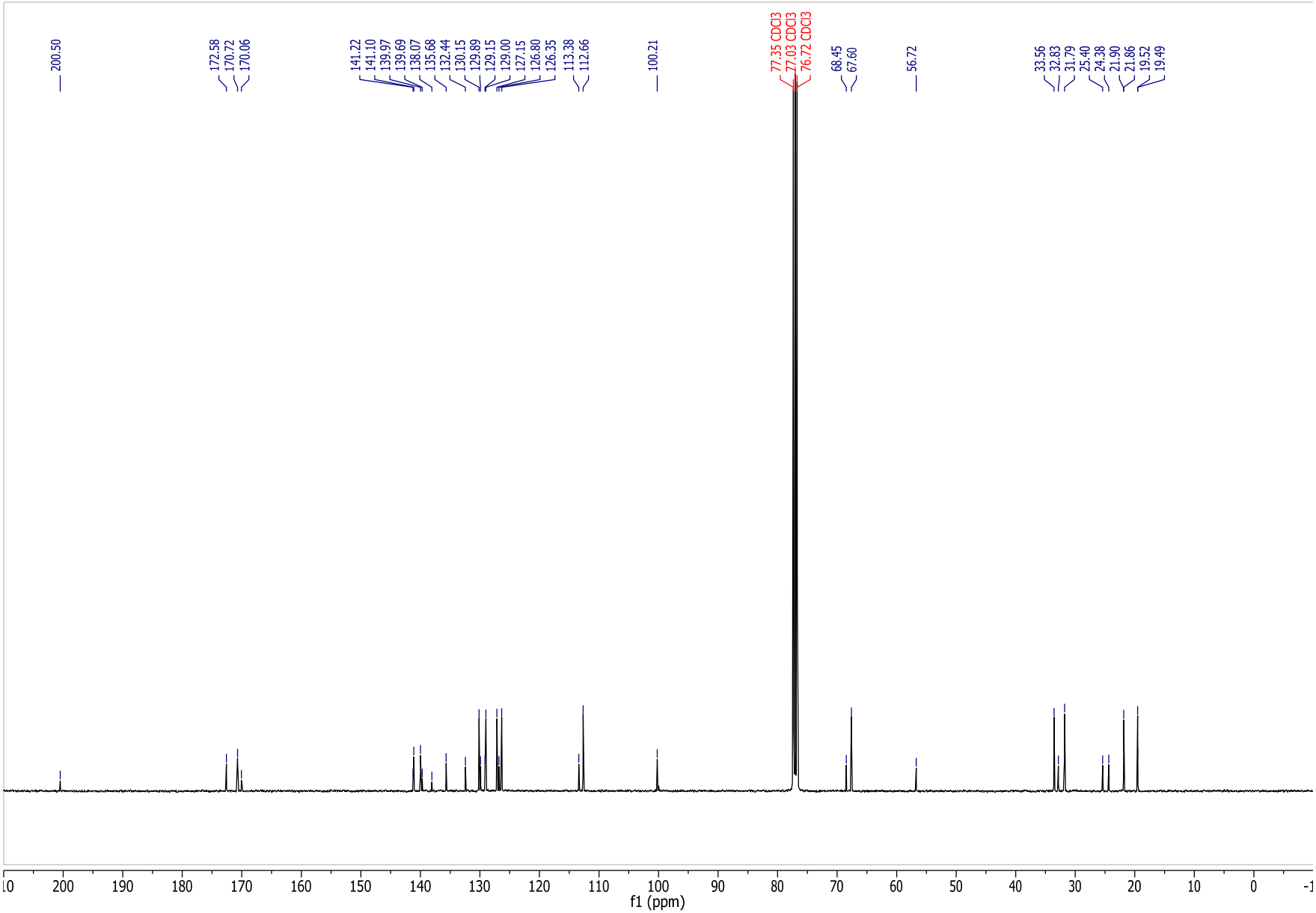
$CDCl_3$
100.1 MHz

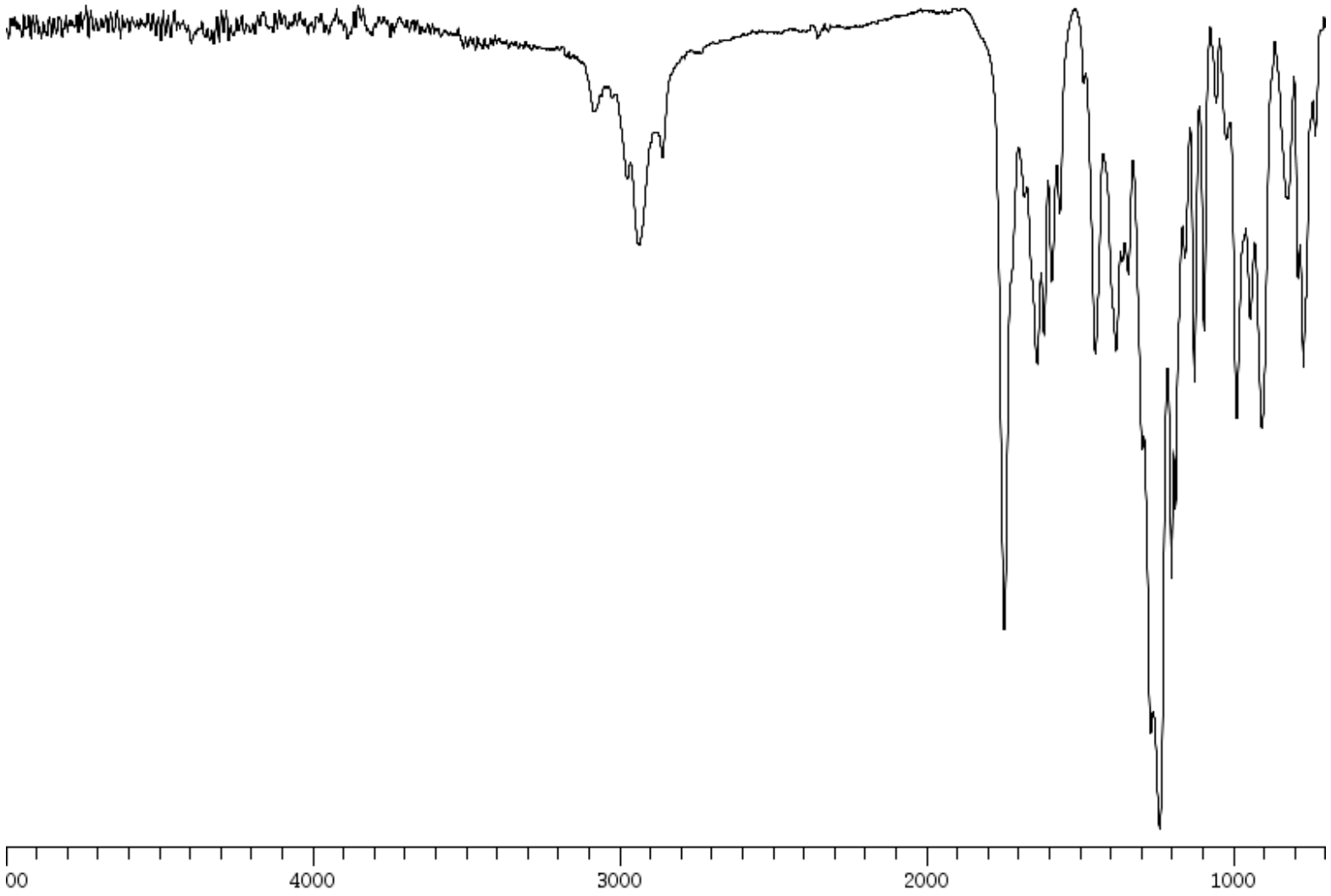



00
4000
3000
2000
1000

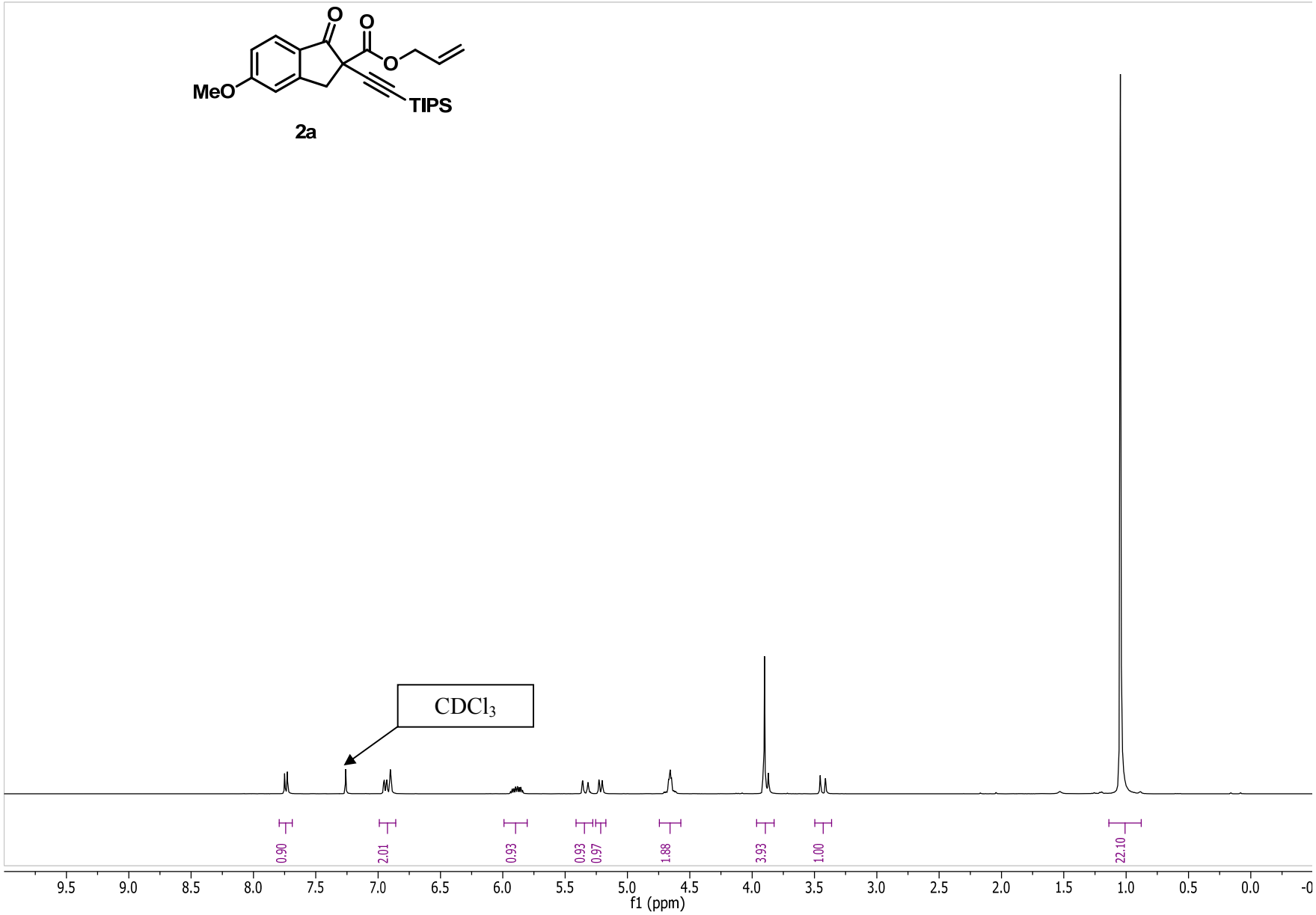

CDCl3
400 MHz
3o
CDCl3
0.34
1.00
0.38
2.47
1.36
0.97
0.32
0.95
0.17
2.01
0.74
0.33
0.68
2.14
5.16
0.31
3.12
1.04
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

$CDCl_3$
100.1 MHz

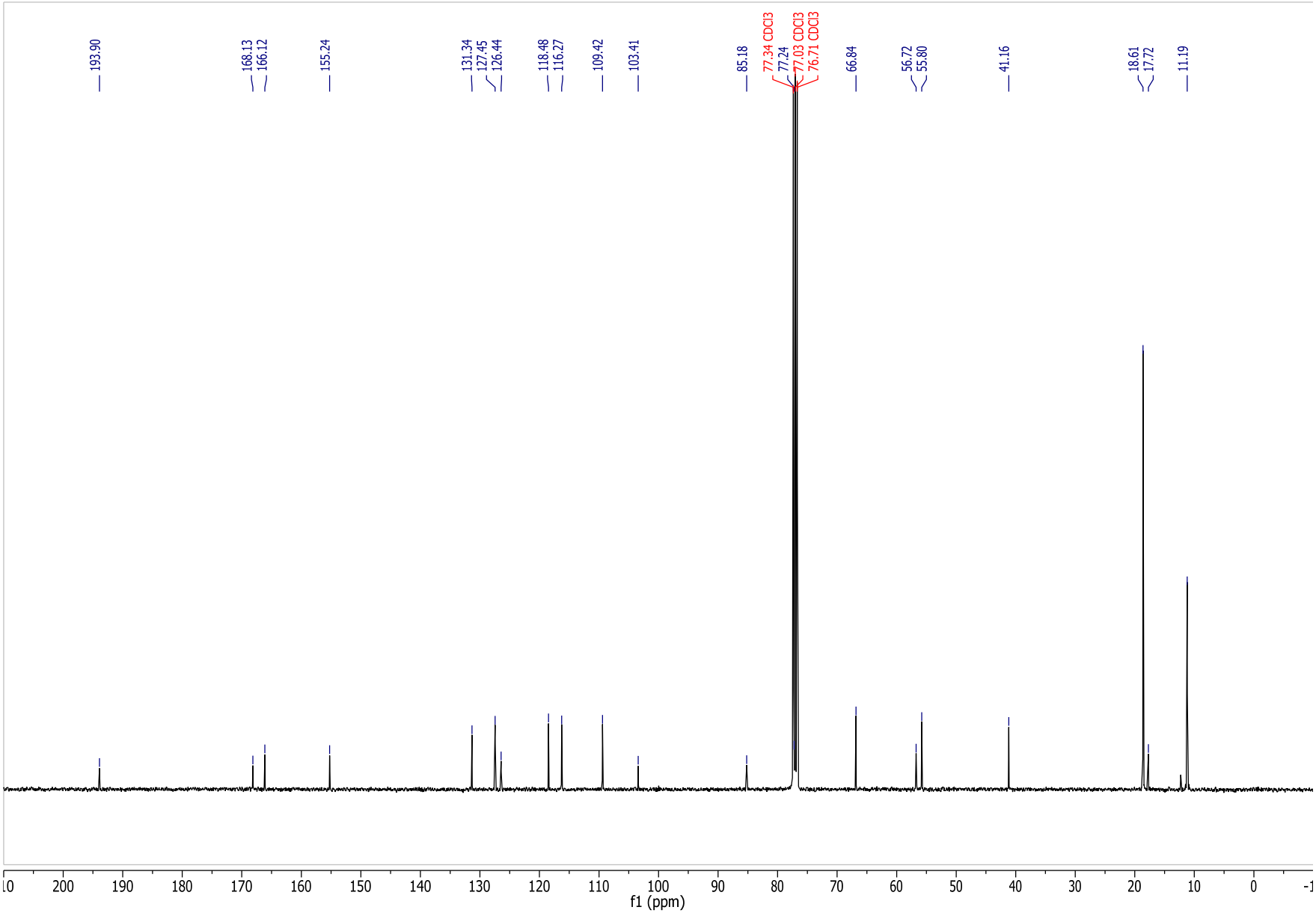


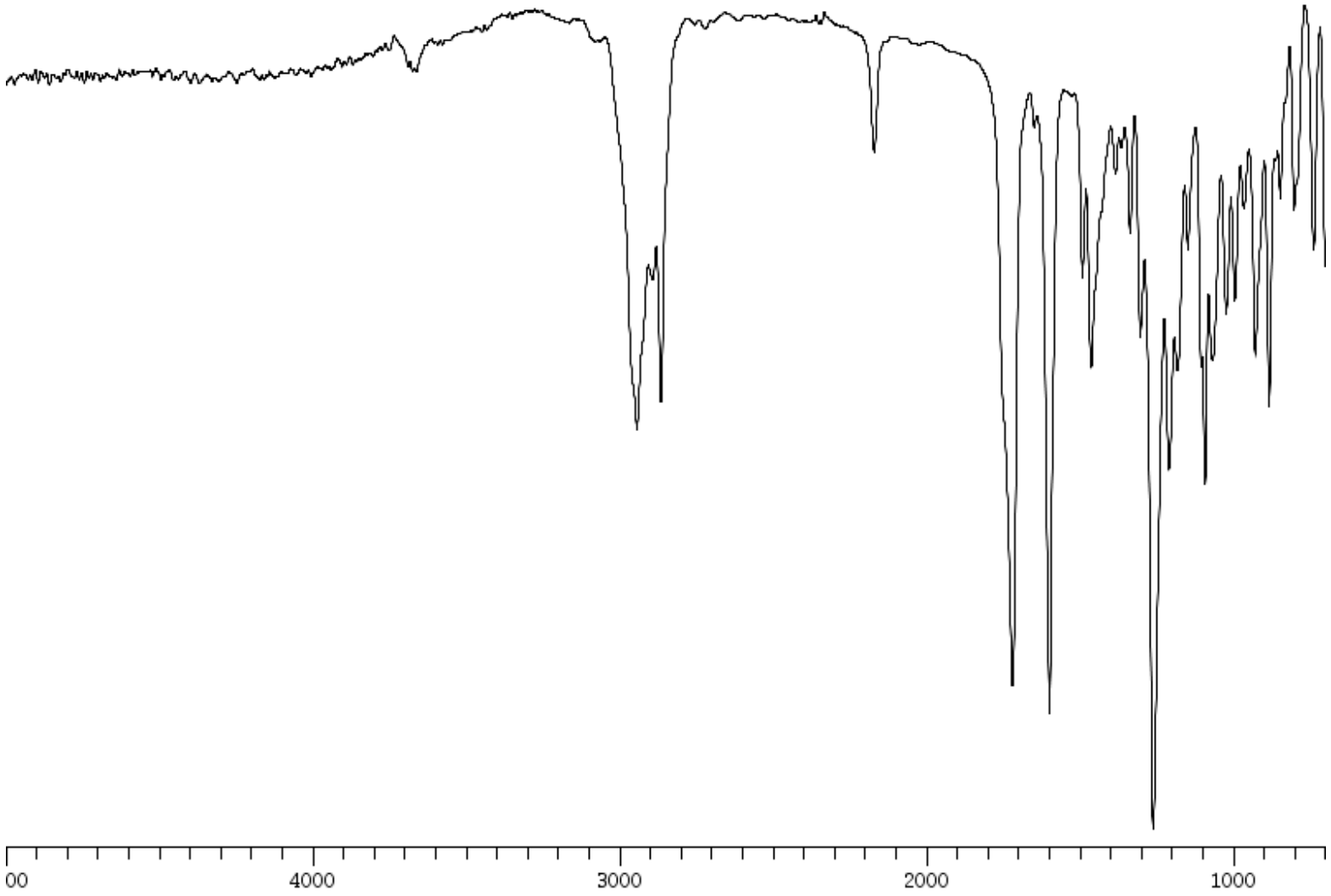

00
4000
3000
2000
1000

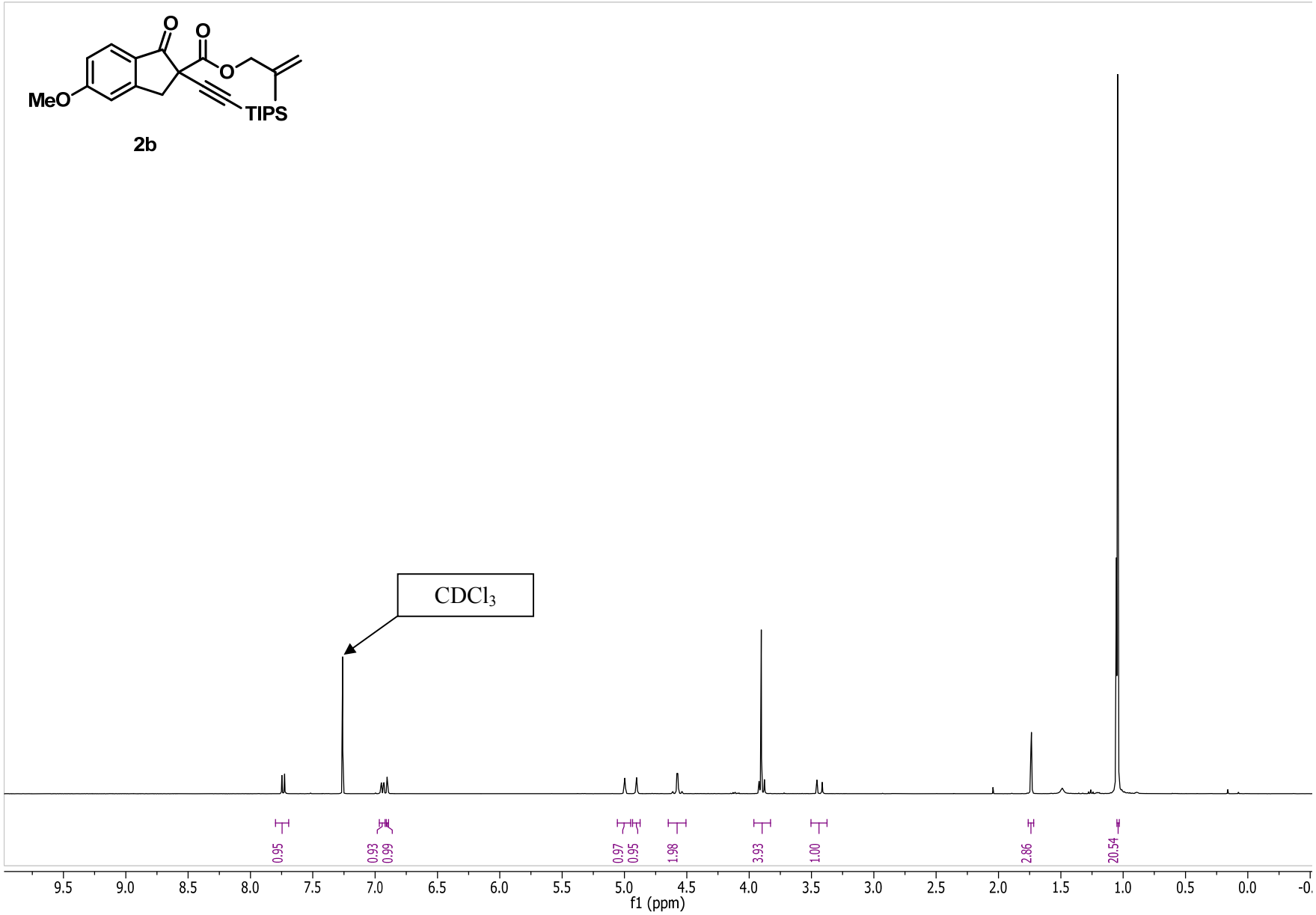
$CDCl_3$
400 MHz



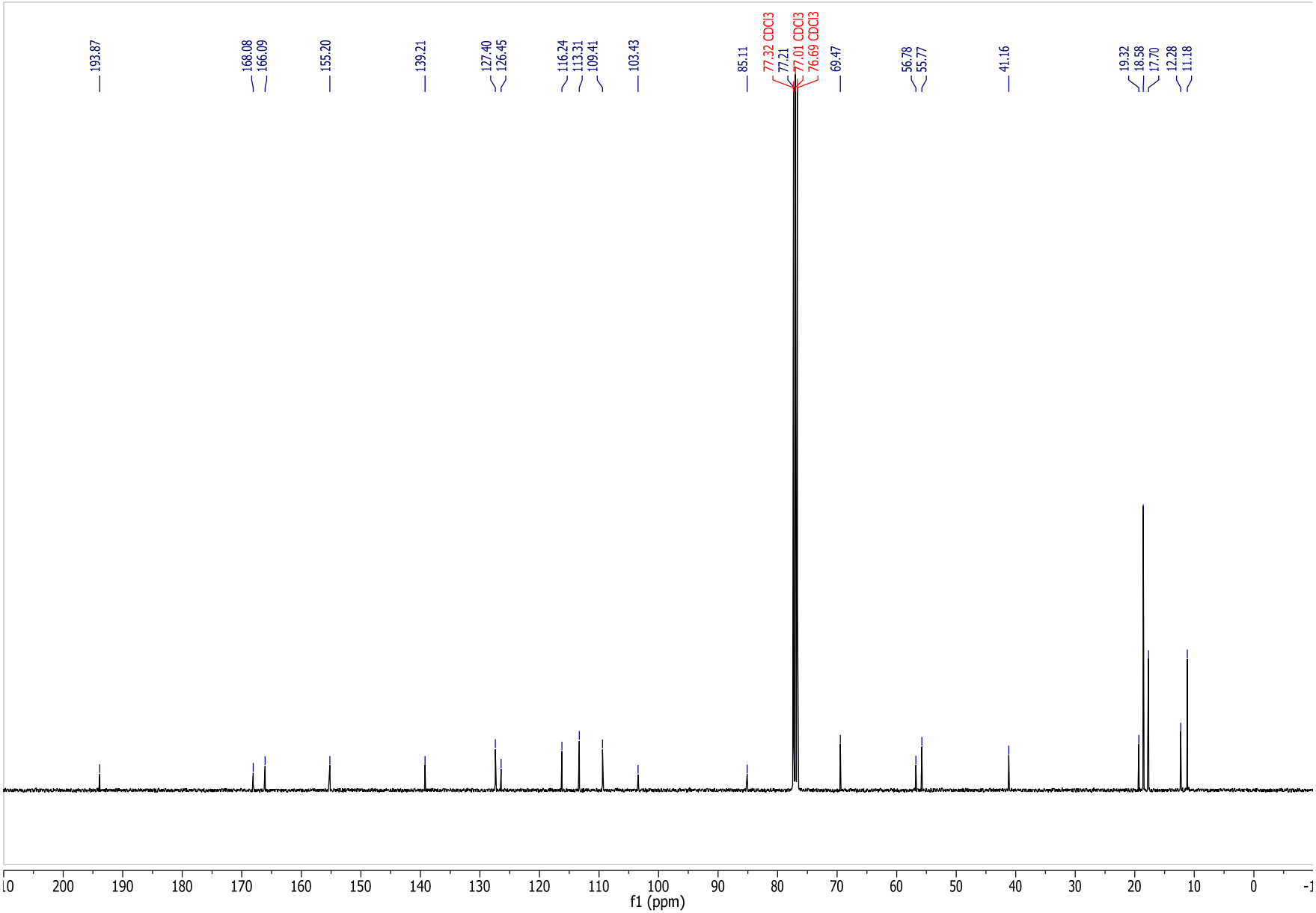
$CDCl_3$
100.1 MHz

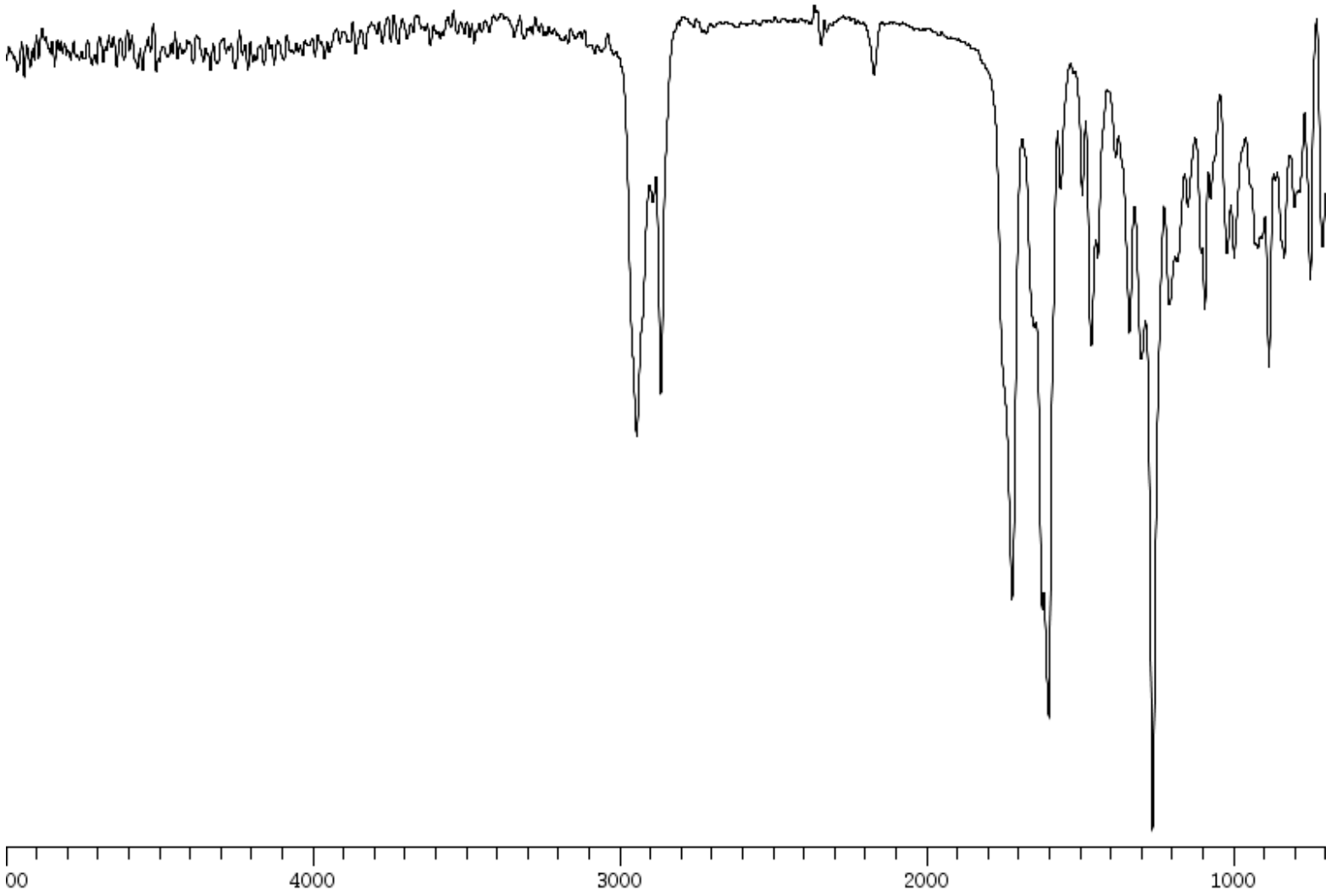



00
4000
3000
2000
1000

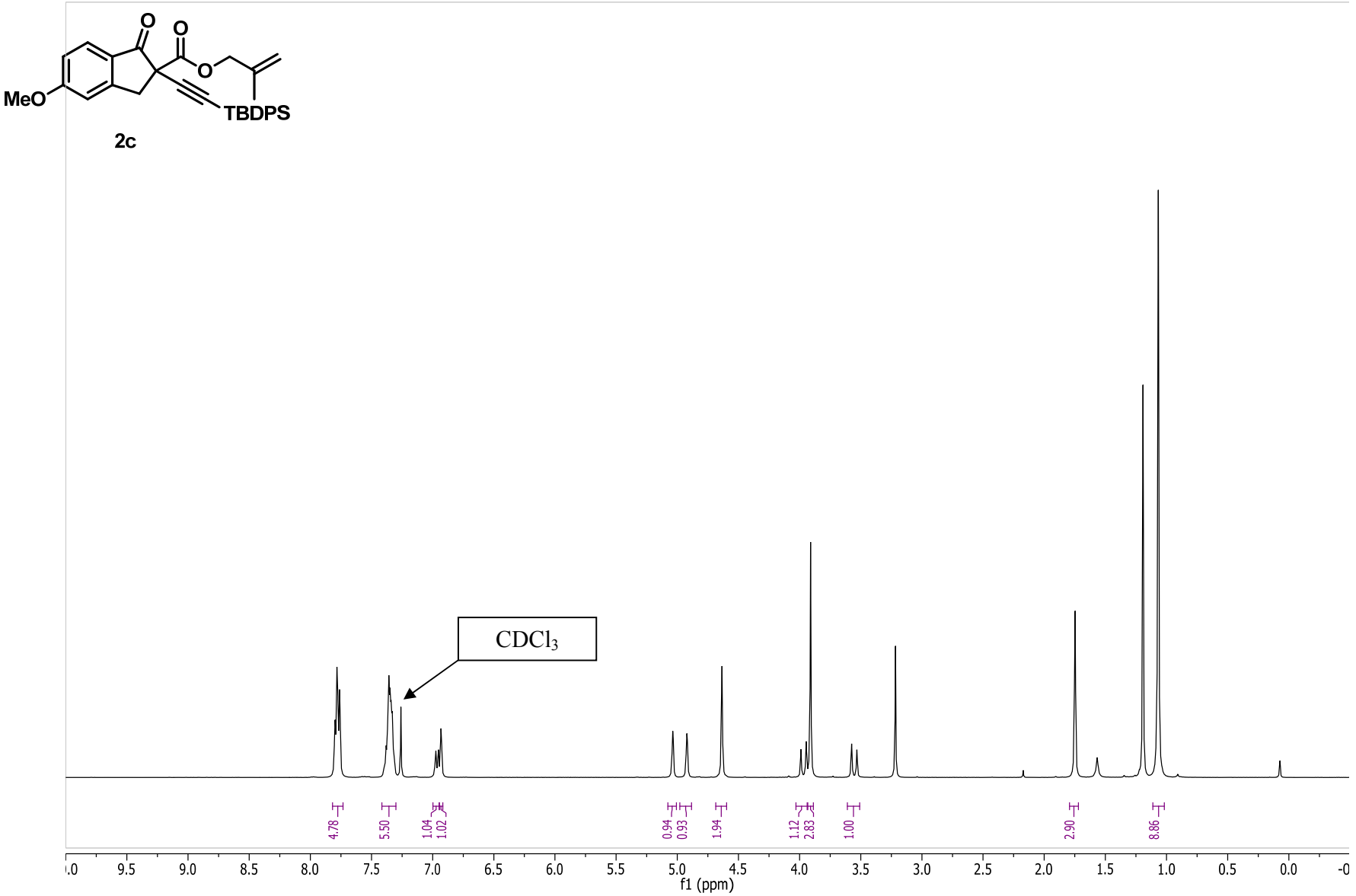

CDCl3
400 MHz
MeO
O
O
O
TIPS
2b
CDCl3
0.95
0.93
0.99
0.97
0.95
1.98
3.93
1.00
2.86
20.54
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

$CDCl_3$
100.1 MHz

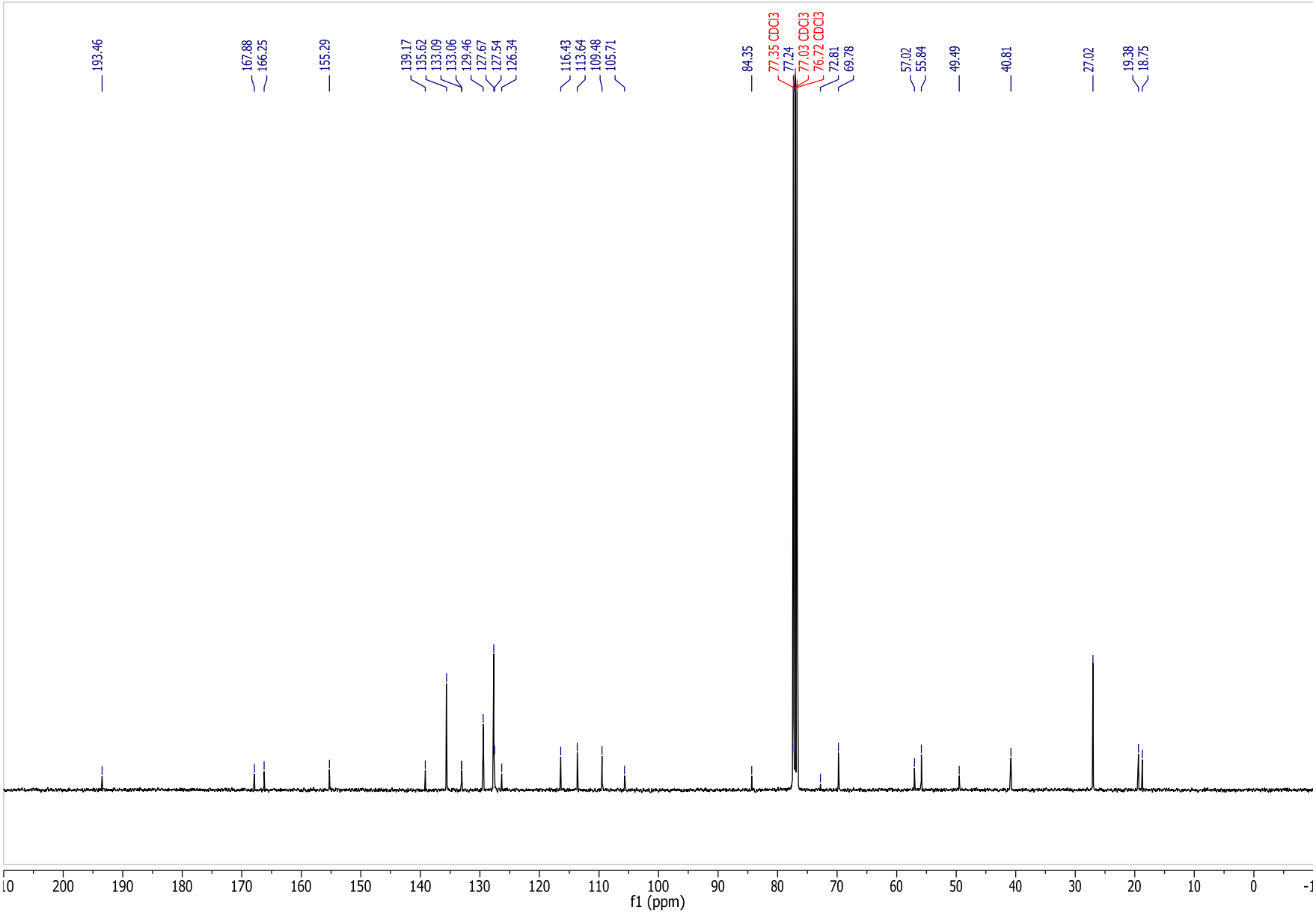


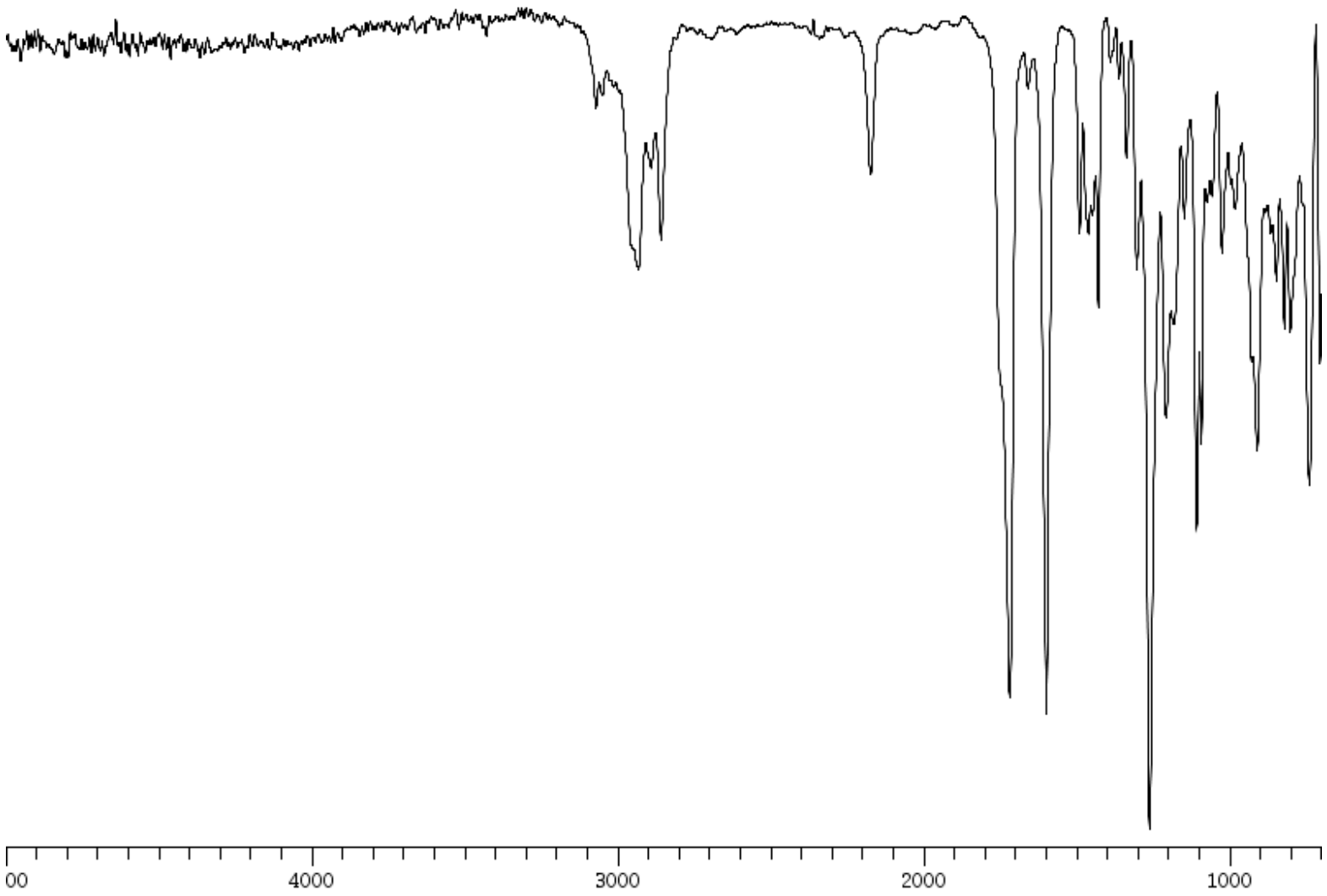

00
4000
3000
2000
1000

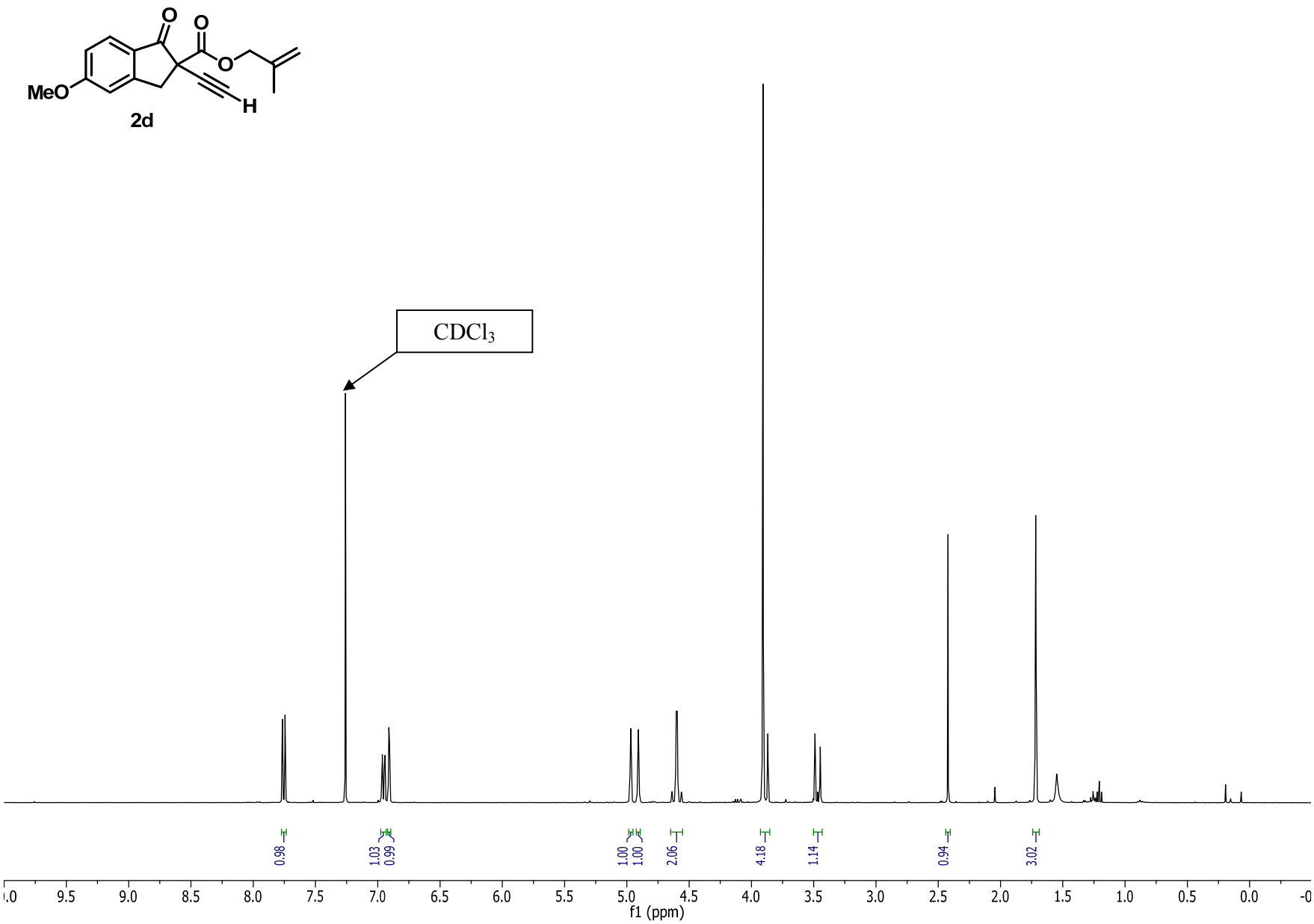
$CDCl_3$
400 MHz

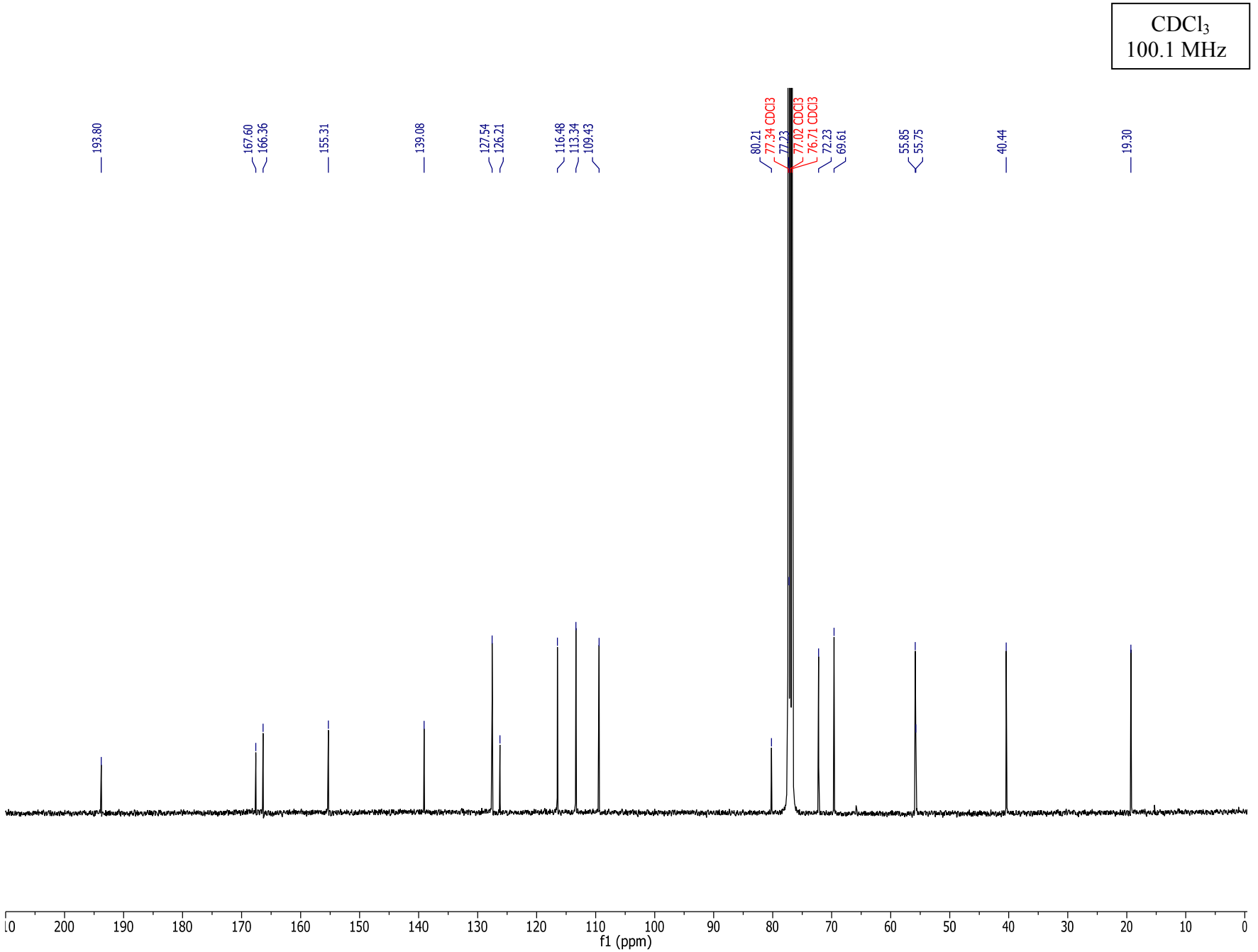


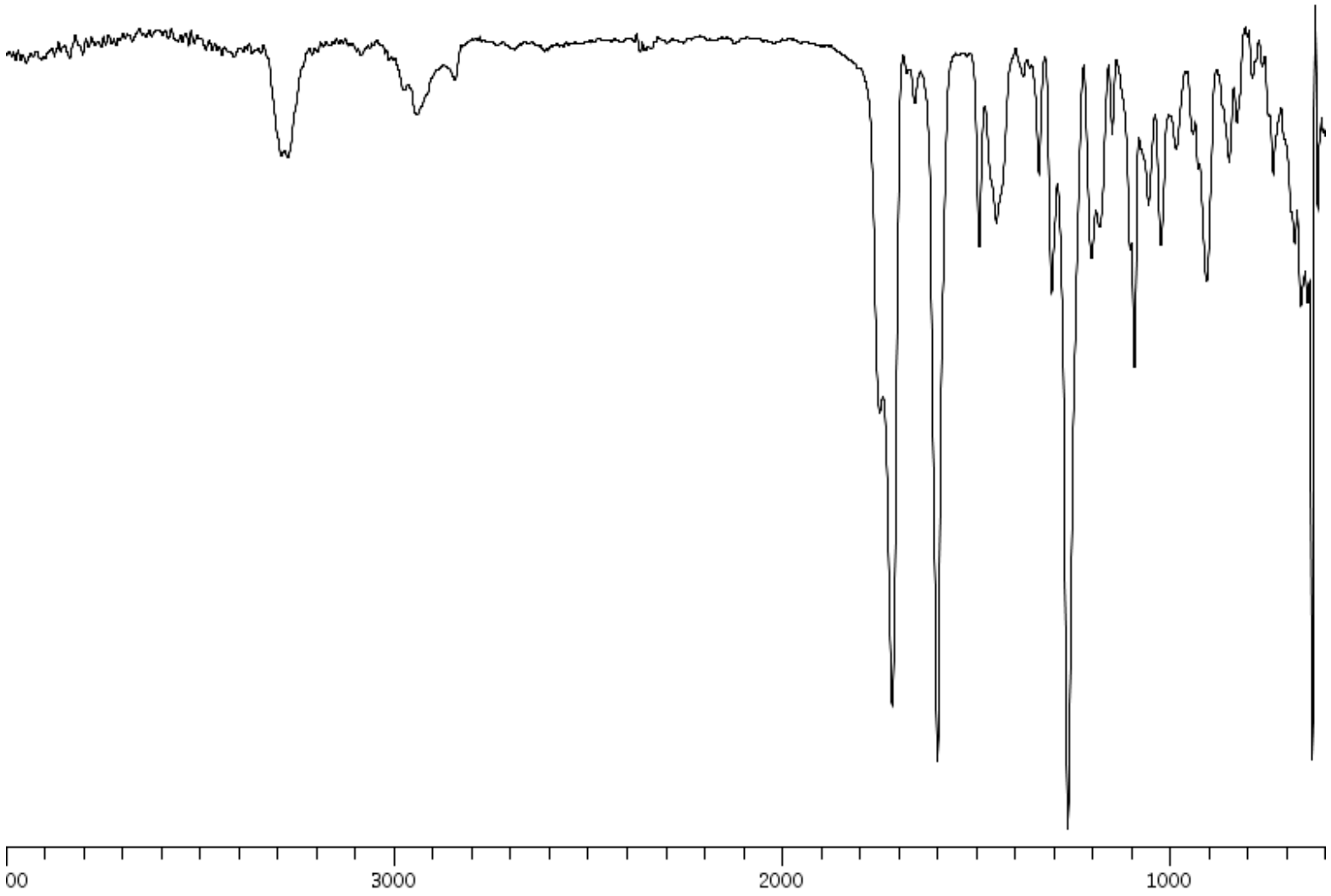
$CDCl_3$
100.1 MHz

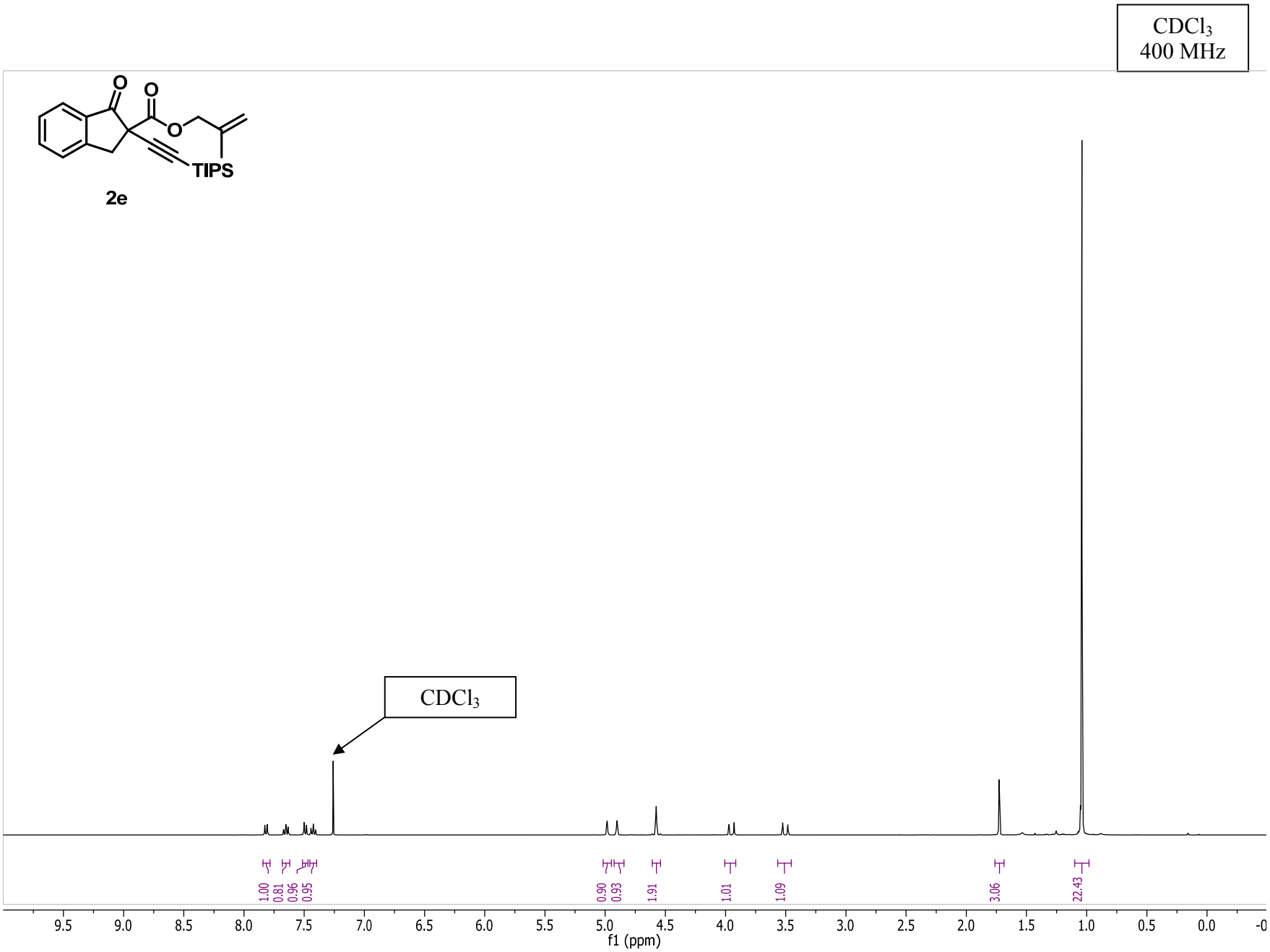



00
4000
3000
2000
1000

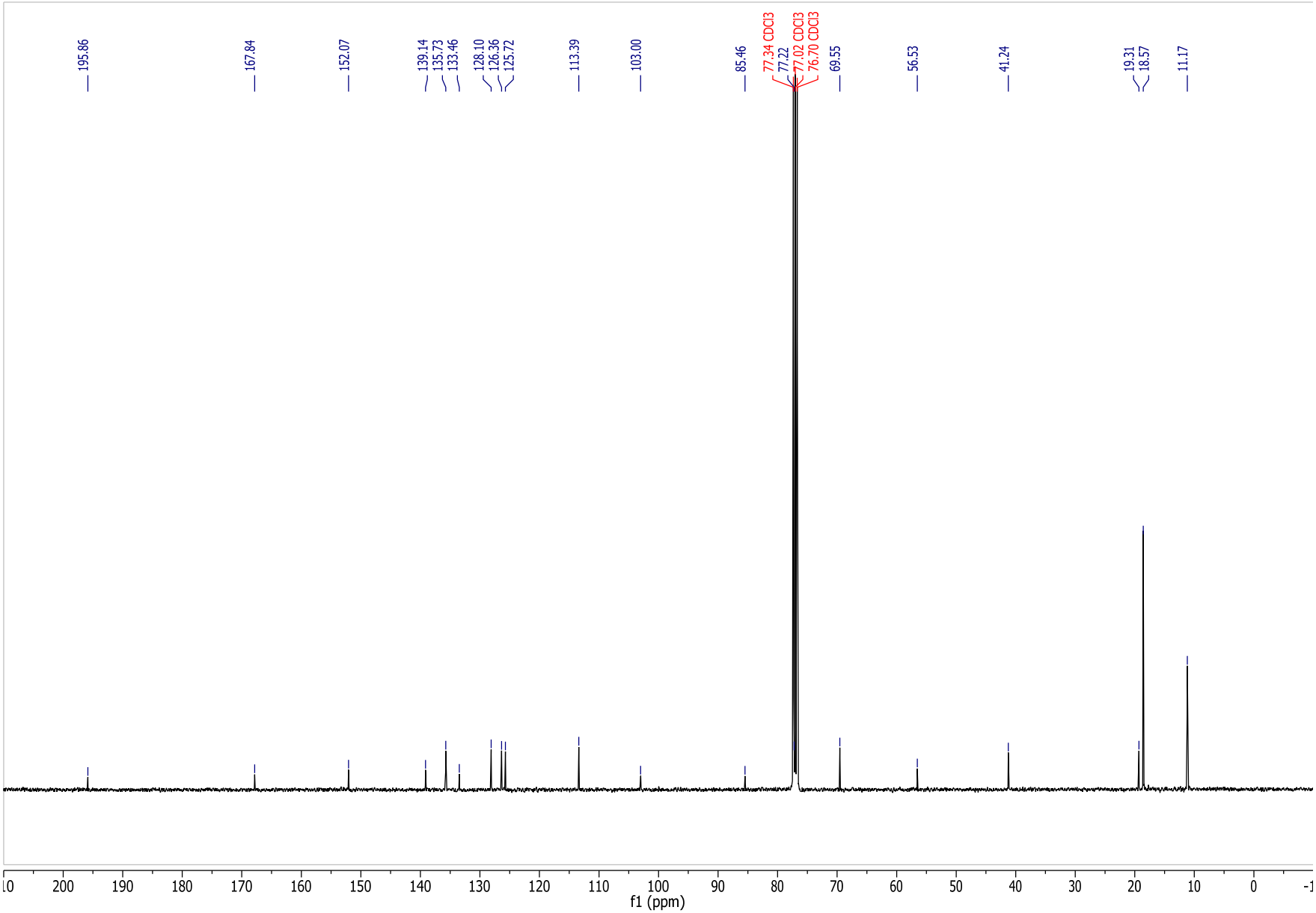

CDCl3
400 MHz
MeO
O
O
O
H
2d
CDCl3
0.98
1.03
0.99
1.00
1.00
2.06
4.18
1.14
0.94
3.02
f1 (ppm)

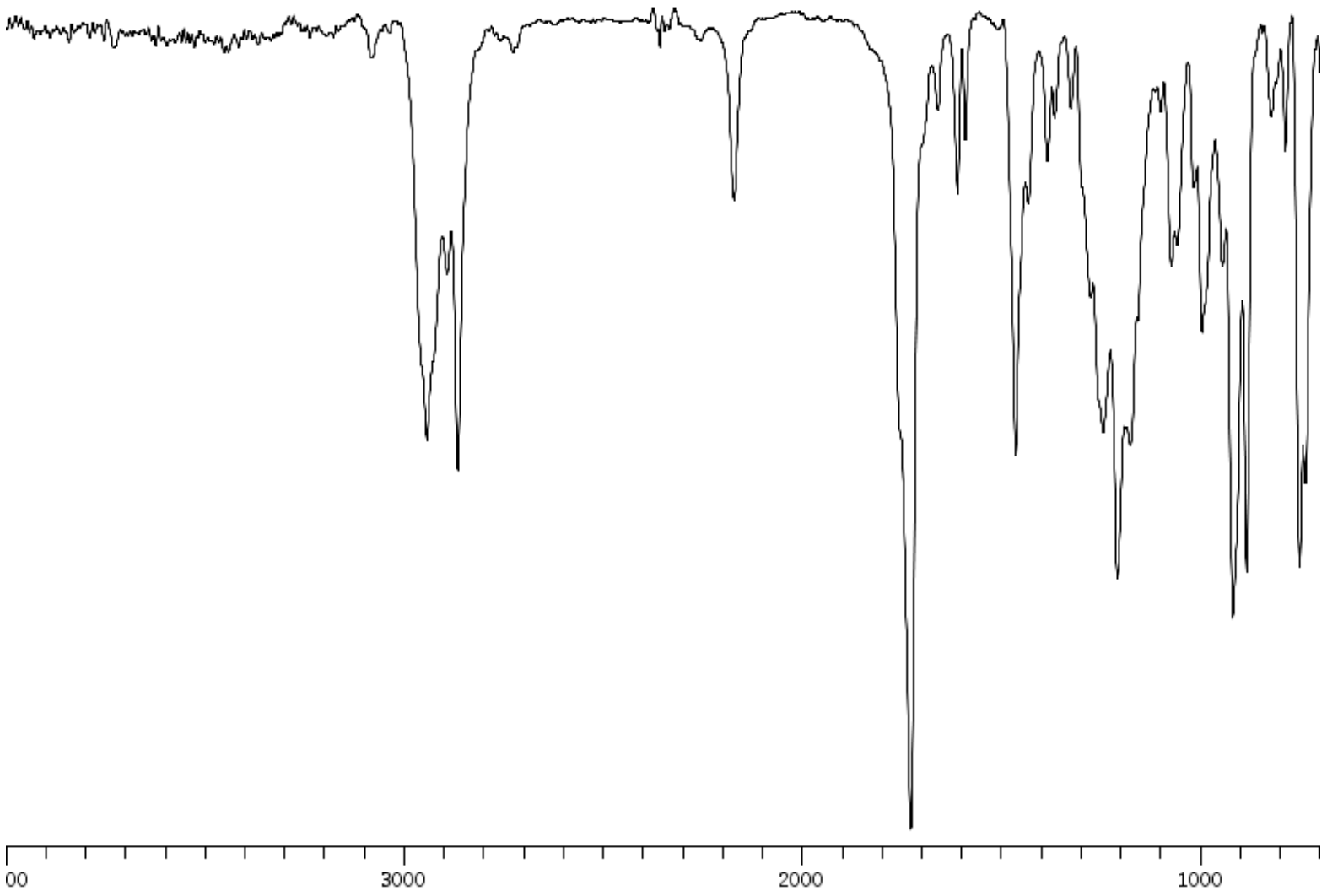

CDCl3
100.1 MHz
193.80
167.60
166.36
155.31
139.08
127.54
126.21
116.48
113.34
109.43
80.21
77.34 CDCl3
77.23
77.02 CDCl3
76.71 CDCl3
72.23
69.61
55.85
55.75
40.44
19.30
f1 (ppm)

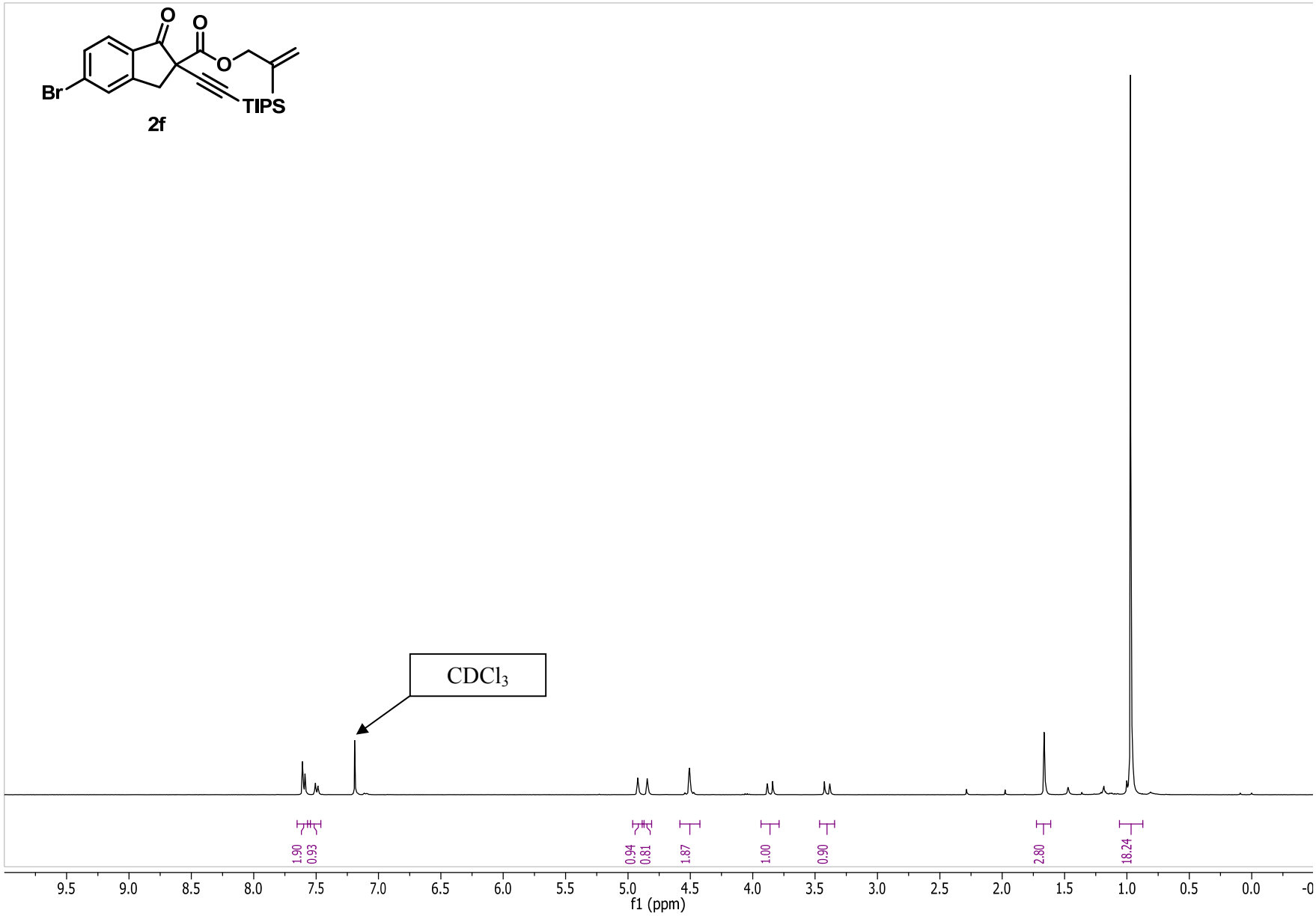

00
3000
2000
1000


CDCl3
400 MHz
TIPS
2e
CDCl3
1.00
0.81
0.96
0.95
0.90
0.93
1.91
1.01
1.09
3.06
22.43
f1 (ppm)

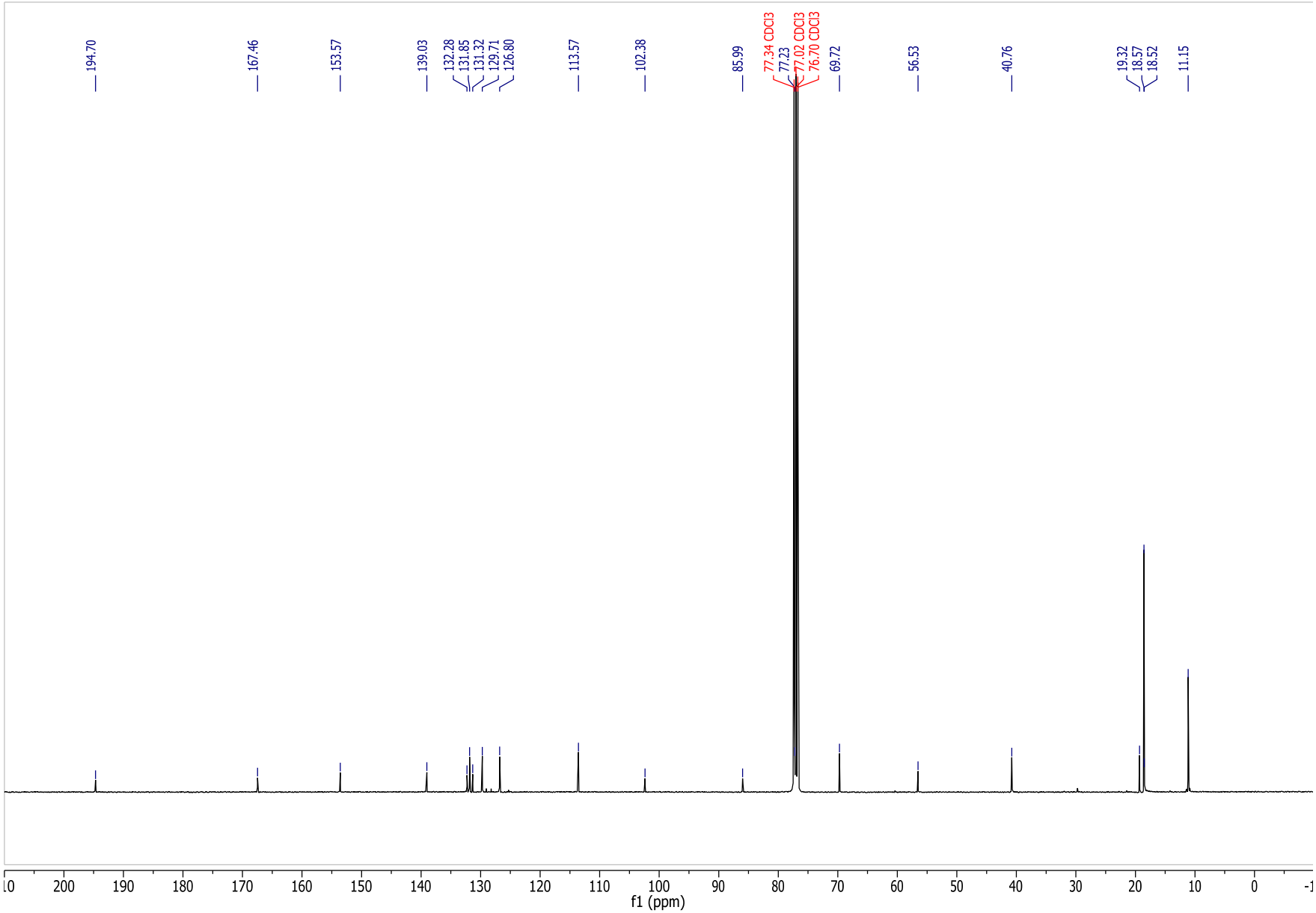
$CDCl_3$
100.1 MHz

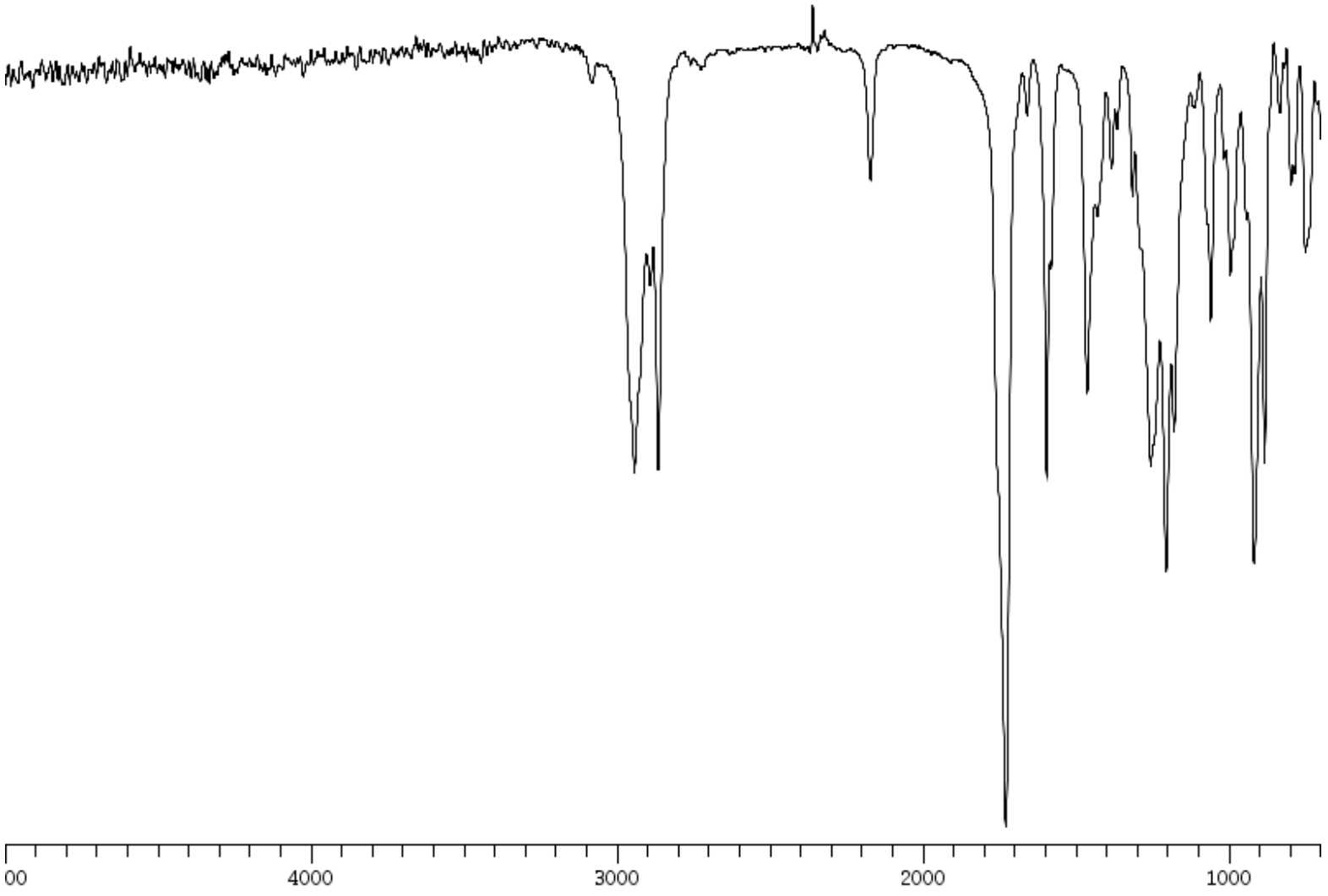


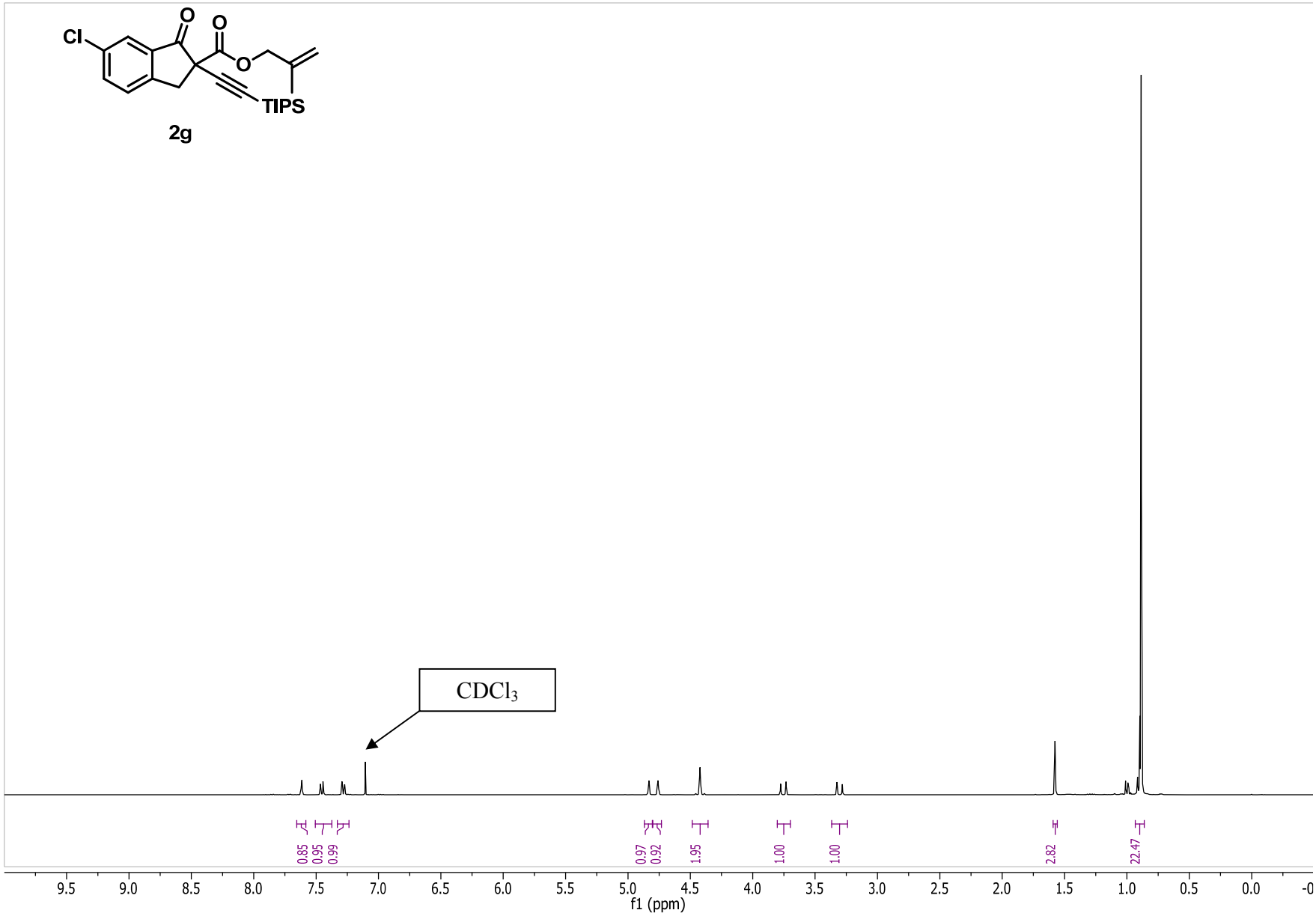

00
3000
2000
1000


CDCl3
400 MHz
Br
O
O
O
TIPS
2f
CDCl3
1.90
0.93
0.94
0.81
1.87
1.00
0.90
2.80
18.24
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

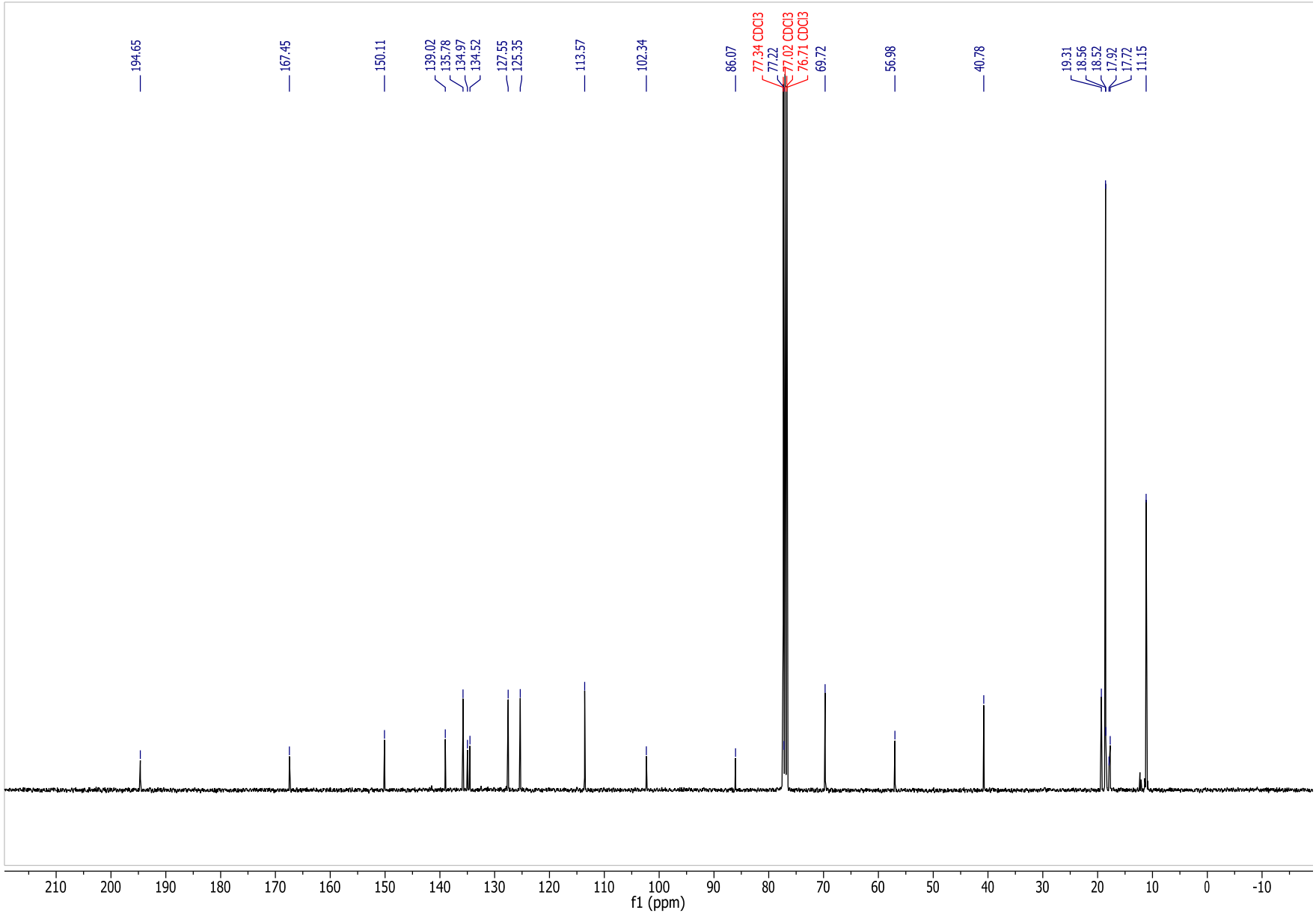
$CDCl_3$
100.1 MHz

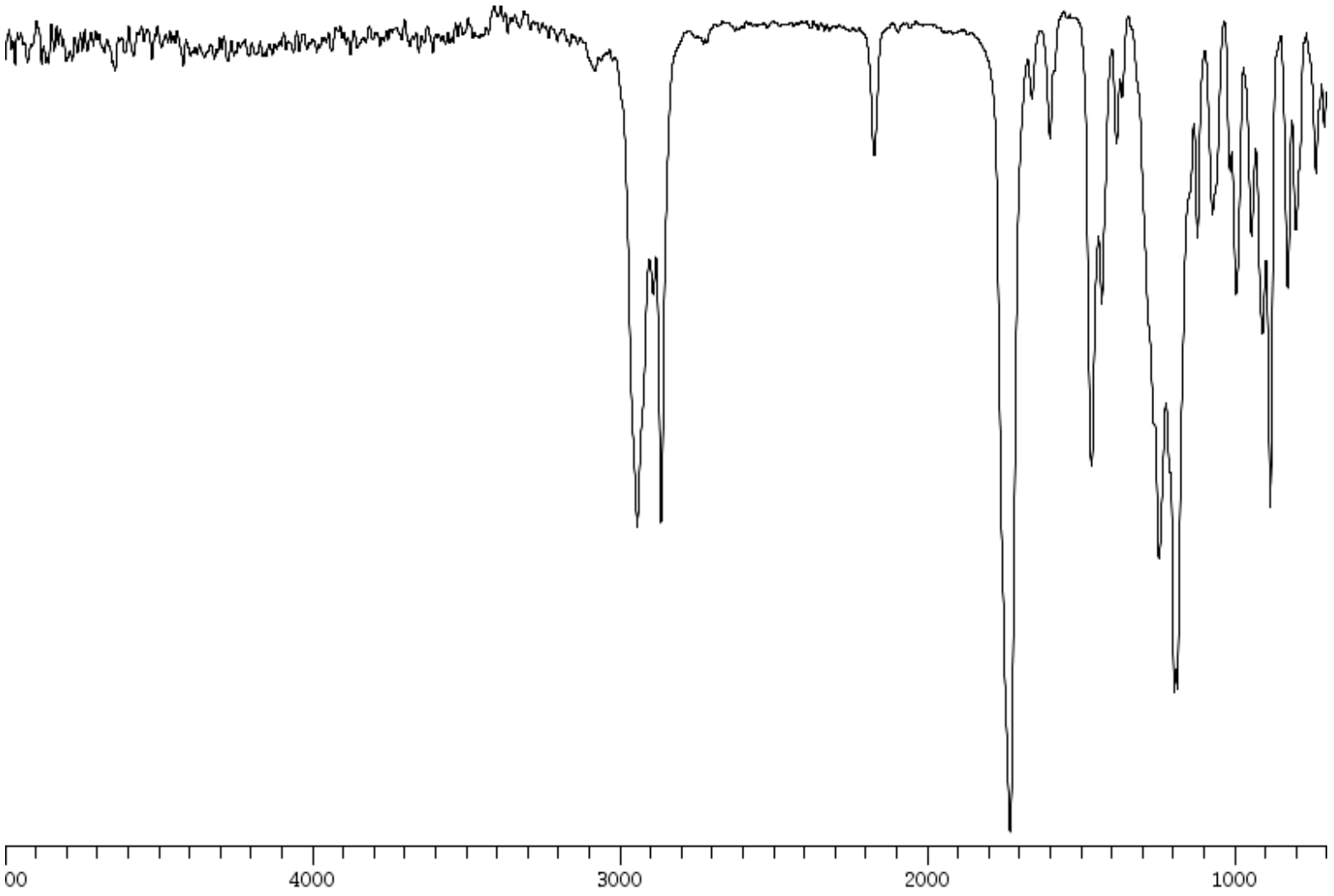


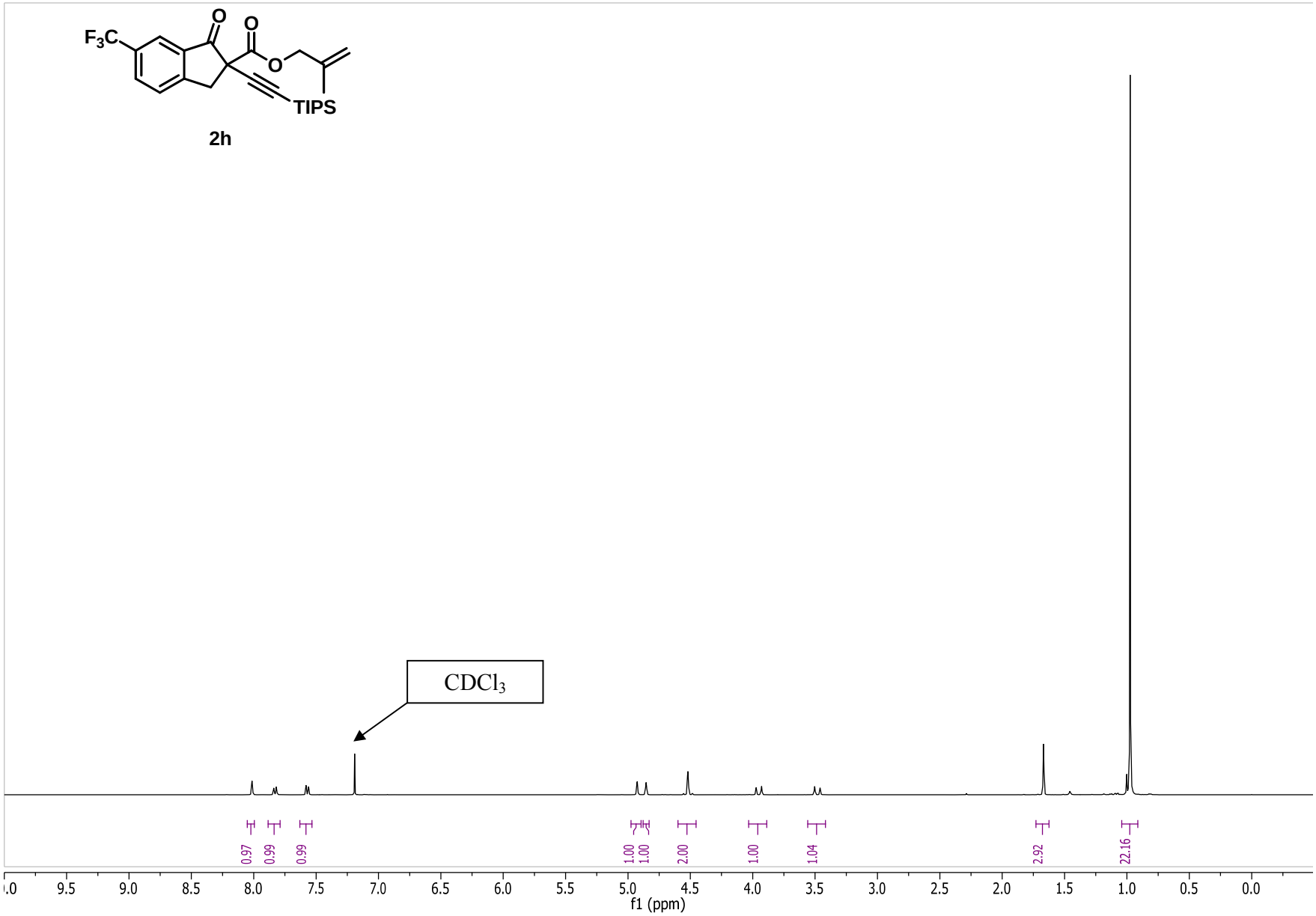

00
4000
3000
2000
1000


CDCl3
400 MHz
Cl
O
O
O
TIPS
2g
CDCl3
0.85
0.95
0.99
0.97
0.92
1.95
1.00
1.00
2.82
22.47
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

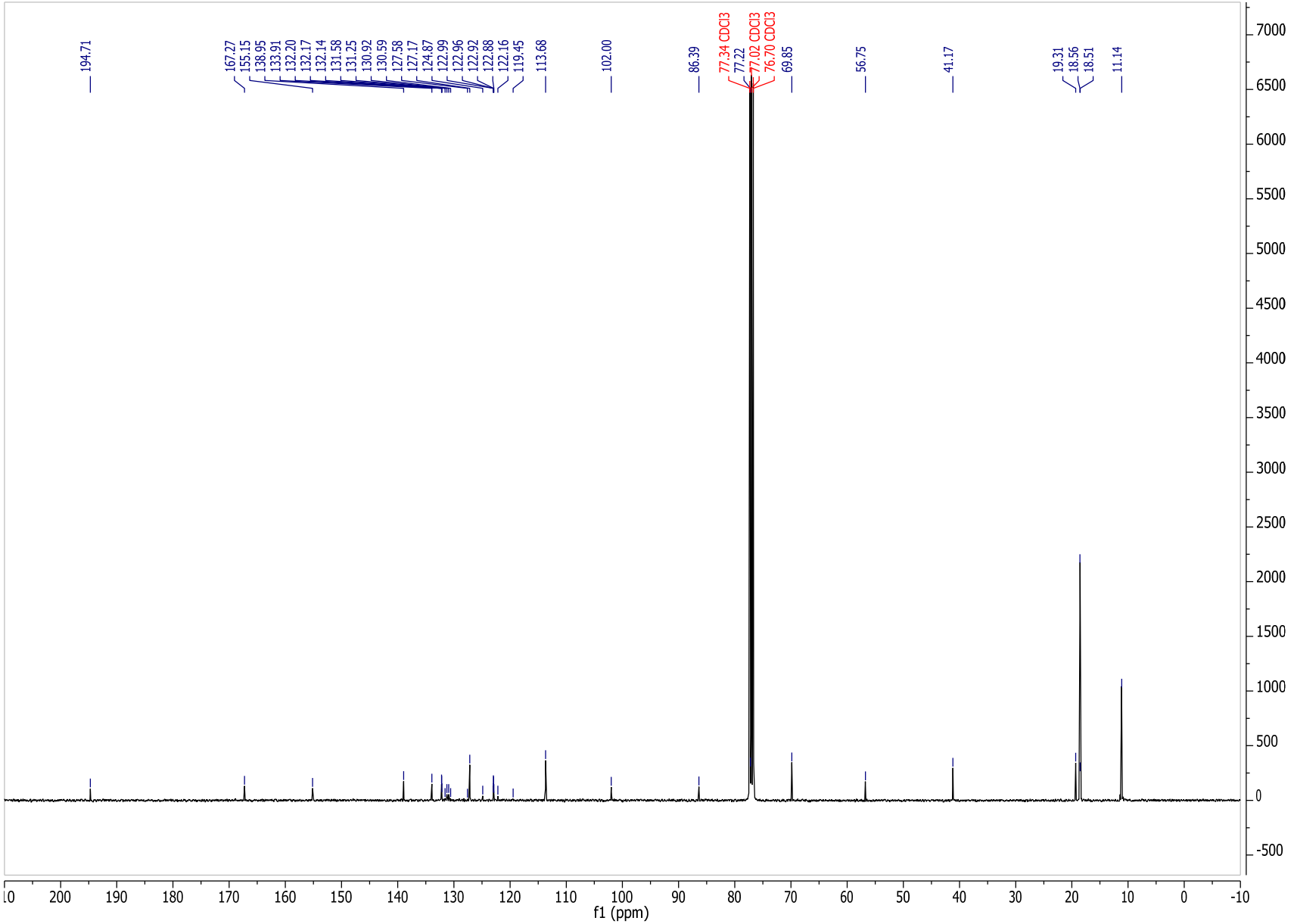
$CDCl_3$
100.1 MHz

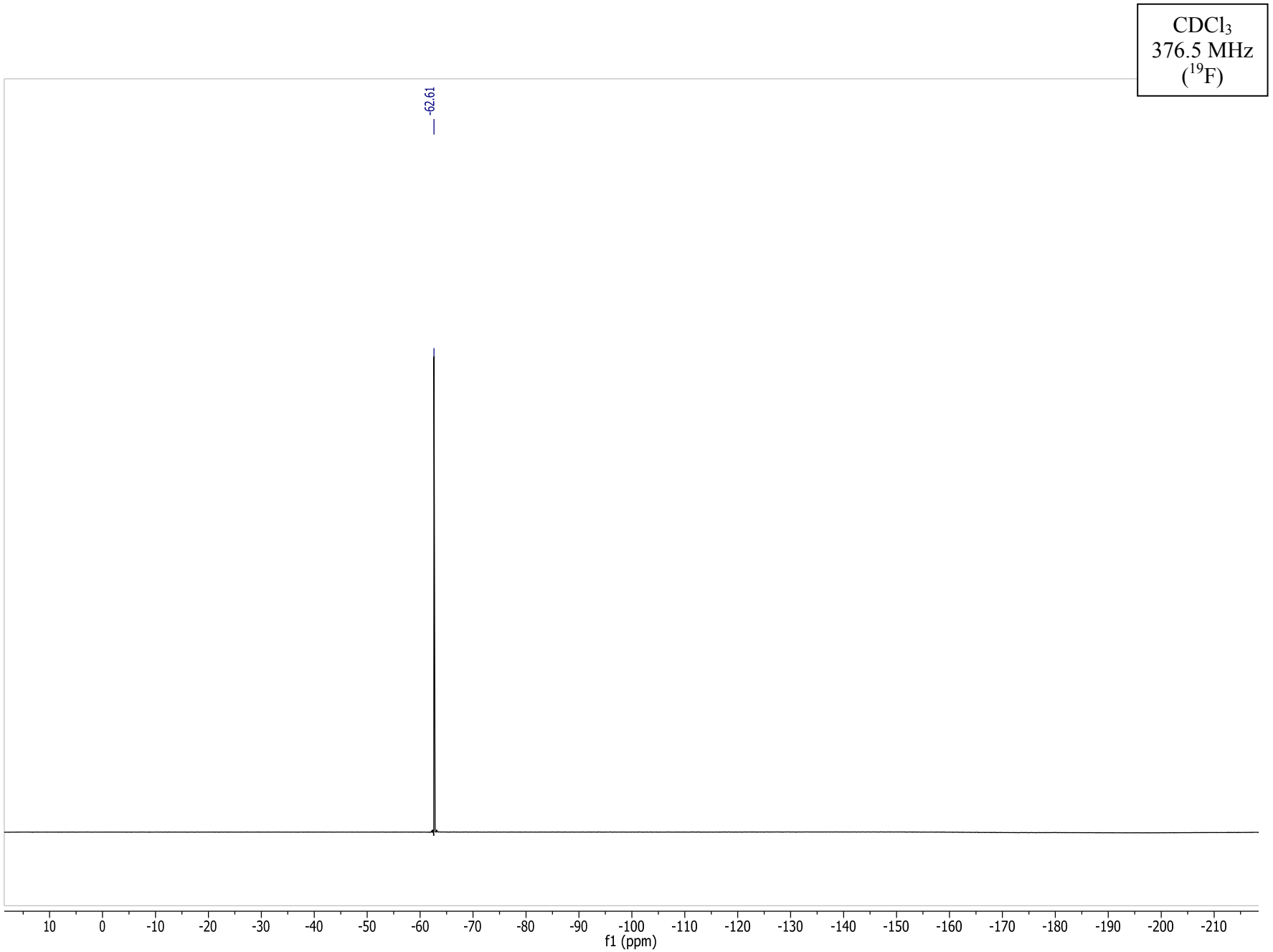


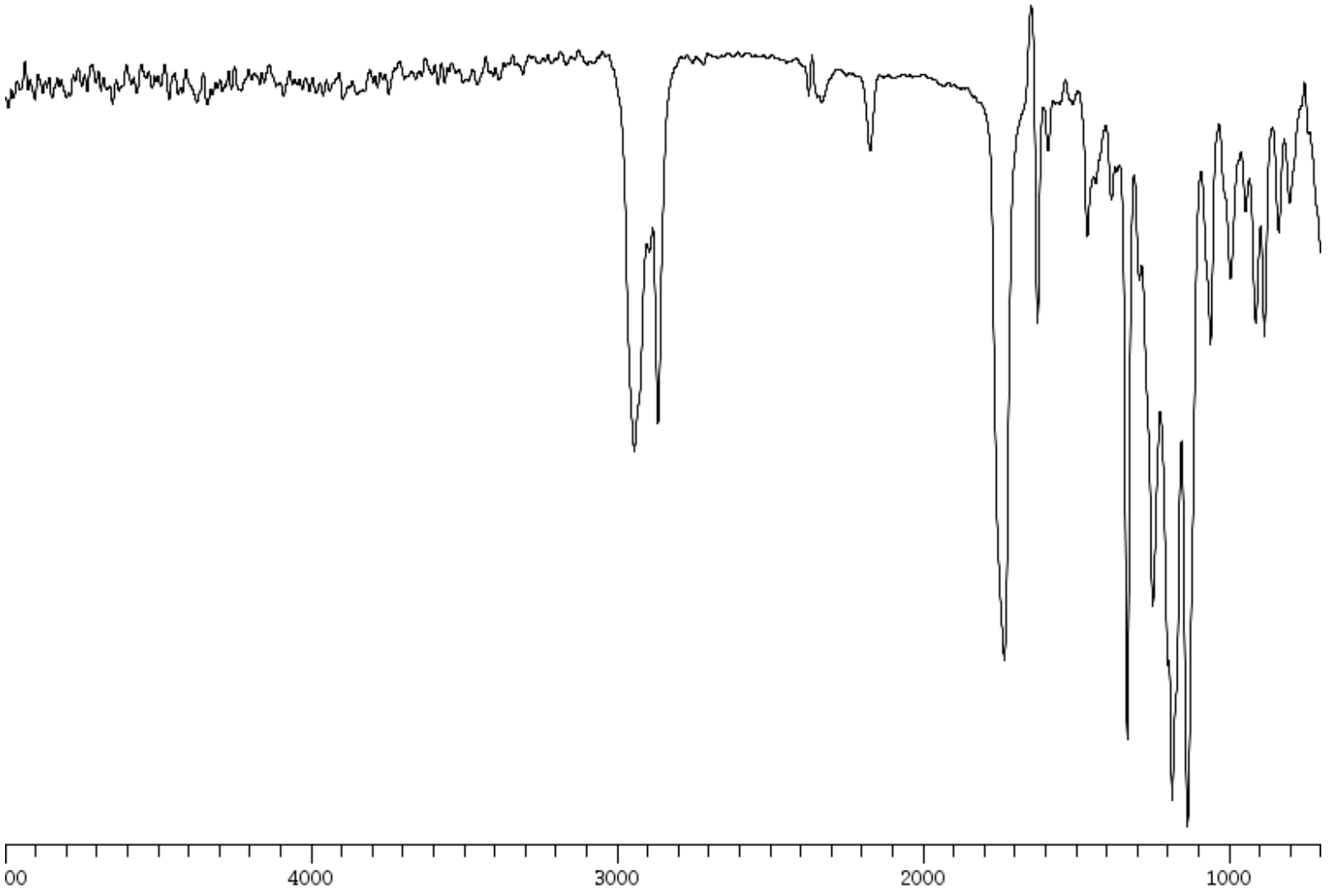

00
4000
3000
2000
1000


CDCl3
400 MHz
F3C
O
O
O
TIPS
2h
CDCl3
0.97
0.99
0.99
1.00
1.00
2.00
1.00
1.04
2.92
22.16
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

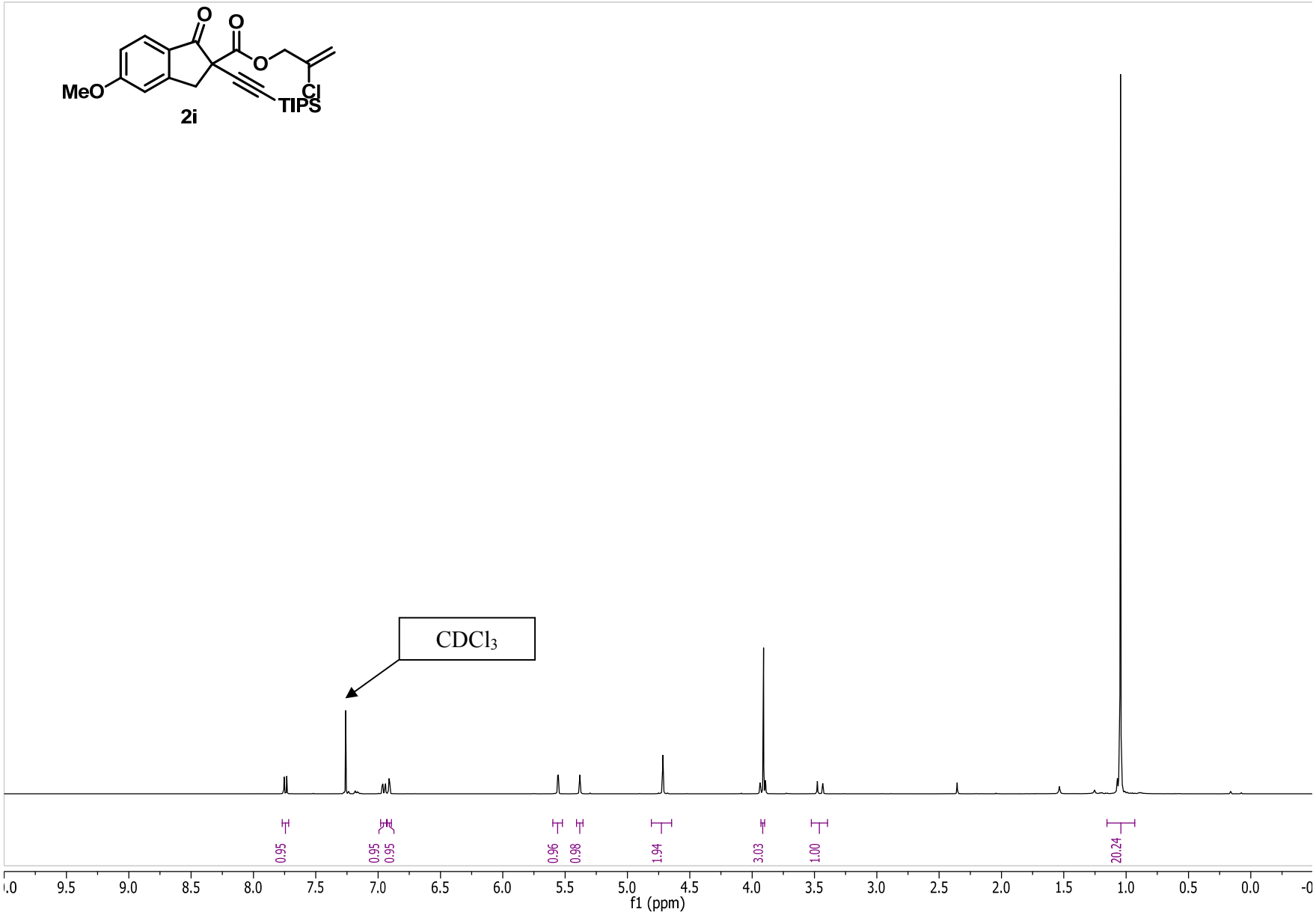
$CDCl_3$
100.1 MHz



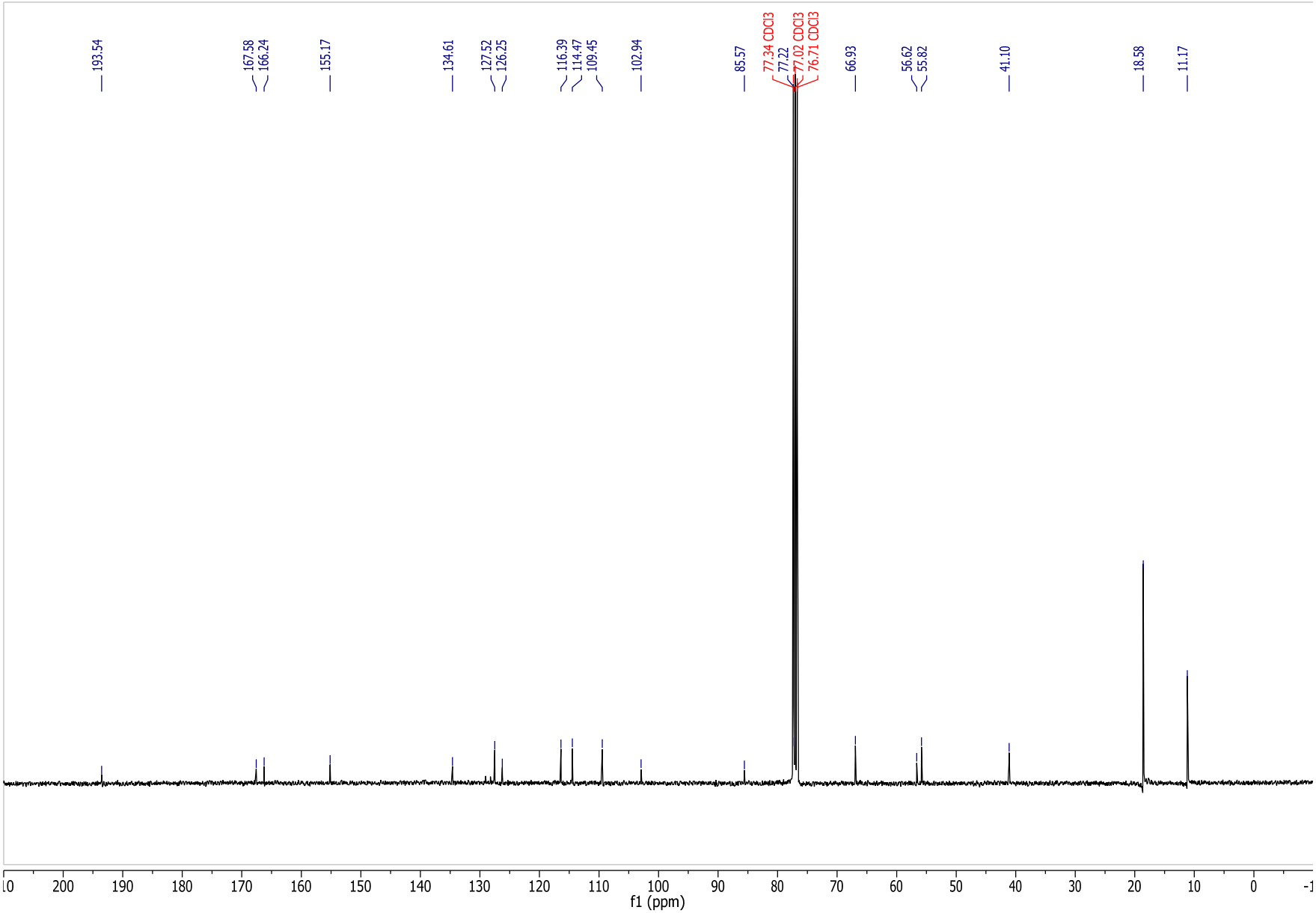

$CDCl_3$
376.5 MHz
(^{19}F)
-62.61
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

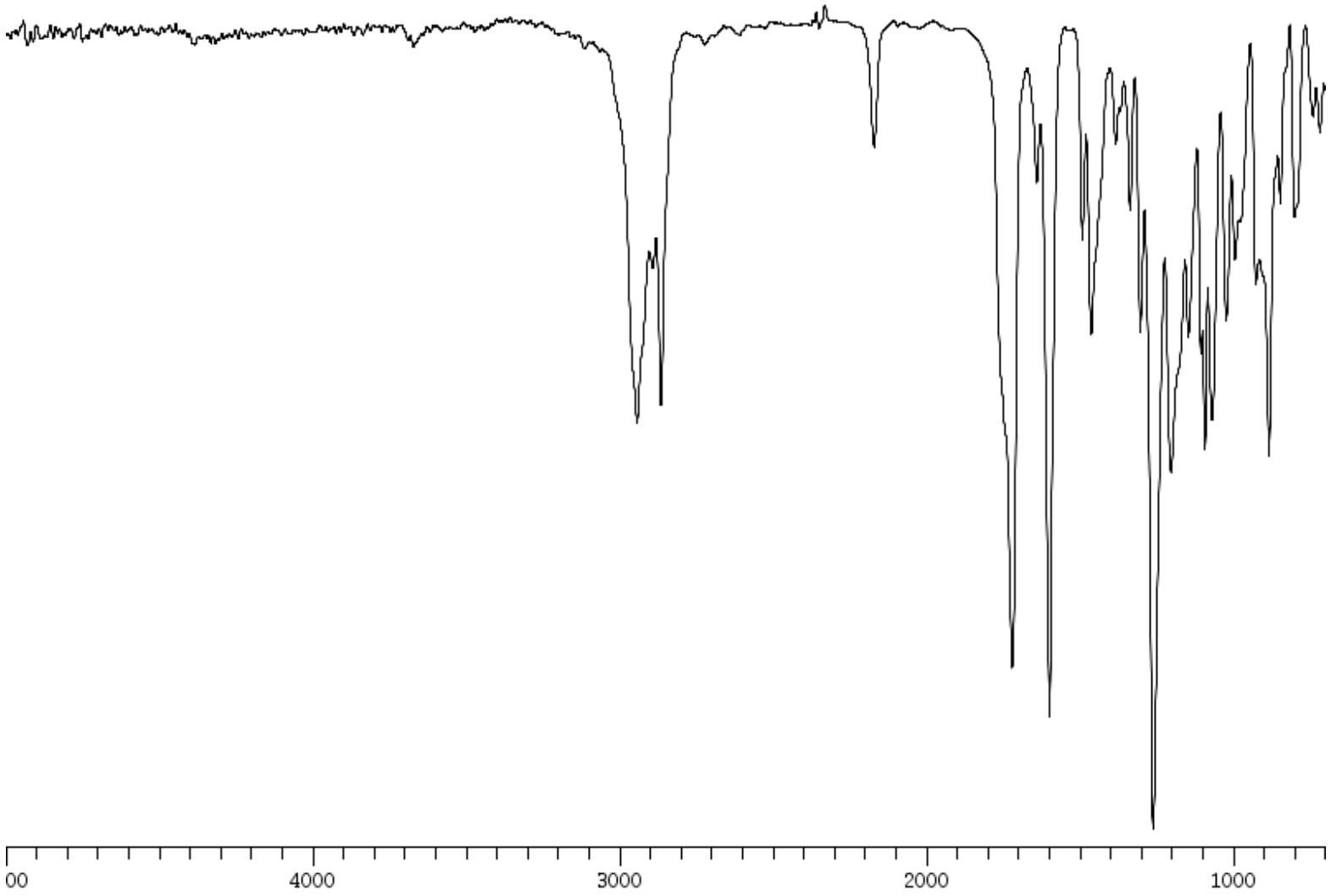

00
4000
3000
2000
1000

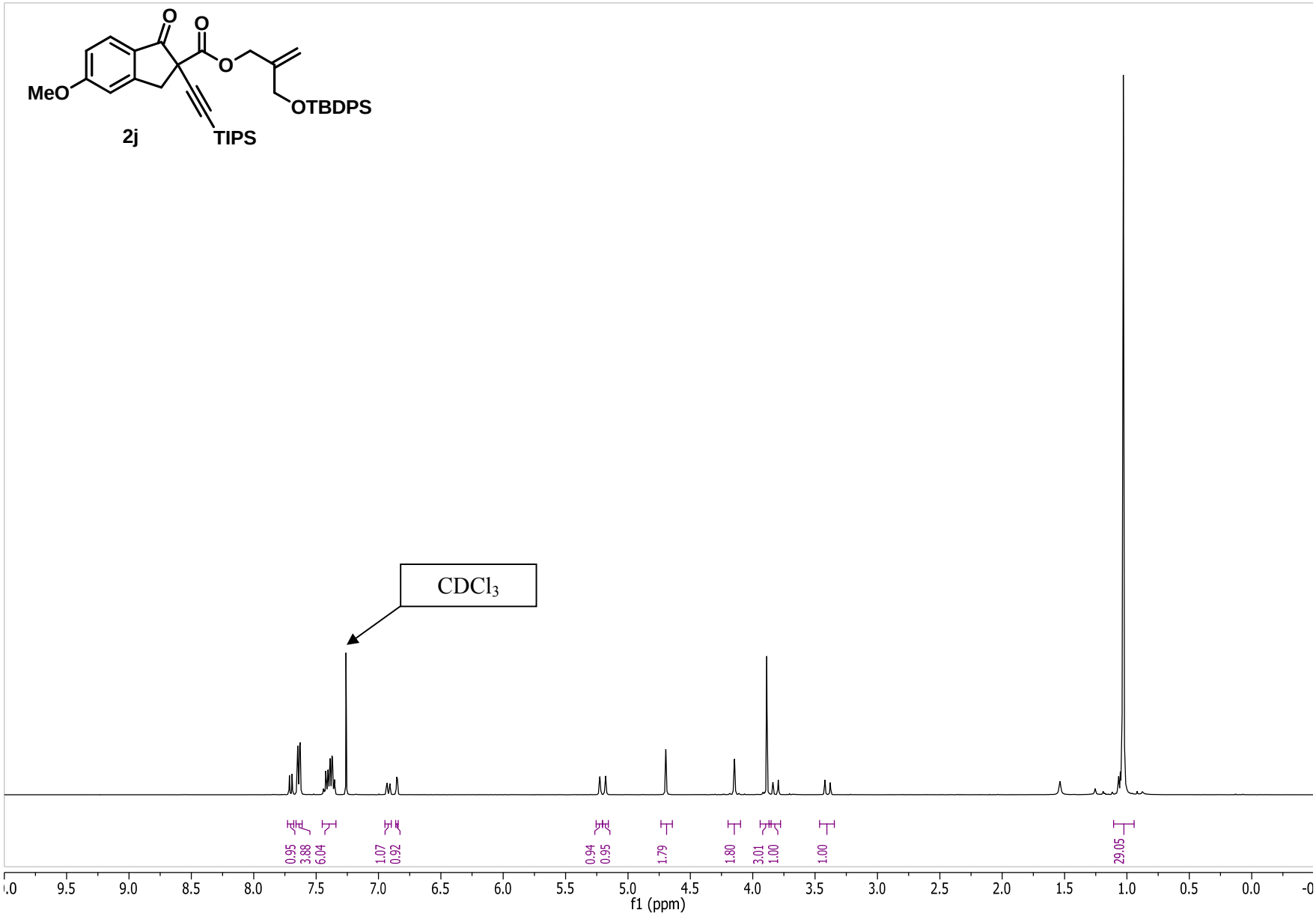
$CDCl_3$
400 MHz



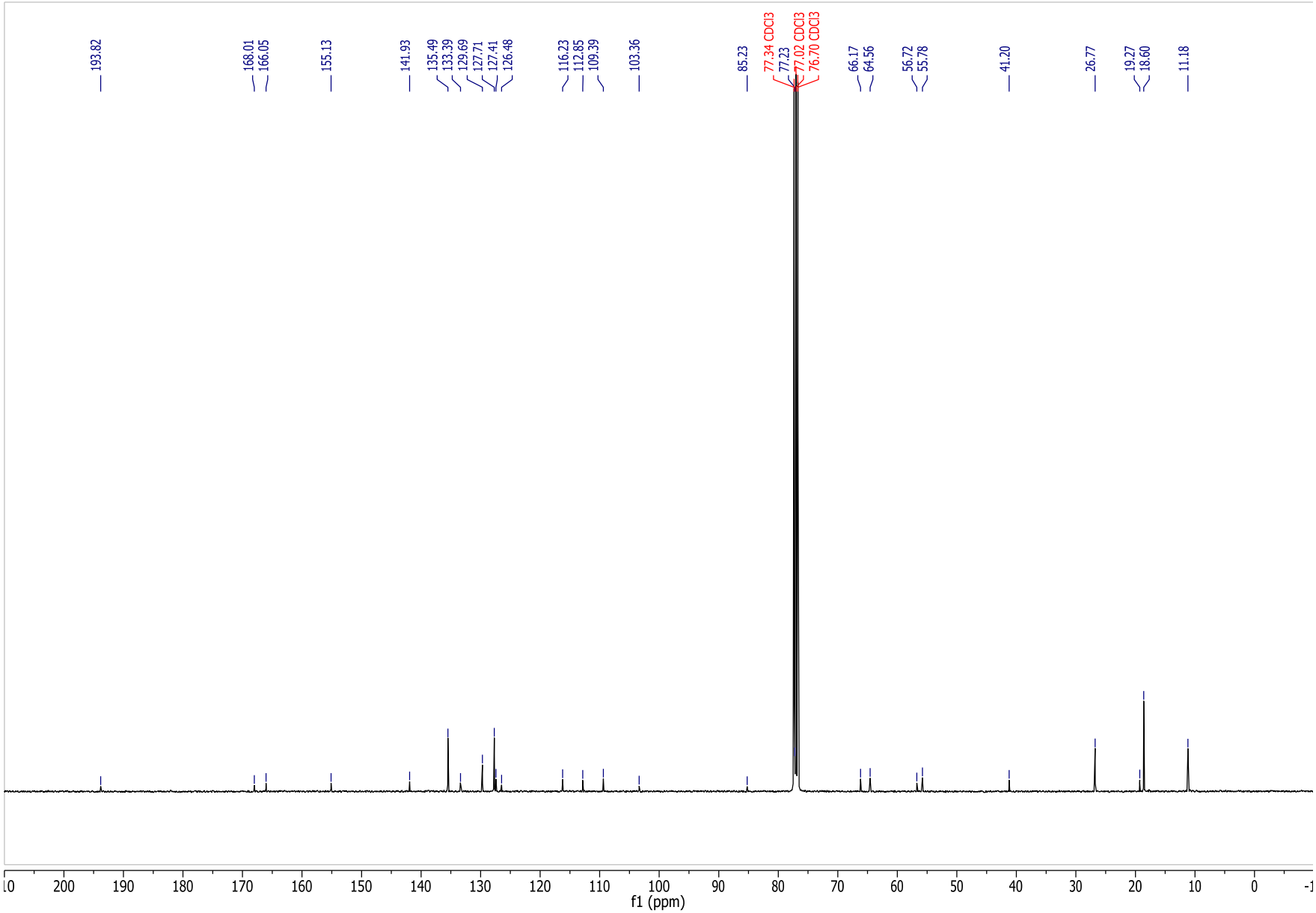
$CDCl_3$
100.1 MHz

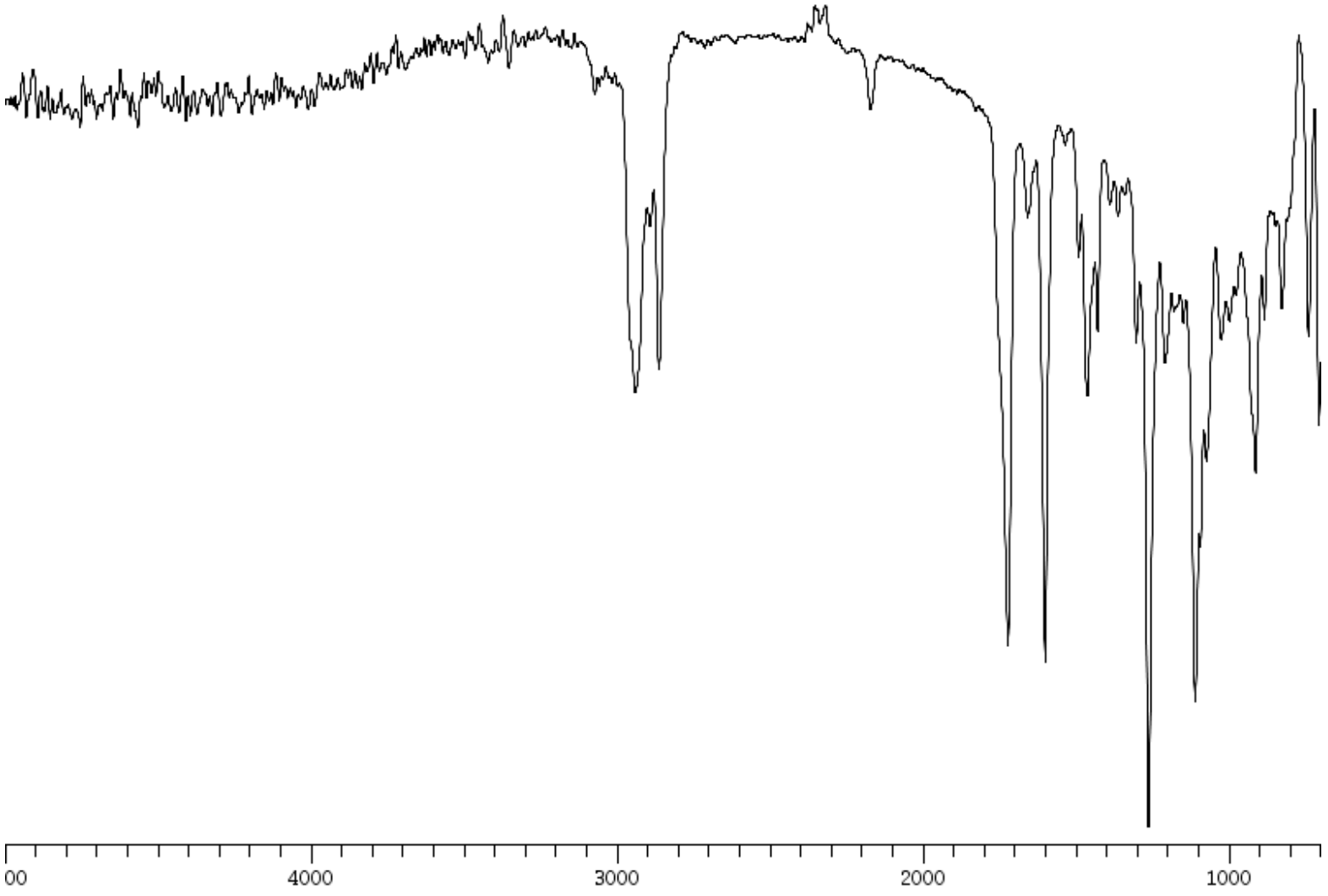



00
4000
3000
2000
1000


CDCl3
400 MHz
MeO
O
O
O
OTBDPS
2j
TIPS
CDCl3
0.95
3.88
6.04
1.07
0.92
0.94
0.95
1.79
1.80
3.01
1.00
1.00
29.05
f1 (ppm)

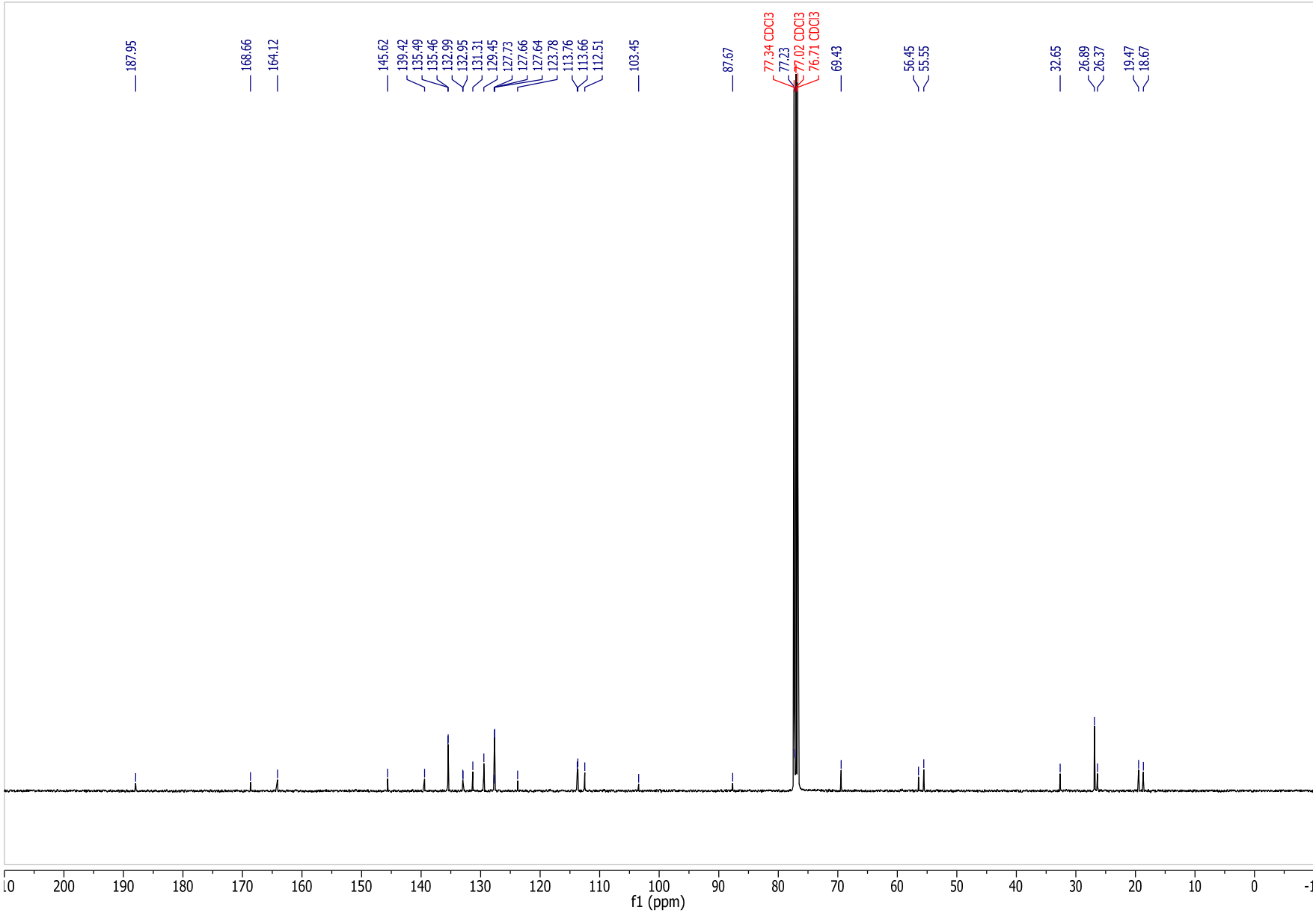
$CDCl_3$
100.1 MHz

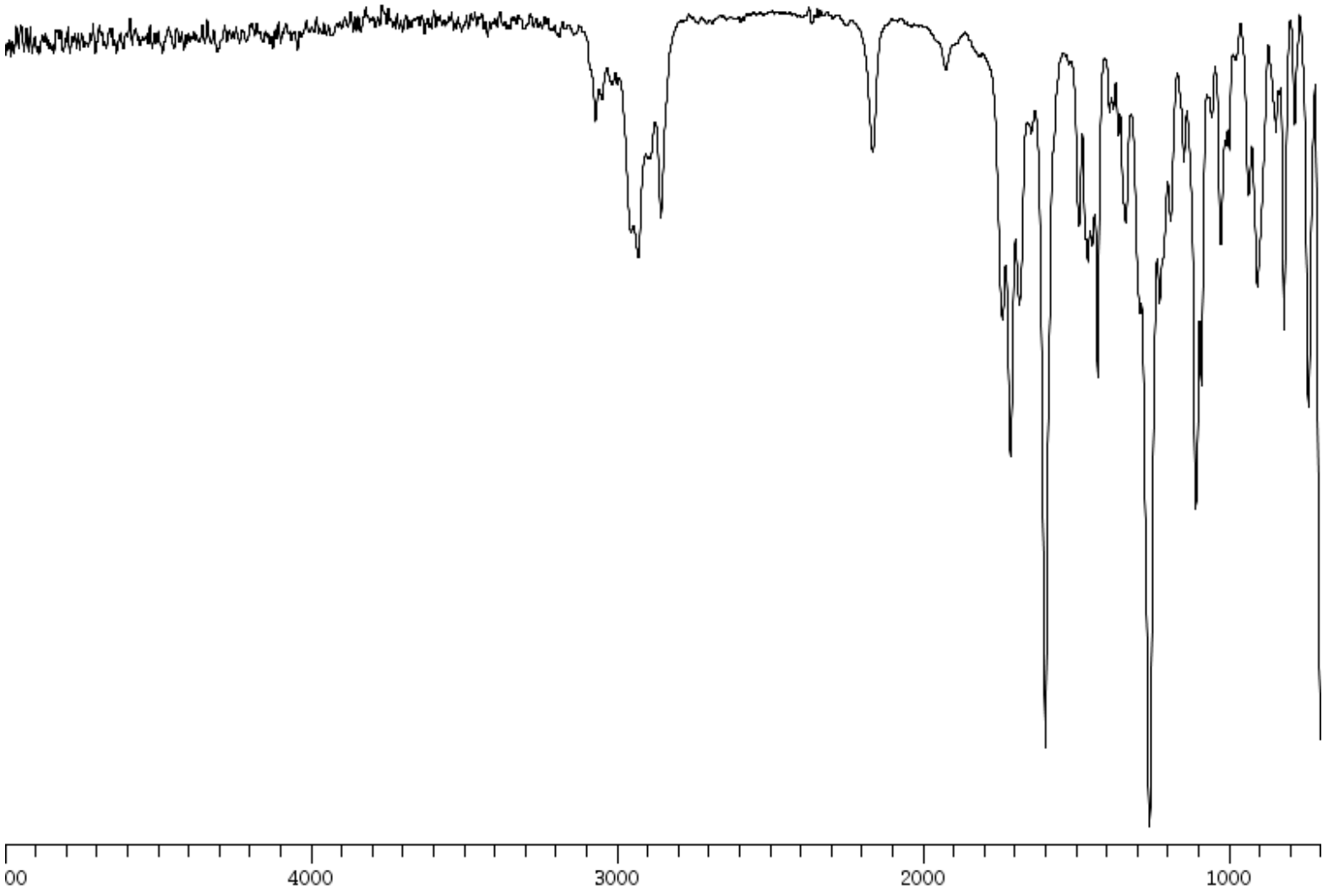



00
4000
3000
2000
1000

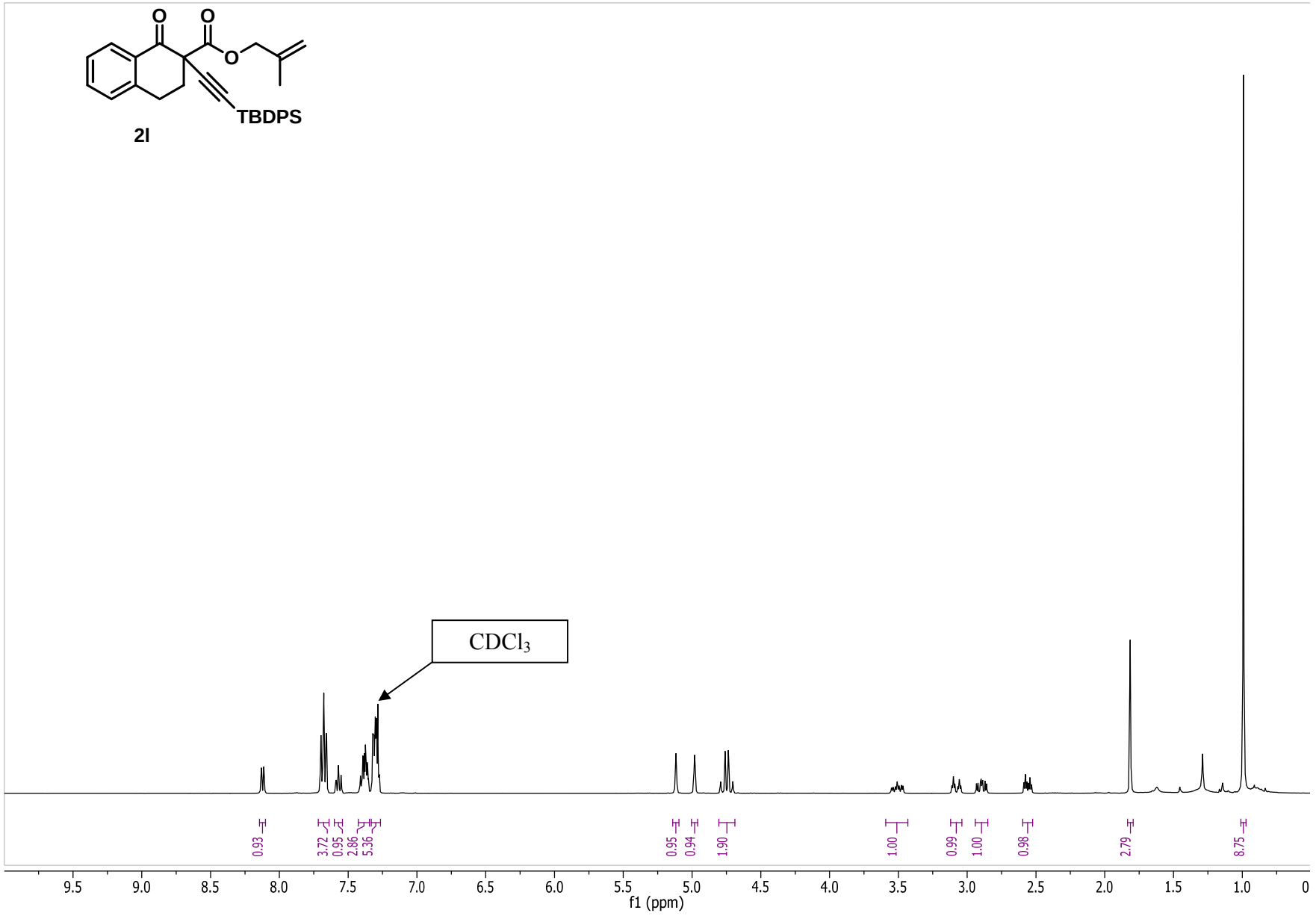
$CDCl_3$
400 MHz

$CDCl_3$
100.1 MHz

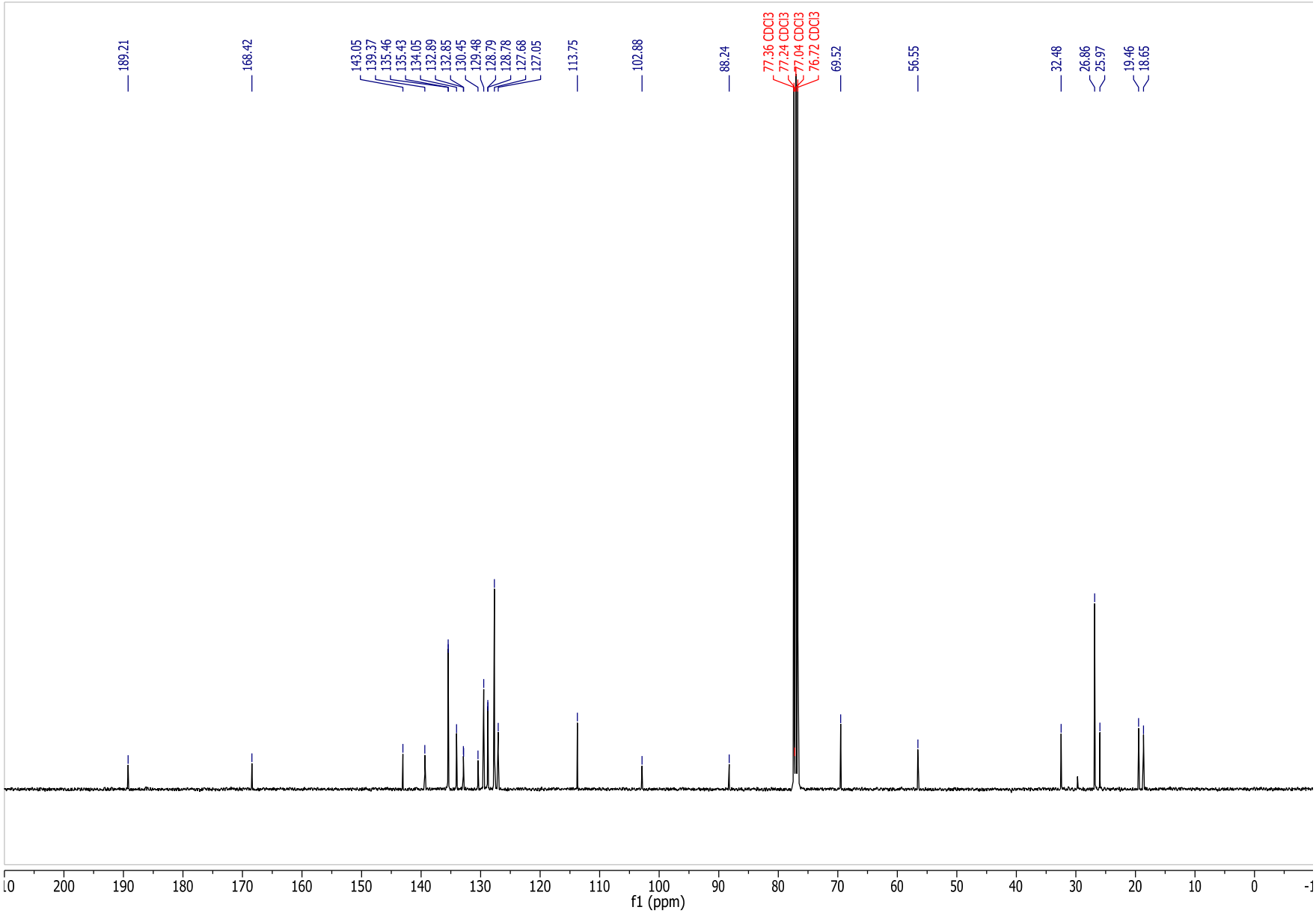


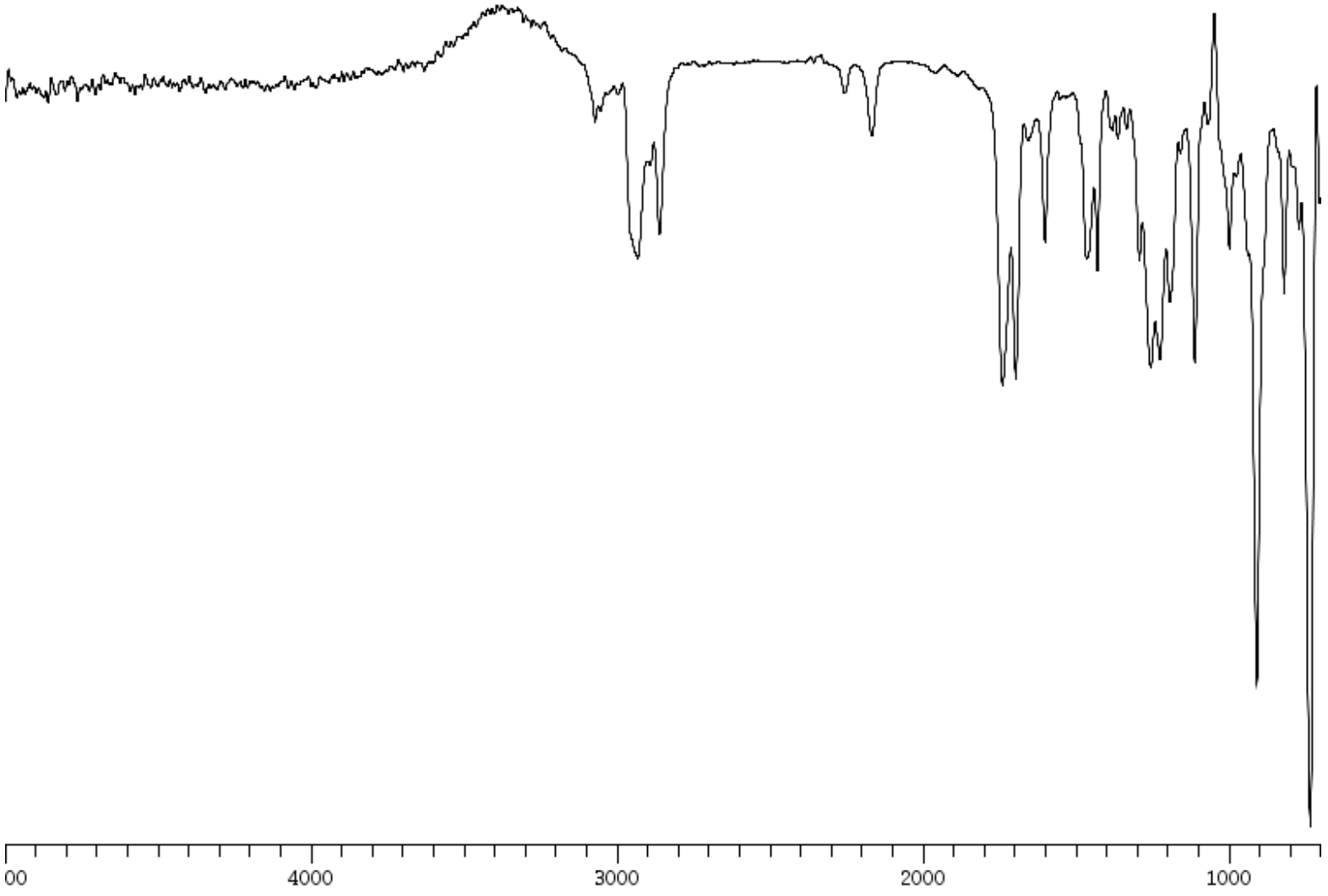

00
4000
3000
2000
1000

$CDCl_3$
400 MHz

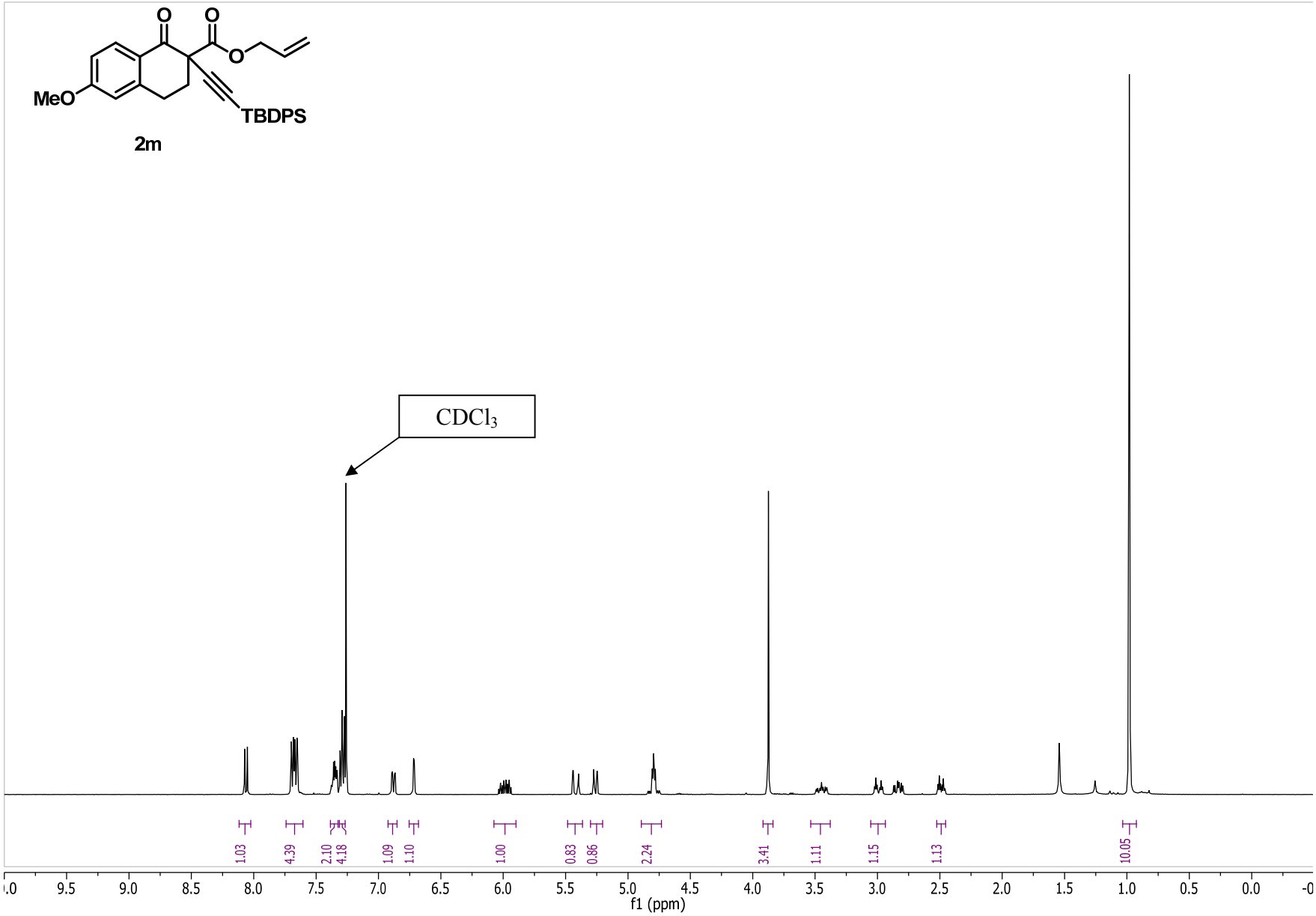


$CDCl_3$
100.1 MHz

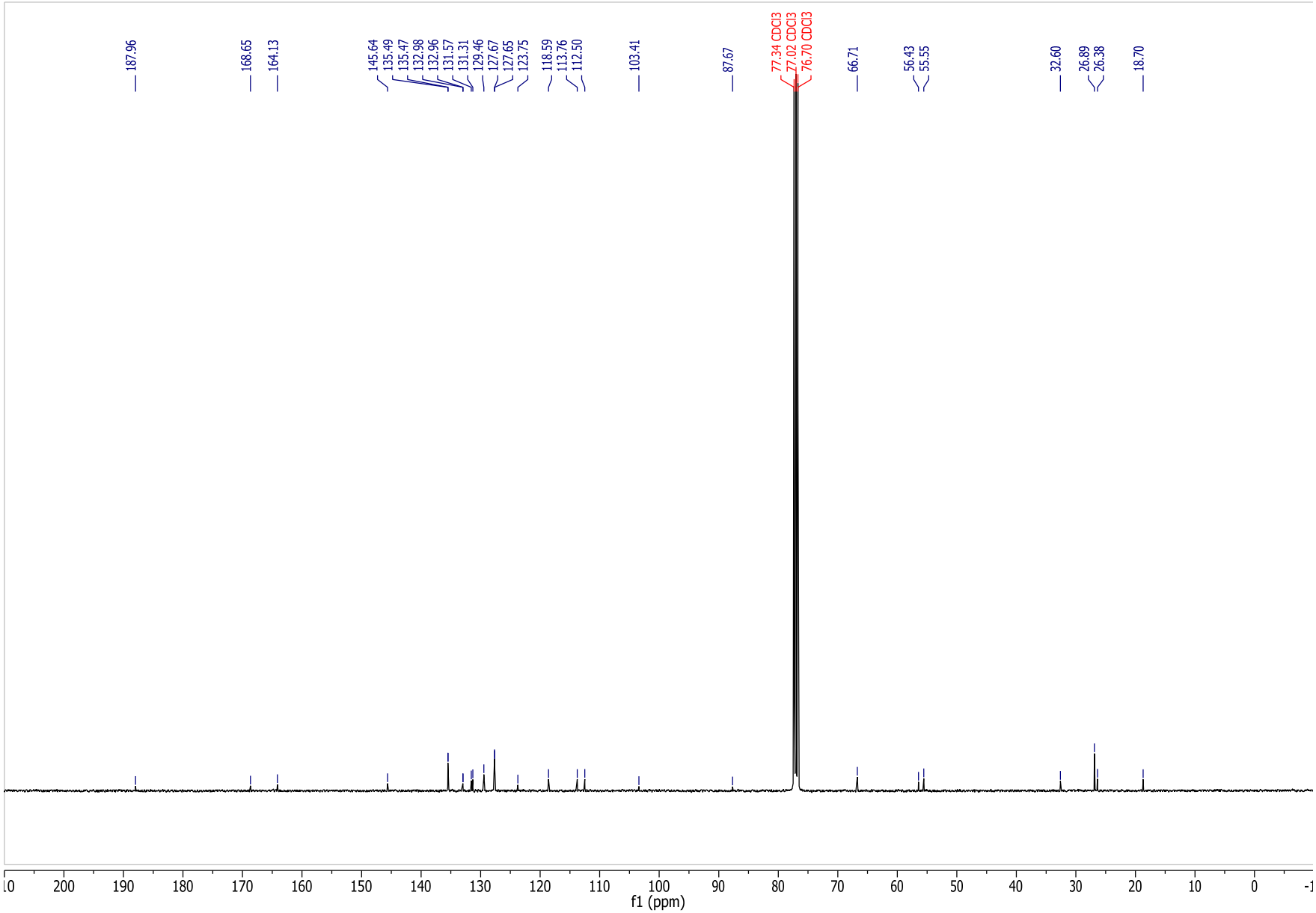


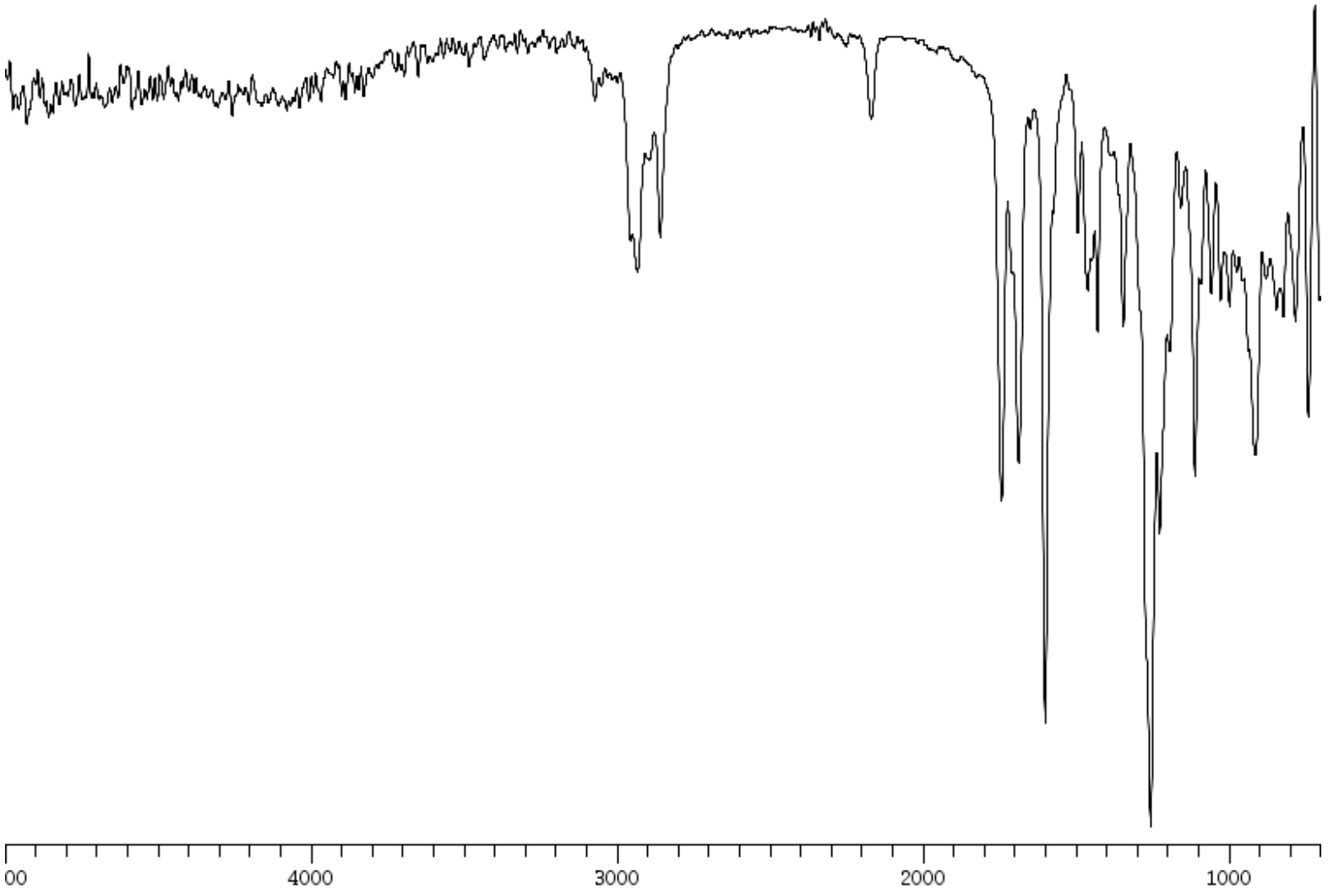

00
4000
3000
2000
1000

$CDCl_3$
400 MHz

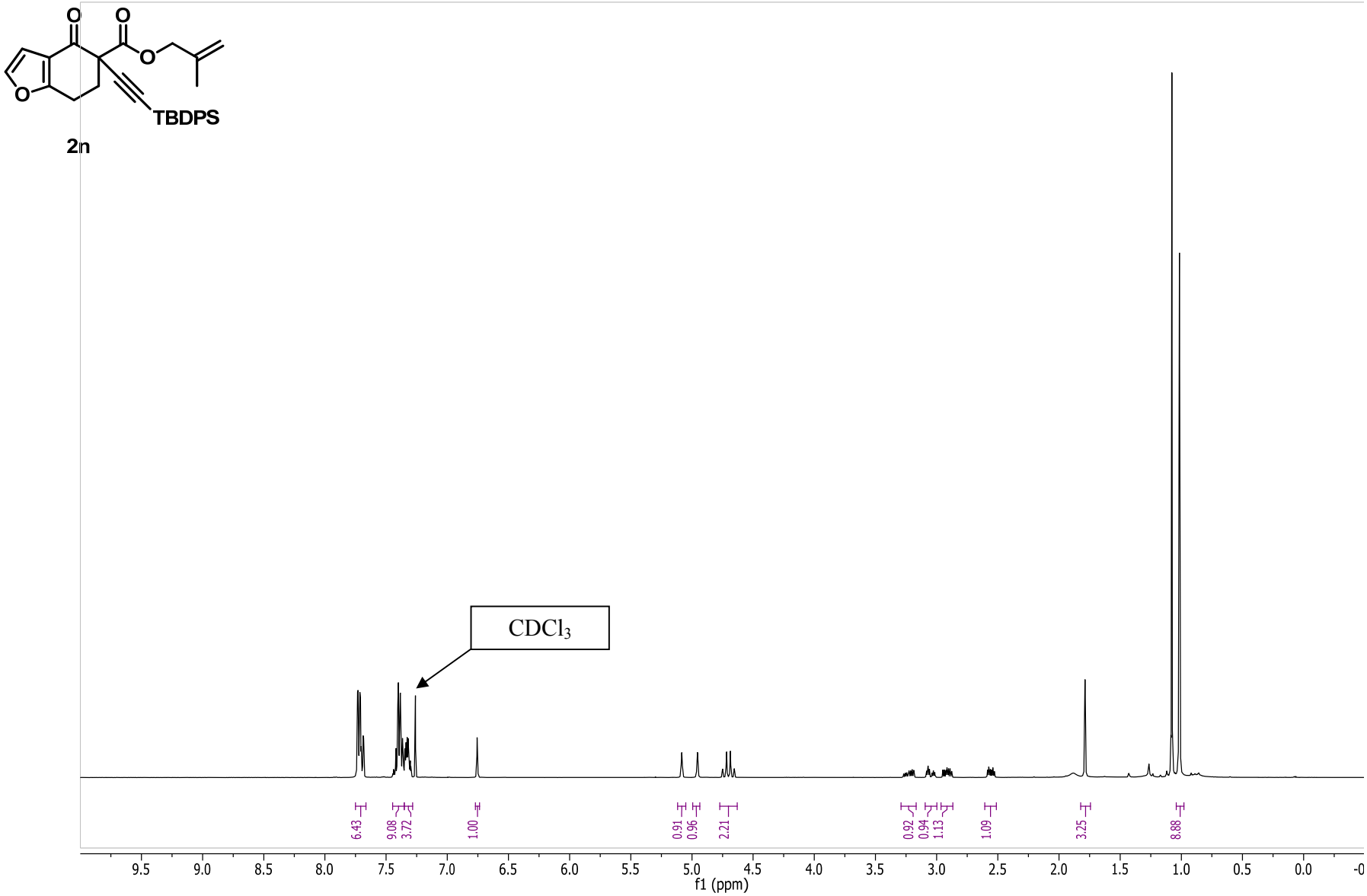


$CDCl_3$
100.1 MHz

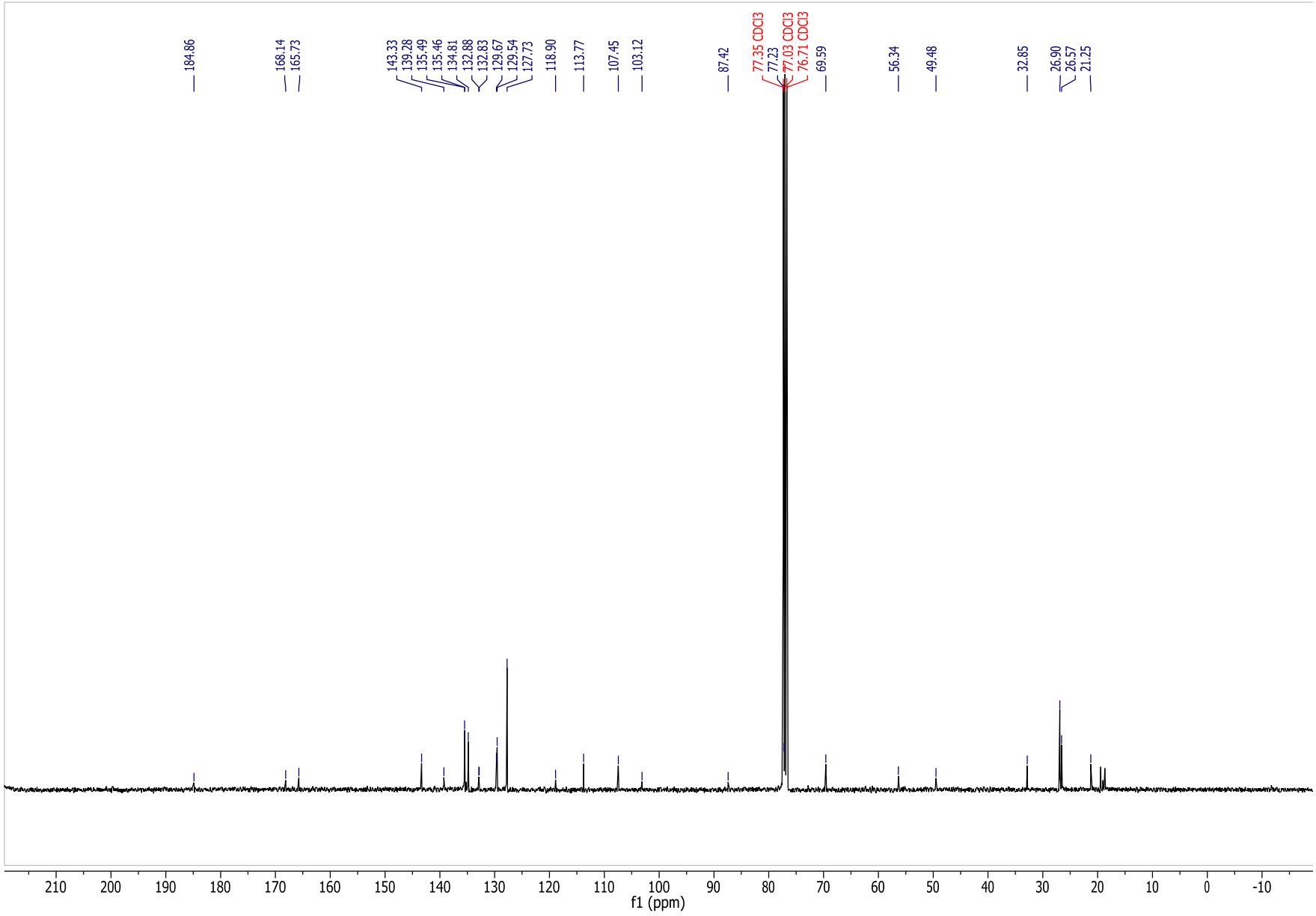


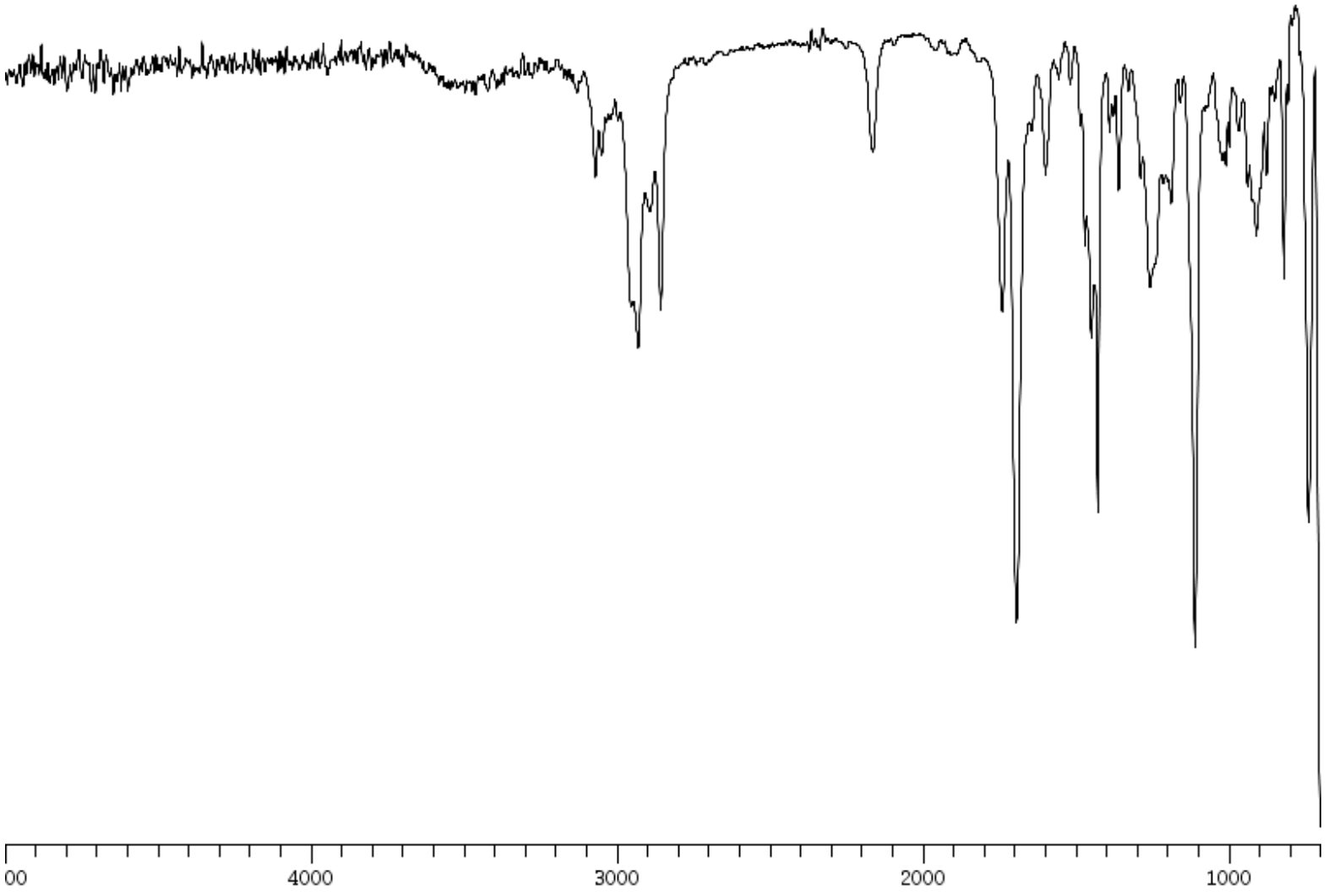

00
4000
3000
2000
1000

$CDCl_3$
400 MHz

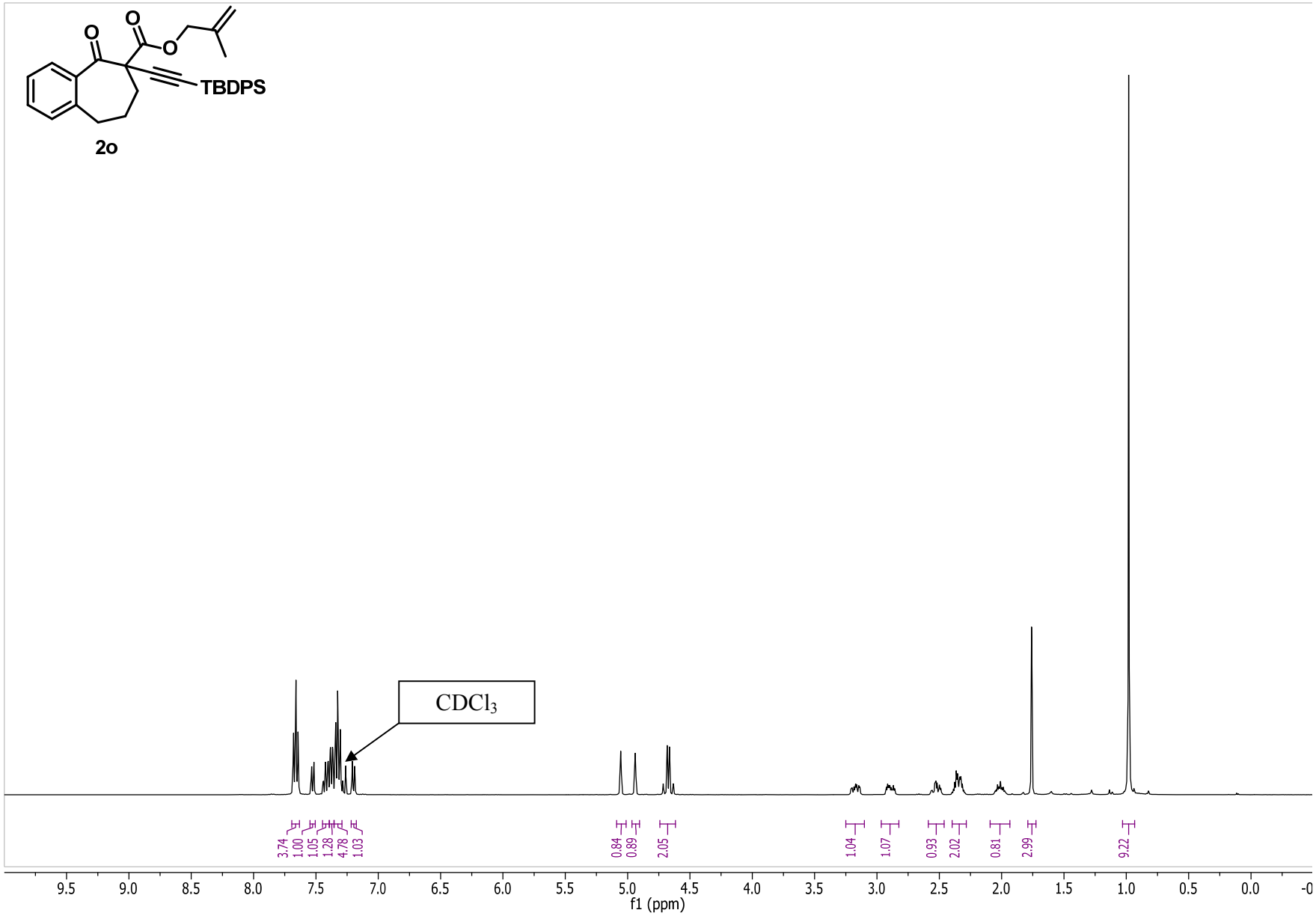


$CDCl_3$
100.1 MHz

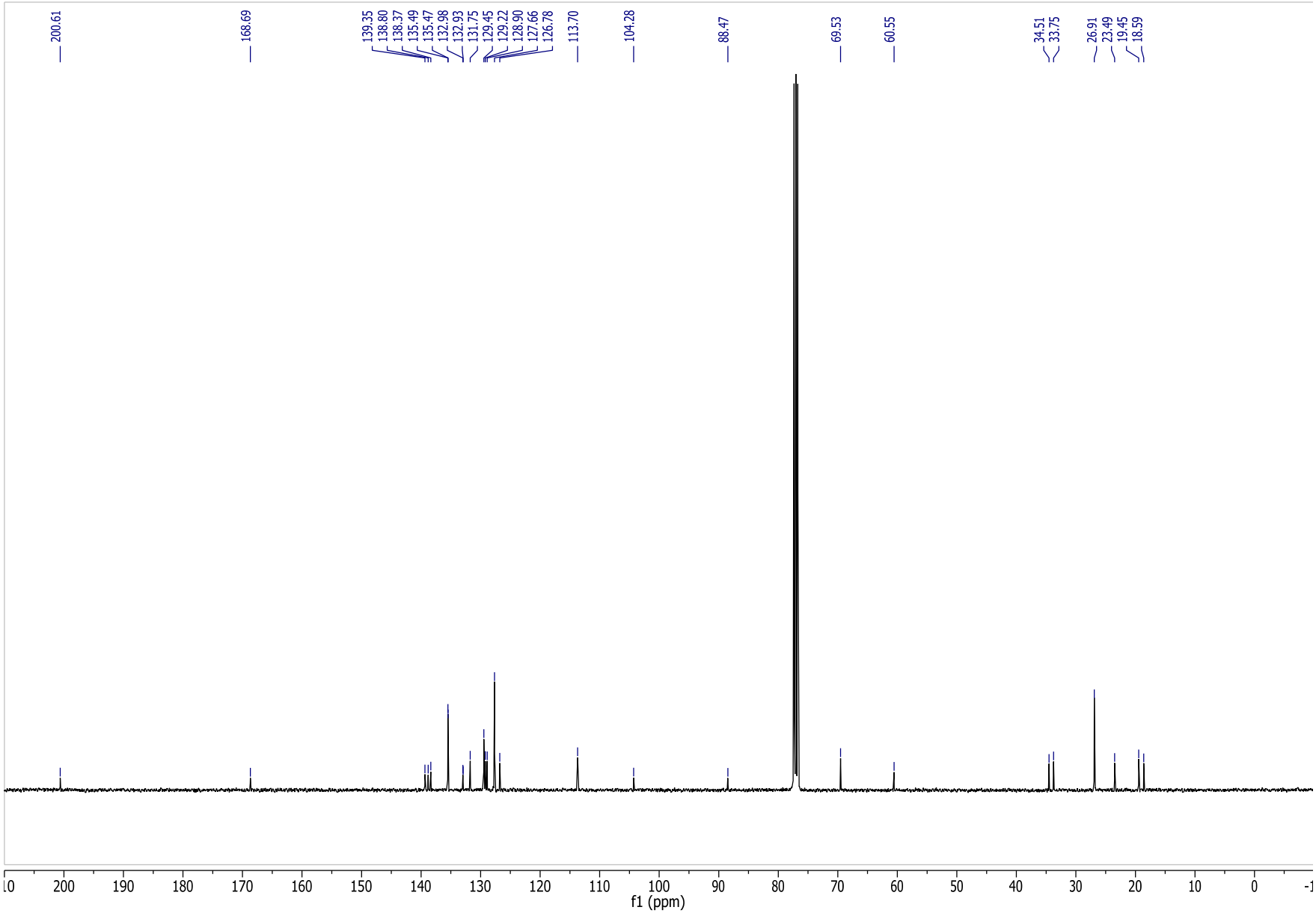


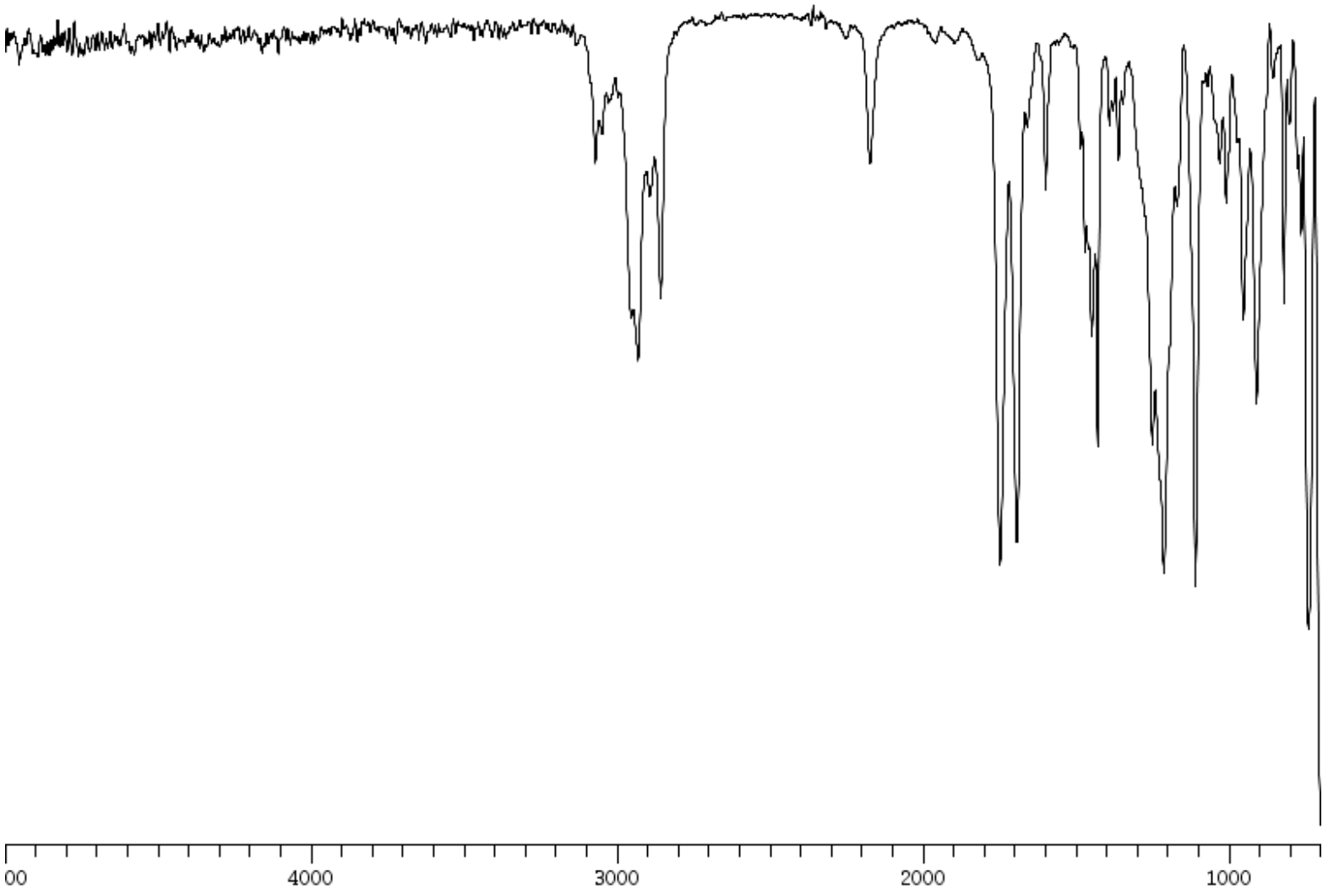

00
4000
3000
2000
1000

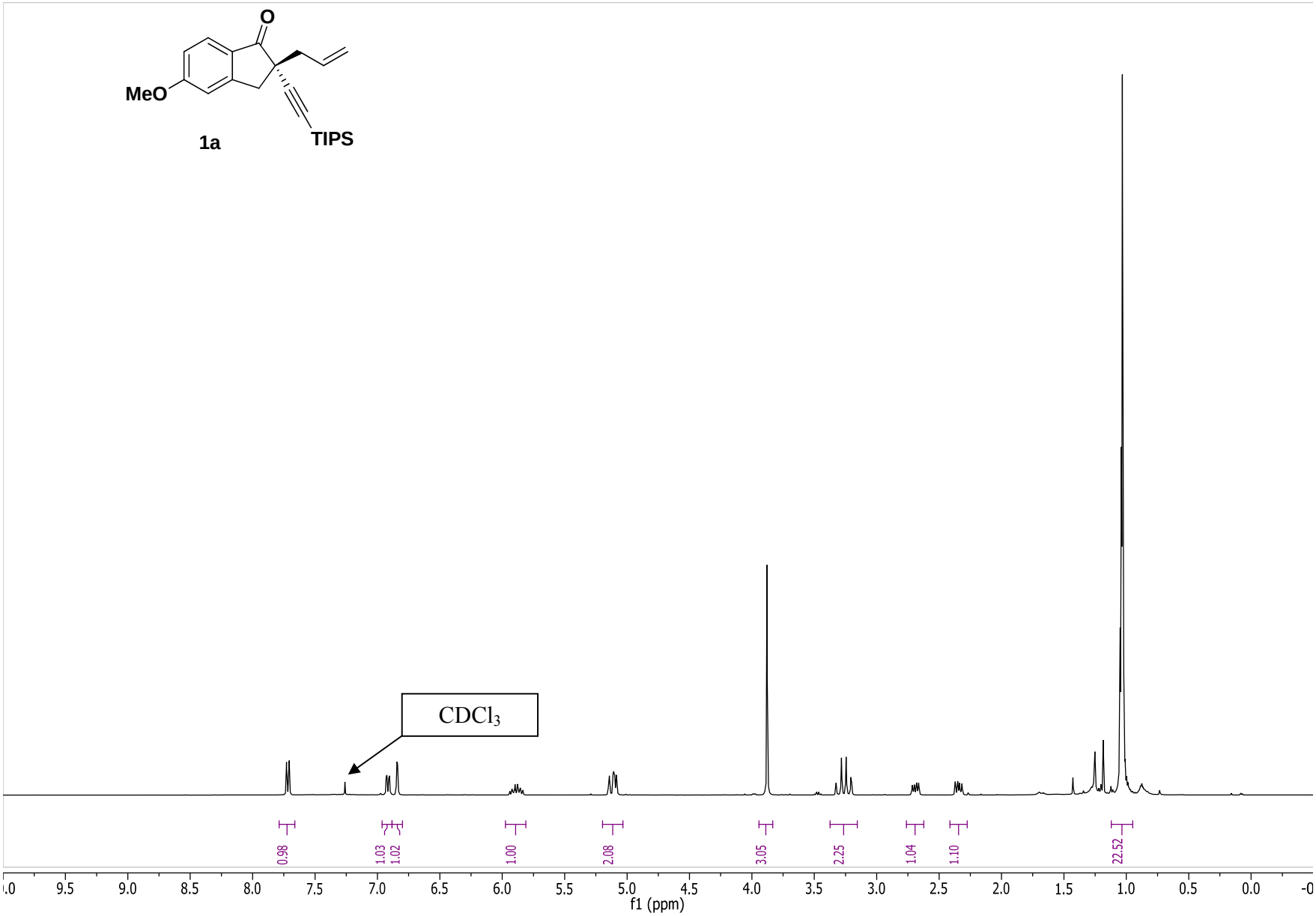
$CDCl_3$
400 MHz



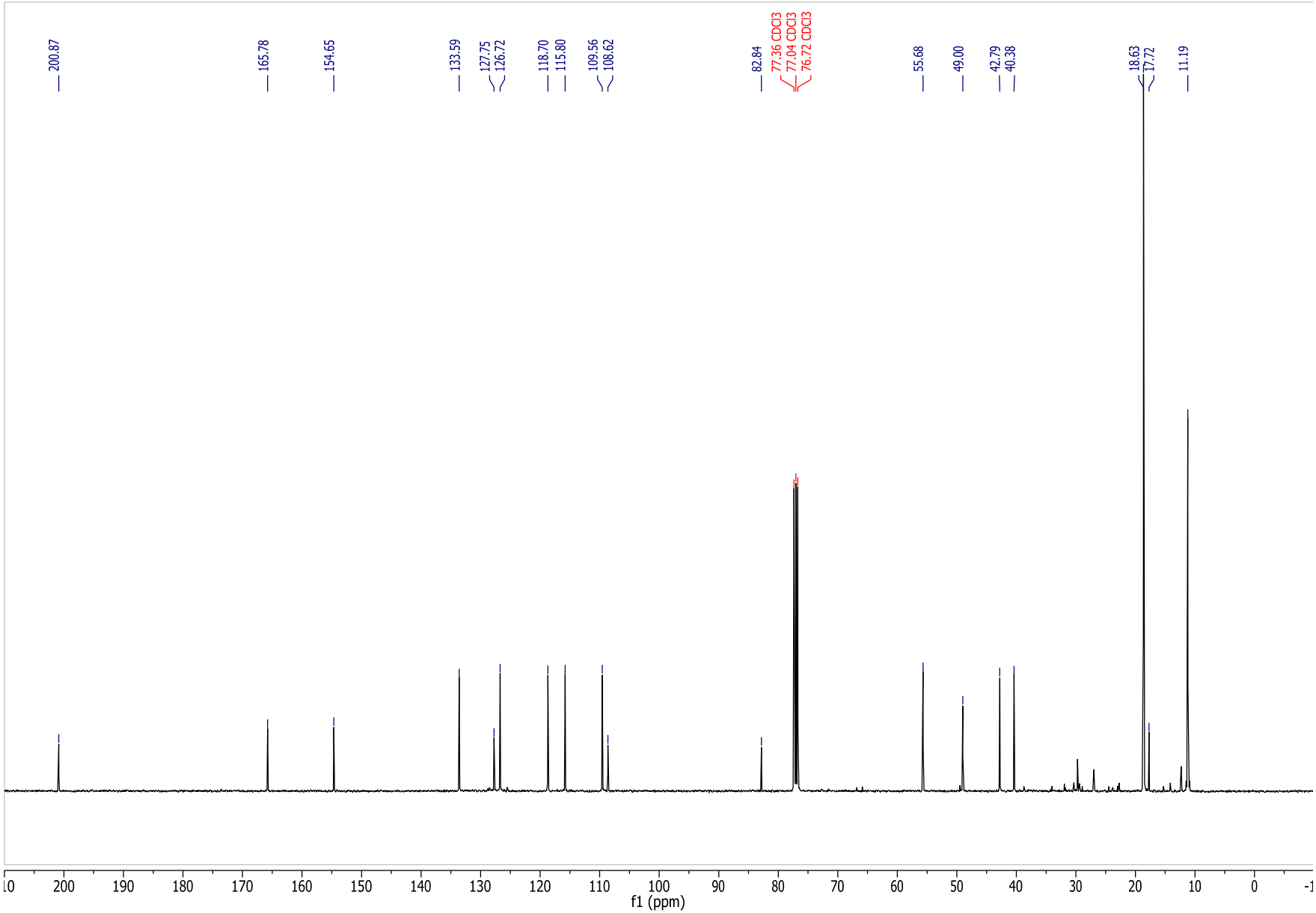
$CDCl_3$
100.1 MHz

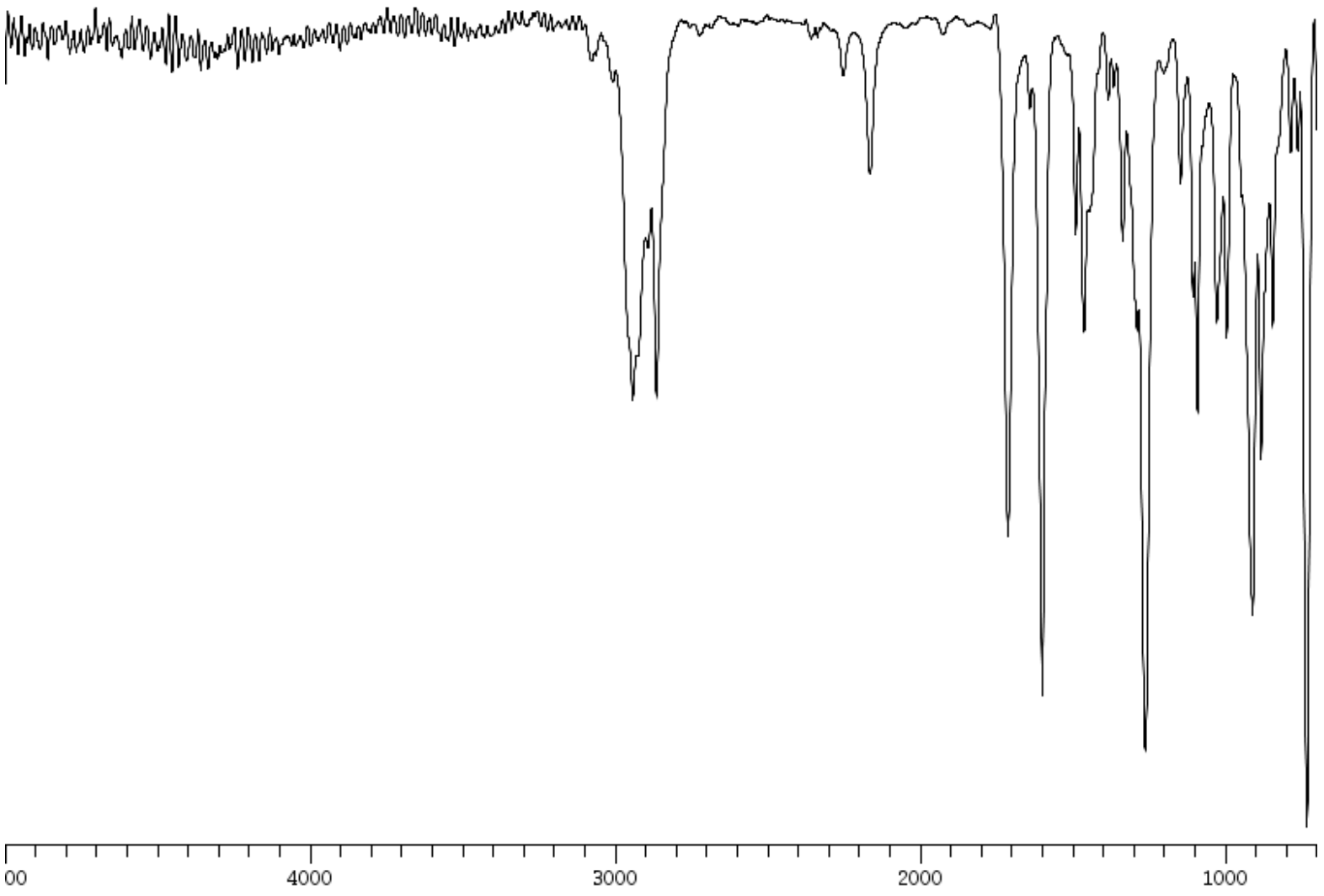


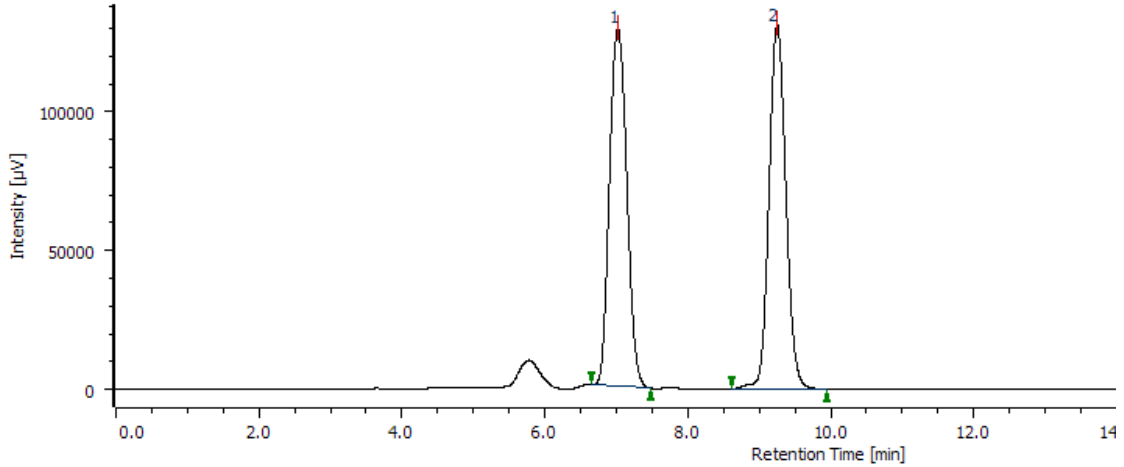

00
4000
3000
2000
1000


CDCl3
400 MHz
O
MeO
1a
TIPS
CDCl3
0.98
1.03
1.02
1.00
2.08
3.05
2.25
1.04
1.10
22.52
f1 (ppm)

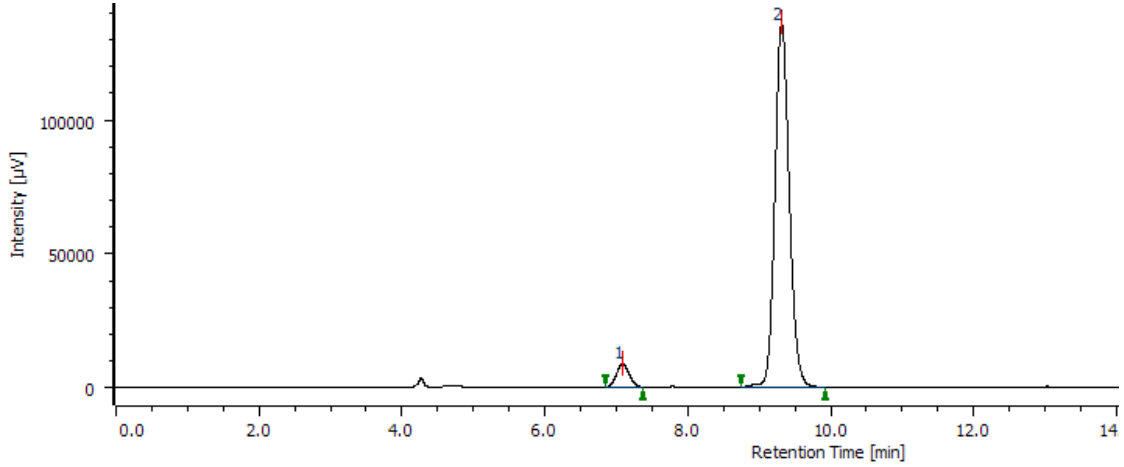
$CDCl_3$
100.1 MHz




00
4000
3000
2000
1000

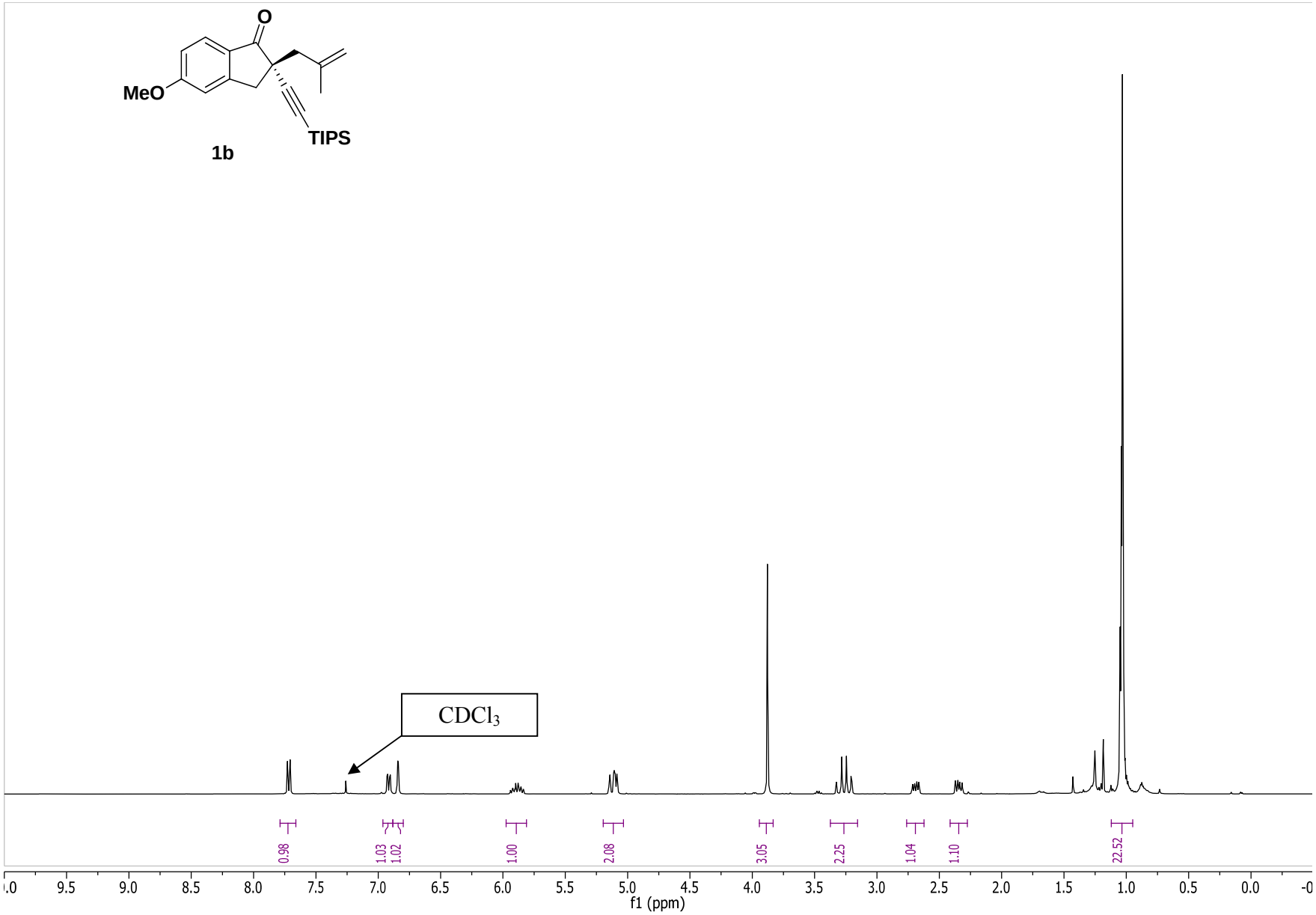


#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	7.013	2155179	128187	50.124	49.430	N/A	3748	5.040	1.110	
2	Unknown	1	9.240	2144485	131146	49.876	50.570	N/A	7468	N/A	1.100	

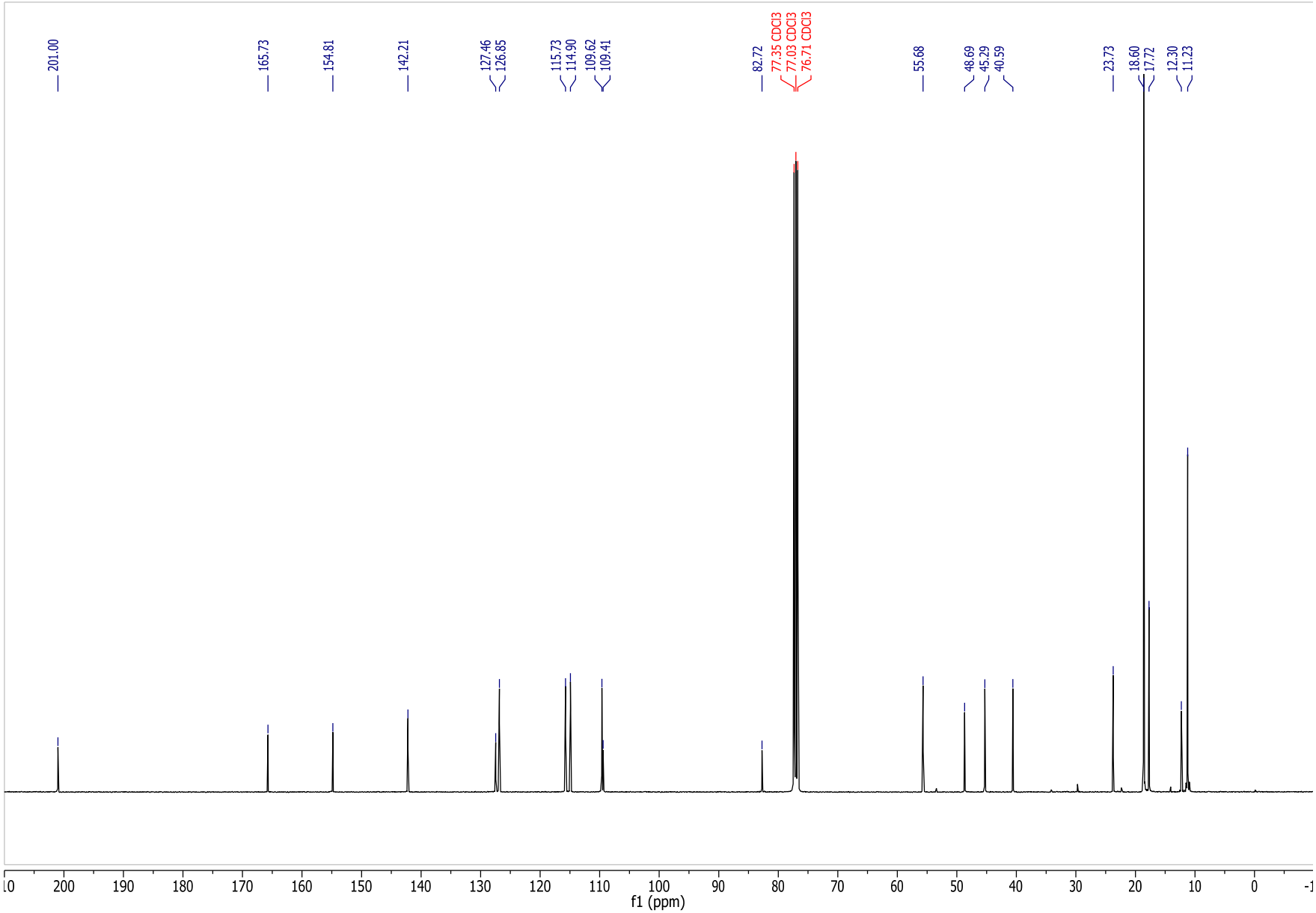


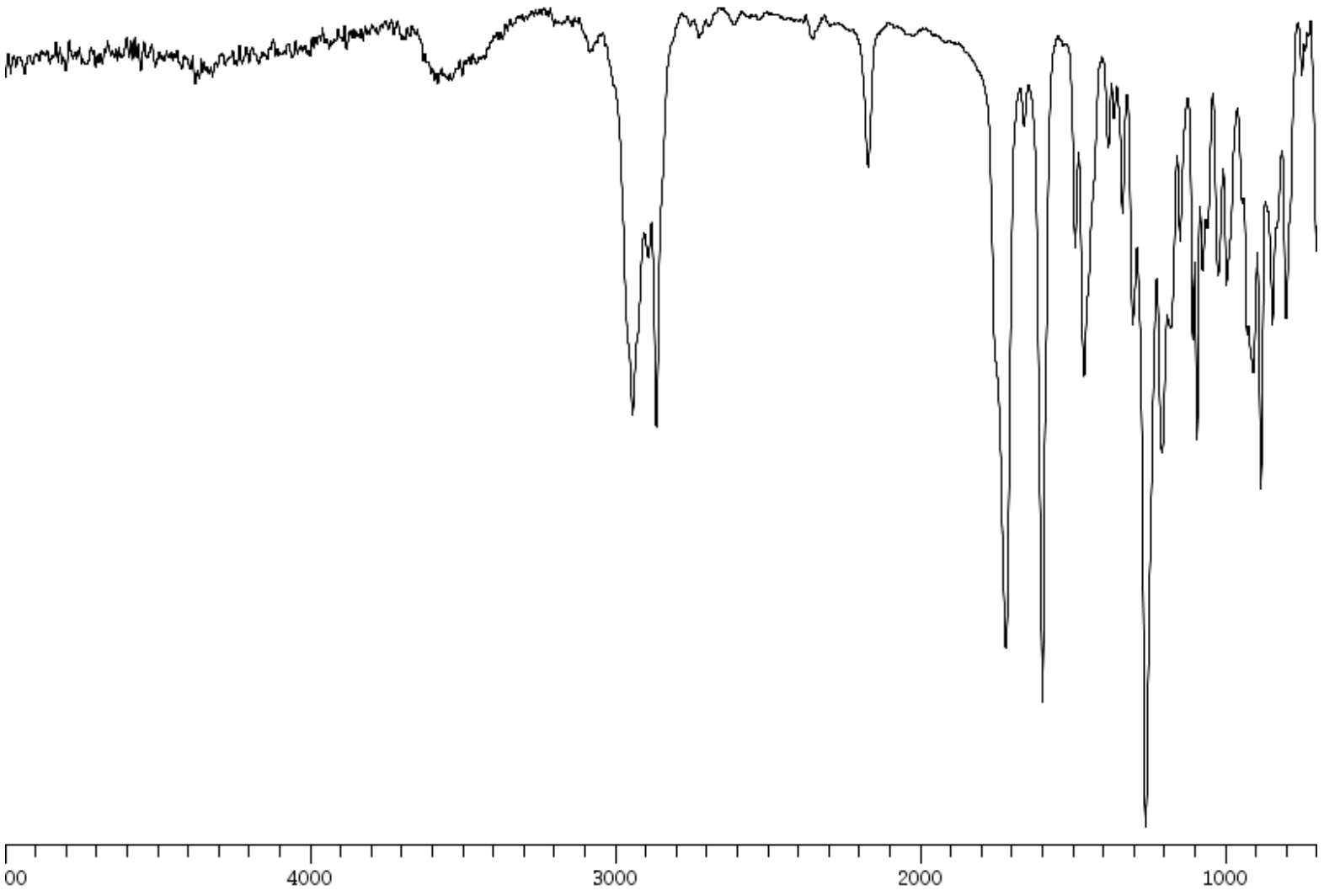
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	7.080	106296	8464	5.299	5.864	N/A	7088	6.386	1.102	
2	Unknown	1	9.303	1899770	135883	94.701	94.136	N/A	10580	N/A	1.138	

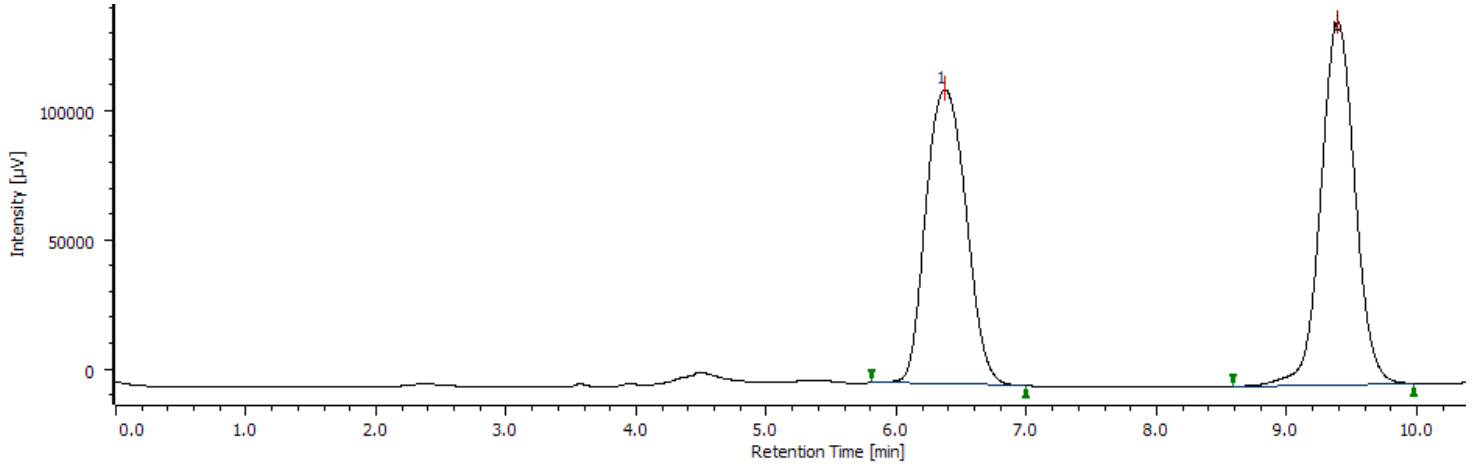
$CDCl_3$
400 MHz



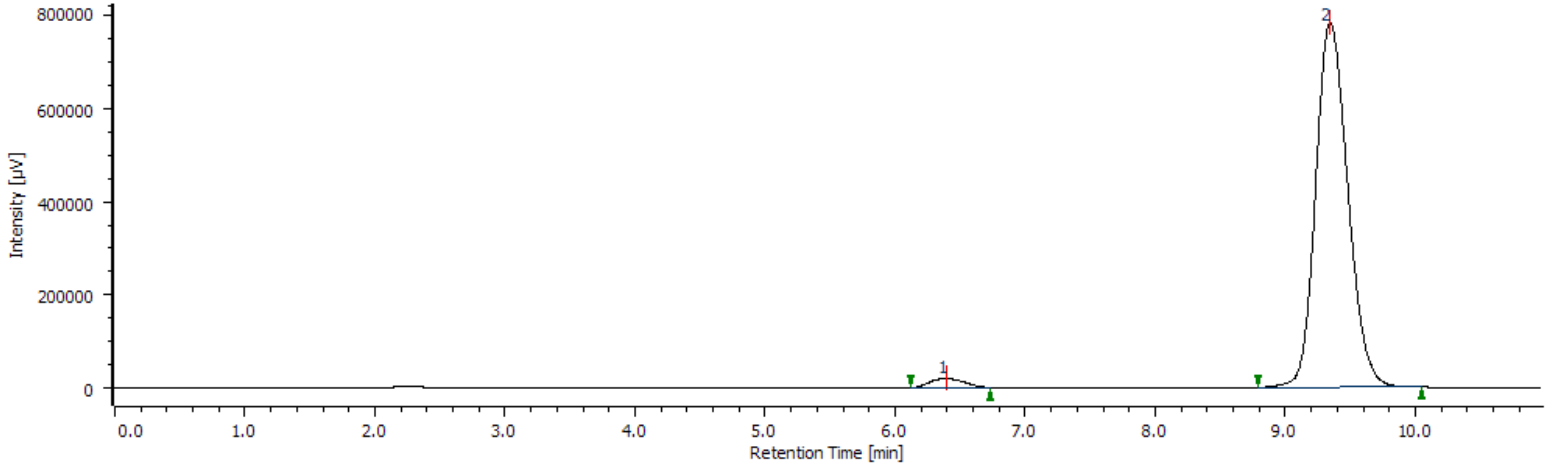
$CDCl_3$
100.1 MHz




00
4000
3000
2000
1000

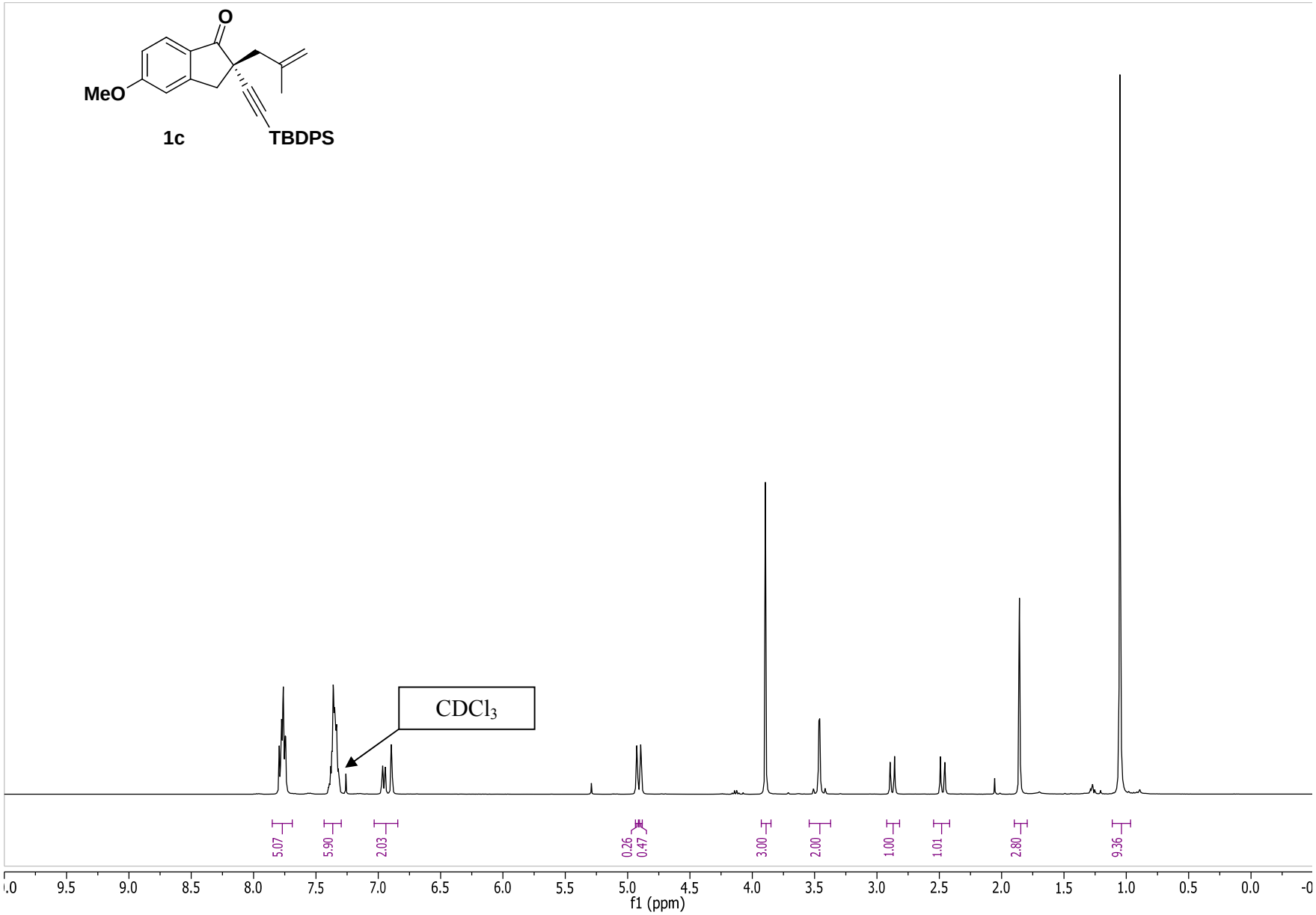


#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	6.367	2446354	113526	49.013	44.788	N/A	1843	5.684	1.120	
2	Unknown	1	9.383	2544913	139950	50.987	55.212	N/A	6348	N/A	1.032	

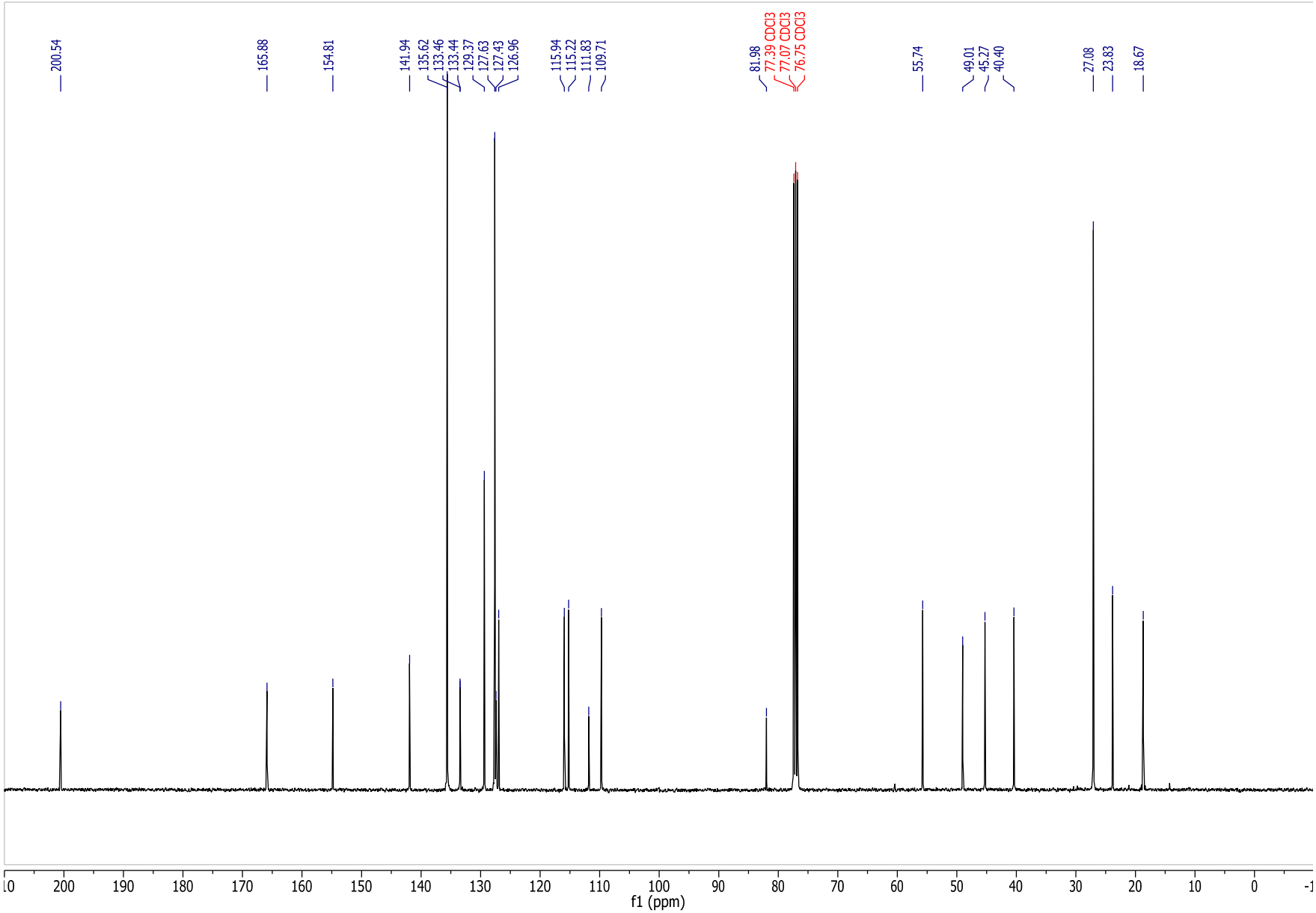


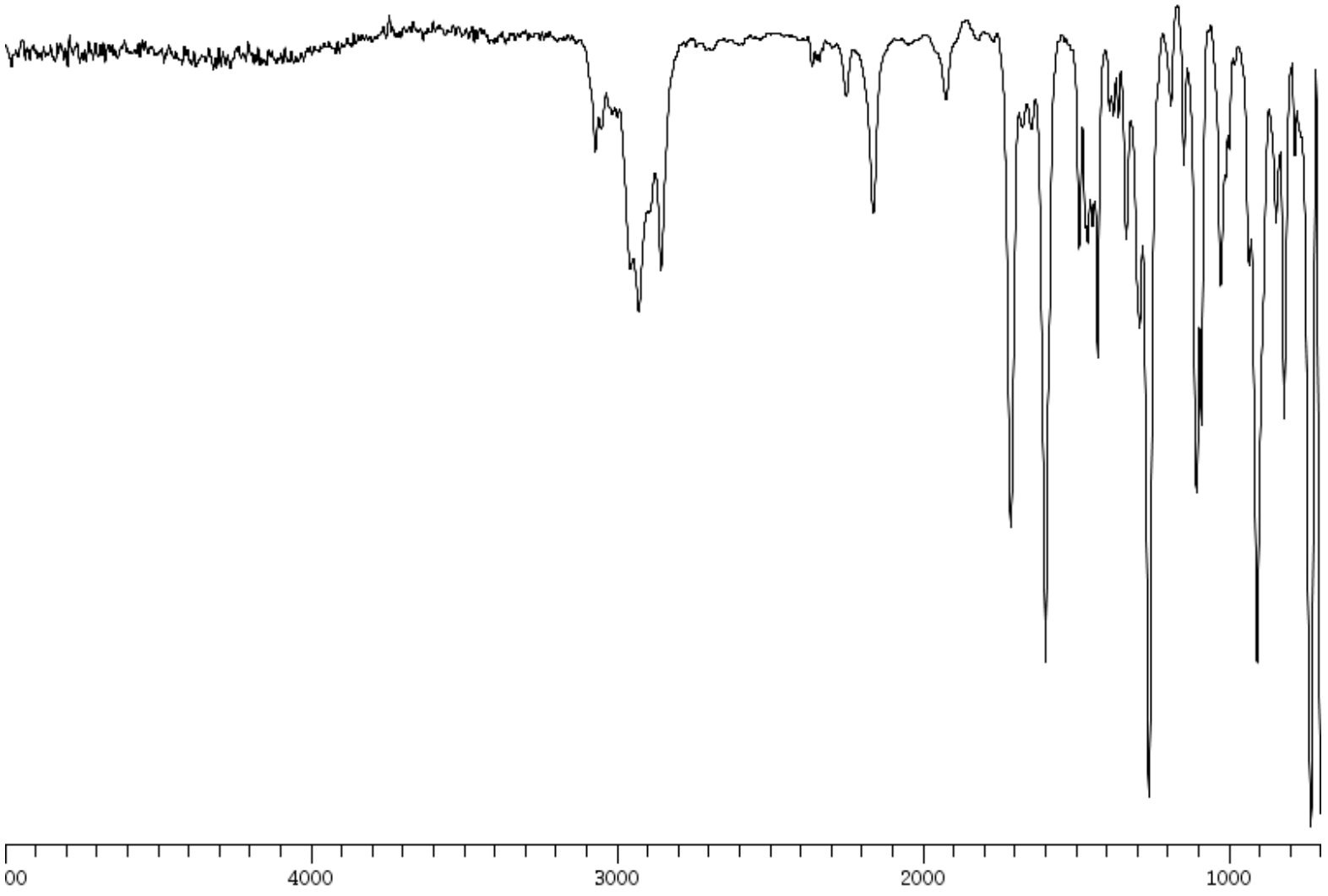
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	6.383	357755	19360	2.596	2.421	N/A	2420	6.104	1.128	
2	Unknown	1	9.337	13421227	780297	97.404	97.579	N/A	6852	N/A	1.174	

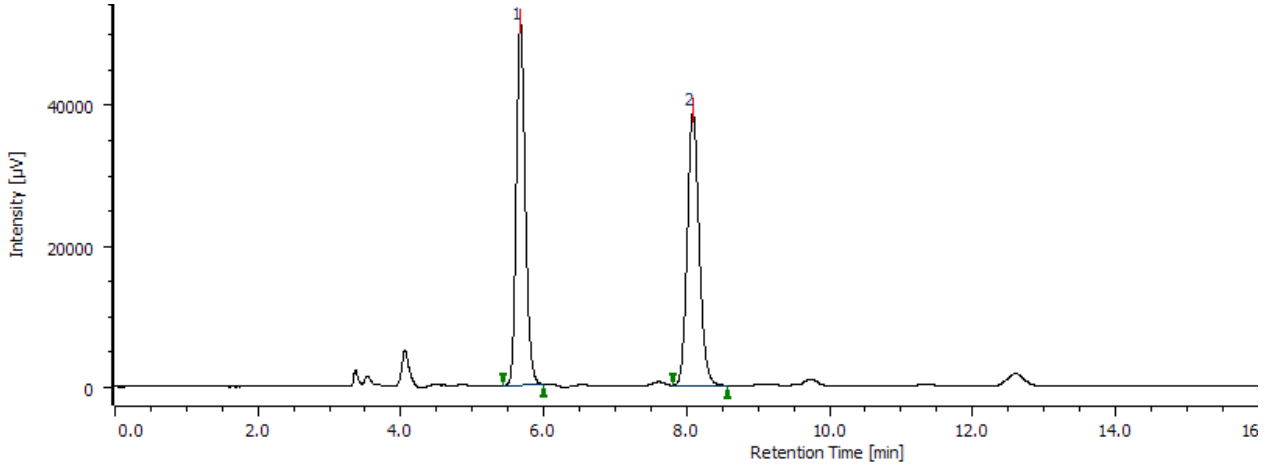
$CDCl_3$
400 MHz



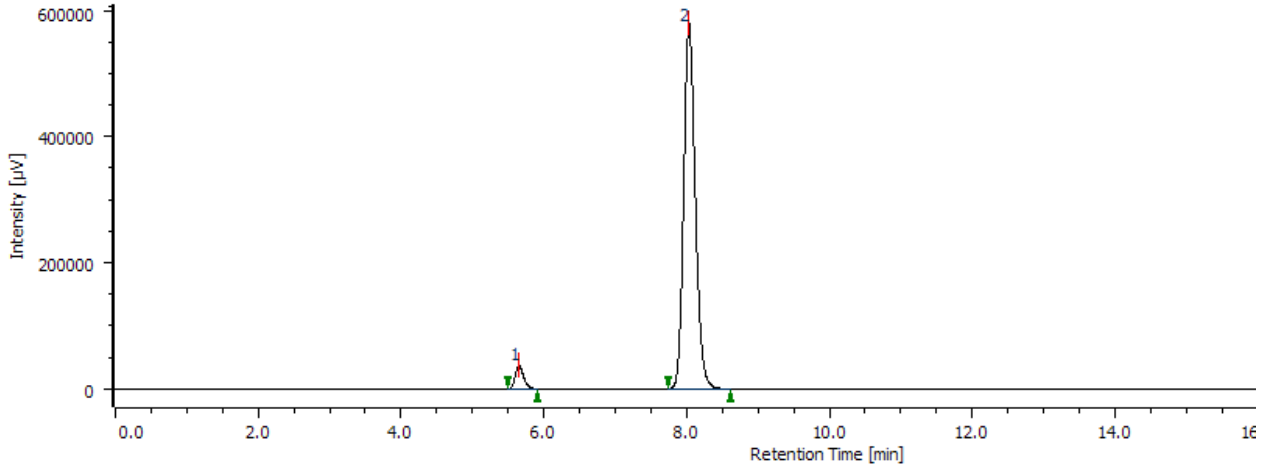
$CDCl_3$
100.1 MHz




00
4000
3000
2000
1000

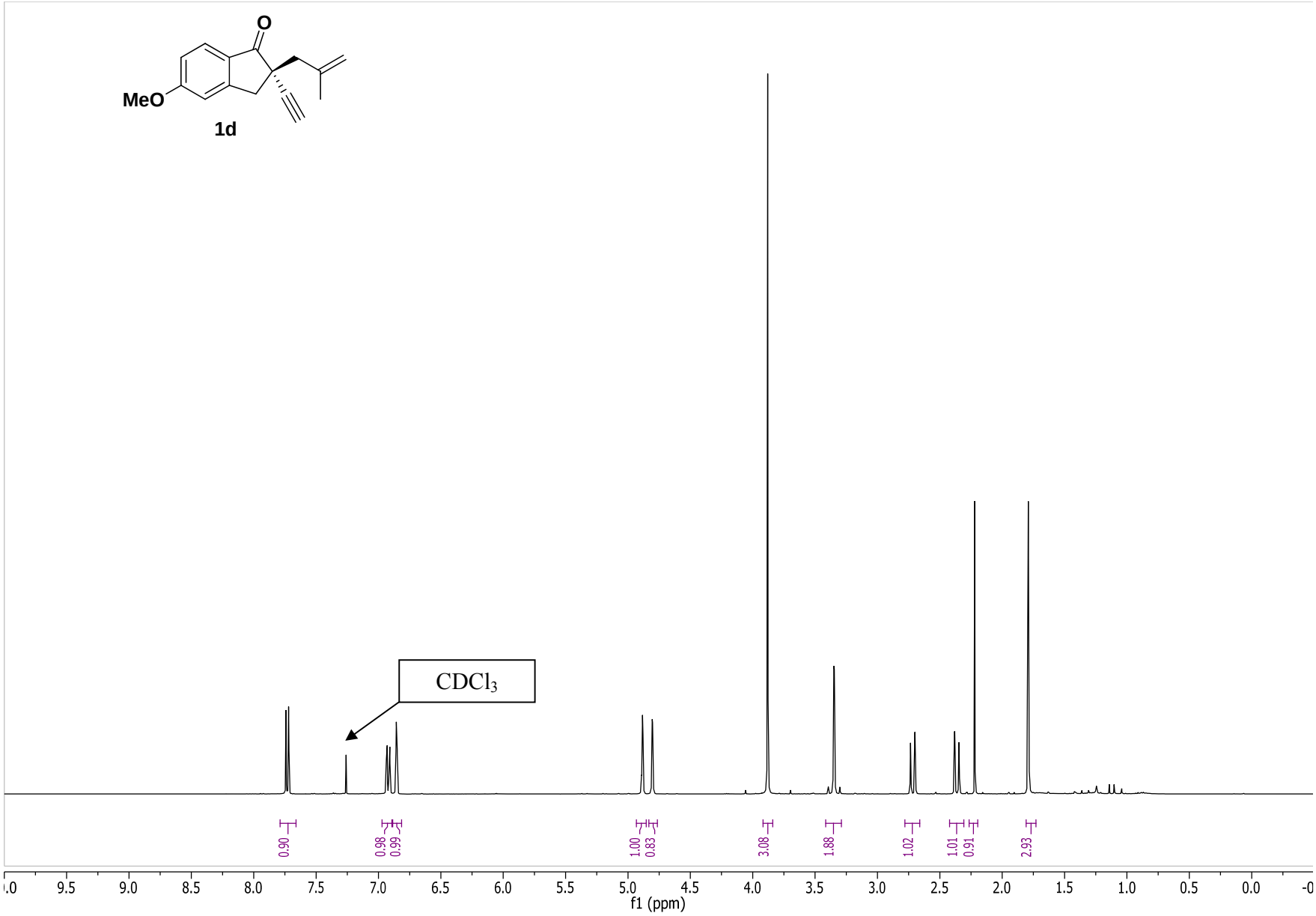


#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	2	5.670	445281	51357	49.893	56.972	N/A	10224	9.243	1.172	
2	Unknown	2	8.080	447184	38788	50.107	43.028	N/A	11718	N/A	1.129	

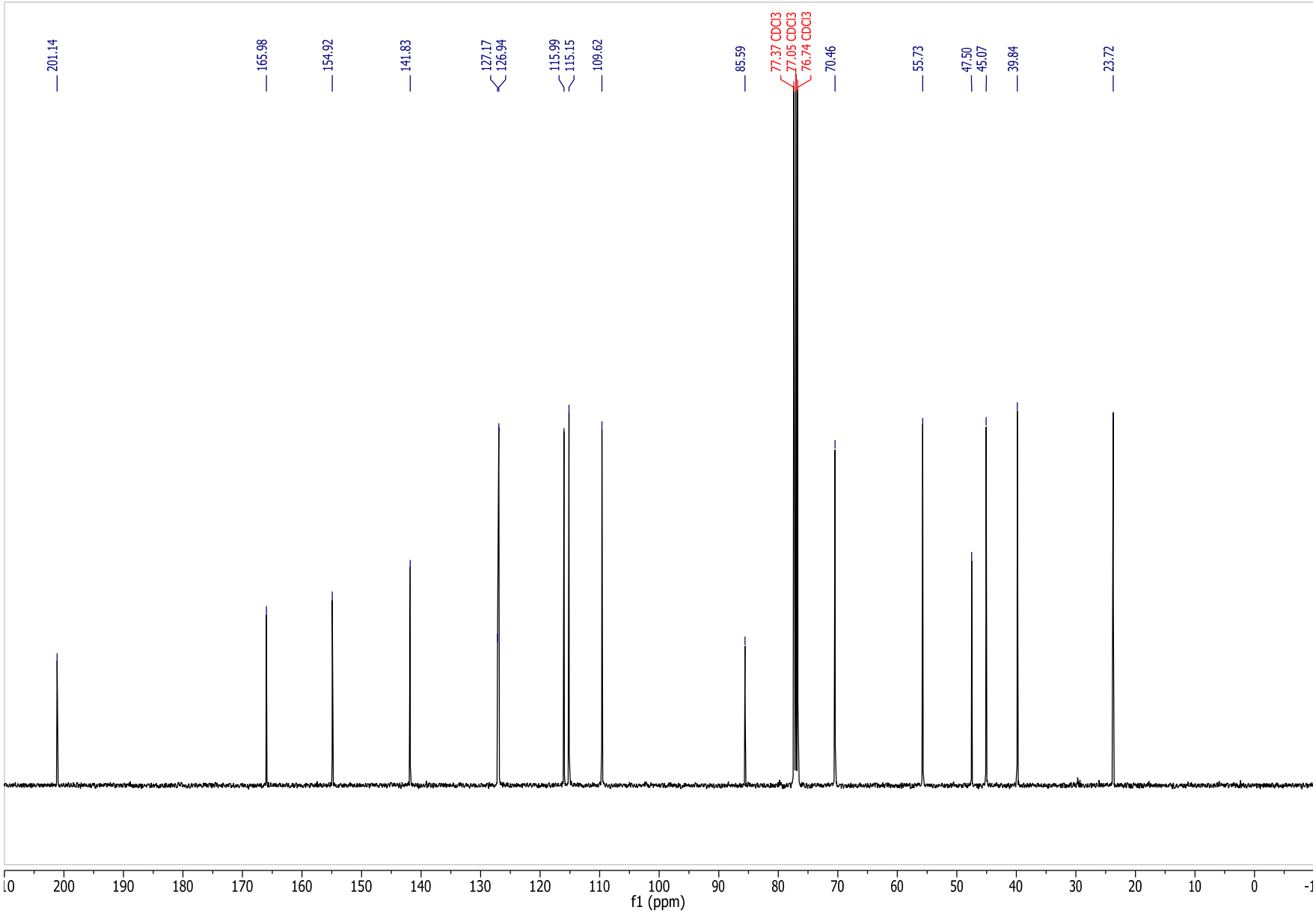


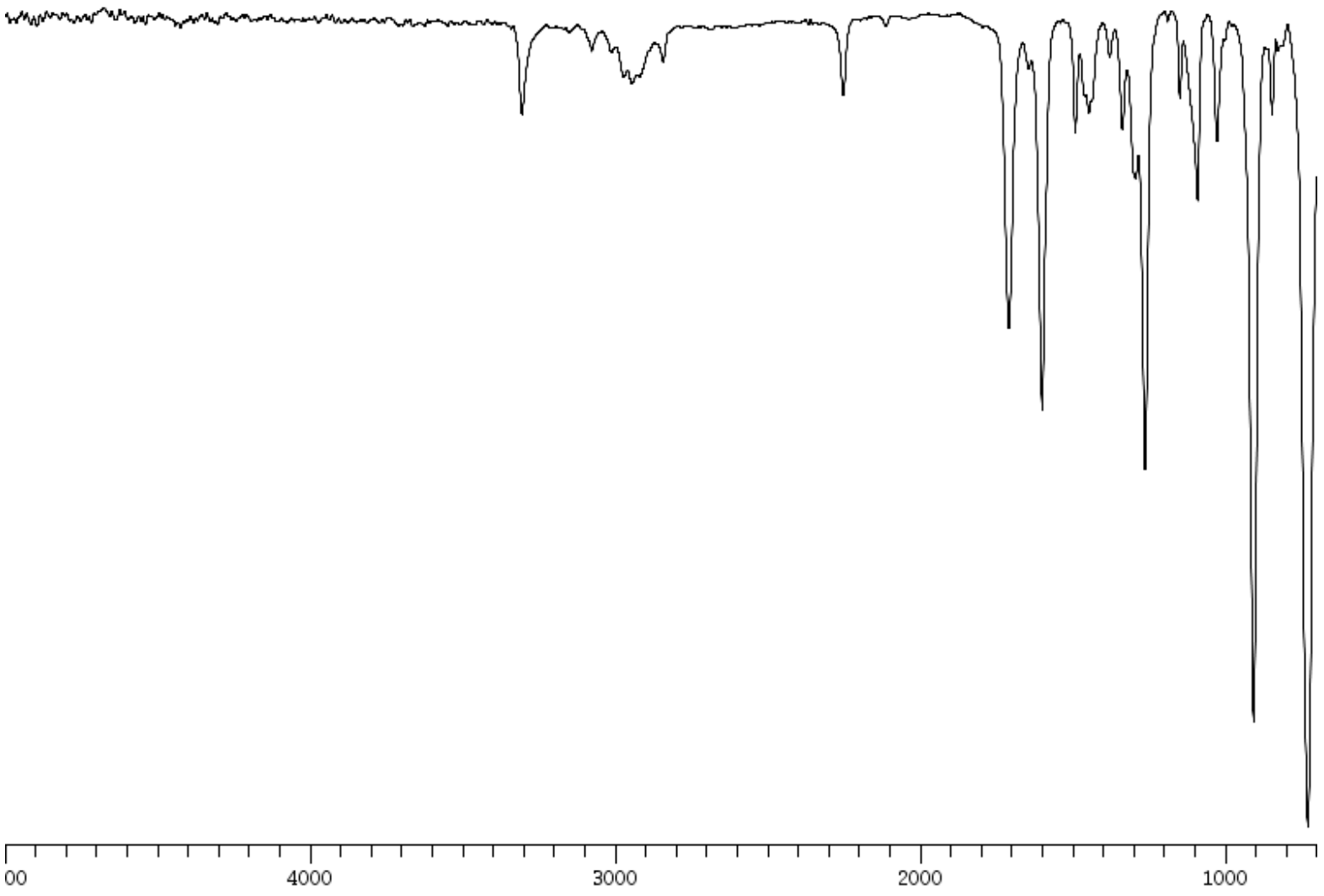
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	2	5.647	301647	36826	4.405	5.991	N/A	11217	9.439	1.213	
2	Unknown	2	8.027	6545917	577879	95.595	94.009	N/A	12057	N/A	1.171	

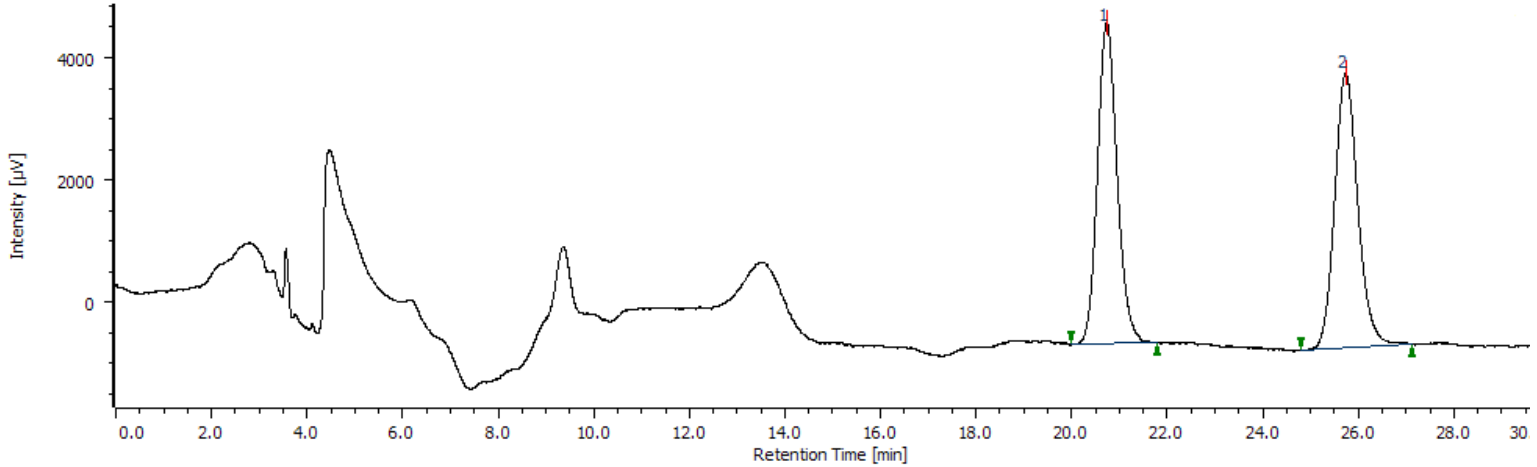
$CDCl_3$
400 MHz



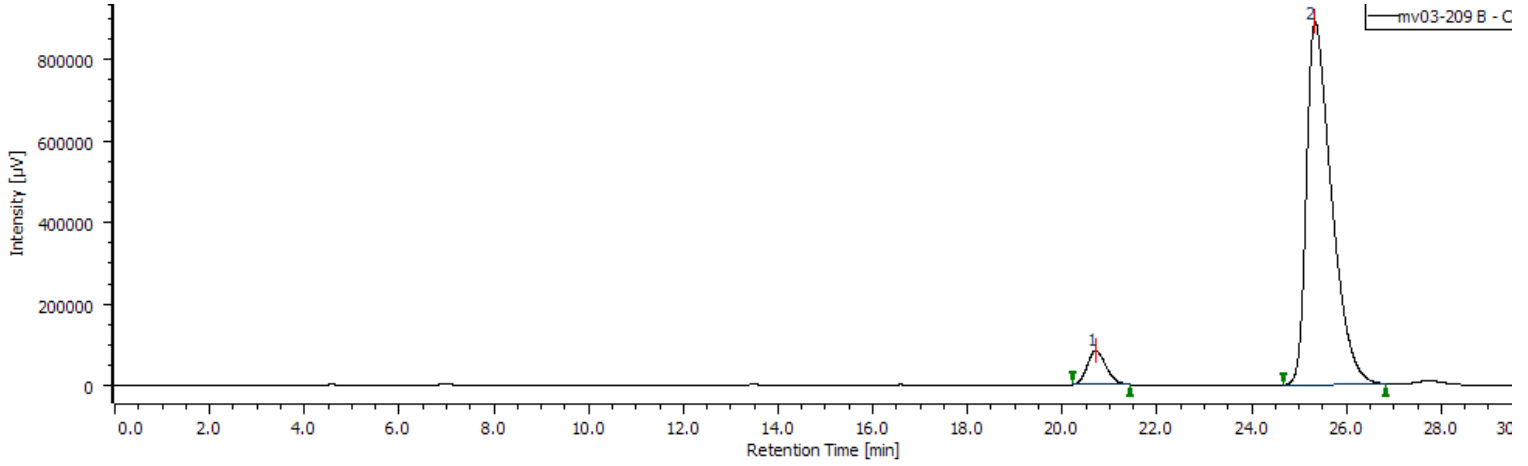
$CDCl_3$
100.1 MHz




00
4000
3000
2000
1000

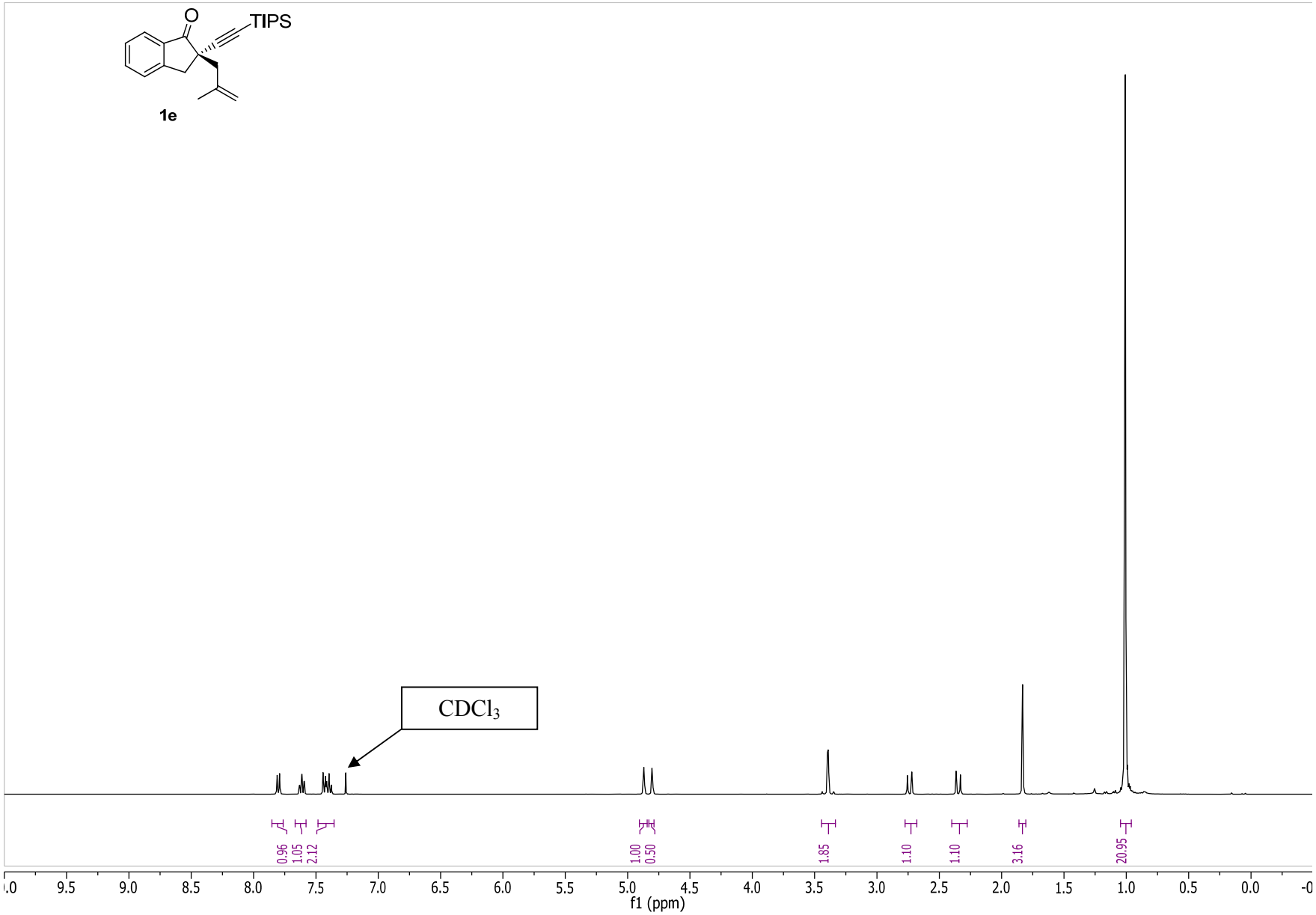


#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	20.713	149081	5222	49.745	53.852	N/A	12659	6.259	1.154	
2	Unknown	1	25.710	150611	4475	50.255	46.148	N/A	14152	N/A	1.133	

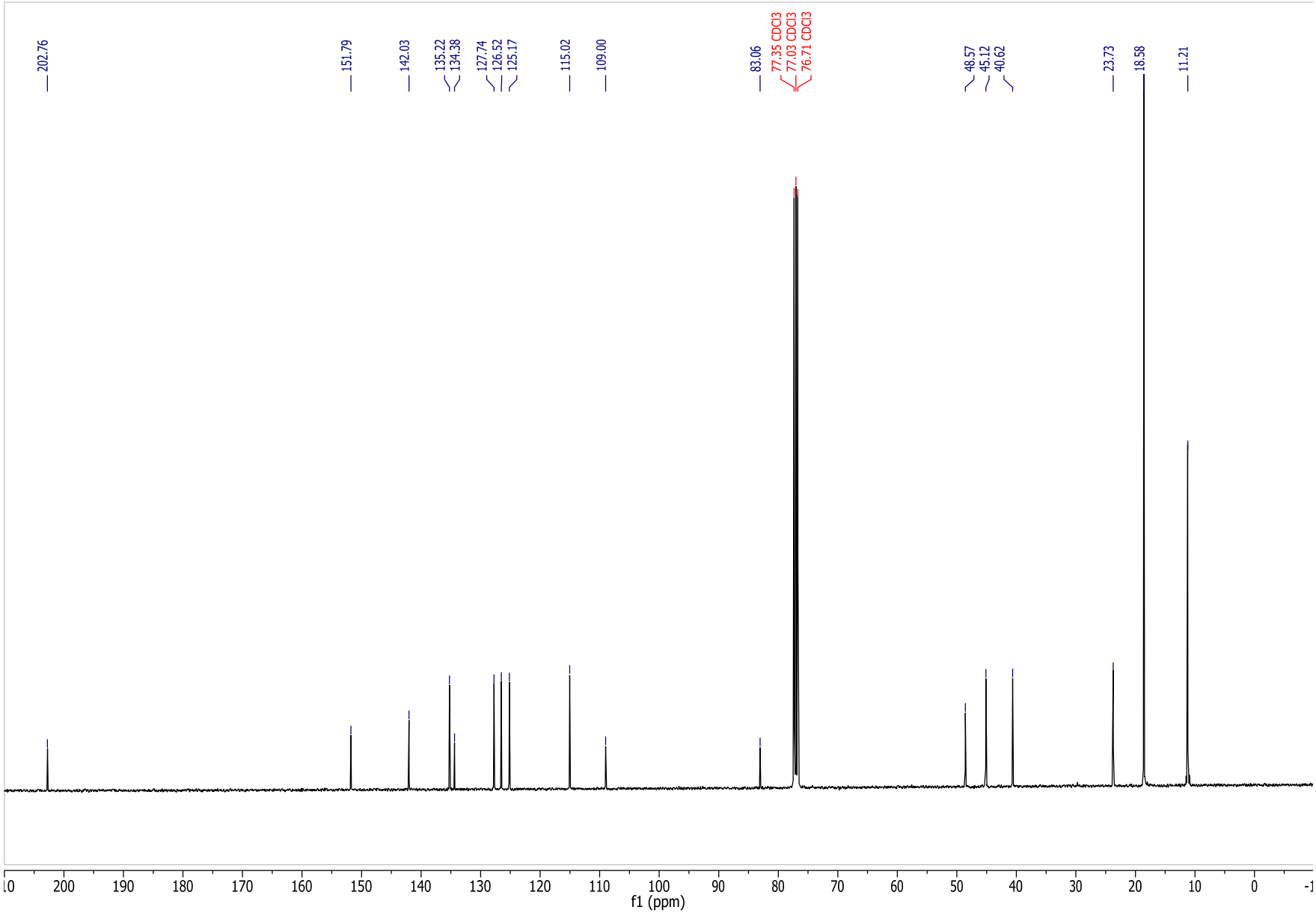


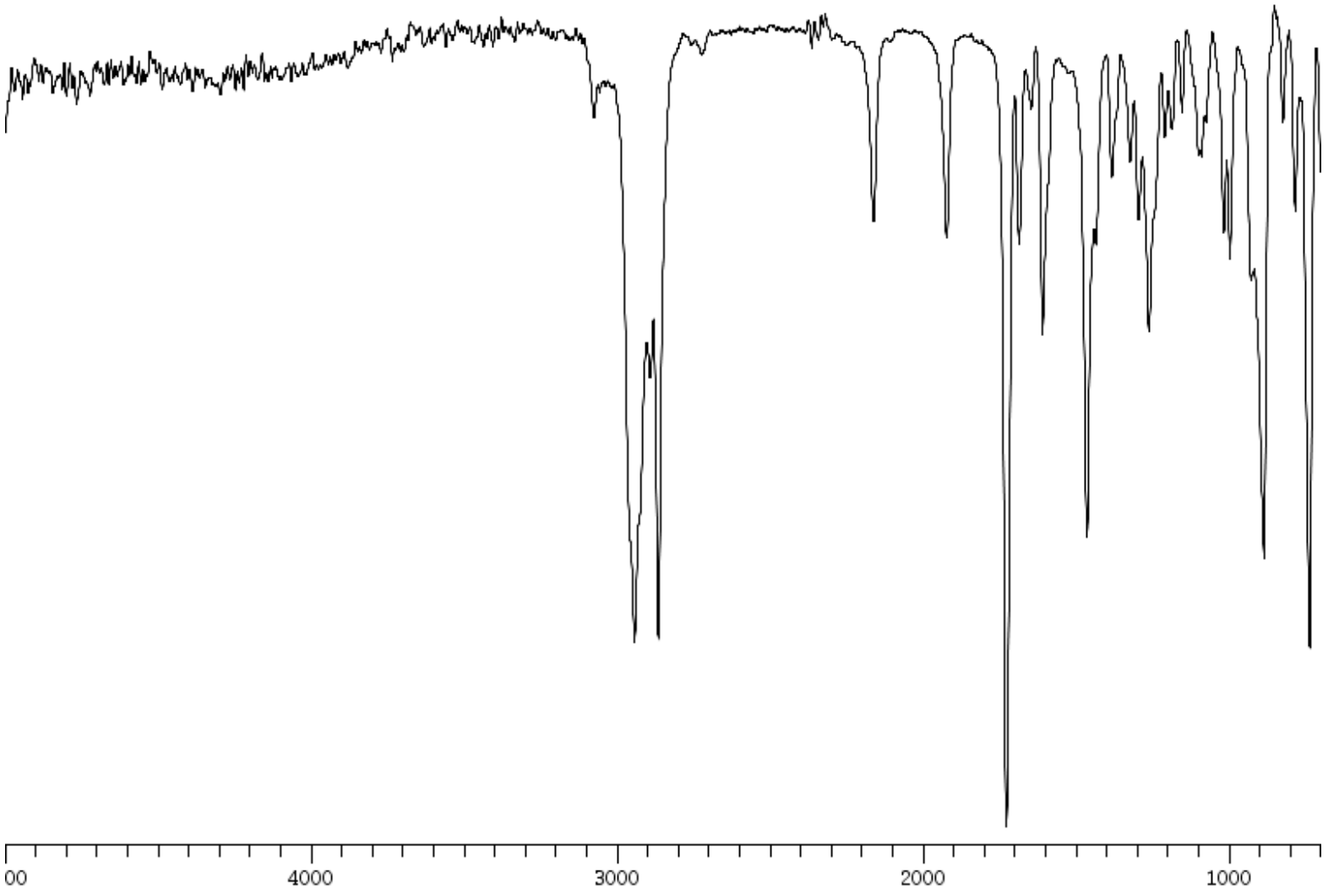
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	20.687	2265879	82670	6.490	8.513	N/A	13155	5.559	1.179	
2	Unknown	1	25.310	32648533	888467	93.510	91.487	N/A	11447	N/A	1.647	

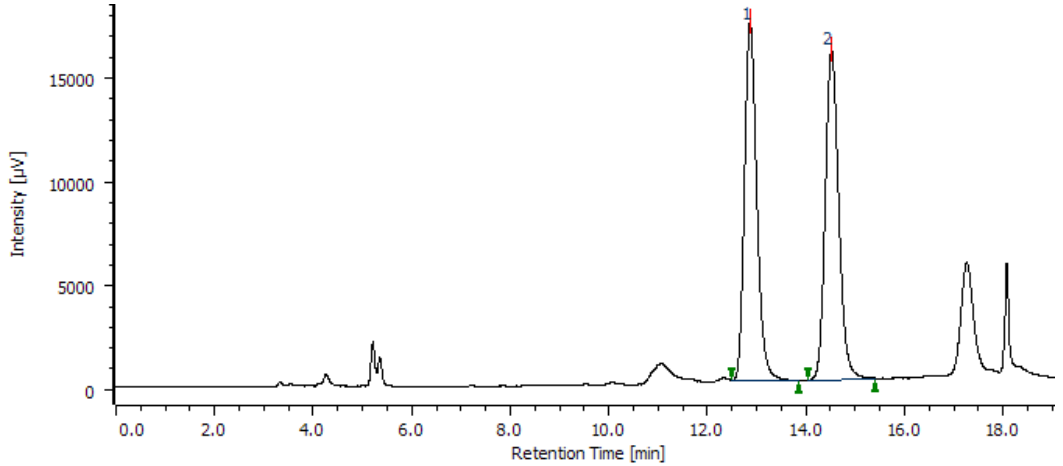
$CDCl_3$
400 MHz



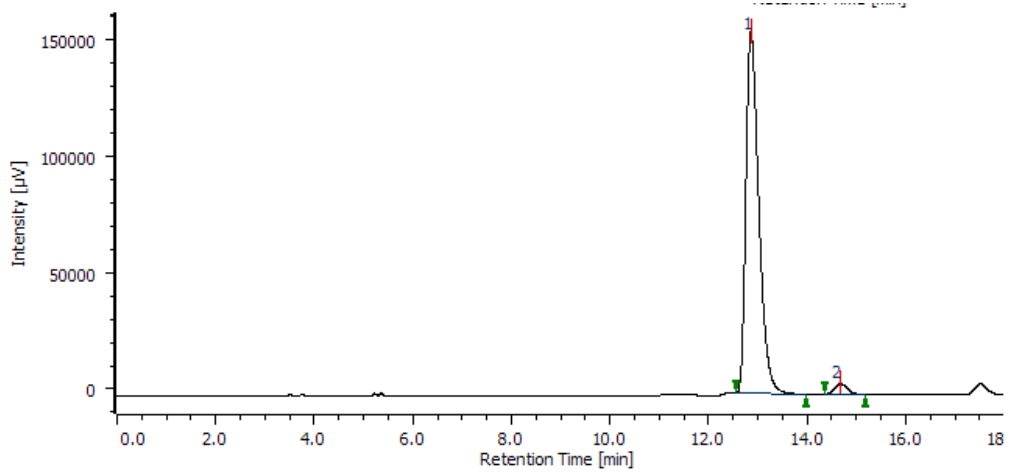
$CDCl_3$
100.1 MHz




00
4000
3000
2000
1000

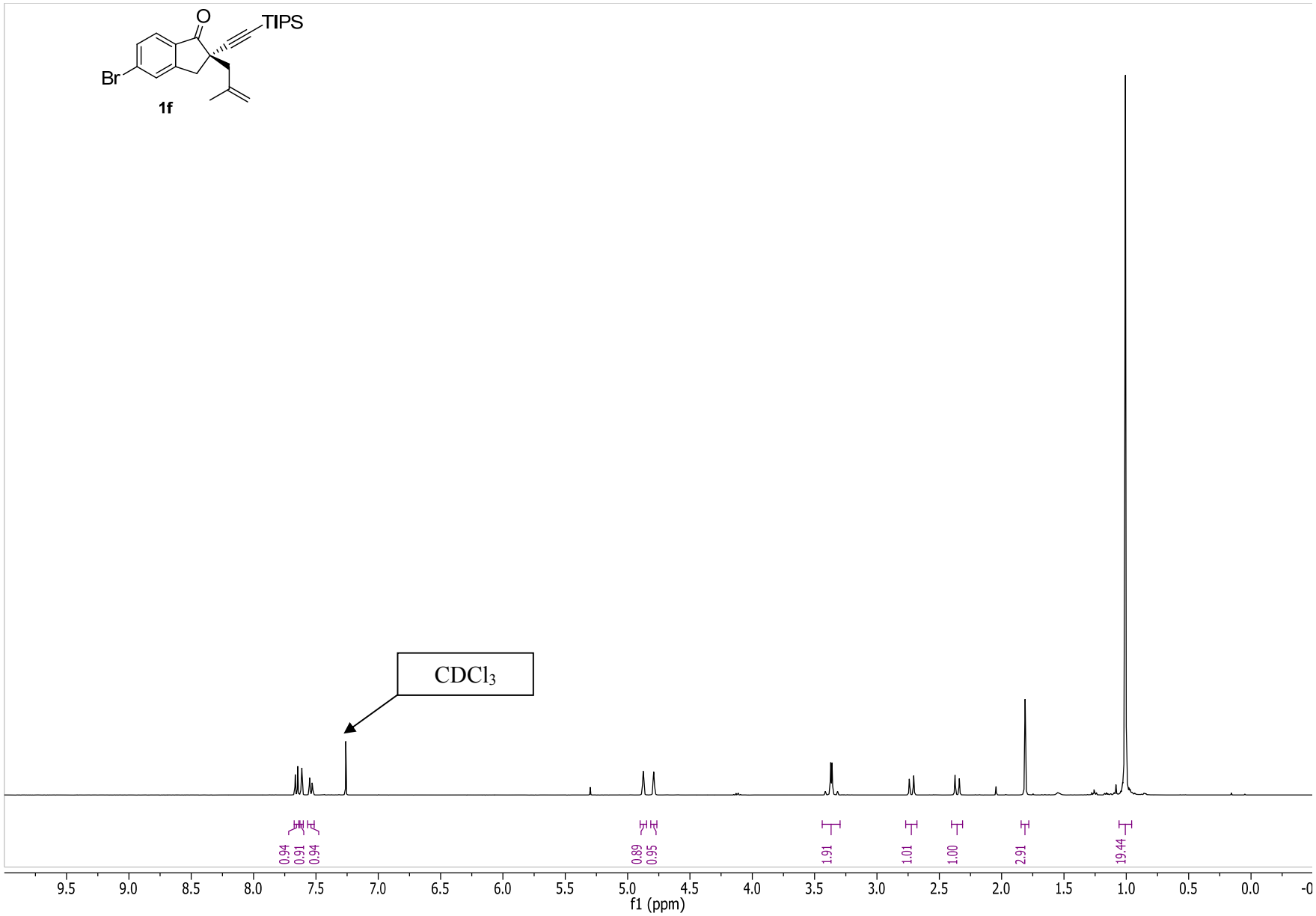


#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	3	12.853	297398	17236	49.744	52.101	N/A	13445	3.545	1.226	
2	Unknown	3	14.503	300462	15846	50.256	47.899	N/A	14013	N/A	1.159	

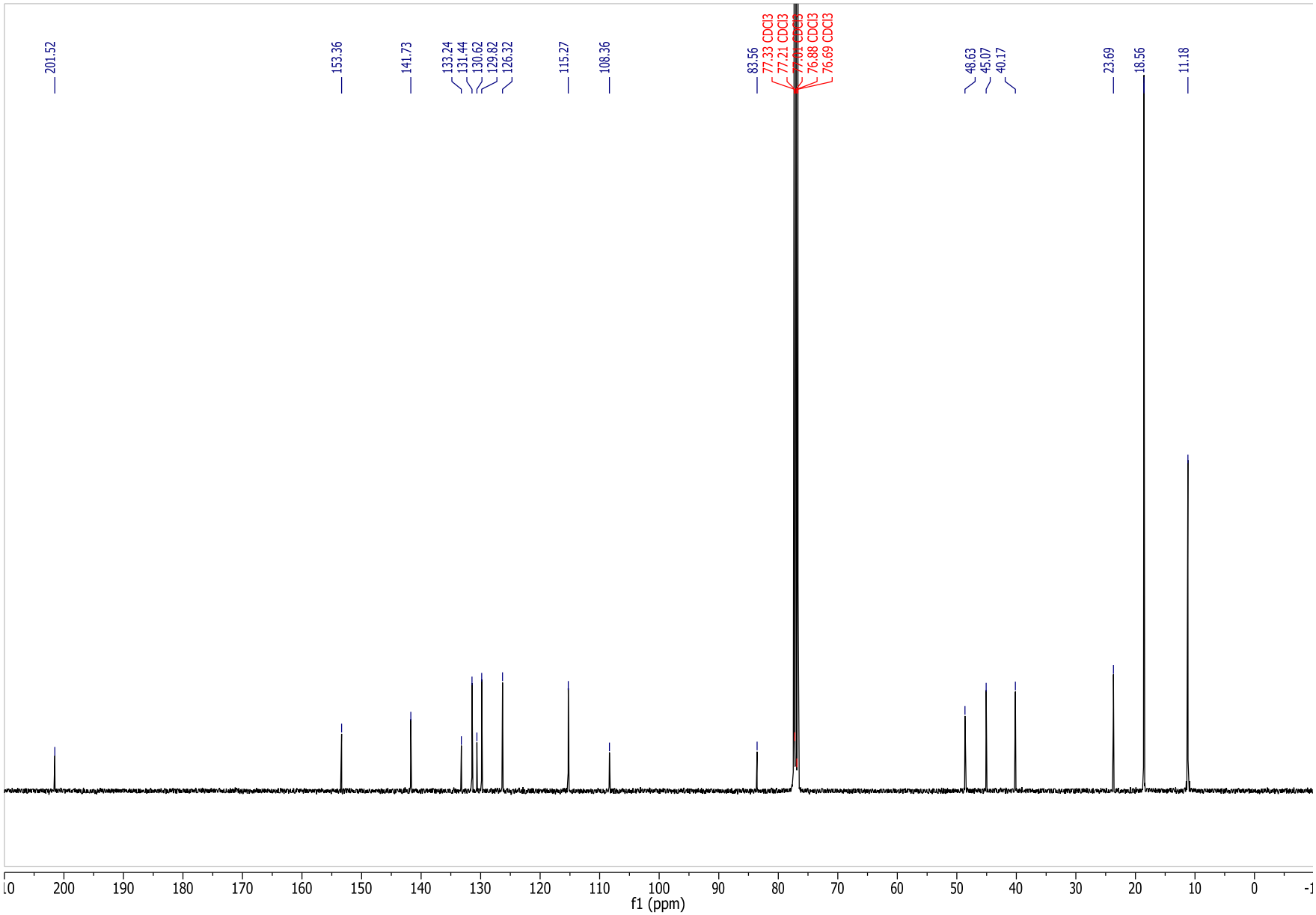


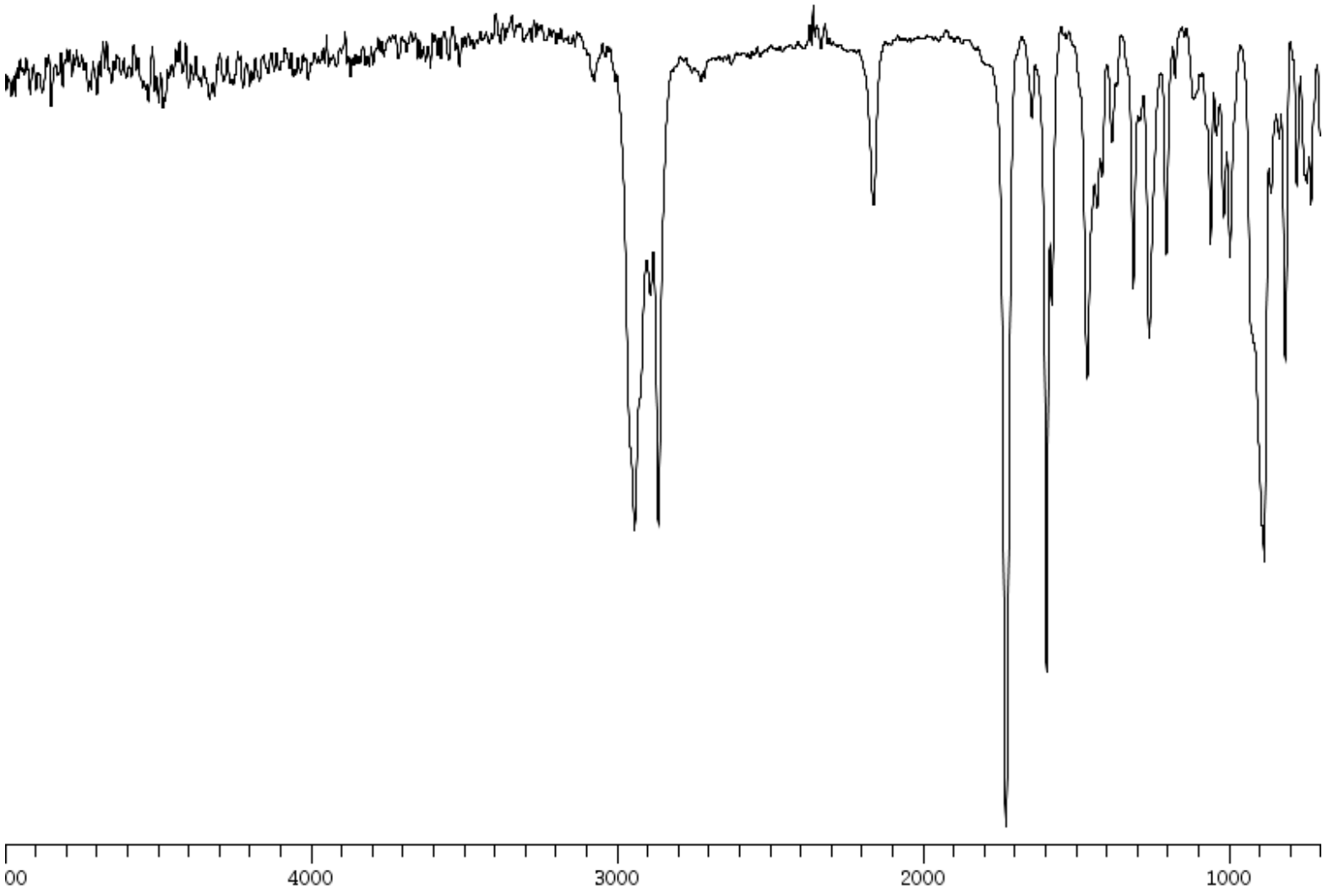
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	3	12.847	2813362	155161	97.111	97.150	N/A	12054	3.809	1.482	
2	Unknown	3	14.660	83690	4552	2.889	2.850	N/A	14527	N/A	1.146	

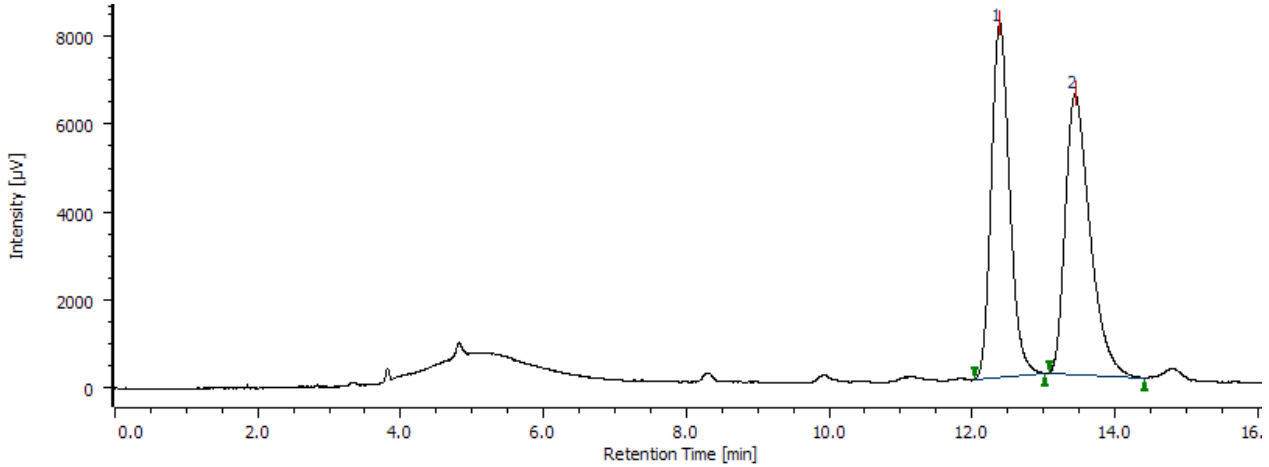
$CDCl_3$
400 MHz



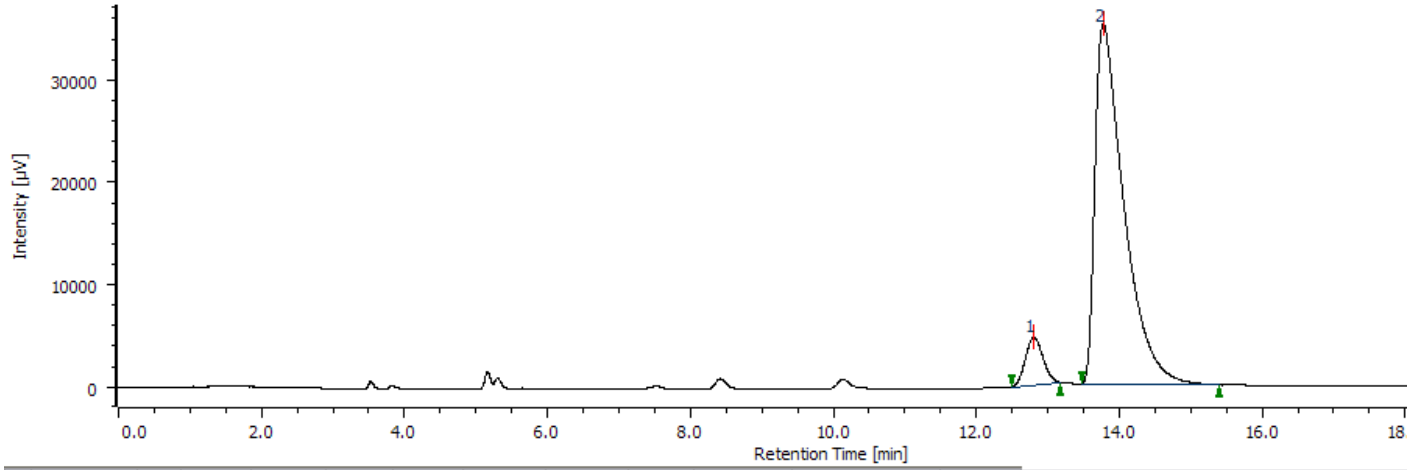
$CDCl_3$
100.1 MHz




00
4000
3000
2000
1000

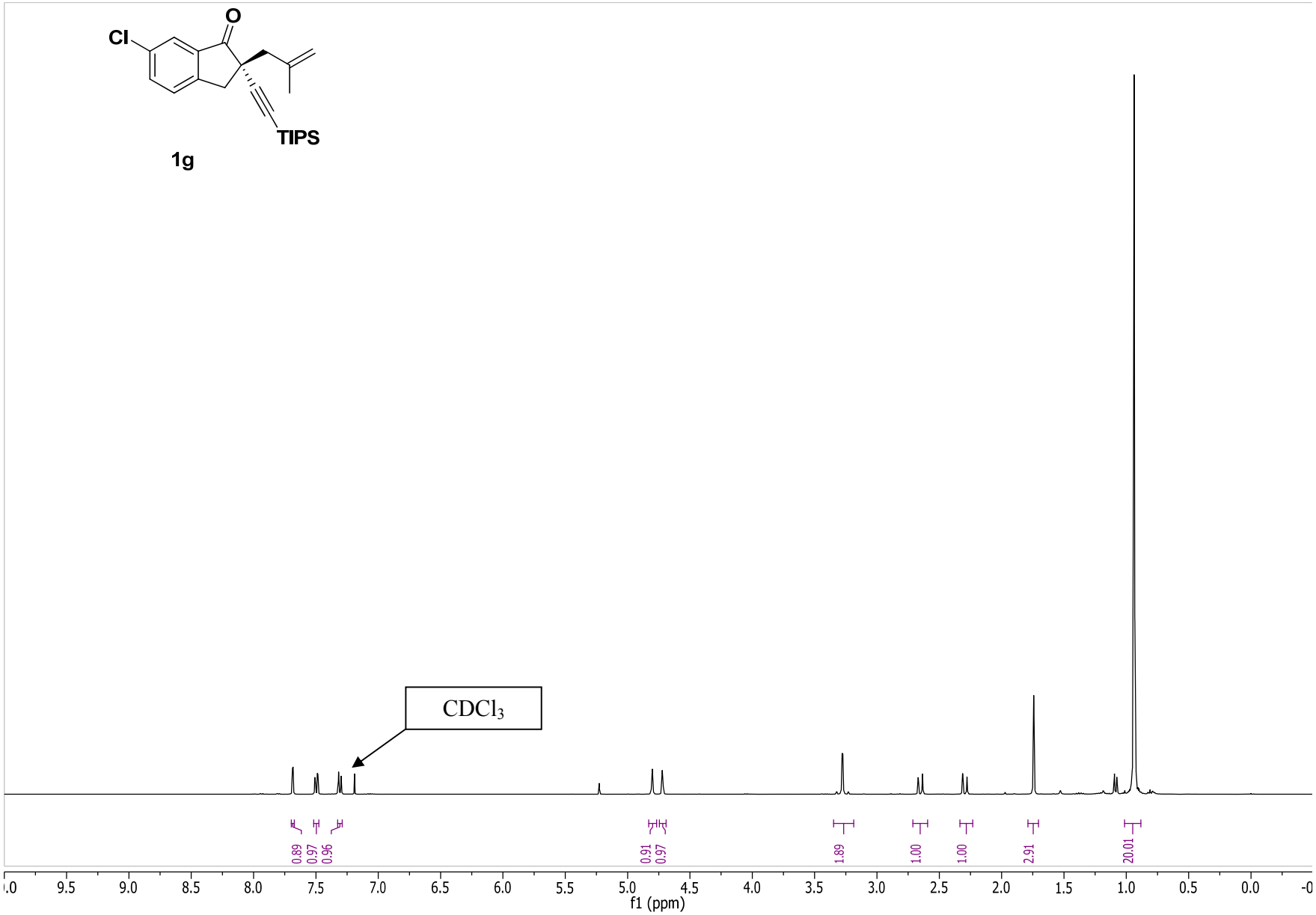


#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	12.377	143567	8033	48.419	55.868	N/A	11492	1.955	1.204	
2	Unknown	1	13.433	152945	6346	51.581	44.132	N/A	7464	N/A	1.468	

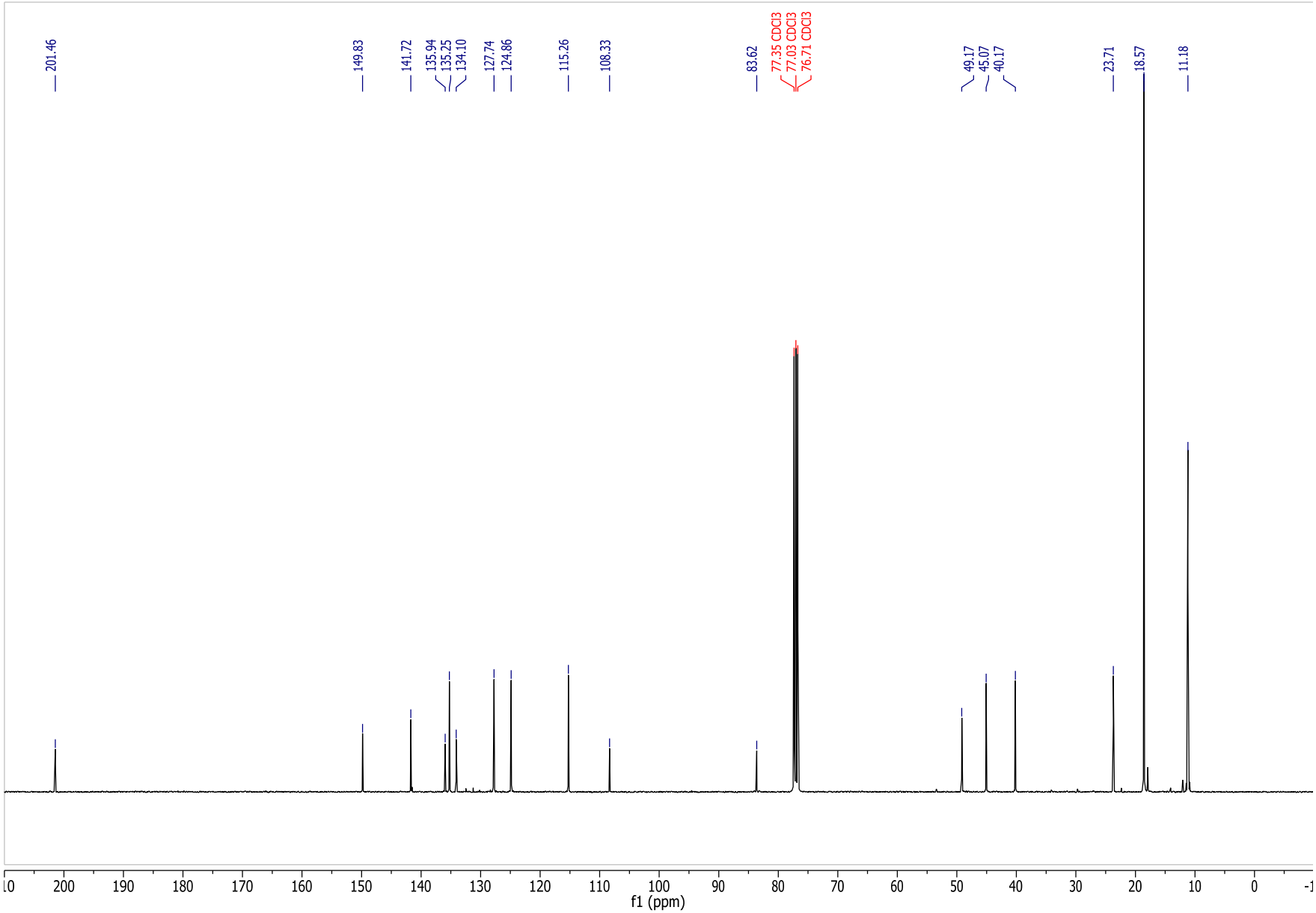


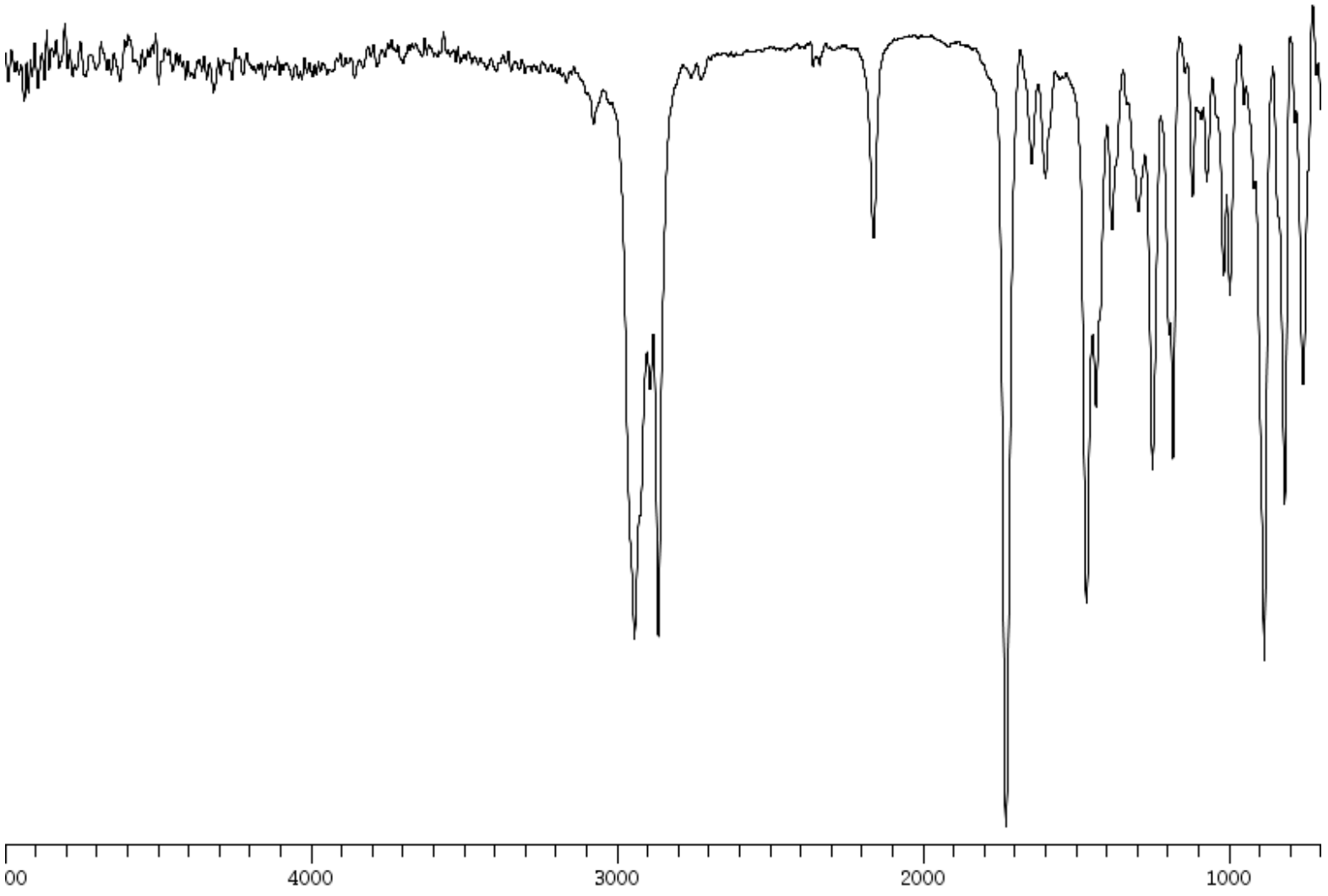
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	12.797	79605	4617	7.453	11.629	N/A	12268	1.659	1.077	
2	Unknown	1	13.763	988429	35091	92.547	88.371	N/A	6074	N/A	2.289	

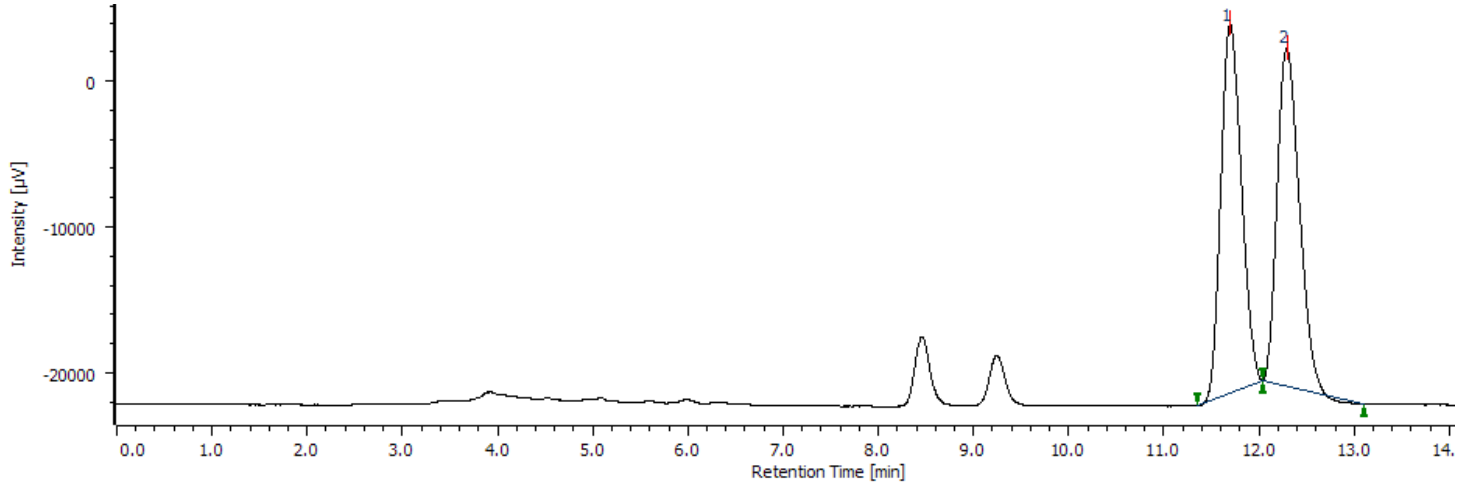
$CDCl_3$
400 MHz



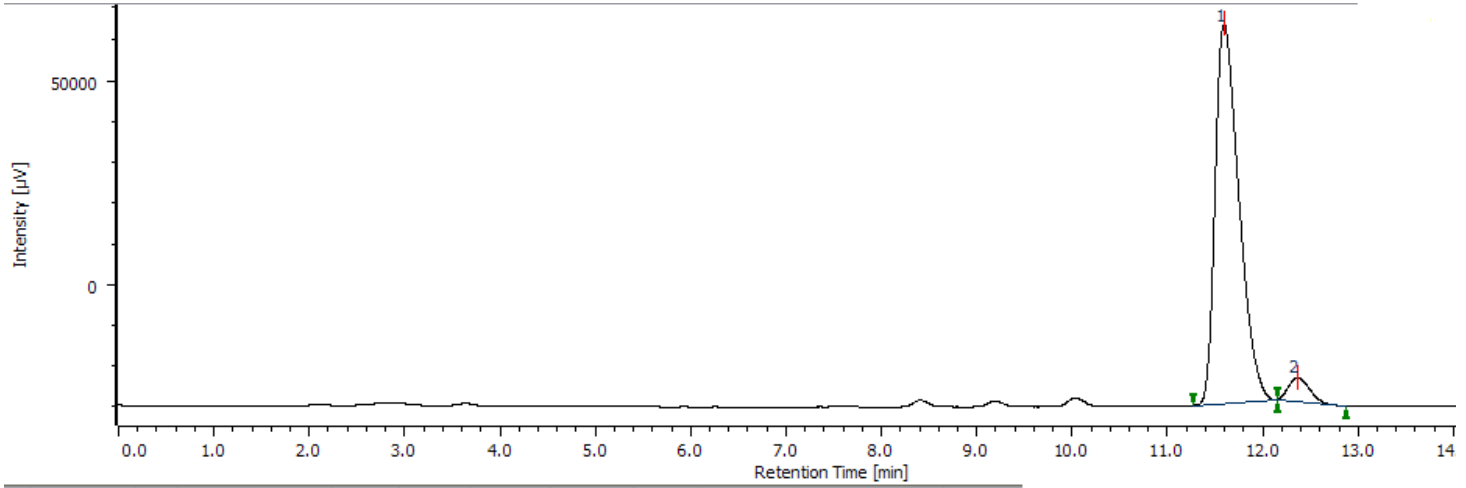
$CDCl_3$
100.1 MHz




00
4000
3000
2000
1000

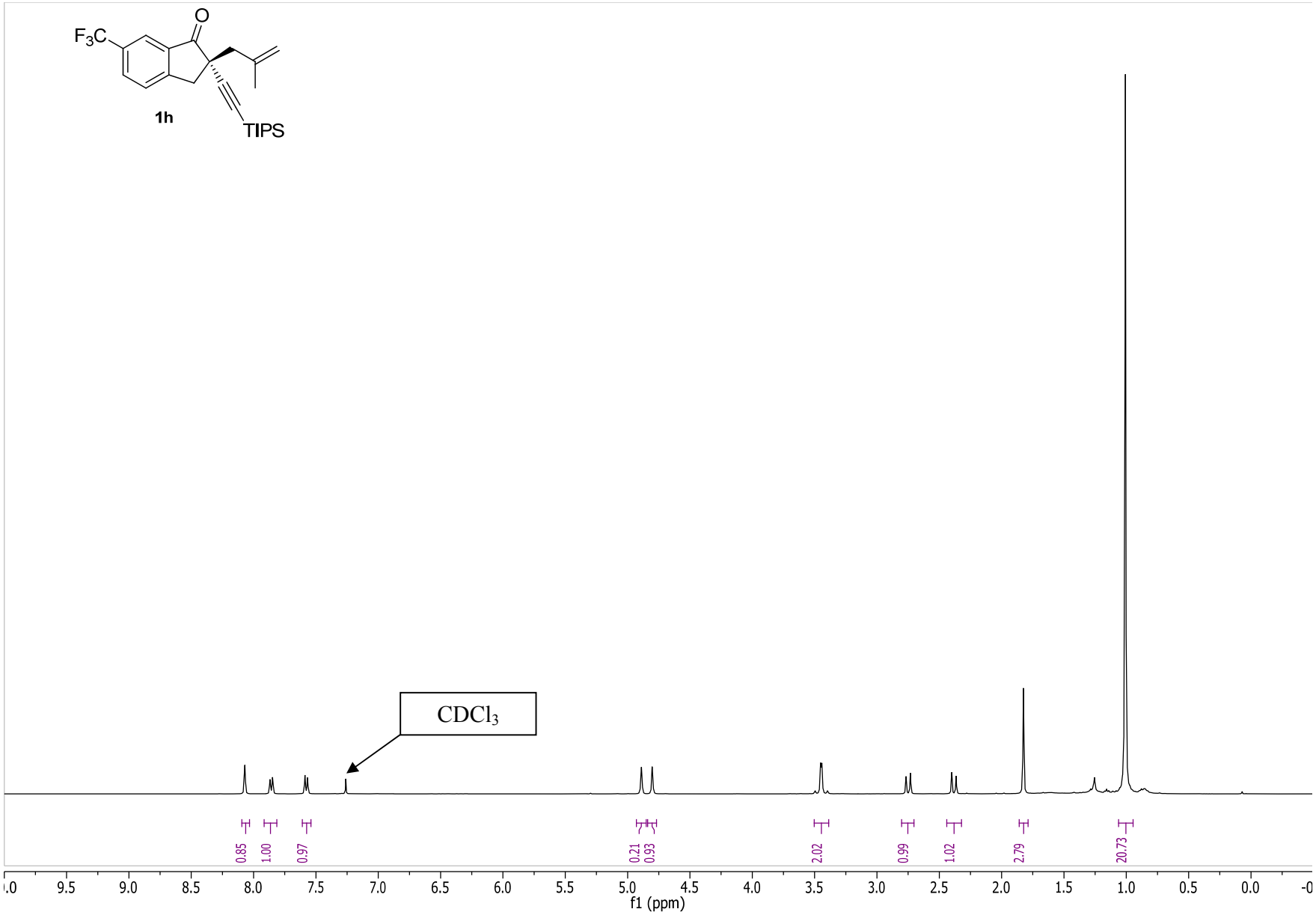


#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	11.683	378304	25230	50.236	52.136	N/A	13370	1.429	1.173	
2	Unknown	1	12.280	374756	23162	49.764	47.864	N/A	12858	N/A	1.271	

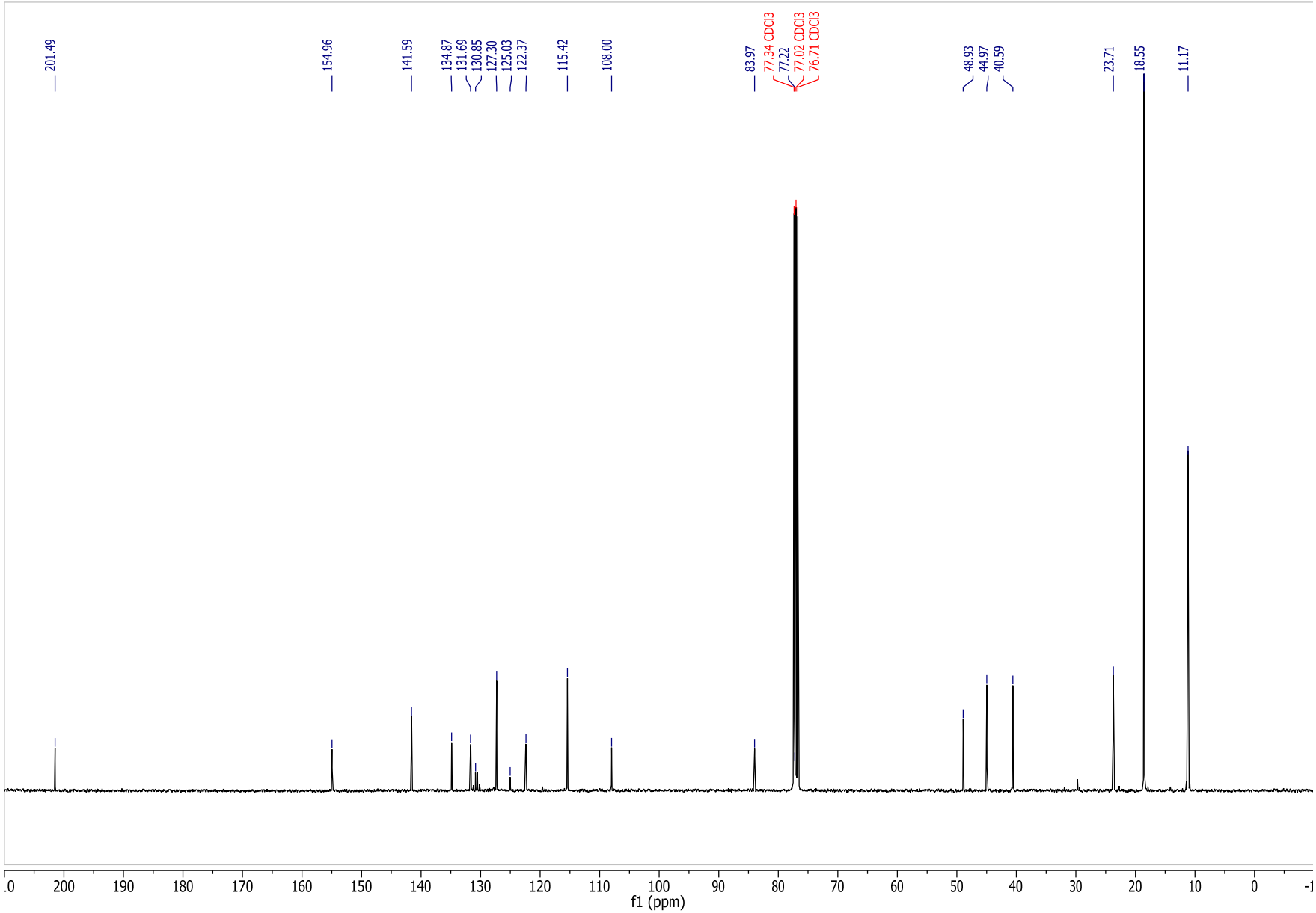


#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	11.583	1604076	92639	94.751	94.072	N/A	10185	1.772	1.498	
2	Unknown	1	12.357	88866	5837	5.249	5.928	N/A	14099	N/A	1.200	

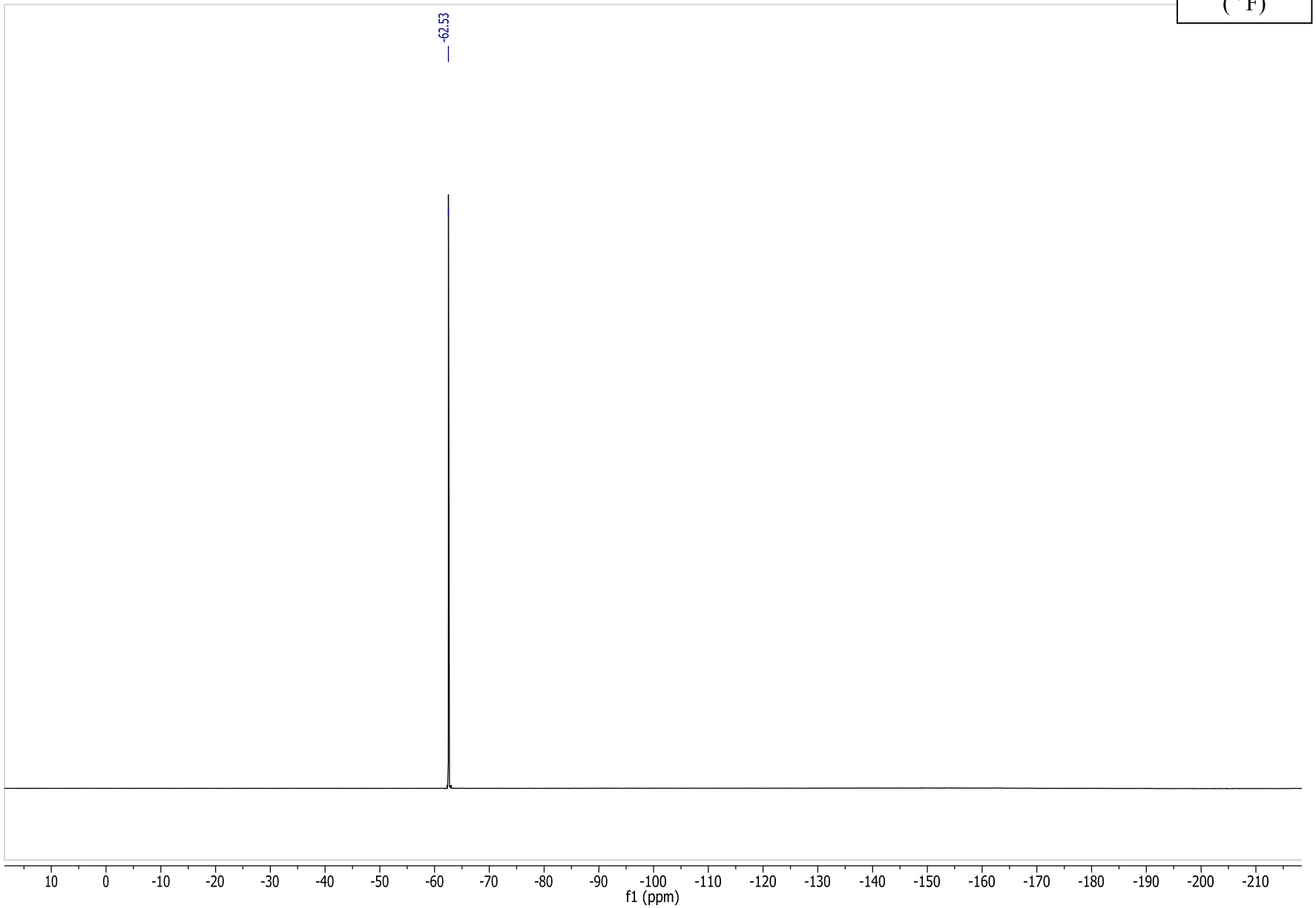
$CDCl_3$
400 MHz

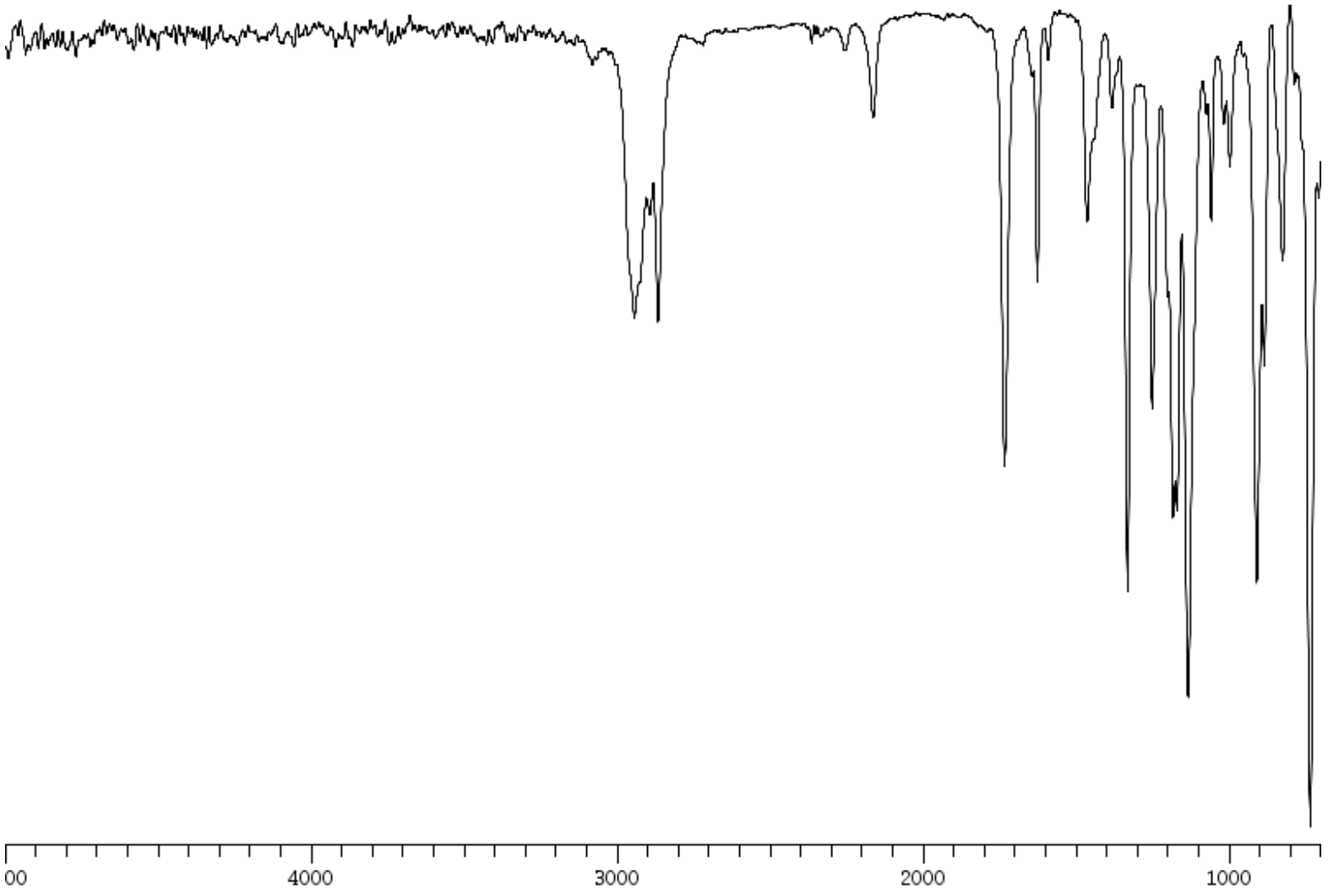


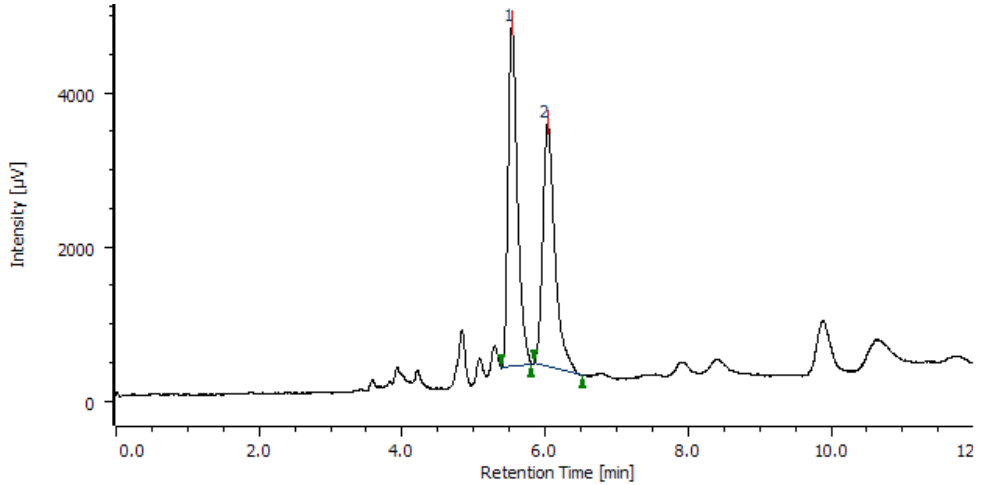
$CDCl_3$
100.1 MHz



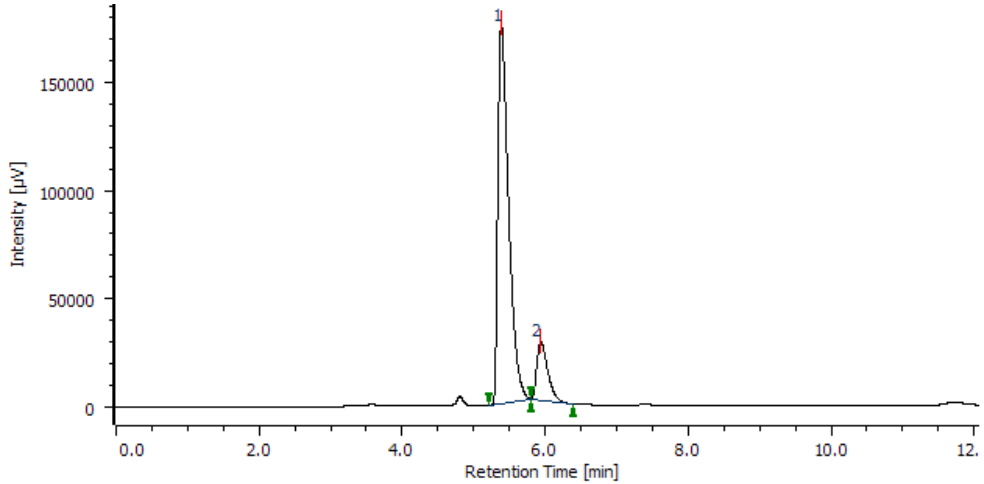
$CDCl_3$
376.5 MHz
(^{19}F)




00
4000
3000
2000
1000

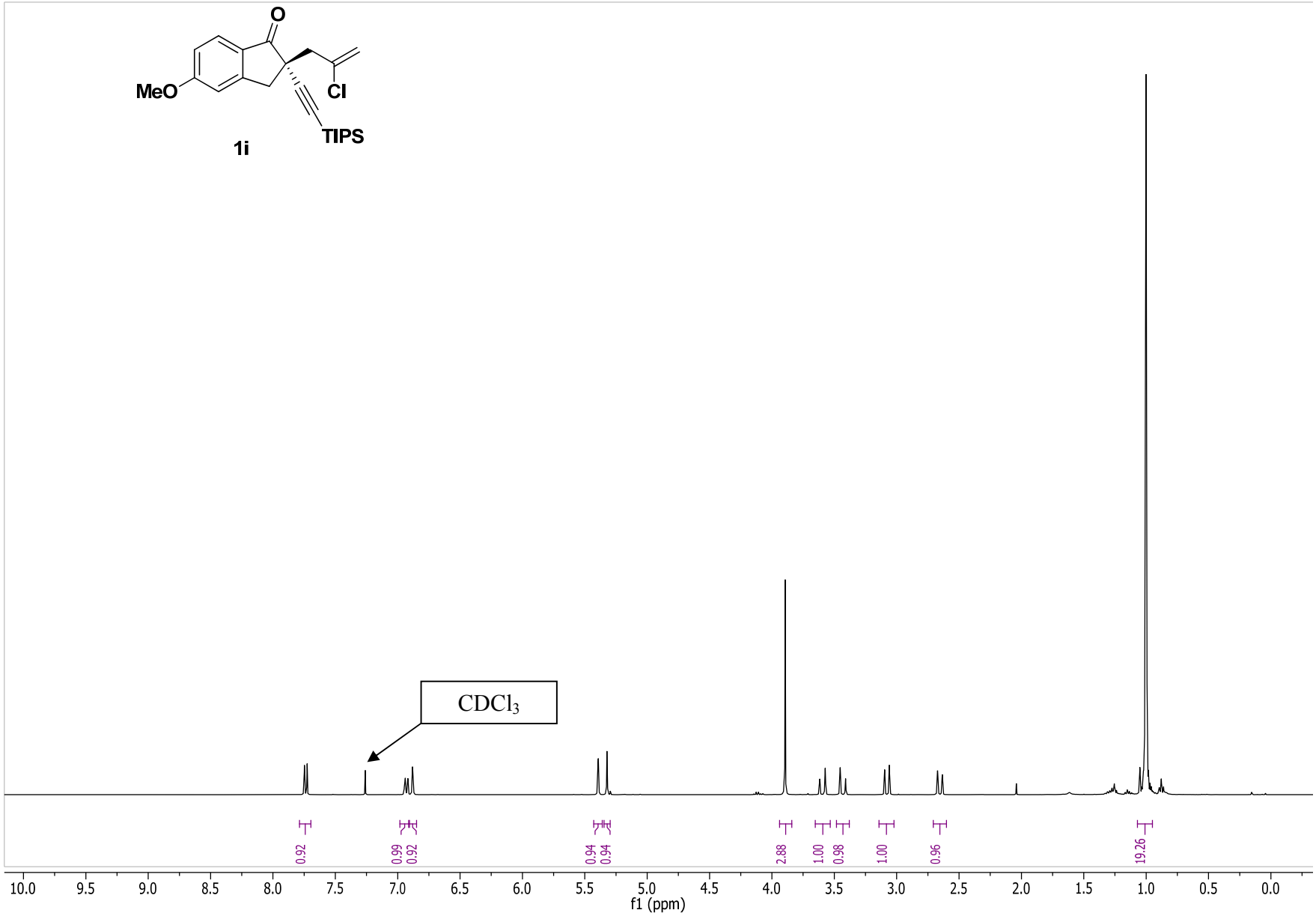


#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	2	5.530	39954	4426	51.945	58.433	N/A	9146	1.931	1.464	
2	Unknown	2	6.030	36963	3149	48.055	41.567	N/A	7020	N/A	1.496	

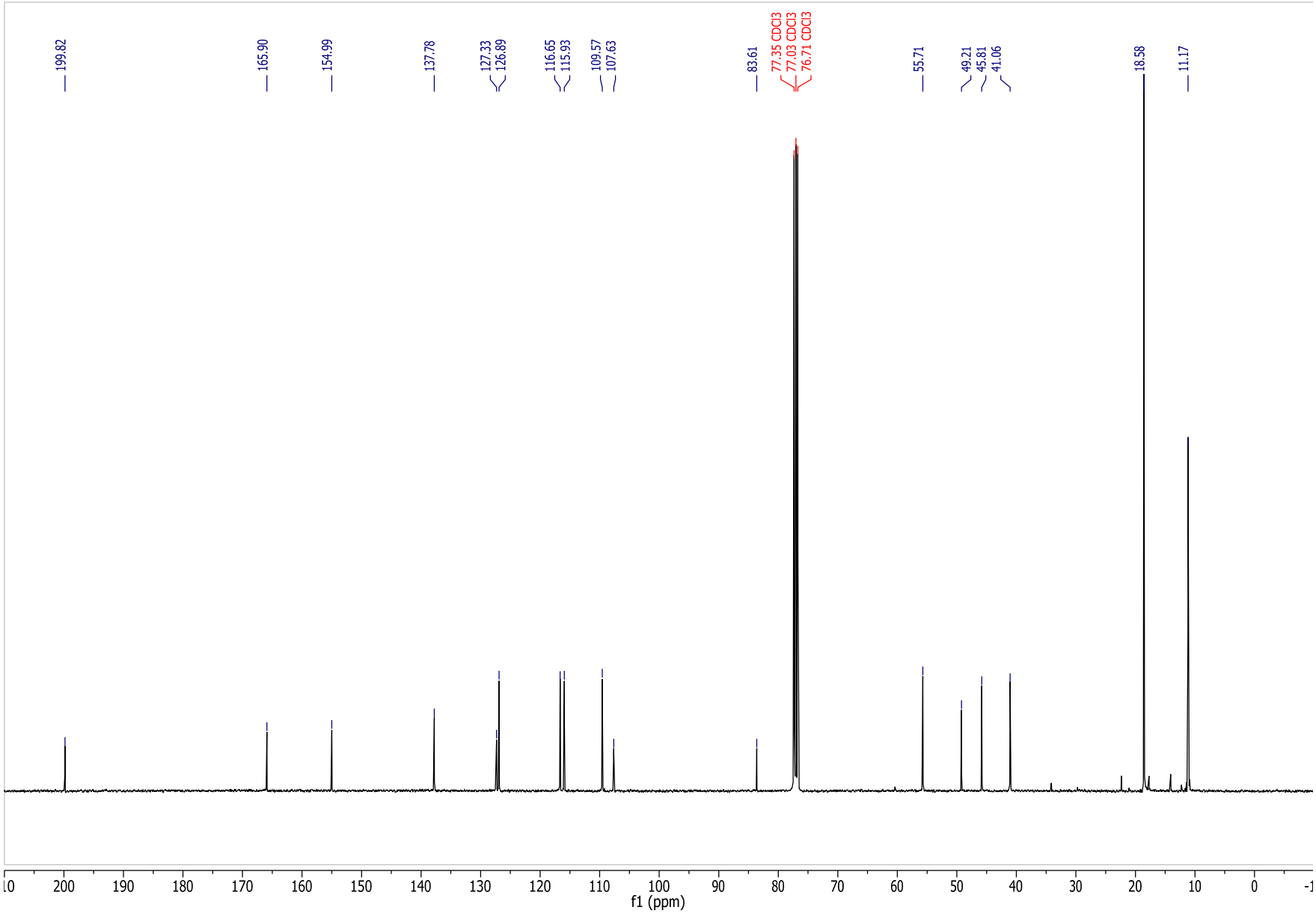


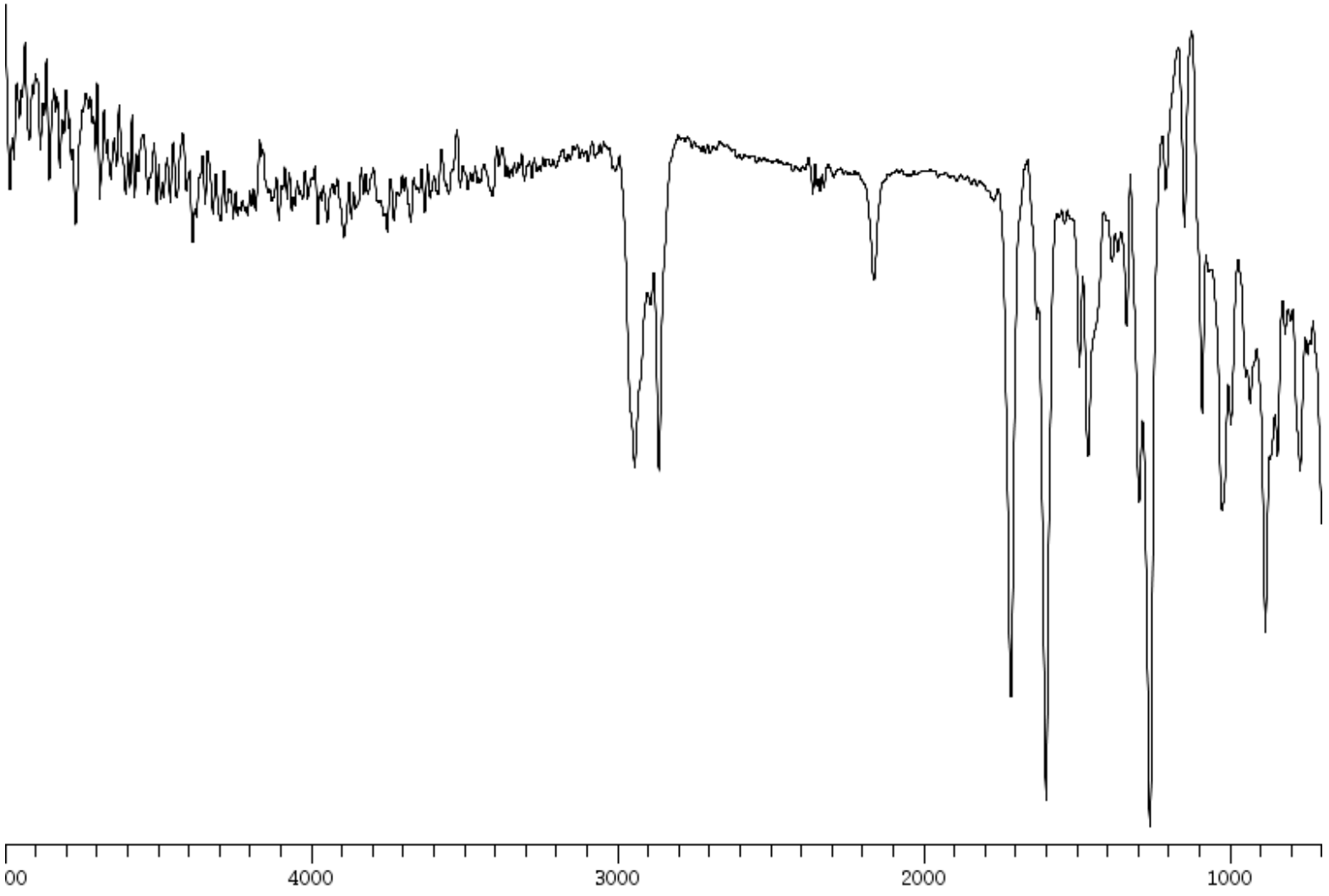
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	2	5.383	1817498	174912	86.445	86.679	N/A	6482	2.029	1.964	
2	Unknown	2	5.933	284990	26881	13.555	13.321	N/A	7391	N/A	1.640	

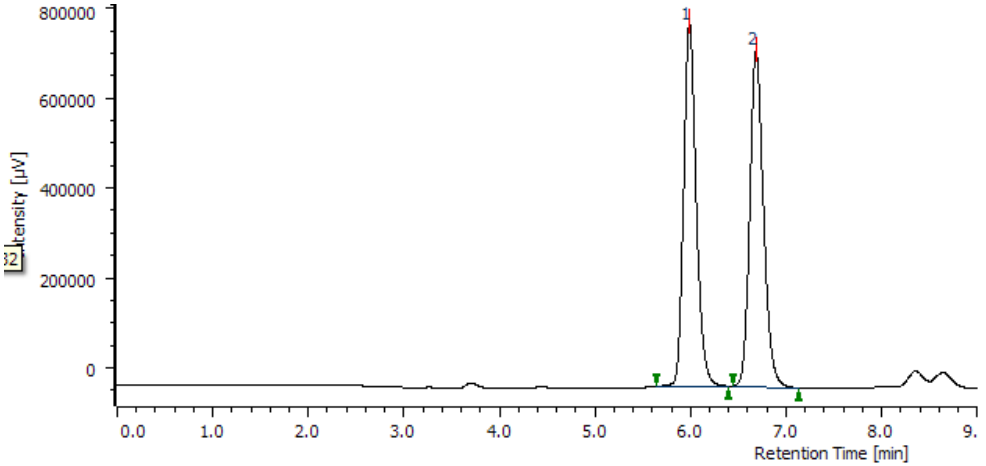
$CDCl_3$
400 MHz



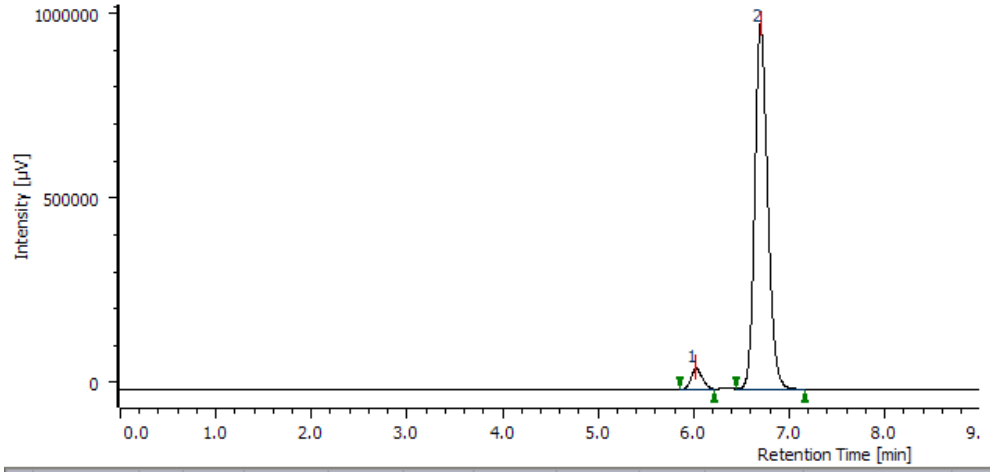
$CDCl_3$
100.1 MHz



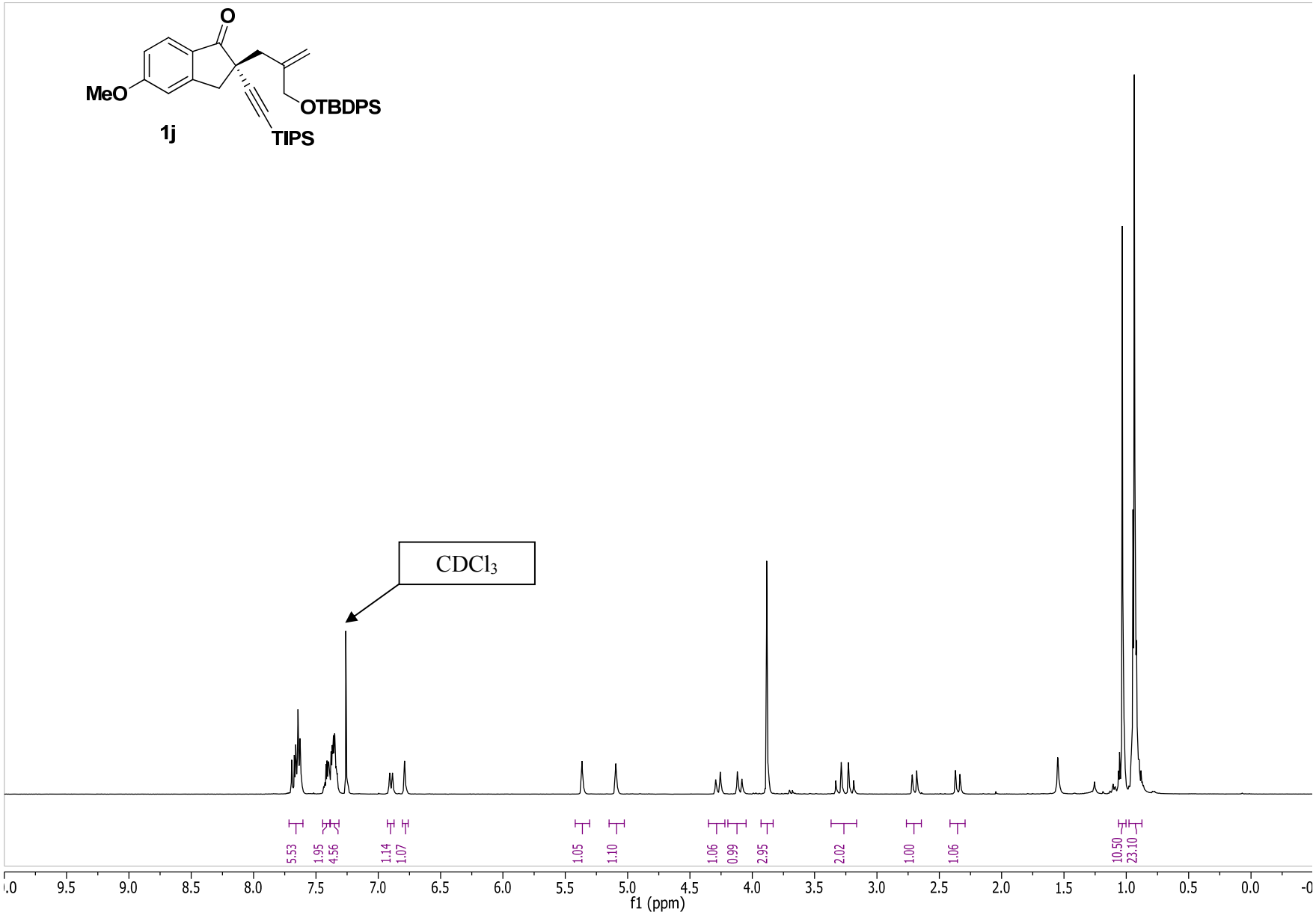

00
4000
3000
2000
1000



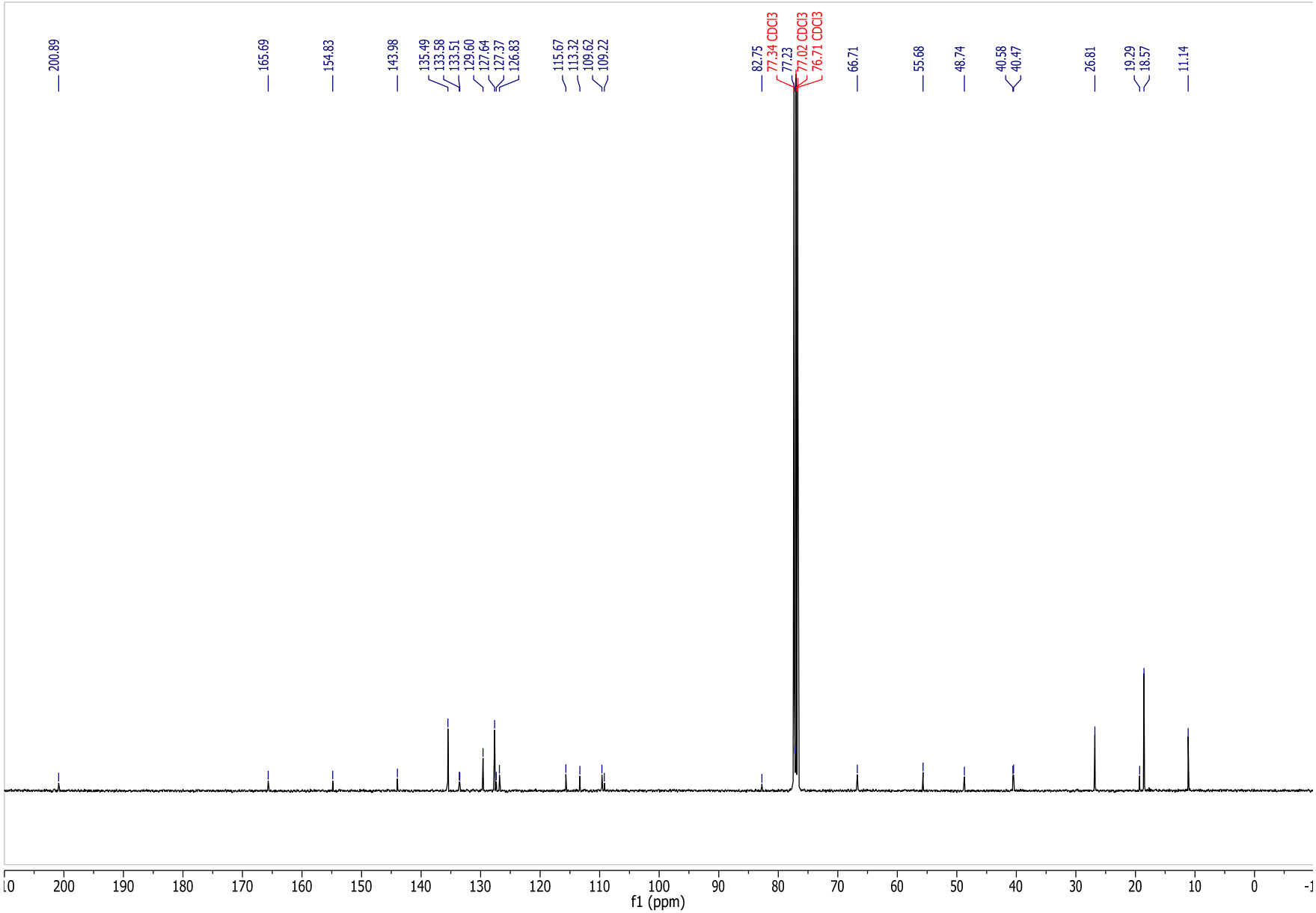
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	2	5.983	7385497	808935	49.869	52.036	N/A	10472	2.850	1.197	
2	Unknown	2	6.680	7424418	745643	50.131	47.964	N/A	10872	N/A	1.183	

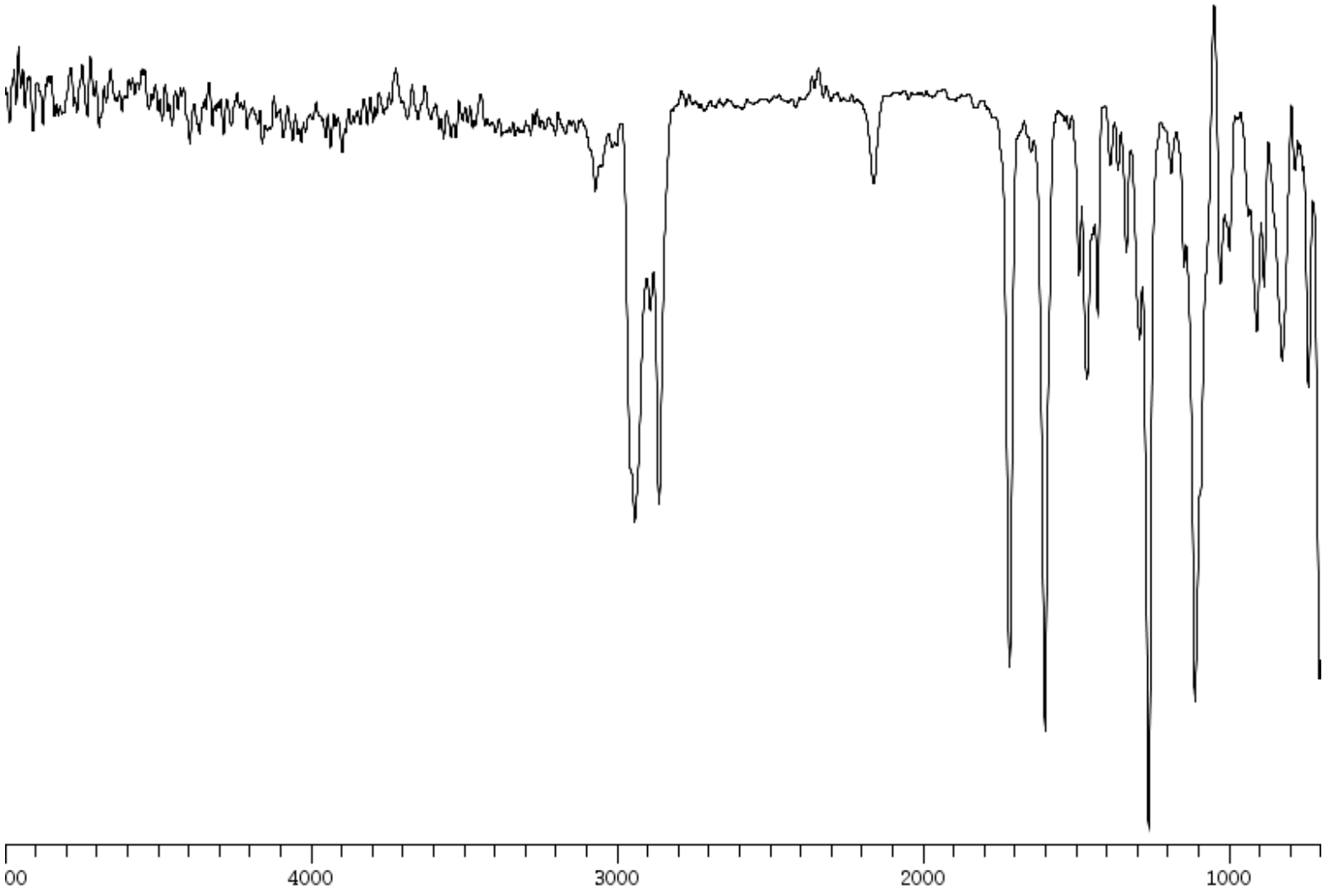


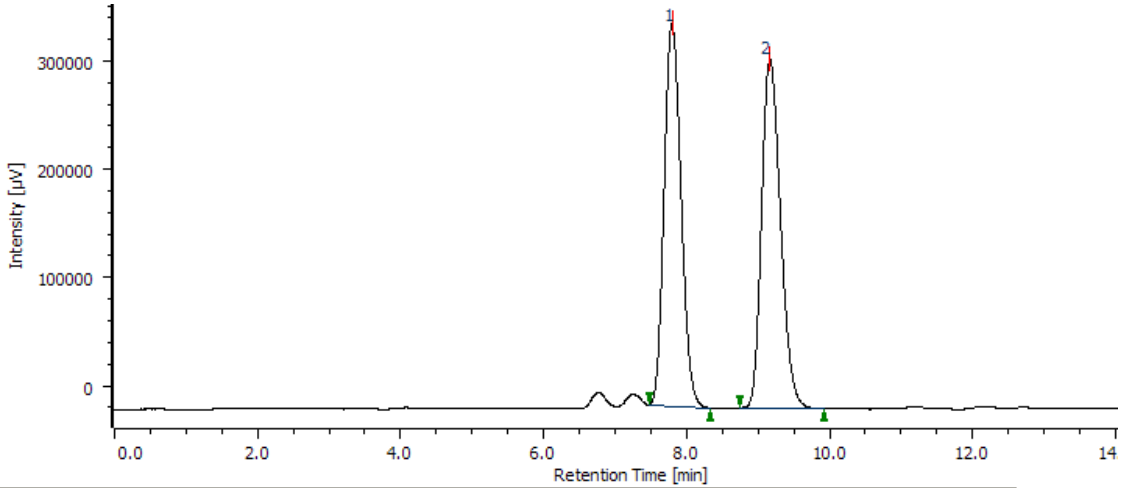
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	2	6.020	456112	56236	4.706	5.402	N/A	12555	2.952	1.146	
2	Unknown	2	6.693	9235589	984722	95.294	94.598	N/A	12184	N/A	1.193	


CDCl3
400 MHz
O
MeO
OTBDPS
TIPS
1j
CDCl3
5.53
1.95
4.56
1.14
1.07
1.05
1.10
1.06
0.99
2.95
2.02
1.00
1.06
10.50
23.10
f1 (ppm)

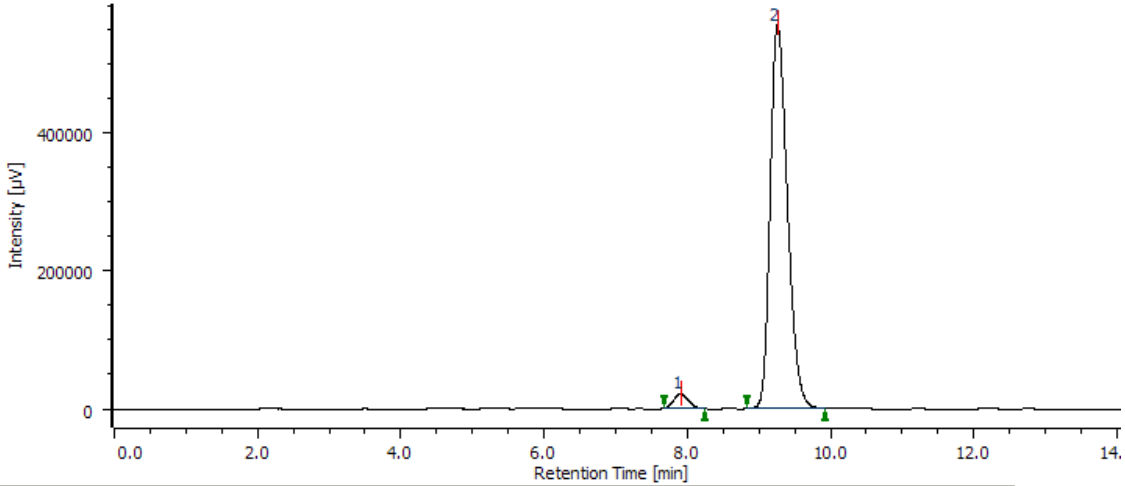
$CDCl_3$
100.1 MHz




00
4000
3000
2000
1000

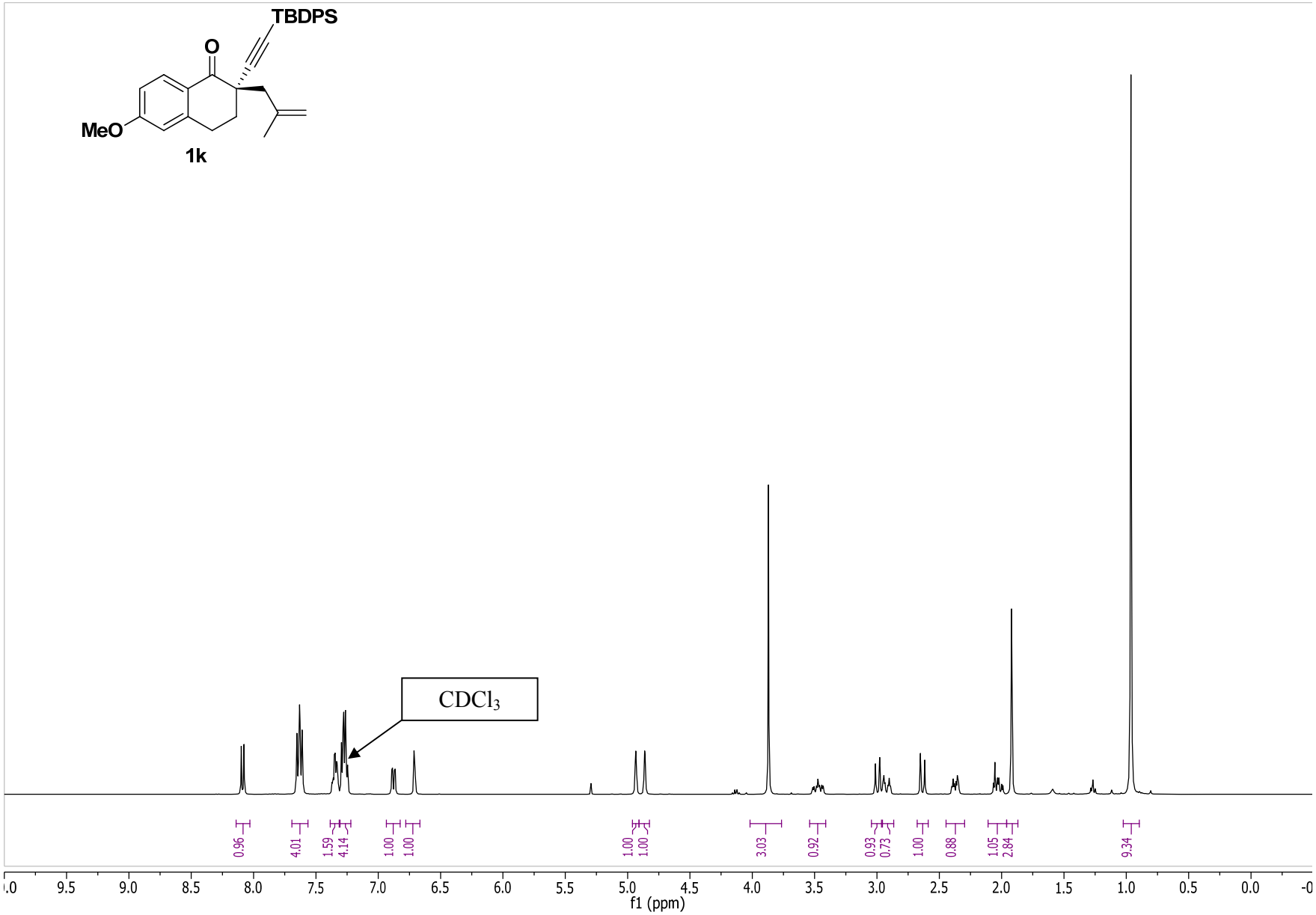


#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	7.790	5789731	351480	49.513	52.260	N/A	4998	2.955	1.143	
2	Unknown	1	9.157	5903625	321075	50.487	47.740	N/A	5666	N/A	1.241	

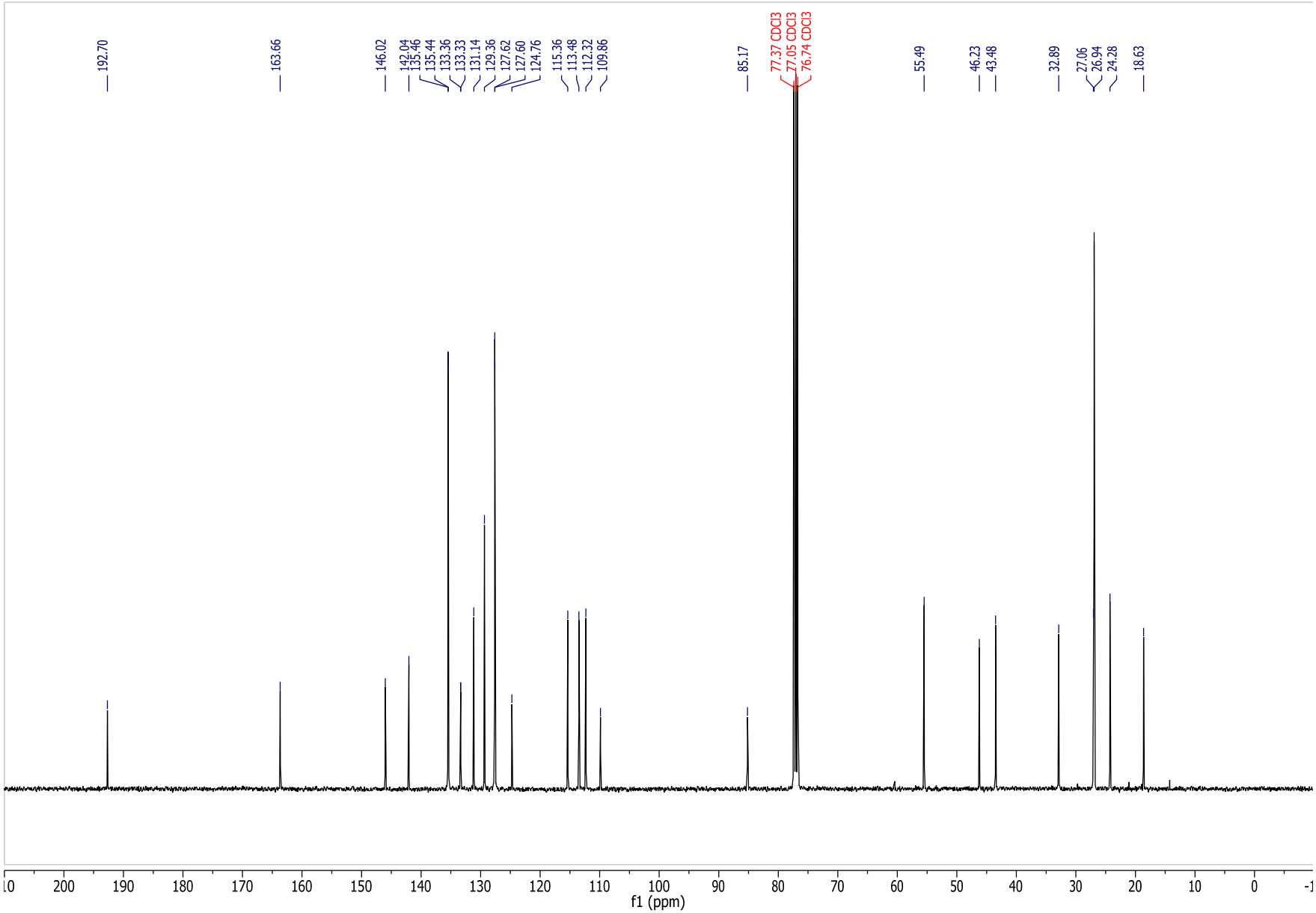


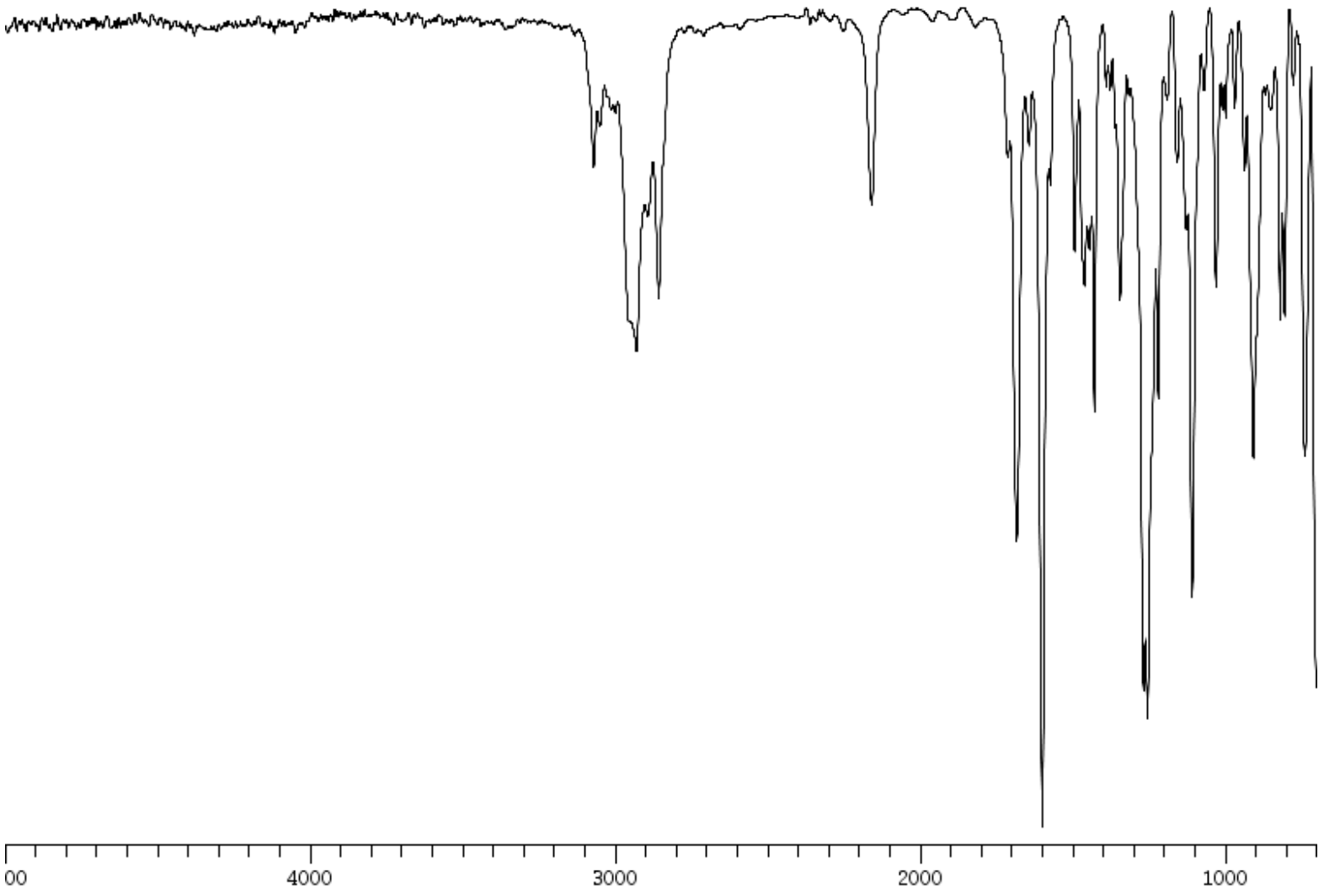
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	7.903	300309	21047	3.147	3.655	N/A	6770	3.285	1.103	
2	Unknown	1	9.250	9241745	554867	96.853	96.345	N/A	7143	N/A	1.299	

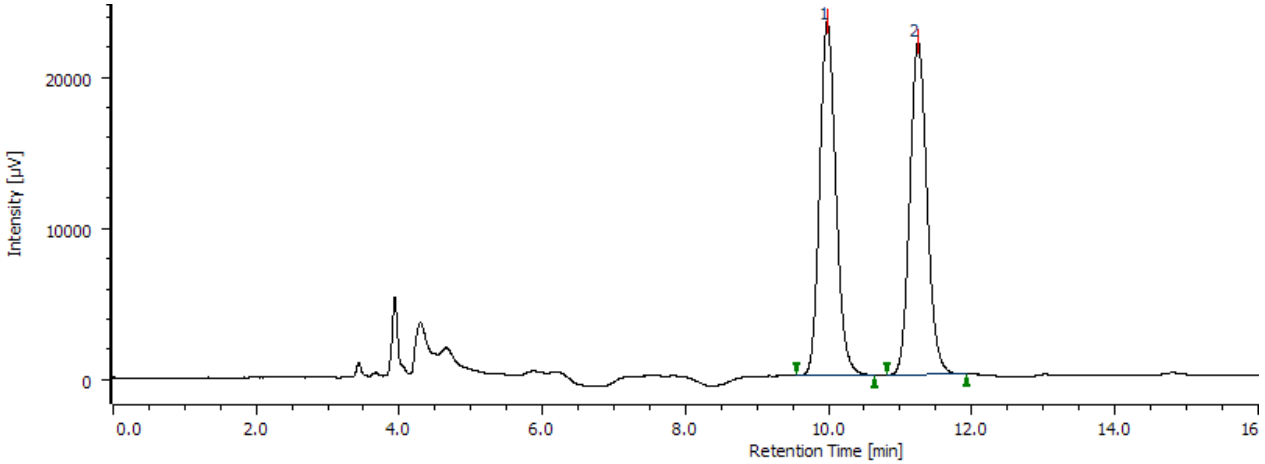
$CDCl_3$
400 MHz



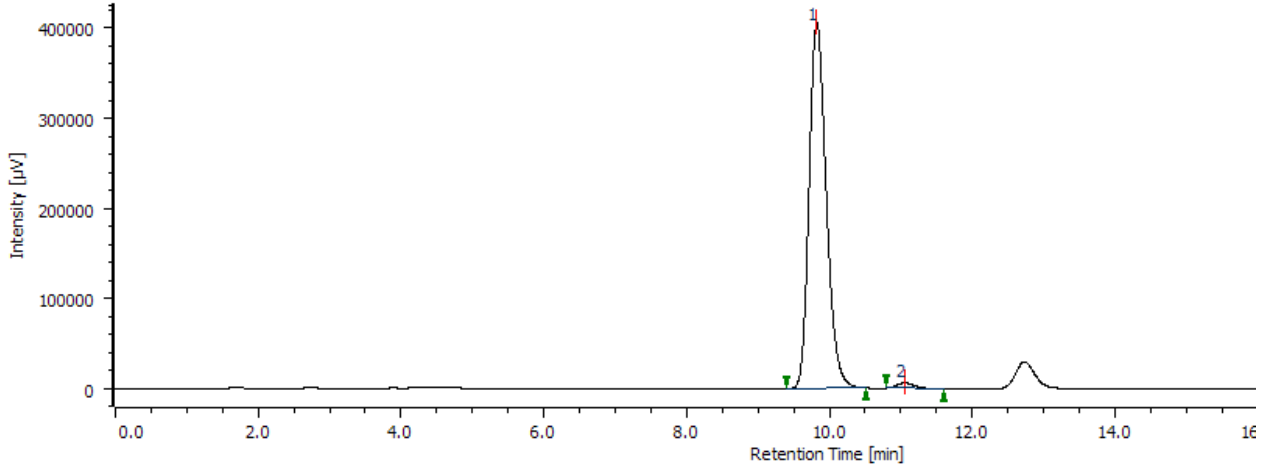
$CDCl_3$
100.1 MHz




00
4000
3000
2000
1000

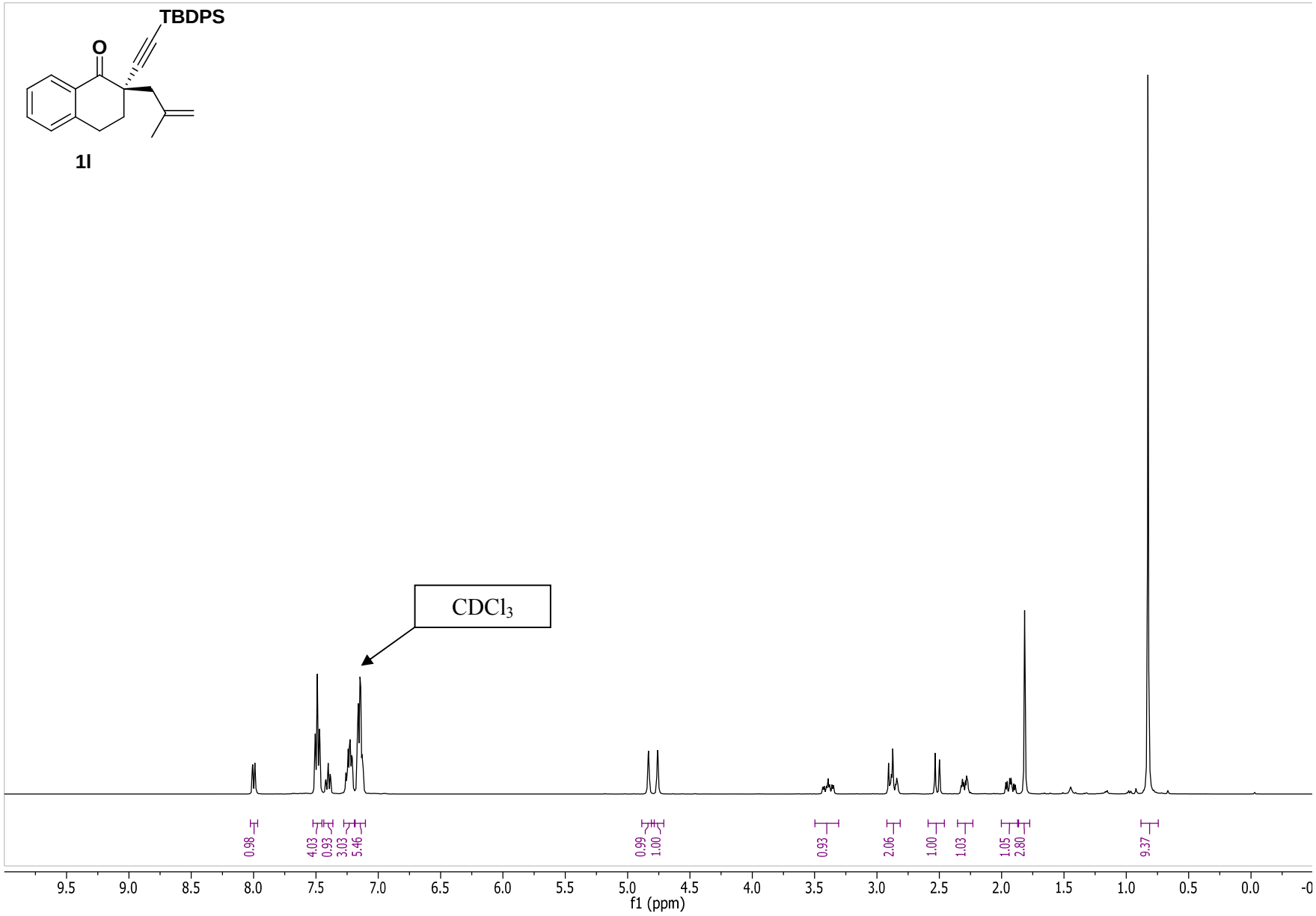


#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	2	9.973	367724	23322	50.145	51.559	N/A	9488	3.018	1.148	
2	Unknown	2	11.243	365600	21912	49.855	48.441	N/A	10722	N/A	1.108	

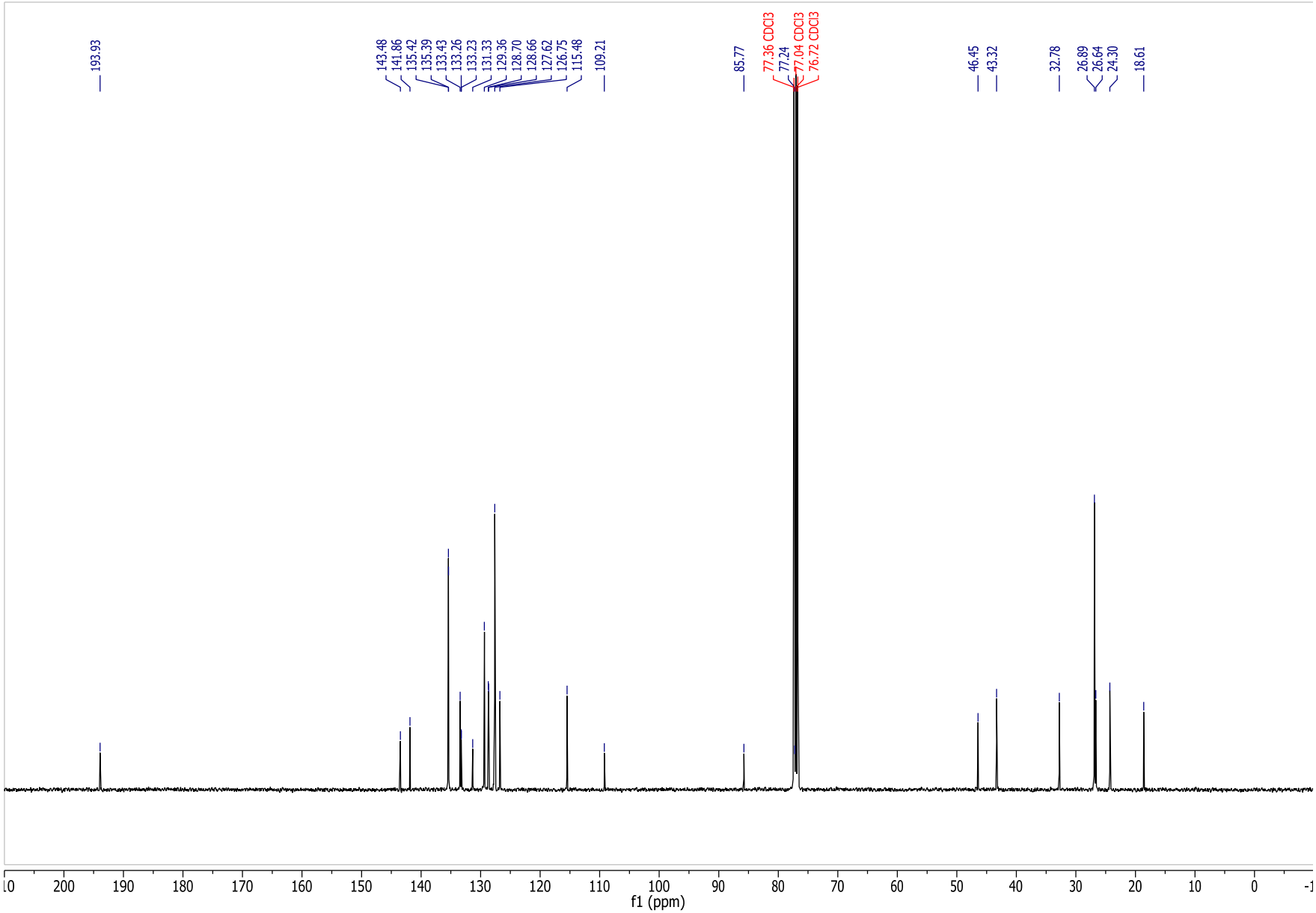


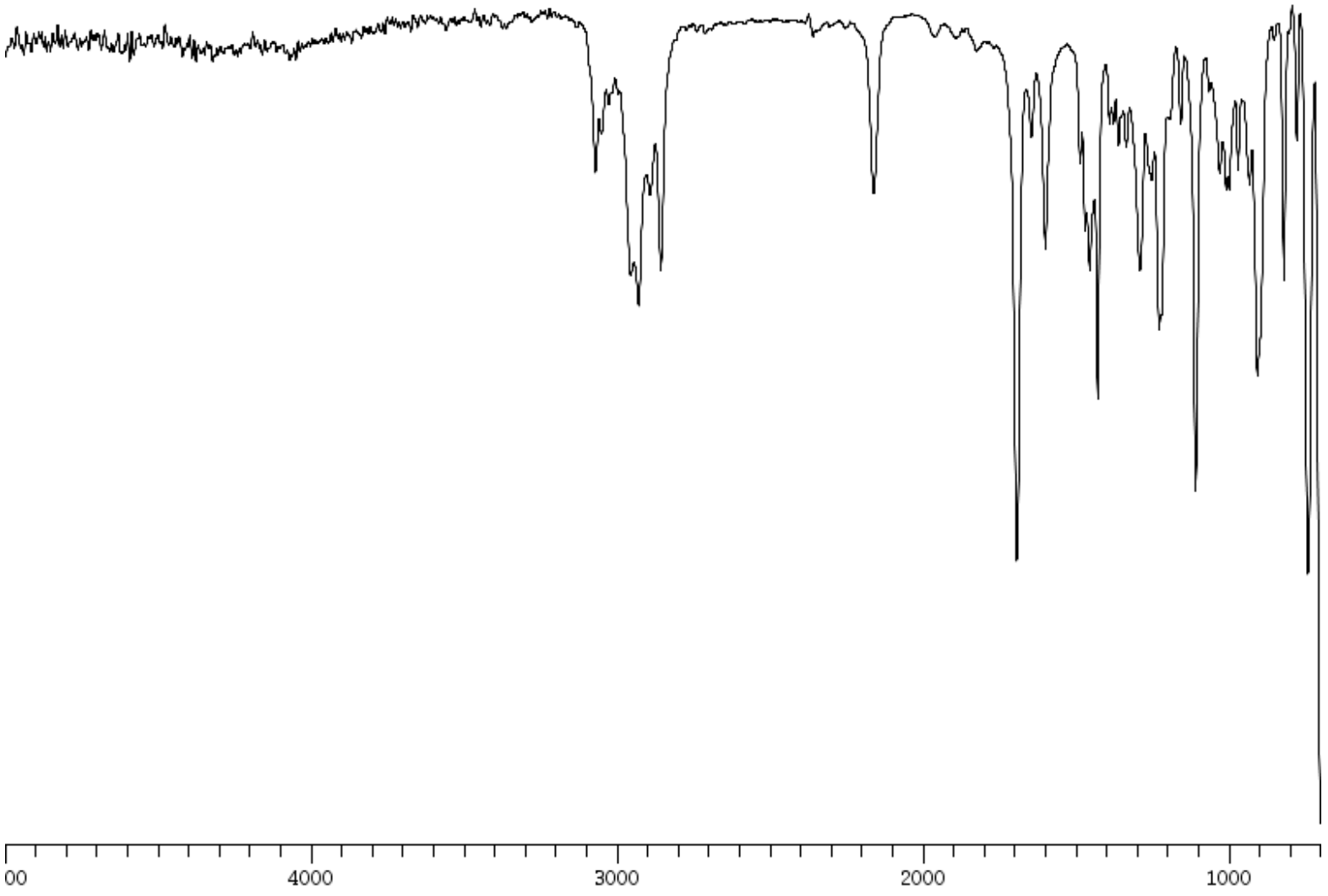
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	2	9.813	6733417	404338	98.604	98.563	N/A	8160	2.850	1.237	
2	Unknown	2	11.047	95303	5894	1.396	1.437	N/A	10401	N/A	1.131	

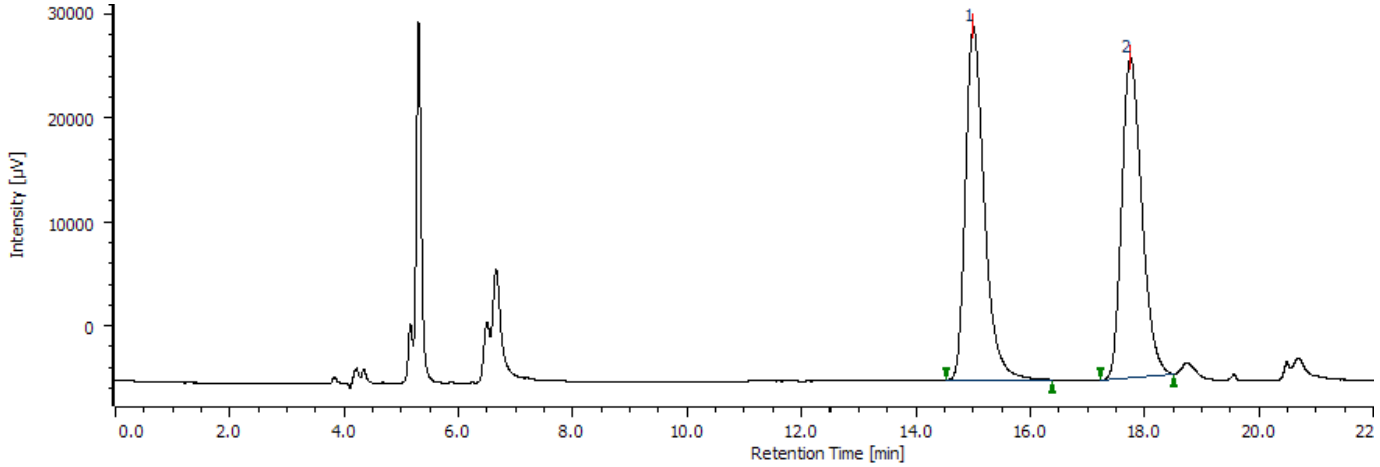
$CDCl_3$
400 MHz



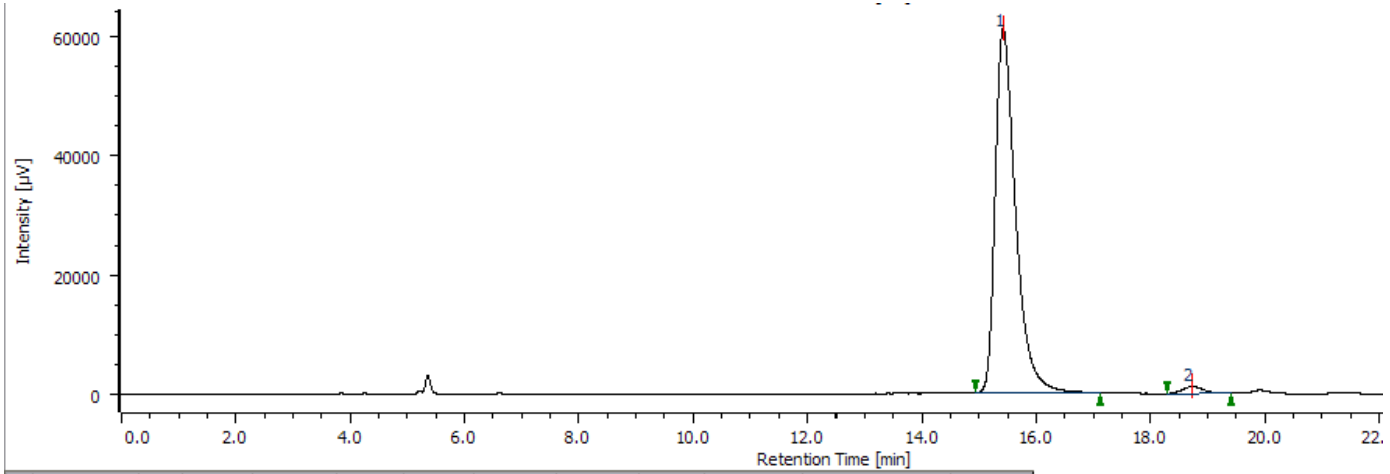
$CDCl_3$
100.1 MHz




00
4000
3000
2000
1000



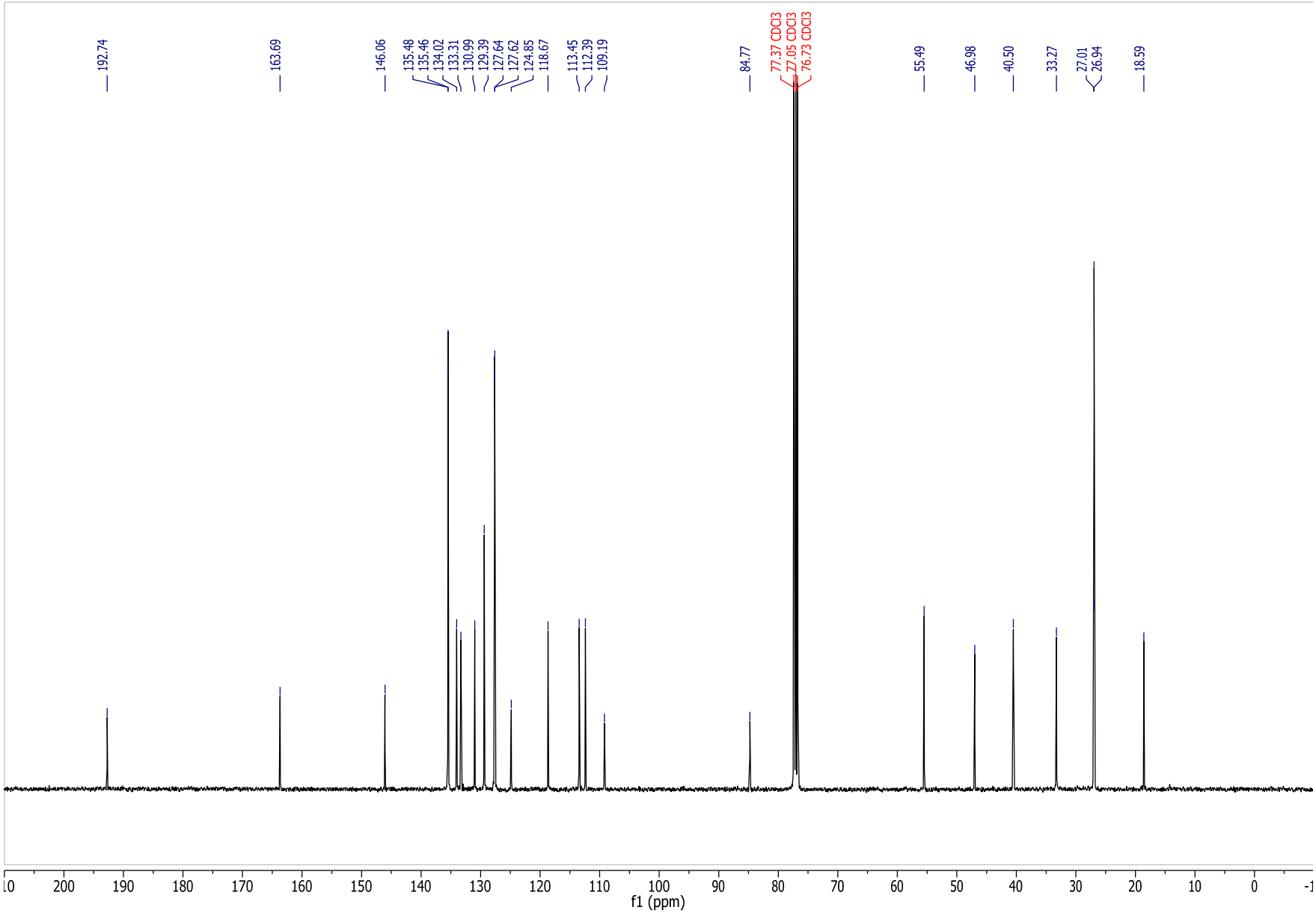
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	14.990	776237	33844	50.840	52.371	N/A	10718	4.531	1.401	
2	Unknown	1	17.740	750597	30780	49.160	47.629	N/A	12377	N/A	1.271	

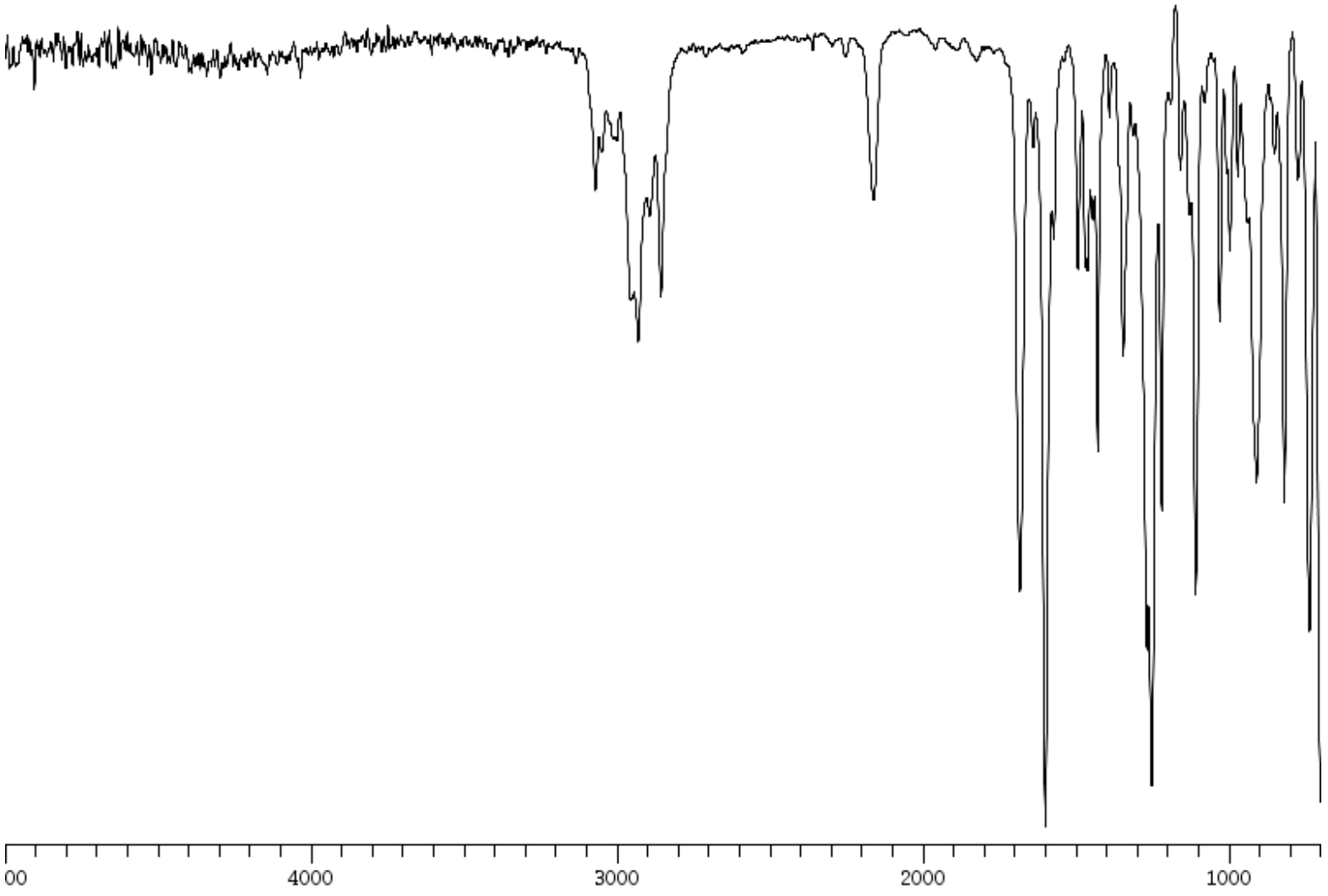


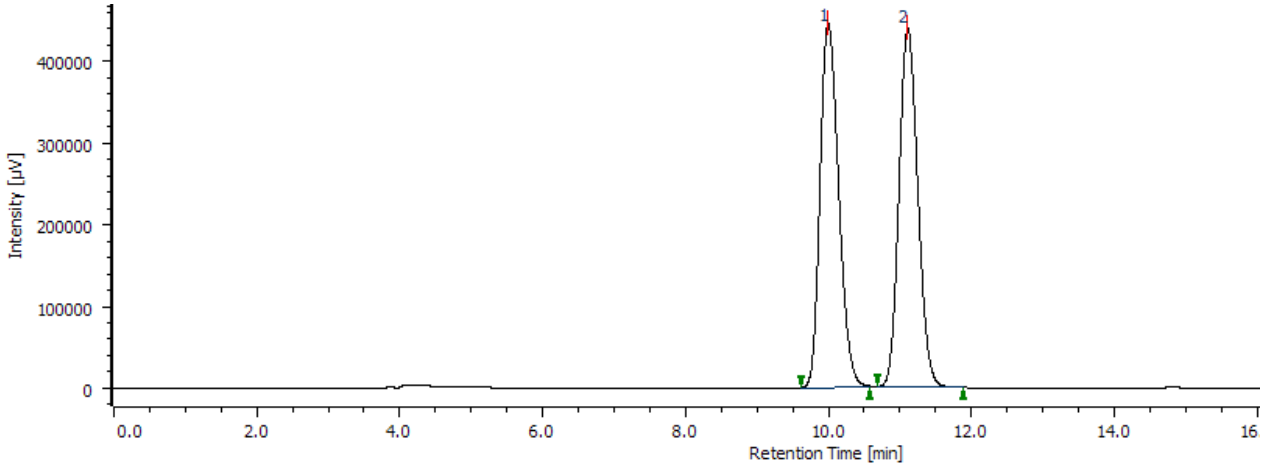
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	15.407	1508633	60877	98.040	98.153	N/A	9792	5.062	1.541	
2	Unknown	1	18.717	30154	1145	1.960	1.847	N/A	11823	N/A	1.172	


CDCl3
400 MHz
TBDPS
O
MeO
1m
CDCl3
1.13
4.66
2.34
5.03
1.16
1.09
1.00
2.29
3.54
1.19
0.31
1.05
1.15
1.18
1.14
10.64
f1 (ppm)

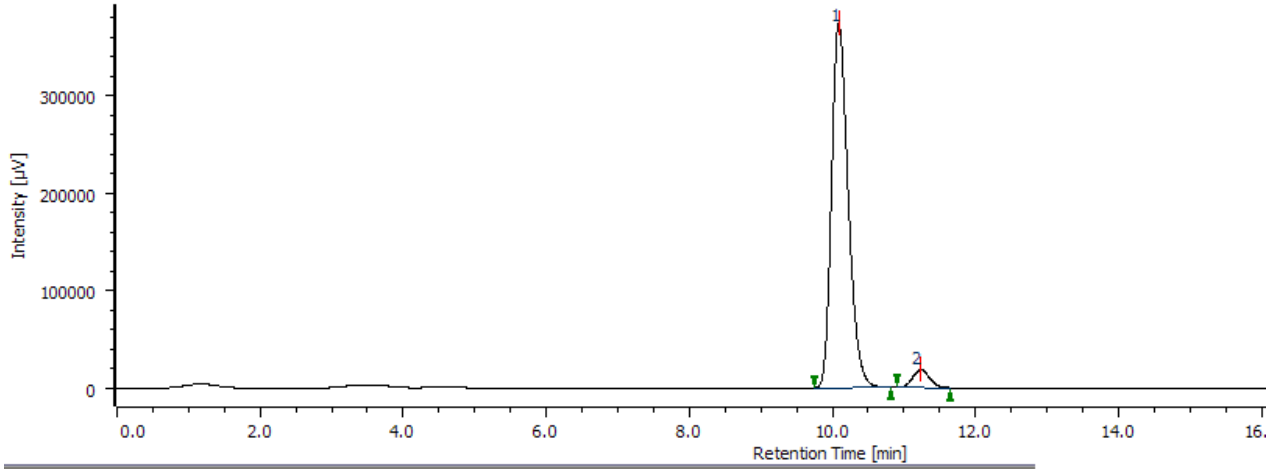
$CDCl_3$
100.1 MHz



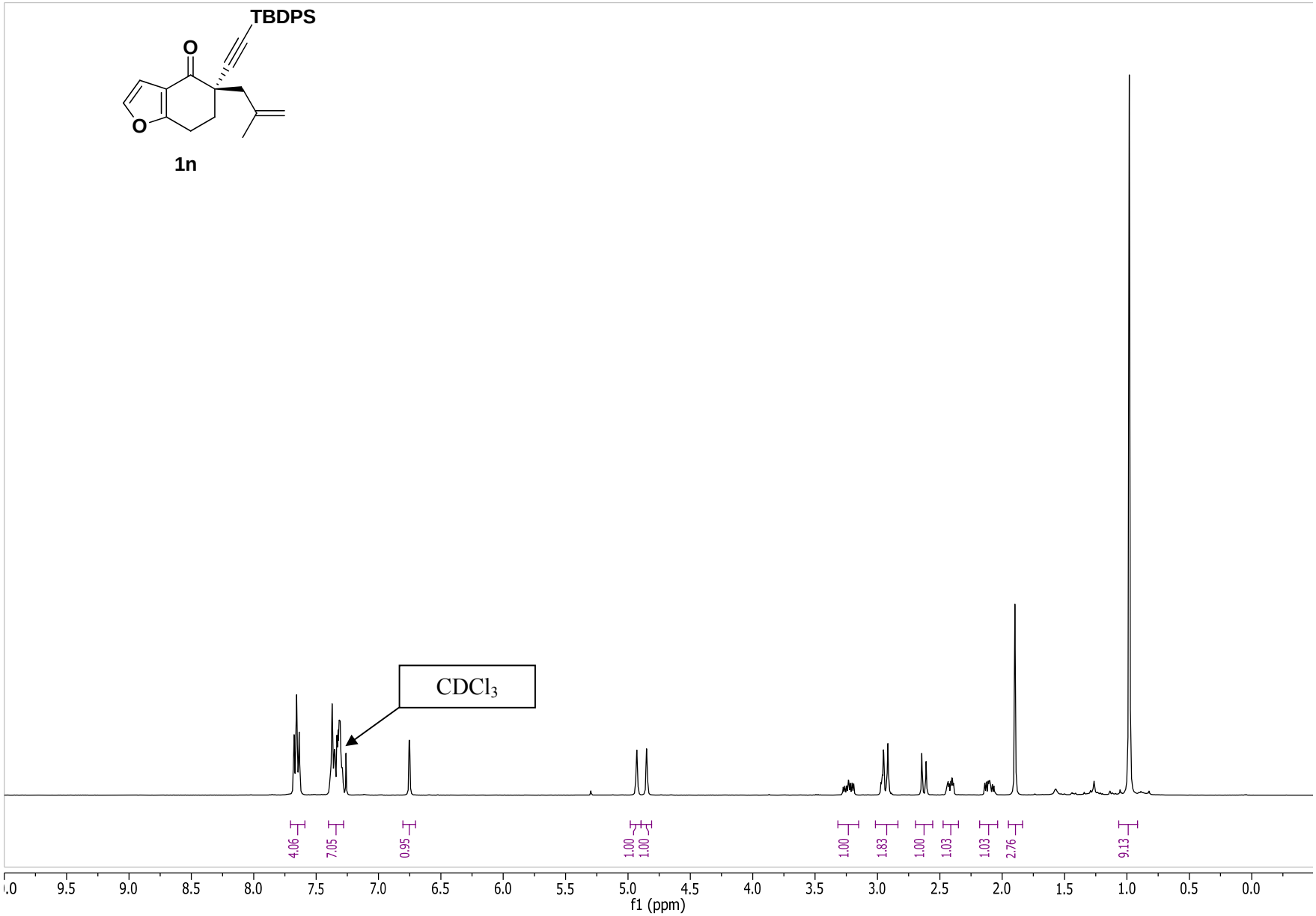

00
4000
3000
2000
1000



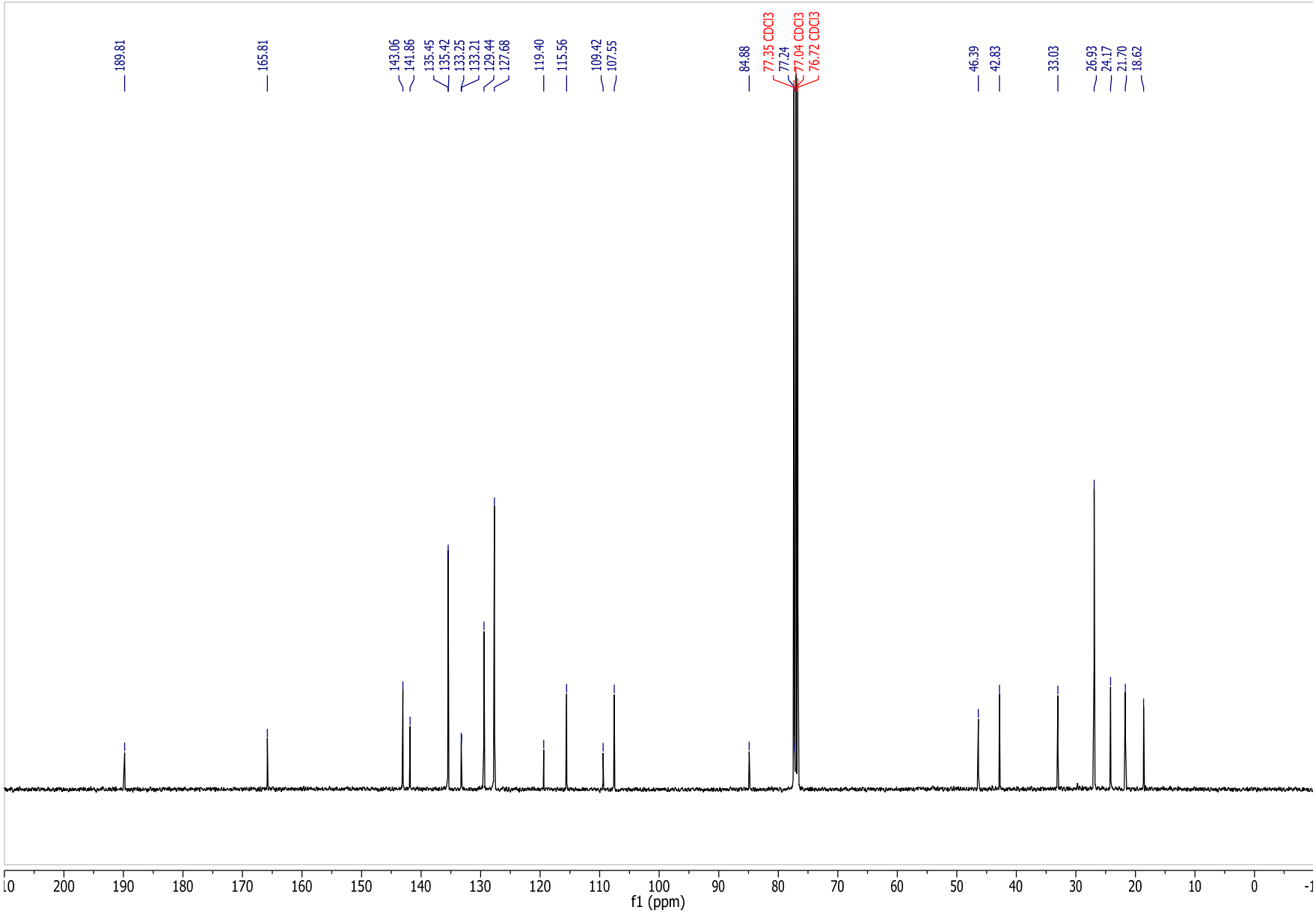
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	2	9.987	7968948	443352	49.910	50.383	N/A	6989	2.318	1.237	
2	Unknown	2	11.100	7997775	436618	50.090	49.617	N/A	8363	N/A	1.129	

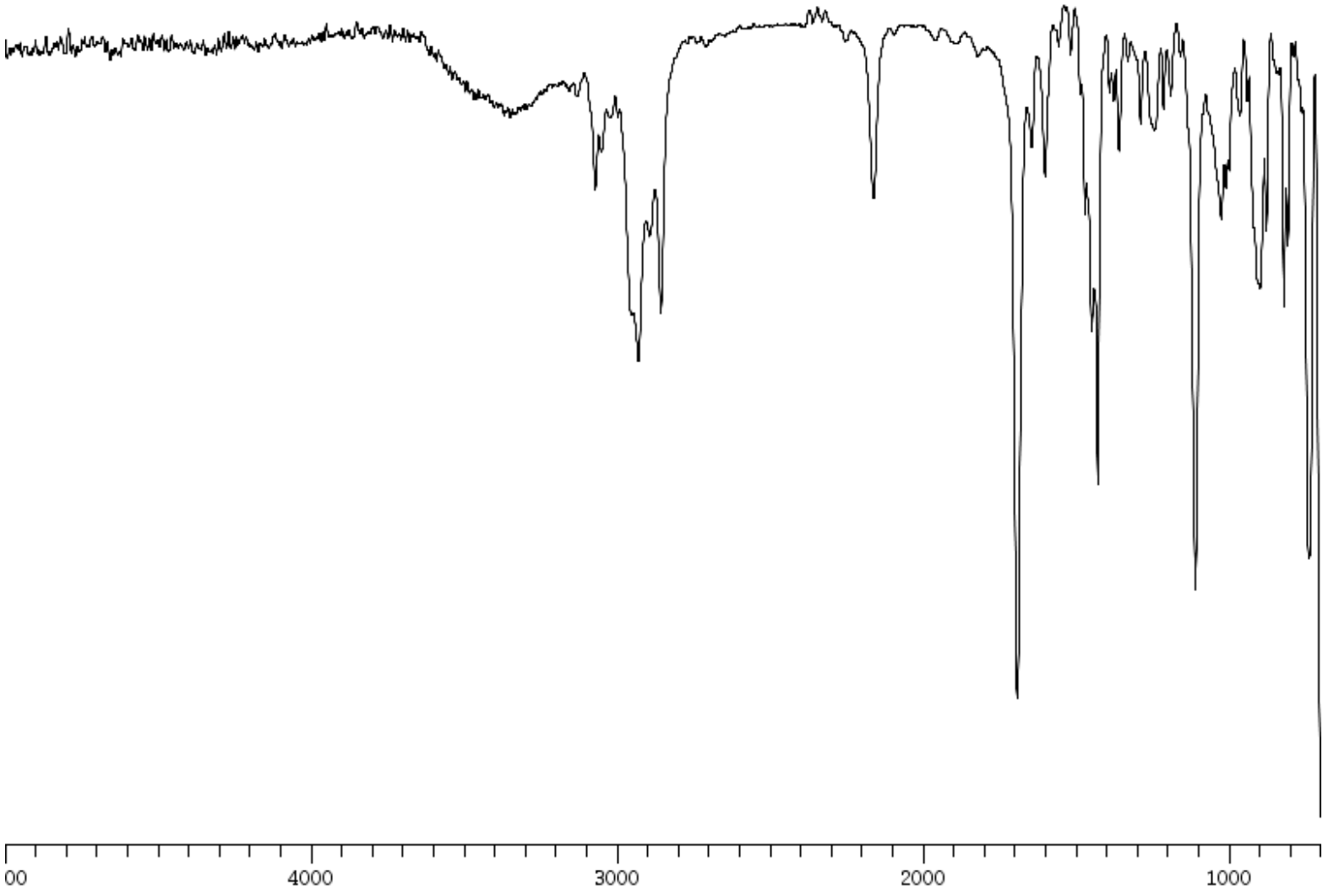


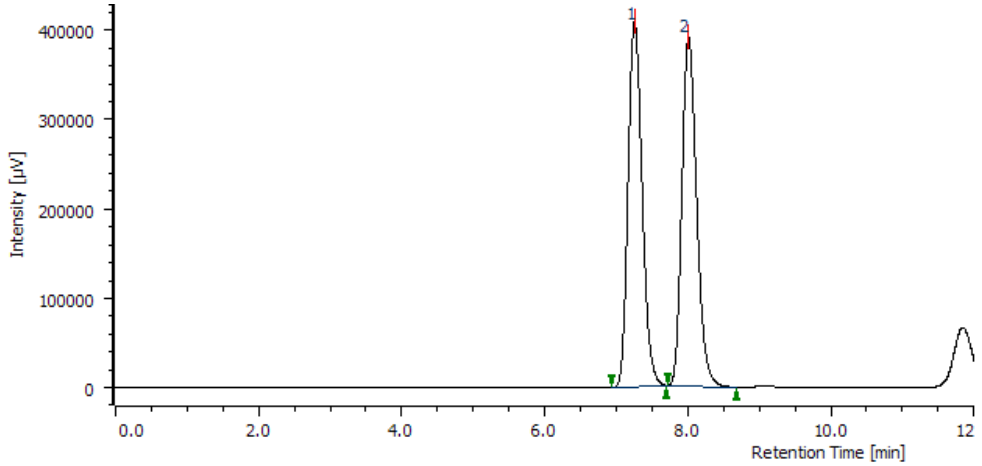
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	2	10.080	6006386	372093	95.262	95.320	N/A	9164	2.685	1.284	
2	Unknown	2	11.223	298737	18269	4.738	4.680	N/A	10767	N/A	1.101	


CDCl3
400 MHz
TBDPS
O
O
1n
CDCl3
4.06
7.05
0.95
1.00
1.00
1.00
1.83
1.00
1.03
1.03
2.76
9.13
f1 (ppm)

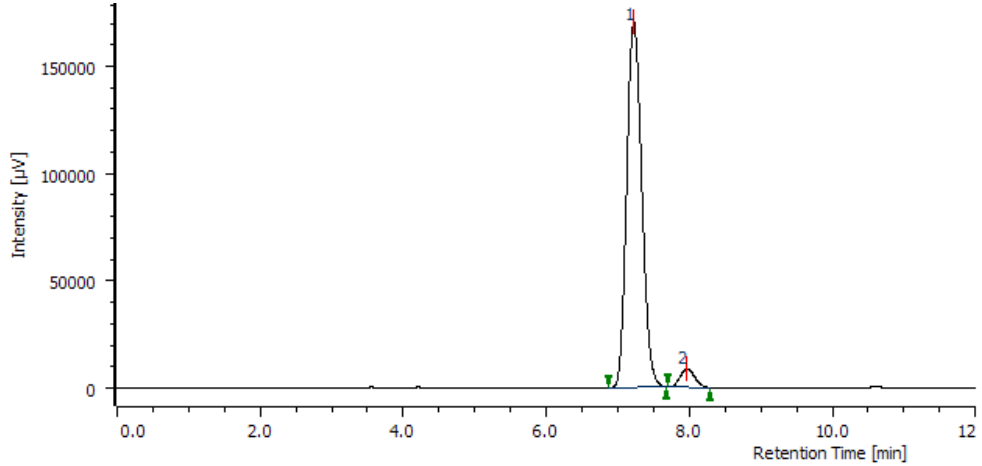
$CDCl_3$
100.1 MHz




00
4000
3000
2000
1000

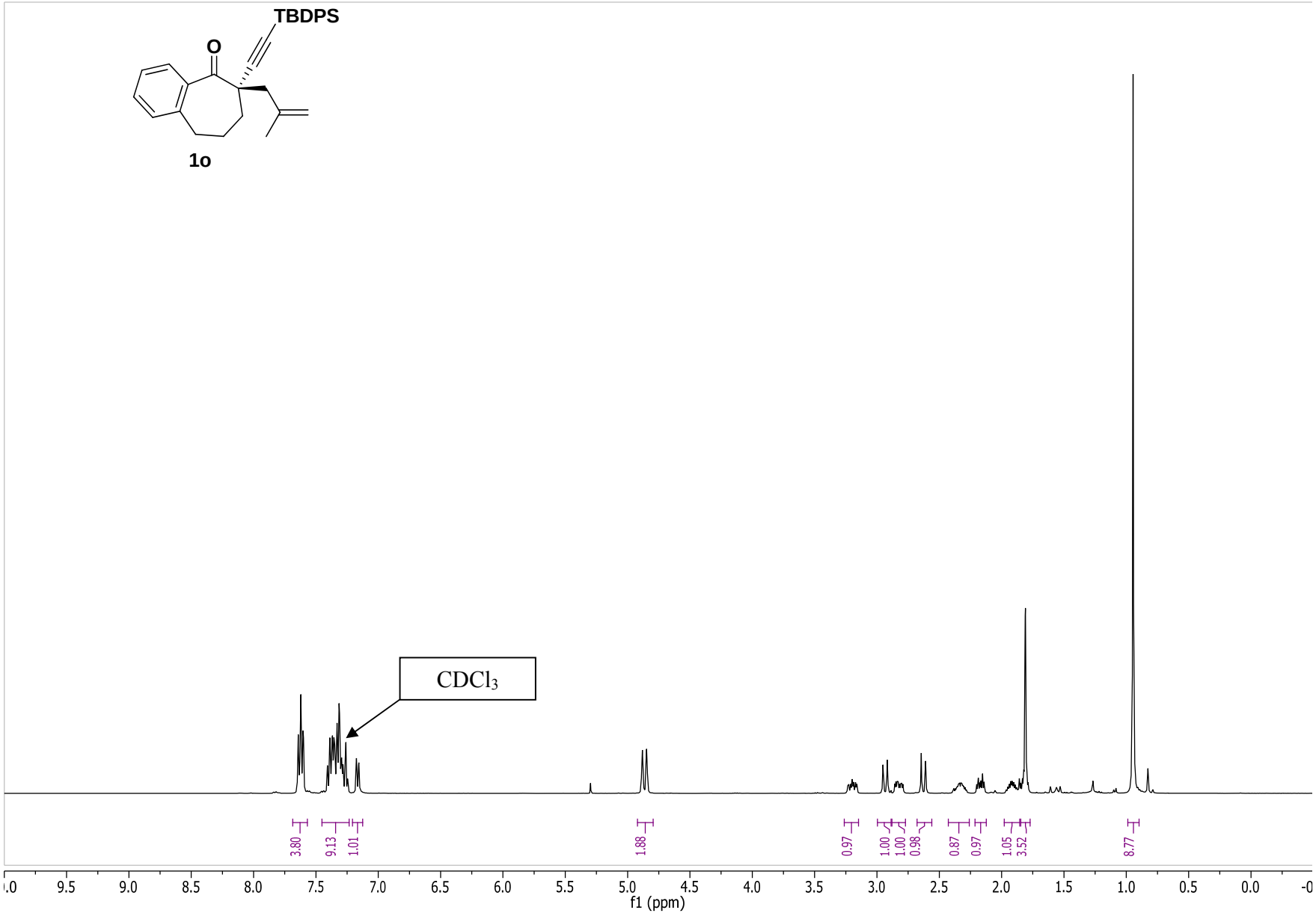


#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	7.250	5557646	406708	49.882	51.122	N/A	6521	2.056	1.182	
2	Unknown	1	8.003	5583967	388848	50.118	48.878	N/A	7263	N/A	1.221	

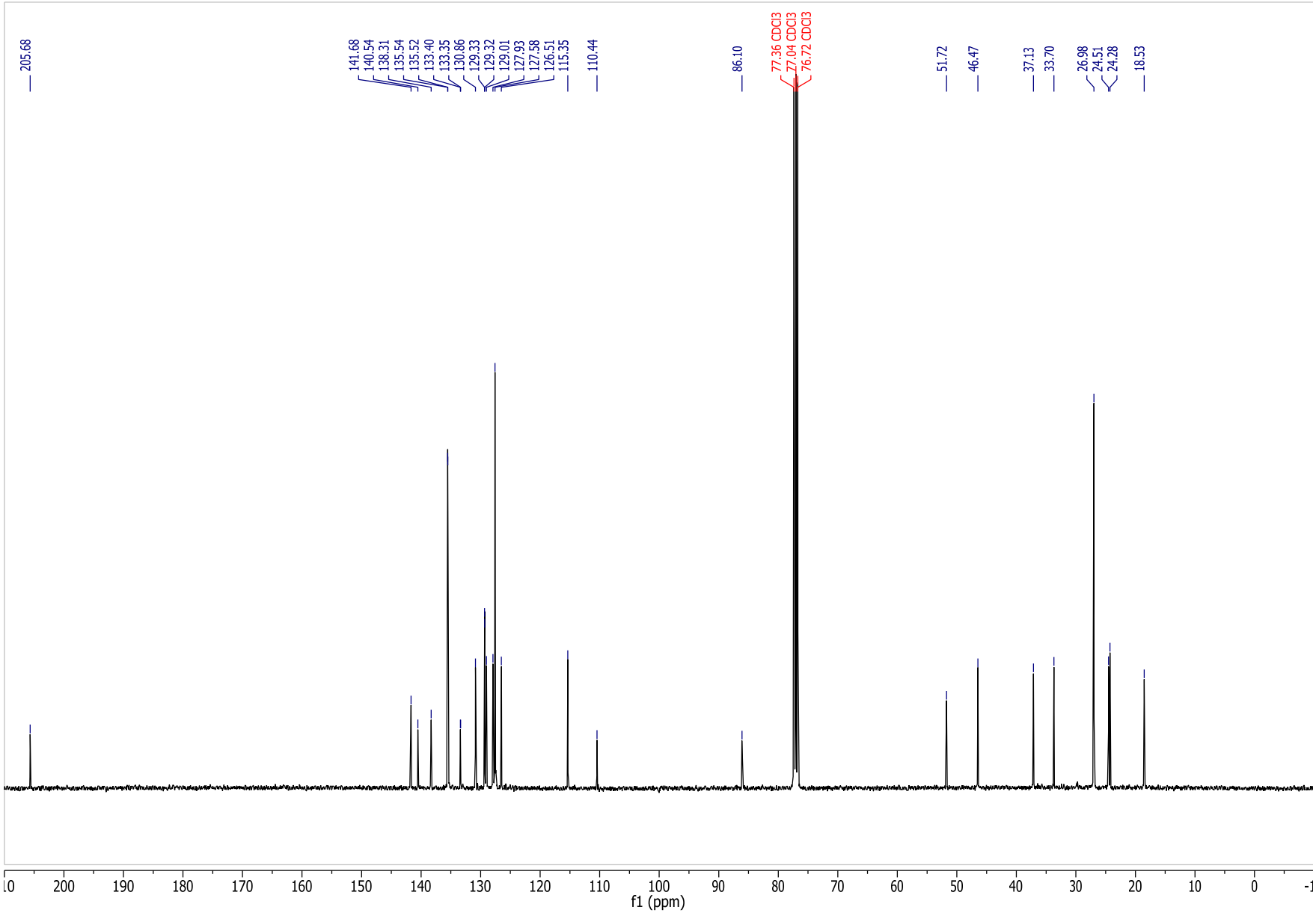


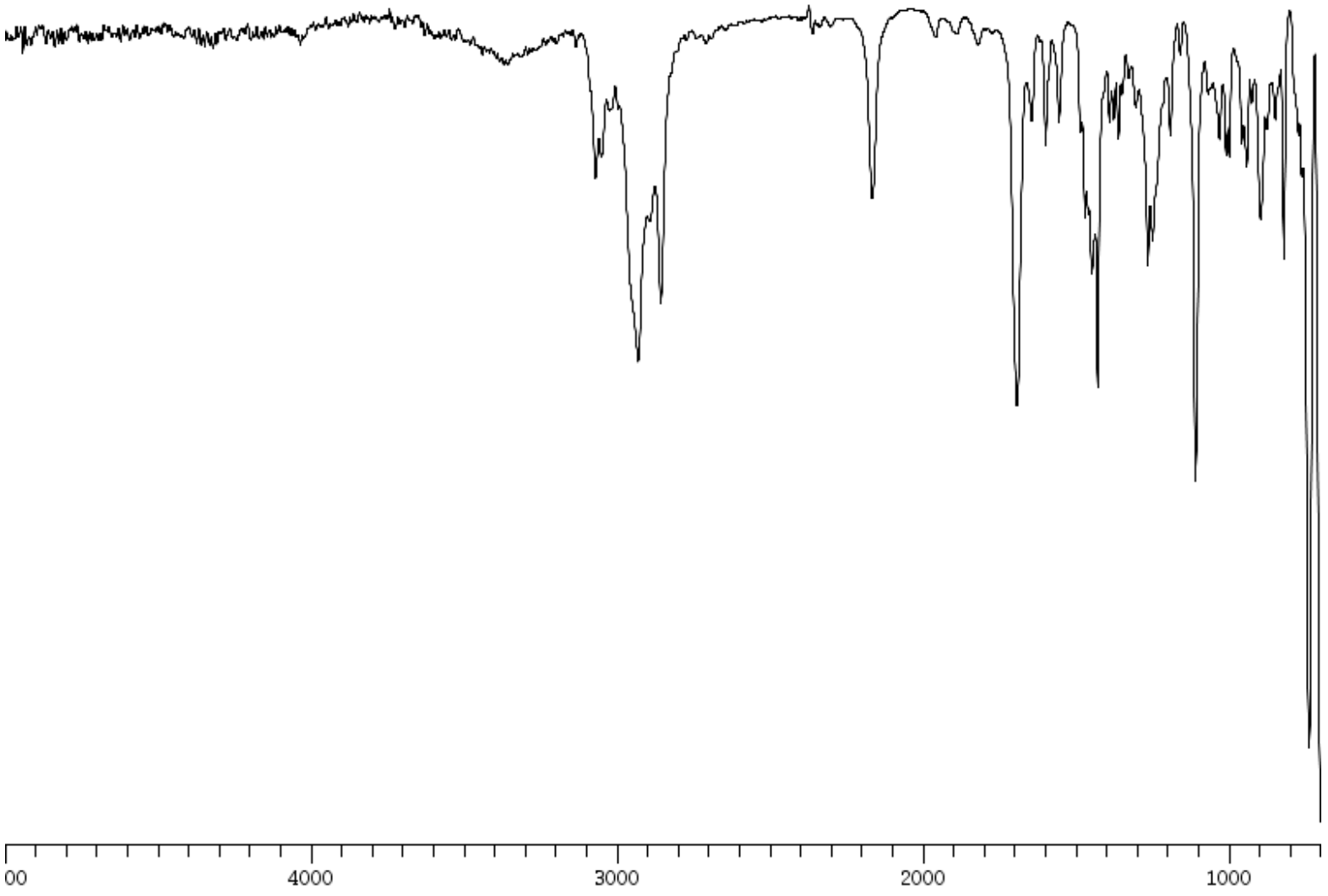
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	7.217	2489015	169651	95.306	95.284	N/A	5454	1.896	1.140	
2	Unknown	1	7.960	122596	8397	4.694	4.716	N/A	6484	N/A	1.117	

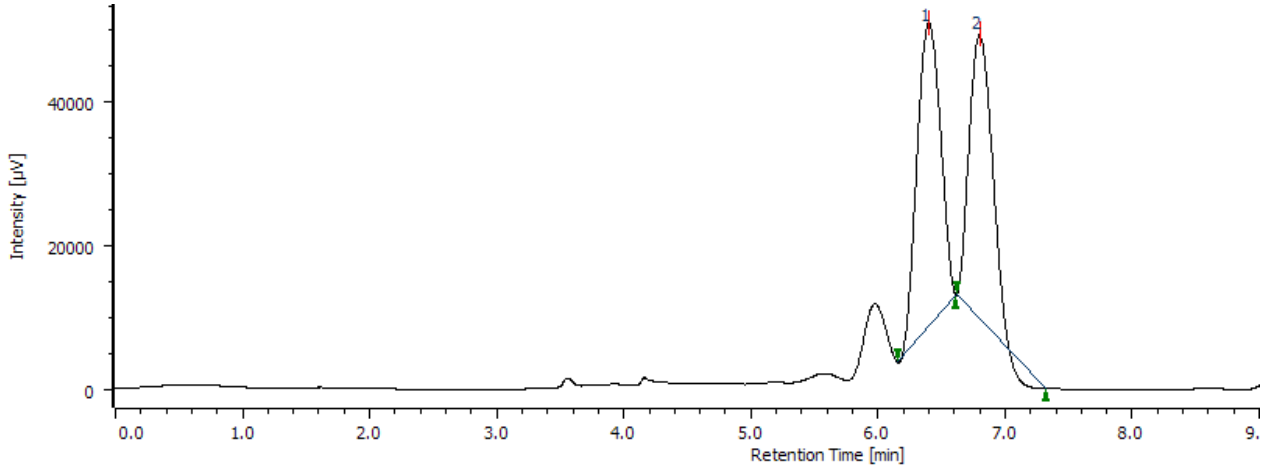
$CDCl_3$
400 MHz



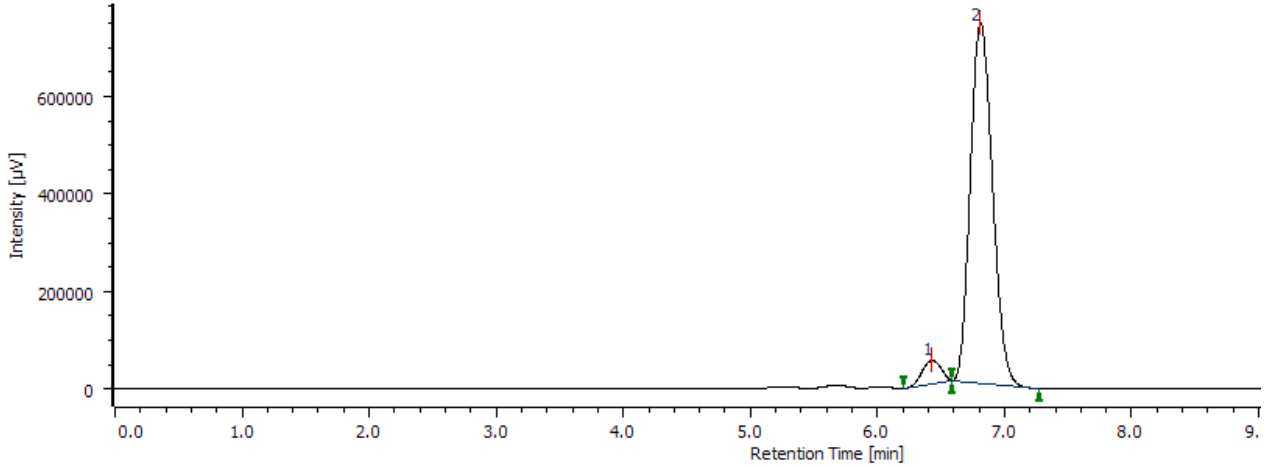
$CDCl_3$
100.1 MHz



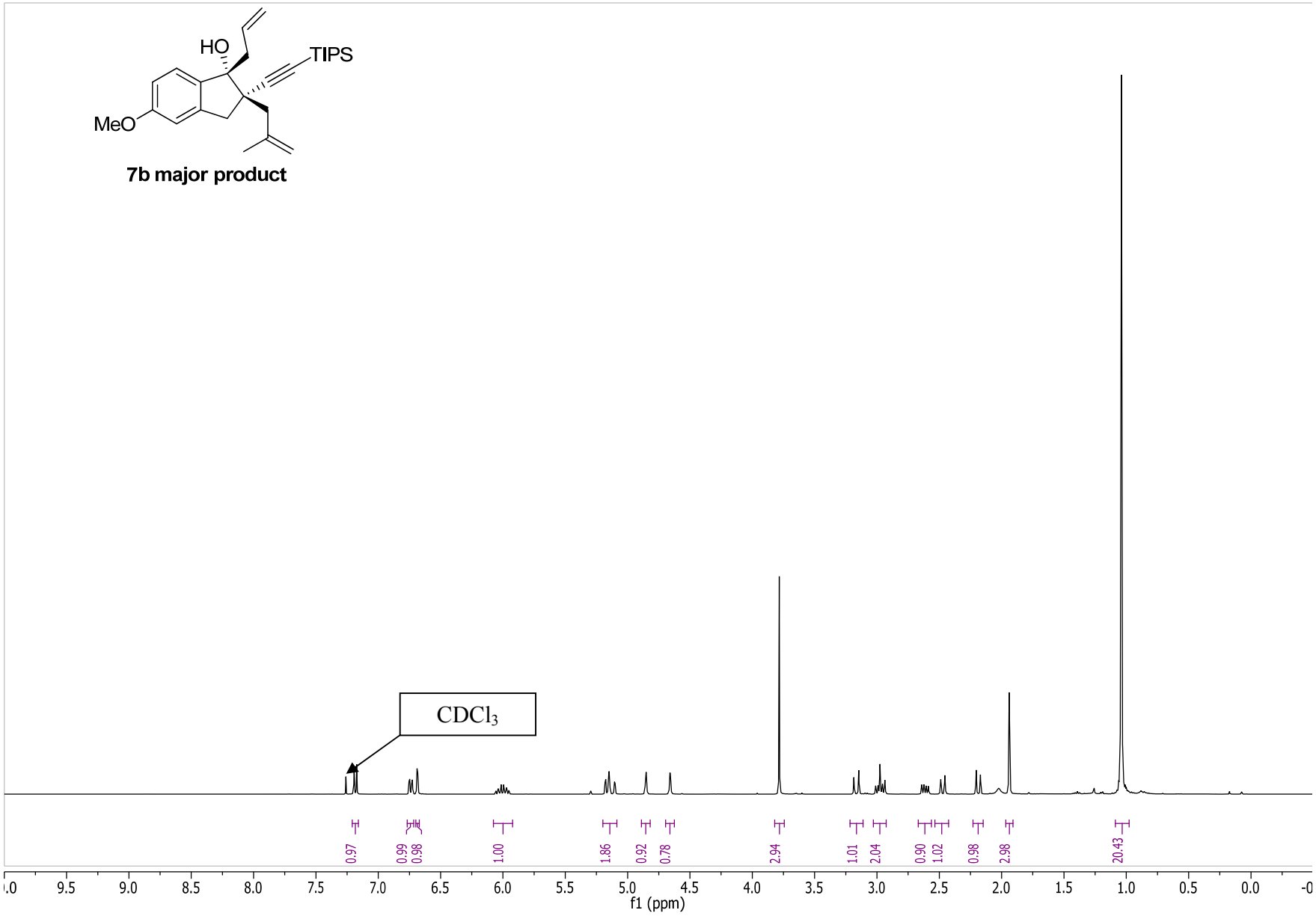

00
4000
3000
2000
1000



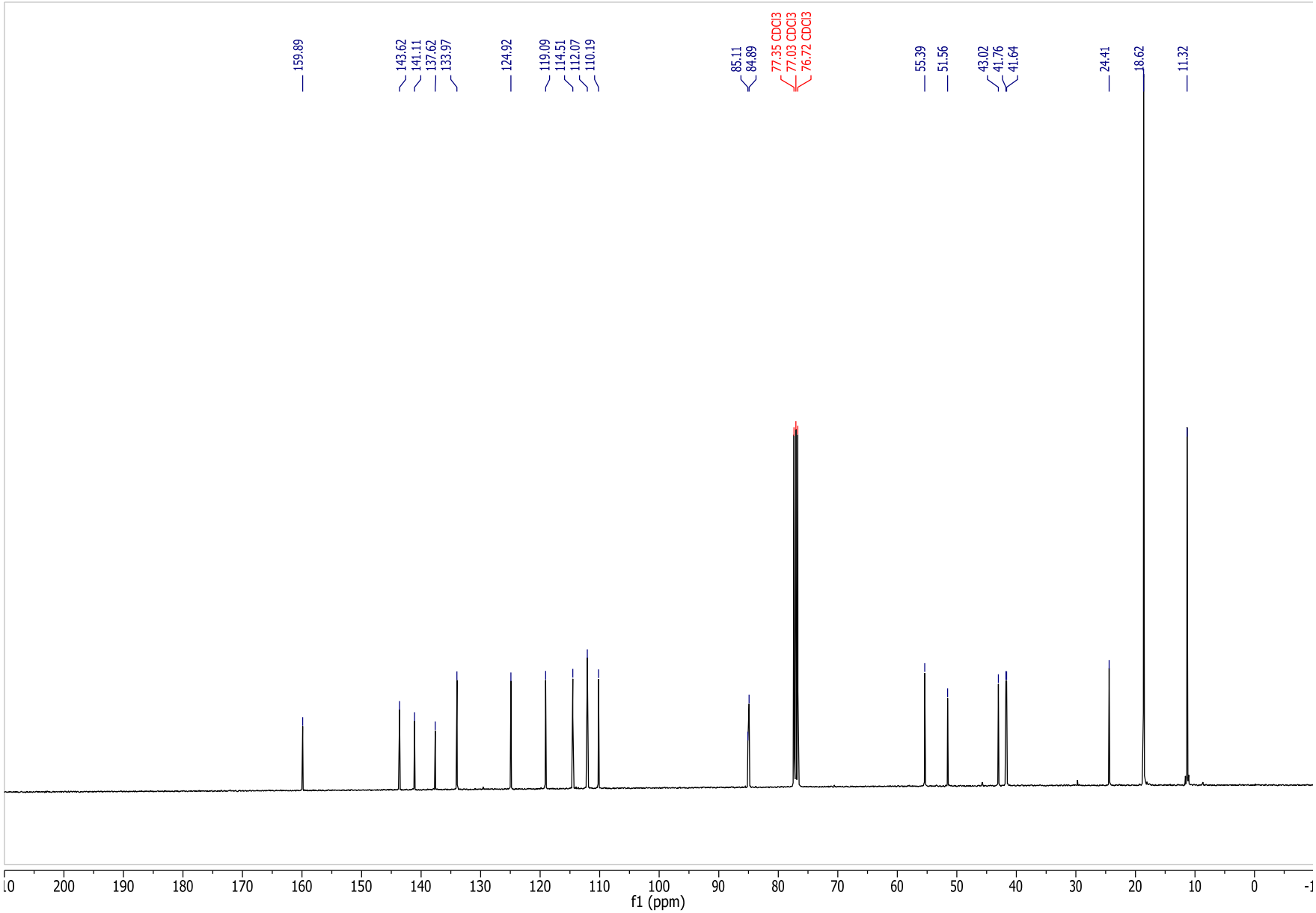
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	6.393	539135	42034	52.142	51.700	N/A	5012	1.123	1.009	
2	Unknown	1	6.793	494835	39271	47.858	48.300	N/A	5916	N/A	1.161	

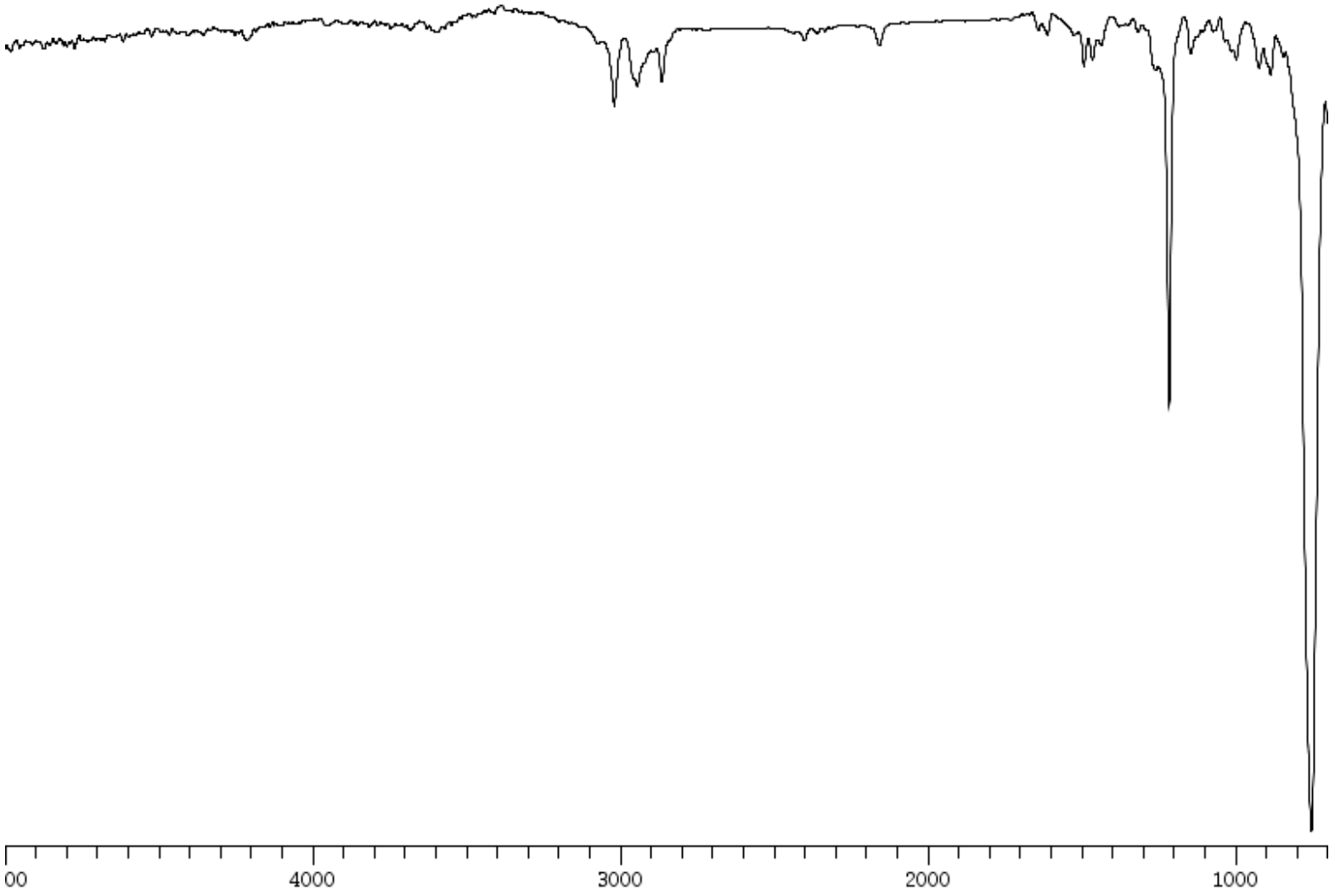


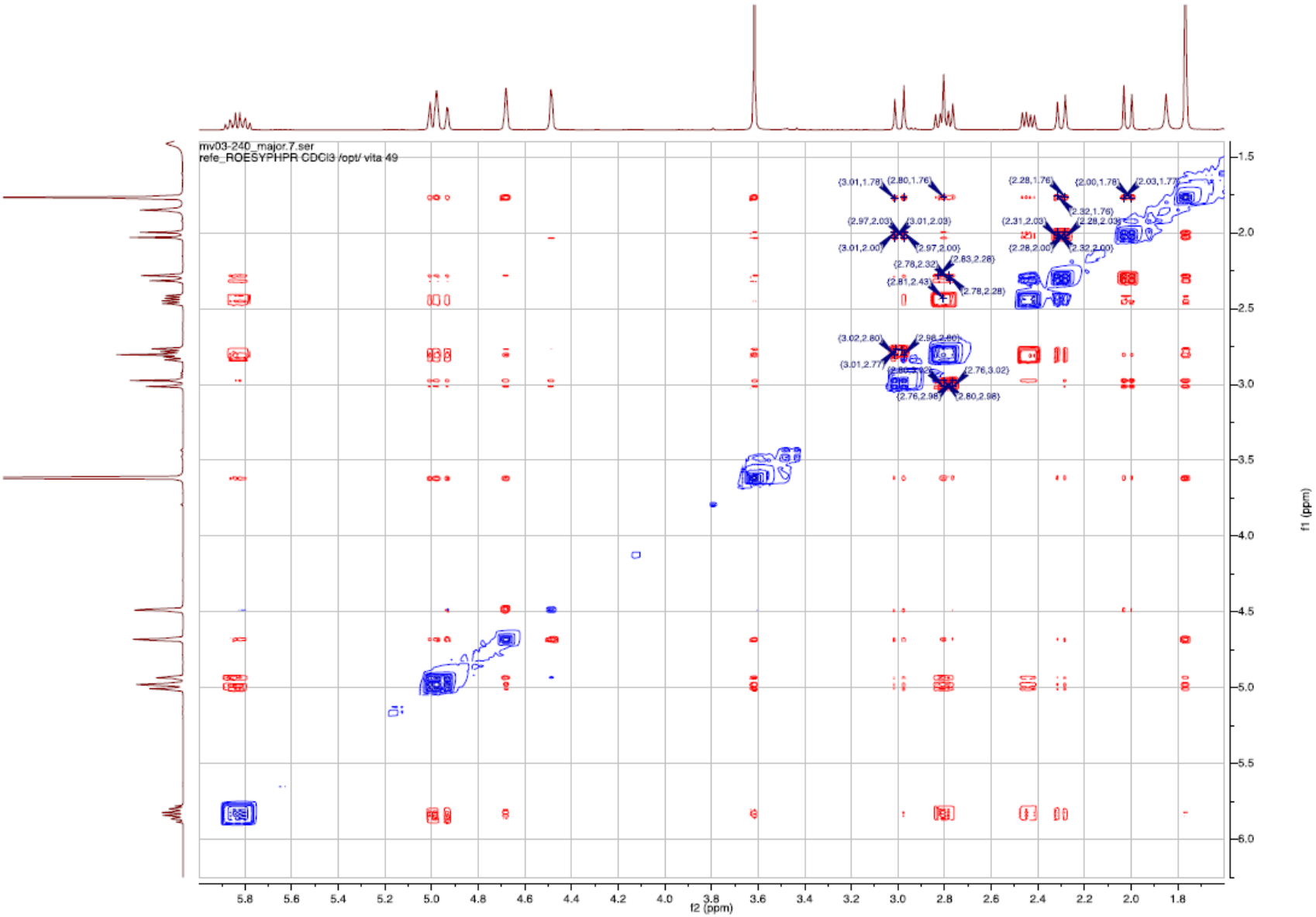
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	6.423	493679	48170	5.259	6.141	N/A	7953	1.244	0.947	
2	Unknown	1	6.803	8894258	736255	94.741	93.859	N/A	7044	N/A	1.163	


CDCl3
400 MHz
HO
TIPS
MeO
7b major product
CDCl3
0.97
0.99
0.98
1.00
1.86
0.92
0.78
2.94
1.01
2.04
0.90
1.02
0.98
2.98
20.43
f1 (ppm)

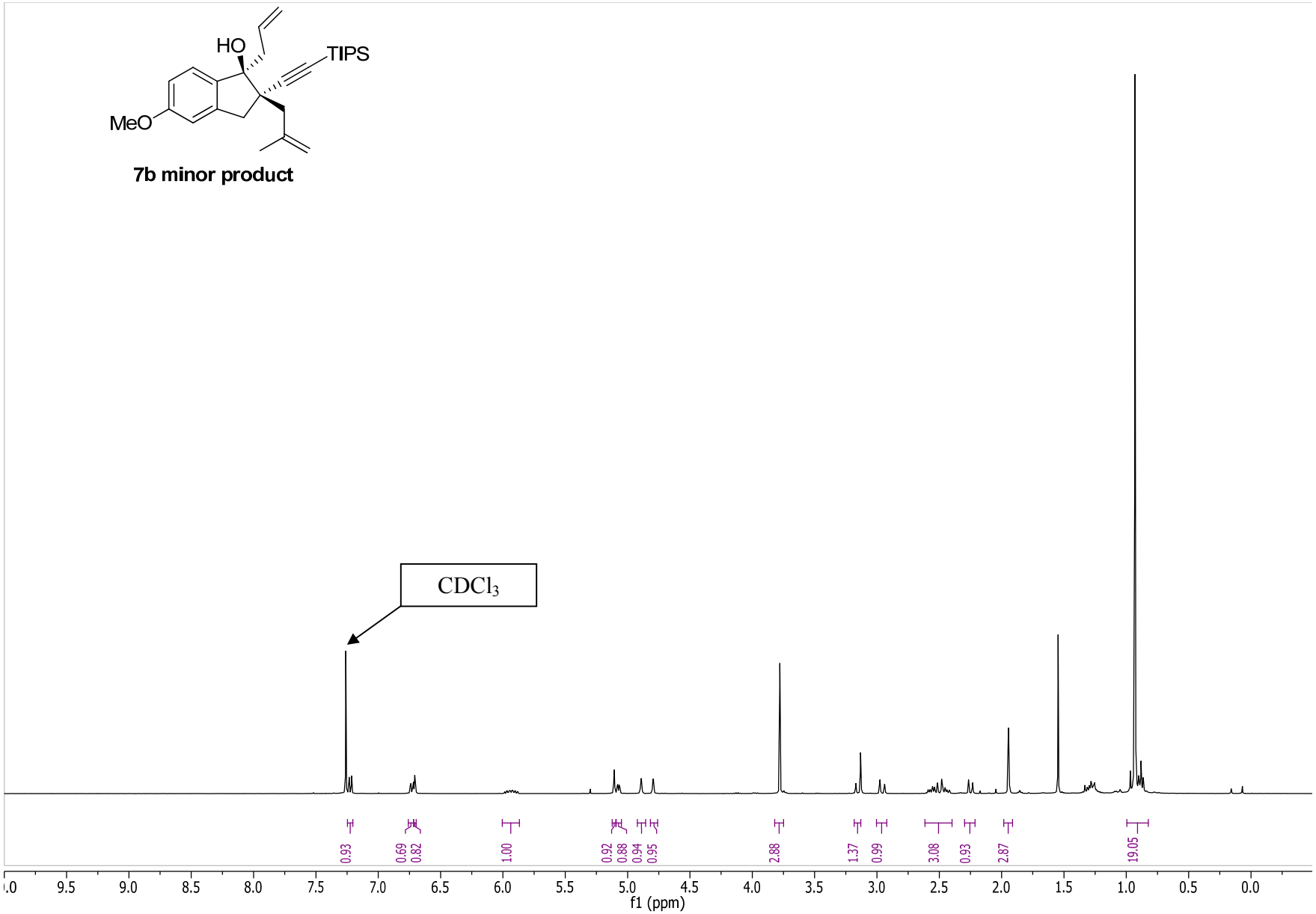
$CDCl_3$
100.1 MHz



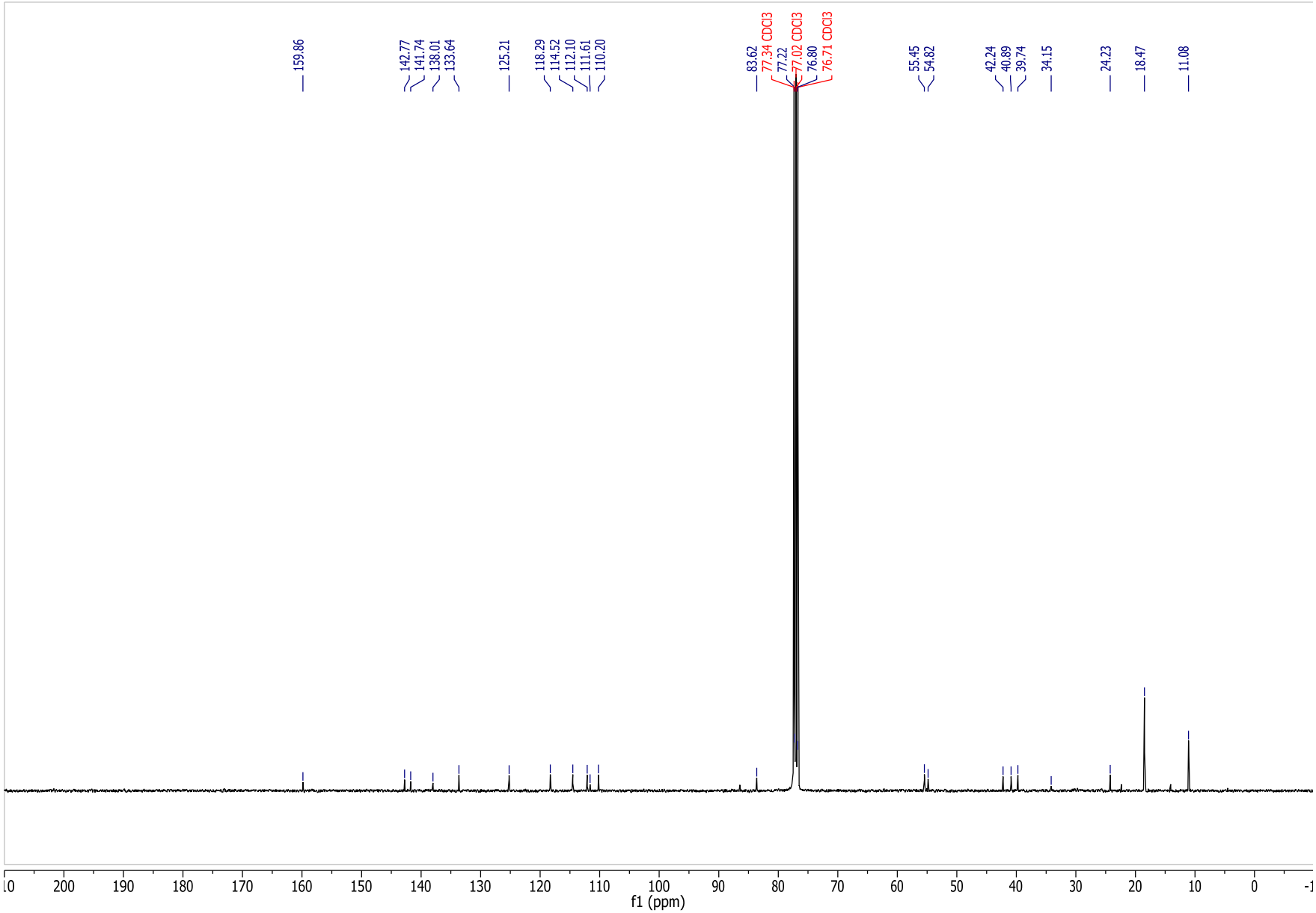

00
4000
3000
2000
1000

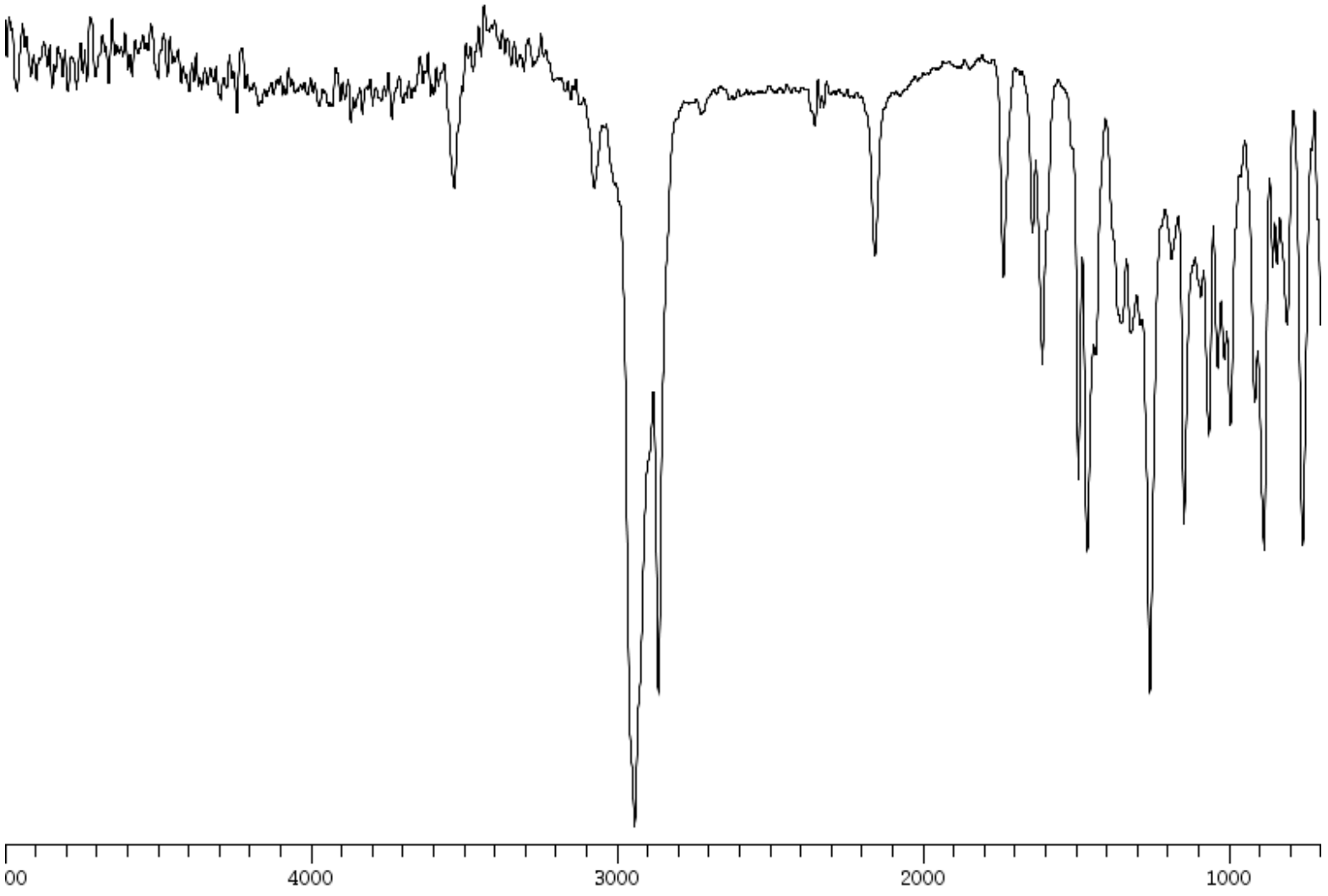

CDCl3
400 MHz
ROESY
mv03-240_major.7.ser
refe_ROESYPHPR CDCl3 /opt/ vita 49
f2 (ppm)
f1 (ppm)

$CDCl_3$
400 MHz

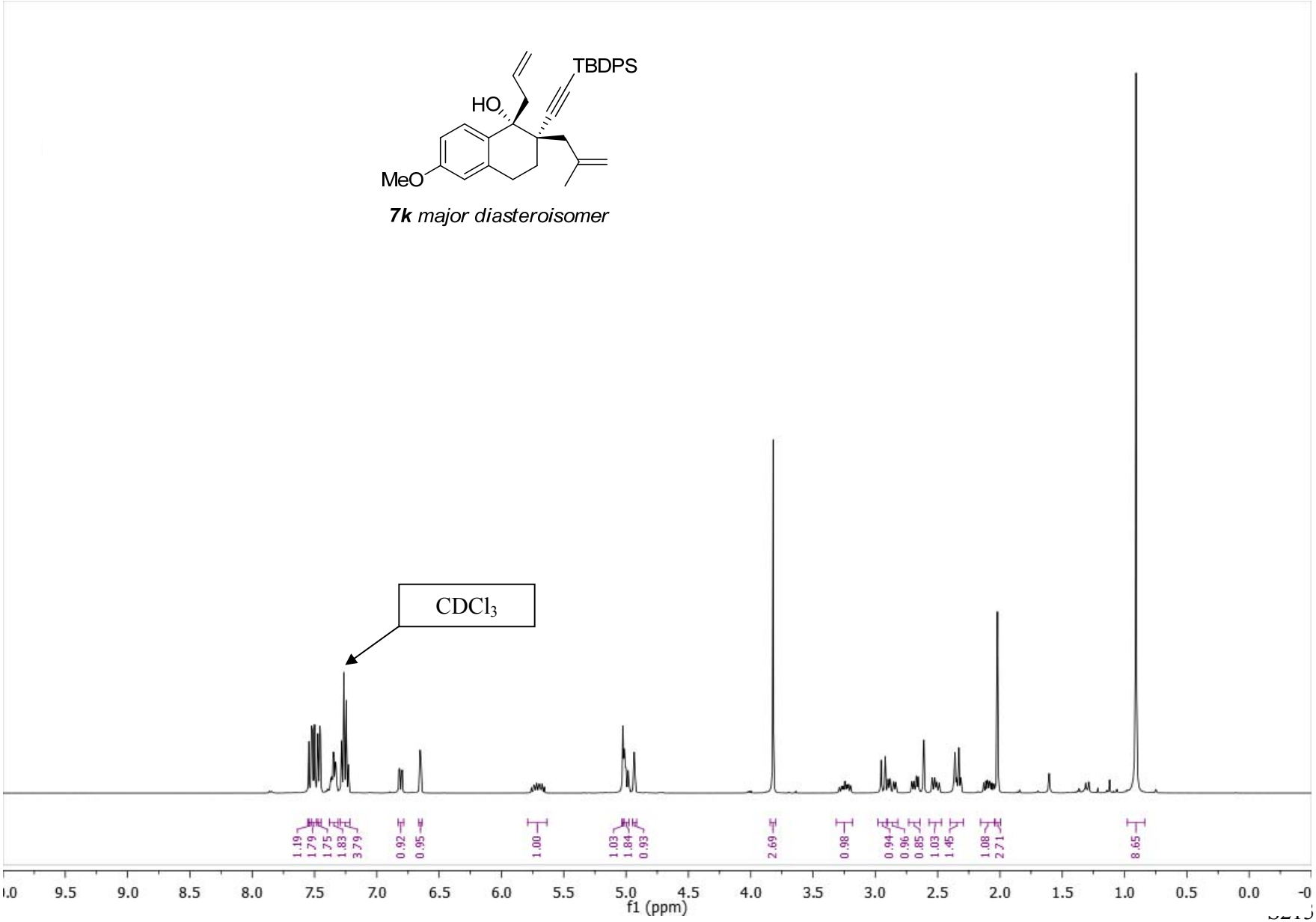


$CDCl_3$
100.1 MHz

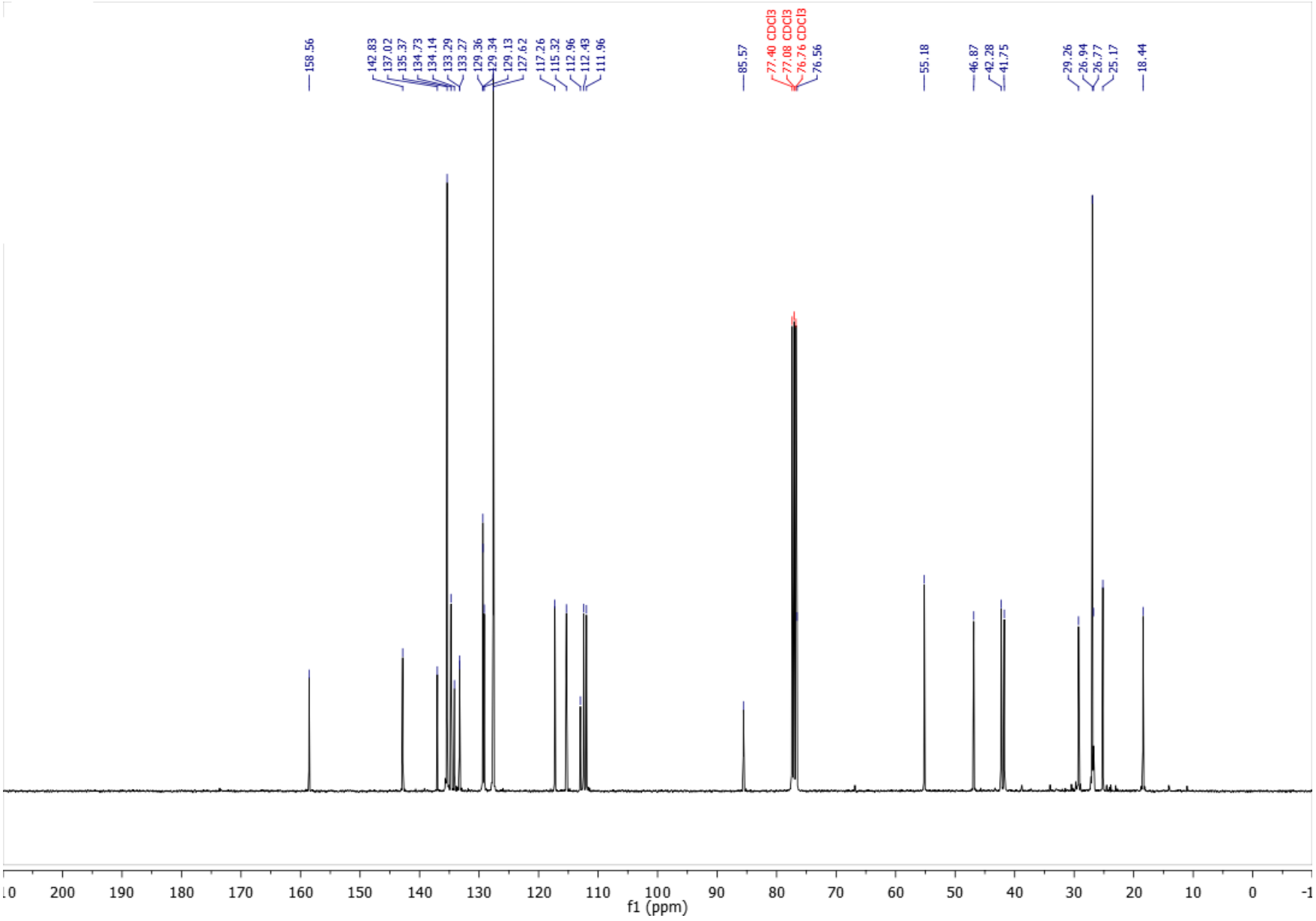


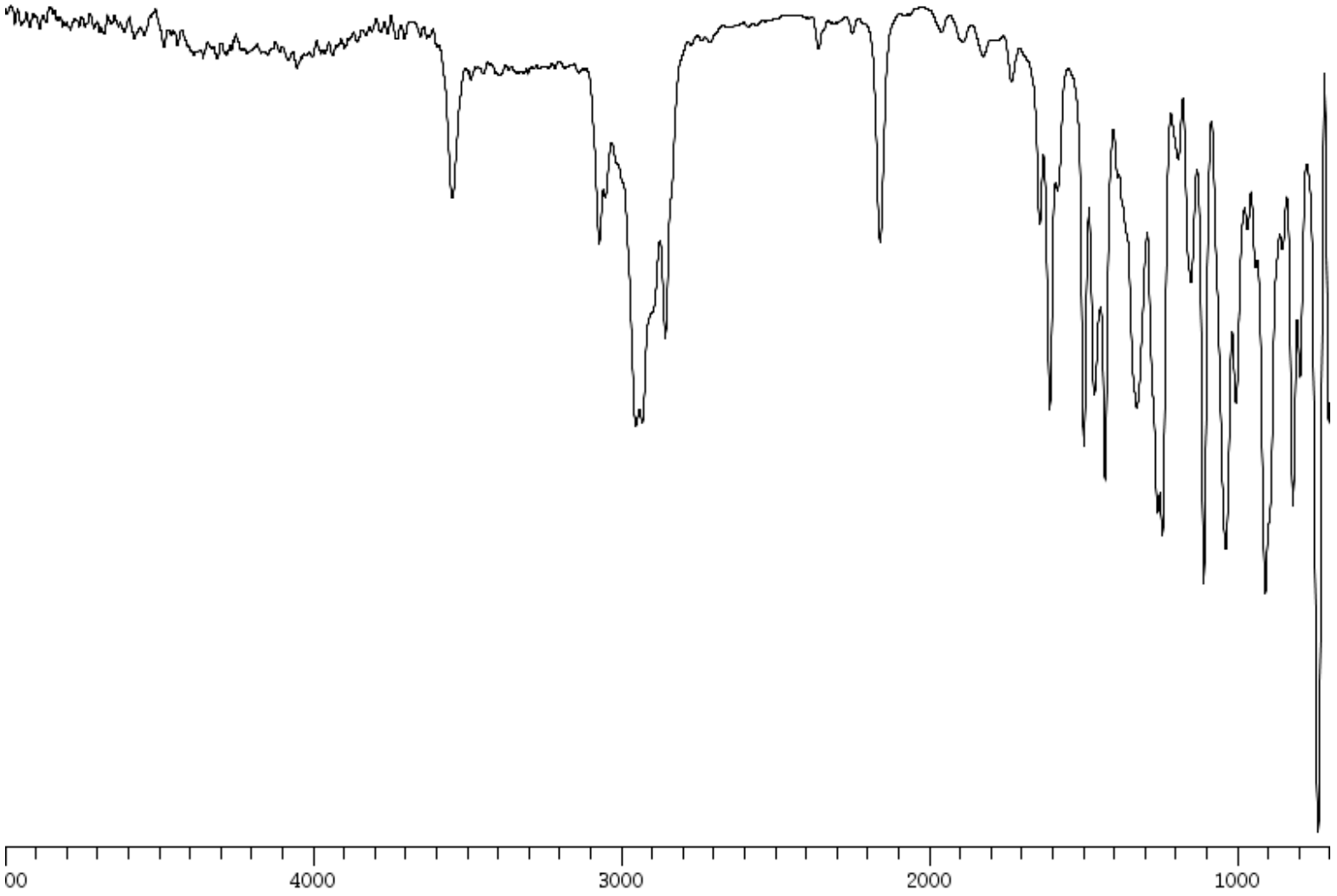

00
4000
3000
2000
1000

$CDCl_3$
400 MHz

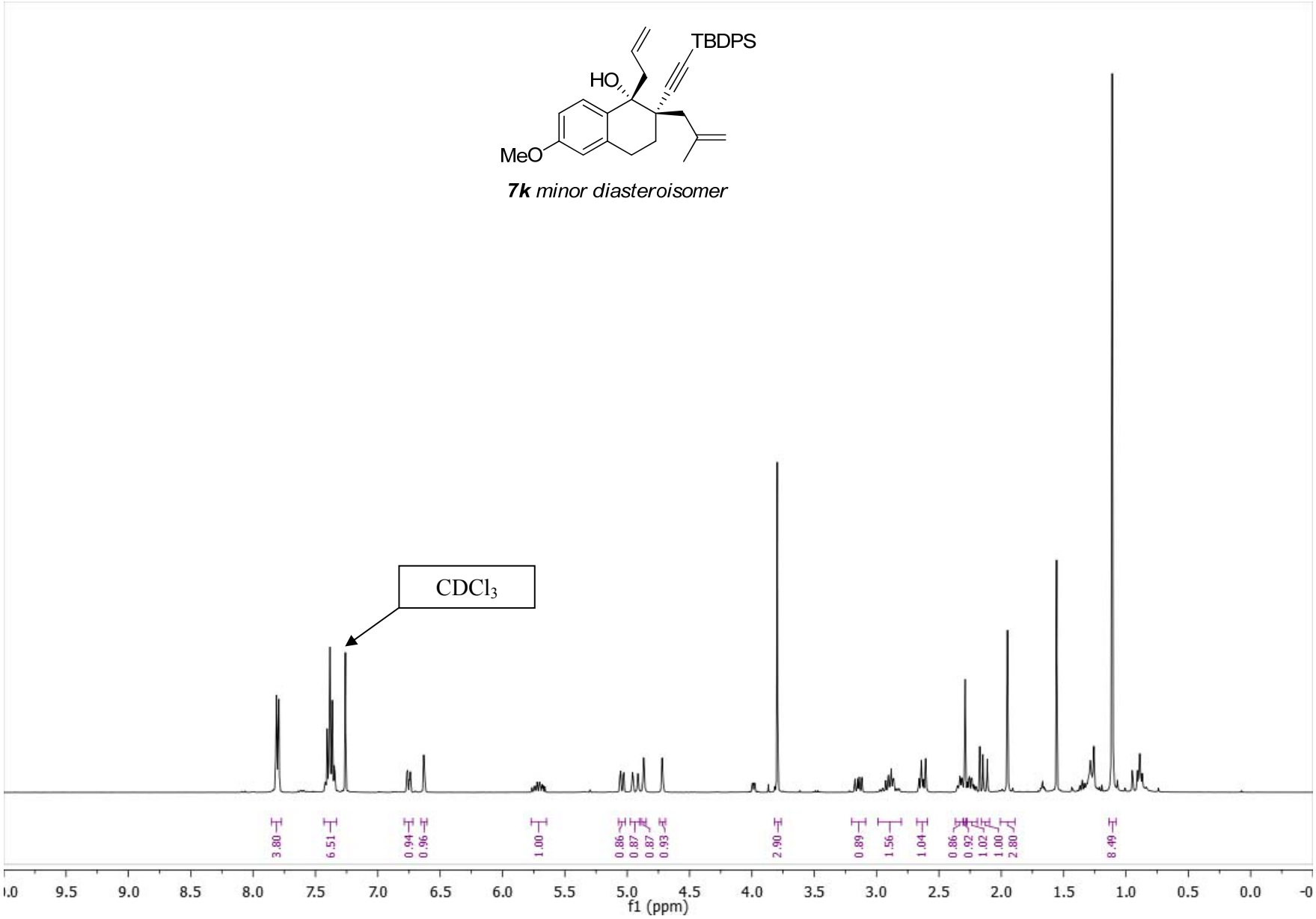


$CDCl_3$
100.1 MHz

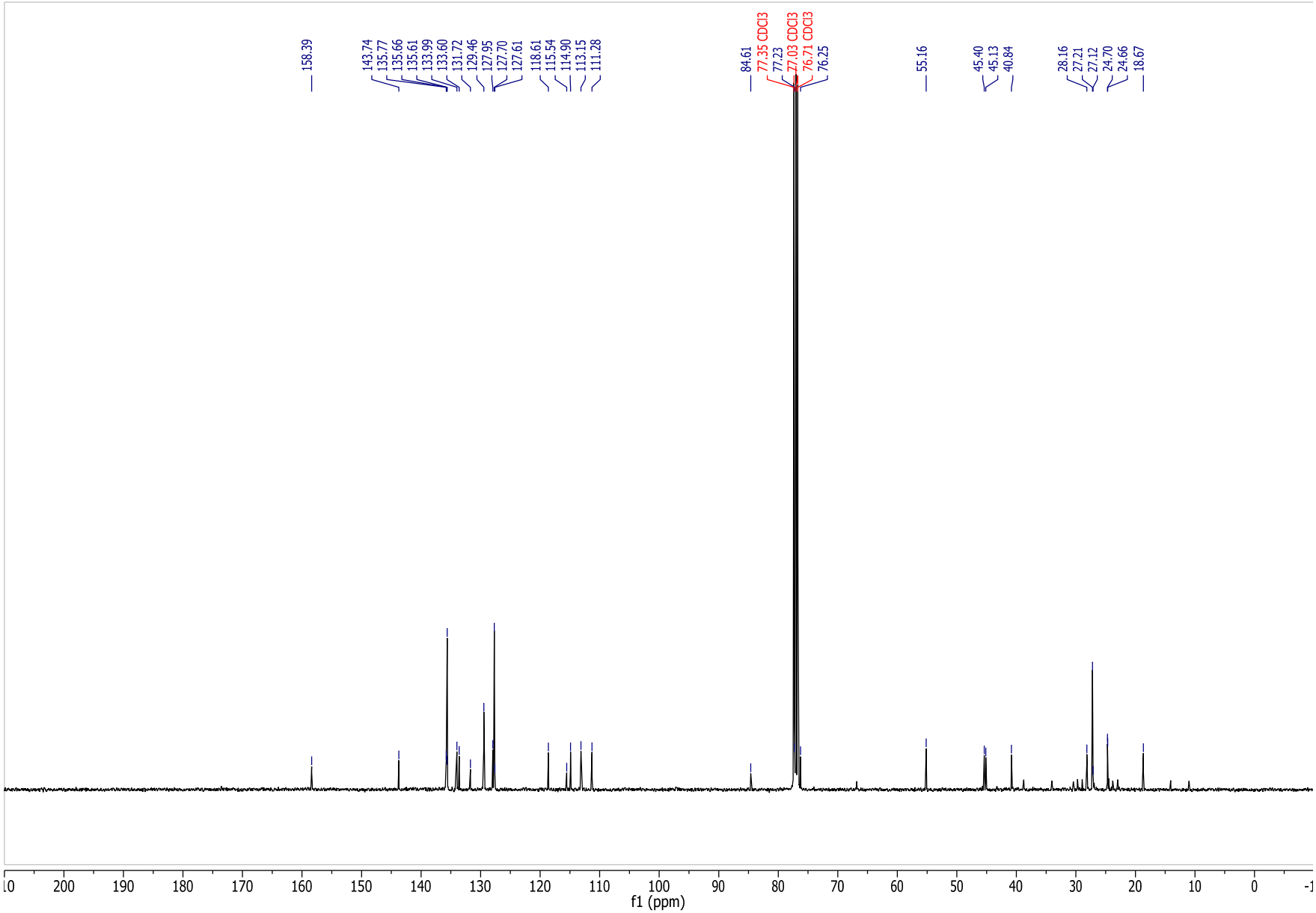


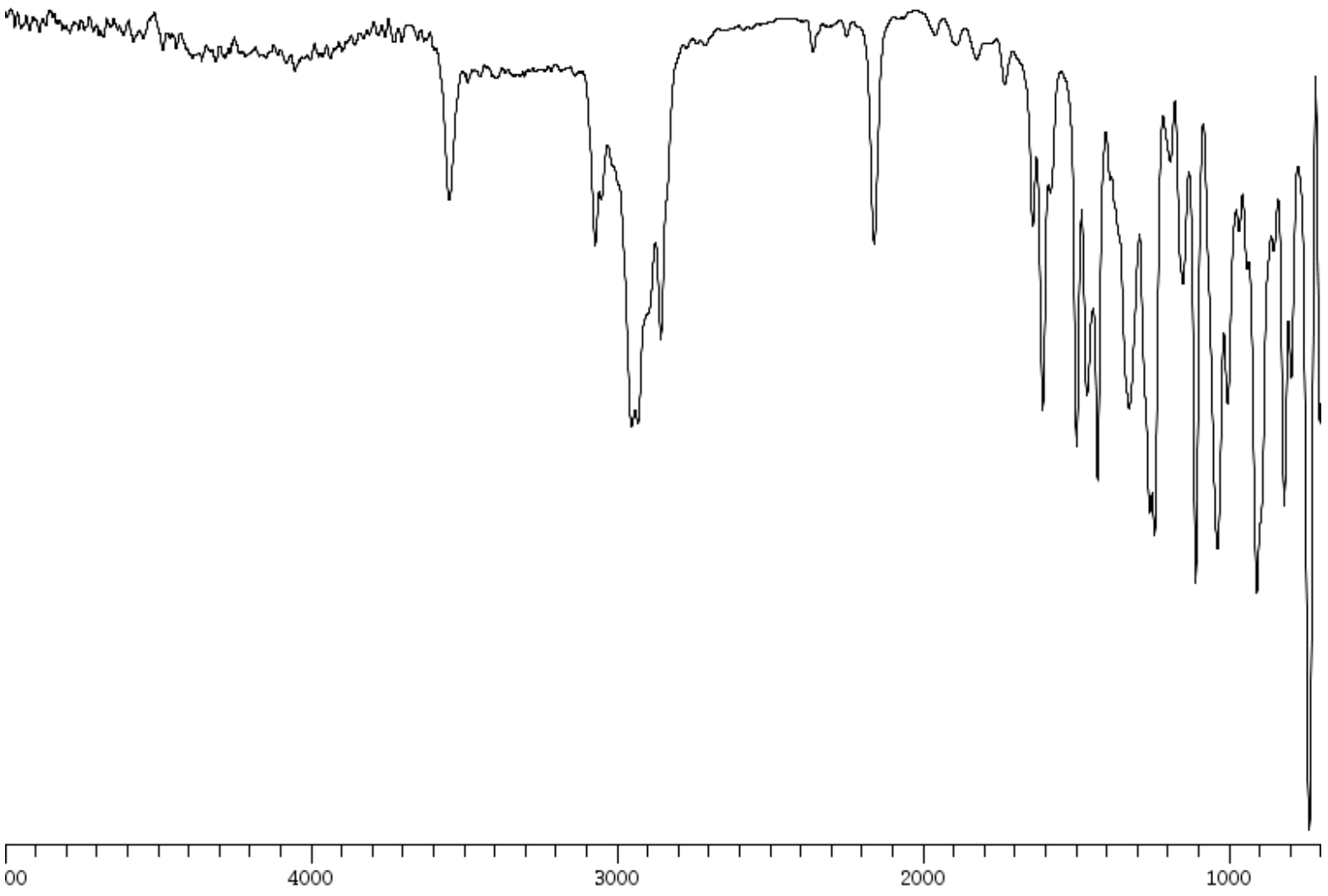

00
4000
3000
2000
1000

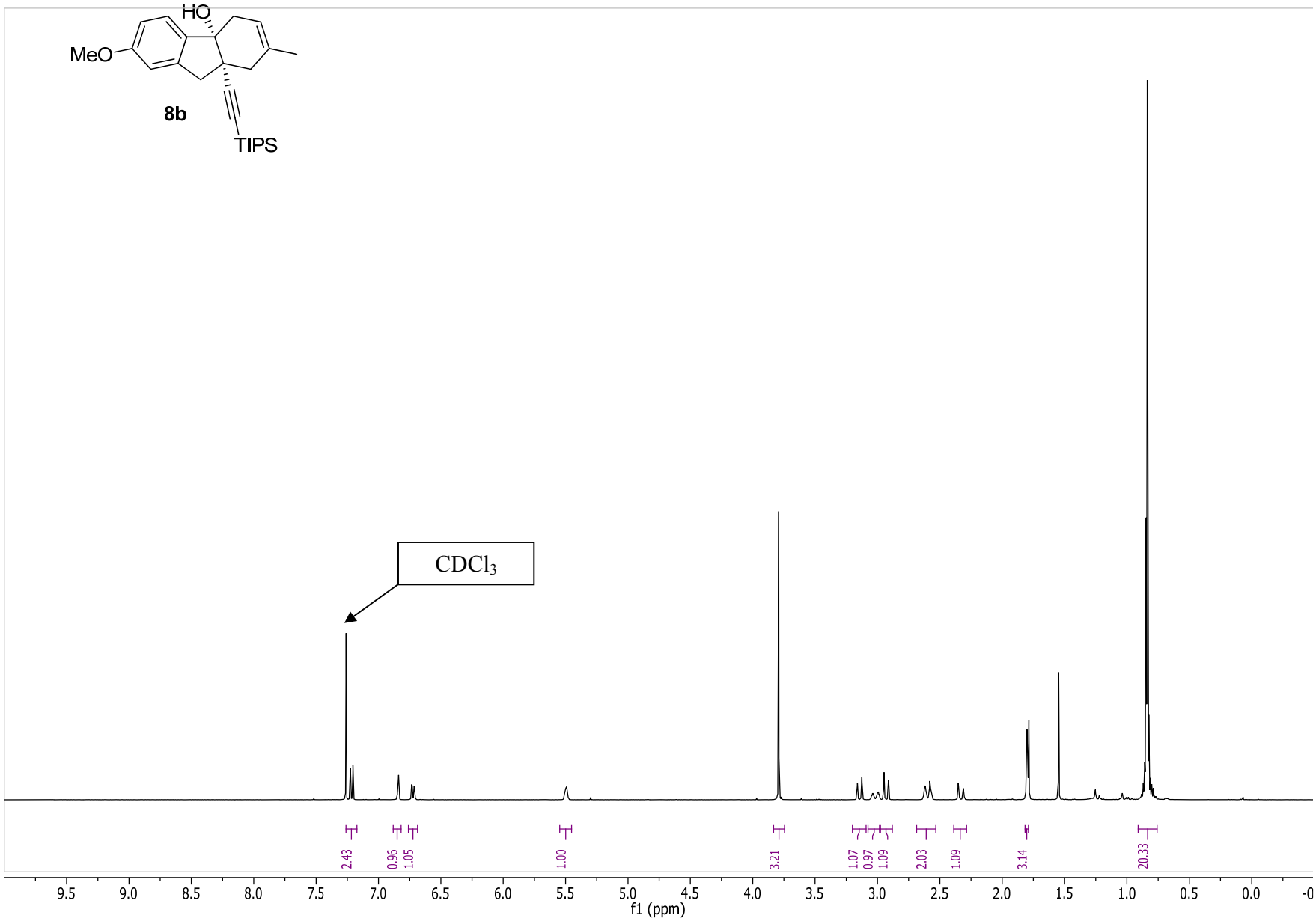
$CDCl_3$
400 MHz



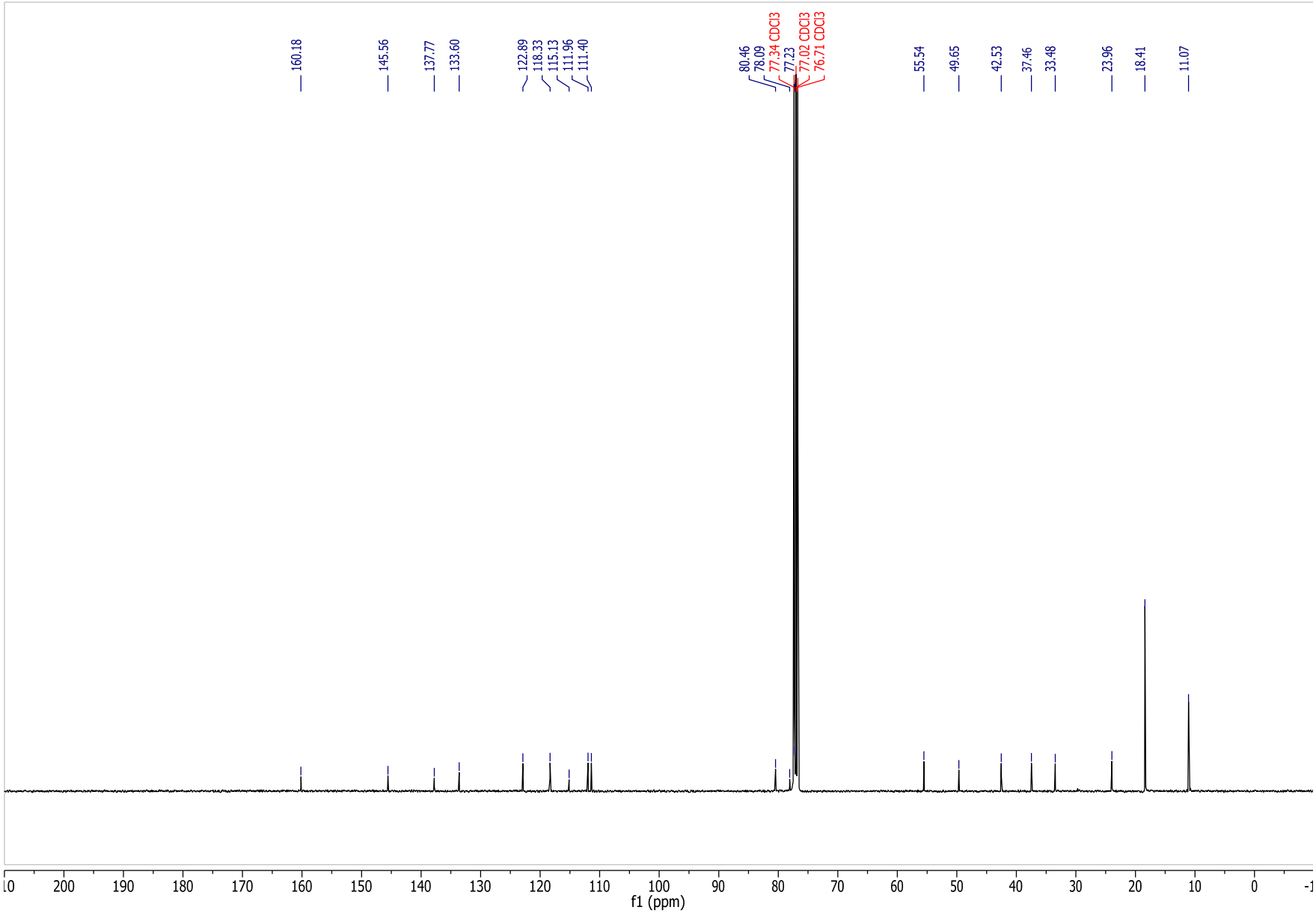
$CDCl_3$
100.1 MHz

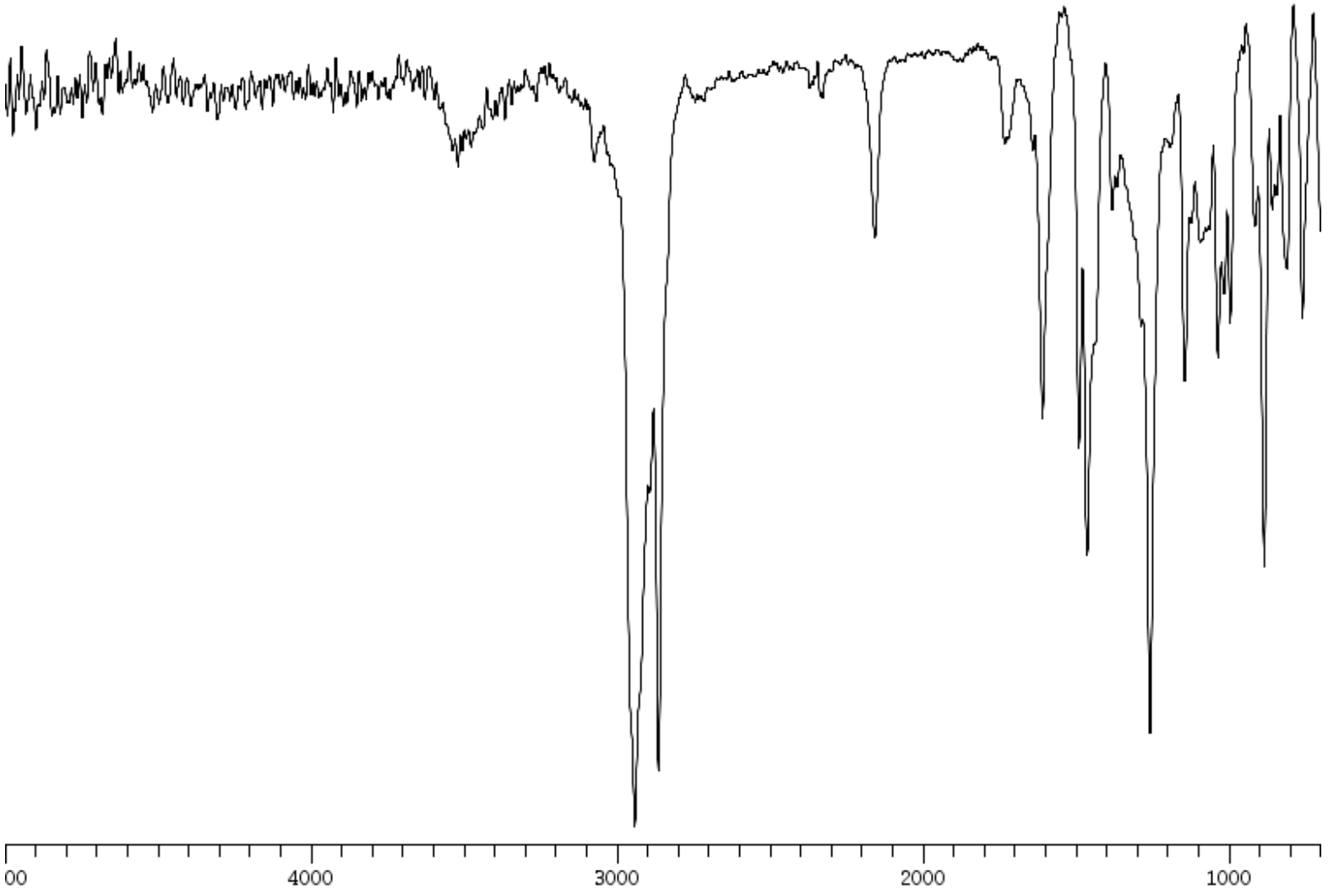



00
4000
3000
2000
1000

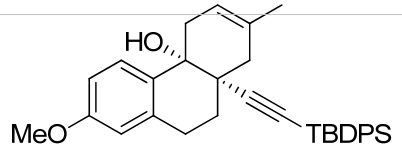

CDCl3
400 MHz
HO
MeO
8b
TIPS
CDCl3
2.43
0.96
1.05
1.00
3.21
1.07
0.97
1.09
2.03
1.09
3.14
20.33
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)

$CDCl_3$
100.1 MHz



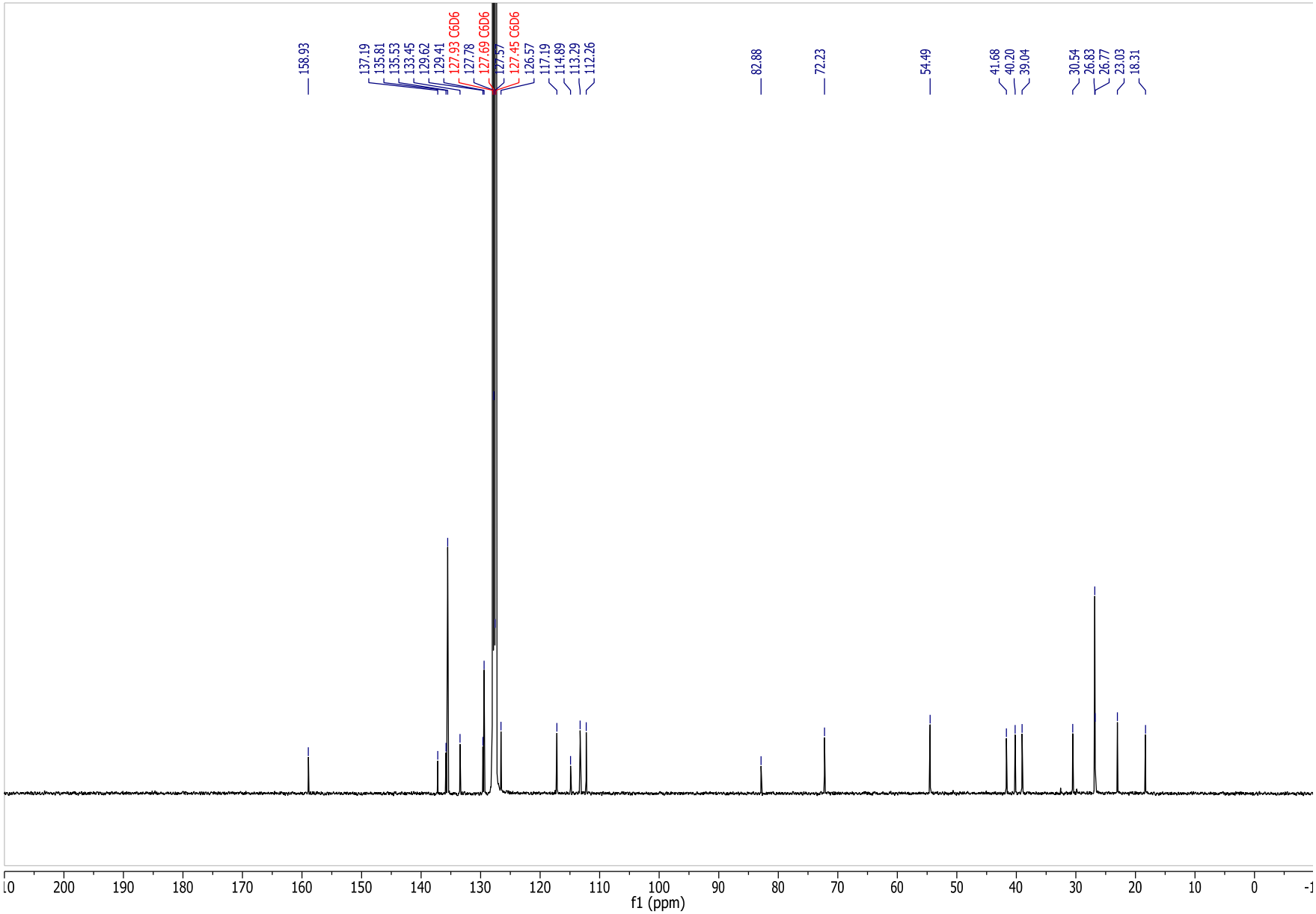

00
4000
3000
2000
1000

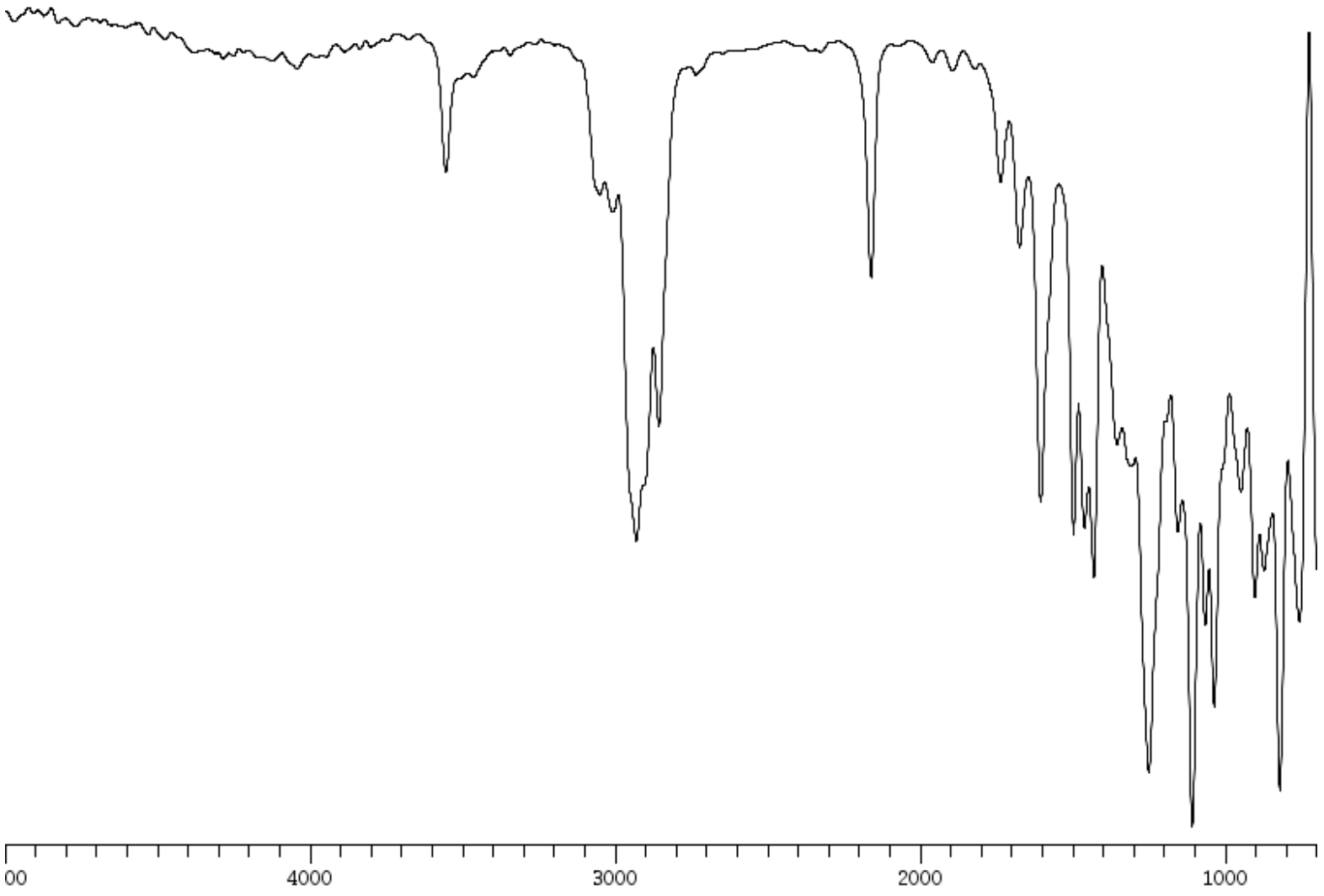
C_6D_6
400 MHz

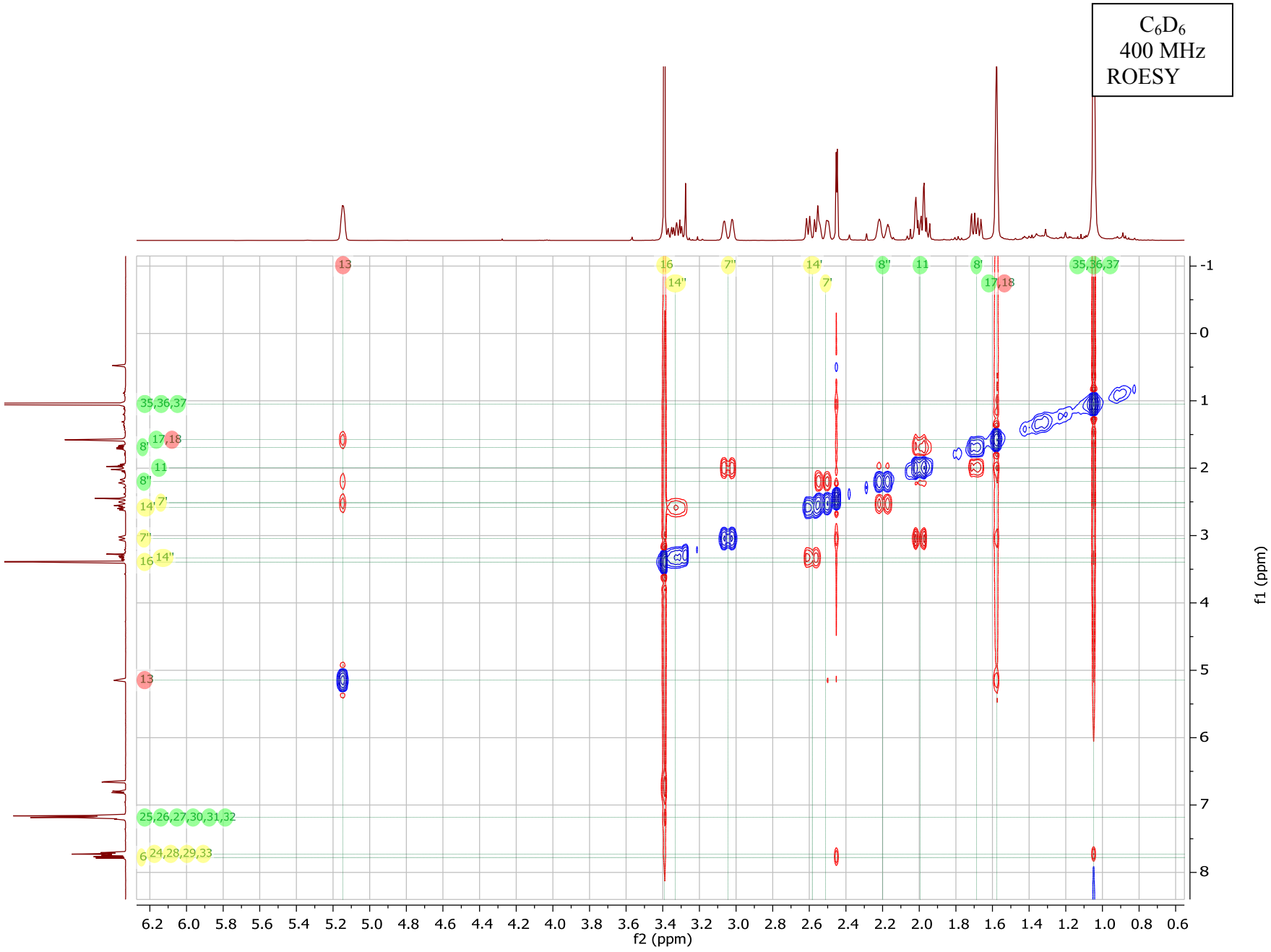


8k *major product*

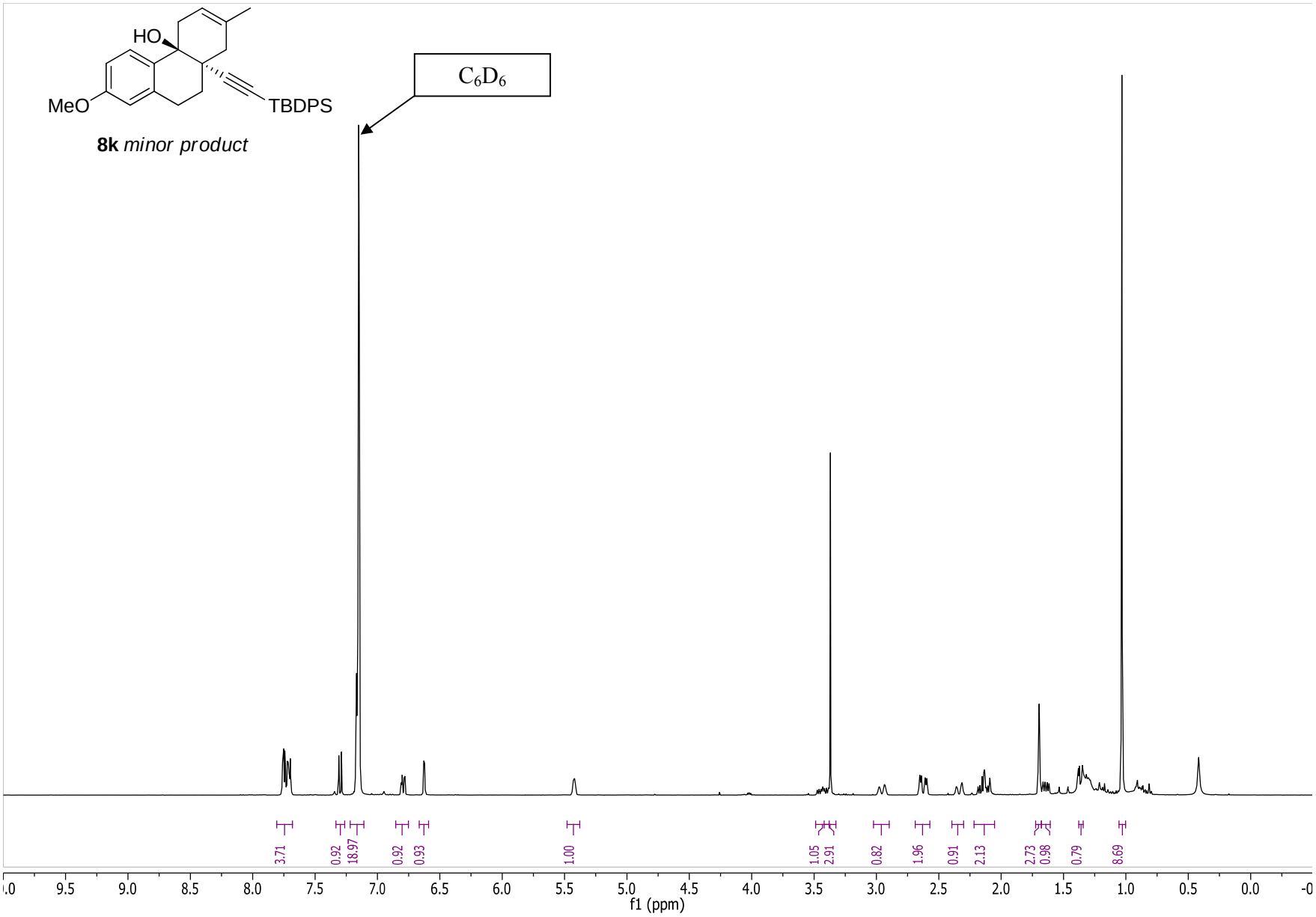
C_6D_6
100.1 MHz



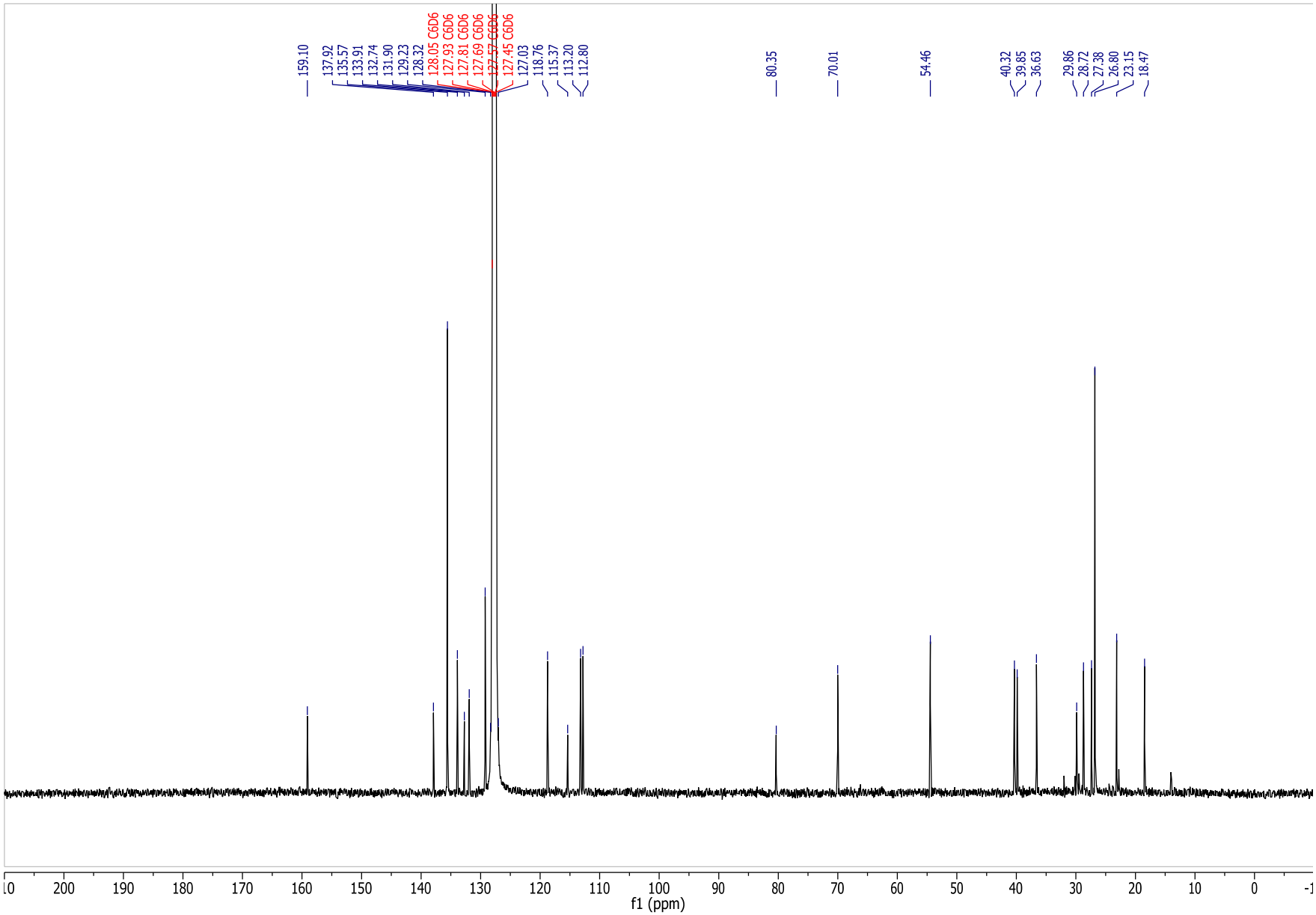

00
4000
3000
2000
1000

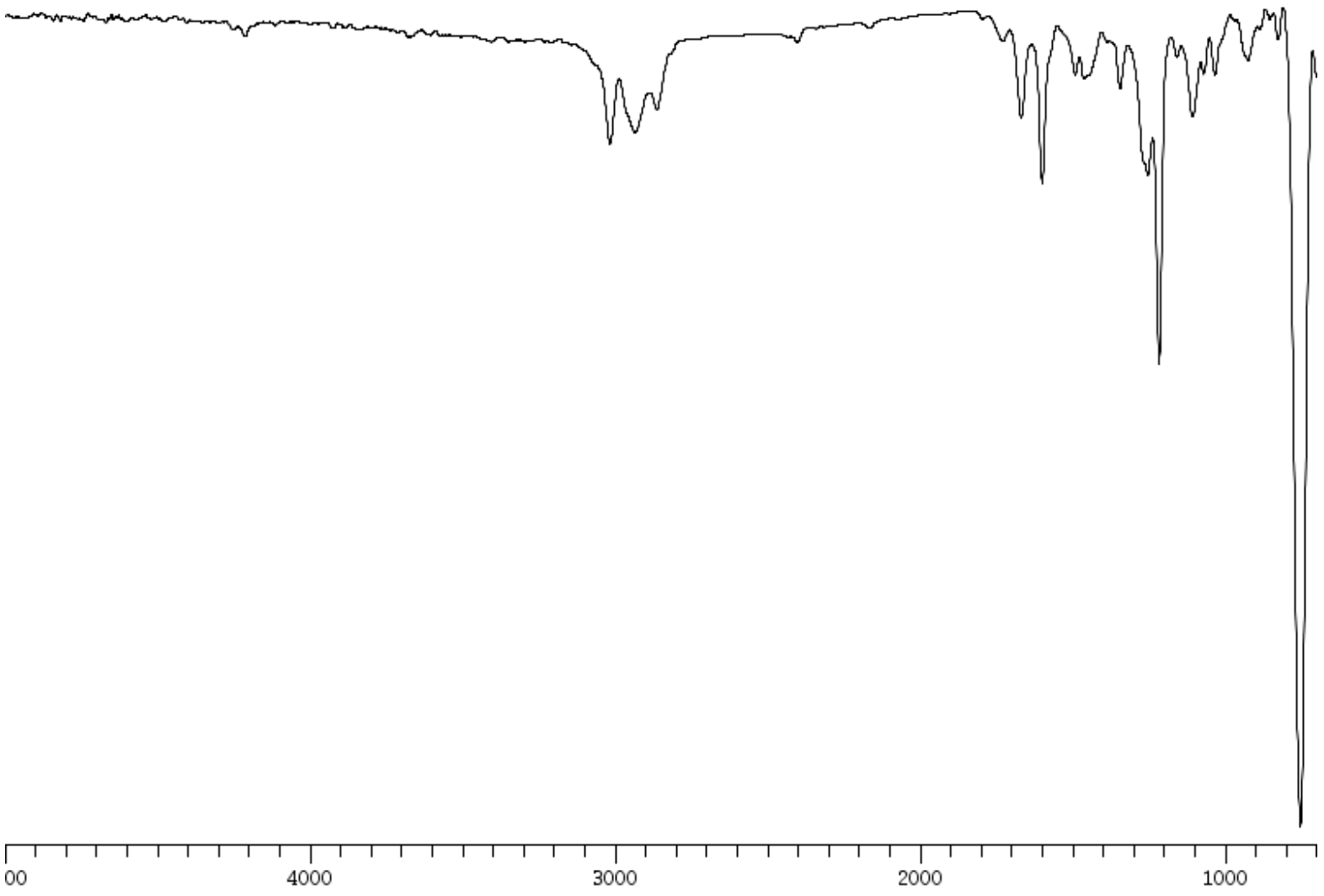

C6D6
400 MHz
ROESY
f2 (ppm)
f1 (ppm)

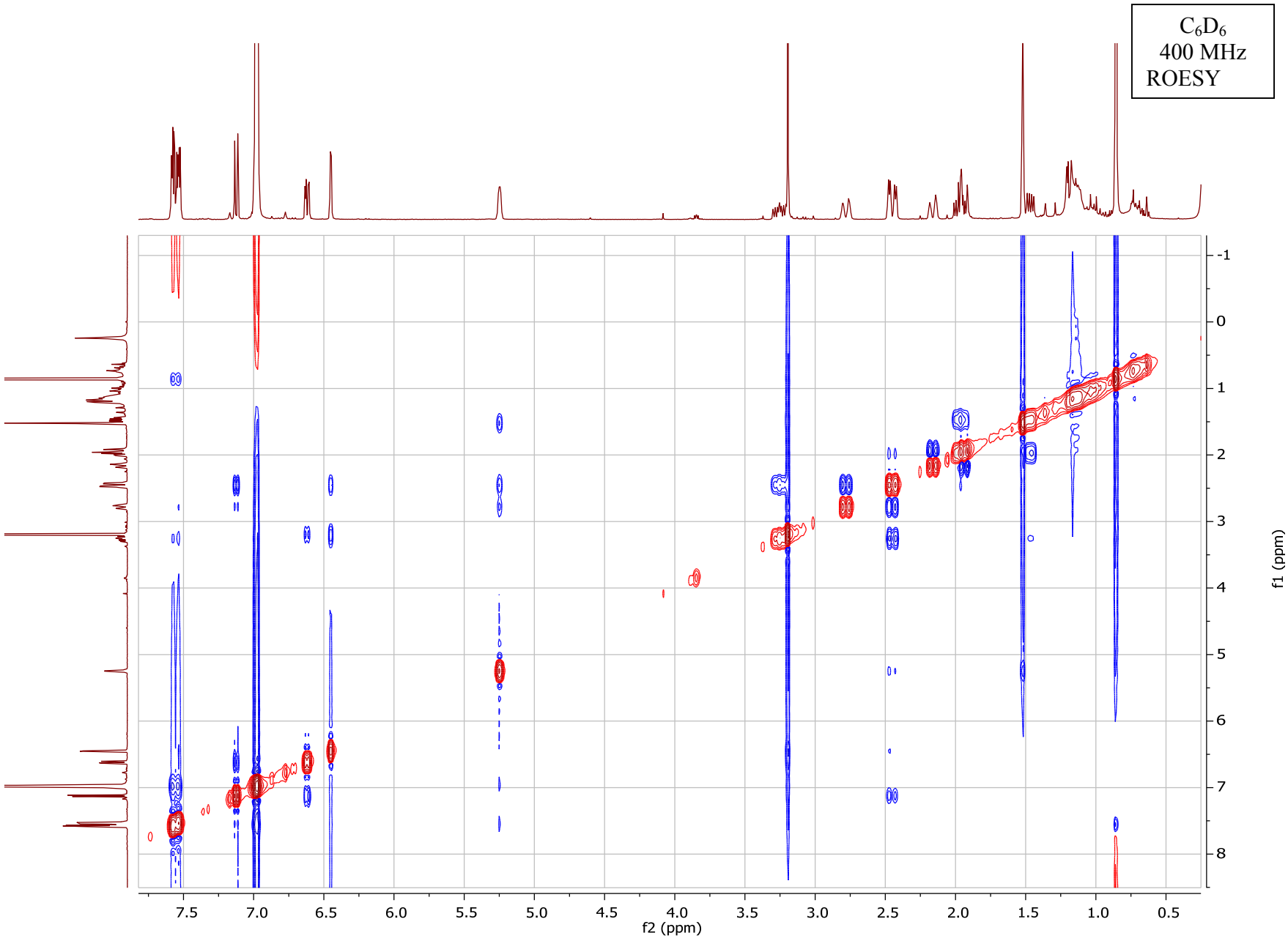
C_6D_6
400 MHz


HO
MeO
TBDPS
8k minor product
C6D6
3.71
0.92
18.97
0.92
0.93
1.00
1.05
2.91
0.82
1.96
0.91
2.13
2.73
0.98
0.79
8.69
f1 (ppm)

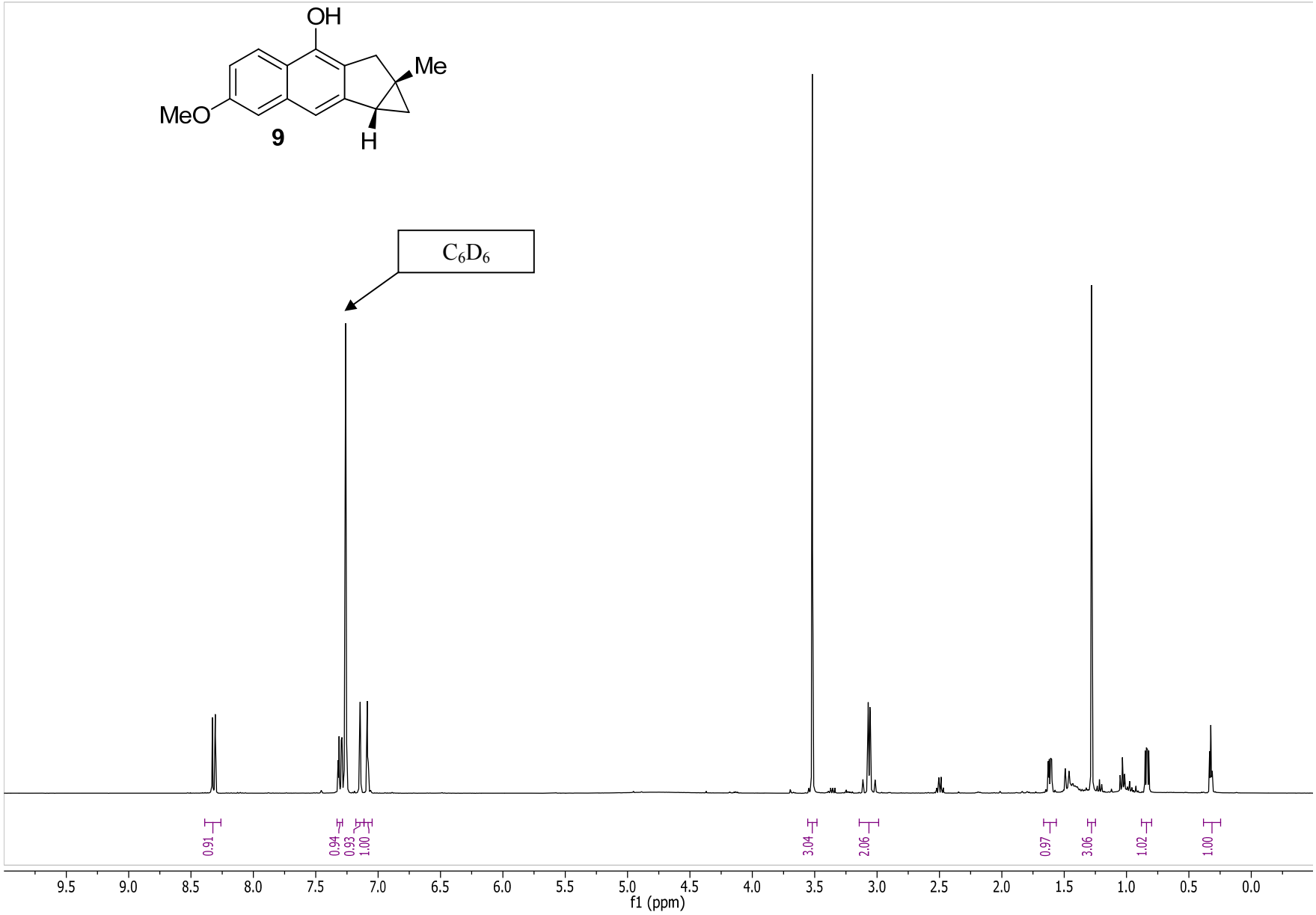
C_6D_6
100.1 MHz



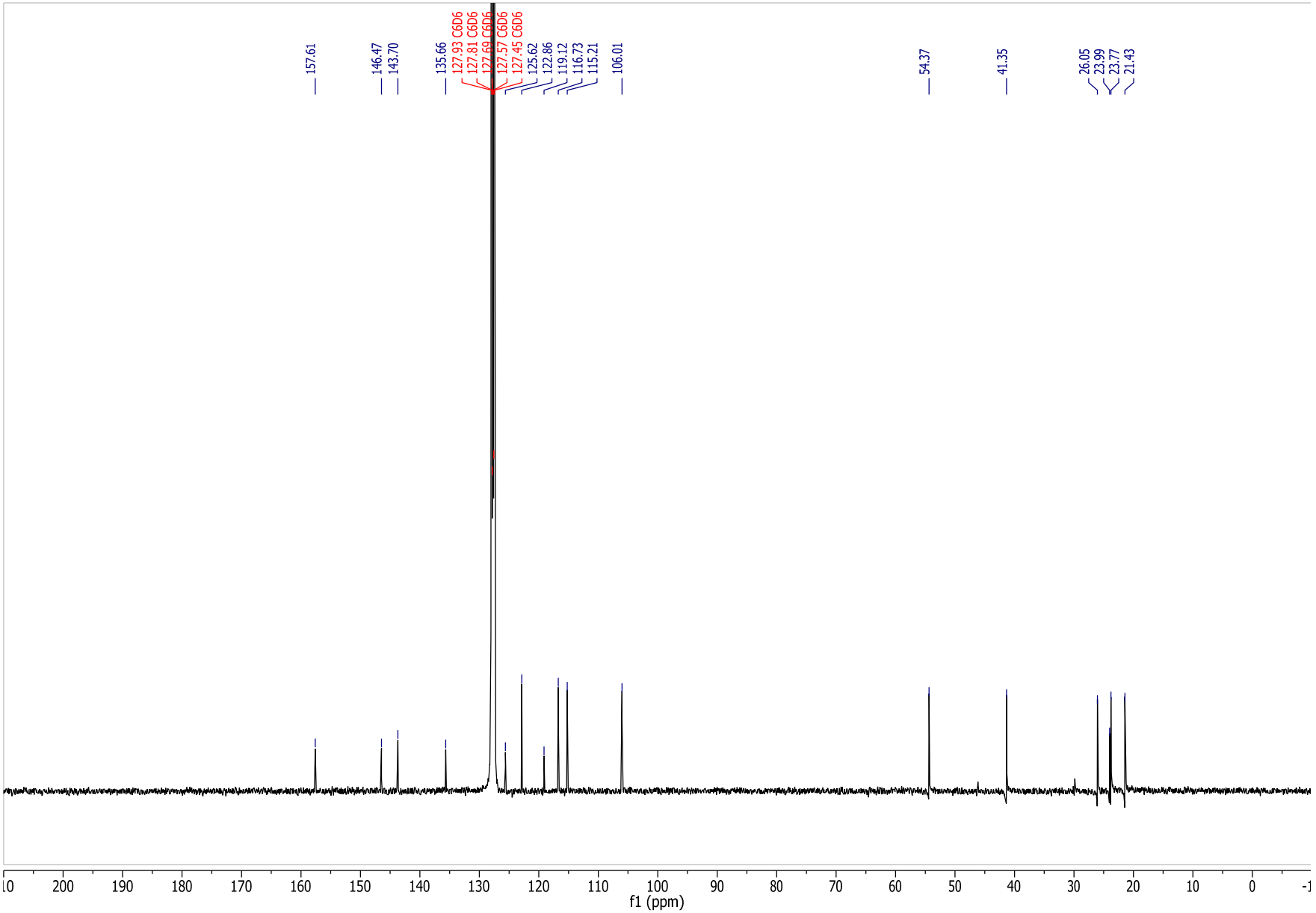

00
4000
3000
2000
1000

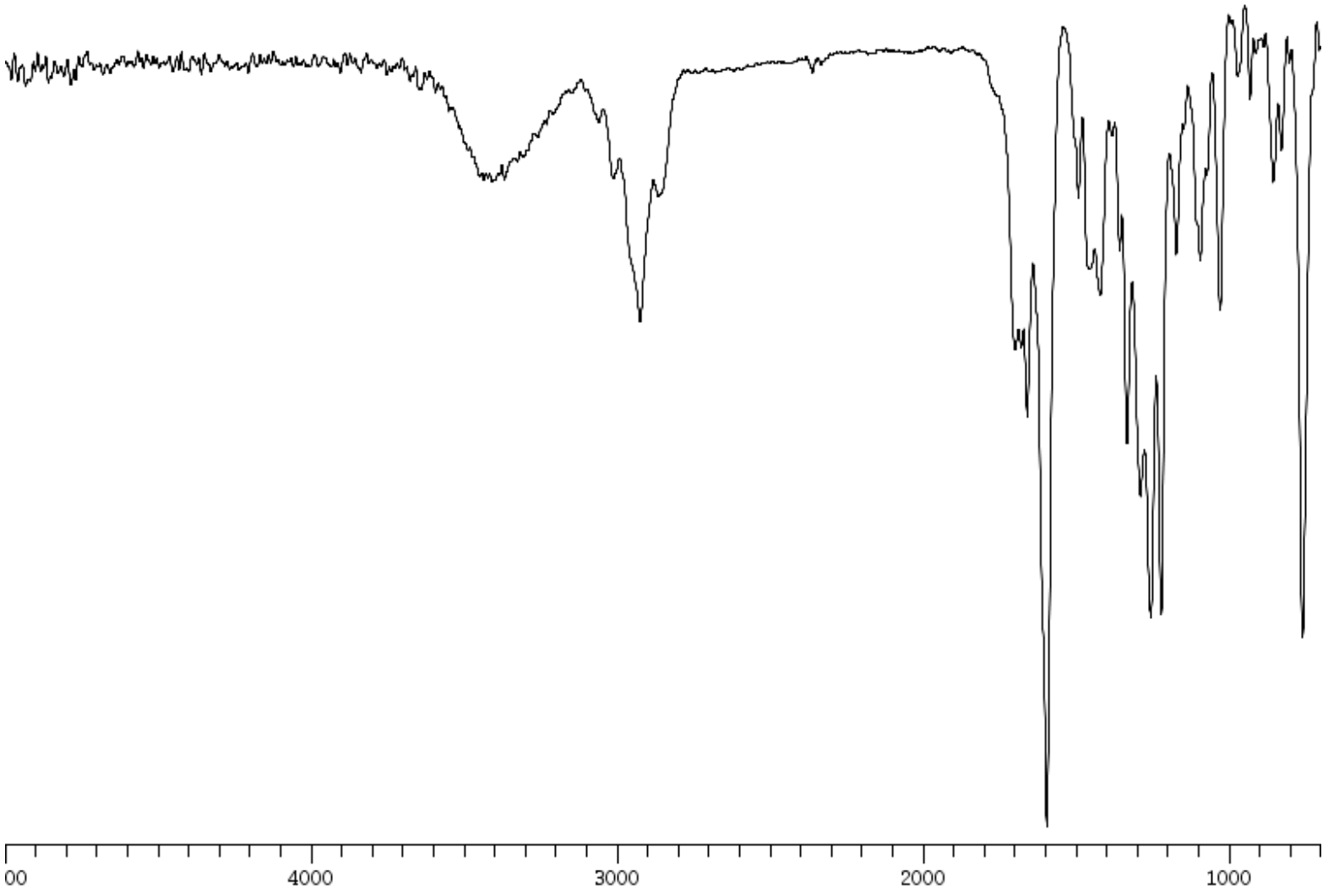

C_6D_6
400 MHz
ROESY
f2 (ppm)
f1 (ppm)

C_6D_6
400 MHz

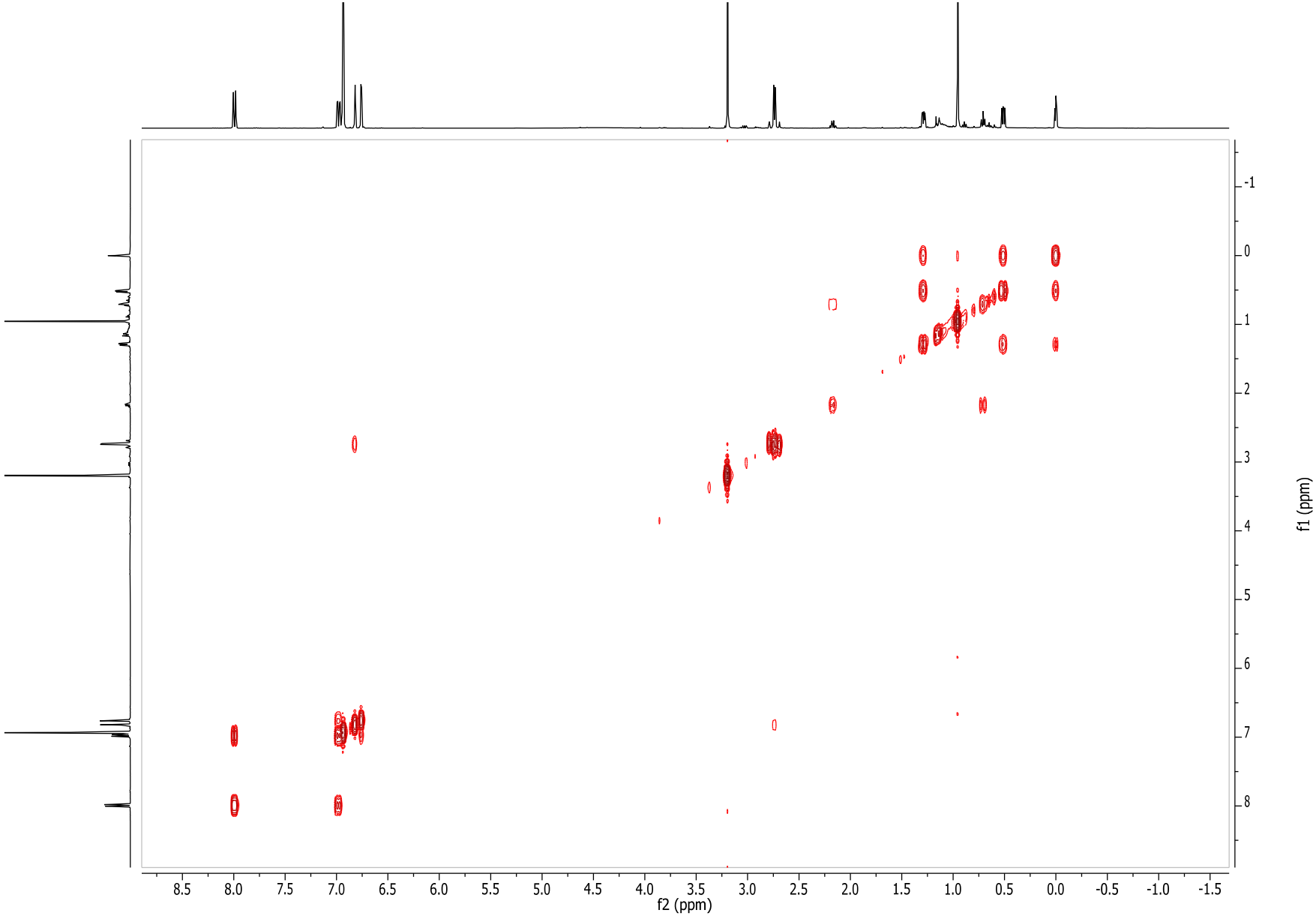

OH
Me
MeO
9
H
C6D6
0.91
0.94
0.93
1.00
3.04
2.06
0.97
3.06
1.02
1.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

C_6D_6
100.1 MHz

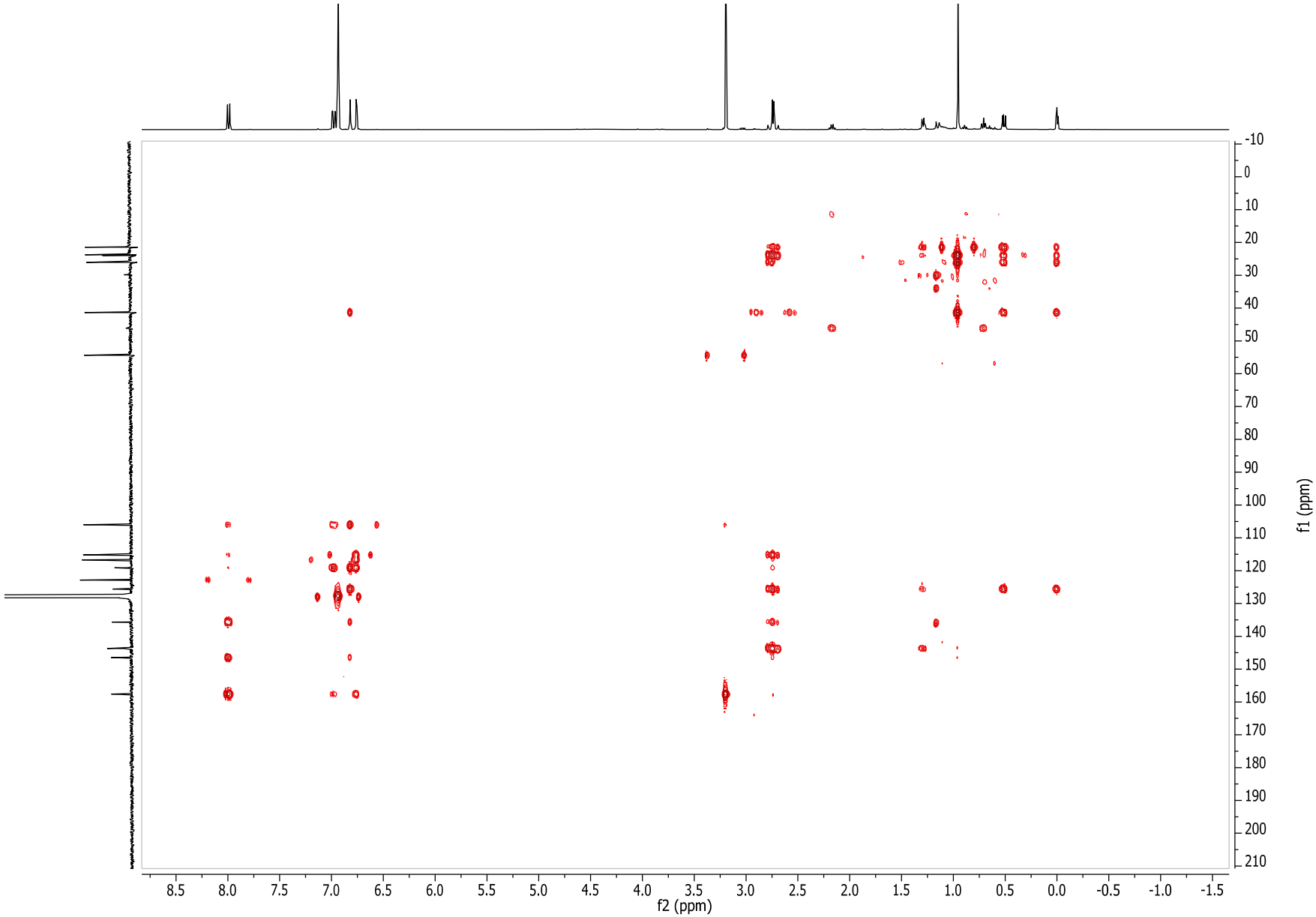



00
4000
3000
2000
1000

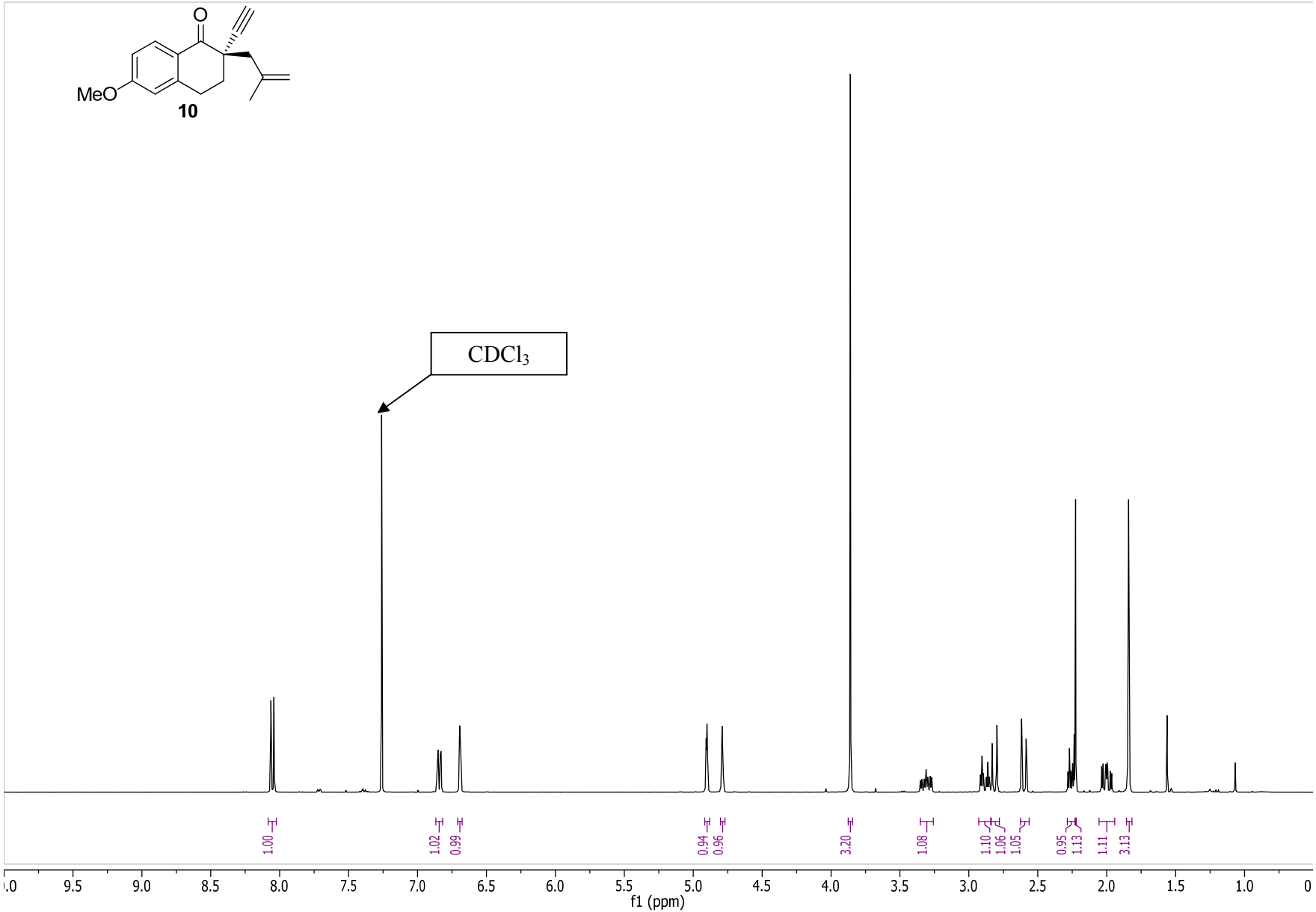
COSY


8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
f2 (ppm)
-1
0
1
2
3
4
5
6
7
8
f1 (ppm)

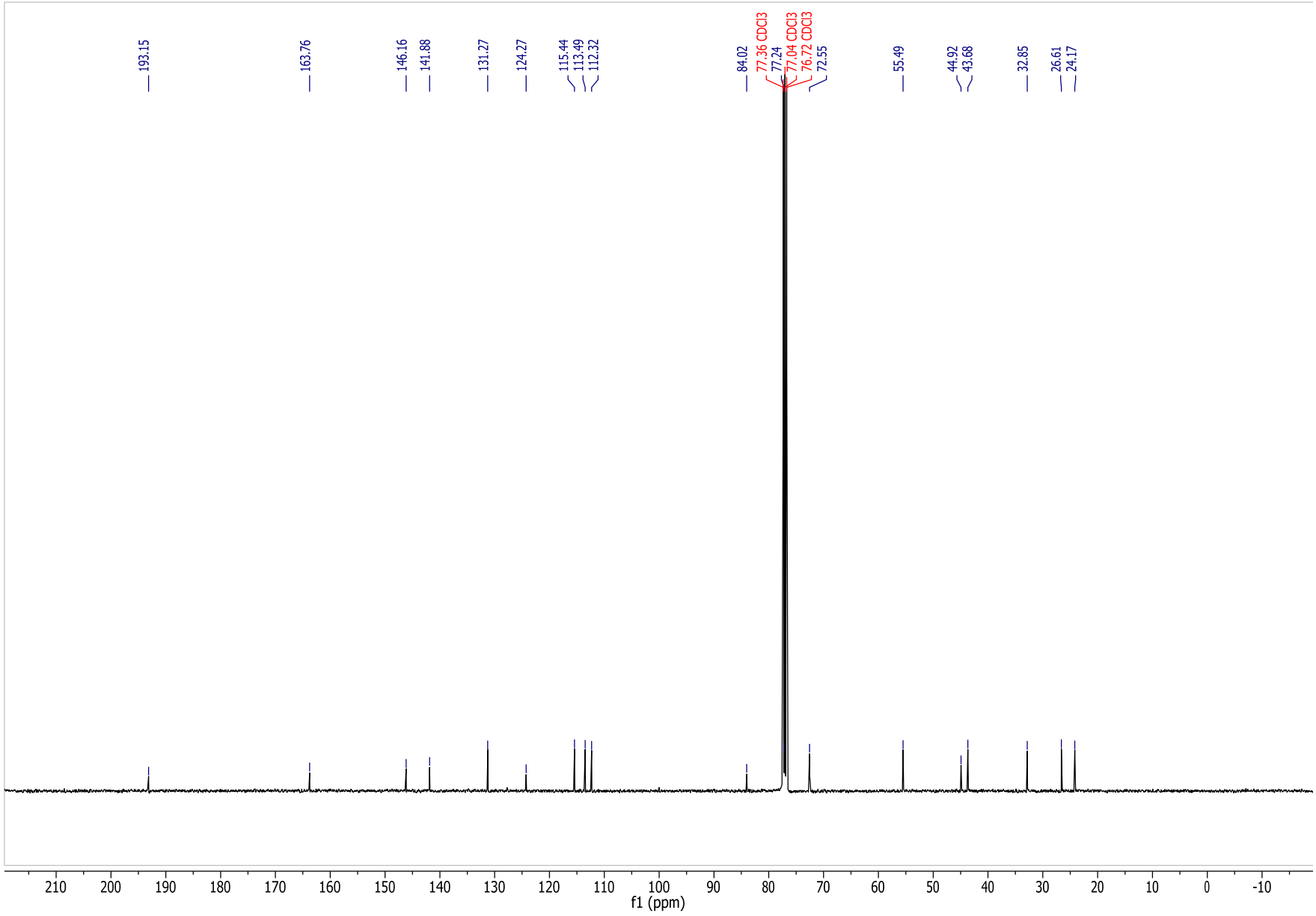
HMBC

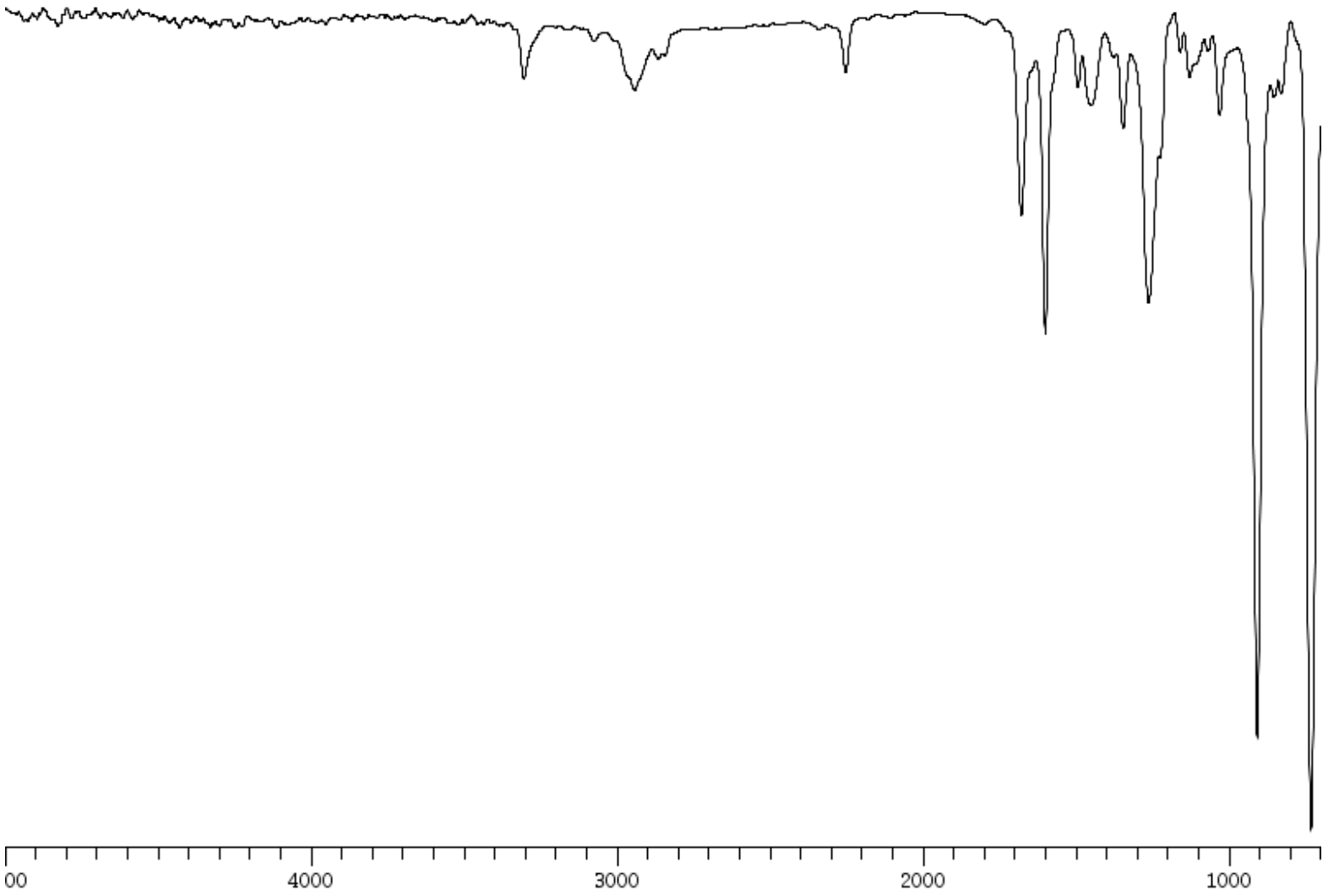


$CDCl_3$
400 MHz

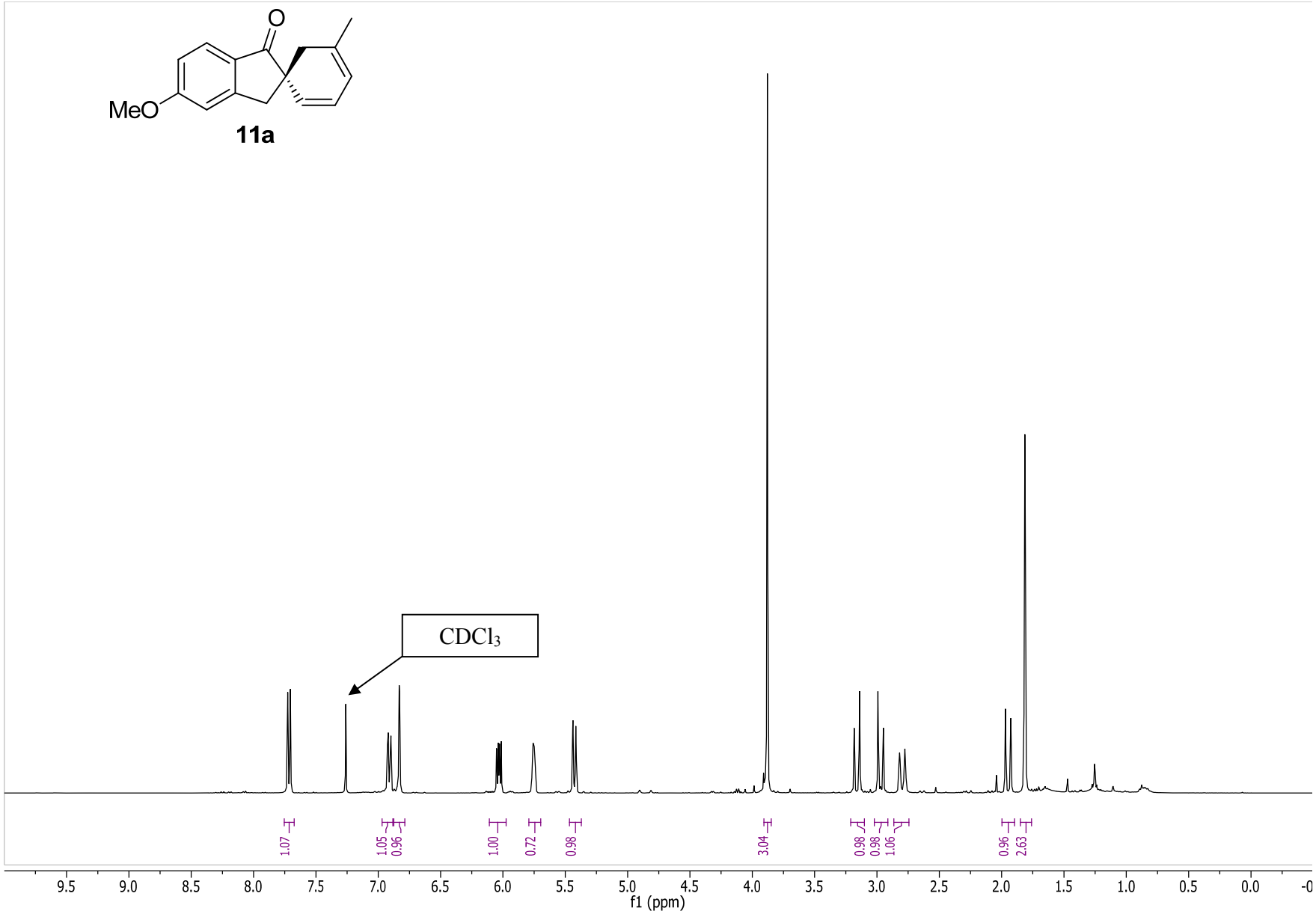


$CDCl_3$
100.1 MHz

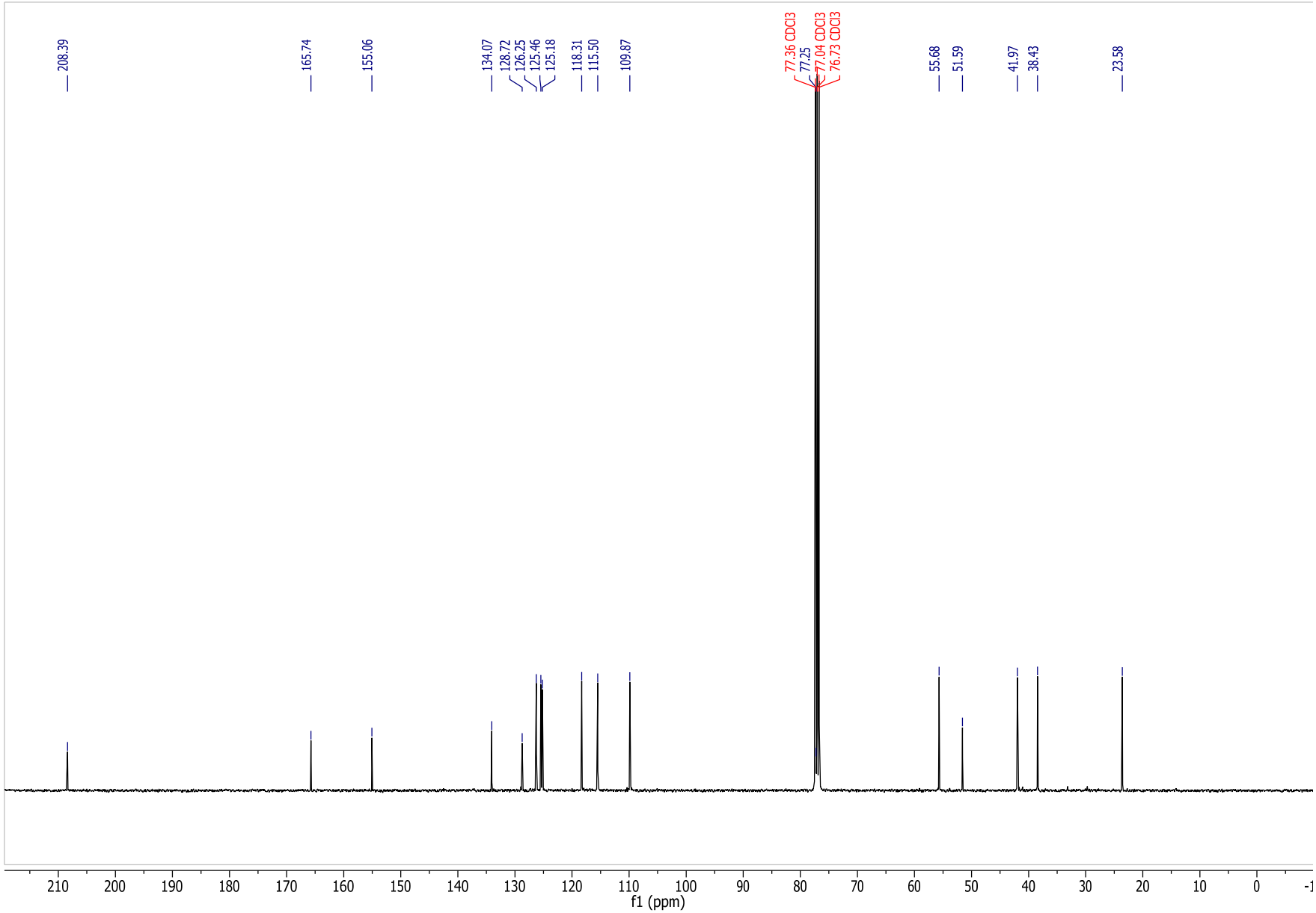


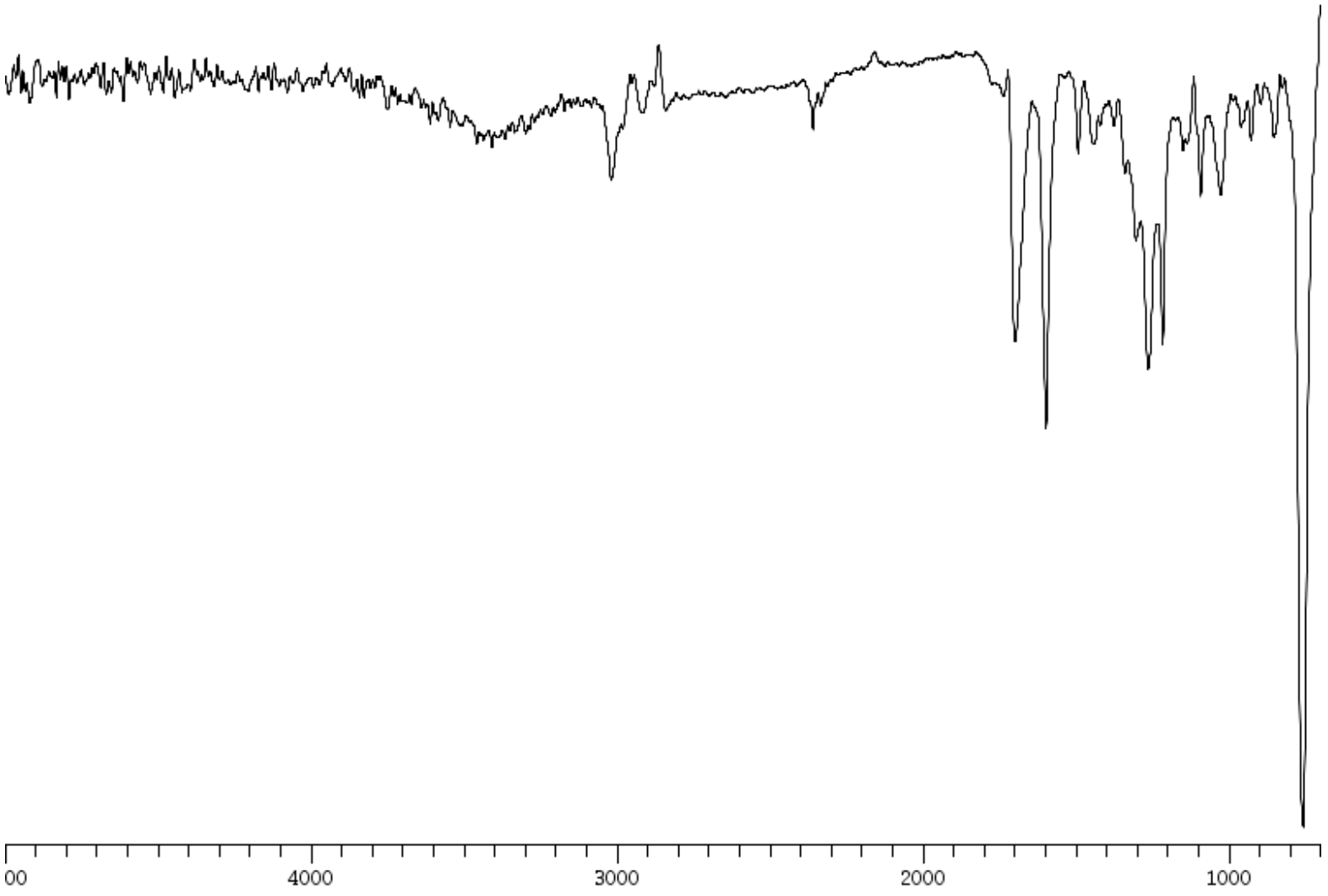

00
4000
3000
2000
1000

$CDCl_3$
400 MHz

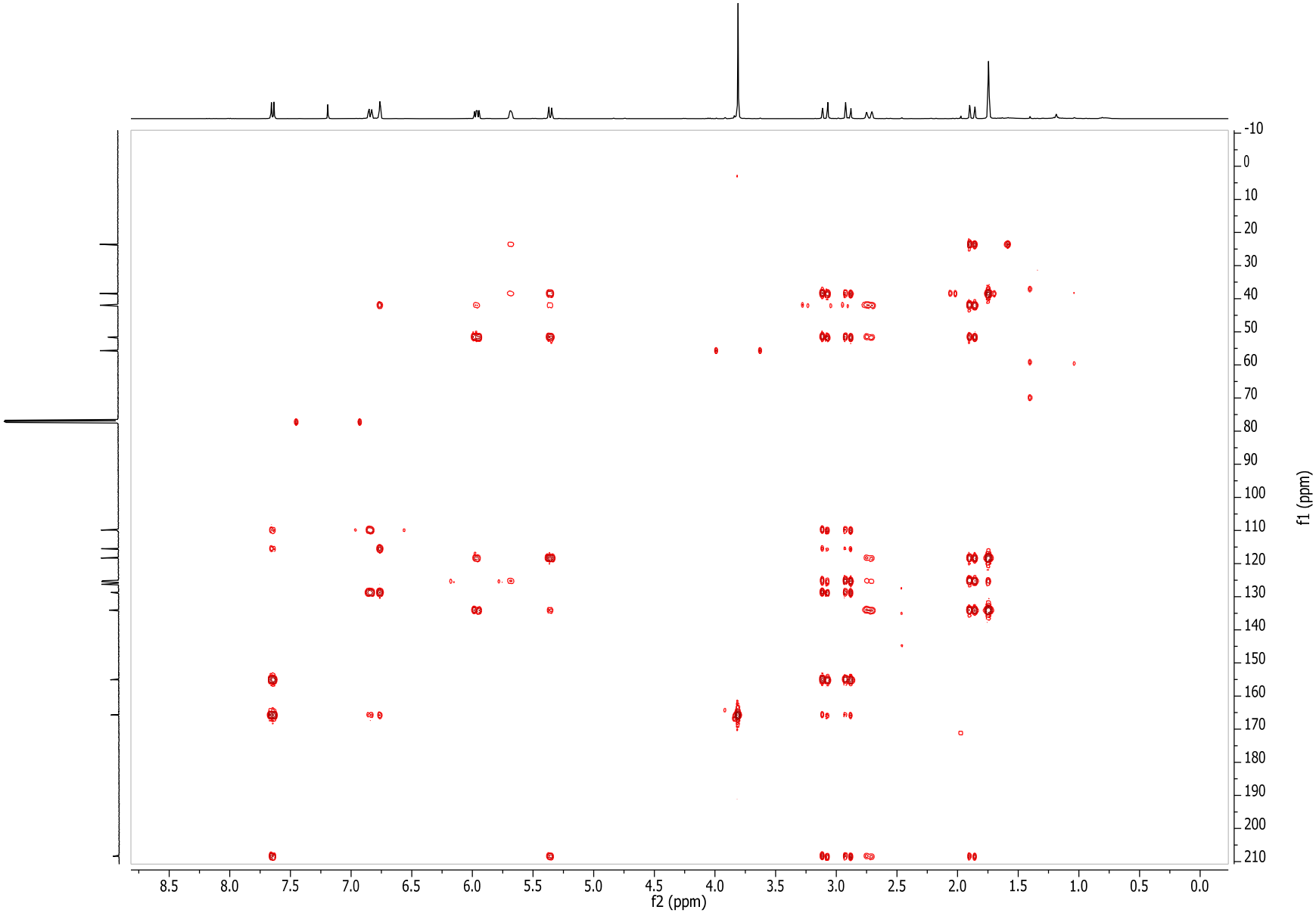


$CDCl_3$
100.1 MHz

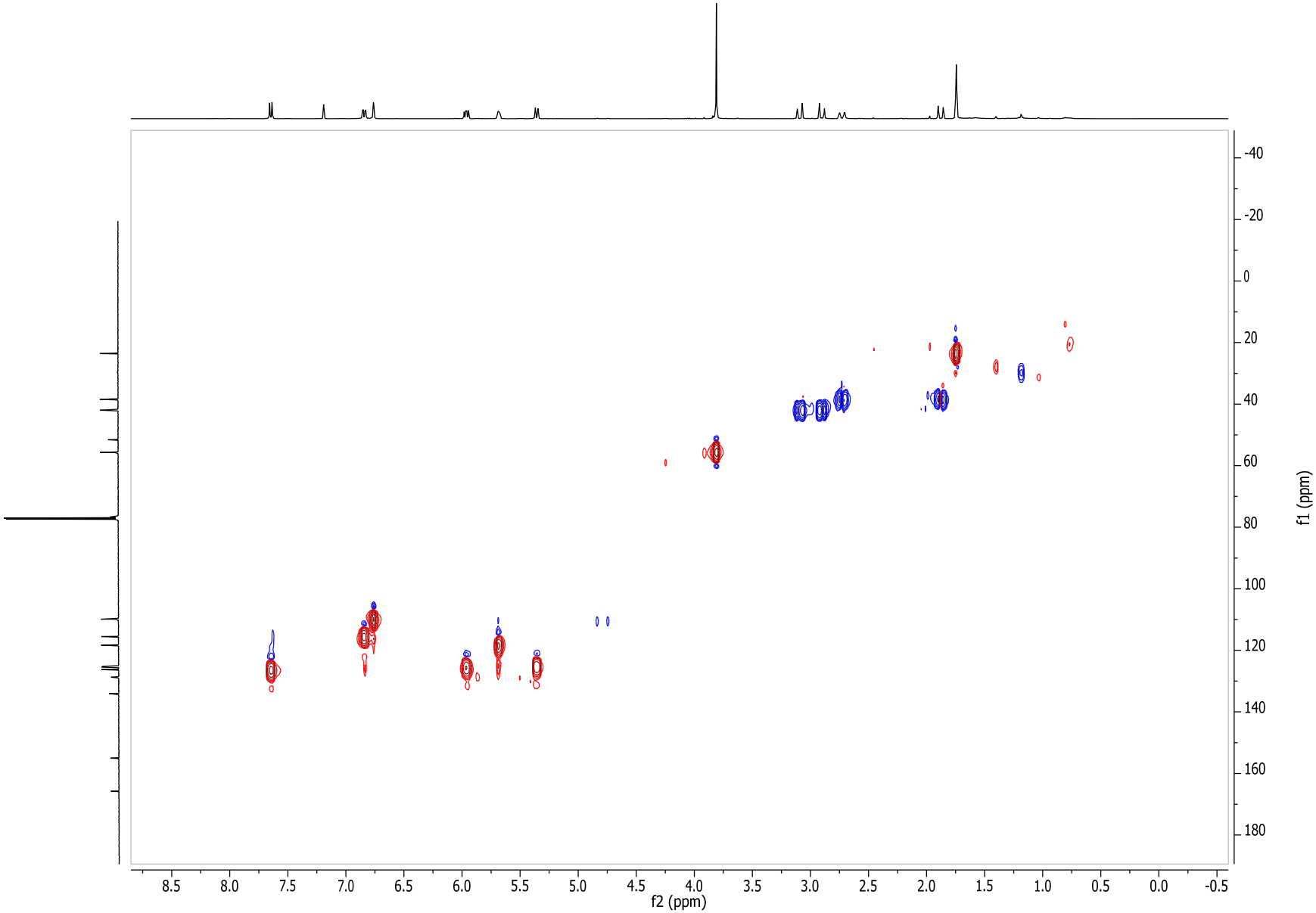



00
4000
3000
2000
1000

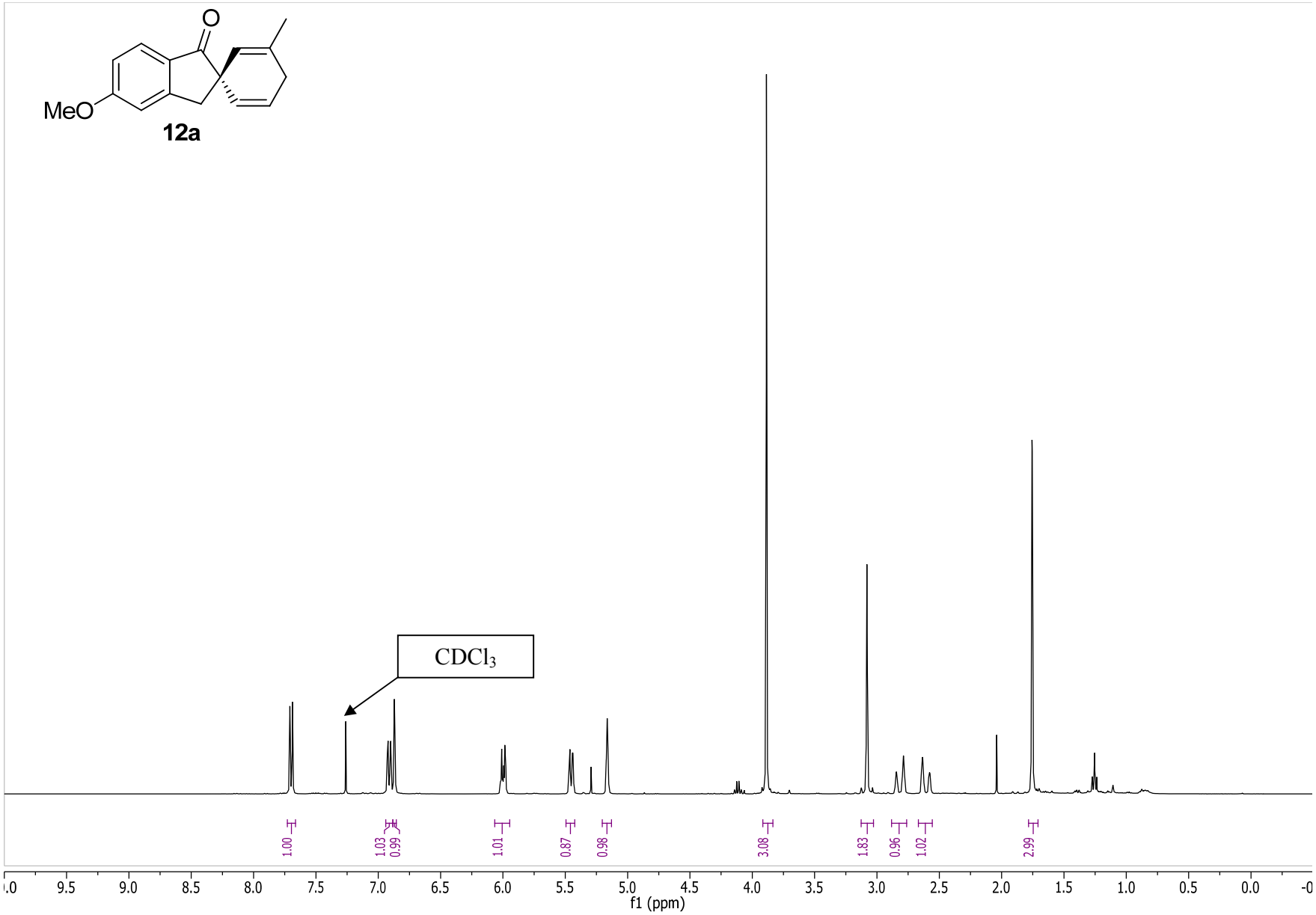
HMBC



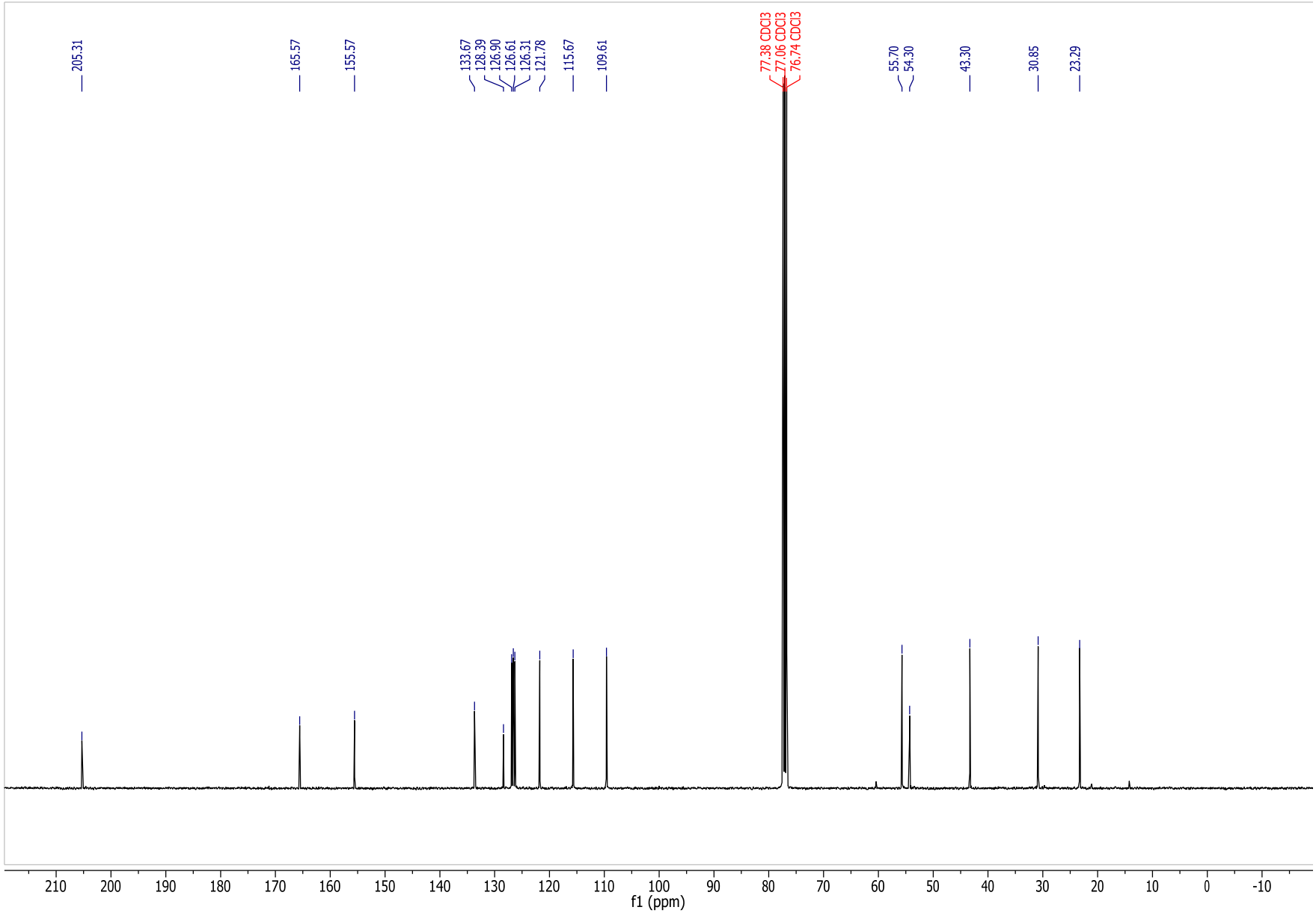
HSQC

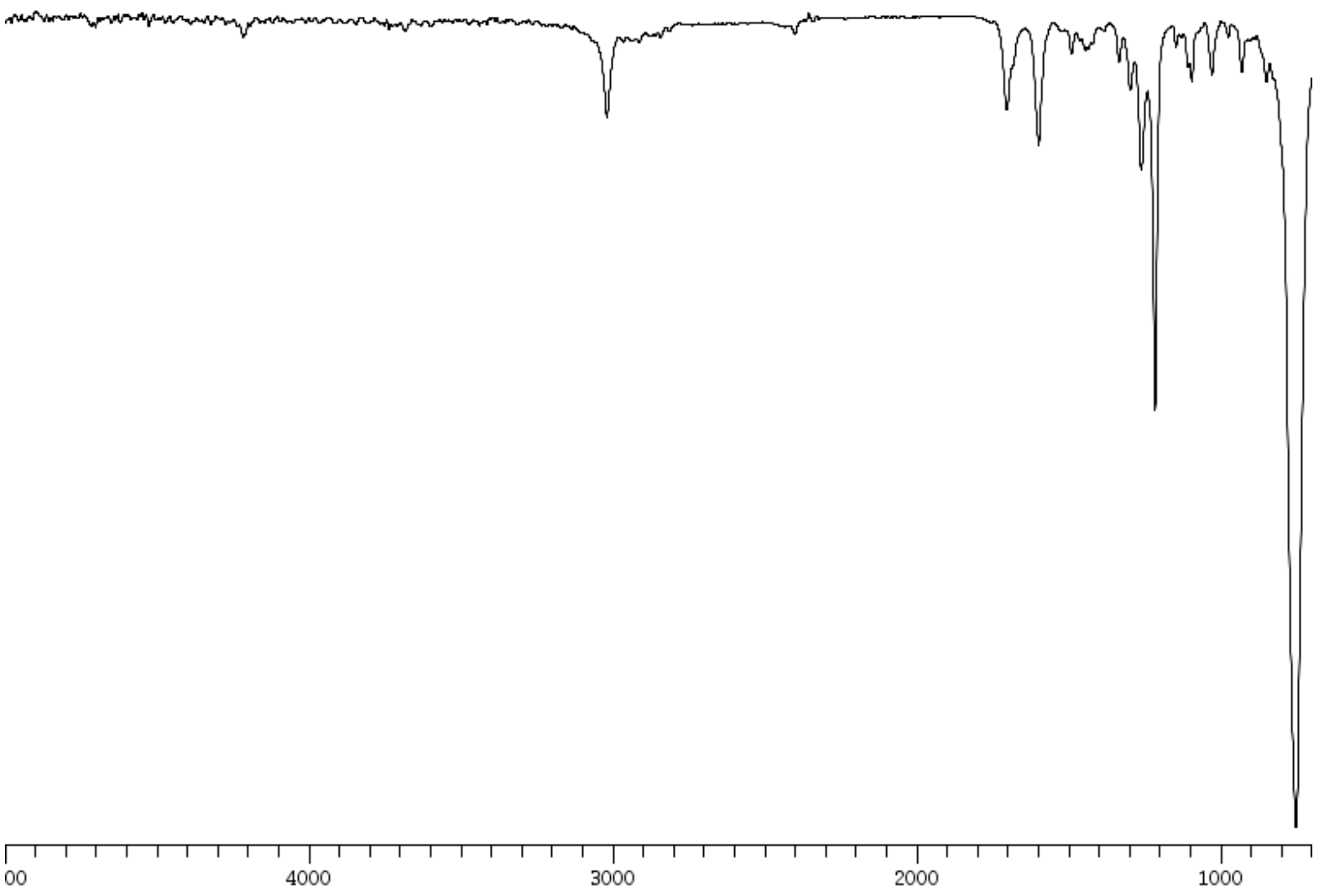

-40
-20
0
20
40
60
80
100
120
140
160
180
f1 (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f2 (ppm)

$CDCl_3$
400 MHz

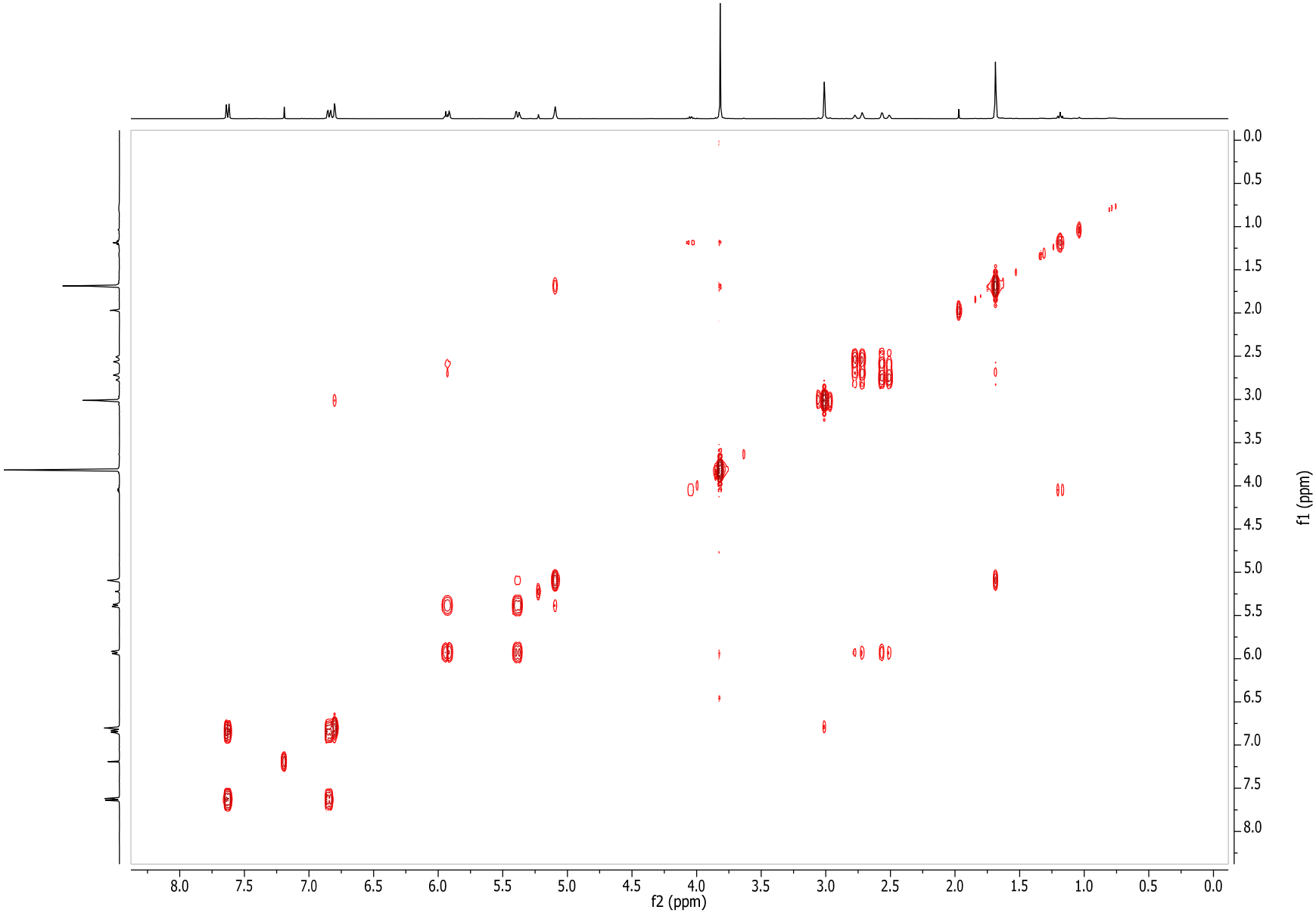


$CDCl_3$
100.1 MHz

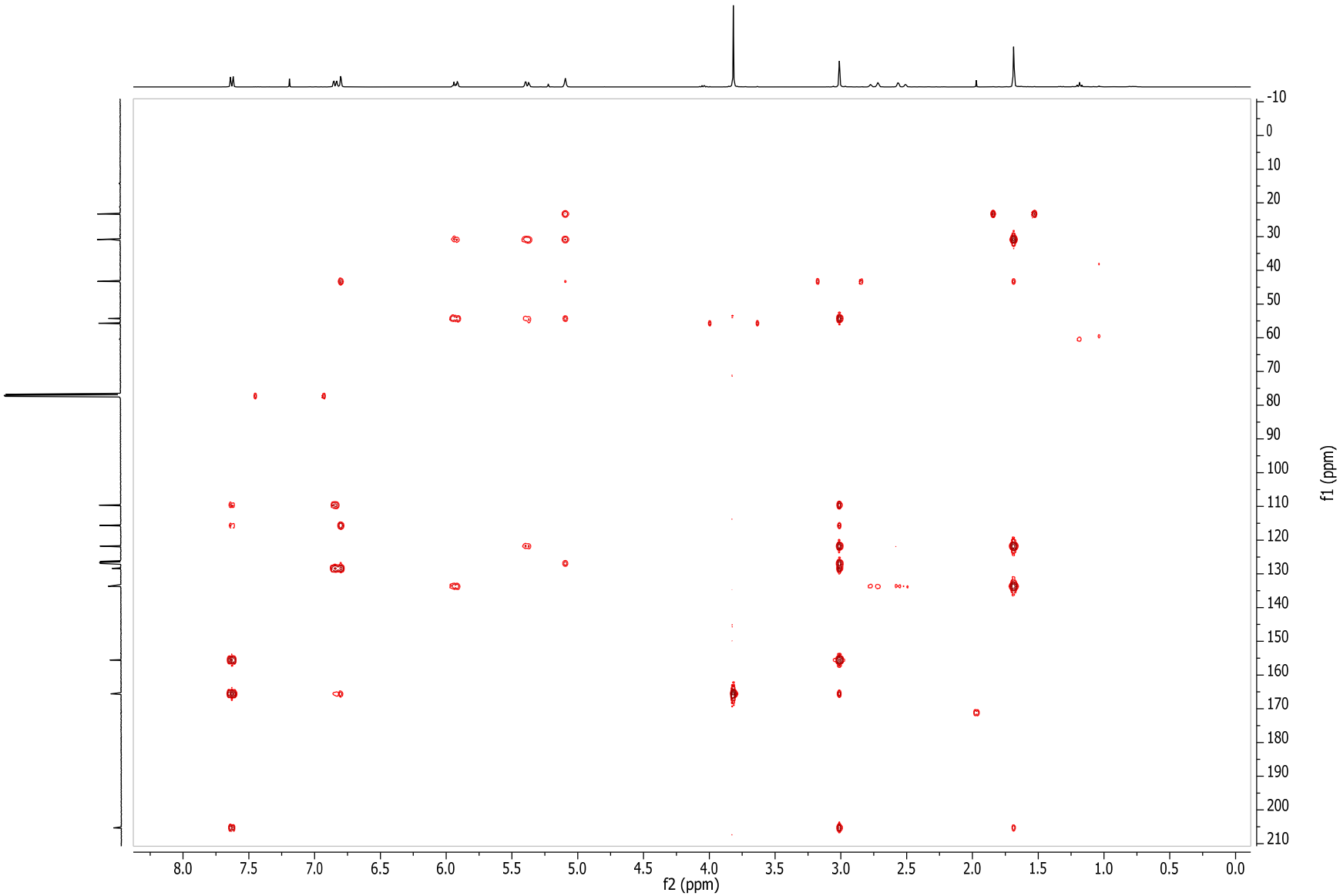



00
4000
3000
2000
1000

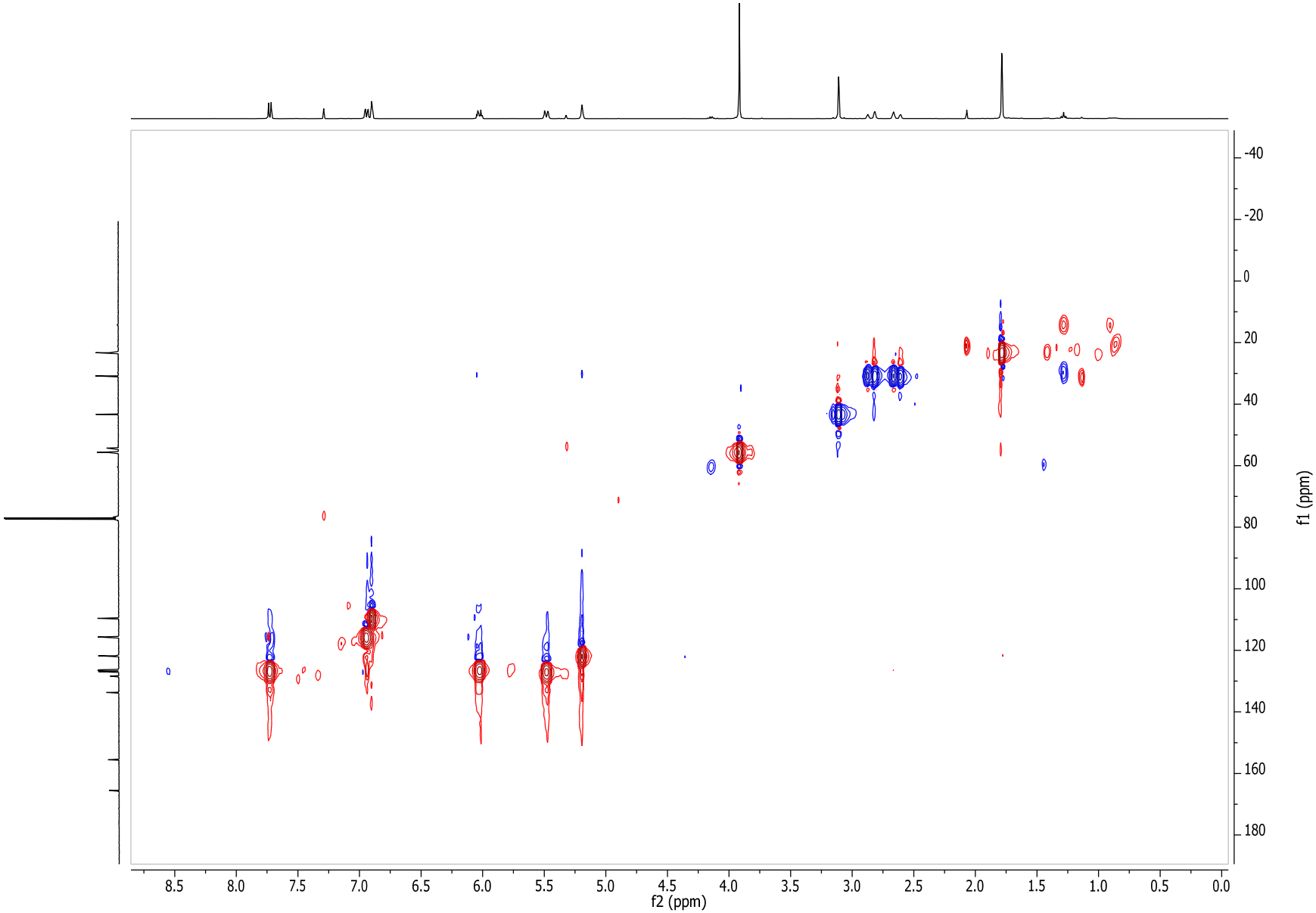
COSY


8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f2 (ppm)
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
f1 (ppm)

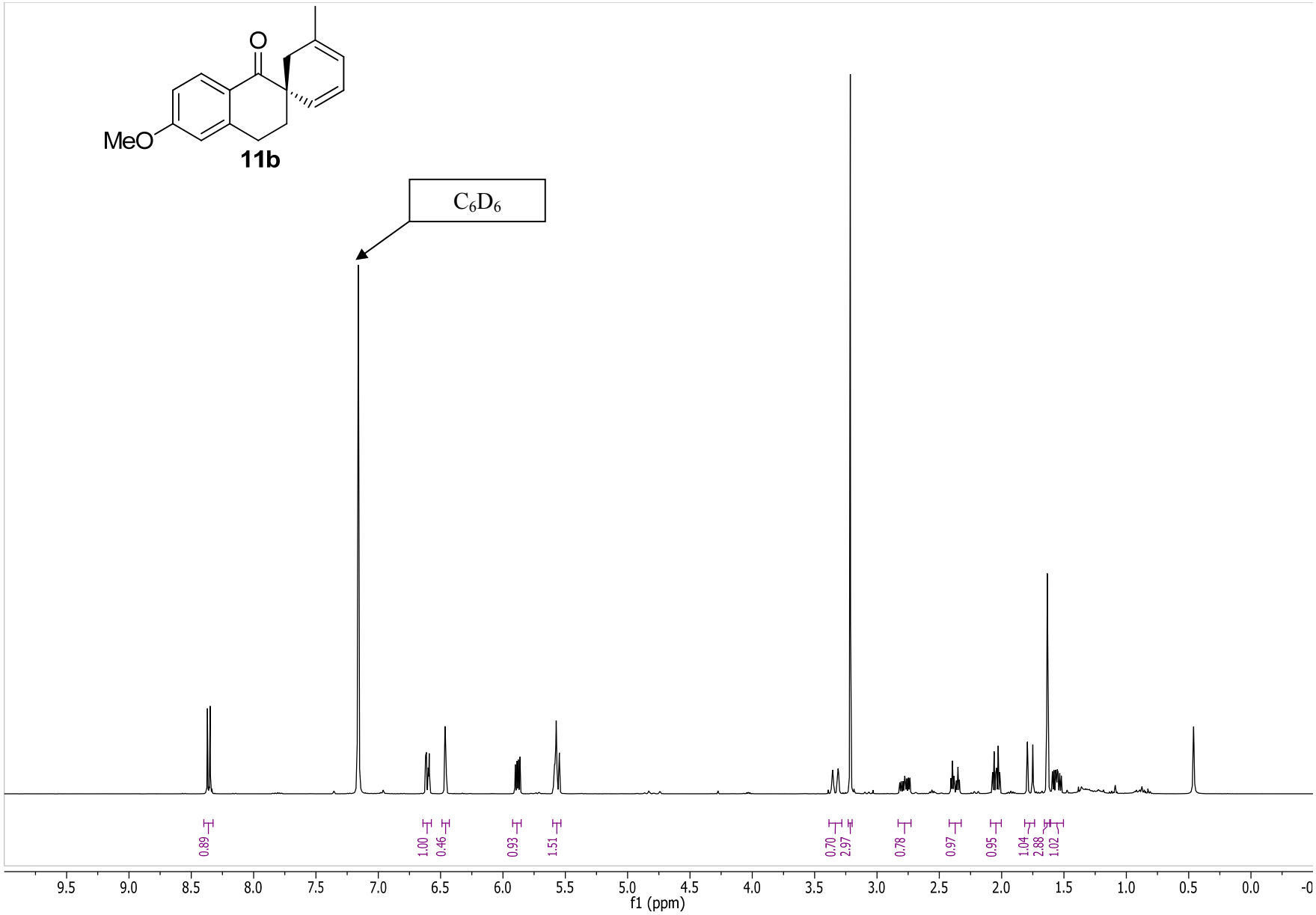
HMBC



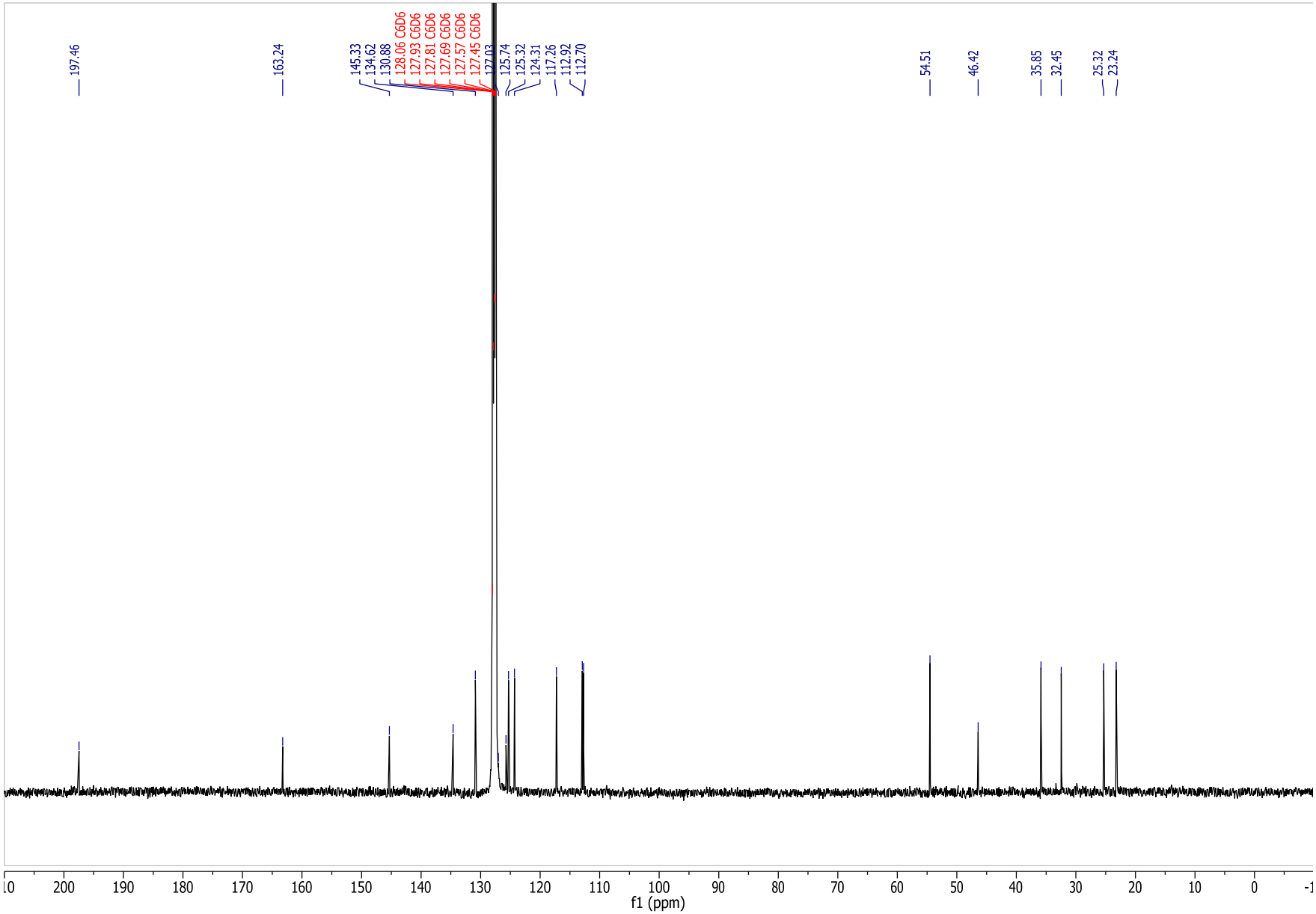
HSQC

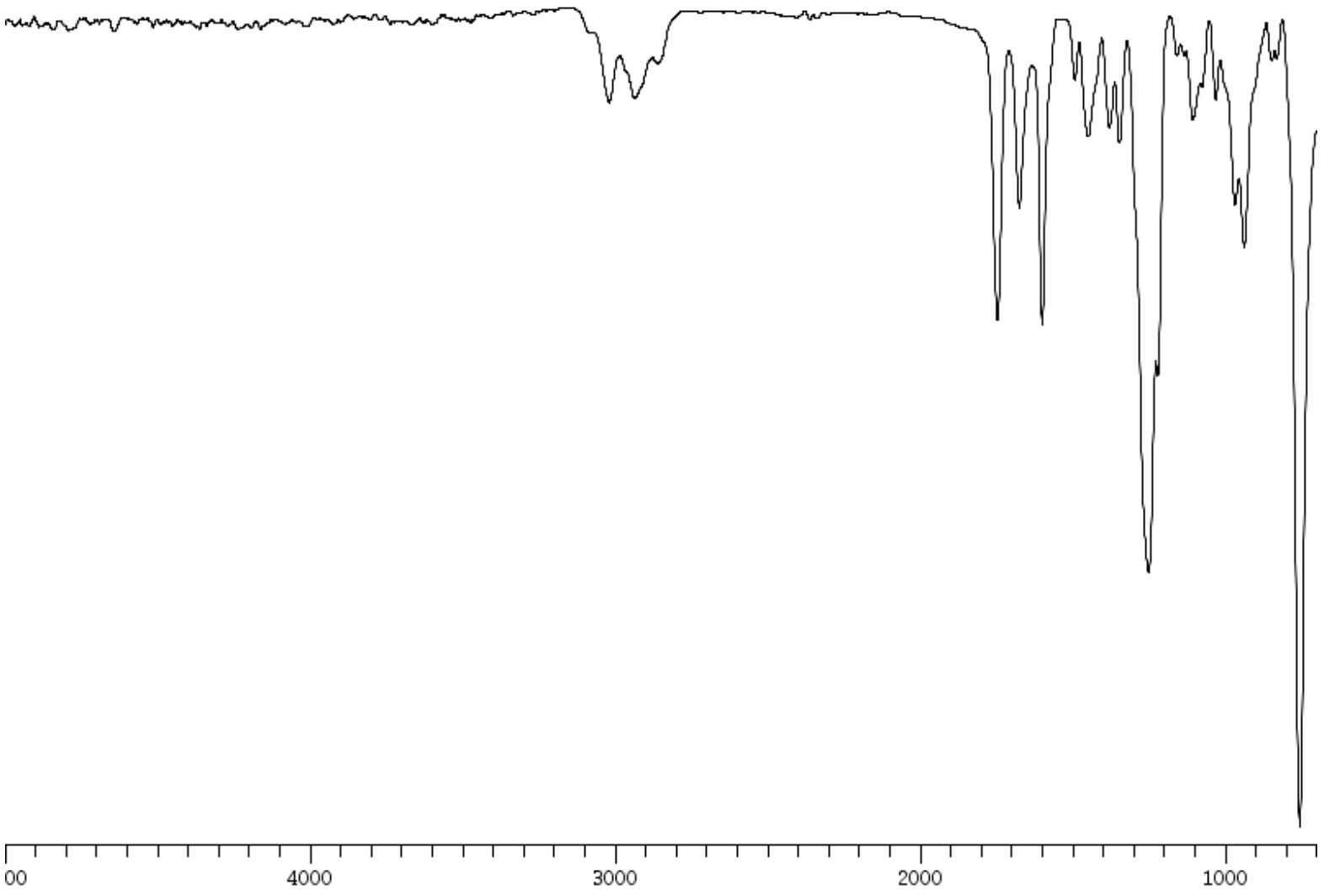

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f2 (ppm)
-40
-20
0
20
40
60
80
100
120
140
160
180
f1 (ppm)

C_6D_6
400 MHz

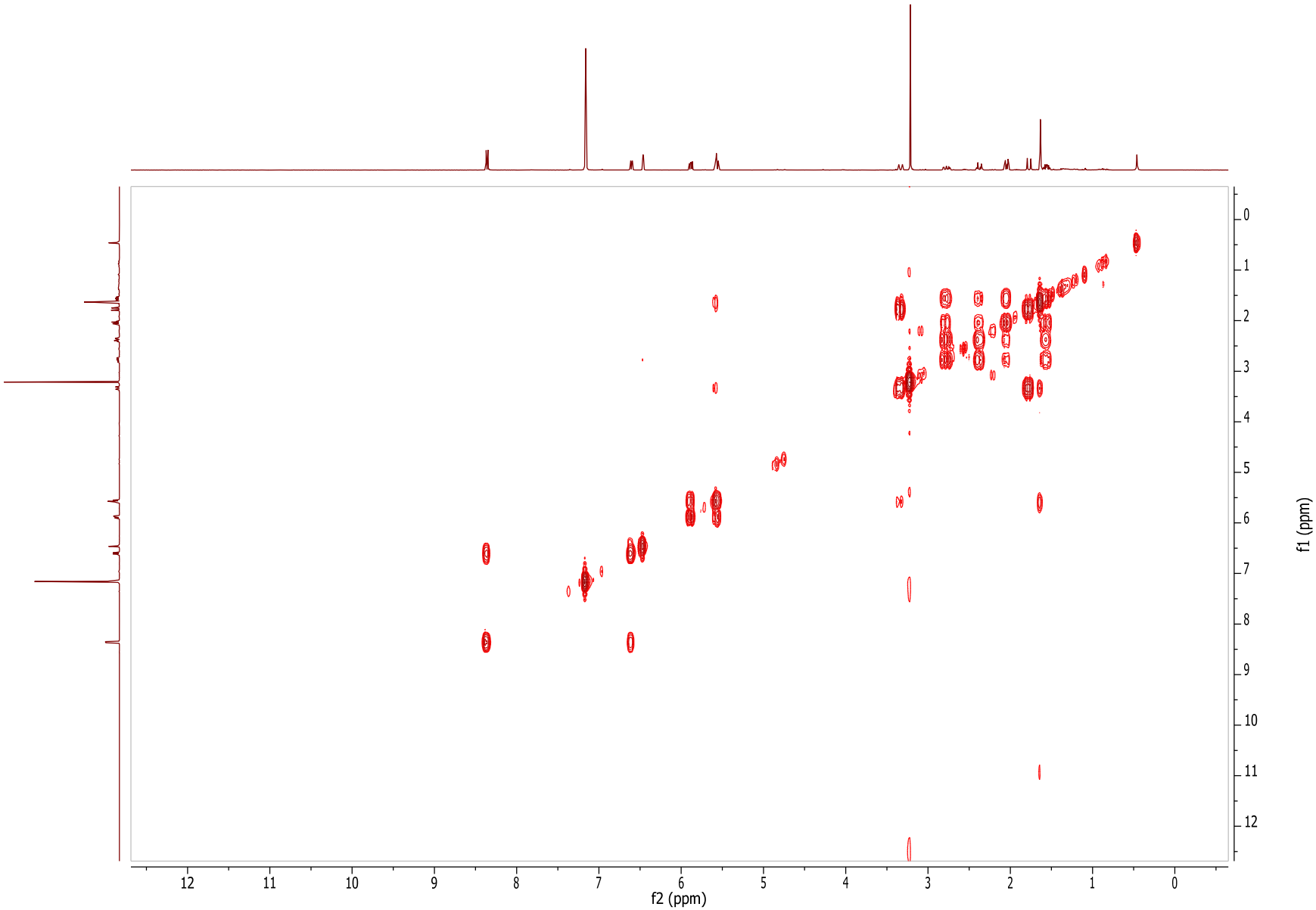

O
MeO
11b
C_6D_6
0.89
1.00
0.46
0.93
1.51
0.70
2.97
0.78
0.97
0.95
1.04
2.88
1.02
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)

C_6D_6
100.1 MHz

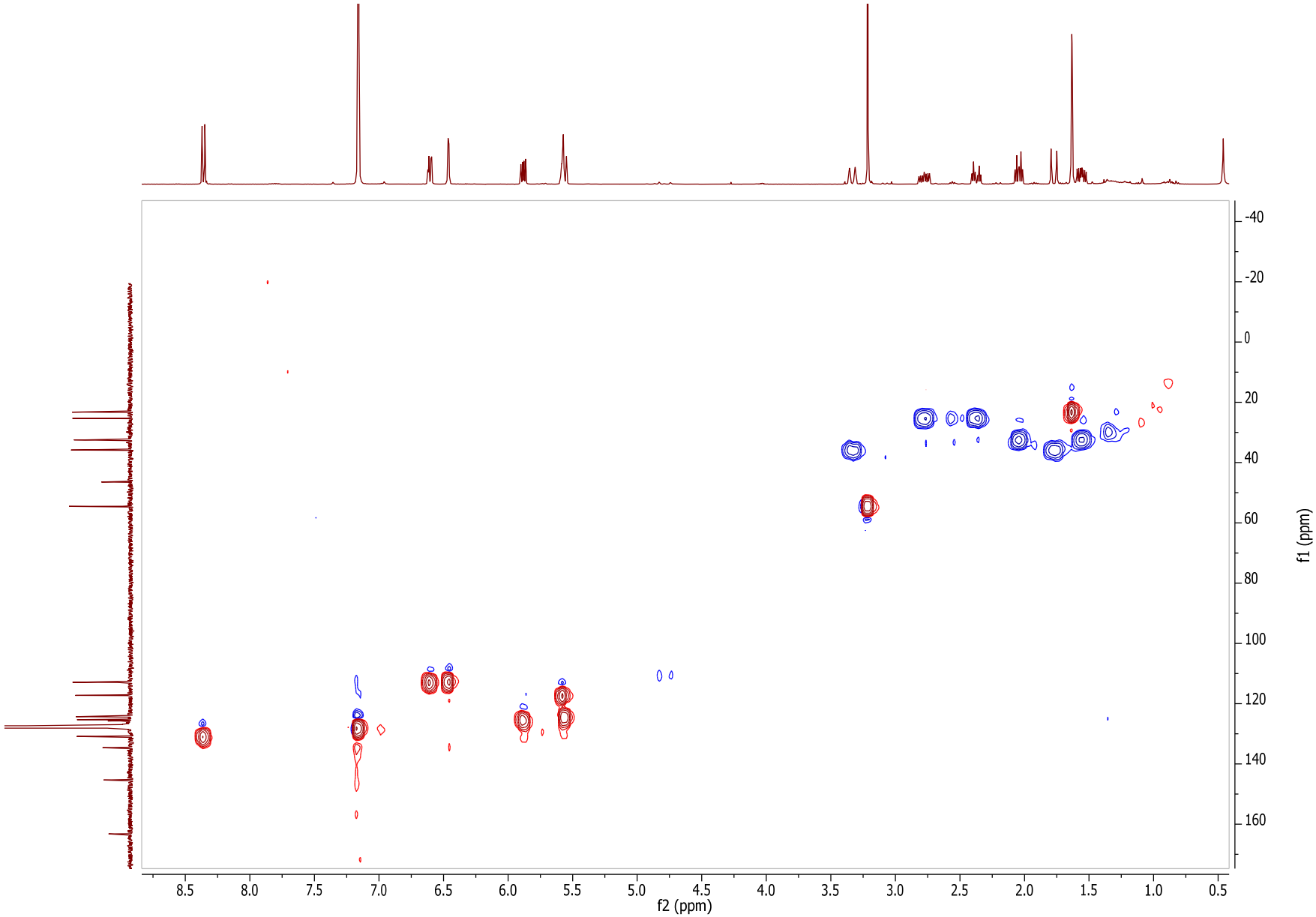



00
4000
3000
2000
1000

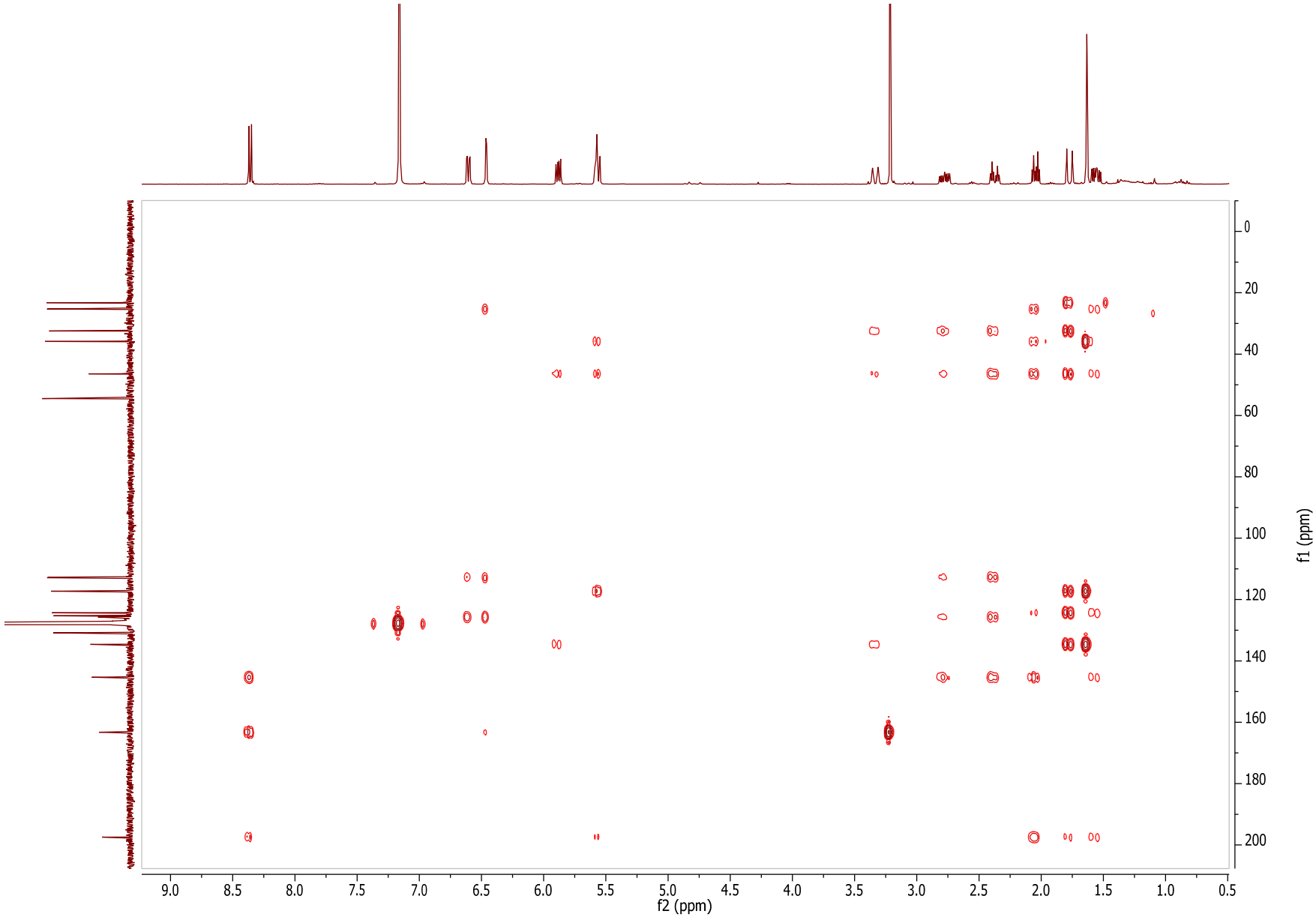
COSY

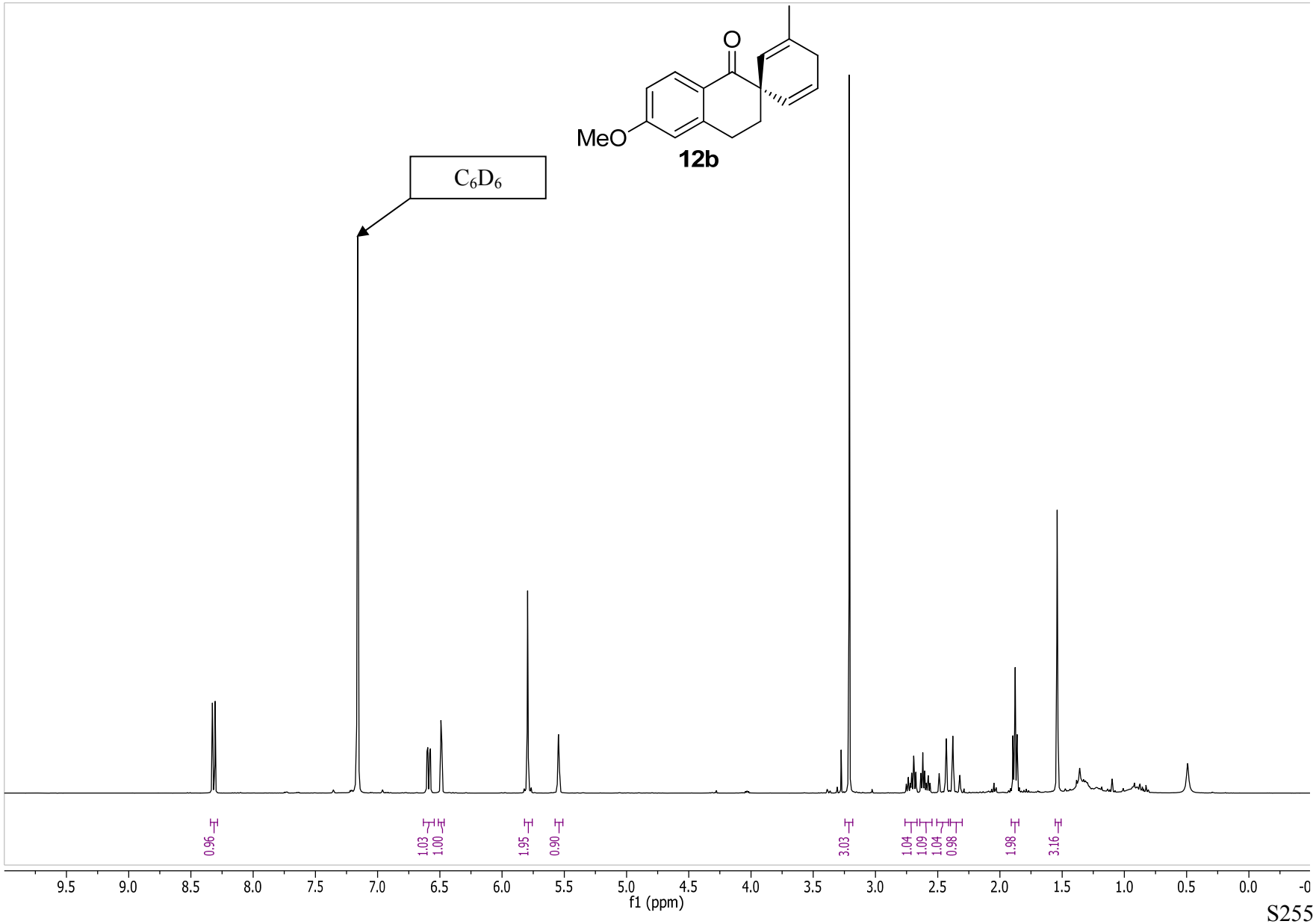


HSQC

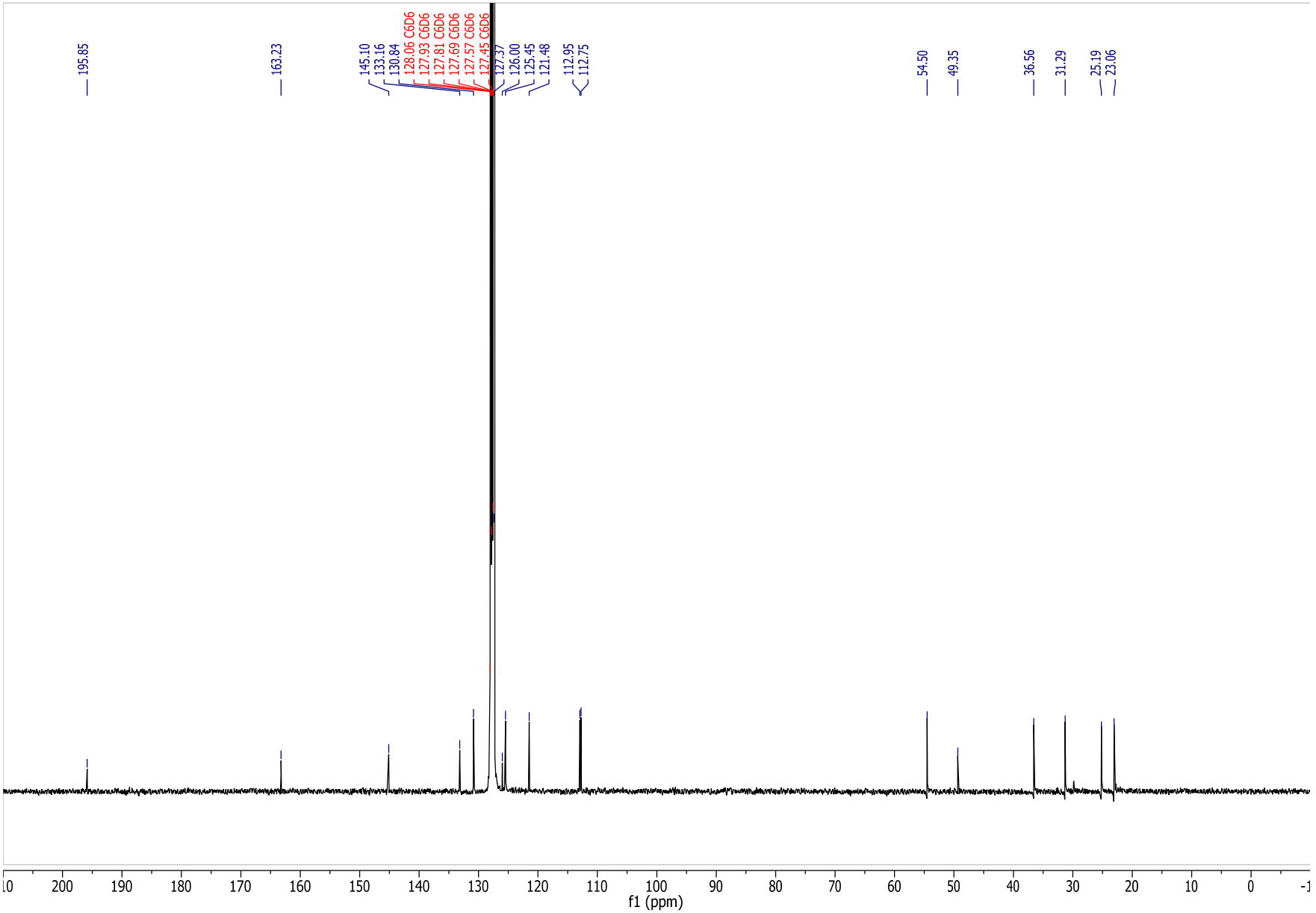

-40
-20
0
20
40
60
80
100
120
140
160
f1 (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f2 (ppm)

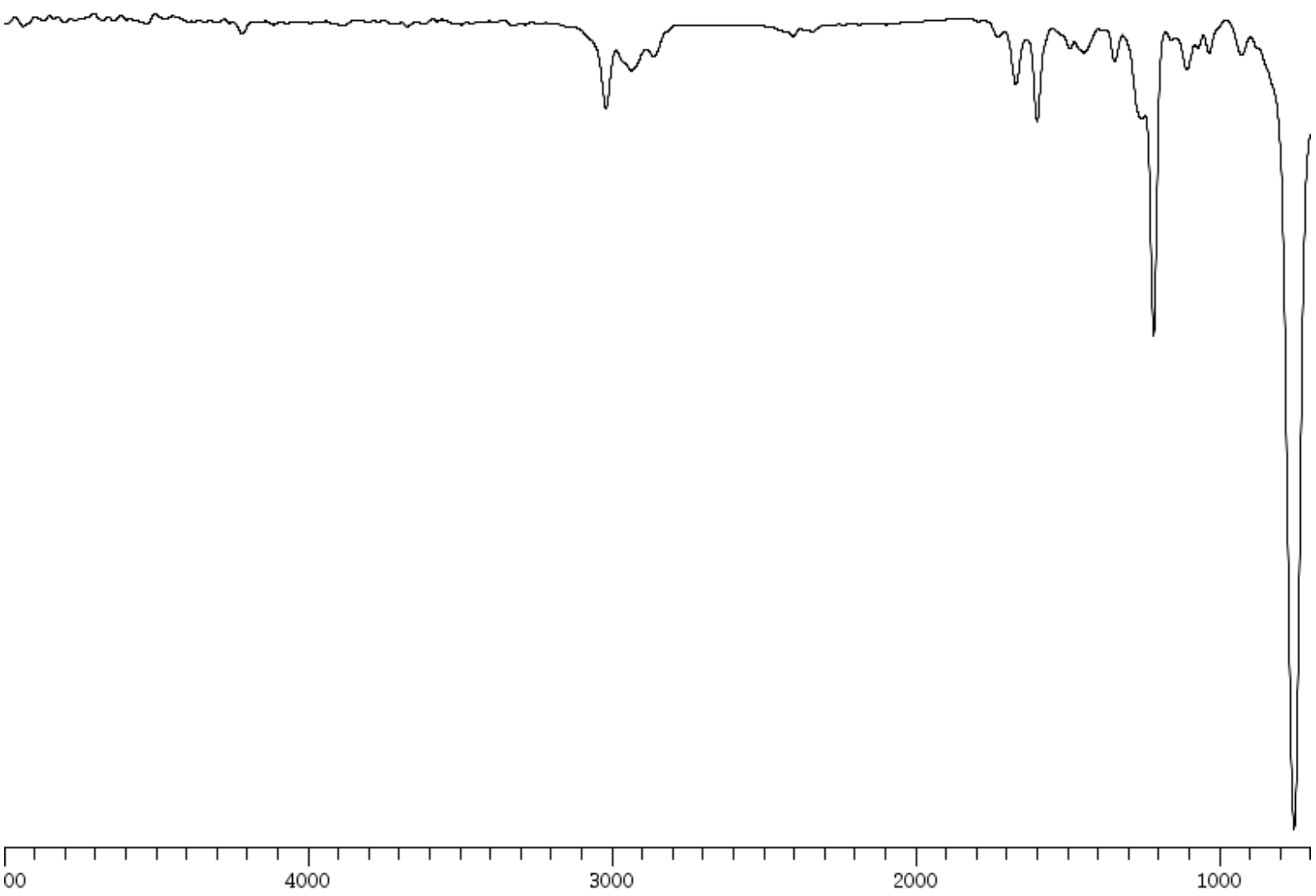
HMBC


9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f2 (ppm)
0
20
40
60
80
100
120
140
160
180
200
f1 (ppm)

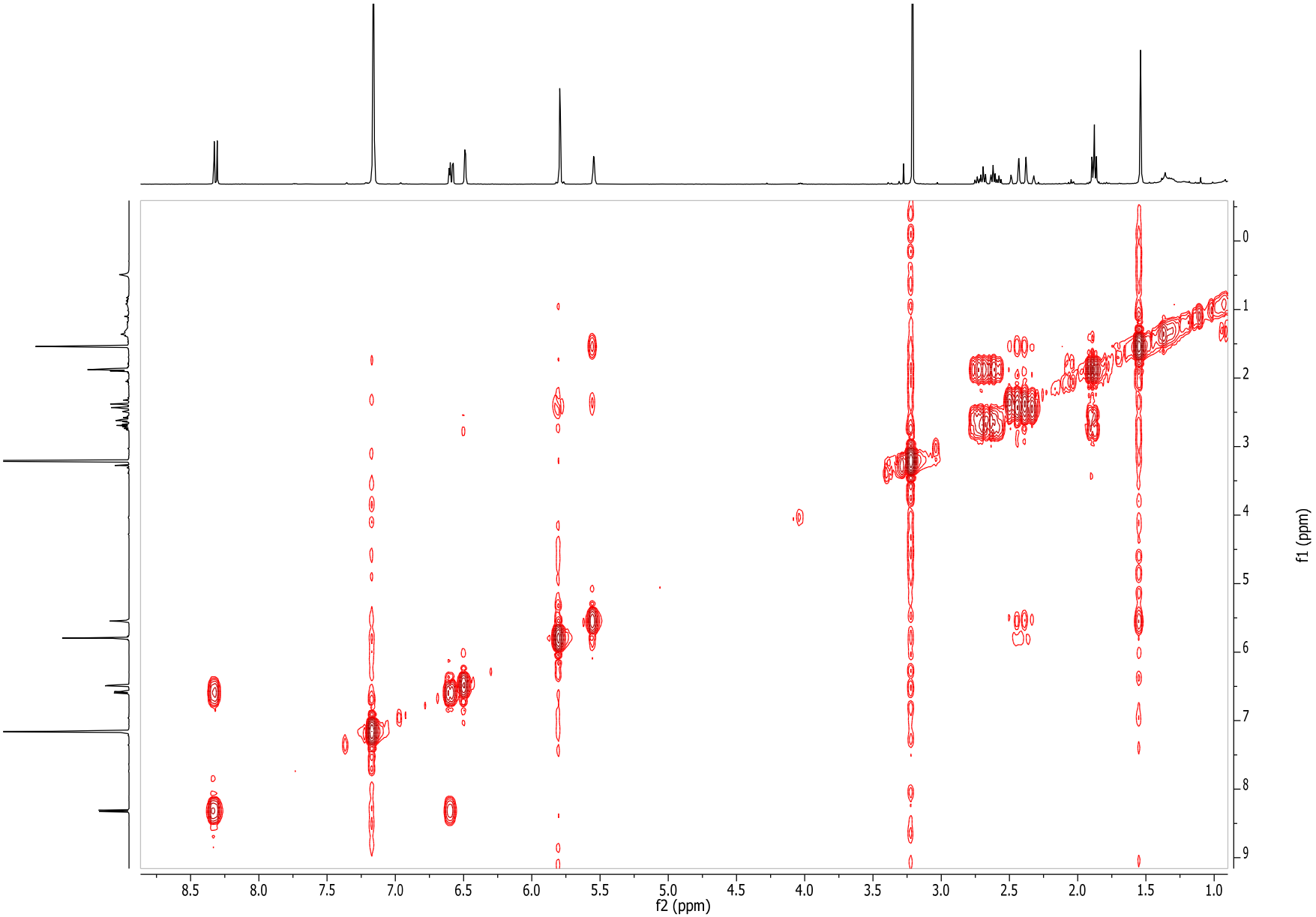

C6D6
400 MHz
O
MeO
12b
C6D6
0.96
1.03
1.00
1.95
0.90
3.03
1.04
1.09
1.04
0.98
1.98
3.16
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

C_6D_6
100.1 MHz

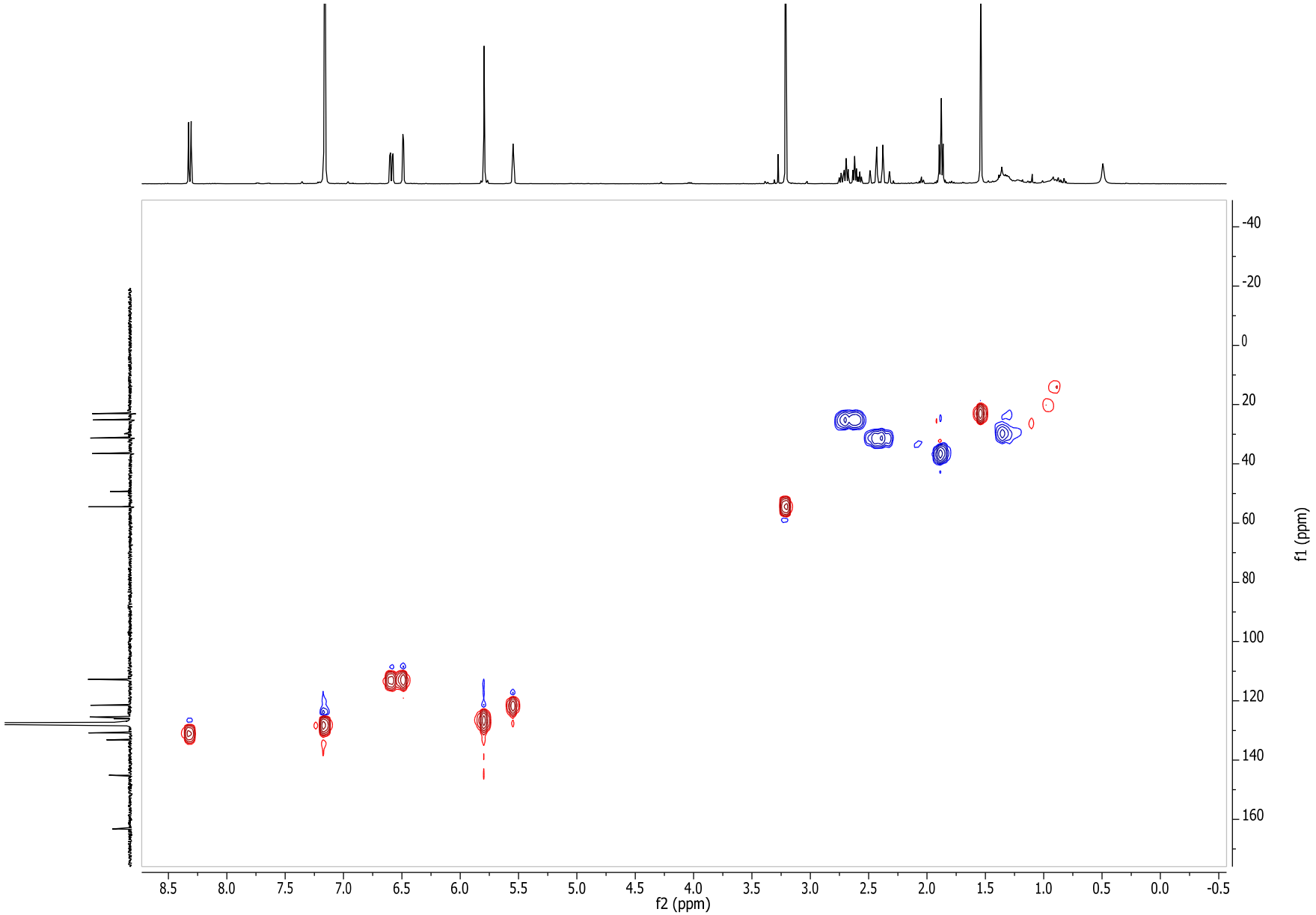



00
4000
3000
2000
1000

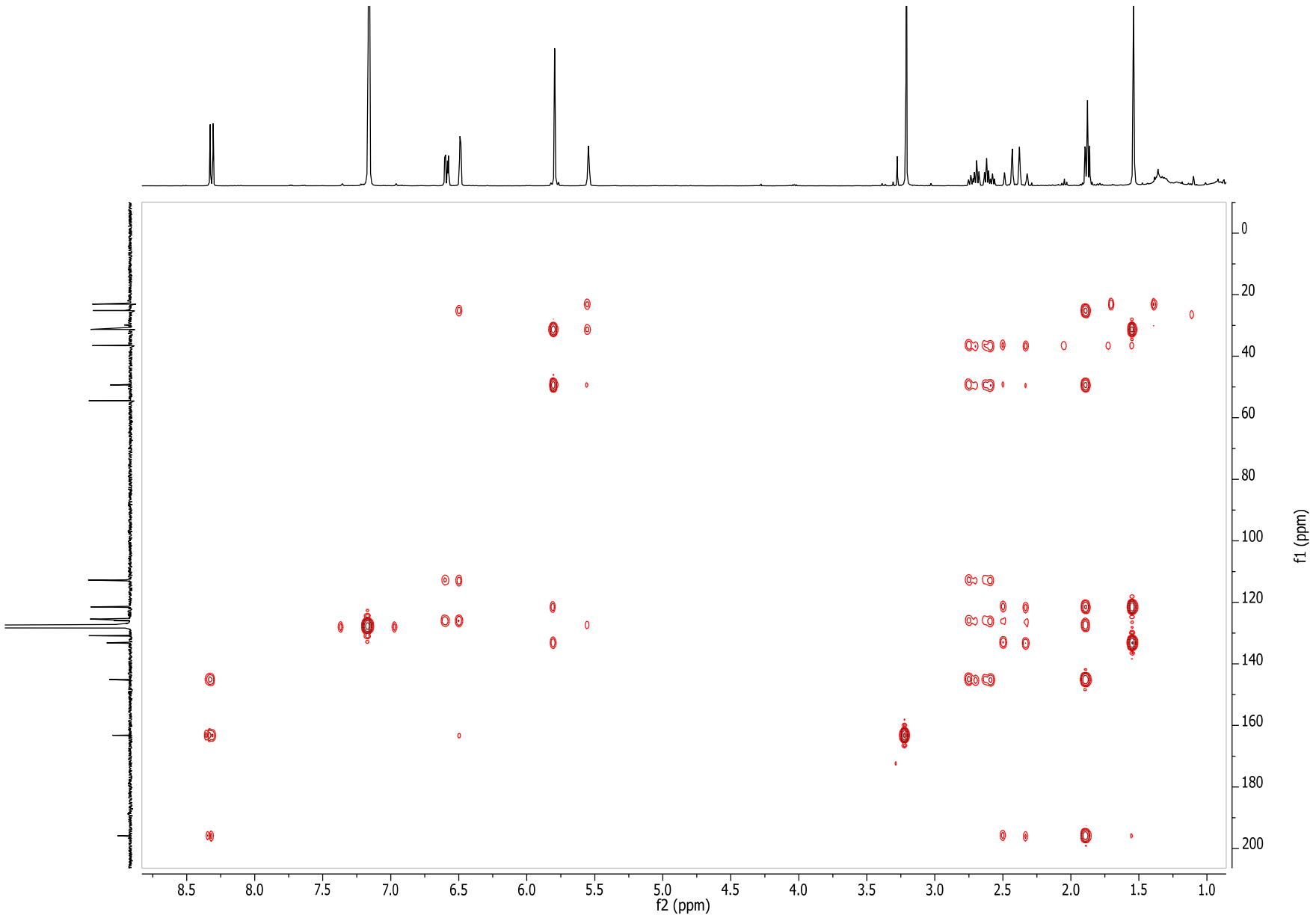
COSY

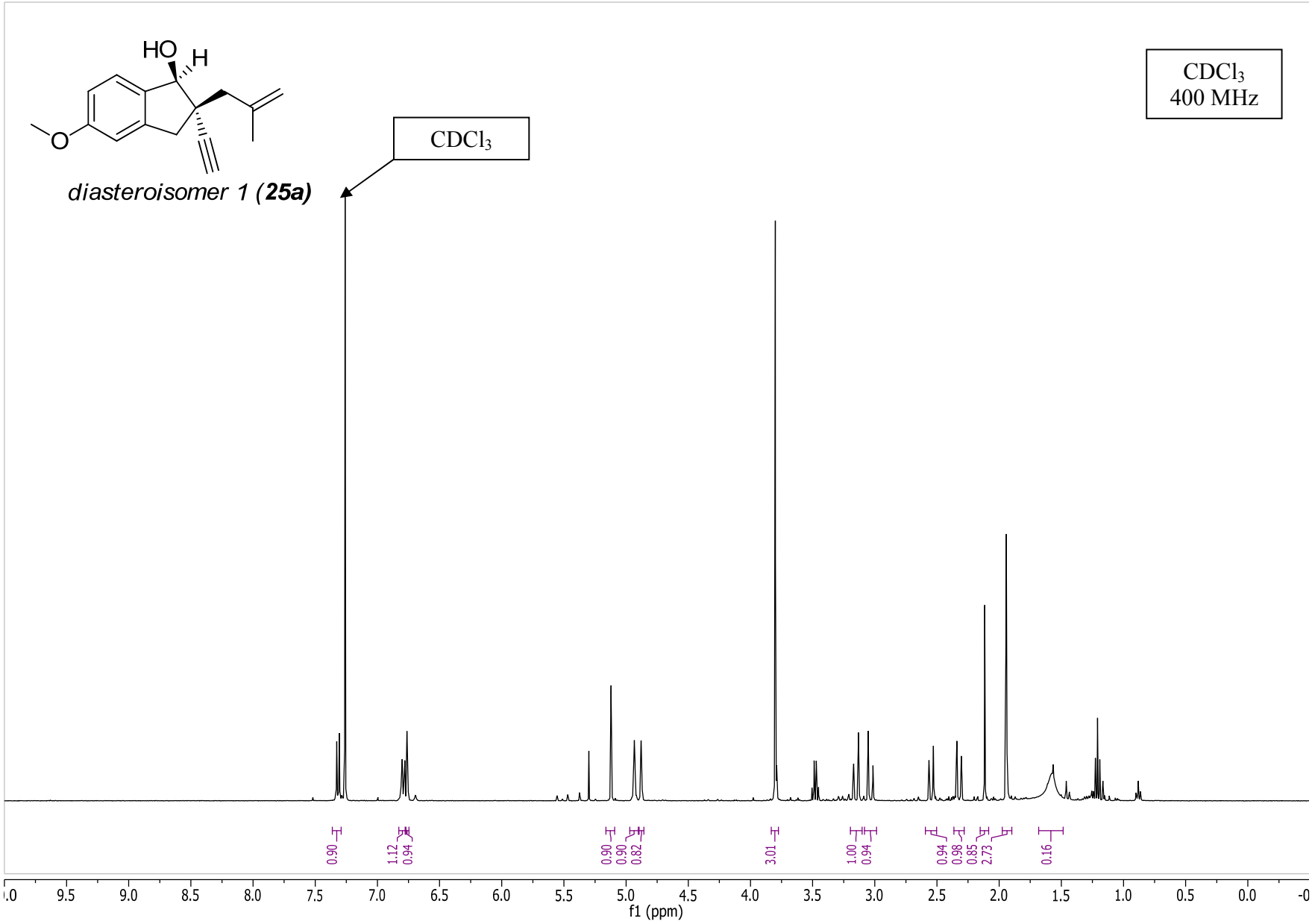

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f2 (ppm)
0
1
2
3
4
5
6
7
8
9
f1 (ppm)

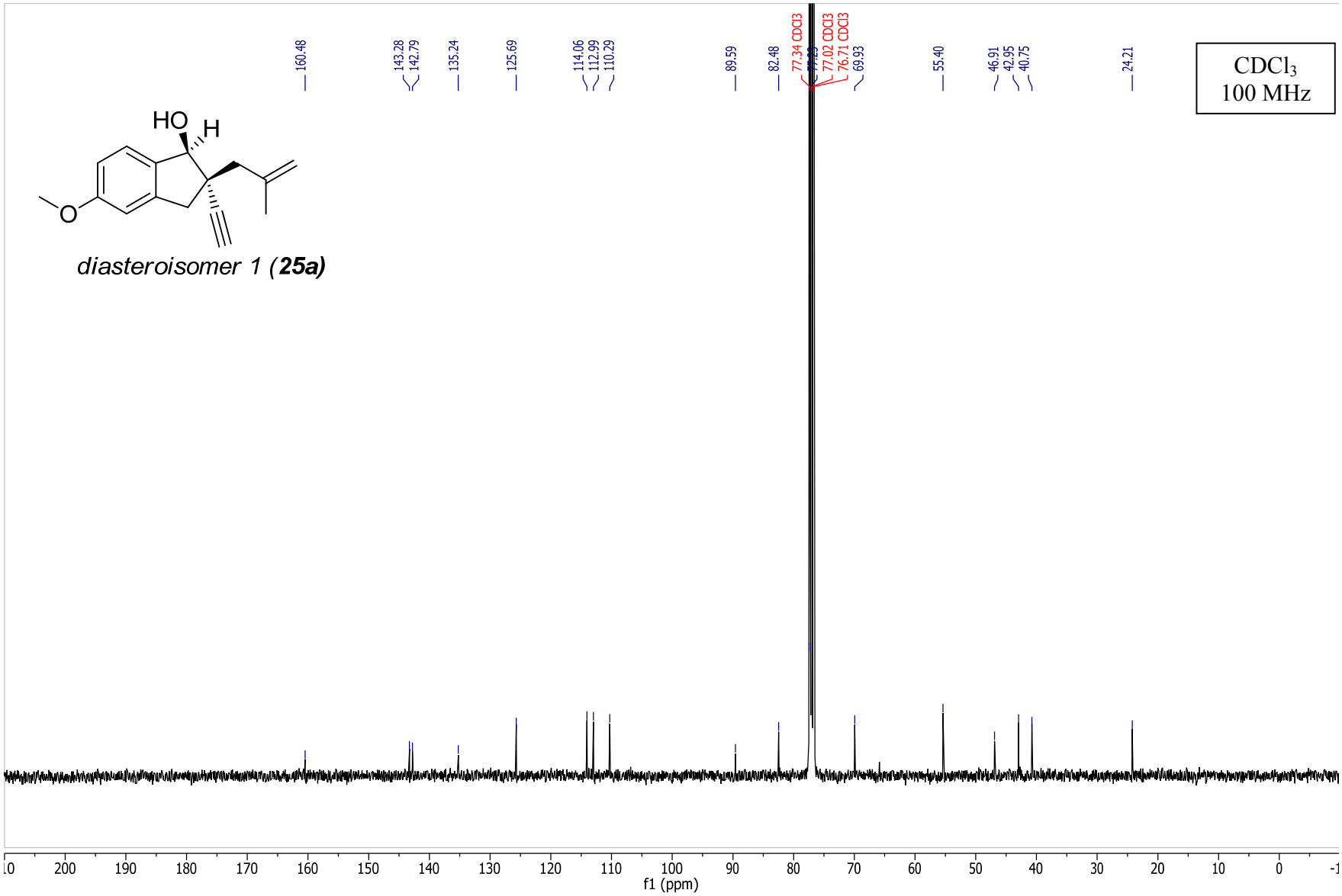
HSQC


8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f2 (ppm)
-40
-20
0
20
40
60
80
100
120
140
160
f1 (ppm)

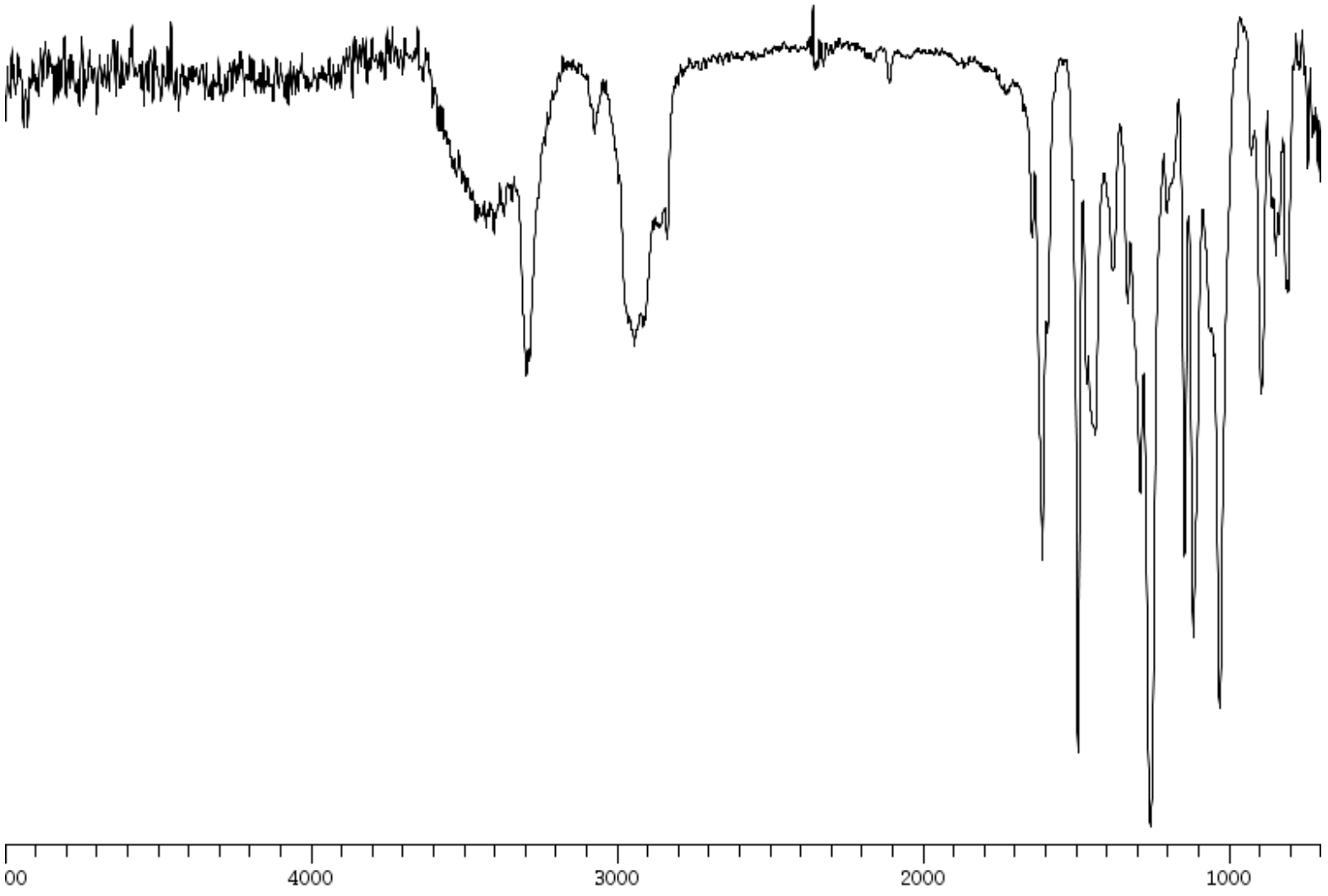
HMBC

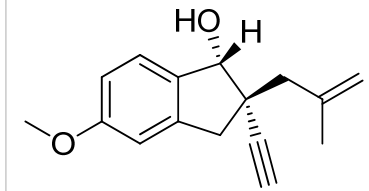

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f2 (ppm)
0
20
40
60
80
100
120
140
160
180
200
f1 (ppm)


HO
H
O
diasteroisomer 1 (25a)
CDCl3
CDCl3
400 MHz
0.90
1.12
0.94
0.90
0.90
0.82
3.01
1.00
0.94
0.94
0.98
0.85
2.73
0.16
f1 (ppm)

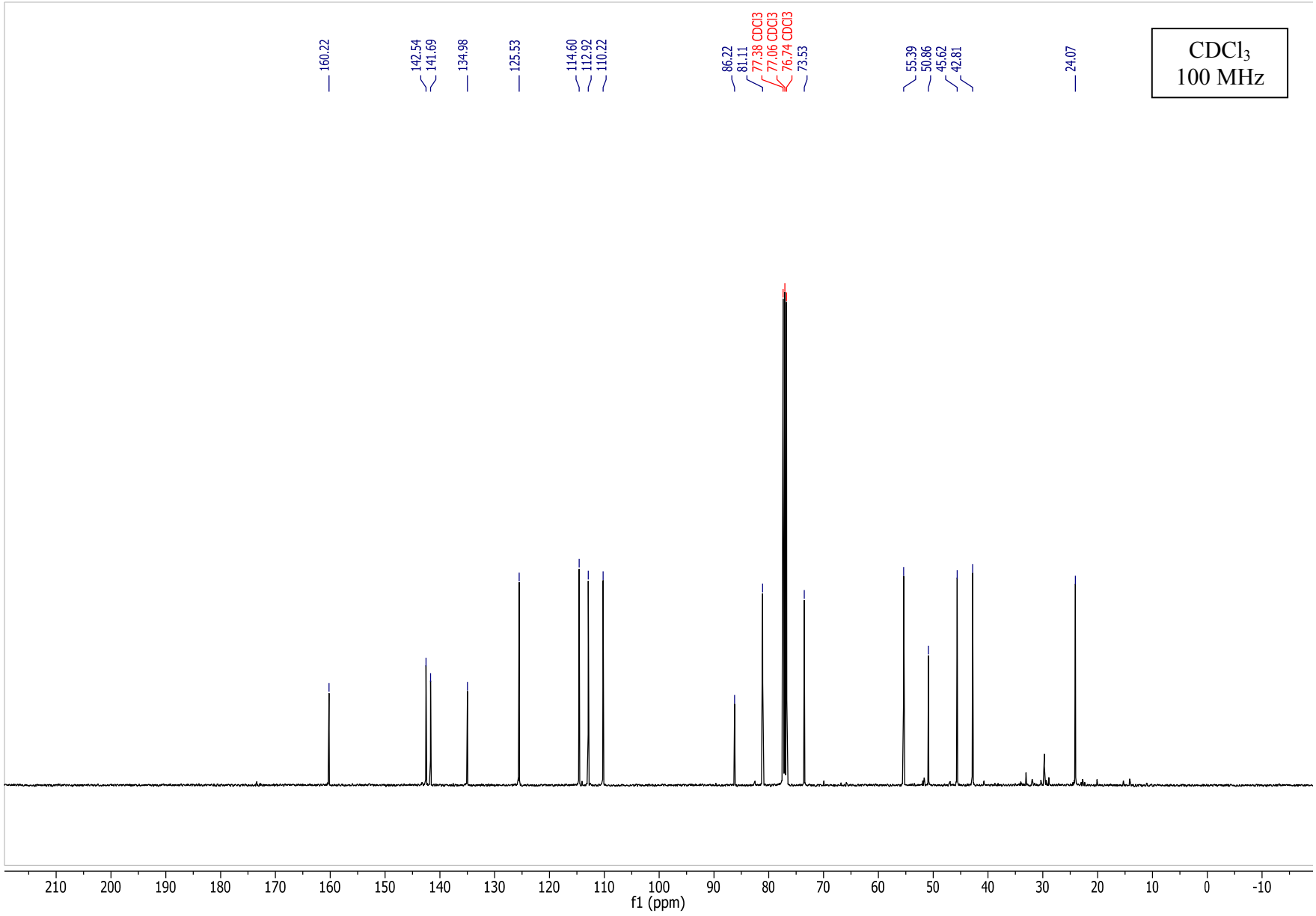


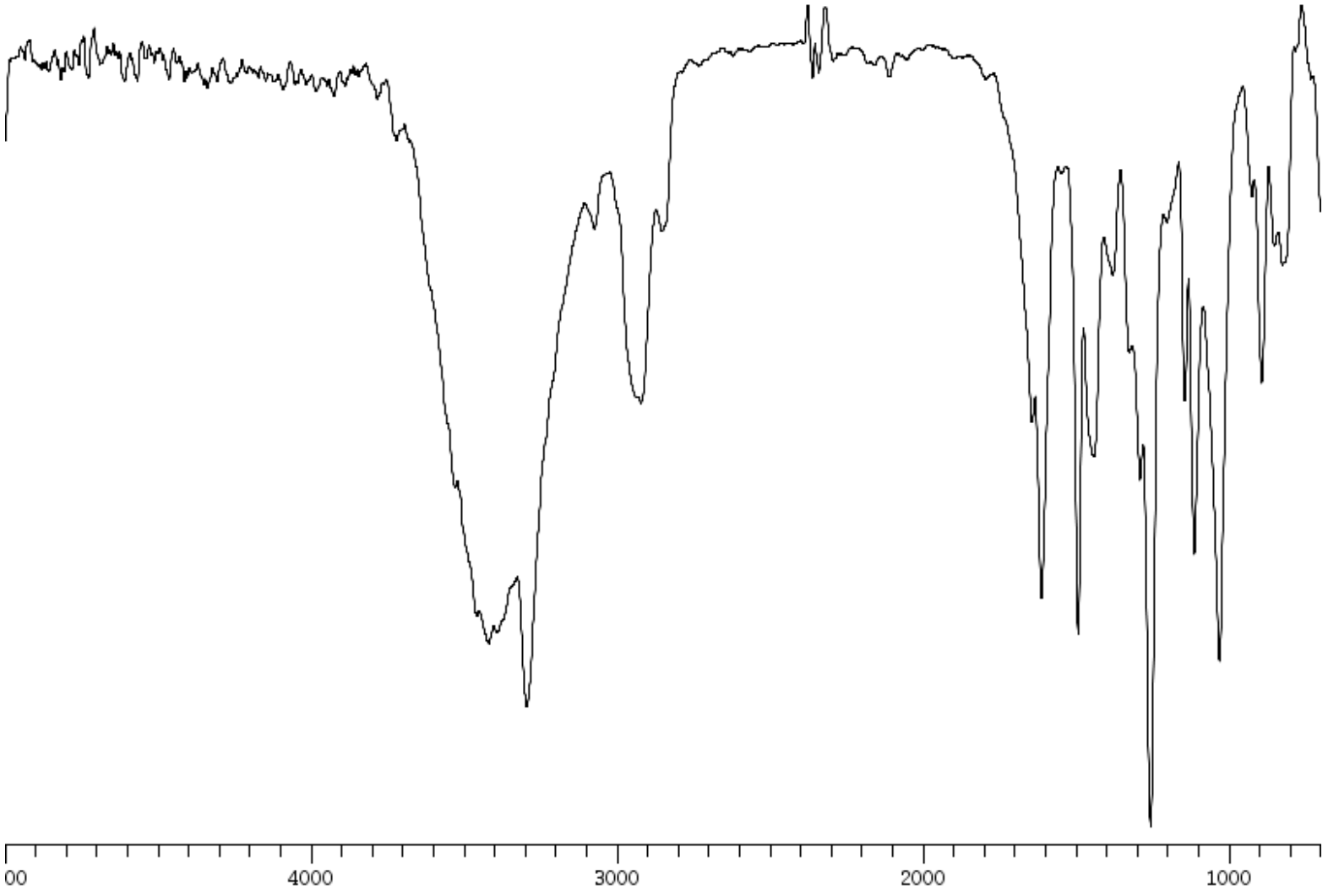
*diasteroisomer 1 (**25a**)*


00
4000
3000
2000
1000

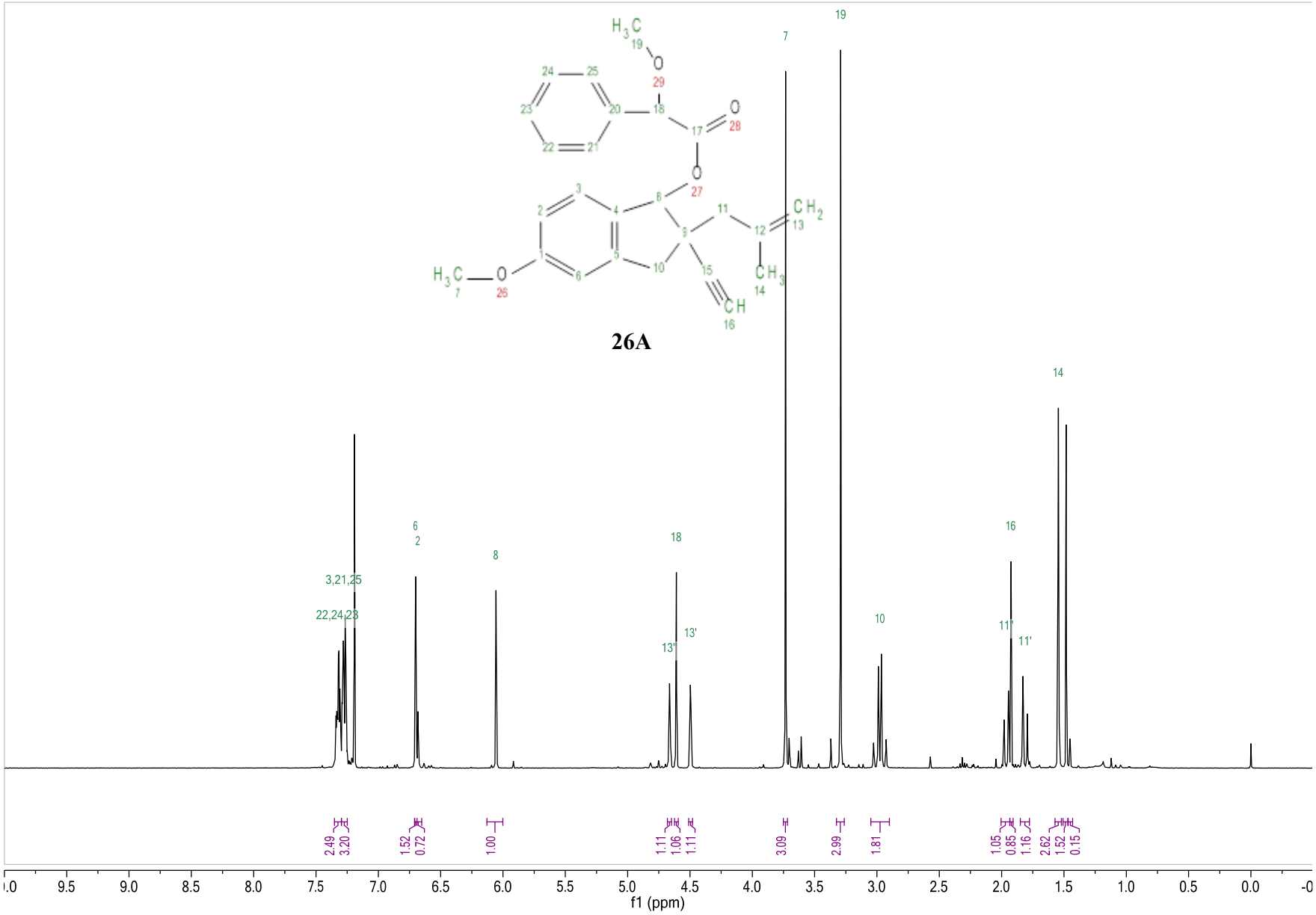


*diasteroisomer 2 (**25b**)*

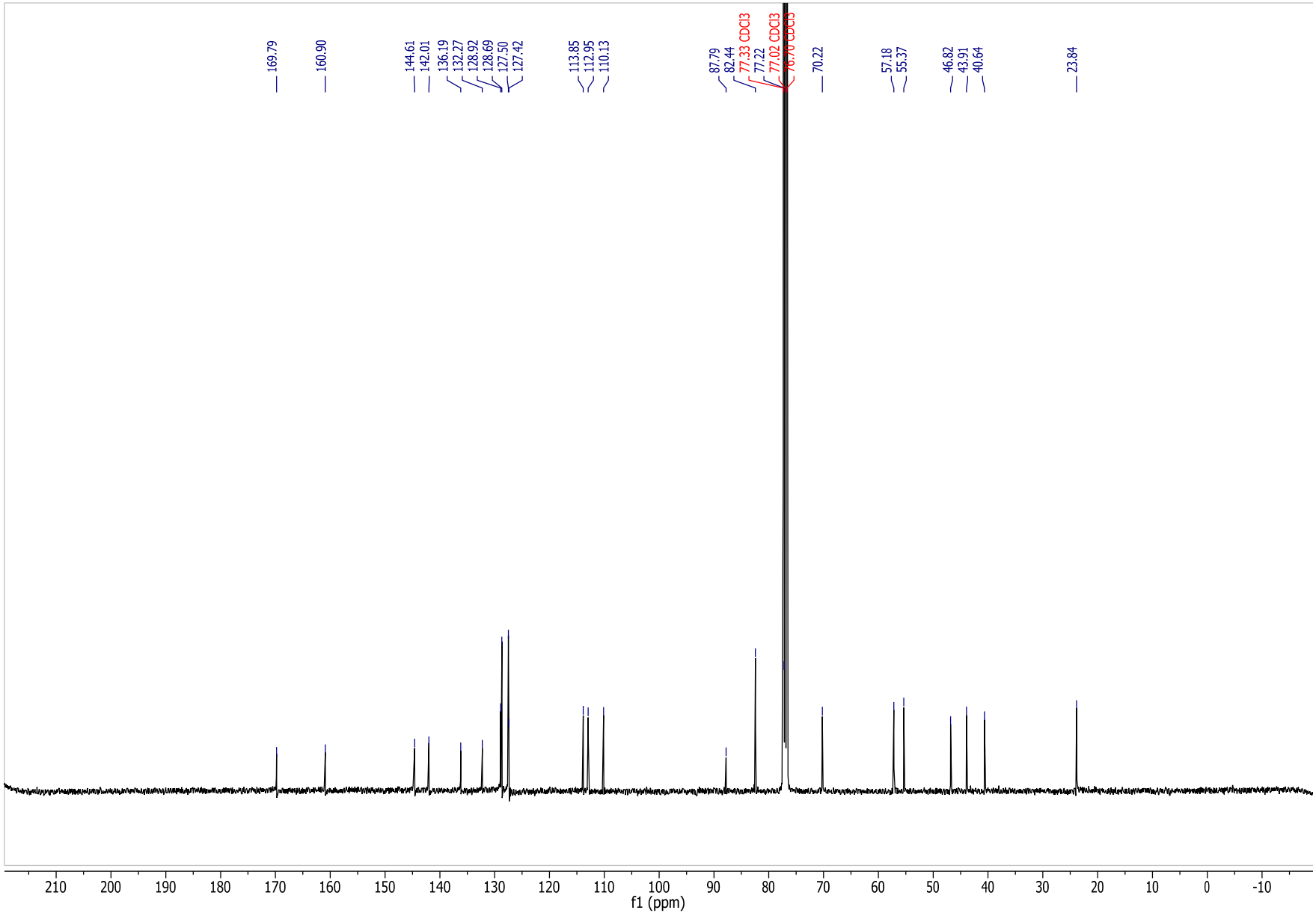

160.22
142.54
141.69
134.98
125.53
114.60
112.92
110.22
86.22
81.11
77.38 CDCl3
77.06 CDCl3
76.74 CDCl3
73.53
55.39
50.86
45.62
42.81
24.07
CDCl3
100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

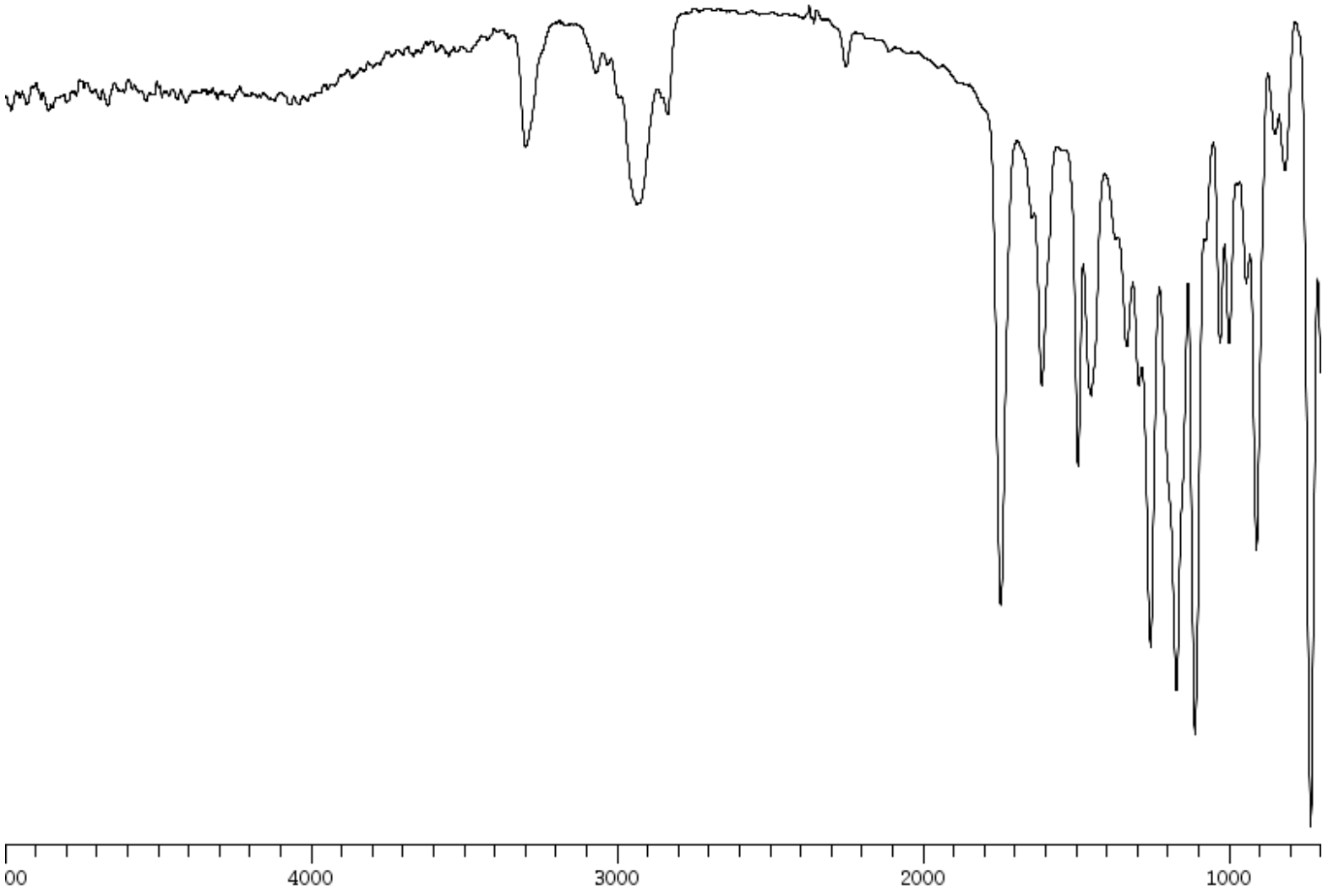

00
4000
3000
2000
1000

$CDCl_3$
400 MHz

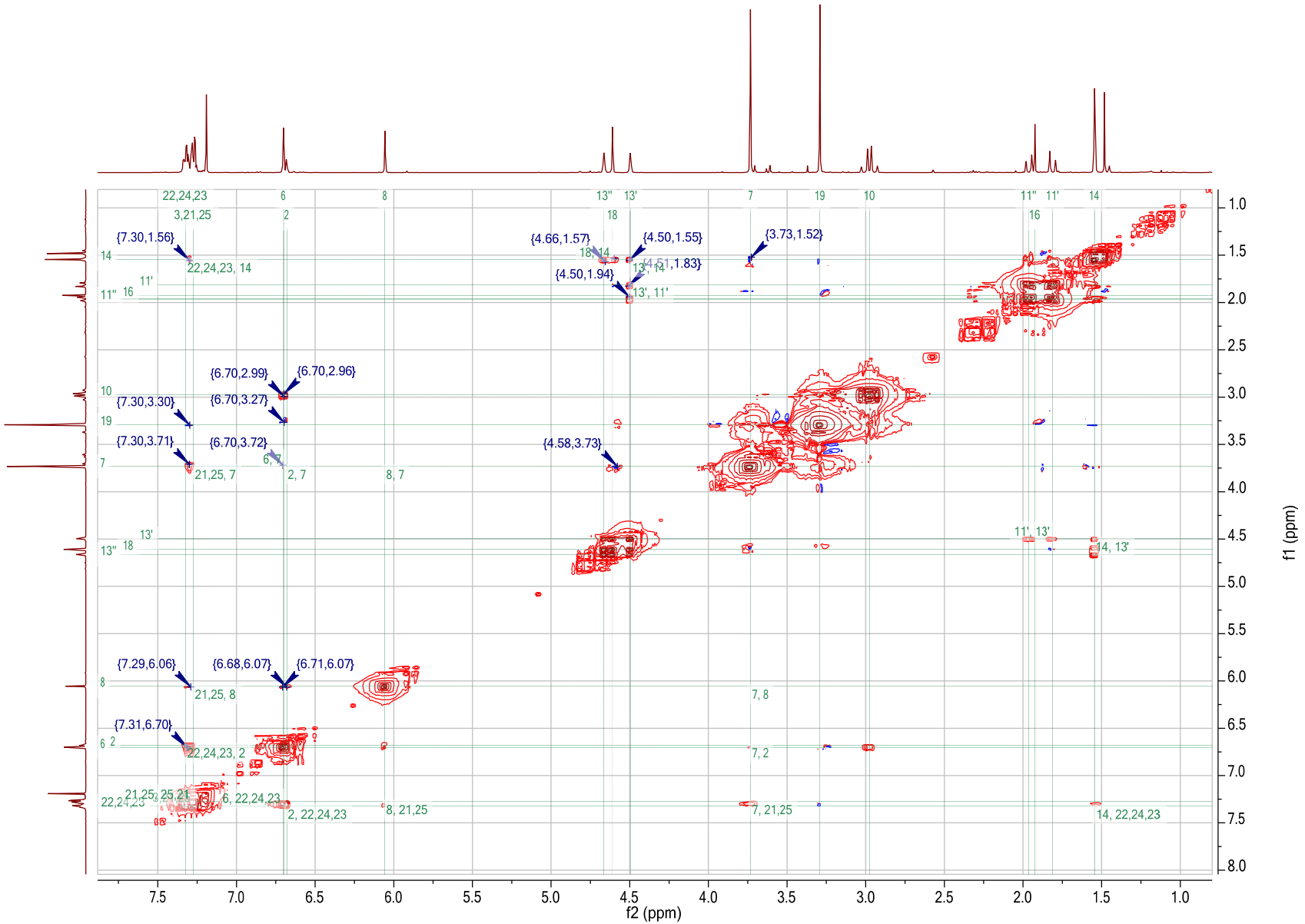


$CDCl_3$
100.1 MHz

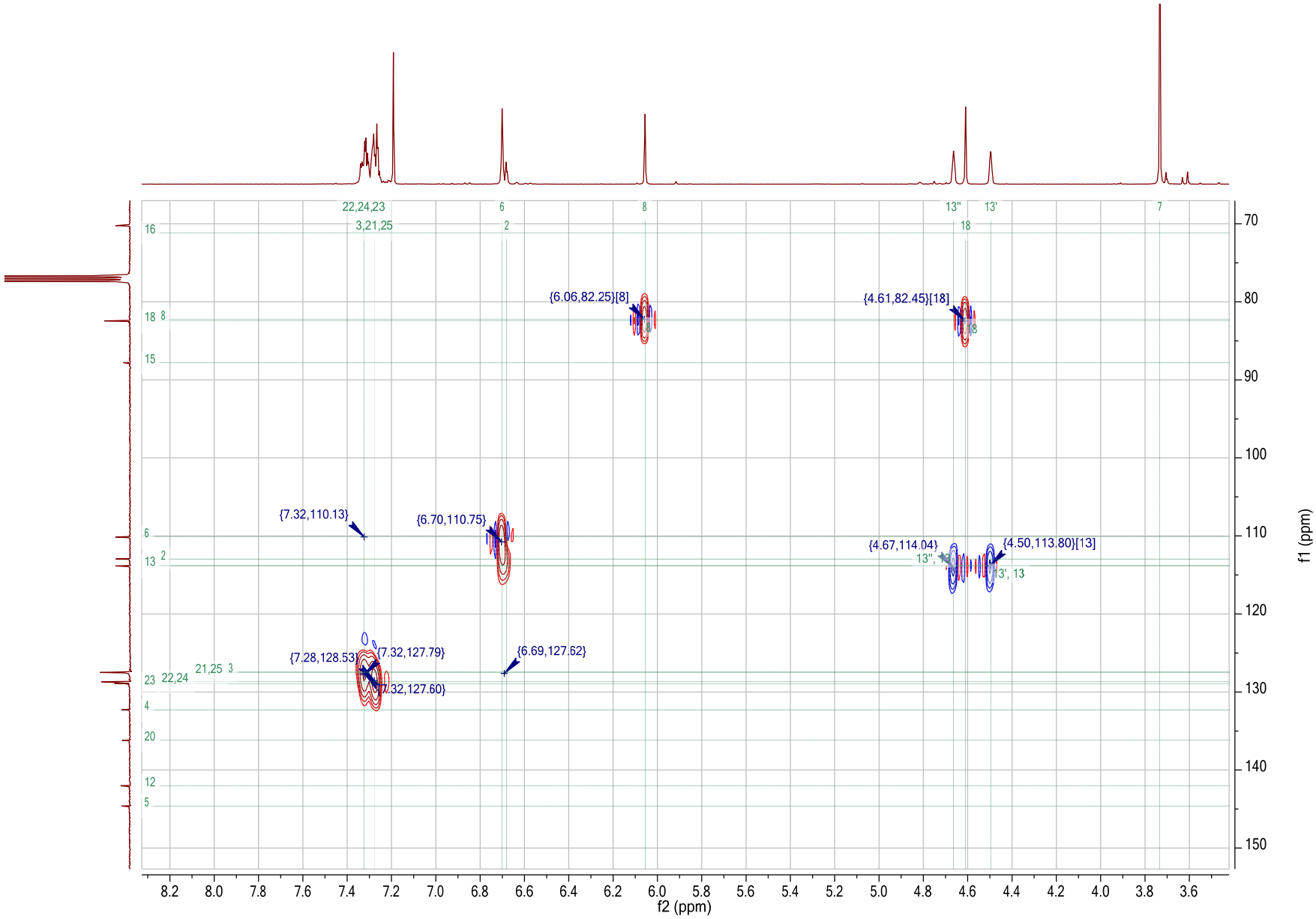



00
4000
3000
2000
1000

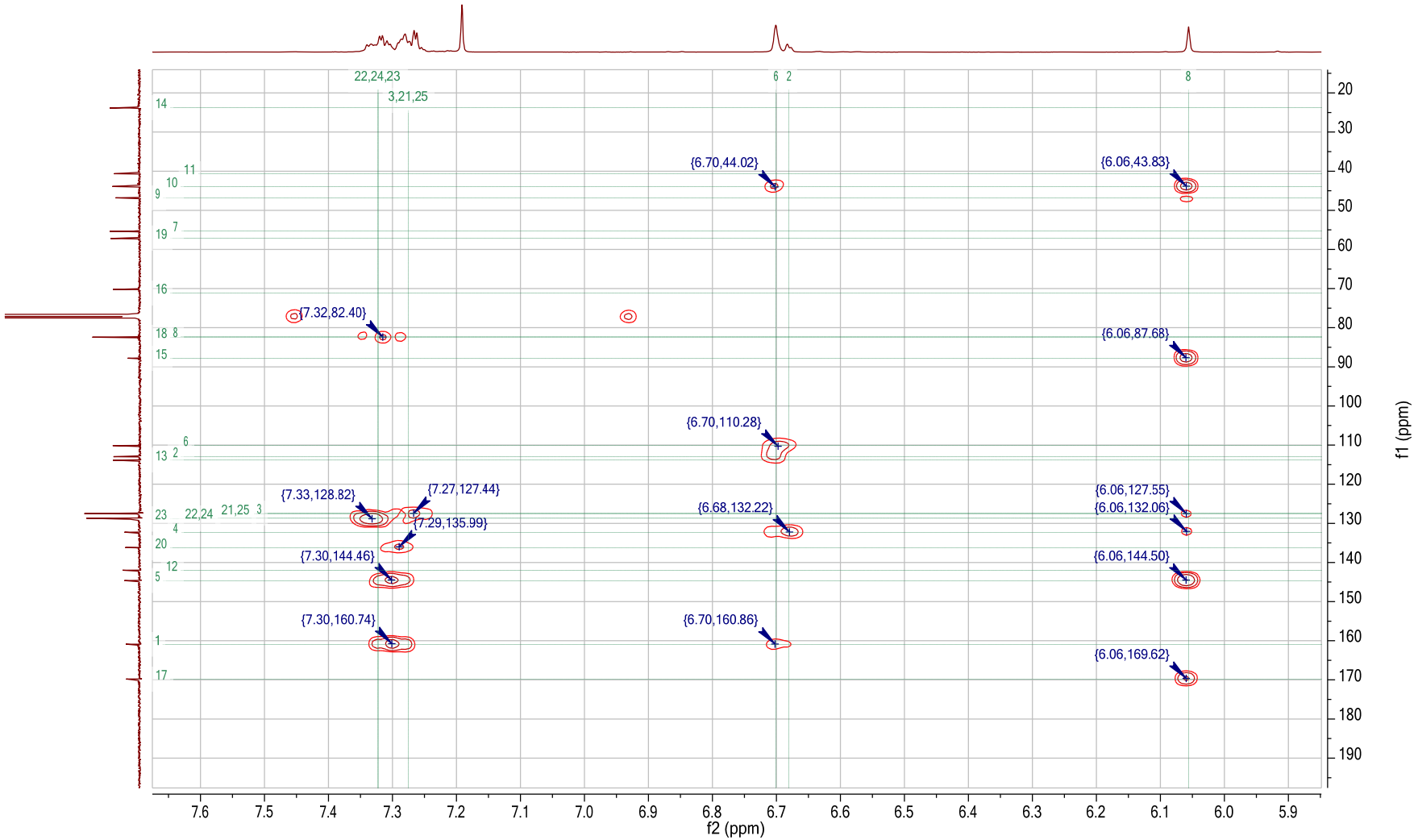
COSY

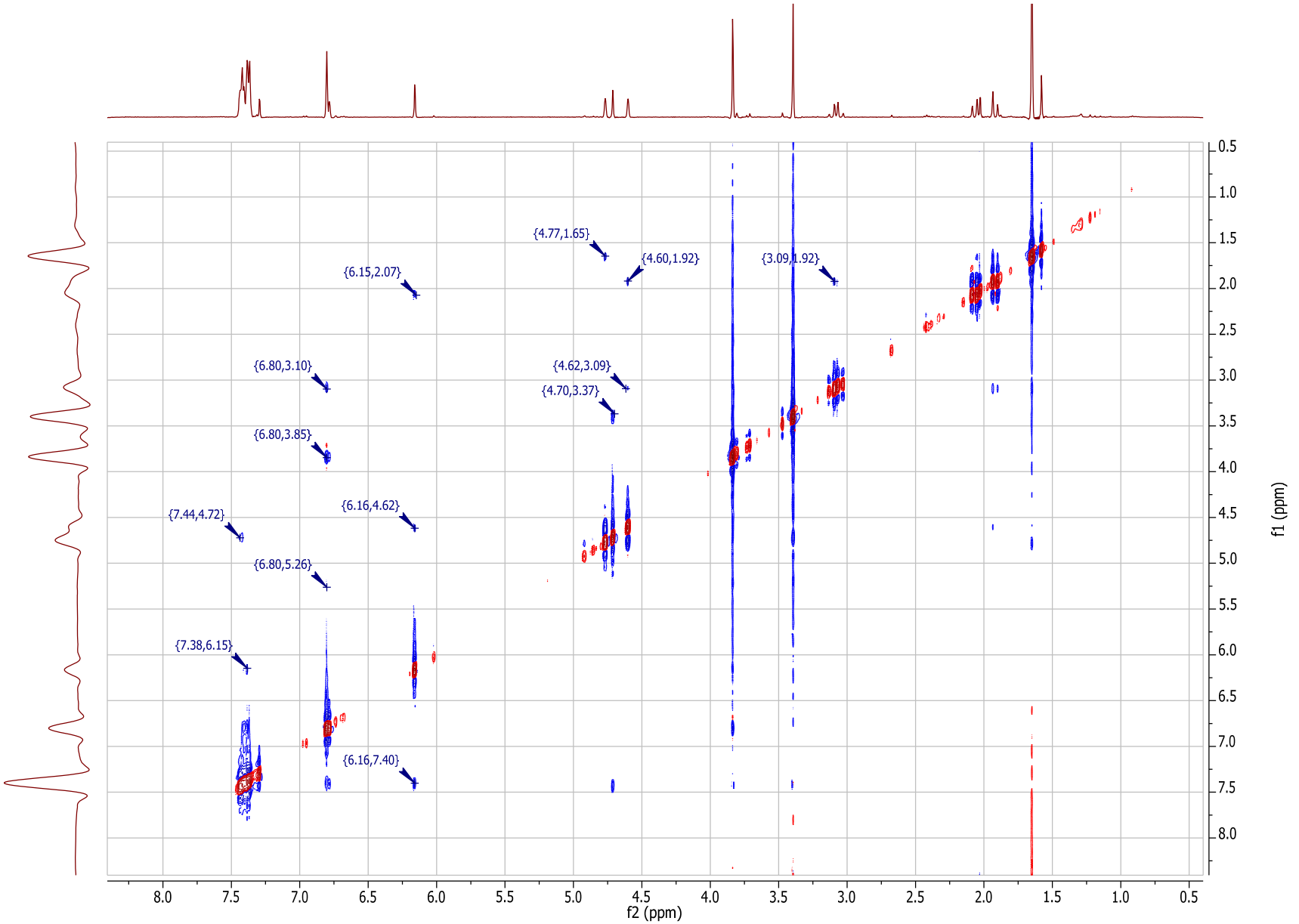

f2 (ppm)
f1 (ppm)
{7.30,1.56}
{4.66,1.57}
{4.50,1.55}
{3.73,1.52}
{4.50,1.94}
{6.70,2.99}
{6.70,2.96}
{7.30,3.30}
{6.70,3.27}
{7.30,3.71}
{6.70,3.72}
{4.58,3.73}
{7.29,6.06}
{6.68,6.07}
{6.71,6.07}
{7.31,6.70}

HSQC

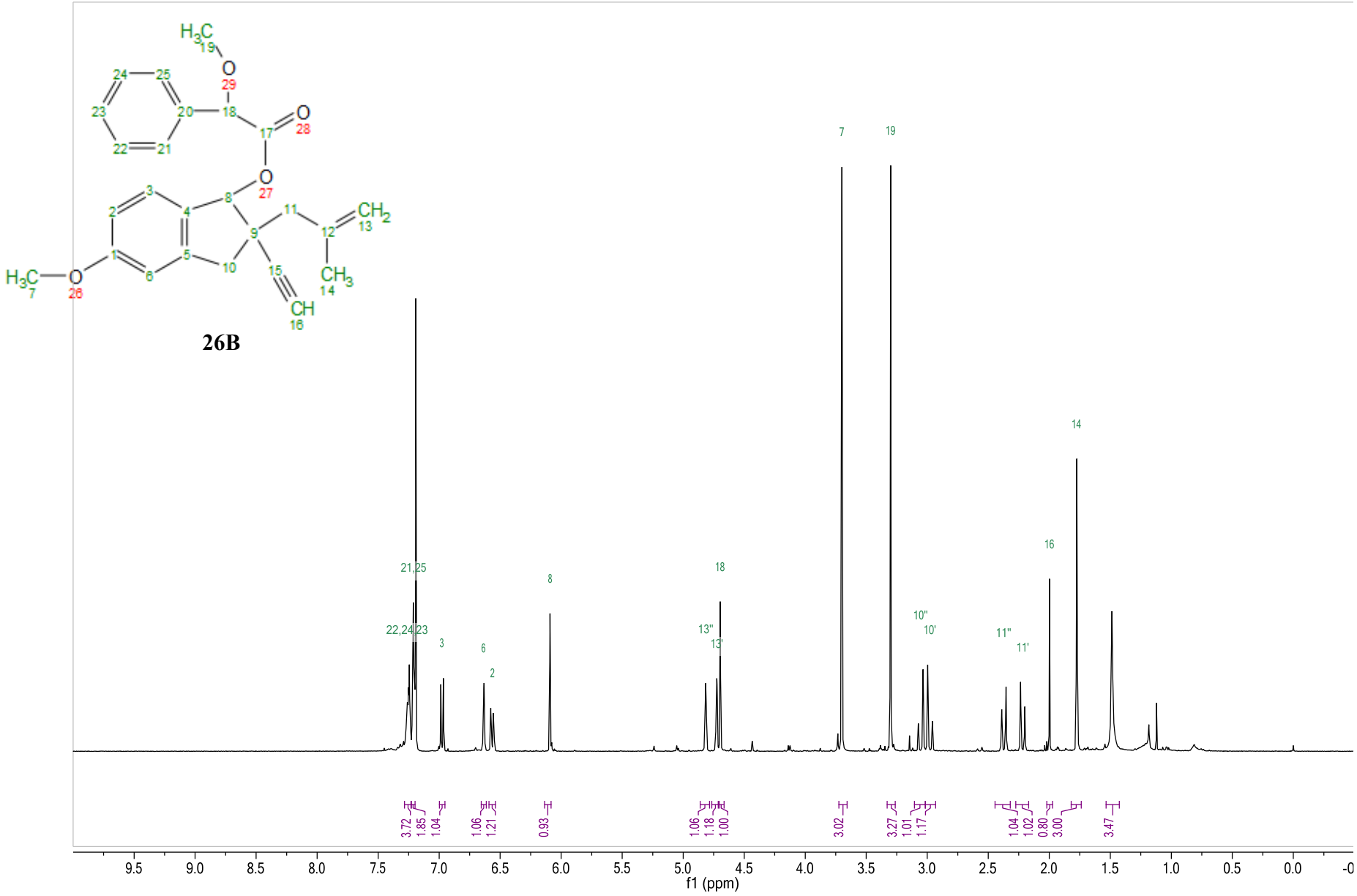

22,24,23
3,21,25
6
2
8
13''
13'
18
7
{6.06,82.25}[8]
{4.61,82.45}[18]
{7.32,110.13}
{6.70,110.75}
{4.67,114.04}
{4.50,113.80}[13]
13', 13
{7.28,128.53}
{7.32,127.79}
{6.69,127.62}
{7.32,127.60}
f2 (ppm)
f1 (ppm)

HMBC


22,24,23
3,21,25
6 2
8
{6.70,44.02}
{6.06,43.83}
{7.32,82.40}
{6.06,87.68}
{6.70,110.28}
{7.33,128.82}
{7.27,127.44}
{7.29,135.99}
{6.68,132.22}
{6.06,127.55}
{6.06,132.06}
{7.30,144.46}
{6.06,144.50}
{7.30,160.74}
{6.70,160.86}
{6.06,169.62}
22,24
21,25
f2 (ppm)
f1 (ppm)

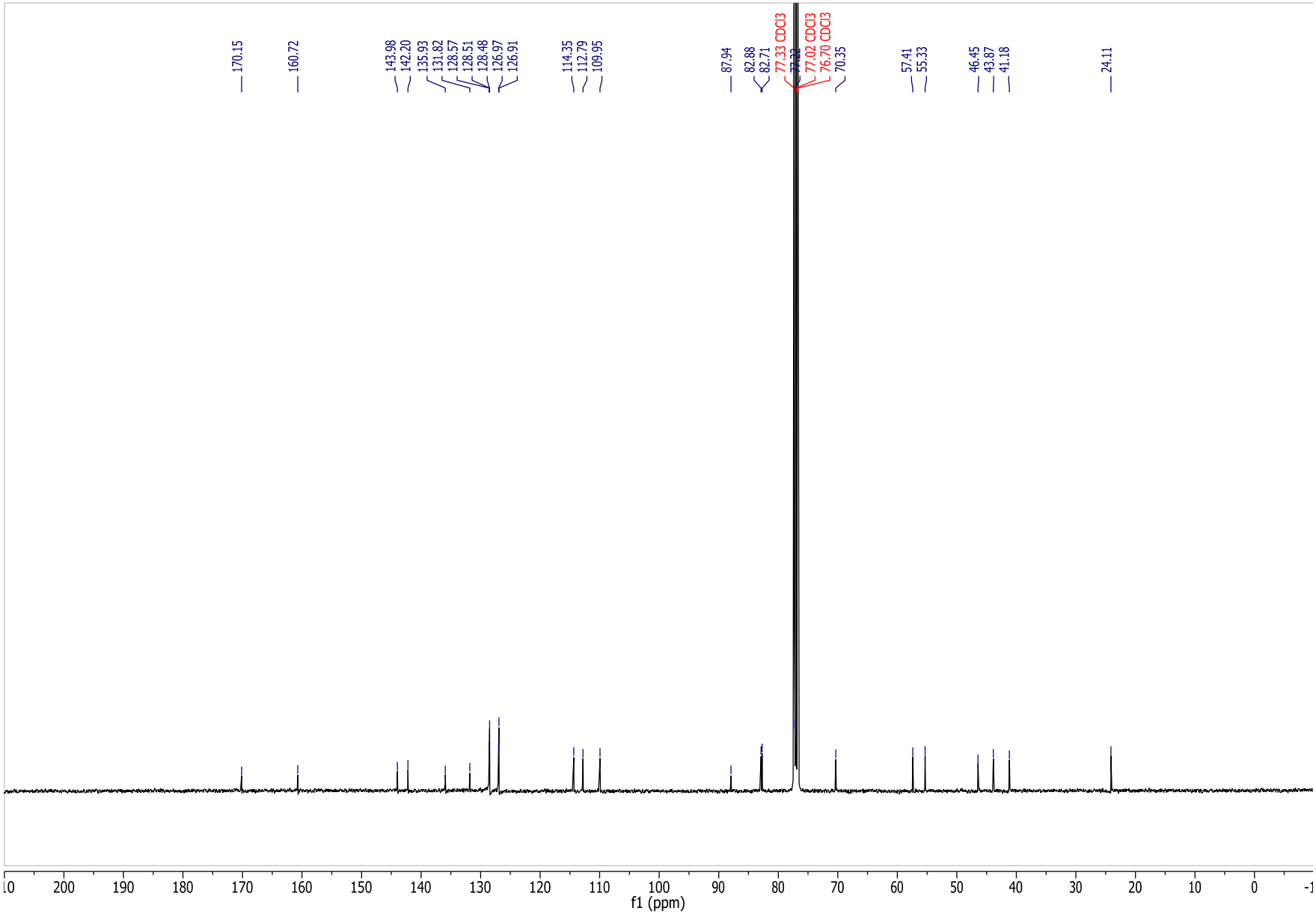

{4.77,1.65}
{4.60,1.92}
{3.09,1.92}
{6.15,2.07}
{6.80,3.10}
{4.62,3.09}
{4.70,3.37}
{6.80,3.85}
{6.16,4.62}
{7.44,4.72}
{6.80,5.26}
{7.38,6.15}
{6.16,7.40}
f2 (ppm)
f1 (ppm)

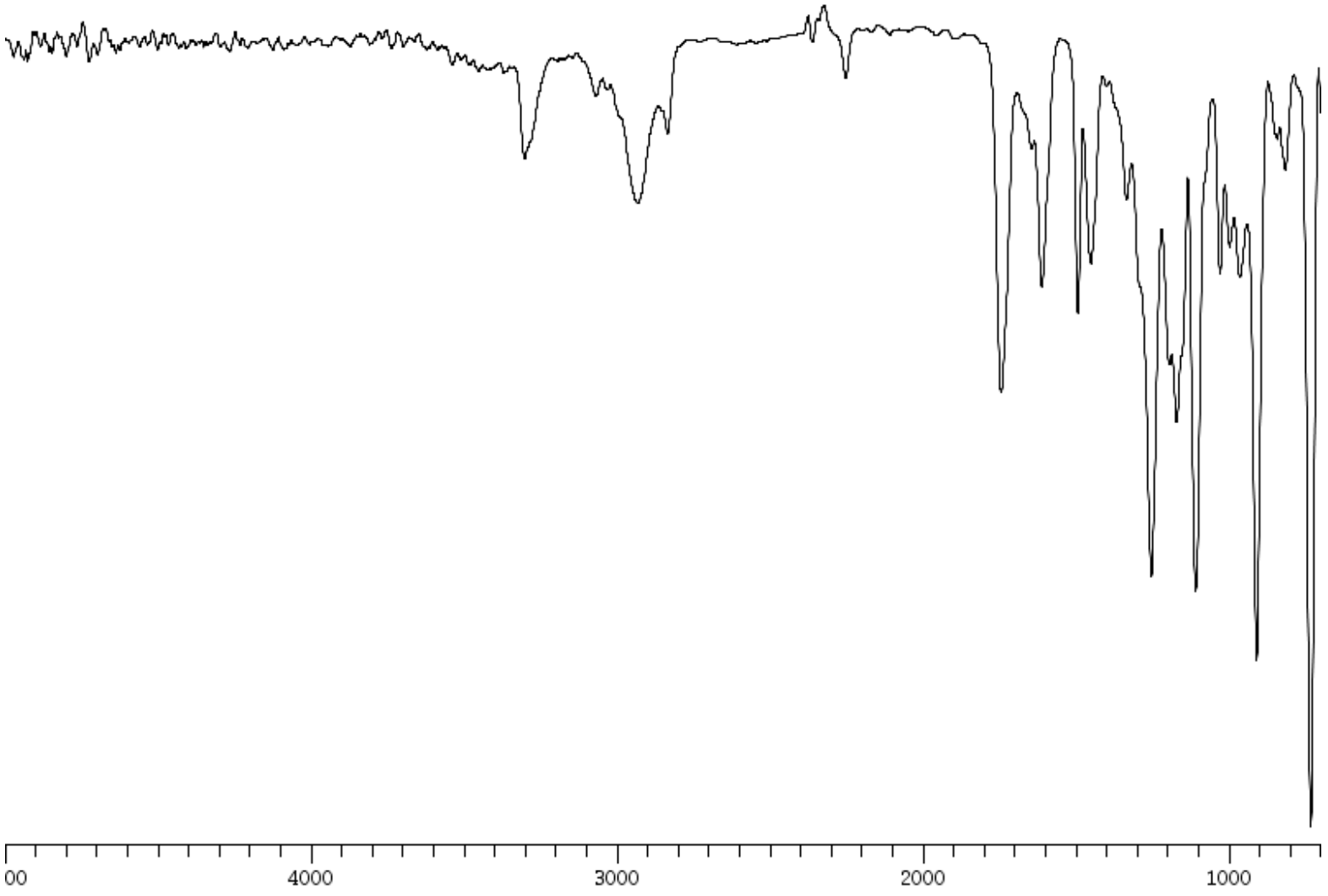
$CDCl_3$
400 MHz



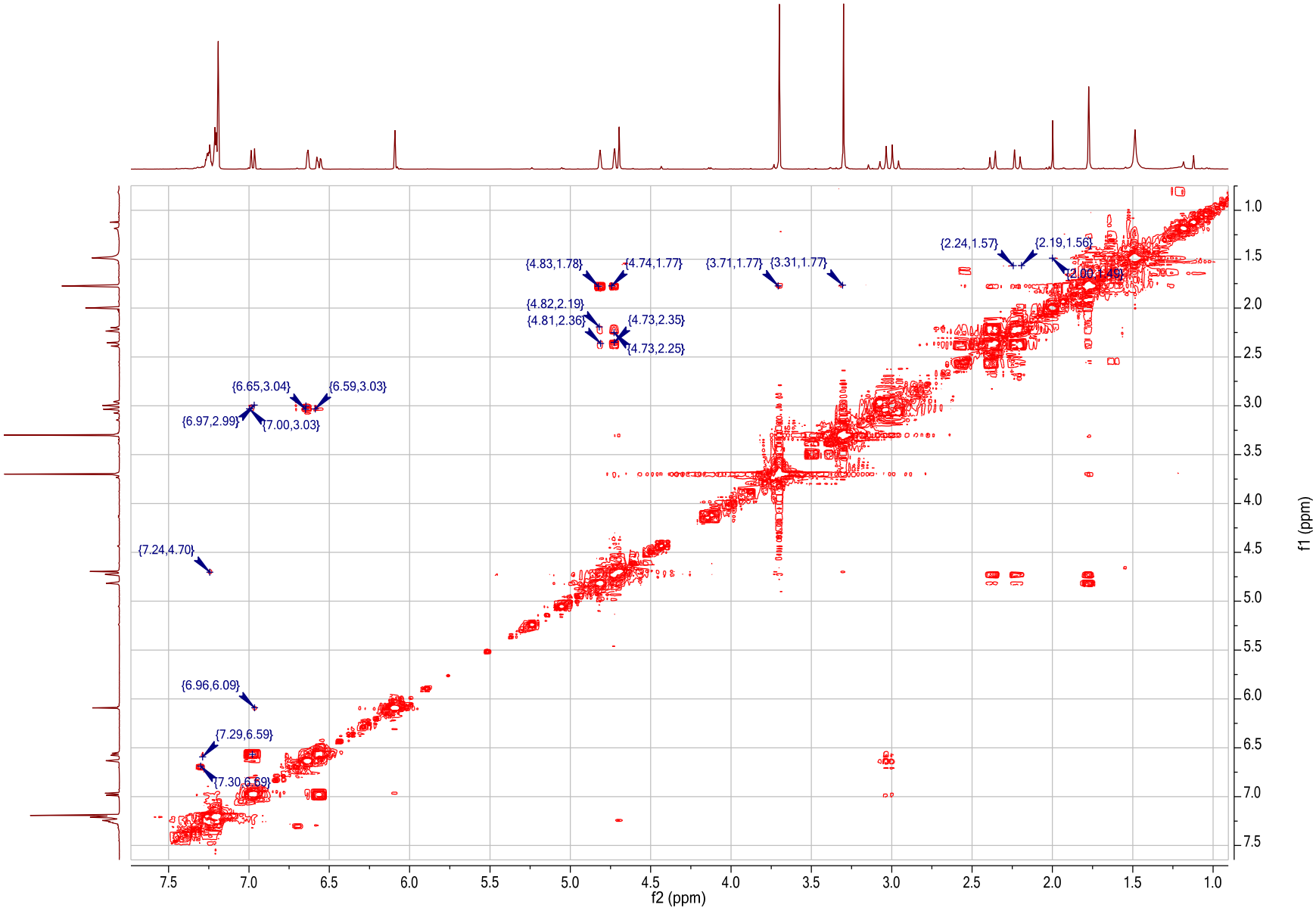
26B

$CDCl_3$
100.1 MHz

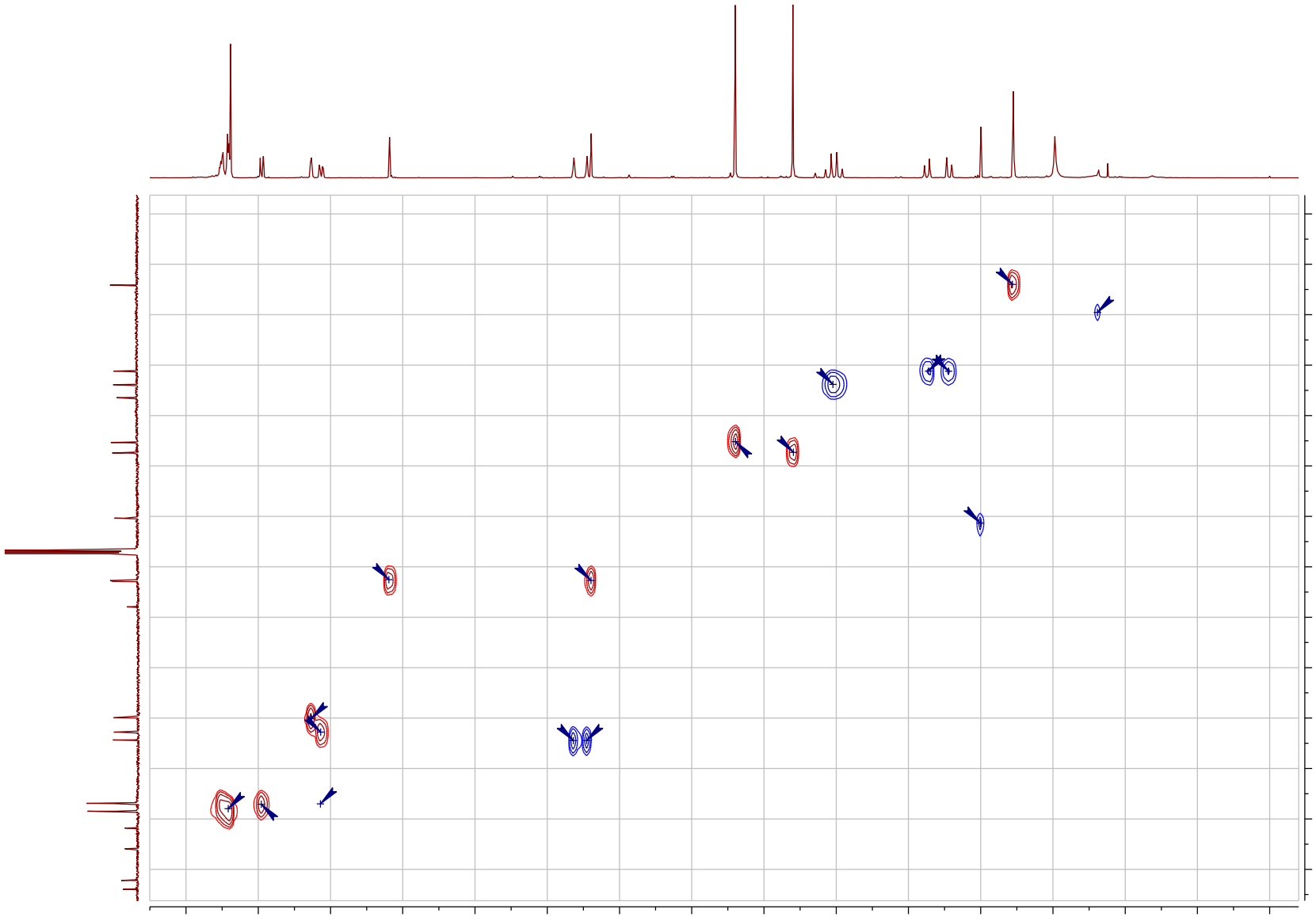



00
4000
3000
2000
1000

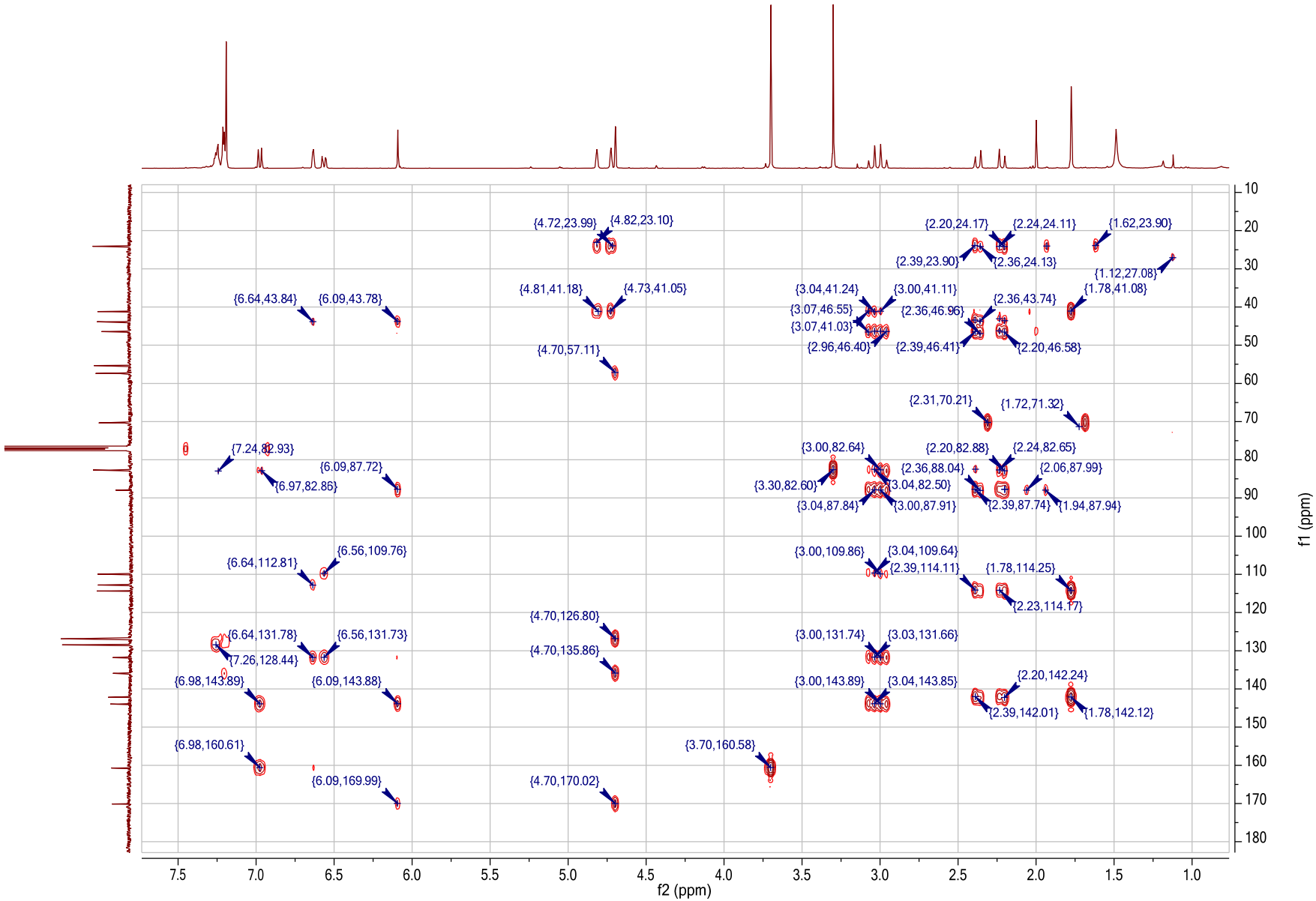
COSY


{4.83,1.78}
{4.74,1.77}
{3.71,1.77}
{3.31,1.77}
{2.24,1.57}
{2.19,1.56}
{2.00,1.49}
{4.82,2.19}
{4.81,2.36}
{4.73,2.35}
{4.73,2.25}
{6.65,3.04}
{6.59,3.03}
{6.97,2.99}
{7.00,3.03}
{7.24,4.70}
{6.96,6.09}
{7.29,6.59}
{7.30,6.59}
f2 (ppm)
f1 (ppm)

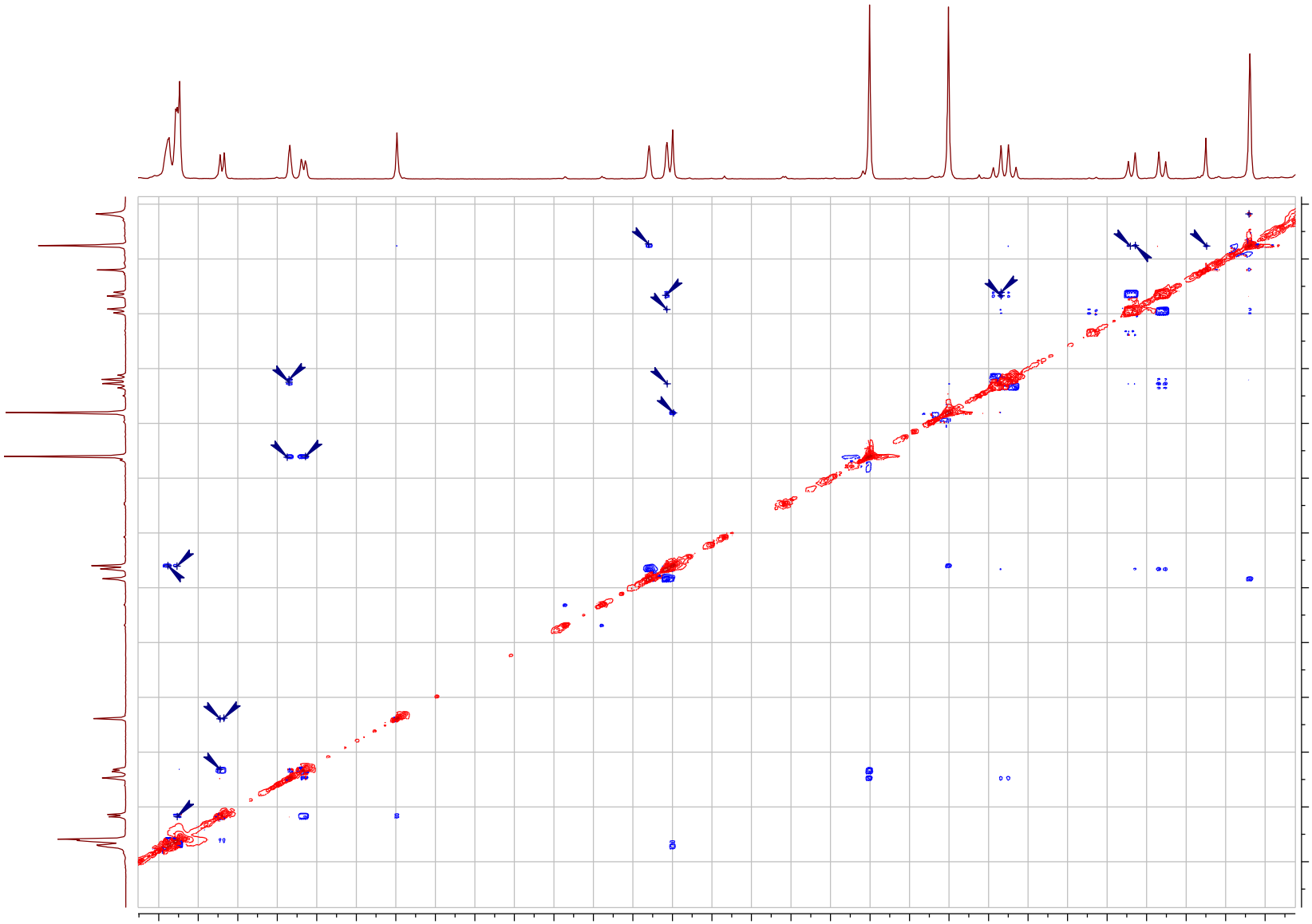
HSQC



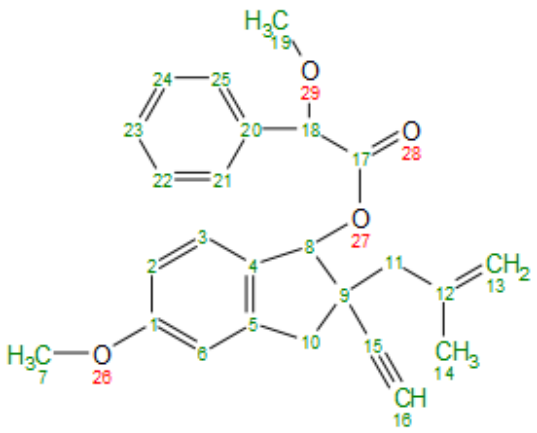
HMBC


{4.72,23.99}
{4.82,23.10}
{2.20,24.17}
{2.24,24.11}
{1.62,23.90}
{2.39,23.90}
{2.36,24.13}
{1.12,27.08}
{6.64,43.84}
{6.09,43.78}
{4.81,41.18}
{4.73,41.05}
{3.04,41.24}
{3.00,41.11}
{1.78,41.08}
{3.07,46.55}
{2.36,46.96}
{2.36,43.74}
{3.07,41.03}
{2.96,46.40}
{2.39,46.41}
{2.20,46.58}
{4.70,57.11}
{2.31,70.21}
{1.72,71.32}
{7.24,82.93}
{6.09,87.72}
{6.97,82.86}
{3.00,82.64}
{2.20,82.88}
{2.24,82.65}
{2.36,88.04}
{2.06,87.99}
{3.30,82.60}
{3.04,82.50}
{3.04,87.84}
{3.00,87.91}
{2.39,87.74}
{1.94,87.94}
{6.64,112.81}
{6.56,109.76}
{3.00,109.86}
{3.04,109.64}
{2.39,114.11}
{1.78,114.25}
{2.23,114.17}
{4.70,126.80}
{6.64,131.78}
{6.56,131.73}
{7.26,128.44}
{4.70,135.86}
{3.00,131.74}
{3.03,131.66}
{6.98,143.89}
{6.09,143.88}
{3.00,143.89}
{3.04,143.85}
{2.20,142.24}
{2.39,142.01}
{1.78,142.12}
{6.98,160.61}
{6.09,169.99}
{4.70,170.02}
{3.70,160.58}
f2 (ppm)
f1 (ppm)

NOESY

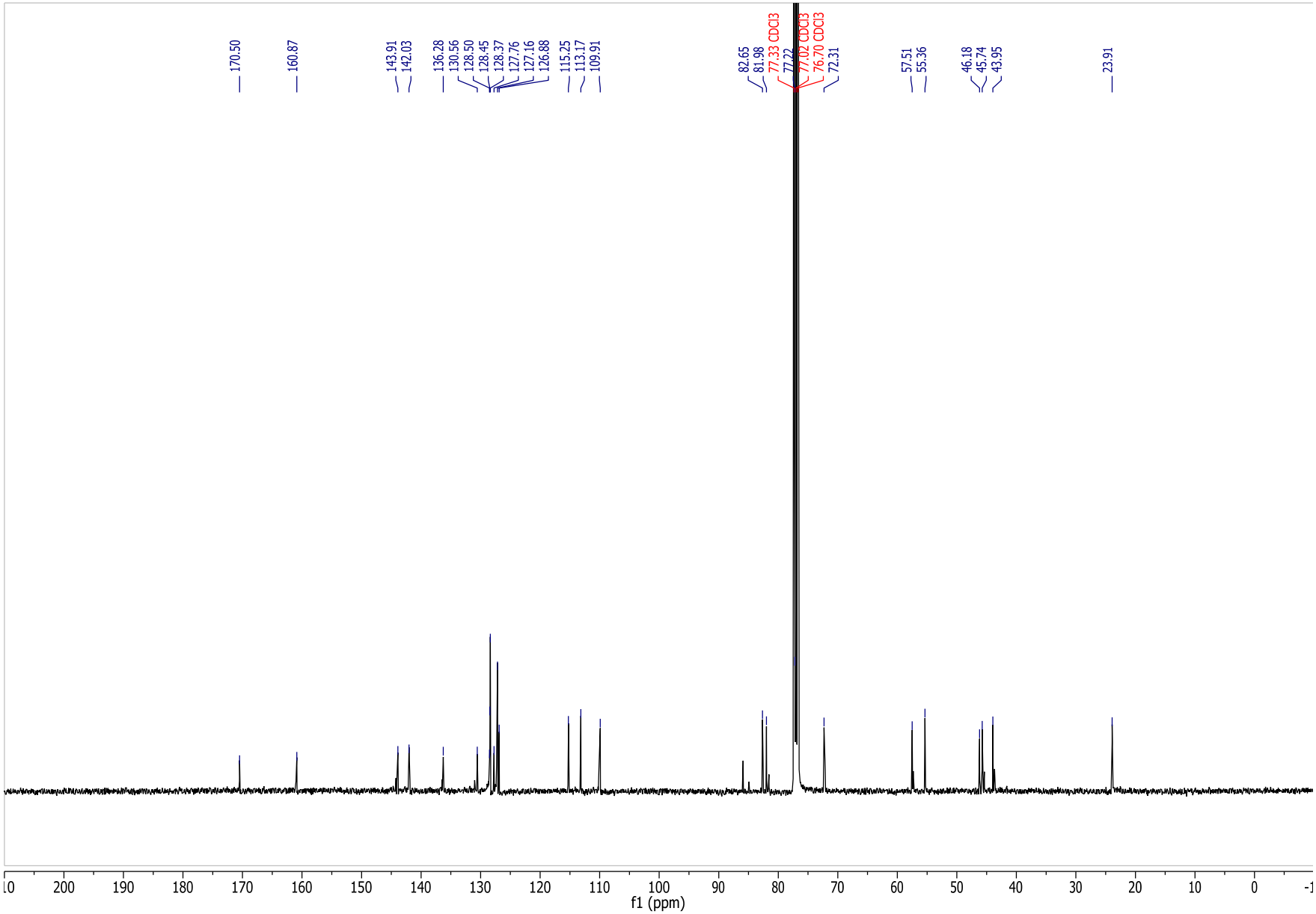


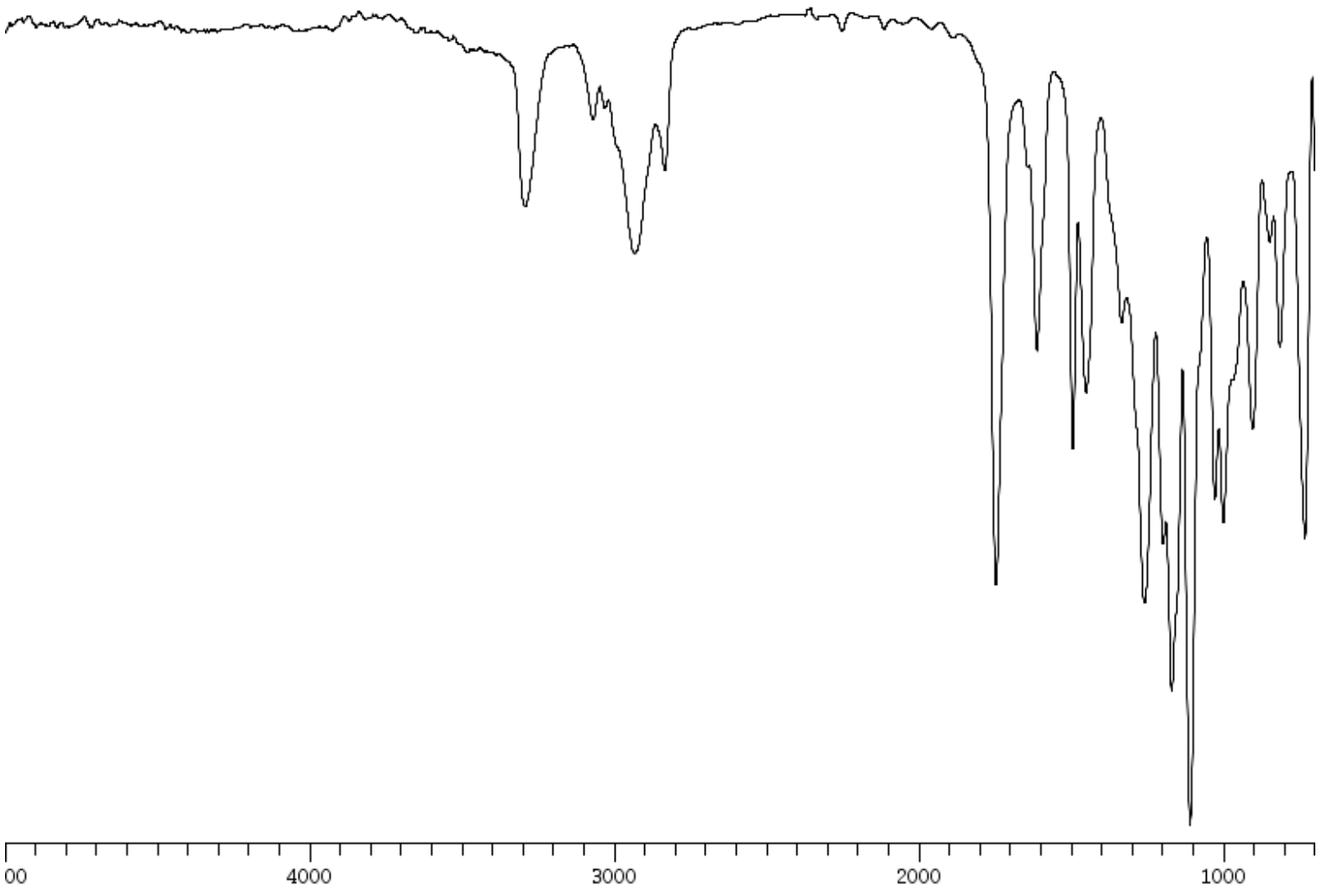
$CDCl_3$
400 MHz



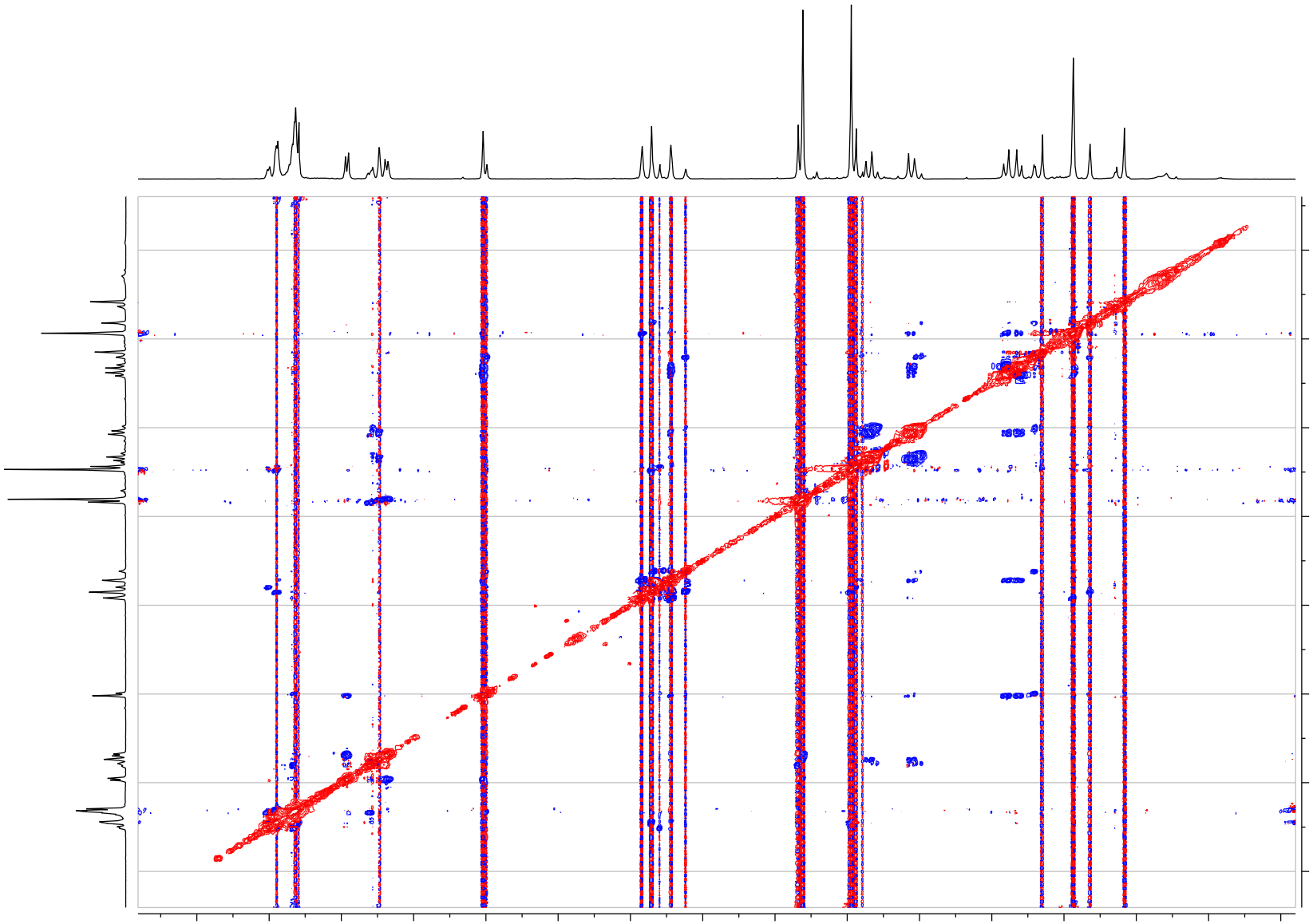
26C

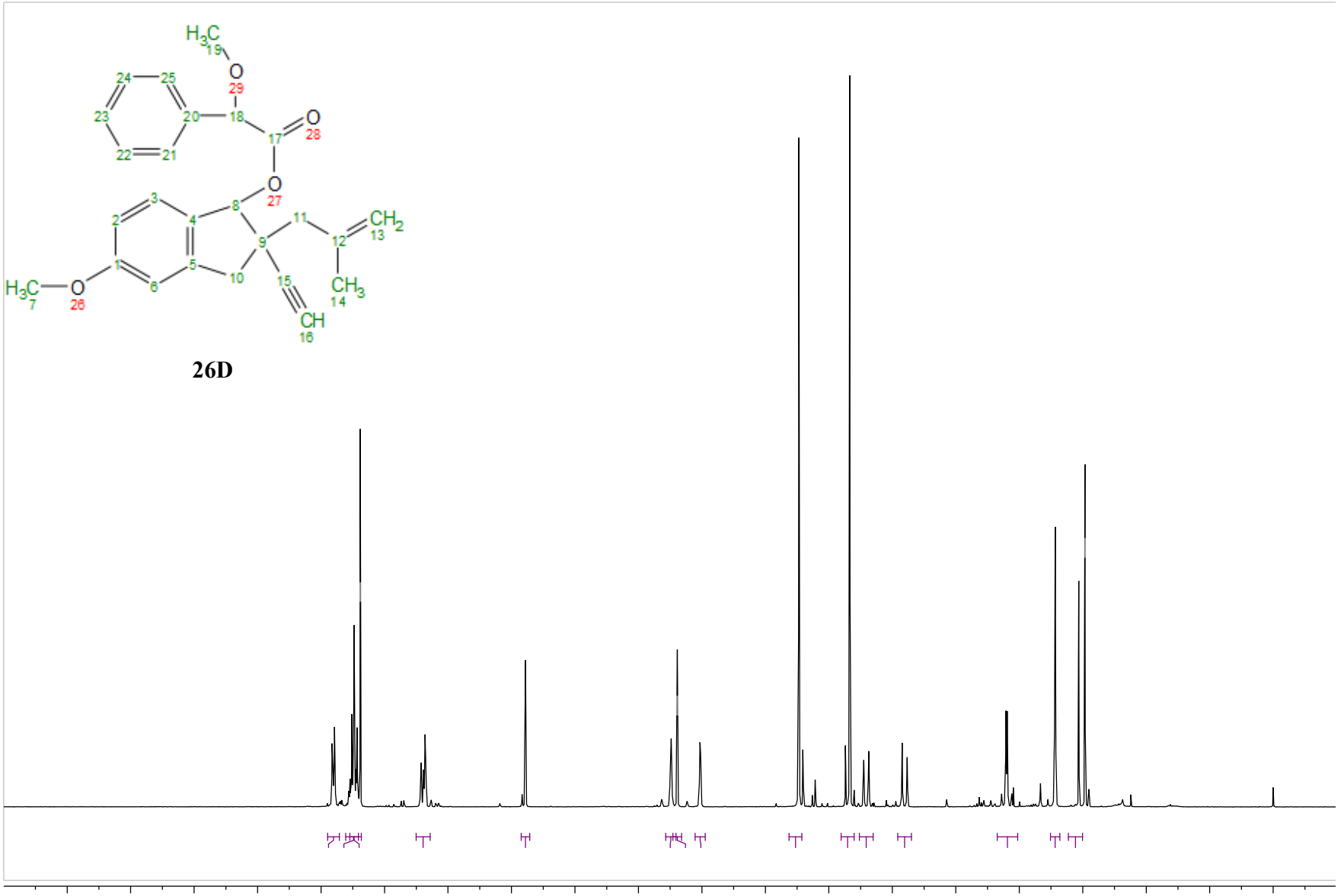
$CDCl_3$
100.1 MHz




00
4000
3000
2000
1000

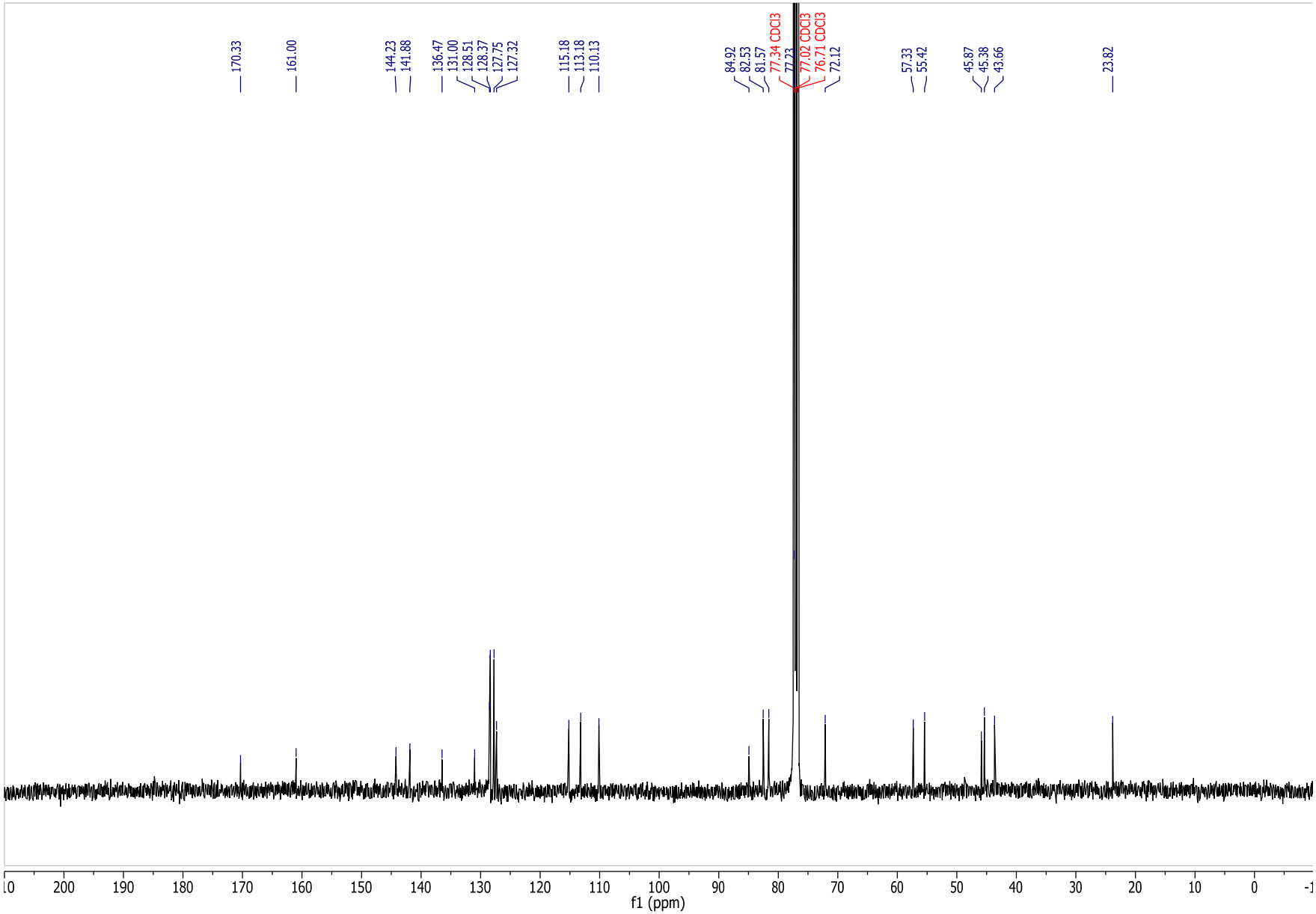
NOESY

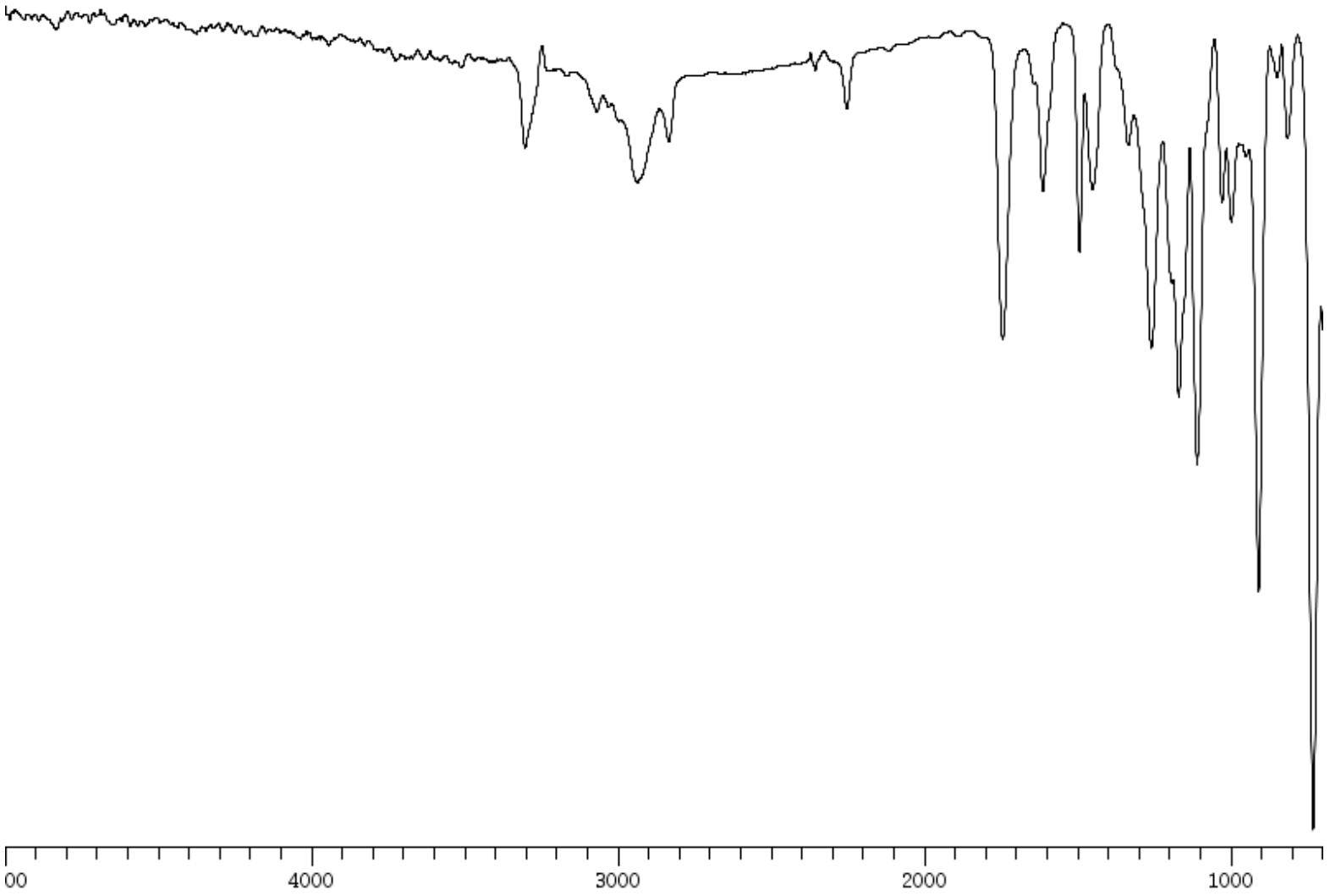



H3C
19
O
29
24
25
23
20
18
O
28
17
22
21
O
27
3
8
11
CH2
13
2
4
12
9
1
5
10
15
CH3
14
H3C
7
O
26
6
CH
16

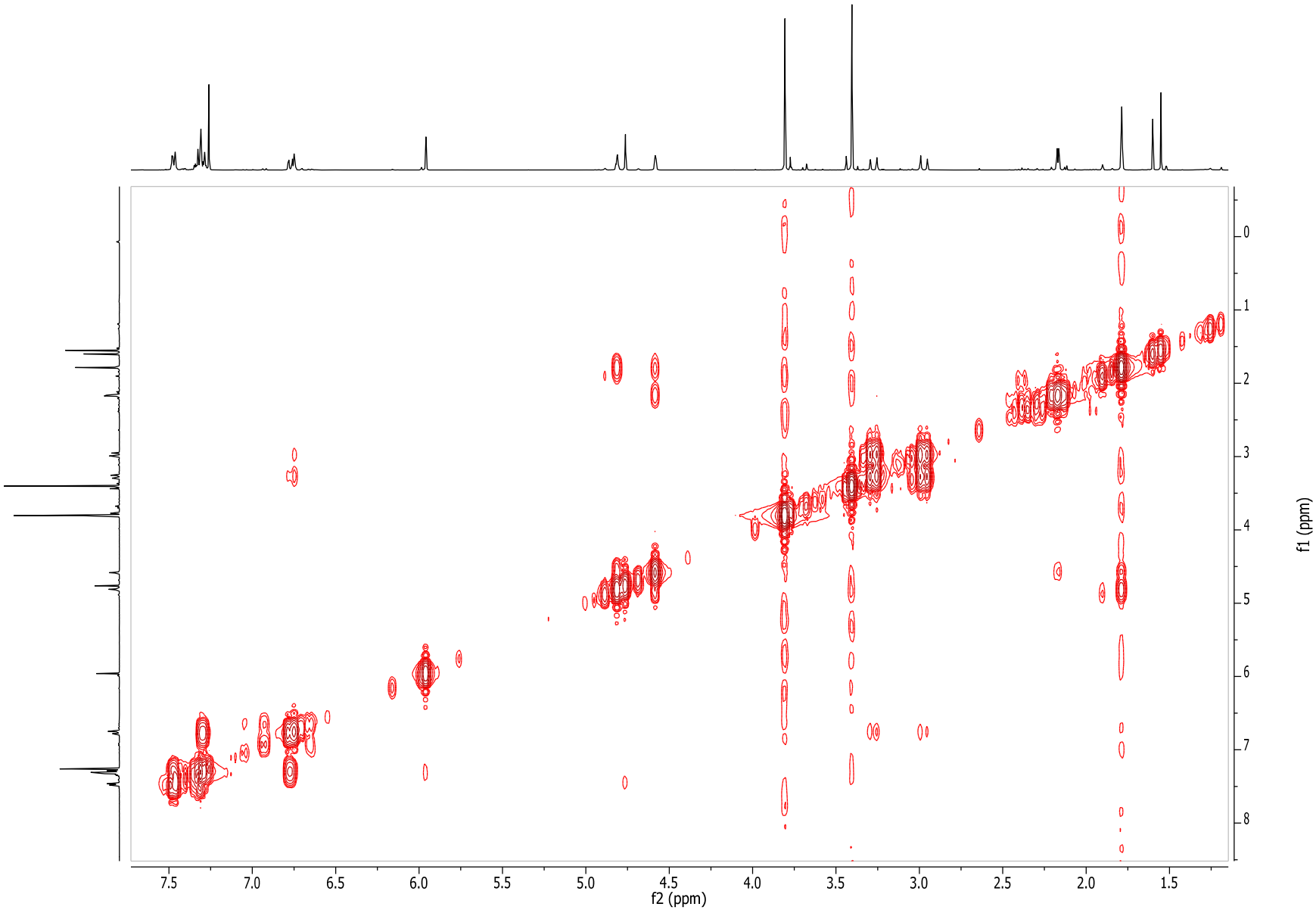
26D

$CDCl_3$
100.1 MHz




00
4000
3000
2000
1000

COSY



NOESY