# Radical-Mediated Reactions Involving Fluorinated Reagents and Sulfones

Inaugural dissertation
of the Faculty of Science,
University of Bern

presented by

Gulsana Sissengaliyeva

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Supervisor of the doctoral thesis:
Prof. Dr. Philippe Renaud

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Accepted by the Faculty of Science.

Bern, **19.07.2024**

The Dean
Prof. Dr. Marco Herwegh

“Ғылымды, ақылды сақтайтұғын мінез деген сауыт болады.”

Абай Құнанбайұлы

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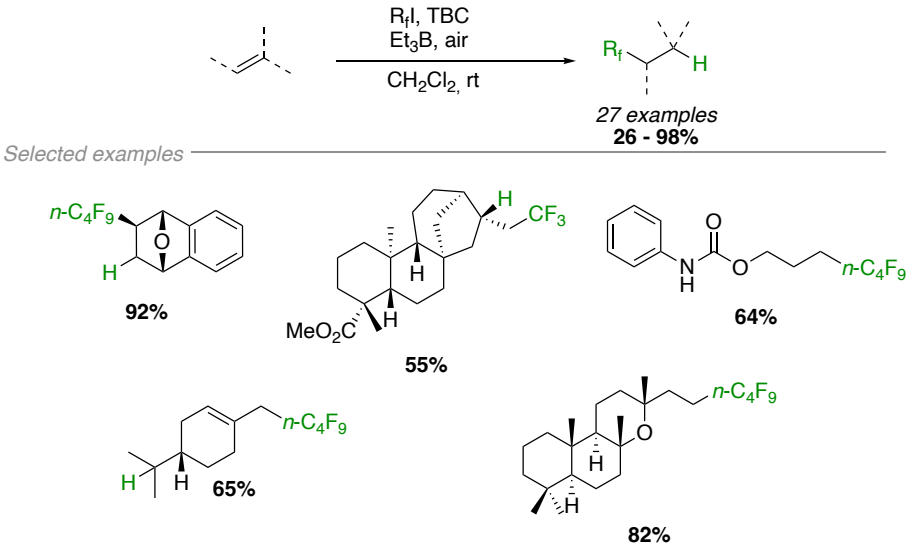
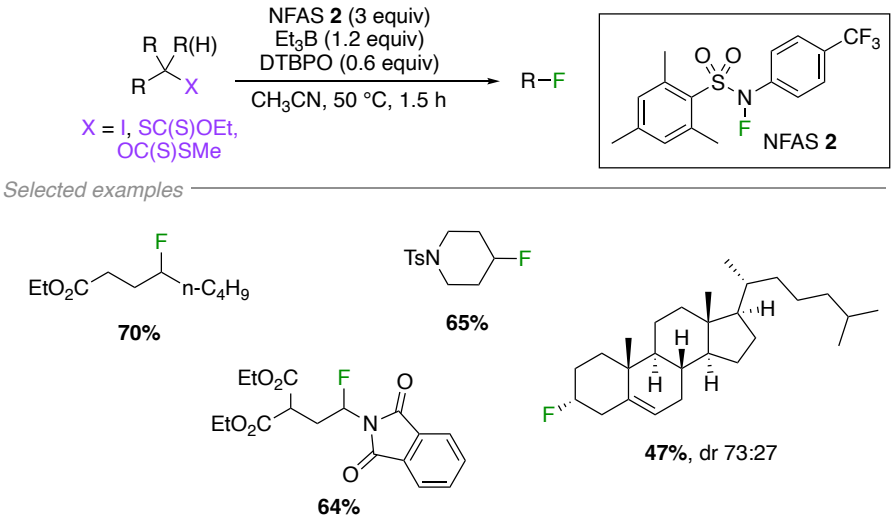
# Abstract

Fluorinated compounds hold significant importance across medicinal, agrochemical, and materials chemistry due to their unique impact on the properties of drug candidates. In this context, the first part of the thesis was dedicated to hydroperfluoroaklylation of unactivated alkenes. This is due to a strong demand for selective, general, and efficient techniques to incorporate trifluoromethyl and other perfluoroalkyl groups into compounds. The direct hydroperfluoroalkylation of various unactivated alkenes, including isoprenoid natural products, has been successfully performed. The process occurs at room temperature using commercially available iodoperfluoroalkanes, with 4-*tert*-butylcatechol as the hydrogen atom source and triethylborane (Scheme 1). Additionally, hydrotrifluoromethylation was achieved under similar conditions using gaseous trifluoromethyl iodide, and a straightforward two-step, one-pot hydrotrifluoromethylation method has also been developed using trifluoromethanesulfonyl chloride, which is a convenient source of trifluoromethyl radicals.



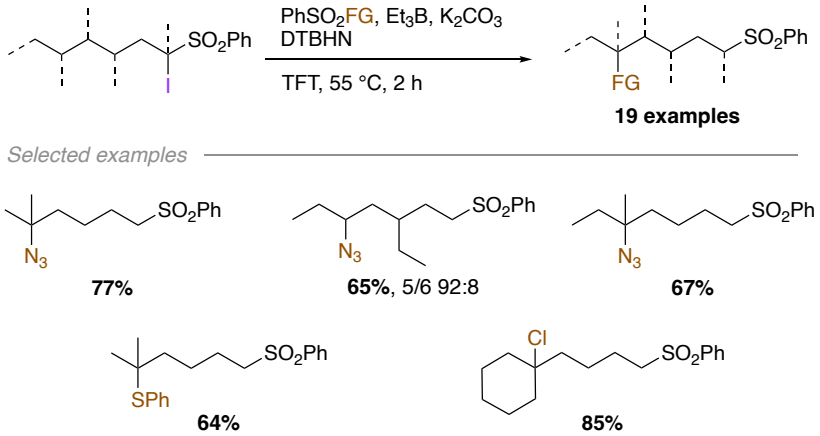

Scheme 1. Hydroperfluoroalkylation of unactivated alkenes

Next, a single fluorination process was investigated utilising the recently developed *N*-fluoro-*N*-arylsulfonamides (NFASs) in the group, representing the third generation of fluorinating agents. This technique facilitated the direct fluorination of secondary and tertiary alkyl iodides and S-alkyl xanthates (Scheme 2). Moreover, carbofluorination reactions with unactivated alkenes were successfully carried out under optimised conditions.




Scheme 2. Radical dehalo- and dethio-flurorination examples.

Due to the versatility of sulfones in organic synthesis, prominently featured in numerous natural compounds and their analogues, the intramolecular 1,5-hydrogen atom transfer (HAT) reactions using α-sulfonyl radicals were investigated as the last part of the thesis. The isomerisation reactions utilising the 1,5-iodine atom transfer (IAT) process and remote C-H functionalisation were successfully executed using α-mono- and bis-sulfonyl radicals across a diverse array of 1-iodoalkyl sulfones. Moreover, allylation and deuteration reactions were explored to analyse the 1,5-HAT translocation patterns, broadening our investigation with α-sulfonyl radicals.




Scheme 3. Remote C-H functionalisation of 1-mono-sulfones through 1,5-HAT.

# List of abbreviations and symbols

| | |
|---|---|
| $\alpha_D$ | optical rotation |
| Ac | Acetyl |
| AIBN | Azobisisobutyronitrile |
| Alox | aluminium oxide |
| aq. | aqueous |
| Ar | Aryl group |
| ATRA | Atom Transfer Radical Addition |
| BDE | Bond Dissociation Energy |
| Boc | *tert*-Butyloxycarbonyl |
| *c* | concentration |
| cat. | catalytic |
| dr | diastereomeric ratio |
| DBU | 1,8-Diazabicyclo[5.4.0]undec-7-ene |
| DCE | 1,2-dichloroethane |
| DCM | dichloromethane |
| DIPEA | *N,N*-Diisopropylethylamine |
| DLP | dilauroyl peroxide |
| DMA | *N,N*-Dimethylacetamid |
| DMAP | 4-diemthylaminopyridine |
| DMF | *N,N*-dimethylformamide |
| DMSO | dimethylsulfoxide |
| DTBHN | di-*tert*-butylhyponitrite |
| Eq. | equation |
| equiv. | equivalents |
| ESI | Electron spray ionization |
| Et | Ethyl |
| $Et_2O$ | Diethyl ether |
| $Et_3B$ | Triethylborane |
| EtOAc | Ethyl acetate |

| | |
|---|---|
| EWG | Electron Withdrawing Group |
| FC | Flash Chromatography |
| GC | Gas Chromatography |
| HAT | Hydrogen Atom Transfer |
| HRMS | High-Resolution Mass Spectrometry |
| *hv* | light irradiation |
| IR | Infrared spectroscopy |
| *J* | coupling constant (in Hz) |
| *k* | rate constant |
| M | Molarity (mol/L) |
| M. p. | Melting point |
| m/z | Mass-to-charge-ratio |
| MeCN / $CH_3CN$ | Acetonitrile |
| mol% | 0,01 equiv. |
| NMR | Nuclear Magnetic Resonance |
| ppm | parts per million |
| quant. | quantitative |
| rt | room temperature |
| sat. | saturated |
| SET | Single Electron Transfer |
| TBC | 4-*tert*-butylcatechol |
| TEA | triethylamine |
| TFT | α,α,α-Trifluorotoluene |
| THF | tetrahydrofuran |
| TLC | Thin Layer Chromatography |
| UV | ultra-violet |
| δ | chemical shift (ppm) |

# General table of contents

Chapter 1

# Radical Hydroperfluoro-alkylations of Olefins

# Chapter 1 – Radical Hydroperfluoroalkylations of Olefins

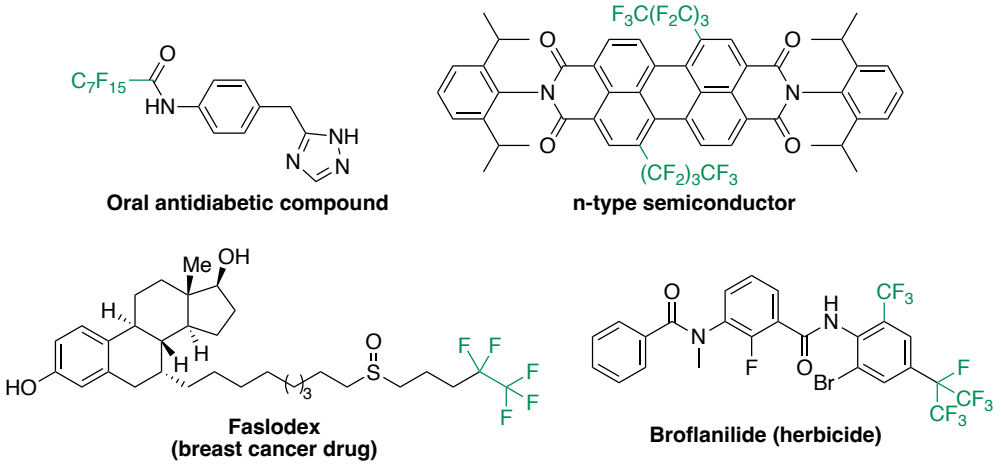
## 1.1 Introduction

The contemporary interest in this field stems from the beneficial properties fluorine substitution can provide to molecules, making it valuable for applications in pharmaceuticals, agrochemicals, materials science, and radiotracers for positron emission tomography (PET).[1]

Fluorine's high electronegativity strengthens the carbon-fluorine bond due to the coulombic attraction in the polarised covalent bond.[2],[3] This strong polarisation enables the C–F fragment to interact attractively with hydrogen-bond donors,[4] other fluorinated molecules,[5],[6] polar groups like carbonyls,[7] and hydrophobic regions.[8] Fluorinated compounds often demonstrate increased binding affinity to proteins, likely because of these polar interactions. However, this effect is typically observed empirically and rationalised afterwards, making it hard to predict.[9],[10],[11] Additionally, most fluorinated compounds show enhanced metabolic stability by resisting unwanted oxidative metabolism pathways.[12] Incorporating fluorine into a molecule can impart many beneficial properties. Fluorine substitution can modulate the $pK_aH$ value of nearby functional groups,[13],[14] leading to increased membrane penetration at physiological pH.[15] Fluorinated arenes are more lipophilic than their non-fluorinated counterparts,[13],[16] which is advantageous in drug development.[13,17–21] In medicinal chemistry, fluorine is sometimes used as an isostere for hydrogen, although its van der Waals radius is closer to that of oxygen (1.47 Å for fluorine versus 1.52 Å for oxygen and 1.20 Å for hydrogen).[22] Additionally, fluorinated compounds can be strategically employed as transition-state inhibitors.[18]

The addition of fluoroalkyl groups to organic molecules has attracted significant interest among synthetic, medicinal, and materials science chemists due to the unique properties these groups confer.[19,23,24] Fluoroalkylation can improve metabolic stability, lipophilicity, and bioavailability with minimal structural changes to the organic scaffolds.[24] For instance, although the trifluoromethyl group is technically a fluorine-substituted methyl group, its reactivity is so distinct that it is considered a separate functional group. Despite the acknowledged advantages of perfluoroalkyl groups in enhancing the functionality of small

molecules, the European Chemicals Agency has restricted the use of polyfluorinated alkanes, labelling them as highly persistent substances.[25] This has hindered the large-scale production of fluorinated precursors.[26] However, extensive research is being conducted into environmentally friendly methods for degrading long polyfluorinated chains.[27] Research has primarily focused on incorporating trifluoromethyl,[35] difluoromethyl,[36] and other less fluorinated groups (such as monofluoroalkyl,[37,38] tetrafluoroethyl,[39] and trifluoroethyl groups[40]) into organic substrates. Conversely, perfluoroalkylation reactions, which introduce longer perfluoroalkyl chains ($C_nF_{2n+1}$, n > 1), are less explored, even though some perfluoroalkyl-substituted compounds exhibit exceptional properties compared to their $CF_3$ or $CF_2H$ counterparts (Scheme 1).[29]



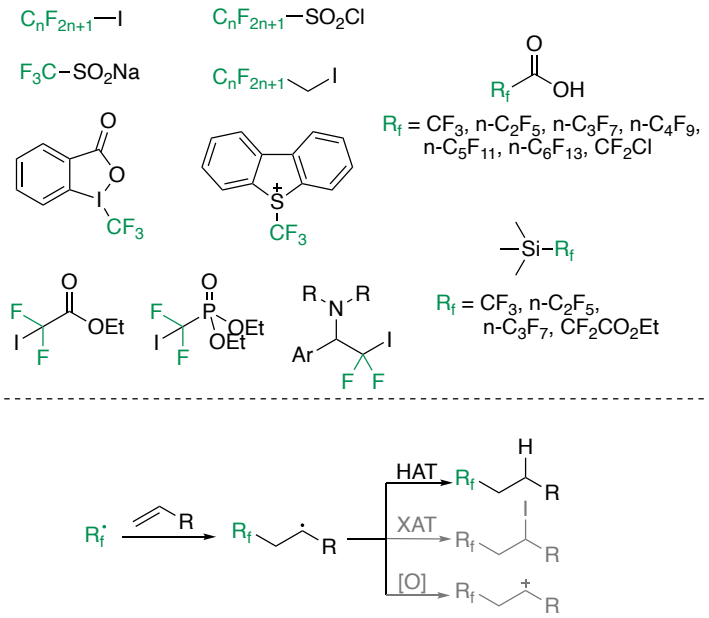

Scheme 1. Representative compounds with perfluoroalkyl groups.[28–34]

Additionally, unactivated alkenes are widely prevalent and often used as carbon sources in producing commodity chemicals.[41] Due to their abundance, numerous catalytic reactions have been developed to functionalise alkenes by forming carbon-carbon or carbon-heteroatom bonds.[42–45] Among these, direct hydroalkylation stands out as a crucial transformation with a wide array of applications, from industrial manufacturing to the creation of pharmaceutical agents.[46–50] Despite significant advances in the field, hydrotrifluoromethylation and hydroperfluoroalkylation of alkenes still require further development.

## 1.2 Reagents as sources of $R_f$ radicals

Organic motifs with small fluorous "ponytails" (e.g., $C_4F_9$, $C_6F_{13}$, $C_8F_{17}$) are known as light fluorous molecules, while heavy fluorous reagents typically have longer fluorous tags with

more than 10 perfluorinated atoms. Light fluorous reagents are convenient and widely used in various fields because they can often be utilised under the same conditions as their non-fluorous counterparts.[51] Several perfluoroalkylation reagents have been developed to create perfluoroalkylated compounds in organic synthesis, materials science, and medicinal chemistry (Scheme 2).[52–55] These reagents include sodium perfluoroalkylsulfinates ($R_FSO_2Na$),[56] perfluoroalkylsulfonyl chlorides ($R_FSO_2Cl$),[57] *S*-(fluoroalkyl)diphenylsulfonium salts,[58] perfluoroalkyl carboxylic acids,[59] $TMSC_nF_{2n+1}$,[60–64] perfluoroacid anhydrides,[65–68] $R_F$-hypervalent iodine reagents,[69] and perfluoroalkyl halides ($R_F$–X).[51,70–73]




Scheme 2. Representatives of some reagents used as a source of $R_f$-radicals and illustration of perfluoroalkylation pathways.[70]

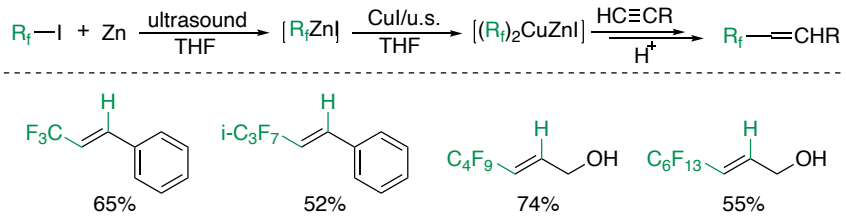
Among these, perfluoroalkyl halides are particularly popular due to their commercial availability, stability, and ease of use. Radical protocols using perfluoroalkyl iodides ($R_F$–I) as radical precursors have been extensively studied.[74,75] Since 2018, various perfluoroalkyl reagents (reagent-$C_nF_{2n+1}$, n > 1) have been employed for the perfluoroalkylation of aliphatic substrates, including perfluoroalkyl halides, perfluoroacid anhydrides, sodium perfluoroalkylsulfinates, $R_F$-hypervalent iodine reagents, *S*-(perfluoroalkyl)diphenylsulfonium salts, and perfluoroalkylated sulfoximines.[76]

## 1.3 Reductive fluoroalkylations of unsaturated systems

### 1.3.1 Hydroperfluoroalkylation

Hydroperfluoroalkylation reactions have been recognised for many years, involving the reductive addition of perfluorinated groups to alkenes.[77] A crucial aspect of these reactions is the role of a hydrogen atom donor, which captures a radical intermediate created when a fluorinated radical is added to an alkene. For these reactions to be effective, it is essential that the fluorinated radical interacts with the double bond more rapidly than it does with the hydrogen atom donor, leading to the product of fluoroalkyl iodide reduction. Additionally, the hydrogen donor must be active enough to inhibit the attachment of a new radical to subsequent alkene molecules. Achieving hydroperfluoroalkylation of alkenes (and alkynes) with perfluoroalkyl halides is challenging due to the competing simple dehalogenation of the perfluoroalkyl halide and Kharasch-type halogen atom transfer radical addition (ATRA).[78]

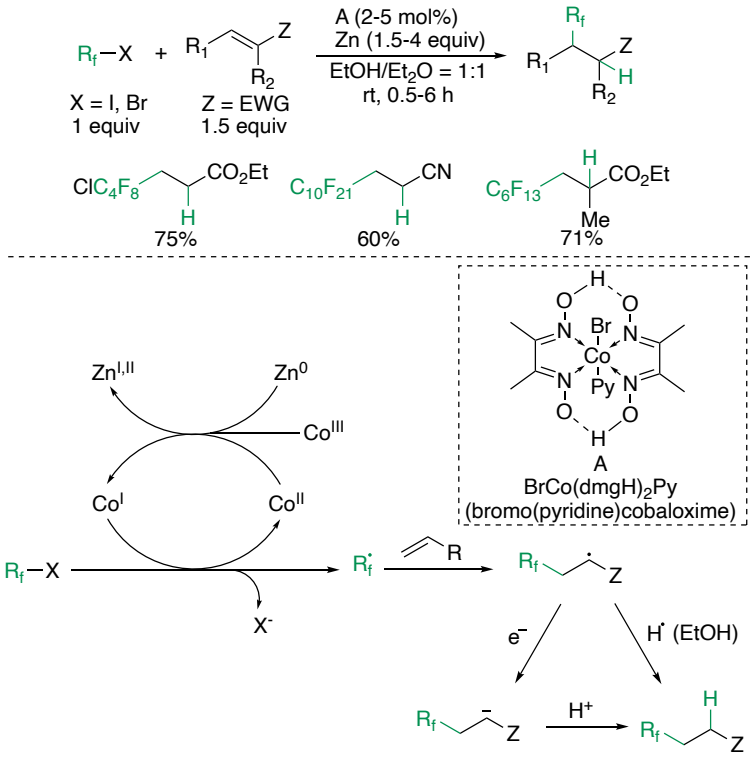
Ishikawa successfully developed a method to hydroperfluoroalkylated carbon-carbon triple bonds using perfluoroalkylzinc iodide in the presence of copper(I) iodide, all under ultrasonic irradiation.[79] The ultrasound-promoted hydroperfluoroalkylation of alkynes using perfluoroalkyl cuprates, which are formed in situ from perfluoroalkyl iodides and zinc in the presence of copper(I) iodide in tetrahydrofuran (THF), proceeded smoothly. The copper metal, generated by reducing copper(I) iodide with zinc powder under ultrasonic dispersion, significantly enhanced the perfluoroalkylation reaction (Scheme 3). The reaction failed to occur without ultrasonic irradiation, highlighting the essential role of ultrasound in driving this chemical process.




Scheme 3. Hydroperfluoroalkylation of alkynes.

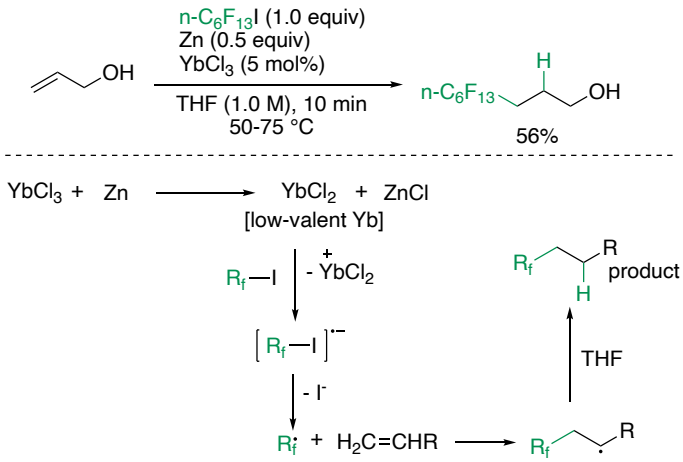
One of the first studies that reported the reductive addition of perfluoroalkyl iodides to alkenes was published by Hu *et al.* in 1991.[80,81] They introduced a bimetallic redox couple, cobalt-oxime(III)/Zn, which promoted the hydroperfluoroalkylation of electron-deficient

alkenes (Scheme 4). The parallel experiments' results show that zinc alone could initiate the reaction, though this led to dramatically reduced yields, primarily producing $R_fH$. Satisfactory yields were achieved even with just 0.5 mol % of cobaloxime present. On the other hand, perfluoroalkyl bromides underwent successful reactions only in the presence of cobaloxime and zinc. However, a higher temperature and extended reaction time were necessary for effective outcomes.



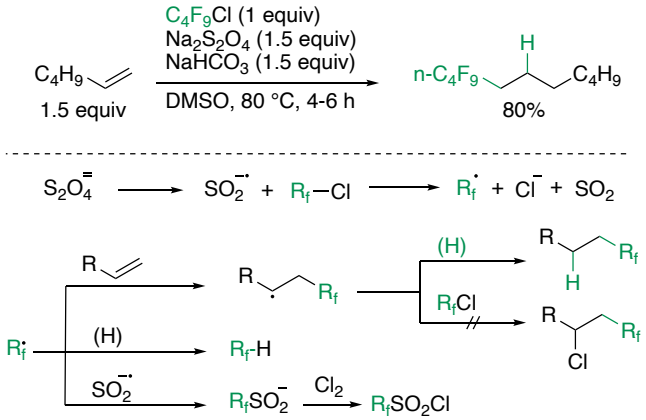

Scheme 4. Hydroperfluoroalkylation of electron-deficient alkenes with cobaloxime(III).

Furthermore, alkenes affording hydroperfluoroalkylated products were reported by Ding and co-workers in 1993.[82] The process was efficiently catalysed using ytterbium chloride ($YbCl_3$) and utilised less than a stoichiometric quantity of zinc powder in THF as a source of the hydrogen atoms and a solvent, completing within a few minutes (Scheme 5). However, it was observed that the reaction failed to proceed when ethanol (EtOH) or benzene was used as the solvent. Alkenes containing functional groups such as esters, hydroxyls, and phosphonates were compatible under the given reaction conditions.




Scheme 5. $YbCl_3$(cat.)/Zn promoted hydroperfluoroalkylation of alkenes and the possible mechanism.

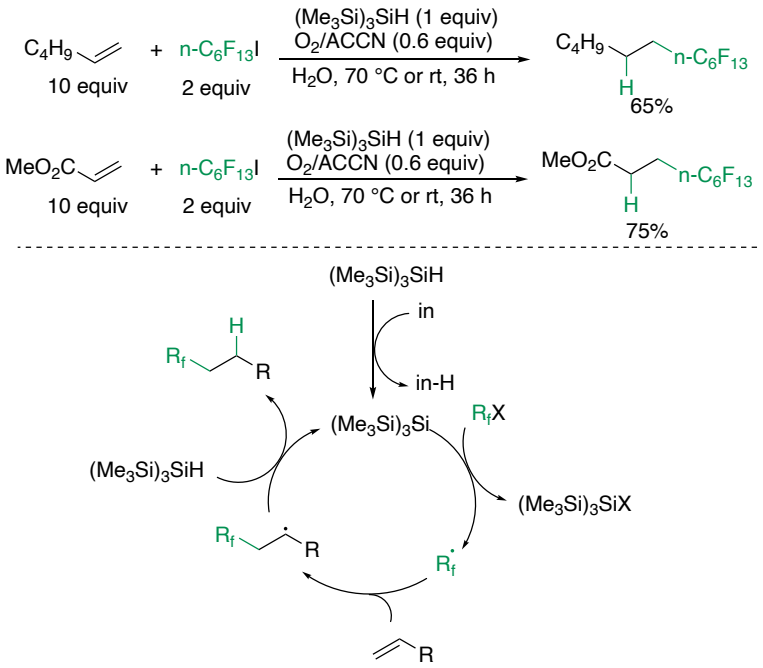
Chen and Long described another reductive procedure in 1999.[83] They used perfluoroalkyl chlorides and sodium dithionite ($Na_2S_2O_4$) in DMSO at elevated temperatures to react with alkenes and alkynes (Scheme 6). According to the authors, the solvent choice plays a crucial role in activating carbon-chlorine bonds in perfluoroalkyl chlorides. Unlike the other solvents that have been tested, dimethyl sulfoxide (DMSO) appears to be essential for this activation process. This is likely because DMSO, similar to hexamethylphosphoramide (HMPA) and dimethylformamide (DMF), is typically considered a suitable solvent for electron transfer (ET) reactions. Additionally, they have established that perfluoroalkyl chlorides can be directly converted to the corresponding sulfinate salts under the same conditions without alkene.




Scheme 6. Hydroperfluoroalkylation of alkenes with perfluoroalkyl chlorides and suggested reaction mechanism.

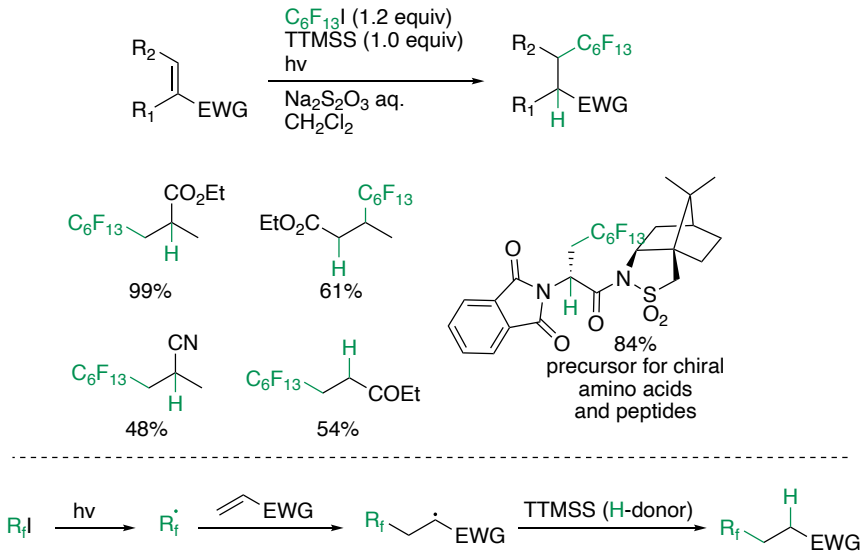
In 2010, Postigo and co-workers investigated the intermolecular addition of perfluoroalkyl radicals to electron-rich alkenes and alkenes with electron-withdrawing groups in water using silyl radicals as mediators.[84] The initiation of the radical reactions was achieved through the

thermal decomposition of an azo compound, specifically 1,10-azobis(cyclohexanecarbonitrile) (ACCN), and through dioxygen initiation, but primer gave higher yields (Scheme 7). Water significantly influences the rates of perfluoroalkyl radical additions to double bonds and hydrogen atom abstraction from the silane.



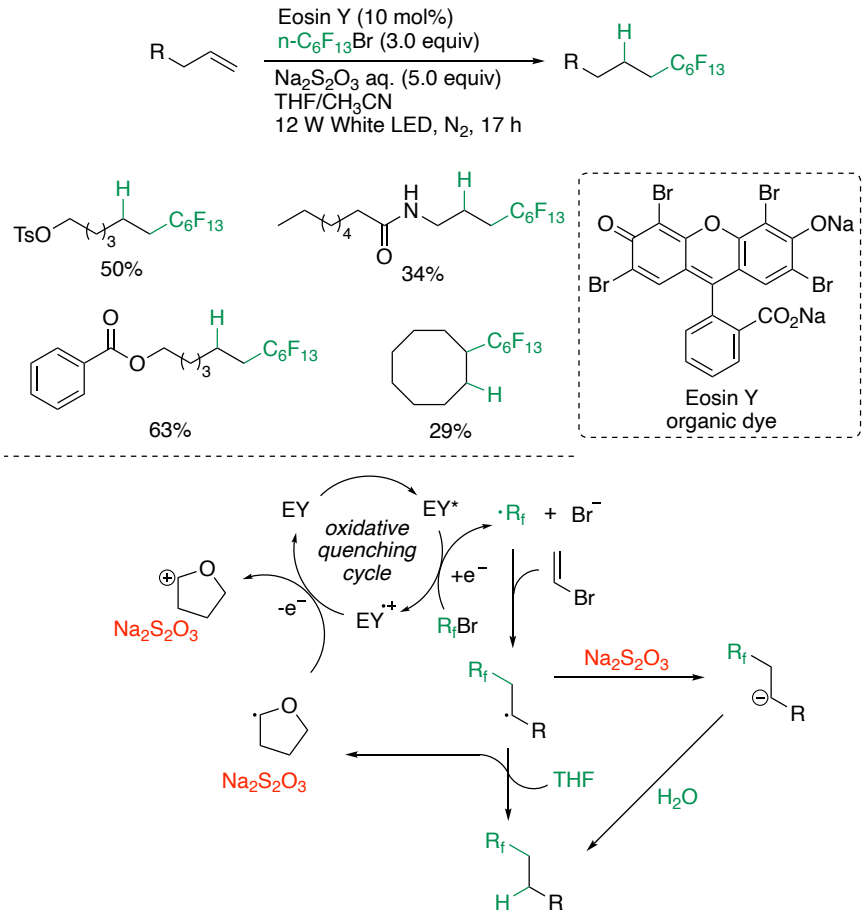

Scheme 7. Hydroperfluoroalkylation of electron-rich and poor alkenes and suggested reaction mechanism.

Yajima and co-workers reported the photoinduced radical hydroperfluoroalkylation of electron-deficient olefins and *N*-phthalimide dehydroamino acid derivatives in 2013.[85] They performed the reaction with tris(trimethylsilyl)silane (TTMSS) as a hydrogen donor and a perfluoroalkyl iodide as a radical precursor in the presence of aqueous sodium thiosulfate ($Na_2S_2O_3$) (Scheme 8). This method proved to be effective with various perfluoroalkyl iodides. In addition, employing camphorsultam as a chiral auxiliary led to high stereoselectivity, and the products were readily converted into corresponding amino acids and peptide derivatives.




Scheme 8. Photoinduced hydroperfluoroalkylation of electron-deficient olefins and the reaction mechanism.

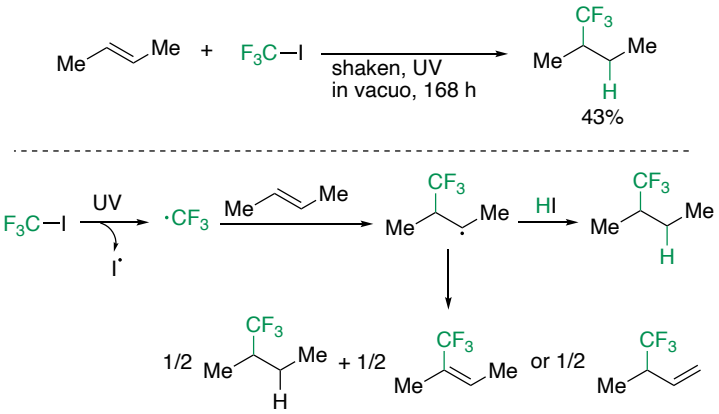
An organic dye-catalyzed (Eosin Y) visible light-induced hydroperfluoroalkylation of unactivated alkenes was introduced by Yajima later in 2019.[86] This method proceeds with perfluoroalkyl bromides and alkenes using either a reductive pathway in the presence of $Na_2S_2O_3$ where water is the hydrogen source or with THF being the hydrogen donor, as shown in Scheme 9. The hydroperfluoroalkylations of internal alkenes and alkynes proceed with relatively poor yields. The reaction with unprotected alcohol afforded traces of the desired product, resulting in perfluoroalkylated THF-protected alcohol as a major side product. They have evolved this procedure to the hydroperfluoroalkylation of electron-deficient alkenes under similar conditions but using *N,N*-diisopropylethylamine (DIPEA) as a reducing agent and water as the hydrogen source.[87] Moreover, under slightly modified conditions in the same group, this study was further extended to the hydroxy- and hydro-perfluoroalkylation of styrenes.[88]




Scheme 9. Hydroperfluoroalkylation of alkenes with Eosin Y and reaction mechanism.

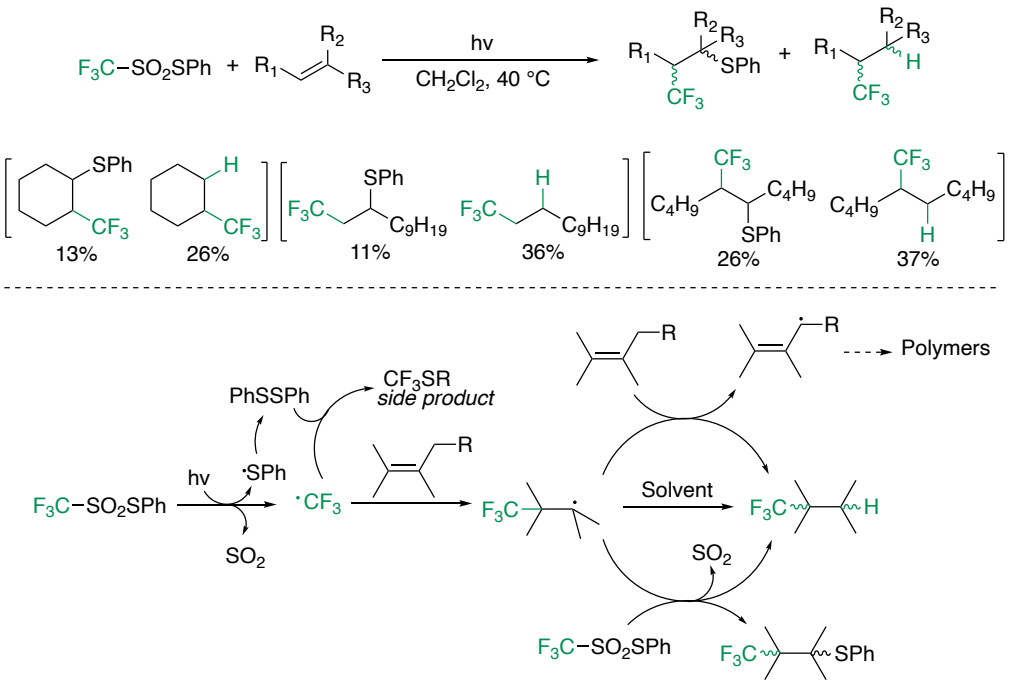
## 1.3.2 Hydrotrifluoromethylation

According to the literature[35], the first report on hydrotrifluoroalkylation was published in 1969 by Haszeldine and co-workers.[89] The study explored the hydrotrifluoromethylation of 2-butene using $CF_3I$ under both photochemical and thermal conditions (200 °C). This reaction process was hampered by several side reactions. The homolytic cleavage of $CF_3I$ generates a $CF_3$ radical, which then attacks the alkene, forming a $CF_3$-containing alkyl radical (Scheme 10). It was proposed that hydrogen iodide acts as a hydrogen source, which could be produced during side reactions like iodotrifluoromethylation and subsequent elimination. Furthermore, the possibility of disproportionation of the $CF_3$-containing alkyl radical, leading to the formation of the proposed hydro-trifluoromethylated product, was also considered.



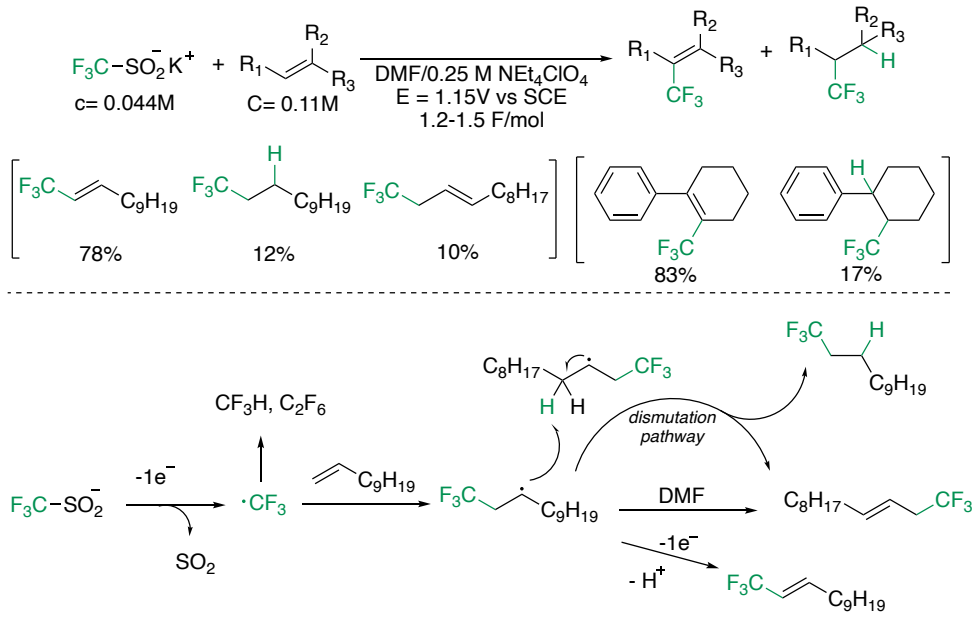

Scheme 10. Hydrotrifluoromethylation of 2-butene with $CF_3I$.

Also, the hydrotrifluoromethylation product was observed by Davies et al. in 1980 when adding $CF_3I$ to but-2-ene as a side product.[77] Later, in 1985 by Muller, during the electrochemical decarboxylative addition of trifluoroacetic acid into acrylic acids.[90] In their pioneering work in 2000, Langlois and his team accomplished desulfitative hydro-trifluoromethylation under UV irradiation using thioesters derived from trifluoroacetic (TFA) or triflic acid. They determined that the hydrogen incorporated into the product came from the allylic hydrogen of the substrate, limiting the maximum yield to 50% (Scheme 11). They also found that the yields were higher with TFA-derived thioesters than those derived from triflic acid. This difference was explained by the strong electron-withdrawing properties of the $CF_3SO_2$ group in the triflic acid-derived thioesters, which increased the electrophilicity of the thioester and favoured thio-trifluoromethylation with the nucleophilic $CF_3$-containing radical.

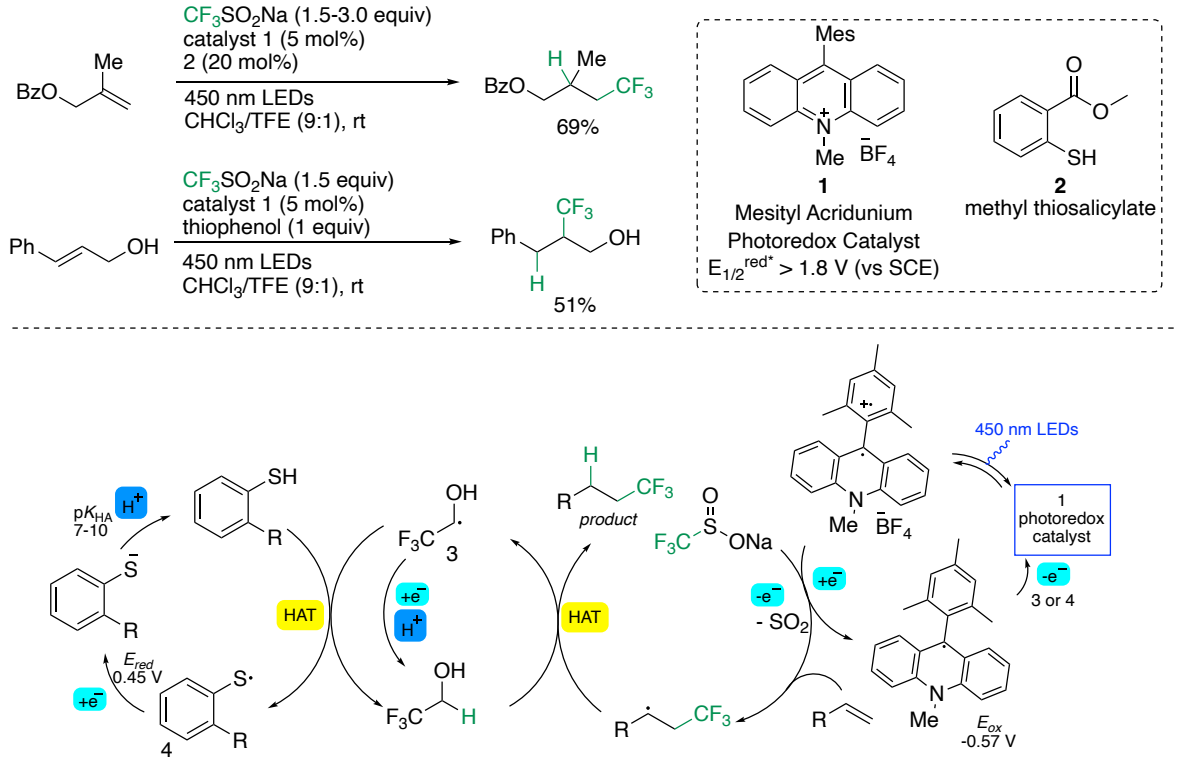



Scheme 11. Hydrotrifluoromethylation of alkenes under photolysis and suggested reaction mechanism.

This work was continued by investigating potassium trifluoromethane sulfinate as a source of $CF_3$ radical, involved in trifluoromethylation reactions under electrochemical oxidation with Tommasino et al.[92] The outcome of this approach afforded low-yield products as a mixture of saturated and unsaturated products (Scheme 12). This method was further extended by Nicewicz and co-workers as a metal-free approach to the hydrotrifluoromethylation of alkenes, using the oxidative capabilities of a commercially available sodium trifluoromethane sulfinate salt ($CF_3SO_2Na$).[93] This transformation is catalysed by *N*-Me-9-mesityl acridinium (**1**) through a photoredox mechanism. Methyl thiosalicylate is a substoichiometric hydrogen atom donor for aliphatic alkenes, while thiophenol is a stoichiometric donor for styrenyl substrates (Scheme 13). Trifluoroethanol (TFE) was used both as a cosolvent and hydrogen donor. The method applies to mono-, di-, and trisubstituted aliphatic alkenes and styrenes, which usually achieve high regioselectivity.




Scheme 12. Hydrotrifluoromethylation of alkenes under electrochemical oxidation and suggested reaction mechanism.

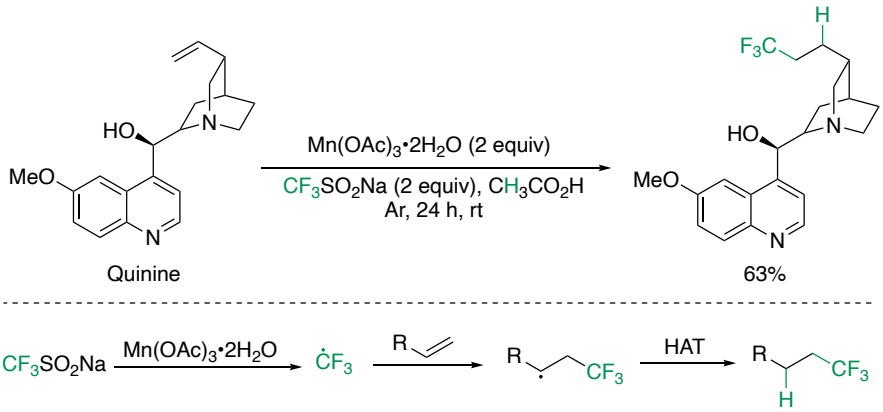



Scheme 13. Hydrotrifluoromethylation of alkene and styrene via photoredox system and suggested reaction mechanism.

Several studies are using Langlois reagent[91] under photoinduced conditions; for example, Lefebvre, Hoffmann, Rueping, and their teams demonstrated the hydrotrifluoromethylation of electron-deficient olefins such as maleimide derivatives, maleic anhydride, and dimethyl

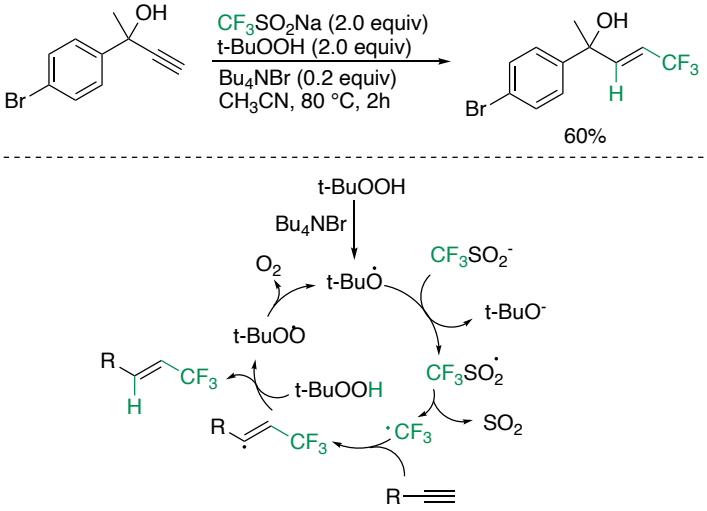
maleate through photoredox organocatalysis.[94] They used 4,4-dimethoxybenzophenone as a catalyst under visible light irradiation. The proposed mechanism suggests that the excited catalyst facilitates the generation of $CF_3$ radicals from the Langlois reagent. In contrast, the protonated ketyl radical generated during the reaction is a hydrogen source. They also used another photocatalyst, $Ir[dF\text{-}(CF_3)ppy]_2(dtbbpy)PF_6$, achieving comparable yields. In a related study, Yao and coworkers reported a metal-free hydrotrifluoromethylation of vinyl phosphonates or phosphine oxides using the Langlois reagent in acetone.[95] They developed two reaction conditions: acetone/HCl under UV irradiation and diacetyl/formic acid under blue LED irradiation, with acetone and diacetyl acting as radical initiators. The mechanism proposed in this work was like the mentioned method, and a significant amount of acetone or diacetyl was required to facilitate the reaction. Additionally, there are works of Zhang, Xu and co-workers[96] and Tlili and colleagues[97] utilising Langlois reagent in hydrotrifluoromethylation of alkenes under visible light irradiation with a photoredox catalyst 2,4,5,6-tetra(9*H*-carbazol-9-yl)isophthalonitrile (4CzIPN) in 1,4-dioxane/MeOH and with change of the solvent to DMSO in the latter case. As the photoinduced technology is trendy among hydrotrifluoromethylation reactions, there are an exhaustive number of studies conducted,[51,91,98,99] including the use of Langlois reagent, and some of them will be discussed further in the review.

Hydro-trifluoromethylation reactions using Langlois reagent can also be performed under thermal conditions without photoirradiation. In 2018, Duan, Li, and their colleagues reported on a $Mn(OAc)_3$-mediated hydro-trifluoromethylation of alkenes using acetic acid ($CH_3CO_2H$) as the solvent.[100] They suggest that $Mn(OAc)_3$ facilitates the generation of $CF_3$ radicals through the oxidation of the Langlois reagent (Scheme 14). In this process, the α-hydrogen of the acetic acid is identified as the source of hydrogen for the reaction.




Scheme 14. Hydrotrifluoromethylation of quinine as an example.

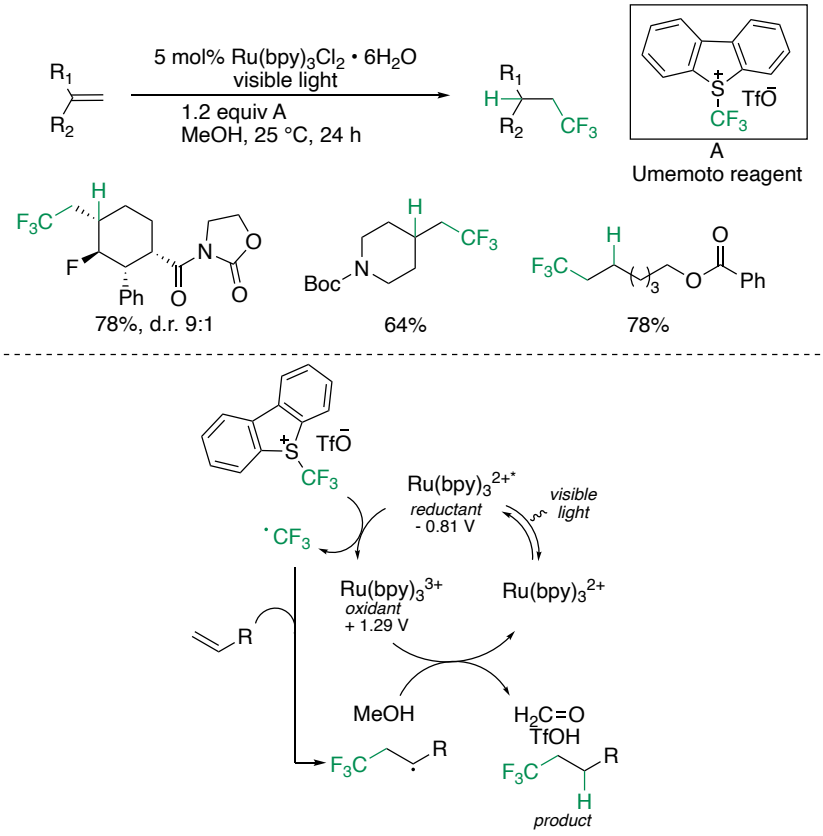
The same year, Antonchick and Matcha demonstrated a transition metal-free hydro-trifluoromethylation of alkynes through a radical chain mechanism, using a combination of Langlois reagent and *t*-BuOOH, with $Bu_4NBr$ serving as a radical initiator.[101] In the initiation step, $Bu_4NBr$ generates a *t*-BuO radical from *t*-BuOOH. This radical then reacts with the Langlois reagent through a single electron transfer (SET), forming a $CF_3$ radical (Scheme 15). This $CF_3$ radical interacts with the alkyne, forming a vinyl radical. The vinyl radical subsequently abstracts hydrogen from *t*-BuOOH to produce the hydro-trifluoromethylated product and *t*-BuOO•. The decomposition of *t*-BuOO• releases $O_2$ and regenerates the *t*-BuO• radical, continuing the propagation of the reaction. The synthesised alkenes using the developed method demonstrated excellent trans-selectivity due to the quaternary stereocenter adjacent to the alkynes.



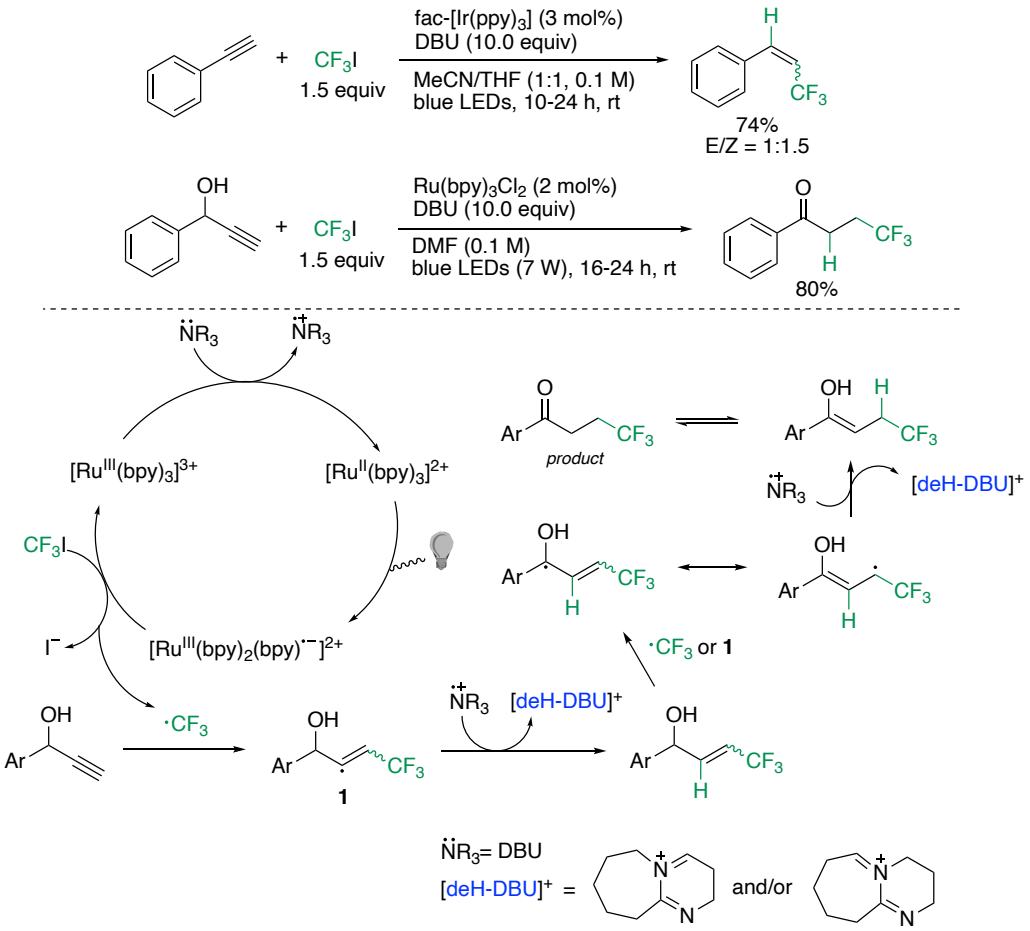

Scheme 15. Hydrotrifluoromethylation of alkynes and reaction mechanism.

Gouverneur has reported a method for the hydrotrifluoromethylation of unactivated alkenes

using visible light.[102] This technique employs the Umemoto reagent as a source of the $CF_3$ group and methanol (MeOH) as the reducing agent and solvent. 5 mol% of $Ru(bpy)_3Cl_2$ facilitates the reaction, which can be conducted at room temperature (Scheme 16). The method is notable for its simplicity and tolerance of various functional groups. The following year, Cho and colleagues reported the iridium-photocatalyzed hydrotrifluoromethylation of alkynes, which relies on adding (1,8-diazabicyclo[5.4.0]undec-7-ene) (DBU) (Scheme 17).[103] DBU serves two key roles: reducing the oxidised Ir(III) photocatalyst during the oxidative quenching cycle and acting as a hydrogen source in its radical-cation form. Additionally, Joo, Cho, and their team synthesised β-trifluoromethylated ketones via the photocatalytic hydrotrifluoromethylation of propargylic alcohols using $CF_3I$, employing $Ru(bpy)_3Cl_2$ as the catalyst due to its lower cost and cleaner reaction profile, despite iridium catalysts giving comparable results.[104] The use of DBU was critical in these reactions. Following hydrotrifluoromethylation, the $CF_3$-substituted allylic alcohol undergoes isomerisation to form a vinyl alcohol intermediate, which then tautomerises to yield the desired product.

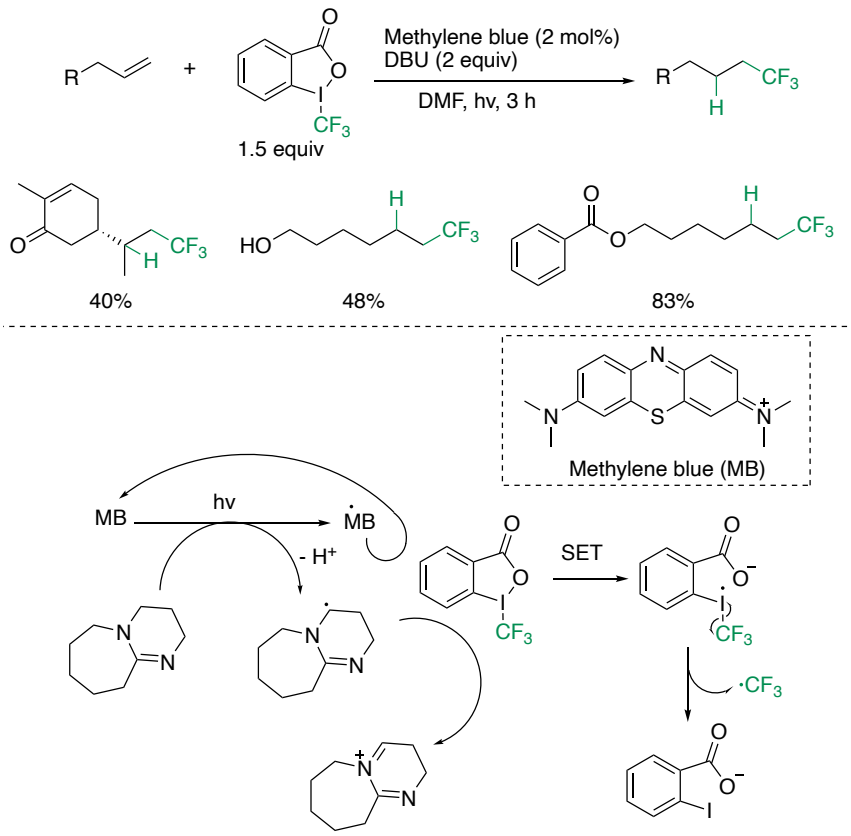



Scheme 16. Hydrotrifluoromethylation of terminal alkenes under visible light irradiation and suggested reaction mechanism.



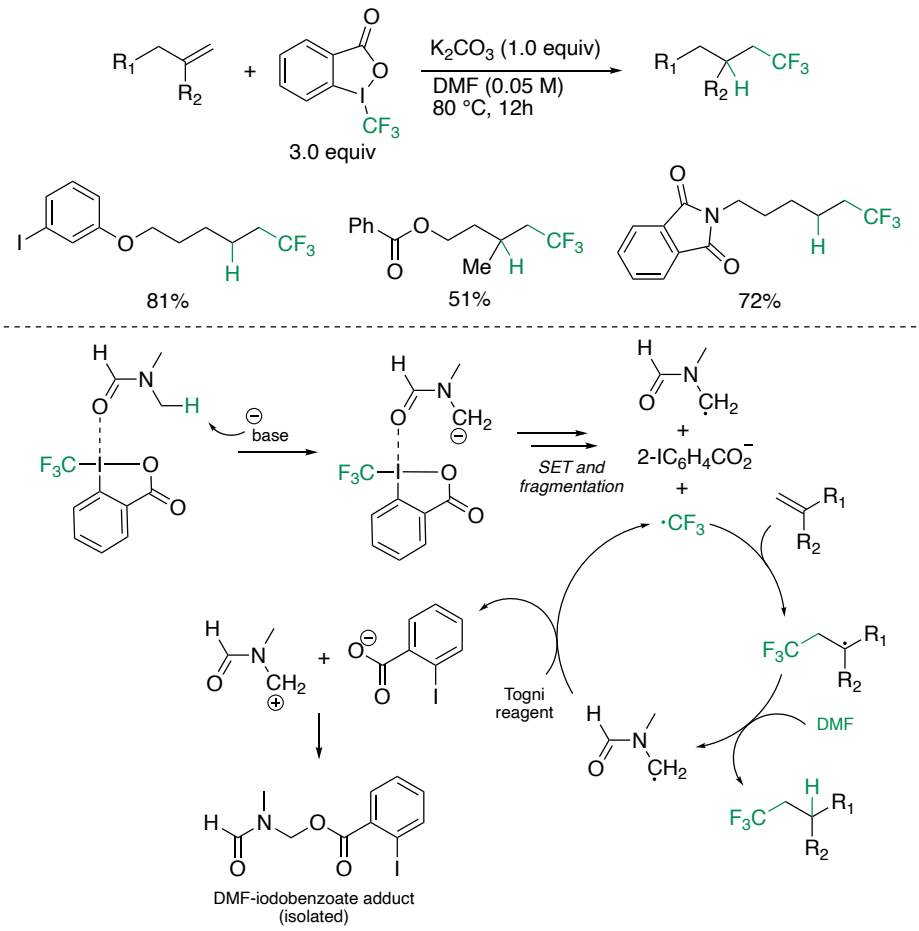

Scheme 17. Photocatalytic hydrotrifluoromethylation of alkynes with $CF_3I$.

In this context, a similar approach was developed by Scaiano and co-workers employing methylene blue as a photocatalyst in combination with Togni's reagent as the $CF_3$ source in the catalytic radical trifluoro- and hydrotrifluoromethylation of electron-rich heterocycles, as well as terminal alkenes and alkynes, under visible light irradiation (Scheme 18).[105] Initially, this reaction was designed to afford just trifluoromethylated products, but obtained reduced products allowed the extension of the scope with electron-rich alkenes. A potential mechanism for the catalytic formation of $CF_3$ radicals involves the action of methylene blue (MB) under visible light irradiation. Upon irradiation, the triplet state of MB can be quenched by DBU. This interaction results in the formation of the semireduced MB radical and an α-amino radical. Both radicals can reduce Togni's reagent, leading to the release of a $CF_3$ radical and the subsequent formation of 2-iodobenzoate. This approach is advertised as being free from toxic transition metal catalysts. These reactions are characterised by moderate to good yields, low catalyst concentrations, and notably short irradiation times.



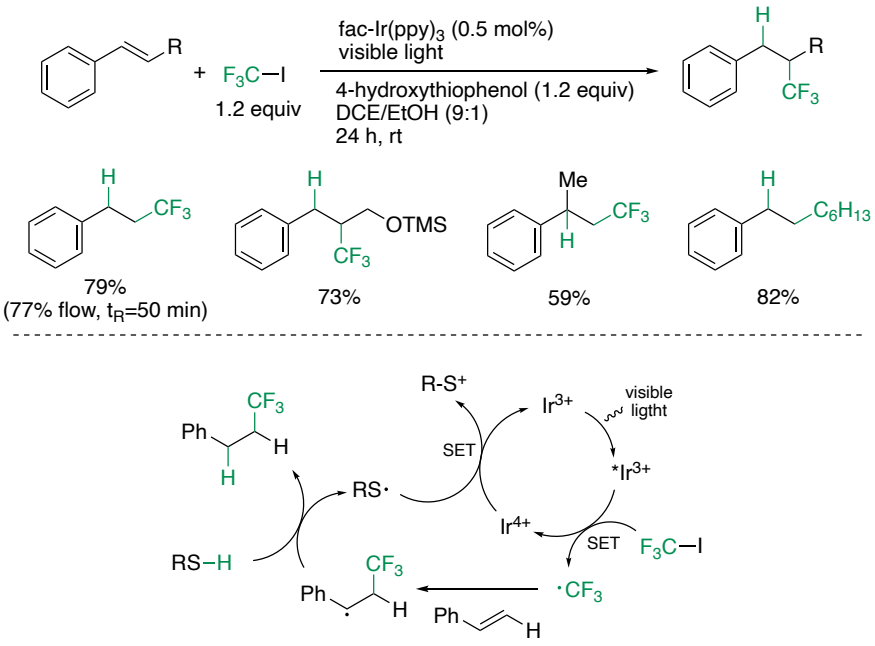

Scheme 18. Hydrotrifluoromethylation of terminal alkenes under visible light with Togni's reagent and mechanism for $CF_3$ radical formation.

The following year, Sodeoka and colleagues developed a metal-free hydrotrifluoromethylation of alkenes using Togni's reagent, with $K_2CO_3$ as an additive and dimethylformamide (DMF) as the solvent under thermal conditions.[106] DMF acts as both a hydrogen source and an electron donor, reducing the Togni reagent in the presence of the base (Scheme 19). The authors postulated a radical chain mechanism, which involves the formation of DMF radicals, facilitating the reaction process.



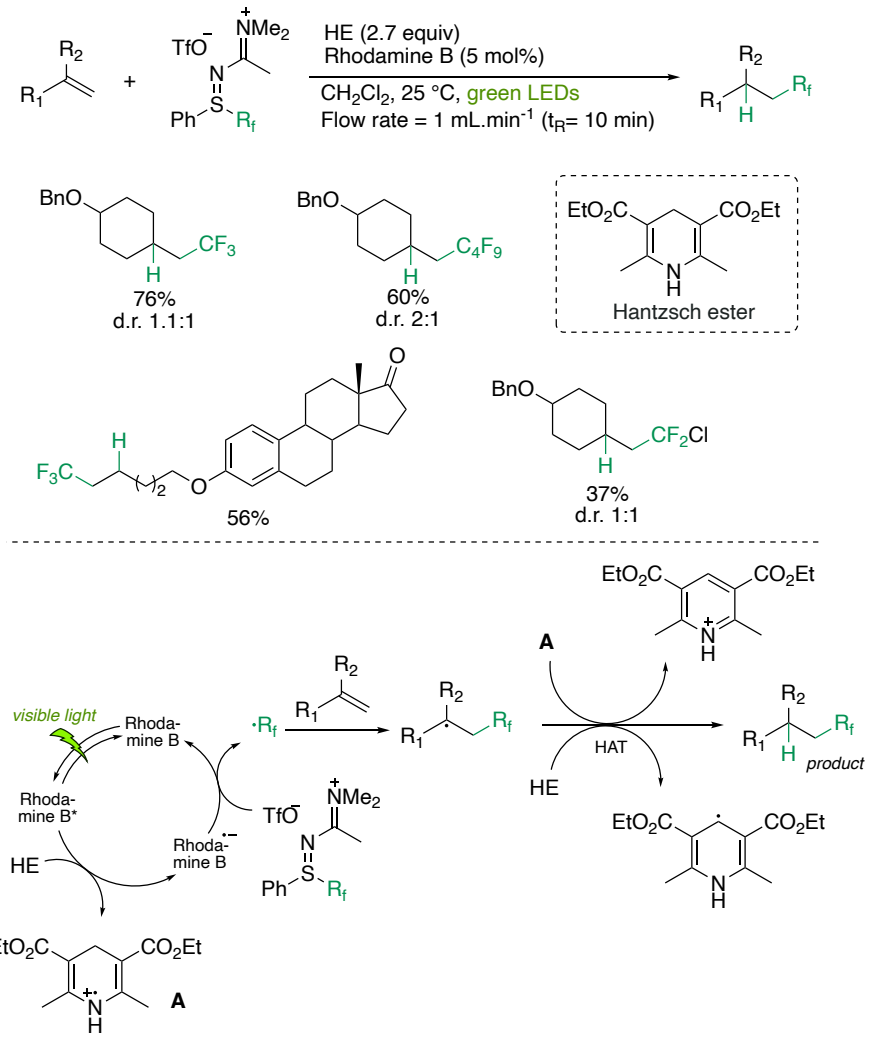

Scheme 19. DMF/base-promoted hydrotrifluoromethylation of alkenes and reaction mechanism.

The photochemical reaction conditions were applied to proceed radical trifluoromethylation and hydrotrifluoromethylation of simple styrenes by Noël and co-workers.[107] In this work, they have employed *fac*-Ir(ppy)$_3$ catalyst under visible light with $CF_3I$ and 4-hydroxythiophenol as the hydrogen atom source (Scheme 20). The reaction was also performed under continuous-flow photochemical conditions, allowing short reaction time and improving the yields in some cases. Different derivatives of styrenes were examined, including 2-vinylnaphthalene, styrenes with hydroxy, acetyl-protected hydroxy, halogen functional groups, as well as 4-vinylpyridine; some of them are illustrated below. They also tested hydroperfluoroalkylation with perfluorohexyliodide to yield the corresponding styrene derivative in 82%. Zhang and colleagues reported a hydrotrifluoromethylation method for alkenes and alkynes using the same photoredox catalyst under visible light in 2018.[108] They used $CF_3Br$, employing THF as both solvent and hydrogen donor, while the specific role of $K_2CO_3$ in this reaction remains unclear. This base produced better results than other inorganic bases such as $Na_2CO_3$, $Cs_2CO_3$, $K_3PO_4$, and $K_2HPO_4$.




Scheme 20. Photocatalytic hydrotrifluoromethylation of styrenes and reaction mechanism.

Magnier reported a similar method, but one that is metal-free, for the photoredox-catalyzed continuous flow technique for hydrotrifluoromethylation.[109] They used Rhodamine B as a photocatalyst and $CF_3$-sulfilimino iminium to generate $R_f$ radicals (Scheme 21). The reaction conditions are suitable for unactivated alkenes with diverse functional groups and were applied on steroid derivatives and a natural compound like (+)-Nootkatone, demonstrating its suitability for the late-stage functionalisation of small, complex molecules and extended to alkynes.




Scheme 21. Hydrotrifluoromethylation of alkenes in flow and reaction mechanism.

An approach using alkylzirconocene (Schwartz reagent) to promote the difluoroalkylation of both alkyl- and silyl-alkenes was reported by Zhang and co-workers.[110] In this method, various unactivated difluoroalkyl iodides and bromides are employed under visible light irradiation without a catalyst and *N*-Methyl-2-pyrrolidone (NMP) is used as a solvent and the hydrogen atom source. They also applied the reaction to introduce trifluoromethyl, perfluoroalkyl, monofluoroalkyl, and nonfluorinated alkyl groups. The proposed mechanism indicates that the reaction occurs via a single electron transfer (SET) pathway, triggered by a Zr(III) species produced by the photolysis of alkyl zirconocene with blue light.

Over the past decade, various conditions for hydrotrifluoromethylation have been extensively explored. Typically, these reactions involve hydrogen abstraction by a $CF_3$-containing alkyl or vinyl radical sourced from an external hydrogen donor or directly from an activated hydrogen

atom within the substrate. In intermolecular setups, photochemical methods are commonly employed.[51,91] Choosing the right hydrogen source and, in some instances, specific additives is crucial for achieving efficient photocatalyst turnover. Additionally, reactions conducted under thermal conditions have been successfully executed through intricate designs incorporating SET events. These developments highlight the evolving complexity and efficiency of hydrotrifluoromethylation techniques in modern synthetic chemistry.

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# Chapter 2

# Radical Mediated Hydroperfluoroalkylation of Unactivated Alkenes

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*The reactions yielding compounds **20, 21** and **22** were carried by Dr. V. Girbu.*

# Chapter 2 – Radical Mediated Hydroperfluoroalkylation of Unactivated Alkenes


## Abstract

The direct hydroperfluoroalkylation of a wide range of unactivated alkenes has been achieved at room temperature with readily available iodoperfluoroalkanes using 4-*tert*-butylcatechol as a source of hydrogen atom and triethylborane. The hydrotrifluoromethylation could also be achieved under these conditions using gaseous trifluoromethyl iodide. An experimentally simple two-step, one-pot hydrotrifluoromethylation process has also been developed using the easy-to-use trifluoromethanesulfonyl chloride as the source of trifluoromethyl radicals. Using these two approaches, a broad range of substrates, including isoprenoid natural products, were efficiently derivatised.



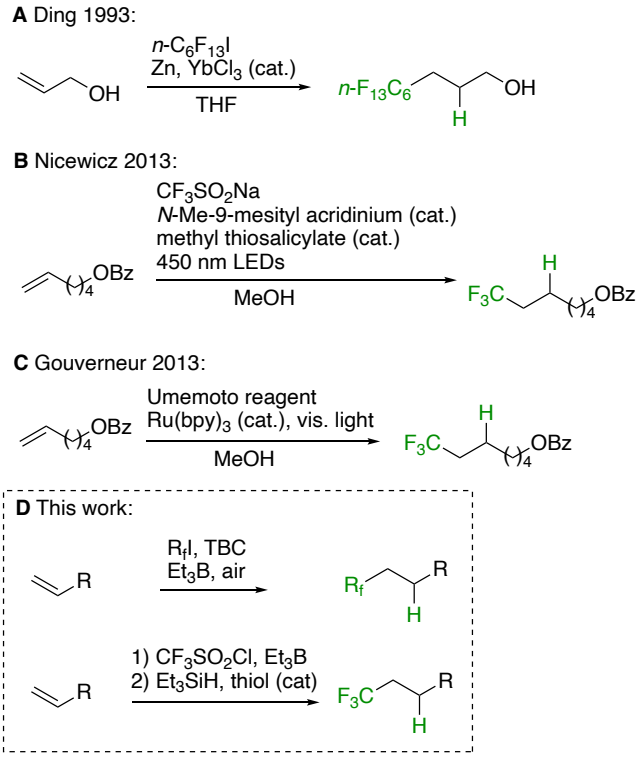
## Keywords

radical, hydroalkylation, carbohydrogenation, fluorine, perfluoroalkyl, trifluoromethyl, catechol, triethylborane


## 2.1 Introduction

Fluorinated compounds are highly interested in medicinal, agrochemical, and material chemistry owing to the unique ability of fluorinated residues to modulate the physical (polarity, lipophilicity, solubility) and chemical (metabolic stability) properties of drug candidates.[1–4] Selective, general and efficient methods for the introduction of trifluoromethyl and other perfluoroalkyl groups are still very much needed and have attracted a great deal of attention in the last decades. The hydroperfuoroalkylation of alkenes represents a very attractive method to achieve this goal. The hydroperfluoroalkylation of electron-deficient alkenes such as acrylates has been developed under reducing conditions.[5–17] The reaction involving the less reactive, unactivated alkenes is more challenging. The reaction can be performed via a two-step procedure using iodine/bromine atom transfer radical addition (ATRA) followed by a dehalogenation process.[18–20] This procedure is,

however, not very practical for hydrotrifluoromethylation due to the gaseous nature of trifluoromethyl iodide. The hydrotrifluoromethylation has been observed as a side reaction by Davies et al. during the addition of $CF_3I$ to alkenes[21] and by Muller during the electrochemical decarboxylation of trifluoroacetic acid in the presence of alkenes.[22] Ding and co-workers reported hydroperfluoroalkylation of alkenes with perfluoroalkyl iodide promoted by zinc and a catalytic amount of ytterbium (III) in THF as both the solvent and the source of hydrogen atom (Scheme 1, A).[23] A similar reductive process was described by Chen and Long using in situ generated perfluoroalkyl iodides and sodium dithionite.[24] Desulfitative processes have been examined by Langlois and co-workers[25] and by Tommasino et al.[26] In these two reactions, the solvent was also the source of hydrogen atom, leading to rather inefficient processes. This approach was nicely extended by Nicewicz and co-workers, who developed a photoredox catalysed trifluoromethylation of styrene and unactivated alkenes using an aromatic thiol as a catalytic source of hydrogen atom (Scheme 1, B).[27] Gouverneur and co-workers reported the hydrotrifluoromethylation of unactivated alkenes using Umemoto reagent as the $CF_3\cdot$ source under photoredox catalysis using methanol as the hydrogen atom source (Scheme 1, C).[28] A related photocatalytic hydrotrifluoromethylation reaction was reported by Scaiano and co-workers using Togni reagent II as a source of $CF_3\cdot$, methylene blue as a catalyst and amines such as TMEDA and DBU as sources of hydrogen atoms.[29] A flow process was developed by Noël and coworkers for the iridium photocatalysed hydrotrifluoromethylation of styrene derivatives with trifluoromethyl iodide and 4-hydroxythiophenol as a source of the hydrogen atom.[30] A similar hydroperfluoroalkylation in flow using sulfilimino iminiums as a source of perfluorinated radicals was proposed by Magnier and wo-workers.[31] The hydroperfluoroalkylation of unactivated alkenes under visible light irradiation of perfluoroalkyl bromide was achieved in the presence of eosin Y as a catalyst under reductive conditions ($Na_2S_2O_3$) or using THF as a source of hydrogen atoms.[32] More recently, the eosin Y photocatalysed radical addition was coupled with the use of ascorbic acid as a reducing agent.[33]




Scheme 1. Hydroperfluoroalkylation of unactivated alkenes.

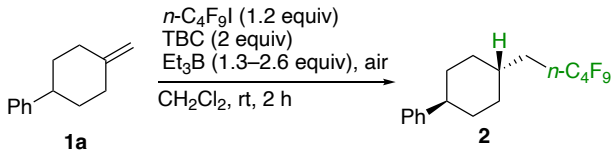
Iodine ATRA reaction of perfluoroalkyl iodides to alkenes using triethylborane/air as an initiator has been pioneered by Utimoto, Oshima and co-workers.[34] Recently, we have developed an efficient radical-mediated chain reaction for the hydroalkylation of unactivated, electron-rich alkenes employing 4-*tert*-butylcatechol (TBC) as a source of hydrogen atoms and triethylborane as a chain transfer reagent.[35–38] This process proved to be efficient with a broad range of electrophilic radicals, and its efficiency was attributed to its very favourable polar effects and unprecedented repair mechanism.[39,35] Considering the simplicity and efficiency of the method, we envisaged that it could be extended to the hydroperfluoroalkylation of unactivated alkenes (Scheme 1, D). We also report a practical method for the hydrotrifluoromethylation of alkenes that does not rely on the use of gaseous $CF_3I$ or expensive radical precursors such as Togni or Uemoto reagents.[40] The submitted version of this manuscript has been posted on a preprint server.[41]

## 2.2 Results and Discussion

### 2.2.1 Hydroperfluoroalkylation with perfluoroalkyl iodides

The hydroperfluoroalkylation of 4-phenyl-1-methylenecyclohexene **1a** with commercially

available nonafluoro-1-iodobutane was investigated first (Scheme 2). Reactions were performed with 4-*tert*-butylcatechol (TBC, 2 equivalents) as a source of hydrogen atoms and triethylborane as a chain transfer reagent. To make the reaction more attractive, the excess of the perfluoroalkyl iodide was limited to 1.2 equivalents relative to the alkene. Reagents were mixed under an inert atmosphere and the reaction vessel was then open to air to initiate the radical process. The first run with 2 equivalents TBC and 1.3 equivalents $Et_3B$ added at once at the beginning of the reaction provided the desired product **2** in 80% yield together with only traces of the iodine ATRA product. Portion-wise addition of TBC (2 × 1 equiv) and triethylborane (2 × 1.3 equiv) provided **2** in 88% yield without traces of the iodine ATRA product.

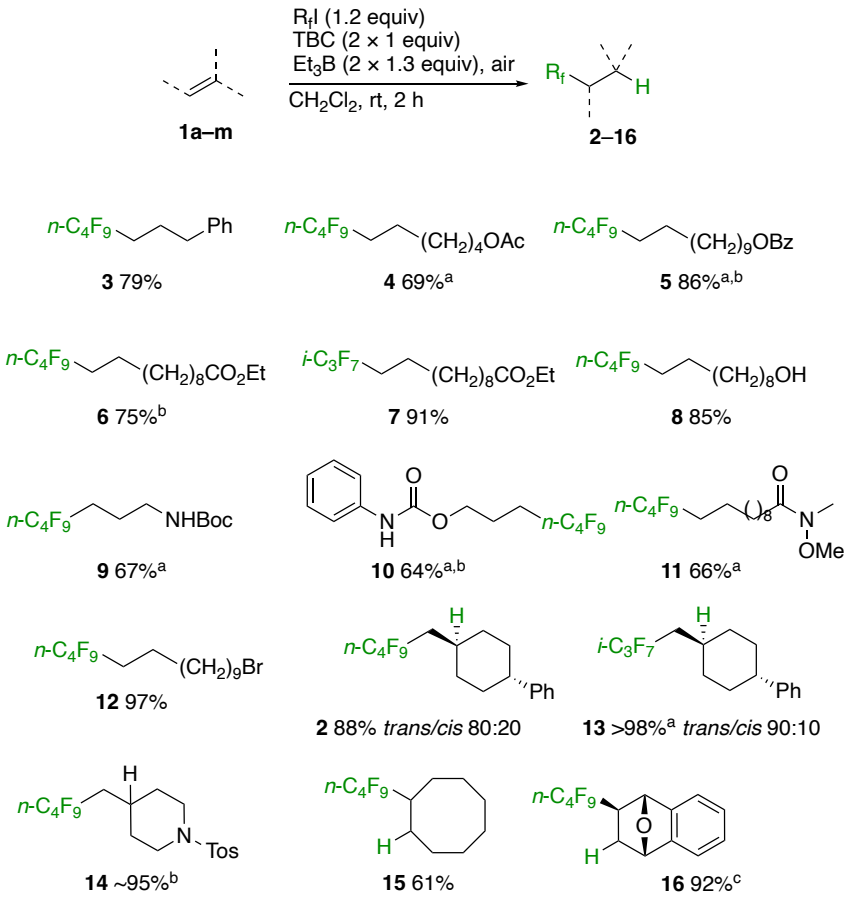



| | |
|---|---|
| TBC (2 equiv)<br>$Et_3B$ (1.3 equiv) | **2** 80% (*trans/cis* 80:20)<br>traces of ATRA product) |
| TBC (2 × 1 equiv)<br>$Et_3B$ (2 × 1.3 equiv) | **2** 88% (*trans/cis* 80:20) |

Scheme 2. Optimised conditions for the hydroperfluoroalkylation of **1a**.

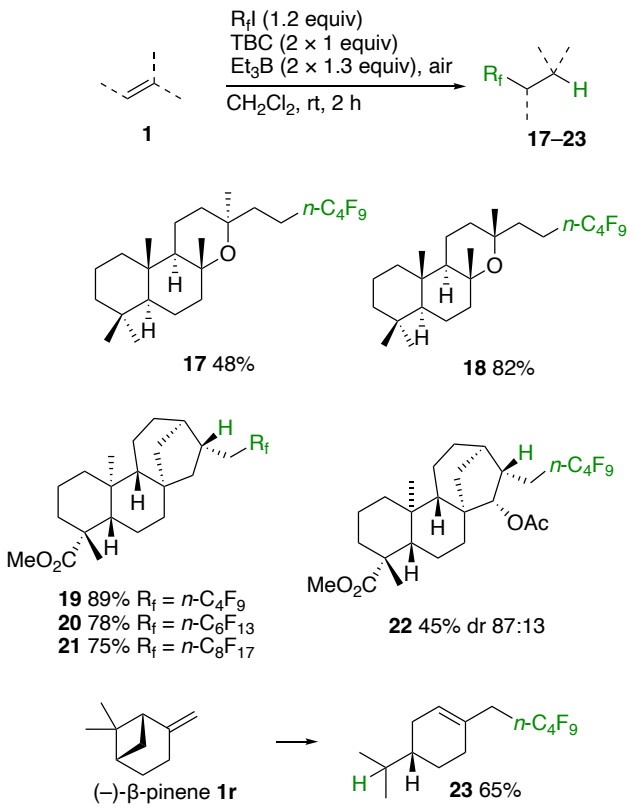
These optimised reaction conditions were employed to investigate the scope of the process with a wide range of alkenes (Scheme 3). Terminal, monosubstituted alkenes were investigated first. Reaction with allylbenzene **1b** gave **3** in 79% yield. Ester containing alkenes **1c**–**1e** gave products **4**–**6** in good to high yields (69–86%). The preparation of **5** from the benzoate ester **1d** worked more efficiently when 10 mol% of $K_2CO_3$ was added to minimise the formation of unsaturated side-products arising from the decomposition of the intermediate iodine ATRA product. The reaction of the ω-unsaturated ethyl ester alkene **1e** with perfluoro-*i*-propyl iodide gave **7** in 91% yield. In this case, a small amount of the iodine atom transfer product (6%) was also isolated and characterised. Perfluoroalkylation of alkenes containing a free hydroxy group (**1f**), carbamates (**1g** and **1h**), a Weinreb amide (**1i**) and a bromide (**1j**) were efficiently hydroperfluoroalkylated to **8**–**12**, demonstrating further the good functional group compatibility of the reaction. Reactions with representative 1,1-disubstituted alkenes were investigated next. The hydroperfluoroalkylation of 4-phenyl-1-methylenecyclohexene **1a** was performed with perfluoro-*n*-butyl iodide and perfluoro-*i*-

propyl iodide providing **2** and **13** in high yields. The hydroperfluoroalkylated product **14** also obtained a high yield (95%) from 1-*p*-toluenesulfonyl-4-methylenepiperidine **1k**. More examples of hydroperfluoroalkylation of 1,1-disubstituted alkenes (terpenoids) are described in Scheme 4. Finally, the reaction was attempted with non-terminal alkenes. The addition of carbon-centered radicals to internal alkenes is challenging and this is particularly true for perfluoroalkyl radicals due to their highly electrophilic nature that favors hydrogen atom transfer from allylic positions.[42] The reaction with cyclooctene **1l** afforded the desired perfluoroalkylated cyclooctane **15** in 61% yield when the reaction was run with 3 equivalents of TBC, which competes favourably with other hydroperfluoroalkylation procedures.[32] The reaction with the more reactive naphthalene-1,4-oxide **1m** proved to be more problematic. Under our standard conditions, only the product of iodine atom transfer was obtained, indicating that the TBC-mediated deiodination was, in this case, inefficient. The origin of this observation is not fully understood. However, the presence of the β-oxygen atom is presumably playing a role in slowing down the rate of hydrogen atom transfer from TBC due to less favourable polar effects (decrease in the nucleophilicity of the radical adduct).[43] At the same time, the bicyclic iodide intermediate is also probably less prone to iodine atom abstraction by an ethyl radical due to less favourable thermodynamic effects, thus preventing the one-pot deiodination process to take place (see mechanistic discussion). Gratifyingly, the desired product of hydroperfluoroalkylation **16** could be obtained in high yield via a two-step procedure involving our recently developed di-*tert*-butylhyponitrite (DTBHN) mediated iodine ATRA reaction,[44] followed by deiodination with hypophosphorous acid according to Barton's procedure.[45,46]




Scheme 3. Hydroperfluoroalkylation of alkenes. a) With 3 equivalents TBC. b) With 10 mol% $K_2CO_3$. c) Using a two-step procedure.

The hydroperfluoroalkylation of terpenoids was investigated next, and the results are presented in Scheme 4. Treatment of *epi*-manoyl oxide **1n** under the standard reaction conditions gave **17** in 48%. The same reaction using manoyl oxide **1o** provided the hydroperfluoroalkylated product **18** in high yield (82%). Finally, the hydroperfluoroalkylation of methyl *ent*-kaurenoate **1p** was investigated with different perfluoroalkyl iodides. The desired products **19**–**21** were obtained in 75–89% yields as single diastereomers. The hydroperfluoroalkylation of methyl 15α-acetoxy-*ent*-kaurenoate **1q** provided the desired product **22** in 45% yield as an 87:13 mixture of diastereomers. Finally, the reaction of (–)-β-pinene **1r** was examined. The reaction afforded, as anticipated for a radical process, the ring-opened product **23** in 65% yield. Overall, these examples demonstrate the utility of our hydroperfluoroalkylation process for the modification of terpenic natural products.

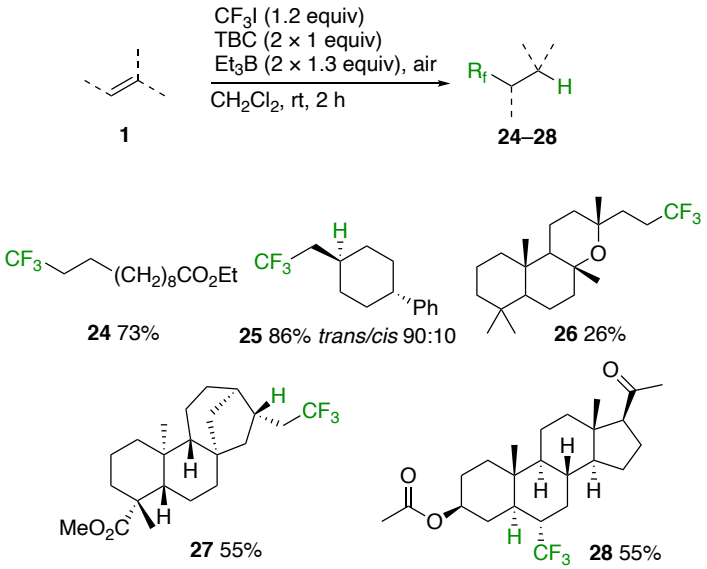



Scheme 4. Hydroperfluoroalkylation of terpenoids.

### 2.2.2 Hydrotrifluoromethylation with trifluoromethyl iodide and trifluoromethanesulfonyl chloride

The good results obtained with perfluoroalkyl iodides incited us to extend the reaction to the hydrotrifluoromethylation of alkenes using trifluoromethyl iodide. The gaseous nature of this reagent made the reaction experimentally more demanding. However, a practical procedure was developed by using a Schlenk flask of a defined total volume (25 mL = 1.2 mmol, 10 mL = 0.5 mmol), which was filled at room temperature and atmospheric pressure with gaseous $CF_3I$ (see supplementary material for details). The closed Schlenk flask was cooled down with liquid nitrogen to condense $CF_3I$, and the system was set under an inert $N_2$ atmosphere and placed in a dry ice ethanol bath at –78 °C. A solution of the alkene and TBC in dichloromethane was added, followed by $Et_3B$. After placing the reaction mixture at –20 °C, air was added via a syringe and the mixture was stirred at this temperature for 1 h, then allowed to warm up to room temperature and further stirred open to air until completion of the reaction. Using this procedure, the monosubstituted alkene **1e** was hydrotrifluoromethylated to **24** in 73% yield (Scheme 5). Similar results were obtained with the *exo*-methylene cyclohexane derivative **1a**

affording **25** in 86% yield as a *trans/cis* 9:1 mixture. The terpenoids manoyl oxide **1o** and methyl *ent*-kaurenoate **1p** afforded **26** and **27** in 26% and 55% yields, respectively. Gratifyingly, hydrotrifluoromethylation of the more challenging non-terminal alkene *O*-acetyl pregnenolone **1s** afforded the desired product **28** in 55% yield. In several reactions, small amounts of alkenes, presumably resulting from HI elimination of the intermediate iodine ATRA products, were also observed.

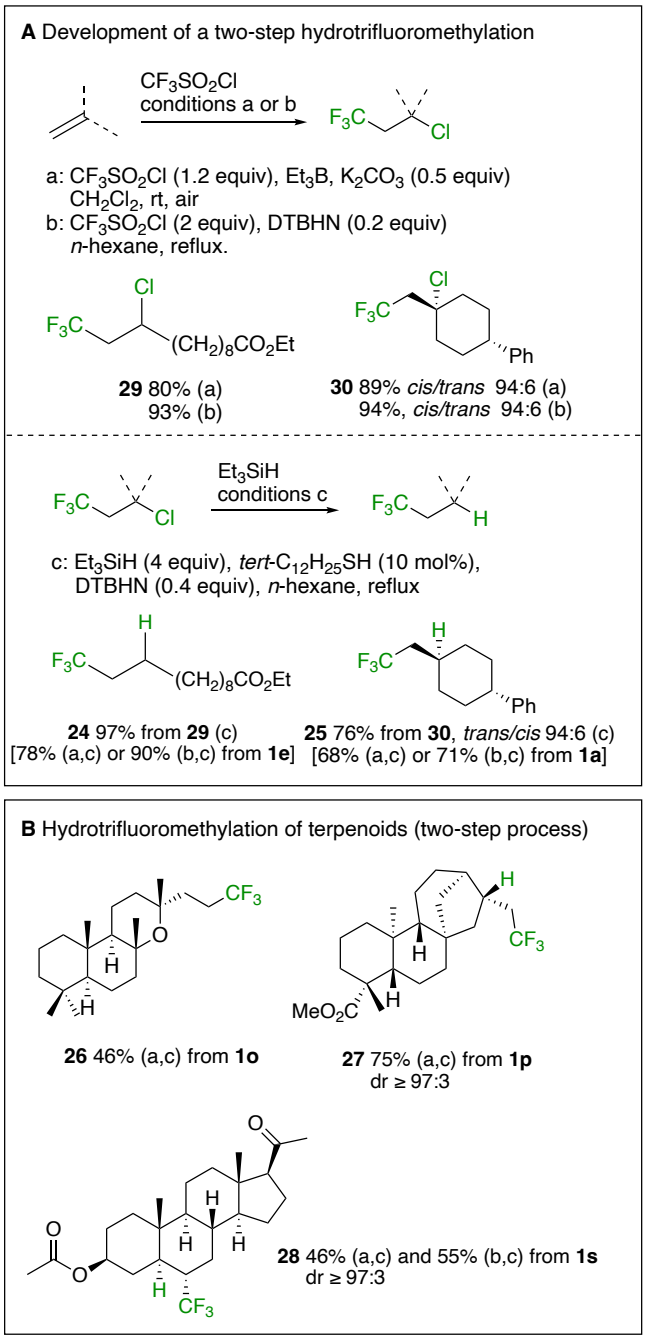



Scheme 5. Hydrotrifluoromethylation with $CF_3I$.

Since working with gaseous trifluoromethyl iodide is tedious and costly, we looked for an alternative procedure based on the use of a commercially available, affordable, and easy-to-handle reagent. Recently, we reported that desulfitative processes are particularly efficient to run chloro- and thio- and azidoalkylation of alkenes.[47–49] Trifluoromethanesulfonyl chloride is a very common and commercially available reagent. Its use for the chlorotrifluoromethylation of alkenes[50] was pioneered by Kamigata et al. using metal catalysis,[51–54] a reaction that could also be run under photoredox conditions,[55–61] as well as under classical radical initiation.[62] Therefore, we decided to employ it for the development of a two-step alkene hydrotrifluoromethylation process. The first step, a chlorine ATRA process, was investigated first with ethyl-10-undecenoate **1e** and 4-phenyl-1-methylenecyclohexane **1a**. The reaction proved to be efficient upon initiation with triethylborane/air at room temperature in dichloromethane using 1.2 equivalents of trifluoromethanesulfonyl chloride (procedure a). The addition of potassium carbonate proved

to be beneficial to the reaction by minimising side product formation, presumably by neutralising small amounts of triflic acid and HCl generated by hydrolysis of the trifluoromethanesulfonyl chloride. Under these conditions, the products of chlorotrifluoromethylation **29** and **30** were isolated in 80% and 89% yields, respectively (Scheme 6, A). Interestingly, by using the procedure we have recently developed for iodine ATRA reaction using di-*tert*-butylhyponitrite (DTBHN) as an initiator,[44] improved yields were obtained, and the use of a base was not anymore necessary. The reaction also proved to work efficiently in *n*-hexane as a solvent, a critical aspect for the development of an operationally simple one-pot procedure (vide infra). Under these conditions (procedure b), chlorides **29** and **30** were obtained in 93% and 94% yields, respectively (Scheme 6, A).

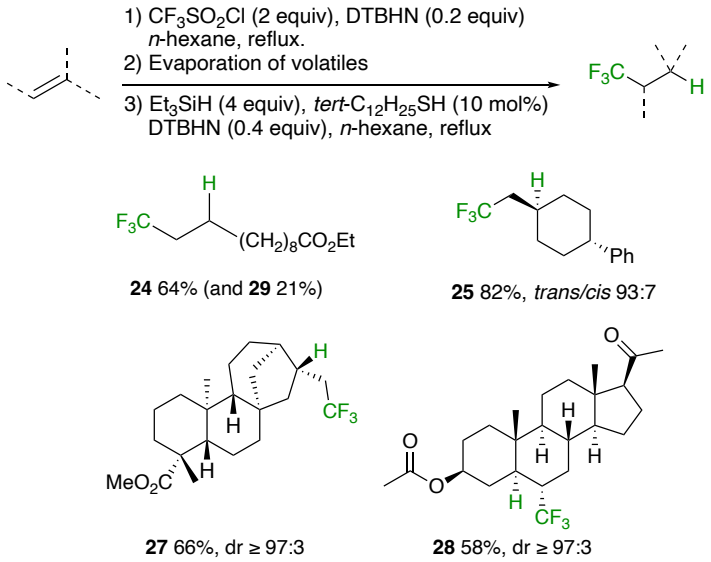
The dechlorination step was investigated next using the mildest possible reaction conditions, i.e., avoiding the use of strong reducing agents such as metals and metal hydrides. For this purpose, the very mild radical method developed by Roberts and co-workers with triethylsilane and *tert*-dodecanethiol was selected.[63,64] By using 4 equivalents of $Et_3SiH$ and 10 mol% of a thiol catalyst under initiation with di-*tert*-butylhyponitrite (procedure c), the desired hydrotrifluoromethylated products **24** and **25** were obtained from chlorides **29** and **30** in 97% and 76%, respectively (Scheme 6, A). Using this two-step approach that combines procedures b and c, alkenes **1e** and **1a** were hydrotrifluoromethylated to **24** and **25** with overall yields of 90% and 71%, respectively. These results compare well with the $CF_3I$ mediated process described in Scheme 5. This two-step approach was then applied for the hydrotrifluoromethylation of isoprenoid substrates (Scheme 6, B). Using procedures a and c, manoyl oxide **1o** and methyl *ent*-kaurenoate **1p** afforded **26** and **27** in 46% and 75% yield, respectively. The challenging non-terminal alkene *O*-acetyl pregnenolone **1s** was then examined and it afforded the desired product **28** in 46% (procedures a and c) and 55% (procedures b and c).




Scheme 6. Two-step hydrotrifluoromethylation with $CF_3SO_2Cl$.

Since the same initiator (DTBHN) and solvent (*n*-hexane) were used for both the desulfitative chlorine ATRA and the dechlorination processes (Scheme 6, conditions b and c), the possibility of running the hydrotrifluoromethylation as a two-step, one-pot process was envisaged. The hydrotrifluoromethylation of a series of alkenes was attempted without purification of the intermediate chlorides (Scheme 7). The reaction conditions used for the two-step process could be kept unchanged provided that, after the chlorine ATRA process, the excess of the volatile trichloromethyl sulfonyl chloride was evaporated before performing the

dechlorination. Using this approach, the alkene **1e** was converted to **24** in 64% yield, together with the non-dechlorinated product **29** (21%). The reaction of **1a** provided **25** in 82% yield as a *trans/cis* 93:7 mixture. The isoprenoids **1p** and **1s** were also subjected to this one-pot process, providing **27** and **28** in 66% and 58% yields, respectively, as single detectable diastereomers (dr ≥ 93:7).

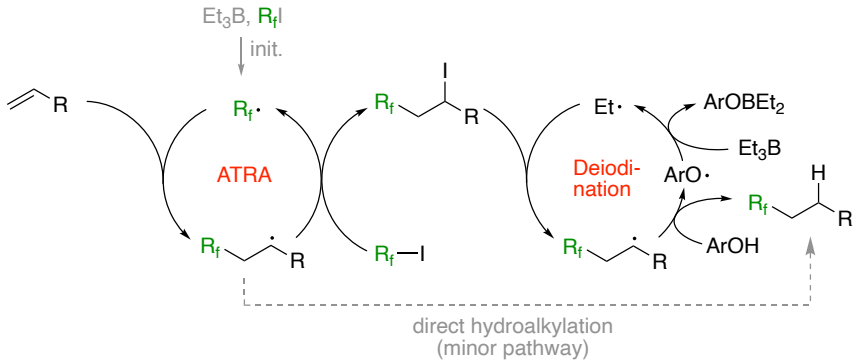



Scheme 7. One-pot hydrotrifluoromethylation with $CF_3SO_2Cl$.

## 2.3 Mechanism

The hydrotrifluoromethylation with perfluorinated alkyl iodides is expected to proceed via the mechanism previously described for α-iodoesters and related compounds.[35] Due to the very likely high rate of iodine atom transfer involving perfluoroalkyl iodides[65] relative to the rate of hydrogen atom transfer from TBC by alkyl radical ($k_H = 1.5 \times 10^6$ $M^{-1}$ $s^{-1}$ for secondary alkyl radicals),[66] the major reaction pathway presumably involves first an iodine ATRA reaction, delivering the iodoperfluoroalkylated intermediate, followed by a deiodination process mediated by the system triethylborane/4-*tert*-butylcatechol (Scheme 8). This mechanism, in which $Et_3B$ plays the role of both the initiator and a chain transfer reagent, is supported by the isolation of iodine ATRA products when the amount of $Et_3B$ is reduced. The product of iodine atom transfer was also isolated during the hydroperfluoroalkylation of naphthalene 1,4-oxide **1m** (Scheme 3, compound **16**). In this specific case, the deiodination cycle is not taking place due to an inefficient abstraction of the iodine atom from the ATRA

product by the ethyl radical. Direct hydrogen atom abstraction from TBC by the intermediate radical adduct is presumably a minor pathway (Scheme 8, grey arrow), except when the intermediate radical adduct is tertiary. Indeed, compared to secondary radicals, tertiary radicals are more nucleophilic and, therefore, react faster with TBC, and, at the same time, their increased stability makes them less reactive for iodine atom abstraction. As discussed previously, the efficacy of this system relies on a particularly efficient chain reaction due to favourable polar effects and, presumably, a chain repair mechanism allowing to overcome chain disrupting processes involving undesired hydrogen atom transfers leading to stabilised allylic radicals. The formation of allylic radicals and the involvement of this chain repair process have not been probed in this particular case but are nevertheless very likely due to the strong hydrogen atom abstracting character of perfluorinated alkyl radicals.[42]




Scheme 8. Simplified reaction mechanism of the hydroperfluoroalkylation with perfluorinated alkyl iodides.

## 2.4 Conclusion

The direct hydroperfluoroalkylation of unactivated alkenes with perfluoroalkyl iodides, including gaseous trifluoromethyl iodide, has been achieved in good to high yields under mild conditions using 4-*tert*-butylcatechol as a source of hydrogen atom and triethylborane as a chain transfer agent. The reaction has been shown to work with terminal alkenes as well as di- and trisubstituted internal alkenes, including those of complex isoprenoids of natural origin. For the trifluoromethylation reaction, a practical alternative to the use of gaseous and expensive $CF_3I$ has been developed by taking advantage of a desulfitative chlorine atom transfer process followed by a thiol-catalyzed dechlorination process. This two-step procedure maintains the mildness of reaction conditions and can be performed without purification of the chloride intermediate in a one-pot procedure.

**Acknowledgements**

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## 2.5 Experimental Section

### General and instrumentations

The $^{13}C$ and $^{1}H$ NMR spectra were recorded on either a Bruker Avance 300 ($^{1}H$: 300.18 MHz, $^{13}C$: 75.48 MHz) or a Bruker Avance II 400 spectrometer ($^{1}H$: 400.13 MHz, $^{13}C$: 101 MHz). Chemical shifts are reported in units of δ (ppm). For $^{1}H$ NMR spectra, the internal standard, tetramethylsilane (TMS), was set to δ = 0.000 ppm or the residual protonated solvents were used to reference the spectra ($CHCl_3$ δ = 7.262 ppm; $CH_2Cl_2$ δ = 5.320 ppm). For $^{13}C$ NMR spectra, the internal standard, tetramethylsilane (TMS), was set to δ = 0.00 ppm or the deuterated solvents were used to reference the spectra ($CDCl_3$ δ = 77.16 ppm; $CD_2Cl_2$ δ = 53.84). $^{13}C$ NMR spectra were run using a proton-decoupled pulse sequence. Due to coupling to the $^{19}F$ nucleus (spin = 1/2), the carbons with fluorine atoms attached to them have multiplet signals in $^{13}C$ NMR and cannot be interpreted or assigned. The following abbreviations were used to describe the multiplicities: s (singlet), d (doublet), t (triplet), q (quadruplet), quin (quintet), sept (septet), m (multiplet), br (broad). Coupling constants (J) are reported in Hertz (Hz) with an accuracy of one unit of the last digit. The number of carbon atoms for each signal is indicated only when superior to one, and when two signals are very close, they are reported with two decimal places. HRMS analyses were recorded on an Applied Biosystems Sciex QSTAR Pulsar (hybrid quadrupole time-of-flight mass spectrometer) using positive electron spray. Infrared spectra were recorded neat equipped with a diamond ATR System and are reported in wave numbers ($cm^{-1}$). Reported are the first six signals (with decreasing wave number) and characteristic functional groups. The following abbreviations were used to explain the intensities: w (weak), m (medium), s (strong), and br (broad), e.g. for OH peaks. Only the stretching frequency of the characteristic functional group was reported, and when the compound did not contain one, the most relevant frequencies were listed. For flash chromatography (FC), silica gel 40-63 µm (230-400 mesh) and aluminium oxide CAMAG 5016-A-I basic (40-300 µm) were used. Thin layer chromatography (TLC) was performed using Silicycle glass-backed TLC extra hard layer, 259 µm, 60 Å, F-254 analytical plates; visualisation under UV (254 nm and/or 366 nm) or/and by staining with a solution of potassium permanganate ($KMnO_4$); phosphomolybdic acid ($H_3PMo_{12}O_{40}$) and cerium sulfate ($Ce(SO_4)_2$), and subsequent heating.

Unless otherwise stated, all yields are isolated yields. Ambient (or room) temperatures were

generally in the 21–25 °C range. All reactions were run under an argon atmosphere, and solids were added quickly or under a blanket of flowing argon unless otherwise specified. All glassware was oven-dried overnight at 140 °C, assembled hot, and cooled under a stream of dry argon gas or flame-dried under vacuum.

## Reagents and starting materials

## Preparation of reagents

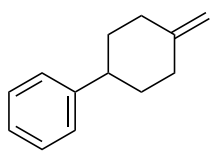
### Di-tert-butyl hyponitrite (DTBHN)[1]

t-BuON=NOt-Bu
$C_8H_{18}N_2O_2$
MW: 174.24

DTBHN was prepared using a slightly altered procedure. In a 250 mL three-neck flask equipped with a stirring bar, sodium *trans*-hyponitrite hydrate (8.15 g) was loaded and dried to a constant weight (5.58 g, 45.0 mmol). In another flask, $ZnCl_2$ hydrate (14 g, 101.0 mmol) was melted under stirring *in vacuo* (3 ×) in order to dry it. From the resulting block of grey solid, pieces with a total weight of 8.6 g (63.1 mmol) were (quickly) transferred into a two-neck flask, dried another 10 min under vacuum, and then suspended in $Et_2O$ (35 mL), first with stirring for 2 h then with sonication for another 20 min until no more pieces of $ZnCl_2$ were visible. To the dry sodium *trans*-hyponitrite was added $Et_2O$ (30 mL) and *tert*-butylbromide (47 mL, 418 mmol) and the resulting milky white mixture was cooled to –10 °C (internal temperature) using an ice/NaCl/water bath. Then, the $ZnCl_2$ suspension was added using a cannula (Ø = 1 mm) at such a rate that the internal temperature did not exceed –5 °C. After complete addition, the mixture was allowed to reach room temperature and stirred for another 1.5 h. The reaction mixture was filtered, and the remaining solid was washed with $Et_2O$ (3 × 10 mL). The resulting yellow solution was transferred into a separatory funnel, and water was added. The aqueous layer was extracted with $Et_2O$ (3 × 20 mL), and the combined organic layers were washed with brine, dried over $Na_2SO_4$ and the volatiles were removed under reduced pressure (bath temperature 20 °C, 400 mbar, end to 50 mbar for a short time). The obtained solid was crystallised from *n*-pentane to furnish almost colourless crystals in three crops (all crops were washed with cold pentane). Recrystallisation from pentane of the combined crops furnished the product as colourless, transparent crystals (3.43 g, 37%). Spectral data is in accordance with the literature. DTBHN was stored for months at 4 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 1.39 (s, 18H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 81.3 (2C, $C_q$), 27.9 (6C, $CH_3$).

## Preparation of alkenes

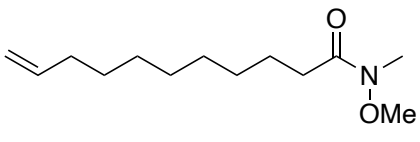
### (4-Methylenecyclohexyl)benzene (1a)[2]



$C_{13}H_{16}$
MW: 172,27

A flame-dried two-neck 250 mL flask was charged under Ar with *t*-BuOK (98% purity, 5.15 g, 45.0 mmol) and $Et_2O$ (60 mL) and the mixture was cooled with an ice bath. Then methyl(triphenyl)phosphonium bromide (16.4 g, 45.0 mmol) was added under vigorous stirring, the cooling bath was removed, and the yellow solution was stirred at rt for 30 min. Meanwhile, 4-phenylcyclohexanone (5.23 g, 30.0 mmol) was dissolved in $Et_2O$ (20 mL) and transferred to the reaction mixture. The flask was equipped with a condenser and heated under reflux for 2.5 h, by which time TLC analysis indicated complete conversion of the starting ketone. The cooled reaction mixture was washed with water (3 × 60 mL), and then the aqueous phases were further extracted with $Et_2O$ (1 × 50 mL). The ethereal phases were washed with brine, dried under $Na_2SO_4$, and filtered through a cotton pad. During concentration under vacuum, triphenylphosphine oxide precipitated. It was removed by filtration through a short pad of silica gel (pentane/$Et_2O$ 8:2). The obtained crude residue was then submitted to FC (heptanes/EtOAc 95:5) to afford the compound as a clear liquid (3.53 g, 20.5 mmol, 68%). $R_f$ = 0.55 (100% pentane). $^1$H NMR (300 MHz, $CD_2Cl_2$): $\delta$ 7.36–7.19 (m, 5H), 4.68 (t, *J* = 1.7 Hz, 2H), 2.69 (tt, *J* = 12.2, 3.4 Hz, 1H), 2.50–2.43 (m, 2H), 2.29–2.16 (m, 2H), 2.07–1.99 (m, 2H), 1.54 (qd, *J* = 12.5, 3.8 Hz, 2H). $^{13}$C NMR (75 MHz, $CD_2Cl_2$): $\delta$ 149.4 (Cq), 147.5 ($C_q$), 128.7 (2×$CH_{Ar}$), 127.2 (2x$CH_{Ar}$), 126.3 (CH), 107.4 (=$CH_2$), 44.5 (CH), 36.0 (2×$CH_2$), 35.5 (2×$CH_2$). IR ($\nu$, $cm^{-1}$): 2927 (w), 2854 (w), 1649 (w), 1492 (w), 887 (m), 753 (m), 696 (m).

### N-methoxy-N-methylundec-10-enamide (1i)[3]



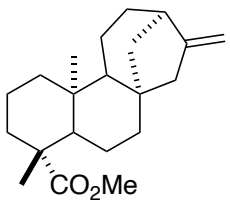

$C_{13}H_{25}NO_2$
MW: 227,35

Step 1: A flame-dried two-neck 100 mL flask was equipped with a condenser and two scrubbers (trap for HCl formed during the reaction) filled with 3M NaOH, in series, and Ar flow. 10-Undecenoic acid (97%, 28.5 g, 150 mmol) and DMF (1.0 mL, 3.0 mmol) were transferred to the flask and then stirred while heating at 80 °C. Thionyl chloride (99.7 %, 16.5 mL, 225 mmol) was added dropwise to the reaction mixture under a flow of Ar. When the addition was complete the Ar balloon was removed, and the

reaction was kept for 6 h at 80 °C. The scrubbers were exchanged for a cold trap (high vacuum), and the excess of DMF and thionyl chloride were removed under vacuum. Then, the cold trap was replaced by a distillation head, and the content was distilled ($2.7\times10^{-1}$ mbar, 40 °C). The first 2 mL were discarded and the distillation provided undec-10-enoyl chloride (14.9 g, 73.3 mmol, 50%) as a colorless oil. $^{1}$H NMR (300 MHz, $CDCl_3$): *δ* 5.76 (ddt, *J* = 17.0, 10.5, 6.7 Hz, 1H), 5.01 – 4.82 (m, 2H), 2.84 (t, *J* = 7.3 Hz, 2H), 2.01 (q, *J* = 6.9 Hz, 2H), 1.65 (q, *J* = 7.1 Hz, 2H), 1.41–1.22 (m, 10H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 173.2 (C=O), 138.8 (CH), 114.1 (CH=*C*$H_2$), 47.0 (*C*$H_2$C=O), 33.7 ($CH_2$), 29.2 ($CH_2$), 29.02 ($CH_2$), 28.98 ($CH_2$), 28.9 ($CH_2$), 28.4 ($CH_2$), 25.0 ($CH_2$).

Step 2: A flame dried 100 mL one-neck flask was loaded with *N,O*-dimethylhydroxylamine hydrochloride (98%, 40 mmol, 4.0 g) and dry $CH_2Cl_2$ (40 mL, 0.3 M). The reaction mixture was cooled to 0 °C with ice/water bath and triethylamine (98%, 11.2 mL, 80 mmol) was added to the reaction mixture that turned to white fluffy mixture and solidified at 0 °C. A solution of undec-10-enoyl chloride (**SI-1**) (20 mmol, 4.054 g) in dry $CH_2Cl_2$ (10 mL) was added dropwise. The cooling bath was removed and the reaction mixture was stirred overnight at rt. Volatiles were removed under high vacuo, the residue was diluted with TBME (100 mL) and partitioned with aq. 1.0 M HCl (100 mL). The ethereal phase was washed again with aq. 1.0 M HCl (100 mL), and the combined aqueous phases were back-extracted with TMBE (10 mL). The combined ethereal phases were washed with aq. 1.0 M NaOH (100 mL), sat. aq. $NaHCO_3$ (100 mL), and sat. aq. NaCl (100 mL), then dried over $Na_2SO_4$, filtered through a plug of silicagel protected with a cotton pad, and concentrated in vacuo to furnish a pale yellow oil that was purified by FC (heptanes/EtOAc 90:10, then 85:15 and finally 80:20) affording **1i** (2.67 g, 11.8 mmol, 59%) as a pale-yellow oil. $R_f$ = 0.44 (heptanes/EtOAc 70:30). $^{1}$H NMR (300 MHz, $CDCl_3$): δ 5.77 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 4.99–4.86 (m, 2H), 3.65 (s, 3H), 3.14 (s, 3H), 2.38 (t, *J* = 7.6 Hz, 2H), 2.04–1.96 (m, 2H), 1.64–1.54 (m, 2H), 1.41–1.21 (m, 10H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 174.8 (C=O, broad signal), 139.2 (=CH), 114.2 (=$CH_2$), 61.2 ($OCH_3$), 33.9 ($CH_2$), 32.3 ($CH_3$, broad signal), 32.0 ($CH_2$, broad signal), 29.5 ($CH_2$), 29.43 ($CH_2$), 29.40 ($CH_2$), 29.2 ($CH_2$), 29.0 ($CH_2$), 24.7 ($CH_2$).

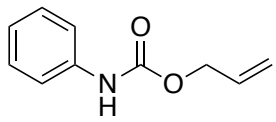
### Methyl (4R,6aS,9R,11bS)-4,11b-dimethyl-8-methylenetetradecahydro-6a,9-methanocyclohepta[a]naphthalene-4-carboxylate (1p)[4]




$C_{21}H_{32}O_2$
MW: 316,49

A flame-dried one neck 25 mL flask was charged with kaur-16-en-19-oic acid (0.2 mmol, 61 mg), benzene (7.0 mL) and methanol (3.0 mL) under Ar at rt. (Trimethylsilyl)diazomethane (0.35 mmol, 0.175 mL, 2 M) was added under Ar, and the reaction mixture was stirred for 1 h at rt. The excess of (trimethylsilyl)diazomethane was allowed to react with acetic acid (0.2 mmol, 11 μL) for 5 min until the yellow mixture turned colourless. To the reaction mixture was basified by adding a few drops of 0.5 M aq. $K_2CO_3$ then washed with water (2 × 5 mL), brine (1 × 10 mL), and dried over $Na_2SO_4$ and concentrated under reduced pressure. The crude product was submitted to FC (pentane/$Et_2O$ 99:1) to afford **1p** as a colorless solid (63 mg, 0.2 mmol, quantitative). $R_f$ = 0.73 (pentane/$Et_2O$ = 98:2). M.p. 79–82 °C (not corrected). $[\alpha]_D^{20}$ = –12.36; c=1.0 (in $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$): δ 4.81–4.78 (m, 1H), 4.73–4.74 (m, 1H), 3.64 (s, 3H), 2.66–2.60 (m, 1H), 2.20–2.13 (m, 1H), 2.06–2.03 (m, 2H), 1.96 (dd, *J* = 11.2, 2.1 Hz, 1H), 1.90–1.69 (m, 4H), 1.64–1.38 (m, 7H), 1.17 (s, 3H), 1.12 (ddt, *J* = 11.4, 5.2, 1.7 Hz, 1H), 1.07–0.94 (m, 3H), 0.83 (s, 3H), 0.83–0.74 (m, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 178.1 (C=O), 155.9 (=CH), 103.0 (=$CH_2$), 57.1 (CH), 55.1 (CH), 51.1 ($CH_3$), 49.0 ($CH_2$), 44.2 (Cq), 43.83 (CH), 43.81 (Cq), 41.3 ($CH_2$), 40.8 ($CH_2$), 39.7 ($CH_2$), 39.4 (Cq), 38.1 ($CH_2$), 33.1 ($CH_2$), 28.8 ($CH_3$), 21.9 ($CH_2$), 19.2 ($CH_2$), 18.4 ($CH_2$), 15.4 ($CH_3$). IR (ν, $cm^{-1}$): 2946 (w), 2930 (w), 2850 (w), 1721 (s), 1146 (s), 870 (s).

### Allyl phenylcarbamate (1h)[5]

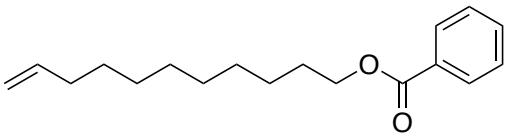



$C_{10}H_{11}NO_2$
MW: 177,20

A 100 mL flask equipped with a stirring bar was charged with allyl alcohol (98%, 0.593 g, 10.0 mmol), phenyl isocyanate (98%, 1.10 mL, 10.0 mmol) and THF (20 mL). The mixture was flushed with Ar and cooled to 0 °C. Triethylamine (1.41 mL, 10.0 mmol) was added by syringe over 5 min and the reaction mixture was warmed up to rt. The homogeneous reaction mixture was stirred for 2 h. The reaction was followed by TLC. The solvent was removed under reduced pressure to afford the crude **1h** as a colorless solid that used without further purification (1.77 mg, 10.0 mmol, 99%). Colorless solid. $R_f$ = 0.4 (10% $Et_2O$/pentane). M.p. 63–64 °C (not corrected). $^1$H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 8.0 Hz, 2H), 7.35–7.28 (m, 2H),

7.09–7.05 (m, 1H), 6.71 (broad s, 1H), 5.97 (ddt, *J* = 17.2, 10.5, 5.7 Hz, 1H), 5.37 (dt, *J* = 17.2, 1.6 Hz, 1H), 5.27 (dq, *J* = 10.4, 1.3 Hz, 1H), 4.67 (dt, *J* = 5.7, 1.4 Hz, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 153.4 (C=O), 137.9 ($Cq_{Ar}$), 132.6 (=CH), 129.2 (2 × $CH_{Ar}$), 123.7 ($CH_{Ar}$), 118.9 (2 × $CH_{Ar}$, broad signal), 118.4 (=$CH_2$), 66.0 ($CH_2$).

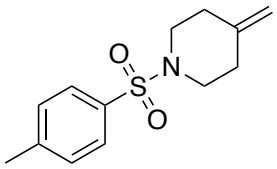
### Undec-10-en-1-yl benzoate (1d)[3]




$C_{18}H_{26}O_2$
MW: 274,40

A 100 mL one-neck round bottom flask with a stirring bar was charged with undec-10-en-1-ol (99%, 2.03 mL, 10.0 mmol) in $CH_2Cl_2$ (45 mL) under Ar. Pyridine (0.968 mL, 12 mmol) was added, and the reaction mixture was cooled with an ice bath to 0 °C. Benzoyl chloride (1.29 mL, 11 mmol) was added slowly, and the reaction mixture was warmed up to rt and then stirred for one day at rt. The reaction mixture was concentrated under vacuum, diluted with $Et_2O$ (40 mL) and washed with aq. 1.0 M HCl (1 × 40 mL). The ethereal phase was washed with $H_2O$ (1 × 40 mL), and the combined aqueous phases were extracted with $Et_2O$ (1 × 10 mL). The combined ethereal phases were washed once more with aq. 1.0 M HCl (1 × 40 mL), then with saturated aq $NaHCO_3$ (2 × 40 mL) and brine (1 × 40 mL), and dried over $Na_2SO_4$. Concentration under vacuum afforded a crude product that was purified by FC (heptanes/EtOAc 99:1, then 98:2 and finally 97:3) to afford **1d** (2.72 g, 9.91 mmol, 99%) as a colourless liquid. $R_f$ = 0.68 (heptanes/EtOAc 95:5). $^1$H NMR (400 MHz, $CDCl_3$): δ 8.09–8.03 (m, 2H), 7.53–7.57 (m, 1H), 7.46–7.41 (m, 2H), 5.81 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 4.99 (dq, *J* = 17.1, 1.7 Hz, 1H), 4.95–4.91 (m, 1H), 4.32 (t, *J* = 6.7 Hz, 2H), 2.07–2.01 (m, 2H), 1.82–1.73 (m, 2H), 1.49–1.27 (m, 12H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 166.9 (C=O), 139.3 (=CH), 132.9 ($CH_{Ar}$), 130.7 ($Cq_{Ar}$), 129.7 (2 × $CH_{Ar}$), 128.4 (2 × $CH_{Ar}$), 114.3 (=$CH_2$), 65.3 ($CH_2$), 33.9 ($CH_2$), 29.6 ($CH_2$), 29.5 ($CH_2$), 29.4 ($CH_2$), 29.2 ($CH_2$), 29.1 ($CH_2$), 28.9 ($CH_2$), 26.2 ($CH_2$). IR (ν, $cm^{-1}$): 2976 (w), 2924 (w), 2853 (w), 1717 (s), 1268 (s), 1109 (m), 707 (s).

## 4-Methylene-1-tosylpiperidine (1k)[6]



$C_{13}H_{17}NO_2S$
MW: 251,34

Step 1: A 500 mL two-neck round bottom flask equipped with a stirring bar was charged with 4-piperidone ethylene acetal (6.59 mL, 50 mmol), triethylamine (10.6 mL, 75 mmol) and $CH_2Cl_2$ (100 mL) under Ar at rt. A solution of tosyl chloride (11.6 g, 60 mmol) in dry $CH_2Cl_2$ (50 mL) was then cannulated dropwise, and the reaction mixture was stirred overnight at rt. Water (100 mL) was added, and the mixture was extracted with $CH_2Cl_2$ (3 × 100 mL). The combined organic phases were washed with aq. sat. $NaHCO_3$ (1 × 100 mL) and brine (1 × 100 mL) were dried over $Na_2SO_4$ and concentrated under reduced pressure to afford a reddish oil, which solidified upon drying. The pale pinkish crude solid was purified by FC (heptanes/EtOAc 60:40) to afford 8-(*p*-tolylsulfonyl)-1,4-dioxa-8-azaspiro[4.5]decane **SI-2** as a colourless solid (14.9 g, 50 mmol, 99%). $^1$H NMR (300 MHz, $CD_2Cl_2$): *δ* 7.68–7.57 (m, 2H), 7.40–7.31 (m, 2H), 3.86 (s, 4H), 3.09 (dd, *J* = 7.0, 4.6 Hz, 4H), 2.44 (s, 3H), 1.80–1.70 (m, 4H). $^{13}$C NMR (75 MHz, $CD_2Cl_2$): *δ* 144.2, 133.7, 130.1, 128.0, 106.3, 64.7, 45.0 (2 × $CH_2$), 34.8 (2 × $CH_2$), 21.7 ($CH_3$).

Step 2: A 1 L one neck round bottom flask equipped with a stirring bar was charged by 8-(p-tolylsulfonyl)-1,4-dioxa-8-azaspiro[4.5]decane (**SI-2**) (14.9 g, 50.1 mmol), THF (200 mL) and water (distilled, 100 mL), followed by dropwise addition of the conc. $H_2SO_4$ (96%, 50 mL, 90 mmol) within 30 min at 0 °C. The reaction was then heated under reflux for 3 h. Upon completion (GC monitoring), EtOAc (200 mL) was added. The organic phase was separated and washed with brine (1 × 200 mL), dried over $Na_2SO_4$ and concentrated under reduced pressure to afford 1-(*p*-Tolylsulfonyl)piperidin-4-one **SI-3** (12.7 g, 50 mmol, 99%) as a colourless solid, which was used for the next step without further purification. $^1$H NMR (300 MHz, $CD_2Cl_2$): δ 7.73–7.63 (m, 2H), 7.40–7.34 (m, 2H), 3.35 (t, *J* = 6.2 Hz, 4H), 2.49 (t, *J* = 6.3 Hz, 4H), 2.43 (s, 3H). $^{13}$C NMR (75 MHz, $CD_2Cl_2$): δ 205.7, 144.7, 133.8, 130.3, 127.9, 46.4, 41.0, 21.7.

Step 3: A 250 mL two-neck flask was filled with *t*-BuOK (98%, 8.61 g, 75.2 mmol), and dry THF (90 mL) was placed under Ar at rt. Methyl(triphenyl)phosphonium bromide (26.9 g, 75.2 mmol) was added giving a yellow color immediately and the reaction mixture was stirred for 30 min at rt. 1-(*p*-Tolylsulfonyl)piperidin-4-one **SI-3** (12.7 g, 50.1 mmol) was placed in a separate 100 mL flask, dissolved in dry THF (30 mL) and cannulated to the main reaction

mixture. The reaction mixture was heated under reflux for 1.5 h under Ar when the TLC analysis indicated complete conversion of the starting ketone. The reaction mixture was partitioned between $Et_2O$ (80 mL) and water (80 mL). The aqueous phase was extracted with $Et_2O$ (1 × 60 mL), washed with brine (1 × 60 mL), dried over $Na_2SO_4$ and concentrated under vacuum. The crude product was purified by FC (heptane/EtOAc 90:10) to afford the **1k** as a colourless solid (8.75 g, 35 mmol, 69 %). $R_f$ = 0.33 (heptane/EtOAc 90:10). M.p. 130.3–131.1 °C (not corrected). $^1$H NMR (300 MHz, $CD_2Cl_2$): δ 7.63–7.59 (m, 2H), 7.36–7.31 (m, 2H), 4.70–4.68 (m, 2H), 3.01 (t, *J* = 5.8 Hz, 4H), 2.42 (s, 3H), 2.31–2.26 (m, 4H). $^{13}$C NMR (75 MHz, $CD_2Cl_2$): δ 144.2 (Cq), 144.1 (Cq), 133.8 (Cq), 130.0 (2 × $CH_{Ar}$), 128.0 (2 × $CH_{Ar}$), 109.9 (=$CH_2$), 48.2 (2 × $CH_2$), 34.2 (2 × $CH_2$), 21.6 ($CH_3$). IR (ν, cm$^{-1}$): 2902 (w), 2845 (w), 1332 (s), 1159 (s), 729 (m).

## Hydroperfluoroalkylation

### General procedure for the hydroperfluoroalkylation with perfluoroalkyl iodides

#### General Procedure 1. Hydroperfluoroalkylation (standard procedure)

To a solution of alkene (1.0 mmol) and 4-*tert*-butylcatechol (TBC) (170 mg, 1.0 mmol) in $CH_2Cl_2$ (2.8 mL, 0.25 M) was added at rt, the perfluoroalkyl iodide (1.2 mmol), followed by $BEt_3$ solution (1.15 M in hexane, 1.13 mL, 1.3 mmol). The reaction mixture was stirred at rt for 1 h in an open-to-air flask protected from moisture by a $CaCl_2$ tube. Then, the second portion of TBC (170 mg, 1.0 mmol) and $BEt_3$ solution (1.15 M in hexane, 1.13 mL, 1.3 mmol) were added, and the solution was stirred for 1 h. The reaction mixture was filtered over a short pad of neutral $Al_2O_3$ eluting with $Et_2O$ or EtOAc in order to remove polar TBC and boron derivatives. The resulting crude filtrate was concentrated under reduced pressure and purified by FC (pentane/$Et_2O$ or heptanes/EtOAc).

#### General Procedure 1'. Modified Hydroperfluoroalkylation procedure

To a solution of alkene (0.16 mmol) and perfluoroalkyl iodide (0.24 mmol) in $CH_2Cl_2$ (10 mL, 0.015M) was added 4-*tert*-butylcatechol (50 mg, 0.3 mmol), followed by $Et_3B$ (0.2 mL, 0.2 mmol, 1M solution in hexane). The resulting solution was stirred at rt in the presence of air and protected from moisture by a $CaCl_2$ guard tube. After 2 h, the reaction mixture was filtered over a short pad of neutral $Al_2O_3$ using $Et_2O$ to remove the catechol derivatives and

boron-containing side products. The resulting crude filtrate was concentrated under reduced pressure and purified by FC (pentane/EtOAc).

### General procedure 2. Hydroperfluoroalkylation in the presence of $K_2CO_3$

To a solution of alkene (1.0 mmol), 4-*tert*-butylcatechol (TBC) (170 mg, 1.0 mmol) and $K_2CO_3$ (13.8 mg, 0.1 mmol) in $CH_2Cl_2$ (2.8 mL, 0.25 M) was added the perfluoroalkyl iodide (1.2 mmol) followed by $BEt_3$ (1.15 M in hexane, 1.13 mL, 1.3 mmol) at rt. The reaction mixture was stirred at rt for 1 h in an open-to-air flask protected from moisture by a $CaCl_2$ tube. Then, a second portion of TBC (170 mg, 1.0 mmol) and $BEt_3$ (1.15 M in hexane, 1.13 mL, 1.3 mmol.) was added, and the mixture was stirred for another 2h. The reaction mixture was then washed with water (2 × 5 mL), and the combined aqueous phases were extracted with $Et_2O$ or EtOAc (2 × 5–10 mL). The combined organic phases were washed with brine (1 × 10 mL), dried over $Na_2SO_4$ and concentrated under reduced pressure. The crude mixture was filtered over a short pad of neutral $Al_2O_3$ using $Et_2O$ or EtOAc to remove polar TBC and boron derivatives. The resulting filtrate was concentrated again under reduced pressure and purified by FC (pentane/$Et_2O$ or heptanes/EtOAc).

### General Procedure 3. Hydrotrifluoromethylation with gaseous $CF_3I$

A 25 mL Schlenk flask was connected to a vacuum/$N_2$ line and to a $CF_3I$ cylinder via its side three-way stopcock and to a gas bubbler via the top ground glass joint using a two-way stopcock. The flask was vacuumed, and gaseous $CF_3I$ was carefully introduced. The overpressure was suppressed by opening the two-way stopcock leading to the bubbler. Using this procedure, gaseous $CF_3I$ (25 mL, 1.2 mmol) was introduced in the flask. Then, the Schlenk flask was closed and cooled down with liquid $N_2$ to condense $CF_3I$ as a colourless solid. The cooled system was set under $N_2$, and the top ground joint was equipped with a septum. The flask was placed in a dry ice-ethanol cooling bath (–78 °C), and a solution of the alkene (1.0 mmol), TBC (339 mg, 2.0 mmol) in $CH_2Cl_2$ (2.8 mL) was added through a syringe followed by a solution of $BEt_3$ (1.15 M in hexane, 1.13 mL, 1.3 mmol). Air (1–2 mL) was introduced by syringe into the reaction mixture. The cooling bath was then replaced by an ice/water/NaCl bath (–20 °C), and the reaction mixture was stirred at this temperature for 1 h. A second portion of

TBC (170 mg, 1.0 mmol) and $BEt_3$ (1.15 M in hexane, 1.13 mL, 1.3 mmol) were added, the cooling bath was removed, the septum was replaced by a $CaCl_2$ tube, and the reaction mixture was stirred open to the air for 2h at rt. After 2 h, the reaction mixture was filtered over a short pad of neutral $Al_2O_3$ using $Et_2O$ or EtOAc to remove TBC and boron derivatives. The crude filtrate was concentrated under reduced pressure and purified by FC (pentane/$Et_2O$ or heptanes/EtOAc).

### General procedure for the hydrotrifluoromethylation with methanesulfonyl chloride

#### General Procedure 4. $Et_3B$-initiated desulfitative chlorine atom transfer (conditions A)

The alkene (1.0 mmol) was placed in a 10 mL flask, and $CH_2Cl_2$ (2.8 mL) was added, followed by $K_2CO_3$ (69 mg, 0.5 mmol) under Ar. Then, trifluoromethanesulfonyl chloride (0.13 mL, 1.2 mmol) and a $BEt_3$ solution (1.15 M in hexane, 1.13 mL, 1.3 mmol) were added quickly. The reaction mixture was stirred at rt in an open-to-air flask with a $CaCl_2$ tube for 2 h. The reaction mixture was washed with water and brine, dried over $Na_2SO_4$ and concentrated under reduced pressure. The crude product was filtered over a short pad of neutral $Al_2O_3$ using $Et_2O$ or EtOAc to remove boron-containing side products. The resulting filtrate was concentrated under reduced pressure and purified by FC (pentane/$Et_2O$ or heptanes/EtOAc) to give the desired chloride.

#### General Procedure 5. DTBHN-initiated desulfitative chlorine atom transfer (conditions B).

In a 10 mL flask containing *n*-hexane (3 mL), the alkene (1.0 mmol) and trifluoromethanesulfonyl chloride (0.22 mL, 2 mmol) were added. DTBHN (34.8 mg, 0.2 mmol) was added, and the reaction mixture was heated under reflux under Ar for 30 min. The cooled reaction mixture was then concentrated under reduced pressure, and the resulting crude product was purified by FC (pentane/$Et_2O$ or heptanes/EtOAc) to give the desired chloride.

#### General Procedure 6. Dechlorination (conditions C)

Under Ar atmosphere, the alkyl chloride (1.0 mmol) was dissolved in *n*-hexane (3.3 mL), and triethylsilane (0.65 mL, 4.0 mmol) was added, followed by *tert*-dodecanethiol (12.4 µL, 50 µmol) and DTBHN (17.6 mg, 0.1 mmol). The reaction mixture was heated under reflux for 1

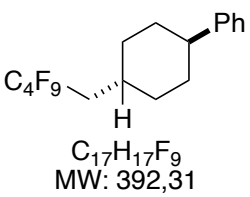
h. A second portion of *tert*-dodecanethiol (12.4 µL, 50 µmol) and DTBHN (17.6 mg, 0.1 mmol) were added, and the solution was further heated under reflux for 1 h. The cooled reaction mixture was washed with aq. sat. $NaHCO_3$ (2 × 10 mL), water and brine. After drying over $Na_2SO_4$, the organic phase was concentrated under reduced pressure, and the residue was purified by FC (pentane/$Et_2O$ or heptanes/EtOAc) to afford the product of hydrotrifluoromethylation.

### General procedure 7. One-pot hydrotrifluoromethylation with $CF_3SO_2Cl$.

In a 10 mL flask was added *n*-hexane (3 mL), the alkene (1.0 mmol), trifluoromethanesulfonyl chloride (0.22 mL, 2 mmol) and DTBHN (34.8 mg, 0.20 mmol). The reaction mixture was heated under reflux for 30 min under Ar. The volatiles (*n*-hexane and excess $CF_3SO_2Cl$) were then removed by evaporation under vacuum at the Schlenk line. *n*-Hexane (3 × 2 mL) was added for efficient co-evaporation of the volatiles. The crude alkyl chloride intermediate was dissolved in *n*-hexane (1.8 mL) under Ar. Triethylsilane (1.61 mL, 10 mmol), *tert*-dodecanethiol (71.3 µL, 0.3 mmol) and DTBHN (35.2 mg, 0.2 mmol) were added, and the reaction mixture was heated under reflux for 1 h. The solution was cooled down and a second portion of *tert*-dodecanethiol (71.3 µL, 0.3 mmol) and DTBHN (35.2 mg, 0.2 mmol) were added, and the reaction mixture was further heated under reflux for 1 h. The cooled reaction mixture was washed with aq. sat. $NaHCO_3$ (2 × 10 mL), water and brine. After drying over $Na_2SO_4$ and concentration under reduced pressure, the crude product was purified by FC (pentane/$Et_2O$ or heptanes/EtOAc) to afford the product of hydrotrifluoromethylation.

## Hydroperfluoroalkylation products

### ((1*R*,4*R*)-4-(2,2,3,3,4,4,5,5,5-nonafluoropentyl)cyclohexyl)benzene **2**

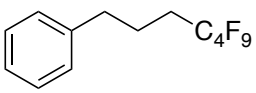



$C_{17}H_{17}F_9$
MW: 392,31

According to general procedure 1 from (4-methylenecyclohexyl)benzene (**1a**) (181 mg, 1.05 mmol) and perfluorobutyl iodide (0.226 ml, 1.26 mmol). The crude product was submitted to FC (100% pentane) to afford **2** (364 mg, 0.926 mmol, 88%, *trans/cis* 83:16) as a colourless crystalline solid. $R_f$ = 0.42 (100% pentane). M.p. 49.5–51.7 °C (uncorrected).

Major isomer: $^{1}$H NMR (400 MHz, $CD_2Cl_2$): $\delta$ 7.33–7.15 (m, 5H), 2.50 (tt, $J$ = 12.2, 3.5 Hz, 1H), 2.13–1.84 (m, 7H), 1.55 (qd, $J$ = 13.0, 3.2 Hz, 2H), 1.28 (qd, $J$ = 13.0, 3.3 Hz, 2H). $^{13}$C NMR (100 MHz, $CD_2Cl_2$): $\delta$ 147.2 ($C_q$), 128.3 (2 × $CH_{Ar}$), 126.7 (2 × $CH_{Ar}$), 125.9 ($CH_{Ar}$), 43.7 ($CHC_6H_5$), 37.1 (t, $J$ = 21.4 Hz, $CH_2C_4F_9$), 33.87 ($CH_2$), 33.82 ($CH_2$), 30.8 (t, $J$ = 2.3 Hz, $CHCH_2C_4F_9$). $^{19}$F NMR (376 MHz, $CD_2Cl_2$) $\delta$ –81.5 ($CF_3$), –112.7 ($CF_2$), –124.9 ($CF_2$), –126.2 ($CF_2$). IR ($\nu$, $cm^{-1}$): 2927 (w), 2855 (w), 1222 (s), 1132 (s). HRMS (EI): calculated for $[C_{17}H_{17}F_9]^+$: 392.1181; found: 392.1178.
Minor isomer (characteristic signals): $^{1}$H NMR (400 MHz, $CD_2Cl_2$): $\delta$ 2.63 (tt, $J$ = 10.6, 3.4 Hz, 1H), 2.39–2.33 (m, 1H), 2.28–2.16 (m, 2H), 1.82–1.62 (m, 8H).
$^{13}$C NMR (100 MHz, $CD_2Cl_2$): δ 146.8 (Cq), 126.8 (2x$CH_{Ar}$), 125.8 ($CH_{Ar}$), 42.9 (CH), 30.7 ($CH_2$), 28.6 ($CH_2$), 26.2 (CH). $^{19}$F NMR (376 MHz, $CD_2Cl_2$) $\delta$ –114.2 ($CF_2$), –124.7 ($CF_2$).

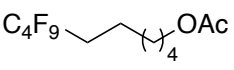
### (4,4,5,5,6,6,7,7,7-Nonafluoroheptyl)benzene **3**




$C_{13}H_{11}F_9$
MW: 338,22

According to general procedure 1 from allylbenzene (125 mg, 1.04 mmol) and perfluorobutyl iodide (435 mg, 1.35 mmol). The crude product was submitted to FC (100% pentane) to afford **3** (236 mg, 0.819 mmol, 79%) as a colourless oil. $R_f$ = 0.65 (100% pentane). $^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.35–7.28 (m, 2$H_{Ar}$), 7.26–7.15 (m, 3$H_{Ar}$), 2.72 (t, $J$ = 7.5 Hz, 2H, $CH_2C_6H_5$), 2.18–2.01 (m, 2H, $CH_2C_4F_9$), 2.01–1.90 (m, 2H, $CH_2CH_2C_4F_9$). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 140.6 ($Cq_{Ar}$), 128.6 (2 × $CH_{Ar}$), 128.3 (2 × $CH_{Ar}$), 126.3 ($CH_{Ar}$), 35.0 ($CH_2C_6H_5$), 30.2 (t, $J$ = 22.3 Hz, $CH_2C_4F_9$), 21.8 ($CH_2CH_2C_4F_9$). $^{19}$F NMR (376 MHz, $CDCl_3$): δ –81.1 ($CF_3$), –114.4 ($CF_2$), –124.4 ($CF_2$), –126.1 (m, $CF_2$). IR ($\nu$, $cm^{-1}$): 3030 (w), 2929 (w), 2053 (w), 1605 (w), 1215 (s), 1130 (s). HRMS (EI): calculated for $[C_{13}H_{10}F_9]^+$: 337.0633; found: 337.0632.

### 7,7,8,8,9,9,10,10,10-Nonafluorodecyl acetate **4**

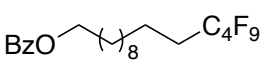



$C_{12}H_{15}F_9O_2$
MW: 362,24

According to general procedure 1 from 5-hexenyl acetate (147 mg, 1.03 mmol), perfluorobutyl iodide (435 mg, 1.24 mmol). The reaction was run using more TBC (351 mg, 2.07 mmol) at the beginning. After 1 h, TBC (175.1 mg, 1.03 mmol) was added and was continued for further 1 h. The crude product was submitted to FC (heptanes/EtOAc 98:2) to afford **4** (260 mg, 0.718 mmol, 69%) as a pale-yellow oil. $R_f$ = 0.45 (heptanes/EtOAc 9:1). $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 4.05 (t, $J$ = 6.6 Hz, 2H,

C*H*$_2$O), 2.14–1.94 (m, 2H, C*H*$_2$C$_4$F$_9$), 2.03 (s, 3H, CH$_3$), 1.71–1.53 (m, 4H, C*H*$_2$CH$_2$O, C*H*$_2$CH$_2$C$_4$F$_9$), 1.47–1.33 (m, 4H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 171.1 (C=O), 64.2 (*C*H$_2$O), 30.7 (t, *J* = 22.3 Hz, *C*H$_2$C$_4$F$_9$), 28.6 (CH$_2$), 28.3 (*C*H$_2$CH$_2$O), 25.5 (CH$_2$), 20.8 (CH$_3$), 20.0 (t, *J* = 3.8 Hz, *C*H$_2$CH$_2$C$_4$F$_9$,). $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ –81.2 (CF$_3$), –114.7 (CF$_2$), –124.6 (CF$_2$), –126.2 (CF$_2$). IR ($\nu$, cm$^{-1}$): 2949 (w), 2865 (w), 1739 (s), 1216 (s), 1166 (m), 1130 (s), 717 (m). HRMS (ESI): calculated for [C$_{12}$H$_{15}$O$_2$F$_9$Na]$^+$: 385.0821; found: 385.0811.

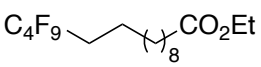
### 12,12,13,13,14,14,15,15,15-Nonafluoropentadecyl benzoate **5**




$C_{22}H_{27}F_9O_2$
MW: 494,44

According to general procedure 2 from undec-10-enyl benzoate (274 mg, 1.0 mmol), perfluorobutyl iodide (424 mg, 1.21 mmol). The reaction was run using more TBC (339 mg, 2.0 mmol) at the beginning. After 2 h, TBC (170 mg, 1.0 mmol) was added and was continued for further 2 h. The crude product was submitted to FC (heptanes/EtOAc 99:1) to afford **5** (423 mg, 0.856 mmol, 86%) as a colourless oil which crystallised when stored in the fridge. $R_f$ = 0.41 (heptanes/EtOAc 95:5). M.p. = 30–30.1 °C (uncorrected). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.06–8.03 (m, 2H$_{Ar}$), 7.55–7.52 (m, 1H$_{Ar}$), 7.46–7.42 (m, 2H$_{Ar}$), 4.32 (t, *J* = 6.7 Hz, 2H, CO$_2$C*H*$_2$), 2.13–1.96 (m, 2H, C*H*$_2$C$_4$F$_9$), 1.80–1.73 (m, 2H, CO$_2$CH$_2$C*H*$_2$), 1.64–1.53 (m, 2H, C*H*$_2$CH$_2$C$_4$F$_9$), 1.50–1.40 (m, 2H, CO$_2$CH$_2$CH$_2$C*H*$_2$), 1.39–1.24 (m, 12H, 6x CH$_2$). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 166.7 (C=O), 132.8 (CH$_{Ar}$), 130.5 (Cq$_{Ar}$), 129.5 (2xCH$_{Ar}$), 128.3 (2xCH$_{Ar}$), 65.1 (CO$_2$*C*H$_2$), 30.8 (t, *J* = 22.3 Hz, *C*H$_2$C$_4$F$_9$), 29.44 (CH$_2$), 29.42 (CH$_2$), 29.3 (CO$_2$CH$_2$CH$_2$CH$_2$*C*H$_2$), 29.22 (CH$_2$), 29.18 (CH$_2$), 29.07 (*C*H$_2$CH$_2$CH$_2$C$_4$F$_9$), 28.7 (CH$_2$), 26.0 (CH$_2$), 20.1 (t, *J* = 3.6 Hz, *C*H$_2$CH$_2$C$_4$F$_9$). $^{19}$F NMR (376 MHz, CDCl$_3$): $\delta$ –81.07 (m, CF$_3$), –114.6 (m, CF$_2$), –124.5 (m, CF$_2$), –126.1 (m, CF$_2$). IR ($\nu$, cm$^{-1}$): 2927 (w), 2857 (w), 1719 (s), 1271 (s), 1217 (s), 1131 (s), 1110 (s), 709 (s). HRMS (ESI): calculated for [C$_{22}$H$_{28}$O$_2$F$_9$]$^+$: 495.1940; found: 495.1922.

### Ethyl 12,12,13,13,14,14,15,15,15-nonafluoropentadecanoate **6**

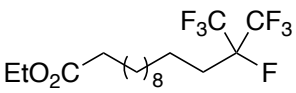



$C_{17}H_{25}F_9O_2$
MW: 432,37

According to general procedure 1 from, ethyl-10-undecenoate (219 mg, 1.0 mmol) and perfluorobutyl iodide (419 mg, 1.2 mmol). The crude product was submitted to FC (heptanes/EtOAc 93:7) to afford **6** (323 mg, 0.747 mmol, 75%) as a pale-yellow oil which crystallised when stored in the fridge. $R_f$ =

0.4 (heptanes/EtOAc 93:7, $KMnO_4$ only, UV inactive). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 4.12 (q, $J$ = 7.1 Hz, 2H, C$H_2$CH$_3$), 2.28 (t, $J$ = 7.5 Hz, 2H, C$H_2$C=O), 2.14–1.94 (m, 2H, C$H_2$C$_4$F$_9$), 1.68–1.53 (m, 4H, C$H_2$CH$_2$C=O, C$H_2$CH$_2$C$_4$F$_9$), 1.42–1.27 (m, 12H, 6xCH$_2$), 1.25 (t, $J$ = 7.1 Hz, 3H, CH$_2$C$H_3$). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 173.9 (C=O), 60.1 (C$H_2$CH$_3$), 34.3 (C$H_2$C=O), 30.8 (t, $J$ = 22.3 Hz, C$H_2$C$_4$F$_9$), 29.29 (CH$_2$), 29.25 (CH$_2$), 29.17 (CH$_2$), 29.15 (CH$_2$), 29.08 (CH$_2$), 29.05 (CH$_2$), 24.9 (C$H_2$CH$_2$C=O), 20.03 (t, $J$ = 3.8 Hz, C$H_2$CH$_2$C$_4$F$_9$), 14.21 (CH$_3$). $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ –81.1 (CF$_3$), –114.6 (CF$_2$), –124.5 (CF$_2$), –126.1 (CF$_2$). IR ($\nu$, cm$^{-1}$): 2978 (w), 2929 (w), 2857 (w), 1735 (s), 1220 (s), 1164 (s). HRMS (ESI): calculated for $[C_{17}H_{26}O_2F_9]^+$: 433.1784; found: 433.1776.

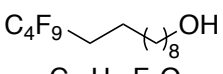
### Ethyl 12,13,13,13-tetrafluoro-12-(trifluoromethyl)tridecanoate **7**




$C_{16}H_{25}F_7O_2$
MW: 382,36

According to general procedure 1 from ethyl under-10-enoate (219 mg, 1.0 mmol) and perfluoroisopropyl iodide (362 mg, 1.2 mmol). The crude product was submitted to FC (heptanes/EtOAc 95:5) to afford **7** (346 mg, 0.905 mmol, 91%) as a colourless oil. $R_f$ = 0.5 (heptanes/EtOAc 90:10). $^1$H NMR (400 MHz, $CDCl_3$): δ 4.12 (q, $J$ = 7.1 Hz, 2H, C$H_2$CH$_3$), 2.28 (t, $J$ = 7.5 Hz, 2H, C$H_2$CO$_2$), 2.11–1.96 (m, 2H, C$H_2$CF(CF$_3$)$_2$), 1.67–1.47 (m, 4H, C$H_2$CH$_2$CO$_2$, C$H_2$CH$_2$CF(CF$_3$)$_2$), 1.39–1.27 (m, 12H, 6x CH$_2$), 1.25 (t, $J$ = 7.2 Hz, 3H, C$H_3$CH$_2$). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 173.9 (C=O), 60.1 (C$H_2$CH$_3$), 34.3 (C$H_2$CO$_2$), 29.6 (C$H_2$CH$_2$CH$_2$CF(CF$_3$)$_2$), 29.28 (CH$_2$), 29.26 (CH$_2$), 29.16 (CH$_2$), 29.07 (CH$_2$), 29.02 (CH$_2$), 28.88 (C$H_2$CF(CF$_3$)$_2$), 24.9 (C$H_2$CH$_2$CO$_2$), 21.3 (C$H_2$CH$_2$CF(CF$_3$)$_2$), 14.2 (C$H_3$CH$_2$). $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ –76.4 (d, $J$ = 6.9 Hz, CF$_3$), –183.7 (th, $J$ = 20.4, 6.8 Hz, CF). IR ($\nu$, cm$^{-1}$): 2928 (w), 2857 (w), 1736 (s), 1216 (s), 1158 (s), 1110 (m), 1033 (m), 719 (m). HRMS (ESI): calculated for $[C_{16}H_{26}O_2F_7]^+$: 383.1827; found: 383.1820.

### 11,11,12,12,13,13,14,14,14-Nonafluorotetradecan-1-ol **8**

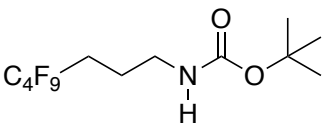



$C_{14}H_{21}F_9O$
MW: 376,31

According to general procedure 1 from 10-undecen-1-ol (172 mg, 1.0 mmol) and perfluorobutyl iodide (419 mg, 1.2 mmol). The crude product was submitted to FC (pentane/Et$_2$O 75:25 to 100% Et$_2$O) to afford **8** (331 mg, 0.848 mmol, 85%) as a colourless solid. $R_f$ = 0.30 (pentane/Et$_2$O 70:30). M.p. 35.5–36.5

°C (uncorrected). $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 3.64 (t, $J$ = 6.7 Hz, 2H, C$H_2$OH), 2.15–1.91 (m, 2H, C$H_2C_4F_9$), 1.65–1.50 (m, 4H, C$H_2CH_2C_4F_9$ and C$H_2CH_2$OH), 1.41–1.26 (m, 12H, 6x$CH_2$). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 63.2 (*C*$H_2$OH), 33.0 (*C*$H_2CH_2$OH), 30.9 (t, $J$ = 22.3 Hz, *C*$H_2C_4F_9$), 29.69 ($CH_2$), 29.61 ($CH_2$), 29.55 ($CH_2$), 29.49 ($CH_2$), 29.35 ($CH_2$), 29.24 ($CH_2$), 25.9 ($CH_2$), 20.2 (t, $J$ = 3.6 Hz, *C*$H_2CH_2C_4F_9$). $^{19}$F NMR **(**376 MHz, $CDCl_3$): $\delta$ -81.1 ($CF_3$), –114.6 ($CF_2$), –124.5 ($CF_2$), –126.1 ($CF_2$). IR ($\nu$, $cm^{-1}$): 3341 (w), 2928 (w), 2856 (w), 1132 (m), 1218 (m), 747 (s). HRMS (EI): calculated for $[C_{13}H_{16}F_9]^+$: 343.1099, found: 343.1099; calculated for $[C_{12}H_{14}F_9]^+$: 329.0944, found: 329.0944; calculated for $[C_{11}H_{12}F_9]^+$: 315.0787 found: 315.0787.

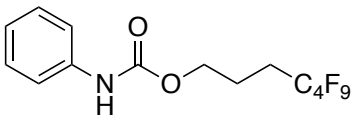
### *Tert*-butyl (4,4,5,5,6,6,7,7,7-nonafluoroheptyl)carbamate **9**




$C_{12}H_{16}F_9NO_2$
MW: 377,25

According to general procedure 1 from *N*-Boc-allylamine (160 mg, 1.0 mmol), perfluorobutyl iodide (0.209 mL, 1.2 mmol). The reaction was run by using more TBC (339 mg, 2.0 mmol) at the beginning. After 1 h, TBC (170 mg, 1.0 mmol) was added and was continued for further 1 h. The crude product was submitted to FC (grad. pentane/$Et_2O$ 95:5, then 90:10, and finally 80:20) to afford **9** (252 mg, 0.668 mmol, 67%) as a pale-yellow oil. $R_f$ = 0.30 (pentane/$Et_2O$ 85:15,). $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 4.68 (t, $J$ = 6.6 Hz, 1H, NH), 3.20 (q, $J$ = 6.7 Hz, 2H, C$H_2$NH), 2.17–2.03 (m, 2H, C$H_2C_4F_9$), 1.82–1.75 (m, 2H, C$H_2CH_2C_4F_9$), 1.43 (s, 9H, 3 × $CH_3$). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 156.0 (C=O), 79.5 ($C_q$), 39.6 (*C*$H_2$NH), 28.3 (3 × $CH_3$), 28.2 (t, $J$ = 22.5 Hz, *C*$H_2C_4F_9$), 21.2 (*C*$H_2CH_2C_4F_9$). $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ –81.2 ($CF_3$), –114.5 ($CF_2$), –124.5 ($CF_2$), –126.2 $CF_2$). IR ($\nu$, $cm^{-1}$): 3348 (w), 2981 (w), 1686 (m), 1217 (s), 1165 (s), 1131 (s), 716 (m). HRMS (ESI): calculated for $[C_{12}H_{16}O_2NF_9Na]^+$: 400.0930; found: 400.0921.

### 4,4,5,5,6,6,7,7,7-Nonafluoroheptyl phenylcarbamate **10**



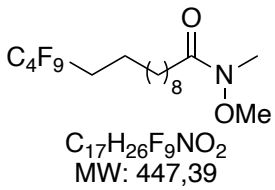

$C_{14}H_{12}F_9NO_2$
MW: 397,24

According to general procedure 2 from allyl *N*-phenylcarbamate (**1p**) (181 mg, 1.0 mmol), perfluorobutyl iodide (419 mg, 1.2 mmol). The reaction was run by using more TBC (339 mg, 2.0 mmol) at the beginning. After 1 h, TBC (170 mg, 1.0 mmol) was added and was continued for further 1 h. The crude product was

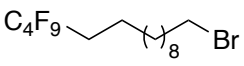
submitted to FC (heptanes/EtOAc 90:10) to afford **10** (254 mg, 0.639 mmol, 64%) as a colourless solid. $R_f$ = 0.38 (heptanes/EtOAc 90:10). M.p. 71.5–72.5 °C (uncorrected). $^1$H NMR (400 MHz, $CD_2Cl_2$): δ 7.46–7.36 (m, 2$H_{Ar}$), 7.36–7.25 (m, 2$H_{Ar}$), 7.08 (ddt, *J* = 8.6, 7.3, 1.3 Hz, 1H), 6.72 (bs, 1H, NH), 4.23 (t, *J* = 6.2 Hz, 2H, $CO_2CH_2$), 2.35–2.16 (m, 2H, $CH_2C_4F_9$), 2.07–1.94 (m, 2H, $CH_2CH_2C_4F_9$). $^{13}$C NMR (100 MHz, $CD_2Cl_2$): δ 153.1 (C=O), 137.9 ($C_q$), 129.0 (2 × $CH_{Ar}$), 123.4 ($CH_{Ar}$), 118.6 (2 × $CH_{Ar}$), 63.5 ($CO_2CH_2$), 27.7 (t, *J* = 22.3 Hz, $CH_2C_4F_9$), 20.2 $CH_2CH_2C_4F_9$). $^{19}$F NMR (376 MHz, $CD_2Cl_2$): δ –81.4 (m, $CF_3$), –114.9 ($CF_2$), –124.6 ($CF_2$), –126.3 ($CF_2$). IR (ν, $cm^{-1}$): 3313 (m), 3138 (w), 3057 (w), 2971 (w), 2907 (w), 1704 (s), 1598 (m), 1542 (m), 1444 (m), 1318 (m), 1213 (s), 1130 (s), 1068 (s), 1026 (s), 715 (s). HRMS (ESI): calculated for $[C_{14}H_{13}O_2NF_9]^+$: 398.0797; found: 398.0791.

### 12,12,13,13,14,14,15,15,15-Nonafluoro-*N*-methoxy-*N*-methylpentadecanamide **11**

According to general procedure 1 from *N*-Methoxy-*N*-methylundec-10-enamide (**1h**) (277 mg, 1.22 mmol), perfluorobutyl iodide (252 mL, 1.46 mmol). The reaction was run by using more TBC (406 mg, 2.44 mmol) at the beginning. After 1 h, TBC (203 mg, 1.22 mmol) was added and was continued for further 1 h. The crude product was submitted to FC (heptanes/EtOAc 95:5, 90:10, 80:20) to afford **11** (362 mg, 0.809 mmol, 66%) as a colourless oil. $R_f$ = 0.39 (heptanes/EtOAc 79:30). $^1$H NMR (400 MHz, $CDCl_3$): *δ* 3.67 (s, 3H, $CH_3O$), 3.16 (s, 3H, $CH_3N$), 2.40 (*t*, *J* = 7.6 Hz, 2H, $CH_2C$=O), 2.13–1.94 (m, 2H, $CH_2C_4F_9$), 1.68–1.51 (m, 4H, $CH_2CH_2C$=O and $CH_2CH_2C_4F_9$), 1.42–1.22 (m, 12H, 6x$CH_2$). $^{13}$C NMR (100 MHz, $CDCl_3$): *δ* 174.8 (C=O), 61.1 ($CH_3O$), 32.1 ($CH_3N$), 31.9 ($CH_2C$=O), 30.7 (t, *J* = 22.3 Hz, $CH_2C_4F_9$), 29.37 ($CH_2$), 29.32 (2 × $CH_2$), 29.27 ($CH_2$), 29.14 ($CH_2$), 29.03 ($CH_2$), 24.6 ($CH_2$), 20.0 (t, *J* = 3.8 Hz, $CH_2CH_2C_4F_9$). $^{19}$F NMR (376 MHz, $CDCl_3$): *δ* –81.2 ($CF_3$), –114.7 ($CF_2$), –124.6 ($CF_2$), –126.1 ($CF_2$). IR (ν, $cm^{-1}$): 2956 (w), 2927 (w), 1669 (m), 1216 (s), 1131 (s), 1002 (m), 878 (m). HRMS (ESI): calculated for $[C_{17}H_{26}O_2NF_9Na]^+$: 470.1712; found: 470.1697.



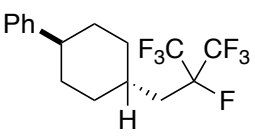
15-Bromo-1,1,1,2,2,3,3,4,4-nonafluoropentadecane **12**




$C_{15}H_{22}BrF_9$
MW: 453,23

According to general procedure 1 from 11-bromo-1-undecene (233 mg, 1.0 mmol) and perfluorobutyl iodide (419 mg, 1.2 mmol). The crude product was submitted to FC (100% pentane) to afford **12** (441 mg, 0.973 mmol, 97%) as a colourless oil. $R_f$ = 0.76 (100% pentane). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 3.41 (t, $J$ = 6.8 Hz, 2H, C$H_2$Br), 2.14–1.95 (m, 2H, C$H_2$C$_4$F$_9$), 1.91–1.80 (m, 2H, C$H_2$CH$_2$Br), 1.65–1.54 (m, 2H, C$H_2$CH$_2$C$_4$F$_9$), 1.48–1.23 (m, 14H, C$H_2$(CH$_2$)$_2$Br and 6xCH$_2$). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 34.0 (*C*H$_2$Br), 32.8 (*C*H$_2$CH$_2$Br), 30.8 (t, $J$ = 22.4 Hz, *C*H$_2$C$_4$F$_9$), 29.39 (CH$_2$), 29.35 (CH$_2$), 29.29 (CH$_2$), 29.17 (CH$_2$), 29.06 (CH$_2$), 28.7 (CH$_2$), 28.1 (*C*H$_2$(CH$_2$)$_2$Br), 20.0 (t, $J$ = 3.6 Hz, *C*H$_2$CH$_2$C$_4$F$_9$). $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ –81.1 ($CF_3$), –114.6 ($CF_2$), –124.5 ($CF_2$), –126.1 ($CF_2$). IR ($\nu$, cm$^{-1}$): 2976 (w), 22827 (w), 2857 (w), 1456 (w), 1220 (s), 1165 (m), 1131 (s), 717 (m). HRMS (EI): calculated for [$C_4H_8Br$]$^+$: 134.9804; found: 134.9803; and calculated for [$C_{11}H_{14}F_9$]$^+$: 317.0946; found: 317.0943.

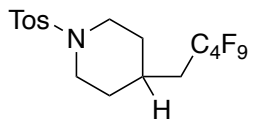
(4-(2,3,3,3-Tetrafluoro-2-(trifluoromethyl)propyl)cyclohexyl)benzene **13**




$C_{16}H_{17}F_7$
MW: 342,30

According to general procedure 1 from (4-methylenecyclohexyl)benzene (**1a**) (174 mg, 1.0 mmol), perfluoroisopropyl iodide (362 mg, 1.2 mmol). The reaction was run by using more TBC (339 mg, 2.0 mmol) at the beginning. After 1 h, TBC (170 mg, 1.0 mmol) was added and was continued for further 1 h. The crude product was submitted to FC (100% pentane) to afford **13** (341 mg, 0.996 mmol, 99%, *trans/cis* 9:1, contaminated with ca. 5% of alkene) as a colourless oil. $R_f$ = 0.55 (100% pentane). Major isomer: $^1$H NMR (400 MHz, $CD_2Cl_2$): $\delta$ 7.33–7.25 (m, 2H$_{Ar}$), 7.23–7.14 (m, 2H$_{Ar}$), 2.49 (tt, $J$ = 12.2, 3.5 Hz, 1H, C*H*C$_6$H$_5$), 2.10–1.79 (m, 7H, C$H_2$CF(CF$_3$)$_2$, C*H*CH$_2$CF(CF$_3$)$_2$, C$H_2$CHCH$_2$CF(CF$_3$)$_2$, 2x CH*H*CHC$_6$H$_5$), 1.53 (qd, $J$ = 13.1, 3.2 Hz, 2H, 2 x C*H*HCHC$_6$H$_5$), 1.23 (qd, $J$ = 13.1, 3.1 Hz, 2H, C$H_2$CHCH$_2$CF(CF$_3$)$_2$). $^{13}$C NMR (100 MHz, $CD_2Cl_2$): $\delta$ 147.2 (Cq$_{Ar}$), 128.3 (2 × CH$_{Ar}$), 126.7 (2 × CH$_{Ar}$), 125.9 (CH$_{Ar}$), 43.7 (CHC$_6$H$_5$), 35.3 (d, $J$ = 19.3 Hz, *C*H$_2$CF(CF$_3$)$_2$), 34.30 (CH$_2$), 34.29 (CH$_2$), 33.8 (2x*C*HHCHC$_6$H$_5$), 32.1 (*C*HCH$_2$CF(CF$_3$)$_2$). $^{19}$F NMR (376 MHz, $CD_2Cl_2$): $\delta$ –77.2 (d, $J$ = 6.6 Hz, 2xCF$_3$), –184.4 (th, $J$ = 24.2, 6.8 Hz, CF). IR ($\nu$, cm$^{-1}$): 3028 (w), 2927 (w), 2855 (w), 1213 (s), 1154 (s), 1037 (m), 948 (m), 697 (s). HRMS (EI): calculated for [$C_{16}H_{17}F_7$]$^+$: 342.1206; found: 342.1206.

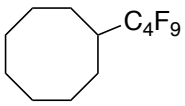
### 4-(2,2,3,3,4,4,5,5,5-Nonafluoropentyl)-1-tosylpiperidine **14**




$C_{17}H_{18}F_9NO_2S$
MW: 471,38

According to general procedure 2 from 4-methylene-1-(p-tolylsulfonyl)piperidine (**1r**) (126 mg, 0.50 mmol) and perfluorobutyl iodide (210 mg, 0.6 mmol). The reaction was run by using TBC (85 mg, 0.5 mmol), $K_2CO_3$ (7 mg, 0.05 mmol) and $BEt_3$ (0.565 mL, 0.650 mmol, 1.15 M in hexane) at the beginning. After 1 h, TBC (85 mg, 0.5 mmol) and $BEt_3$ (0.565 mL, 0.650 mmol, 1.15 M in hexane) were added, and the reaction continued for a further 1 h. The crude product was submitted to FC (heptanes/EtOAc 85:15) to afford **14** (254 mg, 0.539 mmol, 95%) as a colourless powder. $R_f$ = 0.34 (heptanes/EtOAc 85:15). M.p. 141.7–142.9 °C (uncorrected). $^1$H NMR (400 MHz, $CD_2Cl_2$): $\delta$ 7.65–7.58 (m, 2H$_{Ar}$), 7.36 (d, $J$ = 8.1 Hz, 2H$_{Ar}$), 3.77–3.72 (m, 2H), 2.44 (s, 3H, $CH_3$), 2.24 (td, $J$ = 12.1, 2.6 Hz, 2H), 2.09–1.94 (m, 2H, C$H_2$C$_4$F$_9$), 1.86 (broad d, $J$ = 13.6, 2H), 1.79–1.68 (m, 1H, C$H$CH$_2$C$_4$F$_9$), 1.51–1.38 (m, 2H). $^{13}$C NMR (100 MHz, $CD_2Cl_2$): $\delta$ 143.8 (Cq$_{Ar}$), 132.8 (Cq$_{Ar}$), 129.6 (2 × C$H_{Ar}$), 127.6 (2 × C$H_{Ar}$), 46.1 (2 × NC$H_2$), 36.1 (t, $J$ = 21.4 Hz, C$H_2$C$_4$F$_9$), 31.8 (2 × CH$_2$), 28.7 (C$H$CH$_2$C$_4$F$_9$), 21.2 (C$_q$C$H_3$). $^{19}$F NMR (376 MHz, $CD_2Cl_2$): $\delta$ –79.5 ($CF_3$), –110.9 ($CF_2$), –122.9 ($CF_2$), –124.3 ($CF_2$). IR ($\nu$, cm$^{-1}$): 2981 (w), 1262 (s), 1163 (s), 1131 (s), 749 (s). HRMS (EI): calculated for [$C_{17}H_{18}O_2NF_9S$]$^+$: 471.0909, found: 471.0904; and calculated for [$C_{10}H_{11}NF_9$]$^+$: 316.0742, found: 316.0738; and calculated for [$C_7H_7O_2S$]$^+$: 155.0161, found: 155.0161.

### (Perfluorobutyl)cyclooctane **15**

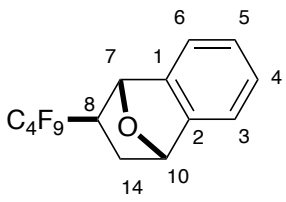



$C_{12}H_{15}F_9$
MW: 330,24

According to general procedure 1 from cyclooctene (116 mg, 1.0 mmol), perfluorobutyl iodide (419 mg, 1.2 mmol). The reaction was run by using more TBC (339 mg, 2.0 mmol) at the beginning. After 1 h, TBC (170 mg, 1.0 mmol) was added and was continued for further 1 h. The crude product was submitted to FC (100% pentane) to afford **15** (203 mg, 0.615 mmol, 62%) as a colourless oil. $R_f$ = 1 (100% pentane). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 2.47–2.30 (m, 1H, C$H$C$_4$F$_9$), 1.94–1.88 (m, 2H), 1.83–1.72 (m, 2H), 1.68–1.44 (m, 10H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 40.2 (t, $J$ = 20.0 Hz, C$H$C$_4$F$_9$), 26.6 (CH$_2$), 26.3 (2 × CH$_2$), 25.2 (2 × CH$_2$), 24.7 (m, 2 × CH$_2$). $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ –81.0 ($CF_3$), –116.4 ($CF_2$), –120.8 ($CF_2$), –126.2 ($CF_2$). IR ($\nu$, cm$^{-1}$): 3341 (w), 2928 (w), 2856

(w), 1132 (m), 1218 (m), 747 (s). HRMS (EI): calculated for $[C_{12}H_{14}F_9]^+$: 329.0946; found: 329.0944.

### (1*R*,2*R*,4*S*)-2-(perfluorobutyl)-1,2,3,4-tetrahydro-1,4-epoxynaphthalene **16**



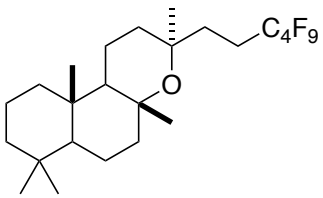

$C_{14}H_9F_9O$
MW: 364,21

1,4-Epoxy-1,4-dihydronaphthalene (147 mg, 1.00 mmol) was placed under A r in a 10 mL two-neck flask equipped with a condenser. The flask from light with an aluminium foil and perfluorobutyl iodide (0.348 mL, 2.0 mmol) was added, followed by EtOAc (3 mL) and DTBHN (35 mg, 0.2 mmol). The mixture was stirred vigorously while the reaction mixture was heated under reflux for 30 min. After cooling down, it was concentrated under reduced pressure, and the crude iodide-ATRA product was directly used in the dehalogenation step.

The crude iodide was dissolved in 1,4-dioxane (2 mL), and hypophosphorous acid (1.09 mL, 10 mmol) was added, followed by triethylamine (1.55 mL, 11 mmol) and AIBN (32 mg, 0.2 mmol) under Ar covered with Al foil. The reaction mixture was heated under reflux for 1.5 h. A second portion of the AIBN (32 mg, 0.2 mmol) was added, and the reaction was stirred for another 2 h under reflux. TBME (25 mL) and water were added to the reaction mixture, the ethereal phase was washed with 1.0 M NaOH (2 × 15 mL). The aqueous phases were combined and extracted with TBME (10 mL). The combined organic phases were washed with $NaHCO_3$ (2 × 20 mL), brine, dried over $Na_2SO_4$, and concentrated under reduced pressure. The crude product was purified by FC (pentane/$Et_2O$ 97:3) to afford **16** (341 mg, 0.936 mmol, 92%) as a pale-yellow oil. $R_f$ = 0.34 (pentane/$Et_2O$ 97:3), CAM, UV active $^1$H NMR (400 MHz, $CDCl_3$): *δ* 7.34–7.27 (m, 2$H_{Ar}$), 7.25–7.18 (m, 2$H_{Ar}$), 5.67 (s, 1H, C*H*O), 5.51 (br dd, *J* = 5.1, 1.7 Hz, 1H, C*H*O), 2.52–2.37 (m, 1H, C*H*$C_4F_9$-8), 2.35–2.29 (m, 1H), 1.78 (dd, *J* = 12.1, 8.6 Hz, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$): *δ* 145.2 ($Cq_{Ar}$), 144.1 ($Cq_{Ar}$), 127.5 ($CH_{Ar}$), 127.2 ($CH_{Ar}$), 119.6 ($CH_{Ar}$), 118.9 ($CH_{Ar}$), 78.6 (*C*H-O), 78.2 (*C*H-O), 43.0 (dd, *J* = 22.2, 19.8 Hz, *C*H$C_4F_9$), 29.03 ($CH_2$). $^{19}$F NMR (376 MHz, $CDCl_3$) δ –81.0 ($CF_3$), –113.8 (dq, *J* = 275.5, 14.5 Hz, 1F of $CF_2$), –116.7 (dq, *J* = 275.4, 15.5 Hz, 1F of $CF_2$), –122.3 ($CF_2$), –126.0 ($CF_2$). IR (ν, $cm^{-1}$): 2963 (w), 1231 (s), 1213 (s), 1187 (s), 1130 (s), 751 (s). HRMS (EI): calculated for $[C_{14}H_9OF_9]^+$: 364.0504, found: 364.0499; and calculated for $[C_{14}H_8OF_9]^+$: 363.0426, found: 363.0424.

The stereochemistry of **16** was attributed according to the following reference.[3]

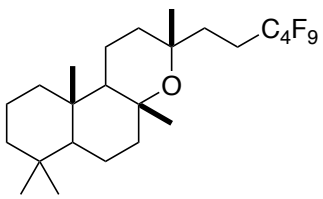
(3*S*,4a*R*,10a*S*)-3,4a,7,7,10a-pentamethyl-3-(3,3,4,4,5,5,6,6,6-nonafluorohexyl)dodecahydro-1*H*-benzo[*f*]chromene **17**




$C_{24}H_{35}F_9O$
MW: 510,53

According to general procedure 1 from *epi*-manoyl oxide (145 mg, 0.5 mmol) and perfluorobutyl iodide (212 mg, 0.6 mmol). The crude product was submitted to FC (pentane/$Et_2O$ 98:2) to afford **17** (122 mg, 0.239 mmol, 48%) as a colourless oil. $R_f$ = 0.53 (pentane/$Et_2O$ 97:3). $[\alpha]_D^{20}$ = 11.78 (c = 1.0, $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 2.40–2.21 (m, 1H), 2.20–2.05 (m, 2H), 1.86–1.72 (m, 2H), 1.70–0.76 (m, 15H), 1.25 (s, 3H), 1.11 (s, 3H), 0.86 (s, 3H), 0.79 (s, 3H), 0.77 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 75.4 ($C_q$, *C*($CH_3$)OC($CH_3$)), 71.6 ($C_q$, *C*($CH_3$)$CH_2CH_2C_4F_9$), 57.6 (CH), 56.5 (CH), 43.5 ($CH_2$), 42.1 ($CH_2$), 39.2 ($CH_2$), 38.2 ($CH_2$), 37.0 ($C_q$), 33.30 ($CH_3$), 33.26 ($C_q$), 30.7 ($CH_2$), 30.0 ($CH_3$), 26.1 (t, *J* = 21.7 Hz, *C*$H_2C_4F_9$), 23.7 ($CH_3$), 21.2 ($CH_3$), 20.0 ($CH_2$), 18.6 ($CH_2$), 15.7 ($CH_3$), 15.2 ($CH_2$). $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ –81.1 ($CF_3$), –114.5 ($CF_2$), –124.3 ($CF_2$), –126.0 ($CF_2$). IR ($\nu$, $cm^{-1}$): 2976 (w), 2926 (w), 2868 (w), 1220 (s), 1133 (s), 1051 (s). HRMS (EI): calculated for $[C_{23}H_{34}F_9O]^+$: 509.2460; found: 509.2469.

(3*R*,4a*R*,10a*S*)-3,4a,7,7,10a-pentamethyl-3-(3,3,4,4,5,5,6,6,6-nonafluorohexyl)dodecahydro-1*H*-benzo[*f*]chromene **18**

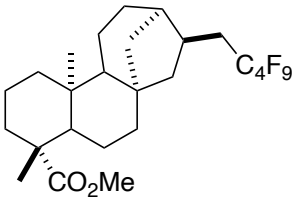



$C_{24}H_{35}F_9O$
MW: 510,53

According to general procedure 2 from manoyl oxide (145 mg, 0.5 mmol) and perfluorobutyl iodide (0.1 mL, 0.6 mmol). The reaction was run by using TBC (85 mg, 0.5 mmol), $K_2CO_3$ (69.1 mg, 0.5 mmol) and $BEt_3$ (0.57 mL, 0.65 mmol, 1.15 M in hexane) at the beginning. After 2 h, TBC (85 mg, 0.5 mmol) and $BEt_3$ (0.57 mL, 0.65 mmol, 1.15 M in hexane) were added and was continued for further 2 h. The crude product was purified by FC (pentane 100% to pentane/$Et_2O$ 98:2) to afford **18** (208 mg, 0.407 mmol, 82%) as a colourless solid. $R_f$ = 0.2 (pentane/$Et_2O$ 99:1). M.p. 46.3–46.4 °C (uncorrected). $[\alpha]_D^{20}$ = 1.52 (c = 1.0, $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 2.24–2.10 (m, 2H, C$H_2C_4F_9$), 1.75–1.20 (m, 14H), 1.26 (s, 3H), 1.24 (s, 3H), 1.15 (td, *J* = 13.4, 4.4 Hz, 1H), 1.07–1.03 (m, 1H, C*H*$C_q$($CH_3$)O), 0.96–0.91 (m, 1H, C*H*$C_q$$CH_3$), 0.90–0.82 (m, 1H), 0.86 (s, 3H), 0.79

(s, 3H), 0.77 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 74.9 (Cq), 71.2 (Cq), 58.2 (CH), 56.4 (CH), 42.9 ($CH_2$), 42.1 ($CH_2$), 39.1 ($CH_2$), 36.8 (Cq), 36.4 ($CH_2$), 35.1 ($CH_2CH_2C_4F_9$), 33.3 ($C_q(CH_3)_2$ and $C_qCH_3$), 27.7 ($CH_3$), 25.5 (t, $J$ = 21.9 Hz, $CH_2C_4F_9$), 24.6 ($CH_3$), 21.2 ($CH_3$), 19.8 ($CH_2$), 18.6 ($CH_2$), 15.7 ($CH_3$), 15.3 ($CH_2$). $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ –81.1 ($CF_3$), –114.3 ($CF_2$), –124.2 (m, $CF_2$), –126.1 ($CF_2$). IR ($\nu$, cm$^{-1}$): 2976 (w), 2927 (w), 2864 (w), 1232 (s), 1221 (s), 1132 (s), 1120 (s). HRMS (ESI): calculated for $[C_{24}H_{36}OF_9]^+$: 511.2617; found: 511.2608.

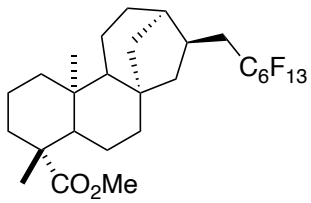
Methyl (4*R*,6a*S*,8*R*,9*R*,11b*S*)-4,11b-dimethyl-8-(2,2,3,3,4,4,5,5,5-nonafluoropentyl)tetradecahydro-6a,9-methanocyclohepta[*a*]naphthalene-4-carboxylate **19**




$C_{25}H_{33}F_9O_2$
MW: 536,52

According to general procedure 1 from methyl *ent*-kaurenoate (**1l**) (63.3 mg, 0.2 mmol) and perfluorobutyl iodide (83.9 mg, 0.24 mmol). The reaction was run by using more TBC (67.8 mg, 0.4 mmol) at the beginning, and $BEt_3$ (0.226 mL, 0.26 mmol, 1.15 M in hexane). After 1 h, TBC (33.9 mg, 0.2 mmol) and $BEt_3$ (0.226 mL, 0.26 mmol, 1.15 M in hexane) were added and was continued for further 1 h. The crude product was submitted to FC (pentane/$Et_2O$ 99:1) to afford **19** (95 mg, 0.177 mmol, 89%, dr >95:5) as a colourless solid. $R_f$ = 0.47 (pentane/$Et_2O$ 98:2). M.p. 72.2–74.6 °C (not corrected). $[\alpha]_D^{20}$ = -3.01 (c = 1.0, $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 3.64 (s, 3H, $CO_2CH_3$), 2.33 (ddq, $J$ = 12.1, 8.5, 6.1 Hz, 1H, $CHCH_2C_4F_9$), 2.27–2.04 (m, 4H), 2.01 (dt, $J$ = 11.6, 1.4 Hz, 1H, $C_qCHHCHCH_2C_4F_9$), 1.92–1.66 (m, 5H), 1.63–1.38 (m, 7H), 1.17–1.09 (m, 1H), 1.16 (s, 3H, $CH_3CCO_2Me$), 1.08–0.94 (m, 4H), 0.88–0.73 (m, 1H), 0.82 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 178.0 (C=O), 57.0 (CH), 56.2 (CH), 51.1 ($CO_2CH_3$), 47.1 ($CH_2$), 44.5 (Cq), 43.8 (Cq), 41.8 ($CH_2$), 40.7 ($CH_2$), 40.1 ($CH_2$), 39.5 (CH), 39.4 (Cq), 38.1 ($CH_2$), 32.1 (CH), 31.8 (t, $J$ = 21.5 Hz, $CH_2C_4F_9$), 28.7 ($CH_3$), 25.9 ($CH_2$), 22.1 ($CH_2$), 19.1 ($CH_2$), 19.0 ($CH_2$), 15.3 ($CH_3$). $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ –81.1 ($CF_3$), –113.1 (ddq, $J$ = 269.9, 26.4, 13.0 Hz, 1F of $CF_2$), –114.3 (ddq, $J$ = 270.4, 26.9, 13.1 Hz, 1F of $CF_2$), –124.5 ($CF_2$), –125.9 ($CF_2$). IR ($\nu$, cm$^{-1}$): 2995 (w), 2945 (w), 2853 (w), 1721 (s), 1230 (s), 1212 (s), 1129 (s), 725 (s). HRMS (ESI): calculated for $[C_{25}H_{34}O_2F_9]^+$: 537.2410; found: 537.2400.

Methyl (4R,6aS,8S,9R,11bS)-4,11b-dimethyl-8-(2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoroheptyl) tetradecahydro-6a,9-methanocyclohepta[a]naphthalene-4-carboxylate **20**




$C_{27}H_{33}F_{13}O_2$
MW: 636,54

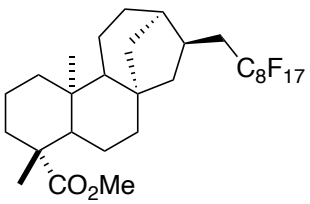
According to general procedure 1' from methyl *ent*-kaurenoate **1p** (50 mg, 0.16 mmol) and perfluoro-1-iodo-*n*-hexane (52 µL, 0.24 mmol). The crude product was purified by FC (pentane/EtOAc 97:3) to give **20** (79 mg, 78%, dr >95:5) as a colourless oil, contaminated with the traces of eliminated side product. $[a]_D^{20}$ = –34.1 (*c* = 4.5, $CHCl_3$). $^1$H NMR (300 MHz, $CDCl_3$): *δ* 3.64 (s, 3H), 2.40–0.73 (m, 24H), 1.16 (s, 3H) , 0.82 (s, 3H).

$^1$H NMR (300 MHz, $CDCl_3$) δ 3.64 (s, 3H), 2.41 – 2.25 (m, 1H), 2.24 – 2.04 (m, 4H), 2.04 – 1.96 (m, 1H), 1.90 – 1.67 (m, 6H), 1.67 – 1.35 (m, 5H), 1.16 (s, 4H), 1.14 – 0.92 (m, 3H), 0.90 – 0.71 (m, 6H).

Major isomer:

$^{13}$C NMR (75 MHz, $CDCl_3$) δ 178.2 (Cq, C=O), 57.1 (CH), 56.3 (CH), 51.2 ($CO_2CH_3$), 47.3 ($CH_2$), 44.6 (Cq), 43.9 (Cq), 41.9 ($CH_2$), 40.9 ($CH_2$), 40.3 ($CH_2$), 39.6 (CH), 39.5 (Cq), 38.2 ($CH_2$), 32.3 (CH), 32.1 (t, *J* = 21.7 Hz, $CH_2C_6F_{13}$), 28.9 ($CH_3$), 26.0 ($CH_2$), 22.3 ($CH_2$), 19.3 ($CH_2$), 19.1 ($CH_2$), 15.5 ($CH_3$). $^{19}$F NMR (282 MHz, $CDCl_3$): *δ* –80.8 ($CF_3$), –112.7 to –113.5 (m, 1F of $CF_2$), –114.2 (ddq, *J* = 268.9, 27.7, 13.1 Hz, 1F of $CF_2$), –121.9 ($CF_2$), –122.9 ($CF_2$), –123.6 ($CF_2$), –126.2 ($CF_2$). IR (ν, $cm^{-1}$): 2932, 2360, 2341, 1725, 1142, 707. HRMS (ESI): calculated for $[C_{27}H_{33}F_{13}O_2]^+$: 637.2351; found: 637.2346.

Methyl (4R,6aS,8S,9R,11bS)-8-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,9-heptadecafluorononyl)-4,11b-dimethyltetradecahydro-6a,9-methanocyclohepta[a]naphthalene-4-carboxylate **21**




$C_{29}H_{33}F_{17}O_2$
MW: 736,55

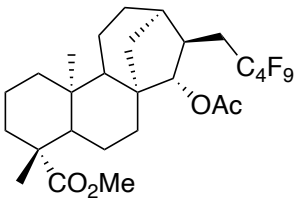
According to general procedure 1' from methyl *ent*-kaurenoate **1p** (50 mg, 0.16 mmol) and perfluoro-*n*-octyl iodide (62 µL, 0.24 mmol). The crude product was purified by FC (pentane/EtOAc 97:3) to give **21** (85 mg, 75%, dr >95:5) as a colourless oil, contaminated with the traces of eliminated side product. $[a]_D^{20}$ = –26.4° (*c* = 4.8, $CHCl_3$).

Major isomer:

$^1$H NMR (300 MHz, $CDCl_3$): *δ* 3.64 (s, 3H), 2.41–0.72 (m, 24H), 1.16 (s, 3H), 0.82 (s, 3H).

$^{1}$H NMR (300 MHz, $CDCl_3$) δ 3.64 (s, 3H), 2.42 – 2.25 (m, 1H), 2.24 – 2.03 (m, 4H), 2.01 (d, *J* = 11.5 Hz, 1H), 1.93 – 1.68 (m, 5H), 1.68 – 1.35 (m, 8H), 1.16 (s, 4H), 1.14 – 0.89 (m, 4H), 0.84 (m, 4H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 178.2 (C=O), 57.1 (CH), 56.4 (CH), 51.2 ($CO_2CH_3$), 47.3 ($CH_2$), 44.6 (Cq), 43.9 (Cq), 41.9 ($CH_2$), 40.9 ($CH_2$), 40.3 ($CH_2$), 39.6 (CH), 39.5 (Cq), 38.2 ($CH_2$), 32.3 (CH), 32.1 (t, *J* = 22.1 Hz, $CH_2C_8F_{17}$), 28.8 ($CH_3$), 26.0 ($CH_2$), 22.3 ($CH_2$), 19.3 ($CH_2$), 19.1 ($CH_2$), 15.5 ($CH_3$). $^{19}$F NMR (282 MHz, $CDCl_3$): *δ* –80.8 ($CF_3$), –113.0 (ddq, *J* = 268.8, 27.7, 13.9 Hz, 1F of $CF_2$), –114. 2 (ddq, *J* = 268.8, 26.9, 13.2 Hz, 1F of $CF_2$), –121.7 ($CF_2$) , –121.9 (4F, 2x$CF_2$), –122.7 ($CF_2$), –123.5 ($CF_2$), –126.1 ($CF_2$). IR (v, cm$^{-1}$): 2359, 2341, 1717, 1240, 1111, 906, 728, 647. HRMS (ESI): calculated for $[C_{27}H_{33}F_{13}O_2]^+$: 737.2287; found: 737.2282.

Methyl (4R,6aR,7S,8S,9R,11bS)-7-acetoxy-4,11b-dimethyl-8-(2,2,3,3,4,4,5,5,5-nonafluoropentyl) tetradecahydro-6a,9-methanocyclohepta[a]naphthalene-4-carboxylate **22**




$C_{27}H_{35}F_9O_4$
MW: 594,56

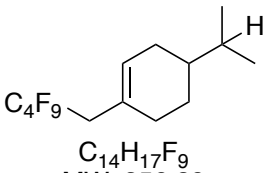
According to general procedure 1' from methyl 15-α-acetoxy-*ent*-kaurenoate **1q** (50 mg, 0.13 mmol), nonafluoro-1-iodobutane (45 µL, 0.24 mmol), 4-methoxycatechol (38 mg, 0.27 mmol) and $BEt_3$ (0.17 mL, 0.17 mmol). The crude product was purified by FC (pentane/EtOAc 93:7) to give **22** (35 mg, 45%, dr 87:13) as a yellowish oil.

Major diastereomer (8-α):

$^{1}$H NMR (300 MHz, $CDCl_3$ ): *δ* 4.71 (d, *J* = 3.5 Hz, 1H), 3.63 (s, 3H), 2.35–0.75 (m, 23H), 2.06 (s, 3H), 1.15 (s, 3H), 0.83 (s, 3H).

$^{1}$H NMR (300 MHz, $CDCl_3$) δ 4.75 – 4.69 (m, 1H), 3.64 (s, 3H), 2.35 – 2.26 (m, 3H), 2.16 (d, *J* = 14.4 Hz, 1H), 2.06 (s, 3H), 1.89 – 1.80 (m, 4H), 1.72 – 1.58 (m, 4H), 1.56 – 1.39 (m, 5H), 1.17 – 1.15 (m, 4H), 1.08 – 0.93 (m, 3H), 0.84 - 0.83 (m, 4H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 178.1 (C=O), 171.2 (OC=O), 86.8 (*C*HCOAc), 56.6 (CH), 53.5 (CH), 51.3 ($CO_2CH_3$), 47.3 ($CH_2$), 43.8 (Cq), 41.8 ($CH_3$), 40.5 ($CH_2$), 39.7 ($C_q$), 38.5 ($CH_2$), 38.0 ($CH_2$), 37.9 (CH), 34.9 ($CH_2$), 29.8 (t, *J* = 20.8 Hz, $CH_2C_4F_9$), 28.7 ($CH_3$), 25.0 ($CH_2$), 21.2 (CH), 21.1 ($CH_2$), 19.2 ($CH_2$), 18.7 ($CH_2$), 15.7 ($CH_3$). $^{19}$F NMR (282 MHz, $CDCl_3$ ): *δ* –81.1 (3F, $CF_3$), –114.1 ($CF_2$), –124.3 ($CF_2$) , –125.9 ($CF_2$). IR (v, cm$^{-1}$): 2933, 1725, 1228, 1131, 1026, 729. HRMS (ESI): calculated for $[C_{27}H_{35}F_9O_6Na]^+$: 617.2289; found: 617.2284.

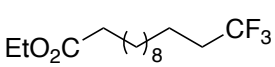
### 4-Isopropyl-1-(2,2,3,3,4,4,5,5,5-nonafluoropentyl)cyclohex-1-ene **23**




$C_{14}H_{17}F_9$
MW: 356,28

According to general procedure 1 from (1*S*)-(–)-beta-pinene (158 mg, 1.0 mmol). The crude product was submitted to FC (100% pentane) to afford **23** (309 mg, 0.867 mmol, 87%) as a colourless liquid. $R_f$ = 0.73 (100% pentane). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 5.76–5.58 (m, 1H, C*H*=CCH$_2$C$_4$F$_9$), 2.82–2.56 (m, 2H, C*H*$_2$C$_4$F$_9$), 2.24–1.97 (m, 3H), 1.87–1.69 (m, 2H), 1.55–1.42 (m, 1H), 1.38–1.15 (m, 2H), 0.90 (d, *J* = 6.8, 3H), 0.89 (d, *J* = 6.8 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 130.1 (*C*H=CCH$_2$C$_4$F$_9$), 126.5 (t, *J* = 2.0 Hz, C$_q$), 39.4 (CH), 38.6 (t, *J* = 22.0 Hz, *C*H$_2$C$_4$F$_9$), 32.1 (CH), 30.2 (*C*H$_2$), 29.2 (*C*H$_2$), 26.3 (CH$_2$), 19.9 (CH$_3$), 19.6 (CH$_3$). $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ –81.1 (CF$_3$), –111.7 to –112.6 (m, 1F of CF$_2$), –112.9 to –113.8 (m, 1F of CF$_2$), –124.2 (CF$_2$), –126.0 (CF$_2$). IR ($\nu$, cm$^{-1}$): 2930 (w), 2875 (w), 1213 (s), 1130 (s); HRMS (EI): calculated for [$C_{14}H_{17}F_9$]$^+$: 356.1181; found: 356.1186.

### Ethyl 12,12,12-trifluorododecanoate **24**




$C_{14}H_{25}F_3O_2$
MW: 282,35

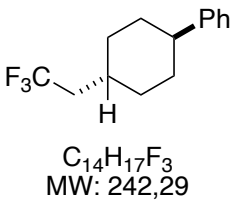
According to general procedure 3 from ethyl-10-undecenoate (219 mg, 1.0 mmol). The reaction was run by using less TBC (170 mg, 1.0 mmol) at the beginning. After 1 h, TBC (170 mg, 1.0 mmol) was added and was continued for further 1 h. The crude product was submitted to FC (heptanes/EtOAc 95:5) to afford **24** (206 mg, 0.73 mmol, 73%) as yellow oil.

From **29** (285 mg, 0.90 mmol) according to general procedure 6. The crude product was submitted to FC (heptanes/EtOAc 95:5) to afford **24** (246 mg, 0.87 mmol, 97%) as a stinky colourless oil which crystallised when stored in the fridge.

According to general procedure 7 from ethyl-10-undecenoate (219 mg, 1.0 mmol), the desired product **24** (180 mg, 0.64 mmol, 64%) was obtained as a colourless oil as a mixture with the intermediate chloride **29** (68 mg, 0.21 mmol, 21%). $R_f$ = 0.55 (heptanes/EtOAc 9:1). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 4.12 (q, *J* = 7.1 Hz, 2H, C*H*$_2$CH$_3$), 2.28 (t, *J* = 7.5 Hz, 2H, C*H*$_2$CO$_2$), 2.13–1.96 (m, 2H, C*H*$_2$CF$_3$), 1.65–1.50 (m, 4H, C*H*$_2$CH$_2$CO$_2$ and C*H*$_2$CH$_2$CF$_3$), 1.39–1.27 (m, 12H), 1.25 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 173.9 (C=O), 127.3 (q, *J* = 276.3 Hz, CF$_3$), 60.1 (*C*H$_2$CH$_3$), 34.3 (*C*H$_2$CO$_2$), 33.7 (q, *J* = 28.2 Hz, *C*H$_2$CF$_3$), 29.3 (CH$_2$), 29.2 (CH$_2$), 29.2 (CH$_2$), 29.11 (CH$_2$), 29.07 (CH$_2$), 28.7 (CH$_2$), 24.9 (*C*H$_2$CH$_2$CO$_2$), 21.8 (q, *J* = 2.9 Hz, *C*H$_2$CH$_2$CF$_3$), 14.2 (*C*H$_2$CH$_3$). $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ –66.5 (t, *J* = 11.0 Hz, CF$_3$). IR ($\nu$, cm$^{-}$

[1]): 2927 (w), 2856 (w), 1734 (s), 1252 (s), 1155 (s), 1132 (s), 1031 (s). HRMS (ESI): calculated for $[C_{14}H_{26}O_2F_3]^+$: 283.1879; found: 283.1872.

### ((1*R*,4*R*)-4-(2,2,2-trifluoroethyl)cyclohexyl)benzene **25**




$C_{14}H_{17}F_3$
MW: 242,29

According to general procedure 3 from 4-methylenecyclohexyl)benzene (174 mg, 1.0 mmol). The crude product was purified by FC (100% pentane) to afford **25** (209 mg, 0.86 mmol, 86%, *trans/cis* 9:1) containing traces (c.a. 4% of alkene).

From **30** (140 mg, 0.5 mmol) according to general procedure 6. The crude product was purified by FC (pentane) to afford **25** (92 mg, 0.38 mmol, 76%) as a *trans/cis* 94:6 mixture.

According to general procedure 7 from 4-methylenecyclohexyl)benzene (174 mg, 1.0 mmol). The desired product **25** (198 mg, 0.82 mmol, 82%, *trans/cis* 93:7) was obtained.

Colourless oil crystallises when stored in the fridge, as it has a low melting point: M.p. 37 °C (uncorrected). $R_f$ = 0.45 (100% pentane).

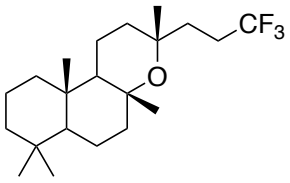
Major isomer: $^1$H NMR (400 MHz, $CD_2Cl_2$): δ 7.31–7.26 (m, 2H$_{Ar}$), 7.24–7.08 (m, 3H$_{Ar}$ ), 2.50 (tt, *J* = 12.3, 3.7 Hz, 1H, C*H*C$_6$H$_5$), 2.08 (tt, *J* = 11.7, 5.7 Hz, 2H, C*H*$_2$CF$_3$), 2.02–1.90 (m, 4H), 1.82–1.72 (m, 1H, C*H*CH$_2$CF$_3$), 1.53 (qd, *J* = 12.9, 3.4 Hz, 2H), 1.23 (qd, *J* = 12.8, 3.4 Hz, 2H). $^{13}$C NMR (100 MHz, $CD_2Cl_2$): *δ* 147.3 (C$_q$), 128.3 (2CH$_{Ar}$), 127.33 (q, J = 277.3 Hz, CF$_3$), 126.7 (2CH$_{Ar}$), 125.9 (CH$_{Ar}$), 43.8 (*C*HC$_6$H$_5$), 40.5 (q, *J* = 26.9 Hz, *C*H$_2$CF$_3$), 33.8 (2xCH$_2$), 33.2 (2xCH$_2$), 31.8 (d, *J* = 2.4 Hz, *C*HCH$_2$CF$_3$). $^{19}$F NMR (376 MHz, $CD_2Cl_2$): *δ* –63.1 (t, *J* = 10.9 Hz).. IR (ν, cm$^{-1}$): 2929 (w), 2853 (w), 1274 (s), 1259 (s), 752 (s). HRMS (EI): calculated for $[C_{14}H_{17}F_3]^+$: 242.1276; found: 242.1276.

Minor isomer (characteristic signal): $^{19}$F NMR (376 MHz, $CD_2Cl_2$): *δ* –64.4 (t, *J* = 11.5 Hz).

### (3*R*,4a*R*,10a*S*)-3,4a,7,7,10a-pentamethyl-3-(3,3,3-trifluoropropyl)dodecahydro-1*H*-benzo-[*f*]chromene **26**

According to general procedure 3 from manoyl oxide (145 mg, 0.5 mmol). The crude product was purified by FC (pentane/Et$_2$O 99.5:0.5) to afford **26** (46 mg, 0.128 mmol, 26%).

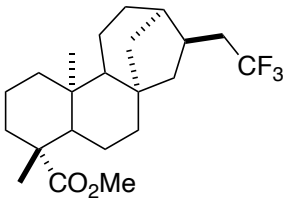
From chloride **33** (119 mg, 0.301 mmol) according to general procedure 6. The crude product was purified by FC (pentane/Et$_2$O 99.5:0.5) to afford **26** (83 mg, 0.231 mmol, 77%). Colourless



$C_{21}H_{35}F_3O$
MW: 360,51

solid. $R_f$ = 0.42 (pentane/$Et_2O$ 99.5:0.5). M.p. 80–82 °C (uncorrected). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 2.27–2.10 (m, 2H), 1.77–1.20 (m, 14H), 1.26 (s, 3H), 1.23 (s, 3H), 1.21–1.07 (m, 1H), 1.07–0.99 (m, 1H), 0.93 (dd, $J$ = 11.9, 2.6 Hz, 1H), 0.88–0.80 (m, 1H), 0.86 (s, 3H), 0.79 (s, 3H), 0.76 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$):) $\delta$ 128.2 (q, $J$ = 276.0 Hz), 75.0 (Cq), 71.3 (Cq), 58.5 (CH), 56.7 (CH), 43.1 ($CH_2$), 42.3 ($CH_2$), 39.4 ($CH_2$), 37.2 (q, $J$ = 2.5 Hz, $CH_2$), 37.0 (Cq), 36.5 ($CH_2$), 33.47 ($CH_3$), 33.46 (Cq), 28.7 (q, $J$ = 28.3 Hz, $CH_2CF_3$), 27.9 ($CH_3$), 24.8 ($CH_3$), 21.4 ($CH_3$), 20.0 ($CH_2$), 18.8 ($CH_2$), 15.9 ($CH_3$), 15.5 ($CH_2$). $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ –66.1 (t, $J$ = 11.2 Hz). IR ($\nu$, $cm^{-1}$): 2997 (w), 2947 (w), 2921 (w), 2859 (w), 2841 (w), 1318 (s), 1254 (s), 1120 (s). HRMS (EI): calculated for $[C_{21}H_{35}OF_3]^+$: 360.2635, found: 360.2637; and calculated for $[C_{20}H_{32}OF_3]^+$: 345.2400, found: 345.2399; and calculated for $[C_{20}H_{30}F_3]^+$: 327.2294, found: 327.2294.

Methyl (4*R*,6a*S*,8*R*,9*R*,11b*S*)-4,11b-dimethyl-8-(2,2,2-trifluoroethyl)tetradecahydro-6a,9-methanocyclohepta[*a*]naphthalene-4-carboxylate **27**



$C_{22}H_{33}F_3O_2$
MW: 386,50

According to general procedure 3 from methyl *ent*-kaurenoate (63.3mg, 0.2 mmol). The reaction was run by using more TBC (67.8 mg, 0.4 mmol) at the beginning, and $BEt_3$ (0.23 mL, 0.26 mmol, 1.15 M in hexane). After 1 h, TBC (33.9 mg, 0.2 mmol) and $BEt_3$ (0.23 mL, 0.26 mmol, 1.15 M in hexane) were added and was continued for further 1 h. The crude product was purified by FC (pentane/$Et_2O$ 98:2) to afford **27** (30 mg, 0.077 mmol, 39%) as a single diastereomer. A second fraction of **27** (12.5 mg, 0.032 mmol, 16%) contaminated with 7% of alkene) was also isolated, combined yield of **27** (42.4 mg, 0.11 mmol, 55%). The crude product was purified by FC (pentane/$Et_2O$ 98:2) to afford **27** (43 mg, 0.11 mmol, 55%) as a single diastereomer contaminated with traces (ca. 3-4%) of alkene.

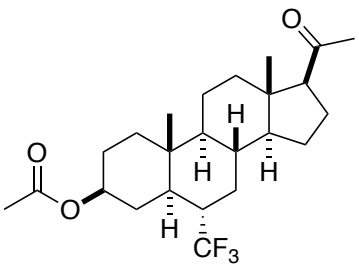
From chloride **31** (67 mg, 0.159 mmol), according to general procedure 6. The crude product was purified by FC (pentane/$Et_2O$ 98:2) to afford **27** (58 mg, 0.150 mmol, 94%) as a single diastereomer. The product was contaminated with about 6% of an alkene, presumably resulting from HCl elimination.

From methyl *ent*-kaurenoate (63.3mg, 0.2 mmol) according to general procedure 7.

Purification by FC afforded **27** (51 mg, 0.13 mmol, 66%, as single diastereomer) contaminated with ca. 4-5% of alkene. The chloride **31** (8 mg, 0.02 mmol, 8%) was also isolated.

Colourless oil. $R_f$ = 0.48 ($Et_2O$/pentane 2:98). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 3.64 (s, 3H, $CO_2CH_3$), 2.29–2.12 (m, 4H), 2.12–2.06 (m, 1H), 1.99 (dd, *J* = 11.6, 1.8 Hz, 1H), 1.89–1.64 (m, 5H), 1.62–1.37 (m, 7H), 1.16 (s, 3H), 1.15–1.05 (m, 1H), 1.05–0.94 (m, 4H), 0.86–0.74 (m, 1H), 0.82 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 178.2 (C=O), 127.74 (q, *J* = 277.1 Hz, $CF_3$), 57.2 (CH), 56.4 (CH), 51.3 ($CO_2CH_3$), 46.74 ($CH_2$), 44.6 ($C_q$), 44.0 ($C_qCO_2Me$), 42.0 ($CH_2$), 40.9 ($CH_2$), 40.31 ($CH_2$), 39.6 (Cq), 39.2 (CH), 38.3 ($CH_2$), 35.4 (q, *J* = 27.2 Hz, $CH_2CF_3$), 33.7 (CH), 28.9 ($CH_3$), 26.0 ($CH_2$), 22.3 ($CH_2$), 19.3 ($CH_2$), 19.1 ($CH_2$), 15.5 ($CH_3$). $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ –65.0 (t, *J* = 10.7 Hz). IR ($\nu$, $cm^{-1}$): 2987 (w), 2832 (w), 2849 (w), 1723 (s), 1254 (s), 1142 (s), 1116 (s), 1079 (s). HRMS (EI): calculated for $[C_{22}H_{33}O_2F_3]^+$: 386.2427; found: 386.2433; and calculated for $[C_{20}H_{30}F_3]^+$: 327.2294; found: 327.2297.

(3*S*,6*S*,8*R*,9*S*,10*R*,13*S*,14*S*,17*S*)-17-acetyl-10,13-dimethyl-6-(trifluoromethyl)hexadecahydro -1*H*-cyclopenta[*a*]phenanthren-3-yl acetate **28**




$C_{24}H_{35}F_3O_3$
MW: 428,54

According to general procedure 3 from pregnenolone acetate (362 mg, 1.0 mmol). The crude product was purified by FC (heptane/EtOAc 85:15) to afford **28** (237 mg, 0.55 mmol, 55%, dr >95:5) as a single diastereomer.

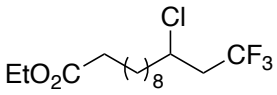
From chloride **32** (238 mg, 0.514 mmol) according to general procedure 6. The crude product was purified by FC (heptane/EtOAc 9:1) to afford **28** (195 mg, 0.455 mmol, 89%) as a single diastereomer. The product was contaminated by 4% of an alkene resulting from HCl elimination.

From pregnenolone acetate (362 mg, 1.0 mmol) according to general procedure 7. $K_2CO_3$ (138 mg, 1 mmol) was added to neutralise small amounts of triflic acid and HCl generated by hydrolysis of the trifluoromethanesulfonyl chloride by residual moisture and thus avoid epimerisation at C(17). The desired product **28** (250 mg, 58%, dr > 95:5) was obtained as a single diastereomer.

Colourless solid. $R_f$ = 0.18 (heptane/EtOAc 9:1). M.p. 131.4–132.9 °C (uncorrected). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 4.69–4.55 (m, 1H), 2.51 (t, *J* = 8.9 Hz, 1H), 2.27 (m, 1H, $CHCF_3$), 2.21–2.09

(m, 1H), 2.11 (s, 3H), 2.05–1.99 (m, 1H), 2.03 (s, 3H), 1.96 (ddd, *J* = 14.5, 3.8, 1.5 Hz, 1H), 1.89–1.77 (m, 4H), 1.74–1.06 (m, 11H), 1.06–0.96 (m, 1H), 0.93 (d, *J* = 1.7 Hz, 3H), 0.71 (td, *J* = 11.2, 4.1 Hz, 1H), 0.63 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): *δ* 209.4 (C=O), 170.8 (C=O), 128.5 (q, *J* = 282.0 Hz, *C*$F_3$), 74.0 (CH), 63.8 (CH), 56.5 (CH), 54.6 (CH), 44.8 (CH), 44.3 (Cq), 42.2 (q, *J* = 25.5 Hz, *C*H$CF_3$), 39.7 ($CH_2$), 39.0 ($CH_2$), 35.2 (Cq), 32.8 (q, *J* = 2.4 Hz, $CH_2$), 32.0 (CH), 31.6 ($CH_3$), 31.3 (q, *J* = 2.5 Hz, $CH_2$), 27.6 ($CH_2$), 24.5 ($CH_2$), 22.9 ($CH_2$), 21.5 ($CH_3$), 21.1 ($CH_2$), 14.5 (q, *J* = 4.0 Hz, $CH_3$), 13.6 ($CH_3$). $^{19}$F NMR (376 MHz, $CDCl_3$): *δ* –61.0 (d, *J* = 12.2 Hz, $CF_3$). IR (ν, $cm^{-1}$): 2975 (w), 2946 (w), 2930 (w), 2849 (w), 1721 (s), 1147 (s), 870 (s). HRMS (ESI): calculated for $[C_{24}H_{36}O_3F_3]^+$: 429.2611, found: 429.2605; and calculated for $[C_{24}H_{35}O_3F_3Na]^+$: 451.2431, found: 451.2423. Minor isomer: $^{19}$F NMR (376 MHz, $CDCl_3$): *δ* –66.1 (d, *J* = 12.0 Hz).

### Ethyl 10-chloro-12,12,12-trifluorododecanoate **29**



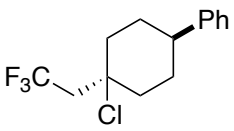

$C_{14}H_{24}ClF_3O_2$
MW: 316,79

From ethyl-10-undecenoate (219 mg, 1.0 mmol) according to general procedure 4. The crude product was submitted to FC (heptanes/EtOAc 95:5) to afford **29** (230 mg, 0.726 mmol, 73%).

From ethyl-10-undecenoate (219 mg, 1.0 mmol), according to general procedure 5, the desired product **29** (294 mg, 0.93 mmol, 93%) was isolated accordingly.

Colourless oil. $^1$H NMR (400 MHz, $CDCl_3$): *δ* 4.11 (q, *J* = 7.2 Hz, 2H), 4.11–4.06 (m, 1H, C*H*Cl), 2.70–2.42 (m, 2H, C*H*$_2$$CF_3$), 2.27 (t, *J* = 7.5 Hz, 2H, $CO_2$C*H*$_2$), 1.87–1.66 (m, 2H, C*H*$_2$CHCl), 1.65–1.27 (m, 12H), 1.24 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): *δ* 174.0 (C=O), 125.5 (q, *J* = 277.6 Hz, $CF_3$), 60.3 (*C*$H_2$$CH_3$), 54.3 (q, *J* = 3.3 Hz, *C*HCl), 42.6 (q, *J* = 28.3 Hz, *C*$H_2$$CF_3$), 38.2 (*C*$H_2$CHCl), 34.5 (*C*$H_2$$CO_2$), 29.31 ($CH_2$), 29.23 ($CH_2$), 29.18 ($CH_2$), 28.9 ($CH_2$), 26.0 ($CH_2$), 25.1 ($CH_2$), 14.4 ($CH_3$). $^{19}$F NMR (376 MHz, $CDCl_3$): *δ* –63.9 (t, *J* = 10.2 Hz, $CF_3$). IR (ν, $cm^{-1}$): 2930 (w), 2857 (w), 1731 (s), 1240 (s), 1240, 1145 (s), 1114 (s), 630 (m). HRMS (ESI): calculated for $[C_{14}H_{25}O_2ClF_3]^+$: 317.1490; found: 317.1500.

(4-Chloro-4-(2,2,2-trifluoroethyl)cyclohexyl)benzene **30**



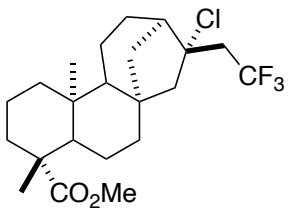

$C_{14}H_{16}ClF_3$
MW: 276,73

According to general procedure 4 from 4-methylene-cyclohexyl)benzene **1a** (174 mg, 1.0 mmol). The crude product was purified by FC (100% pentane) to afford the chloride **30** (247 mg, 0.89 mmol, 89%, *trans/cis* 94:6).

According to general procedure 5 from 4-methylene-cyclohexyl)benzene **1a** (174 mg, 1.0 mmol). The chloride **30** (259 mg, 0.94 mmol, 94%) was obtained as a *trans/cis* 94:6 mixture of stereoisomers.

Colourless crystalline compound. M.p. 83.5–85.5 °C (uncorrected). $^1$H NMR (400 MHz, $CD_2Cl_2$): δ 7.37–7.25 (m, 4H$_{Ar}$), 7.24–7.18 (m, 1H), 2.76 (q, *J* = 10.9 Hz, 2H, C*H*$_2$CF$_3$), 2.54 (tt, *J* = 12.2, 3.6 Hz, 1H, C*H*C$_6$H$_5$), 2.28–2.14 (m, 2H), 2.13–1.98 (m, 2H), 1.93–1.78 (m, 4H). $^{13}$C NMR (101 MHz, $CD_2Cl_2$): *δ* 146.3 (Cq$_{Ar}$), 128.4 (2 × CH$_{Ar}$), 126.8 (2 × CH$_{Ar}$), 126.2 (CH$_{Ar}$), 125.4 (q, *J* = 278.8 Hz, *C*F$_3$), 68.1 (q, *J* = 2.2 Hz), 48.4 (q, *J* = 27.4 Hz, *C*H$_2$CF$_3$), 42.9 (*C*HC$_6$H$_5$), 39.3 (q, *J* = 1.5 Hz, 2C), 29.56 (2C). $^{19}$F NMR (376 MHz, $CD_2Cl_2$): *δ* –59.9 (t, *J* = 10.9 Hz, CF$_3$). IR (ν, cm$^{-1}$): 3030 (w), 2930 (w), 2856 (w), 1262 (s), 1131 (s), 737 (s). HRMS (EI): calculated for [$C_{14}H_{16}ClF_3$]+: 276.0887; found: 276.0884.

Methyl (4*R*,6a*S*,8*S*,9*R*,11b*S*)-8-chloro-4,11b-dimethyl-8-(2,2,2-trifluoroethyl)tetradecahydro-6a,9-methanocyclohepta[*a*]naphthalene-4-carboxylate **31**

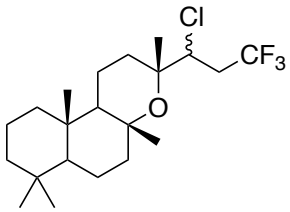



$C_{22}H_{32}ClF_3O_2$
MW:420,94

From methyl *ent*-kaurenoate (**1p**) (63.3 mg, 0.20 mmol) according to general procedure 5. The crude product was purified by FC (pentane/Et$_2$O 99:1) to afford **31** (67 mg, 0.159 mmol, 80%, as a single diastereomer. Colourless solid. R$_f$ = 0.36 (pentane/Et$_2$O 98:2). $[\alpha]_D^{20}$ = –6.26 (c = 1.0, $CH_2Cl_2$). M.p. 90–92 °C (uncorrected). $^1$H NMR (400 MHz, $CDCl_3$): *δ* 3.65 (s, 3H, CO$_2$C*H*$_3$), 2.75 (qd, *J* = 10.2, 1.8 Hz, 2H, C*H*$_2$CF$_3$), 2.49–2.38 (m, 1H), 2.24–2.14 (m, 2H), 2.07–1.91 (m, 3H), 1.89–1.59 (m, 8H), 1.51–1.31 (m, 3H), 1.17 (s, 3H), 1.07–0.93 (m, 3H), 0.84 (d, *J* = 2.2 Hz, 3H), 0.78 (td, *J* = 13.5, 5.0 Hz, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$): *δ* 178.0 (C=O), 126.0 (q, *J* = 278.6 Hz, *C*F$_3$), 73.9 (q, *J* = 2.3 Hz), 57.8 (CH$_2$), 56.9 (CH), 55.9 (CH), 51.3 (CH$_3$), 50.9 (CH), 45.3 (C$_q$), 43.9 (C$_q$), 42.8 (q, *J* = 28.1 Hz, *C*H$_2$CF$_3$), 41.8 (CH$_2$), 40.8 (CH$_2$), 39.6 (C$_q$), 38.2 (CH$_2$), 37.5 (CH$_2$), 28.8 (CH$_3$), 27.4 (CH$_2$), 22.1 (CH$_2$), 19.2 (CH$_2$), 18.3 (CH$_2$), 15.5 (CH$_3$). $^{19}$F NMR (376 MHz, $CDCl_3$): *δ* –59.5 (t, *J* = 10.2 Hz, CF$_3$). IR (ν, cm$^{-1}$): 2986

(w), 2848 (w), 2871 (w), 2851 (w), 1719 (s), 1124 (s), 1108 (s). HRMS (EI): calculated for $[C_{22}H_{32}O_2ClF_3]^+$: 420.2037; found: 420.2046.

(3*S*,5*S*,6*R*,8*S*,9*S*,10*R*,13*S*,14*S*,17*S*)-17-acetyl-5-chloro-10,13-dimethyl-6-(trifluoromethyl)-hexadecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl acetate **32**




$C_{21}H_{34}ClF_3O$
MW:394,95

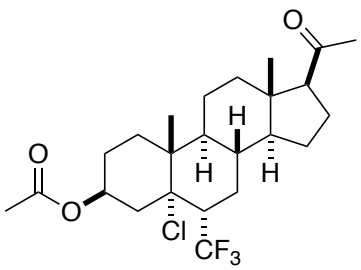
From pregnenolone acetate **1s** (138 mg, 1.0 mmol) according to general procedure 4 in the presence of $K_2CO_3$ (138 mg, 1.0 mmol). The crude product was purified by FC (heptane/EtOAc 9:1) to afford **32** (238 mg, 0.51 mmol, 51%, dr > 95:5) as a single diastereomer.

From pregnenolone acetate **1s** (138 mg, 1.0 mmol) according to general procedure 5. The chloride **32** (294 mg, 0.64 mmol, 64%) was obtained as a single diastereomer.

Colourless crystalline compound. $R_f$ = 0.27 (heptane/EtOAc 9:1). $[\alpha]_D^{20}$ = 1.58 (c = 1.0, $CH_2Cl_2$). M.p. 146.5–147.4 °C (uncorrected). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 5.39 (tt, *J* = 10.6, 5.4 Hz, 1H), 2.84 (qd, *J* = 12.1, 6.8 Hz, 1H, C*H*$CF_3$), 2.54 (t, *J* = 8.7 Hz, 1H), 2.42 (ddd, *J* = 13.8, 10.3, 2.0 Hz, 1H), 2.31 (ddd, *J* = 13.9, 5.1, 1.8 Hz, 1H), 2.24–2.00 (m, 3H), 2.11 (s, 3H), 2.03 (s, 3H), 1.96 (ddt, *J* = 11.6, 5.6, 2.0 Hz, 1H), 1.85–1.52 (m, 9H), 1.47 (td, *J* = 12.5, 3.9 Hz, 1H), 1.34–1.19 (m, 3H), 1.14 (s, 3H), 0.62 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): $\delta$ 209.4 (C=O), 170.5 (C=O), 126.4 (q, *J* = 282.4 Hz, *C*$F_3$), 84.7 (Cq), 70.8 (CH), 63.6 (CH), 56.0 (CH), 51.0 (q, *J* = 25.7 Hz, *C*H$CF_3$), 46.4 (CH), 44.3 (Cq), 40.5 (Cq), 40.1 (q, *J* = 2.9 Hz, *C*$H_2$CCl), 38.8 ($CH_2$), 34.6 ($CH_2$), 32.0 (CH), 31.6 ($CH_3$), 26.7 ($CH_2$), 26.14 ($CH_2$), 24.3 ($CH_2$), 23.0 ($CH_2$), 21.5 ($CH_3$), 21.0 ($CH_2$), 16.6 (q, *J* = 4.1 Hz, $CH_3$), 13.4 ($CH_3$). $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ –60.0 (d, *J* = 12.0 Hz, $CF_3$). IR ($\nu$, $cm^{-1}$): 2943 (w), 2881 (w), 2851 (w), 1730 (s), 1707 (s), 1257 (s), 1142 (s), 1118 (s), 1107 (s), 750 (s). HRMS (ESI): calculated for $[C_{24}H_{35}O_3ClF_3]^+$: 463.2219; found: 463.2221.

(3*R*,4a*R*,10a*S*)-3-((*S*)-1-chloro-3,3,3-trifluoropropyl)-3,4a,7,7,10a-pentamethyldodeca-hydro-1*H*-benzo[*f*]chromene **33**

From manoyl oxide (145 mg, 0.5 mmol) according to general procedure 4 in the presence of $K_2CO_3$ (34.6 mg, 0.25 mmol) The crude product was purified by FC (pentane/$Et_2O$ 99.5:0.5) to



$C_{24}H_{34}ClF_3O_3$
MW: 462,98

afford **33** (122 mg, 0.31 mmol, 62%, dr 2:1). The major diastereomer of **33** is a colourless solid. M.p. 105.0–107.1 °C (uncorrected). $R_f$ = 0.33 (100% pentane). The minor diastereomer is a colourless oil. $R_f$ = 0.14 (100% pentane).

Major diastereomer:

$^1$H NMR (400 MHz, $CDCl_3$): *δ* 3.77 (d, *J* = 10.3 Hz, 1H), 3.06 (dqd, *J* = 15.4, 11.1, 1.4 Hz, 1H), 2.28 (dp, *J* = 15.5, 9.9 Hz, 1H), 2.03–1.90 (m, 1H), 1.74–1.20 (m, 11H), 1.25 (s, 3H), 1.23 (s, 3H), 1.19–1.09 (m, 2H), 0.96–0.81 (m, 2H), 0.86 (s, 3H), 0.79 (s, 3H), 0.77 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): *δ* 126.7 (q, *J* = 277.0 Hz, *C*$F_3$), 76.2 (Cq), 74.2 (Cq), 63.0 (q, *J* = 2.8 Hz, CH), 57.7 (CH), 56.6 (CH), 43.0 ($CH_2$), 42.2 ($CH_2$), 39.2 ($CH_2$), 37.1 (q, *J* = 28.2 Hz), 37.0 (Cq), 36.5 ($CH_2$), 33.5 (CH), 33.4 (Cq), 24.8 ($CH_3$), 21.4 ($CH_3$), 20.8 ($CH_3$), 20.0 ($CH_2$), 18.7 ($CH_2$), 15.8 ($CH_3$), 15.2 ($CH_2$). $^{19}$F NMR (376 MHz, $CDCl_3$): *δ* –64.2 (t, *J* = 10.2 Hz). IR (ν, $cm^{-1}$): 2984 (w), 2968 (w), 2924 (w), 2857 (w), 1376 (m), 1136 (s), 1103 (s), 1075 (s). EI-MS (ESI): calculated for $[C_{21}H_{34}OClF_3]^+$: 394.2244; found: 394.2245.

Minor diastereomer:

$^1$H NMR (400 MHz, $CDCl_3$): *δ* 3.81 (dd, *J* = 10.1, 1.5 Hz, 1H), 3.05 (dqd, *J* = 15.5, 11.1, 1.6 Hz, 1H), 2.39 (dp, *J* = 15.5, 9.9 Hz, 1H), 1.79–1.22 (m, 12H), 1.41 (s, 3H), 1.29 (s, 3H), 1.15 (td, *J* = 13.4, 4.2 Hz, 1H), 1.05–0.99 (m, 1H), 0.96–0.91 (m, 1H), 0.95–0.81 (m, 1H), 0.86 (s, 3H), 0.80 (s, 3H), 0.77 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ 126.8 (q, *J* = 277.0 Hz), 76.3, 74.9, 61.8 (q, *J* = 2.9 Hz), 58.8, 56.6, 42.9, 42.2, 39.3, 37.5 (q, *J* = 28.5 Hz), 37.1, 33.4 (q, *J* = 4.6 Hz), 31.7, 25.5, 24.6, 21.4, 19.9, 18.7, 16.0, 15.0. $^{19}$F NMR (376 MHz, $CDCl_3$): *δ* –63.8 (t, *J* = 10.6 Hz). IR (ν, $cm^{-1}$) (ATRA minor): 2924 (w), 2865 (w), 1262 (m), 1125 (s), 1107 (s). EI-MS (ESI): calculated for $[C_{21}H_{34}OClF_3]^+$: 394.2245; found: 394.2245.

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Chapter 3

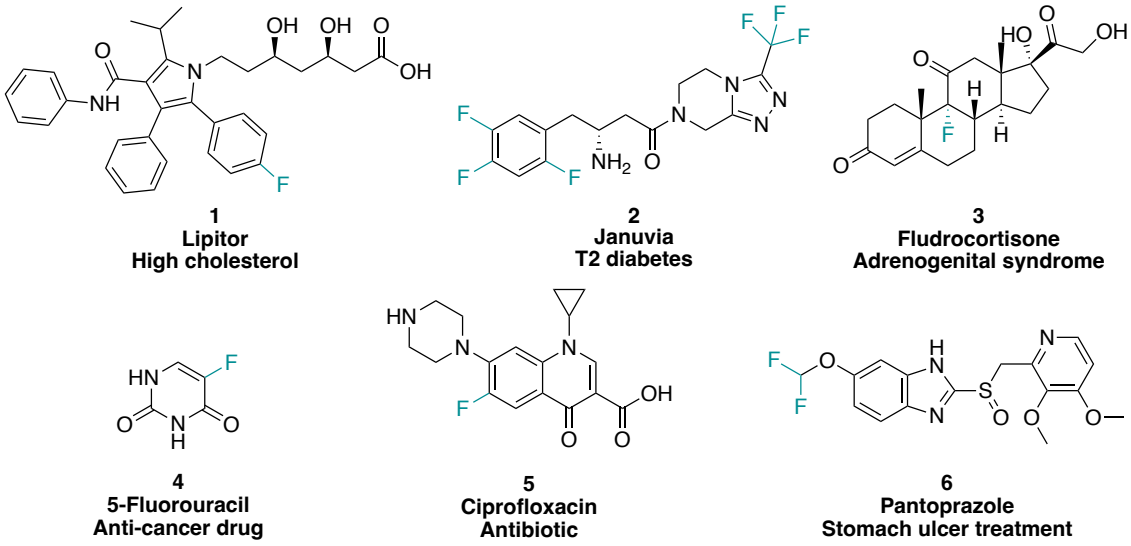
# Radical Fluorination: development of radical fluorinating agents

# Chapter 3 – Radical Fluorination: development of radical fluorinating agents

## 3.1 Introduction

Organofluorine compounds are a critical family of molecules with substantial applications in medicinal, agrochemical, and material sciences, mainly due to the unique properties of the fluorine atom.[1–4] Introducing a fluorine atom into organic compounds can significantly alter properties such as $pK_a$, lipophilicity, protein binding affinity, and metabolic stability.[2] As a result, numerous pharmaceuticals featuring fluoro-aliphatic, -aromatic, and -heterocyclic units have been developed. Notable examples include Prozac™, Lipitor®, Emtriva®, Flonase®, Sovaldi®, Januvia®, and Crestor®.[5,6]

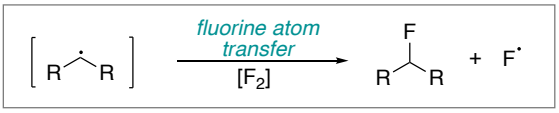
Historically, the potent effects of fluorination were demonstrated in 1954 when Fried and Sabo discovered that introducing a single fluorine atom into the corticosteroid **3** (fludrocortisone) increased its potency tenfold (Scheme 1).[7] The anti-cancer drug 5-fluorouracil **4** and its anti-fungal analogue 5-fluorocytosine were developed, highlighting the therapeutic potential of fluorinated compounds.[8] The 1980s saw the development of 6-fluoroquinolones, a significant class of bactericides, with ciprofloxacin **5** becoming one of the most widely used antibiotics globally. More recent years have seen the diversification of pharmaceuticals containing $–CF_2$, $–CF_3$, and $–CF_2CF_3$ moieties, such as Pantoprazole **6**, which is used to treat stomach ulcers and esophagitis and was among the most prescribed medications in the United States in 2017.[9] These developments underscore fluorine's ongoing importance and impact in drug development and other scientific fields.




Scheme 1. Examples of drugs with fluorine incorporation.

Fluorine is the most abundant halogen in various ores within the Earth's crust. The principal mineral sources of fluorine include fluorspar ($CaF_2$), cryolite ($Na_3AlF_6$), and fluorapatite ($Ca_5(PO_4)_3F$).[10,11] Despite its mineral prevalence, organofluorine compounds are exceedingly rare.[12] Currently, all fluorine atoms utilised in organofluorine chemistry are derived from fluorspar. This mineral is processed into anhydrous hydrogen fluoride (aHF) using aqueous sulfuric acid. aHF is a critical reagent directly employed in numerous industrial processes. Notably, it is used in the Balz-Schiemann and Swarts halogen exchange processes, which are essential to producing fluoroaromatic and trifluoromethylaromatic derivatives, respectively.[11] These processes underscore the significance of aHF in synthesising essential organofluorine compounds vital to various sectors, including pharmaceuticals and materials science.

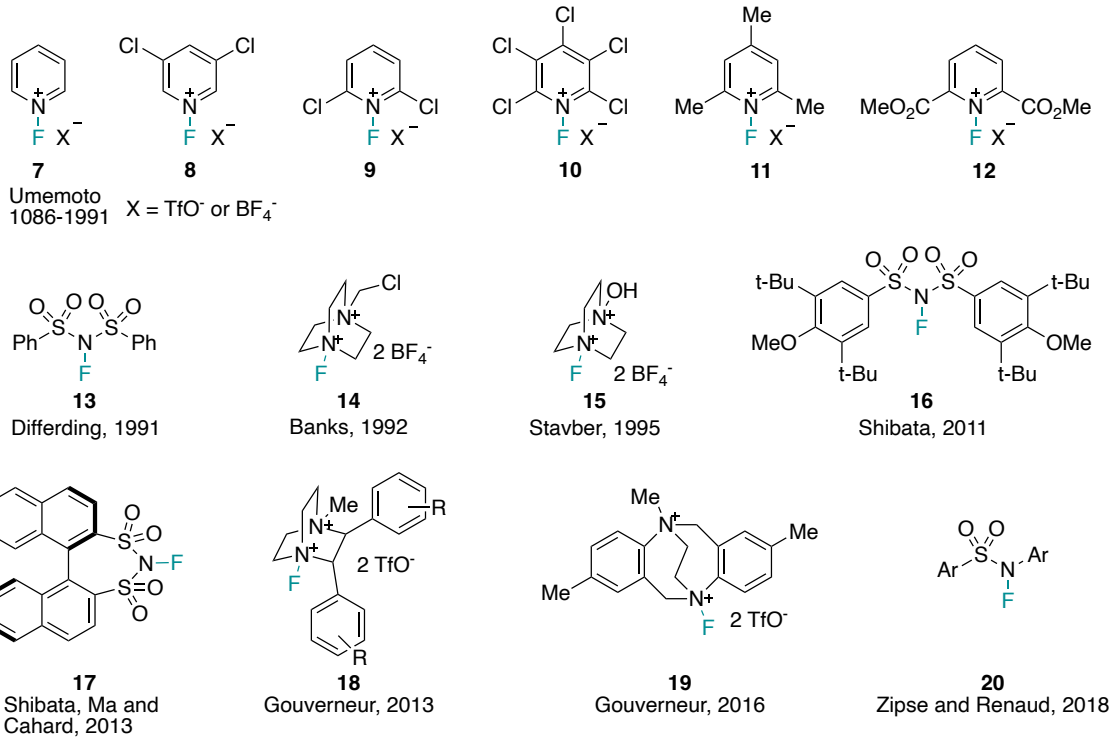
Early investigations into developing electrophilic fluorinating agents primarily focused on those containing an O–F bond, such as $CF_3OF$,[13,14] $ClO_3F$,[15,16] $CF_3COOF$,[17] $CH_3COOF$,[18] and $CsSO_4F$,[19] or an Xe–F bond as seen in $XeF_2$.[20,21] However, these reagents often presented challenges due to their high reactivity, lack of selectivity, complex synthesis, and limited commercial availability. Elemental fluorine ($F_2$) has been successfully used to fluorinate a range of nucleophilic substrates, utilising batch and flow techniques.[22–28] Despite its effectiveness, the use of elemental fluorine requires specialised handling techniques and equipment, making it less accessible for routine use in both laboratory and industrial settings due to safety concerns.




Scheme 2. Fluorination of radicals, general mechanism.

The introduction of bench-stable electrophilic fluorinating reagents with N–F bonds in the 1980s dramatically transformed the field.[29] These N–F reagents are selective and easy to handle, offering sources of electrophilic fluorine, many of which are now commercially available without requiring specialised handling procedures. There are two main categories of N–F reagents: (i) neutral N–F reagents and (ii) quaternary ammonium N–F reagents, with the latter being the most electrophilic. The popularity and widespread synthetic application of N–F reagents are partly attributed to their long shelf lives and the fact that they can be safely handled in standard laboratory glassware. This ease of use and stability makes N–F reagents particularly valuable in various chemical synthesis processes, enhancing their utility in academic and industrial settings.

From 1964 to 2018, numerous N–F reagents have been developed as the second generation of fluorinating agents, each contributing uniquely to the field of fluorination chemistry. Key commercial reagents include (Scheme 3) N-fluoropyridinium salts (such as salts **7-12**) developed by Umemoto et al.,[30–32] NFSI (N-fluorobenzenesulfonimide, **13**) by Differding,[33] and Selectfluor® (1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis[tetrafluoroborate], **14**) by Banks et al.[34] Stavber and co-workers introduced an analogue of Selectfluor® named Accufluor™ (1-fluoro-4-hydroxy-1,4-diazoniabicyclo[2.2.2]octane bis[tetrafluoroborate], **15**).[35]

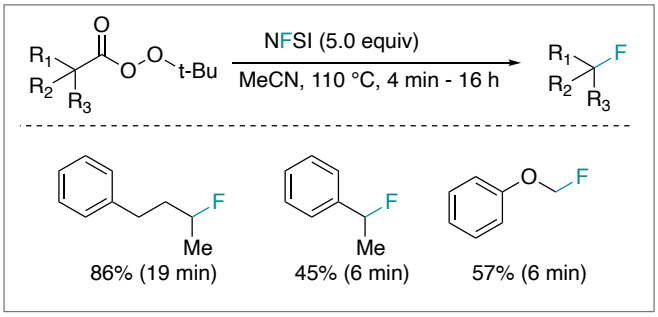



Scheme 3. Some examples of N-F class fluorinating reagents.

The ongoing innovation in fluorinating reagents is further evidenced by the introduction of new compounds by researchers like Shibata, Toste, and Gouverneur. Shibata reported a sterically demanding version of NFSI, N-fluoro-(3,5-di-tert-butyl-4-methoxy)benzenesulfonimide (NFBSI, **16**),[36] and chiral analogues (**17**).[37] Gouverneur et al. introduced chiral Selectfluor® derivatives in 2013 (**18**),[38] and a novel N–F reagent derived from ethano-Tröger's base in 2016 (**19**).[39] Most recently, in 2018, Zipse and Renaud reported a new generation of radical N–F fluorinating reagents based on N-fluoro-N-arylsulfonamides (**20**),[40] highlighting the continuous growth and diversification in the development of these crucial synthetic tools.

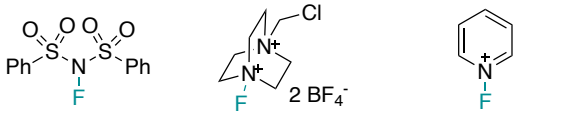
## 3.2 N-Fluorobenzensulfonimide (NFSI)

A pivotal discovery of NFSI by Differding[33] catalysed the rapid development of radical C–H fluorination and further revitalised the broader field of radical fluorination made by the Sammis group.[41] They reported that carbon radicals, generated via the decarboxylation of peresters, could react with electrophilic N–F reagents to produce fluorinated products (Scheme 4).




Scheme 4. Decarboxylative fluorination with NFSI.

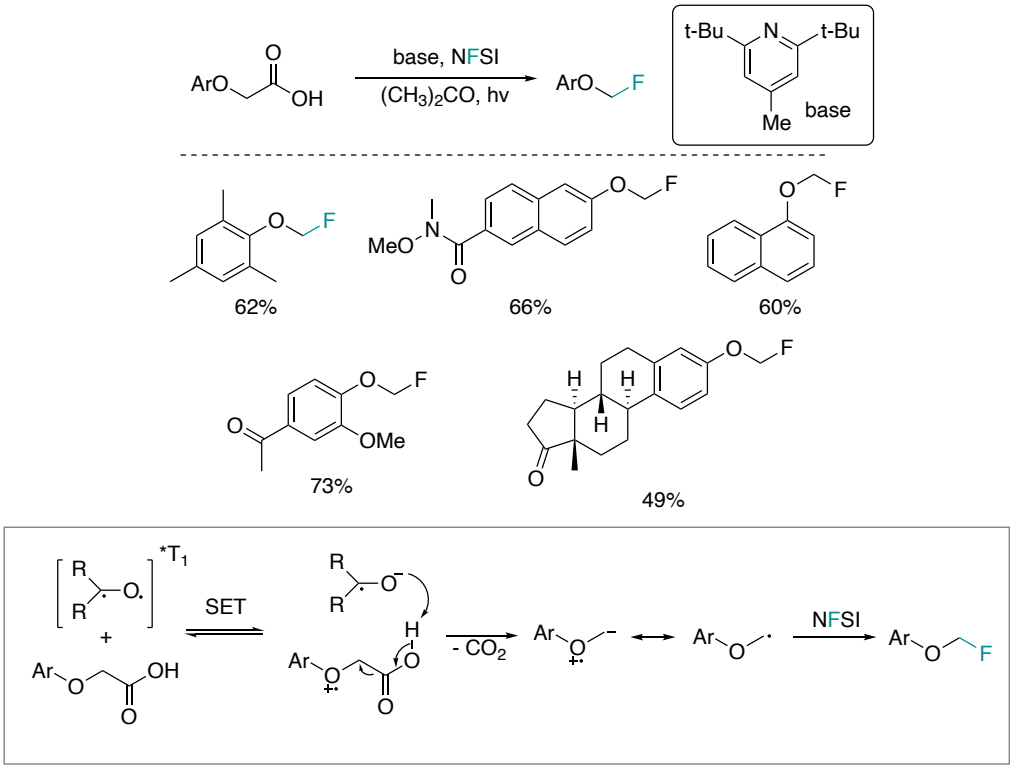
Sammis and colleagues leveraged the relatively low N–F bond dissociation energies (BDEs) of 63.1 and 60.9 kcal/mol (in MeCN) for NFSI and Selectfluor®, respectively, underscoring their potential as fluorine atom transfer reagents (Scheme 5). In contrast, N-fluoropyridinium, commonly used in Pd(II)-catalysed C–H fluorination, was calculated to have a higher BDE of 75.1 kcal/mol. Experimentally, N-fluoropyridinium salts failed to react and,[41] as a result, have been less frequently considered as fluorine atom sources in subsequent studies.[42] This finding significantly influenced the strategic selection of N–F reagents in developing efficient fluorination protocols.




**NFSI** 63.1 kcal mol$^{-1}$ | **Selectfluor** 60.9 kcal mol$^{-1}$ | **N-fluoropyridinium** 75.1 kcal mol$^{-1}$

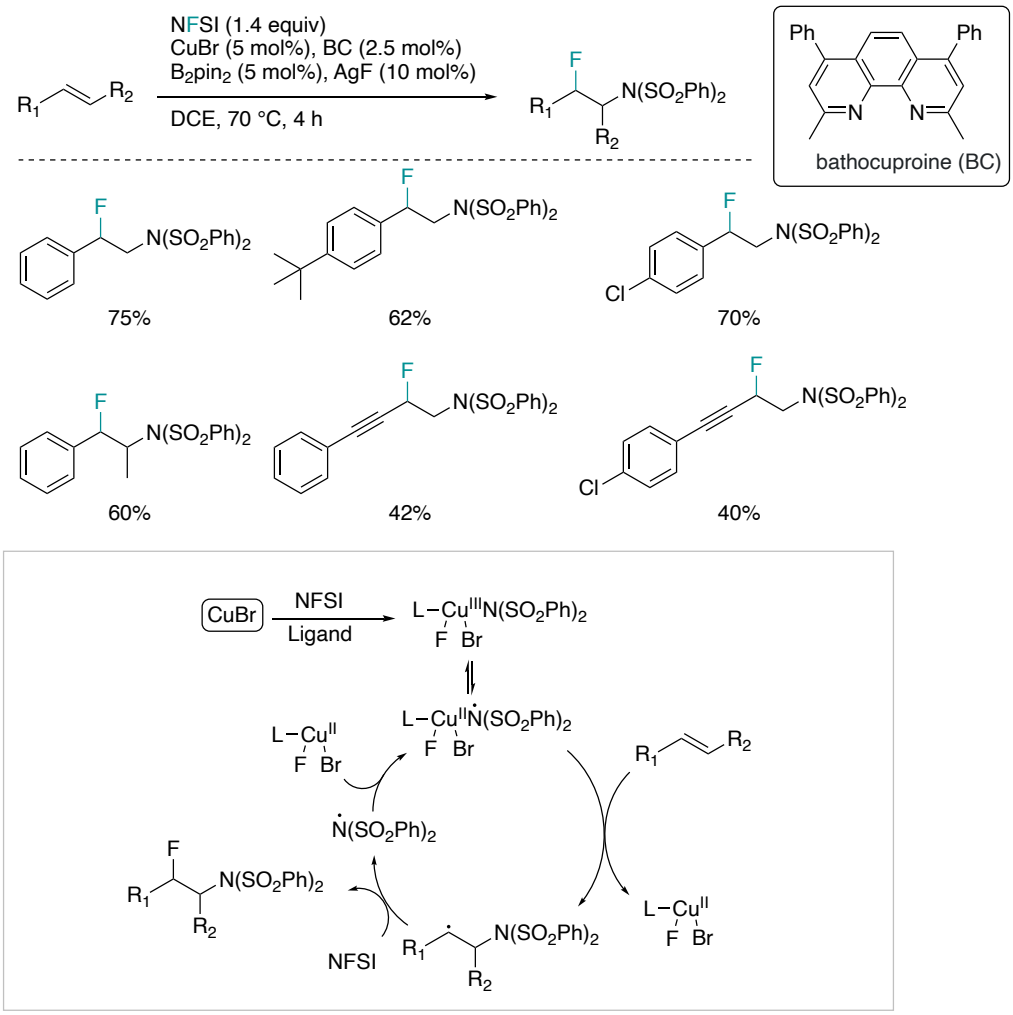
Scheme 5. N-F BDEs of some electrophilic fluorinating agents.

In 2015, the Sammis group further advanced their work by developing a photoinduced decarboxylative procedure designed explicitly for the fluorination of α-aryloxy carboxylic acids.[43] While initial attempts to fluorinate simple alkyl radicals without α-oxygenation were unsuccessful, the method demonstrated a nice scope and good functional group tolerance when applied to more complex structures (as detailed in Scheme 6).



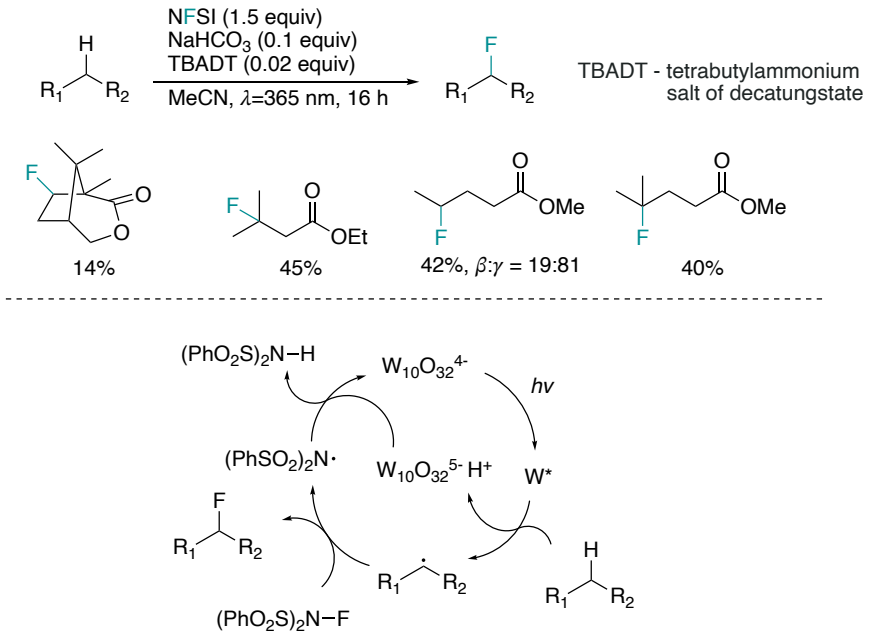

Scheme 6. Photodecarboxylative fluorination with NFSI.

Zhang *et al.* have successfully realised the copper-catalyzed radical aminofluorination of styrenes using NFSI.[44] with high regioselectivity, producing aminofluorination products with regioselectivities opposite to those observed in palladium-catalyzed and noncatalysed processes. This development represents a novel approach to copper-catalyzed regioselective radical aminofluorination reactions between styrenes and NFSI (Scheme 7). Notably, this method marks the first instance of NFSI being used simultaneously as a radical nitrogen and fluorine source, making it an exceptionally valuable reagent for synthetic applications.



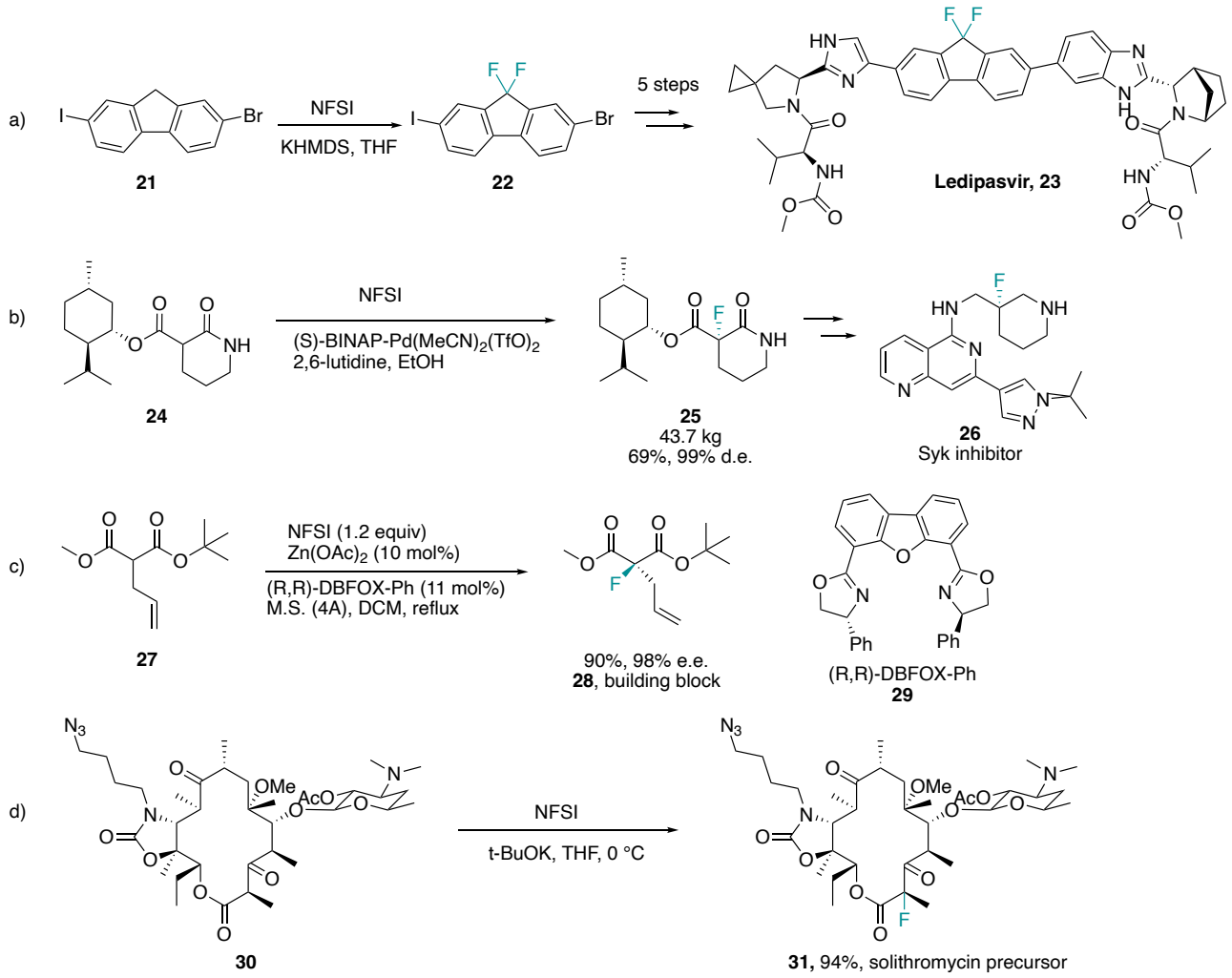

Scheme 7. Aminofluorination of styrenes with NFSI.

The same year, Britton and co-workers made a cost-effective and convenient process for the direct fluorination of unactivated C–H bonds, leveraging the hydrogen abstracting capabilities of a tetrabutylammonium salt of decatungstate photocatalyst in conjunction with the mild fluorine atom transfer reagent, NFSI (Scheme 8).[45] This operationally straightforward reaction facilitates direct access to a wide array of fluorinated organic molecules, encompassing structurally complex natural products, acyl fluorides, and fluorinated amino acid derivatives, but with relatively low yields. By exploiting the hydrogen abstraction capacity of a readily prepared and inexpensive decatungstate photocatalyst alongside the fluorine-transfer agent NFSI, they have developed an efficient method for fluorinating unactivated C($sp^3$)–H bonds.




Scheme 8. Photocatalytic fluorination with NFSI and TBADT.

Despite the non-radical introduction of fluorine atoms, several companies successfully expanded the application of NFSI. In 2014, Gilead Sciences used NFSI to achieve the difluorination of fluorene, leading to the synthesis of ledipasvir (**23**), a therapeutic agent for treating hepatitis C (Scheme 9a).[46]

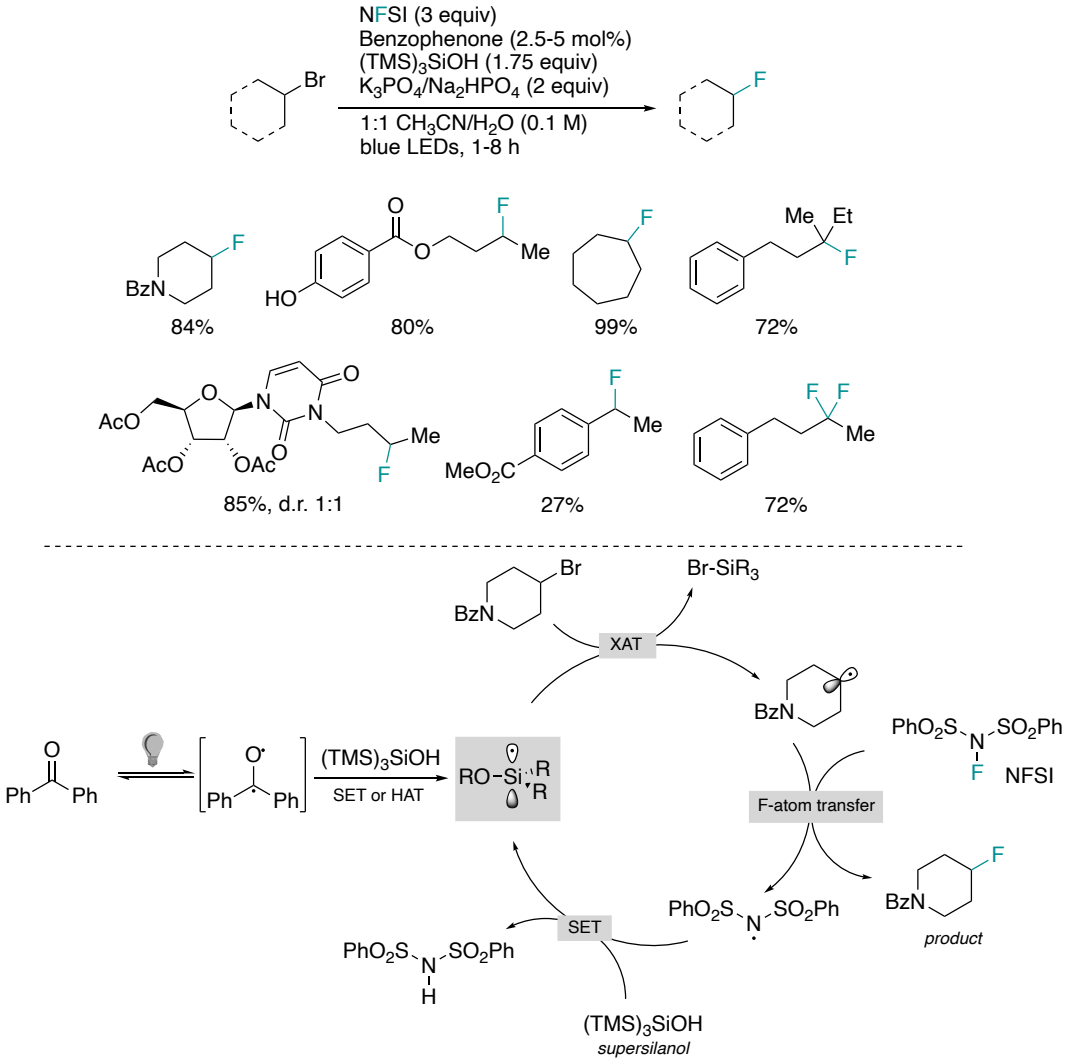



Scheme 9. Synthesis of fluorine-containing pharmaceutically relevant targets using NFSI.

GlaxoSmithKline reported a kilogram-scale enantioselective fluorination in 2015 using NFSI to synthesise a tyrosine kinase (Syk) inhibitor **26**, aimed at preclinical drug development (Scheme 9b).[47] NFSI was also employed in the asymmetric fluorination of prochiral malonate esters. These esters were subsequently used as building blocks for preparing pharmaceutically relevant compounds, including fluorinated β-amino acids, β-lactams, and protease inhibitors (Scheme 9c).[48] Additionally, synthesising the fluorine-containing antibiotic solithromycin involved reacting compound **30** with NFSI to produce the solithromycin precursor **31** (Scheme 9d).[49] These examples highlight the versatility and effectiveness of N–F reagents, particularly NFSI, in facilitating crucial fluorination steps across various therapeutic categories.

MacMillan presented in 2019 a procedure for fluorinating alkyl bromides, combining silyl

radical-mediated halogen-atom abstraction with benzophenone photosensitisation.[50] Despite expectations favouring Si–F bond formation, this technique selectively targets alkyl bromides using an N–F bond electrophilic fluorinating agent (Scheme 10). According to the authors, mechanistic and computational studies confirmed a radical chain mechanism, with Si–Br abstraction preferred due to polar effects and halogen polarizability in the transition state. This metal-free method tolerates various functional groups and has been applied to create gem-difluorinated structures, which are valuable in medicinal chemistry and agriculture.

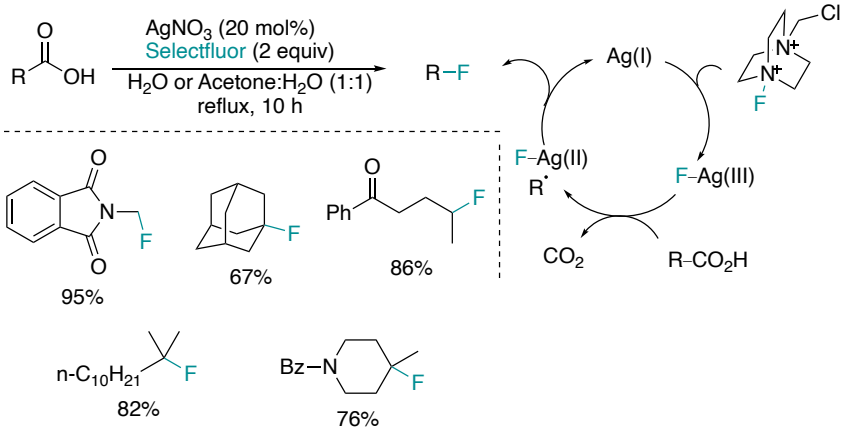



Scheme 10. Silyl-radical-mediated radical fluorination of alkyl bromides with NFSI.

The development of NFSI has been a milestone in advancing fluorination techniques within organic chemistry. NFSI stands out due to its distinct properties, which include high stability, excellent selectivity, and a good safety profile compared to earlier fluorinating agents. Exploring the following primary N-F reagents is a logical progression as the field advances.

## 3.3 Selectfluor®

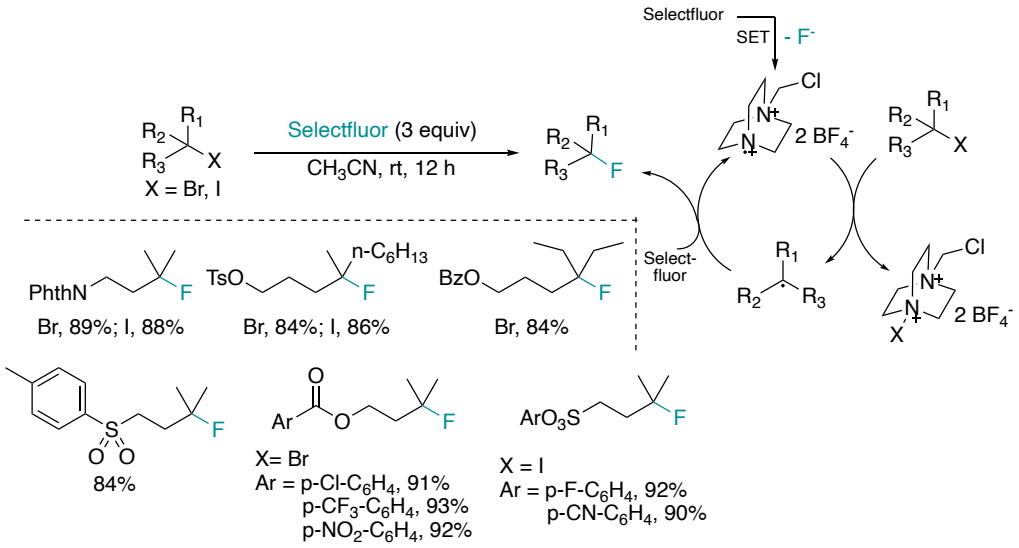
First developed by Banks et al.[34] in 1992, Selectfluor® became the most common reagent for radical fluorination reactions.[51] The fluorodecarboxylation work of Li has pioneered the field of silver-catalysed radical fluorinations with Selectfluor® (Scheme 11).[52] His approach includes using $AgNO_3$ as a catalyst and Selectfluor® in the decarboxylative fluorination of various aliphatic carboxylic acids in an aqueous solution. The proposed mechanism for this reaction involves Ag(III)-mediated single electron transfer (SET) formed by oxidation of Ag(I) with Selectfluor®. Carboxylate anion oxidation with Ag(III)-F species results in CO2 loss and subsequent formation of Ag(II)-F species and alkyl radicals. The latter is trapped by the fluorine atom of Ag(II)-F, affording the product and regenerating the Ag(I) catalyst. Therefore, suggesting silver-catalysed decarboxylative fluorination occurs through SET and fluorine atom transfer in sequence. Following this work, other scholars have investigated the decarboxylative fluorination pathway with this approach.[53–56] The fluorinative deboronation of alkyl pinacol boranes and alkyl boronic acids catalysed by Ag(I) with Selectfluor® was published by Li[57] and Aggarwal[58] in 2014 and 2015, respectfully. Additionally, numerous publications have featured the use of Ag(I) alongside Selectfluor®,[59–67] and it would be too extensive to list them all. Therefore, I will focus on more relevant studies to my research topic.




Scheme 11. Ag(I)-catalysed decarboxylative fluorination of carboxylic acids.

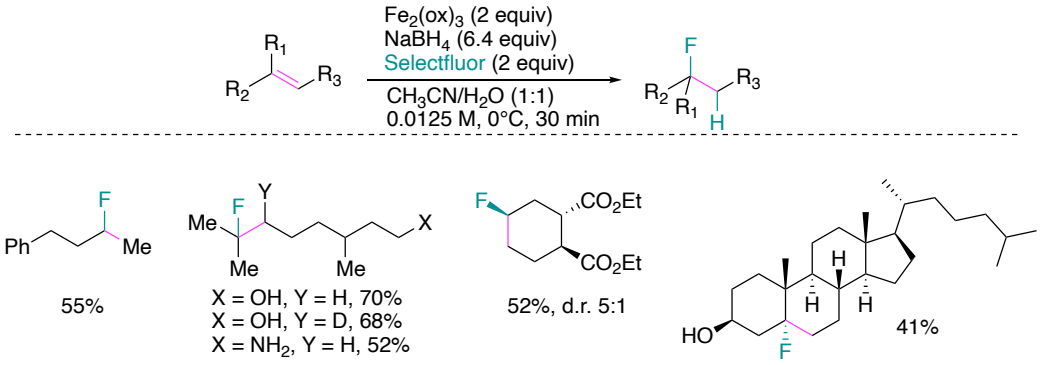
The direct fluorination of tertiary alkyl bromides and iodides using Selectfluor® was described by Li and co-workers as an efficient approach due to the metal-free conditions and the specific reactivity towards tertiary alkyl halides (Scheme 12).[68] The reaction takes place at room temperature in acetonitrile. It tolerates a wide range of functional groups, and the mechanism takes place through homolytic cleavage of the carbon-halogen bond facilitated by the unique

properties of Selectfluor®. The reaction's selectivity is highlighted by its indifference toward alkyl chlorides and primary and secondary alkyl bromides, which remain unaffected under the reaction conditions. This specificity is advantageous because it allows for selective fluorination in complex mixtures without protecting groups. In the reaction, due to the strong electrophilic nature of Selectfluor®, secondary alkyl iodides form unstable alkyl iodine(III) difluorides decompose in water to yield hydroxylation products via carbocationic intermediates.



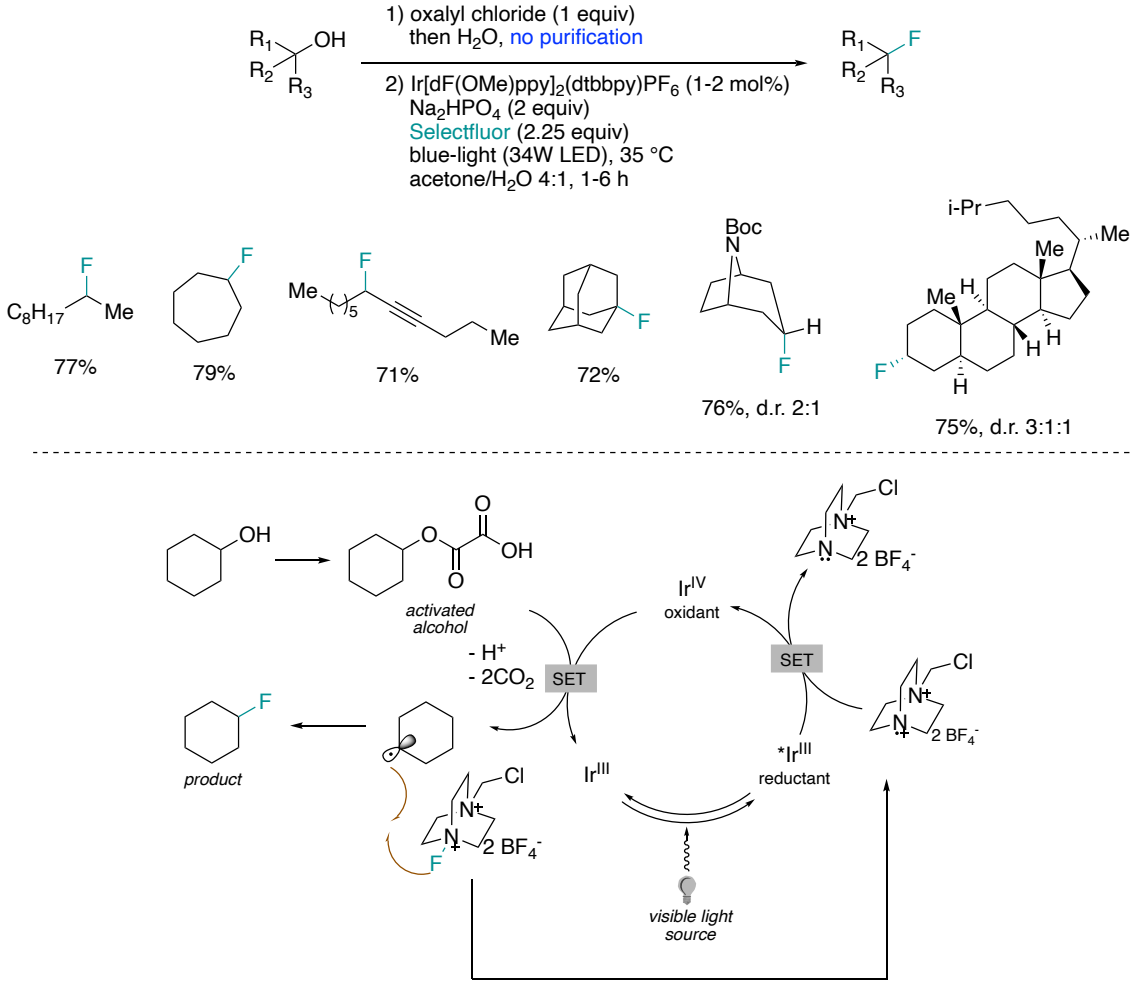

Scheme 12. Fluorination of tertiary alkyl halides.

Boger and Barker developed a potent Fe(III)/$NaBH_4$-mediated free radical hydrofluorination of unactivated alkenes using Selectfluor® as the fluorine source, achieving exclusive Markovnikov addition 2012.[69] Unlike traditional, challenging free radical hydrofluorinations, this Fe(III)/$NaBH_4$-mediated method operates under exceptionally mild conditions (0°C, 5 min, $CH_3CN/H_2O$), as shown in Scheme 13. The reaction is air-tolerant, uses water as a cosolvent, and shows remarkable substrate scope and functional group tolerance.




Scheme 13. Hydrofluorination of unactivated alkenes with Selectfluor®.

MacMillan and co-workers developed a deoxyfluorination of alcohols using an electrophilic fluorine source facilitated by visible-light photoredox catalysis in 2019 (Scheme 14).[70]



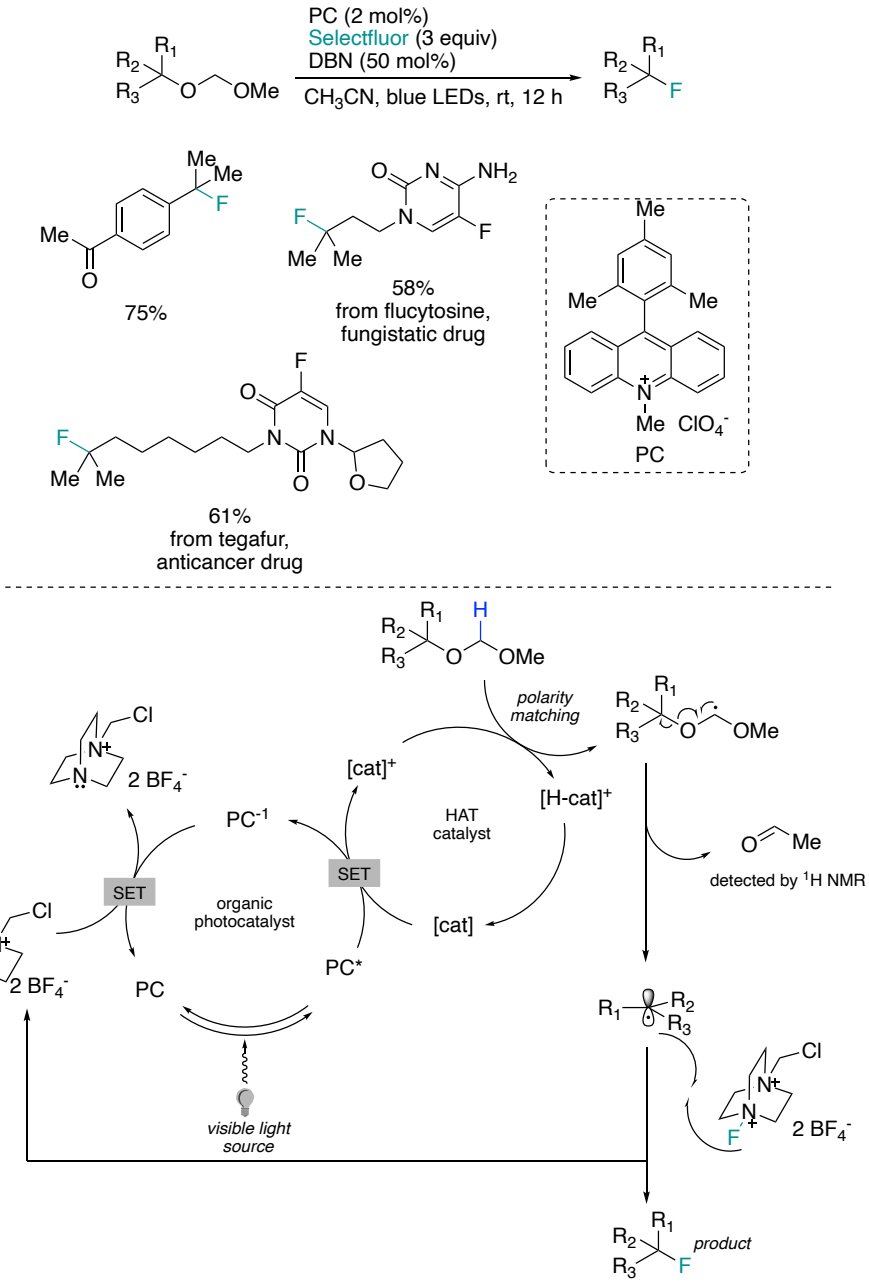

Scheme 14. Photoredox deoxyfluorination of alcohols via their oxalates and mechanism.

This radical-mediated C-F coupling efficiently fluorinates secondary and tertiary alcohols, converting alcohols to their corresponding oxalates in a straightforward, single-step process without the need for purification. This technique complements earlier nucleophilic

deoxyfluorination methods, which are particularly beneficial for tertiary alcohols where an $S_N2$-type mechanism is notably tricky.

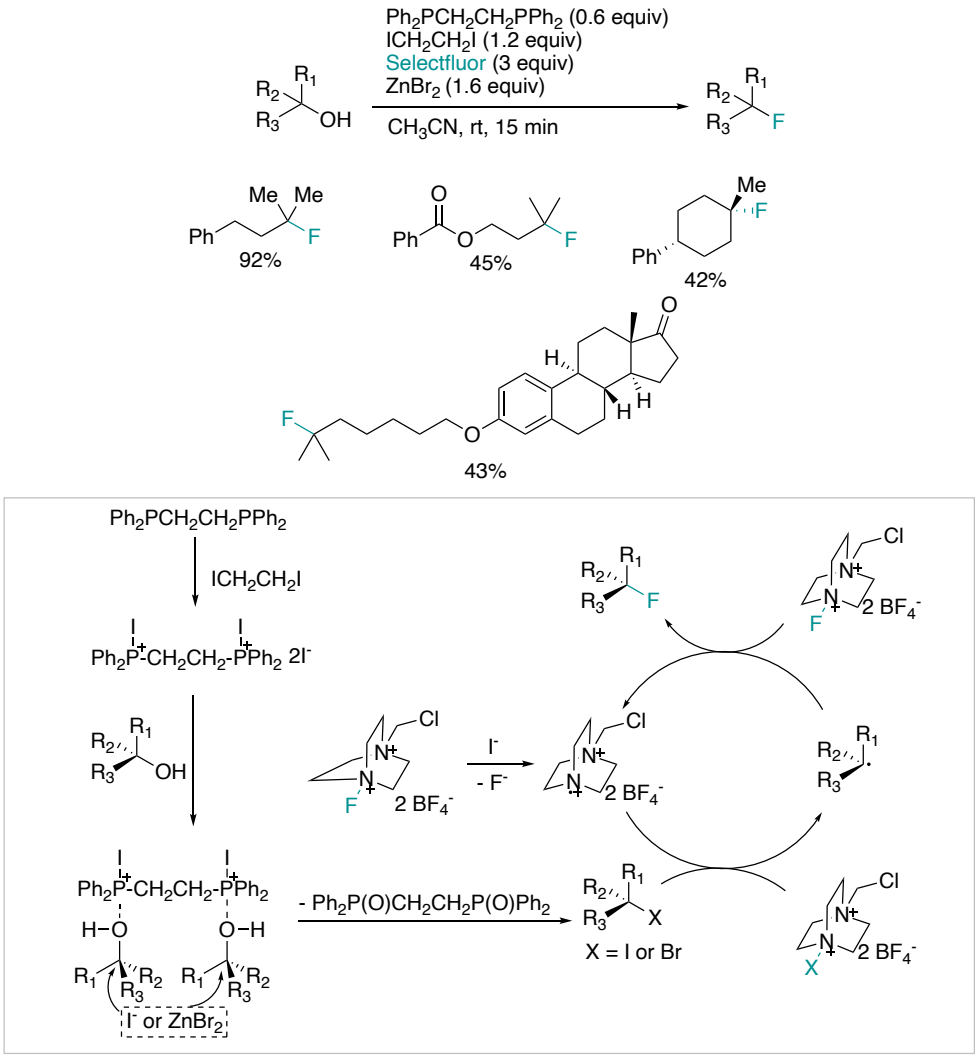
In their studies on deoxygenative fluorination of activated alcohols as caesium oxalates, Brioche and co-workers employ comparable techniques with a notable variation in the choice of catalysts, in one using *fac*-Ir(ppy)$_3$ as a photocatalyst, and in the other $AgNO_3$.[71,72] They mainly focus on the tertiary alcohol deoxyfluorinations in the photoredox catalysed method and broaden the scope with secondary and primary alcohol modifications with the $AgNO_3$ approach. As a complementing radical approach of deoxyfluorination, the group of Gómez-Suàrez suggested a light-mediated catalyst-free methodology.[73] This work also succeeds in the deoxyfluorination of tertiary alcohols, some benzylic and propargylic alcohol derivatives, but with considerably lower yields for the latter two.

Also, a very similar approach but with methoxymethyl (MOM) ethers was presented by Xie et al.[74] This process is facilitated by a synergistic combination of photocatalysis and organocatalysis and achieves exclusive fluorination of tertiary C–O bonds under mild conditions, even when competing reaction sites are present. Under irradiation with the visible-light the photocatalyst (9-mesityl-10-methylacridin-10-ium perchlorate) undergoes SET oxidation of the HAT catalyst 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) to give the radical cation, which goes rapid polarity-matches HAT with the tertiary ether to form the alkoxyl radical (Scheme 15). The latter undergoes subsequent C-O homolysis, generating alkyl radicals trapped by Selectfluor®. Not mentioned before, Selectfluor® also plays an additional role as an oxidant to close the photocatalytic cycle by accepting an electron from the photocatalyst.



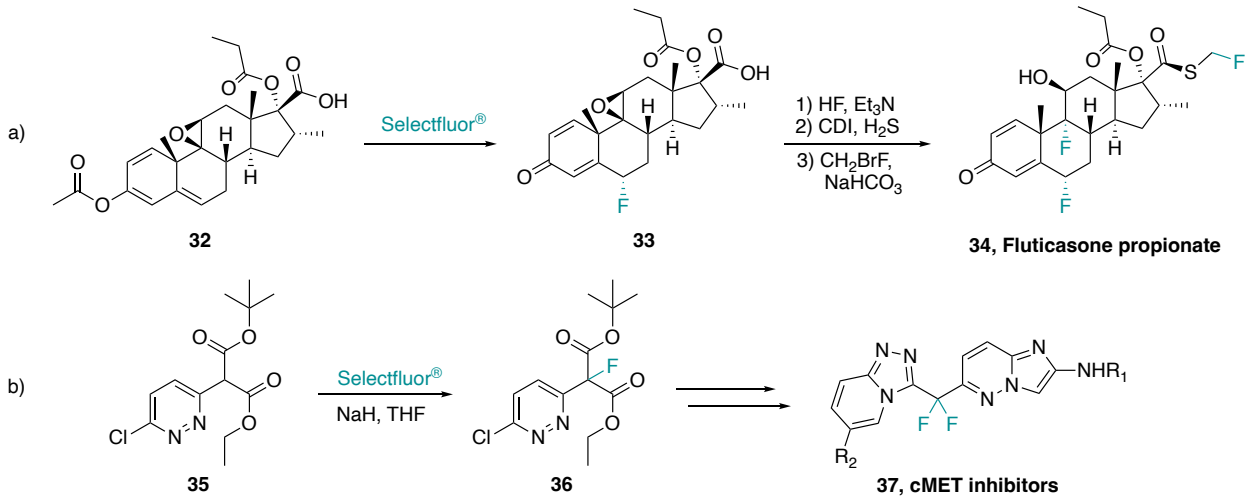

Scheme 15. Photoredox radical fluorination of tertiary ethers and late-stage modification of complex molecules.

Lin and Xiao developed a method for dehydroxylative fluorination of tertiary alcohols using Selectfluor®, activated by a $Ph_2PCH_2CH2PPh_2/ICH_2CH_2I$ system as a one-step procedure (Scheme 16).[75] Despite the apparent incompatibility of the reagents (Selectfluor® with the phosphine and in situ generated I—), the reactions proceed, yielding the desired products in moderate to high yields. The advantage of this approach is that it is fast and utilises readily available alcohols, and the authors claim it can be used in $^{18}F$-labelling processes.




Scheme 16. Dehydroxylative fluorination of tertiary alcohols.

Since its introduction, Selectfluor® has rapidly become a highly popular N–F reagent and is now produced commercially on a multi-ton scale.[76] Approximately 25 tonnes of Selectfluor® are sold annually, generating around $7.5 million in sales.[77] This reagent is extensively utilised across both small-scale laboratory settings and moderate-scale industrial syntheses, and it plays a significant role in medicinal and drug discovery applications. Selectfluor® is thermally stable up to 195 °C[76] and exhibits moderate to high solubility and stability in polar solvents such as water, MeCN, DMF, methanol, and THF. It is also characterised by low toxicity. Notably, 80% of all commercially available fluorosteroids are synthesised industrially using Selectfluor®,[77] which has replaced more corrosive agents like perchloryl fluoride ($ClO_3F$).[6,78]

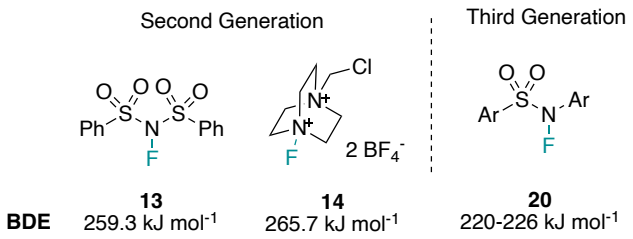



Scheme 17. Dehydroxylative fluorination of tertiary alcohols.

One of the prominent pharmaceutical products derived from this reagent is fluticasone propionate **34** (Scheme 17a), with global sales of therapeutics containing fluticasone propionate reaching approximately $17 billion between 2009 and 2012.[77] A team at Merck employed Selectfluor® to fluorinate the sodium salt of malonate **35** in THF. This step was part of the synthesis process for cMET tyrosine kinase inhibitors used in anti-cancer therapies (Scheme 17b).[79] N–F reagents have been widely utilised for fluorinating several drug targets, as demonstrated in the previous part, and their critical role in pharmaceutical development is shown here.[80]

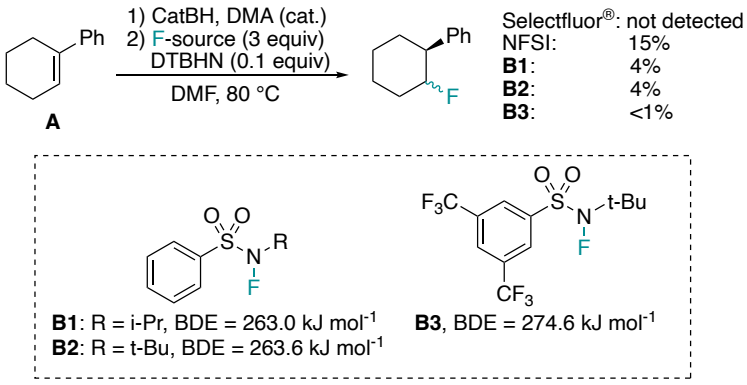
## 3.4 N-Fluoro-N-arylsulfonamides (NFASs)

There was a distinct need for a third generation of reagents capable of operating effectively under mild radical reaction conditions without participating in electrophilic or electron transfer processes.[81,82] In this context, our group introduced N-fluoro-N-arylsulfonamides (NFASs) as a new generation of radical fluorinating agents.[40] The bond dissociation energies of NFASs are 30–45 kJ/mol lower than those of NFSI and Selectfluor®, which promotes smoother radical processes by minimising side reactions typically caused by the electrophilic and oxidant properties of earlier radical fluorinating agents (Scheme 18).




Scheme 18. BDE of N-F bonds in fluorinating agents.

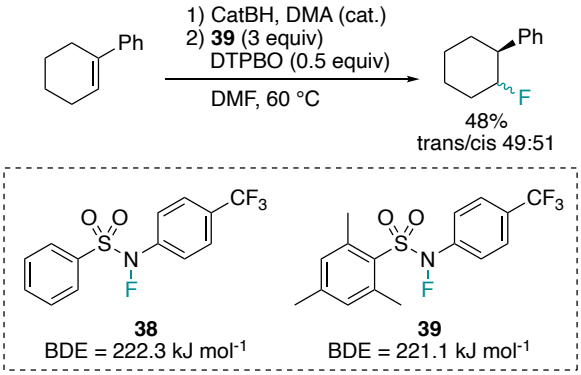
Initial experiments into the hydrofluorination of alkenes began with the hydroboration of 1-phenyl-1-cyclohexene **A** using catecholborane, followed by a reaction with fluorinating agents Selectfluor® and NFSI (as illustrated in Scheme 19). The reaction involving Selectfluor® proved highly exothermic and led to the decomposition of the intermediate B-alkylcatecholborane, with no trace of the desired fluoride product detectable by GC analysis. On the other hand, the reaction with NFSI yielded product, but only at a 15% yield. To minimise undesired side reactions caused by the electrophilicity of the fluorinating agents, tests were conducted with less electrophilic N–F reagents. Benzenesulfonamides (**B1** – **B2**) and benzamide (**B3**) were synthesised by the fluorination of corresponding amides and tested; however, all three N-fluoroamides were inefficient, yielding less than 4%.




Scheme 19. Initial attempts of hydrofluorination via *B*-alkylcatecholboranes.

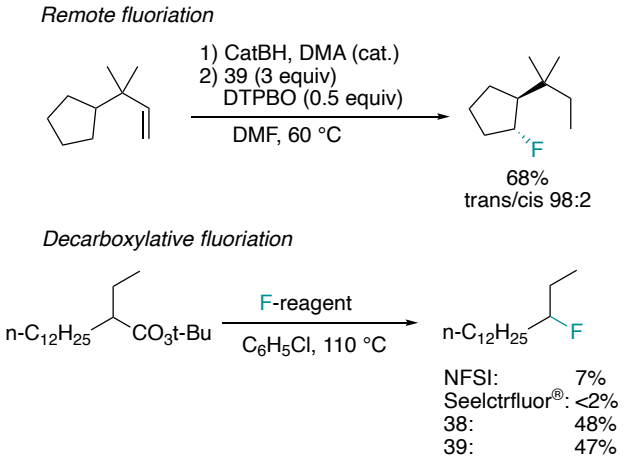
After these disappointing results, the investigation of NFASs was conducted to reduce the N–F BDE while retaining sufficient polar effects to facilitate the fluorination of nucleophilic alkyl radicals. The calculation of BDE of N-F in **38** (222.3 kJ mol$^{-1}$) supported the theory that N-aryl substituents can lower N–F BDEs by stabilising the corresponding amidyl radical via delocalisation onto the aromatic ring. Thus, several NFASs were prepared by fluorination of the amides with $Cs_2CO_3$ and NFSI, and their BDE lay between 220.0 – 226.1 kJ mol$^{-1}$. The prepared NFASs with lower BDE were tested under the reaction conditions, and the best outcome was achieved with **39**, where the desired product was isolated at 48% or 51% of GC

yield (Scheme 20).




Scheme 20. Hydrofluorination of non-terminal alkene with NFASs.

When applied with appropriate substrates, the radical hydrofluorination technique facilitates efficient remote fluorination through a 1,5-hydrogen atom transfer (HAT) mechanism. Additionally, a related method for remote fluorination that employs photoredox-generated iminyl radicals has been recently documented.[53] Also, the decarboxylative fluorination being heavily studied in the field, as was reviewed earlier, was tested under the action of the new fluorinating agent. The results of these reactions are exemplified by the hydrofluorination of terminal alkene, which yields fluoride with a 68% yield and exhibits outstanding trans diastereoselectivity. Decarboxylative fluorination of *t*-Bu peresters yields 48% and 47% of the product with both **38** and **39** NFASs, respectively (Scheme 21); in the latter case, test of other fluorinating reagents such as NFSI and Selectfluor® being insufficient with traces of the product.




Scheme 21. Remote and decarboxylative fluorination of alkenes and *t*-Bu peresters, respectively, with NFASs.

In both the hydrofluorination and decarboxylation processes, NFSI yielded fluorinated products at lower rates than NFASs despite exhibiting a higher rate constant for fluorine atom

transfer. Analysis of the crude reaction mixtures indicated a greater production of alkenes when using NFSI compared to NFASs. The formation of these alkenes could be attributed to three competitive reactions:

1. A single electron transfer (SET) from the fluorinating agent to the secondary alkyl radical leads to cation formation followed by the loss of a proton.
2. An acid-catalyzed HF elimination after fluorination.
3. A radical cross-disproportionation between the alkyl radical and the imidyl radical in NFSI or amidyl radicals in NFASs. The latter is less prompt to undergo hydrogen abstraction due to the stabilisation from the aromatic ring.

NFASs have been successfully employed in a metal-free hydrofluorination method that involves hydroboration with catecholborane, followed by radical deborylative fluorination. Using monoisopinocampheylborane ($IpcBH_2$) for hydroboration facilitates the asymmetric hydrofluorination of trisubstituted alkenes. Additionally, NFASs have proven superior to NFSI in the decarboxylative fluorination of tert-butyl peresters, highlighting their effectiveness across a broad spectrum of radical-mediated fluorination processes. These advancements suggest that NFASs have the potential to significantly transform the field of radical fluorination, enabling more powerful transformations under conditions milder than those required by previous generations of fluorinating agents.

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# Chapter 4

# A Mild Radical Procedure for Deiodofluorination of Secondary and Tertiary Alkyl Iodides and Related Processes

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*This chapter is a Draft manuscript. This reasearch was started by Dr. Daniel Meyer and continued by Dr. Camilo Meléndez, then finished by my part. Their contributions are gratefully acknowledged, and results are included here. Personal contribution comprises expansion of the substrate scope with xanthates: the fluorination of S-alkyl dithionocarbonates – dethioflurorination of tertiary xanthate (**4f**), fluorination alpha to nitrogen (**4s**) and fluorination of mannose derivative (**4l**), which appeared to be challenging, and including the update of the draft and combining and preparing the experimental parts.*

# Chapter 4 – A Mild Radical Procedure for Deiodofluorination of Secondary and Tertiary Alkyl Iodides and Related Processes


## Abstract

Using the recently developed *N*-fluoro-*N*-arylsulfonamides (NFASs) as a third generation of fluorinating reagents, direct fluorination of secondary, tertiary alkyl iodides and *S*-alkyl xanthates was performed. Unlike classical reagents (NFSI, Selectfluor®), NFASs have lower electrophilicity, allowing a mild and selective introduction of the fluorine atom under radical conditions. Carbofluorination reactions with unactivated alkenes under optimised conditions could also be achieved.



## Keywords

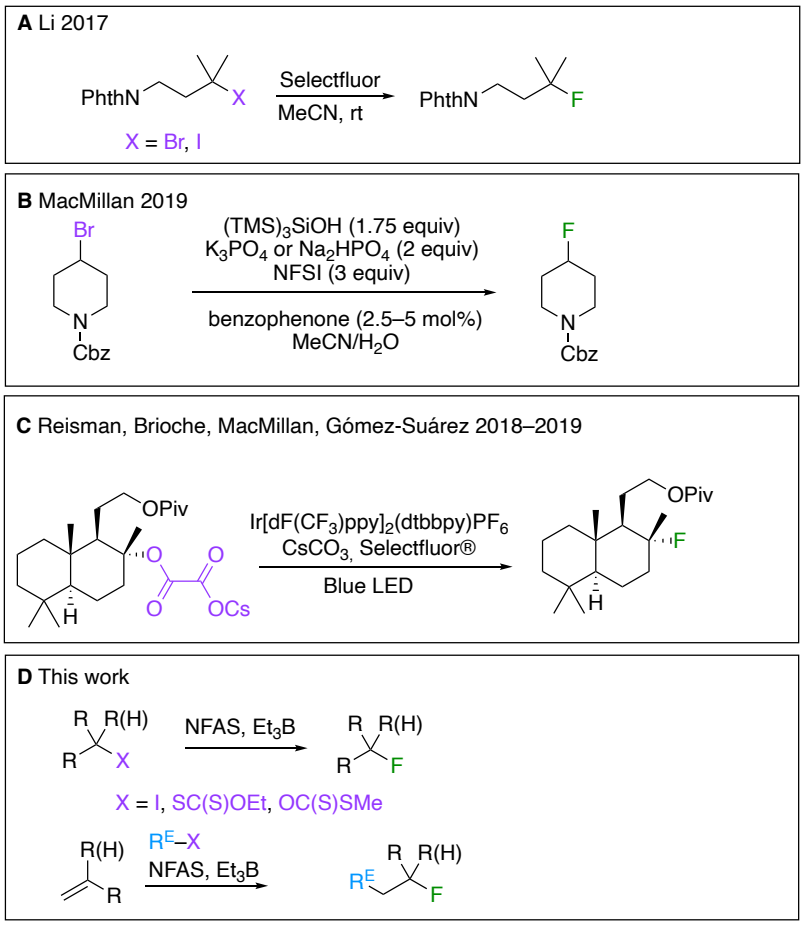
Fluorination, *S*-alkyl xanthates, NFAS, triethylborane, carbofluorination, alkyl iodides


## 4.1 Introduction

The insertion of fluorine atoms into organic molecules is well known to modulate their properties. This includes increased lipophilicity, biological potency, and stability to enzymatic degradation. As a result, fluorinated compounds have found numerous applications in material science, crop protection and drug development.[1–6] $^{18}$F-Labeled molecules are also highly important as contrast agents for positron emission tomography (PET). The growing importance of fluorine-containing compounds has created a strong demand for efficient methods to address their preparation. In this context, besides the direct fluorination of C–H bonds,[7,8] the halogen-exchange fluorination of alkyl halides represents one of the most straightforward methods to insert fluorine in a molecule. Nucleophilic fluorinations of allylic,[9–11] primary, and some secondary halides[12,13] have been successfully developed. Very recently, Gouverneur and coworkers reported such nucleophilic displacement using a mixture of acid-grade fluorspar (>97% $CaF_2$) and dipotassium hydrogen phosphate ($K_2HPO_4$) under mechanochemical conditions as the source of fluoride.[14] One drawback of the aforementioned nucleophilic displacement of halides approach is that most secondary and

tertiary substrates are challenging due to steric hindrance. However, examples of successful halogen-exchange fluorinations to access tertiary fluorides were reported with $Cu_2O$-HF-THF,[15] $HF_x$·Py,[16] silver fluoride,[17,18] fluorine gas,[19] xenon difluoride,[20–22] iodonium fluoride[23] and *p*-iodotoluene[24] difluorides as fluorine sources. These reactions proceed via carbocation intermediates. Besides the classical nucleophilic[25] and electrophilic[26] fluorination processes, radical fluorination is becoming a valuable alternative. Amongst the possible approaches to achieve a C–F bond under radical conditions,[27] the preparation of alkyl fluorides from alkyl halides has remained elusive. *N*-aryl-α-bromoamides have been selectively converted into the corresponding fluorides using a combination of CsF and a copper(II) catalyst.[28] Li and coworkers described the fluorination of alkyl bromides and iodides with 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (Selectfluor®) (Scheme 1, A).[27] This reaction is limited to tertiary alkyl bromides and iodides, and a mechanism involving the Selectfluor® mediated fluorination of a radical intermediate was proposed. Due to the strong electrophilic nature of Selectfluor®, secondary iodides are converted to alkyl iodine(III) difluorides, which decompose during aqueous workup to give the corresponding alcohols. MacMillan reported in 2019 a procedure for the fluorination of unactivated secondary and tertiary alkyl bromides using *N*-fluorobenzenesulfonimide (NFSI) as the source of fluorine atom for the carbon-centred radical generated upon irradiation of the super silanol ($(TMS)_3SiOH$) in the presence of benzophenone as a photosensitiser (Scheme 1, B).[29]

Procedures for the radical deoxyfluorination of alcohols via their oxalate monoesters with Selectfluor® were reported by Reisman, Brioche, MacMillan and Gómez-Suárez (Scheme 1, C),[30–34] and deoxyfluorination via their methoxymethyl ethers (MOM-ethers) was reported by Xie.[35] Lin and Xiao reported the conversion of tertiary alcohols into the corresponding fluorides via in situ transformation into the tertiary iodides or bromides in the presence of the $Ph_2PCH_2CH_2PPh_2$/ $ICH_2CH_2I$ /$ZnBr_2$ system.[36]




Scheme 1. Radical dehalofluorination and related reactions.

Recently, we have reported the use of *N*-fluoro-*N*-arylsulfonamides (NFASs)[37] as a new class of radical fluorinating agents and showed that these proved remarkably efficient in converting alkylbenzo[*d*][1,3,2]dioxaboroles (alkyl-Bcat) into the corresponding fluoroalkanes via a radical chain mechanism. Due to their reduced electrophilicity compared to classical reagents such as NFSI and Selectfluor®, NFASs opened new opportunities for mild and selective introduction of fluorine atoms under radical conditions. Herein, we report that NFASs can be applied to converting alkyl iodides and xanthates into the corresponding fluorides under mild conditions. Additionally, this chemistry could be extended to the carbofluorination of alkenes (Scheme 1, D).[38,39]

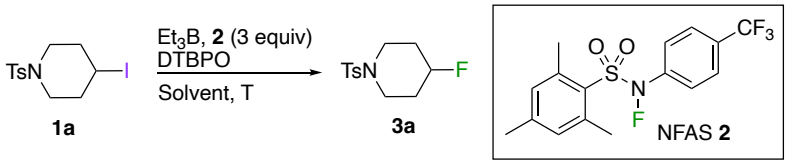
## 4.2 Results and Discussion

### 4.2.1 Deiodofluorination

The *N*-*p*-toluenesulfonyl-4-iodopiperidine **1a** was used as the model substrate to optimise the reaction conditions. All reactions were performed with the *N*-fluoro-2,4,6-trimethyl-*N*-(4-

(trifluoromethyl)phenyl)benzenesulfonamide (NFAS) **2** (3 equiv) and triethylborane (1.1 equiv) was selected as the chain transfer reagent. Initiation with air was attempted first but failed to give reproducible results. Better results were obtained with di-*tert*-butylhyponitrite or di-*tert*-butyl peroxalate (DTBPO) (1 equiv), ultimately preferred for simplicity and economic reasons. Using these unoptimised standard conditions, the influence of the solvent was examined first. Interestingly, very similar results were obtained in benzene, 1,2-dichloroethane, *tert*-butyl methyl ether, ethyl acetate or DMF, the fluorinated piperidine **3a** being obtained in ca. 50% yield (Table 1, entries 1–5). A slightly higher yield was obtained in acetonitrile using 1 equivalent of DTBPO at 60 °C (Table 1, entry 6), and this solvent was adopted for the rest of our study. Decreasing the amount of DTBPO to 0.5 equivalent did not alter the reaction yield (Table 1, entry 7). The slow addition of 1.2 equivalents of triethylborane over 2 hours favoured the formation of the desired fluoride **2a** (Table 1, entry 8, 65%). Using potassium carbonate as a base led to a slight decrease in the yield (Table 1, entry 9). Increasing the quantity of triethylborane to 2.0 equivalents proved detrimental to the reaction (Table 1, entry 10). Notably, the major side product observed in this case was the corresponding deiodinated *N*-*p*-toluenesulfonylpiperidine, mainly produced via a hydrogen atom abstraction process between the secondary alkyl radical and triethylborane.[40,41] Finally, decreasing the amount of DTBPO to 0.3 equivalent also led to a marked decrease in the yield (Table 1, entry 11).

Table 1. Optimisation of the iodine-fluorine exchange reaction.

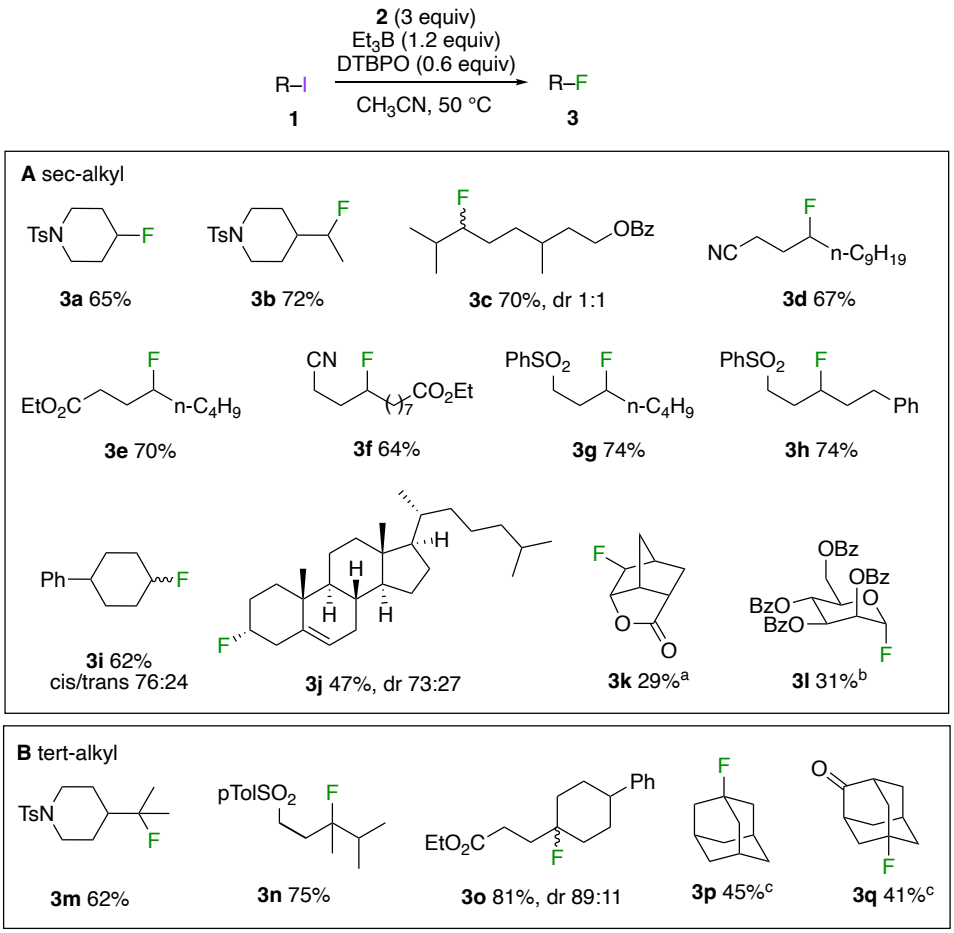



| Entry | $Et_3B$ [equiv] | DTBPO [equiv] | Solvent | T [°C] | Reaction time | **3a** |
|---|---|---|---|---|---|---|
| 1 | 1.1 | 1 | benzene | 60 | 1 | 50% |
| 2 | 1.1 | 1 | DCE | 60 | 1 | 50% |
| 3 | 1.1 | 1 | TBME | 55 | 1 | 47% |
| 4 | 1.2 | 0.6 | EtOAc | 60 | 1 | 52% |

| | | | | | | |
|---|---|---|---|---|---|---|
| 5 | 1.2 | 0.6 | DMF | 60 | 4[a] | 51% |
| 6 | 1.1 | 1 | MeCN | 60 | 1 | 55% |
| 7 | 1.1 | 0.5 | MeCN | 60 | 1 | 54% |
| 8 | 1.2 | 0.6 | MeCN | 50 | 4[a] | 65% |
| 9 | 1.2 | 0.6 | MeCN | 50 | 4[a,b] | 60% |
| 10 | 2 | 0.6 | MeCN | 50 | 4[a] | 50% |
| 11 | 1.2 | 0.3 | MeCN | 50 | 4[a] | 30% |

[a] Syringe pump addition of $Et_3B$ and DTBPO over 2 h followed by a 2 h reaction. [b] $K_2CO_3$ (2 equiv).

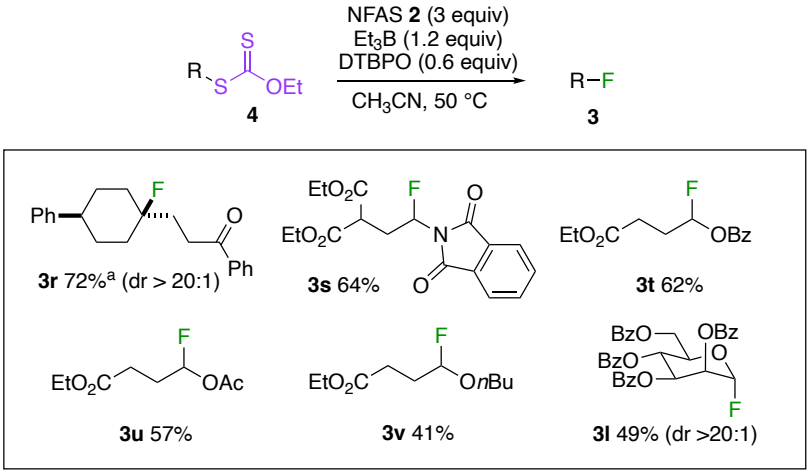
The scope of the fluorine-iodine exchange reaction was examined first on a range of secondary alkyl iodides (Scheme 2, A). Acyclic iodides **1b**–**h** and cyclohexyl iodides **3a** and **3i** were efficiently converted into the corresponding fluorides **3a**–**i** in 62–74% yields. Cholesteryl iodide **1j** was converted to the corresponding fluoride **3j** in 47% yield. A lower yield was obtained for the fluorolactone **1k** (29%), presumably due to a reduced nucleophilicity of the β-oxygenated radical intermediates.[42] Interestingly, the fluorinated mannose derivative **3l** was obtained with a moderate yield from the corresponding bromide. Tertiary iodides (Scheme 2, B) were investigated next. Excellent yields were obtained with acyclic and monocyclic iodides, affording the **3m**–**o** tertiary fluorides in 62–81% yields. Despite their volatility, adamantyl iodides **1p** and **1q** afforded the corresponding fluorides **3p** and **3q** in moderate 45% and 41% isolated yields. As anticipated, an attempt to run the iodine-fluorine exchange process with a primary alkyl iodide gave only traces of the fluoride, presumably due to the inefficiency of the iodine atom transfer process and the lower reactivity of primary radicals towards NFAS reagent **2**.[37]




Scheme 2. Fluorination of alkyl iodides. [a] In DCE with $K_2CO_3$ (2 equiv). [b] Starting from the anomeric bromide. [c] Using 2 equiv of **2** in DCE.

### 4.2.2 Dethiofluorination of S-alkyl O-ethyl dithiocarbonates

The successful conversion of iodides to fluorides using our NFAS reagent prompted us to investigate a similar reaction with *S*-alkyl *O*-ethyl dithiocarbonates. Based on the pioneering work of Zard, this type of xanthates are well-established radical precursors that are equaling, and even surpassing, iodides for many applications.[43–45] Their stability makes them attractive for various synthetic applications. To our delight, tertiary xanthate **4r** afforded the fluoride **3r** in good yield. Fluorination alpha to a nitrogen atom was achieved from xanthate **4s**, delivering fluoride **3s** in 64% yield. Interestingly, the *S*-(1-acyloxyalkyl) xanthates **4t** and **4u** reacted smoothly to afford the α-acyloxy fluorides **3t** and **3u** in 62% and 57% yields, respectively. Similarly, *S*-(1-alkoxyalkyl) xanthates **4v** and **4l** were converted to the α-alkoxy fluorides **3v** and **3l** in moderate yields (Scheme 3).



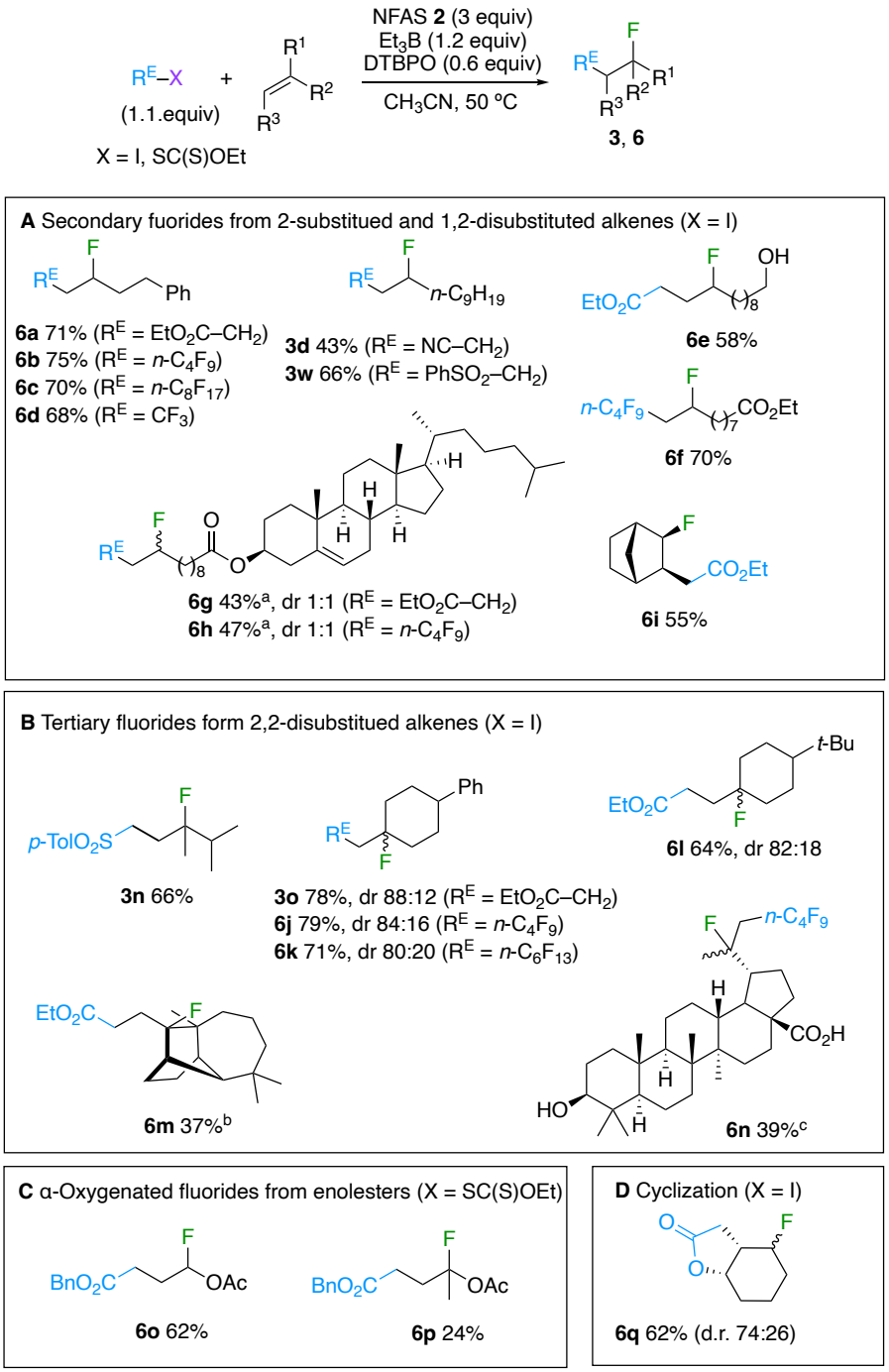

Scheme 3. Fluorination of *S*-alkyl dithionocarbonates **4** (dethioflurorination). [a] characterised as the 2,4-dinitrophenylhydrazone (overall yield for the 2 steps).

### 4.2.3 Carbofluorination of alkenes

Introducing a fluorine atom via a radical mechanism offers the possibility of combining the C–F bond formation with the creation of a new C–C bond. Heinrich reported the carbofluorination of alkenes from arylhydrazines as the source of aryl radicals, with Selectfluor acting as both an oxidant and the radical fluorine source.[46,47] Decarboxylative approaches have been employed to achieve the acyl-fluorination,[48] alkyl-fluorination[49] of styrenes, and the fluoroalkoxycarbonylation of alkenes.[50] The carbofluorination of alkenes has also been achieved using aryl diazonium salts,[51] and the fluorotrifluoromethylation of alkenes has also been reported.[52] Li and coworkers reported a silver-catalyzed radical carbofluorination of unactivated alkenes with acetic acid.[53] The same group also reported an attractive copper(II)-mediated procedure for the carbofluorination of alkenes,[54] as well as the carbofluorination of alkenes with acetone or malonyl derivatives and Selectfluor® in the presence of silver acetate.[55] The cyano-fluorination of easily oxidisable vinyl azides[56] and vinylethers[57] have been reported using TMSCN in the presence of Selectfluor®. In this case, the proposed mechanism involves oxidation of the electron-rich C=C bond by Selectfluor® to give a radical cation, which then abstracts the fluorine atom, followed by the cyanide trapping of the resulting carbocation. Finally, Molander reported the synthesis of α-fluoro-α-amino acids via the carbofluorination of dehydroalanine with alkyltrifluoroborates upon irradiation in the presence of an acridinium catalyst and Selectfluor® as the source of fluorine.[58]

Extension of the deiodofluorination reaction to the carbofluorination of alkenes with NFSA

agent **2** was investigated next (Scheme 4). The reaction was attempted first with terminal monosubstituted alkenes and 1,2-disubstituted alkenes (Scheme 4, A). The use of only a slight excess of the iodide $R^E$–I (1.1 equivalents) as a source of electrophilic radicals $R^E$• was necessary together with an excess of NFAS **2** (3 equivalents) and triethylborane (1.2 equivalents). The reaction of 4-phenylbut-1-ene with ethyl iodoacetate and perfluroroalkyl iodides (including trifluoromethyl iodide) afforded the desired products of carbofluorination **6a**–**d** in 68–75% yield. The reaction was extended to undec-1-ene with iodoacetonitrile and iodomethylphenyl sulfone as radical precursors to produce the corresponding fluoronitrile **3d** and fluorosulfone **3w.** The reaction of alkenes containing non-protected alcohols, esters and internal alkene gave the desired fluorides **6e**–**h** in satisfactory yields (43–70%). The highly reactive norbornene was also a suitable substrate for this transformation, yielding **6i** in 55%. In this case, the reaction initially afforded a mixture of the desired fluorinated compound **6i** and the corresponding iodide arising from the ATRA reaction. Further addition of 0.3 equivalent triethylborane and 10 mol% of DTBPO was required to complete the reaction. Next, the carbofluorination of 2,2-disubstituted alkenes leading to tertiary fluorides was examined (Scheme 4, B). The products **3n**, **3o**, and **6j**–**l** were obtained with simple alkenes in good yields. The more challenging natural products, longifolene and betulinic acids that contain a free hydroxy and a free carboxy group, were carbofluorinated to **6m** and **6n** in acceptable 37% and 39% yields, respectively. The preparation of the secondary and tertiary α-oxygenated fluorides **6o** and **6p** proved feasible using xanthate radical precursors (Scheme 4, C). The modest 24% yield for forming **6p** is still remarkable since they are only accessible via carbofluorination due to the instability of the corresponding tertiary xanthates. Finally, a cyclisation reaction starting from cyclohex-1-en-3-yl iodoacetate afforded the fluorolactone **6q** in 62% yield (Scheme 4, D).



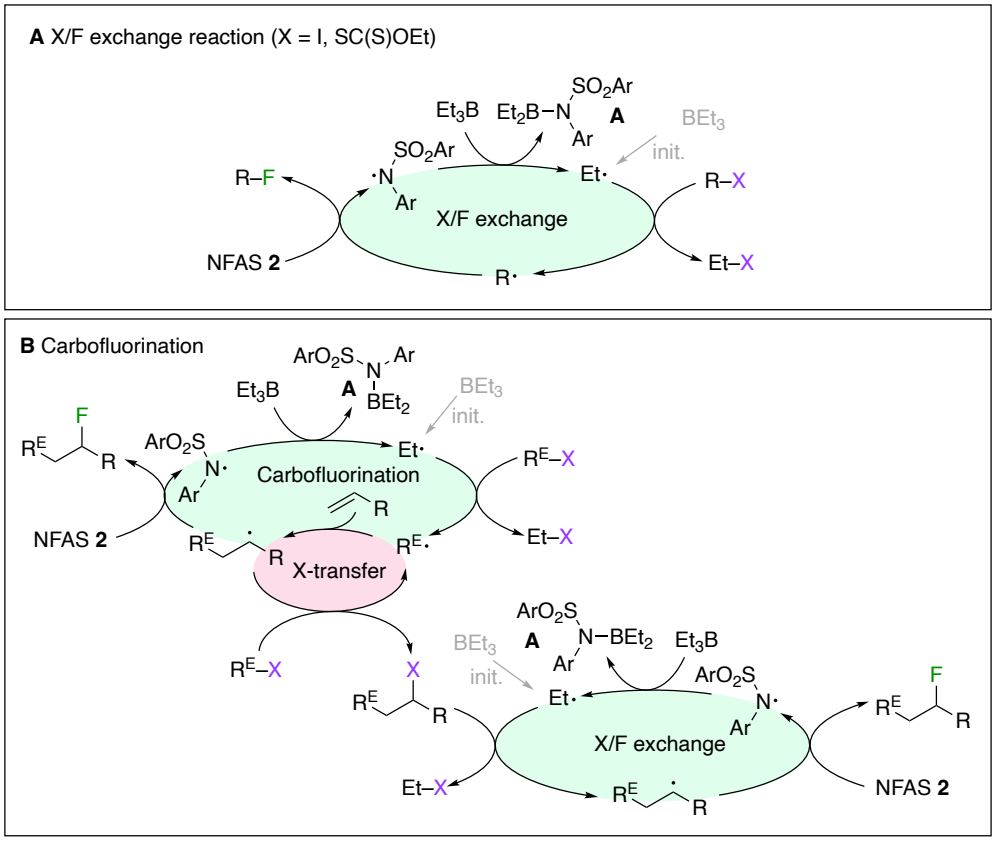

Scheme 4. Carbofluorination of alkenes. [a] A mixture of MeCN/DCE (3:1) was used. [b] Using 2 equiv of **2** in DCE.

[c] DCE/EtOAc/DMF (4:2:1).

## 4.3 Mechanism

The X/F exchange reaction has been designed as a chain process involving triethylborane as a chain transfer agent, according to Scheme 5, A. The fact that 0.6 equivalents of the radical initiator DTBPO are required to reach complete conversion of the iodide indicates that the chain length is probably short. The mechanism of the carbofluorination process is slightly

more complex. The fluorination can follow a direct mechanism where the electrophilic radical $R^E\bullet$ adds to the alkene, and the resulting radical adduct gets fluorinated by NFAS **2** (Scheme 5, B, carbofluorination). This mechanism probably only operates at the end of the reaction when the concentration of the radical precursor $R^E$—X is much lower than that of NFAS **2**. Before reaching this situation, a fast competing X-transfer process (Scheme 5, B, X-transfer) can take place, and the radical adduct can then enter a second fluorination chain transfer process (Scheme 5, B, X/F exchange) identical to the one described in Scheme 5, A. The X-transfer followed by the X/F exchange process is expected to dominate with iodides. Indeed, the rate of iodine atom transfer between alkyl radical and ethyl iodoacetate ($k_{IAT}$ = 2.6 × $10^7$ $M^{-1}$ $s^{-1}$ at 50 °C for a primary alkyl radical) is much larger than the rate of fluorination with NFAS ($k_{FAT}$ ≈ 3 × $10^4$ $M^{-1}$ $s^{-1}$ at 80 °C for a secondary alkyl radical). A similar situation is also probably operating for the *S*-alkyl xanthates.




Scheme 5. Proposed mechanism for the X/F exchange (A) and the carbofluorination (B) reactions.

## 4.4 Conclusion

Using the mild radical fluorinating agent NFAS **2** has allowed the development of an efficient method to convert secondary and tertiary alkyl iodides and *S*-alkyl xanthates into fluorides.

The reaction occurs under mild conditions and is compatible with various functional groups. Finally, a one-pot procedure for the carbofluorination of unactivated alkenes and electron-rich alkenes such as enol esters and enol ethers was developed, taking advantage of the mild, non-oxidative reaction conditions.

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## 4.5 Experimental Section

*In this experimental section only the products made by me are presented.*

### General and instrumentations

The $^{13}C$ and $^{1}H$ NMR spectra were recorded on a Bruker Avance 300 ($^{1}H$: 300.18 MHz, $^{13}C$: 75.48 MHz). Some $^{1}H$ and $^{13}C$ NMR were recorded on a Bruker Avance II 400 spectrometer ($^{1}H$: 400.13 MHz, $^{13}C$: 101 MHz). Chemical shifts are reported in units of δ (ppm). For $^{1}H$ NMR spectra, the internal standard, tetramethylsilane (TMS), was set to δ = 0.000 ppm or the residual protonated solvents were used to reference the spectra ($CHCl_3$ δ = 7.262 ppm; $CH_2Cl_2$ δ = 5.320 ppm). For $^{13}C$ NMR spectra, the internal standard, tetramethylsilane (TMS), was set to δ = 0.00 ppm or the deuterated solvents were used to reference the spectra ($CDCl_3$ δ = 77.16 ppm; $CD_2Cl_2$ δ = 53.84). $^{13}C$ NMR spectra were run using a proton-decoupled pulse sequence. Due to coupling to the $^{19}F$ nucleus (spin = 1/2), the carbons with fluorine atoms attached to them have multiplet signals in $^{13}C$ NMR and mostly cannot be interpreted or assigned. The following abbreviations were used to describe the multiplicities: s (singlet), d (doublet), t (triplet), q (quadruplet), quin (quintet), sept (septet), m (multiplet), br (broad). Coupling constants (J) are reported in Hertz (Hz) with an accuracy of one unit of the last digit. The number of carbon atoms for each signal is indicated only when superior to one, and when two signals are very close, they are reported with two decimal places. HRMS analyses were recorded on an Applied Biosystems Sciex QSTAR Pulsar (hybrid quadrupole time-of-flight mass spectrometer) using positive electron spray. Infrared spectra were recorded neat equipped with a diamond ATR System and are reported in wave numbers ($cm^{-1}$). Reported are the first six signals (with decreasing wave number) and characteristic functional groups. The following abbreviations were used to explain the intensities: w (weak), m (medium), s (strong), and br (broad), e.g. for OH peaks. Only the stretching frequency of the characteristic functional group was reported, and when the compound did not contain one, the most relevant frequencies were listed. For flash chromatography (FC), silica gel 40-63 µm (230-400 mesh) and aluminium oxide CAMAG 5016-A-I basic (40-300 µm) were used. Thin layer chromatography (TLC) was performed using Silicycle glass-backed TLC extra hard layer, 259 µm, 60 Å, F-254 analytical plates; visualisation under UV (254 nm and/or 366 nm) or/and by staining with a solution of potassium permanganate ($KMnO_4$); phosphomolybdic acid ($H_3PMo_{12}O_{40}$) and cerium sulfate ($Ce(SO_4)_2$), and subsequent heating.

Unless otherwise stated, all yields are isolated yields. Ambient (or room) temperatures were generally in the 21–25 °C range. All reactions were run under an argon atmosphere, and solids were added quickly or under a blanket of flowing argon unless otherwise specified. All glassware was oven-dried overnight at 140 °C, assembled hot, and cooled under a stream of dry argon gas or flame-dried under vacuum.

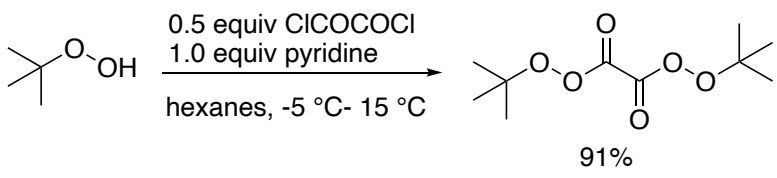
Solvents for reactions: a) distilled acetonitrile ($CH_3CN$) was filtered through dried alumina columns under a positive argon pressure. b) DCE was obtained from commercial sources and used without prior distillation: It was filtered through a pad of basic AlOx, collected with molecular sieves and allowed to stand over 24 hours. c) In some cases, DMF (0.3-1 mL, dry - Sigma Aldrich) was added to the reaction mixture to ensure complete solubilisation of the fluorinating agents. Solvents for extractions and flash column chromatography were of technical grade and were distilled before use, as in the case of DCM. Commercial triethylborane (neat) was used as a solution in benzene (1.15 M, considering additive volumes).

## Reagents and starting materials

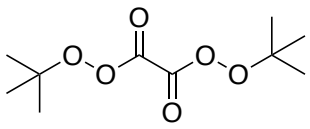
### Preparation of Triethylborane Solution

To an appropriate volume of dry and degassed (freeze-thaw method) benzene triethylborane (neat, argon atmosphere) was added via syringe while keeping the tip of the needle underneath the solvent. To prepare the 30.0 mL, 1.15 M solution of $Et_3B$, 5.0 mL of neat $Et_3B$ was added to 25.0 mL of benzene. Analysis by NMR suggested that the concentration does not fluctuate considerably over a period of 1-25 days (solution kept in a desiccator under an argon atmosphere).

### Di-tert-butyl peroxyoxalate (DTBPO)[1]



*DTBPO is sensitive to heat and shock and, therefore, a potent explosive. This compound should only be handled with extreme care and appropriate safety precautions (small scale, avoid scratching, use of a blast shield and cut protection gloves).*



$C_{10}H_{18}O_6$
MW: 234,25

A solution of freshly opened oxalyl chloride (0.86 mL, 10.0 mmol) in dry hexane (10 mL) was added to a stirred solution of pyridine (1.61 mL, 20.0 mmol) and tert-butyl hydroperoxide (3.64 mL, 5.5 mol/L in decane, 20.0 mmol) in dry hexane (20 mL) at −5 °C. The mixture was allowed to warm up to 15 °C, filtered and washed with pentane. The filtrate was cooled to −78 °C, and the liquid was removed with a syringe. The solid residue was diluted with pentane (20 mL), cooled to −78 °C, and then the liquid was removed with a syringe. This process was repeated twice. The residue was crystallised from pentane at −25 °C overnight. The liquid was removed with a needle, and the crystals were dried under a high vacuum at 0 C, which afforded di-tert-butyl peroxyoxalate as colourless crystals (2.14 g, 91%). Storage: portions of ca. 500 mg in glass vials can be stored in freezer at −20 °C. $^{1}$H-NMR (300 MHz, $CDCl_3$): δ 1.38 (s, 18H); $^{13}$C-NMR (75 MHz, $CDCl_3$): δ 154.3 (very weak signal), 85.9, 26.1.

## Preparation of the fluorinating agent (N-fluoro-2,4,6-trimethyl-N-(4-(trifluoromethyl)phenyl)benzenesulfonamide) **2**

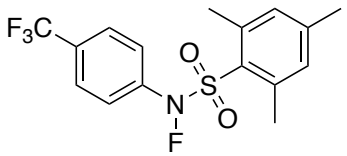
### *First stage*

4-(trifluoromethyl)aniline (60 mmol) was added to a mixture of pyridine (2 equiv) in DCM (0.3 M) and cooled down to 0 °C. Then, mesitylene sulfonyl chloride (1 equiv) in dry DCM was added, and the mixture was stirred at room temperature overnight. The crude mixture was diluted with a 1M HCl solution the next day and extracted with a diethyl ether/pentane (2:1) mixture. The organic layers were washed with 1M HCl solution twice, washed three times with water, dried over $Na_2SO_4$, and concentrated. The resulting solid was purified by recrystallisation from hot heptane, yielding the desired 2,4,6-trimethyl-N-(4-(trifluoromethyl)phenyl)benzenesulfonamide.

### *Second Stage*

The sulfonamide obtained from the first stage (60 mmol) was dissolved in Dry DCM (0.3 mmol). $Cs_2CO_3$ (1.3 equiv) was then added, stirring the resulting mixture at room

temperature for 60 min. NFSI (1.3 equiv) was added, and the mixture was stirred at room temperature for an additional 3h. The crude mixture was diluted with pentane, and the solid residue was filtered off. Afterwards, the volatiles were removed under reduced pressure to yield the crude product. Using a sonication bath, the latter solid was triturated with a hot mixture of Pentane/diethyl ether (1.5:1). After standing in a freezer (c.a -9 ºC) for 1 hour, the so-formed solid was separated by filtration, and the procedure was repeated twice. After this, the resulting solid was recrystallised from hot heptane. The solvent was removed under reduced pressure to yield the desired fluorinating reagent as white crystals (Further dried in vacuo for 5 hours before use).

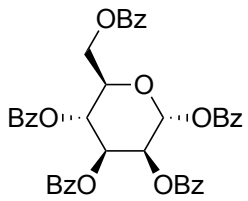


$C_{16}H_{15}F_4NO_2S$
MW: 361,35

$^1$H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.3 Hz, 2H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.05 (s, 2H), 2.64 (s, 6H), 2.36 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 145.4 ($C_{Ar}$-$CH_3$), 142.8 ($2C_{Ar}$-$CH_3$), 141.7 (d, *J* = 9.3 Hz, ($C_{Ar}$-NF), 132.34 (2*C*H), 132.34 ($C_{Ar}$-$CF_3$), 131.4 (dq, *J* = 32.9, 1.8 Hz, *C*$F_3$), 127.5, 125.9 (dt, *J* = 5.0, 3.4 Hz, $2C_{Ar}$-($CCF_3$)), 124.1 (d, *J* = 10.2 Hz, $2C_{Ar}$-CNF), 23.1 ($2CH_3$), 21.2 ($CH_3$). $^{19}$F NMR (376 MHz, $CDCl_3$) δ 36.3 (s), 62.7 (s). HRMS (ESI): calculated for $[C_{16}H_{15}O_2NF_4NaS]^+$: 384.0652, found: 384.0641. IR (neat): 1598, 1352, 1321, 1194, 1167, 1132, 1106, 1063, 1038, 1016.

## Preparation of xanthates

### (2R,3S,4S,5R,6R)-6-((benzoyloxy)methyl)tetrahydro-2H-pyran-2,3,4,5-tetrayl tetrabenzoate



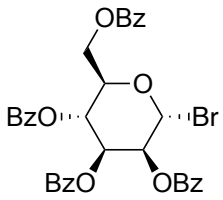
$C_{41}H_{32}O_{11}$
MW: 700,70

The experimental procedure and spectroscopic characterisations correspond with the literature.[2]

$^1$H NMR (300 MHz, $CDCl_3$) δ 8.25 – 8.16 (m, 2H), 8.14 – 8.04 (m, 4H), 8.01 – 7.92 (m, 2H), 7.91 – 7.82 (m, 2H), 7.73 – 7.26 (m, 15H), 6.63 (d, *J* = 2.0 Hz, 1H), 6.29 (t, *J* = 10.1 Hz, 1H), 6.07 (dd, *J* = 10.3, 3.3 Hz, 1H), 5.95 – 5.88 (m, 1H), 4.70 (dd, *J* = 12.1, 2.4 Hz, 1H), 4.54 (ddd, *J* = 21.7, 12.8, 3.5 Hz, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 166.2, 165.8, 165.4, 165.2, 163.9 (each C=O), 134.2, 133.8, 133.7, 133.5, 133.2, 130.3, 130.1, 129.97, 129.93, 129.93, 129.1, 128.97, 128.97, 128.95, 128.86, 128.8, 128.6, 128.58, 128.58, 128.55 (Ar-C and CH), 91.5, 71.3, 70.1, 69.5, 66.3, 62.5.

(2R,3R,4S,5S,6R)-2-((benzoyloxy)methyl)-6-bromotetrahydro-2H-pyran-3,4,5-triyl tribenzoate **1l**

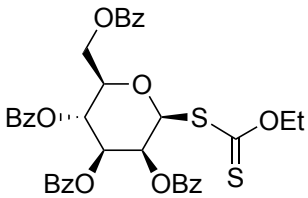
The experimental procedure and spectroscopic characterisations correspond with the literature.[2]




$C_{34}H_{27}BrO_9$
MW: 659,49

$^1$H NMR (300 MHz, $CDCl_3$) δ 8.11 (m, 2H), 8.01 (m, 4H), 7.89 – 7.80 (m, 2H), 7.65 – 7.49 (m, 3H), 7.49 – 7.34 (m, 7H), 7.29 (m, 2H), 6.59 (d, *J* = 1.7 Hz, 1H), 6.35 – 6.18 (m, 2H), 5.91 (dd, *J* = 2.8, 1.7 Hz, 1H), 4.75 (dd, *J* = 12.4, 2.4 Hz, 1H), 4.70 – 4.61 (m, 1H), 4.51 (dd, *J* = 12.4, 3.7 Hz, 1H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 166,1, 165,5, 165.4, 165,1, 133.9, 133.8, 133.5, 133.3, 130.04, 130.04, 129.95, 129.93, 128.93, 128.87, 128.85, 128,81, 128.69, 128.65, 128.65, 128.5, 83.4, 73.2, 73.1, 69.2, 66.0, 61.9.

(2R,3R,4S,5S)-2-((benzoyloxy)methyl)-6-((ethoxycarbonothioyl)thio)tetrahydro-2H-pyran-3,4,5-triyl tribenzoate **4l**

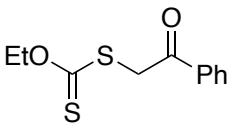



$C_{37}H_{32}O_{10}S_2$
MW: 700,77

A flame-dried two-neck 250 mL flask was charged with (3,4,5-tribenzoyloxy-6-bromo-tetrahydropyran-2-yl)methyl benzoate (5.12 g, 7.77 mmol) and dissolved in acetonitrile (39 mL) at rt. Then potassium ethyl xanthogenate (1.93 g, 11.7 mmol) was added. The resulting solution was stirred overnight at rt. The completion was monitored with TLC (heptane/EtOAc 8:2, $KMnO_4$, CAM, UV active). On the next day, water was added and extracted with $CH_2Cl_2$ and dried under $Na_2SO_4$ (no brine wash, separates very hardly forming emulsion), filtered and concentrated. The resulting crude was submitted to FC, and a gradual increase of polarity helped to have better purification (pentane/$Et_2O$ 75:25 to 100% $Et_2O$) to yield the product as a white solid **4l** (2.5 g, 3.2 mmol, 41%). $R_f$ = 0.31. M. p. = 78.1 – 80 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ 8.13 – 8.08 (m, 2H), 8.07 – 8.02 (m, 2H), 7.94 – 7.91 (m, 2H), 7.83 – 7.79 (m, 2H), 7.66 – 7.54 (m, 2H), 7.53 – 7.48 (m, 1H), 7.47 – 7.39 (m, 6H), 7.38 – 7.33 (m, 2H), 7.30 – 7.24 (m, 3H), 6.15 (dd, J = 3.3, 1.1 Hz, 1H), 6.04 (d, J = 1.2 Hz, 1H), 6.03 (t, J = 10.1 Hz, 1H), 5.76 (dd, J = 10.1, 3.4 Hz, 1H), 4.71 (dd, J = 12.2, 2.6 Hz, 1H), 4.65 (qd, J = 7.1, 4.6 Hz, 2H), 4.52 (dd, J = 12.3, 5.0 Hz, 1H), 4.32 (ddd, J = 10.0, 5.0, 2.7 Hz, 1H), 1.39 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 209.74, 166.11, 165.57, 165.26, 165.07, 133.61, 133.53, 133.32, 133.06, 130.03, 129.82, 129.80, 129.78, 128.92, 128.77, 128.73, 128.61,

128.46, 128.43, 128.37, 128.31, 85.32, 77.21, 72.73, 70.94, 70.86, 66.32, 63.03, 13.67. IR (ν, $cm^{-1}$): 3063 (w), 2978 (w), 1720 (str.), 1256 (str.). HRMS (ESI): calculated for $[C_{37}H_{32}O_{10}NaS_2]^+$: 723.1329, found: 723.1322.

### (4-Methylenecyclohexyl)benzene

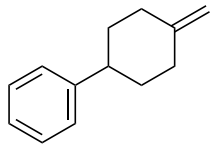



$C_{11}H_{12}O_2S_2$
MW: 240,34

The experimental procedure and spectroscopic characterisations correspond with the literature.[5]

$^1$H NMR (300 MHz, $CD_2Cl_2$): *δ* 7.36–7.19 (m, 5H), 4.68 (t, *J* = 1.7 Hz, 2H), 2.69 (tt, *J* = 12.2, 3.4 Hz, 1H), 2.50–2.43 (m, 2H), 2.29–2.16 (m, 2H), 2.07–1.99 (m, 2H), 1.54 (qd, *J* = 12.5, 3.8 Hz, 2H). $^{13}$C NMR (75 MHz, $CD_2Cl_2$): *δ* 149.4, 147.5, 128.7, 127.2, 126.3, 107.4, 44.5, 36.0, 35.5.

### O-ethyl S-(2-oxo-2-phenylethyl) carbonodithioate



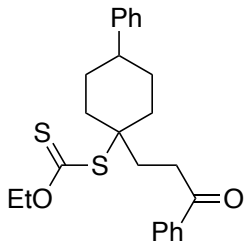
$C_{13}H_{16}$
MW: 172,27

The experimental procedure and spectroscopic characterisations correspond with the literature.[6]

$^1$H NMR (300 MHz, $CDCl_3$) δ 8.07 – 7.99 (m, 2H), 7.67 – 7.57 (m, 1H), 7.55 – 7.46 (m, 2H), 4.70 – 4.58 (m, 4H), 1.39 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 213.4, 192.4, 135.9, 133.8, 128.9, 128.6, 70.8, 43.7, 13.8.

### O-ethyl S-(1-(3-oxo-3-phenylpropyl)-4-phenylcyclohexyl) carbonodithioate **4r**

The experimental procedure and spectroscopic characterisations correspond with the literature.[6]

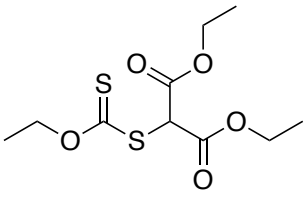



$C_{24}H_{28}O_2S_2$
MW: 412,61

$^1$H NMR (300 MHz, $CDCl_3$) δ 8.02 – 7.94 (m, 2H), 7.62 – 7.53 (m, 1H), 7.53 – 7.43 (m, 2H), 7.35 – 7.16 (m, 5H), 4.65 (q, *J* = 7.1 Hz, 2H), 3.27 – 3.16 (m, 2H), 2.53 (tt, *J* = 12.2, 3.8 Hz, 1H), 2.45 – 2.32 (m, 4H), 2.07 – 1.86 (m, 2H), 1.78 (dd, *J* = 14.1, 3.6 Hz, 2H), 1.65 – 1.48 (m, 3H), 1.41 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 213.16, 199.94, 146.50, 136.90, 133.28, 128.77, 128.55, 128.25, 127.00, 126.35, 69.89, 59.94, 44.23, 36.56, 35.98, 34.08, 29.79, 13.80.

### Diethyl 2-ethoxycarbothioylsulfanylpropanedioate

The experimental procedure and spectroscopic characterisations correspond with the literature.[3]

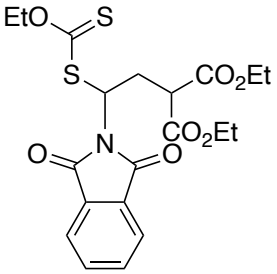


$C_{10}H_{16}O_5S_2$
MW: 280,4

$^1$H NMR (400 MHz, $CDCl_3$) δ 5.27 (s, 1H), 4.63 (q, *J* = 7.1 Hz, 2H), 4.25 (q, *J* = 7.1 Hz, 4H), 1.41 (t, *J* = 7.1 Hz, 3H), 1.28 (t, *J* = 7.2 Hz, 6H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 210.31 (C=S), 165.25 (C=O), 71.10, 62.95, 56.46, 14.07, 13.73.

### Diethyl 2-(2-(1,3-dioxoisoindolin-2-yl)-2-((ethoxycarbonothioyl)thio)ethyl)malonate **4s**

The experimental procedure and spectroscopic characterisations correspond with the literature.[4]



$C_{20}H_{23}NO_7S_2$
MW: 453,52

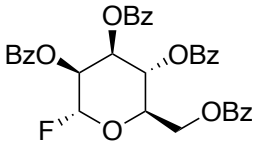
$^1$H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.74 (dd, *J* = 5.5, 3.1 Hz, 2H), 6.37 (dd, *J* = 9.3, 6.8 Hz, 1H), 4.62 (q, *J* = 7.1 Hz, 2H), 4.21 (qd, *J* = 7.1, 1.8 Hz, 2H), 4.16 – 3.99 (m, 2H), 3.43 (t, *J* = 7.3 Hz, 1H), 2.94 – 2.72 (m, 2H), 1.40 (t, *J* = 7.1 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.20 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 210.1 (C=S), 168.0, 167.8 (C=O ester), 166.50, 166,50 (C=O amide), 134.4, 131.5, 123.6 (Ar-C and CH), 70.5 (α-N-CH), 61.9, 61.8, 55.6, 49.5 (CH), 32.1, 13.97, 13.90, 13.6.

## General procedures

### General Procedure (Fluorination of Alkyl Xanthates)

The corresponding alkyl xanthate (0.5 mmol) and **2** (0.542 g, 1.5 mmol) were dissolved in dry acetonitrile (2 mL, 0.2 M). The mixture can be briefly sonicated to ensure complete solubilisation of the fluorinating agent. Then, the $BEt_3$ solution (0.522 mL, 0.6 mmol, 1.15 M in benzene,) and solid DTBPO (70.3 mg, 0.3 mmol) were added, and the resulting mixture was stirred for 1.5 h at 50 °C. The reaction mixture passed through AlOx, then concentrated, and the crude was purified by FC (pentane/$Et_2O$ or heptanes/EtOAc).

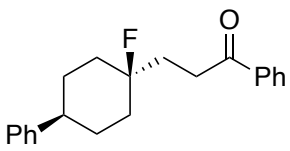
(3,4,5-tribenzoyloxy-6-fluoro-tetrahydropyran-2-yl)methyl benzoate **3l**




$C_{34}H_{27}FO_9$
MW: 598,58

According to General Procedure (3,4,5-tribenzoyloxy-6-ethoxycarbothioylsulfanyl-tetrahydropyran-2-yl)methyl benzoate (350 mg, 0.5 mmol) was dissolved in acetonitrile (1 mL), and DTBPO (70.3 mg, 0.3 mmol, dissolved in 1 mL of acetonitrile). TLC (heptane/EtOAc 8:2, CAM, KMnO4, UV active). The crude was submitted to high-resolution Au column - Combi Flash FC (heptane/EtOAc 97.5:2.5– 95:5 – 92.5:7.5 – 90:10 – 87.5:12.5 – 85:15 – 80:20 to 100% EtOAc) to yield the product as a white crystalline solid (146 mg, 0.253 mmol, 49%). $R_f$ = 0.31. M. p. = 59.3 – 60.7 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ 8.17 – 8.10 (m, 2H), 8.07 – 8.01 (m, 2H), 7.99 – 7.93 (m, 2H), 7.88 – 7.81 (m, 2H), 7.65 – 7.56 (m, 2H), 7.55 – 7.49 (m, 1H), 7.48 – 7.35 (m, 7H), 7.31 – 7.25 (m, 2H), 6.22 (t, J = 10.2 Hz, 1H), 5.97 – 5.79 (m, 3H) {5.87 (dd, J = 48.2, 1.8 Hz, 1H); 5.87 (dd, J = 3.3, 2.0 Hz, 1H); 5.93 (ddd, J = 10.3, 3.4, 1.8 Hz, 1H)}, 4.78 (dd, J = 12.4, 2.4 Hz, 1H), 4.61 (ddd, J = 10.2, 3.8, 2.5 Hz, 1H), 4.50 (dd, J = 12.4, 3.8 Hz, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 166.01, 165.35, 165.28, 165.05, 133.72, 133.59, 133.34, 133.13, 129.89, 129.82, 129.79, 129.76, 128.78, 128.72, 128.66, 128.50, 128.47, 128.35, 104.91 (d, J = 223.9 Hz), 71.19 (d, J = 2.5 Hz), 69.16 (d, J = 1.6 Hz), 68.55 (d, J = 39.7 Hz), 65.75, 62.11. $^{19}$F NMR (376 MHz, $CDCl_3$): δ -138.16 (d, J = 48.3 Hz). IR (ν, $cm^{-1}$): 3063 (w), 2960 (w), 1721 (str.), 1090 (str.), 703 (str.). HRMS (ESI): calculated for $[C_{34}H_{28}O_9F]^+$: 599.1712, found: 599.1708.

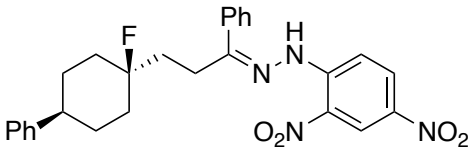
(Z)-1-(2,4-dinitrophenyl)-2-(3-(1-fluoro-4-phenylcyclohexyl)-1-phenylpropylidene)hydrazine **3r**




$C_{21}H_{23}FO$
MW: 310,41

According to General Procedure O-ethyl [1-(3-oxo-3-phenyl-propyl)-4-phenyl-cyclohexyl]sulfanylmethanethio ate (145 mg, 0.351 mmol) and NFAS (0.548 g, 1.5 mmol) were dissolved in acetonitrile (1 mL), followed by triethylborane (0.367 mL, 0.422 mmol, 1.15 M in benzene) and DTBPO (49.4 mg, 0.211 mmol) latter dissolved in 1 mL of MeCN. TLC (heptane/EtOAc 9:1, UV active, weakly visible under CAM). The crude was submitted to high-resolution Au column - Combi Flash FC (heptane/EtOAc 100:0 – 98:2 – 97:3 – 96:4 – 95:5 – 90:10 to 100% EtOAc) to yield the product as a yellow oil, contaminated (78.4 mg, 0.253 mmol, 72%). It was subjected to derivatisation to get the product pure from

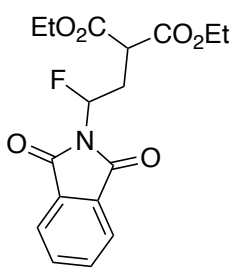
contaminants.



$C_{27}H_{27}FN_4O_4$
MW: 490,54

To an ~4 mL glass vial with a stirring bar, 3-(1-fluoro-4-phenyl-cyclohexyl)-1-phenyl-propan-1-one (76.6 mg, 0.247 mmol) was placed, followed by MeOH (1.5 mL) and $H_2SO_4$ conc. (0.21 mL), then (2,4-dinitrophenyl)hydrazine (75.6 mg, 0.37 mmol) was added and stirred at rt for 20 min. The red precipitate formed instantly. The formed precipitate was filtered, washed with a small amount of MeOH, and dried under a vacuum. The product was obtained as an orange powder cis:trans 95:5 (84 mg, 0.171 mmol, 69% over two steps), and a small amount of impurity present 91:9, probably eliminated (oxidised) product, as the tertiary fluorides are very unstable in acidic condition (decompose in $CDCl_3$ and slowly in $C_6D_6$). $R_f$ = 0.44. M. p. = 169 – 171 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ 11.54 (s, 1H), 9.17 (d, J = 2.6 Hz, 1H), 8.36 (dd, J = 9.6, 2.6 Hz, 1H), 8.14 (d, J = 9.6 Hz, 1H), 7.88 (ddd, J = 7.7, 6.7, 3.8 Hz, 2H), 7.48 (dd, J = 5.1, 2.0 Hz, 3H), 7.37 – 7.27 (m, 2H), 7.27 – 7.15 (m, 3H), 3.13 – 2.95 (m, 2H), 2.58 (ddd, J = 16.1, 8.2, 5.2 Hz, 1H), 2.25 – 2.13 (m, 2H), 2.04 – 1.78 (m, 6H), 1.69 (td, J = 13.6, 4.6 Hz, 1H), 1.59 (td, J = 13.6, 4.6 Hz, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 155.59, 146.58, 145.23, 138.45, 136.21, 130.44, 130.25, 129.87, 129.02, 128.59, 126.95, 126.62, 126.35, 123.65, 116.93, 94.14 (d, J = 172.9 Hz), 43.48, 36.47 (d, J = 23.6 Hz), 35.13 (d, J = 22.7 Hz), 29.19, 21.21 (d, J = 4.9 Hz). $^{19}$F NMR (376 MHz, $CDCl_3$): δ -161.85 (dddp, J = 40.2, 30.4, 20.1, 10.8, 9.7 Hz), -163.47 (dddq, J = 48.7, 28.5, 19.1, 9.6, 8.5 Hz). IR (ν, $cm^{-1}$): 3308 (w), 2930 (w), 2856 (w), 1615 (m), 1590 (m), 1509 (str.), 1491 (str.), 1107 (str.). HRMS (ESI): calculated for $[C_{27}H_{28}O_4N_4F]^+$: 491.2089, found: 491.2105.

### Diethyl 2-(2-(1,3-dioxoisoindolin-2-yl)-2-fluoroethyl)malonate **3s**



$C_{17}H_{18}FNO_6$
MW: 351,33

According to General Procedure (diethyl 2-[2-(1,3-dioxoisoindolin-2-yl)-2-ethoxycarbothioylsulfanyl-ethyl]propanedioate (227 mg, 0.5 mmol). TLC (heptane/EtOAc 7:3, UV active, weakly visible under CAM). The crude was submitted to high-resolution Au column - Combi Flash FC (heptane/EtOAc 95:5 – 90:10 – 87.5.5:12.5 – 85:15 – 80:20 to 100% EtOAc) to yield the product as a pale-yellow oil (112 mg, 0.32 mmol, 64%). $R_f$ = 0.41. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.91 (dd, J = 5.5, 3.1 Hz, 2H), 7.79 (dd, J = 5.5, 3.0 Hz,

2H), 6.28 (ddd, J = 48.4, 8.4, 5.2 Hz, 1H), 4.26 – 4.16 (m, 4H), 3.55 (dd, J = 8.4, 6.5 Hz, 1H), 3.27 (dddd, J = 14.8, 9.1, 8.4, 6.5 Hz, 1H), 2.87 – 2.71 (m, 1H), 1.27 (td, J = 7.1, 1.0 Hz, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 168.34, 168.26, 166.63, 166.61, 134.95, 131.56, 124.16, 88.18 (d, J = 201.7 Hz), 62.06, 48.25 (d, J = 4.1 Hz), 30.62 (d, J = 28.6 Hz), 14.11. $^{19}$F NMR (376 MHz, $CDCl_3$): δ -147.33 (ddd, J = 48.3, 25.7, 9.1 Hz). IR (ν, $cm^{-1}$): 2982 (w), 2938 (w), 1721 (str.). HRMS (ESI): calculated for $[C_{17}H_{18}O_6NFNa]^+$: 374.1010, found: 374.1010.

## References


[1] P. D. Bartlett, E. P. Benzing, R. E. Pincock, *J. Am. Chem. Soc.* **1960**, *82*, 1762–1768.

[2] L. M. Doyle, S. O'Sullivan, C. Di Salvo, M. McKinney, P. McArdle, P. V. Murphy, *Org. Lett.* **2017**, *19*, 5802–5805.

[3] C. Chay, R. Cansino, C. Pinzón, R. Torres-Ochoa, R. Martínez, *Mar. Drugs* **2014**, *12*, 1757–1772.

[4] B. Quiclet-Sire, G. Revol, S. Z. Zard, *Tetrahedron* **2010**, *66*, 6656–6666.

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[6] N. D. C. Tappin, P. Renaud, *Adv. Synth. Catal.* **2021**, *363*, 275–282.

Chapter 5

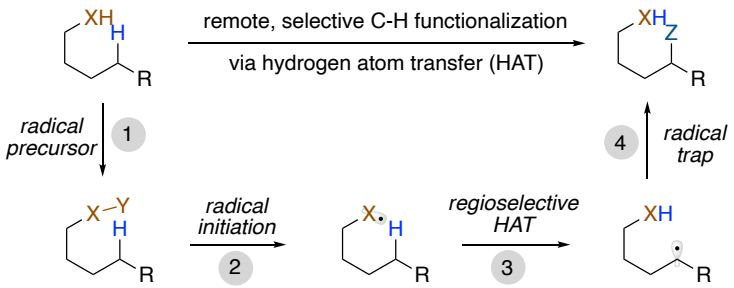
# Intramolecular Hydrogen Atom Transfers

# Chapter 5 – Intramolecular Hydrogen Atom Transfers

## 5.1 General introduction of remote functionalization via selective hydrogen atom transfer (HAT)

The modification of C–H bonds is likened to adding the final touches to a painting, where precision and selectivity are paramount. The transformative role of intramolecular hydrogen atom transfer (HAT) in the selective functionalization of remote C–H bonds within organic molecules is a method to correct or modify molecules without starting from scratch, emphasising its importance in refining complex synthetic processes. Although older than metal-based methods,[1–3] a radical-mediated approach offers a novel reactivity that significantly contrasts conventional closed-shell pathways. While metal-based C–H activation techniques are more commonly used due to their effectiveness in addressing chemo-, regio-, and stereoselectivity, radical-mediated C–H functionalization, despite being known longer, has been underutilised mainly due to the harsh conditions traditionally required for radical generation. Modern methods allowing milder radical generation—such as iodonium reagents[4–6] and photoredox catalysts[7–9]—are highlighted for enabling more profound exploration of the inherent selectivity of C–H functionalizations via single-electron transfer (SET) pathways.[10–13] Several general reviews and chapters discuss the C-H functionalisation enabled by remote HAT to carbon-centred radicals, some of which will be referenced later in the chapter.[14–19]

### 5.1.1 The general strategy for remote, directed C–H functionalization via HAT

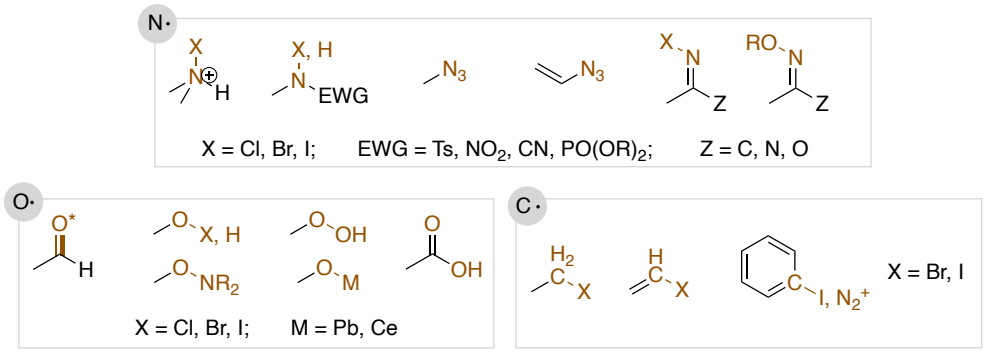



Scheme 1. Schematic representation of remote and selective C-H functionalization via HAT.

The general strategy for remote, directed C–H functionalization via HAT encompasses four principal steps essential to the mechanism of all intramolecular HAT reactions (Scheme 1).[17]

### 5.1.1.1 Generation and types of radical precursors

This initial step involves creating a precursor that can easily transform into a radical. This precursor often includes a weak bond that facilitates the formation of a radical upon mild activation. The radical precursors are generally prepared and utilised across different types of radicals (see Scheme 2).[10]




Scheme 2. Representation of different types of radical precursors.

*N-centred radicals* are typically generated through single-electron transfer (SET) reduction or the homolysis of a weak nitrogen-halide (N–X) bond, where X could be a halogen or a diazonium group ($N_2$ nucleofuge). The radical initiation often involves a halogen chemical reductant (such as $R_3Sn•$, $(TMS)_3Si•$) or chalcogen irradiator to break the N–X bond, releasing a nitrogen-centred radical that is highly reactive and suitable for initiating HAT. *O-centred radicals* are commonly accessed by the homolysis of a weak O–X bond, where X is usually a halogen or by photoexciting a carbonyl group. Photolysis is particularly effective for carbonyls, where the energy from the light promotes an electron to an excited state, facilitating the loss of a neighbouring group and forming the radical. *C-centred radicals* include alkyl, aryl, and vinyl radicals, typically generated from weak C–X bonds (X is a halogen or a diazonium group), addition to unsaturated systems (alkynes, allenes and alkenes) or from C–$N_2$ precursors where the $N_2$ group acts as a leaving group upon activation. These radicals are often formed through thermal or photochemical processes that induce the homolysis of the C–X bond, releasing a carbon-centred radical.

### 5.1.1.2 Initiation of the radical process

Once the precursor is prepared, the radical is generated through thermal decomposition, photolysis, or chemical reaction. This step is crucial as it sets the stage for the selective

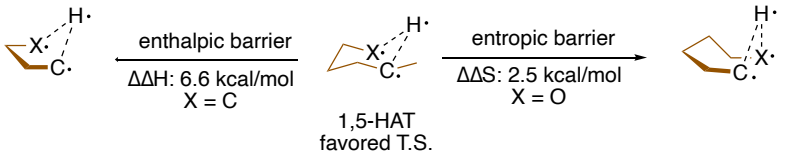
hydrogen atom transfer. Traditionally, radical initiation has involved using strong acids, high temperatures, or unstable and hazardous materials such as peroxides and toxic organotin reagents. Additionally, high-energy ultraviolet (UV) light has been a standard method to induce the necessary energy for radical formation. These conditions pose safety risks and environmental concerns and limit functional group compatibility, potentially degrading sensitive molecular frameworks or necessitating protective groups. Recent methodologies have shifted towards using more sustainable and less toxic metal catalysts. Metals like iron (Fe), copper (Cu), and nickel (Ni) have become popular due to their abundance and relatively mild reaction conditions. These metals can facilitate electron transfer reactions necessary for radical generation without the extreme conditions previously required.[17]

Hypervalent iodine reagents, including radical reactions, have proven exceptionally useful in organic synthesis. It offers a versatile toolkit for initiating radicals under controlled and less harsh conditions, broadening the scope of radical-mediated transformations. Visible-light-mediated photoredox catalysis has revolutionised radical initiation, allowing for the generation of radicals under ambient conditions using visible light. Photoredox catalysts, often based on earth-abundant metals or organic dyes, absorb visible light and transfer energy to substrates, forming radicals in a controlled and sustainable manner, allowing for greater control over the radical generation process and enhancing the selectivity of HAT and reducing side reactions. This control is crucial for achieving high regio- and stereoselectivity in complex molecule synthesis, particularly in intermolecular HAT. By reducing the reliance on hazardous chemicals and energy-intensive conditions, these modern techniques align better with the principles of green chemistry, offering more sustainable and safer alternatives for radical initiation in industrial and laboratory settings.

#### 5.1.1.3 Regioselective intramolecular HAT

Following initiation, the radical species abstracts a hydrogen atom from a specific C–H bond within the molecule. This step is usually highly regioselective, often favouring the removal of hydrogen from a particular position due to steric and electronic factors. Since HAT is significantly influenced by bond dissociation energy (BDE) and HAT from tertiary C–H sites, it generally occurs faster than from secondary and primary sites in each system. Although other modes of intramolecular HAT are possible,[20] the 1,5-HAT is the most prevalent pathway due

to a six-membered cyclic transition state, which allows for a nearly linear alignment of the C–H–X (where X is the radical) bonds. This geometric arrangement facilitates the adequate orbital overlap necessary for HAT, resulting in a more favourable transition state and a smoother hydrogen transfer. The geometry, typically observed at around 153° for oxygen-centred radicals (O•), enhances the precision of hydrogen abstraction, making the 1,5-HAT highly selective and efficient (illustrated in Scheme 3).[21]




Scheme 3. Regioselective HAT process.

For carbon-centred radicals (C•), there's a marked preference for 1,5-HAT over 1,4-HAT, with a difference in enthalpy changes (ΔΔH) of about 6.6 kcal/mol.[22] This significant enthalpic advantage arises because the 1,5-HAT often involves less strained transitions than 1,4-HAT. The preference for 1,5-HAT over 1,6-HAT is mainly due to lower entropic barriers (ΔΔS, about 8.3 eu 2.5 kcal/mol) lower in the pathway involving O• radicals.[23] This lower entropic barrier results in a faster and more favourable hydrogen abstraction process, enhancing the overall efficiency of the reaction. In addition, the Thorpe–Ingold effect also plays a crucial role, especially in cases of intramolecular HAT. This effect enhances the reaction rate by favouring the formation of a more stable, less strained cyclic transition state in the molecular structure.[24–26]

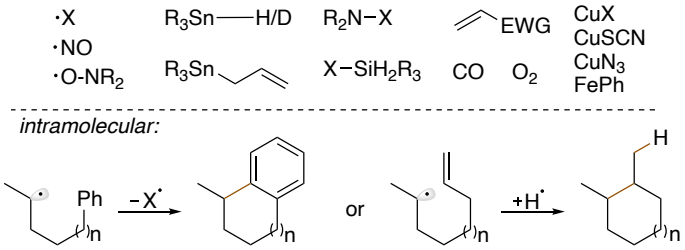
The kinetic rate for 1,5-HAT is significantly higher than other pathways, reaching $2.7 \times 10^7$ $s^{-1}$.[27] This rate enhancement underscores the effectiveness of the six-membered ring transition state in facilitating rapid and selective hydrogen abstraction. Despite the general preference for 1,5-HAT, exceptions occur where this pathway is less favourable. For instance, other pathways might dominate if the fifth carbon (C5) lacks a hydrogen atom or the adjacent C–H bonds are inherently weaker (e.g., benzylic, tertiary, α-oxy C–H bonds).[20] Additionally, geometric constraints that prevent the formation of a stable six-membered ring can divert the reaction to less typical pathways. Selective 1,5-HAT typically leads to forming a δ-carbon radical, which can then be trapped to introduce functional groups or form various molecular architectures. This selectivity is crucial for designing synthetic strategies that require precise

modification of complex molecules, often enabling transformations that are difficult to achieve through other synthetic routes.

Another critical factor influencing the efficiency and selectivity of hydrogen atom transfer (HAT) is radical philicity, or the polarity of the radical involved.[28–33] This philicity, whether electrophilicity or nucleophilicity, can be quantified using the free radicals' ionisation potential (IP) and electron affinity (EA).

### 5.1.1.4 Trapping of the relayed radical

After the H-atom transfer, a suitable trapping agent quickly traps or stabilises the resultant radical intermediate. This can lead to the formation of various functional groups or initiate further transformations, finalising the C–H functionalization process.




Scheme 4. Radical traps.

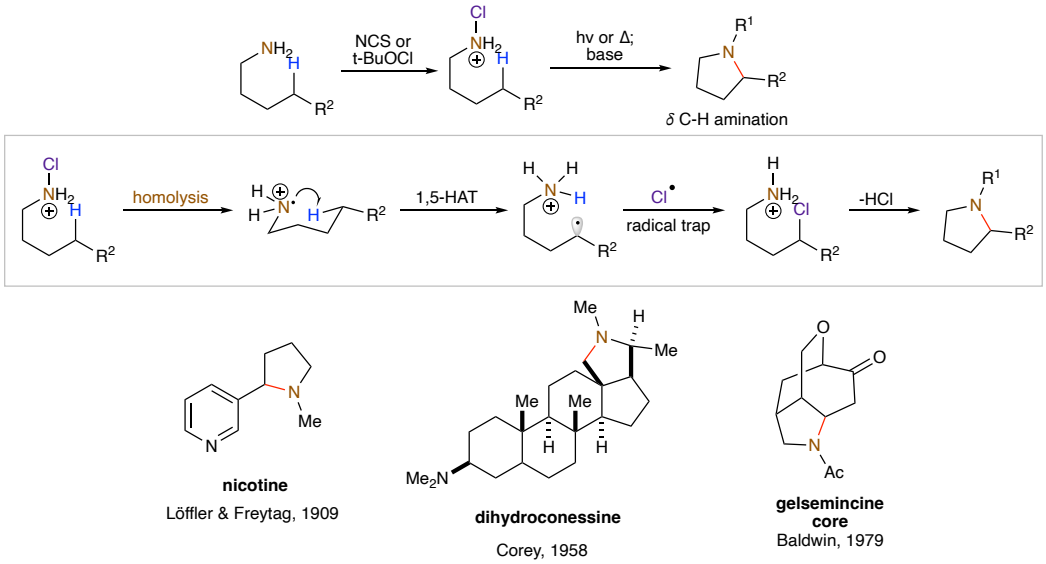
Radical traps are diverse, offering a wide range of possibilities for reaction design, differing significantly from the options typically used in metal-mediated reactions. Compounds like halogens (X•), nitric oxide (NO•), and nitroso (ON•) groups can act as radical traps (Scheme 4). These species are stable under certain conditions but can react with intermediate radicals generated during HAT to form new bonds. Elements such as nitrogen (N–X), silicon (Si–X), and tin (Sn–H, Sn–allyl) can form weakly bonded intermediates that readily react with carbon-centred radicals. These interactions often lead to the formation of new functional groups or stabilisation of the radical intermediate. Copper salts like CuX, CuSCN, and $CuN_3$ are particularly effective in trapping radicals. These metal complexes can engage in further redox reactions, adding to the complexity and diversity of the possible outcomes. Alkenes and arenes provide a rich platform for radical trapping, where the radical can add across a double bond (in alkenes) or form radical aromatic substitution products (in arenes).[17] This is a kind of flexibility offered by the formation of unique bonds and structures that might be inaccessible through traditional metal-based methods. The use of radical traps in HAT

processes enables the exploration of synthetic routes that complement other methodologies. For instance, directly trapping radicals with π-systems or weakly bonded molecules can simplify reaction sequences and reduce the need for protective group strategies or harsh reaction conditions. The broad array of available radical traps allows chemists to tailor the reactivity according to the needs of the synthetic target. This versatility makes radical trapping an essential tool in the arsenal of C–H functionalization techniques, providing the ability to influence the complexity and functionality of the synthesised molecules directly.

## 5.2 Intramolecular HAT with heteroatom-centred radicals

### 5.2.1 Nitrogen-centred radicals

In intramolecular HAT chemistry, *N*-centered radicals hold a crucial position.[34] Historically, they were the first type of radicals used to initiate remote hydrogen atom transfers. Their structure allows for customisation through *N*-substitution, which finely adjusts their polarity and dramatically affects their reactivity in HAT.[35] The first documented case of selective C–H functionalization via HAT was reported by Hofmann in 1883,[36] a process that is now recognised as the Hofmann–Löffler–Freytag (HLF) reaction (Scheme 5).

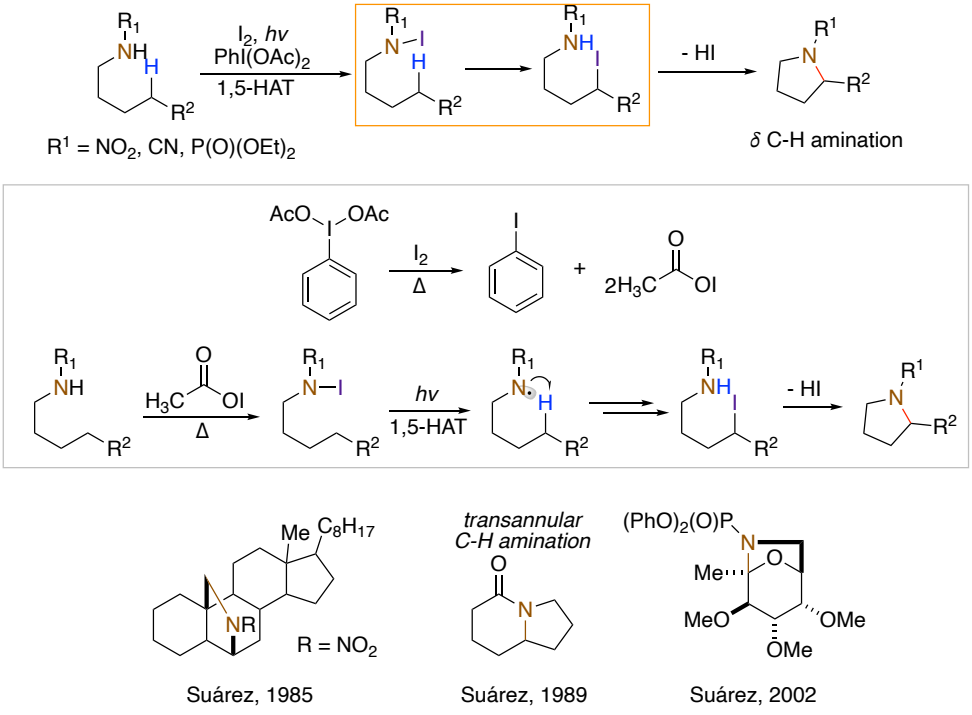



Scheme 5. Hofmann-Löffler-Freytag reaction, δ C-H amination via N-centred radicals.

This reaction involves the photolytic homolysis of a cationic *N*-haloamine,[37,38] forming a polarised aminium radical cation. This radical can abstract a hydrogen atom from the δ carbon, creating a new C-centred radical.[35] A chair-like transition state determines the site selectivity of the 1,5-HAT in this reaction. The generated δ C-radical is subsequently trapped

by recombination with a caged radical (X•) or reaction with N–X, forming an δ halide. This halide is then displaced through base-induced intramolecular cyclisation, a mechanism facilitating the direct synthesis of pyrrolidines from amines via δ C–H amination. This technique has streamlined the synthesis of various natural products and their derivatives. Notably, Löffler and Freytag utilised this reaction in 1909 to synthesise nicotine,[39] while in 1958, Corey and Hertler applied it to produce a series of cycloaminated steroid derivatives.[40] In 1979, Baldwin and Doll expanded its use to amides for the total synthesis of gelsemincine.[41] The HLF reaction has proven to be a robust radical-mediated C–H functionalization method, demonstrating significant selectivity and utility in organic synthesis. This radical approach, discovered in the 19th century, is known for its high regioselectivity and exergonic nature. Despite these advantages, it did not become prominent among mainstream C–H functionalization methods until advancements were made in the mild generation of radicals.[17,18,20,42–45]

Nearly a century after the original discovery, in 1985, Suárez and his team developed a method that eliminated the need to perform the *N*-haloamine to initiate radical reactions. Instead, they innovatively produced N–I in situ using molecular iodine and a hypervalent iodine oxidant, $PhI(OAc)_2$ (Scheme 6).



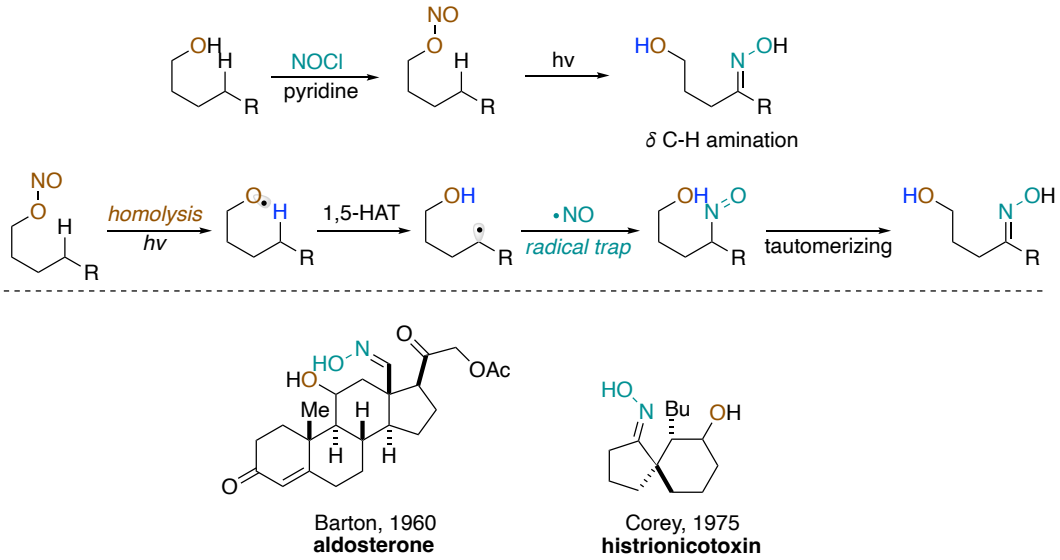

Scheme 6. Suárez modification, δ C-H amination via in situ N-I formation and homolysis.

This approach leads to the formation of transient AcOI, from which N–I is generated. The relatively weak N–I bond is then cleaved by light, forming a corresponding electrophilic nitrogen-centred radical. Thus, the main difference from the original HFL reaction is the replacement of one hydrogen atom attached to the nitrogen by an electron-withdrawing group. Through these modifications, the synthesis of steroid derivates, bicyclic lactams and δ C–H amination of carbohydrates were implemented.[46–49] Suárez's modifications to the HLF reaction paved the way for further advancements by various research groups. Notably, the Herrera[50] and Muñiz[51,52] groups independently explored and developed these modifications in 2015 and the following years. Their contributions have significantly expanded the scope and applicability of the HLF reaction. For a comprehensive review of these and other modern HLF modifications, interested readers can refer to the extensive literature on this topic.[17]

### 5.2.2 Oxygen-centred radicals

Another prevalent atom in intramolecular HAT processes is the oxygen-centred radical. The oxygen atom's high electronegativity (χ = 3.4), second only to fluorine, creates a strong driving force for HAT for two main reasons: (1) The formation of an open-shell on this highly electronegative atom is generally disfavoured, which promotes HAT, and (2) the O–H bond formed during HAT is particularly strong (Bond Dissociation Energy, BDE = 110 kcal/mol for O–H versus less than 100 kcal/mol for N–H and C–H). These factors make O-centred radicals incredibly versatile for synthetic applications, allowing for introducing halogen, heteroatom, and even alkyl groups in the remote intermediate carbon radical. However, generating radicals on such an electronegative atom poses significant challenges, including the possibility of fragmentation of alkoxy radicals by generating aldehydes and side products. The three most common methods for initiating these radicals include carbonyl photoexcitation and alkoxy or non-alkoxy radical initiation. Since alcohols are highly versatile in synthesis, developing O-centred radicals from alcohols has catalysed numerous C–H functionalization techniques. Sir Derek Barton demonstrated this in 1960.[53–55] Barton synthesised a precursor with a weak N–O bond by reacting an alcohol with nitrosyl chloride, which, upon photolytic homolysis, produced both a persistent •NO radical and a transient alkoxy radical (Scheme 7). This led to 1,5-HAT, forming an δ-nitroso alcohol tautomerised into an δ-aminated oxime. This method has proven pivotal in synthesising complex molecules like steroids (aldosterone)[56] and histrionicotoxin.[57] It has been applied to functionalities like the δ-amination of $Me_{10}$-

carborane by Hawthorne and colleagues, showcasing its broad utility in remote C–H amination.[58]




Scheme 7. The Barton reaction: δ C-H amination via O-centred radicals.

In the following decades, Čeković[59–61] and his co-workers developed many applications of this approach using O-SPh derivatives as radical precursors, with further investigations by other scholars like in 2014, Taniguchi[62] converting alkenes into hydroperoxides under Fe(Pc), $O_2$ and $NaBH_4$ media, resulting in the formation of 1,4-diol, through the peroxide-based HAT process. Also, Chen and co-workers, in 2016, were able to trap the δ radical with allyl sulfones, enabling δ C-H allylation;[63] in the same year, Meggers and co-workers published an asymmetric alkylation photoredox method with Ir & chiral Rh-based catalysts being the first and only method as such.[64]

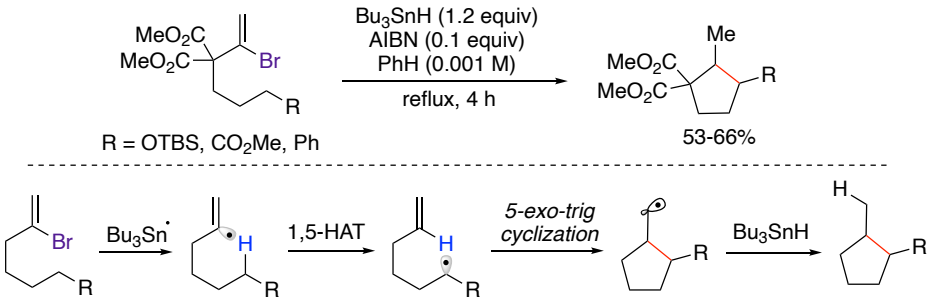
### 5.2.3 $sp^2$ Carbon-centred radicals: *vinyl and aryl derived*

Carbon-centred radical-mediated HAT was first reported in 1954,[16,65] and in 1967, Heiba and Dessau investigated the reactions of vinyl radicals generated by adding $CCl_3$ radicals to open-chain $>C_6$ alkynes.[66] The relative reactivities of these radicals in hydrogen abstraction and chlorine transfer reactions with $CCl_4$ and the influence of different solvents and reaction temperatures for these transfers were studied. However, carbon-centred radical-mediated HAT was not used in organic synthesis until the late 1980s.[67,68] Over the past decade, it has seen rapid and widespread adoption in synthetic applications, reflecting significant advancements in radical chemistry and its integration into mainstream synthetic

methodologies.

HAT processes mediated by C-centred radicals are less common than those initiated by heteroatoms like nitrogen and oxygen. In N• and O• initiated mechanisms, a C–H bond is typically replaced with a stronger N–H or O–H bond.[34] However, C-centered radical pathways face challenges because both the HAT precursor and product feature a C–H bond, requiring a significant driving force for reaction. Often, this involves exchanging a C($sp^2$)-centred radical for a more stable C($sp^3$) radical, forming a more robust aryl C–H bond from an alkyl C–H bond. While bond dissociation energy (BDE) is not the sole determinant of HAT reactivity due to the often irreversible and exothermic nature of these reactions with early transition states,[69] BDE remains a helpful indicator for predicting outcomes in these transformations.[70] For radicals with similar BDE differences, an electrophilic radical is likely to preferentially undergo HAT from a more hydridic (electron-rich) C–H site and conversely for a nucleophilic radical.[71–73] In instances of a polarity mismatch, an alternative HAT agent can be utilised for polarity reversal catalysis, effectively modifying the reaction pathway to achieve the desired outcome.[74–76]

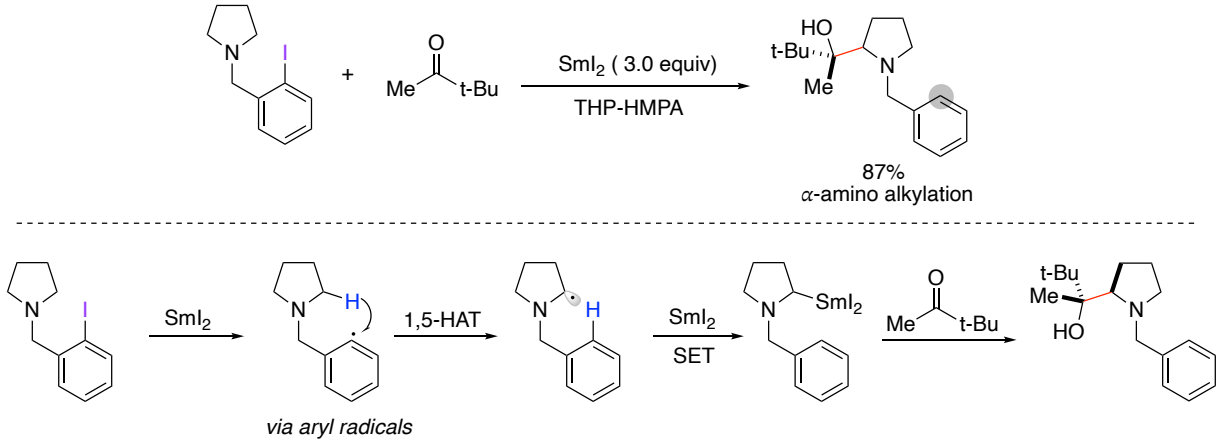
Curran and colleagues systematically studied C• sites translocating via intramolecular HAT between C–H bonds and subsequent cyclisations (Scheme 8).[68,77,78] They investigated the energy difference between C($sp^2$) and C($sp^3$) radicals to facilitate HAT from an alkyl C–H to a vinyl radical. This study marked a significant advance in understanding and utilising HAT for complex organic transformations. An insightful review by Dénès, Beaufils, and Renaud[79] highlights significant advancements in synthesising five-membered rings through the translocation of vinyl radicals followed by cyclisation.




Scheme 8. δ Alkylation via C($sp^2$)-centred radicals.

Ito and colleagues[80] demonstrated that amines could undergo HAT using an o-iodobenzyl

precursor (Scheme 9). Utilising $SmI_2$ as a radical initiator, the process involves α-amino C–H abstraction followed by trapping with a ketone, forming α C–H alkylated amines. Undheim and his colleagues further extended this work to α C–H alkylated amines with alkene traps, such as acrylates.



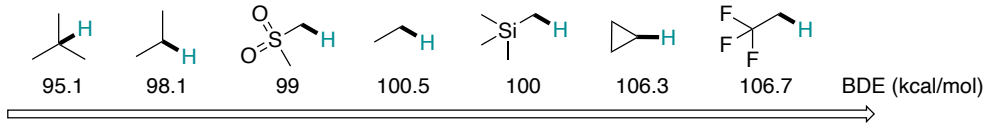

Scheme 9. C-H alkylation of α-amines via aryl radicals.

### 5.2.4 $sp^3$ Carbon-centred radicals

Alkanes are among the most abundant resources on Earth, serving as fundamental starting materials for chemical transformations. In an atom- and step-economic mode, alkanes with inert C($sp^3$)–H bonds are traditionally converted into valuable building blocks for pharmaceuticals, agrochemicals, and polymers. However, the intrinsic inertness of C($sp^3$)–H bonds and the susceptibility of other functional groups make selective transformations of these bonds exceedingly challenging in synthetic chemistry. The challenge with HAT initiated by C($sp^3$)-centred radicals is the minimal energetic difference between the initial and resultant C• after HAT.

Selective and efficient C–H bond functionalisation involving intramolecular HAT from unactivated C($sp^3$)–H to alkyl radical remains challenging.[81] Alkyl radicals exhibit weaker H-atom abstracting ability than nitrogen- or oxygen-centred radicals, aryl or vinyl radicals. Additionally, BDE differences between C($sp^3$)–H bonds and the radical polarity of corresponding alkyl radical species are comparable, making mutual HAT processes between alkyl radicals potentially reversible. Moreover, unactivated C($sp^3$)–H bonds, lacking p-π conjugation and stabilisation by lone pair electrons of heteroatoms, possess higher BDEs

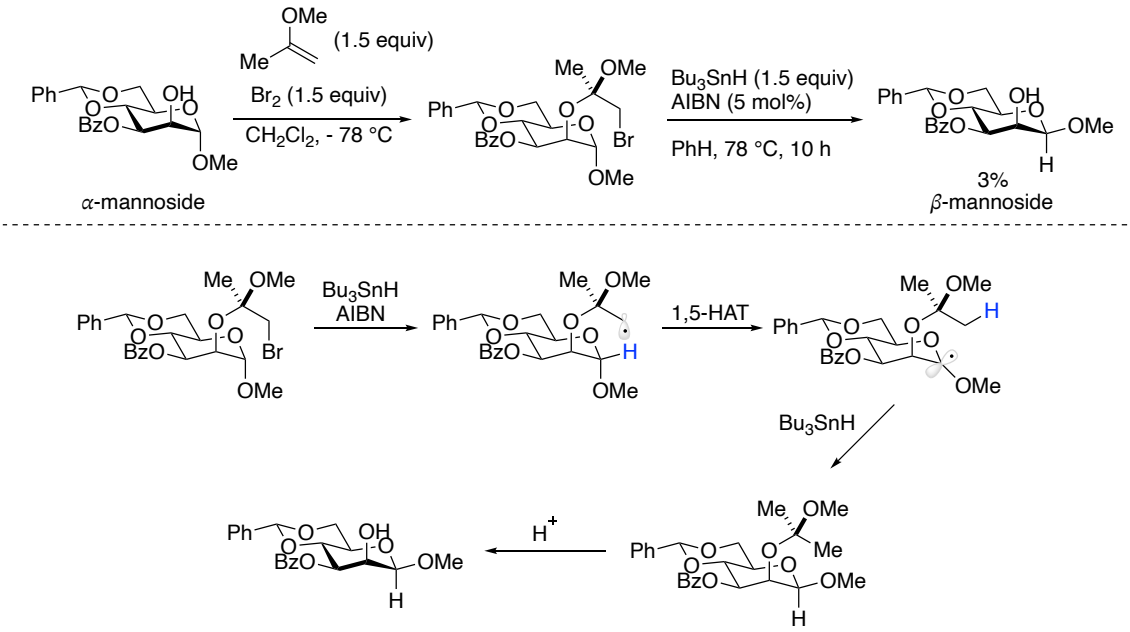
(some examples of BDE of C(sp$^3$)–H bonds used in the literature are given in Scheme 10).[82,83] Therefore, efficient and regioselective functionalisation of unactivated C(sp$^3$)–H bonds is substantially valuable but highly challenging.




Scheme 10. Examples of bond dissociation energy of C(sp$^3$)-H.

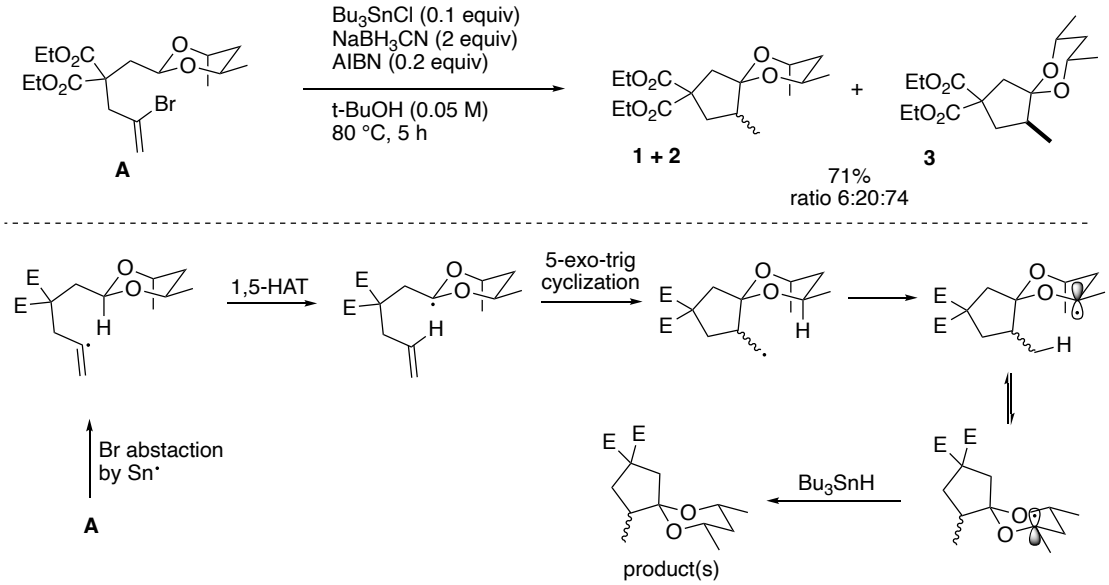
### 5.2.4.1 Non-substituted and related alkyl radicals

Crich and colleagues[84] developed a solution by generating a more stable α-oxy radical as the driving force (Scheme 11). In a unique example of sp$^3$ C• initiated HAT, they achieved the epimerisation of α-mannoside to β-mannoside, although in low yield, successfully overcoming the inherent anomeric stereo preference, which presented its own challenges.



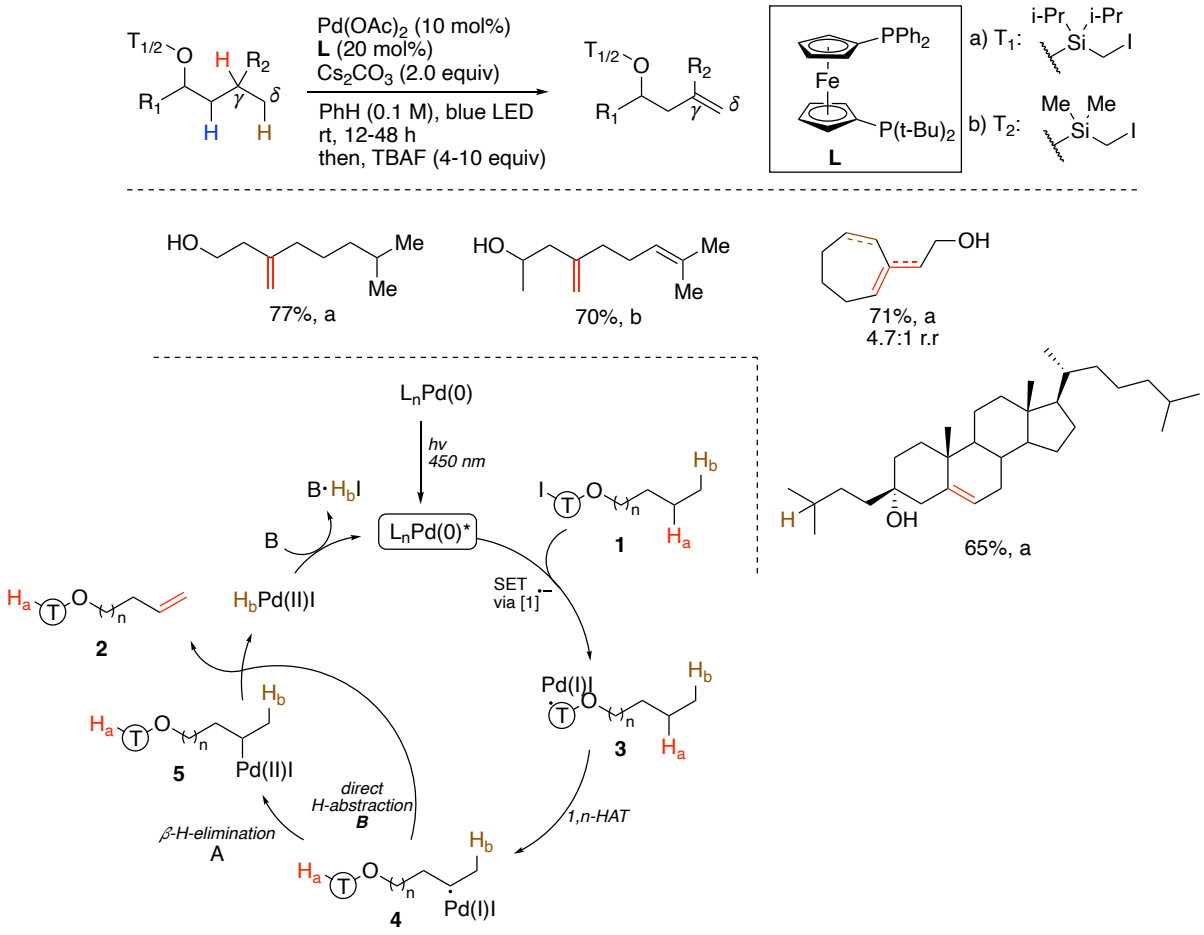

Scheme 11. Generating stable α-oxy radical as the driving force for sp$^3$ C• initiated HAT.

Crich and Bertrand have reported several studies on 5-*exo* cyclisation of conformationally constrained 2,3-dioxolanyl radicals.[85–87] They investigated chiral 1,3-dioxolan-2-yl radicals derived from acetals engaged in intramolecular hydrogen abstraction and subsequent 5-*exo*-trig cyclisation when treated with tributyltin hydride and AIBN, yielding products with modest and contrasting stereoselectivities (Scheme 12). The higher degree of substitution on the alkene in this reaction led to almost complete diastereoselectivity in the stereocontrolled cyclisation.




Scheme 12. Diastereoselective 5-exo-trig cyclisation of 1,3-dioxolan-2-yl radicals via intramolecular 1,5-HAT.

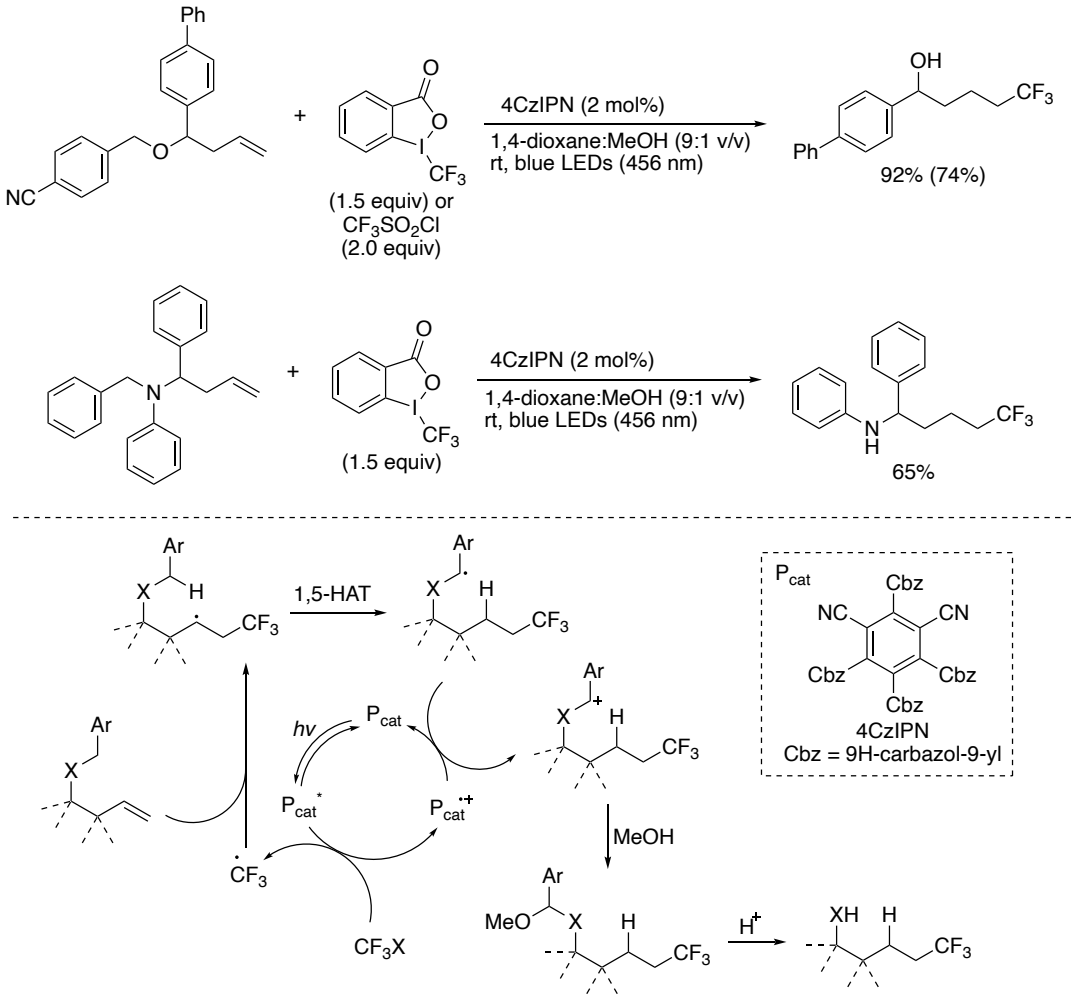
In 2017, Gevorgyan[88] and his team introduced a method for the remote desaturation of aliphatic alcohols using Pd-photocatalysis (Scheme 13). The HAT at unactivated C($sp^3$)−H sites is facilitated by Si-auxiliaries, utilising (halomethyl)silanes that are easily installable and removable. The formation of key hybrid alkyl Pd-radical intermediates is efficiently triggered by visible light from alkyl iodides and Pd(0) complexes. This approach involves SET reduction, regioselective HAT, and Pd-catalyzed β-hydrogen elimination, culminating in aliphatic alcohol's selective, remote desaturation. Notably, desaturations mostly occur at tertiary positions, which mainly trigger 1,6-HAT in these transformations. Remarkably, this method operates without the need for external photosensitisers or oxidants.




Scheme 13. Remote desaturation via C($sp^3$)-I using Pd-catalyst.

### 5.2.4.2 1,5-HAT with neighbouring fluorinated groups

The study reported by Zhang and Xu introduced a novel method for the hydrotrifluoromethylation of benzyl-protected homoallylic alcohol and amine derivatives using 2,4,5,6-tetra(9*H*-carbazol-9-yl)isophthalonitrile (4CzIPN) as a catalyst.[89] This metal-free photoredox catalysis facilitates the activation of various fluoromethylation agents like $CF_3SO_2Cl$, Togni's reagent, 2-bromo-2,2-difluoroacetate through oxidative quenching, and $CF_3SO_2Na$ via reductive quenching. The reaction efficiently produces δ-fluoromethylated free alcohols and amines through 1,5-HAT and removes the benzyl-protecting groups concurrently under mild irradiation conditions (Scheme 14). This process extends the applicability of 4CzIPN to effectively hydrotrifluoromethylate simple alkenes and Michael acceptors.

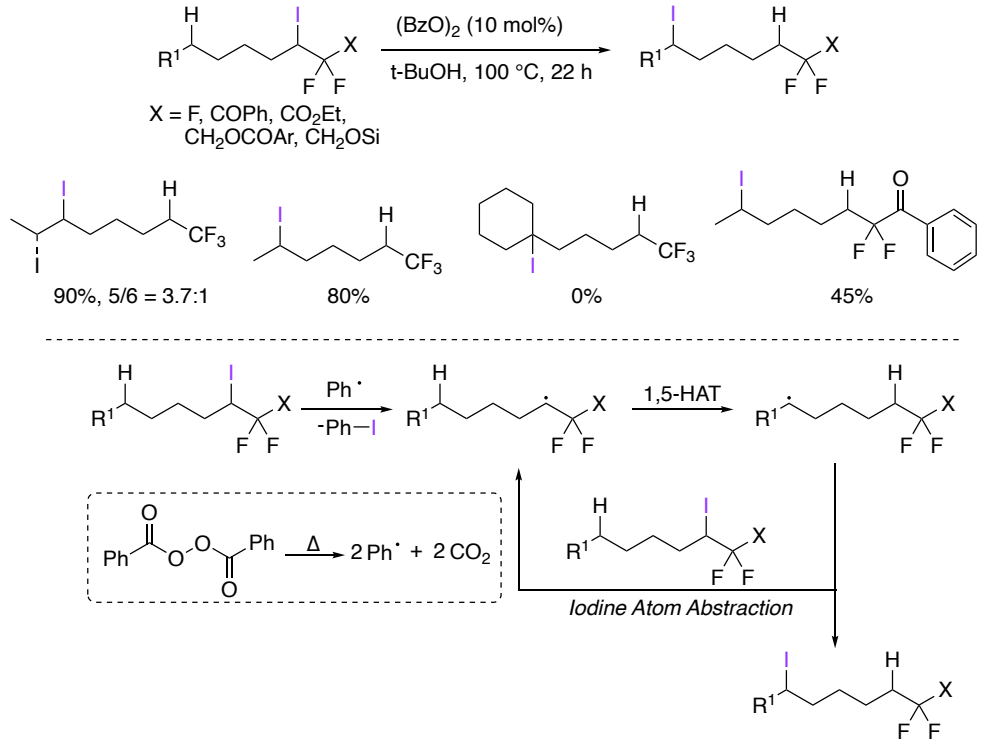



Scheme 14. Synthesis of alcohols and amines via 1,5-HAT with γ-$CF_3$ radicals and reaction mechanism.

Different scholars have carried out several works on remote C-H functionalisation via carbocations. One is Sodeoka, which uses the same Togni reagent under CuI catalysis at elevated temperatures.[90] Also, Nevado and co-workers developed a remote oxidative fluoroalkylation of long-chain alkenes with an Ir(III)-photocatalyst under visible light irradiation.[91] The vast majority of these studies are listed in the review by Li and Xu,[16] and they also mention several studies employing remote C-H functionalisation via carbanions.

In 2022, Inamoto and Abe et al. developed a straightforward iodine atom transfer in fluorinated alkyl iodides utilising 1,5-HAT (Scheme 15).[92] The radicals connected to the fluorinated functional groups promote the 1,5-HAT due to electrophilic properties and facilitate site-selective iodination of unreactive C($sp^3$)–H bonds, producing di—and tri-fluorinated alkyl iodides with good yields. It also demonstrates excellent atom economy and high tolerance for some functional groups. However, no products were obtained with the

substrates possessing tertiary and benzylic C-H bonds.




Scheme 15. Iodine atom transfer in fluorinated alkyl iodides via 1,5-HAT.

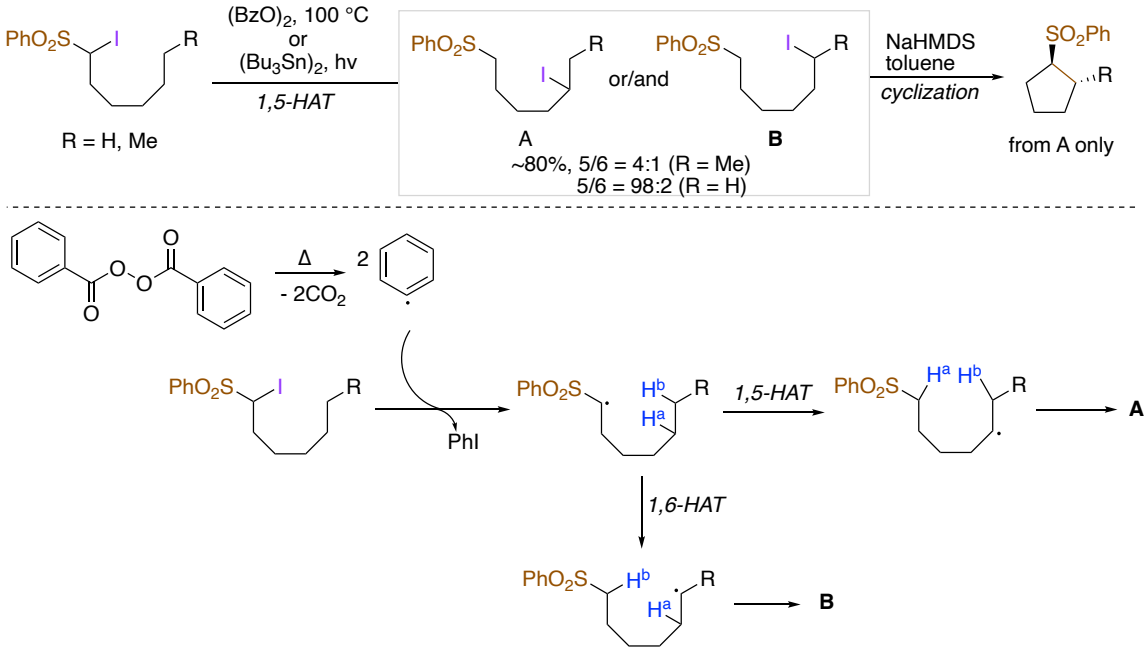
There are more recent works on remote C-H functionalization via carbon radicals; the nicely reviewed work of Li was published in 2023[16] and by Wu in 2024.[81] The review will continue in the next part of the chapter for more studies focused on α-sulfonyl radicals in 1,5-HAT. This will include further discussion and analysis of advancements and methodologies pertinent to the topic, enhancing the depth of understanding and application in this field.

### 5.2.4.3 C(sp$^3$) α-Sulfonyl carbon radicals in remote functionalization via 1,5-HAT

Sulfonyl groups are privileged moieties in natural products and synthetic building blocks. The electron-withdrawing effect exerted by the sulfonyl group endows α-sulfonyl alkyl radicals with electrophilic properties. However, previous works have demonstrated that sulfonyl groups offer little or no stabilisation to the radical species.[93–95] This is clearly different from the stabilisation seen in alkyl radicals of α-esters or ketones.[93,96] In other words, the electrophilic property and the instability of α-sulfonyl alkyl radicals might be favourable for abstracting hydrogen atoms from unactivated C(sp$^3$)–H bonds.

One of the first examples of facilitating HAT via a sp$^3$ C• using an α-EWG halide, where the C–X bond is weaker than the secondary C–X bond involved in the translocation, on remote

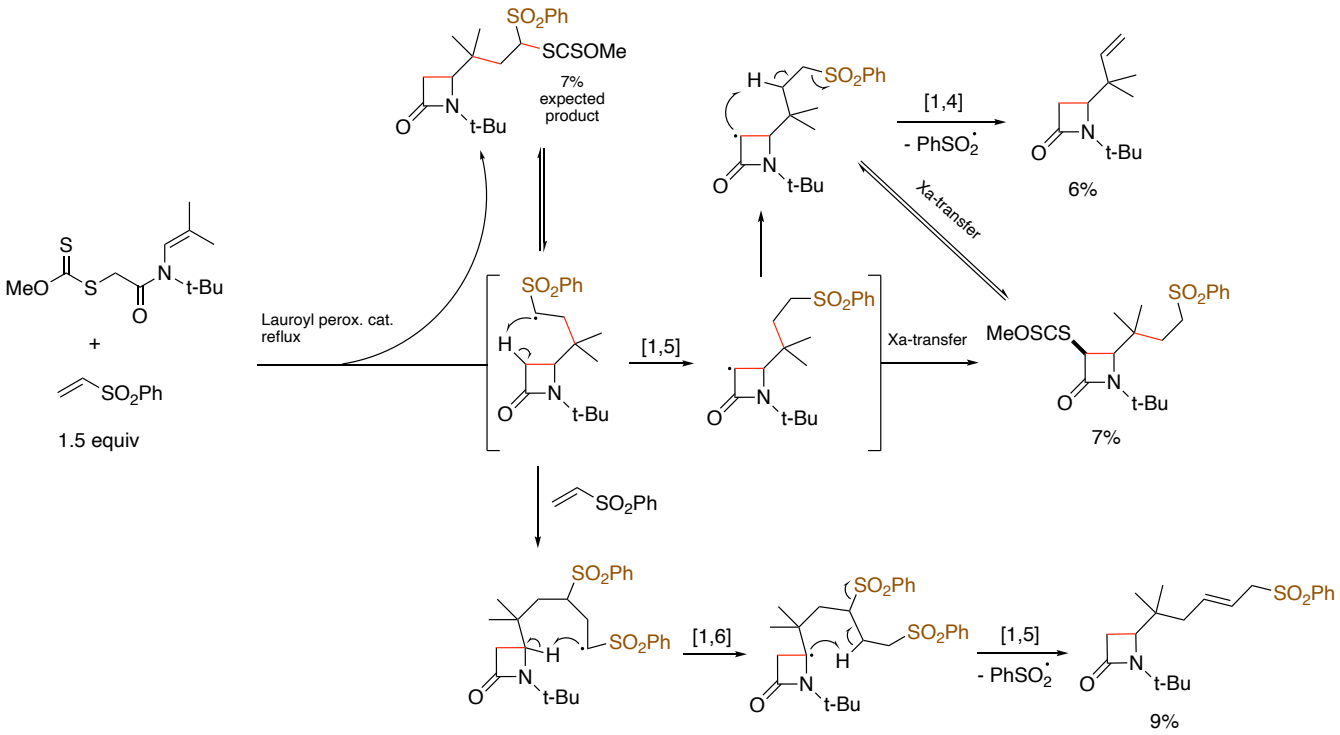
functionalisation was conducted by Masnyk in 1997.[97] The work of Masnyk explores the radical reactions of α-iodoalkylphenyl sulfones (Scheme 16). He introduced an α-sulfonyl iodide as a radical precursor to induce HAT-driven cyclisation, forming cyclopentanes from acyclic alkanes through δ C–H functionalization as a process analogous to the all-carbon version of the HLF reaction. The research shows that these compounds, when containing sufficiently long alkyl chains ($C_5$ or longer), undergo radical rearrangement to 5-iodo-1-phenylsulfonyl derivatives at 100 °C in the presence of benzoyl peroxide or when irradiated with a sunlamp in the presence of hexabutylditin. These methods produce predominantly 1,5-shift products, although some 1,6-shift products are also formed. The resulting 5-iodo-1-phenylsulfonyl derivatives are versatile intermediates in organic synthesis. They can undergo intramolecular nucleophilic substitution upon treatment with bases to provide cyclic phenylsulfonyl derivatives in good yield, with a high degree of stereoselectivity, yielding only single stereoisomers.




Scheme 16. Masnyk's work, δ C-H alkylation via atom transfer.

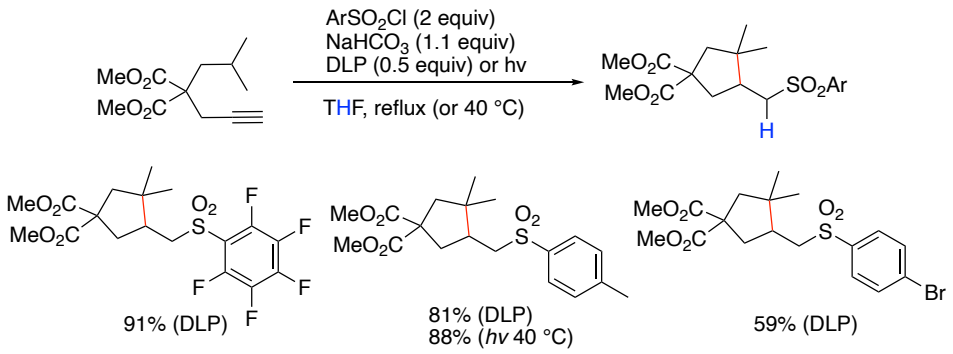
The following year, Zard and colleagues published[98] a study documenting an unexpected 1,5-HAT product involving an α-phenyl sulfone radical while synthesising a β-lactam. To favour the formation of the β-lactam, they tried to couple the cyclisation with an irreversible carbon-carbon bond formation step using a phenyl vinyl sulfone. Thus, they isolated four different products instead of one desired, coming from the sequence of different HAT processes due to the relatively long life of the intermediate radicals (Scheme 17). In addition, one can note

that after 1,5-HAT, there is a back 1,4-HAT taking place, as well as 1,6-HAT involving α-phenyl sulfone, followed by another 1,5-HAT process. Although it was not the focus of the research and no further investigations were pursued in this case, this finding again demonstrates that an alkyl radical adjacent to a sulfonyl group can act as a hydrogen atom abstractor by merging HAT and functional group (FG) transfer processes.



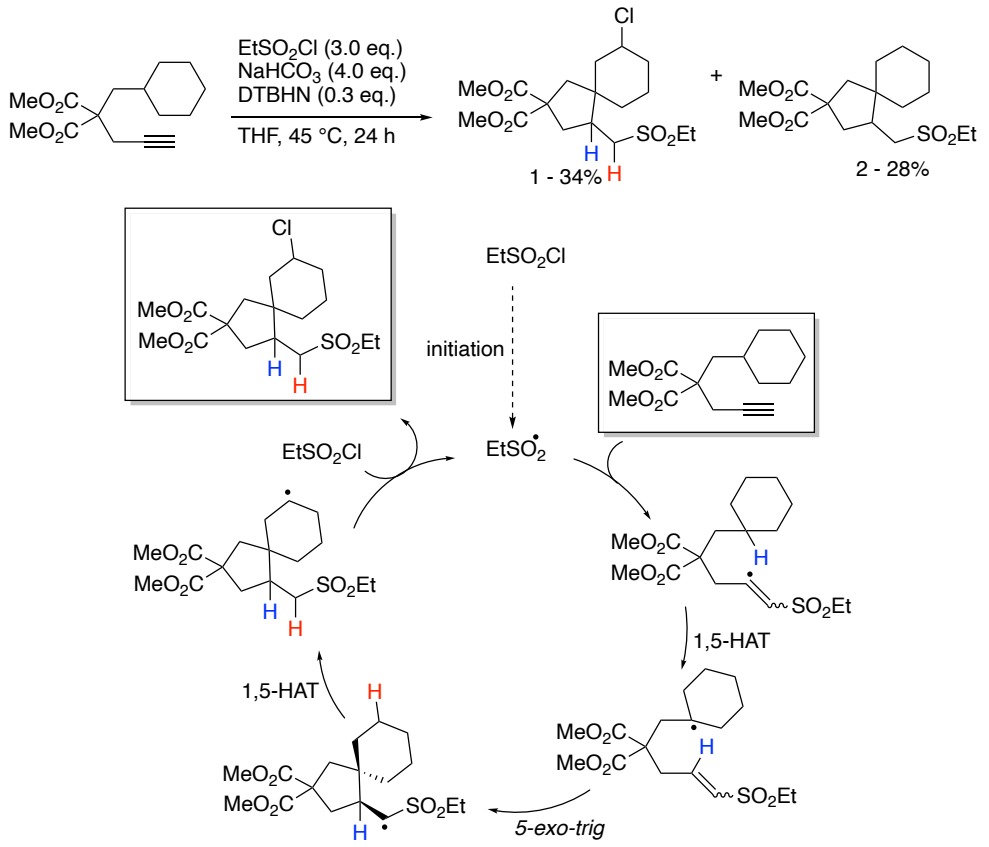

Scheme 17. Unexpected 1,5-HAT involving α-$SO_2$ radical in ATRA reactions and 1,4 and 1,6-HAT side processes.

The work of Renaud[99] in 2017 also showcased the involvement of α-sulfonyl radical in the intermolecular HAT process after 5-*exo*-trig cyclisation (Scheme 18). In this case, α-sulfonyl radical is not chlorinating but abstracting a hydrogen atom from THF due to polar effects. Even though this is not a direct example of 1,5-HAT via an α-sulfonyl radical, it presented the possibility for further investigations into this area.



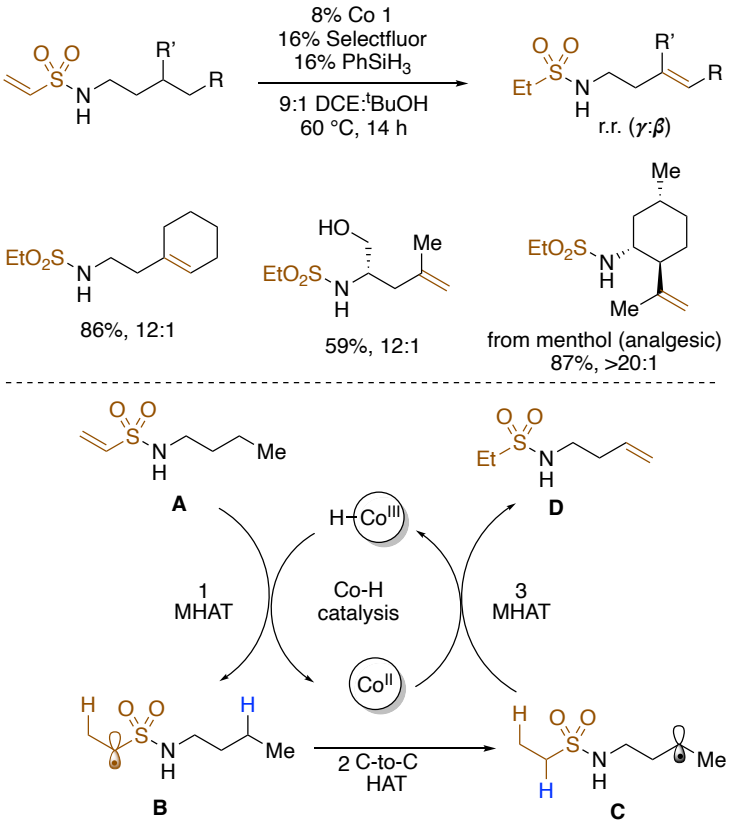

Scheme 18. Hydrosulfonylation with arenesulfonyl chlorides and THF.

After some deep diving into this work, we encountered actual intramolecular 1,5-HAT via α-sulfonyl radical after cyclisation when a longer chain was present on the other part of the molecule (Scheme 19). This part of the work has not yet been published and presented as part of Lise Benoist's master thesis.[100]



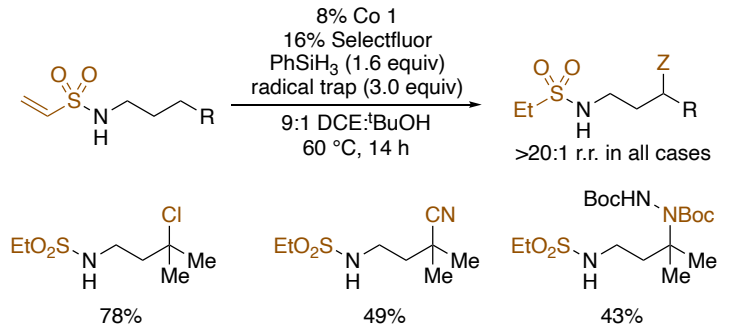

Scheme 19. Hydrosulfonylation via 1,5-HAT and chlorination with ethylsulfonyl chlorides.

In 2022, Nagib, RajanBabu and co-workers developed an elegant cobalt-catalyzed γ-C($sp^3$)–H bond functionalization of amines using a triple HAT strategy.[101] They introduced a new sulfonyl radical chaperone to enable remote desaturation of amines, amino acids, and peptides with excellent chemo-, regio-, and site-selectivity (Scheme 20).



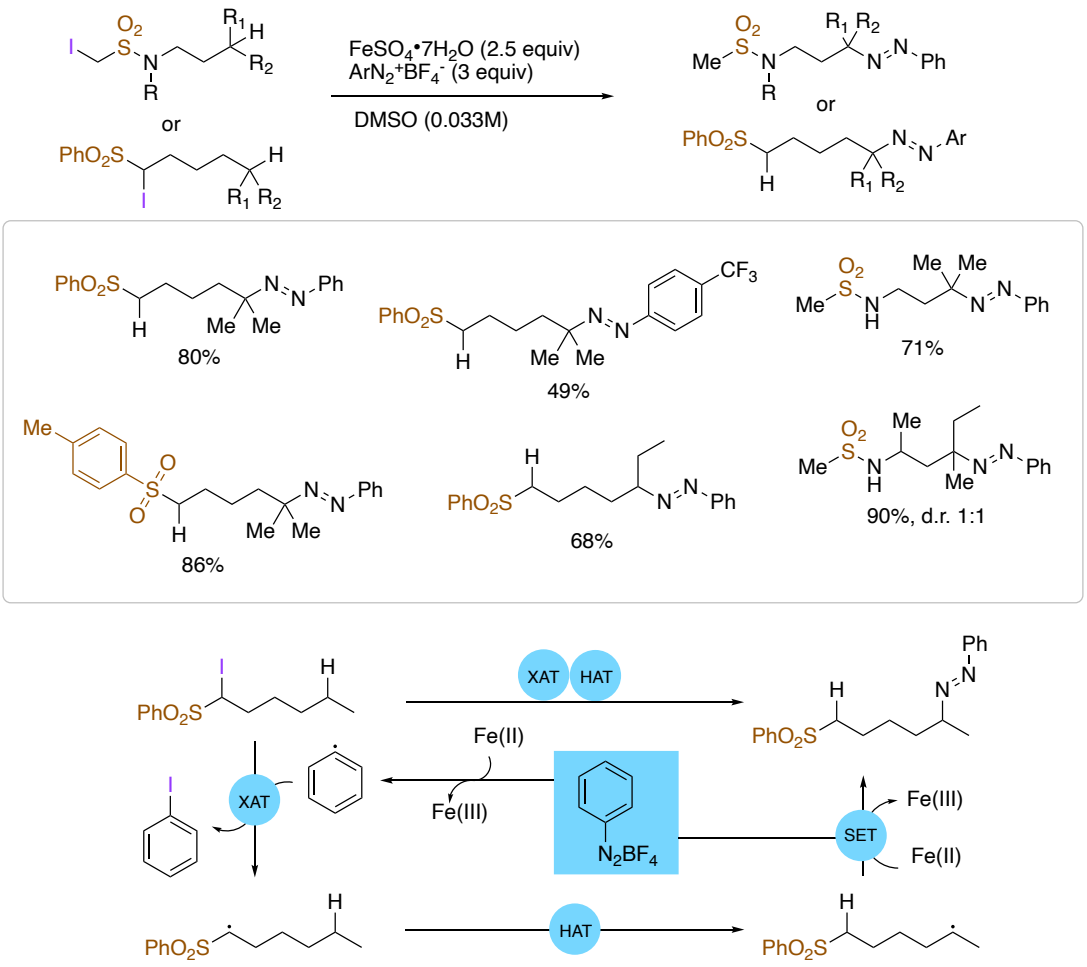

Scheme 20. Remote desaturation via triple HAT.

This reaction's key and challenging step involves HAT from C-to-C, meeting thermodynamic and kinetic requirements, as confirmed by DFT calculations. The reaction sequence begins with a metal H-atom transfer (MHAT) to generate an α-sulfonyl alkyl radical, which then participates in a HAT process to produce a remote alkyl radical, the desaturated product produced in a third HAT between this radical and a CoH species. DFT calculations indicated that the 1,6-HAT process is kinetically favoured over the 1,5- and 1,7-HAT processes. This approach also achieved γ-selective C–Cl, C–CN, and C–N bond formations with TsCl, TsCN, and di-tert-butyl azodicarboxylate (D*t*BAD) radical traps, with exceptional regioselectivities (Scheme 21).




Scheme 21. γ-C-H functionalisation by interrupted radical cascade.

While the PhD work was conducted, a study involving the use of an α-sulfonyl group for remote functionalization was reported by the group of Wu in 2023.[102] Their approach, closely aligned with our research, demonstrates a novel strategy for constructing remote C($sp^3$)–N bonds. This method employs an iron salt and diazonium salt at room temperature to facilitate aryl radical-mediated halogen atom transfer combined with intramolecularly regioselective HAT. Wu's team tested this methodology using aliphatic sulfones, sulfonamides, and sulfonates, showcasing its versatility in synthesising aryl diazo-compounds (Scheme 22). However, reactions with different diazonium salts gave moderate yields, and substituted sulfones delivered similar results, notably increasing the yield in tertiary positions. A study on sulphonamides' scope also shows higher yields with tertiary substrates and average with secondary—a few trials with sulfonates delivered poor to moderate yield with isomerisation of azo product.




Scheme 22. Remote functionalization via 1,5-HAT with diazonium salts.

Considering the extensive research documented in the literature regarding the use of sulfones

as precursors for 1,5-HAT and their potential for further functionalization, we were inspired to pursue additional investigations in this direction. These studies will be presented in the next chapter, where we aim to explore and expand upon the existing methodologies, possibly uncovering new synthetic applications and enhancing the understanding of sulfone chemistry in organic synthesis.

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# Chapter 6

# Remote C-H Functionalisation Using α-Sulfonyl Radicals

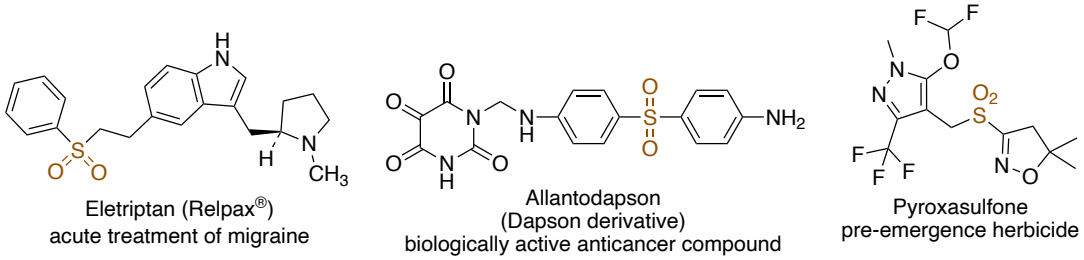
This chapter includes a Draft manuscript.

# Chapter 6 – Remote C-H Functionalisation Using α-Sulfonyl Radicals

## 6.1 Draft manuscript

### 6.1.1 Introduction

Sulfones are essential and versatile compounds in organic synthesis, featuring prominently in various natural compounds[1] and analogues[2,3] that exhibit biological activities, including antifungal, antibacterial, and anti-HIV properties. As representatives, some examples are Eletriptan, which is used in the acute treatment of migraine,[4,5] Allantodapson is a biologically active anticancer compound,[6] and Pyroxasulfone, which is used as a pre-emergence herbicide[7,8] illustrated in Scheme 1.




Scheme 1. Biologically active compounds containing sulfone group.

The remarkable versatility of sulfonyl groups is well-documented; a carbon atom attached to a sulfone can be converted into an anion, a cation, a radical, or some combination of these under varying conditions. While the rich chemistry of sulfones is widely acknowledged and has been extensively explored in many books[9,10] and reviews,[11–24] the literature could be more comprehensive. Specifically, compounds with bis-sulfonyl groups are still in need of further investigation.[25]

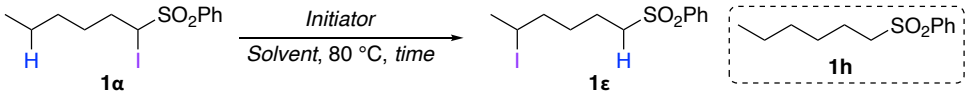
Intramolecular 1,5-hydrogen atom transfer (HAT) reactions are prevalent in free radical chemistry, typically involving heteroatoms or carbon-centred radicals.[26] Inspired by Masnyk's work from 1997,[27] we explored the process further and expanded it to remote C-H functionalisation. During this study, we witnessed experimental evidence of the reversibility of the 1,5-HAT process and extended the study on bis-sulfones for the first time.

## 6.1.2 Results with mono-sulfones

### a) Optimisations of the 1,5-HAT process with 1-iodoalkyl mono-sulfones

The optimisation trials were conducted with an easily accessible substrate ((1-iodohexyl)sulfonyl)benzene[28] **1α** in different solvents such as benzene (PhH), ethyl acetate (EtOAc) and α,α,α-trifluorotoluene (TFT) using mainly di-*t*-butyl hyponitrite (DTBHN) as the initiator (Table 1). Reagents were mixed under an inert atmosphere of argon, and the reaction vessel was quickly immersed in the pre-heated oil bath at 80 °C to initiate the radical process. It was protected from light with aluminium foil. [1]

Table 1. Optimisation of the 1,5-Iodine atom transfer process (IAT). The reactions were performed on a 1.0 mmol scale in 0.2 M concentration.[1]



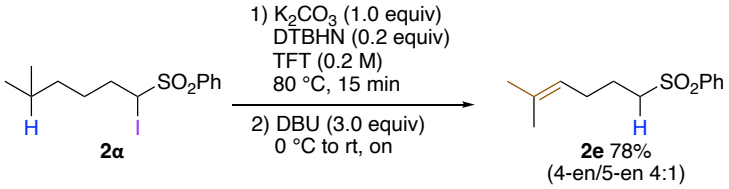

| Entry | Solvent | Initiator | Time | Yield |
|---|---|---|---|---|
| 1 | PhH | DTBHN 20 mol%[a] | 3 h | 63%[b] |
| 2 | EtOAc | DTBHN 20 mol%[a] | 2 h | 33%[c] |
| 3 | EtOAc | DLP 100 mol% | 2 h | 41%[d] |
| 4 | TFT | DTBHN 40 mol%[a] | 2 h | 75% |

[a] Added in two portions. [b] 11% of ((1-iodohexyl)sulfonyl)benzene **1α** back. [c] 53% of ((1-iodohexyl)sulfonyl)benzene **1α** back. [d] ~30% reduced product (hexylsulfonyl)benzene **1h** was isolated.

The first reaction ran with 10 mol% of DTBHN, with the second portion added after 1.5 hours in benzene as a solvent, yielding the desired 1,5-iodine atom transfer (IAT) product **1ε** in 63% with 11% of the starting material **1α** back as a separate fraction. EtOAc was tested under similar conditions, using a shorter reaction time (2 hours). The desired product **1ε** was obtained in 33% yield, with 53% of unreacted **1α**. Low conversion indicates that the initiator load might have been insufficient, and EtOAc might not be the best solvent for this process. The reaction was repeated with 1.0 equivalent of DLP under the same reaction conditions. It provided a slight increase in yield of 41% compared to entry 2, but the formation of

[1] The letters used in the numbering of the compounds has been used as follow: α: functionalization at position 1 relative to the sulfonyl group; ε: functionalization at position 5 relative to the sulfonyl group; h: deiodinated product; d: deuterated product; e eliminated product resulting from HI elimination; r: rearranged product.

deiodinated product **1h** (30%) was observed. The latter is believed to be formed through H-atom abstraction from DLP. Considering all the trials and the need for a non-H-atom donor solvent with a high boiling point and low toxicity, α,α,α-trifluorotoluene (TFT) was our next choice. It is commonly used in the industry. Running the reaction in TFT with slightly increased 0.2 equivalents of DTBHN and the second portion added after 1 hour afforded clean product **1ε** in 75% yield. Interestingly, no starting material or other side products were isolated, and this was the best result we could get with 1,5-HAT to a secondary radical. Under these optimised conditions, the reaction of **2α** provided a complex mixture of iodide **2ε** and alkenes **2e**. A one-pot, two-step approach leading to alkene **2e** was developed. Potassium carbonate was added in the first step to neutralise the traces of HI formed during the reaction. Using 0.2 equivalents of DTBHN in TFT at 80 °C, the 1,5-HAT process was fully finished in 15 minutes (Scheme 2). Then, the addition of 3.0 equivalents of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) at 0 °C for the next step[29] stirred overnight afforded the product **2e** in 78% as (4-en/5-en 4:1).



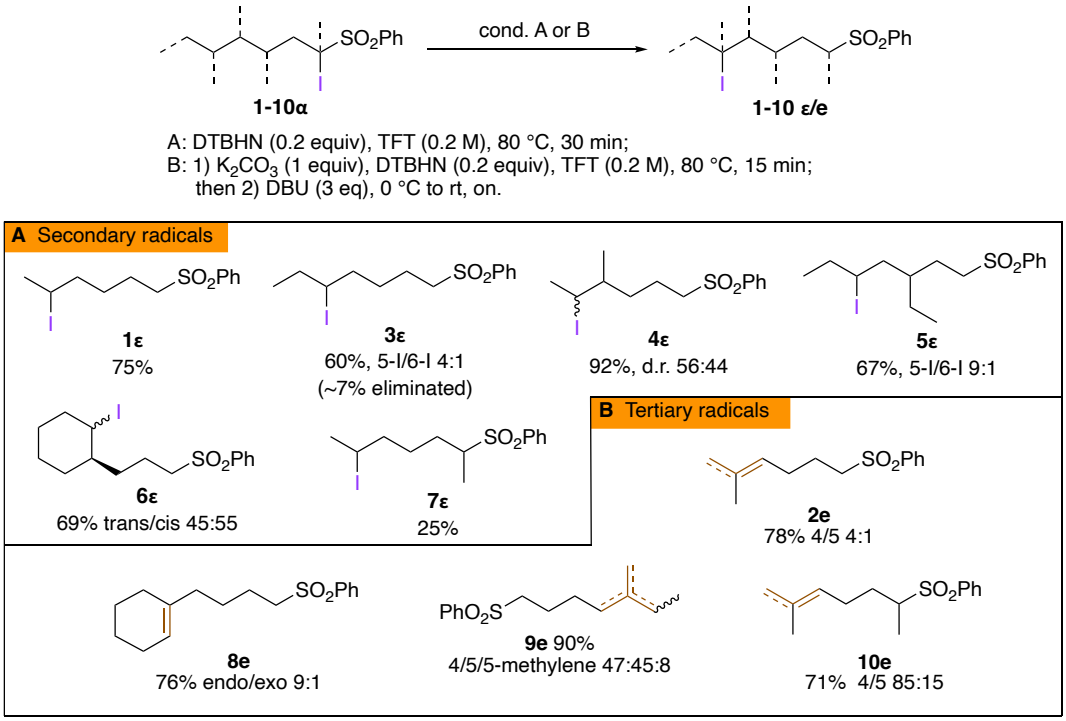

Scheme 2. 1,5-HAT followed by an elimination process for a tertiary 1-iodoalkyl mono-sulfone.

## b) The isomerisation of 1-iodoalkyl mono-sulfones through 1,5-HAT

The optimised conditions from Table 1 (conditions A) were applied to a wide range of 1-iodoalkyl mono-sulfones to investigate the scope of the 1,5-IAT process, shown in Scheme 3. Secondary radical precursors were investigated first. The simplest 1-iodoalkyl mono-sulfone ((1-iodoheptyl)sulfonyl)benzene **1α** delivered product **1ε** in 75% as a clean product. A substrate **3α** with the longer chain provided **3ε** in 60% as a 4:1 mixture of 1,5- and 1,6-IAT products, respectively, and 7% of the eliminated side product was also isolated. Under condition A, reactions were finished in 30 minutes. Substituted substrates with methyl and ethyl groups on the alkyl chain were also tested. ((1-Iodo-4-methylhexyl)sulfonyl)benzene (**4α**) delivered the desired product **4ε** as a 1:1 mixture of diastereomers in 92% yield. Product **5α** was obtained from **5ε** as a 9:1 mixture of 1,5- and 1,6-IAT, respectively, in 67% yield. Compared to the outcome of product **3ε**, we can see that substituents slightly increase the

selectivity of 1,5- over 1,6-HAT. Sterically rigid substrate **6α** was also tested, which gave the same results as in Masnyk's work,[27] yielding product **6ε** in 69% yield as a *cis/trans* 55:45 mixture. Finally, the tertiary α-iodosulfone **7α** was examined. It gave **7ε** in 25% yield together with the deiodinated starting material and alkenes.

Tertiary radical precursors were investigated next, using the one-pot, two-step procedure from Scheme 3 (conditions B). Substrate **2α** delivered product **2e** in 78%. α-Iodosulfone **8α** gave **8e** in 76%. A tertiary radical precursor with longer alkyl chain **9α** was also investigated, providing **9e** in 90% yield as a mixture of three regioisomers. The α-iodo-α-methylsulfone **10α** delivered the alkene **10e** in 71%.



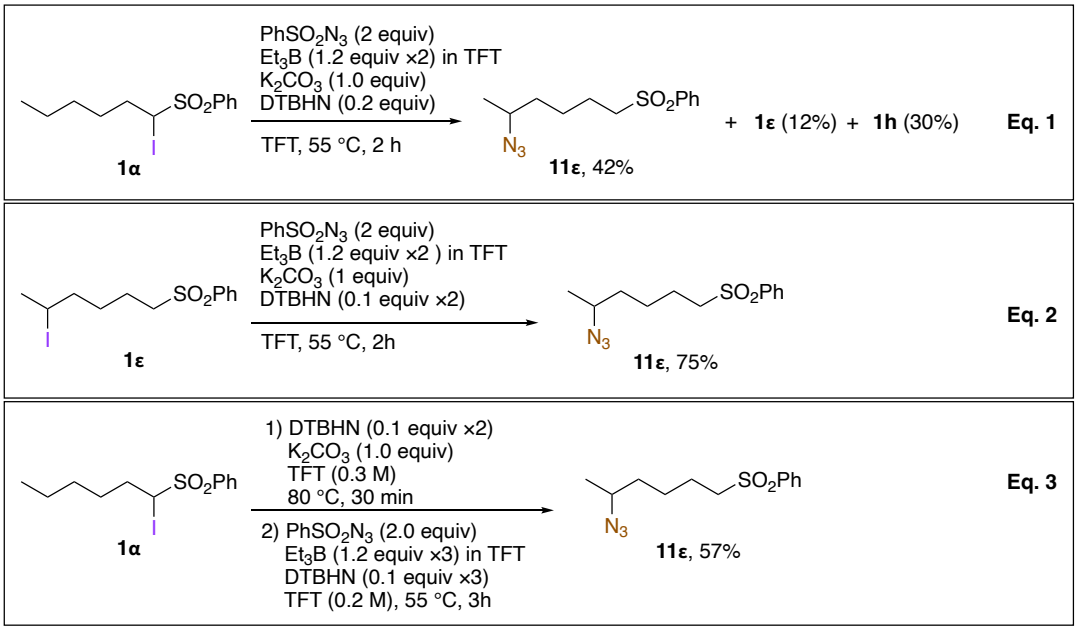

Scheme 3. Isomerisation of 1-monosulfones through 1,5-HAT. The reactions were performed on a 0.5 mmol scale.

## c) ε-C-H functionalisation

Remote azidation was investigated first with substrate **1α** and benzenesulfonyl azide ($PhSO_2N_3$). Reactions were performed in TFT with triethylborane as a chain transfer reagent and DTBHN as an initiator. Adding potassium carbonate positively impacted the reaction by neutralising a small amount of HI produced during the reaction, minimising the formation of unsaturated side products. All reagents were mixed under an Ar atmosphere, protected from

light and immersed in the pre-heated oil bath to initiate the radical process. Under these conditions, **1α** afforded the azide **11ε** in 42% yield together with the ε-iodide **1ε** (12%) and the deiodinated product **1h** (30%) (Scheme 4, eq. 1).

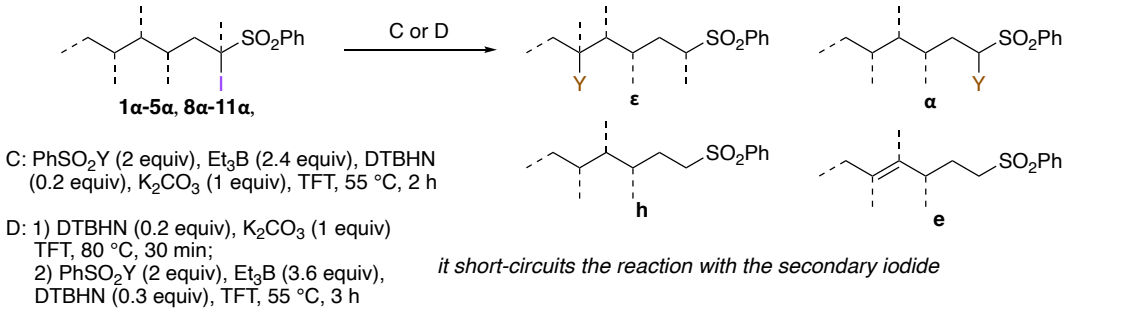
To check the efficacy of the azidation step, the ε-iodosulfone **1ε** was azidated under the same reaction conditions (Scheme 4, eq. 2). This resulted in 75% of the desired product **11ε** with traces (3%) of starting substrate **1ε**. This indicates that the 1,5-HAT process from the α-sulfonyl radical is slower than its competing reduction, most probably by abstracting an H-atom from $Et_3B$. To avoid the formation of the deiodinated product **1h** observed in equation 1 (Scheme 4), a one-pot, two-step azidation procedure was developed (Scheme 4, eq. 3). First, compound **1α** with $K_2CO_3$ (1 equiv) was treated with DTBHN according to conditions closely related to the one developed in Scheme 2. Then, benzenesulfonyl azide (2.0 equiv), $Et_3B$ (1.2 equiv in three portion) and DTBHN (10 mol% in three portions) were added to the reaction mixture containing mainly the translocated ε-iodide **1ε**. The reaction was stirred at 55 °C for 3 hours to afford the desired azide **11ε** in 57% yield.

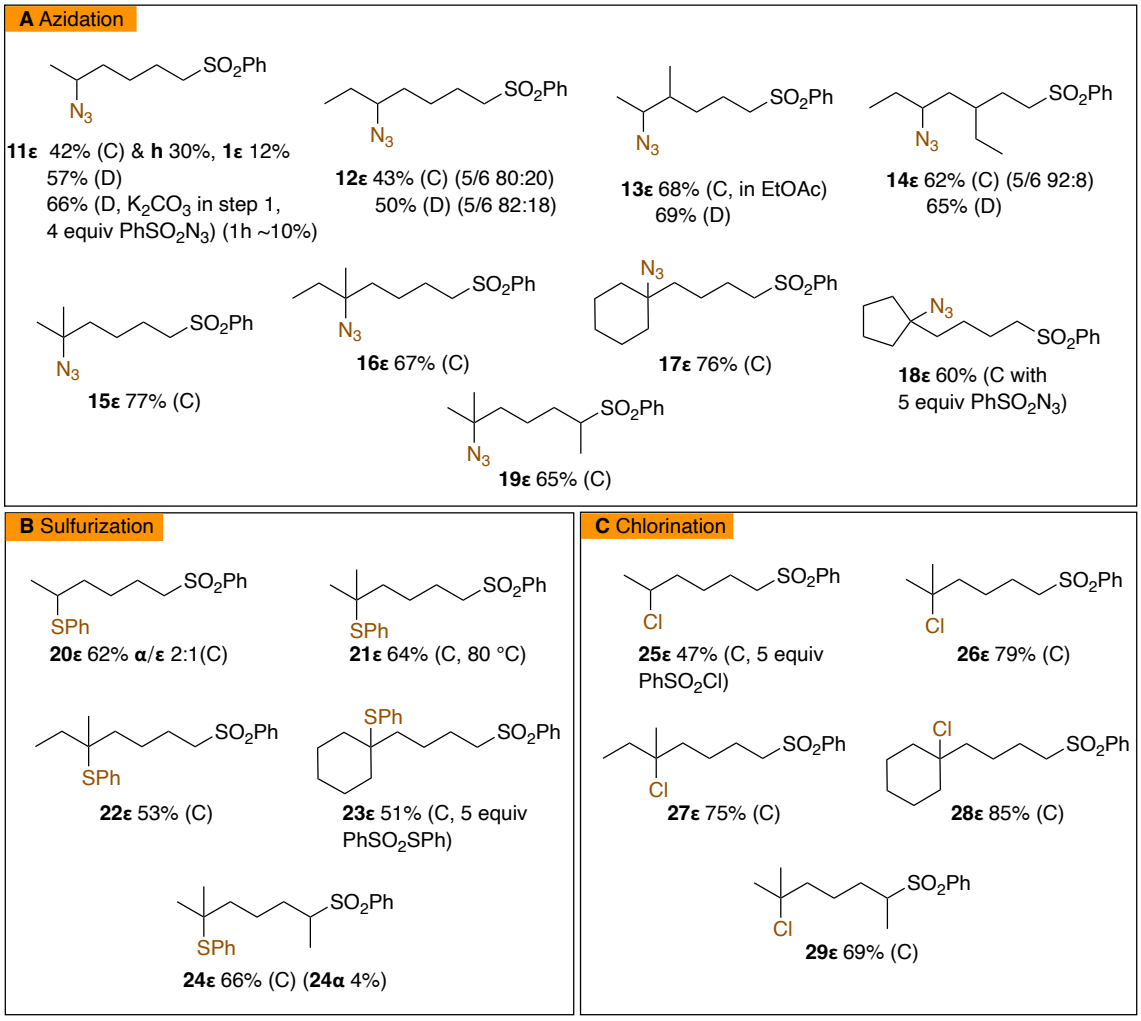



Scheme 4. Optimisation of the remote C-H azidation with mono-sulfones. The reactions were performed on a 0.5 or 1.0 mmol scale, in 0.2 M concentration.

Next, the scope of the remote C-H functionalisation of different 1-iodoalkyl mono-sulfones was investigated. The azidation was investigated first using $PhSO_2N_3$ as an azidating agent. Reactions were run either in one-step (method C) or two-step (method D) reaction conditions.

Results are summarised in Scheme 5 (A). Under condition C, the secondary radical precursors **1α, 3α–5α** delivered the desired azidation products **11ε–14ε** in moderate to good yields. The main trend is that the substituted substrates delivered higher yields than non-substituted ones. The regioselectivity (5/6 80:20) for product **12ε** was the same as for product **3ε** in Scheme 3. Condition D provided slightly better yields in all cases where it was used. Next, azidation of tertiary radicals was investigated with **2α**, **8α–11α** delivering the products **15ε–19ε** in good yields under condition A. Interestingly, the α-methylated iodide **7α** provided the translocated azide **19ε** in 65% yield. Other sulfonyl radical traps were investigated. The sulfurisation with $PhSO_2SPh$ was attempted first (Scheme 5, B). The secondary radical precursor **1α** was examined first and afforded an ε/α 34:66 mixture of the thioester **20** in 62% yield. Reactions involving tertiary radicals generated from **2α**, **8α–9α** afforded the tertiary sulfides **21ε–23ε** in 51-64% yields. The α-methylated iodide **10α** afforded the sulfide **24ε** in 66% yield together with a small amount of **24α** (4%). The more electrophilic $PhSO_2Cl$ radical trap was also examined (Scheme 5, C). The reaction with **1α** gave the chloride **25ε**. No chlorination occurs at the α position, presumably due to the increased electrophilicity of $PhSO_2Cl$ compared to $PhSO_2SPh$. In this case, the translocated iodide **1ε** (27%) was also formed despite the use of a 5-fold excess of the fluorinating agent. Attempts to convert the translocated iodide **1ε** to **25ε** upon treatment with $PhSO_2Cl$ under the same reaction condition failed to give the desired chloride, presumably due to a fast reaction of the ethyl radicals generated from $Et_3B$ with the chlorinated trap. This process short-circuits the abstraction of the secondary iodide, indicating that the two-step procedure D used successfully for the azidation reaction is unsuitable for the chlorination process. Tertiary chlorides **26ε–29ε** were obtained in good yields.



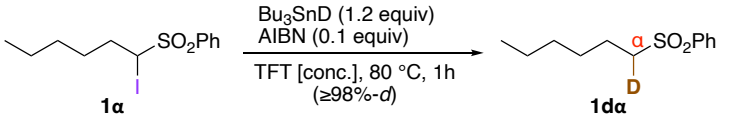

Scheme 5. Remote C-H functionalisation of 1-mono-sulfones through 1,5-HAT. The reactions were performed on a 0.5 mmol scale.

## d) Reversibility of 1,5-HAT process in α-sulfonyl radicals

### *Deuteration reactions*

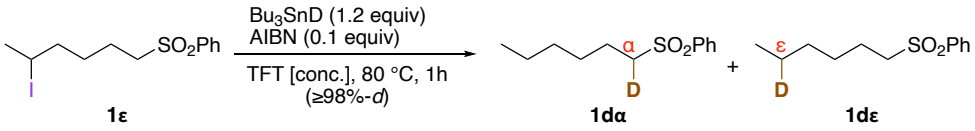
To get a better understanding of this reaction, the possibility that the 1,5-HAT step is reversible was examined. For this purpose, deuteration experiments were run first. The deuteration reactions with $Bu_3SnD$ were run with the secondary iodides **1α** and **1ε**. The

results are summarised in Scheme 6. Starting from **1α** (Scheme 6, eq. 1), only the α-deuterated product **1dα** was obtained in excellent yields with ≥98% deuterium incorporation. This demonstrates that the deuteration of an α-radical is faster than the 1,5-HAT process, even in diluted conditions. The reaction starting with **1ε** was investigated next (Scheme 6, eq. 2). At the highest concentration (0.5 M), only ε-deuterated product **1dε** was observed. At 0.05 M and 0.01 M, α/ε 3:97 mixtures of **1d** were obtained in ≥98% and 92% yields, respectively. Under more diluted reaction conditions (0.005 M), an α/ε 18:82 mixture was obtained in 92% yield. These results indicate that the hydrogen atom transfer from the ε to α-position competes at the highest dilution with the deuterium atom transfer from $Bu_3SnD$ to the secondary alkyl radical.




Eq. 1

| 1α | yield | α/ε |
|---|---|---|
| 0.5 M | 95% | >98:2 |
| 0.05 M | ≥98% | >95:5 |
| 0.005 M | >98% | >95:5 |

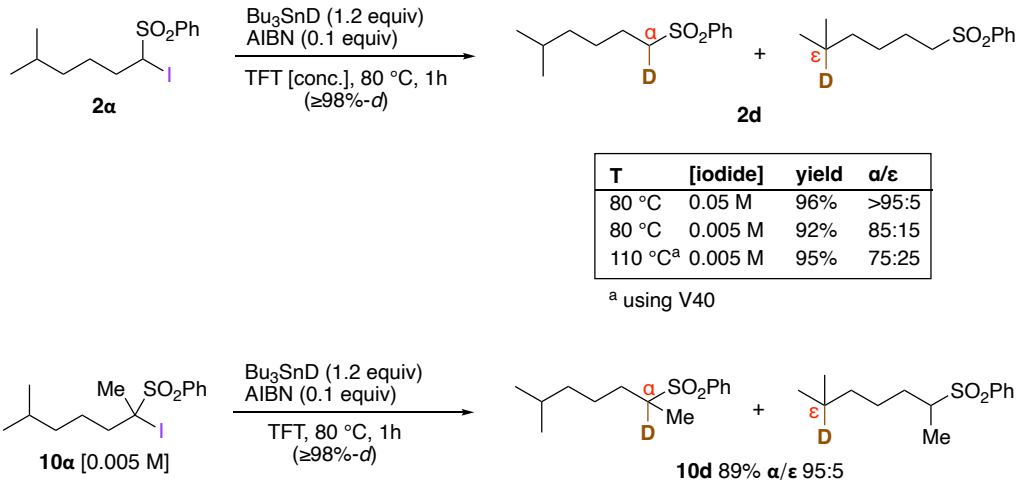



Eq. 2

| 1ε | yield | α/ε |
|---|---|---|
| 0.5 M | 90% | <2:98 |
| 0.05 M | ≥98% | 3:97 |
| 0.01 M | 92% | 3:97 |
| 0.005 M | 92% | 18:82 |

Scheme 6. Deuterations **1α** and **1ε**.

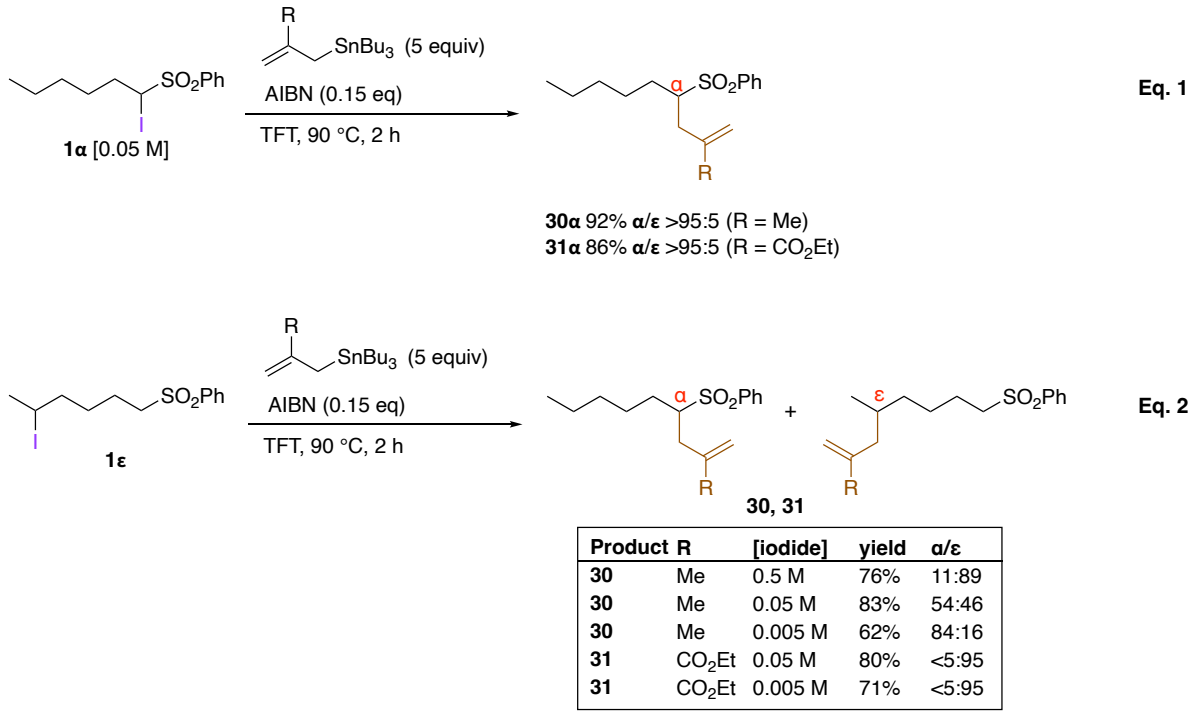
Deuteration reactions with **2α** and **10α** were also conducted at different concentrations (Scheme 7). At 80 °C and 0.05 M concentration, **2α** delivered only α-deuterated product **2dα** in 96%. Diluting further the reaction to 0.005 M provided **2d** in 92% yield as an α/ε 85:15 mixture. By running the reaction at a high temperature (110 °C) using 1,1'-azobis(cyclohexane-1-carbonitrile) (V40) as an initiator, the amount of ε-product was increased to an α/ε 75:25 ratio. Finally, deuteration of the α-methylated α-iodosulfone **10α** at the highest dilution (0.005 M) gave **10d** as an α/ε 95:5 mixture in 89% yield.




Scheme 7. Deuterations **2α** and **10α**.

### *Allylation reactions*

The reversibility of the HAT involving α-sulfonyl radicals was further investigated with allylation reaction. Two series of experiments starting from either the α-iodosulfone **1α** or from the ε-iodosulfone **1ε** were run. Starting from **1α** (0.05 M) and tributyl(2-methylallyl)stannane (5.0 equiv) only α-allylated product **30α** was isolated in 92% yield. This was expected due to the electrophilic properties of α-sulfonyl radical and excess of the allylstannane derivative (Scheme 8, eq. 1). Then, the more electrophilic ethyl 2-((tributylstannyl)methyl)acrylate was used under the same conditions, which also delivered only α-allylated product **31α** in 86% yield. Reactions starting from ((5-iodohexyl)sulfonyl)benzene **1ε** were investigated next (Scheme 8, eq. 2). With the electron-rich 2-methylallylsulfone, at 0.5 M concentration in **1ε**, an α/ε 11:89 mixture of **30** was obtained in 76% yield. At 0.05 M concentration, an α/ε 54:46 mixture was obtained in 83% yield. Further dilution (0.005 M) resulted in an α/ε 84:16 mixture of **30** in 62% yield. Translocations from the ε to the α-position were observed with the electron-rich radical trap due to a mismatch in polarity with the ε secondary alkyl radical. As anticipated, allylation reactions with the electron-deficient substituted allylstannane (R = $CO_2Me$) gave the **31ε** exclusively, even at the lowest 0.005 M concentration (Scheme 8, eq. 2). In this case, a polarity match between the nucleophilic secondary alkyl radical and the electron-deficient radical trap favours the direct trapping of the radical over the ε to α 1,5-HAT transfer.




| Product | R | [iodide] | yield | α/ε |
|---|---|---|---|---|
| **30** | Me | 0.5 M | 76% | 11:89 |
| **30** | Me | 0.05 M | 83% | 54:46 |
| **30** | Me | 0.005 M | 62% | 84:16 |
| **31** | $CO_2Et$ | 0.05 M | 80% | <5:95 |
| **31** | $CO_2Et$ | 0.005 M | 71% | <5:95 |

Scheme 8. Reaction of **1α** and **1ε** with allylstannanes.

## 6.1.3 HAT with bis-sulfone

The adaptability of sulfones to their chemical environments makes molecules containing two or more sulfones rich in synthetic potential, especially when these groups are attached to a single carbon atom. In such structures, termed geminal bis-sulfones, each carbon-sulfur (C-S) bond can be activated independently, allowing the central carbon to act as a platform for generating diverse and unique synthons. Even more unusual reactive species can arise if the central carbon of the bis-sulfone possesses hydrogen atoms, as these acidic C-H bonds can be deprotonated and further functionalised.[24,30] Cronyn highlighted bis-sulfones' potential to mimic highly reactive intermediates as early as 1952.[31] It showed that bis-sulfones could act as surrogates for otherwise challenging to generate synthons like the methane dianion, despite the stringent conditions required to break the C-S bonds. This early work paved the way for understanding the full synthetic utility of bis-sulfones.

Since the initial findings, the synthetic community has increasingly recognised the versatility of geminal bis-sulfones as surrogates for reactive intermediates that are otherwise challenging or impossible to access directly. The central carbon of a geminal bis-sulfone can participate in up to four new bond-forming reactions, establishing it as a potent synthetic

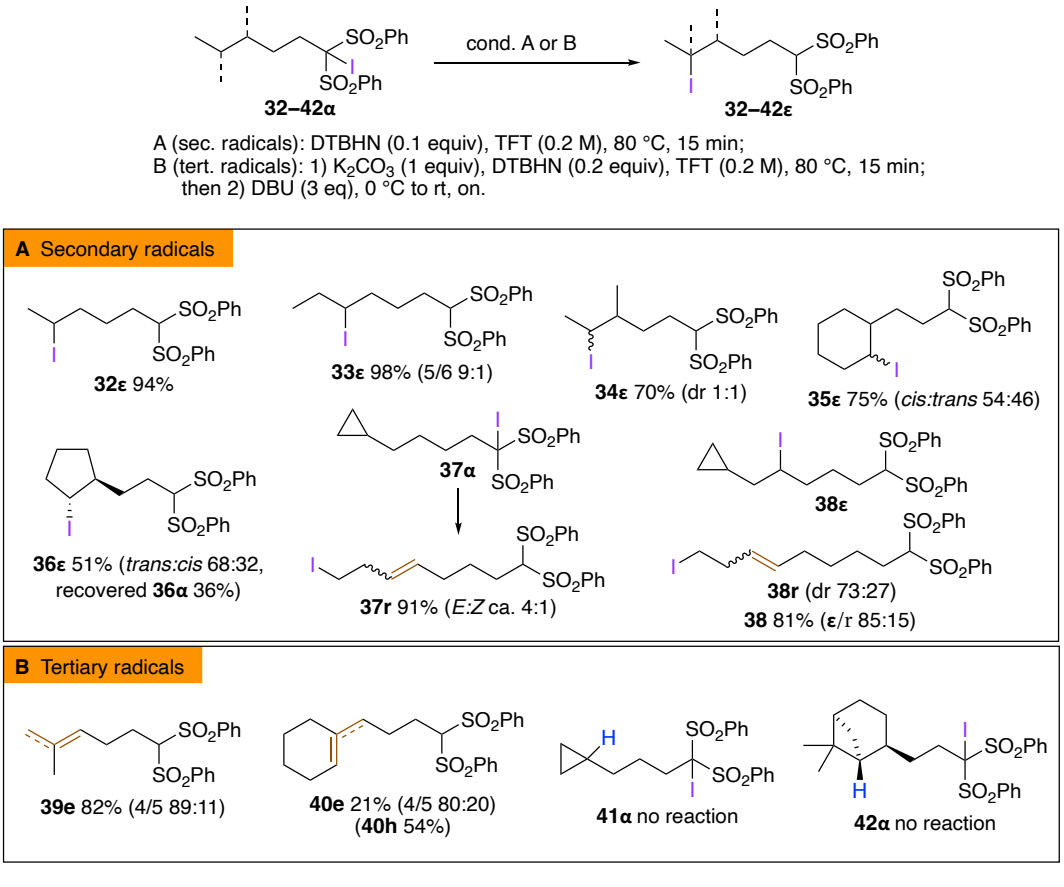
linchpin.[24,30] Bis-sulfones like bis(phenylsulfonyl)methane (BPSM) or 1,3-benzodithiole tetroxide (BDT) are frequently used in organic synthesis to create synthons that originate from methane. Unlike the anionic chemistry of gem-bis-sulfones, their radical chemistry is very limited.[32–36] α-Iodo-α-alkyl-gem-bis-sulfones are readily prepared by alkylation and iodination from bis(benzenesulfonyl) methane. They are, therefore, very attractive substrates for remote activation of the C-H bond under the conditions used for the mono-sulfones. The geminal bis-sulfone moiety should enhance the electrophilicity of the generated α-bis-sulfonyl radical and hopefully favour the 1,5-HAT processes.

## a) Isomerisation of 1-iodoalkyl bis-sulfones

The optimised conditions from Scheme 3 were applied to 1-iodoalkyl bis-sulfones to investigate the scope of the 1,5-IAT process. A series of experiments were run with substrates suitable for the generation of secondary alkyl radicals via 1,5-HAT (Scheme 9, A). The isomerisation of (1-iodohexane-1,1-diyldisulfonyl)dibenzene **32α** delivered the ε-iodide **32ε** in 94% yield. The reaction was clean, high-yielding, and fast (15 minutes). Only 0.1 equivalent of DTBHN was required to reach complete conversion. Other α-iodoalkyl-bis-sulfones **33α**–**38α** affording secondary alkyl radicals were investigated. Translocated products **33ε**–**35ε** were obtained in high yields. The iodinated 5-membered ring system **36ε** was less efficient, and a substantial amount of the starting iodide **36α** was recovered. Iodide **37α** provided, as expected, the ring-opened product **37r** in high yield. The iodide **38α** provided an 85:15 mixture of **38ε** and **38r** (dr 73:27). This example was examined to investigate possible reversibility of the 1,5-HAT that could favour a slower 1,6-HAT transfer process leading to the ring opening product **38r**. By comparing the 1,5-HAT ratio observed for compound **33α** (5/6 90:10) with substrate **38α** (ε/r 85:15), only a slight increase of the 1,6-translocation product was observed, indicating that only marginal (if any) reversibility is involved in this process. The high efficacy of the examples described here (in Scheme 9, A) demonstrates that bis-sulfones are more efficient at promoting translocation processes leading to secondary alkyl iodides than the corresponding mono-sulfones.

Precursors leading to tertiary radicals were examined next using the two-step procedure used for related mono-sulfones (Scheme 9, B). The acyclic **39α** delivered the alkene **39e** in 82% yield. The cyclohexyl containing **40α** gave **40e** in a low 21% yield. The major product in this

case was the deiodinated sulfone **40h**. Attempts to activate a tertiary cyclopropane C–H bond with **41α,** a tertiary bridgehead position of the (–)-nopol derivative **42α** failed to give any isomerised iodide and the starting iodides were recovered. This short study indicates that alkene generation via transient tertiary radicals is less efficient with bis-sulfones than with mono-sulfones.

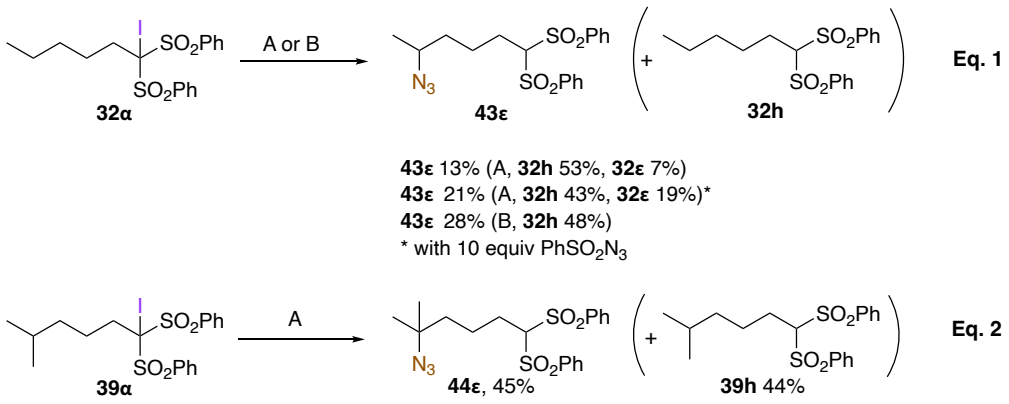



Scheme 9. The isomerisation of α-bis-sulfones through 1,5-HAT.

## b) Remote C-H functionalisation of 1-iodoalkyl bis-sulfones

Attempts to prepare azides from α-iodo-bis-sulfones via reaction with benzenesulfonyl azide prove to be more challenging than expected. The reaction of **32α** using the one-step cascade reaction run with $Et_3B$ and DTBHN provided the azide **43** in low yield (13%) together with the deiodinated sulfone **32h** (53%) (Scheme 10, eq. 1). Increasing the excess of $PhSO_2N_3$ to 10.0 equivalents had only a marginal effect on the result. Using the two-step process (condition B) developed with mono-sulfone (Scheme 4, eq. 3) led to only to a slightly improved yield as **43ε** (28%) was obtained. The major product remained the deiodinated sulfone **32h** (48%). Azidation of **39α** provided the tertiary azide **44** in 45% yield using the one-pot two-step procedure B (Scheme 10, eq. 2). In this case, too, a large amount of the deiodinated bis-

sulfone **39h** (44%) was obtained.

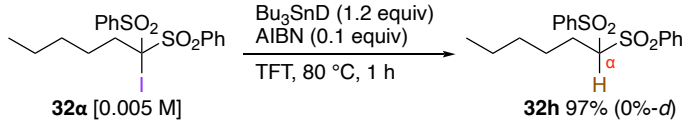



Scheme 10. Remote C-H functionalisation of bis-sulfones.

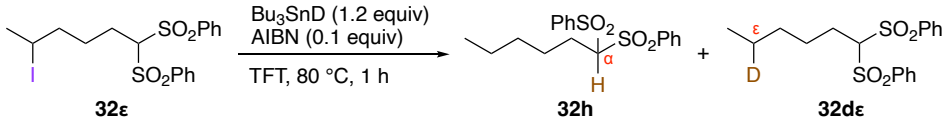
## c) Deuteration reactions

Deuteration reactions of **32α** with $Bu_3SnD$ were investigated at 80 °C (Scheme 11, eq. 1). At the most diluted concentration of 0.005 M, **32α** delivered the deiodinated but not-deuterated product **32h** in 97%. The absence of deuterium incorporation was attributed to a fast D/H exchange process occurring during the work-up and purification processes. The following experiments further demonstrated the rapid erosion of the deuterium content. A deprotonation of **32h** with sodium hydride in THF and deuteration with the addition of 2 equivalents of $D_2O$ stirred for 1 hour were performed. The $^1H$ NMR analysis of the crude sample with no work-up showed **32dα** with no H-signal at the α-position, which can be depicted as full D-incorporation at the α-position. However, after work-up with diethyl ether and water followed by evaporation and drying in the vacuum, the $^1H$ NMR spectra of crude product indicated only **32h** (74% yield) with no D-incorporation. Furthermore, a reaction of a 0.5 M solution of **32α** with an excess of $Bu_3SnD$ (1.2 equiv) in the presence of AIBN was performed. After evaporation of the volatiles, $^{13}C$ and $^2H$-NMR analyses of the crude product prior to work-up and purification showed the presence of the deuterated **32dα** with about 50% deuterium incorporation. Next, 5-iodo alkyl bis-sulfone **32ε** was deuterated at three concentrations (Scheme 11, eq. 2). At 0.5 M, product **32dε** was isolated with 74% D-incorporation at position ε. The D-incorporation at position ε went down to 36% at 0.05 M and less than 1% at 0.005 M. At the three concentrations, no D-incorporation was observed

at the α-position after work-up and purification by chromatography on silica gel. Based on these observations, we assume that the α/ε ratio can be directly deduced from the %D-incorporation at position ε.




**32α** [0.005 M] **32h** 97% (0%-*d*) **Eq. 1**

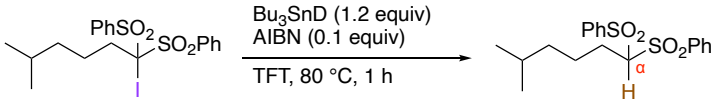



**32ε** **32h** **32dε** **Eq. 2**

| [32ε] | yield | D-inc. α | D-inc. ε | est. α/ε |
|---|---|---|---|---|
| 0.5 M | 91% | 0% | 74% | 26:74 |
| 0.05 M | 89% | 0% | 36% | 64:36 |
| 0.005 M | >98% | 0% | <1% | >99:1 |

Scheme 11. Deuterations of bis-sulfone **32**.

The deuteration of the tertiary radical precursor **39α**, at 0.005 M concentration, gave **39h** in 97% yield, and no D-incorporation (Scheme 12) further confirmed the very fast reaction of the α-sulfonylated radical with tin hydride relative to the 1,5-HAT.



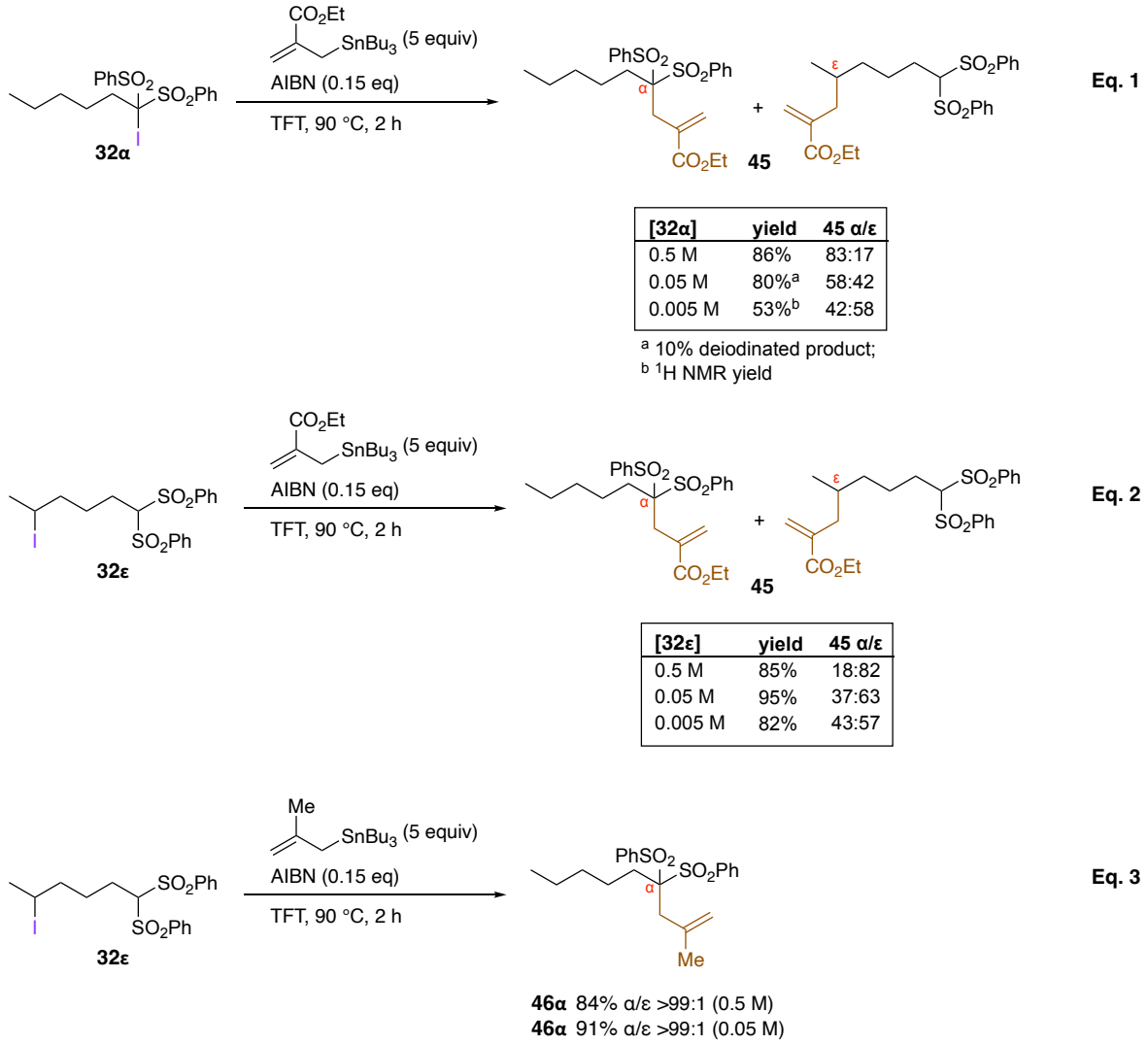

**39α** [0.005 M] **39h** 97% (0%-d)

Scheme 12. Deuterations of bis-sulfone **39α**.

## d) Allylation of bis-sulfones

First, (1-Iodohexane-1,1-diyldisulfonyl)dibenzene **32α** was allylated with the electron-deficient ethyl 2-((tributylstannyl)methyl)acrylate trap at the highest concentration (0.5 M) delivering an α/ε 83:17 mixture **45** in 86% yield (Scheme 13, eq.1). At 0.05 M, the reaction gave an α/ε 58:42 mixture of **45** in 80% yield. Traces of the deiodinated alkyl bis-sulfone 32h were observed. At the most diluted reaction conditions (0.005 M), an α/ε 42:58 mixture of **45** was obtained in 53%. The allylation was also performed with the ε-iodosulfone **32ε** (Scheme 13, eq. 2). At 0.5 M, it gave **45** in 85% yield as an α/ε 18:82 mixture. At 0.05 M concentration, an α/ε 37:63 mixture of **45** was obtained in 95% yield. Finally, at 0.005 M concentration, **45** was obtained in 82% yield as an α/ε 43:57 mixture. Interestingly, this ratio is nearly identical to the one obtained from **32α**, suggesting an equilibrium between the α and the ε radical has

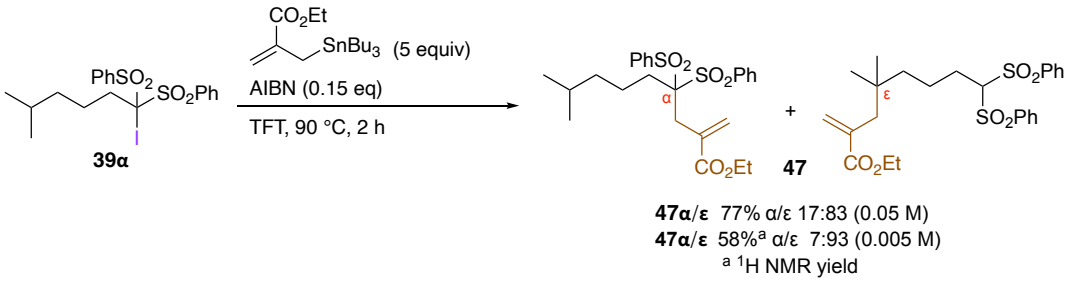
been reached. Allylation of **32ε** with the electron-rich tributyl(2-methylallyl)stannane at 0.05 M and 0.5 M concentrations delivered only the α-allylated product **46α** in 91% and 84% yield, respectively (Scheme 13, eq. 3). This is a further confirmation of the rapidity of the 1,5-HAT process when bis-sulfones are used. Under these conditions, the two radicals α and ε are in fast equilibrium, and the product ratio is determined by the different rates of allylation. The electrophilic bis-sulfonylated α radical reacts much faster with the electron-rich 2-methylallylstanane than the secondary ε alkyl radical.




Scheme 13. Allylation of bis-sulfone **32**.

Allylation of **39α** with the electron-deficient ethyl 2-((tributylstannyl)methyl)acrylate gave **47** as an α/ε 17:83 mixture at 0.05 M concentration and 7:93 at 0.005 M in 77% and 58% yield, respectively (Scheme 14). By analogy to the results in Scheme 13 (eq. 1 and 2), we assume that at 0.005 M, the α and ε radicals are in equilibrium, and the trapping by the allyltin

derivative is slower.

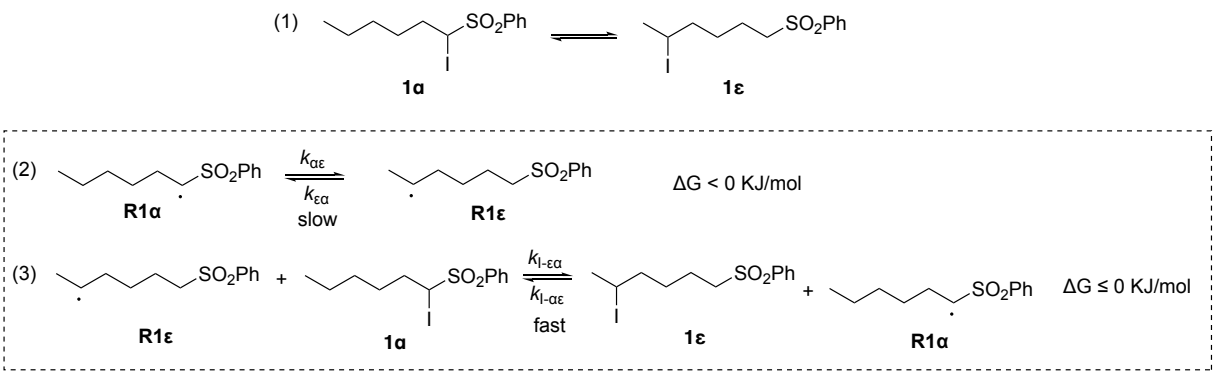



Scheme 14. Allylation of bis-sulfone **39α**.

## 6.1.4 Discussion

### *Iodine atom transfer*

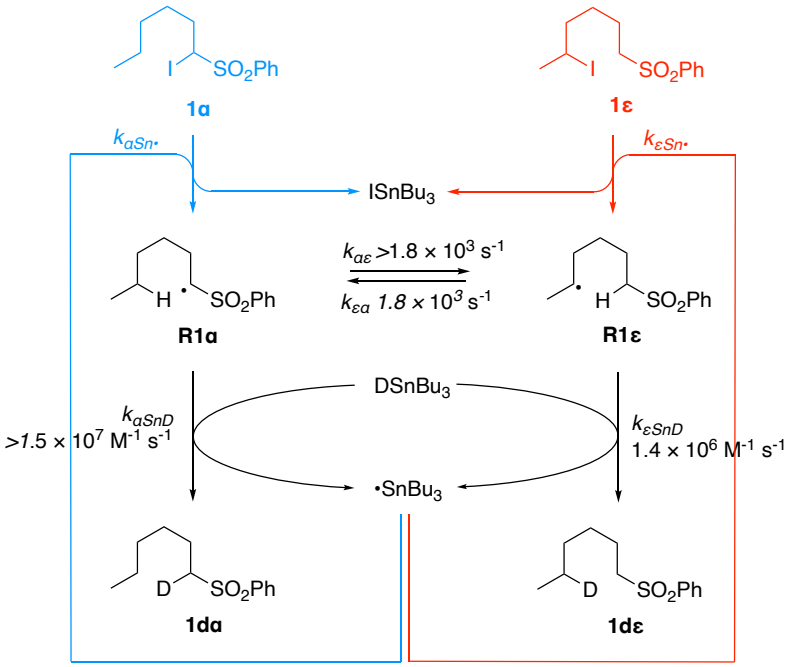
The efficiency of the isomerisation of the α-iodoalkyl sulfone **1α** to ε-iodoalkyl sulfone **1ε** may be the result of a thermodynamic control involving a reversible hydrogen atom transfer. This would imply that ε-iodoalkyl sulfone **1ε** is more stable than the α-iodoalkyl sulfone **1α** (Scheme 15, eq.1). The efficacy of this process is strongly favoured by the fact that the isomerisation process **R1α** to **R1ε** (Scheme 15, eq. 2) is an exergonic process since sulfonyl group have been reported to destabilise radicals slightly.[37] Interestingly, the second step of this chain process (Scheme 15, eq. 3) is also exothermic (or at least close to thermoneutral) even though it converts the more stable radical **R1ε** into the less stable **R1α**. This thermodynamically unfavored process is compensated by the higher stability of the ε-iodoalkyl sulfone **1ε** relative to the α-iodoalkyl sulfone **1α**. The presence of an electron-withdrawing sulfonyl group at the carbon centre bearing the iodide weakens the α-C–I bond. Porter postulated a similar weakening of a C–Br bond to explain the role of Lewis acids in radical bromine atom transfer reactions. In that case, the complexation of an amide moiety by a Lewis acid was weakening an adjacent C–Br bond.[38] This chemistry illustrates once again the unique reactivity of sulfones. By comparison, ester groups are unsuitable for such isomerisation reactions, as the radical translocation step is highly endergonic. Finally, this simple thermodynamic analysis of the isomerisation process rationalises well why the isomerisation leading to tertiary iodides (or alkene after HI elimination) is less efficient even though the isomerisation step (eq. 2) is extremely favourable. Still, the iodine atom transfer step (eq. 3) is now, at best, thermoneutral or even slightly endergonic.




Scheme 15. Thermodynamic aspects of the isomerisation of iodide **1α**.

### *Deuteration of the mono-sulfone **1***

The deuteration experiments, starting with regioisomeric **1α** (blue) and **1ε** (red), follow the mechanism depicted in Scheme 16.




Scheme 16. Mechanism for the deuteration of **1**.

The deuteration experiment starting from **1α** indicates clearly that deuteration of the radical **R1α** by $Bu_3SnD$ is faster than the 1,5-HAT (**R1α** to **R1ε**) even at the lowest 0.005 M concentration tested. Interestingly, the same deuteration starting with **1ε** affords the deuterated product **1d** as an α/ε 18:82 ratio, indicating in this case that the 1,5-HAT (**R1ε** to **R1α**) competes with the reaction of **R1ε** with $Bu_3SnD$. Since the rate of HAT between secondary alkyl radicals and $Bu_3SnH$ has been determined, it is possible to estimate the rate constant $k_{\varepsilon\alpha}$ for the 1,5-HAT from **R1ε** to **R1α**. The rate constant for the reaction of isopropyl

radical with $Bu_3SnH$ has been determined at 300 K as $k_{HAT}$ = 1.5 × $10^6$ $M^{-1}$ $s^{-1}$.[39] The Arrhenius parameters for this reaction are log *A* = 8.71 $M^{-1}$ $s^{-1}$ and $E_a$ = +14.5 ± 2.1 kJ $mol^{-1}$. From this we obtain $k_{SnH}$(80 °C) = 3.7 × $10^6$ l $mol^{-1}$ $s^{-1}$. Moreover, kinetic deuterium isotope effects for $HSnBu_3$/$DSnBu_3$ were determined at KIE = 2.7 for cyclohexyl and KIE = 2.8 for *tert*-Bu radicals.[40]

$$[\mathbf{1d\alpha}]/[\mathbf{1d\varepsilon}] = k_{\varepsilon\alpha}/k_{\varepsilon SnD} \times [DSnBu_3]$$

At 0.005 M in **1ε**, the $Bu_3SnD$ concentration during the reaction can be estimated to be 0.0035 M, the average value between the concentration at the beginning of the reaction (0.006 M) and the end (0.001 M) since 1.2 equivalents of $Bu_3SnD$ were used.

$$[\mathbf{1d\alpha}]/[\mathbf{1d\varepsilon}] = 18/82 = k_{\varepsilon\alpha}/k_{\varepsilon SnD} \times 0.0035\ M)$$

If we take $k_{\varepsilon SnD}$ at 80 °C as 3.7 × $10^6$/2.7 = 1.4 × $10^6$ $M^{-1}$ $s^{-1}$ (that is assuming an H/D isotope effect of 2.7) and, we obtain:

$$k_{\varepsilon\alpha} = (18/82) \times 1.4 \times 10^6\ M^{-1}\ s^{-1} \times 0.0035\ M$$

$$k_{\varepsilon\alpha} = 1.1 \times 10^3\ s^{-1}$$

Based on the simple analysis of Scheme 15, eq. 2, we assume that rate constant $k_{\alpha\varepsilon}$ for the 1,5-HAT from **R1α** to **R1ε** is larger than the reverse process $k_{\varepsilon\alpha}$ = 1.1 × $10^3$ $s^{-1}$.

$$k_{\alpha\varepsilon} > k_{\varepsilon\alpha} = 1.1 \times 10^3\ s^{-1}$$

From the reaction of **1α** with $Bu_3SnD$ at the lowest 0.005 M concentration giving **1d** with an α/ε ratio >98:2, we can write:

$$[\mathbf{1d\alpha}]/[\mathbf{1d\varepsilon}] = k_{\varepsilon SnD} \times [DSnBu_3]/k_{\alpha\varepsilon}$$

$$k_{\varepsilon SnD} = ([\mathbf{1d\alpha}]/[\mathbf{1d\varepsilon}]) \times (k_{\alpha\varepsilon}/[DSnBu_3])$$

$$k_{\varepsilon SnD} = (>98/2) \times (>1.1 \times 10^3/0.0035)$$

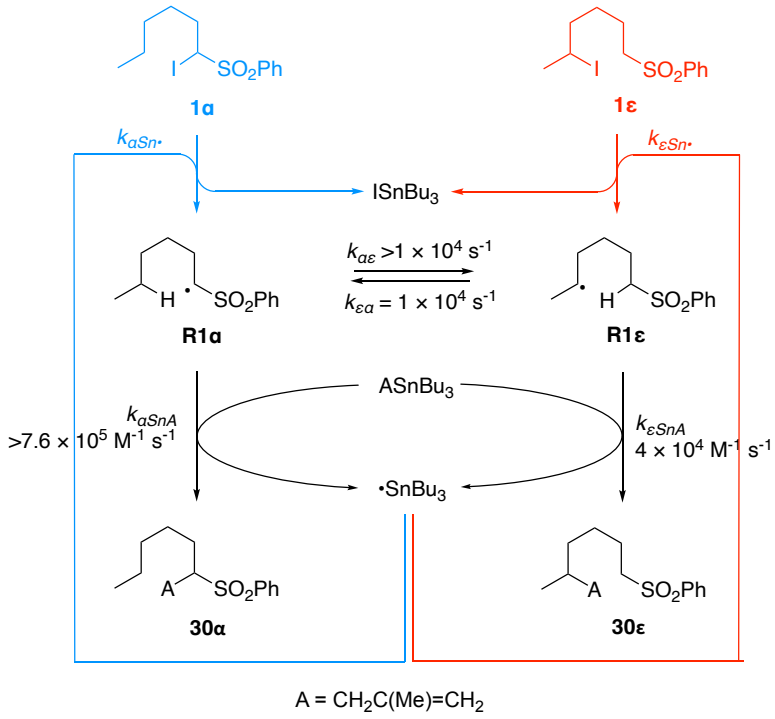
$$k_{\varepsilon SnD} > 1.5 \times 10^7$$

This implies that radical **R1α** is extremely rapidly reduced by the $Bu_3SnD$, pointing towards very strong polar effects.

### *Allylation of the mono-sulfone **1***

The allylation of **1α** with the (2-methylallyl)tributylstannane (5 equivalents) provided only the α-allylated product **30α** at 0.05 M concentration. Interestingly, the ε-iodoalkyl sulfone **1ε** provided **30** as an α/ε mixture at concentrations ranging from 0.5 to 0.005 M. A constant of $k_{\varepsilon SnA}$ = 4 × $10^4$ $M^{-1}$ $s^{-1}$ has been reported for the reaction of secondary radicals with allyltributylstannane.[41] We assume this rate is close to the one for the reaction with the 2-

methylallyl derivative. Therefore, it is possible to analyse the allylation reaction (Scheme 17) similarly to the deuteration reaction.




Scheme 17. Mechanism of allylation of monosulfone **1α** with (2-methylallyl)tributylstannane.

By introducing $k_{\varepsilon SnA} = 4 \times 10^4$ $M^{-1}$ $s^{-1}$ at 80 °C and [allylstannane] = 2.5, 0.25, and 0.025 for [**1α**] = 0.5, 0.05, and 0.005 M, respectively:

$$[\mathbf{30\alpha}]/[\mathbf{30\varepsilon}] = k_{\varepsilon\alpha}/(k_{\varepsilon SnA} \times [Bu_3SnA])$$

$$k_{\varepsilon\alpha} = [\mathbf{30\alpha}]/[\mathbf{30\varepsilon}] \times k_{\varepsilon SnA} \times [Bu_3SnA]$$

$$k_{\varepsilon\alpha} = 11/89 \times 4 \times 10^4 \times 2.5 = 1.2 \times 10^4 \text{ at 0.5M}$$

$$k_{\varepsilon\alpha} = 54/46 \times 4 \times 10^4 \times 0.25 = 1.2 \times 10^4 \text{ at 0.05 M}$$

$$k_{\varepsilon\alpha} = 84/16 \times 4 \times 10^4 \times 0.025 = 5 \times 10^3 \text{ at 0.005 M}$$

$k_{\varepsilon\alpha} = 1.0 \times 10^4$ $s^{-1}$ (average value at 80 °C)

Based on that, we can estimate the $k_{\alpha SnA}$

$$k_{\alpha SnA} = ([\mathbf{30\alpha}]/[\mathbf{30\varepsilon}]) \times (k_{\alpha\varepsilon}/[Bu_3SnA])$$

$$k_{\alpha SnA} = (>95/5) \times (>1.0 \times 10^4 \text{ } s^{-1}/0.25 \text{ M})$$

$k_{\alpha SnA} > 7.6 \times 10^5$ $M^{-1}$ $s^{-1}$

This value is reasonable for the reaction of an electrophilic radical with an electron-rich alkene. The two analyses reported in Schemes 16 and 17 predict the rate of α/ε isomerisation in close accordance ($k_{\varepsilon\alpha} = 1.1 \times 10^3$ $s^{-1}$ (deuteration) and $k_{\varepsilon\alpha} = 1.0 \times 10^4$ $s^{-1}$ (allylation). The value for the allylation is probably slightly too high since we have used for $k_{\varepsilon SnA}$ the rate

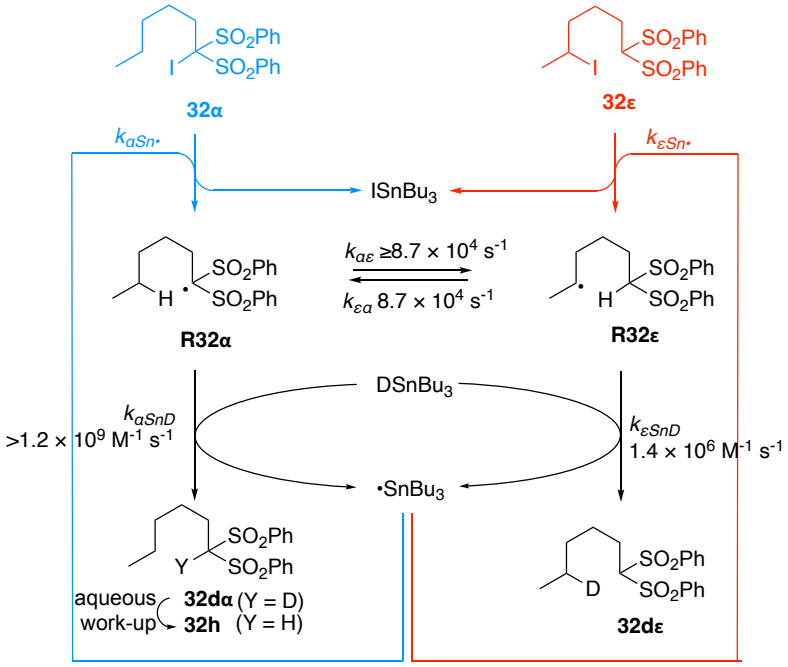
constant for the reaction with the simple allyltributylstannane, and we have run the reactions with the more electron-rich 2-methylallyltributylstannane.

### *Deuteration of the bis-sulfone **32***

The same treatment was made for the bis-sulfone **32** (Scheme 18). It is assumed that the lack of deuteration at the α-position was exclusively due to a fast D/H-exchange process occurring during the work-up. The percentage of deuteration at the end of the reaction at the α-position was assumed to be equal to the percentage of product non-deuterated at position ε:

$$\%d\text{-}\mathbf{32d\alpha} = 100\text{-}(\%d\text{-}\mathbf{32d\varepsilon})$$

This is based on the very reasonable hypothesis that the deuteration of the iodides **32α** and **32ε** is taking place with 100% D-incorporation.




Scheme 18. Mechanism of deuteration with bis-sulfone **32**.

The result with **32ε** indicates that the rate constant for the radical translocation (**R32ε** to **R32α**) is larger than the one estimated for **R1ε**. Indeed, at the highest 0.005 M dilution, only the product **32α** is observed, indicating a complete 1,5-HAT. At the higher concentration of 0.05 M, an α/ε 64:36 ratio was obtained. By using the same analysis as for the mono-sulfone **1**, this leads to the following rate constant:

$$(64/36) \times 1.4 \times 10^6\ M^{-1}\ s^{-1} \times 0.035\ mol\ l^{-1} = k_{\varepsilon\alpha} = 8.7 \times 10^4\ s^{-1}$$

The deuteration reaction starting from **32α** afforded, even at the highest dilution of 0.005M, exclusively the α product, indicating that the DAT from $Bu_3SnD$ is much faster than the 1,5-

HAT **32Rα** to **32Rε**.

$k_{\alpha SnD}$ involving **R32α** can also be estimated according to the same approach as for **R1α,** assuming that the conversion of the bis-sulfonylated **R32α** to **R32ε** is exergonic or thermoneutral (to be confirmed by calculations).

$$[\mathbf{32h}]/[\mathbf{32d\varepsilon}] = k_{\alpha SnD} \times [DSnBu_3]/k_{\alpha\varepsilon}$$

$$k_{\alpha SnD} = ([\mathbf{32h}]/[\mathbf{32d\varepsilon}]) \times (k_{\alpha\varepsilon}/[DSnBu_3])$$

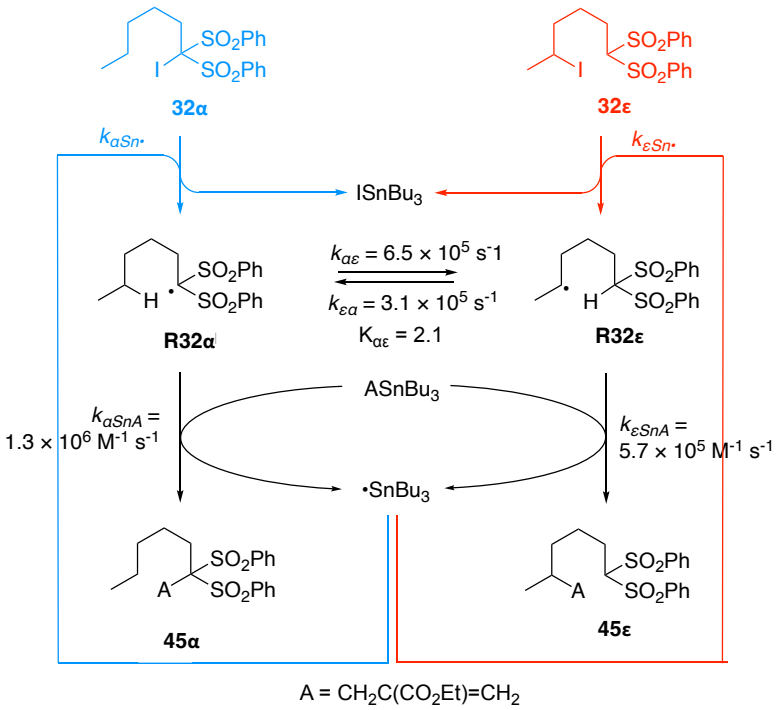
$$k_{\varepsilon SnD} = (>98/2) \times (>8.7 \times 10^4/0.0035)$$

$$k_{\varepsilon SnD} > 1.2 \times 10^9\ M^{-1}\ s^{-1}$$

This rate constant suggests that the rate of the reaction between **R32α** and $Bu_3SnD$ is diffusion-controlled. Calculations are currently performed to support this surprising hypothesis. Interestingly, the isomerisation rate of the bis-sulfonylated radical derived from **32α** is about one order of magnitude faster than the mono-sulfone **1α**.

### *Allylation of bis-sulfone **32***

The reaction of **32** with (2-methoxycarbonylallyl)tributylstannane is very interesting since both **32α** and **32ε** provide α/ε mixtures of **45** (Scheme 19). At the lowest concentration (0.005 M), both **32α** and **32ε** provide the same mixture of **45α**/**45ε**, i.e 42:58 and 43:57, respectively. This indicates, that at this concentration, the equilibration between **R32α** and **R32ε** is faster than the reaction of both radicals with the (2-methoxycarbonylallyl)tributylstannane present at a 0.025 M concentration.




Scheme 19. Mechanism of the allylation of the bis-sulfone **32**.

To the best of our knowledge, the rate constant for the radical addition to (2-methoxycarbonylallyl)tributylstannane is not reported. Still, we assume it is close to the rate of addition of a secondary alkyl radical to methyl methacrylate. A value of $k_{\varepsilon SnA}$ of $5.7 \times 10^5$ $M^{-1}$ $s^{-1}$ (average of rate for methyl $4.9 \times 10^5$ and *tert*-butyl $6.6 \times 10^5$ $M^{-1}$ $s^{-1}$).[42] From the reaction of **32ε** at the highest concentration, one can estimate $k_{\varepsilon\alpha}$:

$$[\mathbf{45\alpha}]/[\mathbf{45\varepsilon}] = k_{\varepsilon\alpha}/(k_{\varepsilon SnA} \times [Bu_3SnA])$$

$$k_{\varepsilon\alpha} = [\mathbf{45\alpha}]/[\mathbf{45\varepsilon}] \times k_{\varepsilon SnA} \times [Bu_3SnA]$$

$$k_{\varepsilon\alpha} = 18/82 \times 5.7 \times 10^5\ M^{-1}\ s^{-1} \times 2.5\ M \text{ (at 0.5 M)}$$

$$k_{\varepsilon\alpha} = 3.1 \times 10^5\ s^{-1}$$

For the reaction starting from **32α**, a similar analysis can be made. The rate constant for the addition of the radical **R32α** to (2-methoxycarbonylallyl)tributylstannane is not reported. However, we have taken the value for the addition of the cyanomethyl radical to methyl acrylate ($k_{\alpha SnA} = 1.3 \times 10^6$). From the reaction of **32α** at the highest concentration, one can estimate $k_{\alpha\varepsilon}$:

$$[\mathbf{45\varepsilon}]/[\mathbf{45\alpha}] = k_{\alpha\varepsilon}/(k_{\alpha SnA} \times [Bu_3SnA])$$

$$k_{\alpha\varepsilon} = [\mathbf{45\varepsilon}]/[\mathbf{45\alpha}] \times k_{\alpha SnA} \times [Bu_3SnA]$$

$$k_{\alpha\varepsilon} = 17/83 \times 1.3 \times 106\ M^{-1}\ s^{-1} \times 2.5 \text{ (at 0.5 M)}$$

$$k_{\alpha\varepsilon} = 6.6 \times 10^5\ s^{-1}$$

Based on these values, the result obtained at the lowest concentration (equilibrium value) can be predicted:

$$[\mathbf{45\alpha}]/[\mathbf{45\varepsilon}] = ([\mathbf{R32\alpha}]/[\mathbf{R32\varepsilon}]) \times (k_{\alpha SnA}/k_{\varepsilon SnA}) = 1/K_{\alpha\varepsilon} \times (k_{\alpha SnA}/k_{\varepsilon SnA})$$

$$K_{\alpha\varepsilon} = [\mathbf{R32\varepsilon}]/[\mathbf{R32\alpha}] = k_{\alpha\varepsilon}/k_{\varepsilon\alpha} = 6.6 \times 10^5\ s^{-1} / 3.1 \times 10^5\ s^{-1} = 2.1$$

$$[\mathbf{45\alpha}]/[\mathbf{45\varepsilon}] = 1/2.1 \times (1.3 \times 10^6\ M^{-1}\ s^{-1} / 5.5 \times 10^5\ M^{-1}\ s^{-1})$$

$$[\mathbf{45\alpha}]/[\mathbf{45\varepsilon}] = 1.1 = 52{:}48 \text{ (predicted)}$$

$$[\mathbf{45\alpha}]/[\mathbf{45\varepsilon}] = 0.7 = 42{:}58 \text{ (experimental)}$$

The values for the rate constant of the translocation determined using deuteration and allylation are also in good agreement: $k_{\varepsilon\alpha} = 8.7 \times 10^4\ s^{-1}$ (deuteration) and $k_{\varepsilon\alpha} = 3.1 \times 10^5\ s^{-1}$ (allylation).

## 6.2 Conclusion

The properties of α-sulfonyl radicals for intramolecular hydrogen atom transfer make them particularly attractive for remote functionalisation of aliphatic C–H bonds. A detailed understanding of the kinetic and thermodynamic aspects should allow the design of a highly efficient process involving one or several HATs. The high synthetic versatility of sulfones makes them particularly attractive for synthetic applications, particularly the synthesis of complex molecules. The unique reactivity of the bis-sulfonylated radicals is particularly attractive, highlighting the importance of the polar effect in HAT processes.

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## 6.3 Experimental Section

### General and instrumentations

The $^{13}C$ and $^{1}H$ NMR spectra were recorded on either a Bruker Avance 300 ($^{1}H$: 300.18 MHz, $^{13}C$: 75.48 MHz) or a Bruker Avance II 400 spectrometer ($^{1}H$: 400.13 MHz, $^{13}C$: 101 MHz). Chemical shifts are reported in units of δ (ppm). For $^{1}H$ NMR spectra, the residual protonated solvents were used to reference the spectra ($CHCl_3$ δ = 7.262 ppm; $CH_2Cl_2$ δ = 5.320 ppm; $C_6C_6$ δ = 7.160 ppm). For $^{13}C$ NMR spectra, the deuterated solvents were used to reference the spectra ($CDCl_3$ δ = 77.16 ppm; $CD_2Cl_2$ δ = 53.84 ppm; $C_6C_6$ δ = 128.060 ppm). $^{13}C$ NMR spectra were run using a proton-decoupled pulse sequence. The following abbreviations were used to describe the multiplicities: s (singlet), d (doublet), t (triplet), q (quadruplet), quin (quintet), sept (septet), m (multiplet), br (broad). Coupling constants (J) are reported in Hertz (Hz) with an accuracy of one unit of the last digit. The number of carbon atoms for each signal is indicated only when superior to one, and when two signals are very close, they are reported with two decimal places. HRMS analyses were recorded on LTQ Orbitrap XL with nano ESI (Thermo) and QStar Pulsar ESI-qTOF-MS (Sciex) (hybrid quadrupole time-of-flight mass spectrometer) using positive electron spray. Infrared spectra were recorded neat equipped with a diamond ATR System and are reported in wave numbers ($cm^{-1}$). Reported are the first six signals (with decreasing wave number) and characteristic functional groups. The following abbreviations were used to explain the intensities: w (weak), m (medium), s (strong), and br (broad), e.g. for OH peaks. Only the stretching frequency of the characteristic functional group was reported, and when the compound did not contain one, the most relevant frequencies were listed. For flash chromatography (FC), silica gel 40–63 µm (230–400 mesh) was used. Thin layer chromatography (TLC) was performed using Silicycle glass-backed TLC extra hard layer, 259 µm, 60 Å, F-254 analytical plates; visualisation under UV (254 nm and/or 366 nm) or/and by staining with a solution of potassium permanganate ($KMnO_4$); phosphomolybdic acid ($H_3PMo_{12}O_{40}$) and cerium sulfate ($Ce(SO_4)_2$), and subsequent heating.

Unless otherwise stated, all yields are isolated yields. Ambient (or room) temperatures were generally in the 21–25 °C range. All reactions were run under an argon atmosphere, and solids were added quickly or under a blanket of flowing argon unless otherwise specified. All glassware was oven-dried overnight at 140 °C, assembled hot, and cooled under a stream of dry argon gas or flame-dried under vacuum.

Unless otherwise stated, all other reagents were obtained commercially and used without further purification. Solvents for reactions (THF, $Et_2O$, $CH_2Cl_2$, *n*-hexane) were first distilled under reduced pressure and then filtered over columns of dried alumina under positive argon pressure.

### Preparation of Triethylborane Solution

To an appropriate volume of dry and degassed (freeze-thaw method) α,α,α-trifluorotoluene (TFT) triethylborane (neat, argon atmosphere) was added via syringe while keeping the tip of the needle underneath the solvent. To prepare the 30.0 mL, 1.15 M solution of $Et_3B$, 5.0 mL of neat $Et_3B$ was added to 25.0 mL of trifluorotoluene. Analysis by NMR suggested that the concentration does not fluctuate considerably over a period of 1-25 days (solution kept in a desiccator under an argon atmosphere).

### Reagents and starting materials

### Preparation of reagents

### Di-tert-butyl hyponitrite (DTBHN)

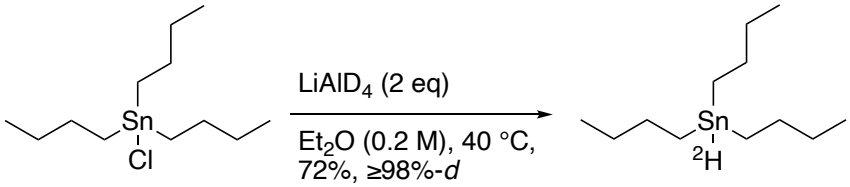
t-BuON=NOt-Bu
$C_8H_{18}N_2O_2$
MW: 174.24

DTBHN was prepared according to a slightly altered reported procedure.[1] In a 250 mL three-neck flask equipped with a stirring bar was loaded sodium *trans*-hyponitrite hydrate (8.15 g), which was then dried to constant weight (5.58 g, 45.0 mmol). In a second flask, $ZnCl_2$ (14.0 g, 101.0 mmol) was dried and melted in vacuo (× 3) to dry it. From the resulting block of grey solid, pieces with a total weight of 8.6 g (63.1 mmol) were quickly transferred into a two-neck flask, dried for 10 min under vacuum, and then suspended in $Et_2O$ (35 mL), first with stirring for 2 h then with sonication for another 20 min until no more pieces of $ZnCl_2$ were visible. To the freshly dried sodium *trans*-hyponitrite (5.58 g, 45.0 mmol) was added $Et_2O$ (30 mL) and *tert*-butylbromide (47 mL, 418 mmol) and the resulting milky reaction mixture was cooled to –10 °C (internal temperature) using an ice/NaCl/water bath. Then, the freshly prepared $ZnCl_2$ solution was added using a cannula (Ø = 1 mm) **at such a rate that the internal temperature did not exceed –5 °C**. After complete addition, the mixture was allowed to reach room temperature and stirred for another 1.5 h. The reaction mixture was filtered on a cotton pad, and the remaining solid was washed with $Et_2O$ (3 × 10 mL). The resulting yellow solution was transferred into a separatory funnel, and

water was added. The aqueous layer was extracted with $Et_2O$ (3 × 20 mL) and the combined organic layers were washed with brine, dried over $Na_2SO_4$ and the volatiles were removed under reduced pressure (**bath temperature not exceeding 20 °C**, 400 mbar, then 50 mbar for a short time). The crude solid was crystallised from *n*-pentane in the freezer to furnish almost colourless crystals in three crops (all crops were washed with cold pentane). Recrystallisation from *n*-pentane of the combined crops furnished the product as colourless, transparent crystals (3.43 g, 37%). Spectral data is in accordance with the literature. DTBHN was stored for months at 4 °C. $^1$H NMR (300 MHz, $CDCl_3$): δ 1.39 (s, 18H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 81.3 (2C, Cq), 27.9 (6C, $CH_3$).

### Tributylstannane-d

The substrate was prepared according to the literature procedure with slight modifications, and the spectral data were in accordance with it.[2]




1) Lithium aluminium deuteride (0.857 g, 20.0 mmol) was introduced in a 50 mL two-neck round-bottom flask equipped with a stirring bar and then dissolved in $Et_2O$ (20 mL, degassed by bubbling Argon for 20 min before use) under Argon at 0 °C. The cold bath was removed, and the solution was stirred for 30 minutes at rt. The resulting $LiAlD_4$ solution (20 mL, 20 mmol, 1.0 M in $Et_2O$) was used without sediments* and added dropwise to a 100 mL two-neck round-bottom flask equipped with stirring bar and condenser containing a solution of tri-*n*-butyl(chloro)stannane (2.8 mL, 10.0 mmol) in $Et_2O$ (20 mL) at 0 °C. The reaction mixture was stirred for 15 minutes at 0 °C, then for 1h at 40 °C. The reaction was monitored by $^1$H and $^{13}$C NMR (see below for details). The reaction mixture was cooled to 0 °C, and then $D_2O$ (2 mL, ca. 100 mmol) was added slowly to quench the remaining active species carefully. Solid dry $Na_2SO_4$ was added to absorb the excess of $D_2O$, and the mixture was stirred for 10 min. The solution was filtered through a Celite/$Na_2SO_4$ dry mixture (volume approx. 35 mL), a small amount of vacuum (50 mL syringe was used as a drying column and 100 mL one-neck dry flask as a receiving jar). The reaction flask was washed with $Et_2O$ (2 × 20 mL) and filtered. The volatiles were removed under a Schlenk line vacuum while stirring and heating at 40 °C for 1–

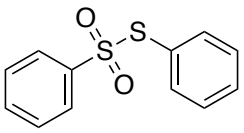
2 hours, yielding the n-$Bu_3SnD$ as a colourless liquid (2.1 g, 72%). $^1$H NMR (400 MHz, $C_6D_6$) δ 1.67–1.45 (m, 6H), 1.41–1.29 (m, 6H), 1.04–0.86 (m, 15H). $^{13}$C NMR (101 MHz, $C_6D_6$) δ 30.3, 27.5, 13.9, 8.3. $^2$H NMR (61 MHz, $C_6D_6$) δ 5.06 (s, 1D). $^{119}$Sn NMR (149 MHz, $C_6D_6$) δ -90.56 (t, *J* = 242.8 Hz).

* The remaining white precipitate was carefully quenched with $Na_2SO_4 \times 10H_2O$ at 0 °C under Argon flow (violent gas evolution).

*NMR check:* A 0.3 mL aliquot was taken from the reaction mixture and placed into an NMR tube (dried under vacuum; septum; Argon atmosphere), and the solvent was removed under high vacuum. $C_6D_6$ (0.5 mL) was added under Ar, and 2–3 drops of $D_2O$ were added to quench the excess of $LiAlD_4$. The NMR tube was sealed with parafilm, and $^{13}$C and $^1$H were measured. Complete conversion was achieved after 1 h.

### S-phenyl benzenesulfonothioate

The substrate was prepared according to the literature, and the spectral data were in accordance with it.[3]

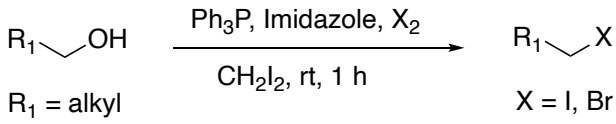


$C_{12}H_{10}O_2S_2$
MW: 250,3

To a suspension of (phenyldisulfanyl)benzene (2.21 g, 10.1 mmol) and sodium benzenesulfinate (5.25 g, 32.0 mmol) in anhydrous DCM (150 mL) was added iodine (5.03 g, 20.0 mmol). The reaction mixture was stirred for 2 h at rt until complete consumption of (phenyldisulfanyl)benzene (TLC monitoring). The reaction mixture was diluted with DCM (100 mL), then successively washed with 5% $Na_2S_2O_3$ (100 mL), water (2 × 100 mL), and brine (2 × 100 mL). The organic phase was dried over $Na_2SO_4$. The colourless crude was purified by flash column chromatography on silica gel (DCM/pentane = 40:60 then 50:50), affording a peachy oil. The pure fraction of the FC was dissolved in methanol and cooled to –78 °C, and then *n*-pentane was added until complete precipitation. The precipitate was collected by filtration under vacuum, washed several times with pentane and dried under vacuum to give the product as a white powder (3.7 g, 74%), M. p. = 44.8 – 46.0 °C (not corrected). $^1$H NMR (300 MHz, $CDCl_3$) δ 7.62–7.53 (m, 3H), 7.51–7.38 (m, 3H), 7.38–7.29 (m, 4H). $^{13}$C NMR (75 MHz,

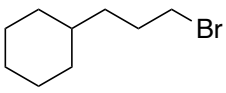
$CDCl_3$) δ 143.1 ($C_q$), 136.7 (2×$CH_{Ar}$), 133.8 ($CH_{Ar}$), 131.6 ($CH_{Ar}$), 129.6 (2×$CH_{Ar}$), 128.9 (2×$CH_{Ar}$), 128.0 ($C_q$), 127.7 (2×$CH_{Ar}$). IR (ν, $cm^{-1}$): 3026, 1441, 1320, 1143, 1077, 746, 680, 585 (w).

## General Procedure 1. Preparation of iodides and bromides (Appel reaction)




To a stirred solution of $PPh_3$ (3.93 g, 15 mmol) in anhydrous dichloromethane (75 mL) was added bromine or iodine (15 mmol) in small portions at room temperature. The reaction mixture was protected from light with an aluminium foil and stirred for 10 min. Imidazole (1.70 g, 25 mmol) was added, and the reaction mixture was stirred at rt for an additional 10 min. The alcohol (10 mmol) was added dropwise to the suspension, and the mixture was stirred for 1 h at rt. Upon completion (TLC monitoring), the reaction mixture was diluted with pentane and filtered through a short pad of silica gel. The pad of silica gel was washed with pentane, and the filtrate was concentrated under reduced pressure. This sequence can be repeated several times if needed. Caution: as some alkyl iodides are volatile, the pressure during evaporation should be lowered carefully (bath temperature max. 40 °C).

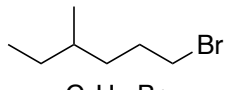
## (3-Bromopropyl)cyclohexane




$C_9H_{17}Br$
MW: 205,14

The title product was obtained following General Procedure 1 with 3-cyclohexyl-1-propanol (1.55 mL, 10.0 mmol), bromine (0.78 mL, 15.0 mmol), $Ph_3P$ (4.14 g, 15.0 mmol), and imidazole (1.71 g, 25.0 mmol) to afford the product as a colourless liquid (2.05 g, quantitative). $^1H$ NMR (300 MHz, $CDCl_3$) δ 3.38 (t, *J* = 6.9 Hz, 2H), 1.94–1.80 (m, 2H), 1.74–1.60 (m, 5H), 1.39–1.02 (m, 5H), 0.99–0.78 (m, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 37.2, 36.1, 34.5, 33.4 (2C), 30.5, 26.7, 26.5 (2C). IR (ν, $cm^{-1}$): 2918, 2848, 1447, 650. HRMS (EI) m/z: $[M]^+$ calculated for $[C_9H_{17}Br]^+$: 204.0508, found: 204.0509. The spectral data were in accordance with the literature reports.[4]

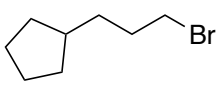
### 1-Bromo-4-methylhexane




$C_7H_{15}Br$
MW: 179,1

The title product was obtained following General Procedure 1 with 4-methylhexan-1-ol (3.40 g, 29.3 mmol), bromine (2.25 mL, 43.9 mmol), $Ph_3P$ (12.12 g, 43.9 mmol), and imidazole (4.98 g, 73.1 mmol) to afford the product as a colourless liquid (4.35 g, 83%). $^1$H NMR (400 MHz, $CDCl_3$) δ 3.40 (td, *J* = 6.9, 1.0 Hz, 2H), 1.95 – 1.77 (m, 2H), 1.51 – 1.41 (m, 1H), 1.34 (m, 2H), 1.27 – 1.21 (m, 1H), 1.19 – 1.09 (m, 1H), 0.87 (d, *J* = 6.4 Hz, 3H), 0.87 (t, *J* = 7.3 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 35.1, 34.3, 33.8, 30.6, 29.3, 19.1, 11.3. IR (ν, $cm^{-1}$): 2959, 2925, 2873, 1460, 643. GCMS (EI) m/z: $[M\text{-}CH_3]^+$ calculated for $[C_6H_{12}Br]^+$: 163.0117, found: 163.0119.

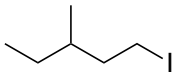
### (3-Bromopropyl)cyclopentane




$C_8H_{15}Br$
MW: 191,1

The title product was obtained following General Procedure 1 with 3-cyclopentylpropan-1-ol (2.12 mL, 15.0 mmol), bromine (1.15 mL, 22.5 mmol), $Ph_3P$ (5.9 g, 22.5 mmol), and imidazole (2.55 g, 37.5 mmol) to afford the product as a colourless liquid (2.87 g, quant.). $^1$H NMR (400 MHz, $CDCl_3$) δ 3.40 (t, *J* = 6.9 Hz, 2H), 1.92–1.82 (m, 2H), 1.82–1.70 (m, 3H), 1.60–1.40 (m, 6H), 1.16–1.01 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 39.6, 34.8, 34.4, 32.8 (2C), 32.3, 25.3 (2C). IR (ν, $cm^{-1}$): 2944, 2865, 1450, 651. GCMS (EI) m/z: $[M]^+$ calculated for $[C_8H_{15}Br]^+$: 190.0352, found: 190.0352.

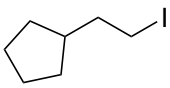
### 1-Iodo-3-methylpentane




$C_6H_{13}I$
MW: 212,1

The title product was obtained following General Procedure 1 with 3-methylpentan-1-ol (3.72 mL; 30.0 mmol), iodine (11.4 g, 45.0 mmol), $Ph_3P$ (11.8 g, 45.0 mmol), and imidazole (5.11 g, 75.0 mmol) to afford the product as a colourless liquid (5.76 g, 91%). $^1$H NMR (400 MHz, $CDCl_3$) δ 3.25 (ddd, *J* = 9.5, 8.5, 5.8 Hz, 1H), 3.17 (ddd, *J* = 9.5, 8.3, 7.2 Hz, 1H), 1.88 (dddd, *J* = 13.9, 8.5, 7.1, 5.4 Hz, 1H), 1.64 (dtd, *J* = 14.0, 8.1, 5.8 Hz, 1H), 1.53–1.43 (m, 1H), 1.52-1.31 (m, 1H), 1.17 (m, 1H), 0.88 (t, *J* = 7.0 Hz, 3H), 0.87 (d, *J* = 7.0 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 40.7, 35.6, 28.9, 18.4, 11.3, 5.5. IR (ν, $cm^{-1}$): 2958, 2924, 2872, 1461, 1234, 1177. GCMS (EI) m/z: $[M\text{-}I]^+$ calculated for $[C_6H_{13}]^+$: 85.1012, found: 85.1012; calculated for $[I]^-$: 126.9045, found: 126.9040.

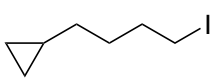
### (2-Iodoethyl)cyclopentane



$C_7H_{13}I$
MW: 224,1

The title product was obtained following the General Procedure 1 as colourless liquid by Dr. Fabrice Dénès and kindly donated to me. $^1$H NMR (400 MHz, $CDCl_3$) δ 3.23 – 3.16 (m, 2H), 1.92 – 1.84 (m, 3H), 1.83 – 1.75 (m, 2H), 1.67 – 1.57 (m, 2H), 1.57 (s, 2H), 1.14 – 1.03 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 41.1, 40.4, 32.0 (2C), 25.2 (2C), 6.2. IR (ν, $cm^{-1}$): 2945, 2863, 1449, 1241, 1199. GCMS (EI) m/z: $[M]^+$ calculated for $[C_7H_{13}I]^+$: 224.0056, found: 224.0062.

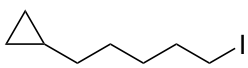
### (4-Iodobutyl)cyclopropane



$C_7H_{13}I$
MW: 224,1

The title product was obtained following General Procedure 1 with 4-cyclopropylbutan-1-ol (3.43 g, 30.0 mmol), iodine (11.42 g, 45.0 mmol), $Ph_3P$ (11.8 g, 45.0 mmol), and imidazole (5.11 g, 75.0 mmol) to afford the product as a colourless liquid (5.64 g, 84%). $^1$H NMR (400 MHz, $CDCl_3$) δ 3.19 (t, *J* = 7.1 Hz, 2H), 1.90–1.82 (m, 2H), 1.58–1.44 (m, 2H), 1.22 (m, 2H), 0.70–0.60 (m, 1H), 0.47–0.35 (m, 2H), 0.06– -0.04 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 33.7, 33.5, 30.8, 10.8, 7.4, 4.6 (2C). IR (ν, $cm^{-1}$): 3073, 2997, 2924, 2850, 1456, 1220, 1179, 1031. GCMS (EI) m/z: $[M]^+$ calculated for $[C_7H_{13}I]^+$: 224.0056, found: 224.0062.

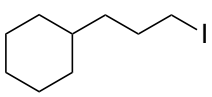
### (5-Iodopentyl)cyclopropane



$C_8H_{15}I$
MW: 238,1

The title product was obtained following General Procedure 1 with 5-cyclopropylpentan-1-ol (1.67 g, 13.0 mmol), iodine (4.95 g, 19.5 mmol), $Ph_3P$ (5.11 g, 19.5 mmol), and imidazole (2.21 g, 32.5 mmol) to afford the product as a colourless liquid (2.35 g, 76%). $^1$H NMR (400 MHz, $CDCl_3$) δ 3.19 (t, *J* = 7.0 Hz, 2H), 1.86–1.76 (m, 2H), 1.47–1.38 (m, 4H), 1.24–1.17 (m, 2H), 0.70–1.58 (m, 1H), 0.45–0.33 (m, 2H), 0.05 – -0.04 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 34.6, 33.8, 30.5, 28.7, 10.9, 7.4, 4.5 (2C). IR (ν, $cm^{-1}$): 3073, 2997, 2921, 2851, 1458, 1212, 1174, 1012. GCMS (EI) m/z: $[M\text{-}C_3H_6]^-$ calculated for $[C_5H_9I]^-$: 195.9743, found: 195.9745.

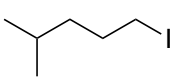
### (3-Iodopropyl)cyclohexane



$C_9H_{17}I$
MW: 252,1

The title product was obtained following General Procedure 1 with 3-cyclohexylpropan-1-ol (6.25 mL, 40.0 mmol), iodine (15.2 g, 60.0 mmol), $Ph_3P$ (15.7 g, 60.0 mmol), and imidazole (6.81 g, 100.0 mmol) to afford the product as a colourless liquid (10.0 g, quant.). $^1$H NMR (400 MHz, $CDCl_3$) δ 3.16 (t, *J* = 7.1 Hz, 2H), 1.89–1.77 (m, 2H), 1.75–1.59 (m, 5H), 1.27 (m, 3H), 1.23 – 1.07 (m, 3H), 0.94–0.84 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 38.5, 37.0, 33.4 (2C), 31.3, 26.7, 26.5 (2C), 7.7. IR (ν, $cm^{-1}$): 2917, 2847, 1446, 1213, 1168. GCMS (EI) m/z: $[M-I]^+$ calculated for $[C_9H_{17}]^+$: 125.1330, found: 125.1326.

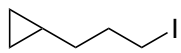
### 1-Iodo-4-methylpentane



$C_6H_{13}I$
MW: 212,1

The title product was obtained following General Procedure 1 with 4-methylpentan-1-ol (4.10 g, 40.0 mmol), iodine (15.23 g, 60.0 mmol), $Ph_3P$ (15.78 g, 60.15 mmol), imidazole (6.62 g, 100.2 mmol) to afford the product as a colourless liquid (3.21 g, 38%). $^1$H NMR (300 MHz, $CDCl_3$) δ 3.17 (t, *J* = 7.1 Hz, 2H), 1.90–1.75 (m, 2H), 1.65–1.52 (m, 1H), 1.36–1.19 (m, 2H), 0.89 (d, *J* = 6.6 Hz, 6H). IR (ν, $cm^{-1}$): 2953, 2927, 2903, 2868, 1466, 1231, 1175.

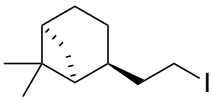
### (3-Iodopropyl)cyclopropane



$C_6H_{11}I$
MW: 210,1

The title product was obtained following General Procedure 1 with 3-cyclopropylpropan-1-ol (3.51 g, 35.0 mmol), iodine (13.30 g, 52.5 mmol), $Ph_3P$ (13.80 g, 52.5 mmol), and imidazole (5.96 g, 87.5 mmol) to afford the product as a colourless liquid (5.45 g, 74%). $^1$H NMR (400 MHz, $CDCl_3$) δ 3.24 (t, *J* = 7.0 Hz, 2H), 1.94 (p, *J* = 7.1 Hz, 2H), 1.30 (q, *J* = 7.0 Hz, 2H), 0.73–0.59 (m, 1H), 0.49–0.36 (m, 2H), 0.09–0.03 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 35.4, 33.9, 10.0, 7.3, 4.5 (2C). IR (ν, $cm^{-1}$): 3073, 2997, 2956, 2914, 2847, 1448, 1234, 1165, 1014, 818. GCMS (EI) m/z: $[M]^+$ calculated for $[C_6H_{11}I]^+$: 209.9900, found: 209.9903.

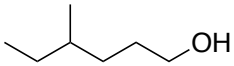
### (1S,2S,5S)-2-(2-iodoethyl)-6,6-dimethylbicyclo[3.1.1]heptane



$C_{11}H_{19}I$
MW: 278,2

The title product was obtained following the General Procedure 1 with 2-((1*S*,2*S*,5*S*)-6,6-dimethylbicyclo[3.1.1]heptan-2-yl)ethan-1-ol (1.30 g, 7.73 mmol), iodine (2.94 g, 11.6 mmol), $Ph_3P$ (3.04 g, 11.6 mmol), and imidazole (1.31 g, 19.3 mmol) to afford the product as a colourless liquid (2.04 g, 95%, d.r. 91:9). Major isomer: $^1$H NMR (400 MHz, $CDCl_3$) δ 3.18 (qt, *J* = 9.5, 7.5 Hz, 2H), 2.35 (dtd, *J* = 9.7, 6.3, 2.2 Hz, 1H), 2.14–2.04 (m, 1H), 2.02–1.81 (m, 7H), 1.48–1.34 (m, 1H), 1.18 (s, 3H), 0.98 (s, 3H), 0.91 (d, *J* = 9.6 Hz, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 45.7, 42.1, 41.36, 41.31, 38.7, 33.5, 28.1, 26.2, 23.2, 21.5, 6.1. IR (ν, $cm^{-1}$): 2982, 2901, 2863, 1466, 1219, 1176. GCMS (EI) m/z: $[M\text{-}CH_3]^+$ calculated for $[C_{10}H_{16}I]^+$: 263.0291, found: 263.0297.

### 4-Methylhexan-1-ol



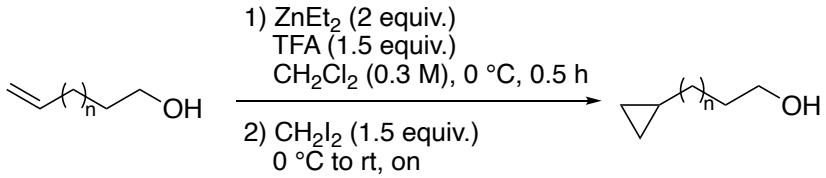

$C_7H_{16}O$
MW: 116,2

To a solution of 4-methylhex-1-ene (35.0 mmol, 4.97 mL) in tetrahydrofuran (15 mL) at 0 °C under Argon was slowly added $BH_3$ (42.0 mL, 42.0 mmol, 1.0 M solution in THF). The reaction mixture was stirred overnight, gradually warming up to rt. The reaction mixture was cooled to 0 °C, and 3.0 M NaOH (12.3 mL) solution and $H_2O_2$ (3.78 mL, 37.0 mmol, 30% aq. solution) were simultaneously added slowly and carefully at 0 °C. The reaction mixture was stirred for 3 h at rt. Upon completion (TLC monitoring), the reaction mixture was diluted with $Et_2O$ and water, and the phases were separated. The aqueous phase was extracted with $Et_2O$ (2 × 50 mL), and the combined organic phases were washed with brine, dried over $Na_2SO_4$ and filtered, and the solvent was removed under reduced pressure. The crude was then purified by flash column chromatography on silica gel (Heptane/EtOAc = 90:10 to 80:20) to yield the product as a colourless liquid (3.47 g, 85%). $^1$H NMR (300 MHz, $CDCl_3$) δ 3.62 (t, *J* = 6.7 Hz, 2H), 1.67–1.52 (m, 2H), 1.43–1.29 (m, 3H), 1.21–1.10 (m, 2H), 0.87 (d, *J* = 4.2 Hz, 3H), 0.86 (t, *J* = 6.8 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 63.6, 34.4, 32.7, 30.5, 29.6, 19.3, 11.5. IR (ν, $cm^{-1}$): 3335, 2958, 2928, 2872, 1460, 1376, 1056. GCMS (EI) m/z: $[M\text{-}H]^+$ calculated for $[C_7H_{15}O]^+$: 115.1117, found: 115.1120.

### General Procedure 2. Preparation of cyclopropylalcohols

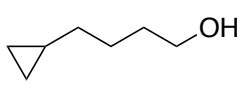
The following cyclopropylalcohols were prepared according to the modified literature

procedure.[5]




To a flame-dried 100-mL two-neck round-bottom flask containing a solution of alcohol (10 mmol) in dichloromethane (30 mL) at 0 °C were successively added dropwise diethylzinc (20 mL, 20 mmol, 1.0 M solution in hexanes) and trifluoroacetic acid (1.15 mL, 15 mmol). [Caution: Diethylzinc is a pyrophoric and highly toxic reagent; therefore, it should be handled with high precaution]. The mixture was stirred for 30 minutes at 0 °C under Argon, and then diiodomethane (1.21 mL, 15 mmol) was added dropwise over 20 minutes. The reaction was stirred for 14 h under Argon while the ice bath was allowed to slowly warm to rt (the reaction mixture turned white, and gas evolution continued). The reaction was carefully quenched with sat. aq. $NH_4Cl$ at 0 °C, then filtered. The phases were separated, and the aqueous layer was extracted with DCM (2 × 20 mL). The combined organic phases were washed with brine (100 mL), dried over $Na_2SO_4$, filtered and concentrated. The crude was then purified by flash column chromatography on silica gel (Pentane/$Et_2O$ = 90:10 to 70:30) to yield the desired product.

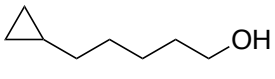
### 4-Cyclopropylbutan-1-ol




$C_7H_{14}O$
MW: 114,2

The title product was obtained following the General Procedure 2 from hex-5-en-1-ol (9.61 mL, 80.0 mmol), $ZnEt_2$ (160 mL, 160.0 mmol,1.0 M in Hexane), trifluoroacetic acid (8.91 mL, 120.0 mmol), dichloromethane (135 mL, 0.3 M) and diiodomethane (9.67 mL, 120.0 mmol) to afford the product as yellow oil (5.64 g, 62%). $^1$H NMR (400 MHz, $CDCl_3$) δ 3.63 (t, *J* = 6.6 Hz, 2H), 1.65–1.54 (m, 2H), 1.51–1.39 (m, 2H), 1.22 (q, *J* = 7.0 Hz, 2H), 0.72–0.60 (m, 1H), 0.45–0.33 (m, 2H), 0.05– -0.05 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 63.2, 34.6, 32.8, 25.9, 10.9, 4.5 (2C). IR (ν, $cm^{-1}$): 3329, 3074, 2999, 2928, 2856, 1458, 1070, 1041, 1013, 818 (w). The spectral data were in accordance with the literature.[5]

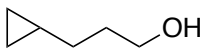
### 5-Cyclopropylpentan-1-ol



$C_8H_{16}O$
MW: 128,2

The title product was obtained following the General Procedure 2 hept-6-en-1-ol (3.50 g, 30.7 mmol), $ZnEt_2$ (61.3 mL, 61.3 mmol, 1.0 M in Hexane), trifluoroacetic acid (3.52 mL, 46.0 mmol), dichloromethane (105 mL, 0.3 M) and diiodomethane (3.7 mL, 46.0 mmol) to afford the product as yellow oil (2.05 g, 52%). $^1$H NMR (400 MHz, $CDCl_3$) δ 3.63 (t, *J* = 6.6 Hz, 2H), 1.56 (p, *J* = 6.8 Hz, 2H), 1.48–1.30 (m, 4H), 1.19 (q, *J* = 7.0 Hz, 2H), 0.69–0.58 (m, 1H), 0.44–0.32 (m, 2H), 0.04– -0.06 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 63.2, 34.8, 33.0, 29.6, 25.7, 11.0, 4.5 (2C). IR (ν, $cm^{-1}$): 3328, 3074, 2998, 2924, 2853, 1460, 1053, 1042, 1012, 819 (w). The spectral data were in accordance with the literature.[6]

### 3-Cyclopropylpropan-1-ol

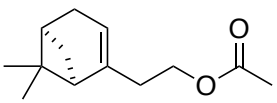


$C_6H_{12}O$
MW: 100,2

The title product was obtained following the General Procedure 2 pent-4-en-1-ol (6.15 mL, 60.0 mmol), $ZnEt_2$ (120 mL, 120.0 mmol, 1.0 M in Hexane), trifluoroacetic acid (6.69 mL, 90.0 mmol), dichloromethane (200 mL, 0.3 M) and diiodomethane (7.25 mL, 90.0 mmol) to afford the product as yellow oil (4.14 g, 69%). $^1$H NMR (400 MHz, $CDCl_3$) δ 3.65 (t, *J* = 6.7 Hz, 2H), 1.72–1.60 (m, 2H), 1.29–1.22 (m, 2H), 0.71–0.59 (m, 1H), 0.46–0.34 (m, 2H), 0.06– -0.03 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 62.9, 32.9, 31.0, 10.7, 4.6 (2C). IR (ν, $cm^{-1}$): 3334, 3075, 2999, 2930, 2853, 1451, 1056, 1042, 1011, 820 (w). The spectral data were in accordance with the literature.[7]

The substrates **S1** and **S2** were prepared according to the literature procedure, and the spectral data were in accordance with it.[8]

### 2-((1R,5S)-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)ethyl acetate **S1**

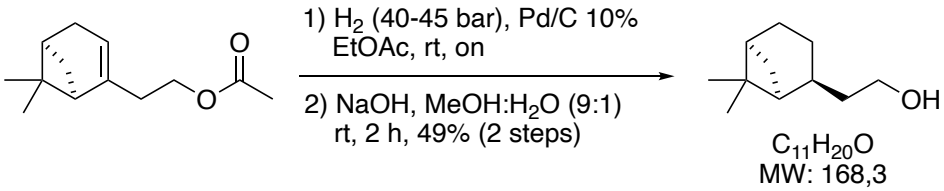


$C_{13}H_{20}O_2$
MW: 208,3

To the solution of (-)-nopol (10.3 mL, 60.0 mmol) in dichloromethane (40 mL) at 0 °C under Argon was added $Et_3N$ (12.5 mL, 90.0 mmol), followed by careful addition of acetyl chloride (5.12 mL, 72.0 mmol). The reaction was stirred at 0 °C for 10 minutes and then warmed up to rt for 30 minutes. Upon completion (TLC monitoring), the reaction mixture was poured into an ice-water mixture (100 mL), and the phases were separated. The aqueous phase was extracted with DCM (2 × 150 mL) and the combined organic phases were washed with brine

and then concentrated under a vacuum. The crude was then purified by flash column chromatography on silica gel (Pentane/$Et_2O$ = 100:0 to 95:5) to yield the product **S1** as a colourless liquid (11.83 g, 95%). $^1$H NMR (400 MHz, $CDCl_3$) δ 5.29 (bs, 1H), 4.12–4.00 (m, 2H), 2.36 (dt, *J* = 8.5, 5.6 Hz, 1H), 2.30–2.15 (m, 4H), 2.10–2.03 (m, 2H), 2.02 (s, 3H), 1.26 (s, 3H), 1.14 (d, *J* = 8.5 Hz, 1H), 0.81 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 171.2, 144.3, 118.9, 62.9, 45.8, 40.9, 38.1, 36.0, 31.8, 31.5, 26.4, 21.2, 21.1. IR (ν, $cm^{-1}$): 2984, 2914, 2833, 1739, 1231, 1031. GCMS (EI) m/z: $[M\text{-}C_2H_4]^+$ calculated for $[C_{11}H_{16}]^+$: 148.1247, found: 148.1249.

### 2-((1S,2S,5S)-6,6-dimethylbicyclo[3.1.1]heptan-2-yl)ethan-1-ol **S2**

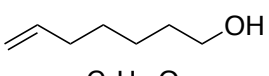



1) To the solution of acetyl protected (-)-nopol (4.17 g, 20.0 mmol) in EtOAc (40 mL) at rt was added Pd/C 10% (0.404 g, 3.8 mmol) carefully and placed inside of an autoclave for hydrogenation and sealed properly. The auclave was filled with $H_2$ (45 bar), and the reaction mixture was stirred vigorously for 16 h at rt. The reaction was stopped, carefully filtered through celite, and washed with EtOAc. [Important: the filter cake on the celite should not be dried during filtration; risk of spontaneous ignition] The crude solution was evaporated under reduced pressure (220 mbar, then gradual decrease to 100 mbar), and the crude product was engaged in the deprotection step without purification.

2) To the solution of NaOH (2.8 g, 70.0 mmol) in MeOH:$H_2O$ (9:1) 44 mL was added the crude reduced nopol derivative and the reaction mixture was stirred for 2 hours ar rt. Upon completion, the reaction mixture was concentrated under reduced pressure, and the crude mixture was diluted with $H_2O$ and extracted with DCM (2 × 100 mL). The combined organic phases were concentrated and afforded the desired product as a colourless oil (1.57 g, 49%, 88:12 dr). $^1$H NMR (400 MHz, $CDCl_3$) δ 3.71–3.57 (m, 2H), 2.36–2.28 (m, 1H), 2.16–2.08 (m, 1H), 2.02 – 1.90 (m, 2H), 1.90 – 1.77 (m, 3H), 1.67 (q, *J* = 7.1 Hz, 2H), 1.52–1.52 (m, 1H), 1.18 (s, 3H), 1.01 (s, 3H), 0.89 (d, *J* = 9.5 Hz, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 61.9, 46.6, 41.6, 40.9, 38.9, 37.7, 33.8, 28.3, 26.6, 23.4, 22.5. IR (ν, $cm^{-1}$): 3318, 2981, 2902, 2864, 1467, 1382, 1057. GCMS (EI) m/z: $[M\text{-}CH_3]^+$ calculated for $[C_{10}H_{17}]^+$: 137.1325, found: 137.1328.

### Hept-6-en-1-ol

The substrate was prepared according to the literature procedure, and the spectral data were in accordance with it.[9]



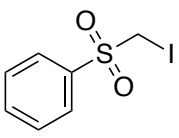
$C_7H_{14}O$
MW: 114,2

To the solution of hept-6-enoic acid (4.06 mL, 30.0 mmol) in tetrahydrofuran (60 mL, 0.5 M) at 0 °C under Argon was added $LiAlH_4$ (8.25 mL, 33.0 mmol, 4.0 M in $Et_2O$) dropwise, then the reaction mixture allowed to warm up to rt and stirred for 3 hours. The reaction mixture was carefully quenched upon completion with 1.0 M HCl aq. solution (100 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic phases were washed with brine, dried over $Na_2SO_4$ and filtered, and concentrated under a reduced pressure. The crude product was then purified by flash column chromatography on silica gel (Pentane/$Et_2O$ = 70:30) to yield the product as a colourless liquid (3.35 g, 98%). $^1$H NMR (400 MHz, $CDCl_3$) δ 5.80 (ddt, *J* = 17.0, 10.2, 6.7 Hz, 1H), 4.99 (dq, *J* = 17.1, 1.7 Hz, 1H), 4.93 (ddt, *J* = 10.2, 2.3, 1.2 Hz, 1H), 3.63 (t, *J* = 6.6 Hz, 2H), 2.06 (tdd, *J* = 6.6, 5.3, 1.4 Hz, 2H), 1.62–1.52 (m, 2H), 1.47–1.31 (m, 4H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.0, 114.5, 63.1, 33.8, 32.7, 28.8, 25.4. IR (ν, $cm^{-1}$): 3330, 3076, 2928, 2857, 1640, 1052, 907.

## Preparation of α-iodoalkyl sulfones

### ((Iodomethyl)sulfonyl)benzene

The substrate was prepared according to the literature procedure, and the spectral data were in accordance with it.[10]

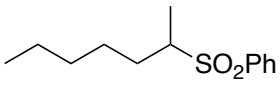


$C_7H_7IO_2S$
MW: 282,1

A mixture of sodium benzene sulfinate (11.7 g, 70.0 mmol), diiodomethane (6.28 mL, 77.2 mmol), and dimethyl sulfoxide (70 mL) was heated to 85 °C for 5–14 h. The mixture was then diluted with water (700 mL) and extracted with dichloromethane (5 × 50 mL). The combined organic phases were successively washed with 5% $Na_2S_2O_3$ (1 × 200 mL), sat. aq. solution of $NaHCO_3$ (1 × 200 mL), water (1 × 200 mL), and brine (1 × 200 mL), then dried over $Na_2SO_4$ and filtered. The solvent was removed under reduced pressure, giving yellow oil as a crude. The crude was then purified by flash column chromatography on silica gel (Heptane/EtOAc = 90:10 to 60:40) to yield the product as a white solid (17.5 g, 89%). $^1$H NMR (300 MHz, $CDCl_3$) δ 8.01–7.94 (m, 2H), 7.76–7.67 (m, 1H), 7.64–7.55 (m, 2H), 4.47 (s, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 136.1 ($C_q$), 134.7

($CH_{Ar}$), 129.5 (2 × $CH_{Ar}$), 129.1 (2 × $CH_{Ar}$), 16.8 ($CH_2$).

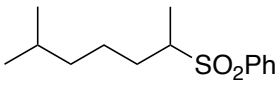
### (Heptan-2-ylsulfonyl)benzene **S3**




$C_{13}H_{20}O_2S$
MW: 240,4

To a solution of (ethylsulfonyl)benzene (1.70 g, 10 mmol) in THF (40 mL) at –78 °C was added dropwise *n*BuLi (4.40 mL, 11 mmol, 2.5 M in hexanes). The reaction mixture was stirred at –78 °C for 45 minutes, and then 1-bromopentane (1.86 mL, 15 mmol) was added. The reaction mixture was stirred and let warm up to rt over 1.5 h. Upon completion (TLC monitoring), water was added slowly. The phases were separated, and the aqueous layer was extracted with EtOAc (2 × 25 mL). The combined organic phases were washed with brine (2 × 50 mL), dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. The crude was then purified by flash column chromatography on silica gel (Heptane/EtOAc = 90:10 to 80:20) to yield the product as a colourless liquid (1.88 g, 78%). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.91–7.85 (m, 2H), 7.69–7.62 (m, 1H), 7.59–7.52 (m, 2H), 3.01 (dqd, *J* = 10.3, 6.9, 3.5 Hz, 1H), 1.99–1.91 (m, 1H), 1.49–1.33 (m, 2H), 1.25 (d, *J* = 6.5 Hz, 3H), 1.32–1.20 (m, 5H), 0.85 (t, *J* = 6.8 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 137.5, 133.6, 129.2, 129.1, 60.3, 31.5, 29.1, 26.4, 22.5, 14.1, 13.3. IR (ν, $cm^{-1}$): 2953, 2930, 2860 (w), 1446, 1301, 1289, 1141, 1083 (str.). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $[C_{13}H_{20}O_2SNa]^+$: 263.1076, found: 263.1074

### ((6-Methylheptan-2-yl)sulfonyl)benzene **S4**



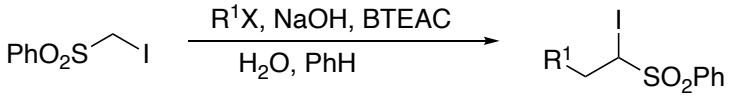

$C_{14}H_{22}O_2S$
MW: 254,4

To a solution of (ethylsulfonyl)benzene (1.70 g, 10 mmol) in THF (40 mL) at –78 °C was added dropwise *n*BuLi (4.40 mL, 11 mmol, 2.5 M in hexanes). The reaction mixture was stirred at –78 °C for 45 min, then 1-bromo-4-methylpentane (2.18 mL, 15 mmol) was added, and the reaction mixture was warmed up to rt over 1.5 h. Upon completion (TLC monitoring), the reaction was quenched with water (volume). The phases were separated, and the aqueous layer was extracted with EtOAc (volume × 2). The combined organic phases were washed with brine (volume × 2), dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. The crude was purified by flash column chromatography on silica gel (Heptane/EtOAc = 90:10 to 80:20) to yield the product as a colourless liquid (1.84 g, 73%). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.91–7.85 (m, 2H), 7.68–7.60 (m, 1H), 7.59–7.52 (m, 2H), 3.02 (dqd, *J* = 10.2, 6.9, 3.5 Hz, 1H), 2.00–1.86 (m, 1H),

1.54–1.33 (m, 3H), 1.26 (d, *J* = 6.9 Hz, 3H), 1.29 – 1.18 (m, 1H), 1.19–1.07 (m, 2H), 0.84 (d, *J* = 6.6, Hz, 3H), 0.83 (d, *J* = 6.6, Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 137.5 (Cq), 133.7 ($CH_{Ar}$), 129.17 (2 × $CH_{Ar}$), 129.16 (2 × $CH_{Ar}$), 60.3 (CH), 38.6 ($CH_2$), 29.4 ($CH_2$), 27.9 (CH), 24.5 ($CH_2$), 22.7 ($CH_3$), 22.5 ($CH_3$), 13.3 ($CH_3$). IR (ν, $cm^{-1}$): 2951, 2867 (w), 1446, 1302, 1141, 1084 (str.). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $[C_{14}H_{22}O_2SNa]^+$: 277.1233, found: 277.1239.

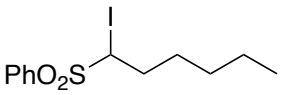
## General Procedure 3. Alkylation of ((iodomethyl)sulfonyl)benzene

Alpha-sulfonyl iodides were prepared according to the literature procedure.[11]




A mixture of ((iodomethyl)sulfonyl)benzene (2.82 g, 10.0 mmol) in benzene (10 mL, 1.0 M), benzyltriethylammonium chloride (BTEAC) (182 mg, 0.8 mmol), alkyl halide (12–15 mmol) in 50% aqueous NaOH (0.4 M) was stirred at rt for 2–14 h. The mixture was then diluted with water (10 × the volume of the reaction mixture) and extracted with DCM (3 × 100 mL). Combined organic phases were washed with brine, dried over $Na_2SO_4$, filtered, and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography on silica gel (Heptane/EtOAc = 90:10).

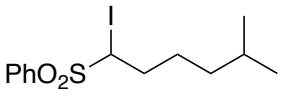
## ((1-Iodohexyl)sulfonyl)benzene **1α**




$C_{12}H_{17}IO_2S$
MW: 352,23

The title compound was prepared following General Procedure 3 with iodomethylsulfonylbenzene (1.41 g, 5.0 mmol), 50% NaOH (12.5 mL), benzyl(triethyl)ammonium chloride (46 mg, 0.2 mmol) and 1-bromopentane (1.13 g, 7.5 mmol) to afford as a yellow solid (1.47 g, 84%). m.p. = 37.6–38.8 °C (not corrected). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.01–7.92 (m, 2H), 7.75–7.66 (m, 1H), 7.61–7.55 (m, 2H), 4.87 (dd, *J* = 11.1, 3.1 Hz, 1H), 2.05 (dddd, *J* = 14.5, 9.5, 6.0, 3.1 Hz, 1H), 1.88 (dddd, *J* = 14.4, 11.2, 9.4, 4.4 Hz, 1H), 1.66–1.53 (m, 1H), 1.40–1.15 (m, 5H), 0.86 (t, *J* = 6.9 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 135.3 ($C_q$), 134.5 ($CH_{Ar}$), 130.1 (2 × $CH_{Ar}$), 129.2 (2 × $CH_{Ar}$), 45.4 (CH), 33.0 ($CH_2$), 30.6 ($CH_2$), 28.9 ($CH_2$), 22.4 ($CH_2$), 14.0 ($CH_3$). IR (ν, $cm^{-1}$): 2962, 2936, 2919, 2850 (w), 1300, 1291 (str.), 1141, 1079 (str.). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $[C_{12}H_{17}O_2INaS]^+$: 379.9886, found: 379.9874.

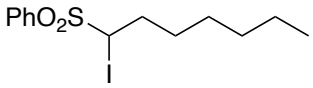
((1-Iodo-5-methylhexyl)sulfonyl)benzene **2α**



$C_{13}H_{19}IO_2S$
MW: 366,26

The title compound was prepared following General Procedure 3 with iodomethylsulfonylbenzene (0.564 g, 2.0 mmol), benzyl(triethyl)ammonium chloride (0.08 mmol, 18.4 mg), 50% NaOH (5 mL) and 1-bromo-4-methylpentane (3.0 mmol, 0.45 mL) to afford as a yellow dense oil (0.56 g, 76%). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.99–7.92 (m, 2H), 7.73–7.67 (m, 1H), 7.60–7.54 (m, 2H), 4.87 (dd, *J* = 11.1, 3.1 Hz, 1H), 2.02 (dddd, *J* = 14.3, 9.5, 6.4, 3.1 Hz, 1H), 1.86 (dddd, *J* = 14.4, 11.0, 9.7, 4.4 Hz, 1H), 1.68–1.54 (m, 1H), 1.54–1.42 (m, 1H), 1.39–1.23 (m, 1H), 1.22–1.05 (m, 2H), 0.84 (dd, *J* = 6.6, 1.2 Hz, 6H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 135.2 (Cq), 134.4 ($CH_{Ar}$), 130.0 (2 × $CH_{Ar}$), 129.2 (2 × $CH_{Ar}$), 45.4 (CH), 37.6 ($CH_2$), 33.2 ($CH_2$), 27.8 (CH), 27.1 ($CH_2$), 22.7 ($CH_3$), 22.4 ($CH_3$). IR (ν, $cm^{-1}$): 2951, 2866 (w), 1321, 1307, 1149, 1080 (str.). HRMS (EI) m/z: calculated for $[C_{13}H_{19}O_2S]^+$: 239.1100, found: 239.1105; calculated for $[C_7H_{14}I]^+$: 225.0135, found: 235.0139; calculated for $[C_6H_7O_2S]^+$: 143.0161, found: 143.0164.

((1-Iodoheptyl)sulfonyl)benzene **3α**

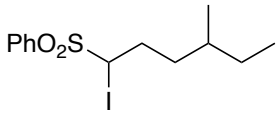


$C_{13}H_{19}IO_2S$
MW: 366,26

The title compound was prepared following General Procedure 3 with iodomethylsulfonylbenzene (1.41 g, 5.0 mmol), benzene (2 mL), benzyl(triethyl)ammonium chloride (92 mg, 0.4 mmol), 50% NaOH (10.5 mL) and 1-bromohexane (1.07 mL, 7.5 mmol) to afford as a pale yellow solid (1.65 g, 91%). m.p. = 70.8–72.8 °C (not corrected). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.01–7.93 (m, 2H), 7.75–7.65 (m, 1H), 7.64–7.54 (m, 2H), 4.87 (dd, *J* = 11.1, 3.1 Hz, 1H), 2.05 (dddd, *J* = 14.4, 9.4, 6.0, 3.1 Hz, 1H), 1.88 (dddd, *J* = 14.4, 11.2, 9.4, 4.5 Hz, 1H), 1.67–1.52 (m, 1H), 1.40–1.15 (m, 7H), 0.86 (t, *J* = 6.9 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 135.2 ($C_q$), 134.5 ($CH_{Ar}$), 130.0 (2 × $CH_{Ar}$), 129.2 (2 × $CH_{Ar}$), 45.4 (CH), 33.0 ($CH_2$), 31.4 ($CH_2$), 29.2 ($CH_2$), 28.1 ($CH_2$), 22.6 ($CH_2$), 14.1 ($CH_3$). IR (ν, $cm^{-1}$): 2965, 2951, 2934, 2915, 2852 (w), 1309, 1289, 1141, 1079 (str.). HRMS (ESI) m/z: $[M+H]^+$ calculated for $[C_{13}H_{20}IO_2S]^+$: 367.0215, found: 367.0215; $[M+Na]^+$ calculated for $[C_{13}H_{19}IO_2SNa]^+$: 389.0033, found: 389.0033.

((1-Iodo-4-methylhexyl)sulfonyl)benzene **4α**

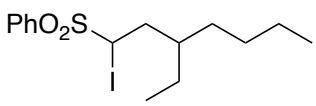
The title compound was prepared following General Procedure 3 with ((iodomethyl)sulfonyl)benzene (2.821 g, 10.0 mmol), 50% NaOH (25 mL), TEBA (91 mg, 0.4




$C_{13}H_{19}IO_2S$
MW: 366,26

mmol) and 1-bromo-3-methylpentane (2.476 g, 15.0 mmol) to afford as a colourless oil (2.23 g, 6 mmol, 61%; dr = 1:1). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.01–7.92 (m, 2H dia 1 + 2H dia 2), 7.74–7.65 (m, 1H dia 1 + 1H dia 2), 7.62–7.56 (m, 2H dia 1 + 2H dia 2), 4.83 (dd, *J* = 11.0, 3.1 Hz, 1H dia 1 + 1H dia 2), 2.15–1.97 (m, 1H dia 1 + 1H dia 2), 1.93–1.74 (m, 1H dia 1 + 1H dia 2), 1.56 (dddd, *J* = 13.3, 10.7, 6.2, 4.4 Hz, 1H, dia 1), 1.39–0.97 (m, 4H dia 1 + 5H dia 2), 0.88–0.77 (m, 6H dia 1 + 6H dia 2). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 135.10 (Cq), 135.06 (Cq), 134.4 ($CH_{Ar}$, dia 1 + dia 2), 129.8 (2 × $CH_{Ar}$, dia 1 + dia 2), 129.1 (2 × $CH_{Ar}$, dia 1 + dia 2), 45.71 (CH), 45.65 (CH), 35.8 ($CH_2$), 35.5 ($CH_2$), 33.6 (CH), 33.4 (CH), 30.9 ($CH_2$), 30.6 ($CH_2$), 29.6 ($CH_2$), 28.6 ($CH_2$), 19.4 ($CH_3$), 18.6 ($CH_3$), 11.4 ($CH_3$), 11.1 ($CH_3$). IR (ν, $cm^{-1}$): 2957, 2923, 2871 (w), 1446, 1320, 1307, 1147, 1080 (str.). HRMS (EI) m/z: $[M-I]^+$ calculated for $[C_{13}H_{19}O_2S]^+$: 239.1100, found: 239.1104.

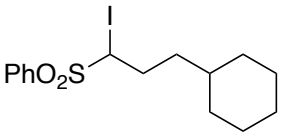
### (3-Ethyl-1-iodoheptyl)sulfonyl)benzene **5α**




$C_{15}H_{23}IO_2S$
MW: 394,31

The title compound was prepared following General Procedure 3 with iodomethylsulfonylbenzene (1.41 g, 5.0 mmol), benzene (2 mL), benzyl(triethyl)ammonium chloride (92 mg, 0.4 mmol), 50% NaOH (10.5 mL) and 3-(bromomethyl)heptane (1.07 mL, 7.5 mmol) to afford as a greenish dense oil (0.81 g, 41%), d.r. 1:1. $^1$H NMR (400 MHz, $CDCl_3$) δ 8.00–7.93 (m, 4H, dia 1 + dia 2), 7.73–7.66 (m, 2H, dia 1 + dia 2), 7.61–7.55 (m, 4H, dia 1 + dia 2), δ 4.89 (dd, *J* = 11.8, 2.9 Hz, 1H, dia 1), 4.88 (dd, *J* = 11.8, 2.9 Hz, 1H, dia 2), 1.98–1.89 (m, 2H, dia 1 + dia 2), 1.84–1.77 (m, 2H, dia 1 + dia 2), 1.57–0.96 (m, 18H, dia 1 + dia 2), 0.87 (t, *J* = 6.8 Hz, 3H), 0.841 (t, *J* = 7.5 Hz, 3H), 0.837 (t, *J* = 7.2 Hz, 3H), 0.70 (t, *J* = 7.5 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 135.21 (Cq, dia 1), 135.20 (Cq, dia 2), 134.5 (2 × $CH_{Ar}$, dia 1 + dia 2), 130.01 (2 × $CH_{Ar}$), 129.99 (2 × $CH_{Ar}$), 129.24 (4 × $CH_{Ar}$, dia 1 + dia 2), 44.43 (CH), 44.37 (CH), 38.5 (CH), 37.9 (CH), 37.0 ($CH_2$), 36.61 ($CH_2$), 32.6 ($CH_2$), 30.9 ($CH_2$), 28.9 ($CH_2$), 27.4 ($CH_2$), 26.2 ($CH_2$), 23.8 ($CH_2$), 23.1 ($CH_2$), 23.0 ($CH_2$), 14.2 (2 × $CH_3$), 11.1 ($CH_3$), 9.2 ($CH_3$). IR (ν, $cm^{-1}$): 2956, 2924, 2856 (w), 1320, 1308, 1149, 1080 (str.). HRMS (ESI) m/z: $[M+H]^+$ calculated for $[C_{15}H_{24}IO_2S]^+$: 395.0541, found: 395.0541; (EI): calculated for $[C_{15}H_{24}IO_2S]^+$: 395.0536, found: 395.0533.

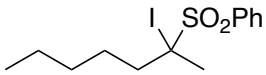
((3-Cyclohexyl-1-iodopropyl)sulfonyl)benzene **6α**




$C_{15}H_{21}IO_2S$
MW: 392,30

The title compound was prepared following General Procedure 3 with iodomethylsulfonylbenzene (0.846 g, 3.0 mmol), benzyl(triethyl)ammonium chloride (26.7 mg, 0.12 mmol), 50% NaOH (7.5 mL) and (2-bromoethyl)cyclohexane (0.72 mL, 4.5 mmol) to afford as a yellow oil (0.52 g, 44%). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.02–7.93 (m, 2H), 7.74–7.65 (m, 1H), 7.64–7.53 (m, 2H), 4.83 (dd, *J* = 11.1, 3.0 Hz, 1H), 2.12 (dddd, *J* = 14.4, 10.3, 5.7, 3.0 Hz, 1H), 1.91–1.81 (m, 1H), 1.73–1.54 (m, 5H), 1.53–1.39 (m, 1H), 1.34–1.03 (m, 5H), 0.94–0.79 (m, 2H).$^{13}$C NMR (101 MHz, $CDCl_3$) δ 135.3 (Cq), 134.5 ($CH_{Ar}$), 130.1 (2 × $CH_{Ar}$), 129.2 (2 × $CH_{Ar}$), 45.7 (CH), 36.8 (CH), 36.7 ($CH_2$), 33.7 ($CH_2$), 32.7 ($CH_2$), 30.8 ($CH_2$), 26.6 ($CH_2$), 26.4 ($CH_2$), 26.3 ($CH_2$). IR (ν, $cm^{-1}$): 2918, 2847 (w), 1319, 1307, 1146, 1080 (str.). HRMS (ESI) m/z: $[M+H]^+$ calculated for $[C_{15}H_{22}IO_2S]^+$: 393.0373, found: 393.0373.

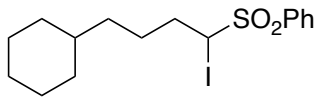
((2-Iodoheptan-2-yl)sulfonyl)benzene **7α**




$C_{13}H_{19}IO_2S$
MW: 366,3

To a solution of (heptan-2-ylsulfonyl)benzene (1.80 g, 7.5 mmol) in THF (50 mL) at – 78 °C was added dropwise n-BuLi (3.30 mL, 8.25 mmol, 2.5 M in hexanes). The reaction mixture was stirred at –78 °C for 1 h, then a freshly prepared solution of iodine (2.28 g, 9 mmol) in dry THF (5 ml) was added, and the reaction mixture was slowly warmed up to rt over 30 min. Upon completion, water was added slowly, the phases were separated, and the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic phases were successively washed with 5% $Na_2S_2O_3$ solution, water, and brine, then dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. The crude was purified by flash column chromatography on silica gel (Heptane/EtOAc = 90:10 to 70:30) to yield the product as a white solid (2.16 g, 79%). M.p. = 42.2–44.0 °C (not corrected). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.03–7.97 (m, 2H), 7.73–7.66 (m, 1H), 7.61–7.54 (m, 2H), 2.16–2.07 (m, 1H), 2.09 (s, 3H), 1.70–1.55 (m, 2H), 1.51–1.39 (m, 1H), 1.38–1.23 (m, 4H), 0.91–0.87 (m, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 134.3 ($CH_{Ar}$), 133.3 (Cq), 131.9 (2 × $CH_{Ar}$), 128.8 (2 × $CH_{Ar}$), 64.6 (Cq), 40.3 ($CH_2$), 31.5 ($CH_2$), 28.8 ($CH_3$), 27.9 ($CH_2$), 22.6 ($CH_2$), 14.1 ($CH_3$). IR (ν, $cm^{-1}$): 2953, 2926, 2868 (w), 1447, 1303, 1135, 1080 (str.). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $[C_{13}H_{19}IO_2SNa]^+$: 389.0043, found: 389.0037.

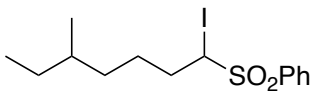
((4-Cyclohexyl-1-iodobutyl)sulfonyl)benzene **8α**




$C_{16}H_{23}IO_2S$
MW: 406,32

The title compound was prepared following General Procedure 3 with iodomethylsulfonylbenzene (1.41 g, 5.0 mmol), benzyl(triethyl)ammonium chloride (92 mg, 0.4 mmol), 50% NaOH (12.5 mL) and (3-bromopropyl)cyclohexane (1.54 g, 7.5 mmol) to afford as a dark orange oil (1.66 g, 81%). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.00–7.93 (m, 2H), 7.74–7.65 (m, 1H), 7.61–7.56 (m, 2H), 4.87 (dd, *J* = 11.2, 3.1 Hz, 1H), 2.01 (dddd, *J* = 14.3, 9.5, 6.4, 3.1 Hz, 1H), 1.86 (dddd, *J* = 14.2, 11.1, 9.6, 4.4 Hz, 1H), 1.73–1.55 (m, 6H), 1.38–1.27 (m, 1H), 1.27–1.01 (m, 6H), 0.91–0.75 (m, 2H).$^{13}$C NMR (101 MHz, $CDCl_3$) δ 135.2 (Cq), 134.5 ($CH_{Ar}$), 130.0 (2 × $CH_{Ar}$), 129.2 (2 × $CH_{Ar}$), 45.5 (CH), 37.3 (CH), 36.1 ($CH_2$), 33.5 ($CH_2$), 33.3 ($CH_2$), 33.2 ($CH_2$), 26.70 ($CH_2$), 26.6 ($CH_2$), 26.41 ($CH_2$), 26.37 ($CH_2$). IR (ν, $cm^{-1}$): 2917, 2846 (w), 1321, 1308, 1147, 1080 (str.). HRMS (ESI) m/z: $[M+H]^+$ calculated for $[C_{16}H_{24}IO_2S]^+$: 407.0541, found: 407.0541.

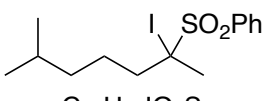
((1-Iodo-5-methylheptyl)sulfonyl)benzene **9α**




$C_{14}H_{21}IO_2S$
MW: 380,3

The title compound was prepared following General Procedure 3 with iodomethylsulfonylbenzene (2.82 g, 10.0 mmol), benzene (10 mL), benzyl(triethyl)ammonium chloride (182 mg, 0.8 mmol), 50% NaOH (15.8 mL) and 1-bromo-4-methylhexane (2.69 g, 15 mmol) to afford as an orange-red dense oil (2.21 g, 58%, dr = 1:1). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.00–7.93 (m, 4H, dia 1 + dia 2), 7.73–7.67 (m, 2H, dia 1 + dia 2), 7.63–7.56 (m, 4H, dia 1 + dia 2), 4.878 (dd, *J* = 11.1, 3.2 Hz, 1H, dia 1), 4.875 (dd, *J* = 11.2, 3.2 Hz, 1H, dia 2), 2.07–1.98 (m, 2H, dia 1 + dia 2), 1.93–1.82 (m, 2H, dia 1 + dia 2), 1.71–1.51 (m, 2H, dia 1 + dia 2), 1.42–1.18 (m, 8H, dia 1 + dia 2), 1.18–1.02 (m, 4H, dia 1 + dia 2), 0.87–0.80 (m, 12H, dia 1 + dia 2). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 135.2 (2 × Cq), 134.3 (2 × $CH_{Ar}$), 129.9 (4 × $CH_{Ar}$), 129.1 (4 × $CH_{Ar}$), 45.3 (2 × CH), 35.2 ($CH_2$), 35.1 ($CH_2$), 34.1 (CH), 34.0 (CH), 33.3 ($CH_2$), 33.1 ($CH_2$), 29.5 ($CH_2$), 29.1 ($CH_2$), 26.8 ($CH_2$), 26.7 ($CH_2$), 19.1 ($CH_3$), 18.9 ($CH_3$), 11.3 ($CH_3$), 11.2 ($CH_3$). IR (ν, $cm^{-1}$): 2956, 2925, 2870 (w), 1446, 1320, 1307 (str.), 1148, 1080 (str.), 745. HRMS (ESI) m/z: $[M+Na]^+$ calculated for $[C_{14}H_{21}IO_2SNa]^+$: 403.0199, found: 403.0188.

((2-Iodo-6-methylheptan-2-yl)sulfonyl)benzene **10α**

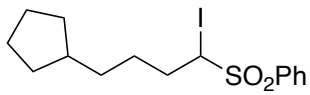



$C_{14}H_{21}IO_2S$
MW: 380,3

To a solution of ((6-methylheptan-2-yl)sulfonyl)benzene (1.75 g, 6.8 mmol) in THF (50 mL) at – 78 °C was added *n*BuLi (3.11 mL, 7.78 mmol, 2.5 M in hexanes) dropwise. The reaction mixture was stirred at –78 °C for 1 h, and then a freshly prepared solution of iodine (2.16 g, 8.49 mmol) in THF (5 ml) was added. The reaction mixture was stirred and slowly warmed to rt over 30 min. Upon completion, the reaction mixture was quenched with water (100 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (2 × 100 mL). The combined organic phases were successively washed with 5% $Na_2S_2O_3$ solution, water and brine, then dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. The crude was purified by flash column chromatography on silica gel (Heptane/EtOAc = 90:10 to 70:30) to yield the product as an orange oil (2.43 g, 90%). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.05–7.97 (m, 2H), 7.74–7.66 (m, 1H), 7.62–7.55 (m, 2H), 2.13–2.05 (m, 1H), 2.10 (s, 3H), 1.68–1.44 (m, 4H), 1.27–1.20 (m, 2H), 0.88 (d, *J* = 6.7 Hz, 6H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 134.4 ($CH_{Ar}$), 133.3 (Cq), 131.9 (2 × $CH_{Ar}$), 128.8 (2 × $CH_{Ar}$), 64.7 (Cq), 40.5, 38.6 ($CH_2$), 28.8 ($CH_2$), 27.9 ($CH_3$), 26.1 (CH), 22.68 ($CH_3$), 22.64 ($CH_3$).

IR (ν, $cm^{-1}$): 2951, 2900, 2866 (w), 1446, 1320, 1305, 1141, 1065 (str.). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $[C_{14}H_{21}IO_2SNa]^+$: 403.0199, found: 403.0192.

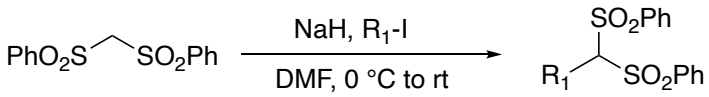
((4-Cyclopentyl-1-iodobutyl)sulfonyl)benzene **18α**




$C_{15}H_{21}IO_2S$
MW: 392,3

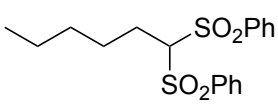
The title compound was prepared following General Procedure 3 with iodomethylsulfonylbenzene (2.82 g, 10.0 mmol), benzene (10 mL), benzyl(triethyl)ammonium chloride (182 mg, 0.8 mmol), 50% NaOH (15.8 mL) and (3-bromopropyl)cyclopentane (2.48 g, 13 mmol) to afford as a dark orange oil (1.6 g, 41%). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.00–7.92 (m, 2H), 7.74–7.67 (m, 1H), 7.64–7.54 (m, 2H), 4.87 (dd, *J* = 11.2, 3.1 Hz, 1H), 2.04 (dddd, *J* = 14.4, 9.5, 6.1, 3.1 Hz, 1H), 1.94–1.82 (m, 1H), 1.76–1.42 (m, 8H), 1.40–1.18 (m, 3H), 1.08–0.96 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 135.3 (Cq), 134.5 ($CH_{Ar}$), 130.1 (2 × $CH_{Ar}$), 129.2 (2 × $CH_{Ar}$), 45.5 (CH), 39.8 (CH), 34.8 ($CH_2$), 33.2 ($CH_2$), 32.8 ($CH_2$), 32.6 ($CH_2$), 28.5 ($CH_2$), 25.24 ($CH_2$), 25.23 ($CH_2$). IR (ν, $cm^{-1}$): 2940, 2857 (w), 1446, 1321, 1133, 1307, 1145, 1080 (str.), 738. HRMS (ESI) m/z: $[M+Na]^+$ calculated for $[C_{15}H_{21}IO_2SNa]^+$: 415.0199, found: 415.0207.

### General Procedure 4. Alkylation of bis(phenylsulfonyl)methane




A two-neck round-bottom flask equipped with a gas exhaustion tube was charged with NaH (12 mmol; 55% dispersion in mineral oil) while under Argon. NaH was washed with *n*-pentane (10 mL × 3) and suspended in anhydrous DMF (20 mL). The suspension was cooled to 0 °C, and bis-sulfone (10 mmol) was added slowly (with control of the gas exhaustion). The reaction mixture was stirred at 0 °C for 30–60 min and alkyliodide (12 mmol) was added dropwise at 0 °C. The reaction mixture was protected from light and stirred at room temperature for 30 min. Upon completion (TLC monitoring), the reaction mixture was quenched with 1.0 M HCl (100 mL) and extracted with EtOAc (200 mL). The aq. phase was extracted with EtOAc (2 × 100 mL), and then the combined OP was washed with water (3 × 50 mL) and brine (3 × 50 mL), dried over $Na_2SO_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (Heptane/EtOAc = 90:10 to 70:30).

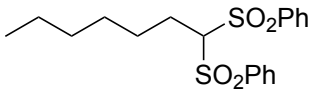
### Hexane-1,1-diyldisulfonyl)dibenzene




$C_{18}H_{22}O_4S_2$
MW: 366,5

The title compound was prepared following General Procedure 4 with bis(phenylsulfonyl)methane (4.49 g, 15 mmol), NaH (0.69 g, 18 mmol, 55% in mineral oil), 1-iodopentane (2.4 mL, 18 mmol) and to afford as a white solid (5.16 g, 94 %), M.p. = 105–107 °C (not corrected). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.00–7.92 (m, 4H), 7.74–7.66 (m, 2H), 7.63–7.53 (m, 4H), 4.37 (t, *J* = 5.6 Hz, 1H), 2.16–2.11 (m, 2H), 1.61–1.48 (m, 2H), 1.28–1.15 (m, 4H), 0.83 (t, *J* = 6.9 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 137.9 (2 × Cq), 134.5 (2 × $CH_{Ar}$), 129.6 (4 × $CH_{Ar}$), 129.1 (4 × $CH_{Ar}$), 83.8 (CH), 31.1 ($CH_2$), 27.8 ($CH_2$), 25.6 ($CH_2$), 22.0 ($CH_2$), 13.8 ($CH_3$). IR (ν, $cm^{-1}$): 2954, 2916, 2860 (w), 1330, 1309, 1159, 1076 (str.). HRMS (EI) m/z: $[M+H]^+$ calculated for $[C_{18}H_{23}O_2S]^+$: 367.1032, found: 367.1037.

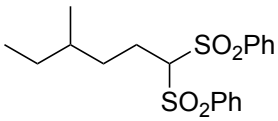
### (Heptane-1,1-diyldisulfonyl)dibenzene




$C_{19}H_{24}O_4S_2$
MW: 380,5

The title compound was prepared following General Procedure 4 with bis(phenylsulfonyl)methane (5.93 g, 20 mmol), NaH (0.92 g, 24 mmol, 55% in mineral oil), 1-iodohexane (3.54 mL, 24 mmol) to afford as a white solid (6.22 g, 82 %), M.p. = 91.2–92.2 °C (not corrected). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.00–7.92 (m, 4H), 7.75–7.65 (m, 2H), 7.63–7.53 (m, 4H), 4.37 (t, *J* = 5.6 Hz, 1H), 2.19–2.09 (m, 2H), 1.60–1.48 (m, 2H), 1.30–1.12 (m, 6H), 0.85 (t, *J* = 6.9 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 138.1 (2 × Cq), 134.7 (2 × $CH_{Ar}$), 129.7 (4 × $CH_{Ar}$), 129.2 (4 × $CH_{Ar}$), 84.0 (CH), 31.2 ($CH_2$), 28.8 ($CH_2$), 28.2 ($CH_2$), 25.8 ($CH_2$), 22.5 ($CH_2$), 14.1 ($CH_3$). IR (ν, cm$^{-1}$): 2954, 2931, 2869, 2860 (w), 1331, 1307, 1292, 1156, 1140, 1078 (str.). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $[C_{19}H_{24}O_4S_2Na]^+$: 403.1008, found: 403.1000.

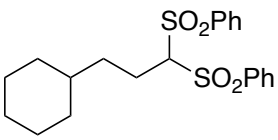
### (4-Methylhexane-1,1-diyldisulfonyl)dibenzene




$C_{19}H_{24}O_4S_2$
MW: 380,5

The title compound was prepared following General Procedure 4 with bis(phenylsulfonyl)methane (2.96 g, 10 mmol), NaH (0.48 g, 12 mmol, 55% in mineral oil), and 1-iodo-3-methylpentane (2.54 g, 12 mmol) to afford as a white solid (0.776 g, 20 %), M.p. = 85.3–86.2 °C (not corrected). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.00–7.94 (m, 4H), 7.74–7.67 (m, 2H), 7.63–7.56 (m, 4H), 4.33 (t, *J* = 5.6 Hz, 1H), 2.24–2.05 (m, 2H), 1.60–1.48 (m, 1H), 1.39–1.30 (m, 1H), 1.30–1.18 (m, 2H), 1.15–1.02 (m, 1H), 0.80 (t, *J* = 7.3 Hz, 3H), 0.77 (d, *J* = 6.4 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 138.1 (2 × Cq), 134.7 (2 × $CH_{Ar}$), 129.8 (4 × $CH_{Ar}$), 129.2 (4 × $CH_{Ar}$), 84.3 (CH), 35.1 ($CH_2$), 34.3 (CH), 29.0 ($CH_2$), 23.6 ($CH_2$), 18.8 ($CH_3$), 11.3 ($CH_3$). IR (ν, cm$^{-1}$): 3061, 2963, 2928, 2873 (w), 1446, 1307, 1293, 1152, 1142, 1077 (str.). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $[C_{19}H_{24}O_4S_2Na]^+$: 403.1008, found: 403.1016.

### (3-Cyclohexylpropane-1,1-diyldisulfonyl)dibenzene



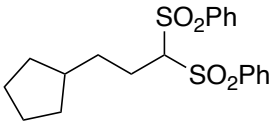

$C_{21}H_{26}O_4S_2$
MW: 406,6

The title compound was prepared following General Procedure 4 with bis(phenylsulfonyl)methane (0.296 g, 1.0 mmol), NaH (48 mg, 1.2 mmol, 55% in mineral oil), and (2-bromoethyl)cyclohexane (0.229 g, 1.2 mmol) to afford as a white solid (0.279 g, 69 %), M.p. = 127.8–128.8 °C (not corrected). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.00–7.93 (m, 4H), 7.75–7.64 (m, 2H),

7.64–7.52 (m, 4H), 4.33 (t, *J* = 5.6 Hz, 1H), 2.20–2.10 (m, 2H), 1.72–1.50 (m, 6H), 1.46–1.37 (m, 2H), 1.19–1.09 (m, 3H), 0.86–0.73 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 138.1 (2 × Cq), 134.7 (2 × $CH_{Ar}$), 129.7 (4 × $CH_{Ar}$), 129.2 (4 × $CH_{Ar}$), 84.3 (CH), 37.5 (CH), 35.9 ($CH_2$), 32.9 (2 × $CH_2$), 26.5 ($CH_2$), 26.2 (2 × $CH_2$), 23.4 ($CH_2$). IR (ν, $cm^{-1}$): 2927, 2854 (w), 1446, 1309, 1291, 1154, 1141, 1078 (str.). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $[C_{21}H_{26}O_4S_2Na]^+$: 429.1165, found: 429.1157.

### (3-Cyclopentylpropane-1,1-diyldisulfonyl)dibenzene

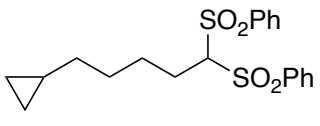
The title compound was obtained following the General Procedure 4 as a white solid by Dr. Fabrice Dénès and kindly donated to me.




$C_{20}H_{24}O_4S_2$
MW: 392,5

M.p. = 137–140 °C (not corrected). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.03–7.92 (m, 4H), 7.75–7.66 (m, 2H), 7.65–7.54 (m, 4H), 4.36 (t, *J* = 5.6 Hz, 1H), 2.21–2.10 (m, 2H), 1.73–1.61 (m, 3H), 1.61–1.40 (m, 6H), 1.06–0.92 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 138.1 (2 × Cq), 134.7 (2 × $CH_{Ar}$), 129.8 (4 × $CH_{Ar}$), 129.2 (4 × $CH_{Ar}$), 84.2 (CH), 39.8 (CH), 34.7 ($CH_2$), 32.4 (2 × $CH_2$), 25.2 (2 × $CH_2$), 25.1 ($CH_2$). IR (ν, $cm^{-1}$): 3063, 2949, 2932, 2859 (w), 1446, 1306, 1294, 1156, 1141, 1078 (str.). HRMS (EI) m/z: $[M+H]^+$ calculated for $[C_{20}H_{25}O_4S_2]^+$: 393.1189, found: 393.1196.

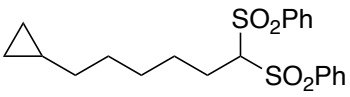
### (5-Cyclopropylpentane-1,1-diyldisulfonyl)dibenzene




$C_{20}H_{24}O_4S_2$
MW: 392,5

The title compound was prepared following General Procedure 4 with bis(phenylsulfonyl)methane (2.96 g, 10 mmol), NaH (0.48 g, 12 mmol, 55% in mineral oil), (4-iodobutyl)cyclopropane (1.37 g, 12 mmol) to afford as a white solid (2.08 g, 53 %), M.p. = 80.5–82.5 °C (not corrected). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.04–7.97 (m, 4H), 7.80–7.70 (m, 2H), 7.68–7.58 (m, 4H), 4.42 (t, *J* = 5.6 Hz, 1H), 2.24–2.14 (m, 2H), 1.68–1.56 (m, 2H), 1.42–1.32 (m, 2H), 1.15 (q, *J* = 7.1 Hz, 2H), 0.66–0.57 (m, 1H), 0.48–0.36 (m, 2H), 0.05– -0.04 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 138.1 (2 × Cq), 134.7 (2 × $CH_{Ar}$), 129.7 (4 × $CH_{Ar}$), 129.2 (4 × $CH_{Ar}$), 84.0 (CH), 34.1 ($CH_2$), 29.2 ($CH_2$), 28.1 ($CH_2$), 25.8 ($CH_2$), 10.7 (CH), 4.5 (2 × $CH_2$). IR (ν, $cm^{-1}$): 3057, 3000, 2971, 2930, 2850 (w), 1446, 1306, 1292, 1155, 1140, 1078 (str.). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $[C_{20}H_{24}O_4S_2Na]^+$: 415.1008, found: 415.1001.

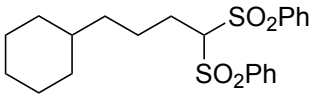
### (6-Cyclopropylhexane-1,1-diyldisulfonyl)dibenzene




$C_{21}H_{26}O_4S_2$
MW: 406,6

The title compound was prepared following General Procedure 4 with bis(phenylsulfonyl)methane (2.96 g, 10 mmol), NaH (12 mmol, 0.52 g, 55% in mineral oil), and (5-iodopentyl)cyclopropane (2.86 g, 12.0 mmol) and to afford as a white solid (1.71 g, 42 %), M.p. = 97–98 °C (not corrected). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.00–7.92 (m, 4H), 7.75–7.66 (m, 2H), 7.63–7.53 (m, 4H), 4.37 (t, *J* = 5.6 Hz, 1H), 2.20–2.10 (m, 2H), 1.59–1.51 (m, 2H), 1.38–1.18 (m, 4H), 1.12 (q, *J* = 7.0 Hz, 2H), 0.67–0.52 (m, 1H), 0.44–0.32 (m, 2H), 0.02– -0.08 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 138.1 (2 × Cq), 134.7 (2 × $CH_{Ar}$), 129.7 (4 × $CH_{Ar}$), 129.2 (4 × $CH_{Ar}$), 84.0 (CH), 34.6 ($CH_2$), 29.1 ($CH_2$), 29.0 ($CH_2$), 28.3 ($CH_2$), 25.8 ($CH_2$), 10.9 (CH), 4.5 (2 × $CH_2$). IR (ν, $cm^{-1}$): 3062, 2994, 2921, 2854 (w), 1448, 1311, 1291, 1157, 1144, 1078 (str.). HRMS (ESI) m/z: $[M+H]^+$ calculated for $[C_{21}H_{27}O_4S_2]^+$: 407.1345, found: 407.1336.

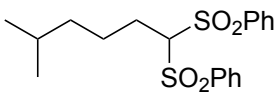
### (4-Cyclohexylbutane-1,1-diyldisulfonyl)dibenzene




$C_{22}H_{28}O_4S_2$
MW: 420,6

The title compound was prepared following General Procedure 4 with bis(phenylsulfonyl)methane (4.45 g, 15 mmol), NaH (0.72 g, 18 mmol, 55% in mineral oil), and (3-iodopropyl)cyclohexane (4.54 g, 18 mmol) to afford as a white solid (3.71 g, 59 %), M.p. = 115.7–117.3 °C (not corrected). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.01–7.92 (m, 4H), 7.76–7.66 (m, 2H), 7.62–7.54 (m, 4H), 4.37 (t, *J* = 5.6 Hz, 1H), 2.16–2.05 (m, 2H), 1.74–1.48 (m, 7H), 1.29–1.02 (m, 6H), 0.88–0.74 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 138.1 (2 × Cq), 134.7 (2 × $CH_{Ar}$), 129.7 (4 × $CH_{Ar}$), 129.2 (4 × $CH_{Ar}$), 84.0 (CH), 37.2 (CH), 36.9 ($CH_2$), 33.3 (2 × $CH_2$), 26.7 ($CH_2$), 26.4 (2 × $CH_2$), 26.0 ($CH_2$), 25.6 ($CH_2$). IR (ν, $cm^{-1}$): 2919, 2849 (w), 1448, 1313, 1292, 1156, 1141, 1078 (str.). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $[C_{22}H_{28}O_4S_2Na]^+$: 443.1321, found: 443.1329.

### (5-Methylhexane-1,1-diyldisulfonyl)dibenzene

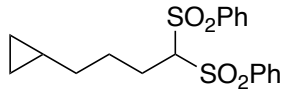



$C_{19}H_{24}O_4S_2$
MW: 380,5

The title compound was prepared following General Procedure 4 with bis(phenylsulfonyl)methane (3.70 g, 12.5 mmol), NaH (0.575 g, 15.0 mmol, 55% in mineral oil), and 1-iodo-4-methylpentane (3.18 g, 15.0 mmol) to afford as a white solid (4.45 g, 94 %), M.p. = 63–65 °C (not corrected). $^1$H NMR (400

MHz, $CDCl_3$) δ 8.06–7.94 (m, 4H), 7.76–7.67 (m, 2H), 7.66–7.56 (m, 4H), 4.40 (t, *J* = 5.6 Hz, 1H), 2.25–2.10 (m, 2H), 1.60–1.40 (m, 3H), 1.15–1.05 (m, 2H), 0.83 (d, *J* = 6.6 Hz, 6H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 138.1 (2 × Cq), 134.7 (2 × $CH_{Ar}$), 129.7 (4 × $CH_{Ar}$), 129.2 (4 × $CH_{Ar}$), 84.0 (CH), 38.3 ($CH_2$), 27.6 (CH), 26.1 ($CH_2$), 26.0 ($CH_2$), 22.5 (2 × $CH_3$). IR (ν, $cm^{-1}$): 2958, 2815, 2867 (w), 1448, 1330, 1296, 1158, 1076 (str.). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $[C_{19}H_{25}O_4S_2]^+$: 381.1189, found: 381.1183.

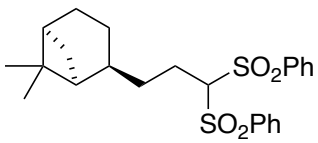
### (4-Cyclopropylbutane-1,1-diyldisulfonyl)dibenzene




$C_{19}H_{22}O_4S_2$
MW: 378,5

The title compound was prepared following General Procedure 4 with bis(phenylsulfonyl)methane (2.96 g, 10.0 mmol), NaH (0.524 g, 12.0 mmol, 55% in mineral oil), and (3-iodopropyl)cyclopropane (2.52 g, 12.0 mmol) and to afford as a white solid (2.03 g, 54 %), M.p. = 132.2–134.2 °C (not corrected). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.01–7.92 (m, 4H), 7.77–7.66 (m, 2H), 7.64–7.54 (m, 4H), 4.38 (t, *J* = 5.7 Hz, 1H), 2.24–2.13 (m, 2H), 1.72–1.60 (m, 2H), 1.14 (q, *J* = 7.1 Hz, 2H), 0.61–0.48 (m, 1H), 0.44–0.31 (m, 2H), -0.01– -0.07 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 137.8 (2 × Cq), 134.4 (2 × $CH_{Ar}$), 129.5 (4 × $CH_{Ar}$), 128.9 (4 × $CH_{Ar}$), 83.8 (CH), 33.9 ($CH_2$), 28.1 ($CH_2$), 25.3 ($CH_2$), 10.0 (CH), 4.3 (2 × $CH_2$). IR (ν, $cm^{-1}$): 3060, 2992, 2951, 2924, 2866 (w), 1446, 1323, 1306, 1293, 1156, 1144, 1078 (str.). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $[C_{19}H_{22}O_4S_2Na]^+$: 401.0852, found: 401.0845.

### (1S,2S,5S)-2-(3,3-bis(phenylsulfonyl)propyl)-6,6-dimethylbicyclo[3.1.1]heptane



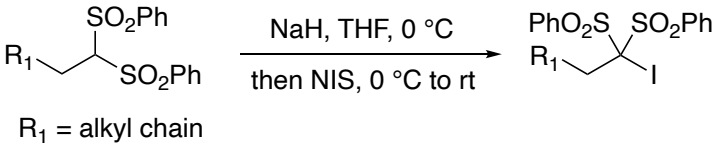

$C_{24}H_{30}O_4S_2$
MW: 446,6

The title compound was prepared following General Procedure 4 with bis(phenylsulfonyl)methane (1.48 g, 5.0 mmol), NaH (0.262 g, 6.0 mmol, 55% in mineral oil), and (1*S*,2*S*,5*S*)-2-(2-iodoethyl)-6,6-dimethylbicyclo[3.1.1]heptane (1.67 g, 6.0 mmol) to afford as a white solid (2.14 g, 96 %), M.p. = 73–75 °C (not corrected). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.98–7.94 (m, 4H), 7.75–7.66 (m, 2H), 7.63–7.54 (m, 4H), 4.33 (t, *J* = 5.5 Hz, 1H), 2.29 (dtd, *J* = 9.5, 6.2, 2.1 Hz, 1H), 2.21–2.02 (m, 2H), 1.95–1.72 (m, 5H), 1.74–1.69 (m, 1H), 1.67–1.55 (m, 2H), 1.32–1.24 (m, 1H), 1.14 (s, 3H), 0.90 (s, 3H), 0.81 (d, *J* = 9.6 Hz, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 138.2 (Cq), 138.1 (Cq), 134.7 (2 × $CH_{Ar}$), 129.8 (2 × $CH_{Ar}$), 129.7 (2 × $CH_{Ar}$), 129.3 (4 × $CH_{Ar}$), 84.2 (CH), 46.0 (CH), 41.5 (CH), 41.2 (CH), 38.7 (Cq), 36.2 ($CH_2$), 33.7 ($CH_2$), 28.2 ($CH_3$), 26.4

($CH_2$), 24.5 ($CH_2$), 23.3 ($CH_3$), 22.0 ($CH_2$). IR (ν, $cm^{-1}$): 2922 (w), 1446, 1320, 1308, 1147, 1078 (str.). HRMS (ESI) m/z: $[M+H]^+$ calculated for $[C_{24}H_{31}O_4S_2]^+$: 447.1658, found: 447.1652.

## General Procedure 5. Iodination

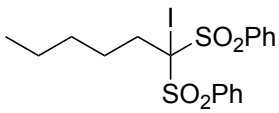
A modified literature procedure was used to obtain the iodides, as shown below.[12]




$R_1$ = alkyl chain

A two-neck round-bottom flask equipped with a gas exhaustion tube was charged with NaH (654 mg, 15 mmol, 55% dispersion in mineral oil). The mineral oil was removed by washing with *n*-pentane (10 mL × 3), and THF (30 mL) was added. The resulting suspension was cooled to 0 °C, and the bis-sulfone derivative (10 mmol) was added slowly in portion-wise (with control of the gas exhaustion). The reaction mixture was stirred at 0 °C for 30–60 min, and a solution of NIS (3.37 g, 15 mmol) in THF (7 mL) was added dropwise. The reaction mixture was protected from light and stirred at room temperature for 30 min. The reaction mixture was filtered through a plug of silica, which was then washed with EtOAc, and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography on silica gel (Heptane/EtOAc = 9:1 to 7:3). The products could be stored at 4 °C in the dark, and no degradation was observed.

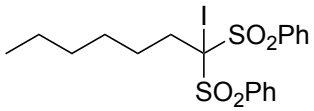
## (1-Iodohexane-1,1-diyldisulfonyl)dibenzene **32α**




$C_{18}H_{21}IO_4S_2$
MW: 492,4

The title compound was prepared following General Procedure 5 with (hexane-1,1-diyldisulfonyl)dibenzene (0.730 g, 2.0 mmol), *N*-Iodosuccinimide (0.585 g, 2.6 mmol) and NaH (0.115 g, 3.0 mmol, 55% in mineral oil) to afford as a dense orange oil (0.641 g, 67 %, contaminated with 6% of SM). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.17–8.11 (m, 4H), 7.77–7.70 (m, 2H), 7.64–7.55 (m, 4H), 2.25–2.14 (m, 2H), 1.79–1.72 (m, 2H), 1.36–1.23 (m, 4H), 0.87 (t, J = 6.9 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 135.2 (2 × Cq), 135.0 (2 × $CH_{Ar}$), 132.4 (4 × $CH_{Ar}$), 128.5 (4 × $CH_{Ar}$), 84.4 (Cq), 36.3 ($CH_2$), 31.8 ($CH_2$), 29.4 ($CH_2$), 22.2 ($CH_2$), 14.0 ($CH_3$). IR (ν, $cm^{-1}$): 2955, 2925, 2869 (w), 1446, 1331, 1309, 1142, 1073 (str.). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $[C_{18}H_{21}O_4IS_2Na]^+$: 514.9818, found: 514.9800.

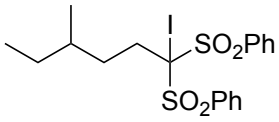
### (1-Iodoheptane-1,1-diyldisulfonyl)dibenzene **33α**




$C_{19}H_{23}IO_4S_2$
MW: 506,4

The title compound was prepared following General Procedure 5 with (heptane-1,1-diyldisulfonyl)dibenzene (5.71 g, 15.0 mmol), *N*-Iodosuccinimide (4.39 g, 19.5 mmol) and NaH (0.862 g, 22.5 mmol, 55% in mineral oil) to afford as a yellowish sticky oil (6.12 g, 81 %, contaminated with ca. 10% of starting material). $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.19–8.09 (m, 4H), 7.78–7.69 (m, 2H), 7.65–7.54 (m, 4H), 2.25–2.16 (m, 2H), 1.81–1.68 (m, 2H), 1.37–1.20 (m, 6H), 0.87 (t, *J* = 6.9 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 135.3 (2 × Cq), 135.1 (2 × $CH_{Ar}$), 132.5 (4 × $CH_{Ar}$), 128.6 (4 × $CH_{Ar}$), 84.5 (Cq), 36.4 ($CH_2$), 31.5 ($CH_2$), 29.8 ($CH_2$), 29.4 ($CH_2$), 22.6 ($CH_2$), 14.1 ($CH_3$). IR (ν, $cm^{-1}$): 2953, 2922, 2869 (w), 1446, 1330, 1310, 1142, 1073 (str.). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $[C_{19}H_{23}O_4IS_2Na]^+$: 528.9975, found: 528.9960.

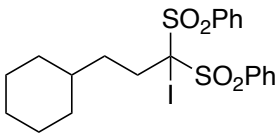
### (1-Iodo-4-methylhexane-1,1-diyldisulfonyl)dibenzene **34α**




$C_{19}H_{23}IO_4S_2$
MW: 506,4

The title compound was prepared following General Procedure 5 with (4-methylhexane-1,1-diyldisulfonyl)dibenzene (1.65 g, 4.34 mmol), *N*-Iodosuccinimide (1.46 g, 6.5 mmol) and NaH (0.26 g, 6.5 mmol, 55% in mineral oil) to afford as an orange sticky oil (1.92 g, 87 %, contaminated with 7 % of starting material). $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.16–8.11 (m, 4H), 7.77–7.70 (m, 2H), 7.66–7.54 (m, 4H), 2.26 (ddd, *J* = 14.9, 11.7, 4.8 Hz, 1H), 2.16 (ddd, *J* = 14.9, 11.5, 4.4 Hz, 1H), 1.78 (ddt, *J* = 13.4, 11.6, 4.7 Hz, 1H), 1.57 (dddd, *J* = 13.5, 11.9, 7.2, 4.8 Hz, 1H), 1.37–1.23 (m, 2H), 1.22–1.09 (m, 1H), 0.86 (t, *J* = 7.2 Hz, 3H), 0.85 (d, *J* = 6.9 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 135.37 (Cq), 135.35 (Cq), 135.15 (2 × $CH_{Ar}$), 132.57(2 × $CH_{Ar}$), 132.55 (2 × $CH_{Ar}$), 128.62 (2 × $CH_{Ar}$), 128.61 (2 × $CH_{Ar}$), 85.1 (Cq), 36.1 ($CH_2$), 35.1 (CH), 34.5 ($CH_2$), 29.3 ($CH_2$), 19.2 ($CH_3$), 11.5 ($CH_3$). IR (ν, $cm^{-1}$): 2957, 2922, 2872 (w), 1446, 1331, 1310, 1143, 1074 (str.). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $[C_{19}H_{23}O_4IS_2Na]^+$: 528.9975, found: 528.9968.

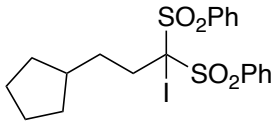
(3-Cyclohexyl-1-iodopropane-1,1-diyldisulfonyl)dibenzene **35α**




$C_{21}H_{25}IO_4S_2$
MW: 532,5

The title compound was obtained following the General Procedure 5 with (3-Cyclohexylpropane-1,1-diyldisulfonyl)dibenzene as yellow sticky oil by Dr. Fabrice Dénès and kindly donated to me. $^1$H NMR (400 MHz, $CDCl_3$) δ 8.18–8.10 (m, 4H), 7.78–7.65 (m, 2H), 7.67–7.52 (m, 4H), 2.28–2.18 (m, 2H), 1.75–1.57 (m, 7H), 1.25–1.05 (m, 4H), 0.96–0.84 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 135.4 (2 × Cq), 135.1 (2 × $CH_{Ar}$), 132.6 (4 × $CH_{Ar}$), 128.6 (4 × $CH_{Ar}$), 85.2 (Cq), 38.3 (CH), 37.0 ($CH_2$), 34.3 ($CH_2$), 33.2 (2 × $CH_2$), 26.6 ($CH_2$), 26.4 (2 × $CH_2$). IR (ν, $cm^{-1}$): 2919 (w), 1446, 1328, 1309, 1142, 1074 (str.). HRMS (ESI) m/z: $[M+H]^+$ calculated for $[C_{21}H_{26}O_4IS_2]^+$: 533.0312, found: 533.0301.

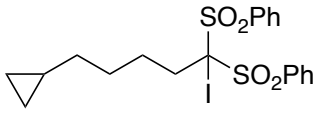
(3-Cyclopentyl-1-iodopropane-1,1-diyldisulfonyl)dibenzene **36α**




$C_{20}H_{23}IO_4S_2$
MW: 518,4

The title compound was obtained following the General Procedure 5 with (3-cyclopentylpropane-1,1-diyldisulfonyl)dibenzene as yellow sticky oil by Dr. Fabrice Dénès and kindly donated to me. $^1$H NMR (400 MHz, $CDCl_3$) δ 8.18–8.10 (m, 4H), 7.78–7.69 (m, 2H), 7.67–7.55 (m, 4H), 2.25–2.21 (m, 2H), 1.81–1.73 (m, 2H), 1.73–1.65 (m, 3H), 1.65–1.45 (m, 4H), 1.15–1.03 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 135.4 (2 × Cq), 135.2 (2 × $CH_{Ar}$), 132.6 (4 × $CH_{Ar}$), 128.6 (4 × $CH_{Ar}$), 84.8 (Cq), 40.4 (CH), 35.85 ($CH_2$), 35.83 ($CH_2$), 32.5 (2 × $CH_2$), 25.2 (2 × $CH_2$). IR (ν, $cm^{-1}$): 2920, 2863 (w), 1446, 1330, 1310, 1140, 1074 (str.). HRMS (ESI) m/z: $[M+H]^+$ calculated for $[C_{20}H_{24}O_4IS_2]^+$: 519.0155, found: 519.0144.

(5-Cyclopropyl-1-iodopentane-1,1-diyldisulfonyl)dibenzene **37α**

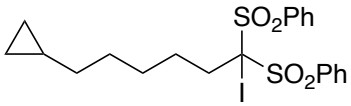



$C_{20}H_{23}IO_4S_2$
MW: 518,4

The title compound was prepared following General Procedure 5 with (5-cyclopropylpentane-1,1-diyldisulfonyl)dibenzene (1.96 g, 5.0 mmol), *N*-Iodosuccinimide (1.69 g, 7.5 mmol) and NaH (0.3 g, 7.5 mmol, 55% in mineral oil) to afford as a yellow solid (2.375 g, 92 %, contaminated with 6 % of starting material). M.p. = 83.5–85.5 °C (not corrected). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.20–8.11 (m, 4H), 7.81–7.69 (m, 2H), 7.68–7.55 (m, 4H), 2.23–2.18 (m, 2H), 1.80–1.71 (m, 2H), 1.40 (tt, *J* = 7.6, 6.2 Hz, 2H), 1.19 (app. q, *J* = 7.1 Hz, 2H), 0.70–0.56 (m, 1H), 0.42–0.38 (m, 2H), 0.04– -0.05 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 135.3 (2 × Cq),

135.1 (2 × $CH_{Ar}$), 132.5 (4 × $CH_{Ar}$), 128.6 (4 × $CH_{Ar}$), 84.4 (Cq), 36.5 ($CH_2$), 34.3 ($CH_2$), 29.8 ($CH_2$), 29.7 ($CH_2$), 10.8 (CH), 4.6 (2 × $CH_2$). IR (ν, $cm^{-1}$): 3069, 2993, 2913, 2850 (w), 1445, 1328, 1305, 1138, 1072 (str.). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $[C_{20}H_{23}O_4IS_2Na]^+$: 540.9975, found: 540.9965.

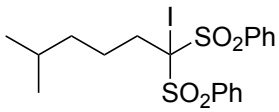
### (6-Cyclopropyl-1-iodohexane-1,1-diyldisulfonyl)dibenzene **38α**




$C_{21}H_{25}IO_4S_2$
MW: 532,5

The title compound was prepared following General Procedure 5 with (6-cyclopropylhexane-1,1-diyldisulfonyl)dibenzene (1.60 g, 3.94 mmol), *N*-Iodosuccinimide (1.33 g, 5.9 mmol) and NaH (0.258 g, 5.9 mmol, 55% in mineral oil) to afford as a yellow solid (1.85 g, 88 %, contaminated with 6 % of starting material), M.p. = 90.7–92.3 °C (not corrected). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.21–8.10 (m, 4H), 7.79–7.69 (m, 2H), 7.65–7.53 (m, 4H), 2.23–2.18 (m, 2H), 1.79–1.71 (m, 2H), 1.43–1.29 (m, 4H), 1.17 (q, *J* = 7.0 Hz, 2H), 0.68–0.56 (m, 1H), 0.46–0.33 (m, 2H), 0.06– -0.06 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 135.4 (2 × Cq), 135.1 (2 × $CH_{Ar}$), 132.5 (4 × $CH_{Ar}$), 128.6 (4 × $CH_{Ar}$), 84.5 (Cq), 36.4 ($CH_2$), 34.6 ($CH_2$), 29.9 ($CH_2$), 29.6 ($CH_2$), 29.3 ($CH_2$), 10.9 (CH), 4.5 (2 × $CH_2$). IR (ν, $cm^{-1}$): 2992, 2954, 2915, 2852 (w), 1446, 1331, 1319, 1310, 1144, 1073 (str.). HRMS (ESI) m/z: $[M+H]^+$ calculated for $[C_{21}H_{26}O_4IS_2]^+$: 533.0312, found: 533.0302.

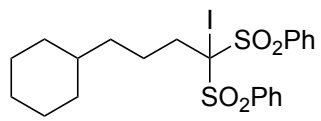
### (1-Iodo-5-methylhexane-1,1-diyldisulfonyl)dibenzene **39α**




$C_{19}H_{23}IO_4S_2$
MW: 506,4

The title compound was prepared following General Procedure 5 with (5-methylhexane-1,1-diyldisulfonyl)dibenzene (1.90 g, 5.0 mmol), *N*-Iodosuccinimide (1.46 g, 6.5 mmol) and NaH (0.30 g, 7.5 mmol, 55% in mineral oil) to afford as a yellow solid (2.25 g, 89 %, contaminated with 4 % of starting material), M.p. = 110.3–111.4 °C (not corrected). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.18–8.09 (m, 4H), 7.78–7.69 (m, 2H), 7.65–7.54 (m, 4H), 2.20–2.16 (m, 2H), 1.80–1.67 (m, 2H), 1.53 (dhept, *J* = 13.3, 6.6 Hz, 1H), 1.22–1.10 (m, 2H), 0.87 (d, *J* = 6.6 Hz, 6H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 135.2 (2 × Cq), 135.0 (2 × $CH_{Ar}$), 132.4 (4 × $CH_{Ar}$), 128.5 (4 × $CH_{Ar}$), 84.4 (Cq), 38.8 ($CH_2$), 36.4 ($CH_2$), 27.7 (CH + $CH_2$), 22.5 (2 × $CH_3$). IR (ν, $cm^{-1}$): 2955, 2920, 2866 (w), 1447, 1328, 1319, 1308, 1141, 1072 (str.). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $[C_{19}H_{23}O_4IS_2Na]^+$: 528.9975, found: 528.9962.

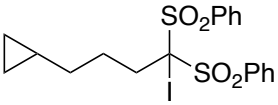
### (4-Cyclohexyl-1-iodobutane-1,1-diyldisulfonyl)dibenzene **40α**




$C_{22}H_{27}IO_4S_2$
MW: 546,5

The title compound was prepared following General Procedure 5 with (4-cyclohexylbutane-1,1-diyldisulfonyl)dibenzene (2.94 g, 7.0 mmol), *N*-Iodosuccinimide (2.05 g, 9.1 mmol) and NaH (0.42 g, 10.5 mmol, 55% in mineral oil) to afford as a red sticky oil (2.49 g, 65 %, contaminated with 5 % of starting material). $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.16–8.11 (m, 4H), 7.77–7.70 (m, 2H), 7.64–7.55 (m, 4H), 2.20– 2.15 (m, 2H), 1.78–1.60 (m, 6H), 1.24–1.04 (m, 6H), 0.93–0.79 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 135.2 (2 × Cq), 135.0 (2 × $CH_{Ar}$), 132.4 (4 × $CH_{Ar}$), 128.5 (4 × $CH_{Ar}$), 84.4 (Cq), 37.38 ($CH_2$), 37.32 (CH), 36.5 ($CH_2$), 33.3 (2 × $CH_2$), 27.2($CH_2$), 26.6 ($CH_2$), 26.3 (2 × $CH_2$). IR (ν, $cm^{-1}$): 2918, 2826 (w), 1446, 1373, 1331, 1143, 1073 (str.). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $[C_{22}H_{27}O_4IS_2Na]^+$: 569.0288, found: 569.0299.

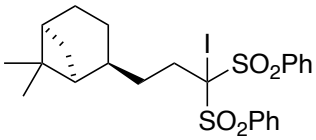
### (4-Cyclopropyl-1-iodobutane-1,1-diyldisulfonyl)dibenzene **41α**




$C_{19}H_{21}IO_4S_2$
MW: 504,4

The title compound was prepared following General Procedure 5 with (4-cyclopropylbutane-1,1-diyldisulfonyl)dibenzene (1.90 g, 5.0 mmol), *N*-Iodosuccinimide (1.69 g, 7.5 mmol) and NaH (0.327 g, 7.5 mmol, 55% in mineral oil) to afford as a yellow solid (2.19 g, 87%, contaminated with 4% of starting material), M.p. = 91.5–93.5 °C (not corrected). $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.18–8.11 (m, 4H), 7.78–7.67 (m, 2H), 7.65–7.54 (m, 4H), 2.27–2.23 (m, 2H), 1.92–1.86 (m, 2H), 1.22 (q, *J* = 7.1 Hz, 2H), 0.66–0.53 (m, 1H), 0.43–0.38 (m, 2H), 0.00– -0.06 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 135.4 (2 × Cq), 135.2 (2 × $CH_{Ar}$), 132.6 (4 × $CH_{Ar}$), 128.6 (4 × $CH_{Ar}$), 84.6 (Cq), 36.3 ($CH_2$), 34.7 ($CH_2$), 30.1 ($CH_2$), 10.5 (CH), 4.8 (2 × $CH_2$). IR (ν, $cm^{-1}$): 3064, 2995, 2980, 2967, 2925, 2887, 2840 (w), 1445, 1331, 1307, 1142, 1076 (str.). HRMS (ESI) m/z: $[M+H]^+$ calculated for $[C_{19}H_{22}O_4IS_2]^+$: 504.9999, found: 504.9993.

(*1S,2S,5S*)-2-(3-iodo-3,3-bis(phenylsulfonyl)propyl)-6,6-dimethylbicyclo[3.1.1]heptane **42α**



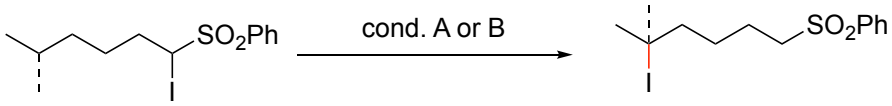

$C_{24}H_{29}IO_4S_2$
MW: 572,5

The title compound was prepared following General Procedure 5 with (1*S*,2*S*,5*S*)-2-(3,3-bis(phenylsulfonyl)propyl)-6,6-dimethylbicyclo- [3.1.1]heptane (2.00 g, 4.48 mmol), *N*-Iodosuccinimide (1.51 g, 6.72 mmol) and NaH (0.293 g, 6.72 mmol, 55% in mineral oil) to afford as a yellow solid (1.95 g, 76%, contaminated with 4 % of starting material), M.p. = 66.7–67.3 °C (not corrected). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.19–8.09 (m, 4H), 7.77–7.71 (m, 2H), 7.61–7.58 (m, 4H), 2.32 (dtd, *J* = 9.5, 6.3, 2.1 Hz, 1H), 2.27–2.10 (m, 2H), 1.97–1.78 (m, 8H), 1.46–1.39 (m, 1H), 1.18 (s, 3H), 1.03 (s, 3H), 0.83 (d, *J* = 9.7 Hz, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 135.44 (Cq), 135.38 (Cq), 135.15 ($CH_{Ar}$), 135.13 ($CH_{Ar}$), 132.58 (2 × $CH_{Ar}$), 132.54 (2 × $CH_{Ar}$), 128.64 (2 × $CH_{Ar}$), 128.63 (2 × $CH_{Ar}$), 85.1 (Cq), 46.2 (CH), 41.7 (CH), 41.6 (CH), 38.8 (Cq), 37.1 ($CH_2$), 35.3 ($CH_2$), 33.8 ($CH_2$), 28.2 ($CH_3$), 26.5 ($CH_2$), 23.3 ($CH_3$), 22.2 ($CH_2$). IR (ν, $cm^{-1}$): 2905 (w), 1445, 1332, 1309, 1141, 1075 (str.). HRMS (ESI) m/z: $[M+H]^+$ calculated for $[C_{24}H_{30}O_4IS_2]^+$: 573.0625, found: 573.0619.

## Remote functionalisation

### General procedure for the isomerisation of α-iodoalkyl mono- and bis-sulfones through 1.5-HAT process

### General Procedure 6. Isomerisation of α-iodoalkyl mono- and bis-sulfones

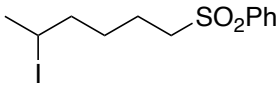



**A:** DTBHN (0.2 equiv), TFT (0.2 M), 80 °C;
**B:** 1) $K_2CO_3$ (1 equiv), DTBHN (0.2 equiv), TFT (0.2 M), 80 °C, 15 min; then 2) DBU (3 eq), 0 °C to rt, on.

**Conditions A**: A 10 mL two-neck round-bottom flask equipped with a condenser and under Argon was charged with α-iodoalkyl mono- or bis-sulfones (0.5 mmol) and dissolved in anhydrous trifluorotoluene (2 mL). DTBHN (17.4 mg, 0.1 mmol) was then quickly added, and the reaction flask was immersed in the pre-heated oil bath at 80 °C and stirred for 15 minutes. The reaction mixture was protected from light with Aluminium foil. Upon completion (TLC monitoring), the volatiles were removed under reduced pressure and the crude product was purified by flash column chromatography on silica gel (Heptane/EtOAc = 90:10 to 80:20).

**Conditions B**: A 10 mL two-neck round-bottom flask equipped with a condenser and under Argon was charged with α-iodoalkyl mono- or bissulfones (0.5 mmol), $K_2CO_3$ (69.1 mg, 0.5 mmol) an anhydrous trifluorotoluene (2 mL). DTBHN (17.4 mg, 0.1 mmol) was then quickly added, and the reaction flask was immersed in the pre-heated oil bath at 80 °C and stirred for 15 minutes. The reaction mixture was protected from light with Aluminium foil. Upon completion (TLC monitoring), the reaction mixture was cooled to 0 °C and 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) (228 mg, 1.5 mmol) was added. The reaction mixture was stirred at rt for 14h. Then, the volatiles were removed under reduced pressure, and the crude product was purified by flash column chromatography on silica gel (Heptane/EtOAc = 90:10 to 80:20).

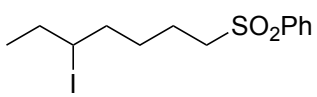
((5-Iodohexyl)sulfonyl)benzene **1ε**




$C_{12}H_{17}IO_2S$
MW: 352,23

The title compound was prepared following General Procedure 6 (conditions A) with ((1-iodohexyl)sulfonyl)benzene (0.704 g, 2.0 mmol), trifluorotoluene (6 mL), and DTBHN (69 mg, 0.4 mmol) to afford as a colourless liquid (0.528 g, 75 %). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.93–7.87 (m, 2H), 7.69–7.62 (m, 1H), 7.60–7.55 (m, 2H), 4.10 (dqd, *J* = 8.7, 6.8, 4.2 Hz, 1H), 3.10 (t, *J* = 8.0 Hz, 2H), 1.88 (d, *J* = 6.8 Hz, 3H), 1.85–1.64 (m, 3H), 1.63–1.51 (m, 2H), 1.52–1.38 (m, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.3 (2 × Cq), 133.9 ($CH_{Ar}$), 129.5 (2 × $CH_{Ar}$), 128.2 (2 × $CH_{Ar}$), 56.2 ($CH_2$), 42.2 ($CH_2$), 29.1 (CH), 29.0 ($CH_3$), 28.6 ($CH_2$), 22.0 ($CH_2$). IR (ν, $cm^{-1}$): 2916, 2860 (w), 1302, 1289, 1142, 1084 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{12}H_{17}IO_2SNa]^+$: 374.9874, found: 374.9874.

((5-Iodoheptyl)sulfonyl)benzene **3ε**




$C_{13}H_{19}IO_2S$
MW: 366,3

The title compound was prepared following General Procedure 6 (conditions A) with ((1-iodoheptyl)sulfonyl)benzene (0.5 mmol, 0.183 g), and DTBHN (18 mg, 0.1 mmol) (30 min) to afford as a pale yellow oil (110 mg, 60%; 4:1 mixture of regioisomers).

((5-Iodoheptyl)sulfonyl)benzene (Major regioisomer):

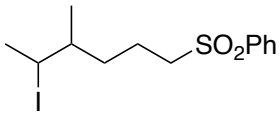
$^1$H NMR (400 MHz, $CDCl_3$) δ 7.95–7.88 (m, 2H), 7.70–7.63 (m, 1H), 7.61–7.54 (m, 2H), 3.99 (tt, *J* = 8.7, 4.2 Hz, 1H), 3.16–3.05 (m, 2H), 1.87–1.54 (m, 7H), 1.54–1.31 (m, 1H), 0.99 (t, *J* = 7.2

Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.2 (Cq), 133.69 ($CH_{Ar}$), 129.31 (2 × $CH_{Ar}$), 128.0 (2 × $CH_{Ar}$), 56.08 ($CH_2$), 40.8 (CH), 39.5 ($CH_2$), 33.7 ($CH_2$), 28.3 ($CH_2$), 21.9 ($CH_2$), 14.0 ($CH_3$). IR (ν, $cm^{-1}$): 2961, 2933, 2871 (w), 1445, 1302, 1142, 1084 (str.). HRMS (EI) m/z: $[M-I]^+$ calculated for $[C_{13}H_{19}O_2S_2]^+$: 239.1100, found: 239.1099; calculated for $[I]^+$: 126.9039, found: 126.9040.

((5-Iodoheptyl)sulfonyl)benzene (minor regioisomer, characteristic signals):

$^1$H NMR (400 MHz, $CDCl_3$) δ 4.12 (dqd, *J* = 8.8, 6.9, 4.5 Hz, 1H), 1.89 (d, *J* = 6.8 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.2 (Cq), 133.65 ($CH_{Ar}$), 129.29 (2 × $CH_{Ar}$), 56.12 ($CH_2$), 42.3 ($CH_2$), 29.8 (CH), 29.2 ($CH_2$), 28.9 ($CH_3$), 27.4 ($CH_2$), 22.5 ($CH_2$).

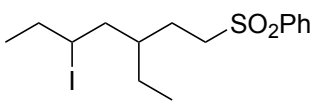
### ((5-Iodo-4-methylhexyl)sulfonyl)benzene **4ε**




$C_{13}H_{19}IO_2S$
MW: 366,26

The title compound was prepared following General Procedure 6 (conditions A) with ((1-iodo-4-methylhexyl)sulfonyl)benzene (0.733 g, 2.0 mmol), trifluorotoluene (6 mL), and DTBHN (35 mg, 0.2 mmol) to afford as a yellow oil (0.675 g, 92 %; dr 56:44). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.94–7.87 (m, 2H, dia 1 + dia 2), 7.69–7.63 (m, 1H, dia 1 + dia 2), 7.61–7.54 (m, 2H, dia 1 + dia 2), 4.30–4.18 (m, 1H, dia 1 + dia 2), 3.11–3.06 (m, 2H, dia 1 + dia 2), 1.85 (d, *J* = 7.0 Hz, 3H, 1 dia), 1.82 (d, *J* = 7.0 Hz, 3H, 1 dia), 1.85–1.66 (m, 2H, dia 1 + dia 2), 1.59–1.48 (m, 1H, 1 dia), 1.45–1.27 (m, 2H, 1 dia), 1.27–1.15 (m, 1H dia 1 + 1H dia 2), 0.95 (d, *J* = 6.2 Hz, 3H, 1 dia), 0.86 (d, *J* = 6.0 Hz, 3H, 1 dia), 0.84–0.76 (m, 1H, 1 dia). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.3 (Cq, dia 1 + dia 2), 133.87 (2 × $CH_{Ar}$), 133.85 (2 × $CH_{Ar}$), 129.5 (2 × $CH_{Ar}$, dia 1 + dia 2), 128.1 (2 × $CH_{Ar}$, dia 1 + dia 2), 56.44 ($CH_2$), 56.36 ($CH_2$), 40.7 (CH), 41.4 (CH), 39.7 (CH), 38.5 (CH), 36.0 ($CH_2$), 33.2 ($CH_2$), 26.4 ($CH_3$), 25.4 ($CH_3$), 20.5 ($CH_2$), 20.3 ($CH_2$), 18.5 ($CH_3$), 17.0 ($CH_3$). IR (ν, $cm^{-1}$): 2962, 2915, 2871 (w), 1301, 1142, 1084 (str.). HRMS (ESI): $[M+H]^+$ calculated for $[C_{13}H_{20}IO_2S]^+$: 367.0228, found: 367.0228.

### ((3-Ethyl-5-iodoheptyl)sulfonyl)benzene **5ε**



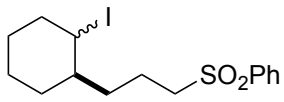

$C_{15}H_{23}IO_2S$
MW: 394,3

The title compound was prepared following General Procedure 6 (conditions A) with ((3-ethyl-1-iodoheptyl)sulfonyl)benzene (0.197 g, 0.5 mmol) and DTBHN (9 mg, 0.05 mmol) to afford as a white solid (0.132 g, 67 %; 9:1 mixture of regioisomers, dr = 1:1).

Major regioisomer (dr = ca. 1:1):

$^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.97–7.88 (m, 4H, dia 1 + dia 2), 7.71–7.63 (m, 2H, dia 1 + dia 2), 7.62–7.54 (m, 4H, dia 1 + dia 2), 4.02–3.90 (m, 2H, dia 1 + dia 2), 3.16–2.99 (m, 4H, dia 1 + dia 2), 1.97–1.85 (m, 1H, 1 dia), 1.85–1.55 (m, 11H, dia 1 + dia 2), 1.55–1.13 (m, 6H, dia 1 + dia 2), 1.001 (t, *J* = 7.2 Hz, 3H, 1 dia), 0.999 (t, *J* = 7.2 Hz, 3H, 1 dia), 0.81 (t, *J* = 7.3 Hz, 3H, 1 dia), 0.79 (t, *J* = 7.3 Hz, 3H, 1 dia). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.2 (Cq), 139.1 (Cq), 133.71 ($CH_{Ar}$), 133.68 ($CH_{Ar}$), 129.32 (2 × $CH_{Ar}$), 129.31 (2 × $CH_{Ar}$), 128.0 (2 × $CH_{Ar}$, dia 1 + dia 2), 54.0 ($CH_2$), 53.4 ($CH_2$), 43.8 ($CH_2$), 43.7 ($CH_2$), 39.5 (CH), 39.1 (CH), 37.9 (2 × CH), 34.2 ($CH_2$), 34.0 ($CH_2$), 25.5 ($CH_2$), 25.4 ($CH_2$), 24.4 ($CH_2$), 24.2 ($CH_2$), 14.07 ($CH_3$), 14.03 ($CH_3$), 10.4 ($CH_3$), 9.7 ($CH_3$). IR (ν, $cm^{-1}$): 2957, 2928, 2871 (w), 1445, 1294, 1271, 1142, 1084 (str.). HRMS (EI) m/z: $[M-I]^+$ calculated for $[C_{15}H_{23}O_2S_2]^+$: 267.1413, found: 267.1414; calculated for $[I]^+$: 126.9039, found: 126.9040.

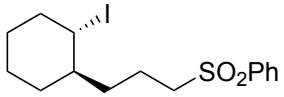
### ((3-((1R,2S)- and ((3-((1R,2R)-2-Iodocyclohexyl)propyl)sulfonyl)benzene **6ε**




$C_{15}H_{21}IO_2S$
MW: 392.2955

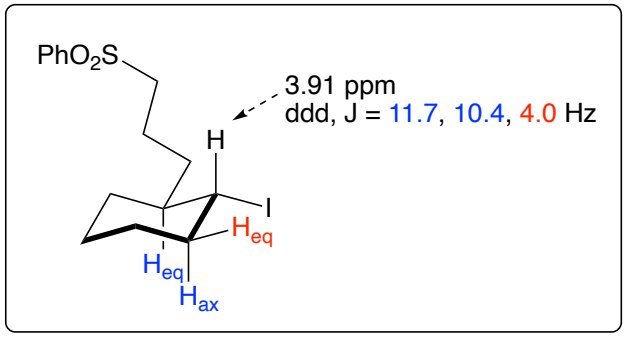
The title compound was prepared following General Procedure 6 (conditions A) with ((3-cyclohexyl-1-iodopropyl)sulfonyl)benzene (0.203 g, 0.52 mmol) and DTBHN (18 mg, 0.1 mmol) (2 h) to afford as a colourless oil (69%, trans/cis 45:55). The two isomers could be separated to give *trans* (63.76 mg, 31%, $R_f$ = 0.56) and *cis* isomers (76.34 mg, 38%, $R_f$ = 0.5).

<u>((3-((1*R*,2*S*)-2-Iodocyclohexyl)propyl)sulfonyl)benzene (*trans* isomer):</u>

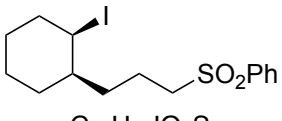



$C_{15}H_{21}IO_2S$
MW: 392,3

$R_f$ = 0.56. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.95–7.89 (m, 2H), 7.69–7.63 (m, 1H), 7.61–7.55 (m, 2H), 3.91 (ddd, *J* = 11.7, 10.4, 4.0 Hz, 1H), 3.18–2.99 (m, 2H), 2.53–2.44 (m, 1H), 2.13–2.00 (m, 1H), 1.89–1.49 (m, 7H), 1.35–1.21 (m, 3H), 1.07–0.97 (m, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.4 (Cq), 133.8 ($CH_{Ar}$), 129.5 (2 × $CH_{Ar}$), 128.2 (2 × $CH_{Ar}$), 56.4 ($CH_2$), 46.3 (CH), 41.6 (CH + $CH_2$), 36.9 ($CH_2$), 31.9 ($CH_2$), 29.1 ($CH_2$), 25.7 ($CH_2$), 19.5 ($CH_2$). IR (ν, $cm^{-1}$): 2925, 2853 (w), 1445, 1302, 1142, 1084 (str.). HRMS (ESI): $[M+H]^+$ calculated for $[C_{15}H_{22}IO_2S]^+$: 393.0379, found: 393.0379.

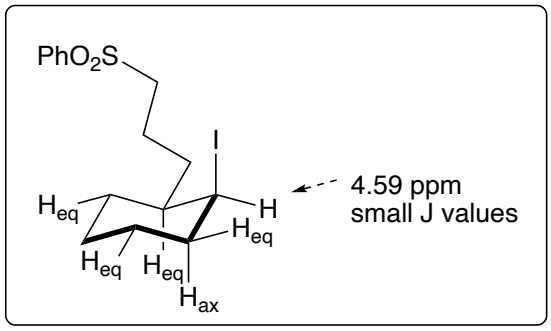



((3-((1*R*,2*R*)-2-Iodocyclohexyl)propyl)sulfonyl)benzene (*cis* isomer):

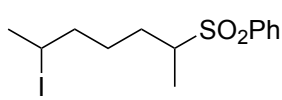



$C_{15}H_{21}IO_2S$
MW: 392,3

$R_f$ = 0.5. Brown solid. M.p. = 67–69 °C (not corrected). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.95–7.88 (m, 2H), 7.71–7.63 (m, 1H), 7.61–7.54 (m, 2H), 4.60–4.58 (m, 1H), 3.15–3.00 (m, 2H), 2.22–2.11 (m, 1H), 1.84–1.59 (m, 5H), 1.59–1.51 (m, 1H), 1.45–1.38 (m, 1H), 1.36–1.16 (m, 4H), 0.42 (dtt, *J* = 10.2, 6.6, 3.1 Hz, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.3 (Cq), 133.8 ($CH_{Ar}$), 129.5 (2 × $CH_{Ar}$), 128.2 (2 × $CH_{Ar}$), 56.4 ($CH_2$), 46.7 (CH), 42.2 (CH), 36.9 ($CH_2$), 36.7 ($CH_2$), 28.9 ($CH_2$), 25.5 ($CH_2$), 22.8 ($CH_2$), 19.6 ($CH_2$). IR (ν, $cm^{-1}$): 2922, 2874, 2848 (w), 1445, 1300, 1276, 1149, 1084 (str.). HRMS (ESI): $[M+H]^+$ calculated for $[C_{15}H_{22}IO_2S]^+$: 393.0379, found: 393.0379.




((6-Iodoheptan-2-yl)sulfonyl)benzene **7ε**

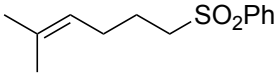



$C_{13}H_{19}IO_2S$
MW: 366,3

The title compound was prepared following General Procedure 6 (conditions A) with ((2-iodoheptan-2-yl)sulfonyl)benzene (91.6 mg, 0.25 mmol) and DTBHN (18 mg, 0.1 mmol) (30 min) to afford as a yellow oil (22.8 mg, 25%, dr = 1:1). $R_f$ = 0.48. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.97–7.85 (m, 4H, dia 1 + dia 2), 7.72–7.66 (m, 2H, dia 1 + dia 2), 7.60–7.55 (m, 4H, dia 1 + dia 2), 4.17–4.07 (m, 2H, dia 1 + dia 2), 3.07–2.99 (m, 2H, dia 1 + dia 2), 2.12–1.95 (m, 2H, dia 1 + dia 2), 1.903 (d, *J* = 6.8 Hz, 3H, dia 1), 1.895 (d, *J* = 6.8 Hz, 3H, dia 2), 1.87–1.36 (m, 10H,

dia 1 + dia 2), 1.30 (d, *J* = 6.9 Hz, 6H, dia 1 + dia 2). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 137.3 (Cq, dia 1 + dia 2), 133.7 ($CH_{Ar}$, dia 1 + dia 2), 129.1 (2 × $CH_{Ar}$, dia 1 + dia 2), 129.0 (2 × $CH_{Ar}$, dia 1 + dia 2), 60.0 (CH), 59.9 (CH), 42.4 ($CH_2$), 42.1 ($CH_2$), 29.4 (CH), 29.1 (CH), 29.0 ($CH_3$), 28.8 ($CH_3$), 28.3 ($CH_2$), 28.0 ($CH_2$), 27.0 ($CH_2$), 26.9 ($CH_2$), 13.4 ($CH_3$), 13.3 ($CH_3$). IR (ν, $cm^{-1}$): 2932, 2864 (w), 1445, 1300, 1141, 1082 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{13}H_{19}IO_2SNa]^+$: 389.0043, found: 389.0038.

### ((5-Methylhex-4-en-1-yl)sulfonyl)benzene **2e**

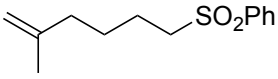



$C_{13}H_{18}O_2S$
MW: 238,3

The title compound was prepared following General Procedure 6 (conditions B) with ((1-iodo-5-methylhexyl)sulfonyl)benzene (0.183 g, 0.5 mmol), trifluorotoluene (2.2 mL), $K_2CO_3$ (69.1 mg, 0.5 mmol), DTBHN (17.4 mg, 0.1 mmol), and DBU (0.229 mL, 1.5 mmol) to afford as a colorless oil (92.9 mg, 78%; ratio internal:terminal alkene 4:1).

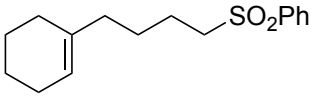
((5-Methylhex-4-en-1-yl)sulfonyl)benzene (major isomer): $R_f$ = 0.58. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.94–7.87 (m, 2H), 7.69–7.62 (m, 1H), 7.61–7.52 (m, 2H), 5.00–4.95 (, 1H), 3.08–3.04 (m, 2H), 2.04 (q, *J* = 7.3 Hz, 2H), 1.78–1.68 (m, 2H), 1.65 (bs, 3H), 1.54 (bs, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.2 (Cq), 133.7 (=Cq), 133.6 ($CH_{Ar}$), 129.23 (2 × $CH_{Ar}$), 128.1 (2 × $CH_{Ar}$), 122.1 (=CH), 55.7 ($CH_2$), 26.4 ($CH_2$), 25.7 ($CH_3$), 22.8 ($CH_2$), 17.7 ($CH_3$). IR (ν, $cm^{-1}$): 2915, 2870 (w), 1446, 1303, 1145, 1085 (str.). HRMS (ESI): $[M+H]^+$ calculated for $[C_{13}H_{19}O_2S]^+$: 239.1100, found: 239.1105.

((5-Methylhex-5-en-1-yl)sulfonyl)benzene (minor, characteristic signals): $^1$H NMR (400 MHz, $CDCl_3$) δ 4.69–4.66 (m, 1H), 4.61–4.69 (m, 1H), 3.11–3.06 (m, 2H), 1.97 (t, *J* = 7.6 Hz, 2H), 1.67–1.75 (m, 2H), 1.65 (bs, 3H), 1.52–1.43 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 110.6 (=$CH_2$), 56.1 ($CH_2$), 26.1 ($CH_2$), 22.22 ($CH_2$), 22.15 ($CH_3$).




$C_{13}H_{18}O_2S$
MW: 238.3450

### ((4-(Cyclohex-1-en-1-yl)butyl)sulfonyl)benzene **8e**



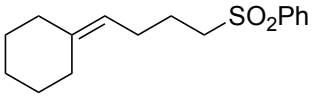

$C_{16}H_{22}O_2S$
MW: 278,4

The title compound was prepared following General Procedure 6 ( conditions B) with ((4-cyclohexyl-1-iodobutyl)sulfonyl)benzene (0.203 g, 0.5 mmol), trifluorotoluene (2.2 mL), $K_2CO_3$ (69.1 mg, 0.5 mmol), DTBHN (17.4 mg, 0.1 mmol), and DBU (0.229 mL, 1.5 mmol)

to afford as a colorless oil (106 mg, 76%; *endo/exo* 9:1).

((4-(Cyclohex-1-en-1-yl)butyl)sulfonyl)benzene (Major): $R_f$ = 0.6. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.94–7.86 (m, 2H), 7.72–7.62 (m, 1H), 7.61–7.52 (m, 2H), 5.31 (tp, *J* = 3.0, 1.3 Hz, 1H), 3.14–3.02 (m, 2H), 1.96–1.85 (m, 4H), 1.85–1.78 (m, 2H), 1.71–1.62 (m, 2H), 1.60–1.38 (m, 6H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.2 ($Cq_{Ar}$), 136.5 (=Cq), 133.6 ($CH_{Ar}$), 129.2 (2 × $CH_{Ar}$), 128.0 (2 × $CH_{Ar}$), 121.7 (=CH), 56.1 ($CH_2$), 37.2 ($CH_2$), 28.0 ($CH_2$), 26.1 ($CH_2$), 25.1 ($CH_2$), 22.9 ($CH_2$), 22.4 ($CH_2$), 22.2 ($CH_2$). IR (ν, $cm^{-1}$): 2922, 2855, 2833 (w), 1446, 1303, 1144, 1085 (str.). HRMS (ESI): $[M+H]^+$ calculated for $[C_{16}H_{23}O_2S]^+$: 279.1413, found: 279.1415.

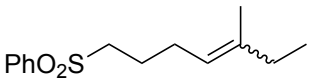
((4-Cyclohexylidenebutyl)sulfonyl)benzene (minor, characteristic signals):



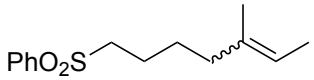

$C_{16}H_{22}O_2S$
MW: 278,4

$^1$H NMR (400 MHz, $CDCl_3$) δ 4.92 (tt, *J* = 7.3, 1.3 Hz, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 142.0 (=Cq), 118.6 (=CH).

## ((5-Methylhept-4-en-1-yl)sulfonyl)benzene and/or ((5-methylhept-5-en-1-yl)sulfonyl)benzene **9e**

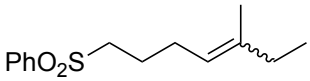



$C_{14}H_{20}O_2S$
MW: 252,4



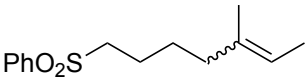

The title compound was prepared following General Procedure 6 (conditions B) with ((1-iodo-5-methylheptyl)sulfonyl)benzene (0.190 g, 0.5 mmol), trifluorotoluene (2.0 mL), $K_2CO_3$ (69.1 mg, 0.5 mmol), DTBHN (17.4 mg, 0.1 mmol), and DBU (0.229 mL, 1.5 mmol) to afford as a colourless oil (113.1 mg, 90 %, ratio = 47:45:8). $R_f$ = 0.6. 4/5/5 = 47:45:8. The relative configuration of the two major regioisomers was tentatively assigned as *E*:*Z* = ca. 3:1 (ratio estimated by integration of the alkenyl CH signals in $^{13}$C NMR) based on the multiplicity of the signals at 5.16–5.09 and 5.00–4.95 ppm.

((5-Methylhept-4-en-1-yl)sulfonyl)benzene (characteristic signals):



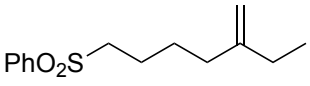

$^1$H NMR (400 MHz, $CDCl_3$) δ 7.92–7.89 (m, 2H), 7.69–7.62 (m, 1H), 7.61–7.53 (m, 2H), 5.01–5.94 (m, 1H, major), 4.94–4.90 (m, 1H, minor), 3.14–3.03 (m, 2H, minor + major), 2.10–2.00 (m, 2H, minor + major), 2.00–1.90 (m, 2H, minor + major), 1.79–1.66 (m, 2H), 1.65–1.64 (m, 3H, minor), 1.54 (bs, 3H, major), 0.95 (t, *J* = 7.4 Hz, 3H, major), 0.91 (t, *J* = 7.6 Hz, 3H, minor). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 121.7 (=CH, minor), 120.5 (=CH, major). IR (ν, $cm^{-1}$): 2963, 2931, 2871 (w), 1445, 1303, 1145, 1085 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{14}H_{20}O_2SNa]^+$: 275.1076, found: 275.1072.

((5-Methylhept-5-en-1-yl)sulfonyl)benzene (characteristic signals)*:*



$^{1}$H NMR (400 MHz, $CDCl_3$) 5.23–5.17 (m, 1H, minor), 5.13 (dtt, *J* = 8.3, 5.3, 1.6 Hz, 1H, major), $^{13}$C NMR (101 MHz, $CDCl_3$) δ 128.1 (=CH, minor), 119.3 (=CH, major).

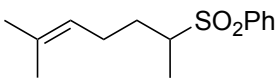
((5-ethyleneheptyl)sulfonyl)benzene (minor, characteristic signals): $^{1}$H NMR (400 MHz, $CDCl_3$)



$C_{14}H_{20}O_2S$
MW: 252,4

4.70–4.67 (m, 1H), 4.63–4.61 (m, 1H), 0.98 (t, *J* = 7.4 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 108.3 (=$CH_2$), 12.3 ($CH_3$).

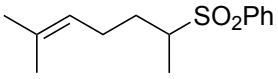
## ((6-Methylhept-5-en-2-yl)sulfonyl)benzene **10e**



$C_{14}H_{20}O_2S$
MW: 252,4

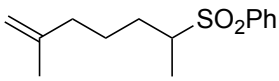
The title compound was prepared following General Procedure 6 (conditions B) with ((2-iodo-6-methylheptan-2-yl)sulfonyl)benzene (0.190 g, 0.5 mmol), trifluorotoluene (2.0 mL), $K_2CO_3$ (69.1 mg, 0.5 mmol), DTBHN (17.4 mg, 0.1 mmol), and DBU (0.229 mL, 1.5 mmol) to afford as a yellow oil (89.04 mg, 71 %; regioisomeric ratio = 85:15), contaminated with 8% of reduced side product. $R_f$ = 0.7.

((6-methylhept-5-en-2-yl)sulfonyl)benzene (major): $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.92–7.84 (m,



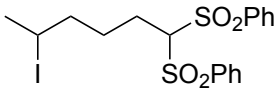
2H), 7.70–7.61 (m, 1H), 7.60–7.53 (m, 2H), 4.99–4.93 (m, 1H), 3.09–2.96 (m, 1H), 2.17–2.06 (m, 1H), 2.04–1.91 (m, 2H), 1.66 (bs, 3H), 1.56 (bs, 3H), 1.47–1.37 (m, 1H), 1.26 (d, *J* = 6.9 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 137.5 (=Cq), 133.7 ($CH_{Ar}$), 133.5 ($Cq_{Ar}$), 129.2 (4 × $CH_{Ar}$), 122.5 (=CH), 59.6 (CH), 29.3 ($CH_2$), 25.8 ($CH_3$), 25.0 ($CH_2$), 17.9 ($CH_3$), 13.2 ($CH_3$). IR (ν, $cm^{-1}$): 2930, 2866 (w), 1446, 1301, 1142, 1083 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{14}H_{20}O_2SNa]^+$: 275.1076, found: 275.1074.

((6-methylhept-6-en-2-yl)sulfonyl)benzene (minor): $^{1}$H NMR (400 MHz, $CDCl_3$) 4.69–4.67 (m,



1H), 4.62–4.60 (m, 1H), 1.66 (bs, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 110.7 (=$CH_2$), 37.4 ($CH_2$).

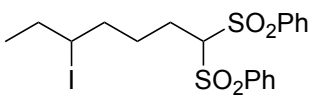
(5-Iodohexane-1,1-diyldisulfonyl)dibenzene **32ε**



$C_{18}H_{21}IO_4S_2$
MW: 492,4

The title compound was prepared following General Procedure 6 (conditions A) with (1-iodohexane-1,1-diyldisulfonyl)dibenzene (0.492 g, 1.0 mmol), trifluorotoluene (4 mL), and DTBHN (17.4 mg, 0.1 mmol) to afford as a yellow oil (466.9 mg, 94 %). $R_f$ = 0.32. $^1$H NMR (400 MHz, $CDCl_3$) δ 8.01–7.91 (m, 4H), 7.76–7.66 (m, 2H), 7.64–7.53 (m, 4H), 4.38 (t, *J* = 5.6 Hz, 1H), 4.07 (dqd, *J* = 8.3, 6.8, 4.5 Hz, 1H), 2.27–2.08 (m, 2H), 1.87 (d, *J* = 6.8 Hz, 3H), 1.82–1.64 (m, 3H), 1.64–1.52 (m, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 137.97 (Cq), 137.93 (Cq), 134.8 (2 × $CH_{Ar}$), 129.77 (2 × $CH_{Ar}$), 129.76 (2 × $CH_{Ar}$), 129.34 (2 × $CH_{Ar}$), 129.33 (2 × $CH_{Ar}$), 83.7 (CH), 42.2 ($CH_2$), 29.0 ($CH_3$), 28.4 (CH-I + $CH_2$), 24.9 ($CH_2$). IR (ν, $cm^{-1}$): 3061, 2961, 2938, 2914 (w), 1446, 1322, 1309, 1144, 1077 (str.). HRMS (ESI): $[M+H]^+$ calculated for $[C_{18}H_{22}O_4S_2I]^+$: 492.9999, found: 492.9988.

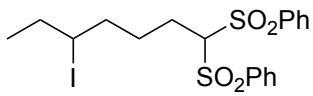
(5-Iodoheptane-1,1-diyldisulfonyl)dibenzene **33ε**



$C_{19}H_{23}IO_4S_2$
MW: 506,4

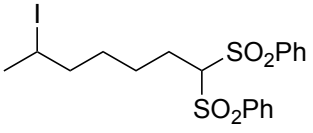
The title compound was prepared following General Procedure 6 (conditions A) with (1-iodoheptane-1,1-diyldisulfonyl)dibenzene (0.127 g, 0.25 mmol), trifluorotoluene (1 mL), DTBHN (4 mg, 0.025 mmol) to afford as a yellow oil (115 mg, 98 %; 9:1 mixture of regioisomers). $R_f$ = 0.4.

<u>(5-Iodoheptane-1,1-diyldisulfonyl)dibenzene (major)</u>:



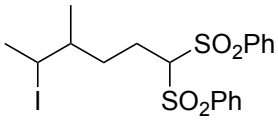
$^1$H NMR (400 MHz, $CDCl_3$) δ 8.01–7.92 (m, 4H), 7.76–7.66 (m, 2H), 7.56–7.61 (m, 4H), 4.38 (t, *J* = 5.6 Hz, 1H), 3.96 (tt, *J* = 8.4, 4.4 Hz, 1H), 2.27–2.08 (m, 2H), 1.86–1.60 (m, 6H), 0.99 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 138.0 (Cq), 137.9 (Cq), 134.8 (2 × $CH_{Ar}$), 129.77 (2 × $CH_{Ar}$), 129.75 (2 × $CH_{Ar}$), 129.34 (2 × $CH_{Ar}$), 129.32 (2 × $CH_{Ar}$), 83.7 (CH), 40.3 (CH–I), 39.6 ($CH_2$), 33.8 ($CH_2$), 28.3 ($CH_2$), 14.2 ($CH_2$). IR (ν, $cm^{-1}$): 2962, 2924, 2872 (w), 1446, 1325, 1309, 1143, 1077 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{19}H_{23}O_4S_2INa]^+$: 528.9975, found: 528.9966.

<u>(6-iodoheptane-1,1-diyldisulfonyl)dibenzene (minor, characteristic signals)</u>:



$^1$H NMR (400 MHz, $CDCl_3$) 4.11 (ddt, *J* = 8.9, 7.0, 5.9 Hz, 1H), 1.89 (d, *J* = 6.8 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 29.8 (CH–I), 28.9 ($CH_3$).

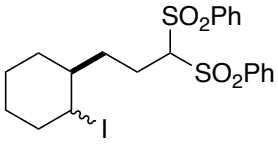
(5-Iodo-4-methylhexane-1,1-diyldisulfonyl)dibenzene **34ε**




$C_{19}H_{23}IO_4S_2$
MW: 506,4

The title compound was prepared following General Procedure 6 (conditions A) with (1-iodo-4-methylhexane-1,1-diyldisulfonyl)dibenzene (0.127 g, 0.25 mmol), trifluorotoluene (1.2 mL), DTBHN (9 mg, 0.05 mmol) to afford as an orange oil (89.3 mg, 70 %, dr = 1:1). $R_f$ = 0.4. $^1$H NMR (400 MHz, $CDCl_3$) δ 8.01–7.91 (m, 8H, dia 1 + dia 2), 7.76–7.66 (m, 4H, dia 1 + dia 2), 7.61–7.55 (m, 8H, dia 1 + dia 2), 4.36 (t, *J* = 5.6 Hz, 1H, dia 1), 4.35 (t, *J* = 5.6 Hz, 1H, dia 2), 4.24–4.15 (m, 2H, dia 1 + dia 2), 2.30–2.07 (m, 4H, dia 1 + dia 2), 1.83 (d, *J* = 7.0 Hz, 3H, 1 dia), 1.80 (d, *J* = 7.0 Hz, 3H, 1 dia), 1.80–1.73 (m, 1H, 1 dia) 1.66–1.52 (m, 1H, 1 dia), 1.54–1.43 (m, 1H, 1 dia), 1.36 (dddd, *J* = 13.1, 10.5, 9.1, 5.2 Hz, 1H, 1 dia), 1.27–1.18 (m, 1H, 1 dia), 0.91 (d, *J* = 6.6 Hz, 3H), 0.84–0.78 (m, 4H, 1 dia). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 138.07 (Cq), 138.02 (Cq), 137.9 (Cq), 137.8 (Cq), 134.84 ($CH_{Ar}$), 134.81 (3 × $CH_{Ar}$), 129.8 ($CH_{Ar}$), 129.74 (2 × $CH_{Ar}$), 129.72 ($CH_{Ar}$), 129.36 (2 × $CH_{Ar}$), 129.33 (2 × $CH_{Ar}$), 83.9 (CH), 83.8 (CH), 41.6 (CH), 40.9 (CH), 39.0 (CH), 37.8 (CH), 35.8 ($CH_2$), 33.2 ($CH_2$), 26.3 ($CH_3$), 25.3 ($CH_3$), 23.6 ($CH_2$), 23.3 ($CH_2$), 18.4 ($CH_3$), 17.0 ($CH_3$). IR (ν, $cm^{-1}$): 2964, 2922 (w), 1446, 1324, 1309, 1144, 1077 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{19}H_{23}O_4S_2INa]^+$: 528.9975, found: 528.9965.

(3-(2-Iodocyclohexyl)propane-1,1-diyldisulfonyl)dibenzene **35ε**



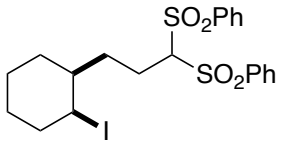

$C_{21}H_{25}IO_4S_2$
MW: 532,45

The title compound was prepared following General Procedure 6 (conditions A) with (3-cyclohexyl-1-iodopropane-1,1-diyldisulfonyl)dibenzene (0.133 g, 0.25 mmol), trifluorotoluene (1.2 mL), DTBHN (9 mg, 0.05 mmol) to afford as a yellow solid (overall 100.4 mg, 75 %; *cis*:*trans* = 54:46). $R_f$ = 0.4. M.p. = 47–49 °C (not corrected).

Mixture of isomers (dr = 54:46): $^1$H NMR (400 MHz, $CDCl_3$) δ 8.00–7.96 (m, 8H), 7.74–7.69 (m, 4H), 7.62–7.55 (m, 8H), 4.53–4.48 (m, 1H), 4.39 (dd, *J* = 5.9, 4.6 Hz, 1H), 4.36 (t, *J* = 5.7 Hz, 1H), 3.87 (ddd, *J* = 11.5, 10.0, 4.1 Hz, 1H), 2.52-2.43 (m, 1H), 2.31–1.96 (m, 7H), 1.82–1.12 (m, 17H), 0.44 (dtt, *J* = 9.8, 6.3, 3.0 Hz, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 138.21 (Cq), 138.11 (Cq), 137.90 (Cq), 137.83 (Cq), 134.78 (2 × $CH_{Ar}$), 134.76 ($CH_{Ar}$), 134.71 ($CH_{Ar}$), 129.83 (2 × $CH_{Ar}$), 129.80 (2 × $CH_{Ar}$), 129.73 (2 × $CH_{Ar}$), 129.71 (2 × $CH_{Ar}$), 129.37 (2 × $CH_{Ar}$), 129.32 (6 × $CH_{Ar}$), 83.84 (CH), 83.82 (CH), 46.47 (CH), 45.92 (CH–I), 42.38 (CH), 41.44 ($CH_2$), 40.95 (CH–I), 36.75 ($CH_2$), 36.63

($CH_2$), 36.60 ($CH_2$), 31.85 ($CH_2$), 28.96 ($CH_2$), 28.72 ($CH_2$), 25.56 ($CH_2$), 25.40 ($CH_2$), 22.77 ($CH_2$), 22.71 ($CH_2$), 22.69 ($CH_2$). IR (ν, $cm^{-1}$): 2921, 2850 (w), 1446, 1325, 1310, 1145, 1078 (str.). HRMS (ESI): $[M+H]^+$ calculated for $[C_{21}H_{26}O_4S_2I]^+$: 533.0312, found: 533.0303.

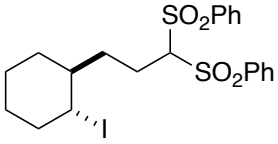
<u>*Cis*-isomer (major, characteristic signals)</u>:




$C_{21}H_{25}IO_4S_2$
MW: 532,45

$^1$H NMR (400 MHz, $CDCl_3$) δ 8.00–7.96 (m, 4H), 7.74– 7.69 (m, 2H), 7.62–7.55 (m, 4H), 4.53–4.48 (m, 1H), 4.36 (t, *J* = 5.7 Hz, 1H), 0.44 (dtt, *J* = 9.8, 6.3, 3.0 Hz, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 45.8 (CH–I), 42.2 (CH).

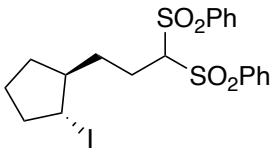
<u>(3-((1*S*,2*R*)-2-iodocyclohexyl)propane-1,1-diyldisulfonyl)dibenzene (characteristic signals):</u>




$C_{21}H_{25}IO_4S_2$
MW: 532,45

*Trans*-isomer (minor)*:* $^1$H NMR (400 MHz, $CDCl_3$) δ 4.39 (dd, *J* = 5.9, 4.6 Hz, 1H), 3.87 (ddd, *J* = 11.5, 10.0, 4.1 Hz, 1H), 2.52-2.43 (m, 1H), 2.08–2.00 (m, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 83.7 (CH), 41.3 ($CH_2$), 40.8 (CH–I).

### (3-(2-Iodocyclopentyl)propane-1,1-diyldisulfonyl)dibenzene **36ε**

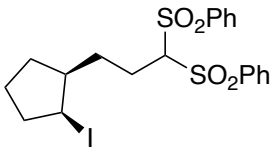



$C_{20}H_{23}IO_4S_2$
MW: 518,4

The title compound was prepared following General Procedure 6 (conditions A) with (3-cyclopentyl-1-iodopropane-1,1-diyldisulfonyl)dibenzene (0.130 g, 0.25 mmol), trifluorotoluene (1.2 mL), and DTBHN (9 mg, 0.05 mmol) to afford as a yellow oil (66 mg, 51%; *trans*:*cis* = 68:32). $R_f$ = 0.35. Along with the desired product, 36% of the starting material and 12% of the reduced side product were also isolated.

<u>*Trans*-isomer (major)</u>: $^1$H NMR (400 MHz, $CDCl_3$) δ 8.01–7.95 (m, 4H), 7.75–7.67 (m, 2H), 7.62–7.55 (m, 4H), 4.40–4.36 (m, 1H), 3.62 (td, *J* = 8.5, 7.1 Hz, 1H), 2.32–1.88 (m, 6H), 1.79–1.35 (m, 4H), 1.18–1.06 (m, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 138.0 (Cq), 137.6 (Cq), 134.67 ($CH_{Ar}$), 134.61 ($CH_{Ar}$), 129.7 (2 × $CH_{Ar}$), 129.6 (2 × $CH_{Ar}$), 129.19 (2 × $CH_{Ar}$), 129.17 (2 × $CH_{Ar}$), 83.8 (CH), 51.2 (CH), 39.1 ($CH_2$), 32.3 ($CH_2$), 31.1 (CH–I), 29.3 ($CH_2$), 24.2 ($CH_2$), 23.8 ($CH_2$). IR (ν, $cm^{-1}$): 2921, 2866 (w), 1446, 1324, 1309, 1143, 1077 (str.). HRMS (ESI): $[M+H]^+$ calculated for $[C_{20}H_{24}O_4S_2I]^+$: 519.0155, found: 519.0146.

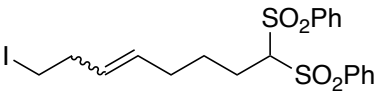
<u>(3-((1*S*,2*S*)-2-iodocyclopentyl)propane-1,1-diyldisulfonyl)dibenzene (Characteristic signals):</u>




$C_{20}H_{23}IO_4S_2$
MW: 518,4

*Cis-isomer (minor):* $^1$H NMR (400 MHz, $CDCl_3$) δ 8.01–7.95 (m, 4H), 7.75–7.67 (m, 2H), 7.62–7.55 (m, 4H), 4.40–4.36 (m, 2H), 2.30–2.09 (m, 4H), 1.84–1.95 (m, 1H), 1.76–1.54 (m, 2H), 1.36–1.28 (m, 1H), 0.92–0.81 (m, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 137.9 (Cq), 137.7 (Cq), 134.64 (2 × $CH_{Ar}$), 83.6 (CH), 46.5 (CH), 43.1 (CH), 38.8 ($CH_2$), 35.3 ($CH_2$), 28.7 ($CH_2$), 24.2 ($CH_2$), 21.6 ($CH_2$).

## (8-Iodooct-5-ene-1,1-diyldisulfonyl)dibenzene **37ε**




$C_{20}H_{23}IO_4S_2$
MW: 518,4

The title compound was prepared following General Procedure 6 (conditions A) with (5-cyclopropyl-1-iodopentane-1,1-diyldisulfonyl)dibenzene (0.130 g, 0.25 mmol), trifluorotoluene (1.2 mL), and DTBHN (9 mg, 0.05 mmol) to afford as a yellow oil (118.8 mg, 91%; *E*:*Z* = ca. 4:1*). $R_f$ = 0.4. (* Ratio estimated by $^{13}$C NMR).

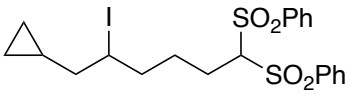
Major isomer: $^1$H NMR (400 MHz, $CDCl_3$) δ 7.95–7.93 (m, 4H), 7.74–7.67 (m, 2H), 7.61–7.55 (m, 4H), 5.43–5.28 (m, 2H), 4.39 (t, *J* = 5.7 Hz, 1H), 3.12 (t, *J* = 7.2 Hz, 2H), 2.52 (td, *J* = 7.6, 5.9 Hz, 2H), 2.16–2.12 (m, 2H), 2.02–1.95 (m, 2H), 1.74–1.61 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 137.9 (2 × Cq), 134.6 (2 × $CH_{Ar}$), 131.4 (=CH), 129.9 (=CH), 129.6 (4 × $CH_{Ar}$), 129.1 (4 × $CH_{Ar}$), 83.7 (CH), 36.6 ($CH_2$), 31.8 ($CH_2$), 27.6 ($CH_2$), 25.1 ($CH_2$), 5.7 ($CH_2$–I). IR (ν, $cm^{-1}$): 2921 (w), 1446, 1325, 1309, 1144, 1077 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{20}H_{23}O_4S_2INa]^+$: 540.9975, found: 540.9969.

Minor isomer (Characteristic signals): $^1$H NMR (400 MHz, $CDCl_3$) δ 4.37 (t, J = 5.5 Hz, 1H), 3.11 (t, *J* = 7.2 Hz, 2H) 2.57 (q, *J* = 7.0 Hz, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 137.8 (2 × Cq), 134.6 (2 × $CH_{Ar}$), 130.5 (=CH), 129.6 (4 × $CH_{Ar}$), 129.3 (=CH), 129.1 (4 × $CH_{Ar}$), 83.7 (CH), 31.4 ($CH_2$), 27.9 ($CH_2$), 26.9 ($CH_2$), 25.3 ($CH_2$), 5.2 ($CH_2$–I).

## (6-Cyclopropyl-5-iodohexane-1,1-diyldisulfonyl)dibenzene **38ε**

The title compound was prepared following General Procedure 6 (conditions A) with (6-cyclopropyl-1-iodohexane-1,1-diyldisulfonyl)dibenzene (0.133 g, 0.25 mmol), trifluorotoluene (1.2 mL), and DTBHN (9 mg, 0.05 mmol) to afford as a 85:15 mixture of 1.5-IAT and primary iodide as yellow oil (108 mg, 81%), $R_f$ = 0.46.

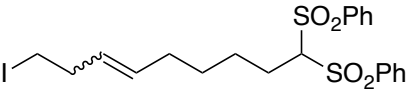
(6-Cyclopropyl-5-iodohexane-1,1-diyldisulfonyl)dibenzene (Major):




$C_{21}H_{25}IO_4S_2$
MW: 532,5

$^1$H NMR (400 MHz, $CDCl_3$) δ 8.01–7.92 (m, 4H), 7.75–7.66 (m, 2H), 7.64–7.54 (m, 4H), 4.38 (t, *J* = 5,7 Hz, 1H), 4.08 (tdd, *J* = 8.2, 5.8, 4.0 Hz, 1H), 2.28–2.10 (m, 2H), 1.91 (ddd, *J* = 14.4, 7.9, 6.3 Hz, 1H), 1.86–1.64 (m, 4H), 1.54 (ddd, *J* = 14.7, 7.1, 5.8 Hz, 1H), 0.92–0.78 (m, 1H), 0.58–0.44 (m, 2H), 0.20–0.12 (m, 1H), 0.09–0.01 (m, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 137.83 (Cq), 137.77 (Cq), 134.7 (2 × $CH_{Ar}$), 129.62 (2 × $CH_{Ar}$), 129.60 (2 × $CH_{Ar}$), 129.19 (2 × $CH_{Ar}$), 129.17 (2 × $CH_{Ar}$), 83.5 (CH), 45.7 ($CH_2$), 39.4 ($CH_2$), 37.2 (CH–I), 28.2 ($CH_2$), 24.8 ($CH_2$), 11.2 (CH), 4.5 ($CH_2$), 4.3 ($CH_2$). IR (ν, $cm^{-1}$): 3063, 3000, 2927 (w), 1446, 1322, 1309, 1142, 1077 (str.). HRMS (ESI): $[M+H]^+$ calculated for $[C_{21}H_{26}O_4S_2I]^+$: 533.0312, found: 533.0304.

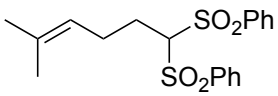
(9-Iodonon-6-ene-1,1-diyldisulfonyl)dibenzene (minor, d.r. = 73:27, Characteristic signals):




$C_{21}H_{25}IO_4S_2$
MW: 532,5

$^1$H NMR (400 MHz, $CDCl_3$) 5.48–5.39 (m, 1H), 5.37–5.28 (m, 1H), 3.14 (t, *J* = 7.1 Hz, 1H, major), 3.13 (t, *J* = 7.1 Hz, 1H, minor), 2.61–2.56 (m, 2H, minor), 2.55–2.50 (m, 2H, major). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 132.5 (=CH), 129.08 (=CH), 83.7 (CH), 36.6 ($CH_2$, major), 31.7 ($CH_2$, minor), 6.2 ($CH_2$–I, major), 5.5 ($CH_2$–I, minor).

## (5-Methylhex-4-ene-1,1-diyldisulfonyl)dibenzene **39e**



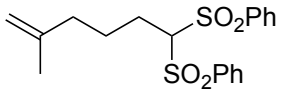

$C_{19}H_{22}O_4S_2$
MW: 378,5

The title compound was prepared following General Procedure 6 (conditions B) with (1-iodo-5-methylhexane-1,1-diyldisulfonyl)dibenzene (0.253 g, 0.5 mmol), trifluorotoluene (2.0 mL), $K_2CO_3$ (69 mg, 0.5 mmol), DTBHN (17 mg, 0.1 mmol), and DBU (0.229 mL, 1.5 mmol) to afford as a pale yellow solid (155 mg, 82%; *endo:exo* = 89:11). $R_f$ = 0.5. M.p. = 95.5–96.4 °C. (contain 11% of reduced product).

(5-Methylhex-4-ene-1,1-diyldisulfonyl)dibenzene (major): $^1$H NMR (400 MHz, $CDCl_3$) δ 8.00–7.90 (m, 4H), 7.72–7.65 (m, 2H), 7.64–7.53 (m, 4H), 4.77–4.70 (m, 1H), 4.38 (t, *J* = 5.8 Hz, 1H), 2.27 (q, *J* = 7.0 Hz, 2H), 2.21–2.16 (m, 2H), 1.62 (bs, 3H), 1.57 (bs, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 138.0 (2 × Cq), 135.3 (=Cq), 134.5 (2 × $CH_{Ar}$), 129.6 (4 × $CH_{Ar}$), 129.1 (4 × $CH_{Ar}$), 121.1 (=CH), 82.3 (CH), 26.2 ($CH_2$), 25.8 ($CH_3$), 25.6 ($CH_2$), 17.9 ($CH_3$). IR (ν, $cm^{-1}$): 2915 (w), 1446, 1343, 1327, 1308, 1157, 1077 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{19}H_{22}O_4S_2Na]^+$:

401.0852, found: 401.0841.

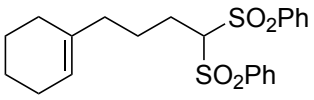
(5-methylhex-5-ene-1,1-diyldisulfonyl)dibenzene (minor):



$C_{19}H_{22}O_4S_2$
MW: 378.50

$^1$H NMR (400 MHz, $CDCl_3$) 4.70–4.68 (m, 1H), 4.61–4.58 (m, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 111.1 (=$CH_2$).

## (4-(Cyclohex-1-en-1-yl)butane-1,1-diyldisulfonyl)dibenzene **40e**



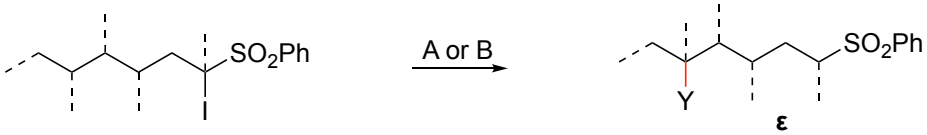
$C_{22}H_{26}O_4S_2$
MW: 418,6

The title compound was prepared following General Procedure 6 (conditions B) with (4-cyclohexyl-1-iodobutane-1,1-diyldisulfonyl)dibenzene (0.137 g, 0.25 mmol), trifluorotoluene (1.2 mL), $K_2CO_3$ (35 mg, 0.25 mmol), DTBHN (9 mg, 0.05 mmol), and DBU (0.112 mL, 0.75 mmol) to afford as a white solid (21.9 mg, 21%; *endo:exo* = 80:20), inseparable from the reduced by-product (. $R_f$ = 0.55. M.p. = 105.4–106.4 °C (not corrected). Mixture of 20:80 = Product: Reduced side product;

Characteristic signals: $^1$H NMR (400 MHz, $CDCl_3$) δ 5.34–5.30 (m, 1H), 1.99–1.91 (m, 2H), 1.88 (t, *J* = 7.4 Hz, 2H), 1.84–1.77 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 122.2 (=CH), 37.3 ($CH_2$), 28.0 ($CH_2$), 25.2 ($CH_2$). IR (ν, $cm^{-1}$): 2954, 2921, 2869 (w), 1720, 1448, 1313, 1125, 1078 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{22}H_{26}O_4S_2Na]^+$: 441.1165, found: 441.1154.

## General procedure for remote functionalisation of α-iodoalkyl mono- and bis-sulfones

### General Procedure 7. Remote functionalisation




A: $PhSO_2Y$ (2 equiv), $Et_3B$ (2.4 equiv), DTBHN (0.2 equiv), $K_2CO_3$ (1 equiv), TFT, 55 °C

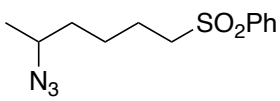
B: 1) DTBHN (0.2 equiv), $K_2CO_3$ (1 equiv), TFT, 80 °C.
2) $PhSO_2Y$ (2 equiv), $Et_3B$ (3.6 equiv), DTBHN (0.3 equiv), TFT, 55 °C

**Conditions A:** A 10 mL two-neck round-bottom flask equipped with a condenser and an Argon inlet was charged with α-iodoalkyl mono- or bissulfones (0.5 mmol) and $K_2CO_3$ (69.1 mg, 0.5 mmol). Anhydrous trifluorotoluene (2 mL) was added, and the reaction mixture was protected from light with Aluminium foil. The arylsulfonyl radical trap $PhSO_2$–Y trap (2.0 mmol) was

added to the reaction mixture, followed by quick addition of $Et_3B$ (0.52 mL, 1.2 mmol, 1.15 M in TFT) and DTBHN (9 mg, 0.05 mmol). The reaction flask was immersed in the pre-heated oil bath at 55 °C, and the reaction mixture was stirred for 1 h. The reaction mixture was removed from the oil bath, and a second portion of $Et_3B$ (0.52 mL, 1.2 mmol, 1.15 M in TFT) and DTBHN (9 mg, 0.05 mmol) was added. The reaction mixture was then stirred for another 1 h at 55 °C. Upon completion (TLC monitoring), the volatiles were removed under reduced pressure and the crude product was purified by flash column chromatography on silica gel (Heptane/EtOAc = 90:10 to 80:20).

**Conditions B:** A 10 mL two-neck round-bottom flask equipped with a condenser and an Argon inlet was charged with α-iodoalkyl mono- or bissulfones (0.5 mmol) and $K_2CO_3$ (69.1 mg, 0.5 mmol). Anhydrous trifluorotoluene (2 mL) was added, followed by DTBHN (17.4 mg, 0.1 mmol). The reaction flask was protected from light with Aluminium foil and then immersed in a pre-heated oil bath at 80 °C. The reaction mixture was stirred for 15 min ( TLC monitoring), then cooled to 0 °C. The arylsulfonyl radical trap $PhSO_2$–Y (2.0 mmol), $Et_3B$ (0.52 mL, 1.2 mmol, 1.15 M in TFT) and DTBHN (9 mg, 0.05 mmol) were sequentially added and the reaction flask immersed in the pre-heated oil bath at 55 °C and the reaction mixture stirred for 1h. Then, a second portion of $Et_3B$ (0.52 mL, 1.2 mmol, 1.15 M in TFT) and DTBHN (9 mg, 0.05 mmol) were added (after cooling the reaction mixture) and the mixture was stirred for another hour at 55 °C. A third portion of $Et_3B$ (0.52 mL, 1.2 mmol, 1.15 M in TFT) and DTBHN (9 mg, 0.05 mmol) were added (after cooling the reaction mixture) and the reaction mixture stirred 1 h more. The volatiles were removed under reduced pressure, and the crude product was purified by flash column chromatography on silica gel (Heptane/EtOAc = 90:10 to 80:20).

### ((5-Azidohexyl)sulfonyl)benzene **11ε**




$C_{12}H_{17}N_3O_2S$
MW: 267,35

The title compound was prepared following General Procedure 7 (condition A) with ((1-iodohexyl)sulfonyl)benzene (176 mg, 0.5 mmol), $K_2CO_3$ (69 mg, 0.5 mmol), $PhSO_2N_3$ (83 mg, 1.0 mmol), trifluorotoluene (2 mL), $Et_3B$ (1.04 mL, 1.2 mmol, 1.15 M in TFT) and DTBHN (18 mg, 0.1 mmol) to afford as a colorless oil (55.6 mg, 42%). $R_f$ = 0.4.

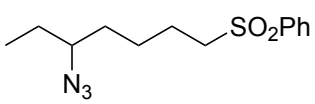
The title compound was prepared following General Procedure 7 (conditions B) with ((1-iodohexyl)sulfonyl)benzene (176 mg, 0.5 mmol), DTBHN (18 mg, 0.1 mmol), trifluorotoluene

(2 mL), at 80 °C for 30 minutes. Then $PhSO_2N_3$ (1.0 mmol, 183 mg), $K_2CO_3$ (69 mg, 0.5 mmol), $Et_3B$ (1.57 mL, 1.8 mmol, 1.15 M in TFT) and DTBHN (27 mg, 0.15 mmol) to afford as a colourless oil (75.6 mg, 57%).

The same procedure using $K_2CO_3$ (69 mg, 0.5 mmol) from the first step and 4 equiv. of $PhSO_2N_3$ (366 mg, 2.0 mmol) afforded the product (88 mg, 66%). Also, the reduced product was isolated in ~10% yield and contaminated with traces of eliminated side product.

$^1$H NMR (400 MHz, $CDCl_3$) δ 7.93–7.87 (m, 2H), 7.69–7.62 (m, 1H), 7.61–7.53 (m, 2H), 3.38 (hex, *J* = 6.4 Hz, 1H), 3.10–3.06 (m, 2H), 1.78–1.67 (m, 2H), 1.52–1.36 (m, 4H), 1.21 (d, *J* = 6.5 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.2 (Cq), 133.8 ($CH_{Ar}$), 129.4 (2 × $CH_{Ar}$), 128.1 (2 × $CH_{Ar}$), 57.6 (CH), 56.2 ($CH_2$), 35.7 ($CH_2$), 24.9 ($CH_2$), 22.6 ($CH_2$), 19.5 ($CH_3$). IR (ν, $cm^{-1}$): 2933, 2870, 2094 (w), 1141, 1085 (str.). HRMS (ESI): $[M+H]^+$ calculated for $[C_{12}H_{18}N_3O_2S]^+$: 268.1114, found: 268.1113.

### ((5-Azidoheptyl)sulfonyl)benzene **12ε**

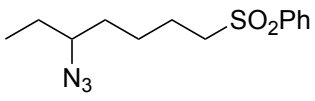



$C_{13}H_{19}N_3O_2S$
MW: 281,4

The title compound was prepared following General Procedure 7 (condition A) with ((1-iodoheptyl)sulfonyl)benzene (183 mg, 0.5 mmol), $K_2CO_3$ (69 mg, 0.5 mmol), $PhSO_2N_3$ (183 mg, 1.0 mmol), trifluorotoluene (2 mL), $Et_3B$ (1.04 mL, 1.2 mmol, 1.15 M in TFT) and DTBHN (18 mg, 0.1 mmol) to afford as a colorless oil (60.5 mg, 43%; 5-$N_3$/6-$N_3$ = 80:20). $R_f$ = 0.5.

The title compound was also prepared following General Procedure 7 (conditions B) with ((1-iodoheptyl)sulfonyl)benzene (183 mg, 0.5 mmol), DTBHN (18 mg, 0.1 mmol), trifluorotoluene (2 mL), at 80 °C for 30 minutes. Then $PhSO_2N_3$ (183 mg, 1.0 mmol), $K_2CO_3$ (69 mg, 0.5 mmol), $Et_3B$ (1.57 mL, 1.8 mmol, 1.15 M in TFT) and DTBHN (27 mg, 0.15 mmol) to afford as a colourless oil (71 mg, 50%), 5/6 = 82:18.

<u>((5-Azidoheptyl)sulfonyl)benzene (major)</u>:

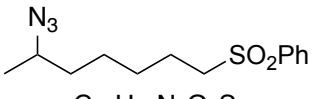



$C_{13}H_{19}N_3O_2S$
MW: 281,4

$^1$H NMR (400 MHz, $CDCl_3$) δ 7.98–7.87 (m, 2H), 7.70–7.63 (m, 1H), 7.59–7.55 (m, 2H), 3.17–3.05 (m, 3H), 1.83–1.65 (m, 2H), 1.59–1.34 (m, 6H), 0.95 (t, *J* = 7.4 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.2 (Cq), 133.7 ($CH_{Ar}$), 129.3 (2 × $CH_{Ar}$), 128.0 (2 × $CH_{Ar}$), 64.0 (CH), 56.1 ($CH_2$), 33.4 ($CH_2$), 27.3 ($CH_2$), 24.9 ($CH_2$), 22.5 ($CH_2$), 10.4 ($CH_3$). IR (ν, $cm^{-1}$): 2937, 2874 (w),

2092 (str.), 1446, 1303, 1288, 1141, 1085 (str.). HRMS (ESI): $[M+H]^+$ calculated for $[C_{13}H_{20}N_3O_2S]^+$: 282.1264, found: 282.1264.

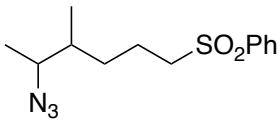
((6-Azidoheptyl)sulfonyl)benzene (minor regioisomer):




$C_{13}H_{19}N_3O_2S$
MW: 281,4

$^1$H NMR (400 MHz, $CDCl_3$) 3.43–3.34 (m, 1H), 1.22 (d, *J* = 6.5 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.2 (Cq), 133.6 ($CH_{Ar}$), 129.27 (2 × $CH_{Ar}$), 128.0 (2 × $CH_{Ar}$), 57.7 (CH), 56.1 ($CH_2$), 35.8 ($CH_2$), 28.0 ($CH_2$), 25.5 ($CH_2$), 19.4 ($CH_3$).

### ((5-Azido-4-methylhexyl)sulfonyl)benzene **13ε**



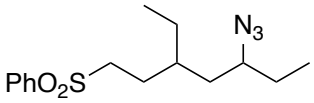

$C_{13}H_{19}N_3O_2S$
MW: 281,37

The title compound was prepared following General Procedure 7 (condition A) with ((1-iodo-4-methylhexyl)sulfonyl)benzene (183 mg, 0.5 mmol), $K_2CO_3$ (69 mg, 0.5 mmol), $PhSO_2N_3$ (145 mg, 0.75 mmol), EtOAc (2 mL), $Et_3B$ (1.04 mL, 1.2 mmol, 1.15 M in TFT) and DTBHN (18 mg, 0.1 mmol) to afford as a colourless oil (96.1 mg, 68%, dr = 1:1). $R_f$ = 0.4.

The title compound was prepared following General Procedure 7 (conditions B) with ((1-iodo-4-methylhexyl)sulfonyl)benzene (183 mg, 0.5 mmol), DTBHN (9 mg, 0.05 mmol), trifluorotoluene (2 mL), at 80 °C for 15 minutes. Then $PhSO_2N_3$ (183 mg, 1.0 mmol), $K_2CO_3$ (69 mg, 0.5 mmol), $Et_3B$ (1.57 mL, 1.8 mmol, 1.15 M in TFT) and DTBHN (27 mg, 0.15 mmol) to afford as a colourless oil (97 mg, 69%, dr = 1:1). Eliminated side product was also isolated in ~21% yield.

$^1$H NMR (400 MHz, $CDCl_3$) δ 7.97–7.87 (m, 4H, dia 1 + dia 2), 7.71–7.63 (m, 2H, dia 1 + dia 2), 7.62–7.52 (m, 4H, dia 1 + dia 2), 3.42 (qd, *J* = 6.7, 4.0 Hz, 1H, dia 1), 3.31 (p, *J* = 6.5 Hz, 1H, dia 2), 3.15–3.00 (m, 4H, dia 1 + dia 2), 1.91–1.57 (m, 4H, dia 1 + dia 2), 1.55–1.40 (m, 4H, dia 1 + dia 2), 1.29–1.22 (m, 2H, dia 1 + dia 2), 1.20 (d, *J* = 6.8 Hz, 3H, dia 1), 1.18 (d, *J* = 6.4 Hz, 3H, dia 2), 0.867 (d, *J* = 6.9 Hz, 3H, dia 2), 0.860 (d, *J* = 6.7 Hz, 3H, dia 1). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.3 (2 × Cq, dia 1 + dia 2), 133.9 (2 × $CH_{Ar}$, dia 1 + dia 2), 129.4 (4 × $CH_{Ar}$, dia 1 + dia 2), 128.1 (4 × $CH_{Ar}$, dia 1 + dia 2), 62.2 (CH), 61.7 (CH), 56.46 ($CH_2$), 56.44 ($CH_2$), 38.01 (CH), 37.96 (CH), 31.8 ($CH_2$), 31.5 ($CH_2$), 20.5 ($CH_2$), 20.4 ($CH_2$), 16.2 ($CH_3$), 15.9 ($CH_3$), 15.4 ($CH_3$), 14.7 ($CH_3$). IR (ν, $cm^{-1}$): 2965, 2928, 2876 (w), 2089, 1142, 1085 (str.). HRMS (ESI): $[M+H]^+$ calculated for $[C_{13}H_{20}N_3O_2S]^+$: 282.1271, found: 282.1272.

((5-Azido-3-ethylheptyl)sulfonyl)benzene **14ε**



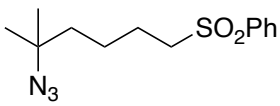
$C_{15}H_{23}N_3O_2S$
MW: 309,43

The title compound was prepared following General Procedure 7 (condition A) with ((3-ethyl-1-iodoheptyl)sulfonyl)benzene (197 mg, 0.5 mmol), $K_2CO_3$ (69 mg, 0.5 mmol), $PhSO_2N_3$ (183 mg, 1.0 mmol), trifluorotoluene (2 mL), $Et_3B$ (1.04 mL, 1.2 mmol, 1.15 M in TFT) and DTBHN (18 mg, 0.1 mmol) to afford as a colorless oil (91.9 mg, 62%; 5-$N_3$/6-$N_3$ = 92:8, dr = 45:55) $R_f$ = 0.5.

The title compound was prepared following General Procedure 7 (conditions B) with ((3-ethyl-1-iodoheptyl)sulfonyl)benzene (197 mg, 0.5 mmol), DTBHN (9 mg, 0.05 mmol), trifluorotoluene (2 mL), at 80 °C for 15 minutes. Then $PhSO_2N_3$ (183 mg, 1.0 mmol), $K_2CO_3$ (69 mg, 0.5 mmol), $Et_3B$ (1.57 mL, 1.8 mmol, 1.15 M in TFT) and DTBHN (27 mg, 0.15 mmol) to afford as a colourless oil (100.6 mg, 65%), 48% clean fraction, other 17% contaminated with traces of 1.5-IAT and eliminated side products.

$^1$H NMR (400 MHz, CDCl3) δ 7.94–7.89 (m, 4H, dia1 + dia 2), 7.70–7.63 (m, 2H, dia1 + dia2), 7.60–7.56 (m, 4H, dia1 + dia 2), 3.21–3.03 (m, 6H, dia 1 + dia 2), 1.81–1.16 (m, 18H, dia 1 + dia 2), 0.957 (t, *J* = 7.4 Hz, 3H, 1 dia), 0.954 (t, *J* = 7.5 Hz, 3H, 1 dia), 0.807 (t, *J* = 7.4 Hz, 3H, 1 dia), 0.800 (t, *J* = 7.4 Hz, 3H, 1 dia). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.14 (Cq), 139.08 (Cq), 133.71 ($CH_{Ar}$), 133.68 ($CH_{Ar}$), 129.30 (2 × $CH_{Ar}$), 129.28 (2 × $CH_{Ar}$), 128.0 (4 × $CH_{Ar}$), 62.1 (CH), 61.6 (CH), 53.9 ($CH_2$), 53.6 ($CH_2$), 37.5 ($CH_2$), 37.2 ($CH_2$), 34.9 (2 × CH), 27.9 ($CH_2$), 27.8 ($CH_2$), 25.88 ($CH_2$), 25.83 ($CH_2$), 25.1 ($CH_2$), 24.9 ($CH_2$), 10.48 ($CH_3$), 10.41 ($CH_3$), 10.38 ($CH_3$), 10.0 ($CH_3$). IR (ν, $cm^{-1}$): 2964, 2932, 2876 (w), 2093 (str.), 1304, 1143, 1085 (str.). HRMS (ESI): $[M+H]^+$ calculated for $[C_{15}H_{24}O_2N_3S]^+$: 310.1584, found: 310.1581.

((5-azido-5-methylhexyl)sulfonyl)benzene **15ε**



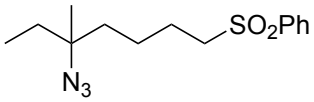
$C_{13}H_{19}N_3O_2S$
MW: 281,37

The title compound was prepared following General Procedure 7 (condition A) with ((1-iodo-5-methylhexyl)sulfonyl)benzene (183 mg, 0.5 mmol), $K_2CO_3$ (0.5 mmol, 69.1 mg), $PhSO_2N_3$ (183 mg, 1.0 mmol), trifluorotoluene (2 mL), $Et_3B$ (1.04 mL, 1.2 mmol, 1.15 M in TFT) and DTBHN (18 mg, 0.1 mmol) to afford as a colorless liquid (108 mg, 77%). $R_f$ = 0.5.

$^1$H NMR (400 MHz, $CDCl_3$) δ 7.92–7.88 (m, 2H), 7.70–7.63 (m, 1H), 7.59–7.55 (m, 2H), 3.11–3.07 (m, 2H), 1.79–1.64 (m, 2H), 1.46–1.36 (m, 4H), 1.21 (s, 6H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ

139.2, 133.8, 129.4, 128.2, 61.3, 56.2, 41.0, 26.0, 23.2, 23.0. IR (ν, $cm^{-1}$): 2967, 2943, 2871, (w), 2090, 1142, 1085 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{13}H_{19}N_3O_2SNa]^+$: 304.1096, found: 304.1089.

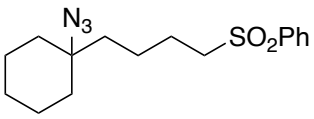
### ((5-Azido-5-methylheptyl)sulfonyl)benzene **16ε**




$C_{14}H_{21}N_3O_2S$
MW: 295,4

The title compound was prepared following General Procedure 7 (condition A) with ((1-iodo-5-methylheptyl)sulfonyl)benzene (190 mg, 0.5 mmol), $K_2CO_3$ (69 mg, 0.5 mmol), $PhSO_2N_3$ (183 mg, 1.0 mmol), trifluorotoluene (2 mL), $Et_3B$ (1.04 mL, 1.2 mmol, 1.15 M in TFT) and DTBHN (18 mg, 0.1 mmol) to afford as a colorless oil (99.7 mg, 67%). $R_f$ = 0.3. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.93–7.89 (m, 2H), 7.70–7.64 (m, 1H), 7.61–7.55 (m, 2H), 3.14–3.06 (m, 2H), 1.76–1.69 (m, 2H), 1.51 (qd, *J* = 7.5, 1.4 Hz, 2H), 1.46–1.35 (m, 4H), 1.17 (s, 3H), 0.89 (t, *J* = 7.5 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.3 (Cq), 133.9 ($CH_{Ar}$), 129.5 (2 × $CH_{Ar}$), 128.2 (2 × $CH_{Ar}$), 64.2 (Cq), 56.3 ($CH_2$), 38.5 ($CH_2$), 32.1 ($CH_2$), 23.1 ($CH_2$), 22.9 ($CH_2$), 22.8 ($CH_3$), 8.4 ($CH_3$). IR (ν, $cm^{-1}$): 2969, 2940, 2878 (w), 2087 (str.), 1446, 1304, 1288, 1154, 1143, 1086 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{14}H_{21}N_3O_2SNa]^+$: 318.1247, found: 318.1251.

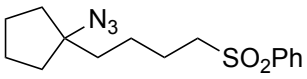
### ((4-(1-azidocyclohexyl)butyl)sulfonyl)benzene **17ε**




$C_{16}H_{23}N_3O_2S$
MW: 321,44

The title compound was prepared following General Procedure 7 (condition A) with ((4-cyclohexyl-1-iodobutyl)sulfonyl)benzene (0.5 mmol, 203 mg), $K_2CO_3$ (0.5 mmol, 69.1 mg), $PhSO_2N_3$ (1.0 mmol, 183 mg), trifluorotoluene (2 mL, 0.2 M), $Et_3B$ (1.2 mmol, 1.04 mL, 1.15 M in TFT) and DTBHN (0.1 mmol, 18 mg) to afford as a colorless liquid (122 mg, 76%). $R_f$ = 0.5. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.97–7.87 (m, 2H), 7.70–7.62 (m, 1H), 7.61–7.54 (m, 2H), 3.12–3.08 (m, 2H), 1.76–1.68 (m, 2H), 1.66–1.38 (m, 11H), 1.36–1.16 (m, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.1 (Cq), 133.7 ($CH_{Ar}$), 129.3 (2 × $CH_{Ar}$), 128.0 (2 × $CH_{Ar}$), 63.7 (Cq), 56.1 ($CH_2$), 39.5 ($CH_2$), 34.5 (2 × $CH_2$), 25.4 ($CH_2$), 23.0 ($CH_2$), 22.12 ($CH_2$), 22.06 (2 × $CH_2$). IR (ν, $cm^{-1}$): 2930, 2857 (w), 2095 (str.), 1143, 1085 (str.). HRMS (ESI): $[M+H]^+$ calculated for $[C_{16}H_{24}N_3O_2S]^+$: 322.1588, found: 322.1588.

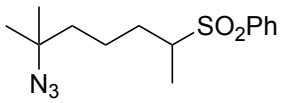
((4-(1-Azidocyclopentyl)butyl)sulfonyl)benzene **18ε**




$C_{15}H_{21}N_3O_2S$
MW: 307,4

The title compound was prepared following General Procedure 7 (condition A) with ((4-cyclopentyl-1-iodobutyl)sulfonyl)benzene (0.25 mmol, 98.1 mg), $K_2CO_3$ (0.25 mmol, 34.6 mg), $PhSO_2N_3$ (1.25 mmol, 229 mg), trifluorotoluene (1 mL, 0.2 M), $Et_3B$ (0.6 mmol, 0.52 mL, 1.15 M in TFT) and DTBHN (0.05 mmol, 9 mg) to afford as a yellow oil (46.2 mg, 60%). $R_f$ = 0.45. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.95–7.88 (m, 2H), 7.70–7.63 (m, 1H), 7.62–7.54 (m, 2H), 3.12–3.07 (m, 2H), 1.82–1.63 (m, 8H), 1.61–1.55 (m, 2H), 1.54–1.43 (m, 4H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.3 (Cq), 133.8 ($CH_{Ar}$), 129.4 (2 × $CH_{Ar}$), 128.2 (2 × $CH_{Ar}$), 73.3 (Cq), 56.3 ($CH_2$), 38.7 ($CH_2$), 37.0 (2 × $CH_2$), 24.1 ($CH_2$), 23.8 (2 × $CH_2$), 23.1 ($CH_2$). IR (ν, cm$^{-1}$): 2945, 2871 (w), 2091 (str.), 1446, 1303, 1257, 1142, 1085 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{15}H_{21}N_3O_2SNa]^+$: 330.1247, found: 330.1242.

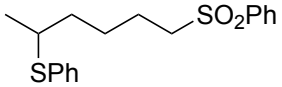
((6-Azido-6-methylheptan-2-yl)sulfonyl)benzene **19ε**




$C_{14}H_{21}N_3O_2S$
MW: 295,4

The title compound was prepared following General Procedure 7 (condition A) with ((2-iodo-6-methylheptan-2-yl)sulfonyl)benzene (95 mg, 0.25 mmol), $K_2CO_3$ (34.6 mg, 0.25 mmol), $PhSO_2N_3$ (91.6 mg, 0.5 mmol), trifluorotoluene (1 mL), $Et_3B$ (0.52 mL, 0.6 mmol, 1.15 M in TFT) and DTBHN (9 mg, 0.05 mmol) to afford as a colourless oil (48.3 mg, 65%), $R_f$ = 0.48. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.92–7.83 (m, 2H), 7.71–7.63 (m, 1H), 7.62–7.53 (m, 2H), 3.07–2.99 (m, 1H), 2.01–1.90 (m, 1H), 1.60–1.27 (m, 6H), 1.27 (d, *J* = 6.9 Hz, 3H), 1.24 (s, 3H), 1.23 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 137.4 (Cq), 133.8 ($CH_{Ar}$), 129.3 (2 × $CH_{Ar}$), 129.2 (2 × $CH_{Ar}$), 61.4 (Cq), 60.1 (CH), 41.2 ($CH_2$), 29.4 ($CH_2$), 26.12 ($CH_3$), 26.07 ($CH_3$), 21.5 ($CH_2$), 13.5 ($CH_3$). IR (ν, cm$^{-1}$): 2970, 2872 (w), 2092 (str.), 1446, 1302, 1263, 1140, 1084 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{14}H_{21}N_3O_2SNa]^+$: 318.1247, found: 318.1243.

Phenyl(6-(phenylsulfonyl)hexan-2-yl)sulfane **20ε**

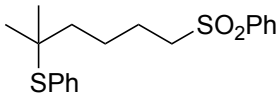



$C_{18}H_{22}O_2S_2$
MW: 334,5

The title compound was prepared following General Procedure 7 (conditions A) with ((1-iodohexyl)sulfonyl)benzene (176 mg, 0.5 mmol), $K_2CO_3$ (69 mg, 0.5 mmol), $PhSO_2SPh$ (376 mg, 1.5 mmol), trifluorotoluene (2 mL), $Et_3B$ (1.57 mL, 1.8 mmol, 1.15 M in TFT) and

DTBHN (27 mg, 0.15 mmol) for 3 h to afford as yellow oil (35.4 mg, 21%, contain 10% 1,5-IAT), $R_f$ = 0.67. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.98–7.87 (m, 2H), 7.71–7.63 (m, 1H), 7.63–7.53 (m, 2H), 7.38–7.32 (m, 2H), 7.31–7.19 (m, 3H), 3.20–3.11 (m, 1H), 3.11–3.03 (m, 2H), 1.83–1.66 (m, 2H), 1.64–1.44 (m, 4H), 1.23 (d, *J* = 6.7 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 133.7, 132.1, 129.3, 128.8, 128.0, 126.9, 56.1, 43.0, 35.9, 25.6, 22.5, 21.1. IR (ν, $cm^{-1}$): 2922, 2861 (w), 1145, 1303, 1142, 1084 (str.). HRMS (ESI): $[M+H]^+$ calculated for $[C_{18}H_{23}O_2S_2]^+$: 335.1134, found: 335.1132.

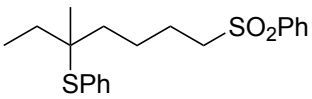
### (2-Methyl-6-(phenylsulfonyl)hexan-2-yl)(phenyl)sulfane **21ε**




$C_{19}H_{24}O_2S_2$
MW: 348,5

The title compound was prepared following General Procedure 7 (conditions A) with ((1-iodo-5-methylhexyl)sulfonyl)benzene (183 mg, 0.5 mmol), $K_2CO_3$ (69 mg, 0.5 mmol), $PhSO_2SPh$ (250 mg, 1.0 mmol), trifluorotoluene (2 mL), $Et_3B$ (1.04 mL, 1.2 mmol, 1.15 M in TFT) and DTBHN (18 mg, 0.1 mmol), at 80 °C to afford as a brown oil (111 mg, 64%), $R_f$ = 0.5. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.94–7.89 (m, 2H), 7.69–7.64 (m, 1H), 7.60–7.56 (m, 2H), 7.47–7.43 (m, 2H), 7.38–7.27 (m, 3H), 3.14–3.05 (m, 2H), 1.77–1.63 (m, 2H), 1.60–1.49 (m, 2H), 1.44–1.36 (m, 2H), 1.18 (s, 6H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.3 (Cq), 137.5 (2 × $CH_{Ar}$), 133.8 ($CH_{Ar}$), 132.0 (Cq), 129.4 (2 × $CH_{Ar}$), 129.0 ($CH_{Ar}$), 128.7 (2 × $CH_{Ar}$), 128.2 (2 × $CH_{Ar}$), 56.4 ($CH_2$), 49.1 (Cq), 41.8 ($CH_2$), 28.8 (2 × $CH_3$), 23.8 ($CH_2$), 23.1 ($CH_2$). IR (ν, $cm^{-1}$): 3058, 2940, 2866 (w), 1146, 1301, 1143, 1085 (str.). HRMS (ESI): $[M+H]^+$ calculated for $[C_{19}H_{25}O_2S_2]^+$: 349.1290, found: 349.1289.

### (3-Methyl-7-(phenylsulfonyl)heptan-3-yl)(phenyl)sulfane **22ε**

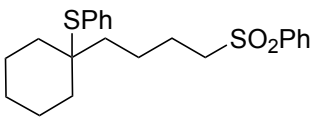



$C_{20}H_{26}O_2S_2$
MW: 362,5

The title compound was prepared following General Procedure 7 (conditions A) with ((1-iodo-5-methylheptyl)sulfonyl)benzene (190 mg, 0.5 mmol), $K_2CO_3$ (69 mg, 0.5 mmol), $PhSO_2SPh$ (250 mg, 1.0 mmol), trifluorotoluene (2 mL), $Et_3B$ (1.04 mL, 1.2 mmol, 1.15 M in TFT) and DTBHN (18 mg, 0.1 mmol) to afford as an orange oil (96 mg, 53%), $R_f$ = 0.36. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.93–7.86 (m, 2H), 7.70–7.63 (m, 1H), 7.62–7.53 (m, 2H), 7.46–7.40 (m, 2H), 7.37–7.25 (m, 3H), 3.14–3.05 (m, 2H), 1.75–1.63 (m, 2H), 1.58–1.47 (m, 2H), 1.43 (q, *J* = 7.5 Hz, 2H), 1.40–1.31 (m, 2H), 1.10 (s, 3H), 0.94 (t, *J* = 7.4 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$)

δ 139.2 (Cq), 137.4 (2 × $CH_{Ar}$), 133.7 ($CH_{Ar}$), 131.8 (Cq), 129.3 (2 × $CH_{Ar}$), 128.7 ($CH_{Ar}$), 128.5 (2 × $CH_{Ar}$), 128.1 (2 × $CH_{Ar}$), 56.2 ($CH_2$), 53.0 (Cq), 38.6 ($CH_2$), 32.2 ($CH_2$), 25.7 ($CH_3$), 23.2 ($CH_2$), 23.0 ($CH_2$), 8.7 ($CH_3$). IR (ν, $cm^{-1}$): 2963, 2936, 2871 (w), 1146, 1302, 1144, 1085 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{20}H_{26}O_2S_2Na]^+$: 385.1266, found: 385.1267.

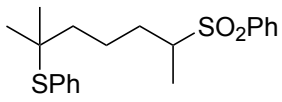
### Phenyl(1-(4-(phenylsulfonyl)butyl)cyclohexyl)sulfane **23ε**




$C_{22}H_{28}O_2S_2$
MW: 388,6

The title compound was prepared following General Procedure 7 (conditions A) with ((4-cyclohexyl-1-iodobutyl)sulfonyl)benzene (203 mg, 0.5 mmol), $K_2CO_3$ (69 mg, 0.5 mmol), $PhSO_2SPh$ (626 mg, 2.5 mmol), trifluorotoluene (2 mL), $Et_3B$ (1.04 mL, 1.2 mmol, 1.15 M in TFT) and DTBHN (18 mg, 0.1 mmol), at 80 °C to afford as an orange oil (98.9 mg, 51%), $R_f$ = 0.57. $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.8 Hz, 2H), 7.66 (q, *J* = 7.1 Hz, 1H), 7.57 (q, *J* = 7.1 Hz, 2H), 7.40 (d, *J* = 7.5 Hz, 1H), 7.35–7.16 (m, 4H), 3.23–2.97 (m, 2H), 2.12–1.22 (m, 16H). $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 139.2, 137.3, 133.6, 129.2, 129.1, 128.5, 128.1, 56.3 ($CH_2$), 53.8 (Cq), 36.2 (2 × $CH_2$), 25.9 ($CH_2$), 22.9 ($CH_2$), 22.4 ($CH_2$), 22.1 (2 × $CH_2$). IR (ν, $cm^{-1}$): 2925, 2853 (w), 1145, 1302, 1143, 1084 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{22}H_{28}O_2S_2Na]^+$: 411.1423, found: 411.1415.

### (2-Methyl-6-(phenylsulfonyl)heptan-2-yl)(phenyl)sulfane **24ε**

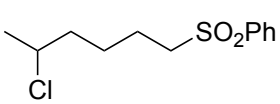



$C_{20}H_{26}O_2S_2$
MW: 362,5

The title compound was prepared following General Procedure 7 (conditions A) with ((2-iodo-6-methylheptan-2-yl)sulfonyl)benzene (95 mg, 0.25 mmol), $K_2CO_3$ (35 mg, 0.25 mmol), $PhSO_2SPh$ (125 mg, 0.5 mmol), trifluorotoluene (1 mL), $Et_3B$ (0.52 mL, 0.6 mmol, 1.15 M in TFT) and DTBHN (9 mg, 0.05 mmol) to afford as an orange oil (56.5 mg, 62%), $R_f$ = 0.57. Contain α-SPh product as a mixture with the ε-SPh product = 6:94; overall 66%. $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.91–7.85 (m, 2H), 7.71–7.62 (m, 1H), 7.59–7.54 (m, 2H), 7.49–7.43 (m, 2H), 7.39–7.28 (m, 3H), 3.10–3.00 (m, 1H), 1.98–1.88 (m, 1H), 1.69–1.33 (m, 5H), 1.29 (d, *J* = 6.9 Hz, 3H), 1.19 (s, 6H). $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 137.4 (2 × $CH_{Ar}$), 133.6 ($CH_{Ar}$), 132.0 (Cq), 129.08, 129.03 (2 × $CH_{Ar}$), 129.00 (2 × $CH_{Ar}$), 128.8 ($CH_{Ar}$), 128.5 (2 × $CH_{Ar}$), 60.1 ($CH_2$), 49.0 (Cq), 41.9 ($CH_2$), 29.4 ($CH_2$), 28.81 ($CH_3$), 28.75 ($CH_3$), 22.0 ($CH_2$), 13.3 ($CH_3$). IR (ν, $cm^{-1}$): 2954, 2865 (w), 1145, 1301, 1141, 1084 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{20}H_{26}O_2S_2Na]^+$:

385.1266, found: 385.1261.

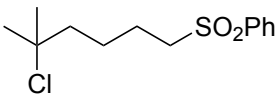
### ((5-Chlorohexyl)sulfonyl)benzene **25ε**




$C_{12}H_{17}ClO_2S$
MW: 260,8

The title compound was prepared following General Procedure 7 (conditions A) with ((1-iodohexyl)sulfonyl)benzene (0.5 mmol, 176 mg), $K_2CO_3$ (69 mg, 0.5 mmol), $PhSO_2Cl$ (0.32 mL, 2.5 mmol), trifluorotoluene (2 mL), $Et_3B$ (1.04 mL, 1.2 mmol, 1.15 M in TFT) and DTBHN (18 mg, 0.1 mmol) to afford as a yellow oil (108.9 mg, 47%), $R_f$ = 0.39. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.93–7.86 (m, 2H), 7.69–7.63 (m, 1H), 7.63–7.54 (m, 2H), 4.00–3.92 (m, 1H), 3.10 (t, *J* = 8.0 Hz, 2H), 1.82–1.42 (m, 6H), 1.47 (d, *J* = 6.5 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.3 (Cq), 133.9 ($CH_{Ar}$), 129.5 (2 × $CH_{Ar}$), 128.2 (2 × $CH_{Ar}$), 58.2 (CH–Cl), 56.2 ($CH_2$), 39.7 ($CH_2$), 25.51 ($CH_2$), 25.45 ($CH_3$), 22.4 ($CH_2$). IR (ν, $cm^{-1}$): 2926, 2867 (w), 1146, 1303, 1291, 1141, 1085 (str.). HRMS (ESI): $[M+H]^+$ calculated for $[C_{12}H_{18}O_2SCl]^+$: 261.0711, found: 261.0712.

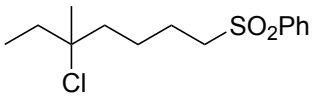
### ((5-Chloro-5-methylhexyl)sulfonyl)benzene **26ε**




$C_{13}H_{19}ClO_2S$
MW: 274,8

The title compound was prepared following General Procedure 7 (conditions A) with ((1-iodo-5-methylhexyl)sulfonyl)benzene (91.5 mg, 0.25 mmol), $K_2CO_3$ ( 35 mg, 0.25 mmol), $PhSO_2Cl$ (64.5 μL, 0.5 mmol), trifluorotoluene (1 mL), $Et_3B$ (0.52 mL, 0.6 mmol, 1.15 M in TFT) and DTBHN (9 mg, 0.05 mmol) to afford as a colorless oil (54.4 mg, 79%). $R_f$ = 0.52. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.93–7.89 (m, 2H), 7.69–7.63 (m, 1H), 7.60–7.54 (m, 2H), 3.15–3.07 (m, 2H), 1.79–1.64 (m, 4H), 1.61–1.51 (m, 2H), 1.53 (s, 6H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.3 (Cq), 133.9 ($CH_{Ar}$), 129.5 (2 × $CH_{Ar}$), 128.2 (2 × $CH_{Ar}$), 70.4 (Cq), 56.3 ($CH_2$), 45.4 ($CH_2$), 32.5 (2 × $CH_3$), 24.1 ($CH_2$), 22.9 ($CH_2$). IR (ν, $cm^{-1}$): 2969, 2943, 2870 (w), 1146, 1302, 1143, 1085 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{13}H_{19}O_2ClNaS]^+$: 297.0686, found: 297.0685.

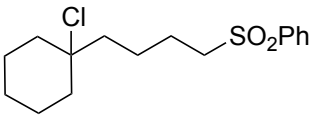
((5-Chloro-5-methylheptyl)sulfonyl)benzene **27ε**




$C_{14}H_{21}ClO_2S$
MW: 288,8

The title compound was prepared following General Procedure 7 (conditions A) with ((1-iodo-5-methylheptyl)sulfonyl)benzene (190 mg, 0.5 mmol), $K_2CO_3$ (69 mg, 0.5 mmol), $PhSO_2Cl$ (0.13 mL, 1.0 mmol), trifluorotoluene (2 mL), $Et_3B$ (1.04 mL, 1.2 mmol, 1.15 M in TFT) and DTBHN (18 mg, 0.1 mmol) to afford as an orange oil (108.3 mg, 75%). $R_f$ = 0.5. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.96–7.87 (m, 2H), 7.71–7.62 (m, 1H), 7.60–7.55 (m, 2H), 3.15–3.08 (m, 2H), 1.80–1.61 (m, 6H), 1.58–1.48 (m, 2H), 1.45 (s, 3H), 0.97 (t, *J* = 7.4 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.1 (Cq), 133.7 ($CH_{Ar}$), 129.3 (2 × $CH_{Ar}$), 128.1 (2 × $CH_{Ar}$), 74.6 (Cq), 56.1 ($CH_2$), 43.0 ($CH_2$), 36.8 ($CH_2$), 29.1 ($CH_3$), 23.5 ($CH_2$), 22.8 ($CH_2$), 9.1 ($CH_3$). IR (ν, $cm^{-1}$): 2669, 2939, 2878 (w), 1146, 1303, 1144, 1085 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{14}H_{21}O_2ClNaS]^+$: 311.0843, found: 311.0839.

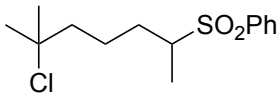
((4-(1-chlorocyclohexyl)butyl)sulfonyl)benzene **28ε**




$C_{16}H_{23}ClO_2S$
MW: 314,9

The title compound was prepared following General Procedure 7 (conditions A) with ((4-cyclohexyl-1-iodobutyl)sulfonyl)benzene (203 mg, 0.5 mmol), $K_2CO_3$ (69 mg, 0.5 mmol), $PhSO_2Cl$ (130 µL, 1.0 mmol), trifluorotoluene (2 mL), $Et_3B$ (1.04 mL, 1.2 mmol, 1.15 M in TFT) and DTBHN (18 mg, 0.1 mmol) to afford as an orange oil (134.3 mg, 85%), $R_f$ = 0.61. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.96–7.86 (m, 2H), 7.70–7.62 (m, 1H), 7.61–7.53 (m, 2H), 3.18–3.02 (m, 2H), 1.93–1.83 (m, 2H), 1.80–1.40 (m, 13H), 1.28–1.13 (m, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.3 (Cq), 133.8 ($CH_{Ar}$), 129.4 (2 × $CH_{Ar}$), 128.2 (2 × $CH_{Ar}$), 75.5 (Cq), 56.3 ($CH_2$), 44.8 ($CH_2$), 39.8 (2 × $CH_2$), 25.6 ($CH_2$), 23.0 ($CH_2$), 22.8 ($CH_2$), 22.4 (2 × $CH_2$). IR (ν, $cm^{-1}$): 2931, 2859 (w), 1145, 1302, 1142, 1085 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{16}H_{23}O_2ClNaS]^+$: 337.0999, found: 337.0998.

((6-Chloro-6-methylheptan-2-yl)sulfonyl)benzene **29ε**

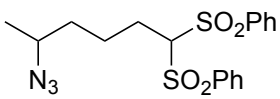



$C_{14}H_{21}ClO_2S$
MW: 288,8

The title compound was prepared following General Procedure 7 (conditions A) with ((2-iodo-6-methylheptan-2-yl)sulfonyl)benzene (95 mg, 0.25 mmol), $K_2CO_3$ ( 35 mg, 0.25 mmol), $PhSO_2Cl$ (64.5 µL, 0.5 mmol), trifluorotoluene (1 mL), $Et_3B$ (0.52 mL, 0.6 mmol, 1.15 M in

TFT) and DTBHN (9 mg, 0.05 mmol) to afford as a yellow oil (49.9 mg, 69%), $R_f$ = 0.5. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.92–7.84 (m, 2H), 7.69–7.61 (m, 1H), 7.61–7.53 (m, 2H), 3.05 (dqd, *J* = 9.4, 6.9, 3.7 Hz, 1H), 2.05–1.92 (m, 1H), 1.73–1.60 (m, 3H), 1.54 (s, 6H), 1.51–1.37 (m, 2H), 1.28 (d, *J* = 6.9 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 137.5 (Cq), 133.8 ($CH_{Ar}$), 129.24 (2 × $CH_{Ar}$), 129.16 (2 × $CH_{Ar}$), 70.5 (Cq), 60.1 (CH), 45.6 ($CH_2$), 32.58 ($CH_3$), 32.54 ($CH_3$), 29.2 ($CH_2$), 22.4 ($CH_2$), 13.4 ($CH_3$). IR (ν, $cm^{-1}$): 2972, 2934, 2870 (w), 1146, 1301, 1142, 1084 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{14}H_{21}O_2ClNaS]^+$: 311.0843, found: 311.0840.

### (5-Azidohexane-1,1-diyldisulfonyl)dibenzene **43ε**

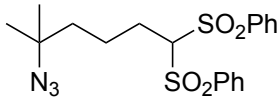



$C_{18}H_{21}N_3O_4S_2$
MW: 407,5

The title compound was prepared following General Procedure 7 (conditions B) with (1-iodohexane-1,1-diyldisulfonyl)dibenzene (123 mg, 0.25 mmol), $K_2CO_3$ (35 mg, 0.25 mmol), DTBHN (9 mg, 0.05 mmol), trifluorotoluene (1 mL), at 80 °C for 15 minutes. Then $PhSO_2N_3$ (92 mg, 0.5 mmol), $Et_3B$ (0.78 mL, 0.9 mmol, 1.15 M in TFT) and DTBHN (13 mg, 0.075 mmol) to afford as a yellow oil (28.1 mg, 28%). The reduced side product was also isolated (44.4 mg, 48%).

$^1$H NMR (400 MHz, $CDCl_3$) δ 8.00–7.90 (m, 4H), 7.76–7.65 (m, 2H), 7.65–7.52 (m, 4H), 4.37 (t, *J* = 5.6 Hz, 1H), 3.38 (hex, *J* = 6.5 Hz, 1H), 2.24–2.08 (m, 2H), 1.74–1.57 (m, 2H), 1.40 (td, *J* = 7.8, 6.5 Hz, 2H), 1.22 (d, *J* = 6.5 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 137.96 (Cq), 137.91 (Cq), 134.8 (2 × $CH_{Ar}$), 129.75 (2 × $CH_{Ar}$), 129.73 (2 × $CH_{Ar}$), 129.31 (4 × $CH_{Ar}$), 83.7 (CH), 57.3 (CH), 35.6 ($CH_2$), 25.5 ($CH_2$), 24.8 ($CH_2$), 19.5 ($CH_3$). IR (ν, $cm^{-1}$): 3064, 2966, 2927 (w), 2097 (str.), 1146, 1325, 1310, 1140, 1076 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{18}H_{21}O_4N_3NaS_2]^+$: 430.0866, found: 430.0853.

### (5-Azido-5-methylhexane-1,1-diyldisulfonyl)dibenzene **44ε**

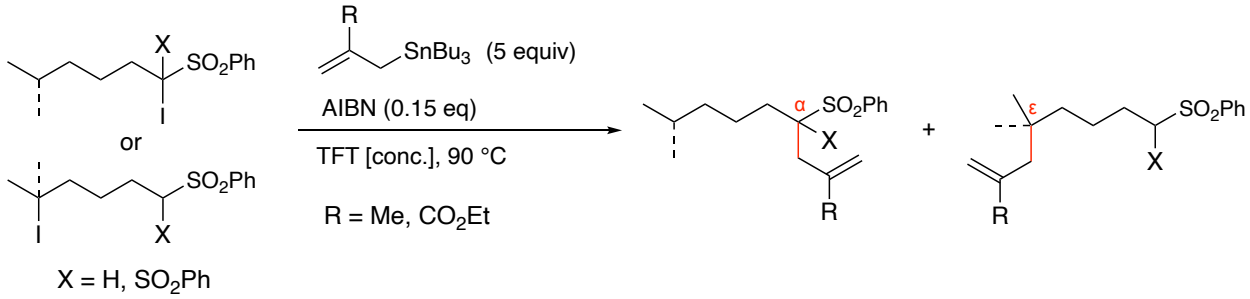



$C_{19}H_{23}N_3O_4S_2$
MW: 421,5

The title compound was prepared following General Procedure 7 (conditions A) with (1-iodo-5-methylhexane-1,1-diyldisulfonyl)dibenzene (127 mg, 0.25 mmol), $K_2CO_3$ (35 mg, 0.25 mmol), $PhSO_2N_3$ (92 mg, 0.5 mmol), trifluorotoluene (1 mL), $Et_3B$ (0.52 mL, 0.6 mmol, 1.15 M in TFT) and DTBHN (9 mg, 0.05 mmol) to afford as a whitish oil (47.5 mg, 45%). $R_f$ = 0.33. $^1$H NMR (400 MHz, $CDCl_3$) δ 8.00–7.93 (m, 4H), 7.76–7.68 (m, 2H),

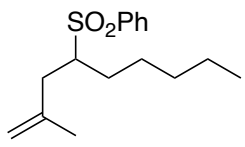
7.65–7.54 (m, 4H), 4.38 (t, *J* = 5.6 Hz, 1H), 2.16 (td, *J* = 7.8, 5.6 Hz, 2H), 1.67–1.56 (m, 2H), 1.41–1.33 (m, 2H), 1.21 (s, 6H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 137.8 (2 × Cq), 134.6 (2 × $CH_{Ar}$), 129.6 (4 × $CH_{Ar}$), 129.2 (4 × $CH_{Ar}$), 83.6 (CH), 61.1 (Cq), 40.7 ($CH_2$), 25.9 (2 × $CH_3$), 25.8 ($CH_2$), 23.0 ($CH_2$). IR (ν, $cm^{-1}$): 2966, 2923 (w), 2091 (str.), 1147, 1326, 1310, 1143, 1078 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{19}H_{23}O_4N_3NaS_2]^+$: 444.1022, found: 444.1018.

## General Procedure 8. Remote allylation α- or ε-iodoalkyl mono- and bis-sulfones




A 10 mL two-neck round-bottom flask equipped with a condenser was charged with α- or ε-iodoalkyl mono- or bis-sulfones (0.25 mmol) and tributyl(2-methylallyl)stannane (**A**) or ethyl 2-((tributylstannyl)methyl)acrylate (**B**) (1.25 mmol) were dissolved in anhydrous trifluorotoluene (see description for volume) while under Argon. The reaction mixture was protected from light with Aluminium foil. Then AIBN (0.038 mmol) was added quickly, and the reaction mixture was immersed in the pre-heated oil bath at 90 °C and stirred for 2 h. Upon completion (TLC monitoring), the reaction mixture was cooled to rt and filtered through a short pad of $SiO_2/K_2CO_3$ (9:1). The pad was washed with EtOAc, the volatiles were removed under reduced pressure, and the crude product was purified by flash column chromatography on $SiO_2/K_2CO_3$ (9:1) (Heptane/EtOAc = 95:5 to 90:10).

### ((2-Methylnon-1-en-4-yl)sulfonyl)benzene **30α**



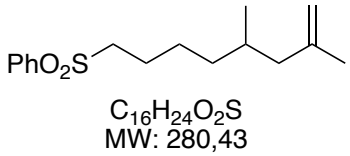

$C_{16}H_{24}O_2S$
MW: 280,43

The title compound was prepared following General Procedure 8 with ((1-iodohexyl)sulfonyl)benzene (176 mg, 0.5 mmol), tributyl(2-methylallyl)stannane **A** (0.61 mL, 2.5 mmol), trifluorotoluene (9 mL, 0.05 M), and AIBN (12.6 mg, 0.075 mmol) to afford as a colourless oil (128.9 mg, 92%), α:ε > 95:5, $R_f$ = 0.71.

The title compound was prepared following General Procedure 8 with ((5-iodohexyl)sulfonyl)benzene (88.1 mg, 0.25 mmol), tributyl(2-methylallyl)stannane **A** (0.29 mL, 1.25 mmol), trifluorotoluene (50 mL, 0.005 M), and AIBN (6 mg, 0.038 mmol) to afford 30α (36.2 mg, 52%) and 30ε (7.3 mg, 10%) ( overall 62%; α:ε = 84:16) as colorless oils.

$^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.94–7.84 (m, 2H), 7.69–7.62 (m, 1H), 7.60–7.52 (m, 2H), 4.81–4.79 (m, 1H), 4.72–4.70 (m, 1H), 3.10 (dtd, *J* = 9.5, 5.6, 3.7 Hz, 1H), 2.58 (dd, *J* = 14.4, 3.7 Hz, 1H), 2.19 (ddd, *J* = 14.3, 10.1, 0.8 Hz, 1H), 1.81 (ddt, *J* = 14.6, 9.4, 6.1 Hz, 1H), 1.63 (bs, 3H), 1.60–1.51 (m, 1H), 1.46–1.33 (m, 2H), 1.28–1.33 (m, 4H), 0.84 (t, *J* = 7.0 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 140.8 (Cq), 138.2 (Cq), 133.7 ($CH_{Ar}$), 129.2 (2 × $CH_{Ar}$), 129.1 (2 × $CH_{Ar}$), 114.2 (=$CH_2$), 62.6 (CH), 37.2 ($CH_2$), 31.9 ($CH_2$), 28.2 ($CH_2$), 26.8 ($CH_2$), 22.4 ($CH_2$), 21.9 ($CH_3$), 14.1 ($CH_3$). IR (ν, $cm^{-1}$): 2922, 2869 (w), 1303, 1143, 1085 (str.). HRMS (ESI): $[M+H]^+$ calculated for $[C_{16}H_{25}O_2S]^+$: 281.1575, found: 281.1575.

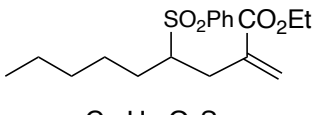
### ((5,7-Dimethyloct-7-en-1-yl)sulfonyl)benzene **30ε**




$C_{16}H_{24}O_2S$
MW: 280,43

The title compound was prepared following General Procedure 8 with ((5-iodohexyl)sulfonyl)benzene (88.1 mg, 0.25 mmol), tributyl(2-methylallyl)stannane **A** (0.29 mL, 1.25 mmol), trifluorotoluene (0.21 mL, 0.5 M), and AIBN (6 mg, 0.038 mmol) to afford 30α and 30ε as colourless oil (5.8 mg, 8%) and (48 mg, 68%) respectively (overall 76%, α:ε = 11:89). $R_f$ = 0.65. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.94–7.87 (m, 2H), 7.69–7.62 (m, 1H), 7.60–7.54 (m, 2H), 4.75–4.79 (m, 1H), 4.62–4.60 (m, 1H) , 3.08 (t, *J* = 8.1 Hz, 2H), 1.94 (ddd, *J* = 13.6, 6.5, 1.2 Hz, 1H), 1.77 (ddd, *J* = 13.6, 8.1, 1.0 Hz, 1H), 1.73–1.65 (m, 2H), 1.64 (bs, 3H), 1.60–1.49 (m, 1H), 1.46–1.19 (m, 3H), 1.09–0.99 (m, 1H), 0.79 (d, *J* = 6.6 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 144.6 (Cq), 139.4 (Cq), 133.7 ($CH_{Ar}$), 129.4 (2 × $CH_{Ar}$), 128.2 (2 × $CH_{Ar}$), 111.7 (=$CH_2$), 56.5 ($CH_2$), 46.0 ($CH_2$), 36.2 ($CH_2$), 30.4 (CH), 25.9 ($CH_2$), 23.1 ($CH_2$), 22.3 ($CH_3$), 19.5 ($CH_3$). IR (ν, $cm^{-1}$): 2954, 2925, 2856 (w), 1303, 1144 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{16}H_{24}O_2SNa]^+$: 303.1389, found: 303.1380.

### Ethyl 2-methylene-4-(phenylsulfonyl)nonanoate **31α**

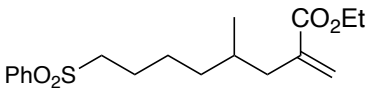



$C_{18}H_{26}O_4S$
MW: 338,5

The title compound was prepared following General Procedure 8 with ((1-iodohexyl)sulfonyl)benzene (88.1 mg, 0.25 mmol), ethyl 2-((tributylstannyl)methyl)acrylate **B** (504 mg, 1.25 mmol), trifluorotoluene (5 mL), and AIBN (6.2 mg, 0.038 mmol) to afford as a colorless oil (72.7 mg, 86%; α:ε > 95:5). $R_f$ = 0.52.

$^1$H NMR (400 MHz, $CDCl_3$) δ 7.90–7.87 (m, 2H), 7.69–7.62 (m, 1H), 7.59–7.52 (m, 2H), 6.22–6.19 (m, 1H), 5.63–5.61 (m, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 3.39 (dq, *J* = 9.0, 5.4 Hz, 1H), 2.80 (ddd, *J* = 14.3, 5.3, 1.3 Hz, 1H), 2.49 (ddd, *J* = 14.2, 9.0, 0.9 Hz, 1H), 1.88 (dddd, *J* = 14.5, 9.7, 6.2, 5.2 Hz, 1H) , 1.54 (ddt, *J* = 14.3, 10.4, 5.8 Hz, 1H), 1.48–1.33 (m, 2H), 1.27–1.09 (m, 4H), 1.23 (t, *J* = 7.1 Hz, 3H), 0.83 (t, *J* = 7.0 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.2 (Cq), 138.4 (Cq), 136.4 (Cq), 133.7 ($CH_{Ar}$), 129.2 (2 × $CH_{Ar}$), 128.9 (2 × $CH_{Ar}$), 128.6 (=$CH_2$), 62.5 (CH), 61.0 ($CH_2$), 32.3 ($CH_2$), 31.7 ($CH_2$), 27.7 ($CH_2$), 26.7 ($CH_2$), 22.4 ($CH_2$), 14.3 ($CH_3$), 14.1 ($CH_3$). IR (ν, $cm^{-1}$): 2956, 2929, 2870 (w), 1710, 1446, 1301, 1142, 1083 (str.). HRMS (ESI): $[M+H]^+$ calculated for $[C_{18}H_{27}O_4S]^+$: 339.1625, found: 339.1631.

### Ethyl 4-methyl-2-methylene-8-(phenylsulfonyl)octanoate **31ε**




$C_{18}H_{26}O_4S$
MW: 338,5

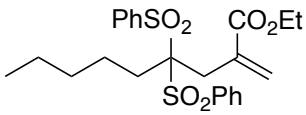
The title compound was prepared following General Procedure 8 with ((5-iodohexyl)sulfonyl)benzene (88 mg, 0.25 mmol), ethyl 2-((tributylstannyl)methyl)acrylate **B** (504 mg, 1.25 mmol), trifluorotoluene (5 mL, 0.05 M), and AIBN (6 mg, 0.038 mmol) to afford as colorless oil (67.7 mg, 80%; α:ε < 5:95). $R_f$ = 0.51.

The title compound was also prepared following General Procedure 8 with ((5-iodohexyl)sulfonyl)benzene (0.25 mmol, 88.1 mg), ethyl 2-((tributylstannyl)methyl)acrylate **B** (504 mg, 1.25 mmol), trifluorotoluene (50 mL, 0.005 M), and AIBN (6 mg, 0.038 mmol) to afford as colorless oil (59.7 mg, 71%; α:ε < 5:95).

$^1$H NMR (400 MHz, $CDCl_3$) δ 7.93–7.88 (m, 2H), 7.69–7.63 (m, 1H), 7.60–7.53 (m, 2H), 6.14 (d, *J* = 1.7 Hz, 1H), 5.45–5.44 (m, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.14–3.02 (m, 2H), 2.29 (ddd, *J* = 13.6, 5.8, 1.2 Hz, 1H), 2.00 (ddd, *J* = 13.7, 8.2, 1.0 Hz, 1H), 1.77–1.64 (m, 2H), 1.64–1.51 (m, 1H), 1.45–1.22 (m, 3H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.08 (dddd, *J* = 13.1, 10.5, 8.2, 5.6 Hz, 1H), 0.80 (d, *J* = 6.7 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 167.5 (Cq), 139.7 (Cq), 139.4 (Cq), 133.7 ($CH_{Ar}$),

129.4 (2 × $CH_{Ar}$), 128.2 (2 × $CH_{Ar}$), 125.9 (=$CH_2$), 60.7 ($CH_2$), 56.4 ($CH_2$), 39.7 ($CH_2$), 36.2 ($CH_2$), 31.8 (CH), 25.9 ($CH_2$), 23.0 ($CH_2$), 19.3 ($CH_3$), 14.3 ($CH_3$). IR (ν, $cm^{-1}$): 2926, 2870 (w), 1710, 1446, 1304, 1143, 1085 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{18}H_{26}O_4SNa]^+$: 361.1444, found: 361.1450.

### Ethyl 2-methylene-4-(phenylsulfonyl)-4-((phenylthio)peroxy)nonanoate **45α**




$C_{24}H_{30}O_6S_2$
MW: 478,6

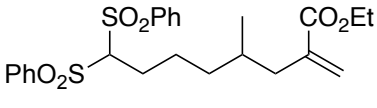
The title compound was prepared following General Procedure 8 with ((1-iodo-1-(phenylsulfonyl)hexyl)peroxy)(phenyl)sulfane (123 mg, 0.25 mmol), ethyl 2-((tributylstannyl)methyl)acrylate **B** (504 mg, 1.25 mmol), trifluorotoluene (0.5 mL, 0.5 M), and AIBN (6 mg, 0.038 mmol) to afford 45α as a colorless oil (76.5 mg, 71%; contaminated with 12% of reduced product) and 45ε (15.8 mg, 15%) (overall 86%; α:ε = 83:17). $R_f$ = 0.53.

The title compound was also prepared following General Procedure 8 with ((1-iodo-1-(phenylsulfonyl)hexyl)peroxy)(phenyl)sulfane (123 mg, 0.25 mmol), ethyl 2-((tributylstannyl)methyl)acrylate **B** (504 mg, 1.25 mmol), trifluorotoluene (5 mL, 0.05 M), and AIBN (6 mg, 0.038 mmol) to afford 45α as colorless oil (55.2 mg, 46%; contaminated with 10% of reduced product) and 45ε (41.1 mg, 34%) (overall 80%; α:ε = 58:42).

Following General Procedure 8 with ((1-iodo-1-(phenylsulfonyl)hexyl)peroxy)(phenyl)sulfane (123 mg, 0.25 mmol), ethyl 2-((tributylstannyl)methyl)acrylate **B** (504 mg, 1.25 mmol), trifluorotoluene (50 mL, 0.005 M), and AIBN (6 mg, 0.038 mmol), the title compound was obtained as a 42:58 mixture of regioisomers (overall 53% NMR yield (standard = 1,3,5-trimethoxybenzene); α:ε = 42:58).

$^1$H NMR (400 MHz, $CDCl_3$) δ 8.10–8.02 (m, 4H), 7.75–7.66 (m, 2H), 7.61–7.54 (m, 4H), 6.41–6.40 (m, 1H), 5.99–5.98 (m, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.38 (bs, 2H), 2.18–2.11 (m, 2H), 1.65–1.54 (m, 2H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.27–1.10 (m, 4H), 0.84 (d, *J* = 7.0 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 167.2 (Cq), 137.8 (2 × Cq), 134.6 (2 × $CH_{Ar}$), 134.3 (=Cq), 131.6 (4 × $CH_{Ar}$), 130.8 (=$CH_2$), 128.8 (4 × $CH_{Ar}$), 92.2 (CH), 61.4 ($CH_2$), 32.8 ($CH_2$), 31.7 ($CH_2$), 31.4 ($CH_2$), 24.1 ($CH_2$), 22.3 ($CH_2$), 14.2 ($CH_3$), 14.1 ($CH_3$). IR (ν, $cm^{-1}$): 2956, 2928, 2871 (w), 1713, 1446, 1327, 1308, 1140, 1074 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{24}H_{30}O_6S_2Na]^+$: 501.1376, found: 501.1382.

### Ethyl 4-methyl-2-methylene-8,8-bis(phenylsulfonyl)octanoate **45ε**



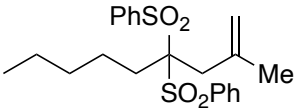

$C_{24}H_{30}O_6S_2$
MW: 478,6

The title compound was prepared following General Procedure 8 with (5-iodohexane-1,1-diyldisulfonyl)dibenzene (123 mg, 0.25 mmol), ethyl 2-((tributylstannyl)methyl)acrylate B (504 mg, 1.25 mmol), trifluorotoluene (0.5 mL, 0.5 M), and AIBN (4 mg, 0.025 mmol) to afford 45α (18.4 mg, 15%) and 45ε (84.2 mg, 70%) (overall 85%; α:ε = 18:82) as colorless oils. $R_f$ = 0.4.

The title compound was also prepared following General Procedure 8 with (5-iodohexane-1,1-diyldisulfonyl)dibenzene (123 mg, 0.25 mmol), ethyl 2-((tributylstannyl)methyl)acrylate **B** (504 mg, 1.25 mmol), trifluorotoluene (5 mL, 0.05 M), and AIBN (6 mg, 0.038 mmol) to afford 45α (38.1 mg, 35%, contaminated with ca. 7% of reduced product) and 45ε (64.7 mg, 60%) (overall 95%; α:ε = 37:63) as colorless oils.

The title compound was prepared following General Procedure 8 with (5-iodohexane-1,1-diyldisulfonyl)dibenzene (123 mg, 0.25 mmol), ethyl 2-((tributylstannyl)methyl)acrylate B (504 mg, 1.25 mmol), trifluorotoluene (50 mL, 0.005 M), and AIBN (4 mg, 0.025 mmol) to afford 45α (42.2 mg, 35%) and 45ε (55.9 mg, 47%) (overall 82%; α:ε = 43:57) as colorless oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.98–7.93 (m, 4H), 7.72–7.66 (m, 2H), 7.61–7.54 (m, 4H), 6.16 (d, *J* = 1.6 Hz, 1H), 5.46–5.44 (m, 1H), 4.38 (t, *J* = 5.6 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 2.27 (ddd, *J* = 13.7, 5.9, 1.2 Hz, 1H), 2.13 (td, *J* = 7.9, 5.6 Hz, 2H), 2.01 (ddd, *J* = 13.7, 8.2, 1.0 Hz, 1H), 1.67–1.44 (m, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.29–1.18 (m, 1H), 1.04 (dddd, *J* = 13.3, 10.3, 7.9, 5.4 Hz, 1H), 0.79 (d, *J* = 6.6 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 167.4 (Cq), 139.6 (=Cq), 138.08 (Cq), 138.07 (Cq), 134.7 (2 × $CH_{Ar}$), 129.8 (4 × $CH_{Ar}$), 129.2 (4 × $CH_{Ar}$), 126.0 (=$CH_2$), 83.9 (CH), 60.8 ($CH_2$), 39.6 ($CH_2$), 36.1 ($CH_2$), 31.6 (CH), 25.9 ($CH_2$), 25.7 ($CH_2$), 19.3 ($CH_3$), 14.4 ($CH_3$). IR (ν, $cm^{-1}$): 2955, 2924, 2870, 2851 (w), 1709, 1447, 1325, 1310, 1143, 1078 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{24}H_{30}O_6S_2Na]^+$: 501.1376, found: 501.1366.

### ((2-Methyl-4-(phenylsulfonyl)non-1-en-4-yl)peroxy)(phenyl)sulfane **46α**




$C_{22}H_{28}O_4S_2$
MW: 420,6

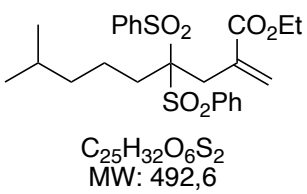
The title compound was prepared following General Procedure 8 with (5-iodohexane-1,1-diyldisulfonyl)dibenzene (123 mg, 0.25 mmol), **A** (0.29 mL, 1.25 mmol), trifluorotoluene (0.5 mL, 0.5 M), and AIBN (6 mg, 0.038 mmol) to afford as colorless oil (88.2 mg, 84%; α:ε

> 99:1). $R_f$ = 0.48.

The title compound was also prepared following General Procedure 8 with (5-iodohexane-1,1-diyldisulfonyl)dibenzene (123 mg, 0.25 mmol), tributyl(2-methylallyl)stannane **A** (0.29 mL, 1.25 mmol), trifluorotoluene (5 mL, 0.05 M), and AIBN (6 mg, 0.038 mmol) to afford as colourless oil (95.6 mg, 91%; α:ε > 99:1).

$^1$H NMR (400 MHz, $CDCl_3$) δ 8.09–8.01 (m, 4H), 7.74–7.65 (m, 2H), 7.60–7.52 (m, 4H), 5.04–5.02 (m, 1H), 5.02–5.00 (m, 1H), 3.02 (s, 2H), 2.36–2.31 (m, 2H), 1.75–1.68 (m, 2H), 1.75 (bs, 3H), 1.38–1.18 (m, 4H), 0.89 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 138.2 (=Cq), 137.5 (2 × Cq), 134.5 (2 × $CH_{Ar}$), 131.7 (4 × $CH_{Ar}$), 128.6 (4 × $CH_{Ar}$), 118.1 (=$CH_2$), 93.6 (CH), 36.0 ($CH_2$), 32.5 ($CH_2$), 29.9 ($CH_2$), 24.9 ($CH_3$), 24.0 ($CH_2$), 22.4 ($CH_2$), 14.2 ($CH_3$). IR (ν, $cm^{-1}$): 2958, 2926, 2871, 2850 (w), 1447, 1327, 1308, 1138, 1074 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{22}H_{28}O_4S_2Na]^+$: 443.1321, found: 443.1312.

### Ethyl 8-methyl-2-methylene-4-(phenylsulfonyl)-4-((phenylthio)peroxy)nonanoate **47α**

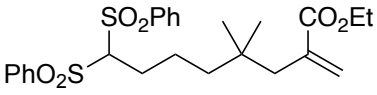



$C_{25}H_{32}O_6S_2$
MW: 492,6

The title compound was prepared following General Procedure 8 with ((1-iodo-5-methyl-1-(phenylsulfonyl)hexyl)peroxy)(phenyl) sulfane (127 mg, 0.25 mmol), ethyl 2-((tributylstannyl)methyl)acrylate **B** (504 mg, 1.25 mmol), trifluorotoluene (5 mL, 0.05 M), and AIBN (6 mg, 0.038 mmol) to afford 47α (16.5 mg, 13%, contaminated with ca. 13% of reduced product) and 47ε (79 mg, 64%) (overall 77%; α:ε = 17:83) as colorless oil. $R_f$ = 0.47.

$^1$H NMR (400 MHz, $CDCl_3$) δ 8.10 – 8.02 (m, 4H), 7.75 – 7.64 (m, 2H), 7.58 (tt, *J* = 7.5, 1.6 Hz, 4H), 6.40 (d, *J* = 1.0 Hz, 1H), 6.02 – 5.96 (m, 1H), 4.15 (q, *J* = 7.2 Hz, 2H), 3.38 (d, *J* = 0.9 Hz, 2H), 2.12 (ddd, *J* = 8.4, 6.6, 4.8 Hz, 2H), 1.66 – 1.57 (m, 2H), 1.45 (dtd, *J* = 13.3, 6.6, 1.7 Hz, 1H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.13 – 1.05 (m, 2H), 0.81 (d, *J* = 6.6 Hz, 7H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 167.06, 137.66, 134.49, 134.12, 131.45, 130.61, 129.7, 92.1, 61.4, 39.9, 31.7, 31.6, 27.9, 22.7, 22.3, 14.2. IR (ν, $cm^{-1}$): 2957, 2930, 2869 (w), 1710, 1446, 1327, 1309, 1145, 1078 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{25}H_{32}O_6S_2Na]^+$: 515.1533, found: 515.1544.

### Ethyl 4,4-dimethyl-2-methylene-8,8-bis(phenylsulfonyl)octanoate **47ε**



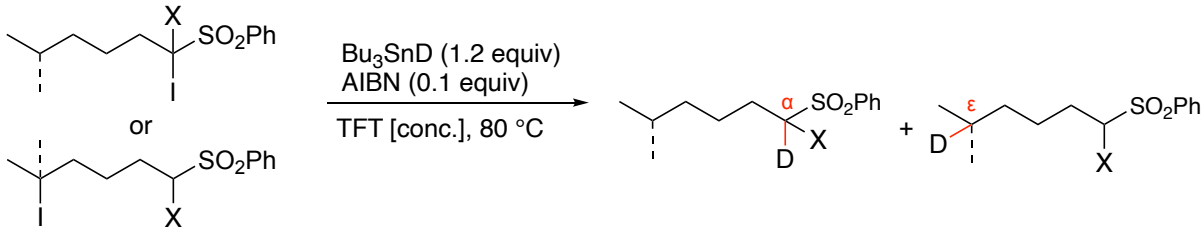

$C_{25}H_{32}O_6S_2$
MW: 492,6

The title compound was prepared following General Procedure 8 with ((1-iodo-5-methyl-1-(phenylsulfonyl)hexyl)peroxy)(phenyl) sulfane (127 mg, 0.25 mmol), ethyl 2-((tributylstannyl)methyl)acrylate **B** (504 mg, 1.25 mmol), trifluorotoluene (50 mL, 0.005 M), and AIBN (6 mg, 0.038 mmol) to afford 47α and 47ε (58% NMR yield (standard = 1,3,5-trimethoxybenzene); α:ε = 7:93). $R_f$ = 0.33.

$^1$H NMR (400 MHz, $CDCl_3$) δ 7.98–7.94 (m, 4H), 7.72–7.66 (m, 2H), 7.63–7.54 (m, 4H), 6.17 (d, *J* = 1.7 Hz, 1H), 5.43–5.41 (m, 1H), 4.40 (t, *J* = 5.6 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 2.21 (bs, 2H), 2.11 (td, *J* = 7.8, 5.5 Hz, 2H), 1.55–1.46 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.12–1.05 (m, 2H), 0.75 (s, 6H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 168.3 (Cq), 138.6 (=Cq), 138.1 (2 × Cq), 134.7 (2 × $CH_{Ar}$), 129.8 (4 × $CH_{Ar}$), 129.2 (4 × $CH_{Ar}$), 127.4 (=$CH_2$), 83.8 (CH), 60.9 ($CH_2$), 42.7 ($CH_2$), 41.6 ($CH_2$), 40.0 (Cq), 26.50 (2 × $CH_3$), 26.45 ($CH_2$), 23.1 ($CH_2$), 14.3 ($CH_3$). IR (ν, $cm^{-1}$): 2957, 2930, 2869 (w), 1710, 1446, 1327, 1309, 1145, 1078 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{25}H_{32}O_6S_2Na]^+$: 515.1533, found: 515.1544.

### General procedure for remote deuteration of α- or ε-iodoalkyl mono- or bis-sulfones

### General Procedure 9. Deuteration

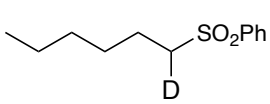



X = H, $SO_2Ph$

A two-neck 10 mL round-bottom flask equipped with a condenser was charged with α- or ε-iodoalkyl mono- or bis-sulfones (0.5 mmol), and tributylstannane-*d* (0.6 mmol) were dissolved in anhydrous trifluorotoluene (see description for volume) while under Argon, protected from light with Aluminium foil. Then, AIBN (0.05 mmol) was added. The reaction mixture was immersed in the pre-heated oil bath at 80 °C, and the reaction mixture was stirred for 1 h at 80 °C (TLC monitoring). The reaction mixture was cooled to rt and filtered through a short pad of $SiO_2/K_2CO_3$ (9:1). The pad was washed with EtOAc, and the volatiles were removed under

reduced pressure. The crude product was purified by flash column chromatography on $SiO_2/K_2CO_3$ (9:1) mixture (Heptane/EtOAc = 95:5 to 90:10).

### ((Hexyl-1-d)sulfonyl)benzene **1dα**




$C_{12}H_{17}DO_2S$
MW: 227,3

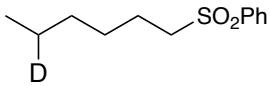
The title compound was prepared following General Procedure 9 with ((1-iodohexyl)sulfonyl)benzene (176 mg, 0.5 mmol), tributylstannane-*d* (175 mg, 0.6 mmol), trifluorotoluene (1 mL, 0.5 M), and AIBN (8 mg, 0.05 mmol) to afford as white solid (107.7 mg, 95%; α:ε > 98:2, ≥98%-*d*)$R_f$ = 0.62. M.p. = 40.5–42.5 °C (not corrected).

The title compound was prepared following General Procedure 9 with ((1-iodohexyl)sulfonyl)benzene (176 mg, 0.5 mmol), tributylstannane-*d* (175 mg, 0.6 mmol), trifluorotoluene (10 mL, 0.05 M), and AIBN (8.4 mg, 0.05 mmol) to afford as white solid (114 mg, ≥98%; α:ε > 98:5, ≥98%-*d*).

The title compound was prepared following General Procedure 9 with ((1-iodohexyl)sulfonyl)benzene (88.1 mg, 0.25 mmol), tributylstannane-*d* (87.6 mg, 0.3 mmol), trifluorotoluene (50 mL, 0.005 M), and AIBN (4.1 mg, 0.025 mmol) to afford X as white solid (56 mg, ≥ 98%; α:ε > 98:5, ≥ 98%-*d*).

$^1$H NMR (400 MHz, $CDCl_3$) δ 7.92–7.85 (m, 2H), 7.67–7.60 (m, 1H), 7.59–7.51 (m, 2H), 3.04 (tt, *J* = 8.0, 1.9 Hz, 1H), 1.67 (q, *J* = 7.8 Hz, 2H), 1.39–1.26 (m, 2H), 1.26–1.18 (m, 4H), 0.82 (t, *J* = 6.8 Hz, 3H). $^2$H NMR (61 MHz, $CDCl_3$) δ 3.03 (s, 1D). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.3 (Cq), 133.7 ($CH_{Ar}$), 129.3 (2 × $CH_{Ar}$), 128.1 (2 × $CH_{Ar}$), 56.0 (t, $J_{C\text{-}D}$ = 20 Hz, CHD), 31.2 ($CH_2$), 27.9 ($CH_2$), 22.5 ($CH_2$), 22.3 ($CH_2$), 13.9 ($CH_3$). IR (ν, $cm^{-1}$): 2954, 2929, 2870, 2858 (w), 1446, 1302, 1146, 1085 (str.). HRMS (ESI): $[M+H]^+$ calculated for $[C_{12}H_{18}{}^2HO_2S]^+$: 228.1163, found: 228.1163.

### ((Hexyl-5-d)sulfonyl)benzene **1dε**




$C_{12}H_{17}DO_2S$
MW: 227,3

The title compound was prepared following General Procedure 9 with ((5-iodohexyl)sulfonyl)benzene (176 mg, 0.5 mmol), tributylstannane-*d* (175 mg, 0.6 mmol), trifluorotoluene (1 mL, 0.5 M), and AIBN (8.4 mg, 0.05 mmol) to afford as colorless oil (102.5 mg, 90%; α:ε < 2:98, ≥98%-*d*). $R_f$ = 0.53.

The title compound was prepared following General Procedure 9 with ((5-iodohexyl)sulfonyl)benzene (176 mg, 0.5 mmol), tributylstannane-*d* (175 mg, 0.6 mmol),

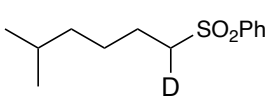
trifluorotoluene (10 mL, 0.05 M), and AIBN (8.4 mg, 0.05 mmol) to afford as colorless oil (113.1 mg, ≥98%; α:ε = 3:97, ≥98%-*d*).

The title compound was prepared following General Procedure 9 with ((5-iodohexyl)sulfonyl)benzene (88.1 mg, 0.25 mmol), tributylstannane-*d* (87.6 mg, 0.3 mmol), trifluorotoluene (25 mL, 0.01 M), and AIBN (4.1 mg, 0.025 mmol) to afford as colorless oil (52.1 mg, 92%; α:ε = 3:97, ≥98%-*d*).

The title compound was prepared following General Procedure 9 with ((5-iodohexyl)sulfonyl)benzene (88.1 mg, 0.25 mmol), tributylstannane-*d* (87.6 mg, 0.3 mmol), trifluorotoluene (50 mL, 0.005 M), and AIBN (4.1 mg, 0.025 mmol) to afford as colorless oil (52.3 mg, 92%; α:ε = 18:82, ≥98%-*d*).

$^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.93–7.84 (m, 2H), 7.65–7.60 (m, 1H), 7.58–7.50 (m, 2H), 3.09–3.01 (m, 2H), 1.73–1.63 (m, 2H), 1.38–1.28 (m, 2H), 1.27–1.15 (m, 3H), 0.84–0.79 (m, 3H). $^{2}$H NMR (61 MHz, $CDCl_3$) δ 1.18 (s, 1D). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.3 (Cq), 133.7 ($CH_{Ar}$), 129.3 (2 × $CH_{Ar}$), 128.1 (2 × $CH_{Ar}$), 56.4 ($CH_2$), 31.1 ($CH_2$), 27.9 ($CH_2$), 22.7 ($CH_2$), 21.9 (t, $J_{C\text{-}D}$ = 19 Hz, CHD), 13.8 ($CH_3$). IR (ν, $cm^{-1}$): 2952, 2921, 2870, 2856 (w), 1446, 1303, 1141, 1085 (str.). HRMS (ESI): $[M+H]^+$ calculated for $[C_{12}H_{18}{}^{2}HO_2S]^+$: 228.1163, found: 228.1164.

### ((5-Methylhexyl-1-d)sulfonyl)benzene **2dα**




$C_{13}H_{19}DO_2S$
MW: 241,4

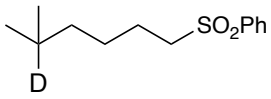
The title compound was prepared following General Procedure 9 with ((1-iodo-5-methylhexyl)sulfonyl)benzene (91.6 mg, 0.25 mmol), tributylstannane-*d* (87.6 mg, 0.3 mmol), trifluorotoluene (5 mL, 0.05 M), and AIBN (4.1 mg, 0.025 mmol) to afford as colorless oil (58.1 mg, 96%; α:ε = >95:5, ≥98%-*d*). $R_f$ = 0.48.

The title compound was prepared following General Procedure 9 with ((1-iodo-5-methylhexyl)sulfonyl)benzene (91.6 mg, 0.25 mmol), tributylstannane-*d* (87.6 mg, 0.3 mmol), trifluorotoluene (50 mL, 0.005 M), and AIBN (4.1 mg, 0.025 mmol) to afford as colorless oil (55.2 mg, 92%; α:ε = 85:15, ≥98%-*d*).

The title compound was prepared following General Procedure 9 with ((1-iodo-5-methylhexyl)sulfonyl)benzene (91.6 mg, 0.25 mmol), tributylstannane-*d* (87.6 mg, 0.3 mmol), trifluorotoluene (50 mL, 0.005 M), and V40 (6.1 mg, 0.025 mmol) at 110 °C to afford as colorless oil (57 mg, 95%; α:ε = 75:25, ≥ 98%-*d*).

$^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.95–7.86 (m, 2H), 7.67–7.62 (m, 1H), 7.59–7.55 (m, 2H), 3.06 (tt, *J* = 7.6, 1.9 Hz, 1H), 1.68 (q, *J* = 7.8 Hz, 2H), 1.55–1.41 (m, 1H), 1.38–1.30 (m, 2H), 1.16–1.09 (m, 2H), 0.83 (d, *J* = 6.6 Hz, 6H). $^{2}$H NMR (61 MHz, $CDCl_3$) δ 3.09 (s, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.4 (Cq), 133.7 ($CH_{Ar}$), 129.4 (2 × $CH_{Ar}$), 128.2 (2 × $CH_{Ar}$), 56.15 (t, $J_{CD}$ = 21 Hz, CHD), 38.4 ($CH_2$), 27.8 (CH), 26.1 ($CH_2$), 22.9 ($CH_2$), 22.6 (2 × $CH_3$). IR (ν, $cm^{-1}$): 2952, 2868 (w), 1447, 1303, 1147, 1086 (str.). HRMS (ESI): $[M+H]^+$ calculated for $[C_{13}H_{20}{}^{2}HO_2S]^+$: 242.1323, found: 242.1322.

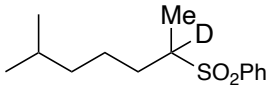
((5-Methylhexyl-5-*d*)sulfonyl)benzene **2dε**




$C_{13}H_{19}DO_2S$
MW: 241,4

$^{2}$H NMR (61 MHz, $CDCl_3$) δ 3.08 (s, 0.75D), 1.46 (s, 0.25D).

((6-Methylheptan-2-yl-2-d)sulfonyl)benzene **10dα**

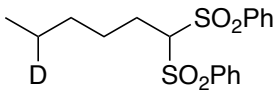



$C_{14}H_{21}DO_2S$
MW: 255,4

The title compound was prepared following General Procedure 9 with ((2-iodo-6-methylheptan-2-yl)sulfonyl)benzene (95.1 mg, 0.25 mmol), tributylstannane-*d* (87.6 mg, 0.3 mmol), trifluorotoluene (50 mL, 0.005 M), and AIBN (4.1 mg, 0.025 mmol) to afford as colorless oil (56.6 mg, 89%; α:ε = 95:5, ≥ 98%-*d*). $R_f$ = 0.5.

$^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.89–7.84 (m, 2H), 7.69–7.60 (m, 1H), 7.60–7.51 (m, 2H), 1.96–1.88 (m, 1H), 1.52–1.33 (m, 3H), 1.30–1.19 (m, 1H), 1.25 (bs, 3H), 1.16–1.09 (m, 2H), 0.834 (d, *J* = 6.6 Hz, 3H), 0.829 (d, *J* = 6.6 Hz, 3H). $^{2}$H NMR (61 MHz, $CDCl_3$) δ 3.02 (s, 0.95D), 1.44 (s, 0.05D).$^{13}$C NMR (101 MHz, $CDCl_3$) δ 137.5 (Cq), 133.6 ($CH_{Ar}$), 129.2 (2 × $CH_{Ar}$), 129.1 (2 × $CH_{Ar}$), 59.83 (t, $J_{CD}$ = 21 Hz, CHD), 38.6 ($CH_2$), 29.3 ($CH_2$), 27.8 (CH), 24.4 ($CH_2$), 22.7 ($CH_3$), 22.5 ($CH_3$), 13.2 ($CH_3$). IR (ν, $cm^{-1}$): 2951, 2867 (w), 1463, 1299, 1132, 1076 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{14}H_{21}{}^{2}HO_2SNa]^+$: 278.1295, found: 278.1293.

### (Hexane-1,1-diyldisulfonyl-5-d)dibenzene **32dε**




$C_{18}H_{21}DO_4S_2$
MW: 367,5

The title compound was prepared following General Procedure 9 with (5-iodohexane-1,1-diyldisulfonyl)dibenzene (123 mg, 0.25 mmol), tributylstannane-*d* (87.6 mg, 0.3 mmol), trifluorotoluene (0.5 mL, 0.5 M), and AIBN (4.1 mg, 0.025 mmol) to afford as white solid (84 mg, 91%; α:ε = 25:75, 75%-*d*). M. p. = 94.8–95.3 °C (not corrected). $R_f$ = 0.43.

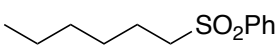
The title compound was prepared following General Procedure 9 with (5-iodohexane-1,1-diyldisulfonyl)dibenzene (116 mg, 0.24 mmol), tributylstannane-*d* (82.4 mg, 0.28 mmol), trifluorotoluene (4.8 mL, 0.05 M), and AIBN (3.9 mg, 0.024 mmol) to afford as white solid (76.8 mg, 89%; α:ε = 64:36, ≥36%-*d*).

The title compound was prepared following General Procedure 9 with (5-iodohexane-1,1-diyldisulfonyl)dibenzene (123 mg, 0.25 mmol), tributylstannane-*d* (87.6 mg, 0.3 mmol), trifluorotoluene (5 mL, 0.05 M), and AIBN (4.1 mg, 0.025 mmol)at 0–36 °C using sun lamp irradiation (300 W), to afford as white solid (84.8 mg, 92%; α:ε = 50:50, ≥50%-*d*)

$^1$H NMR (400 MHz, $CDCl_3$) δ 7.98 –7.92 (m, 4H), 7.75–7.65 (m, 2H), 7.61–7.55 (m, 4H), 4.37 (t, *J* = 5.6 Hz, 1H), 2.17–2.11 (m, 2H), 1.59–1.50 (m, 2H), 1.27–1.15 (m, 3H), 0.83 (d, *J* = 6.9 Hz, 3H). $^2$H NMR (61 MHz, $CDCl_3$) δ 1.23 (s, D). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 138.1 (2 × Cq), 134.7 (2 × $CH_{Ar}$), 129.8 (4 × $CH_{Ar}$), 129.2 (4 × $CH_{Ar}$), 83.98 (CH), 31.19 ($CH_2$), 27.93 ($CH_2$), 25.7 ($CH_2$), 21.76 (t, $J_{CD}$ = 19 Hz, CHD), 13.87 ($CH_3$). IR (ν, cm$^{-1}$): 2956, 2924, 2857 (w), 1445, 1328, 1306, 1292, 1156, 1145, 1078 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{18}H_{21}{}^2HO_4S_2Na]^+$: 390.0914, found: 390.0914.

## Characterisation of side products

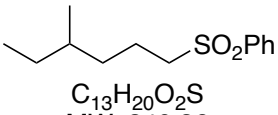
### (Hexylsulfonyl)benzene




$C_{12}H_{18}O_2S$
MW: 226,33

Colourless liquid. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.93–7.88 (m, 2H), 7.69–7.62 (m, 1H), 7.58–7.54 (m, 2H), 3.10–3.04 (m, 2H), 1.75–1.65 (m, 2H), 1.40–1.29 (m, 2H), 1.29–1.17 (m, 4H), 0.85 (t, *J* = 6.9 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.4 (Cq), 133.7 ($CH_{Ar}$), 129.4 (2 × $CH_{Ar}$), 128.2 (2 × $CH_{Ar}$), 56.5 ($CH_2$), 31.3 ($CH_2$), 28.1 ($CH_2$), 22.7 ($CH_2$), 22.4 ($CH_2$), 14.0 ($CH_3$). IR (ν, cm$^{-1}$): 2954, 2925, 2857 (w), 1303, 1286, 1142, 1085 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{12}H_{18}O_2SNa]^+$: 249.0915, found: 249.0915.

### ((4-methylhexyl)sulfonyl)benzene




$C_{13}H_{20}O_2S$
MW: 240,36

Colourless liquid. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.95–7.88 (m, 2H), 7.68–7.63 (m, 1H), 7.60–7.54 (m, 2H), 3.11–3.11 (m, 2H), 1.82–1.60 (m, 2H), 1.41–1.21 (m, 3H), 1.20–1.03 (m, 2H), 0.86–0.78 (m, 6H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.5 (Cq), 133.7 ($CH_{Ar}$), 129.4 (2 × $CH_{Ar}$), 128.2 (2 × $CH_{Ar}$), 56.8 ($CH_2$), 35.2 ($CH_2$), 34.1 (CH), 29.3 ($CH_2$), 20.5 ($CH_2$), 19.0 ($CH_3$), 11.4 ($CH_3$). IR (ν, $cm^{-1}$): 2958, 2922, 2873 (w), 1303, 1142, 1085 (str.). HRMS (ESI): $[M+Na]^+$ calculated for $[C_{13}H_{20}O_2SNa]^+$: 263.1072, found: 263.1072.

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# 7 Appendix

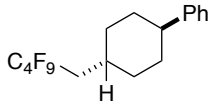
## NMR Spectra

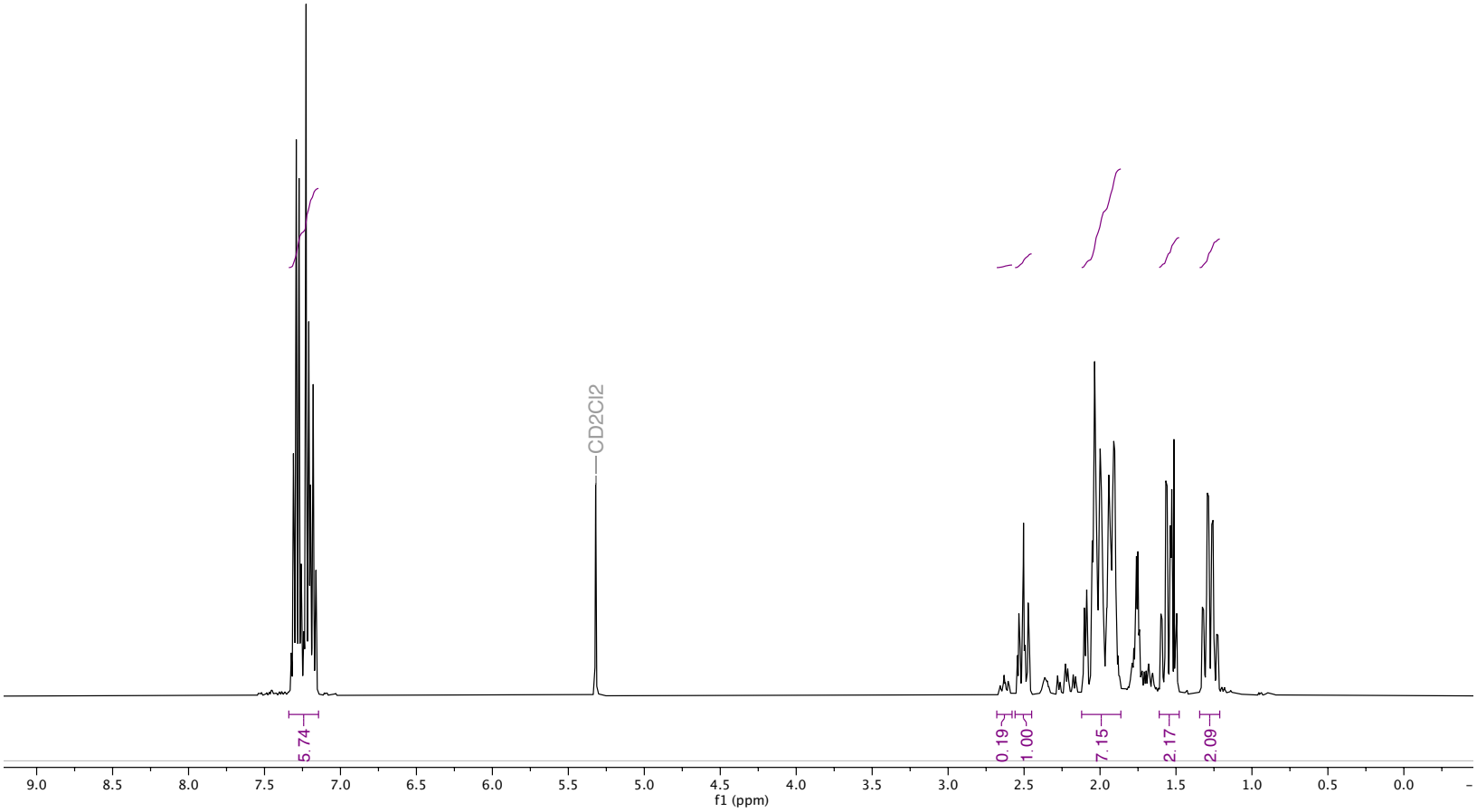
## 7.1 NMR Spectra Chapter 2

**Radical Mediated Hydroperfluoroalkylation of Unactivated Alkenes**

((1*R*,4*R*)-4-(2,2,3,3,4,4,5,5,5-nonafluoropentyl)cyclohexyl)benzene **(2)**

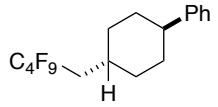
$^1$H-NMR (400 MHz, $CD_2Cl_2$)

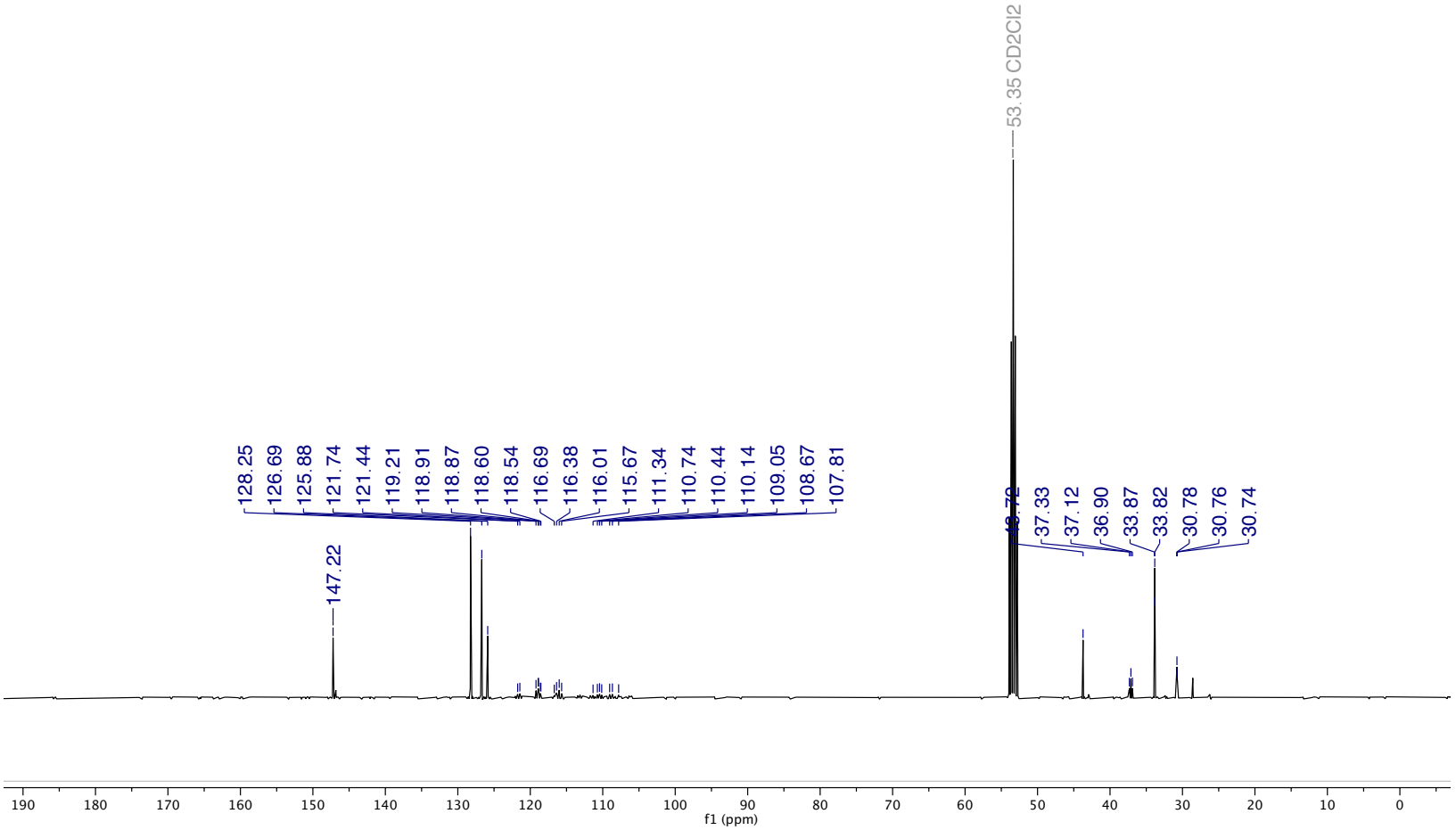


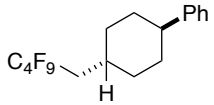
((1*R*,4*R*)-4-(2,2,3,3,4,4,5,5,5-nonafluoropentyl)cyclohexyl)benzene **(2)**

$^{13}$C-NMR (100 MHz, $CD_2Cl_2$)

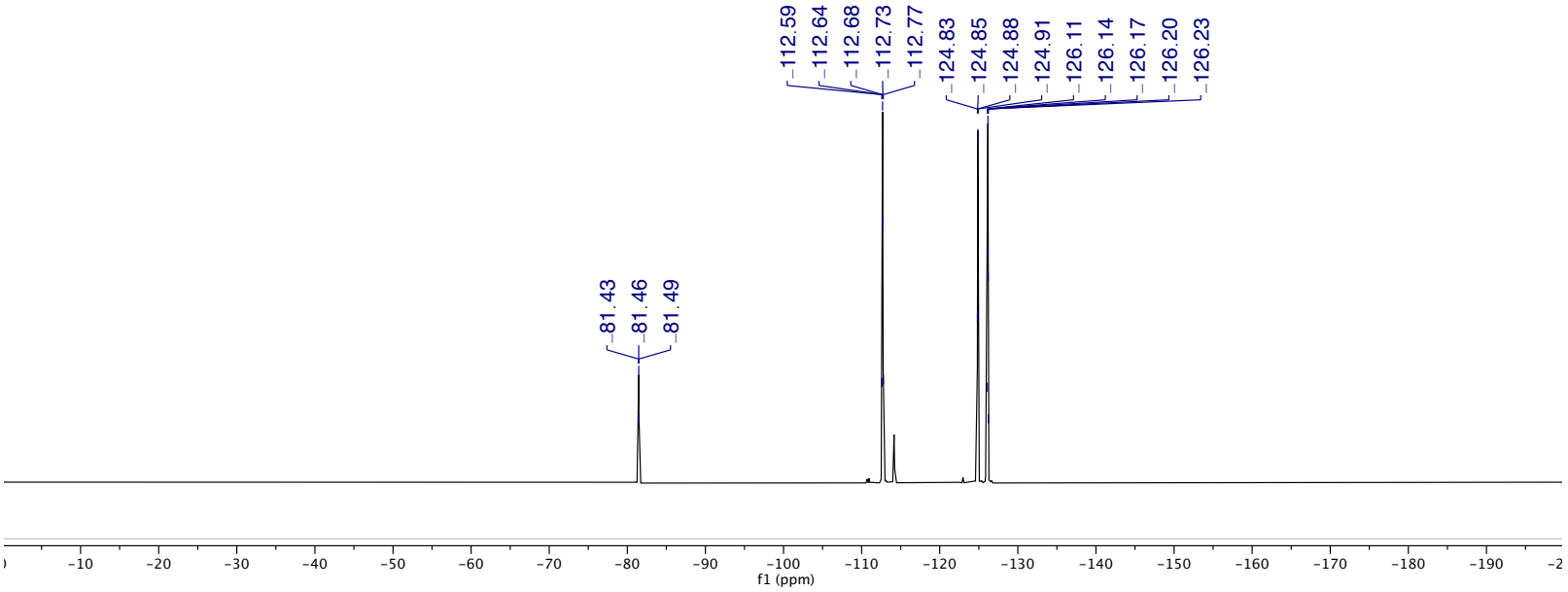


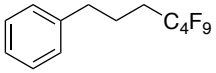
((1*R*,4*R*)-4-(2,2,3,3,4,4,5,5,5-nonafluoropentyl)cyclohexyl)benzene **(2)**



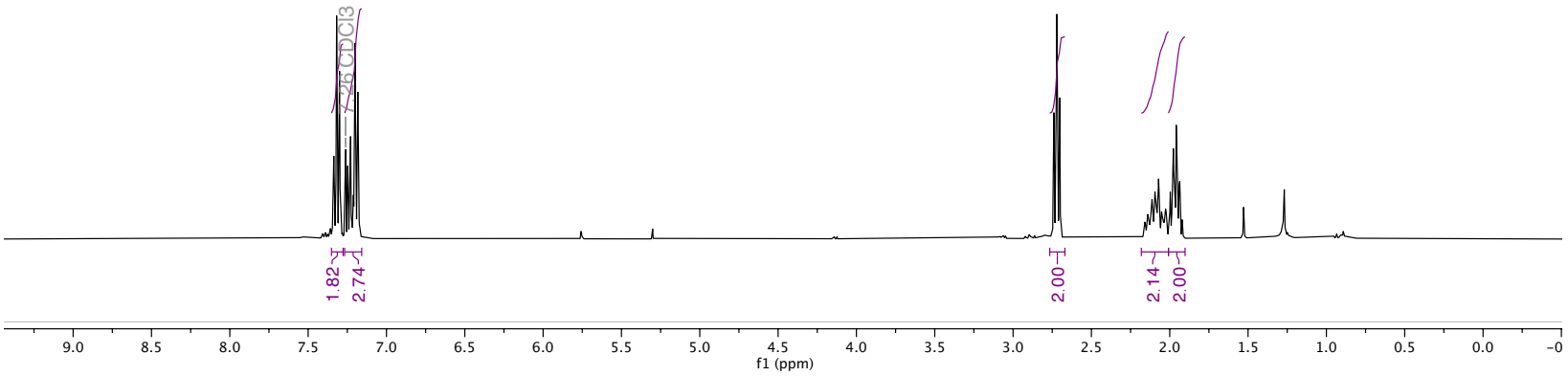

$^{19}$F-NMR (376 MHz, $CD_2Cl_2$)



(4,4,5,5,6,6,7,7,7-Nonafluoroheptyl)benzene **(3)**

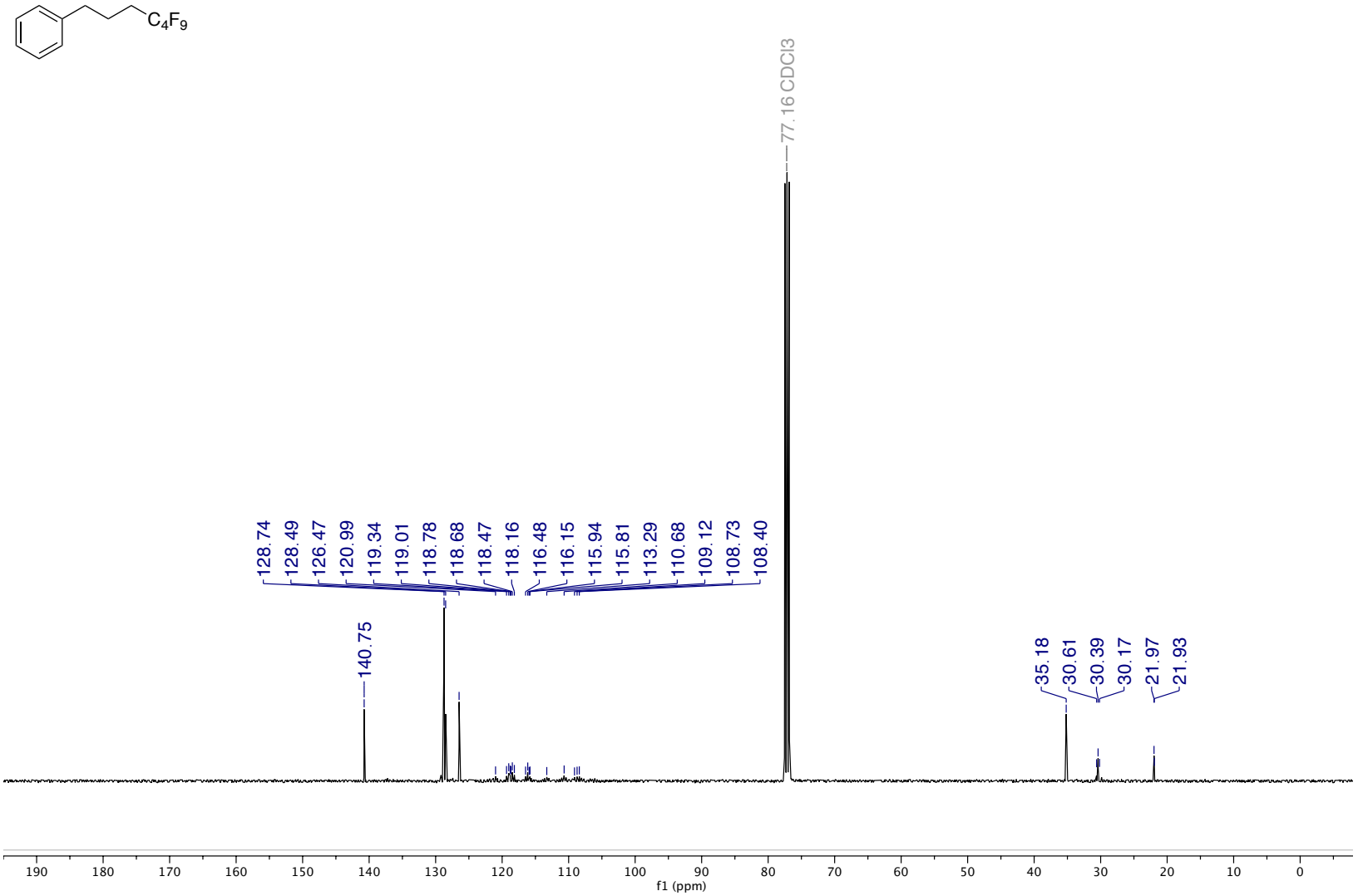



$^1$H-NMR (400 MHz, $CDCl_3$)

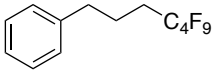


(4,4,5,5,6,6,7,7,7-Nonafluoroheptyl)benzene **(3)**

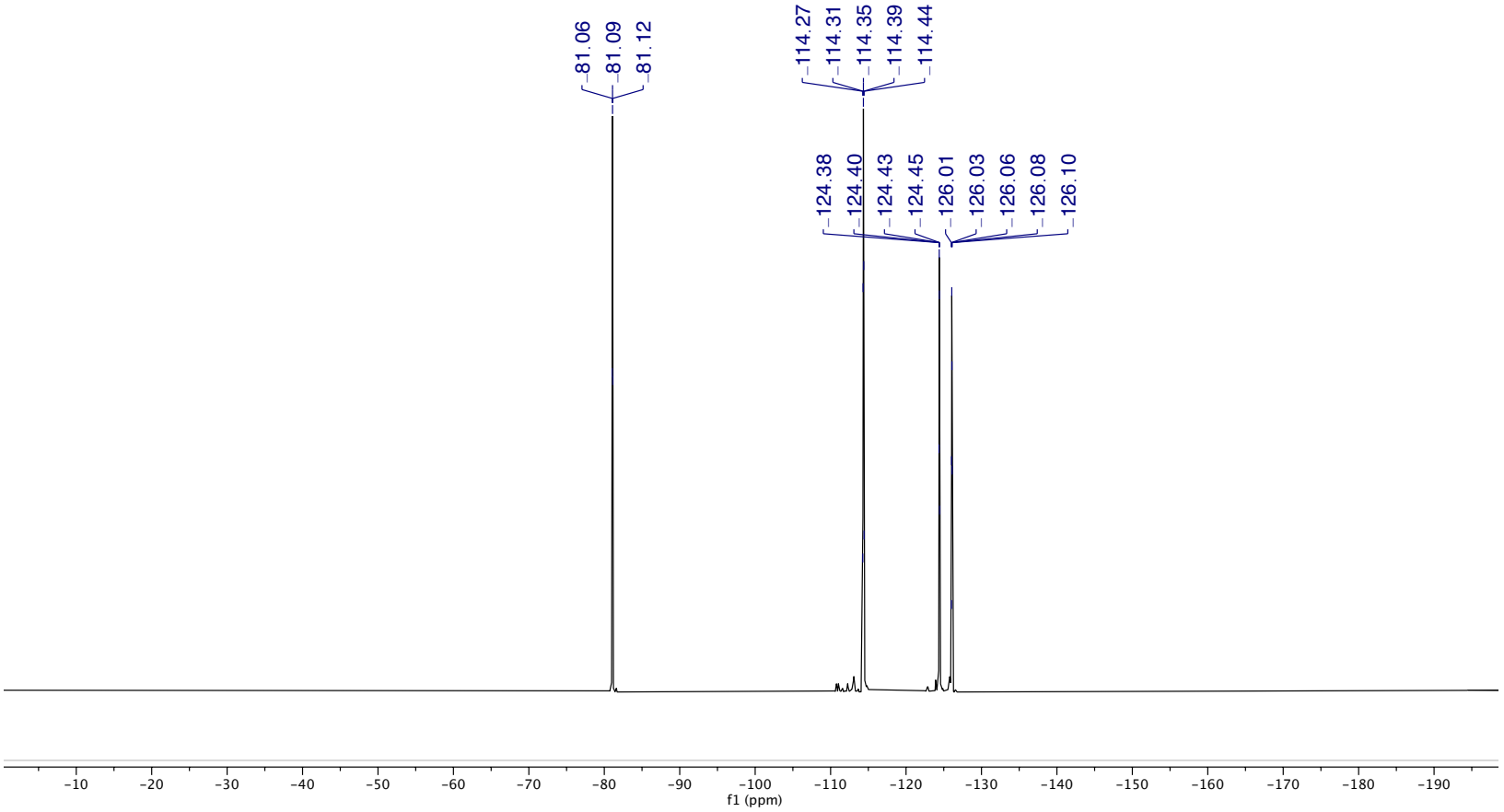
$^{13}$C-NMR (100 MHz, $CDCl_3$)



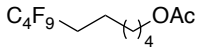
(4,4,5,5,6,6,7,7,7-Nonafluoroheptyl)benzene **(3)**



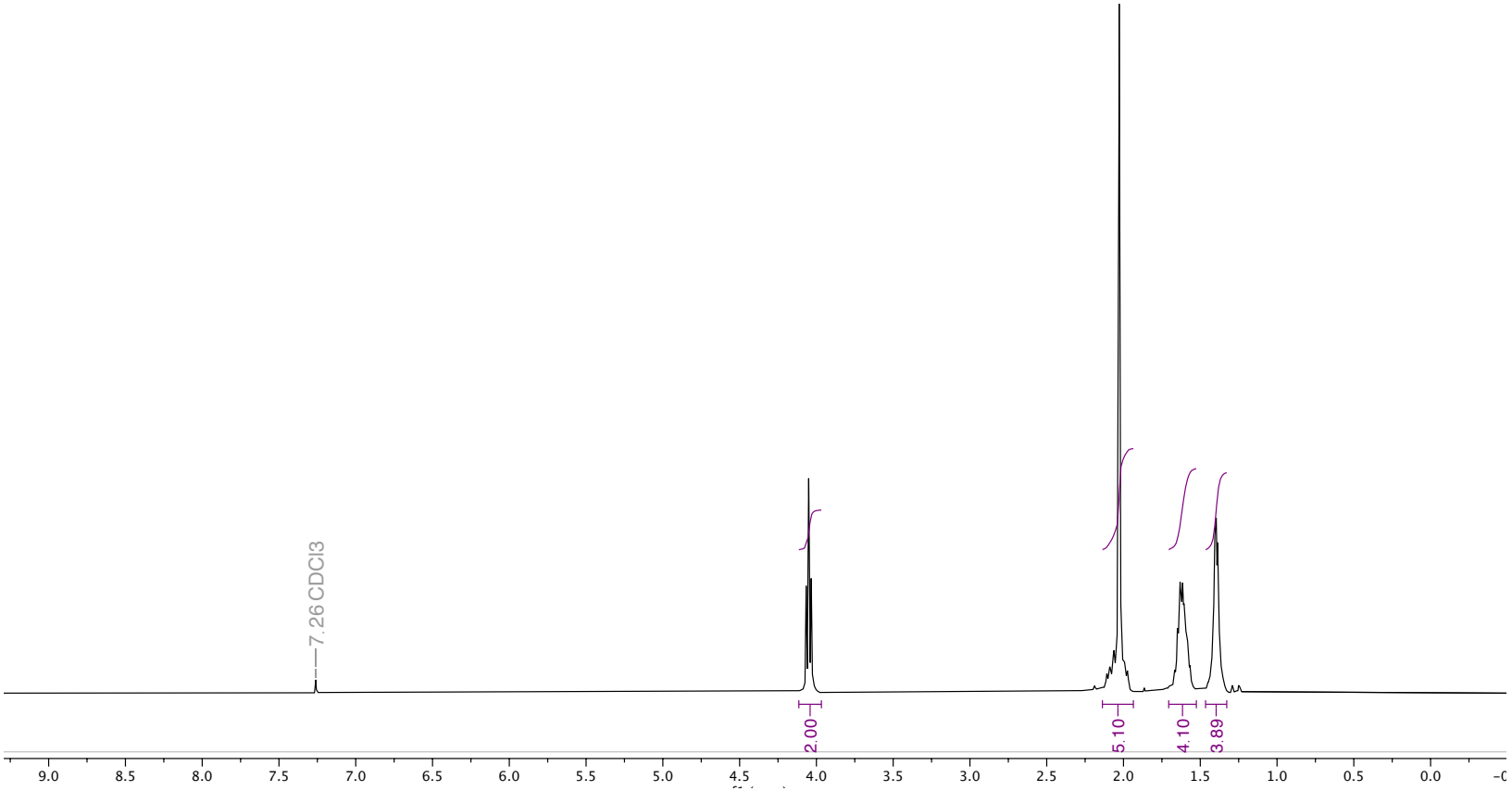

$^{19}$F-NMR (376 MHz, $CDCl_3$)



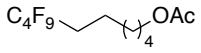
7,7,8,8,9,9,10,10,10-Nonafluorodecyl acetate **(4)**



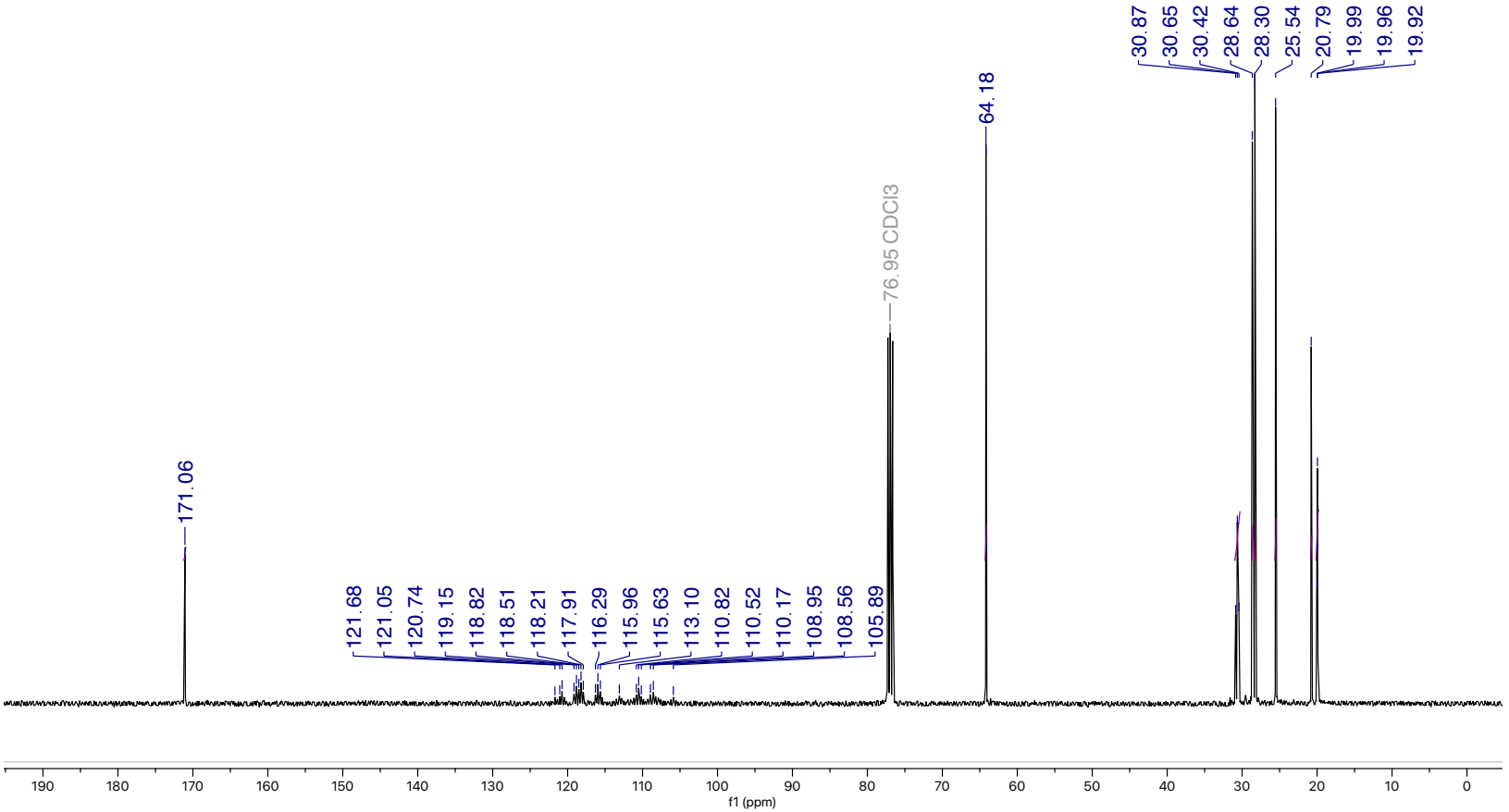

$^{1}$H-NMR (400 MHz, $CDCl_3$)



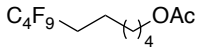
7,7,8,8,9,9,10,10,10-Nonafluorodecyl acetate **(4)**



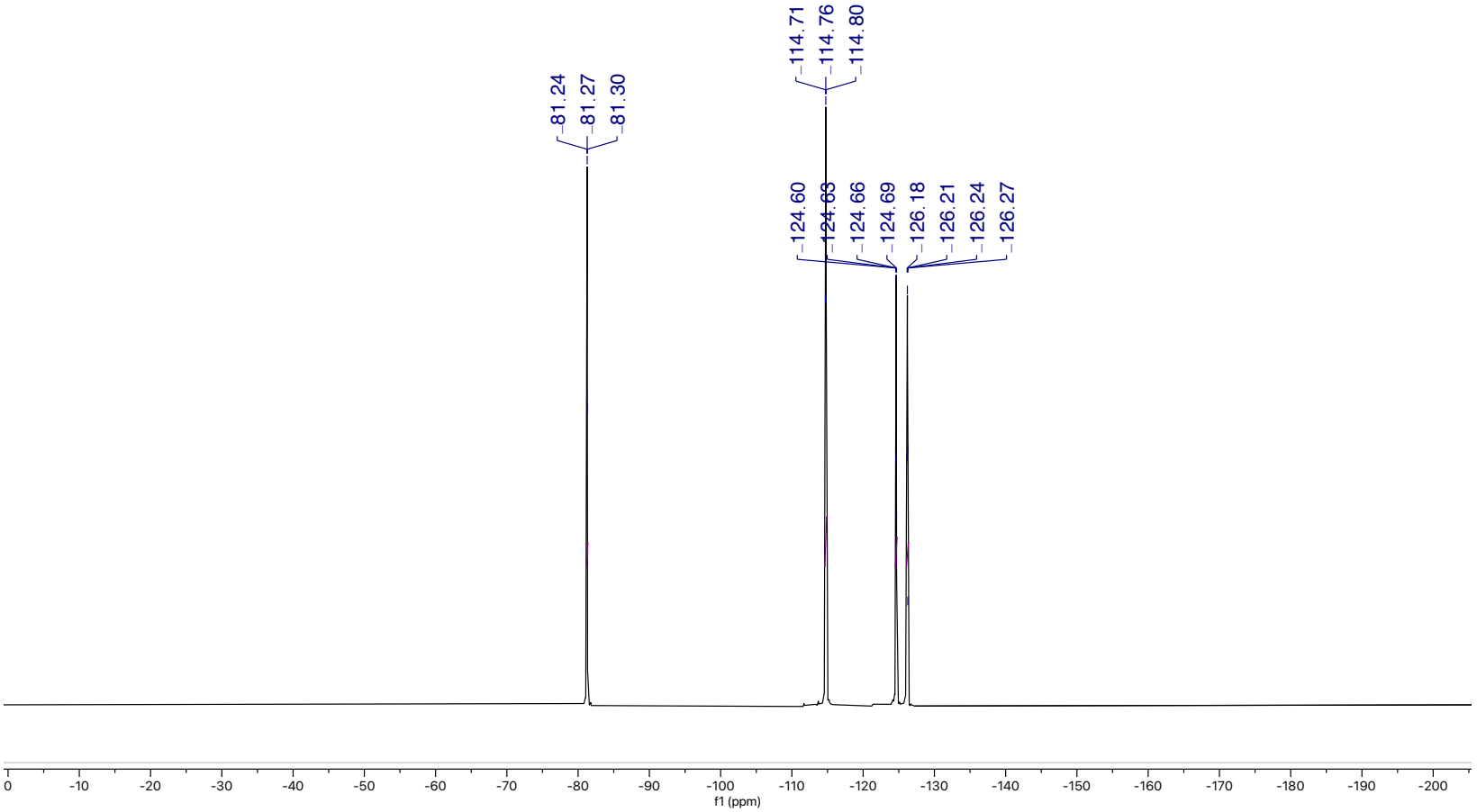

$^{13}$C-NMR (100 MHz, $CDCl_3$)



7,7,8,8,9,9,10,10,10-Nonafluorodecyl acetate **(4)**

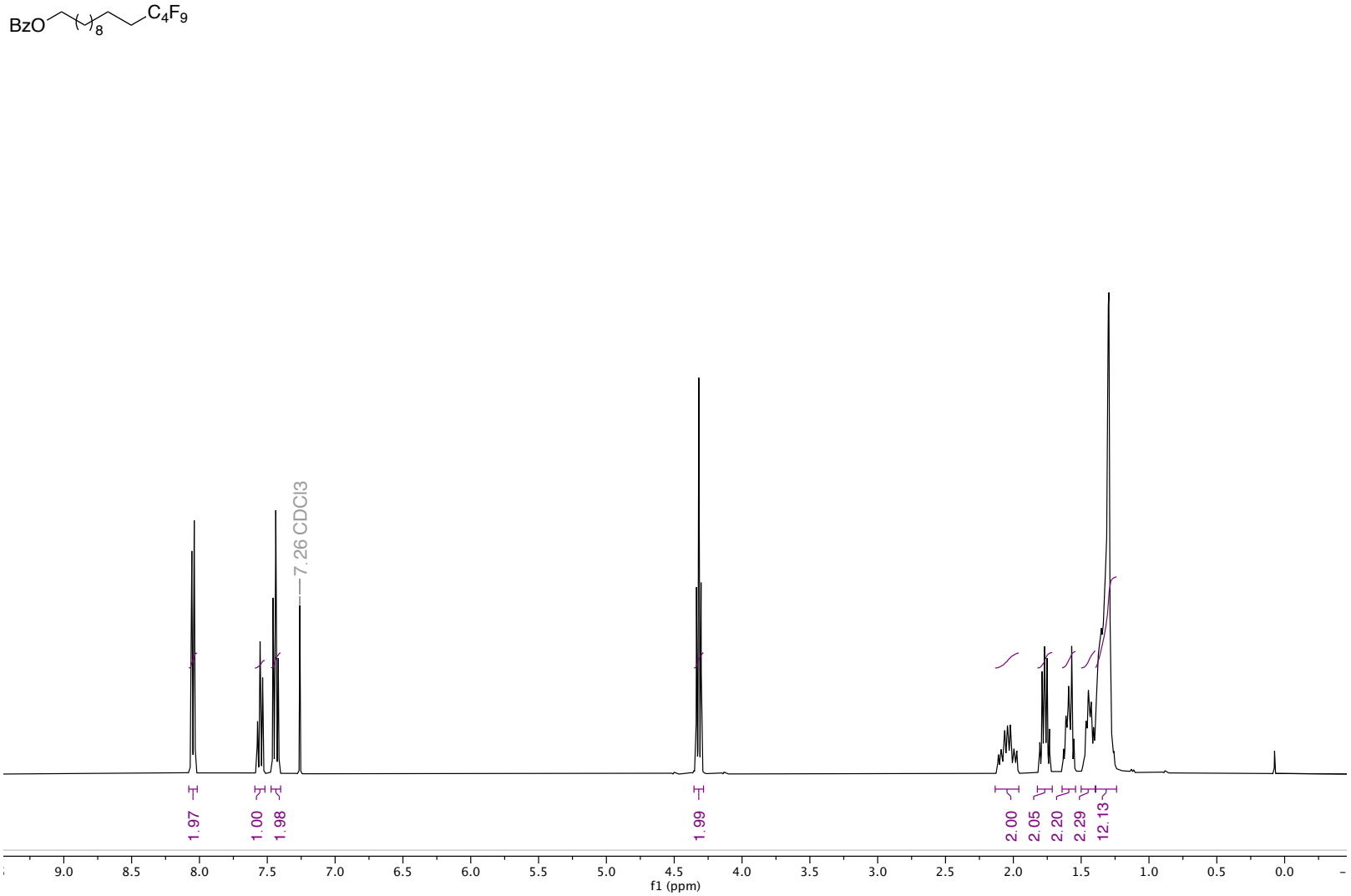



$^{19}$F-NMR (376 MHz, $CDCl_3$)

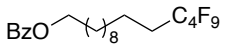


12,12,13,13,14,14,15,15,15-Nonafluoropentadecyl benzoate **(5)**

$^1$H-NMR (400 MHz, $CDCl_3$)

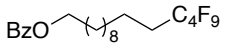


12,12,13,13,14,14,15,15,15-Nonafluoropentadecyl benzoate **(5)**

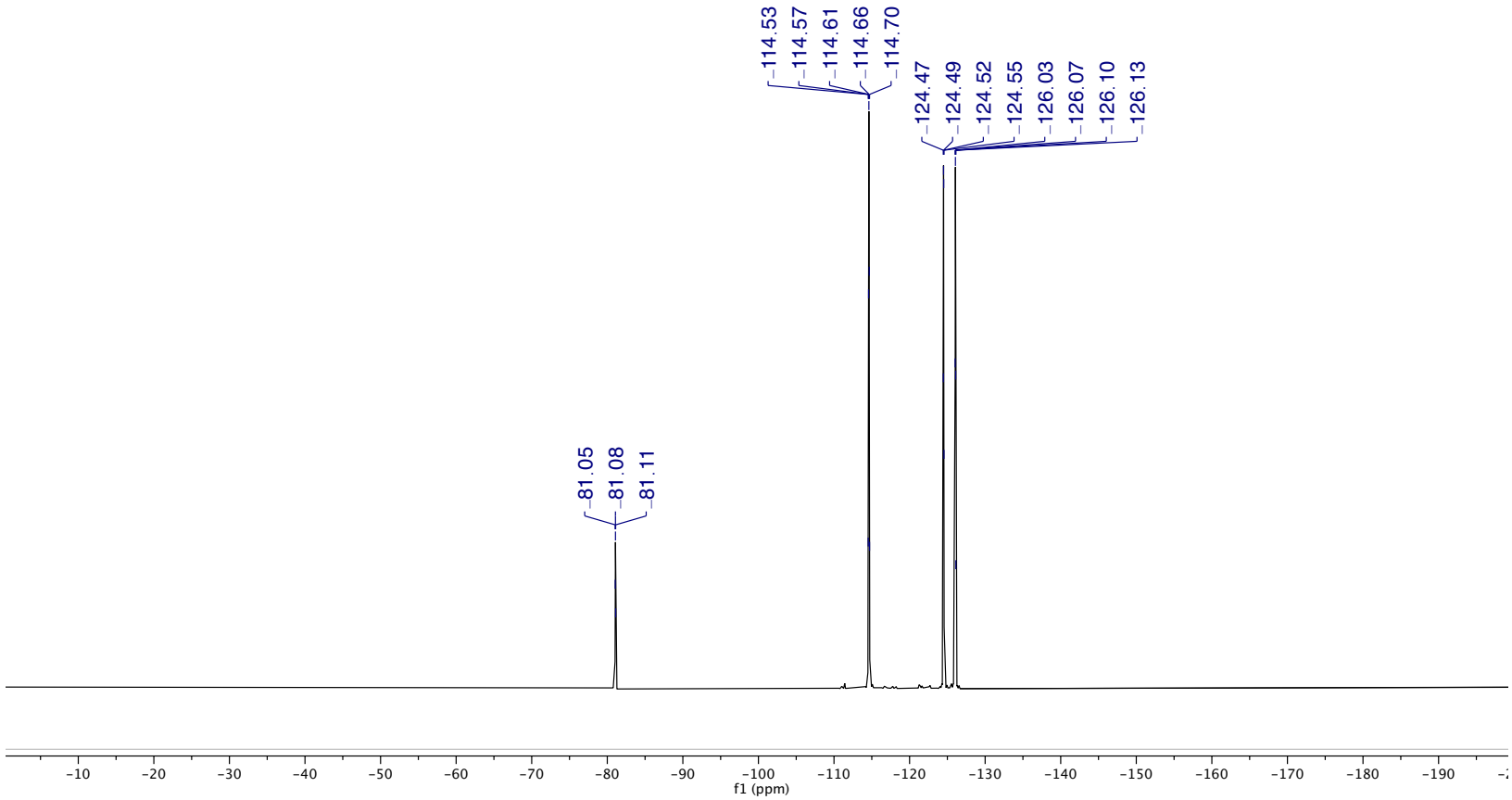



$^{13}$C-NMR (100 MHz, $CDCl_3$)

12,12,13,13,14,14,15,15,15-Nonafluoropentadecyl benzoate **(5)**

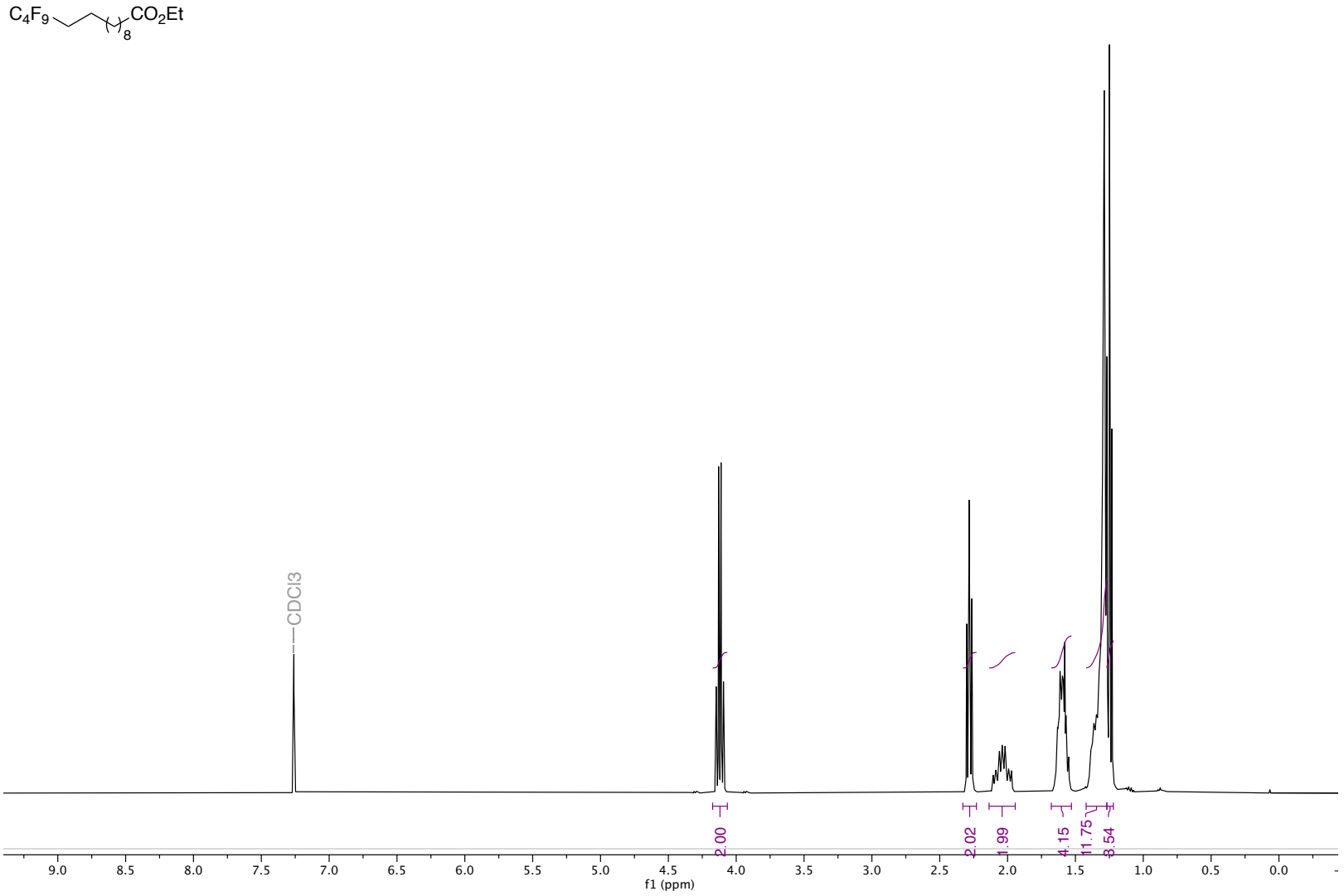



$^{19}$F-NMR (376 MHz, $CDCl_3$)



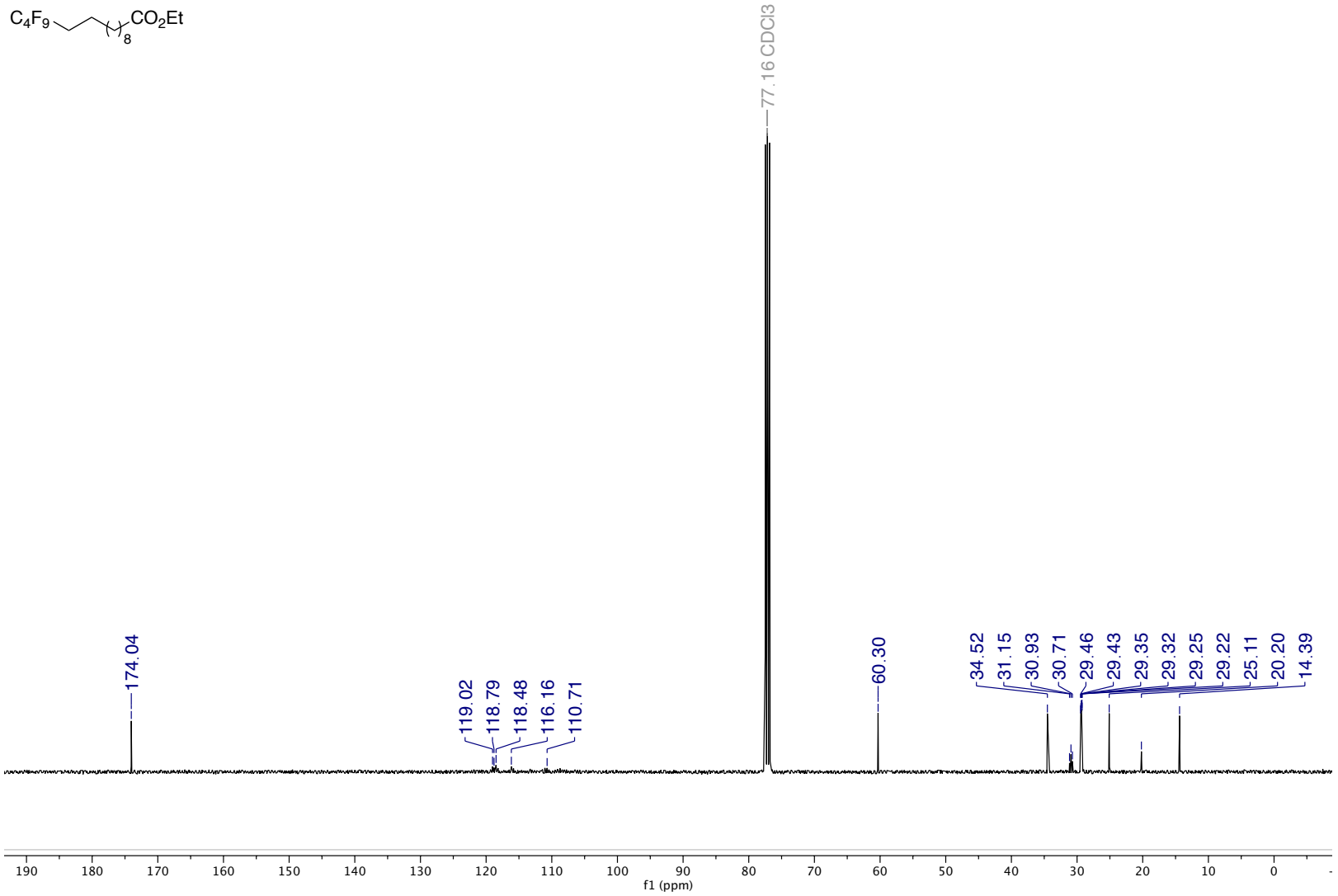
Ethyl 12,12,13,13,14,14,15,15,15-nonafluoropentadecanoate **(6)**

$^1$H-NMR (400 MHz, $CDCl_3$)

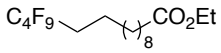


Ethyl 12,12,13,13,14,14,15,15,15-nonafluoropentadecanoate **(6)**

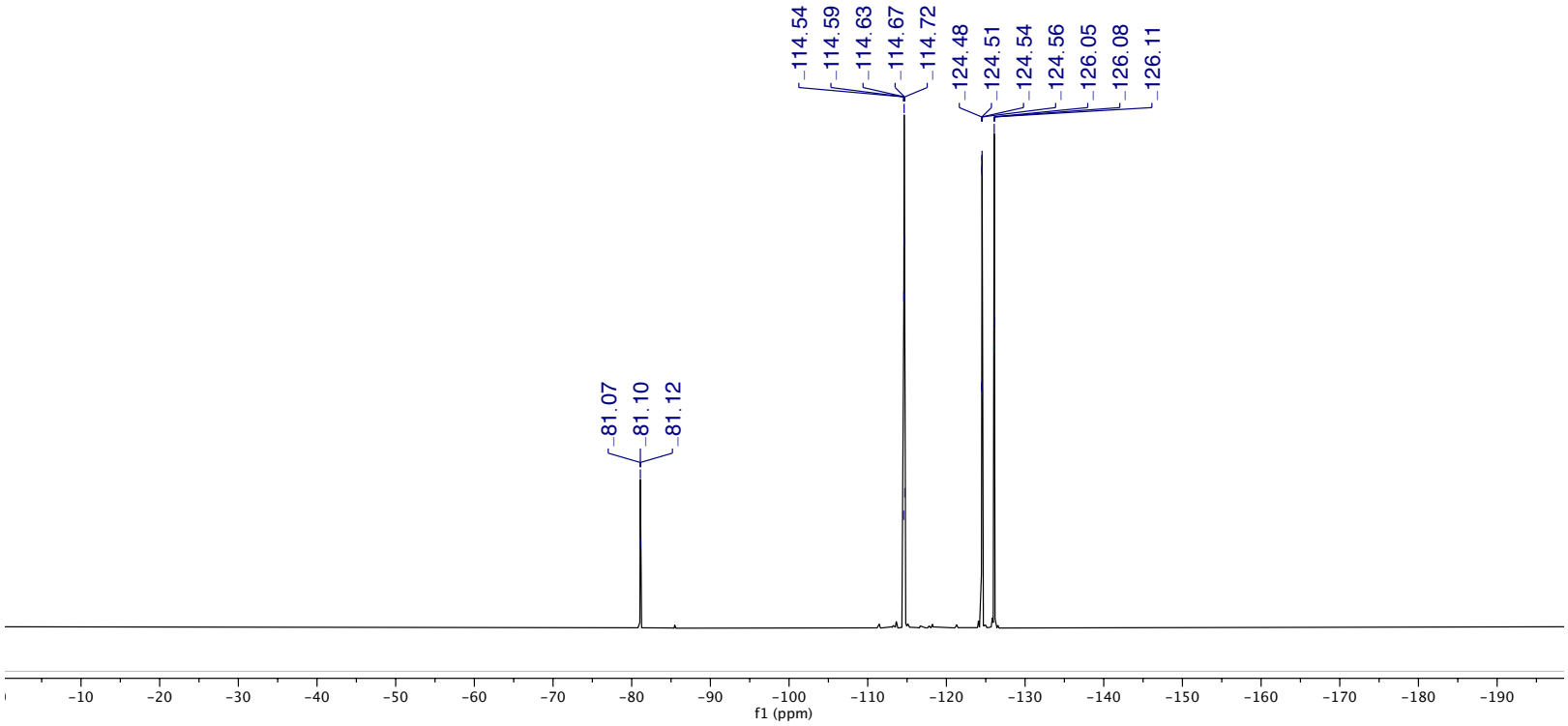
$^{13}$C-NMR (100 MHz, $CDCl_3$)



Ethyl 12,12,13,13,14,14,15,15,15-nonafluoropentadecanoate **(6)**

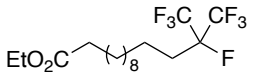


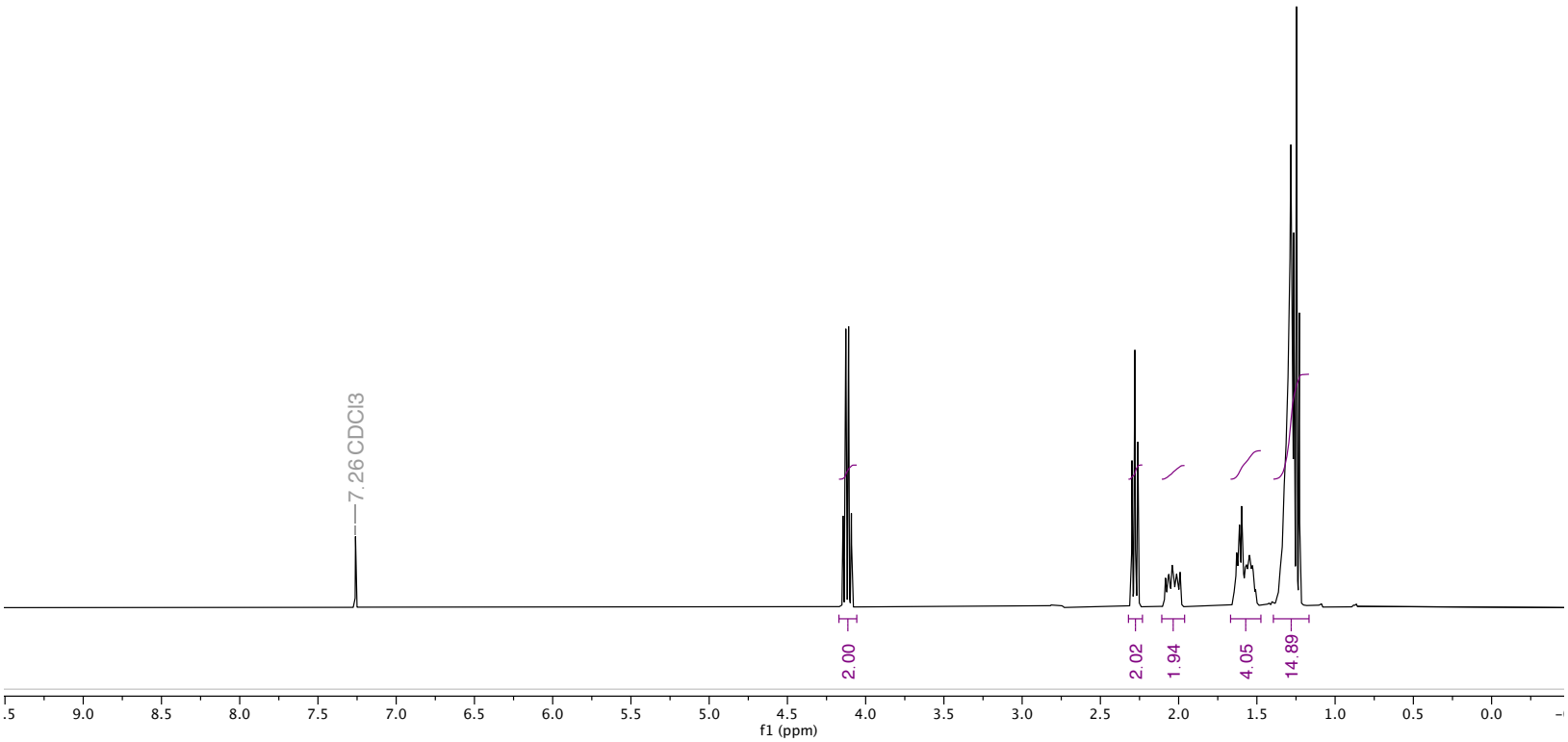

$^{19}$F-NMR (376 MHz, $CDCl_3$)



Ethyl 12,13,13,13-tetrafluoro-12-(trifluoromethyl)tridecanoate **(7)**

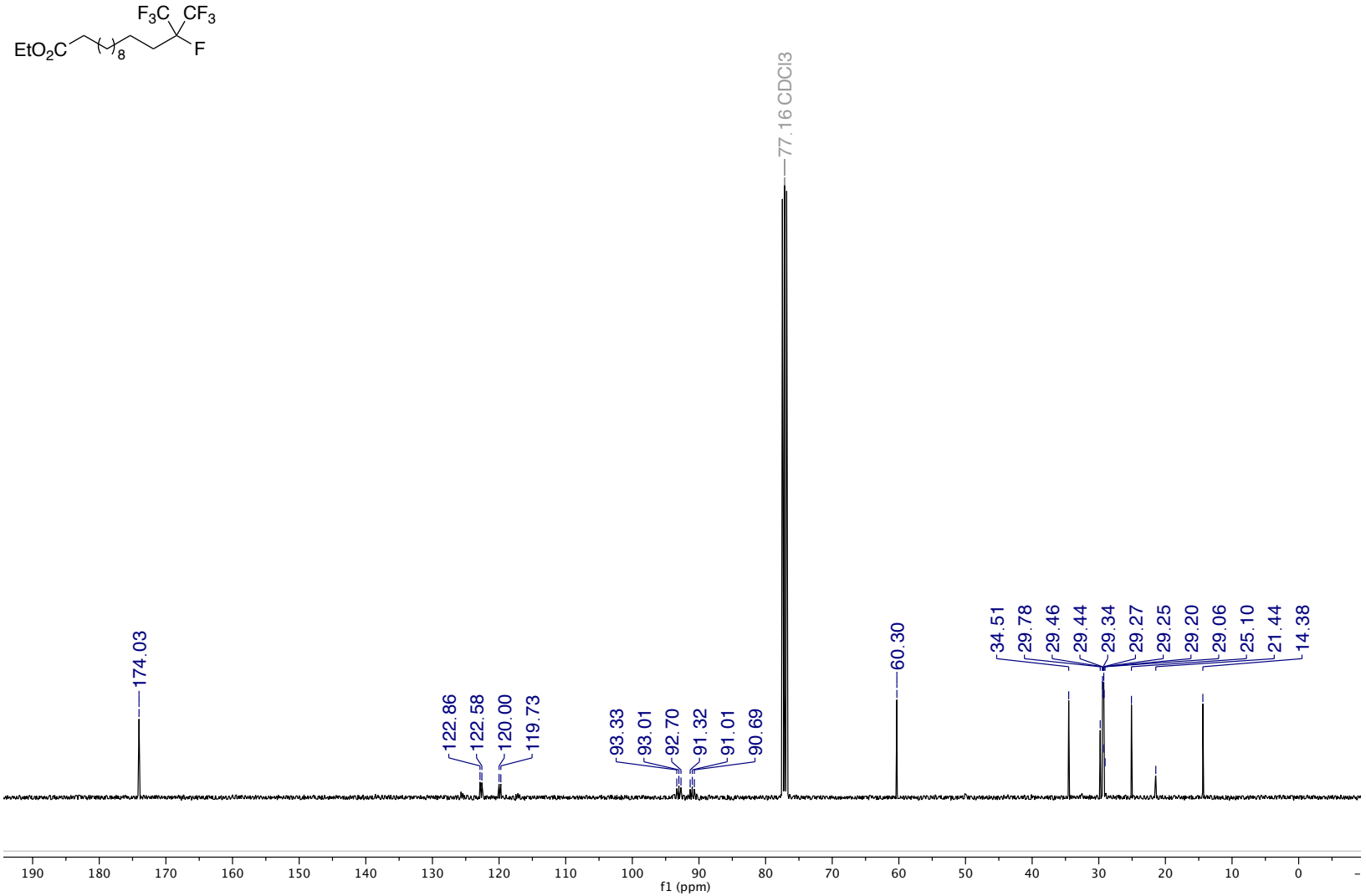
$^1$H-NMR (400 MHz, $CDCl_3$)



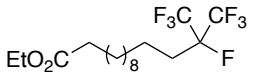



Ethyl 12,13,13,13-tetrafluoro-12-(trifluoromethyl)tridecanoate **(7)**

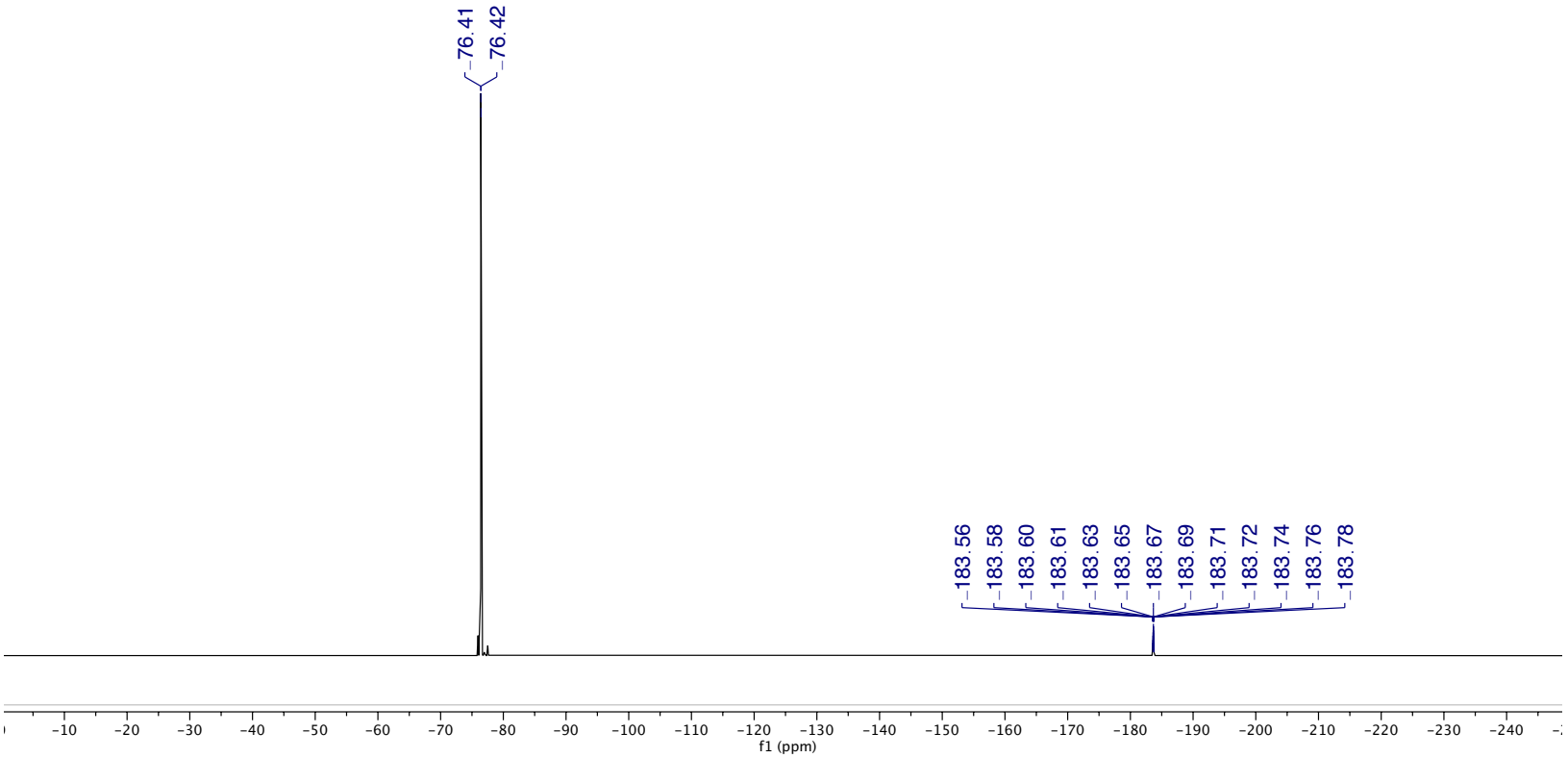
$^{13}$C-NMR (100 MHz, $CDCl_3$)



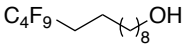
Ethyl 12,13,13,13-tetrafluoro-12-(trifluoromethyl)tridecanoate **(7)**



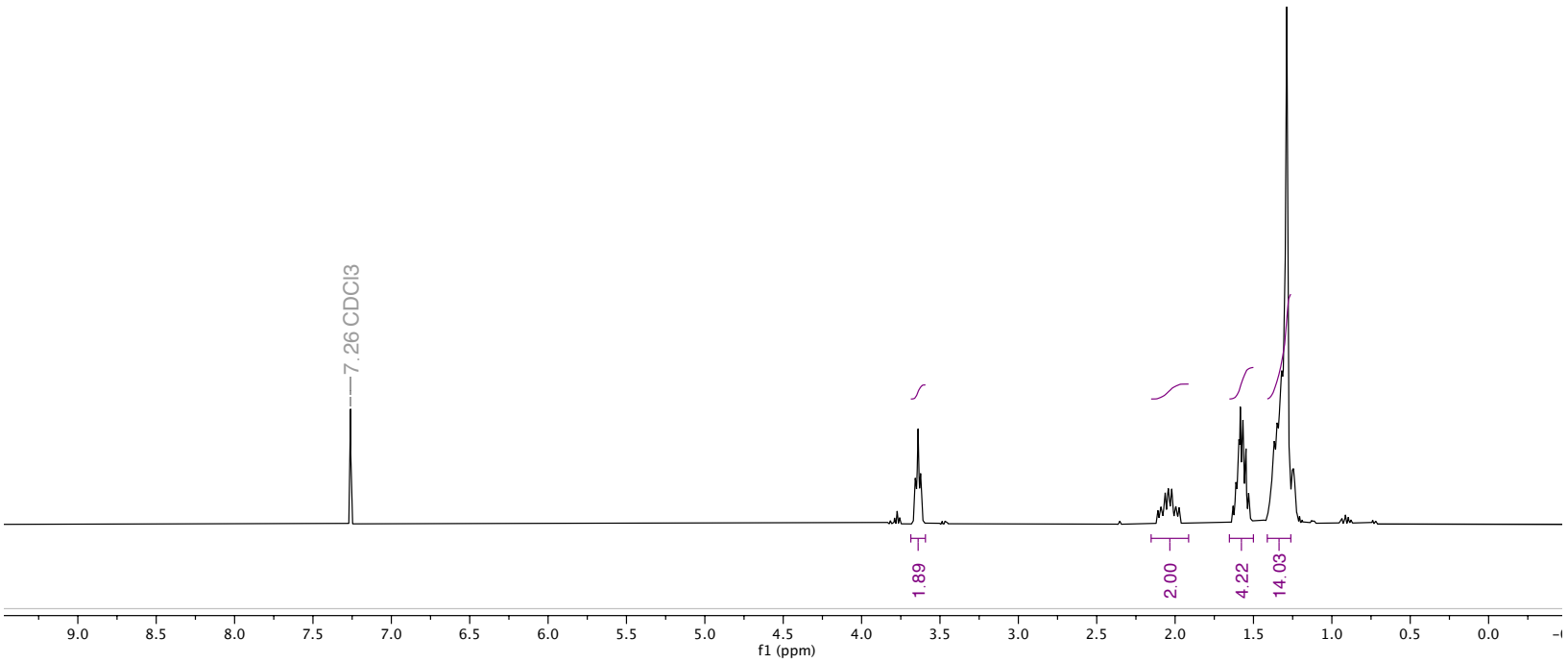

$^{19}$F-NMR (376 MHz, $CDCl_3$)



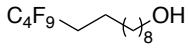
11,11,12,12,13,13,14,14,14-Nonafluorotetradecan-1-ol **(8)**




$^{1}$H-NMR (400 MHz, $CDCl_3$)

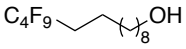


11,11,12,12,13,13,14,14,14-Nonafluorotetradecan-1-ol **(8)**

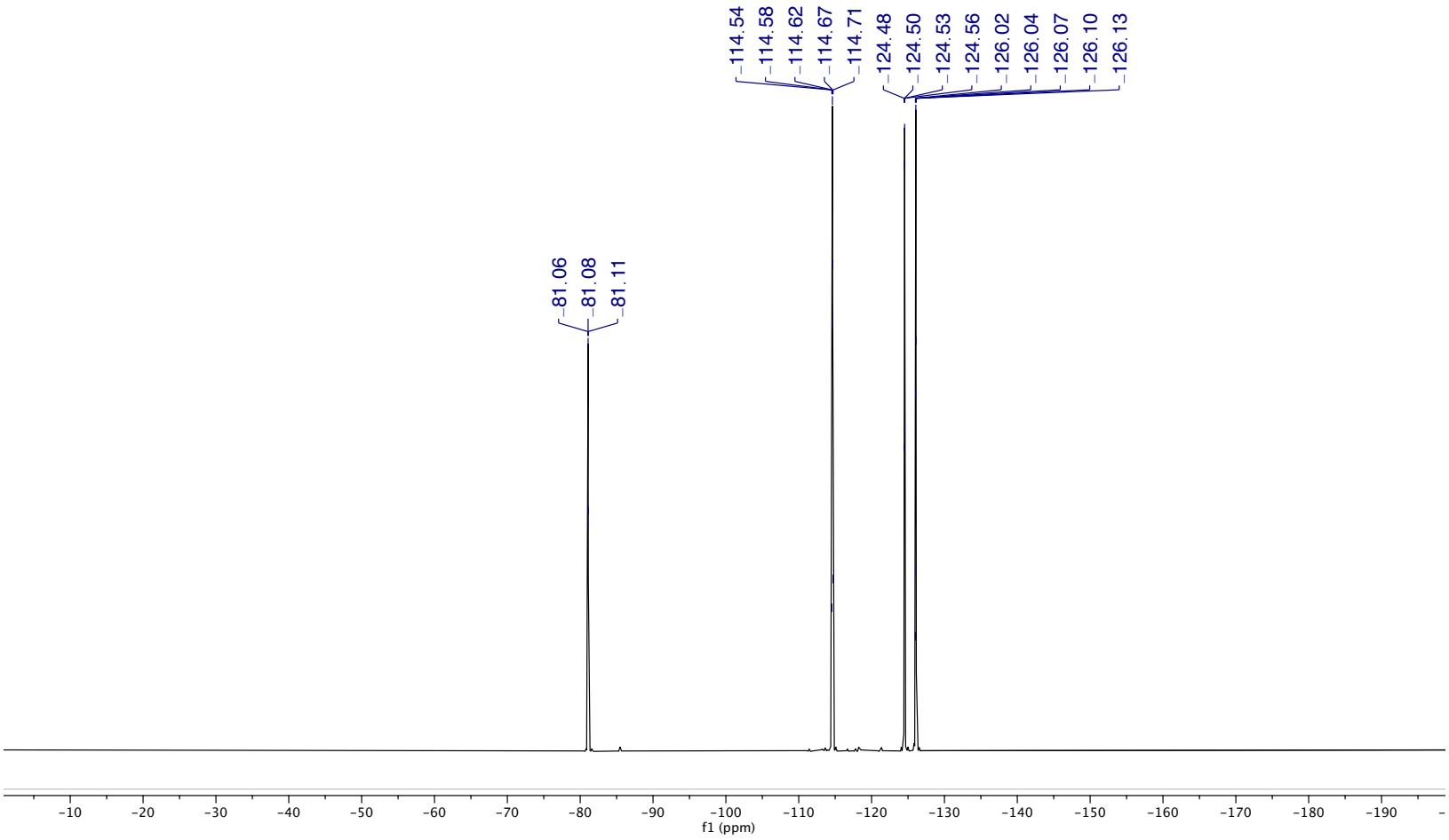



$^{13}$C-NMR (100 MHz, $CDCl_3$)

11,11,12,12,13,13,14,14,14-Nonafluorotetradecan-1-ol **(8)**

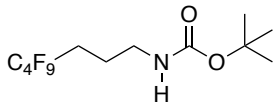


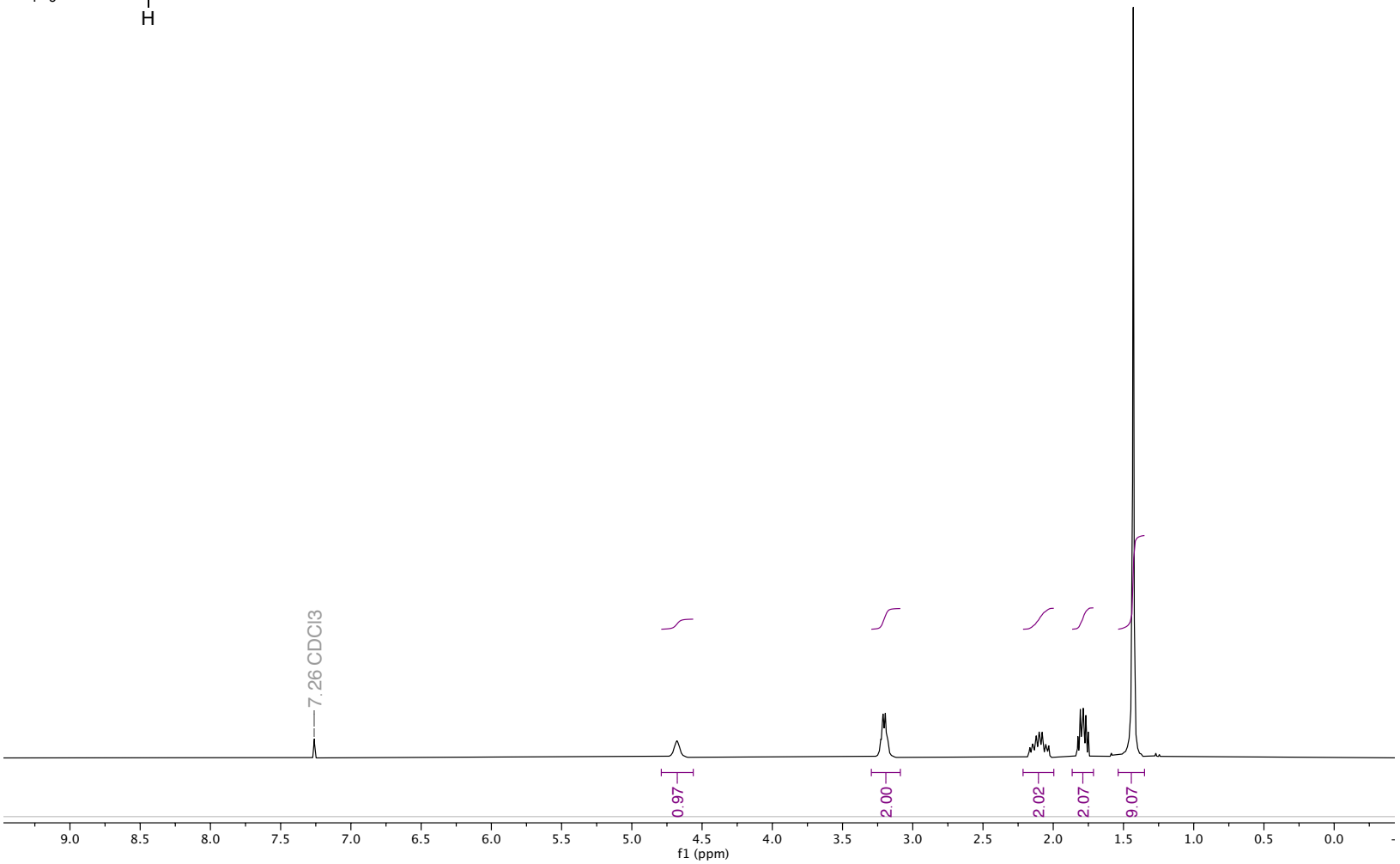

$^{19}$F-NMR (376 MHz, $CDCl_3$)



*Tert*-butyl (4,4,5,5,6,6,7,7,7-nonafluoroheptyl)carbamate **(9)**

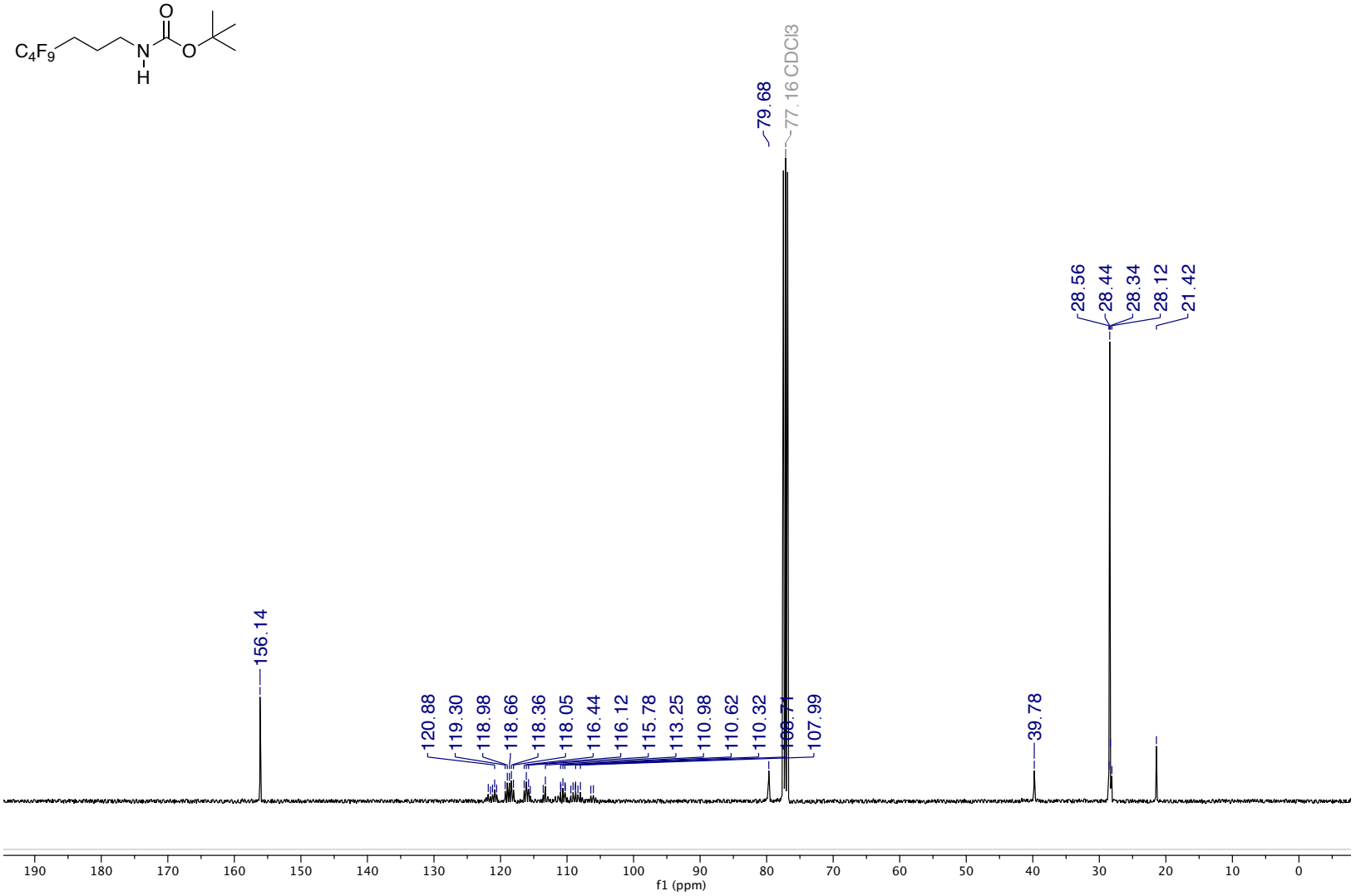
$^1$H-NMR (400 MHz, $CDCl_3$)



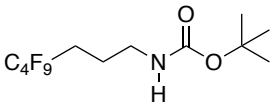



*Tert*-butyl (4,4,5,5,6,6,7,7,7-nonafluoroheptyl)carbamate **(9)**

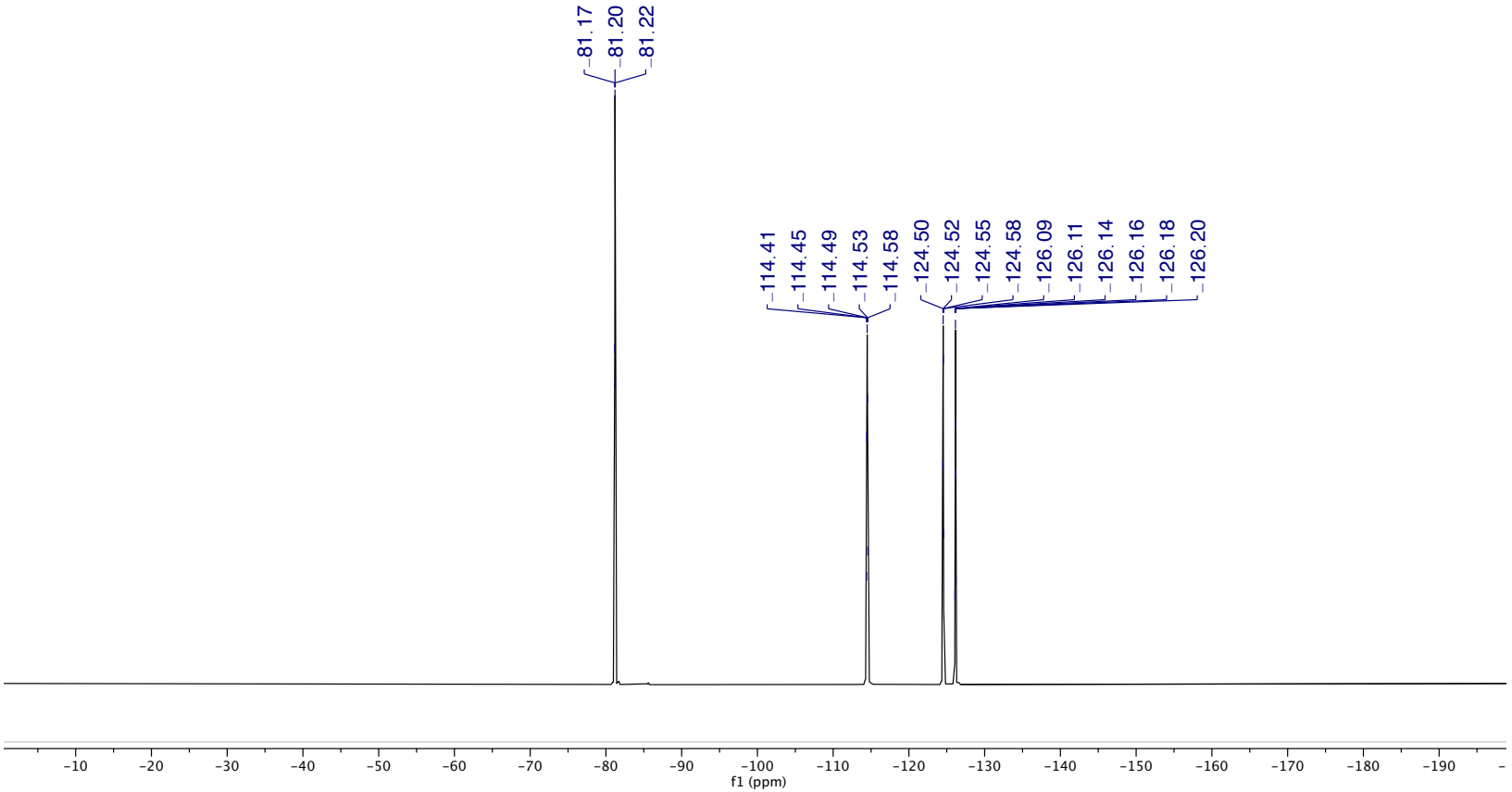
$^{13}$C-NMR (100 MHz, $CDCl_3$)



*Tert*-butyl (4,4,5,5,6,6,7,7,7-nonafluoroheptyl)carbamate **(9)**

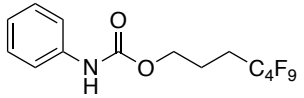


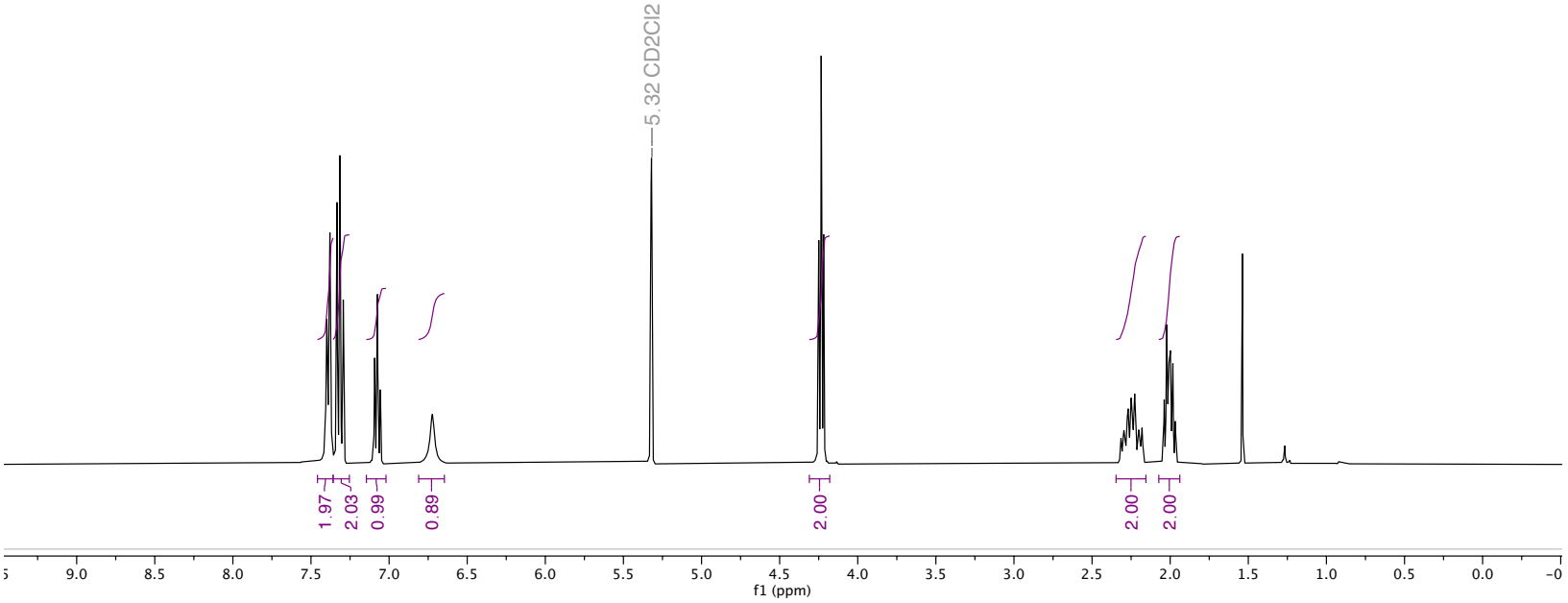

$^{19}$F-NMR (376 MHz, $CDCl_3$)



7,7,7,7,7,7,7,7,7-Nonafluoro-7λ12-hepta-4,6-diyn-1-yl phenylcarbamate **(10)**

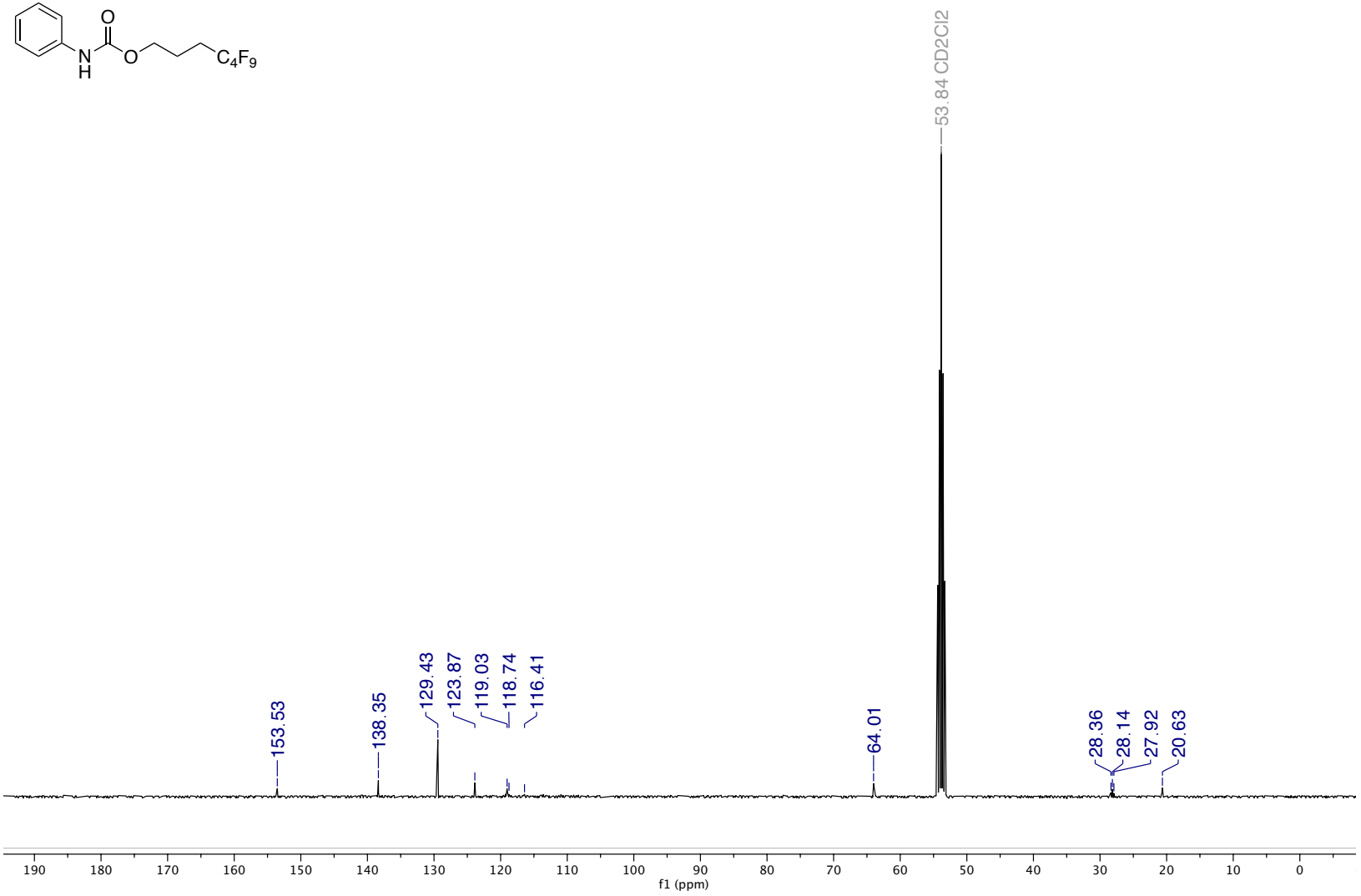
$^{1}$H-NMR (400 MHz, $CDCl_3$)



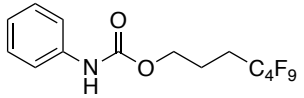
7,7,7,7,7,7,7,7,7-Nonafluoro-7λ12-hepta-4,6-diyn-1-yl phenylcarbamate **(10)**

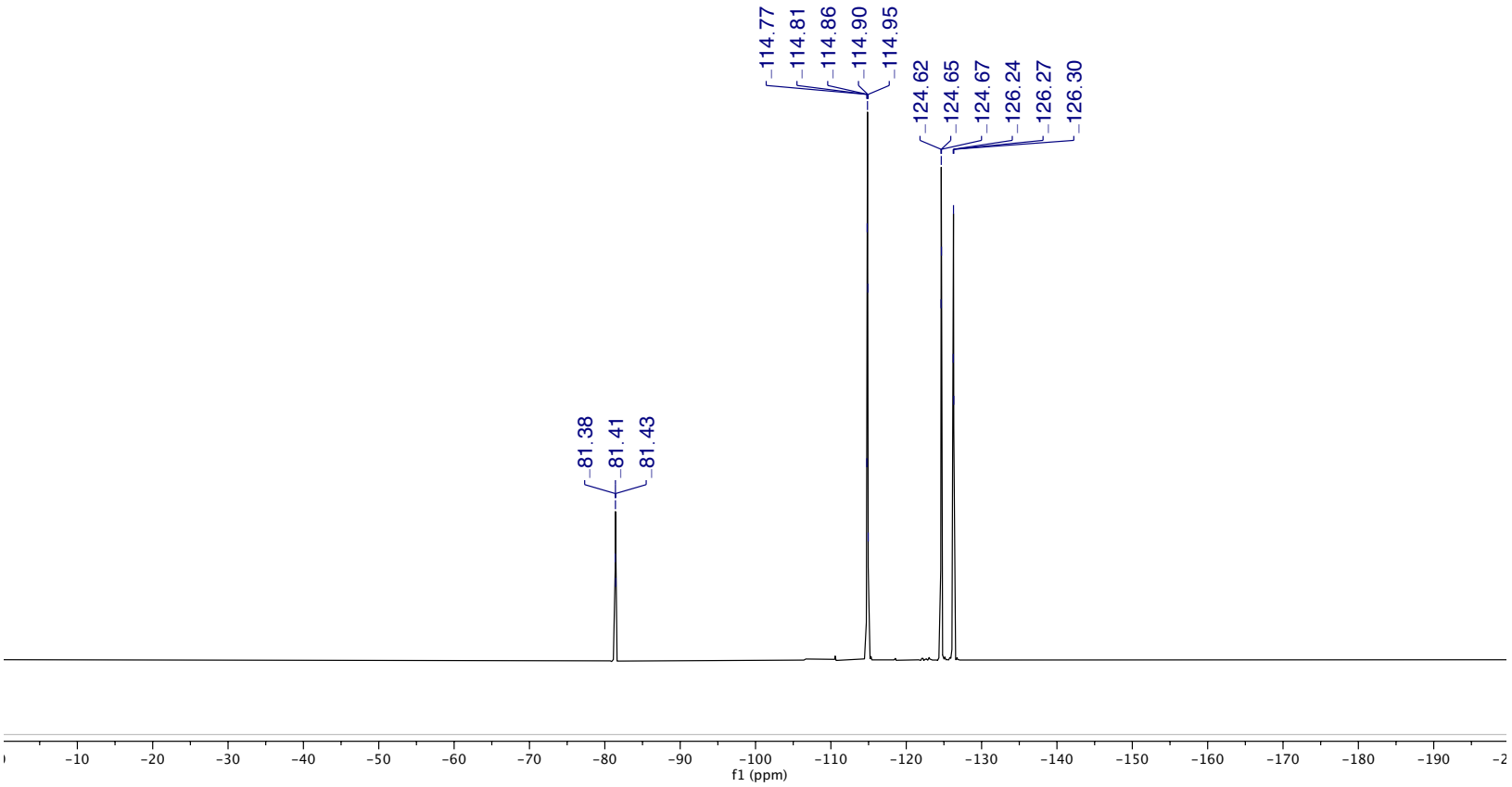
$^{13}$C-NMR (100 MHz, $CDCl_3$)



7,7,7,7,7,7,7,7,7-Nonafluoro-7λ12-hepta-4,6-diyn-1-yl phenylcarbamate **(10)**

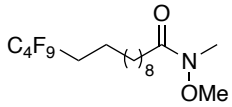
$^{19}$F-NMR (376 MHz, $CDCl_3$)

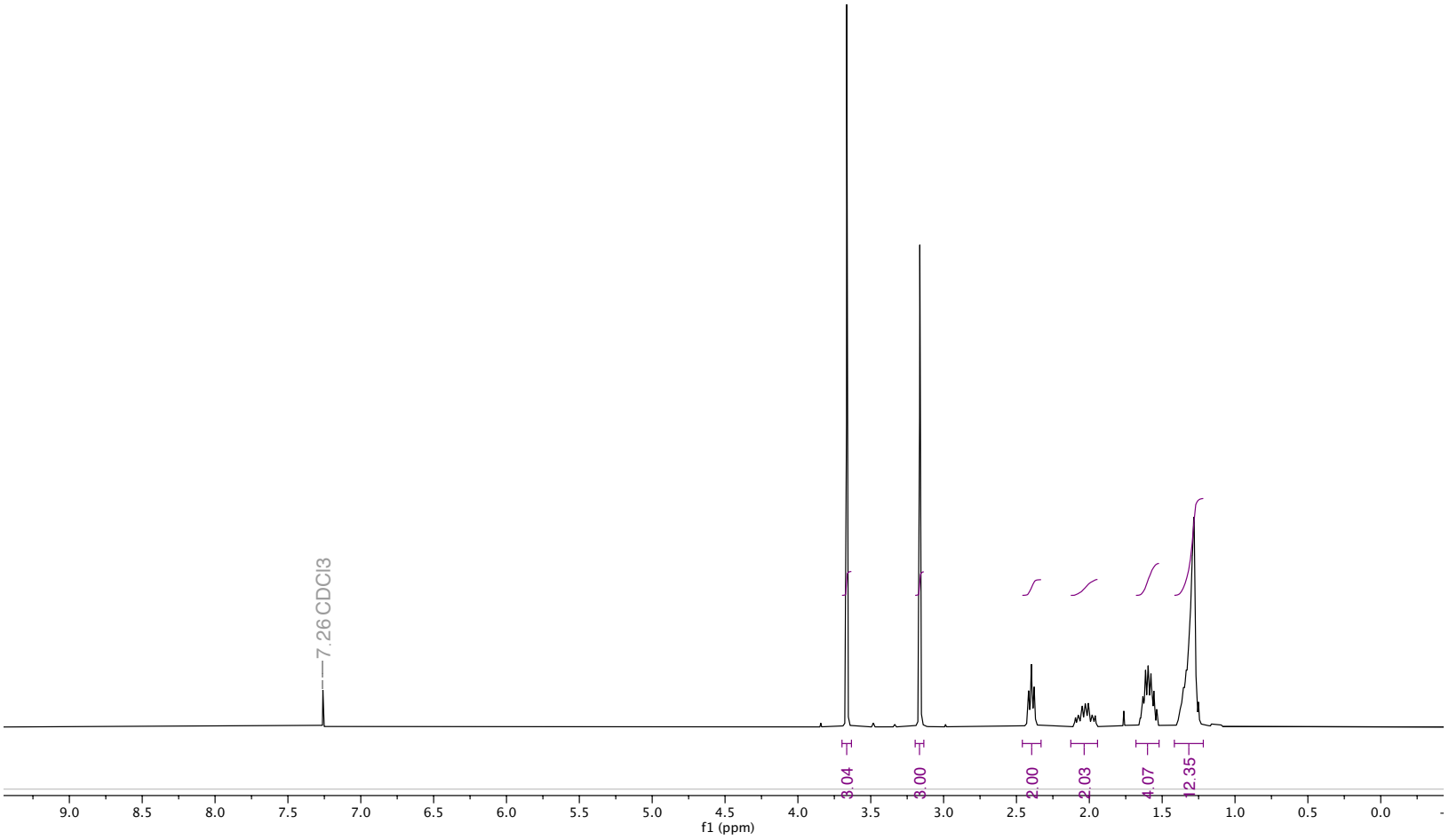


12,12,13,13,14,14,15,15,15-Nonafluoro-*N*-methoxy-*N*-methylpentadecanamide **(11)**

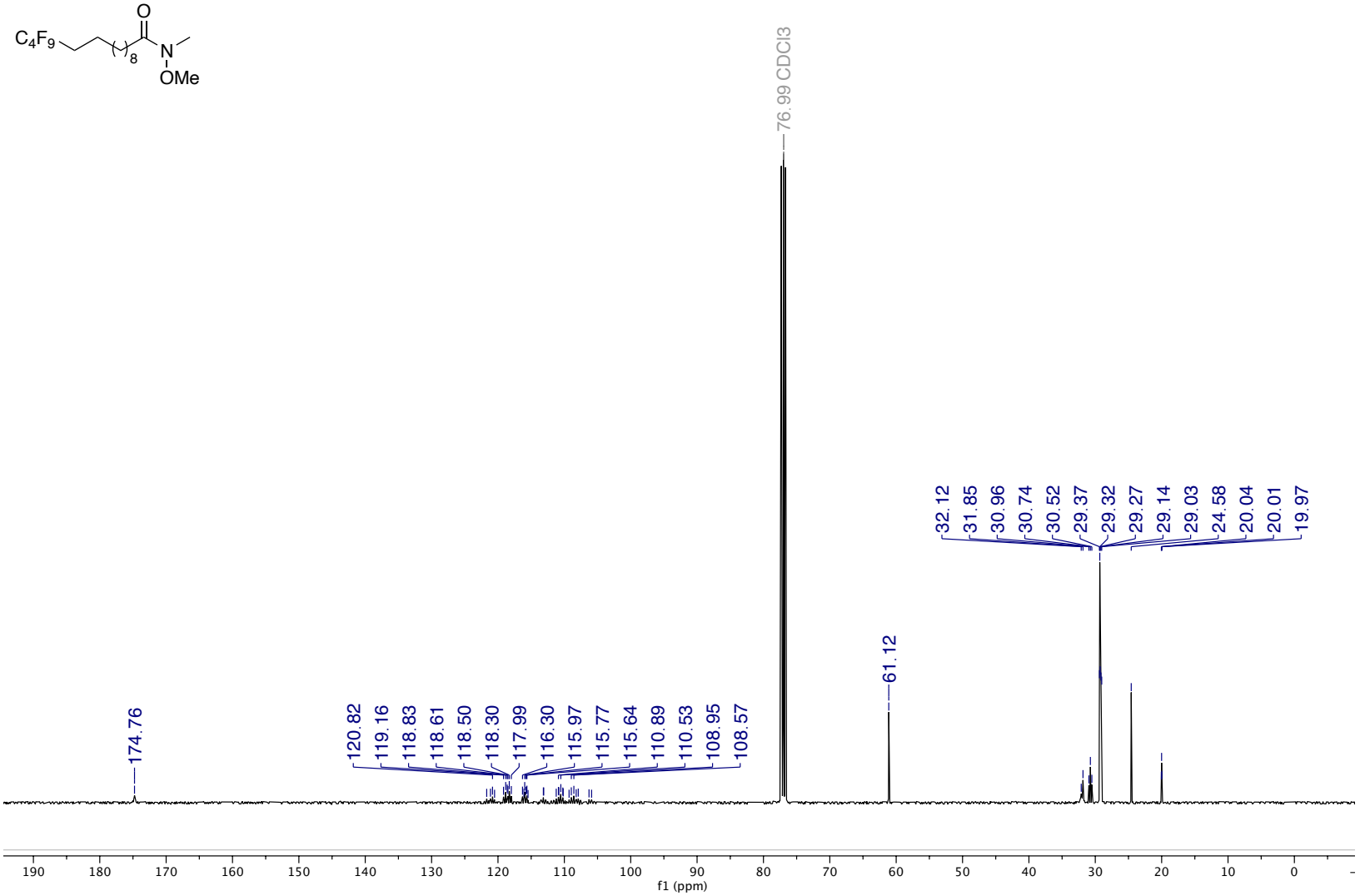
$^1$H-NMR (400 MHz, $CDCl_3$)



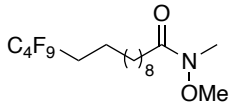
12,12,13,13,14,14,15,15,15-Nonafluoro-*N*-methoxy-*N*-methylpentadecanamide **(11)**

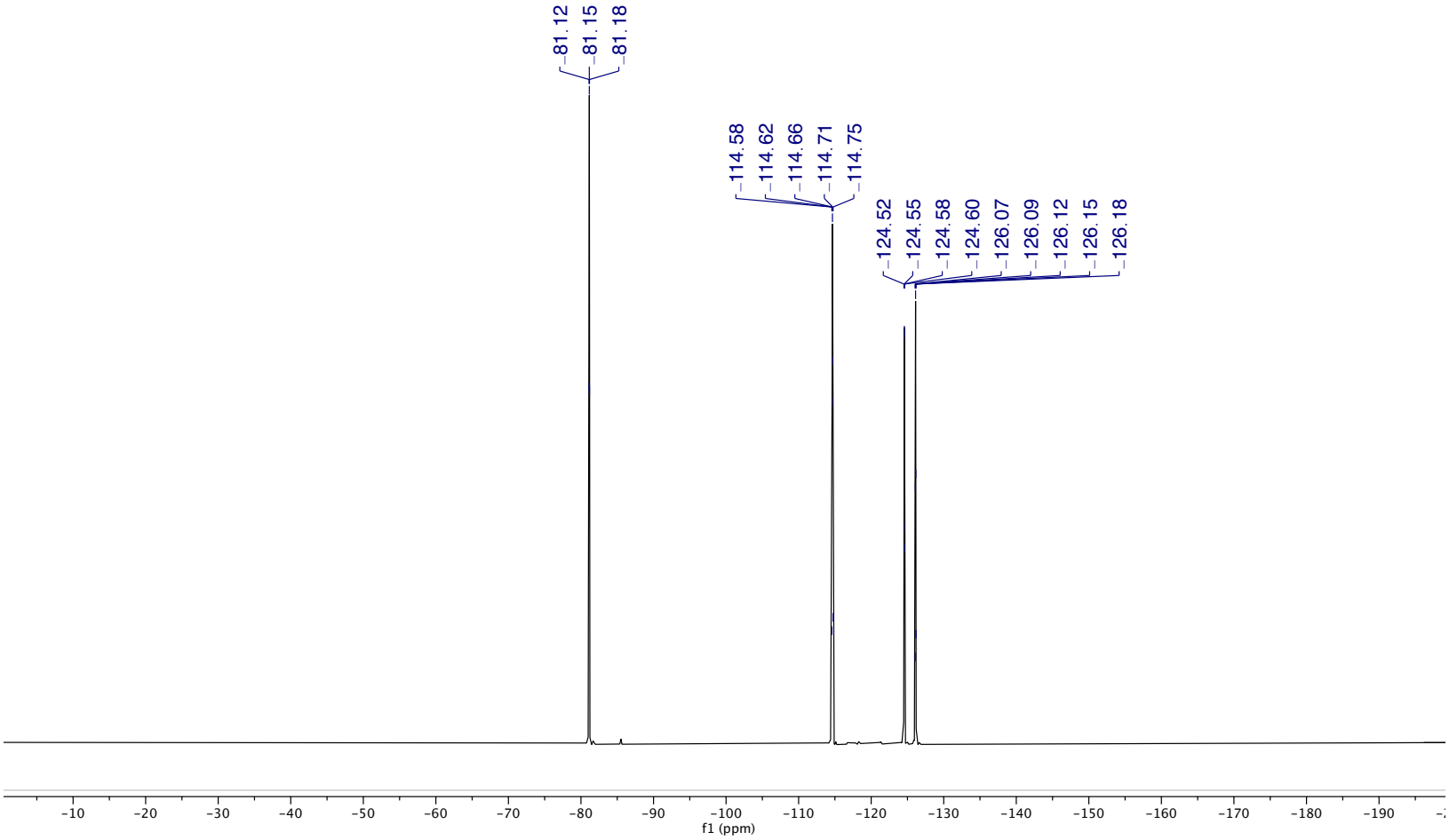
$^{13}$C-NMR (100 MHz, $CDCl_3$)



12,12,13,13,14,14,15,15,15-Nonafluoro-*N*-methoxy-*N*-methylpentadecanamide **(11)**

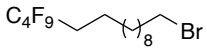
$^{19}$F-NMR (376 MHz, $CDCl_3$)

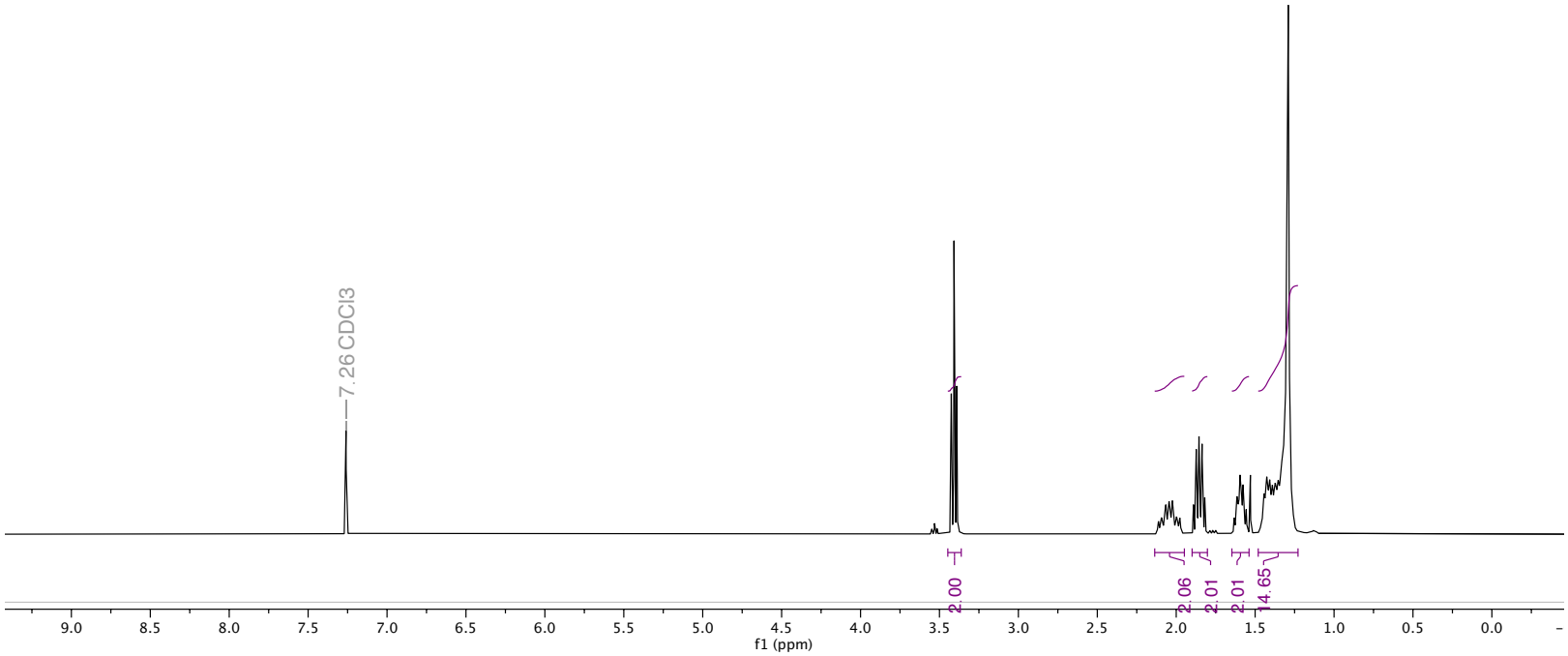


15-Bromo-1,1,1,2,2,3,3,4,4-nonafluoropentadecane **(12)**

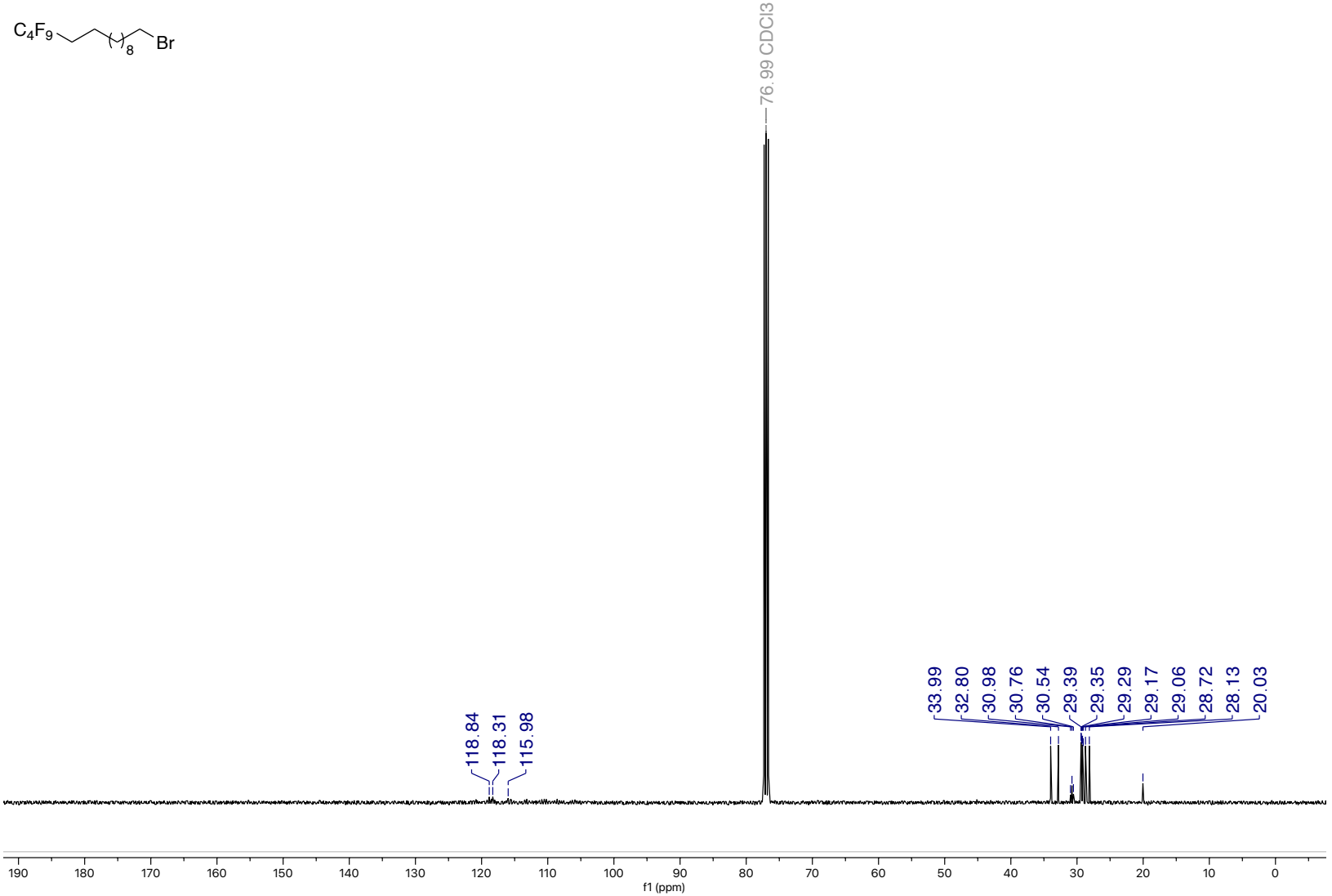
$^1$H-NMR (400 MHz, $CDCl_3$)



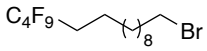



15-Bromo-1,1,1,2,2,3,3,4,4-nonafluoropentadecane **(12)**

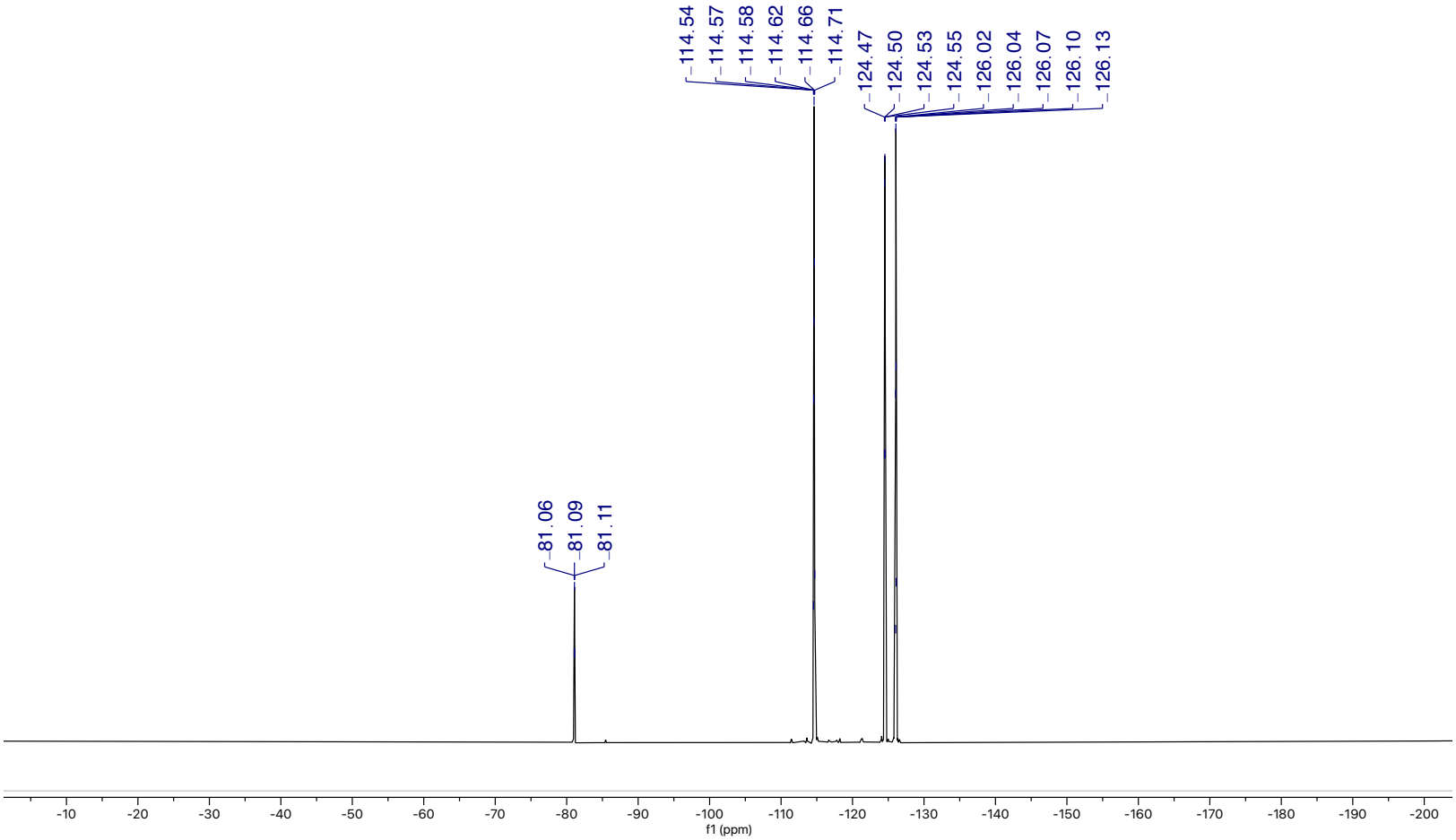
$^{13}$C-NMR (100 MHz, $CDCl_3$)



15-Bromo-1,1,1,2,2,3,3,4,4-nonafluoropentadecane **(12)**

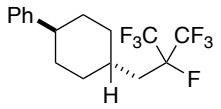


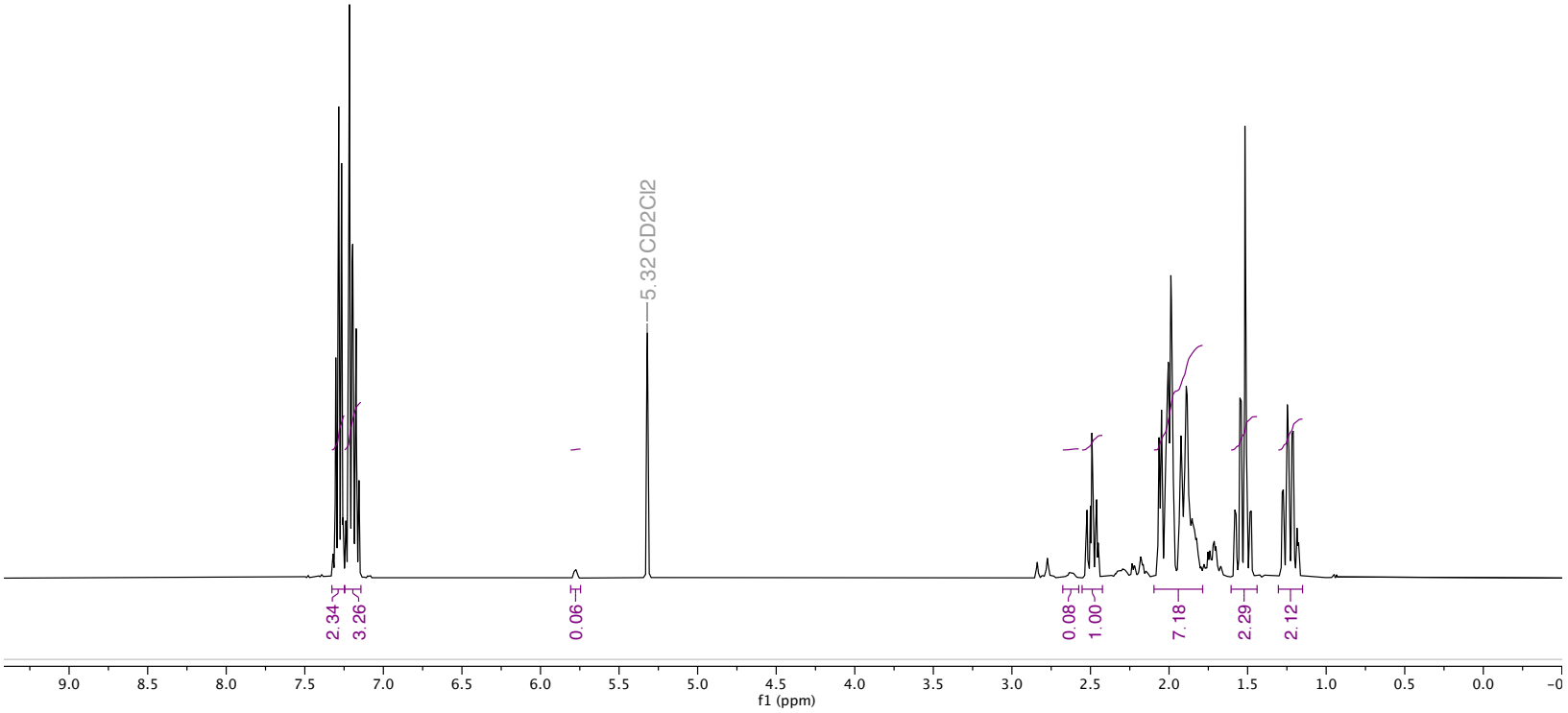

$^{19}$F-NMR (376 MHz, $CDCl_3$)



((1*R*,4*R*)-4-(2,3,3,3-tetrafluoro-2-(trifluoromethyl)propyl)cyclohexyl)benzene **(13)**

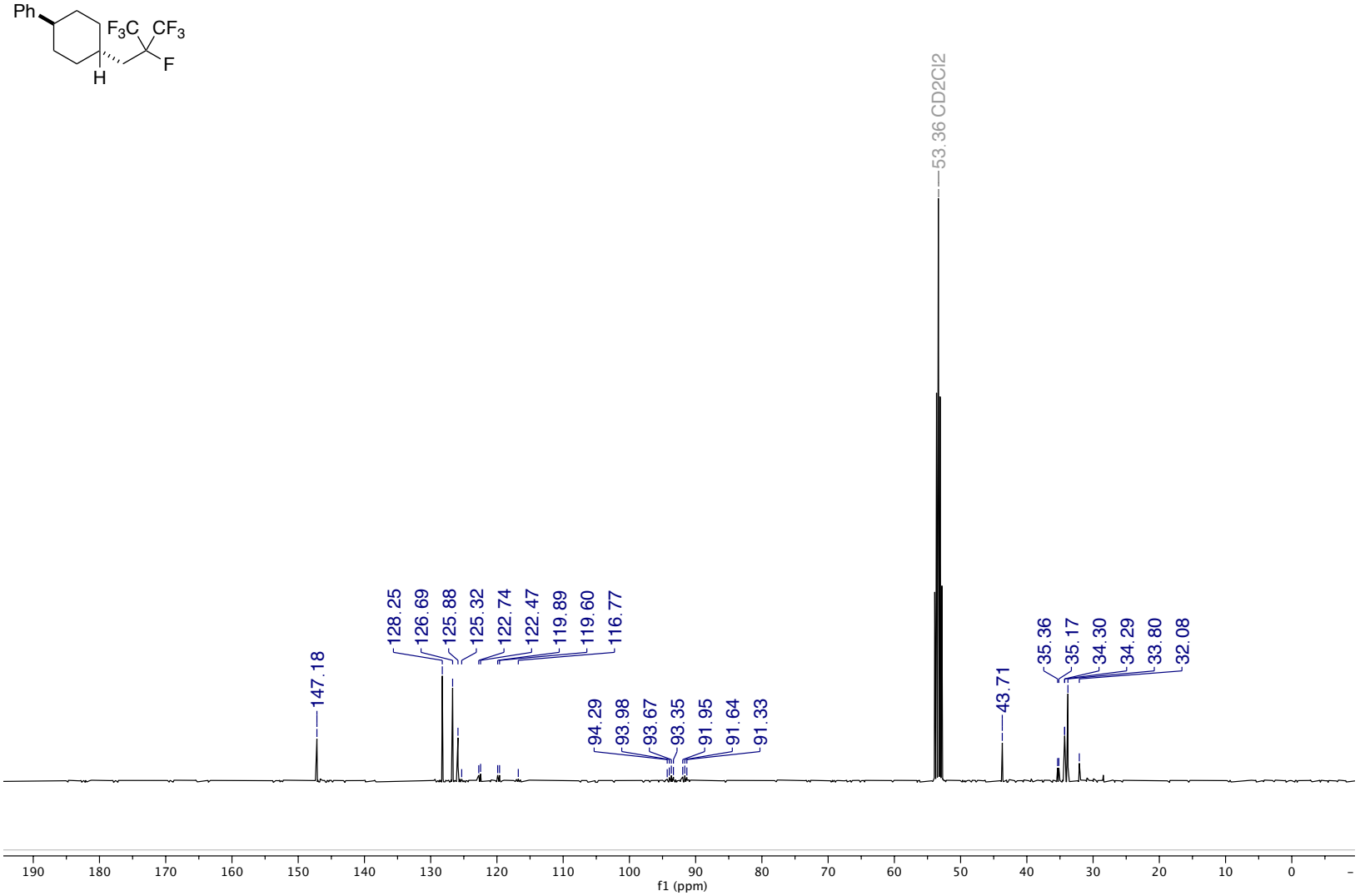
$^{1}$H-NMR (400 MHz, $CD_2Cl_2$)



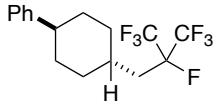
((1*R*,4*R*)-4-(2,3,3,3-tetrafluoro-2-(trifluoromethyl)propyl)cyclohexyl)benzene **(13)**

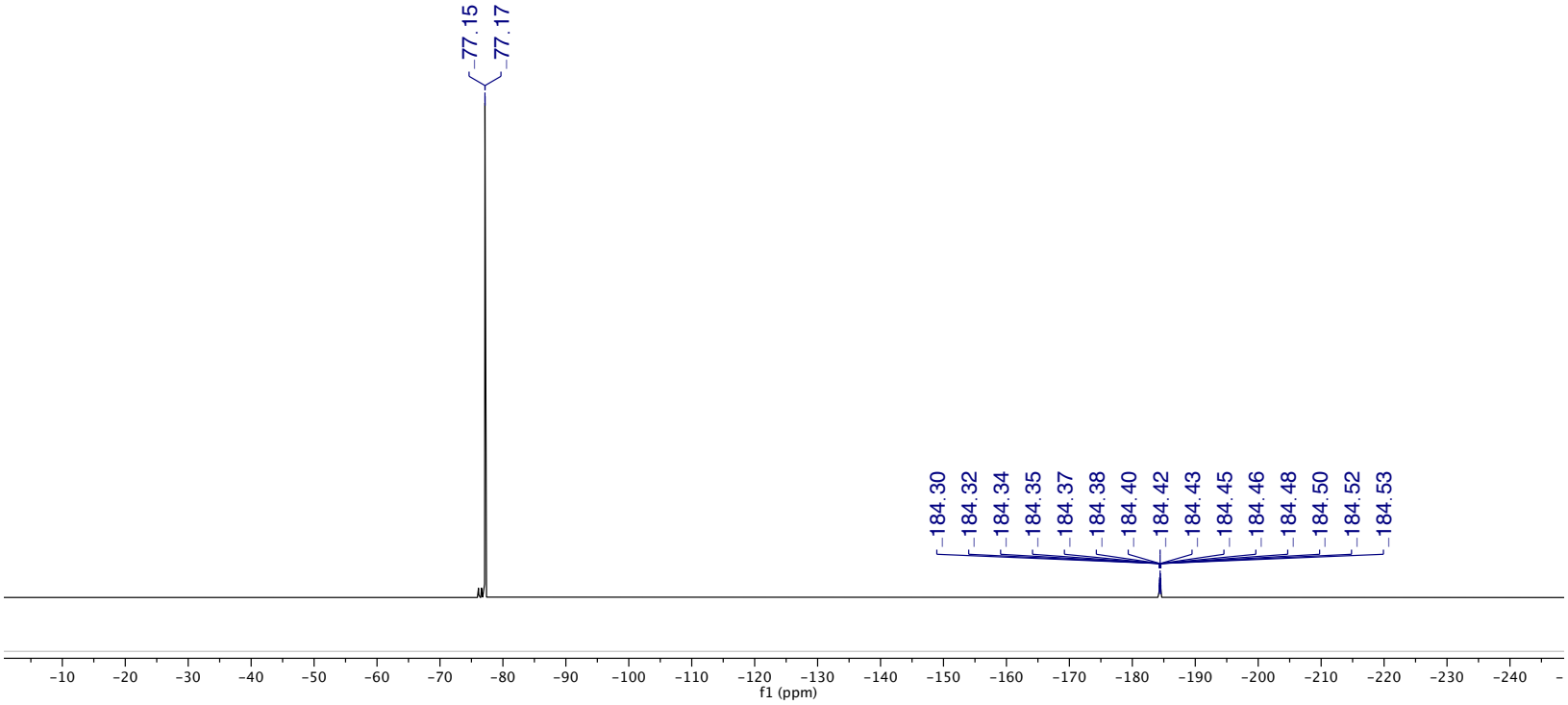
$^{13}$C-NMR (100 MHz, $CD_2Cl_2$)



((1*R*,4*R*)-4-(2,3,3,3-tetrafluoro-2-(trifluoromethyl)propyl)cyclohexyl)benzene **(13)**

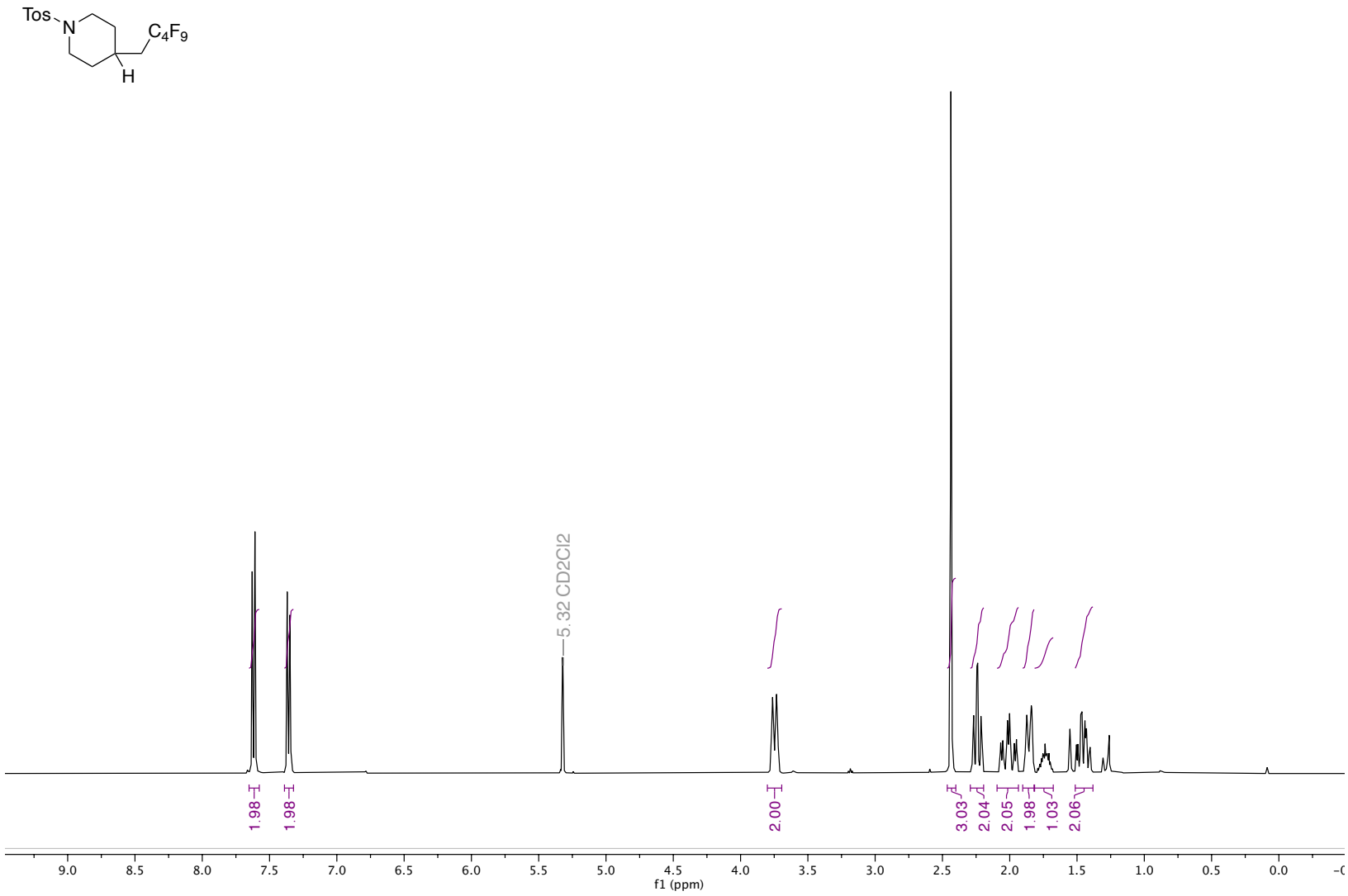
$^{19}$F-NMR (376 MHz, $CD_2Cl_2$)



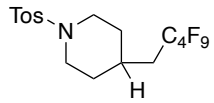



4-(2,2,3,3,4,4,5,5,5-Nonafluoropentyl)-1-tosylpiperidine **(14)**

$^1$H-NMR (400 MHz, $CD_2Cl_2$)



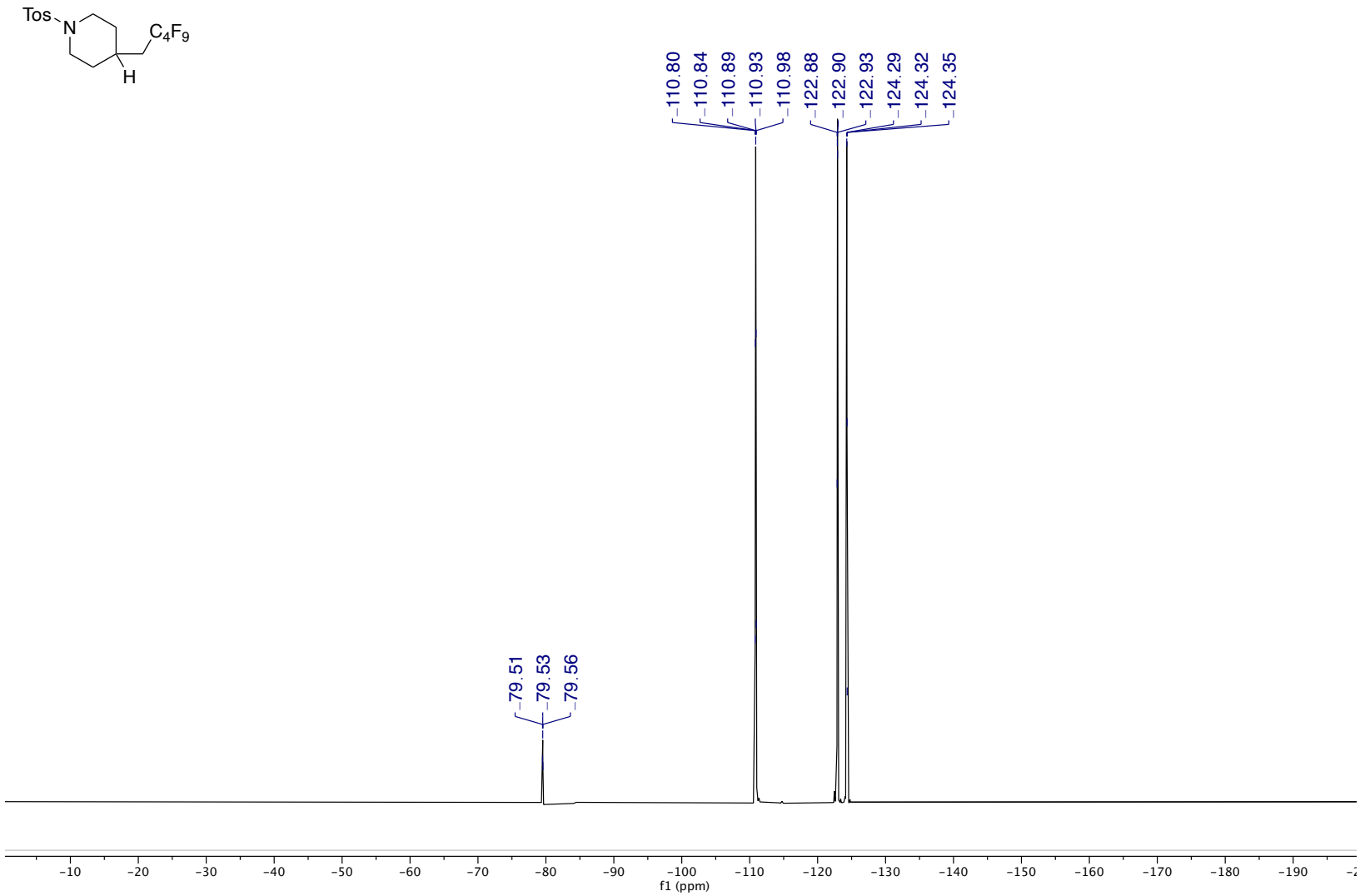
4-(2,2,3,3,4,4,5,5,5-Nonafluoropentyl)-1-tosylpiperidine **(14)**



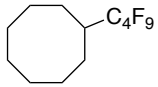

$^{13}$C-NMR (100 MHz, $CD_2Cl_2$)

4-(2,2,3,3,4,4,5,5,5-Nonafluoropentyl)-1-tosylpiperidine **(14)**

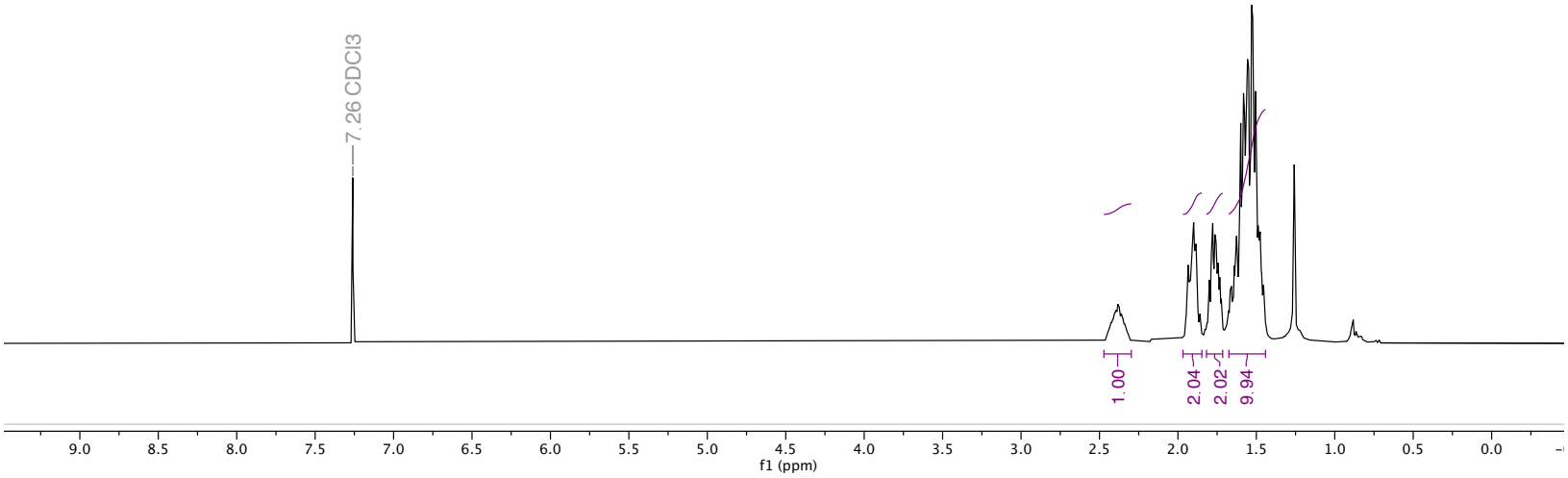
$^{19}$F-NMR (376 MHz, $CD_2Cl_2$)



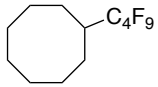
(Perfluorobutyl)cyclooctane **(15)**



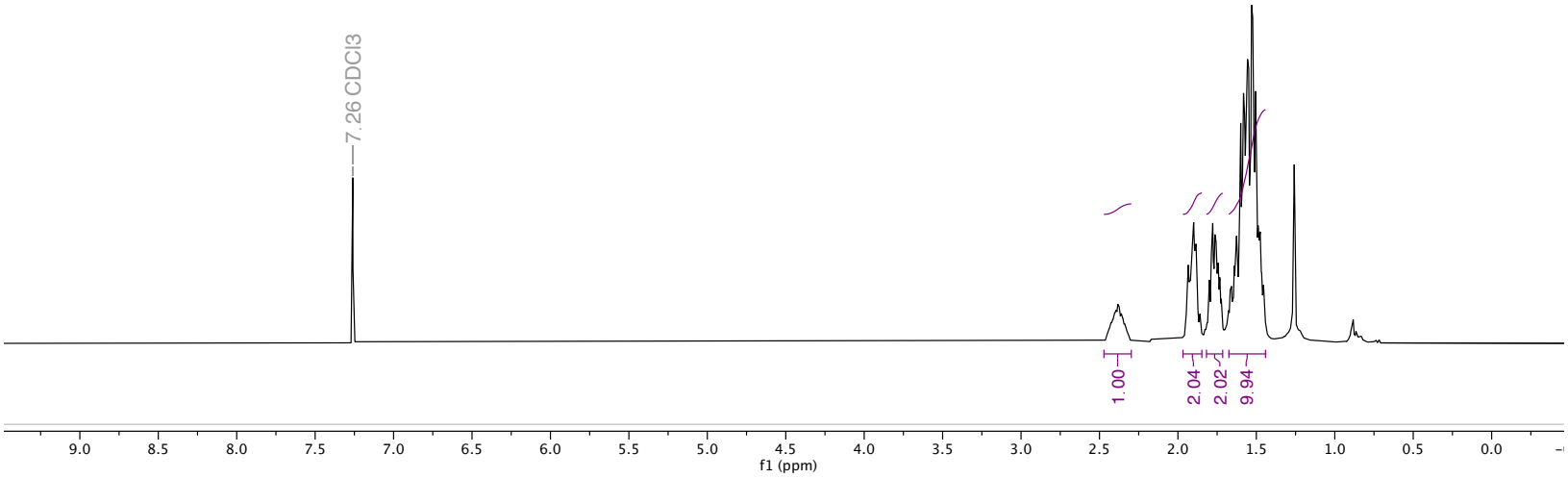

$^1$H-NMR (400 MHz, $CDCl_3$)



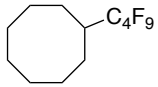
(Perfluorobutyl)cyclooctane **(15)**



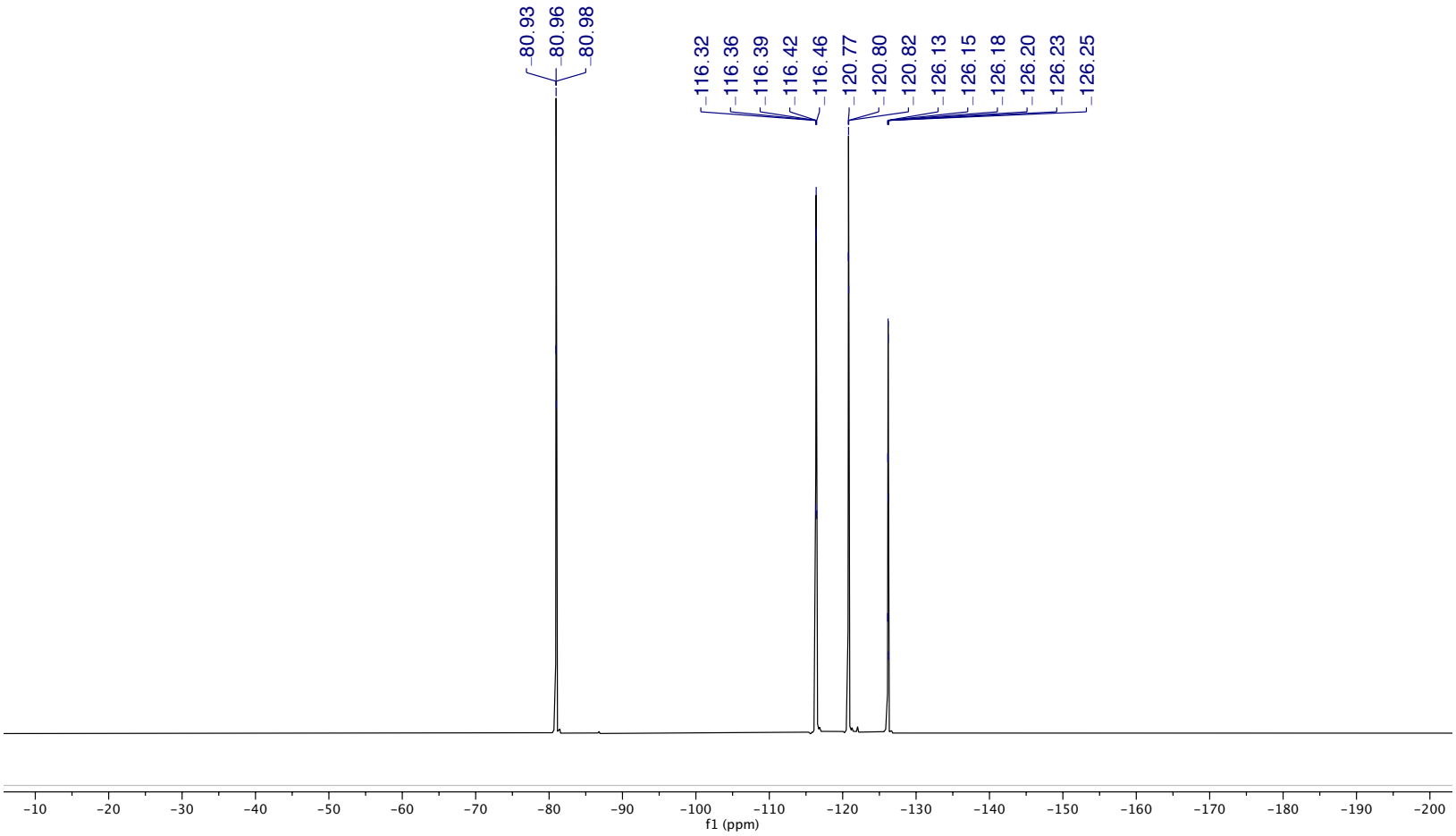

$^1$H-NMR (400 MHz, $CDCl_3$)



(Perfluorobutyl)cyclooctane **(15)**

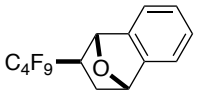


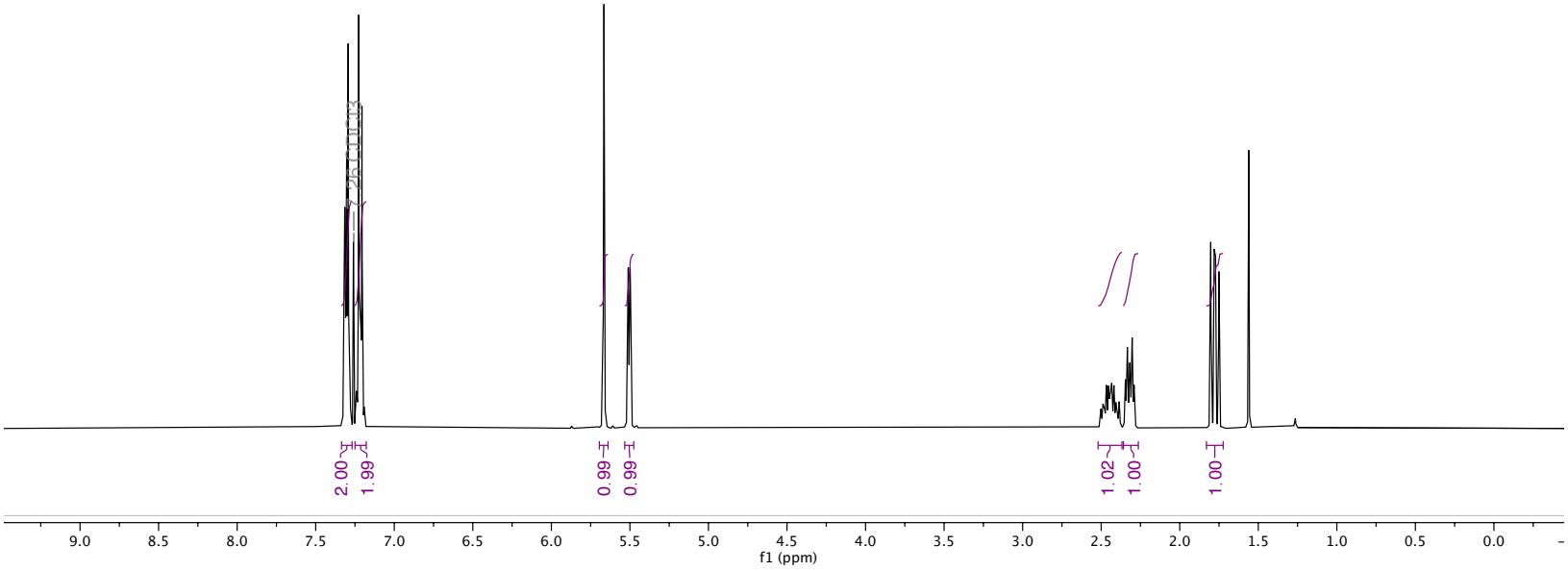

$^{19}$F-NMR (376 MHz, $CDCl_3$)



(1*R*,2*R*,4*S*)-2-(perfluorobutyl)-1,2,3,4-tetrahydro-1,4-epoxynaphthalene **(16)**

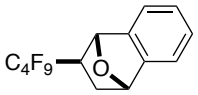
$^1$H-NMR (400 MHz, $CDCl_3$)

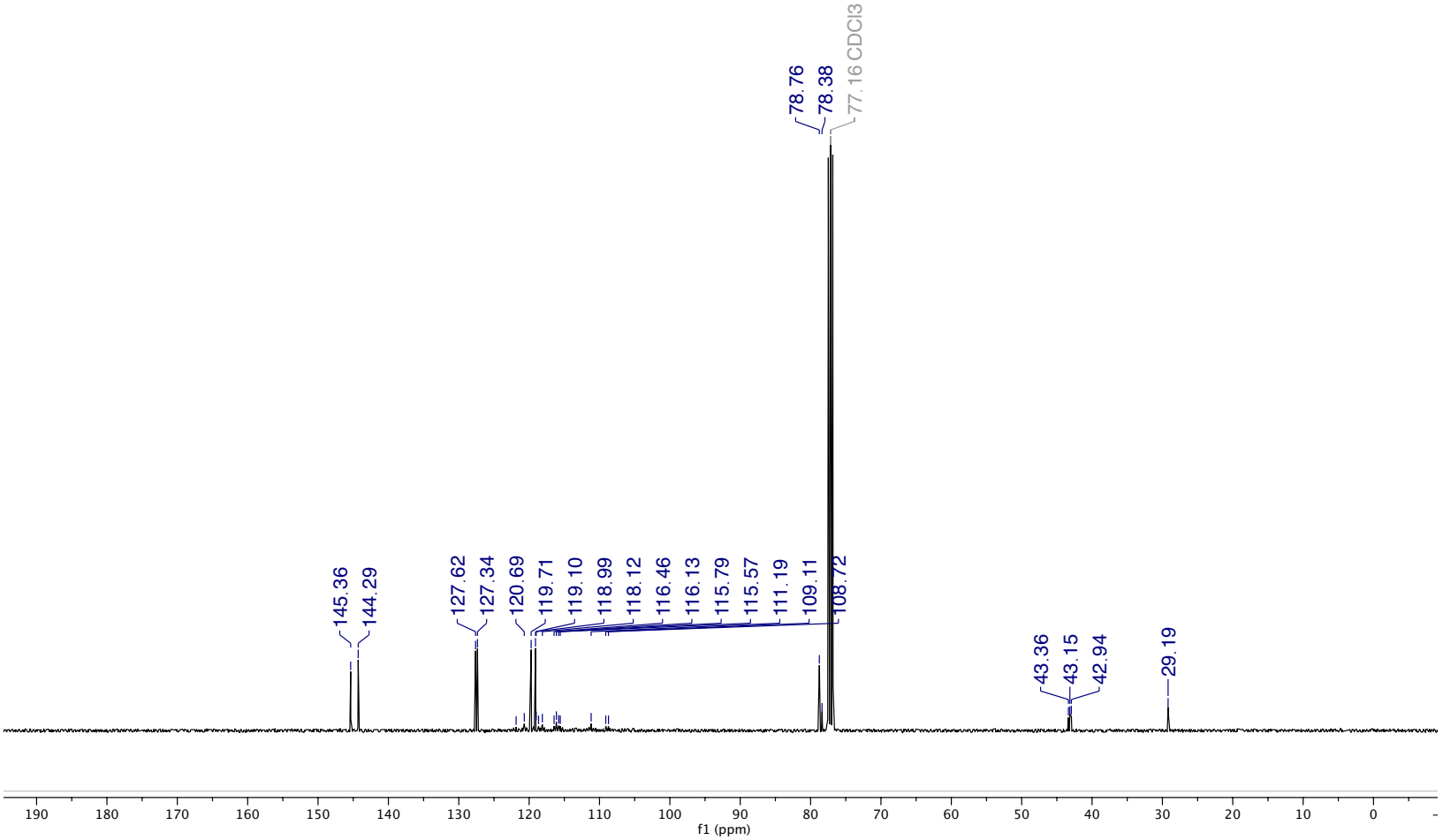


(1*R*,2*R*,4*S*)-2-(perfluorobutyl)-1,2,3,4-tetrahydro-1,4-epoxynaphthalene **(16)**

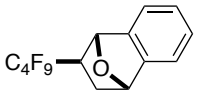
$^{13}$C-NMR (100 MHz, $CDCl_3$)

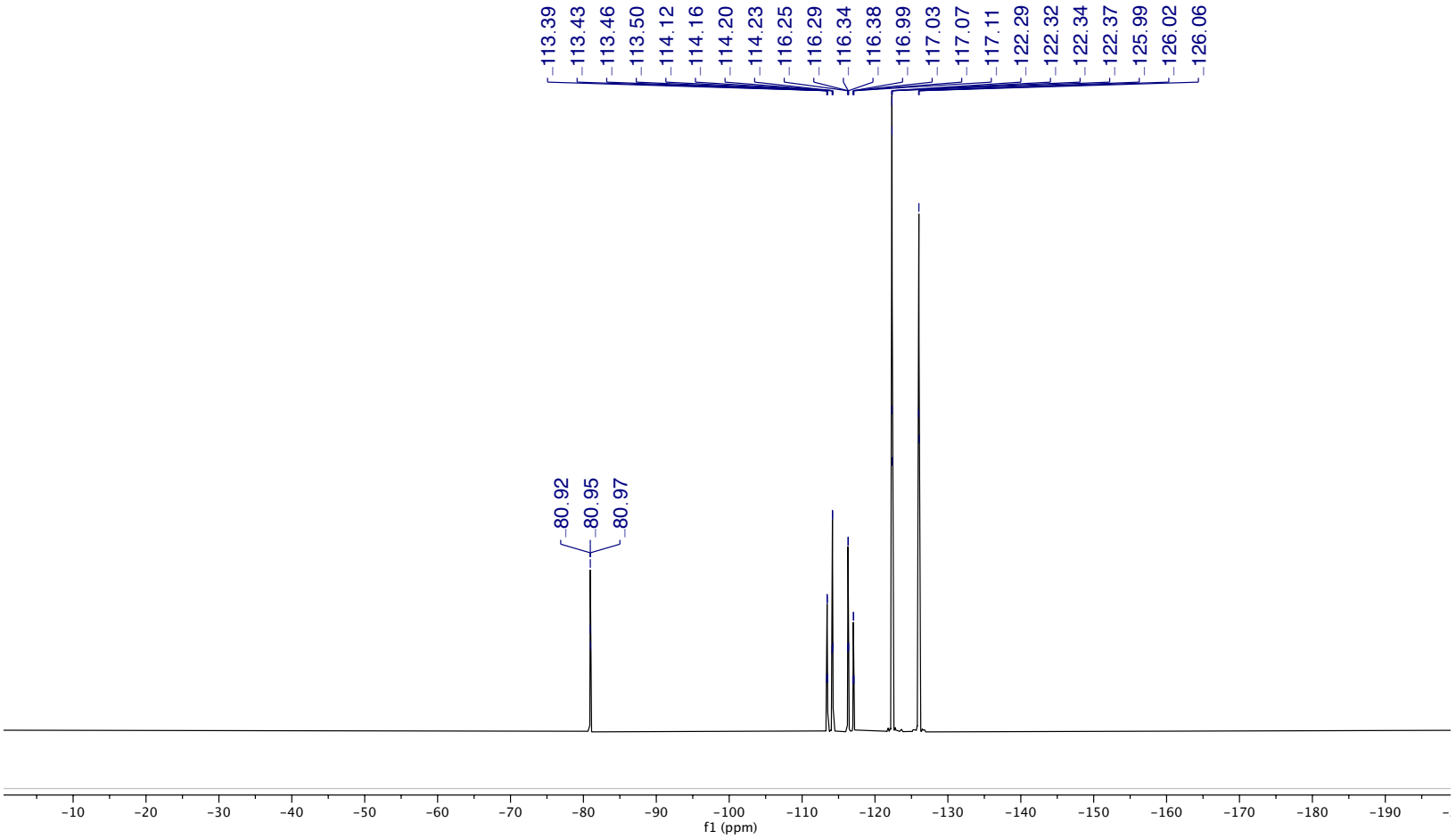


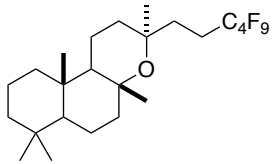
(1*R*,2*R*,4*S*)-2-(perfluorobutyl)-1,2,3,4-tetrahydro-1,4-epoxynaphthalene **(16)**

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

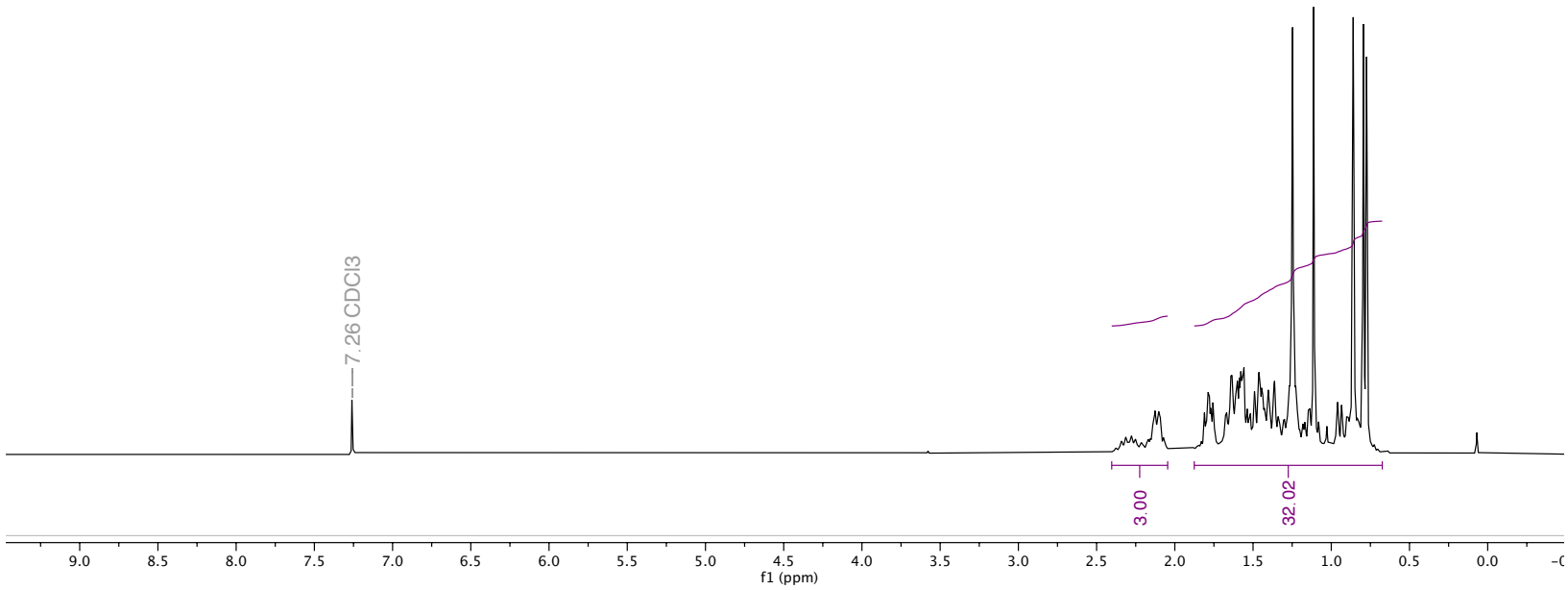


(3*S*,4a*R*,10a*S*)-3,4a,7,7,10a-pentamethyl-3-(3,3,4,4,5,5,6,6,6-nonafluorohexyl)dodecahydro-1*H*-benzo[*f*]chromene **(17)**

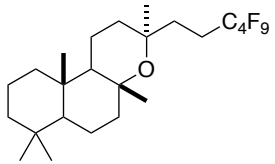



$^1$H-NMR (400 MHz, $CDCl_3$)



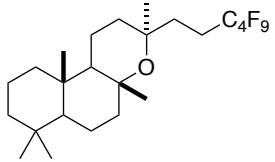
(3*S*,4a*R*,10a*S*)-3,4a,7,7,10a-pentamethyl-3-(3,3,4,4,5,5,6,6,6-nonafluorohexyl)dodecahydro-1*H*-benzo[*f*]chromene **(17)**

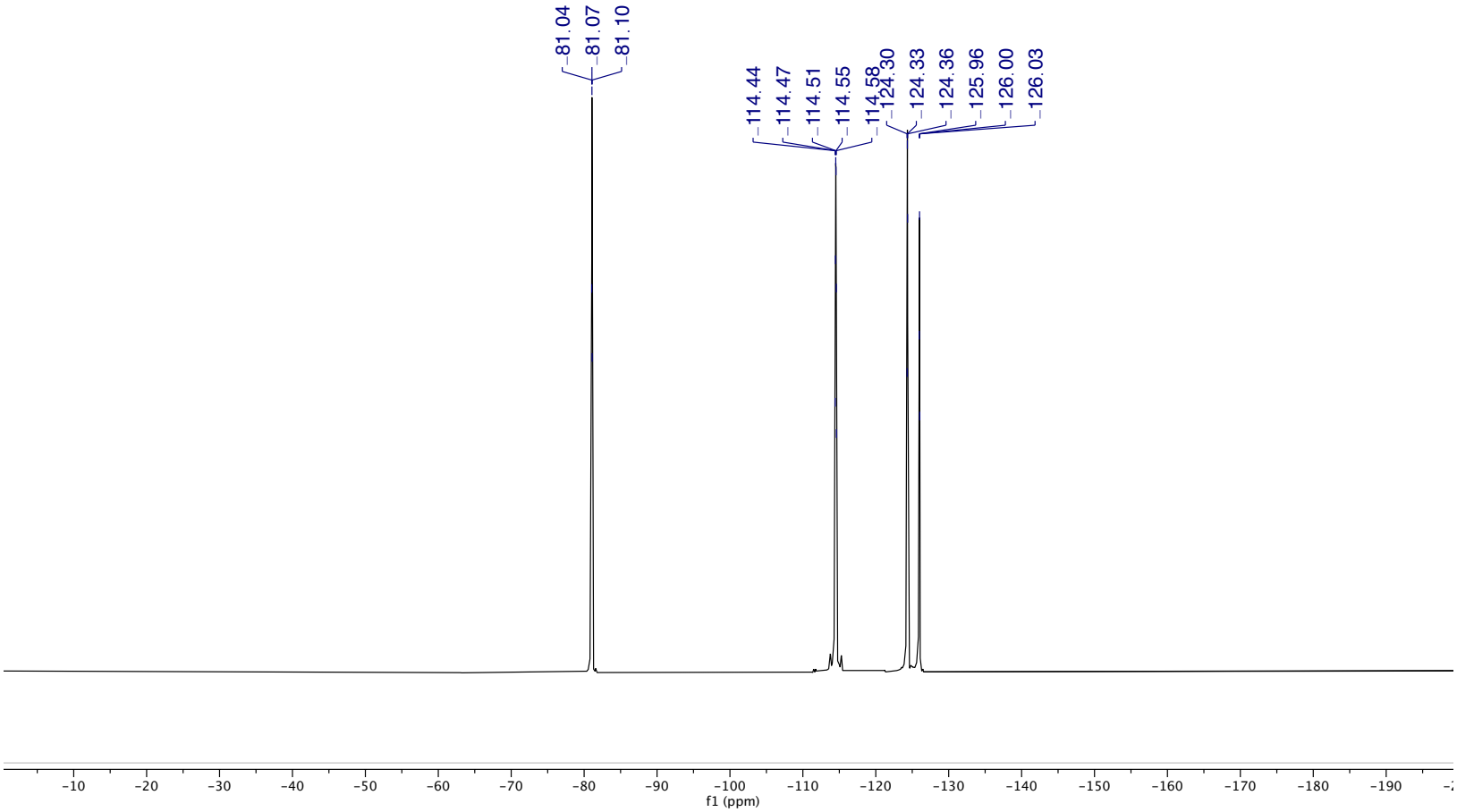
$^{13}$C-NMR (100 MHz, $CDCl_3$)



(3*S*,4a*R*,10a*S*)-3,4a,7,7,10a-pentamethyl-3-(3,3,4,4,5,5,6,6,6-nonafluorohexyl)dodecahydro-1*H*-benzo[*f*]chromene **(17)**

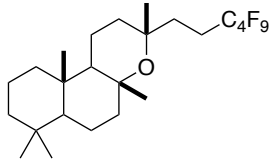
$^{19}$F-NMR (376 MHz, $CDCl_3$)

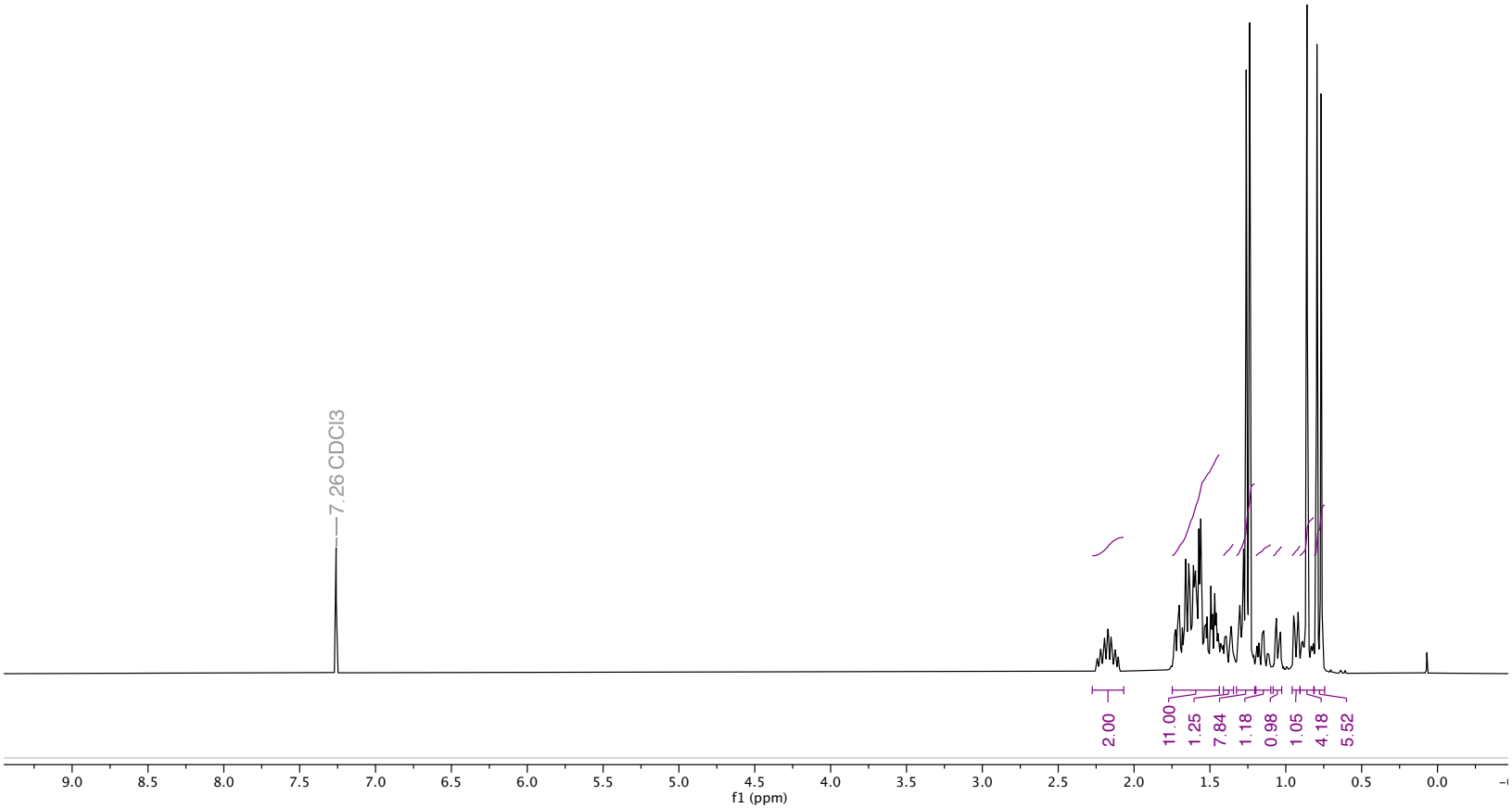


(3*R*,4a*R*,10a*S*)-3,4a,7,7,10a-pentamethyl-3-(6,6,6,6,6,6,6,6,6-nonafluoro-6λ12-hexa-3,5-diyn-1-yl)dodecahydro-1*H*-benzo[*f*]chromene **(18)**

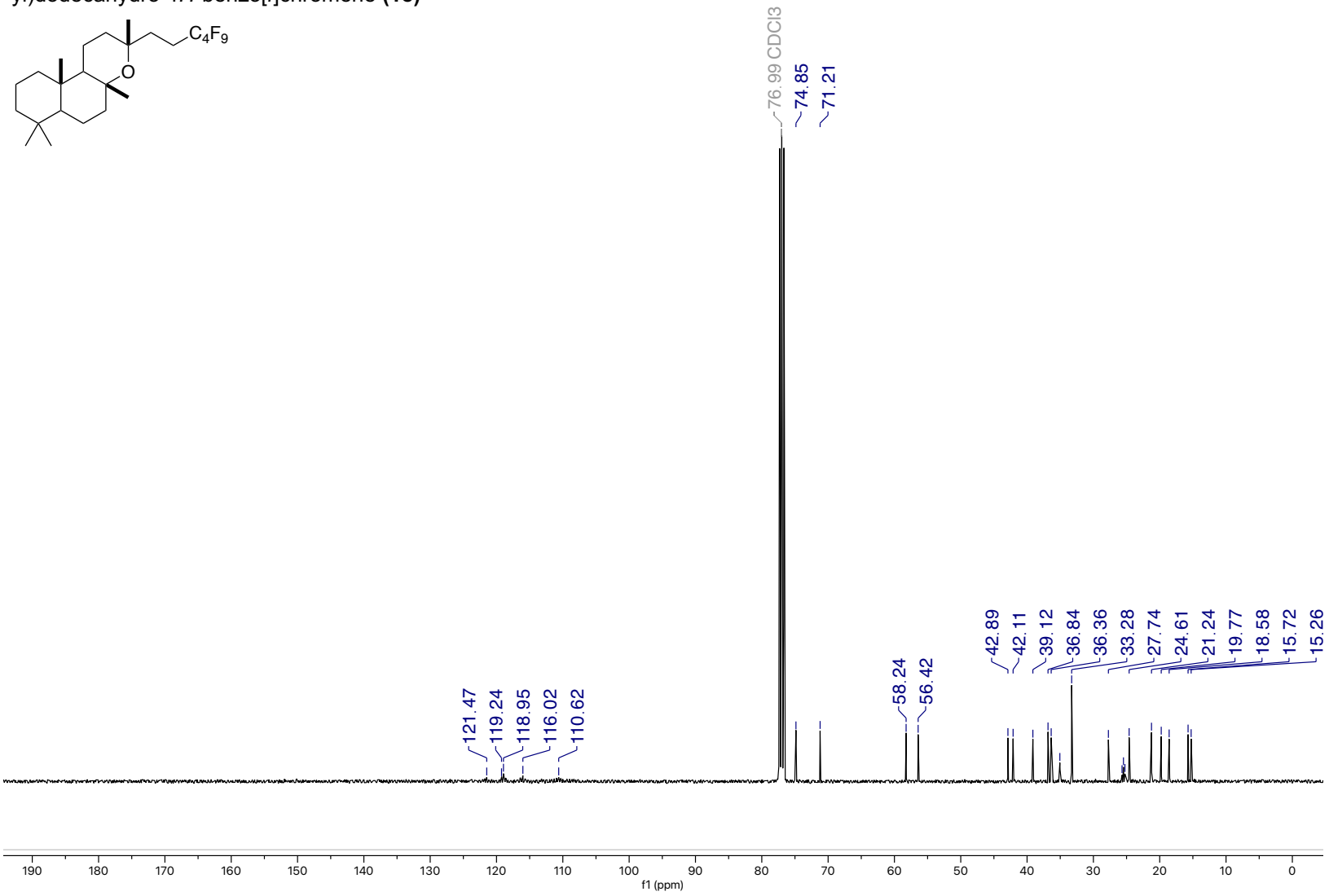
$^1$H-NMR (400 MHz, $CDCl_3$)



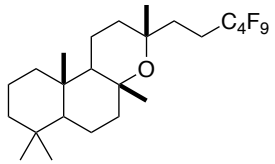



(3*R*,4a*R*,10a*S*)-3,4a,7,7,10a-pentamethyl-3-(6,6,6,6,6,6,6,6,6-nonafluoro-6λ12-hexa-3,5-diyn-1-yl)dodecahydro-1*H*-benzo[*f*]chromene **(18)**

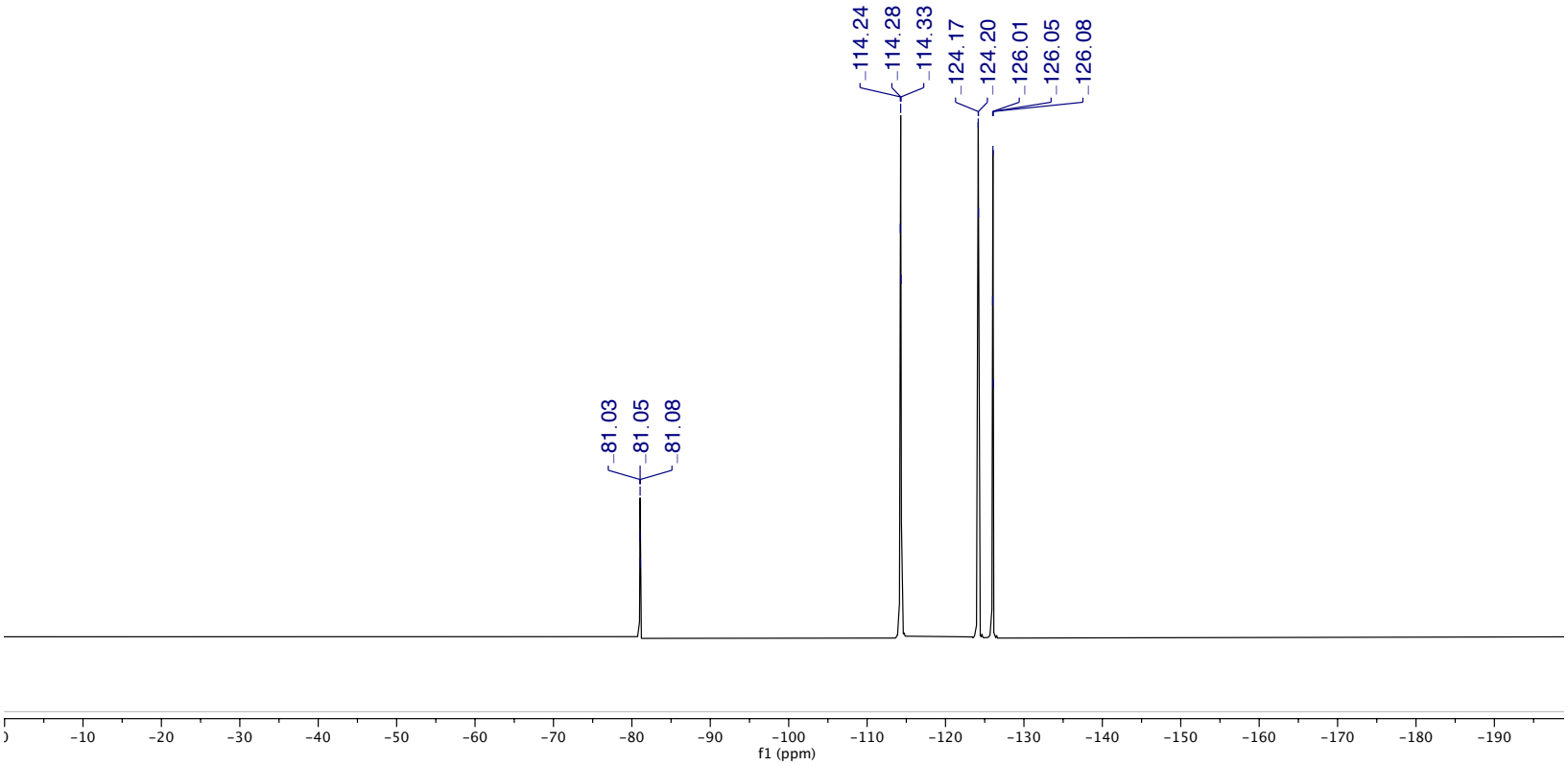
$^{13}$C-NMR (100 MHz, $CDCl_3$)



(3*R*,4a*R*,10a*S*)-3,4a,7,7,10a-pentamethyl-3-(6,6,6,6,6,6,6,6,6-nonafluoro-6λ12-hexa-3,5-diyn-1-yl)dodecahydro-1*H*-benzo[*f*]chromene **(18)**

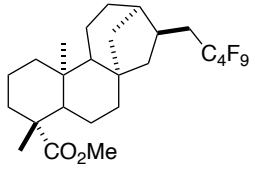


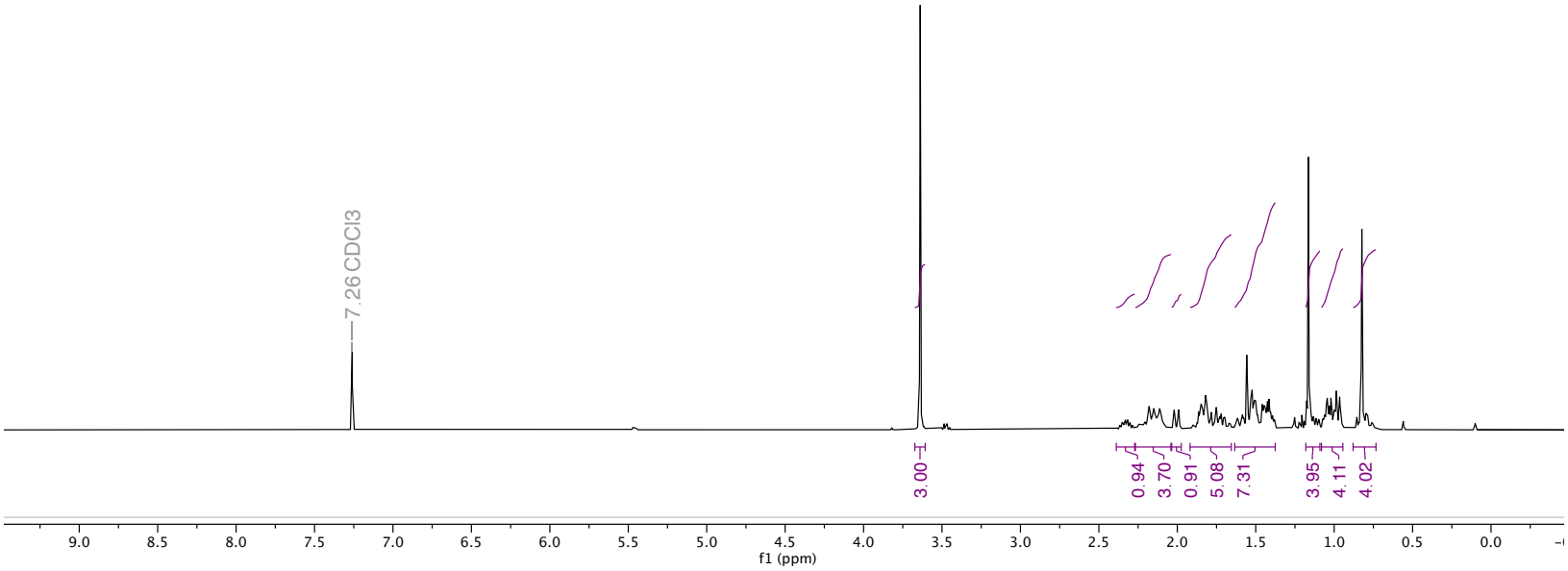

$^{19}$F-NMR (376 MHz, $CDCl_3$)



Methyl (4*R*,6a*S*,8*R*,9*R*,11b*S*)-4,11b-dimethyl-8-(5,5,5,5,5,5,5,5,5-nonafluoro-5λ12-penta-2,4-diyn-1-yl)tetradecahydro-6a,9-methanocyclohepta[*a*]naphthalene-4-carboxylate **(19)**

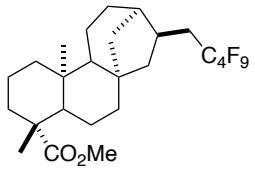
$^1$H-NMR (400 MHz, $CDCl_3$)



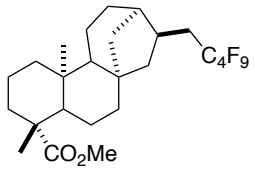
Methyl (4*R*,6a*S*,8*R*,9*R*,11b*S*)-4,11b-dimethyl-8-(5,5,5,5,5,5,5,5,5-nonafluoro-5λ12-penta-2,4-diyn-1-yl)tetradecahydro-6a,9-methanocyclohepta[*a*]naphthalene-4-carboxylate **(19)**

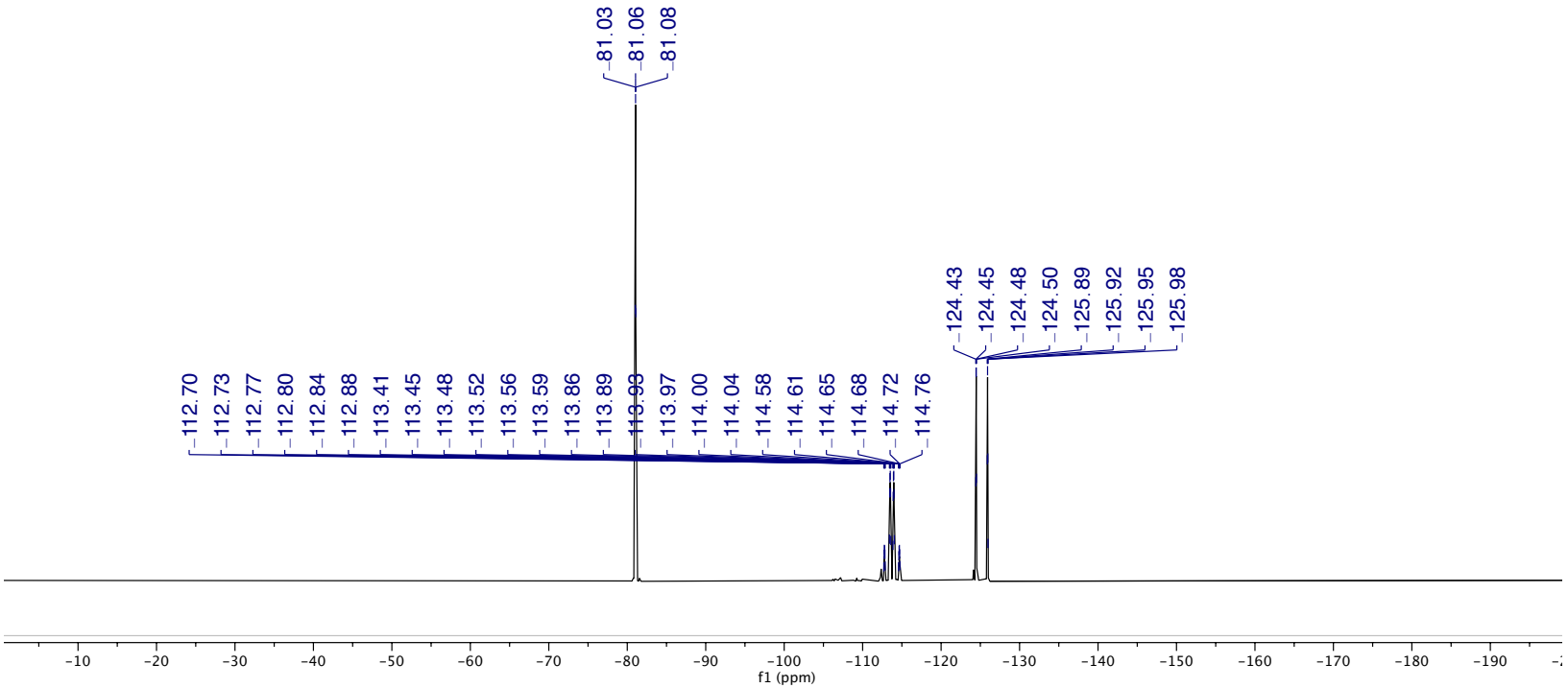
$^{13}$C-NMR (100 MHz, $CDCl_3$)



Methyl (4*R*,6a*S*,8*R*,9*R*,11b*S*)-4,11b-dimethyl-8-(5,5,5,5,5,5,5,5,5-nonafluoro-5λ12-penta-2,4-diyn-1-yl)tetradecahydro-6a,9-methanocyclohepta[*a*]naphthalene-4-carboxylate **(19)**

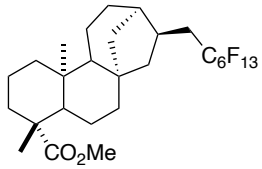
$^{19}$F-NMR (376 MHz, $CDCl_3$)

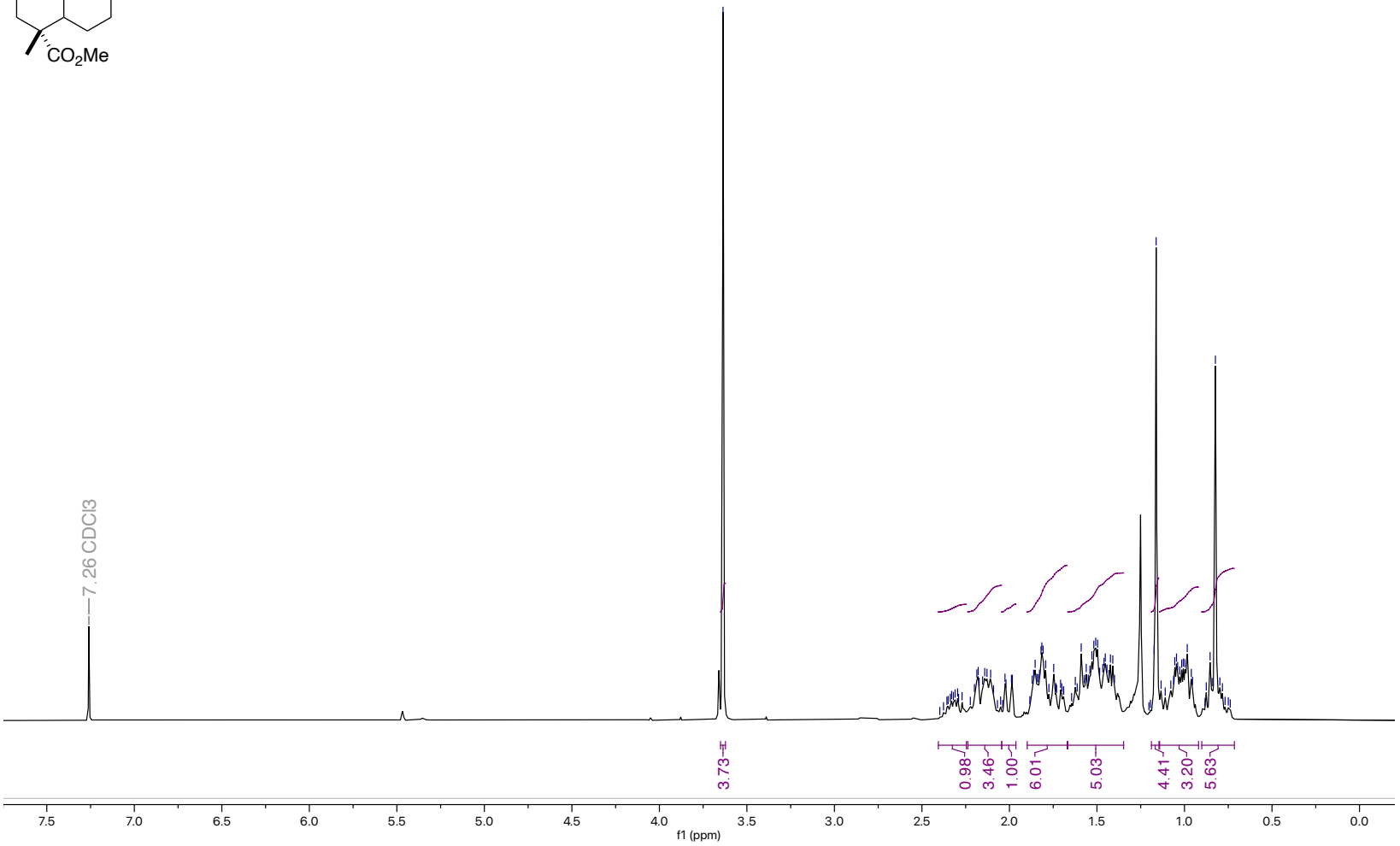


Methyl (4R,6aS,8S,9R,11bS)-4,11b-dimethyl-8-(2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoroheptyl) tetradecahydro-6a,9-methanocyclohepta[a]naphthalene-4-carboxylate **(20)**

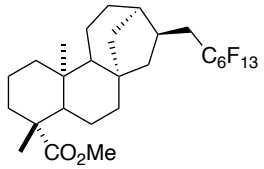
$^1$H-NMR (300 MHz, $CDCl_3$)

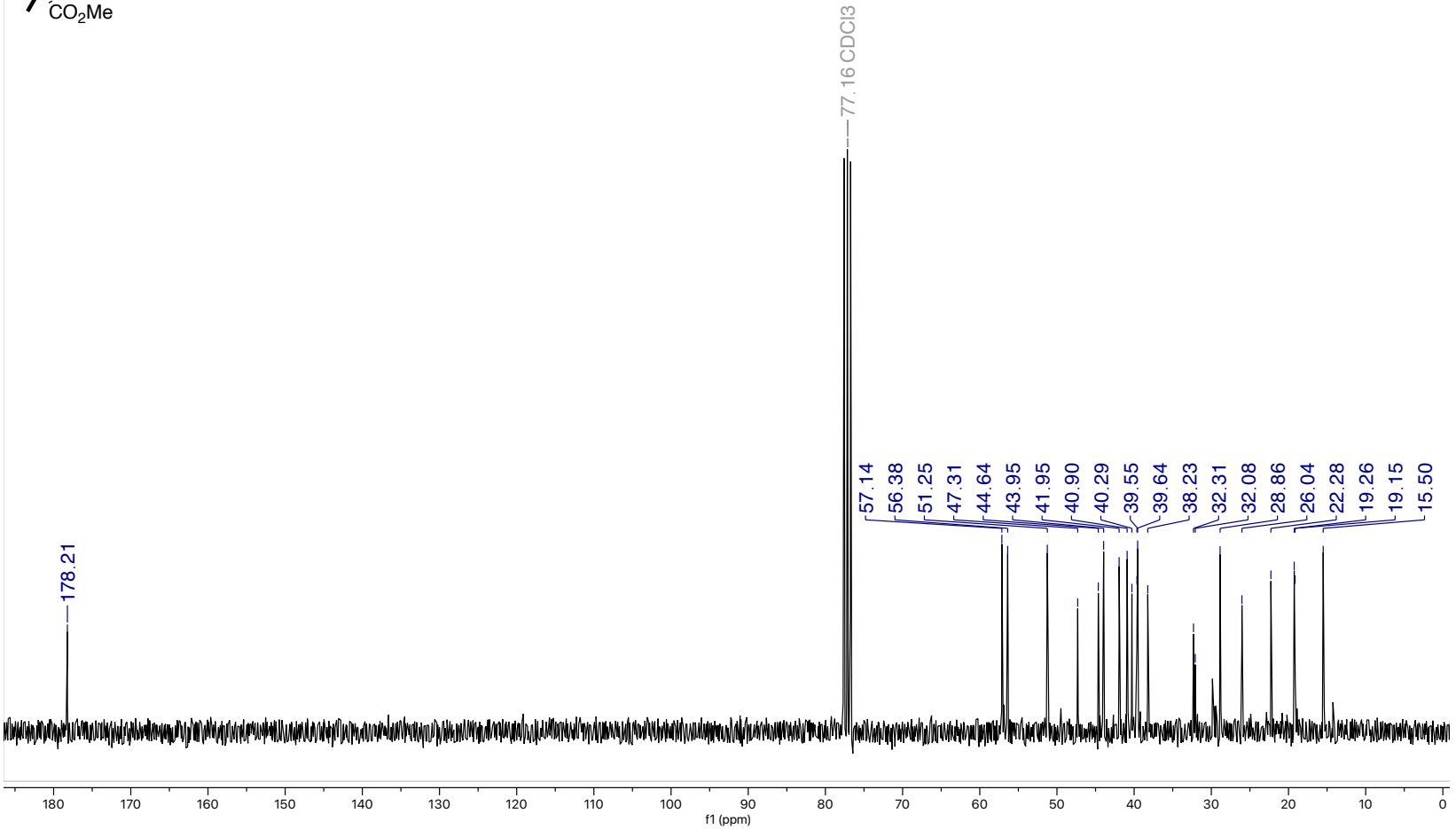


Methyl (4R,6aS,8S,9R,11bS)-4,11b-dimethyl-8-(2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoroheptyl) tetradecahydro-6a,9-methanocyclohepta[a]naphthalene-4-carboxylate **(20)**

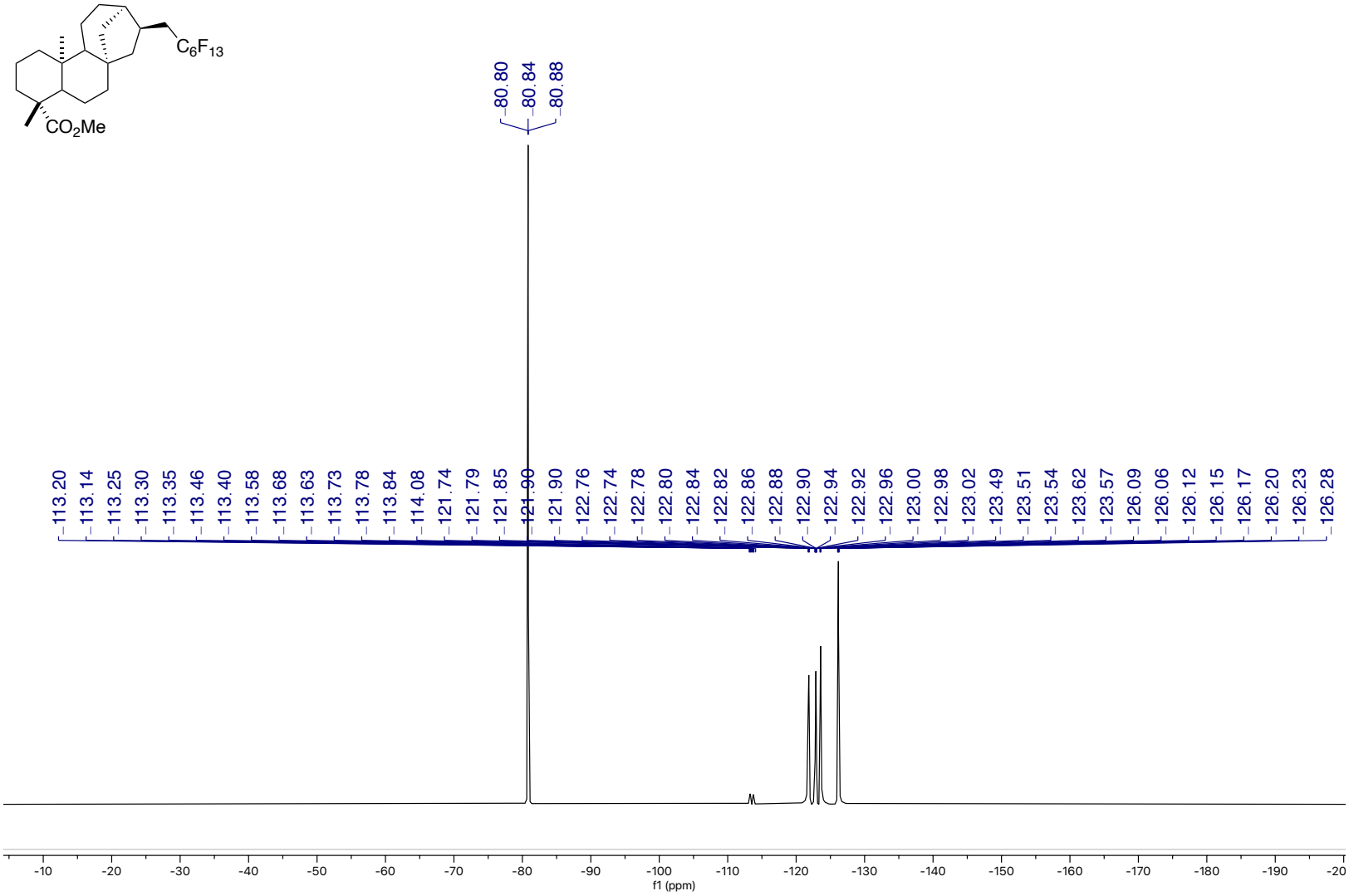
$^{13}$C-NMR (75 MHz, $CDCl_3$)



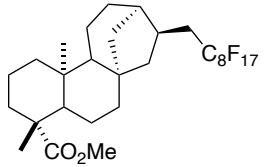
Methyl (4R,6aS,8S,9R,11bS)-4,11b-dimethyl-8-(2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoroheptyl) tetradecahydro-6a,9-methanocyclohepta[a]naphthalene-4-carboxylate **(20)**

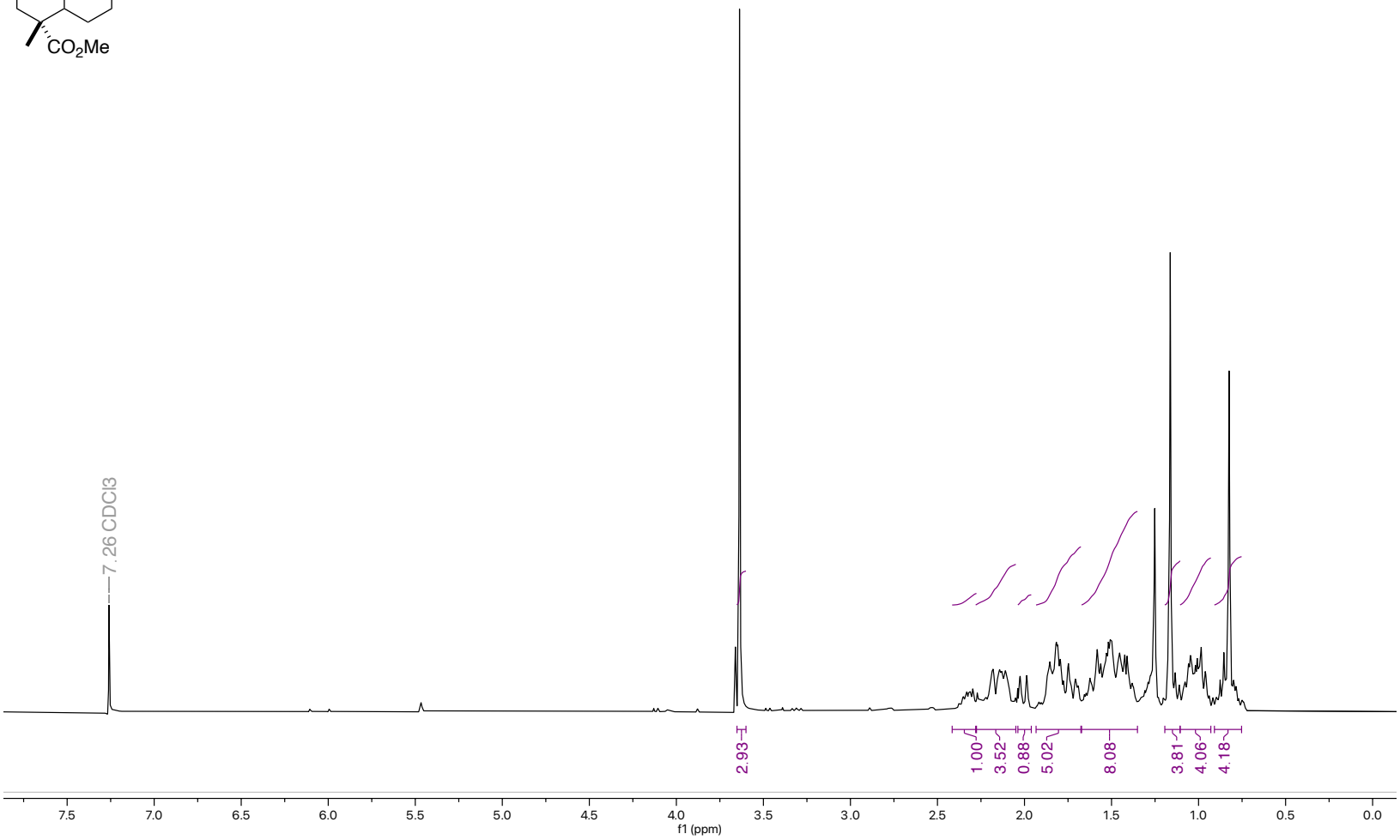
$^{19}$F-NMR (282 MHz, $CDCl_3$)



Methyl (4R,6aS,8S,9R,11bS)-8-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,9-heptadecafluorononyl)-4,11b-dimethyltetradecahydro-6a,9-methanocyclohepta[a]naphthalene-4-carboxylate **(21)**

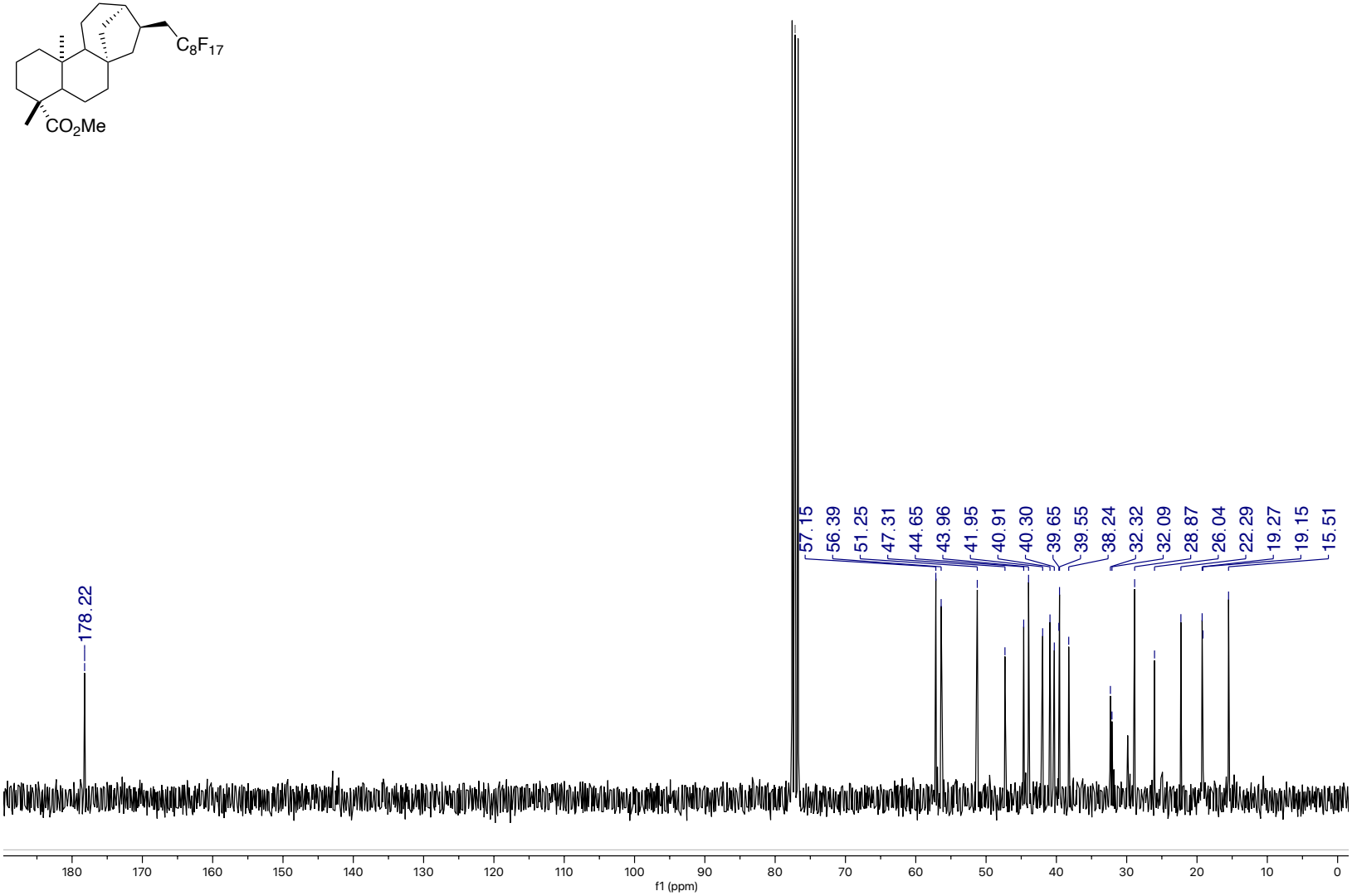
$^1$H-NMR (300 MHz, $CDCl_3$)



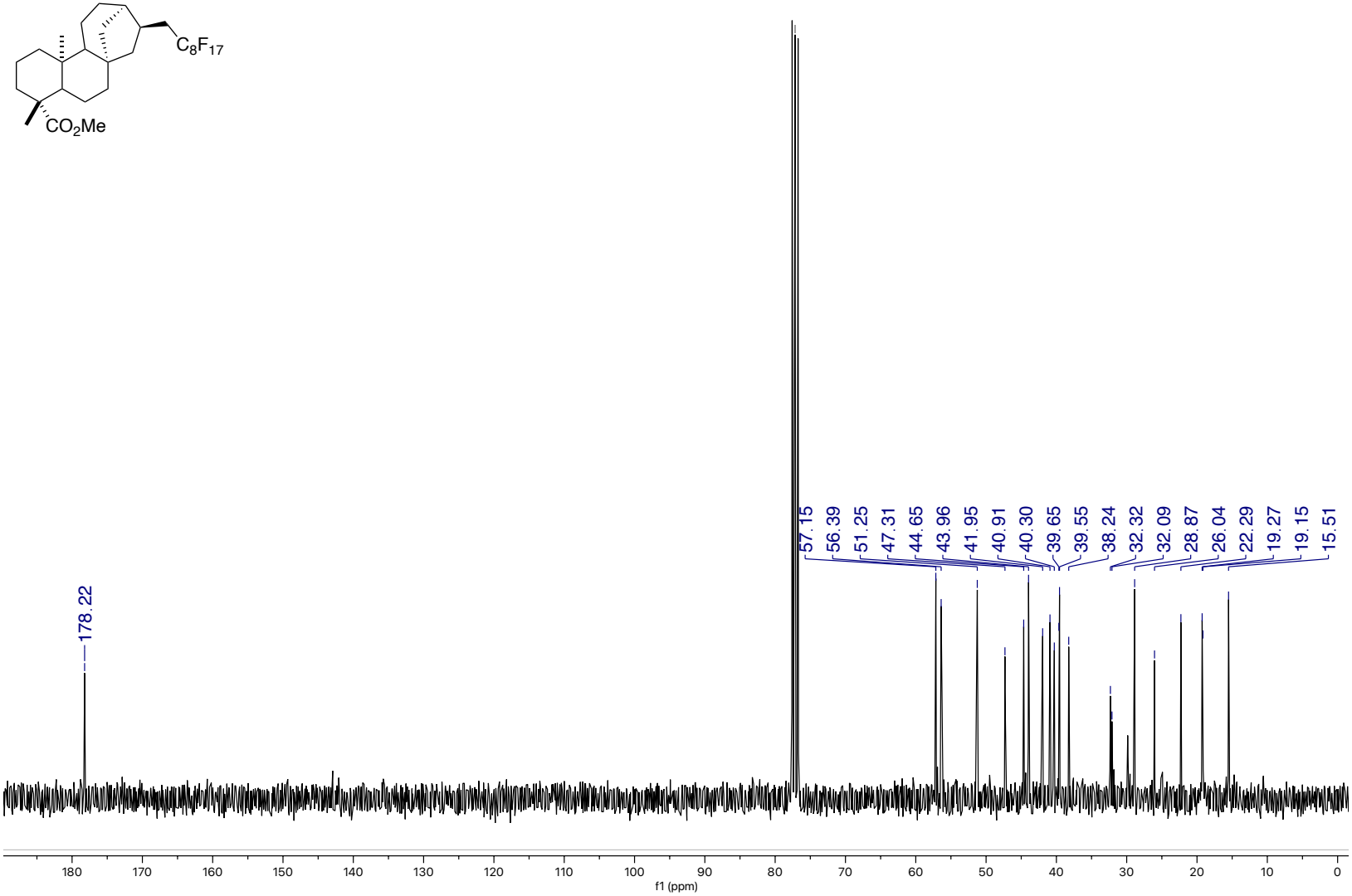
Methyl (4R,6aS,8S,9R,11bS)-8-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,9-heptadecafluorononyl)-4,11b-dimethyltetradecahydro-6a,9-methanocyclohepta[a]naphthalene-4-carboxylate **(21)**

$^{13}$C-NMR (75 MHz, $CDCl_3$)



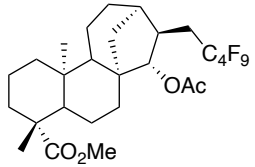
Methyl (4R,6aS,8S,9R,11bS)-8-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,9-heptadecafluorononyl)-4,11b-dimethyltetradecahydro-6a,9-methanocyclohepta[a]naphthalene-4-carboxylate **(21)**

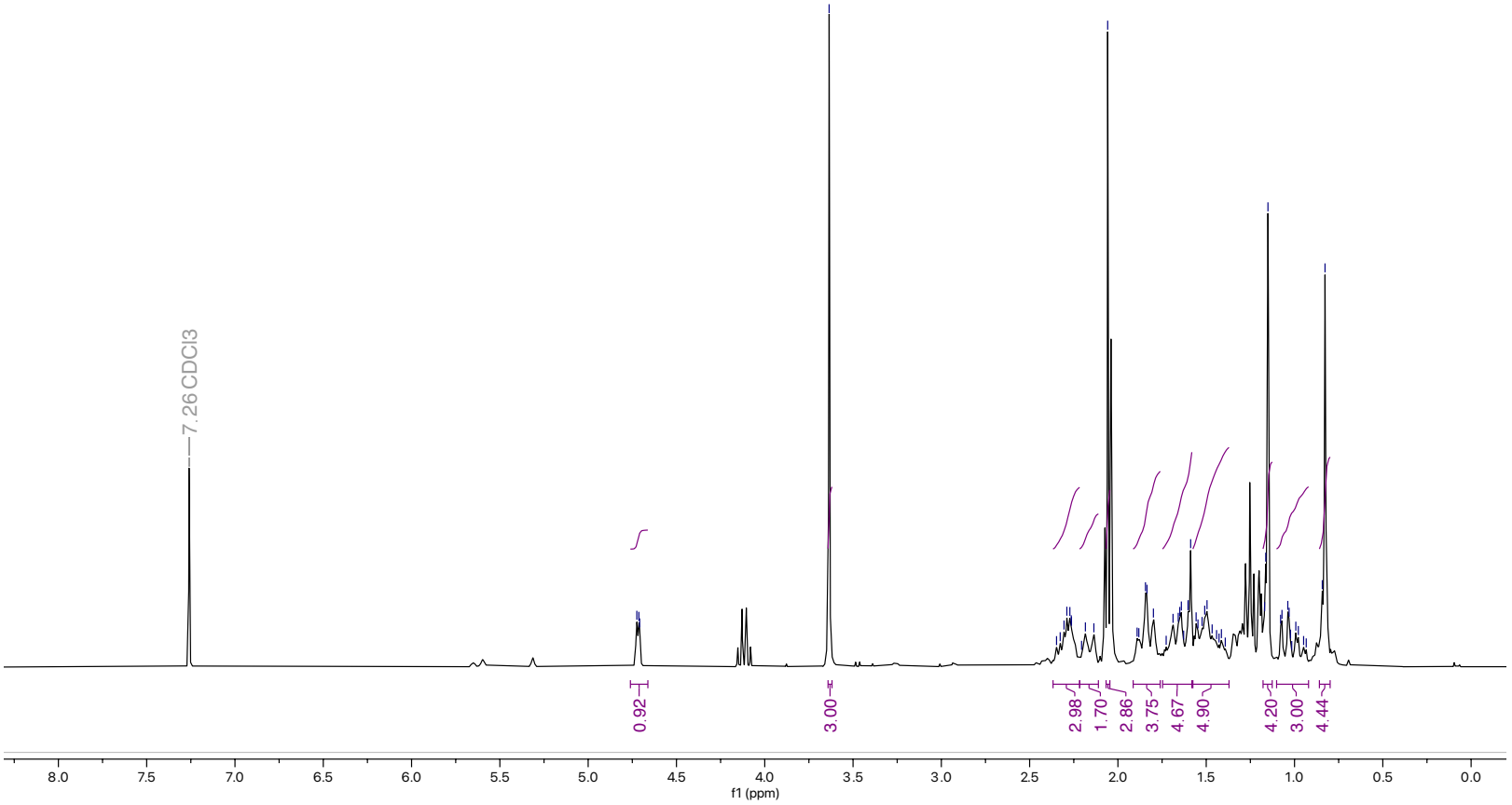
$^{13}$C-NMR (75 MHz, $CDCl_3$)



Methyl (4R,6aR,7S,8S,9R,11bS)-7-acetoxy-4,11b-dimethyl-8-(2,2,3,3,4,4,5,5,5-nonafluoropentyl) tetradecahydro-6a,9-methanocyclohepta[a]naphthalene-4-carboxylate **(22)**

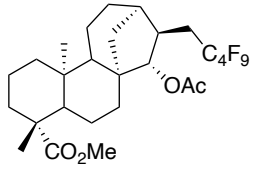
$^1$H-NMR (300 MHz, $CDCl_3$)



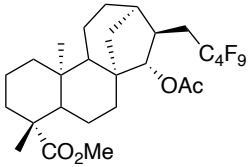
Methyl (4R,6aR,7S,8S,9R,11bS)-7-acetoxy-4,11b-dimethyl-8-(2,2,3,3,4,4,5,5,5-nonafluoropentyl) tetradecahydro-6a,9-methanocyclohepta[a]naphthalene-4-carboxylate **(22)**

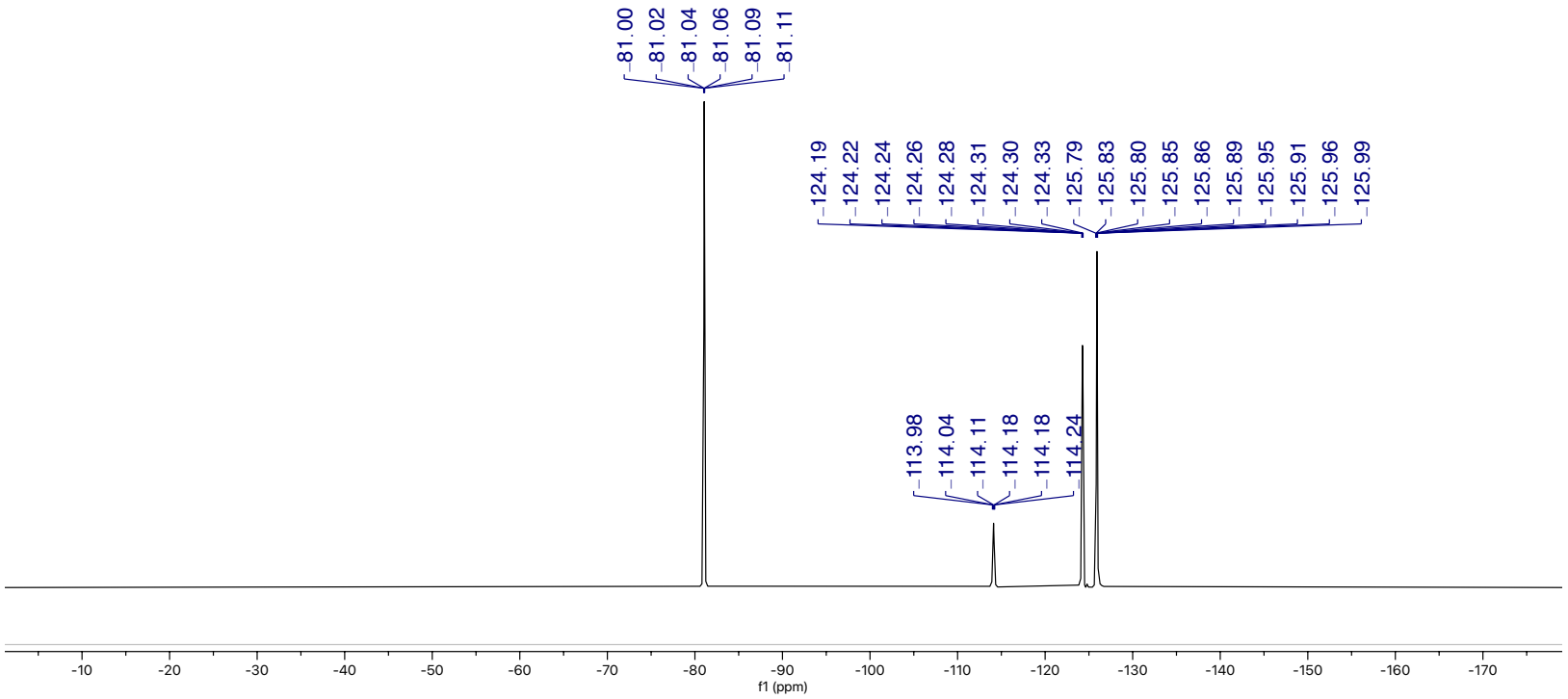
$^{13}$C-NMR (75 MHz, $CDCl_3$)



Methyl (4R,6aR,7S,8S,9R,11bS)-7-acetoxy-4,11b-dimethyl-8-(2,2,3,3,4,4,5,5,5-nonafluoropentyl) tetradecahydro-6a,9-methanocyclohepta[a]naphthalene-4-carboxylate **(22)**

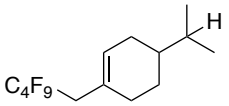
$^{19}$F-NMR (282 MHz, $CDCl_3$)

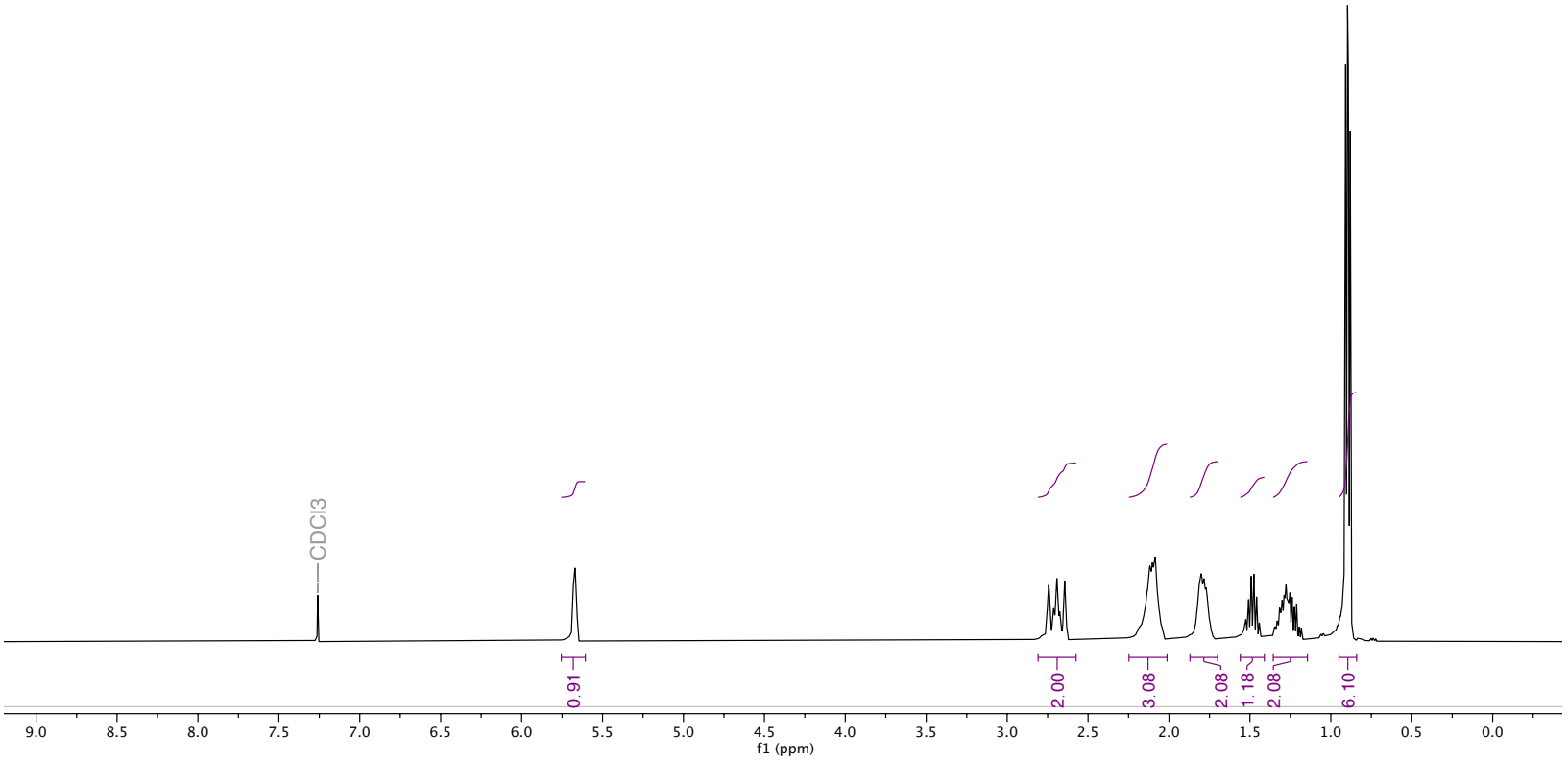


4-Isopropyl-1-(2,2,3,3,4,4,5,5,5-nonafluoropentyl)cyclohex-1-ene **(23)**

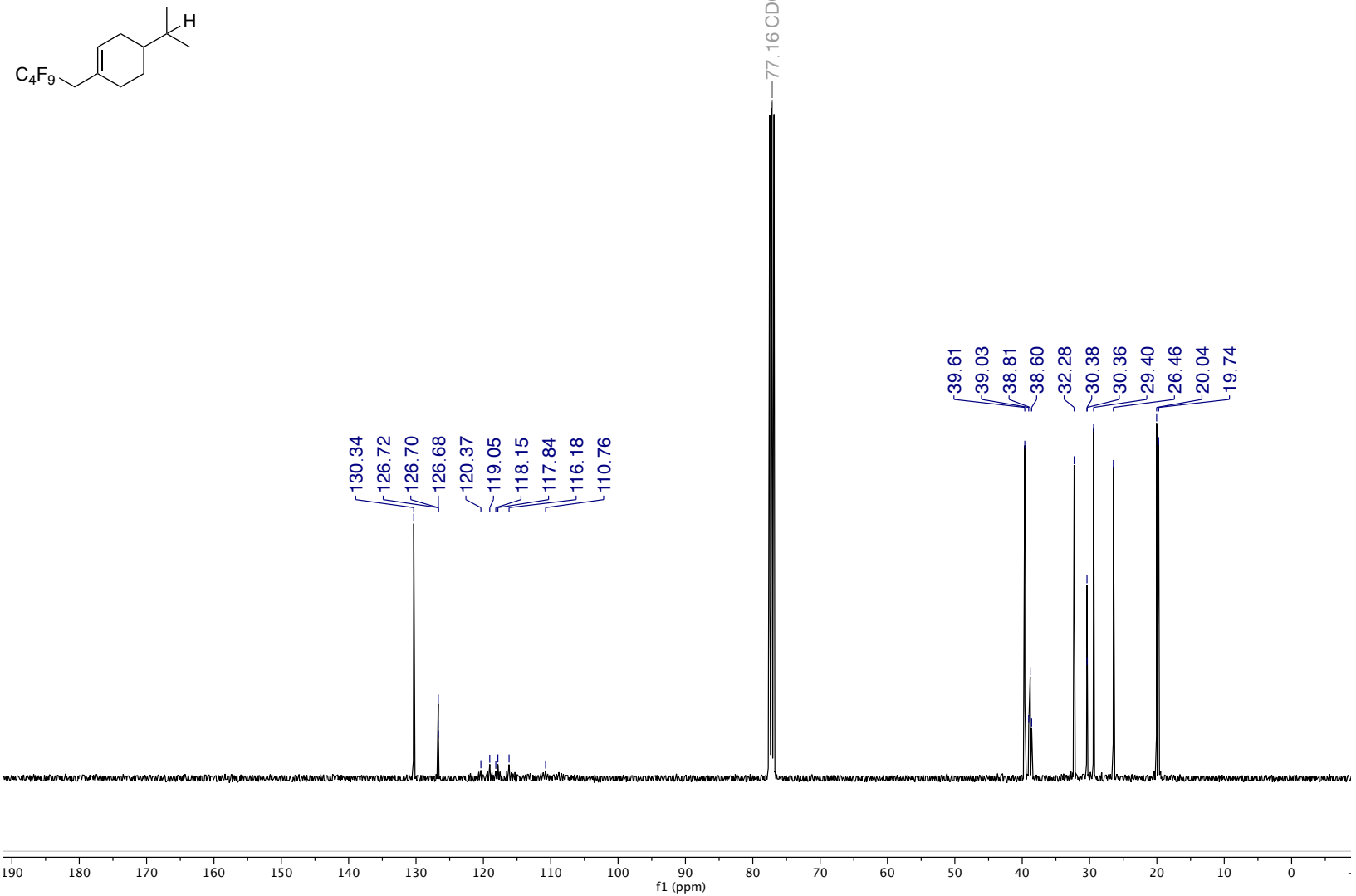
$^1$H-NMR (400 MHz, $CDCl_3$)



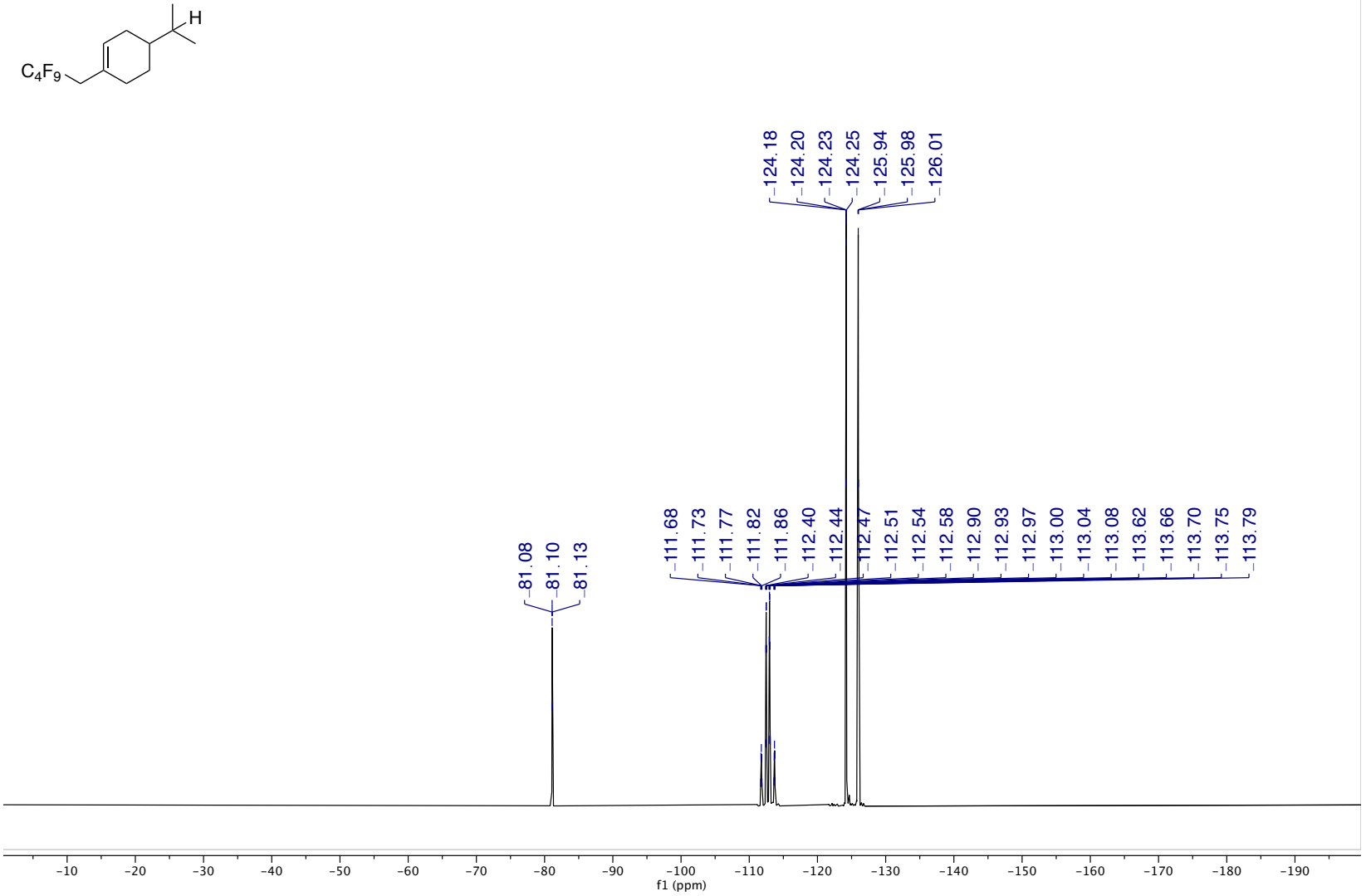
4-Isopropyl-1-(2,2,3,3,4,4,5,5,5-nonafluoropentyl)cyclohex-1-ene **(23)**

$^{13}$C-NMR (100 MHz, $CDCl_3$)

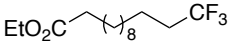


4-Isopropyl-1-(2,2,3,3,4,4,5,5,5-nonafluoropentyl)cyclohex-1-ene **(23)**

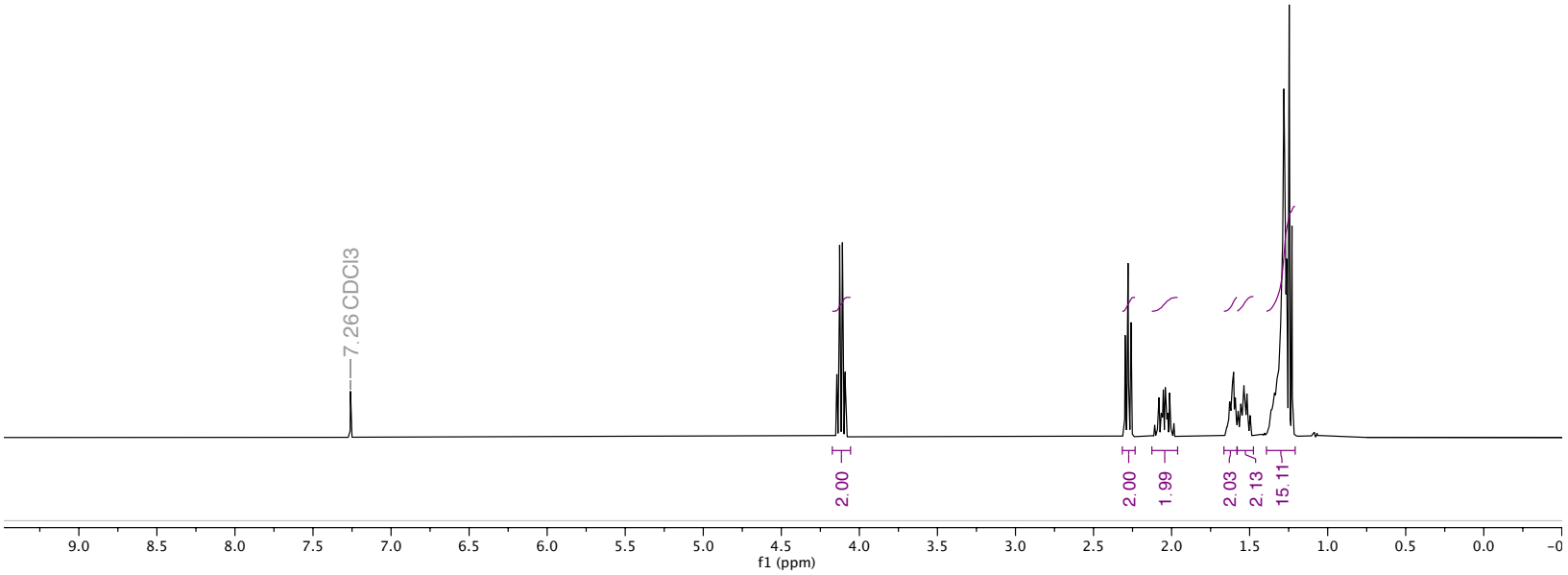
$^{19}$F-NMR (376 MHz, $CDCl_3$)



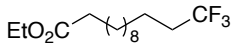
Ethyl 12,12,12-trifluorododecanoate **(24)**



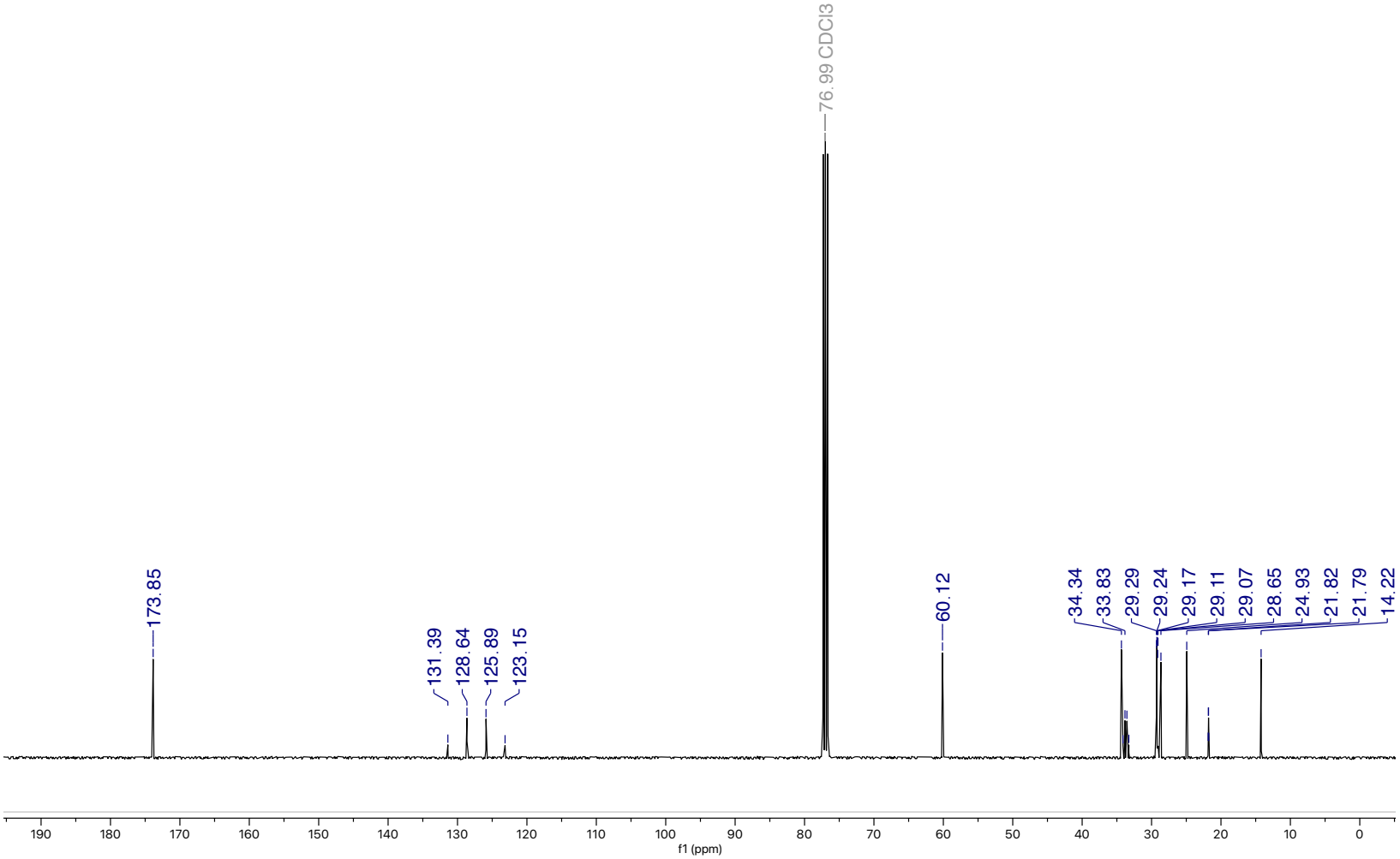

$^{1}$H-NMR (400 MHz, $CDCl_3$)



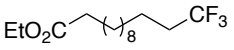
Ethyl 12,12,12-trifluorododecanoate **(24)**



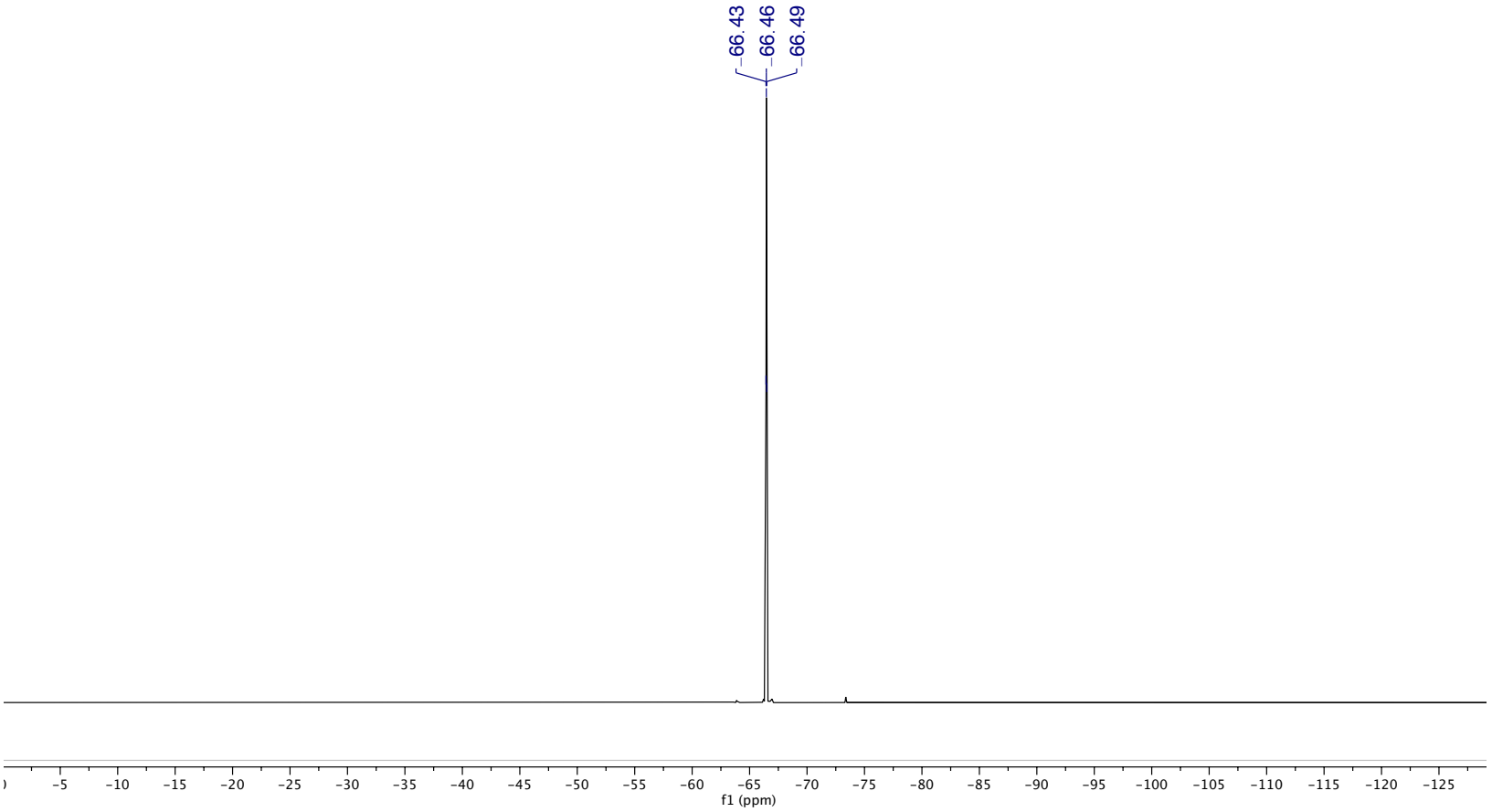

$^{13}$C-NMR (100 MHz, $CDCl_3$)



Ethyl 12,12,12-trifluorododecanoate **(24)**

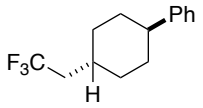


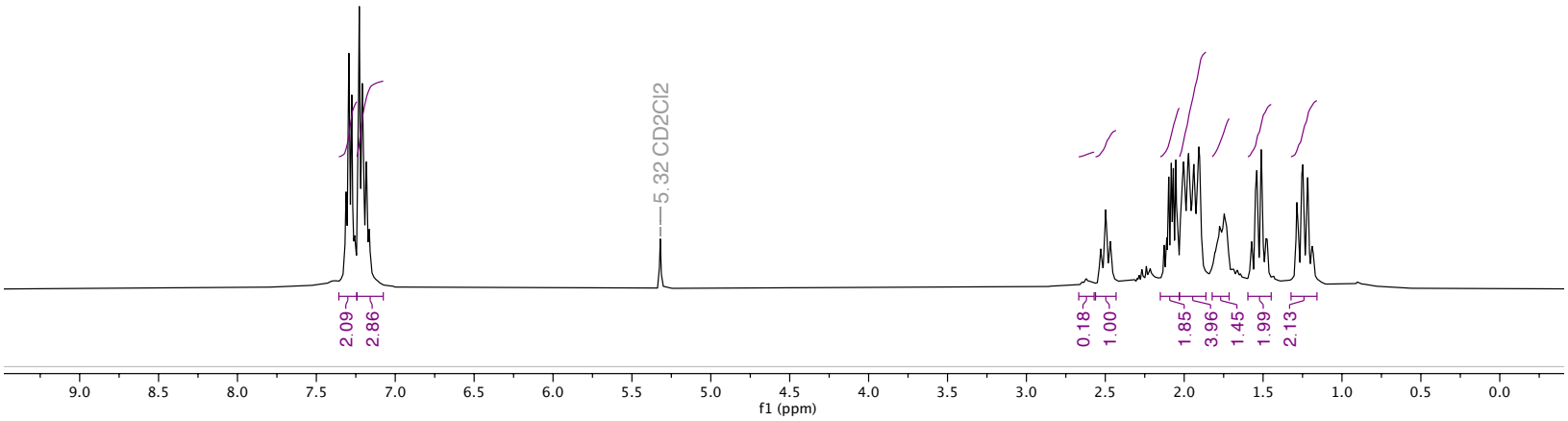

$^{19}$F-NMR (376 MHz, $CDCl_3$)



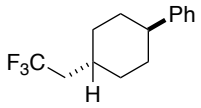
((1*R*,4*R*)-4-(2,2,2-trifluoroethyl)cyclohexyl)benzene **(25)**

$^1$H-NMR (400 MHz, $CD_2Cl_2$)

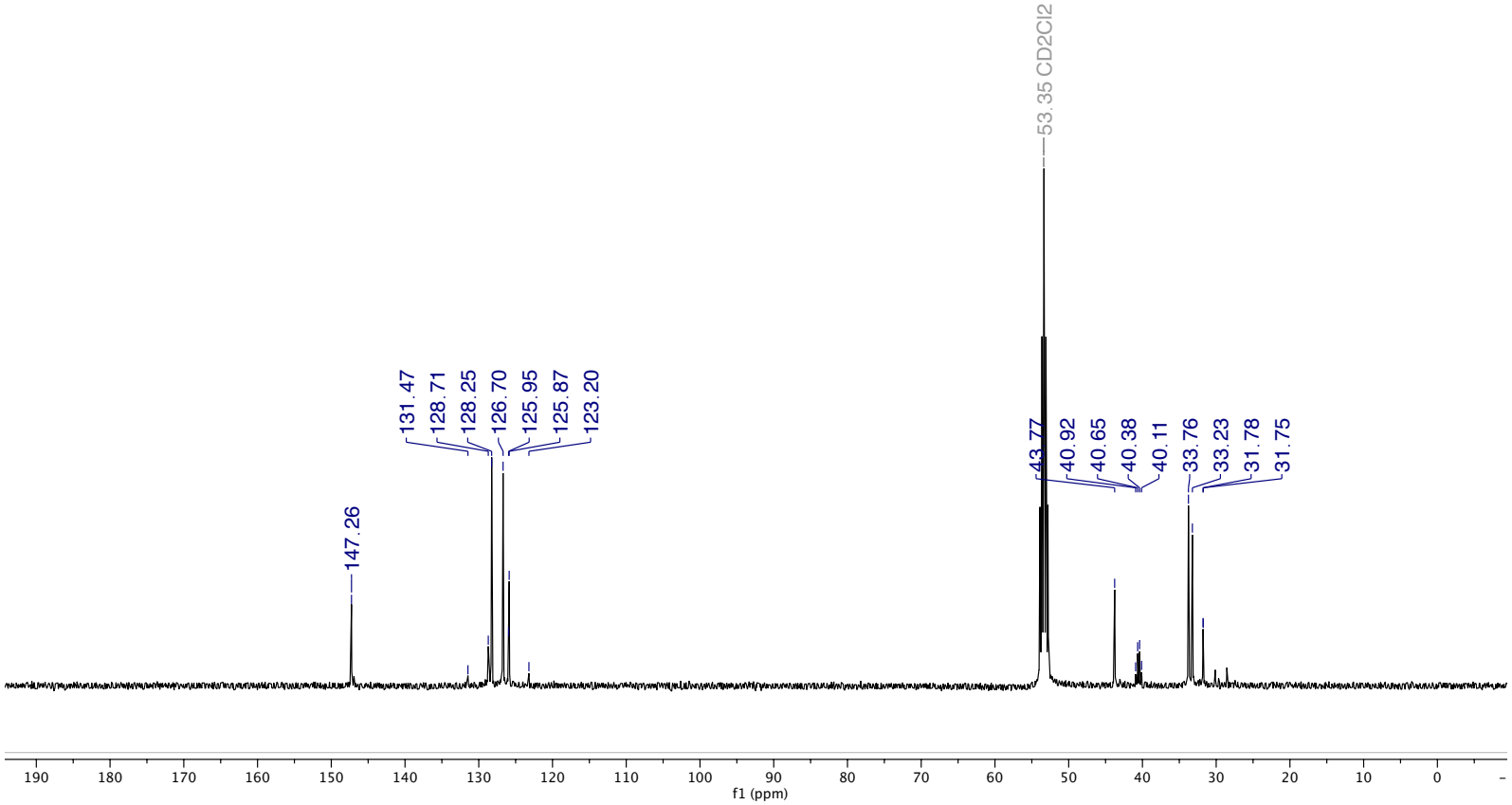


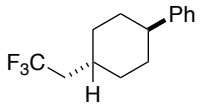
((1*R*,4*R*)-4-(2,2,2-trifluoroethyl)cyclohexyl)benzene **(25)**



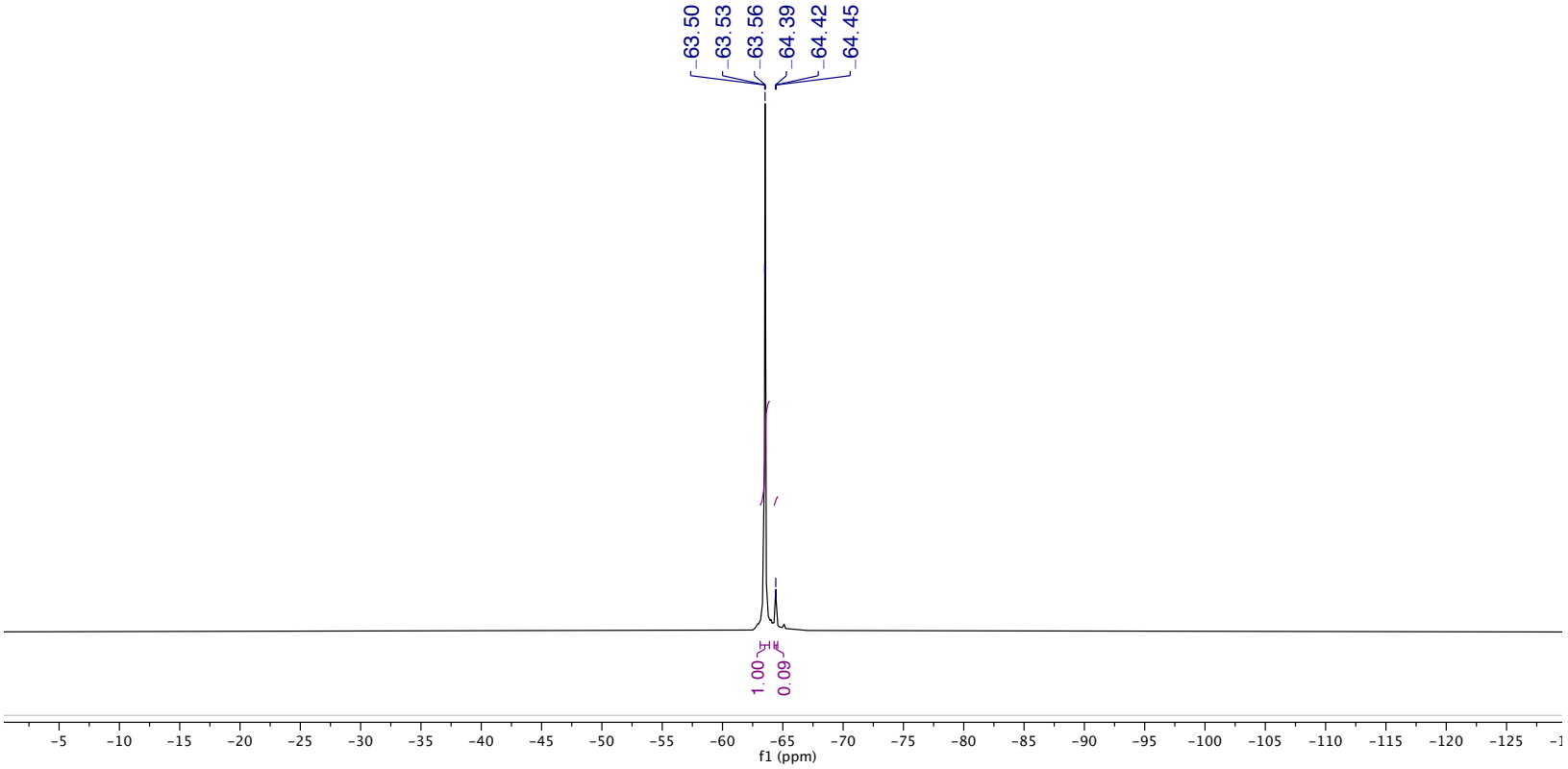

$^{13}$C-NMR (100 MHz, $CD_2Cl_2$)



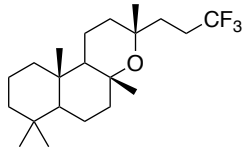
((1*R*,4*R*)-4-(2,2,2-trifluoroethyl)cyclohexyl)benzene **(25)**



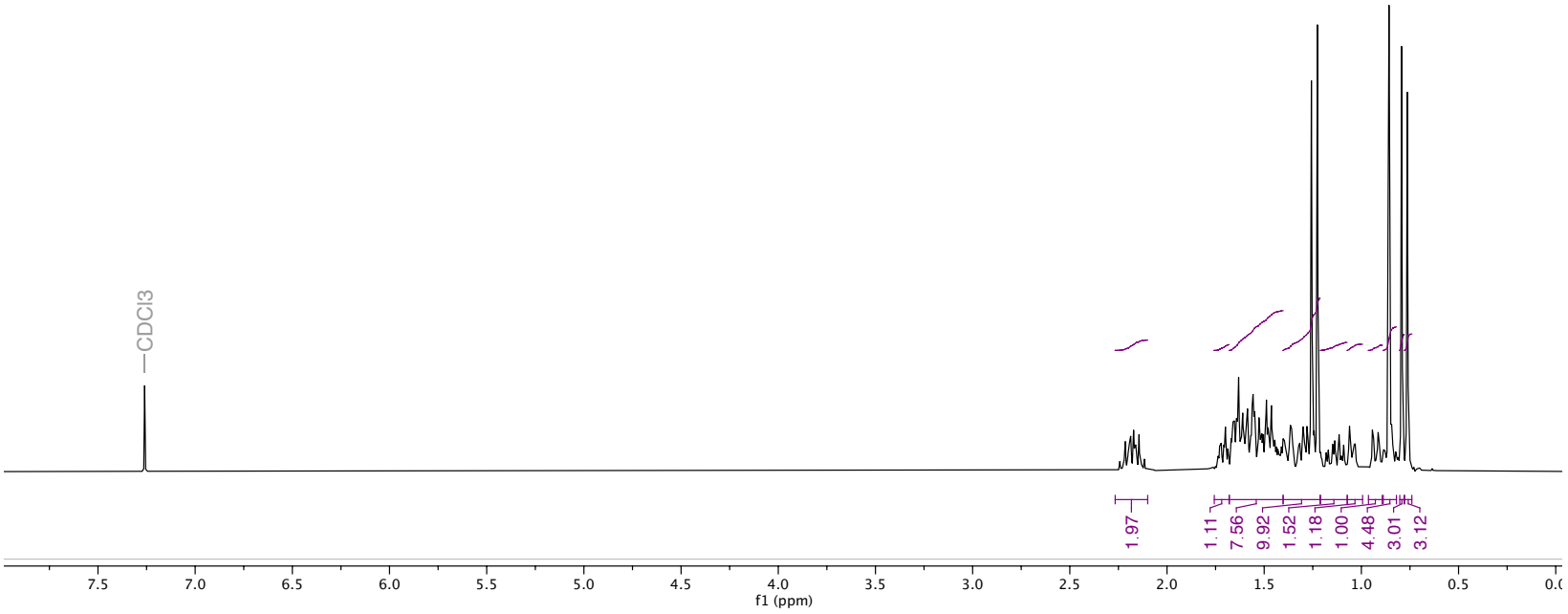

$^{19}$F-NMR (376 MHz, $CD_2Cl_2$)



(3*R*,4a*R*,10a*S*)-3,4a,7,7,10a-pentamethyl-3-(3,3,3-trifluoropropyl)dodecahydro-1*H*-benzo[*f*]chromene **(26)**

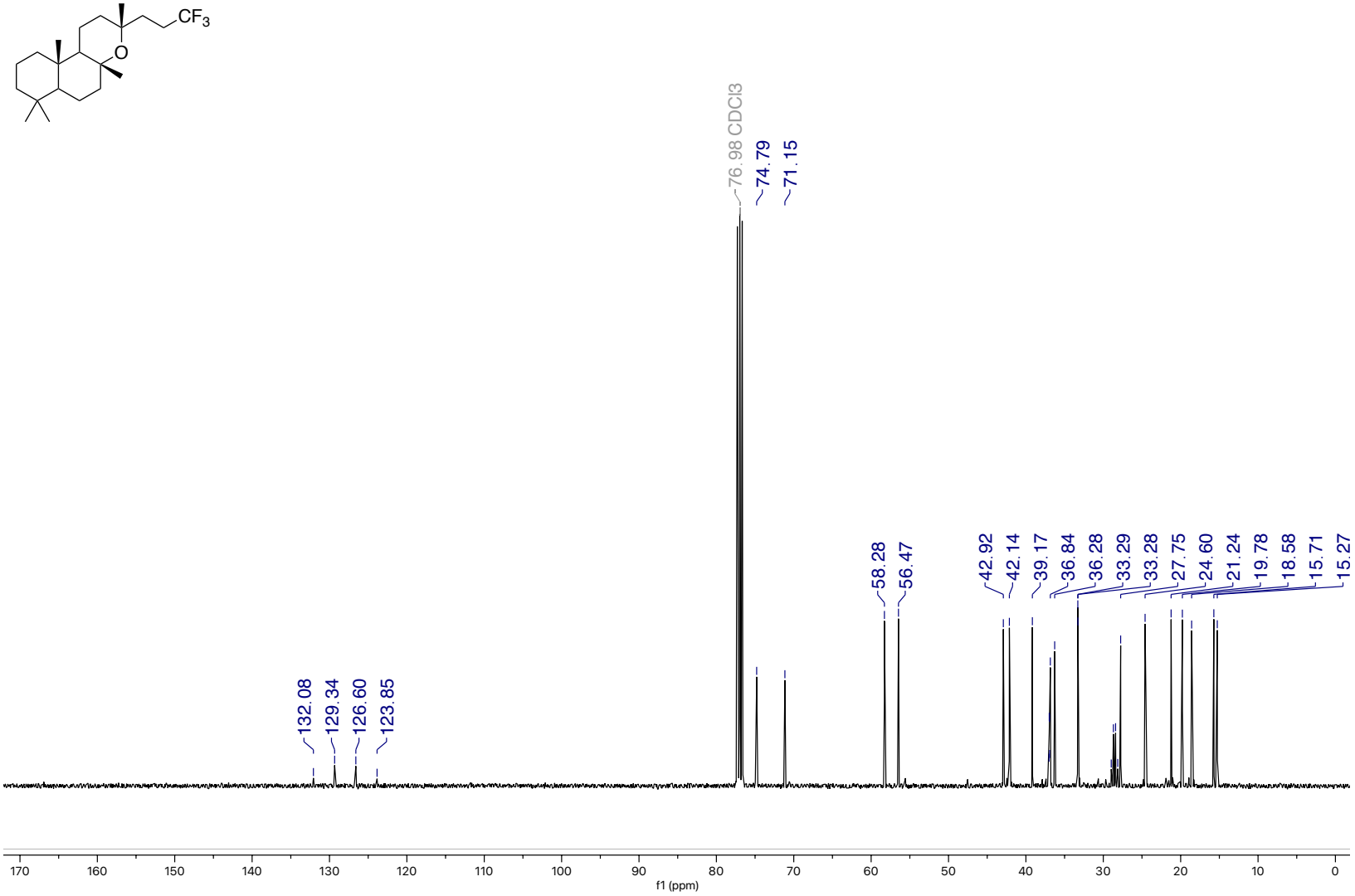



$^1$H-NMR (400 MHz, $CDCl_3$)

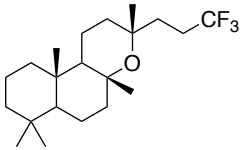


(3*R*,4a*R*,10a*S*)-3,4a,7,7,10a-pentamethyl-3-(3,3,3-trifluoropropyl)dodecahydro-1*H*-benzo[*f*]chromene **(26)**

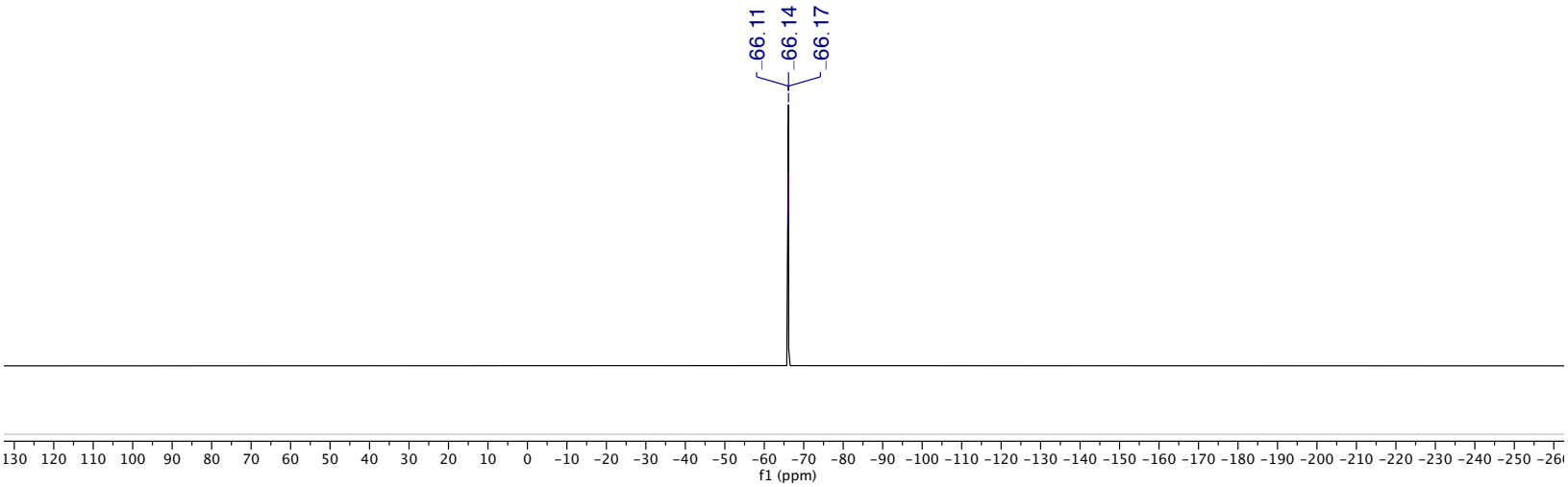
$^{13}$C-NMR (100 MHz, $CDCl_3$)



(3*R*,4a*R*,10a*S*)-3,4a,7,7,10a-pentamethyl-3-(3,3,3-trifluoropropyl)dodecahydro-1*H*-benzo[*f*]chromene **(26)**

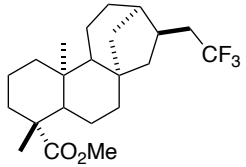


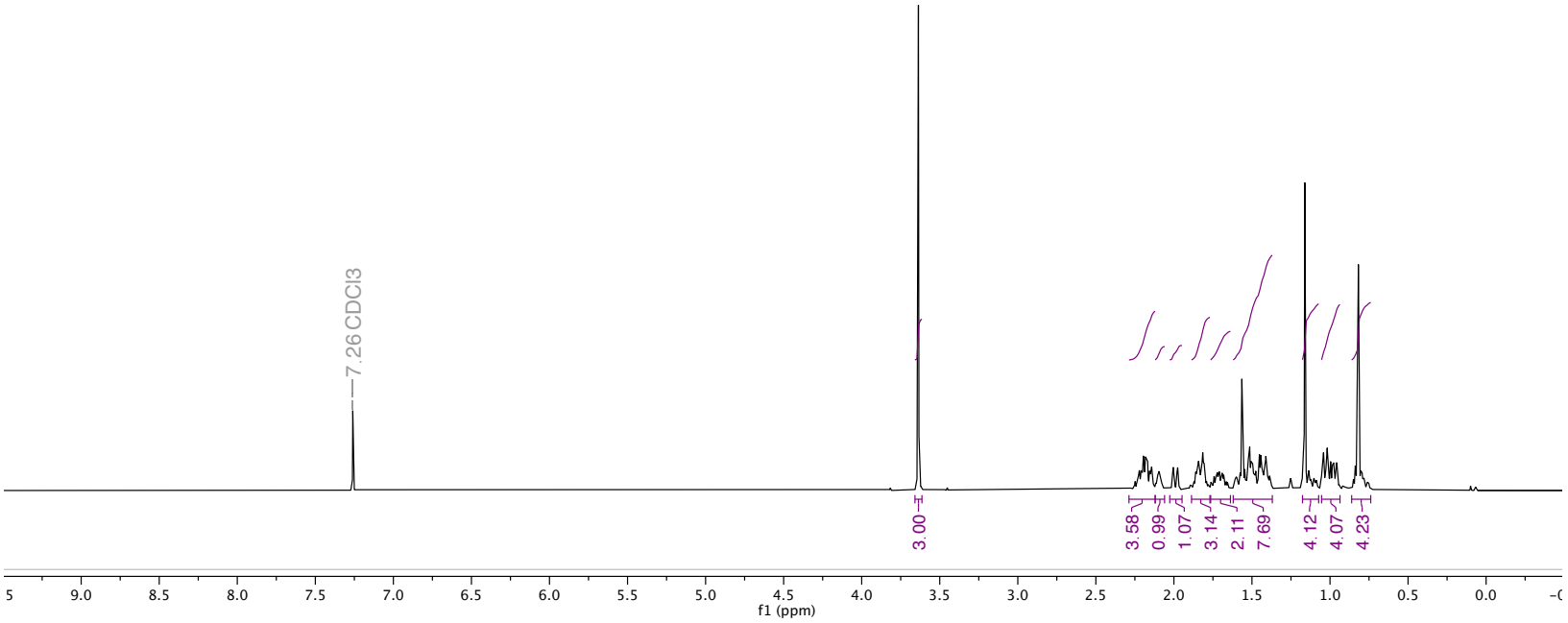

$^{19}$F-NMR (376 MHz, $CDCl_3$)



Methyl (4*R*,6a*S*,8*R*,9*R*,11b*S*)-4,11b-dimethyl-8-(2,2,2-trifluoroethyl)tetradecahydro-6a,9-methanocyclohepta[*a*]naphthalene-4-carboxylate **(27)**

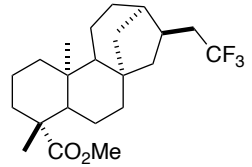
$^1$H-NMR (400 MHz, $CDCl_3$)



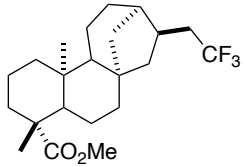



Methyl (4*R*,6a*S*,8*R*,9*R*,11b*S*)-4,11b-dimethyl-8-(2,2,2-trifluoroethyl)tetradecahydro-6a,9-methanocyclohepta[*a*]naphthalene-4-carboxylate **(27)**

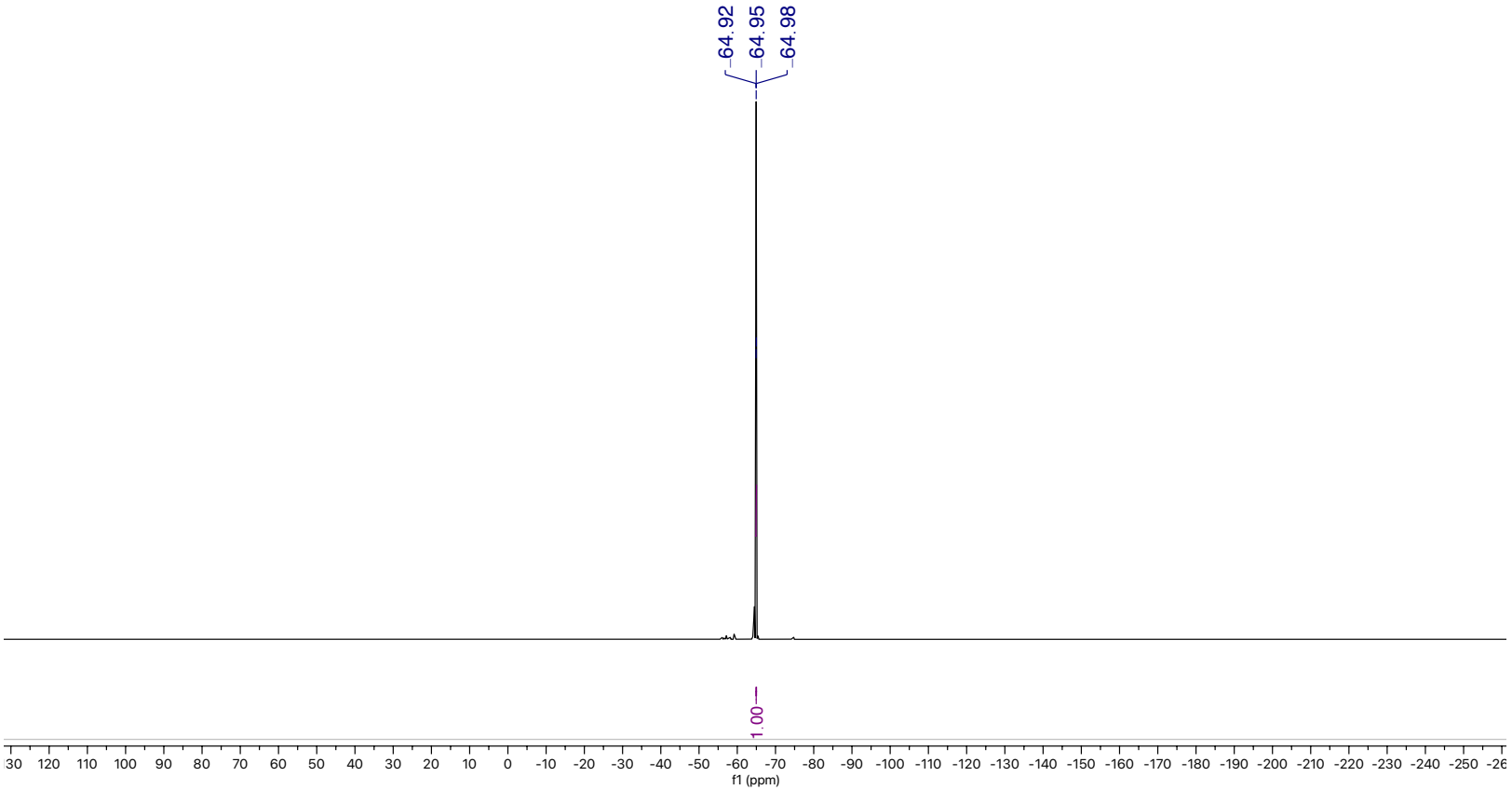
$^{13}$C-NMR (100 MHz, $CDCl_3$)



Methyl (4*R*,6a*S*,8*R*,9*R*,11b*S*)-4,11b-dimethyl-8-(2,2,2-trifluoroethyl)tetradecahydro-6a,9-methanocyclohepta[*a*]naphthalene-4-carboxylate **(27)**

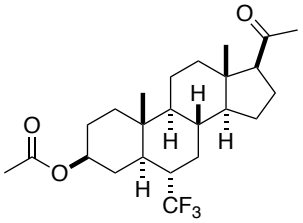


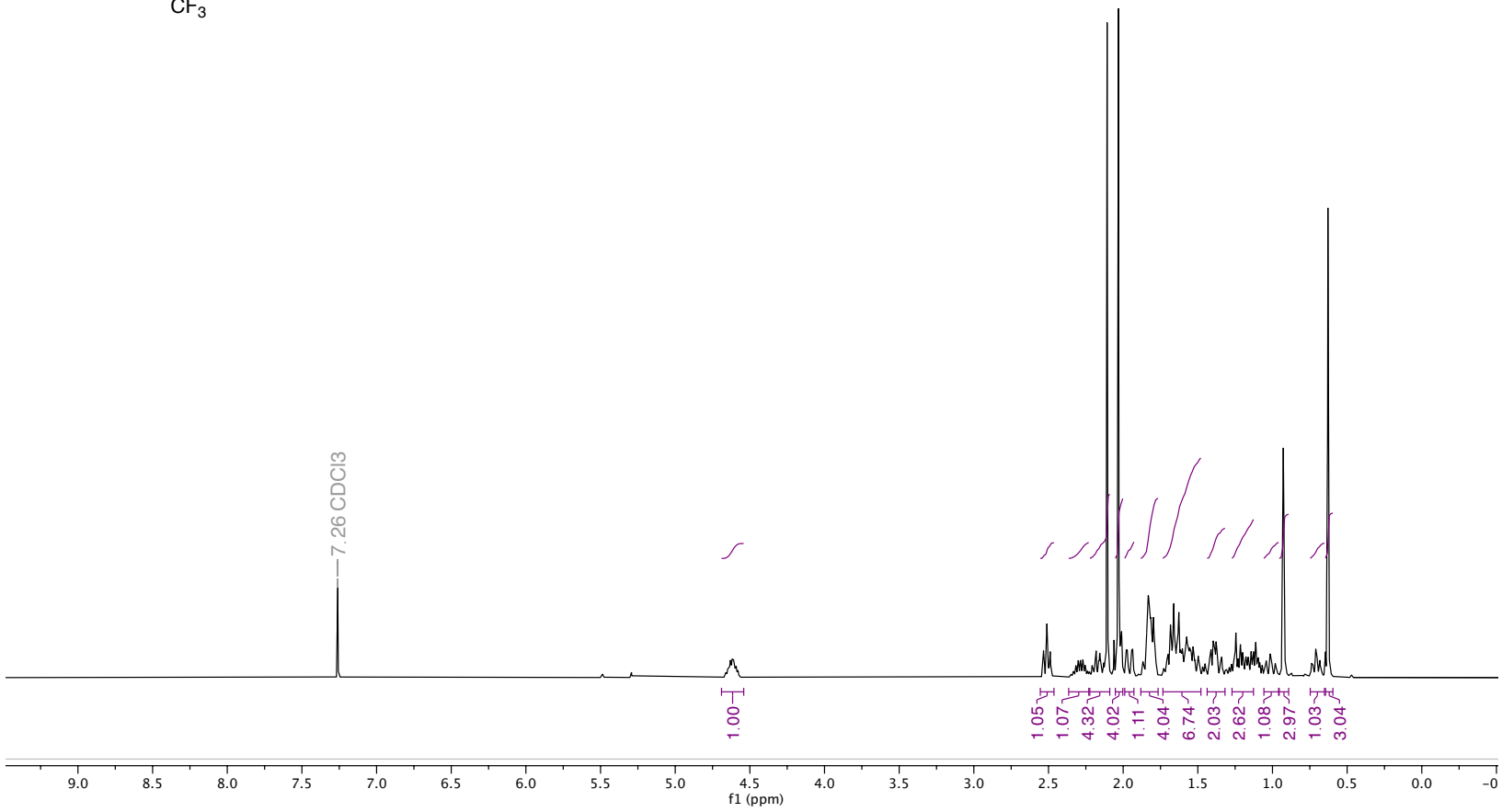

$^{19}$F-NMR (376 MHz, $CDCl_3$)



(3*S*,5*R*,6*S*,8*R*,9*S*,10*R*,13*S*,14*S*,17*S*)-17-Acetyl-10,13-dimethyl-6-(trifluoromethyl)hexadecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl acetate **(28)**

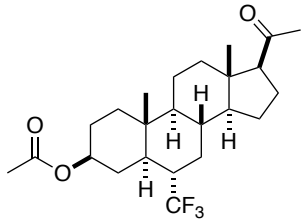
$^1$H-NMR (400 MHz, $CDCl_3$)



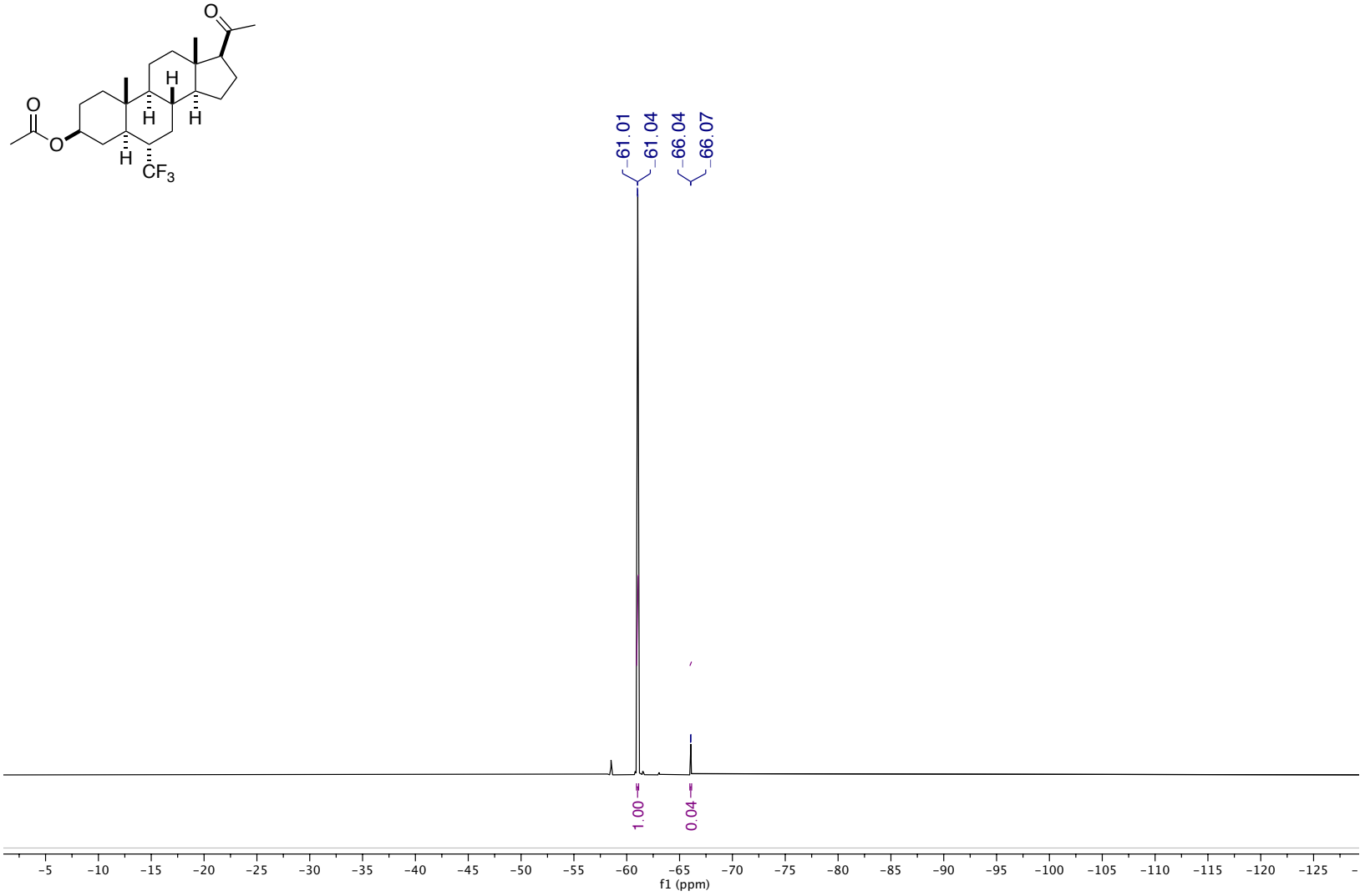
(3*S*,5*R*,6*S*,8*R*,9*S*,10*R*,13*S*,14*S*,17*S*)-17-Acetyl-10,13-dimethyl-6-(trifluoromethyl)hexadecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl acetate **(28)**

$^{13}$C-NMR (100 MHz, $CDCl_3$)



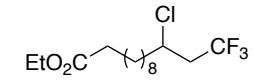
(3*S*,5*R*,6*S*,8*R*,9*S*,10*R*,13*S*,14*S*,17*S*)-17-Acetyl-10,13-dimethyl-6-(trifluoromethyl)hexadecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl acetate **(28)**

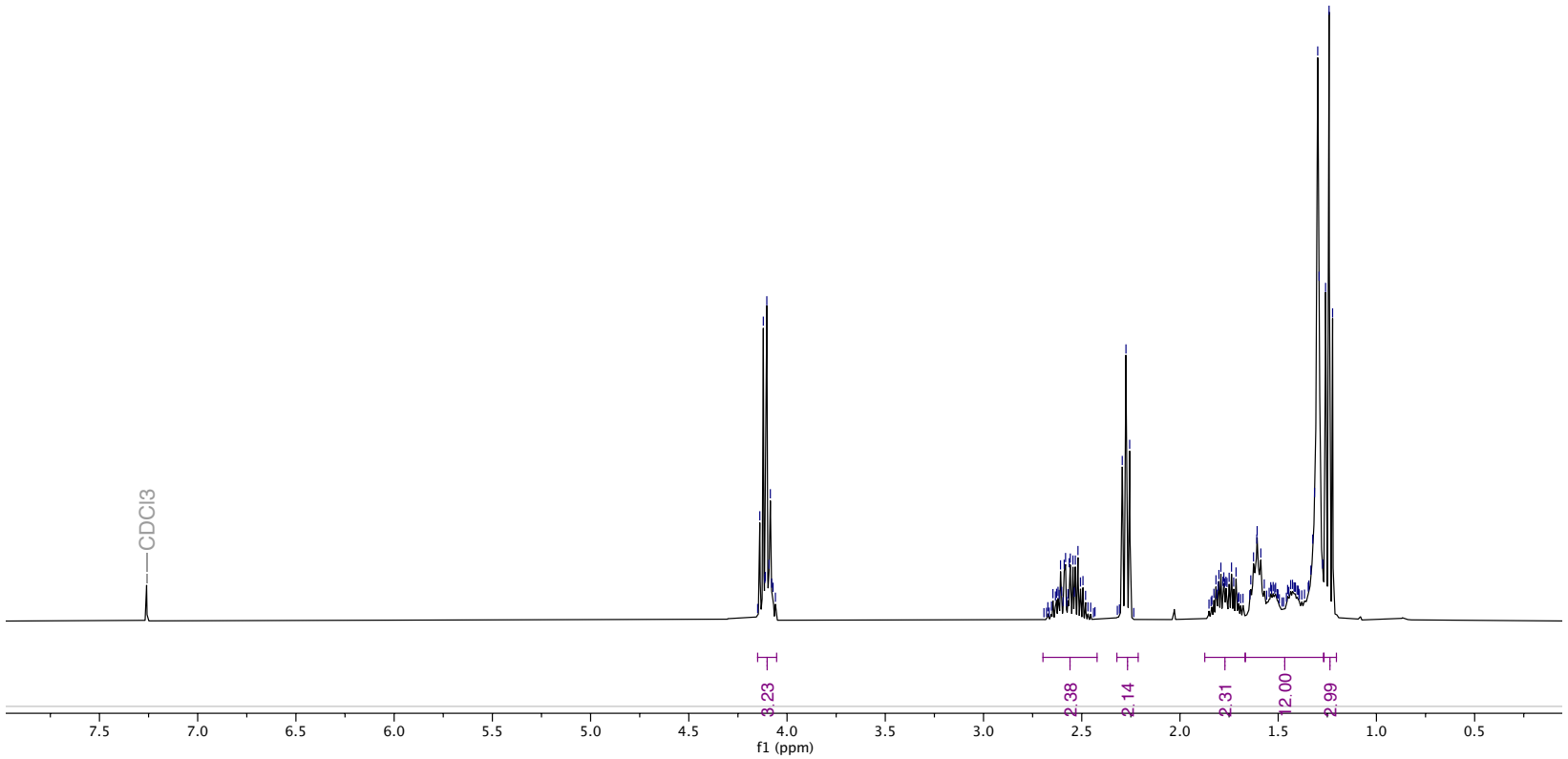
$^{19}$F-NMR (376 MHz, $CDCl_3$)



10-Chloro-2-(ethylperoxy)-12,12,12-trifluorododec-1-ene **(29)**

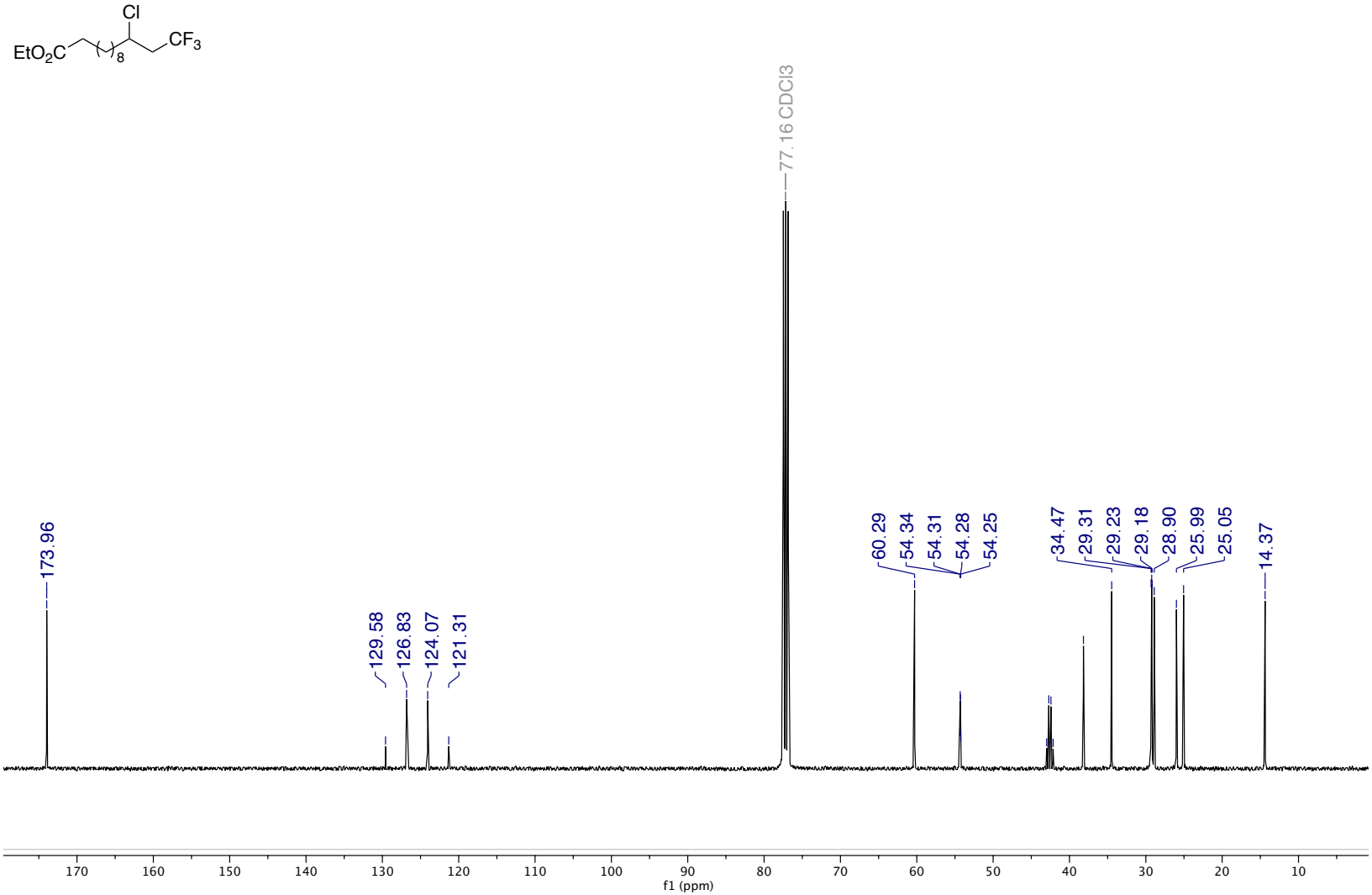
$^1$H-NMR (400 MHz, $CDCl_3$)



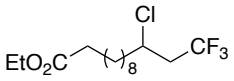



10-Chloro-2-(ethylperoxy)-12,12,12-trifluorododec-1-ene **(29)**

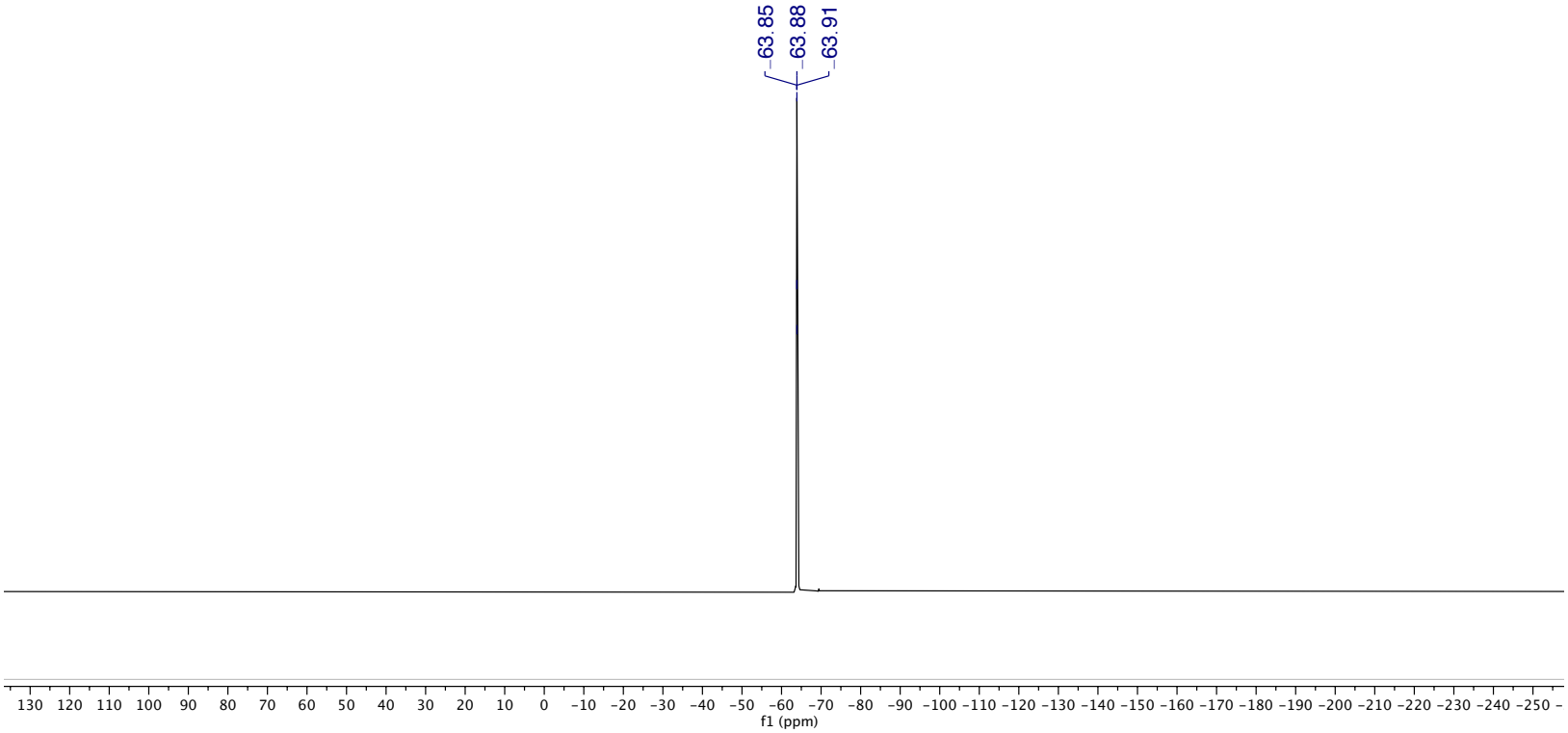
$^{13}$C-NMR (100 MHz, $CDCl_3$)



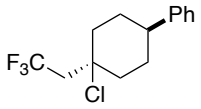
10-Chloro-2-(ethylperoxy)-12,12,12-trifluorododec-1-ene **(29)**



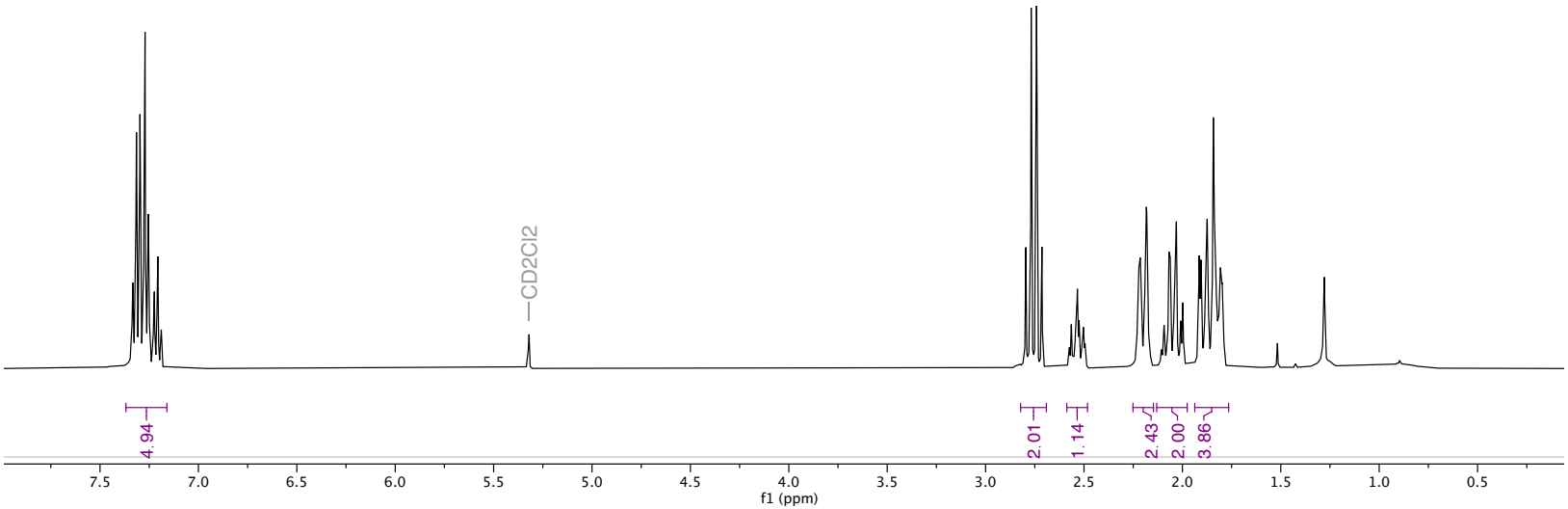

$^{19}$F-NMR (376 MHz, $CDCl_3$)



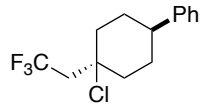
((1*S*,4*S*)-4-chloro-4-(2,2,2-trifluoroethyl)cyclohexyl)benzene **(30)**




$^{1}$H-NMR (400 MHz, $CD_2Cl_2$)



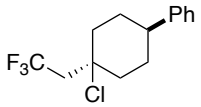
((1*S*,4*S*)-4-chloro-4-(2,2,2-trifluoroethyl)cyclohexyl)benzene **(30)**

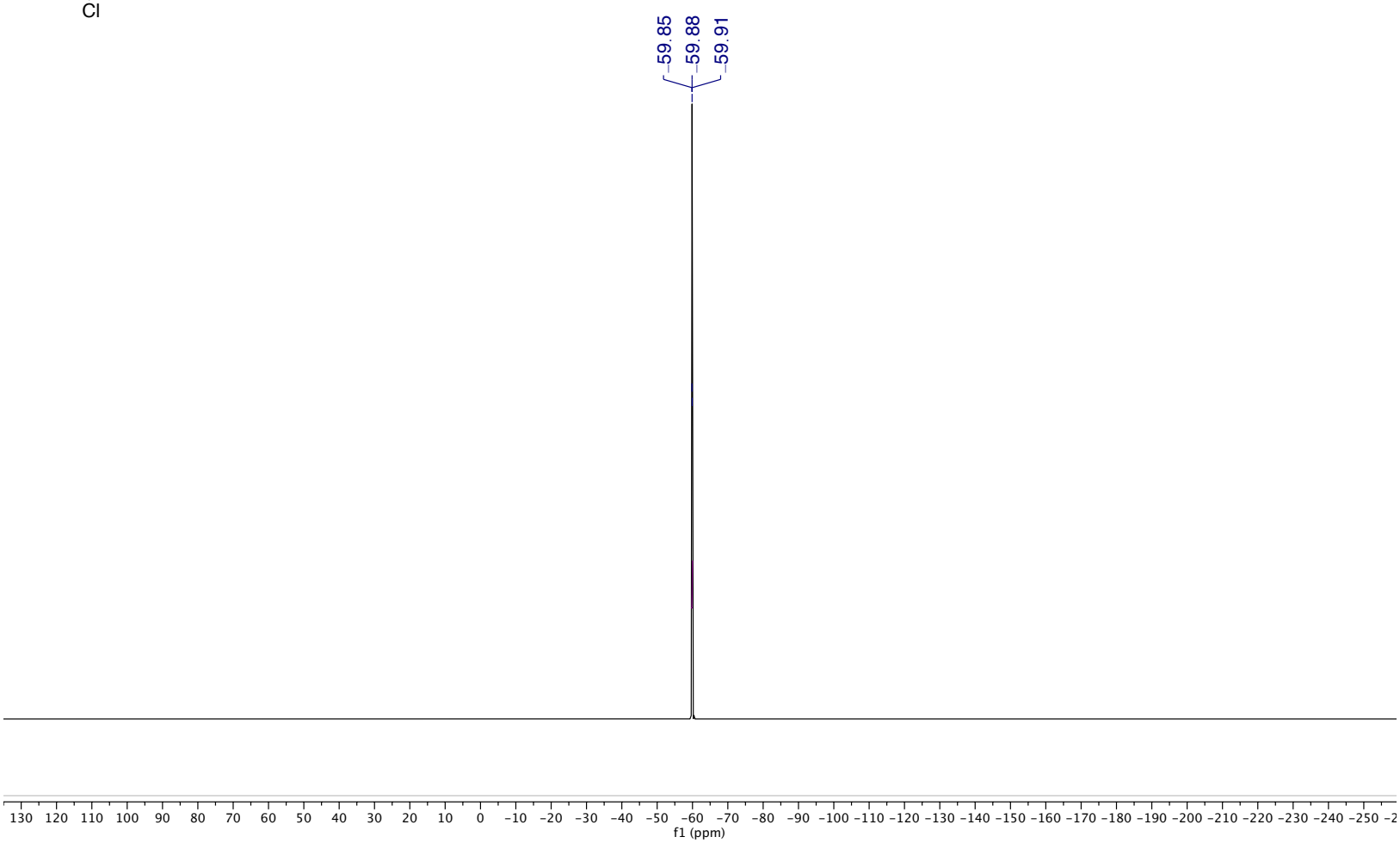



$^{13}$C-NMR (100 MHz, $CD_2Cl_2$)

((1*S*,4*S*)-4-chloro-4-(2,2,2-trifluoroethyl)cyclohexyl)benzene **(30)**

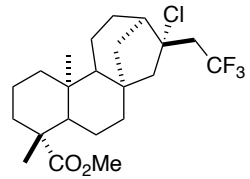
$^{19}$F-NMR (376 MHz, $CD_2Cl_2$)



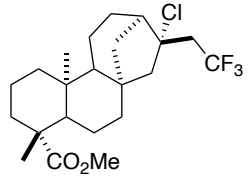
Methyl (4*R*,6a*S*,8*S*,9*R*,11b*S*)-8-chloro-4,11b-dimethyl-8-(2,2,2-trifluoroethyl)tetradecahydro-6a,9-methanocyclohepta[*a*]naphthalene-4-carboxylate **(31)**

$^1$H-NMR (400 MHz, $CDCl_3$)

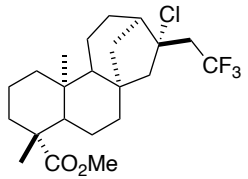


Methyl (4*R*,6a*S*,8*S*,9*R*,11b*S*)-8-chloro-4,11b-dimethyl-8-(2,2,2-trifluoroethyl)tetradecahydro-6a,9-methanocyclohepta[*a*]naphthalene-4-carboxylate **(31)**

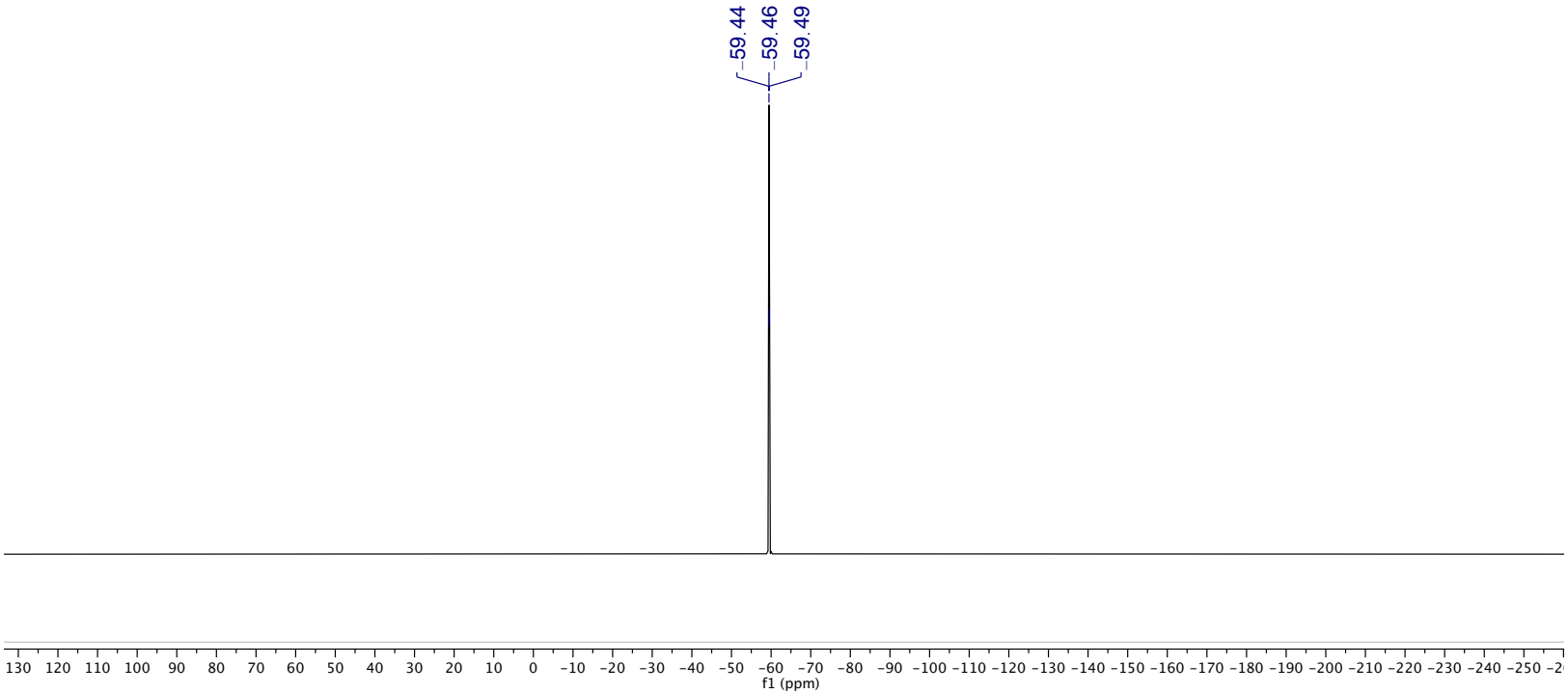
$^{13}$C-NMR (100 MHz, $CDCl_3$)



Methyl (4*R*,6a*S*,8*S*,9*R*,11b*S*)-8-chloro-4,11b-dimethyl-8-(2,2,2-trifluoroethyl)tetradecahydro-6a,9-methanocyclohepta[*a*]naphthalene-4-carboxylate **(31)**

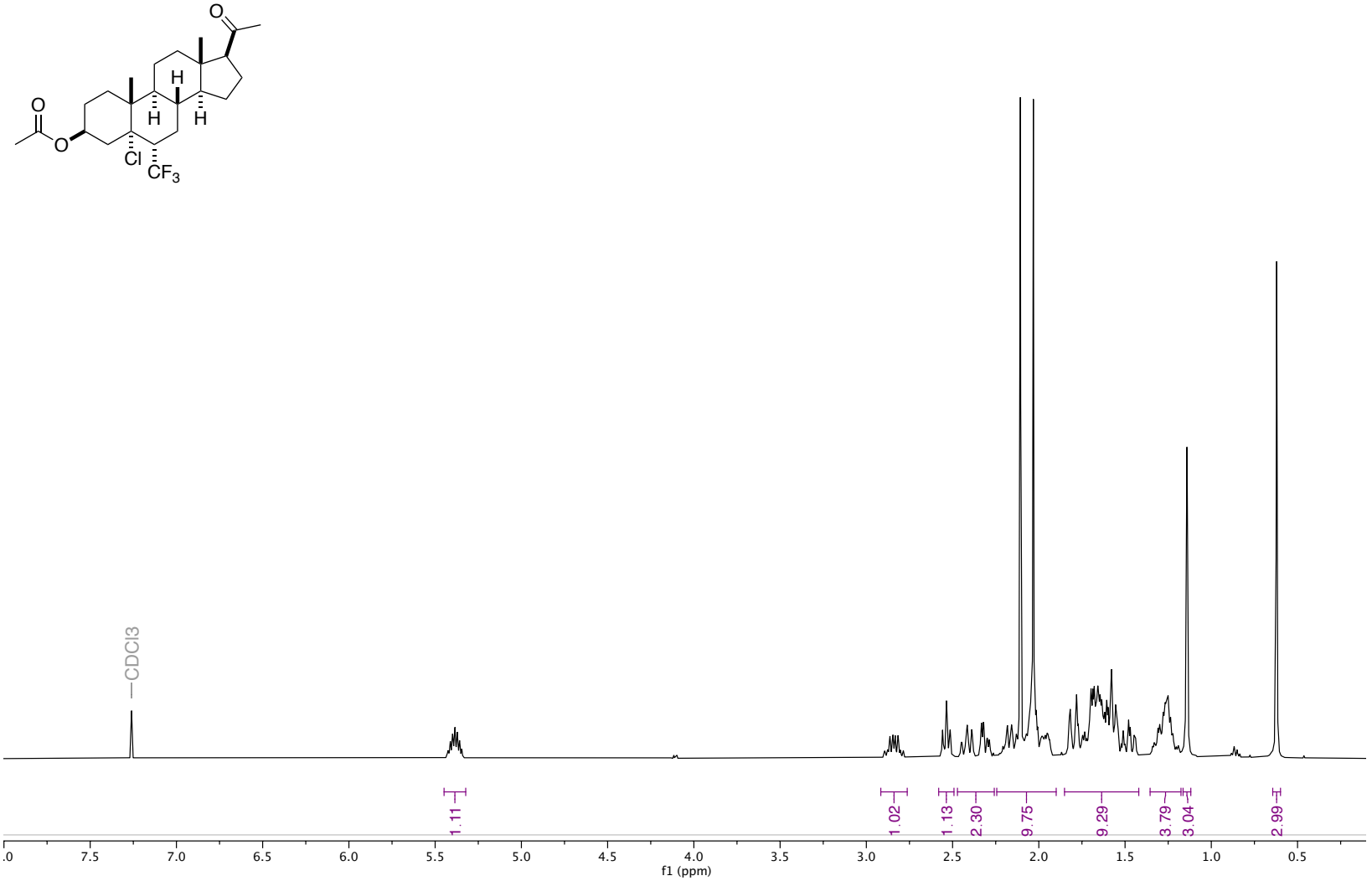



$^{19}$F-NMR (376 MHz, $CDCl_3$)



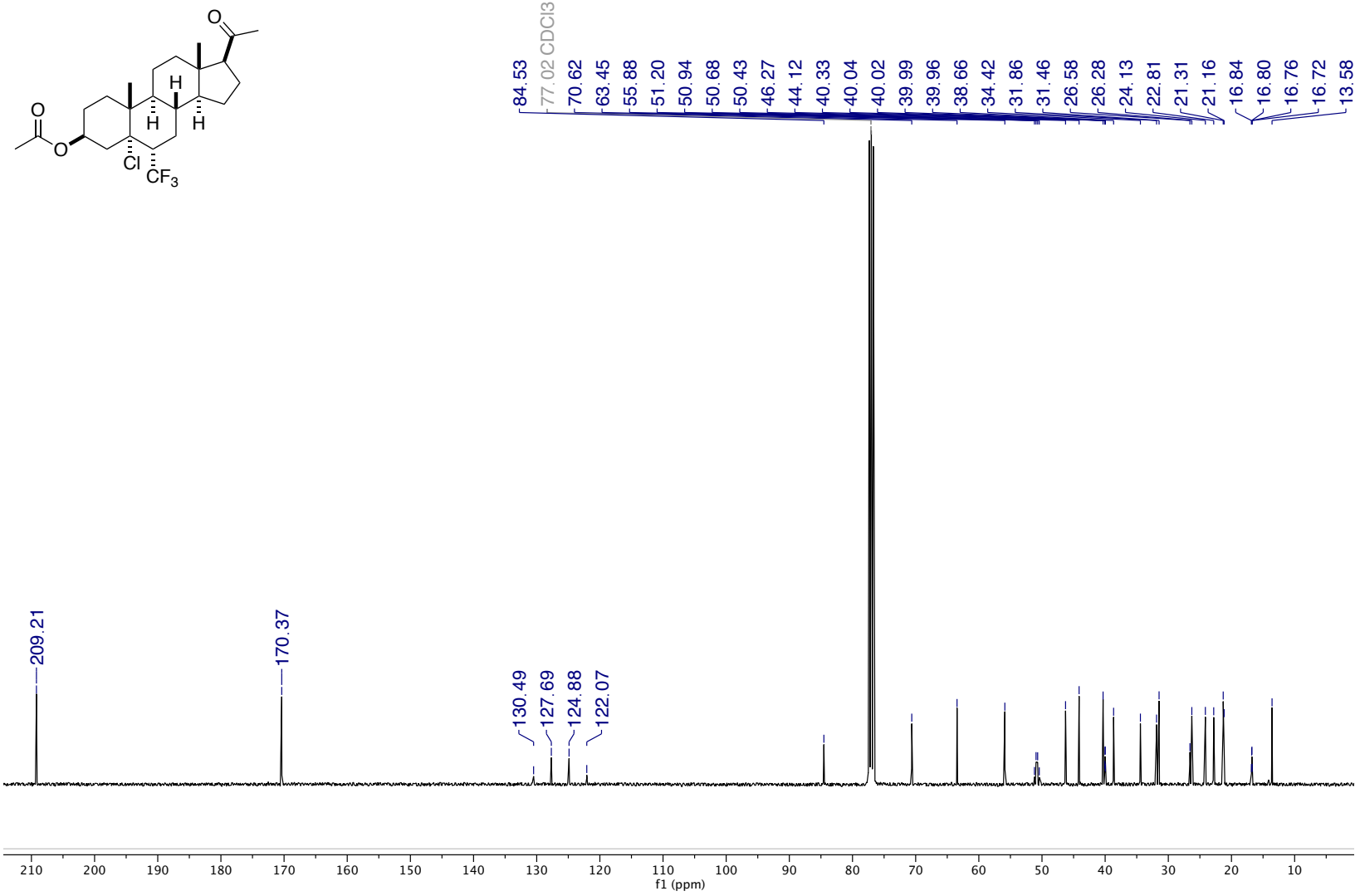
(3*S*,5*S*,6*R*,8*S*,9*S*,10*R*,13*S*,14*S*,17*S*)-17-acetyl-5-chloro-10,13-dimethyl-6-(trifluoromethyl)-hexadecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl acetate **(32)**

$^1$H-NMR (400 MHz, $CDCl_3$)

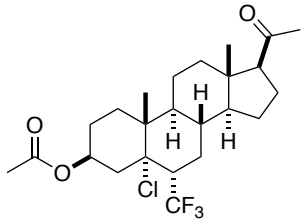


(3*S*,5*S*,6*R*,8*S*,9*S*,10*R*,13*S*,14*S*,17*S*)-17-acetyl-5-chloro-10,13-dimethyl-6-(trifluoromethyl)-hexadecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl acetate **(32)**

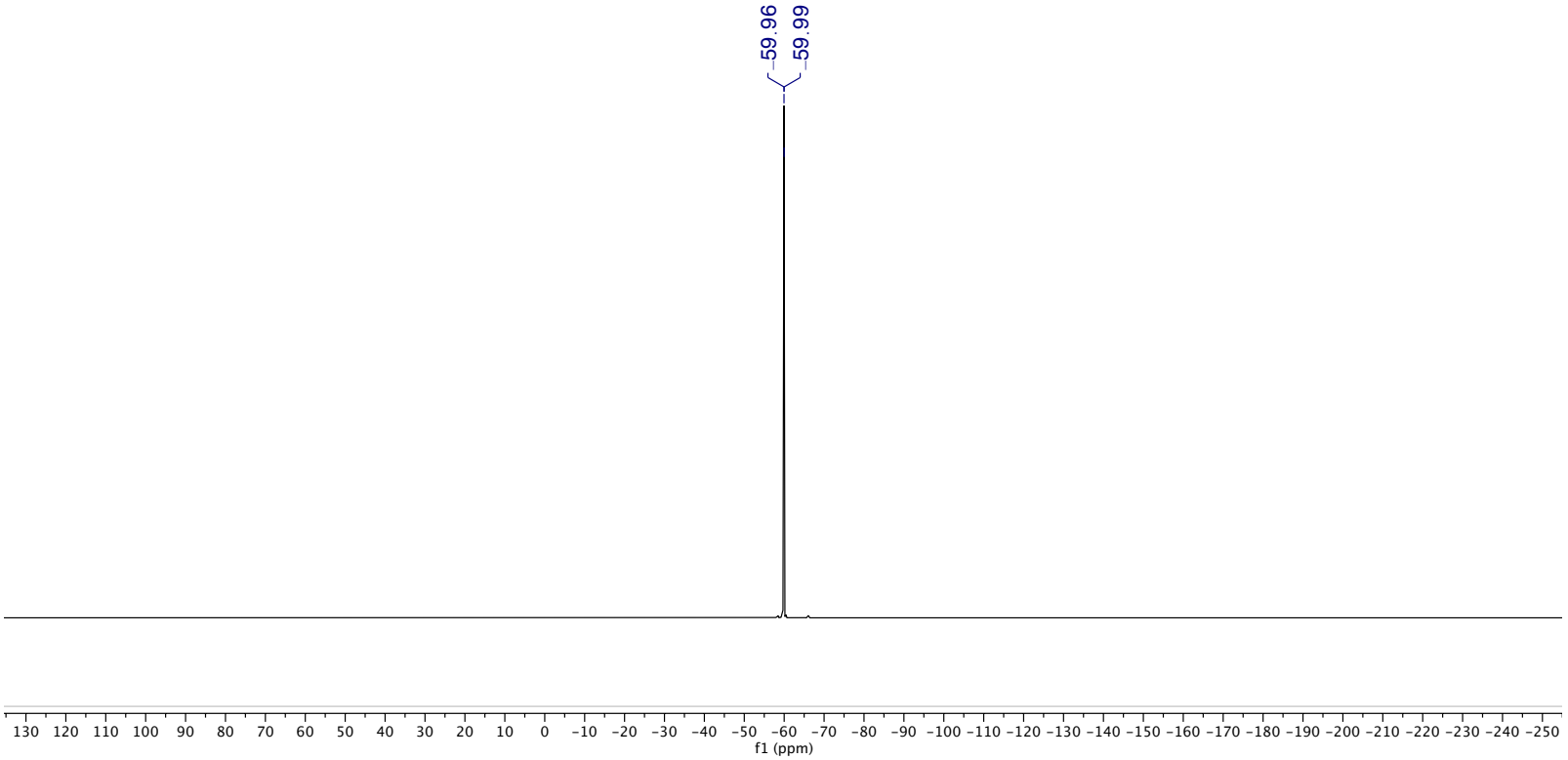
$^{13}$C-NMR (100 MHz, $CDCl_3$)



(3*S*,5*S*,6*R*,8*S*,9*S*,10*R*,13*S*,14*S*,17*S*)-17-acetyl-5-chloro-10,13-dimethyl-6-(trifluoromethyl)-hexadecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl acetate **(32)**

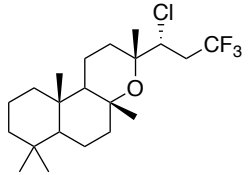


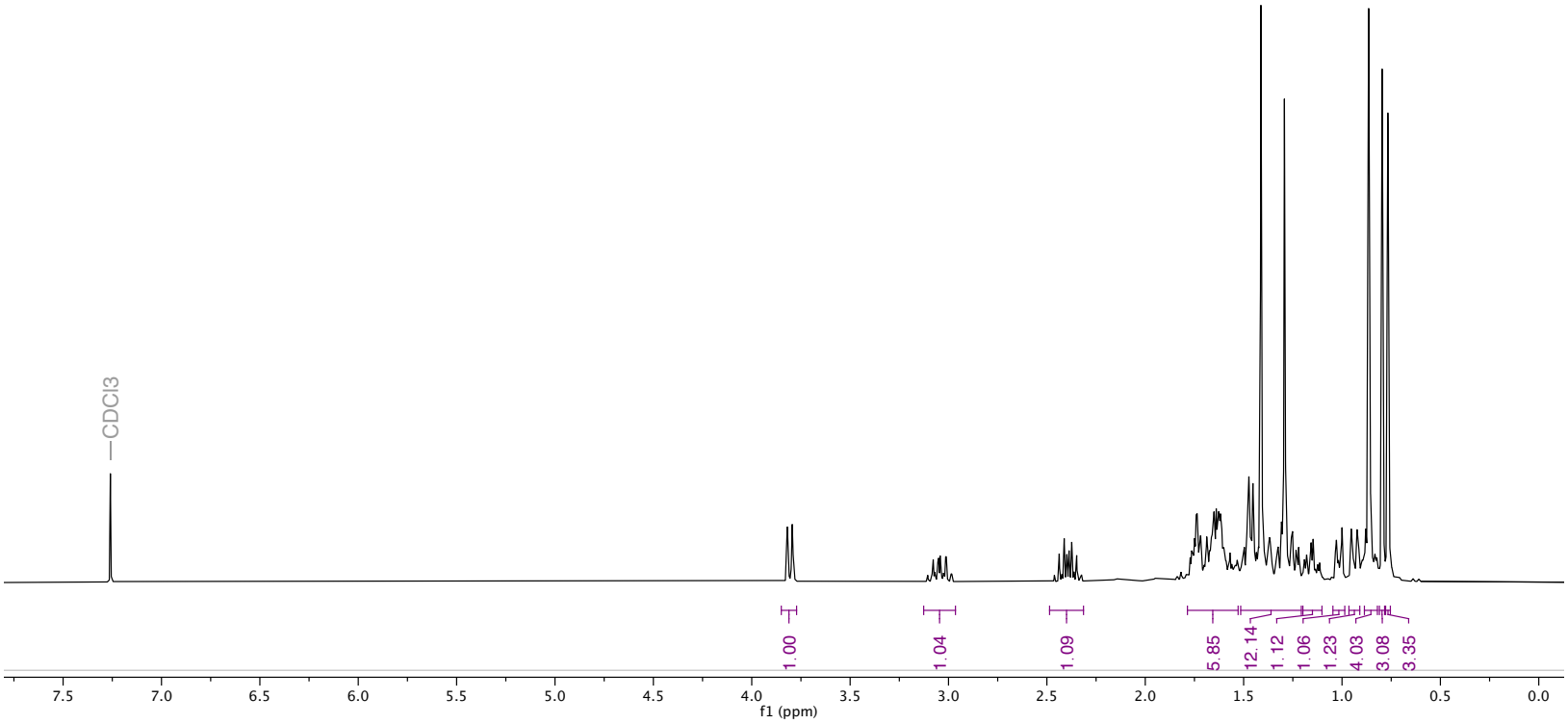

$^{19}$F-NMR (376 MHz, $CDCl_3$)



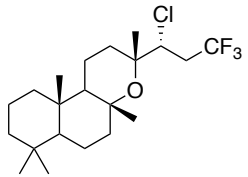
(3*R*,4a*R*,10a*S*)-3-((*R*)-1-chloro-3,3,3-trifluoropropyl)-3,4a,7,7,10a-pentamethyldodecahydro-1*H*-benzo[*f*]chromene (**33**-minor)

$^1$H-NMR (400 MHz, $CDCl_3$)



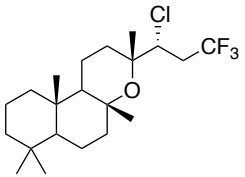



(3*R*,4a*R*,10a*S*)-3-((*R*)-1-chloro-3,3,3-trifluoropropyl)-3,4a,7,7,10a-pentamethyldodecahydro-1*H*-benzo[*f*]chromene (**33**-minor)

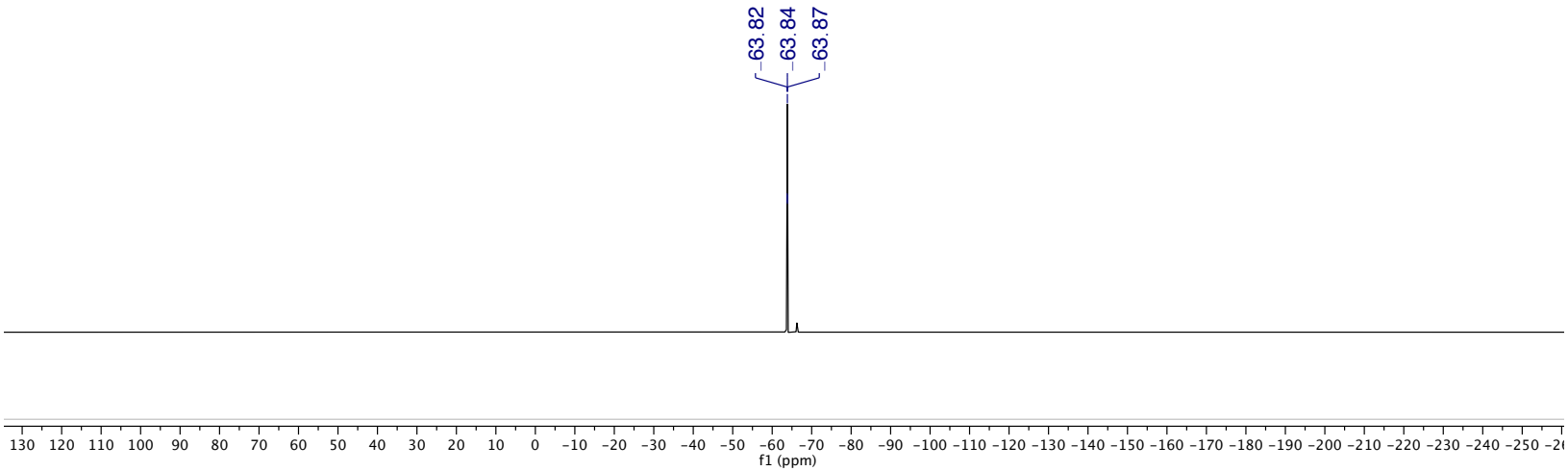



$^{13}$C-NMR (100 MHz, $CDCl_3$)

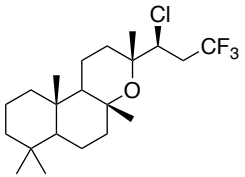
(3*R*,4a*R*,10a*S*)-3-((*R*)-1-chloro-3,3,3-trifluoropropyl)-3,4a,7,7,10a-pentamethyldodecahydro-1*H*-benzo[*f*]chromene (**33**-minor)



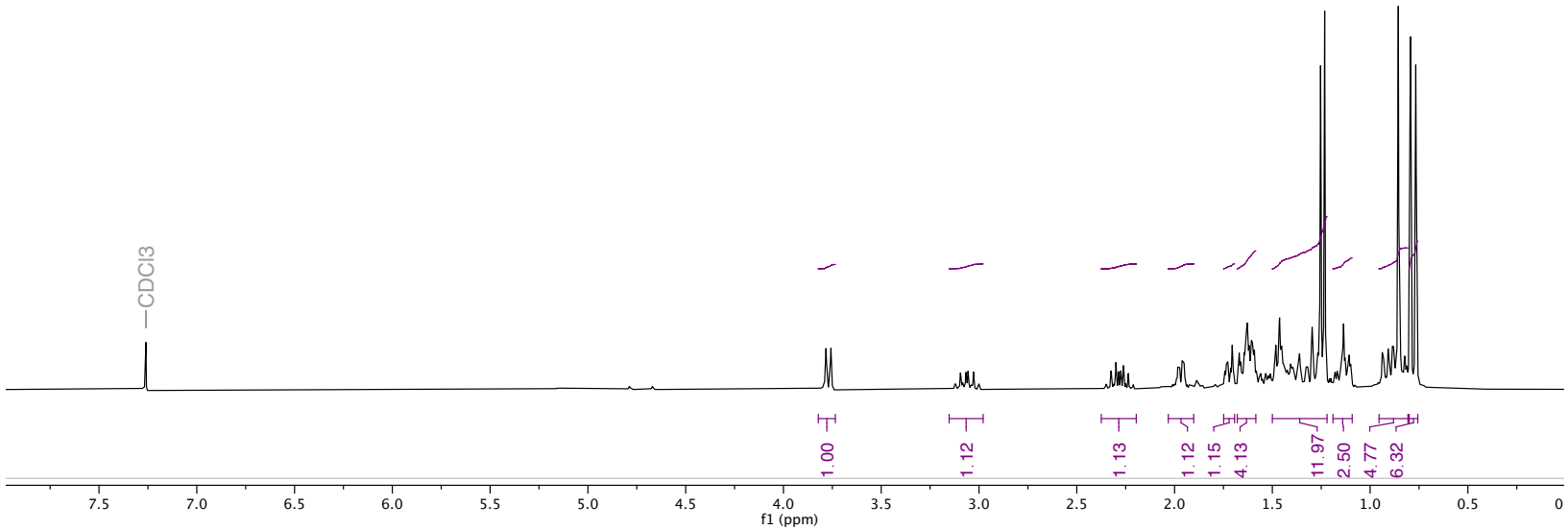

$^{19}$F-NMR (376 MHz, $CDCl_3$)



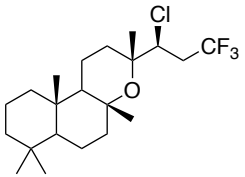
(3*R*,4a*R*,10a*S*)-3-((*S*)-1-chloro-3,3,3-trifluoropropyl)-3,4a,7,7,10a-pentamethyldodecahydro-1*H*-benzo[*f*]chromene (**33**-major)



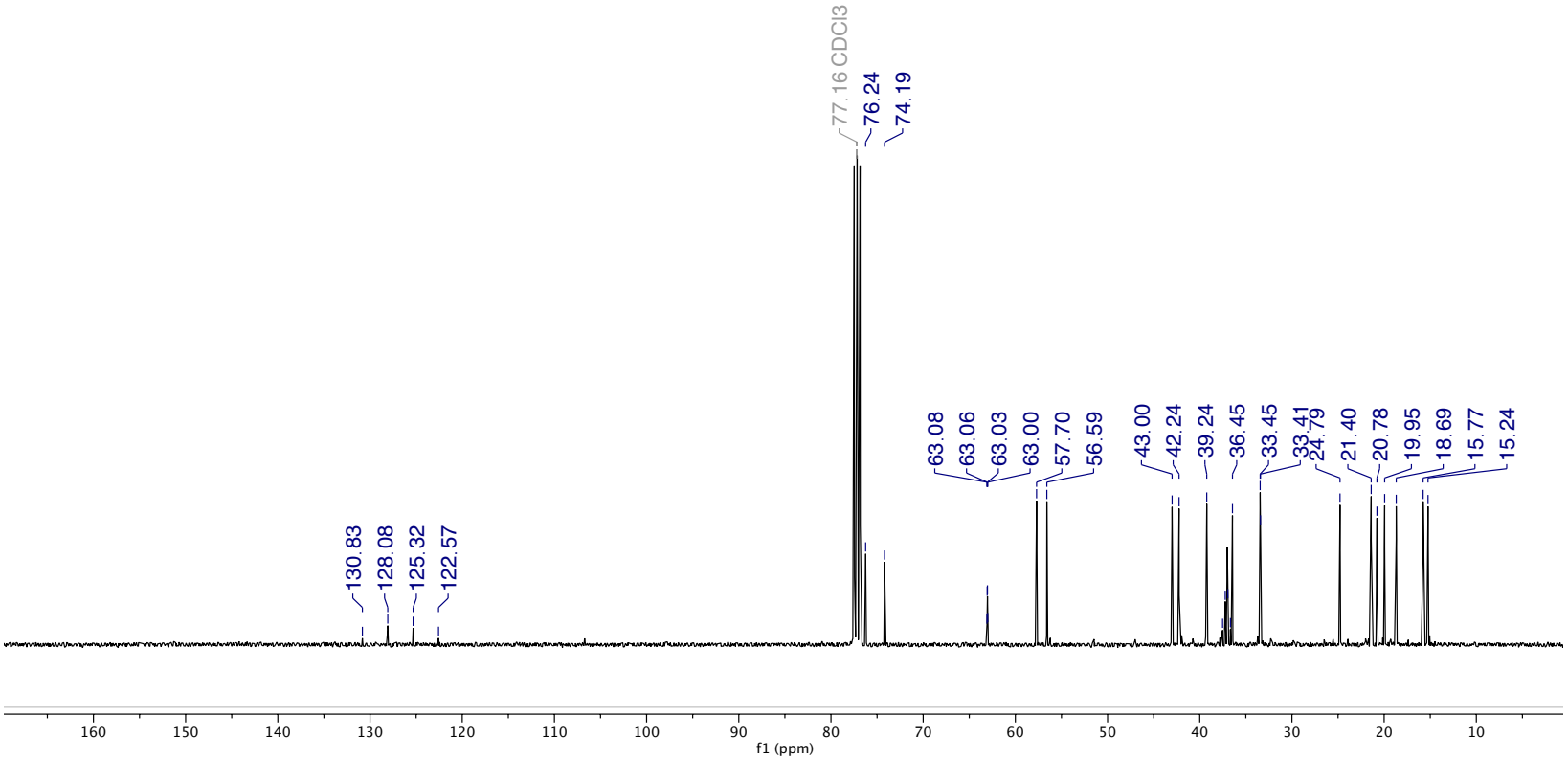

$^1$H-NMR (400 MHz, $CDCl_3$)



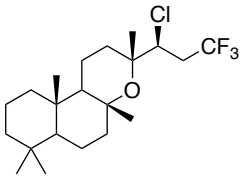
(3*R*,4a*R*,10a*S*)-3-((*S*)-1-chloro-3,3,3-trifluoropropyl)-3,4a,7,7,10a-pentamethyldodecahydro-1*H*-benzo[*f*]chromene (**33**-major)



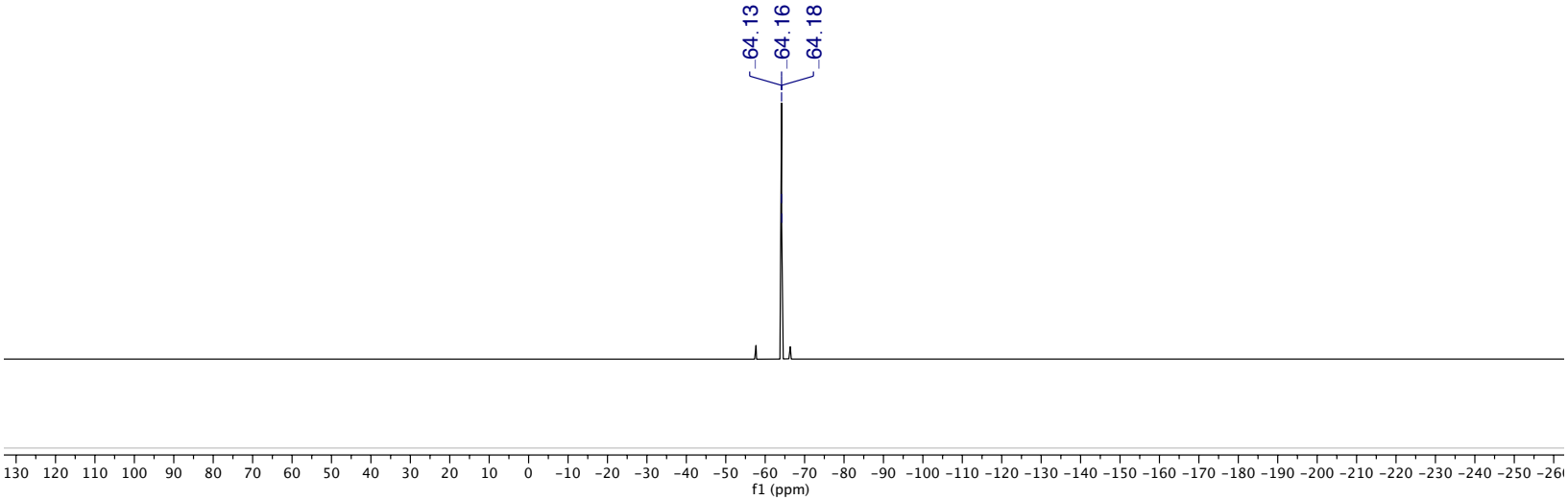

$^{13}$C-NMR (100 MHz, $CDCl_3$)



(3*R*,4a*R*,10a*S*)-3-((*S*)-1-chloro-3,3,3-trifluoropropyl)-3,4a,7,7,10a-pentamethyldodecahydro-1*H*-benzo[*f*]chromene (**33**-major)




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

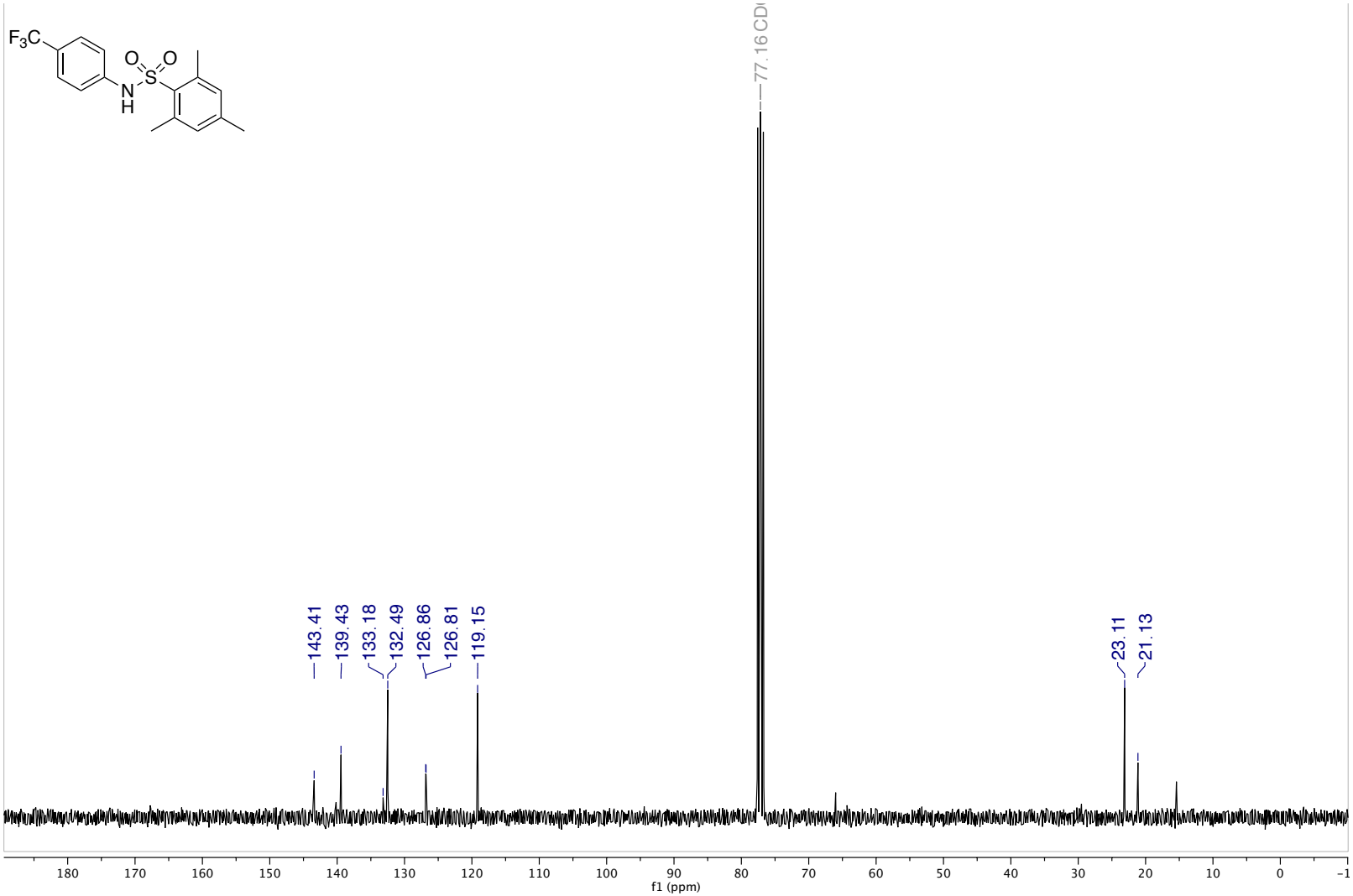


## 7.2 NMR Spectra Chapter 4

**A Mild Radical Procedure for Deiodofluorination of Secondary and Tertiary Alkyl Iodides and Related Processes**

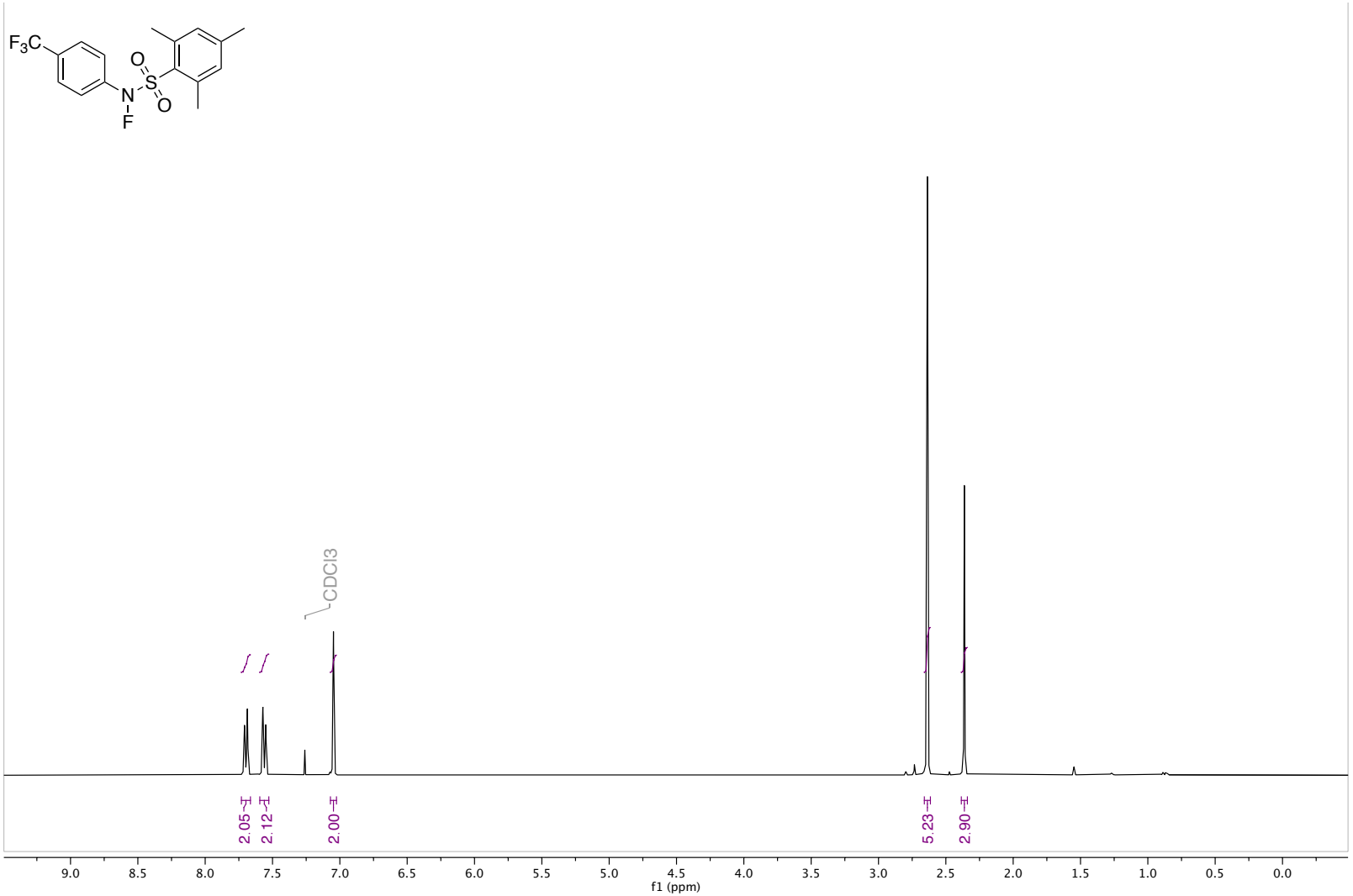
2,4,6-trimethyl-*N*-(4-(trifluoromethyl)phenyl)benzenesulfonamide

$^{13}$C-NMR (75 MHz, $CDCl_3$)



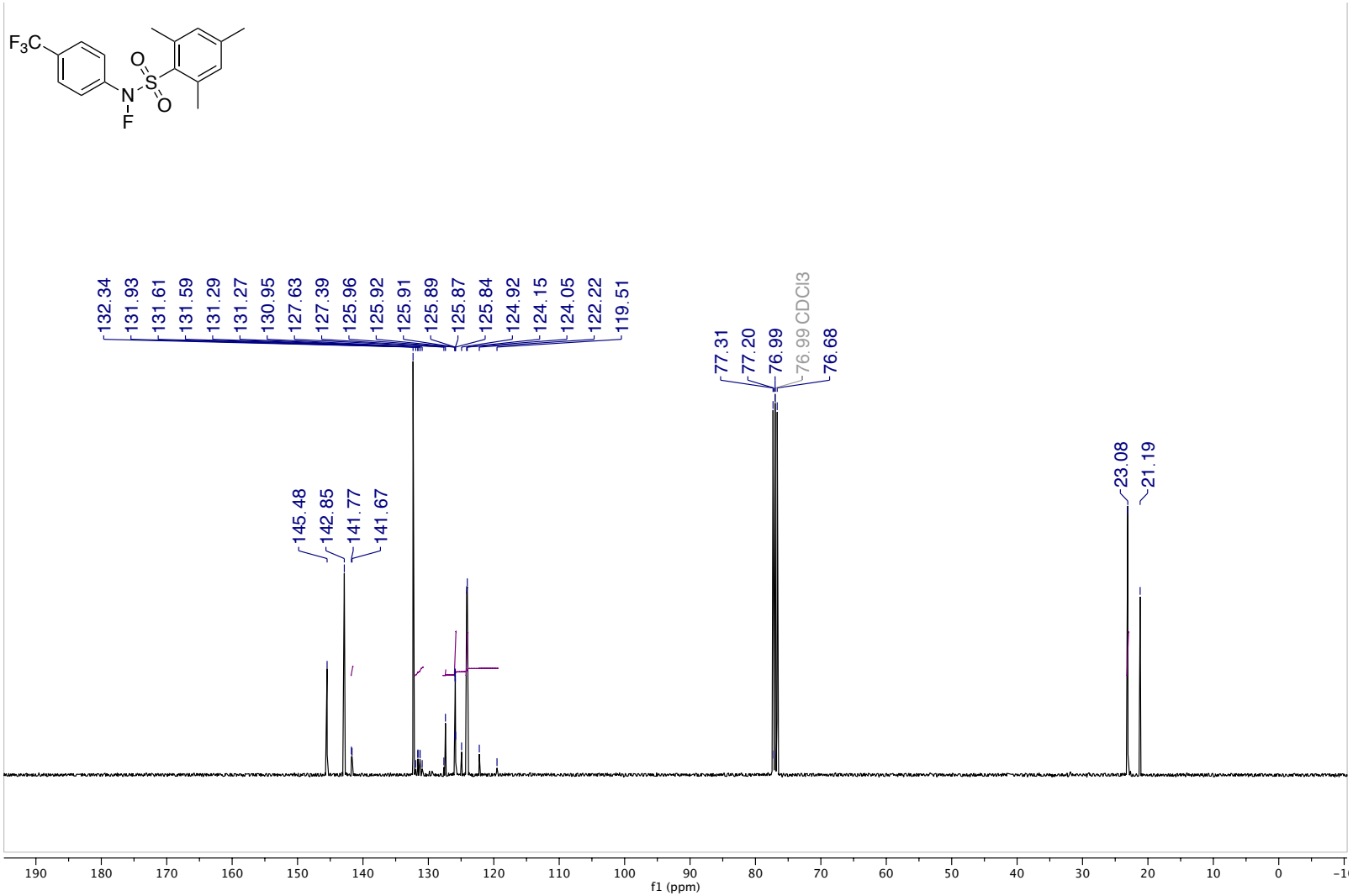
*N*-fluoro-2,4,6-trimethyl-*N*-(4-(trifluoromethyl)phenyl)benzenesulfonamide

$^1$H-NMR (400 MHz, $CDCl_3$)



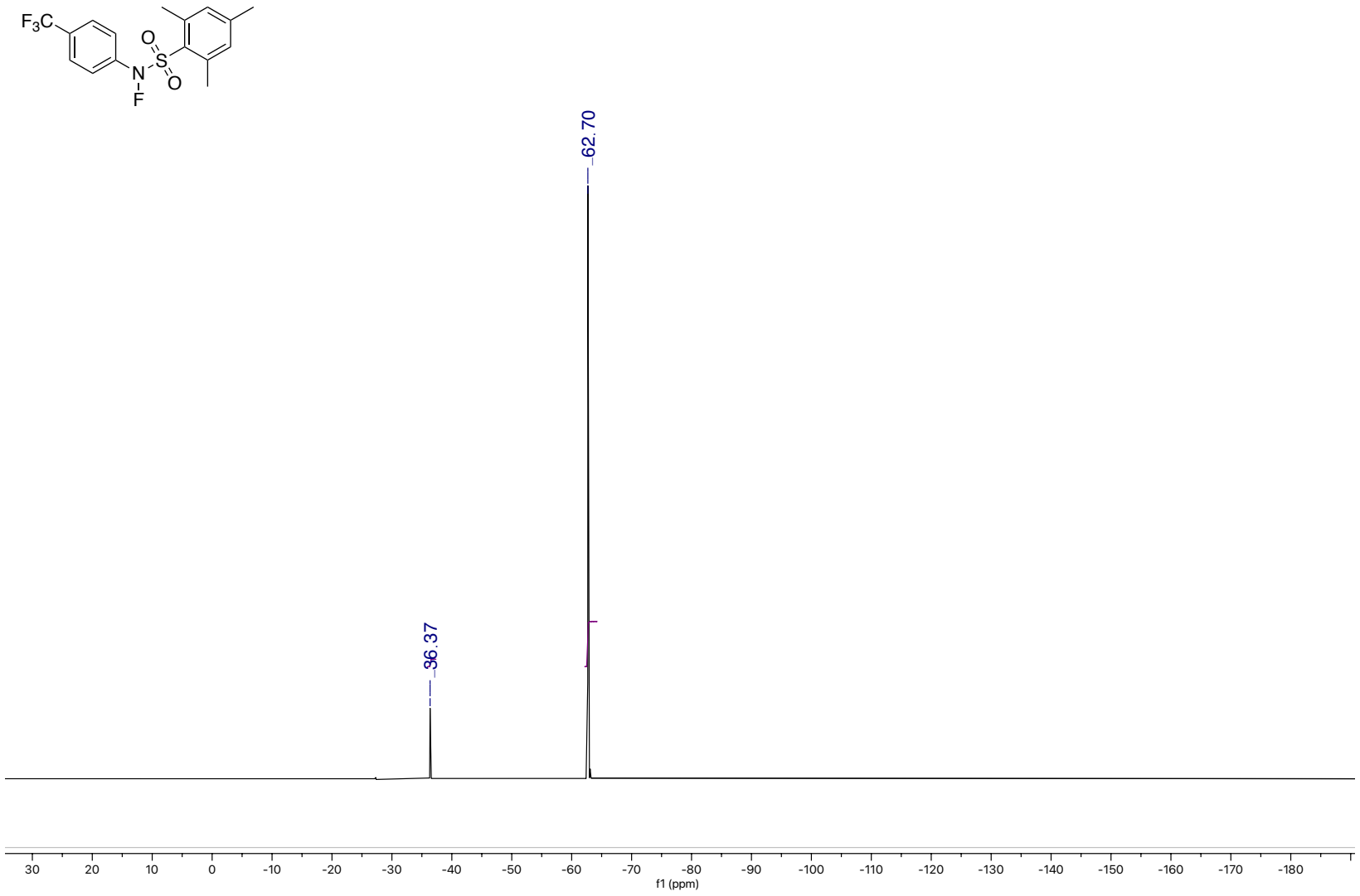
*N*-fluoro-2,4,6-trimethyl-*N*-(4-(trifluoromethyl)phenyl)benzenesulfonamide

$^{13}$C-NMR (100 MHz, $CDCl_3$)



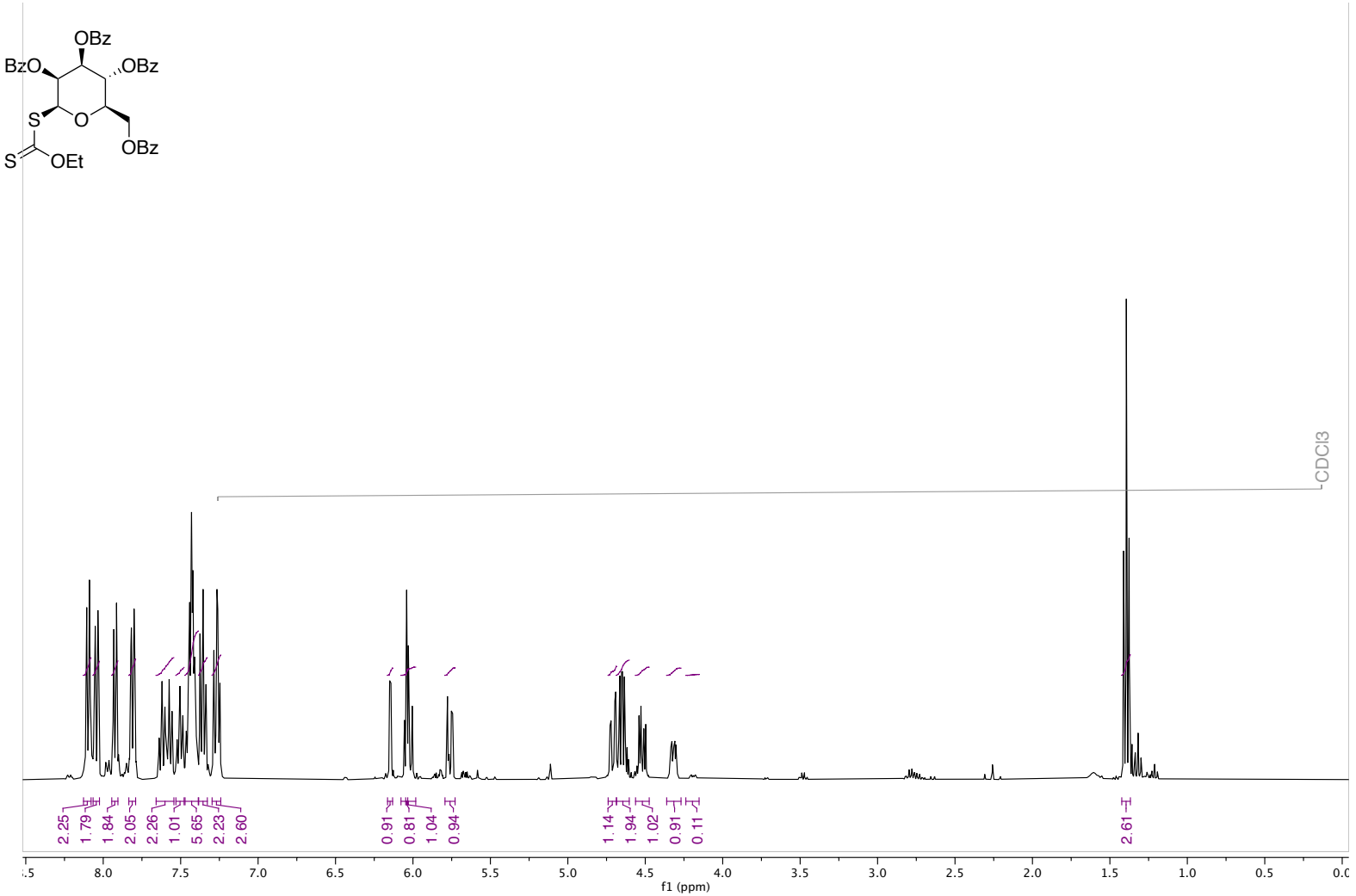
*N*-fluoro-2,4,6-trimethyl-*N*-(4-(trifluoromethyl)phenyl)benzenesulfonamide

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



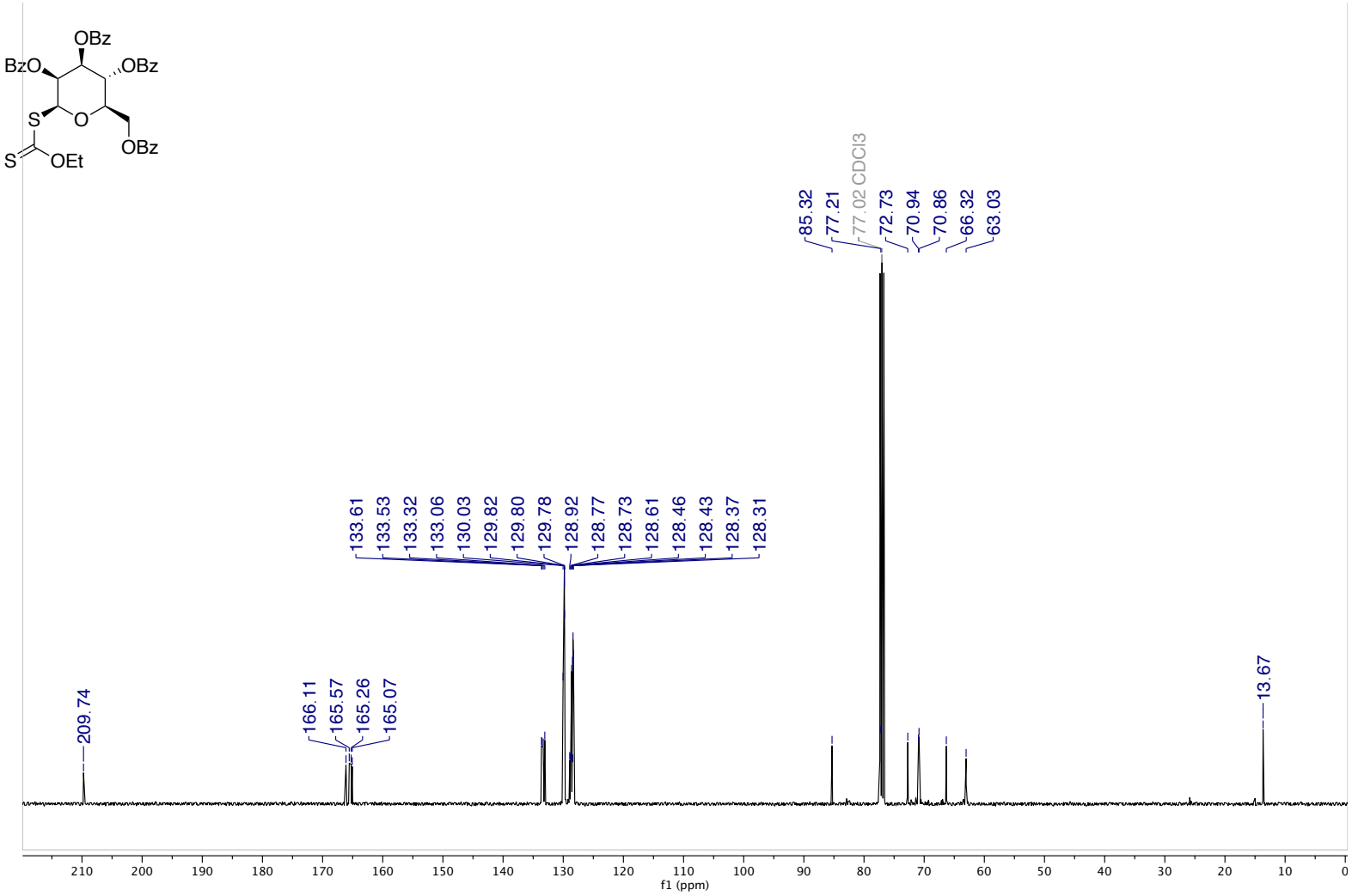
2,3,4,6-Tetra-*O*-benzoyl-α-D-mannopyranosyl xanthate (SI-3)

$^{1}$H-NMR (400 MHz, $CDCl_3$)



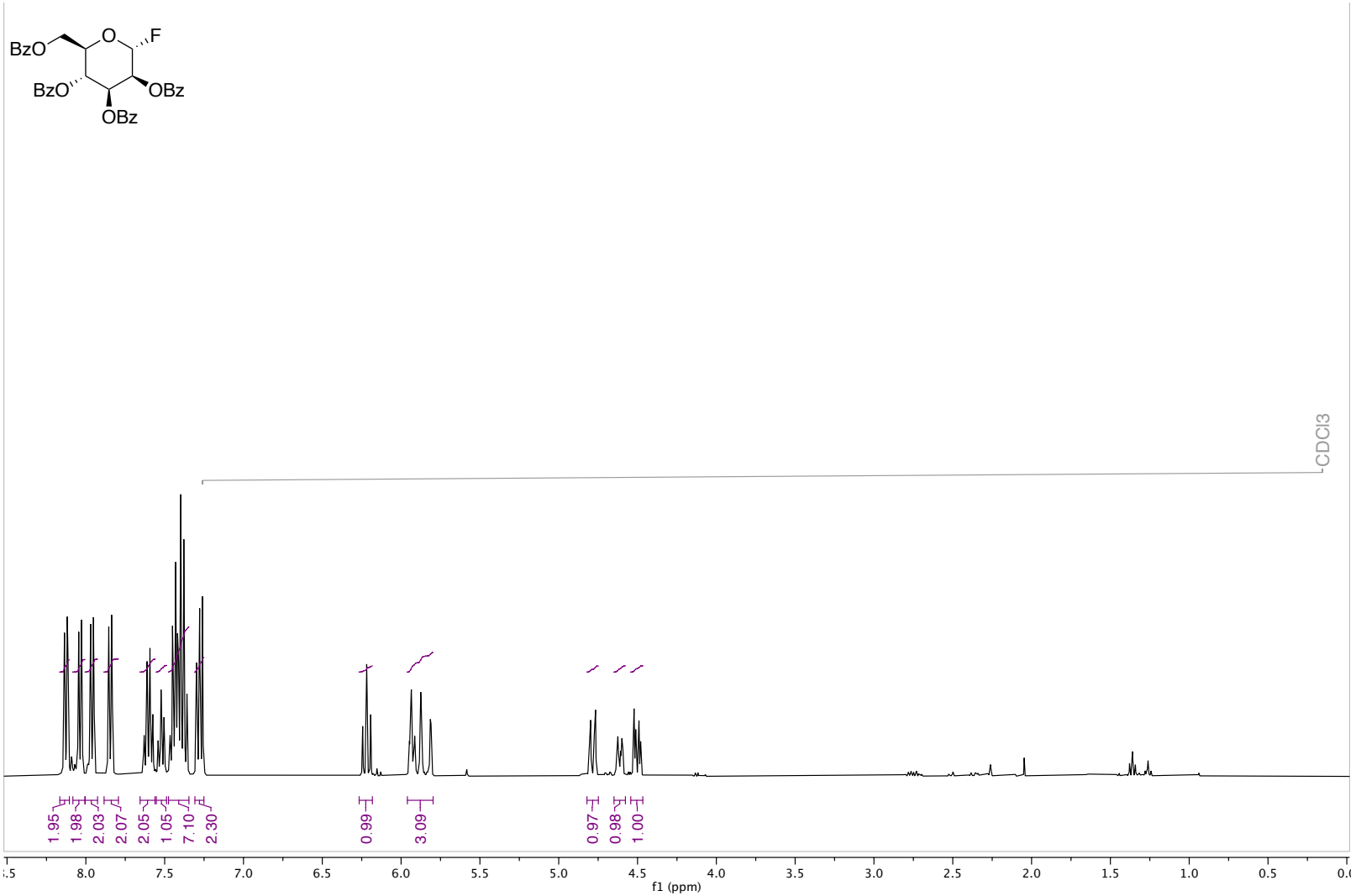
2,3,4,6-Tetra-*O*-benzoyl-α-D-mannopyranosyl xanthate (SI-3)

$^{13}$C-NMR (100 MHz, $CDCl_3$)



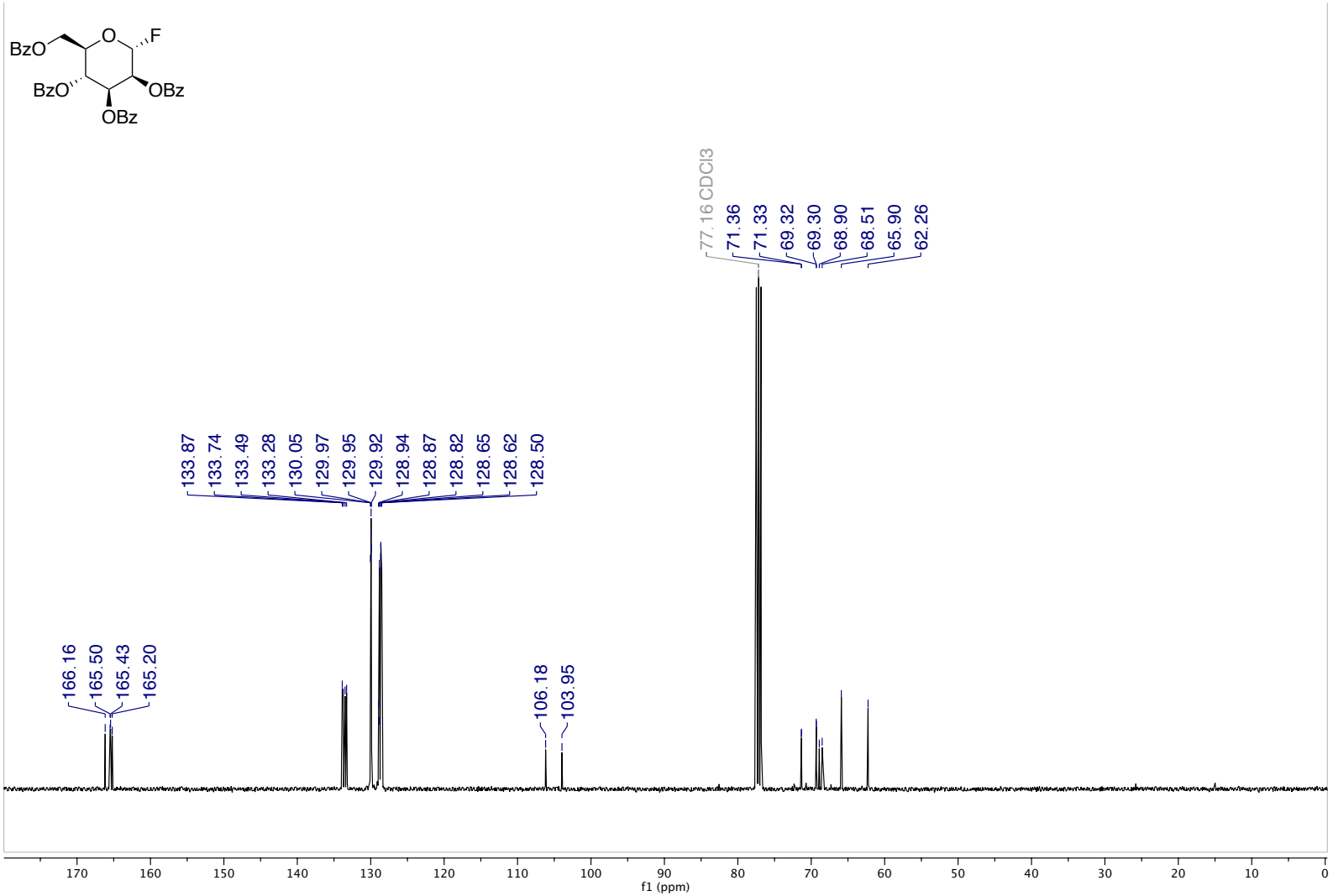
(2*R*,3*R*,4*S*,5*S*,6*R*)-2-((benzoyloxy)methyl)-6-fluorotetrahydro-2*H*-pyran-3,4,5-triyl tribenzoate

$^{1}$H-NMR (400 MHz, $CDCl_3$)



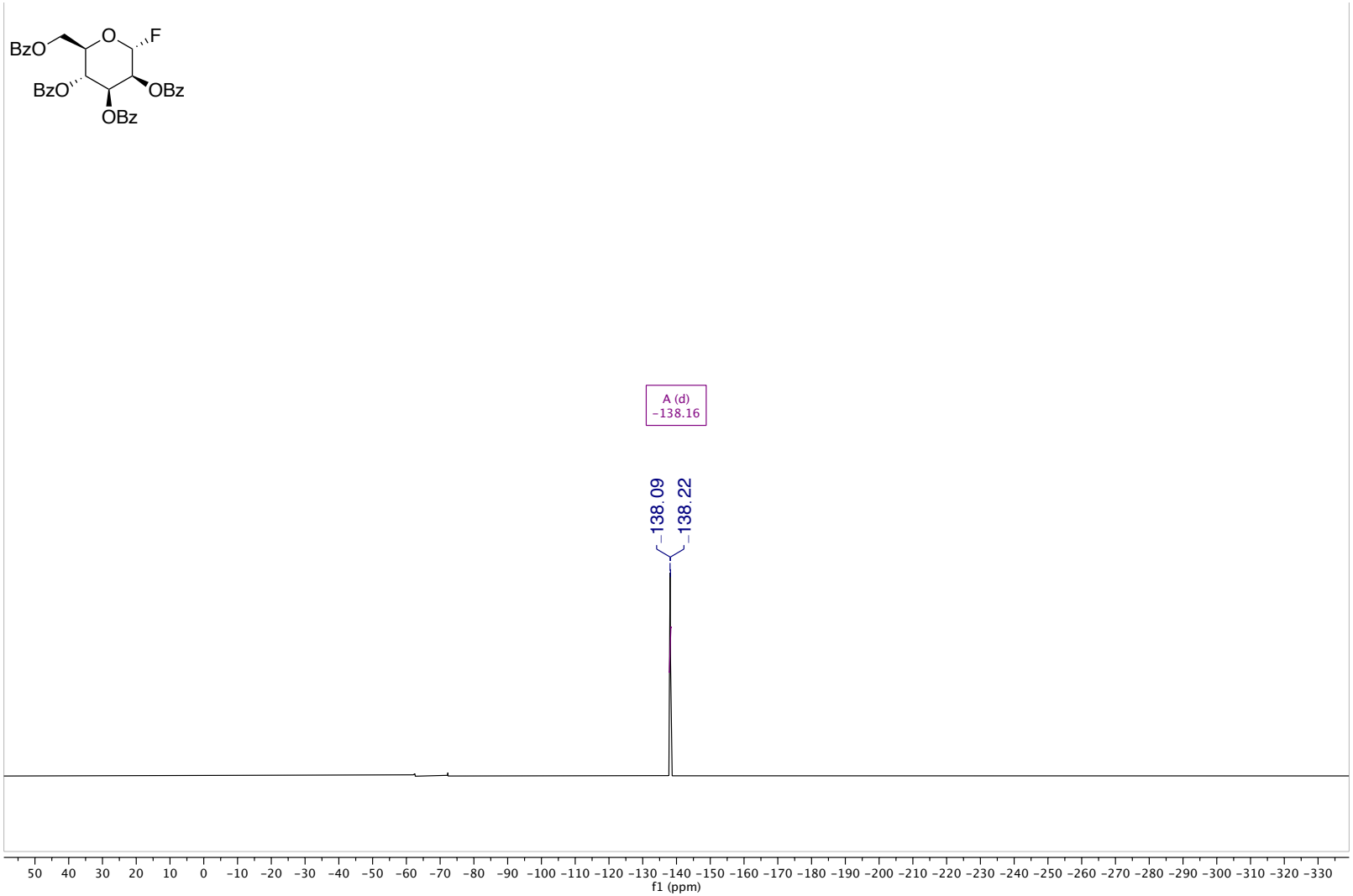
(2*R*,3*R*,4*S*,5*S*,6*R*)-2-((benzoyloxy)methyl)-6-fluorotetrahydro-2*H*-pyran-3,4,5-triyl tribenzoate

$^{13}$C-NMR (100 MHz, $CDCl_3$)



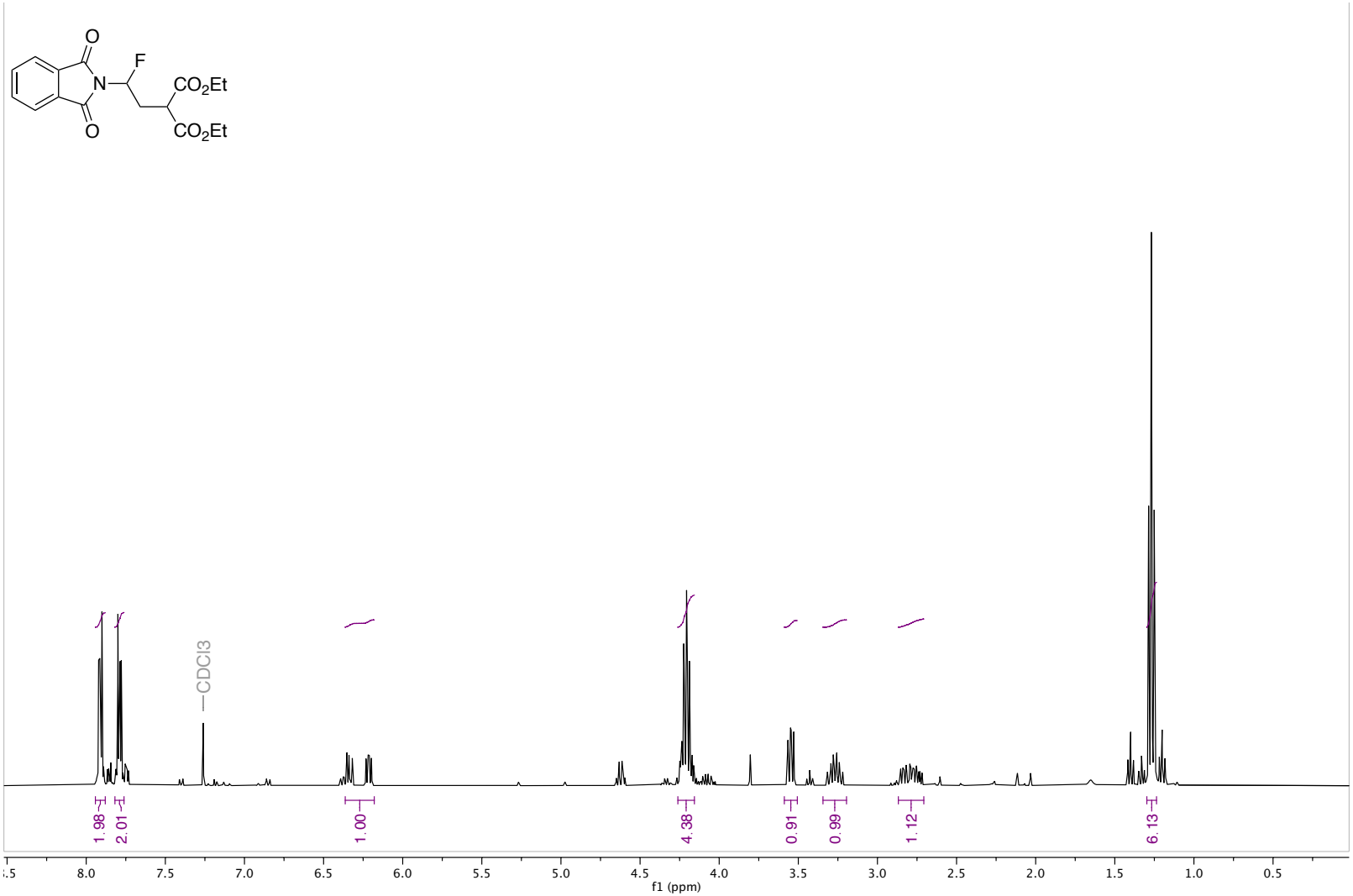
(2*R*,3*R*,4*S*,5*S*,6*R*)-2-((benzoyloxy)methyl)-6-fluorotetrahydro-2*H*-pyran-3,4,5-triyl tribenzoate

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



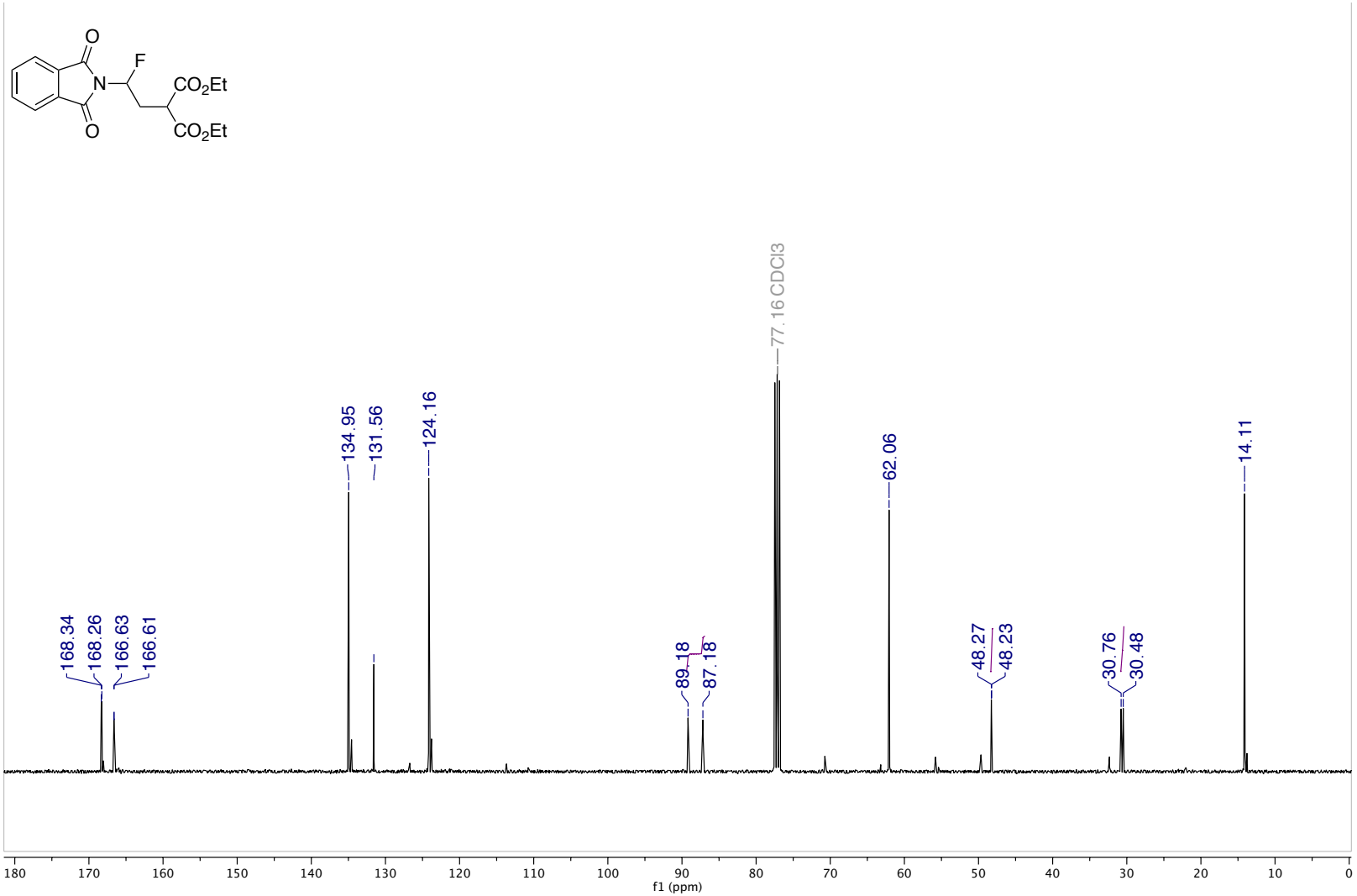
Diethyl 2-(2-(1,3-dioxoisoindolin-2-yl)-2-fluoroethyl)malonate

$^1$H-NMR (400 MHz, $CDCl_3$)



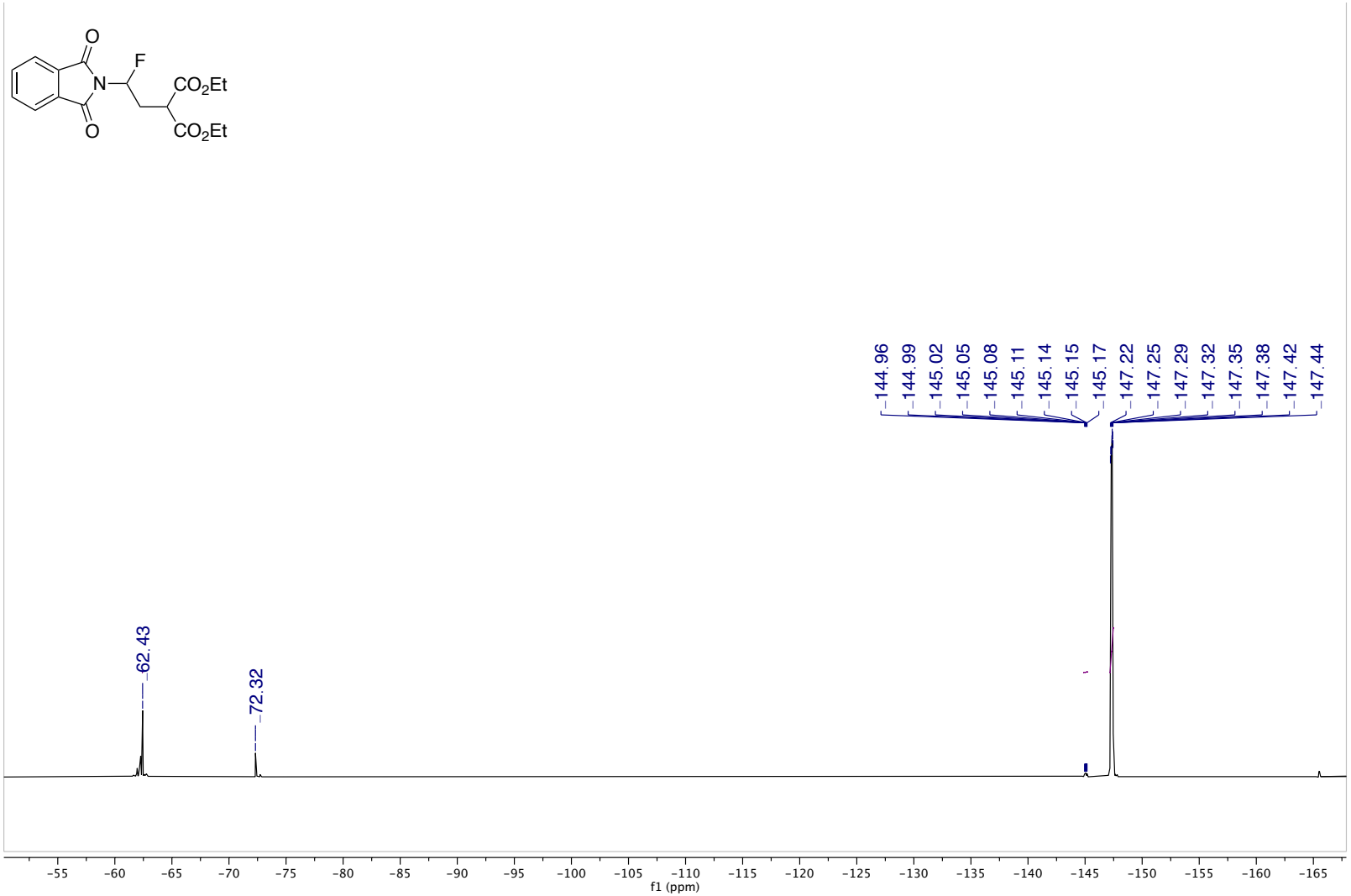
Diethyl 2-(2-(1,3-dioxoisoindolin-2-yl)-2-fluoroethyl)malonate

$^{13}$C-NMR (100 MHz, $CDCl_3$)



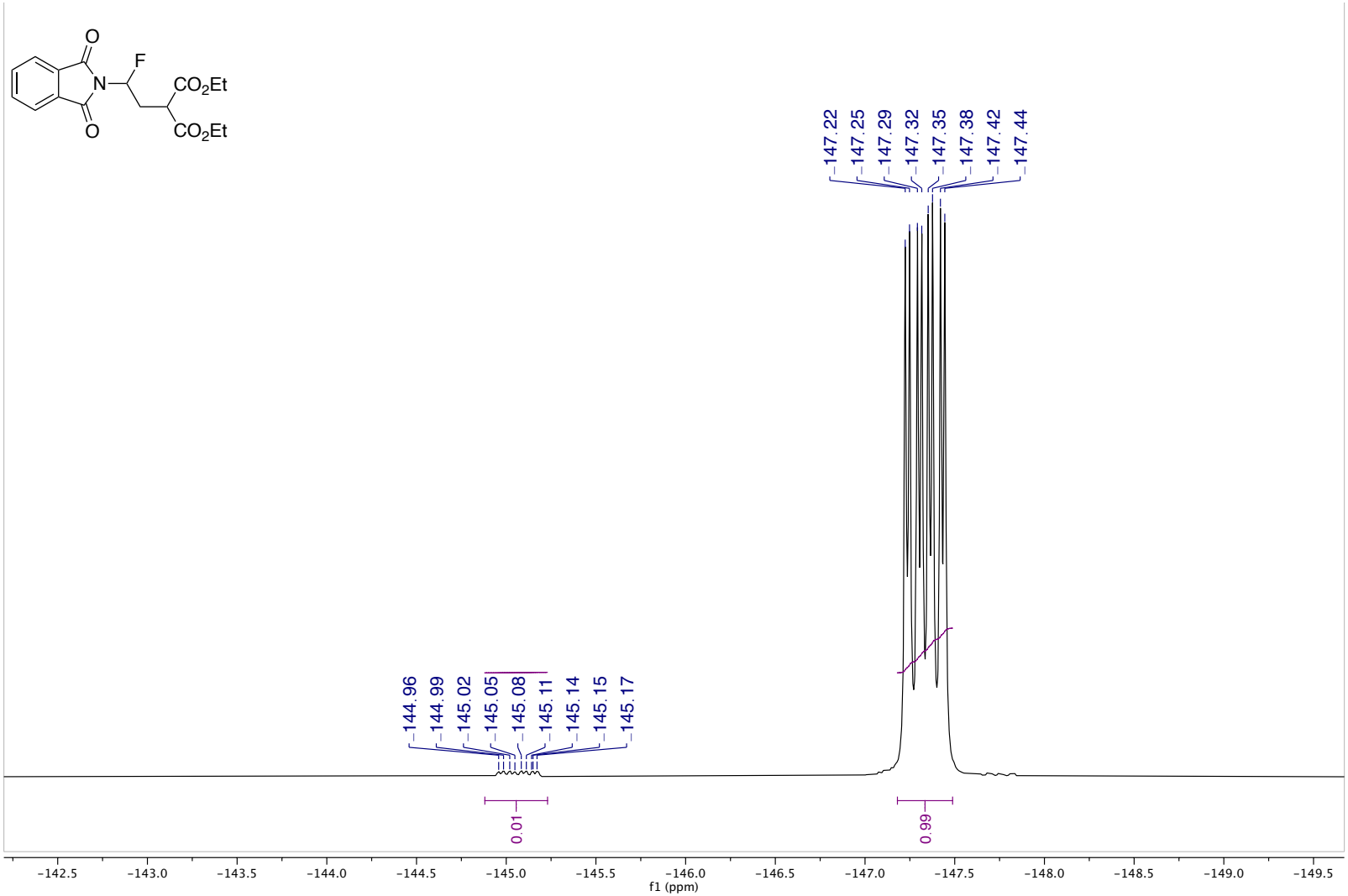
Diethyl 2-(2-(1,3-dioxoisoindolin-2-yl)-2-fluoroethyl)malonate

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



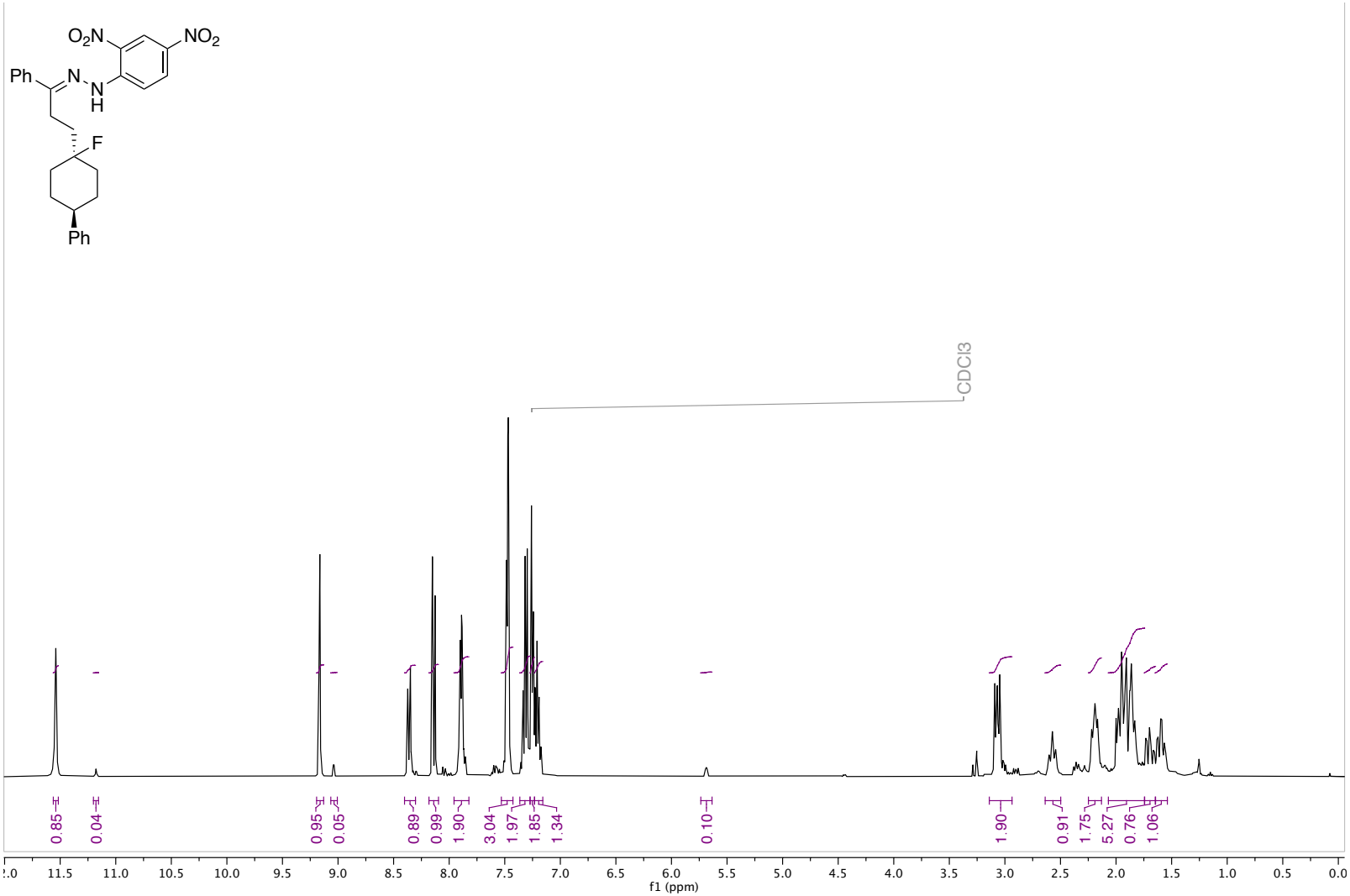
Diethyl 2-(2-(1,3-dioxoisoindolin-2-yl)-2-fluoroethyl)malonate

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



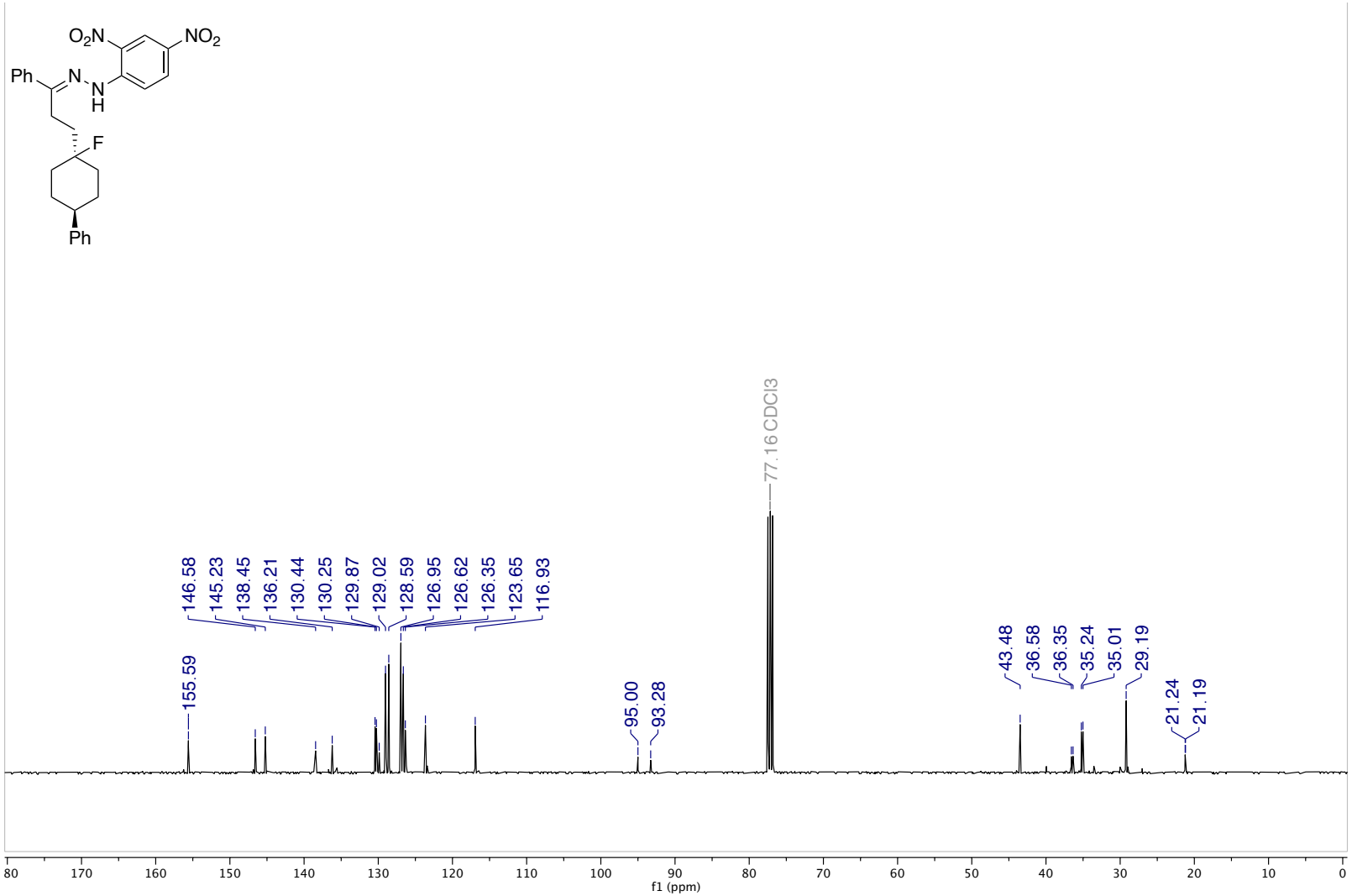
(*E*)-1-(2,4-dinitrophenyl)-2-(3-((1*s*,4*s*)-1-fluoro-4-phenylcyclohexyl)-1-phenylpropylidene)hydrazine

$^1$H-NMR (400 MHz, $CDCl_3$)



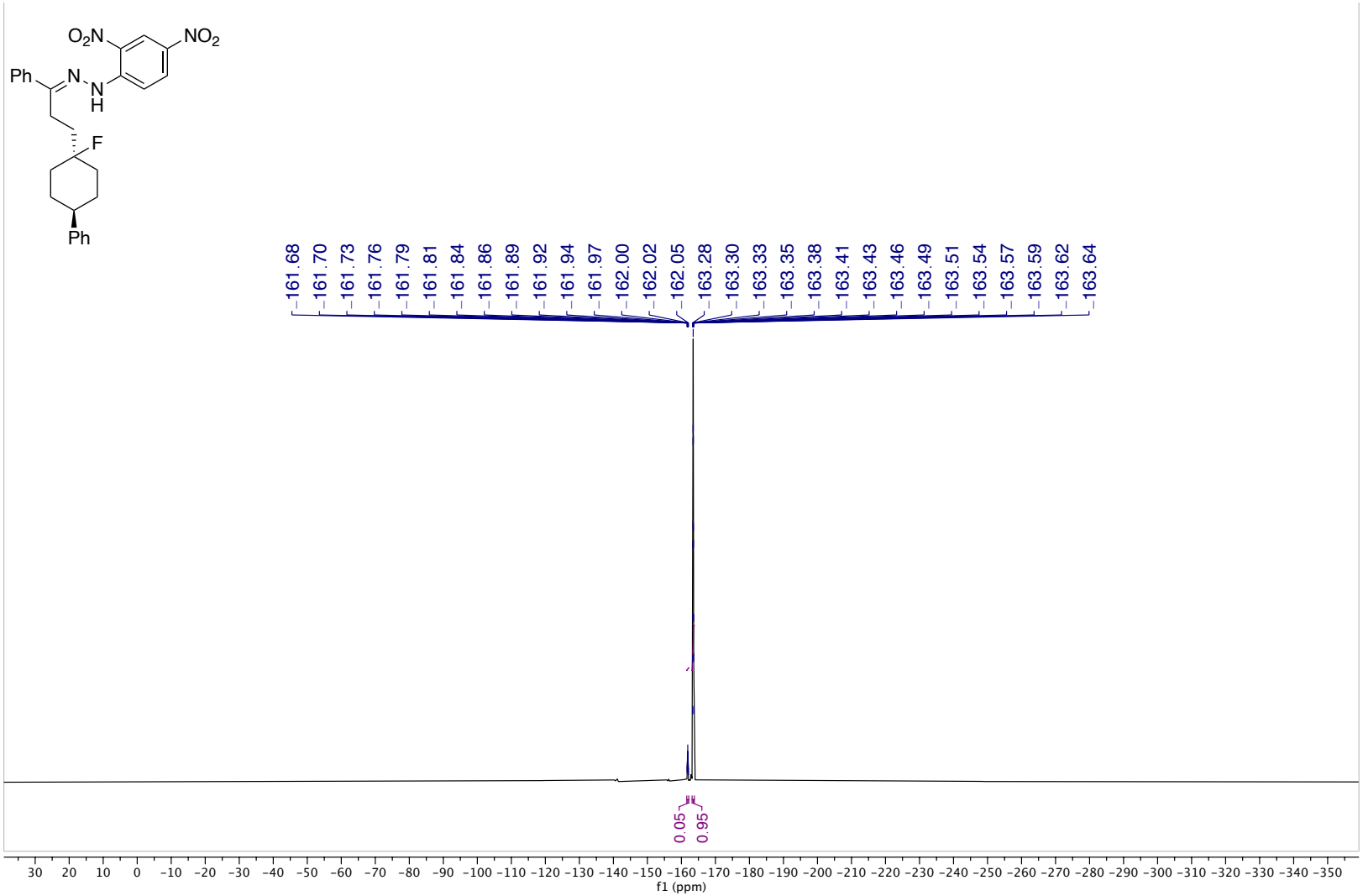
(*E*)-1-(2,4-dinitrophenyl)-2-(3-((1*s*,4*s*)-1-fluoro-4-phenylcyclohexyl)-1-phenylpropylidene)hydrazine

$^{13}$C-NMR (100 MHz, $CDCl_3$)



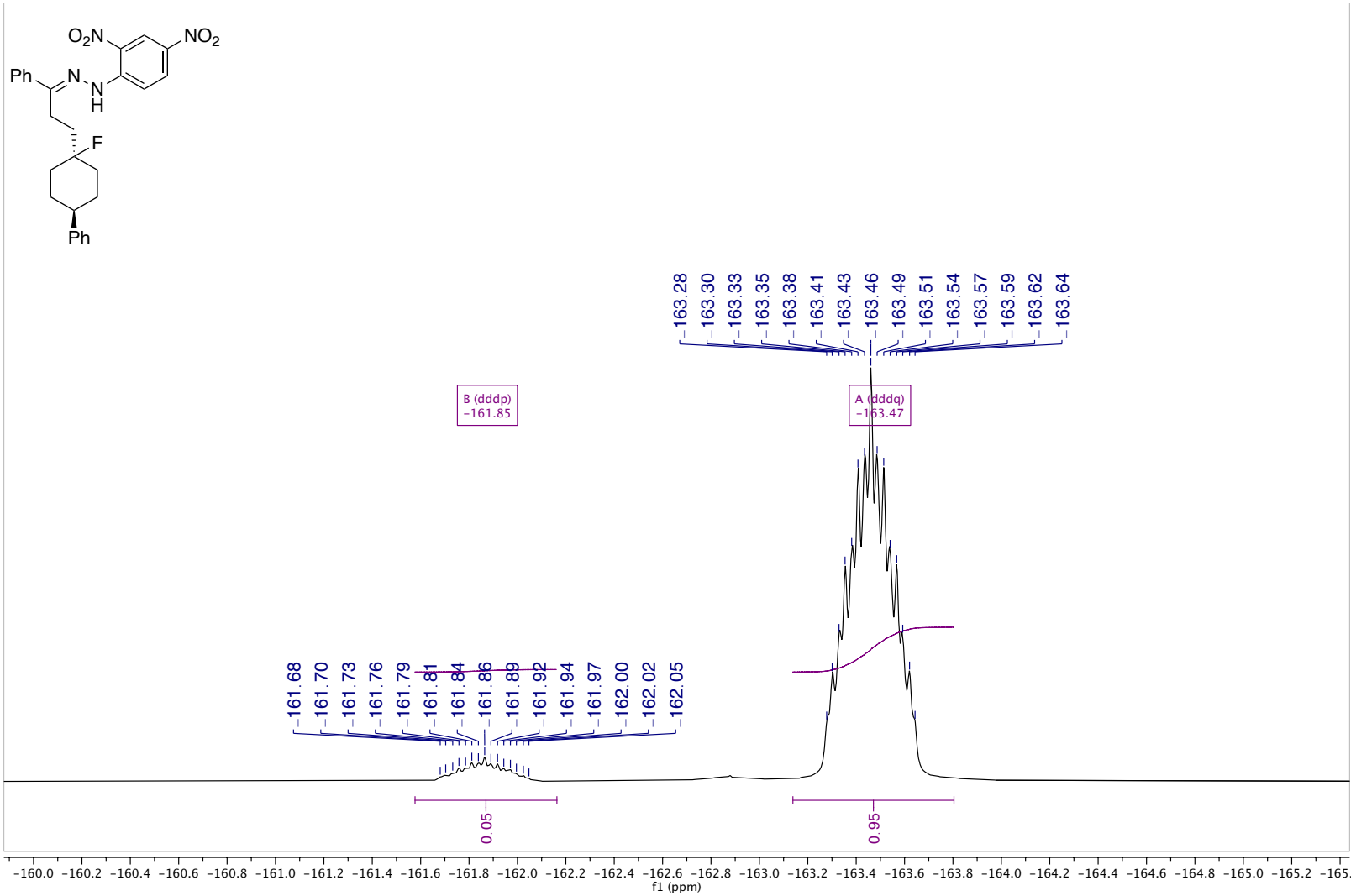
(*E*)-1-(2,4-dinitrophenyl)-2-(3-((1*s*,4*s*)-1-fluoro-4-phenylcyclohexyl)-1-phenylpropylidene)hydrazine

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



(*E*)-1-(2,4-dinitrophenyl)-2-(3-((1*s*,4*s*)-1-fluoro-4-phenylcyclohexyl)-1-phenylpropylidene)hydrazine

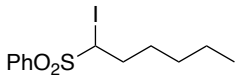
$^{19}$F-NMR (376 MHz, $CDCl_3$)



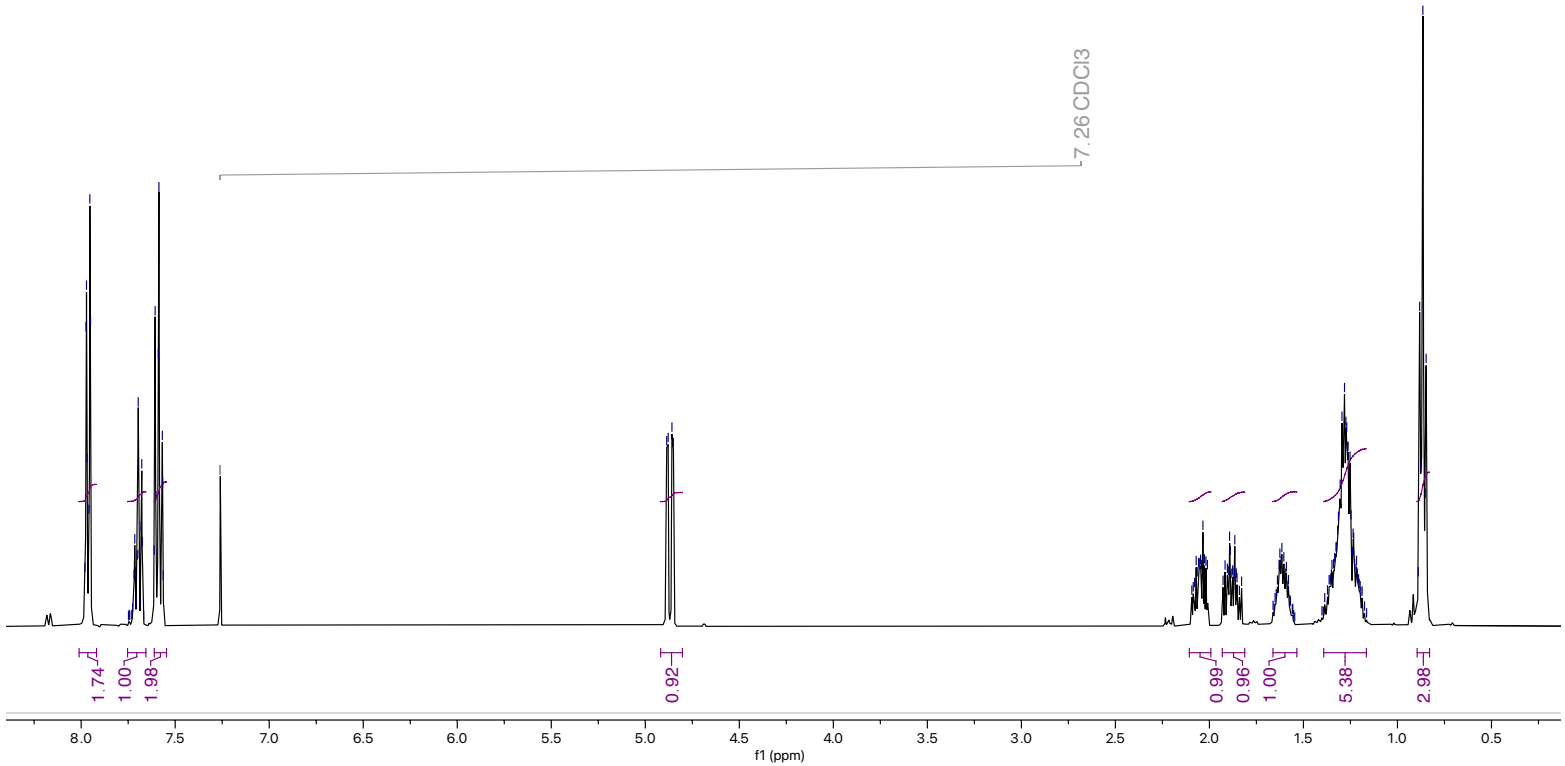
## 7.3 NMR Spectra Chapter 6

**Remote C-H Functionalization Using α-Sulfonyl Radicals**

((1-Iodohexyl)sulfonyl)benzene

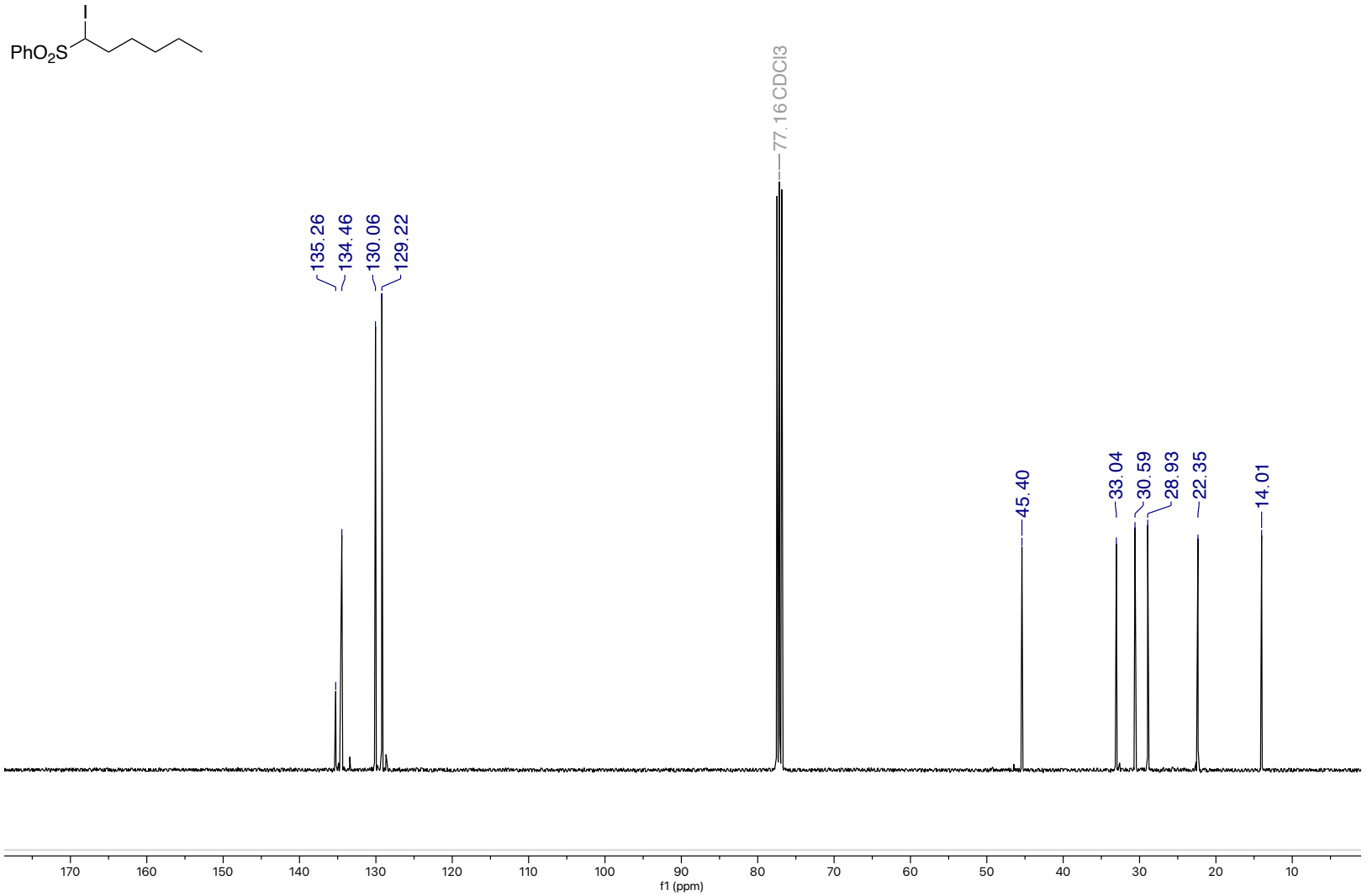



$^{1}$H-NMR (400 MHz, $CDCl_3$)



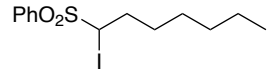
((1-Iodohexyl)sulfonyl)benzene

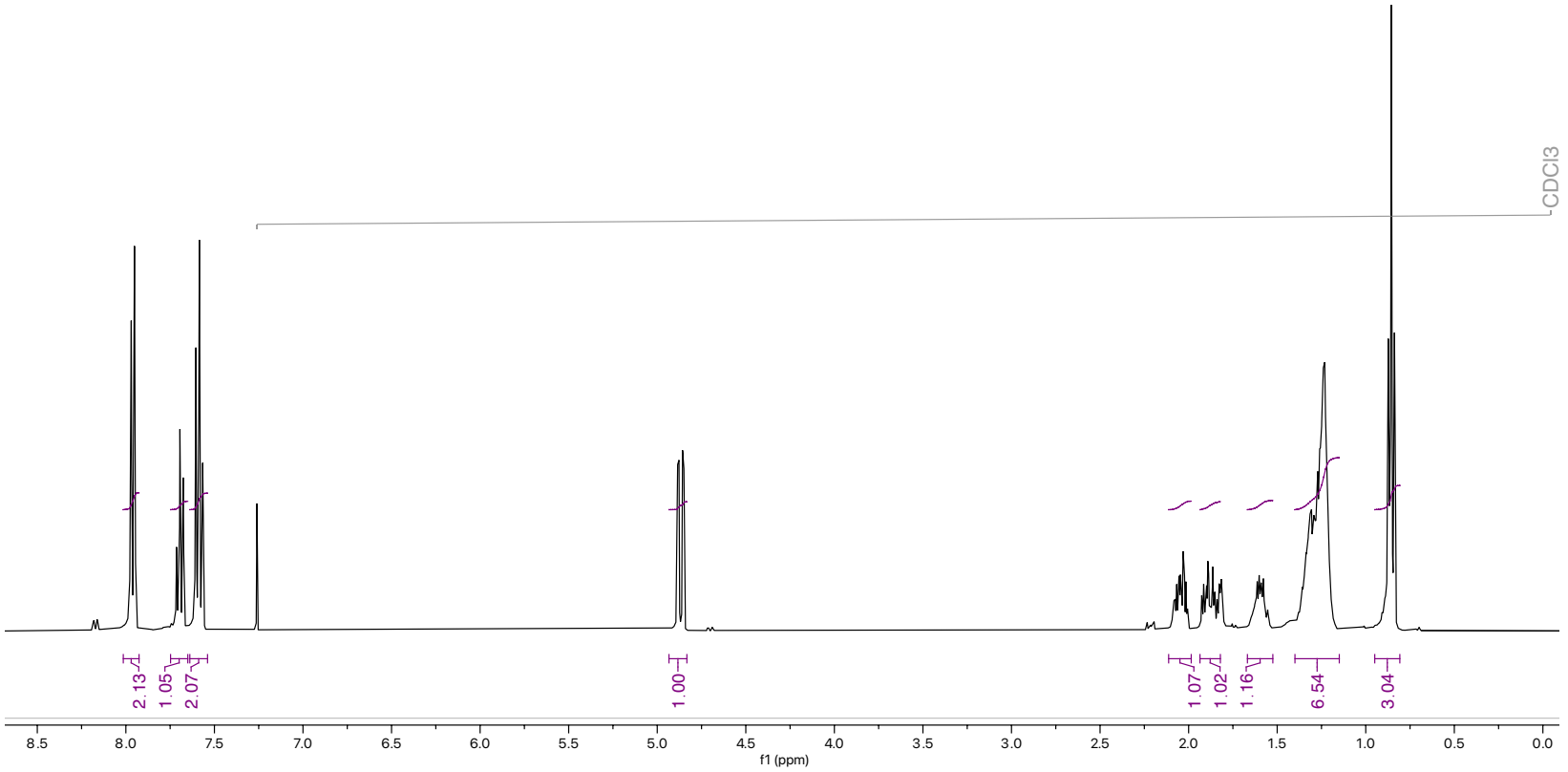
$^{13}$C-NMR (101 MHz, $CDCl_3$)



((1-Iodoheptyl)sulfonyl)benzene

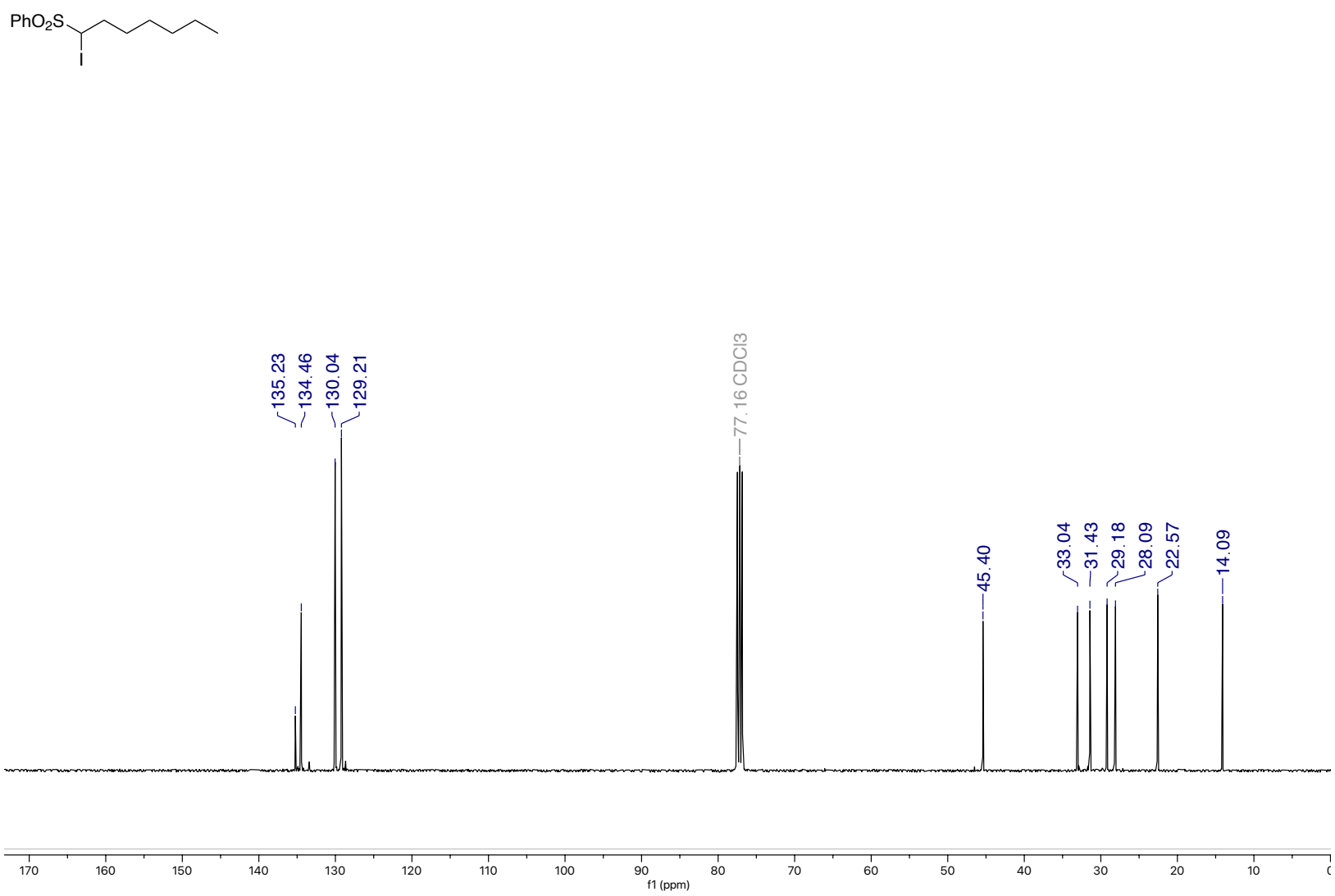
$^1$H-NMR (400 MHz, $CDCl_3$)



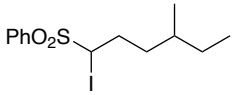
((1-Iodoheptyl)sulfonyl)benzene

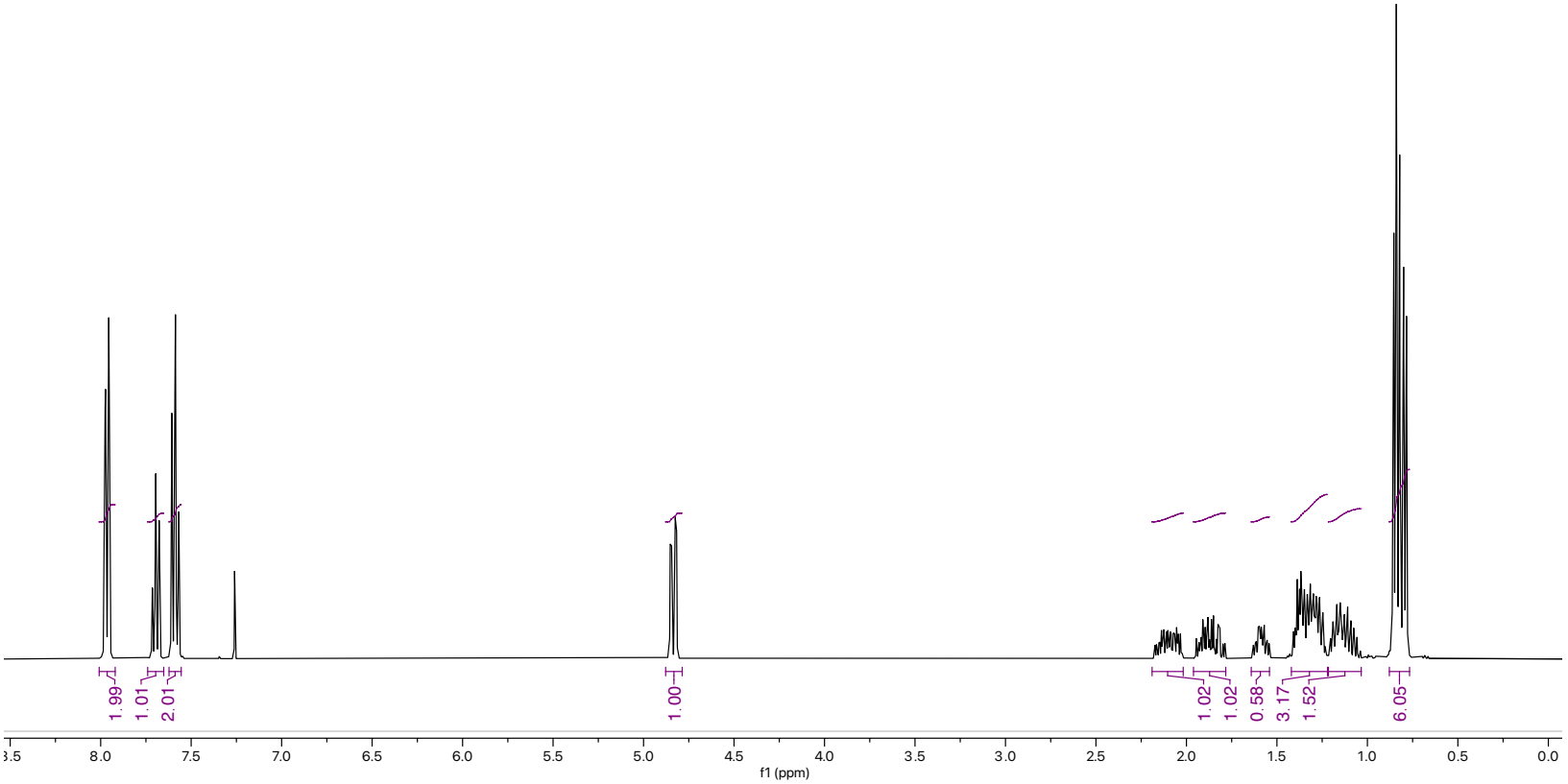
$^{13}$C-NMR (101 MHz, $CDCl_3$)



((1-Iodo-4-methylhexyl)sulfonyl)benzene

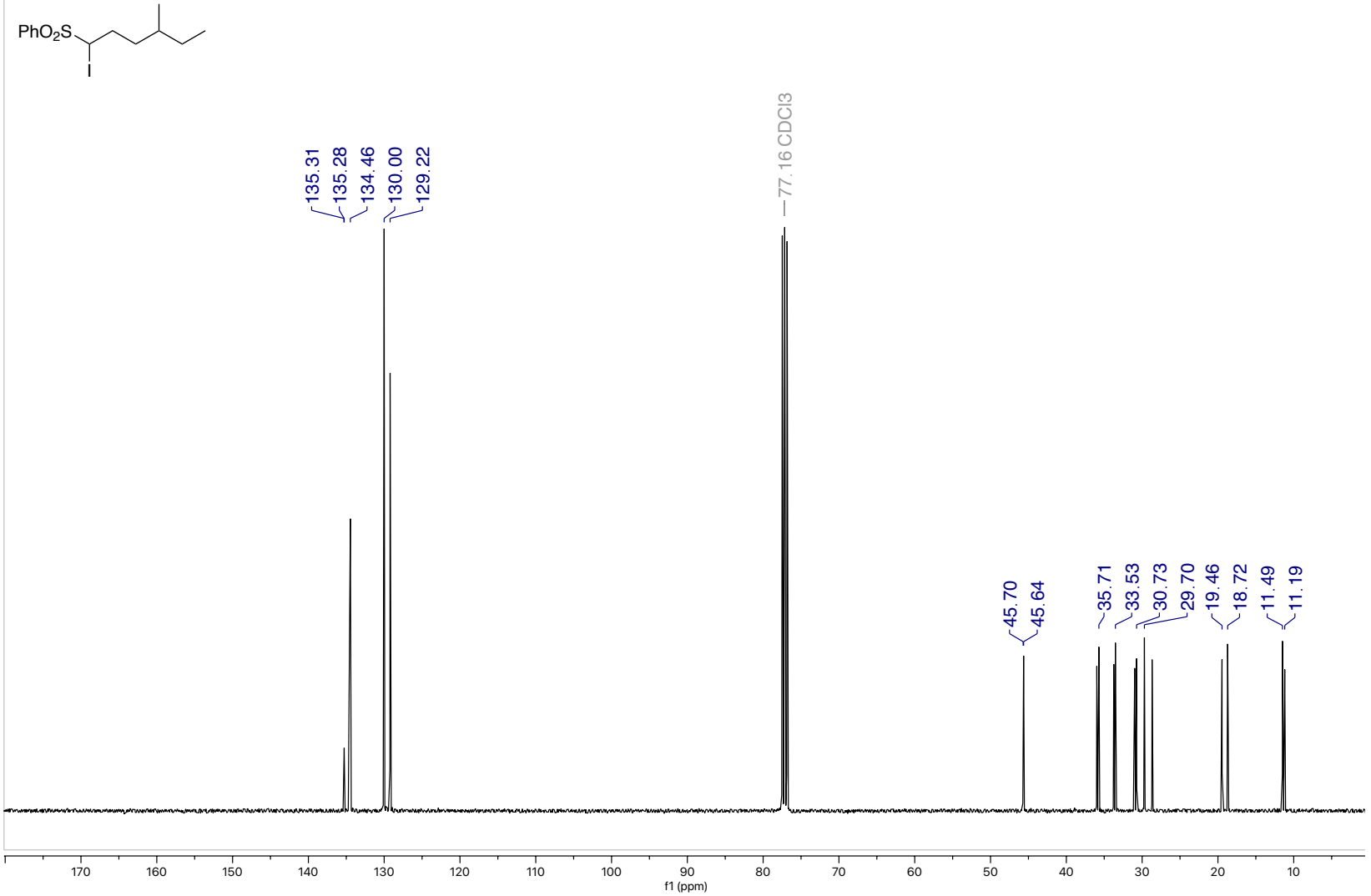
$^1$H-NMR (400 MHz, $CDCl_3$)



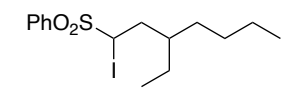
((1-Iodo-4-methylhexyl)sulfonyl)benzene

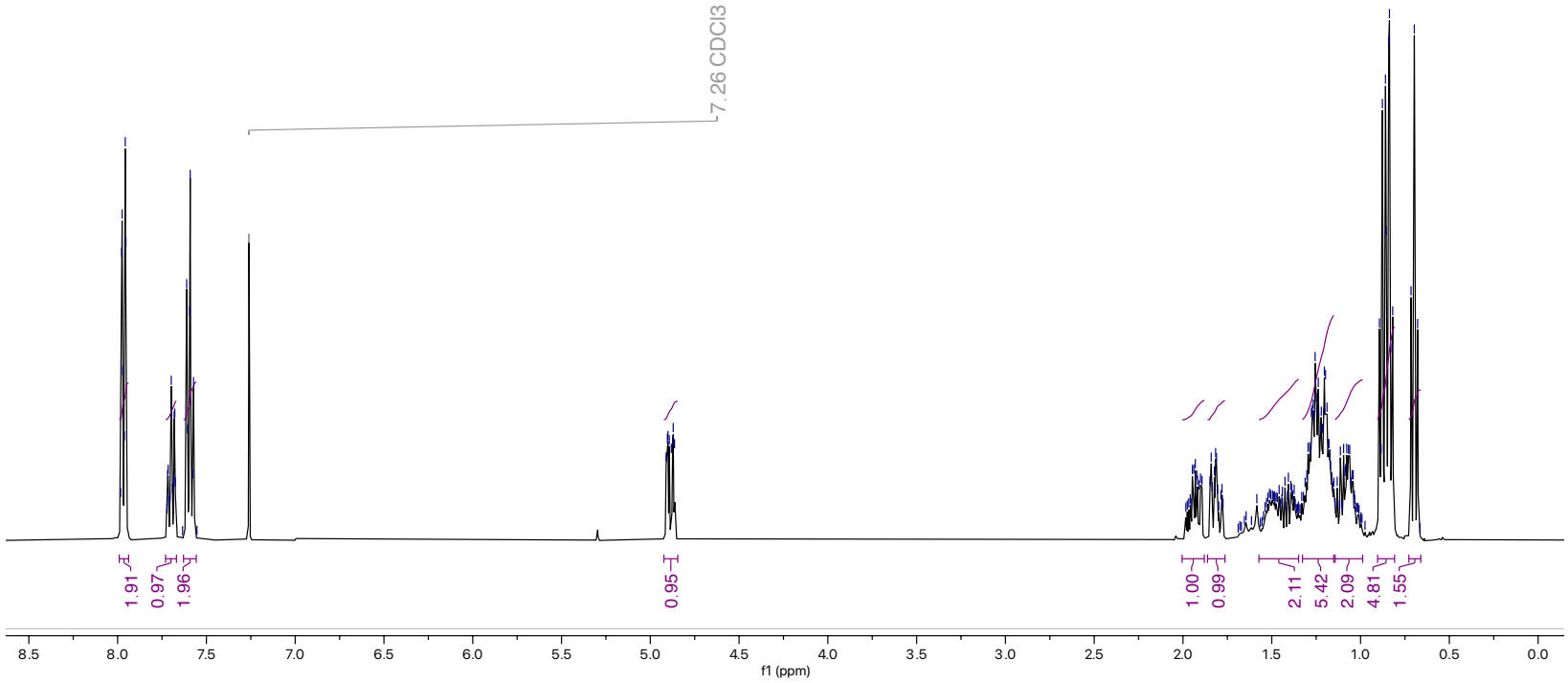
$^{13}$C-NMR (101 MHz, $CDCl_3$)



((3-Ethyl-1-iodoheptyl)sulfonyl)benzene

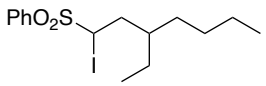
$^1$H-NMR (400 MHz, $CDCl_3$)

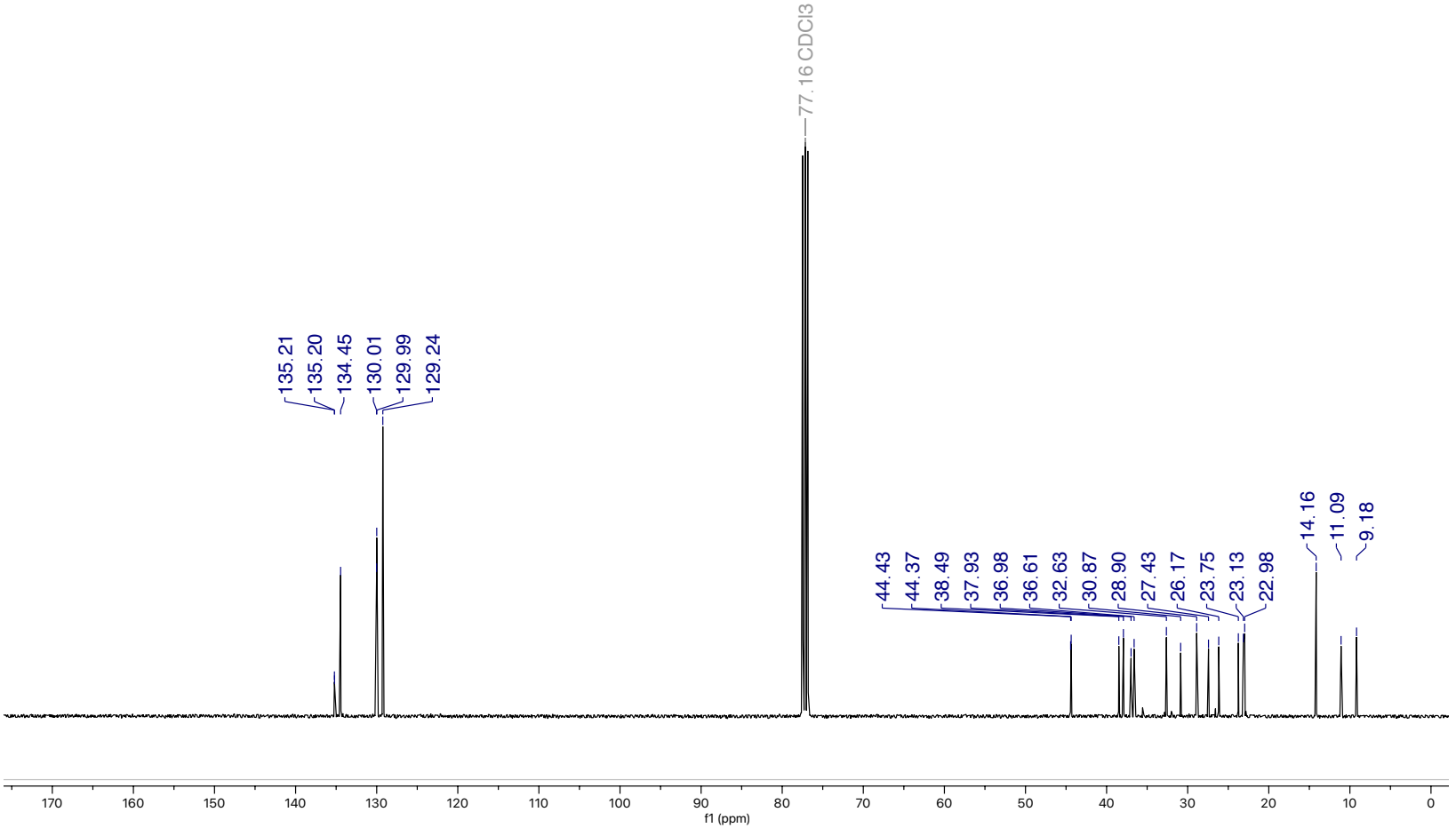


((3-Ethyl-1-iodoheptyl)sulfonyl)benzene

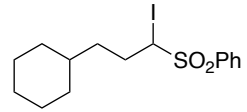
$^{13}$C-NMR (101 MHz, $CDCl_3$)

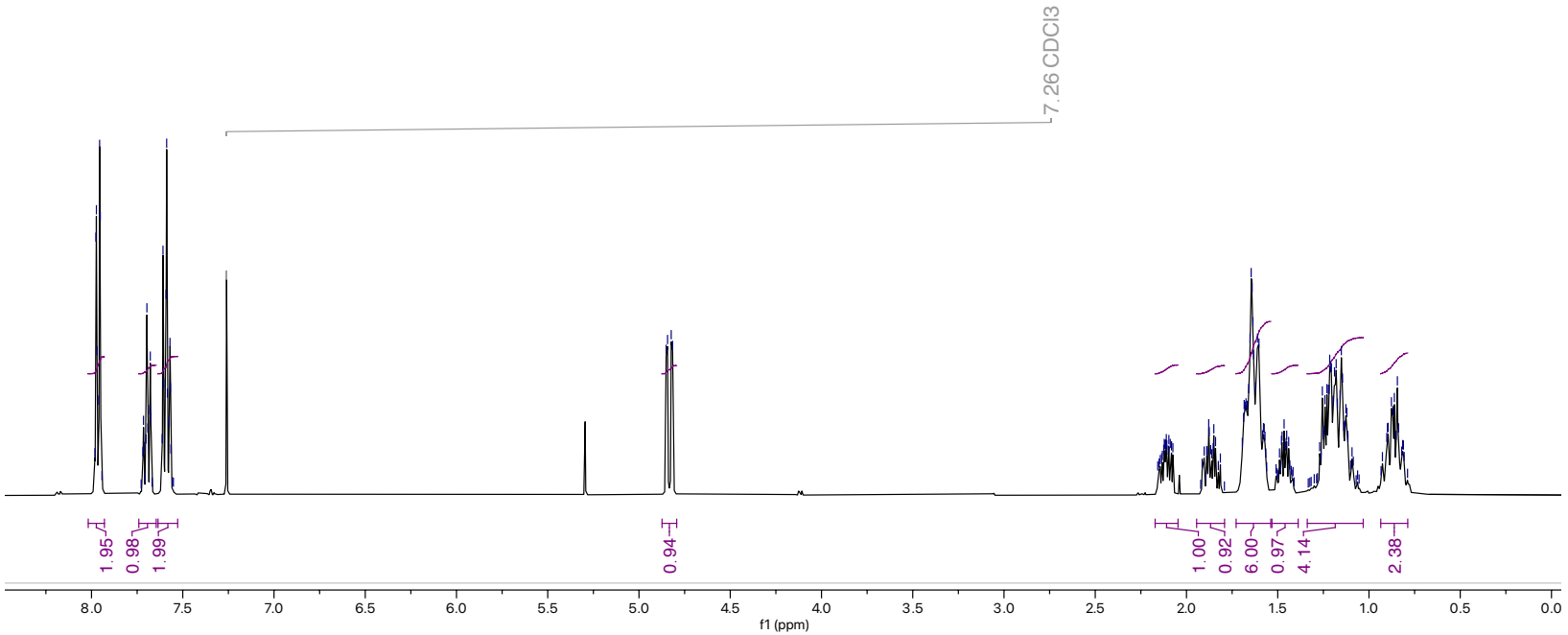


((3-Cyclohexyl-1-iodopropyl)sulfonyl)benzene

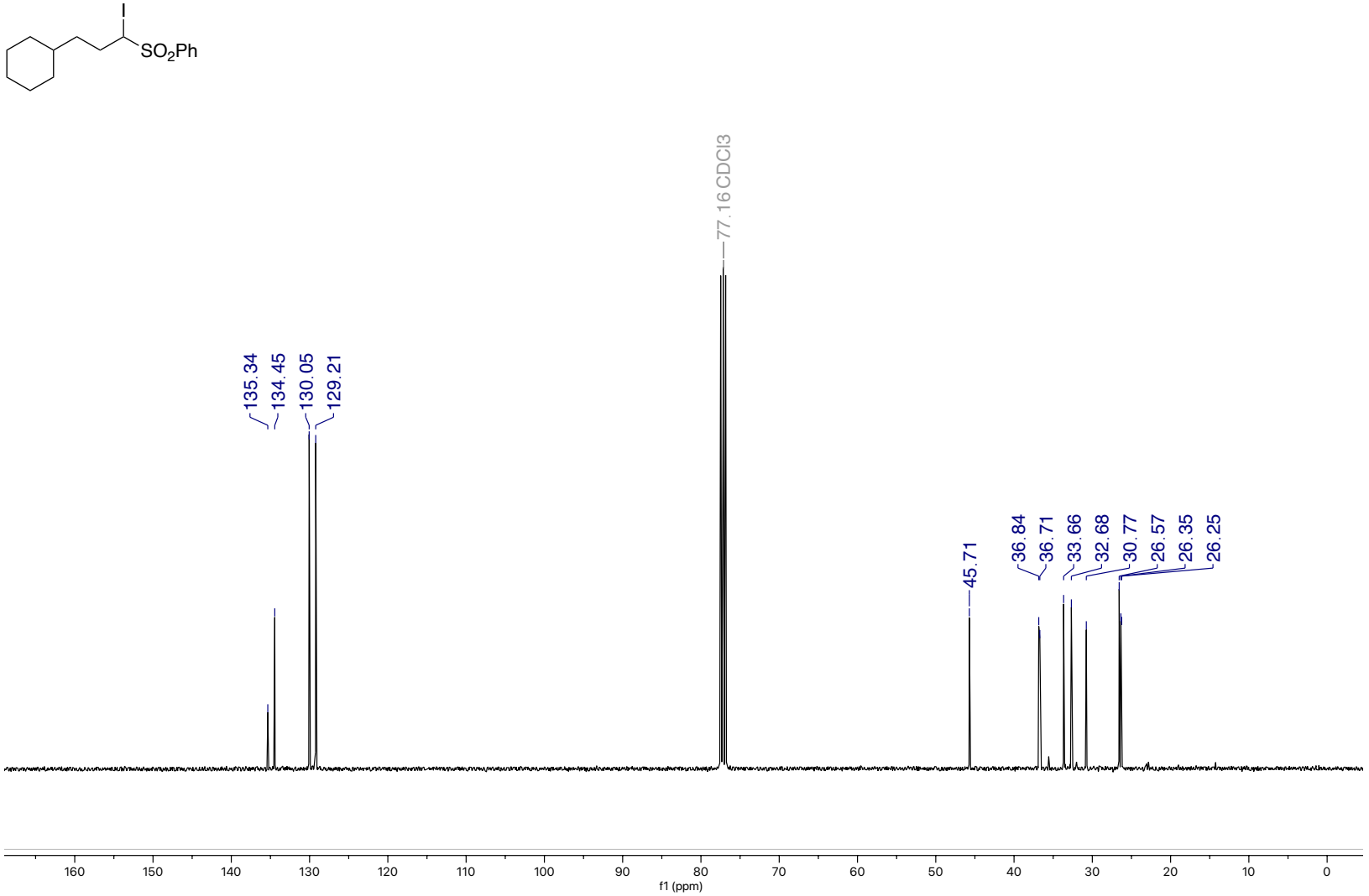
$^1$H-NMR (400 MHz, $CDCl_3$)



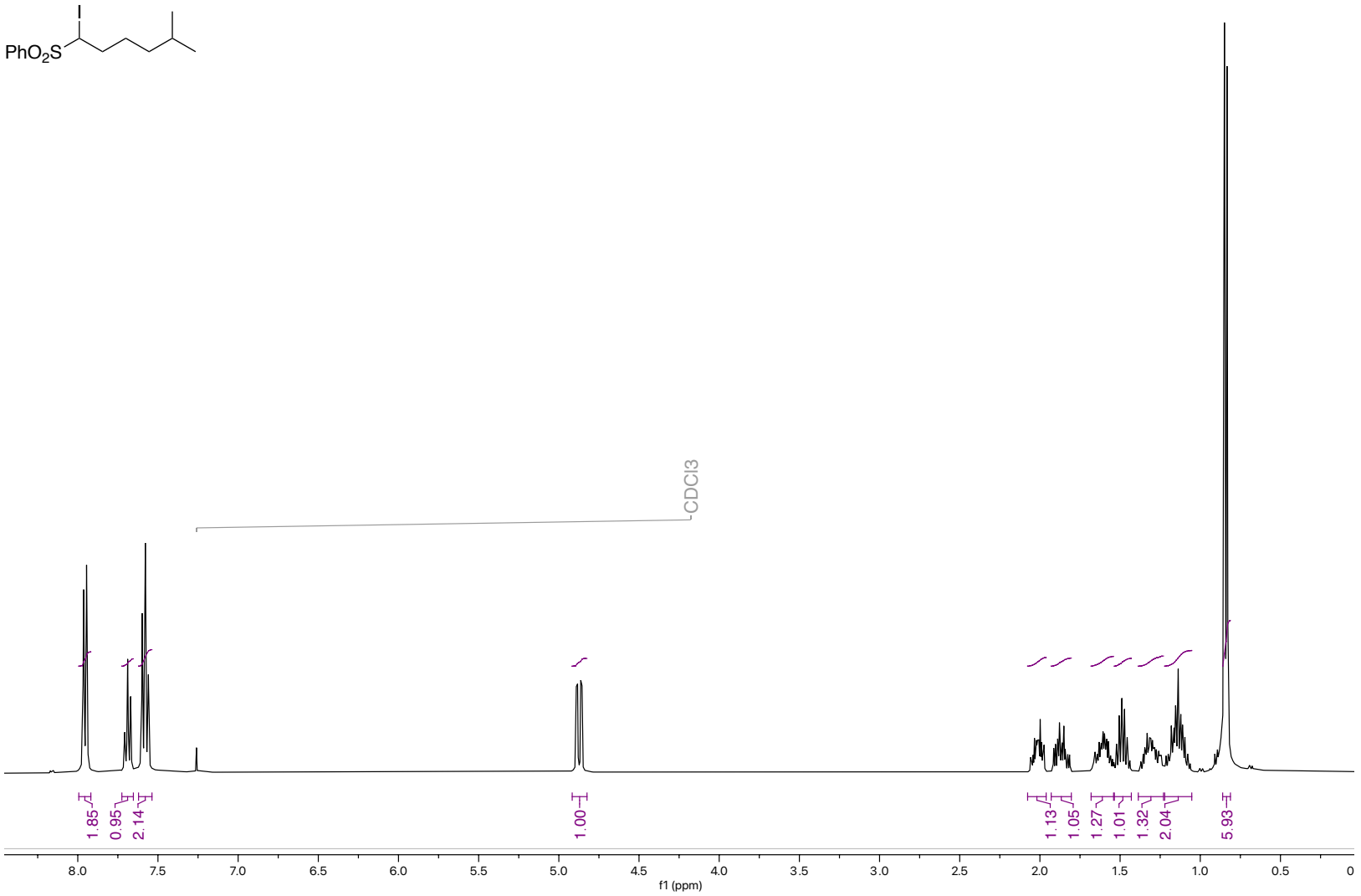
((3-Cyclohexyl-1-iodopropyl)sulfonyl)benzene

$^{13}$C-NMR (101 MHz, $CDCl_3$)

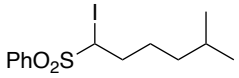


((1-Iodo-5-methylhexyl)sulfonyl)benzene

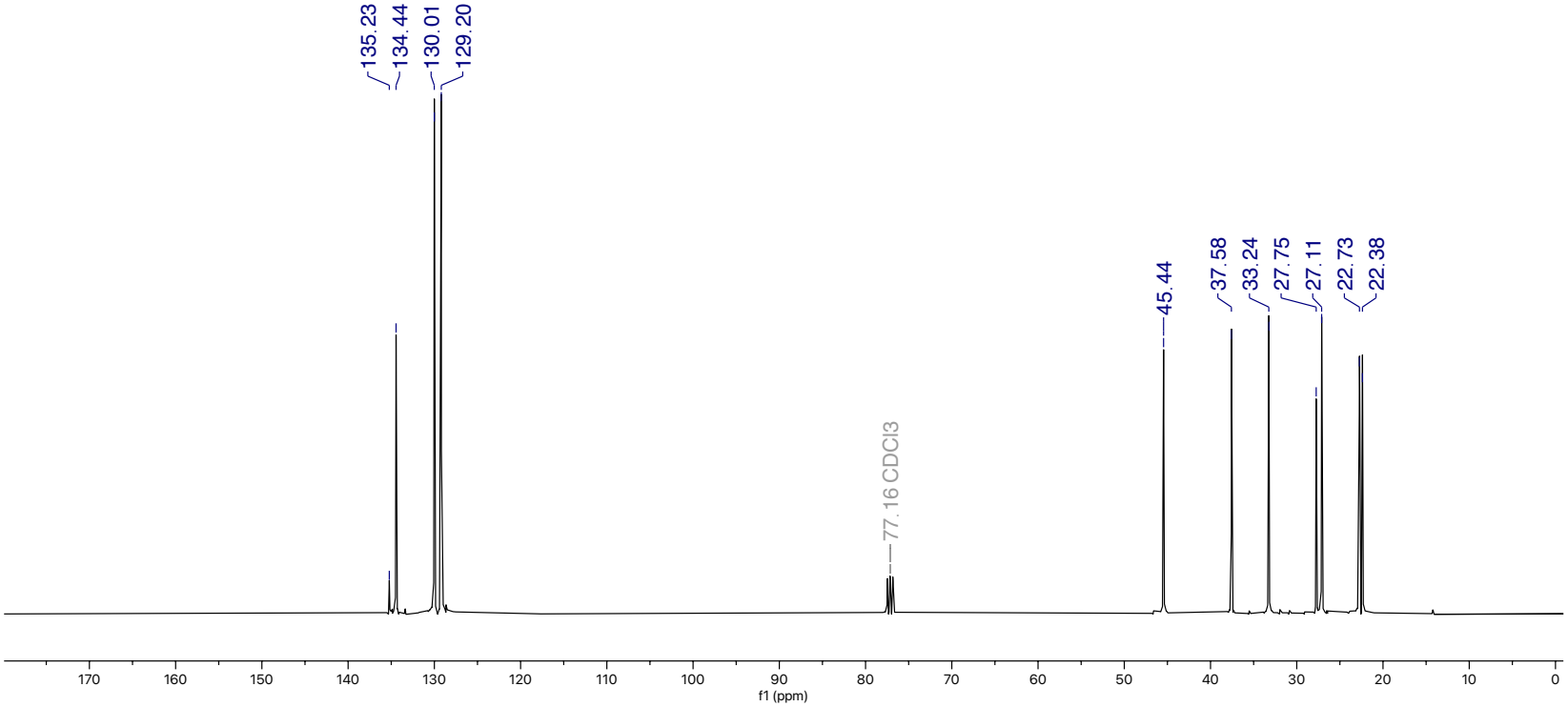
$^1$H-NMR (400 MHz, $CDCl_3$)



((1-Iodo-5-methylhexyl)sulfonyl)benzene

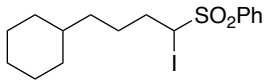


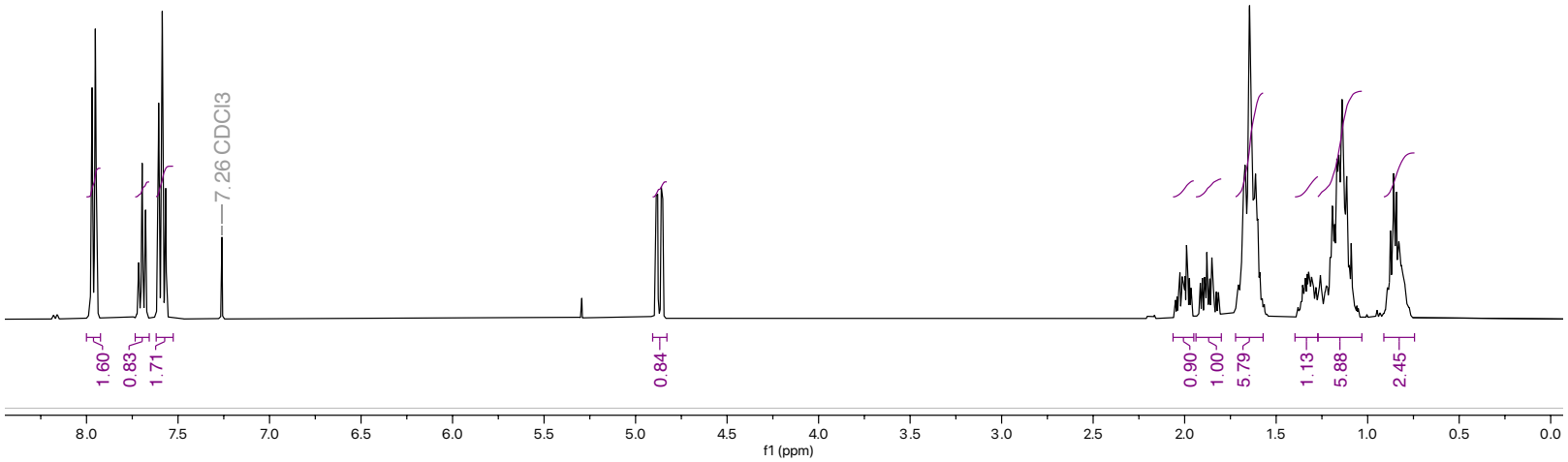

$^{13}$C-NMR (101 MHz, $CDCl_3$)



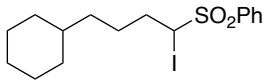
((4-Cyclohexyl-1-iodobutyl)sulfonyl)benzene

$^1$H-NMR (400 MHz, $CDCl_3$)

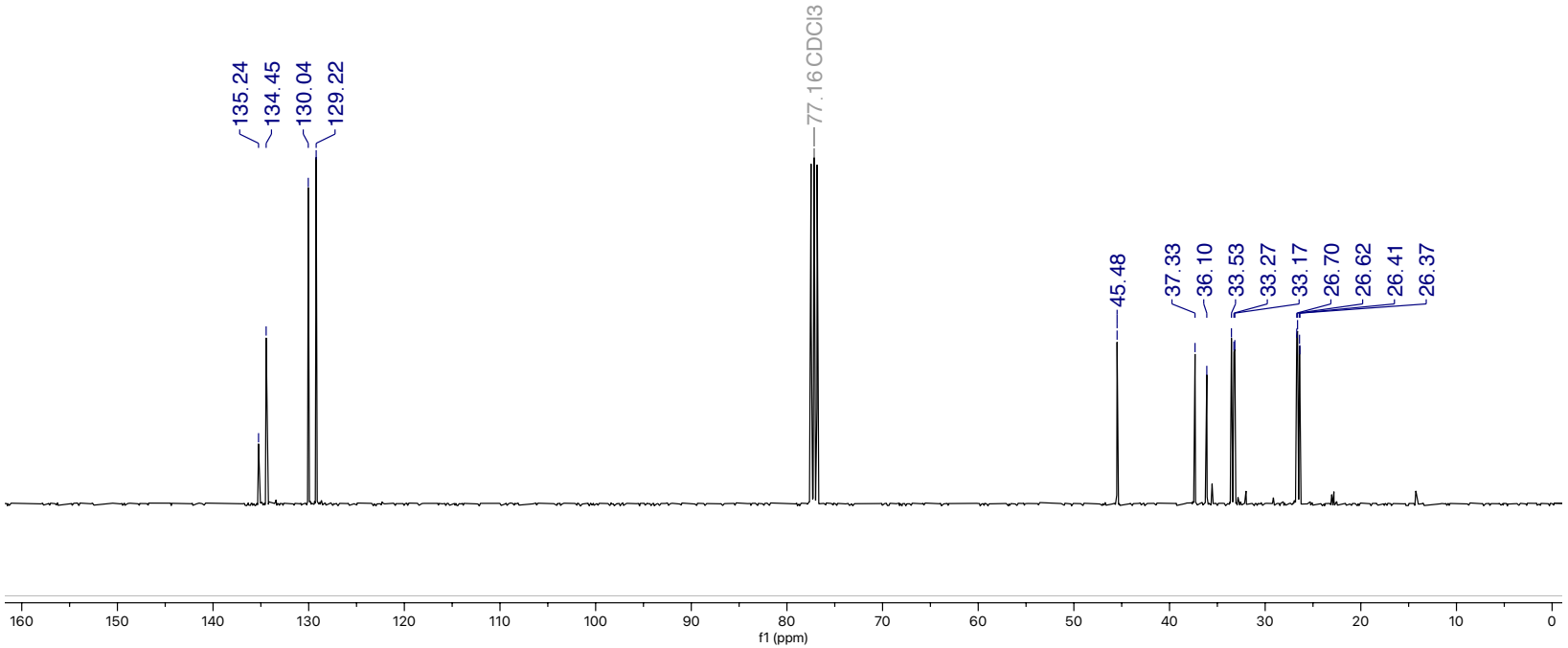


((4-Cyclohexyl-1-iodobutyl)sulfonyl)benzene

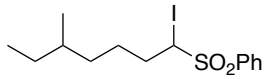


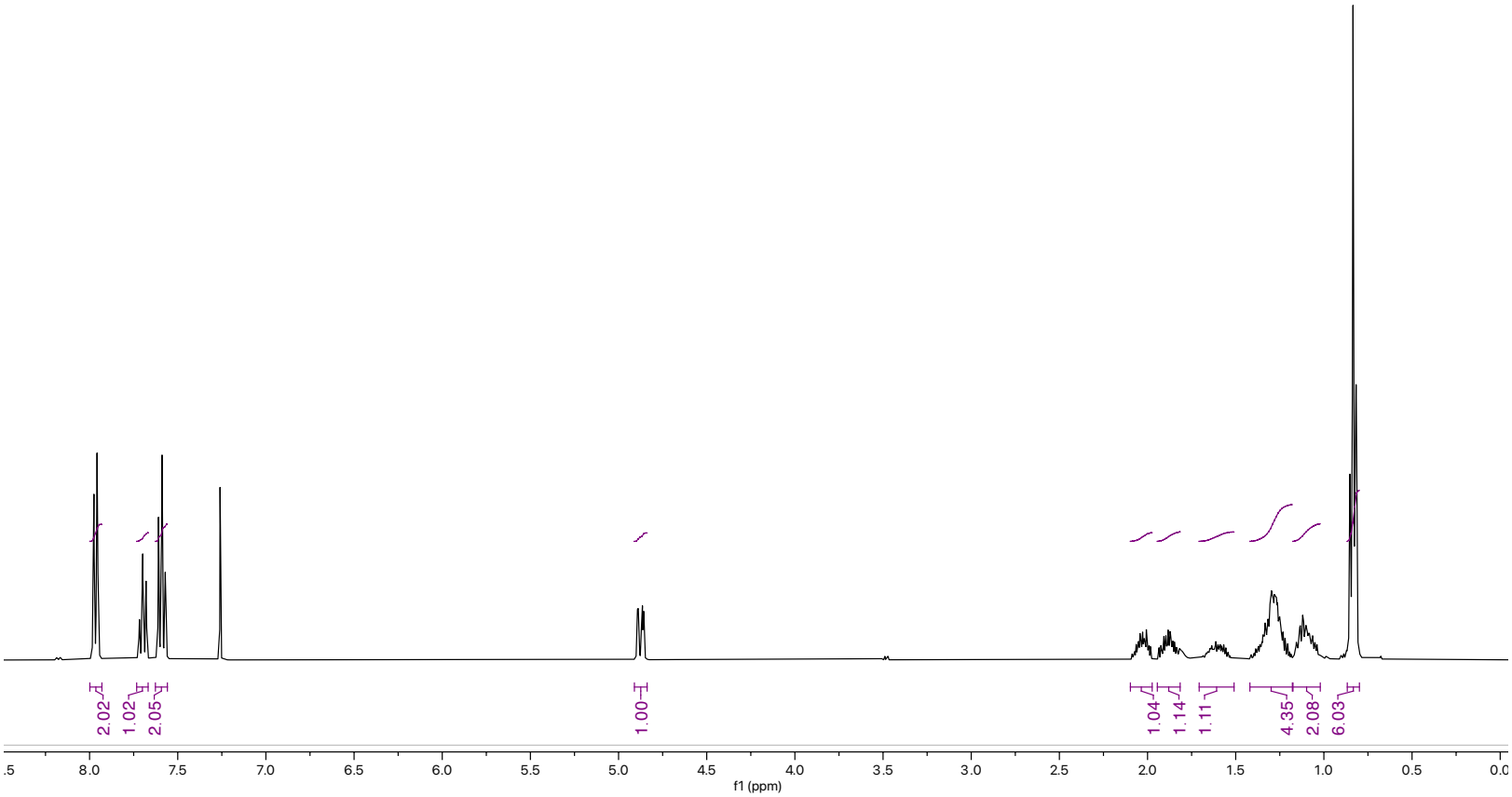

$^{13}$C-NMR (101 MHz, $CDCl_3$)



((1-Iodo-5-methylheptyl)sulfonyl)benzene

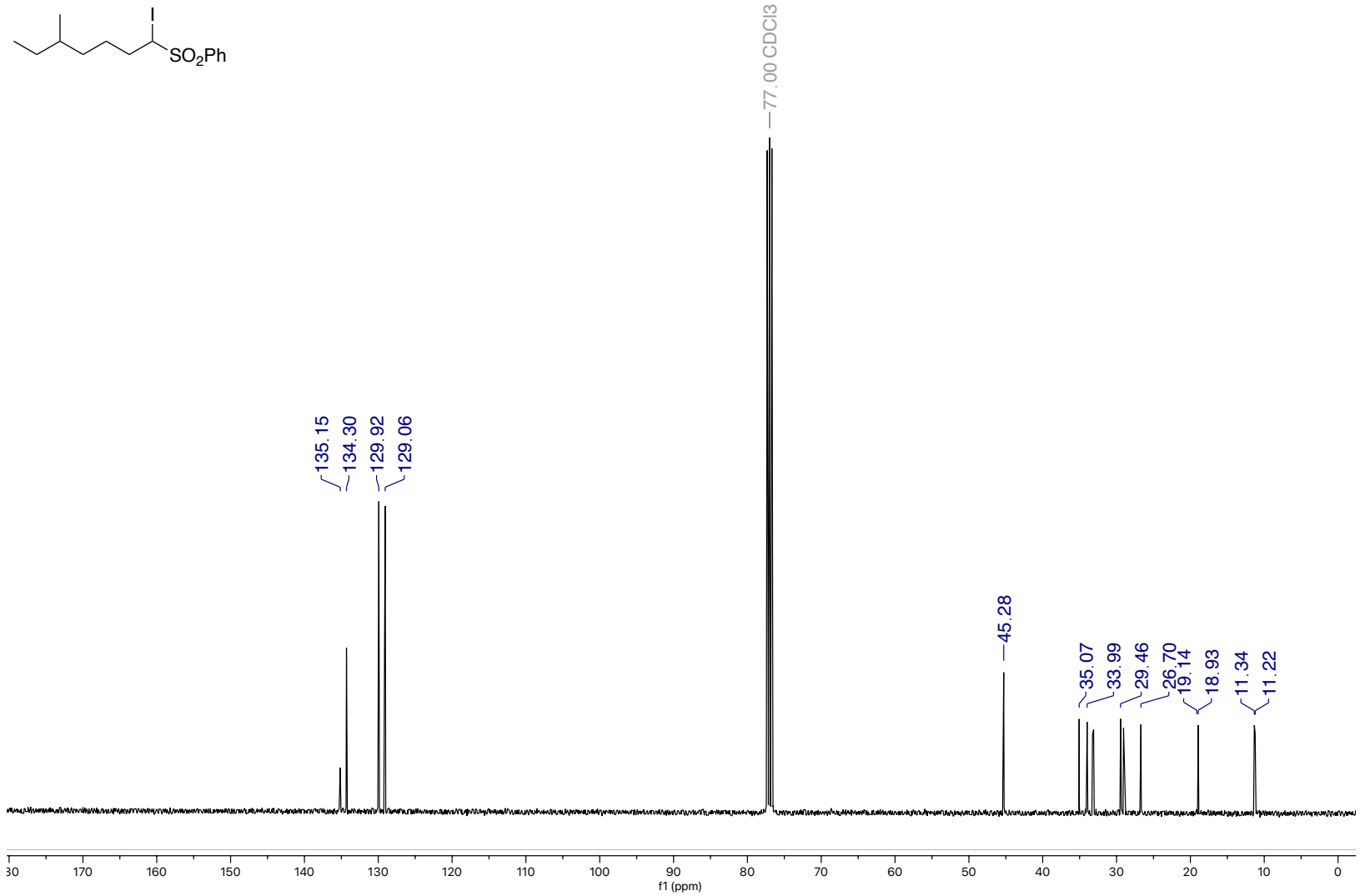
$^1$H-NMR (400 MHz, $CDCl_3$)



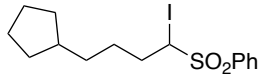
((1-Iodo-5-methylheptyl)sulfonyl)benzene

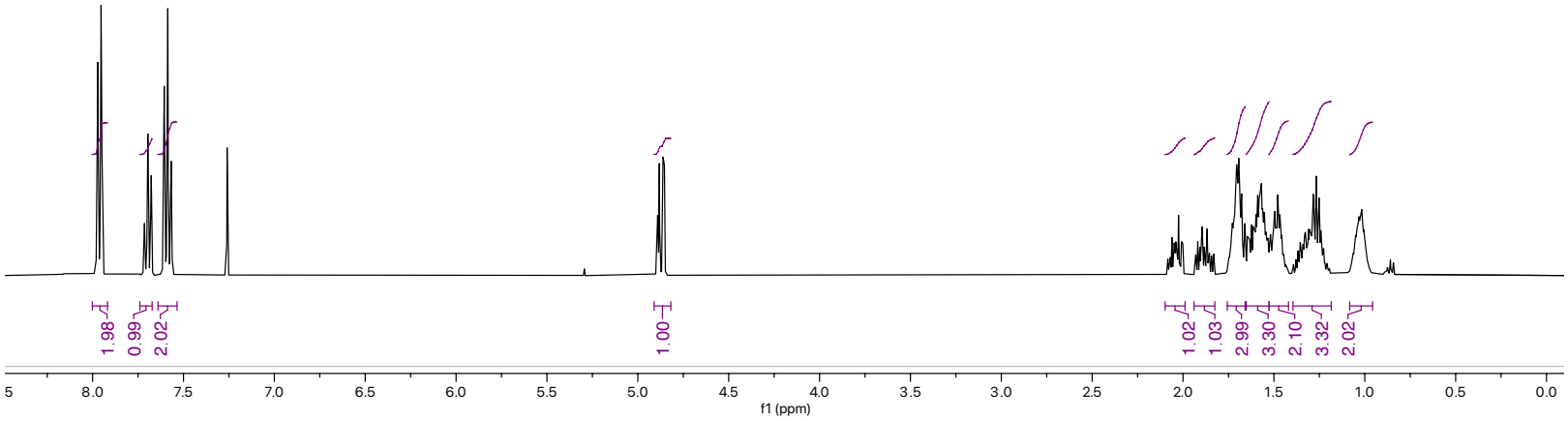
$^{13}$C-NMR (101 MHz, $CDCl_3$)



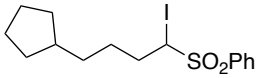
((4-Cyclopentyl-1-iodobutyl)sulfonyl)benzene

$^1$H-NMR (400 MHz, $CDCl_3$)

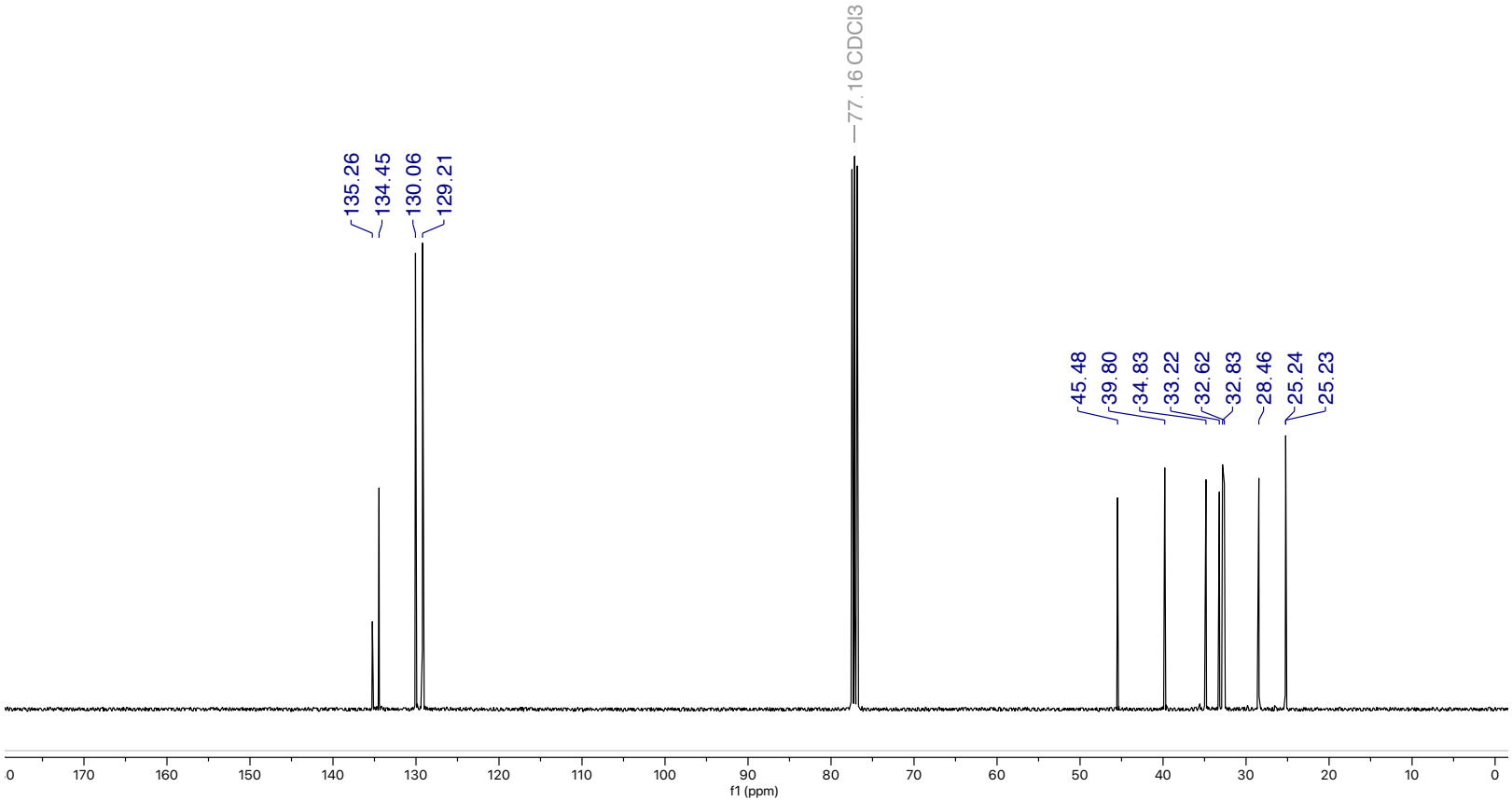


((4-Cyclopentyl-1-iodobutyl)sulfonyl)benzene

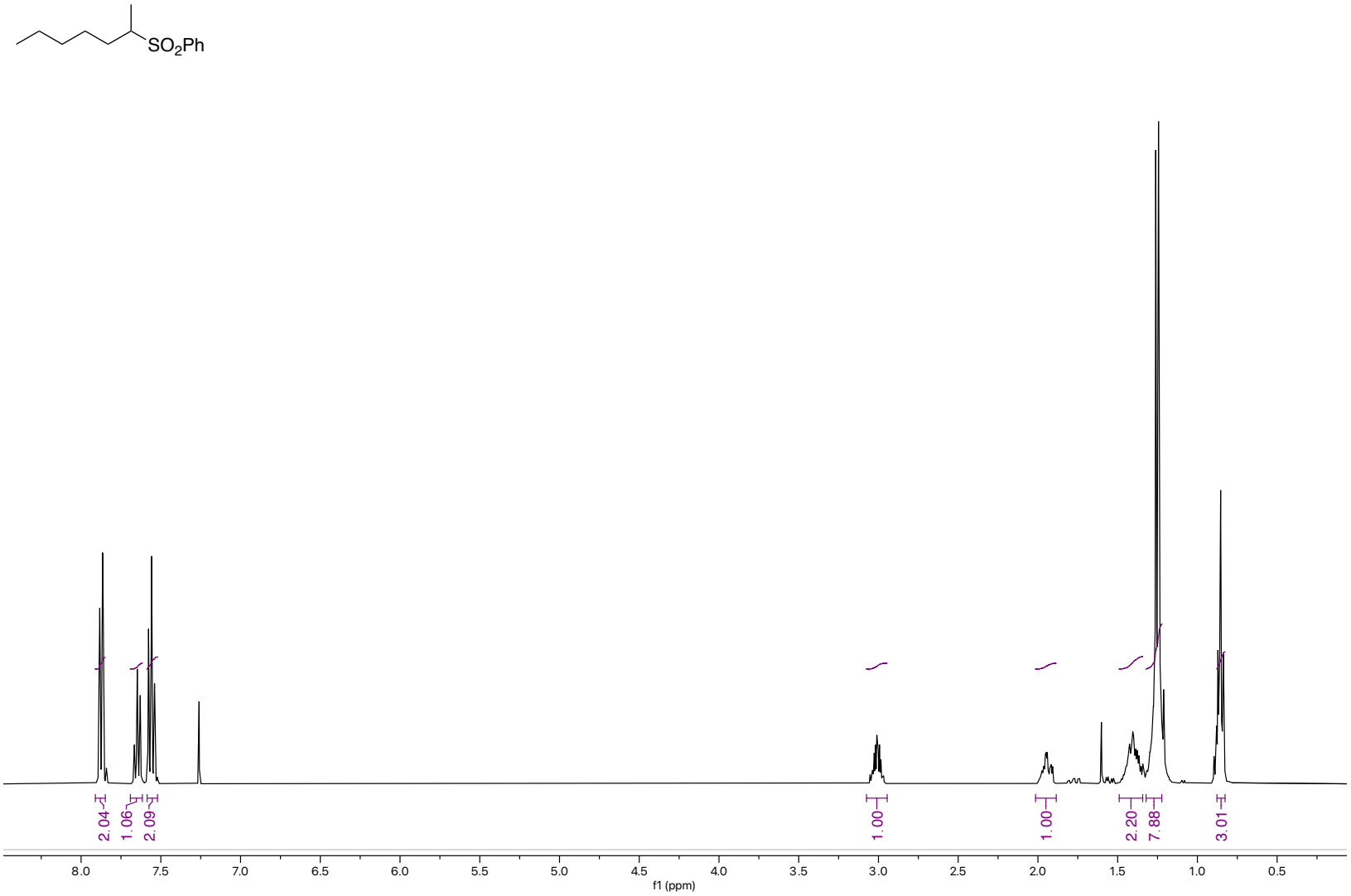



$^{13}$C-NMR (101 MHz, $CDCl_3$)



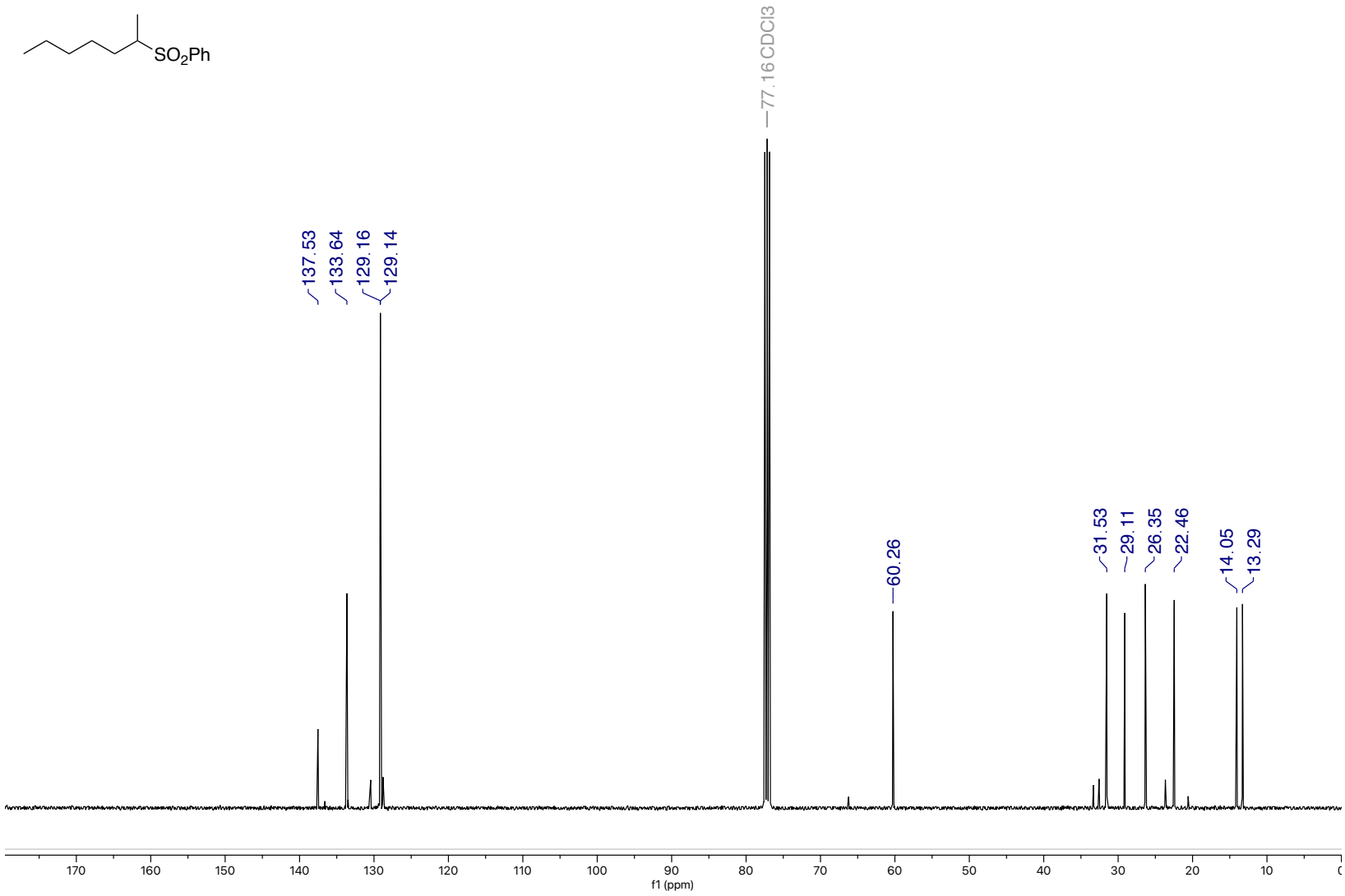
(Heptan-2-ylsulfonyl)benzene

$^1$H-NMR (400 MHz, $CDCl_3$)



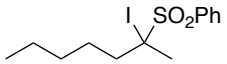
(Heptan-2-ylsulfonyl)benzene

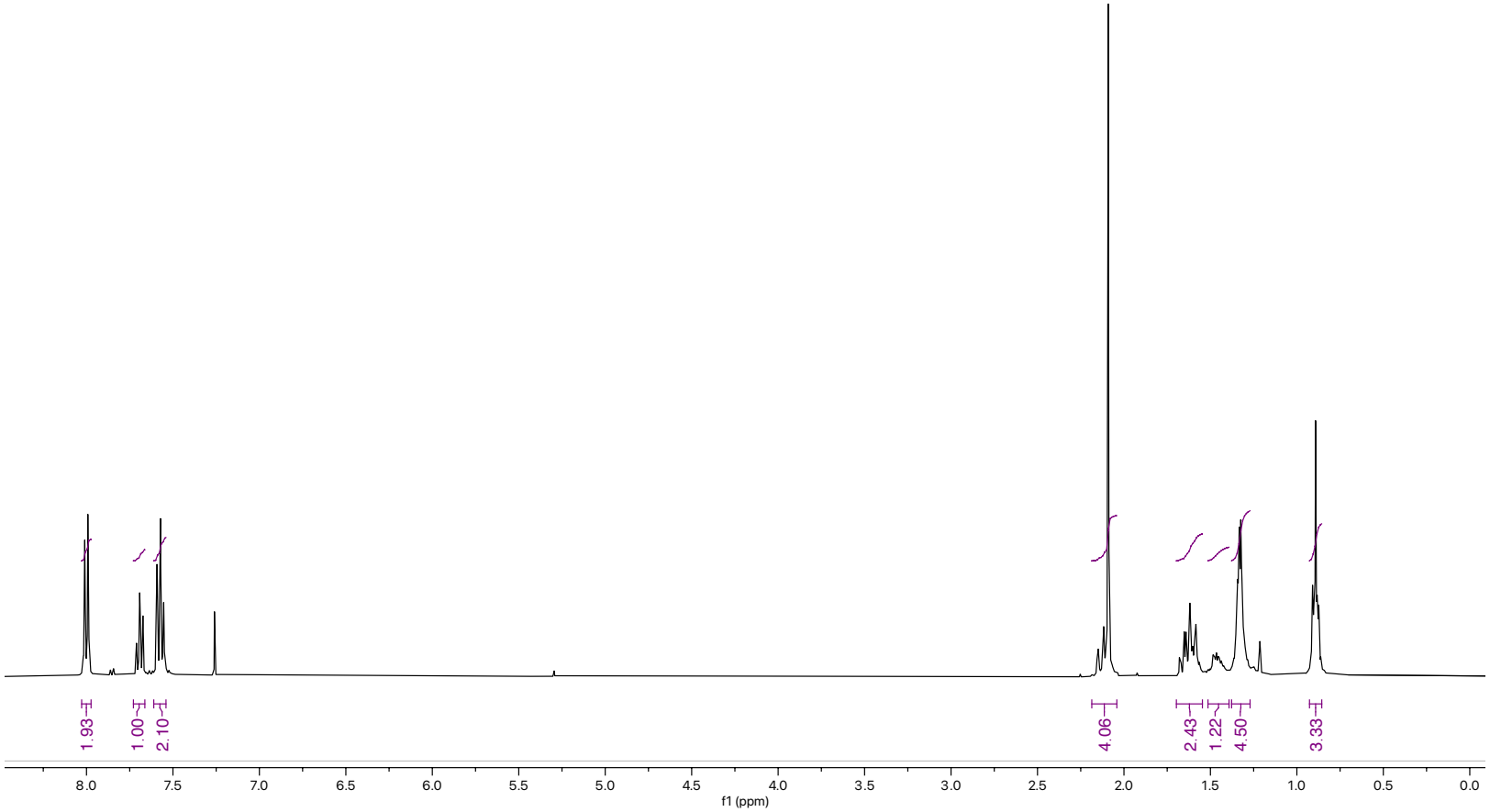
$^{13}$C-NMR (101 MHz, $CDCl_3$)



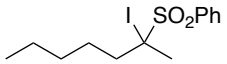
((2-Iodoheptan-2-yl)sulfonyl)benzene

$^1$H-NMR (400 MHz, $CDCl_3$)

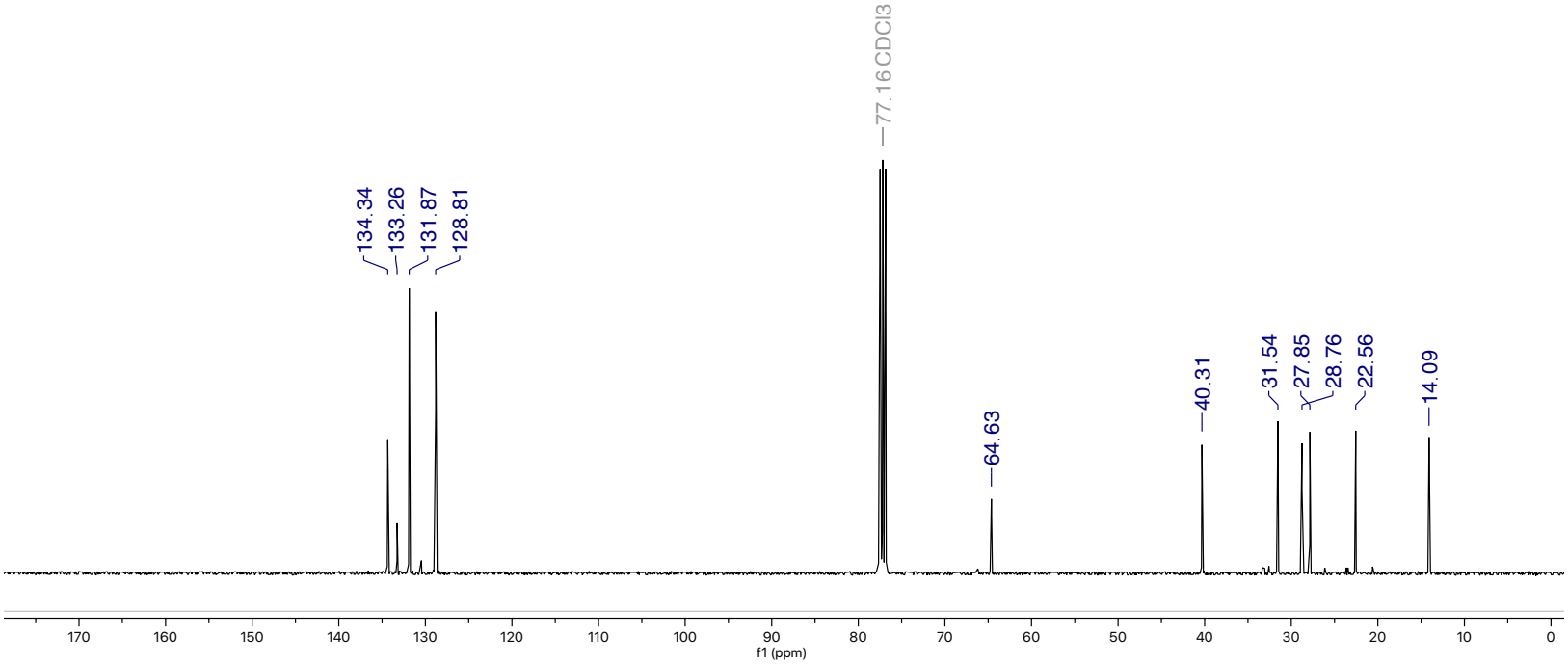


((2-Iodoheptan-2-yl)sulfonyl)benzene

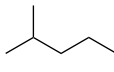


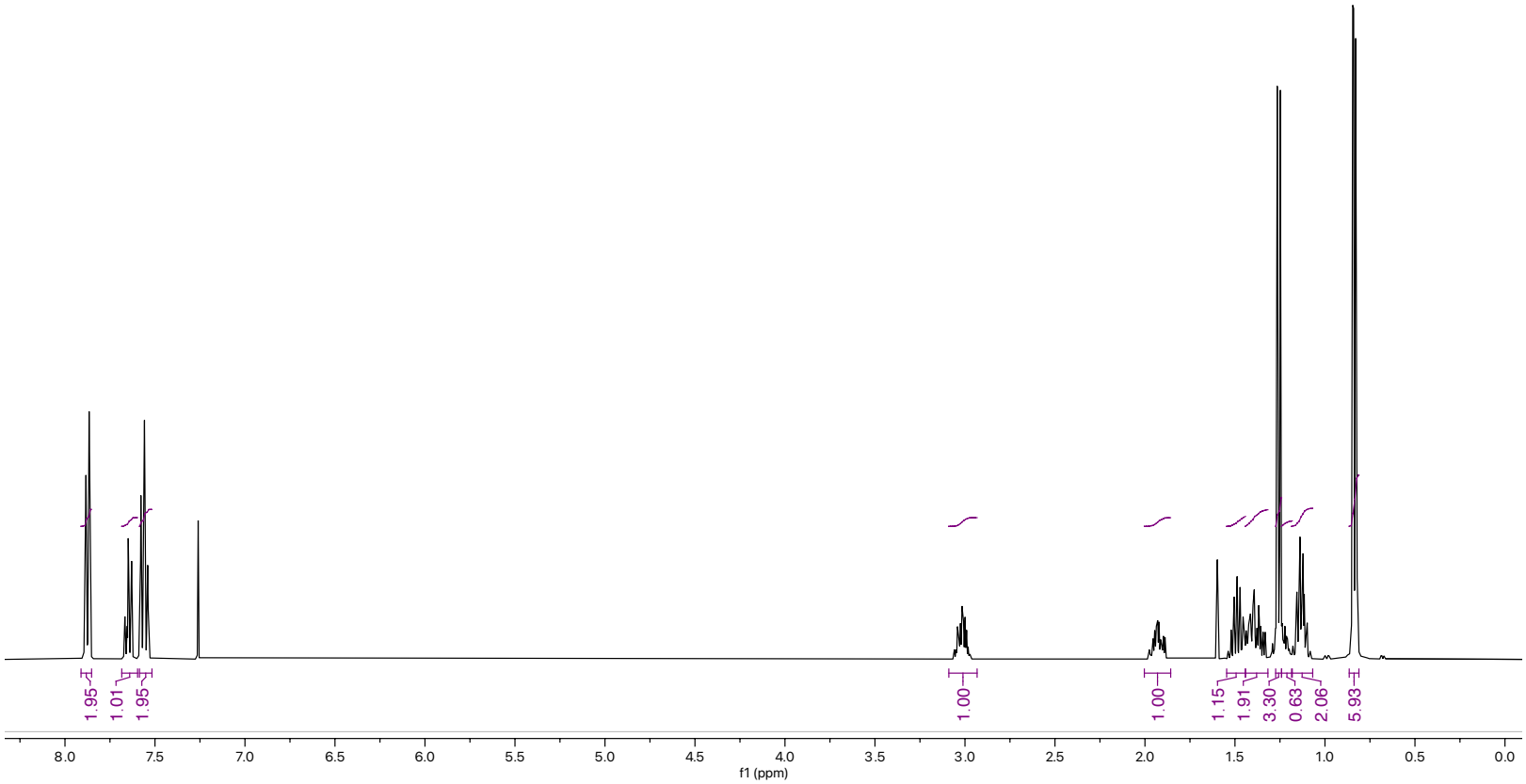

$^{13}$C-NMR (101 MHz, $CDCl_3$)



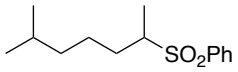
((6-Methylheptan-2-yl)sulfonyl)benzene

$^1$H-NMR (400 MHz, $CDCl_3$)

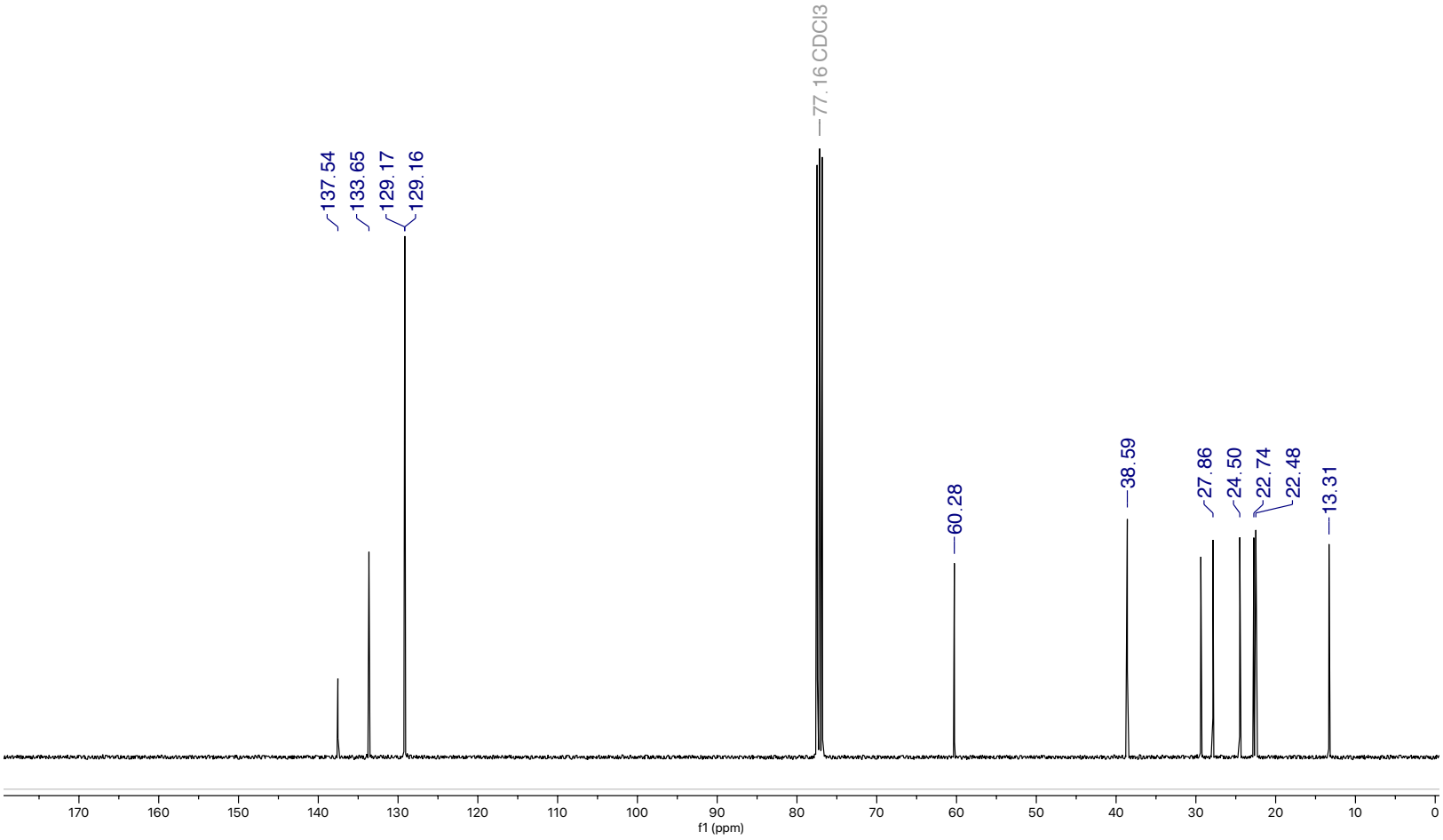


((6-Methylheptan-2-yl)sulfonyl)benzene

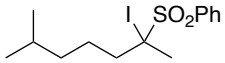


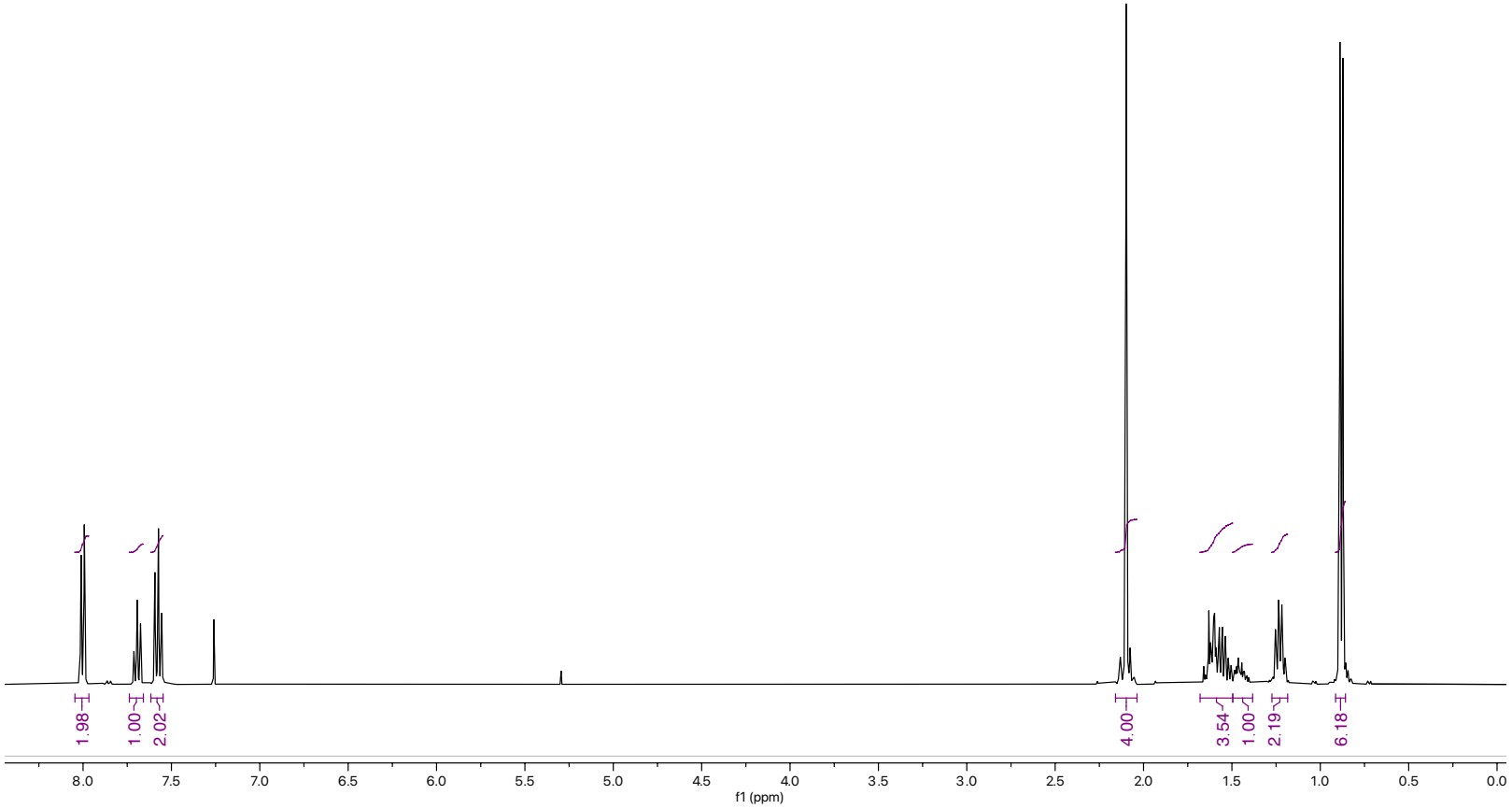

$^{13}$C-NMR (101 MHz, $CDCl_3$)



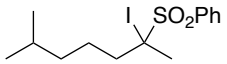
((2-Iodo-6-methylheptan-2-yl)sulfonyl)benzene

$^1$H-NMR (400 MHz, $CDCl_3$)

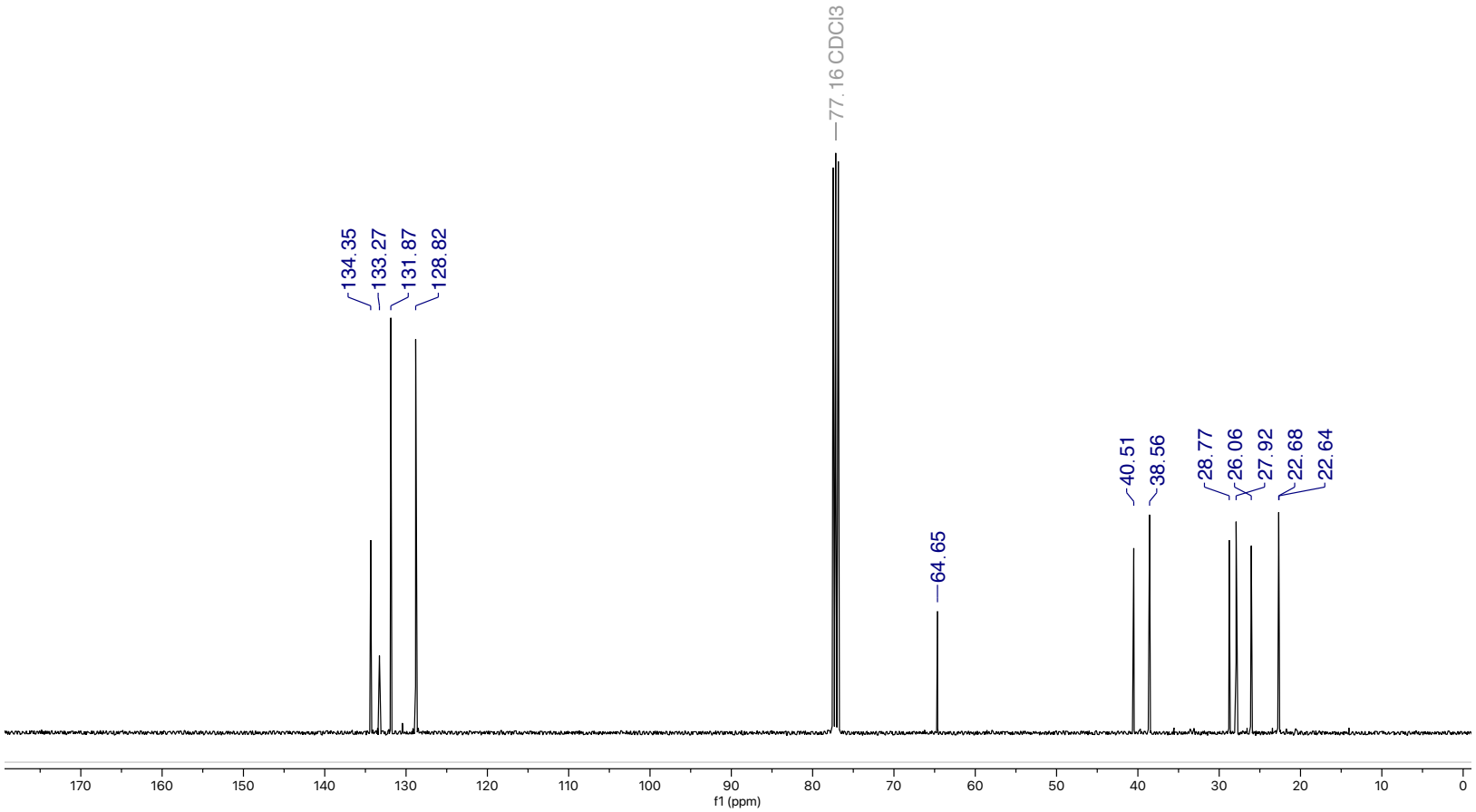


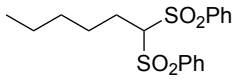
((2-Iodo-6-methylheptan-2-yl)sulfonyl)benzene



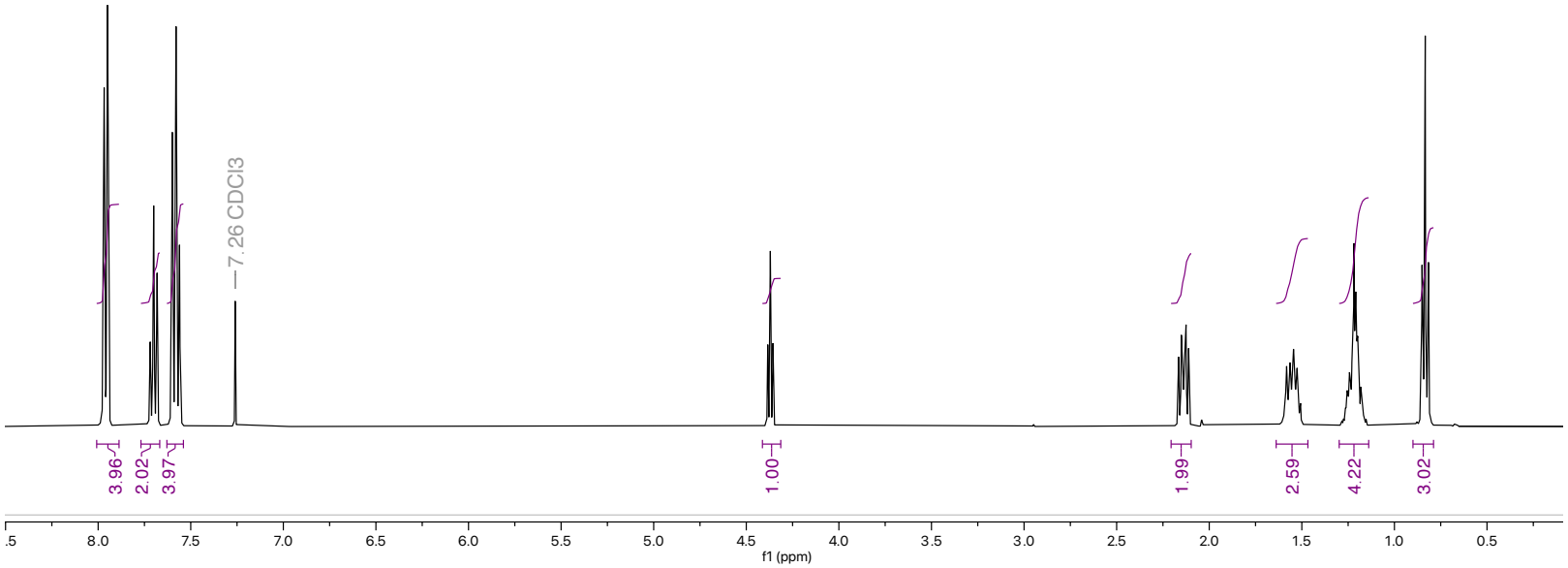

$^{13}$C-NMR (101 MHz, $CDCl_3$)



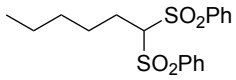
Hexane-1,1-diyldisulfonyl)dibenzene



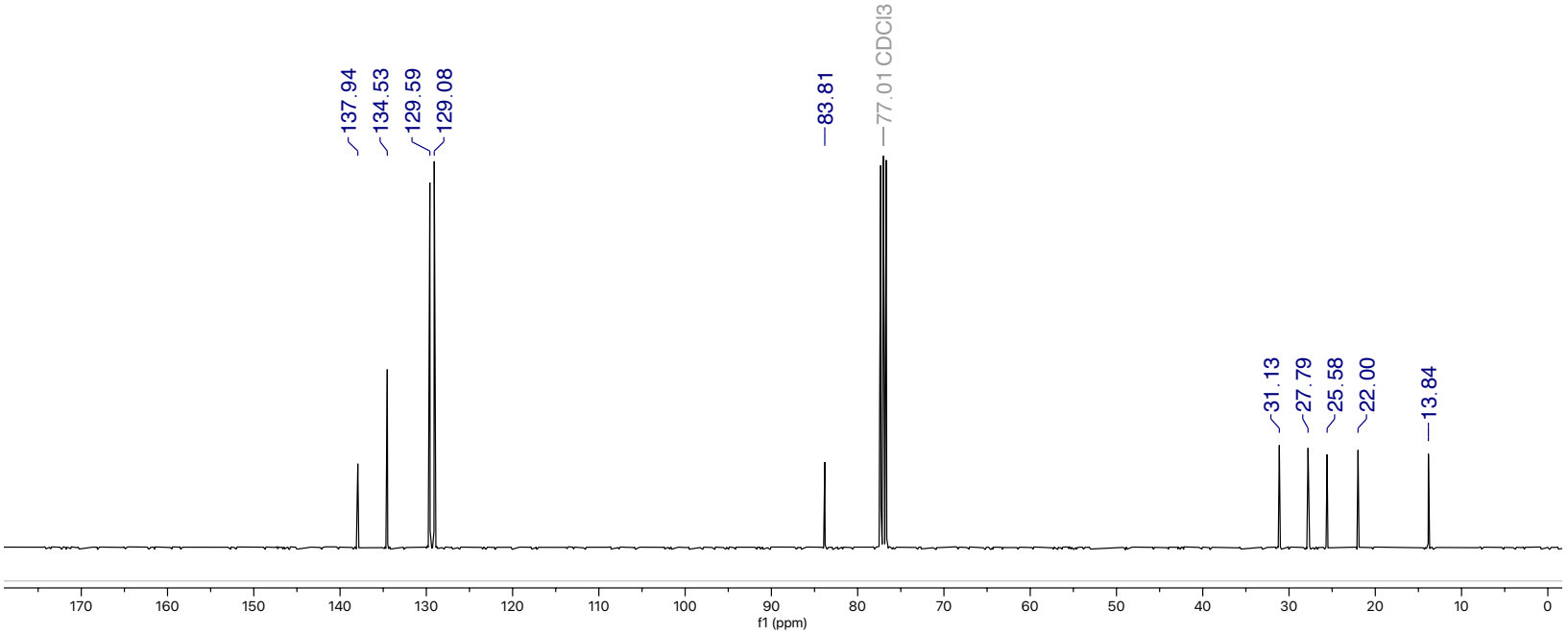

$^{1}$H-NMR (400 MHz, $CDCl_3$)



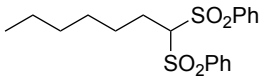
Hexane-1,1-diyldisulfonyl)dibenzene



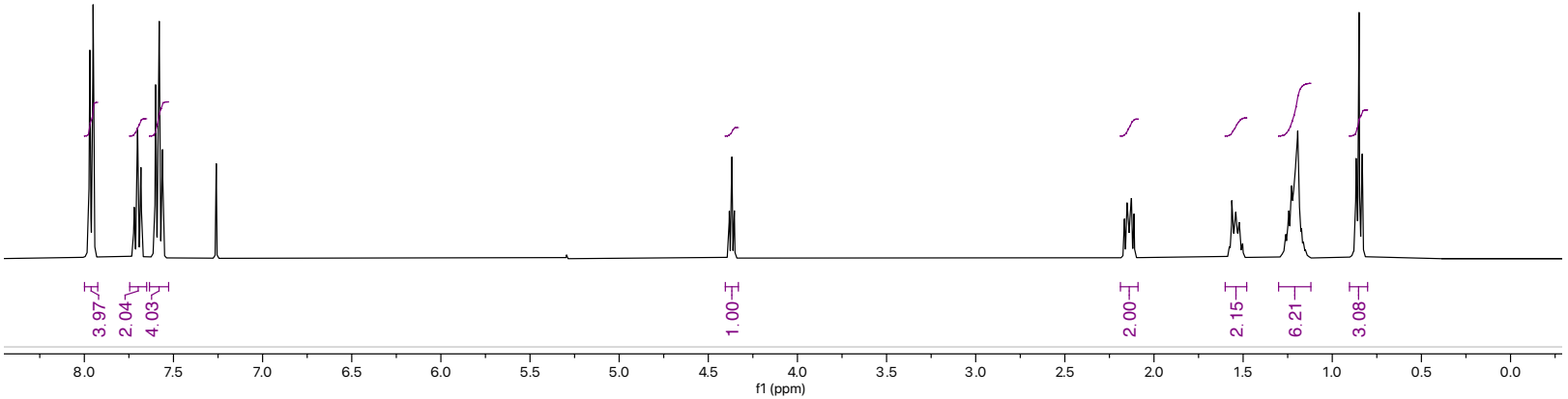

$^{13}$C-NMR (101 MHz, $CDCl_3$)



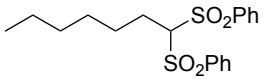
(Heptane-1,1-diyldisulfonyl)dibenzene



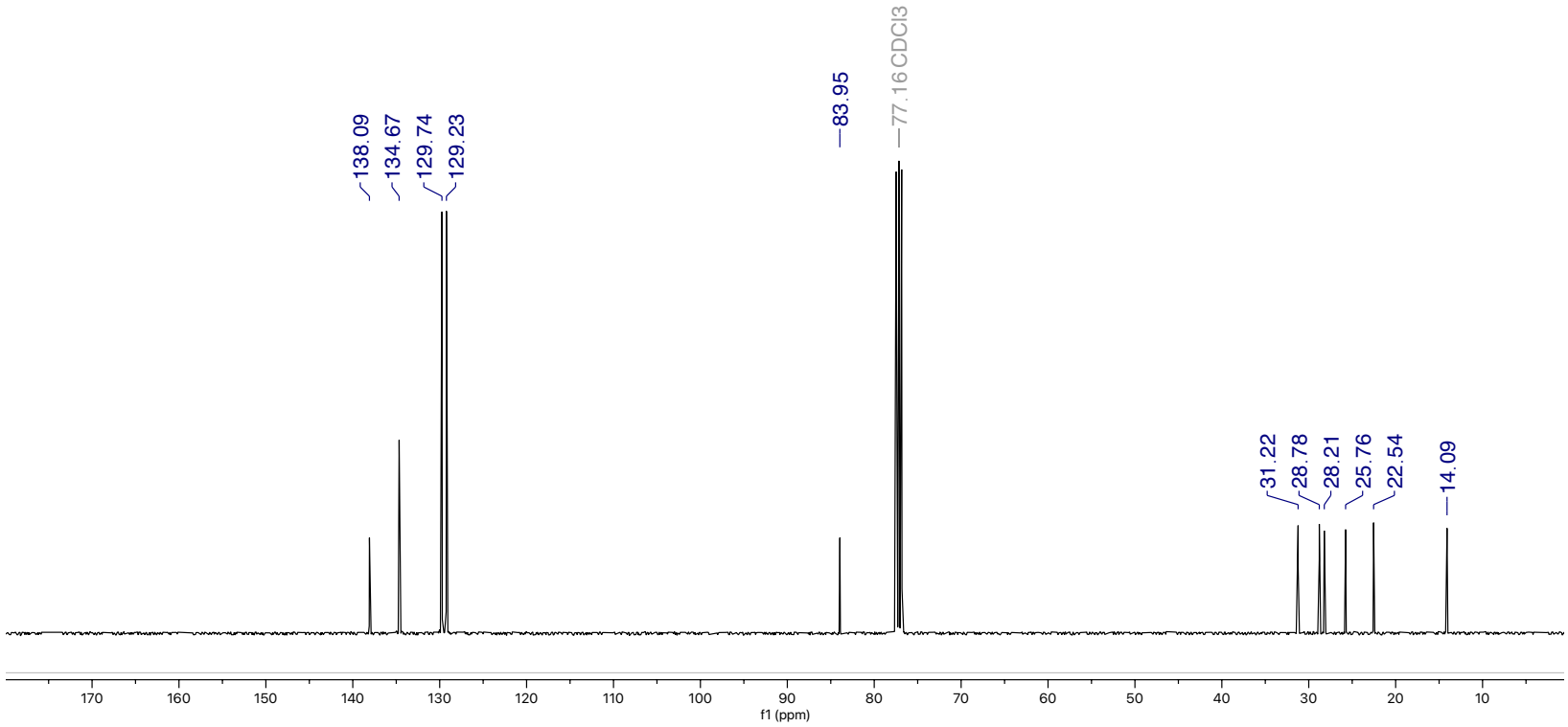

$^{1}$H-NMR (400 MHz, $CDCl_3$)



(Heptane-1,1-diyldisulfonyl)dibenzene



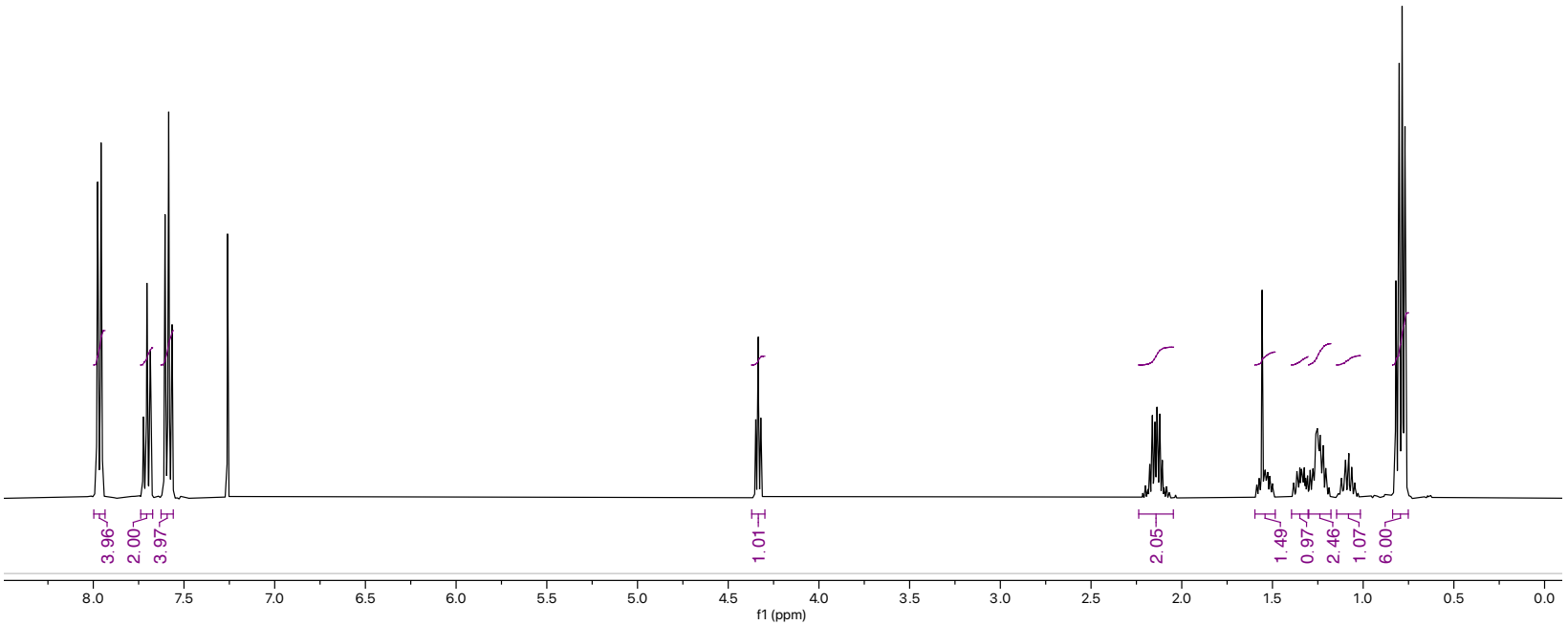

$^{13}$C-NMR (101 MHz, $CDCl_3$)



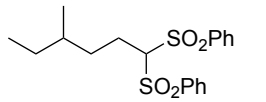
(4-Methylhexane-1,1-diyldisulfonyl)dibenzene

$^1$H-NMR (400 MHz, $CDCl_3$)



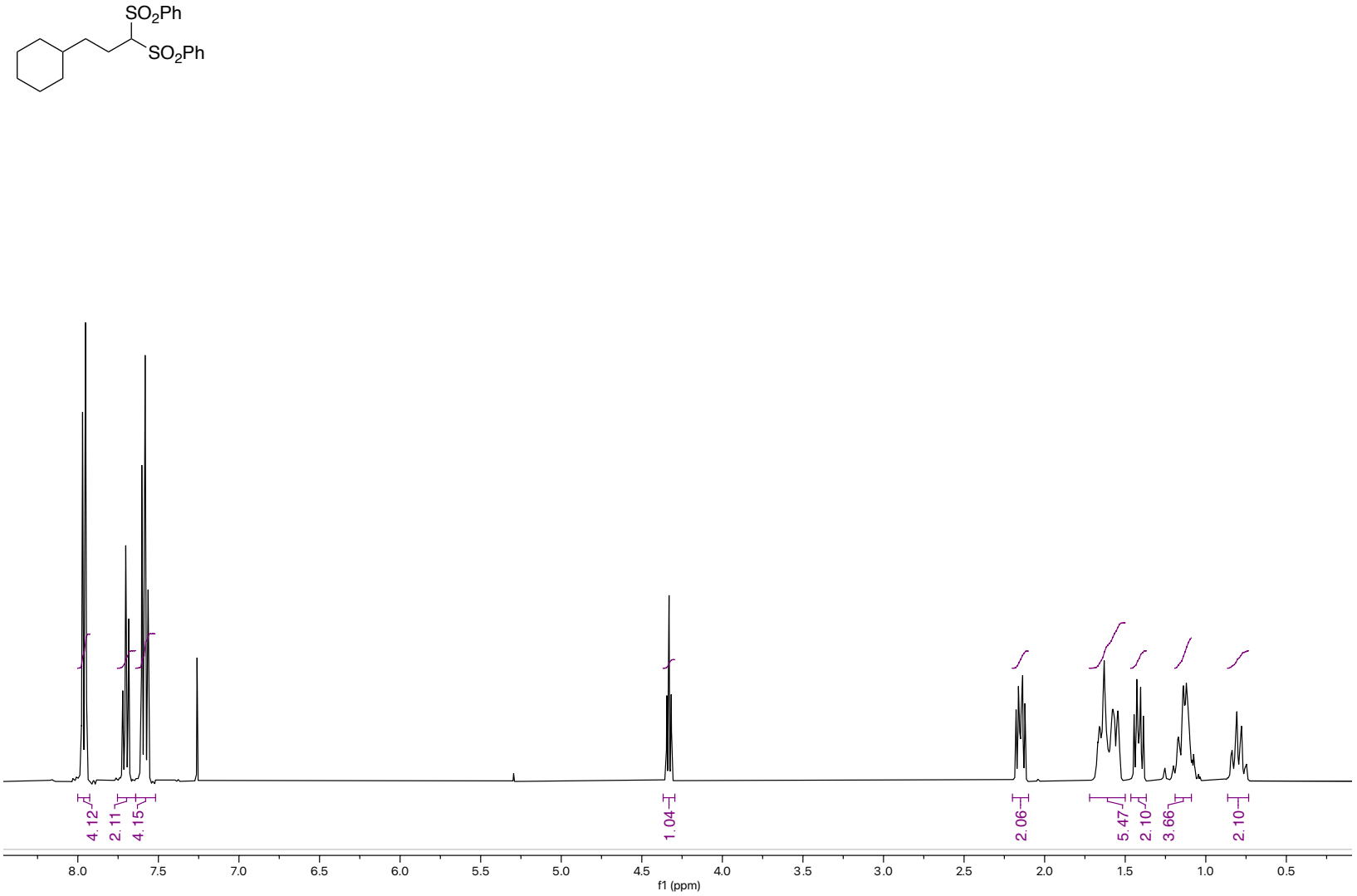
(4-Methylhexane-1,1-diyldisulfonyl)dibenzene




$^{13}$C-NMR (101 MHz, $CDCl_3$)

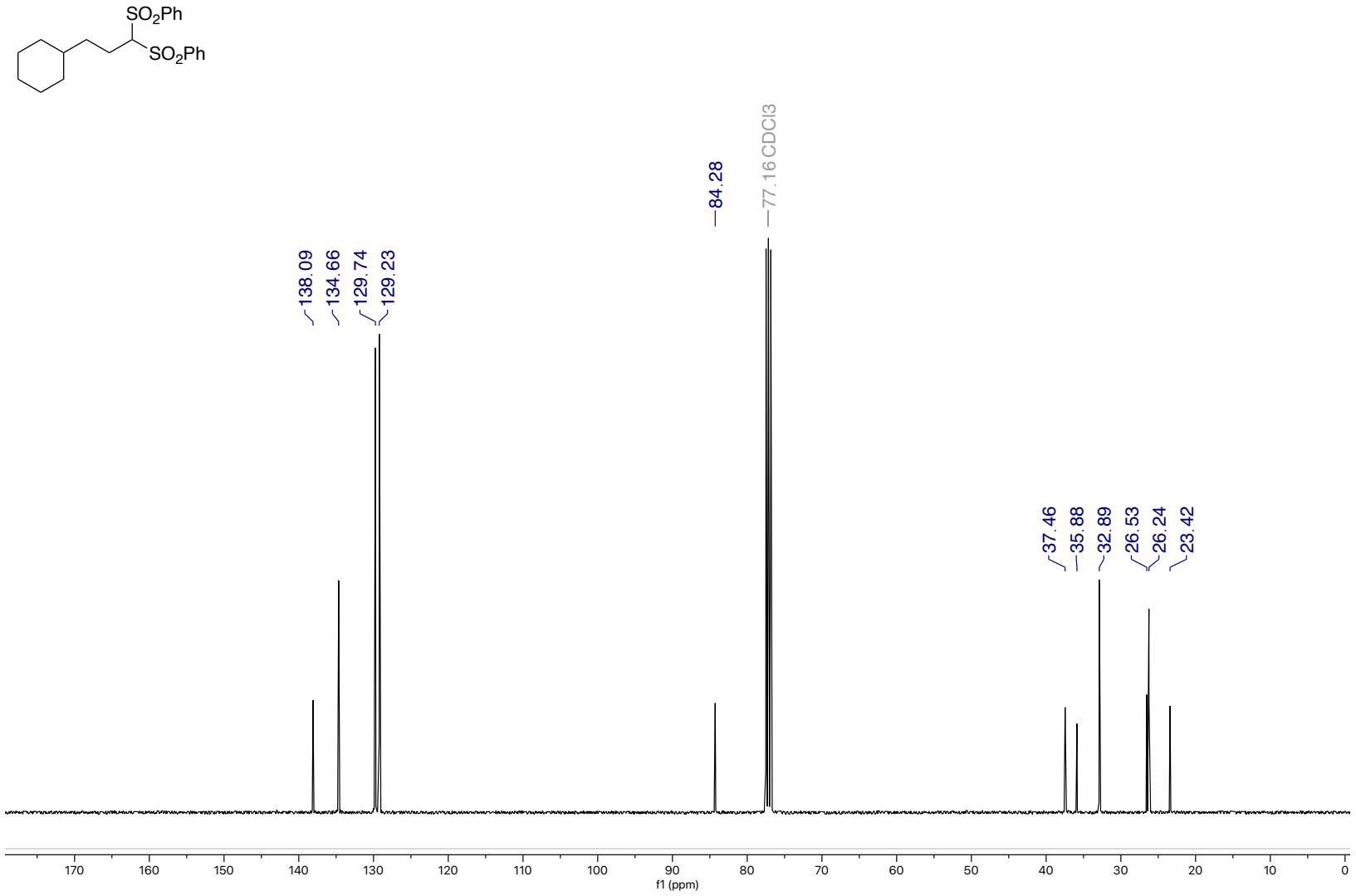
(3-Cyclohexylpropane-1,1-diyldisulfonyl)dibenzene

$^1$H-NMR (400 MHz, $CDCl_3$)



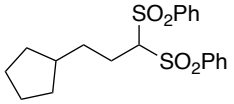
(3-Cyclohexylpropane-1,1-diyldisulfonyl)dibenzene

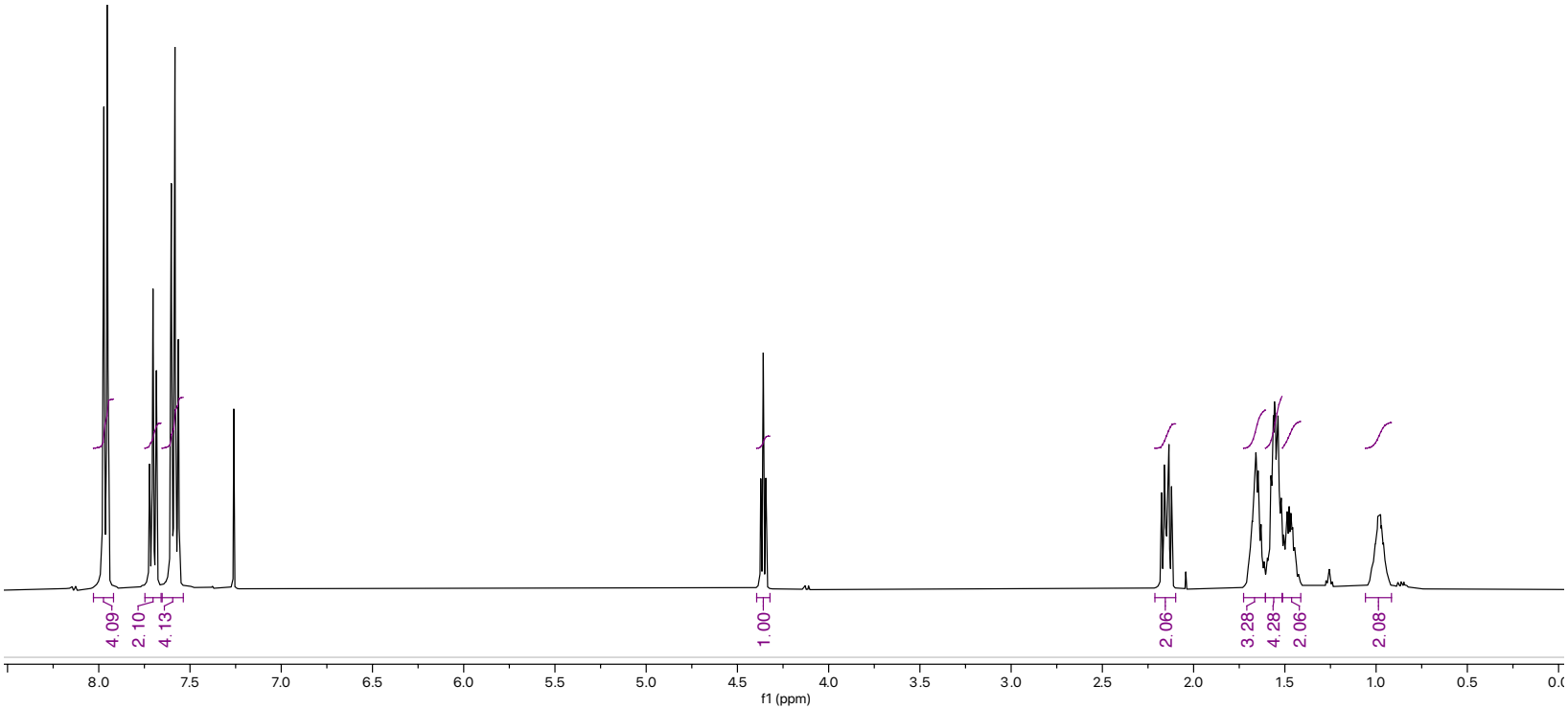
$^{13}$C-NMR (101 MHz, $CDCl_3$)



(3-Cyclopentylpropane-1,1-diyldisulfonyl)dibenzene

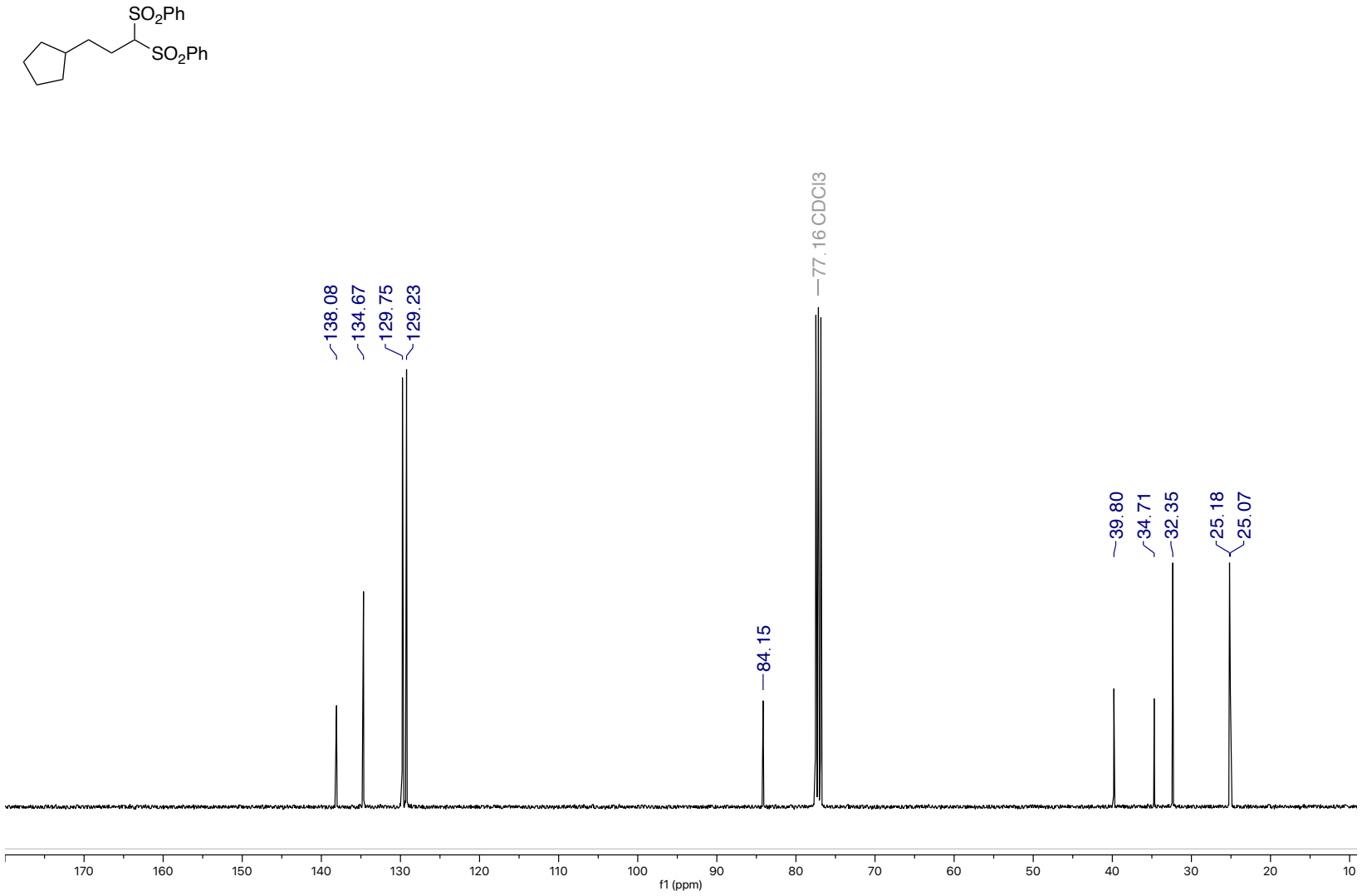
$^1$H-NMR (400 MHz, $CDCl_3$)



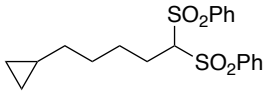
(3-Cyclopentylpropane-1,1-diyldisulfonyl)dibenzene

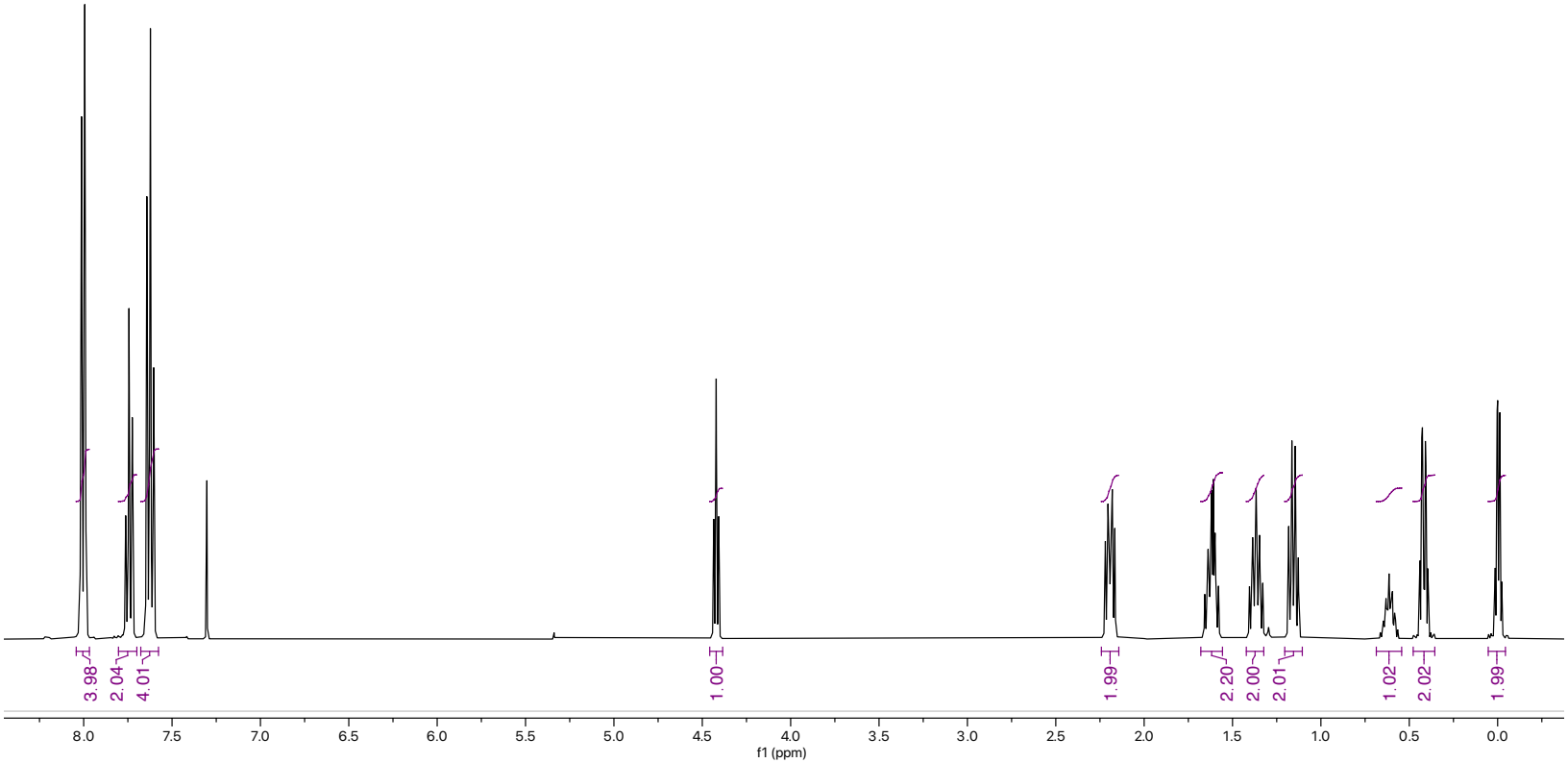
$^{13}$C-NMR (101 MHz, $CDCl_3$)



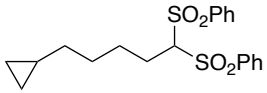
(5-Cyclopropylpentane-1,1-diyldisulfonyl)dibenzene

$^1$H-NMR (400 MHz, $CDCl_3$)

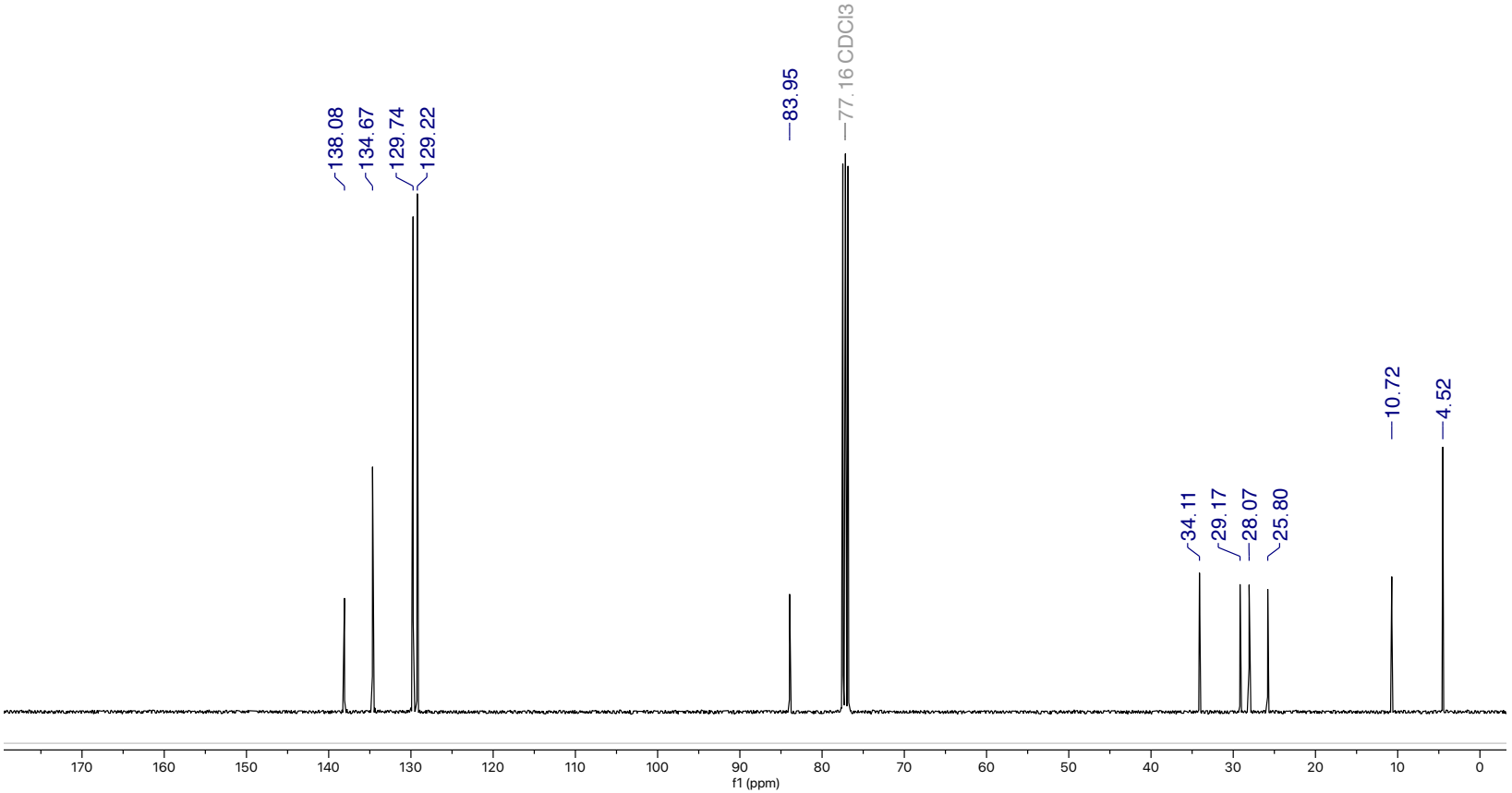


(5-Cyclopropylpentane-1,1-diyldisulfonyl)dibenzene

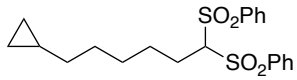


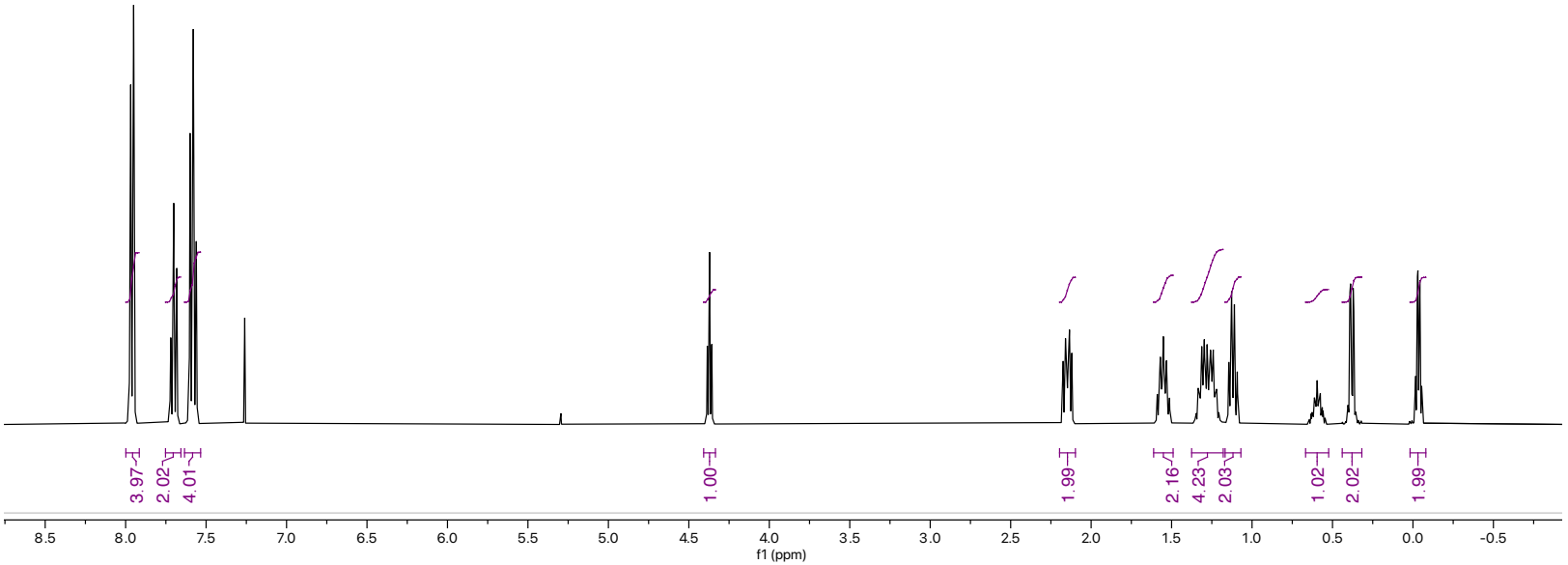

$^{13}$C-NMR (101 MHz, $CDCl_3$)



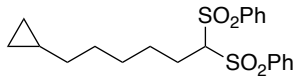
(6-Cyclopropylhexane-1,1-diyldisulfonyl)dibenzene

$^1$H-NMR (400 MHz, $CDCl_3$)

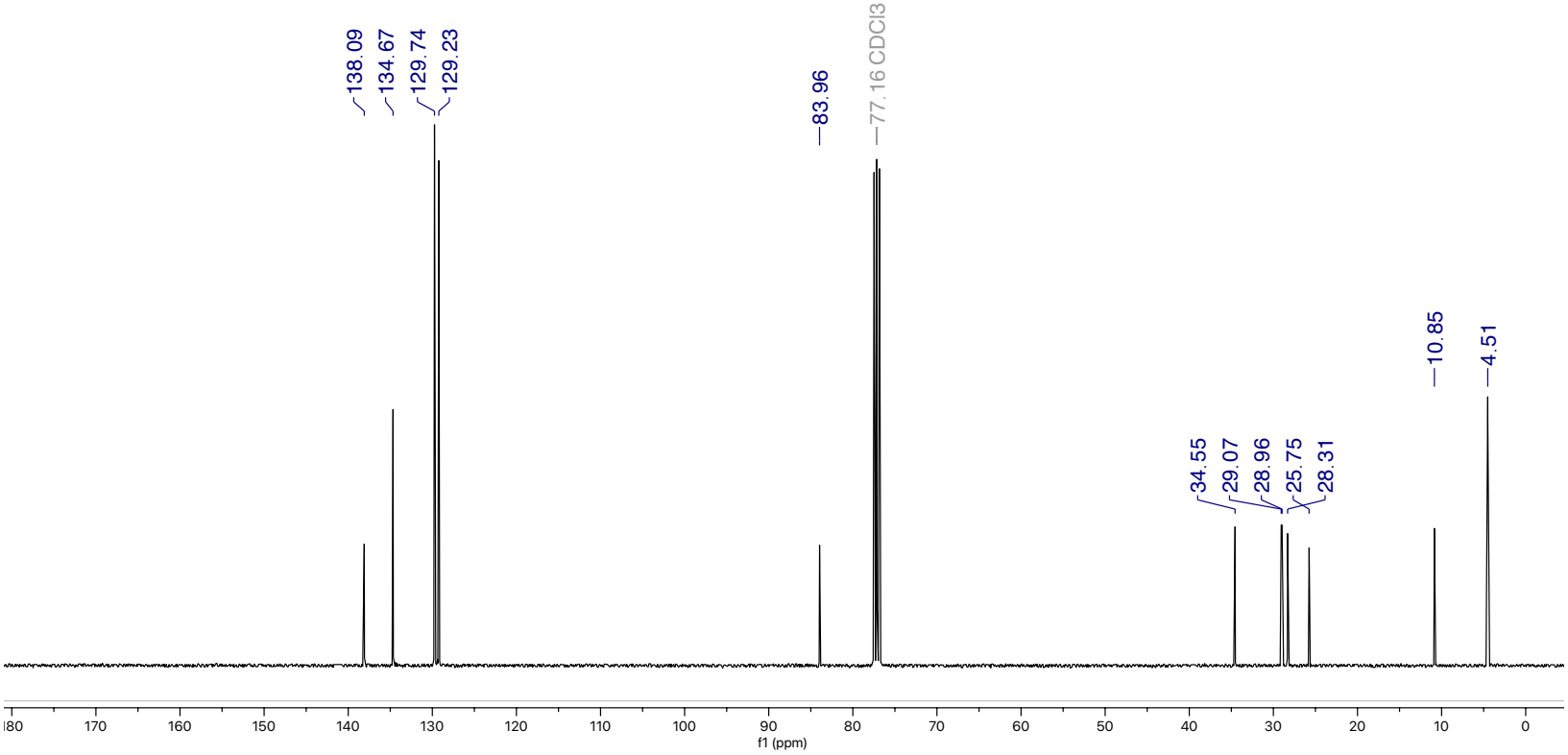


(6-Cyclopropylhexane-1,1-diyldisulfonyl)dibenzene

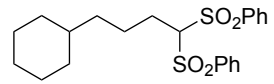


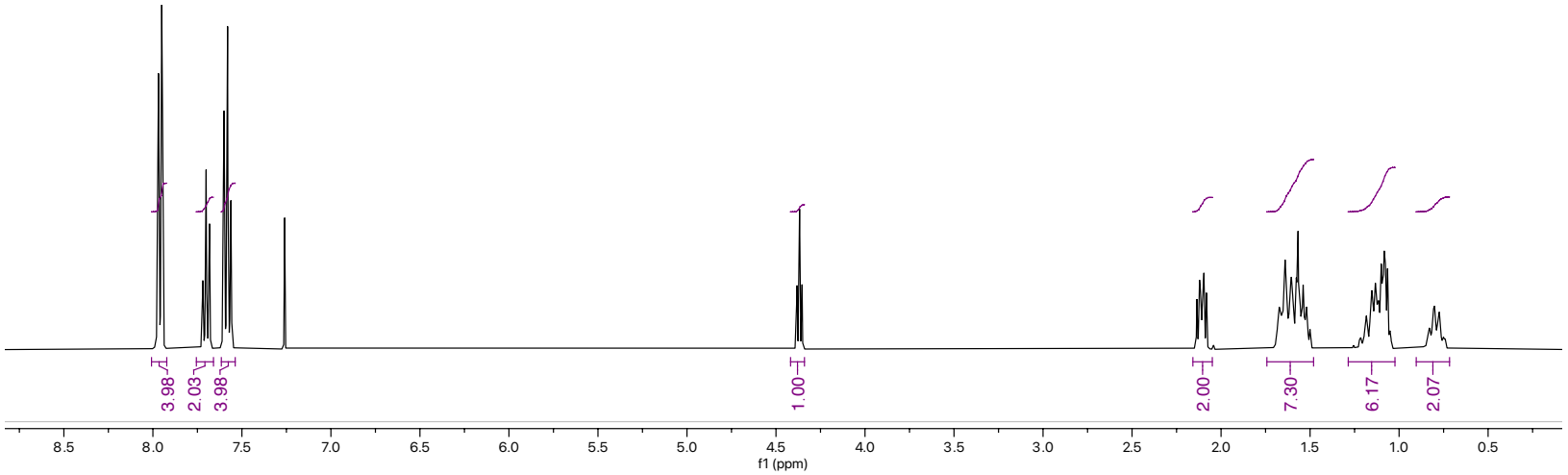

$^{13}$C-NMR (101 MHz, $CDCl_3$)



(4-Cyclohexylbutane-1,1-diyldisulfonyl)dibenzene

$^1$H-NMR (400 MHz, $CDCl_3$)

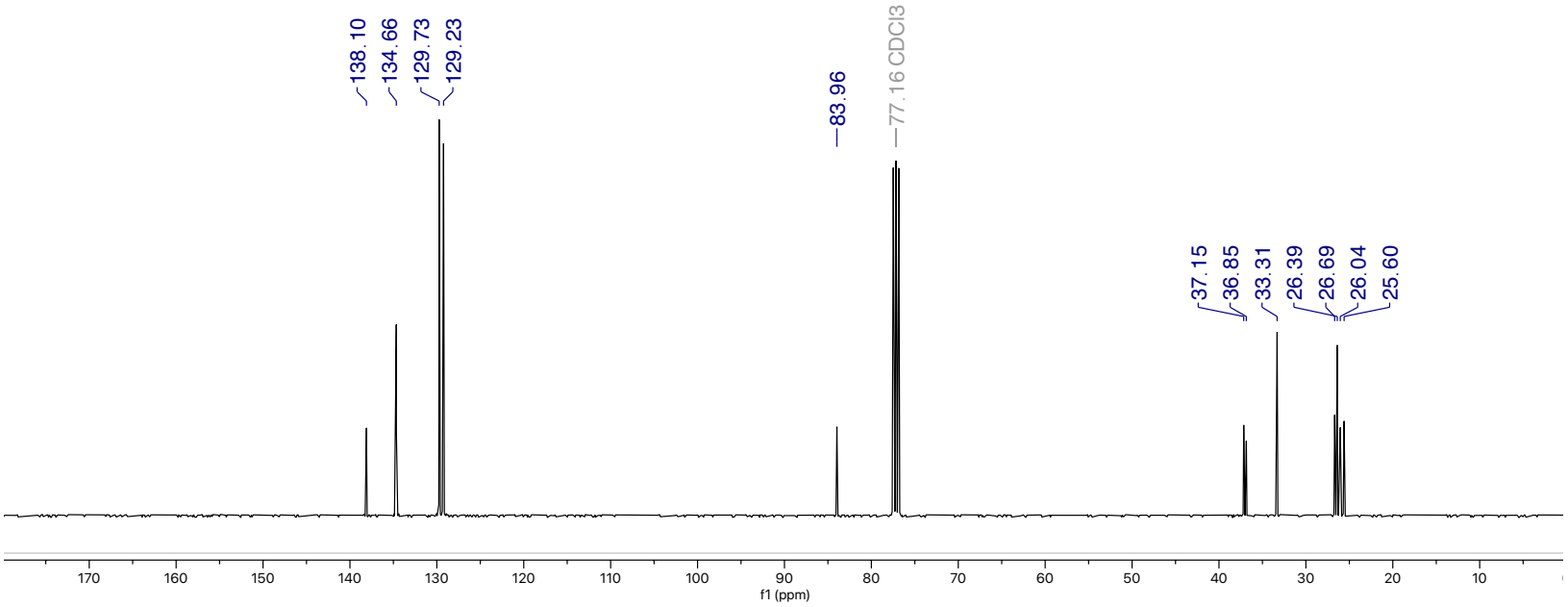


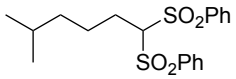
(4-Cyclohexylbutane-1,1-diyldisulfonyl)dibenzene

$^{13}$C-NMR (101 MHz, $CDCl_3$)

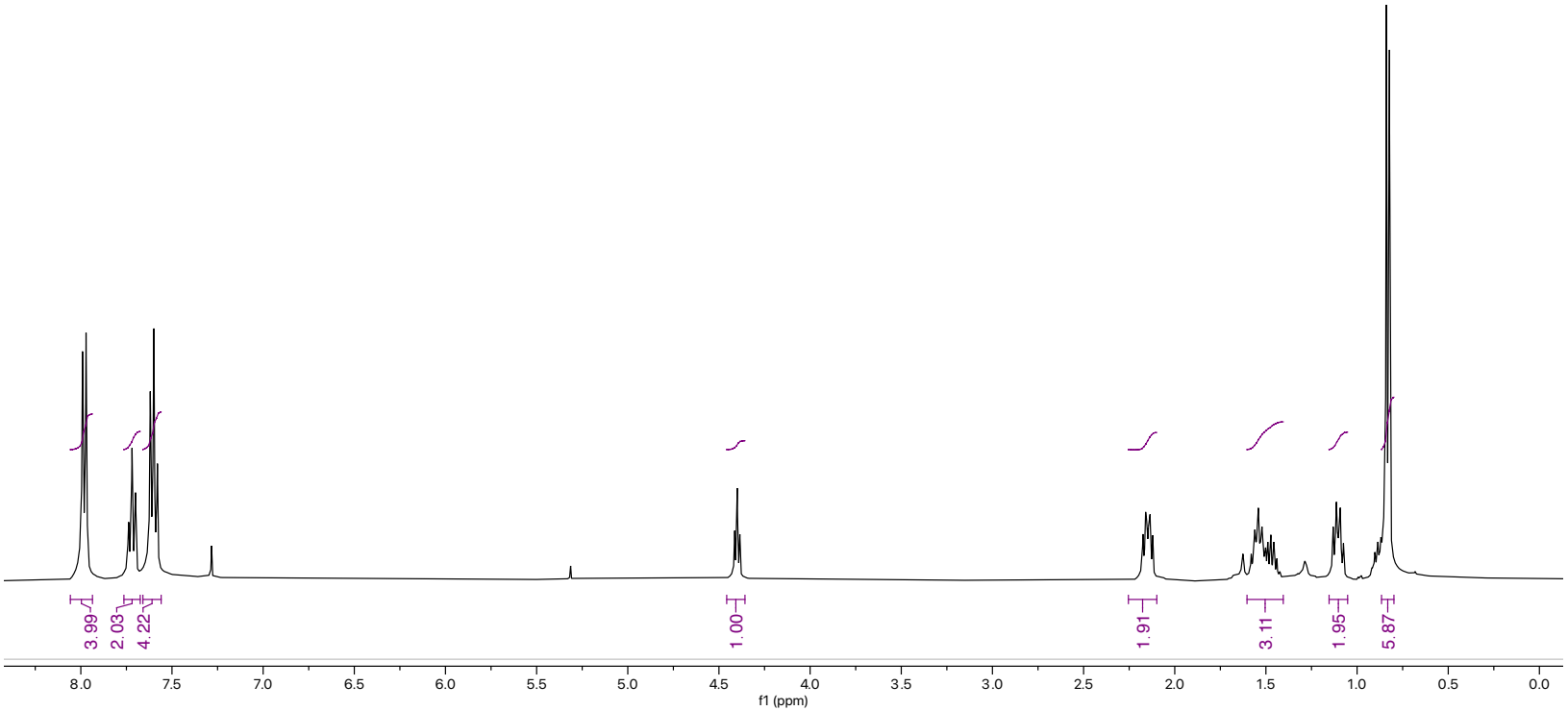


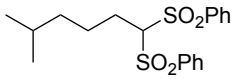
(5-Methylhexane-1,1-diyldisulfonyl)dibenzene



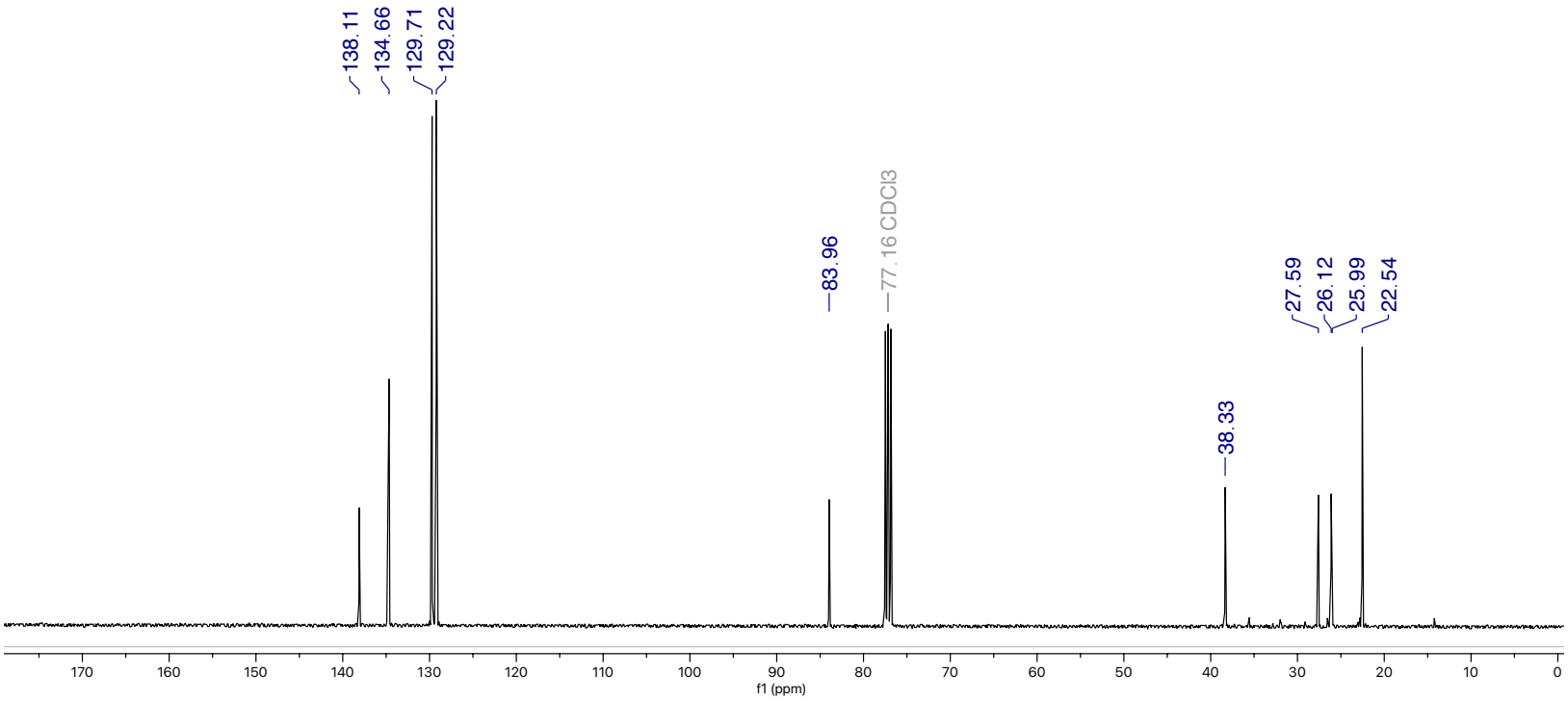

$^1$H-NMR (400 MHz, $CDCl_3$)



(5-Methylhexane-1,1-diyldisulfonyl)dibenzene

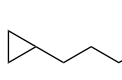


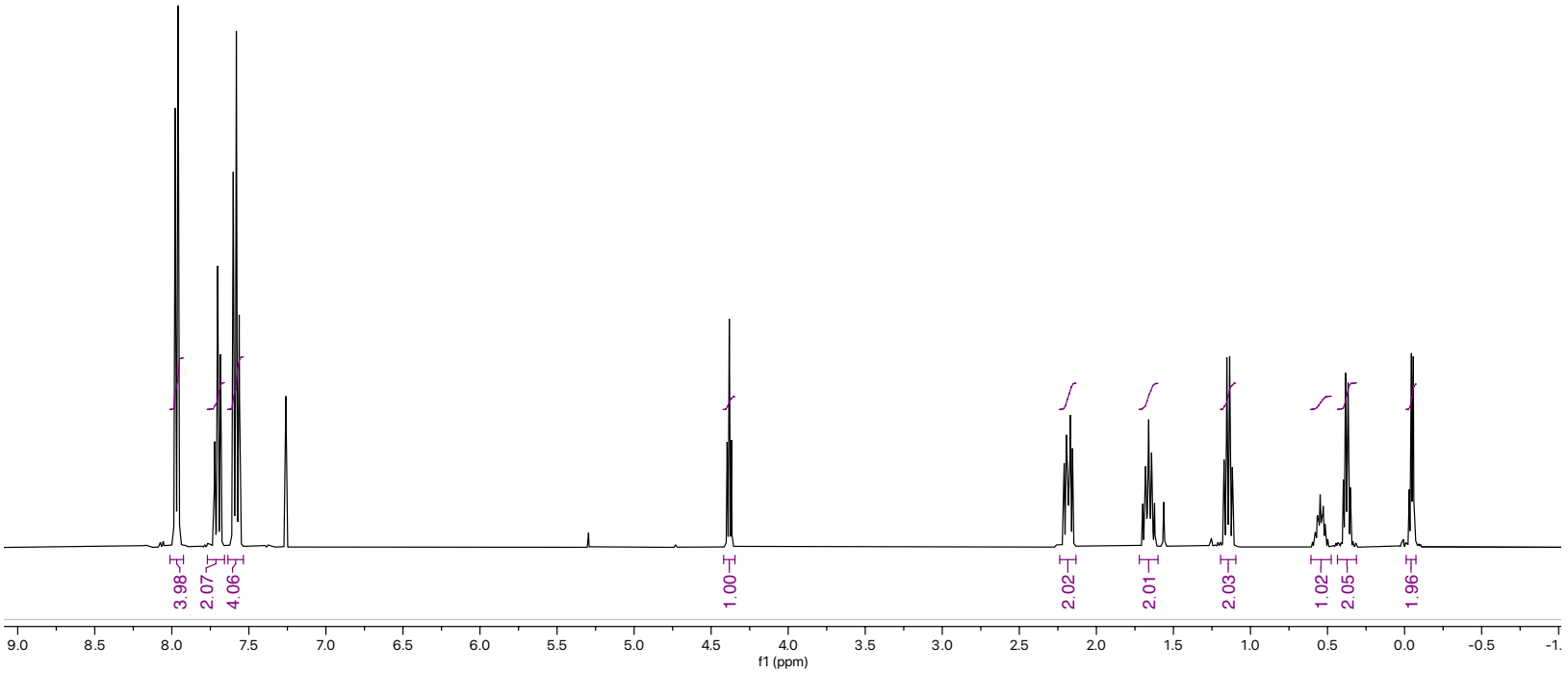

$^{13}$C-NMR (101 MHz, $CDCl_3$)



(4-Cyclopropylbutane-1,1-diyldisulfonyl)dibenzene

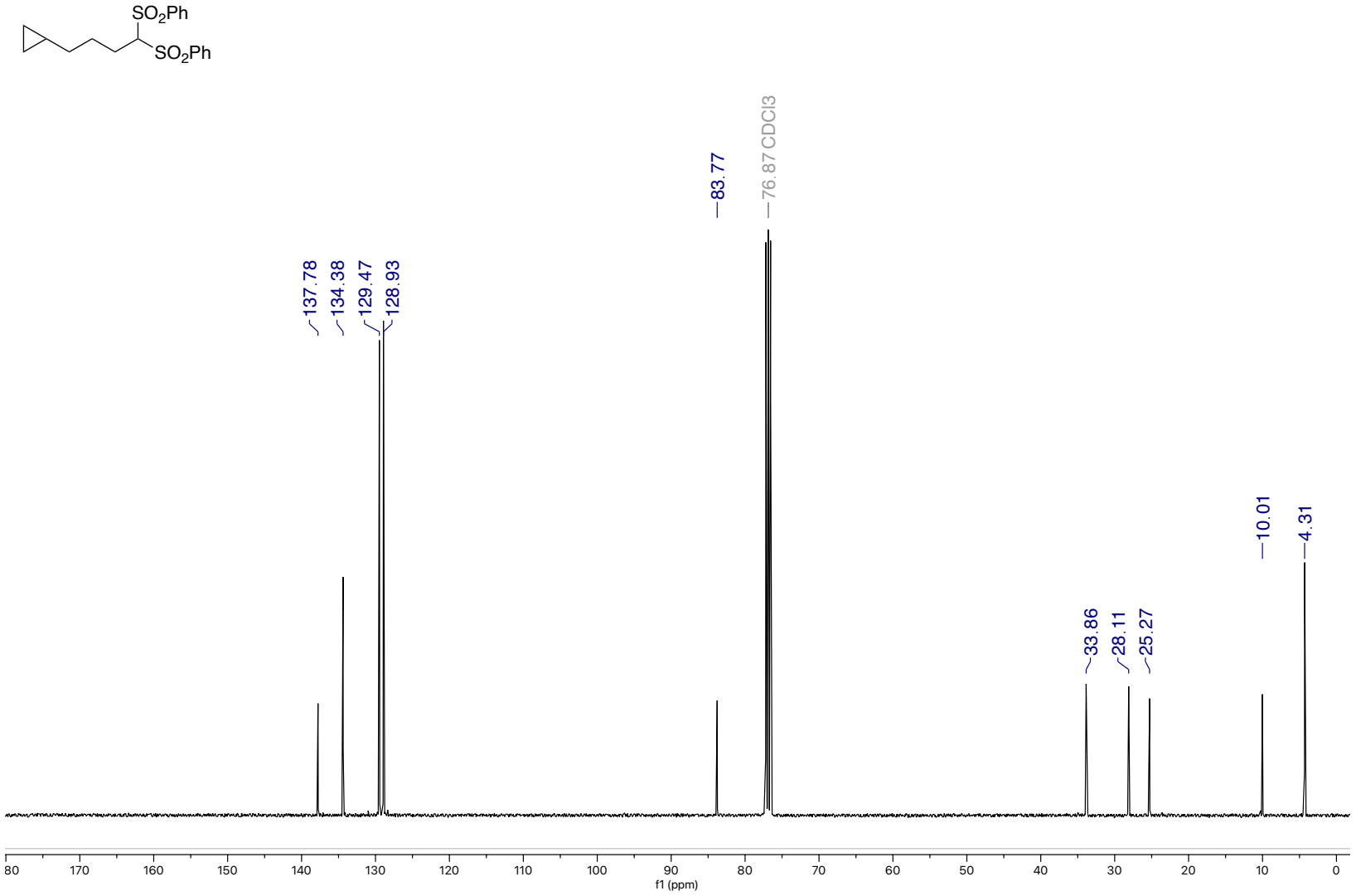
$^1$H-NMR (400 MHz, $CDCl_3$)



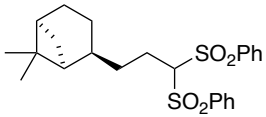
(4-Cyclopropylbutane-1,1-diyldisulfonyl)dibenzene

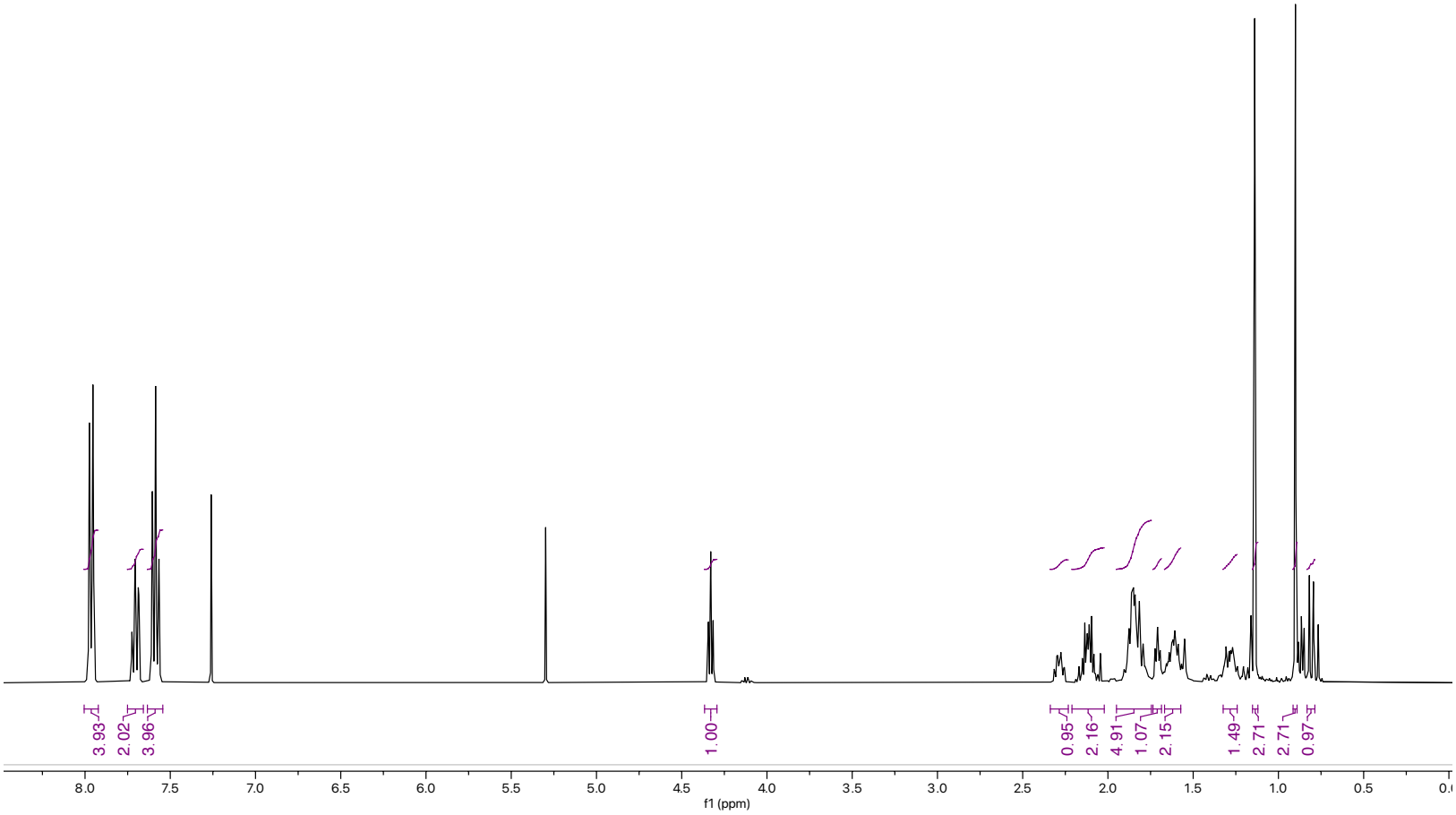
$^{13}$C-NMR (101 MHz, $CDCl_3$)



(1S,2S,5S)-2-(3,3-bis(phenylsulfonyl)propyl)-6,6-dimethylbicyclo[3.1.1]heptane

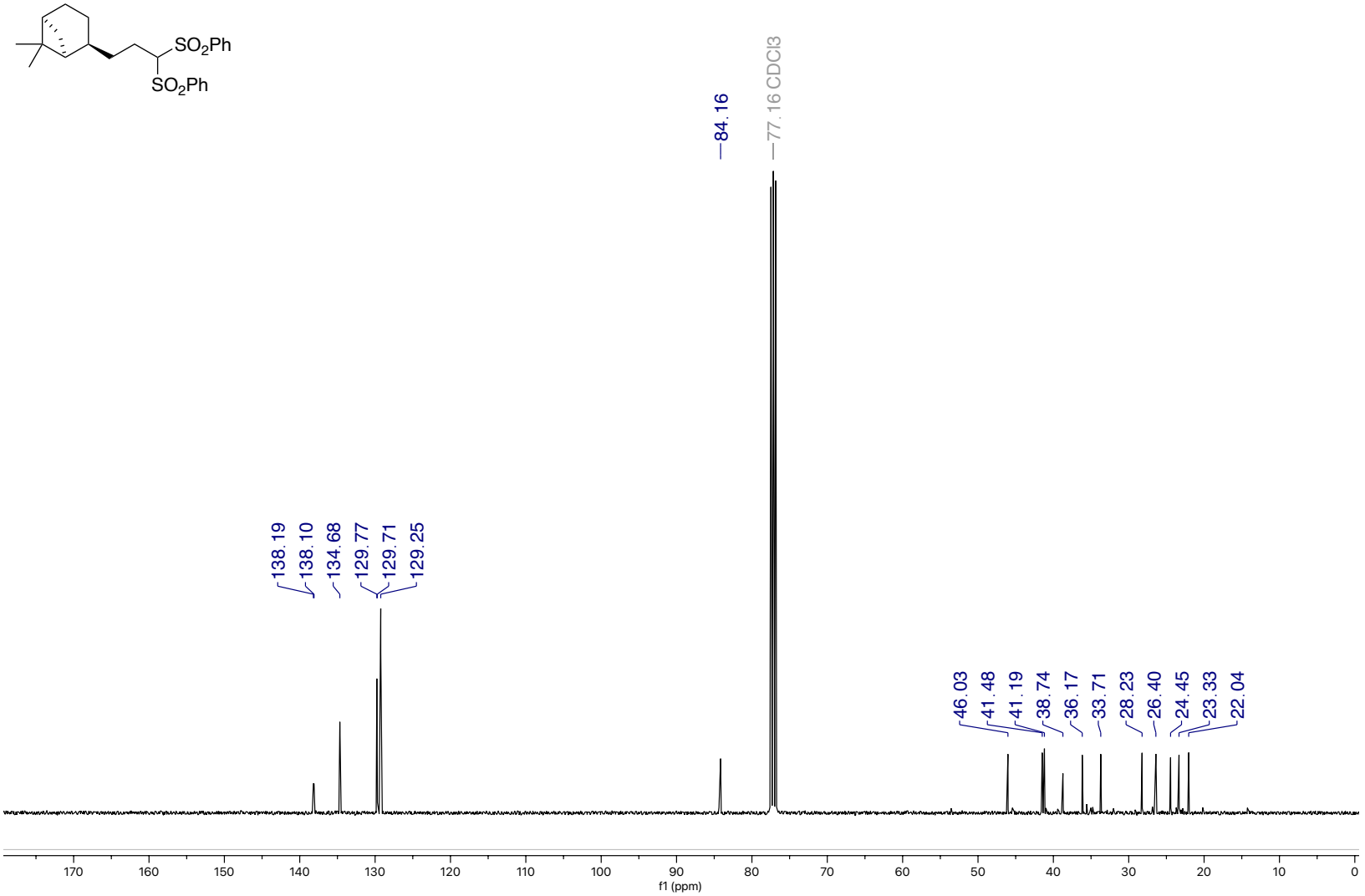
$^1$H-NMR (400 MHz, $CDCl_3$)



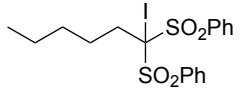
(1S,2S,5S)-2-(3,3-bis(phenylsulfonyl)propyl)-6,6-dimethylbicyclo[3.1.1]heptane

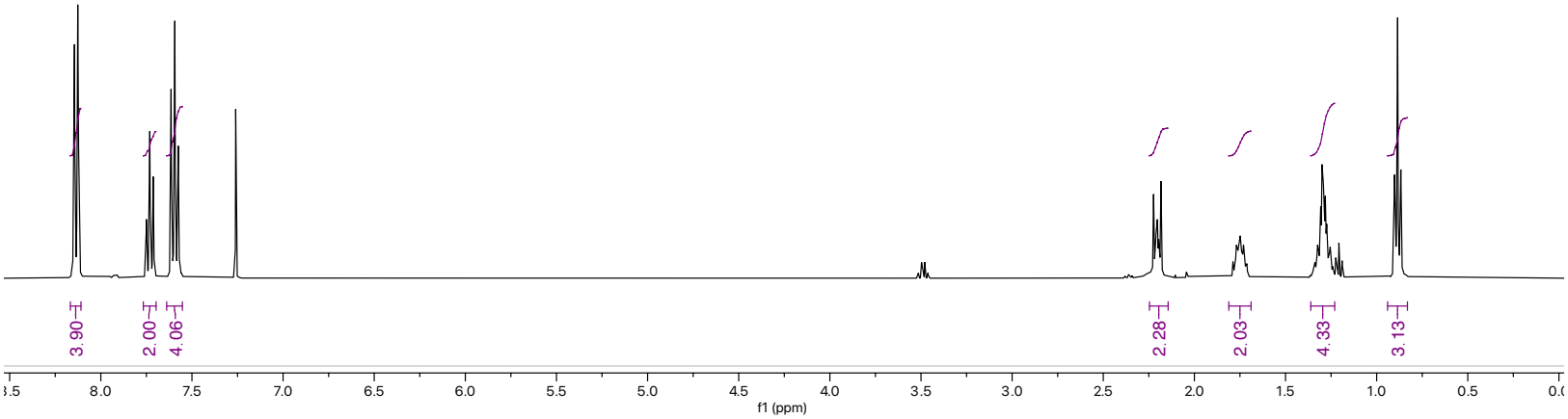
$^{13}$C-NMR (101 MHz, $CDCl_3$)



(1-Iodohexane-1,1-diyldisulfonyl)dibenzene

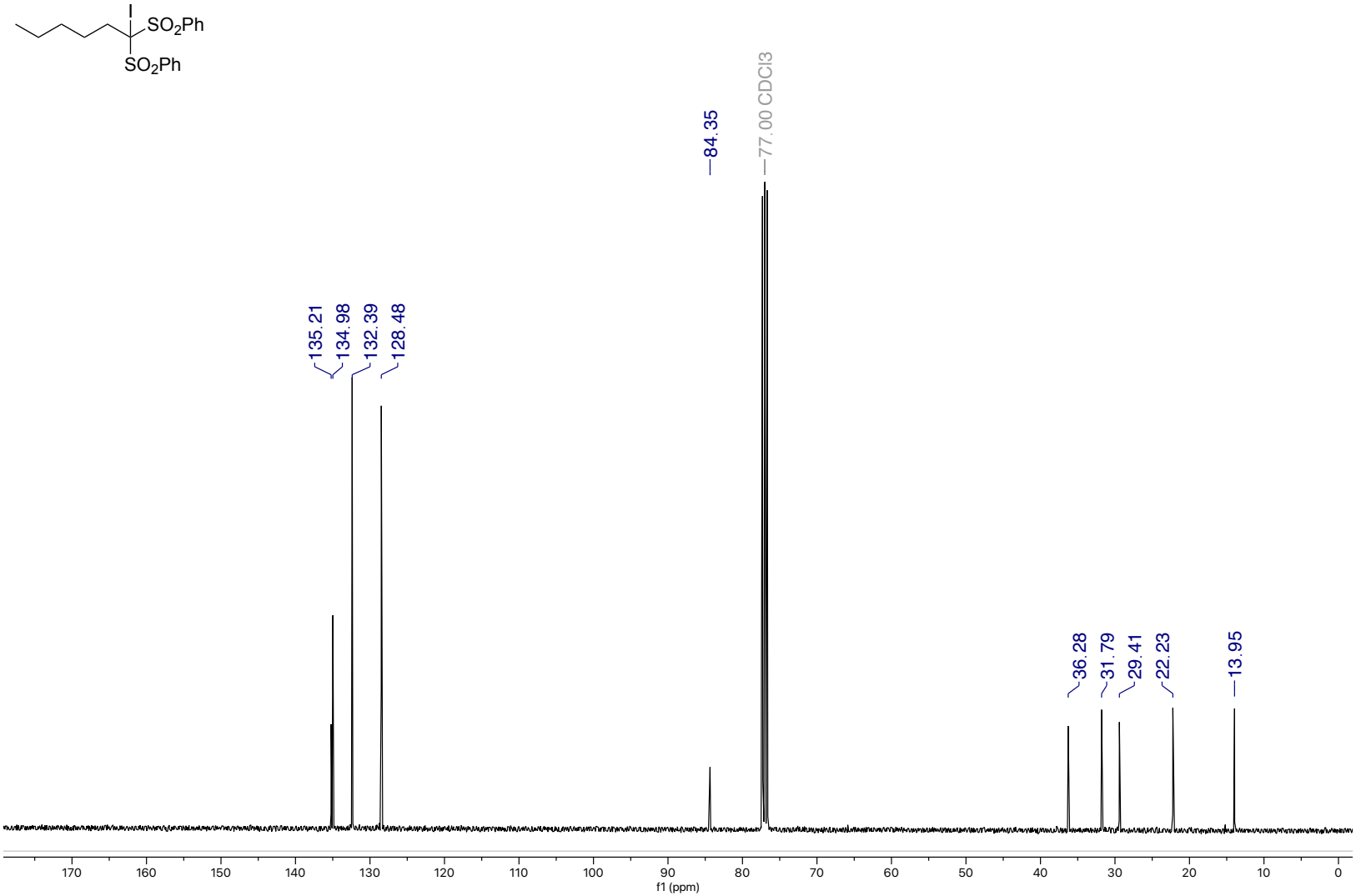
$^1$H-NMR (400 MHz, $CDCl_3$)



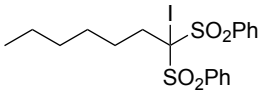



(1-Iodohexane-1,1-diyldisulfonyl)dibenzene

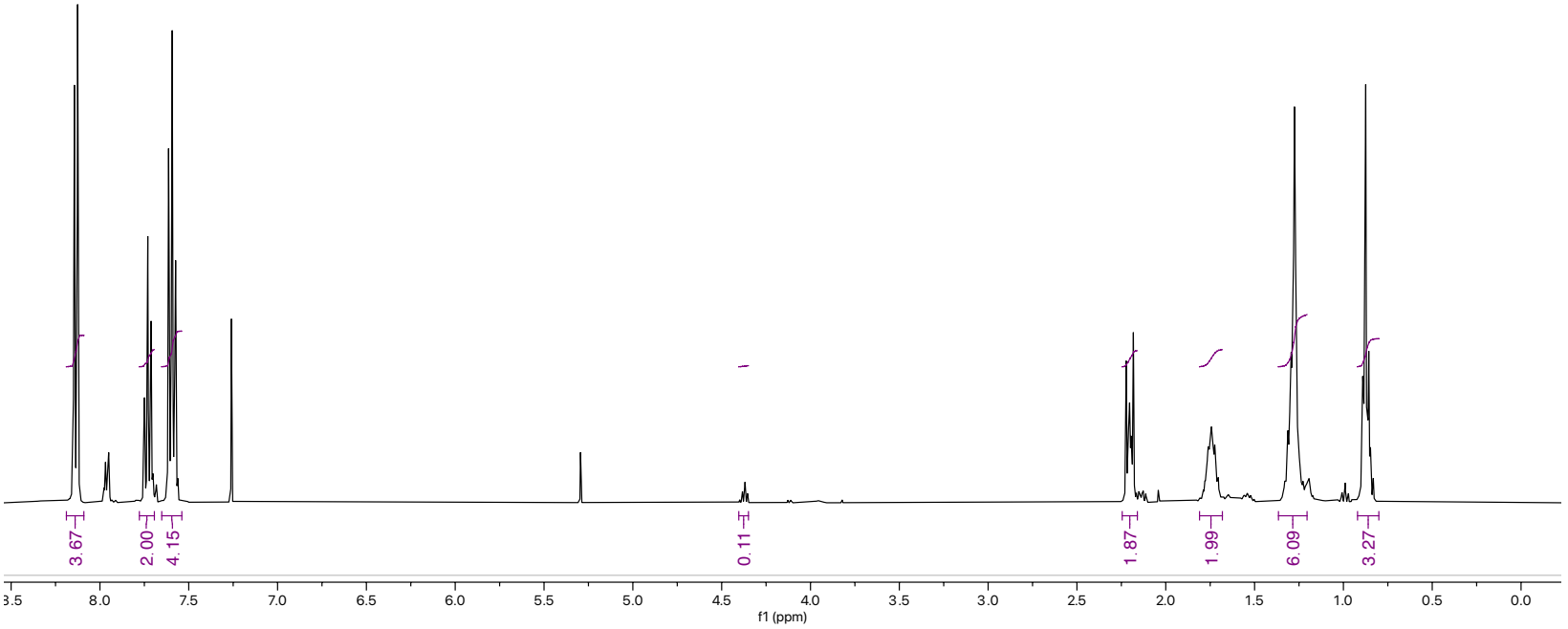
$^{13}$C-NMR (101 MHz, $CDCl_3$)



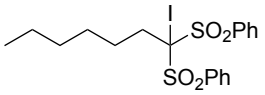
(1-Iodoheptane-1,1-diyldisulfonyl)dibenzene



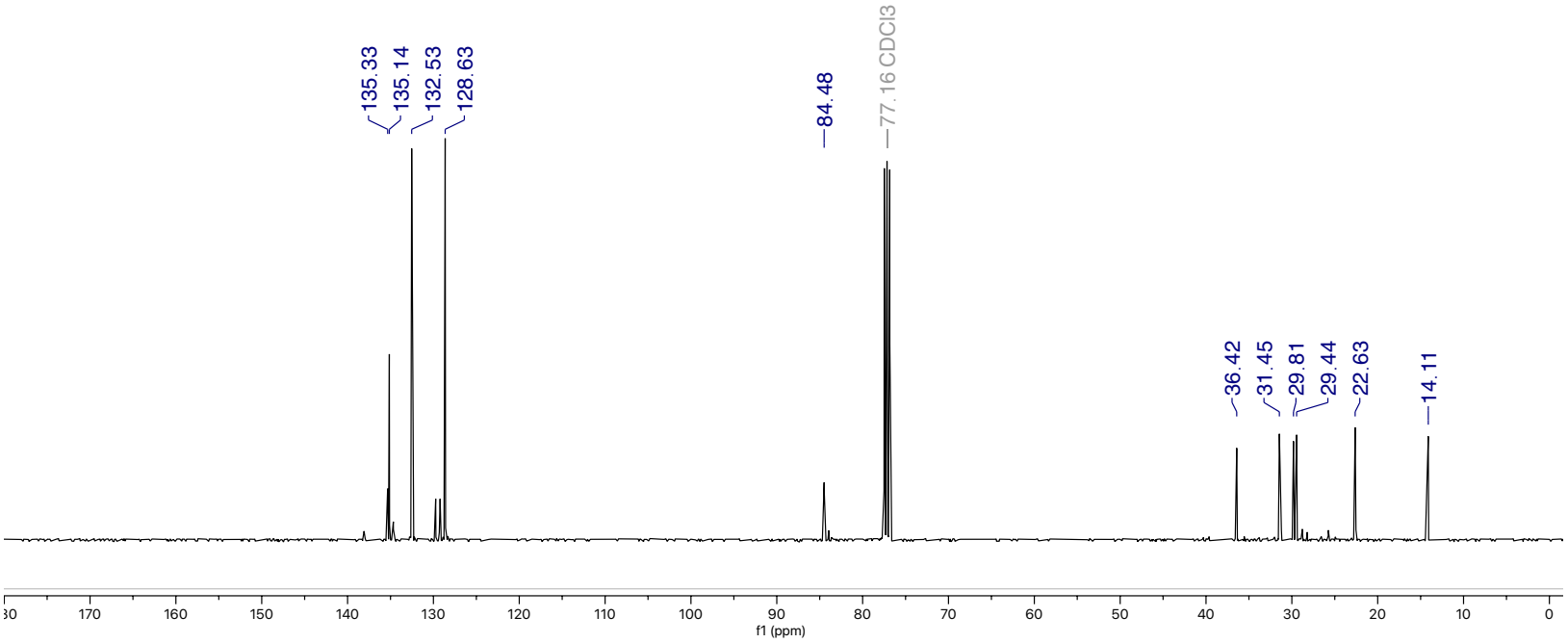

$^1$H-NMR (400 MHz, $CDCl_3$)



(1-Iodoheptane-1,1-diyldisulfonyl)dibenzene

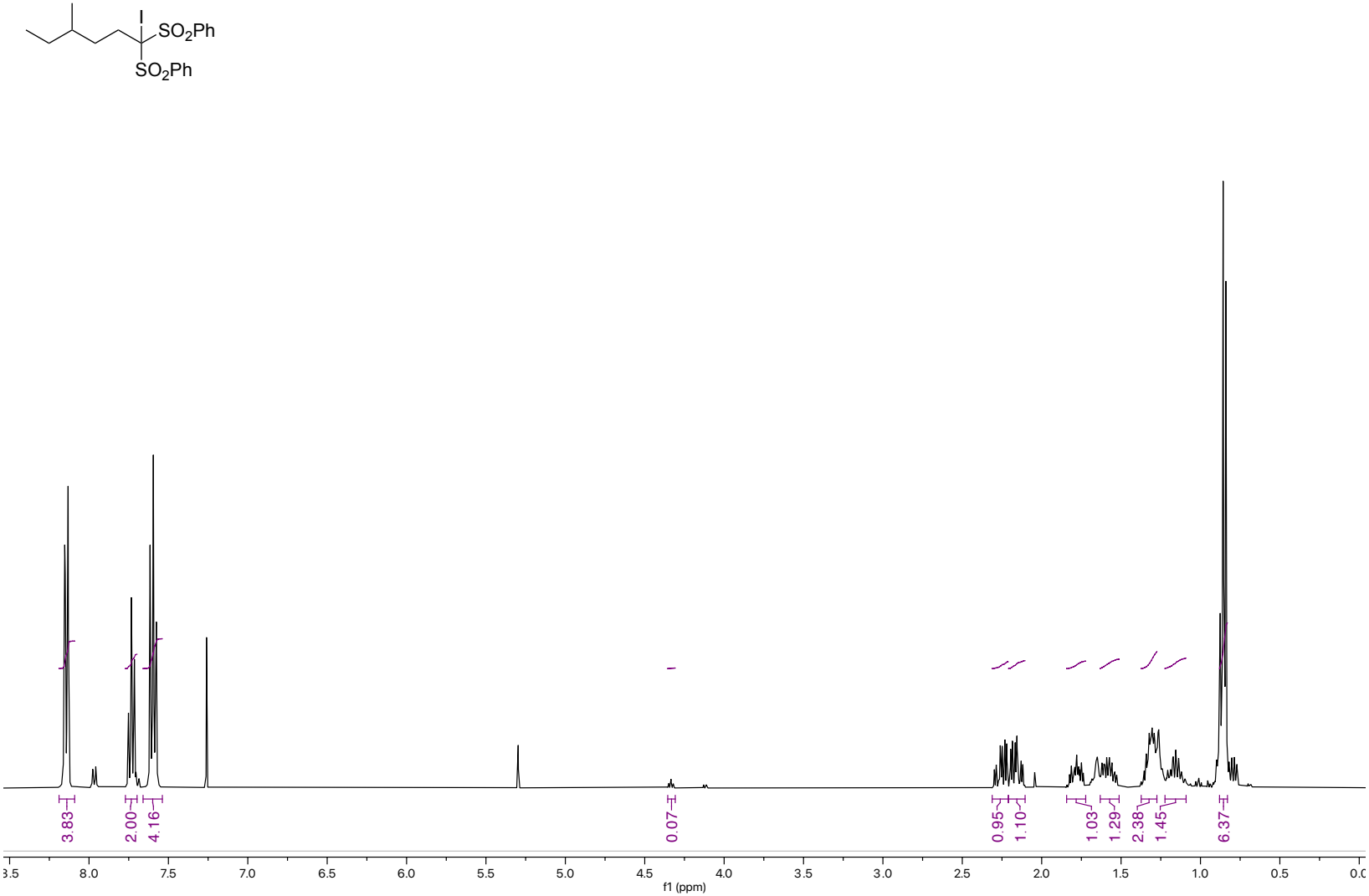



$^{13}$C-NMR (101 MHz, $CDCl_3$)



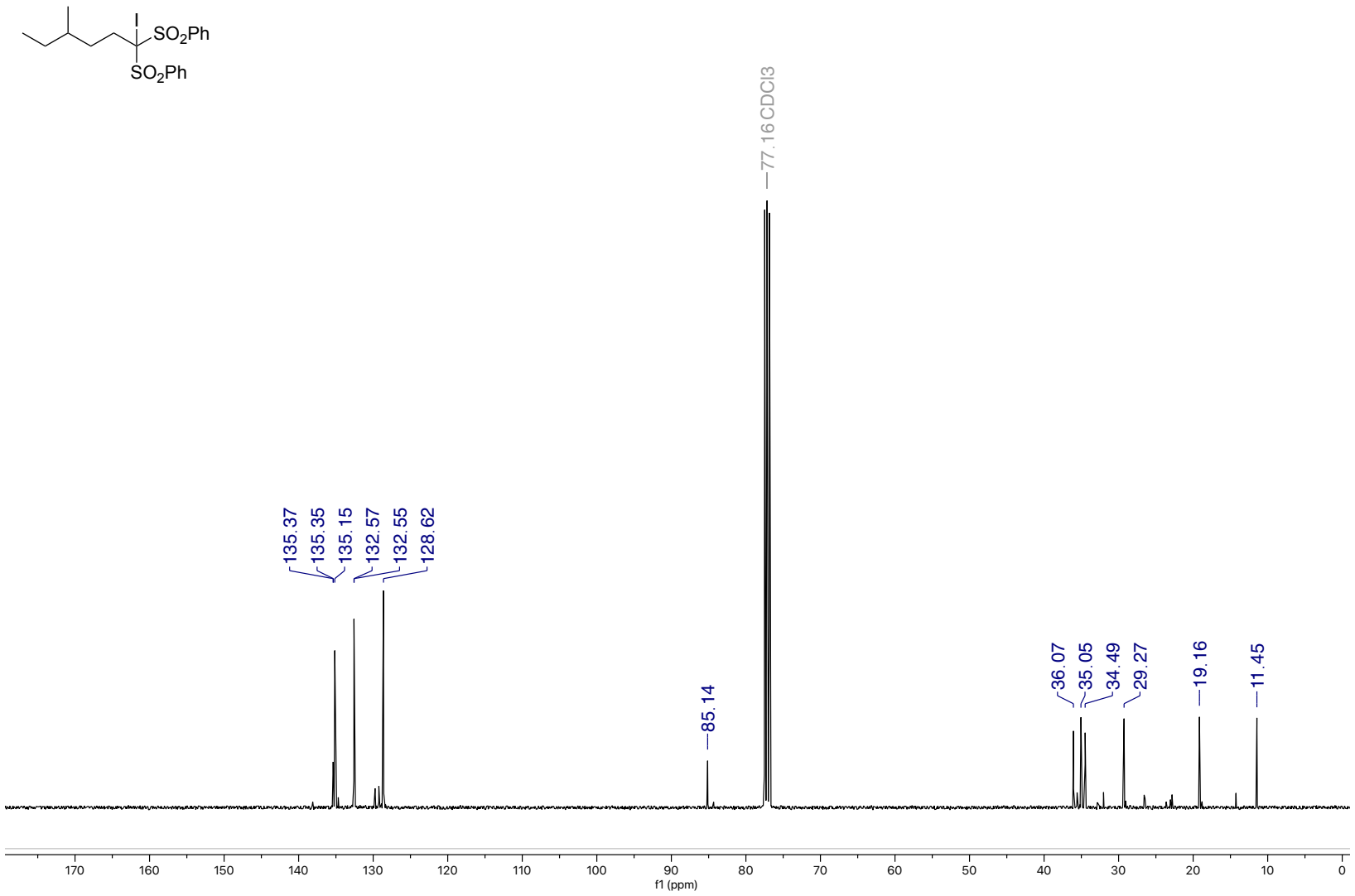
(1-Iodo-4-methylhexane-1,1-diyldisulfonyl)dibenzene

$^1$H-NMR (400 MHz, $CDCl_3$)



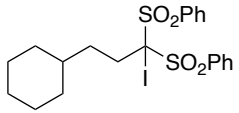
(1-Iodo-4-methylhexane-1,1-diyldisulfonyl)dibenzene

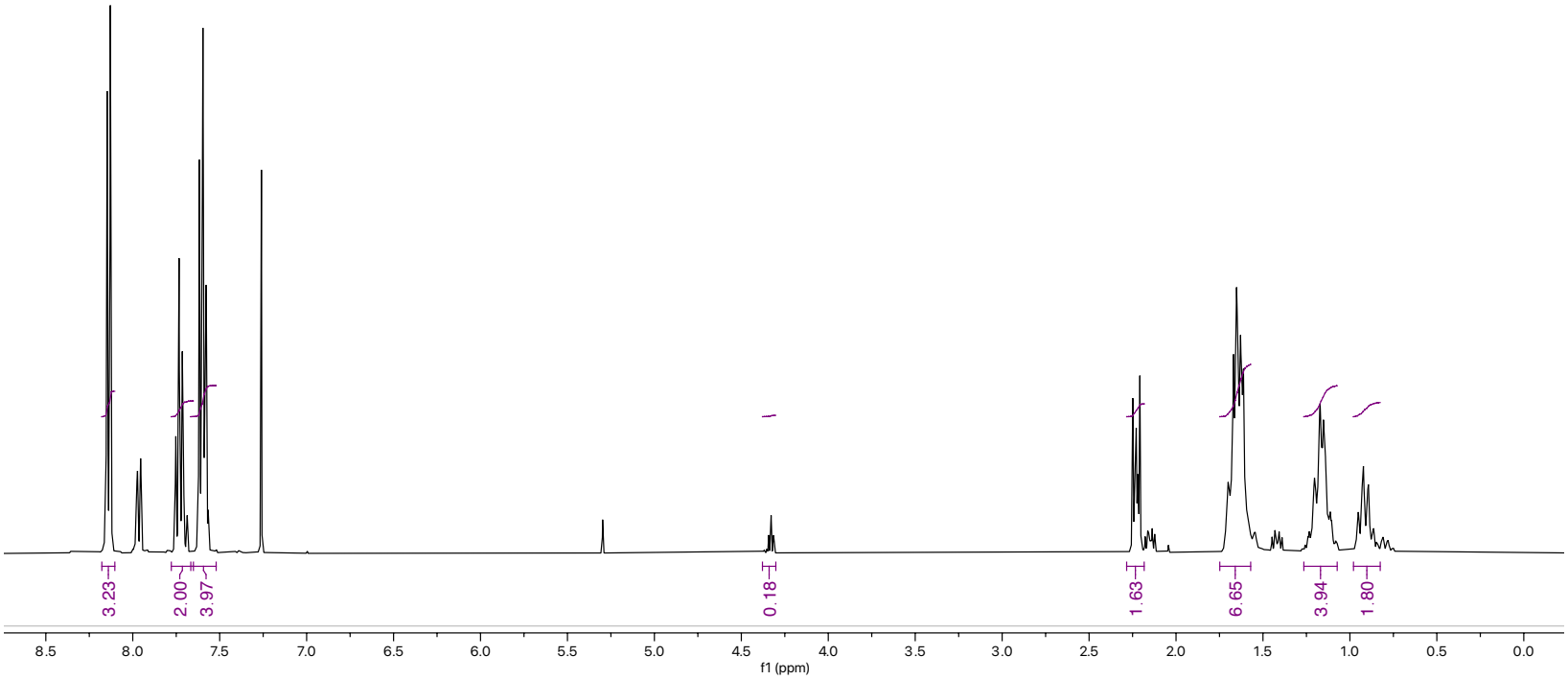
$^{13}$C-NMR (101 MHz, $CDCl_3$)



(3-Cyclohexyl-1-iodopropane-1,1-diyldisulfonyl)dibenzene

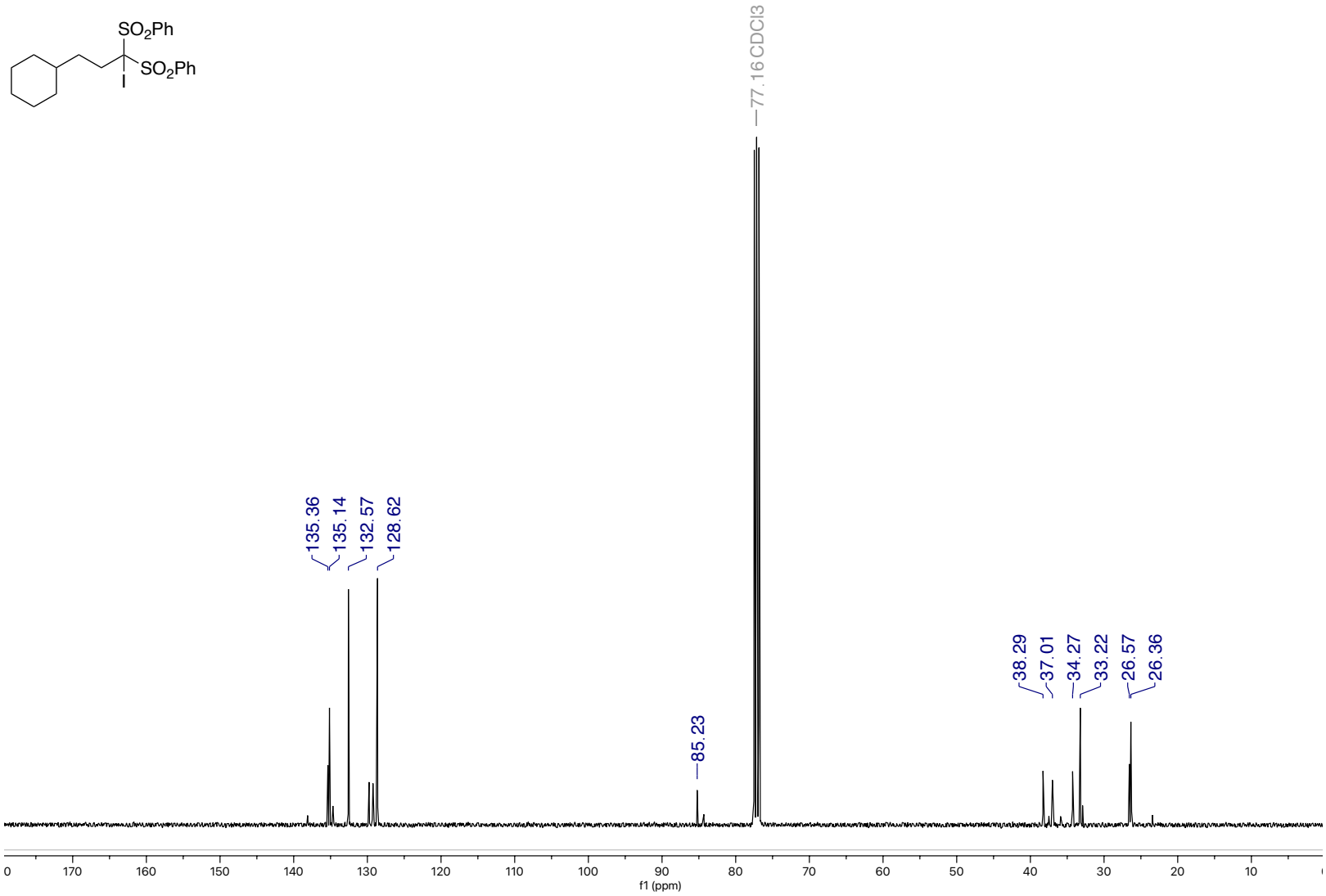
$^1$H-NMR (400 MHz, $CDCl_3$)



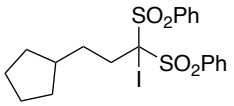
(3-Cyclohexyl-1-iodopropane-1,1-diyldisulfonyl)dibenzene

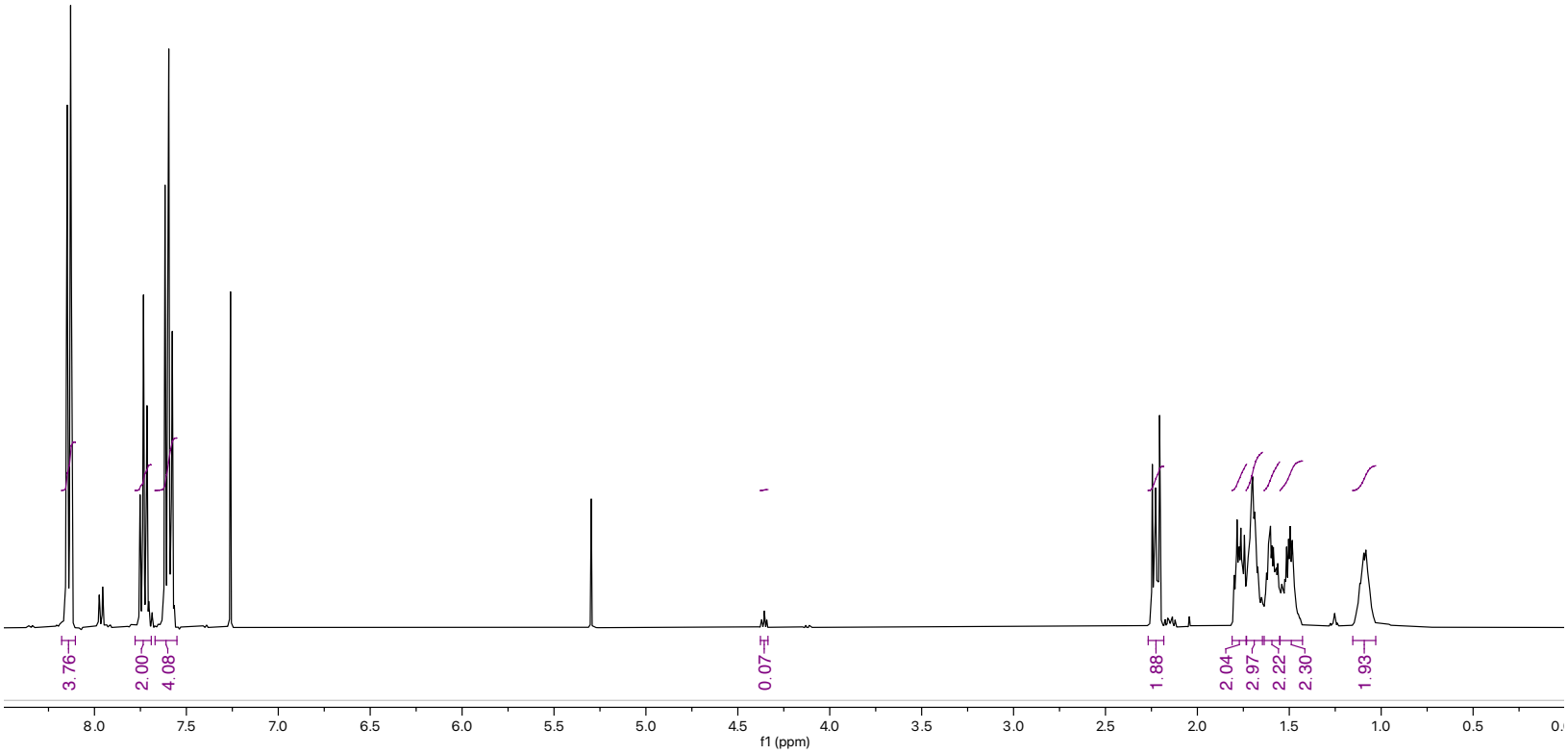
$^{13}$C-NMR (101 MHz, $CDCl_3$)



(3-Cyclopentyl-1-iodopropane-1,1-diyldisulfonyl)dibenzene

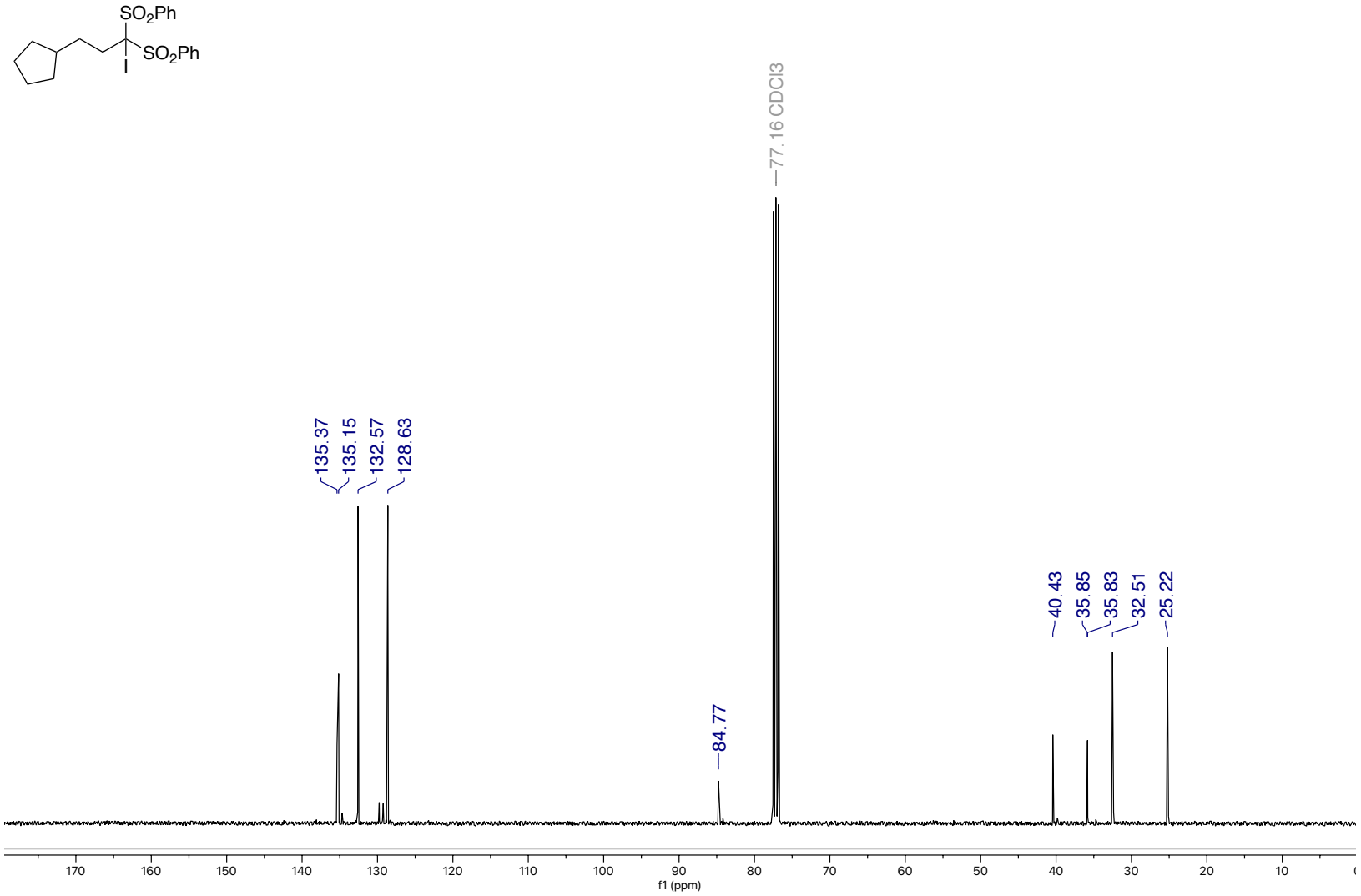
$^1$H-NMR (400 MHz, $CDCl_3$)



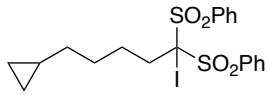
(3-Cyclopentyl-1-iodopropane-1,1-diyldisulfonyl)dibenzene

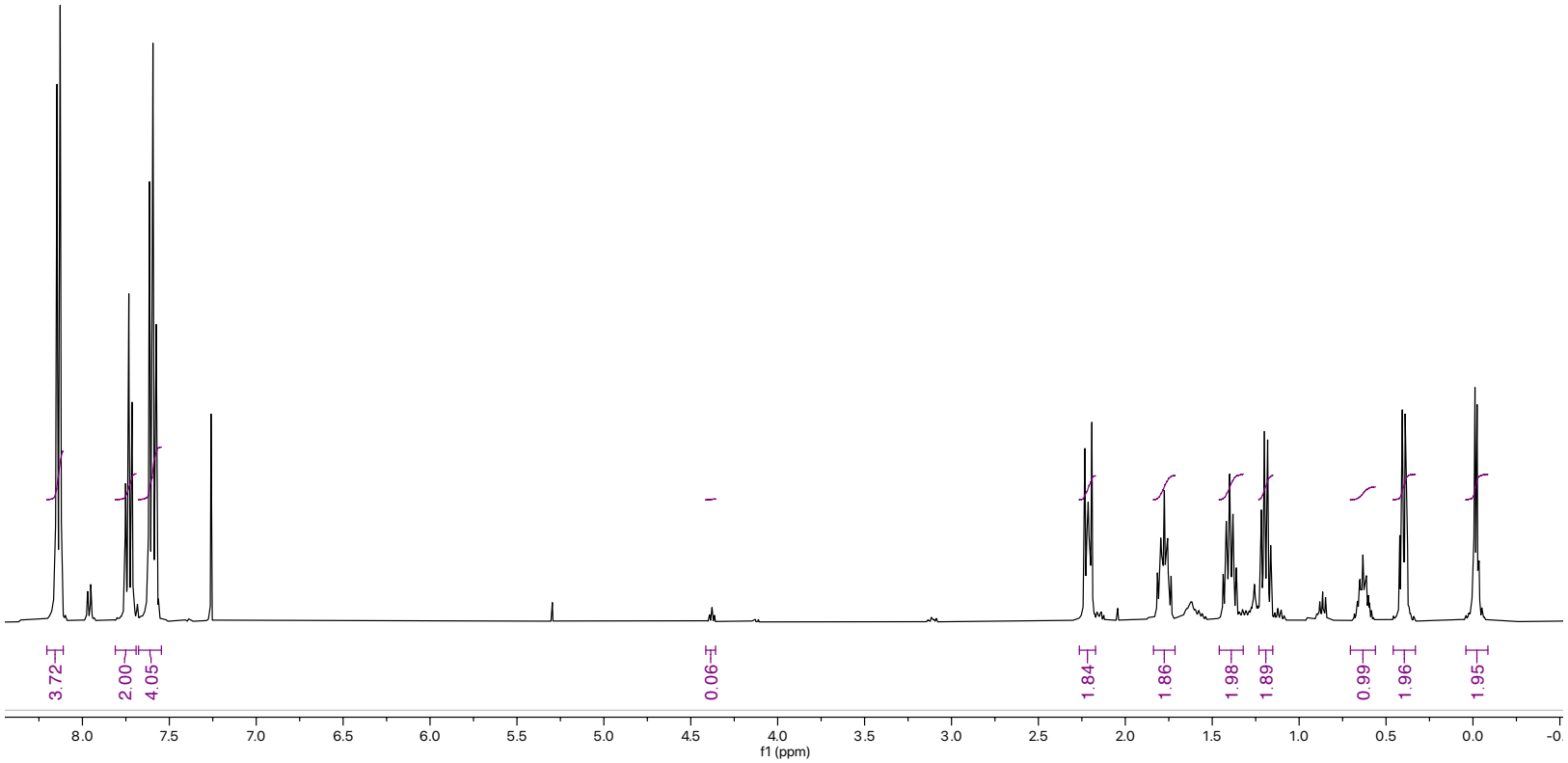
$^{13}$C-NMR (101 MHz, $CDCl_3$)



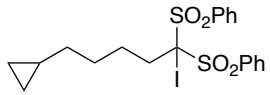
(5-Cyclopropyl-1-iodopentane-1,1-diyldisulfonyl)dibenzene

$^1$H-NMR (400 MHz, $CDCl_3$)

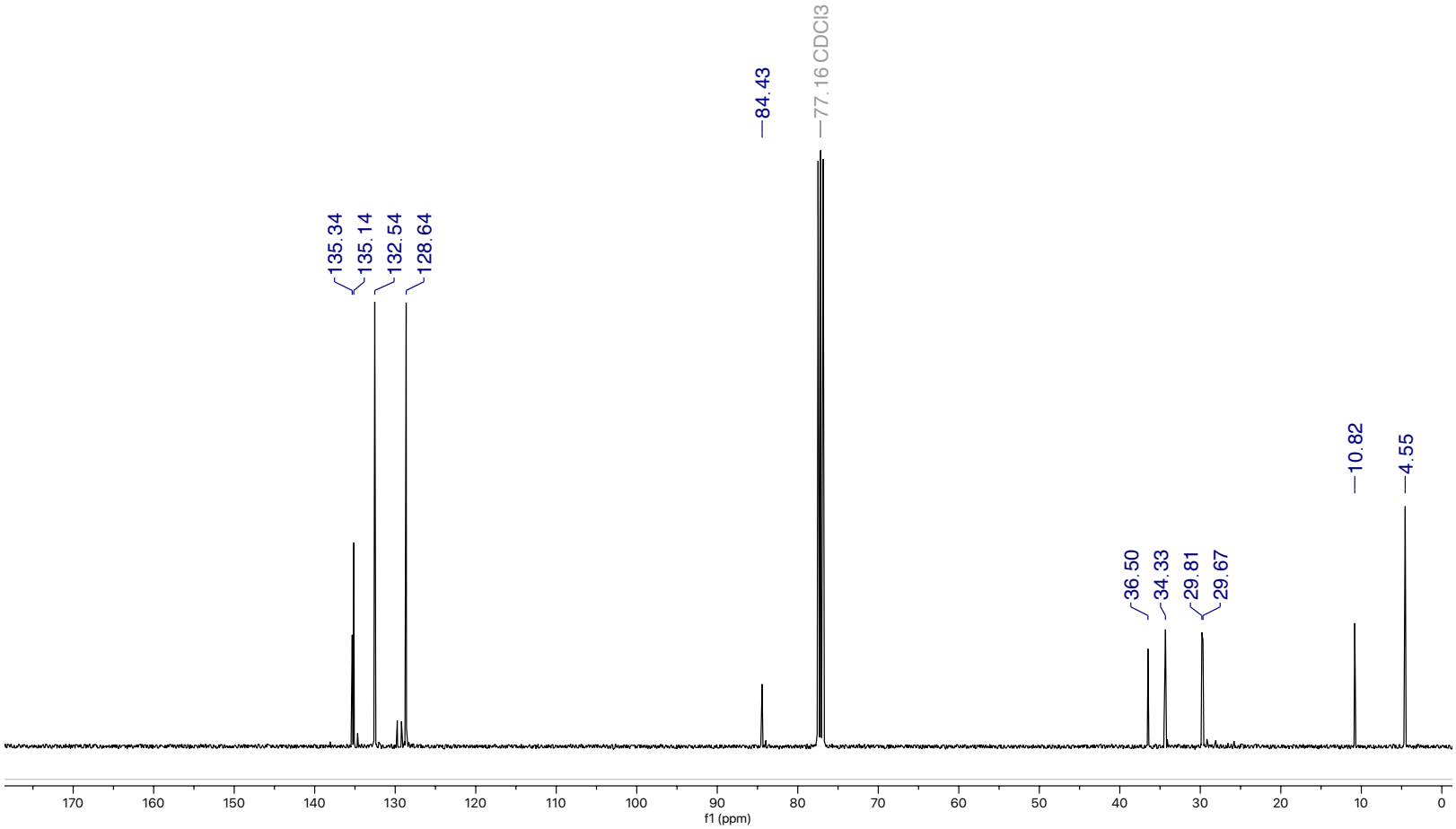


(5-Cyclopropyl-1-iodopentane-1,1-diyldisulfonyl)dibenzene

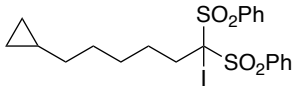


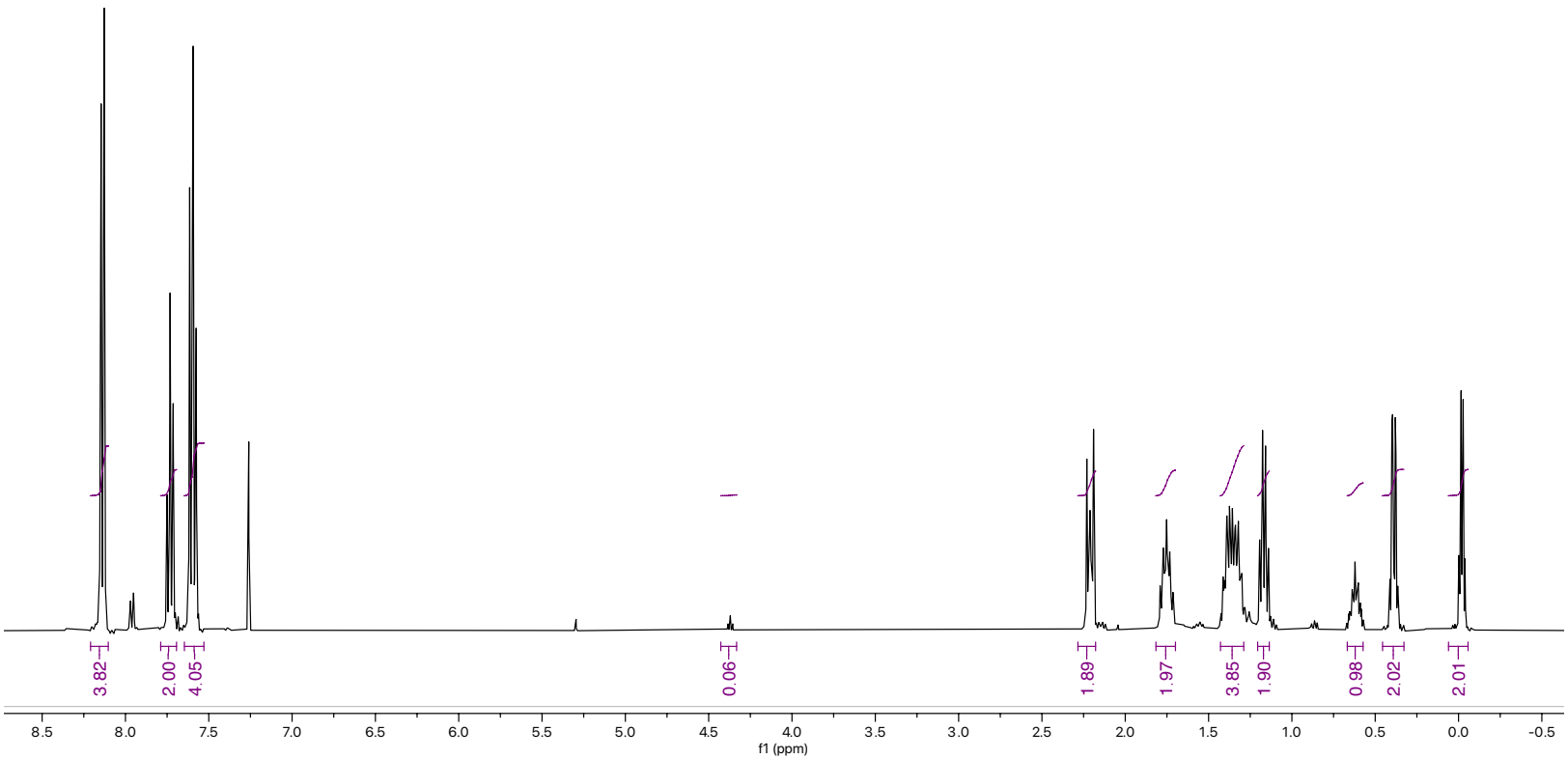

$^{13}$C-NMR (101 MHz, $CDCl_3$)



(6-Cyclopropyl-1-iodohexane-1,1-diyldisulfonyl)dibenzene

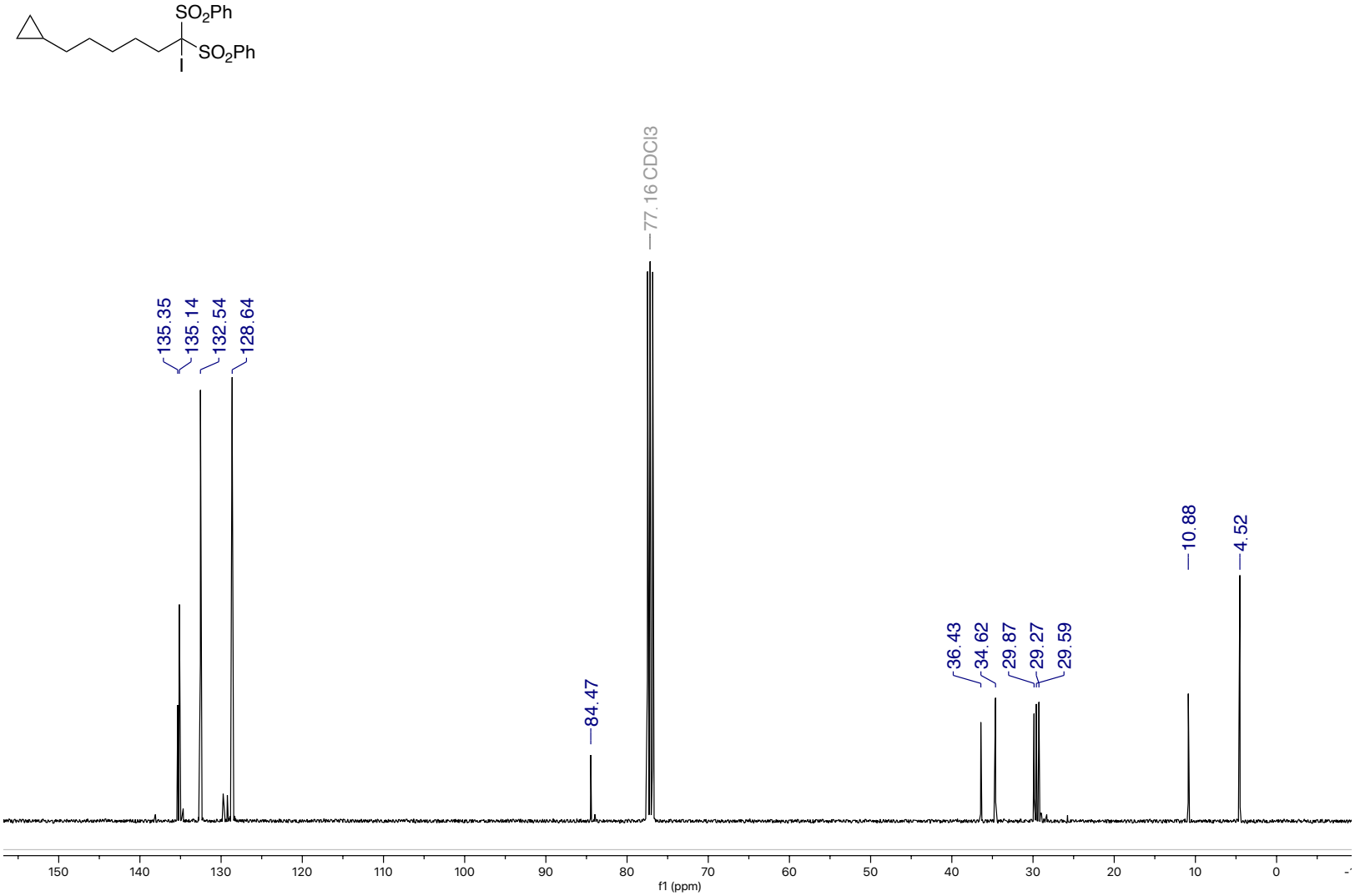
$^1$H-NMR (400 MHz, $CDCl_3$)



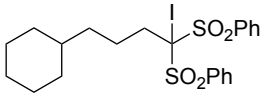
(6-Cyclopropyl-1-iodohexane-1,1-diyldisulfonyl)dibenzene

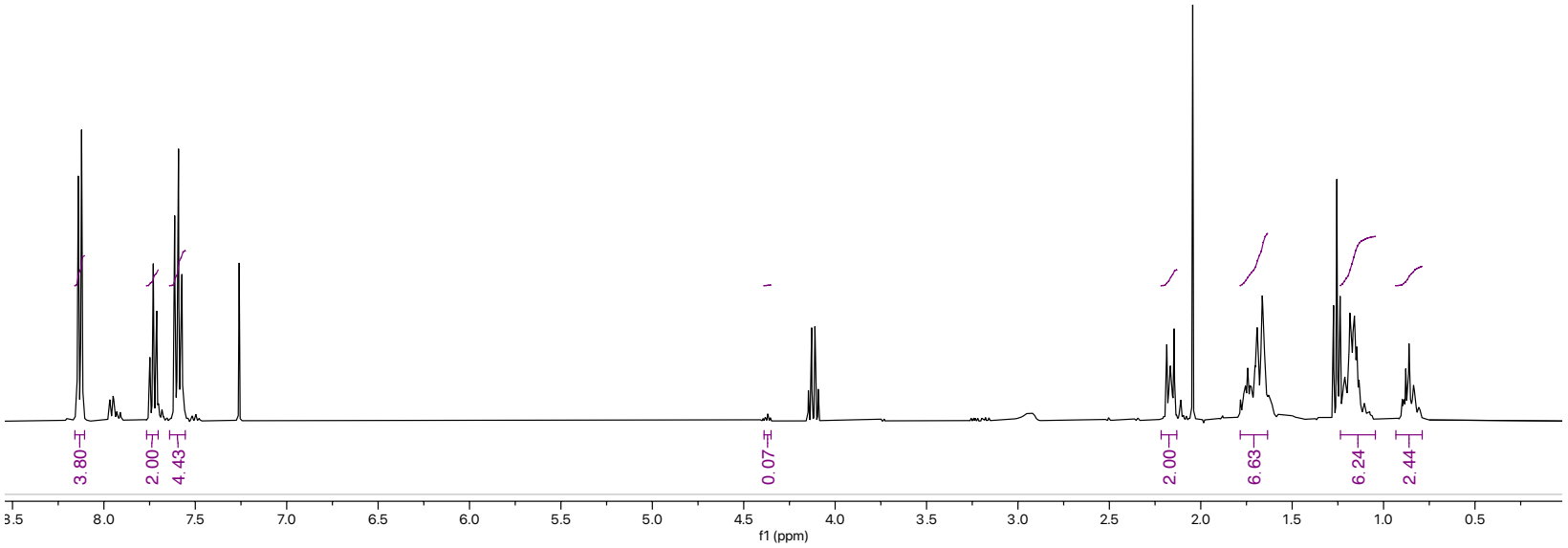
$^{13}$C-NMR (101 MHz, $CDCl_3$)



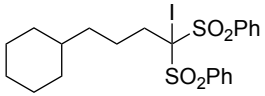
(4-Cyclohexyl-1-iodobutane-1,1-diyldisulfonyl)dibenzene

$^1$H-NMR (400 MHz, $CDCl_3$)

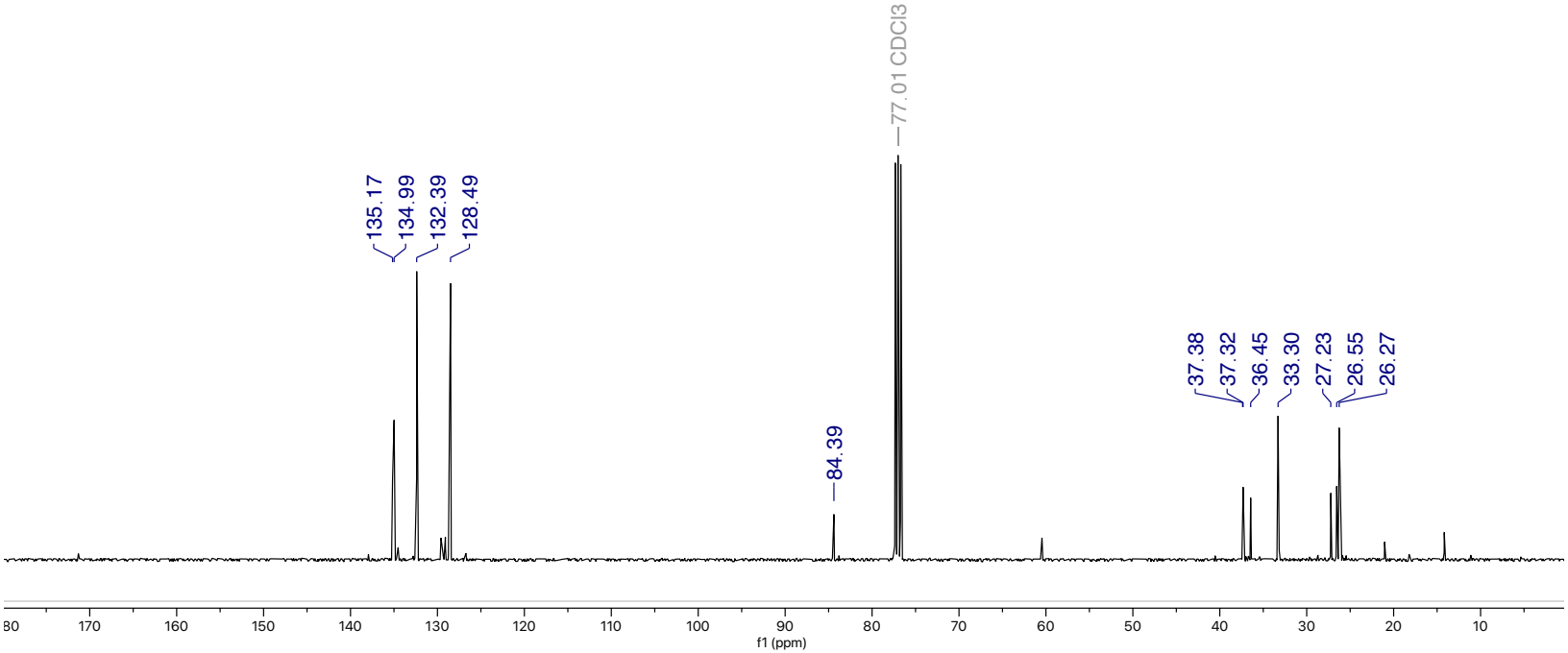


(4-Cyclohexyl-1-iodobutane-1,1-diyldisulfonyl)dibenzene

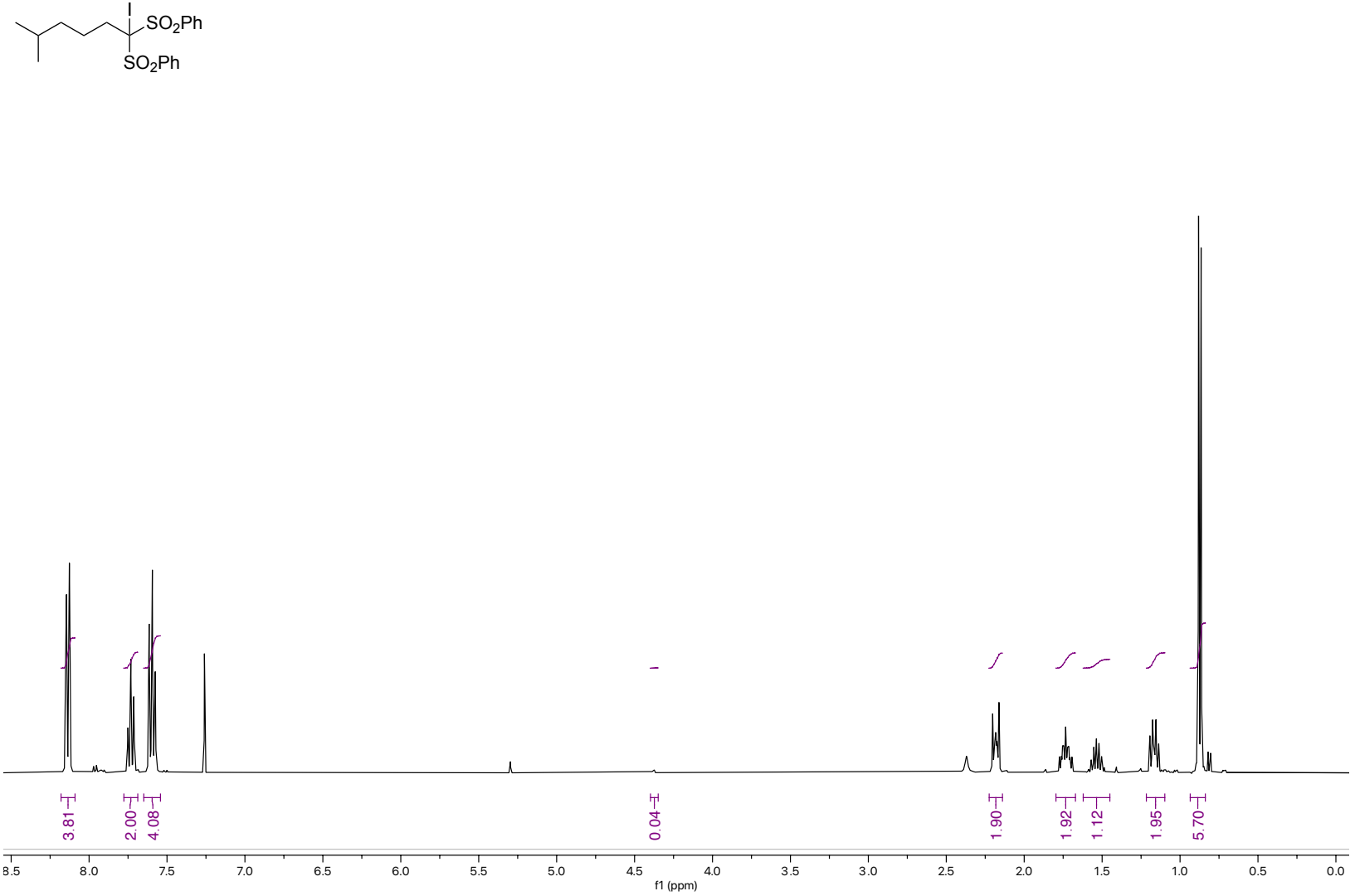



$^{13}$C-NMR (101 MHz, $CDCl_3$)



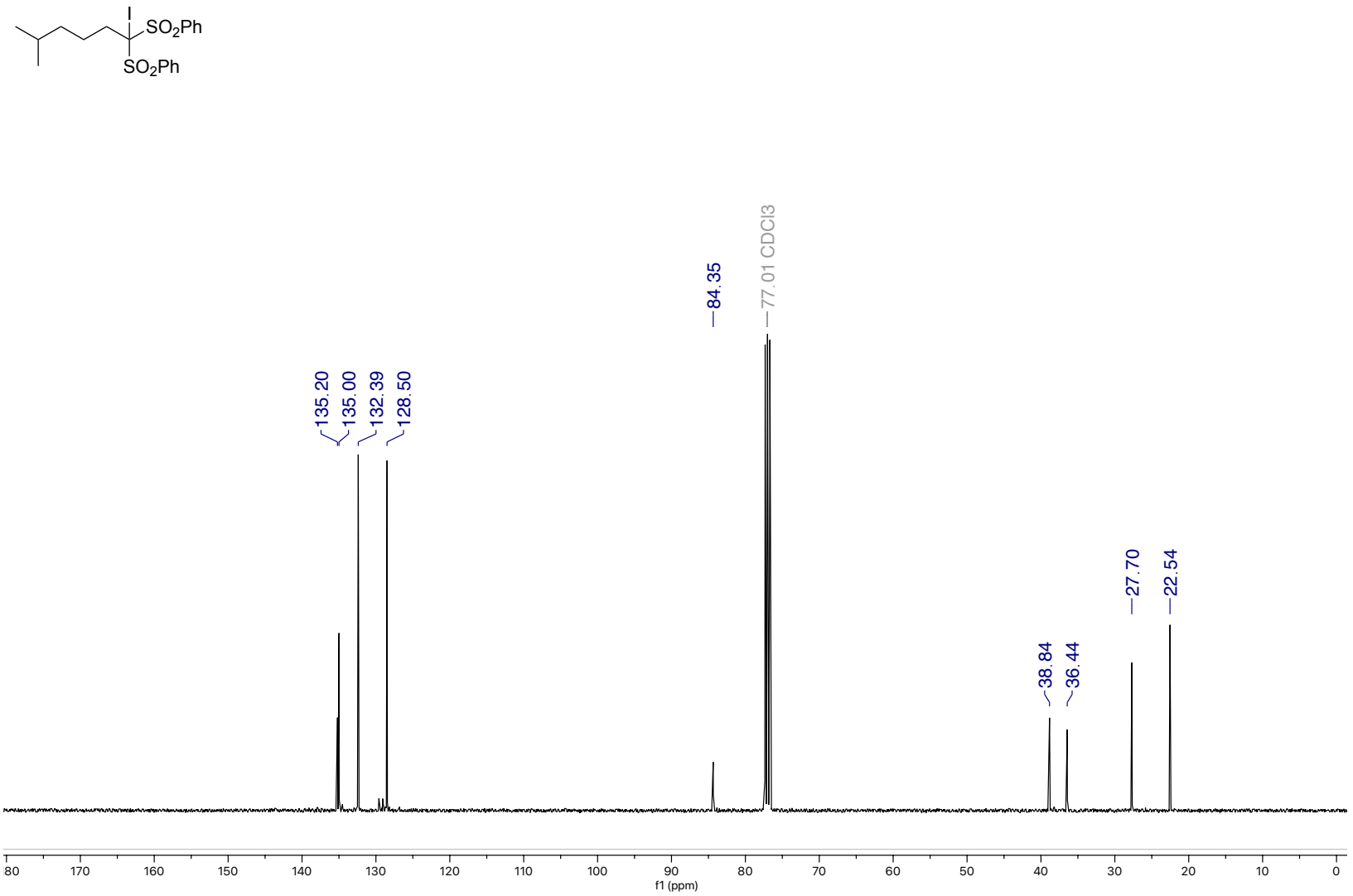
(1-Iodo-5-methylhexane-1,1-diyldisulfonyl)dibenzene

$^1$H-NMR (400 MHz, $CDCl_3$)



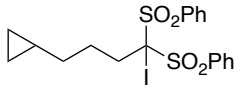
(1-Iodo-5-methylhexane-1,1-diyldisulfonyl)dibenzene

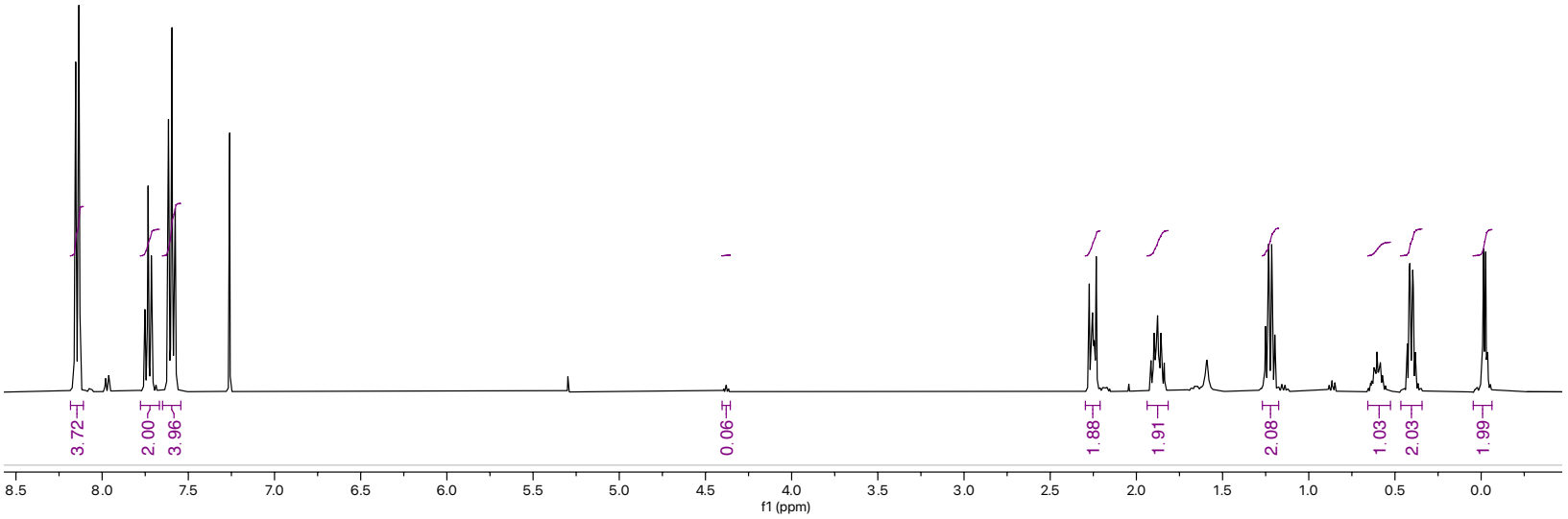
$^{13}$C-NMR (101 MHz, $CDCl_3$)



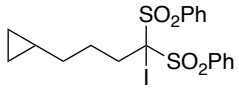
(4-Cyclopropyl-1-iodobutane-1,1-diyldisulfonyl)dibenzene

$^1$H-NMR (400 MHz, $CDCl_3$)



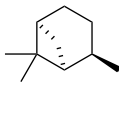
(4-Cyclopropyl-1-iodobutane-1,1-diyldisulfonyl)dibenzene

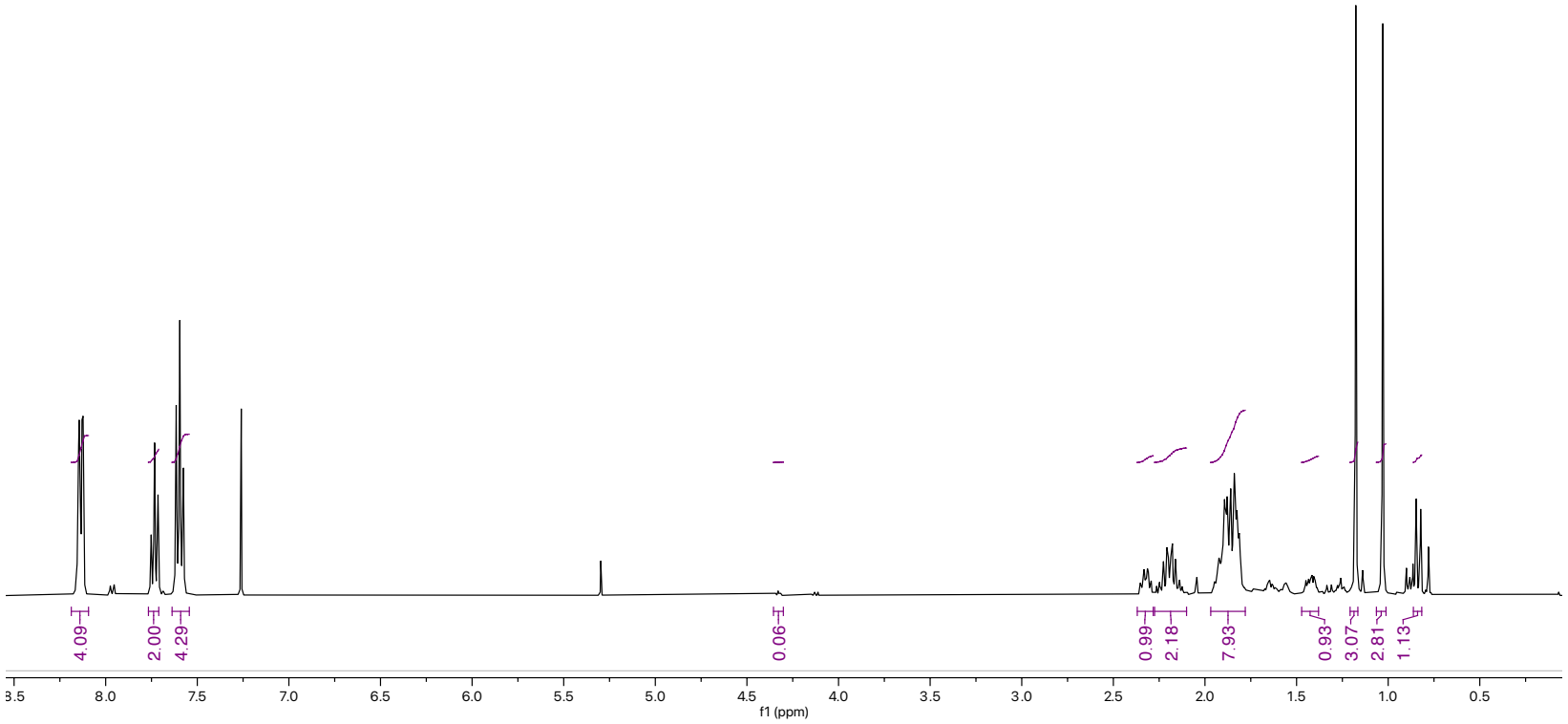



$^{13}$C-NMR (101 MHz, $CDCl_3$)

(1*S*,2*S*,5*S*)-2-(3-iodo-3,3-bis(phenylsulfonyl)propyl)-6,6-dimethylbicyclo[3.1.1]heptane

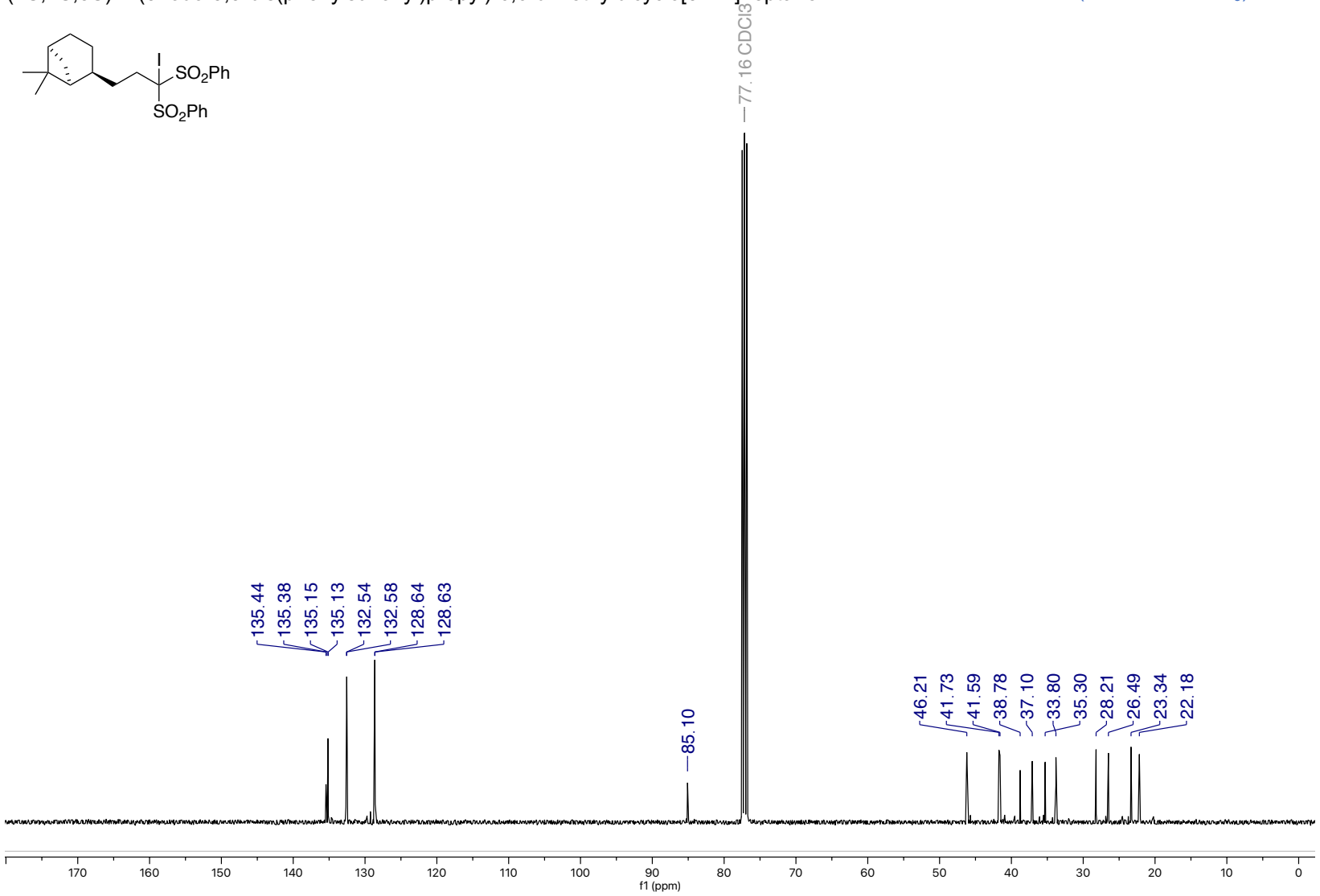
$^1$H-NMR (400 MHz, $CDCl_3$)



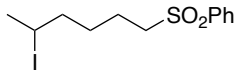



(1*S*,2*S*,5*S*)-2-(3-iodo-3,3-bis(phenylsulfonyl)propyl)-6,6-dimethylbicyclo[3.1.1]heptane

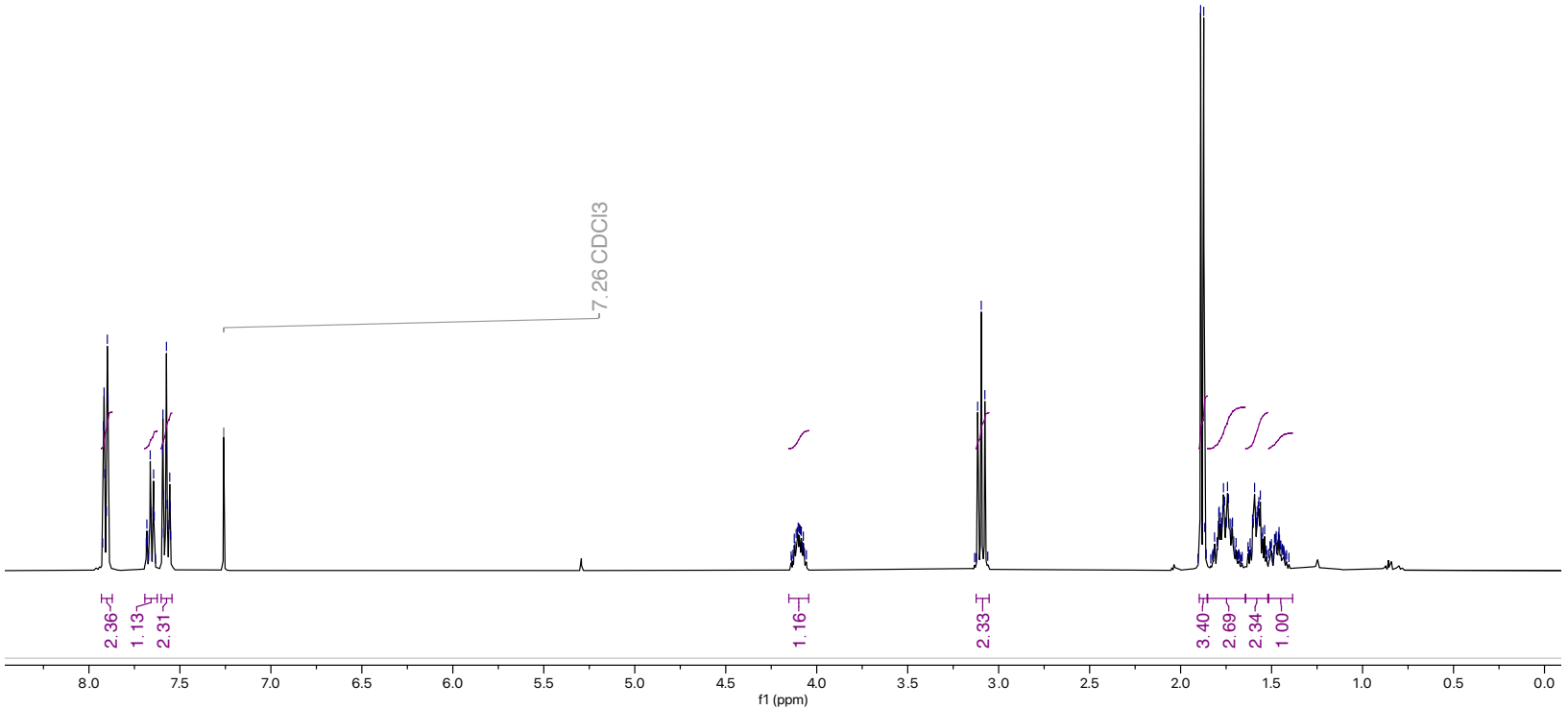
$^{13}$C-NMR (101 MHz, $CDCl_3$)



((5-Iodohexyl)sulfonyl)benzene

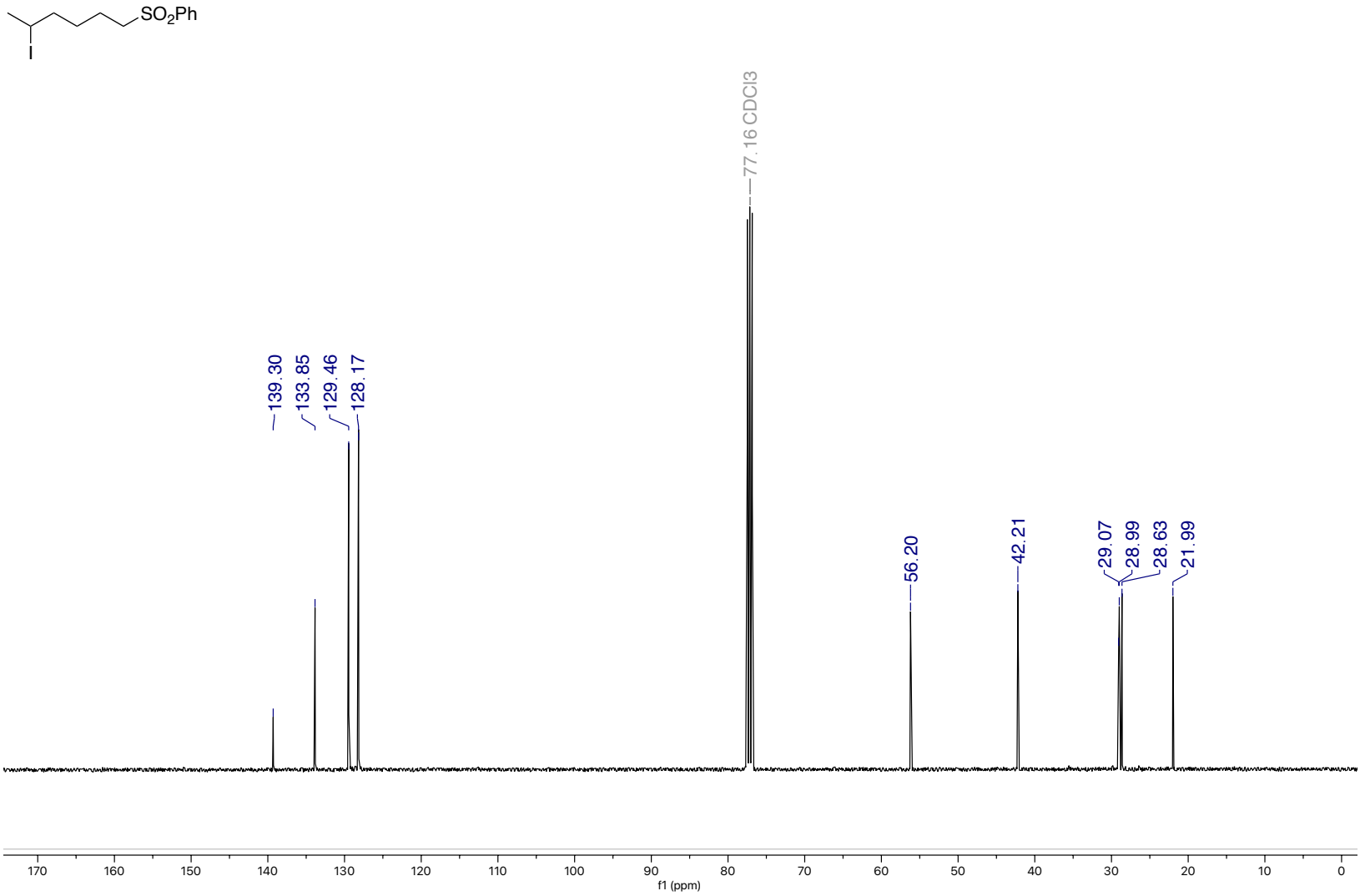



$^{1}$H-NMR (400 MHz, $CDCl_3$)

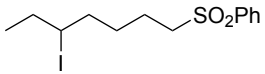


((5-Iodohexyl)sulfonyl)benzene

$^{13}$C-NMR (101 MHz, $CDCl_3$)

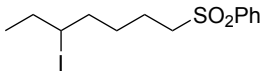


((5-Iodoheptyl)sulfonyl)benzene




$^1$H-NMR (400 MHz, $CDCl_3$)

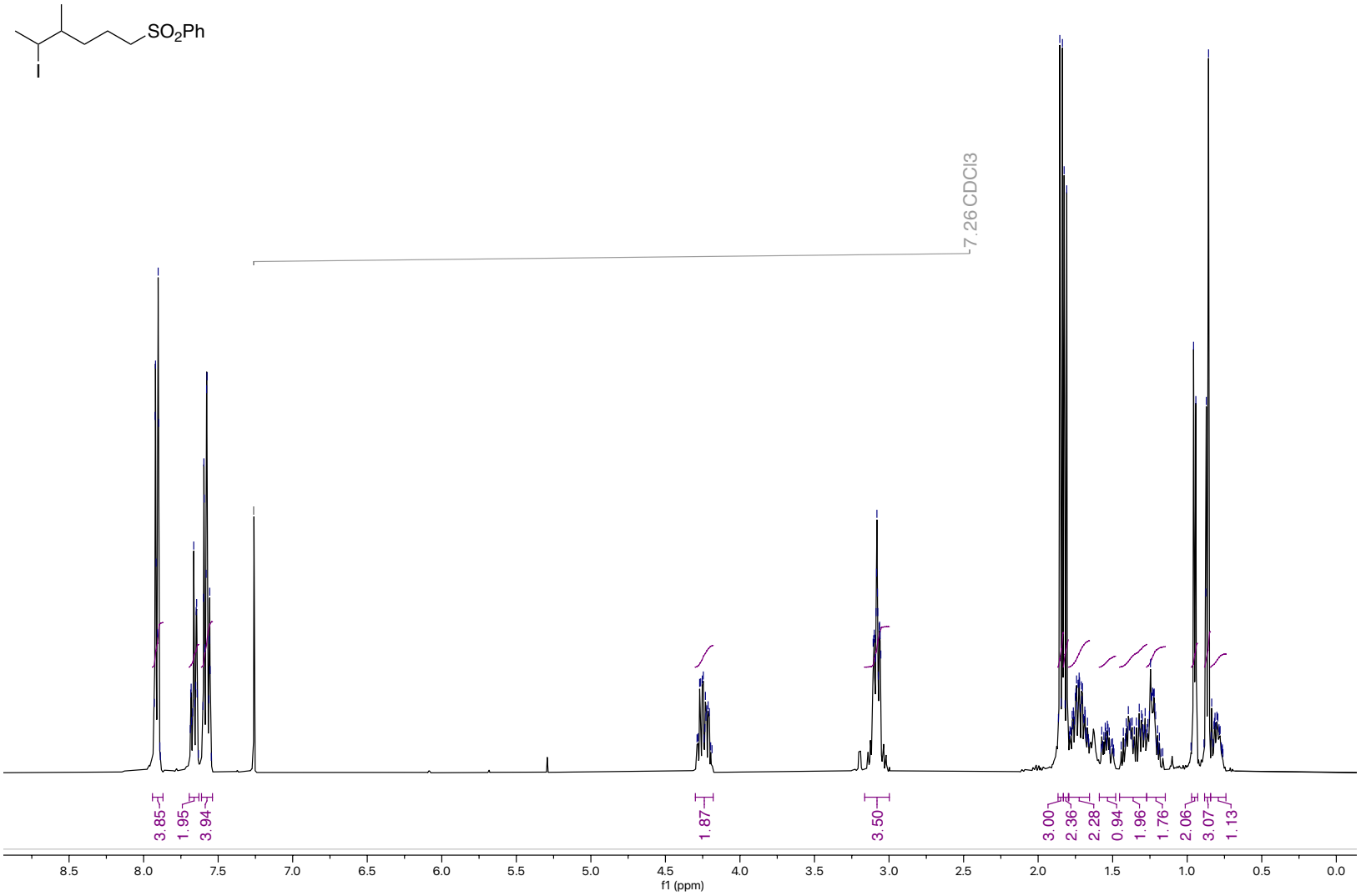
((5-Iodoheptyl)sulfonyl)benzene




$^{13}$C-NMR (101 MHz, $CDCl_3$)

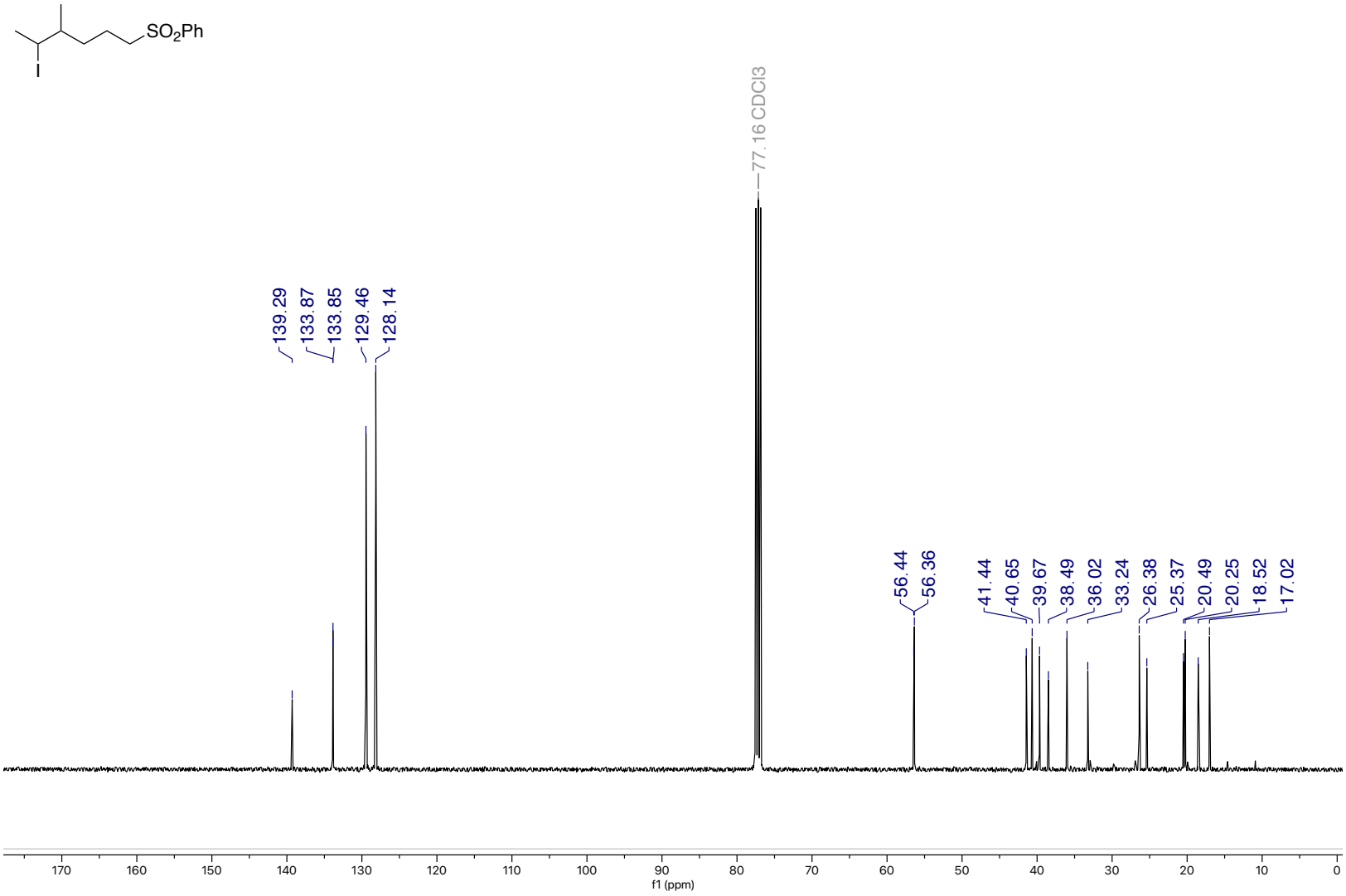
((5-Iodo-4-methylhexyl)sulfonyl)benzene

$^1$H-NMR (400 MHz, $CDCl_3$)

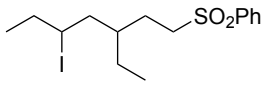


((5-Iodo-4-methylhexyl)sulfonyl)benzene

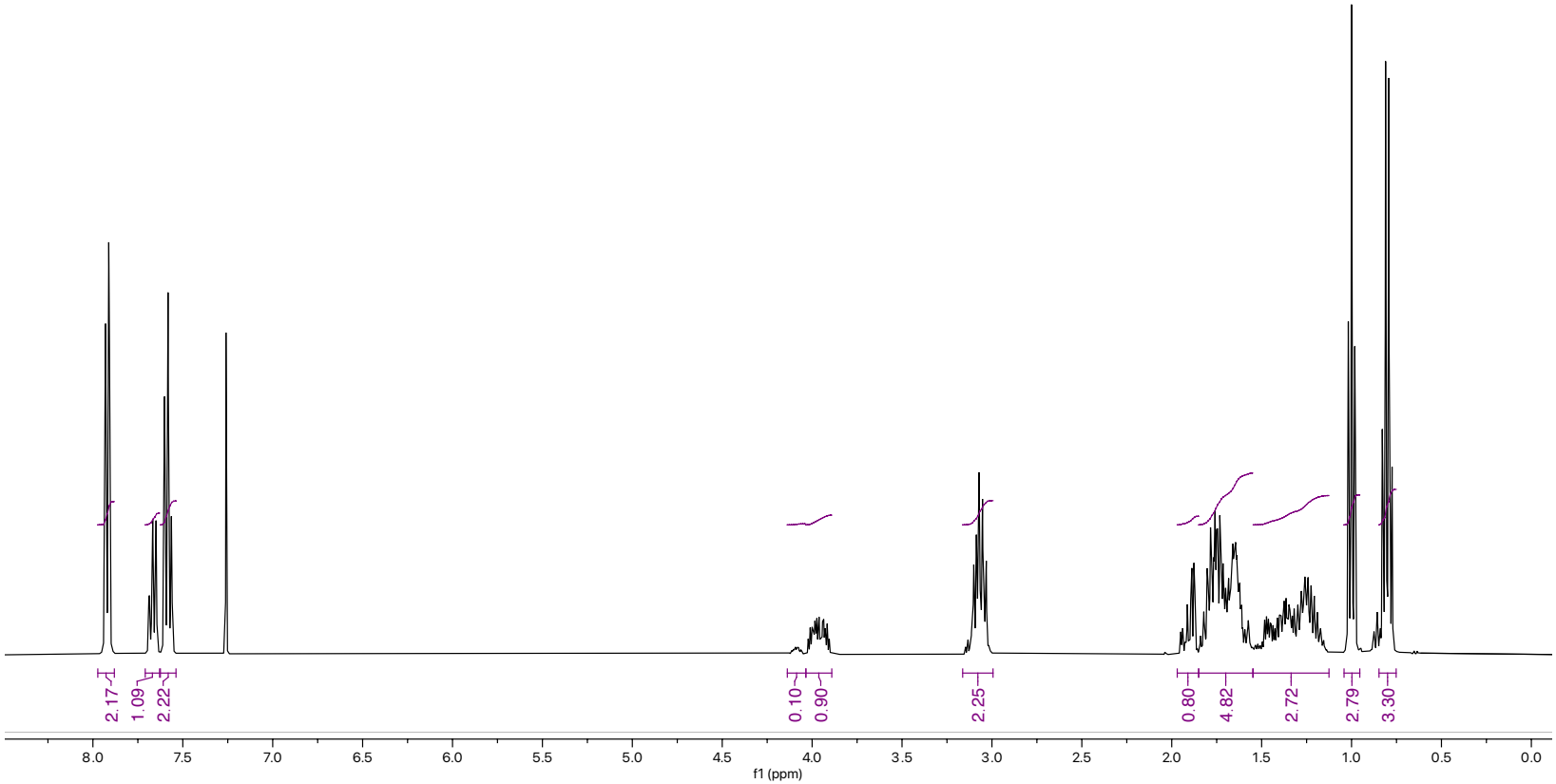
$^{13}$C-NMR (101 MHz, $CDCl_3$)



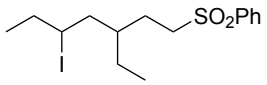
((3-Ethyl-5-iodoheptyl)sulfonyl)benzene




$^{1}$H-NMR (400 MHz, $CDCl_3$)



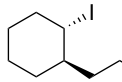
((3-Ethyl-5-iodoheptyl)sulfonyl)benzene

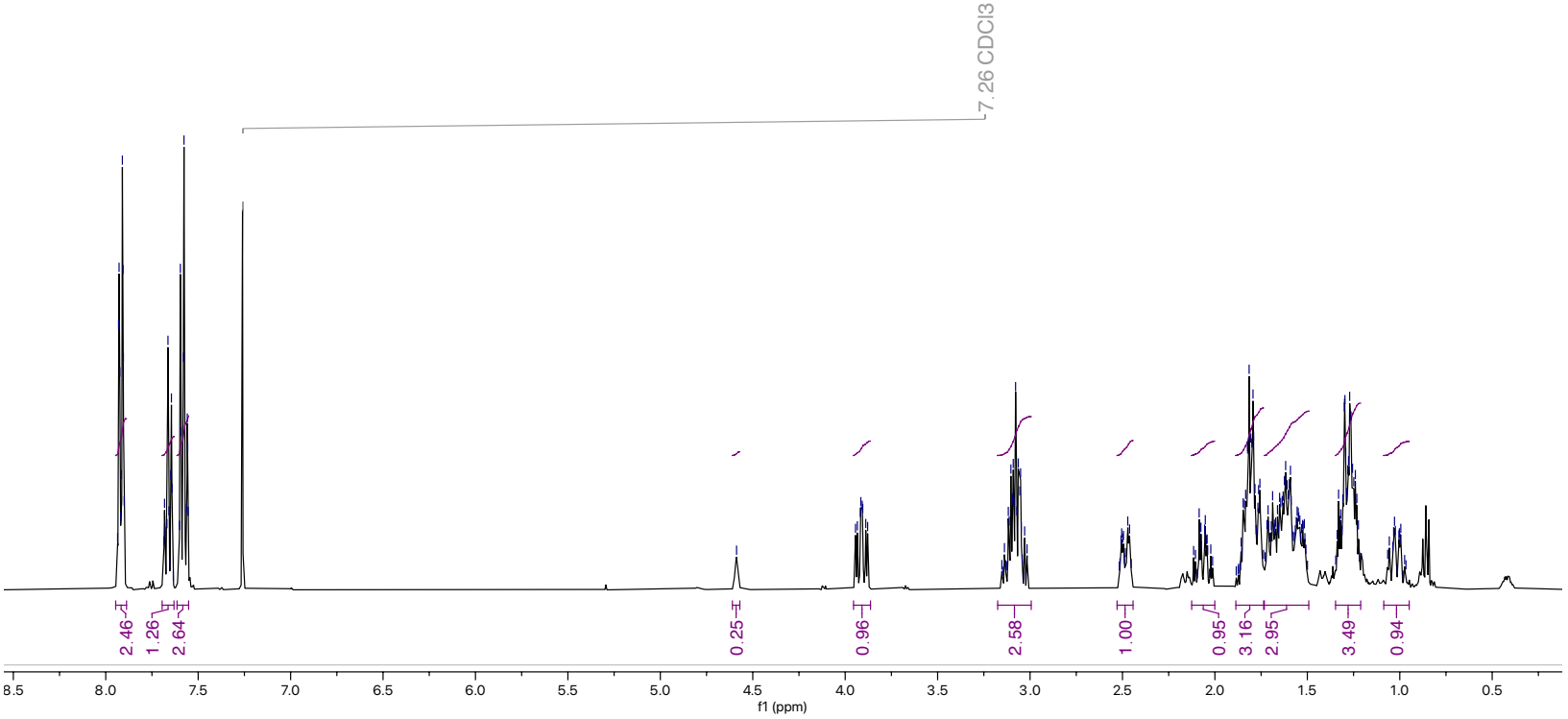



$^{13}$C-NMR (101 MHz, $CDCl_3$)

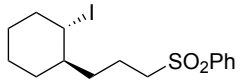
((3-((1*R*,2*S*)-2-iodocyclohexyl)propyl)sulfonyl)benzene

$^1$H-NMR (400 MHz, $CDCl_3$)



((3-((1*R*,2*S*)-2-iodocyclohexyl)propyl)sulfonyl)benzene

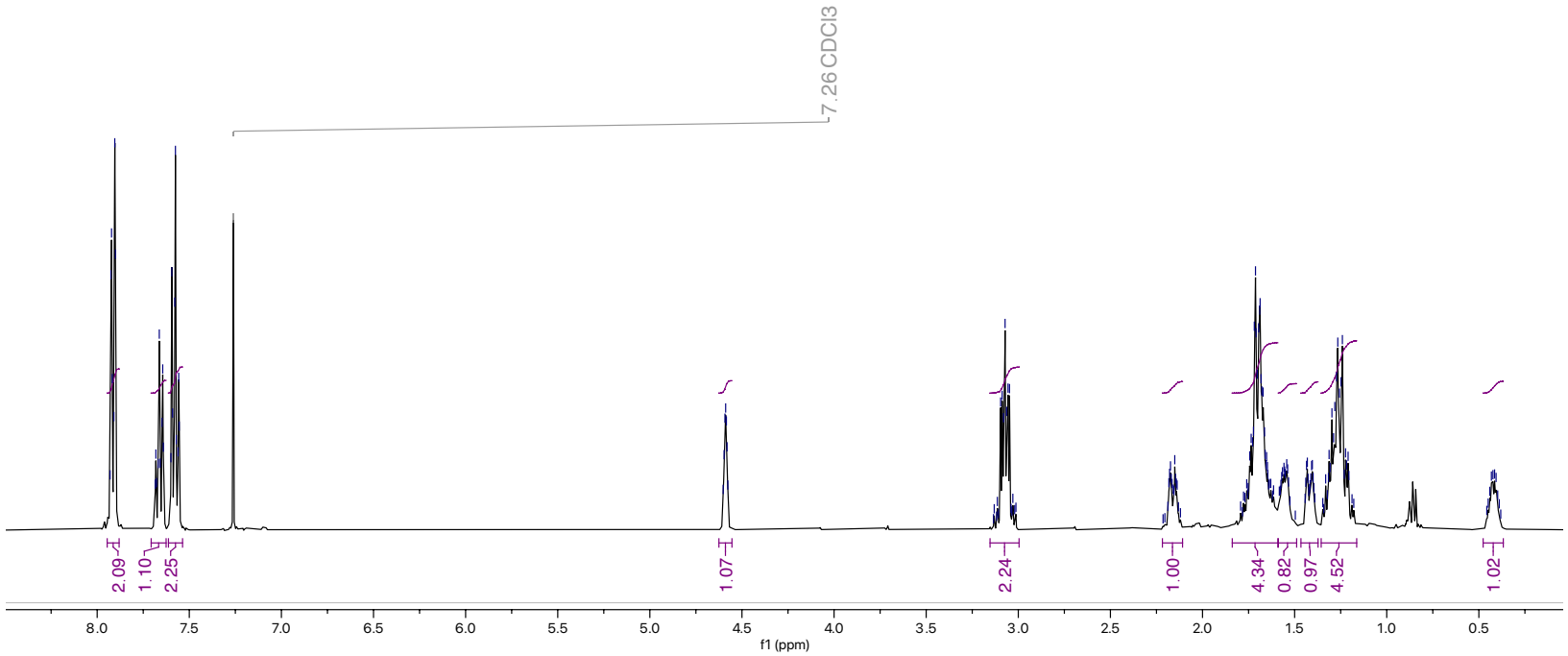



$^{13}$C-NMR (101 MHz, $CDCl_3$)

((3-((1R,2R)-2-iodocycloexyl)propyl)sulfonyl)benzene

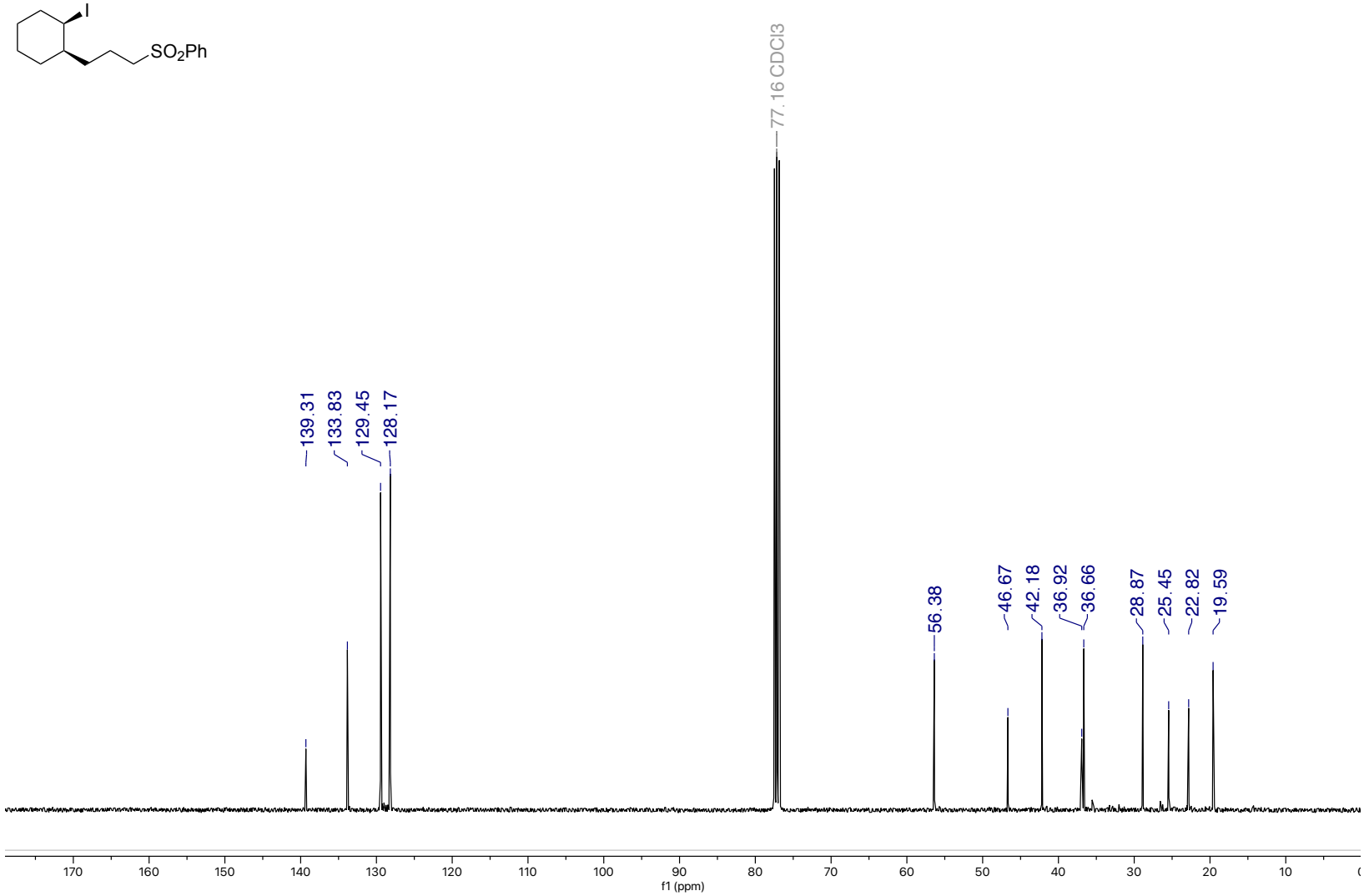
$^1$H-NMR (400 MHz, $CDCl_3$)



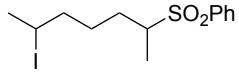



((3-((1R,2R)-2-iodocycloexyl)propyl)sulfonyl)benzene

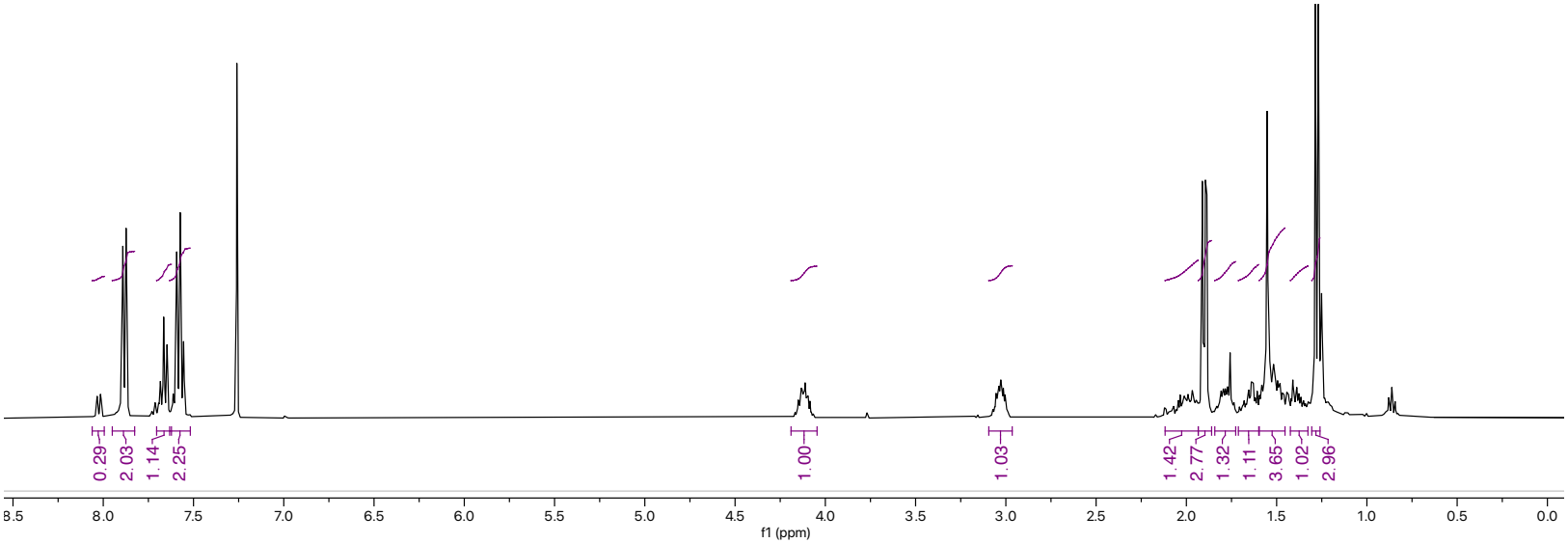
$^{13}$C-NMR (101 MHz, $CDCl_3$)



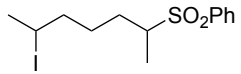
((6-Iodoheptan-2-yl)sulfonyl)benzene




$^{1}$H-NMR (400 MHz, $CDCl_3$)

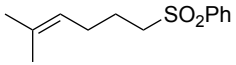


((6-Iodoheptan-2-yl)sulfonyl)benzene

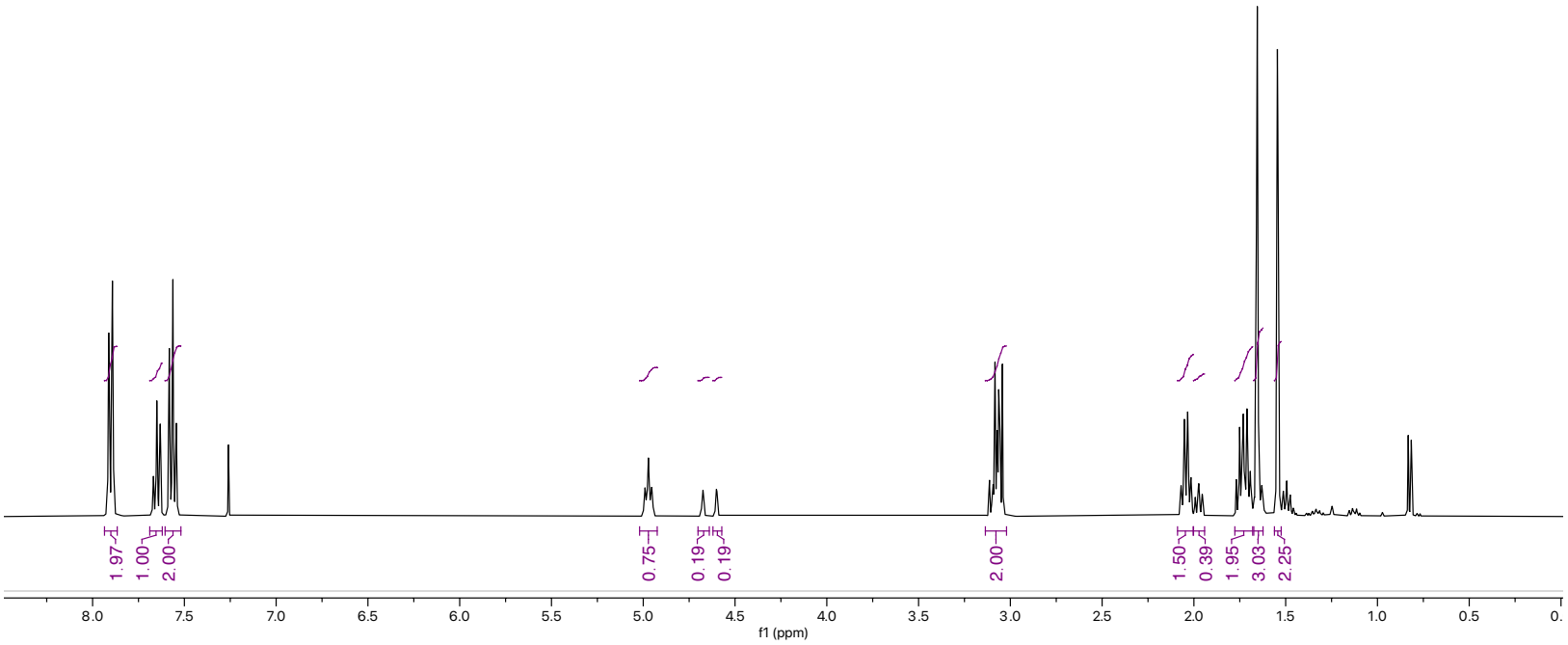



$^{13}$C-NMR (101 MHz, $CDCl_3$)

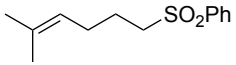
((5-Methylhex-4-en-1-yl)sulfonyl)benzene



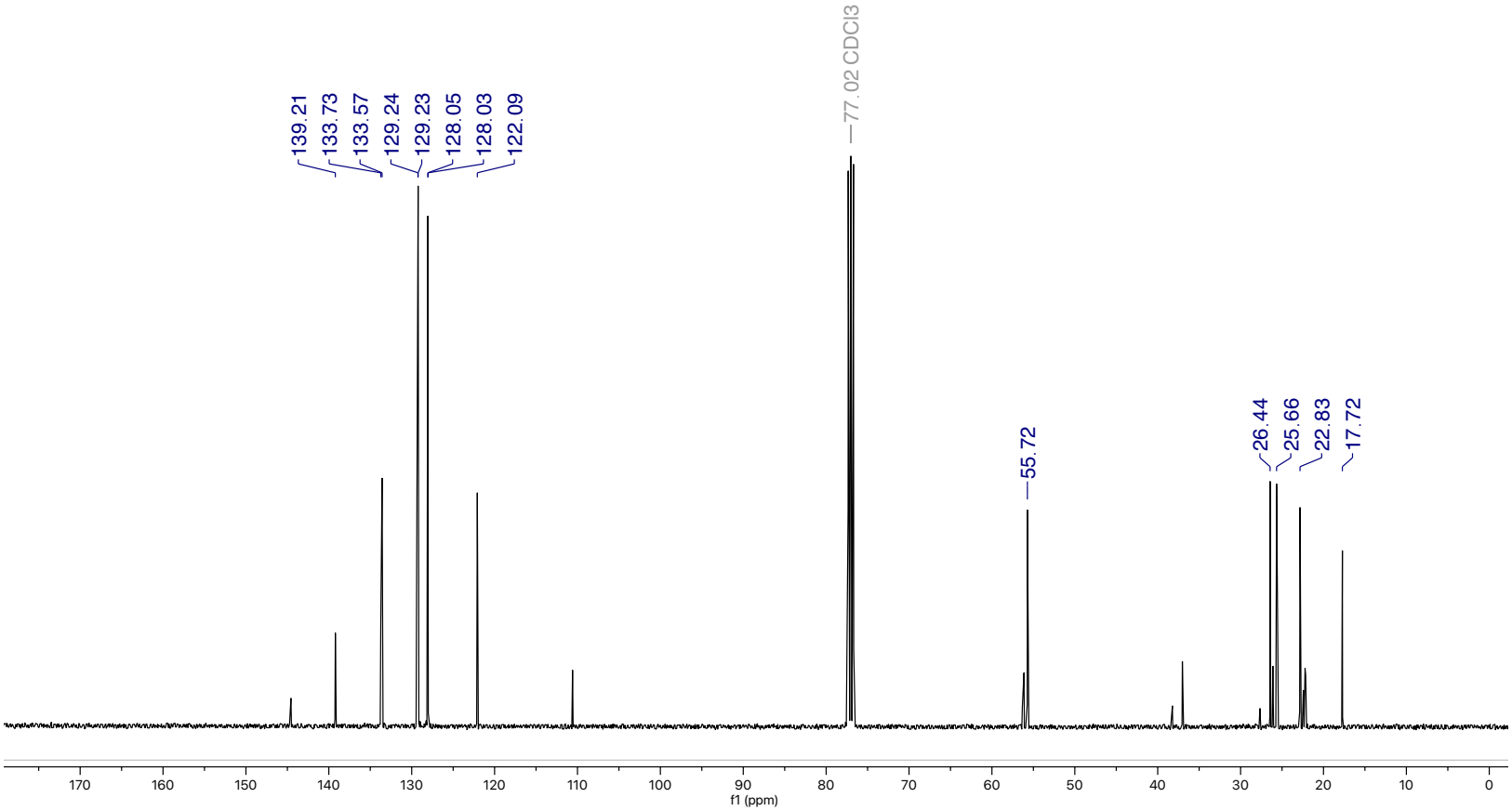

$^1$H-NMR (400 MHz, $CDCl_3$)



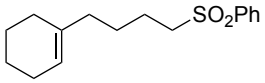
((5-Methylhex-4-en-1-yl)sulfonyl)benzene



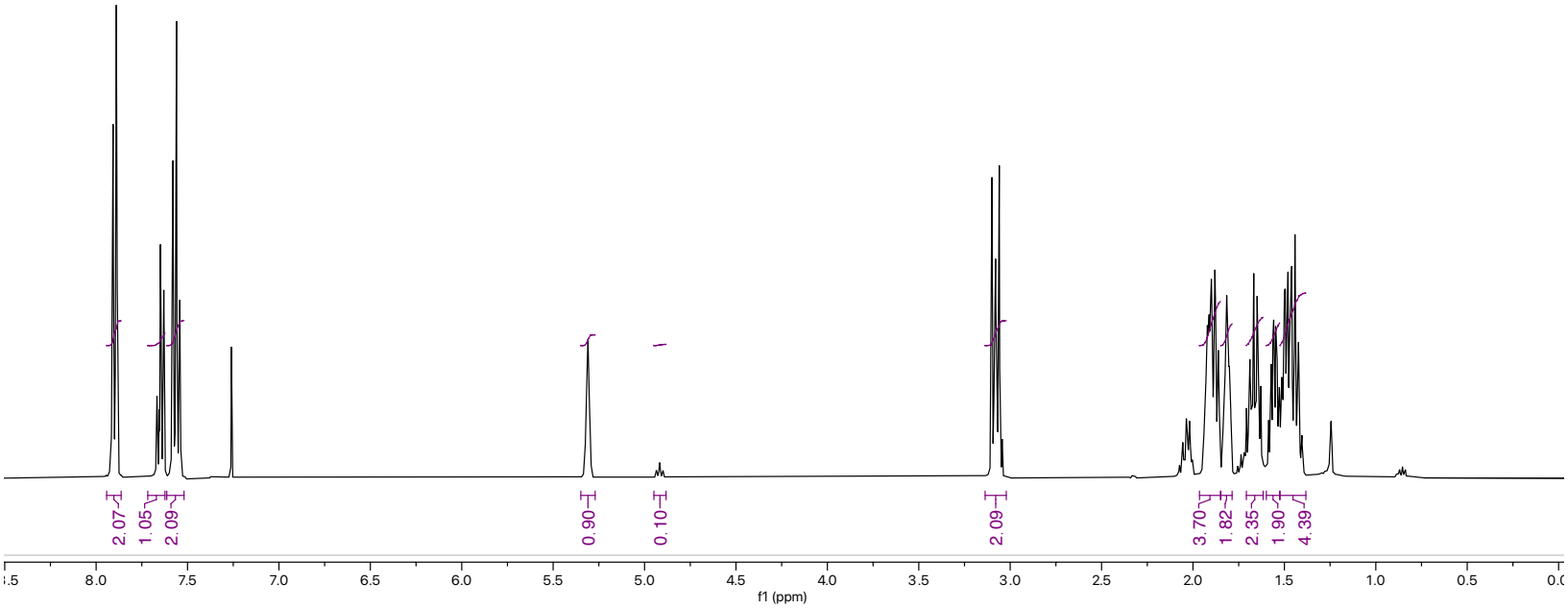

$^{13}$C-NMR (101 MHz, $CDCl_3$)



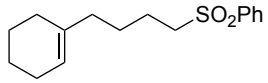
((4-(Cyclohex-1-en-1-yl)butyl)sulfonyl)benzene



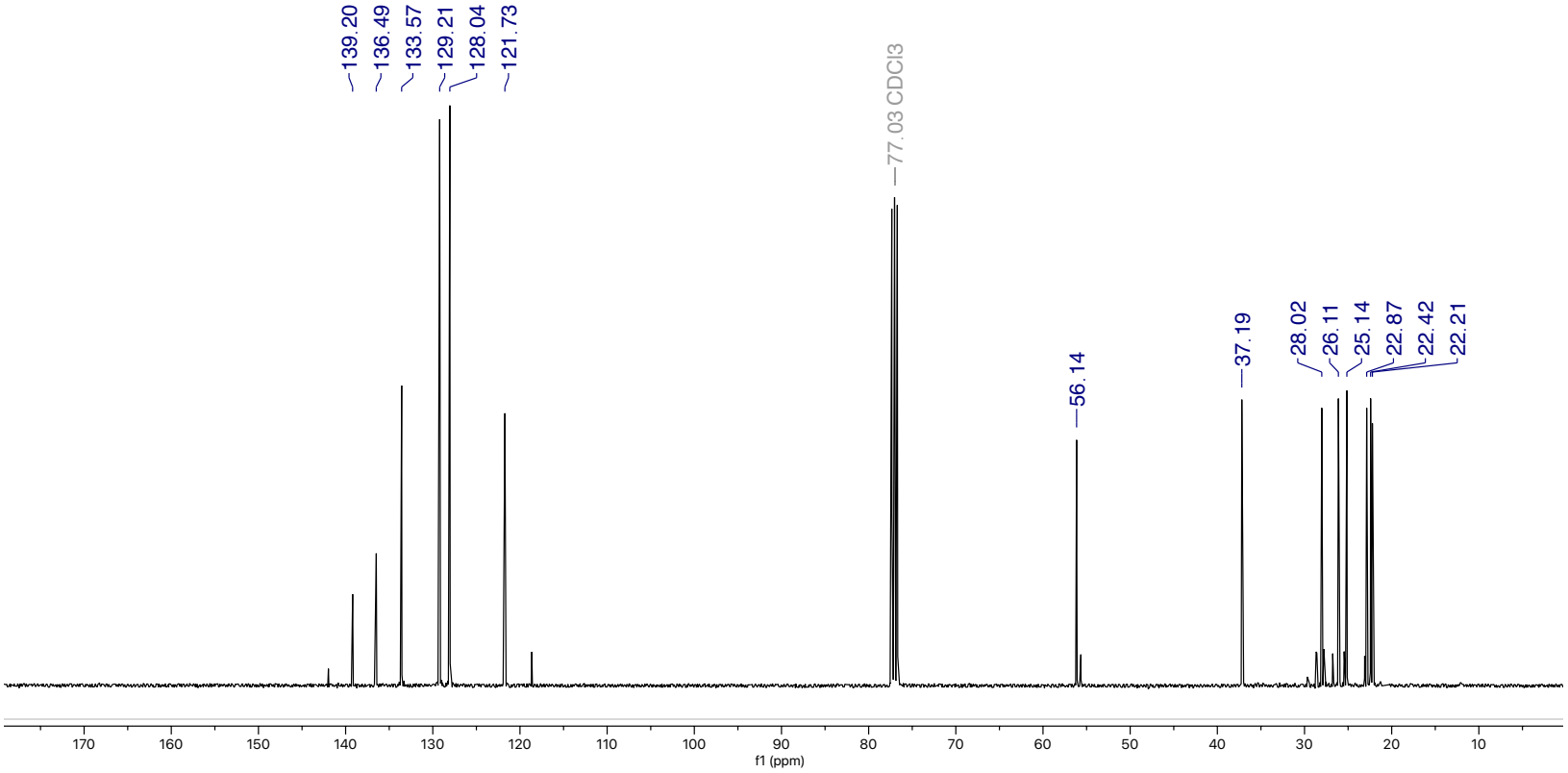

$^1$H-NMR (400 MHz, $CDCl_3$)



((4-(Cyclohex-1-en-1-yl)butyl)sulfonyl)benzene

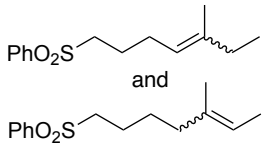


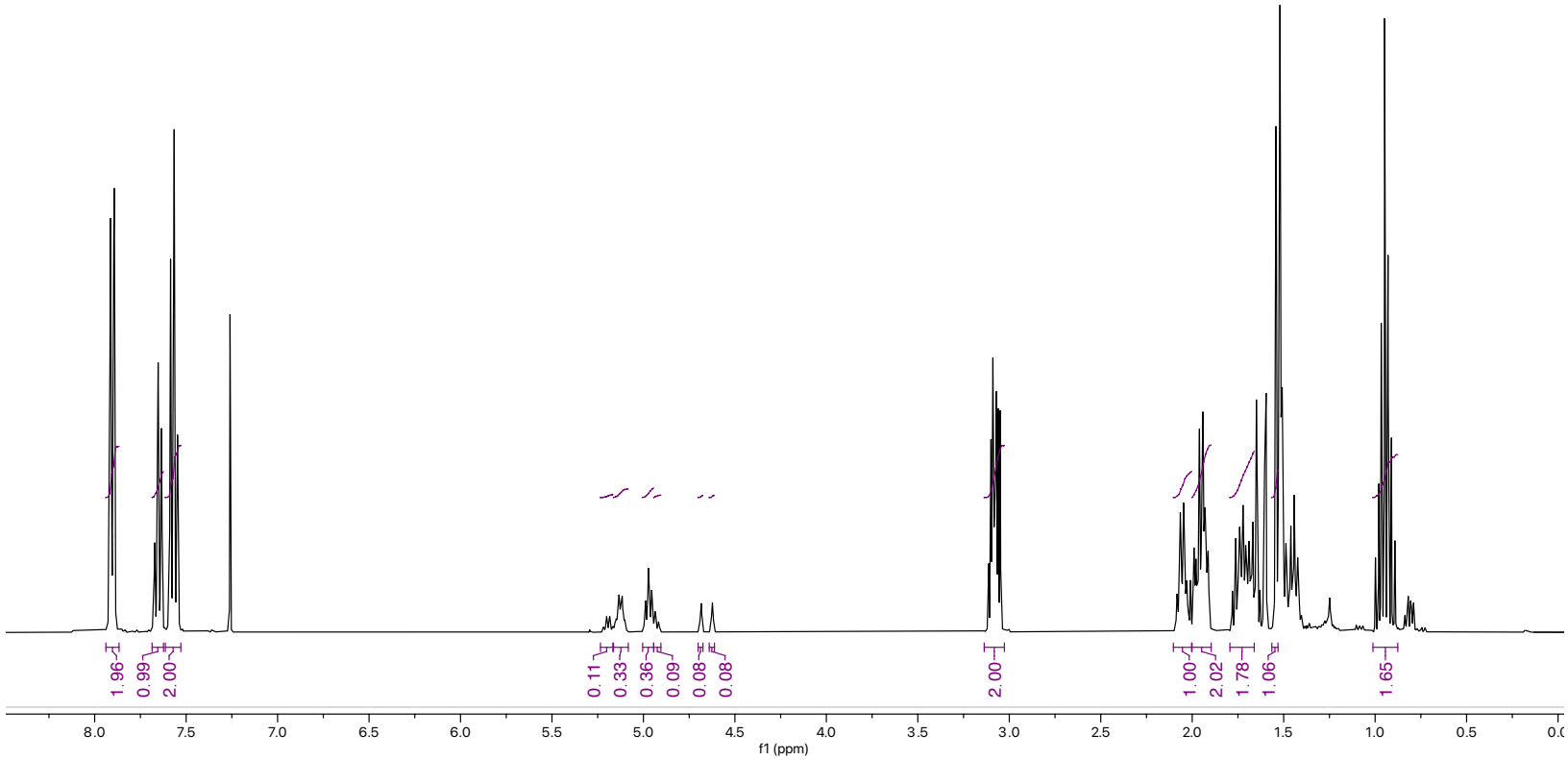

$^{13}$C-NMR (101 MHz, $CDCl_3$)



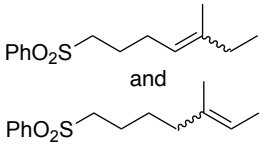
5-Methylhept-4-en-1-yl)sulfonyl)benzene

$^1$H-NMR (400 MHz, $CDCl_3$)

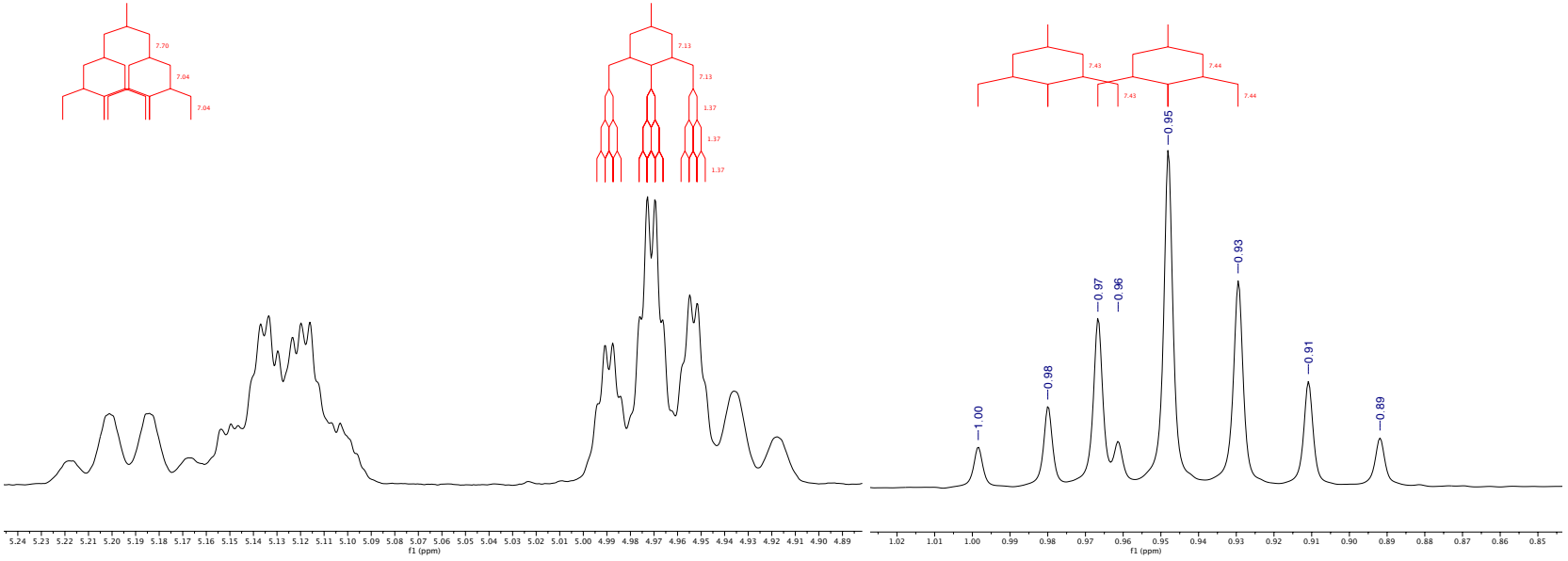


5-Methylhept-4-en-1-yl)sulfonyl)benzene

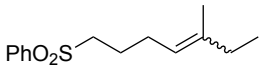


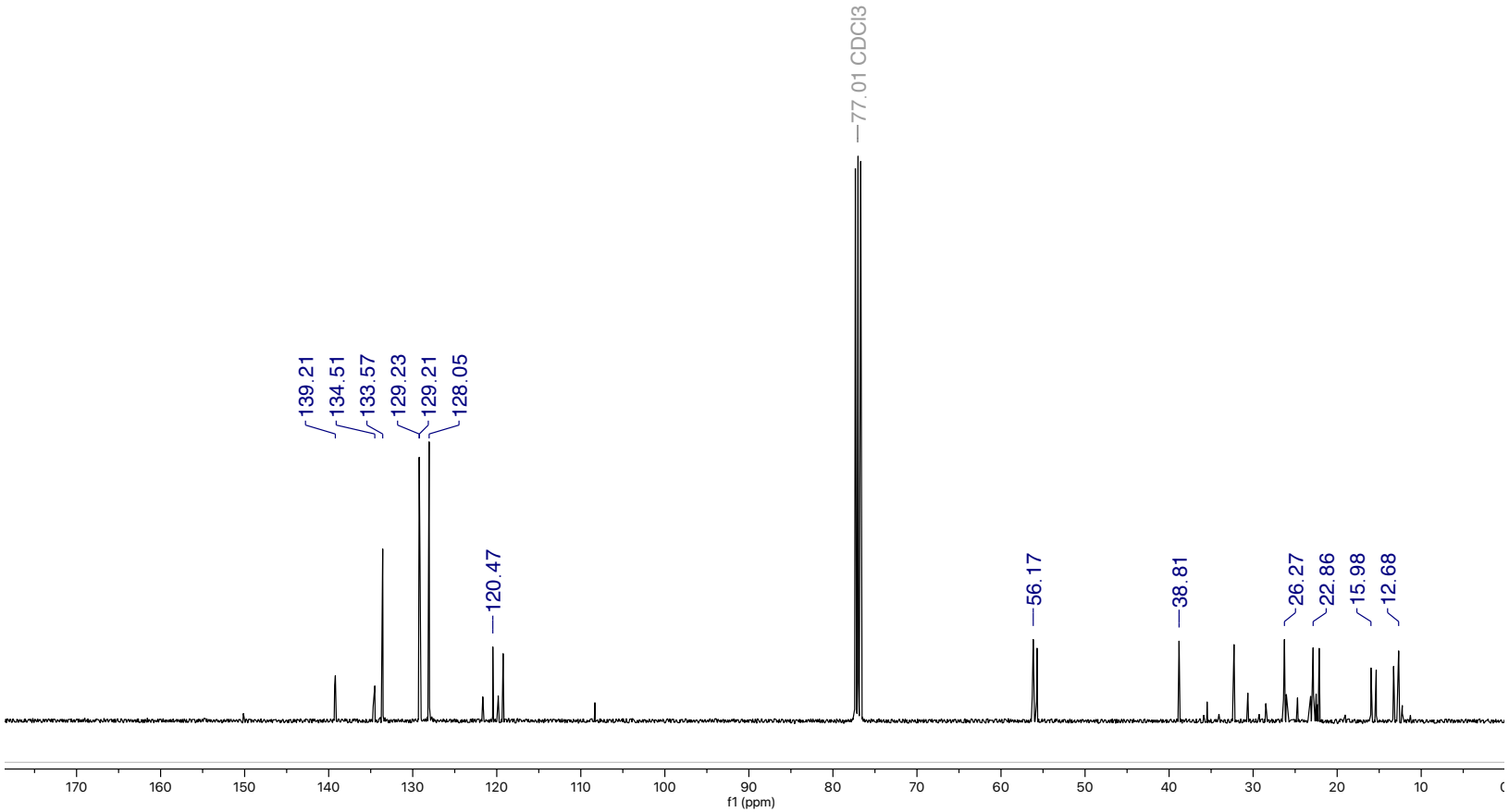

$^{1}$H-NMR (400 MHz, $CDCl_3$)



5-Methylhept-4-en-1-yl)sulfonyl)benzene

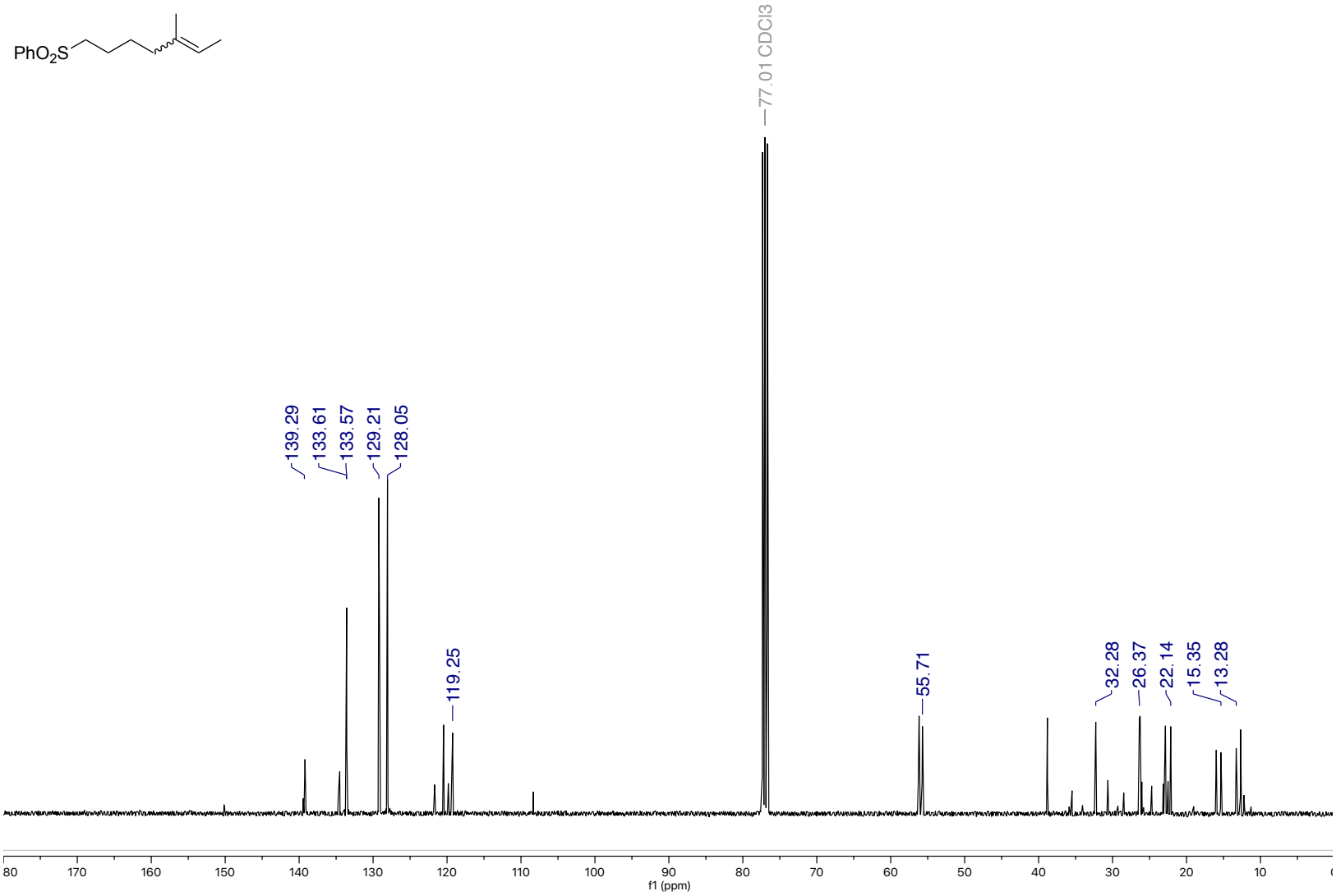
$^{13}$C-NMR (101 MHz, $CDCl_3$)



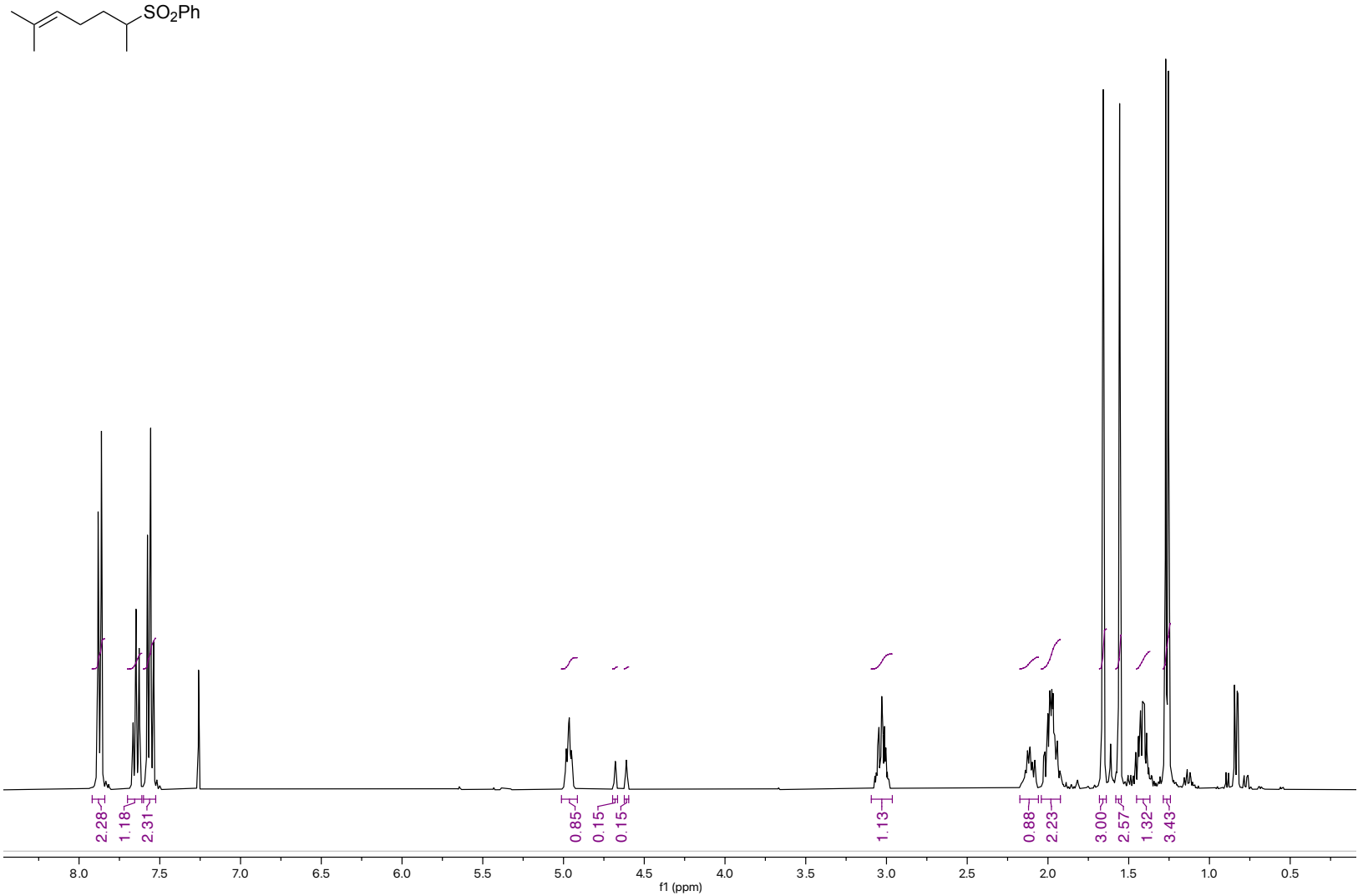
((5-Methylhept-5-en-1-yl)sulfonyl)benzene

$^{13}$C-NMR (101 MHz, $CDCl_3$)

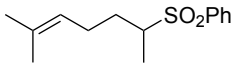


((6-Methylhept-5-en-2-yl)sulfonyl)benzene

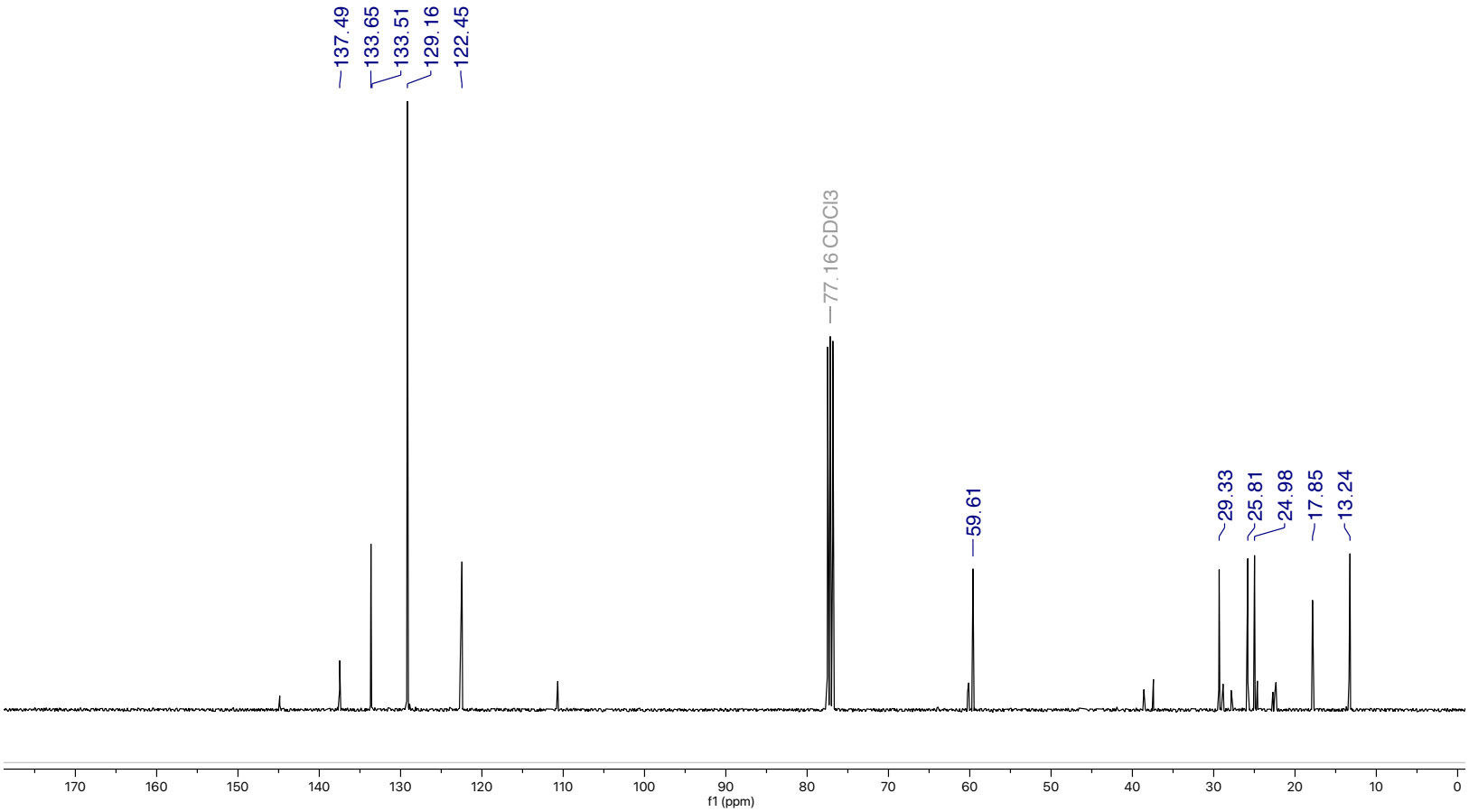
$^1$H-NMR (400 MHz, $CDCl_3$)



((6-Methylhept-5-en-2-yl)sulfonyl)benzene

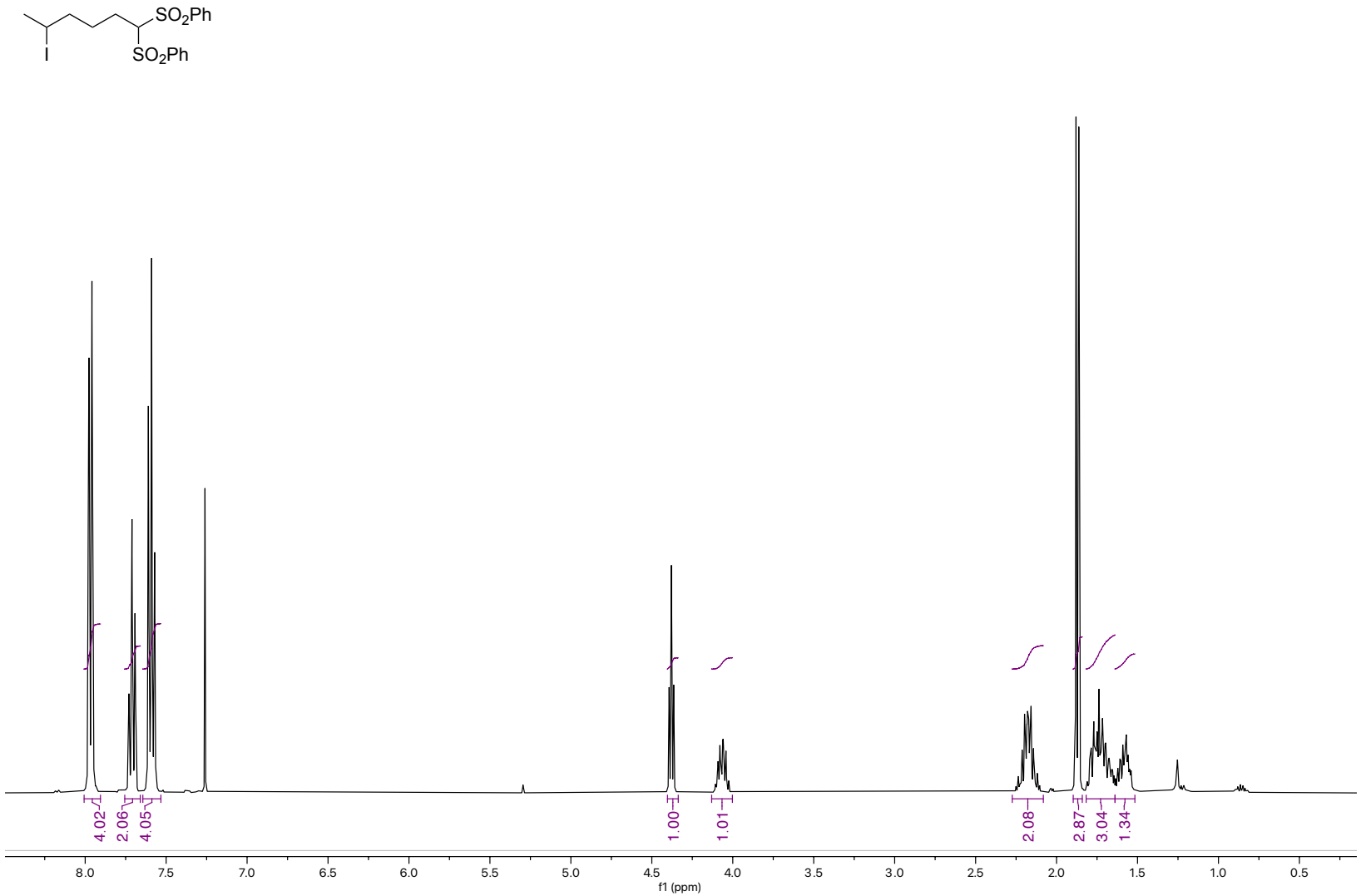



$^{13}$C-NMR (101 MHz, $CDCl_3$)



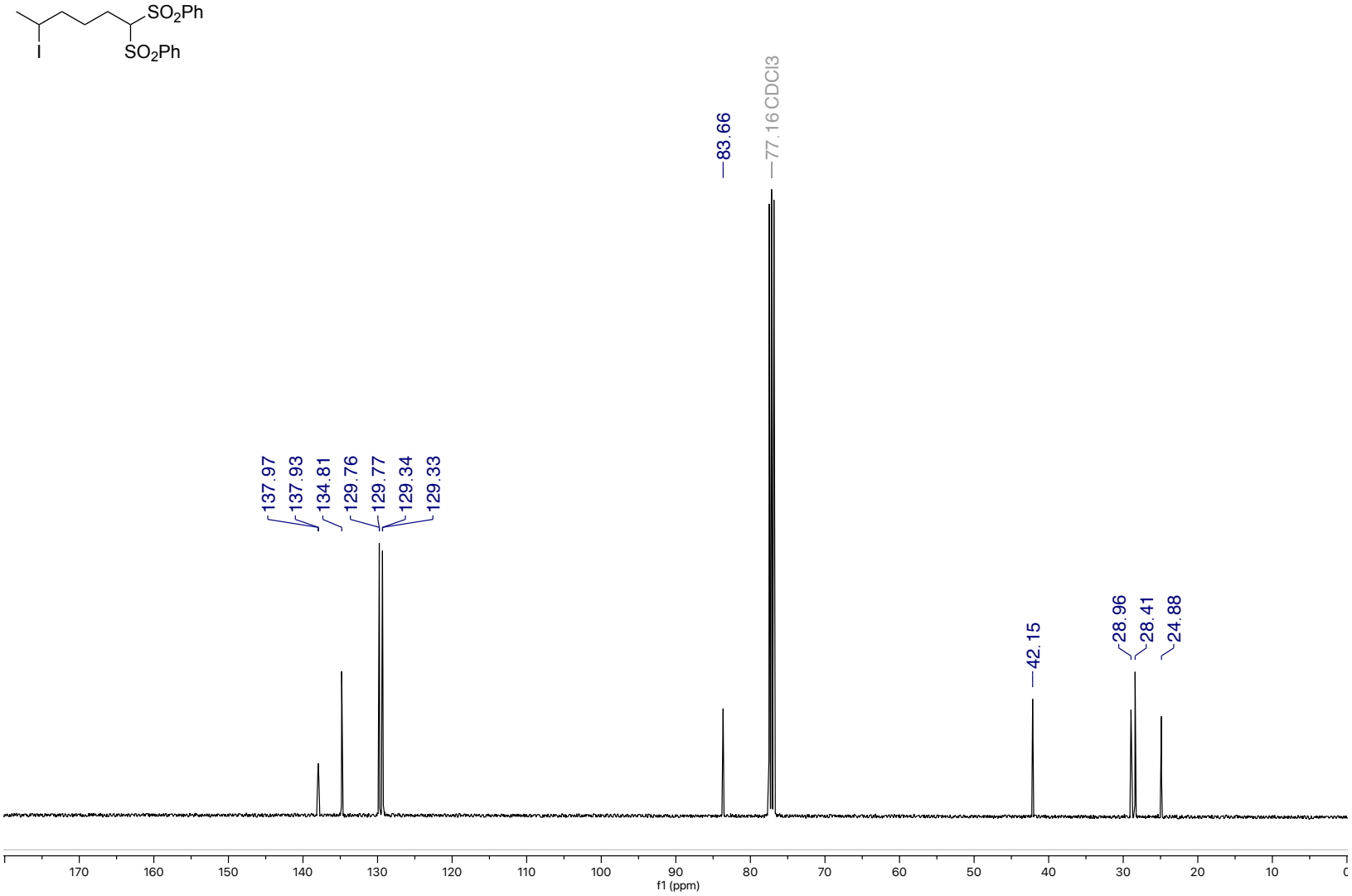
(5-Iodohexane-1,1-diyldisulfonyl)dibenzene

$^1$H-NMR (400 MHz, $CDCl_3$)

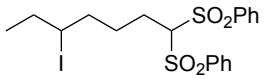


(5-Iodohexane-1,1-diyldisulfonyl)dibenzene

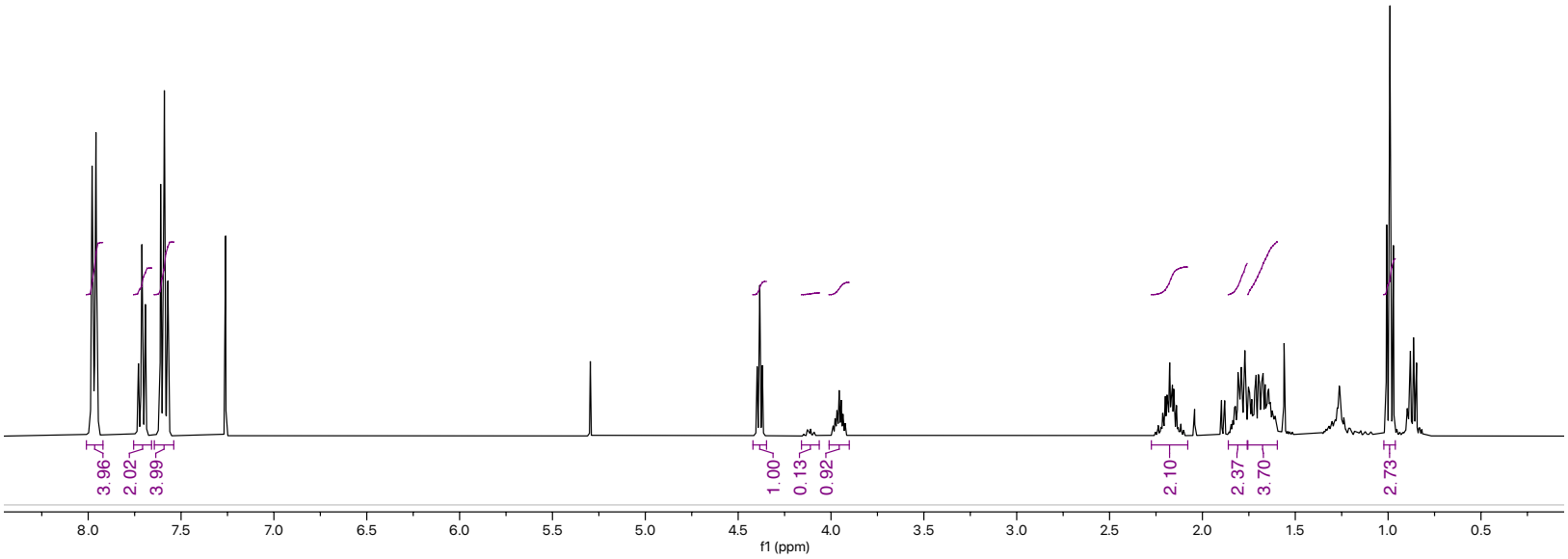
$^{13}$C-NMR (101 MHz, $CDCl_3$)



5-Iodoheptane-1,1-diyldisulfonyl)dibenzene

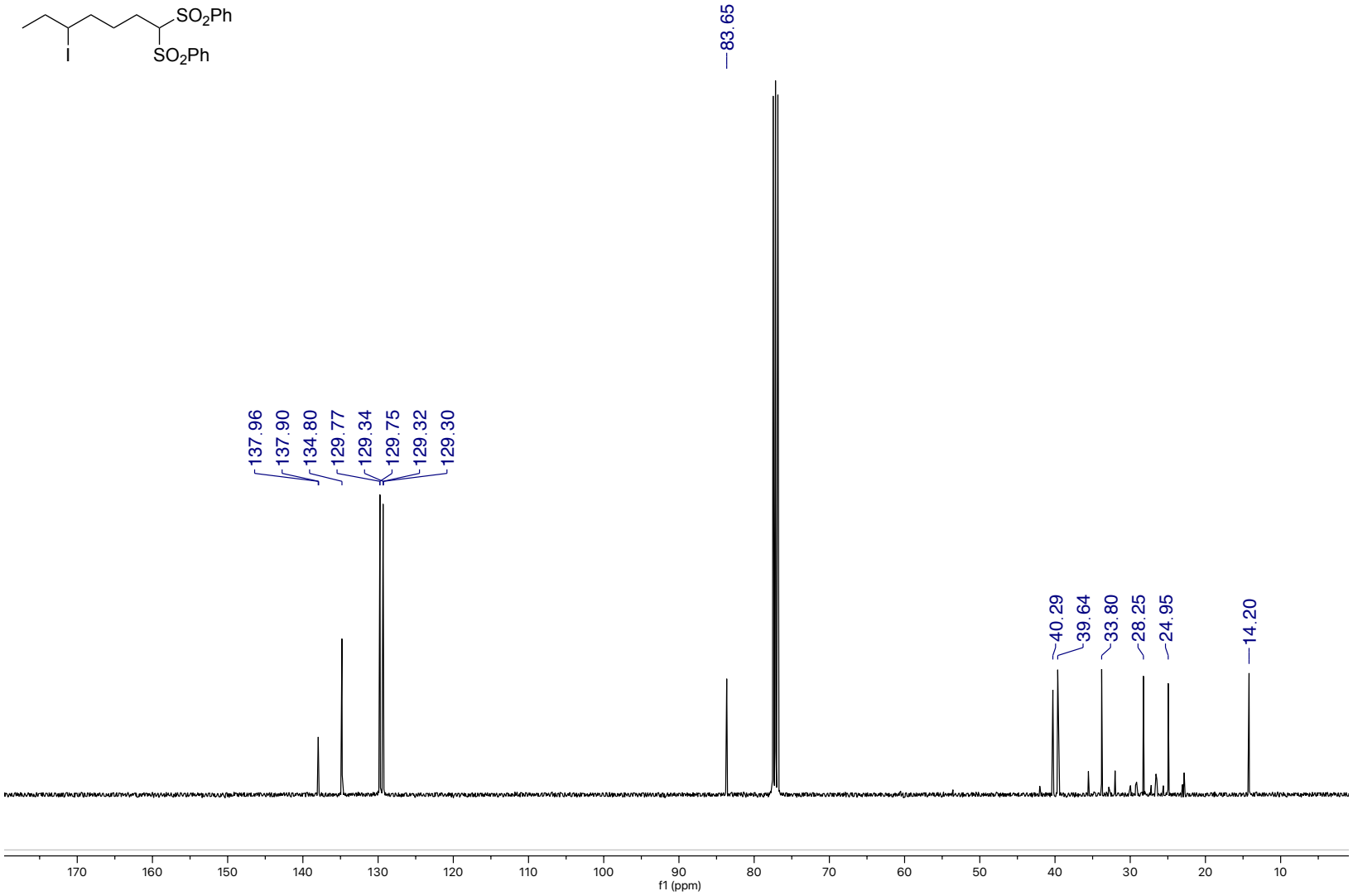



$^{1}$H-NMR (400 MHz, $CDCl_3$)



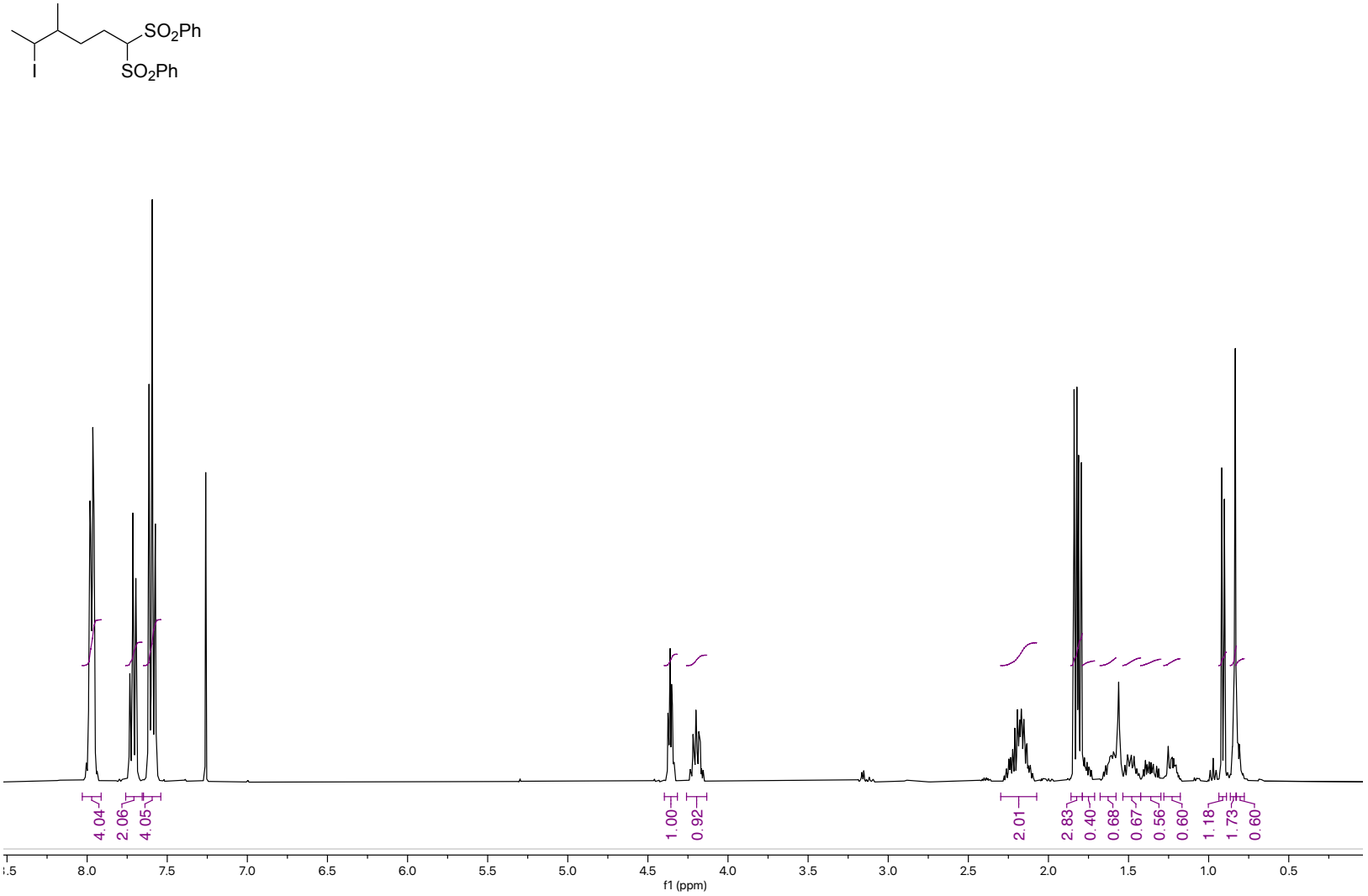
5-Iodoheptane-1,1-diyldisulfonyl)dibenzene

$^{13}$C-NMR (101 MHz, $CDCl_3$)



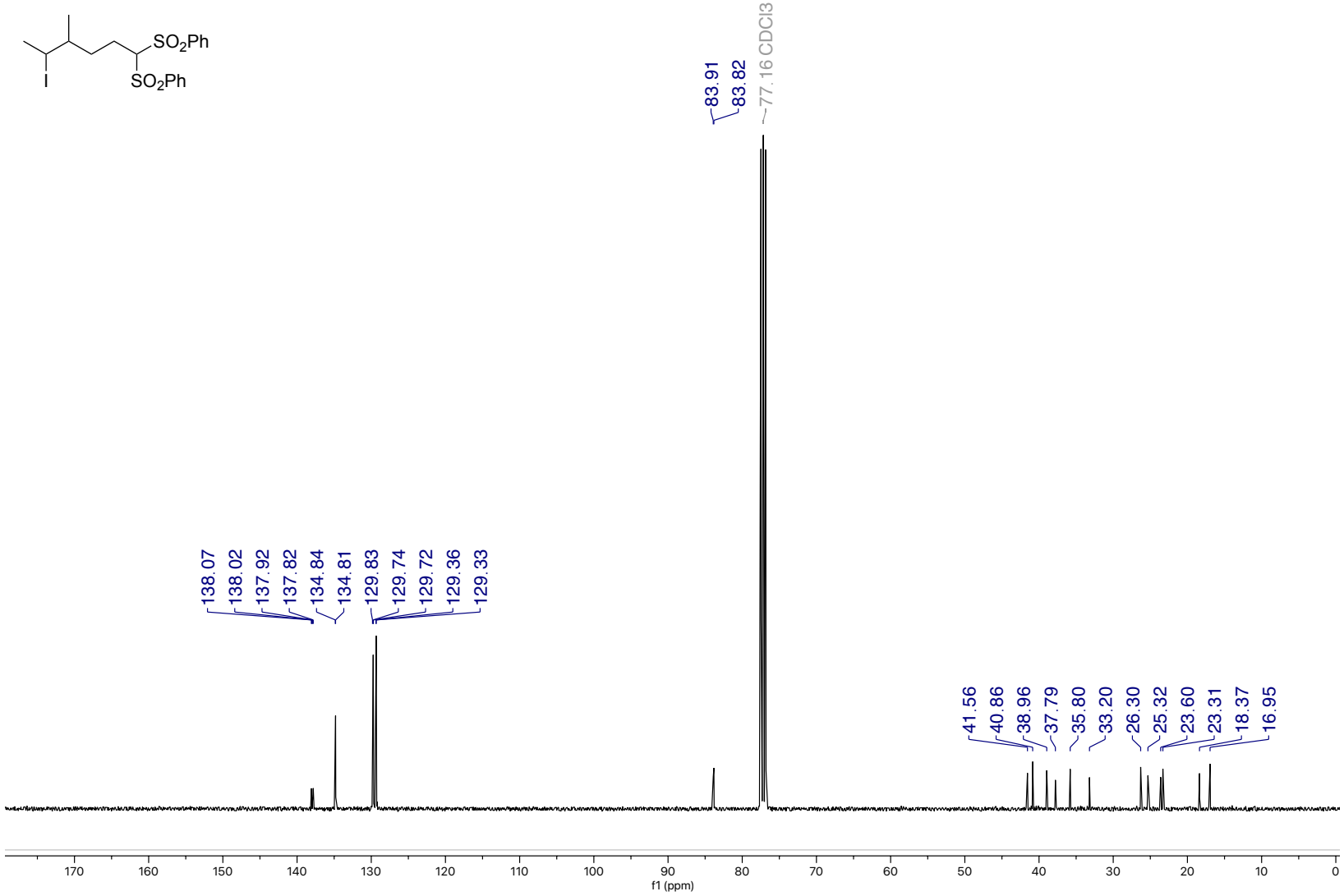
(5-Iodo-4-methylhexane-1,1-diyldisulfonyl)dibenzene

$^1$H-NMR (400 MHz, $CDCl_3$)



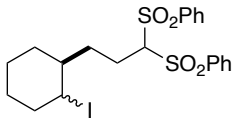
(5-Iodo-4-methylhexane-1,1-diyldisulfonyl)dibenzene

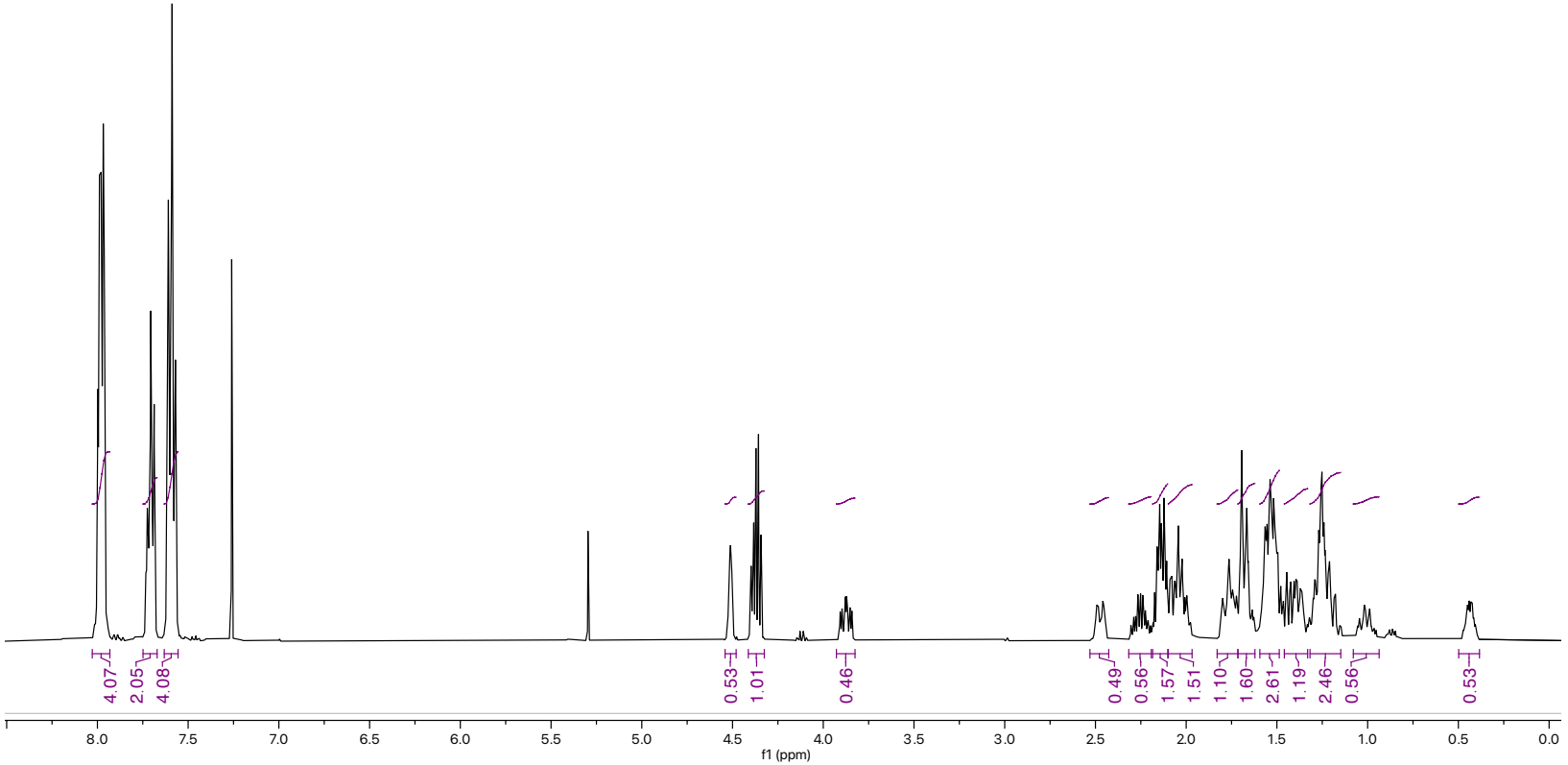
$^{13}$C-NMR (101 MHz, $CDCl_3$)



(3-(2-Iodocyclohexyl)propane-1,1-diyldisulfonyl)dibenzene

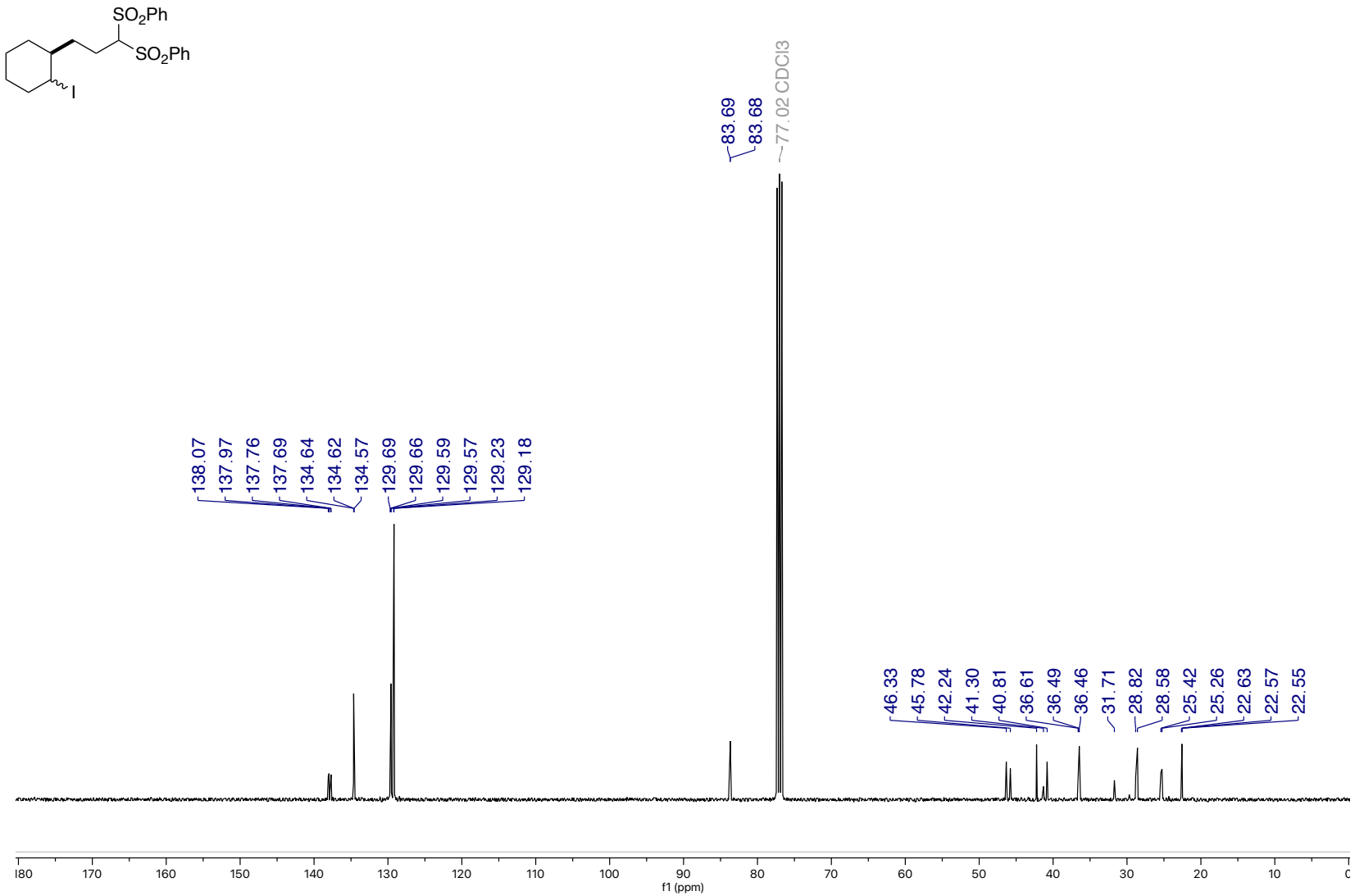
$^1$H-NMR (400 MHz, $CDCl_3$)



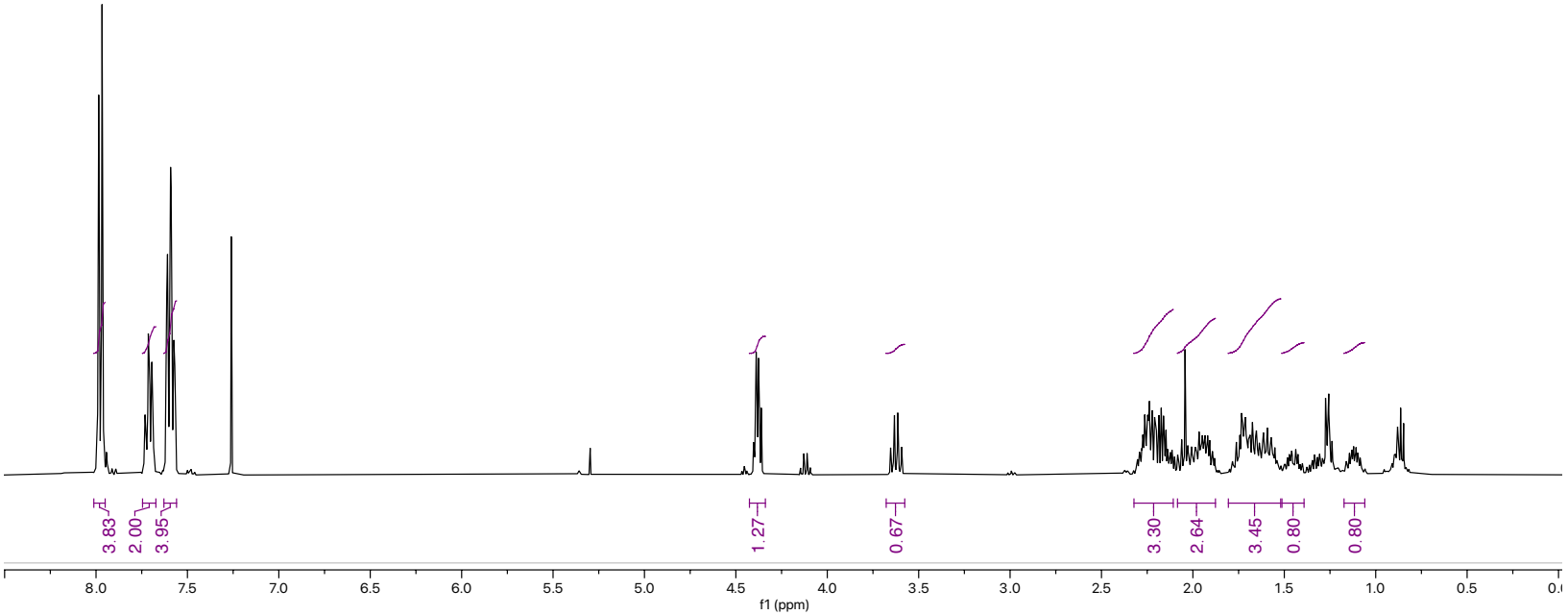
(3-(2-Iodocyclohexyl)propane-1,1-diyldisulfonyl)dibenzene

$^{13}$C-NMR (101 MHz, $CDCl_3$)

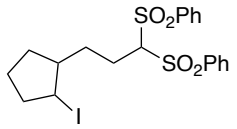


(3-(2-Iodocyclopentyl)propane-1,1-diyldisulfonyl)dibenzene

$^1$H-NMR (400 MHz, $CDCl_3$)

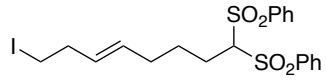
(3-(2-Iodocyclopentyl)propane-1,1-diyldisulfonyl)dibenzene

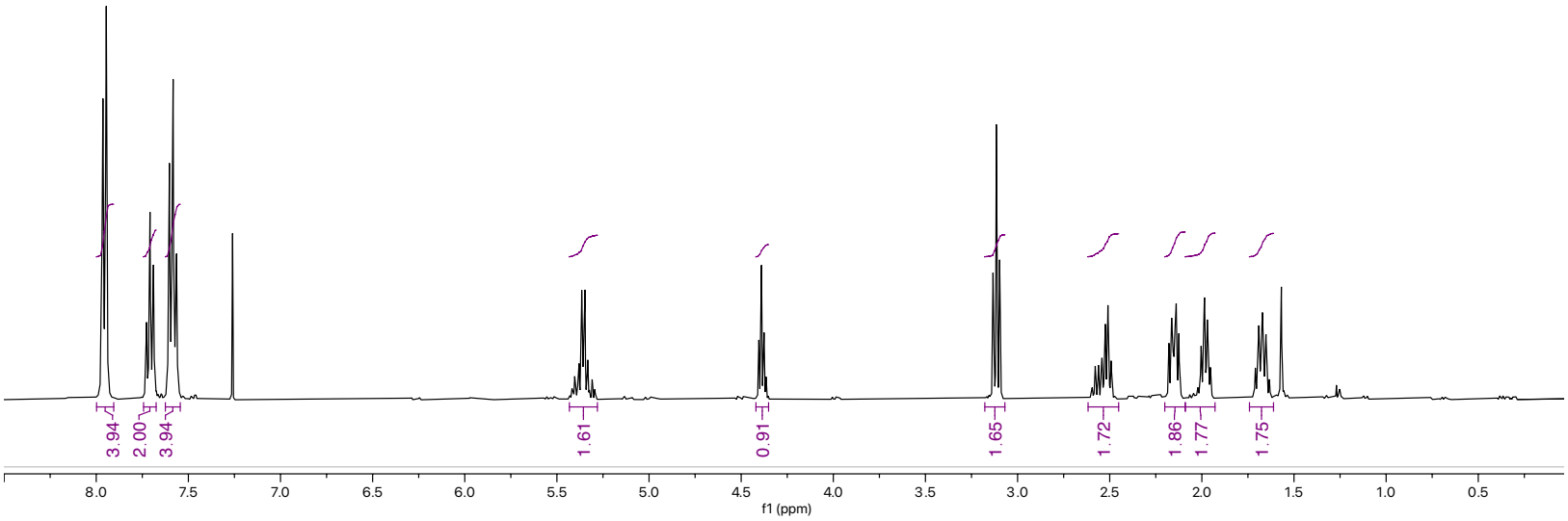



$^{13}$C-NMR (101 MHz, $CDCl_3$)

(8-Iodooct-5-ene-1,1-diyldisulfonyl)dibenzene

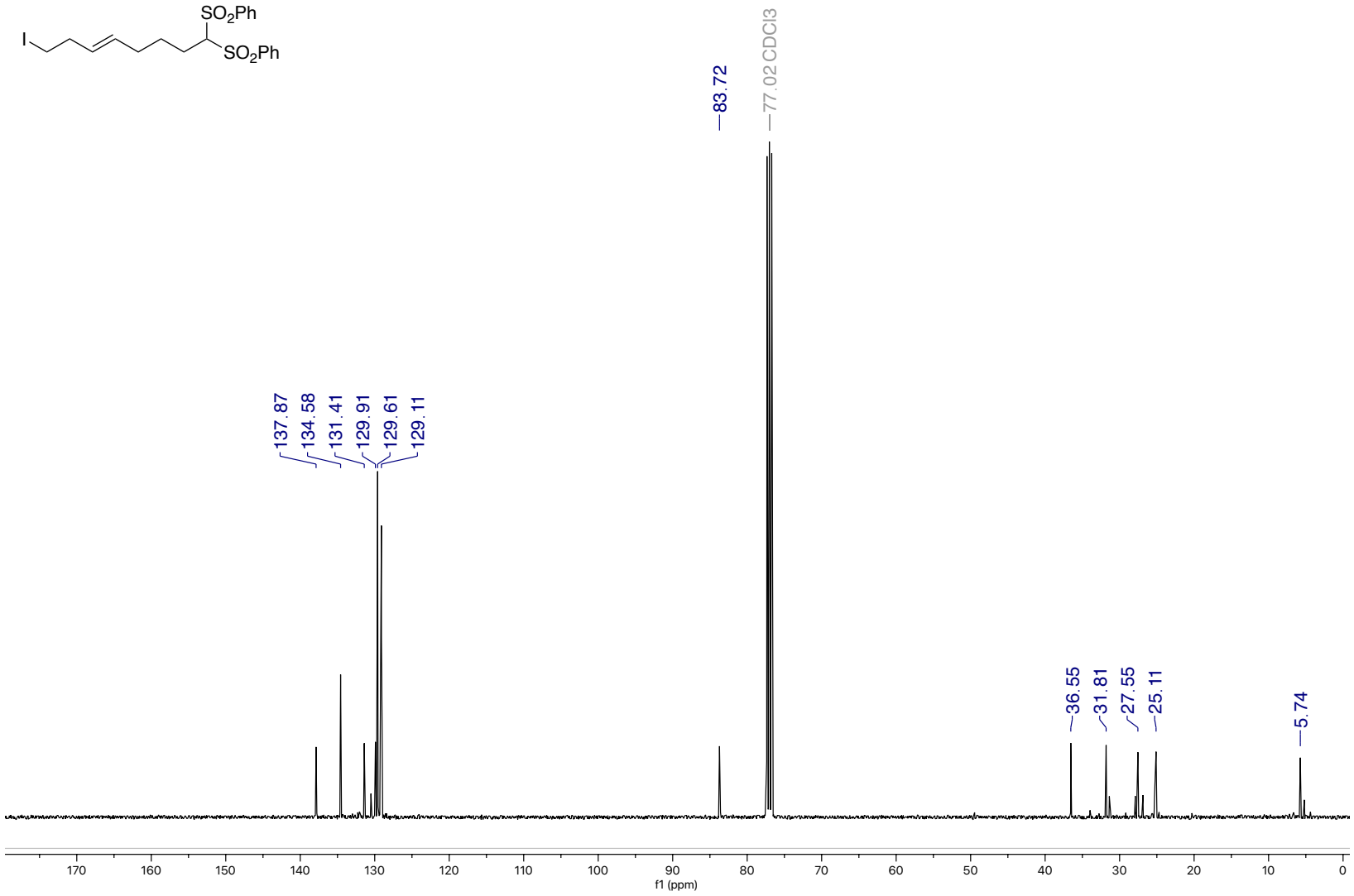
$^1$H-NMR (400 MHz, $CDCl_3$)



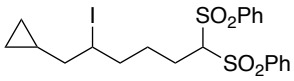
(8-Iodooct-5-ene-1,1-diyldisulfonyl)dibenzene

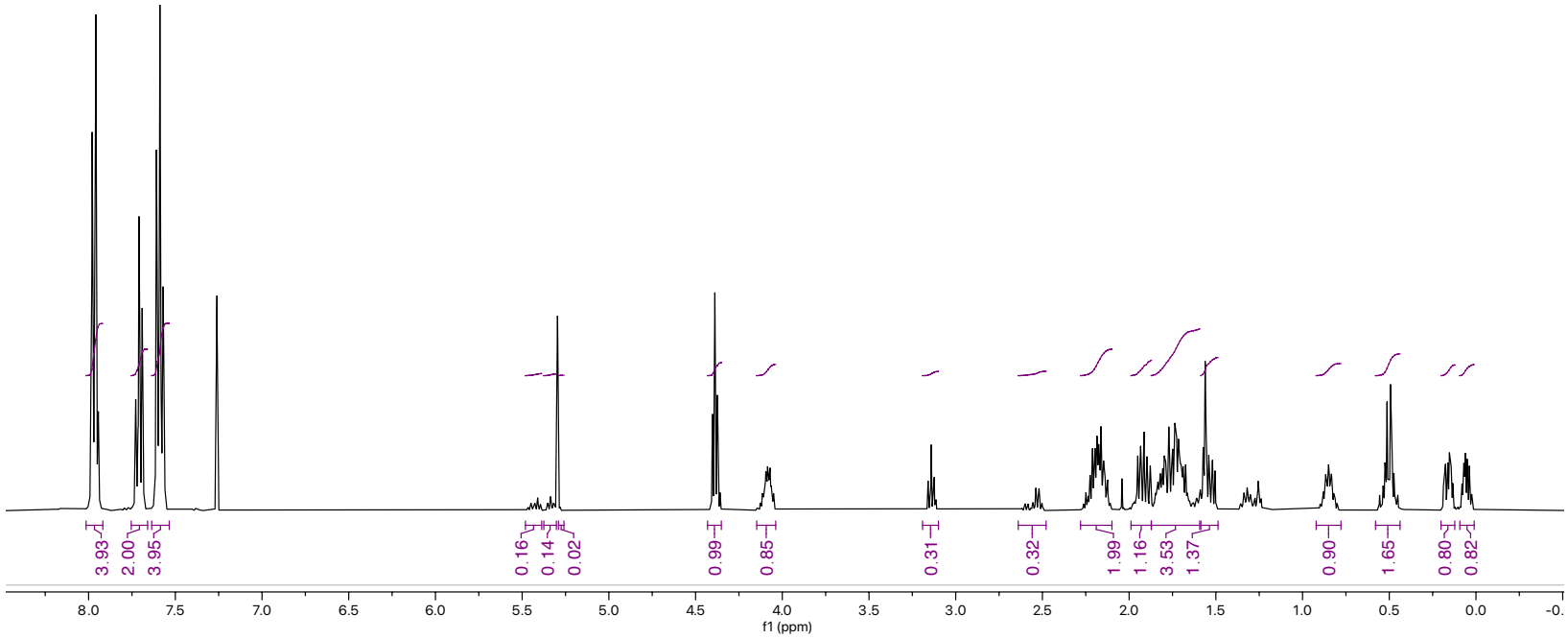
$^{13}$C-NMR (101 MHz, $CDCl_3$)



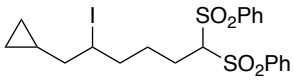
(6-Cyclopropyl-5-iodohexane-1,1-diyldisulfonyl)dibenzene

$^1$H-NMR (400 MHz, $CDCl_3$)



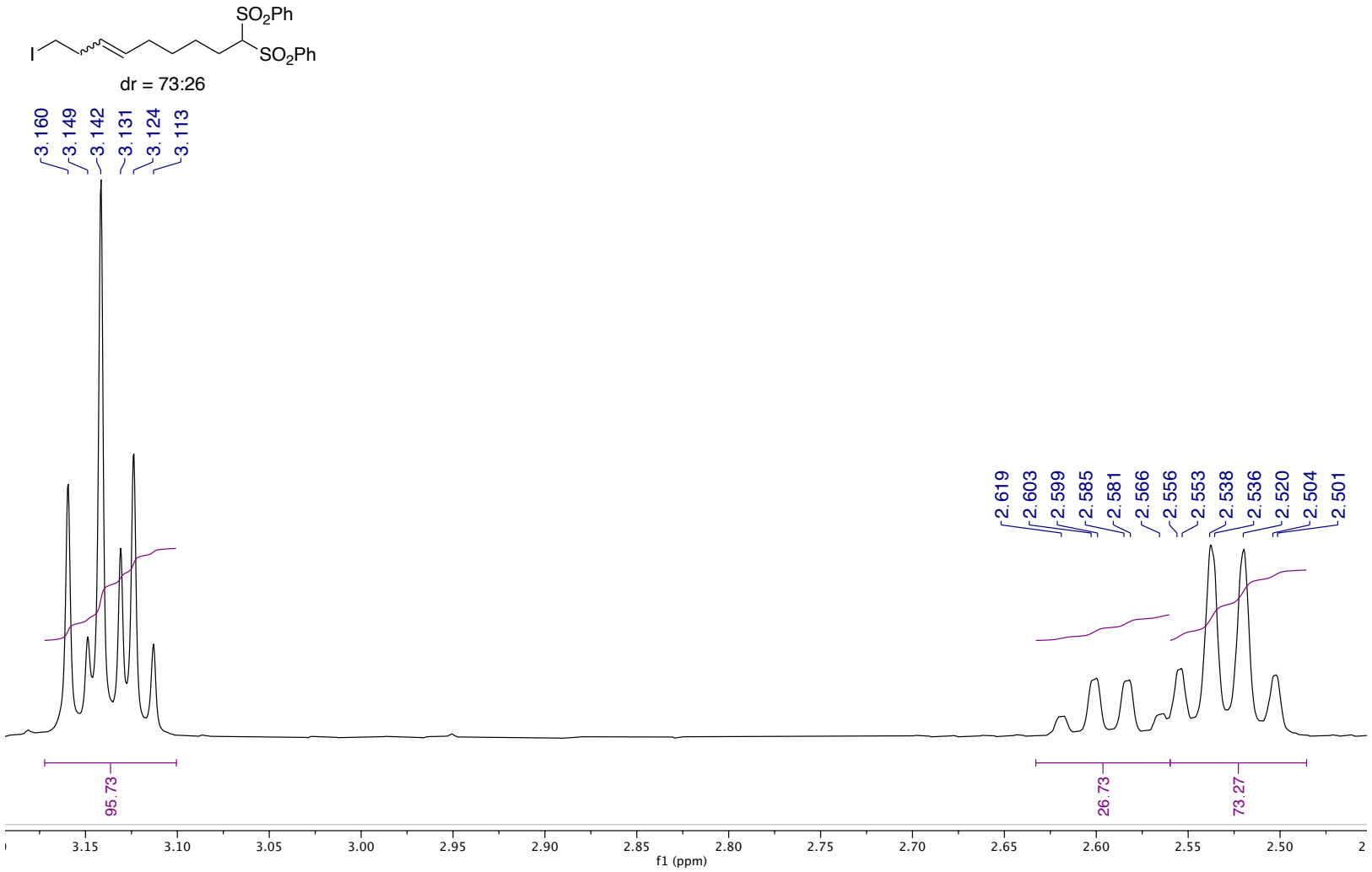
(6-Cyclopropyl-5-iodohexane-1,1-diyldisulfonyl)dibenzene



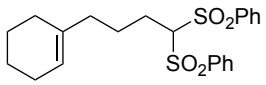

$^{13}$C-NMR (101 MHz, $CDCl_3$)

(9-iodonon-6-ene-1,1-diyldisulfonyl)dibenzene

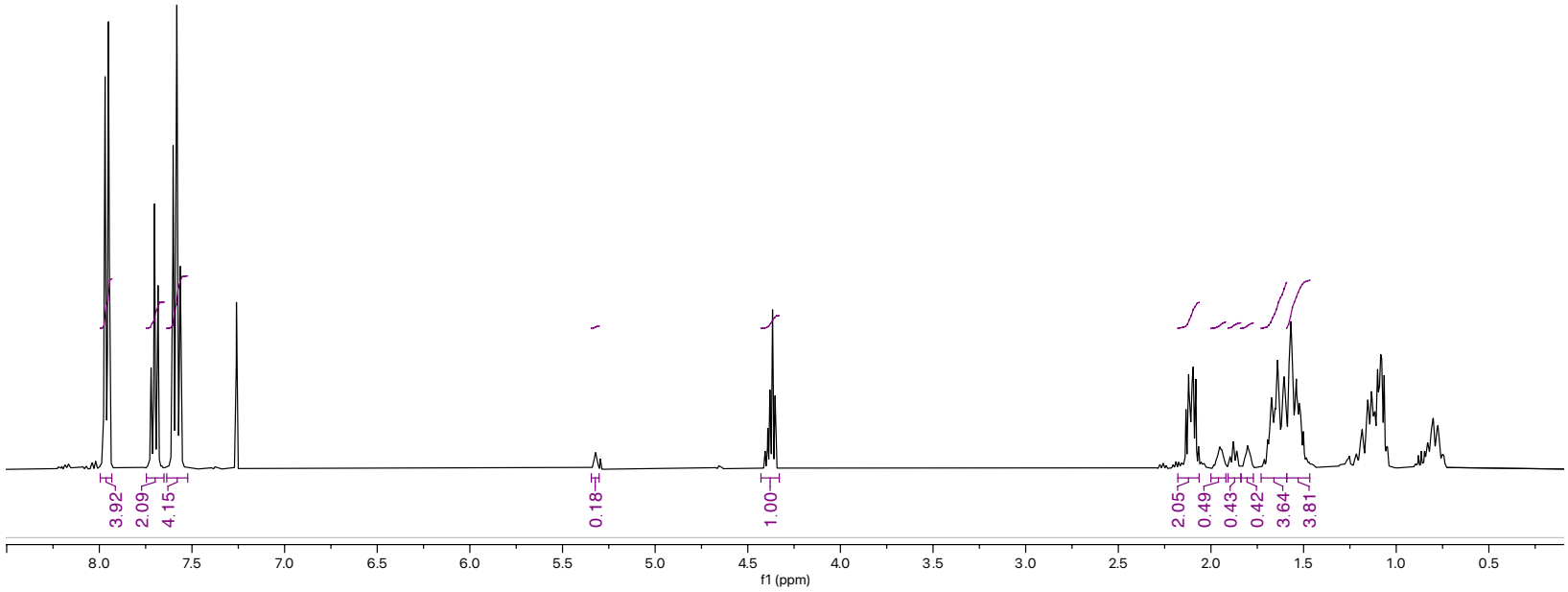
$^1$H-NMR (400 MHz, $CDCl_3$)



(4-(Cyclohex-1-en-1-yl)butane-1,1-diyldisulfonyl)dibenzene

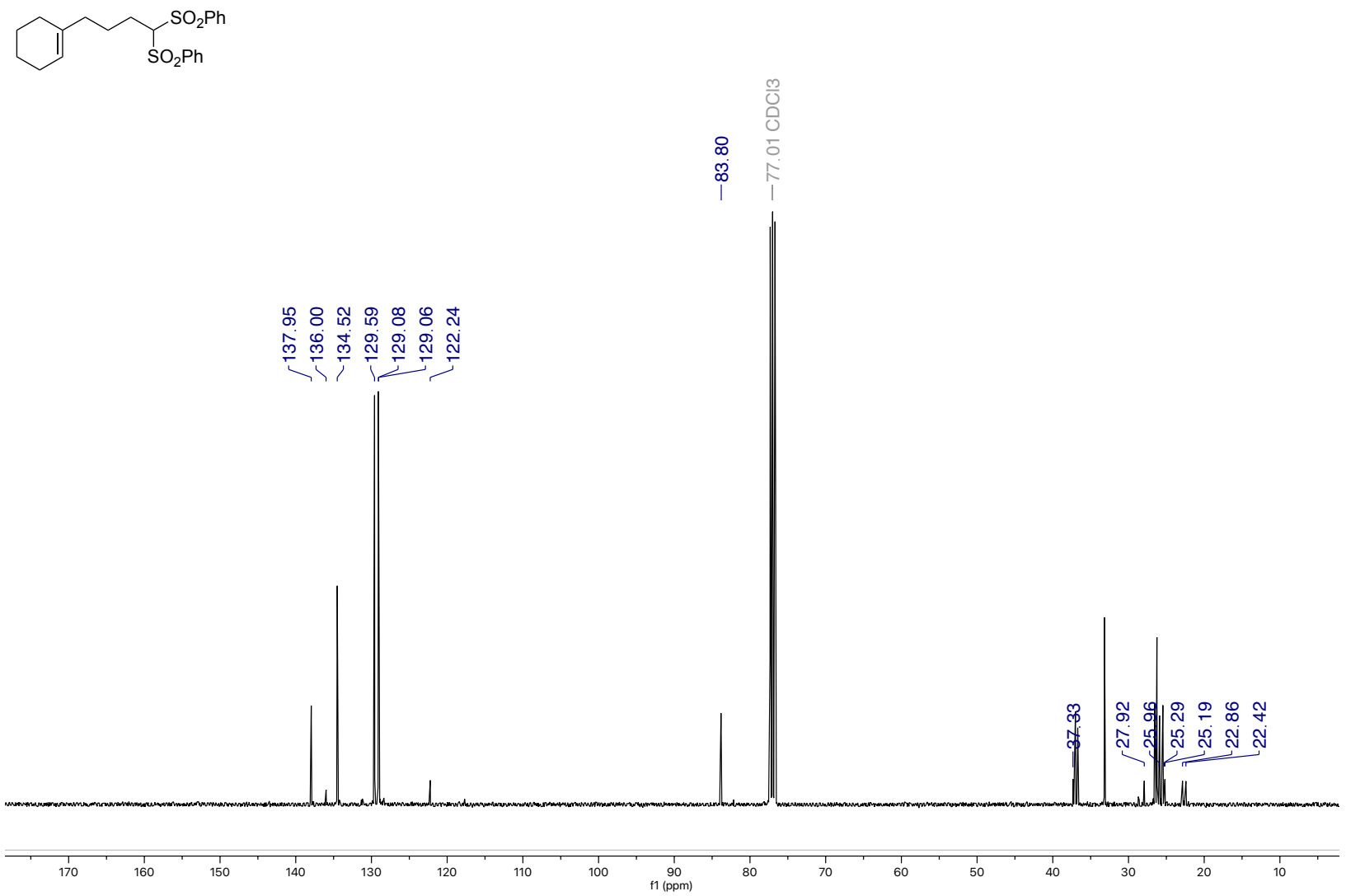



$^1$H-NMR (400 MHz, $CDCl_3$)

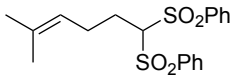


(4-(Cyclohex-1-en-1-yl)butane-1,1-diyldisulfonyl)dibenzene

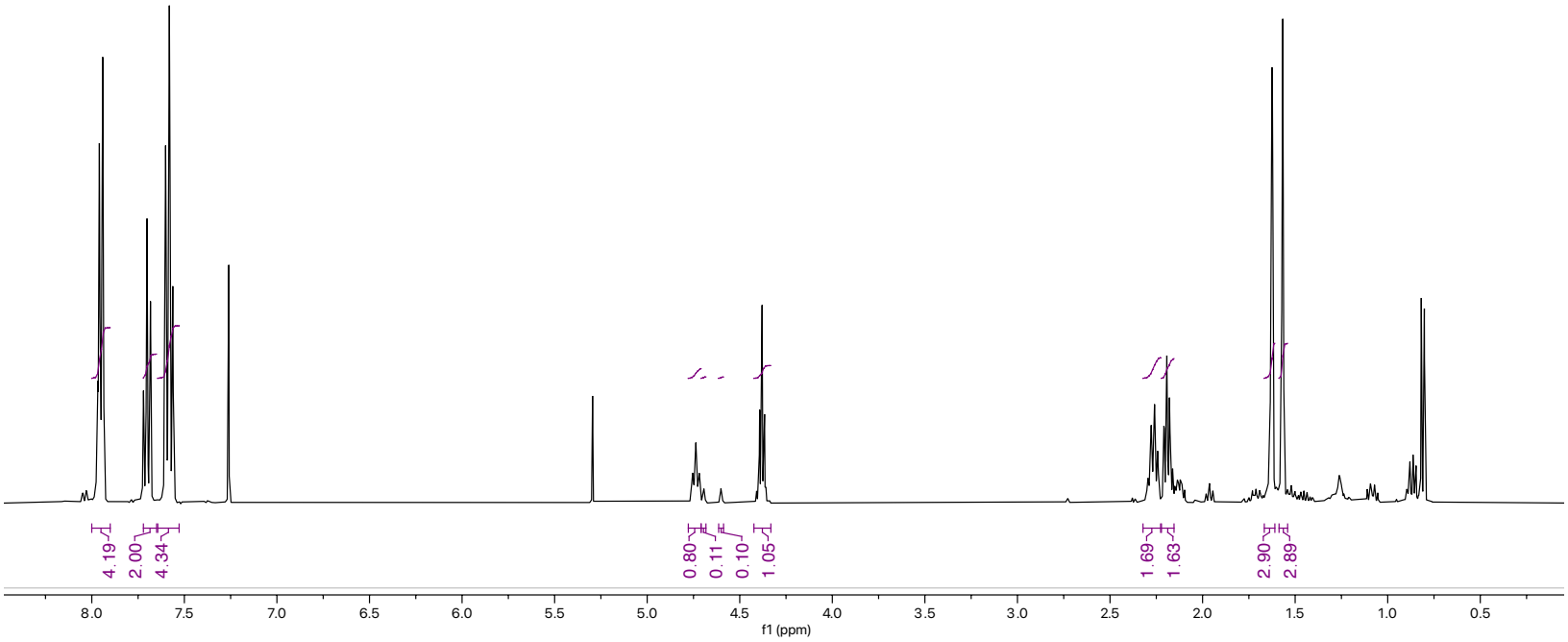
$^{13}$C-NMR (101 MHz, $CDCl_3$)



(5-Methylhex-4-ene-1,1-diyldisulfonyl)dibenzene

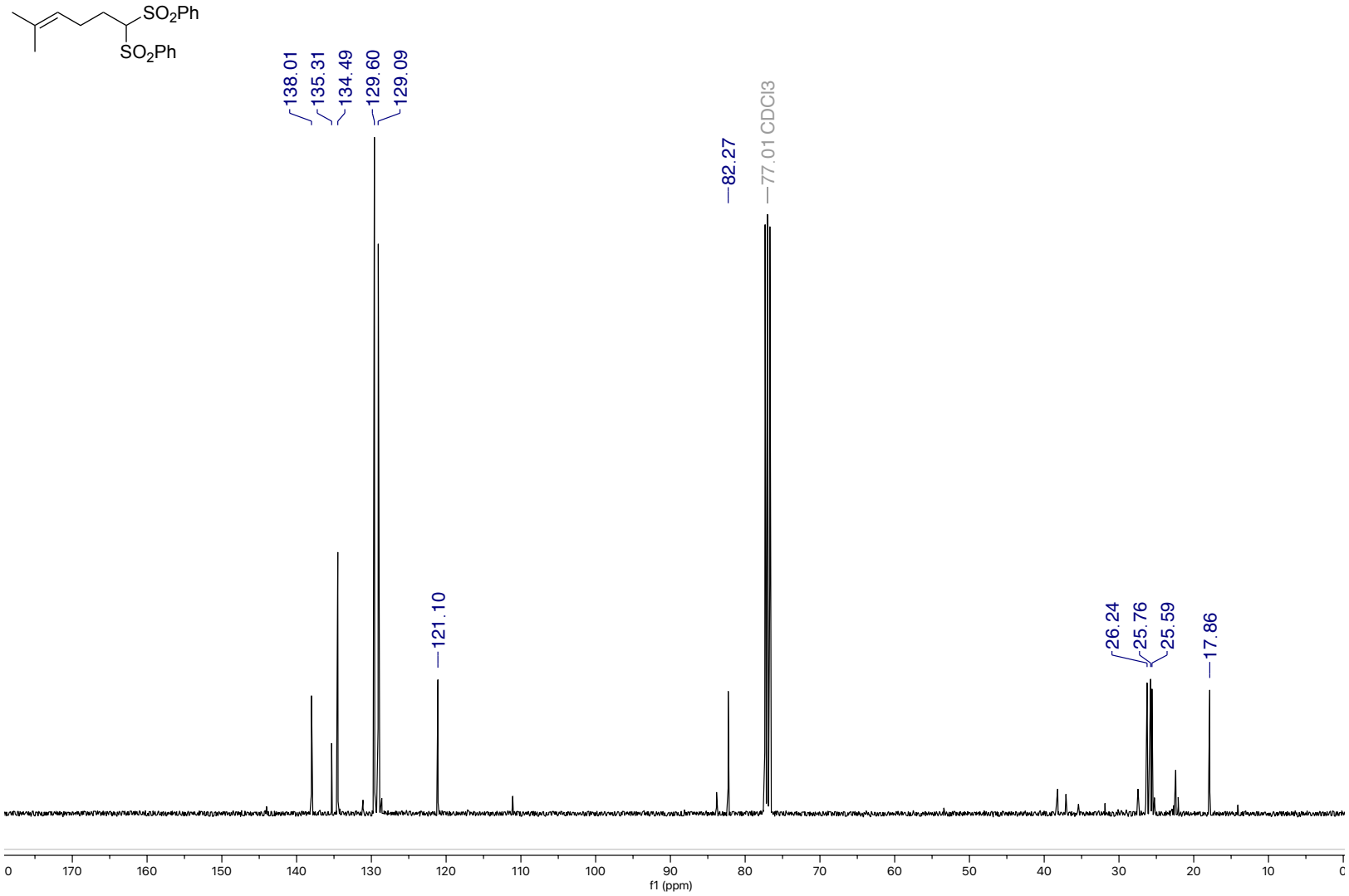



$^1$H-NMR (400 MHz, $CDCl_3$)

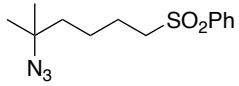


(5-Methylhex-4-ene-1,1-diyldisulfonyl)dibenzene

$^{13}$C-NMR (101 MHz, $CDCl_3$)



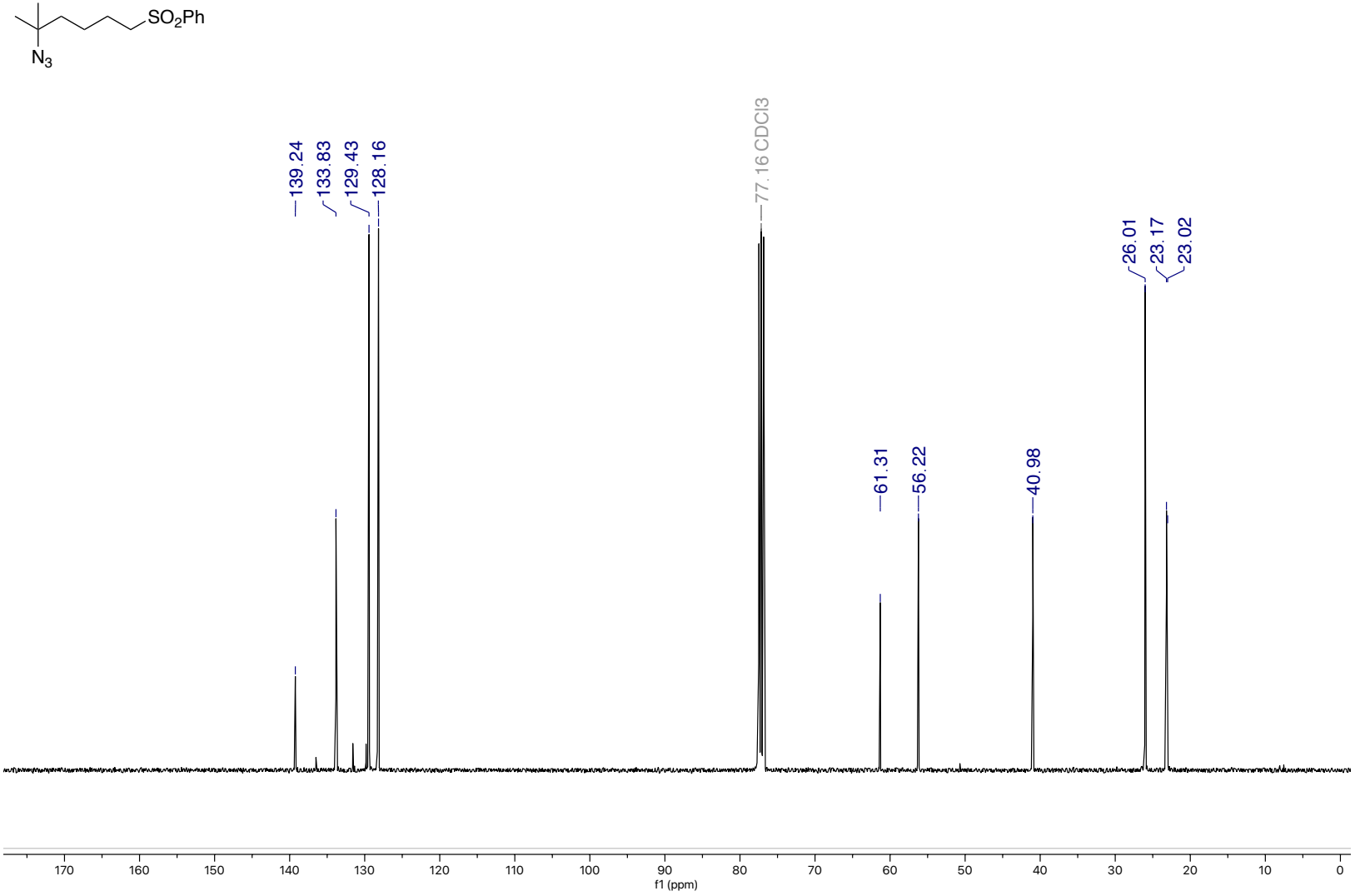
((5-Azido-5-methylhexyl)sulfonyl)benzene




$^1$H-NMR (400 MHz, $CDCl_3$)

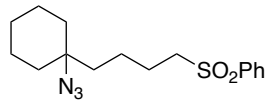
((5-Azido-5-methylhexyl)sulfonyl)benzene

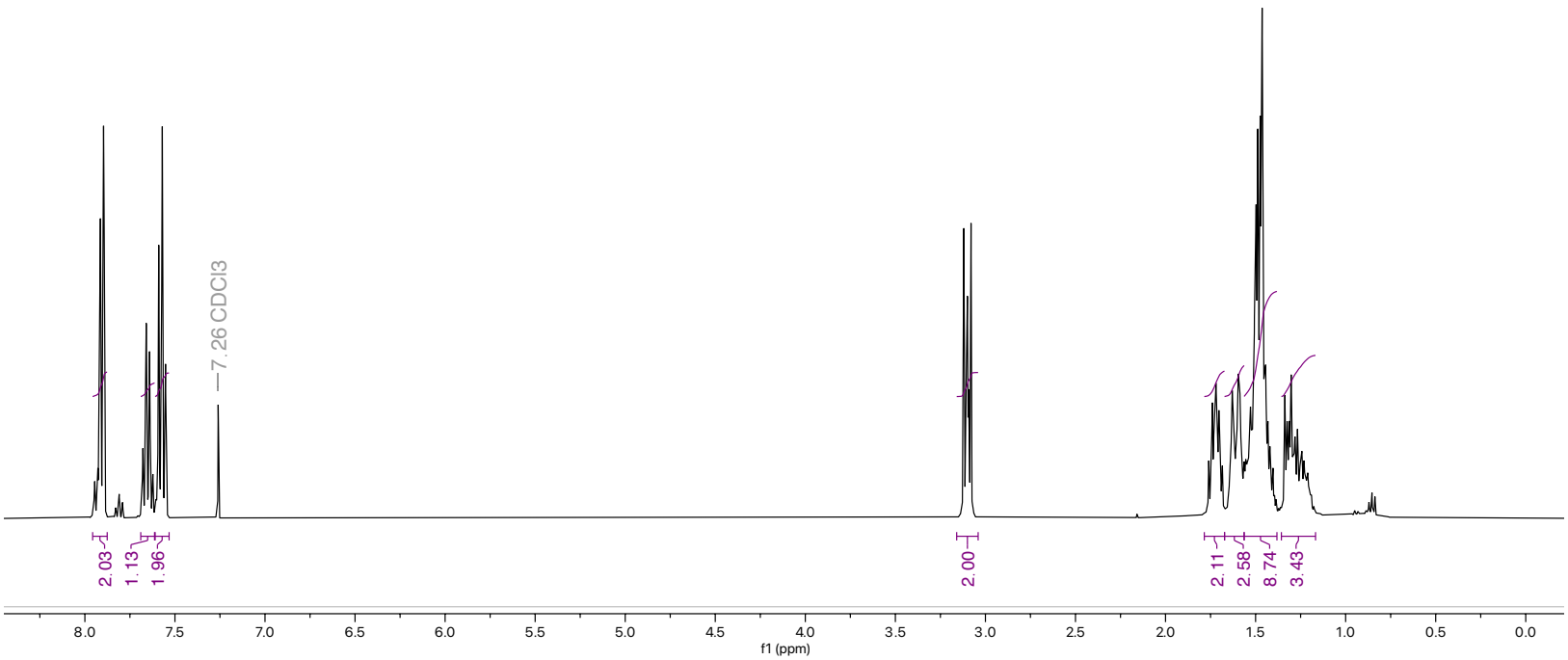
$^{13}$C-NMR (101 MHz, $CDCl_3$)



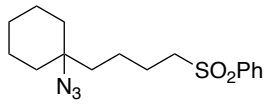
((4-(1-Azidocyclohexyl)butyl)sulfonyl)benzene

$^1$H-NMR (400 MHz, $CDCl_3$)

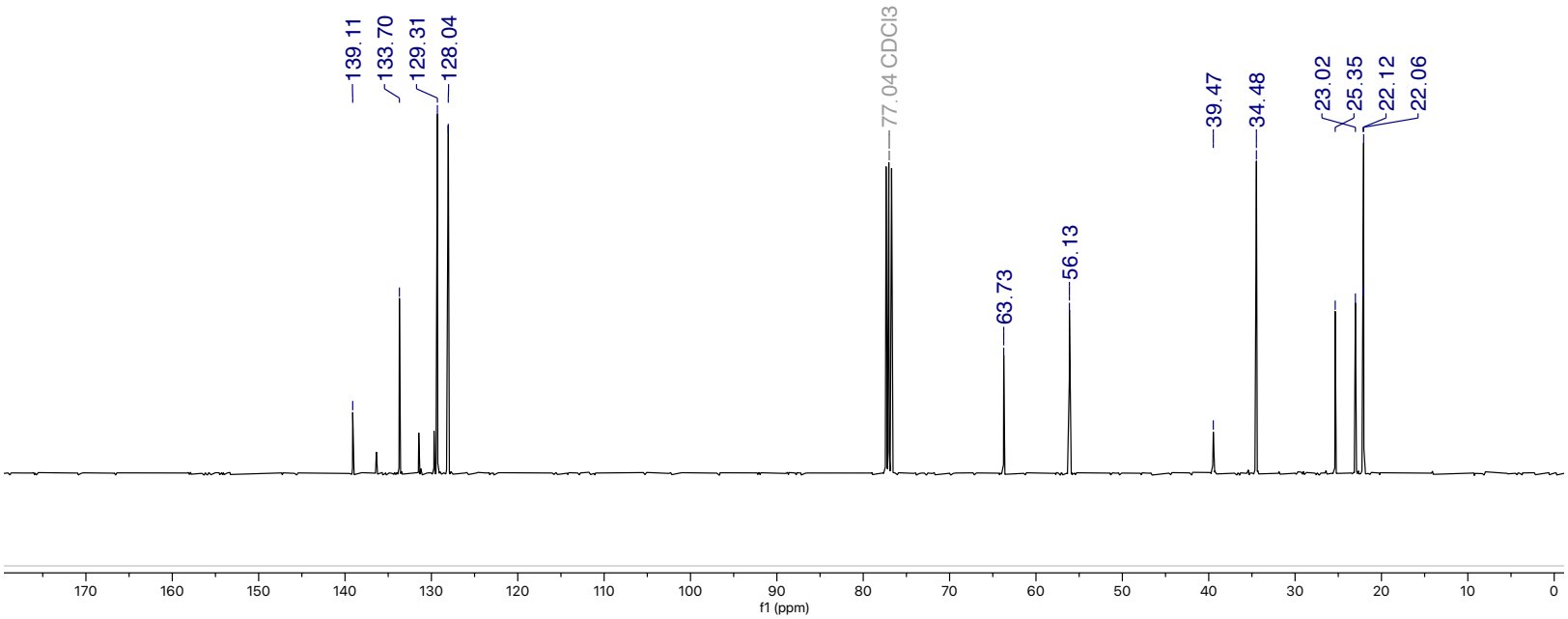


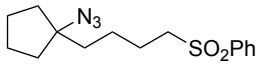
((4-(1-Azidocyclohexyl)butyl)sulfonyl)benzene



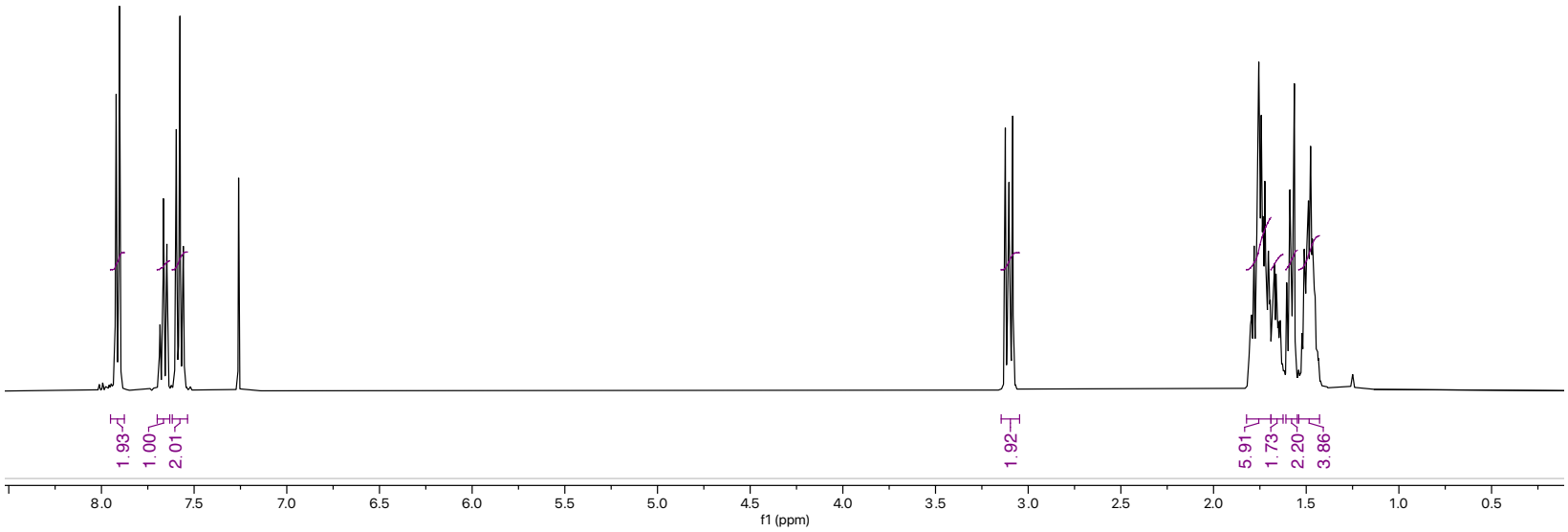

$^{13}$C-NMR (101 MHz, $CDCl_3$)



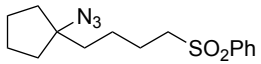
((4-(1-Azidocyclopentyl)butyl)sulfonyl)benzene



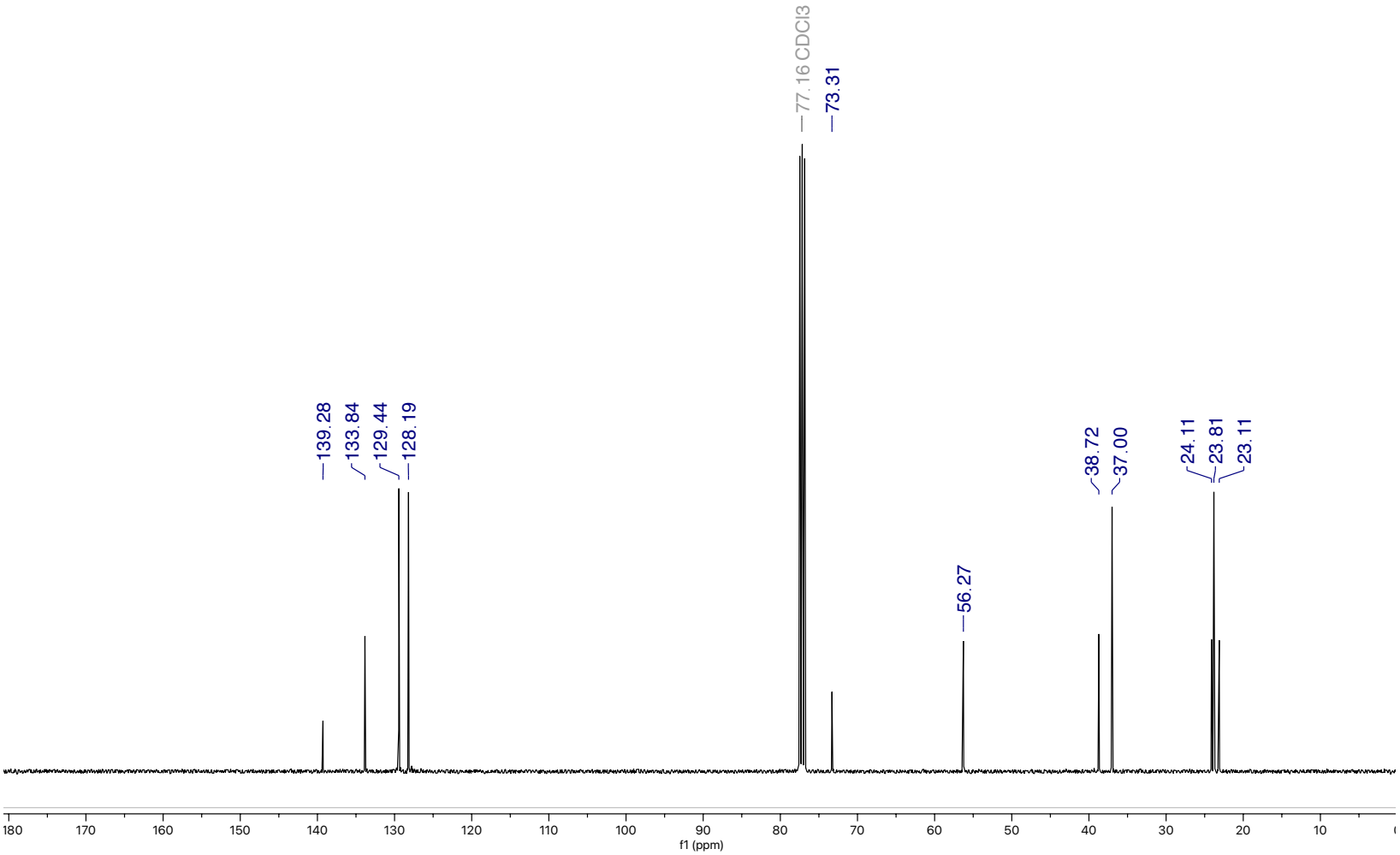

$^{1}$H-NMR (400 MHz, $CDCl_3$)



((4-(1-Azidocyclopentyl)butyl)sulfonyl)benzene

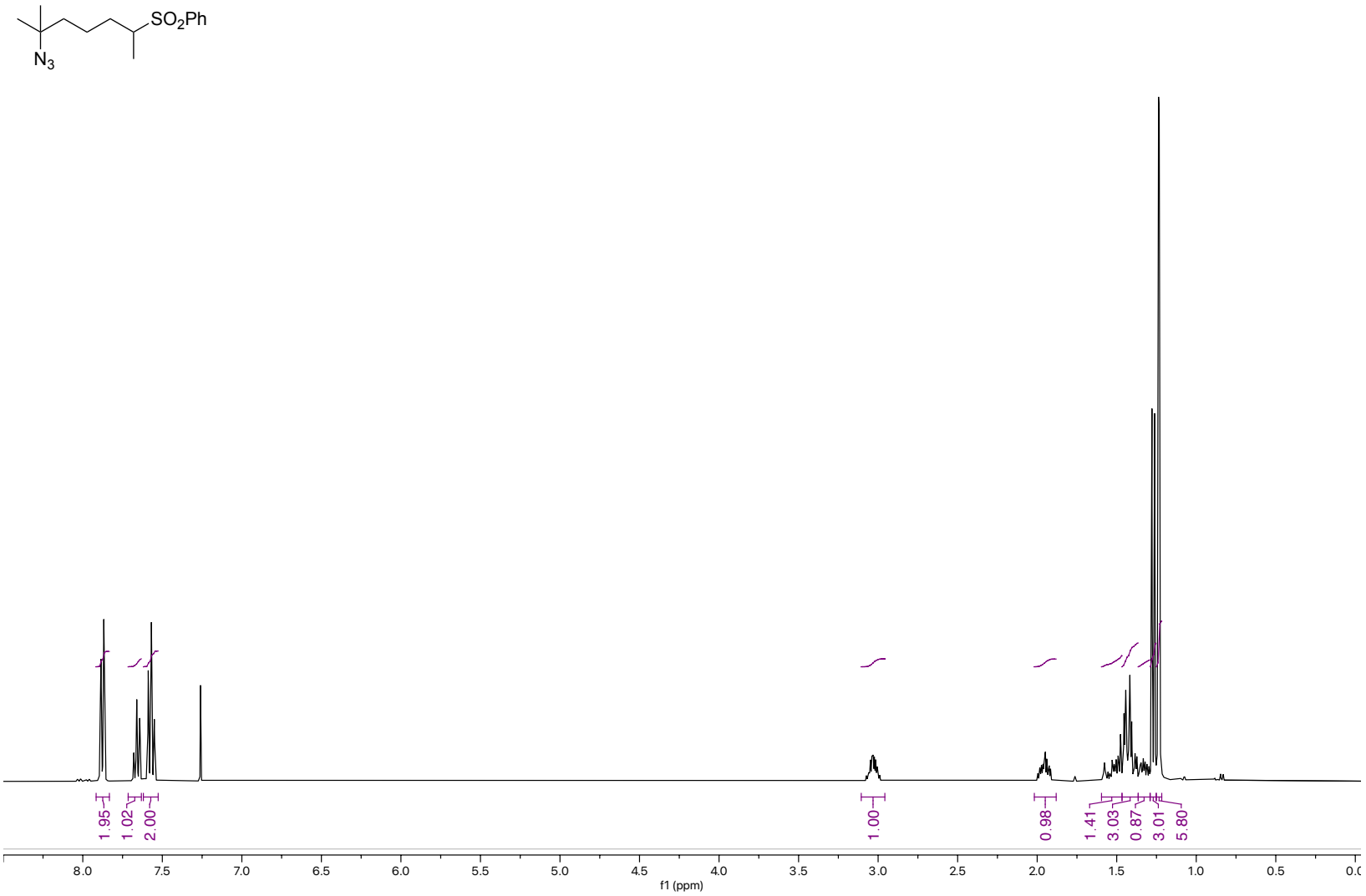



$^{13}$C-NMR (101 MHz, $CDCl_3$)



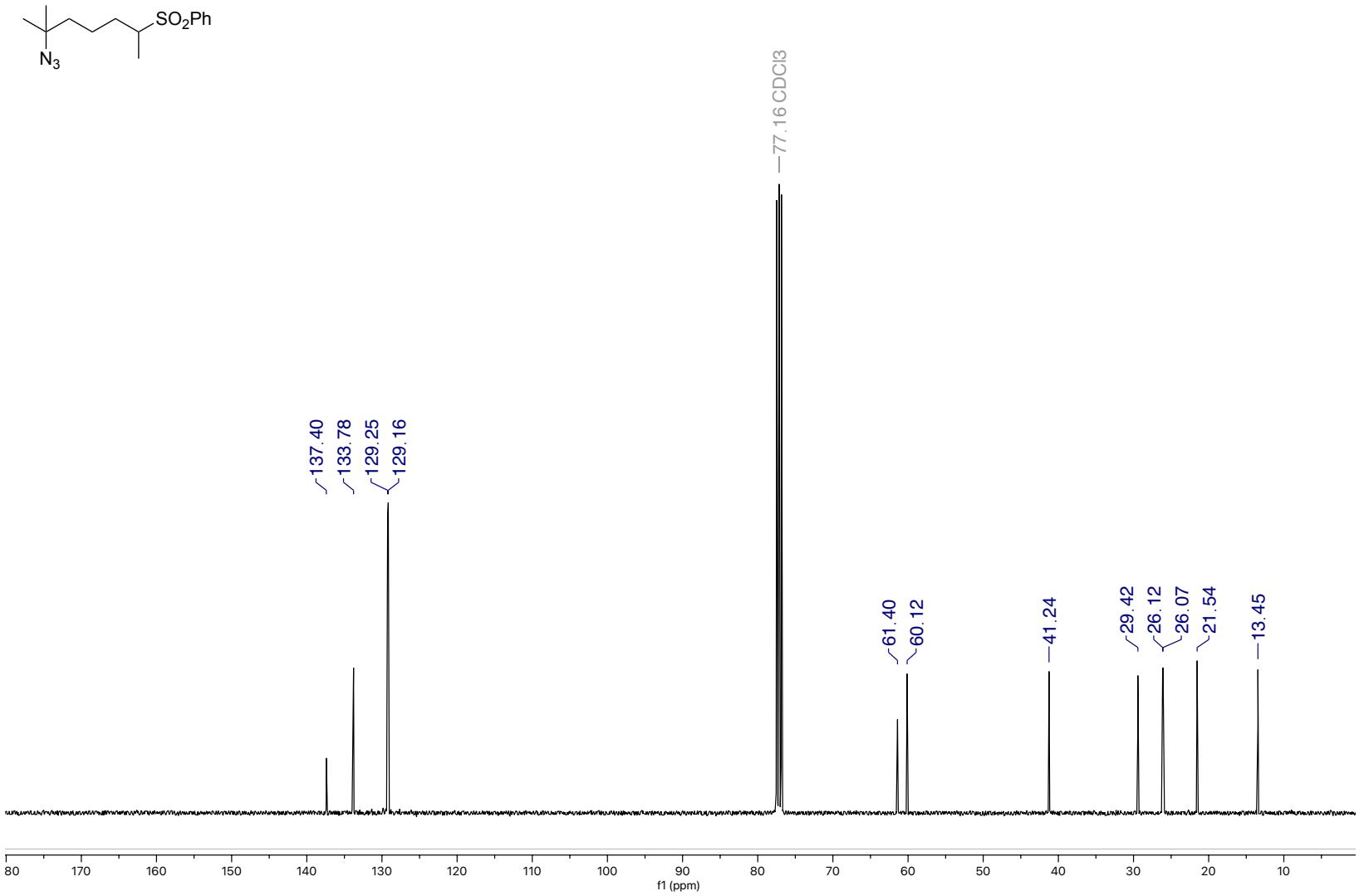
((6-Azido-6-methylheptan-2-yl)sulfonyl)benzene

$^1$H-NMR (400 MHz, $CDCl_3$)

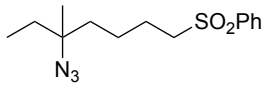


((6-Azido-6-methylheptan-2-yl)sulfonyl)benzene

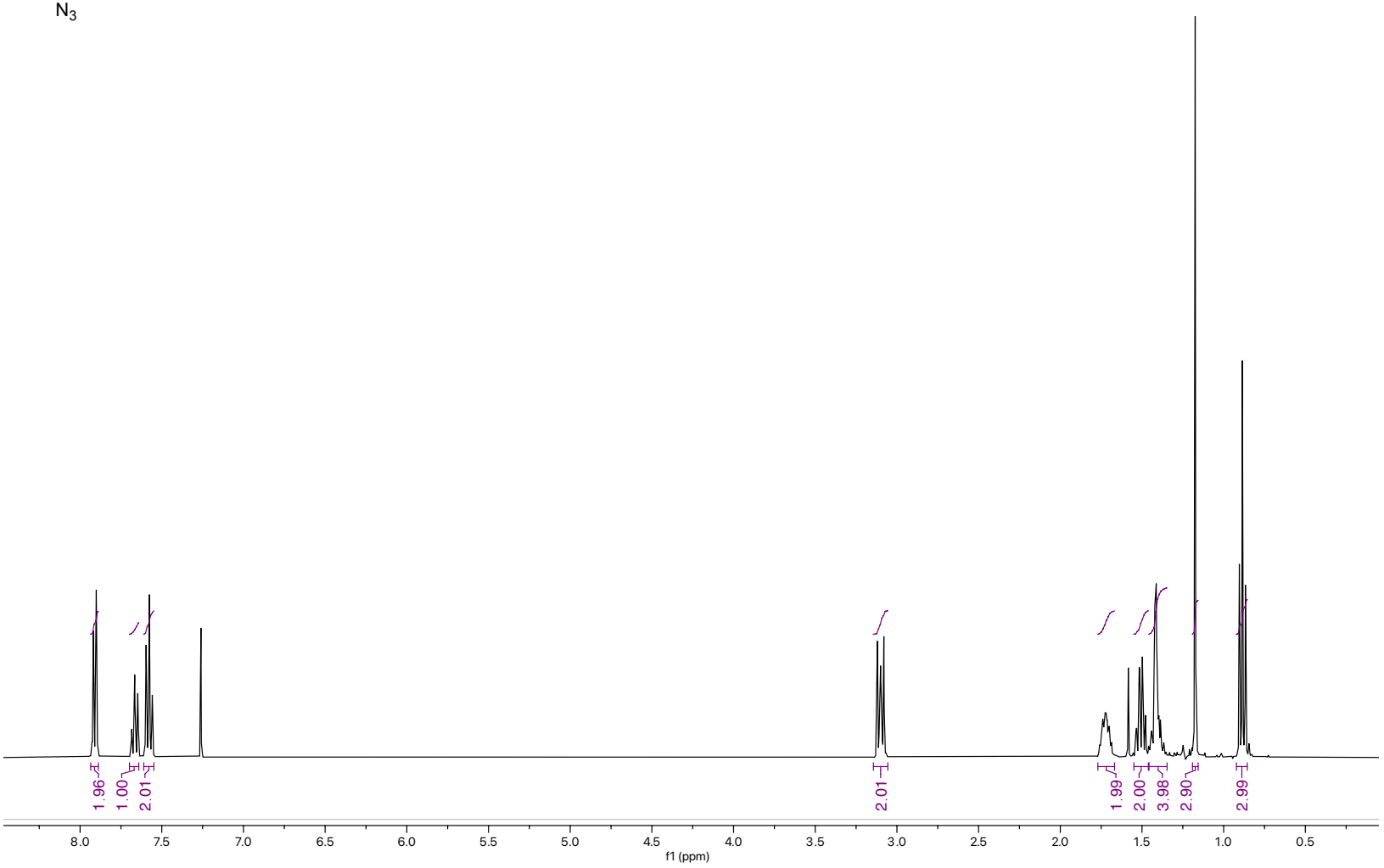
$^{13}$C-NMR (101 MHz, $CDCl_3$)



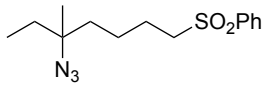
((5-Azido-5-methylheptyl)sulfonyl)benzene



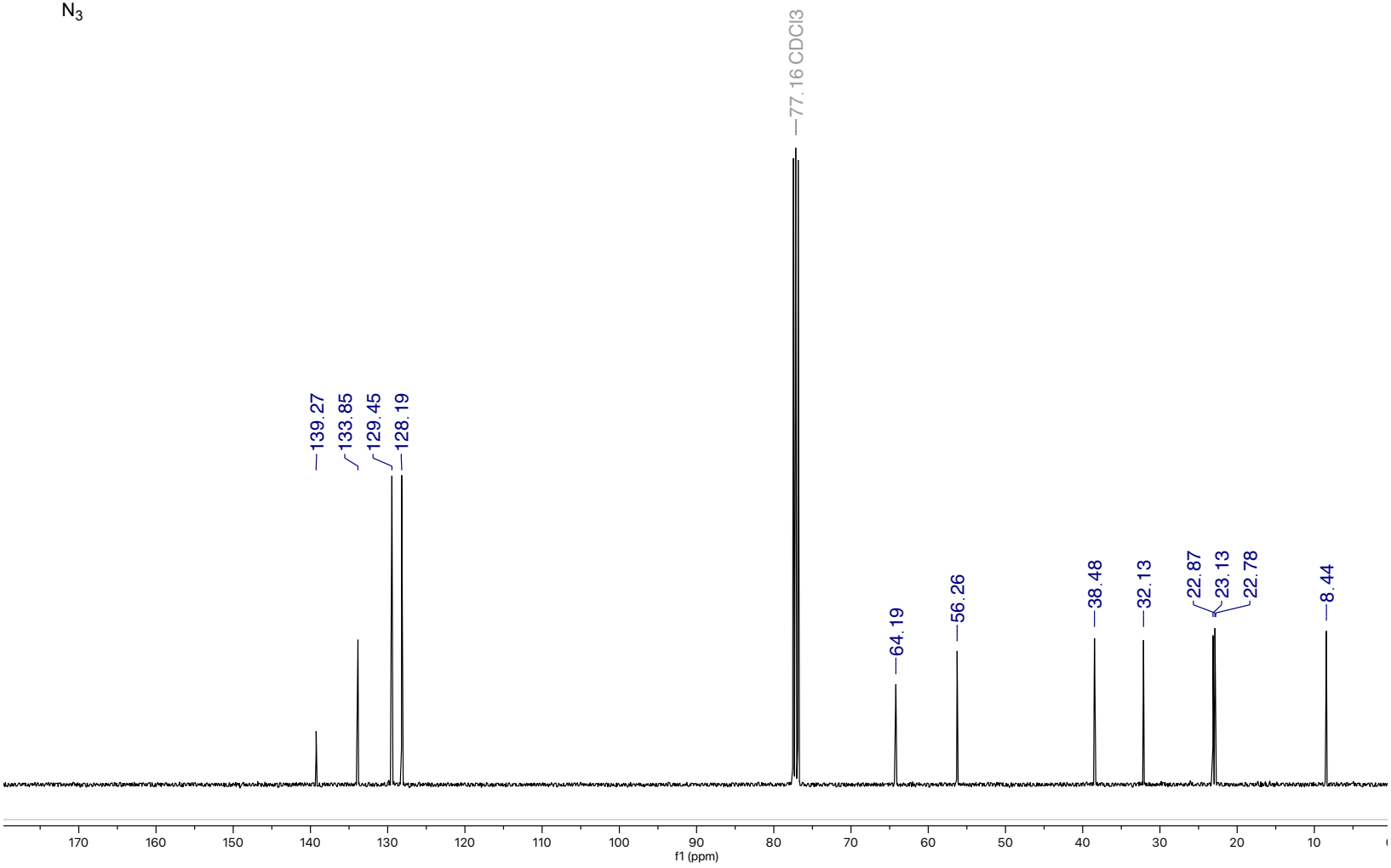

$^{1}$H-NMR (400 MHz, $CDCl_3$)



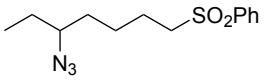
((5-Azido-5-methylheptyl)sulfonyl)benzene



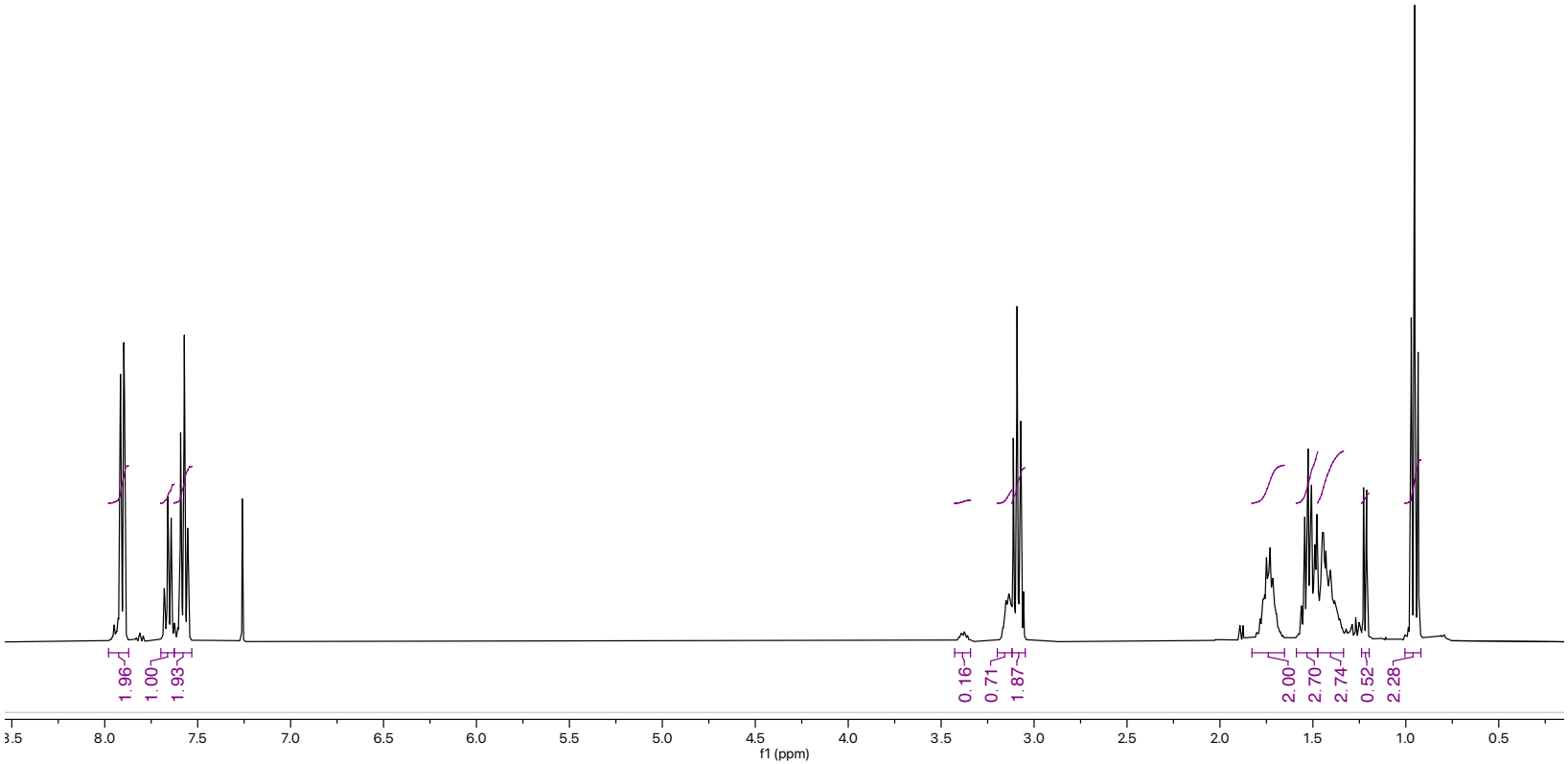

$^{13}$C-NMR (101 MHz, $CDCl_3$)



((5-Azidoheptyl)sulfonyl)benzene

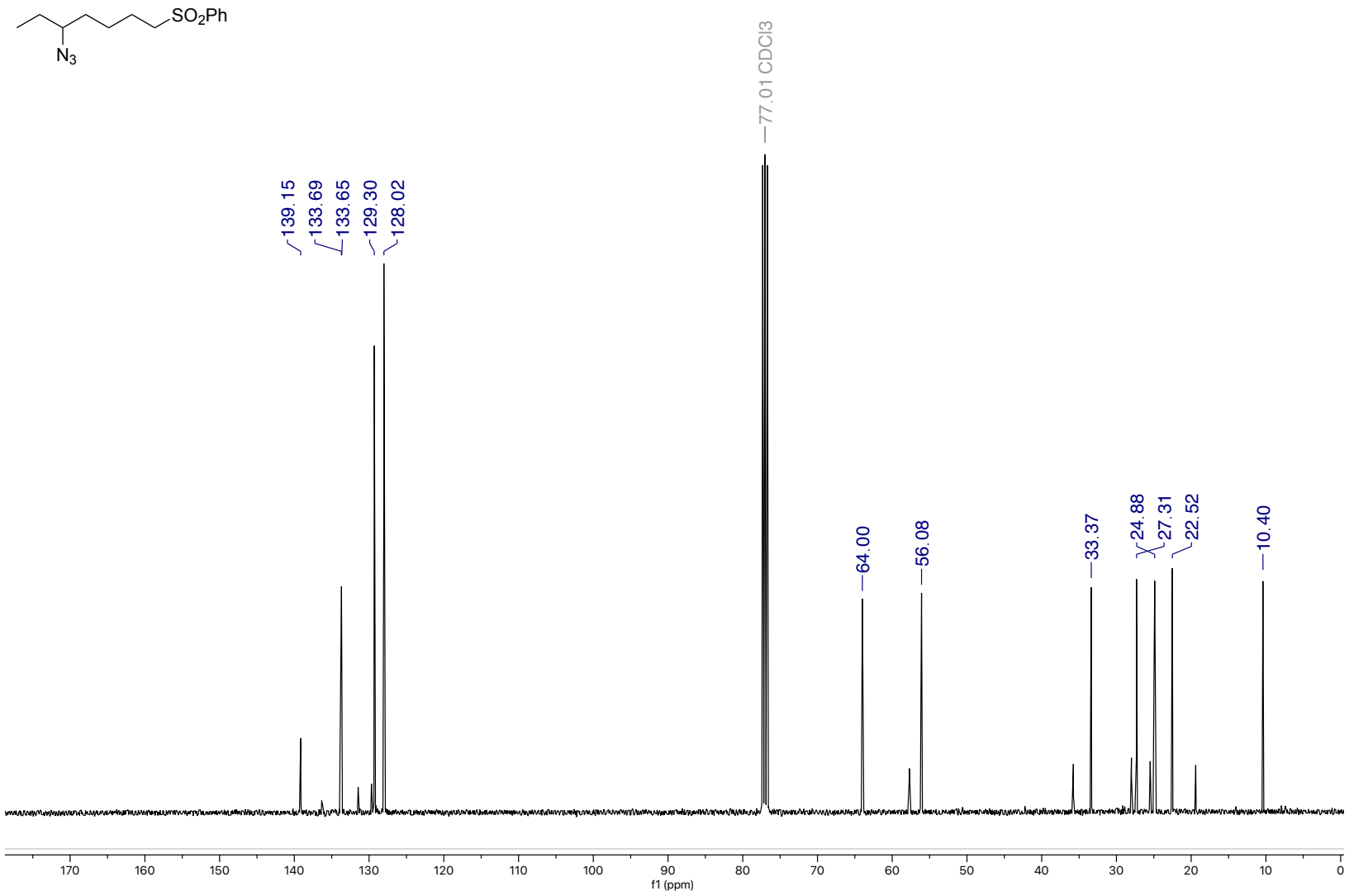



$^{1}$H-NMR (400 MHz, $CDCl_3$)

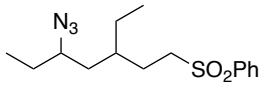


((5-Azidoheptyl)sulfonyl)benzene

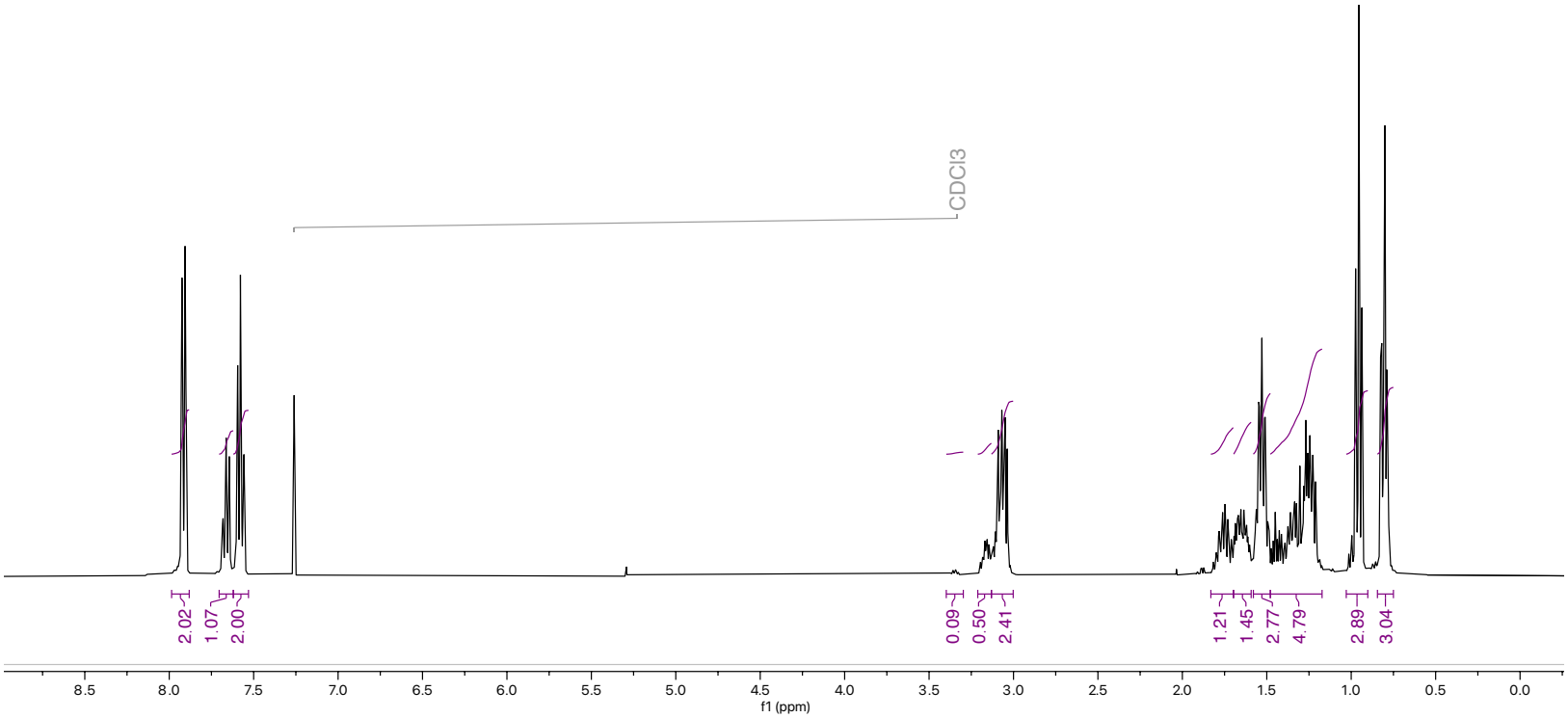
$^{13}$C-NMR (101 MHz, $CDCl_3$)



((5-azido-3-ethylheptyl)sulfonyl)benzene

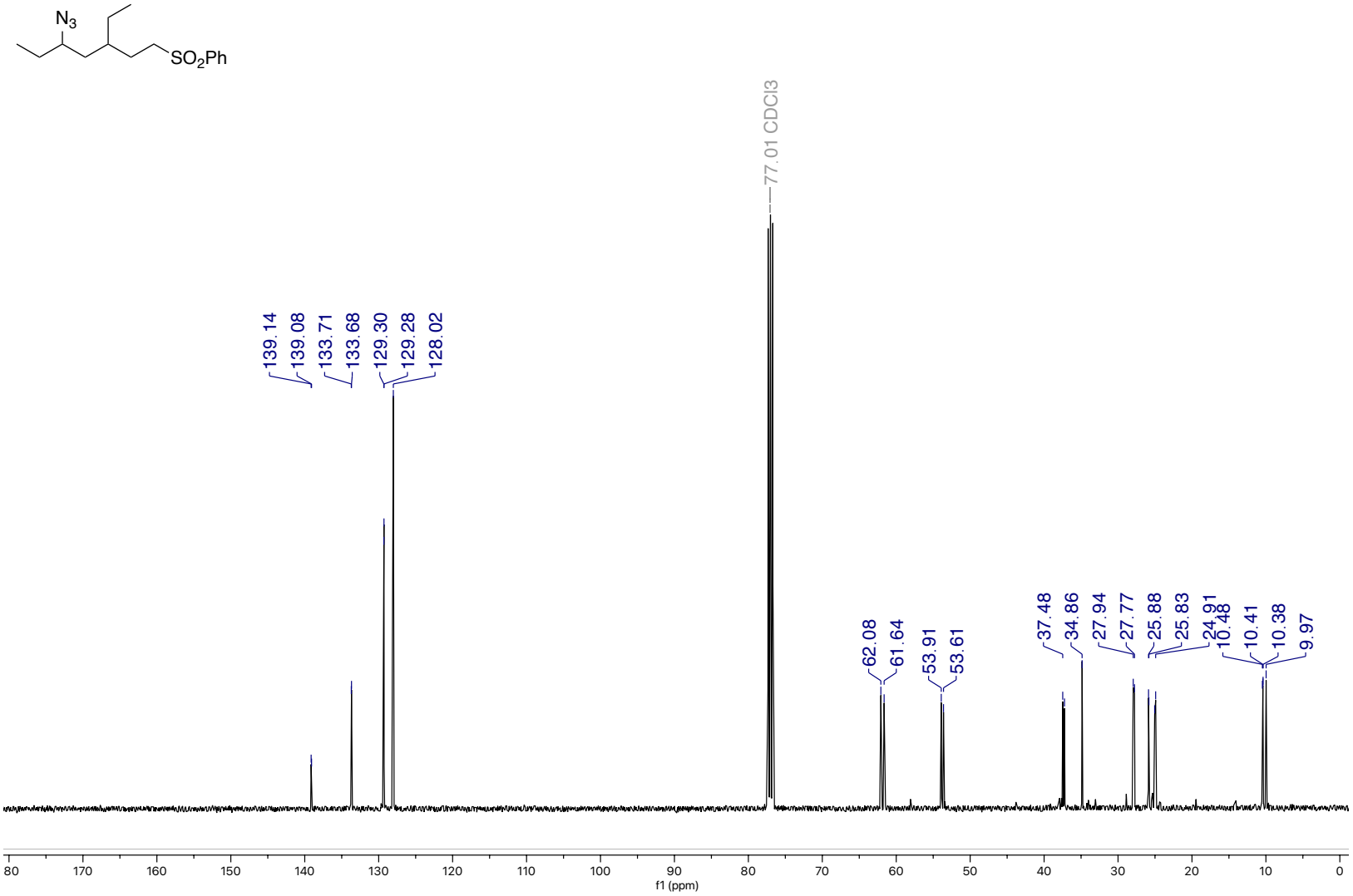



$^{1}$H-NMR (400 MHz, $CDCl_3$)

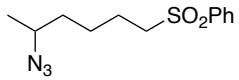


((5-azido-3-ethylheptyl)sulfonyl)benzene

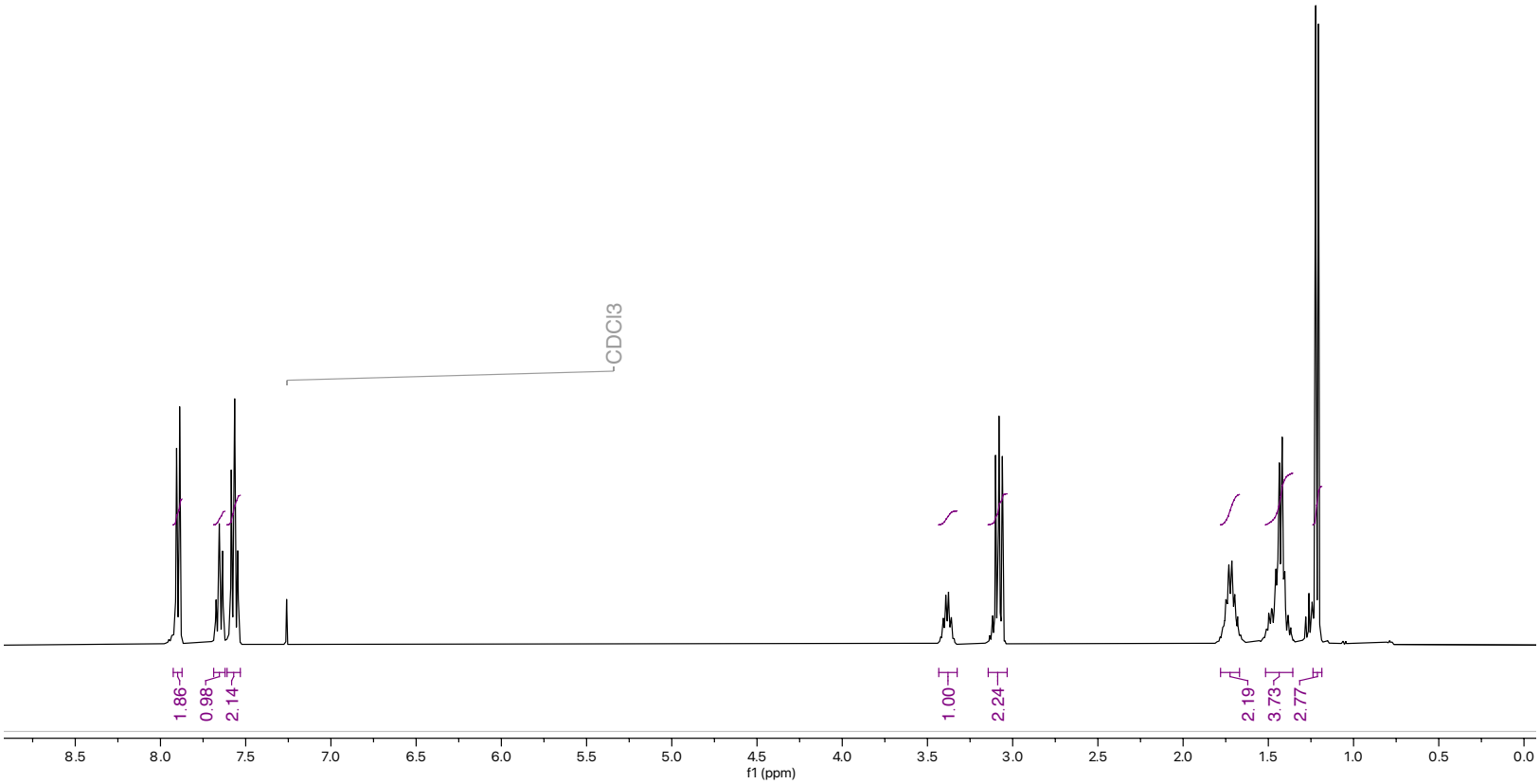
$^{13}$C-NMR (101 MHz, $CDCl_3$)



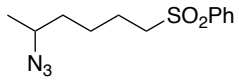
((5-azidohexyl)sulfonyl)benzene



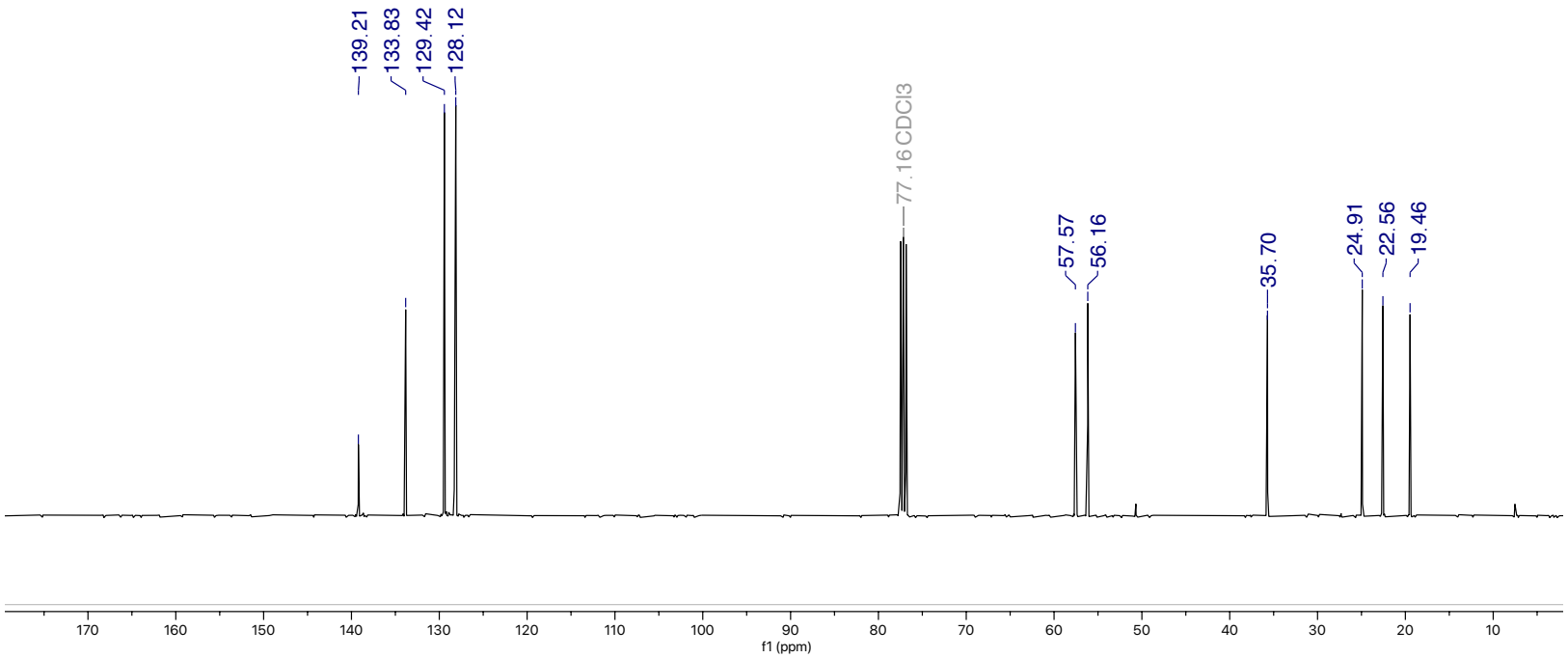

$^{1}$H-NMR (400 MHz, $CDCl_3$)



((5-azidohexyl)sulfonyl)benzene

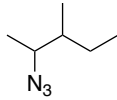


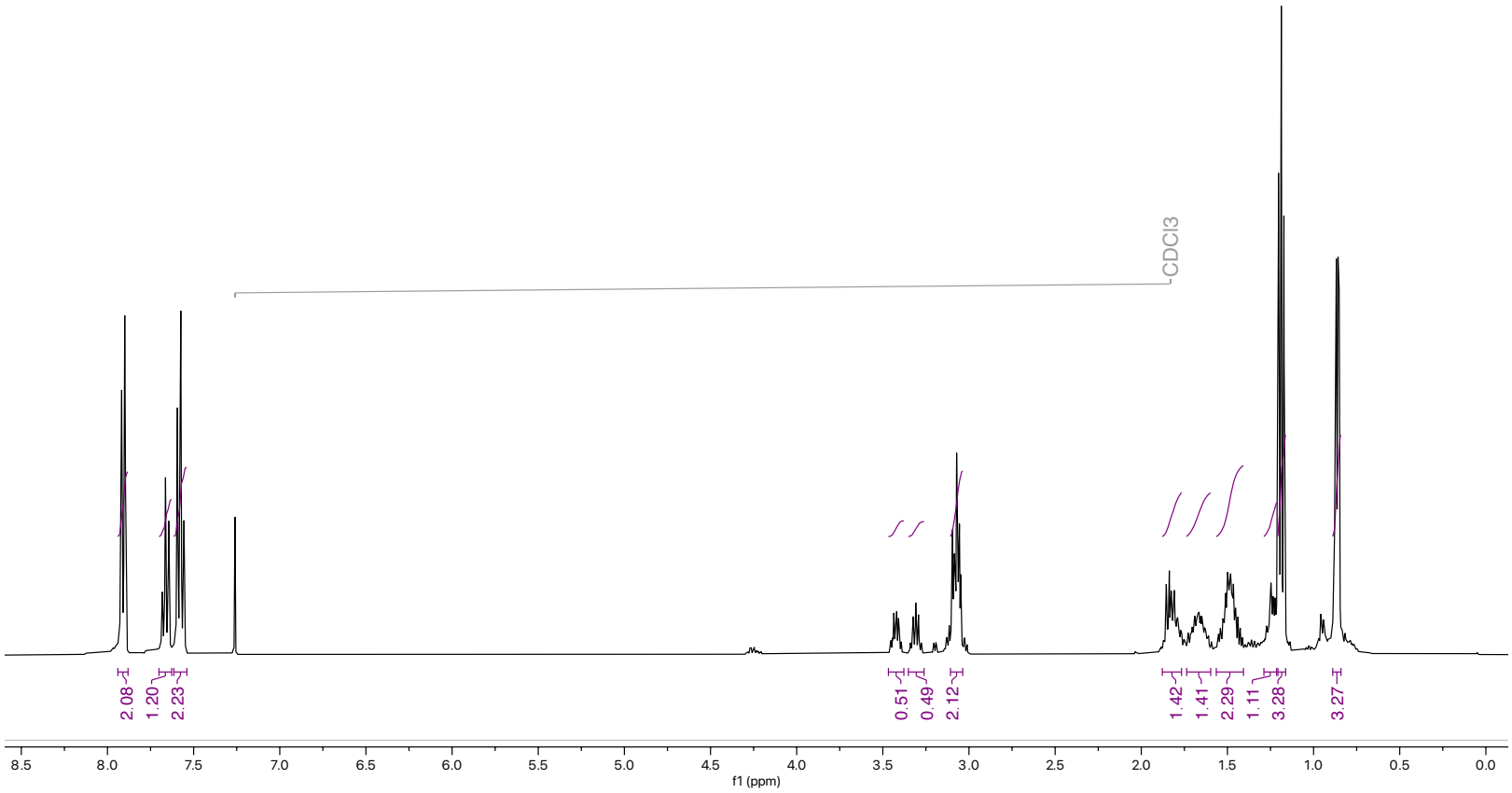

$^{13}$C-NMR (101 MHz, $CDCl_3$)



((5-Azido-4-methylhexyl)sulfonyl)benzene

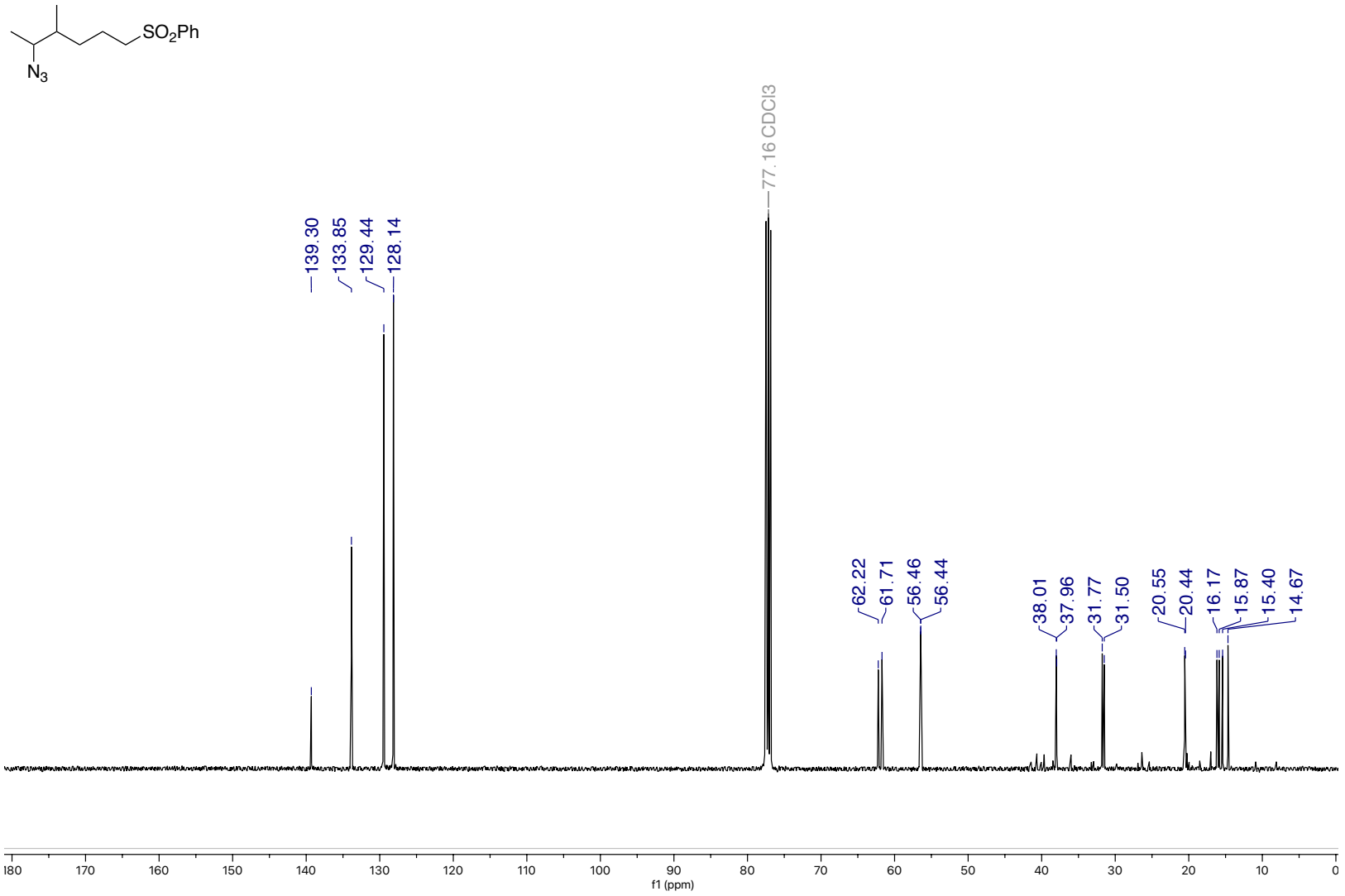
$^1$H-NMR (400 MHz, $CDCl_3$)



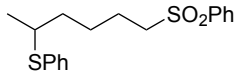



((5-Azido-4-methylhexyl)sulfonyl)benzene

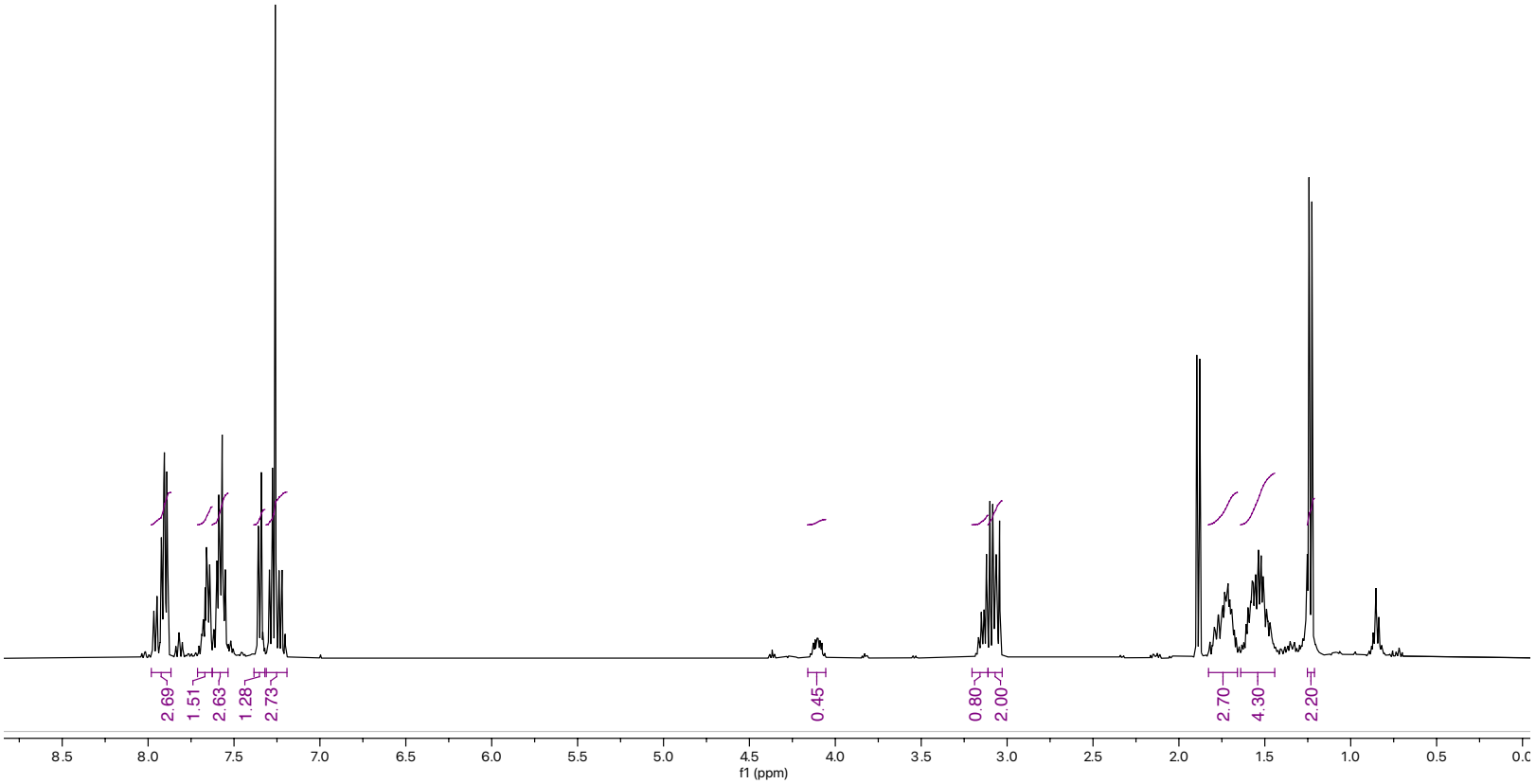
$^{13}$C-NMR (101 MHz, $CDCl_3$)



Phenyl(6-(phenylsulfonyl)hexan-2-yl)sulfane

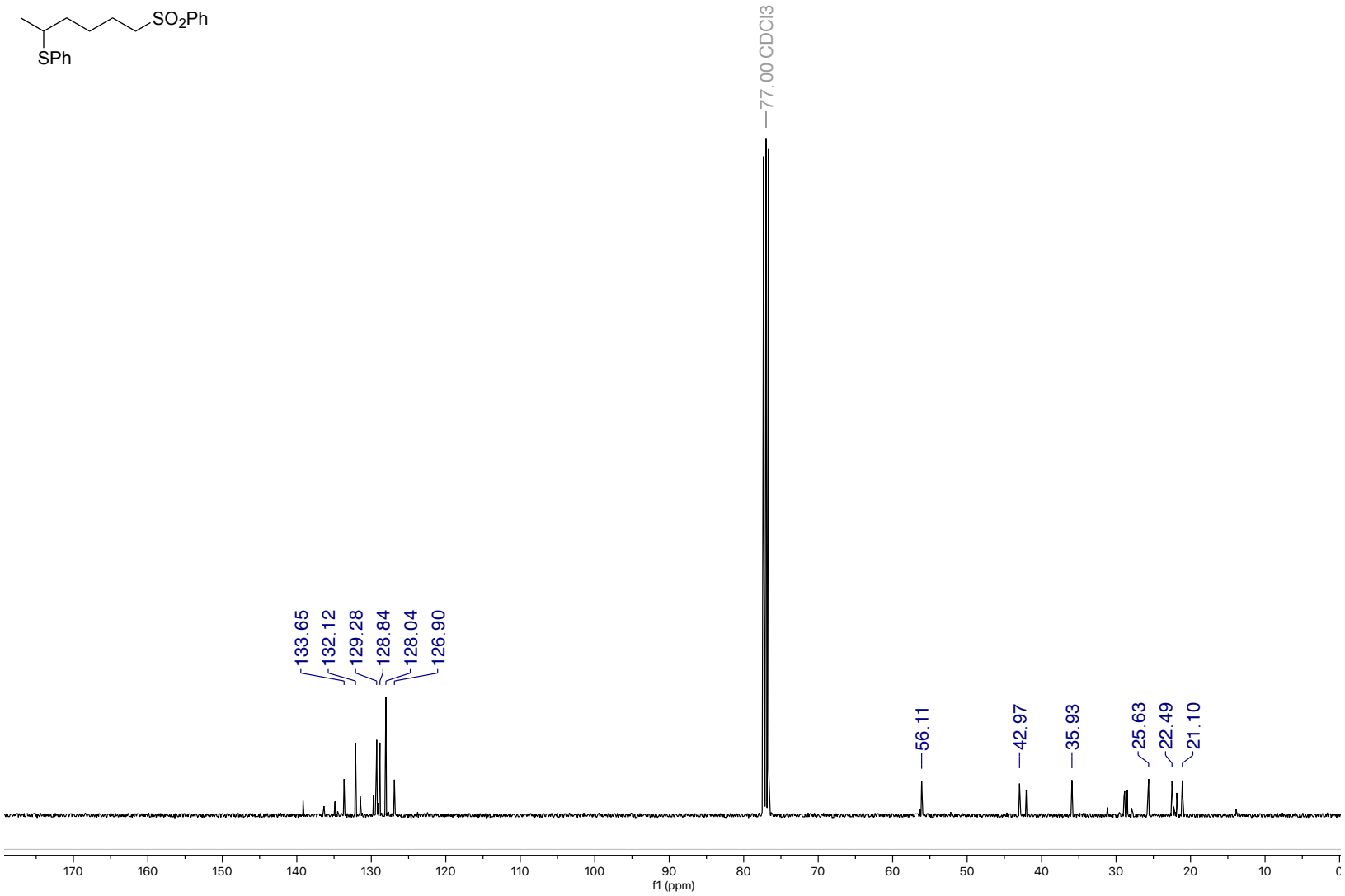



$^1$H-NMR (400 MHz, $CDCl_3$)



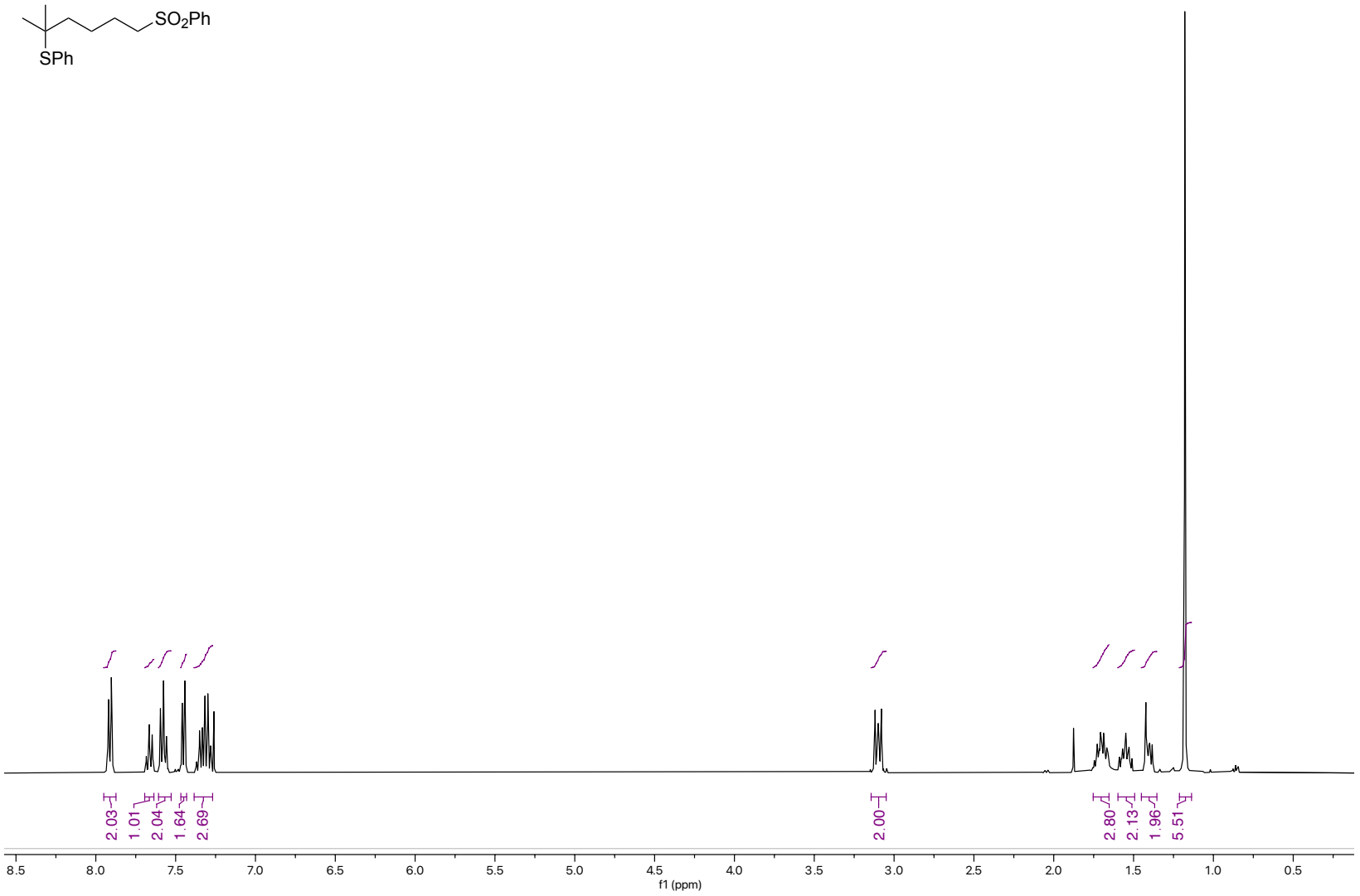
Phenyl(6-(phenylsulfonyl)hexan-2-yl)sulfane

$^{13}$C-NMR (101 MHz, $CDCl_3$)



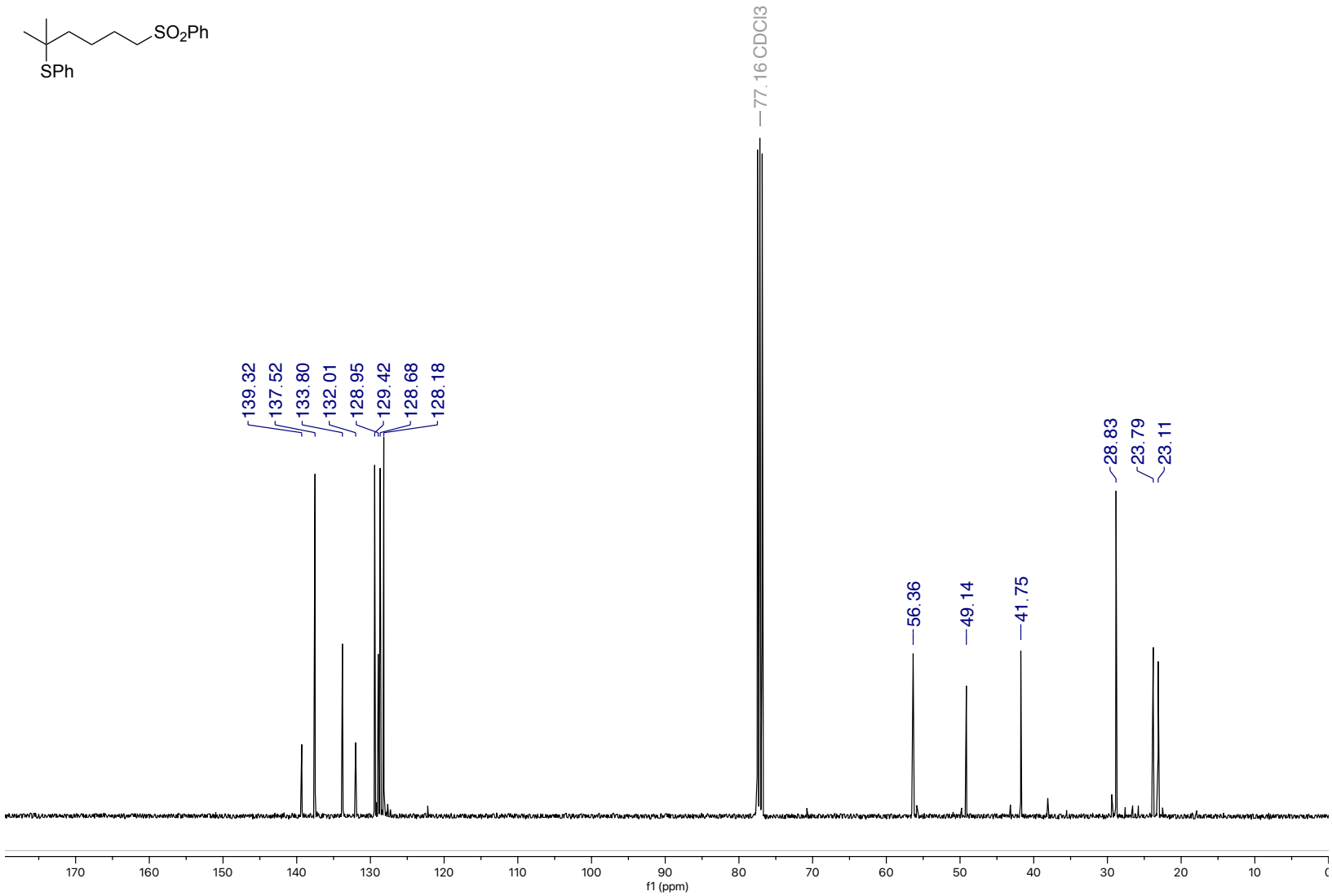
(2-Methyl-6-(phenylsulfonyl)hexan-2-yl)(phenyl)sulfane

$^1$H-NMR (400 MHz, $CDCl_3$)



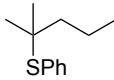
(2-Methyl-6-(phenylsulfonyl)hexan-2-yl)(phenyl)sulfane

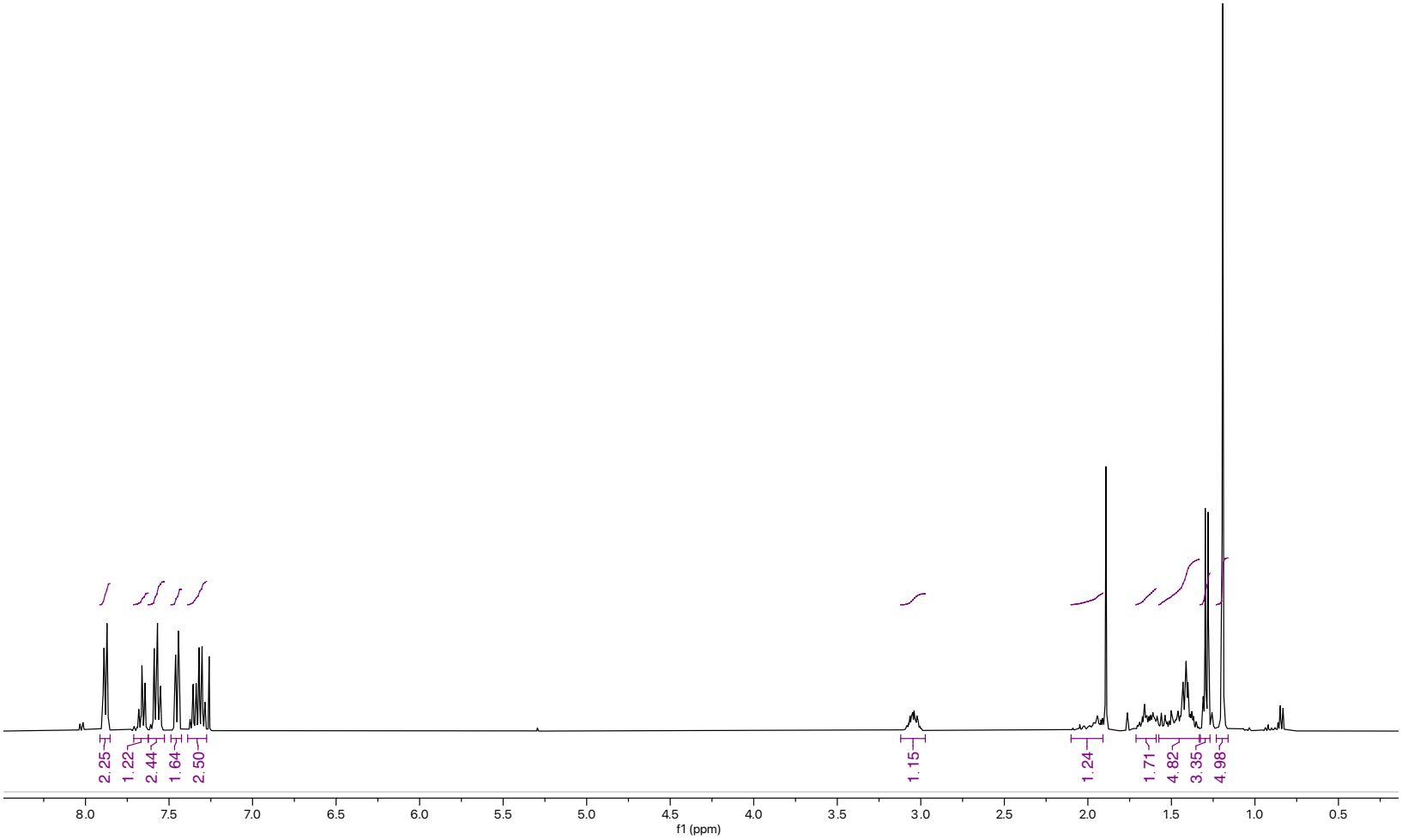
$^{13}$C-NMR (101 MHz, $CDCl_3$)



(2-Methyl-6-(phenylsulfonyl)heptan-2-yl)(phenyl)sulfane

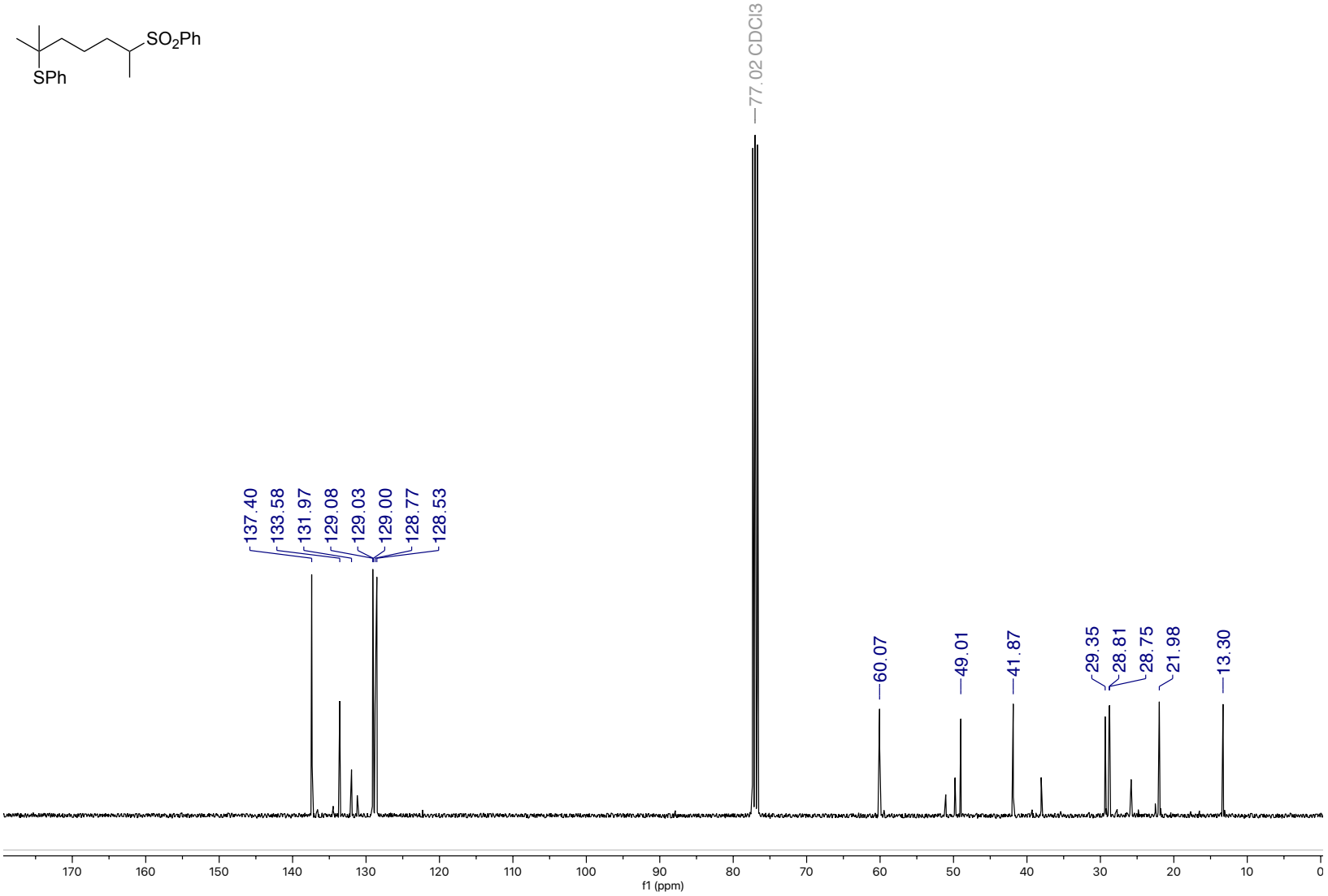
$^1$H-NMR (400 MHz, $CDCl_3$)



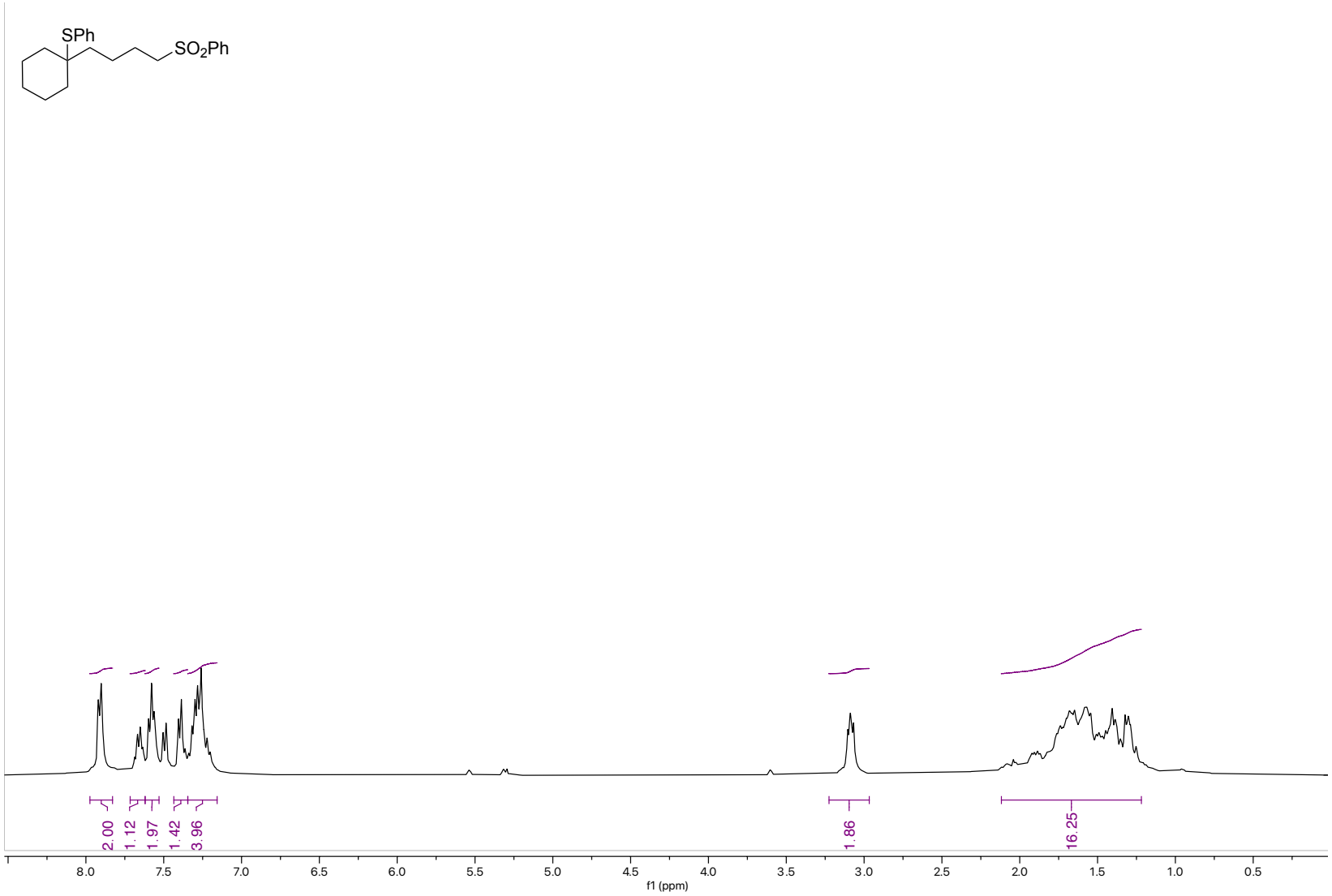
(2-Methyl-6-(phenylsulfonyl)heptan-2-yl)(phenyl)sulfane

$^{13}$C-NMR (101 MHz, $CDCl_3$)



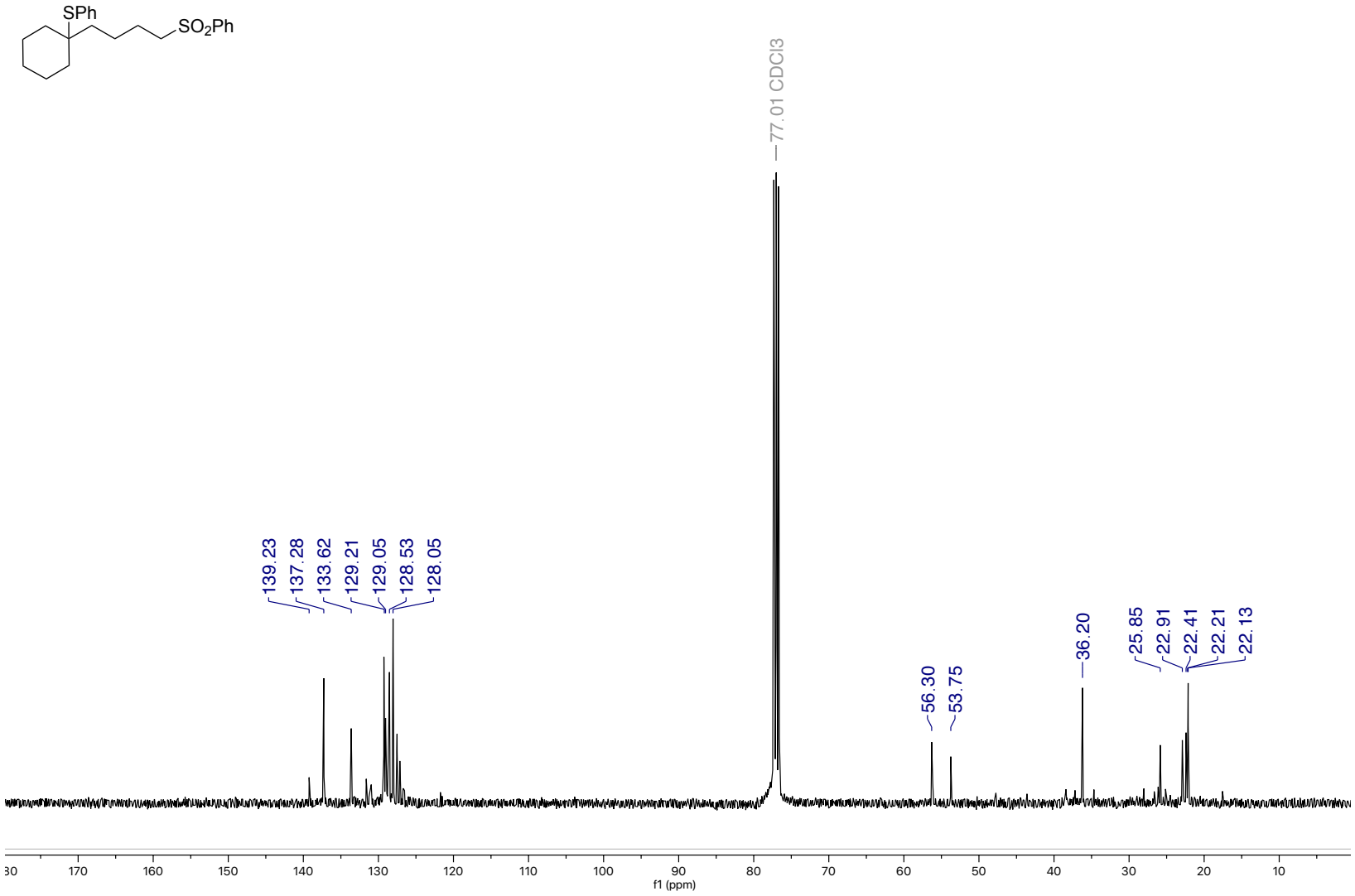
Phenyl(1-(4-(phenylsulfonyl)butyl)cyclohexyl)sulfane

$^1$H-NMR (400 MHz, $CDCl_3$)

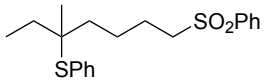


Phenyl(1-(4-(phenylsulfonyl)butyl)cyclohexyl)sulfane

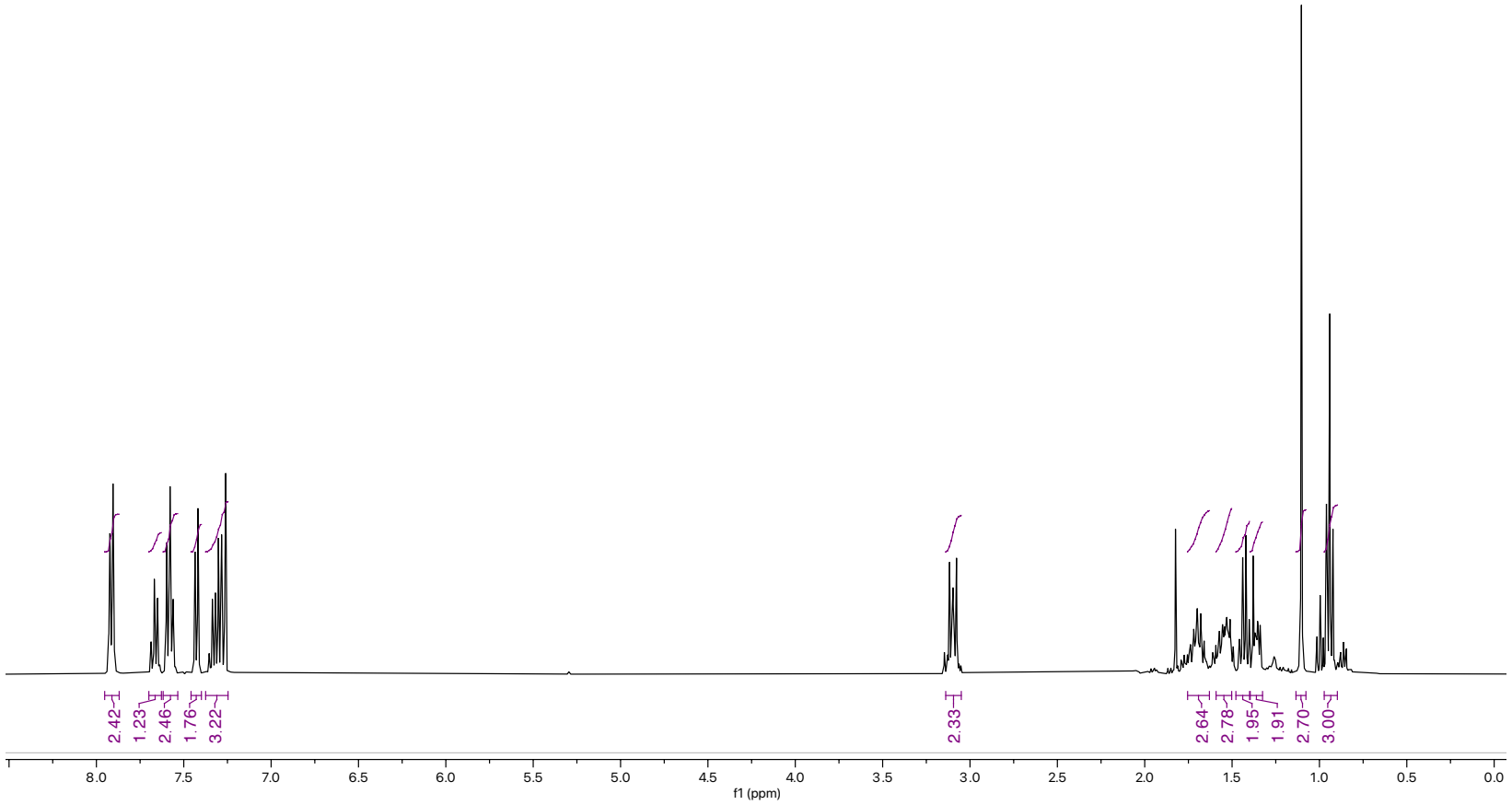
$^{13}$C-NMR (101 MHz, $CDCl_3$)



(3-Methyl-7-(phenylsulfonyl)heptan-3-yl)(phenyl)sulfane

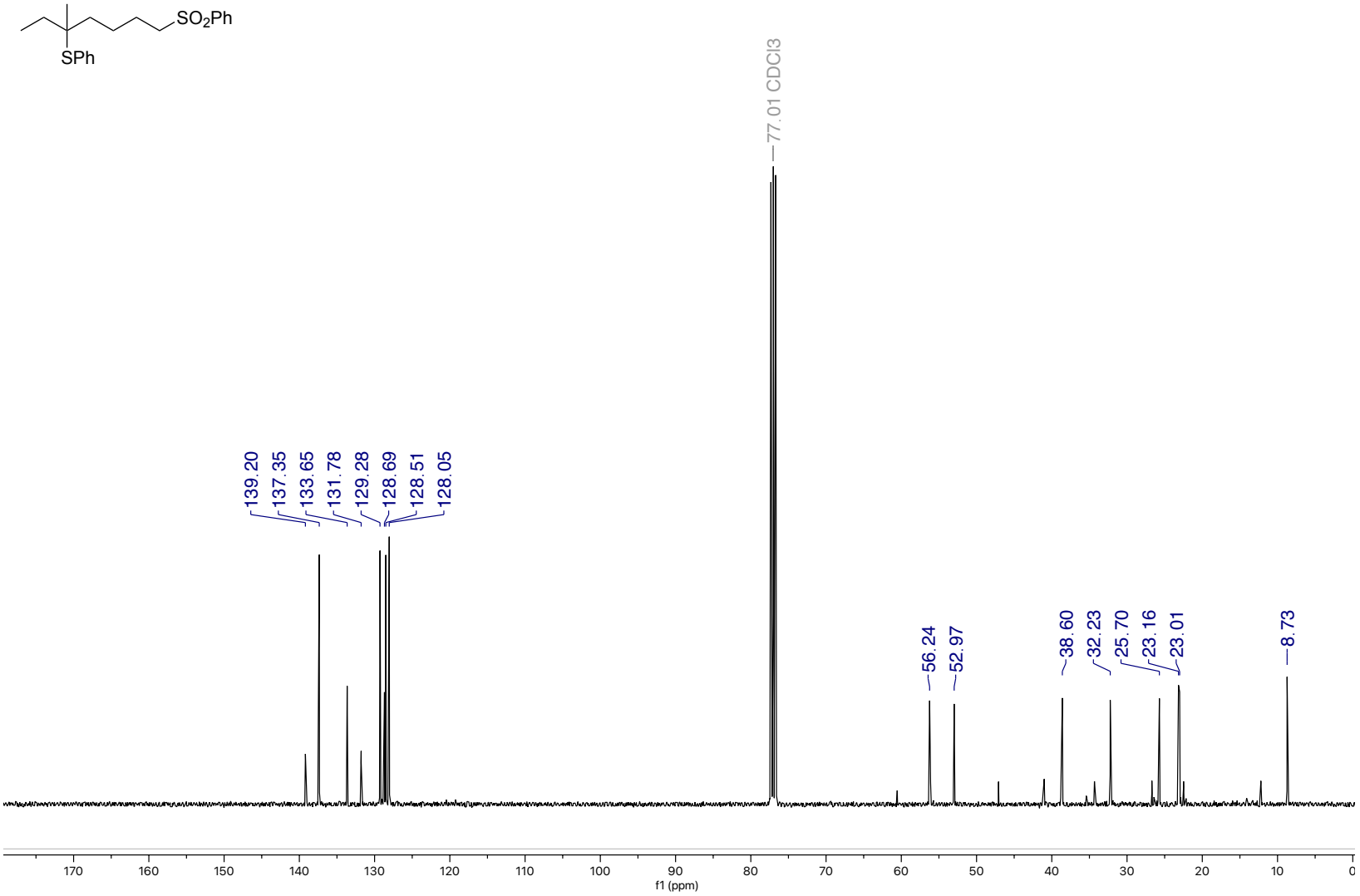



$^1$H-NMR (400 MHz, $CDCl_3$)

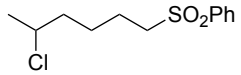


(3-Methyl-7-(phenylsulfonyl)heptan-3-yl)(phenyl)sulfane

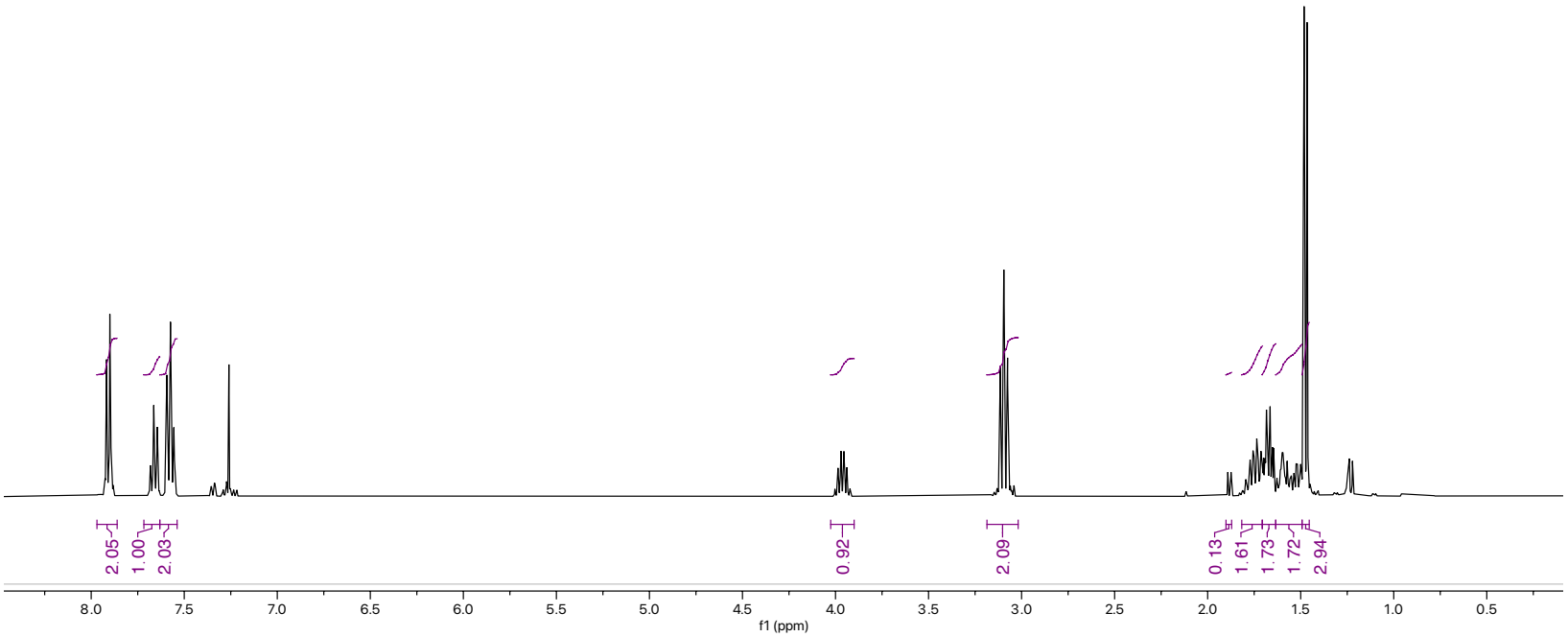
$^{13}$C-NMR (101 MHz, $CDCl_3$)



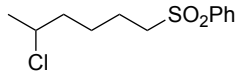
((5-Chlorohexyl)sulfonyl)benzene



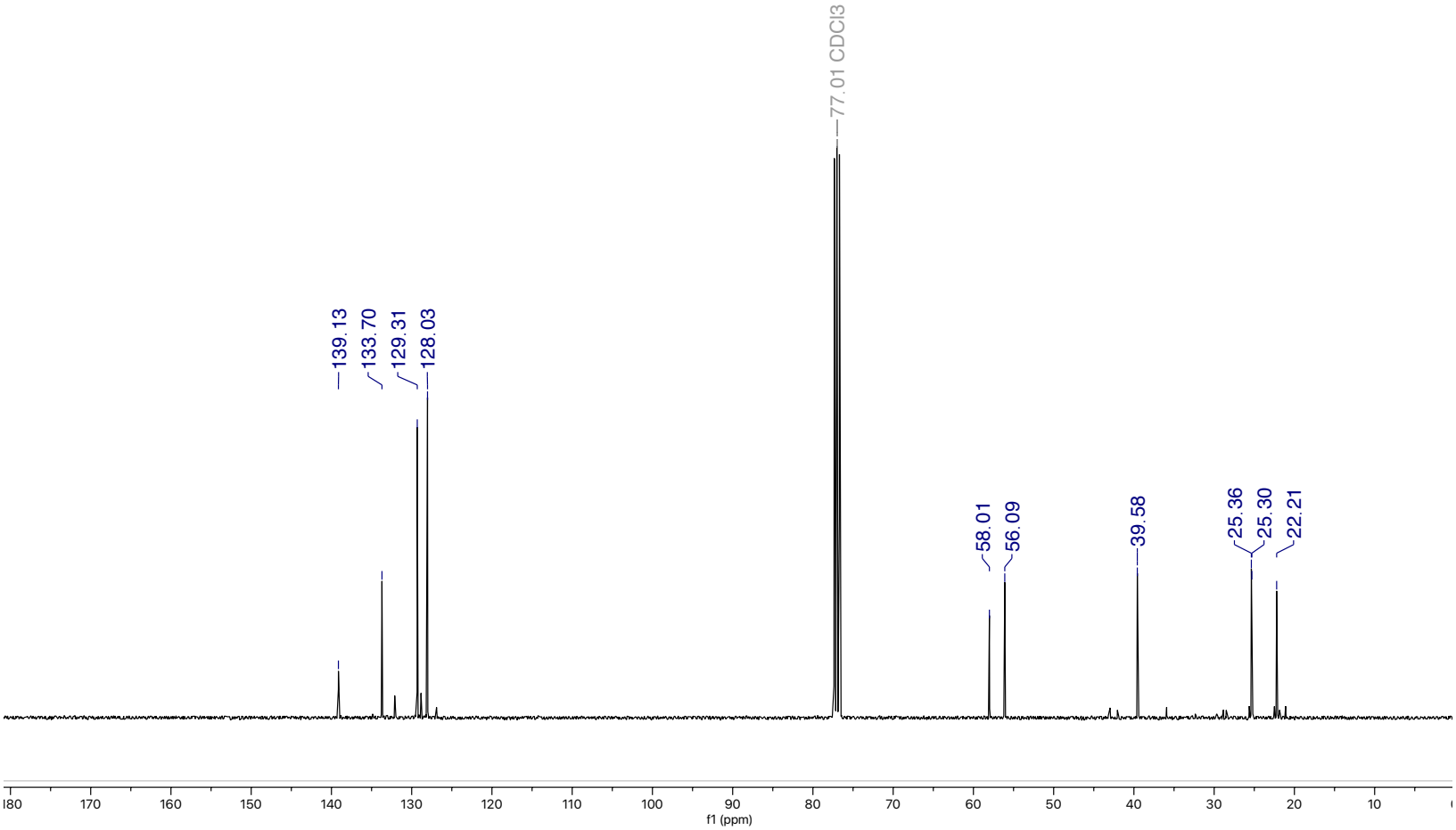

$^{1}$H-NMR (400 MHz, $CDCl_3$)



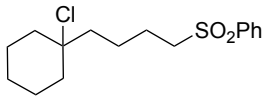
((5-Chlorohexyl)sulfonyl)benzene



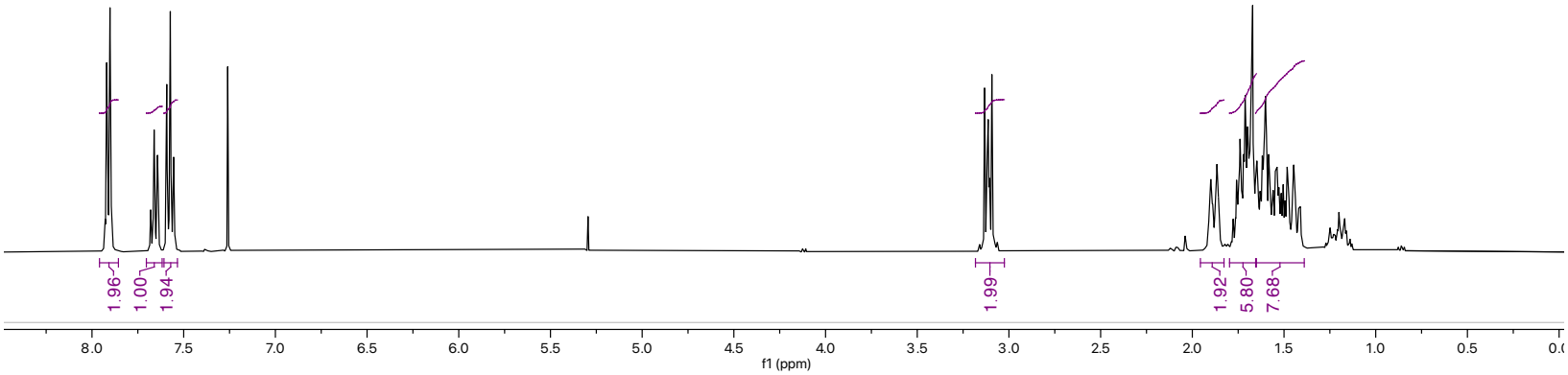

$^{13}$C-NMR (101 MHz, $CDCl_3$)



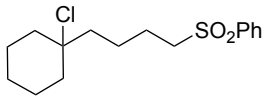
((4-(1-chlorocyclohexyl)butyl)sulfonyl)benzene



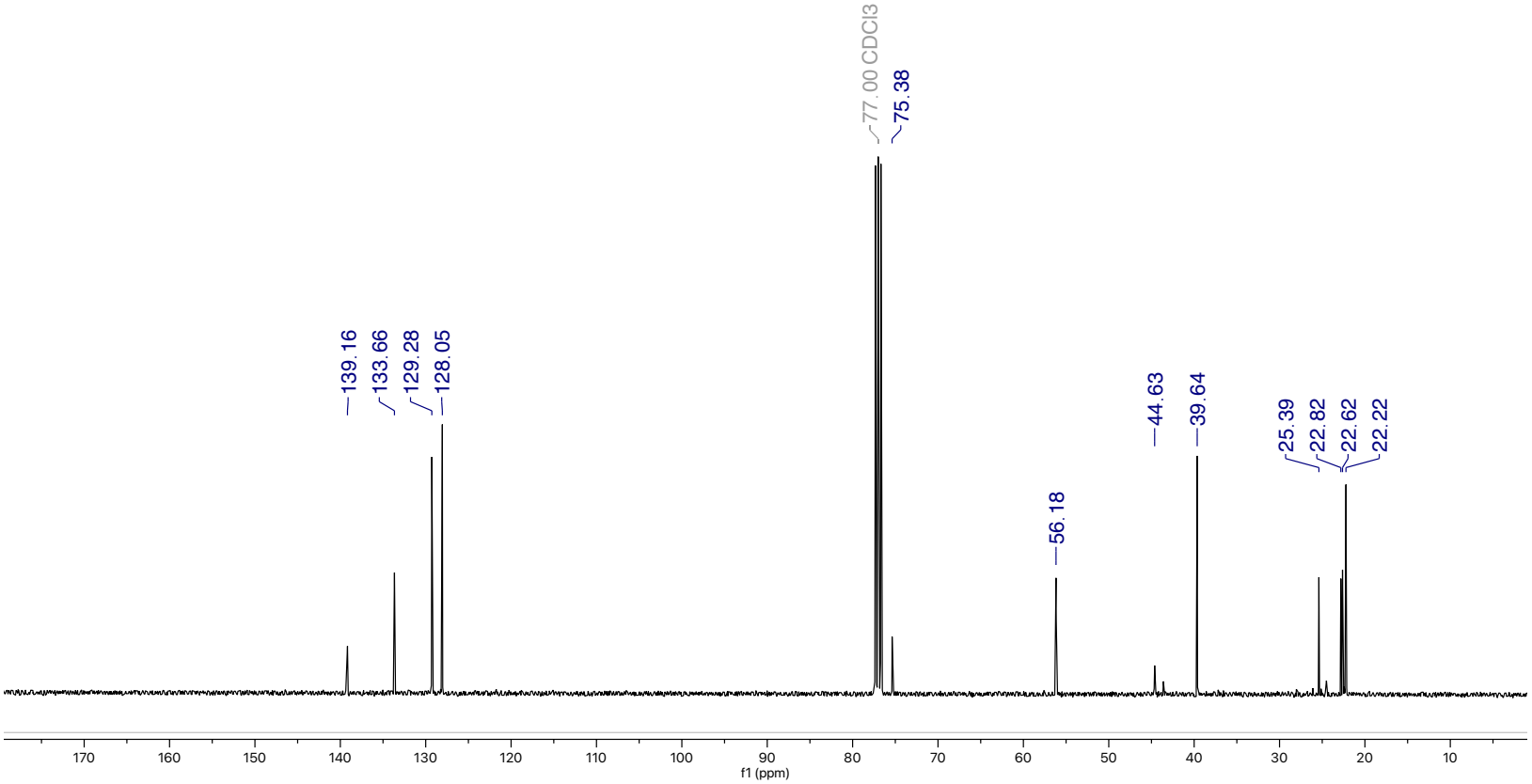

$^1$H-NMR (400 MHz, $CDCl_3$)



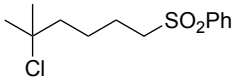
((4-(1-chlorocyclohexyl)butyl)sulfonyl)benzene



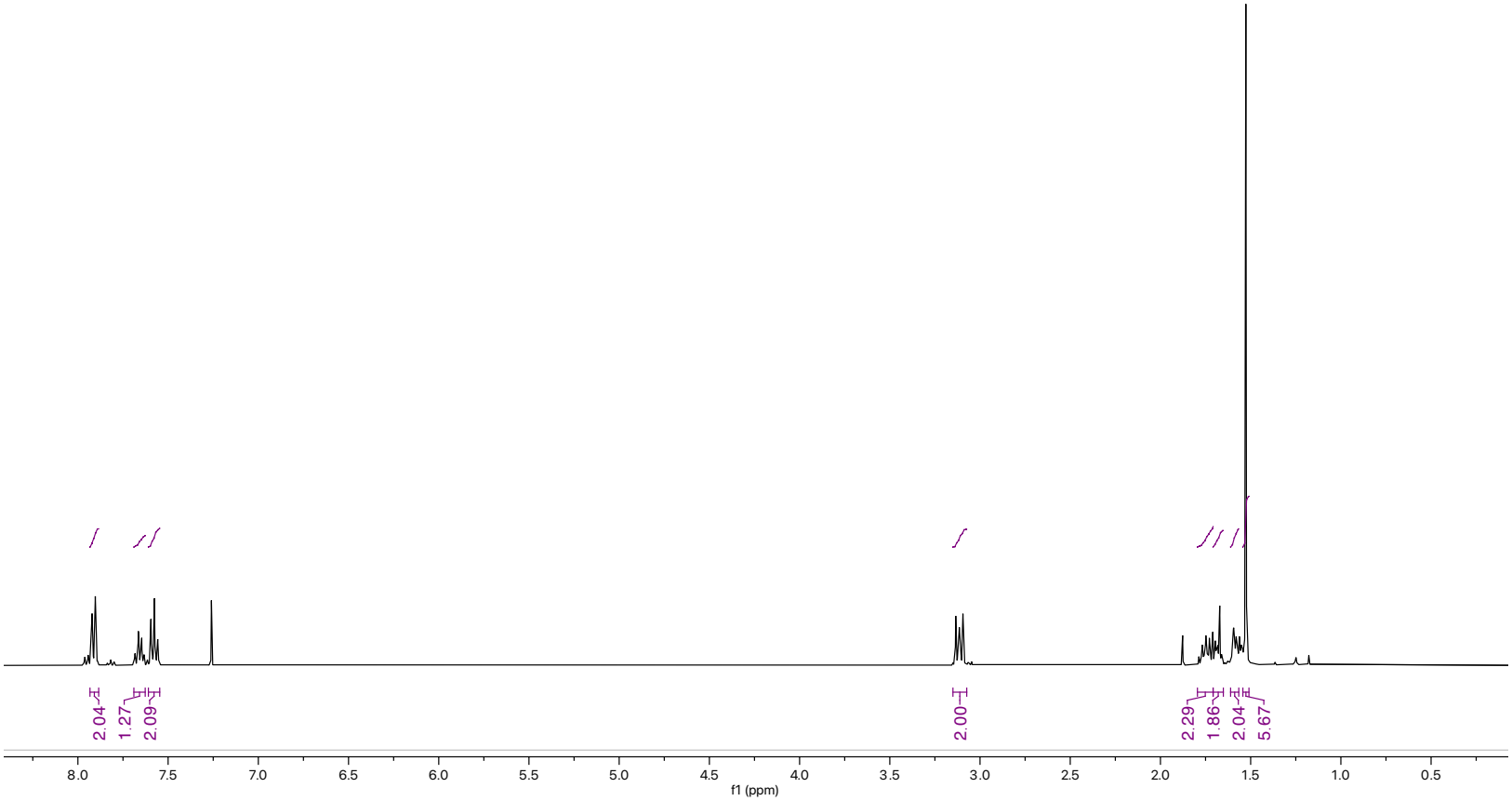

$^{13}$C-NMR (101 MHz, $CDCl_3$)



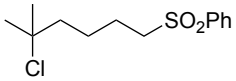
((5-Chloro-5-methylhexyl)sulfonyl)benzene



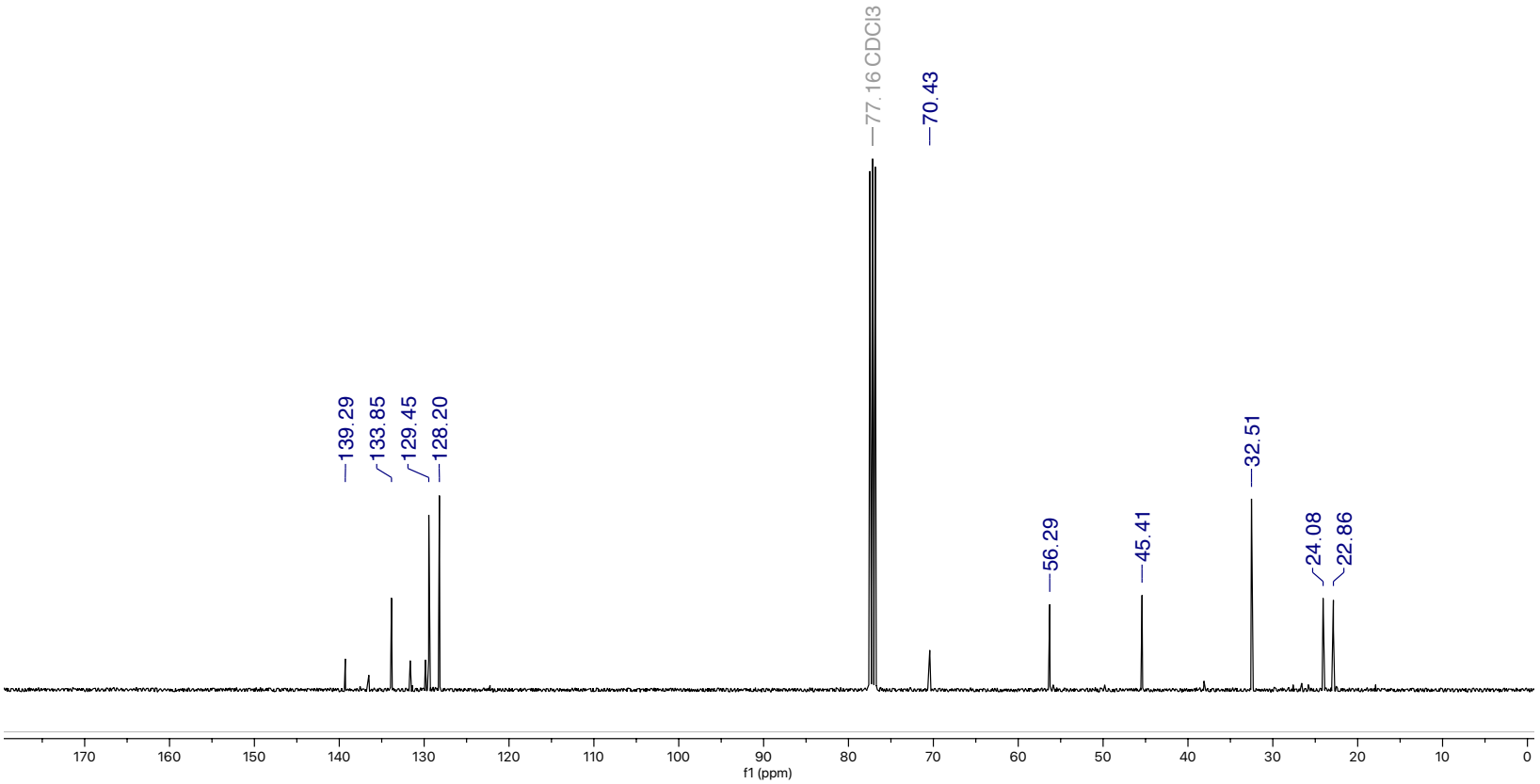

$^{1}$H-NMR (400 MHz, $CDCl_3$)



((5-Chloro-5-methylhexyl)sulfonyl)benzene

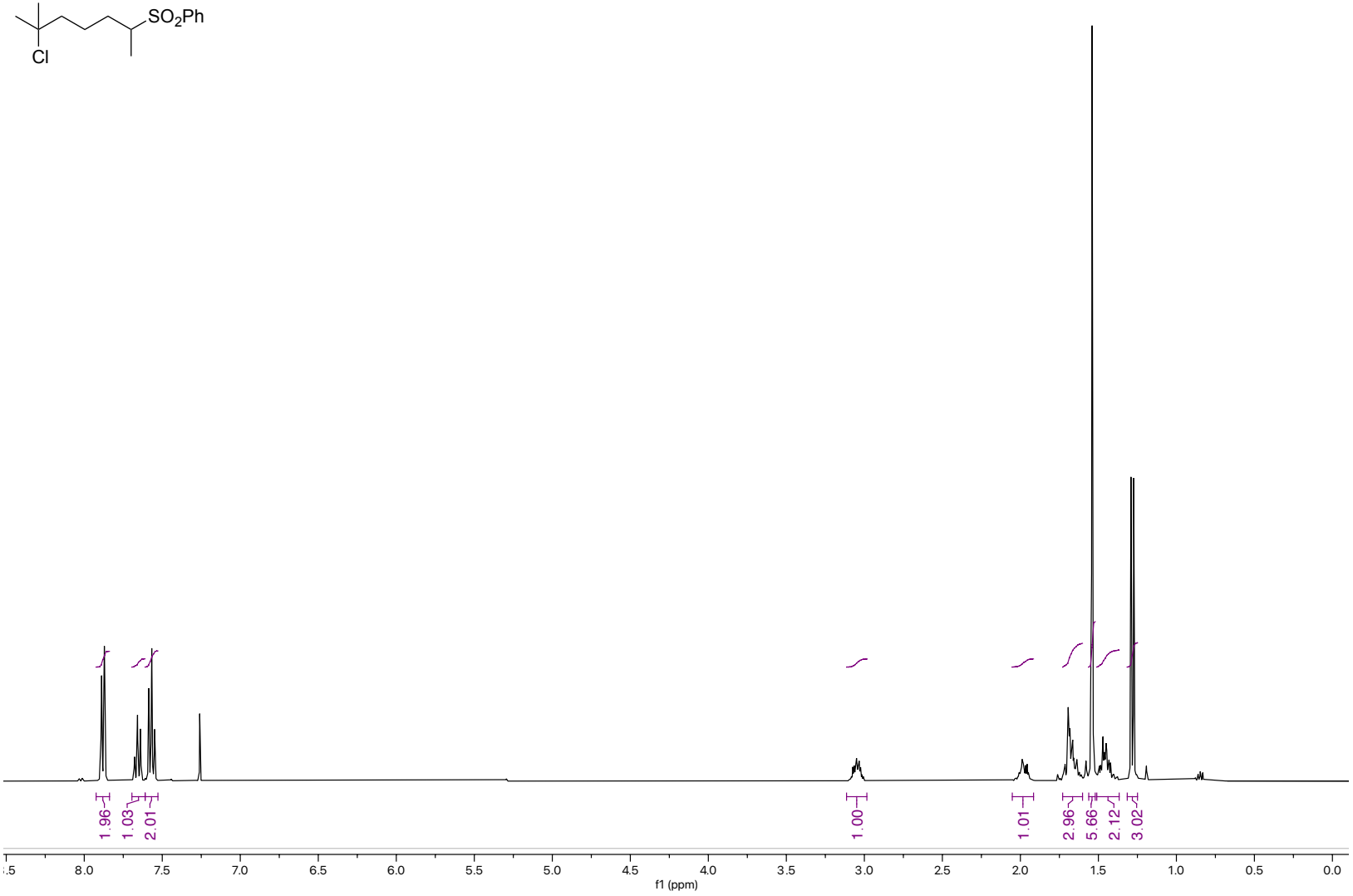



$^{13}$C-NMR (101 MHz, $CDCl_3$)



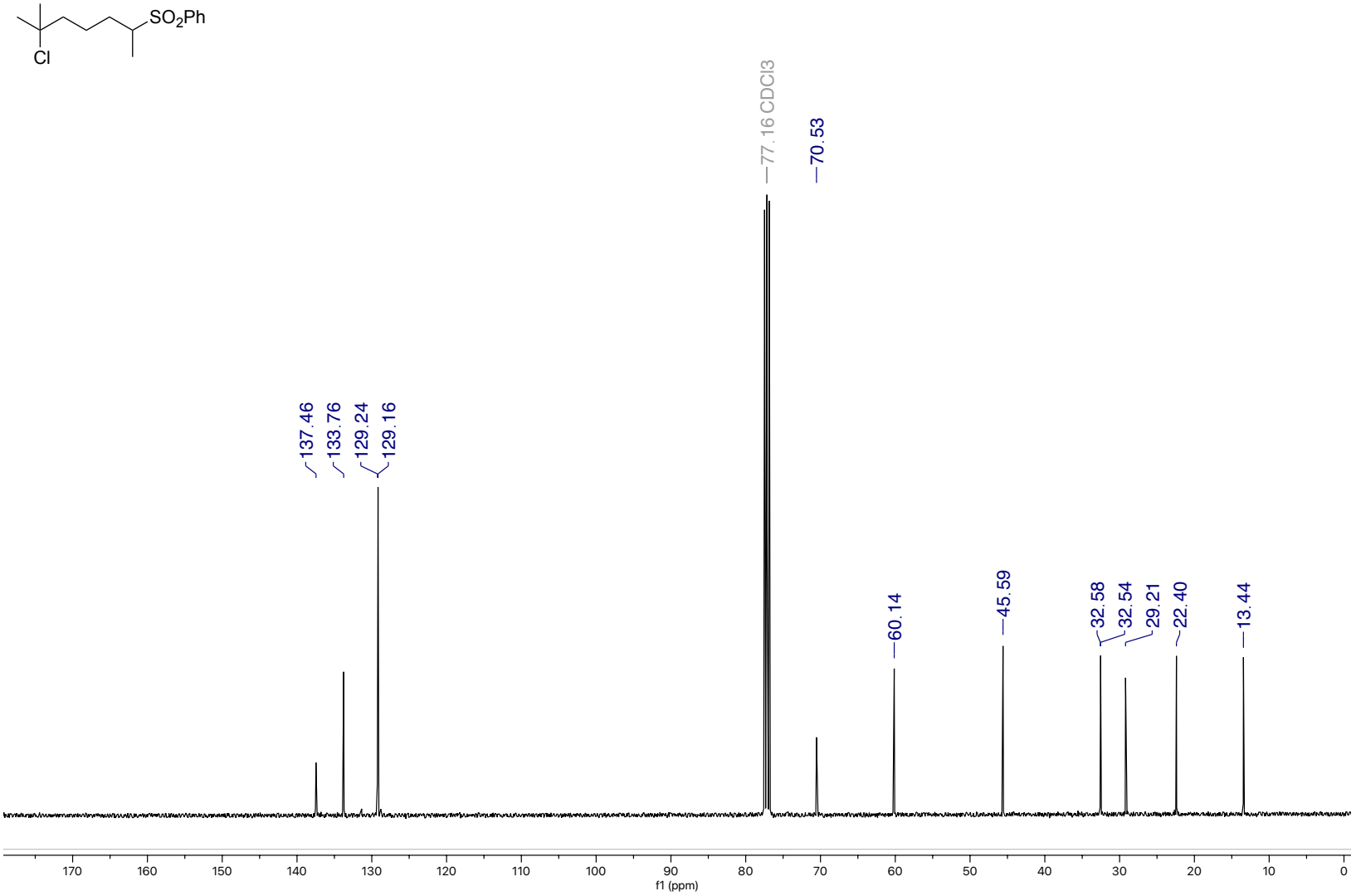
((6-Chloro-6-methylheptan-2-yl)sulfonyl)benzene

$^1$H-NMR (400 MHz, $CDCl_3$)

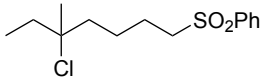


((6-Chloro-6-methylheptan-2-yl)sulfonyl)benzene

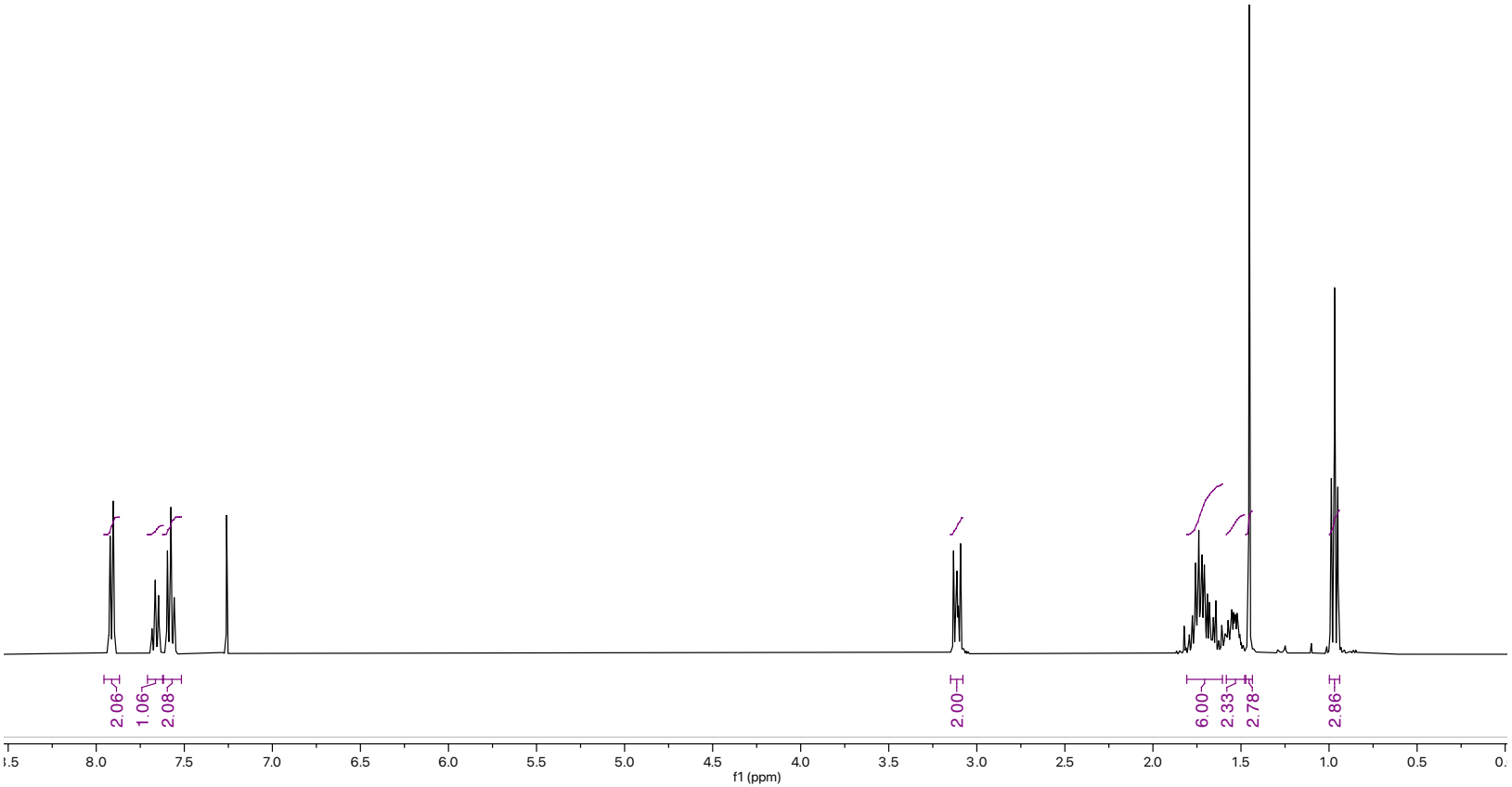
$^{13}$C-NMR (101 MHz, $CDCl_3$)



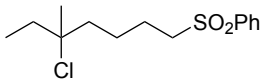
((5-Chloro-5-methylheptyl)sulfonyl)benzene



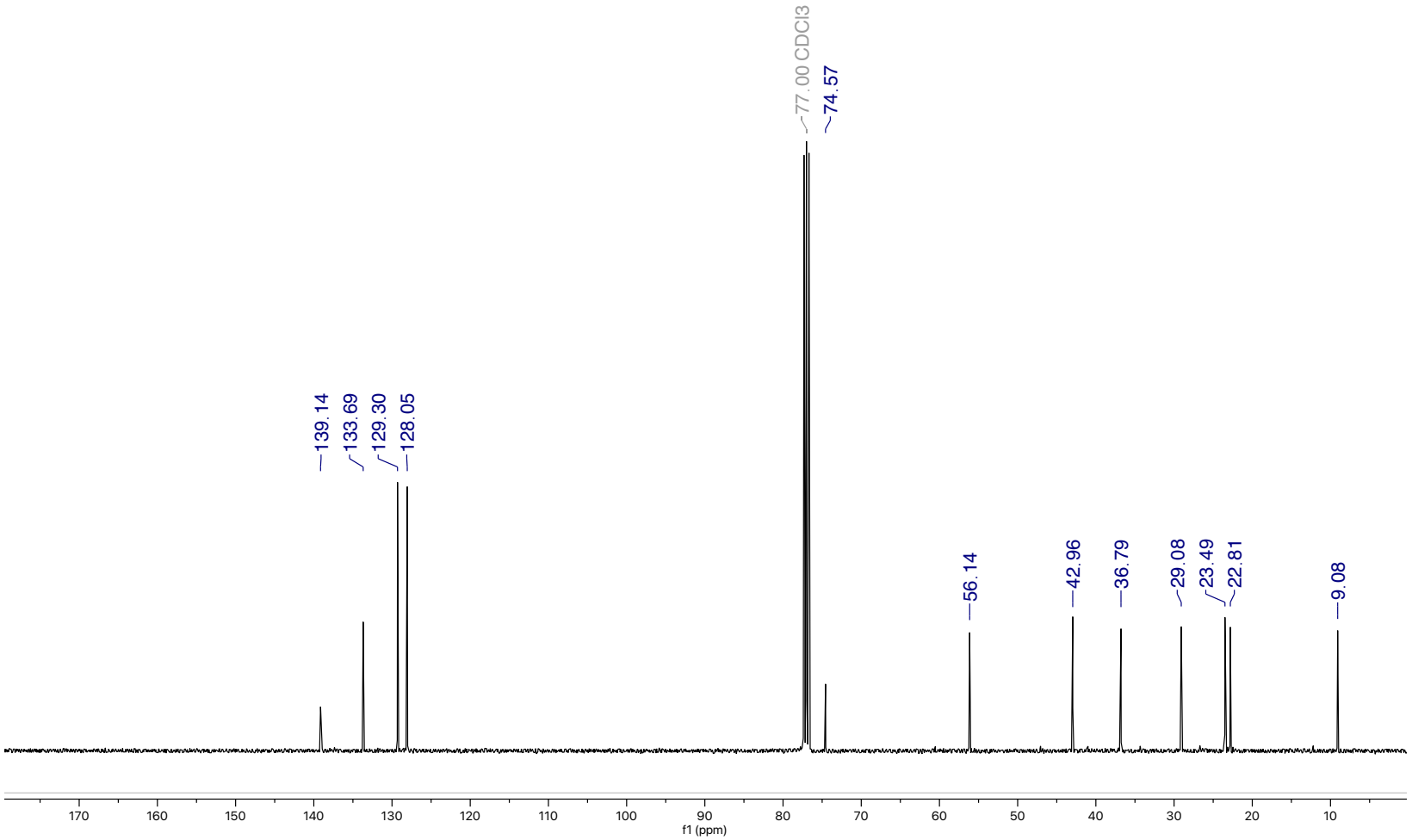

$^1$H-NMR (400 MHz, $CDCl_3$)



((5-Chloro-5-methylheptyl)sulfonyl)benzene

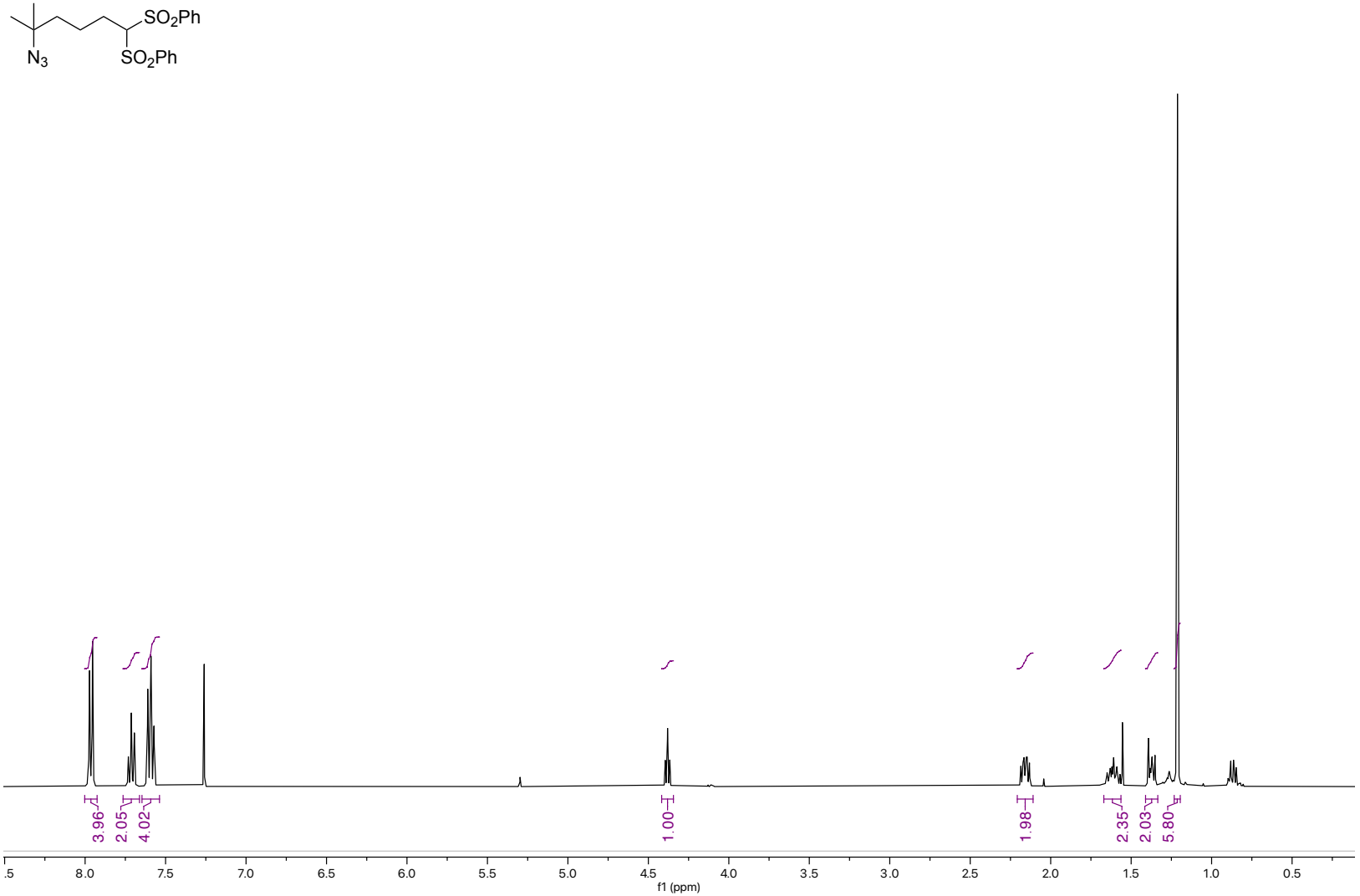



$^{13}$C-NMR (101 MHz, $CDCl_3$)

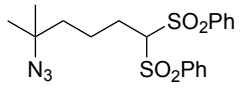


(5-Azido-5-methylhexane-1,1-diyldisulfonyl)dibenzene

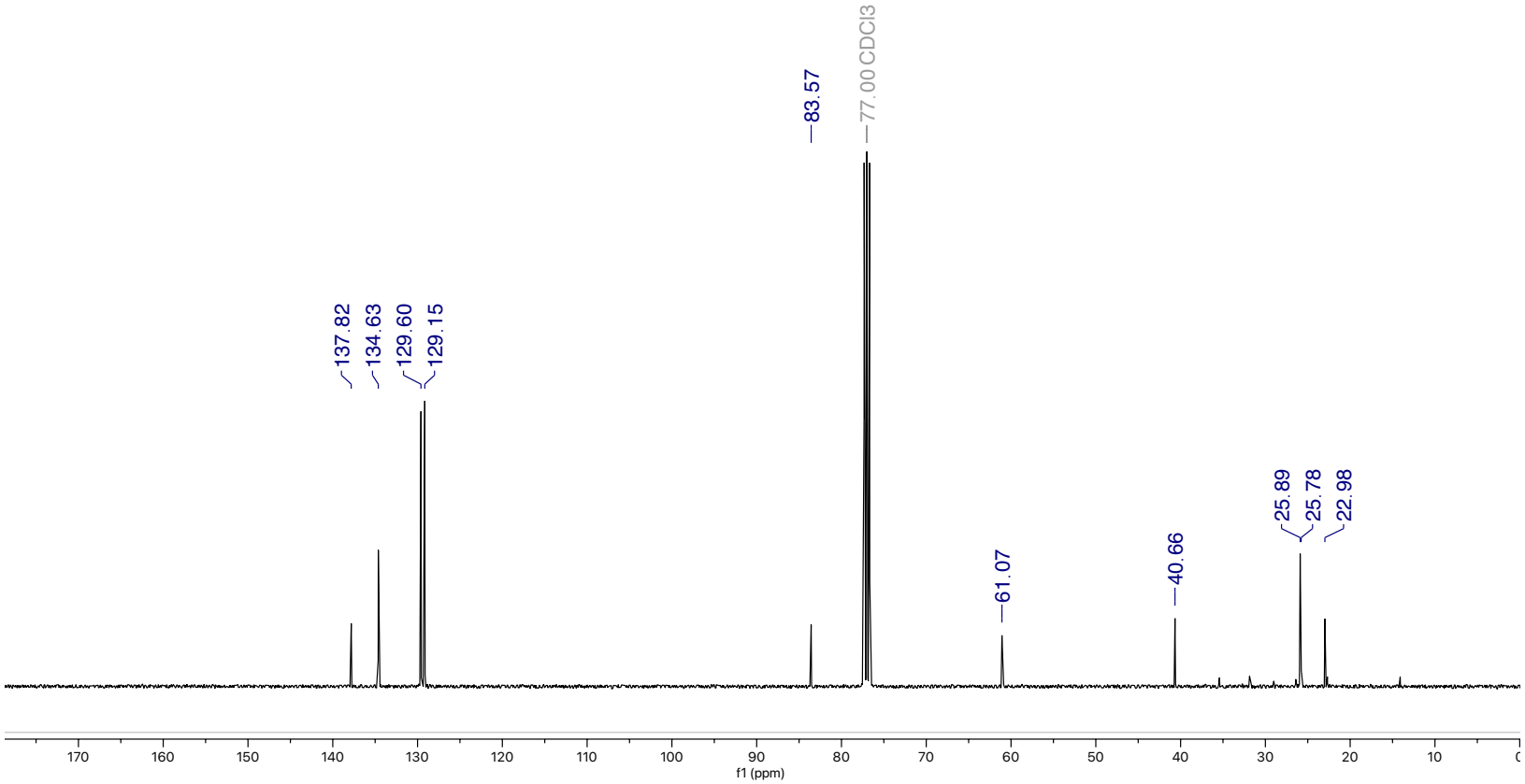
$^1$H-NMR (400 MHz, $CDCl_3$)



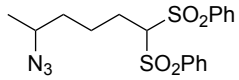
(5-Azido-5-methylhexane-1,1-diyldisulfonyl)dibenzene



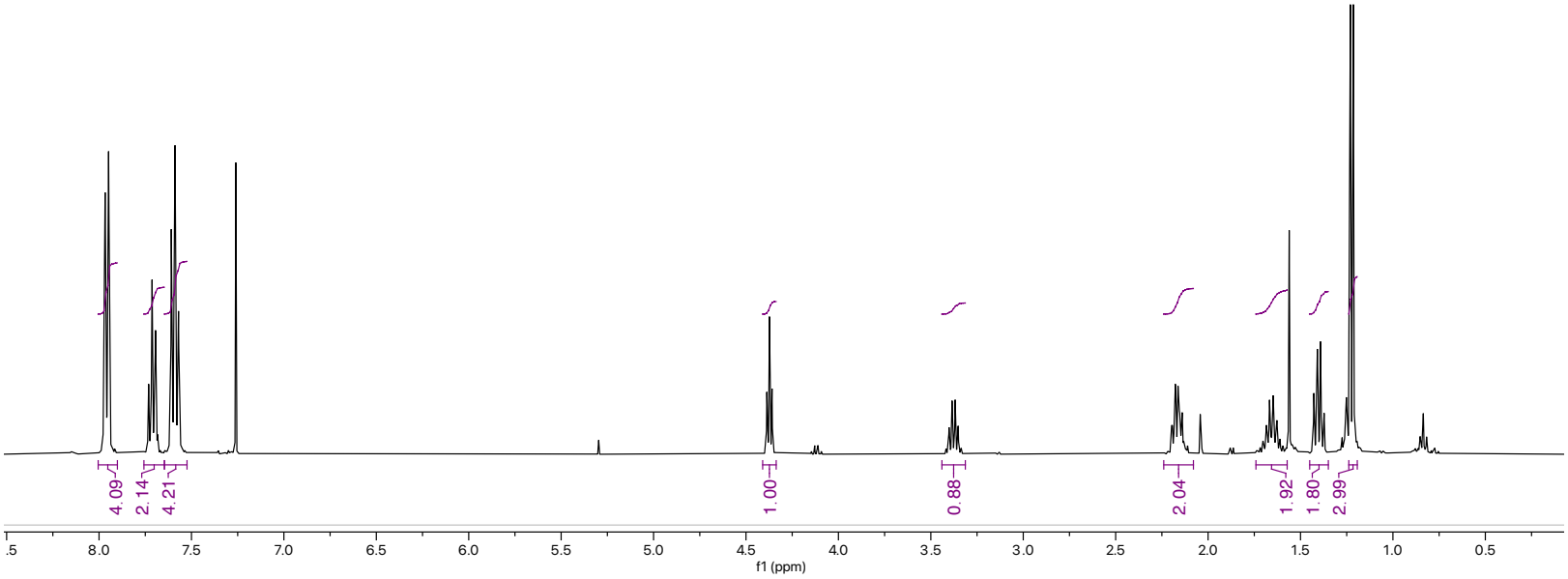

$^{13}$C-NMR (101 MHz, $CDCl_3$)



(5-Azidohexane-1,1-diyldisulfonyl)dibenzene

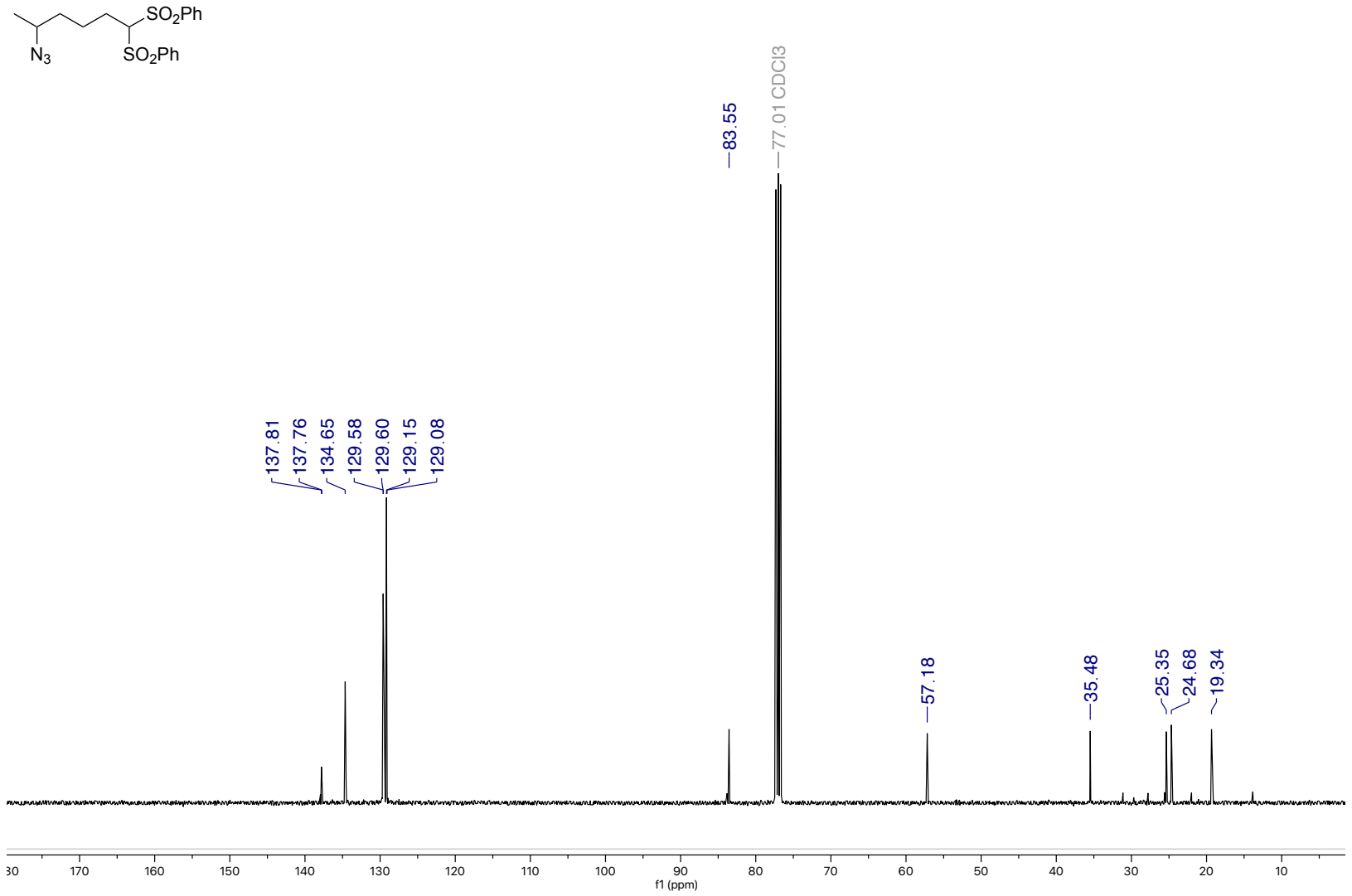



$^1$H-NMR (400 MHz, $CDCl_3$)



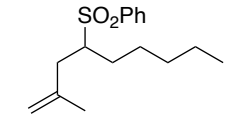
(5-Azidohexane-1,1-diyldisulfonyl)dibenzene

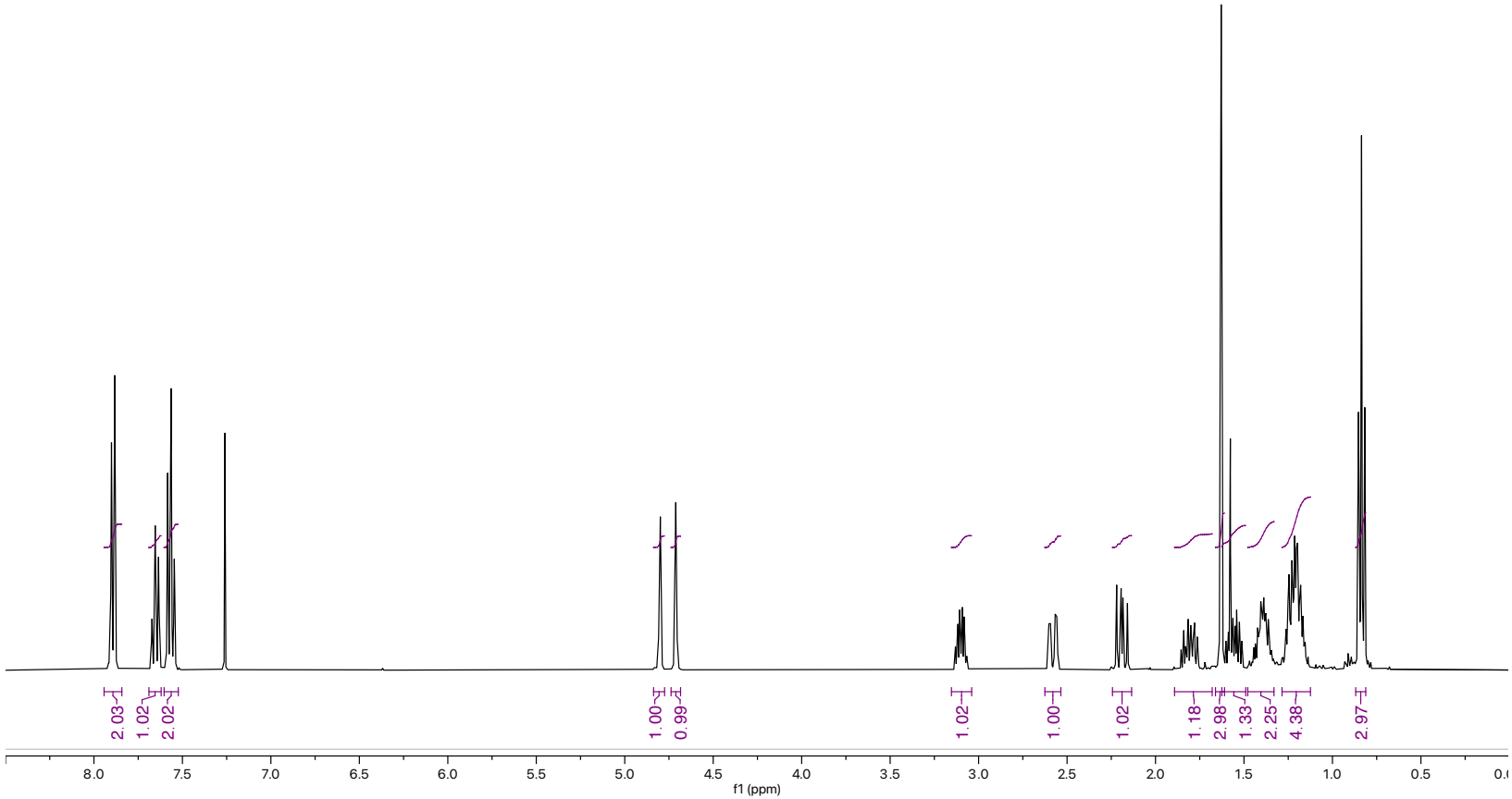
$^{13}$C-NMR (101 MHz, $CDCl_3$)



((2-Methylnon-1-en-4-yl)sulfonyl)benzene

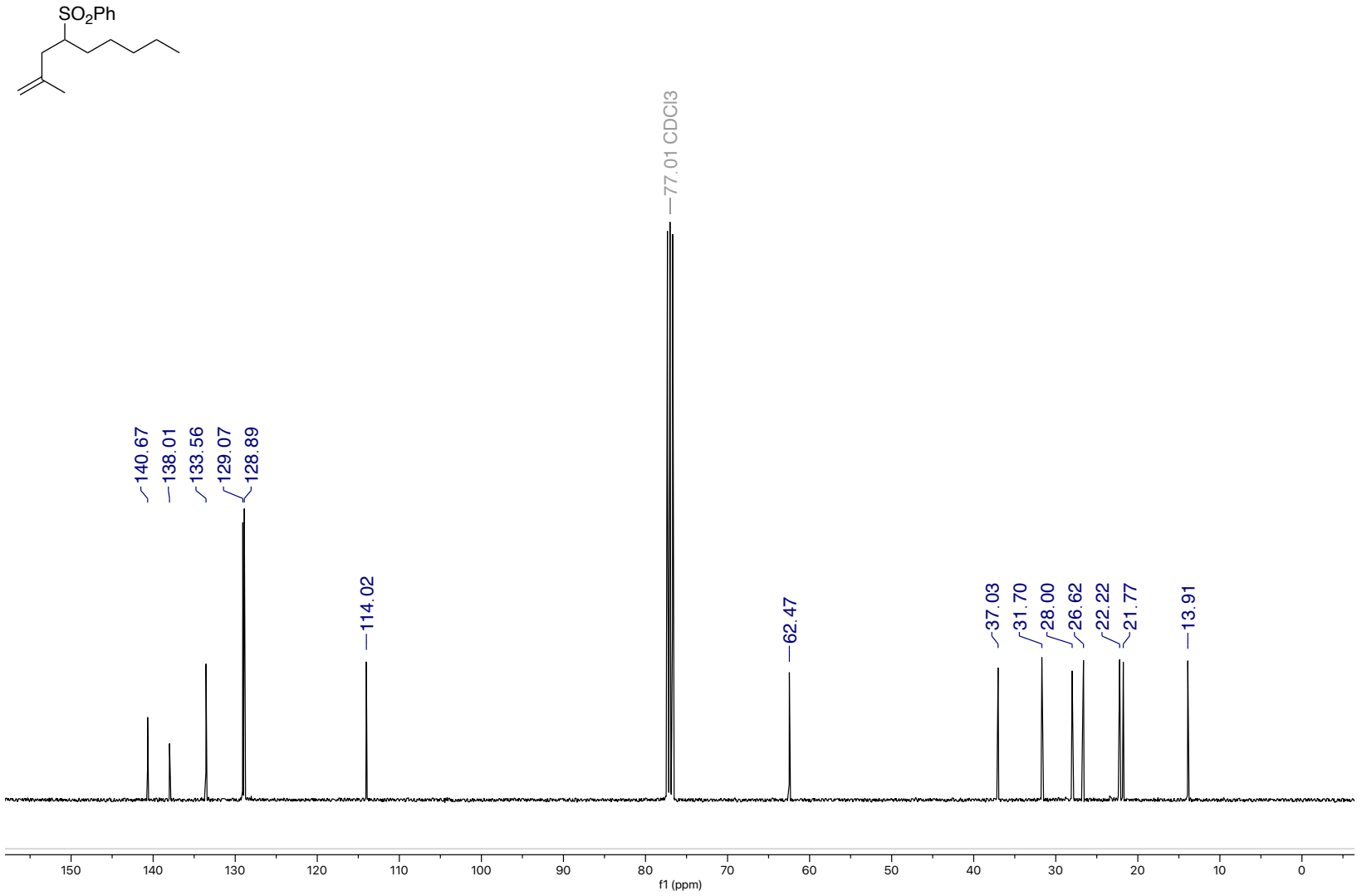
$^1$H-NMR (400 MHz, $CDCl_3$)



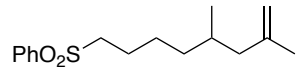
((2-Methylnon-1-en-4-yl)sulfonyl)benzene

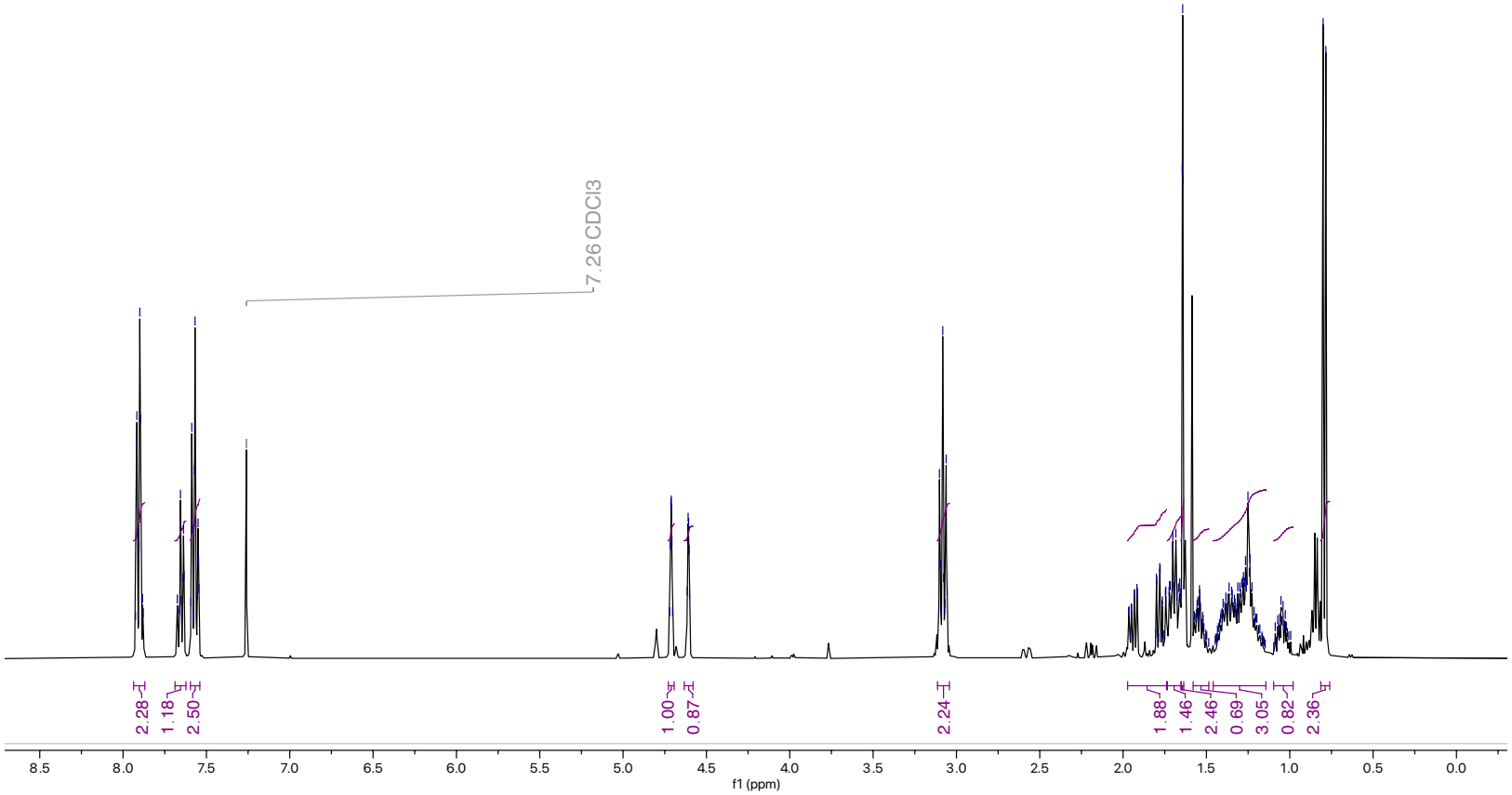
$^{13}$C-NMR (101 MHz, $CDCl_3$)



((5,7-Dimethyloct-7-en-1-yl)sulfonyl)benzene

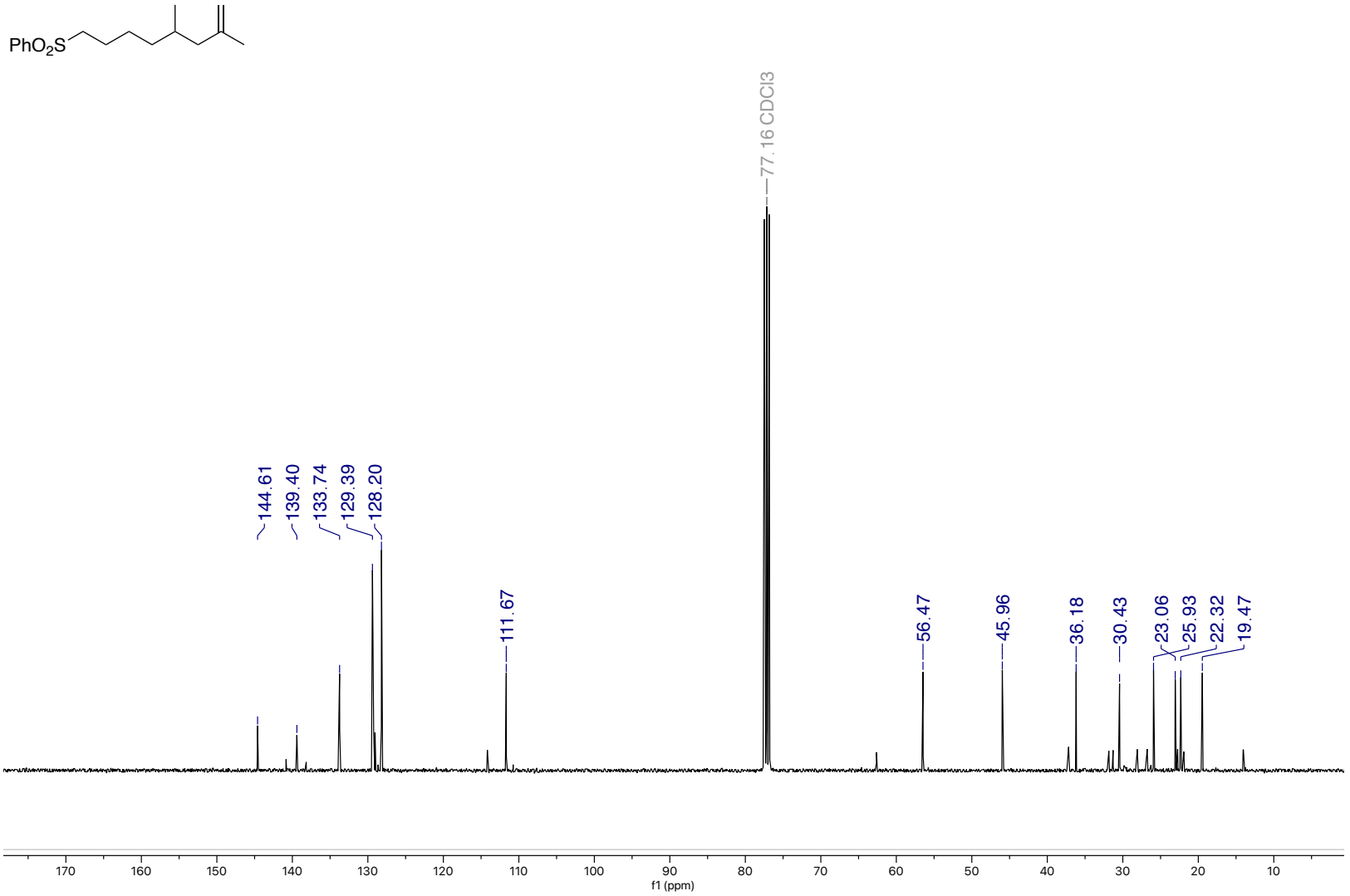
$^1$H-NMR (400 MHz, $CDCl_3$)



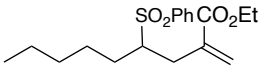



((5,7-Dimethyloct-7-en-1-yl)sulfonyl)benzene

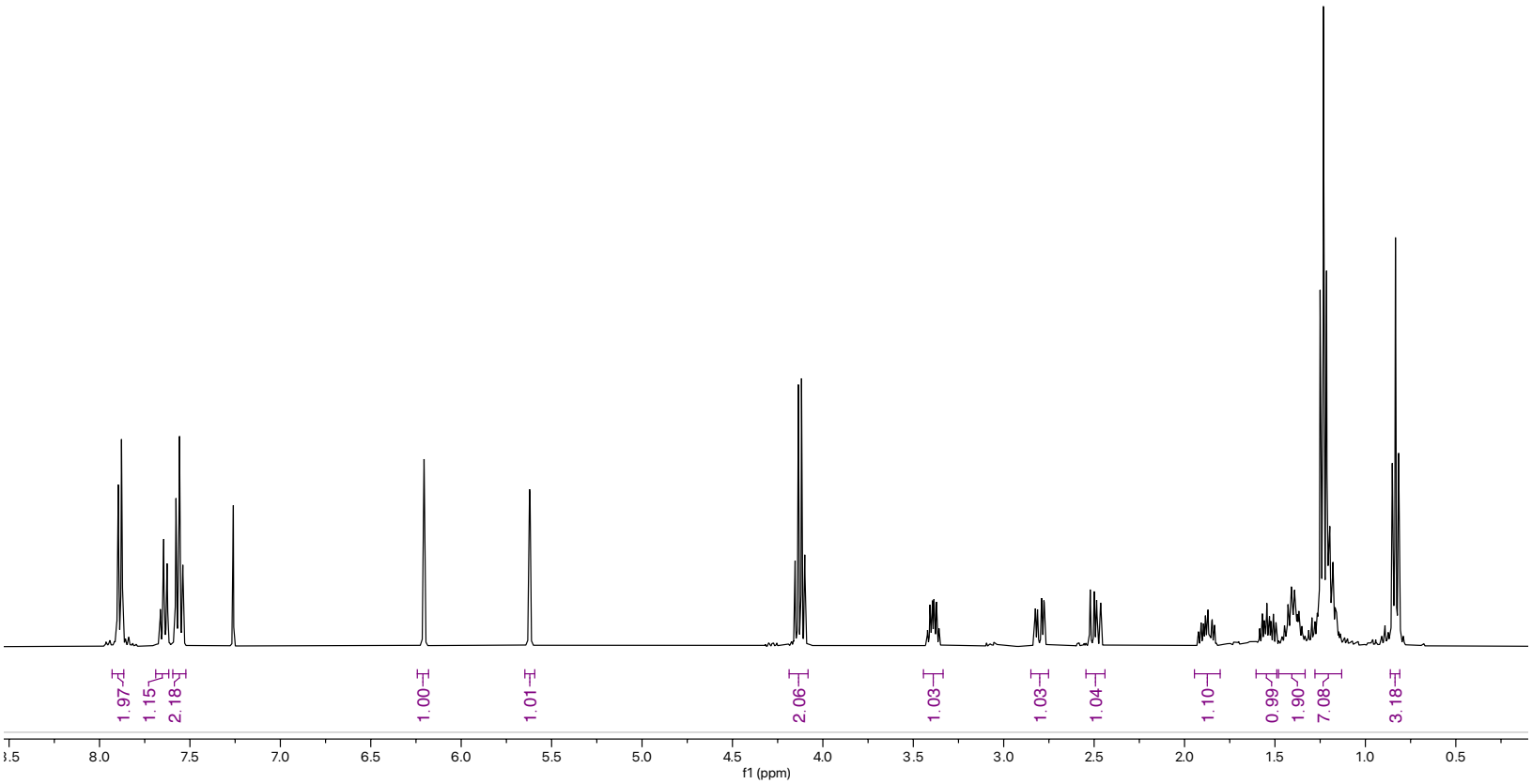
$^{13}$C-NMR (101 MHz, $CDCl_3$)



Ethyl 2-methylene-4-(phenylsulfonyl)nonanoate

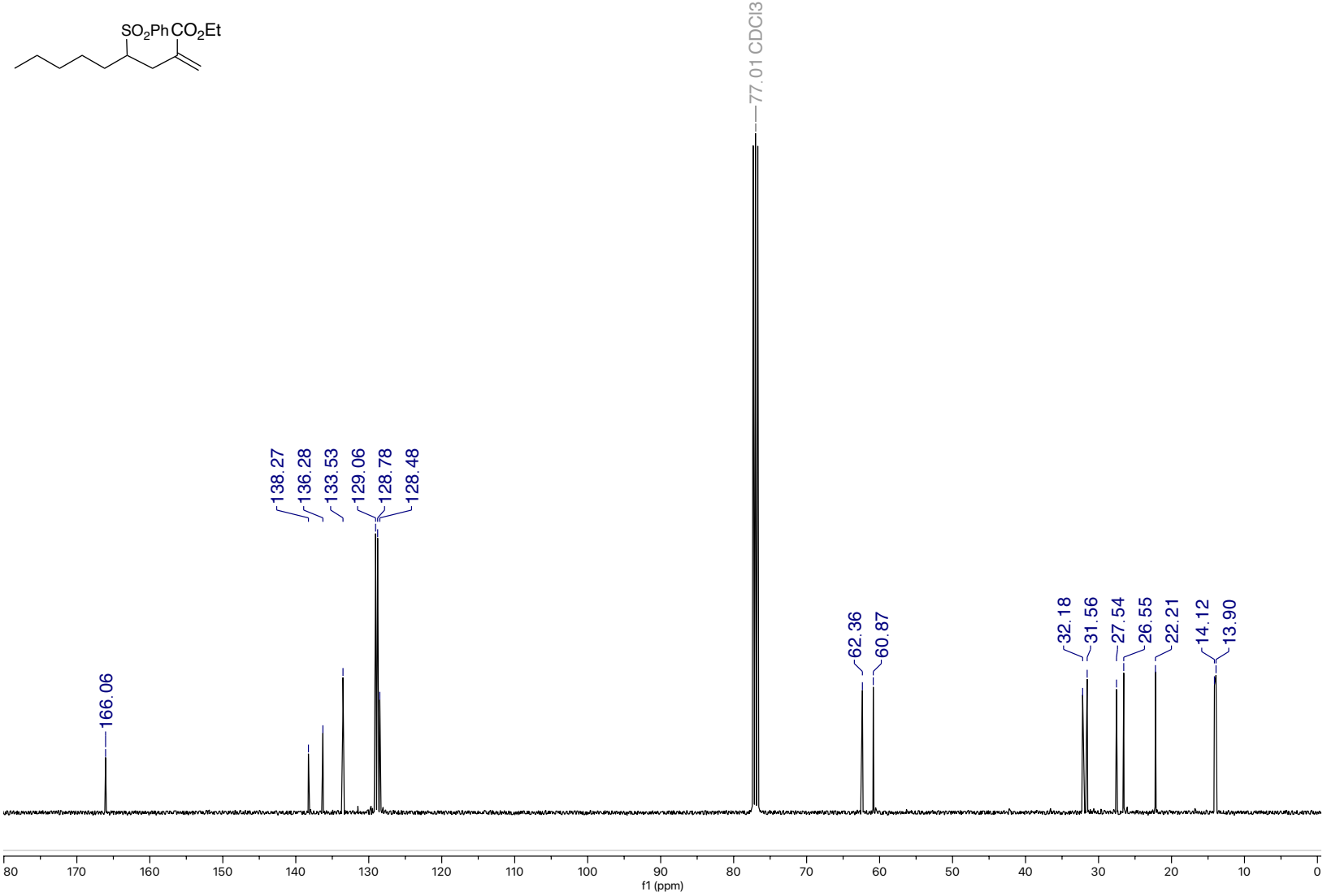



$^1$H-NMR (400 MHz, $CDCl_3$)



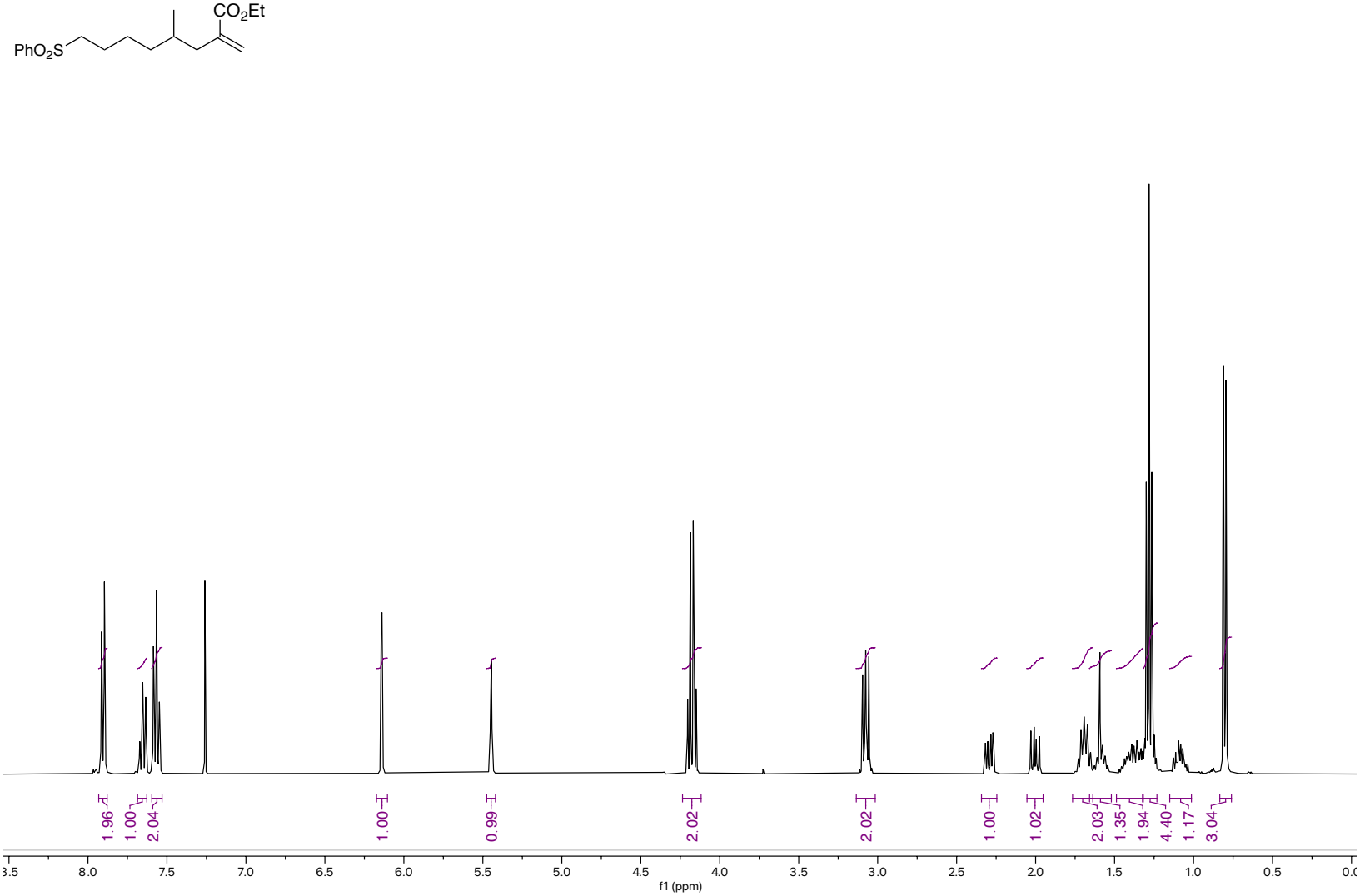
Ethyl 2-methylene-4-(phenylsulfonyl)nonanoate

$^{13}$C-NMR (101 MHz, $CDCl_3$)



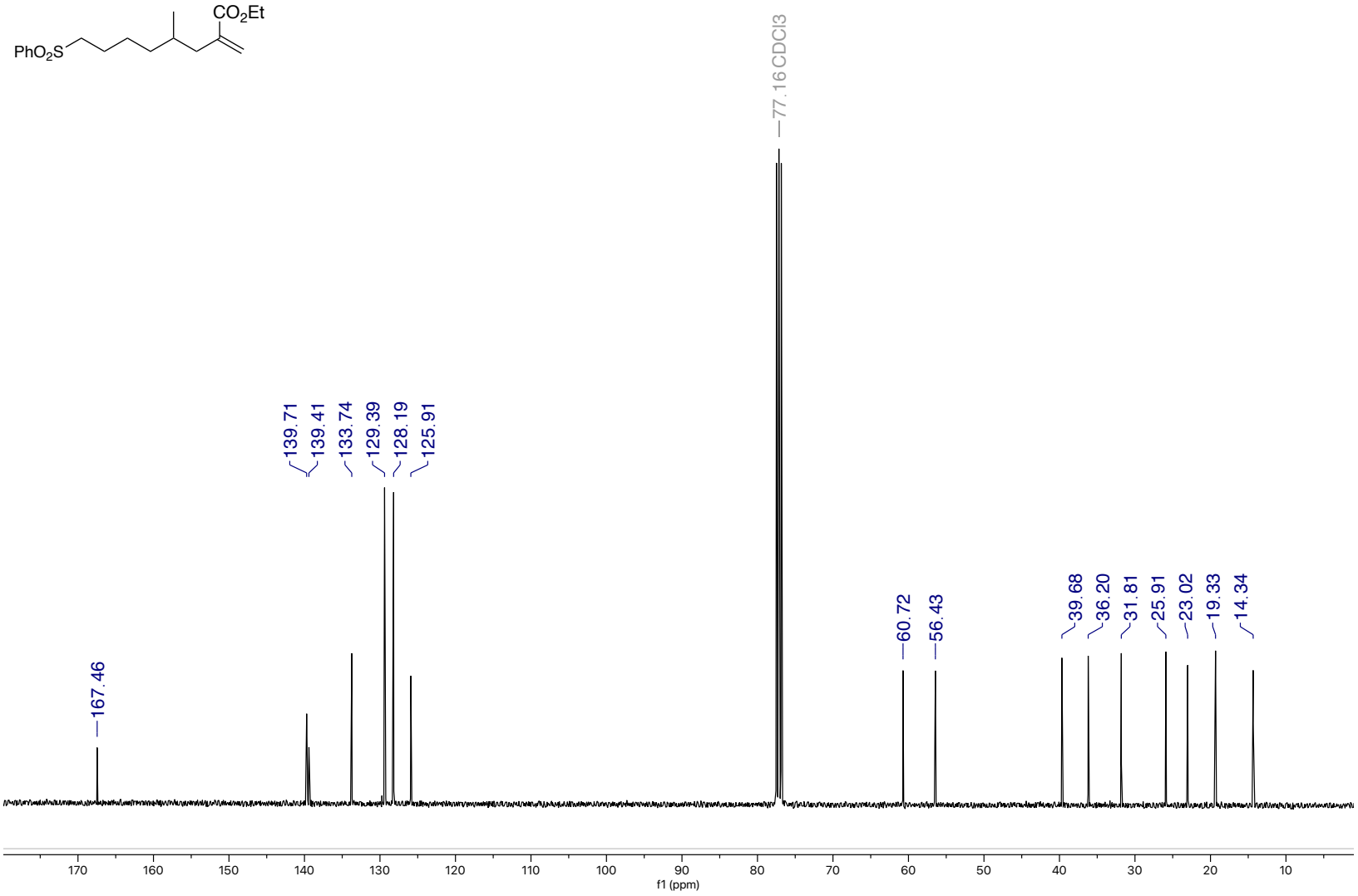
Ethyl 4-methyl-2-methylene-8-(phenylsulfonyl)octanoate

$^1$H-NMR (400 MHz, $CDCl_3$)



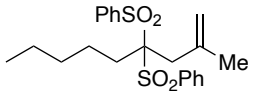
Ethyl 4-methyl-2-methylene-8-(phenylsulfonyl)octanoate

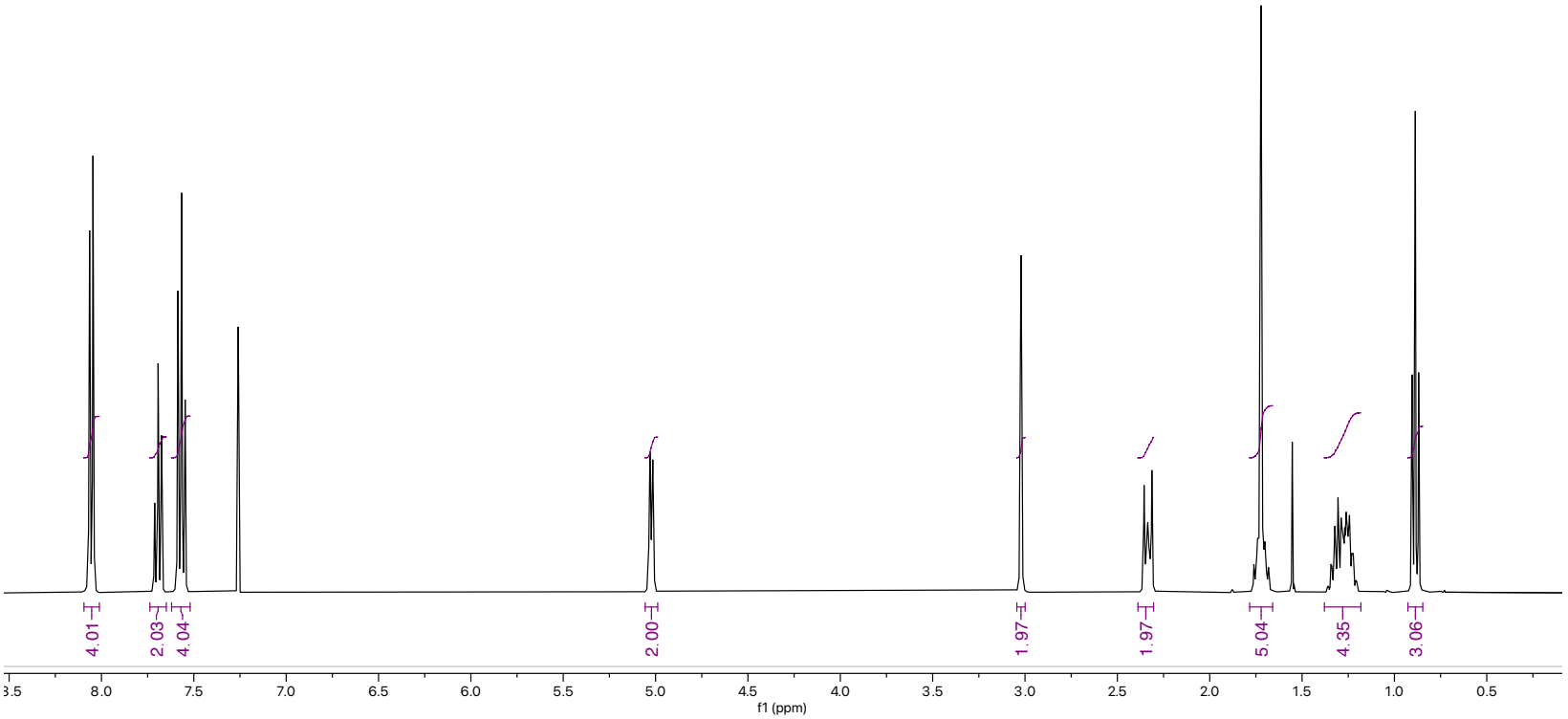
$^{13}$C-NMR (101 MHz, $CDCl_3$)



((2-Methyl-4-(phenylsulfonyl)non-1-en-4-yl)peroxy)(phenyl)sulfane

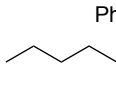
$^1$H-NMR (400 MHz, $CDCl_3$)

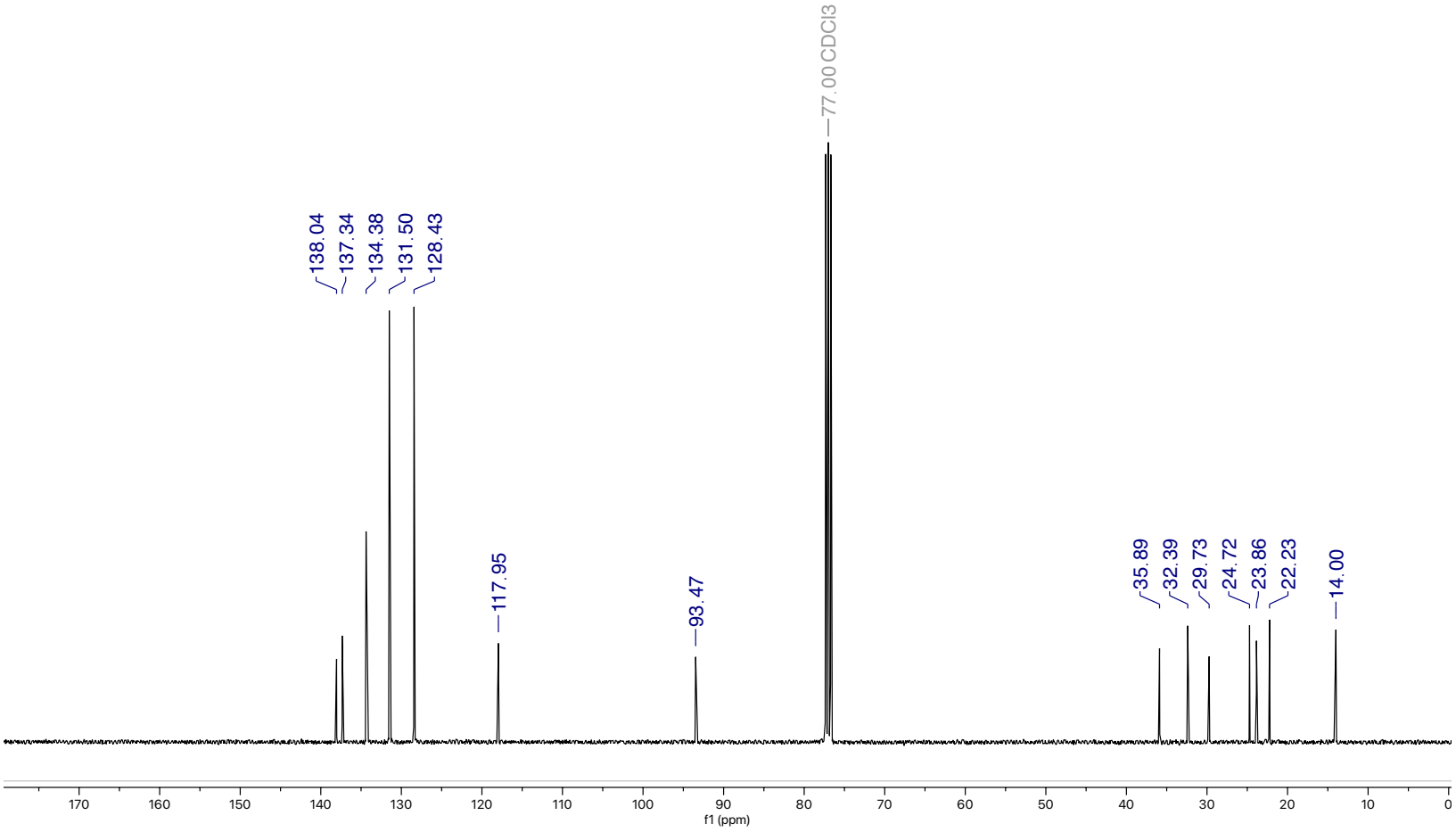


((2-Methyl-4-(phenylsulfonyl)non-1-en-4-yl)peroxy)(phenyl)sulfane

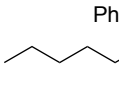
$^{13}$C-NMR (101 MHz, $CDCl_3$)

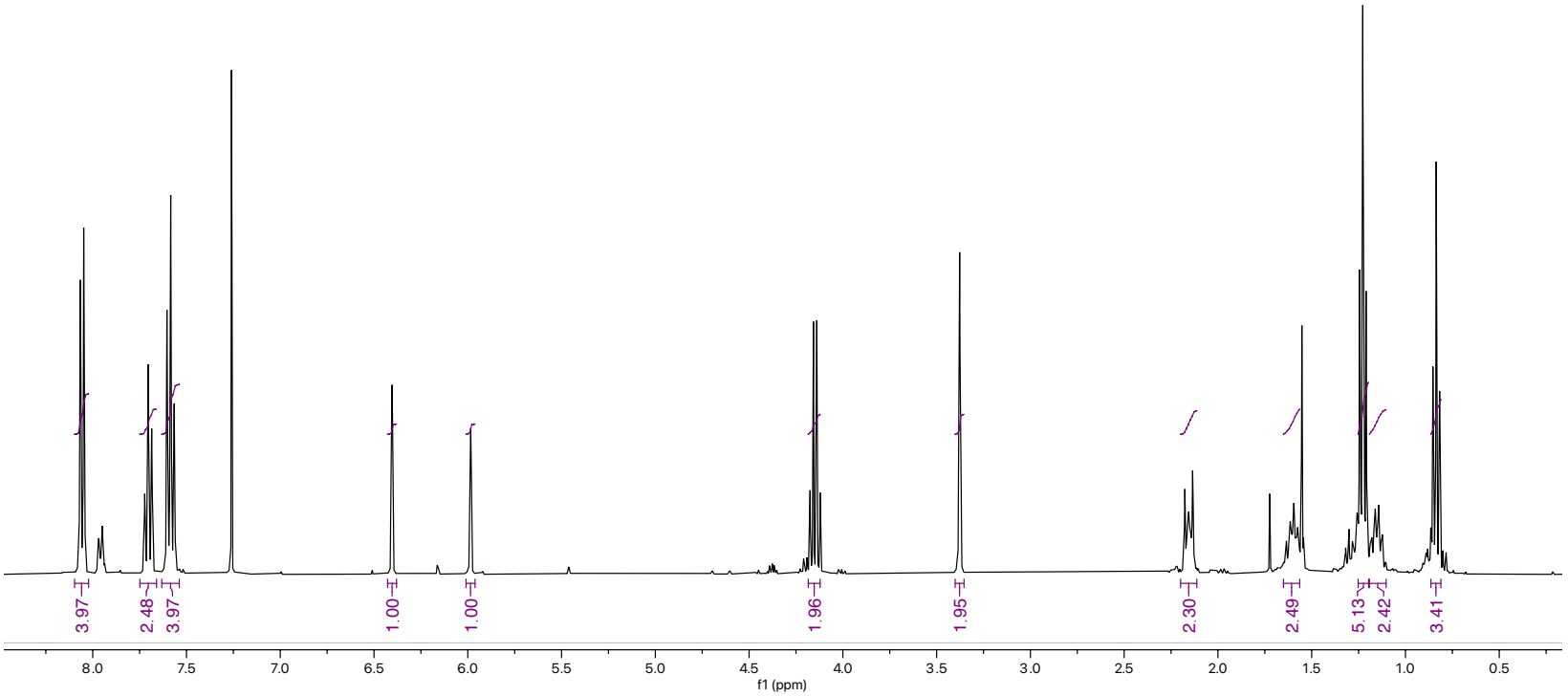


Ethyl 2-methylene-4-(phenylsulfonyl)-4-((phenylthio)peroxy)nonanoate

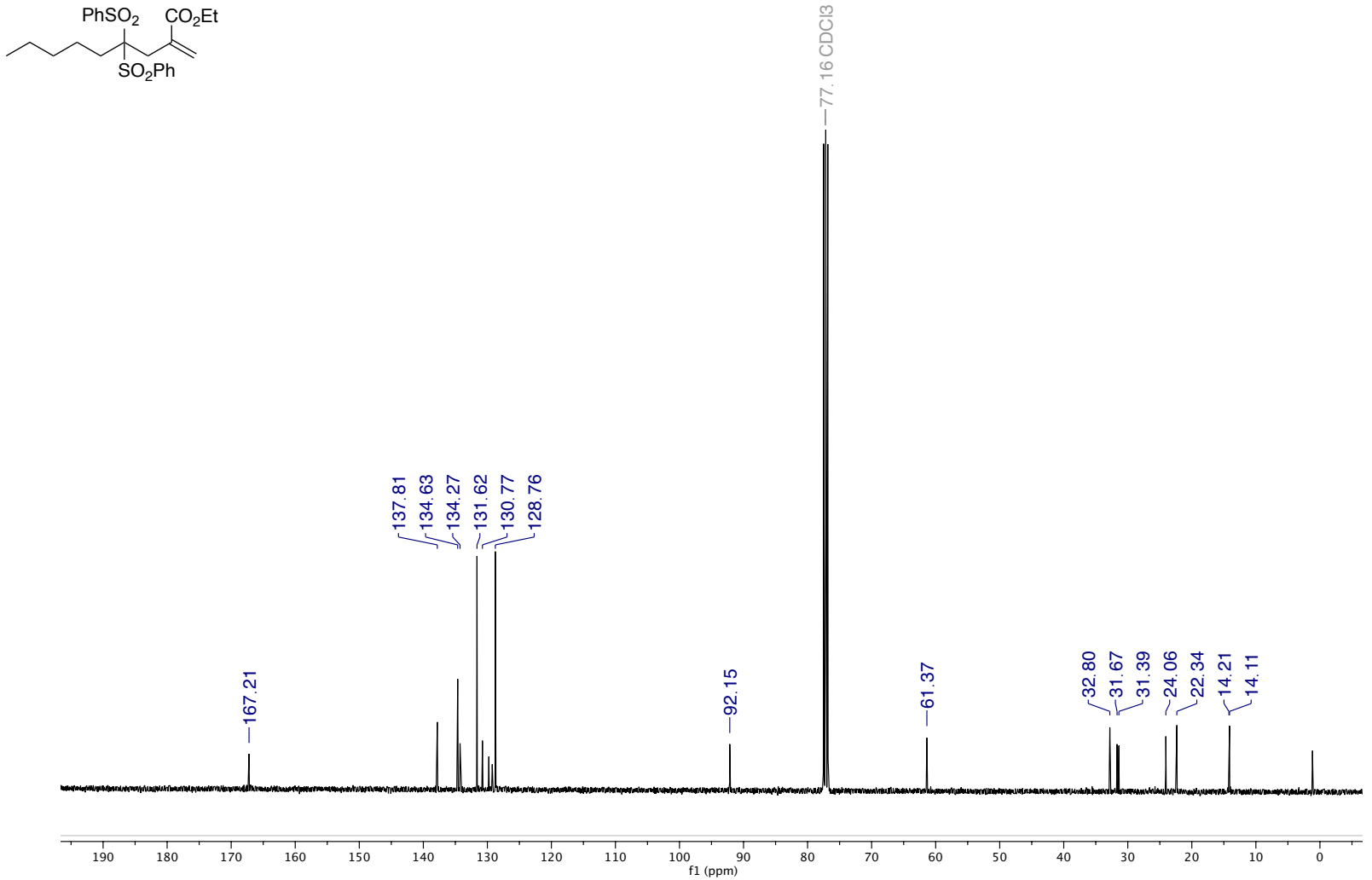
$^1$H-NMR (400 MHz, $CDCl_3$)



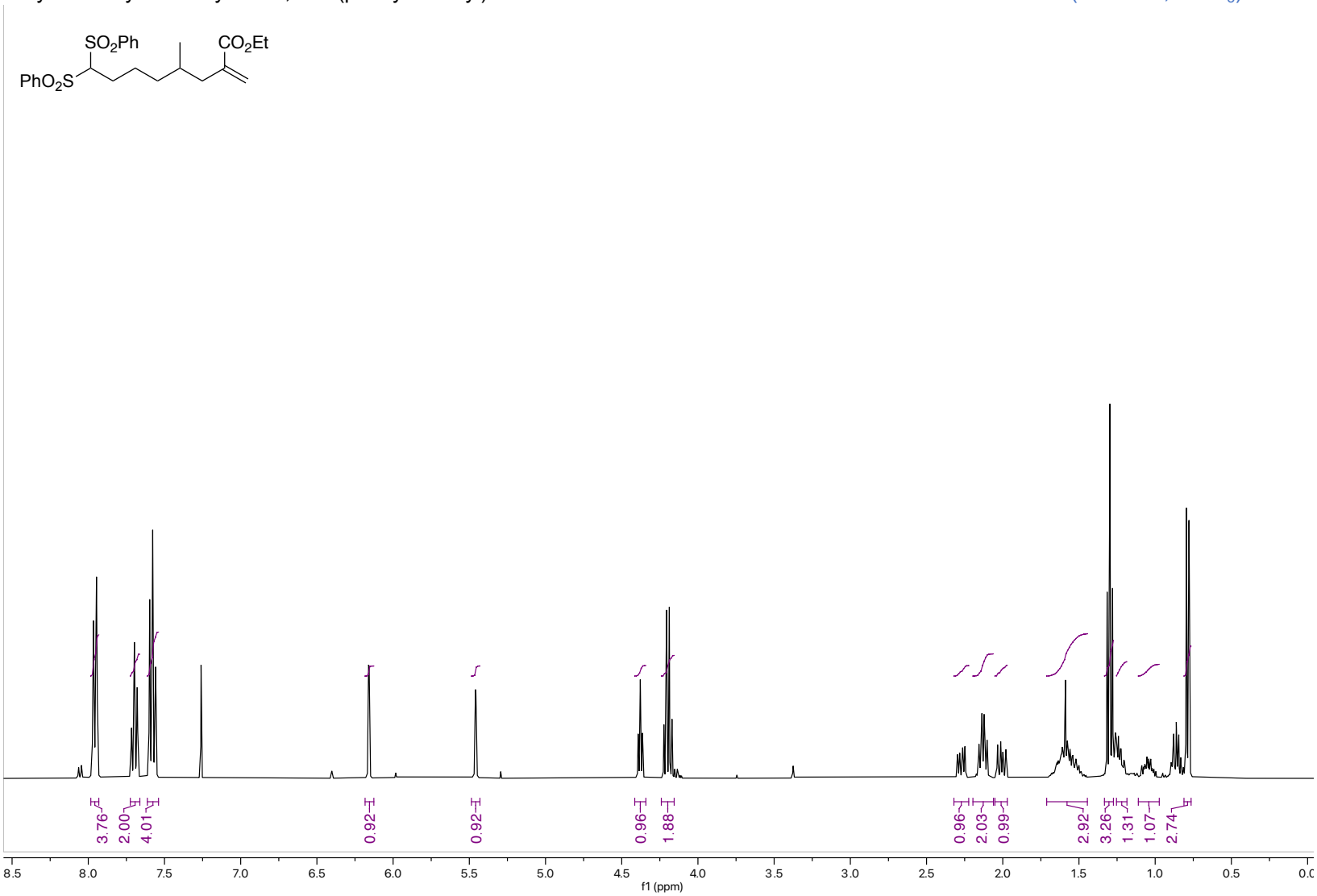
Ethyl 2-methylene-4-(phenylsulfonyl)-4-((phenylthio)peroxy)nonanoate

$^{13}$C-NMR (101 MHz, $CDCl_3$)



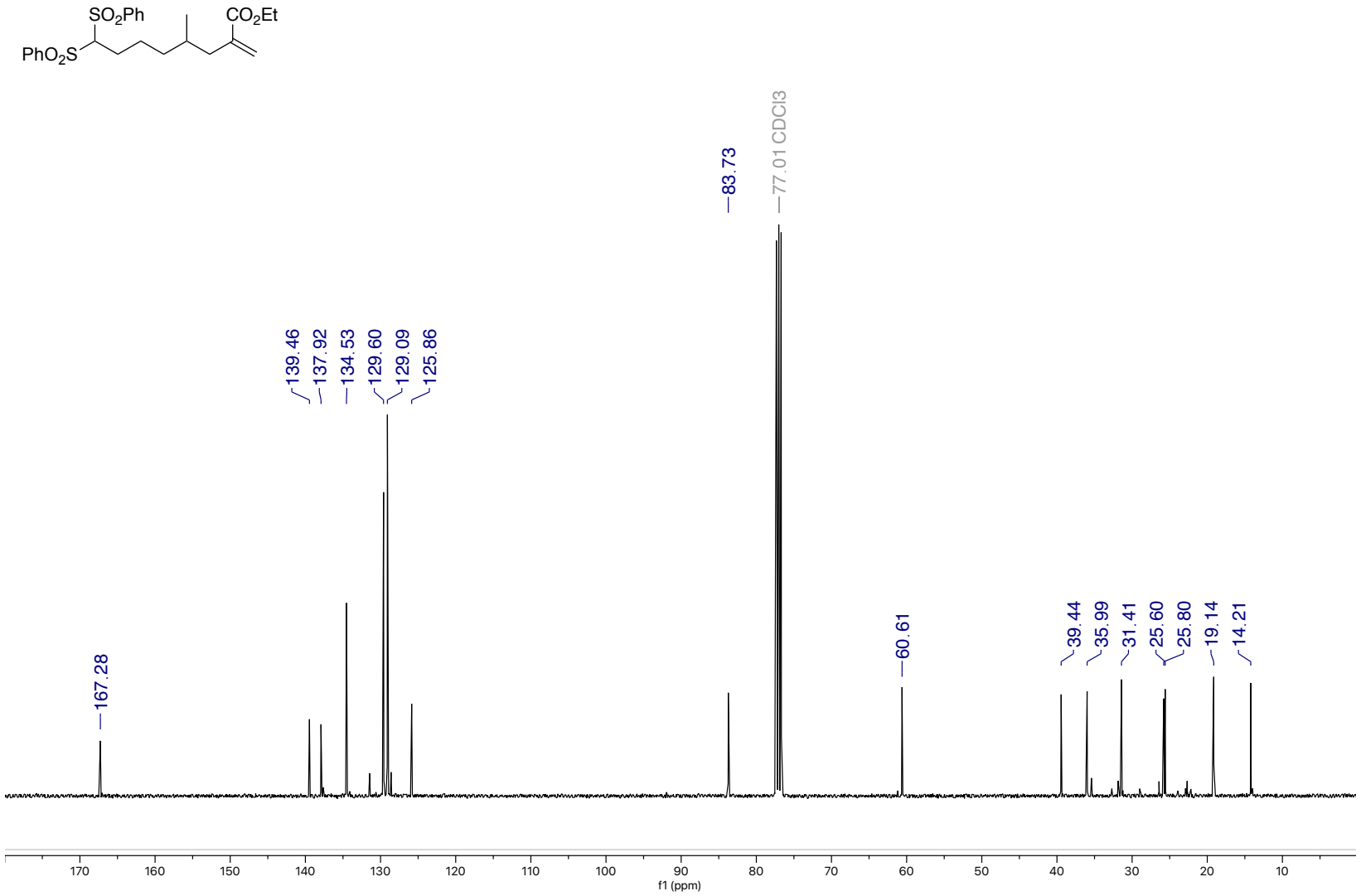
Ethyl 4-methyl-2-methylene-8,8-bis(phenylsulfonyl)octanoate

$^1$H-NMR (400 MHz, $CDCl_3$)



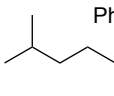
Ethyl 4-methyl-2-methylene-8,8-bis(phenylsulfonyl)octanoate

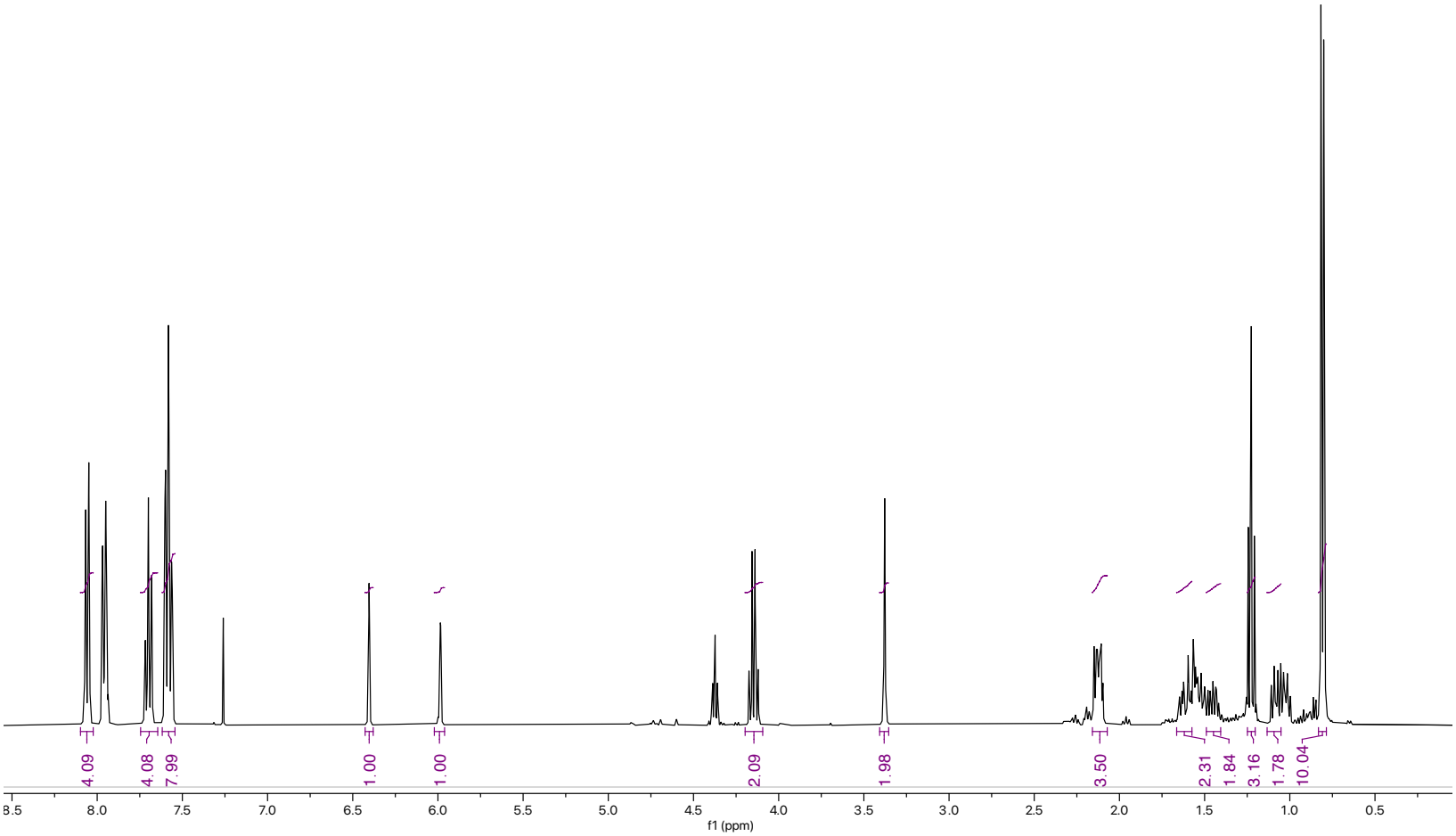
$^{13}$C-NMR (101 MHz, $CDCl_3$)



Ethyl 8-methyl-2-methylene-4-(phenylsulfonyl)-4-((phenylthio)peroxy)nonanoate

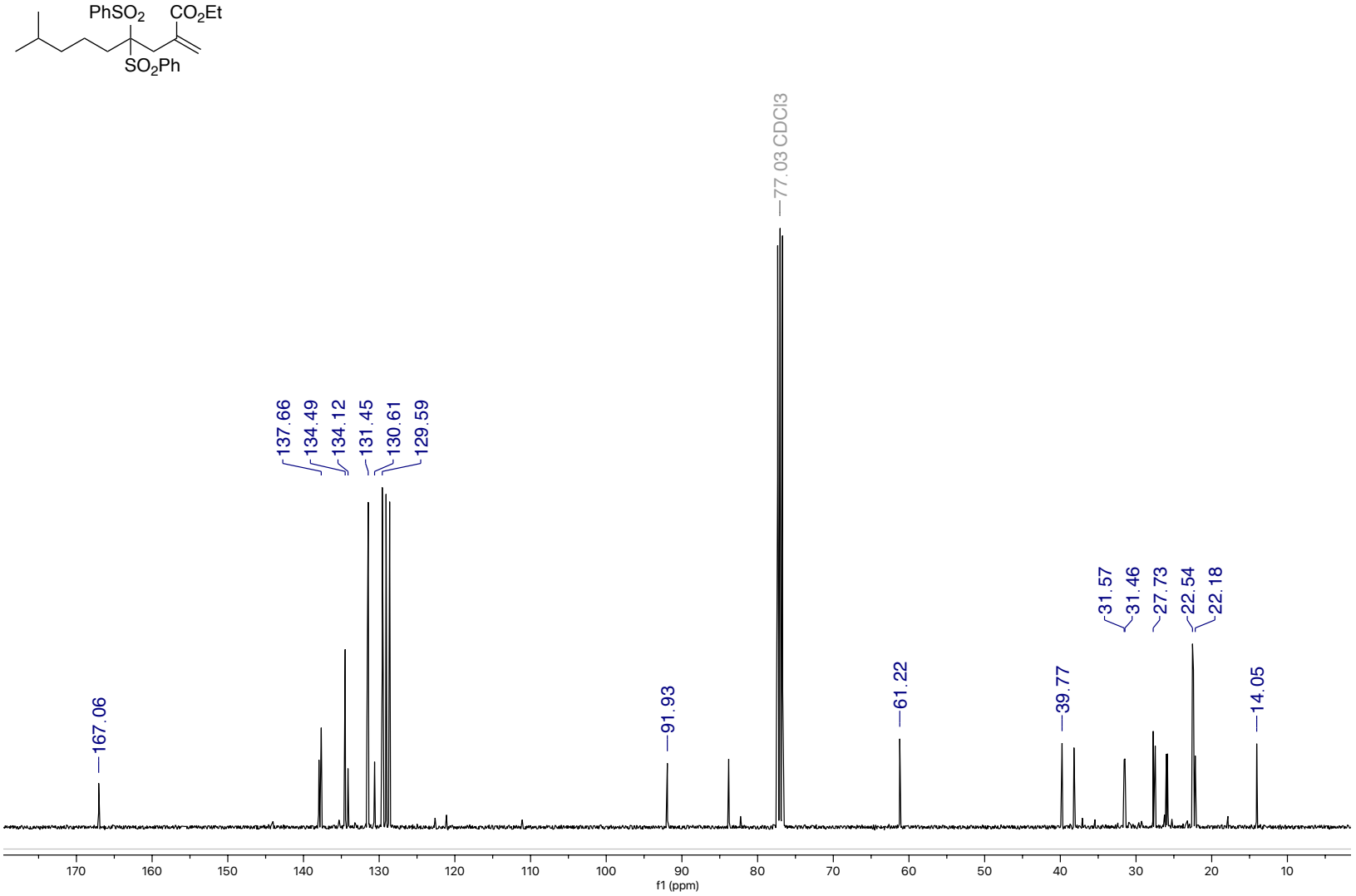
$^1$H-NMR (400 MHz, $CDCl_3$)



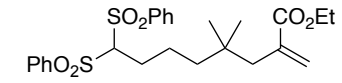
Ethyl 8-methyl-2-methylene-4-(phenylsulfonyl)-4-((phenylthio)peroxy)nonanoate

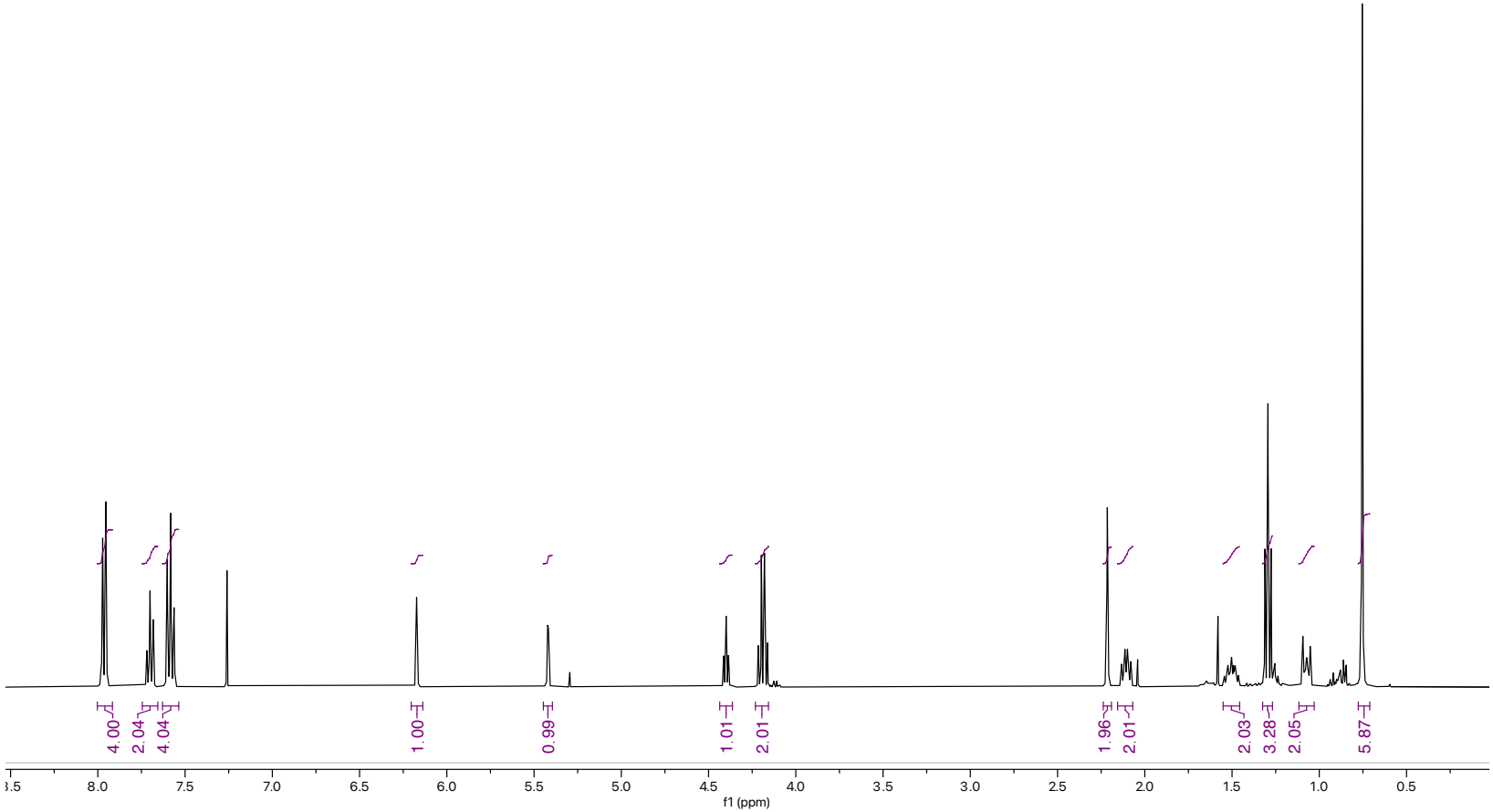
$^{13}$C-NMR (101 MHz, $CDCl_3$)



Ethyl 4,4-dimethyl-2-methylene-8,8-bis(phenylsulfonyl)octanoate

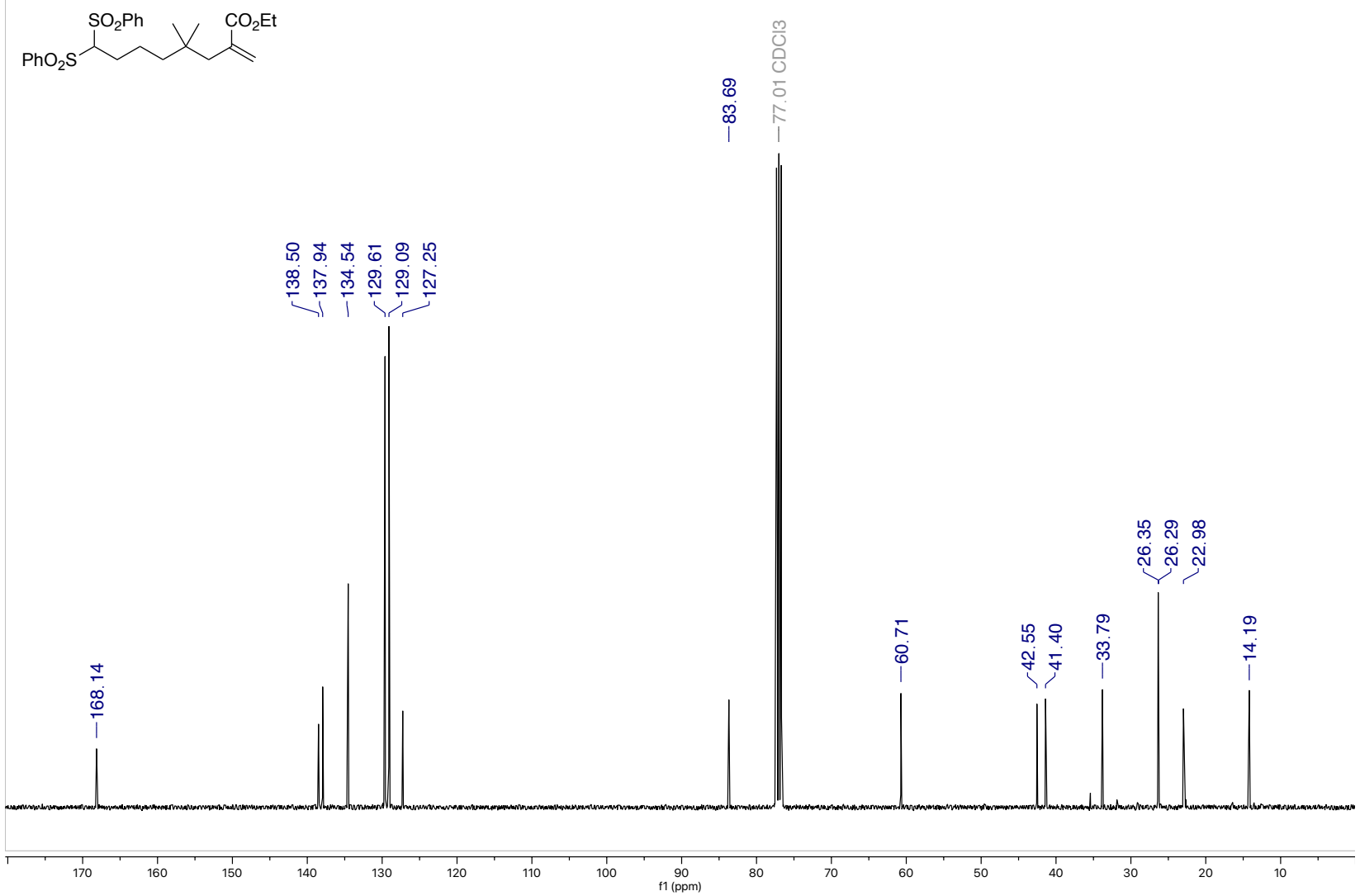
$^1$H-NMR (400 MHz, $CDCl_3$)



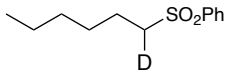



Ethyl 4,4-dimethyl-2-methylene-8,8-bis(phenylsulfonyl)octanoate

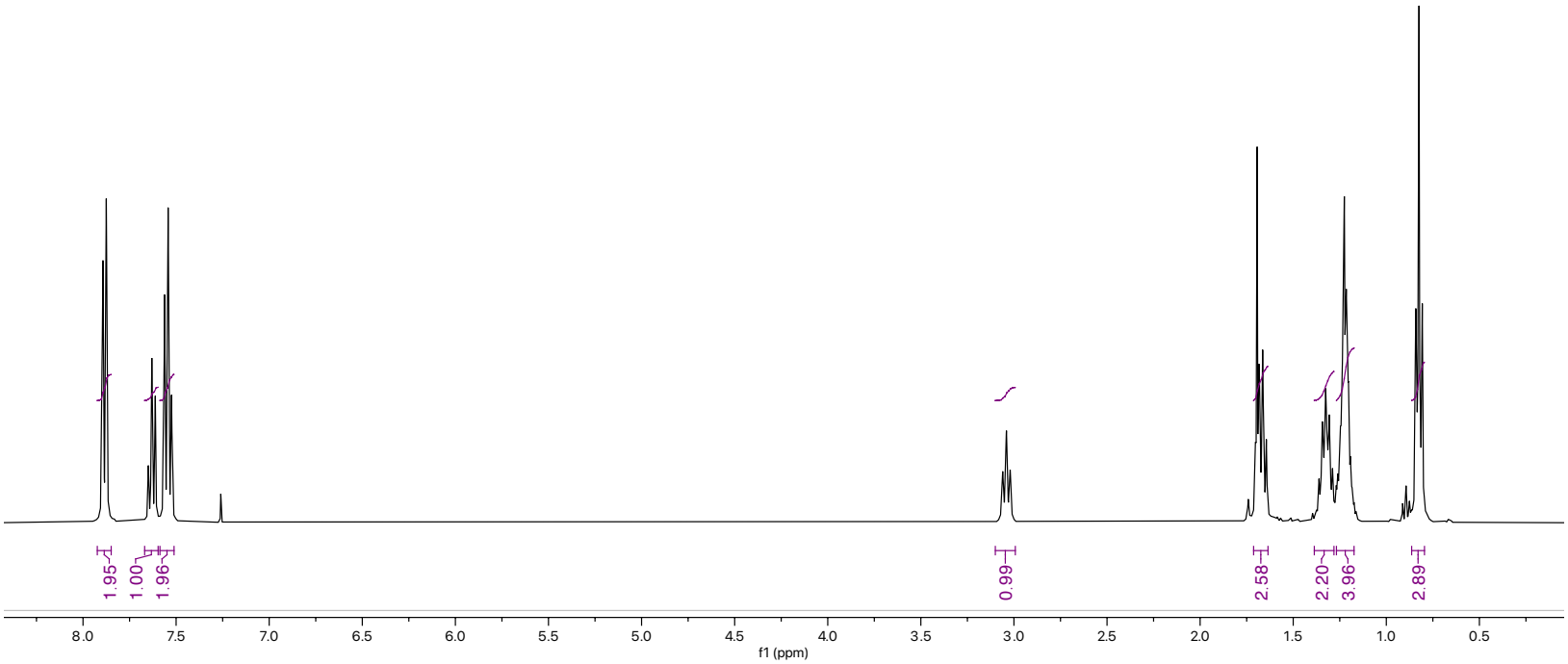
$^{13}$C-NMR (101 MHz, $CDCl_3$)



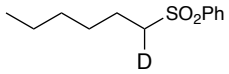
((Hexyl-1-*d*)sulfonyl)benzene



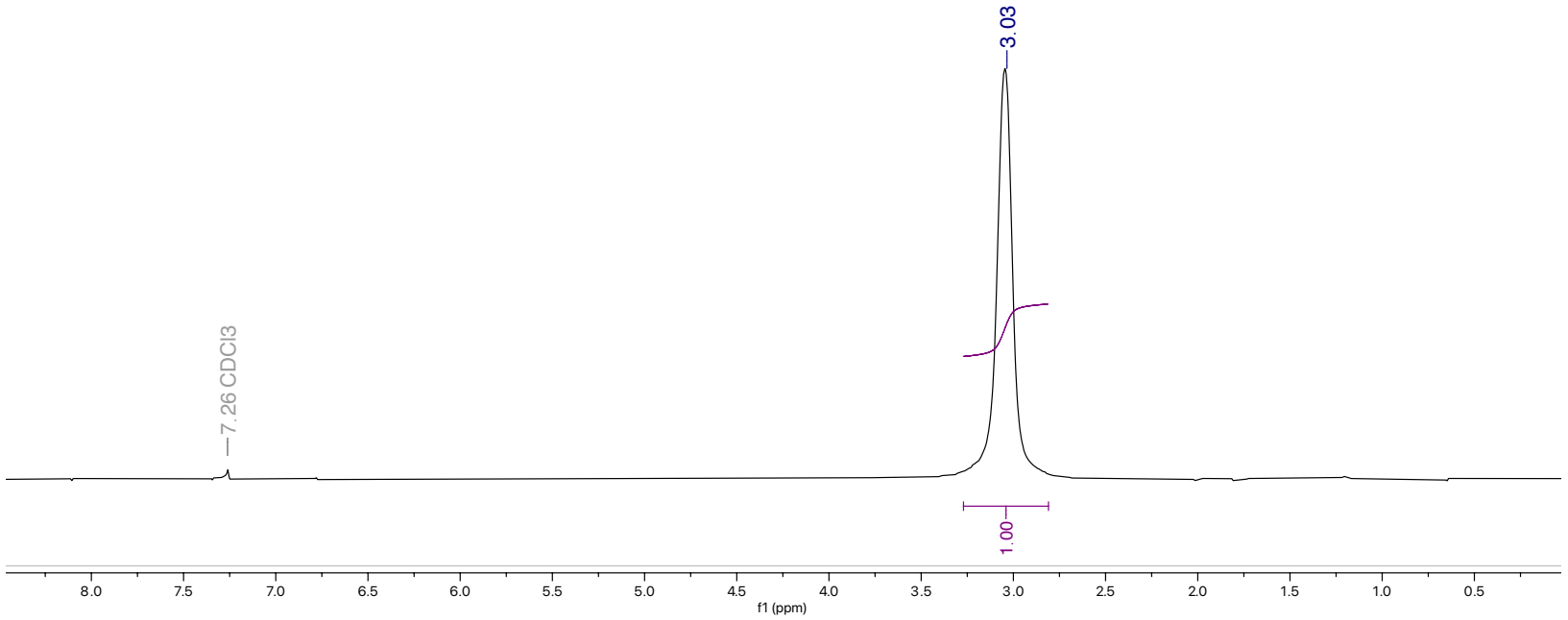

$^{1}$H-NMR (400 MHz, $CDCl_3$)



((Hexyl-1-*d*)sulfonyl)benzene

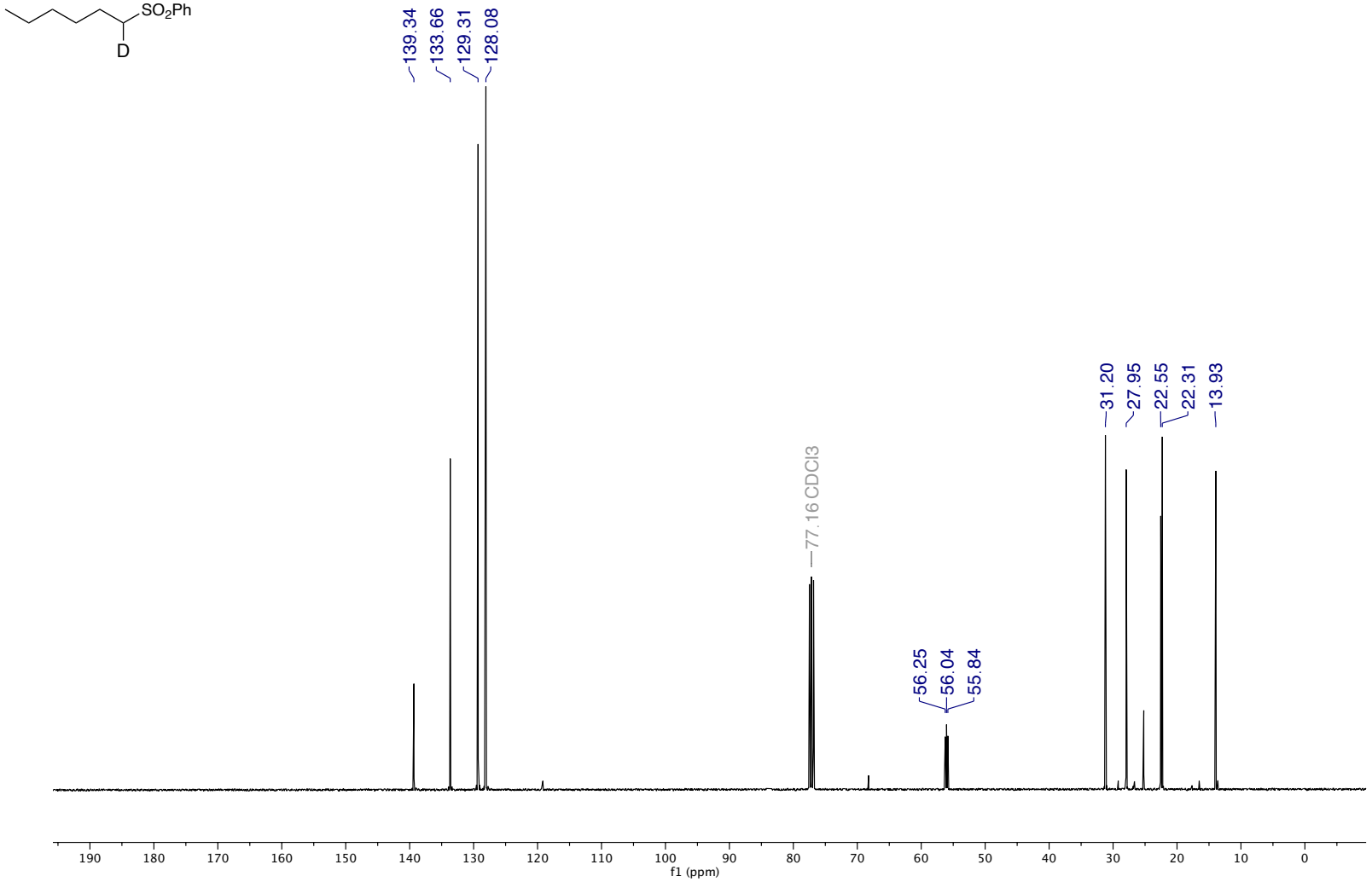



$^{2}$H-NMR (61 MHz, $CDCl_3$)



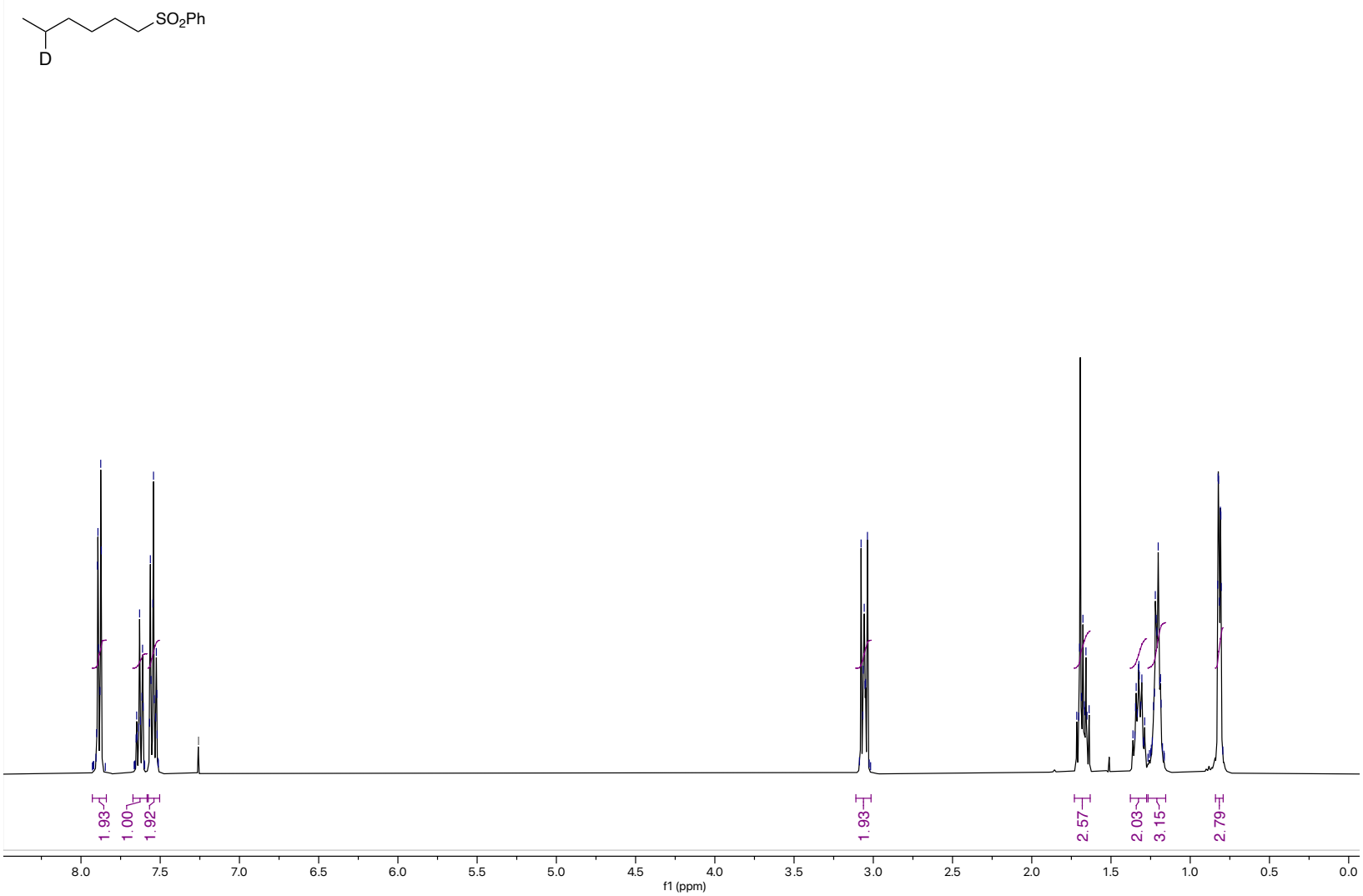
((Hexyl-1-*d*)sulfonyl)benzene

$^{13}$C-NMR (101 MHz, $CDCl_3$)



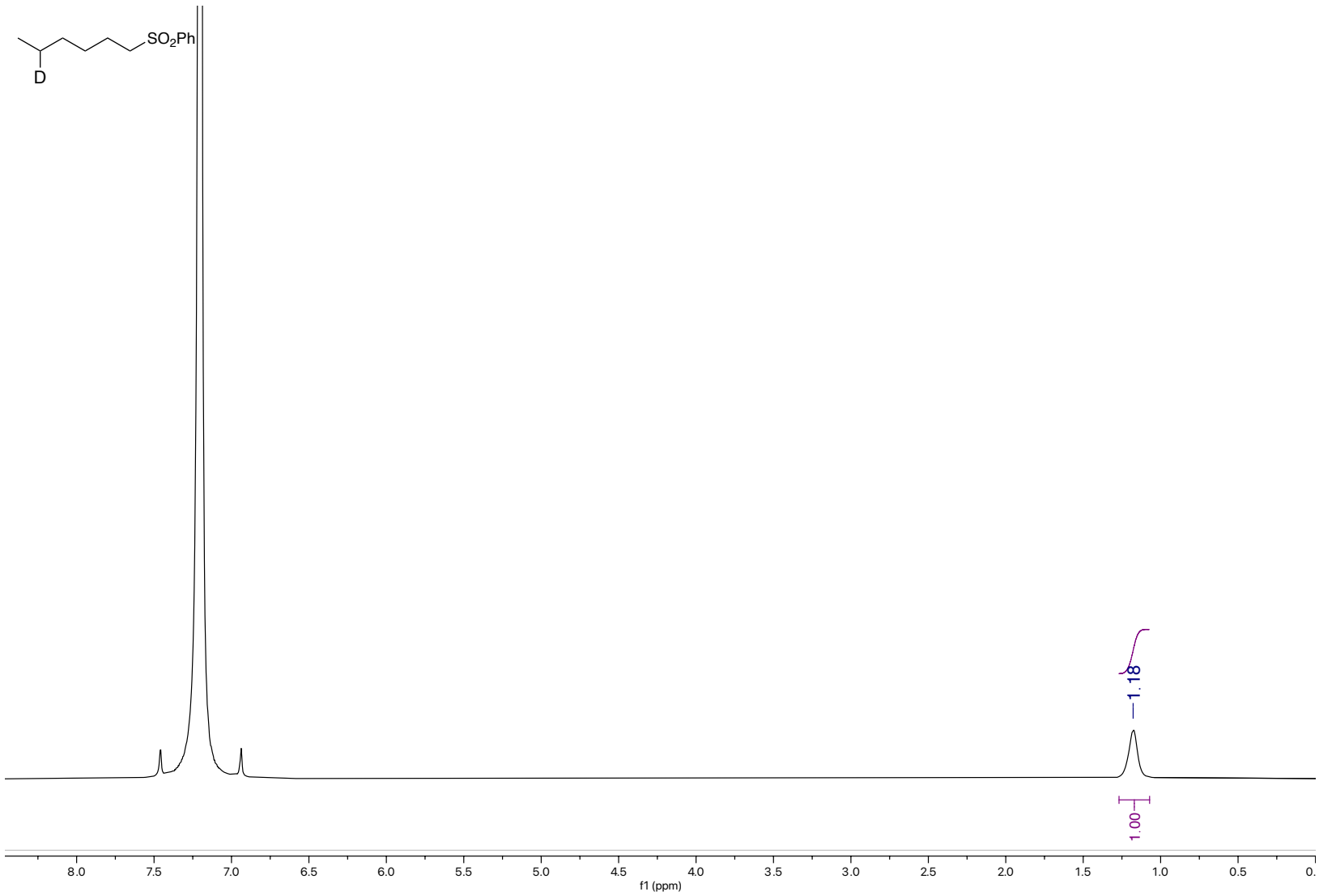
((Hexyl-5-*d*)sulfonyl)benzene

$^1$H-NMR (400 MHz, $CDCl_3$)



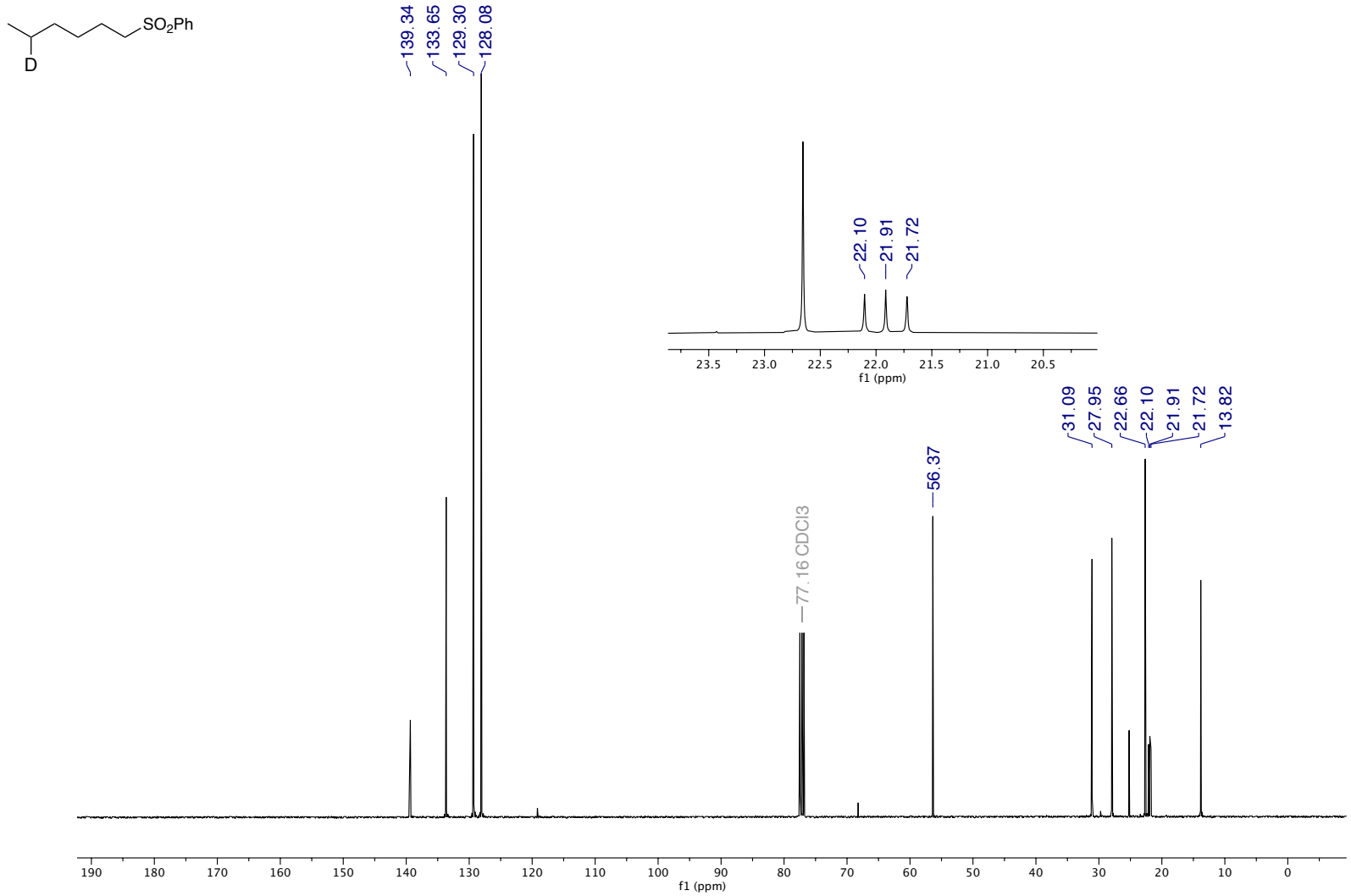
((Hexyl-5-*d*)sulfonyl)benzene

$^2$H-NMR (61 MHz, $CDCl_3$)

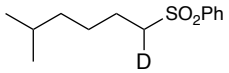


((Hexyl-5-*d*)sulfonyl)benzene

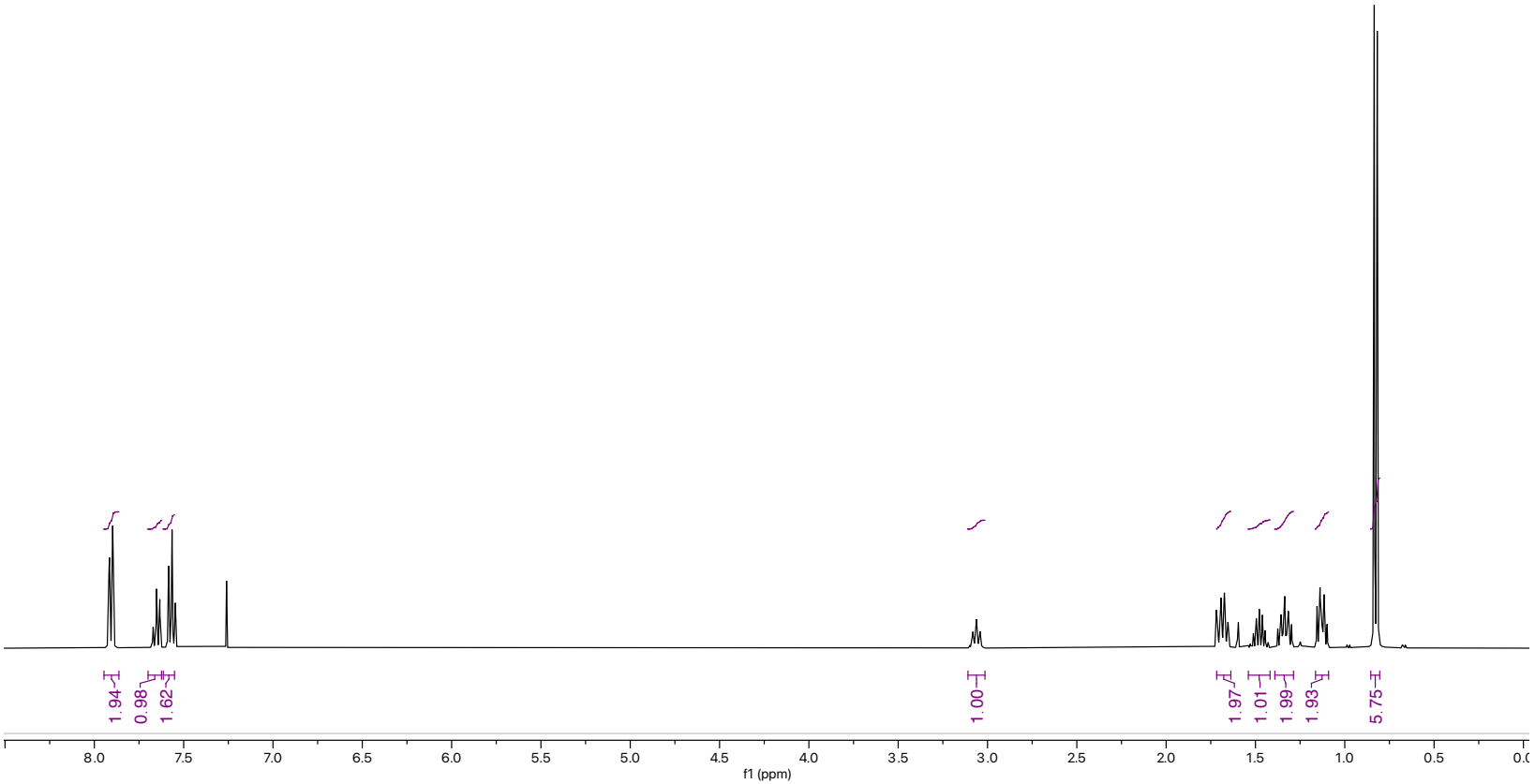
$^{13}$C-NMR (101 MHz, $CDCl_3$)



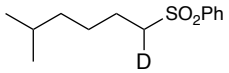
((5-Methylhexyl-1-*d*)sulfonyl)benzene



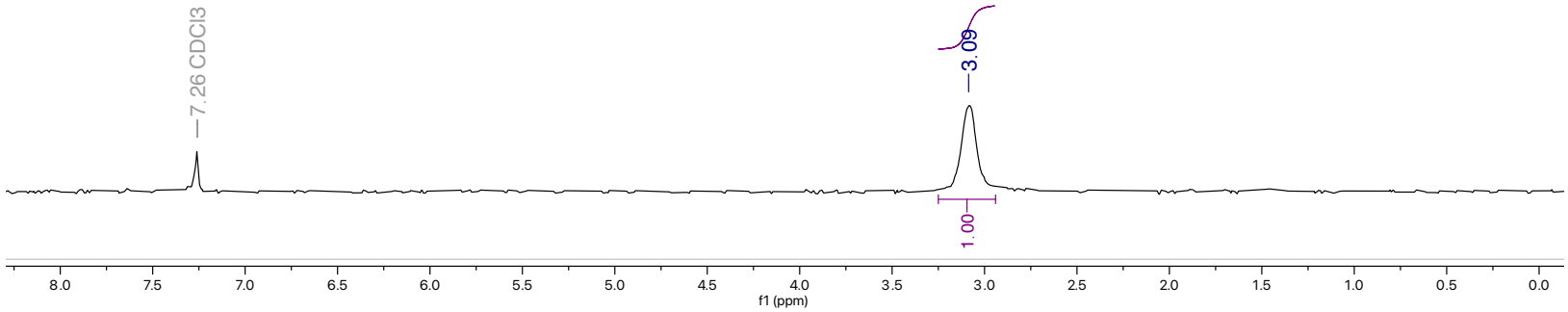

$^{1}$H-NMR (400 MHz, $CDCl_3$)



((5-Methylhexyl-1-*d*)sulfonyl)benzene

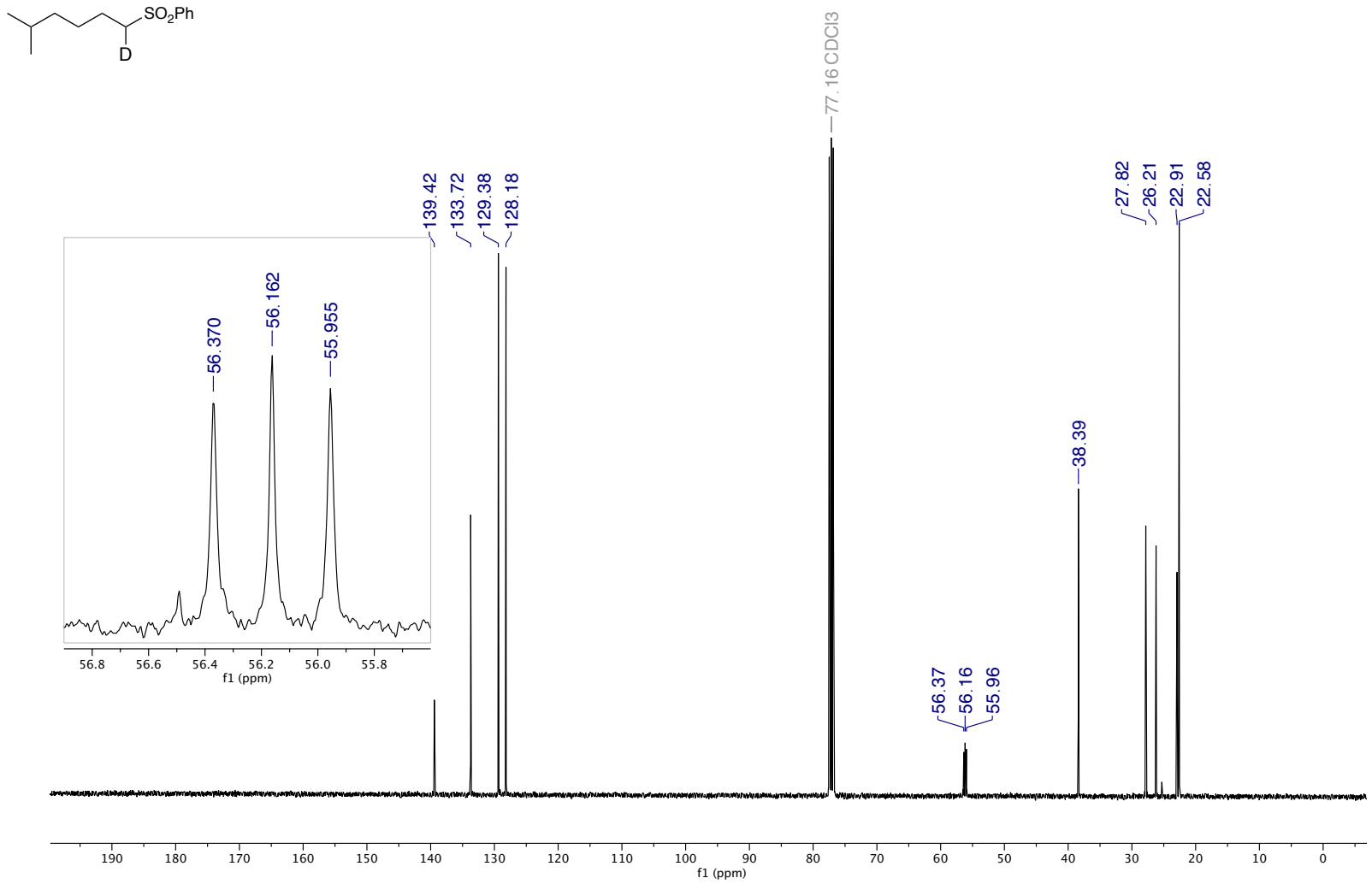



$^{2}$H-NMR (61 MHz, $CDCl_3$)

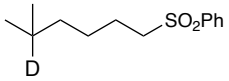


((5-Methylhexyl-1-*d*)sulfonyl)benzene

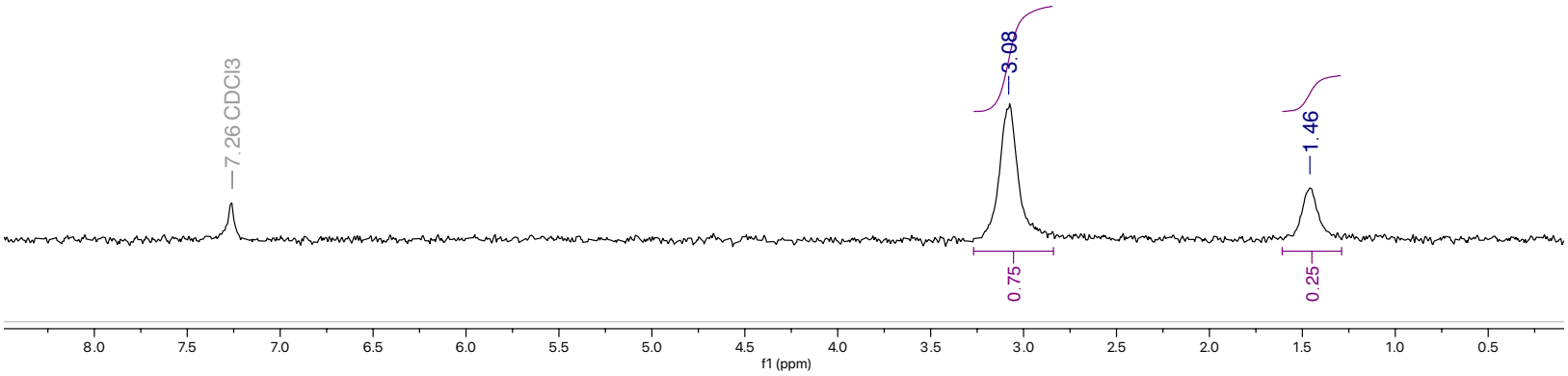
$^{13}$C-NMR (101 MHz, $CDCl_3$)



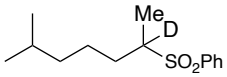
((5-Methylhexyl-5-d)sulfonyl)benzene



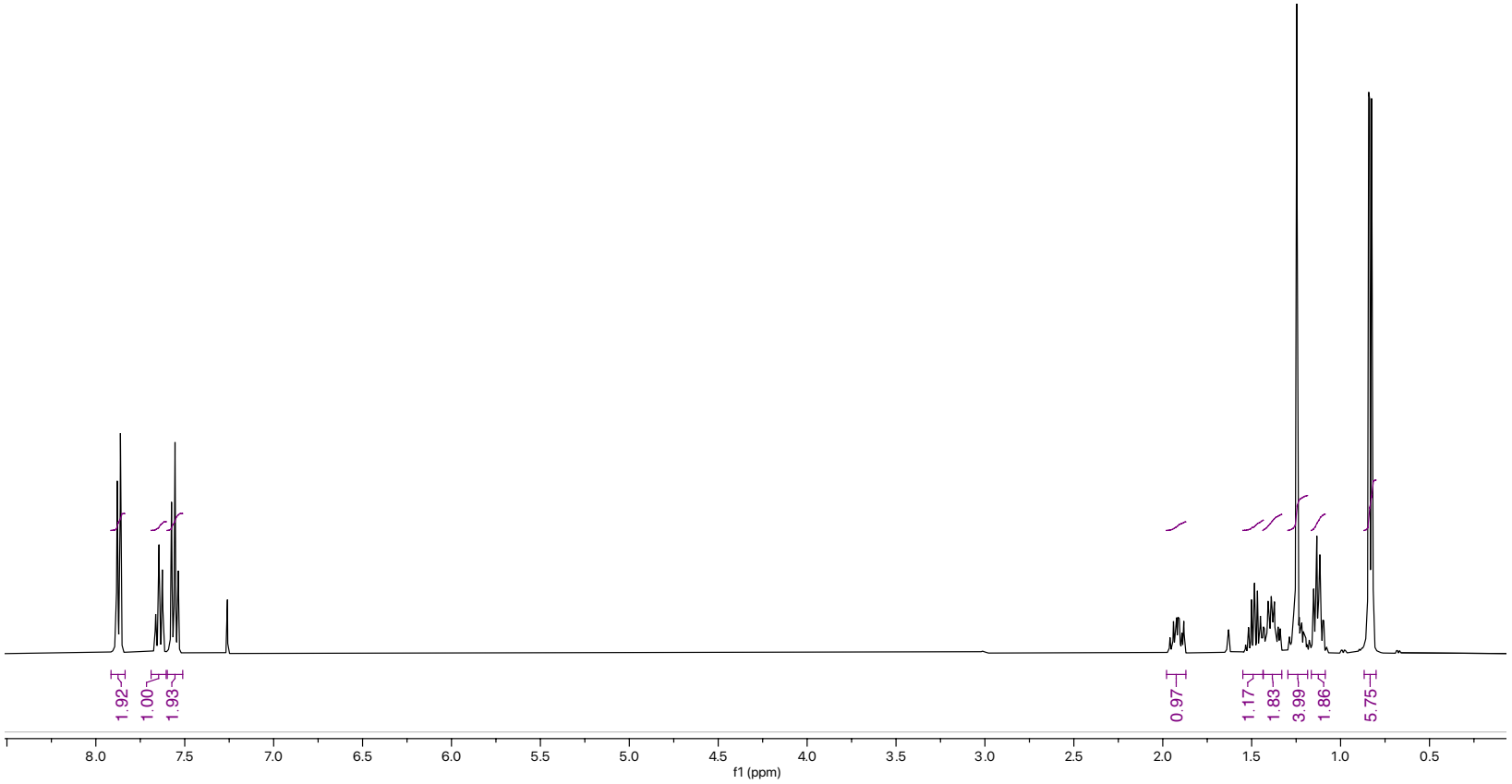

$^{2}$H-NMR (61 MHz, $CDCl_3$)



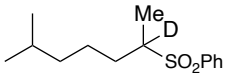
((6-Methylheptan-2-yl-2-*d*)sulfonyl)benzene



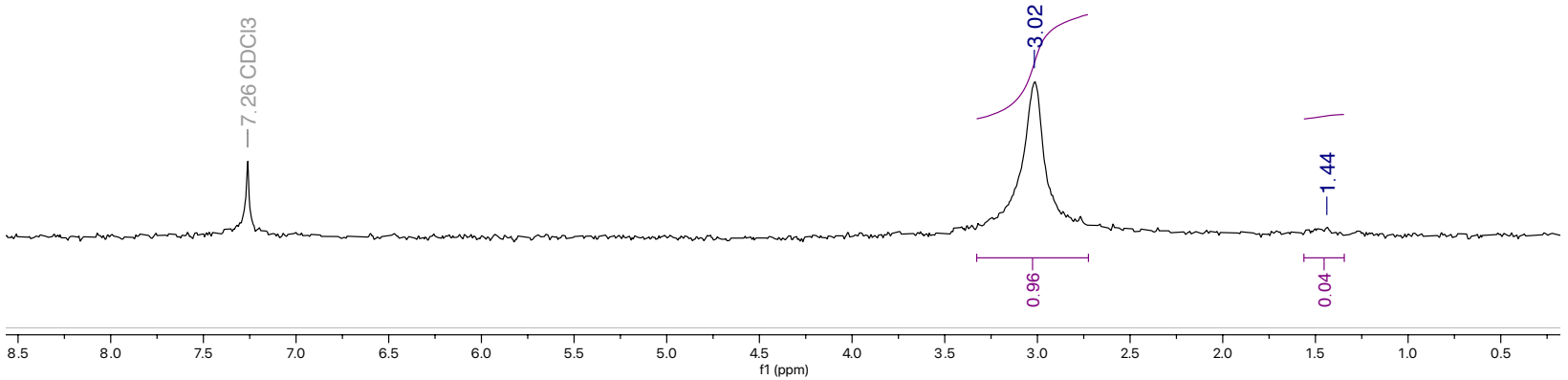

$^{1}$H-NMR (400 MHz, $CDCl_3$)



((6-Methylheptan-2-yl-2-*d*)sulfonyl)benzene

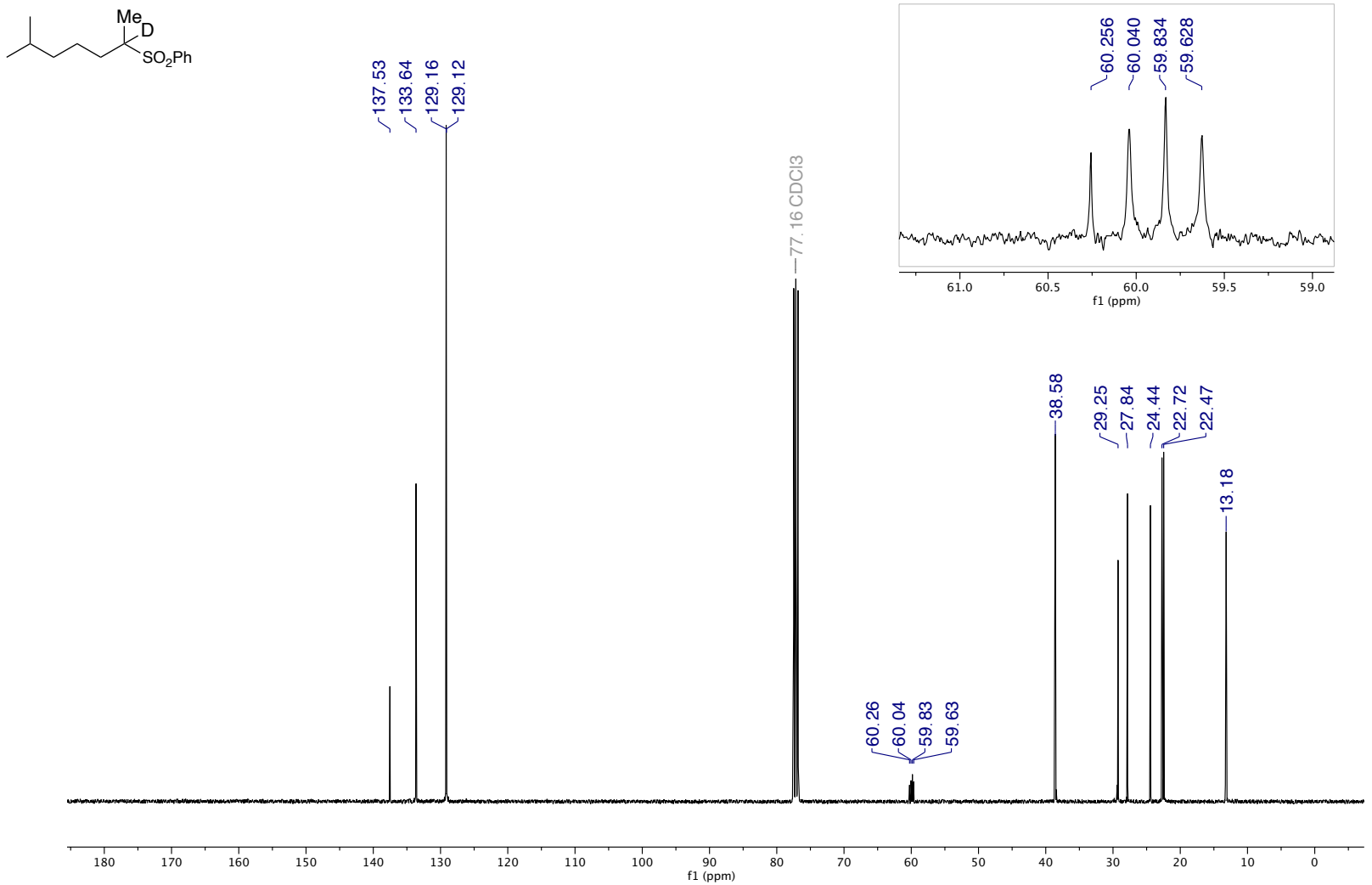



$^{2}$H-NMR (61 MHz, $CDCl_3$)



((6-Methylheptan-2-yl-2-*d*)sulfonyl)benzene

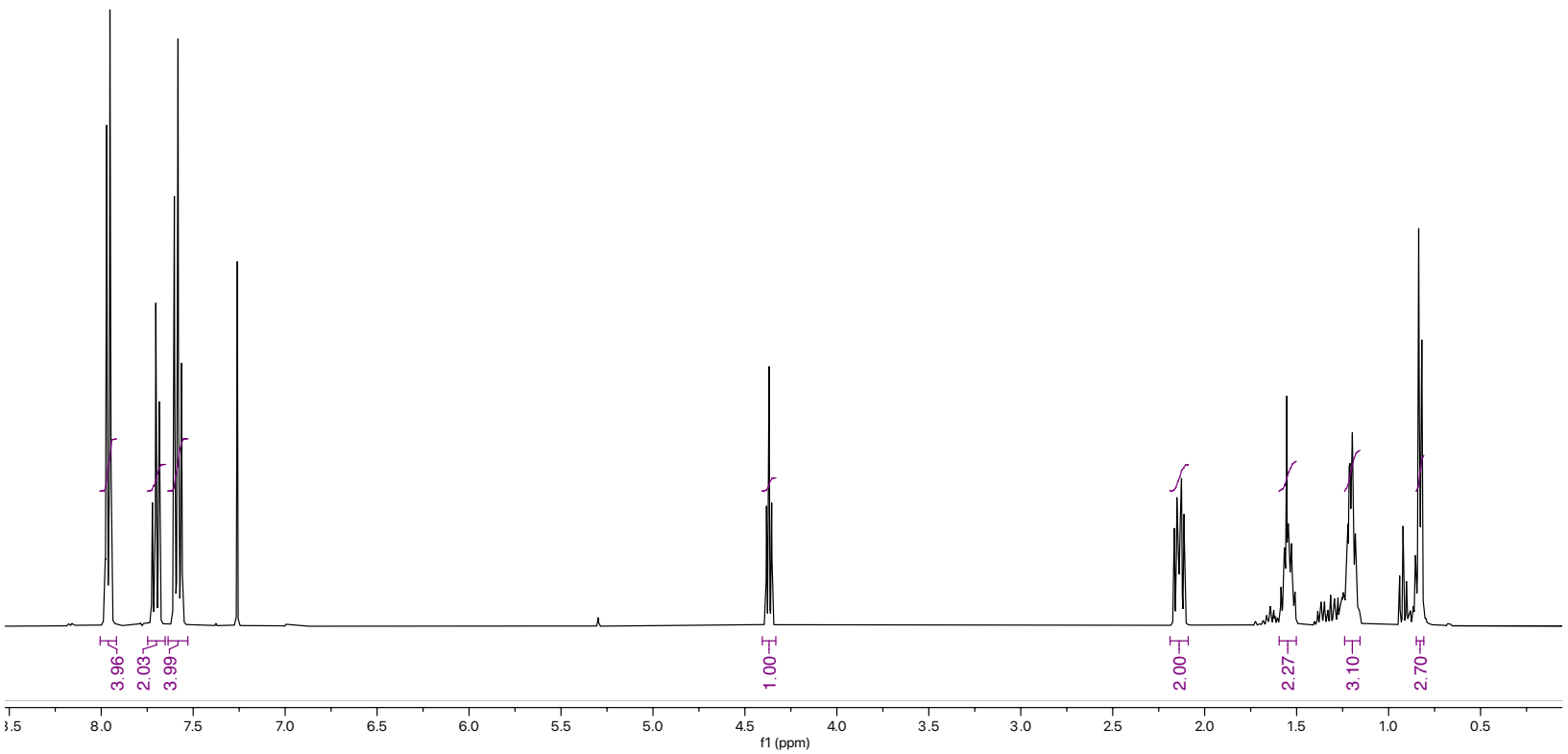
$^{13}$C-NMR (101 MHz, $CDCl_3$)



(Hexane-1,1-diyldisulfonyl-5-*d*)dibenzene

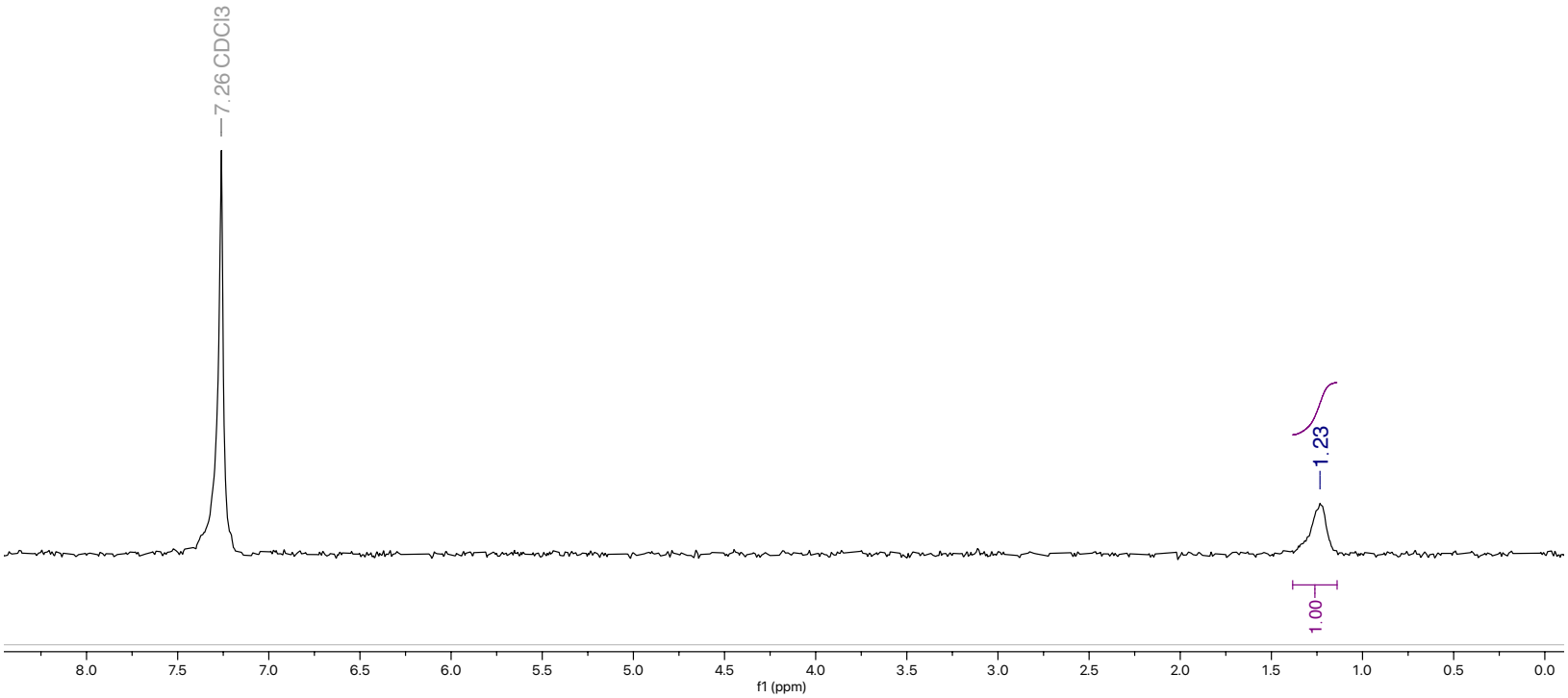
$^1$H-NMR (400 MHz, $CDCl_3$)



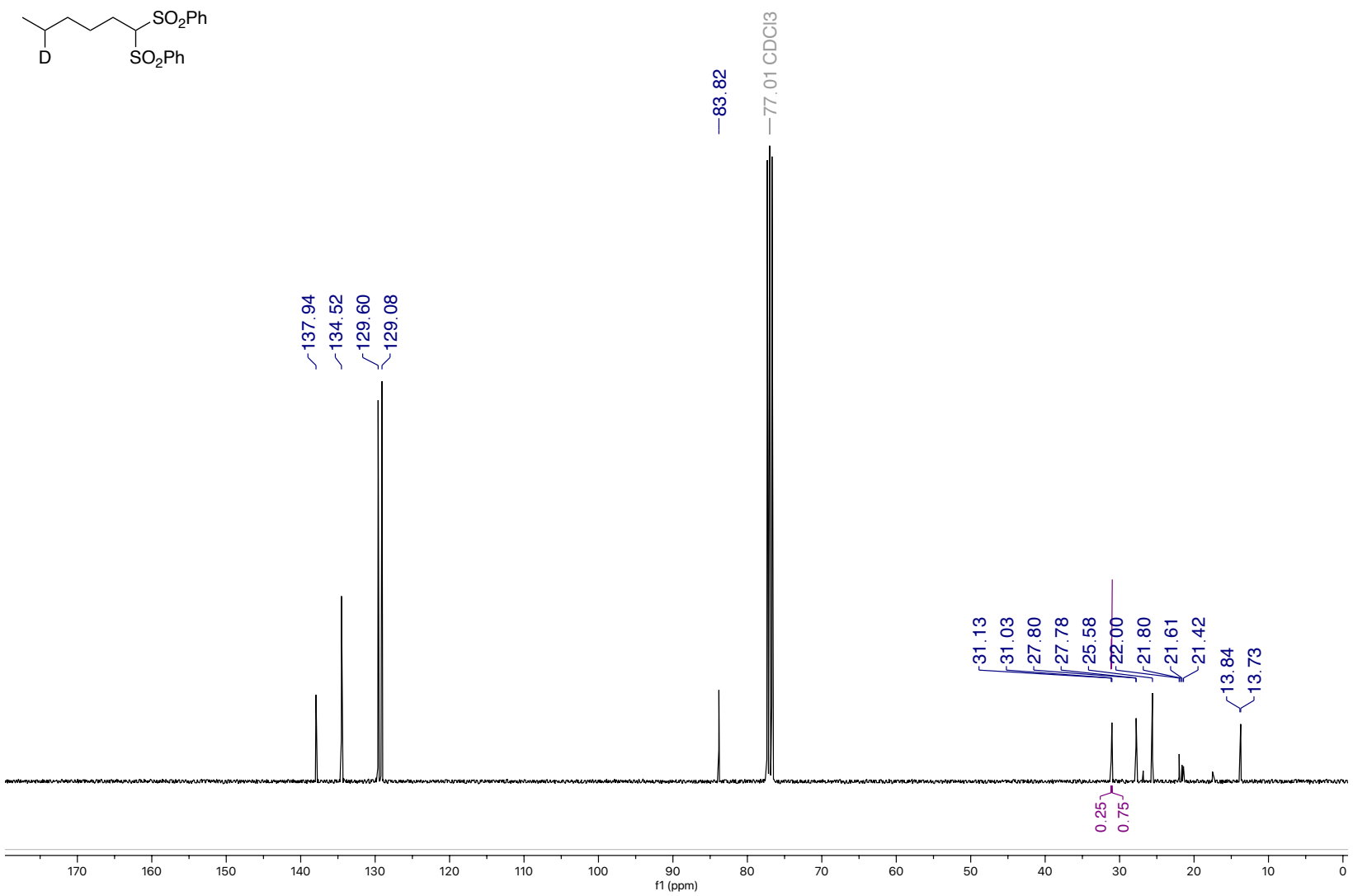
(Hexane-1,1-diyldisulfonyl-5-*d*)dibenzene

$^{2}$H-NMR (61 MHz, $CDCl_3$)

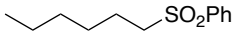


(Hexane-1,1-diyldisulfonyl-5-*d*)dibenzene

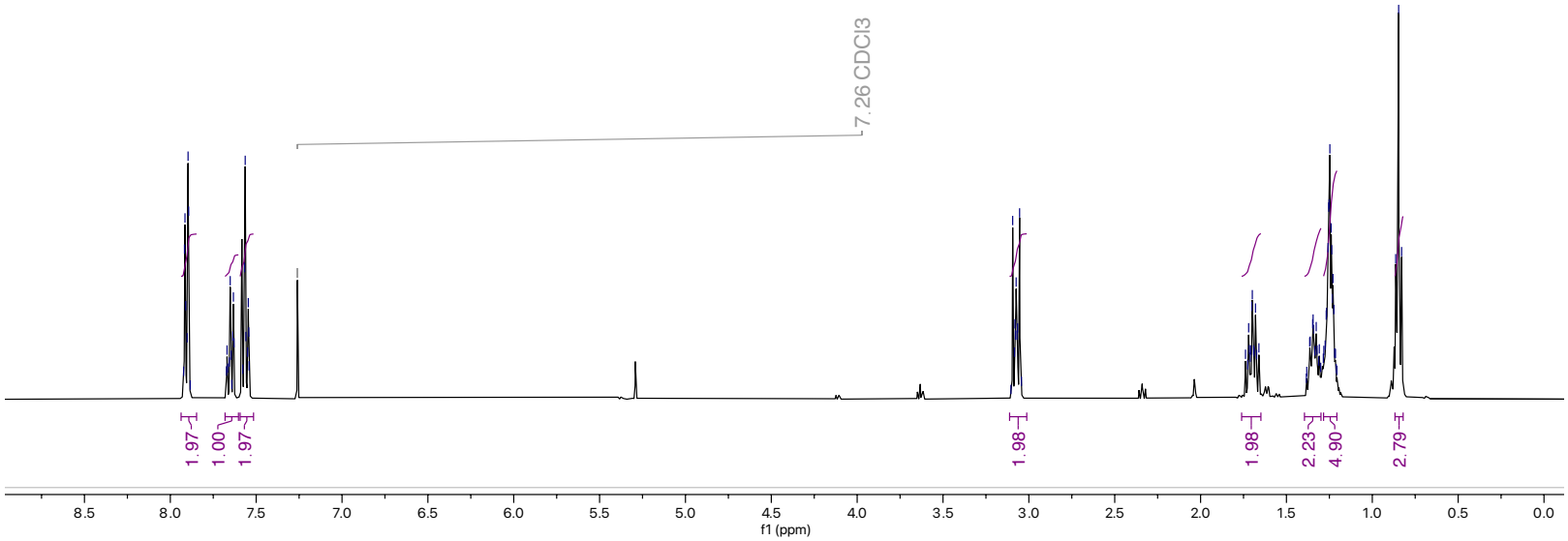
$^{13}$C-NMR (101 MHz, $CDCl_3$)



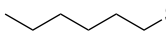
(Hexylsulfonyl)benzene



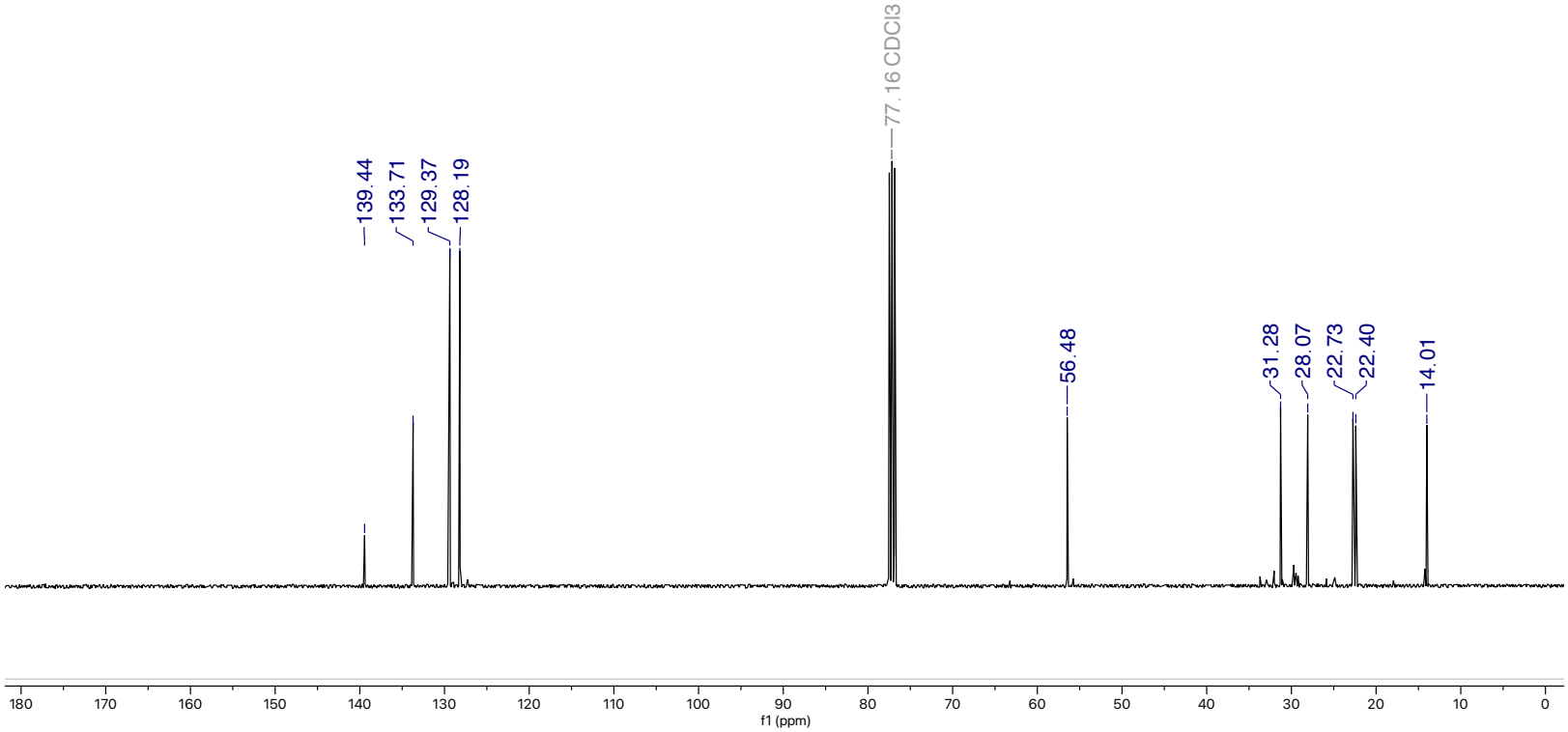

$^1$H-NMR (400 MHz, $CDCl_3$)



(Hexylsulfonyl)benzene

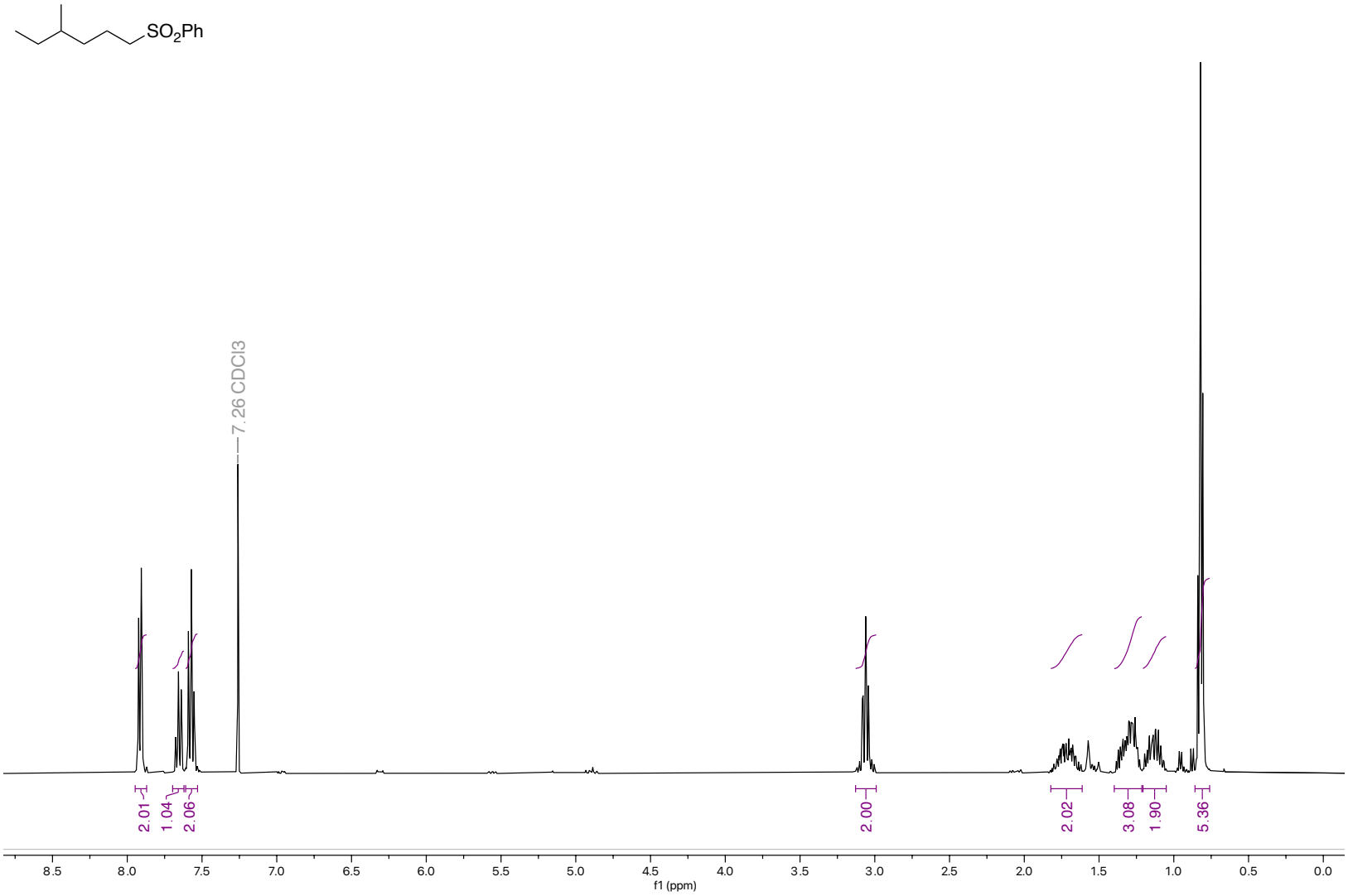



$^{13}$C-NMR (101 MHz, $CDCl_3$)



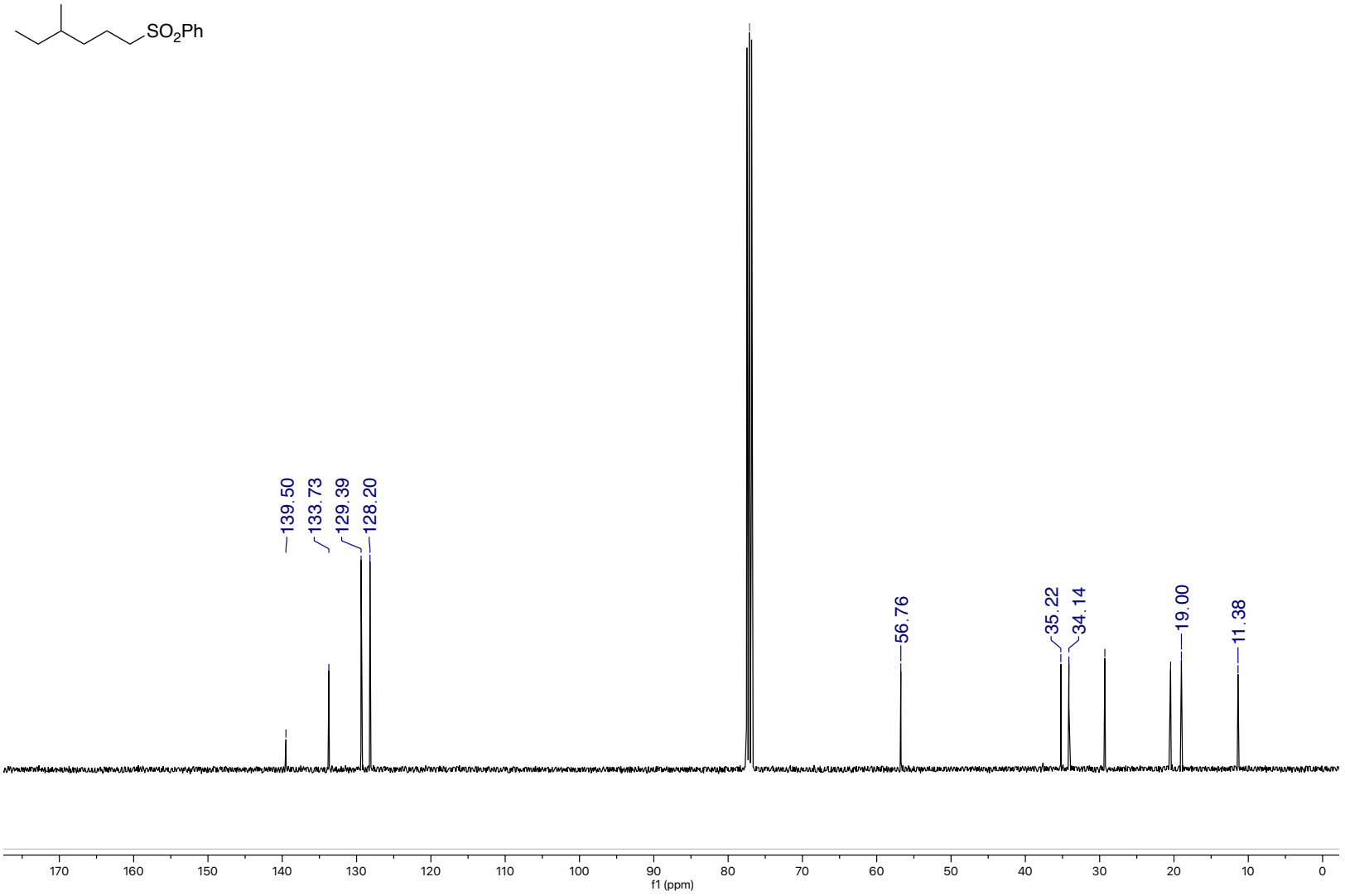
((4-Methylhexyl)sulfonyl)benzene

$^1$H-NMR (400 MHz, $CDCl_3$)



((4-Methylhexyl)sulfonyl)benzene

$^{13}$C-NMR (101 MHz, $CDCl_3$)



# Declaration of consent

on the basis of Article 18 of the PromR Phil.-nat. 19

Name/First Name: Sissengaliyeva Gulsana

Registration Number: 20-113-445

Study program: PhD in Chemistry and Molecular Sciences

Bachelor ☐ Master ☐ Dissertation ☑

Title of the thesis: Radical-Mediated Reactions Involving Fluorinated Reagents and Sulfones

Supervisor: Prof. Dr. Philippe Renaud

I declare herewith that this thesis is my own work and that I have not used any sources other than those stated. I have indicated the adoption of quotations as well as thoughts taken from other authors as such in the thesis. I am aware that the Senate pursuant to Article 36 paragraph 1 litera r of the University Act of September 5th, 1996 and Article 69 of the University Statute of June 7th, 2011 is authorized to revoke the doctoral degree awarded on the basis of this thesis.
For the purposes of evaluation and verification of compliance with the declaration of originality and the regulations governing plagiarism, I hereby grant the University of Bern the right to process my personal data and to perform the acts of use this requires, in particular, to reproduce the written thesis and to store it permanently in a database, and to use said database, or to make said database available, to enable comparison with theses submitted by others.

06.06.2024

Place/Date

Signature