CARBON DIOXIDE-MEDIATED PREPARATION OF AMINE-BORANES

by

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Dedicated to Charles "Charlie" Milliken

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ABSTRACT

Since their discovery by Burg and Schlesinger in 1937, amine-boranes have enjoyed a rich preparative history and have experienced reinvigorated interest as valuable reagents for organic syntheses. Previously, the Herbert C. Brown Center for Borane Research has reported their synthesis from $NaBH_4$ and amines via the intermediacy of $(NH_4)_2SO_4$ or $NaHCO_3$. Described herein is a CO_2-mediated amine-borane synthesis that accommodates all classes of amines, particularly long-chain trialkyl- and pyridine-like heteroarylamines.

CHAPTER 1. PRIOR SYNTHESES OF AMINE-BORANES

1.1 General Background of Amine-Boranes

Formally, amine-boranes can be described as complexes of borane, which acts as a Lewis acid, and an amine, which acts as a Lewis base. In this complex, the nitrogen atom's lone pair of electrons forms a coordinate covalent, also known as a dative, bond via donation into the vacant borane 2*p* orbital (Figure 1.1).[1] Such borane adducts can typically be formed with any Lewis base (molecules containing nitrogen, oxygen, phosphorous, or sulfur, wherein the hetero-atom possesses an available pair of non-bonding electrons). Common, simplistic examples of these classical adducts include ammonia-borane (NH_3-BH_3, AB), borane-tetrahydrofuran (BH_3-THF, BTHF), phosphine-borane (PH_3-BH_3, PB), borane-dimethylsulfide [BH_3-$S(CH_3)_2$, BDMS, DMSB], etc.

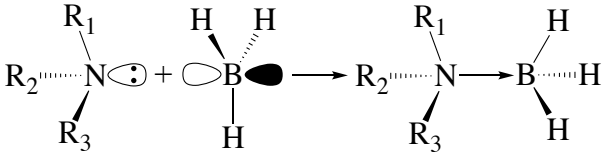


Figure 1.1 $sp^3\sigma$-pσ dative bond formation in an amine-borane

The discovery of a boron-nitrogen dative bond is attributable to Gay-Lussac in 1809[2], and in 1937, Burg and Schlesinger were credited with the first report of an amine-borane, trimethylamine-borane (Figure 1.2).[3] With regards to Gay-Lussac, Burg, and Schlesinger, their initial discoveries have ushered more than three-quarters of a century (and beyond) of research into amine-boranes and their derivatives, with diverse applications ranging from reagents in organic syntheses[4] to hydrogen storage materials[5] to pharmacologically active compounds.[6]

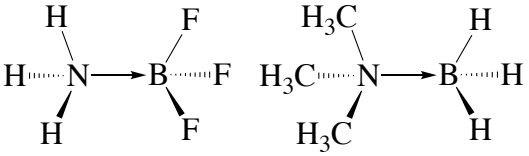


Figure 1.2 Ammonia-trifluoroborane (left) & trimethylamine-borane (right)

The first historical application of amine-boranes is taken to be as reducing agents, as noted in Hutchins et al.'s seminal 1984 review.[7] A full treatment of the numerous applications of amine-boranes and their derivatives, as well as their relatives like phosphine- (or phosphane-) and sulfide-boranes, is not within the scope of this introduction, though such literature serves as the basis for several fine investigations[6c, 8] and reviews (Figure 1.3[9]).[1, 2b, 7, 10]

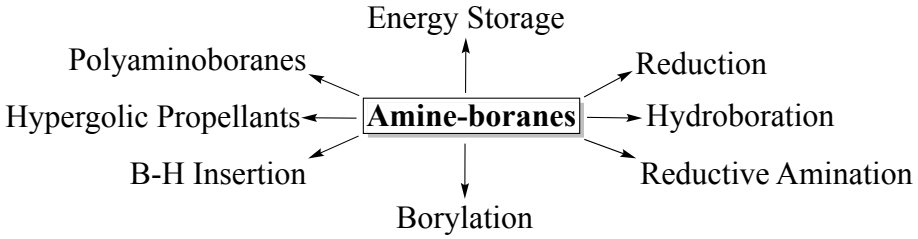


Figure 1.3 Amine-borane applications (Adapted from Kulkarni & Ramachandran, 2017)

Amine-boranes are perhaps most commonly recognized as valuable reagents due to the hydridic nature of the hydrogen atoms on the borane functionality; it is this hydridicity that enables the diverse and unique chemistry of amine-boranes (To illustrate this principle, some older representations of amine-boranes, historically called amine-"borines" or "-borazanes," denote positive and negative charges on the N- and B-atoms, respectively, while maintaining the overall neutrality of the complex) (Figure 1.4).[2b, 10d, 11] It is evident that AB is the structurally simplest of the amine-boranes, regarding the substitution on the N-atom.

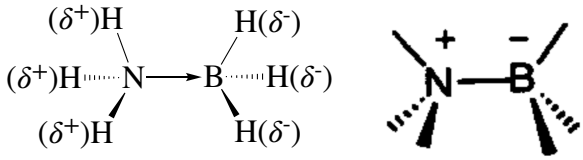


Figure 1.4 General hydridicity of ammonia-borane (left) & historical representation[10d] (right)

By extension, the generally broad classifications of amine-boranes include: ammonia-borane (AB), primary (1°), secondary (2°), tertiary (3°), and heteroaryl (HA) amine-boranes, wherein the N-atom is involved in the aromaticity of the ring; these classifications describe the amount of non-hydrogen substitution on the N-atom. Within the 2° and 3° classifications, there exists the subset of heterocyclic (HC) amine-boranes, e.g., aziridine-borane, wherein the N-atom

is part of the closed ring. Though not as prominent, there are also amine-bisboranes (Bis),[12] with hydrazine-bisborane ($H_3BNH_2NH_2BH_3$) and ethylenediamine-bisborane [$H_3BNH_2(CH_2)_2NH_2BH_3$] as the most recognized examples; there appears to be scant reporting of amine-tris-, tetrakis-, or pentakis-boranes, especially no higher than five -BH_3 groups.[13] Interestingly, a recent (2019) patent describes the preparation of a trisborane complex [*N*,*N*-bis[2-(dicyclohexylphosphino)ethylamine-trisborane], wherein two of the three -BH_3 groups are coordinated to P-atoms and the third -BH_3 group is coordinated to an N-atom, representing a hybrid (Hyb) amine/phosphine-borane.[14] Moreover, there exists a subset within each of the aforementioned categories, barring AB, that includes functionalized (Func) amine-boranes, for instance methan*ol*amine-borane, 2-diethylaminoethane*thiol*-borane, or *allyl*amine-borane; in some instances, these accompanying functional groups are sensitive to boranation, i.e., installment of the -BH_3 group, so care must be taken when choosing a preparative method, as will later be discussed (Figure 1.5).

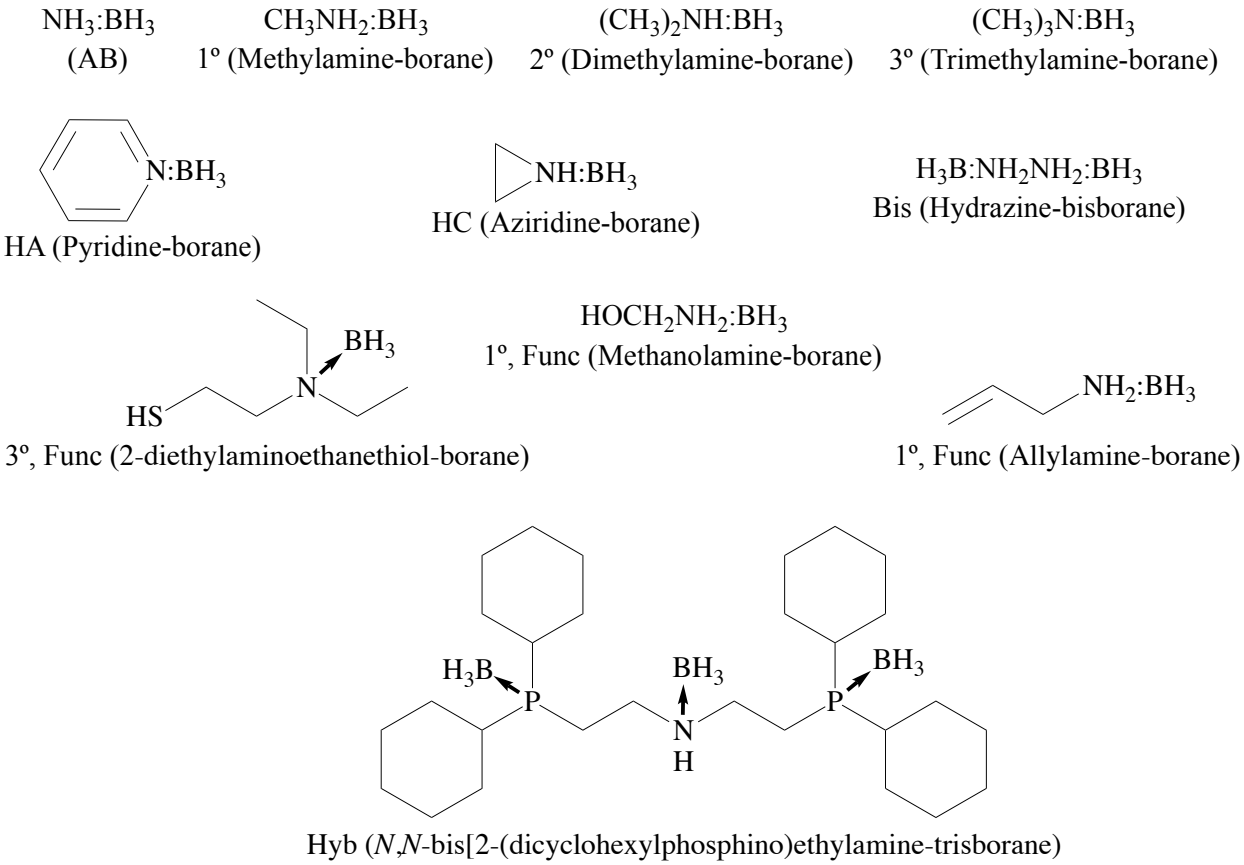


Figure 1.5 Examples of various amine-boranes

In terms of the hydridicity of an amine-borane, this particular property is dependent upon both the N-atom's and the B-atom's substituent(s), though in the case of non-substitution on the B-atom (BH_3), hydride-donating tunability lies with the N-atom. More generally, the overall stability of an amine-borane is contingent on the substitution(s) of the N- and B-atoms. As an extreme example, aniline-borane is stable at -30 °C, the minimum temperature required for its preparation, but can begin to dehydrocouple as ambient temperatures are approached, assuming standard pressure.[2b, 10d, 15] The most notorious factor influencing amine-borane stability is the steric bulk of the group(s) on both the B- and N-atoms. The steric bulk phenomenon has been quantitatively demonstrated by assessing the molar enthalpies of formation (ΔH_f) between certain amines and BTHF; the reported ΔH_f trends are: 1) *n*$BuNH_2$-BH_3 > *n*Bu_2NH-BH_3 > *n*Bu_3N-BH_3 and 2) Et_2NH-BH_3 > *n*Pr_2NH-BH_3 > *n*Bu_2NH-BH_3.[2b, 16] Understandably, the resultant instability from increasingly bulky groups on the B- and/or N-atoms is due to poor orbital overlap (Figure 1.1). There have also been suggestions that increased alkyl bulk on the N-atom entails reduced Lewis basicity by increasing the bond angle around the N-atom, thereby reducing the *p* character of the interacting lone-pair and increasing its *s* character.[2b, 17] As a general rule of thumb, Hutchins et al. posit that a stable adduct can be formed so long as the pK_a of the amine is greater than 5.0 – 5.5.[7] It is also noted that those amines whose pK_a values lie within that range can form the dative bond with borane but that this N-B bond is weaker compared to those amines with pK_a values greater than the specified range.

Invariably, some of the same principles governing the stability of an amine-borane adduct also apply to the hydride-donating capability of the amine-borane; it is understood that the amine-borane adduct must itself be stable in order to react. Most prominently, when describing amine-boranes simply bearing the -BH_3 moiety, the identity of the amine governs reductive capabilities of the hydrides. For example, it has been shown that increasing alkyl substitution on the amine decreases reducing ability, illustrated by the trend AB > RNH_2-BH_3 > R_2NH-BH_3 > R_3N-BH_3.[2b, 7] Regarding the sister compounds, heteroaryl- and *N*-arylamine-boranes, the trend is that those amines with lower pK_a values are better reducing agents. In an application-related example, several different amine-boranes were tested in their reductive abilities towards a gold salt, $AuPPh_3Cl$, for the preparation of nanoparticles, and their capacities to reduce the salt were: AB > *t*-butylamine-borane ≈ triethylamine-borane > morpholine-borane, illustrating the effect of the N-atom's substituents on hydridicity.[10b, 18]

Another interesting facet of hydride-donating governability is the report that acidic, aqueous/mixed aqueous solvents can enhance the reducing ability of some amine-boranes; this has been demonstrated using morpholine-borane and several of its derivatives and relatives.[2b, 10h, 19] In a specific example, without acidification, *N*,*N*,*N*-trimethylamine-borane is unable to reduce cyclohexanone to the corresponding alcohol within 38 hours reaction time. With acidification, the ketone-alcohol transformation is affected within 8 minutes with 80% conversion. It has also been noted that solvent selection and increased temperatures, up to a certain extent ($\sim 70 < T < 100$ °C), can improve amine-borane hydridicity.[7] Finally, the addition of a Lewis acid catalyst, such as $AlCl_3$ or BF_3, markedly improves the reductive effect of certain amine-boranes due to a complexing action of the Lewis acid with the carbonyl oxygen, which in turn facilitates the intermolecular hydride transfer from the amine-borane to the δ^+ carbon.[7, 20]

Within the framework of organic chemistry, amine-boranes are most prominently viewed as reducing agents; Hutchins et al. regard amine-boranes as essential "in the arsenal of reductive weapons available to chemists."[7] Though not definitive, it is within reason to suggest that of the available reducing agents, including amine-boranes, sodium borohydride ($NaBH_4$), also known as sodium tetrahydridoborate, is the most widely used and commonly recognized.[21] In fact, it has been boldly asserted that "every beginning organic text mentions the use of sodium borohydride as a reducing agent."[22] Moreover, *Ullmann's Encyclopedia of Industrial Chemistry* indicates that thousands of metric tons of $NaBH_4$ are annually manufactured and utilized worldwide, representing a multimillion dollar business; such usage warrants the recognition of $NaBH_4$ as "by far the most important commercially available complex hydride."[21b, 23] Other popular, often-employed reducing agents include: lithium aluminum hydride (LAH),[24] lithium borohydride (LBH),[25] lithium triethylborohydride [Superhydride®, LiTEBH],[26] sodium cyanoborohydride ($NaBH_3CN$),[27] lithium aminoborohydrides (LAB reagents),[28] diisobutylaluminum hydride (DIBAL, DIBAL-H),[29] sodium-bis(2-methoxyethoxy)aluminum hydride (SMEAH, Red-Al®),[30] and triethylsilane (TES).[31] A computational study ranks AB, a somewhat representative amine-borane, as roughly in between TES, a weak reducing agent, and BH_4^-, an intermediate reducing agent, in terms of reducing strength, as measured by ΔG values.[21c]

Given such an abundance of reducing agents, one might be prompted to consider how amine-boranes are set apart from their counterparts. With reference to the previous discussion, reducing strength is certainly the most obvious distinction that can be made between amine-

boranes and other reducing agents. However, tunability of amine-borane reducing strength is made possible by 1) manipulating the N-atom's substituent(s), 2) acidifying the solution, 3) varying the solvent, 4) adding a Lewis acid catalyst, and/or 5) adjusting the reaction temperature. It is worthwhile however to note that Brown and coworkers experimented with the tunability of SBH's reducing strength by changing the cation and substituting the H atom(s) with alkyl or alkoxy groups.[32]

Though Heiden and Latham cite AB as a representative amine-borane in their study on "[e]stablishing hydride donor abilities,"[21c] it is difficult to make a generalization about the hydridicity of amine-boranes due to the vastness of this class of compounds. Aside from customizable reducing abilities, amine-boranes are oftentimes far more soluble than their fellow hydride donors in common solvents, both aprotic and protic; some of these solvents include: benzene, dichloromethane, ether, hexane, methanol, tetrahydrofuran, and toluene. Notably, amine-boranes are mostly unreactive towards water and other protic solvents.[2b, 7, 10h] Finally, amine-boranes offer tantalizing advantages, especially over certain reducing agents like LAH, LBH, and Superhydride® as well as boranating agents like diborane (B_2H_6, DB), BTHF, and BDMS, in terms of air- and moisture-sensitivity, pyrophoricity, and toxicity.[2b, 33]

The current discussion would be remiss if one of the more exotic applications of amine-boranes was not discussed prior to their synthetic history. By complexing the -BH_3 moiety with an asymmetric amine [$H_{(3-n)}R_nN$, such that $n = \{2, 3\}$ and $R_1 \neq R_2 \neq R_3$], it is possible to impart stereogenicity to the resultant amine-borane and perform an enantioselective reduction (Figure 1.1).[10d, 34] Similarly, chiral molecules possessing an amine functional group can be boranated and converted to chiral reducing agents.[7, 35] Between those two categories of chiral amine-borane reducing agents, it could be argued that the most infamous example is the Corey-Itsuno, or Corey-Bakshi-Shibata (CBS), reduction. The reaction development was first begun by Itsuno and coworkers in 1981 by reducing prochiral aromatic ketones with chiral alkoxy-amine-borane complexes.[36] Itsuno et al.'s work was extended by Corey, Bakshi, and Shibata in 1987, whereby Corey et al. demonstrated excellent enantioselectivity for the reduction of ketones using chiral oxazaborolidines (Figure 1.6).[37]

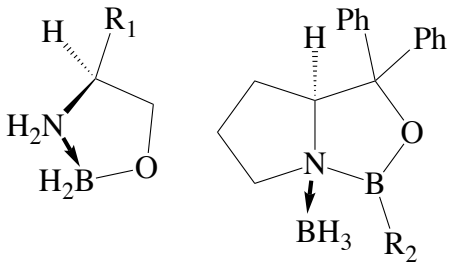


Figure 1.6 Itsuno's alkoxy-amine-borane (left) & Corey's oxazaborolidine-borane (right)

1.2 Chronological Syntheses of Amine-Boranes

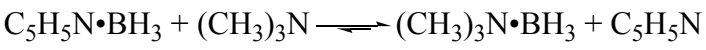
Having provided a cursory overview of amine-boranes and their properties, a chronological history of their most notable preparations can be presented. The emphasis of this timeline is to denote the first report of a particular synthetic style; once these syntheses are initially reported, there are seemingly innumerable accounts wherein most of the methods are employed and occasionally developed further. For clarification, the aim of this chronology is to establish a history of synthetic methods for amine-boranes, of which ammonia-borane is both a prime and unique example. Though some of the following synthetic methods are applicable to the synthesis of AB, not all of the methods can accommodate this parent amine-borane. Likewise, there are synthetic methods for attaining AB that are not amenable to other amine-boranes. As such, the current discussion will not emphasize those preparative methods that are exclusive to AB; there are several reviews that seek to address the vast preparative methods for AB alone.[10j, 33b, 38]

As mentioned earlier, the first report of an amine-borane, trimethylamine-"borine," was contributed by Burg and Schlesinger in 1937 (Scheme 1.1).[3] Brown later described the diborane-based process for preparing "borine trialkyl amines" in 1958.[39]

$$3\ N(CH_3)_3 + B_2H_6 \longrightarrow 2\ N(CH_3)_3{\bullet}BH_3 + N(CH_3)_3$$

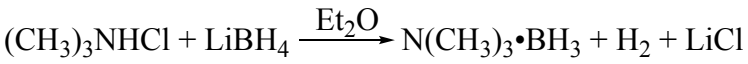
Scheme 1.1 Synthesis of trimethylamine-borine via diborane & free amine

In 1942, Brown, Schlesinger, and Cardon used the diborane protocol to develop a transamination method for synthesizing amine-boranes, wherein the free amine displaces the amine that is already complexed with borane (Scheme 1.2).[40] The transamination method was later expounded upon by Baldwin and Washburn in 1961,[41] as well as several others, including the Ramachandran group.[42]



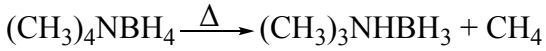
Scheme 1.2 Synthesis of trimethylamine-borane via transamination

More than a decade passed before another novel synthetic procedure for amine-boranes was presented, when Schaeffer and Anderson prepared trimethylamine-borine via LBH in 1949 (Scheme 1.3).[43]



Scheme 1.3 Synthesis of trimethylamine-borine via LBH & amine•hydrochloride

In 1952, Banus, Gibb, Jr., and Bragdon posited a thermal-decomposition method for making amine-boranes (Scheme 1.4).[44] The pyrolysis method was further explored by Safronov, Jalisatgi, and Hawthorne in their 2019 patent investigating the decomposition of organoammonium tetrahydroborates.[45]



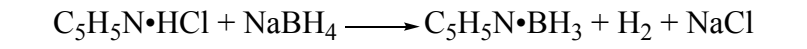
Scheme 1.4 Synthesis of trimethylamine-borine via tetramethylammonium borohydride

In 1953, Schechter presented a unique synthesis of amine-boranes via electrolysis between an anode and cathode of an ionic borohydride in a non-aqueous solvent like an amine (Scheme 1.5).[46]

Scheme 1.5 Synthesis of dimethylamine-borane via electrolysis with Hg cathode and Pt anode

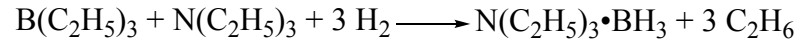
In a similar fashion to Schaeffer and Anderson's LBH preparative method, Taylor, Grant, and Sands synthesized pyridine-borane using SBH with the amine as the solvent in 1955 (Scheme 1.6).[47] It is likely that previous authors did not report a synthesis of amine-boranes via SBH due to difficulties associated with SBH's preparation, though a suitable preparation had in

fact been known for some time.[48] However, due to World War II national security concerns, Schlesinger, Brown, and Finholt were unable to publish their findings.[21b, 21e, 32b, 49] The chemical and patent literature is rife with adjustments and alleged improvements to this particular process.[50]



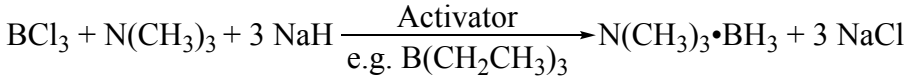
Scheme 1.6 Synthesis of pyridine-borane via SBH & amine•hydrochloride

Shortly after Taylor, Grant, and Sands's synthesis of pyridine-borane, several patents and publications from both academia and the chemical industry began describing the preparation of amine-boranes. First among these descriptions was from Köster in February 1957, wherein he developed a route to amine-boranes using high pressure hydrogenolysis of trialkylboranes (Scheme 1.7).[51]



Scheme 1.7 Synthesis of triethylamine-borane via TEB & free amine

Soon after Köster's work, "Preparation of Amine-Borines" was proposed by Jenkner in March 1957, wherein he prepared various amine-boranes with an emphasis on the addition of boron trichloride to the reaction mixture (Scheme 1.8);[52] other ensuing patents have extended the scope of Jenkner's work.[53]



Scheme 1.8 Synthesis of trimethylamine-borine via BCl_3/NaH & free amine

Concluding 1957 as a popular year for amine-borane related patents, Bragdon described a three-step, amine-carbamate-based preparation in August 1957 (Scheme 1.9).[54]

$$CO_2 + 2\ C_3H_7NH_2 \longrightarrow C_3H_7NHCOOC_3H_7NH_3\ (1)$$
$$NaBH_4 + C_3H_7NHCOOC_3H_7NH_3 \longrightarrow C_3H_7NHCOONa + C_3H_7NH_3BH_4\ (2)$$
$$C_3H_7NH_3BH_4 \longrightarrow C_3H_7NH_2BH_3 + H_2\ (3)$$

Scheme 1.9 Synthesis of isopropylamine-borane via SBH & an amine-carbamate

Following Jenkner's patent, as a corporate entity, Farbenfabriken Bayer Aktiengesellschaft formulated a British patent for an amine-borane synthetic process in May 1959, wherein the amine-borane is obtained from a tertiary amine salt, an aqueous solution of metal borohydride, and an inert solvent (Scheme 1.10).[33b, 55] However, Haberland and Stroh filed an identical U.S. patent earlier in 1958 for the same process.[56] Notably, many other patents have followed suit with "similar yet different" acid-mediated proposals.[57]

$$(CH_3CH_2)_3N + KBH_4 + B(OH)_3 + H_2O \longrightarrow (CH_3CH_2)_3N{\bullet}BH_3 + KB(OH)_4 + H_2$$

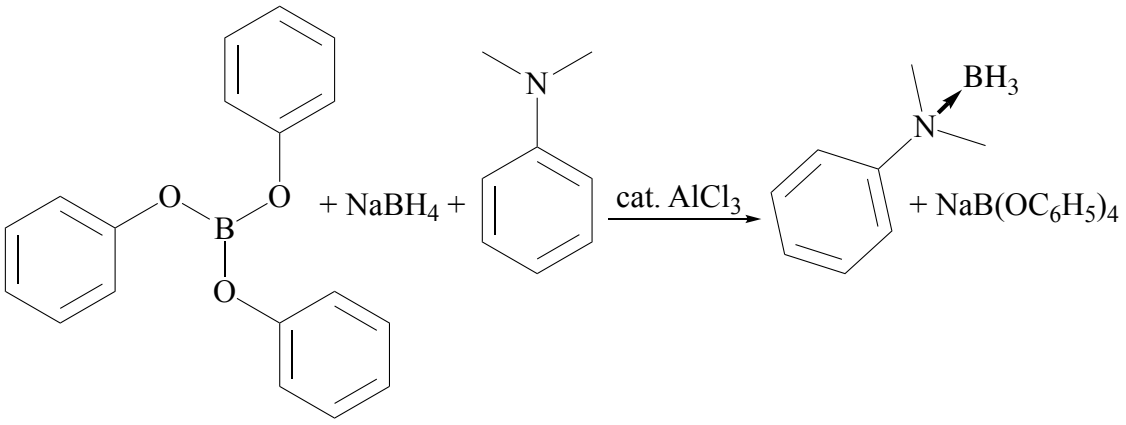
Scheme 1.10 Synthesis of triethylamine-borazane via KBH/boric acid & free amine

Later that same year in July 1959, Lang and Schubert patented an amine-borane synthesis using a metal borohydride and a boron trihalide or boron trihalide etherate (Scheme 1.11).[58] In 1964, Snover extended Lang and Schubert's work through his patent regarding *in-situ* preparation of diborane, subsequent reaction of diborane with a free amine, and isolation of the resultant amine-borane by crystallization from water.[59]

$$4\ (CH_3)_3N + 4\ BF_3{\bullet}O(C_2H_5)_2 + 3\ NaBH_4 \longrightarrow 4\ (CH_3)_3N{\bullet}BH_3 + 4\ (C_2H_5)O + 3\ NaBF_4$$

Scheme 1.11 Synthesis of trimethylamine-borane via boron trifluoride-diethyletherate & SBH

Following Lang and Schubert's work, Ashby in August 1959 defined a synthetic process for amine-boranes characterized by reacting a fully-esterified aryl ester of an oxyacid of boron with a metal borohydride (Scheme 1.12).[60]



Scheme 1.12 Synthesis of dimethyl aniline borane via phenyl borate/SBH & free amine

In February 1960, arguably the most commonly-used method for obtaining amine-boranes was established by Kelly and Edwards, wherein BTHF was used for boranation (Scheme 1.13).[61] There seems to be agreement that this is the first reported use of BTHF as a boranating agent for amines;[33b] this assertion also agrees with the timeline of chemical history since THF was not commercially available until 1956,[62] so applications involving BTHF as a -BH_3 carrier would understandably follow shortly thereafter.

$$(CH_2NH_2)_2 + 2\ C_4H_8O{:}BH_3 \longrightarrow (CH_2NH_2BH_3)_2 + 2\ C_4H_8O$$

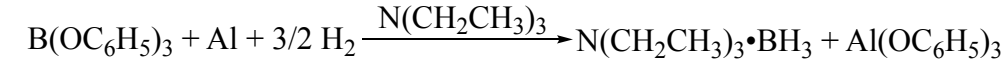
Scheme 1.13 Synthesis of ethane 1,2-diamineborane via BTHF

Soon after Kelly and Edwards' notable procedure, Marshall prepared amine-boranes via a dialkoxyborane and the free amine in March 1960 (Scheme 1.14).[63]

$$3\ BH(OCH_3)_2 + C_5H_5N \xrightarrow{B(OCH_3)_3} C_5H_5N{\bullet}BH_3 + B(OCH_3)_3$$

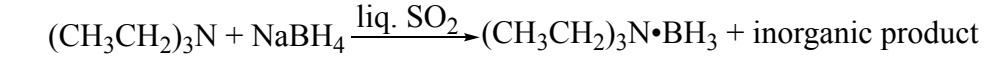
Scheme 1.14 Synthesis of pyridine-borane via dimethoxyborane & free amine

In 1962, Ashby and Foster proposed "A New and Convenient Route to the Amine-Boranes" (Scheme 1.15).[64] Their protocol uses a borate ester with an amine solvent to obtain the amine-borane.



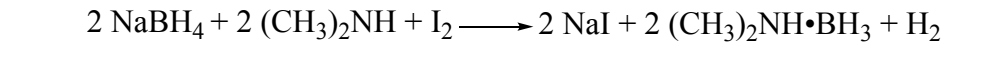
Scheme 1.15 Synthesis of triethylamine-borane via borate ester & free amine as solvent

Following Ashby and Foster's synthesis, Matsumara and Tokura in 1968 published a "superior" preparation using liquid SO_2, with the superiority purportedly owing to the weakly acidic nature of SO_2 relative to other previously used acids.[65] However, the authors fail to fully characterize the reaction, referring to the products as the desired amine-borane and an unidentified "inorganic product," presumed to be sodium sulfoxylate (Scheme 1.16).



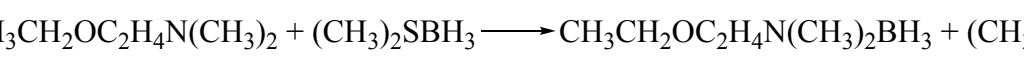
Scheme 1.16 Synthesis of triethylamine-borane via liquid SO_2/SBH & free amine

Later that decade in 1969, Nainan and Ryschkewitsch put forth an amine-borane synthetic procedure involving iodine for the generation of diborane from SBH (Scheme 1.17).[66]



Scheme 1.17 Synthesis of dimethylamine-borane via SBH/iodine & free amine

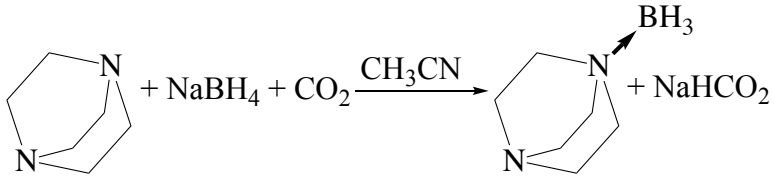
Rivalling BTHF as another popular agent for boranation of amines, BDMS appears to have first been used in a similar manner by Burke and Hough in 1976 as part of their patent, "Water Soluble Tertiary Amine Boranes (Scheme 1.18)."[33b, 67]



Scheme 1.18 Synthesis of 2-ethoxy-*N*,*N*-dimethylethan-1-amine-borane via BDMS & free amine

In 1984, a Czech patent was prepared by Plesek, Stibr, Drdakova, and Jelinek that describes a method similar to Matsumara and Tokura's method, wherein CO_2 acts as a Lewis acid for the amine-borane formation (Scheme 1.19).[68] In 1991, Arduengo developed a method similar to the Czech patent, though Arduengo sought to avoid the water-washing step.[33b, 69] Later

authors (Cao et al., 2012) suggest that the inorganic product is Na_2CO_3 as opposed to $NaHCO_2$, and that $H_{2(g)}$ is in fact a product of the reaction.[70]



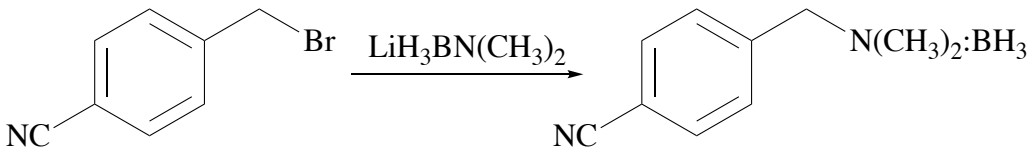
Scheme 1.19 Synthesis of 1,4-diazabicyclo[2.2.2]octane-monoborane via SBH/CO_2

As a unique example, Kampel and Warshawsky in 1994 published an 18-crown-6-mediated synthesis of various amine-boranes in ether (Scheme 1.20).[71]

$$(CH_3)_3N{\bullet}HCl + NaBH_4 \xrightarrow{\text{18-crown-6}} N(CH_3)_3{\bullet}BH_3 + H_2 + NaCl$$

Scheme 1.20 Synthesis of trimethylamine-borane via 18-crown-6 & amine•hydrochloride

Following Kampel and Warshawsky's work, in 1999, Collins, Lanz, Goralski, and Singaram formulated a lithium *N*,*N*-dialkylaminoborohydride-mediated route towards amine-boranes (Scheme 1.21).[72]



Scheme 1.21 Synthesis of *N*,*N*-dimethylcyanobenzylamine-borane via lithium aminoborohydride

There are also several in-house examples of amine-borane synthetic procedures developed in the Brown Center for Borane Research. The first of these described by Ramachandran and Gagare in 2007 focused exclusively on high-purity (>98%) AB synthesis (Scheme 1.22) by fine-tuning a metathesis procedure developed by Geanangel in 1977.[38, 73] The concentration of the reaction medium was critical in obtaining high-purity AB. This method was further modified by the same group for a large-scale preparation of AB involving ammonia as an additive.[74] Ramachandran and Kulkarni then described that the role of ammonia is that of a

reagent (Scheme 1.22).[75] Water can also be used as a promoting additive, as described by them in 2017 (Scheme 1.23).[76]

$$2\ NaBH_4 + (NH_4)_2SO_4 \xrightarrow{5\%\ NH_3} 2\ NH_3{\bullet}BH_3 + Na_2SO_4 + H_2$$

Scheme 1.22 Ammonia-promoted synthesis of ammonia borane

$$2\ NaBH_4 + (NH_4)_2SO_4 \xrightarrow{H_2O} 2\ NH_3{\bullet}BH_3 + Na_2SO_4 + H_2$$

Scheme 1.23 Water-promoted synthesis of ammonia-borane

In 2012, Ramachandran, Raju, and Gagare proposed a one-pot preparation of AB and several trialkylamine-boranes from trimethyl borate, LiH, and $AlCl_3$ in the presence of the desired amine (Scheme 1.24).[77]

$$B(OCH_3)_3 + LiH + N(CH_2CH_3)_3 \xrightarrow{AlCl_3} (CH_3CH_2)_3N{\bullet}BH_3 + LiAl(OMe)_4 + LiCl$$

Scheme 1.24 Synthesis of triethylamine-borane via $B(OMe)_3$/LiH/$AlCl_3$ and free amine

In 2015, the salt metathesis method was expanded to include other amine-boranes aside from AB (Scheme 1.25).[78]

$$NaBH_4 + (NH_4)_2SO_4 + 2\ (CH_3CH_2)_3N \longrightarrow (CH_3CH_2)_3N{\bullet}BH_3 + 2\ NH_3 + Na_2SO_4 + H_2$$

Scheme 1.25 Synthesis of triethylamine-borane via amine-ammonium salt equilibration

Lastly, in 2016, a bicarbonate-mediated process was optimized and developed that accommodates amines of varying degrees as well as functionalized amines (Scheme 1.24).[76]

$$NaBH_4 + NaHCO_3 + (CH_3CH_2CH_2)H_2N + H_2O \longrightarrow (CH_3CH_2CH_2)H_2N{\bullet}BH_3 + H_2$$

Scheme 1.26 Synthesis of 1-propanamine-borane via SBH/$NaHCO_3$ & free amine

Simply by looking at the numerous synthetic strategies, it is evident that amine-boranes have maintained their relevance since their discovery. However, a quick Web of Science™

search using the "Topic" "amine-boranes" reveals an exponentially growing interest in these salient compounds (Figure 1.6). In light of the renewed attention received by amine-boranes and their plentiful applications, it is imperative that new methods are optimized and developed to allow access to as many forms of these compounds as possible, such as the method to be presented herein that is especially amenable to pyridine-like heteroarylamines and long-chain trialkylamines.

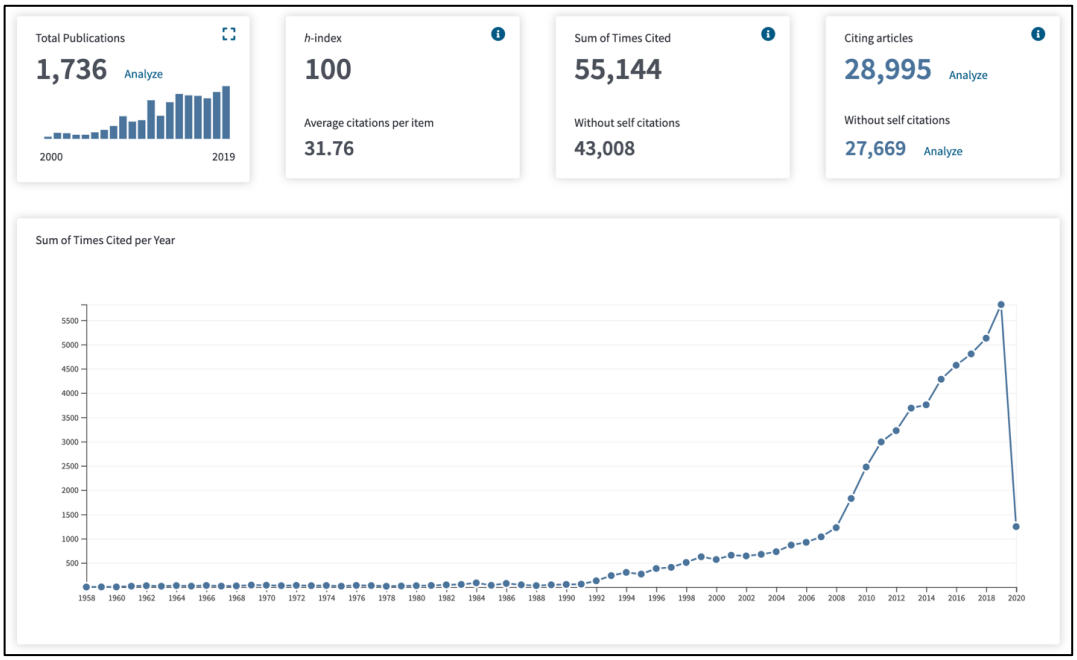


Figure 1.6 Web of Science™ citation report with "amine-boranes" as the Topic from 1937-2020 (per 19-May-2020)

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CHAPTER 2. CO_2-MEDIATED SYNTHESIS OF AMINE-BORANES

2.1 Background

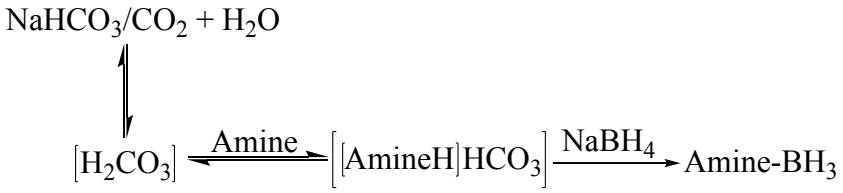
During an ongoing project developing anode materials for lithium ion batteries,[1] quantities of long-chain trialkylamine-boranes, such as tri-*n*-octylamine-borane were needed. Attempted preparation of these compounds using the earlier-reported $NaHCO_3$-mediated synthesis[2] from the Ramachandran laboratory exposed a limitation of the protocol. Failure to obtain even traces of trioctylamine-borane called attention to the need for an efficient synthesis of such amine-boranes.

The goal was to pursue an environmentally friendly, open-air protocol akin to the bicarbonate procedure. As noted, there have been several general reports of acid-mediated preparations of amine-boranes. However, these early procedures require (a) large excesses of the amine (b) reflux conditions (c) reaction times in excess of forty-eight hours (d) laborious purification of the amine-borane and (e) the use of undesirable solvents such as benzene, toluene, and xylene in amounts several times the molar quantity of the borohydride. These limitations have likely been responsible for the reluctance in acceptance of these early protocols for the preparation of amine-boranes in academic and industrial labs. A project was initiated to develop a suitable protocol for the preparation of long-chain trialkylamine-boranes.

2.2 Optimization of the Protocol

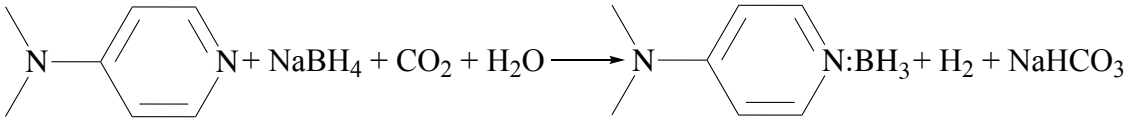
The intermediacy of the *in situ*-generated carbonic acid in the $NaHCO_3$-mediated protocol served as inspiration to systematically examine the CO_2-mediated amine-borane synthesis, which involves a similar mechanism (Scheme 2.1). Accordingly, during the initial optimization, CO_2 was directly introduced as dry ice to a reaction flask containing $NaBH_4$, 4-dimethylaminopyridine (4-DMAP), and THF, followed by the dropwise addition of deionized water. Reaction progress can be monitored by ^{11}B NMR spectroscopy (Note: Anhydrous DMSO is added to the reaction aliquot before running the ^{11}B NMR experiment). Upon completion of the reaction, the reaction contents were filtered through sodium sulfate and Celite®, and the solid residue was washed with THF.

Bicarbonate-mediated synthesis:



Scheme 2.1 General mechanism for HCO_3^-/CO_2-mediated syntheses of amine-boranes

After stirring at room temperature for 24 hours, ^{11}B NMR spectroscopic analysis of a reaction aliquot indicated the formation of 4-DMAP-BH_3; filtration and evaporation of the volatiles under vacuum revealed a quantitative yield, with a 4-DMAP-BH_3:4-DMAP product ratio of 7:3 (Scheme 2.2).



Scheme 2.2 Carbon dioxide-mediated synthesis of 4-DMAP-BH_3

This initial result for a reaction wherein the amine was used in stoichiometric quantities gave the necessary impetus to proceed with the optimization. However, the procedure was marked by the formation of an unintended side-product, which was detected as a triplet centered at δ ~0 ppm in the ^{11}B NMR spectrum (Figure 2.1).

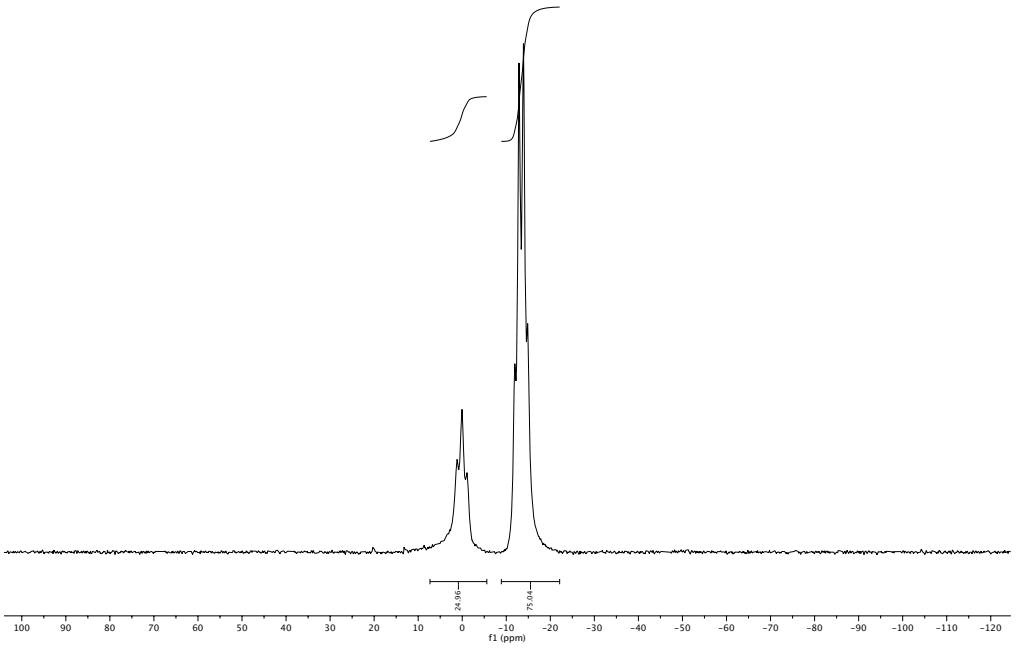


Figure 2.1 ^{11}B NMR spectrum of unoptimized 4-DMAP-BH_3 marked by impurity

This impurity was completely suppressed by lowering the reaction temperature to -78 °C. Careful addition of the dry ice while allowing the reaction mixture to equilibrate slowly to room temperature was enormously critical for the success. This cumbersome exercise prompted the transition to introducing gaseous CO_2 via balloon(s), providing a gentle flow rate with convenient gas transfer. The optimization data for the dry ice method is presented in Table 2.1.

Table 2.1 Initial Dry Ice Optimization Trials

Entry #	Equivalents (Amine:SBH:$CO_{2(s)}$:H_2O)	AB:Amine Conversion (^{1}H NMR)	AB:SBH:Other (^{11}B NMR)	Time (Hrs.)	Cooling Type
1	1:1.5:~4.25:~4.25	100:0	100:0:0	24	-78 °C
2	1:1.5:~4.25:~4.25	---	97:1:2	24	None
3	1:1.5:~4.25:~4.25	92:8	93:1:6	1	None
4	1:1.5:~4.25:~4.25	100:0	88:0:12	1	0 °C
5	1:1.5:~4.25:~4.25	95:5	99:1:0	2.5	-78 °C
6	1:1:~4.25:~4.25	73:27	91:0:9	1	None
7	1:1.5:~4.25:~4.25	---	100:0:0	24	0 °C
8	1:1.5:~4.25:~4.25	---	100:0:0	1.5	-78 °C
9	1:1.5:~4.25:~4.25	---	100:0:0	24	-78 °C

Note that $CO_{2(s)}$ was added to the reaction mixture before H_2O for all trials. 4-dimethylaminopyridine (Entries 1-6); diisopropylamine (Entries 7-8); pyridine (Entry 9) and $CO_{2(s)}$. AB = amine-borane; SBH = sodium borohydride ($NaBH_4$).

During the $CO_{2(g)}$ stage of the optimization, it was again noted that 4-DMAP was boranated completely within 4 hours at room temperature, with minimal-to-no formation of the δ 0 ppm (^{11}B NMR) side product. Additionally, it was also observed that the order of addition of CO_2 and H_2O influenced the efficacy of the reaction. Better results were achieved with the addition of H_2O prior to the introduction of CO_2. Moreover, increasing the molar equivalents of H_2O was shown to hinder the conversion of 4-DMAP to 4-DMAP-BH_3. Conversely, withholding water results in no yield of the amine-borane. Furthermore, portioning the CO_2 that was used to several (3-4) balloons for a steady flow through the system was preferable for increased yield. Finally, a direct CO_2 line with a flow rate of ~50 mL/min. was implemented, and a reaction stoichiometry of 1:1.5:3 of amine:$NaBH_4$:H_2O at ambient temperature was optimal for the reaction. These conditions allowed for the complete conversion of 4-DMAP to 4-DMAP-BH_3

within 30 minutes in quantitative yield (Figure 2.2). The optimization data for the $CO_{2(g)}$ method can be seen in Table 2.2 below.

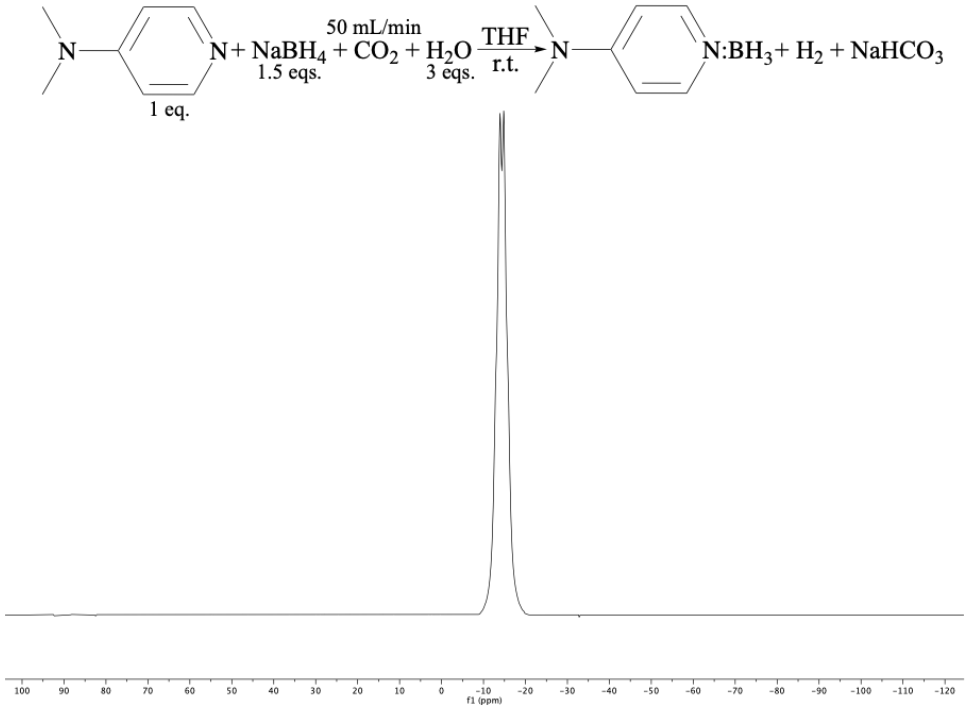


Figure 2.2 Optimized synthesis of 4-DMAP-BH_3 and ^{11}B NMR of purified product

Table 2.2 Optimization Trials Using 4-DMAP and $CO_{2(g)}$

Entry #	Equivalents (Amine:SBH:CO_2:H_2O)	AB:Amine Conversion (^{1}H NMR)	AB:SBH:Other (^{11}B NMR)	Time (Hrs.)	Cooling Type
1	1:1.5:Balloon:4.25	---	96:0:4	24	None
2	1:1.25:Balloon:4.25	98:2	94:0:6	1	None
3	1:1.1:Balloon:4.25	89:11	~100:0:0	---	None
4	1:1.25:Balloon:4.25	---	69:26:5	---	0 °C
5	1:1.25:Balloon:4.25	40:60	~100:0:0	1	-15 °C
6	1:1.25:---:---	~100:0	~100:0:0	---	None
7	1:1.25:Balloon:2.00	~100:0	87:0:13	1	None
8	1:1.25:Balloon:2.00	69:31	98:2:0	1	None
9	1:1.25:Balloon:3.25	60:40	99:1:0	1	None
10	1:1.25:Balloon:3.5	51:49	98:2:0	1	None
11	1:1.25:2 Balloons:3.25	87:13	~100:0:0	1	None
12	1:1.25:2 Balloons:4.77	67:33	~100:0:0	1	None
13	1:1.25:2 Balloons:4.25	75:25	~100:0:0	1	None
14	1:1.25:2 Balloons:3.75	87:13	~100:0:0	1	None
15	1:1.25:2 Balloons:4	54:46	99:1:0	1	None
16	1:1.25:2 Balloons (Stag.):4	81:19	~100:0:0	1	None
17	1:1.25:1 Balloon (2 consec. Flushes):3	---	~100:0:0	1	None
18	1:1.25:1 Balloon w/ vent needle:3	93:7	98:0:2	0.75	None
19	1:1.25:1 Balloon (7 consecutive flushes):3	---	---	1	None

Table 2.2 continued

20	1:1.25:1 Balloon (4 consec., 1,1,1):3	~100:0	~100:0:0	1	None
21	1:1.25:1 Balloon (4 consec., 1,1,1):3	92:8	98:0:2	1	None
22	1:1.25:1 Balloon (4 consec. 1,1,1):3	93:7	~100:0:0	1.33	None
23	1:1.25:1 Balloon (4 consec., 1,1,1):3 (2 M THF)	96:4	~100:0:0	0.75	None
24	1:1.25:Direct line:3	93:7	97:0:3	0.5	None
25	1:1.25:Direct line:4.25	92:8	98:0:2	0.5	None
26	**1:1.5:Direct line:3**	**~100:0**	**~100:0:0**	**0.5**	**None**

Note that for entries 1-7, H_2O was added after $CO_{2(g)}$, and for entries 8-26, H_2O was added before $CO_{2(g)}$. For all entries except entry 23, a 1 M concentration of amine in THF was used. When using a latex balloon as the $CO_{2(g)}$ source, the balloon (which was attached to a plastic syringe tube fitted with a BD PrecisionGlide™ 18G x 1 ½ needle) was filled to roughly maximum volume with $CO_{2(g)}$ and inserted through a rubber septum into the reaction flask. In entry 16, "Stag." indicates that two $CO_{2(g)}$ balloons were used and added in a time-staggered fashion. In entry 17, "2 consec. Flushes" indicates that after the $CO_{2(g)}$-filled balloon was inserted through the septum, two evacuated balloon-syringes were added through the septum consecutively, causing a flow of $CO_{2(g)}$ from the filled balloon through the system and into the evacuated balloon(s). In entry 18, a $CO_{2(g)}$-filled balloon was added through the septum followed by an 18G needle through the septum, allowing for a steady flow of $CO_{2(g)}$ across the system. For entries 20-23, "4 consec., 1,1,1" indicates that after the $CO_{2(g)}$-filled balloon was inserted through the septum, four evacuated balloon-syringes were added through the septum consecutively, followed by the time-staggered addition of three more evacuated balloon-syringes. Beginning with entry 24, a direct $CO_{2(g)}$ line was implemented with a flow rate of ~50 mL $CO_{2(g)}$/min. as measured using a gas burette and stopwatch. Optimal results are highlighted in bold. AB = amine-borane; SBH = sodium borohydride ($NaBH_4$).

2.3 Results

Under the optimized conditions, a variety of primary, secondary, and tertiary alkylamines and heteroarylamines, as well as ammonia, were converted to the corresponding amine-boranes. The borane of ammonia (**1a**) was prepared using both dry ice and $CO_{2(g)}$, though yields were lower than most other amine-boranes. Another gaseous amine, ethylamine (**1b**), was boranated with good yield (65%), with minimal (<5%) ethylammonium borohydride impurity. 1-propanamine (**1c**) and *sec*-butylamine (**1d**) experienced similar borane yields (70%); the yield of

1-propanamine-borane using dry ice (68%) was comparable to the yield provided by $CO_{2(g)}$. The major hurdle to excellent yields with the 1° amines is their susceptibility to carbamate formation.

Of the 2° amines, pyrrolidine (**1e**) afforded the lowest borane yield (42%), followed by piperidine (**1f**) with 61% yield of piperidine-borane, which suggests an inherent difference between the 2° heterocyclic amines and 2° alkylamines that were tested, perhaps owing to basicity factors.[3] Similar to the 1° amines, 2° amines are also vulnerable to direct reaction with CO_2. Diisopropylamine (**1g**) and diethylamine (**1h**) were boranated in good (85%) and excellent (91%) yields; the yield of diethylamine-borane using dry ice (90%) was nearly identical to the $CO_{2(g)}$ yield.

The class of 3° amines, both heterocyclic and trialkyl, consistently provided excellent yields, though the reaction time for these amines was extended to 18 hours. *N*-ethylpiperidine (**1i**) and triethylamine (**1j**) were both boranated in 93% yield, and the yield of triethylamine-borane using dry ice was similar (86%). Most gratifyingly, the long-chain trialkylamines, i.e. tributylamine (**1k**), tridodecylamine (**1l**), and trioctylamine (**1m**), were successfully boranated in >99% yield using the current CO_2 protocol, which delightfully supplements the deficiency in the $NaHCO_3$ procedure. In addition, the heteroarylamines, which included 2-picoline (**1n**), 4-dimethylaminopyridine (**1o**), and pyridine (**1p**), were boranated in >99% yield as well. Moreover, the reaction time for these amines was drastically shortened (30 minutes). All purified, boranated products (**2a**-**p**) were verified to be ≥95% purity by hydride analysis and boron NMR spectroscopy (Table 2.3).[4]

Table 2.3 Summary of Amine-Boranes Prepared Using CO_2-Mediated Protocol

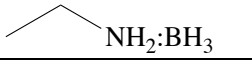
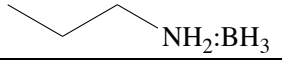
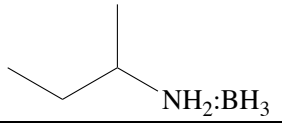
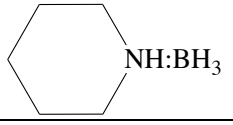
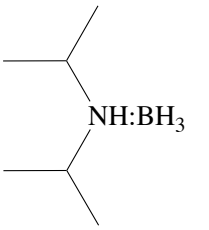
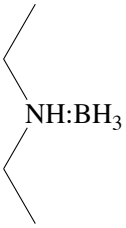
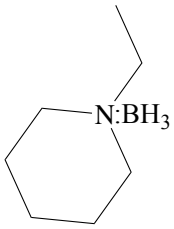
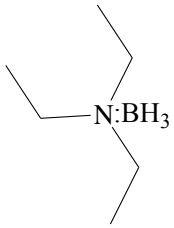
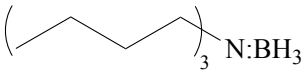
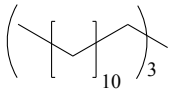
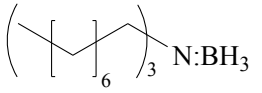
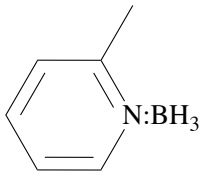
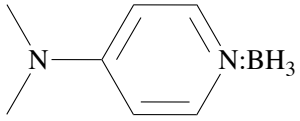
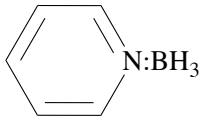
Entry #	Amine Degree	Amine-Borane (N:BH_3)			Rxn Time (Hrs.)	%-Yield[a]
		#	Structure	^{11}B NMR δ (ppm)		
1a	AB	**2a**	NH_3:BH_3	-22.39	0.5	56[b] (32)[c]
1b	1°	**2b**		-20.03	0.5	65
1c	1°	**2c**		-20.08	0.5	70 (68)
1d	1°	**2d**		-20.96	0.5	70
1f	2°	**2f**		-15.65	18	42
1g	2°	**2g**		-21.77	0.5	85
1h	2°	**2h**		-17.22	0.5	91 (90)
1i	3°	**2i**		-13.00	18	93
1j	3°	**2j**		-14.01	18	93 (86)
1k	3°	**2k**		-12.93	18	99[d]
1l	3°	**2l**		-13.88	18	>99[d]

Table 2.3 continued

1m	3°	**2m**		-13.04	18	>99
1n	HA[e]	**2n**		-14.27	0.5	92
1o	HA	**2o**		-14.37	0.5	>99 (>99)
1p	HA	**2p**		-12.61	0.5	>99

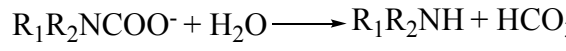
Note: [a]Yield of isolated products based on amount of amine. [b]Yield of gaseous amines (ammonia- and ethylamine-borane) based on amount of $NaBH_4$. [c]Parenthetical yields represent isolated product obtained using dry ice as CO_2 source. [d]0.5 equivalents of amine, 1.5 equivalents of $NaBH_4$, and 3 equivalents of H_2O were used. [e]HA = heteroarylamine.

Using the standardized CO_2 procedure, the amines (**1a**-**p**) corresponding to amine-boranes **2a**-**2p** were boranated within 0.5-18 hours in yields ranging from 56-99% (32-99% for dry ice as the CO_2 source). Generally, the overall yield improves with the degree of substitution of the amine, though pyridine-like heteroarylamines consistently provided excellent yields at room temperature within 30 minutes. The method proved inefficient for the boranation of some *pri*- and *sec*-amines, e.g. benzylamine and *tert*-butylamine, when a noticeable amount of fine, white precipitate was formed upon the addition of CO_2; imidazole, 1-methylimidazole, and tribenzylamine were also incompatible, though for reasons related to the stability of the protonated amine.[5] For the *pri*- and *sec*-amines, the precipitate suggested a competing reaction, likely the formation of ammonium carbamate (Scheme 2.3).[6] Although the formation of amine-boranes from sodium borohydride and ammonium carbamates is known,[7] the loss of an equivalent of amine as the carbamate moiety contributes to the loss of yield; this can be circumvented by using additional equivalents of amine. However, this process could lead to further carbamate formation by uptake of additional amounts of CO_2.

$$CO_2 + 2\ C_3H_7NH_2 \longrightarrow C_3H_7NHCOOC_3H_7NH_3$$

Scheme 2.3 Formation of isopropylamine carbamate from CO_2 and free amine

Carbamates are known to form bicarbonate and free amine with water (Scheme 2.4).[8] Accordingly, an attempt at dissolution of the carbamate[9] and transformation of the resultant free amine/ammonium bicarbonate to the amine-borane was made by the addition of DI water to the "completed" reaction, as well as by trying DI water as the reaction solvent. However, both efforts proved unsuccessful. Moreover, it has been recognized that CO_2 reacts directly with $NaBH_4$,[10] and these carbamate-mitigation techniques seemingly exacerbated this potential side reaction, in addition to the inherent hydrolysis of $NaBH_4$ and to a lesser extent amine-boranes. Moreover, another circumvention was attempted by *ex situ*-generation of $H_2CO_{3(aq)}$ and subsequent transfer of the acidified solution into the reaction mixture. However, due to the rapid dissociation of H_2CO_3, this effort also proved to be unsuccessful, as there was minimal formation of the amine-borane with this approach.



Scheme 2.4 Hydrolysis of a general carbamate

Briefly, there were two cursory investigations into the seemingly unexpected difference between the HCO_3^-- and CO_2-mediated protocols, especially since both methods apparently proceed mechanistically by *in situ*-generation of H_2CO_3 and subsequent complexation of the protonated amine with HCO_3^-, followed by dehydrogenation to give the amine-borane. In the first experiment, a comparison was made between HCO_3^- and CO_3^{2-} for the preparation of AB via the salt metathesis exchange reaction.[11] When prepared via Na_2CO_3, AB was obtained in 80% yield in 4 hours; when prepared via $NaHCO_3$, there was only 34% conversion between AB and SBH by ^{11}B NMR after 4 hours. After 24 hours, the conversion had increased to approximately 66% AB relative to SBH.

Next, the basis of the second inquiry was to examine if the difference between the two methodologies could be attributable to a common-ion effect since the HCO_3^- procedure contains thrice the molar quantity of Na^+ cations as the CO_2 procedure, i.e. 1.5 equivalents of $NaBH_4$ and 3 equivalents of $NaHCO_3$ (4.5 equivalents of Na^+ total) versus solely 1.5 of equivalents $NaBH_4$, respectively. To investigate, the CO_2 protocol was performed using trioctylamine with the addition of 3 equivalents of NaCl as the Na^+ source. Ultimately, trioctylamine-borane was

obtained in identical yield and purity as without NaCl, showing the additional Na^+ (and Cl^-) to be benign.

In conclusion, a synthesis of amine-boranes in varying yields from the free amine, sodium borohydride, and carbon dioxide in wet THF has been developed. This particular CO_2-mediated synthesis extends the previous HCO_3^--mediated protocol to include the class of long-chain trialkylamine-boranes such as trioctyl- and tridodecylamine-borane that had proven inaccessible. Moreover, with the current protocol, reaction times for the preparation of pyridine-like heteroarylamine-boranes were reduced 8-fold, decreasing from 4 hours to 30 minutes. This CO_2-mediated synthesis of amine-boranes will hopefully attract the attention of organic and materials chemists due to the current resurgence of interest in this class of compounds.

2.4 Experimental

General Methods and Materials: ^{11}B, ^{1}H, and ^{13}C NMR spectra were recorded at room temperature on a Varian INOVA or MERCURY 300 MHz NMR instrument. For ^{11}B NMR, chemical shifts (δ values) are reported in parts per million relative to $BF_3 \bullet Et_2O$. Data are reported as: δ value, multiplicity, and integration. All solvents for preparation and isolation of products were reagent-grade. Tetrahydrofuran (THF, Optima®, meets ACS specifications, no preservatives, packaged under N_2, submicron filtered) and stabilized THF (Certified, contains about 0.025% butylated hydroxytoluene i.e., BHT, as a preservative, Safe-Cote®) were purchased from Fisher Chemical; after usage during initial optimization trials, stabilized THF was no longer implemented for further reactions due to the presence of BHT peaks in the ^{1}H and ^{13}C NMRs of purified products.[12] Sodium borohydride (>95.0%) was purchased from Aldrich. Carbon dioxide gas (99%) was purchased from Indiana Oxygen. Deionized water was supplied from an in-house tap. Amines were purchased from commercial sources. Sodium sulfate (Anhydrous, granular, Certified ACS) was purchased from Fisher Chemical, and Celite® was purchased from Oakwood Products, Inc.

Procedure for the Preparation of Ammonia-Borane via $CO_{2(s)}$ (2a): Sodium borohydride (0.57 g, 15.0 mmol) was transferred to the pre-weighed, custom 250 mL round bottom flask with a "porous" side arm for dry ice addition (Figure 2.3), followed by the addition of tetrahydrofuran (10.0 mL, 1 M).

Figure 2.3 Custom dry ice reaction flask with refillable, "porous," and sealable side-arm

To the sealed system, the NH_3 gas line with a mild flow rate and venting outlet were added, and the solution was allowed to briefly saturate at room temperature; the flow of NH_3 was maintained for the entire 30 minutes reaction time. With stirring, deionized water (0.54 mL, 30.0 mmol) was added dropwise through the septum. Approximately 4 grams of dry ice were then added to the dry ice trap at the onset of the reaction, and the trap was maintained with dry ice for 30 minutes. Reaction progress can be monitored by ^{11}B NMR spectroscopy (Note: Anhydrous DMSO is added to the reaction aliquot before running the ^{11}B NMR experiment). Upon completion of the reaction, the reaction contents were filtered through sodium sulfate and Celite®, and the solid residue was washed with THF. Removal of the solvent in vacuo yielded AB (**2a**).

Procedure for the Preparation of Amine-Boranes via $CO_{2(s)}$ (2c, h, j, and o): Sodium borohydride (0.57 g, 15.0 mmol) was transferred to the pre-weighed, custom 250 mL round bottom flask with a "porous" side arm for dry ice addition, followed by the particular amine (10.0 mmol) and 10.0 mL THF (1 M). With stirring, deionized water (0.54 mL, 30.0 mmol) was added dropwise through the septum at room temperature for **2c**, **2h**, and **2o** or 0 °C for **2j**. Approximately 4 grams of dry ice were then added to the dry ice trap at the onset of the reaction, and the trap was maintained with dry ice for 30 minutes for **2c**, **2h**, and **2o** or 4 hours for **2j**. For the preparation of **2j**, the reaction continued for 14 hours with equilibration to room temperature. Reaction progress can be monitored by ^{11}B NMR spectroscopy (Note: Anhydrous DMSO is

added to the reaction aliquot before running the ^{11}B NMR experiment). Upon completion of the reaction, the reaction contents were filtered through sodium sulfate and Celite®, and the solid residue was washed with THF. Removal of the solvent in vacuo yielded the corresponding amine-borane (**2c**, **h**, **j**, and **o**).

General Procedure for the Preparation of Amine-Boranes via Gaseous Amine and $CO_{2(g)}$ (2a and b): Sodium borohydride (0.57 g, 15.0 mmol) was transferred to a pre-weighed, dry round bottom flask, followed by the addition of tetrahydrofuran (10.0 mL, 1M). To the sealed system, the amine gas line with a mild flow rate and venting outlet were added, and the solution was allowed to saturate at room temperature for the preparation of **2a** or 0 °C for **2b**; the flow of $NH_{3(g)}$ was maintained for the entire 30 minutes reaction time, and the flow of $CH_3CH_2NH_{2(g)}$ was maintained for 5 minutes following the addition of $CO_{2(g)}$. With stirring, deionized water (0.54 mL, 30.0 mmol) was added dropwise through the septum. A direct $CO_{2(g)}$ line was added for 30 minutes at room temperature (**2a**) or 0 °C (**2b**). Reaction progress can be monitored by ^{11}B NMR spectroscopy (Note: Anhydrous DMSO is added to the reaction aliquot before running the ^{11}B NMR experiment). Upon completion of the reaction, the reaction contents were filtered through sodium sulfate and Celite®, and the solid residue was washed with THF. Removal of the solvent in vacuo yielded the corresponding amine-borane (**2a** and **b**).

General Procedure for the Preparation of Amine-Boranes via $CO_{2(g)}$ (2c-p): The particular amine (10.0 mmol for **2c**-**j**, and 5.0 mmol for **2k** and **l**) and sodium borohydride (0.57 g, 15.0 mmol) were transferred to a pre-weighed, dry 50 mL round bottom flask, followed by the addition of tetrahydrofuran (10.0 mL, 1 M) at room temperature for the preparation of **2c**, **d**, **g**, **h**, and **n**-**p** or 0 °C for **2e**, **f**, and **i**-**m**. With stirring, deionized water (0.54 mL, 30.0 mmol) was added dropwise through the septum. A direct $CO_{2(g)}$ line and venting outlet were added through the septum for 30 minutes at room temperature (**2c**, **d**, **g**, **h**, and **n**-**p**) or 4 hours at 0 °C (**2e**, **f**, and **i**-**m**) with a flow rate of ~50 mL $CO_{2(g)}$/min. For amines **2e**, **f**, and **i**-**m**, the reaction continued for 14 hours with equilibration to room temperature. Reaction progress can be monitored by ^{11}B NMR spectroscopy (Note: Anhydrous DMSO is added to the reaction aliquot before running the ^{11}B NMR experiment). Upon completion of the reaction, the reaction contents were filtered through sodium sulfate and Celite®, and the solid residue was washed with THF. Removal of the solvent in vacuo yielded the corresponding amine-borane (**2c**-**p**).

General Procedure for Hydride Analysis of Amine-Boranes (2a-p): Approximately 1 mmol of the particular amine-borane was transferred to a pre-weighed, dry 20 mL vial with a septum inlet fitted with a connecting tube. The connecting tube was attached to an analytical gas burette filled with $CuSO_{4(aq)}$ solution (Figure 2.4). A solution of 3 M HCl was syringed into the vial dropwise. The hydrogen generated was measured using the analytical gas burette. The temperature of the reaction was at times raised to ensure complete dehydrogenation. An illustrative calculation to determine sample mass and percent purity is shown (Equation 2.1):

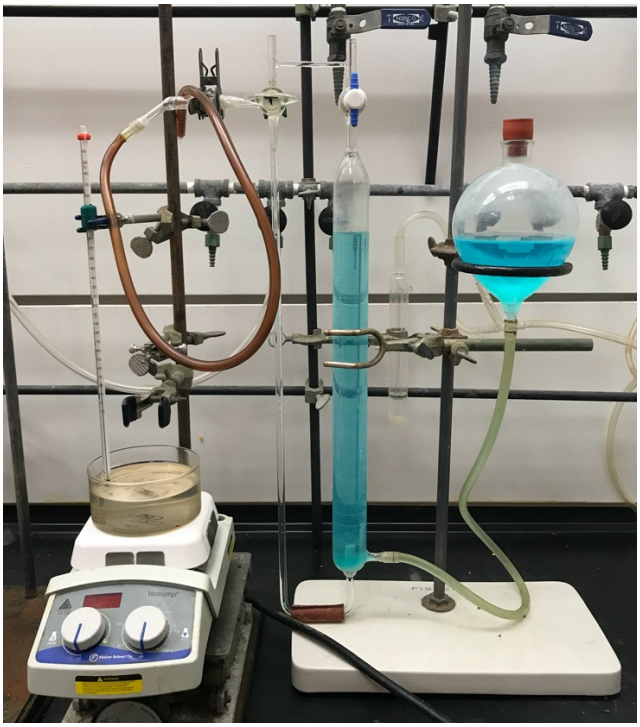


Figure 2.4 Hydride apparatus with oil bath and hot plate for heating/stirring

$$Assuming\ a\ desired\ H_2\ volume\ of \sim 70.0\ mL\ and\ using\ PV = nRT\ at\ 1.0\ atm\ and\ 298\ K:$$

$$(1.0\ atm)(0.07\ L) = n\left(\frac{0.08206\ L \cdot atm}{mol \cdot K}\right)(298\ K)$$

$$n_1 \approx 0.00286\ mol\ H_2, and\ since\ 1\ mol\ of\ amine - borane\ contains\ 3\ hydrides, so$$

$$n_2 \approx 0.000954\ mol\ amine - borane, times\ the\ MW\ to\ give\ the\ sample\ mass.$$

$$Since\ 1\ H^-\ reacts\ with\ 1\ H^+\ to\ give\ H_2, the\ volume\ of\ 3\ M\ HCl\ is\ calculated\ as:$$

$$3\ M\ HCl = \frac{0.00286\ mol\ H^+}{x\ L}, x \approx 0.00095\ L\ (0.95\ mL).$$

$$By\ measuring\ \Delta V\ from\ H_2\ evolution\ in\ the\ analytical\ burette$$

$$and\ accounting\ for\ the\ volume\ of\ HCl\ injected, \% - purity\ is\ given\ as:$$

$$\left(\frac{V_{actual}}{V_{theoretical}}\right)\ x\ 100\% = \left(\frac{66.5\ mL}{70.0\ mL}\right)\ x\ 100\% = 95.0\%\ sample\ purity.$$

Equation 2.1 Sample calculations for hydride analysis of an amine-borane

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APPENDIX A. CHARACTERIZATION OF AMINE-BORANES

Ammonia-borane (2a):

White solid. m.p. = 104 °C.

^{11}B NMR (96 MHz, Tetrahydrofuran) δ -22.39 (q, *J* = 95.1, 94.6 Hz, 3H).

Ethylamine-borane (2b):

White solid. m.p. = 26-27 °C.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 3.88 (s, 2H), 2.80 (q, *J* = 7.0 Hz, 2H), 1.21 (td, *J* = 7.3, 2.0 Hz, 3H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 43.55, 14.45; ^{11}B NMR (96 MHz, Chloroform-*d*) δ -20.03 (q, *J* = 96.0 Hz, 3H).

***n*-Propylamine-borane (2c)**:

White solid. m.p. = 44-46 °C.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 3.91 (s, 2H), 2.67 (q, *J* = 7.2 Hz, 2H), 1.58 (q, *J* = 7.3 Hz, 2H), 0.89 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 50.44, 22.32, 11.16; ^{11}B NMR (96 MHz, Chloroform-*d*) δ -20.08 (q, *J* = 95.7 Hz, 3H).

***sec*-Butylamine-borane (2d)**:

Colorless liquid.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 3.70 (d, *J* = 56.7 Hz, 2H), 2.86 – 2.70 (m, 1H), 1.76 – 1.64 (m, 1H), 1.46 (dtd, *J* = 13.7, 7.6, 1.6 Hz, 1H), 1.21 (dd, *J* = 6.6, 1.7 Hz, 3H), 0.90 (td, *J* = 7.5, 1.6

Hz, 3H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 55.46, 28.74, 18.25, 9.83.; ^{11}B NMR (96 MHz, Chloroform-*d*) δ -20.96 (q, *J* = 95.8 Hz, 3H).

Pyrrolidine-borane (2e):

Colorless liquid.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 4.85 (s, 1H), 3.13 (dq, *J* = 11.3, 5.7 Hz, 2H), 2.55 (dq, *J* = 14.6, 7.9 Hz, 2H), 2.02 – 1.62 (m, 4H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 54.10, 24.64; ^{11}B NMR (96 MHz, Chloroform-*d*) δ -17.34 (q, *J* = 94.9 Hz, 3H).

Piperidine-borane (2f):

White solid. m.p. = 80-82 °C.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 3.89 (s, 1H), 3.17 (d, *J* = 13.5 Hz, 2H), 2.42 (q, *J* = 13.7, 12.5 Hz, 2H), 1.71 (d, *J* = 11.0 Hz, 2H), 1.59 – 1.22 (m, 4H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 53.33, 25.28, 22.56; ^{11}B NMR (96 MHz, Chloroform-*d*) δ -15.65 (q, *J* = 95.8 Hz, 3H).

Diisopropylamine-borane (2g):

Colorless liquid. b.p. = 82 °C.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 3.21 (ddp, *J* = 8.8, 4.9, 2.3 Hz, 2H), 1.24 (ddt, *J* = 6.4, 4.5, 2.1 Hz, 12H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 52.12, 21.11, 19.10; ^{11}B NMR (96 MHz, Chloroform-*d*) δ -21.77 (q, *J* = 96.7 Hz, 3H).

Diethylamine-borane (2h):

Colorless liquid. b.p. = 89-91 °C.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 3.43 (s, 1H), 2.86 – 2.68 (m, 4H), 1.30 – 1.14 (m, 6H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 48.93, 11.76; ^{11}B NMR (96 MHz, Chloroform-*d*) δ -17.22 (q, *J* = 95.9 Hz, 3H).

***N*-Ethylpiperidine-borane (2i)**:

Colorless liquid.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 2.85 (dq, *J* = 21.6, 7.9, 7.2 Hz, 4H), 2.75 – 2.63 (m, 2H), 1.90 – 1.73 (m, 2H), 1.64 – 1.44 (m, 4H), 1.23 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 57.68, 54.79, 22.89, 20.50, 8.92; ^{11}B NMR (96 MHz, Chloroform-*d*) δ -13.00 (q, *J* = 96.7 Hz, 3H).

Triethylamine-borane (2j):

Colorless liquid. b.p. = 97-100 °C.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 2.72 (qd, *J* = 7.3, 3.7 Hz, 6H), 1.29 – 1.04 (m, 9H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 52.37, 8.70; ^{11}B NMR (96 MHz, Chloroform-*d*) δ -14.01 (q, *J* = 96.8 Hz, 3H).

Tributylamine-borane (2k):

Yellow liquid.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 2.65 (dt, *J* = 11.7, 3.3 Hz, 6H), 1.61 (tp, *J* = 11.4, 3.4 Hz, 6H), 1.27 (ddq, *J* = 10.2, 7.4, 3.6, 2.8 Hz, 6H), 0.92 (td, *J* = 7.5, 3.0 Hz, 9H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 59.22, 25.13, 20.73, 13.99; ^{11}B NMR (96 MHz, Chloroform-*d*) δ -12.93 (q, *J* = 100.7, 100.1 Hz, 3H).

Tridodecylamine-borane (2l):

Yellow liquid.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 2.64 (s, 6H), 1.25 (s, 60H), 0.87 (t, *J* = 6.5 Hz, 9H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 59.40, 32.01, 29.74, 29.66, 29.45, 27.50, 23.03, 22.81, 14.25; ^{11}B NMR (96 MHz, Chloroform-*d*) δ -13.88.

Trioctylamine-borane (2m):

Yellow liquid.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 2.81 – 2.54 (m, 6H), 1.71 – 1.49 (m, 7H), 1.23 (dh, *J* = 13.7, 6.9 Hz, 30H), 0.93 – 0.76 (m, 8H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 59.37, 31.82, 29.34, 29.27, 27.46, 22.99, 22.70, 14.16; ^{11}B NMR (96 MHz, Chloroform-*d*) δ -13.04.

2-picoline-borane (2n):

White solid. m.p. = 44-46°C.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.65 (d, *J* = 5.9 Hz, 1H), 7.79 (t, *J* = 7.7 Hz, 1H), 7.34 (d, *J* = 7.8 Hz, 1H), 7.25 (dd, *J* = 7.7, 6.0 Hz, 1H), 2.68 (s, 4H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 157.49, 148.46, 139.58, 126.82, 122.50, 22.63; ^{11}B NMR (96 MHz, Chloroform-*d*) δ -14.27 (q, *J* = 97.5 Hz, 3H).

4-dimethylaminopyridine-borane (2o):

White solid. m.p. = 166-168°C.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.96 – 7.85 (m, 2H), 6.45 – 6.38 (m, 2H), 3.03 (s, 6H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 154.43, 146.42, 106.34, 39.57; ^{11}B NMR (96 MHz, Chloroform-*d*) δ -14.37 (q, *J* = 96.7 Hz, 3H).

Pyridine-borane (2p):

Colorless liquid.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.49 (d, *J* = 5.7 Hz, 2H), 7.89 (t, *J* = 7.8 Hz, 1H), 7.46 (t, *J* = 6.8 Hz, 2H), 2.54 (q, *J* = 89.9 Hz, 3H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 147.19, 139.26, 125.44; ^{11}B NMR (96 MHz, Chloroform-*d*) δ -12.61 (q, *J* = 97.8 Hz, 3H).

APPENDIX B. NMR SPECTRA OF AMINE-BORANES

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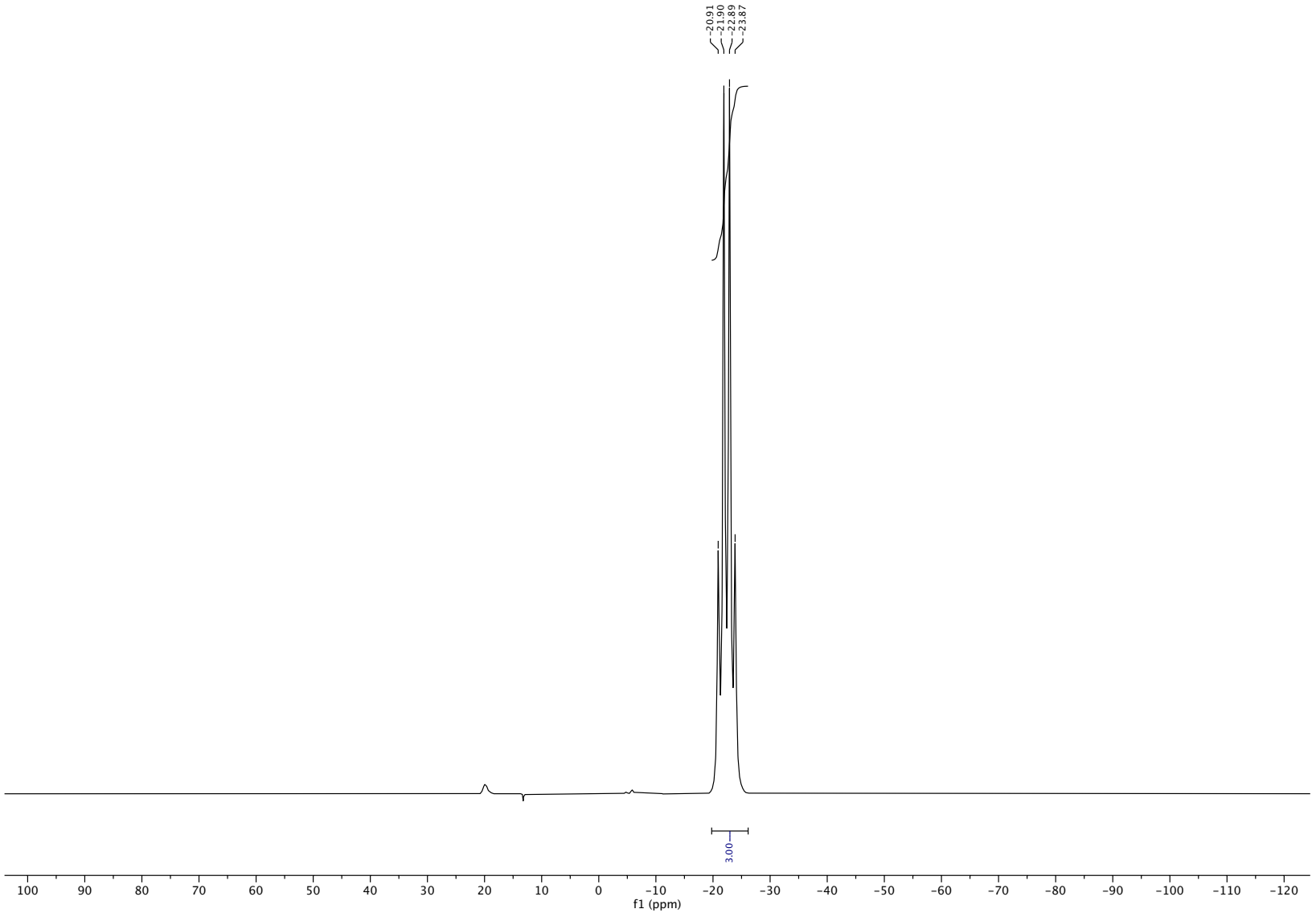
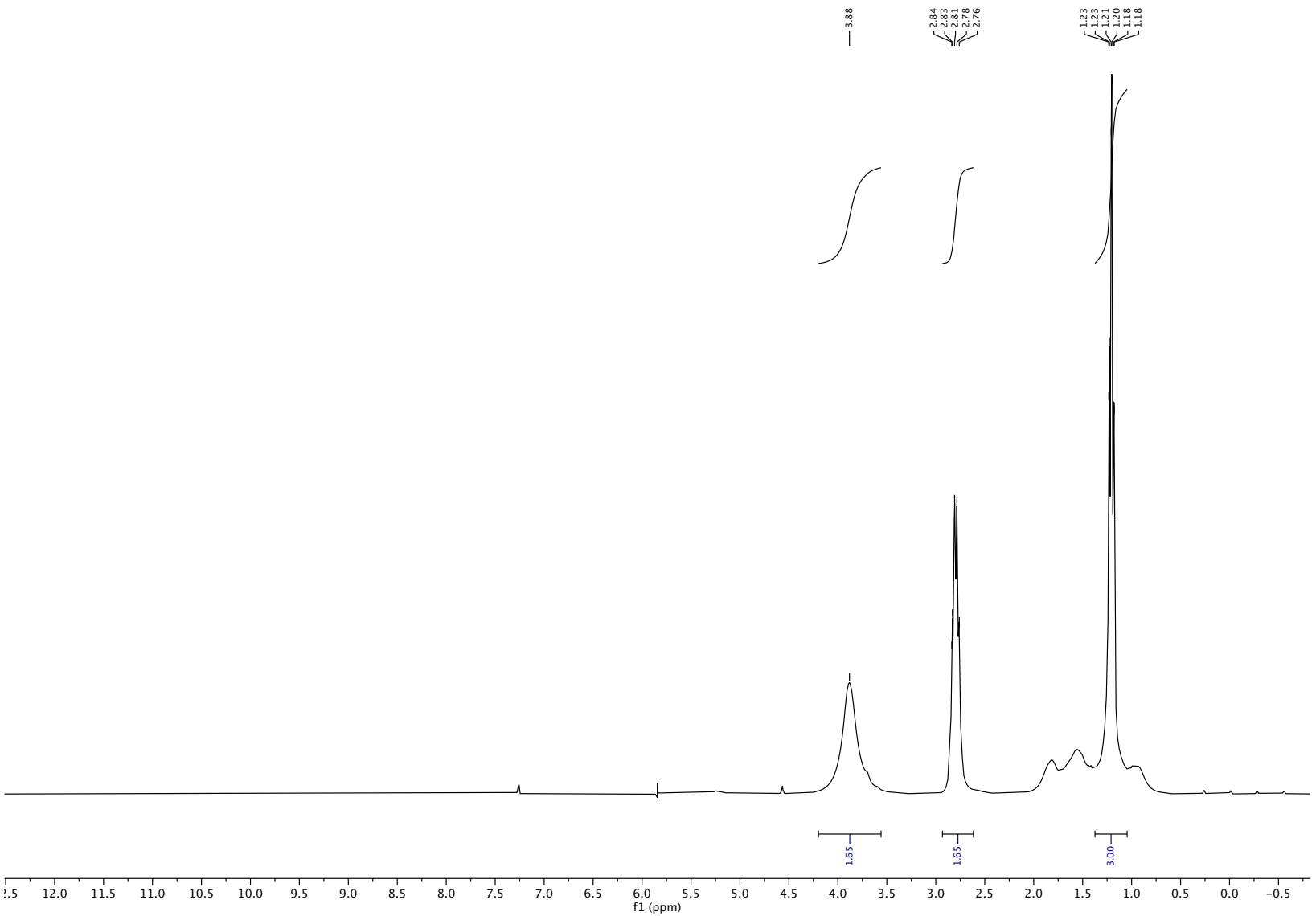
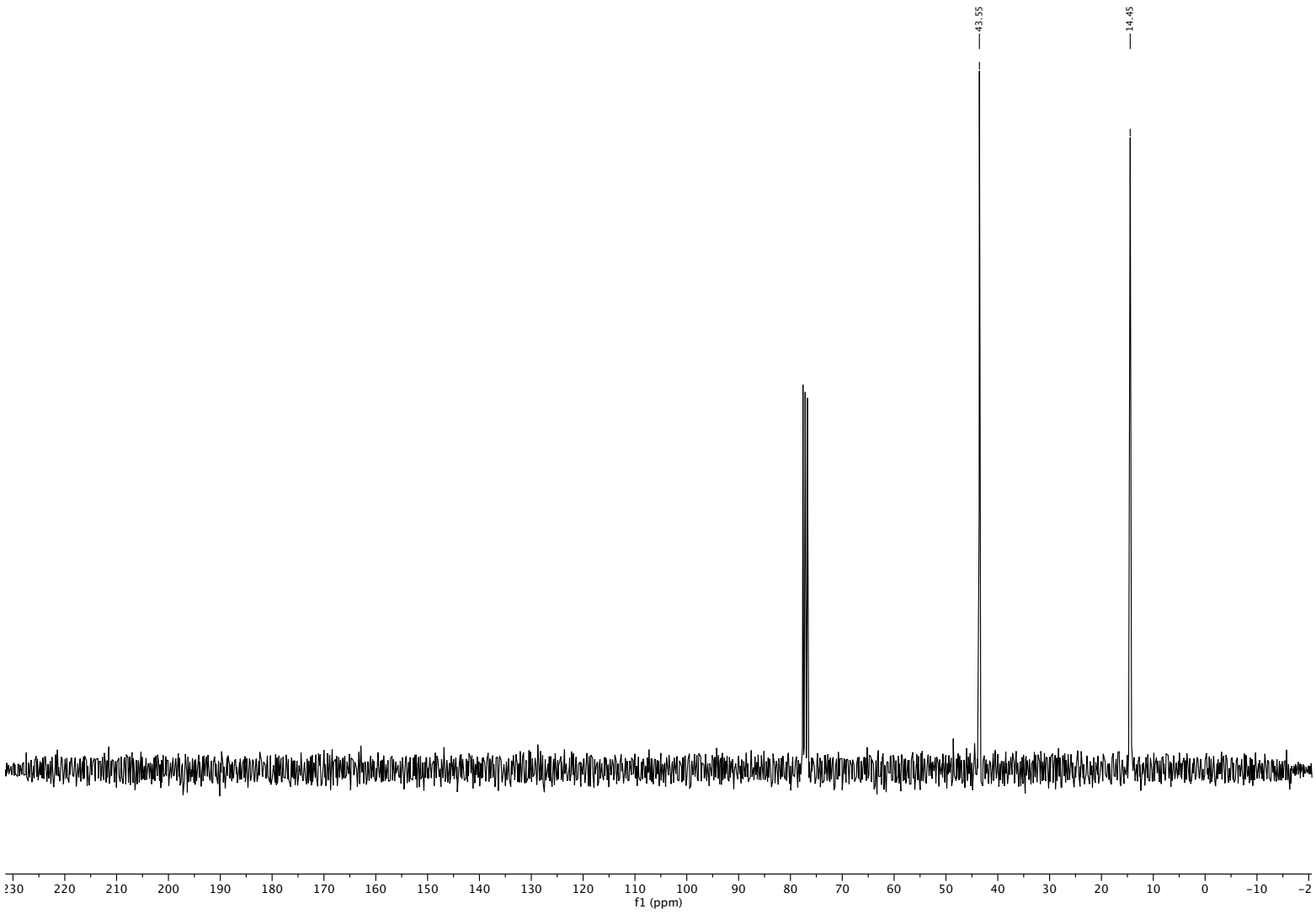


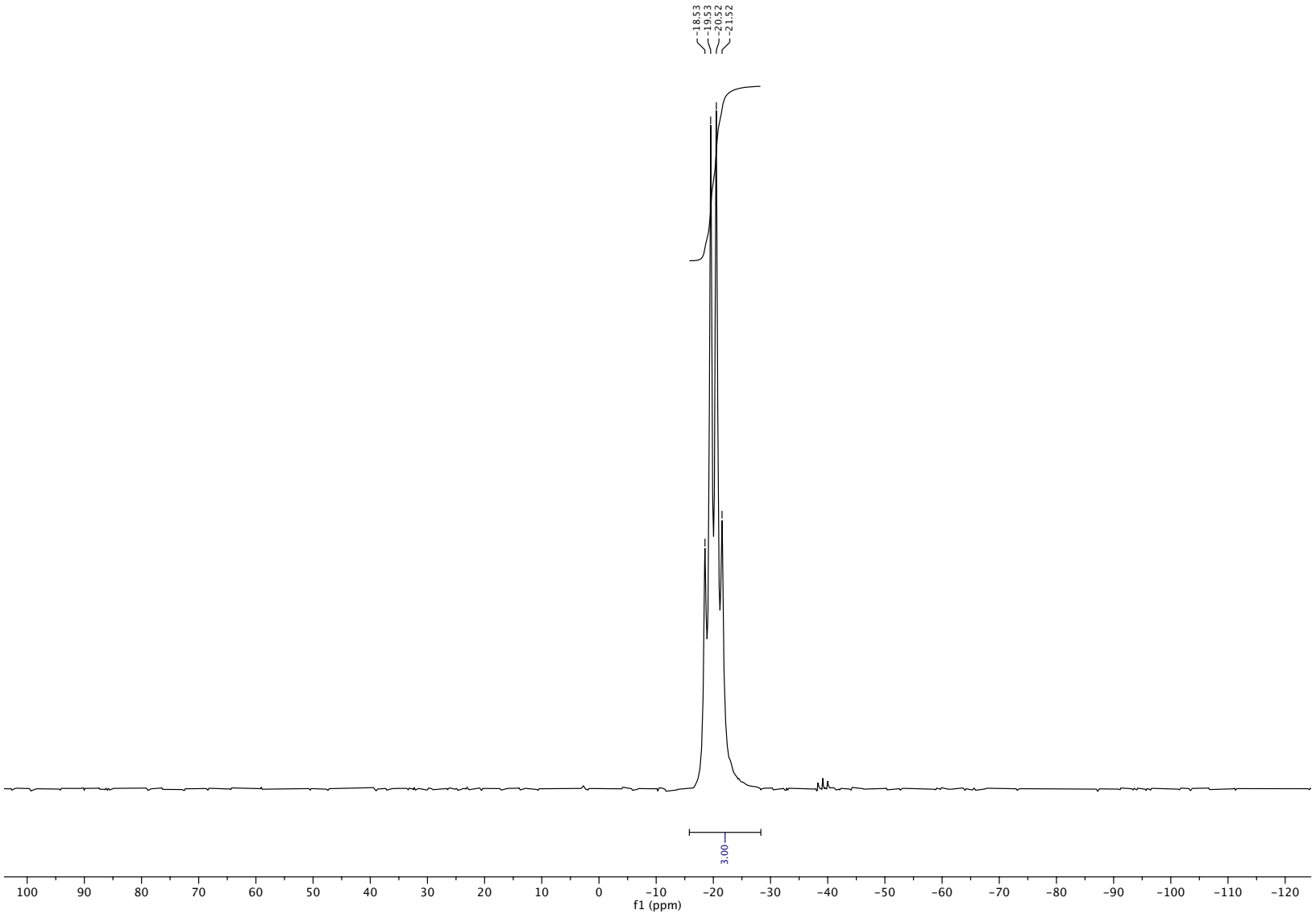
B.1 96 MHz ^{11}B NMR of compound **2a** in THF



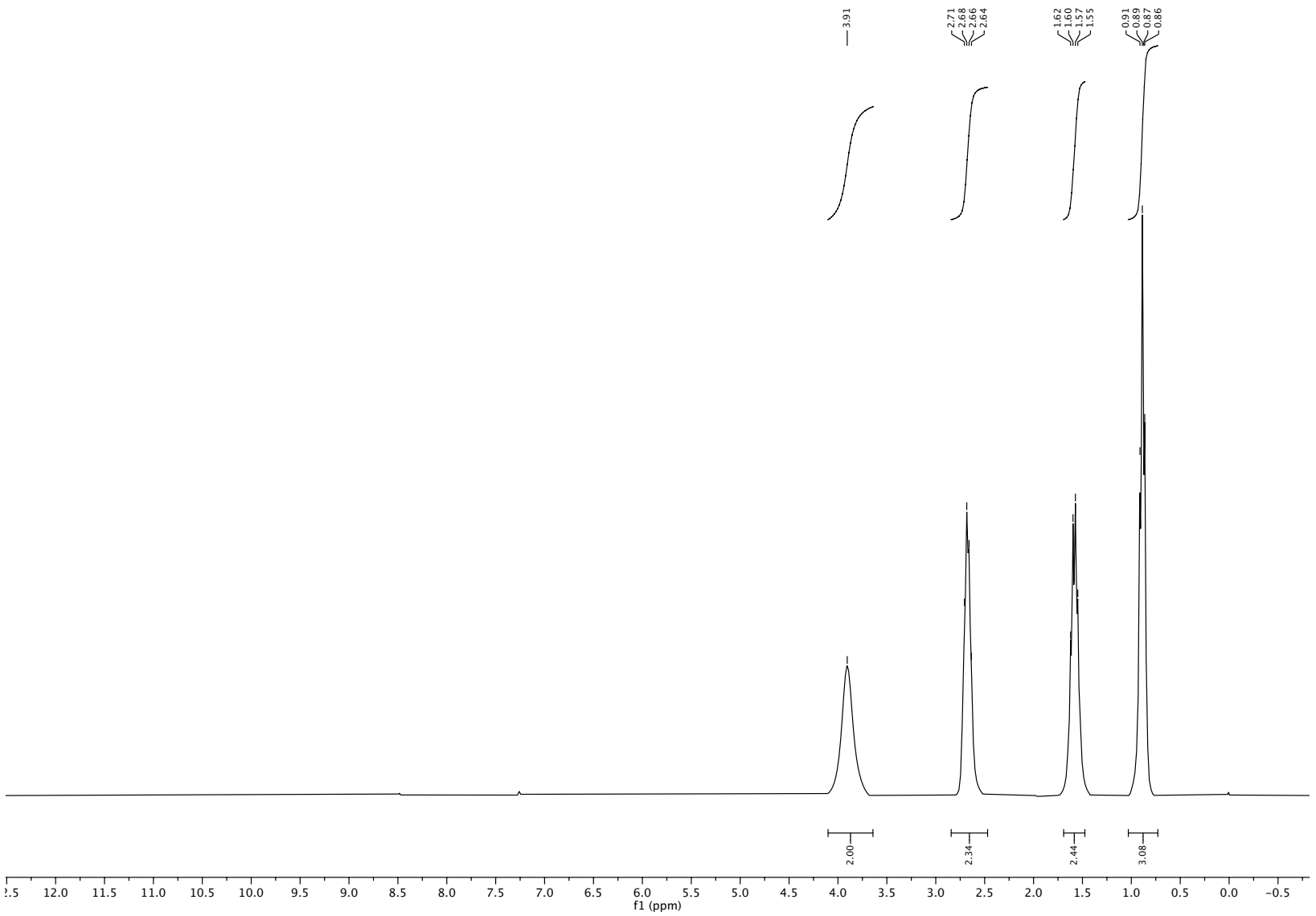
B.2 300 MHz ^{1}H NMR of compound **2b** in $CDCl_3$



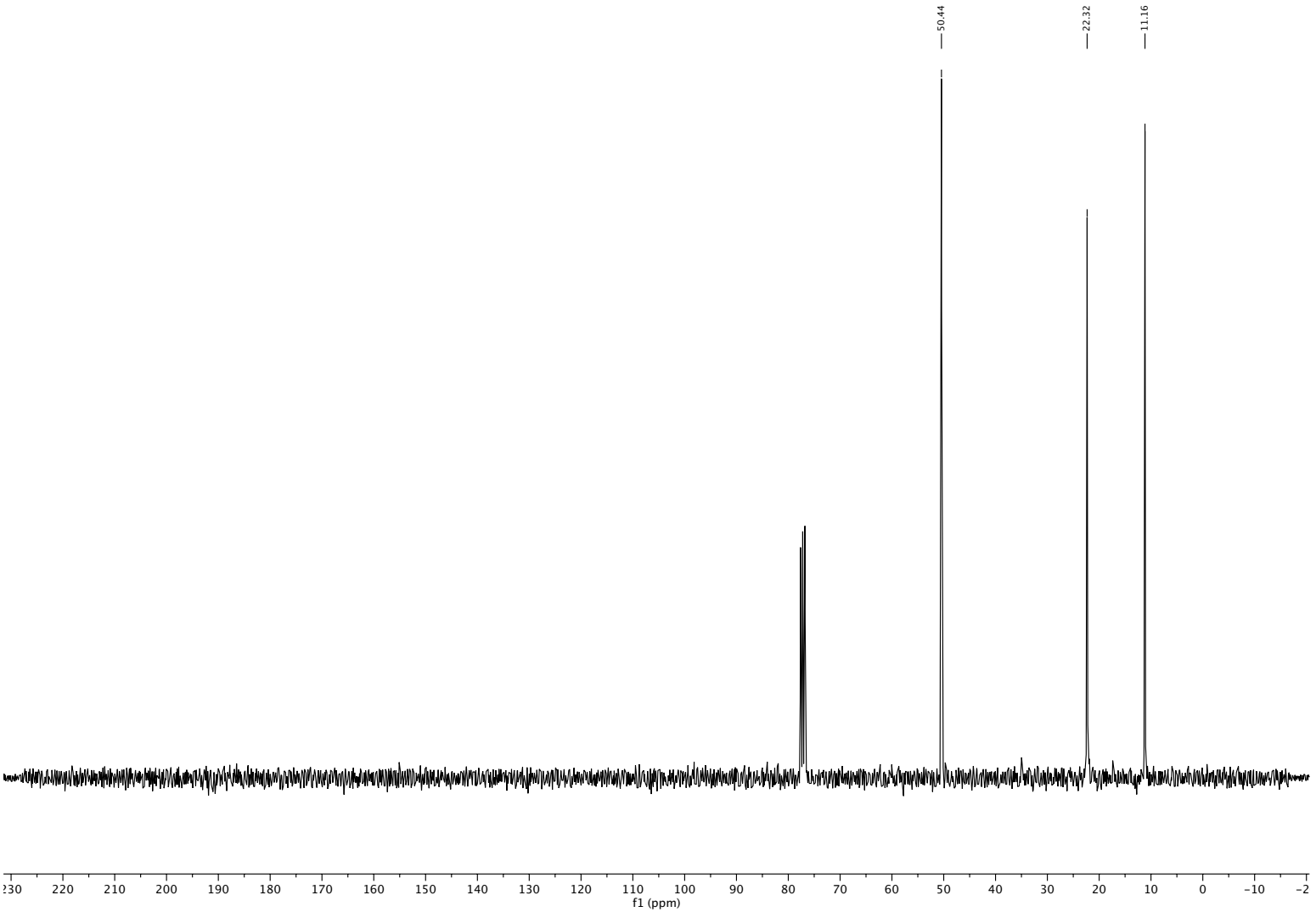
B.3 75 MHz ^{13}C NMR of compound **2b** in $CDCl_3$



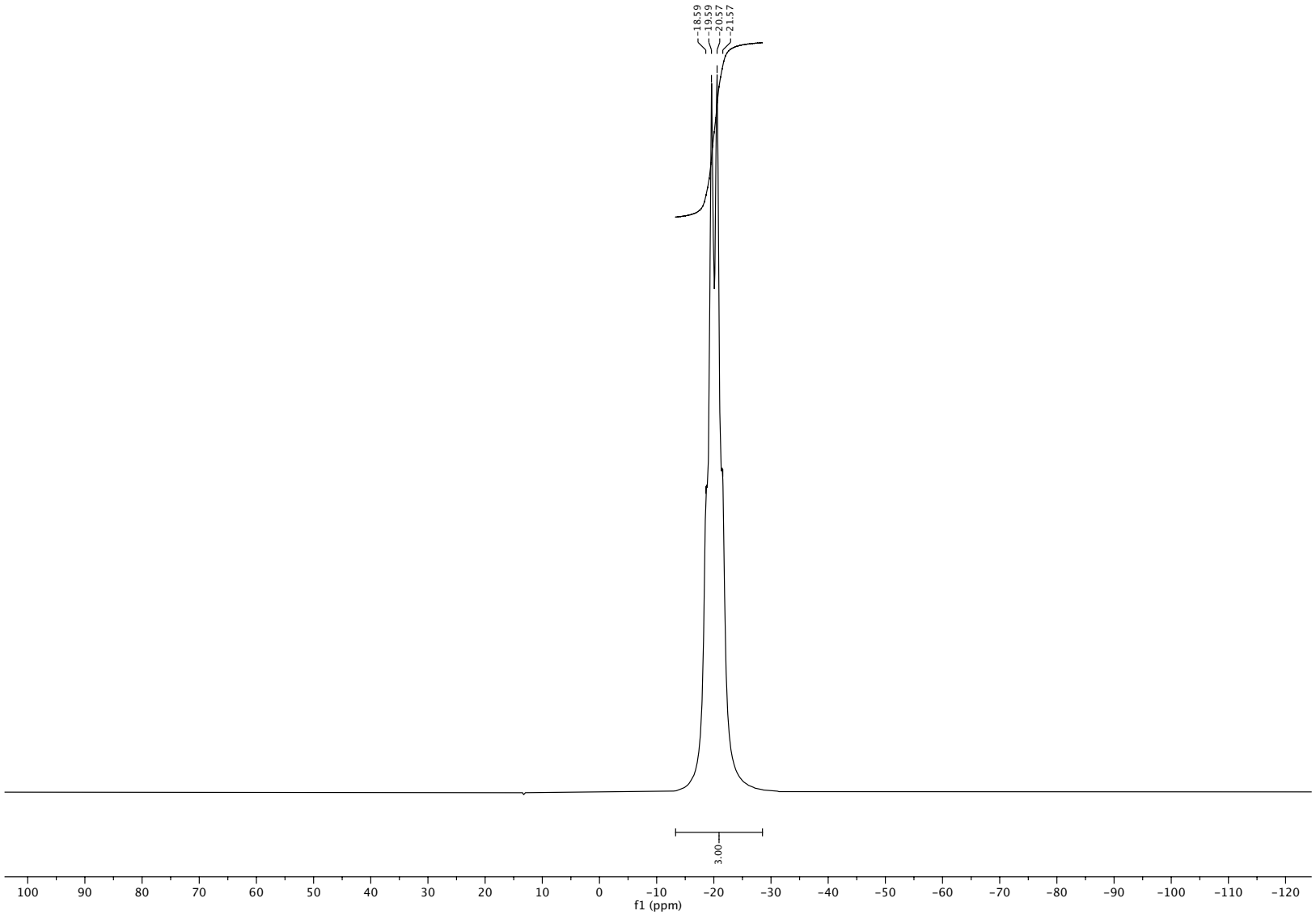
B.4 96 MHz ^{11}B NMR of compound **2b** in $CDCl_3$



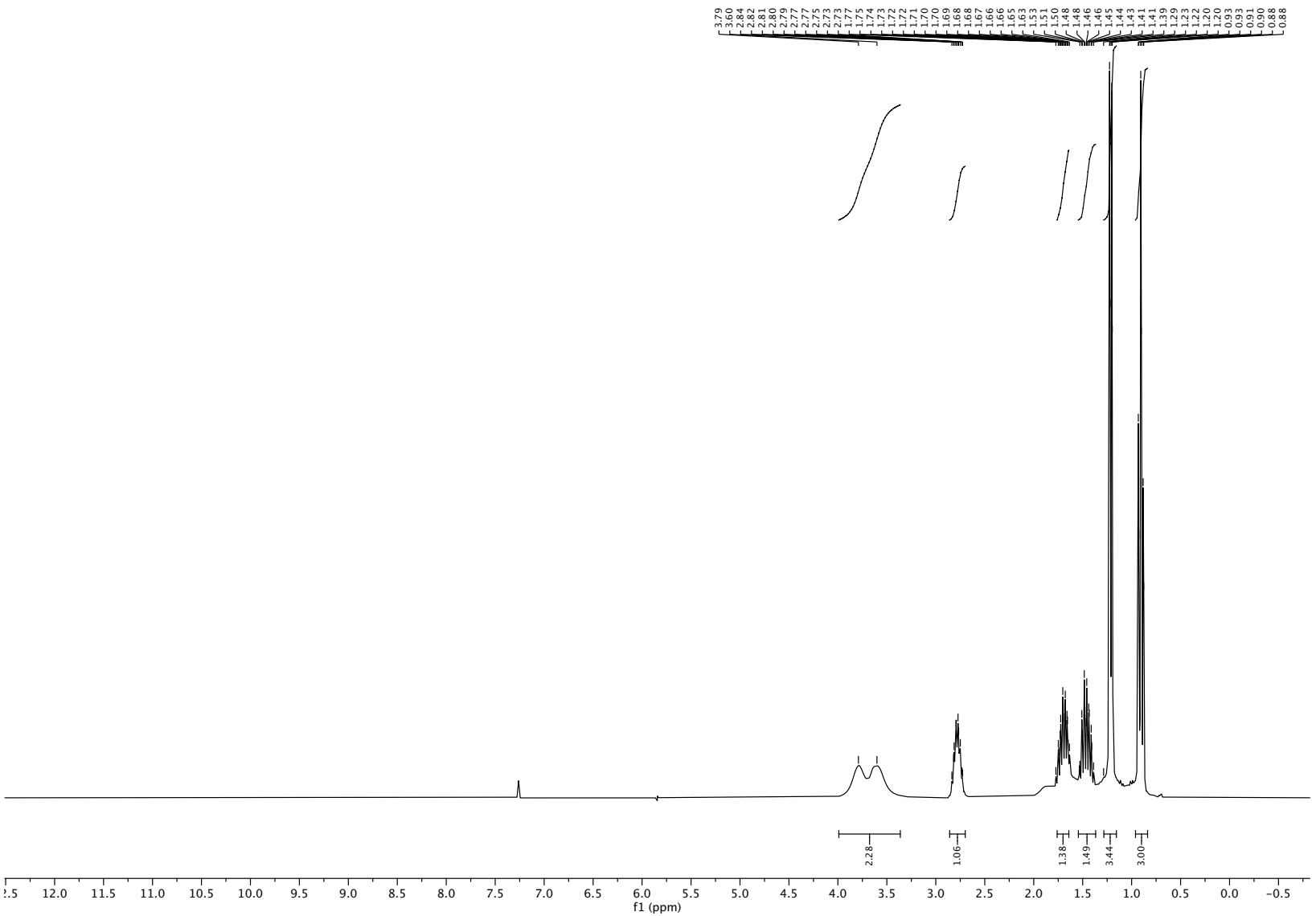
B.5 300 MHz ^{1}H NMR of compound **2c** in $CDCl_3$



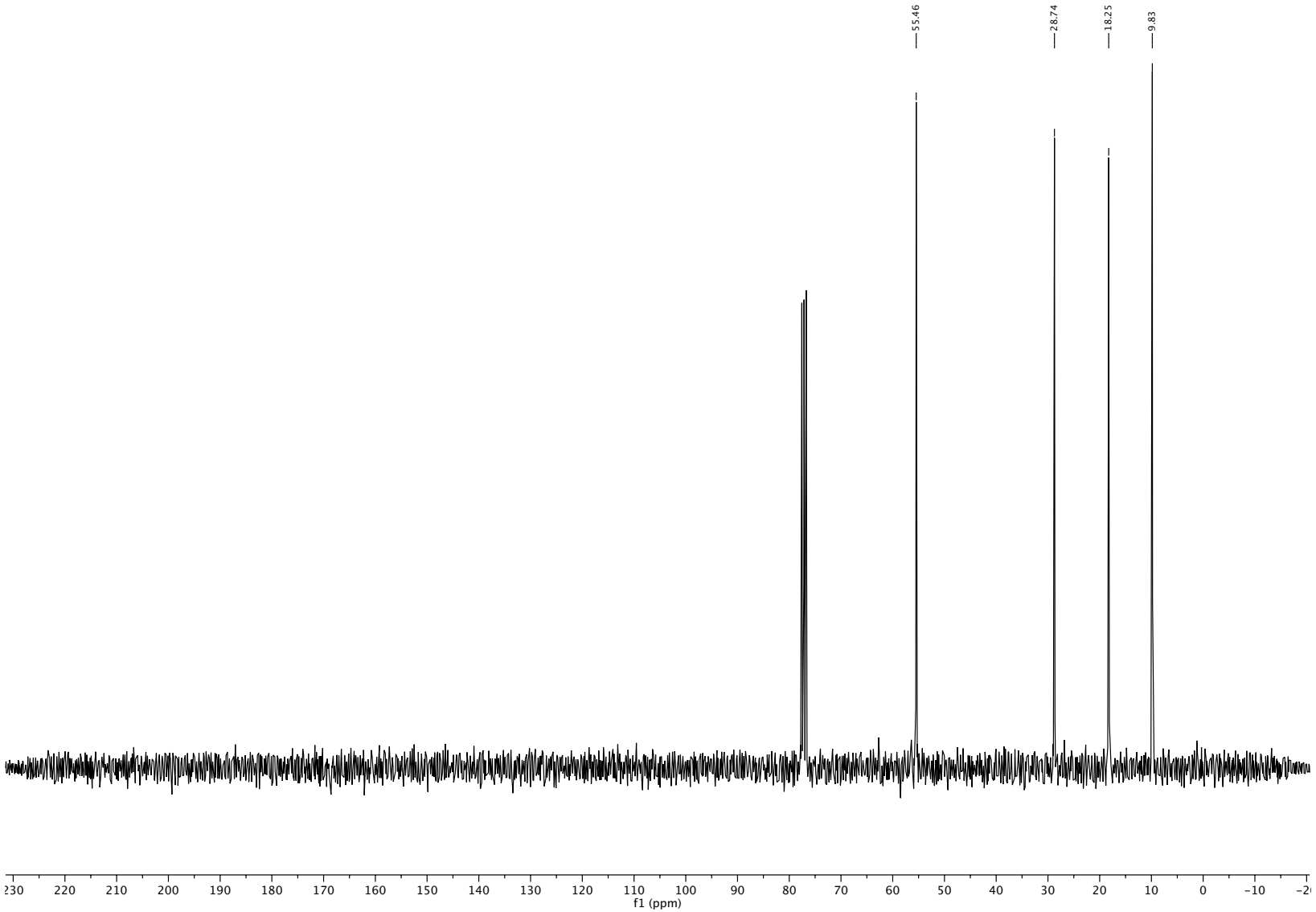
B.6 75 MHz ^{13}C NMR of compound **2c** in $CDCl_3$



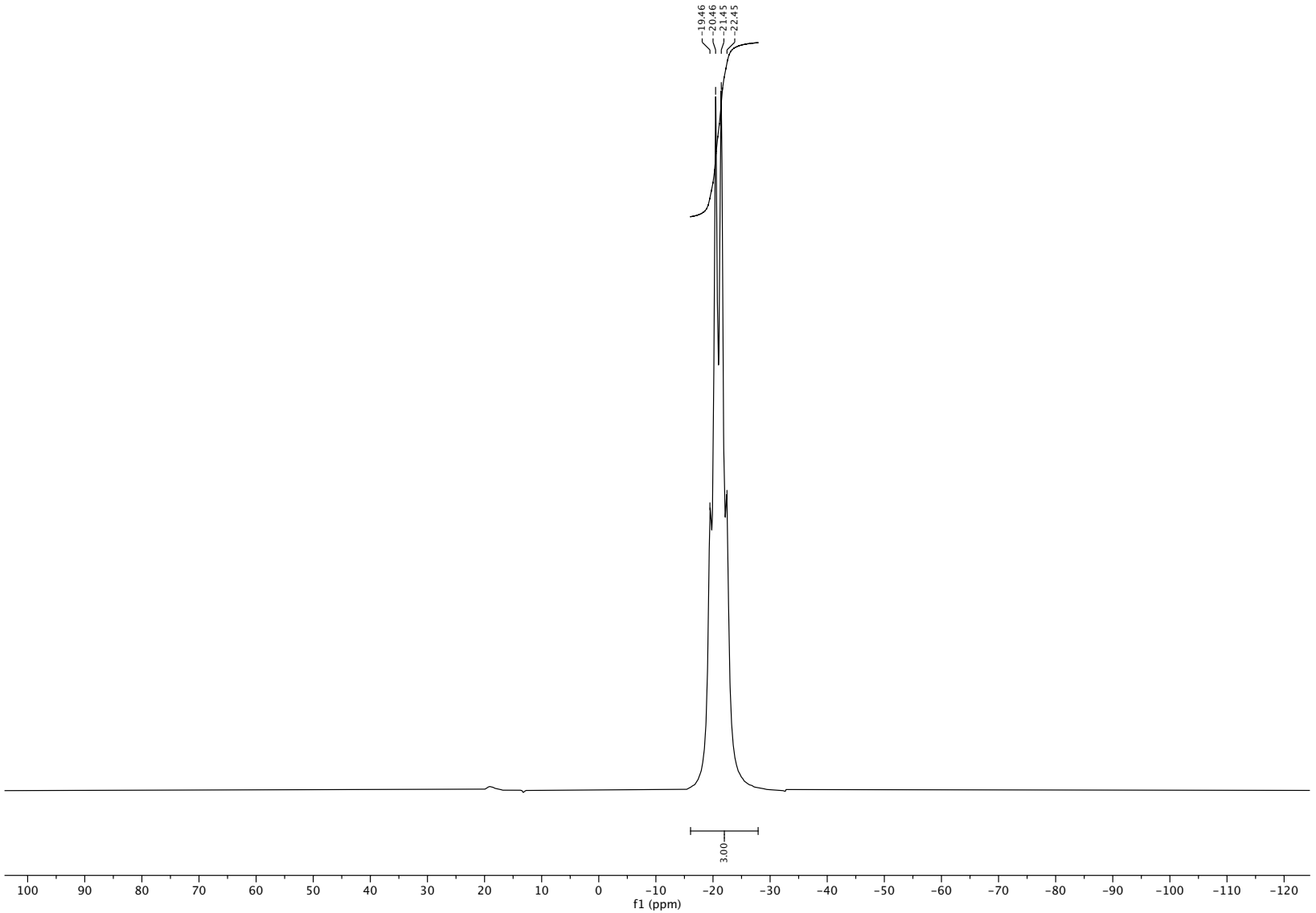
B.7 96 MHz ^{11}B NMR of compound **2c** in $CDCl_3$



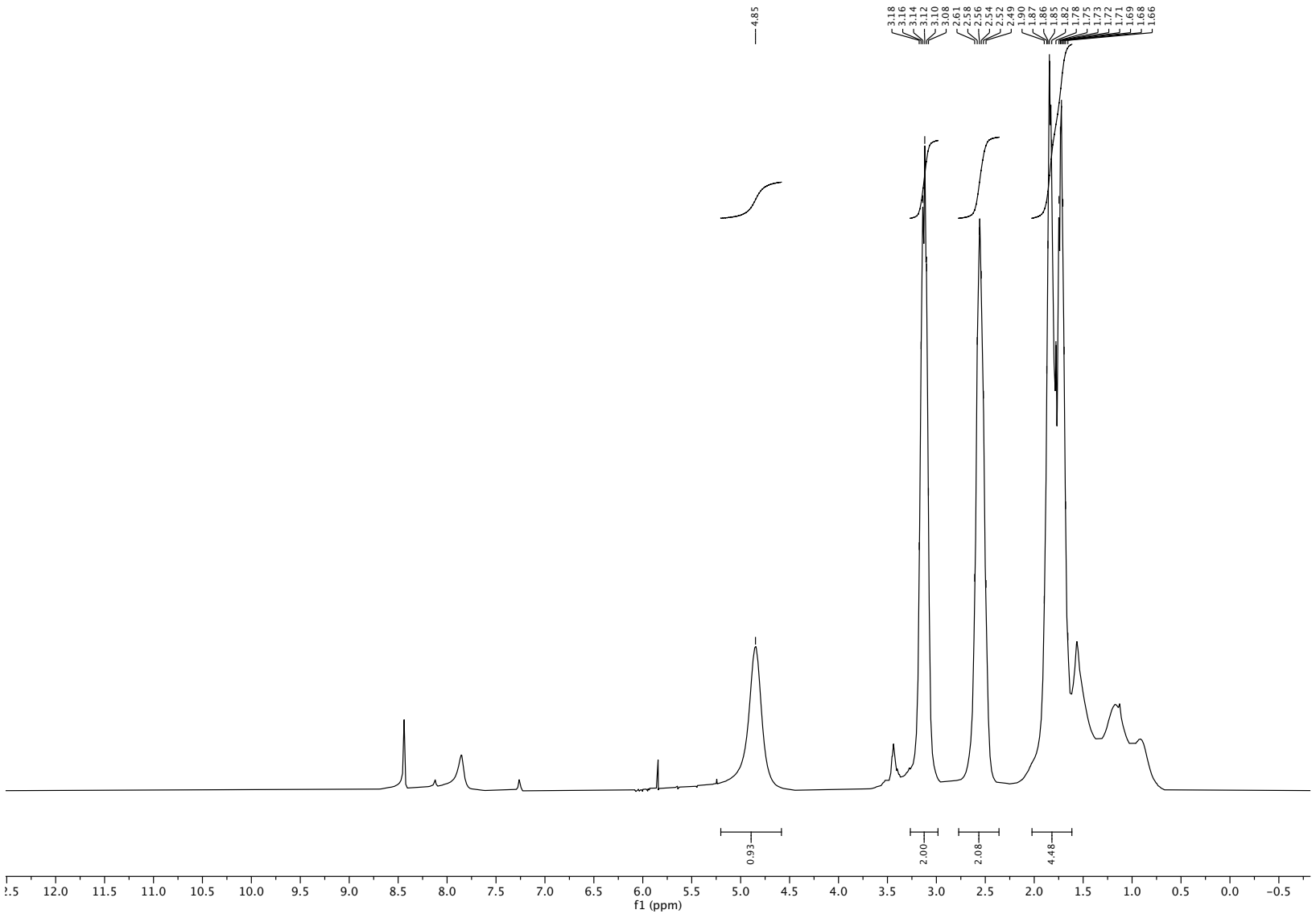
B.8 300 MHz ^{1}H NMR of compound **2d** in $CDCl_3$



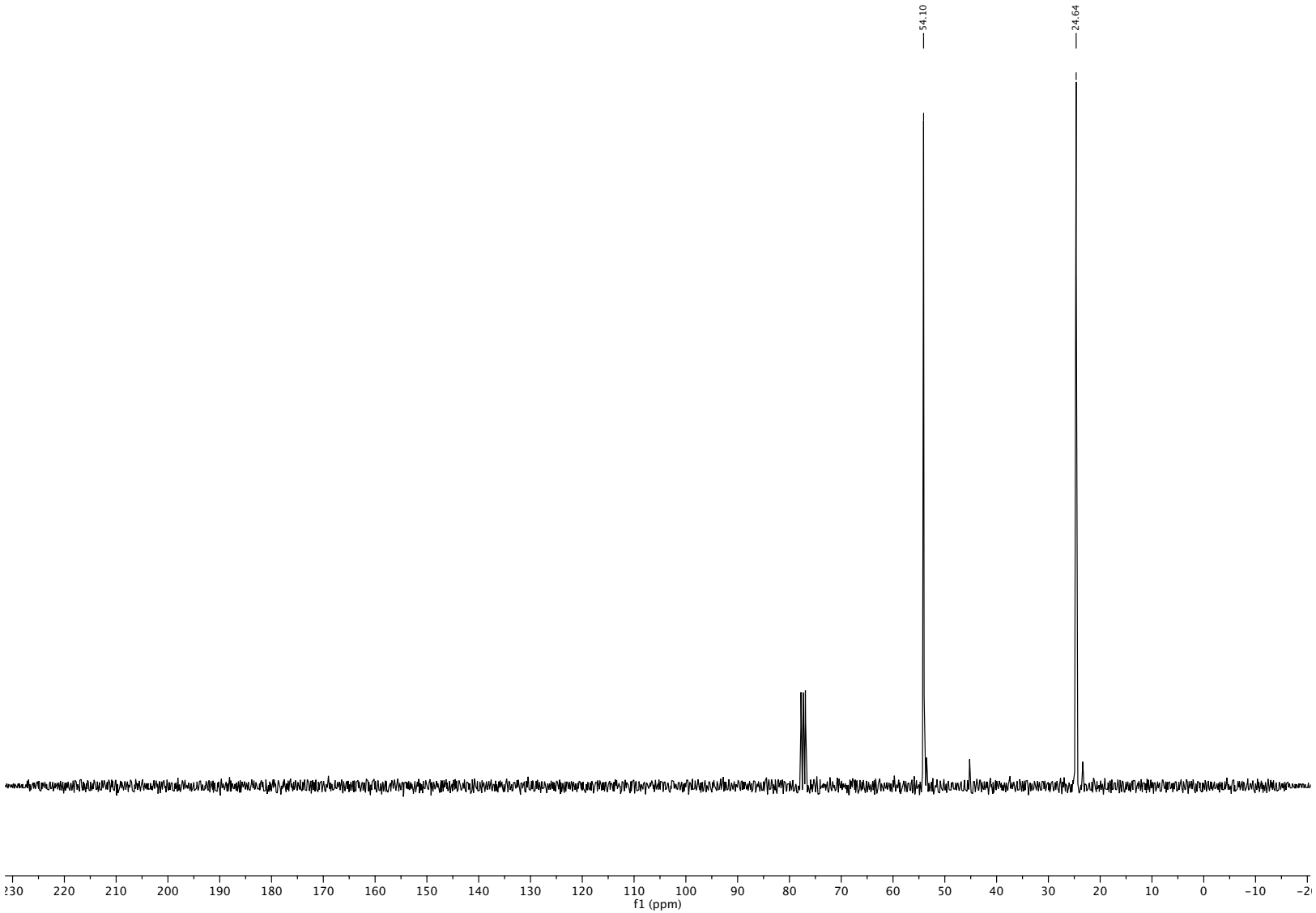
B.9 75 MHz ^{13}C NMR of compound **2d** in $CDCl_3$



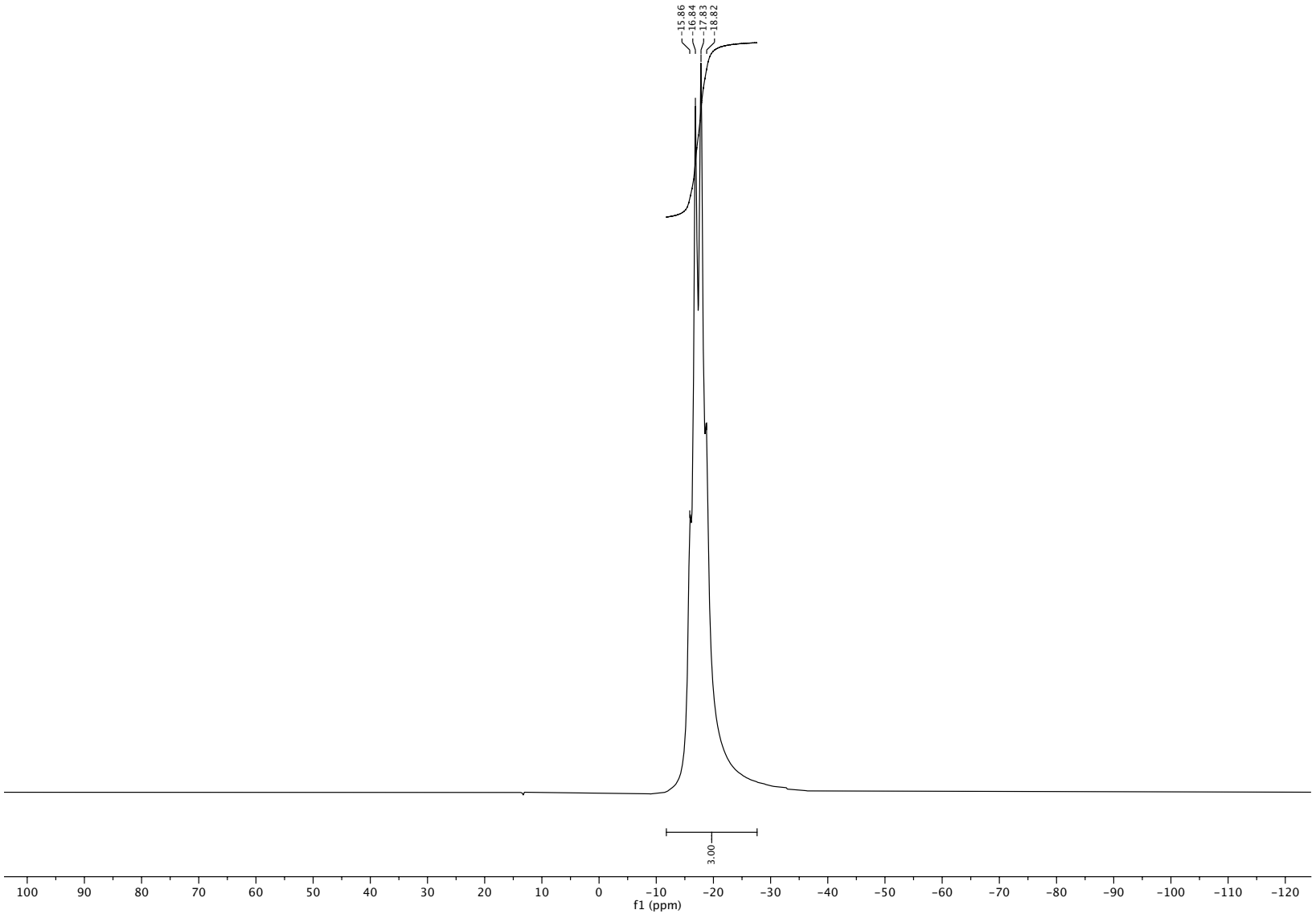
B.10 96 MHz ^{11}B NMR of compound **2d** in $CDCl_3$



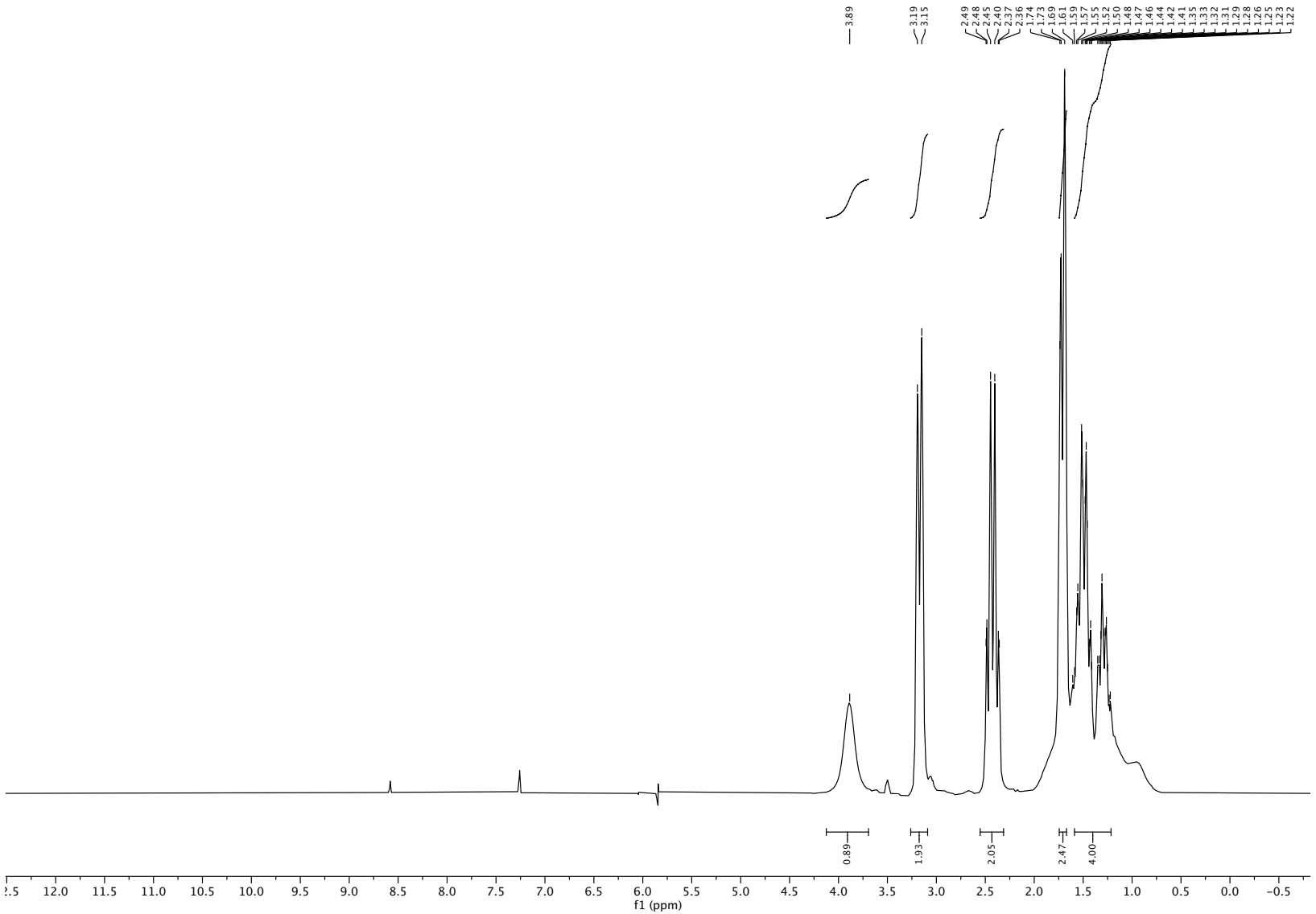
B.11 300 MHz ^{1}H NMR of compound **2e** in $CDCl_3$



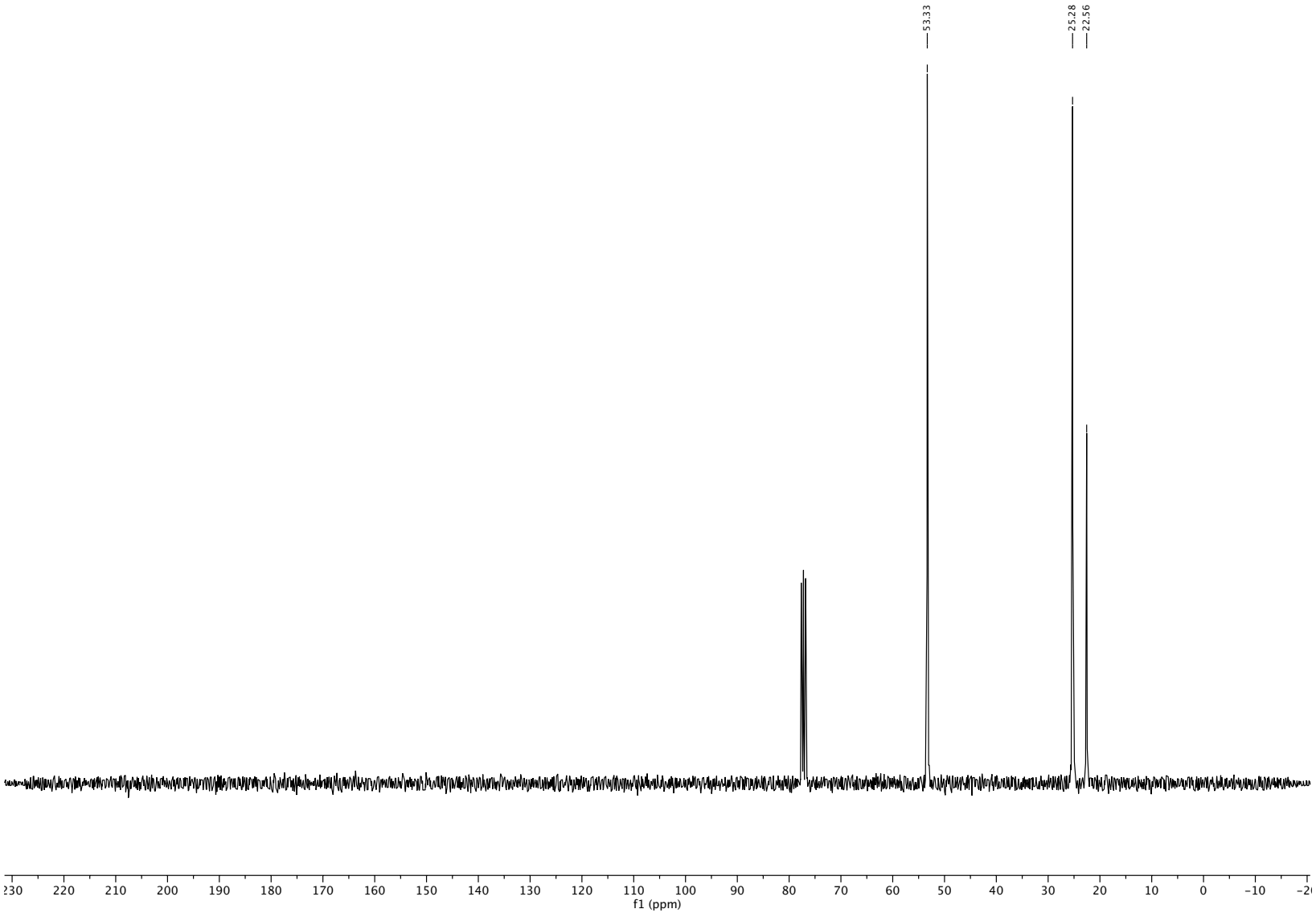
B.12 75 MHz ^{13}C NMR of compound **2e** in $CDCl_3$



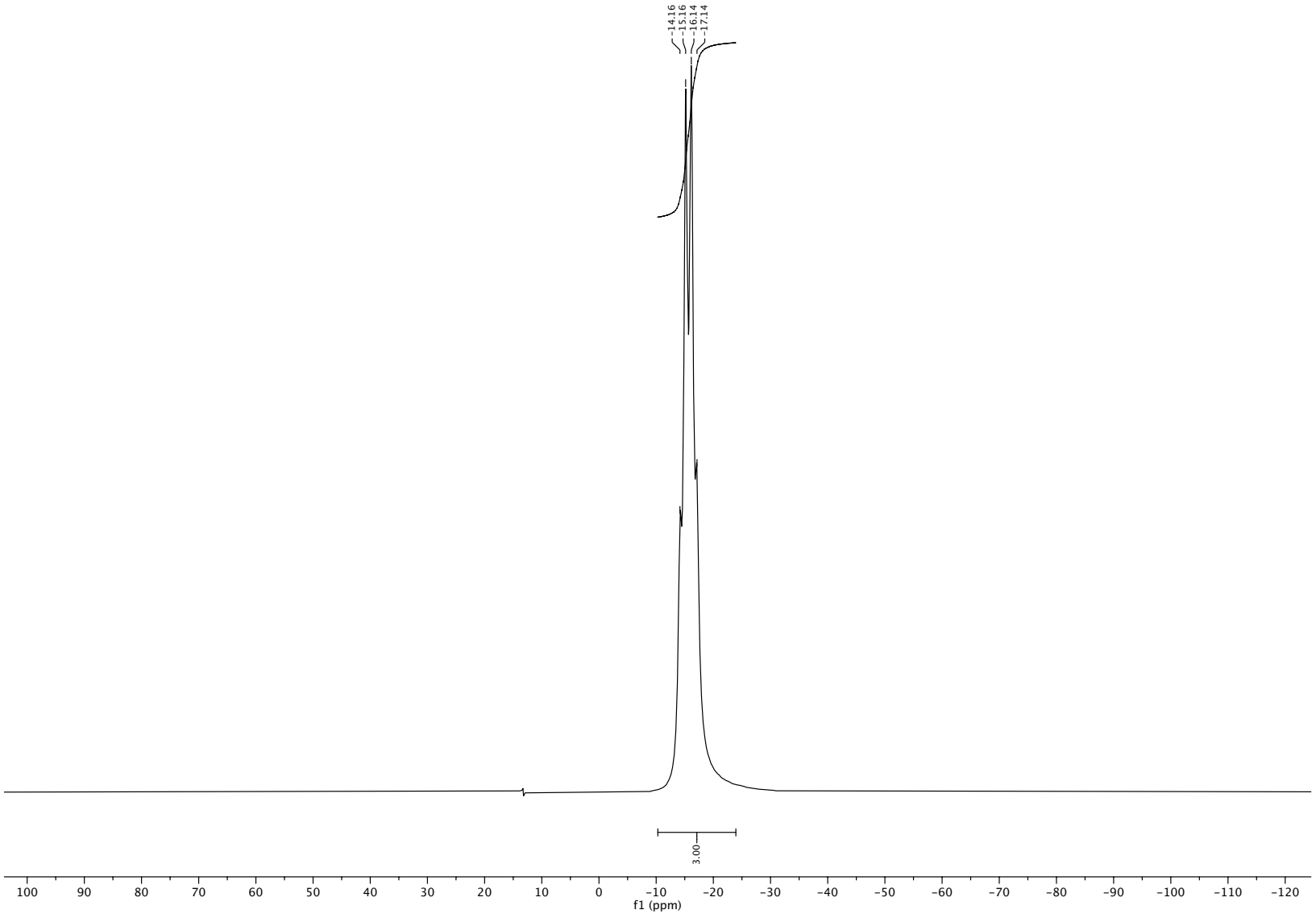
B.13 96 MHz ^{11}B NMR of compound **2e** in $CDCl_3$



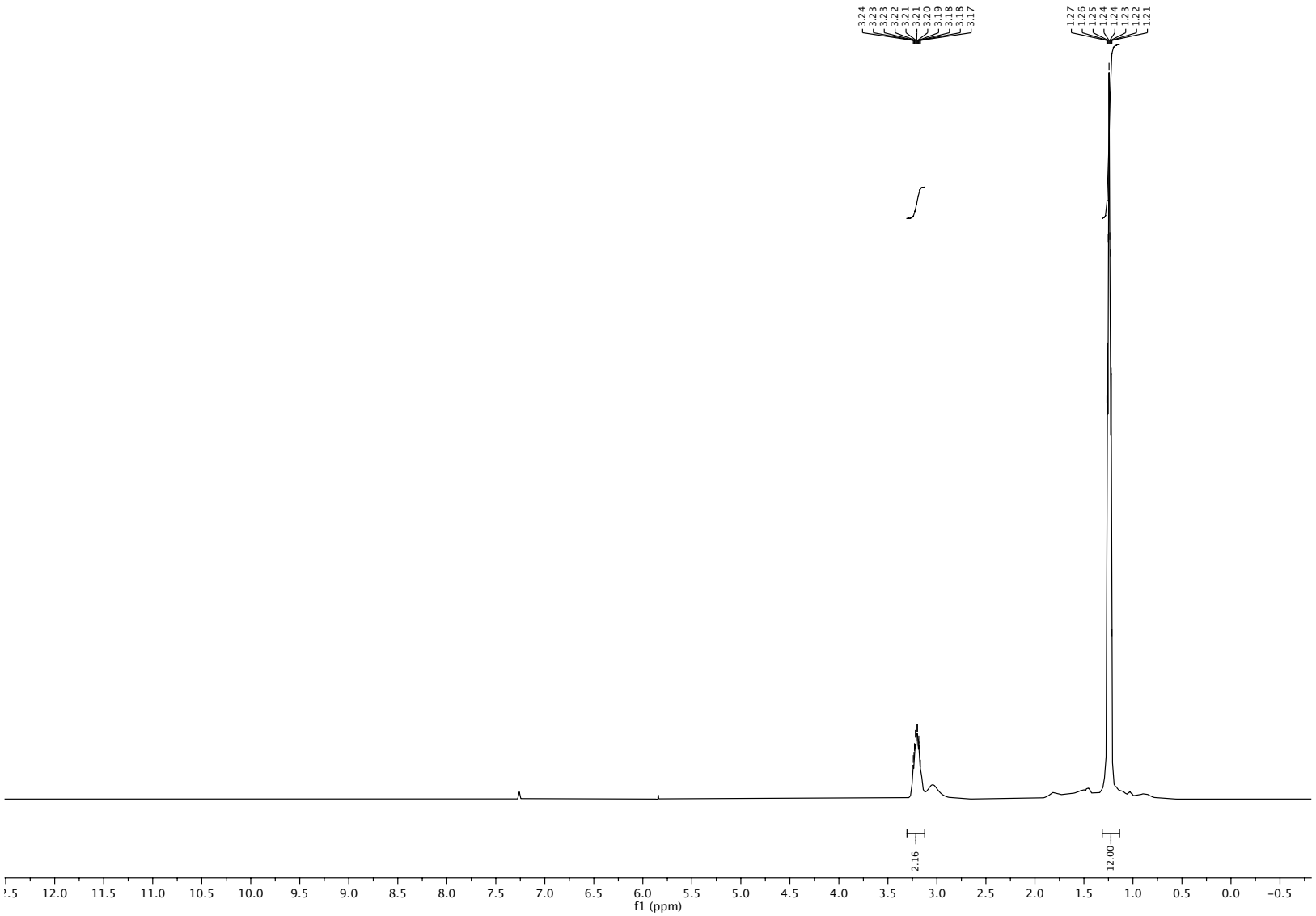
B.14 300 MHz ^{1}H NMR of compound **2f** in $CDCl_3$



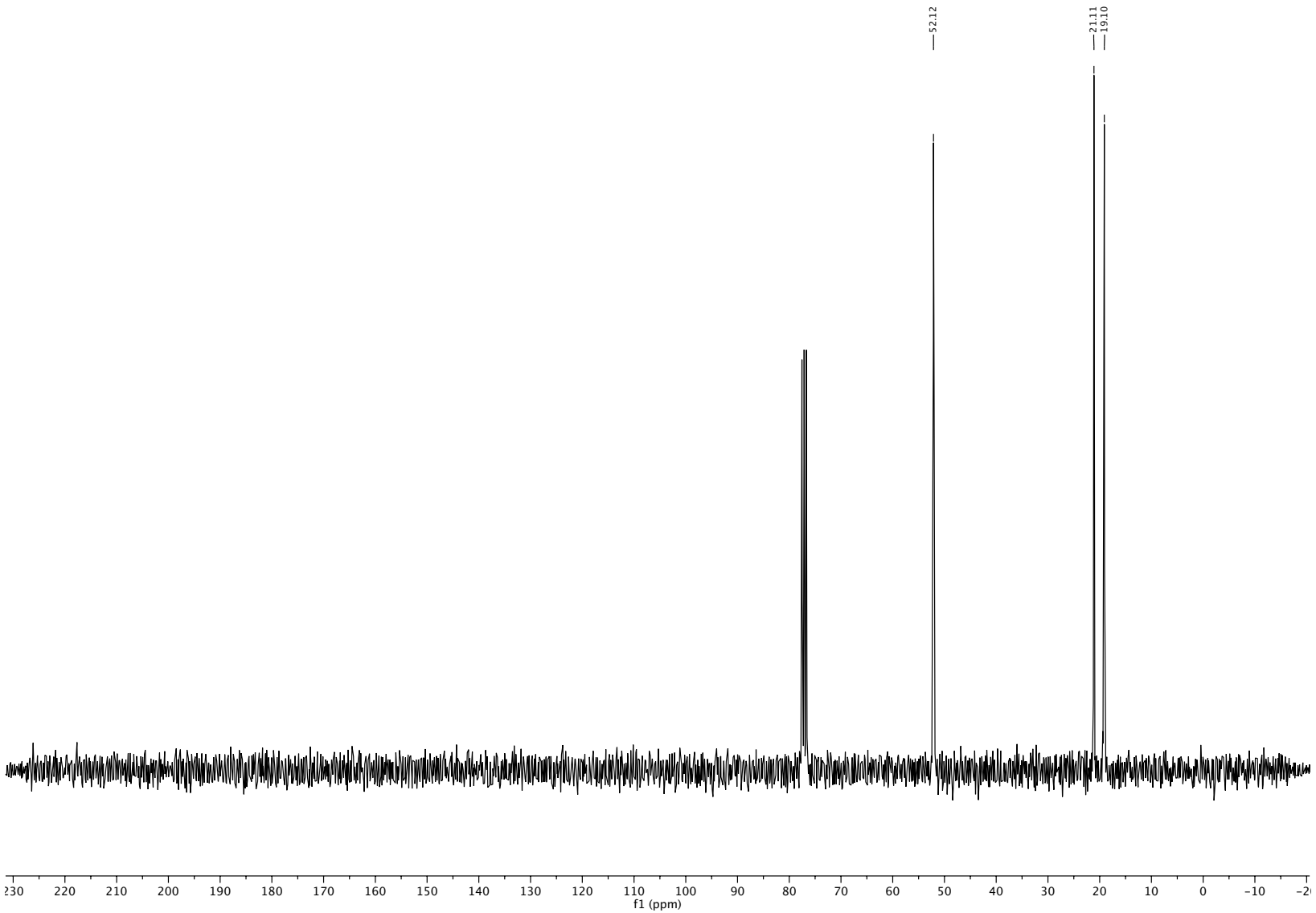
B.15 75 MHz ^{13}C NMR of compound **2f** in $CDCl_3$



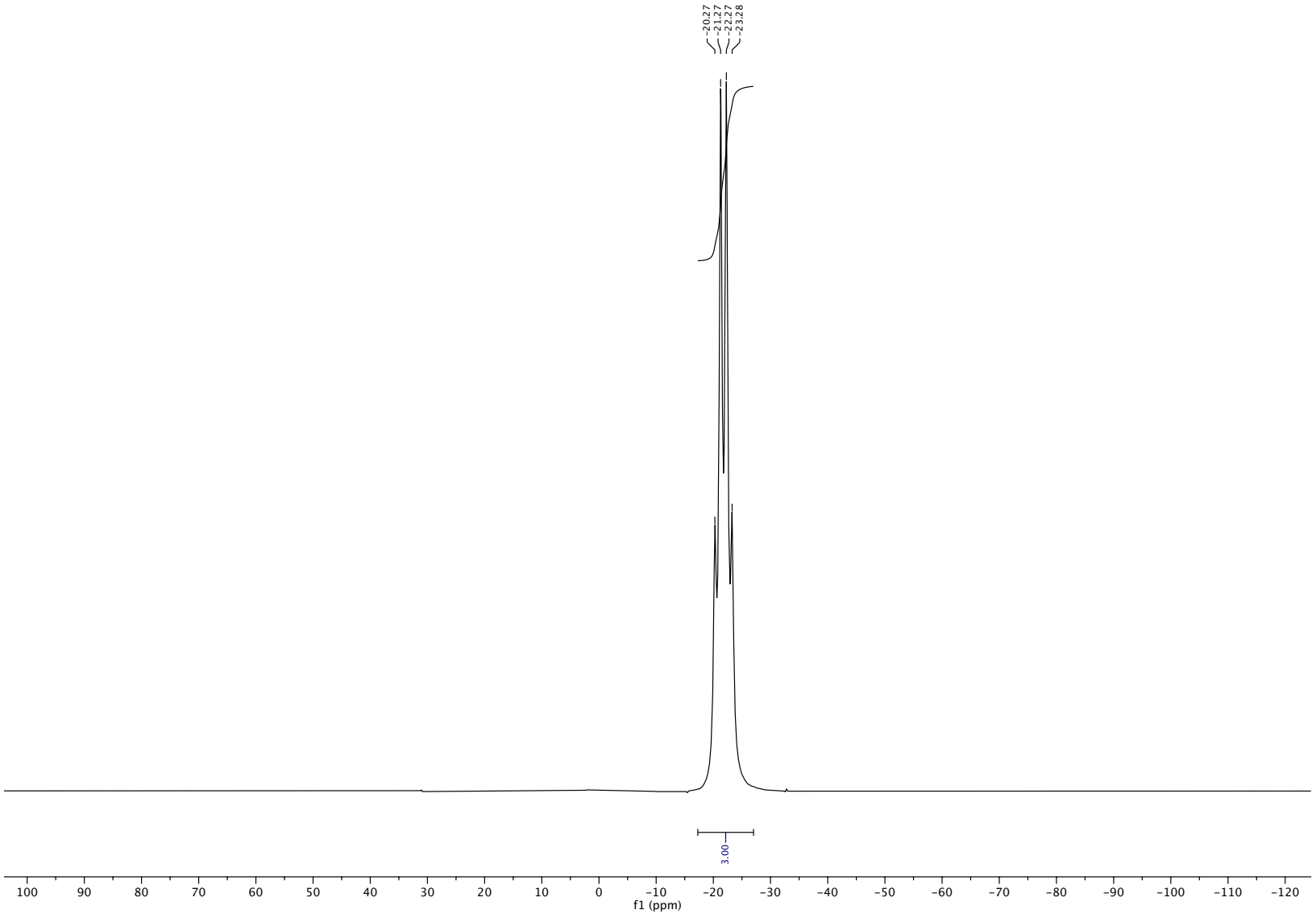
B.16 96 MHz ^{11}B NMR of compound **2f** in $CDCl_3$



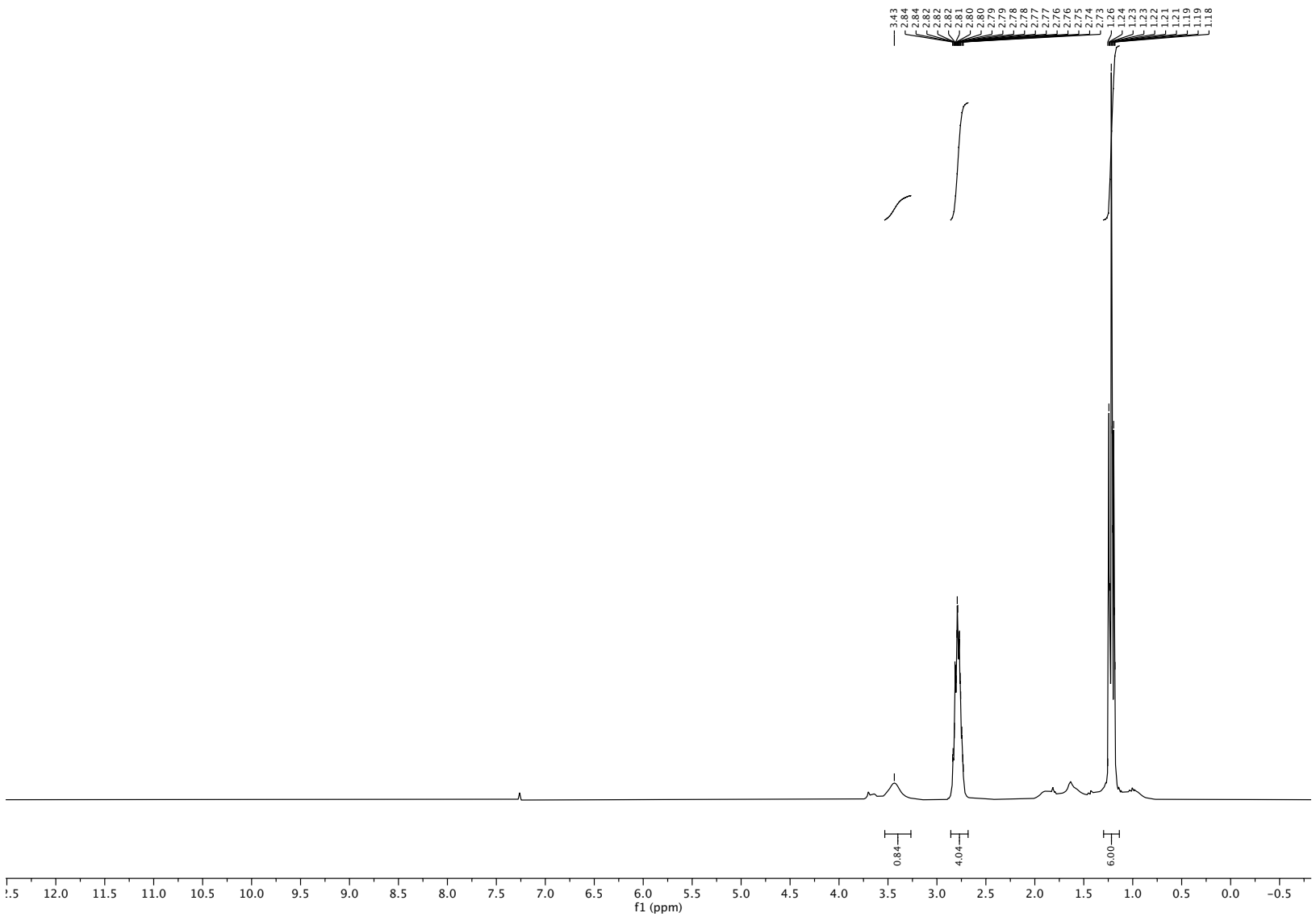
B.17 300 MHz ^{1}H NMR of compound **2g** in $CDCl_3$



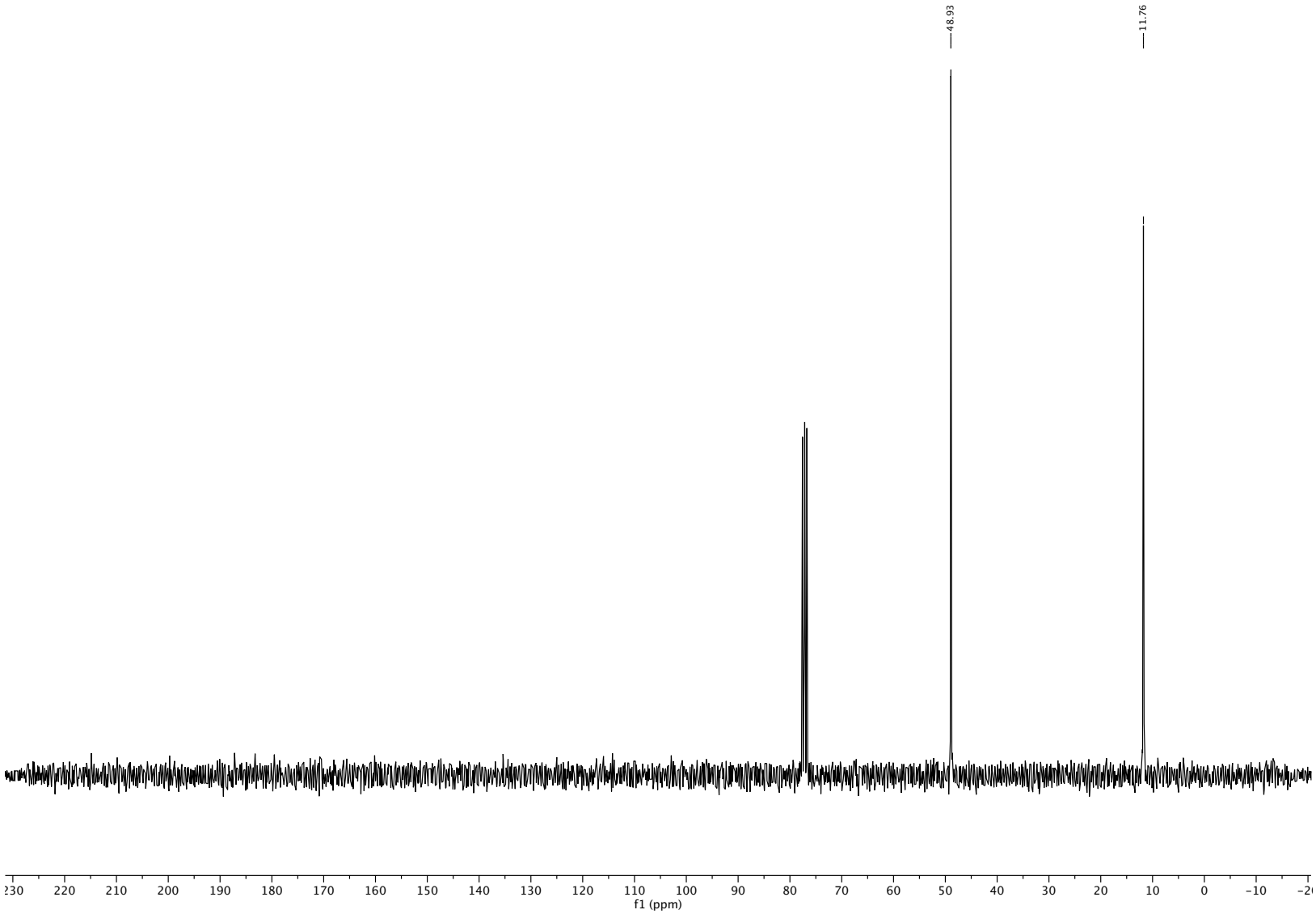
B.18 75 MHz ^{13}C NMR of compound **2g** in $CDCl_3$



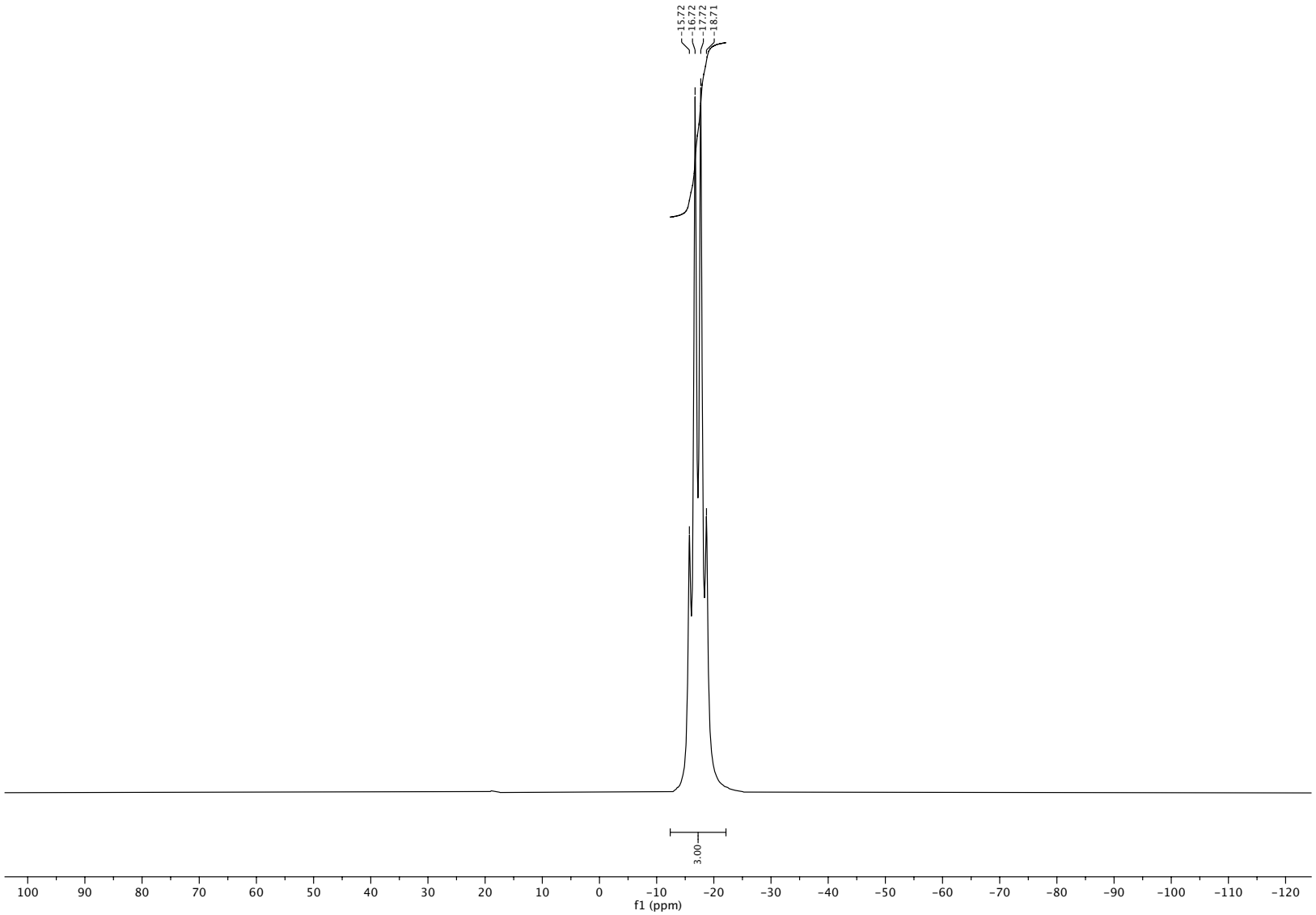
B.19 96 MHz ^{11}B NMR of compound **2g** in $CDCl_3$



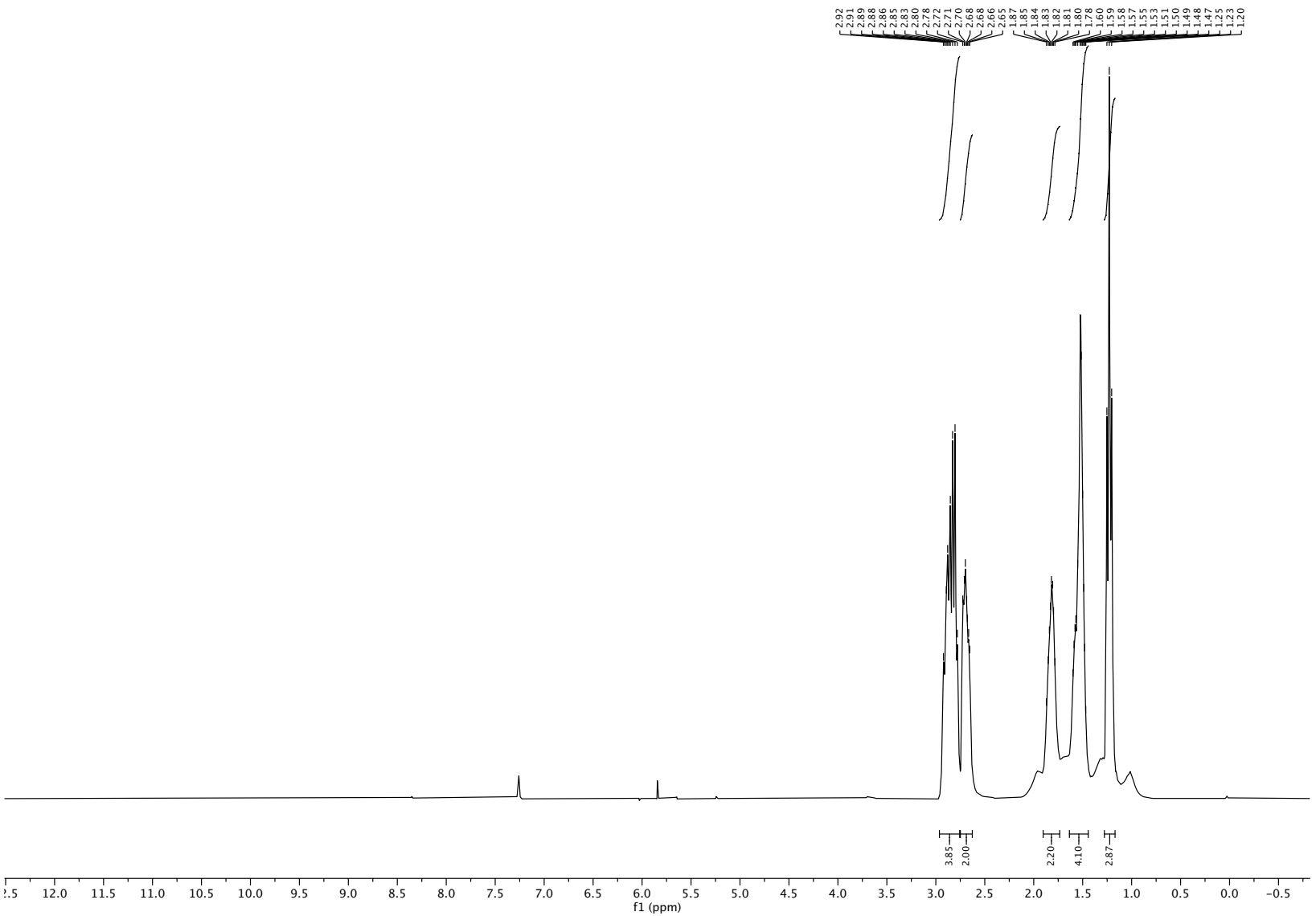
B.20 300 MHz ^{1}H NMR of compound **2h** in $CDCl_3$



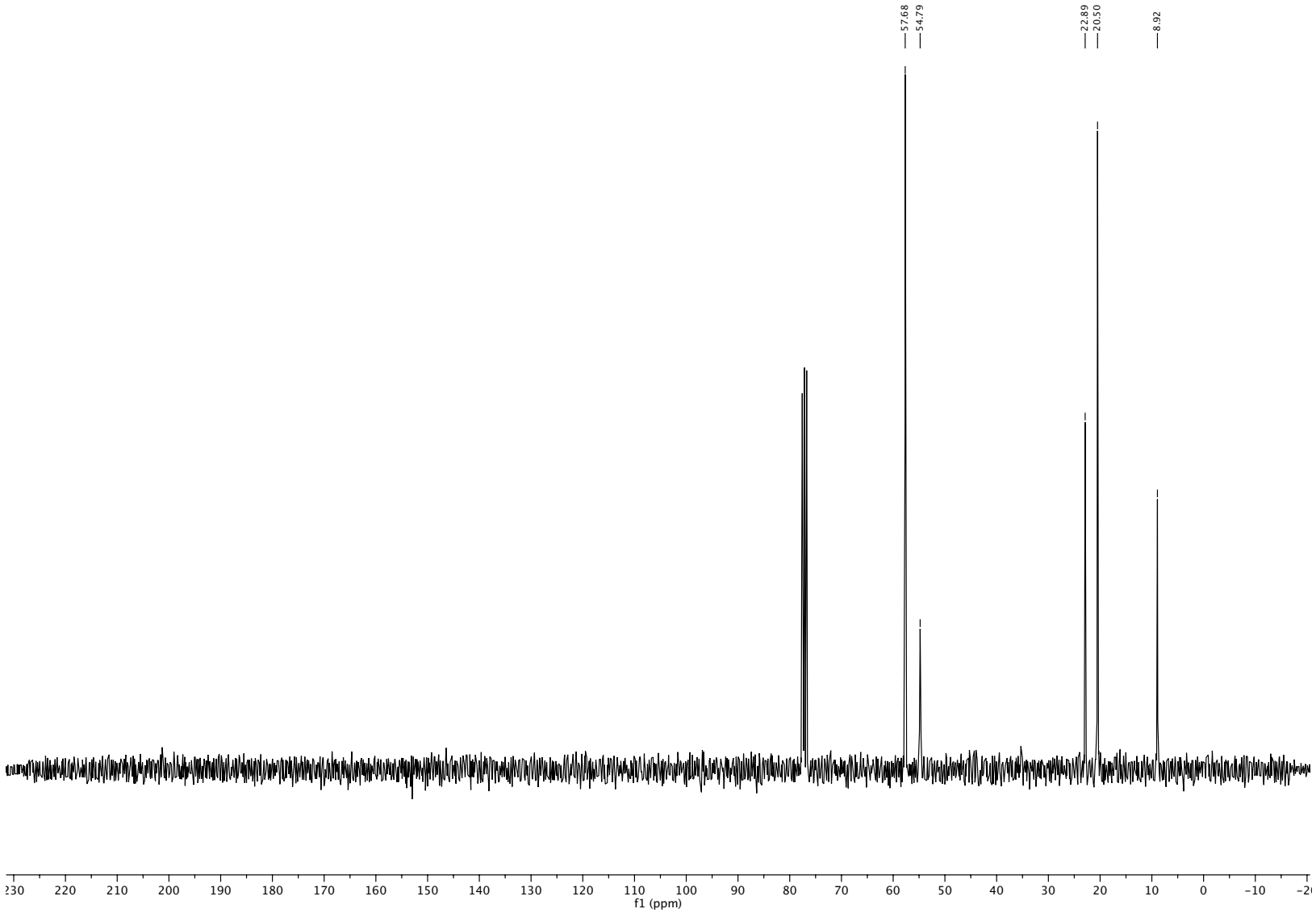
B.21 75 MHz ^{13}C NMR of compound **2h** in $CDCl_3$



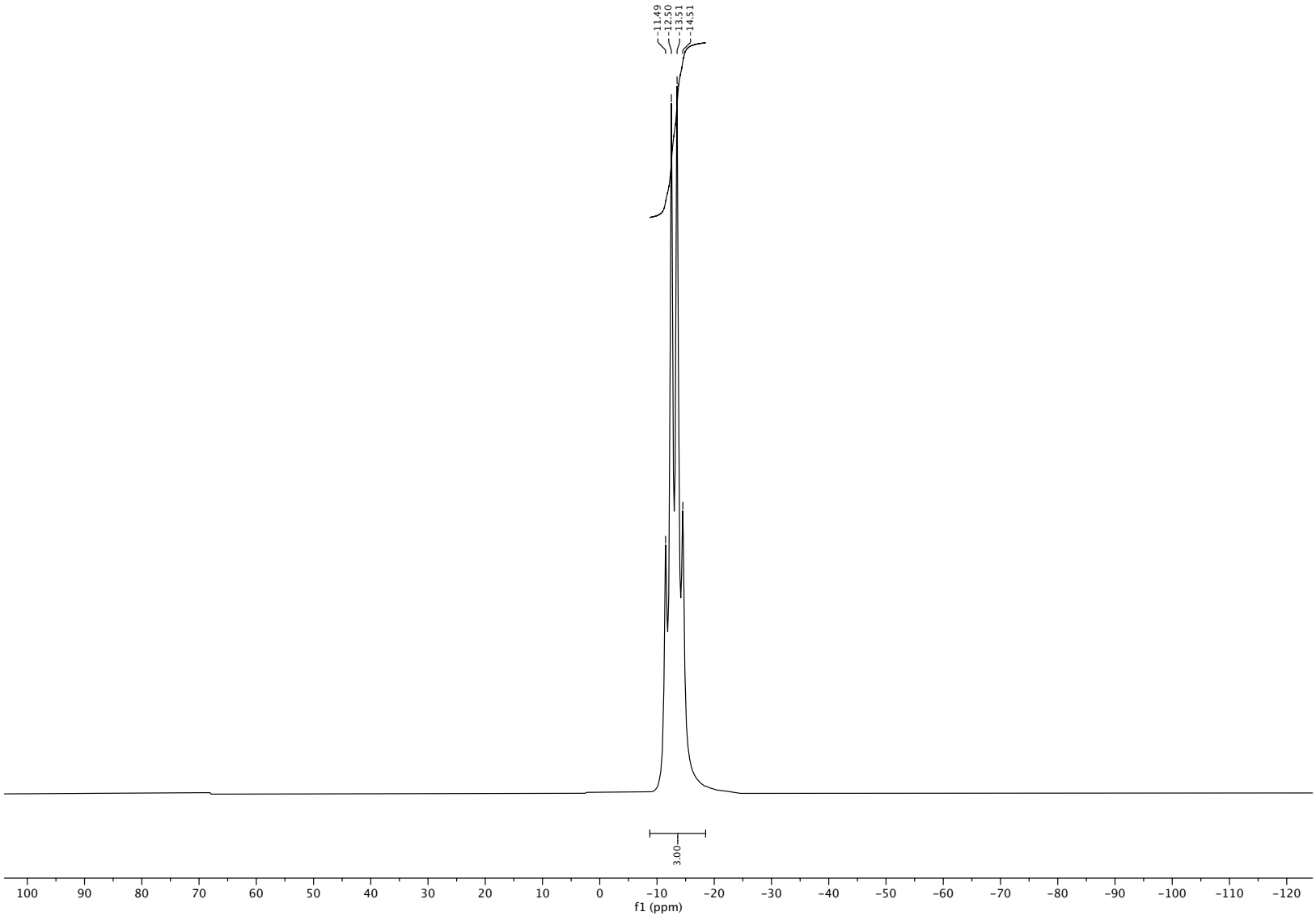
B.22 96 MHz ^{11}B NMR of compound **2h** in $CDCl_3$



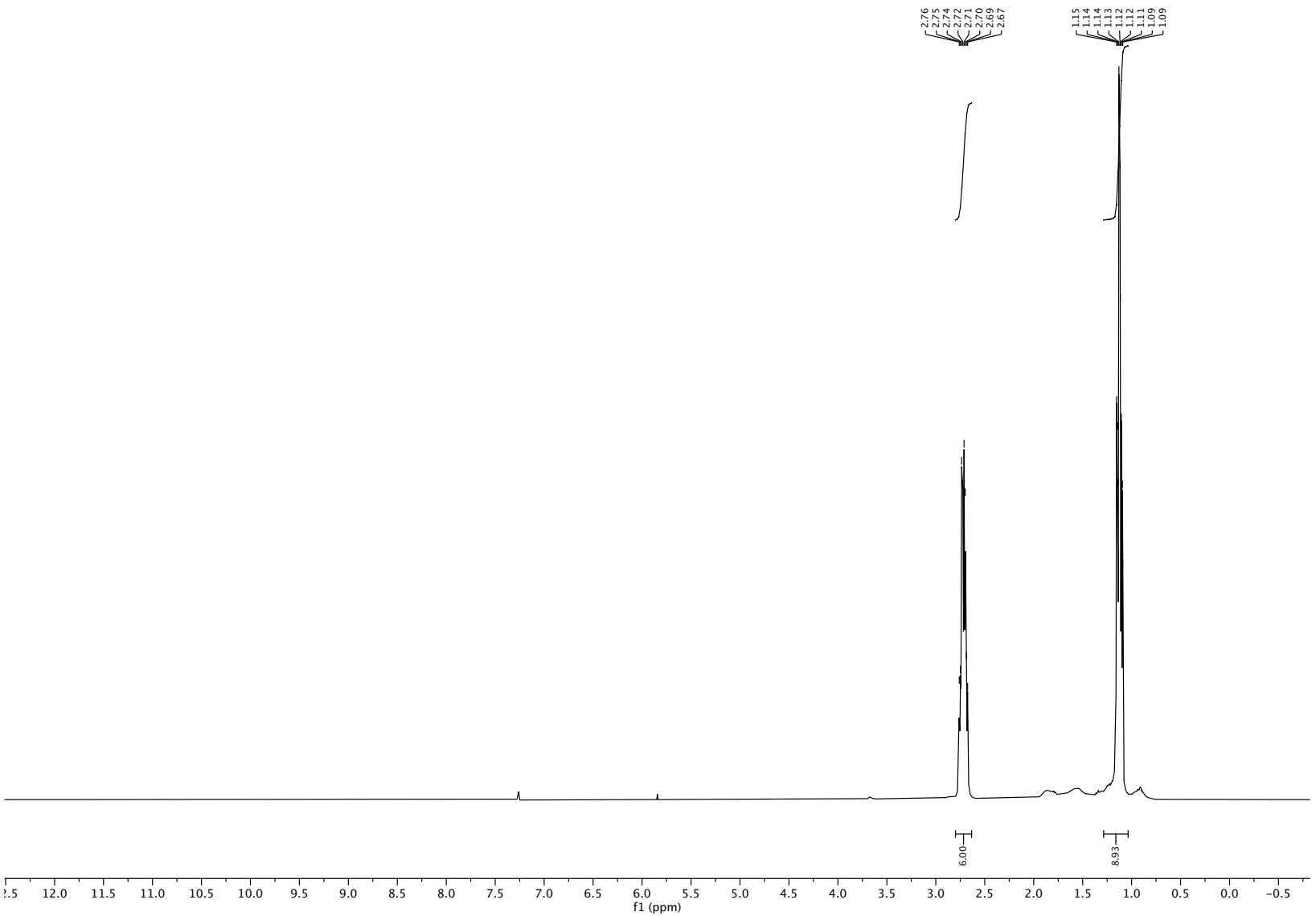
B.23 300 MHz ^{1}H NMR of compound **2i** in $CDCl_3$



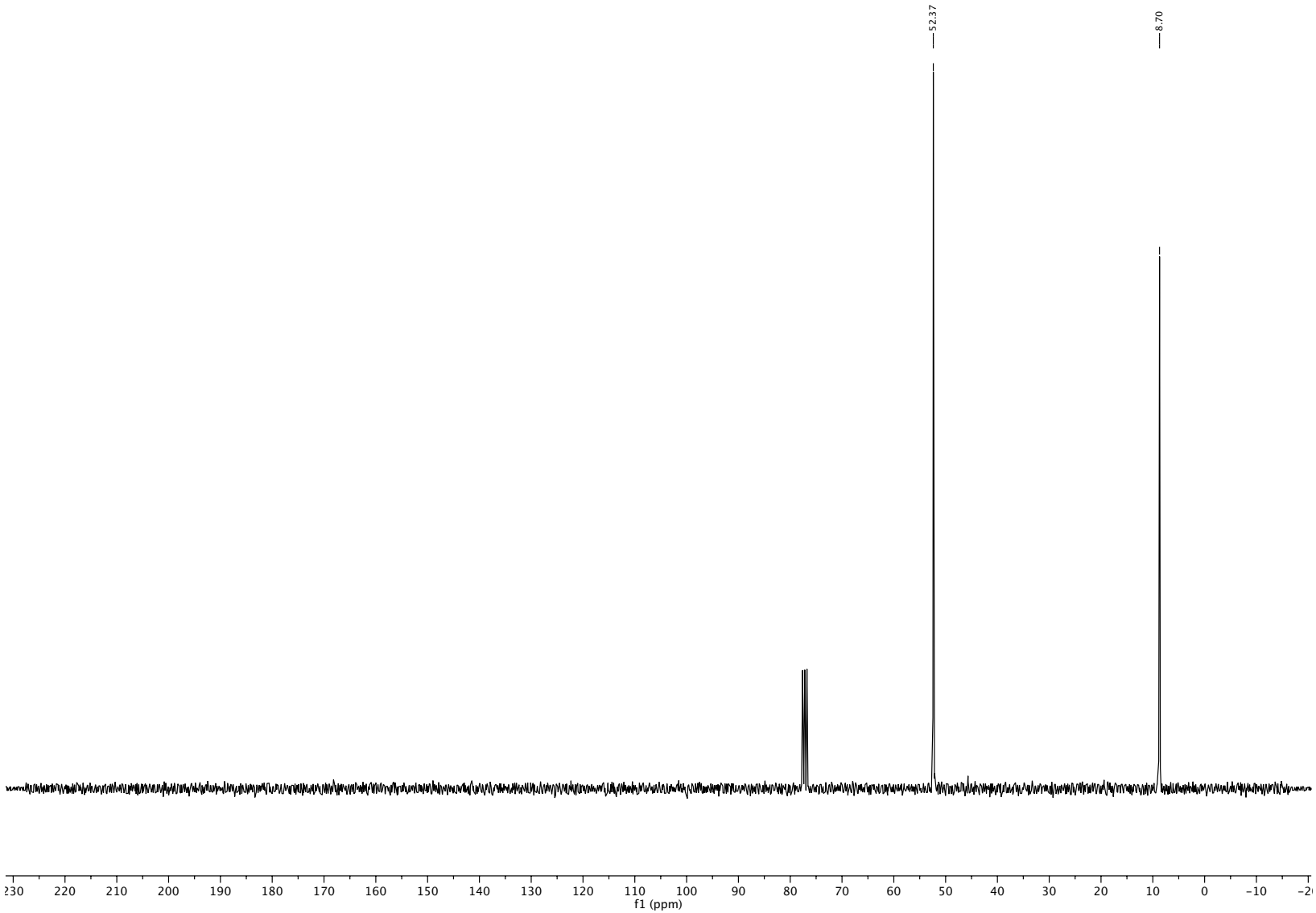
B.24 75 MHz ^{13}C NMR of compound **2i** in $CDCl_3$



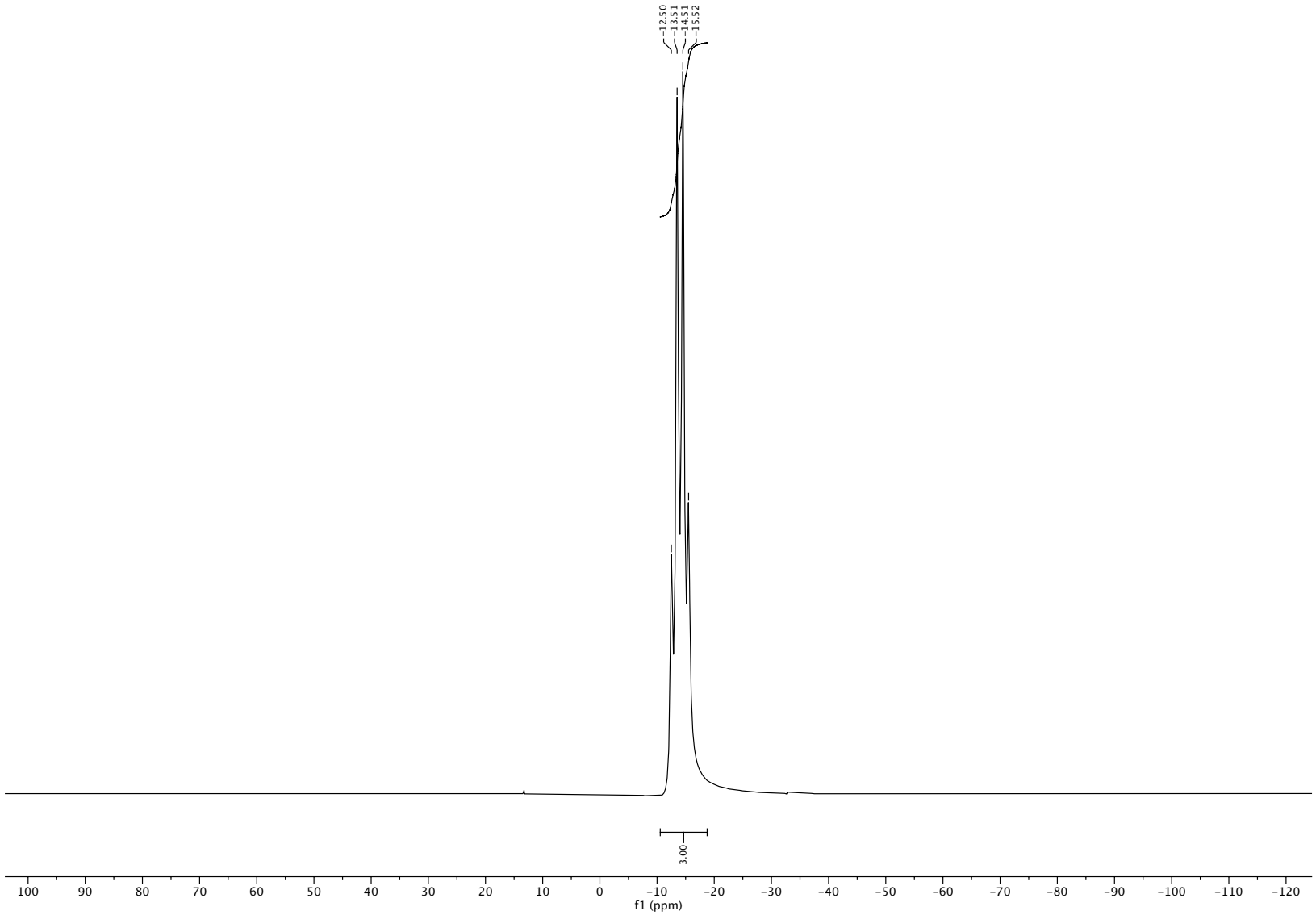
B.25 96 MHz ^{11}B NMR of compound **2i** in $CDCl_3$



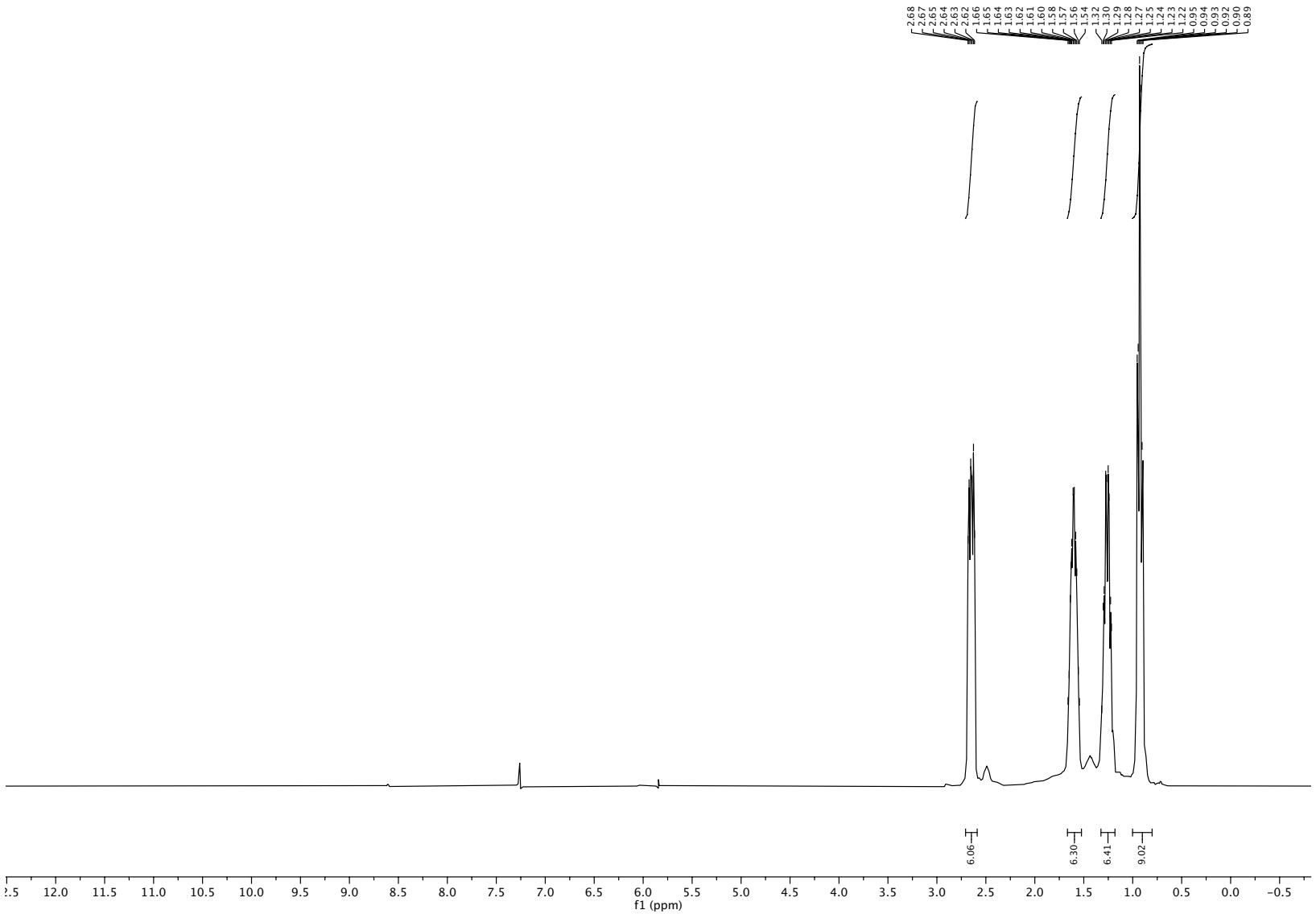
B.26 300 MHz ^{1}H NMR of compound **2j** in $CDCl_3$



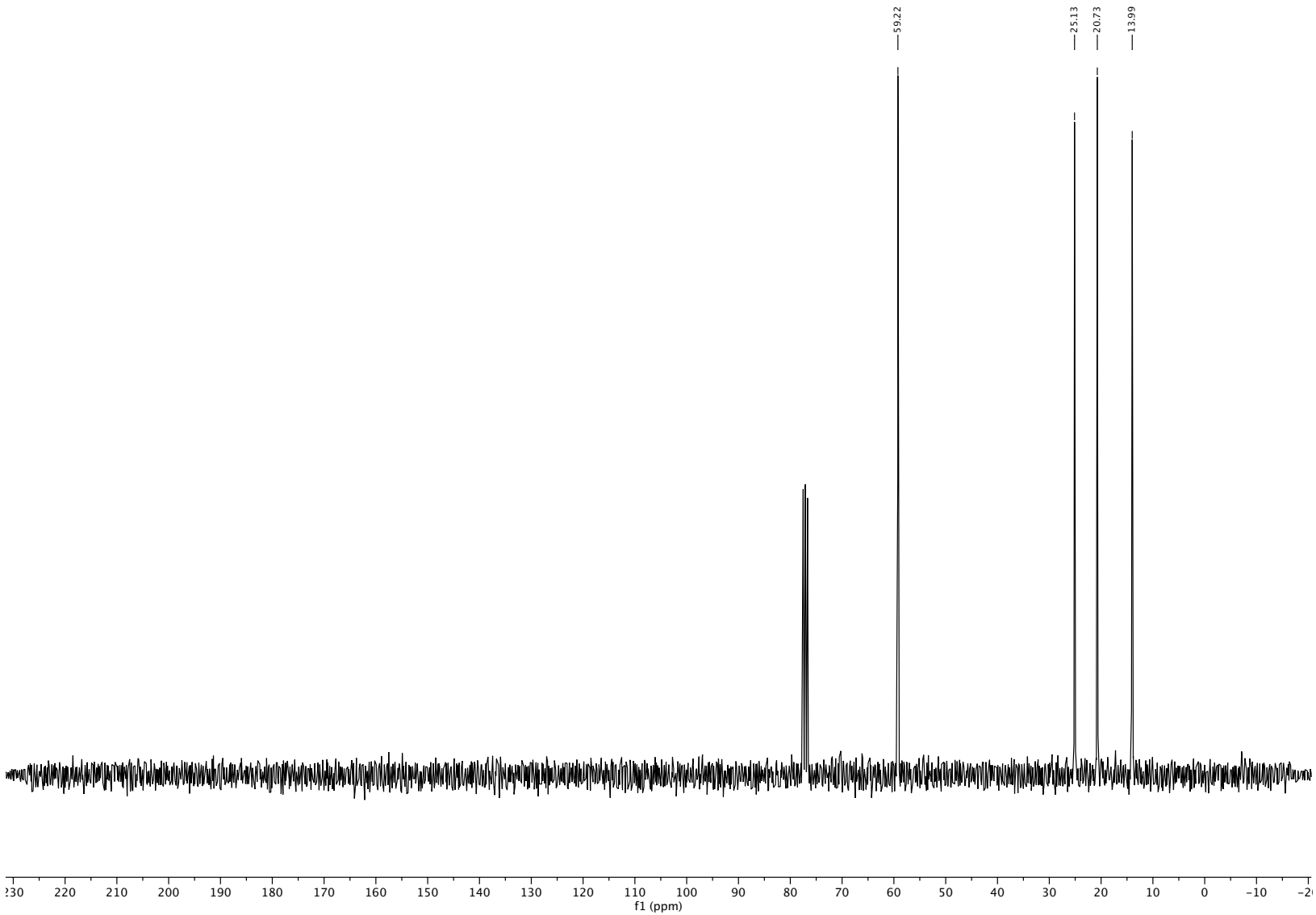
B.27 75 MHz ^{13}C NMR of compound **2j** in $CDCl_3$



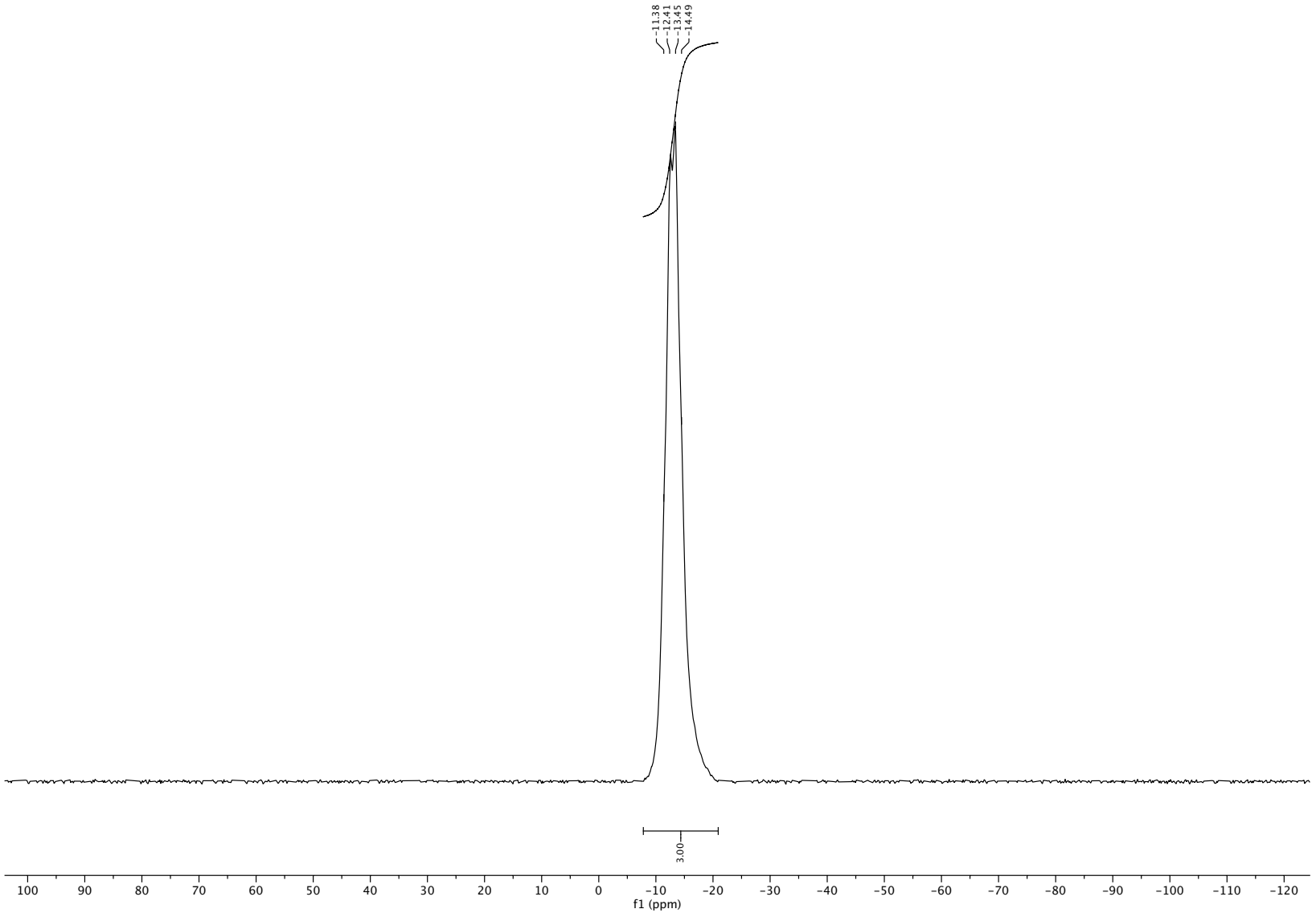
B.28 96 MHz ^{11}B NMR of compound **2j** in $CDCl_3$



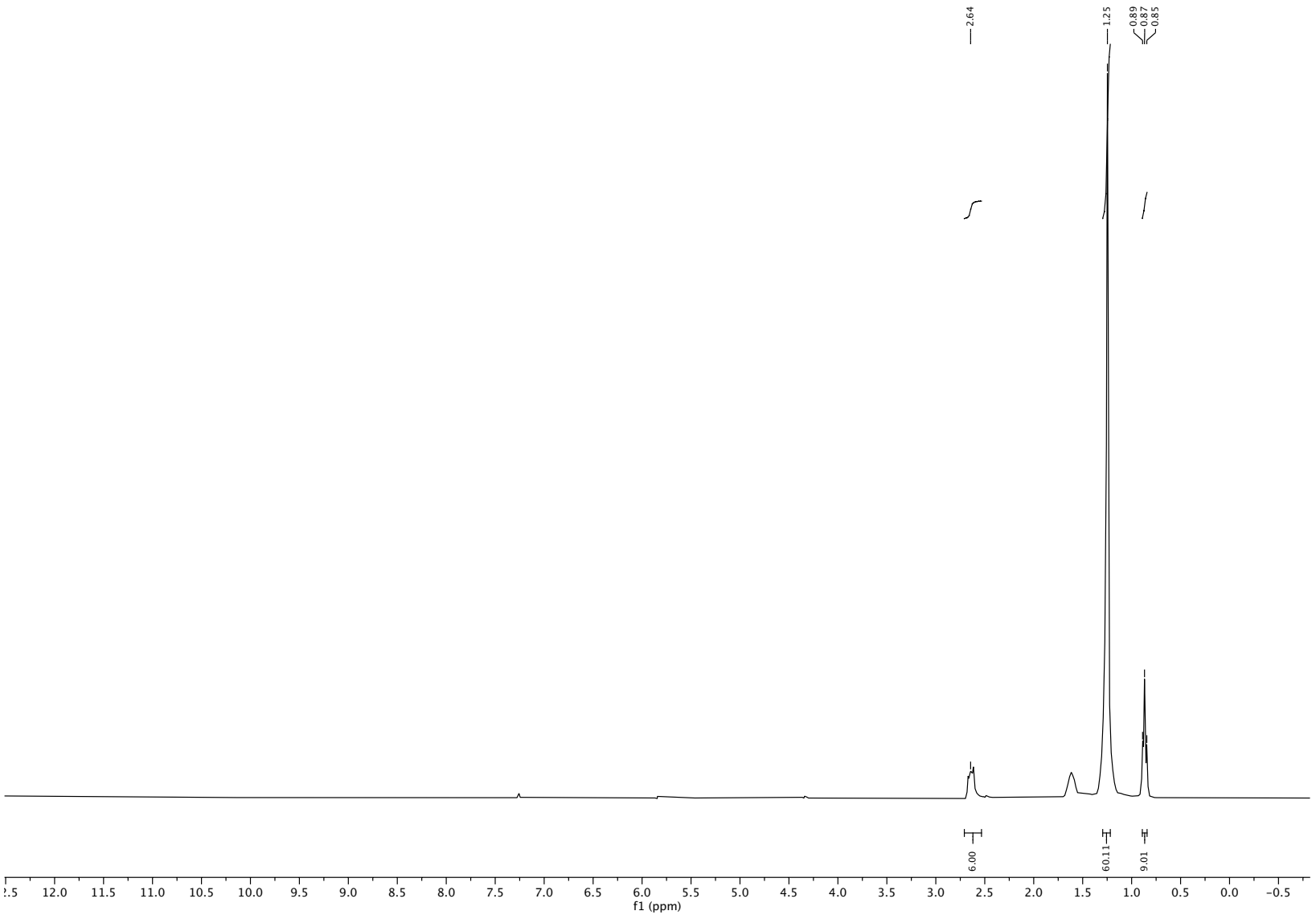
B.29 300 MHz ^{1}H NMR of compound **2k** in $CDCl_3$



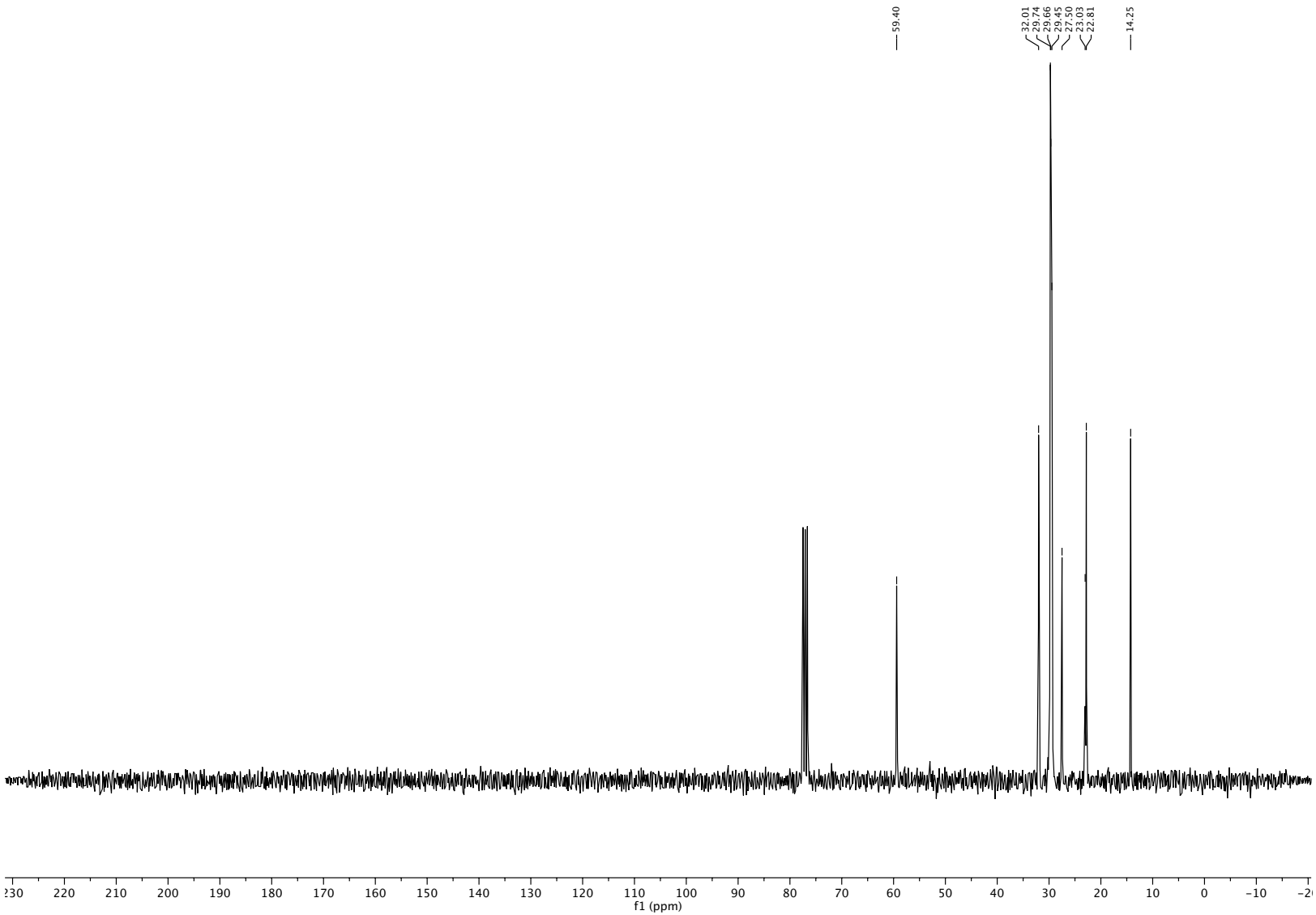
B.30 75 MHz ^{13}C NMR of compound **2k** in $CDCl_3$



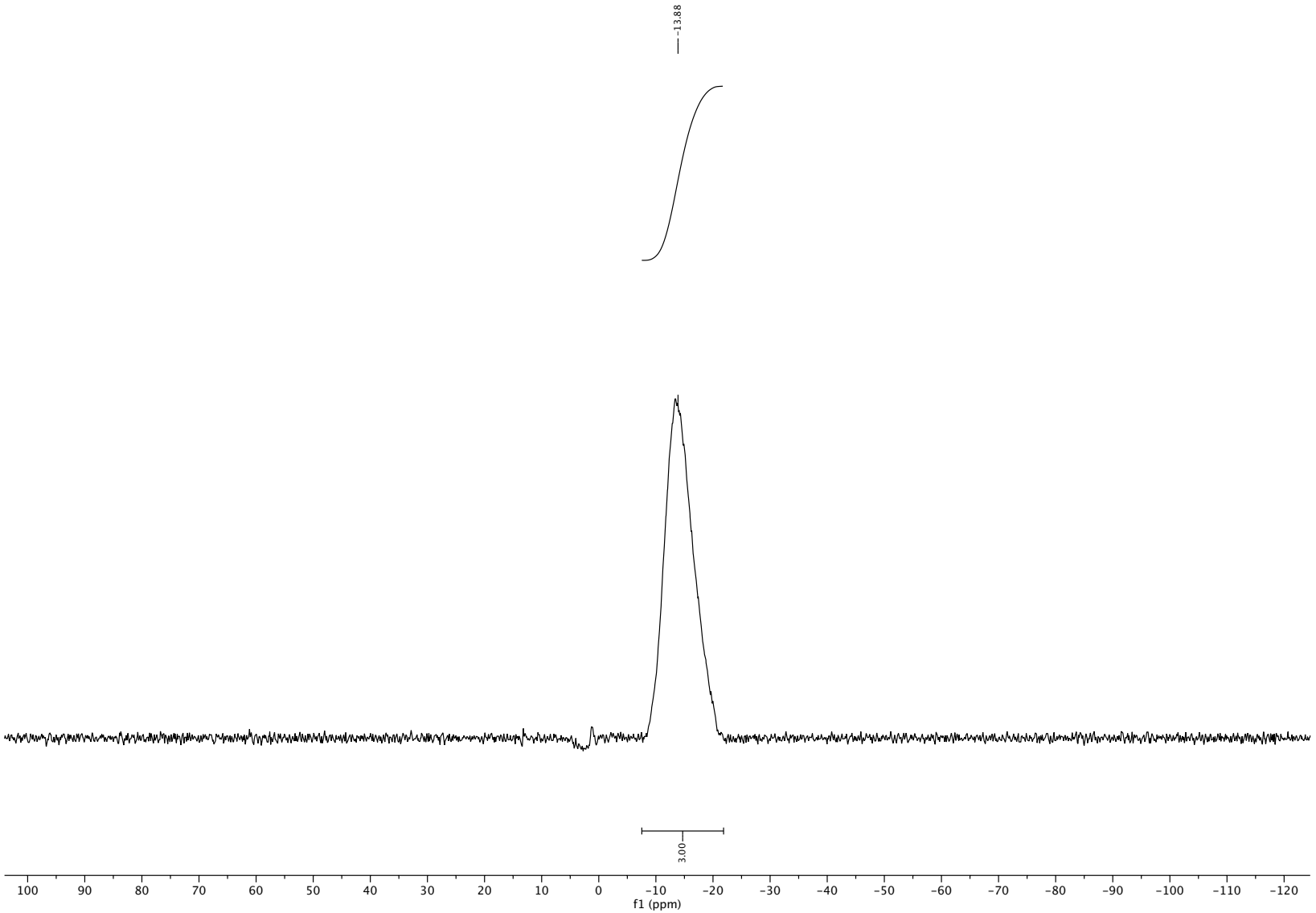
B.31 96 MHz ^{11}B NMR of compound **2k** in $CDCl_3$



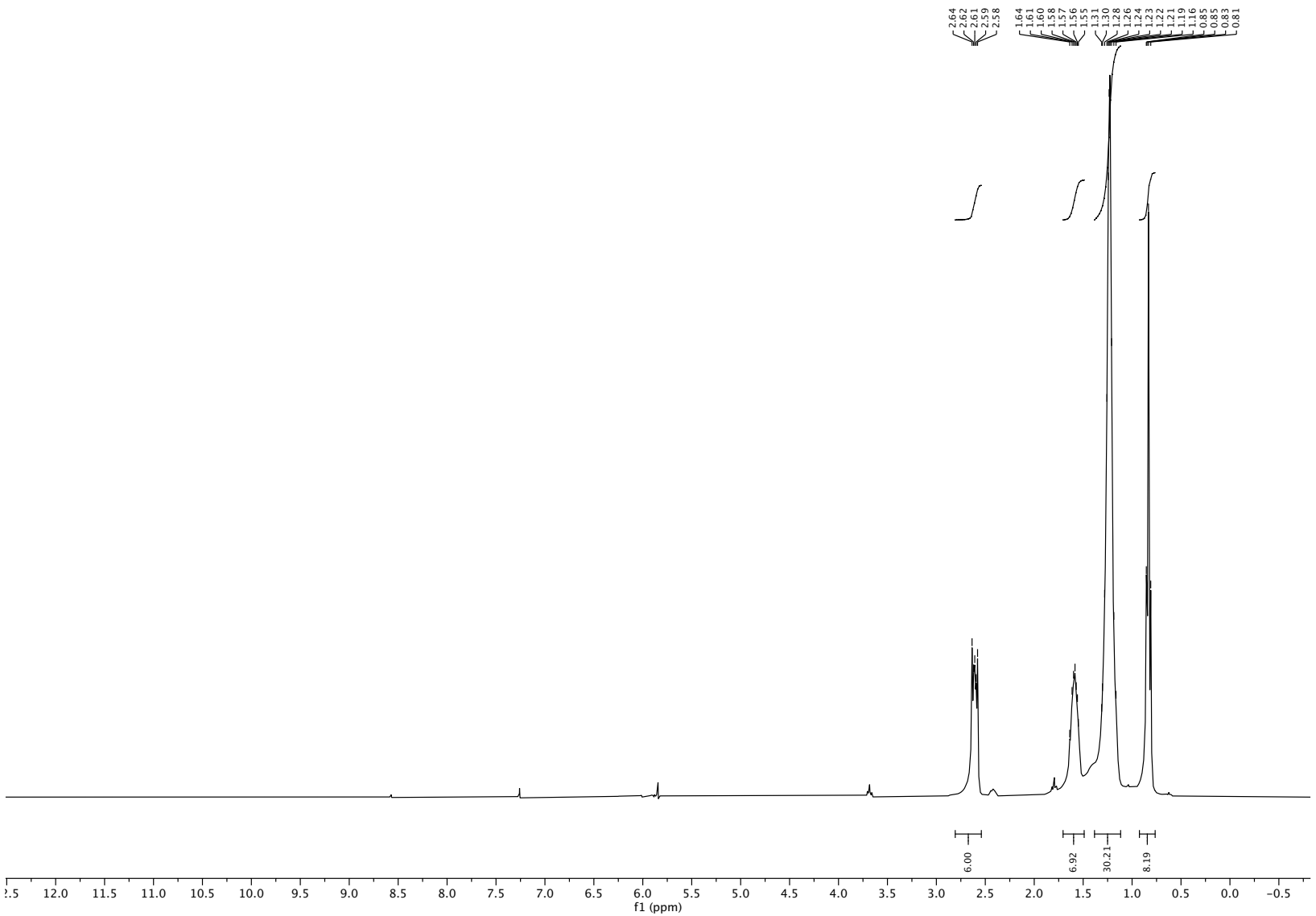
B.32 300 MHz ^{1}H NMR of compound **2l** in $CDCl_3$



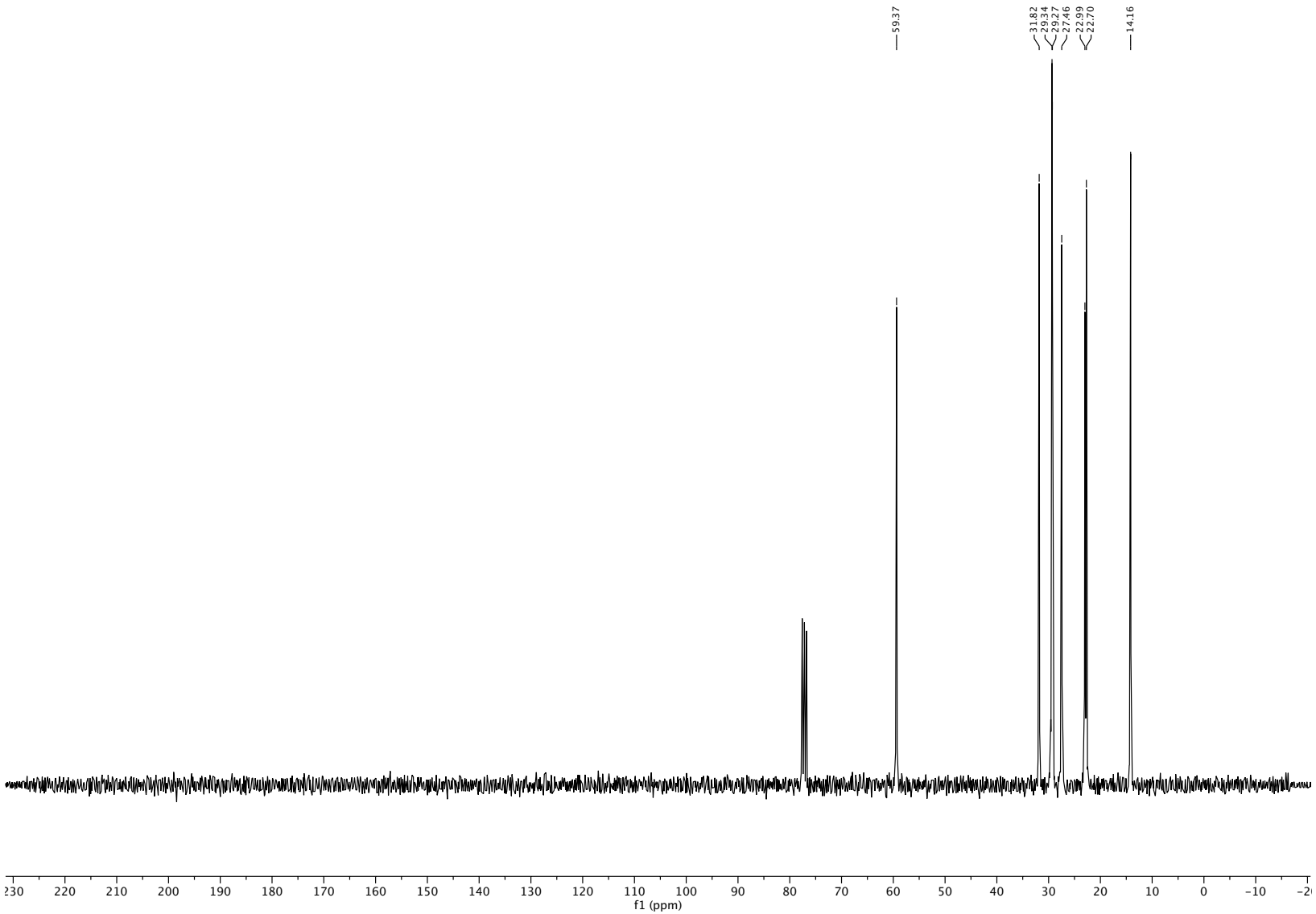
B.33 75 MHz ^{13}C NMR of compound **2l** in $CDCl_3$



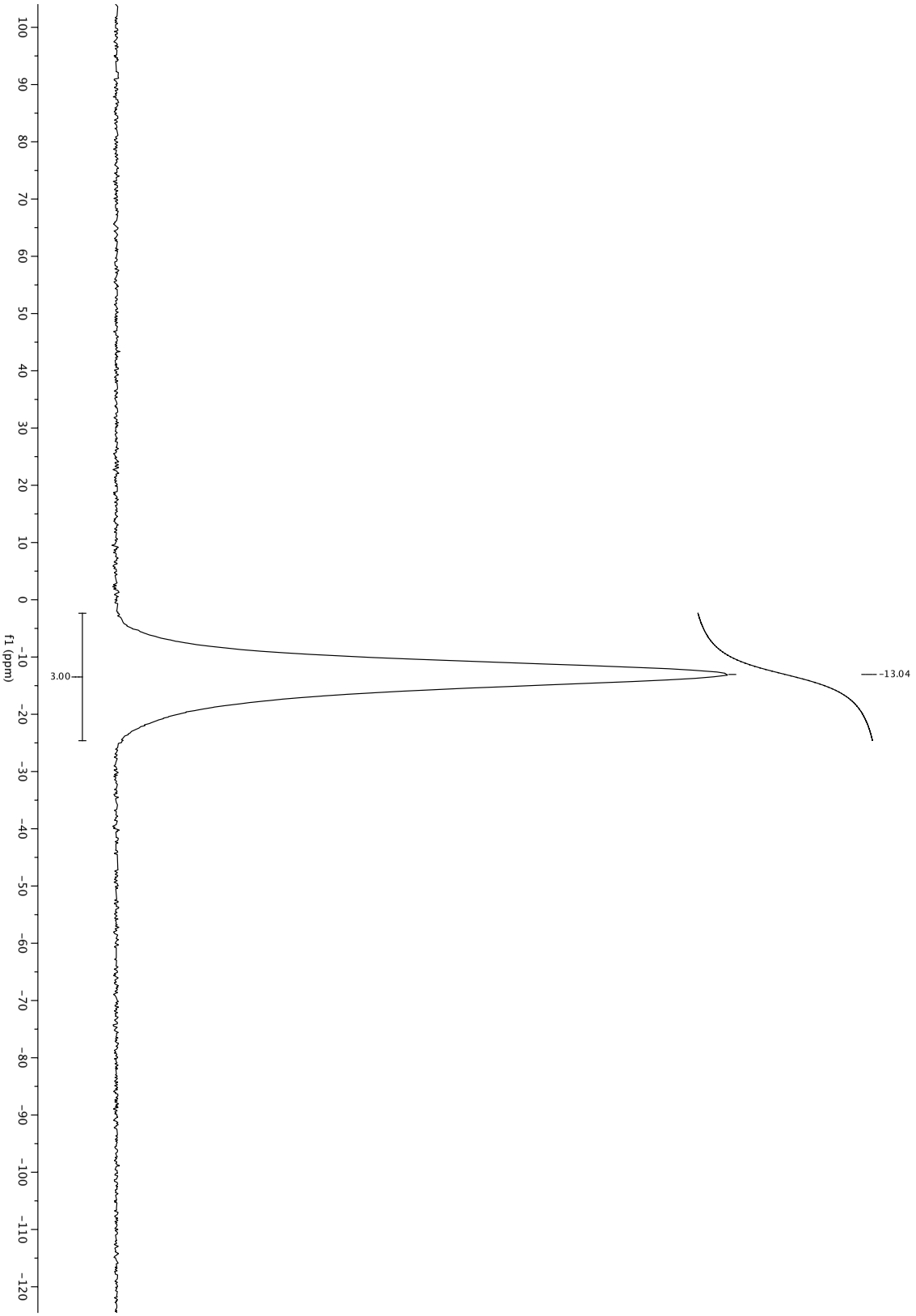
B.34 96 MHz ^{11}B NMR of compound **2l** in $CDCl_3$



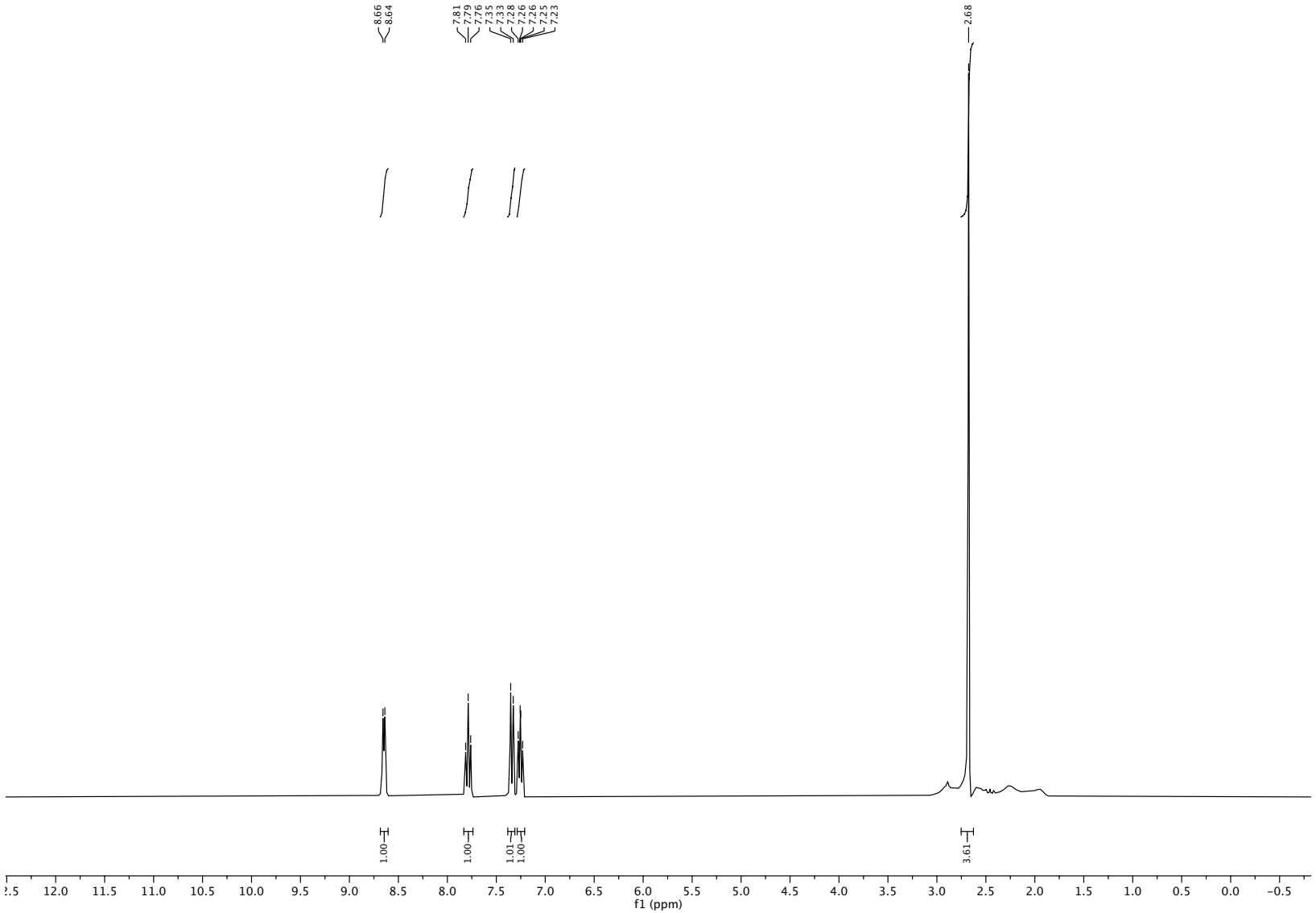
B.35 300 MHz ^{1}H NMR of compound **2m** in $CDCl_3$



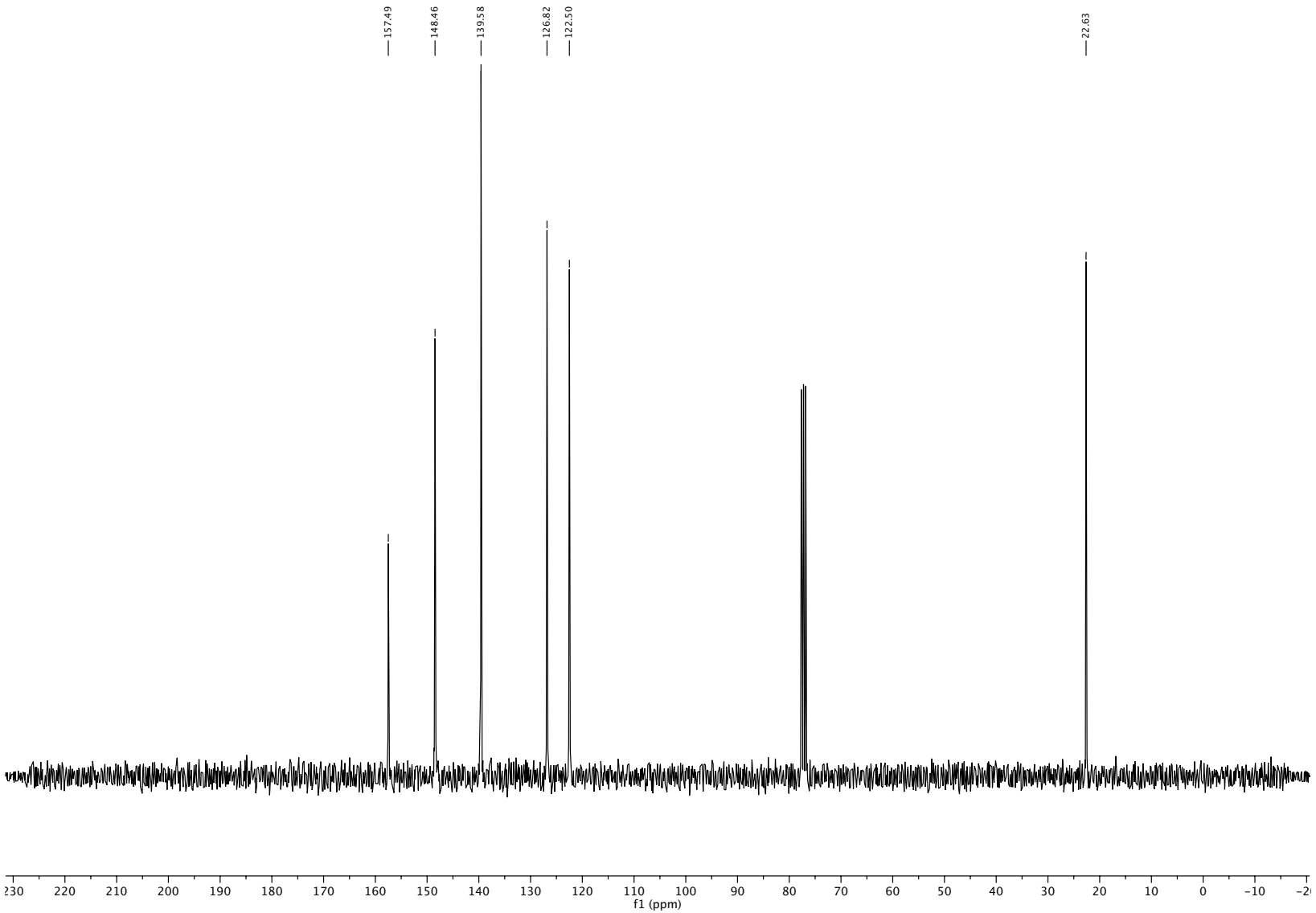
B.36 75 MHz ^{13}C NMR of compound **2m** in $CDCl_3$



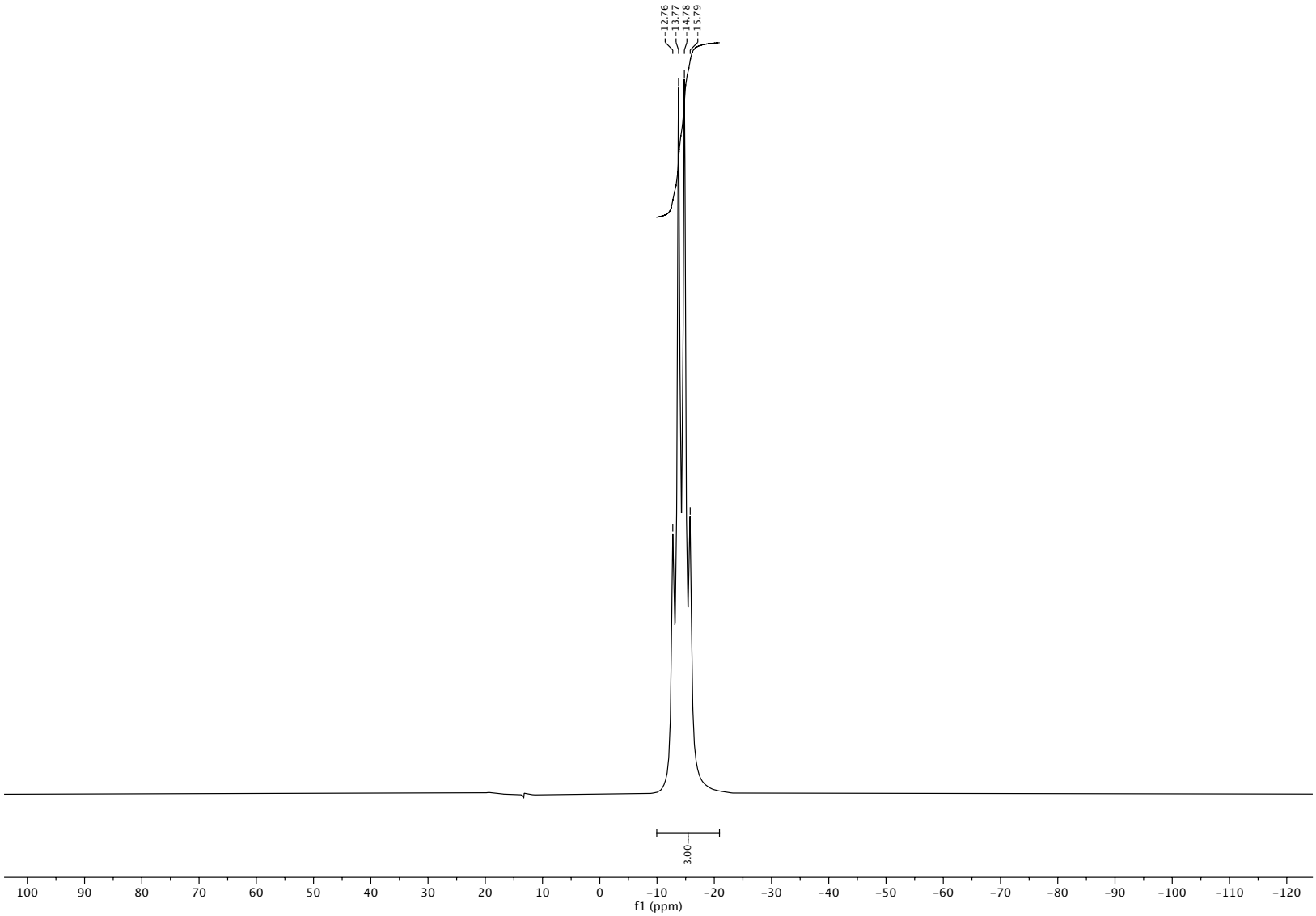
B.37 96 MHz ^{11}B NMR of compound **2m** in $CDCl_3$



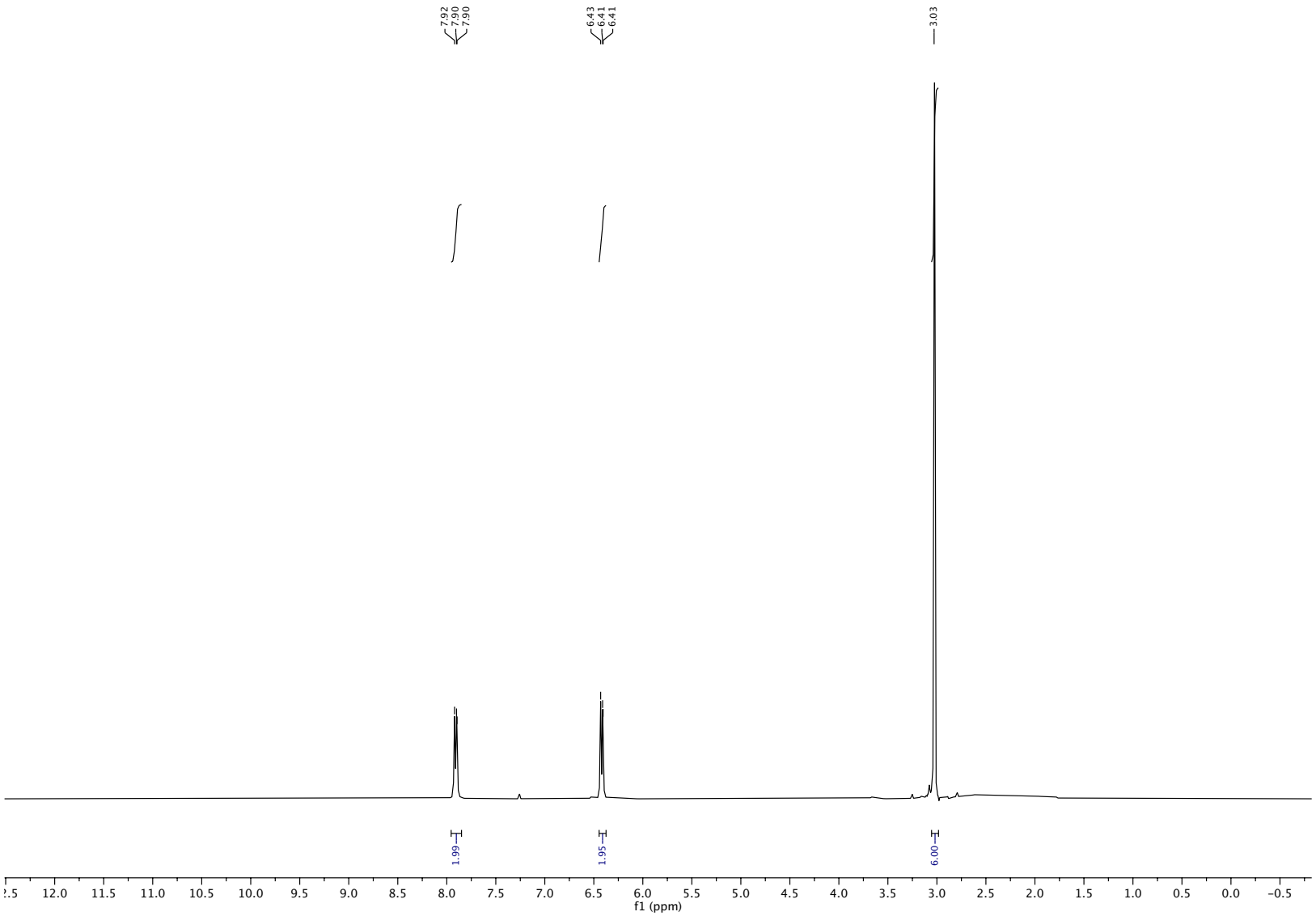
B.38 300 MHz ^{1}H NMR of compound **2n** in $CDCl_3$



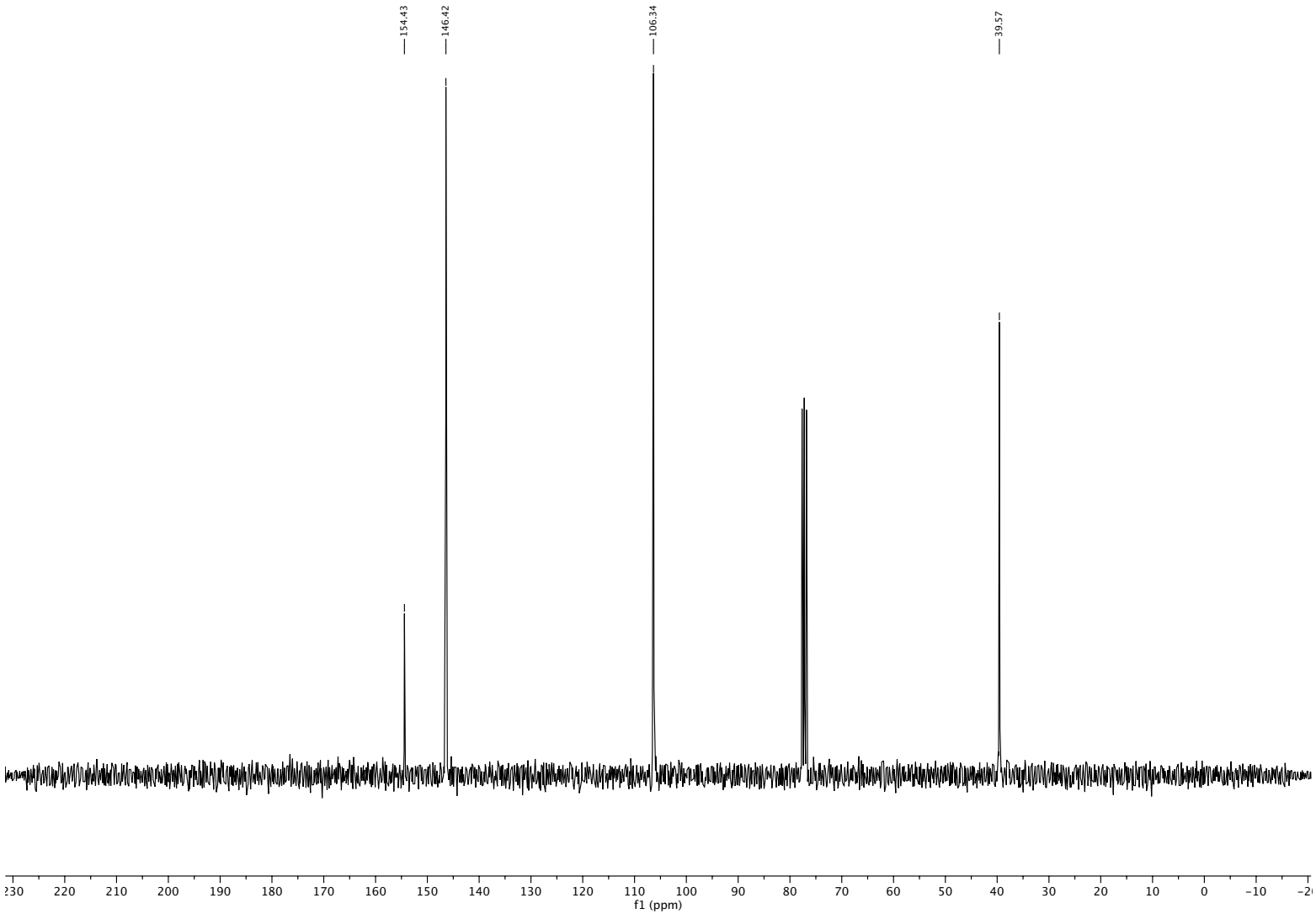
B.39 75 MHz ^{13}C NMR of compound **2n** in $CDCl_3$



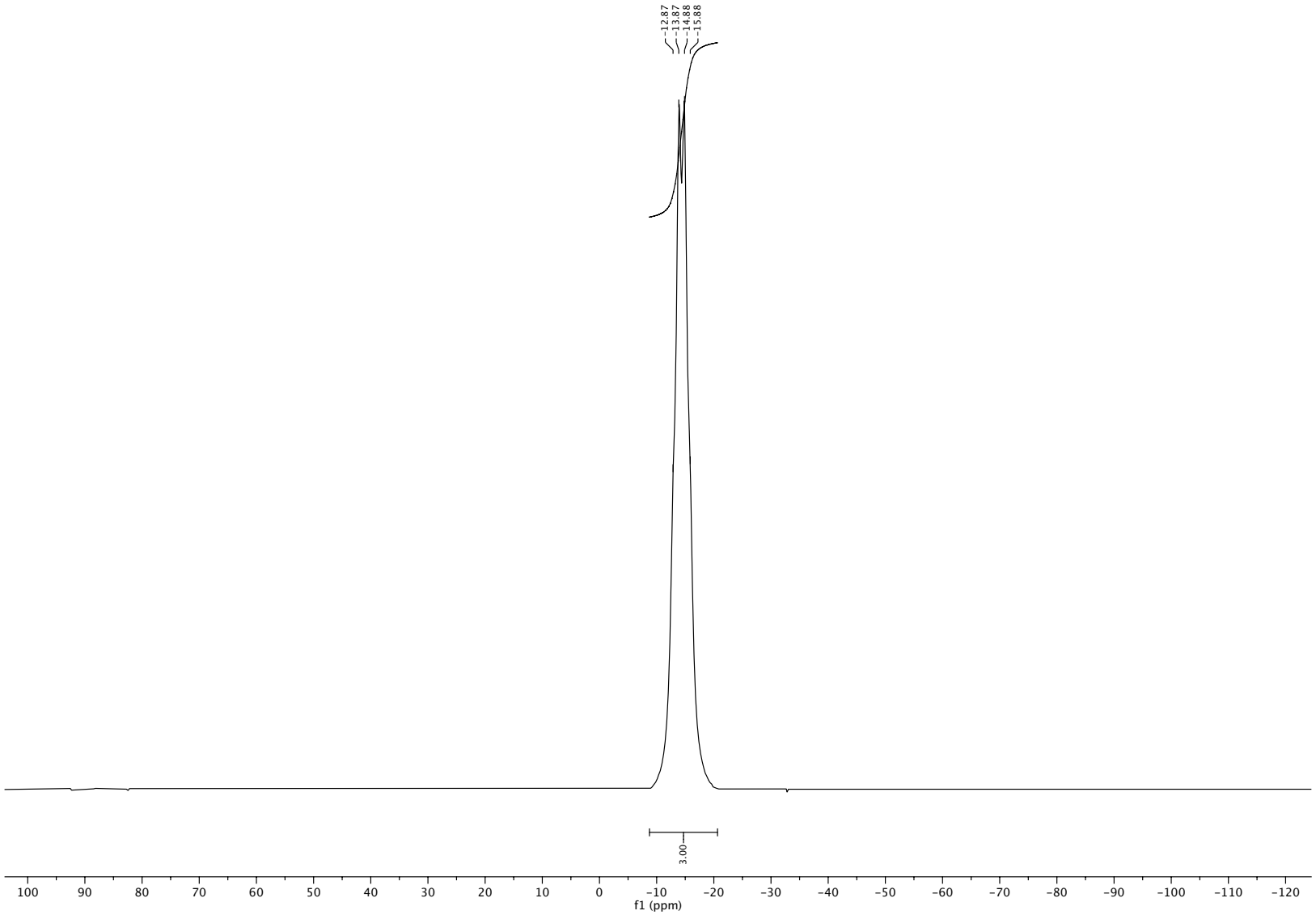
B.40 96 MHz ^{11}B NMR of compound **2n** in $CDCl_3$



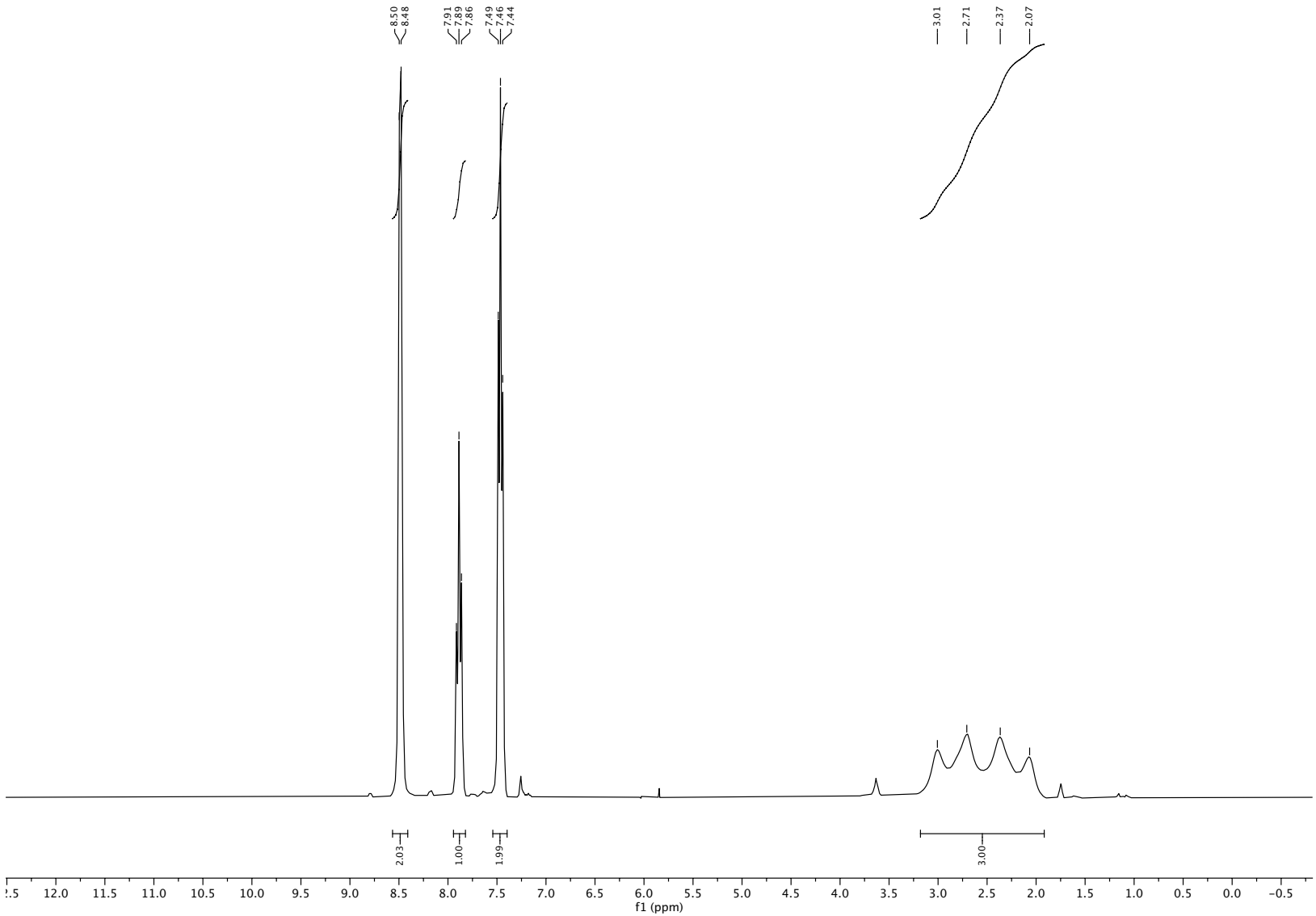
B.41 300 MHz ^{1}H NMR of compound **2o** in $CDCl_3$



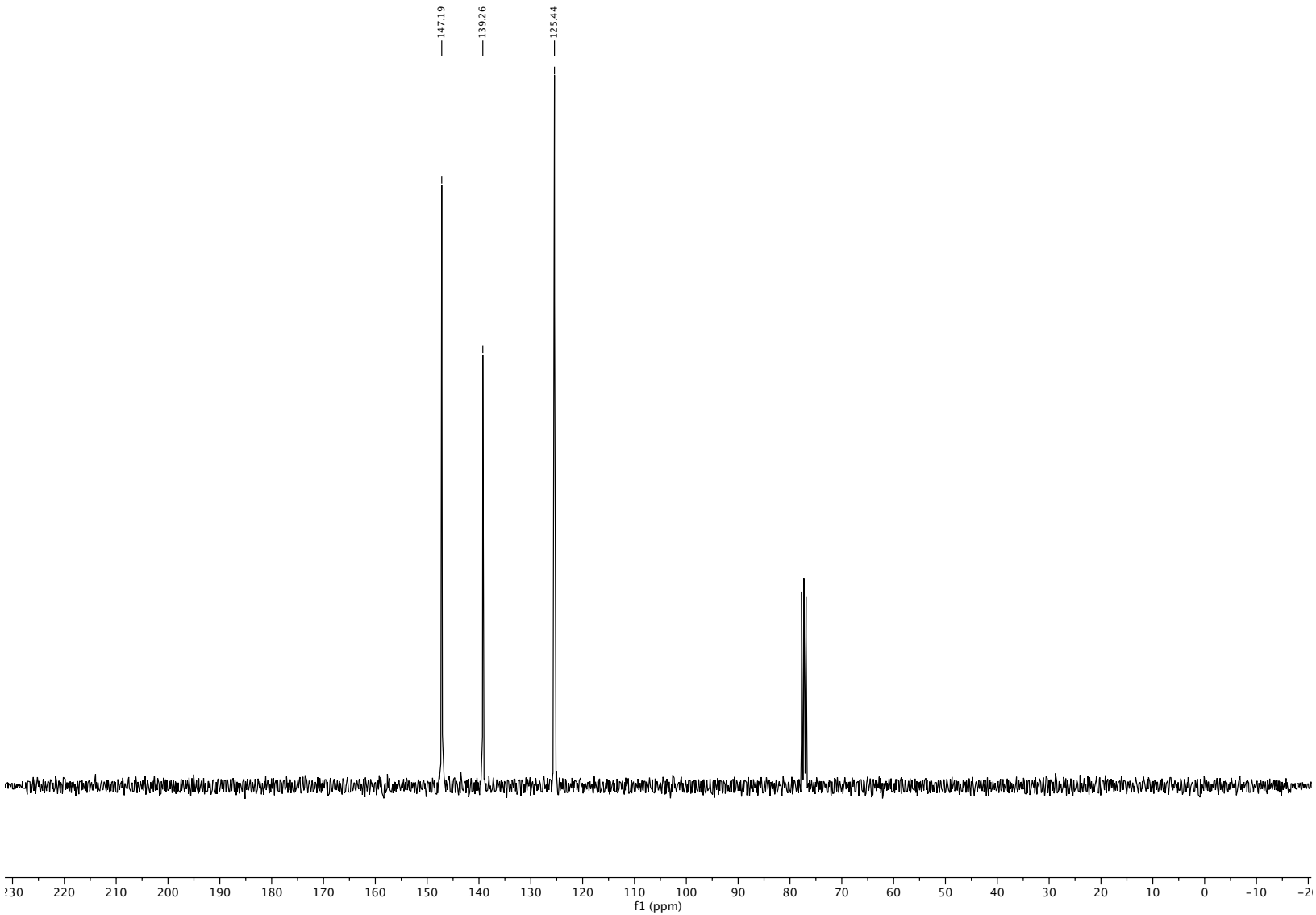
B.42 75 MHz ^{13}C NMR of compound **2o** in $CDCl_3$



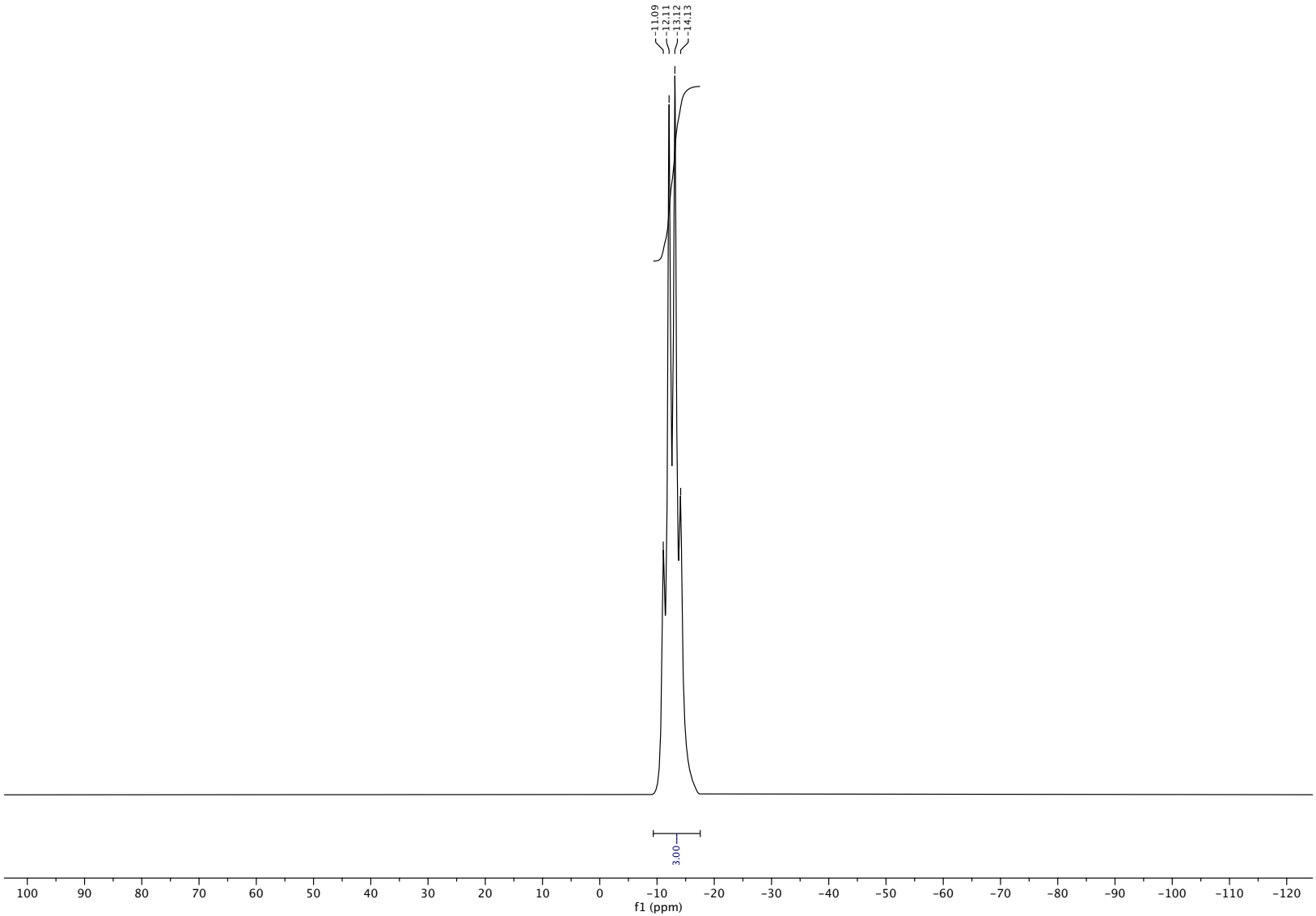
B.43 96 MHz ^{11}B NMR of compound **2o** in $CDCl_3$



B.44 300 MHz ^{1}H NMR of compound **2p** in $CDCl_3$



B.45 75 MHz ^{13}C NMR of compound **2p** in $CDCl_3$



B.46 96 MHz ^{11}B NMR of compound **2p** in $CDCl_3$