Intermolecular Reductive C–N Cross Coupling of Nitroarenes and Boronic Acids by P^{III}/P^{V}=O Catalysis

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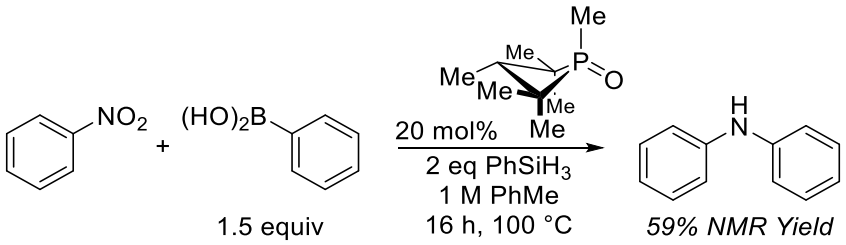
I. General Materials and Methods

All reagents (including commercial phosphorus reagents used in optimization studies) were purchased from commercial vendors (Sigma-Aldrich, Alfa Aesar, Acros, TCI, or Oakwood Chemical, Combi-Blocks) and used without further purification unless otherwise indicated. Nitrobenzene was distilled and stored over molecular sieves prior to use. Dichloromethane, diethyl ether, dimethylformamide, and tetrahydrofuran were purified and collected under argon using a Glass Contour Solvent Purification System. Anhydrous *m*-xylene and dibutyl ether were obtained from a Sigma-Aldrich (sure-seal® bottle) and used as received. All other solvents were ACS grade or better and were used without further purification unless otherwise noted. Manipulations were conducted under an atmosphere of dry N_2 gas unless otherwise noted. According to the reaction scale, the catalytic C–N coupling reactions were carried out in: **1**) glass culture tubes with threaded end (20 x 125 mm; Fisher Scientific part # 14-959-35A), outfitted with a phenolic screw-thread open top cap (Kimble-Chase part #73804-15425), and PTFE-lined silicone septum (Thermo Fisher part # B7995-15); **2**) a 40 mL screw-cap vial with a septum cap; or **3**) a round-bottom flask fitted with a septum. Column chromatography was carried out on silica gel (SiliFlash® Irregular Silica Gel, P60 40-63μm) or aluminum oxide (activated, neutral, Brockmann I) as noted. ^{1}H, ^{13}C, ^{19}F, ^{31}P, and ^{11}B NMR were collected with either Bruker AVANCE-400, DPX 400, VARIAN Inova-500, or JEOL 500 MHz spectrometers and processed using either MestReNova or Bruker software. ^{1}H NMR chemical shifts are given in ppm with respect to solvent residual peak ($CDCl_3$, δ 7.26 ppm; acetone-d_6, δ 2.05 ppm; DMSO-d_6, δ 2.50 ppm; TMS, δ 0.00 ppm). $^{13}C\{^{1}H\}$ NMR shifts are given in ppm with respect to ($CDCl_3$ δ 77.16 ppm, acetone-d_6 δ 29.84 ppm, 206.26 ppm; DMSO-d_6, δ 39.52 ppm). ^{31}P NMR shifts are given in ppm with respect to 85% H_3PO_4 (δ 0.0 ppm) as an external standard. ^{11}B NMR shifts are given in ppm with respect to $BF_3{\cdot}Et_2O$ (δ 0.0ppm) as an external standard. Multiplicities are described as s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, td = triplet of doublets, m = multiplet. Coupling constants are reported in Hertz (Hz). IR spectra were collected using a Nicolet iS5 spectrometer outfitted with an iD5 diamond laminate ATR accessory from *Thermo Scientific*. IR spectra were acquired as neat samples. High-resolution ESI mass spectra were obtained from the Mass Spectrometry Laboratory at the School of Chemical Sciences, University of Illinois at Urbana-Champaign as well as at the MIT department of chemistry instrumentation on a JEOL AccuTOF-DART (JMS-T100LP, ionSense DART source). Additionally, high-resolution mass spectra were collected at Bristol-Myers Squibb on an Agilent 6200 series TOF/6500 series Q-TOF B.06.01 (B6172 SP1).

II. Optimization Studies of the Reductive C–N Cross Coupling Reaction

A. Reaction Discovery



To a 4 mL screw-cap vial fitted with a stir bar was added phenylboronic acid **2a** (91 mg, 0.75 mmol, 1.5 equiv), nitrobenzene **1** (51 µL, 0.50 mmol, 1.0 equiv), phosphine oxide **4•**[O] (17 mg, 0.1 mmol, 0.2 equiv), and a cap. After exchanging atmosphere for nitrogen, toluene (0.50 mL) and phenylsilane (0.12 mL, 1.0 mmol, 2.0 equiv) were added via syringe. The reaction mixture was heated for 16 h, then cooled to room temperature. After filtration over a pad of silica (ethyl acetate rinse), concentration via rotary evaporation, and drying under vaccum, 28 mg of 1,3,5-trimethoxybenzene (TMB, 0.17 mmol) was added. NMR yield was determined based on the relative integration ratio between TMB (6.10 ppm, 1.00, 3H) and diphenylamine (6.94 ppm, 1.17, 2H); 1.17/2 = 0.585.

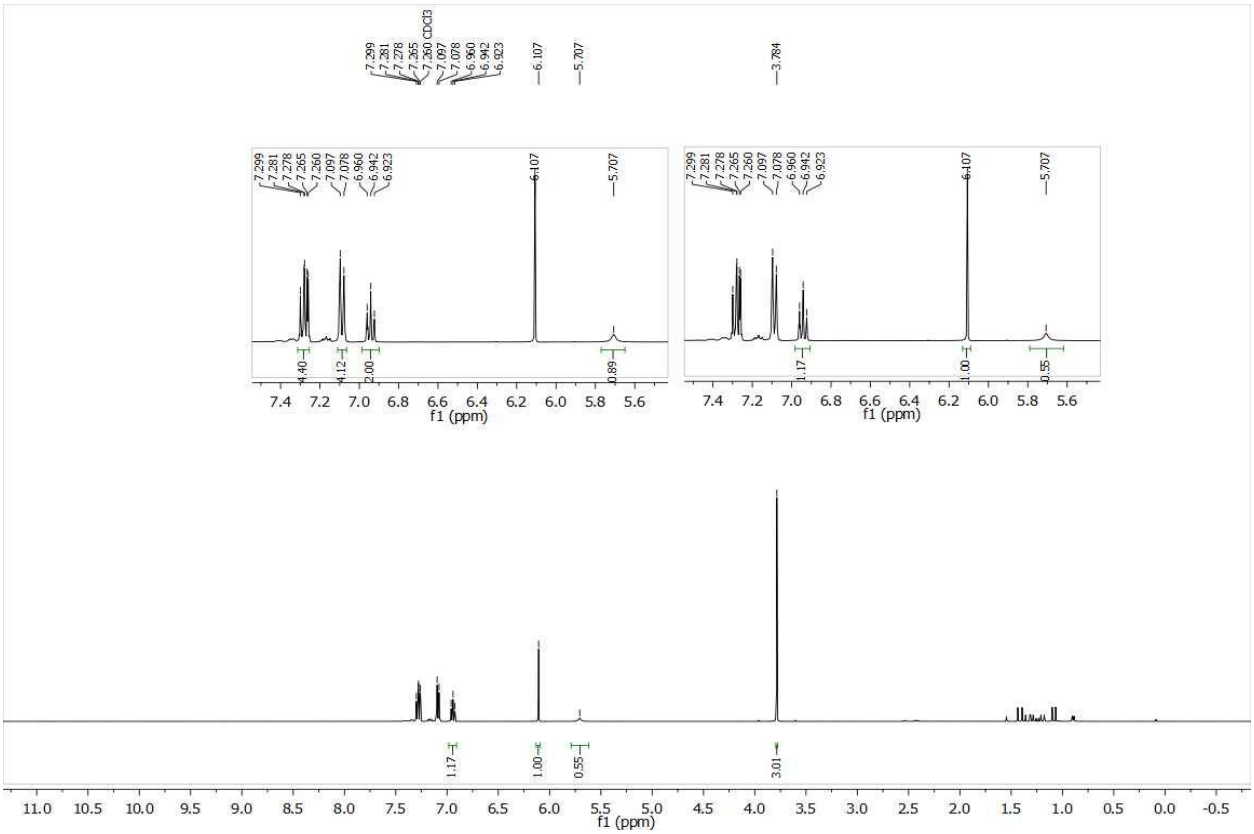
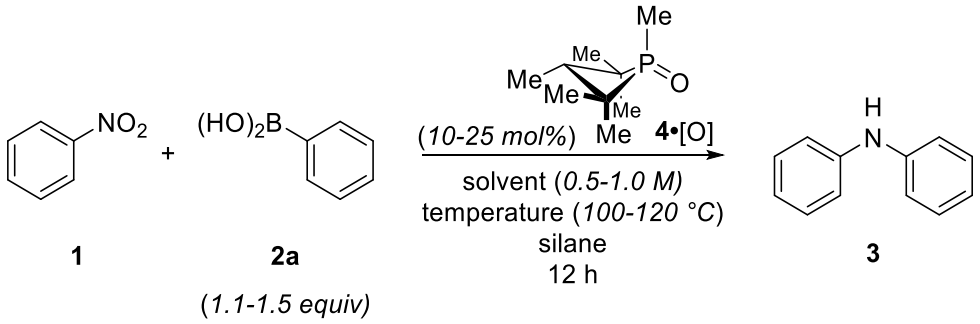


Figure S1. NMR yield determination for initial unoptimized experiment using 1,3,5-trimethoxybenzene as internal standard (59%, chloroform-*d*).

B. Reaction Optimization via Design of Experiments (DoE)



Elucidation of the most optimal reaction conditions was done with the aid of a design of experiments (DoE) approach. DoE is a powerful tool that can aid optimization problems with statistical analysis, helping identify parameters that have the most important influence on a desired outcome.[1]DoE optimization was conducted using JMP® statistical analysis software.[2] A screening design[3] was selected in order to construct an optimization that maximized the yield of diphenylamine **3**. Based on the results of the initial reaction discovery, 6 different parameters (solvent, temperature, concentration, cat. loading, equiv of boronic acid, hydrosilane identity) were evaluated at the indicated ranges or categories (Fig. S2): With these parameters and ranges, a fractional factorial design consisting of 32 runs and no block size was evaluated.

Factors

Continuous | Discrete Numeric | Categorical | Remove | Add N Factors 1

Name	Role	Values	
Solvent	Categorical	Xylene	Butyl Ether
Temperature	Continuous	100	120
Concentration	Continuous	0.5	1
Catalyst Loading	Continuous	0.1	0.25
Equivalents Boronic	Continuous	1.1	1.5
Silane	Categorical	PhSiH3	DEMS

Figure S2. Parameters screened for DoE evaluation for the coupling reaction: temperature (°C), concentration (M), catalyst loading (equivalents relative to **1**), equivalents of boronic acid (referring to **2**, relative to **1**). Two equivalents of phenylsilane or 4 equivalents of DEMS (diethoxymethylsilane) used relative to **1**.

General Procedure for DoE experiments:

A 4 mL screw cap vial equipped with a stir bar was charged with phenylboronic acid (67.1 mg or 91.4 mg) and catalyst (8.7 mg or 21.8 mg). Error on weighing was ±0.3mg. The vials were then sealed and evacuated for 30 sec before backfilling with N_2 (one time). Reactions that were conducted at more dilute concentrations were charged with 0.5 mL of the appropriate solvent. Nitrobenzene and dodecane standard (0.5 mmol per vial) were added via 0.5 mL of a 1 M stock solution made in the appropriate solvent. Lastly, the appropriate silane was added via microliter syringe (123 µL for phenylsilane, 184 µL DEMS). The reaction mixtures were heated for 12 h at the appropriate temperature in aluminum heating blocks. After 12 h, reaction mixtures were cooled to room temperature and diluted with denatured EtOH so that each reaction had a final volume of 2 mL. A 40 µL aliquot of the diluted reaction mixtures were then added to GC vials containing 1.5 mL of denatured EtOH. The yields were then evaluated by GC-FID, ranging from 0 to 90+%. This data was inputted into the JMP® 14 software to construct a model predicting how changing variables will affect future reaction outcomes (Fig. S3).

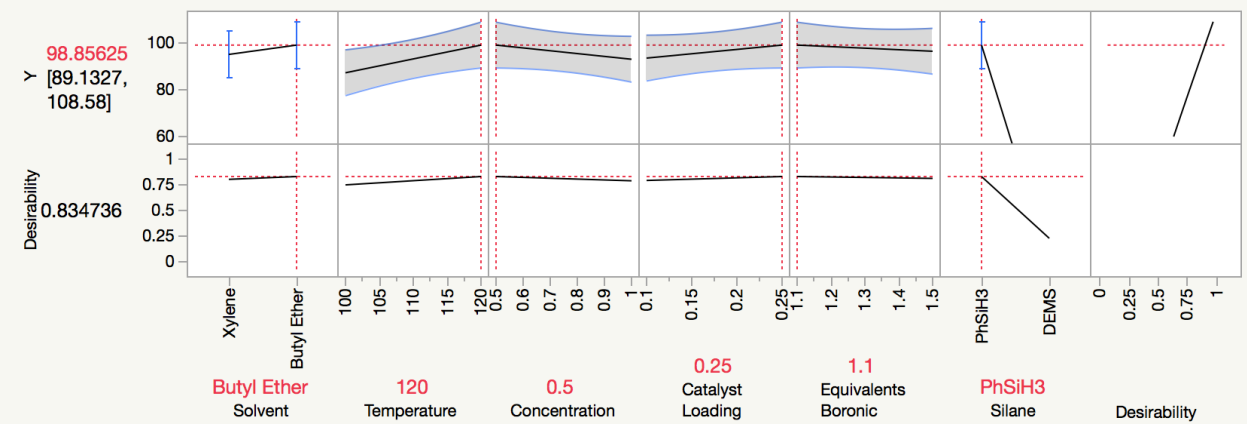


Figure S3. Prediction profiler describing dependency of product yield on reaction variables.

The model predicts higher catalyst loading and temperature give better yields. Little difference is expected between *m*-xylene and dibutyl ether. Little difference in the effects of boronic acid equivalents led to the selection of 1.1 eq. boronic acid. Improved reaction yields at more dilute concentrations (0.5 M) were found to be more ideal. In an effort to minimize catalyst loading, the following conditions were selected:

- 15 mol% catalyst
- T = 120 ˚C.
- *m*-xylene (0.5 M)
- 1.1 equiv boronic acid,
- 2 equiv phenylsilane

C. Impact of Solvent and Borylarene

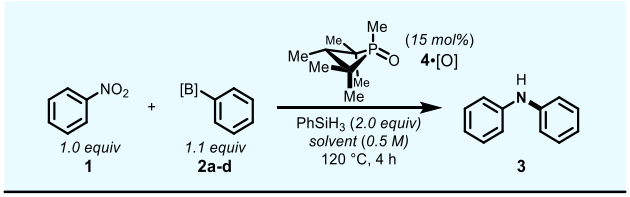
General Procedure:

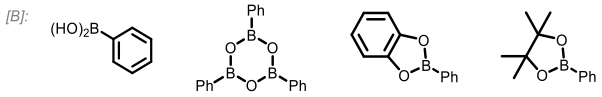
Reaction vessels as described in the General Methods section were equipped with a PTFE stir bar and charged with phosphine oxide catalyst **4**•[O] (13 mg, 0.075 mmol, 15 mol%), phenylboronic acid (67 mg, 0.55 mmol, 1.1 equiv), and dodecane as standard (~0.50 mmol, gravimetrically determined and amount recorded). The vessels were sealed, evacuated on a Schlenk line for 30 sec, and backfilled with N_2 (1 time). Each vessel was then charged with 1 mL of the appropriate solvent via syringe, followed by nitrobenzene (51 μL, 0.50 mmol, 1 equiv) and phenylsilane (123 μL, 1 mmol, 2 equiv) via microliter syringe. The reactions were then heated to 120 ˚C and stirred for 4 h. The reaction mixtures were then cooled to room temperature and diluted with 1 mL of denatured EtOH. After stirring thoroughly, a 40 μL reaction aliquot was taken from each reaction mixture and charged into a GC vial containing 1.5 mL of denatured EtOH. The GC vial was capped and the shaken in order to mix thoroughly. Reaction yields were quantified by GC-FID by reference to calibration curves were made using authentic analytes prior to the start of this study.

GC-FID information:

An Agilent 7890A gas chromatograph was used for the analysis, outfitted with a J&W 127-1012 column (10m X 100 μm X 0.1μm). The initial carrier gas flow rate was 0.38586 mL/min (He) and the temperature program started at 70 ˚C holding for 1 min, then ramped at 50 ºC/min until 250 ºC, and held at that temperature for 2 min. The retention times are as follows: 2.3 minutes (nitrobenzene), 2.7 minutes (dodecane), 3.9 minutes (diphenylamine). Due to overlap issues with PhBcat **2d** (entry 10), the temperature program started at 70 ˚C holding for 3 min, then ramped at 10 ºC/min until 150 ºC, and held at that temperature for 3 min. The retention times are 6.8 min (dodecane), 12.2 min (diphenylamine).

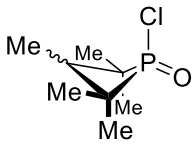
Table S1 (from text): Discovery and optimization of the organophosphorus-catalyzed reductive C-N coupling reaction. Yields were determined through analysis by gas chromatography (GC) with the aid of an internal standard. Yield in parenthesis (entry 1) is for isolated material from a 1.0 mmol reaction scale. 0.37 mmol of **2b** was used in entry 8. Under the conditions of the standard protocol, it is likely that **2a** and **2b** undergo in situ interconversion through reversible hydration/dehydration.





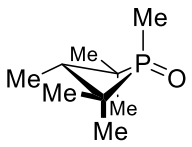
Entry	[B]	Solvent	$R_3P{=}O$	Yield (%)
1	**2a**	*m*-xylene	**4**•[O]	86% (80%)
2	**2a**	*m*-xylene	**4**	82%
3	**2a**	*m*-xylene	none	0%
4	**2a**	*m*-xylene	**4**•[O]; no silane	0%
5	**2a**	dibutyl ether	**4**•[O]	86%
6	**2a**	toluene	**4**•[O]	80%
7	**2a**	DMF	**4**•[O]	17%
8	**2b**	*m*-xylene	**4**•[O]	74%
9	**2c**	*m*-xylene	**4**•[O]	54%
10	**2d**	*m*-xylene	**4**•[O]	2%

D. Preparation of Phosphorus Compounds



S1

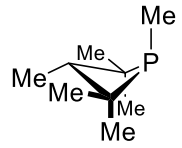
1-Chloro-2,2,3,4,4-pentamethylphosphetane 1-oxide (**S1**): Prepared according to the literature procedure.[4] A round-bottom flask equipped with a stir bar and septum was charged with 6.67 g (50.0 mmol) of $AlCl_3$, then evacuated and back-filled with nitrogen. Methylene chloride (30 mL) was added via syringe and the mixture was cooled to 0 °C with stirring. Phosphorus trichloride (4.36 mL, 50.0 mmol) was added via syringe and stirred for 5 min. 2,4,4-Trimethyl-2-pentene (7.79 mL, 50.0 mmol) was then added via syringe over a period of 10 min and stirring was continued at 0 °C for 2 h. The reaction was cautiously quenched by the slow addition of distilled water (30 mL) over 30 min. The organic phase was separated and the aqueous layer was extracted with methylene chloride (2x50 mL). After setting the aqueous layer aside, the organic layer was washed with an additional portion of water (30 mL) and then the combined aqueous phases were extracted with methylene chloride (50 mL). The combined organic phases were dried over anhydrous sodium sulfate, filtered, and concentrated by rotary evaporation. The product was further dried in vacuo giving product **S1** as a white solid *(8.96 g, 92% yield, dr > 15:1*), which could be used in the next step without additional purification. ^{31}P NMR (162 MHz, $CDCl_3$) δ 81.49 (major, *anti*), 80.63 (minor, *syn*). This compound will slowly hydrolyze in the presence of moisture; it may be stored in a sealed container in a *-20 °C* freezer for an extended period.



4•[O]

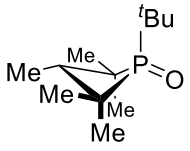
1,2,2,3,4,4-Hexamethylphosphetane 1-oxide (**4•**[O]): Phosphetane oxide **S1** (10.8 g, 62.0 mmol) was added to a two-neck round-bottom flask containing a large stir bar and fitted with a reflux condenser. The top of the reflux condenser and the second neck were both fitted with a rubber septum, and the atmosphere in the vessel was exchanged by evacuation and back-filling with N_2. Diethyl ether (45 mL) was added via syringe, and the mixture was cooled to 0 °C (ice bath) with stirring. A solution of MeMgBr (3 M in diethyl ether, 22.0 mL, 66.0 mmol, 1.06 equiv) was added via syringe over a period of 10 min. After the addition, the mixture was stirred at 35 °C for 4.5 h then cooled to 0 °C (ice bath). The reaction was quenched by addition of saturated aqueous ammonium chloride (12 mL) at which time solids precipitated. The organic and aqueous layers were decanted into a separatory funnel and an additional 25 mL of water was added; the layers were then partitioned and the ether layer was set aside (does not contain product). The precipitated solids in the reaction vessel were triturated with both distilled water (~100 mL) and methylene chloride (~250 mL) until all solids went into solution. After mixing and partitioning, the methylene chloride layer was separated and the aqueous layer was extracted with methylene chloride (2x75 mL). The combined methylene chloride phases were then transferred back into the separatory funnel and washed with water (2x50 mL). Thereafter,

the aqueous phases were back-extracted with methylene chloride (75 mL). The combined methylene chloride phases were dried over anhydrous sodium sulfate, filtered, and concentrated by rotary evaporation. The isolated off-white solid was slurried with diethyl ether (50 mL) and collected by vacuum filtration with rinsing by an additional 30 mL of diethyl ether. Phosphetane oxide **4**•[O] is obtained as a white solid (5.66 g, 52%, *dr 81:1*). Spectra were in agreement with those previously reported[4] and further purification was not necessary. ^{31}P NMR (162 MHz, $CDCl_3$) δ 62.98 (minor, *syn*), 59.38 (major, *anti*).



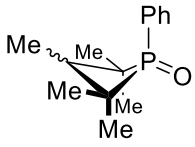
4

1,2,2,3,4,4-Hexamethylphosphetane (**4**): Prepared according to the literature procedure[4] by treatment of **4**•[O] with trichlorosilane (1.05 equiv) and triethylamine (1.05 equiv) in benzene at 75 °C for 20 hours. The sample was stored/handled in an inert atmosphere glovebox. Note that the product is volatile under vacuum and extraction with pentane instead of benzene during the workup is favorable. Spectra are consistent with those previously reported (*dr 23:1)*.[4] ^{31}P NMR (162 MHz, $CDCl_3$) δ 28.77 (major, *anti*), 16.11 (minor, *syn*).



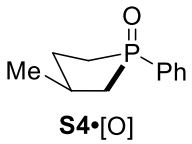
S2•[O]

1-(tert-butyl)-2,2,3,4,4-pentamethylphosphetane 1-oxide (**S2**•[O]): Prepared according to the literature procedure[5] by treatment of 1-chloro-2,2,3-4,4-pentamethylphosphetane 1-oxide **S1** with 1.2 equiv *t*BuLi in pentane. Spectral data were consistent with the literature reported values.[5] The product can be recrystallized from cyclohexane if desired.



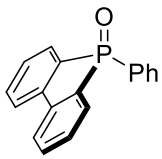
S3•[O]

2,2,3,4,4-pentamethyl-1-phenylphosphetane 1-oxide (**S3**•[O]): Prepared according to the literature procedure by reacting dichlorophenylphosphine (1 equiv) with aluminum trichloride (1 equiv) and 2,4,4-trimethyl-2-pentene (1 equiv) in dichloromethane at 0 °C for 2 hours.[5,6] Recrystallization may be carried out in cyclohexane if necessary. Spectral data were consistent with the literature reported values (6:1 dr, ^{31}P δ 52.8 ppm (major)).



S4•[O]

3-*methyl-1-phenylphospholane 1-oxide* (**S4**•[O]): Prepared according to the literature procedure via hydrogenation (Pd/C) of commercially available 3-methyl-1-phenyl-2-phospholene-1-oxide.[7] Spectral data were consistent with the literature reported values.

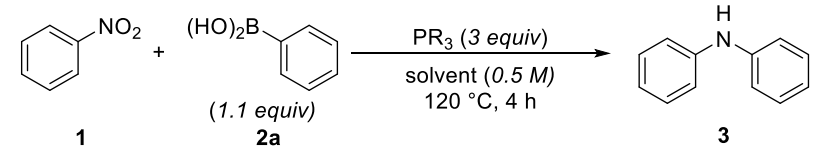


S5•[O]

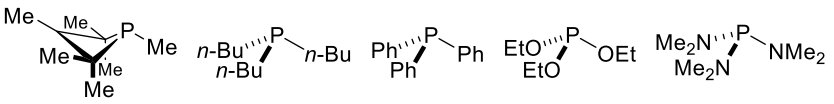
5-phenylbenzo[b]phosphindole 5-oxide (**S5•**[O]): In accordance with literature procedure, triphenylphosphine oxide was treated with phenyllithium and then the corresponding phosphine (5-phenyl-5H-benzo[*b*]phosphindole, **S5**) was oxidized using H_2O_2.[8] The phosphine was purified via column chromatography prior to oxidation (silica, 20% ethyl acetate – 80% hexanes) and **S5•**[O] was recrystallized in ethyl acetate. Spectral data were consistent with the literature reported values.

E. Examples of C–N Coupling Comparing Stoichiometric P(III) Reagents

Table S2: Stoichiometric phosphine reagents were evaluated for their competency in reductive C-N coupling. Four commercial phosphine reagents (**S6**, **S7**, **S8**, **S9**) were compared to 1,2,2,3,4,4-hexamethylphosphetane **4**. The performance of 1,2,2,3,4,4-hexamethylphosphetane **4** (entry 1, 89%) is apparently superior in comparison to tributylphosphine **S6** (entry 2, 66%), triphenyl phosphine **S7** (entry 3, 4%), triethylphosphite **S8** (entry 4, 8%), and tris(dimethylamino)phosphine **S9** (entry 5, 10%). Notably, using three equivalents of 1,2,2,3,4,4-hexamethylphosphetane **4** gives a very similar yield to using 15 mol% of phosphetane oxide **4**•[O] and 2 equivalents of phenylsilane (89% vs 86%).



1 **2a** **3**



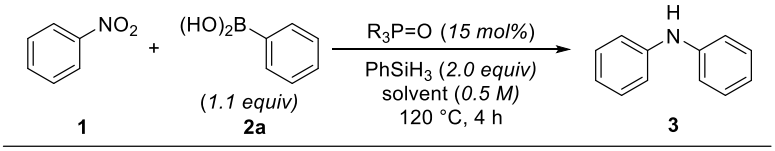
4 **S6** **S7** **S8** **S9**

Entry	R_3P	Solvent	Conversion (%)	Yield (%)
1	**4**	*m*-xylene	99	89
2	**S6**	*m*-xylene	99	66
3	**S7**	*m*-xylene	27	4
4	**S8**	*m*-xylene	19	8
5	**S9**	*m*-xylene	99	10

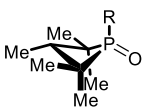
0.5 mmol scale.

F. Comparison of Phosphorus Compounds for Catalytic Reductive Coupling

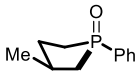
Table S3: Other cyclic and acyclic phosphine oxides assessed were not particularly productive for the desired reaction.



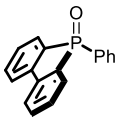
$R_3P{=}O$:



S2•[O] (R = *t*Bu)
S3•[O] (R = Ph)



S4•[O]



S5•[O]

S6•[O] (R = *n*Bu)
S7•[O] (R = Ph)

Entry	$R_3P{=}O$	Solvent	Conversion (%)	Yield (%)
1	**S2**•[O]	*m*-xylene	55	7
2	**S3**•[O]	*m*-xylene	0	0
3	**S4**•[O]	*m*-xylene	5	5
4	**S5**•[O]	*m*-xylene	9	0
5	**S6**•[O]	*m*-xylene	9	0
6	**S7**•[O]	*m*-xylene	25	0

0.5 mmol scale.

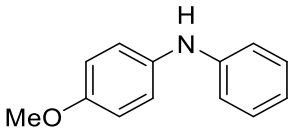
III. Examples of Reductive C–N Coupling

A. General procedure for reductive C–N coupling of boronic acids with nitroaromatic compounds:

To a glass culture tube described in the General Methods section was added a small stir bar, the appropriate nitro substrate (if solid), phosphetane oxide precatalyst **4**•[O] (15 mol% unless otherwise noted), and the appropriate boronic acid. The tube thread was wrapped once with Teflon tape and a phenolic screw-thread open-top cap fitted with a PTFE-lined silicone septum (Thermo Scientific) was screwed on. No special drying of the reaction vessel components was conducted prior. Following evacuation and the introduction of nitrogen on a Schlenk line, dry *m*-xylene (0.5 M) was added via syringe from a sure-seal® bottle. Lastly, phenylsilane (2 equivalents) and nitro substrate (if liquid) was added and the reaction mixture was stirred at 120 °C. When complete, the reaction vessel screw cap was unscrewed (note that in some cases pressure release was observed) and 10 mL of distilled water was added. With the aid of ethyl acetate, the reaction mixture was transferred to a separatory funnel. After mixing and separating the aqueous layer, the organic layer was washed with 10 mL of a 1 M NaOH aqueous solution, and 10 mL of brine. Each aqueous phase was back-extracted with 10 mL portions of ethyl acetate. The combined organic layers were dried over anhydrous sodium sulfate, filtered and concentrated with aid of a rotary evaporator. The crude residues were purified via column chromatography to yield pure coupling products. Columns were primarily slurry packed with hexanes and mobile phase polarity was increased gradually to the mixture indicated. Note: hexanes = Hex, dichloromethane = DCM, ethyl acetate = EA.

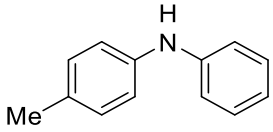
B. Analytical Data for C–N Coupling Products

***4-methoxy-N-phenylaniline* (5):**



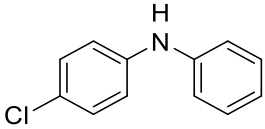
Following the general procedure using phenylboronic acid (268 mg, 2.20 mmol, 1.1 equiv) and 1-methoxy-4-nitrobenzene (306 mg, 2.00 mmol, 1.0 equiv) for 5 h at 120 °C. The product was purified by column chromatography with 8% DCM/ 2% EA/ 90% Hex on silica gel (267 mg, 1.34 mmol, 67%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.22 (t, *J* = 7.9 Hz, 2H), 7.08 (d, *J* = 8.8 Hz, 2H), 6.95 – 6.81 (m, 5H), 5.50 (br s, 1H), 3.81 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.39, 145.28, 135.82, 129.43, 122.33, 119.68, 115.74, 114.78, 55.71. HRMS (ESI) calculated for $C_{13}H_{13}NO$ $[M+H]^+$: 200.1076, Found 200.1080.

***4-methyl-N-phenylaniline* (6):**



Following the general procedure using phenylboronic acid (268 mg, 2.20 mmol, 1.1 equiv) and 1-methyl-4-nitrobenzene (274 mg, 2.00 mmol, 1.0 equiv) for 4 h at 120 °C. The product was purified by column chromatography with 8% DCM/2% EA/ 90% Hex on silica gel (265 mg, 1.44 mmol, 72%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.25 (t, *J* = 7.5 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 7.06 – 6.98 (m, 4H), 6.89 (t, *J* = 7.4 Hz, 1H), 5.61 (br s, 1H), 2.32 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 144.06, 140.39, 131.06, 129.99, 129.44, 120.42, 119.02, 116.97, 20.84. HRMS (ESI) calculated for $C_{13}H_{13}N$ $[M+H]^+$: 184.1126, Found: 184.1129.

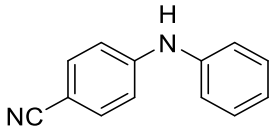
***4-chloro-N-phenylaniline* (7):**



Following the general procedure using phenylboronic acid (268 mg, 2.20 mmol, 1.1 equiv) and 1-chloro-4-nitrobenzene (315 mg, 2.00 mmol, 1.0 equiv) for 3 h at 120 °C. The product was purified by column chromatography with 8% DCM/ 2% EA/ 90% Hex on silica gel (339 mg, 1.66 mmol, 83%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.27 (t, *J* = 7.8 Hz, 2H), 7.21 (d, *J* = 8.8 Hz, 2H), 7.05 (d, *J* = 7.7 Hz, 2H), 7.02 –

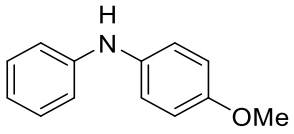
6.93 (m, 3H), 5.67 (br s, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 142.79, 142.01, 129.59, 129.41, 125.65, 121.66, 118.95, 118.25. HRMS (ESI) calculated for $C_{12}H_{10}NCl$ $[M+H]^+$: 204.0580; Found: 204.0582.

4-(phenylamino)benzonitrile **(8):**



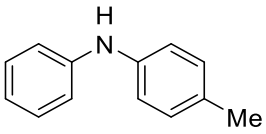
Following the general procedure using phenylboronic acid (268 mg, 2.20 mmol, 1.1 equiv) and 4-nitrobenzonitrile (296 mg, 2.00 mmol, 1.0 equiv) for 2 h at 120 °C. The product was purified by column chromatography with 12% DCM/ 4% EA/ 84% Hex on silica gel (338 mg, 1.74 mmol, 87%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.48 (d, *J* = 8.4 Hz, 2H), 7.36 (t, *J* = 7.7 Hz, 2H), 7.17 (d, *J* = 7.9 Hz, 2H), 7.12 (t, *J* = 7.4 Hz, 1H), 6.97 (d, *J* = 8.5 Hz, 2H), 6.06 (br s, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 148.10, 140.09, 133.92, 129.79, 124.14, 121.38, 120.02, 115.05, 101.71. HRMS (ESI) calculated for $C_{13}H_{10}N_2$ $[M+H]^+$: 195.0922; Found: 195.0927.

4-methoxy-N-phenylaniline **(9):**



Following the general procedure using 4-methoxyphenylboronic acid (334 mg, 2.20 mmol, 1.1 equiv) and nitrobenzene (205 µl, 2.00 mmol, 1.0 equiv) for 4 h at 120 °C. The product was purified by column chromatography with 8% DCM/ 2% EA/ 90% Hex on silica gel (342 mg, 1.72 mmol, 86%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.22 (t, *J* = 7.9 Hz, 2H), 7.08 (d, *J* = 8.8 Hz, 2H), 6.94 – 6.80 (m, 5H), 5.49 (br s, 1H), 3.80 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.40, 145.29, 135.83, 129.44, 122.34, 119.69, 115.75, 114.79, 55.73. HRMS (ESI) calculated for $C_{13}H_{13}NO$ $[M+H]^+$: 200.1075; Found: 200.1079.

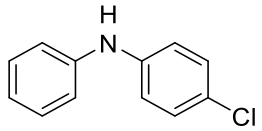
4-methyl-N-phenylaniline **(10):**



Following the general procedure using *p*-tolylboronic acid (299 mg, 2.20 mmol, 1.1 equiv) and nitrobenzene (205 µl, 2.00 mmol, 1.0 equiv) for 4 h at 120 °C. The product was purified by column chromatography with 8% DCM/ 2% EA/ 90% Hex on silica gel (303 mg, 1.65 mmol, 83%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.23 (m, 2H), 7.15 – 7.01 (m, 6H), 6.96 – 6.86 (m, 1H), 5.62 (br s, 1H), 2.33

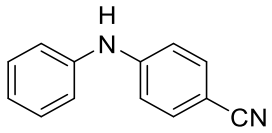
(s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 144.06, 140.40, 131.06, 129.99, 129.44, 120.42, 119.03, 116.98, 20.84. HRMS (ESI) calculated for $C_{13}H_{13}N$ $[M+H]^+$: 184.1126; Found: 184.1126.

4-chloro-N-phenylaniline **(11):**



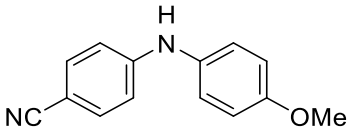
Following the general procedure using 4-chlorophenylboronic acid (344 mg, 2.20 mmol, 1.1 equiv) and nitrobenzene (205 µl, 2.00 mmol, 1.0 equiv) for 6 h at 120 °C. The product was purified by column chromatography with 8% DCM/ 2% EA/ 90% Hex on silica gel (321 mg, 1.57 mmol, 79%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 (t, *J* = 7.9 Hz, 2H), 7.21 (d, *J* = 8.8 Hz, 2H), 7.05 (d, *J* = 7.8 Hz, 2H), 7.03 – 6.93 (m, 3H), 5.67 (br s, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 142.76, 141.97, 129.58, 129.40, 125.61, 121.64, 118.93, 118.22. HRMS (ESI) calculated for $C_{12}H_{10}NCl$ $[M+H]^+$: 204.0580; Found: 204.0586.

4-(phenylamino)benzonitrile **(12):**



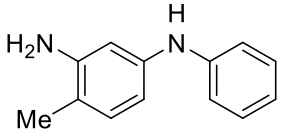
Following the general procedure using 4-cyanophenylboronic acid (323 mg, 2.20 mmol, 1.1 equiv) and nitrobenzene (205 µl, 2.00 mmol, 1.0 equiv) for 6 h at 120 °C. The product was purified by column chromatography with 12% DCM/ 4% EA/ 84% Hex on silica gel (288 mg, 1.48 mmol, 74%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 (d, *J* = 8.7 Hz, 2H), 7.36 (t, *J* = 7.9 Hz, 2H), 7.17 (d, *J* = 7.7 Hz, 2H), 7.12 (t, *J* = 7.4 Hz, 1H), 6.98 (d, *J* = 8.8 Hz, 2H), 6.15 (br s, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 148.14, 140.09, 133.87, 129.74, 124.06, 121.32, 120.06, 115.00, 101.51. HRMS (ESI) calculated for $C_{13}H_{10}N_2$ $[M+H]^+$: 195.0922; Found: 195.0926.

4-((4-methoxyphenyl)amino)benzonitrile **(15):**



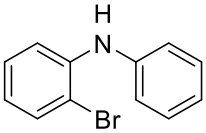
Following the general procedure using 4-methoxyphenylboronic acid (167 mg, 1.10 mmol, 1.1 equiv) and 4-nitrobenzonitrile (148 mg, 1.00 mmol, 1.0 equiv) for 5 h at 120 °C. The product was purified by column chromatography with 8% DCM/2% EA/90% Hex on silica gel (198 mg, 0.88 mmol, 88%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 (d, *J* = 8.8 Hz, 2H), 7.12 (d, *J* = 8.8 Hz, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 6.79 (d, *J* = 8.8 Hz, 2H), 6.01 (br s, 1H), 3.82 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.07, 149.76, 133.82, 132.60, 125.12, 120.31, 114.95, 113.81, 100.26, 55.63. HRMS (ESI) calculated for $C_{14}H_{12}N_2O$ $[M+H]^+$: 225.1028; Found: 225.1032.

4-methyl-N^1-phenylbenzene-1,3-diamine **(18):**



Following the general procedure using phenylboronic acid (134 mg, 1.10mmol, 1.1 equiv) and 2-methyl-5-nitroaniline (152 mg, 1.00 mmol, 1.0 equiv) for 24 h at 120 °C. The product was purified by column chromatography with 30% DCM/10% EA/60% Hex on silica (140 mg, 0.71 mmol, 71%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.24 – 7.19 (m, 2H), 7.00 (dd, *J* = 8.6, 1.1 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 1H), 6.89 – 6.84 (m, 1H), 6.45 – 6.41 (m, 2H), 5.51 (br s, 1H), 3.54 (br s, 2H), 2.10 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 145.40, 143.94, 142.09, 131.23, 129.36, 120.40, 117.44, 115.75, 109.33, 105.19, 16.80. IR (Diamond-ATR, neat): 3418, 3380, 3327, 3050, 2926, 2856, 1625, 1597, 1514, 1495, 1459, 1430, 1379, 1320, 1302, 1277, 1237, 1220, 1155, 1132, 1027, 999, 934, 854, 825, 804, 778, 753, 746, 691, 604 cm^{-1}. HRMS (ESI) calculated for $C_{13}H_{14}N_2$ $[M+H]^+$: 199.1235, Found: 199.1242.

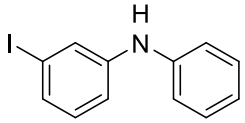
2-bromo-N-phenylaniline **(19):**



Following the general procedure using phenylboronic acid (134 mg, 1.10 mmol, 1.1 equiv) and 1-bromo-2-nitrobenzene (202 mg, 1.00 mmol, 1.0 equiv) for 3 h at 120 °C. The product was purified by column chromatography with 20% DCM/1% EA/79% Hex on silica (214 mg, 0.86 mmol, 86%). ^{1}H NMR (400

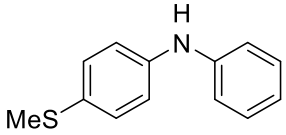
MHz, Chloroform-*d*) δ 7.56 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.40 – 7.32 (m, 2H), 7.32 – 7.27 (m, 1H), 7.23 – 7.16 (m, 3H), 7.08 (t, *J* = 7.4 Hz, 1H), 6.77 (ddd, *J* = 7.9, 7.2, 1.6 Hz, 1H), 6.13 (br s, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 141.67, 141.50, 133.08, 129.56, 128.20, 122.80, 121.00, 120.35, 115.87, 112.28. HRMS (ESI) calculated for $C_{12}H_{10}BrN$ $[M+H]^+$: 248.0075, Found: 248.0078.

3-iodo-N-phenylaniline **(20):**



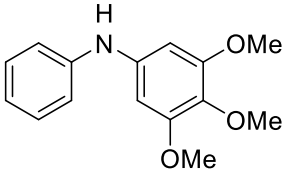
Following the general procedure using phenylboronic acid (134 mg, 1.10 mmol, 1.1 equiv) and 1-iodo-3-nitrobenzene (249 mg, 1.00 mmol, 1.0 equiv) for 3 h at 120 °C. The product was purified by column chromatography with 10% DCM/1% EA/89% Hex on silica (254 mg, 0.86 mmol, 86%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 (s, 1H), 7.30 (t, *J* = 7.9 Hz, 2H), 7.23 (d, *J* = 7.2 Hz, 1H), 7.07 (d, *J* = 7.7 Hz, 2H), 7.03 – 6.92 (m, 3H), 5.65 (br s, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 144.88, 142.01, 130.88, 129.59, 125.69, 122.13, 118.93, 116.35, 95.04. HRMS (ESI) calculated for $C_{12}H_{10}IN$ $[M+H]^+$: 295.9936, Found: 295.9936.

4-(methylthio)-N-phenylaniline **(21):**



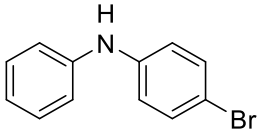
Following the general procedure using phenylboronic acid (134 mg, 1.10 mmol, 1.1 equiv) and 4-nitrothioanisole (169 mg, 1.00 mmol, 1.0 equiv) for 5 h at 120 °C. The product was purified by column chromatography with 10% DCM/1% EA/89% Hex on silica (153 mg, 0.71 mmol, 71%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30 – 7.21 (m, 4H), 7.07 – 6.98 (m, 4H), 6.93 (t, *J* = 7.3 Hz, 1H), 5.66 (br s, 1H), 2.45 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 143.09, 141.44, 129.96, 129.49, 129.16, 121.20, 118.66, 117.85, 17.98. IR (Diamond-ATR, neat): 3392, 3051, 2918, 1604, 1588, 1505, 1484, 1440, 1392, 1316, 1303, 1281, 1236, 1173, 1112, 1092, 1076, 1029, 993, 967, 952, 877, 820, 774, 758, 693 cm^{-1}. HRMS (ESI) calculated for $C_{13}H_{13}NS$ $[M+H]^+$: 216.0847, Found: 216.0847.

***3,4,5-trimethoxy-N-phenylaniline* (22)**



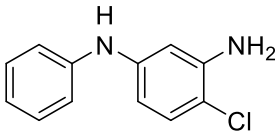
Following the general procedure with slight modification to boronic acid equivalency, 3,4,5-trimethoxyphenylboronic acid (276 mg, 1.30 mmol, 1.3 equiv) and nitrobenzene (103 µL, 1.00 mmol, 1.0 equiv) for 14 h at 120 °C. The product was purified by column chromatography with 40% DCM/10% EA/50% Hex on silica (136 mg, 0.52 mmol, 52%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.27 (t, *J* = 7.9 Hz, 2H), 7.04 (d, *J* = 7.7 Hz, 2H), 6.92 (t, *J* = 7.3 Hz, 1H), 6.34 (s, 2H), 5.65 (br s, 1H), 3.86 – 3.77 (m, 9H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 153.91, 143.69, 139.34, 132.85, 129.51, 120.80, 117.52, 96.31, 61.16, 56.14. HRMS (ESI) calculated for $C_{15}H_{17}NO_3$ $[M+H]^+$: 260.1287, Found: 260.1281.

***4-Bromo-N-phenylaniline* (23):**



Following the general procedure using 4-bromophenylboronic acid (221 mg, 1.10 mmol, 1.1 equiv) and nitrobenzene (103 µL, 1.00 mmol, 1.0 equiv) for 4 h at 120 °C. The product was purified by column chromatography with a gradient of 10-30% DCM in hexanes on neutral alumina (160 mg, 0.65 mmol, 65%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 (d, *J* = 8.8 Hz, 2H), 7.32 – 7.25 (m, 2H), 7.06 (d, *J* = 7.7 Hz, 2H), 7.01 – 6.91 (m, 3H), 5.67 (br s, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 142.55, 142.52, 132.31, 129.59, 121.79, 119.15, 118.42, 112.75. HRMS (ESI) calculated for $C_{11}H_9BrN$ $[M+H]^+$: 260.1287, Found: 260.1281.

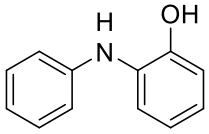
***4-chloro-N^1-phenylbenzene-1,3-diamine* (24):**



Following the general procedure using 3-amino-4-chlorophenylboronic acid (189 mg, 1.10 mmol, 1.1 equiv) and nitrobenzene (103 µL, 1.00 mmol, 1.0 equiv) for 14 h at 120 °C. The product was purified by column chromatography using 20% EA in hexanes on silica (135 mg, 0.62 mmol, 62%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.27 (t, *J* = 7.8 Hz, 2H), 7.10 (d, *J* = 8.5 Hz, 1H), 7.05 (d, *J* = 7.8 Hz, 2H), 6.95 (t,

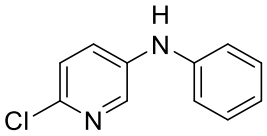
J = 7.3 Hz, 1H), 6.49 (d, *J* = 2.5 Hz, 1H), 6.40 (dd, *J* = 8.5, 2.5 Hz, 1H), 5.58 (br s, 1H), 3.98 (br s, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 143.61, 143.12, 142.88, 130.04, 129.49, 121.46, 118.53, 111.40, 109.17, 104.47. IR (Diamond-ATR, neat): 3448, 3419, 3404, 3391, 3334, 3058, 3031, 1617, 1577, 1510, 1491, 1450, 1398, 1327, 1292, 1239, 1193, 1172, 1145, 1073, 1042, 1022, 972, 931, 894, 843, 799, 789, 736, 693, 662 cm^{-1}. HRMS (ESI) calculated for $C_{12}H_{11}ClN_2$ $[M+H]^+$: 219.0689, Found: 219.0688.

2-(phenylamino)phenol **(25):**



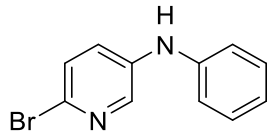
Following the general procedure using 2-hydroxyphenylboronic acid (152 mg, 1.10 mmol, 1.1 equiv) and nitrobenzene (103 µL, 1.00 mmol, 1.0 equiv) for 14 h at 120 °C. Note that acidification of the aqueous layer with 20 mL of 1 M HCl was necessary following standard workup with 1 M NaOH. The product was purified by column chromatography with 7% DCM/20% EA/73% Hex on silica (104mg, 0.56 mmol, 56%). Under an air atmosphere, the white/light tan product was observed to darken in color to brown and then a black solid over time (~one week). Spectral data were collected immediately following isolation and drying on high vac. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 – 7.18 (m, 3H), 7.11 (t, *J* = 7.7 Hz, 1H), 7.00 (d, *J* = 7.9 Hz, 1H), 6.94 – 6.87 (m, 2H), 6.79 (d, *J* = 7.8 Hz, 2H), 5.79 (s, 1H), 5.26 (s, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 151.24, 145.58, 129.55, 129.13, 126.34, 124.95, 121.16, 120.44, 115.94, 115.44. HRMS (ESI) calculated for $C_{12}H_{11}NO$ $[M+H]^+$: 186.0919, Found: 186.0923.

6-chloro-N-phenylpyridin-3-amine **(26):**



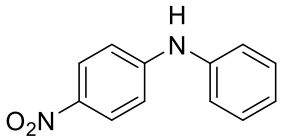
Following the general procedure using phenylboronic acid (402 mg, 3.30 mmol, 1.1 equiv) and 2-chloro-5-nitropyridine (476 mg, 3.00 mmol, 1.0 equiv) for 4 h at 120 °C. The product was purified by column chromatography with 30% DCM/10% EA/60% Hex on silica (552 mg, 2.70 mmol, 90%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.12 (d, *J* = 2.9 Hz, 1H), 7.37 (dd, *J* = 8.6, 3.0 Hz, 1H), 7.36 – 7.26 (m, 2H), 7.17 (d, *J* = 8.6 Hz, 1H), 7.08 – 7.00 (m, 3H), 5.80 (br s, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 142.21, 141.58, 139.29, 139.11, 129.79, 126.65, 124.35, 122.73, 118.79. HRMS (ESI) calculated for $C_{11}H_9ClN_2$ $[M+H]^+$: 205.0533, Found: 205.0530.

***6-bromo-N-phenylpyridin-3-amine* (27):**



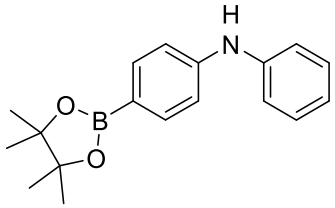
Following the general procedure using phenylboronic acid (134 mg, 1.10 mmol, 1.1 equiv) and 2-bromo-5-nitropyridine (203 mg, 1.00 mmol, 1.0 equiv) for 5 h at 120 °C. The product was purified by column chromatography with 30% DCM/10% EA/60% Hex on silica (161 mg, 0.65 mmol, 65%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (dd, *J* = 2.8, 0.8 Hz, 1H), 7.32 – 7.24 (m, 4H), 7.07 – 6.98 (m, 3H), 5.78 (br s, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 141.33, 139.81, 139.46, 131.40, 129.75, 128.01, 126.23, 122.77, 118.91. HRMS (ESI) calculated for $C_{11}H_9BrN_2$ $[M+H]^+$: 249.0027, Found: 249.0029.

***4-nitro-N-phenylaniline* (28):**



Following the general procedure using phenylboronic acid (134 mg, 1.10 mmol, 1.1 equiv) and 1,4-dinitrobenzene (168 mg, 1.00 mmol, 1.0 equiv) for 2 h at 120 °C. The product was purified by column chromatography with 8% DCM/2% EA/90% Hex on silica (165 mg, 0.77 mmol, 77%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.12 (d, *J* = 9.2 Hz, 2H), 7.39 (t, *J* = 7.9 Hz, 2H), 7.22 (d, *J* = 7.7 Hz, 2H), 7.17 (t, *J* = 7.4 Hz, 1H), 6.94 (d, *J* = 9.2 Hz, 2H), 6.33 (br s, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 150.31, 139.86, 139.60, 129.87, 126.37, 124.80, 122.05, 113.80. IR (Diamond-ATR, neat): 3335, 3043, 1062, 1582, 1541,1524, 1495, 1451, 1430, 1250, 1185, 1100, 1027, 1000, 879, 841, 836, 831, 806, 746, 689, 669, 667 cm^{-1}. HRMS (ESI) calculated for $C_{12}H_{10}N_2O_2$ $[M+H]^+$: 295.9936, Found: 295.9936.

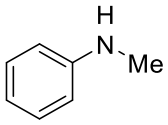
***N-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline* (29):**



Following the general procedure using phenylboronic acid (134 mg, 1.10 mmol, 1.1 equiv) and 4-nitrobenzeneboronic acid pinacol ester (249 mg, 1.00 mmol, 1.0 equiv) for 4 h at 120 °C. The product was purified by column chromatography with 10% DCM/1% EA/89% Hex on silica (170 mg, 0.58 mmol, 58%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.72 (d, *J* = 8.4 Hz, 2H), 7.30 (t, *J* = 7.8 Hz, 2H), 7.14 (d, *J* =

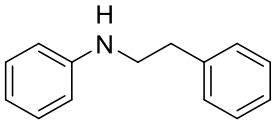
7.8 Hz, 2H), 7.06 – 6.96 (m, 3H), 5.88 (br s, 1H), 1.35 (s, 12H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 146.28, 142.03, 136.43, 129.49, 122.03, 119.24, 115.62, 83.58, 24.99. HRMS (ESI) calculated for $C_{18}H_{22}BNO_2$ $[M+H]^+$: 296.1822, Found: 296.1829.

N-methylaniline **(30):**



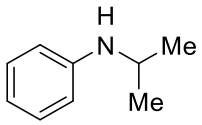
Following the general procedure using methylboronic acid (66 mg, 1.10 mmol, 1.1 equiv) and nitrobenzene (103 µL, 1.00 mmol, 1.0 equiv) for 8 h at 120 °C. The product was purified by column chromatography with 20% DCM/0.4% EA in hexane on silica (53 mg, 0.50 mmol, 50%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.24 – 7.18 (m, 2H), 6.73 (t, *J* = 6.9 Hz, 1H), 6.63 (d, *J* = 7.8 Hz, 2H), 3.70 (br s, 1H), 2.85 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 149.45, 129.33, 117.36, 112.53, 30.86. HRMS (ESI) calculated for C_7H_9N $[M+H]^+$: 108.0813, Found: 108.0814.

N-phenethylaniline **(31):**



Following the general procedure using phenethylboronic acid (165 mg, 1.10 mmol, 1.1 equiv) and nitrobenzene (103 µL, 1.00 mmol, 1.0 equiv) for 4 h at 120 °C. The product was purified by column chromatography with 20% DCM/0.4% EA in hexanes on silica (128 mg, 0.65 mmol, 65%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 (t, *J* = 7.4 Hz, 2H), 7.29 – 7.17 (m, 5H), 6.73 (t, *J* = 7.3 Hz, 1H), 6.64 (d, *J* = 7.8 Hz, 2H), 3.70 (s, 1H), 3.43 (t, *J* = 7.0 Hz, 2H), 2.94 (t, *J* = 7.0 Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 148.12, 139.42, 129.41, 128.92, 128.74, 126.56, 117.59, 113.11, 45.16, 35.64. HRMS (ESI) calculated for $C_{14}H_{15}N$ $[M+H]^+$: 198.1283, Found: 198.1282.

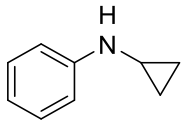
N-isopropylaniline **(32):**



Following the general procedure using isopropylboronic acid (176 mg, 1.10 mmol, 1.1 equiv) and nitrobenzene (103 µL, 1.00 mmol, 1.0 equiv) for 8 h at 120 °C. The product was purified by column chromatography with 10% DCM/0.4% EA in Hexanes on silica (75 mg, 0.55 mmol, 55%). ^{1}H NMR (500

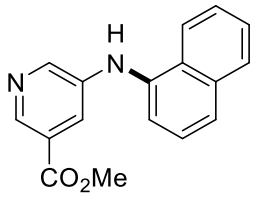
MHz, Chloroform-*d*) δ 7.17 (t, *J* = 7.9 Hz, 2H), 6.67 (t, *J* = 7.3 Hz, 1H), 6.59 (d, *J* = 7.7 Hz, 2H), 3.64 (hept, *J* = 6.3 Hz, 1H), 3.44 (br s, 1H), 1.21 (d, *J* = 6.3 Hz, 6H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 147.64, 129.41, 117.05, 113.33, 44.31, 23.17. HRMS (ESI) calculated for $C_9H_{13}N$ $[M+H]^+$: 136.1126, Found: 136.1125.

N-cyclopropylaniline **(33):**



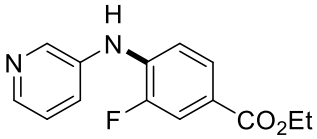
Following the general procedure using cyclopropylboronic acid (95 mg, 1.10 mmol, 1.1 equiv) and nitrobenzene (103 µL, 1.00 mmol, 1.0 equiv) for 8 h at 120 °C. The product was purified by column chromatography with 10% DCM/0.4% EA in hexanes on silica (72 mg, 0.54 mmol, 54%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.20 (t, *J* = 7.9 Hz, 2H), 6.80 (d, *J* = 7.7 Hz, 2H), 6.75 (t, *J* = 7.3 Hz, 1H), 4.17 (s, 1H), 2.43 (tt, *J* = 6.7, 3.6 Hz, 1H), 0.78 – 0.70 (m, 2H), 0.57 – 0.49 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 148.80, 129.24, 117.86, 113.27, 25.36, 7.55. HRMS (ESI) calculated for $C_9H_{13}N$ $[M+H]^+$: 134.0970, Found: 134.0969.

methyl 5-(naphthalen-1-ylamino)nicotinate **(34):**



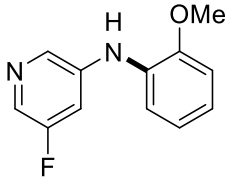
Following the general procedure on 1.0 gram scale. The product was isolated as a light-yellow solid after 2 h (1.15 g, 75%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.71 (br s, 1H), 8.59 (br s, 1H), 8.53 (br s, 1H), 8.23 - 8.07 (m, 1H), 8.01 - 7.84 (m, 1H), 7.76 (br s, 1H), 7.67 (br d, *J*=7.0 Hz, 1H), 7.58 - 7.50 (m, 2H), 7.50 - 7.40 (m, 2H), 3.81 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 165.5, 142.3, 142.0, 139.9, 137.3, 134.4, 128.3, 127.8, 126.3, 126.0, 125.7, 125.6, 123.6, 122.6, 121.0, 116.9, 52.2. IR (Diamond-ATR, neat): 3253, 3050, 2995, 2950, 1723, 1718, 1591, 1578, 1549, 1505, 1457, 1439, 1412, 1399 1335, 1317, 1280, 1258, 1223, 1169, 1108, 1093, 1053, 1022, 990, 966, 902, 885, 796, 790, 778, 773, 765, 740, 697, 650 cm^{-1}. HRMS calculated for $C_{17}H_{14}N_2O_2$ $[M+H]^+$: 279.1128, Found: 279.1131.

***ethyl 3-fluoro-4-(pyridin-3-ylamino)benzoate* (35):**



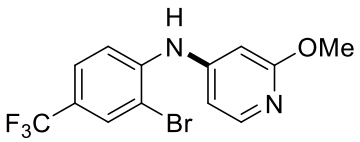
Following the general procedure on 1.0 gram scale. The product was isolated as a white solid after 3 h (1.16 g, 56%). ^{1}H NMR (500 MHz, DMSO-d6) δ 8.70 (br s, 1H), 8.50 (br s, 1H), 8.21 (br d, J=4.0 Hz, 1H), 7.66 (br d, J=5.3 Hz, 1H), 7.64 (s, 1H), 7.58 (br d, J=8.1 Hz, 1H), 7.31 (br dd, J=7.8, 4.7 Hz, 1H), 7.27 (br t, J=8.5 Hz, 1H), 4.25 (q, J=7.0 Hz, 2H), 1.28 (t, J=7.0 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.61, 164.59, 152.23, 150.30, 143.05, 141.93, 137.60, 136.12, 136.04, 126.50, 126.47, 126.21, 123.70, 121.10, 121.05, 116.27, 116.11, 115.15, 115.13, 60.4, 14.1. IR (Diamond-ATR, neat): 3350, 1695, 1614, 1590, 1579, 1538, 1528, 1483, 1476, 1372, 1354, 1345, 1330, 1310, 1286, 1474, 1222, 1191, 1183, 1124, 1088, 1019, 948, 893, 807, 784, 760, 714, 706, 614 cm^{-1}. HRMS calculated for $C_{14}H_{13}FN_2O_2$ $[M+H]^+$: 261.1034, Found: 261.1036.

***5-fluoro-N-(2-methoxyphenyl)pyridin-3-amine* (36):**



Following the general procedure on 674 milligram scale. The product was isolated as a tan solid after 3 h (527 mg, 51%). Spectra were collected for the HCl salt. ^{1}H NMR (500 MHz, DMSO-d_6) δ 15.55 (br s, 1H), 9.55 (br s, 1H), 8.33 (s, 1H), 8.10 (s, 1H), 7.51 (br d, *J*=11.0 Hz, 1H), 7.28 (d, *J*=7.6 Hz, 1H), 7.18 (t, *J*=7.7 Hz, 1H), 7.11 (d, *J*=8.2 Hz, 1H), 6.95 (t, *J*=7.6 Hz, 1H), 3.78 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 161.4, 159.4, 152.4, 146.2, 146.1, 126.9, 126.4, 125.6, 123.6, 120.9, 119.1, 118.8, 113.3, 113.1, 112.6, 55.6. HRMS calculated for $C_{12}H_{11}FN_2O$ $[M+H]^+$: 219.0928, Found: 219.0929.

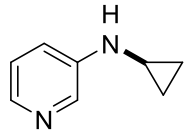
***N-(2-bromo-4-(trifluoromethyl)phenyl)-2-methoxypyridin-4-amine* (37):**



Following the general procedure on 1.00 gram scale. The product was isolated as a white solid after 3 h (0.853 g, 66%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.56 (br s, 1H), 7.99 (br s, 1H), 7.90 (br d, *J*=5.0 Hz, 1H), 7.66 (br d, *J*=7.9 Hz, 1H), 7.57 (br d, *J*=8.1 Hz, 1H), 6.68 (d, *J*=5.0 Hz, 1H), 6.33 (br s, 1H). ^{13}C NMR

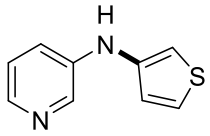
(126 MHz, DMSO-d_6) δ 164.9, 151.7, 147.3, 142.9, 130.37 - 130.27 (m, 1C), 125.82 - 125.21 (m, 1C), 124.6, 124.4, 124.4, 122.5, 116.0, 106.6, 95.1, 52.8. HRMS calculated for $C_{13}H_{10}BrF_3N_2O$ $[M+H]^+$: 347.0001, Found: 347.0002.

N-cyclopropylpyridin-3-amine **(38):**



Following the general procedure on 1.00 gram scale. The product was isolated as a white solid after 3 h (0.595 g, 55%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.07 (d, *J*=2.5 Hz, 1H), 7.81 (dd, *J*=4.4, 1.4 Hz, 1H), 7.13 - 6.91 (m, 2H), 6.31 (br s, 1H), 2.40 - 2.25 (m, 1H), 0.77 - 0.58 (m, 2H), 0.47 - 0.29 (m, 2H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 145.3, 137.3, 135.3, 123.4, 117.9, 24.1, 6.7. HRMS calculated for $C_8H_{10}N_2$ $[M+H]^+$: 135.0916, Found: 135.0916.

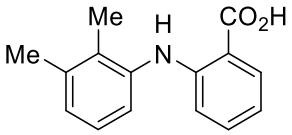
N-(thiophen-3-yl)pyridin-3-amine **(39):**



Following the general procedure on 1.00 gram scale. The product was isolated as a white solid after 3 h (0.781 g, 55%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.58 (s, 1H), 8.43 - 8.29 (m, 1H), 7.98 (br d, *J*=4.3 Hz, 1H), 7.46 (dd, *J*=4.4, 3.1 Hz, 1H), 7.41 (br d, *J*=7.9 Hz, 1H), 7.19 (br dd, *J*=8.1, 4.7 Hz, 1H), 6.97 (br d, *J*=4.6 Hz, 1H), 6.91 (br s, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 141.1, 140.6, 139.4, 137.4, 125.4, 123.8, 122.4, 120.0, 103.9. HRMS calculated for $C_9H_8N_2S$ $[M+H]^+$: 177.0481, Found: 177.0484.

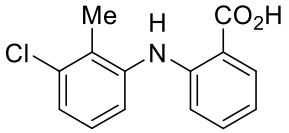
Target synthesis

Mefenamic acid (Ponstel®) (40):[9]



Into a 40 mL vial with a stir bar was added phosphetane oxide precatalyst **4•**[O] (26 mg, 0.15 mmol, 15 mol%), 2,3-dimethylphenylboronic acid (165 mg, 1.10 mmol, 1.1 equiv), and 2-nitrobenzonitrile (148 mg, 1.00 mmol, 1.0 equiv). The vial thread was wrapped with a single piece of Teflon tape and a cap was screwed on. After exchanging air for nitrogen, 2.0 mL of *m*-xylene was added, followed by phenylsilane (0.25 mL, 2.00 mmol, 2.0 equiv). The reaction was heated at 120 °C for 3 h. After cooling the reaction mixture to room temperature, *m*-xylene was removed via rotary evaporator. Then, in a modification of the literature procedure,[10] 10 mL of distilled water was added to the vial, followed by a solution of potassium hydroxide in ethanol (16 mL EtOH, 2.81 g KOH (50 equiv) – heat to solubilize). The reaction mixture was heated at 95 °C for 20 h and then was cooled to room temperature. Ethanol was removed via rotary evaporator and then the aqueous layer was acidified to pH = 3. Extraction was carried out using DCM (4x25 mL) and the organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated by rotary evaporation. The product was purified by column chromatography with 90% DCM/10% EA on silica (161 mg, 0.67 mmol, 67%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.01 (br s, 1H), 9.47 (br s, 1H), 7.89 (d, J = 7.0 Hz, 1H), 7.31 (t, J = 7.8 Hz, 1H), 7.16 – 7.08 (m, 2H), 7.06 – 6.98 (m, 1H), 6.74 – 6.63 (m, 2H), 2.29 (s, 3H), 2.10 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.25, 148.77, 138.35, 137.90, 134.21, 131.73, 131.25, 126.43, 126.04, 122.20, 116.26, 113.09, 111.23, 20.26, 13.70. IR (Diamond-ATR, neat): 3308, 2856, 2569, 1645, 1595, 1575, 1509, 1471, 1445, 1423, 1407 1328, 1278, 1254,1184, 1162, 1151, 1095, 1081, 1064, 1038, 991, 960, 888, 854, 845, 816, 777, 754, 746, 662 cm^{-1}. HRMS (ESI) calculated for $C_{15}H_{15}NO_2$ $[M+H]^+$: 242.1181, Found: 242.1187.

Tolfenamic acid (Clotam®) (41):[11]

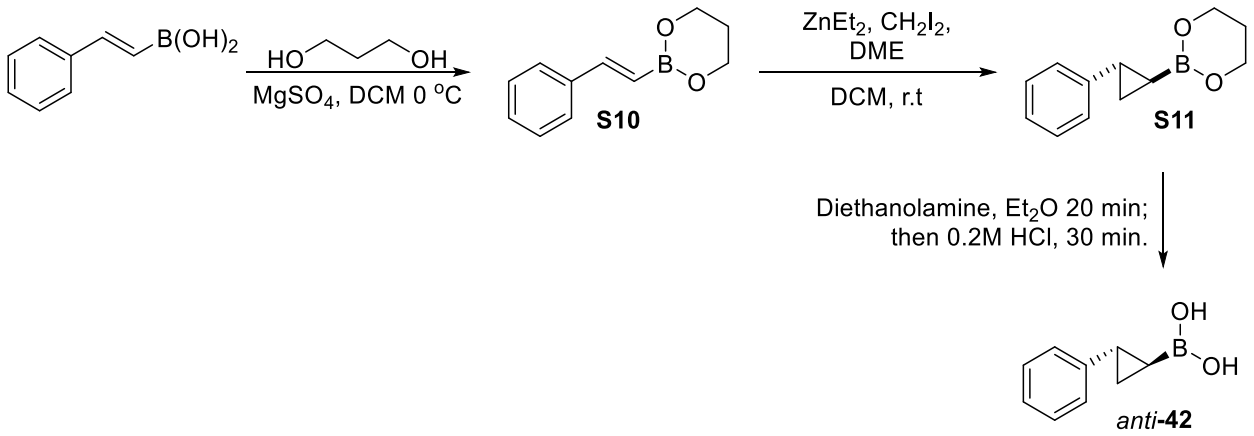


Into a 40 mL vial with a stir bar was added phosphetane oxide precatalyst **4•**[O] (26 mg, 0.15 mmol, 15 mol%), 3-chloro-2-methylphenylboronic acid (187 mg, 1.10 mmol, 1.1 equiv), and 2-nitrobenzonitrile (148 mg, 1.00 mmol, 1.0 equiv). The vial thread was wrapped with a single piece of Teflon tape and a cap was screwed on. After exchanging air for nitrogen, 2 mL of *m*-xylene was added, followed by phenylsilane

(0.25 mL, 2.00 mmol, 2 equiv). The reaction was heated at 120 °C for 5 h. After cooling the reaction mixture to room temperature, *m*-xylene was removed via rotary evaporator. Then, in a modification of the literature procedure,[10] 10 mL of distilled water were added to the vial, followed by a solution of potassium hydroxide in ethanol (16 mL EtOH, 2.81g KOH (50 equiv) – heat to solubilize). The reaction mixture was heated at 95 °C for 16 h and then was cooled to room temperature. Ethanol was removed via rotary evaporator and then the aqueous layer was acidified to pH = 2. Extraction was carried out using DCM (4x25 mL) and the organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated by rotary evaporation. The product was purified by column chromatography with 85% DCM/5% EA/10 Hex on silica (192 mg, 0.73 mmol, 73%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.16 (br s, 1H), 9.59 (br s, 1H), 7.91 (d, J = 7.9 Hz, 1H), 7.41 – 7.20 (m, 4H), 6.87 – 6.73 (m, 2H), 2.26 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.12, 147.54, 140.51, 134.44, 134.30, 131.80, 129.82, 127.58, 124.92, 122.12, 117.35, 113.62, 112.25, 14.73. IR (Diamond-ATR, neat): 3322, 2872, 2565, 1661, 1601, 1582, 1569, 1522, 1449, 1428, 1383, 1328, 1249, 1174, 1159, 1152, 1084, 1049, 1013, 984, 948, 907, 881, 829, 797, 740, 723, 697, 687, 663 cm^{-1}. HRMS (ESI) calculated for $C_{14}H_{12}ClNO_2$ $[M+H]^+$: 262.0635, Found: 262.0646.

IV. Evaluation of Stereospecificity of C–N Coupling

A. Preparation of Cyclopropylboronic Acids *anti*-42 and *syn*-42



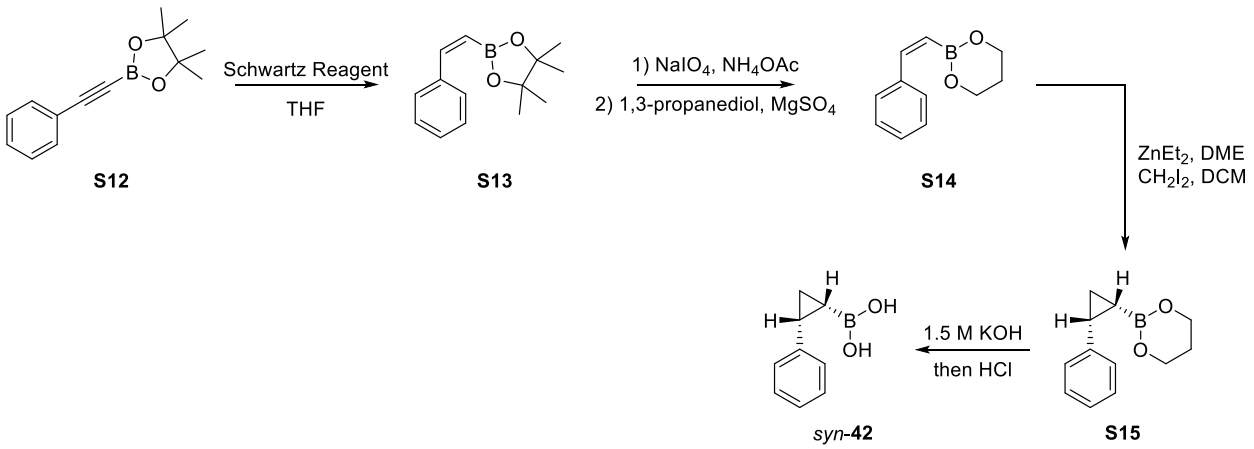
Scheme S1. Synthetic route to *anti*-(2-phenylcyclopropyl)boronic acid (*anti*-**42**).

trans-2-Styryl-1,3,2-dioxaborinane **(S10)** was synthesized according to a modified literature procedure.[12] A 100 mL round bottom flask equipped with a stir bar was charged with *trans*-styrylboronic acid (1.02 g, 6.87 mmol, 1 equiv) and excess $MgSO_4$ **(~**6 grams). The flask was fitted with a septum, then evacuated and backfilled with N_2 (3x). The contents of the flask were then suspended in CH_2Cl_2, and cooled to 0 ˚C using an ice bath. To the reaction was then added 1,3-propanediol (498 μL, 1 equiv 6.87 mmol) in a dropwise fashion. The reaction mixture was then stirred vigorously in the bath—allowing the ice to melt—for 4 h. The reaction progress was monitored by taking ^{1}H NMR. Once the reaction was complete, it was warmed to room temperature, filtered and concentrated in vacuo, resulting in 1.19 g (92% yield) of clear oil. ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.53 – 7.47 (m, 2H), 7.34 (q, *J* = 10.2, 8.5 Hz, 3H), 6.10 (d, *J* = 18.3 Hz, 1H), 4.12 (t, *J* = 5.5 Hz, 4H), 2.04 (p, *J* = 5.5 Hz, 2H). The data agrees with previously reported literature values.[13]

trans-2-(2-phenylcyclopropyl)-1,3,2-dioxaborinane **(S11)** was synthesized according to a modified literature procedure.[14] A 100 mL round bottom flask equipped with a stir bar was flame dried and allowed to cool to room temperature under vacuum. At room temperature, the vessel was charged with $ZnEt_2$ (1M solution in hexanes, 15.7 mL, 15.7 mmol, 2.5 equiv) followed by 1,2-dimethoxyethane (1.64 mL, 15.7 mmol, 2.5 equiv) and DCM (21 mL). The reaction mixture was cooled to 0 ˚C in an ice bath and CH_2I_2 (2.54 mL, 31.5 mmol, 5 equiv, purified by distillation under reduced pressure over CaH_2 before use) was

added dropwise via syringe. The solution was stirred at 0 °C for 25 minutes, then **S10** (1.19 g, 6.31 mmol, 1 equiv) was added to the flask dropwise as a solution in DCM. After the addition, the reaction mixture was stirred at 0 °C for 5 minutes and then warmed to room temperature and stirred vigorously for 12 h (precipitation of a salt may be seen). The reaction was quenched with saturated ammonium chloride solution, diluted with water and the organic layer separated. The aqueous layer was back-extracted with DCM (2x), the organics were combined and washed with brine, dried with Na_2SO_4, filtered and concentrated in vacuo. The resulting oil was purified by silica gel chromatography (3% EtOAc in Hexane) to give 1.05 g of a clear oil (82% yield). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.25 – 7.20 (m, 2H), 7.15 – 7.09 (m, 1H), 7.09 – 7.03 (m, 2H), 3.98 (t, *J* = 5.4 Hz, 4H), 2.04 – 1.98 (m, 1H), 1.98 – 1.90 (m, 2H), 1.08 (ddd, *J* = 8.1, 6.9, 3.5 Hz, 1H), 0.93 (ddd, *J* = 9.8, 5.2, 3.5 Hz, 1H), 0.14 (ddd, *J* = 9.7, 6.9, 5.5 Hz, 1H). The data agrees with previously reported literature values.[13]

anti-(2-phenylcyclopropyl)boronic acid **(***anti*-**42)** was synthesized according to modified literature procedure.[15] To a solution of **S11** (719 mg, 3.56 mmol, 1 equiv) in Et_2O at room temperature was added diethanolamine (412 mg, 3.91 mmol, 1.1 equiv). The reaction mixture was vigorously stirred for 30 minutes, and the precipitate was filtered, collected and washed with Et_2O. The precipitate was then transferred to a 100 mL round bottom flask and suspended in ~20 mL of 0.2 M aqueous HCl solution. This suspension was then treated with 20 mL of Et_2O and the biphasic mixture was stirred vigorously for 30 minutes. The organic layer was then separated and the remaining aqueous layer was extracted 3x with Et_2O. The organics were combined, washed with brine, dried with Na_2SO_4, filtered and concentrated in vacuo to give 319 mg (55% yield) of a white solid. ^{1}H NMR (500 MHz, Acetone-d_6) δ 7.26 – 7.18 (m, 2H), 7.14 – 7.04 (m, 3H), 6.70 (s, 1H, OH, may vary based on amount of anhydride), 1.18 – 1.09 (m, 1H), 0.95 (ddd, *J* = 9.7, 5.1, 3.4 Hz, 1H), 0.13 (ddd, *J* = 9.6, 6.9, 5.5 Hz, 1H). The data agrees with previously reported literature values.[13]



Scheme S2. Synthetic route to *syn*-(2-phenylcyclopropyl)boronic acid (*syn*-**42**).

4,4,5,5-tetramethyl-2-(phenylethynyl)-1,3,2-dioxaborolane **(S12)** was synthesized according to literature procedure[16] in the same manner on 2.00 gram scale with respect to phenylacetylene (19.6 mmol) with exception of the purification method. Once yellow/orange oil was obtained, it was concentrated on a schlenk line overnight to give a yellow/orange solid. This solid was dissolved in acetone (3 mL/gram of crude), cooled in an ice bath, stirred, and precipitated with dropwise addition of water to give a white solid, which was collected by filtration and dried on a schlenk line overnight to give 3.32g (14.6 mmol, 74% yield). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.57 – 7.49 (m, 2H), 7.39 – 7.34 (m, 1H), 7.34 – 7.28 (m, 2H), 1.32 (s, 12H), agrees with reported literature.

cis-4,4,5,5-tetramethyl-2-styryl-1,3,2-dioxaborolane **(S13)** was synthesized according to literature procedure.[17] A 100 mL round bottom flask equipped with a stir bar was charged with Schwartz reagent (2.48g, 9.6 mmol, 1.2 equiv) inside a glovebox. The flask was sealed and removed from the glovebox, and the solid was suspended in 20 mL of THF. Pinacol boronate **S12** (1.83g, 8.0 mmol, 1.0 equiv) was then added dropwise as a solution in THF. The reaction mixture was stirred at room temperature until the solid dissolved and the reaction mixture turned orange in color (approx. 30 minutes). To the reaction mixture was then added excess water (~5 mL) in a dropwise fashion and the reaction was allowed to stir until the orange color disappeared and the reaction turned clear (approx. 30 min). The reaction mixture was then concentrated in order to remove THF. Once formation of a white precipitate was seen the contents of the flask were poured into a separatory funnel and extracted with hexanes (3x ~30 mL). The organics were combined and washed with brine, dried with anhydrous Na_2SO_4, filtered and concentrated in vacuo. The resulting oil was purified by silica gel chromatography (5% to 10% EtOAc in Hexanes) to give 1.32g of

product (5.7 mmol, 71% yield, 96:4 *Z : E)* ^{1}H NMR for the *Z* product (400 MHz, Chloroform-*d*) δ 7.58 – 7.54 (m, 2H), 7.36 – 7.29 (m, 3H), 5.62 (d, *J* = 14.9 Hz, 1H), 1.32 (s, 12H), agrees with reported literature.

***cis-2-styryl-1,3,2-dioxaborinane* (S14)** was synthesized according to modified literature procedure.[12,17] To a solution of **S13** (800 mg, 3.48 mmol, 1.0 equiv) in a 2:1 acetone/water mixture (34 mL) was added $NaIO_4$ (2.23g, 10.4 mmol, 3.0 equiv) and NH_4OAc (804 mg, 10.4 mmol, 3 equiv). The resulting suspension was stirred at room temperature for 33h, monitoring the reaction progress by observing aliquots via ^{1}H NMR (NMR aliquots prepared by extracting ~0.1 mL into EtOAc, concentrating in vacuo, and dissolving residue into $CDCl_3$). Once the reaction was complete, the suspension was concentrated in vacuo to remove acetone and then diluted with EtOAc. The aqueous layer was extracted with EtOAc (3x ~30 mL), and the organics were combined, washed with brine, dried with Na_2SO_4, filtered and concentrated in vacuo. The contents were then transferred in a minimal amount of EtOAc to a 100 mL round bottom flask, to which was then added DCM (30 mL) and $MgSO_4$ (6g). The resulting suspension was then cooled to 0 ˚C, and 1,3-propanediol (276 μL, 3.80 mmol, 1.1 equiv) was added via syringe. The reaction was stirred overnight, filtered, and washed with water to remove excess diol followed by a wash with brine, dried with Na_2SO_4, filtered and concentrated in vacuo. Purified by silica gel chromatography (10% EtOAc in Hexanes) to give 439 mg, of a pale yellow oil. ^{1}H NMR revealed an isomeric mixture of 94 : 6 *Z* : *E*. Characterization for *Z* compound. ^{1}H NMR integration also revealed a 5% impurity (with respect to mmol) corresponding to the free boronic acid of **S13**. This oil was used without further purification into the next step**.** ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 – 7.37 (m, 2H), 7.29 – 7.23 (m, 2H), 7.20 (dt, *J* = 7.8, 2.2 Hz, 1H), 7.05 (d, *J* = 14.9 Hz, 1H), 5.52 (d, *J* = 14.8 Hz, 1H), 3.99 (t, *J* = 5.5 Hz, 4H), 1.95 (p, *J* = 5.5 Hz, 2H).

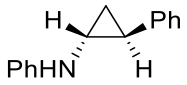
***cis-2-(2-phenylcyclopropyl)-1,3,2-dioxaborinane* (S15)** was synthesized according to modified literature procedure.[14] A 40 mL scintillation vial equipped with a stir bar was flame dried and allowed to cool to room temperature under vacuum. At room temperature, the vessel was charged with $ZnEt_2$ (1M solution in hexanes, 3.05 mL, 3.05 mmol, 2.6 equiv) followed by 1,2-dimethoxyethane (317 μL, 3.05 mmol, 2.6 equiv) and DCM (4.0 mL). The reaction mixture was cooled to 0 ˚C in an ice bath and CH_2I_2 (491 μL, 6.1 mmol, 5.2 equiv, purified by distillation under reduced pressure over CaH_2 before use) was added dropwise via syringe. The solution was stirred at 0 ˚C for 25 minutes, then **S14** (221 mg, 1.17 mmol, 1 equiv,, massed assuming oil was entirely **S14** although containing 5% boronic acid as described above**)** was added to the flask dropwise as a solution in DCM. After the addition, the reaction mixture was stirred at 0 ˚C for 5 minutes and then warmed to room temperature and stirred vigorously for 12h (precipitation of a salt may be seen). The reaction was quenched with saturated ammonium chloride solution, diluted with water and the organic layer separated. The aqueous layer was back-extracted with DCM (2x), the organics were

combined and washed with brine, dried with Na_2SO_4, filtered and concentrated in vacuo. The resulting oil was purified by silica gel chromatography (gradient 10% to 20% EtOAc in Hexane). The *cis* product elutes first and 121 mg of a clear oil (0.598 mmol, 51% yield) was isolated. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.26 (d, *J* = 6.7 Hz, 5H), 7.18 – 7.12 (m, 1H), 3.80 (dt, *J* = 11.0, 5.5 Hz, 2H), 3.70 (dt, *J* = 11.0, 5.5 Hz, 2H), 2.29 (ddd, *J* = 10.3, 8.0, 5.9 Hz, 1H), 1.64 (p, *J* = 5.5 Hz, 2H), 1.14 (ddd, *J* = 7.3, 5.9, 4.0 Hz, 1H), 1.05 (td, *J* = 8.6, 3.9 Hz, 1H), 0.38 (td, *J* = 9.7, 7.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.82, 128.79, 127.71, 125.55, 61.63, 27.29, 21.77, 8.88. Carbon attached directly to boron not visible. ^{11}B NMR (128 MHz, $CDCl_3$) δ 29.08. HRMS (ESI) calculated for $C_{12}H_{15}BO_2$ $[M+H]^+$: 203.1243, Found: 203.1244.

***syn*-(2-phenylcyclopropyl)boronic acid (*syn*-42)** was synthesized according to a modified literature procedure.[13] **S15** (41.8 mg, 0.21 mmol, 1.00 equiv) was treated with 1.5 M KOH (0.8mL, 5.85 equiv). The reaction mixture was stirred at room temperature for 6 hours, and then extracted with Et_2O (3x 1mL). The aqueous layer was extracted treated with 2 M HCl solution (~2mL) and the reaction mixture was then extracted with Et_2O (4x 1 mL). The Et_2O extract from the acidified portion was then filtered through a plug of Na_2SO_4 and concentrated in vacuo and dried on a vacuum line overnight to give 24.8 mg of a white solid. ^{1}H NMR revealed this solid to be a 12:1 mixture of ***syn*-42:S15** which was used directly in the next step. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.28 (d, *J* = 7.0 Hz, 2H), 7.21 (t, *J* = 7.6 Hz, 2H), 7.14 – 7.07 (m, 1H), 2.25 (ddd, *J* = 10.1, 8.2, 5.9 Hz, 1H), 1.17 (td, *J* = 6.8, 4.2 Hz, 1H), 1.05 (td, *J* = 8.7, 3.8 Hz, 1H), 0.41 (td, *J* = 9.7, 7.4 Hz, 1H). ^{13}C NMR (101 MHz, Acetone) δ 206.26, 142.87, 129.39, 128.68, 126.38, 22.26, 10.16. Carbon attached directly to boron not visible. ^{11}B NMR (128 MHz, Acetone) δ 31.21. HRMS not collected for mixture.

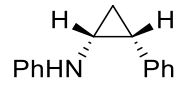
B. Procedures and Analytical Data for C–N Coupling with *anti*-43 and *syn*-43

***anti-N-(2-phenylcyclopropyl)aniline* (*anti*-43):**



Following the general procedure *anti*-(2-phenylcyclopropyl)boronic acid (*anti*-**43**) (89.1 mg, 0.55 mmol, 1.1 equiv), nitrobenzene (51 µL, 0.50 mmol, 1.0 equiv), for 8 h at 120 °C. NMR yield determined using 1,3,5-trimethoxybenzene internal standard (72%). Due to seeming instability on silica and neutral alumina, for characterization purposes the product was isolated on preparative alumina TLC passivated with triethylamine (0.2 mmol scale; 10% DCM/88% Hex/2% TEA, 17 mg, 41%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.33 (t, *J* = 7.6 Hz, 2H), 7.28 – 7.15 (m, 3H), 7.13 (d, *J* = 7.1 Hz, 2H), 6.76 (t, *J* = 7.3 Hz, 1H), 6.72 (d, *J* = 7.6 Hz, 2H), 4.30 (br s, 1H), 2.65 – 2.61 (m, 1H), 2.03 – 1.98 (m, 1H), 1.31 – 1.24 (m, 2H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 148.15, 141.46, 129.36, 128.58, 125.97, 125.85, 118.10, 113.29, 36.50, 26.25, 17.60. HRMS (ESI) calculated for $C_{15}H_{15}N$ $[M+H]^+$: 210.1277, Found: 210.1279.

***syn-N-(2-phenylcyclopropyl)aniline* (*syn*-43):**



Following the general procedure using *syn*-(2-phenylcyclopropyl)boronic acid (*syn*-**43**) (15.8 mg, 0.10 mmol, 1.1 equiv) and nitrobenzene (9.1 µL, 0.09 mmol, 1.0 equiv) for 8 h at 120 °C. For purposes of reaction stoichiometry, 12:1 mixture of *syn*-**42:S15** was massed as if entirely *syn*-**42** (refer to synthetic preparation of *syn*-**42** above). NMR yield determined using dibromomethane internal standard (61%), with no *anti* product detected in the crude. Control experiments with **S15** revealed it to be preserved and inactive in the coupling reaction. Due to seeming instability on silica and neutral alumina, for characterization purposes the product was isolated on preparative alumina TLC passivated with triethylamine (10% DCM/88% Hex/2% TEA, 6.5 mg, 31%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.32 – 7.20 (m, 5H), 7.16 (t, *J* = 7.8 Hz, 2H), 6.75 – 6.66 (m, 3H), 3.64 (br s, 1H), 2.81 (td, *J* = 6.8, 4.3 Hz, 1H), 2.33 (dt, *J* = 9.0, 7.1 Hz, 1H), 1.38 (dt, *J* = 9.1, 6.0 Hz, 1H), 1.02 (ddd, *J* = 6.8, 5.5, 4.3 Hz, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 148.43, 137.18, 129.15, 128.75, 128.17, 126.32, 117.62, 113.13, 31.84, 23.33, 13.97. HRMS (ESI) calculated for $C_{15}H_{15}N$ $[M+H]^+$: 210.1277, Found: 210.1271.

C. Spectroscopic Determination of Reaction Stereospecificity

Stereospecificity of the coupling reactions involving *anti* and *syn*-**42** boronic acids was evaluated using ^{1}H NMR. After conducting the general coupling procedure with nitrobenzene as the partner, the reactions were worked up (according to the general procedure) and compared to the isolated product of opposite stereospecificity. Each isomer was isolated individually for comparison purposes. Note that superimposed spectra were referenced to $CDCl_3$ (δ 7.26) and that peak shift variance in the crude mixtures was estimated to be ±0.03 ppm.

Spectral Assignment of *syn*-43 and *anti*-43.

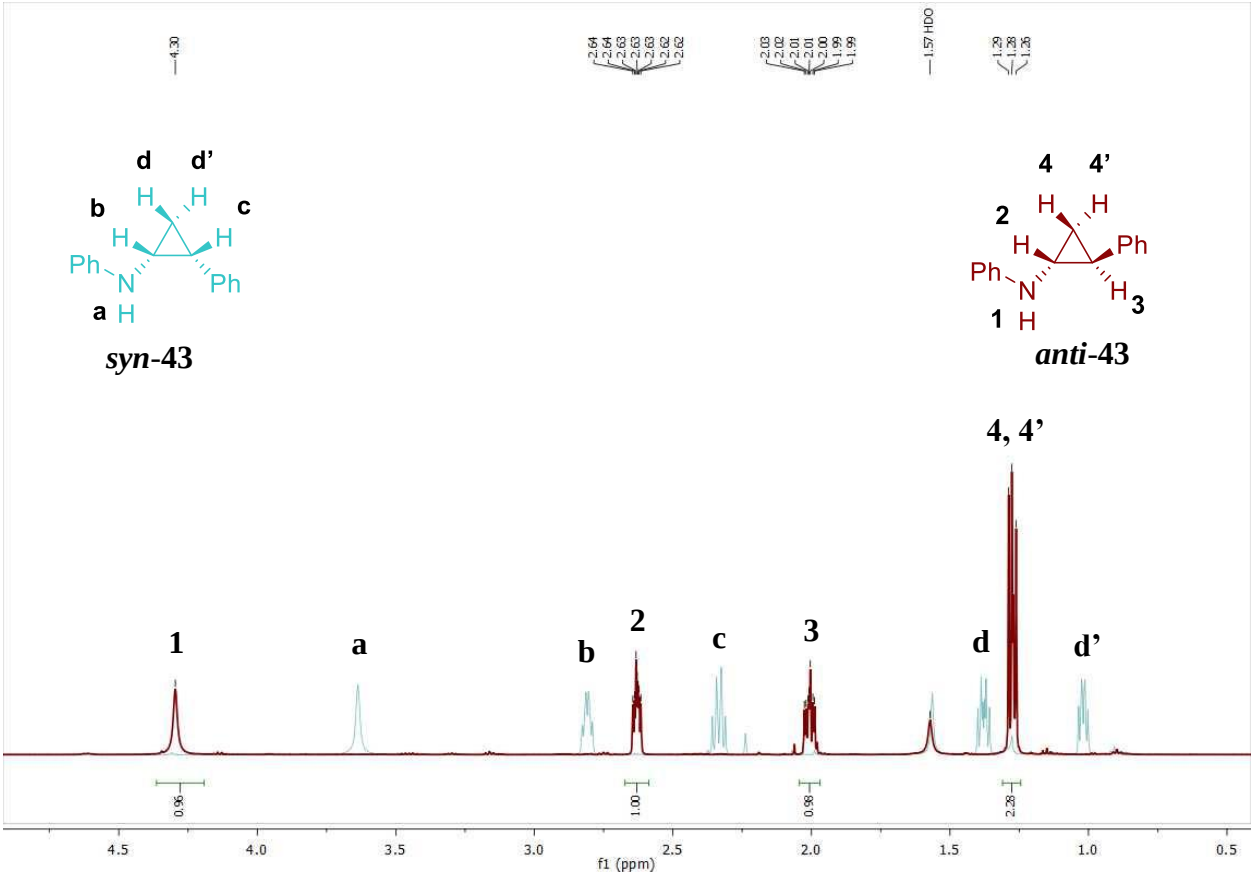


Figure S4. Superimposition of ^{1}H NMR for isolated *anti*-**43** (red) and isolated *syn*-**43** (teal), only aliphatic region shown. Spectral assignments of each isomer are made for future reference. Peak **a** = 3.637 ppm.

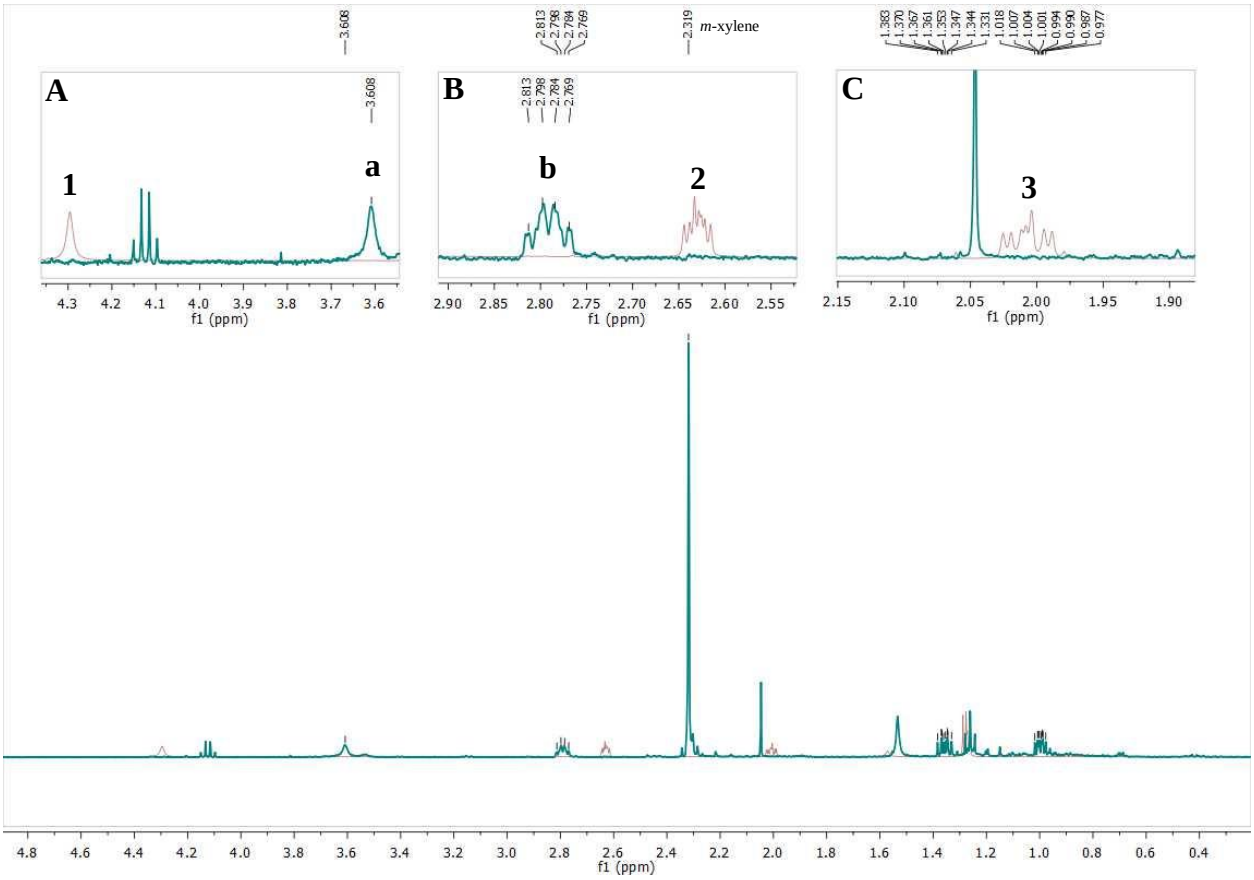


Figure S5. Superimposition of isolated *anti*-**43** (red) and crude reaction mixture of the *syn*-**43** (teal). Key regions of the where the presence of an isomeric mixture should be detected are highlighted. All proton assignments refer to those in Figure S4. Frame **A** shows the characteristic N-H peaks **1** and **a**: no peak corresponding to **1** can be seen in the teal trace. Similarly in frame **B**, proton **2** of the *anti* product is absent in the crude reaction trace. Frame **C** shows the crude trace lacks proton **3** of the *anti* product. The fact that no features of the *anti*-**43** can be seen in the trace of the crude *syn*-**43** led to the determination that the coupling of *syn*-**42** with nitrobenzene (see figure 4C in main text), occurs in a stereoretentive fashion.

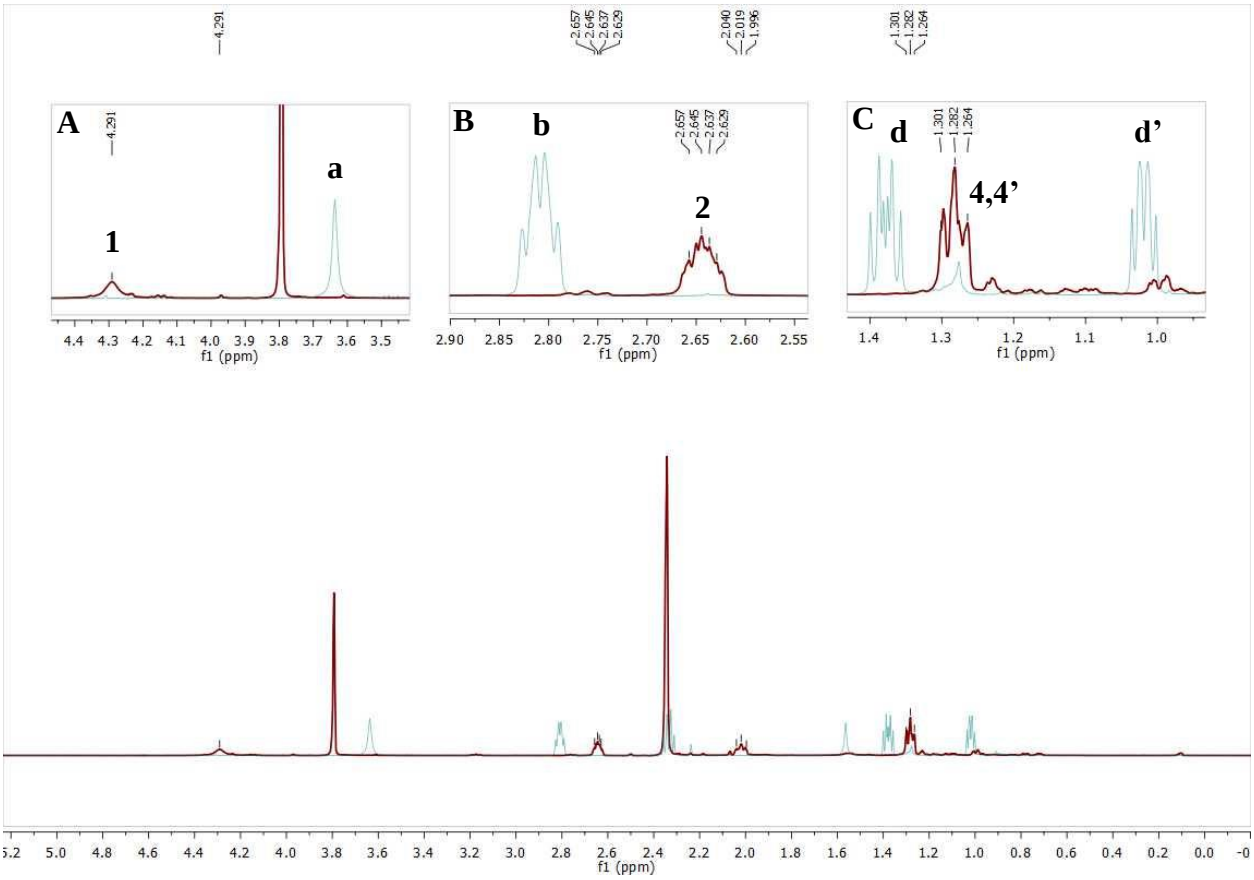
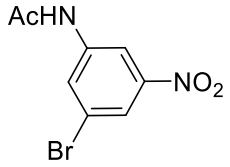


Figure S6. Superimposition of crude *anti*-**43** (red) and isolated *syn*-**43** (teal), peak at 3.82ppm represents 1,3,5-trimethoxybenzene (TMB) used to determine crude NMR yield. Key regions of the where the presence of an isomeric mixture should be detected are highlighted. All proton assignments refer to those in Figure S4. Frame **A** shows the N-H protons **1** and **a**: small signal under **a** represents satellite peak of (TMB). Frame **B** shows no proton **b** in the crude reaction mixture. Critically in frame **C** no signal corresponding to **d** is present, indicating the absence of *syn*-**43** in the coupling of *anti*-**42** with nitrobenzene (see Figure 4C in the main text) and strongly suggesting that such couplings proceed with retention of stereochemistry.

V. Complementarity of the Main Group C–N Coupling Method with Existing Methods

A. Preparation of Substrate 44

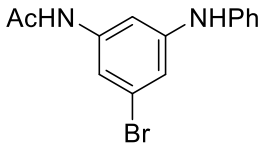
N-(3-bromo-5-nitrophenyl)acetamide **(44):**



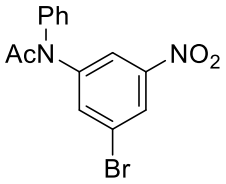
To a 40 mL screw cap scintillation vial fitted with a stir bar was added 3-bromo-5-nitroaniline (647 mg, 2.98 mmol, 1.00 equiv), 4-dimethylaminopyridine (6 mg, 0.05 mmol, 2 mol%), and chloroform (4 mL). Next, triethylamine (0.42 mL, 3.01 mmol, 1.01 equiv) was added via syringe and the reaction mixture was cooled to 0 °C while stirring. After addition of a septum screw cap, acetyl chloride (0.43 mL, 6.03 mmol, 2.02 equiv) was added slowly via syringe. The reaction was then warmed up to room temperature and allowed to stir for 2 hours, at which time TLC and GC/MS indicated consumption 3-bromo-5-nitroaniline. While cooling the reaction mixture in an ice bath, 5 mL of saturated sodium bicarbonate solution was added. The reaction mixture was transferred to a separatory funnel and dichloromethane was used to aid in the transfer of any remaining solids to the funnel. After mixing, the organic layer was separated and then the aqueous phase was extracted with dichloromethane several times until all visible solids were either dissolved in the organic layer or suspended in it. Ethyl acetate was then added to the dichloromethane organic layer until all solids had dissolved. The combined organics were dried over anhydrous sodium sulfate and concentrated. The resulting solid was slurried in hexanes and a small amount of ether, cooled to 0 °C, and filtered cold to give the product (713 mg, 2.75 mmol, 92%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.55 (s, 1H), 8.45 (t, J = 2.0 Hz, 1H), 8.17 (t, J = 1.8 Hz, 1H), 7.99 (t, J = 1.9 Hz, 1H), 2.09 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.31, 148.65, 141.45, 126.56, 121.87, 119.87, 112.19, 24.10. HRMS (ESI) calculated for $C_8H_8N_2O_3Br$ $[M+H]^+$: 258.9718, Found: 258.9706.

B. Procedures and Analytical Data for C–N Coupling Products from 44

***N-(3-bromo-5-(phenylamino)phenyl)acetamide* (45):**

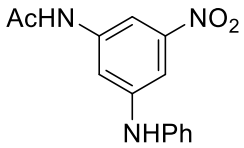


Following the general procedure using phenylboronic acid (67 mg, 0.55 mmol, 1.1 equiv) and *N*-(3-bromo-5-nitrophenyl)acetamide **44** (130 mg, 0.50 mmol, 1.0 equiv) for 4 h at 120 °C. The product was purified by column chromatography with 20% DCM/30% EA/50% Hex on silica (123 mg, 0.403 mmol, 81%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 (s, 1H), 7.28 (t, *J* = 7.9 Hz, 2H), 7.22 (s, 1H), 7.10 – 7.04 (m, 3H), 7.00 (t, *J* = 7.3 Hz, 1H), 6.91 (s, 1H), 5.79 (s, 1H), 2.12 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.80, 145.69, 141.59, 139.92, 129.59, 123.19, 122.57, 119.70, 114.90, 114.45, 106.72, 24.74.HRMS (ESI) calculated for $C_{14}H_{14}N_2OBr$ $[M+H]^+$: 305.0288, Found: 305.0289.



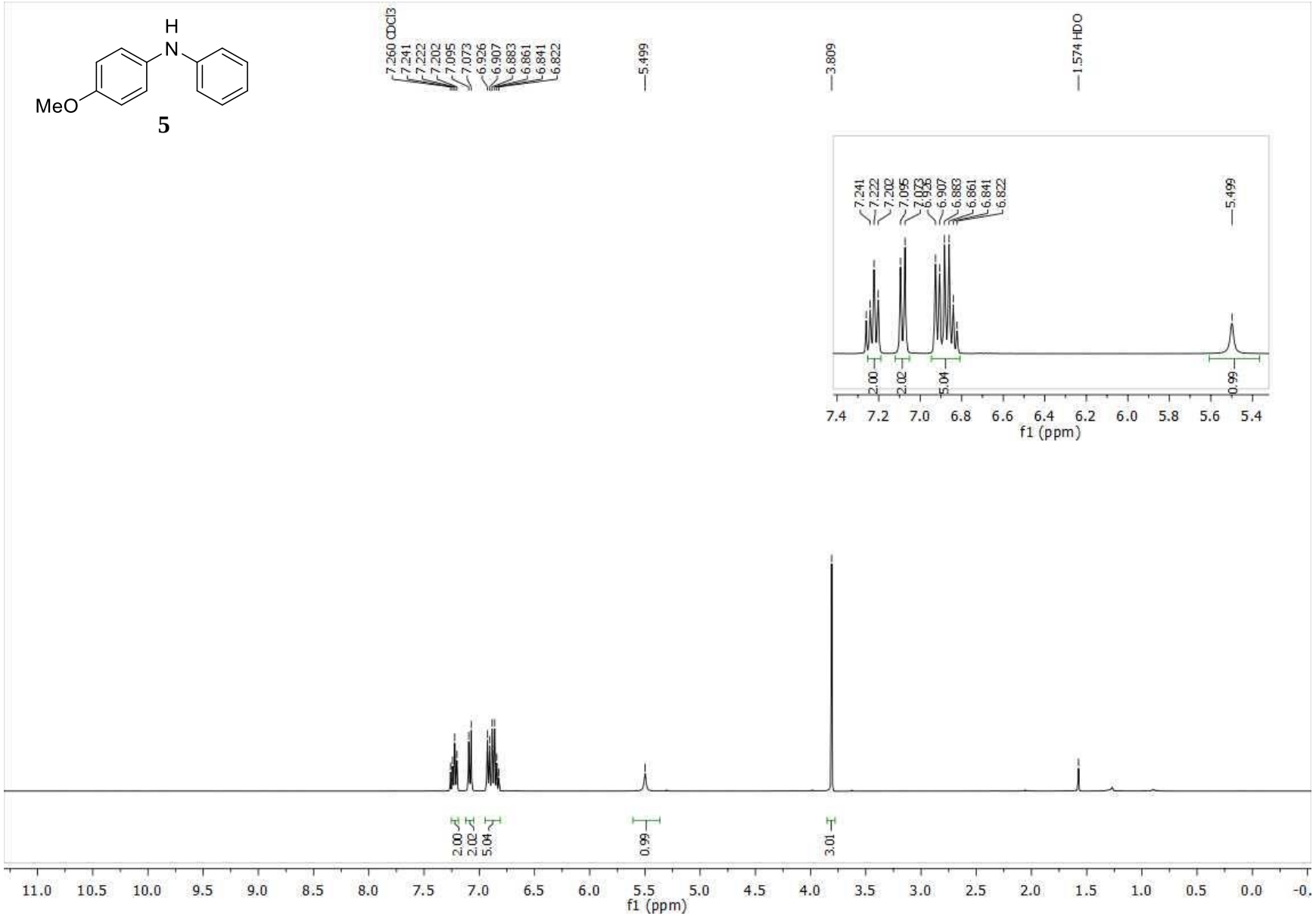
***N-(3-bromo-5-nitrophenyl)-N-phenylacetamide* (46)** was synthesized via a Cham-Lam coupling procedure adapted from the literature.[18] To a glass culture tube equipped with a stir bar was charged **44** (77.7 mg, 0.300 mmol, 1.00 equiv), $Cu(OAc)_2$ (54.5 mg, 0.300 mmol, 1.00 equiv), phenylboronic acid (73.1 mg, 0.600 mmol, 2.00 equiv), and activated 4Å molecular sieves. The tube was then charged with 2.0 mL of ethyl acetate and triethylamine (85 µL, 0.610 mmol., 2.03 equiv) via microsyringe. A phenolic screw-thread open top cap and PTFE-lined silicone septum were added and the tube was stirred and heated at room temperature for 8 hours. At this time, additional reagents were added to the reaction mixture ($Cu(OAc)_2$ (54.5 mg, 0.300 mmol, 1.00 equiv); triethylamine (200 µL, 1.43 mmol., 4.78 equiv); phenylboronic acid (73.1 mg, 0.600 mmol, 2.00 equiv)) and stirring was continued at room temperature for 22 hours. At this time, additional reagents were added to the reaction mixture (same amounts as at 8 hours) and it was heated to 60 °C for 12 hours. The reaction mixture was then absorbed onto silica gel (1.5 g) and purified by silica gel chromatography (5% EA/ 5% DCM in Hex gradient to 10% EA/ 10% DCM in Hex) to isolate the desired product (52.5 mg, 0.157 mmol, 52%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.16 (s, 1H), 8.04 (t, *J* = 1.9 Hz, 1H), 7.81 (t, *J* = 1.9 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 2H), 7.45 (t, *J* = 7.4 Hz, 1H), 7.28 (d, *J* = 7.1 Hz, 2H), 2.07 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 170.72, 148.91, 144.61, 141.69,

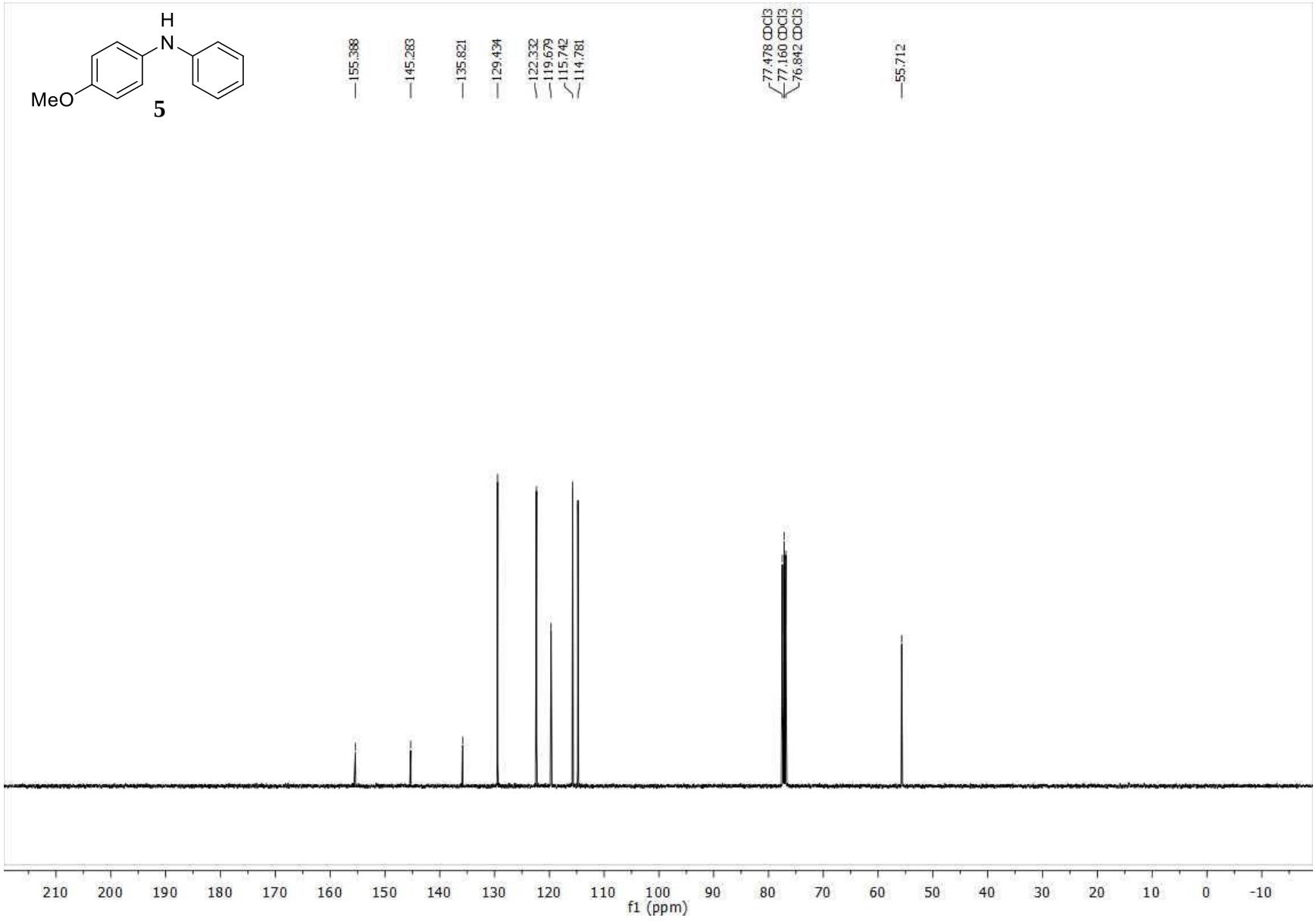
134.58, 130.63, 129.14, 128.71, 123.74, 122.68, 119.68, 24.21. IR (Diamond-ATR, neat): 3122, 3088, 3054, 2851, 1674, 1593, 1569, 1522, 1490, 1449, 1421, 1363, 1336, 1320, 1310, 1292, 1273, 1241, 1204, 1174, 1116, 1078, 1030, 1004, 953, 930, 897, 866, 775, 734, 702, 667, 650, 626, 601, 592 cm^{-1}. HRMS (ESI) calculated for $C_{14}H_{12}N_2O_3Br$ $[M+H]^+$: 335.0031, Found: 335.0018.



N-(3-nitro-5-(phenylamino)phenyl)acetamide **(47)** was synthesized via a Buchwald-Hartwig procedure adapted from the literature.[19] A glass culture tube was equipped with a stir bar and charged with **44** (130 mg, 0.50 mmol, 1.0 equiv), *tert*-BuBrettPhos (4.8 mg, 0.01 mmol, 2 mol%) *tert*-BuBrettPhos Pd G3 (8.5 mg, 0.01 mmol, 2 mol%), and K_2CO_3 (96.7 mg, 0.70 mmol**,** 1.4 equiv). The tube was sealed, then evacuated and backfilled with N_2 three times. The vessel was then charged with 1 mL of *t*-BuOH (previously dried over 4Å molecular sieves), followed by addition of aniline (64 µL, 0.70 mmol, 1.4 equiv). The reaction was heated at 110 ˚C and reaction progress was monitored by silica TLC. After 12 hours significant amounts of starting material were still seen, so the reaction mixture was allowed to cool to room temperature and taken inside of the glovebox, where an additional 1 mol % of *tert*-BuBrettPhos Pd G3 and 1 equivalent of K_2CO_3 were added without exposing the reaction mixture to O_2. Once the addition was complete, the reaction mixture was removed from the glovebox and charged with an additional 1 mL of *t*-BuOH . The reaction mixture was then heated at 110 ˚C for an additional 6 hours, after which TLC showed complete consumption of starting material. The reaction mixture was then allowed to cool to room temperature, diluted with EtOAc (~ 10 mL) and poured into a 60 mL separatory funnel containing ~20 mL of H_2O used to wash the organic layer. The organic layer was separated and the aqueous was extracted one additional time with EtOAc. The organics were combined and washed with brine, dried with Na_2SO_4, filtered and concentrated in vacuo. The reaction mixture was then absorbed onto silica gel (~4 g) using ethyl acetate and purified by silica gel chromatography (10% DCM/ 40% EA/ 50% Hexane) to give the desired product as a red solid (96.6 mg, 0.356 mmol, 71%). ^{1}H NMR (500 MHz, Acetone-*d*6) δ 9.45 (s, 1H), 8.01 (s, 1H), 7.95 (s, 1H), 7.79 (s, 1H), 7.57 (s, 1H), 7.35 (t, *J* = 7.7 Hz, 2H), 7.23 (d, *J* = 8.1 Hz, 2H), 7.02 (t, *J* = 7.3 Hz, 1H), 2.10 (s, 3H). ^{13}C NMR (101 MHz, Acetone-*d*6) δ 169.45, 150.40, 146.86, 142.67, 142.13, 130.28, 123.13, 120.37, 111.51, 105.32, 105.20, 24.35. IR (Diamond-ATR, neat): 3387, 3316, 3107, 1680, 1623, 1589, 1551, 1518, 1495, 1445, 1393, 1365, 1330, 1290 1260, 1233, 1174, 1155, 1007, 992, 984, 956, 938, 909, 871, 852, 831, 800, 756, 744 cm^{-1}. HRMS (ESI) calculated for $C_{14}H_{14}N_3O_3$ $[M+H]^+$: 272.1035, Found: 272.1028.

VI. ^{1}H and ^{13}C NMR Spectra for C–N Coupling Products

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135.821
129.434
122.332
119.679
115.742
114.781
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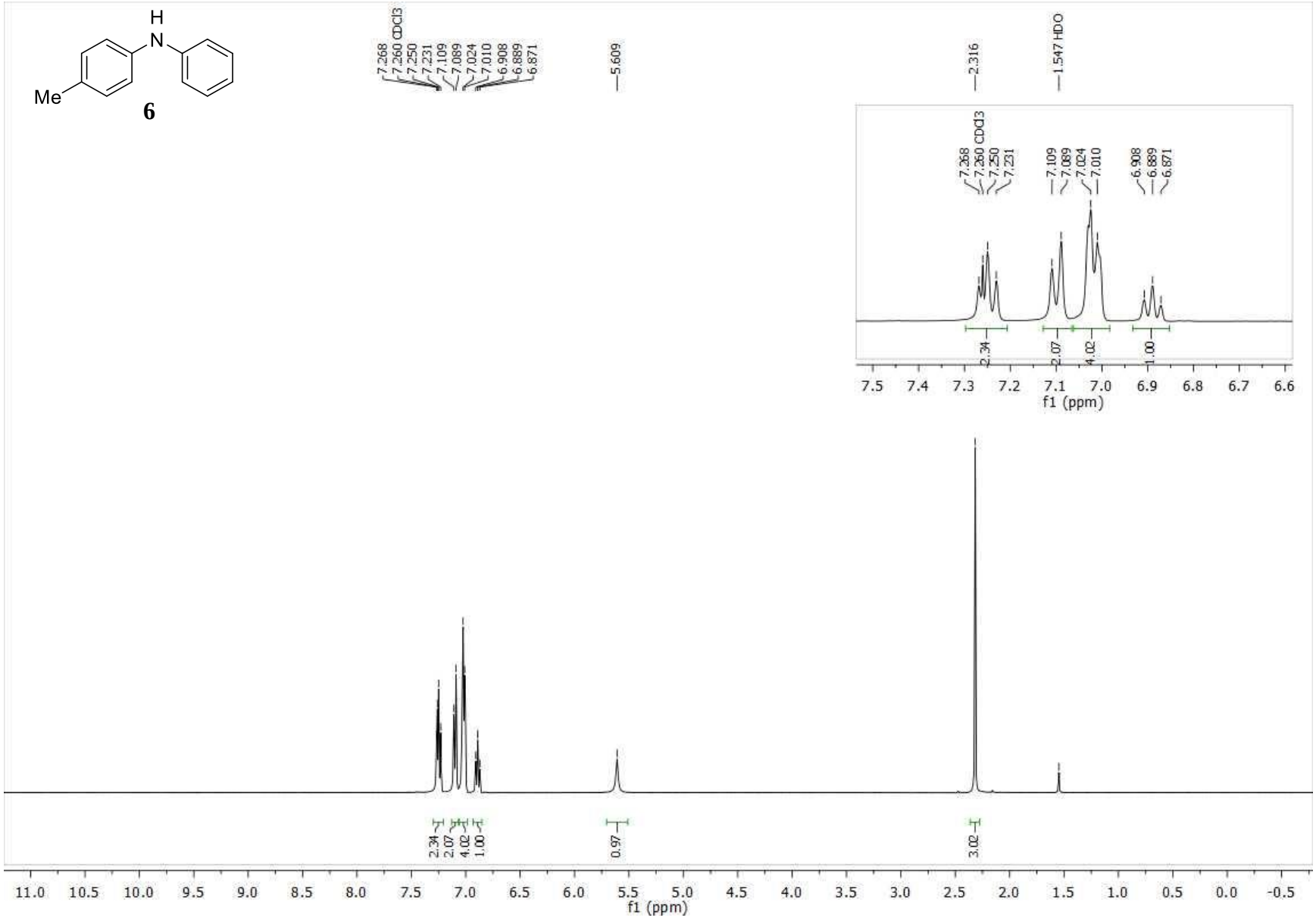
77.160 CDCl3
76.842 CDCl3
55.712
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.109
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7.024
7.010
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6.889
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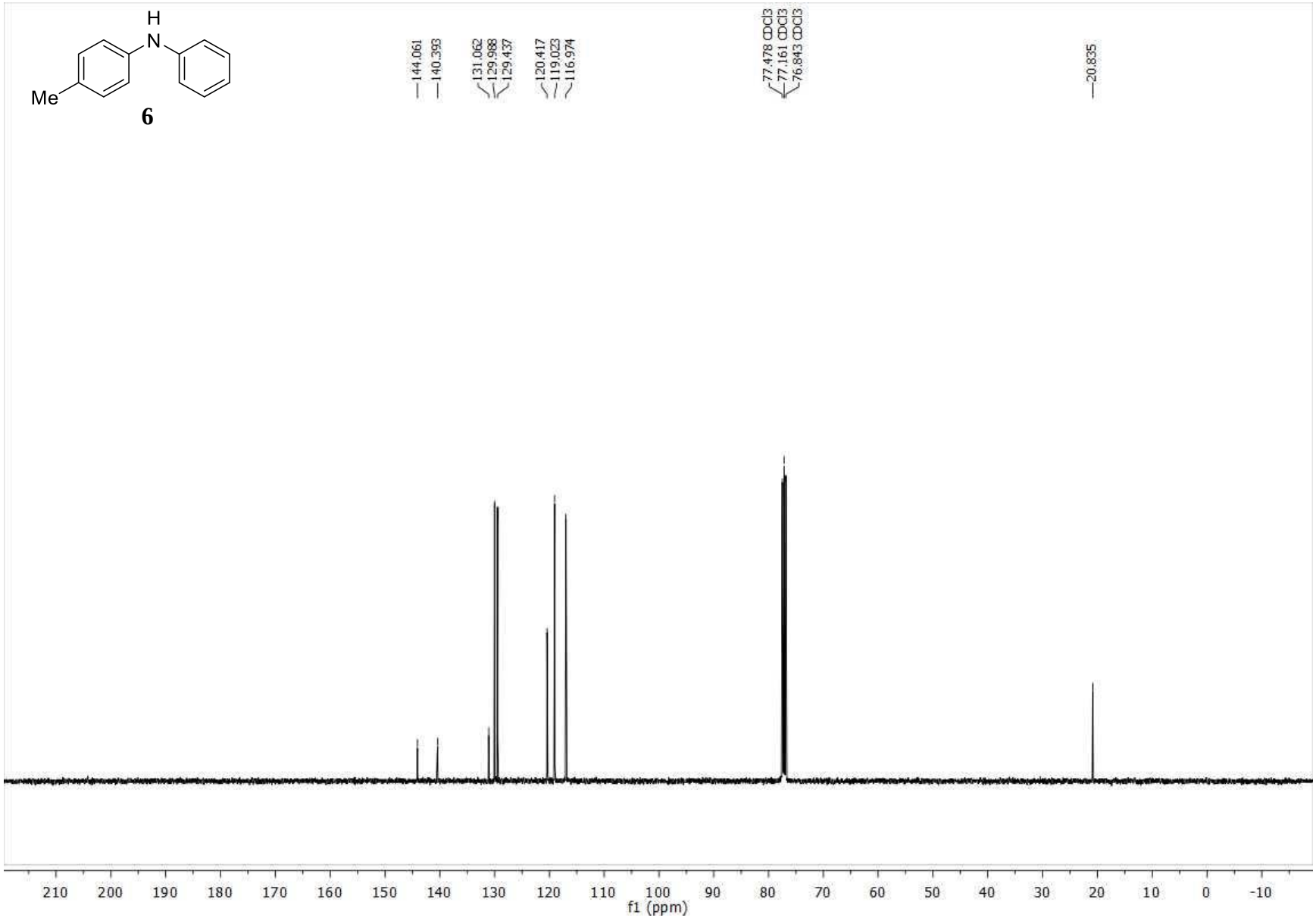
3.02
f1 (ppm)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20.835
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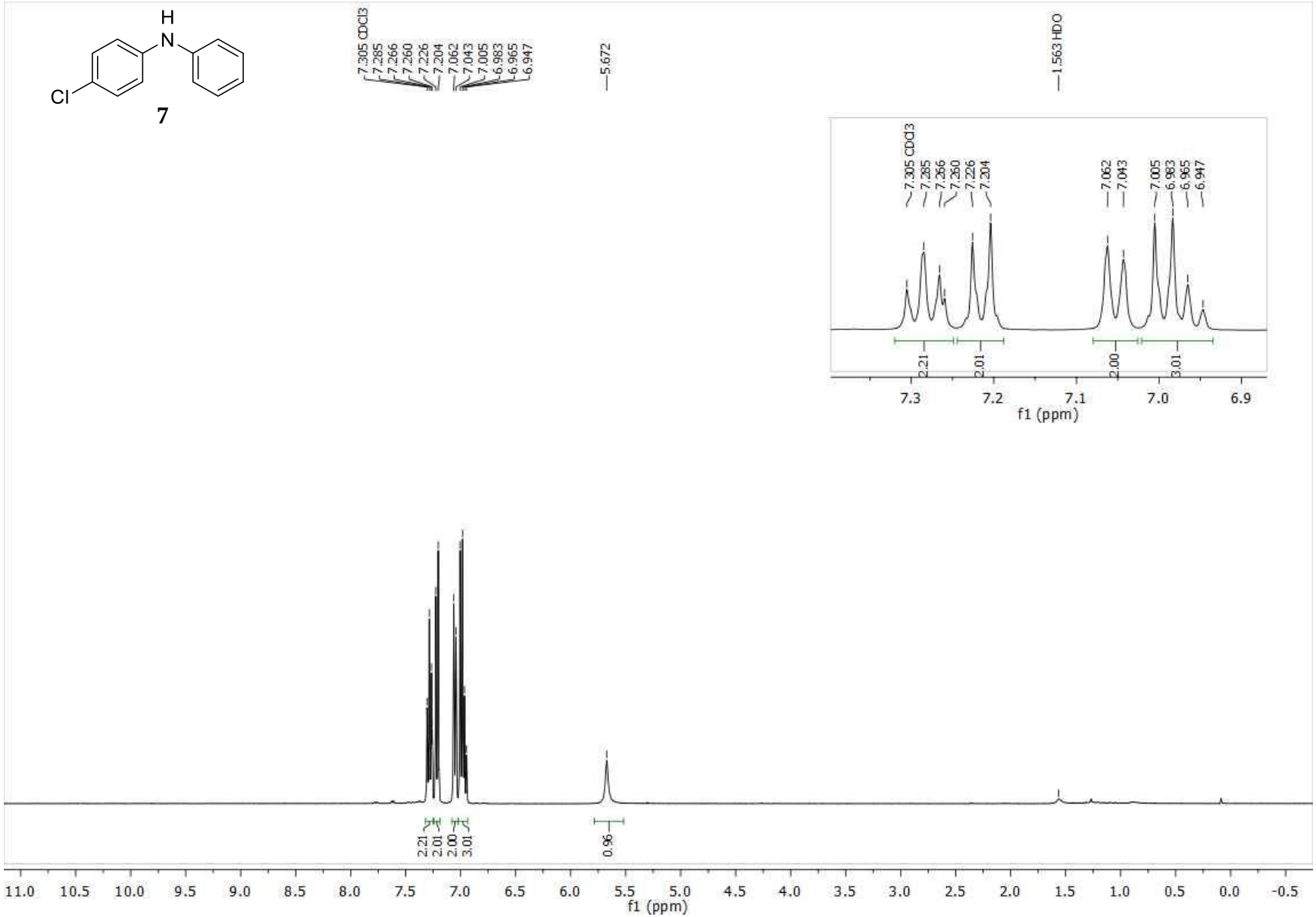
f1 (ppm)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7.062
7.043
7.005
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2.00
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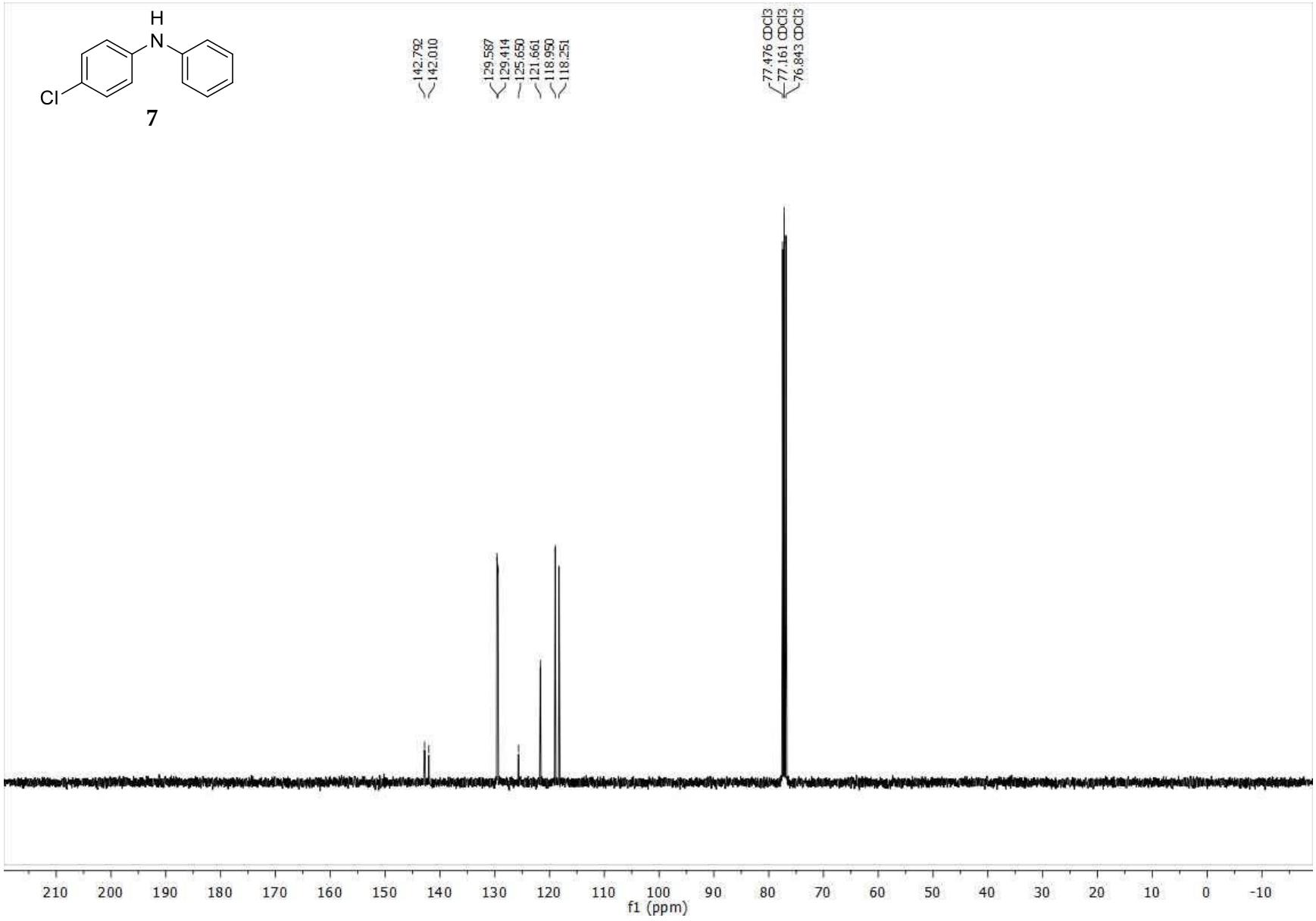
f1 (ppm)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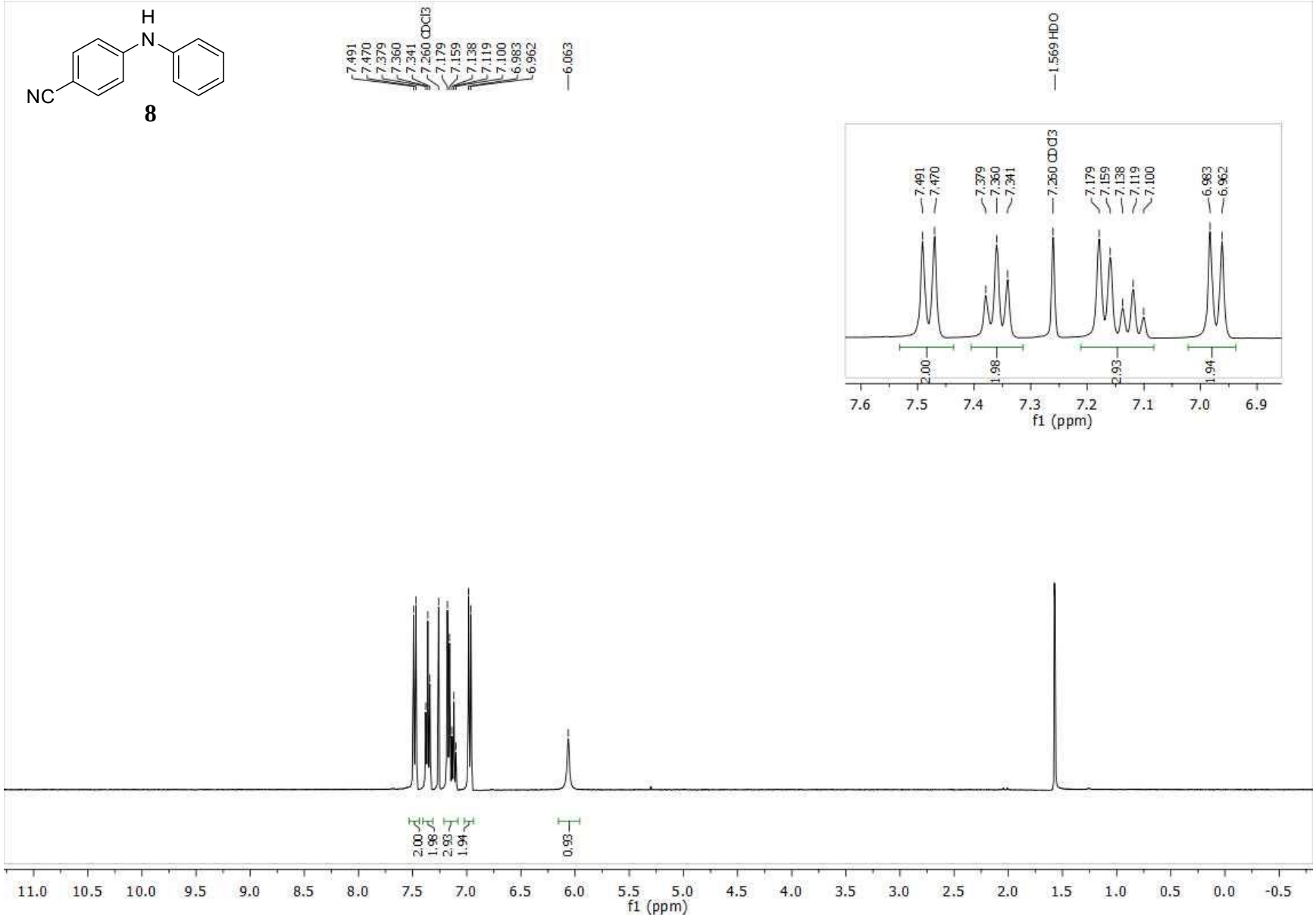
77.161 CDCl3
76.843 CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.119
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6.063
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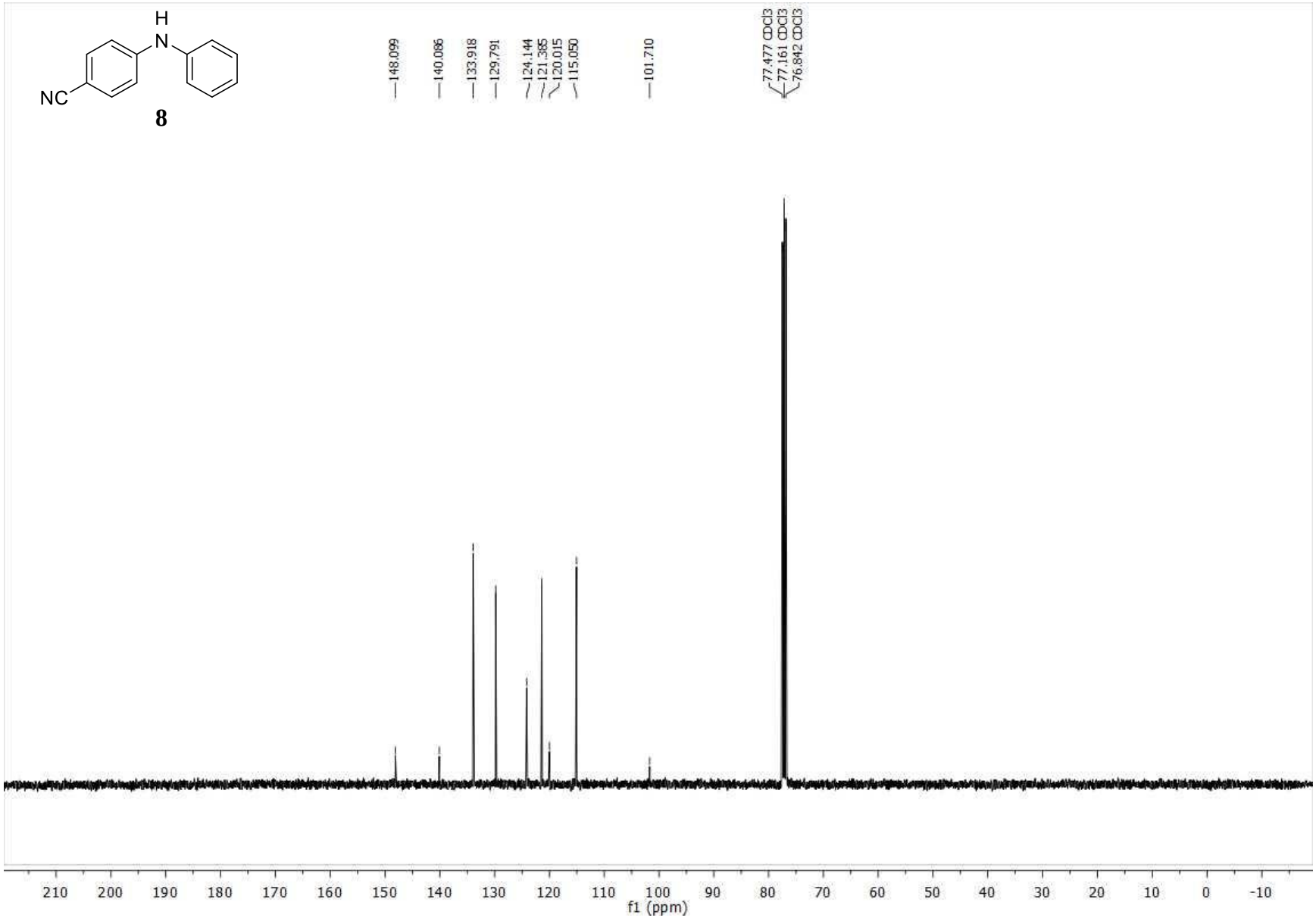
f1 (ppm)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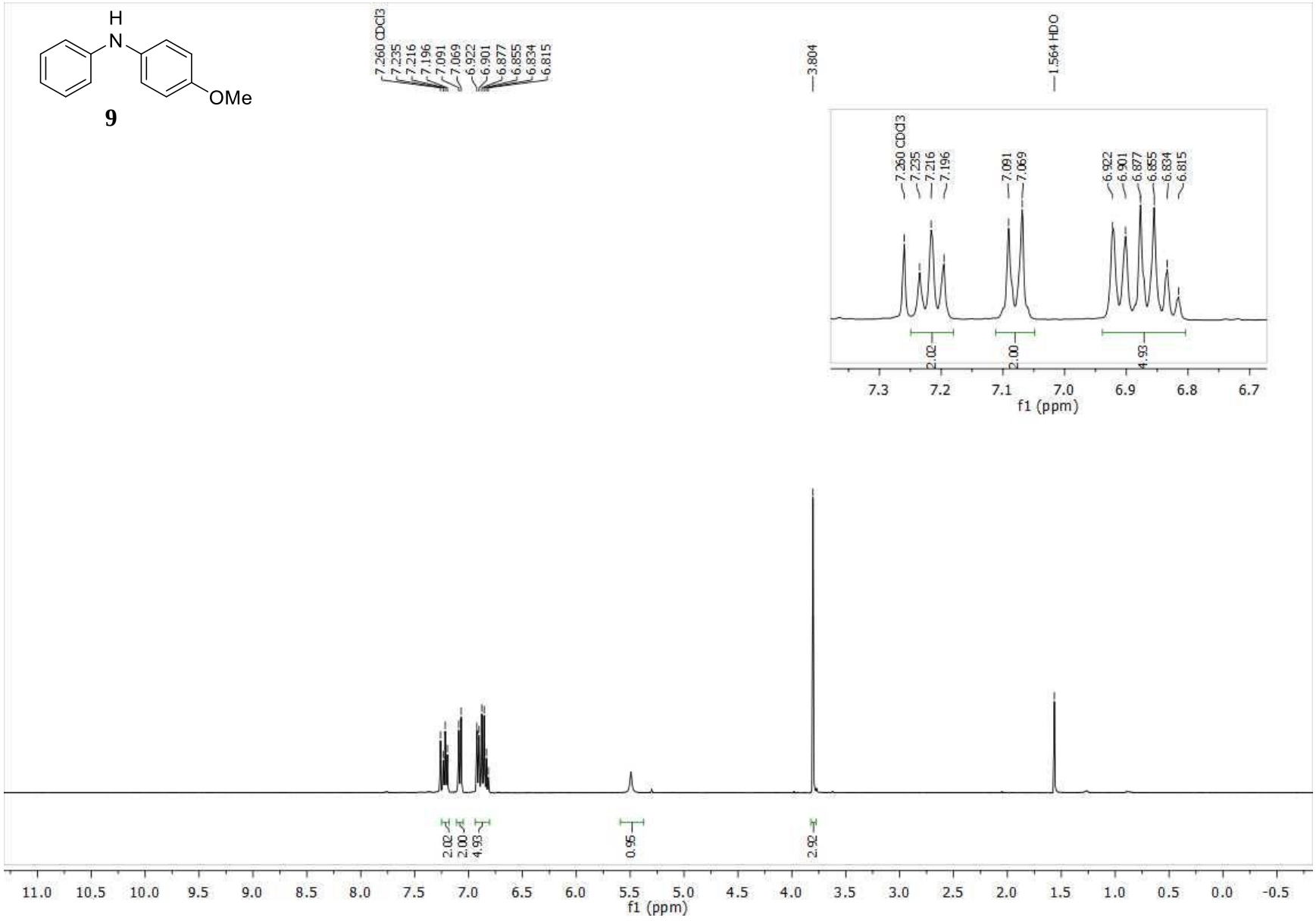
f1 (ppm)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6.877
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6.815
3.804
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2.00
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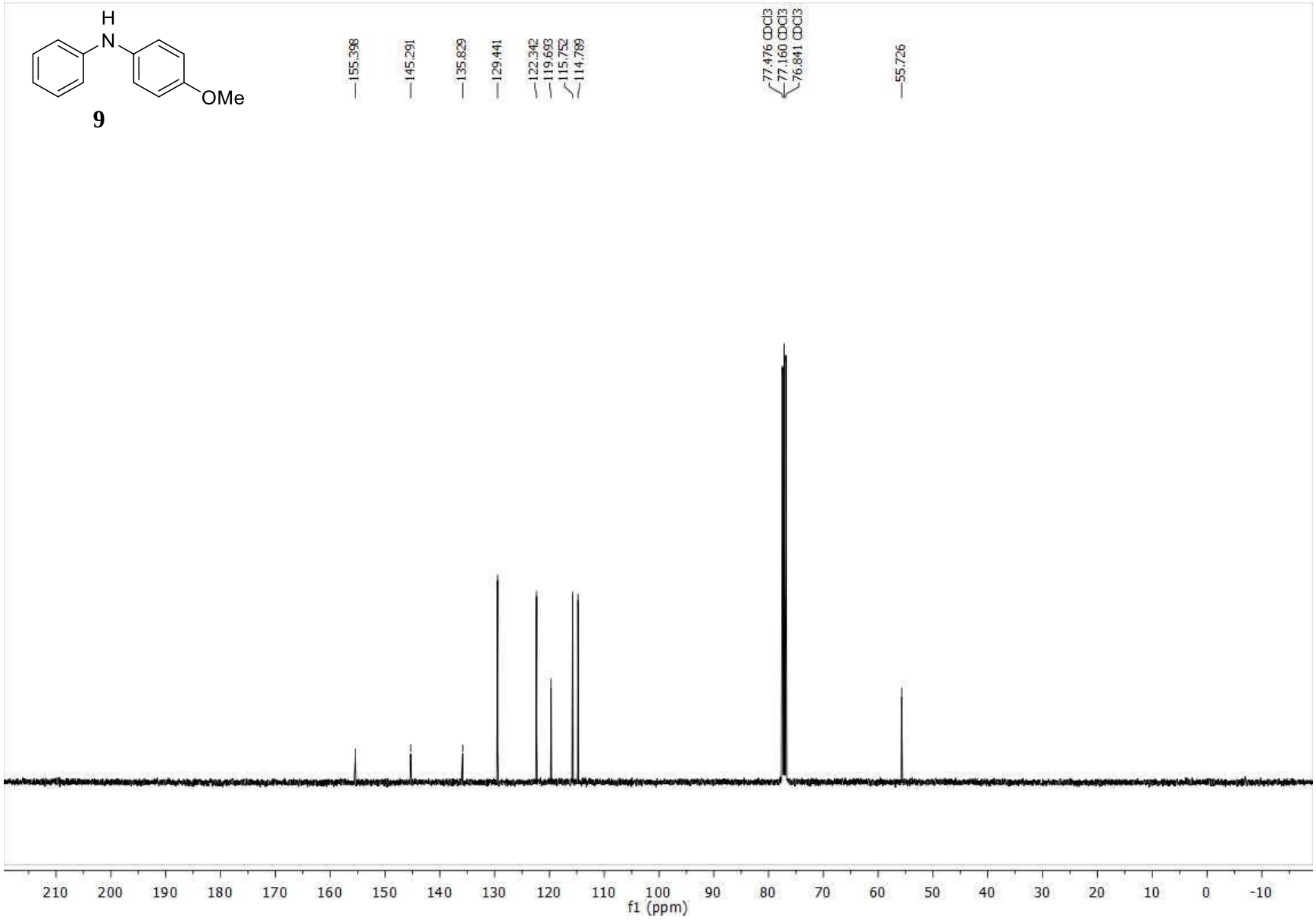
2.92
f1 (ppm)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114.789
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76.841 CDCl3
55.726
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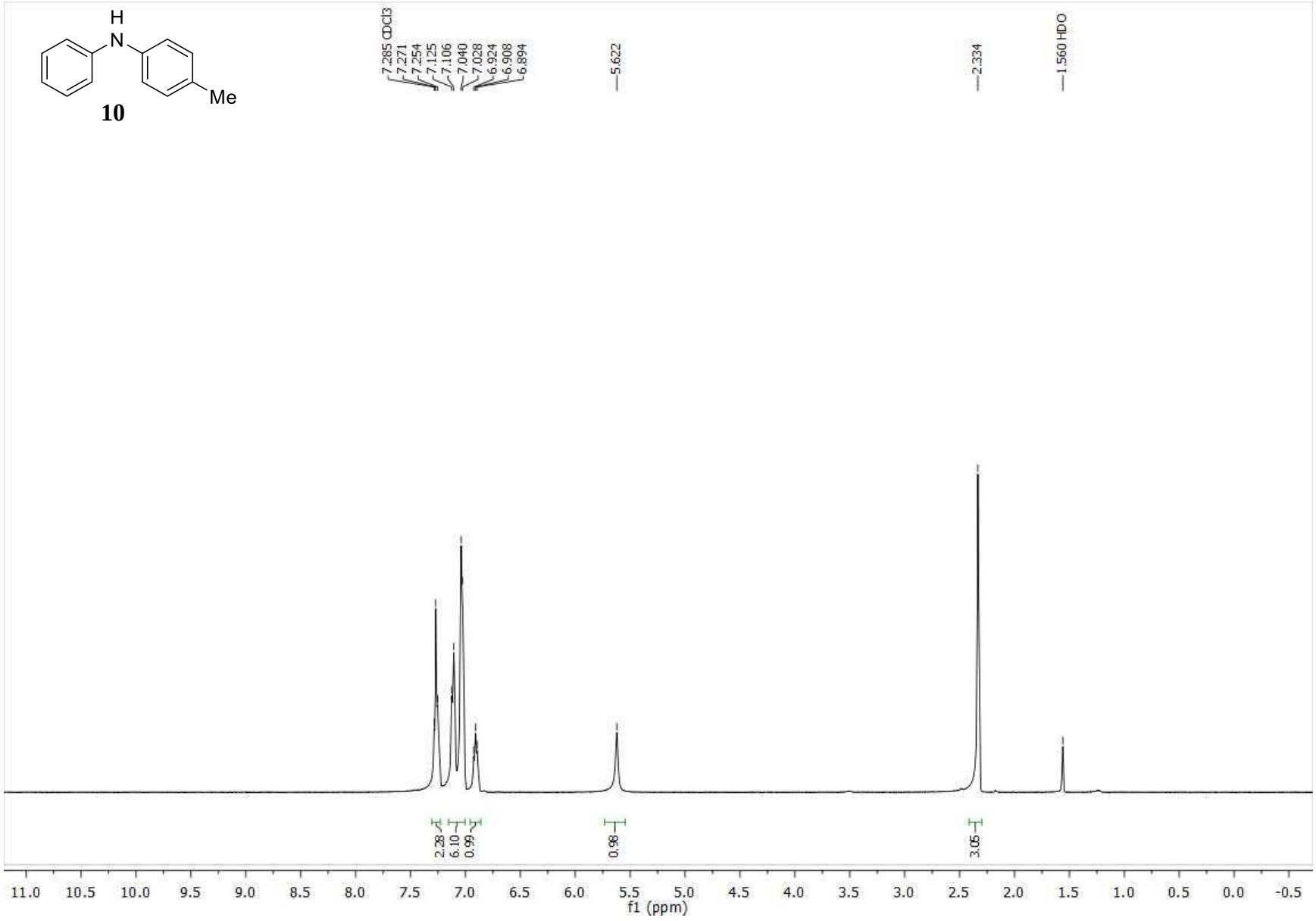
f1 (ppm)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5.622
2.334
1.560 HDO
2.28
6.10
0.99
0.98
3.05
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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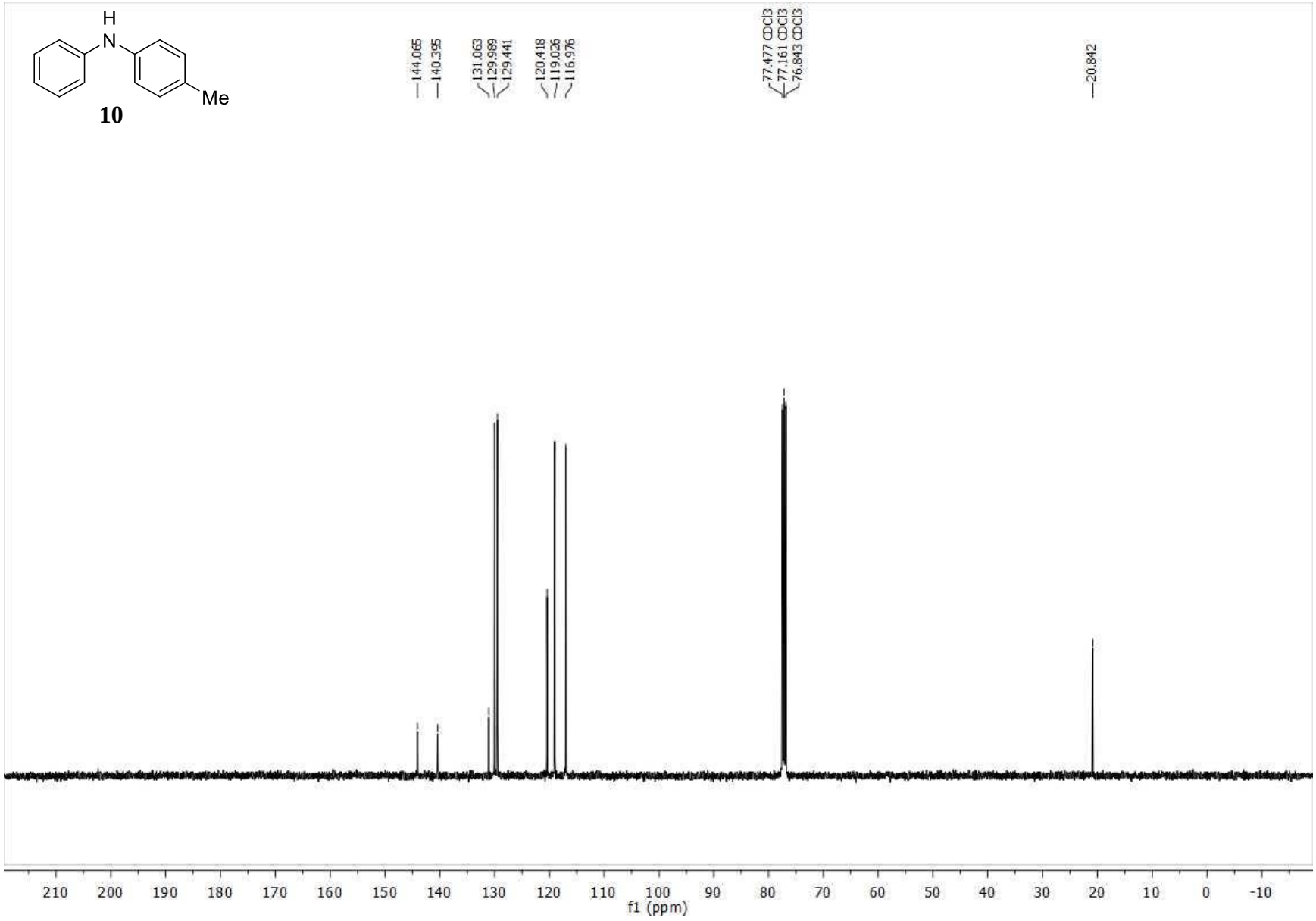
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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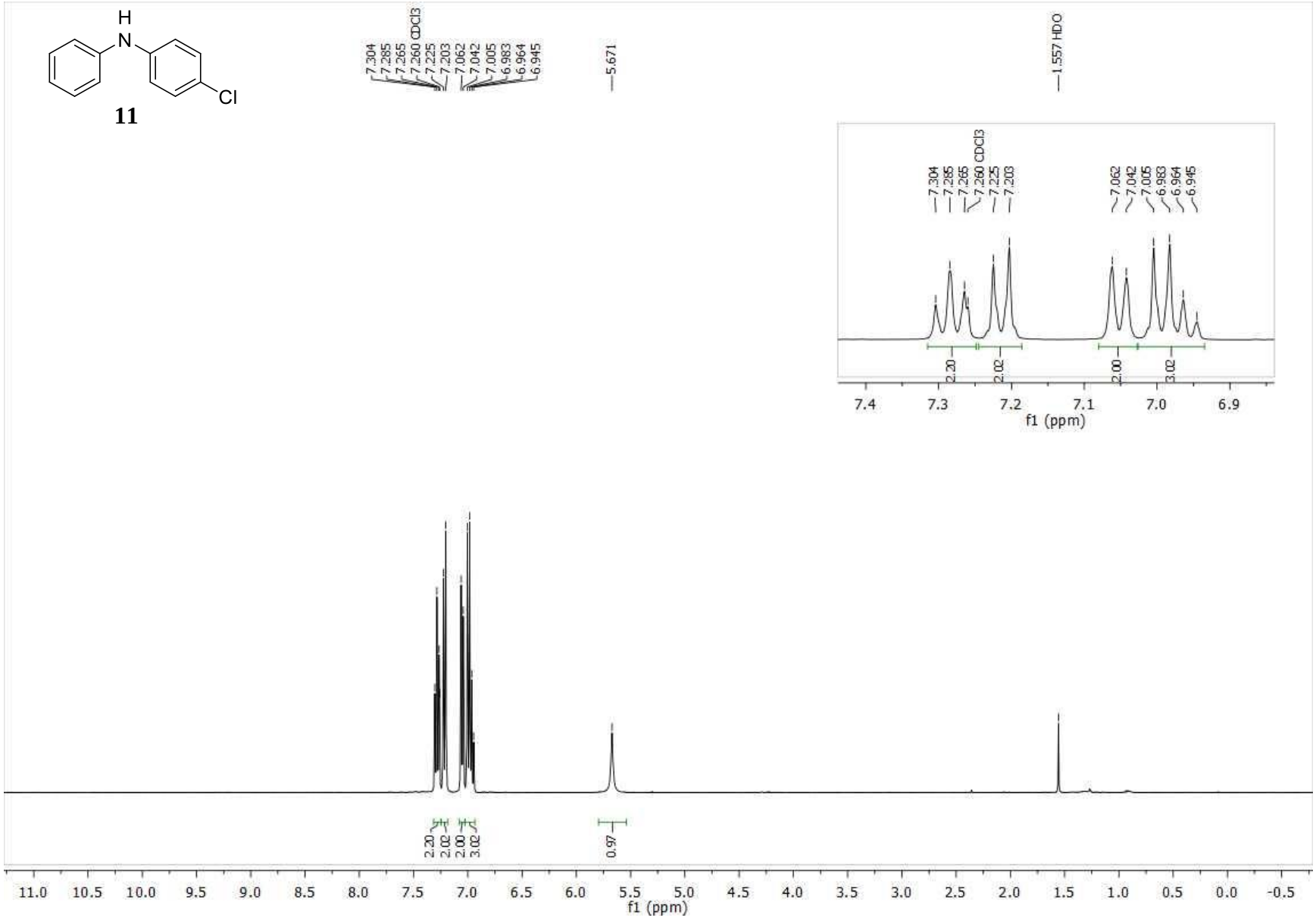
f1 (ppm)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2.00
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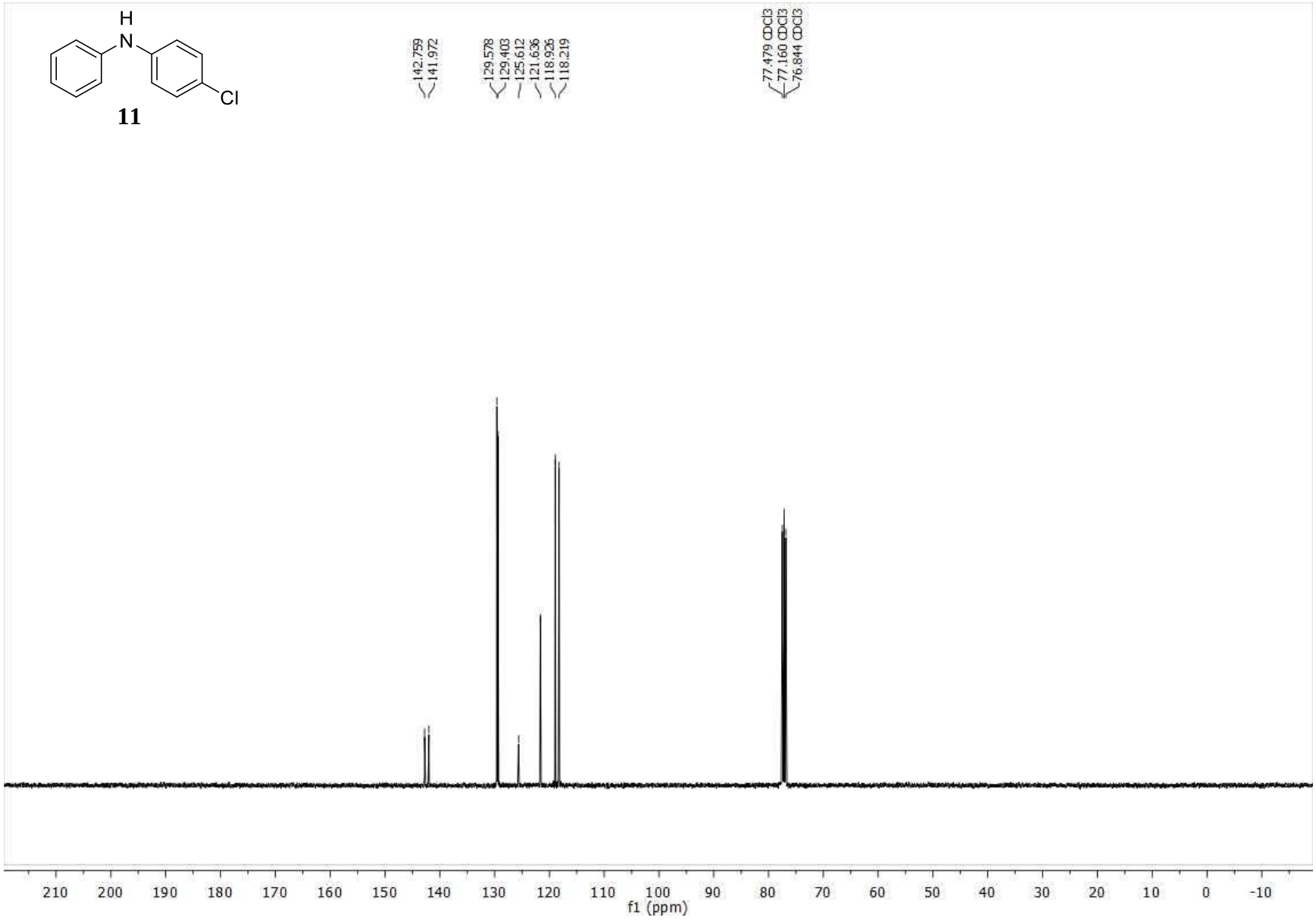
f1 (ppm)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76.844 CDCl3
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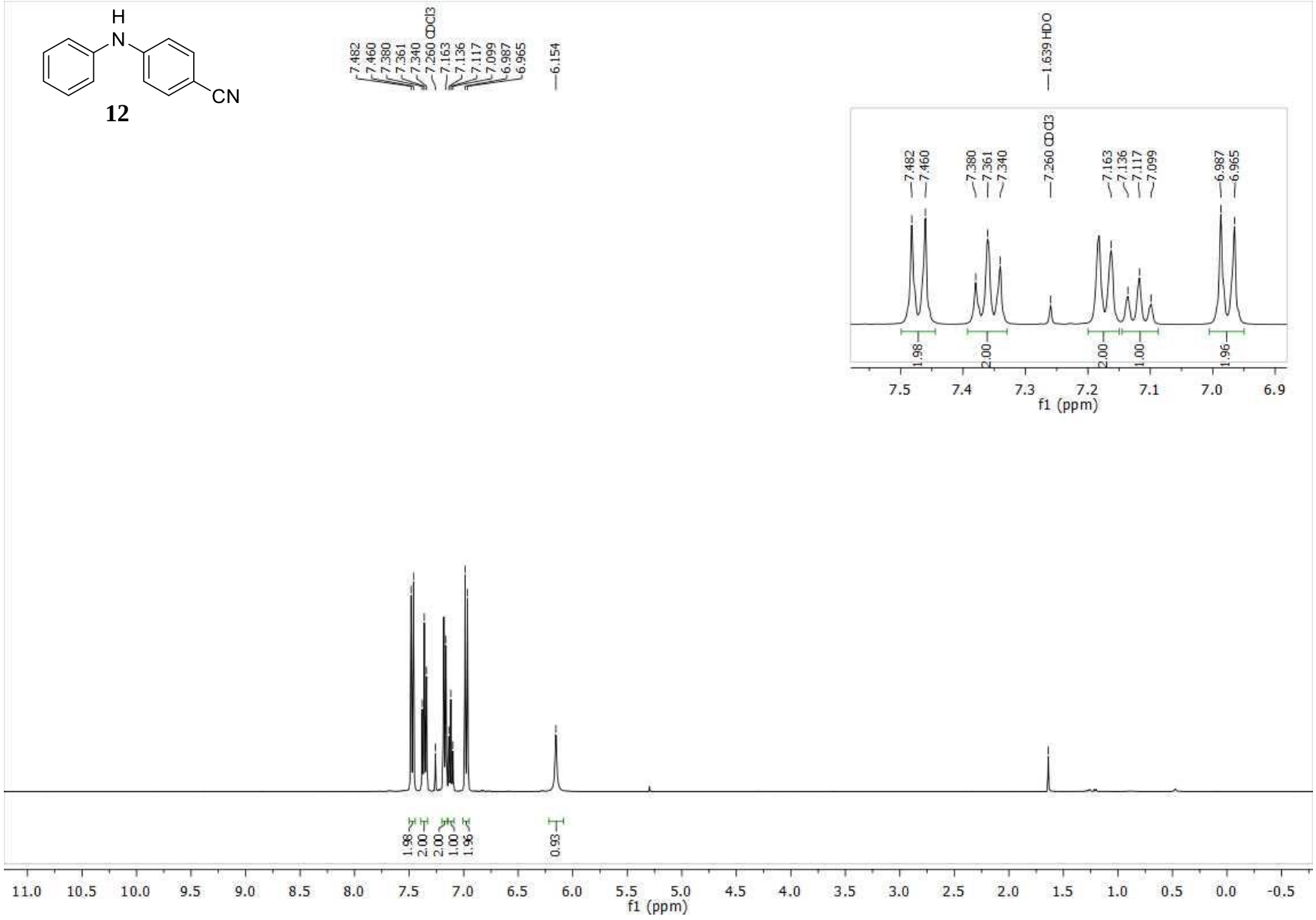
f1 (ppm)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2.00
1.00
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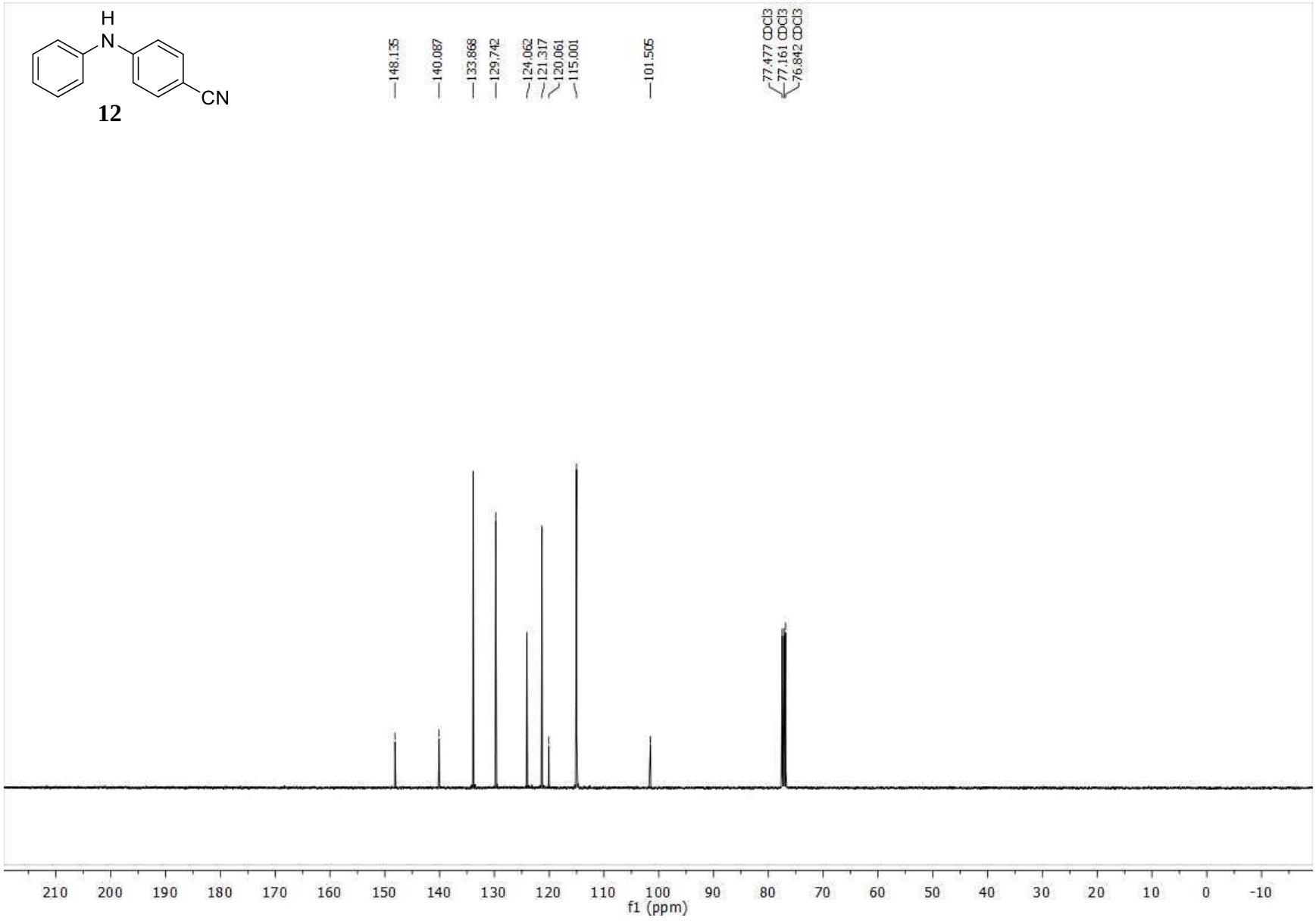
f1 (ppm)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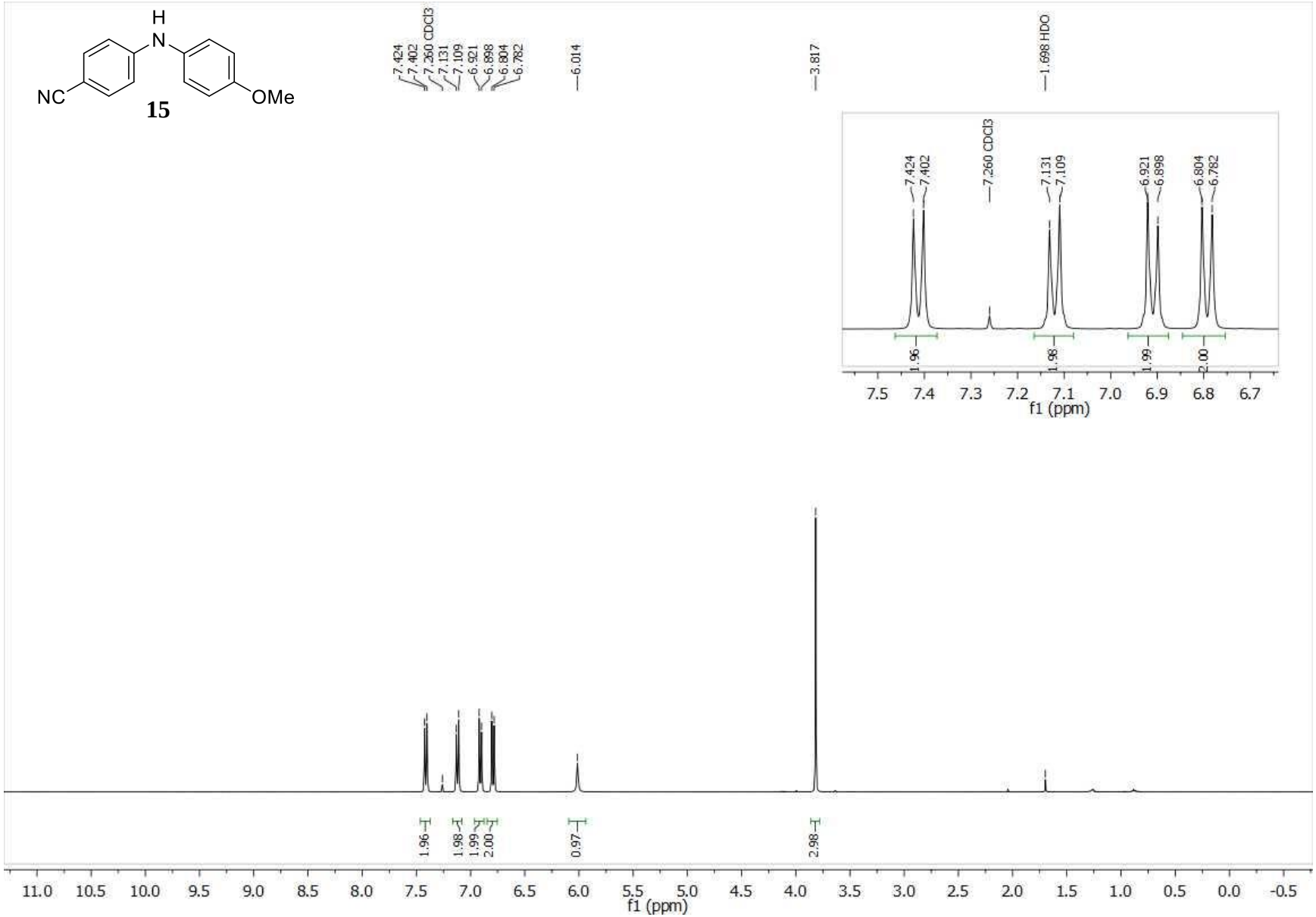
f1 (ppm)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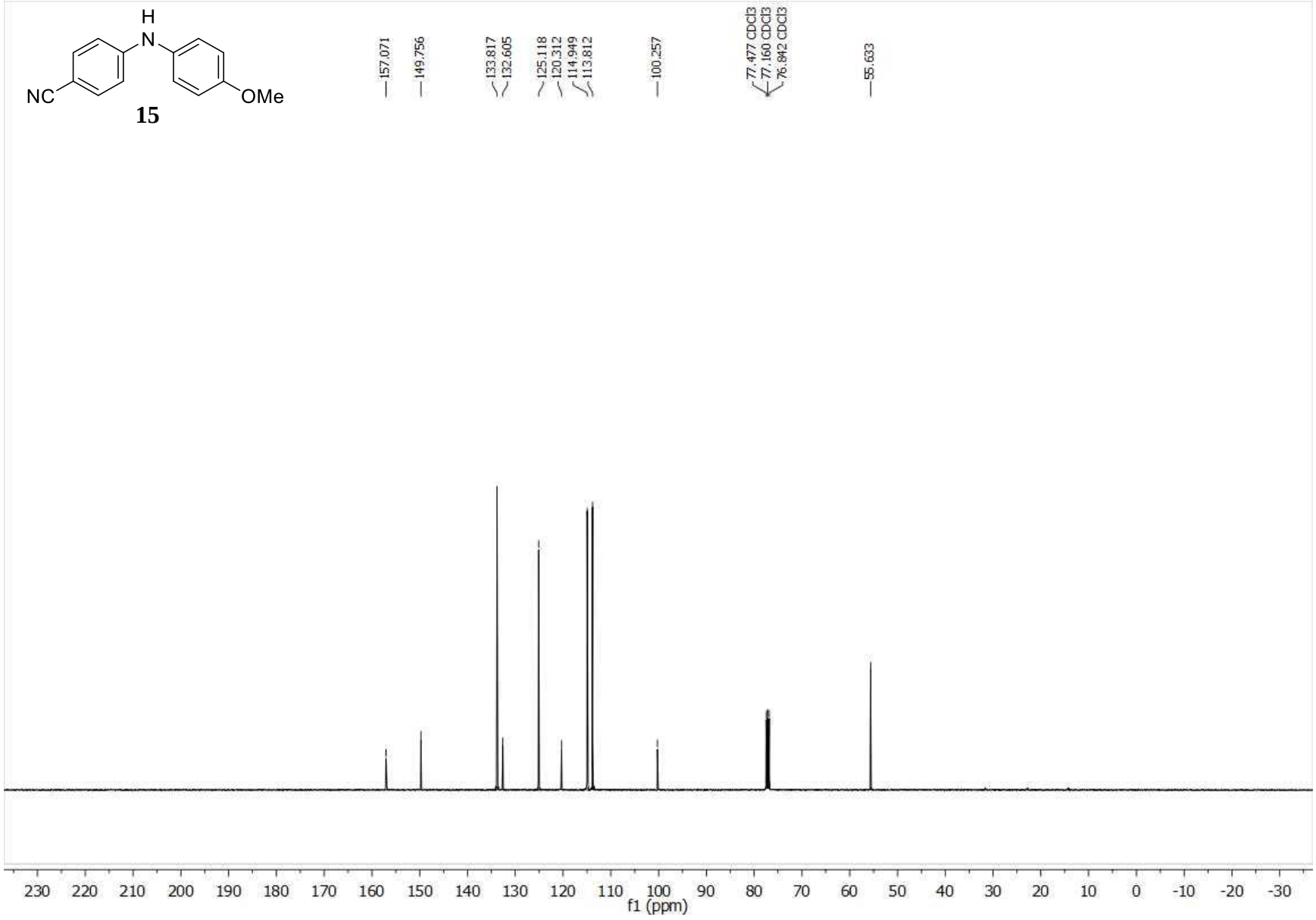
f1 (ppm)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100.257
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55.633
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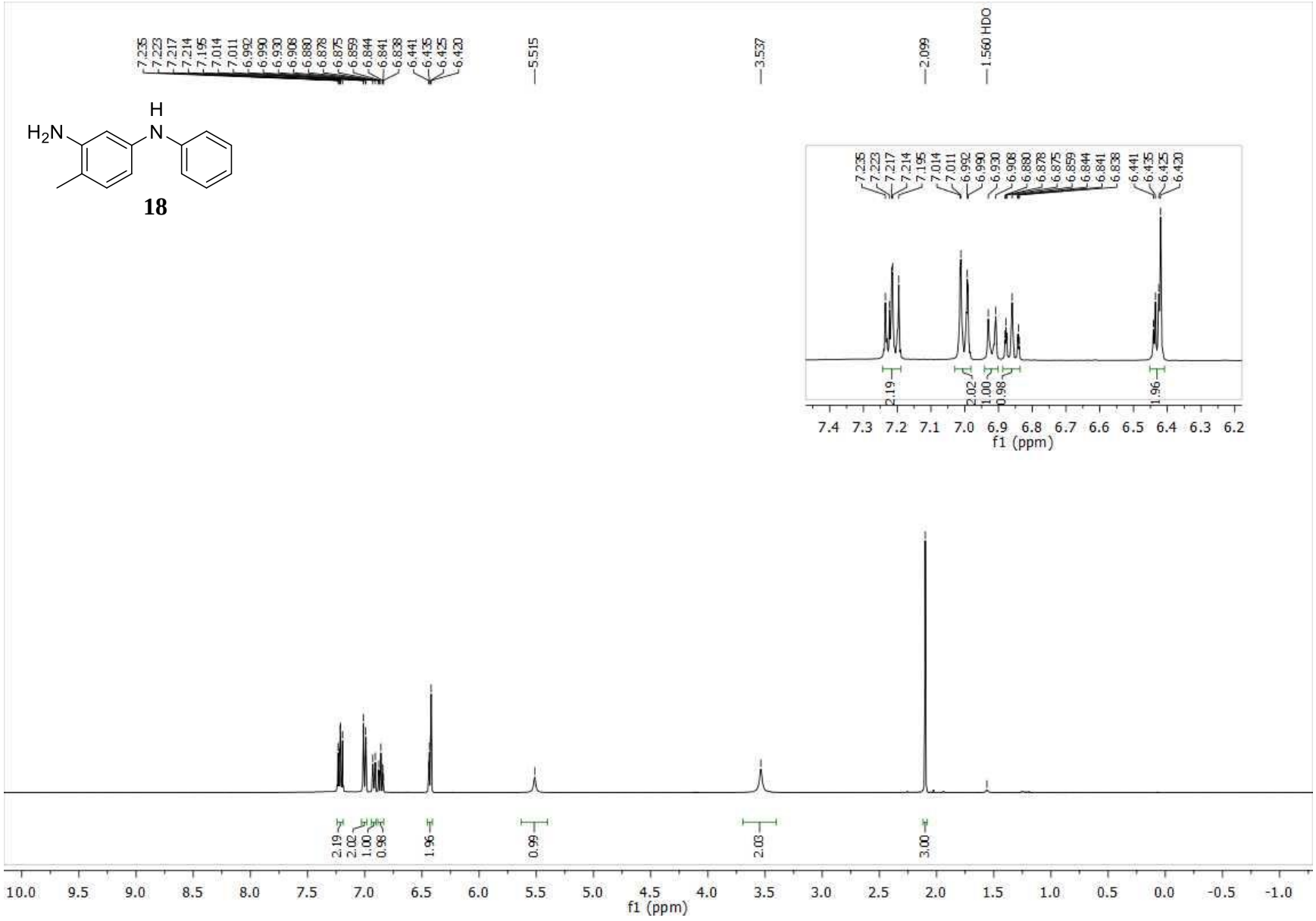
f1 (ppm)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6.859
6.844
6.841
6.838
6.441
6.435
6.425
6.420
5.515
3.537
2.099
1.560 HDO
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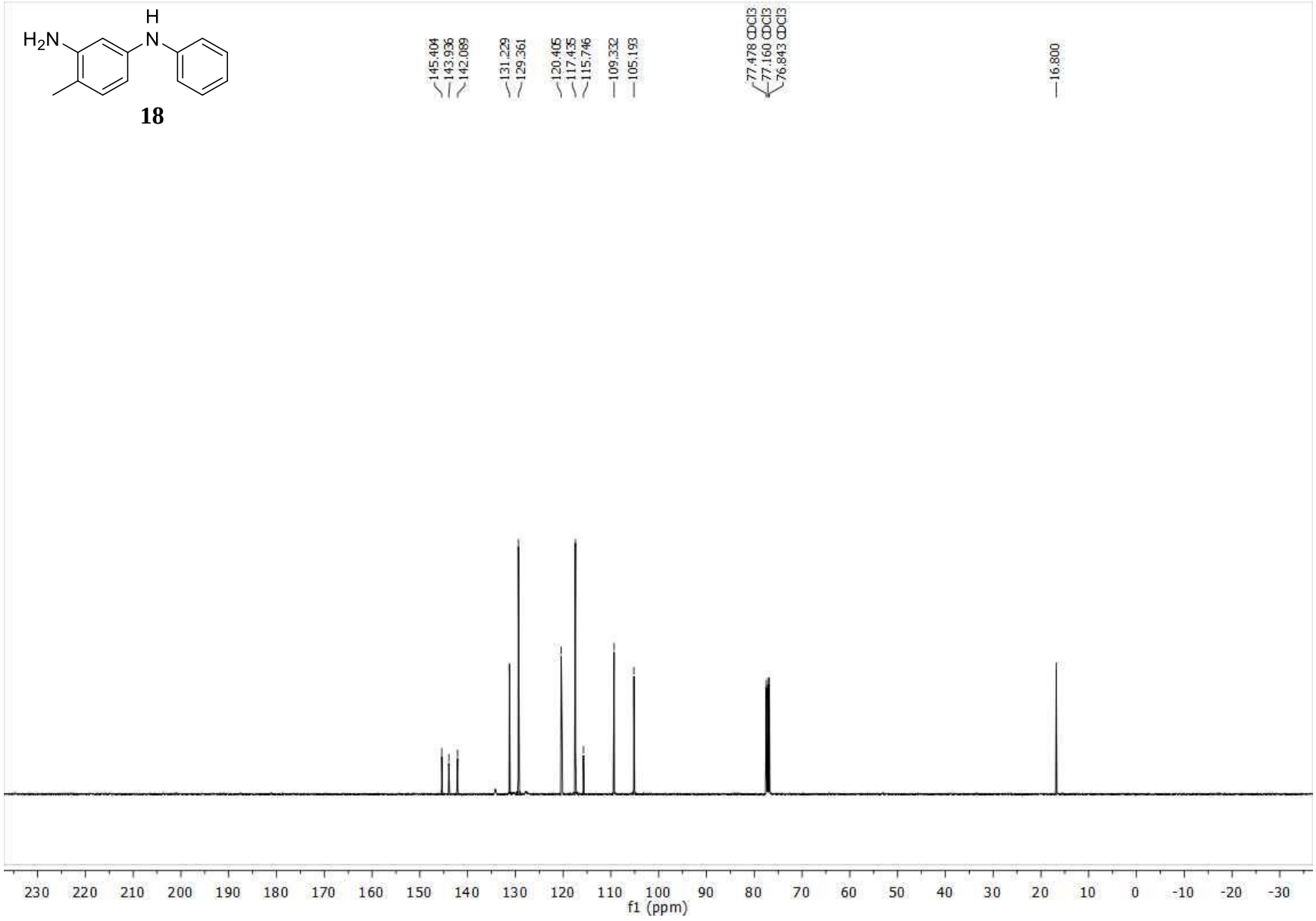
3.00
f1 (ppm)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105.193
77.478 CDCl3
77.160 CDCl3
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16.800
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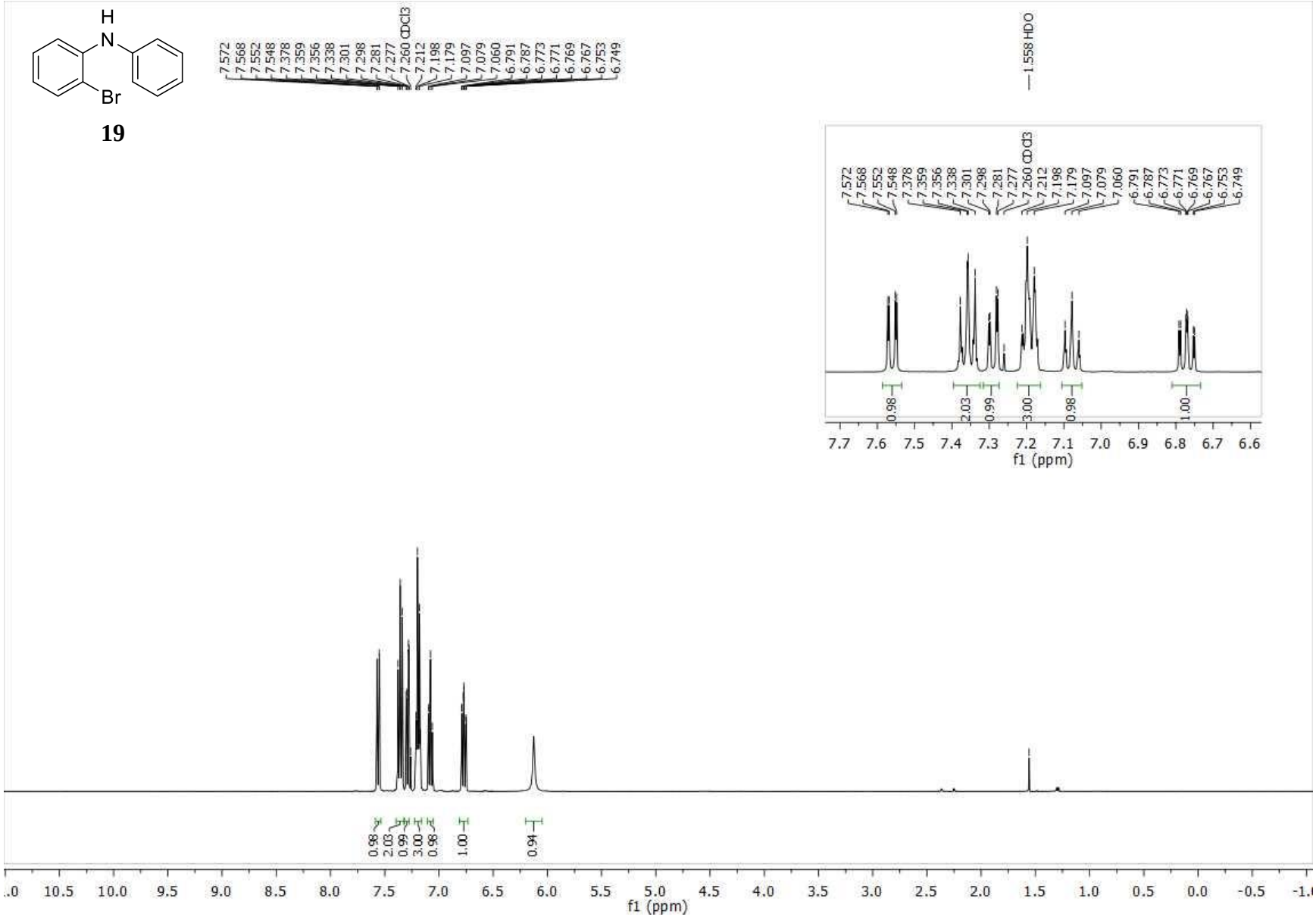
f1 (ppm)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7.277
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7.198
7.179
7.097
7.079
7.060
6.791
6.787
6.773
6.771
6.769
6.767
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0.98
1.00
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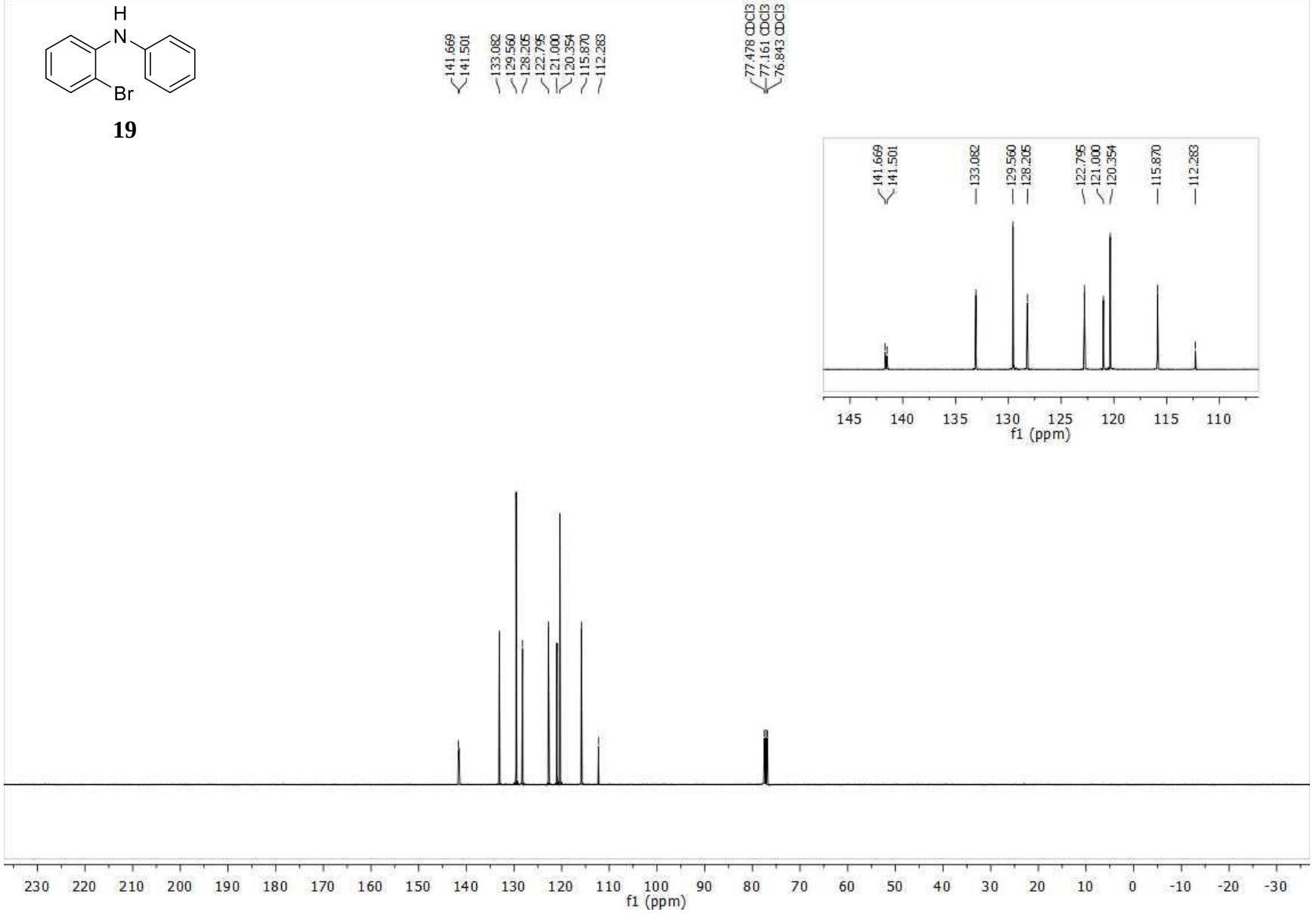
f1 (ppm)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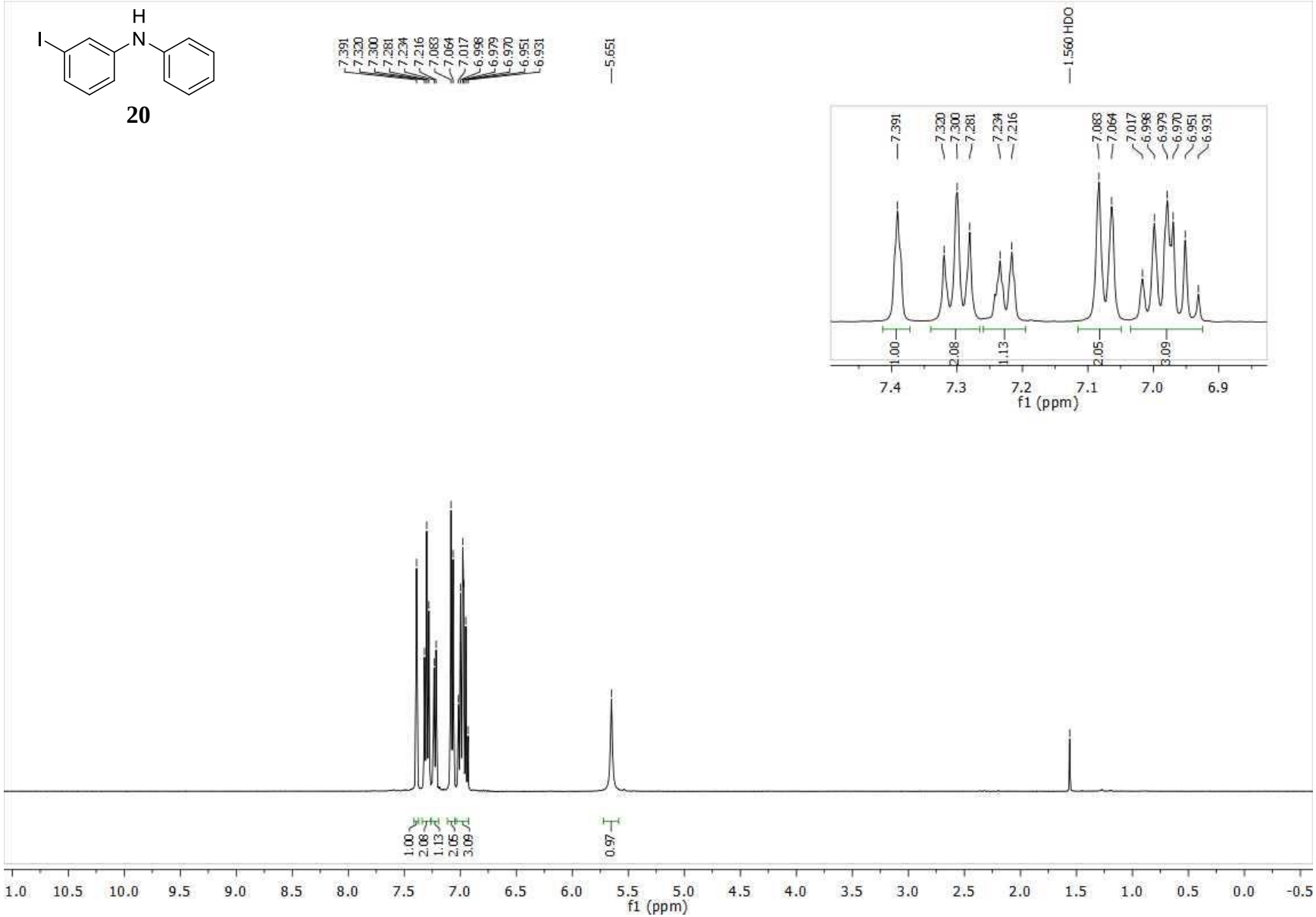
77.161 CDCl3
76.843 CDCl3
f1 (ppm)
f1 (ppm)

19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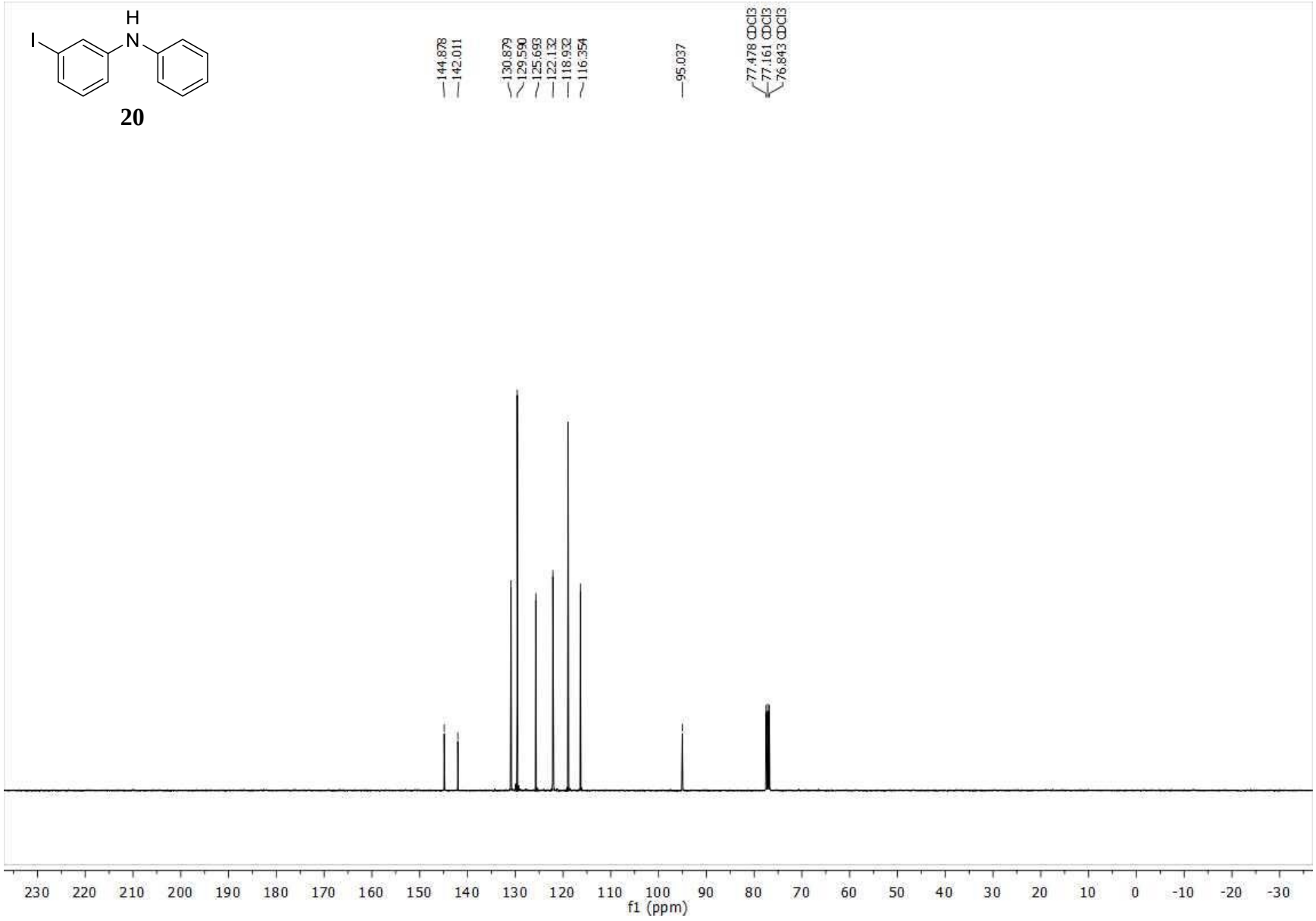
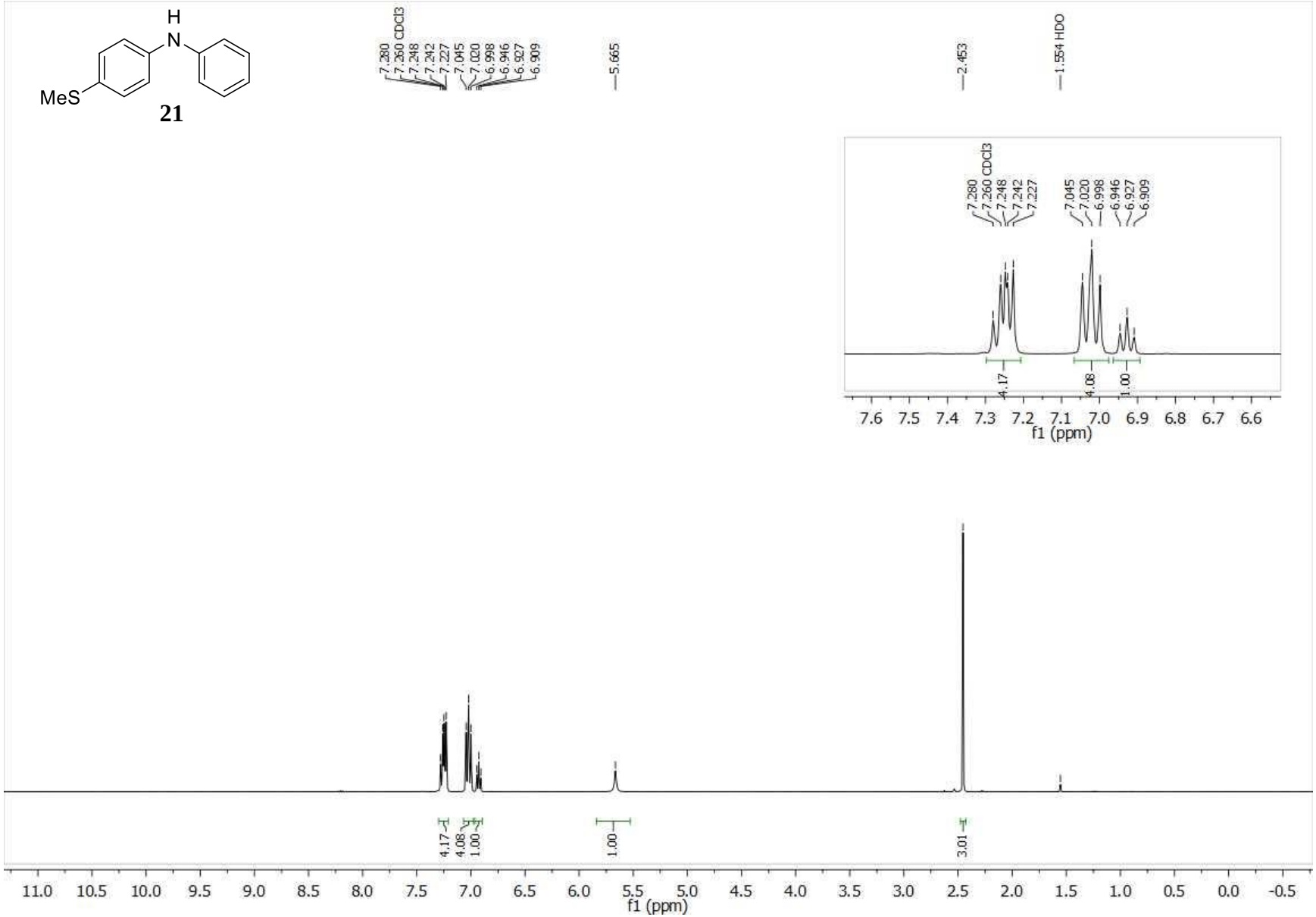
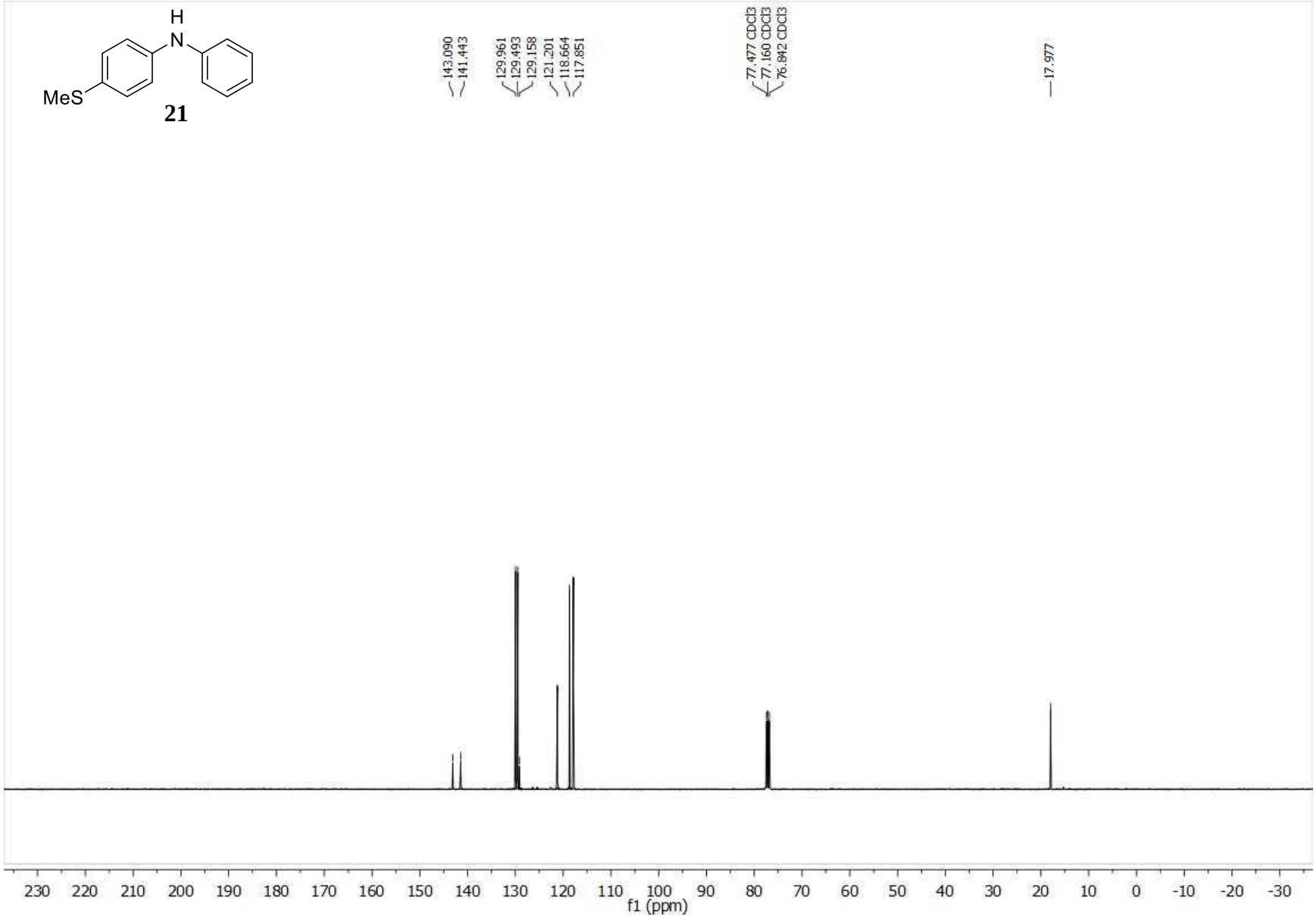
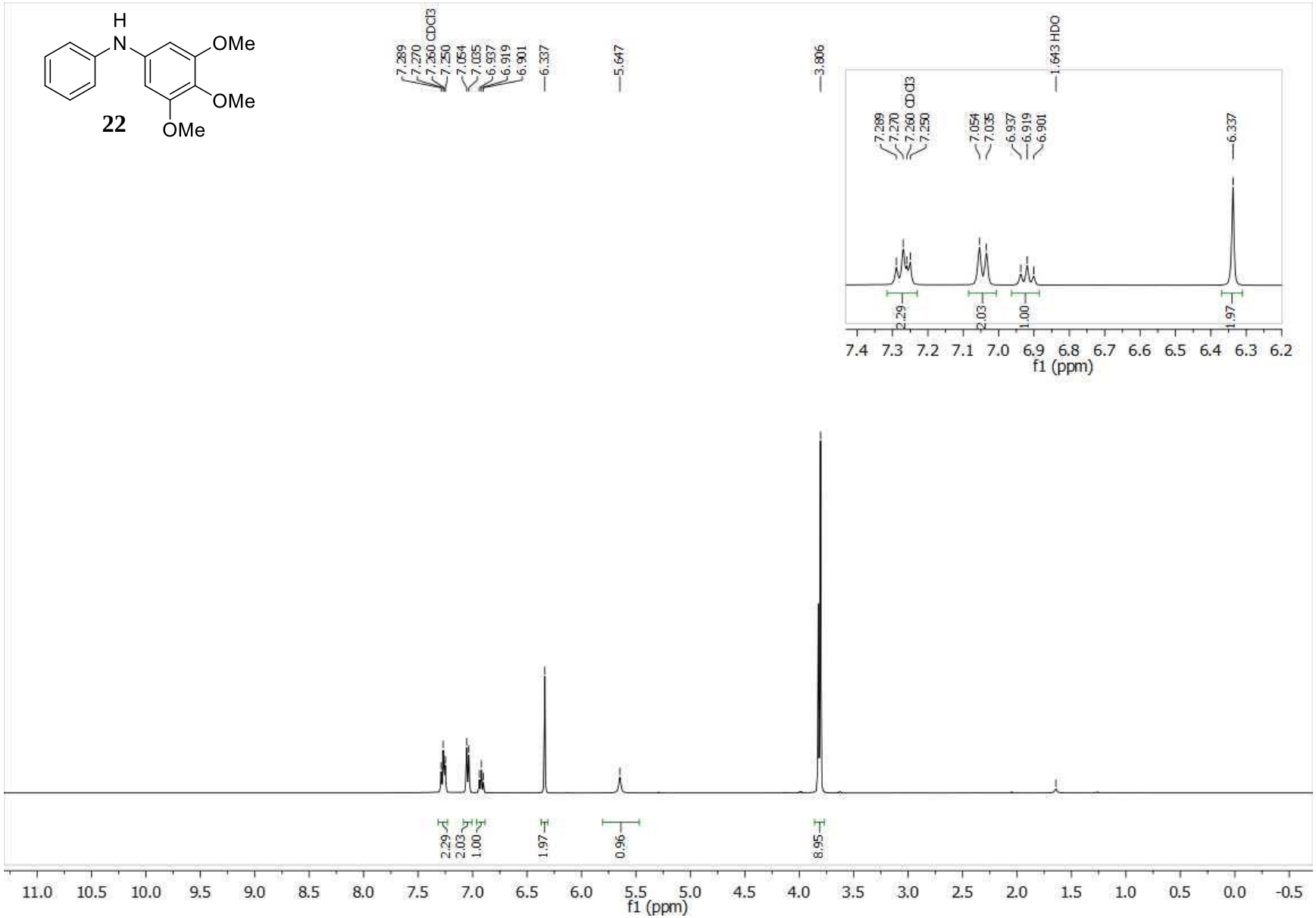
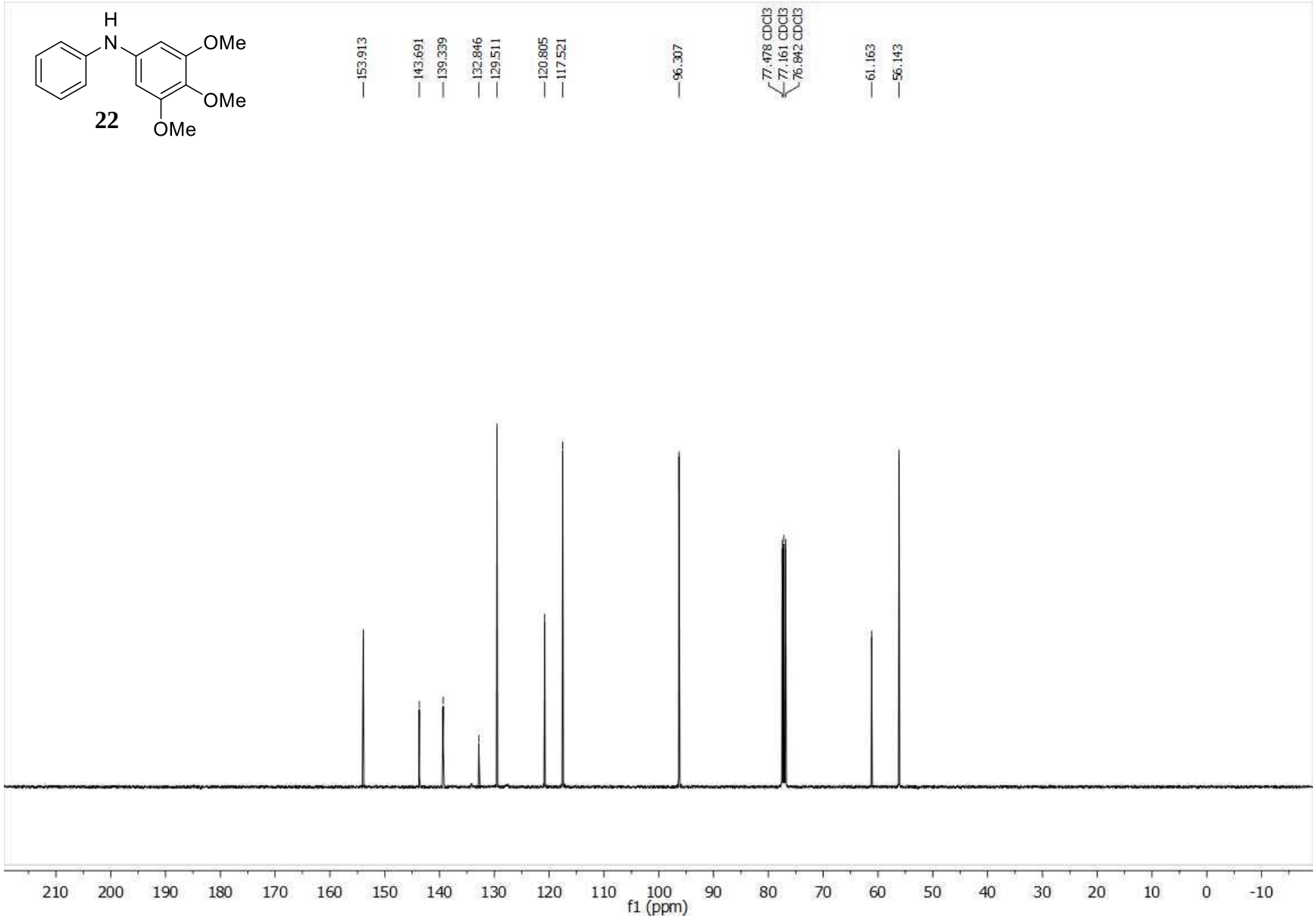
7.064
7.017
6.998
6.979
6.970
6.951
6.931
5.651
1.560 HDO
1.00
2.08
1.13
2.05
3.09
0.97
f1 (ppm)

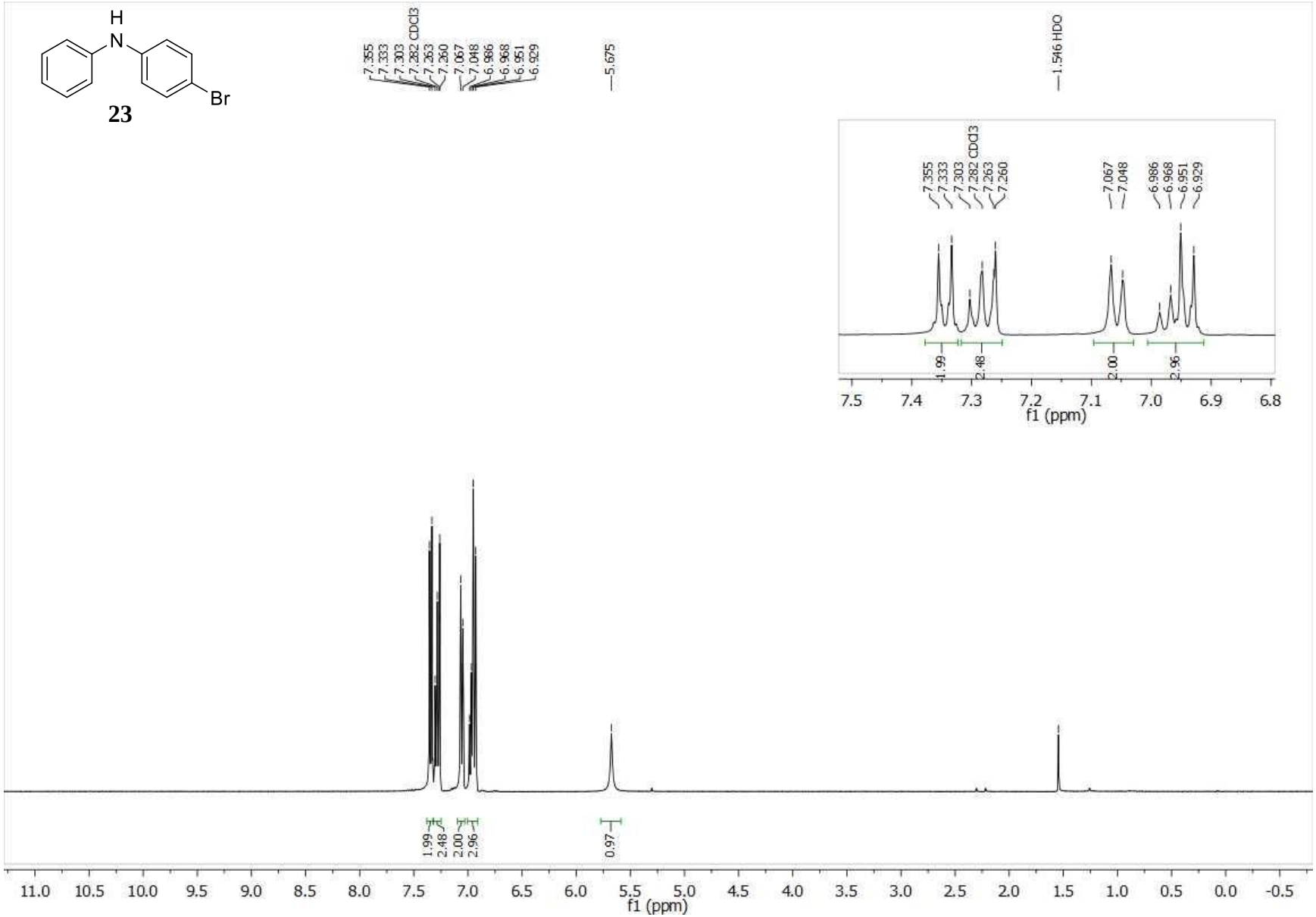

H
N
I
20
144.878
142.011
130.879
129.590
125.693
122.132
118.932
116.354
95.037
77.478 CDCl3
77.161 CDCl3
76.843 CDCl3
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30
f1 (ppm)

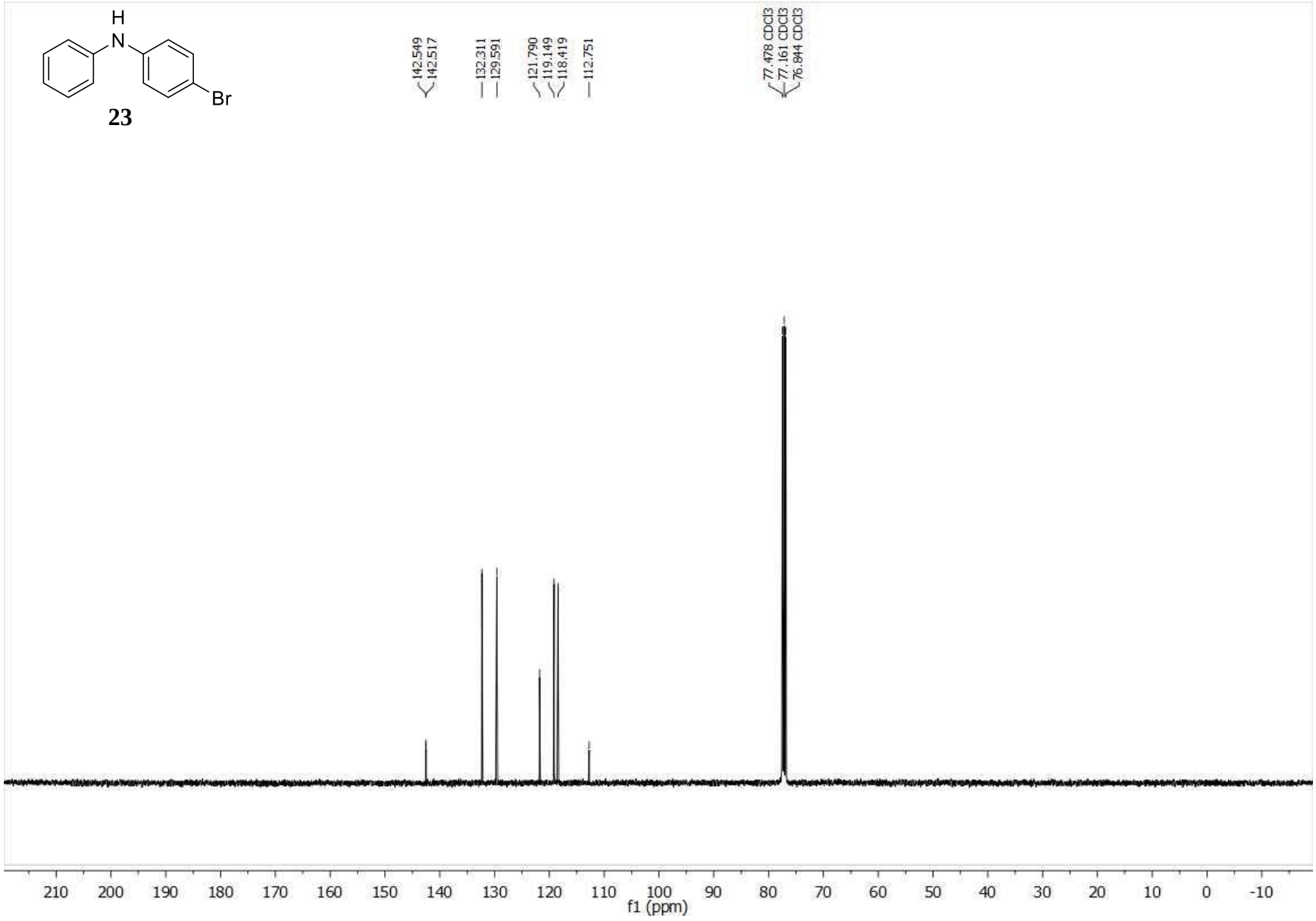

MeS
H
N
21
7.280
7.260 CDCl3
7.248
7.242
7.227
7.045
7.020
6.998
6.946
6.927
6.909
5.665
2.453
1.554 HDO
4.17
4.08
1.00
1.00
3.01
f1 (ppm)

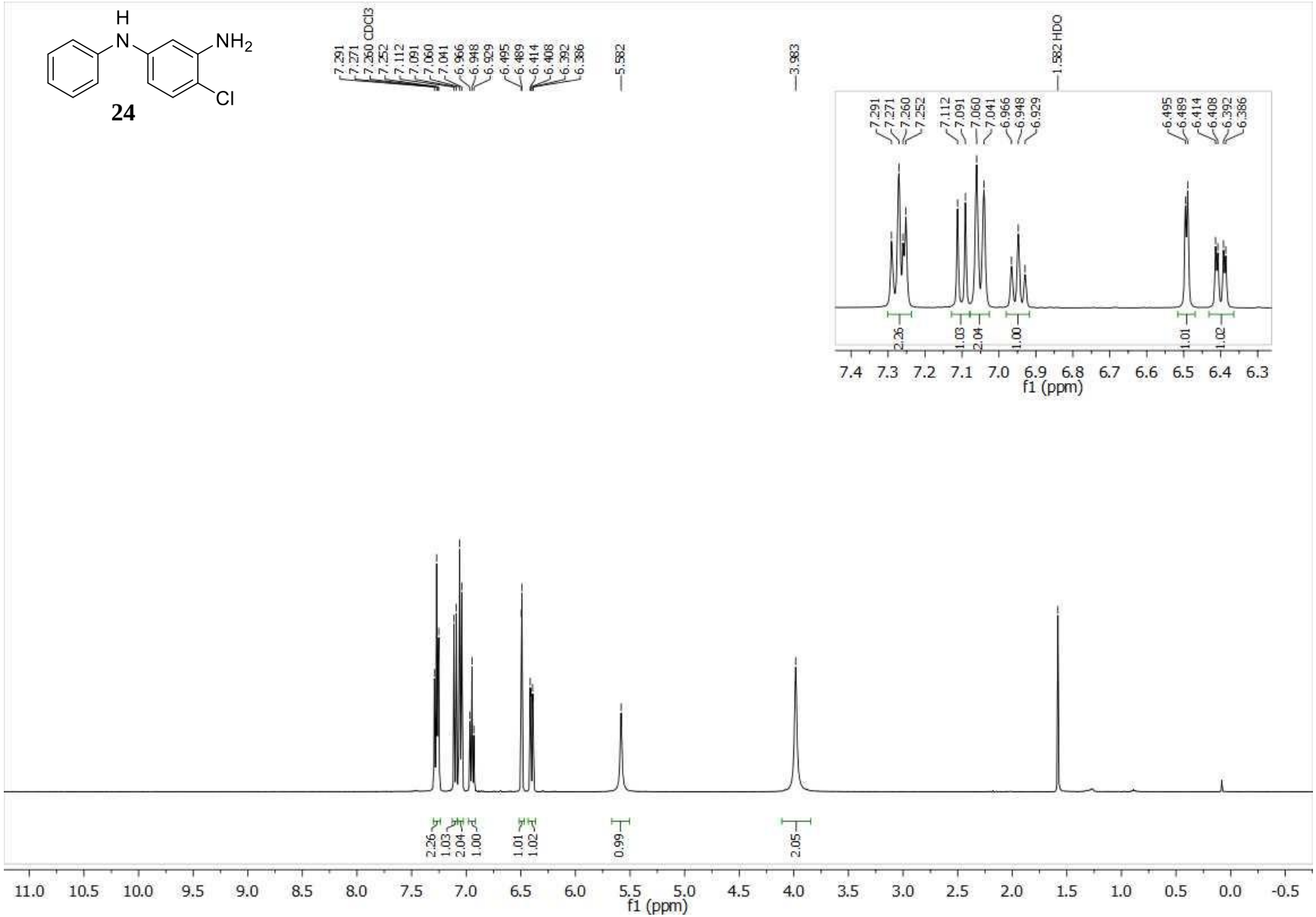

H
N
MeS
21
143.090
141.443
129.961
129.493
129.158
121.201
118.664
117.851
77.477 CDCl3
77.160 CDCl3
76.842 CDCl3
17.977
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30
f1 (ppm)

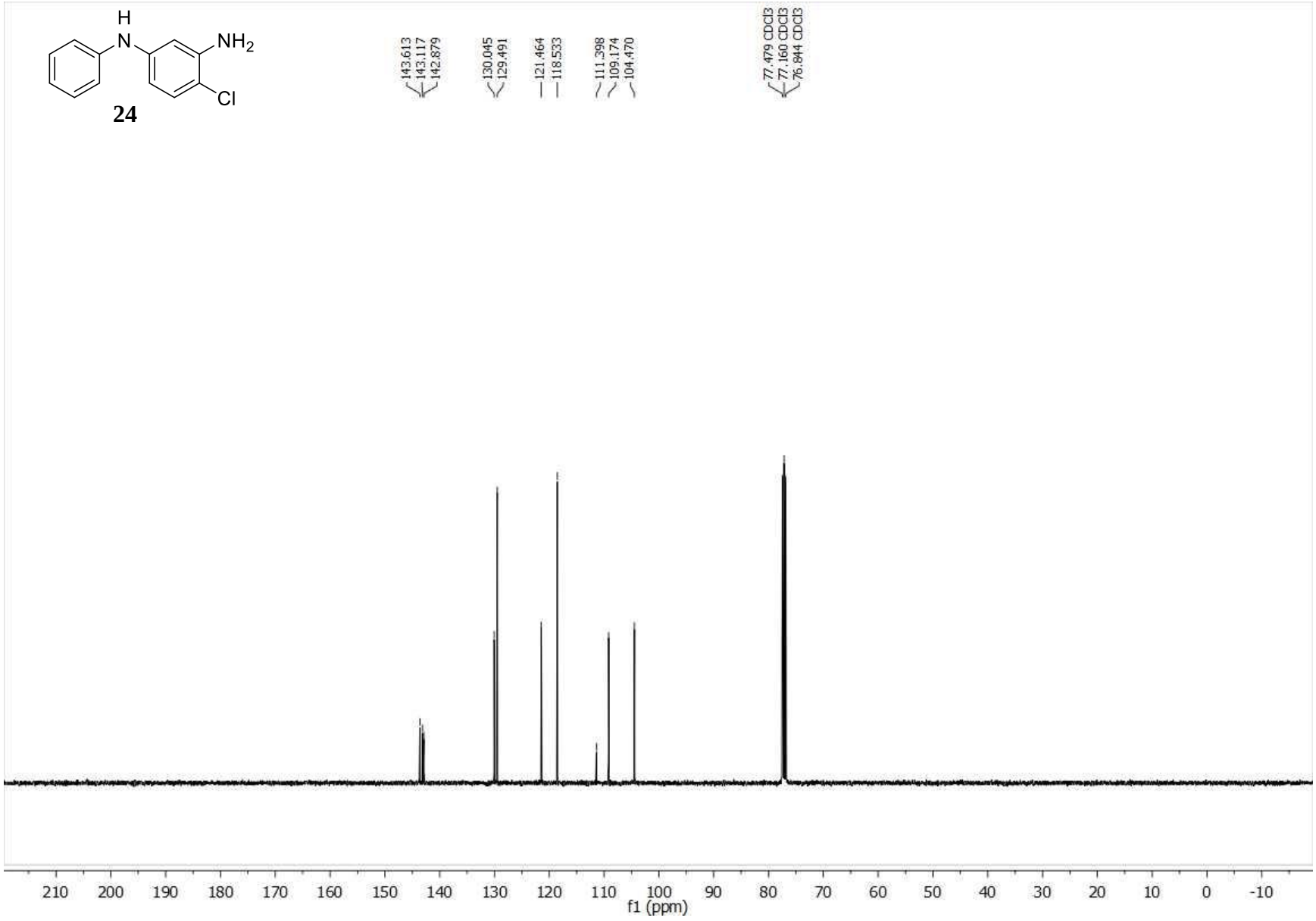

H
N
OMe
OMe
OMe
22
7.289
7.270
7.260 CDCl3
7.250
7.054
7.035
6.937
6.919
6.901
6.337
5.647
3.806
1.643 HDO
2.29
2.03
1.00
1.97
0.96
8.95
f1 (ppm)

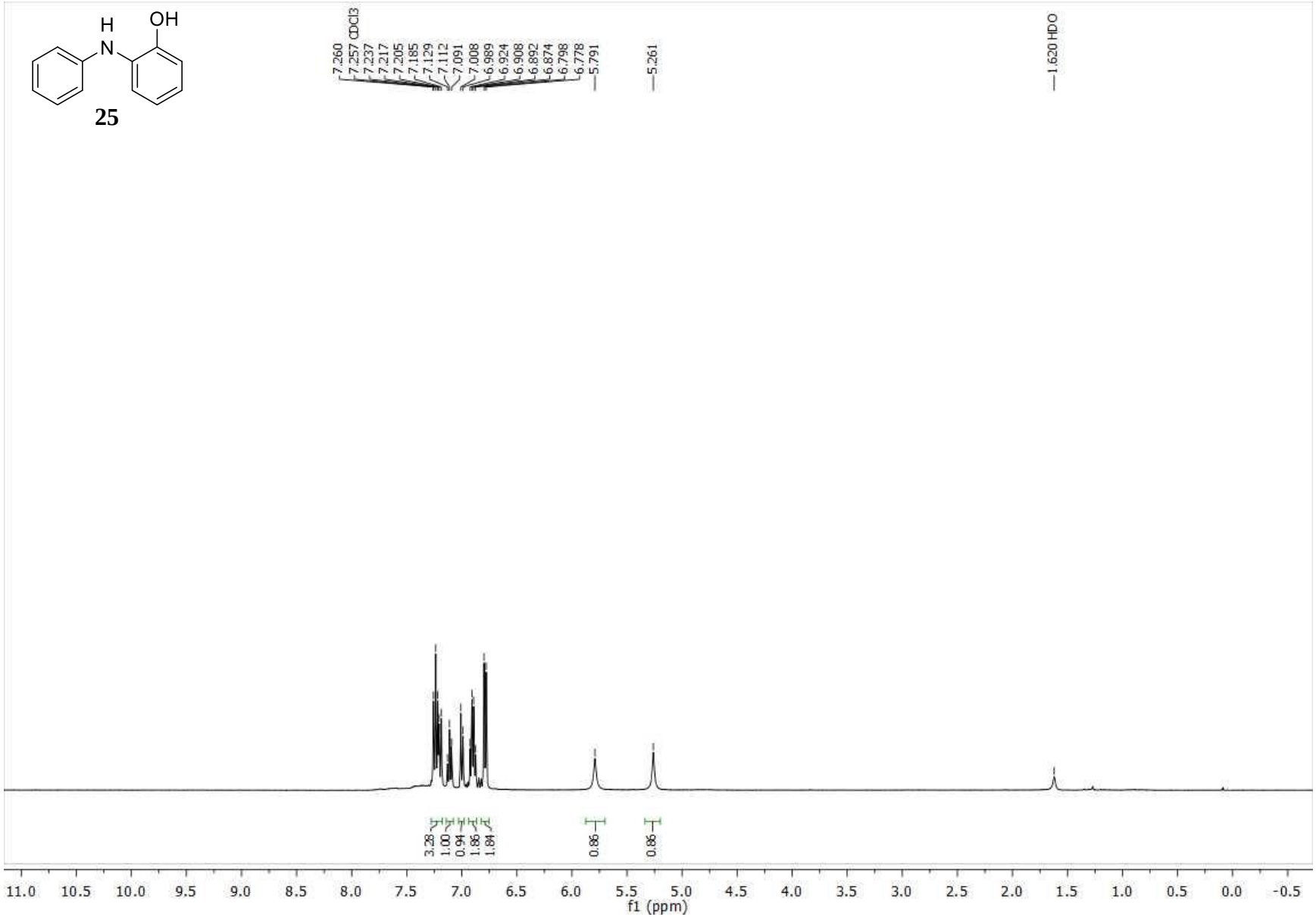

H
N
OMe
OMe
OMe
22
153.913
143.691
139.339
132.846
129.511
120.805
117.521
96.307
77.478 CDCl3
77.161 CDCl3
76.842 CDCl3
61.163
56.143
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

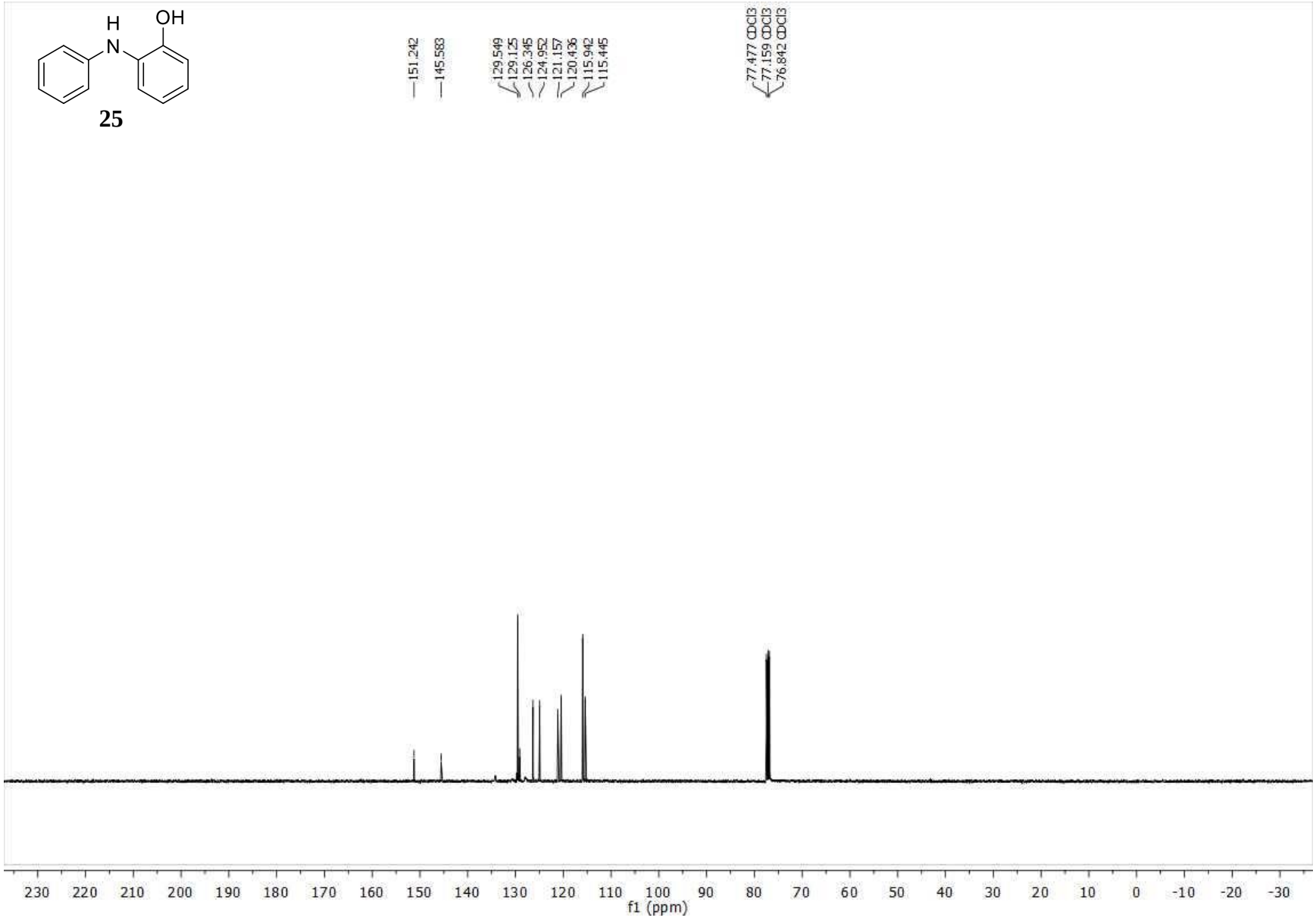

H
N
Br
23
7.355
7.333
7.303
7.282 CDCl3
7.263
7.260
7.067
7.048
6.986
6.968
6.951
6.929
5.675
1.546 HDO
1.99
2.48
2.00
2.96
0.97
f1 (ppm)

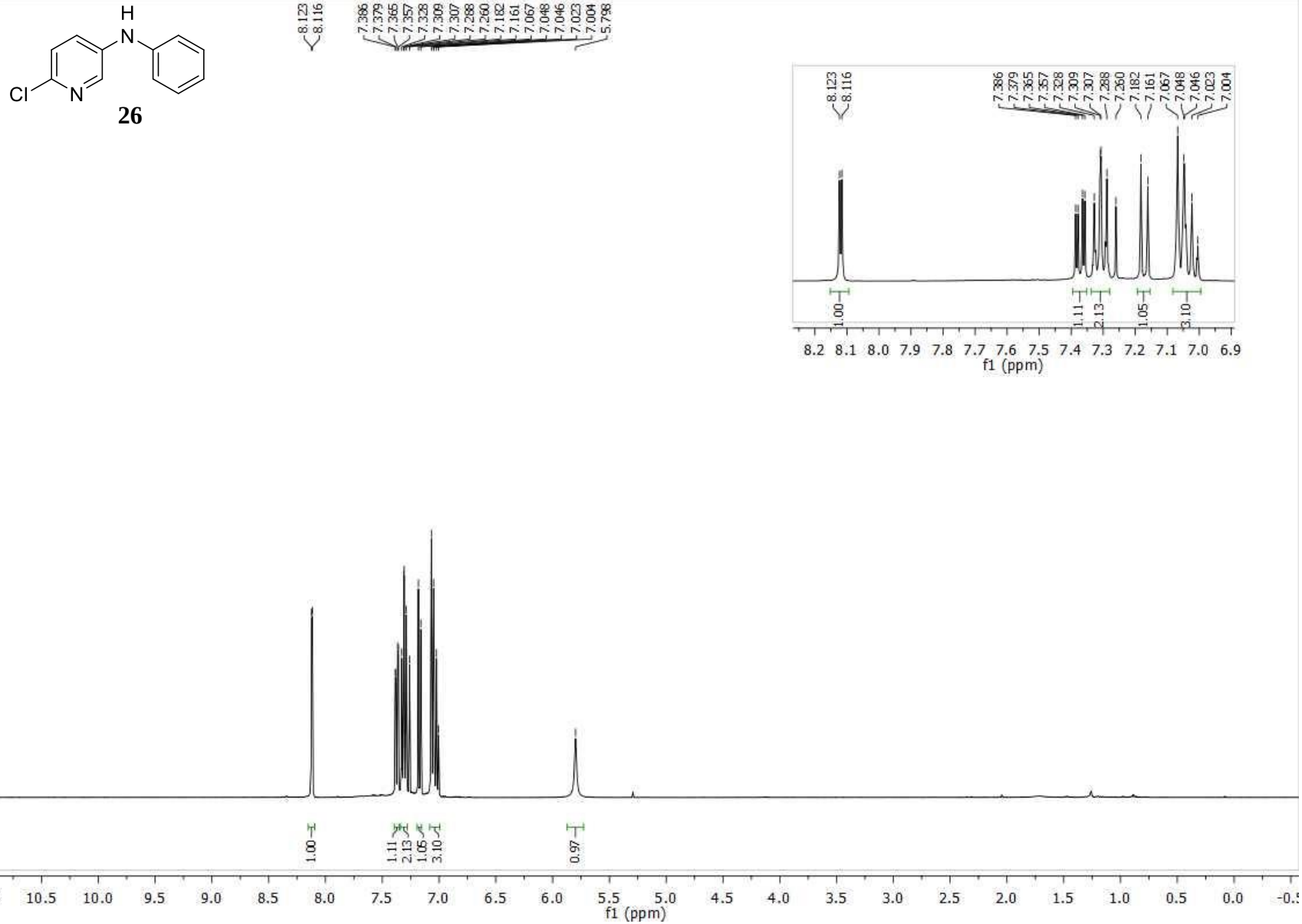

H
N
Br
23
142.549
142.517
132.311
129.591
121.790
119.149
118.419
112.751
77.478 CDCl3
77.161 CDCl3
76.844 CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

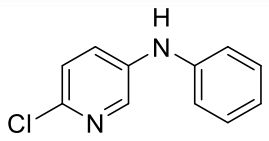

H
N
NH2
Cl
24
7.291
7.271
7.260 CDCl3
7.252
7.112
7.091
7.060
7.041
6.966
6.948
6.929
6.495
6.489
6.414
6.408
6.392
6.386
5.582
3.983
1.582 HDO
2.26
1.03
2.04
1.00
1.01
1.02
0.99
2.05
f1 (ppm)


H
N
NH2
Cl
24
143.613
143.117
142.879
130.045
129.491
121.464
118.533
111.398
109.174
104.470
77.479 CDCl3
77.160 CDCl3
76.844 CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


H
N
OH
25
7.260
7.257 CDCl3
7.237
7.217
7.205
7.185
7.129
7.112
7.091
7.008
6.989
6.924
6.908
6.892
6.874
6.798
6.778
5.791
5.261
1.620 HDO
3.28
1.00
0.94
1.86
1.84
0.86
0.86
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

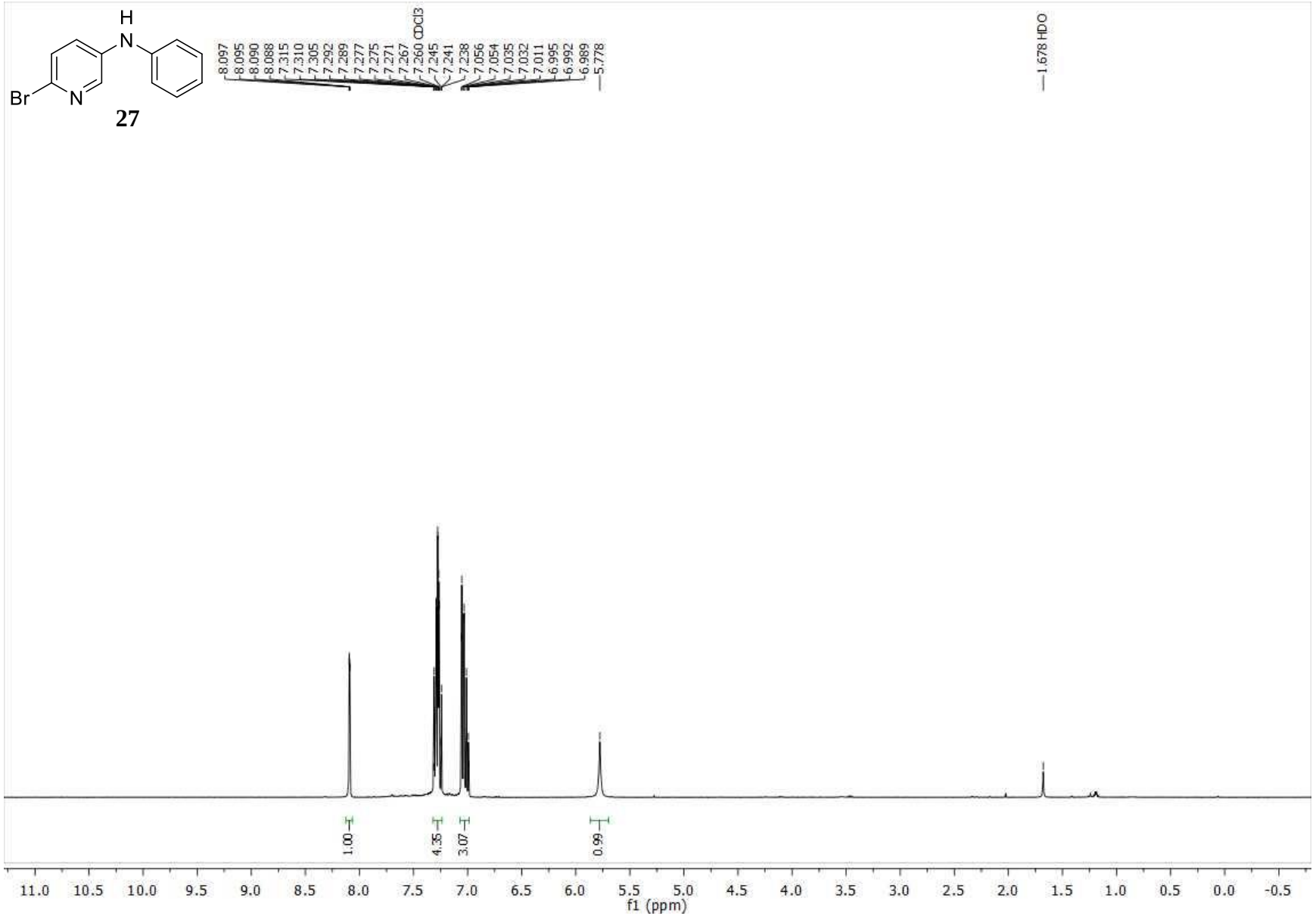

H
N
OH
25
151.242
145.583
129.549
129.125
126.345
124.952
121.157
120.436
115.942
115.445
77.477 CDCl3
77.159 CDCl3
76.842 CDCl3
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30
f1 (ppm)

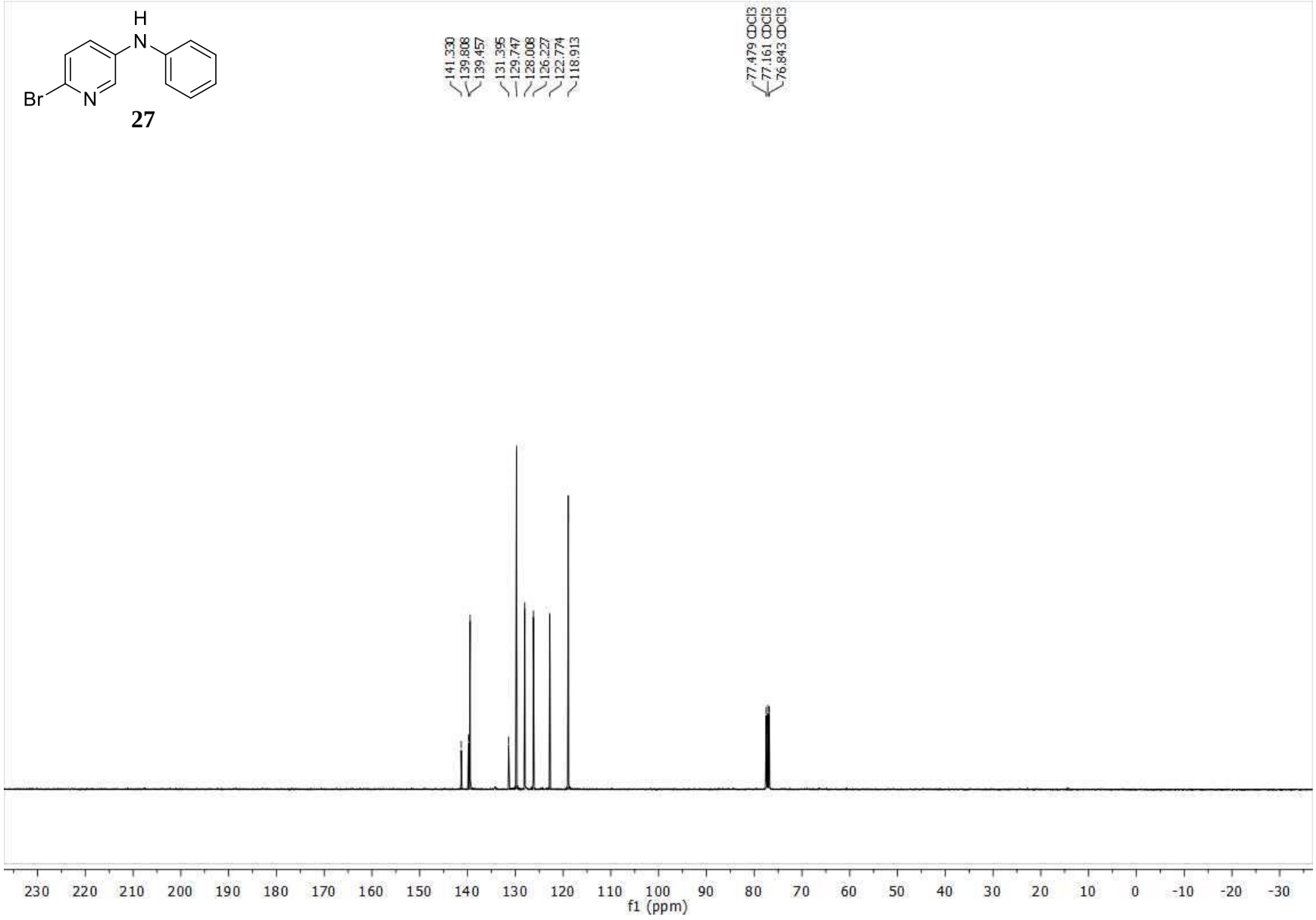

H
N
Cl
N
26
8.123
8.116
7.386
7.379
7.365
7.357
7.328
7.309
7.307
7.288
7.260
7.182
7.161
7.067
7.048
7.046
7.023
7.004
5.798
1.00
1.11
2.13
1.05
3.10
0.97
f1 (ppm)

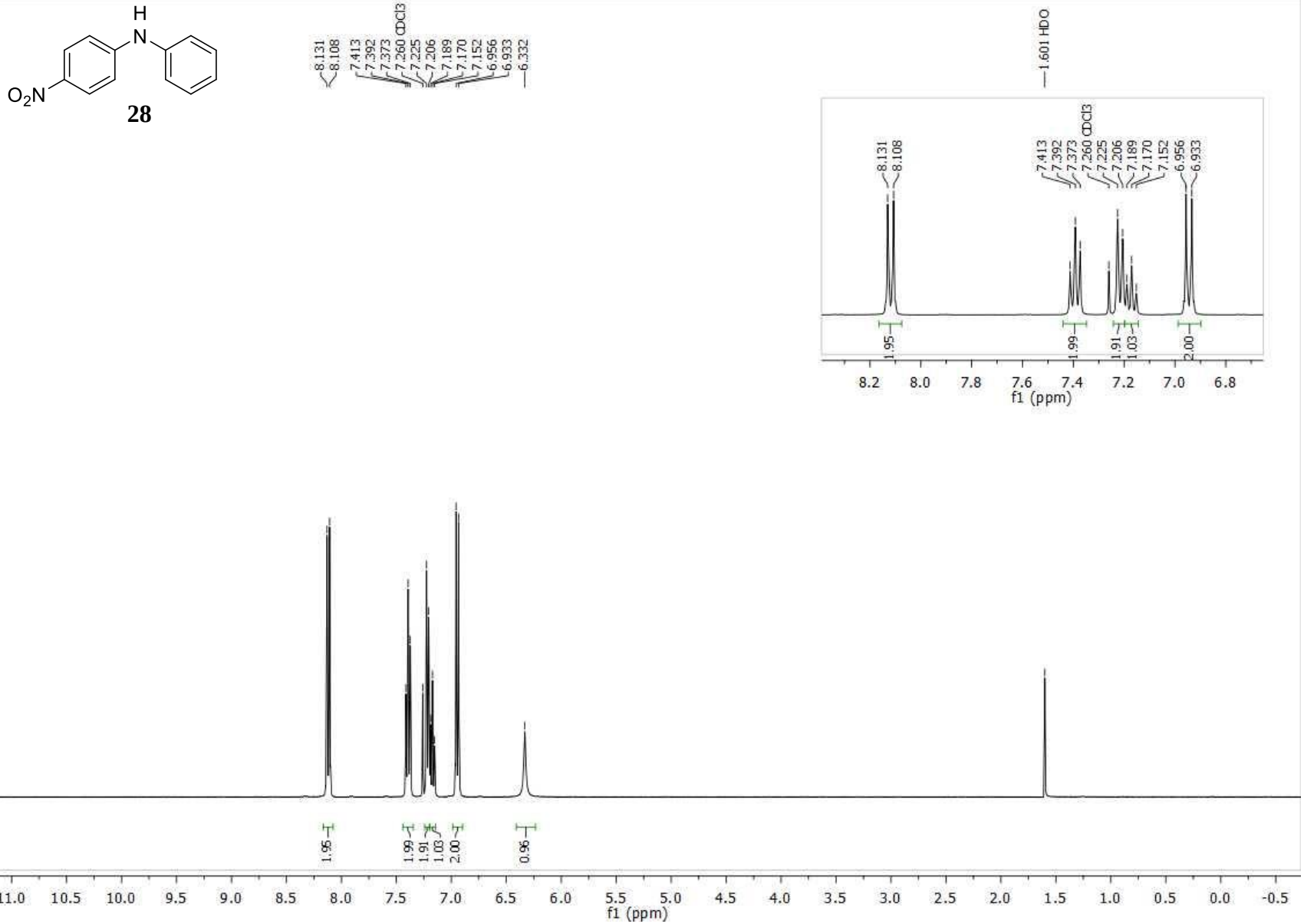

H
N
Cl
N

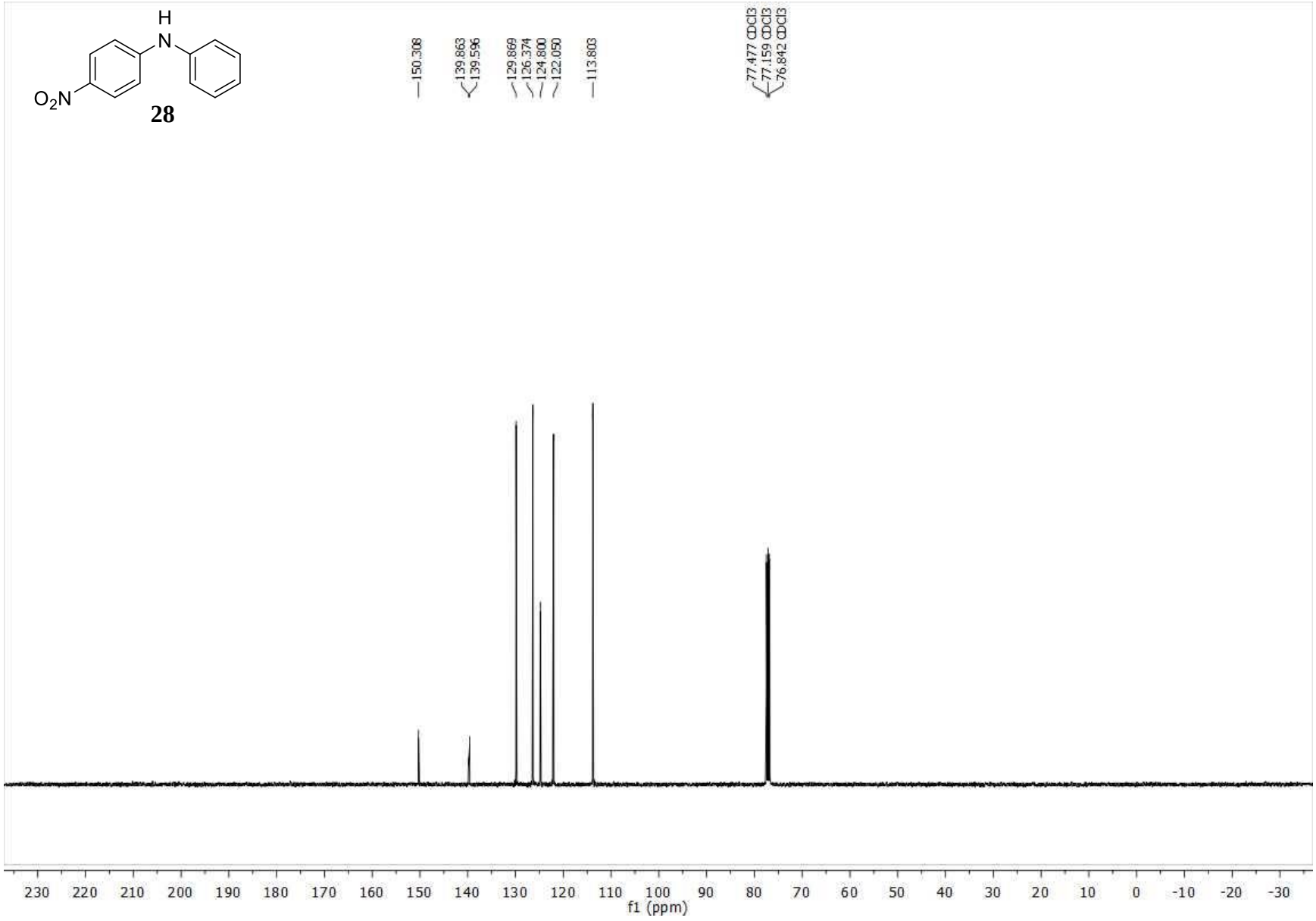
26

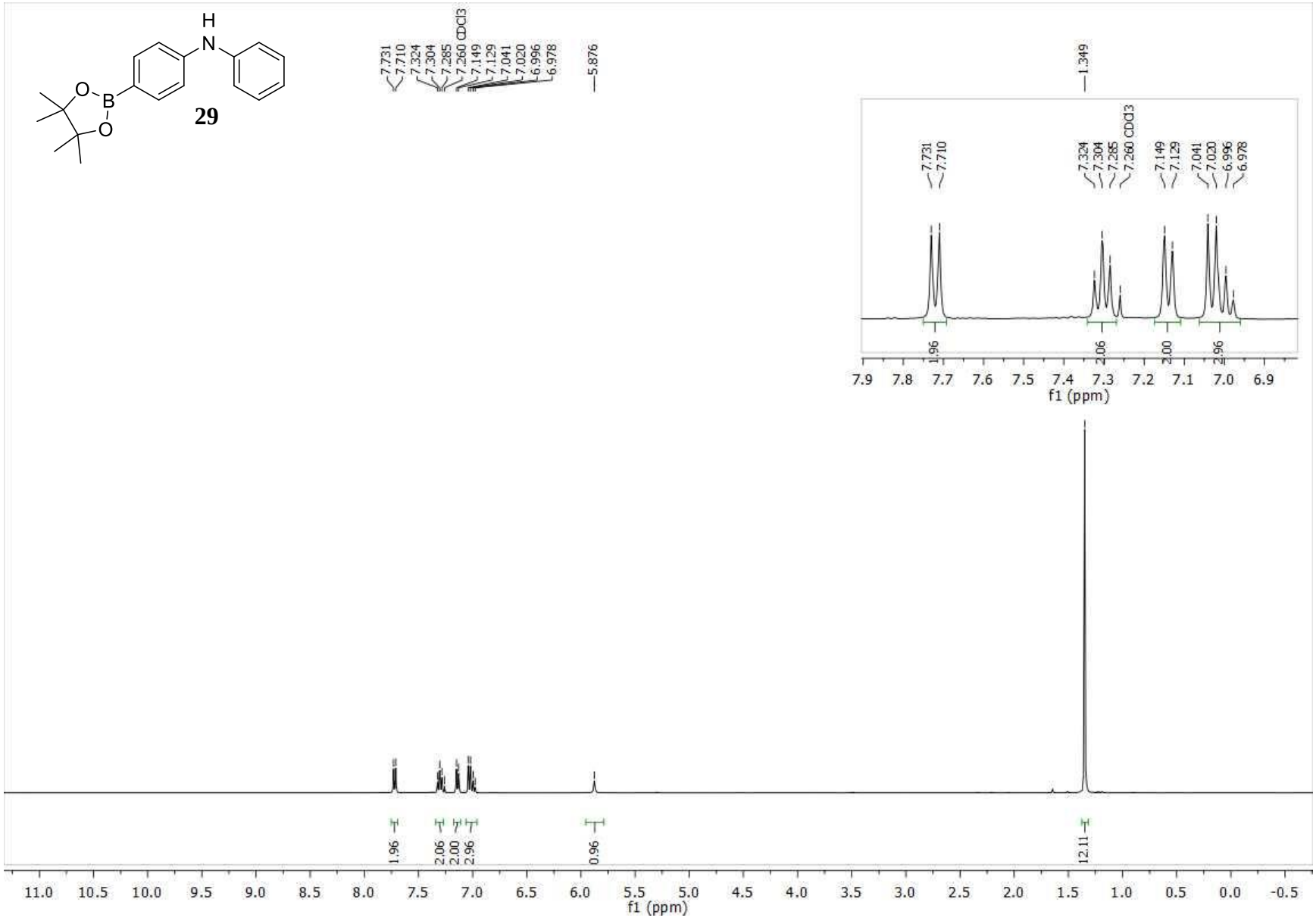
142.213
141.582
139.288
139.107
129.792
126.650
124.349
122.725
118.789
77.477 CDCl3
77.160 CDCl3
76.843 CDCl3
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40
f1 (ppm)

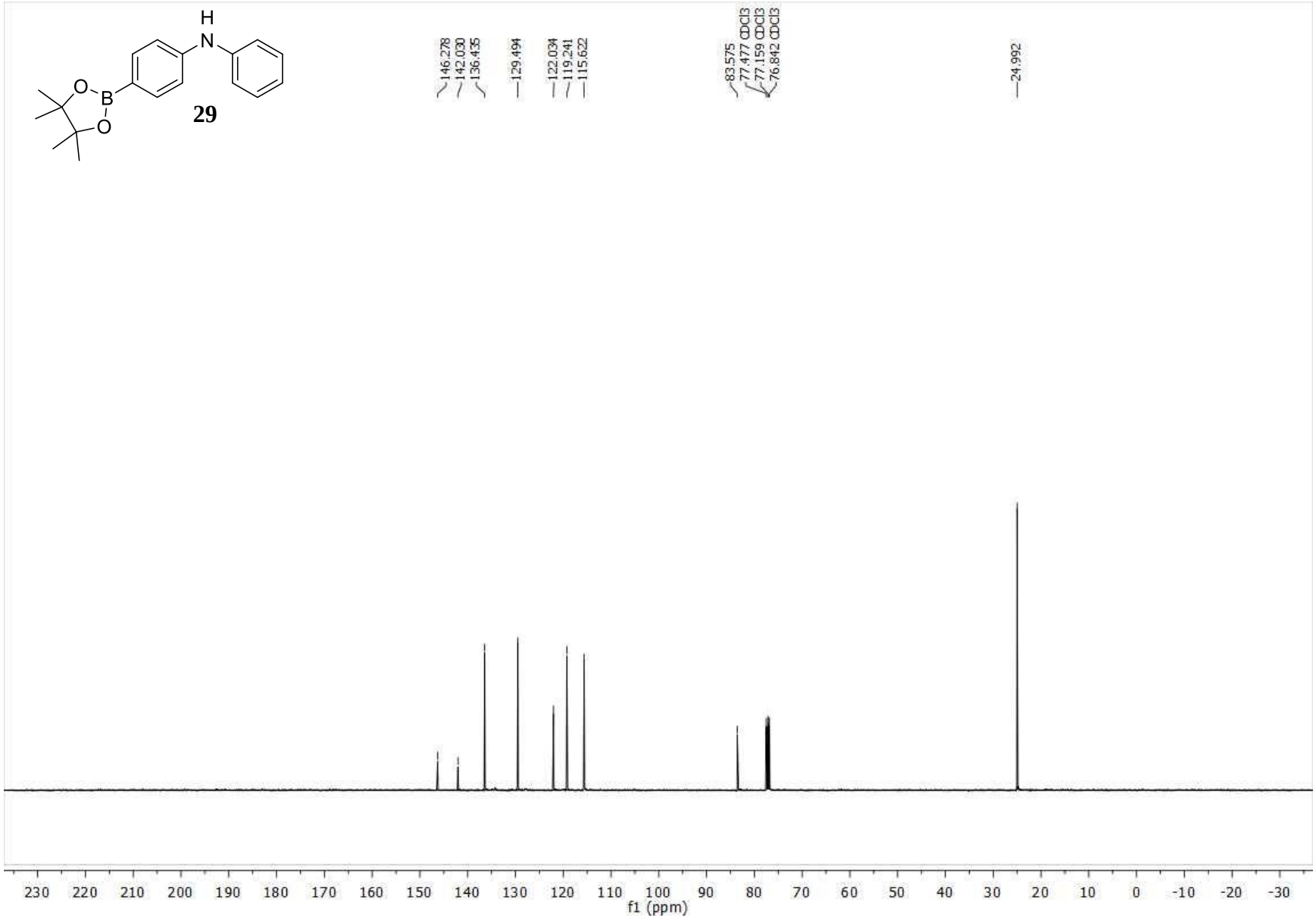

H
N
Br
N
27
8.097
8.095
8.090
8.088
7.315
7.310
7.305
7.292
7.289
7.277
7.275
7.271
7.267
7.260 CDCl3
7.245
7.241
7.238
7.056
7.054
7.035
7.032
7.011
6.995
6.992
6.989
5.778
1.678 HDO
1.00
4.35
3.07
0.99
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

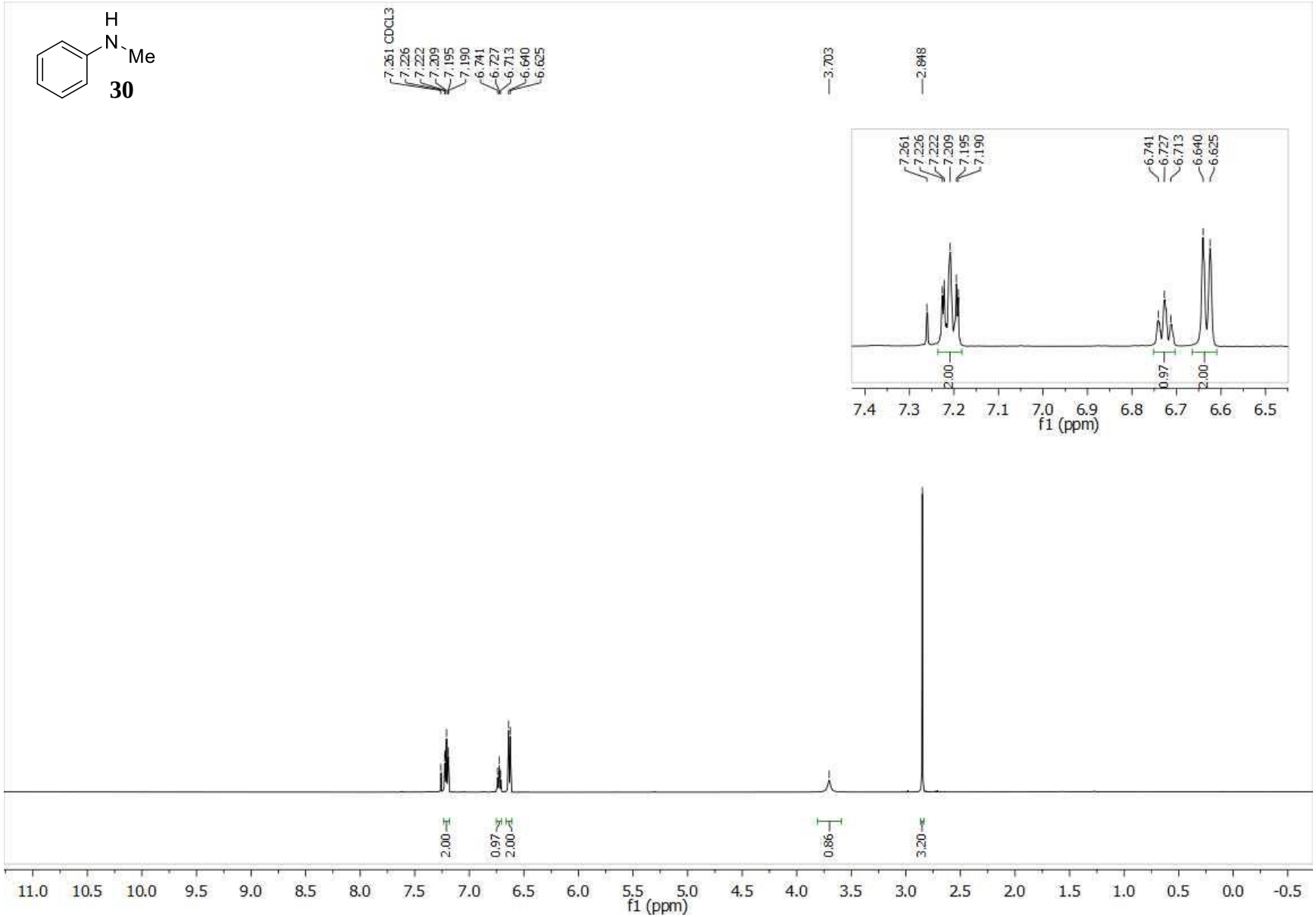

H
N
Br
N
27
141.330
139.808
139.457
131.395
129.747
128.008
126.227
122.774
118.913
77.479 CDCl3
77.161 CDCl3
76.843 CDCl3
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30
f1 (ppm)

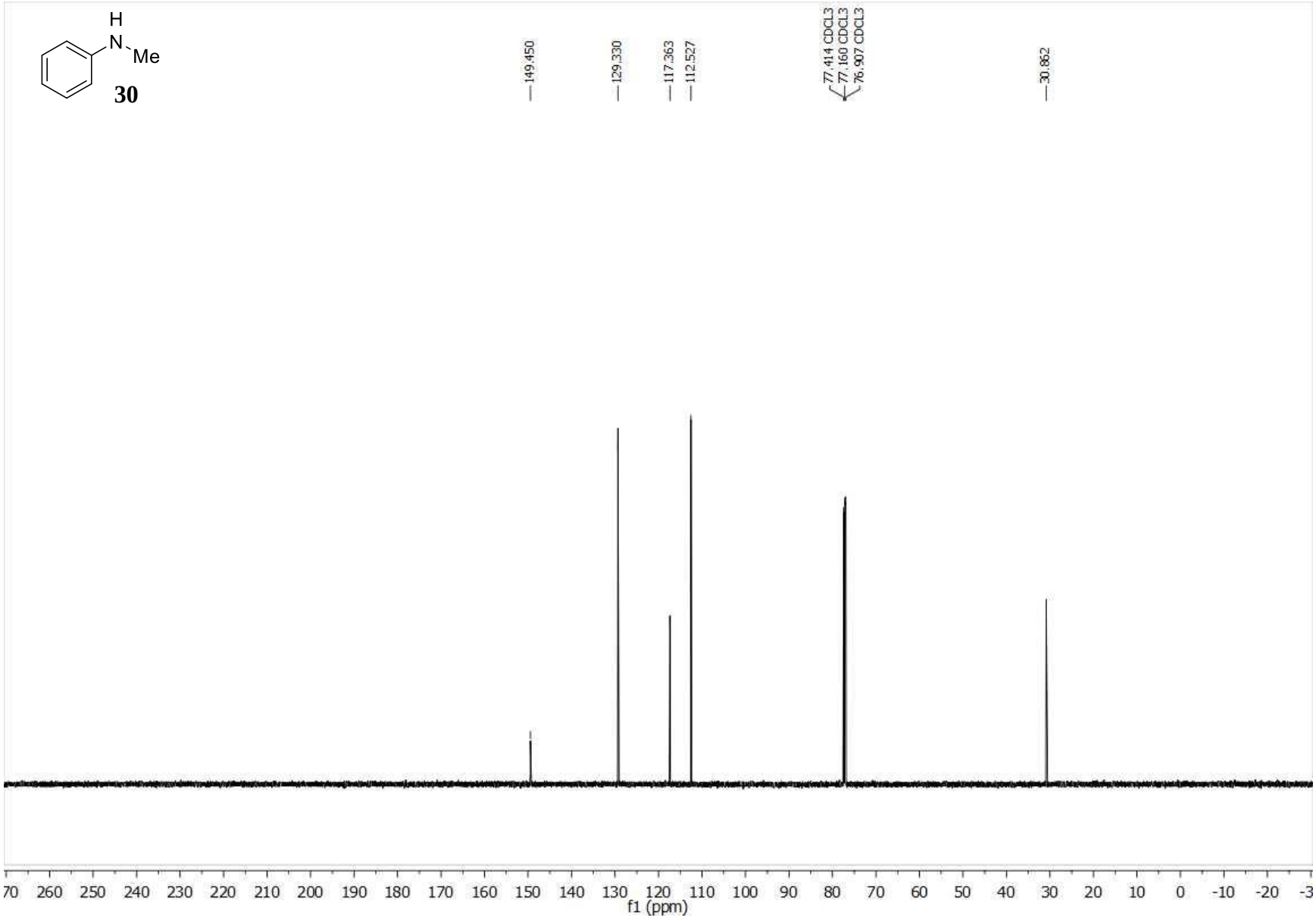

H
N
O2N
28
8.131
8.108
7.413
7.392
7.373
7.260 CDCl3
7.225
7.206
7.189
7.170
7.152
6.956
6.933
6.332
1.601 HDO
1.95
1.99
1.91
1.03
2.00
0.96
f1 (ppm)

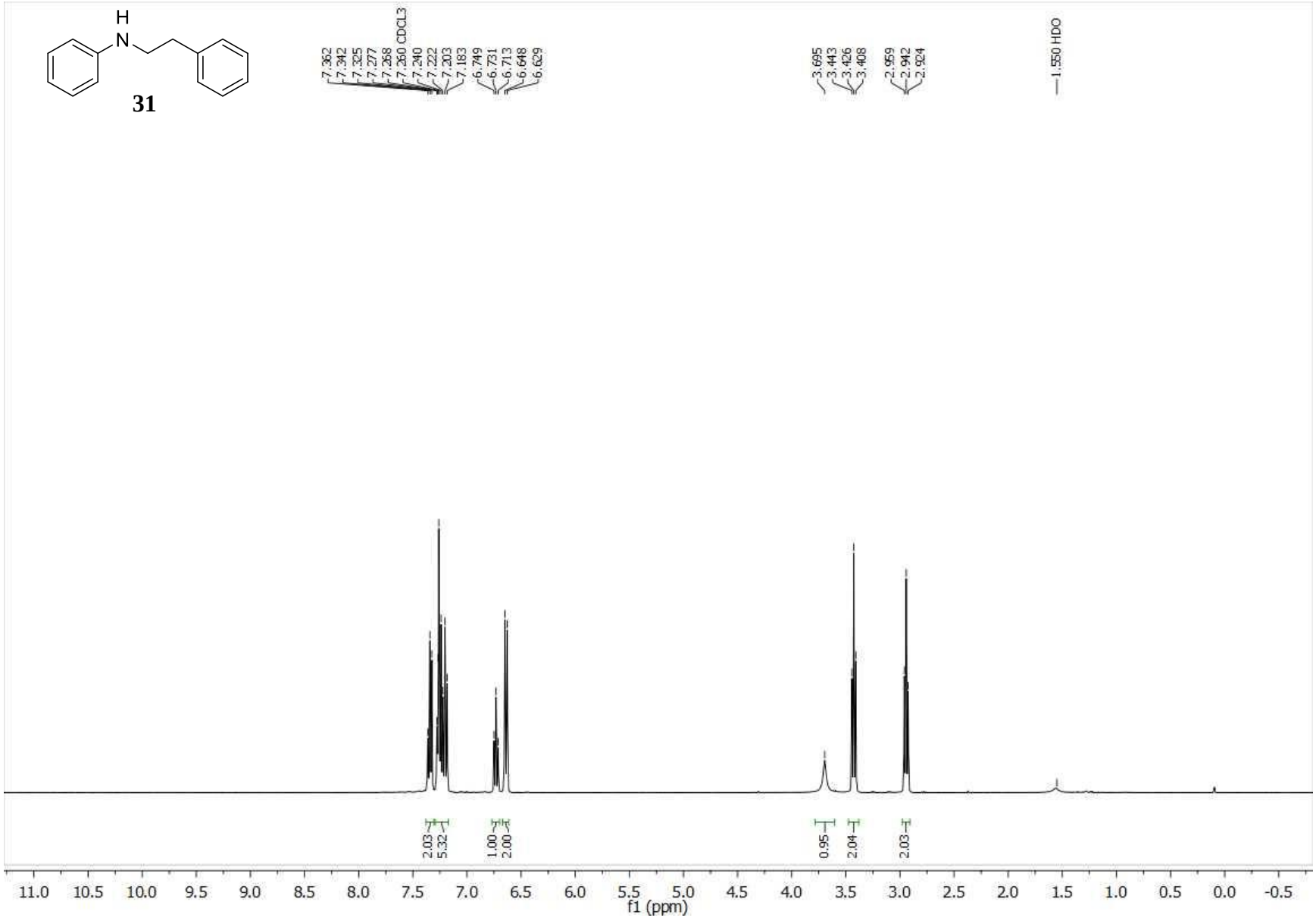

H
N
O2N
28
150.308
139.863
139.596
129.869
126.374
124.800
122.050
113.803
77.477 CDCl3
77.159 CDCl3
76.842 CDCl3
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30
f1 (ppm)

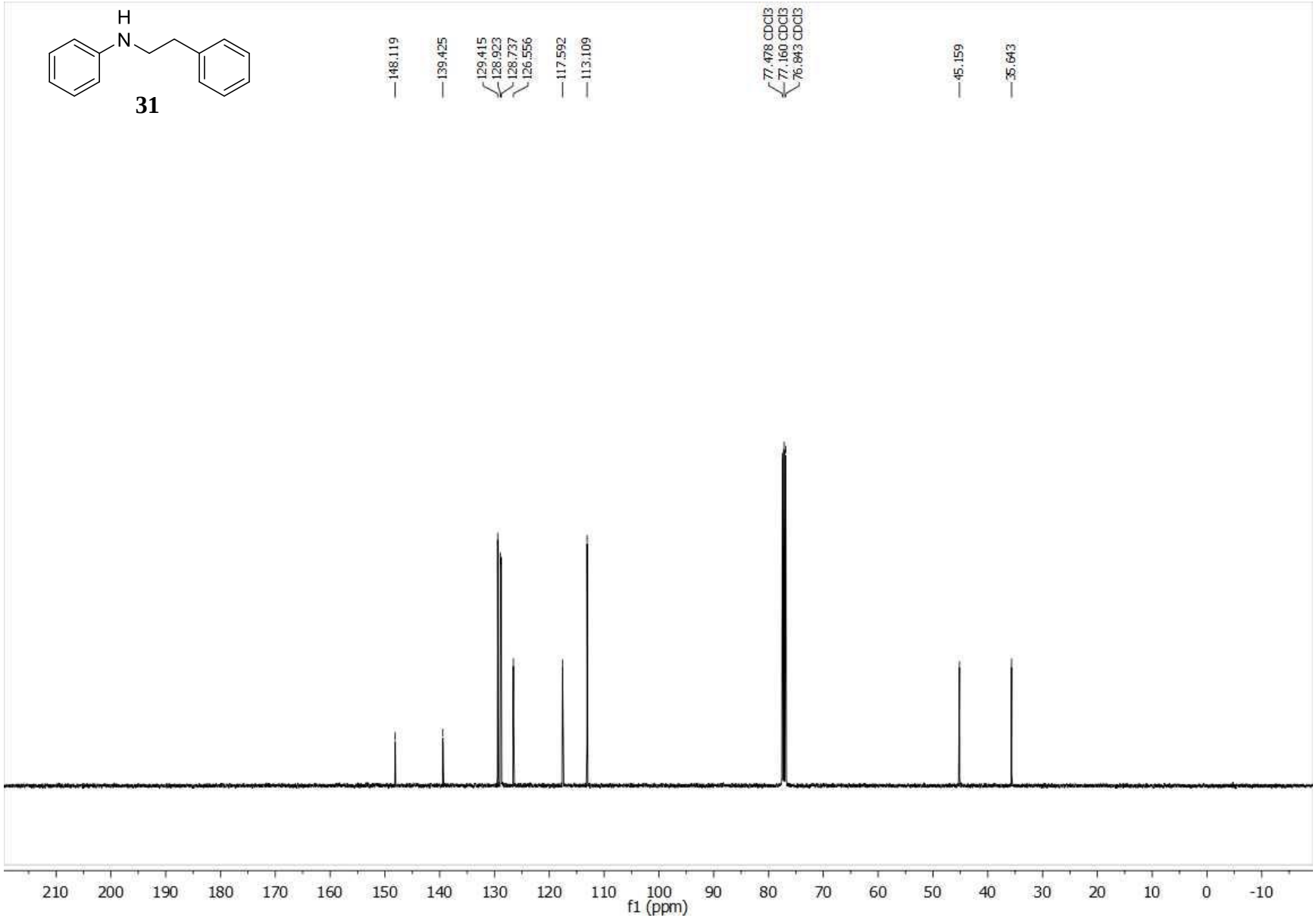

H
N
O
B
O
O
29
7.731
7.710
7.324
7.304
7.285
7.260 CDCl3
7.149
7.129
7.041
7.020
6.996
6.978
5.876
1.349
1.96
2.06
2.00
2.96
0.96
12.11
f1 (ppm)

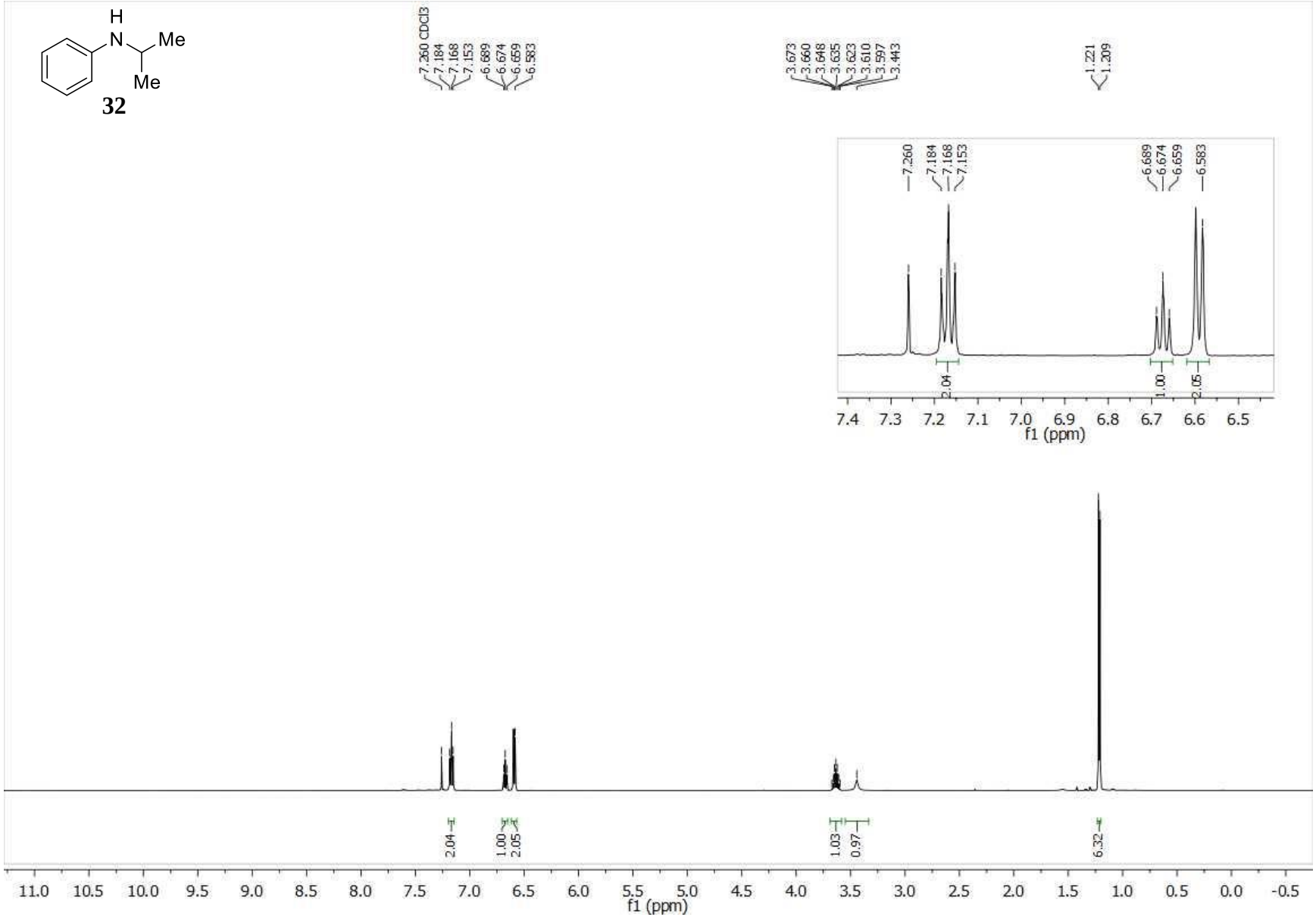

H
N
O
B
O
O
29
146.278
142.030
136.435
129.494
122.034
119.241
115.622
83.575
77.477 CDCl3
77.159 CDCl3
76.842 CDCl3
24.992
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30
f1 (ppm)

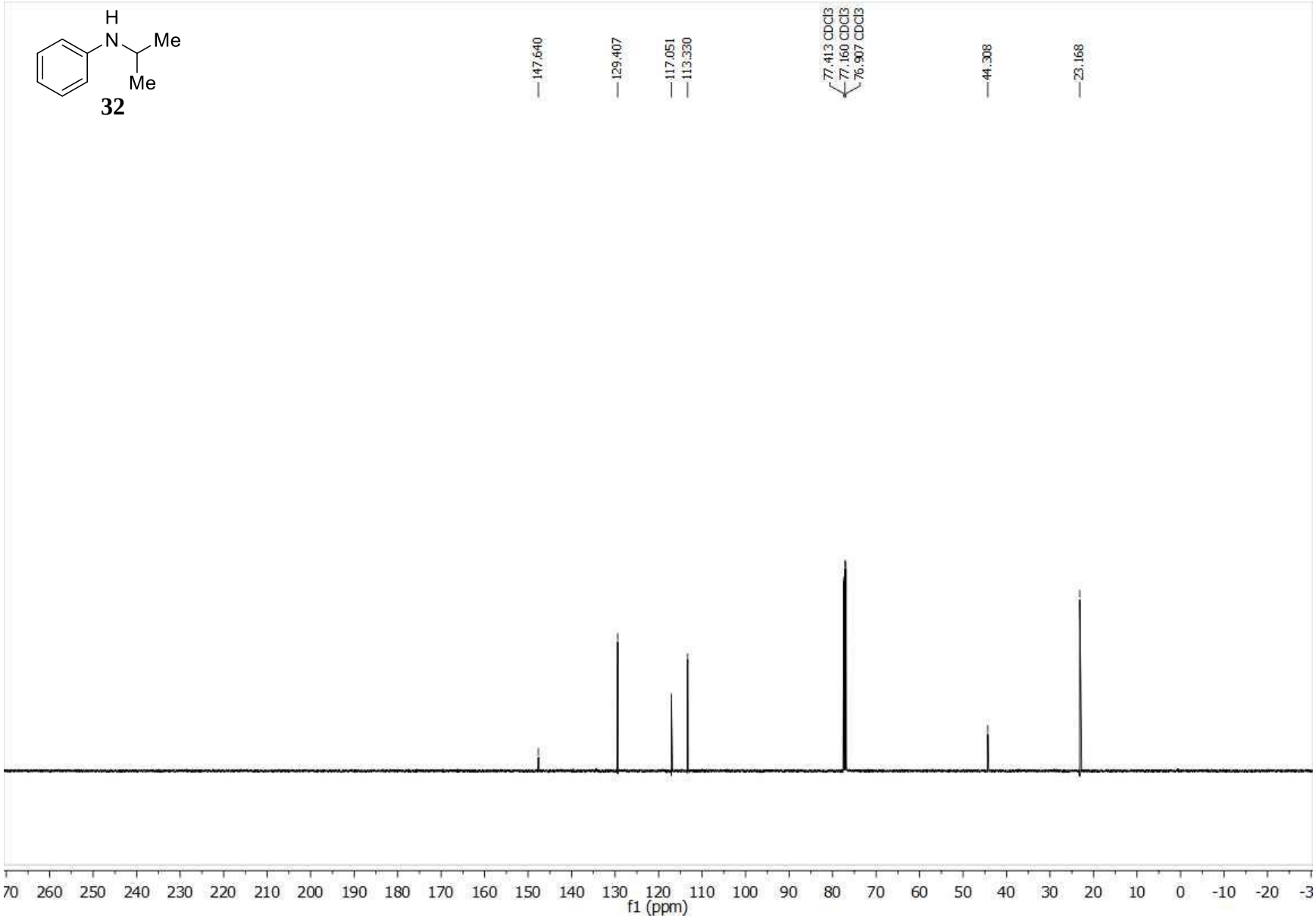

H
N
Me
30
7.261 CDCl3
7.226
7.222
7.209
7.195
7.190
6.741
6.727
6.713
6.640
6.625
3.703
2.848
2.00
0.97
2.00
0.86
3.20
f1 (ppm)

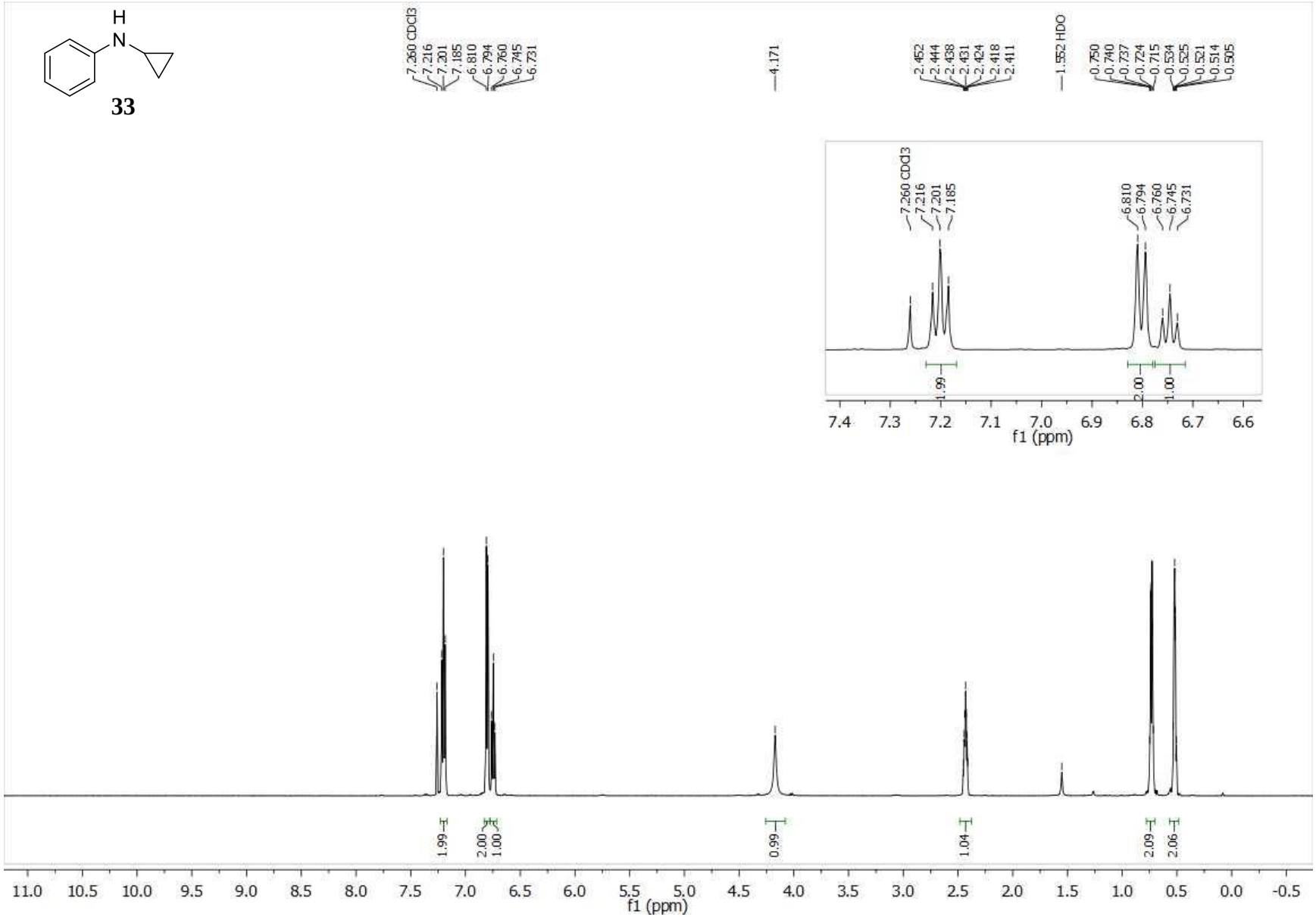

H
N
Me
30
149.450
129.330
117.363
112.527
77.414 CDCl3
77.160 CDCl3
76.907 CDCl3
30.862
f1 (ppm)

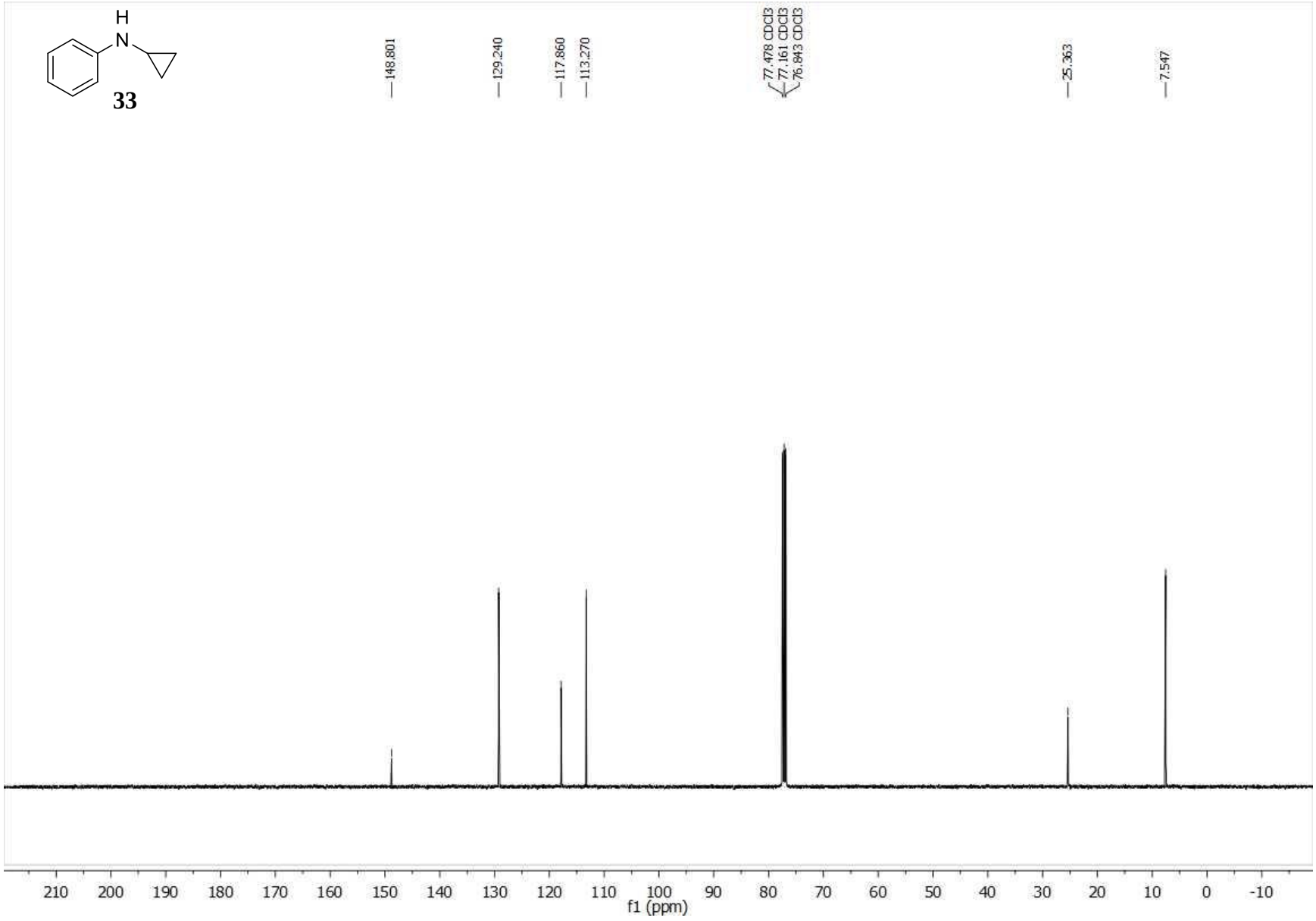

H
N
31
7.362
7.342
7.325
7.277
7.268
7.260 CDCL3
7.240
7.222
7.203
7.183
6.749
6.731
6.713
6.648
6.629
3.695
3.443
3.426
3.408
2.959
2.942
2.924
1.550 HDO
2.03
5.32
1.00
2.00
0.95
2.04
2.03
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

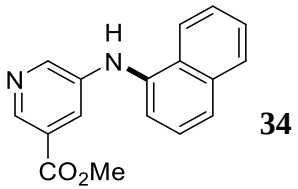

H
N
31
148.119
139.425
129.415
128.923
128.737
126.556
117.592
113.109
77.478 CDCl3
77.160 CDCl3
76.843 CDCl3
45.159
35.643
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


H
N
Me
Me
32
7.260 CDCl3
7.184
7.168
7.153
6.689
6.674
6.659
6.583
3.673
3.660
3.648
3.635
3.623
3.610
3.597
3.443
1.221
1.209
2.04
1.00
2.05
1.03
0.97
6.32
f1 (ppm)

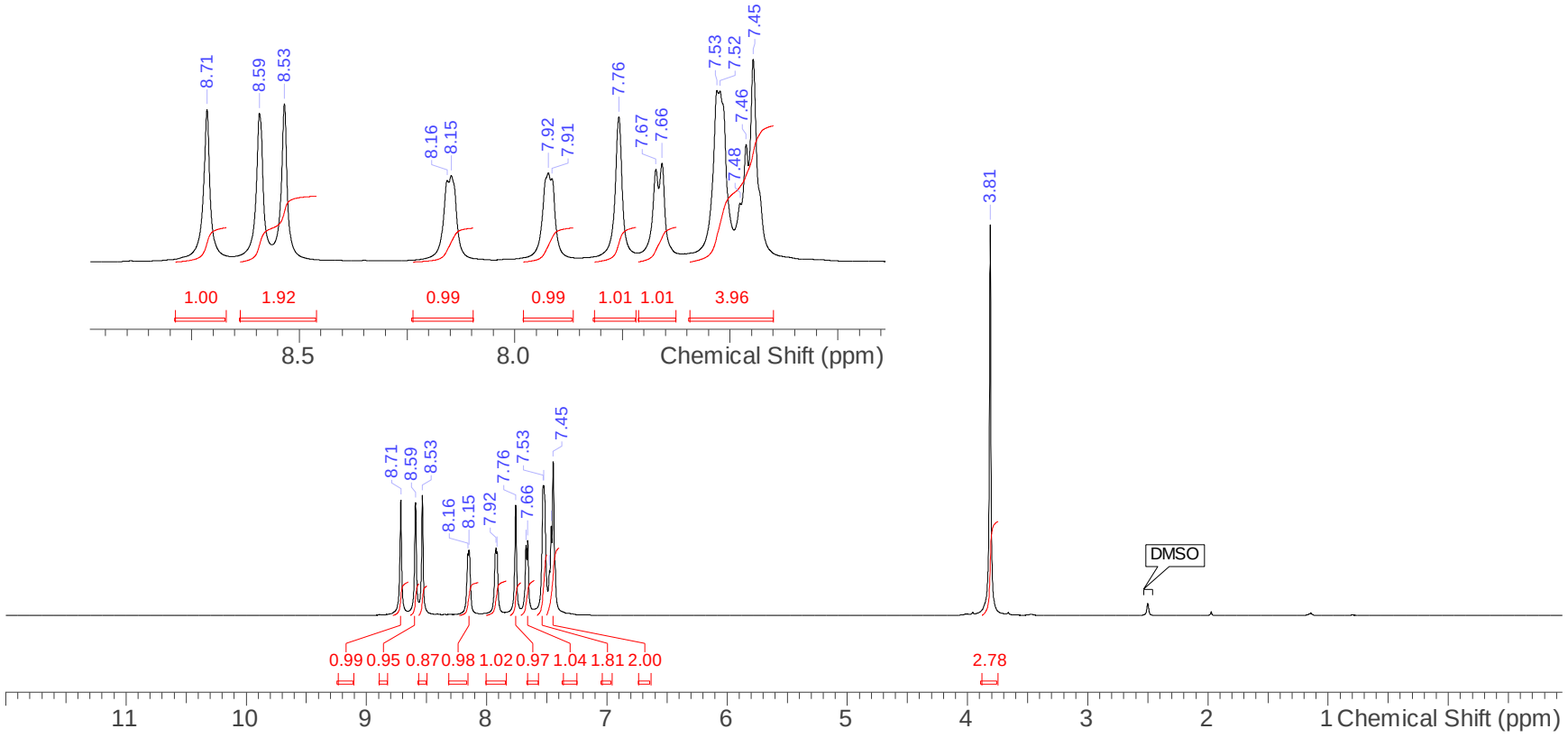

H
N
Me
Me
32
147.640
129.407
117.051
113.330
77.413 CDCl3
77.160 CDCl3
76.907 CDCl3
44.308
23.168
70 260 250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -3
f1 (ppm)

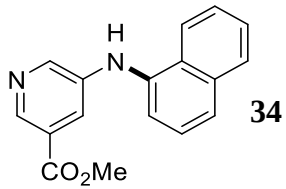

H
N
33
7.260 CDCl3
7.216
7.201
7.185
6.810
6.794
6.760
6.745
6.731
4.171
2.452
2.444
2.438
2.431
2.424
2.418
2.411
1.552 HDO
0.750
0.740
0.737
0.724
0.715
0.534
0.525
0.521
0.514
0.505
1.99
2.00
1.00
0.99
1.04
2.09
2.06
f1 (ppm)


H
N
33
148.801
129.240
117.860
113.270
77.478 CDCl3
77.161 CDCl3
76.843 CDCl3
25.363
7.547
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

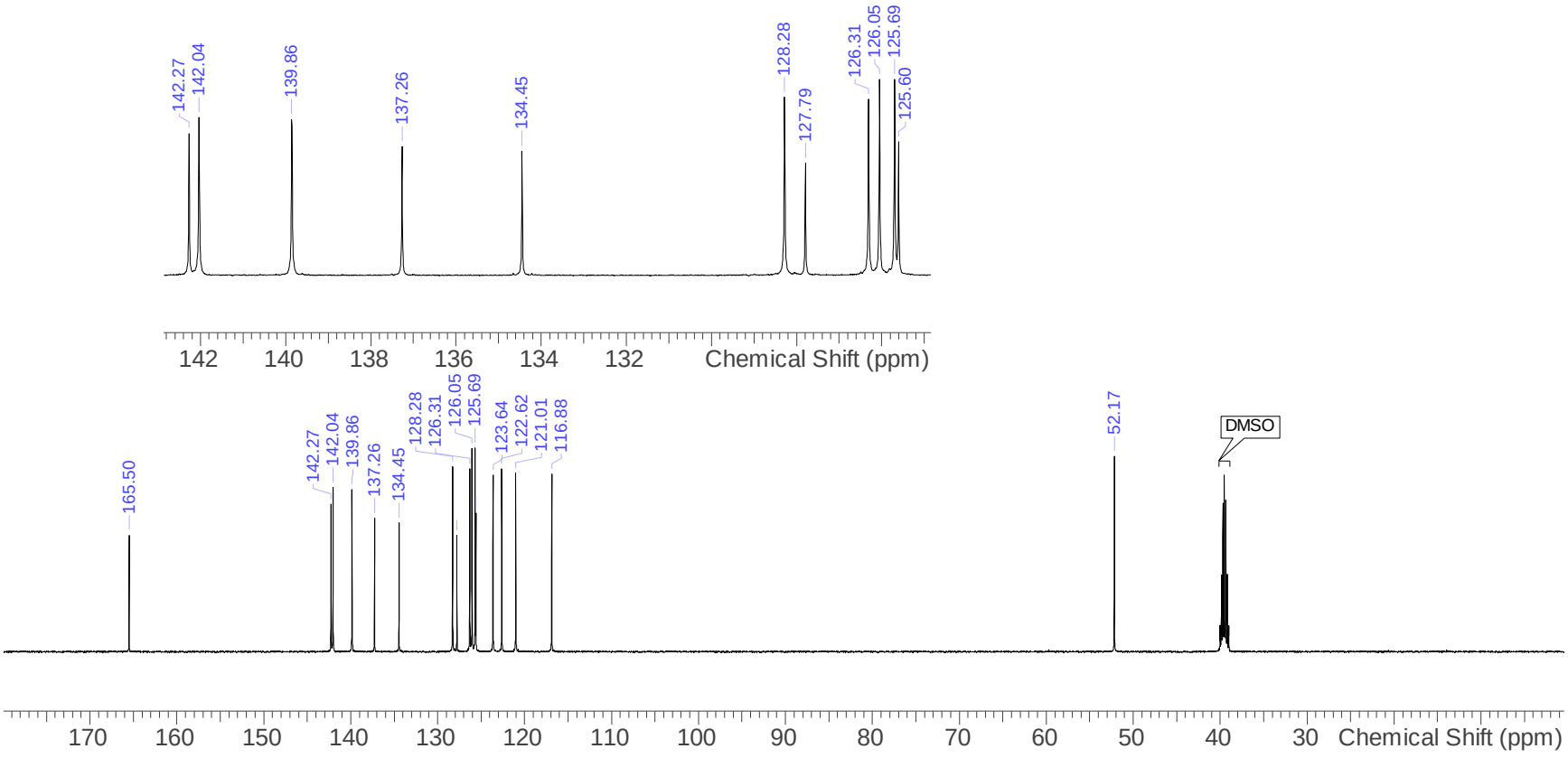

H
N
N
CO2Me

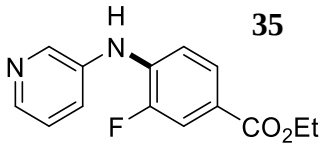
34


8.71
8.59
8.53
8.16
8.15
7.92
7.91
7.76
7.67
7.66
7.53
7.52
7.46
7.48
7.45
1.00
1.92
0.99
0.99
1.01
1.01
3.96
8.5
8.0
Chemical Shift (ppm)
3.81
DMSO
0.99
0.95
0.87
0.98
1.02
0.97
1.04
1.81
2.00
2.78
11
10
9
8
7
6
5
4
3
2
1
Chemical Shift (ppm)

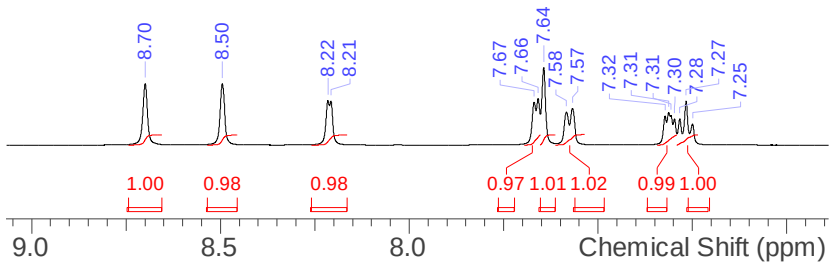

H
N
N
CO2Me

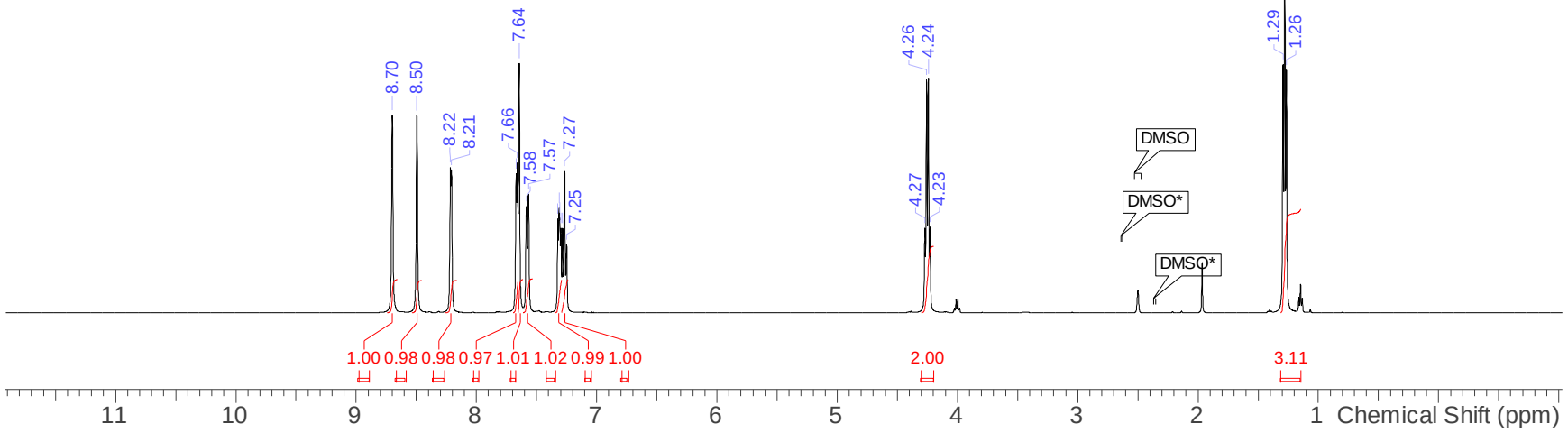
34

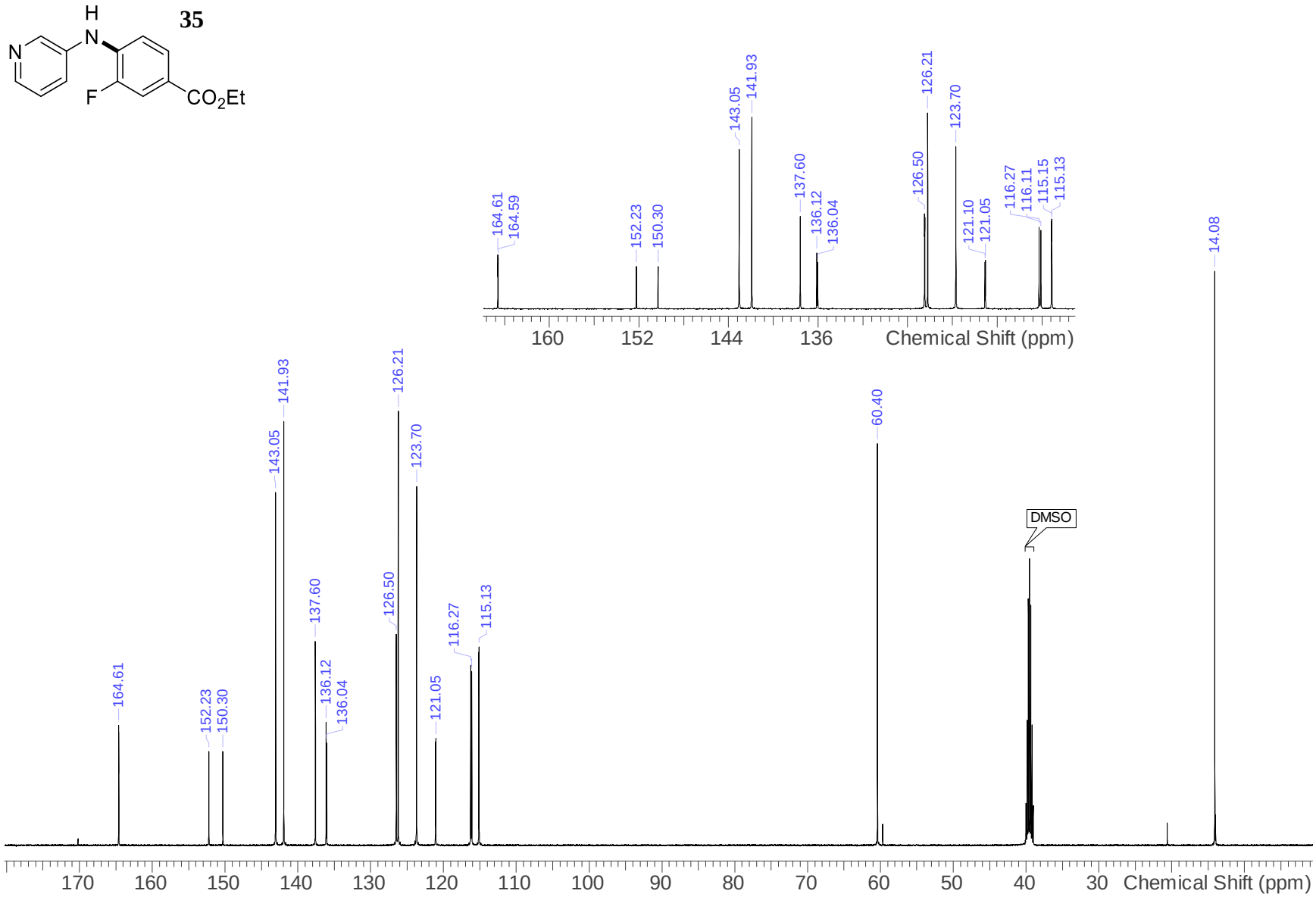

142.27
142.04
139.86
137.26
134.45
128.28
127.79
126.31
126.05
125.69
125.60
142
140
138
136
134
132
Chemical Shift (ppm)
165.50
142.27
142.04
139.86
137.26
134.45
128.28
126.31
126.05
125.69
123.64
122.62
121.01
116.88
52.17
DMSO
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
Chemical Shift (ppm)

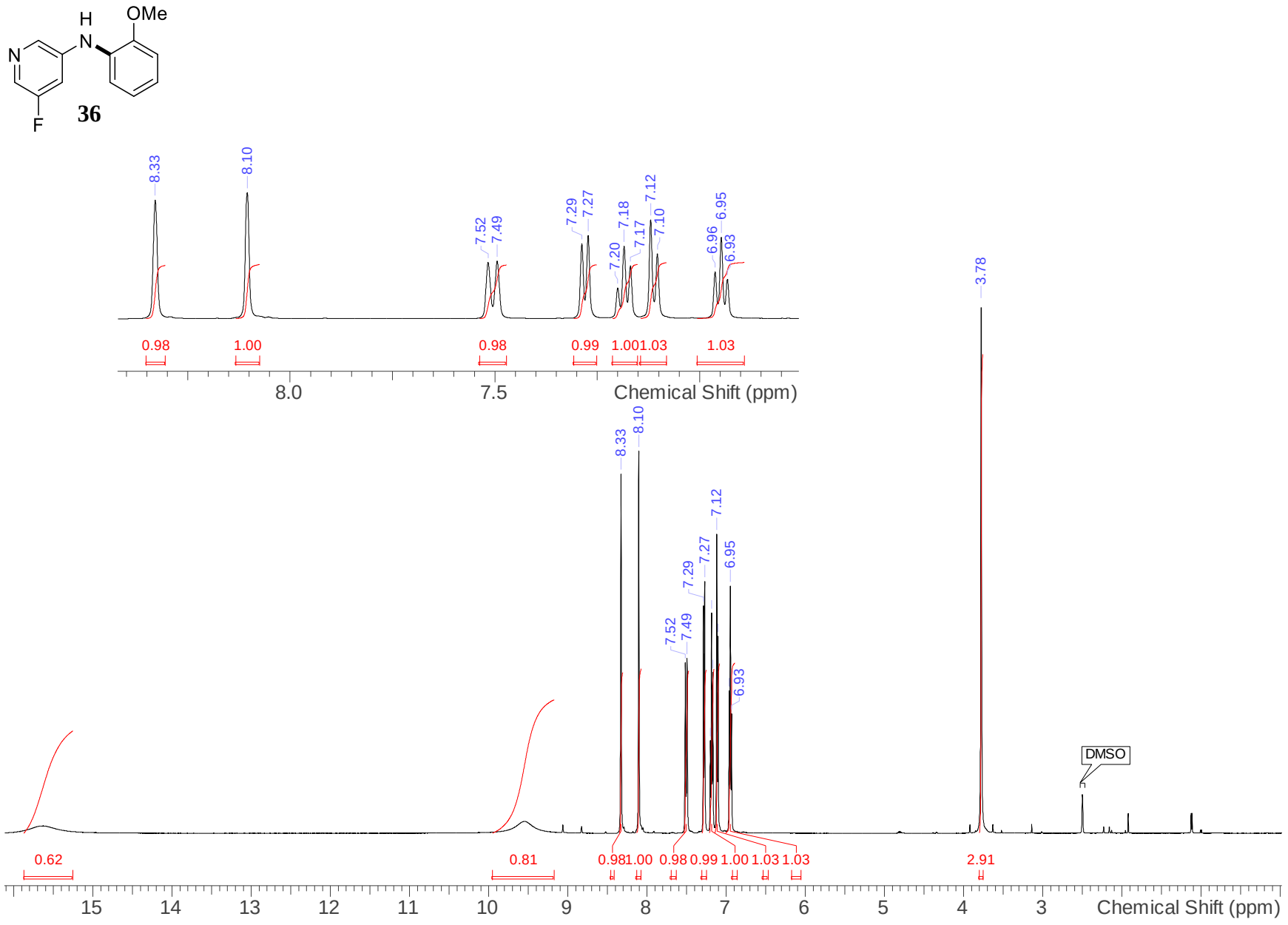

H
N
N
F
CO2Et

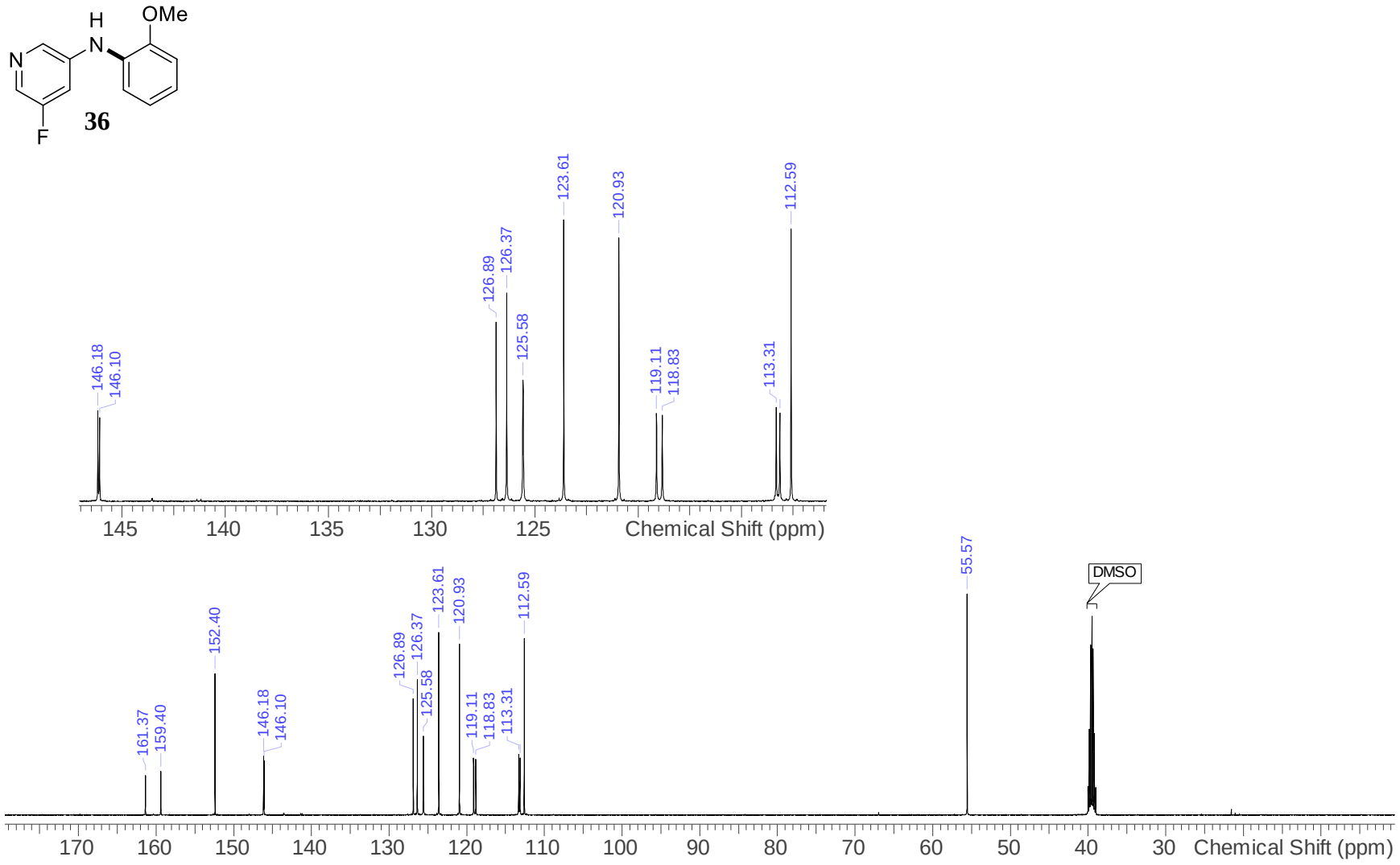
35


8.70
8.50
8.22
8.21
7.67
7.66
7.64
7.58
7.57
7.32
7.31
7.31
7.30
7.28
7.27
7.25
1.00
0.98
0.98
0.97
1.01
1.02
0.99
1.00
9.0
8.5
8.0
Chemical Shift (ppm)

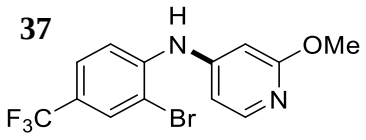

8.70
8.50
8.22
8.21
7.64
7.66
7.58
7.57
7.27
7.25
4.26
4.24
4.27
4.23
DMSO
DMSO*
DMSO*
1.29
1.26
1.28
1.00
0.98
0.98
0.97
1.01
1.02
0.99
1.00
2.00
3.11
11
10
9
8
7
6
5
4
3
2
1
Chemical Shift (ppm)

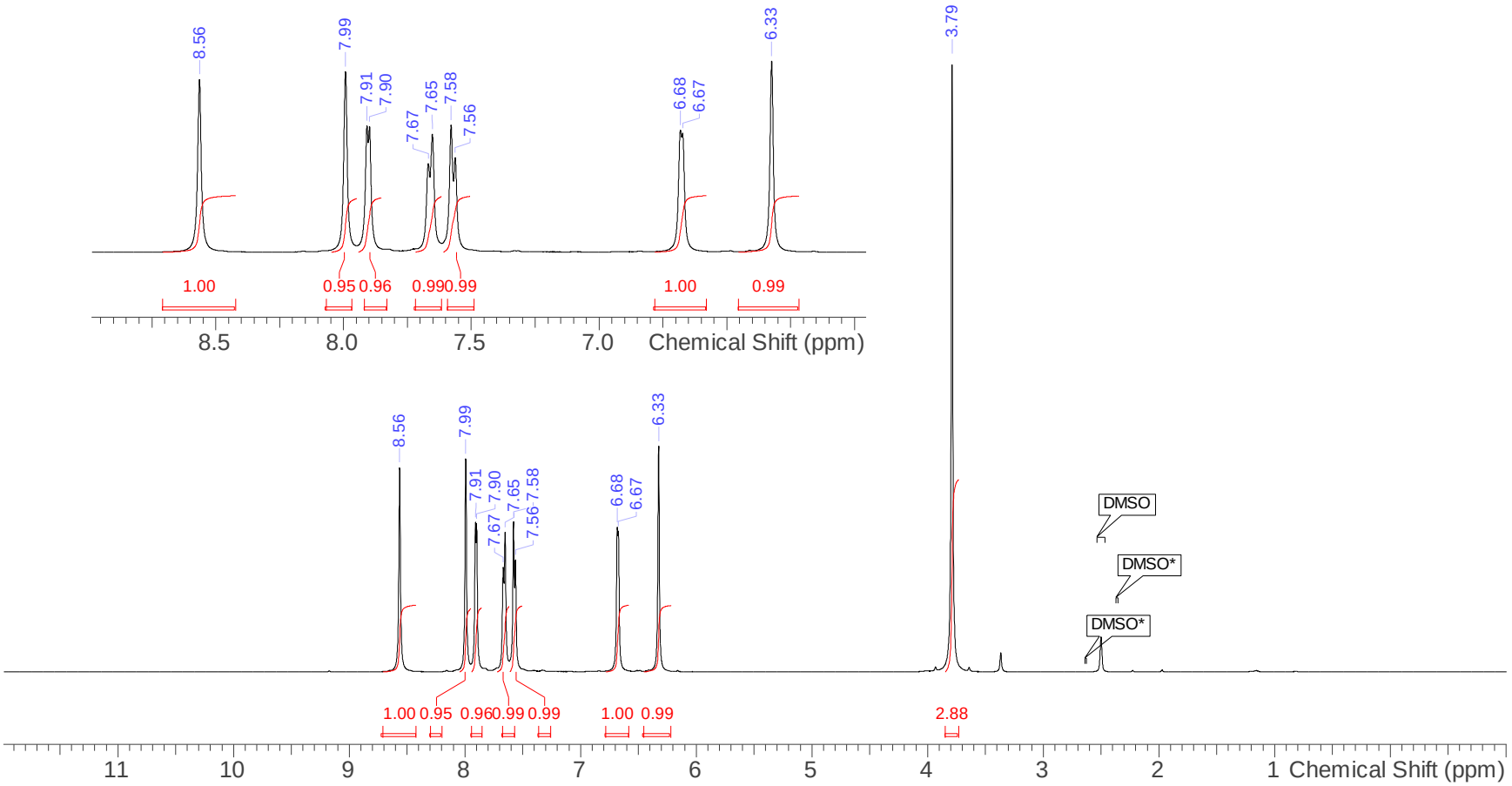

35
H
N
N
F
CO2Et
164.61
164.59
152.23
150.30
143.05
141.93
137.60
136.12
136.04
126.50
126.21
123.70
121.10
121.05
116.27
116.11
115.15
115.13
14.08
160
152
144
136
Chemical Shift (ppm)
60.40
DMSO
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
Chemical Shift (ppm)


H
N
OMe
N
F
36
8.33
8.10
7.52
7.49
7.29
7.27
7.20
7.18
7.17
7.12
7.10
6.96
6.95
6.93
0.98
1.00
0.98
0.99
1.00
1.03
1.03
8.0
7.5
Chemical Shift (ppm)
3.78
DMSO
0.62
0.81
0.98
1.00
0.98
0.99
1.00
1.03
1.03
2.91
15
14
13
12
11
10
9
8
7
6
5
4
3
Chemical Shift (ppm)

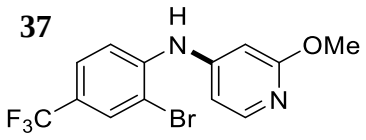

H
N
OMe
N
F
36
146.18
146.10
126.89
126.37
125.58
123.61
120.93
119.11
118.83
113.31
112.59
145
140
135
130
125
Chemical Shift (ppm)
161.37
159.40
152.40
146.18
146.10
126.89
126.37
125.58
123.61
120.93
119.11
118.83
113.31
112.59
55.57
DMSO
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
Chemical Shift (ppm)

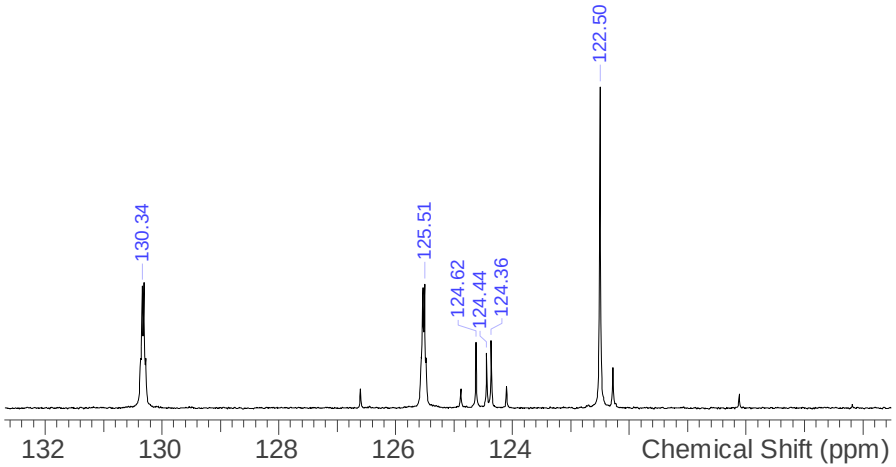
37

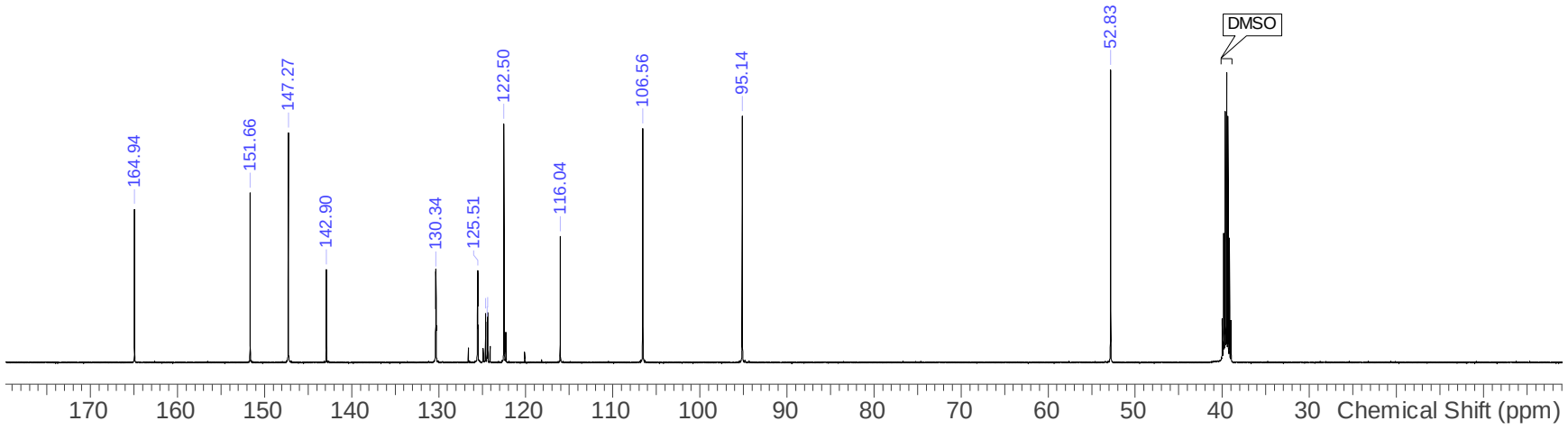

H
N
OMe
N
F3C
Br

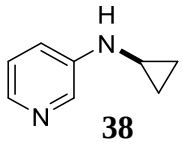

8.56
7.99
7.91
7.90
7.67
7.65
7.58
7.56
6.68
6.67
6.33
3.79
1.00
0.95
0.96
0.99
0.99
1.00
0.99
8.5
8.0
7.5
7.0
Chemical Shift (ppm)
DMSO
DMSO*
DMSO*
2.88
11
10
9
8
7
6
5
4
3
2
1
Chemical Shift (ppm)

37

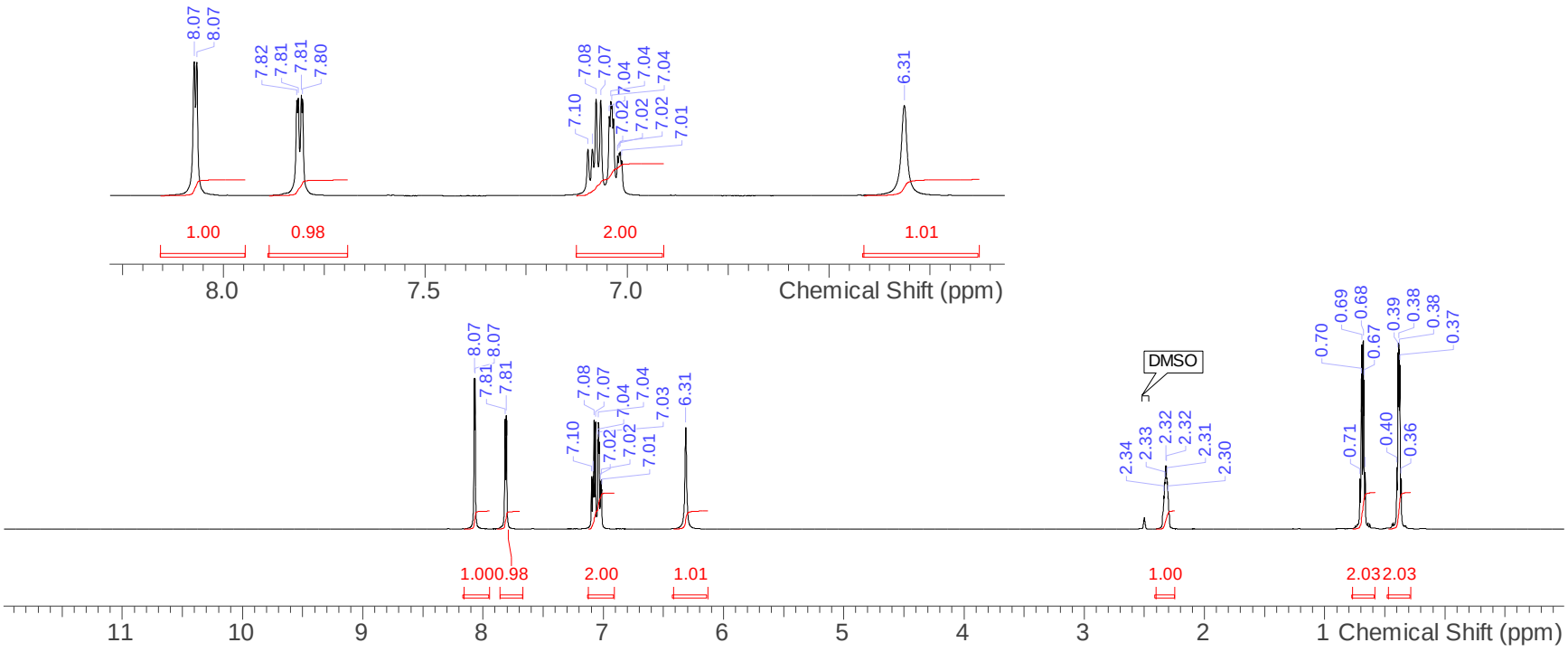

H
N
OMe
N
F3C
Br

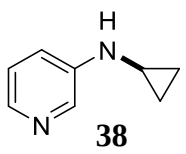

122.50
130.34
125.51
124.62
124.44
124.36
132
130
128
126
124
Chemical Shift (ppm)


52.83
DMSO
164.94
151.66
147.27
142.90
130.34
125.51
122.50
116.04
106.56
95.14
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
Chemical Shift (ppm)


H
N
N

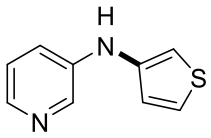
38


8.07
8.07
7.82
7.81
7.81
7.80
7.10
7.08
7.07
7.04
7.04
7.02
7.02
7.02
7.01
6.31
1.00
0.98
2.00
1.01
8.0
7.5
7.0
Chemical Shift (ppm)
8.07
8.07
7.81
7.81
7.10
7.08
7.07
7.04
7.04
7.03
7.02
7.02
7.01
6.31
DMSO
2.34
2.33
2.32
2.32
2.31
2.30
0.70
0.69
0.68
0.67
0.71
0.39
0.38
0.38
0.37
0.40
0.36
1.00
0.98
2.00
1.01
1.00
2.03
2.03
11
10
9
8
7
6
5
4
3
2
1
Chemical Shift (ppm)

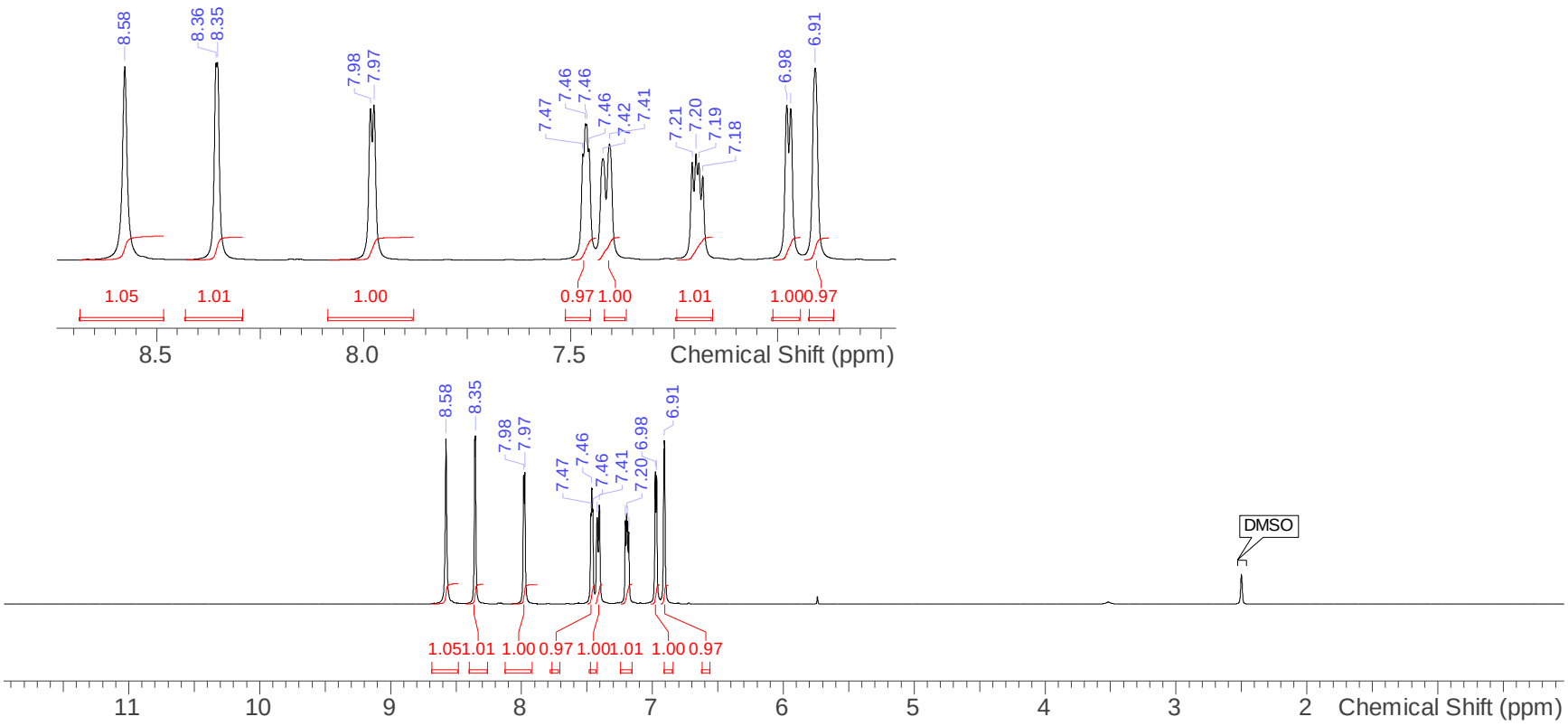


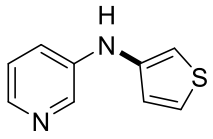
38

145.26
137.29
135.35
123.44
117.93
DMSO
24.08
6.69
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
Chemical Shift (ppm)

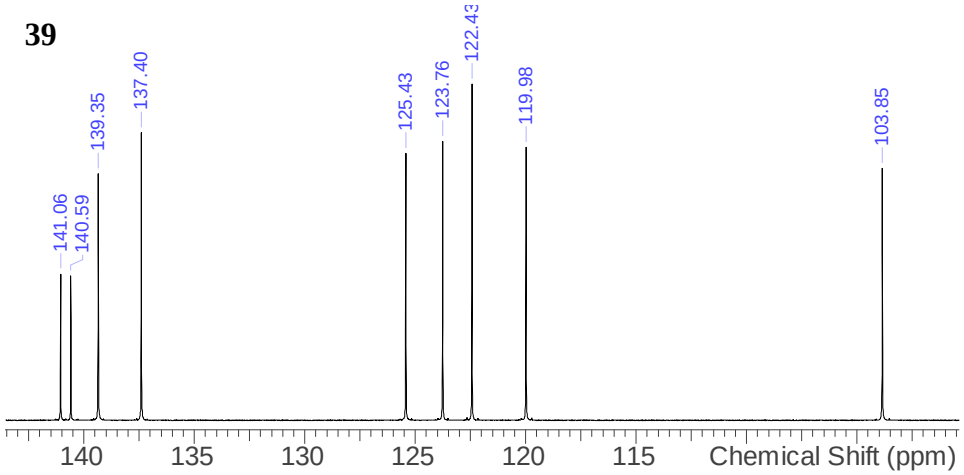


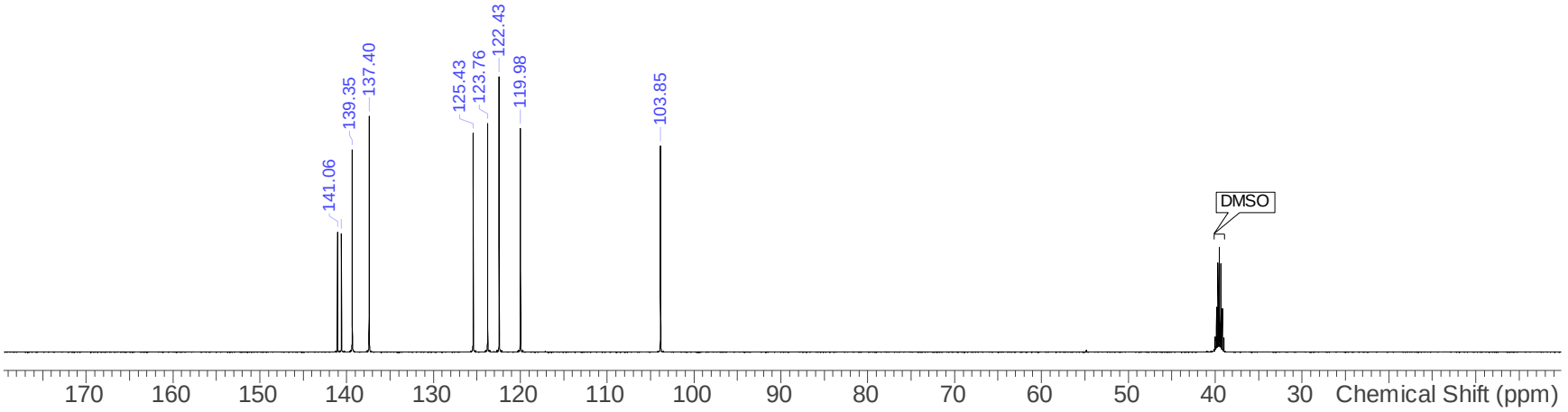
39

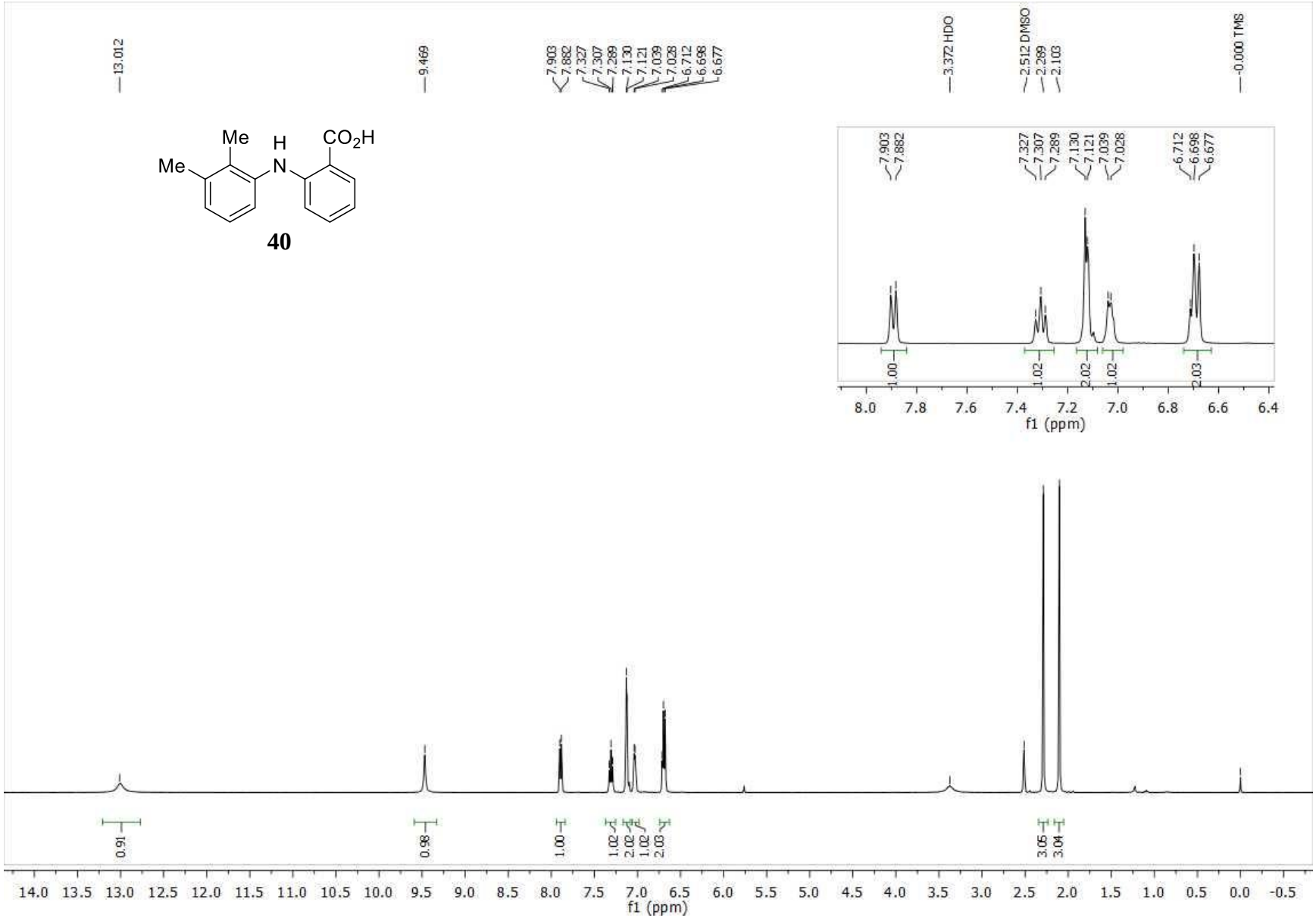

8.58
8.36
8.35
7.98
7.97
7.47
7.46
7.46
7.46
7.42
7.41
7.21
7.20
7.19
7.18
6.98
6.91
1.05
1.01
1.00
0.97
1.00
1.01
1.00
0.97
8.5
8.0
7.5
Chemical Shift (ppm)
8.58
8.35
7.98
7.97
7.47
7.46
7.46
7.41
7.20
6.98
6.91
DMSO
1.05
1.01
1.00
0.97
1.00
1.01
1.00
0.97
11
10
9
8
7
6
5
4
3
2
Chemical Shift (ppm)

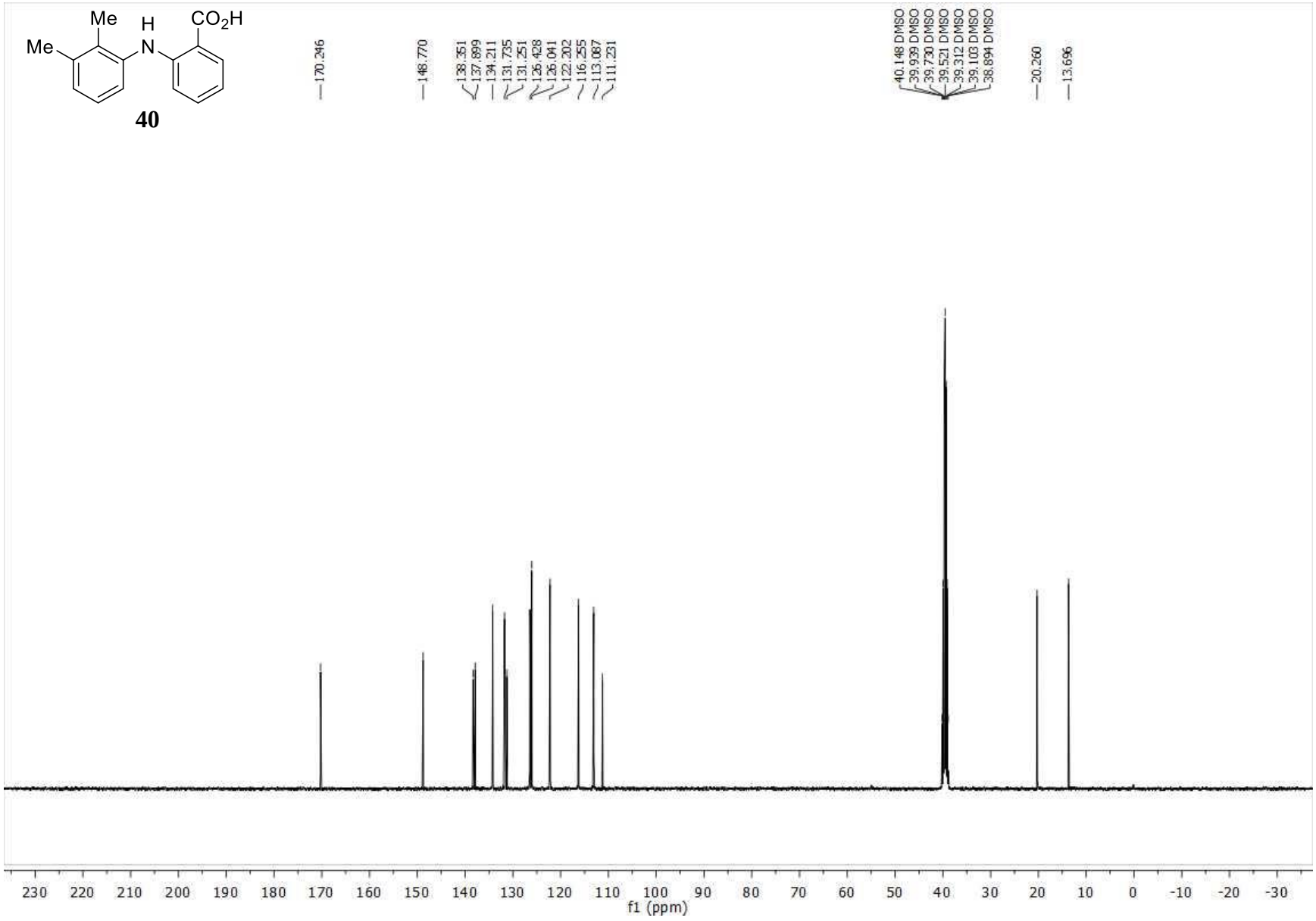

H
N
S
N

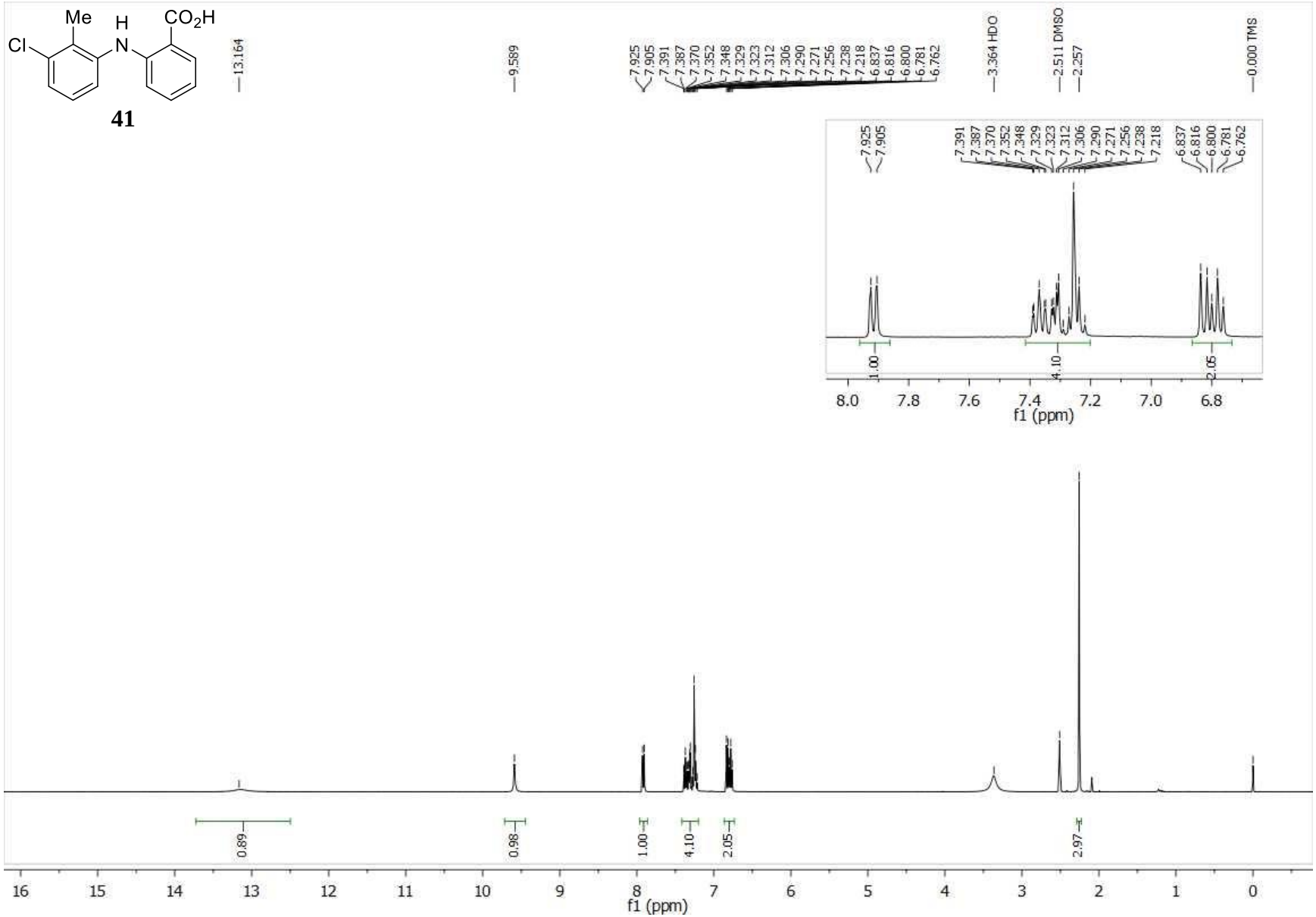
39

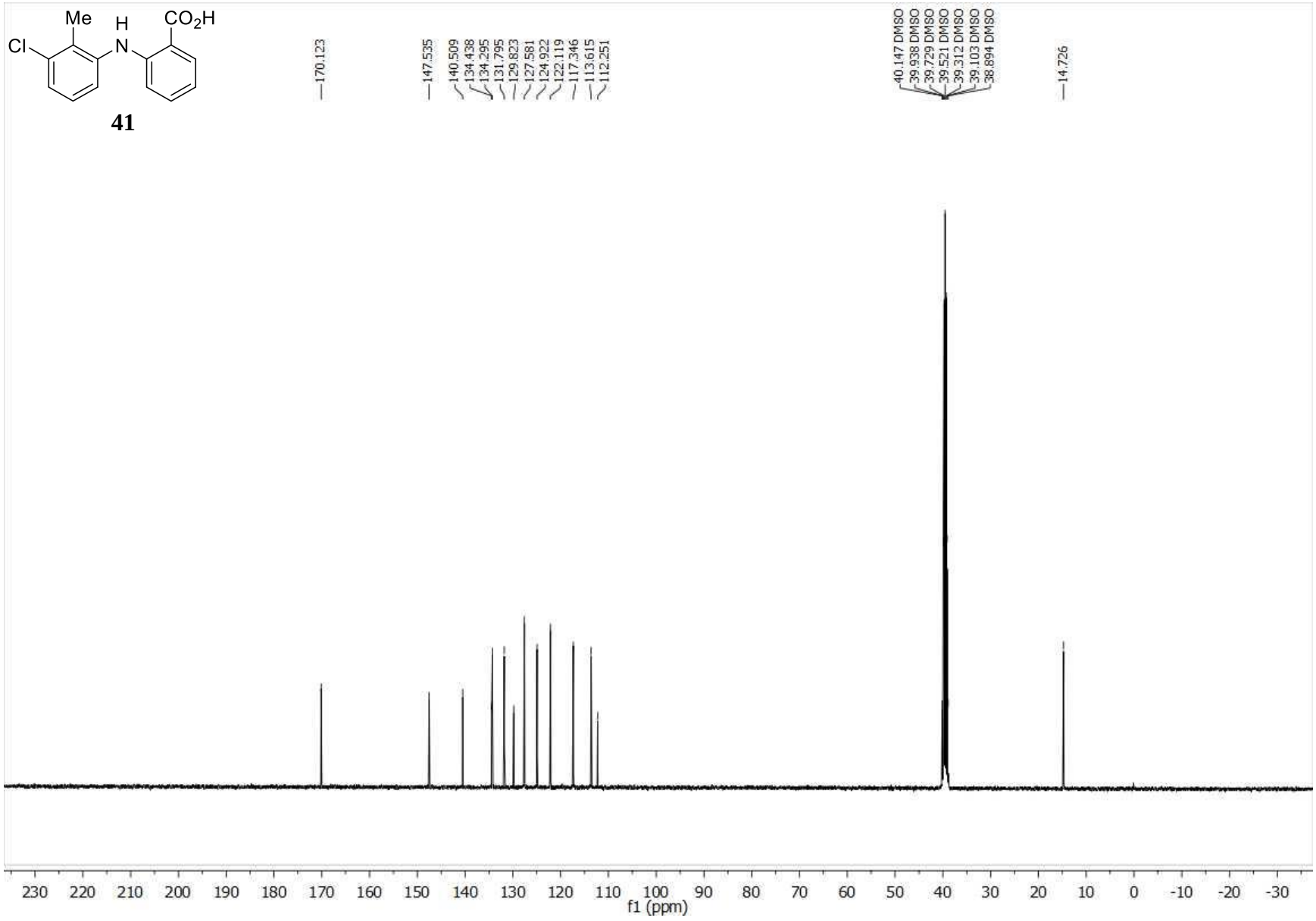

141.06
140.59
139.35
137.40
125.43
123.76
122.43
119.98
103.85
140
135
130
125
120
115
Chemical Shift (ppm)

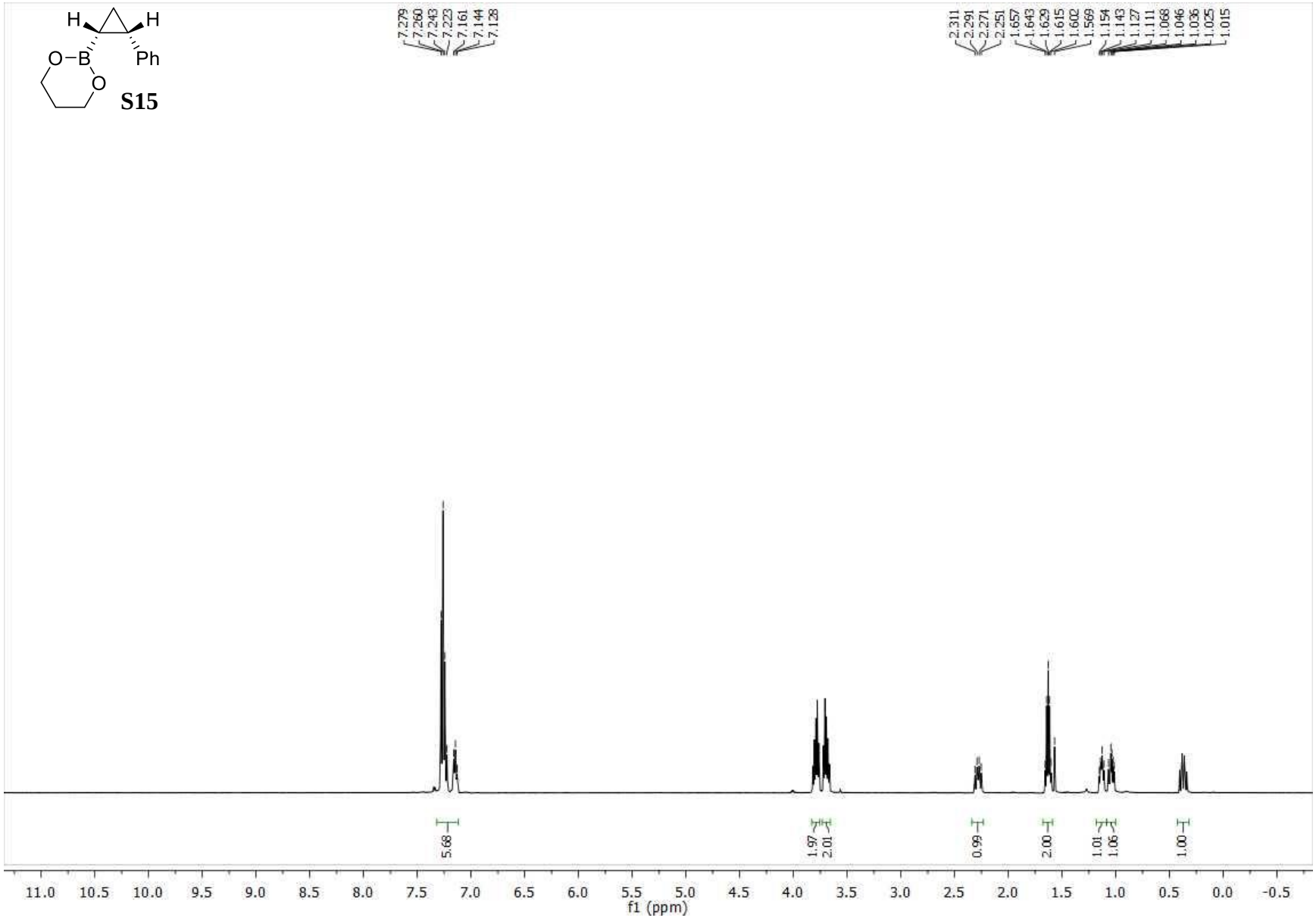

141.06
139.35
137.40
125.43
123.76
122.43
119.98
103.85
DMSO
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
Chemical Shift (ppm)

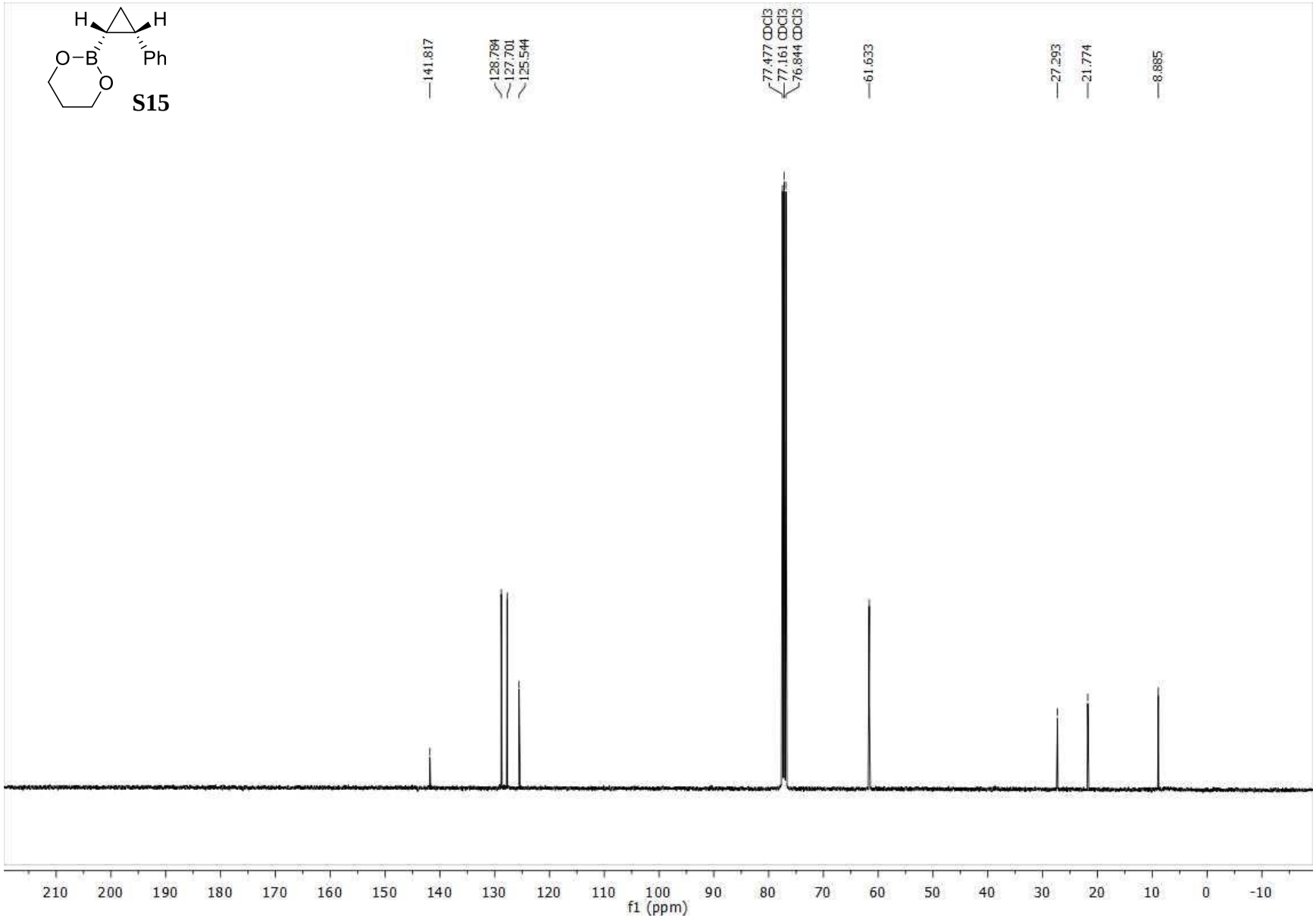

13.012
9.469
7.903
7.882
7.327
7.307
7.289
7.130
7.121
7.039
7.028
6.712
6.698
6.677
3.372 HDO
2.512 DMSO
2.289
2.103
0.000 TMS
Me
H
N
CO2H
Me
40
f1 (ppm)

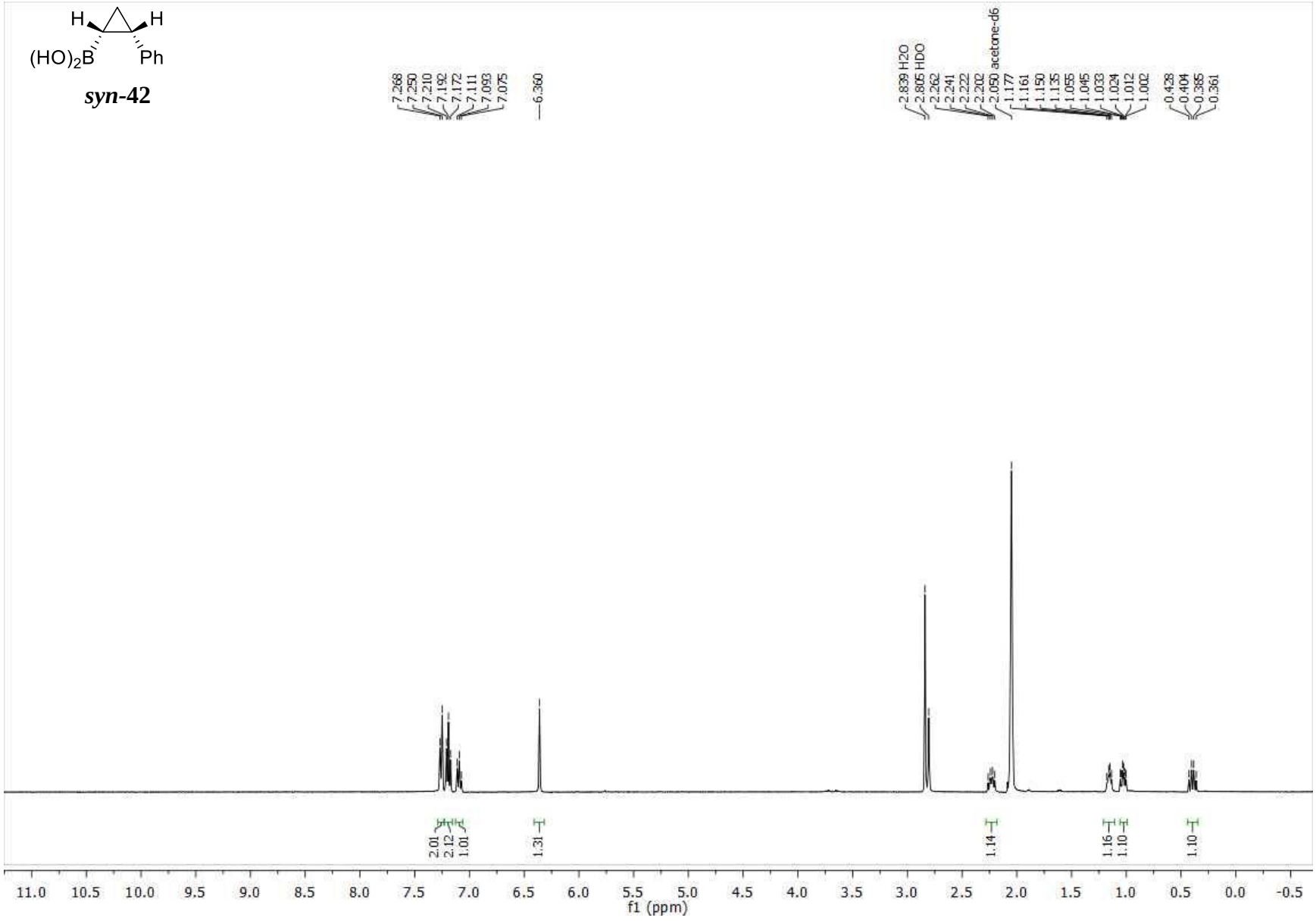

Me
H
N
CO2H
Me
40
170.246
148.770
138.351
137.899
134.211
131.735
131.251
126.428
126.041
122.202
116.255
113.087
111.231
40.148 DMSO
39.939 DMSO
39.730 DMSO
39.521 DMSO
39.312 DMSO
39.103 DMSO
38.894 DMSO
20.260
13.696
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30
f1 (ppm)

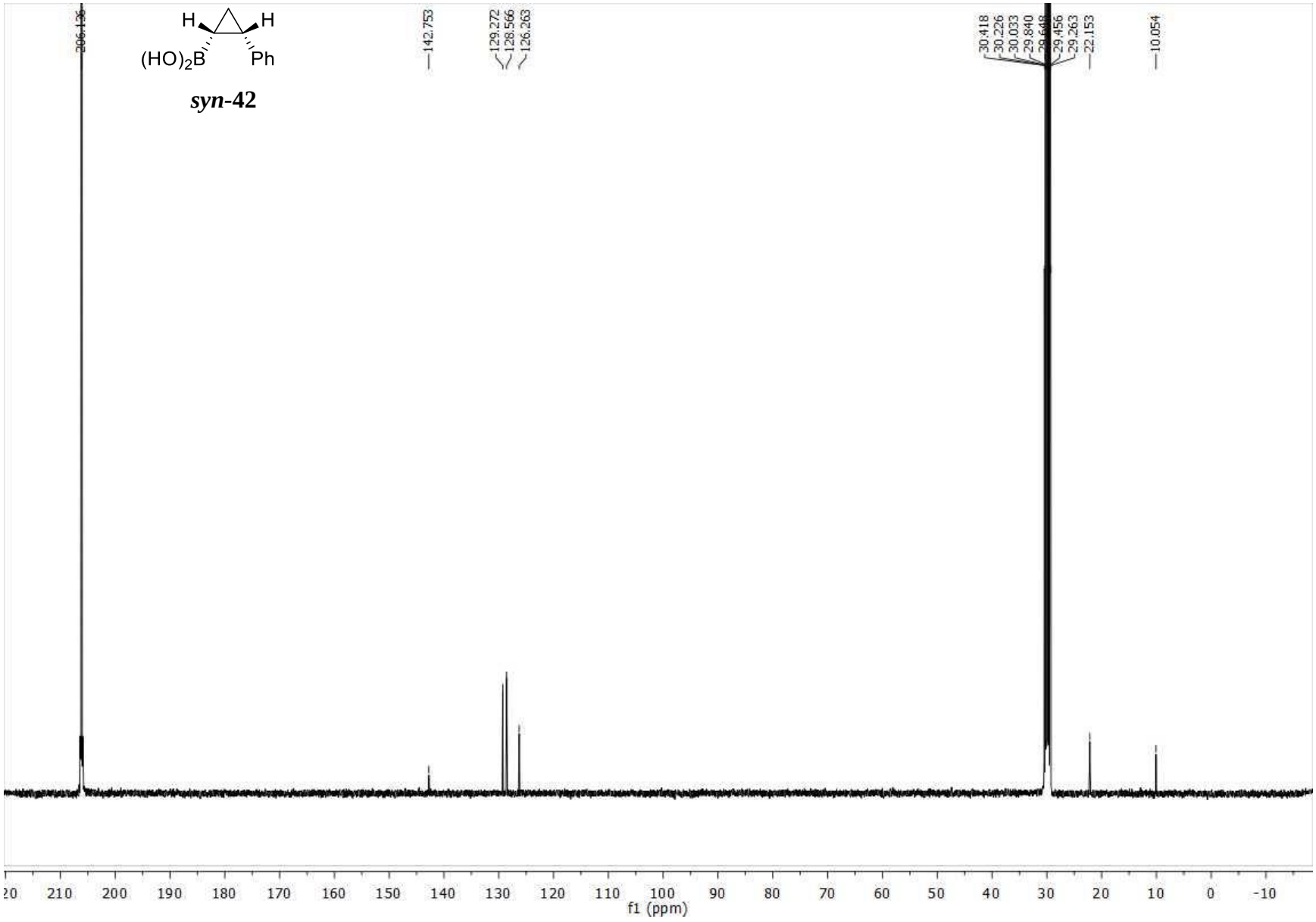

Me
H
N
CO2H
Cl
41
13.164
9.589
7.925
7.905
7.391
7.387
7.370
7.352
7.348
7.329
7.323
7.312
7.306
7.290
7.271
7.256
7.238
7.218
6.837
6.816
6.800
6.781
6.762
3.364 HDO
2.511 DMSO
2.257
0.000 TMS
1.00
4.10
2.05
f1 (ppm)
0.89
0.98
1.00
4.10
2.05
2.97
f1 (ppm)


Me
H
N
CO2H
Cl
41
170.123
147.535
140.509
134.438
134.295
131.795
129.823
127.581
124.922
122.119
117.346
113.615
112.251
40.147 DMSO
39.938 DMSO
39.729 DMSO
39.521 DMSO
39.312 DMSO
39.103 DMSO
38.894 DMSO
14.726
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30
f1 (ppm)

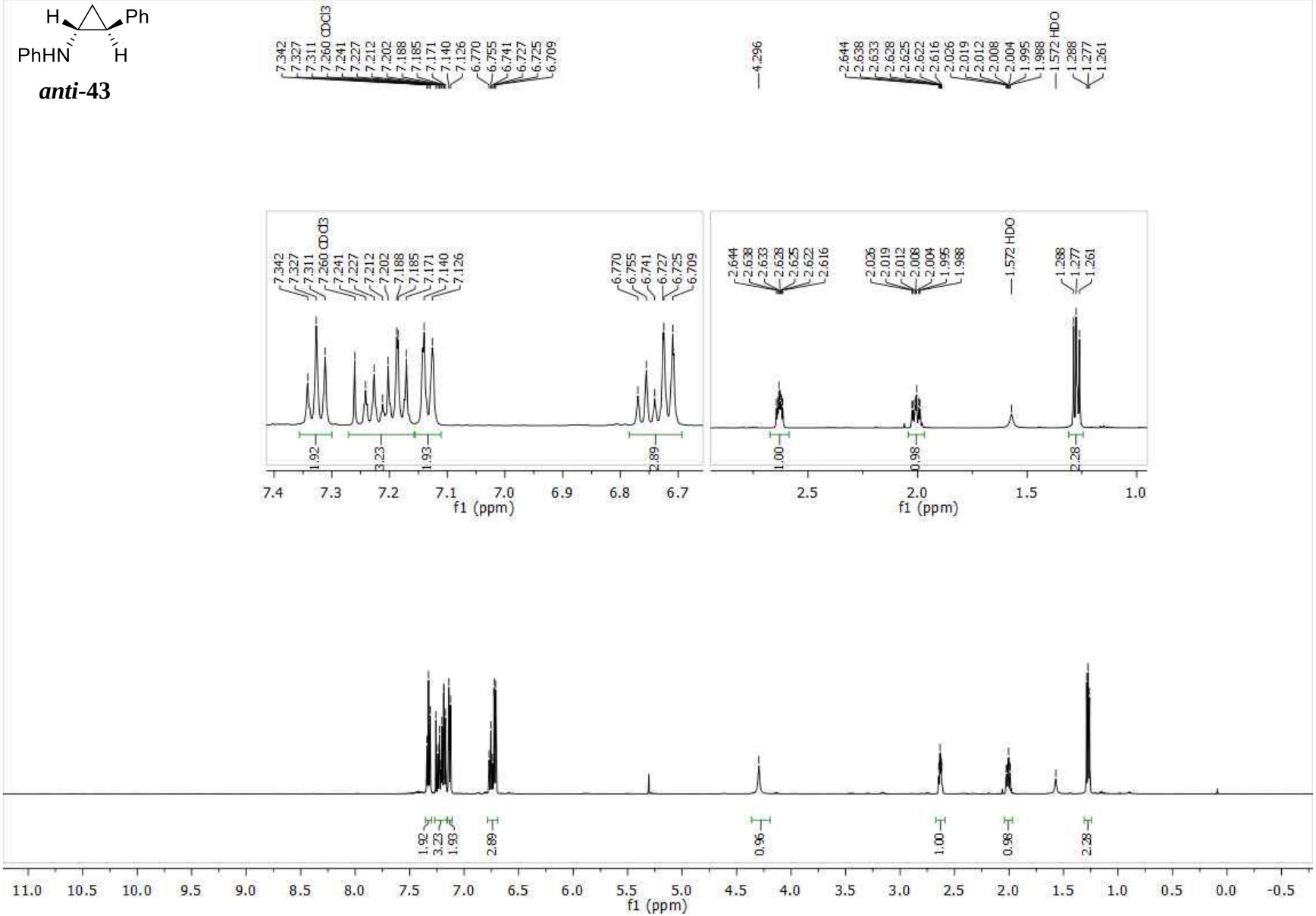

H
H
O
B
O
Ph
S15
7.279
7.260
7.243
7.223
7.161
7.144
7.128
2.311
2.291
2.271
2.251
1.657
1.643
1.629
1.615
1.602
1.569
1.154
1.143
1.127
1.111
1.068
1.046
1.036
1.025
1.015
5.68
1.97
2.01
0.99
2.00
1.01
1.06
1.00
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

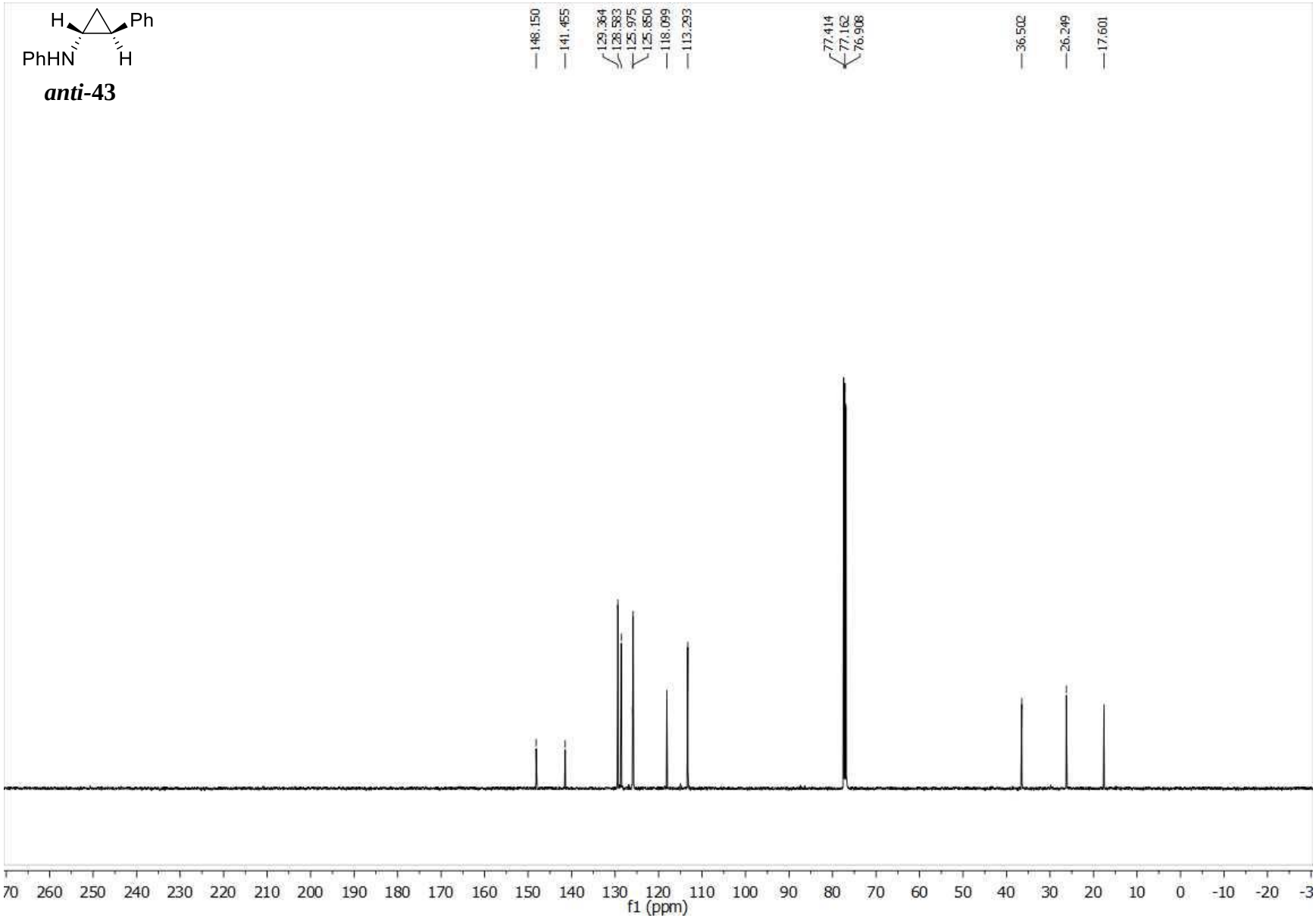

H
H
O−B
Ph
O
S15
141.817
128.784
127.701
125.544
77.477 CDCl3
77.161 CDCl3
76.844 CDCl3
61.633
27.293
21.774
8.885
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

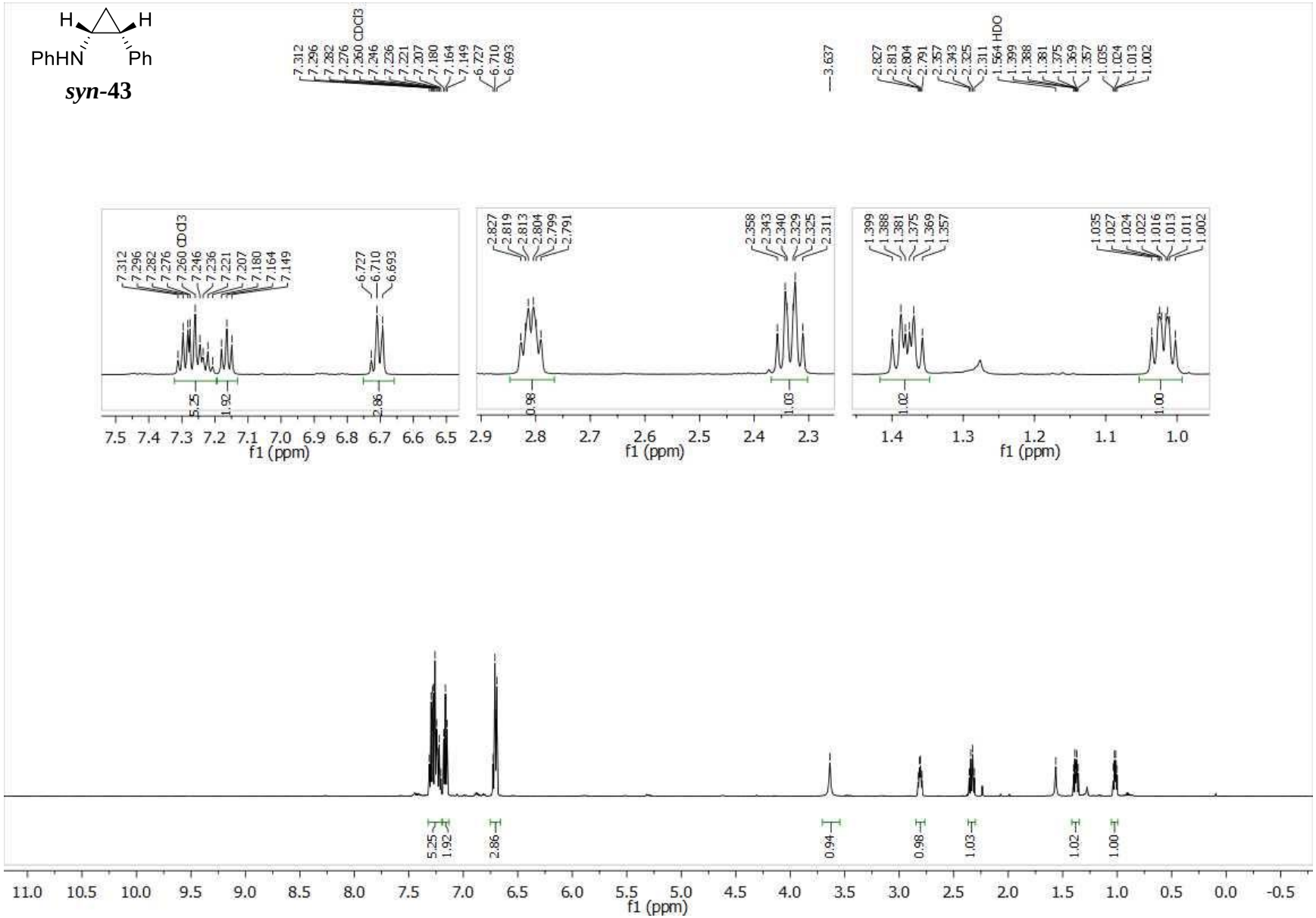

H
H
(HO)2B
Ph
syn-42
7.268
7.250
7.210
7.192
7.172
7.111
7.093
7.075
6.360
2.839 H2O
2.805 HDO
2.262
2.241
2.222
2.202
2.050 acetone-d6
1.177
1.161
1.150
1.135
1.055
1.045
1.033
1.024
1.012
1.002
0.428
0.404
0.385
0.361
2.01
2.12
1.01
1.31
1.14
1.16
1.10
1.10
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

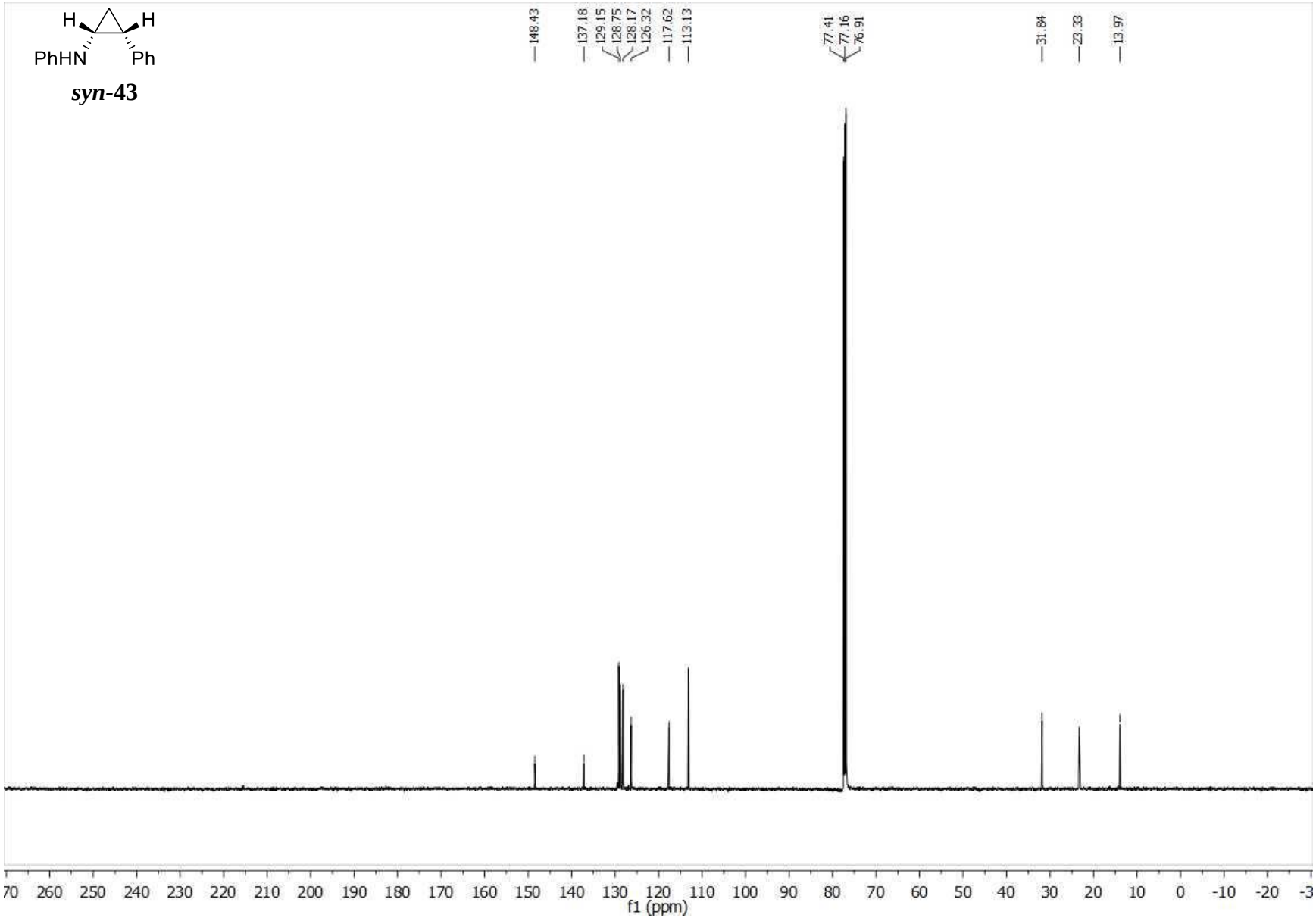

206.136
142.753
129.272
128.566
126.263
30.418
30.226
30.033
29.840
29.648
29.456
29.263
22.153
10.054
H
H
(HO)2B
Ph
f1 (ppm)

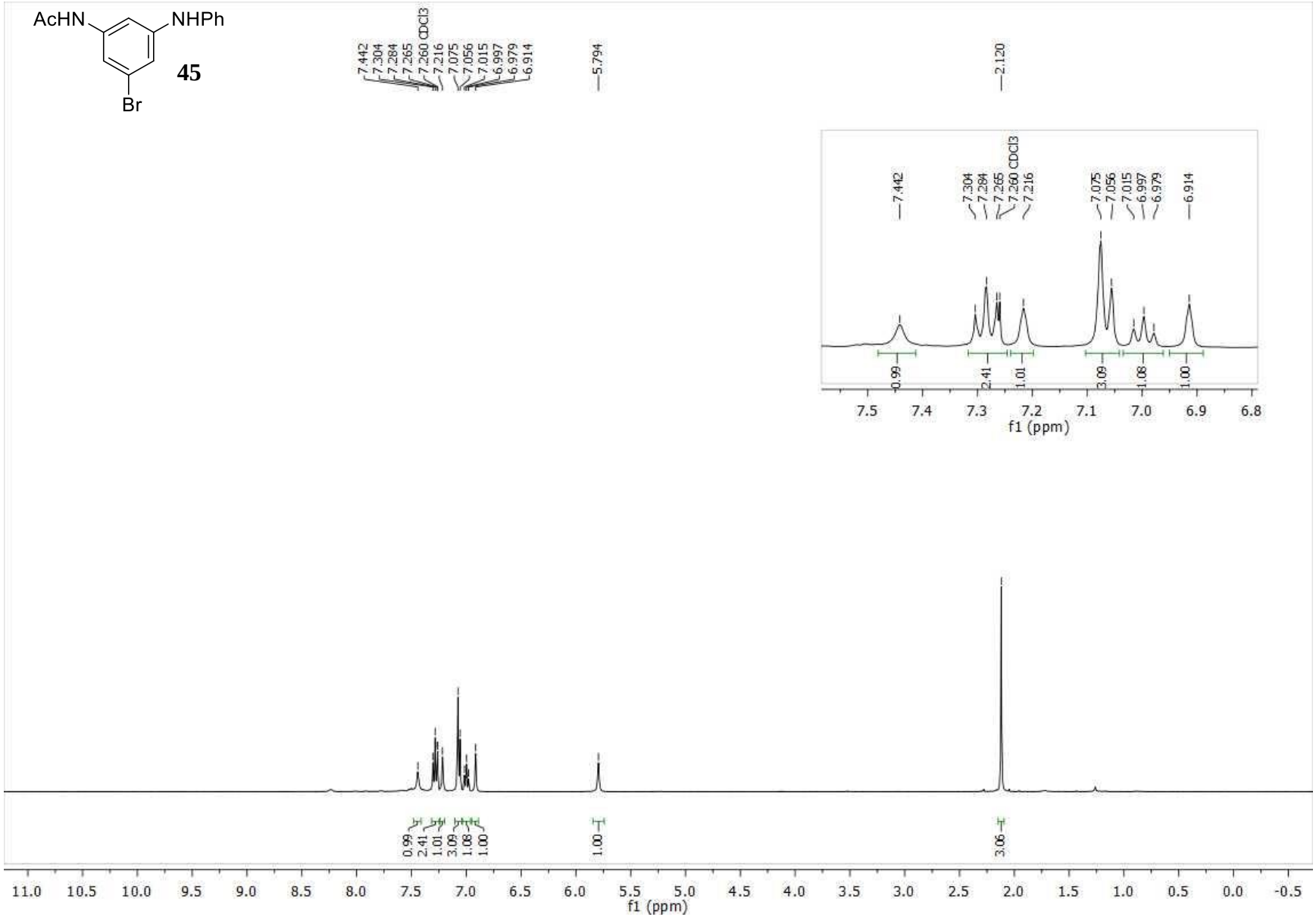
***syn*-42**

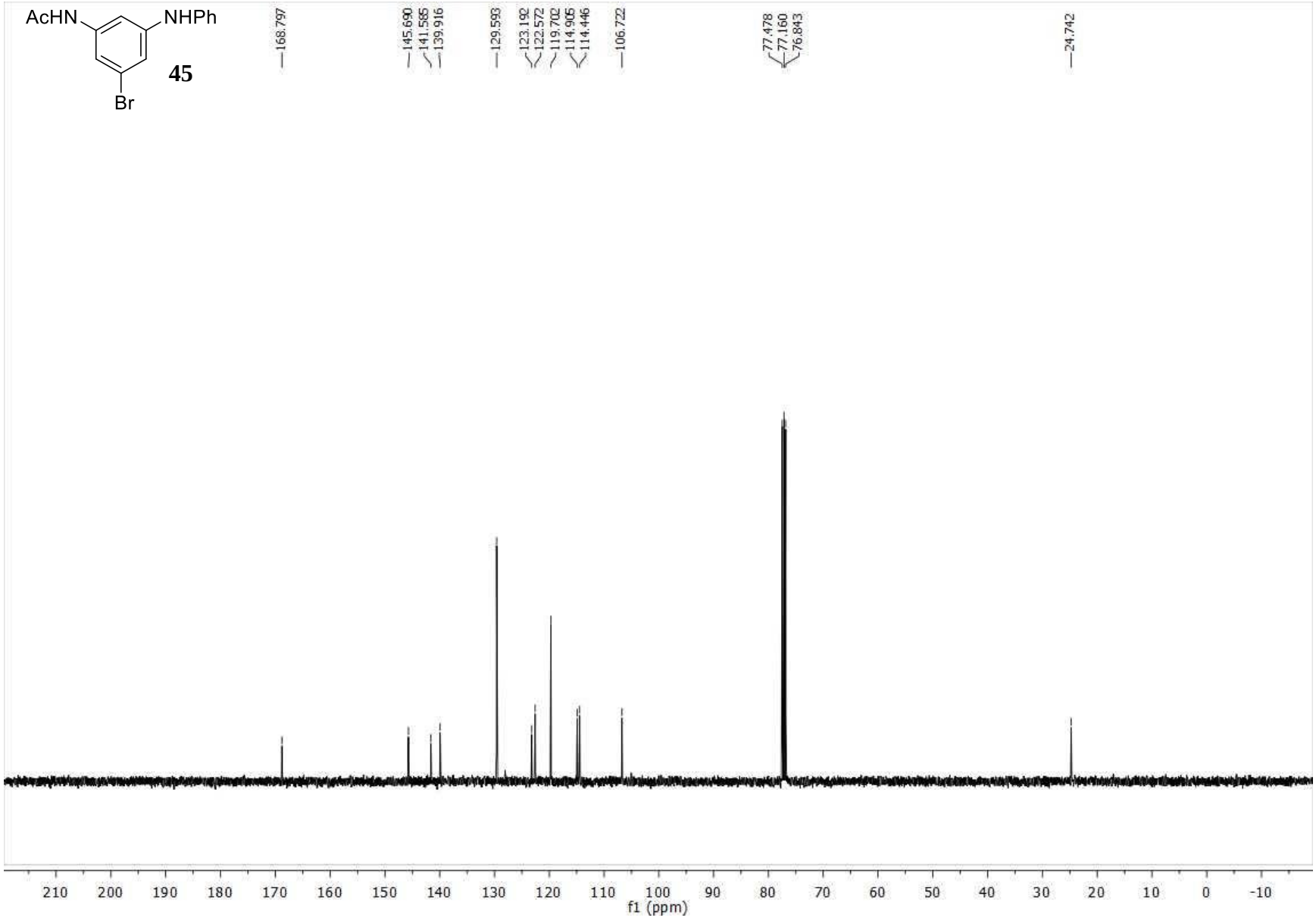

H
Ph
PhHN
H
anti-43
7.342
7.327
7.311
7.260 CDCl3
7.241
7.227
7.212
7.202
7.188
7.185
7.171
7.140
7.126
6.770
6.755
6.741
6.727
6.725
6.709
4.296
2.644
2.638
2.633
2.628
2.625
2.622
2.616
2.026
2.019
2.012
2.008
2.004
1.995
1.988
1.572 HDO
1.288
1.277
1.261
1.92
3.23
1.93
2.89
1.00
0.98
2.28
f1 (ppm)
0.96

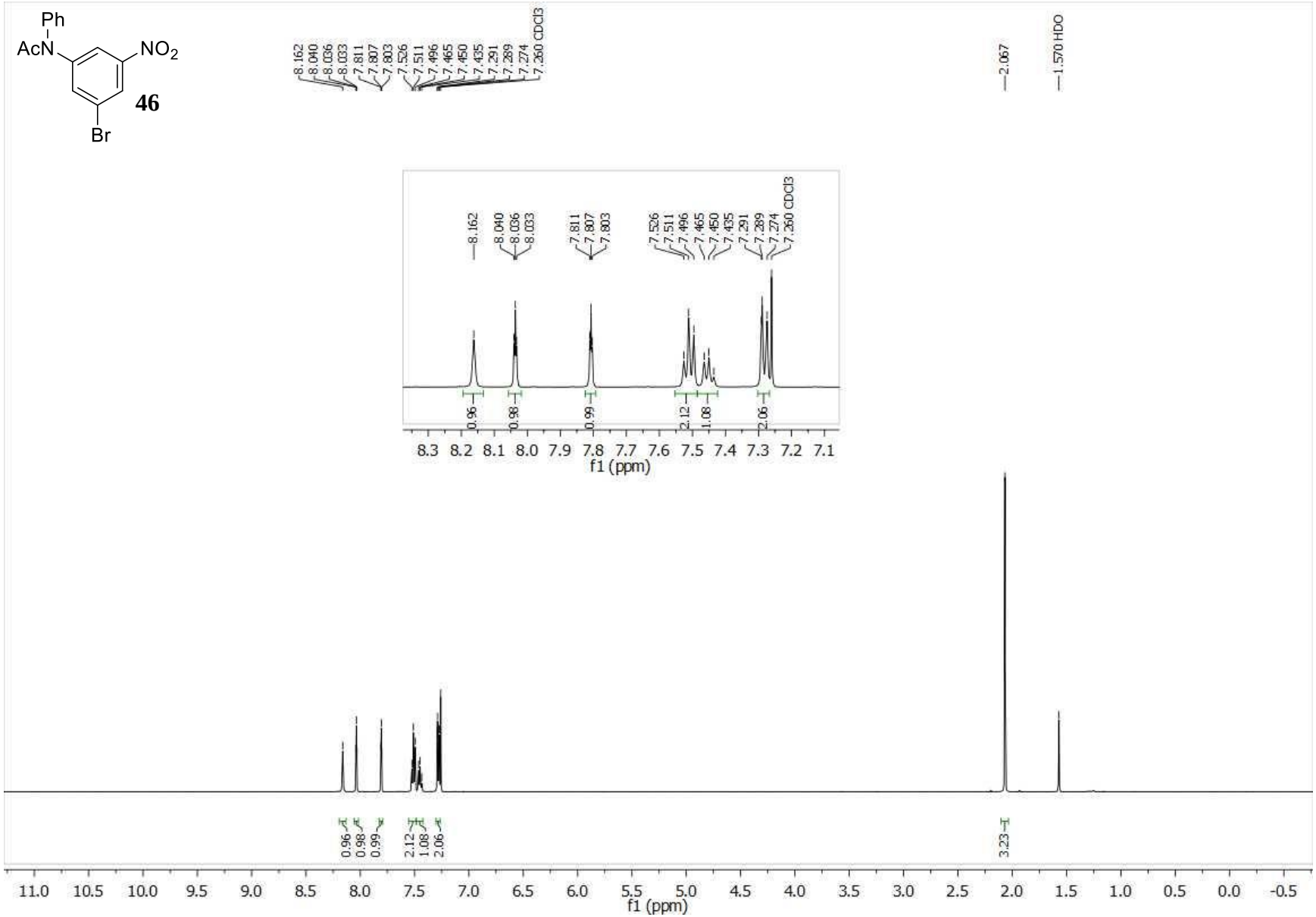

H
Ph
PhHN
H
anti-43
148.150
141.455
129.364
128.583
125.975
125.850
118.099
113.293
77.414
77.162
76.908
36.502
26.249
17.601
f1 (ppm)

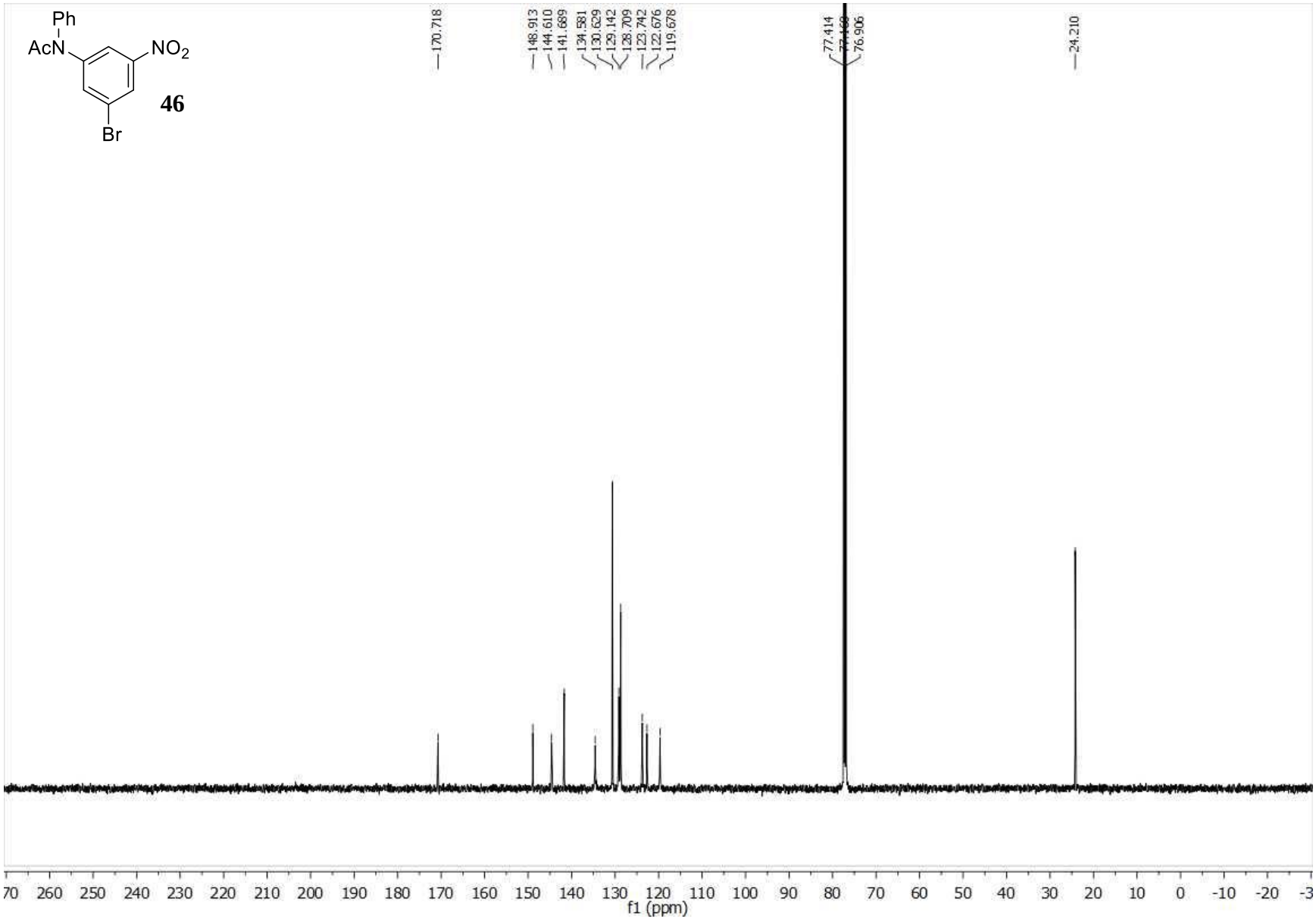

H
H
PhHN
Ph
syn-43
7.312
7.296
7.282
7.276
7.260 CDCl3
7.246
7.236
7.221
7.207
7.180
7.164
7.149
6.727
6.710
6.693
3.637
2.827
2.813
2.804
2.791
2.357
2.343
2.325
2.311
1.564 HDO
1.399
1.388
1.381
1.375
1.369
1.357
1.035
1.027
1.024
1.013
1.002
5.25
1.92
2.86
0.98
1.03
1.02
1.00
0.94
f1 (ppm)

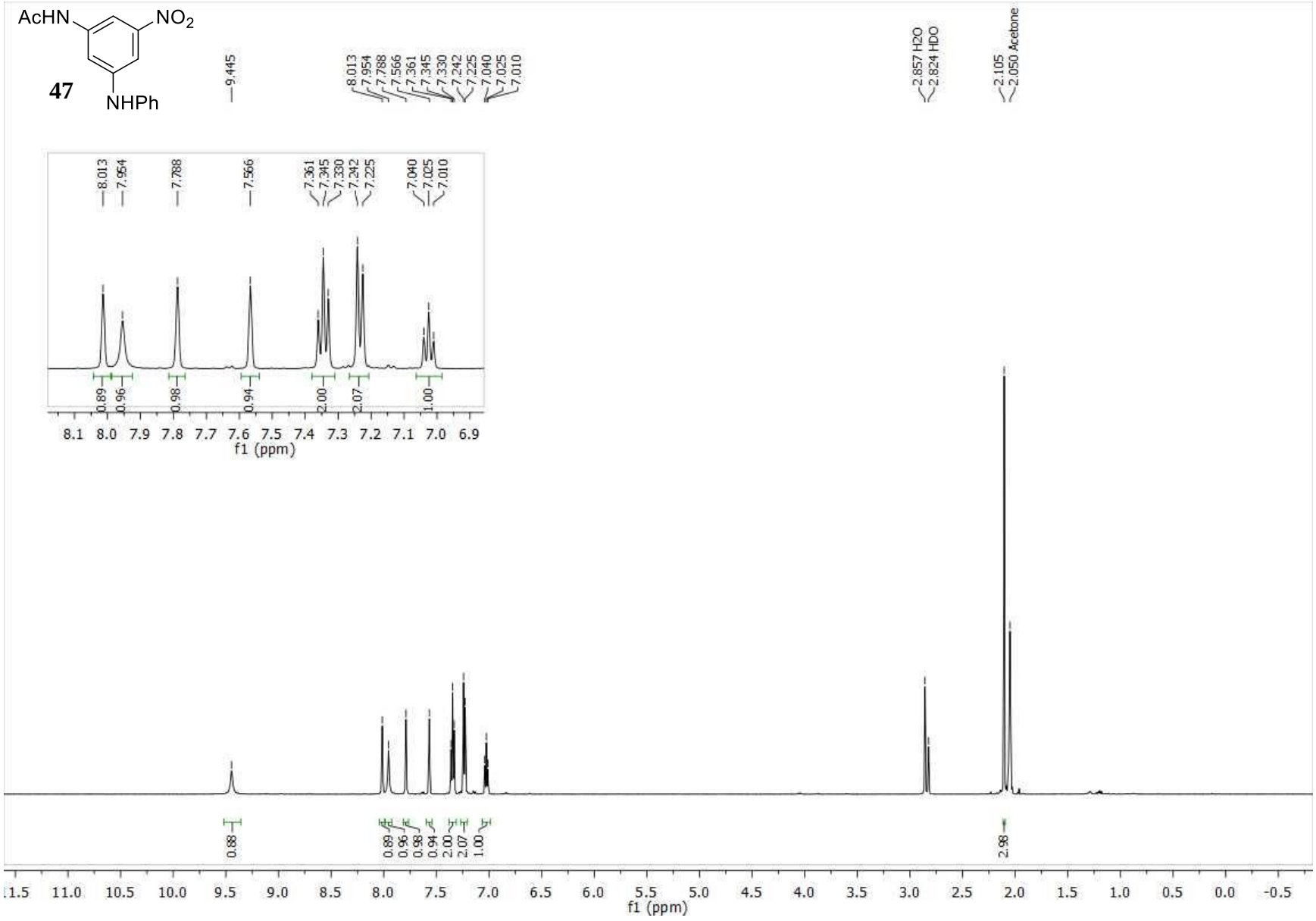

H
H
PhHN
Ph
syn-43
148.43
137.18
129.15
128.75
128.17
126.32
117.62
113.13
77.41
77.16
76.91
31.84
23.33
13.97
f1 (ppm)

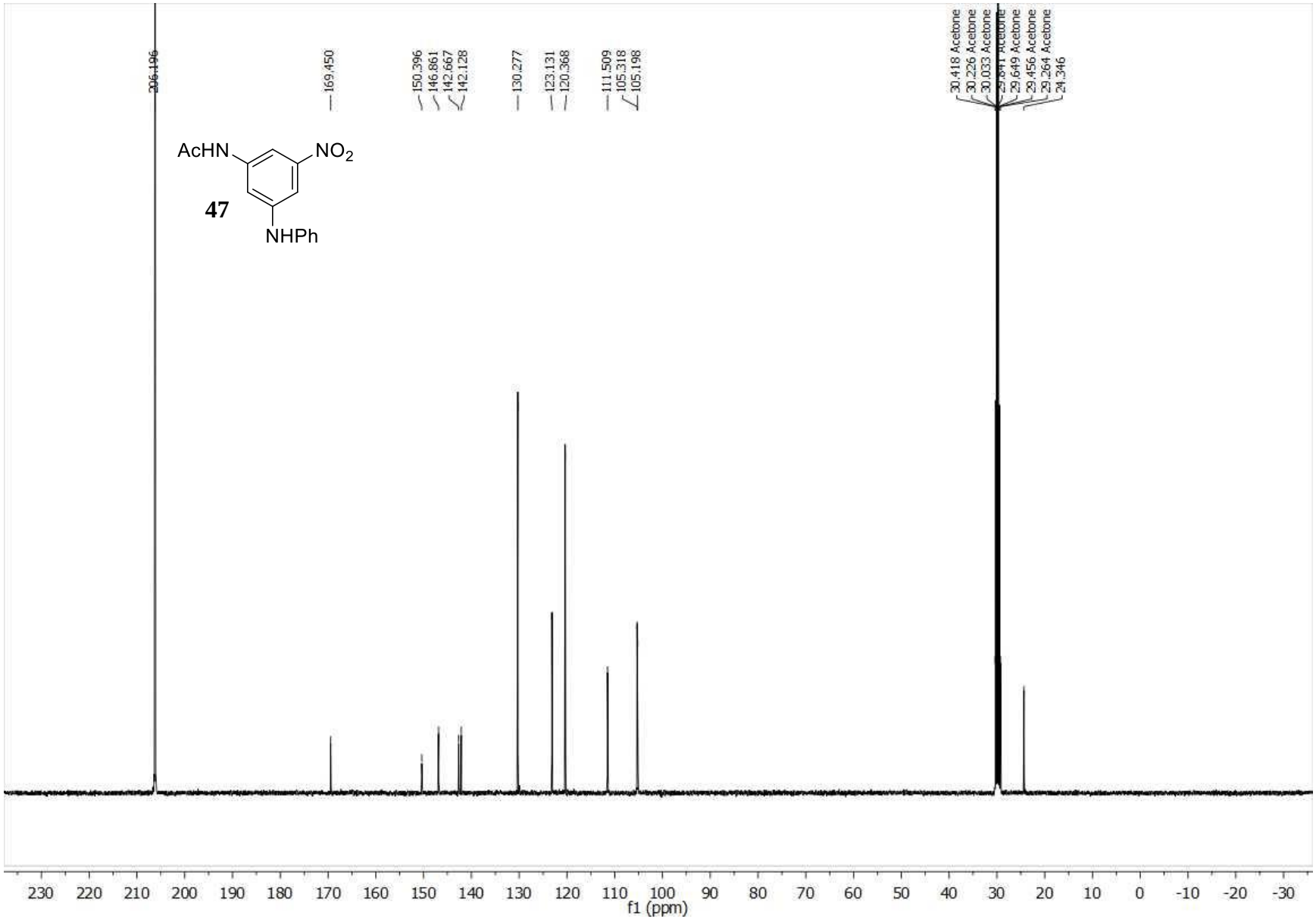

AcHN
NHPh
Br
45
7.442
7.304
7.284
7.265
7.260 CDCl3
7.216
7.075
7.056
7.015
6.997
6.979
6.914
5.794
2.120
0.99
2.41
1.01
3.09
1.08
1.00
1.00
3.06
f1 (ppm)


AcHN
NHPh
Br
45
168.797
145.690
141.585
139.916
129.593
123.192
122.572
119.702
114.905
114.446
106.722
77.478
77.160
76.843
24.742
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Ph
AcN
NO2
Br
46
8.162
8.040
8.036
8.033
7.811
7.807
7.803
7.526
7.511
7.496
7.465
7.450
7.435
7.291
7.289
7.274
7.260 CDCl3
2.067
1.570 HDO
0.96
0.98
0.99
2.12
1.08
2.06
3.23
f1 (ppm)


Ph
AcN
NO2
Br
46
170.718
148.913
144.610
141.689
134.581
130.629
129.142
128.709
123.742
122.676
119.678
77.414
76.906
24.210
f1 (ppm)


AcHN
NO2
NHPh
47
9.445
8.013
7.954
7.788
7.566
7.361
7.345
7.330
7.242
7.225
7.040
7.025
7.010
2.857 H2O
2.824 HDO
2.105
2.050 Acetone
0.89
0.96
0.98
0.94
2.00
2.07
1.00
2.98
f1 (ppm)


206.196
169.450
150.396
146.861
142.667
142.128
130.277
123.131
120.368
111.509
105.318
105.198
30.418 Acetone
30.226 Acetone
30.033 Acetone
29.649 Acetone
29.456 Acetone
29.264 Acetone
24.346
AcHN
NO2
NHPh
47
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30
f1 (ppm)

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