# Preparation of the Core Structure of *Aspidosperma* and *Strychnos* Alkaloids from Aryl Azides by a Cascade Radical Cyclization

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# 1. General Information

### Techniques

All reactions requiring anhydrous conditions were performed in heat-gun, oven or flame dried glassware under an argon atmosphere. An ice bath was used to obtain a temperature of 0 °C. A dry ice/acetone bath was used to obtain −78 and −20 °C. Silica gel 60 Å (40–63 μm) from Silicycle was used for flash column chromatography. Thin layer chromatography (TLC) was performed on Silicycle silica gel 60 $F_{254}$ plates, visualization under UV light (254 nm) and/or by dipping in a solution of $(NH_4)_2MoO_4$ (15.0 g), $Ce(SO_4)_2$ (0.5 g), $H_2O$ (90 mL), conc. $H_2SO_4$ (10 mL); or $KMnO_4$ (3 g), $K_2CO_3$ (20 g) and NaOH 5% (3 mL) in $H_2O$ (300 mL) and subsequent heating. Anhydrous sodium sulfate was used as drying reagent.

### Materials

Commercial reagents were used without further purification unless otherwise stated. Solvents for reactions (predistilled THF, predistilled $Et_2O$, $CH_3CN$, $CH_2Cl_2$, benzene, *n*-hexane, toluene) were filtered over columns of dried neutral aluminium oxide under a positive pressure of argon. Solvents for extractions and flash column chromatography were of technical grade and were distilled prior to use. Triethylborane solutions (1 M in hexane) were prepared from pure triethylborane (BASF or Aldrich, 2.9 mL, 20 mmol, in 17.1 mL of hexane). The solutions were stored at rt under an argon atmosphere in round bottom flasks closed with two septa and were generally used within two months.

### Instrumentations

$^1H$ and $^{13}C$ NMR spectra were recorded on a Bruker AVANCE-300 spectrometer operating at 300 MHz for $^1H$ and 75 MHz for $^{13}C$ at 22 °C unless otherwise stated. Some $^1H$ and $^{13}C$ NMR spectra were recorded on a Bruker Avance II-400 spectrometer ($^1H$: 400 MHz; $^{13}C$: 100 MHz). Chemical shifts ($\delta$) are reported in parts per million (ppm) using the residual solvent ($CHCl_3$: $\delta = 7.26$ for $^1H$ NMR spectra and $CDCl_3$: $\delta = 77.00$ for $^{13}C$ NMR spectra) or $Si(CH_3)_4$ ($\delta = 0.00$ for $^1H$ NMR spectra) as an internal standard. Multiplicities are given as s (singlet), d (doublet), t (triplet), q (quadruplet), m (multiplet), and br (broad). Coupling constants ($J$) are reported in Hz. Infrared spectra were recorded on a Jasco FT-IR-460 Plus spectrometer equipped with a Specac MKII Golden Gate Single Reflection Diamond ATR System and are reported in wave numbers

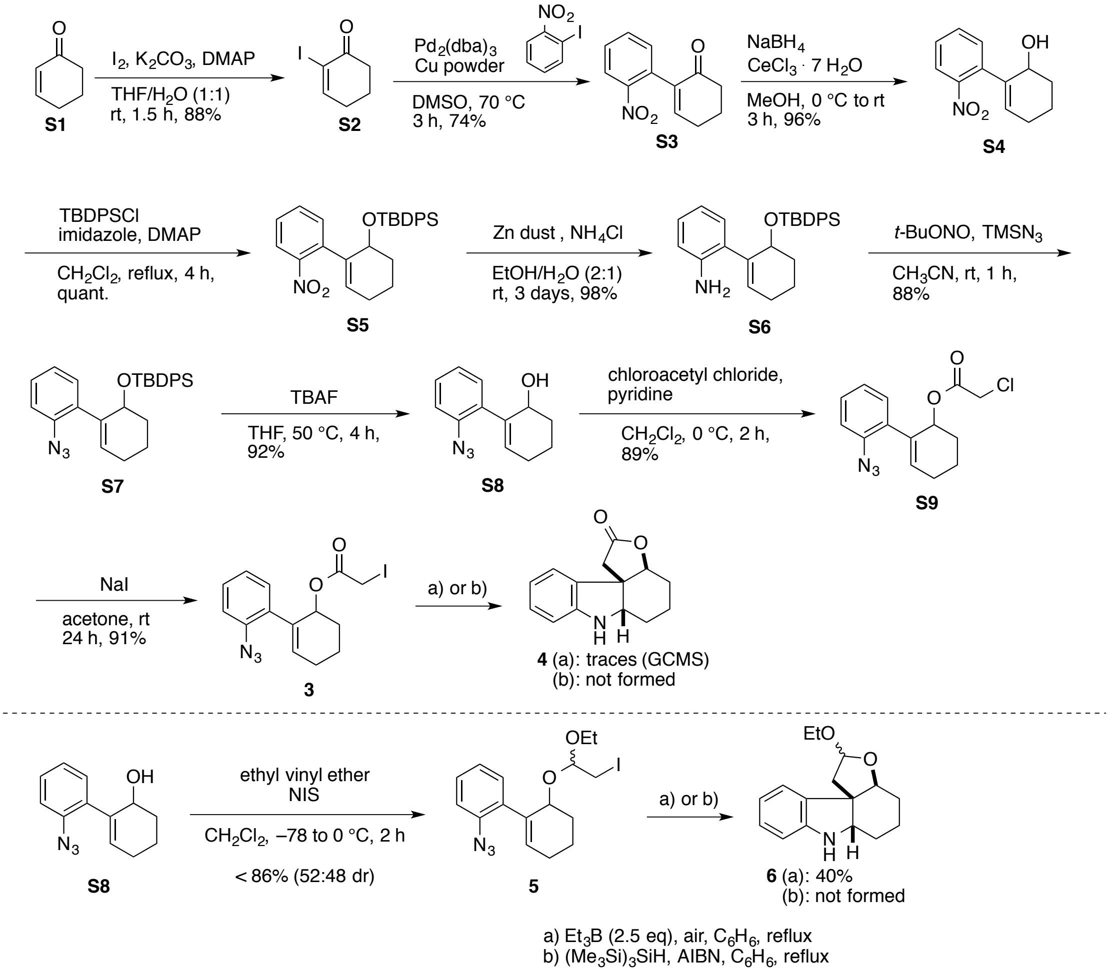
($cm^{-1}$). Low resolution mass spectra were recorded on a Waters Micromass Autospec Q mass spectrometer in EI mode at 70 eV or were taken from GC-MS analyses performed on a Finnigan Trace GC-MS (quadrupole mass analyzer using EI mode at 70 eV) fitted with a Macherey-Nagel Optima delta-3-0.25 μm capillary column (20 m, 0.25 mm); gas carrier: He 1.4 mL/min; injector: 220 °C split mode. HRMS analyses and accurate mass determinations were performed on a Thermo Scientific LTQ Orbitrap XL mass spectrometer using ESI mode at the University of Bern. Melting points were measured on a Büchi B-545 apparatus and are corrected.

***Caution:*** *Since organic azides are capable of exploding, it is strongly recommended to apply standard safety rules and to use a safety shield.*

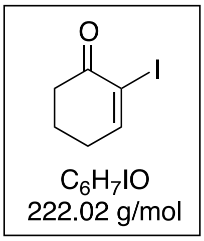
# 2. Experimental Part

## 2.1. Preliminary Studies of the oxygenated analogue of the tetracyclic indoline

Commercially available cyclohex-2-enone **S1** was iodinated in 88% yield. The resulting vinyl iodide **S2** was then coupled with the 1-iodo-2-nitrobenzene in 65% yield using a palladium(0)-catalyzed Ullman cross-coupling reaction developed by Banwell.[1] The resulting ketone **S3** was reduced under Luche conditions,[2] affording the allylic alcohol **S4** in very high yield. The alcohol was protected and the nitro part was transformed to the corresponding aryl azide in a two step procedure[3]. After deprotection of the alcohol an acetyl chain was introduced and after a Finkelstein reaction the desired radical precursor **3** is formed. Alternatively the haloacetamide **5** was prepared as a diastereomeric mixture in 86% yield.

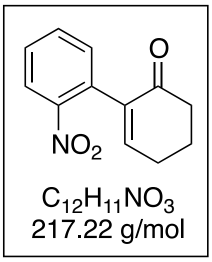


### 2-Iodocyclohex-2-enone (S2)



To a stirred solution of 2-cyclohexenone **S1** (2.0 ml, 20.5 mmol) in THF/$H_2O$ (1:1, 100 mL) was added at rt $K_2CO_3$ (3.3 g, 24 mmol), iodine (10.15 g, 40 mmol) and DMAP (490 mg, 4 mmol) successively. The reaction mixture was stirred for 1.5 h at rt until completion. The solution was then diluted with EtOAc (200 mL), washed with $Na_2S_2O_3$ sat. aq. (1 x 400 mL) and followed by 0.1 M HCl (1 x 400 mL). The organic layer was washed with brine, dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. The crude was purified by flash column chromatography (pentane/$Et_2O$, 4:1) to give the desired product **S2** (3.9 g, 88%). Yellow solid. Physical and spectral data were in accordance with literature data.[4] **m.p.:** 47–50 °C. **$^1$H NMR (300 MHz, $CDCl_3$)** $\delta$ 7.75 (t, $J$ = 4.4 Hz, 1H), 2.66 – 2.62 (m, 2H), 2.45 – 2.40 (m, 2H), 2.11 – 2.04 (m, 2H). **$^{13}$C NMR (75 MHz, $CDCl_3$)** $\delta$ 192.01, 159.34, 103.76, 37.16, 29.85, 22.76. **MS (EI, 70 eV) *m/z* (%):** 222 ($M^+$, 100), 193 (77), 180 (9), 166 (15), 126 (11), 95 (14), 67 (22), 55 (19), 39 (71).

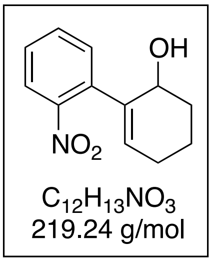
### 2-(2-Nitrophenyl)-2-cyclohexen-1-one (S3)



To a solution of 2-iodocyclohex-2-enone **S2** (1.15 g, 5.2 mmol) and 1-iodo-2-nitrobenzene (2.6 g, 10.4 mmol) in dry DMSO (13 mL) at rt under argon was added $Pd_2(dba)_3\cdot$chloroform complex (270 mg, 0.26 mmol) followed by Cu powder (1.7 g, 26.5 mmol). The mixture was stirred at 70 °C for 3 h. The reaction mixture was then cooled down to rt and $Et_2O$ (150 mL) was added. The mixture was filtered through a pad of Celite (rinsed with Et2O). The filtrate was washed with water (1 x 50 mL), then brine (1 x 50 mL), dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (cyclohexane/AcOEt, 7:1 then 5:1) gave the desired product **S3** (845 mg, 74%).

Yellow solid. Physical and spectral data were in accordance with literature data.[4] **$^1$H NMR (300 MHz, $CDCl_3$)** $\delta$ 8.02 (dd, $J$ = 8.1, 1.2 Hz, 1H), 7.60 (td, $J$ = 7.5, 1.3 Hz, 1H), 7.52 – 7.42 (m, 1H), 7.29 – 7.20 (m, 1H), 7.00 (t, $J$ = 4.2 Hz, 1H), 2.64 – 2.53 (m, 4H), 2.15 (dt, $J$ = 12.3, 6.2 Hz, 2H). **$^{13}$C NMR (75 MHz, $CDCl_3$)** $\delta$ 196.44, 148.65, 146.46, 139.50, 133.25, 132.17, 131.67, 128.74, 124.22, 38.31, 26.29, 22.59. *(contaminated with homo-coupled product)*

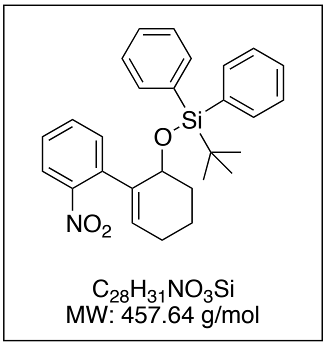
### 2'-Nitro-2,3,4,5-tetrahydro-[1,1'-biphenyl]-2-ol (S4)



To a solution of **S3** (1.99 g, 9.16 mmol) in MeOH at 0 °C under argon was added $CeCl_3 \cdot 7H_2O$ (4.44 g, 11.91 mmol) in one portion. After 10 minutes, $NaBH_4$ (450 mg, 11.91 mmol) was added by portions (3 × 150 mg) in order to keep the temperature of the reaction mixture between 0 and 5 °C. The mixture was then stirred at 0 °C for 1.5 h and then at rt for 1.5 h. Sat. aq. $NH_4Cl$ (70 mL) was added to the mixture and the methanol was removed under reduced pressure. The residue was extracted with $Et_2O$ (3 × 40 mL). The combined organic layers were washed with brine (1 × 40 mL), dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (cyclohexane/AcOEt 5:1) gave **S4** (1.88 g, 8.57 mmol, 94%).

Yellow solid. **m.p.:** 74–77 °C. **$^1$H NMR (300 MHz, $CDCl_3$)** $\delta$ 7.84 (dd, $J$ = 8.1, 1.3 Hz, 1H), 7.56 (td, $J$ = 7.5, 1.3 Hz, 1H), 7.45 – 7.35 (m, 2H), 5.71 (t, $J$ = 3.8 Hz, 1H), 4.46 – 4.38 (m, 1H), 2.25–1.62 (m, 7H). **$^{13}$C NMR (75 MHz, $CDCl_3$)** $\delta$ 149.42, 137.65, 136.82, 132.46, 131.43, 130.22, 127.89, 123.98, 67.59, 32.07, 25.60, 17.72. **IR (neat):** 3560, 3393 (br), 2935, 2863, 2832, 1661, 1606, 1570, 1518, 1342, 1056, 971, 915, 855, 782, 746. **MS (EI, 70 eV) *m/z* (%):** 219 ($M^+$, 1), 185 (22), 169 (47), 168 (84), 167 (100), 166 (23), 156 (16), 146 (32), 129 (28), 120 (29), 115 (36), 104 (16), 92 (21), 77 (32), 55 (20), 51 (23). **HRMS (ESI)** calcd for $C_{12}H_{13}NO_3Na$: 242.0788, found: 242.0782.

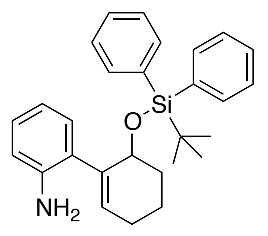
### *tert*-Butyl((2'-nitro-2,3,4,5-tetrahydro-[1,1'-biphenyl]-2-yl)oxy)diphenylsilane (S5)



To a solution of **S4** (2.14 g, 9.77 mmol), imidazole (1.33 g, 19.54 mmol), and DMAP (358 mg, 2.93 mmol) in dry $CH_2Cl_2$ (10 mL) at 0 °C under argon was added TBDPSCl (5.08 mL, 19.54 mmol) dropwise. The reaction mixture was refluxed for 4 h. The mixture was cooled down to rt and water (10 mL) was added. The two layers were separated and the aqueous layer was extracted with $CH_2Cl_2$ (3 × 5 mL). The combined organic layers were washed with brine (1 × 5 mL), dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (cyclohexane/AcOEt 99:1) gave **S5** (4.46 g, 9.75 mmol, quantitative).

Yellow solid. **M.p.:** 84–89 °C. **$^1$H NMR (300 MHz, CDCl$_3$)** $\delta$ 7.86 (dd, $J$ = 8.0, 1.2 Hz, 1H), 7.55–7.26 (m, 11H), 7.24–7.17 (m, 2H), 5.67 (t, $J$ = 3.8 Hz, 1H), 4.50 (t, $J$ = 4.6 Hz, 1H), 2.27–1.99 (m, 2H), 1.93–1.78 (m, 1H), 1.76–1.45 (m, 3H), 0.83 (s, 9H). **$^{13}$C NMR (75 MHz, CDCl$_3$)** $\delta$ 148.18, 139.39, 137.79, 135.82 (2C), 135.67 (2C), 134.52, 133.57, 133.43, 132.38, 129.41, 129.36, 129.19, 127.58, 127.38 (2C), 127.36 (2C), 124.14, 68.75, 31.85, 26.79 (3C), 25.64, 19.17, 17.84. **IR (neat):** 3065, 2930, 2856, 1607, 1570, 1521, 1471, 1427, 1342, 1161, 1104, 1082, 1062, 1005, 997, 926, 898, 821, 737, 699. **MS (EI, 70 eV) *m/z* (%):** 402 (3), 401 (10), 400 (30), 355 (2), 304 (3), 286 (2), 244 (3), 201 (6), 200 (19), 199 (100), 197 (11), 184 (6), 181 (9). **HRMS (ESI)** calcd for $C_{28}H_{31}NO_3SiNa$: 480.1965, found: 480.1952.

### 2'-((*tert*-Butyldiphenylsilyl)oxy)-2',3',4',5'-tetrahydro-[1,1'-biphenyl]-2-amine (S6)



$C_{28}H_{33}NOSi$
MW: 427.65 g/mol

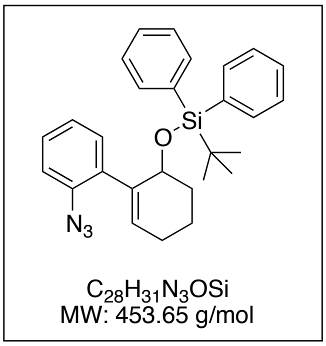
To a suspension of **S5** (1.55 g, 3.38 mmol) in EtOH (21 mL) at rt was added a solution of $NH_4Cl$ (906 mg, 16.93 mmol) in water (11 mL) followed by Zn dust (3.32 g, 50.80 mmol). The reaction mixture was stirred at rt for 3 days. The mixture was then diluted with $CH_2Cl_2$ (20 mL) and water (5 mL) and then filtered through a plug of cotton (rinsed with $CH_2Cl_2$). The filtrate was diluted with water (10 mL) and extracted with $CH_2Cl_2$ (3 × 15 mL). The combined organic layers were dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (cyclohexane/AcOEt 98:2) gave **S6** (1.42 g, 3.32 mmol, 98%).

Colorless oil. **$^1$H NMR (300 MHz, CDCl$_3$)** $\delta$ 7.62 (dd, $J$ = 7.9, 1.5 Hz, 2H), 7.44–7.24 (m, 6H), 7.22–7.14 (m, 2H), 7.08 (td, $J$ = 7.8, 1.6 Hz, 1H), 6.87 (dd, $J$ = 7.7, 1.6 Hz, 1H), 6.74–6.67 (m, 2H), 5.82 (t, $J$ = 3.7 Hz, 1H), 4.45 (t, $J$ = 4.2 Hz, 1H), 3.71 (br s, 2H), 2.28–2.15 (m, 1H), 2.07–1.92 (m, 1H), 1.91–1.75 (m, 1H), 1.68–1.57 (m, 1H), 1.53–1.37 (m, 2H), 0.87 (s, 9H). **$^{13}$C NMR (75 MHz, CDCl$_3$)** $\delta$ 144.70, 138.43, 135.97 (2C), 135.93 (2C), 135.08, 133.57, 130.63, 129.76, 129.40, 129.24, 128.93, 127.75, 127.40 (2C), 127.29 (2C), 118.24, 115.43, 69.44, 32.13, 26.83 (3C), 25.72, 19.09, 17.87. **IR (neat):** 3451 (br), 3362 (br), 2930, 2856, 1611, 1490, 1471, 1451, 1426, 1361, 1291, 1159, 1104, 1061, 1011, 996, 919, 896, 821, 801, 737, 699. **MS (EI, 70 eV) *m/z* (%):** 427 (M$^+$, 1), 372 (5), 371

(16), 370 (54), 292 (11), 274 (6), 226 (4), 201 (6), 200 (20), 199 (100), 197 (5), 181 (7). **HRMS (ESI)** calcd for $C_{28}H_{34}NOSi$: 428.2404, found: 428.2397.

### ((2'-Azido-2,3,4,5-tetrahydro-[1,1'-biphenyl]-2-yl)oxy)(*tert*-butyl)diphenylsilane (S7)

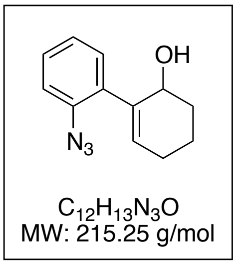
***Cautions:*** *TMSN$_3$ is volatile, latex-permeable and absorbed by the skin. TMSN$_3$ is known to be hydrolytically unstable, resulting in the release of hydrazoic acid, an unstable and very toxic compound. See also General Information.*



To a solution of **S6** (1.41 g, 3.30 mmol) in dry $CH_3CN$ (8 mL) at 0 °C under argon was added *t*-BuONO (90% purity, 0.653 mL, 4.94 mmol) dropwise followed by TMSN$_3$ (0.52 mL, 3.96 mmol) slowly. The reaction mixture was stirred at rt for 1 h. The mixture was concentrated under reduced pressure. Purification by flash column chromatography (pentane then pentane/Et$_2$O 10:1) gave **S7** (1.33 g, 2.93 mmol, 88%).

Yellow oil. **$^1$H NMR (300 MHz, CDCl$_3$)** $\delta$ 7.58–7.53 (m, 2H), 7.43–7.19 (m, 9H), 7.12 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.02 (t, *J* = 7.0 Hz, 1H), 6.95 (d, *J* = 8.0 Hz, 1H), 5.70 (t, *J* = 3.8 Hz, 1H), 4.66 (t, *J* = 4.3 Hz, 1H), 2.28–2.15 (m, 1H), 2.13–1.98 (m, 1H), 1.95–1.82 (m, 1H), 1.80–1.69 (m, 1H), 1.65–1.50 (m, 2H), 0.82 (s, 9H). **$^{13}$C NMR (75 MHz, CDCl$_3$)** $\delta$ 139.60, 137.26, 135.94 (2C), 135.89 (2C), 134.91, 134.56, 133.73, 131.87, 130.37, 129.30, 129.26, 127.99, 127.27 (2C), 127.21 (2C), 124.43, 118.17, 68.21, 31.99, 26.78 (3C), 25.58, 19.12, 17.88. **IR (neat):** 3070, 2930, 2856, 2121, 2089, 1575, 1484, 1472, 1441, 1426, 1288, 1104, 1062, 1013, 997, 922, 897, 859, 820, 737, 699. **MS (EI, 70 eV) *m/z* (%):** the product completely decomposed during the analysis, no detection possible. **HRMS (ESI)** calcd for $C_{28}H_{31}N_3OSiNa$: 476.2129, found: 476.2121.

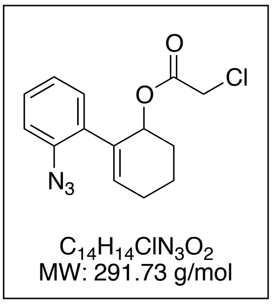
### 2'-Azido-2,3,4,5-tetrahydro-[1,1'-biphenyl]-2-ol (S8)



***Caution:*** *See General Information.*

To a solution of **S7** (1.15 g, 2.54 mmol) in dry THF (48 mL) at 0 °C under argon was added a 1 M solution of TBAF in THF (12.69 mL, 12.69 mmol). The mixture was stirred at 50 °C for 4 h. The mixture was then cooled down to rt and water (150 mL) and $CH_2Cl_2$ (150 mL) were added. The two layers were separated and the aqueous layer was extracted with $CH_2Cl_2$ (3 × 150 mL). The combined organic layers were dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (pentane/$Et_2O$ 15:1 then 5:1) gave **S8** (502 mg, 2.33 mmol, 92%). Yellow oil. **$^1$H NMR (300 MHz, $CDCl_3$)** $\delta$ 7.36–7.28 (m, 1H), 7.22–7.08 (m, 3H), 5.80 (t, *J* = 3.8 Hz, 1H), 4.59 (t, *J* = 4.4 Hz, 1H), 2.32–2.07 (m, 2H), 2.01–1.62 (m, 5H). **$^{13}$C NMR (75 MHz, $CDCl_3$)** $\delta$ 138.74, 137.22, 133.77, 131.28, 131.19, 128.50, 124.93, 118.30, 67.02, 31.51, 25.77, 17.87. **IR (neat):** 3358 (br), 2933, 2858, 2832, 2118, 2085, 1573, 1493, 1440, 1285, 1159, 1147, 1057, 970, 914, 748. **MS (EI, 70 eV) *m/z* (%):** 215 ($M^+$, 1), 187 ($M^+ - N_2$, 12), 170 (28), 169 (45), 168 (71), 167 (39), 143 (17), 131 (26), 130 (100), 115 (22), 103 (15), 89 (12), 77 (20), 63 (11), 51 (15), 39 (16). **HRMS (ESI)** calcd for $C_{12}H_{13}N_3ONa$: 238.0951, found: 238.0949.

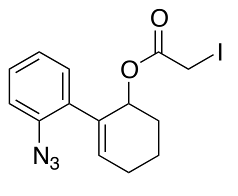
### 2'-Azido-2,3,4,5-tetrahydro-[1,1'-biphenyl]-2-yl 2-chloroacetate (*S9*)



***Caution:*** *See General Information.*

To a solution of **S8** (200 mg, 0.93 mmol) in dry $CH_2Cl_2$ (7.5 mL) at rt under argon was added pyridine (0.150 mL, 1.86 mmol). The reaction mixture was cooled down to 0 °C and chloroacetyl chloride (0.148 mL, 1.86 mmol) was added dropwise. The mixture was stirred at 0 °C for 2 h. The mixture was then diluted with $CH_2Cl_2$ (12 mL) and washed with water (3 × 12 mL). The organic layer was dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (pentane/$Et_2O$ 99:1 then 98:2) gave **S9** (239 mg, 0.82 mmol, 89%). Yellowish oil. **$^1$H NMR (300 MHz, $CDCl_3$)** $\delta$ 7.33–7.27 (m, 1H), 7.15–7.03 (m, 3H), 5.97 (t, *J* = 3.9 Hz, 1H), 5.92 (t, *J* = 4.4 Hz, 1H), 3.85 (q, *J* = 14.7 Hz, 2H), 2.37–2.12 (m, 2H), 2.07–1.91 (m, 2H), 1.85–1.70 (m, 2H). **$^{13}$C NMR (75 MHz, $CDCl_3$)** $\delta$ 166.69, 137.54, 134.30, 134.05, 132.52, 130.90, 128.69, 124.62, 118.38, 71.37, 40.97, 28.43, 25.39, 17.71. **IR (neat):** 2942, 2863, 2832, 2121, 2091, 1752, 1729, 1574, 1484, 1441, 1410, 1278, 1180, 1156, 1091, 1052, 1006, 965, 916, 750. **MS (EI, 70 eV) *m/z* (%):** 291 ($M^+$, 1), 170 (6), 169 (61), 168 (100), 167 (43), 166 (10), 139 (5), 115 (7), 83 (18), 50 (6). **HRMS (ESI)** calcd for $C_{14}H_{14}ClN_3O_2Na$: 314.0667, found: 314.0665.

### 2'-Azido-2,3,4,5-tetrahydro-[1,1'-biphenyl]-2-yl 2-iodoacetate (3)



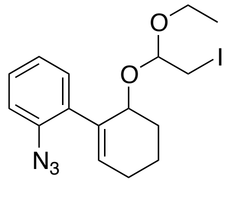
$C_{14}H_{14}IN_3O_2$
MW: 383.18 g/mol

***Caution:*** *See General Information.*

To a solution of **S9** (100 mg, 0.34 mmol) in acetone (2 mL) at rt under argon was added NaI (67 mg, 0.45 mmol). The mixture was stirred at rt for 24 h ***(caution:** flask wrapped in aluminum foil to protect the reaction from light)*. The solvent was then removed under reduced pressure ***(caution:** flask wrapped in aluminum foil)* and the residue was dissolved in a mixture of water (5 mL) and $CH_2Cl_2$ (5 mL). The two layers were separated and the aqueous layer was extracted with $CH_2Cl_2$ (3 × 3 mL). The combined organic layers were successively washed with sat. aq. $Na_2S_2O_3$ (2 × 3 mL) and brine (1 × 3 mL), dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure ***(caution:** flask wrapped in aluminum foil)*. Purification by flash column chromatography (pentane/$Et_2O$ 95:5) gave **3** (120 mg, 0.31 mmol, 91%).

Yellowish oil. **$^1$H NMR (300 MHz, $CDCl_3$)** $\delta$ 7.32–7.26 (m, 1H), 7.18–7.04 (m, 3H), 5.97 (t, *J* = 3.8 Hz, 1H), 5.87 (t, *J* = 4.4 Hz, 1H), 3.50 (s, 2H), 2.37–2.12 (m, 2H), 2.05–1.68 (m, 4H). **$^{13}$C NMR (75 MHz, $CDCl_3$)** $\delta$ 168.23, 137.51, 134.45, 133.91, 132.67, 131.03, 128.59, 124.66, 118.42, 70.96, 28.16, 25.43, 17.80, −5.17. **IR (neat):** 3051, 2939, 2863, 2120, 2090, 1721, 1573, 1484, 1441, 1413, 1248, 1081, 1006, 967, 918, 749, 683. **MS (EI, 70 eV) *m/z* (%):** 170 (8), 169 (57), 168 (100), 167 (49), 166 (11), 139 (8), 83 (23), 63 (5). **HRMS (ESI)** calcd for $C_{14}H_{14}IN_3O_2Na$: 406.0023, found: 406.0015.

### 2'-Azido-2-(1-ethoxy-2-iodoethoxy)-2,3,4,5-tetrahydro-1,1'-biphenyl (5)



$C_{16}H_{20}IN_3O_2$
MW: 413.25 g/mol

***Caution:*** *See General Information.*

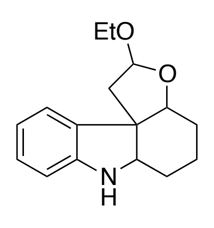
To a solution of **S8** (100 mg, 0.46 mmol) in dry $CH_2Cl_2$ (1 mL) at rt under argon was added ethyl vinyl ether (67 μL, 0.70 mmol). The mixture was cooled down to −78 °C and NIS (157 mg, 0.70 mmol) was added portionwise. The mixture was stirred at −78 °C for 5 minutes then allowed to slowly warm up to 0 °C over 2 h ***(caution:** flask wrapped in aluminum foil to protect the reaction from light)*. The mixture was diluted with $CH_2Cl_2$ (2 mL), then washed with water (1 × 2 mL) and a 10% aqueous $Na_2S_2O_3$ solution (1 × 2 mL), dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure ***(caution:** flask wrapped in aluminum foil)*. Purification by flash column chromatography (pentane/$Et_2O$ 98:2) gave **5** as a mixture of diastereomers contaminated with unidentified side products (166 mg, < 86%, 52:48 dr as determined by $^{1}$H NMR). The diastereomers were inseparable.

Mixture of diastereomers: yellowish oil. **$^{1}$H NMR (300 MHz, $CDCl_3$)** $\delta$ 7.34–7.05 (m, 4H major + 4H minor), 5.85 (t, $J$ = 3.8 Hz, 1H major), 5.81 (t, $J$ = 3.8 Hz, 1H minor), 4.65 (t, $J$ = 5.6 Hz, 1H major), 4.58 (t, $J$ = 3.2 Hz, 1H major), 4.52 (t, $J$ = 4.1 Hz, 1H minor), 4.39 (dd, $J$ = 6.6, 4.2 Hz, 1H minor), 3.54–2.67 (m, 4H major + 4H minor), 2.32–1.61 (m, 6H major + 6H minor), 1.16 (t, $J$ = 7.0 Hz, 3H minor), 0.82 (t, $J$ = 7.0 Hz, 3H major). **IR (neat):** 2973, 2933, 2119, 2086, 1573, 1483, 1441, 1283, 1097, 1045, 1008, 920, 750. **MS (EI, 70 eV) *m/z* (%):** 170 (14), 169 (63), 168 (100), 167 (56), 166 (12), 139 (8), 83 (22). **HRMS (ESI)** calcd for $C_{16}H_{20}IN_3O_2Na$: 436.0492, found: 436.0486.

Major diastereomer: **$^{13}$C NMR (75 MHz, $CDCl_3$)** $\delta$ = 137.33, 136.36, 134.43, 132.54, 131.66, 128.32, 124.63, 118.18, 102.54, 70.92, 61.56, 28.01, 25.55, 16.96, 14.80, 6.10.

Minor diastereomer: **$^{13}$C NMR (75 MHz, $CDCl_3$)** $\delta$ = 137.20, 136.82, 134.29, 132.12, 131.71, 128.46, 124.83, 118.32, 100.00, 72.92, 59.01, 29.84, 25.58, 17.65, 14.99, 5.61.

### 2-Ethoxy-1,2,3a,4,5,6,6a,7-octahydrofuro[2,3-*d*]carbazole (6)



$C_{16}H_{21}NO_2$
MW: 259.34 g/mol

To an open to air solution of **5** (118 mg, 0.28 mmol, 52:48 dr as determined by $^{1}$H NMR) in benzene (0.8 mL) at rt, in a 2-necked 10 mL round bottom flask, was added a 1 M solution of $Et_3B$ in hexane (0.14 mL, 0.14 mmol) with a syringe *(**cautions:** the needle should be immersed into the reaction mixture in order to avoid a direct contact of $Et_3B$ drops with air. Flask wrapped in aluminum foil to protect the reaction from light)*. The reaction mixture was stirred at rt for 30 minutes then $Et_3B$ (0.14 mL, 0.14 mmol) was added. The reaction mixture was stirred at rt for 30 minutes then $Et_3B$ (0.14 mL, 0.14 mmol) was added. After 1 h at rt, the reaction mixture was refluxed and $Et_3B$ (0.14 mL, 0.14 mmol) was added. The mixture was stirred at reflux for 30 minutes then $Et_3B$ (0.14 mL, 0.14 mmol) was added. The reaction mixture was refluxed for 1.5 h then sat. aq. $NaHCO_3$ (5 mL) was added. The two layers were separated and the aqueous layer was extracted with $Et_2O$ (3 × 3 mL). The combined organic layers were washed with brine (1 × 3 mL), dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure at 35 °C. Purification by flash column chromatography (cyclohexane/AcOEt 8:1) gave **6** as a mixture of diastereomers contaminated with unidentified side products (29 mg, < 40%, 55:45 dr as determined by $^{1}H$ NMR). The diastereomers were inseparable.

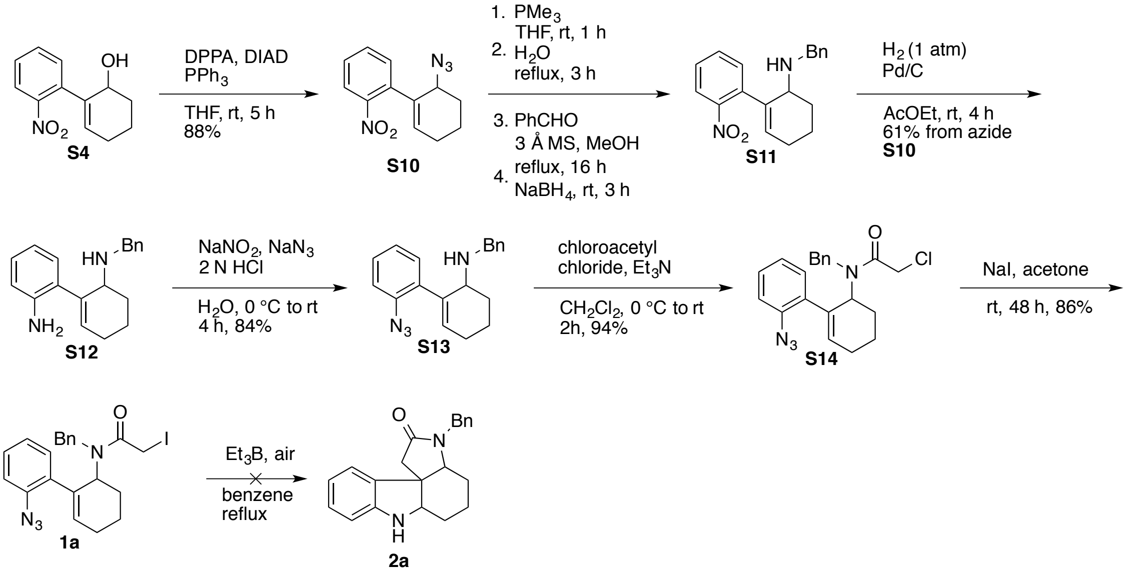
Mixture of diastereomers: yellow oil. *Due to the low purity of the mixture after chromatography, only the $^{1}H$ NMR and GC-MS analyses have been performed.* **$^{1}H$ NMR (300 MHz, $CDCl_3$)** *(the observable signals that confirmed the structure of **6** have been listed)* $\delta$ 7.16 (d, $J$ = 6.9 Hz, 1H major), 7.09–6.64 (m, 3H major + 4H minor), 5.26 (dd, $J$ = 6.0, 1.8 Hz, 1H major), 5.21 (dd, $J$ = 5.8, 4.5 Hz, 1H minor), 4.56 (t, $J$ = 2.6 Hz, 1H minor), 4.30–4.25 (m, 1H major), 4.04 (dd, $J$ = 8.3, 5.3 Hz, 1H major), 3.90–3.77 (m, 1H major + 2H minor), 3.57–3.39 (m, 2H major + 2H minor), 2.72 (dd, $J$ = 13.8, 6.0 Hz, 1H minor).

Major diastereomer: **MS (EI, 70 eV) *m/z* (%):** 259 ($M^+$, 62), 214 (21), 188 (36), 170 (83), 159 (92), 130 (100), 118 (27), 77 (22).

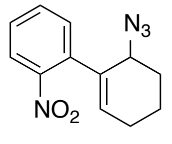
Minor diastereomer: **MS (EI, 70 eV) *m/z* (%):** 259 ($M^+$, 65), 214 (25), 188 (54), 170 (81), 159 (96), 130 (100), 118 (27), 77 (24).

## 2.2. *N*-Benzylated derivative

The synthesis of the amino azide **S13** was finally achieved from the nitro alcohol **S4** after conversion of its hydroxy functionality into an azido group and a Staudinger reaction/hydrolysis/reductive amination sequence. Indeed, *via* a Mitsunobu reaction involving diphenylphosphoryl azide (DPPA), **S4** was readily converted into the azide **S10** in 88% yield.[5] From **S10**, the nitro amine **S11** was successfully prepared using the optimized sequence mentioned above. Since the complete separation of **S11** from small amounts of benzyl alcohol, resulting from the partial reduction of benzaldehyde by $NaBH_4$, was not possible, the nitro amine was used as a crude product in the subsequent reduction step. The aniline **S12** was then obtained in 61% yield from **S10**. Finally, **S12** was converted into the amino azide **S13** in good yield with the $NaNO_2/NaN_3/HCl$ system. After an acetylation with chloroacetylchloride and a Finkelstein reaction the desired radical precursor **1a** is formed.



### 2-Azido-2'-nitro-2,3,4,5-tetrahydro-1,1'-biphenyl (S10)

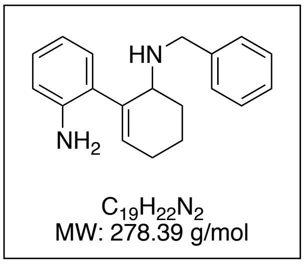


$C_{12}H_{12}N_4O_2$
MW: 244.25 g/mol

To a solution of **S4** (2.02 g, 9.22 mmol) and $PPh_3$ (3.14 g, 11.98 mmol) in dry THF (41 mL) at 0 °C under argon was slowly added DIAD (2.32 mL, 11.98 mmol) followed by DPPA (2.59 mL, 11.98 mmol) dropwise. The reaction mixture was stirred at rt for 5 h. The solvent was then removed under reduced pressure. Purification by flash column chromatography (cyclohexane/toluene 3:1) gave **S10** (1.98 g, 8.11 mmol, 88%).

Yellowish oil. **$^1$H NMR (300 MHz, CDCl$_3$)** $\delta$ 7.98 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.60 (td, *J* = 7.5, 1.2 Hz, 1H), 7.46 (td, *J* = 8.1, 1.5 Hz, 1H), 7.39 (dd, *J* = 7.5, 1.5 Hz, 1H), 5.87 (t, *J* = 3.8 Hz, 1H), 4.14 (t, *J* = 4.3 Hz, 1H), 2.34 – 1.99 (m, 4H), 1.92 – 1.70 (m, 2H). **$^{13}$C NMR (75 MHz, CDCl$_3$)** $\delta$ 148.27, 136.60, 134.43, 133.06, 132.33, 131.53, 128.42, 124.41, 58.83, 28.76, 25.21, 17.62. **IR (neat):** 2939, 2867, 2090, 1607, 1570, 1520, 1438, 1341, 1297, 1243, 1159, 1091, 941, 913, 849, 785, 747. **MS (EI, 70 eV) *m/z* (%):** 244 (M$^+$, 0.1), 202 (77), 184 (36), 170 (35), 168 (46), 167 (31), 131 (25), 130 (73), 115 (100), 104 (80), 92 (69), 91 (56), 89 (53), 77 (96), 76 (54), 63 (41), 55 (52), 51 (44), 39 (34). **HRMS (ESI)** calcd for $C_{12}H_{12}N_4O_2Na$: 267.0852, found: 267.0855.

### *N*²-Benzyl-2,3,4,5-tetrahydro-[1,1'-biphenyl]-2,2'-diamine (S12)

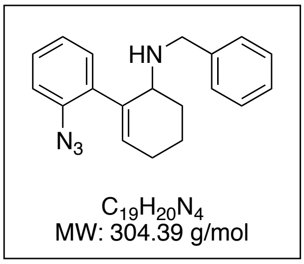


To a solution of **S10** (1.17 g, 4.79 mmol) in dry THF (22 mL) at rt under argon was slowly added a 1 M solution of PMe$_3$ in THF (19.16 mL, 19.16 mmol). The reaction mixture was stirred at rt for 1 h then water (0.60 mL, 33.53 mmol) was added and the mixture was refluxed for 3 h. The mixture was then cooled down to rt, concentrated under reduced pressure, and azeotropically dried with toluene (3 × 40 mL). The residue was dissolved in MeOH (99 mL) then activated 3 Å molecular sieves (20 g) were added followed by freshly distilled benzaldehyde (0.49 mL, 4.79 mmol). The mixture was refluxed for 16 h. The mixture was then cooled down to 0 °C and NaBH$_4$ (200 mg, 5.27 mmol) was added portionwise. The reaction mixture was stirred at rt for 3 h. The mixture was then filtered to remove the solids (rinsed with MeOH) and the filtrate was concentrated under reduced pressure. The residue was dissolved in CH$_2$Cl$_2$ (30 mL) and sat. aq. NaHCO$_3$ (30 mL). The two layers were separated and the aqueous layer was extracted with CH$_2$Cl$_2$ (3 × 10 mL). The combined organic layers were washed with brine (1 × 10 mL), dried over Na$_2$SO$_4$, filtered, and concentrated under reduced pressure. The crude product **S11** (1.53 g) obtained was dissolved in EtOAc (109 mL) at rt under argon and the solution was degassed with argon under a slight vacuum for 5 minutes to remove the oxygen. 5% Pd/C (611 mg, 0.29 mmol) was added under argon and the mixture was degassed with argon for 1 minute. The mixture was stirred under an atmosphere (balloon) of H$_2$ at rt for 4 h. The mixture was then filtered through a pad of Celite (rinsed with EtOAc) and the filtrate was concentrated under reduced pressure. Purification by flash column chromatography ($CH_2Cl_2$ then $CH_2Cl_2/NH_3$ (7 N in MeOH) 99.5:0.5 then 99:1) gave **S12** (810 mg, 2.91 mmol, 61% from azide **S10**).

Yellow liquid. **$^1$H NMR (300 MHz, $CDCl_3$)** $\delta$ 7.26 – 7.15 (m, 3H), 7.11 – 7.03 (m, 3H), 6.93 (dd, *J* = 7.5, 1.4 Hz, 1H), 6.74 – 6.65 (m, 2H), 5.83 (td, *J* = 3.8, 0.9 Hz, 1H), 3.75 (d, *J* = 13.3 Hz, 1H), 3.59 (d, *J* = 13.3 Hz, 1H), 3.46 (t, *J* = 3.7 Hz, 1H), 3.14 (br s, 2H), 2.31 – 2.01 (m, 2H), 1.93 – 1.56 (m, 5H). **$^{13}$C NMR (75 MHz, $CDCl_3$)** $\delta$ 144.47, 140.51, 138.72, 129.81, 129.47, 128.24 (2C), 128.04, 127.98 (2C), 127.89, 126.68, 118.13, 115.47, 54.34, 51.46, 28.13, 25.77, 18.30. **IR (neat):** 3446 (br), 3357 (br), 3023, 2930, 1610, 1490, 1450, 1291, 1156, 1102, 1069, 916, 744, 697. **MS (EI, 70 eV) *m/z* (%):** 278 ($M^+$, 2), 235 (6), 187 (43), 170 (100), 144 (21), 143 (40), 130 (22), 115 (11), 106 (70), 91 (76), 65 (11), 51 (4). **HRMS (ESI)** calcd for $C_{19}H_{23}N_2$: 279.1856, found: 279.1855.

### 2'-Azido-*N*-benzyl-2,3,4,5-tetrahydro-[1,1'-biphenyl]-2-amine (S13)

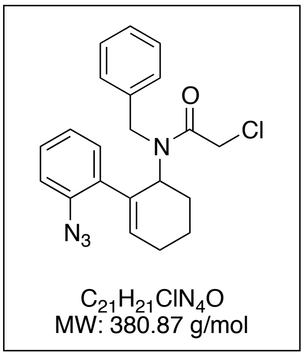
***Cautions:*** *$NaN_3$ is known to release hydrazoic acid, an unstable and very toxic compound, in the presence of acids. See also General Information.*



To a solution of **S12** (796 mg, 2.86 mmol) in a 2 N aqueous HCl solution (80 mL) at 0 °C was added a solution of $NaNO_2$ (217 mg, 3.14 mmol) in water (8 mL). The reaction mixture was stirred at 0 °C for 2 h then a solution of $NaN_3$ (279 mg, 4.29 mmol) in water (8 mL) was added dropwise. The mixture was stirred at rt for 2 h. The mixture was then cooled down to 0 °C and a 25% $NH_4OH$ solution was added dropwise until pH 11. The mixture was extracted with $CH_2Cl_2$ (3 × 10 mL). The combined organic layers were washed with brine (1 × 10 mL), dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography ($CH_2Cl_2$/MeOH 99:1) gave **S13** (734 mg, 2.41 mmol, 84%).

Orange oil. **$^1$H NMR (300 MHz, $CDCl_3$)** $\delta$ 7.34 – 7.26 (m, 1H), 7.23 – 7.14 (m, 4H), 7.12 – 7.05 (m, 2H), 7.04 – 6.99 (m, 2H), 5.75 (td, *J* = 3.8, 1.1 Hz, 1H), 3.70 (d, *J* = 13.4 Hz, 1H), 3.72 – 3.69 (m, 1H), 3.58 (d, *J* = 13.4 Hz, 1H), 2.25 – 2.08 (m, 2H), 1.90 – 1.76 (m, 3H), 1.72 – 1.60 (m, 1H). **$^{13}$C NMR (75 MHz, $CDCl_3$)** $\delta$ 140.72, 139.00, 137.29, 134.47, 131.17, 130.58, 128.21, 128.14 (2C), 128.00 (2C), 126.67, 124.73, 118.30, 53.12, 51.00, 28.21, 25.87, 18.64. **IR (neat):** 3359 (br), 3023, 2928, 2862, 2117, 2086, 1571, 1483, 1441, 1283, 747, 697. **MS (EI, 70 eV)** ***m/z*** **(%):** 170 (6), 169 (61), 168 (100), 167 (51), 166 (10), 139 (7), 115 (4), 83 (20), 77 (5), 63 (3). **HRMS (ESI)** calcd for $C_{19}H_{21}N_4$: 305.1761, found: 305.1758.

### *N*-(2'-Azido-2,3,4,5-tetrahydro-[1,1'-biphenyl]-2-yl)-*N*-benzyl-2-chloroacetamide (S14)

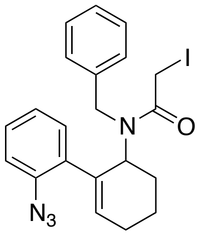


To a solution of **S13** (100 mg, 0.33 mmol) in dry $CH_2Cl_2$ (1.2 mL) at rt under argon was added $Et_3N$ (55 µL, 0.39 mmol). The mixture was cooled down to 0 °C and chloroacetyl chloride (31 µL, 0.39 mmol) was added dropwise. The mixture was stirred at 0 °C for 1 h then at rt for 1 h. The mixture was diluted with $CH_2Cl_2$ (4 mL) and washed with water (3 × 4 mL). The organic layer was dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography ($CH_2Cl_2$/pentane 3:1) gave **S14** contaminated with unidentified side products or the second rotamer (118 mg, < 94%).

Orange oil. **$^1$H NMR (300 MHz, $CDCl_3$)** $\delta$ 7.33 – 7.01 (m, 9H), 6.06 – 6.00 (m, 1H), 5.99 – 5.90 (m, 1H), 4.38 (d, $J$ = 18.3 Hz, 1H), 4.18 (d, $J$ = 18.3 Hz, 1H), 3.56 (q, $J$ = 12.2 Hz, 2H), 2.23 – 1.55 (m, 6H). **$^{13}$C NMR (75 MHz, $CDCl_3$)** $\delta$ 168.08, 137.85, 137.18, 135.29, 134.54, 132.33, 129.87, 128.87 (2C), 128.36, 127.32, 125.49 (2C), 124.74, 118.59, 54.17, 47.94, 41.57, 28.15, 25.37, 21.09. **IR (in $CDCl_3$):** 3020, 2933, 2862, 2122, 2096, 1654, 1484, 1442, 1413, 1289, 752, 728, 699. **MS (EI, 70 eV)** ***m/z*** **(%):** 345 (2), 317 (12), 316 (44), 288 (7), 260 (5), 225 (17), 197 (13), 183 (24), 170 (34), 143 (7), 115 (11), 91 (100), 65 (9). **HRMS (ESI)** calcd for $C_{21}H_{22}ClN_4O$: 381.1477, found: 381.1480.

### *N*-(2'-Azido-2,3,4,5-tetrahydro-[1,1'-biphenyl]-2-yl)-*N*-benzyl-2-iodoacetamide ((*Z*)-1a)

To a solution of **S14** (98 mg, 0.26 mmol) in acetone (2 mL) at rt under argon was added NaI (96 mg, 0.64 mmol). The mixture was stirred at rt for 48 h *(**caution:** flask wrapped in aluminum foil to protect the reaction from light)*. The solvent was then removed under reduced pressure *(**caution:** flask wrapped in aluminum foil)*. Purification by flash column chromatography ($CH_2Cl_2$) gave (*Z*)-**1a** (106 mg, 0.22 mmol, 86%).

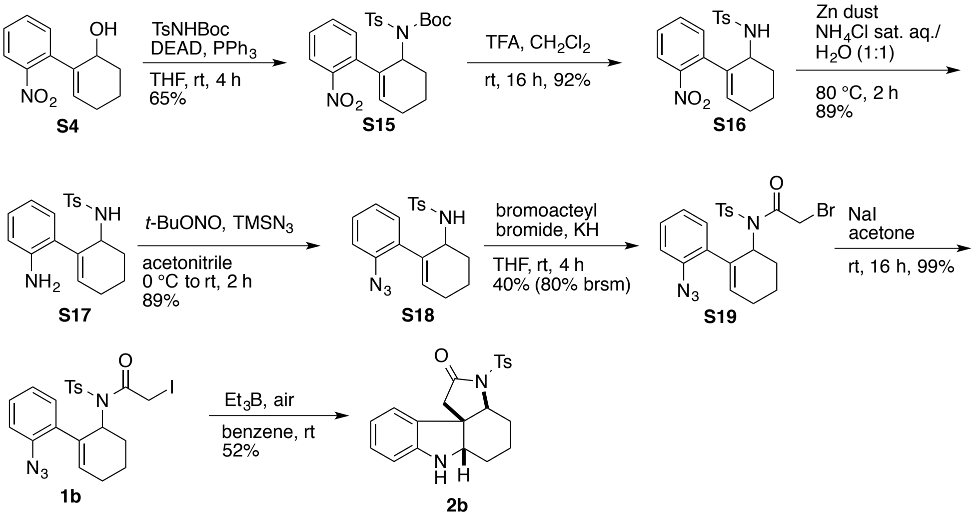


$C_{21}H_{21}IN_4O$
MW: 472.32 g/mol

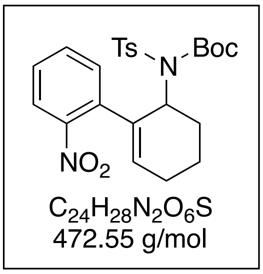
Yellow gum. **$^1$H NMR (300 MHz, CDCl$_3$)** δ 7.34 – 7.03 (m, 9H), 6.03 – 5.95 (m, 2H), 4.43 (d, *J* = 18.3 Hz, 1H), 4.16 (d, *J* = 18.3 Hz, 1H), 3.35 (d, *J* = 9.7 Hz, 1H), 3.21 (d, *J* = 9.7 Hz, 1H), 2.21 – 2.02 (m, 3H), 1.82 – 1.57 (m, 3H). **$^{13}$C NMR (75 MHz, CDCl$_3$)** δ 169.21, 138.10, 137.24, 135.46, 134.75, 132.73, 129.86, 128.82 (2C), 128.32, 127.33, 125.30 (2C), 125.09, 118.83, 53.68, 48.79, 28.32, 25.39, 21.06, −2.74. **IR (neat):** 3020, 2933, 2854, 2121, 2091, 1636, 1484, 1428, 1405, 1290, 1208, 1159, 994, 959, 749, 727, 695. **MS (EI, 70 eV) *m/z* (%):** 317 (15), 316 (48), 288 (10), 260 (7), 225 (24), 197 (17), 183 (28), 170 (42), 143 (10), 115 (16), 91 (100), 65 (11). **HRMS (ESI)** calcd for $C_{21}H_{22}IN_4O$: 473.0833, found: 473.0834.

## 2.3. *N*-Tosylated derivative

The allylic alcohol **S4** was transformed into the tosylamide **S16** *via* a two-step sequence involving a Mitsunobu reaction followed by the Boc-deprotection, in 59% yield for the two steps. The nitro moiety of **S16** was hydrogenated and the resulting aniline **S17** was transformed into the corresponding azido compound **S18** upon treatment with *tert*-butyl nitrite and trimethylsilyl azide[3] in 72% for the two steps. The acylation of the tosylamide **S18** with bromoacetyl bromide gave the bromoacetamide **S19** in 80% yield,[6] that was converted to the iodide **1b** by a Finkelstein reaction.



### *tert*-Butyl-(2'-nitro-2,3,4,5-tetrahydro-[1,1'-biphenyl]-2-yl)(tosyl) carbamate (S15)

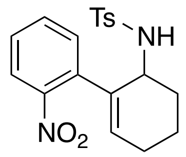


*tert*-Butyl tosylcarbamate (2.564, 9.45 mmol) was dissolved in dry THF (7 mL) and $PPh_3$ (4.957 g, 18.9 mmol) was added. The solution was stirred at rt and the allylic alcohol **S4** (1.384 g, 6.3 mmol) was added followed by DEAD (2.45 mL, 15.75 mmol) dropwise. The mixture was stirred for 4 h until no starting material was left. Then the THF was removed under reduced pressure and the mixture was diluted with EtOAc (30 mL). The solution was successively washed with 1 M NaOH (1 x 20 mL), water (1 x 20 mL) and brine, dried over $Na_2SO_4$ and concentrated under reduced pressure. The crude was purified by flash column chromatography (pentane/$Et_2O$, 2:1) to give **S15** (1.935 g, 65%).

Yellowish solid. **m$_p$:** 121.0 – 121.8 °C. **$^1$H NMR (300 MHz, $CDCl_3$)** $\delta$ 8.05 (dd, $J$ = 7.8, 1.6

Hz, 1H), 7.43 (m, 5H), 7.11 (d, *J* = 8.2 Hz, 2H), 5.86 – 5.77 (m, 1H), 5.77 – 5.61 (m, 1H), 2.49 – 2.31 (m, 1H), 2.37 (s, 3H), 2.30 – 2.10 (m, 3H), 2.00 – 1.88 (m, 2H), 1.30 (s, 9H). **$^{13}$C NMR (75 MHz, CDCl$_3$)** $\delta$ 150.25, 148.24, 143.52, 137.68, 136.28, 132.80, 130.25, 128.96 (2C), 128.13, 127.39 (2C), 124.54, 117.47, 84.08, 57.29, 28.42, 27.84, 25.00, 22.24, 21.47. *(carbonyl carbon peak missing)*. **IR (neat):** 2998, 2937, 1724, 1525, 1344, 1150, 1087, 1005. **MS (EI, 70 eV) *m/z* (%):** 217 (34), 200 (23), 199 (68), 185 (16), 184 (13), 171 (15), 170 (13), 169 (16), 168 (34), 167 (26), 156 (17), 155 (28), 146 (14), 115 (15), 92 (17), 91 (100), 89 (13), 77 (24), 65 (35), 39 (13). **HRMS (ESI)** calcd for $C_{24}H_{28}O_6N_2NaS$: 495.1560, found 495.1549.

## 4-Methyl-*N*-(2'-nitro-2,3,4,5-tetrahydro-[1,1'-biphenyl]-2-yl)benzenesulfonamide (S16)



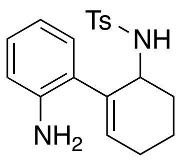
$C_{19}H_{20}N_2O_4S$
372.44 g/mol

To a stirred solution of tosylcarbamate **S15** (1.567 g, 3.3 mmol) in $CH_2Cl_2$ (33 mL) was added dropwise TFA (1.27 mL, 16.6 mmol). The solution was stirred overnight at rt. The solvent was evaporated under reduced pressure and the crude was purified by flash column chromatography (pentane/Et$_2$O, 4:1 to 1:1) to obtain product **S16** (1.14 g, 92%).

White solid. **m$_p$:** 144.8 – 146.0 °C. **$^1$H NMR (300 MHz, CDCl$_3$)** $\delta$ 7.75 – 7.55 (m, 1H), 7.38 (d, *J* = 8.1 Hz, 2H), 7.34 – 7.18 (m, 2H), 7.01 – 6.88 (m, 3H), 5.66 (s, 1H), 5.21 (d, *J* = 6.9 Hz, 1H), 4.03 (s, 1H), 2.34 (s, 3H), 2.22 – 1.96 (m, 3H), 1.96 – 1.78 (m, 1H), 1.71 (m, 2H). **$^{13}$C NMR (75 MHz, CDCl$_3$)** $\delta$ 149.01, 142.55, 137.31, 135.68, 133.83, 132.27, 132.23, 130.79, 129.30 (2C), 127.62, 126.53 (2C), 123.93, 51.27, 30.88, 25.18, 21.39, 17.04. **IR (neat):** 3263(br), 2953, 2871, 1516, 1443, 1417, 1351, 1324, 1152. **MS (EI, 70 eV) *m/z* (%):** 217 (37), 200 (23), 199 (69), 171 (18), 170 (16), 169 (24), 168 (46), 167 (34), 158 (15), 156 (21), 155 (36), 146 (19), 130 (19), 128 (16), 115 (20), 92 (17), 91 (100), 77 (25), 65 (42), 39 (15). **HRMS (ESI)** calcd for $C_{19}H_{21}O_4N_2S$: 373.1217, found 373.1211.

## *N*-(2'-Amino-2,3,4,5-tetrahydro-[1,1'-biphenyl]-2-yl)-4-methylbenzenesulfonamide (S17)

To a solution of nitro compound **S16** (112 mg, 0.3 mmol) in a mixture of EtOH/NH$_4$Cl sat. aq. (1:1, 1 mL) was added zinc dust (98 mg, 1.5 mmol). The reaction mixture was stirred for 2 h at 80 °C. Then it was diluted with EtOAc (10 mL) and $NH_3 \cdot H_2O$ (1 mL)

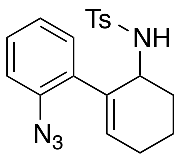


$C_{19}H_{22}N_2O_2S$
342.46 g/mol

was added. The solid was filtered off over a pad of celite and the filtrate was washed with brine, dried over $Na_2SO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography (cyclohexane/EtOAc, 4:1 to 2:1) to get the desired product **S17** (91 mg, 89%).

Yellow solid. **$m_p$:** 97.4 – 100.7 °C. **$^1$H NMR (300 MHz, $CDCl_3$)** $\delta$ 7.27 – 7.25 (m, 2H), 7.04 – 6.90 (m, 3H), 6.56 (d, *J* = 7.9 Hz, 1H), 6.53 – 6.47 (m, 2H), 5.80 (t, *J* = 3.3 Hz, 1H), 5.62 (d, *J* = 5.0 Hz, 1H), 3.75 (s, NH), 3.59 (s, NH2), 2.33 (s, 3H), 2.28 – 1.97 (m, 3H), 1.97 – 1.63 (m, 3H). **$^{13}$C NMR (75 MHz, $CDCl_3$)** $\delta$ 143.19, 142.22, 136.23, 134.94, 132.82, 129.19 (2C), 129.02, 128.01, 127.94, 126.55 (2C), 119.18, 115.83, 52.47, 31.07, 25.29, 21.37, 17.50. **IR (neat):** 3280, 2936, 1615, 1494, 1447, 1326, 1153. **MS (EI, 70 eV) *m/z* (%):** 187 (21), 172 (9), 171 (22), 170 (100) 169 (3), 168 (9), 158 (6), 155 (5), 144 (9), 143 (47), 142 (3), 132 (3), 130 (9), 117 (4), 115 (4), 106 (4), 91 (15), 77 (5), 65 (8), 56 (3). **HRMS (ESI)** calcd for $C_{19}H_{23}O_2N_2S$: 343.1475, found 343.1486.

### *N*-(2'-Azido-2,3,4,5-tetrahydro-[1,1'-biphenyl]-2-yl)-4-methylbenzenesulfonamide (S18)

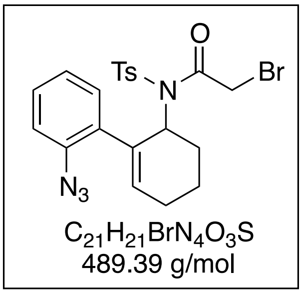


$C_{19}H_{20}N_4O_2S$
368.45 g/mol

Aniline **S17** (171 mg, 0.5 mmol) was dissolved in dry acetonitrile (1 mL) and the solution was cooled to 0 °C (ice bath). To this stirred solution was added *tert*-butylnitrite (90 µL, 0.75 mmol) followed by $TMSN_3$ (79 µL, 0.6 mmol). The resulting solution was stirred for 2 h at rt. Then the reaction mixture was concentrated under reduced pressure and the crude was purified by flash column chromatography (pentane/$Et_2O$, 4:1) to get **S18** (153 mg, 89%).

White solid. **$m_p$:** 156.6 – 158.3 °C. **$^1$H NMR (300 MHz, $CDCl_3$)** $\delta$ 7.35 (d, *J* = 8.3 Hz, 2H), 7.24 – 7.13 (m, 1H), 7.07 – 6.82 (m, 4H), 6.73 (dd, *J* = 8.0, 0.7 Hz, 1H), 5.72 (t, *J* = 3.6 Hz, 1H), 4.52 (d, *J* = 6.6 Hz, 1H), 4.14 (d, *J* = 4.2 Hz, 1H), 2.37 (s, 3H), 2.26 – 1.99 (m, 3H), 1.96 – 1.79 (m, 1H), 1.79 – 1.64 (m, 2H). **$^{13}$C NMR (75 MHz, $CDCl_3$)** $\delta$ 142.54, 137.01, 136.80, 135.05, 133.38, 132.46, 131.05, 129.17 (2C), 128.32, 126.78 (2C), 124.65, 117.85, 50.48, 30.56, 25.31, 21.44, 16.94. **IR (neat):** 3268 (br), 2937 (br), 2121, 1486, 1442, 1327, 1283, 1156. **MS (EI, 70 eV) *m/z* (%):** *the product completely decomposed during the analysis, no detection possible.* **HRMS (ESI)** calcd for $C_{19}H_{20}O_2N_4NaS$ 391.1199, found 391.1196.

### *N*-(2'-Azido-2,3,4,5-tetrahydro-[1,1'-biphenyl]-2-yl)-2-bromo-*N*-tosyl-acetamide (S19)

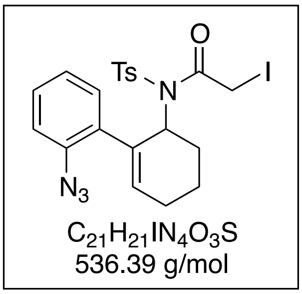


To a suspension of potassium hydride (30% in oil) (220 mg, 1.625 mmol) in dry THF (1 mL) was added dropwise a solution of azido-toluenesulfonamide **S18** (240 mg, 0.65 mmol) in dry THF (2.5 mL) and the mixture was stirred for 3h at rt. Then bromoacetyl bromide (60 µL, 0.65 mmol) was added and it was stirred for 1 h followed by another two additions of bromoacetyl bromide (2 x 60 µL, 0.65 mmol) (1 h stirring in between). After stirring overnight the mixture was quenched with EtOAc (10 mL) and water (5 mL). The two phases were separated and the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layers were washes sequentially with water and brine, dried over $Na_2SO_4$ and concentrated under reduced pressure to give crude. The crude was purified by flash column chromatography (pentane/$Et_2O$, 7:1 for product, resp. 1:1 for recovered starting material) to get **S19** (126 mg, 40%, >80% brsm).

Gray solid. **m$_p$:** 101.1 – 101.8 °C. **$^1$H NMR (300 MHz, CDCl$_3$)** *δ* 7.53 (d, *J* = 8.4 Hz, 2H), 7.27 – 7.22 (m, 3H), 7.02 (dd, *J* = 7.7, 5.3 Hz, 2H), 6.87 (d, *J* = 8.0 Hz, 1H), 5.80 – 5.71 (m, 1H), 5.37 (s, 1H), 4.23 (A part of AB system, *J* = 13.7 Hz, 1H), 3.93 (B part of AB system, *J* = 13.7 Hz, 1H), 2.44 (s, 3H), 2.41 – 2.09 (m, 4H), 2.02 – 1.87 (m, 1H), 1.87 – 1.70 (m, 1H). **$^{13}$C NMR (75 MHz, CDCl$_3$)** *δ* 165.49, 144.95, 137.35, 135.73, 134.65, 132.34, 131.81, 131.29, 129.85 (2C), 128.57, 127.69 (2C), 124.67, 117.71, 59.51, 31.12, 28.10, 24.95, 22.35, 21.62. **IR (neat):** 3061 (br), 2947 (br), 2127, 1701, 1358, 1292, 1169. **MS (EI, 70 eV) *m/z* (%):** 151 (3), 136 (20), 135 (4). 134 (22), 123 (22), 121 (24), 108 (4), 107 (4), 106 (5), 95 (12), 93 (13), 71 (5), 56 (6), 55 (100), 54 (16), 53 (5), 43 (8), 42 (14), 41 (13), 39 (9). **HRMS (ESI)** calcd for $C_{21}H_{21}O_3N_4BrNaS$ 511.0410, found 511.0405.

### *N*-(2'-Azido-2,3,4,5-tetrahydro-[1,1'-biphenyl]-2-yl)-2-iodo-*N*-tosyl-acetamide (1b)

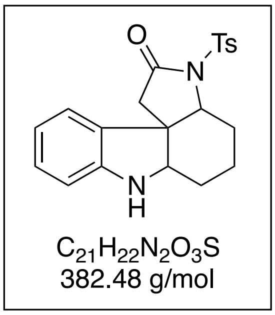
A mixture of tosylacetamide **S19** (48 mg, 0.1 mmol) and sodium iodide (38 mg, 0.25 mmol) in acetone (1 mL) was stirred at rt for 16 h *(**caution:** flask wrapped in aluminum foil)*. The acetone was then removed *(**caution:** flask wrapped in aluminum foil)*. and the residue was diluted with water (10 mL) and $CH_2Cl_2$ (10 mL) and the aqueous layer was extracted with $CH_2Cl_2$ (3 x 10 mL). The organic layers were washed sequentially with



water, $Na_2S_2O_3$ sat. aq. and brine. The organic phase was then dried over $Na_2SO_4$ and concentrated under reduced pressure to give a clean crude **1b** (53 mg, 99%), which was used without further purification.

Yellowish solid. **$^1$H NMR (300 MHz, $CDCl_3$)** $\delta$ 7.55 (d, *J* = 8.4 Hz, 2H), 7.31 – 7.20 (m, 3H), 7.04 (d, *J* = 4.7 Hz, 2H), 6.92 (d, *J* = 8.0 Hz, 1H), 5.82 – 5.71 (m, 1H), 5.49 (s, 1H), 4.06 (A part of AB system, *J* = 11.9 Hz, 1H), 3.89 (B part of AB system, *J* = 11.9 Hz, 1H), 2.44 (s, 3H), 2.37 – 2.12 (m, 4H), 1.93 (s, 1H), 1.88 – 1.73 (m, 1H).

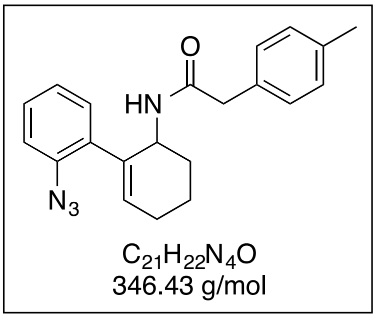
### 3-Tosyl-3a,4,5,6,6a,7-hexahydro-1*H*-pyrrolo[2,3-*d*]carbazol-2(3*H*)-one (2b)



To a solution of aryl azide **1b** (53 mg, 0.1 mmol) was added $Et_3B$ (1 M in *n*-hexane, 0.1 mL, 0.1 mmol) at rt. The mixture was stirred for 1 h and another portion of $Et_3B$ (1 M in *n*-hexane, 0.1 mL, 0.1 mmol) was added. This was repeated once (in total 0.3 mmol of $Et_3B$) and after 3 h stirring, the reaction was complete. The reaction mixture was filtered over a pad of neutral aluminium oxide, rinsed with $Et_2O$ and concentrated under reduced pressure. The residue was purified by flash column chromatography (cyclohexane/EtOAc, 4:1) to get the desired product **2b** (20 mg, 52%) as well as a side product **8** (7 mg, 21%)

White solid. **$m_p$:** 208.5 –209.4 °C. **$^1$H NMR (300 MHz, $CDCl_3$)** $\delta$ 7.81(d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.03 (td, *J* = 7.7, 1.1 Hz, 1H), 6.66 (d, *J* = 7.8 Hz, 1H), 6.43 (td, *J* = 7.4, 0.9 Hz, 1H), 6.30 (dd, *J* = 7.4, 0.7 Hz, 1H), 3.90 (dd, *J* = 11.6, 5.7 Hz, 1H), 3.82 (s, 1H), 3.76 (s, 1H), 2.82 (A part of the AB system, *J* = 17.0 Hz, 1H), 2.47 (s, 3H), 2.47 (B part of the AB system, *J* = 17.0 Hz, 1H), 2.00 – 1.88 (m, 1H), 1.88 – 1.70 (m, 1H), 1.70 – 1.52 (m, 3H), 1.47 – 1.28 (m, 1H). **$^{13}$C NMR (75 MHz, $CDCl_3$)** $\delta$ 171.33, 148.82, 144.98, 135.31, 134.81, 129.38 (2C), 128.54, 128.50 (2C), 121.39, 119.23, 109.78, 66.68, 62.23, 46.28, 38.99, 30.35, 25.86, 21.68, 17.29. **IR (neat):** 1734, 1359, 1169, 1090, 734, 667, 618. **HRMS (ESI)** calcd for $C_{21}H_{23}O_3N_2S$ 383.1424, found 383.1317.

**Side Product 8:**



**$^1$H NMR (300 MHz, $CDCl_3$)** $\delta$ 7.33 – 7.22 (m, 2H), 7.10 – 6.91 (m, 4H), 6.80 (d, *J* = 7.8 Hz, 2H), 5.71 (s, 1H), 5.33 (s, 1H), 4.81 (s, 1H), 3.44 – 3.21 (m, 2H), 2.34 (s, 3H), 2.20 – 1.83 (m, 2H), 1.83 – 1.43 (m, 4H). **$^{13}$C NMR (75 MHz, $CDCl_3$)** $\delta$ 170.43, 137.50, 136.79, 135.29, 133.21, 132.06, 131.52, 130.35, 129.57 (2C), 129.21 (2C), 128.32, 124.58, 118.03, 47.74, 43.44, 29.72, 25.31, 21.10, 18.91. **IR (neat):** 2123, 1642, 1512, 1287, 752, 669. **MS (EI, 70 eV) *m/z* (%):** 382 (2, M+), 345 (16), 329 (4), 281 (5), 207 (27), 195 (3), 170 (20), 169 (100), 168 (98), 167 (42), 166 (6) 154 (11), 149 (6), 143 (3), 140 (3), 139 (4), 133 (3), 115 (3), 106 (8), 105 (18), 103 (3). **HRMS (ESI)** calcd for $C_{21}H_{23}ON_4$ 347.1866, found 347.1875.

## 3. References

(1) Banwell, M. G.; Kelly, B. D.; Kokas, O. J.; Lupton, D. W. *Org. Lett.* **2003**, *5*, 2497.

(2) Luche, J. L. *J. Am. Chem. Soc.* **1978**, *100*, 2226.

(3) Barral, K.; Moorhouse, A. D.; Moses, J. E. *Org. Lett.* **2007**, *9*, 1809.

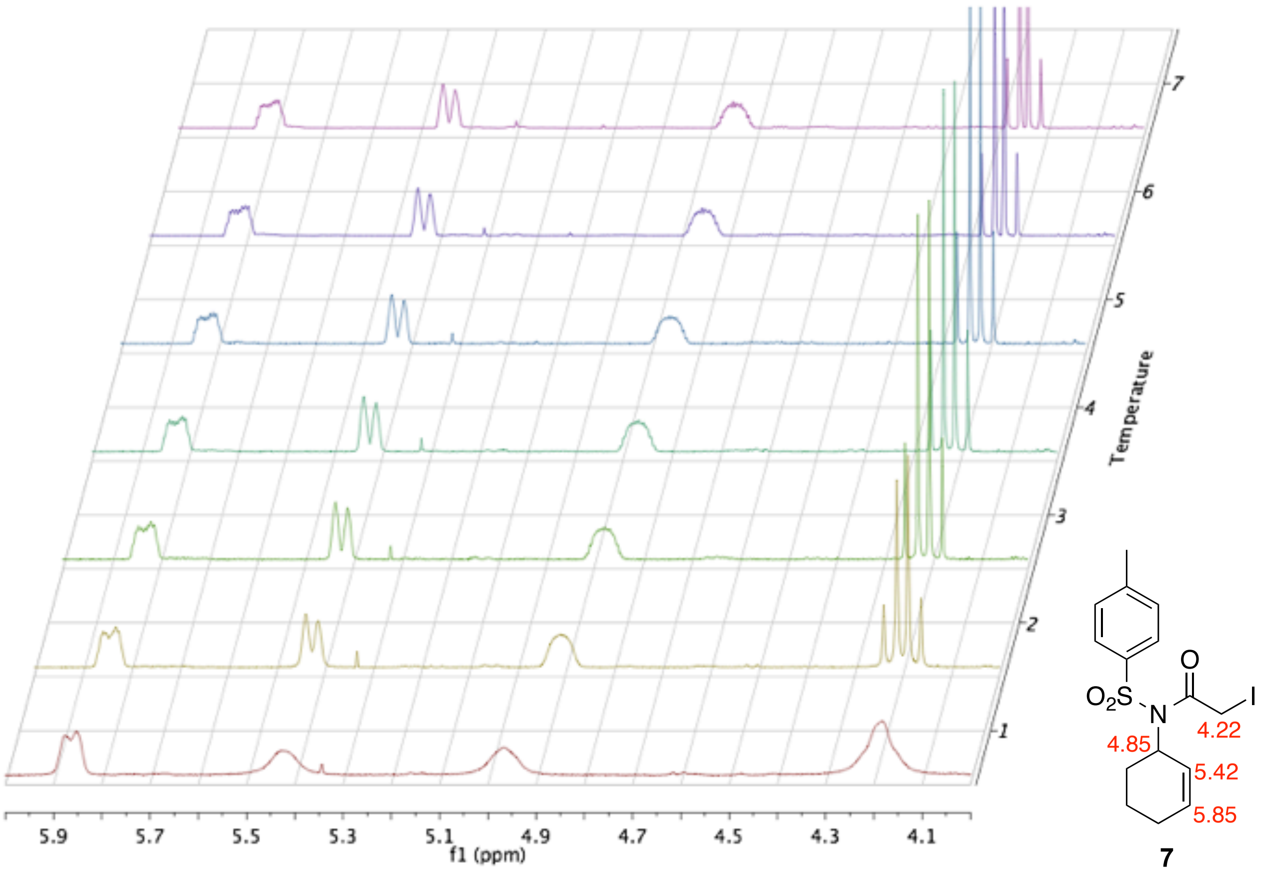
(4) Krafft, M. E.; Cran, J. W. *Synlett* **2005**, 1263.

(5) Chen, J.; Forsyth, C. J. *J. Am. Chem. Soc.* **2003**, *125*, 8734.

(6) brsm = based on recovered starting material

## 4. NMR Spectra

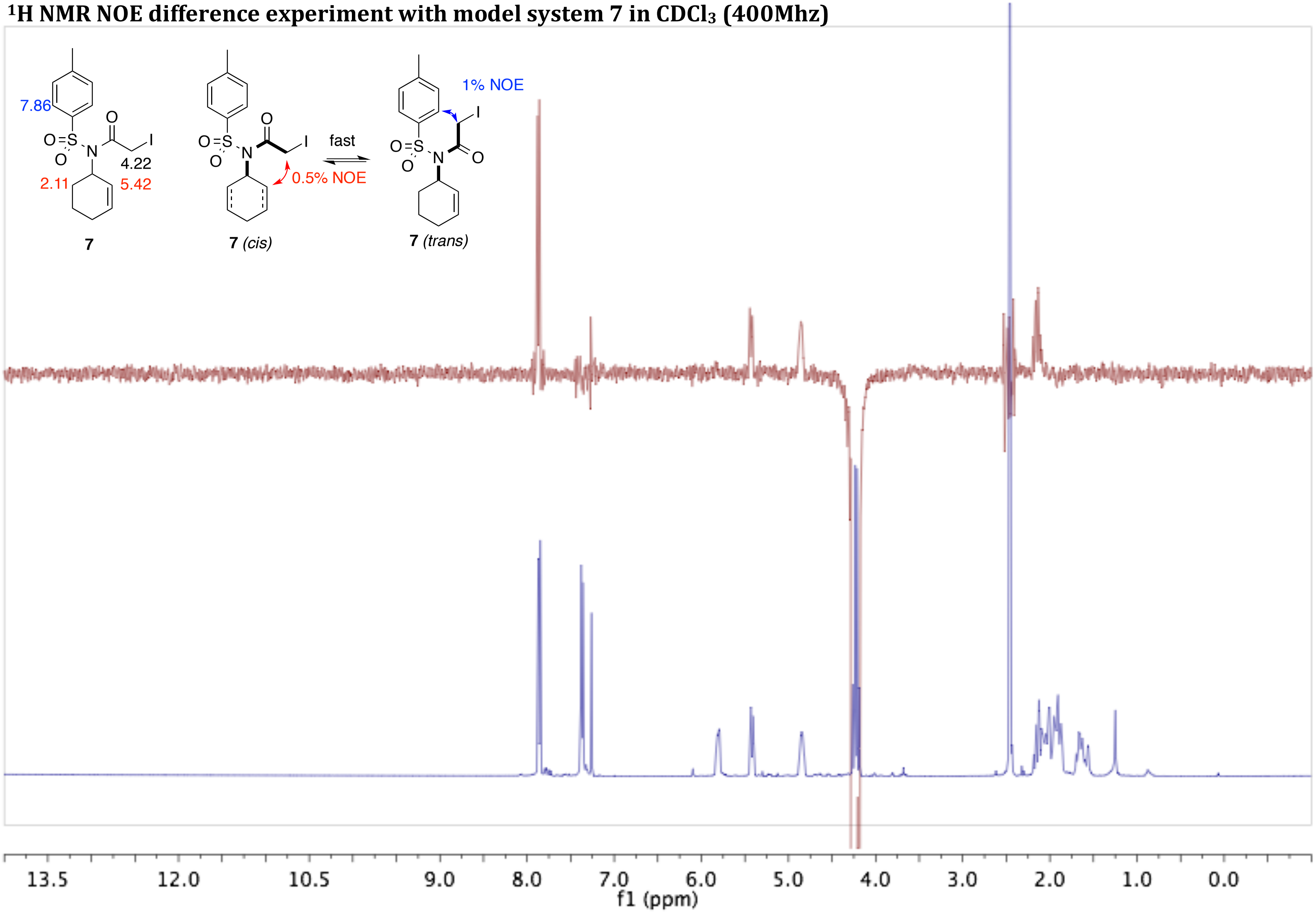
### Variable temperature $^1$H NMR study with model system 7 in $CDCl_3$, 400 Mhz

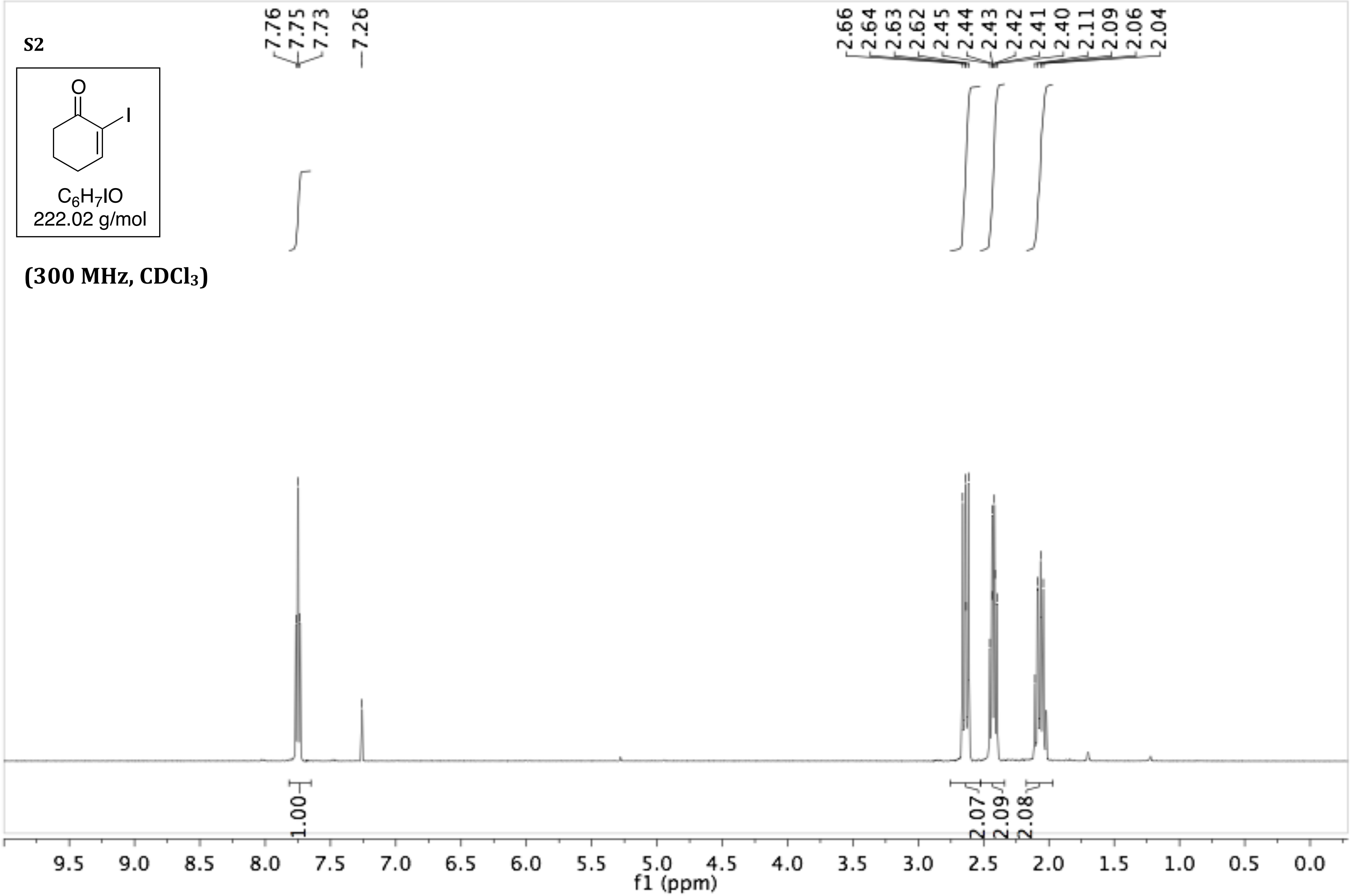


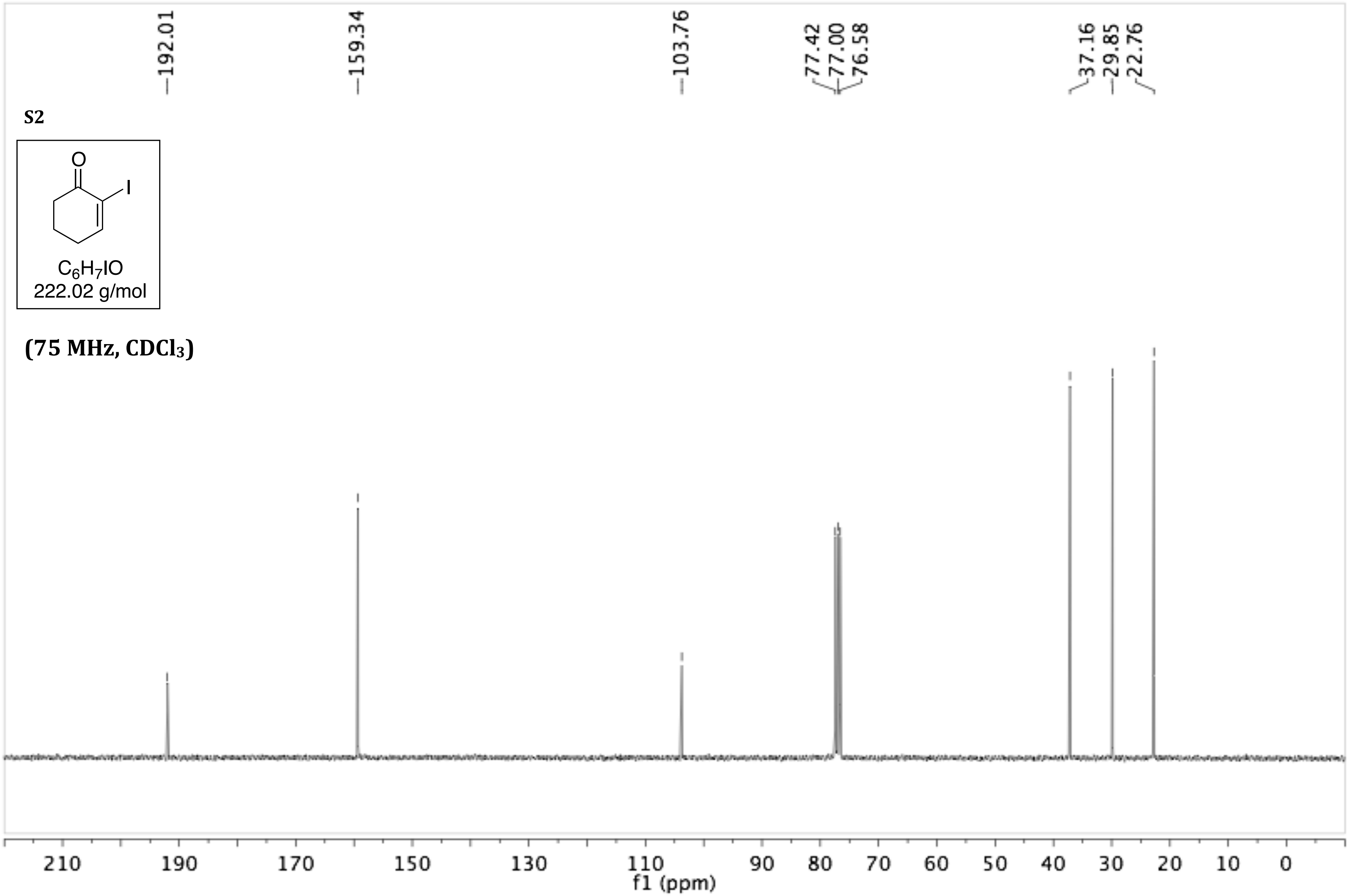
x-axis: chemical shift in ppm
y-axis: 7 different temperatures

1 = –50 °C
2 = –30 °C
3 = –10 °C
4 = 0 °C
5 = 10 °C
6 = 30 °C
7 = 50 °C

# $^1H$ NMR NOE difference experiment with model system 7 in $CDCl_3$ (400Mhz)



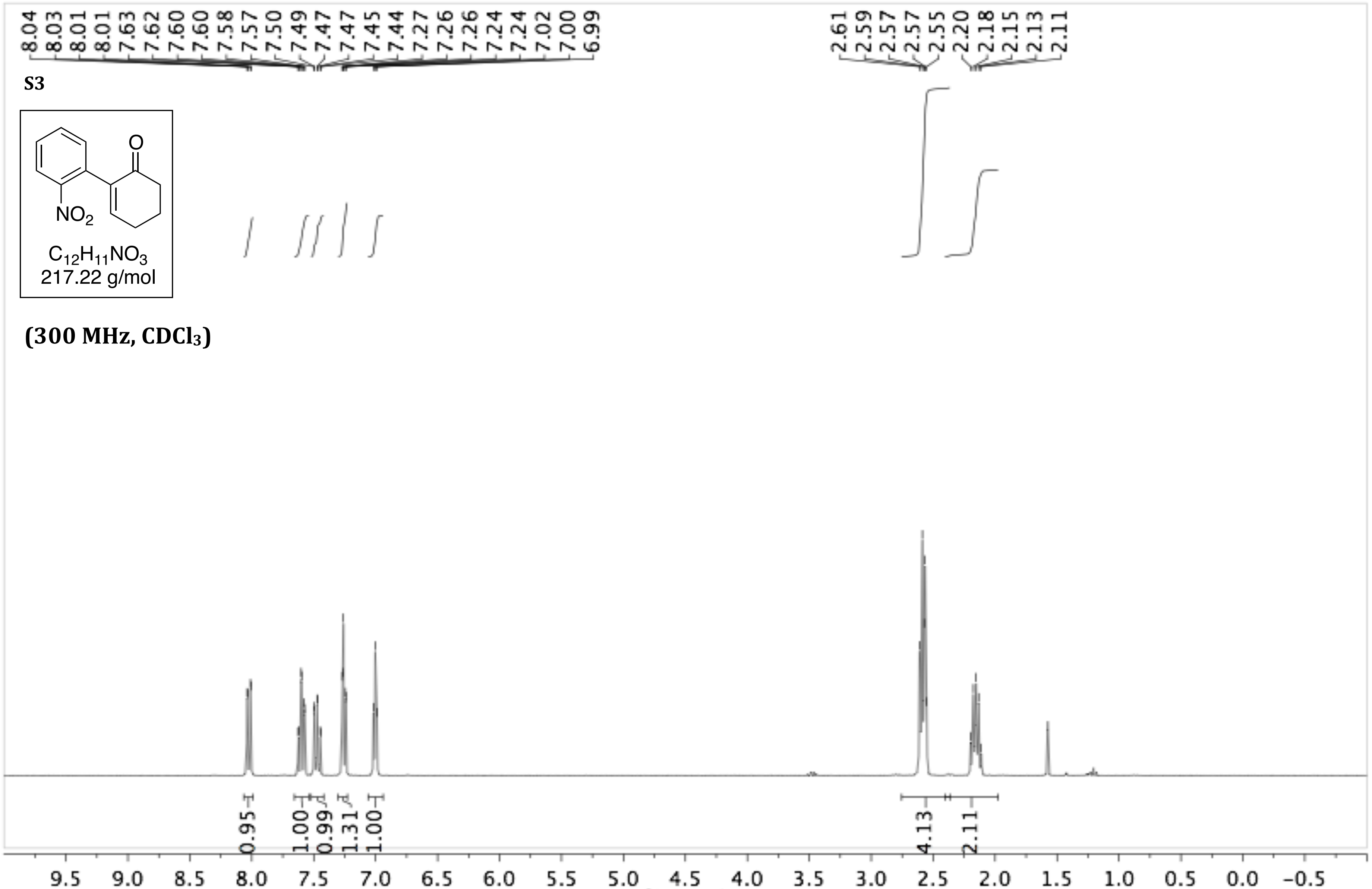

S2
$C_6H_7IO$
222.02 g/mol
(300 MHz, CDCl$_3$)
7.76
7.75
7.73
7.26
2.66
2.64
2.63
2.62
2.45
2.44
2.43
2.42
2.41
2.40
2.11
2.09
2.06
2.04
1.00
2.07
2.09
2.08
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



**S2**

$C_6H_7IO$
222.02 g/mol

**(75 MHz, $CDCl_3$)**

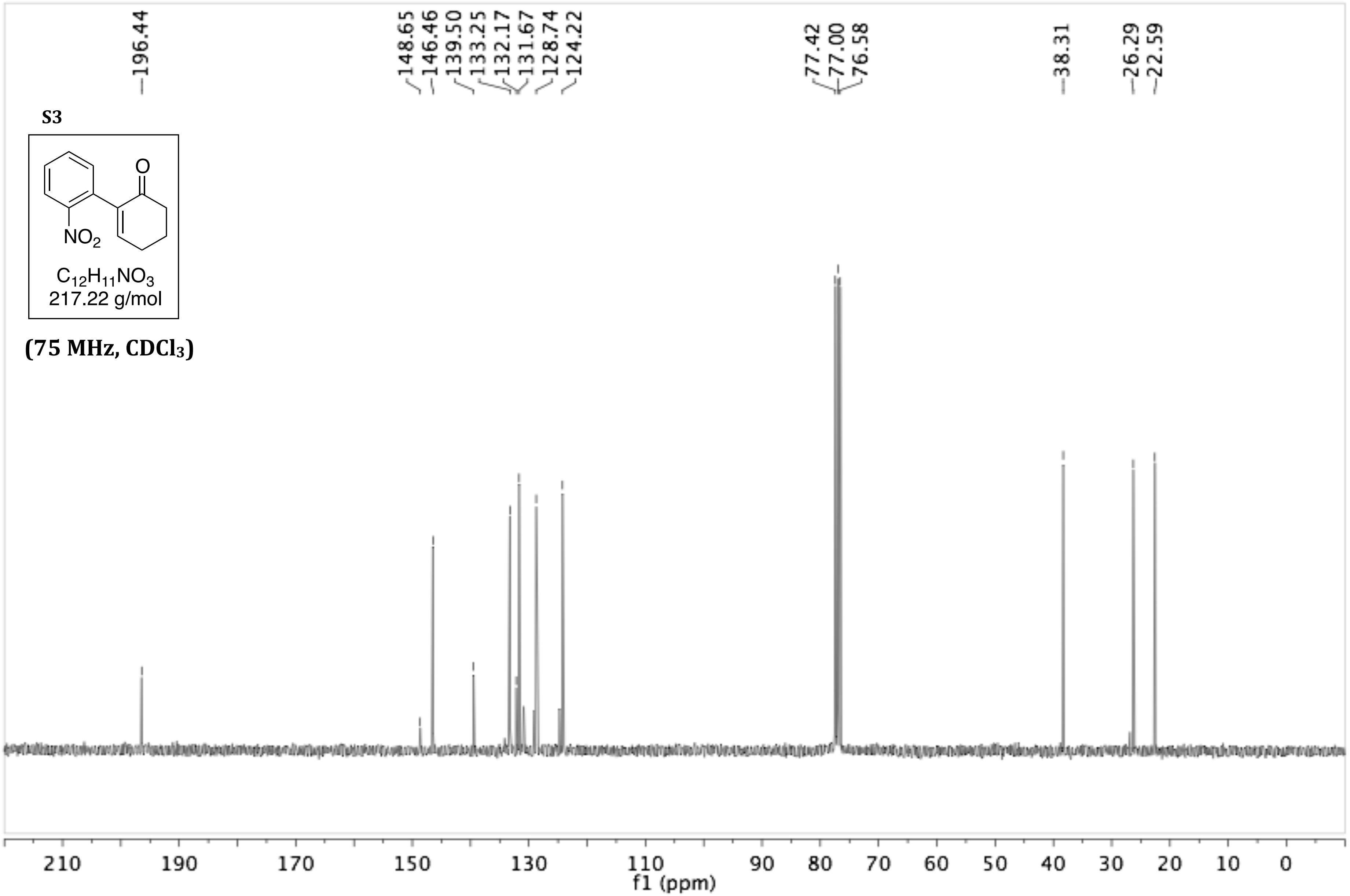


**S3**

$C_{12}H_{11}NO_3$
217.22 g/mol

**(300 MHz, $CDCl_3$)**

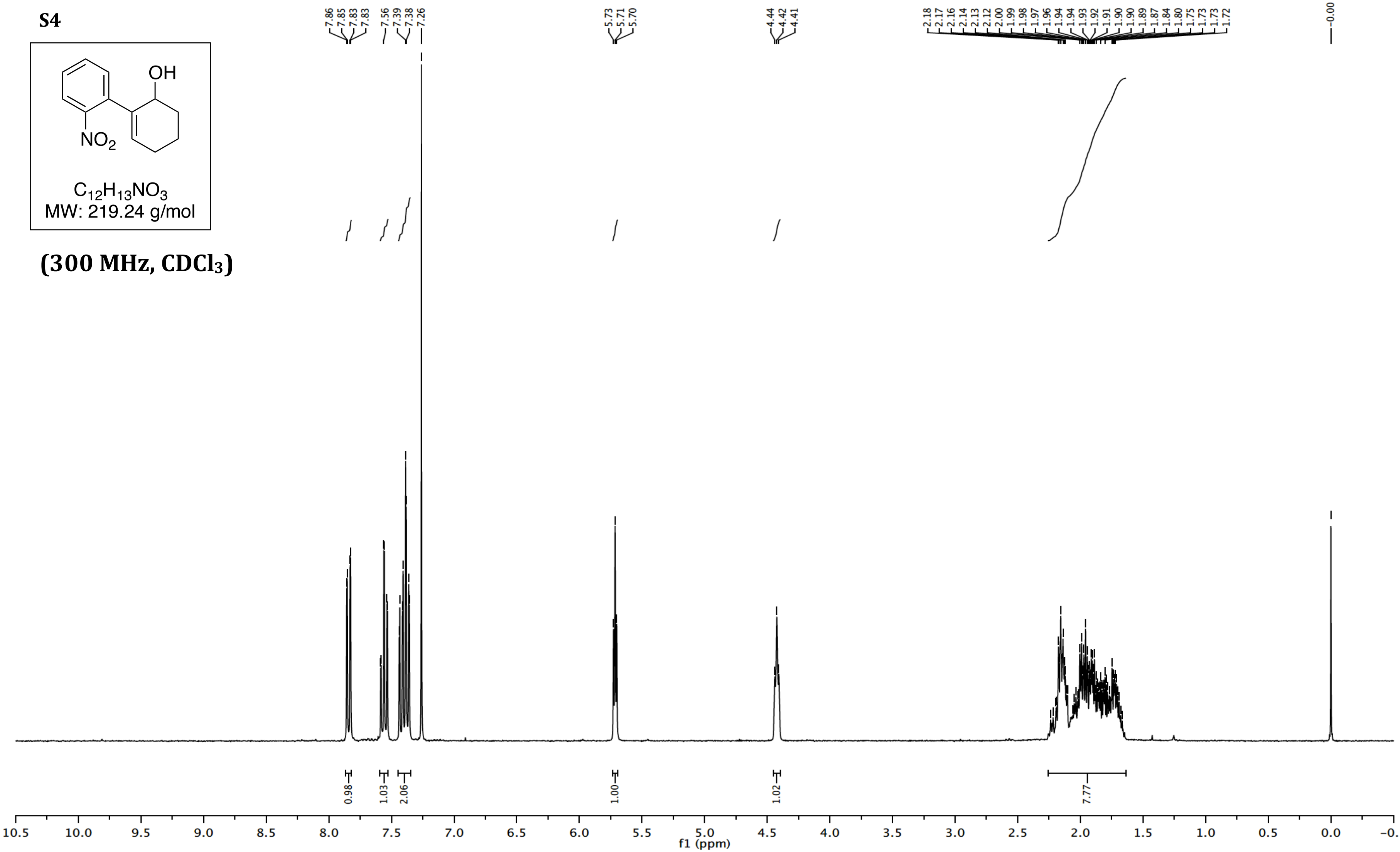
**S3**



$C_{12}H_{11}NO_3$
217.22 g/mol

**(75 MHz, $CDCl_3$)**

**S4**



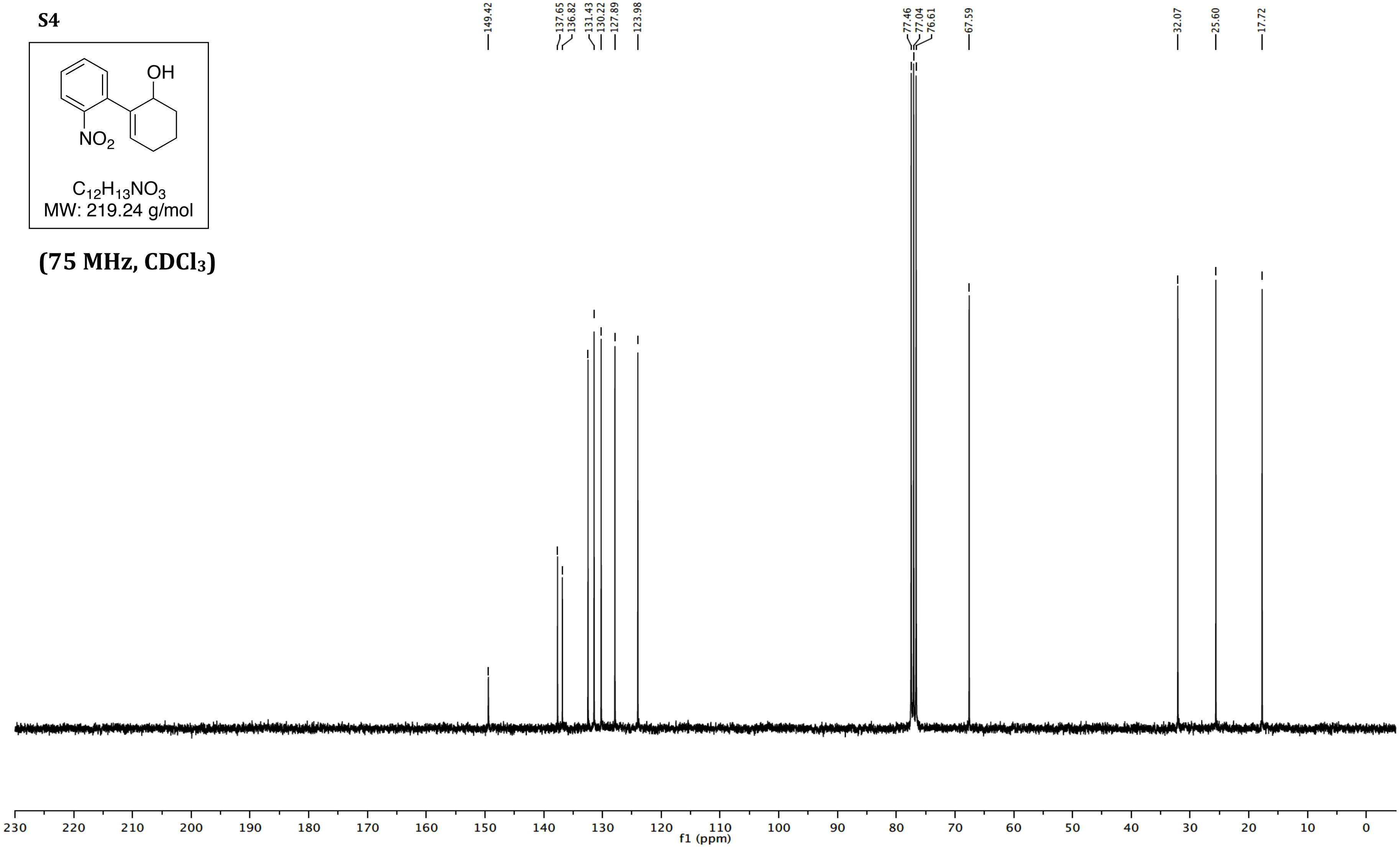
$C_{12}H_{13}NO_3$
MW: 219.24 g/mol

**(300 MHz, $CDCl_3$)**

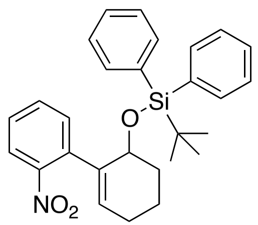
**S4**

$C_{12}H_{13}NO_3$
MW: 219.24 g/mol

**(75 MHz, $CDCl_3$)**

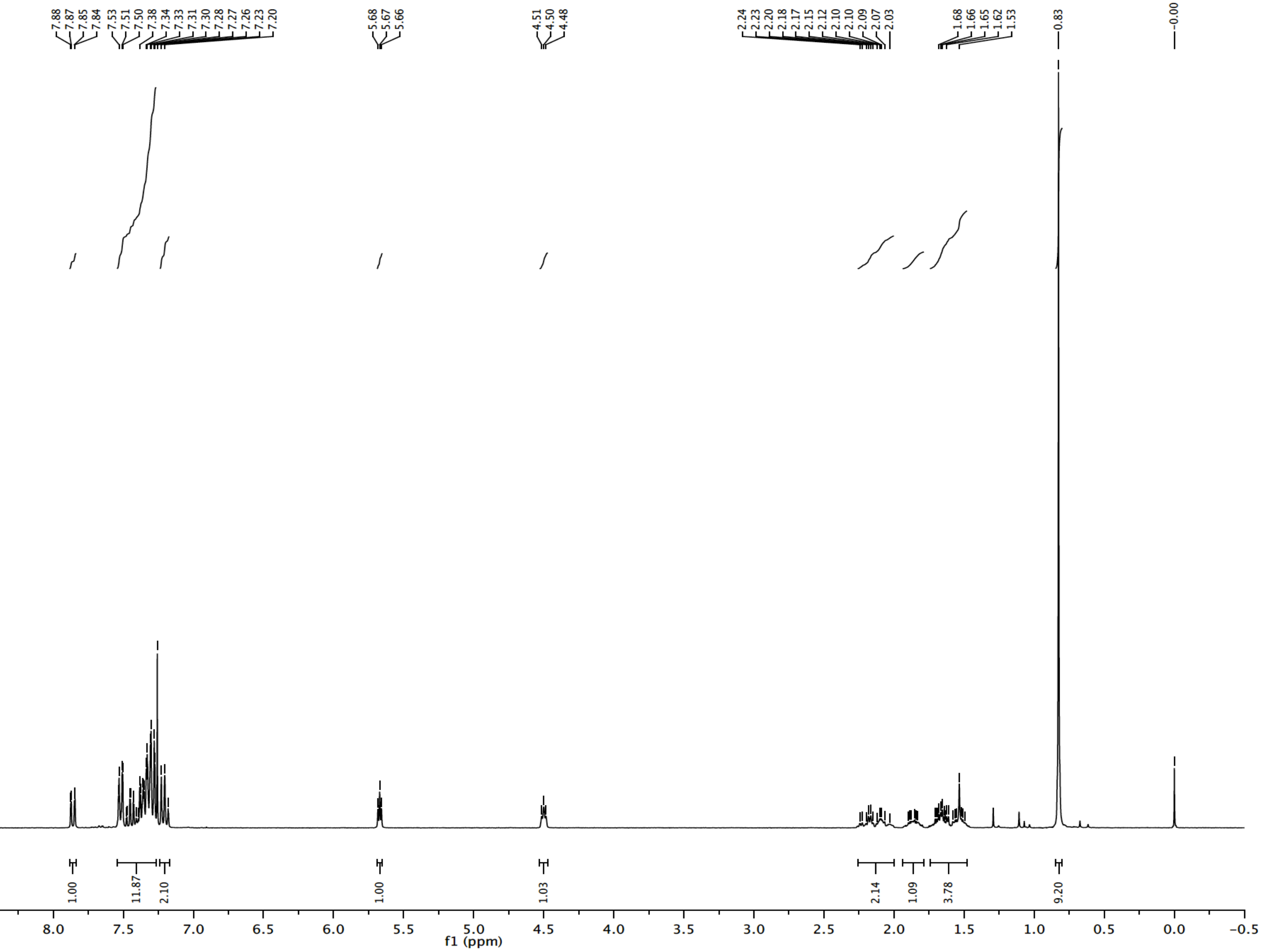


**S5**

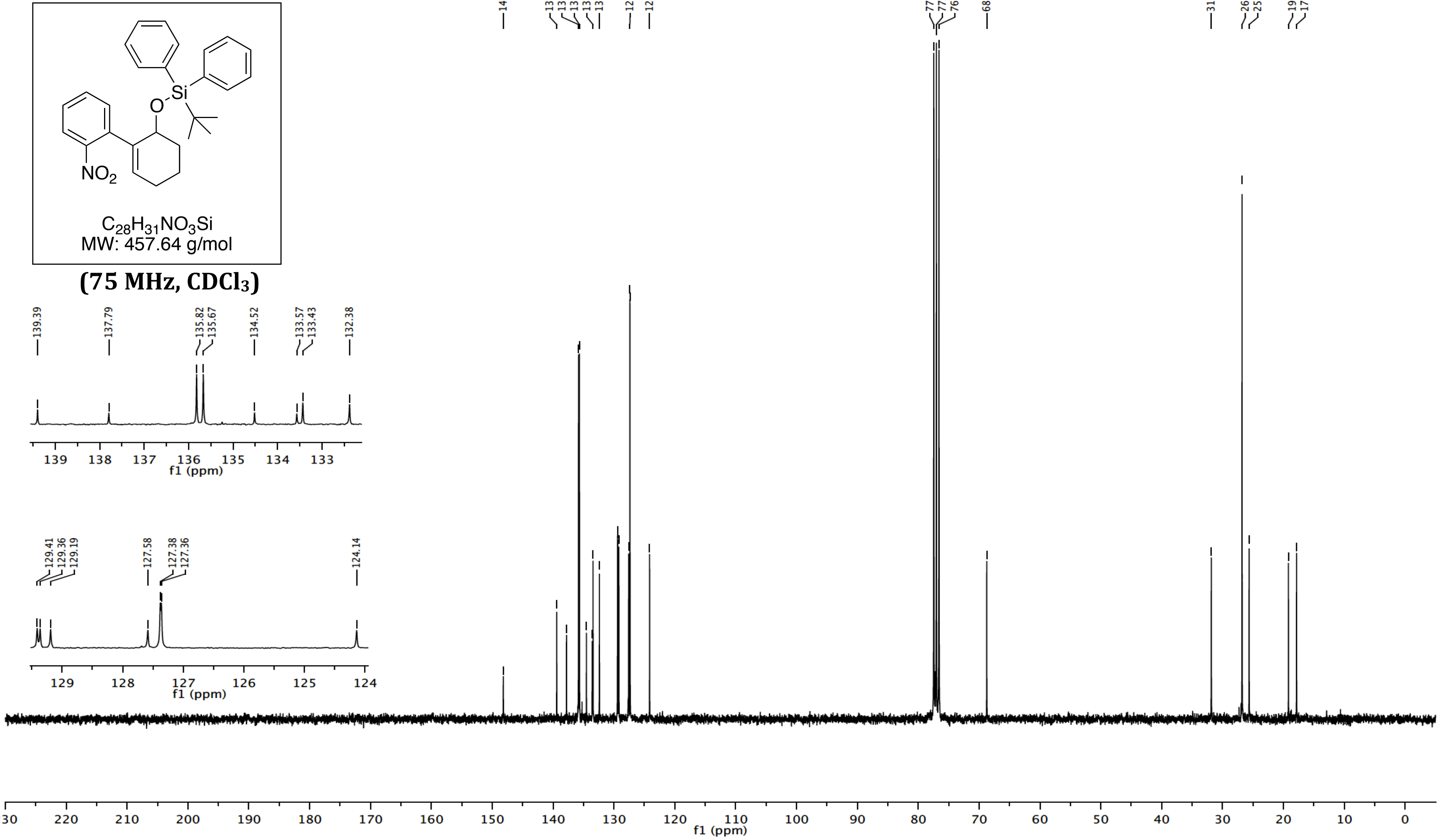


$C_{28}H_{31}NO_3Si$
MW: 457.64 g/mol

**(300 MHz, CDCl$_3$)**



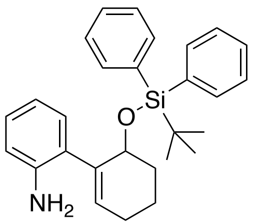
**S5**



$C_{28}H_{31}NO_3Si$
MW: 457.64 g/mol

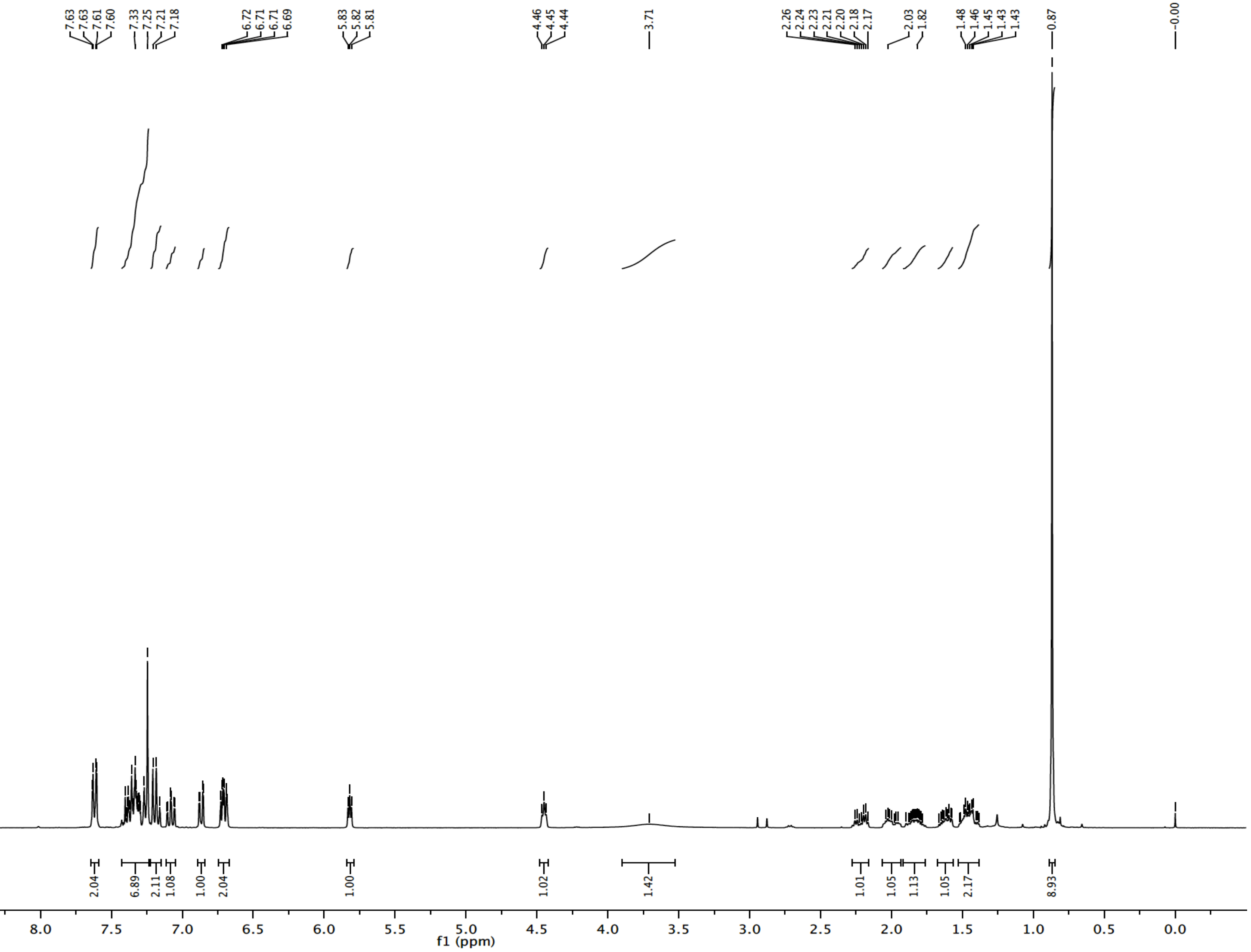
**(75 MHz, $CDCl_3$)**

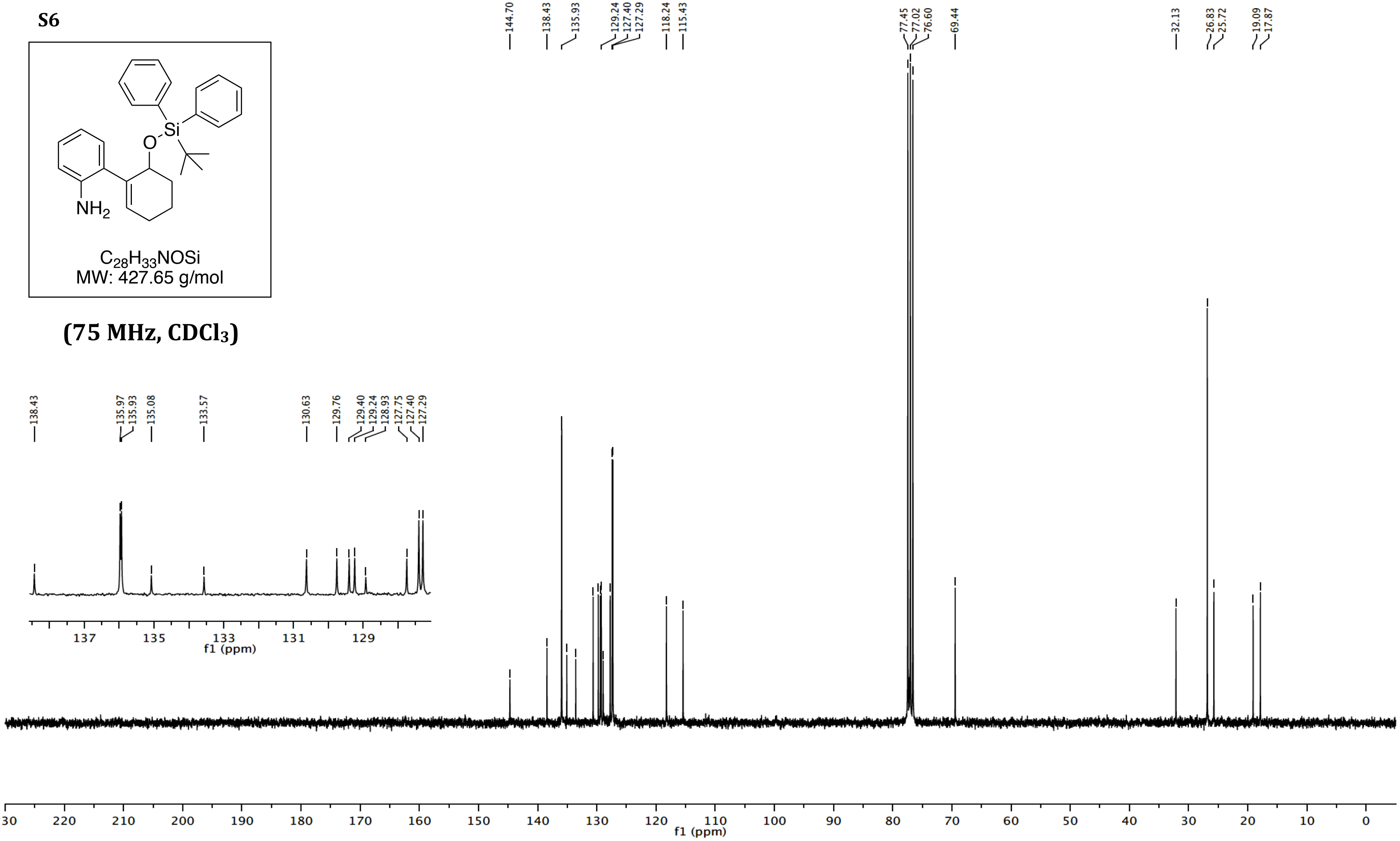
**S6**



$C_{28}H_{33}NOSi$
MW: 427.65 g/mol

**(300 MHz, CDCl$_3$)**





**S6**

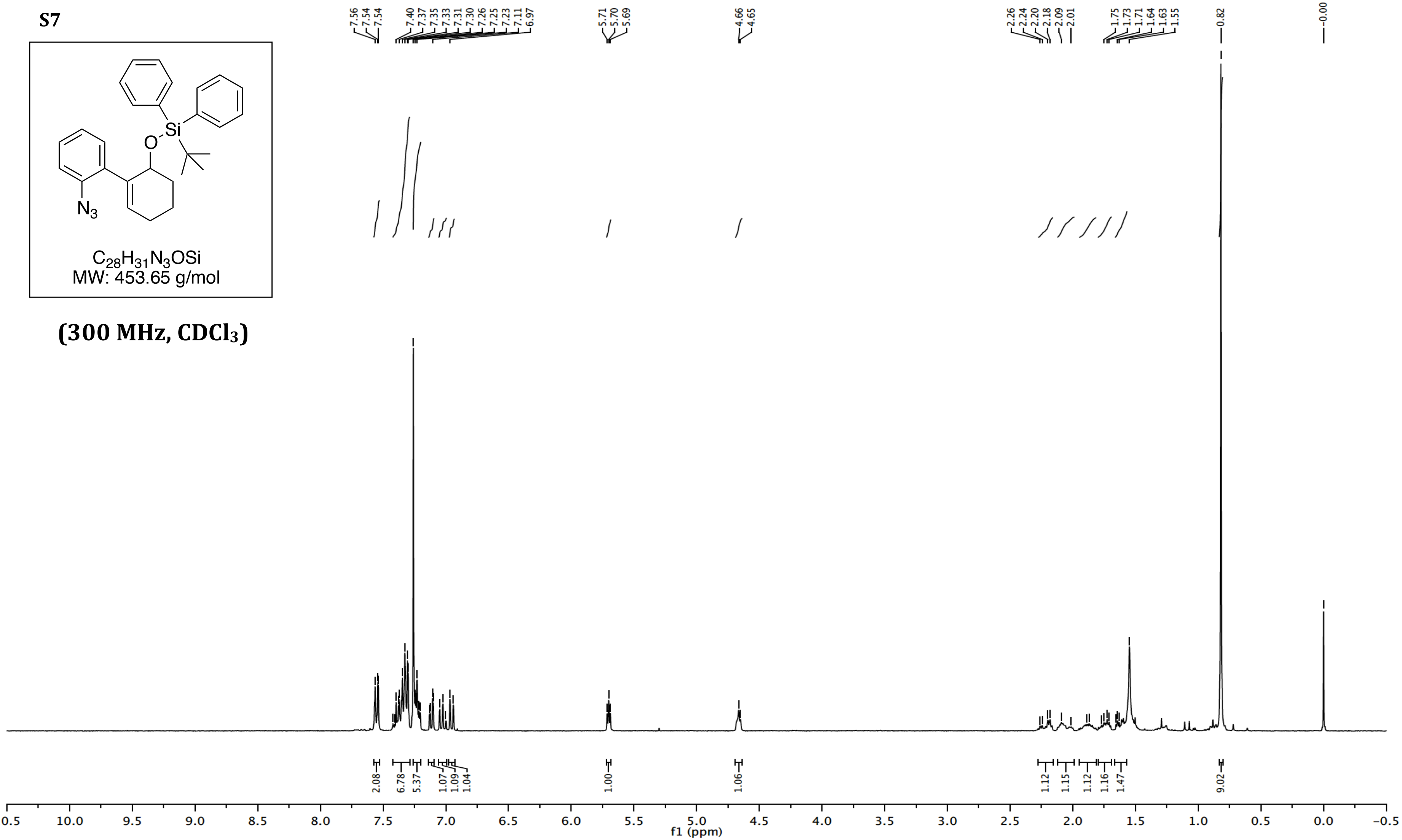
$C_{28}H_{33}NOSi$
MW: 427.65 g/mol

**(75 MHz, CDCl₃)**

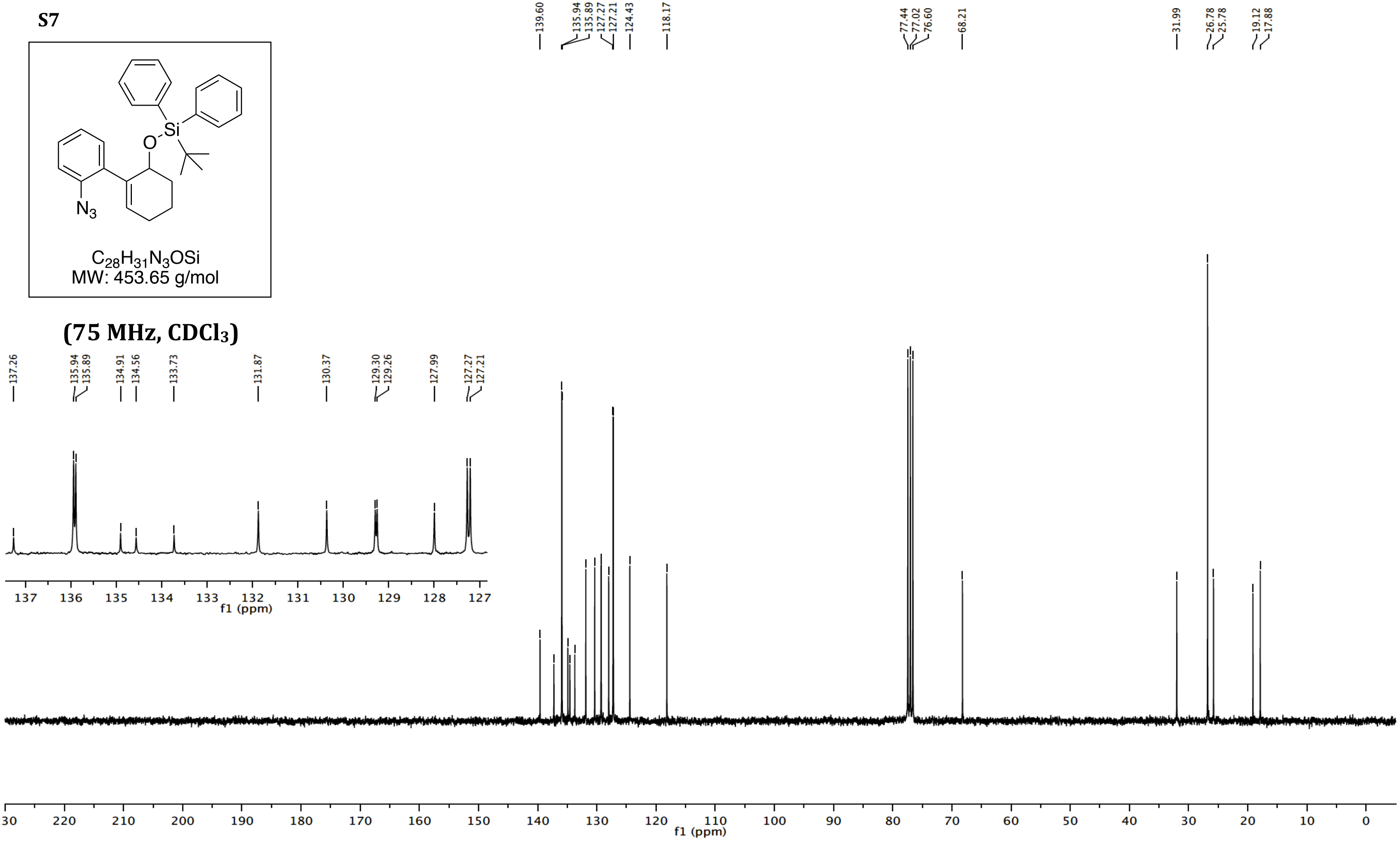
**S7**

$C_{28}H_{31}N_3OSi$
MW: 453.65 g/mol

**(300 MHz, $CDCl_3$)**



**S7**



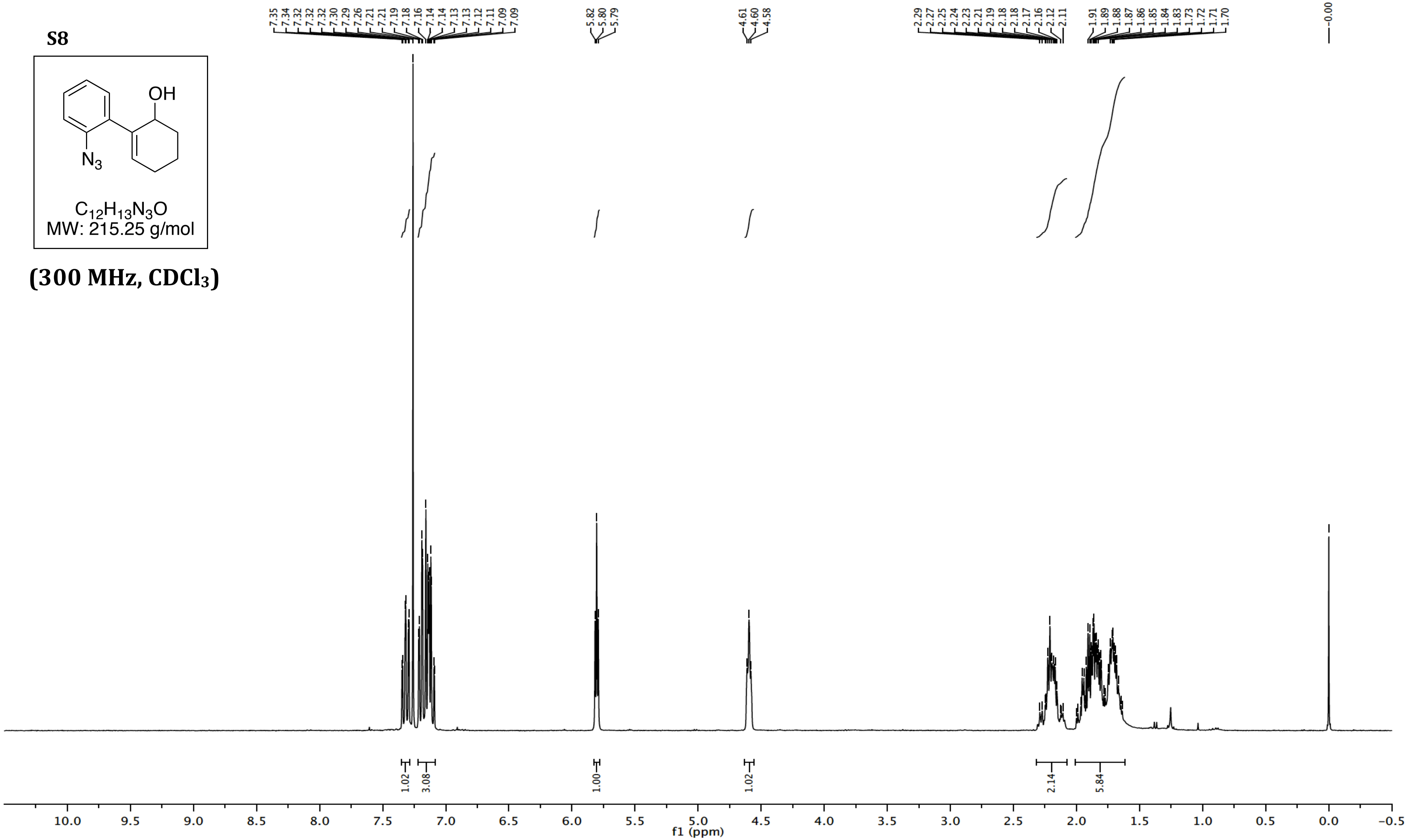
$C_{28}H_{31}N_3OSi$
MW: 453.65 g/mol

**(75 MHz, $CDCl_3$)**

**S8**

$C_{12}H_{13}N_3O$
MW: 215.25 g/mol

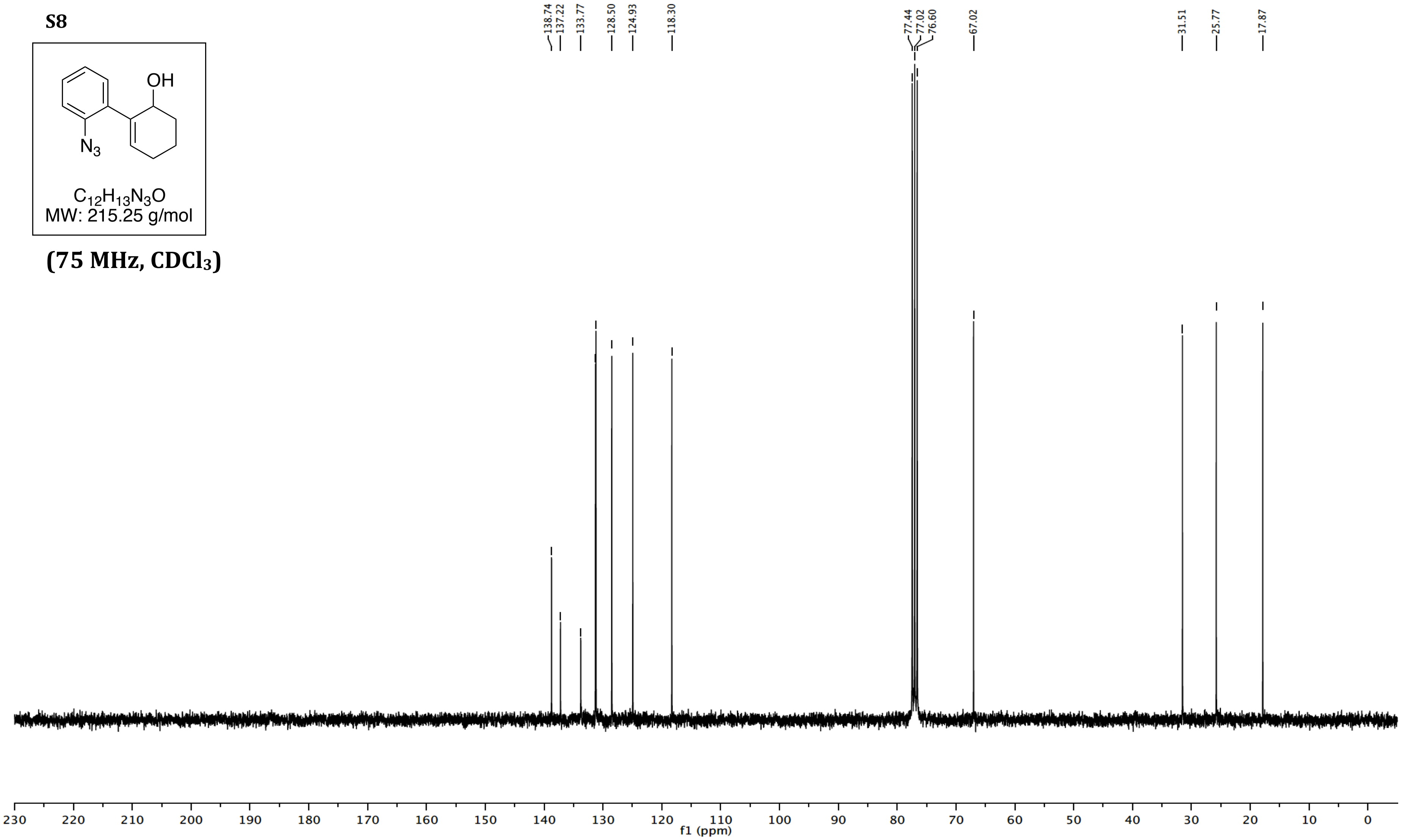
**(300 MHz, CDCl$_3$)**



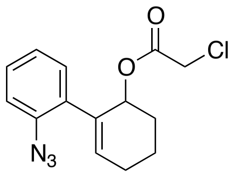
**S8**

$C_{12}H_{13}N_3O$
MW: 215.25 g/mol

**(75 MHz, $CDCl_3$)**

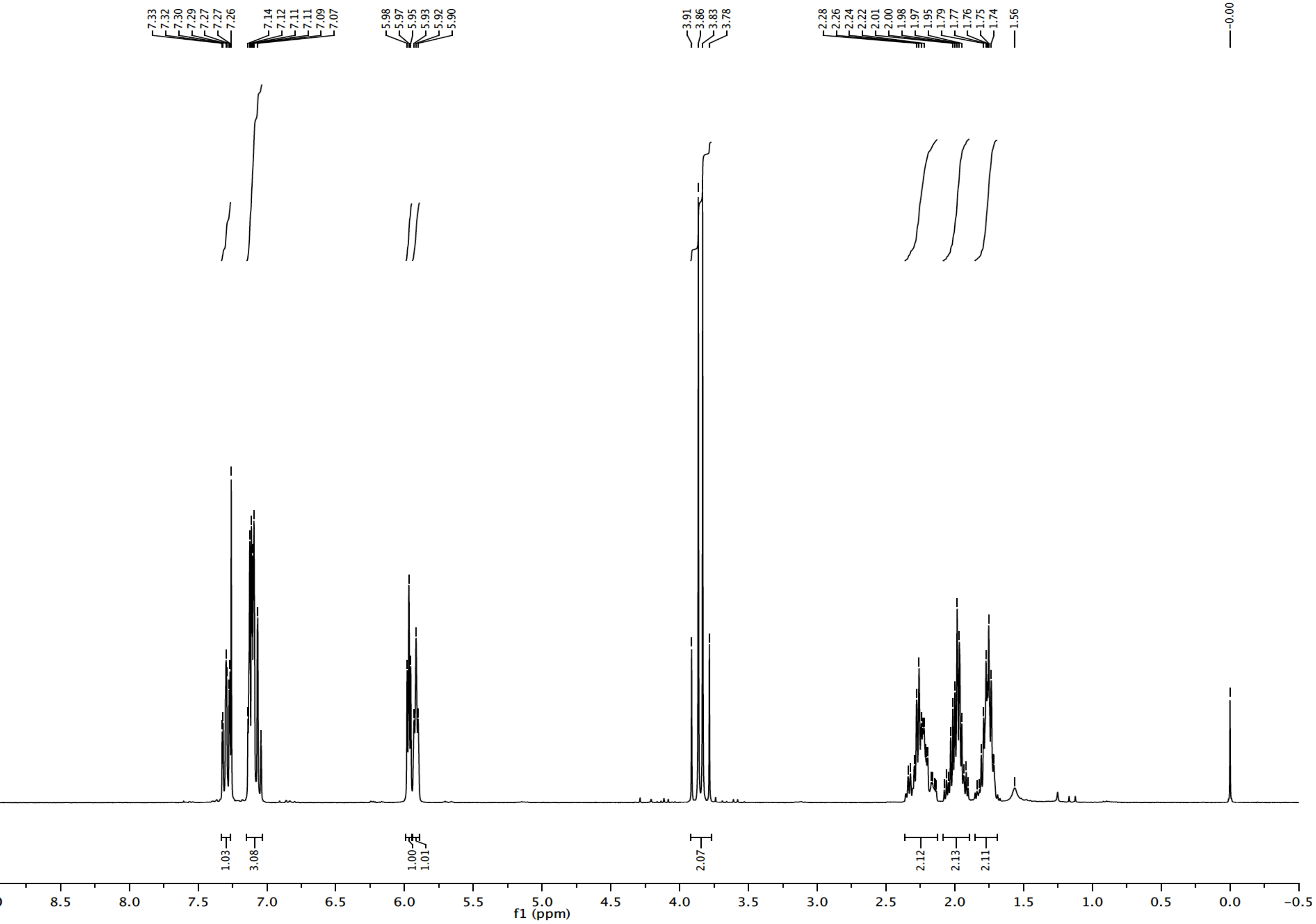


**S9**

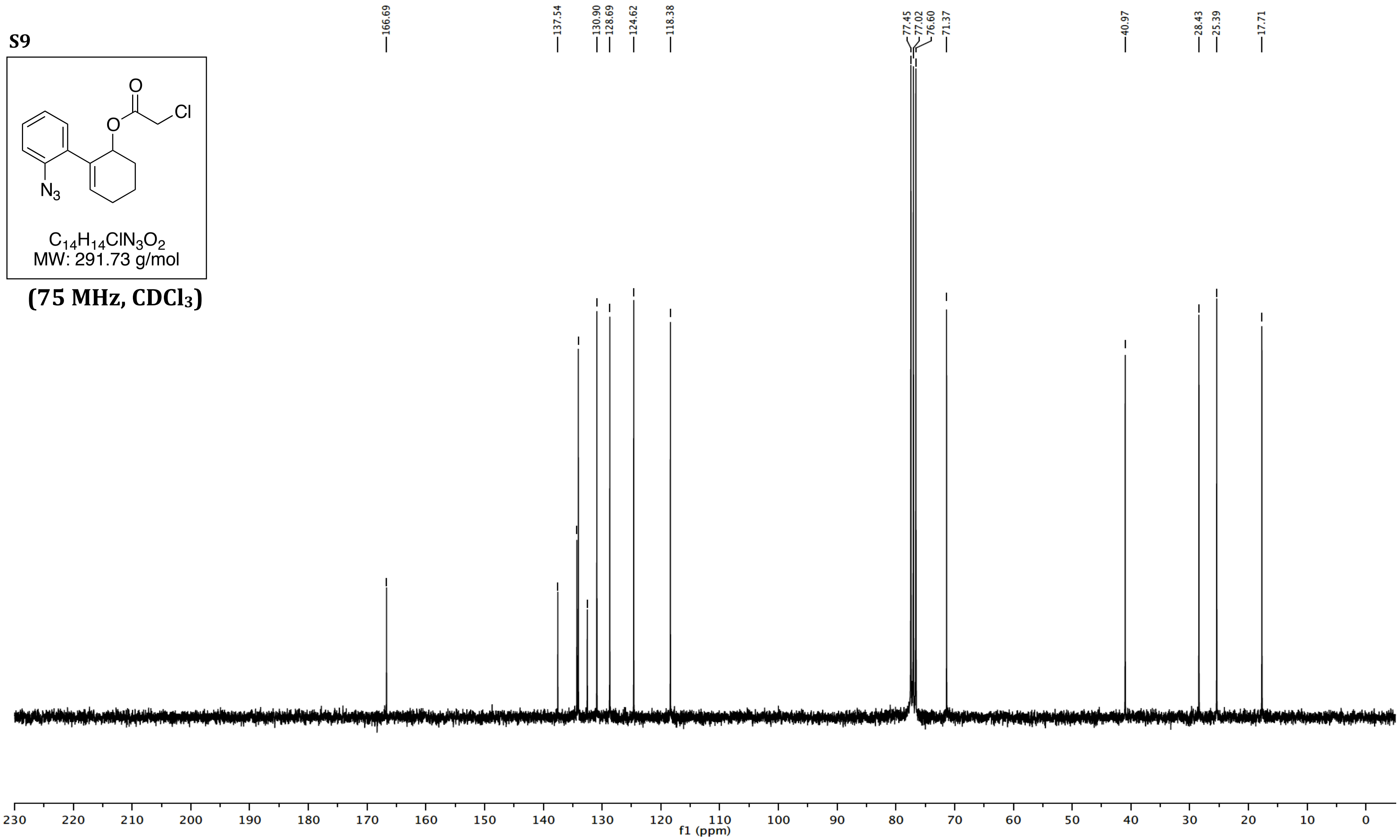


$C_{14}H_{14}ClN_3O_2$
MW: 291.73 g/mol

**(300 MHz, CDCl$_3$)**



**S9**



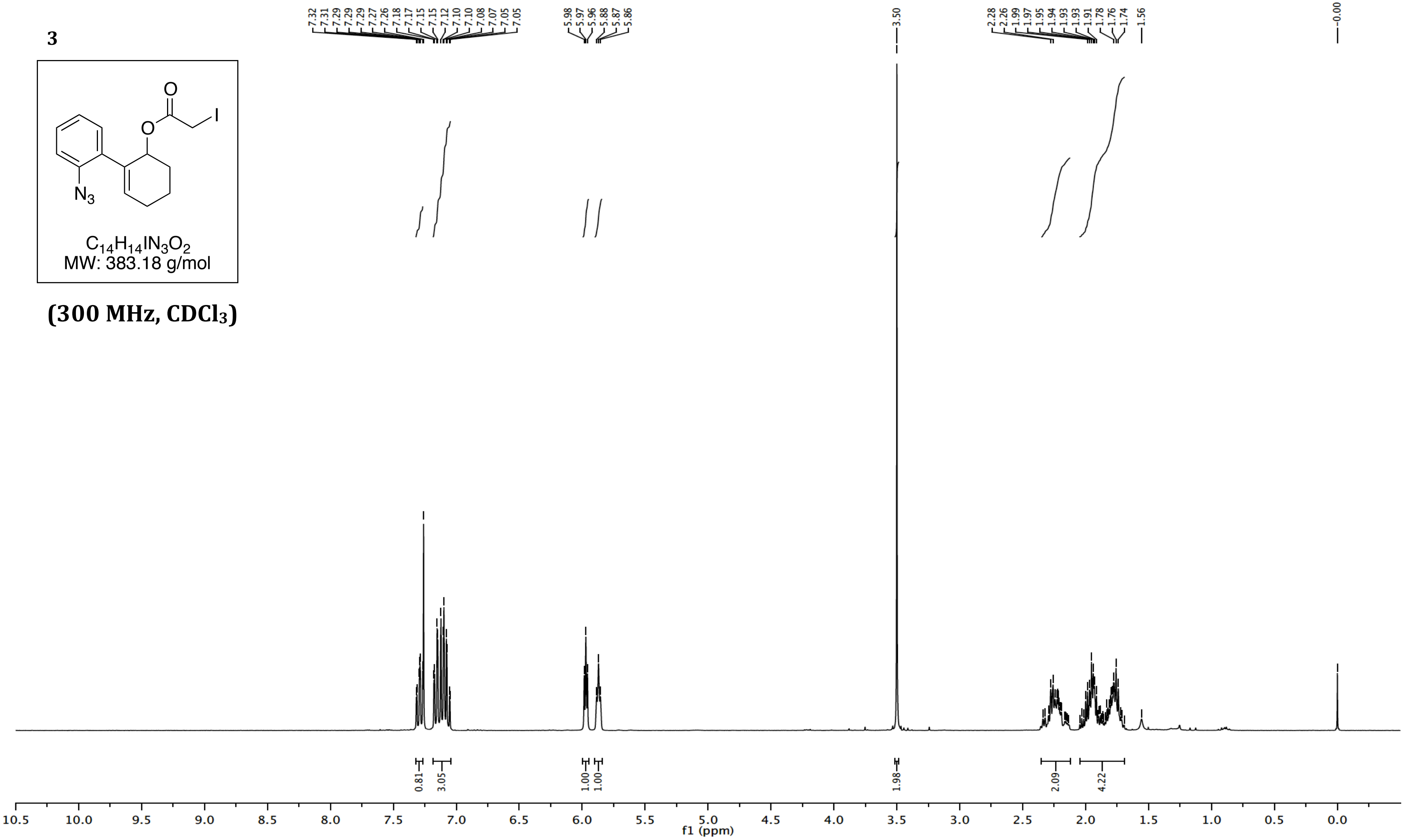
$C_{14}H_{14}ClN_3O_2$
MW: 291.73 g/mol

**(75 MHz, CDCl$_3$)**

**3**

$C_{14}H_{14}IN_3O_2$
MW: 383.18 g/mol

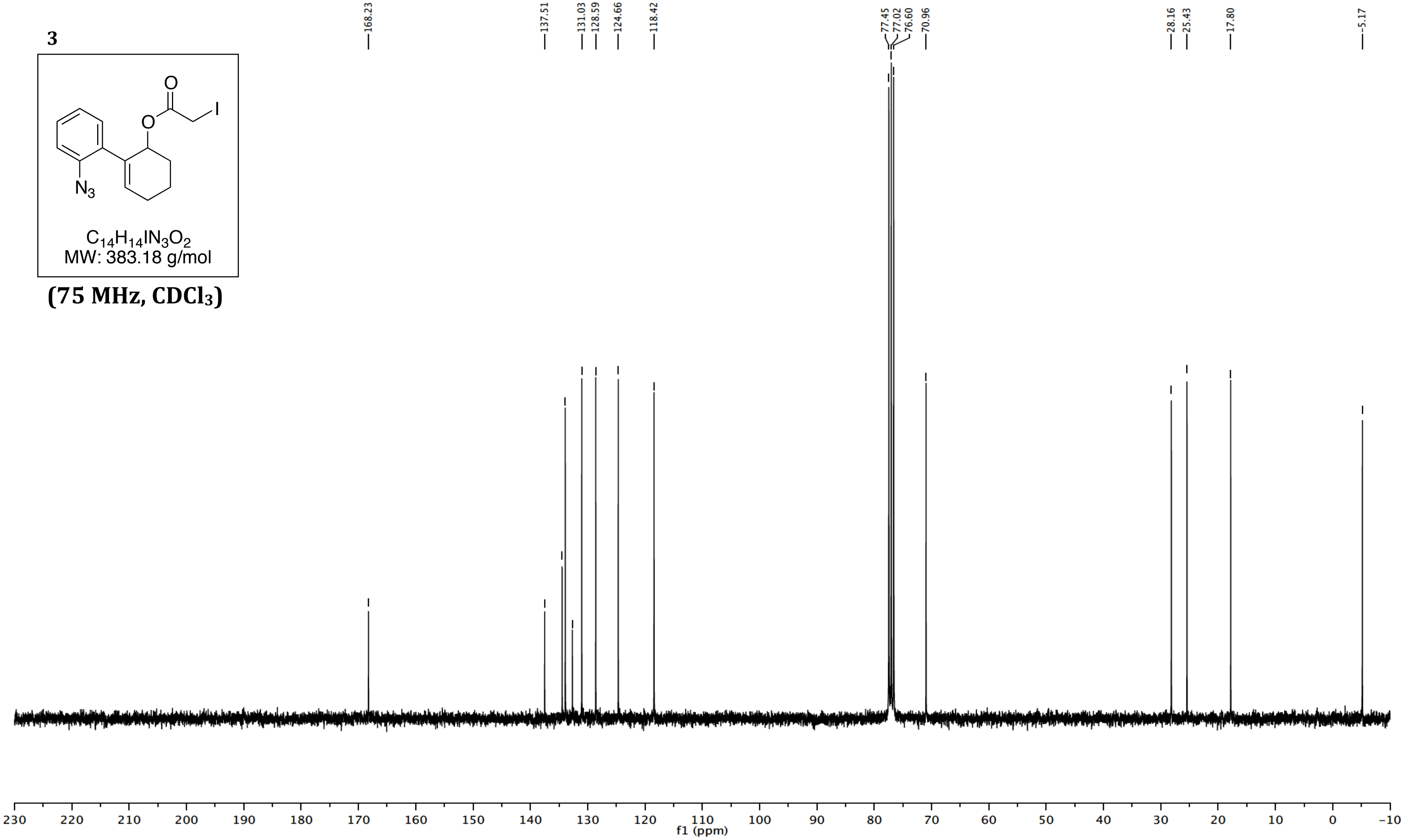
**(300 MHz, $CDCl_3$)**



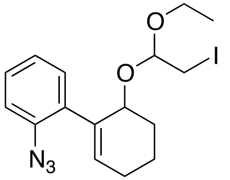
**3**

$C_{14}H_{14}IN_3O_2$
MW: 383.18 g/mol

**(75 MHz, $CDCl_3$)**



**5**

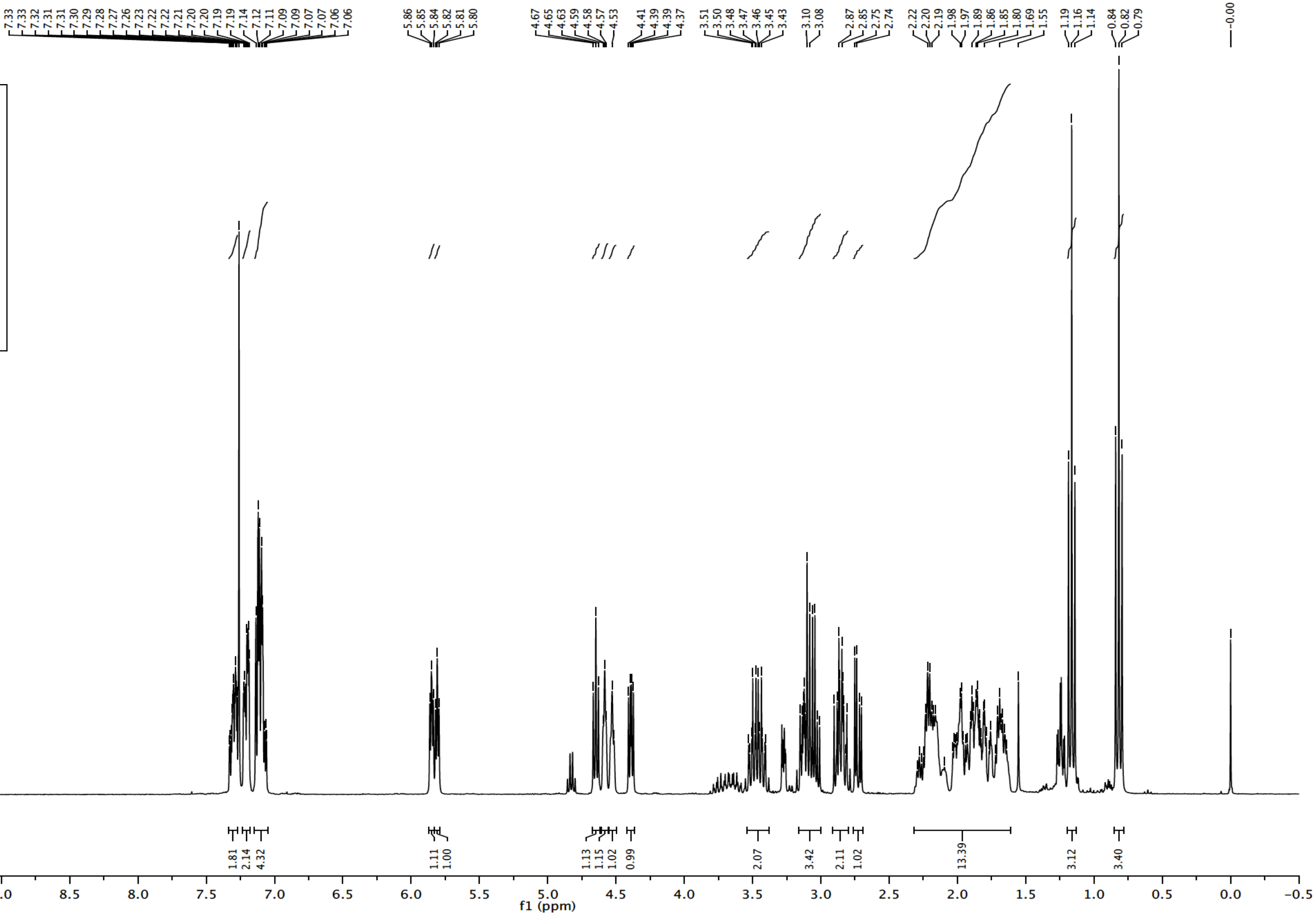


52:48 dr

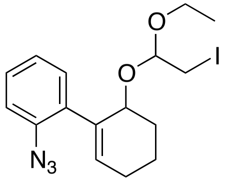
$C_{16}H_{20}IN_3O_2$

MW: 413.25 g/mol

**(300 MHz, CDCl$_3$)**



**5**

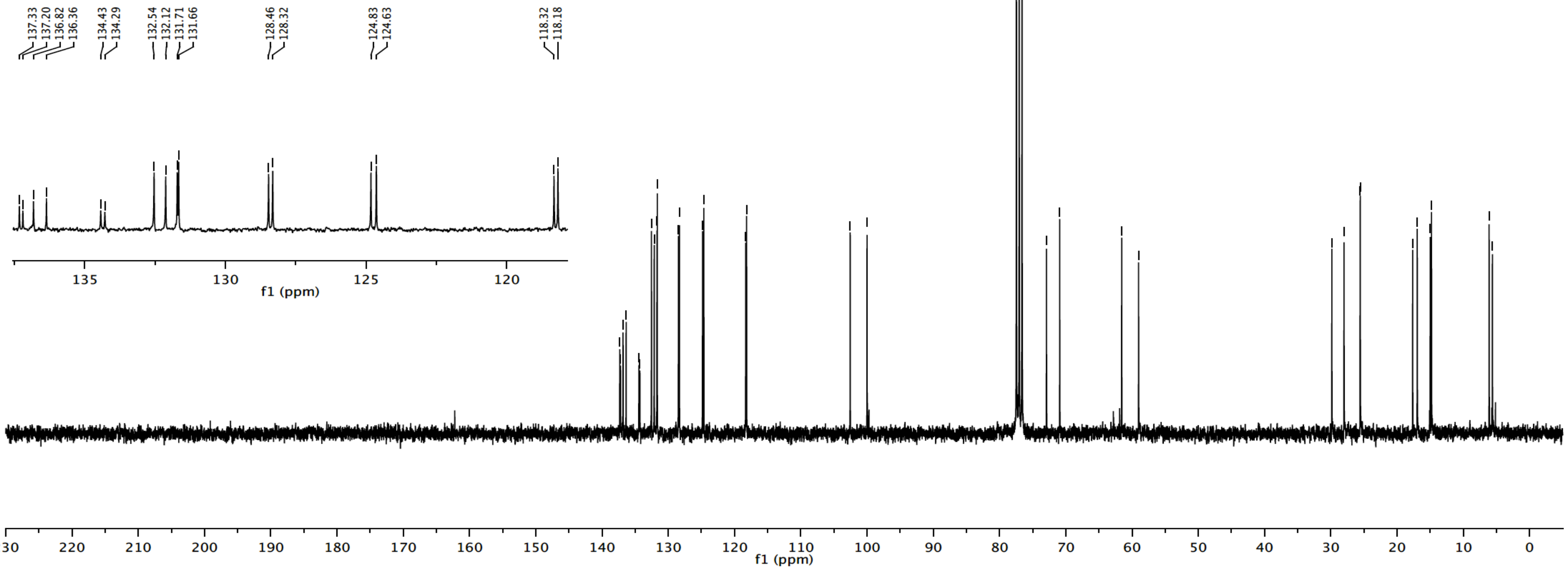


52:48 dr

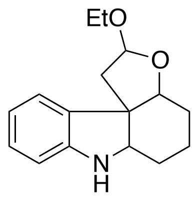
$C_{16}H_{20}IN_3O_2$

MW: 413.25 g/mol

**(75 MHz, CDCl$_3$)**

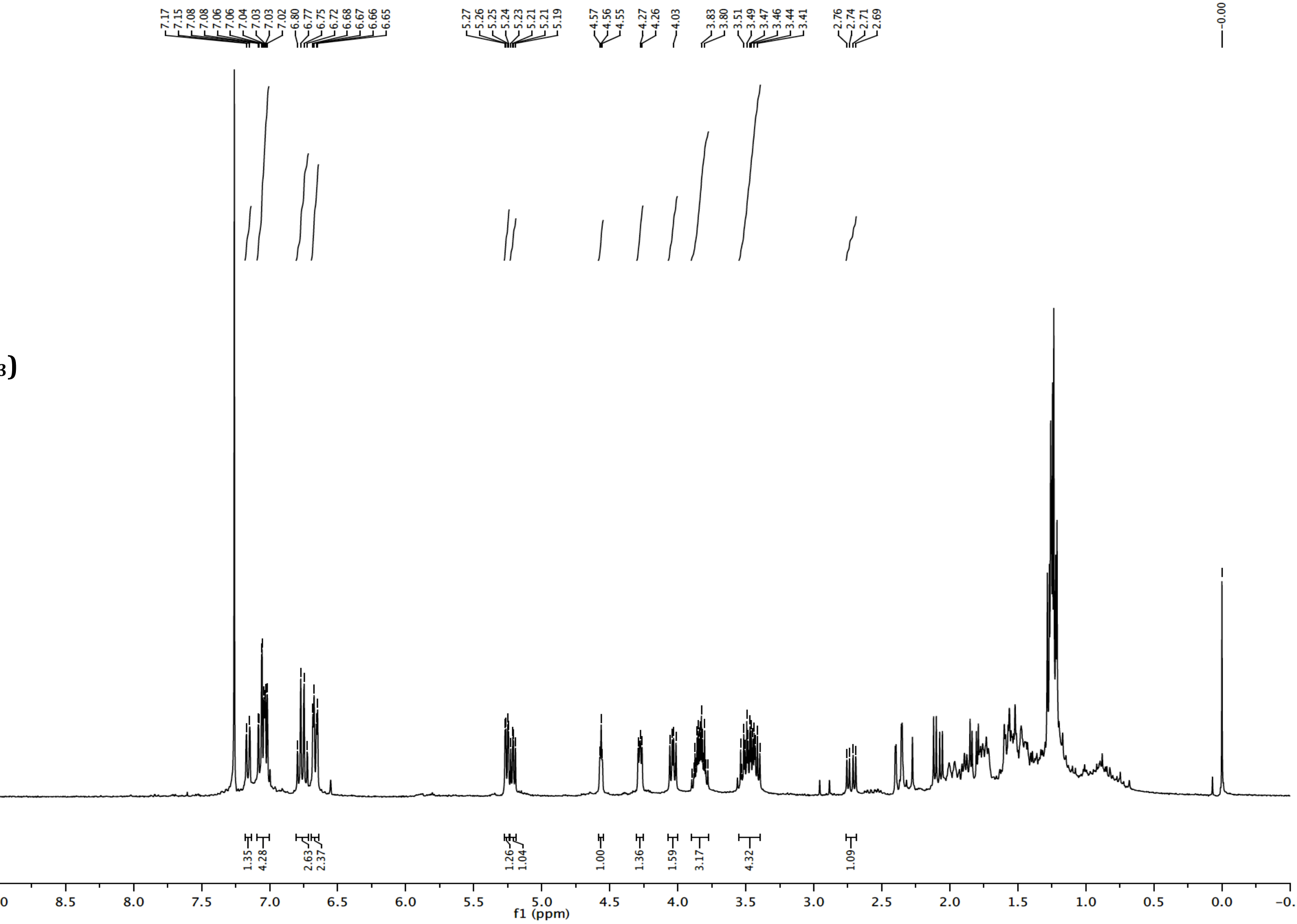


**6**

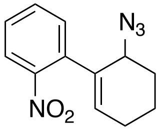


55:45 dr
$C_{16}H_{21}NO_2$
MW: 259.34 g/mol

**(300 MHz, CDCl$_3$)**

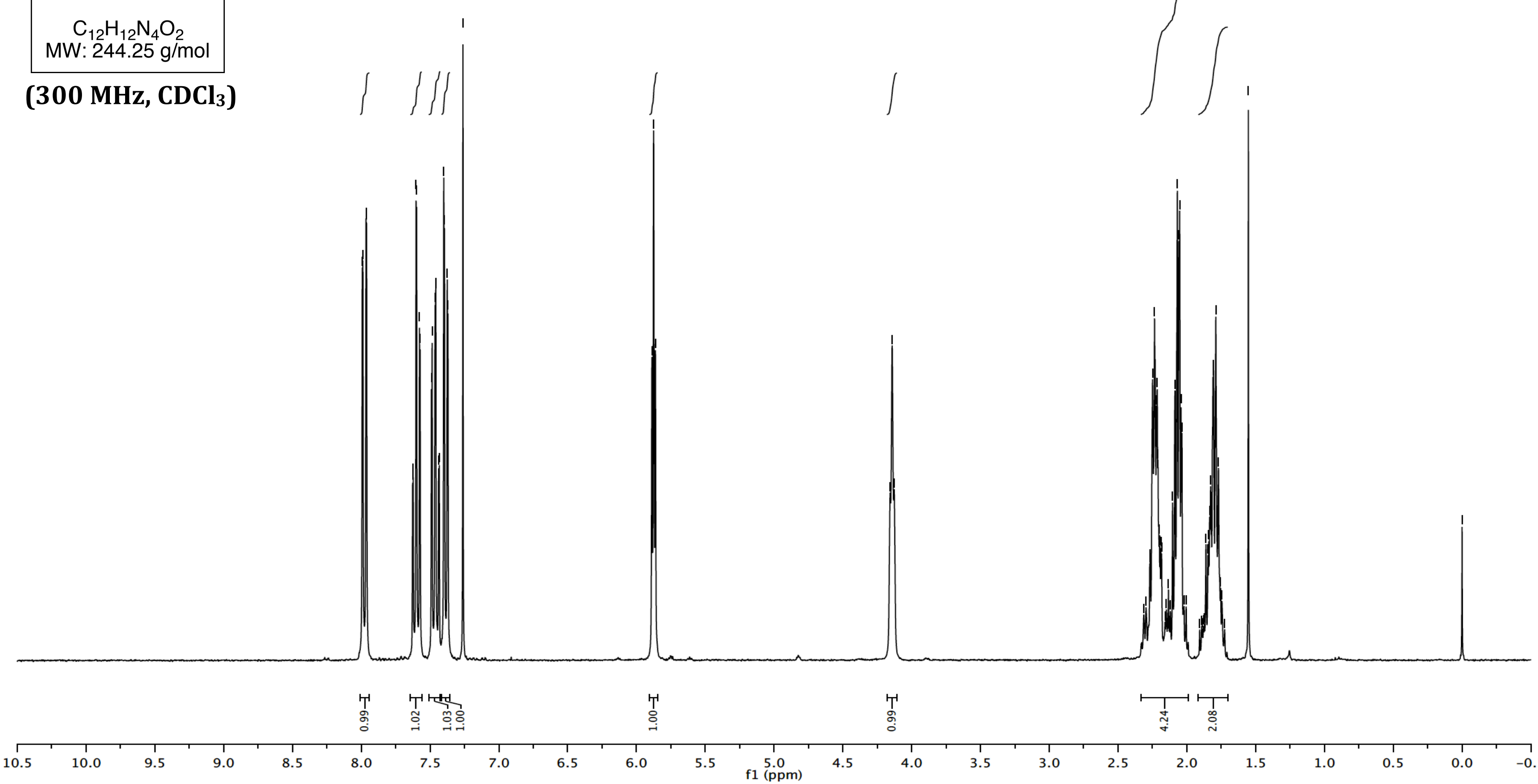


**S10**

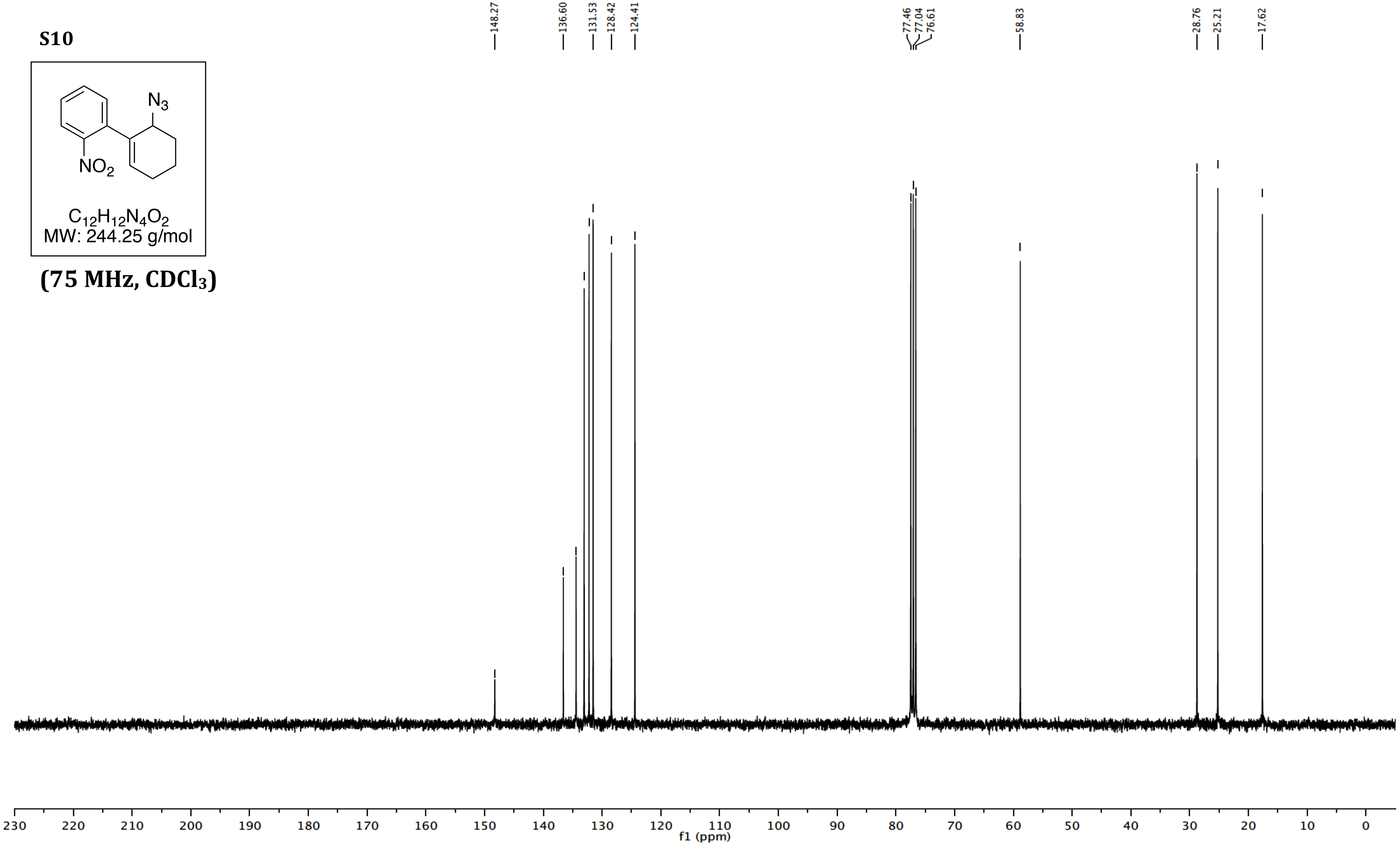


$C_{12}H_{12}N_4O_2$
MW: 244.25 g/mol

**(300 MHz, CDCl$_3$)**



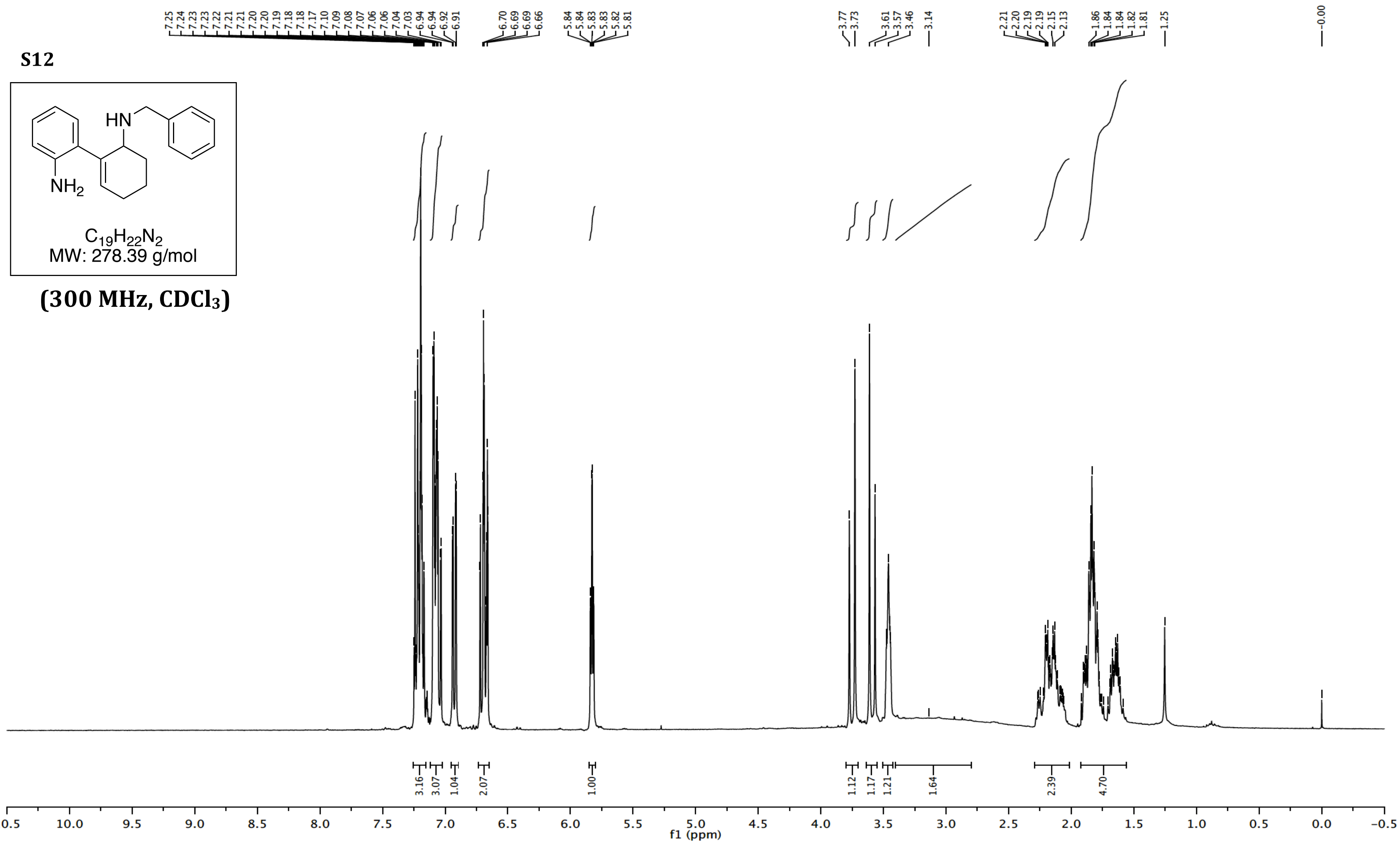
**S10**



$C_{12}H_{12}N_4O_2$
MW: 244.25 g/mol

**(75 MHz, CDCl$_3$)**

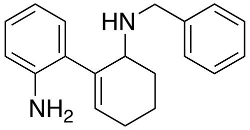
**S12**



$C_{19}H_{22}N_2$
MW: 278.39 g/mol

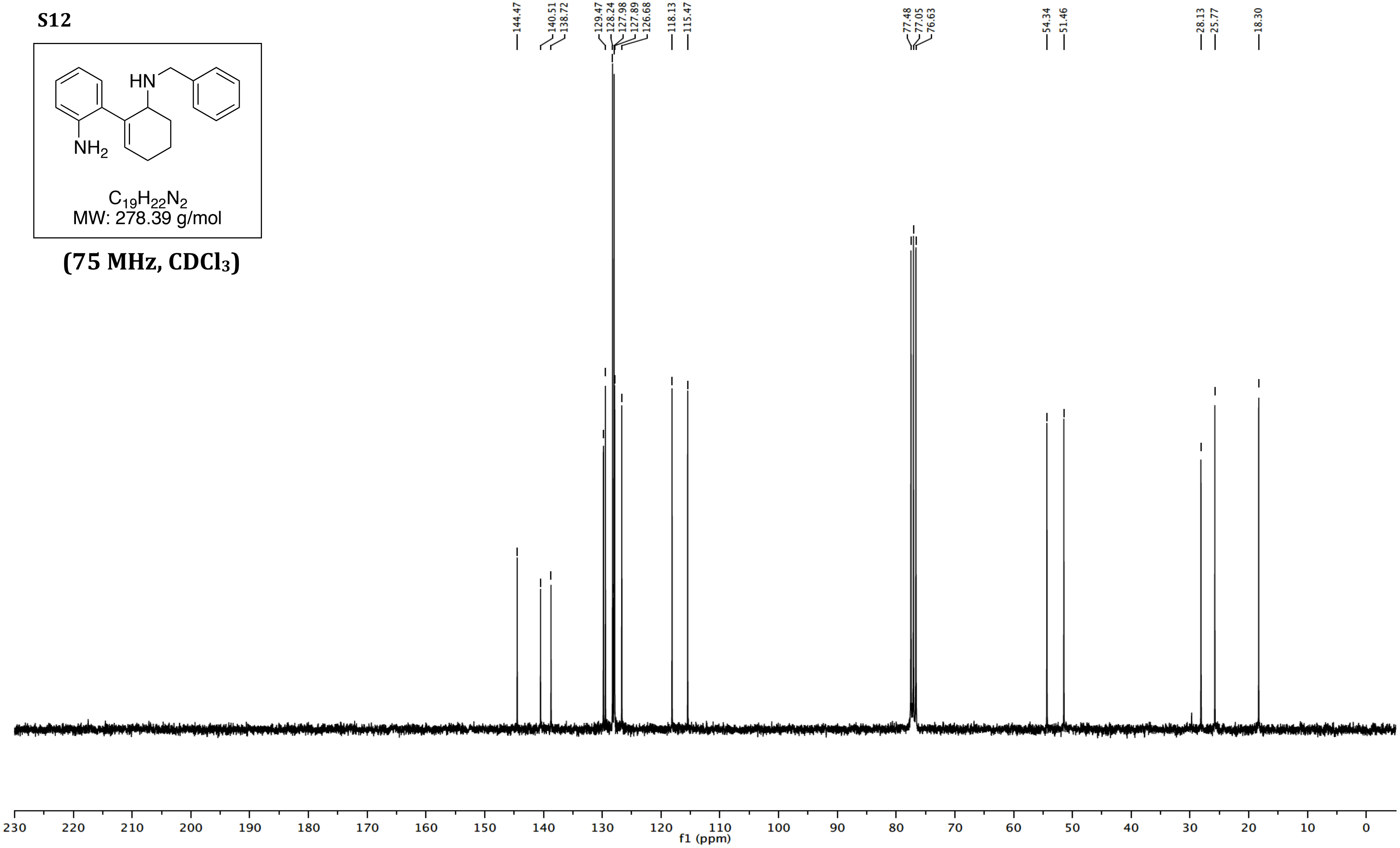
**(300 MHz, $CDCl_3$)**

**S12**

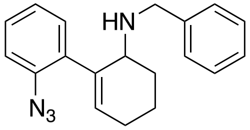


$C_{19}H_{22}N_2$
MW: 278.39 g/mol

**(75 MHz, CDCl$_3$)**

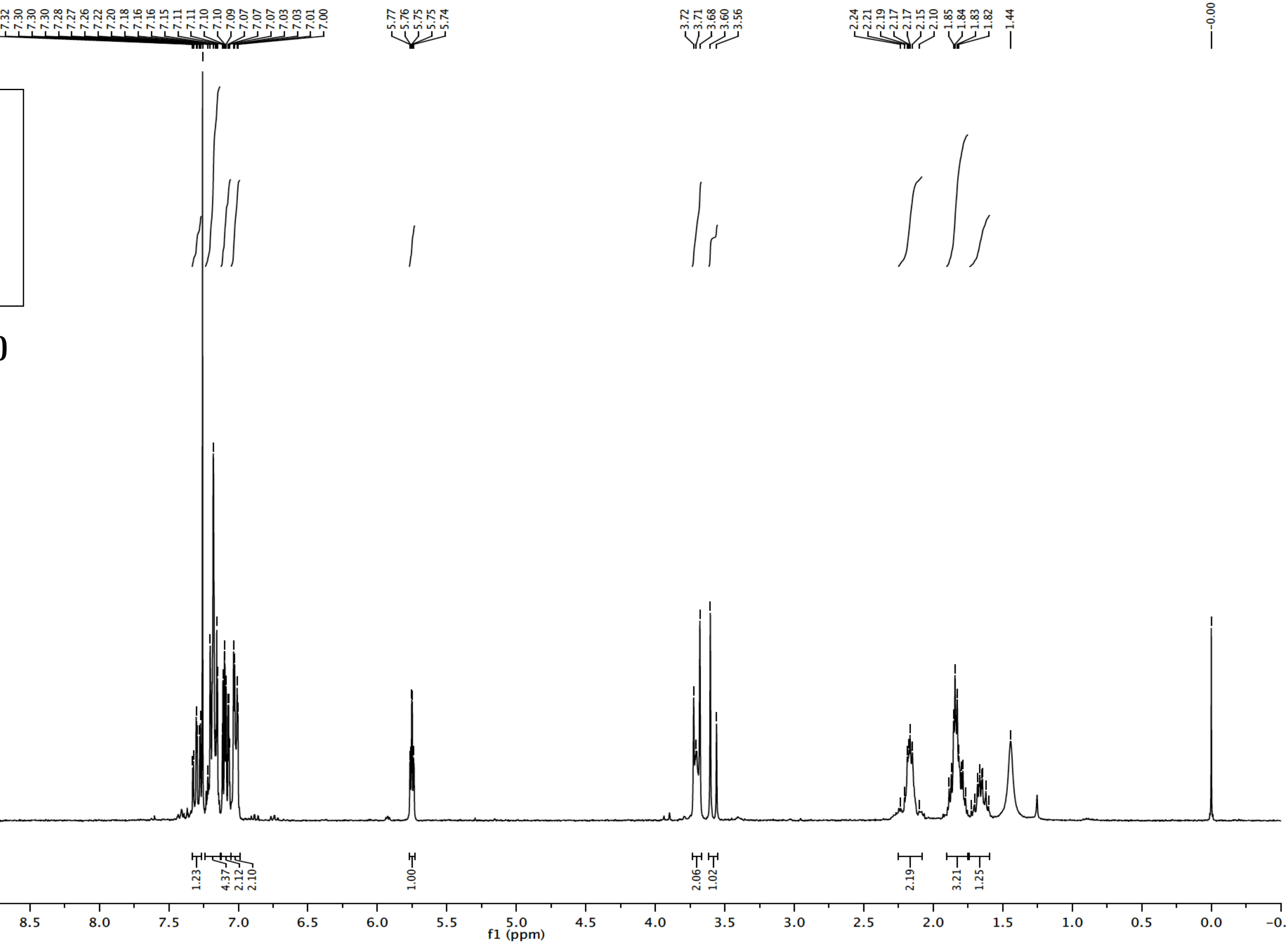


**S13**

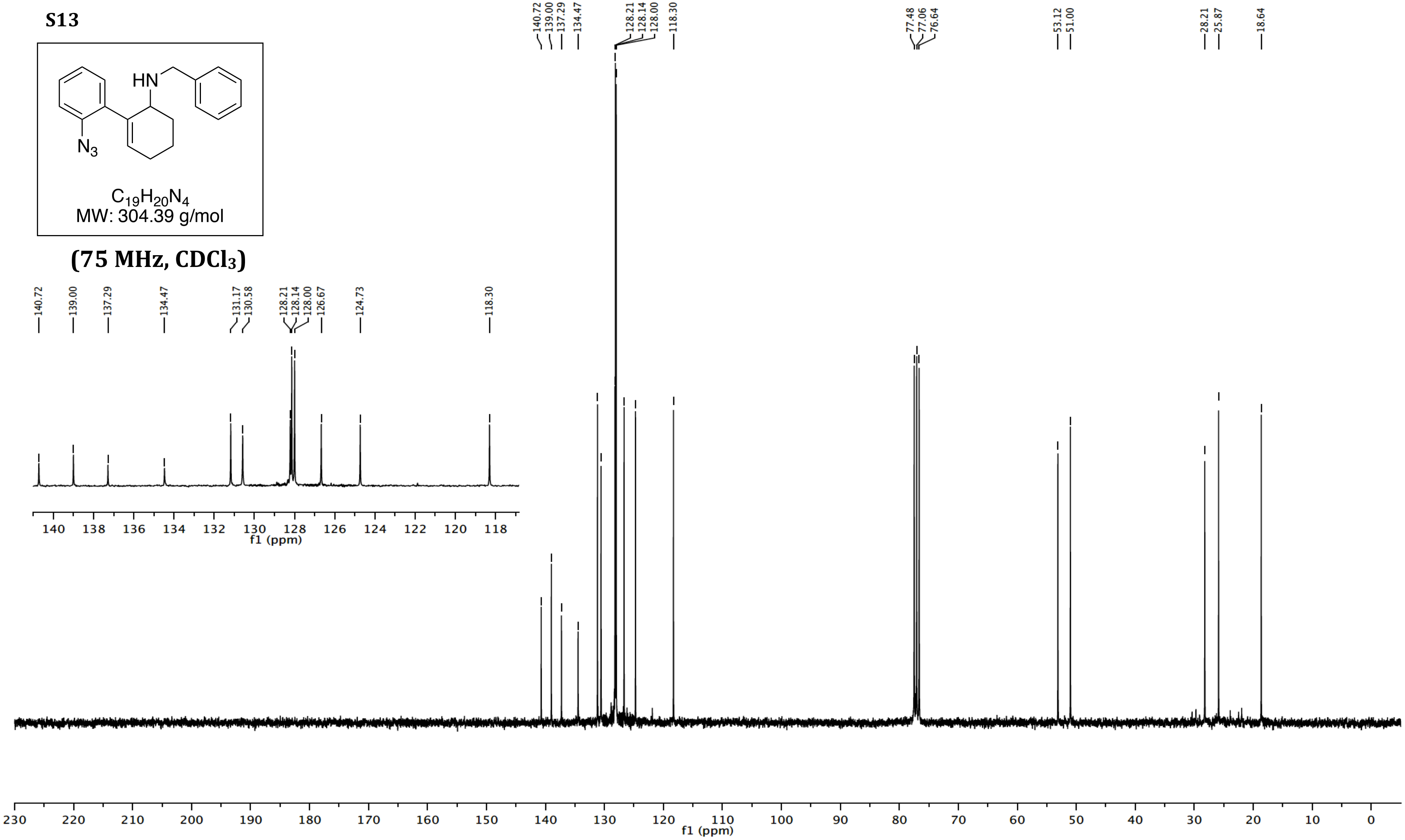


$C_{19}H_{20}N_4$
MW: 304.39 g/mol

**(300 MHz, CDCl$_3$)**



**S13**



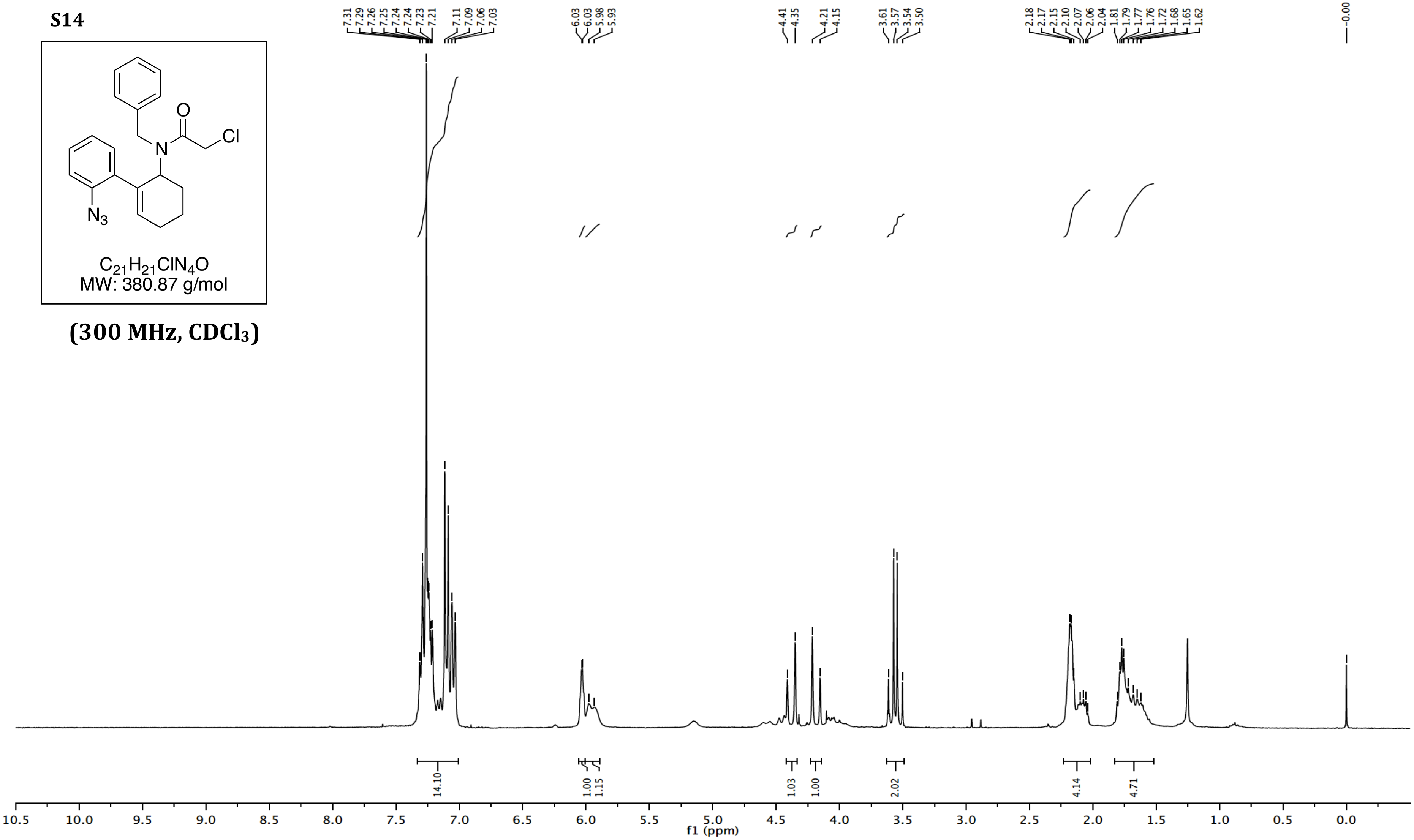
$C_{19}H_{20}N_4$
MW: 304.39 g/mol

**(75 MHz, $CDCl_3$)**

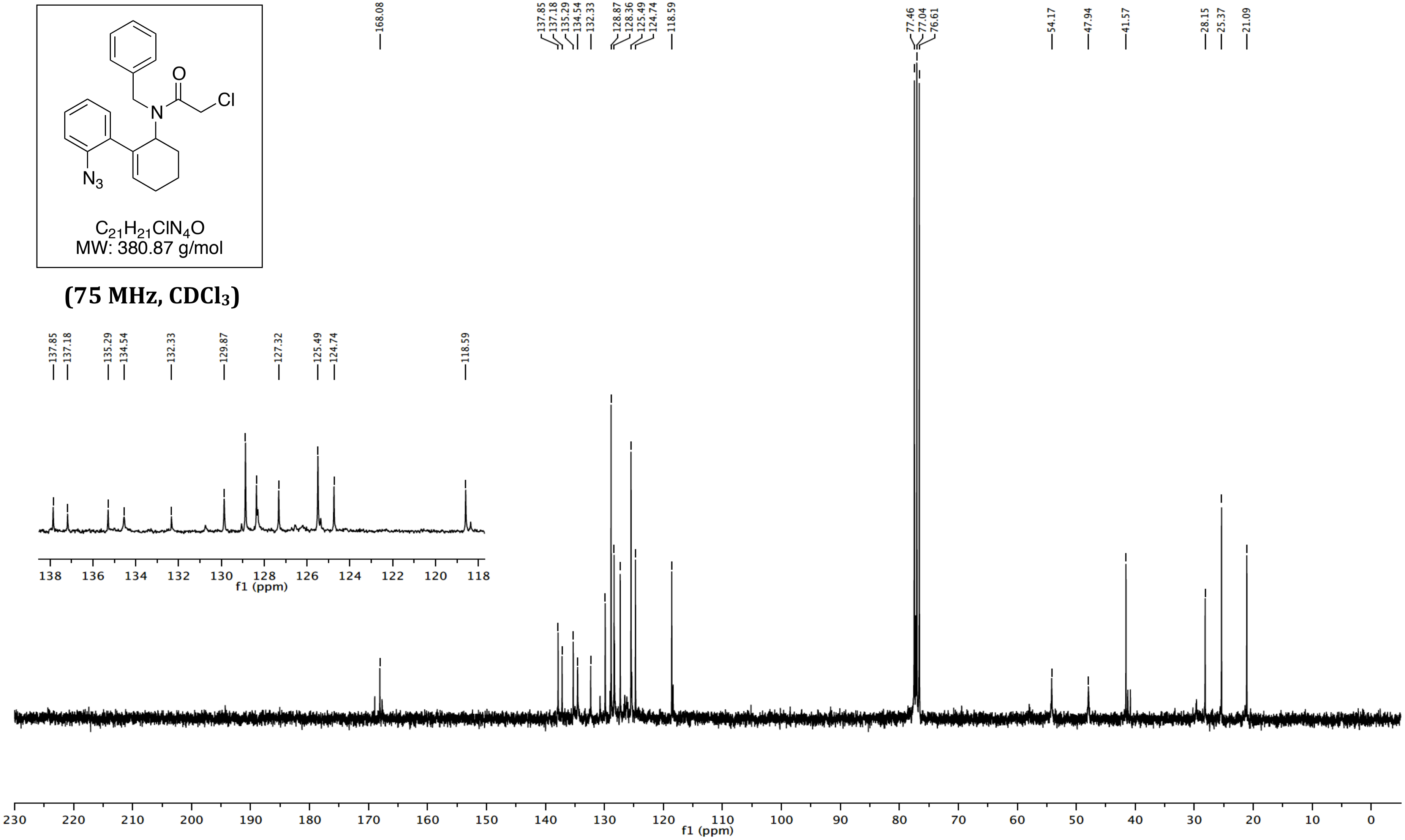
**S14**

$C_{21}H_{21}ClN_4O$
MW: 380.87 g/mol

**(300 MHz, CDCl$_3$)**

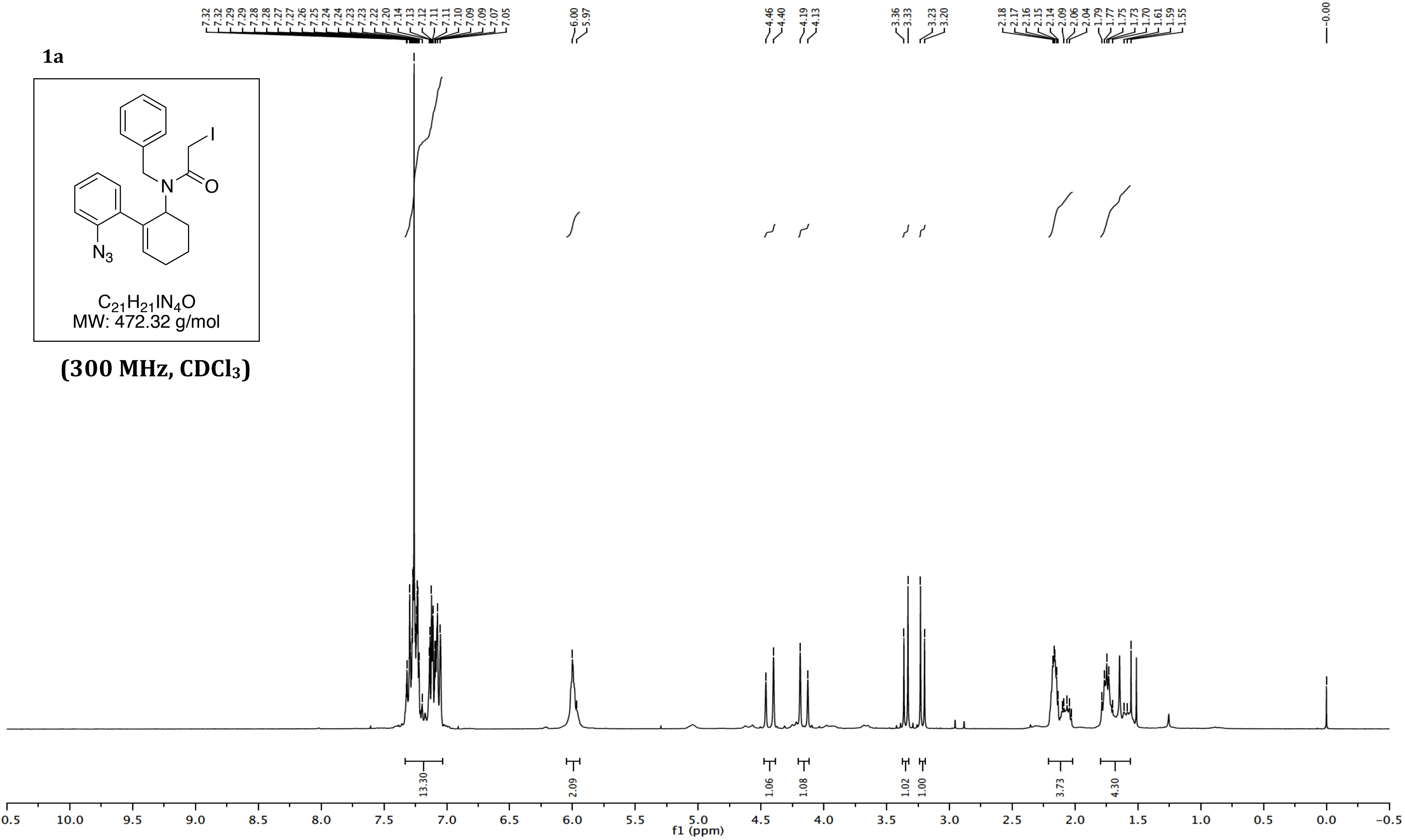


**S14**



$C_{21}H_{21}ClN_4O$
MW: 380.87 g/mol

**(75 MHz, CDCl$_3$)**

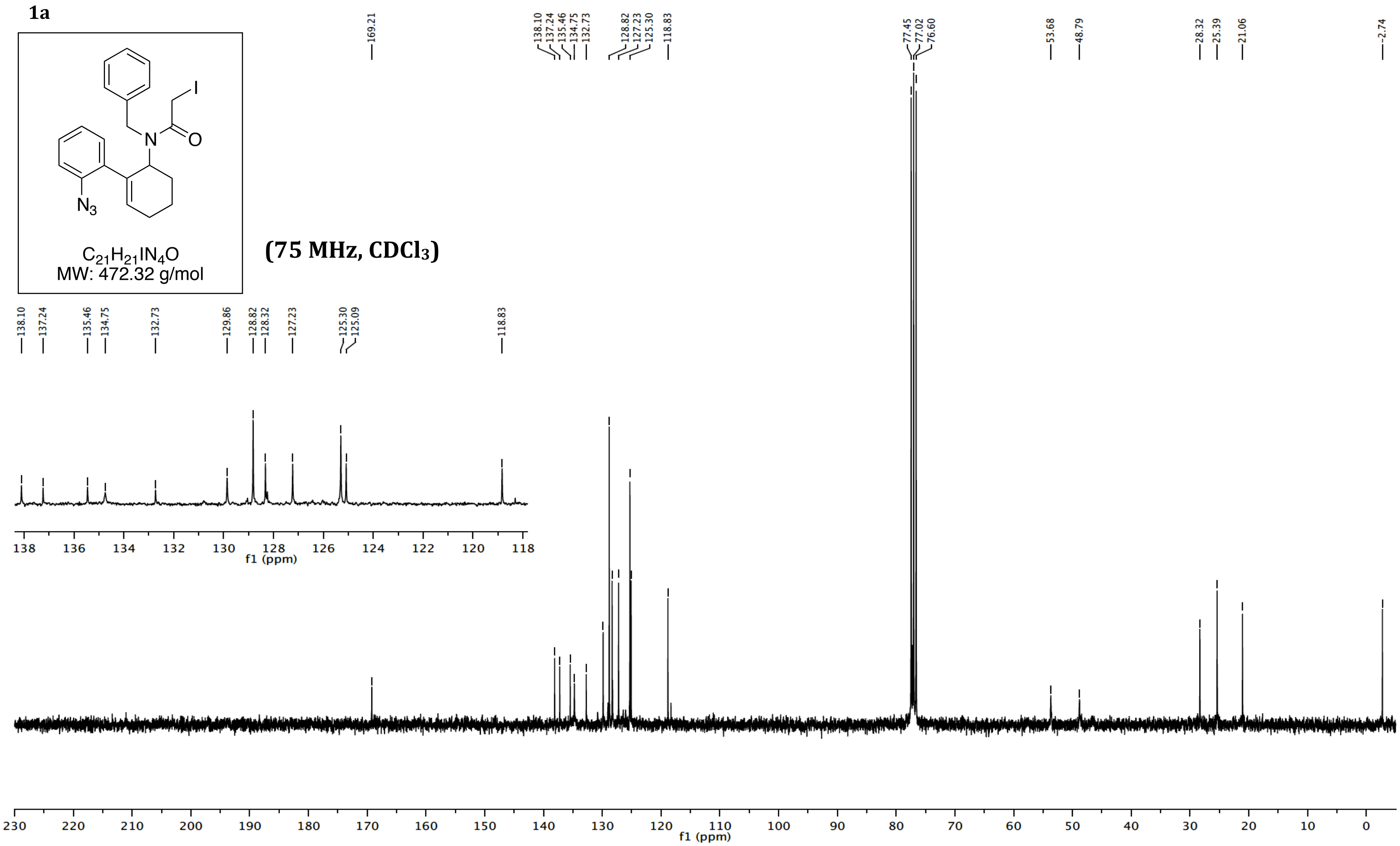


**1a**

$C_{21}H_{21}IN_4O$
MW: 472.32 g/mol

**(300 MHz, $CDCl_3$)**

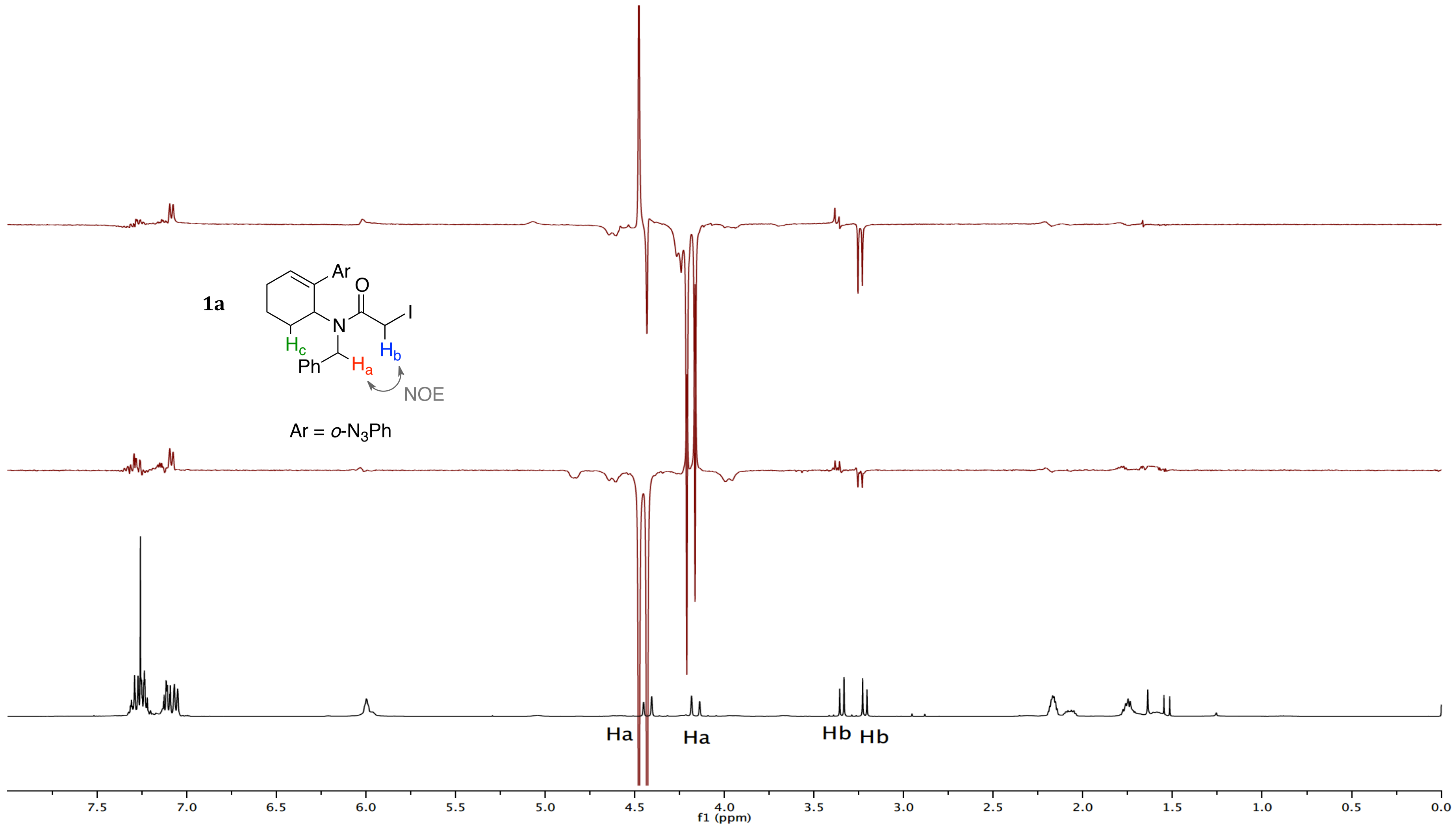
**1a**

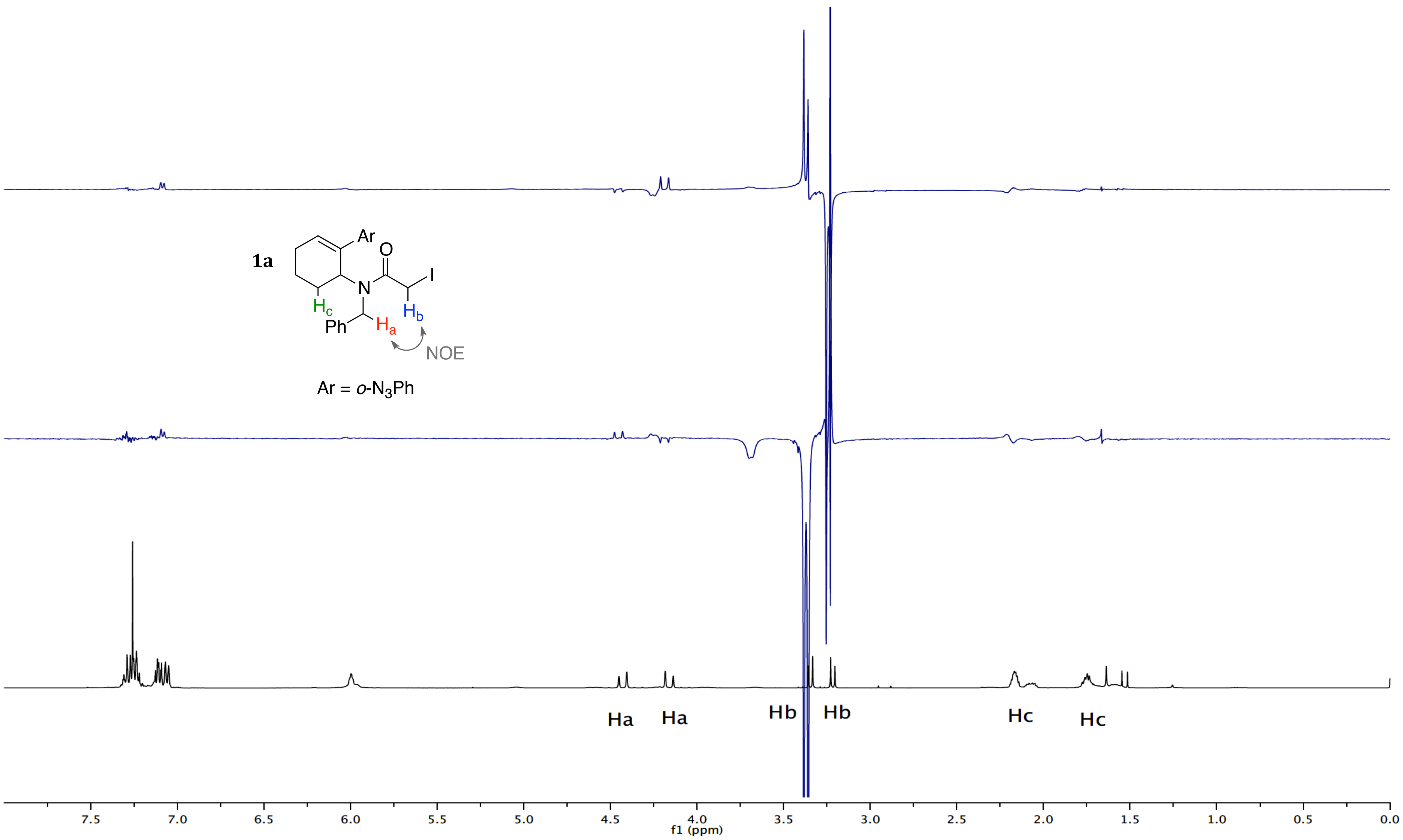


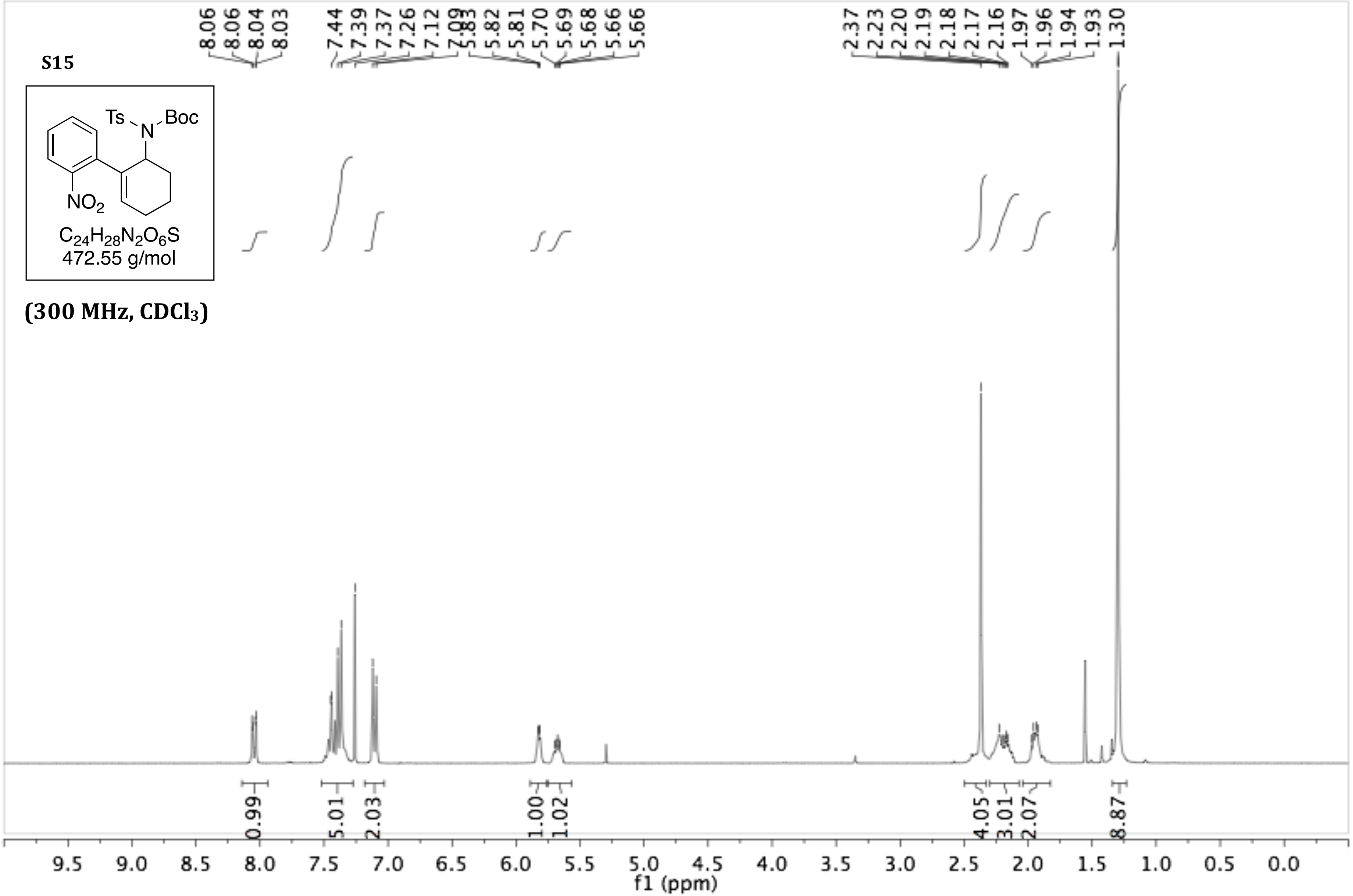
$C_{21}H_{21}IN_4O$
MW: 472.32 g/mol

**(75 MHz, $CDCl_3$)**

<u>NOE experiments:</u> irradiation of $H_a$ and $H_b$. NOE > 0 between $H_a$ and $H_b$. NOE = 0 between $H_b$ and $H_c$. 300 MHz, $CDCl_3$




1a
Ar
O
N
I
Hc
Ph
Ha
Hb
NOE
Ar = o-N3Ph
Ha
Ha
Hb
Hb
Hc
Hc
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
f1 (ppm)
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

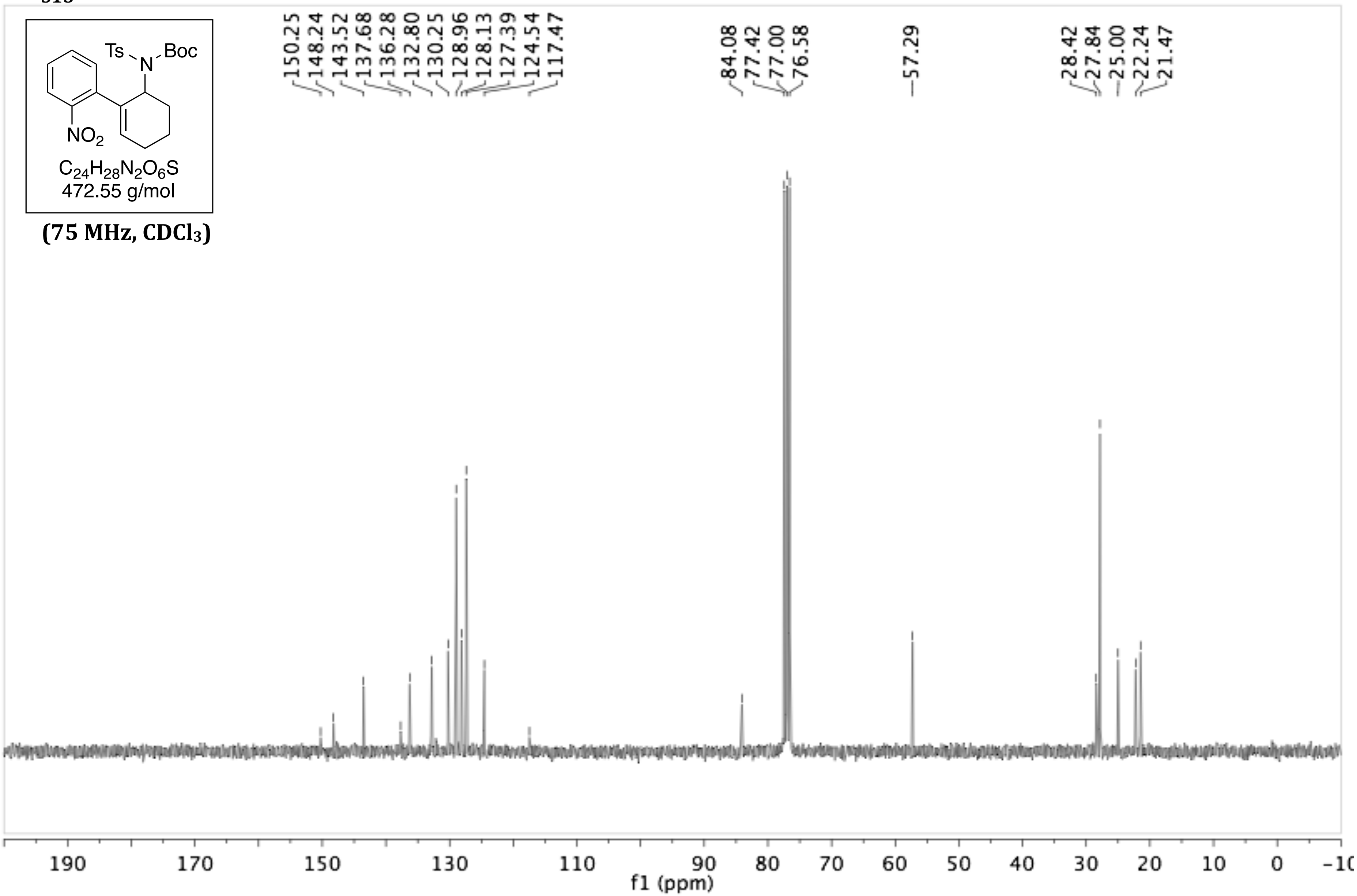


**S15**

$C_{24}H_{28}N_2O_6S$
472.55 g/mol

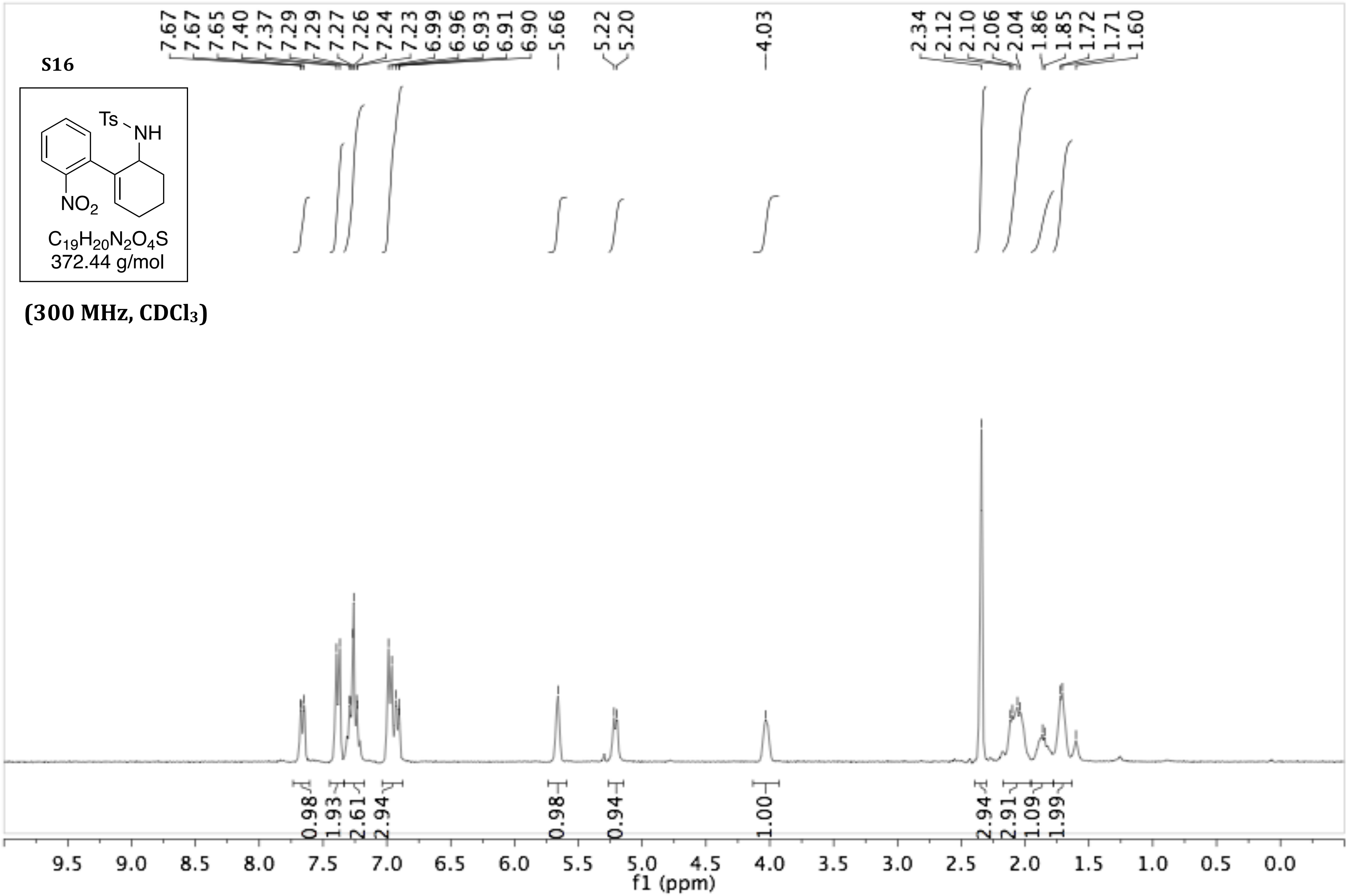
**(300 MHz, CDCl$_3$)**

**S15**



$C_{24}H_{28}N_2O_6S$
472.55 g/mol

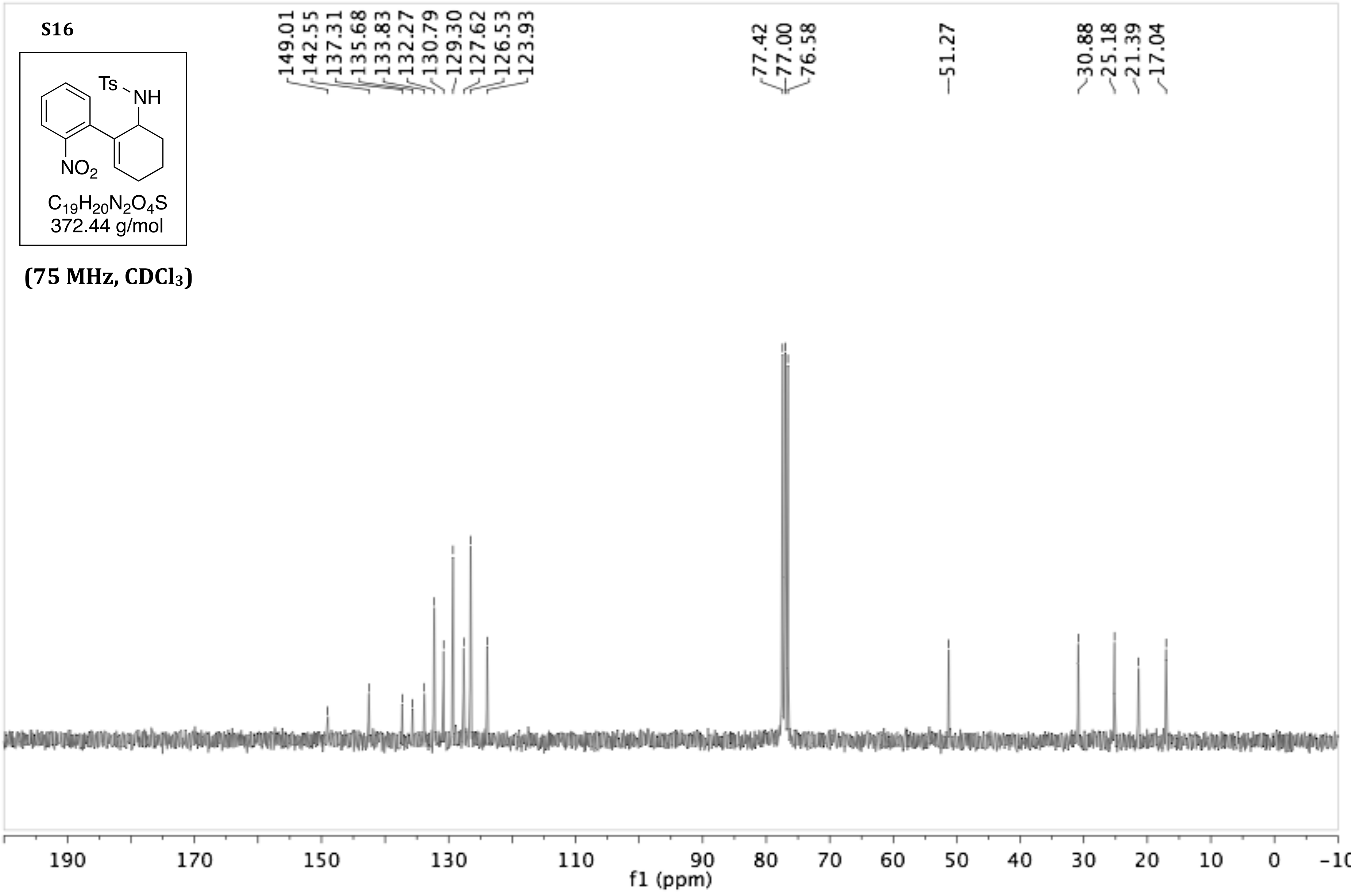
**(75 MHz, CDCl$_3$)**



**S16**

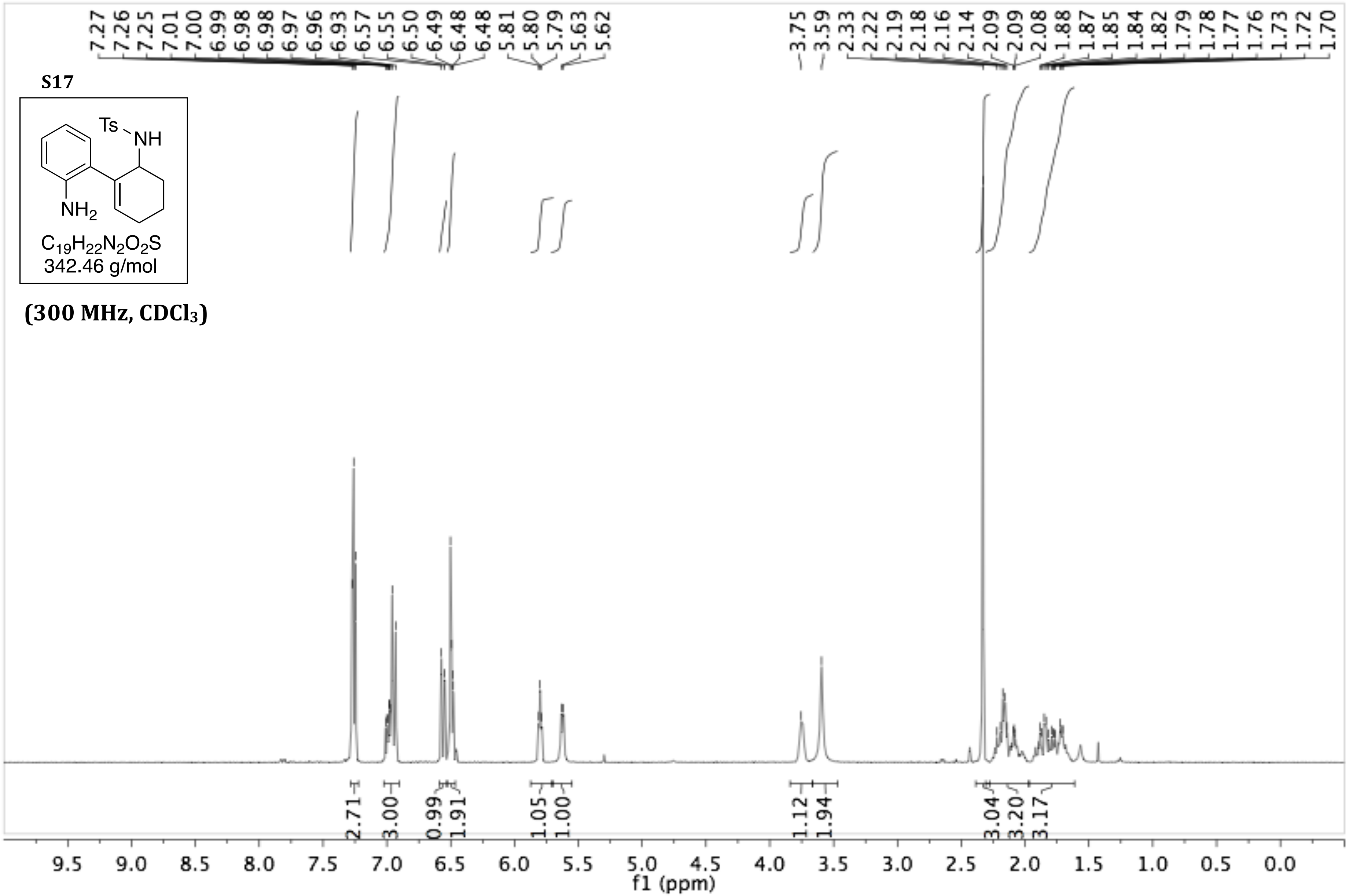
$C_{19}H_{20}N_2O_4S$
372.44 g/mol

**(300 MHz, $CDCl_3$)**


**S16**

$C_{19}H_{20}N_2O_4S$
372.44 g/mol

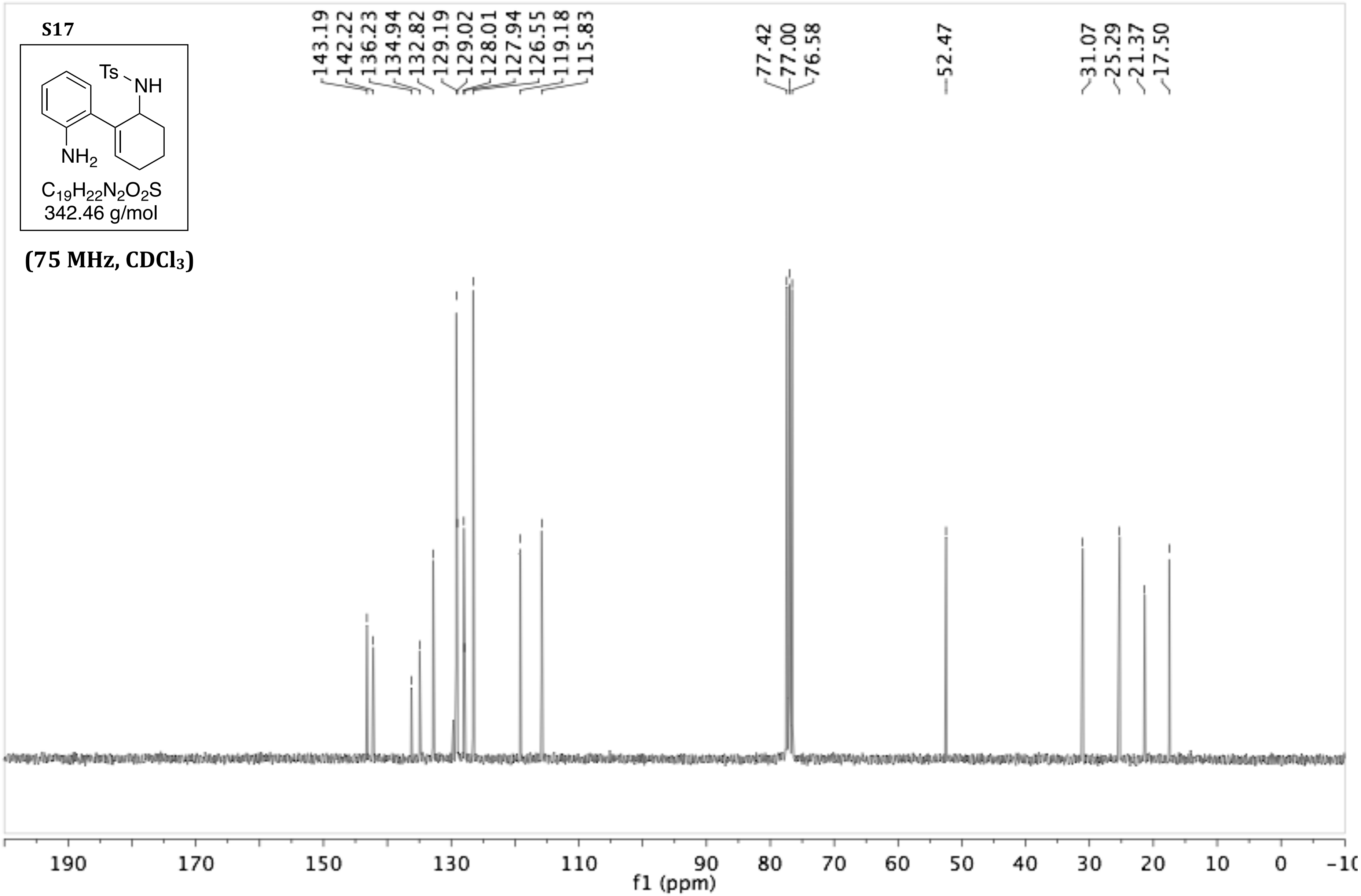
**(75 MHz, $CDCl_3$)**

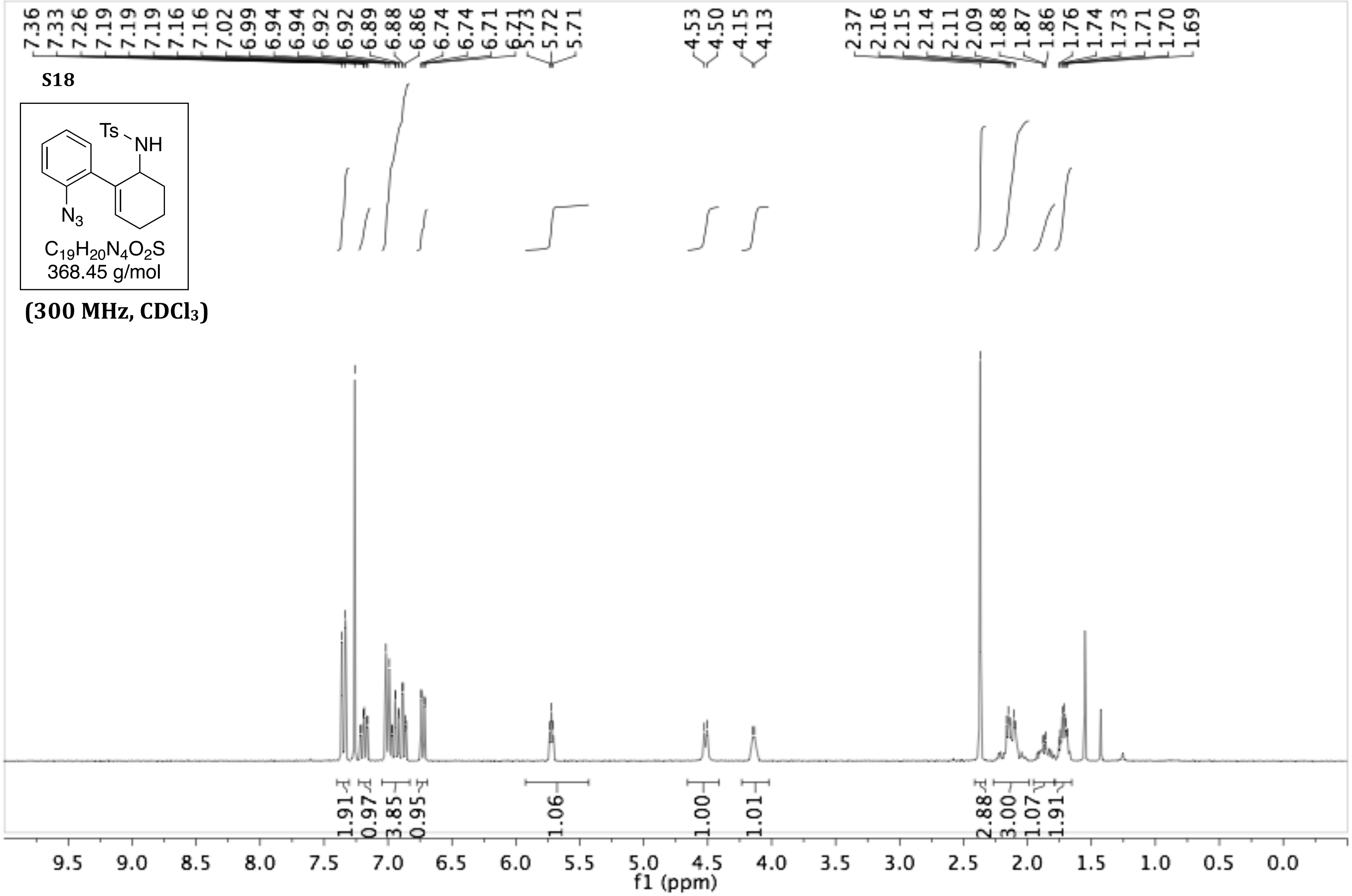


**S17**

$C_{19}H_{22}N_2O_2S$
342.46 g/mol

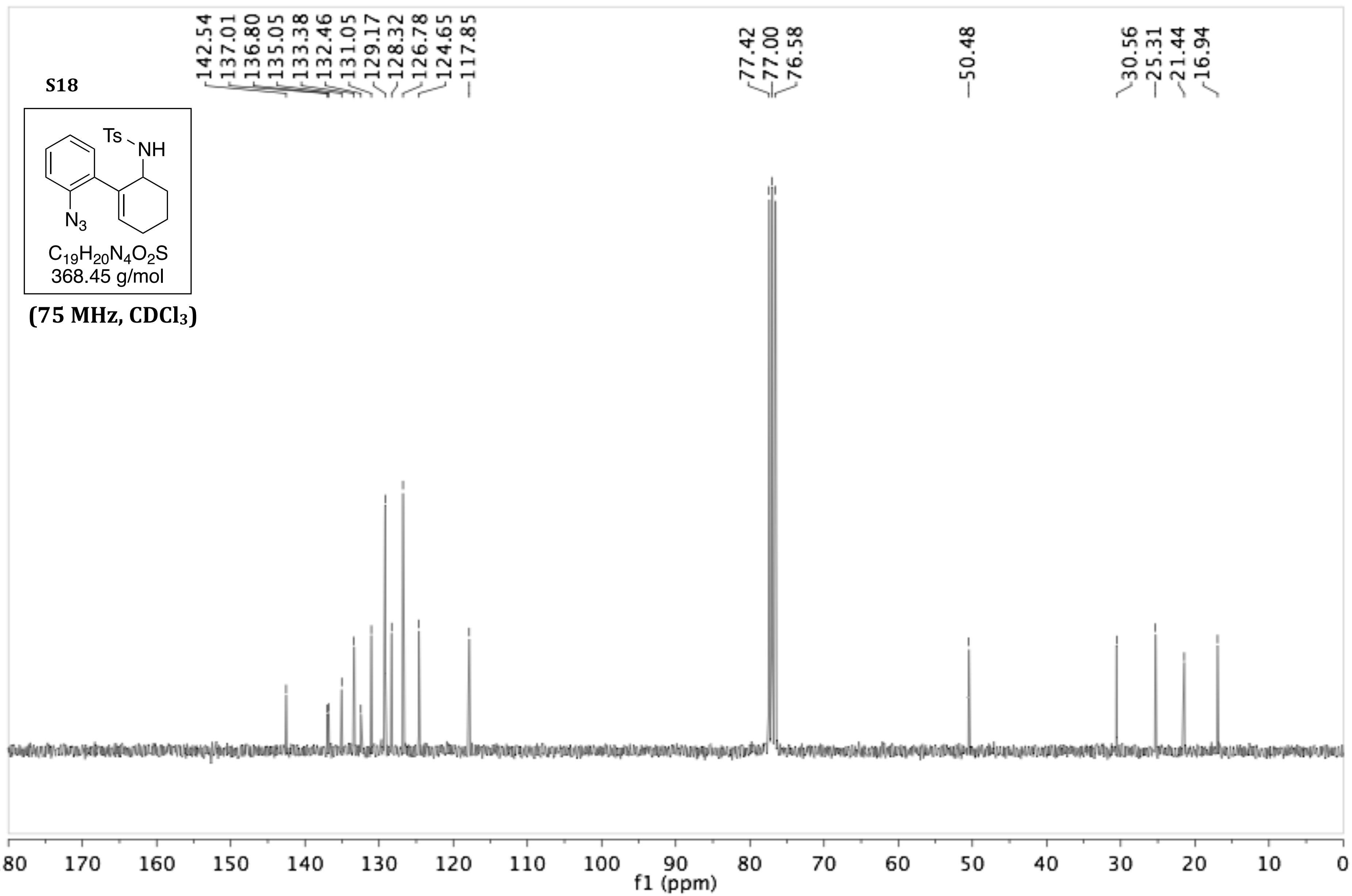
**(300 MHz, CDCl$_3$)**

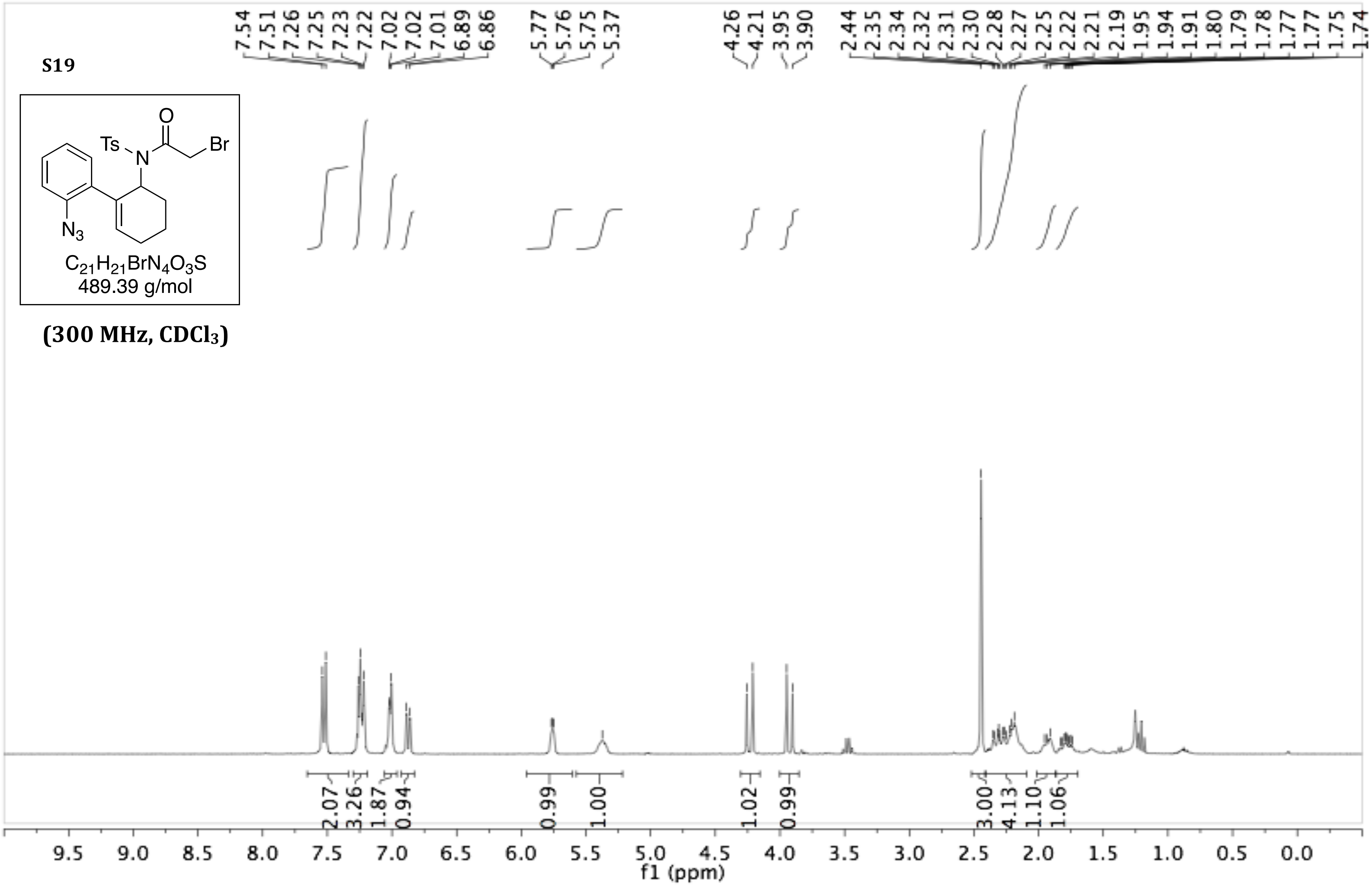

S17
Ts
NH
NH$_2$
$C_{19}H_{22}N_2O_2S$
342.46 g/mol
(75 MHz, $CDCl_3$)
143.19
142.22
136.23
134.94
132.82
129.19
129.02
128.01
127.94
126.55
119.18
115.83
77.42
77.00
76.58
52.47
31.07
25.29
21.37
17.50
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
−1(
f1 (ppm)


**S18**

$C_{19}H_{20}N_4O_2S$
368.45 g/mol

(300 MHz, $CDCl_3$)

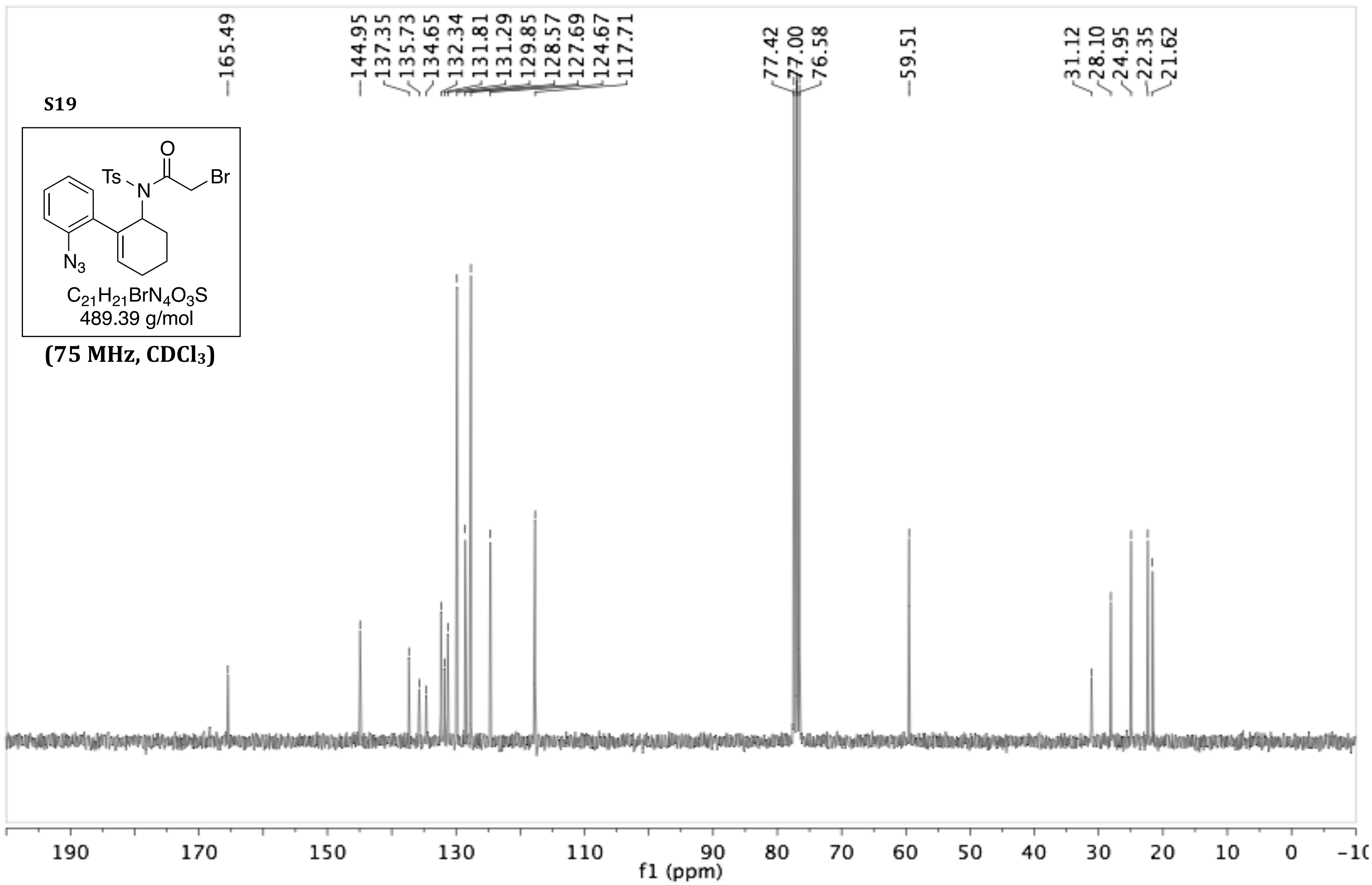

S18
Ts
NH
N3
$C_{19}H_{20}N_4O_2S$
368.45 g/mol
(75 MHz, $CDCl_3$)
142.54
137.01
136.80
135.05
133.38
132.46
131.05
129.17
128.32
126.78
124.65
117.85
77.42
77.00
76.58
50.48
30.56
25.31
21.44
16.94
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



**S19**

$C_{21}H_{21}BrN_4O_3S$
489.39 g/mol

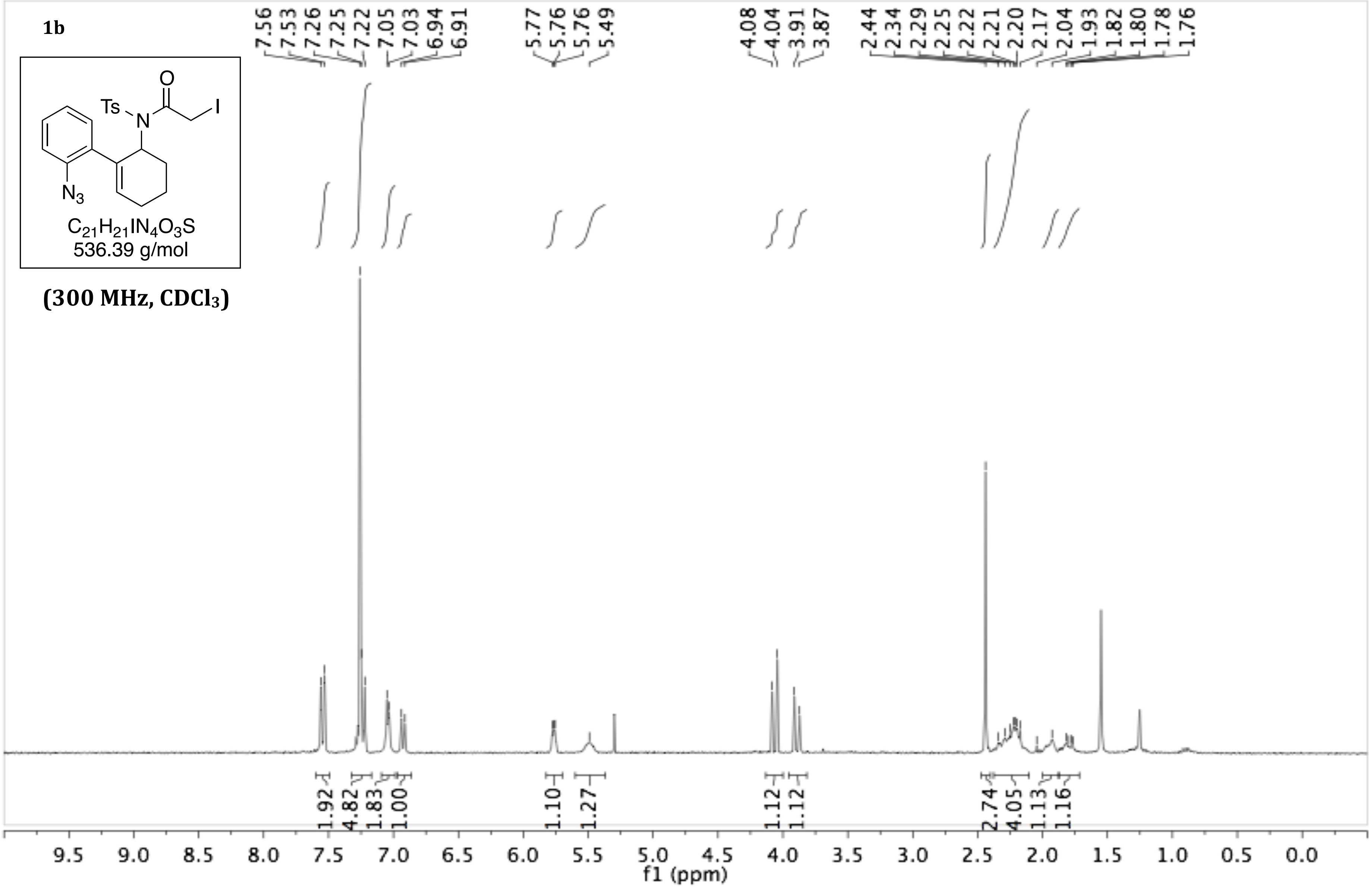
**(300 MHz, $CDCl_3$)**



**S19**

$C_{21}H_{21}BrN_4O_3S$
489.39 g/mol

**(75 MHz, CDCl$_3$)**

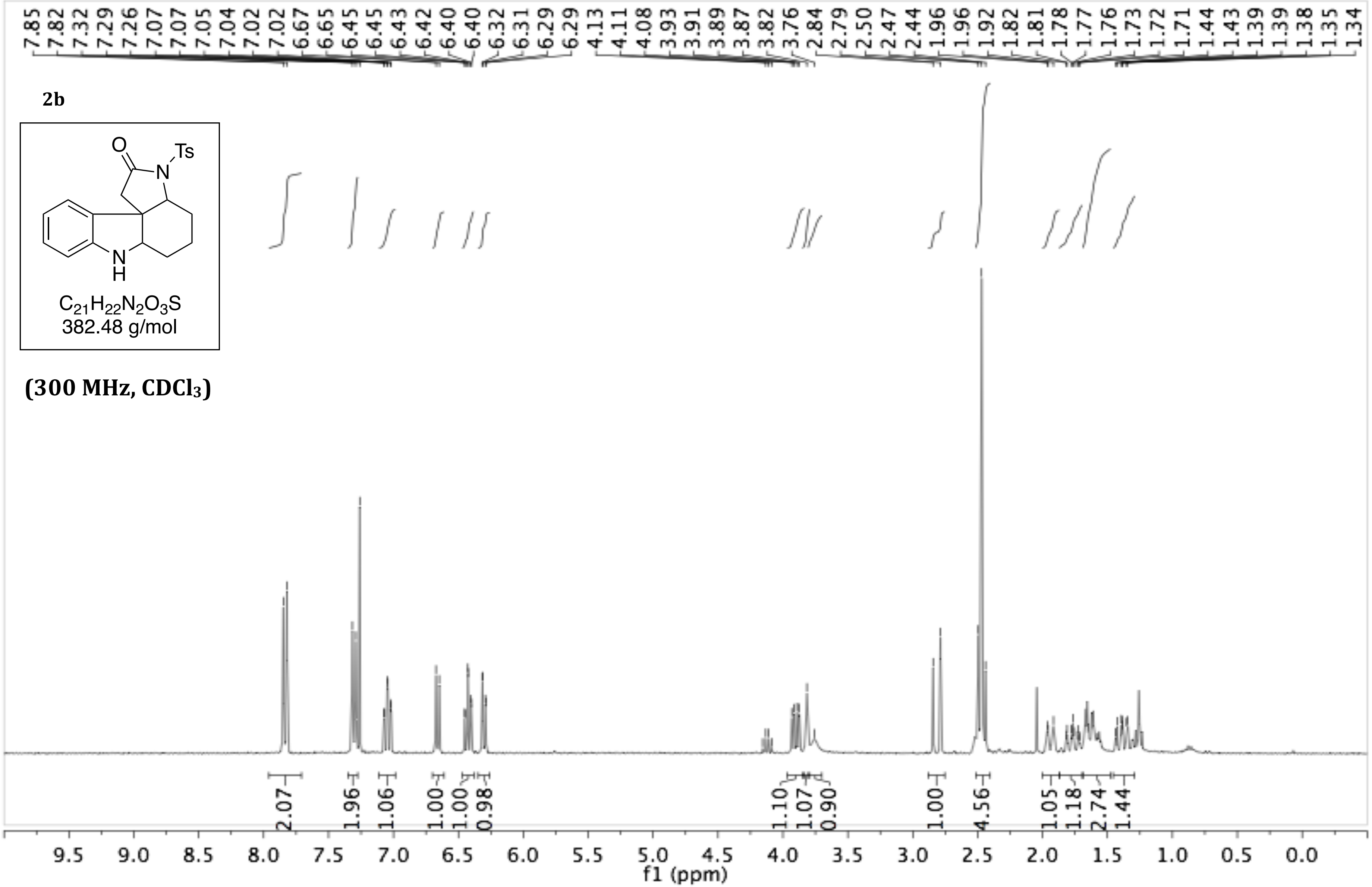


**1b**

$C_{21}H_{21}IN_4O_3S$
536.39 g/mol

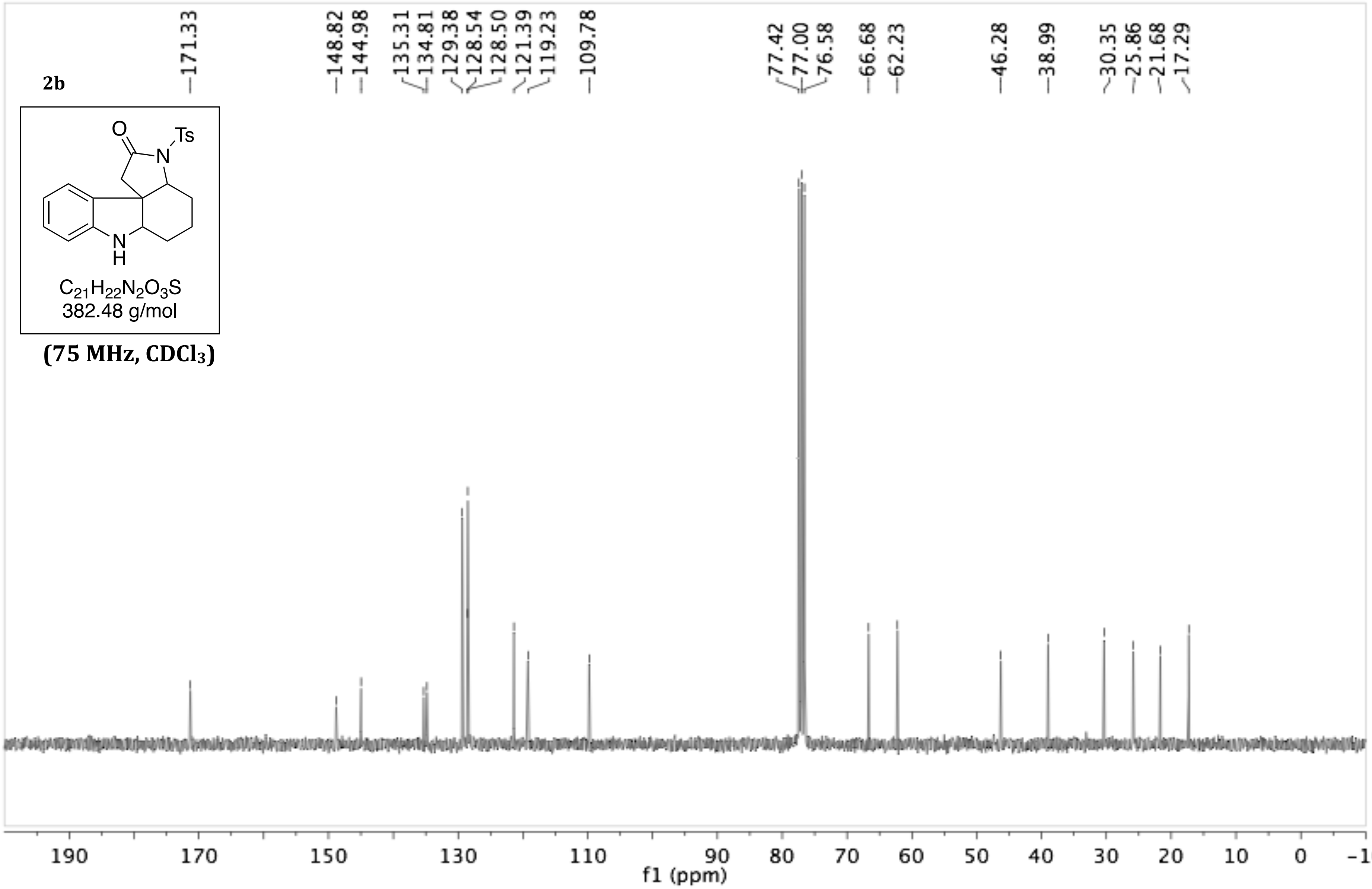
**(300 MHz, CDCl$_3$)**

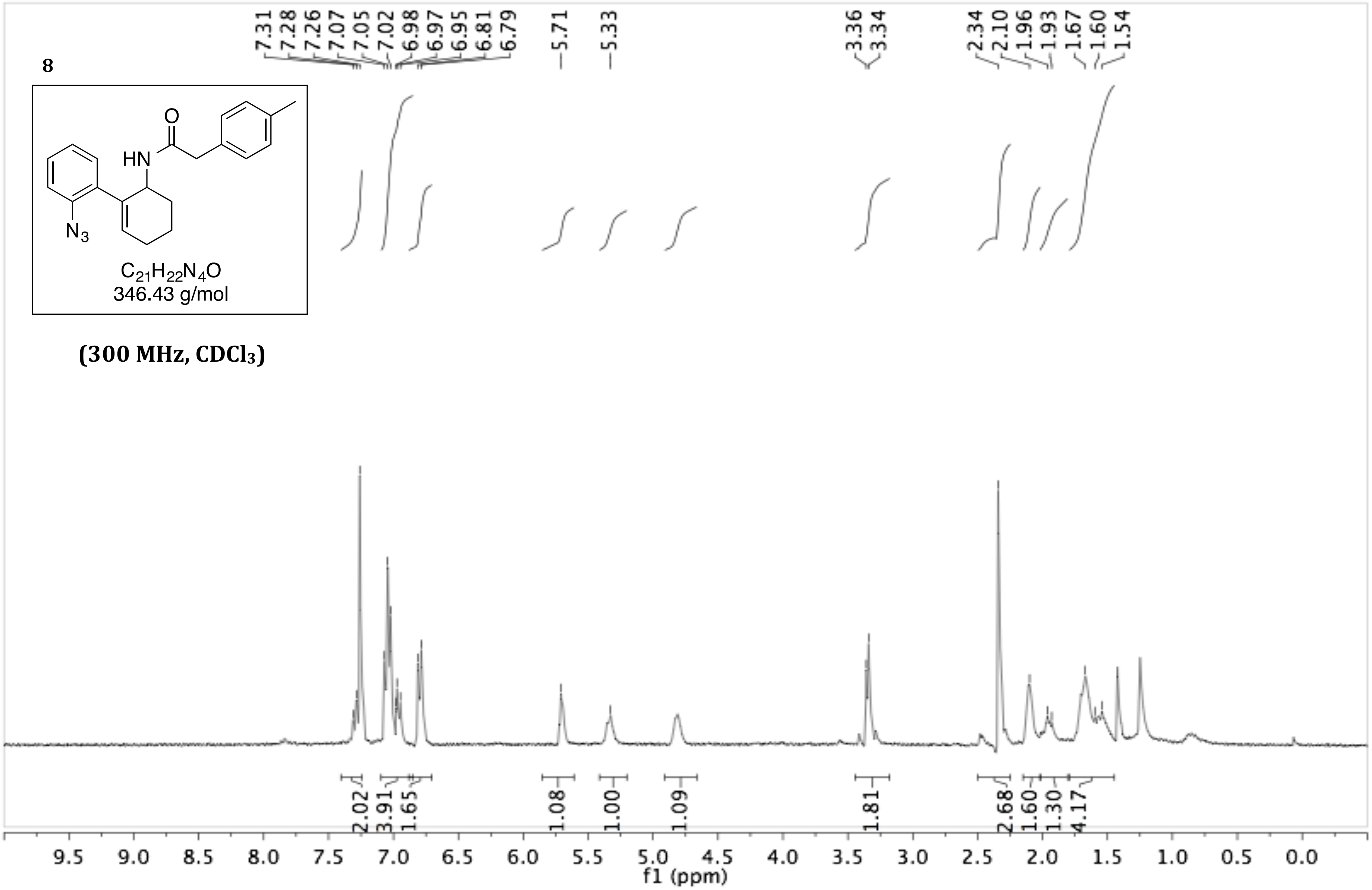
**2b**



$C_{21}H_{22}N_2O_3S$
382.48 g/mol

**(300 MHz, $CDCl_3$)**

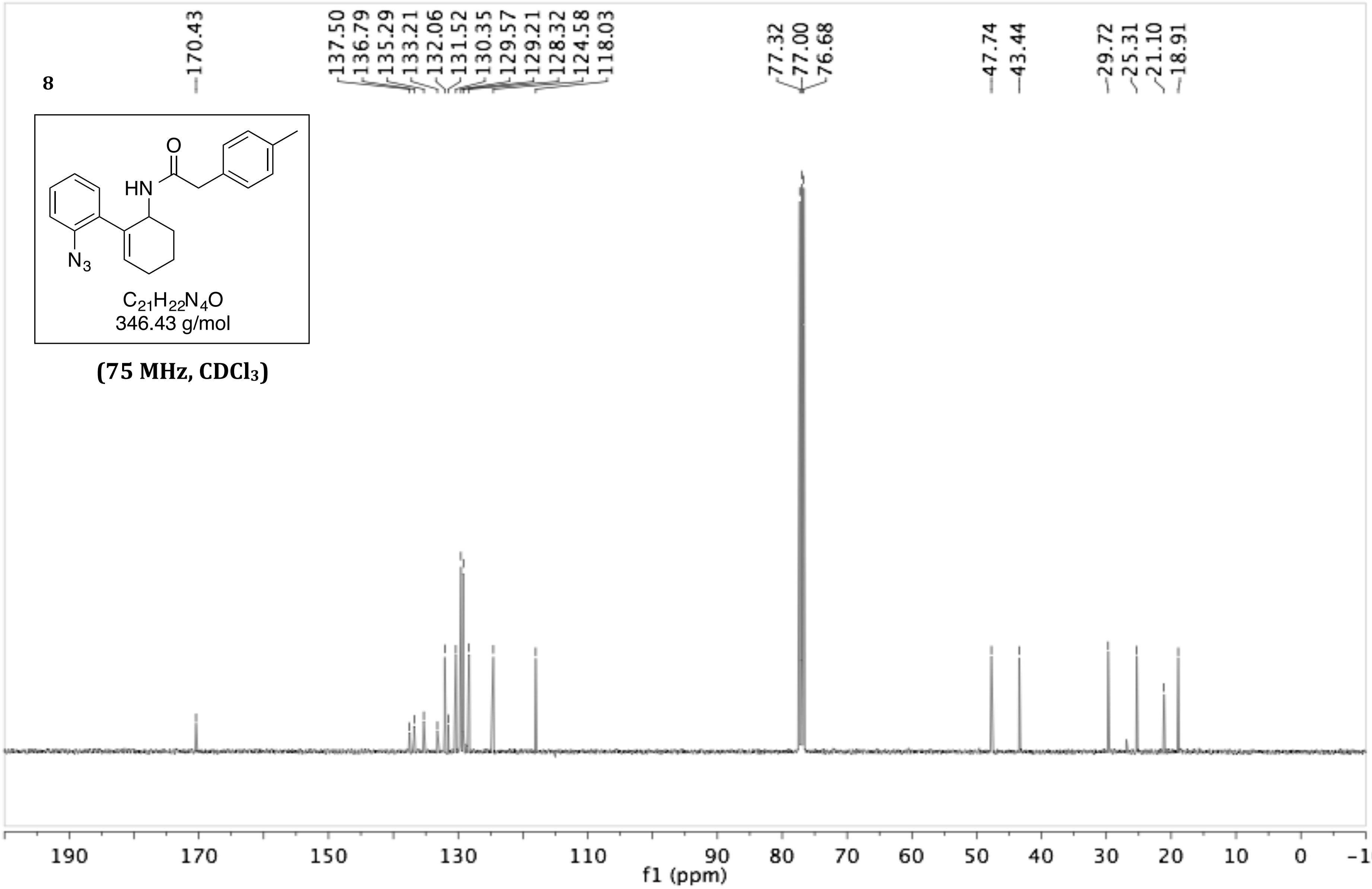

2b
O
N
Ts
N
H
$C_{21}H_{22}N_2O_3S$
382.48 g/mol
(75 MHz, $CDCl_3$)
171.33
148.82
144.98
135.31
134.81
129.38
128.54
128.50
121.39
119.23
109.78
77.42
77.00
76.58
66.68
62.23
46.28
38.99
30.35
25.86
21.68
17.29
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



**8**

$C_{21}H_{22}N_4O$
346.43 g/mol

**(300 MHz, $CDCl_3$)**

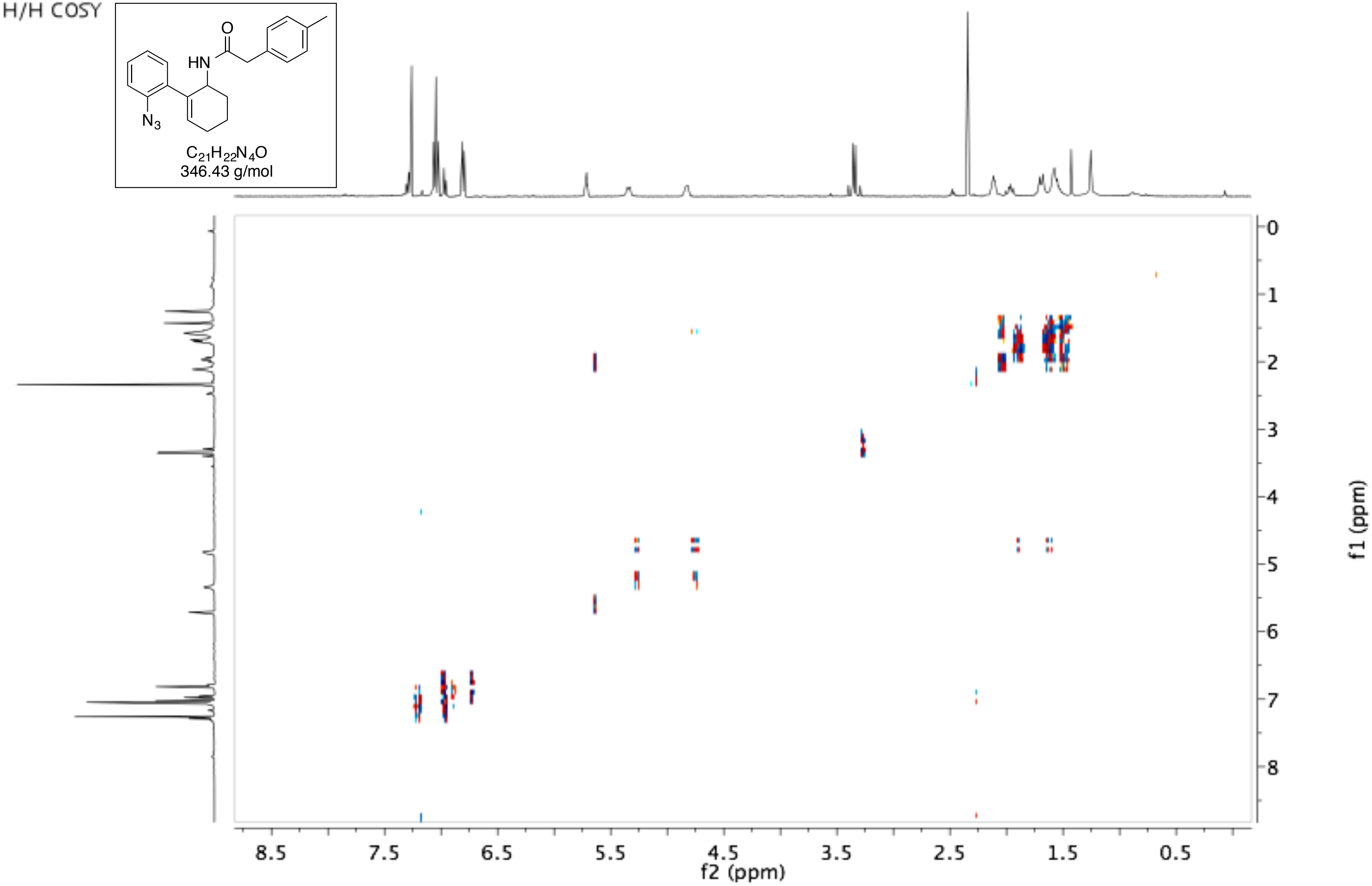


**8**

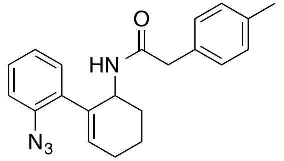
$C_{21}H_{22}N_4O$
346.43 g/mol

**(75 MHz, $CDCl_3$)**

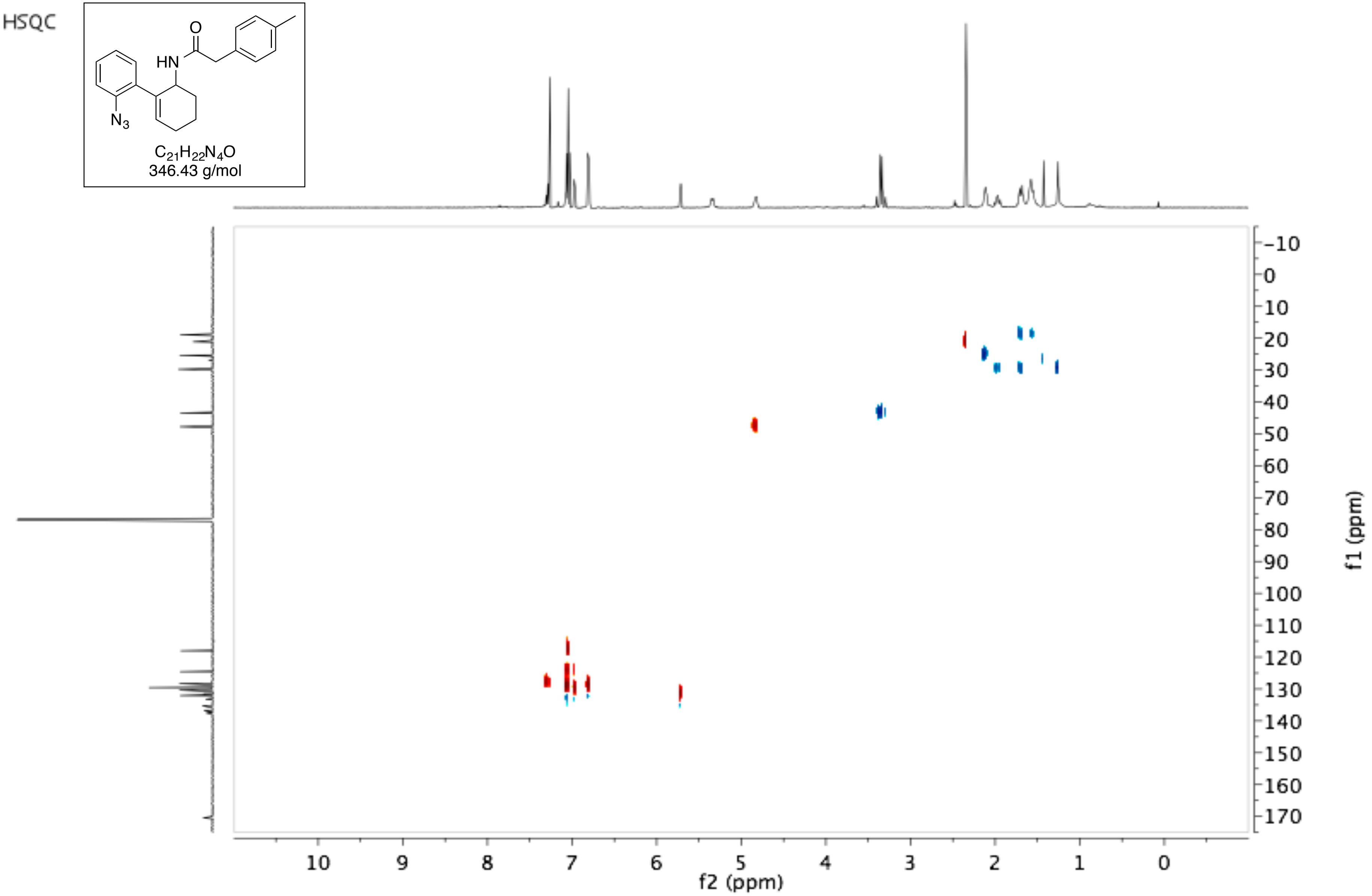
H/H COSY


HN
O
N$_3$
C$_{21}$H$_{22}$N$_4$O
346.43 g/mol
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f2 (ppm)
0
1
2
3
4
5
6
7
8
f1 (ppm)

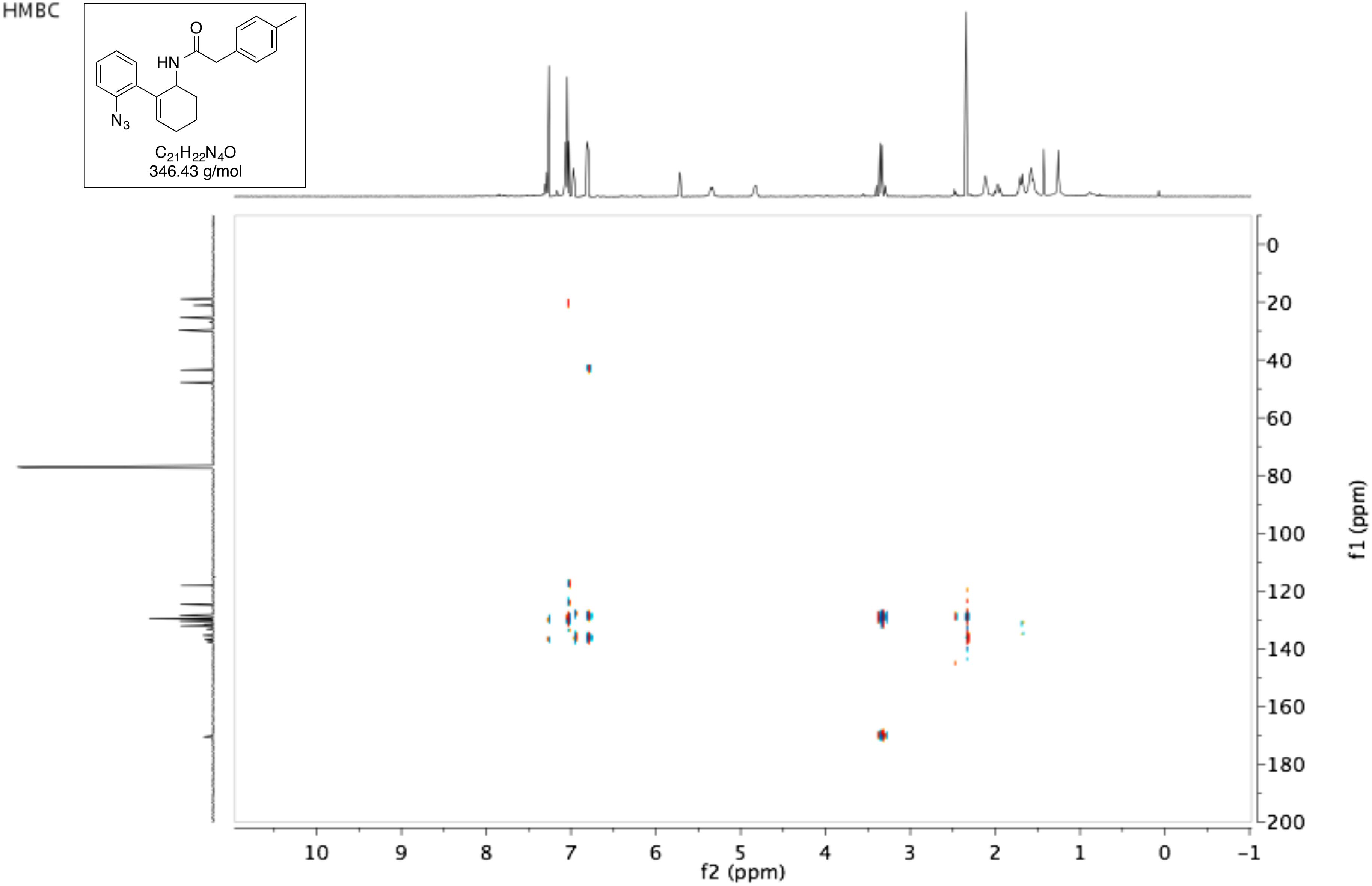
HSQC



$C_{21}H_{22}N_4O$
346.43 g/mol



HMBC



HN
O
$N_3$
$C_{21}H_{22}N_4O$
346.43 g/mol
f2 (ppm)
f1 (ppm)
10
9
8
7
6
5
4
3
2
1
0
−1
0
20
40
60
80
100
120
140
160
180
200