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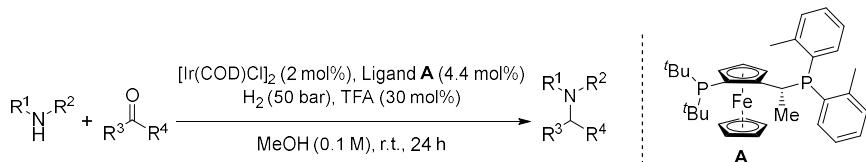
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**Author contribution:** M.J. and T.-M.N. did experimentation, purification, isolation, and characterization as well as writing the supporting information. M.C. and T.R. performed X-ray diffraction studies. M.B performed HPLC analysis. M.J. and R.G.-D. designed and supervised the project as well as writing the manuscript.

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**1. General methods.**

All reactions were carried out under an inert atmosphere of nitrogen using Schlenk line techniques with a dual-bank manifold, unless otherwise noted. All reagents were purchased commercially and used as received, unless otherwise noted. Methanol anhydrous 99.8% was dried under argon atmosphere. Analytical thin-layer chromatography (TLC) was performed on 0.25 mm Merck precoated silica gel plates (60-F254). TLC analysis was performed using hexanes/CH<sub>2</sub>Cl<sub>2</sub>, CH<sub>2</sub>Cl<sub>2</sub>/MeOH or hexanes/AcOEt as the eluent and stained using permanganate stain, ninhydrin stain, and/or UV light (254 nm). Column chromatography was carried out with the same type of silica gel and a Teledyne Isco CombiFlash<sup>(R)</sup> using RediSep Rf Gold Normal-Phase Silica<sup>(R)</sup> columns (60 Å porosity, 20–40 µm). <sup>1</sup>H NMR, <sup>13</sup>C NMR and <sup>19</sup>F NMR were recorded with Bruker FT spectrometers at 300 K unless otherwise noted. <sup>1</sup>H (400, 500 or 600 MHz) and <sup>13</sup>C {<sup>1</sup>H} (100, 126 or 151 MHz) NMR chemical shifts are reported relative to internal TMS ( $\delta$  = 0.00 ppm) CDCl<sub>3</sub> ( $\delta$  = 7.26 ppm); <sup>13</sup>C NMR: CDCl<sub>3</sub> at 77.16 ppm) or to residual protiated solvent, and <sup>19</sup>F NMR (471 MHz) chemical shifts were referenced to external CFCl<sub>3</sub> (0.0 ppm). Chemical shifts are reported in parts per million (ppm). Data are presented as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m = multiplet), coupling constant J (Hz) and integration.

**2. General procedure of the iridium-catalyzed direct reductive amination.**

In an oven dried vial equipped with a stirring bar was added ketone (1.5 mmol, 3 equiv.), amine (0.5 mmol, 1 equiv.), ligand **A** (12.5 mg, 0.022 mmol, 4.4 mol%), [Ir(COD)Cl]<sub>2</sub> (6.7 mg, 0.01 mmol, 2 mol%), anhydrous MeOH (5 mL) and trifluoroacetic acid (17.1 mg, 11.5 µL, 0.15 mmol, 30 mol%) under inert atmosphere,. The vial was placed in an autoclave, which was then sealed, and purged (replacing air with 5 bar of H<sub>2</sub>, three times). The autoclave was charged with 50 bar of H<sub>2</sub> and the reaction mixture was stirred at room temperature for 24 h. Then, the hydrogen from the autoclave was released. LC- and/or GC-MS analysis were performed to calculate the conversion of amine –limiting reagent-. Next, the solution was poured into NaOH 1 M (30 mL). Extraction with ethyl acetate (3 x 20 mL) and drying the organic layer with MgSO<sub>4</sub> before concentration to dryness under reduced pressure afforded a crude residue that was further purified by column chromatography on silica gel (heptane: ethyl acetate 1:0 to 2:1 with 1% triethylamine) to afford the tertiary amine product.

Remark: no glovebox was required for this experiment.

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## 3. Reaction optimization of the iridium-catalyzed direct reductive amination.

**Table S1.** Optimization data of the iridium-catalyzed DRA reaction between aliphatic amine **1** and aliphatic ketone **2.**

The reaction scheme illustrates the optimization of an iridium-catalyzed Direct Reductive Amination (DRA) reaction. The starting materials are aliphatic amine **1** (1-fluorobipiperazine) and aliphatic ketone **a** (2-butane). The reaction conditions involve  $[\text{Ir}(\text{COD})\text{Cl}]_2$  (2 mol%), a specific ligand (4.4 mol%),  $\text{H}_2$  (50 bar), TFA or  $\text{Ti}(\text{OEt})_4$ , and  $\text{MeOH}$  (0.1 M) at room temperature for a specified time. The products are the aminated compound **2** and the catalyst system. To the right of the reaction scheme, five different ligands are shown: **A** (a ferrocene-based phosphine), **B** (a ferrocene-based phosphine), **C** (a bisphosphine), **Xantphos** (a phosphine oxide), and **dppp** (a phosphine).

Entry	Ligand	x	y	$\text{Ti}(\text{OEt})_4$ (mol%)	TFA (mol%)	Time (h)	Conversion of <b>1</b>	Yield of <b>2</b>	Notes
1	<b>A</b>	1	3	100	-	16	55	n.d.	
2	<b>A</b>	1	3	-	30	16	59	n.d.	
3	<b>A</b>	3	1	100	-	16	84	n.d.	
4	<b>A</b>	3	1	-	30	24	80	65	
5	<b>A</b>	1	3	100	-	24	93	70	
6	<b>A</b>	1	3	-	30	24	81	39	
7	<b>A</b>	3	1	100	-	24	86	52	
8	<b>A</b>	3	1	-	30	24	>99	74	<b>optimal conditions</b>
9	<b>A</b>	1	3	-	-	24	6	n.d.	
10	<b>A</b>	1	3	-	100	24	77	n.d.	
11	<b>A</b>	1	3	-	30	24	0	n.d.	without $[\text{Ir}(\text{COD})\text{Cl}]_2$
12	-	1	3	-	30	24	15	n.d.	without any ligand
13	<b>A</b>	1	3	-	30	24	19	n.d.	with $[\text{Ir}(\text{COD})(\text{OMe})]_2$
14	<b>B</b>	1	3	-	30	24	67	29	
15	<b>C</b>	1	3	-	30	24	78	31	
16	<b>D</b>	1	3	-	30	24	97	48	
17	<b>dppp</b>	1	3	-	30	24	74	60	
18	<b>dppe</b>	1	3	-	30	24	48	30	
19	<b>A</b>	1	3	-	30	24	77	n.d.	30 bar $\text{H}_2$ instead of 50
20	<b>A</b>	1	3	-	30	24	80	n.d.	<i>t</i> -AmOH instead of $\text{MeOH}$
21	<b>A</b>	1	3	-	30	24	90	n.d.	0.2 M instead of 0.1M

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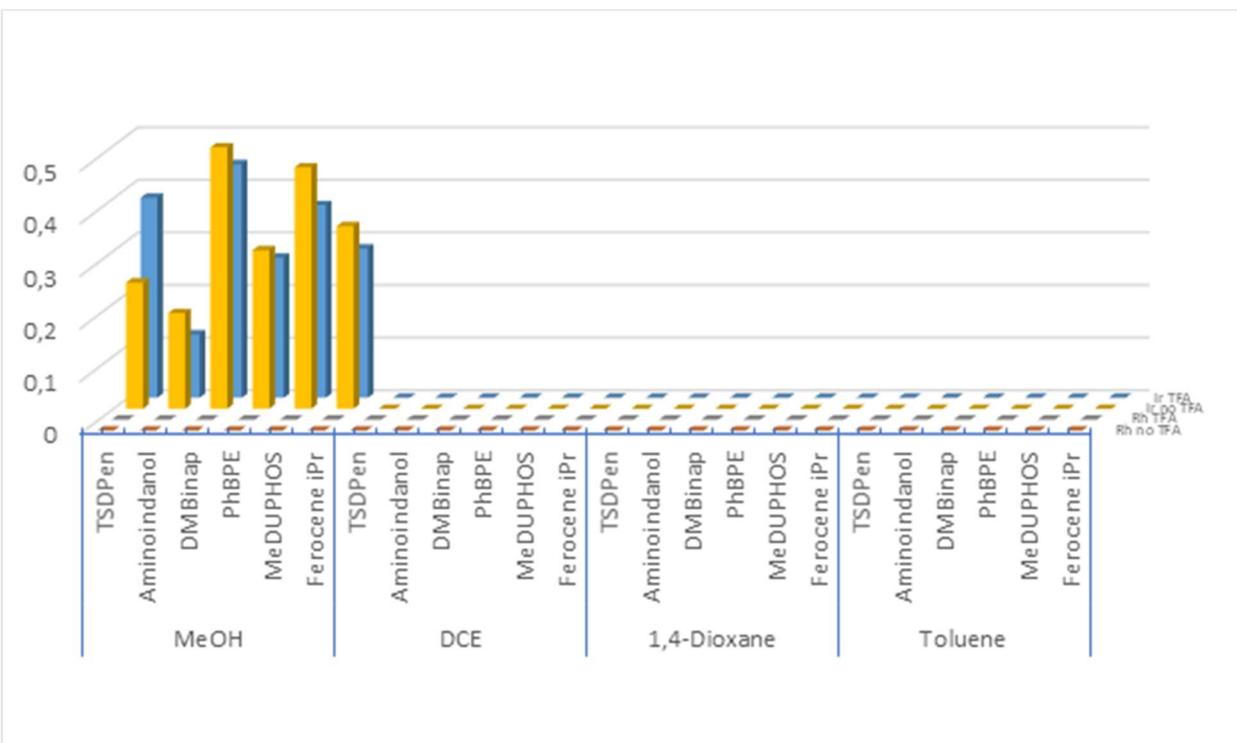
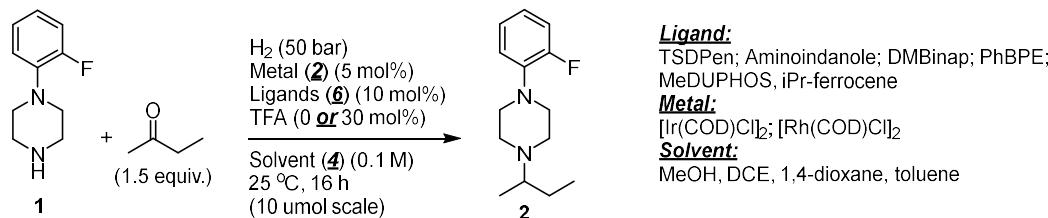
## 4. Reaction optimization of the iridium-catalyzed direct reductive amination by HTE.

## 4.1. General information.

Unless otherwise noted, all reactions were performed in an Innovative glovebox operating on its catalyst bed with oxygen levels typically < 5 ppm. Reaction experimental design was aided by the use of Unchained® Library Studio. Reactions run at 10  $\mu\text{mol}$  scale for the limiting reagent were carried out in 1 mL glass vials (Analytical-Sales, Cat. No. 84001, 8 x 30 mm, 1mL, and transparent well bottom) equipped with magnetic tumble stir bars (V&P Scientific, Cat. No. 7111D-1) in 24 or 96-well reactor blocks (Analytical-Sales, Cat. No. 24249). The various compounds were handled as liquids using single and multi-channel Eppendorf pipettors (10, 100, 200, and 1000  $\mu\text{L}$ ). On completion of solution dosing the plates were covered by a perfluoroalkoxy alkane (PFA) mat (Analytical-Sales, Cat. No. 96967 and 24261), followed by two silicon rubber mats (Analytical-Sales, Cat. No. 96965 and 24262), and an aluminum cover which was tightly and evenly sealed by 9 screws. The plate was removed from the glovebox and placed in a heating block (V&P Scientific, Cat. No. 7111D-1) on the top a magnetic tumble stirrer (500 rpm) and heated to the appropriate temperature. After 16 h, the plate was unsealed and reaction mixtures were diluted with a quench solution containing an internal standard (0.02 M 4,4-di-tert-butylbiphenyl in MeCN/DMSO 4:1, 500  $\mu\text{L}$ ). Aliquots (20  $\mu\text{L}$ ) were taken and introduced into a 96 well HPLC plate, diluted with MeCN (700  $\mu\text{L}$ ) and finally analyzed by UPLC. Finally, data were analyzed using Virscidian Analytical Studio and results expressed as P/IS ratio using Microsoft Excel.

## 4.2. High Throughput Experimentation (HTE) Data.

**Screen 1 (Table S2).** Discovery of direct reductive amination – Variation of solvent, metal, ligand and TFA loading.

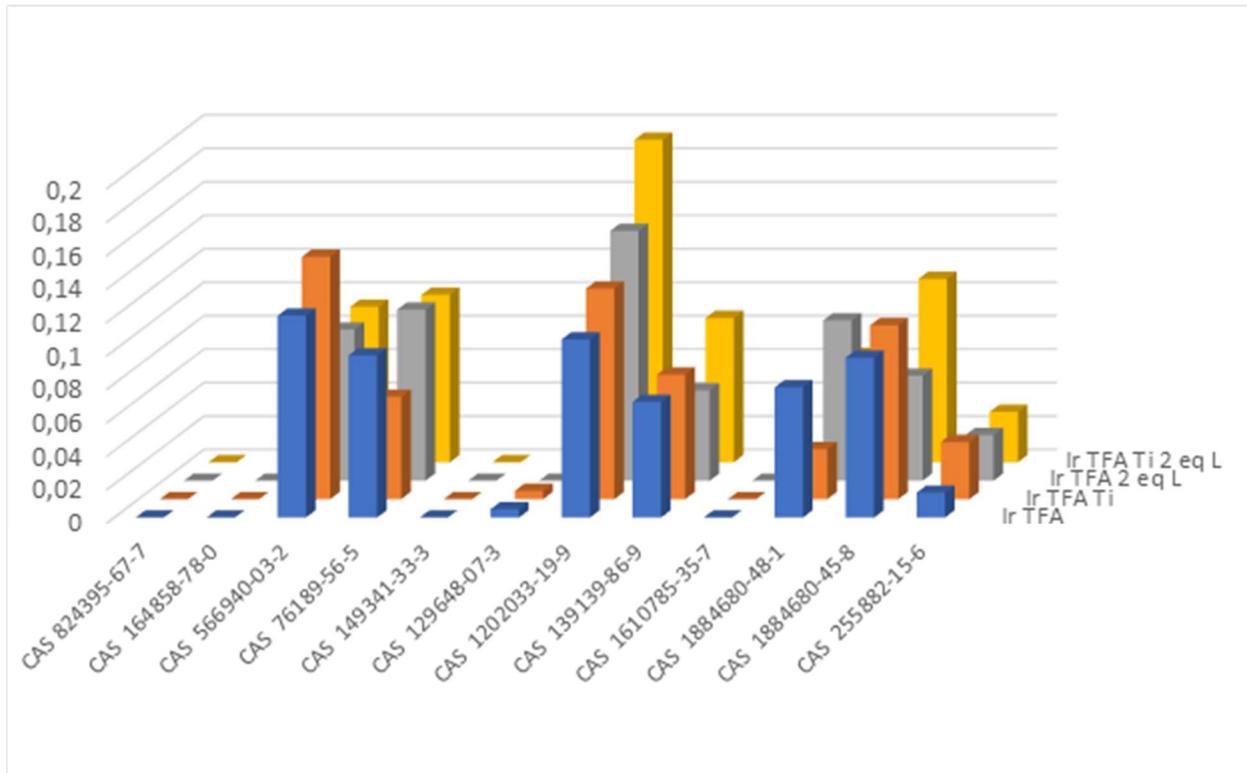
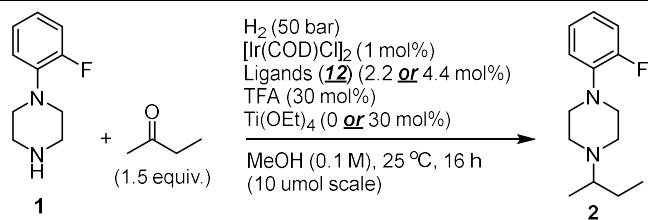


Results: Product only detected with Ir in MeOH. Clear ligand effect.

Best conditions from screen 1: DMBinap; [Ir(COD)Cl]<sub>2</sub>; MeOH.

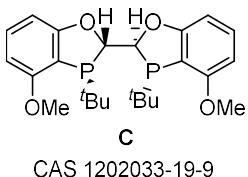
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Screen 2 (Table S3). Optimization of direct reductive amination – Variation of ligand, ligand loading and additive.



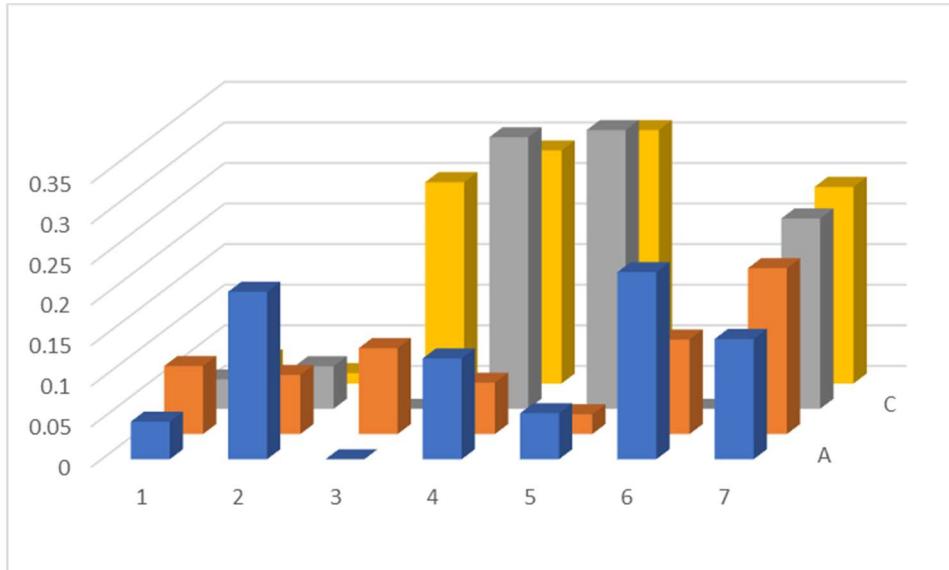
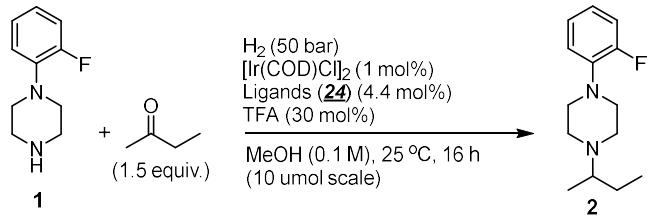
Results: Clear ligand effect with electron rich scaffold affording the highest conversion. Excess ligand (2.2 equiv/Ir) seems superior in some cases. Combination of TFA and  $\text{Ti}(\text{OEt})_4$  seems to improve P/IS, but parameter needs further investigation.

Best conditions from screen 2: Ligand CAS 1202033-19-9



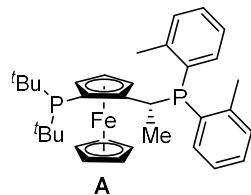
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Screen 3 (Table S4). Optimization of direct reductive amination – Further ligand screen.



	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7 (8.8 mol%)</b>
<b>A</b>	76189-56-5	210169-40-7	137219-86-4	1202033-19-9	139139-86-9	1884680-48-1	603-35-0
<b>B</b>	1884680-45-8	352655-40-4	352655-61-9	145214-57-9	394248-45-4	192138-05-9	5518-52-5
<b>C</b>	256390-47-3	37002-48-5	528814-26-8	158923-11-6	<b>849924-76-1 A</b>	244261-66-3	564483-18-7
<b>D</b>	155806-35-2	2207601-04-3	2207601-10-1	Strem 15-6425	2207601-12-3	223121-07-1	657408-07-6

Best ligand from screen 3: Ligand CAS 849924-76-1

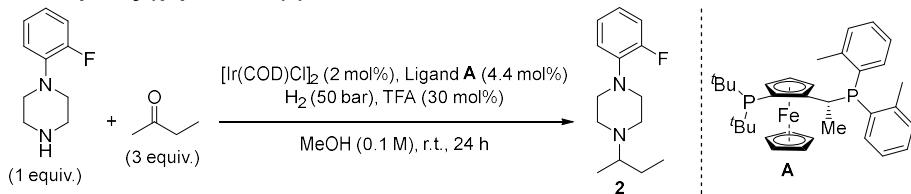


CAS 849924-76-1

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## 5. Characterization of the aliphatic tertiary amine products.

## 1-(sec-Butyl)-4-(2-fluorophenyl)piperazine (2):



**2** was obtained in 74% yield (87 mg, 0.37 mmol) after purification by column chromatography.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.08–6.88 (m, 4H), 3.10 (ddd,  $J$  = 6.0, 3.8, 1.9 Hz, 4H), 2.78–2.64 (m, 4H), 2.50 (dqd,  $J$  = 8.4, 6.6, 5.0 Hz, 1H), 1.63 (dqd,  $J$  = 12.7, 7.5, 5.0 Hz, 1H), 1.39–1.25 (m, 1H), 1.03 (d,  $J$  = 6.5 Hz, 3H), 0.92 (t,  $J$  = 7.4 Hz, 3H) ppm.

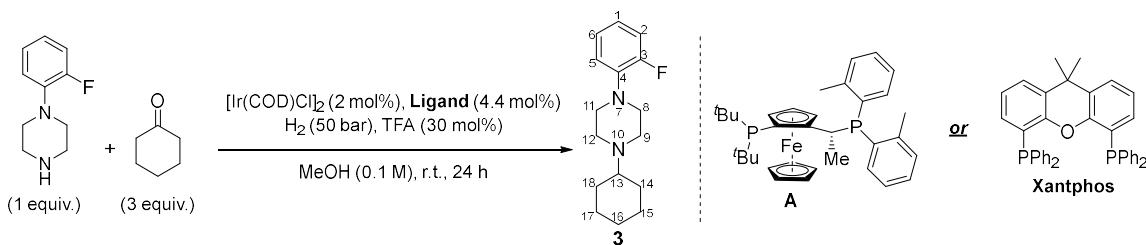
<sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>):  $\delta$  = 155.88 (d,  $J_{C,F}$  = 246.1), 140.51 (d,  $J_{C,F}$  = 8.3), 124.53 (d,  $J_{C,F}$  = 3.6), 122.36 (d,  $J_{C,F}$  = 8.0), 119.04 (d,  $J_{C,F}$  = 3.2), 116.15 (d,  $J_{C,F}$  = 20.8), 60.93, 51.19, 48.54, 26.30, 14.15, 11.49 ppm.

<sup>19</sup>F{<sup>1</sup>H} NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  = -122.74 ppm.

GC:  $t_R$  = 22.1 min; MS (EI): *m/z* = 236 (M<sup>+</sup>, 21), 207 (100), 150 (22), 122 (20), 84 (34), 56 (27).

HRMS (ESI): *m/z* calcd for C<sub>14</sub>H<sub>22</sub>N<sub>2</sub>F 237.1762 [M+H]<sup>+</sup>, found: 237.1760 (1 ppm).

## 1-Cyclohexyl-4-(2-fluorophenyl)piperazine (3):



**3** was obtained in 92% yield (121 mg, 0.46 mmol) using ligand **A** after purification by column chromatography. **3** was also obtained in 80% yield (105 mg, 0.40 mmol) using **Xantphos** after purification by column chromatography. The molecular structure of **3** was unambiguously inferred by a combination of multinuclear and multidimensional NMR studies.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.08–7.04 (m, 1H,  $H_6$ ), 7.06–6.98 (m, 1H,  $H_2$ ), 7.00–6.91 (m, 1H,  $H_5$ ), 6.92 (ddd,  $J$  = 7.9, 4.1, 1.4, 1H,  $H_1$ ), 3.16–3.10 (m, 4H,  $H_8$ ,  $H_{11}$ ), 2.82–2.74 (m, 4H,  $H_9$ ,  $H_{12}$ ), 2.32 (ddq,  $J$  = 11.0, 7.1, 3.4, 1H,  $H_{13}$ ), 1.93 (dd,  $J$  = 9.1, 4.0, 2H,  $H_{14''}$ ,  $H_{18''}$ ), 1.87–1.77 (m, 2H,  $H_{15}$ ,  $H_{17}$ ), 1.69–1.61 (m, 1H,  $H_{16}$ ), 1.26 (td,  $J$  = 9.3, 7.1, 4.2, 4H,  $H_{14}$ ,  $H_{15''}$ ,  $H_{17''}$ ,  $H_{18''}$ ), 1.14 (ddt,  $J$  = 16.2, 12.3, 6.1, 1H,  $H_{16''}$ ) ppm.

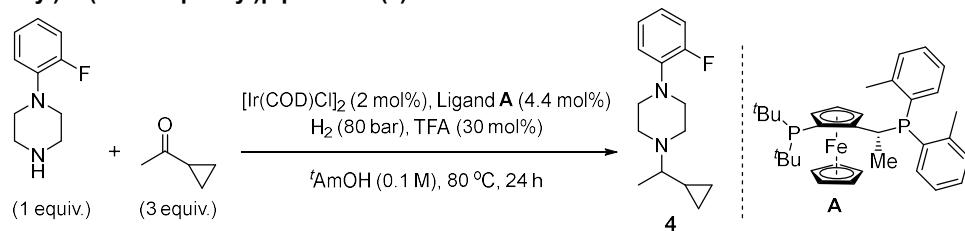
<sup>13</sup>C{<sup>1</sup>H} NMR (126 MHz, CDCl<sub>3</sub>):  $\delta$  = 155.76 (d,  $J_{C,F}$  = 245.9, C<sub>3</sub>), 140.31 (d,  $J_{C,F}$  = 8.3, C<sub>4</sub>), 124.43 (d,  $J_{C,F}$  = 3.7, C<sub>6</sub>), 122.26 (d,  $J_{C,F}$  = 8.0, C<sub>1</sub>), 118.88 (d,  $J_{C,F}$  = 3.2, C<sub>5</sub>), 116.03 (d,  $J_{C,F}$  = 20.7, C<sub>2</sub>), 63.58 (C<sub>13</sub>), 51.06 (C<sub>8</sub>, C<sub>12</sub>), 49.08 (C<sub>9</sub>, C<sub>11</sub>), 29.01 (C<sub>14</sub>, C<sub>18</sub>), 26.35 (C<sub>16</sub>), 25.91 (C<sub>15</sub>, C<sub>17</sub>) ppm.

<sup>19</sup>F{<sup>1</sup>H} NMR (471 MHz, CDCl<sub>3</sub>):  $\delta$  = -122.68 ppm.

GC:  $t_R$  = 12.5 min; MS (EI): *m/z* = 262 (M<sup>+</sup>, 53), 219 (100), 150 (21).

HRMS (ESI): *m/z* calcd for C<sub>16</sub>H<sub>24</sub>N<sub>2</sub>F 263.1918 [M+H]<sup>+</sup>, found: 263.1918 (0 ppm).

## 1-(1-Cyclopropylethyl)-4-(2-fluorophenyl)piperazine (4):



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**4** was obtained in 94% yield (116.6 mg, 0.47 mmol) after purification by column chromatography using modified reaction conditions: *t*-amyl alcohol as solvent, 80 °C, 80 bar.

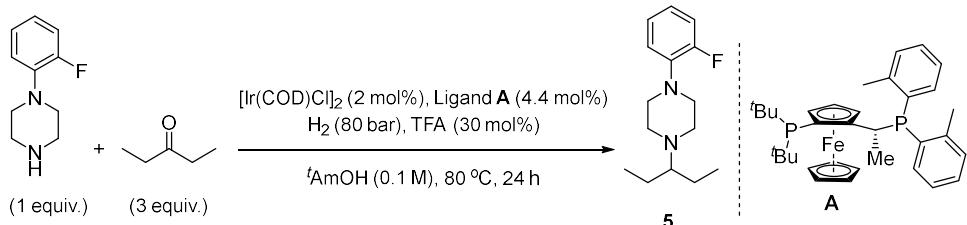
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.09–6.89 (m, 4H), 3.14 (dt,  $J$  = 6.3, 3.2 Hz, 4H), 2.95 (dd,  $J$  = 11.0, 5.2 Hz, 2H), 2.77 (dt,  $J$  = 10.7, 4.9 Hz, 2H), 1.71 (dq,  $J$  = 8.9, 6.5 Hz, 1H), 1.20 (d,  $J$  = 6.6 Hz, 3H), 0.79 (qt,  $J$  = 8.5, 5.1 Hz, 1H), 0.63 (dddd,  $J$  = 9.0, 7.8, 5.8, 4.4 Hz, 1H), 0.53–0.43 (m, 1H), 0.33 (dq,  $J$  = 9.9, 5.0 Hz, 1H), 0.07–0.00 (m, 1H) ppm.

$^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 124.57 (d,  $J_{\text{C},\text{F}}$  = 3.6 Hz), 122.43 (d,  $J_{\text{C},\text{F}}$  = 8.0 Hz), 119.01 (d,  $J_{\text{C},\text{F}}$  = 3.1 Hz), 116.17 (d,  $J_{\text{C},\text{F}}$  = 20.8 Hz), 65.19, 51.02, 50.33, 17.82, 14.35, 6.90, 1.98 ppm ( $x2$   $_{\text{ipso}}\text{C}$  not detected).

$^{19}\text{F}\{\text{H}\}$  NMR (376 MHz,  $\text{CDCl}_3$ ):  $\delta$  = -122.76 ppm.

GC:  $t_{\text{R}}$  = 24.1 min; MS (EI):  $m/z$  = 248 ([M] $^+$ , 33), 233 (100), 207 (38), 150 (41), 122 (34), 56 (52).

HRMS (ESI):  $m/z$  calcd for  $\text{C}_{15}\text{H}_{22}\text{N}_2\text{F}$  249.1762 [M+H] $^+$ , found: 249.1762 (0 ppm).

**1-(2-Fluorophenyl)-4-(pentan-3-yl)piperazine (5):**

**5** was obtained in 78% yield (97.6 mg, 0.39 mmol) after purification by column chromatography using modified reaction conditions: *t*-amyl alcohol as solvent, 80 °C, 80 bar.

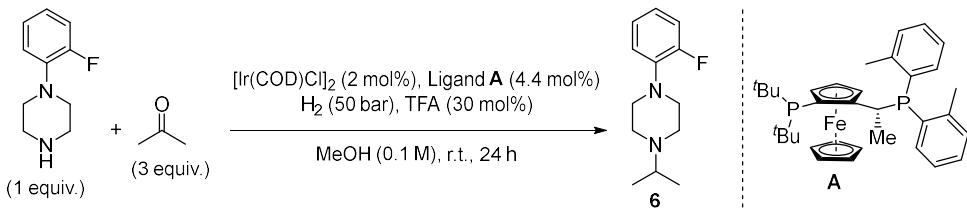
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.09–6.88 (m, 4H), 3.07 (t,  $J$  = 4.8 Hz, 4H), 2.75–2.67 (m, 4H), 2.21 (p,  $J$  = 6.7 Hz, 1H), 1.60–1.49 (m, 2H), 1.35 (dp,  $J$  = 14.3, 7.2 Hz, 2H), 0.93 (t,  $J$  = 7.4 Hz, 6H) ppm.

$^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 124.53 (d,  $J$  = 3.6 Hz), 122.30 (d,  $J$  = 7.9 Hz), 119.07 (d,  $J$  = 3.1 Hz), 116.16 (d,  $J$  = 20.8 Hz), 67.58, 51.43, 48.60, 22.47, 11.91 ppm ( $x2$   $_{\text{ipso}}\text{C}$  not detected).

$^{19}\text{F}\{\text{H}\}$  NMR (376 MHz,  $\text{CDCl}_3$ ):  $\delta$  = -122.68 ppm.

GC:  $t_{\text{R}}$  = 23.2 min; MS (EI):  $m/z$  = 250 ([M] $^+$ , 15), 221 (100), 98 (25).

HRMS (ESI):  $m/z$  calcd for  $\text{C}_{15}\text{H}_{24}\text{N}_2\text{F}$  251.1918 [M+H] $^+$ , found: 251.1918 (0 ppm).

**1-(2-Fluorophenyl)-4-isopropylpiperazine (6):**

**6** was obtained in 84% yield (93.4 mg, 0.42 mmol) after purification by column chromatography.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.06–6.88 (m, 4H), 3.11 (m, 4H), 2.73 (hept,  $J$  = 6.5 Hz, 1H), 2.70 (m, 4H), 1.03 (d,  $J$  = 6.5 Hz, 6H) ppm.

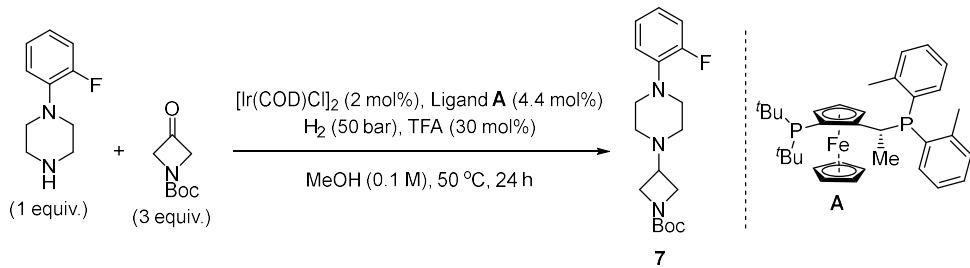
$^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 155.85 (d,  $J_{\text{C},\text{F}}$  = 245.8), 140.37 (d,  $J_{\text{C},\text{F}}$  = 8.5), 124.52 (d,  $J_{\text{C},\text{F}}$  = 3.6), 122.39 (d,  $J_{\text{C},\text{F}}$  = 8.0), 118.98 (d,  $J_{\text{C},\text{F}}$  = 3.1), 116.12 (d,  $J_{\text{C},\text{F}}$  = 20.8), 54.61, 51.00, 48.89, 18.71 ppm.

$^{19}\text{F}\{\text{H}\}$  NMR (376 MHz,  $\text{CDCl}_3$ ):  $\delta$  = -122.73 ppm.

GC:  $t_{\text{R}}$  = 20.7 min; MS (EI):  $m/z$  = 222 (M $^+$ , 50), 207 (100), 150 (22), 122 (27), 84 (40), 71 (25), 56 (60).

HRMS (ESI):  $m/z$  calcd for  $\text{C}_{13}\text{H}_{20}\text{N}_2\text{F}$  223.1605 [M+H] $^+$ , found: 223.1604 (0 ppm).

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**tert-Butyl 3-(4-(2-fluorophenyl)piperazin-1-yl)azetidine-1-carboxylate (7):**

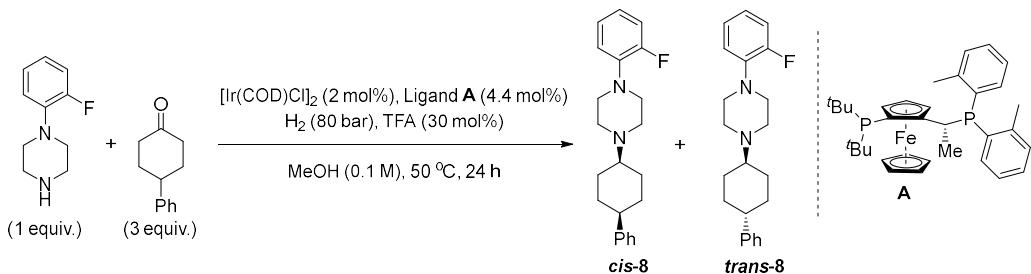
**7** was obtained in 80% yield (134 mg, 0.40 mmol) after purification by column chromatography using modified reaction conditions: 50 °C.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 7.11–6.89 (m, 4H), 3.96 (dd, *J* = 8.7, 7.1 Hz, 2H), 3.85 (dd, *J* = 8.8, 5.3 Hz, 2H), 3.17–3.10 (m, 5H), 2.58–2.51 (m, 4H), 1.44 (s, 9H) ppm.

<sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>): δ = 156.33, 155.73 (d, *J*<sub>C,F</sub> = 245.8 Hz), 139.89 (d, *J*<sub>C,F</sub> = 8.6 Hz), 124.50 (d, *J*<sub>C,F</sub> = 3.5 Hz), 122.66 (d, *J*<sub>C,F</sub> = 8.0 Hz), 118.99 (d, *J*<sub>C,F</sub> = 2.9 Hz), 116.14 (d, *J*<sub>C,F</sub> = 20.6 Hz), 79.50, 53.89, 53.59–52.27 (m), 50.15, 50.11, 49.74, 28.40 ppm.

<sup>19</sup>F{<sup>1</sup>H} NMR (376 MHz, CDCl<sub>3</sub>): δ = -122.80 ppm.

HRMS (ESI): *m/z* calcd for C<sub>18</sub>H<sub>27</sub>FN<sub>3</sub>O<sub>2</sub> 336.2082 [M+H]<sup>+</sup>, found: 336.2079 (2 ppm).

**tert-Butyl 3-(4-(2-fluorophenyl)piperazin-1-yl)azetidine-1-carboxylate (8)**

**8** (2:1 *cis/trans*) was obtained in 93% yield (157 mg, 0.464 mmol) after purification by column chromatography using modified reaction conditions: 50 °C, 80 bar. **cis-8** and **trans-8** were separated by reverse phase chromatography (Stationary phase: RP XBridge Prep C18 OBD- 5μm, 50 x 250mm, Mobile phase: 0.25 % NH<sub>4</sub>HCO<sub>3</sub> solution in water, CH<sub>3</sub>CN).

**cis-8:**

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 7.33–7.26 (m, 2H), 7.24–7.15 (m, 3H), 7.10–6.88 (m, 4H), 3.17–3.10 (m, 4H), 2.81 (dd, *J* = 6.0, 3.8 Hz, 4H), 2.54–2.36 (m, 2H), 2.13–2.05 (m, 2H), 2.05–1.96 (m, 2H), 1.61–1.38 (m, 4H) ppm.

<sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>): δ = 155.78 (d, *J*<sub>C,F</sub> = 245.8 Hz), 146.97, 140.27 (d, *J*<sub>C,F</sub> = 8.5 Hz), 128.35, 126.78, 126.01, 124.47 (d, *J*<sub>C,F</sub> = 3.6 Hz), 122.37 (d, *J*<sub>C,F</sub> = 7.9 Hz), 118.92 (d, *J*<sub>C,F</sub> = 3.0 Hz), 116.07 (d, *J*<sub>C,F</sub> = 20.7 Hz), 63.27, 51.08, 51.05, 49.27, 44.21, 33.57, 29.03 ppm.

<sup>19</sup>F{<sup>1</sup>H} NMR (376 MHz, CDCl<sub>3</sub>): δ = -122.73 ppm.

UPLC (Waters Acuity UPLC BEH C18, 55 °C, [0.1% ammonium bicarbonate in 95% H<sub>2</sub>O + 5% CH<sub>3</sub>CN]/MeOH. = linear gradient from 95/5 to 5/95 in 3.50 min, flow rate = 0.6 mL/min, λ = 210 – 400 nm) t<sub>R</sub> = 2.78 min (*cis*, major).

HRMS (ESI) *m/z* calcd for C<sub>22</sub>H<sub>28</sub>FN<sub>2</sub> 339.2231 [M+H]<sup>+</sup>, found: 339.2228 (2 ppm).

**trans-8:**

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 7.34–7.25 (m, 4H), 7.17 (ddd, *J* = 8.6, 5.7, 2.3 Hz, 1H), 7.08–6.88 (m, 4H), 3.12 (t, *J* = 4.9 Hz, 4H), 2.77–2.61 (m, 5H), 2.33 (d, *J* = 2.9 Hz, 1H), 2.04–1.92 (m, 4H), 1.60 (tdd, *J* = 14.8, 10.7, 6.9 Hz, 4H) ppm.

<sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>): δ = 155.80 (d, *J*<sub>C,F</sub> = 245.8 Hz), 147.15, 140.34 (d, *J*<sub>C,F</sub> = 8.5 Hz), 128.28, 127.05, 125.75, 124.44 (d, *J*<sub>C,F</sub> = 3.6 Hz), 122.22 (d, *J*<sub>C,F</sub> = 7.9 Hz), 118.82 (d, *J*<sub>C,F</sub> = 3.1 Hz), 116.07 (d, *J*<sub>C,F</sub> = 20.8 Hz), 58.95, 51.04, 51.01, 50.00, 42.91, 28.41, 28.05 ppm.

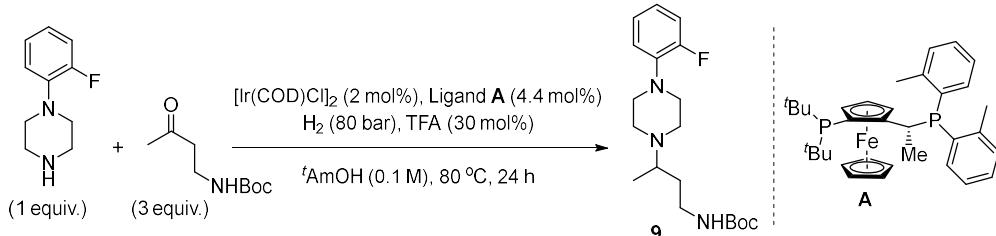
<sup>19</sup>F{<sup>1</sup>H} NMR (376 MHz, CDCl<sub>3</sub>): δ = -122.58 ppm.

## SUPPORTING INFORMATION

UPLC (Waters Acquity UPLC BEH C18, 55 °C, [0.1% ammonium bicarbonate in 95% H<sub>2</sub>O + 5% CH<sub>3</sub>CN]/MeOH. = linear gradient from 95/5 to 5/95 in 3.50 min, flow rate = 0.6 mL/min, λ = 210 - 400 nm) t<sub>R</sub> = 2.67 min (trans, minor).

HRMS (ESI) m/z calcd for C<sub>22</sub>H<sub>28</sub>FN<sub>2</sub> 339.2231 [M+H]<sup>+</sup>, found: 339.2228 (2 ppm).

**tert-Butyl 3-(4-(2-fluorophenyl)piperazin-1-yl)butyl)carbamate (9)**



**9** was obtained in 58% yield (102 mg, 0.29 mmol) after purification by column chromatography using modified reaction conditions: *t*-amyl alcohol as solvent, 80 °C, 80 bar.

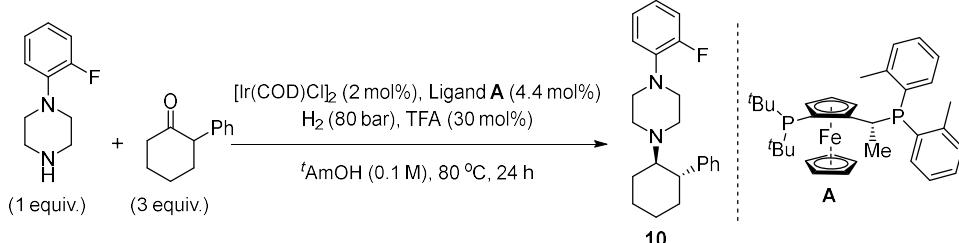
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 7.12–6.87 (m, 4H), 5.90 (s, 1H), 3.34 (d, J = 13.1 Hz, 1H), 3.22–2.99 (m, 5H), 2.88–2.68 (m, 3H), 2.62 (dt, J = 10.5, 4.8 Hz, 2H), 1.81–1.65 (m, 1H), 1.43 (s, 10H), 1.02 (d, J = 6.7 Hz, 3H) ppm.

<sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>): δ = 156.15, 155.79 (d, J<sub>CF</sub> = 245.6 Hz), 140.25 (d, J<sub>CF</sub> = 8.6 Hz), 124.44 (d, J<sub>CF</sub> = 3.6 Hz), 122.44 (d, J<sub>CF</sub> = 7.9 Hz), 118.96 (d, J<sub>CF</sub> = 3.0 Hz), 116.07 (d, J<sub>CF</sub> = 20.8 Hz), 78.67, 58.85, 51.06, 51.03, 48.09, 39.62, 32.62, 28.51, 13.67 ppm.

<sup>19</sup>F{<sup>1</sup>H} NMR (376 MHz, CDCl<sub>3</sub>): δ = -122.84 ppm.

HRMS (ESI) m/z calcd for C<sub>19</sub>H<sub>31</sub>FN<sub>3</sub>O<sub>2</sub> 352.2395 [M+H]<sup>+</sup>, found: 352.2391 (2 ppm).

**1-(2-Fluorophenyl)-4-(2-phenylcyclohexyl)piperazine (10)**



**10** was obtained in 27% yield (46 mg, 0.14 mmol) after purification by column chromatography using modified reaction conditions: *t*-amyl alcohol as solvent, 80 °C, 80 bar.

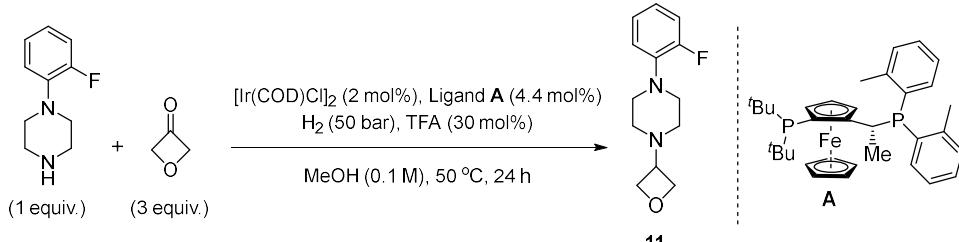
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 7.51 (d, J = 7.5 Hz, 2H), 7.29–7.23 (m, 2H), 7.20–7.13 (m, 1H), 7.05–6.93 (m, 2H), 6.92–6.83 (m, 2H), 3.22 (q, J = 4.7 Hz, 1H), 2.93 (td, J = 4.5, 2.4 Hz, 4H), 2.69–2.54 (m, 3H), 2.47 (dt, J = 10.8, 4.9 Hz, 2H), 2.17–2.06 (m, 1H), 1.98–1.71 (m, 4H), 1.61–1.49 (m, 1H), 1.45 (dq, J = 9.4, 4.7 Hz, 2H) ppm.

<sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>): δ = 155.67 (d, J<sub>CF</sub> = 246.0 Hz), 144.33, 140.24 (d, J<sub>CF</sub> = 8.4 Hz), 129.23, 127.75, 125.51, 124.32 (d, J<sub>CF</sub> = 3.7 Hz), 122.03 (d, J<sub>CF</sub> = 8.0 Hz), 118.69 (d, J<sub>CF</sub> = 3.3 Hz), 115.97 (d, J<sub>CF</sub> = 20.9 Hz), 65.60, 50.99, 50.95, 50.83, 43.47, 31.02, 26.29, 24.86, 22.70 ppm.

<sup>19</sup>F{<sup>1</sup>H} NMR (376 MHz, CDCl<sub>3</sub>): δ = -122.61 ppm.

HRMS (ESI) m/z calcd for C<sub>22</sub>H<sub>28</sub>FN<sub>2</sub> 339.2231 [M+H]<sup>+</sup>, found: 339.2227 (2 ppm).

**1-(2-Fluorophenyl)-4-(oxetan-3-yl)piperazine (11)**



## SUPPORTING INFORMATION

**11** was obtained in 44% yield (57 mg, 0.22 mmol) after purification by column chromatography using modified reaction conditions: 50 °C.

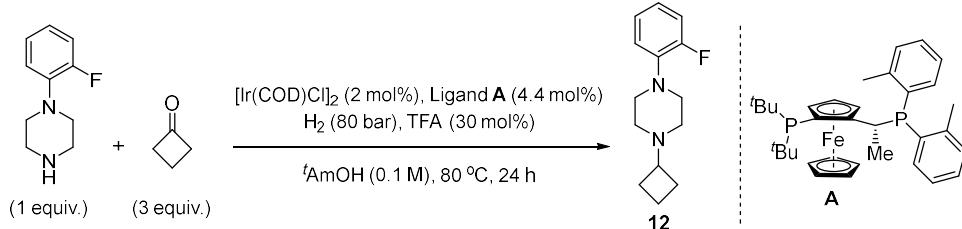
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.11–6.89 (m, 4H), 4.74–4.62 (m, 4H), 3.64–3.53 (m, 1H), 3.19–3.09 (m, 4H), 2.57–2.50 (m, 4H) ppm.

$^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 155.76 (d,  $J_{\text{C},\text{F}} = 245.9$  Hz), 139.99 (d,  $J_{\text{C},\text{F}} = 8.6$  Hz), 124.50 (d,  $J_{\text{C},\text{F}} = 3.6$  Hz), 122.65 (d,  $J_{\text{C},\text{F}} = 8.0$  Hz), 119.01 (d,  $J_{\text{C},\text{F}} = 3.0$  Hz), 116.15 (d,  $J_{\text{C},\text{F}} = 20.6$  Hz), 75.47, 59.27, 50.21, 50.18, 49.73 ppm.

$^{19}\text{F}\{\text{H}\}$  NMR (376 MHz,  $\text{CDCl}_3$ ):  $\delta$  = -122.82 ppm.

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{13}\text{H}_{18}\text{FN}_2\text{O}$  237.1398 [ $\text{M}+\text{H}]^+$ , found: 237.1396 (1 ppm).

**1-Cyclobutyl-4-(2-fluorophenyl)piperazine (12)**



**12** was obtained in 83% yield (97 mg, 0.41 mmol) after purification by column chromatography using modified reaction conditions: *t*-amyl alcohol as solvent, 80 °C, 80 bar.

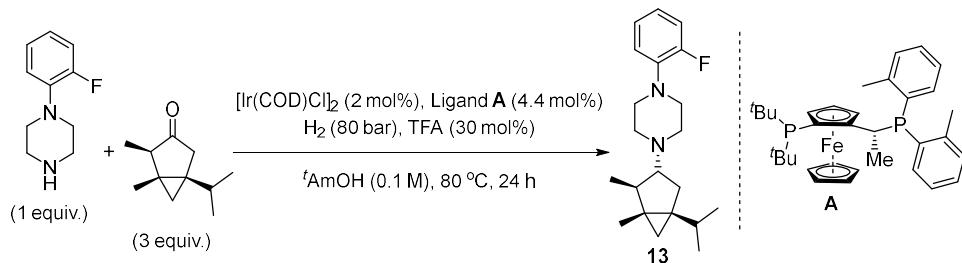
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.10–6.87 (m, 4H), 3.12 (t,  $J = 4.9$  Hz, 4H), 2.88–2.75 (m, 1H), 2.52 (t,  $J = 4.9$  Hz, 4H), 2.13–2.00 (m, 2H), 2.00–1.84 (m, 2H), 1.81–1.64 (m, 2H) ppm.

$^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 155.76 (d,  $J_{\text{C},\text{F}} = 245.8$  Hz), 140.27 (d,  $J_{\text{C},\text{F}} = 8.7$  Hz), 124.46 (d,  $J_{\text{C},\text{F}} = 3.6$  Hz), 122.40 (d,  $J_{\text{C},\text{F}} = 8.0$  Hz), 118.97 (d,  $J_{\text{C},\text{F}} = 3.0$  Hz), 116.07 (d,  $J_{\text{C},\text{F}} = 20.8$  Hz), 60.31, 50.33, 50.30, 49.53, 27.05, 14.31 ppm.

$^{19}\text{F}\{\text{H}\}$  NMR (376 MHz,  $\text{CDCl}_3$ ):  $\delta$  = -122.74 ppm.

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{20}\text{FN}_2$  235.1605 [ $\text{M}+\text{H}]^+$ , found: 235.1603 (1 ppm).

**1-(2-Fluorophenyl)-4-((1*R*,2*R*,5*S*)-5-isopropyl-1,2-dimethylbicyclo[3.1.0]hexan-3-yl)piperazine (13)**



**13** was obtained in 73% yield (113 mg, 0.36 mmol) after purification by column chromatography using modified reaction conditions: *t*-amyl alcohol as solvent, 80 °C, 80 bar.

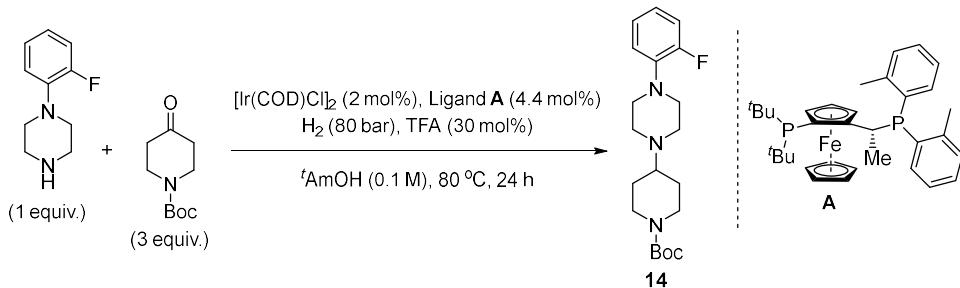
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.09–6.86 (m, 4H), 3.10 (t,  $J = 5.2$  Hz, 4H), 2.59–2.45 (m, 4H), 2.22–2.05 (m, 2H), 1.73 (dd,  $J = 11.5$ , 6.6 Hz, 1H), 1.61–1.51 (m, 1H), 1.29 (hept,  $J = 6.9$  Hz, 1H), 0.98 (d,  $J = 6.8$  Hz, 3H), 0.95–0.85 (m, 7H), 0.56 (dd,  $J = 5.0$ , 3.8 Hz, 1H), 0.20 (ddd,  $J = 8.2$ , 5.0, 1.1 Hz, 1H) ppm.

$^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 155.76 (d,  $J_{\text{C},\text{F}} = 245.8$  Hz), 140.27 (d,  $J_{\text{C},\text{F}} = 8.4$  Hz), 124.42 (d,  $J_{\text{C},\text{F}} = 3.6$  Hz), 122.24 (d,  $J_{\text{C},\text{F}} = 8.0$  Hz), 118.81 (d,  $J_{\text{C},\text{F}} = 3.2$  Hz), 116.05 (d,  $J_{\text{C},\text{F}} = 20.7$  Hz), 65.35, 52.94, 50.40, 50.37, 34.88, 33.27, 31.77, 29.32, 29.17, 20.22, 19.64, 15.78, 13.35 ppm.

$^{19}\text{F}\{\text{H}\}$  NMR (376 MHz,  $\text{CDCl}_3$ ):  $\delta$  = -122.64.

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{20}\text{H}_{30}\text{FN}_2$  317.2388 [ $\text{M}+\text{H}]^+$ , found: 317.2385 (2 ppm).

## SUPPORTING INFORMATION

**tert-Butyl 4-(4-(2-fluorophenyl)piperazin-1-yl)piperidine-1-carboxylate (14)**

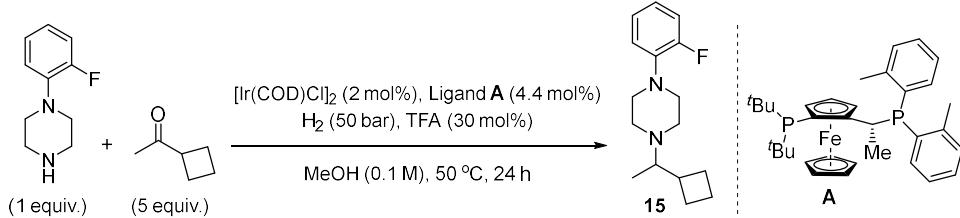
**14** was obtained in 93% yield (169 mg, 0.46 mmol) after purification by column chromatography using modified reaction conditions: *t*-amyl alcohol as solvent, 80 °C, 80 bar.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 7.10–6.88 (m, 4H), 4.16 (br. s, 2H), 3.12 (dd, *J* = 6.2, 3.6 Hz, 4H), 2.78–2.67 (m, 6H), 2.43 (tt, *J* = 11.3, 3.6 Hz, 1H), 1.85 (d, *J* = 12.6 Hz, 2H), 1.46 (s, 9H), 1.51–1.38 (m, 2H) ppm.

<sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>): δ = 155.75 (d, *J*<sub>C,F</sub> = 245.7 Hz), 154.75, 140.12 (d, *J*<sub>C,F</sub> = 8.4 Hz), 124.47 (d, *J*<sub>C,F</sub> = 3.6 Hz), 122.48 (d, *J*<sub>C,F</sub> = 7.9 Hz), 118.90 (d, *J*<sub>C,F</sub> = 3.1 Hz), 116.09 (d, *J*<sub>C,F</sub> = 20.8 Hz), 79.49, 61.97, 50.92, 50.89, 49.21, 43.67, 28.47, 28.30 ppm.

<sup>19</sup>F{<sup>1</sup>H} NMR (376 MHz, CDCl<sub>3</sub>): δ = -122.81 ppm.

HRMS (ESI) *m/z* calcd for C<sub>20</sub>H<sub>31</sub>FN<sub>3</sub>O<sub>2</sub> 364.2395 [M+H]<sup>+</sup>, found: 364.2391 (2 ppm).

**1-(1-Cyclobutylethyl)-4-(2-fluorophenyl)piperazine (15)**

**15** was obtained in 44% yield (57 mg, 0.22 mmol) after purification by column chromatography using modified reaction conditions: 50 °C.

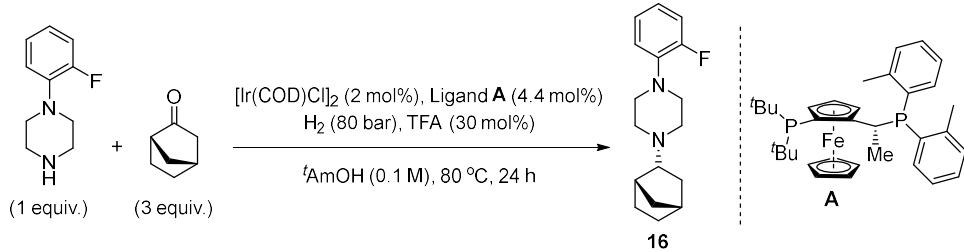
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 7.10–6.86 (m, 5H), 3.07 (t, *J* = 4.9 Hz, 4H), 2.77–2.62 (m, 4H), 2.52 (dq, *J* = 9.2, 6.5 Hz, 1H), 2.47 – 2.34 (m, 1H), 2.10–1.93 (m, 1H), 1.92–1.81 (m, 2H), 1.79–1.62 (m, 2H), 0.92 (d, *J* = 6.5 Hz, 3H) ppm.

<sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>): δ = 155.76 (d, *J*<sub>C,F</sub> = 245.9 Hz), 140.43 (d, *J*<sub>C,F</sub> = 8.5 Hz), 124.40 (d, *J*<sub>C,F</sub> = 3.5 Hz), 122.20 (d, *J*<sub>C,F</sub> = 7.9 Hz), 118.91 (d, *J*<sub>C,F</sub> = 3.2 Hz), 116.02 (d, *J*<sub>C,F</sub> = 20.8 Hz), 65.04, 51.13; 51.10, 49.04, 39.34, 28.56, 26.99, 18.46, 11.75. ppm.

<sup>19</sup>F{<sup>1</sup>H} NMR (376 MHz, CDCl<sub>3</sub>): δ = -122.71 ppm.

HRMS (ESI) *m/z* calcd for C<sub>16</sub>H<sub>24</sub>FN<sub>2</sub> 263.1918 [M+H]<sup>+</sup>, found: 263.1916 (1 ppm).

## SUPPORTING INFORMATION

**1-((1*S*,4*R*)-Bicyclo[2.2.1]heptan-2-yl)-4-(2-fluorophenyl)piperazine (16)**

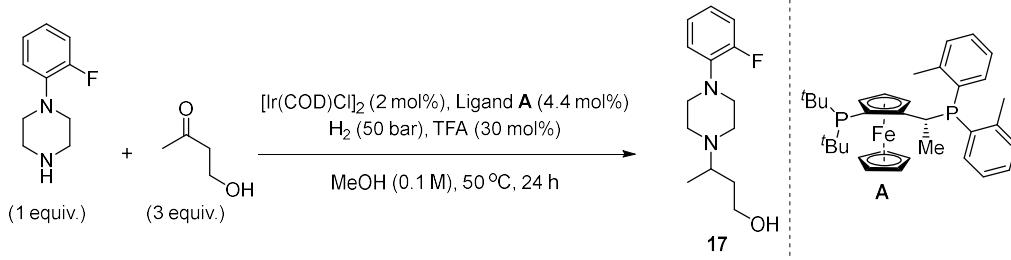
**16** was obtained in 79% yield (108 mg, 0.39 mmol) after purification by column chromatography using modified reaction conditions: *t*-amyl alcohol as solvent, 80 °C, 80 bar. Note: This reaction was also performed on larger scale starting from amine (1.00 g, 5.55 mmol) and norcamphor (1.83 g, 16.65 mmol), affording the desired product in 94% yield after purification by column chromatography

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.09–6.86 (m, 4H), 3.11 (q,  $J$  = 4.9 Hz, 4H), 2.55 (p,  $J$  = 5.7 Hz, 4H), 2.30 (hd,  $J$  = 3.8, 1.5 Hz, 2H), 2.18 (t,  $J$  = 4.7 Hz, 1H), 1.84–1.66 (m, 2H), 1.57–1.43 (m, 1H), 1.38 (dq,  $J$  = 9.6, 1.8 Hz, 1H), 1.35–1.22 (m, 3H), 0.93 (ddd,  $J$  = 12.0, 4.4, 2.8 Hz, 1H) ppm.

$^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 155.76 (d,  $J_{\text{C},\text{F}}$  = 245.9 Hz), 140.34 (d,  $J_{\text{C},\text{F}}$  = 8.5 Hz), 124.41 (d,  $J_{\text{C},\text{F}}$  = 3.6 Hz), 122.19 (d,  $J_{\text{C},\text{F}}$  = 8.0 Hz), 118.83 (d,  $J_{\text{C},\text{F}}$  = 3.2 Hz), 116.03 (d,  $J_{\text{C},\text{F}}$  = 20.8 Hz), 67.65, 52.72, 50.43, 50.39, 38.96, 38.04, 36.83, 35.79, 30.58, 21.05 ppm.

$^{19}\text{F}\{\text{H}\}$  NMR (376 MHz,  $\text{CDCl}_3$ ):  $\delta$  = -122.60 ppm.

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{17}\text{H}_{24}\text{FN}_2$  275.1918 [ $\text{M}+\text{H}]^+$ , found: 275.1915 (2 ppm).

**3-(4-(2-fluorophenyl)piperazin-1-yl)butan-1-ol (17)**

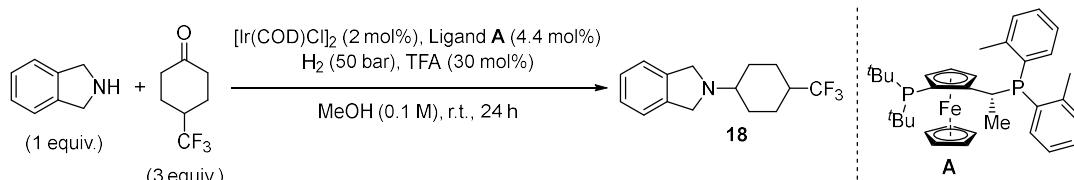
**17** was obtained in 72% yield (91 mg, 0.36 mmol) after purification by column chromatography using modified reaction conditions: 50 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.10–6.88 (m, 4H), 3.93–3.76 (m, 2H), 3.15–2.90 (m, 7H), 2.72–2.62 (m, 2H), 1.92 (ddt,  $J$  = 14.8, 10.7, 4.1 Hz, 1H), 1.41 (ddt,  $J$  = 14.8, 3.7, 2.6 Hz, 1H), 1.06 (d,  $J$  = 6.7 Hz, 3H) ppm.

$^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 155.74 (d,  $J$  = 245.6 Hz), 139.92 (d,  $J$  = 8.7 Hz), 124.51 (d,  $J$  = 3.6 Hz), 122.67 (d,  $J$  = 8.0 Hz), 119.04 (d,  $J$  = 2.9 Hz), 116.09 (d,  $J$  = 20.7 Hz), 64.03, 61.64, 50.94, 50.93, 48.15, 33.57, 13.32 ppm.

$^{19}\text{F}\{\text{H}\}$  NMR (376 MHz,  $\text{CDCl}_3$ ):  $\delta$  = -123.01 ppm.

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{22}\text{FN}_2\text{O}$  253.1711 [ $\text{M}+\text{H}]^+$ , found: 253.1707 (3 ppm).

**2-(4-(Trifluoromethyl)cyclohexyl)isoindoline (18):**

**18** (1:1 *cis/trans*) was obtained in 54% yield (72.6 mg, 0.27 mmol) after purification by column chromatography. Two diastereomers (**18'** and **18''**) were recovered during the purification process and characterized as follow:

Characterization of **18'**:

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.20 (t,  $J$  = 2.0 Hz, 4H), 3.98 (s, 4H), 2.40 (tt,  $J$  = 10.5, 3.8 Hz, 1H), 2.23–2.14 (m, 2H), 2.03 (dd,  $J$  = 7.9, 3.3 Hz, 2H), 1.49–1.25 (m, 5H) ppm.

## SUPPORTING INFORMATION

$^{13}\text{C}\{\text{H}\}$  NMR (101 MHz  $\text{CDCl}_3$ ):  $\delta$  = 139.58, 126.80, 122.33, 61.98, 56.84, 41.63, 41.36, 30.39, 23.70 (d,  $^1\text{J}_{\text{C},\text{F}}$  = 2.7 Hz) ppm.

$^{19}\text{F}\{\text{H}\}$  NMR (376 MHz,  $\text{CDCl}_3$ ):  $\delta$  = -73.62 ppm.

GC:  $t_{\text{R}} = 22.4$  min; MS (EI):  $m/z$  = 269 ( $\text{M}^+$ , 29), 158 (100), 144 (26), 118 (34).

HRMS (ESI):  $m/z$  calcd for  $\text{C}_{15}\text{H}_{19}\text{NF}_3$  270.1464 [ $\text{M}+\text{H}]^+$ , found: 270.1465 (0 ppm).

Characterization of 18”:

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.25–7.19 (m, 4H), 3.93 (s, 4H), 2.68 (p,  $J$  = 3.3 Hz, 1H), 2.08–2.01 (m, 3H), 1.90–1.78 (m, 2H), 1.67 (dt,  $J$  = 13.3, 3.9 Hz, 2H), 1.52 (tt,  $J$  = 13.5, 3.3 Hz, 2H) ppm.

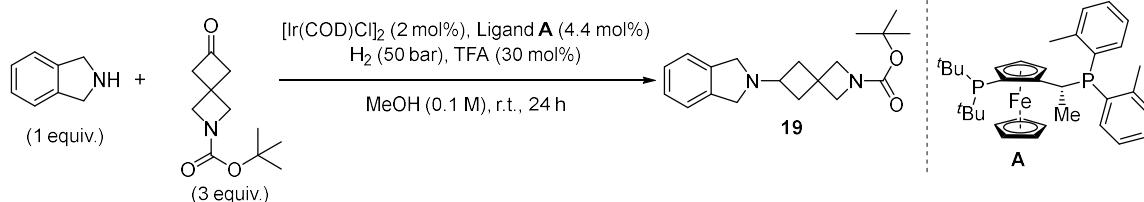
$^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 140.17, 126.70, 122.30, 58.21, 57.07, 41.87, 41.61, 28.94, 19.42 (d,  $^1\text{J}_{\text{C},\text{F}}$  = 2.6 Hz) ppm.

$^{19}\text{F}\{\text{H}\}$  NMR (376 MHz,  $\text{CDCl}_3$ ):  $\delta$  = -73.17 ppm.

GC:  $t_{\text{R}} = 22.9$  min; MS (EI):  $m/z$  = 269 ( $\text{M}^+$ , 27), 158 (100), 144 (24), 118 (33).

HRMS (ESI):  $m/z$  calcd for  $\text{C}_{15}\text{H}_{19}\text{NF}_3$  270.1464 [ $\text{M}+\text{H}]^+$ , found: 270.1463 (0 ppm).

**tert-Butyl 6-(isoindolin-2-yl)-2-azaspiro[3.3]heptane-2-carboxylate (19):**



19 was obtained in 45% yield (72.3 mg, 0.23 mmol) after purification by column chromatography.

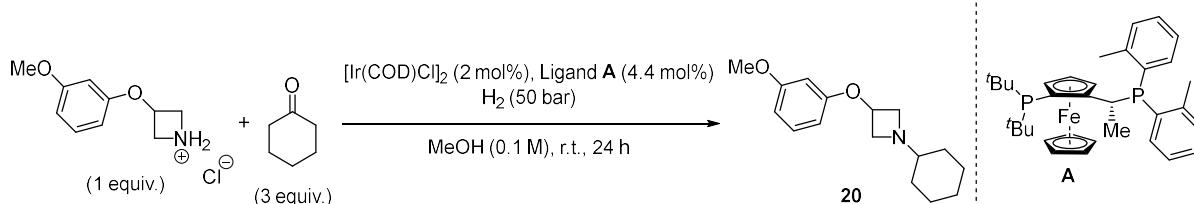
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.18 (s, 4H), 3.94 (s, 2H), 3.85 (s, 2H), 3.83 (s, 4H), 3.13 (p,  $J$  = 7.5 Hz, 1H), 2.39–2.31 (m, 2H), 2.22–2.12 (m, 2H), 1.42 (s, 9H) ppm.

$^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 156.29, 139.87, 126.89, 122.51, 79.34, 56.17, 53.40, 38.54, 32.04, 28.49 ppm.

GC:  $t_{\text{R}} = 40.7$  min; MS (EI):  $m/z$  = 257 ([ $\text{M}-\text{CMe}_3$ ] $^+$ , 13), 144 (34), 118 (100), 57 (20).

HRMS (ESI):  $m/z$  calcd for  $\text{C}_{19}\text{H}_{27}\text{N}_2\text{O}_2$  315.2067 [ $\text{M}+\text{H}]^+$ , found: 315.2065 (1 ppm).

**1-Cyclohexyl-3-(3-methoxyphenoxy)azetidine (20):**



20 was obtained in 36% yield (47.0 mg, 0.18 mmol) after purification by column chromatography using modified reaction conditions: no TFA.

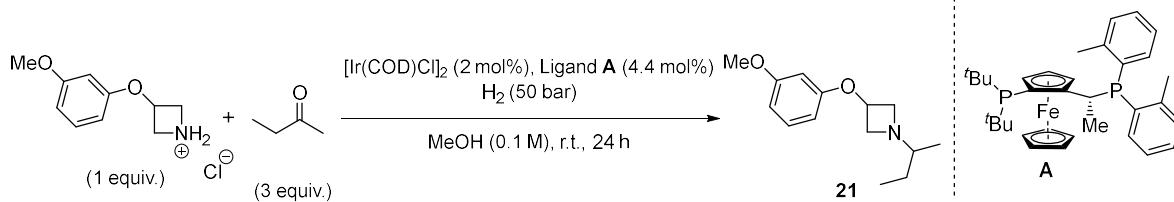
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.18–7.12 (m, 1H), 6.51 (ddd,  $J$  = 8.3, 2.1, 1.0 Hz, 1H), 6.39–6.34 (m, 2H), 4.76 (p,  $J$  = 5.9 Hz, 1H), 3.83–3.78 (m, 2H), 3.77 (s, 3H), 3.09–3.03 (m, 2H), 2.04 (tt,  $J$  = 10.4, 3.5 Hz, 1H), 1.73 (td,  $J$  = 13.2, 8.0, 6.6, 3.9 Hz, 4H), 1.63–1.55 (m, 1H), 1.28–1.12 (m, 3H), 1.00 (qd,  $J$  = 13.6, 12.2, 4.0 Hz, 2H) ppm.

$^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 161.01, 158.53, 130.13, 106.93, 106.75, 101.31, 67.06, 66.39, 59.81, 55.38, 29.96, 25.96, 24.49 ppm.

GC:  $t_{\text{R}} = 29.3$  min; MS (EI):  $m/z$  = 261 ( $\text{M}^+$ , 10), 150 (100), 121 (20).

HRMS (ESI):  $m/z$  calcd for  $\text{C}_{16}\text{H}_{24}\text{NO}_2$  262.1802 [ $\text{M}+\text{H}]^+$ , found: 262.1801 (0 ppm).

## SUPPORTING INFORMATION

**1-(sec-Butyl)-3-(3-methoxyphenoxy)azetidine (21):**

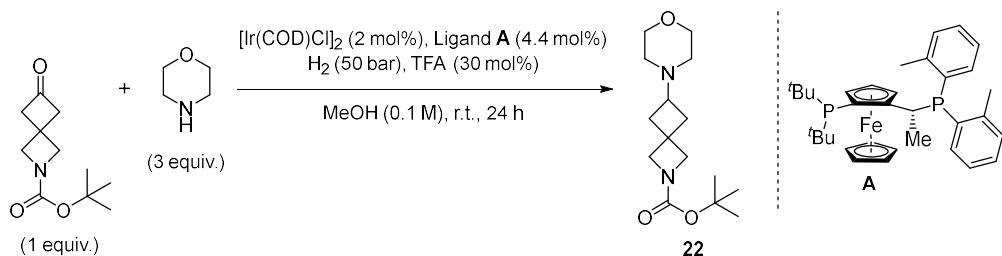
**21** was obtained in 63% yield (75.2 mg, 0.32 mmol) after purification by column chromatography using modified reaction conditions: no TFA.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.20–7.13 (m, 1H), 6.54–6.49 (m, 1H), 6.41–6.34 (m, 2H), 4.76 (p,  $J$  = 5.9 Hz, 1H), 3.87–3.76 (m, 2H), 3.76 (s, 3H), 3.12–3.03 (m, 2H), 2.18 (ddt,  $J$  = 12.5, 6.3, 3.4 Hz, 1H), 1.52 (dtq,  $J$  = 18.4, 7.5, 3.4 Hz, 1H), 1.16 (ddt,  $J$  = 13.4, 8.4, 7.3 Hz, 1H), 0.95 (d,  $J$  = 6.2 Hz, 3H), 0.88 (t,  $J$  = 7.5 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 160.99, 158.47, 130.10, 106.89, 106.74, 101.28, 65.88, 64.94, 60.14, 55.33, 26.34, 16.04, 10.05 ppm.

GC:  $t_{\text{R}} = 23.4$  min; MS (EI):  $m/z$  = 206 ([M-OMe] $^+$ , 10), 150 (100), 121 (25), 58 (34).

HRMS (ESI):  $m/z$  calcd for  $\text{C}_{14}\text{H}_{22}\text{NO}_2$  236.1645 [M+H] $^+$ , found: 236.1646 (0 ppm).

**tert-Butyl 6-morpholino-2-azaspiro[3.3]heptane-2-carboxylate (22):**

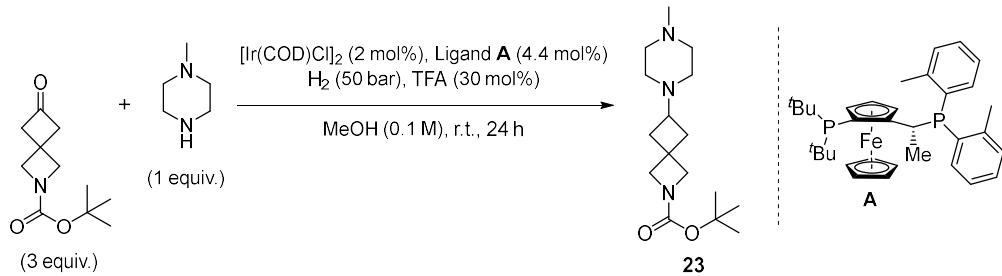
**22** was obtained in 85% yield (121.3 mg, 0.43 mmol) after purification by column chromatography.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 3.91 (s, 2H), 3.80 (s, 2H), 3.68 (t,  $J$  = 4.7 Hz, 4H), 2.62–2.53 (m, 1H), 2.27 (ddd,  $J$  = 12.5, 6.4, 2.7 Hz, 6H), 2.00 (td,  $J$  = 8.8, 2.9 Hz, 2H), 1.41 (s, 9H) ppm.

$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 156.30, 79.44, 66.84, 62.50 (identified by HSQC), 54.96, 50.15, 37.90, 31.25, 28.51 ppm.

GC:  $t_{\text{R}} = 26.8$  min; MS (EI):  $m/z$  = 226 ([M-CMe<sub>3</sub>] $^+$ , 12), 209 (21), 153 (54), 138 (100), 113 (77), 98 (22), 96 (28), 57 (55), 55 (32).

HRMS (ESI):  $m/z$  calcd for  $\text{C}_{15}\text{H}_{27}\text{N}_2\text{O}_3$  283.2016 [M+H] $^+$ , found: 283.2018 (1 ppm).

**tert-Butyl 6-(4-methylpiperazin-1-yl)-2-azaspiro[3.3]heptane-2-carboxylate (23):**

**23** was obtained in 60% yield (88.2 mg, 0.30 mmol) after purification by column chromatography.

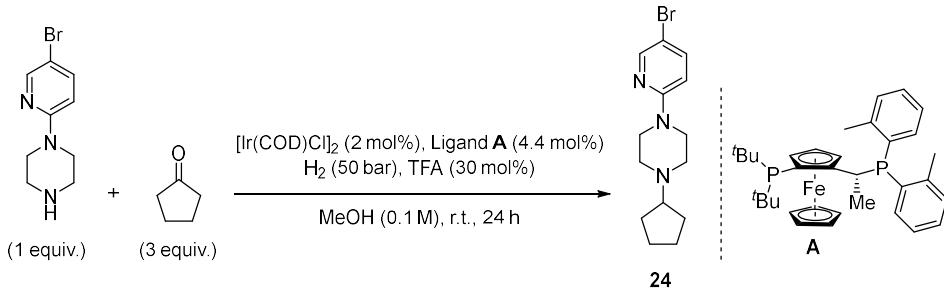
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 3.91 (s, 2H), 3.80 (s, 2H), 2.59 (p,  $J$  = 7.7 Hz, 1H), 2.55–2.25 (m, 10H), 2.28 (s, 3H), 2.01 (td,  $J$  = 9.0, 3.0 Hz, 2H), 1.42 (s, 9H) ppm.

$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 156.22, 79.32, 62.50 (identified by HSQC), 54.72, 54.67, 49.55, 46.04, 38.11, 30.97, 28.43 ppm.

GC:  $t_{\text{R}} = 27.9$  min; MS (EI):  $m/z$  = 222 ([M-CMe<sub>3</sub>] $^+$ , 13), 139 (26), 101 (24), 70 (100), 58 (34).

HRMS (ESI):  $m/z$  calcd for  $\text{C}_{16}\text{H}_{30}\text{N}_3\text{O}_2$  296.2333 [M+H] $^+$ , found: 296.2331 (0 ppm).

## SUPPORTING INFORMATION

**1-(5-Bromopyridin-2-yl)-4-cyclopentylpiperazine (24):**

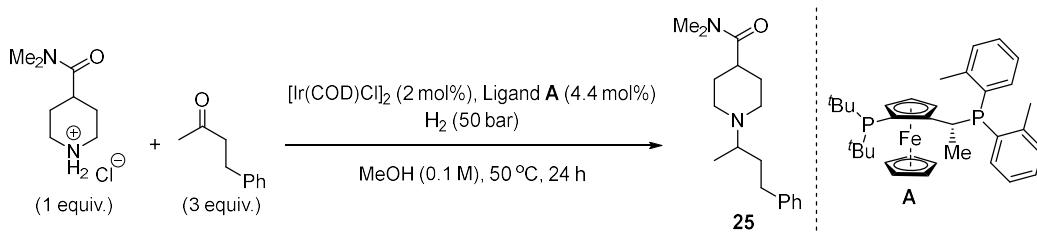
**24** was obtained in 73% yield (114.7 mg, 0.37 mmol) after purification by column chromatography.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 8.18 (d,  $J$  = 2.5 Hz, 1H), 7.51 (dd,  $J$  = 9.0, 2.6 Hz, 1H), 6.52 (d,  $J$  = 9.0 Hz, 1H), 3.55–3.48 (m, 4H), 2.61–2.56 (m, 4H), 2.55–2.46 (m, 1H), 1.93–1.86 (m, 2H), 1.71 (tdd,  $J$  = 9.6, 5.8, 2.2 Hz, 2H), 1.61–1.50 (m, 2H), 1.49–1.38 (m, 2H) ppm.

$^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 158.14, 148.62, 139.77, 108.45, 107.71, 67.58, 52.09, 45.32, 30.57, 24.27 ppm.

GC:  $t_{\text{R}}$  = 37 min; MS (EI):  $m/z$  = 309 ([M] $^+$ , 10), 124 (100), 110 (40), 56 (47).

HRMS (ESI):  $m/z$  calcd for  $\text{C}_{14}\text{H}_{21}\text{N}_3\text{Br}$  310.0913 [M+H] $^+$ , found: 310.0915 (0 ppm).

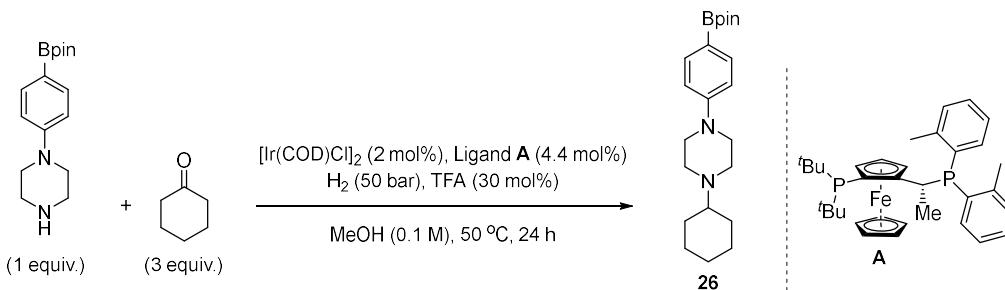
***N,N*-Dimethyl-1-(4-phenylbutan-2-yl)piperidine-4-carboxamide (25)**

**25** was obtained in 60% yield (86 mg, 0.30 mmol) after purification by column chromatography using modified reaction conditions: no TFA, 50 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.66 (s, 0.33H, 1 rotamer), 7.31–7.22 (m, 1H), 7.22–7.12 (m, 3H), 7.10 (s, 0.66H, 1 rotamer), 3.04 (s, 3H), 2.94 (s, 3H), 2.86 (d,  $J$  = 11.4 Hz, 1H), 2.80 (d,  $J$  = 11.5 Hz, 1H), 2.74–2.55 (m, 3H), 2.54–2.34 (m, 2H), 2.20 (t,  $J$  = 11.1 Hz, 1H), 1.94–1.64 (m, 5H), 1.55 (ddt,  $J$  = 13.8, 9.1, 7.1 Hz, 1H), 0.99 (d,  $J$  = 6.6 Hz, 3H) ppm.

$^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 175.25, 142.70, 128.51, 128.25, 125.61, 58.42, 50.11, 45.61, 39.13, 37.05, 35.62, 35.42, 32.93, 28.94, 28.73, 13.62 ppm.

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{18}\text{H}_{29}\text{N}_2\text{O}$  289.2274 [M+H] $^+$ , found: 289.2271 (2 ppm).

**1-cyclohexyl-4-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)piperazine (26)**

**26** was obtained in 83% yield (153 mg, 0.41 mmol) after purification by column chromatography using modified reaction conditions: 50 °C.

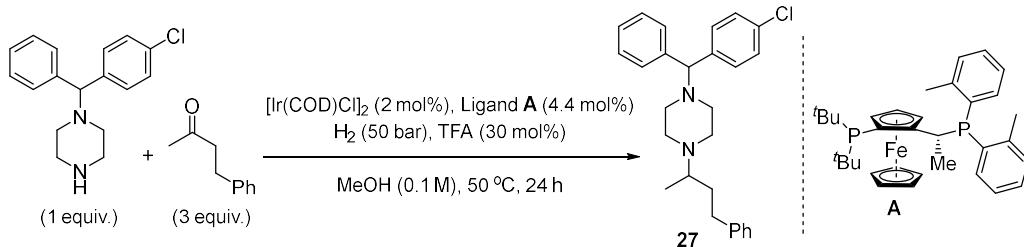
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.74–7.66 (m, 2H), 6.92–6.84 (m, 2H), 3.30–3.23 (m, 4H), 2.74–2.67 (m, 4H), 2.28 (ddd,  $J$  = 11.1, 7.5, 3.6 Hz, 1H), 1.97–1.85 (m, 1H), 1.85–1.74 (m, 1H), 1.69–1.58 (m, 1H), 1.32 (s, 12H), 1.29–1.07 (m, 5H) ppm.

$^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 151.77, 134.37, 112.55, 81.61, 61.80, 47.18, 46.87, 27.27, 24.60, 24.15, 23.14 ppm.

## SUPPORTING INFORMATION

HRMS (ESI)  $m/z$  calcd for  $C_{22}H_{36}N_2O_2B$  371.2864 [M+H]<sup>+</sup>, found: 371.2863 (1 ppm).

**1-((4-Chlorophenyl)(phenyl)methyl)-4-(4-phenylbutan-2-yl)piperazine (27)**



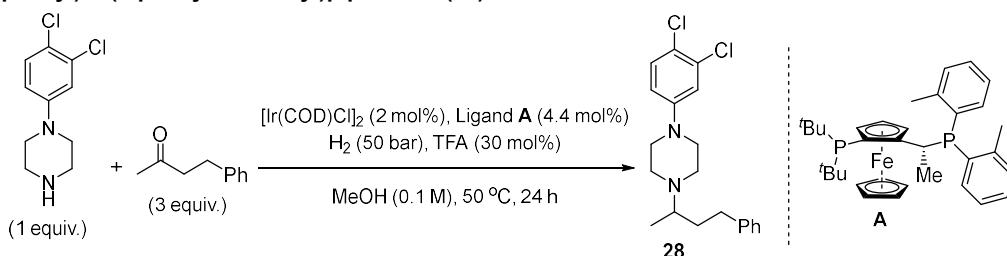
**27** was obtained in 58% yield (121 mg, 0.29 mmol) after purification by column chromatography using modified reaction conditions: 50 °C.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.39–7.31 (m, 4H), 7.30–7.10 (m, 10H), 4.19 (s, 1H), 2.71–2.32 (m, 11H), 1.90–1.77 (m, 1H), 1.54 (ddt,  $J$  = 13.7, 9.6, 7.0 Hz, 1H), 1.01 (d,  $J$  = 6.5 Hz, 3H) ppm.

<sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>):  $\delta$  = 142.75, 142.39, 142.38, 141.59, 141.57, 132.45, 129.25, 128.60, 128.54, 128.43, 128.26, 127.89, 127.08, 125.62, 77.34, 77.23, 77.03, 76.71, 75.63, 57.98, 52.39, 48.18, 35.46, 32.96, 14.06 ppm.

HRMS (ESI)  $m/z$  calcd for  $C_{27}H_{32}ClN_2$  419.2249 [M+H]<sup>+</sup>, found: 419.2246 (2 ppm).

**1-(3,4-Dichlorophenyl)-4-(4-phenylbutan-2-yl)piperazine (28)**



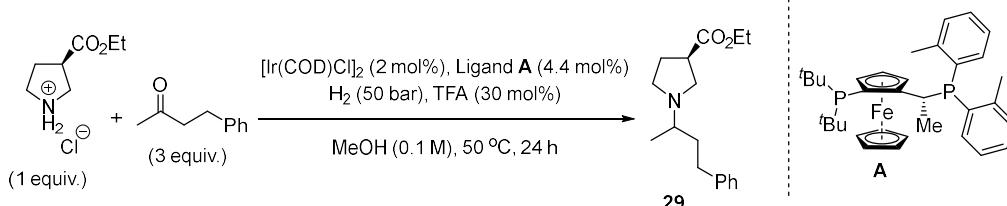
**28** was obtained in 73% yield (132 mg, 0.36 mmol) after purification by column chromatography using modified reaction conditions: 50 °C.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.35–7.21 (m, 3H), 7.23–7.13 (m, 3H), 6.95 (d,  $J$  = 2.8 Hz, 1H), 6.73 (dd,  $J$  = 8.9, 2.9 Hz, 1H), 3.15 (pt,  $J$  = 6.1, 3.5 Hz, 4H), 2.76–2.66 (m, 4H), 2.66–2.52 (m, 3H), 1.87 (ddt,  $J$  = 13.1, 9.2, 6.4 Hz, 1H), 1.60 (ddt,  $J$  = 13.8, 9.2, 7.0 Hz, 1H), 1.02 (d,  $J$  = 6.6 Hz, 3H) ppm.

<sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>):  $\delta$  = 150.90, 142.57, 132.71, 130.36, 128.44, 128.31, 125.70, 121.87, 117.12, 115.24, 58.10, 49.17, 47.79, 35.47, 32.85, 13.84 ppm.

HRMS (ESI)  $m/z$  calcd for  $C_{20}H_{25}Cl_2N_2$  363.1389 [M+H]<sup>+</sup>, found: 363.1387 (1 ppm).

**Ethyl (3*R*)-1-(4-phenylbutan-2-yl)pyrrolidine-3-carboxylate (29)**



**29** was obtained in 71% yield (98 mg, 0.36 mmol) after purification by column chromatography using modified reaction conditions: 50 °C. Product obtained as an inseparable mixture of diastereomer, mixture described below.

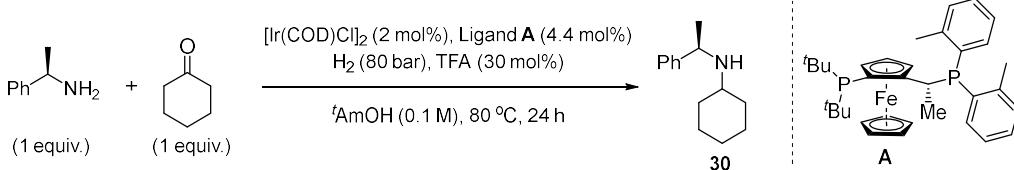
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.29 (tt,  $J$  = 7.1, 0.9 Hz, 2H), 7.22–7.16 (m, 3H), 4.16 (q,  $J$  = 7.1, 2H), 3.45–3.30 (m, 1H), 3.24–3.12 (m, 2H), 3.00–2.88 (m, 1H), 2.85–2.70 (m, 3H), 2.65–2.52 (m, 1H), 2.36–2.26 (m, 1H), 2.18–2.00 (m, 2H), 1.93–1.78 (m, 1H), 1.35–1.22 (m, 6H) ppm.

## SUPPORTING INFORMATION

$^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 172.65, 140.14, 128.66, 128.30, 126.40, 61.61, 59.79, 52.08, 50.26, 41.31, 34.06, 31.88, 27.63, 15.70, 14.11. ppm.

SFC (Stationary phase: Chiralpak IG 20 x 250 mm (two columns installed in series), Mobile phase:  $\text{CO}_2$ ,  $\text{MeOH} + 0.4\% \text{iPrNH}_2$ )  $t_{\text{R}}$  = 9.23 min (isomer 1), 9.45 min (isomer 2).

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{17}\text{H}_{26}\text{NO}_2$  276.1958 [ $\text{M}+\text{H}]^+$ , found: 276.1955 (2 ppm).

**N-(1-phenylethyl)cyclohexanamine (30)**

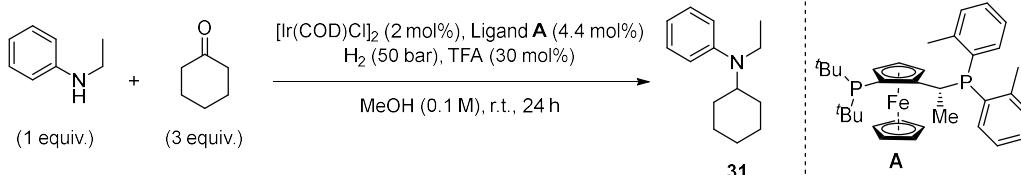
**30** was obtained in 87% yield (88 mg, 0.43 mmol) after purification by column chromatography using modified reaction conditions: *t*-amyl alcohol as solvent, 80 °C, 80 bar.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.55–7.48 (m, 2H), 7.44–7.33 (m, 3H), 6.22–5.28 (br s, 1H), 4.33 (q,  $J$  = 6.7 Hz, 1H), 2.60 (tt,  $J$  = 11.6, 3.9 Hz, 1H), 2.10–1.99 (m, 1H), 1.98–1.91 (m, 1H), 1.80–1.67 (m, 2H), 1.61 (d,  $J$  = 6.8 Hz, 3H), 1.60–1.54 (m, 1H), 1.51–1.33 (m, 2H), 1.18–0.97 (m, 3H) ppm.

$^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 137.26, 129.24, 128.89, 127.51, 55.07, 54.63, 30.17, 28.24, 24.97, 24.64, 24.44, 20.80 ppm.

SFC (Stationary phase: Chiralpak AD 20 x 250 mm, Mobile phase:  $\text{CO}_2$ ,  $\text{MeOH} + 0.4\% \text{iPrNH}_2$ )  $t_{\text{R}}$  = 1.32 min (isomer 1, not detected), 1.52 min (isomer 2).

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{22}\text{N}$  204.1747 [ $\text{M}+\text{H}]^+$ , found: 204.1746 (1 ppm).

**N-(1-Cyclohexyl)-N-ethylaniline (31):**

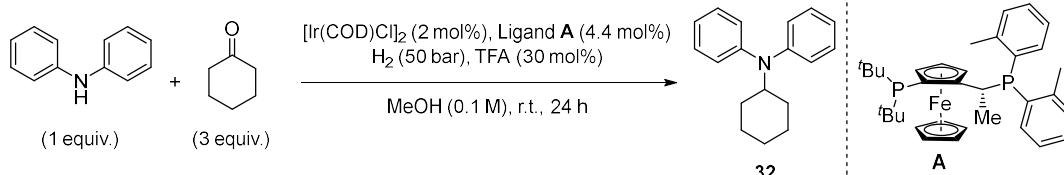
**31** was obtained in 36% yield (36.5 mg, 0.18 mmol) after purification by column chromatography. The spectral data match those found in the literature.<sup>[1]</sup>

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.25–7.20 (m, 2H), 6.78–6.72 (m, 2H), 6.66 (tt,  $J$  = 7.2, 1.1 Hz, 1H), 3.57 (tt,  $J$  = 11.3, 3.2 Hz, 1H), 3.30 (q,  $J$  = 7.0 Hz, 2H), 1.94–1.80 (m, 4H), 1.72 (dddd,  $J$  = 14.2, 6.1, 3.8, 2.2 Hz, 1H), 1.50–1.32 (m, 4H), 1.18 (t,  $J$  = 7.0 Hz, 4H) ppm.

$^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 148.58, 129.33, 115.69, 112.70, 57.34, 39.08, 30.90, 26.44, 26.14, 15.36 ppm.

GC:  $t_{\text{R}}$  = 21.0 min; MS (EI):  $m/z$  = 203 ([ $\text{M}]^+$ , 35), 160 (100), 106 (20), 77 (21).

HRMS (ESI):  $m/z$  calcd for  $\text{C}_{14}\text{H}_{22}\text{N}$  204.1747 [ $\text{M}+\text{H}]^+$ , found: 204.1749 (1 ppm).

**N-Cyclohexyl-N-phenylaniline (32):**

**32** was obtained in 55% yield (70.3 mg, 0.28 mmol) after purification by column chromatography. The spectral data match those found in the literature.<sup>[2]</sup>

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.32–7.24 (m, 4H), 7.00 (tt,  $J$  = 7.4, 1.2 Hz, 2H), 6.87–6.83 (m, 4H), 3.85 (tt,  $J$  = 11.6, 3.4 Hz, 1H), 2.09–1.98 (m, 2H), 1.85–1.76 (m, 2H), 1.70–1.60 (m, 1H), 1.41 (qt,  $J$  = 13.2, 3.5 Hz, 2H), 1.22–0.96 (m, 3H) ppm.

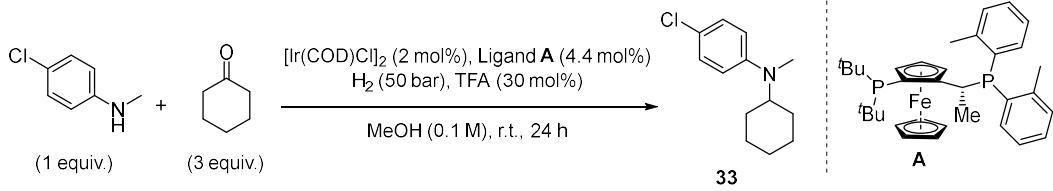
## SUPPORTING INFORMATION

$^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 146.50, 129.25, 122.90, 121.62, 56.78, 31.91, 26.34, 25.92 ppm.

GC:  $t_{\text{R}}$  = 27.9 min; MS (EI):  $m/z$  = 251 ([M] $^+$ , 60), 208 (100), 169 (23).

HRMS (ESI):  $m/z$  calcd for  $\text{C}_{18}\text{H}_{22}\text{N}$  252.1747 [M+H] $^+$ , found: 252.1751 (2 ppm).

**4-Bromo-N-cyclohexyl-N-methylaniline (33):**



33 was obtained in 48% yield (53.7 mg, 0.24 mmol) after purification by column chromatography. The spectral data match those found in the literature.<sup>[3]</sup>

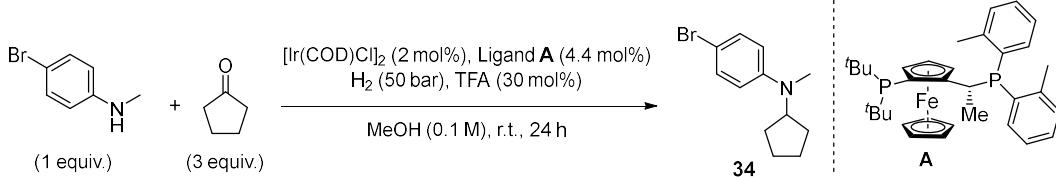
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.18–7.12 (m, 2H), 6.71–6.65 (m, 2H), 3.49 (tt,  $J$  = 11.4, 3.5 Hz, 1H), 2.74 (s, 3H), 1.86–1.83 (m, 2H), 1.78–1.74 (m, 2H), 1.71–1.67 (m, 1H), 1.47–1.31 (m, 4H), 1.15 (tt,  $J$  = 12.6, 3.7 Hz, 1H) ppm.

$^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 128.95, 114.40, 58.55, 31.41, 30.10, 26.30, 26.01 ppm.

GC:  $t_{\text{R}}$  = 23.9 min; MS (EI):  $m/z$  = 223 ([M] $^+$ , 40), 180 (100), 144 (29).

HRMS (ESI):  $m/z$  calcd for  $\text{C}_{13}\text{H}_{19}\text{N}^{35}\text{Cl}$  224.1201 [M+H] $^+$ , found: 224.1199 (1 ppm).

**4-Bromo-N-cyclopentyl-N-methylaniline (34):**



34 was obtained in 93% yield (119.5 mg, 0.47 mmol) after purification by column chromatography.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.33–7.27 (m, 2H), 6.71–6.66 (m, 2H), 4.11 (p,  $J$  = 7.8 Hz, 1H), 2.76 (s, 3H), 1.92–1.83 (m, 2H), 1.77–1.67 (m, 2H), 1.67–1.54 (m, 4H) ppm.

$^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 149.98, 131.67, 115.40, 108.38, 60.29, 32.42, 28.69, 24.32 ppm.

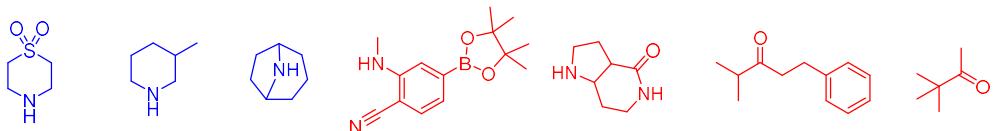
GC:  $t_{\text{R}}$  = 23.8 min; MS (EI):  $m/z$  = 253 ([M] $^+$ , 51), 224 (100), 144 (91).

HRMS (ESI):  $m/z$  calcd for  $\text{C}_{12}\text{H}_{17}\text{N}^{79}\text{Br}$  254.0539 [M+H] $^+$ , found: 254.0543 (2 ppm).

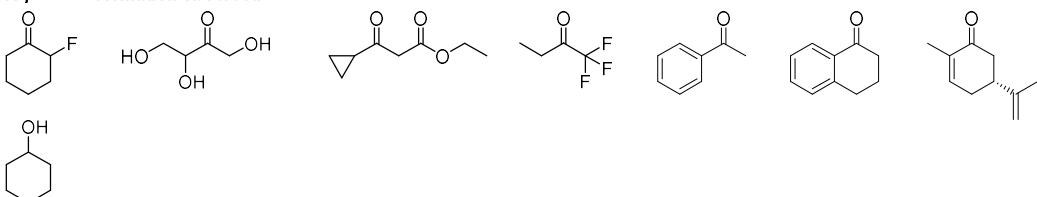
## SUPPORTING INFORMATION

**6. Extended substrate scope.**

*Product detected: Blue >20%, Red <20%*

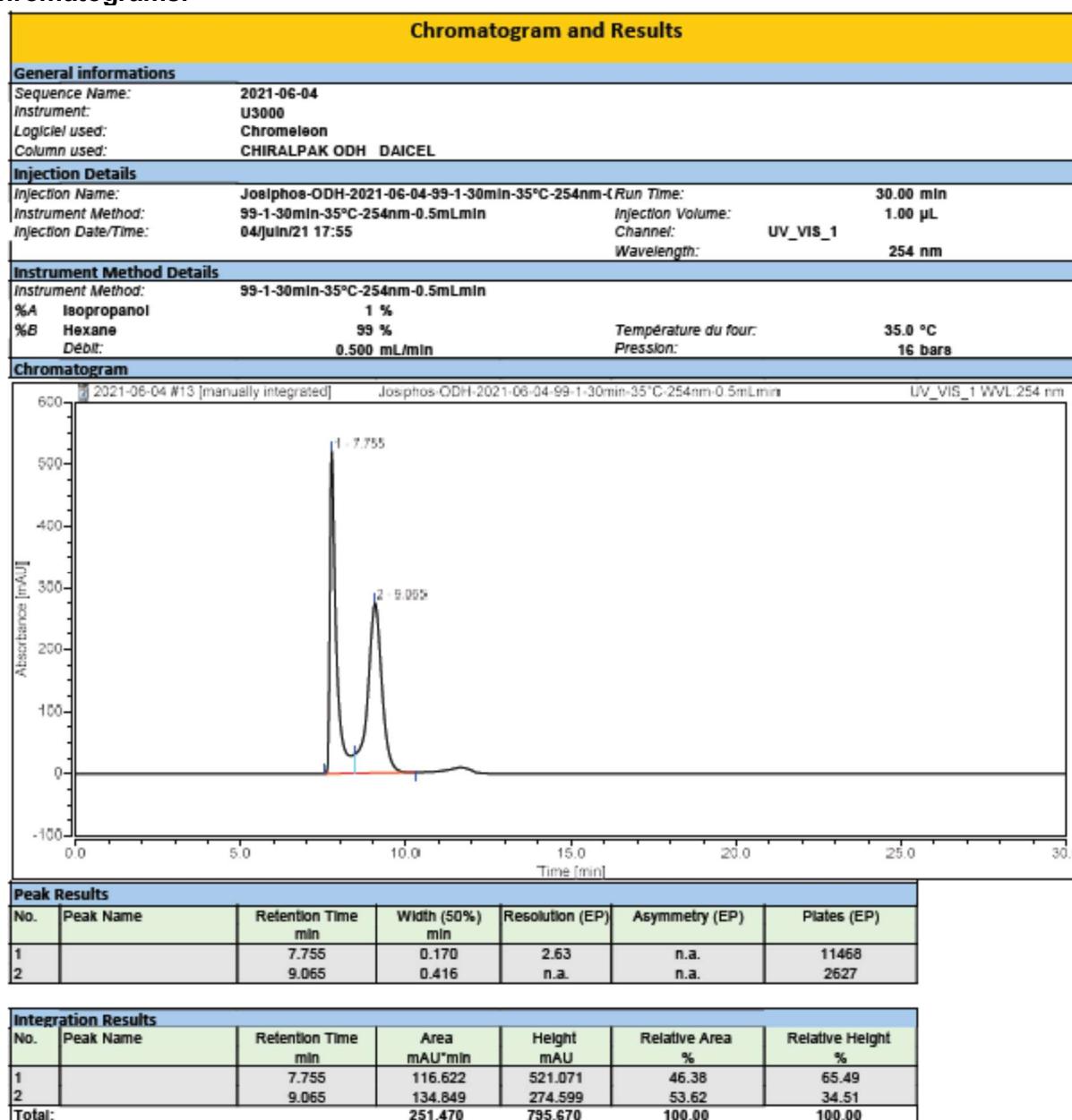


*No product formation observed*



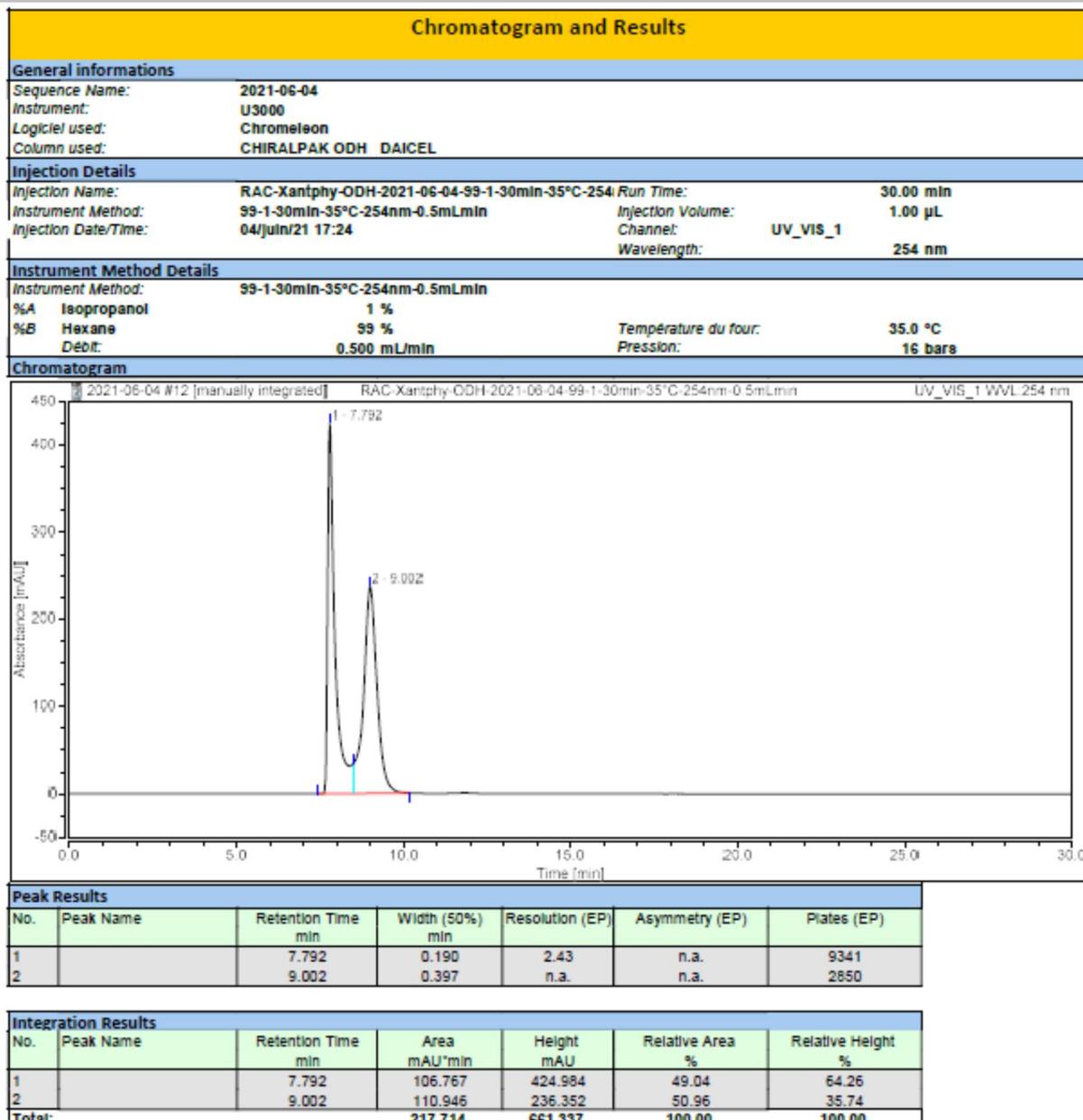
## SUPPORTING INFORMATION

## 7. Chromatograms.



HPLC chromatogram corresponding to product **2** obtained from Table 1, entry 1 (main text) – 8% ee.

## SUPPORTING INFORMATION



HPLC chromatogram corresponding to product **2** obtained from Table 1, entry 2 (main text) – racemic.

## SUPPORTING INFORMATION

Chromatogram and Results											
General informations											
Sequence Name:		2021-07-23									
Instrument:		U3000									
Logiciel used:		Chromeleon									
Column used:		CHIRALPAK ODH DAICEL									
Injection Details											
Injection Name:		Josiphos-ODH-2021-07-23-99-1-30min-35°C-254nm-(Run Time:									
Instrument Method:		99-1-30min-35°C-254nm-0.5mLmin									
Injection Date/Time:		23/juil./21 11:46									
Injection Volume:		1.00 µL									
Channel:		UV_VIS_1									
Wavelength:		254 nm									
Instrument Method Details											
Instrument Method:		99-1-30min-35°C-254nm-0.5mLmin									
%A Isopropanol		1 %									
%B Hexane		99 %									
Débit:		0.500 mL/min									
Température du four:		35.0 °C									
Pression:		17 bars									
Chromatogram											
Peak Results											
No.	Peak Name	Retention Time min	Width (50%) min	Resolution (EP)	Asymmetry (EP)	Plates (EP)					
1		7.257	0.116	2.81	n.a.	21772					
2		8.645	0.467	n.a.	n.a.	1901					
Integration Results											
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %					
1		7.257	33.460	171.274	40.21	64.74					
2		8.645	49.754	93.262	59.79	35.26					
Total:			83.214	264.536	100.00	100.00					

HPLC chromatogram corresponding to product **2** obtained from Table 1, entry 3 (main text) – 20% ee.

## SUPPORTING INFORMATION

Chromatogram and Results						
General informations						
Sequence Name:	2021-07-23					
Instrument:	U3000					
Logiciel used:	Chromeleon					
Column used:	CHIRALPAK ODH DAICEL					
Injection Details						
Injection Name:	MeO BiBOP-ODH-2021-07-24-99-1-30min-35°C-254nm	Run Time:	30.00 min			
Instrument Method:	99-1-30min-35°C-254nm-0.5mLmin	Injection Volume:	1.00 µL			
Injection Date/Time:	23/juil./21 11:15	Channel:	UV_VIS_1			
		Wavelength:	254 nm			
Instrument Method Details						
Instrument Method:	99-1-30min-35°C-254nm-0.5mLmin					
%A Isopropanol	1 %					
%B Hexane	99 %	Température du four:	35.0 °C			
Débit:	0.500 mL/min	Pression:	17 bars			
Chromatogram						
Peak Results						
No.	Peak Name	Retention Time min	Width (50%) min	Resolution (EP)	Asymmetry (EP)	Plates (EP)
1		7.263	0.113	2.80	n.a.	22970
2		8.552	0.431	n.a.	n.a.	2183
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		7.263	79.053	433.722	42.46	66.29
2		8.552	107.126	220.590	57.54	33.71
Total:			186.180	654.312	100.00	100.00

HPLC chromatogram corresponding to product **2** obtained from Table 1, entry 4 (main text) – 15% ee.

## SUPPORTING INFORMATION

NotebookID: mjouffro\_537\_6

Analyst: jdasdore

Method: IG\_MeOH\_column\_coupling (see details below for more info)

Conclusion: N/A

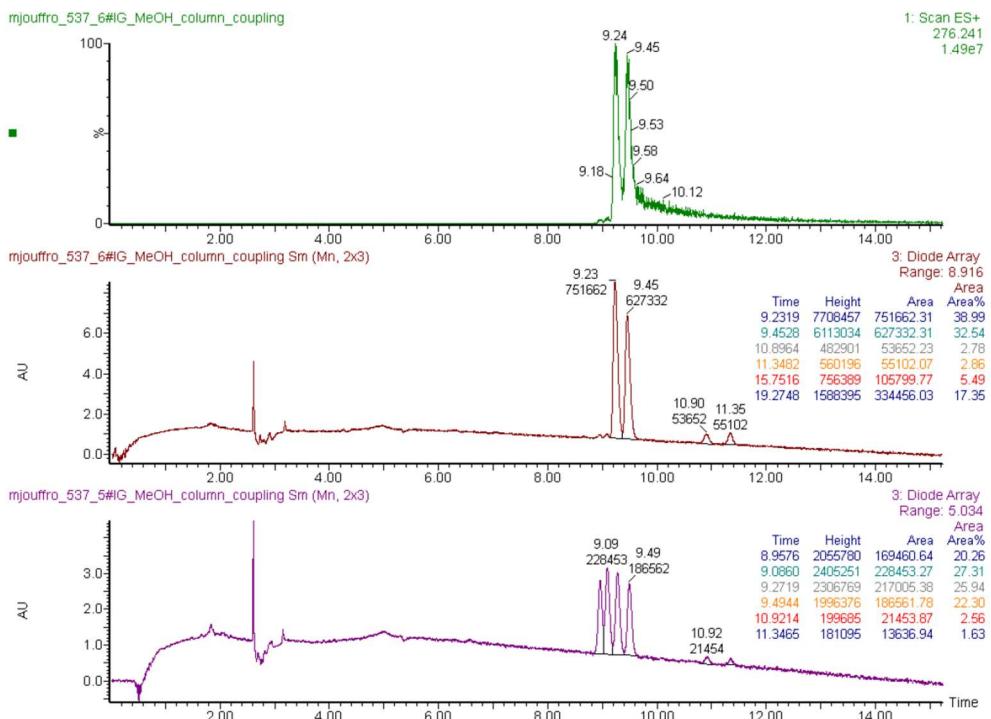
Date: 28/11/2021

Remark: (Rt 8.96 min MS traces of isomer 1), (Rt 9.09 min MS traces of isomer 2), (Rt 9.23 min 38.99% isomer 3), (Rt 9.45 min 32.54% isomer 4).

Retention times of isomer 3 and 4 match with retention times of isomer 3 and isomer 4 of mjouffro\_537\_5

## Conclusion/Chromatogram/spectra

Rt (9.23 min)	UV: 38.99%	isomer 3	MW 275
Rt (9.45 min)	UV: 32.54%	isomer 4	MW 275
Rt (8.96 min)	UV: MS traces	isomer 1	MW 275
Rt (9.09 min)	UV: MS traces	isomer 2	MW 275



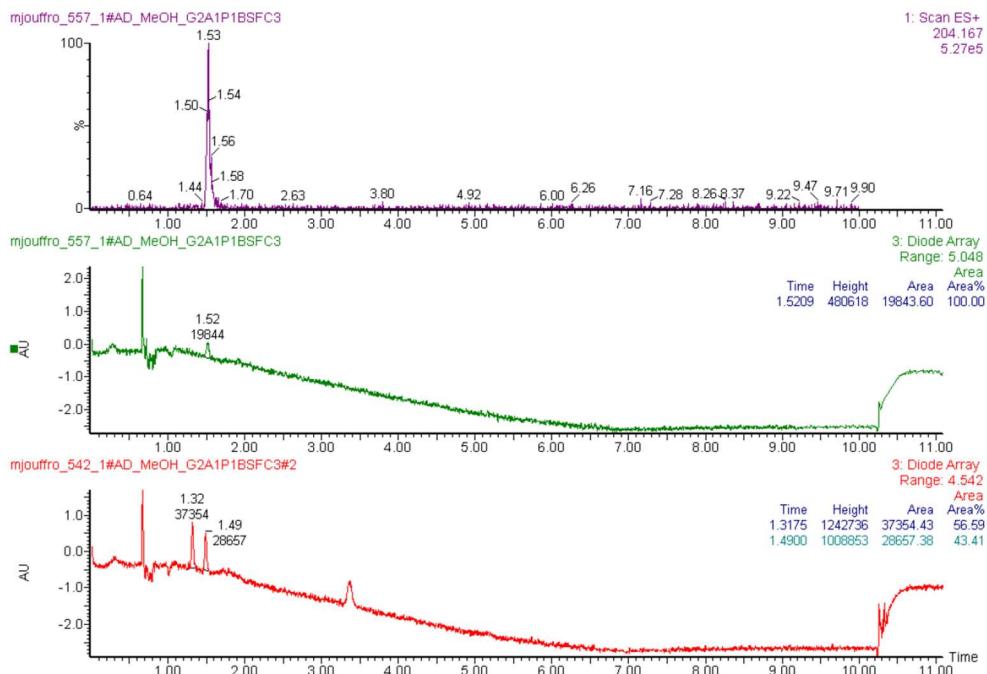
SFC chromatogram corresponding to product **30**. Comparison of chiral SFC spectra of **30** (top, MS spectra; middle, SFC spectra) and mixture of enantiomers obtained from racemic 3-(ethoxycarbonyl)pyrrolidine (bottom).

## SUPPORTING INFORMATION

NotebookID: mjouffro\_557\_1  
Analyst: kraeyma2  
Method: AD\_MeOH\_G2A1P1BSFC3  
Conclusion: N/A  
Date: 30/11/2021  
Remark: (Rt 1.32min 0.00% isomer 1), (Rt 1.52min 100.00% isomer 2)

## Conclusion/Chromatogram/spectra

Rt (1.52 min)	UV: 100.00 %	isomer 2	MW 203
Rt (1.32 min)	UV: 0.00 %	isomer 1	MW 203

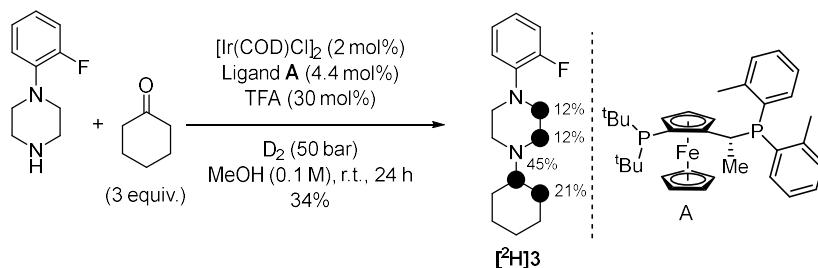


SFC chromatogram corresponding to product **31**. Comparison of chiral SFC spectra of **31** (top, MS spectra; middle, SFC spectra) and mixture of enantiomers obtained from racemic 1-phenylethan-1-amine (bottom).

## SUPPORTING INFORMATION

## 8. Deuteration experiments.

## 8.1. Using deuterium gas



The general procedure of the iridium-catalyzed direct reductive amination was used in this transformation and hydrogen ( $\text{H}_2$ ) was replaced by deuterium ( $\text{D}_2$ ). We observed the formation of the targeted species, though the conversion was significantly reduced compared to the original conditions (34% vs 80%). The isolated product consists of an inseparable mixture of mono-, bis-, and tris-deuterated species according to the MS pattern (**SI-1 to 3**). The formation of these species could result from the metal catalyzed deuteration of the proposed iminium (**SI-1**) or enamine (**SI-2**). This deuterium incorporation could also be explained by the keto-enol equilibrium of cyclohexanone where a proton is exchanged with a deuterium present in the reaction media prior to the DRA reaction, therefore a background reaction was ran using  $\text{H}_2$  in MeOH-d4 (see 8.2).

Deuterium incorporation: 2.10 D/molecule (<sup>1</sup>H-NMR)<sup>[4]</sup>

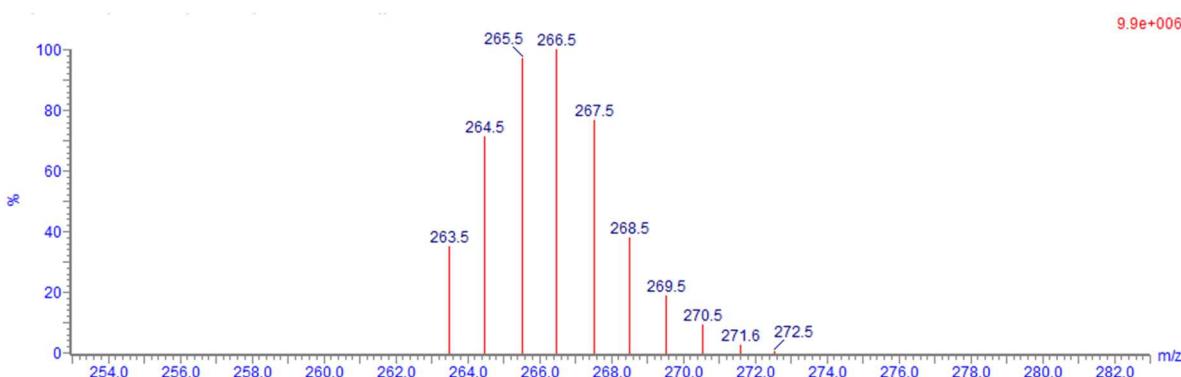
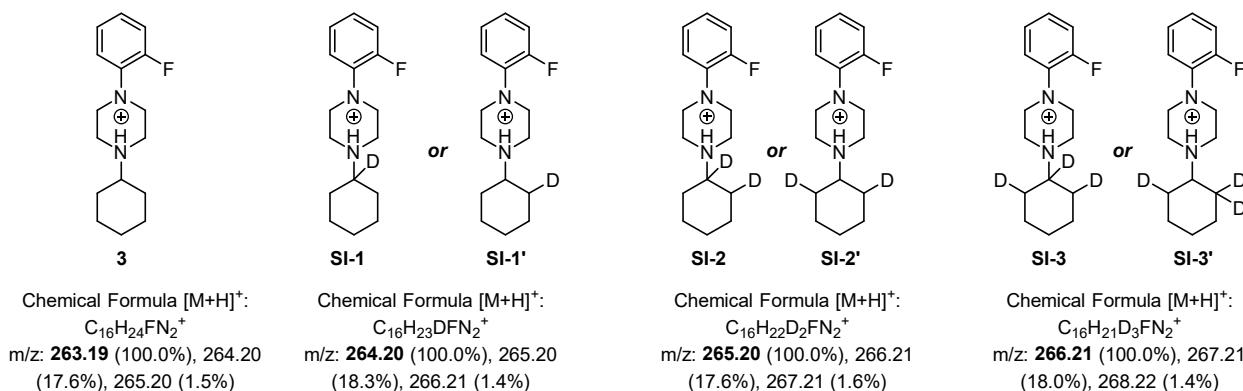


Figure S1. MS spectra of the mixture of deuterated species after basic work up and purification.

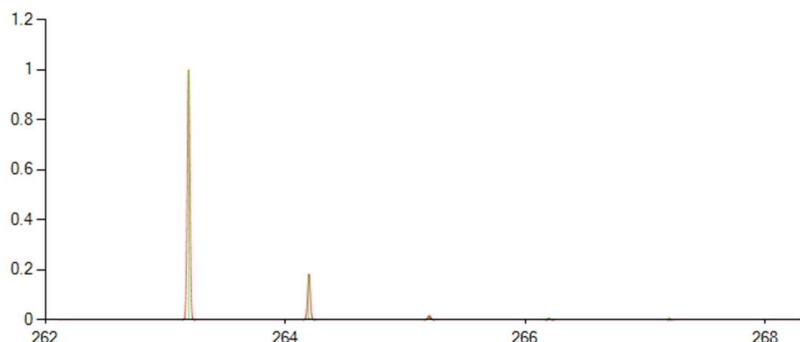
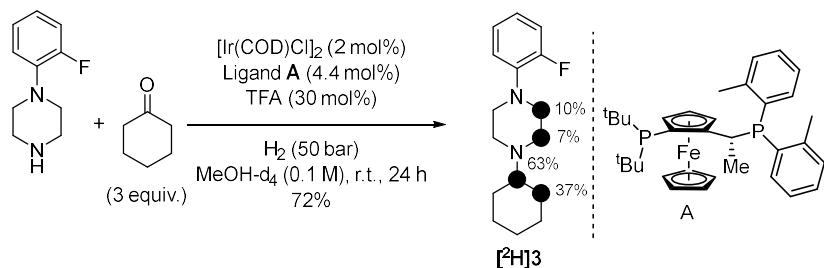


Figure S2. Simulated MS spectra of unlabeled **3**.

## SUPPORTING INFORMATION

## 8.2. Using hydrogen gas in deuterated MeOH



The general procedure of the iridium-catalyzed direct reductive amination was used in this transformation and deuterated MeOH ( $\text{MeOH-d}_4$ ) was used instead of MeOH. We observed the formation of the targeted species with yield similar to the standard reaction (72% vs 80%). The product distribution appears to be different than the previous experiment with a significantly higher amount of mono-deuterated species (**SI-1**), decreased amount of bis-deuterated species (**SI-2**) and a significantly decreased amount of tris-deuterated (**SI-3**) according to the MS pattern. As mentioned above, the formation of these species could be explained by the keto-enol equilibrium of cyclohexanone where a proton is exchanged with a deuterium from the solvent.

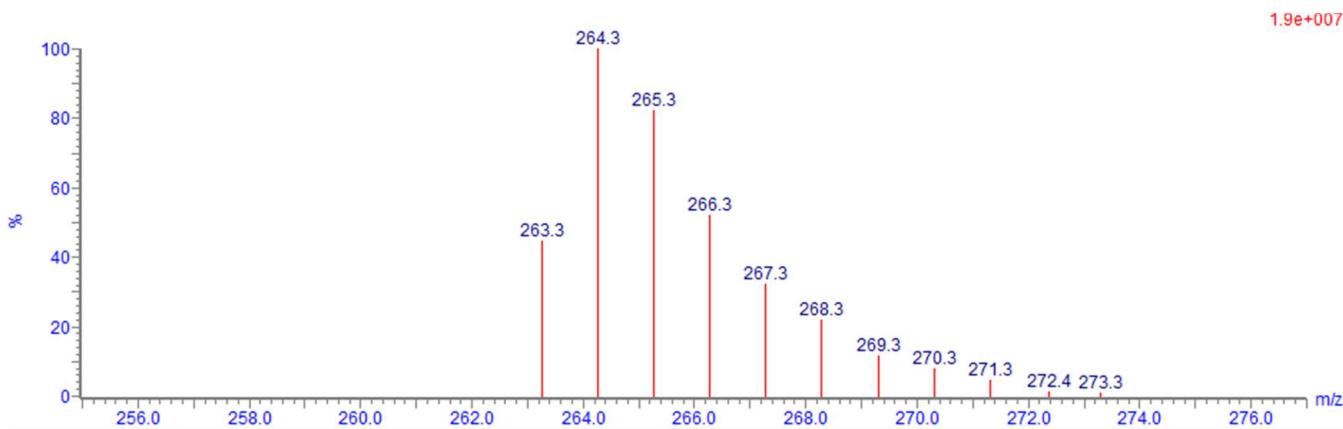
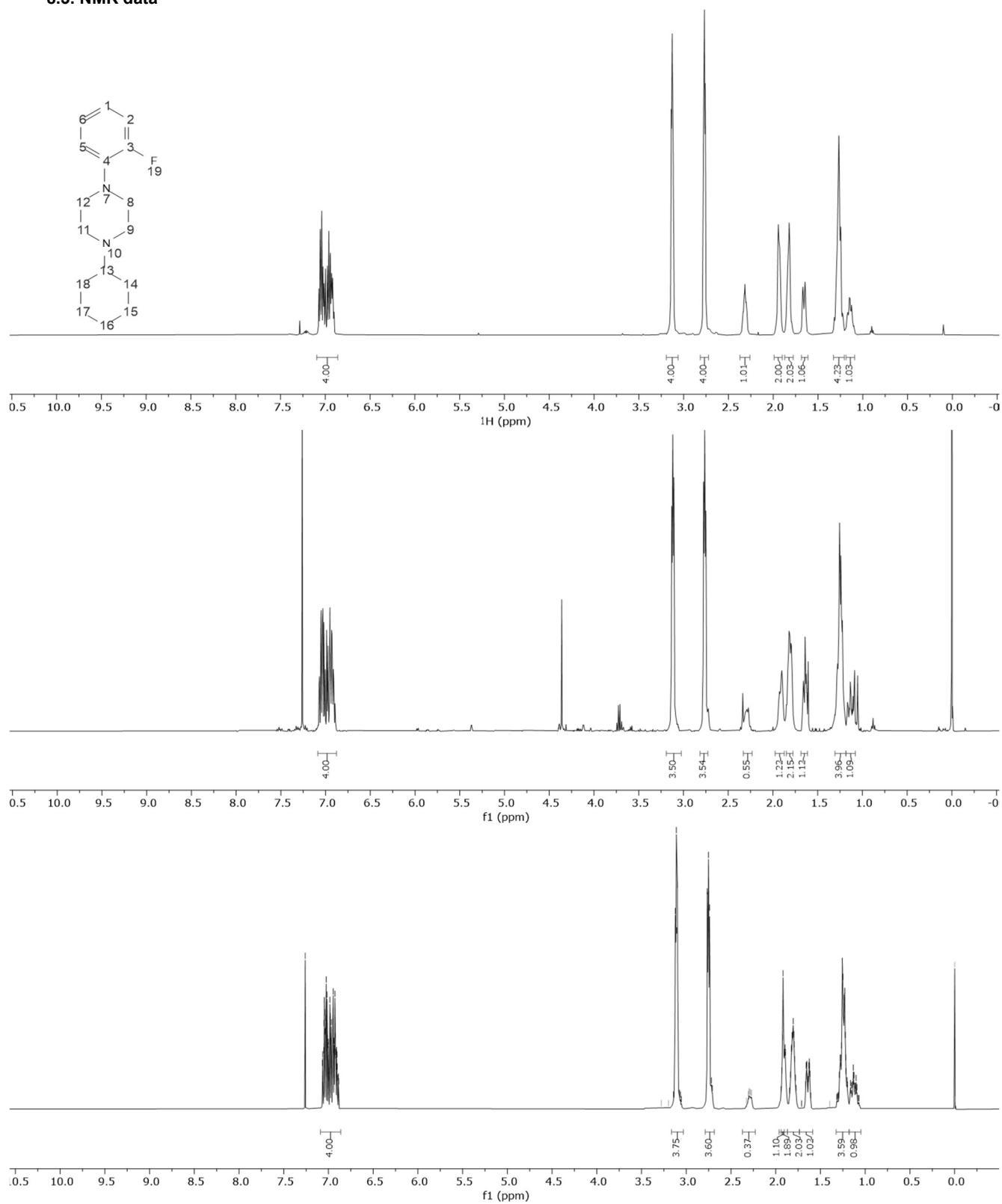


Figure S3. MS spectra of the mixture of deuterated species after basic work up and purification.

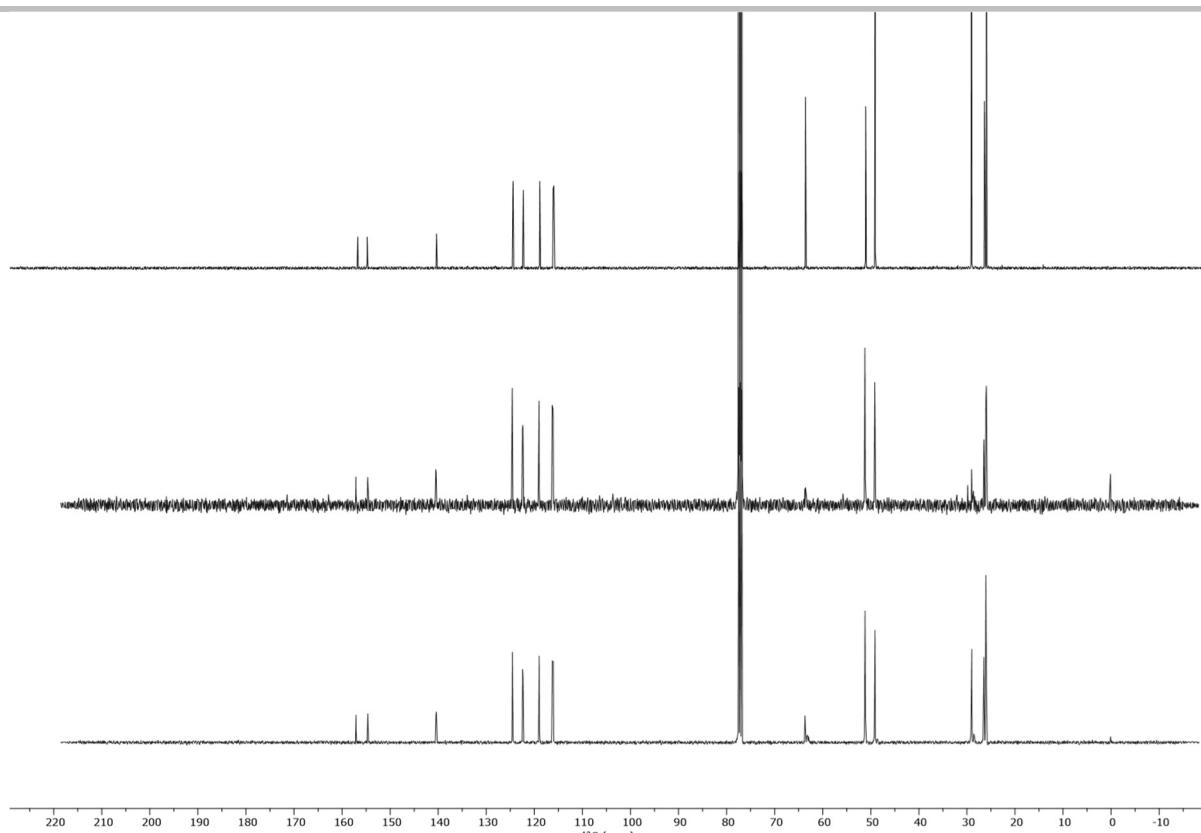
## SUPPORTING INFORMATION

## 8.3. NMR data

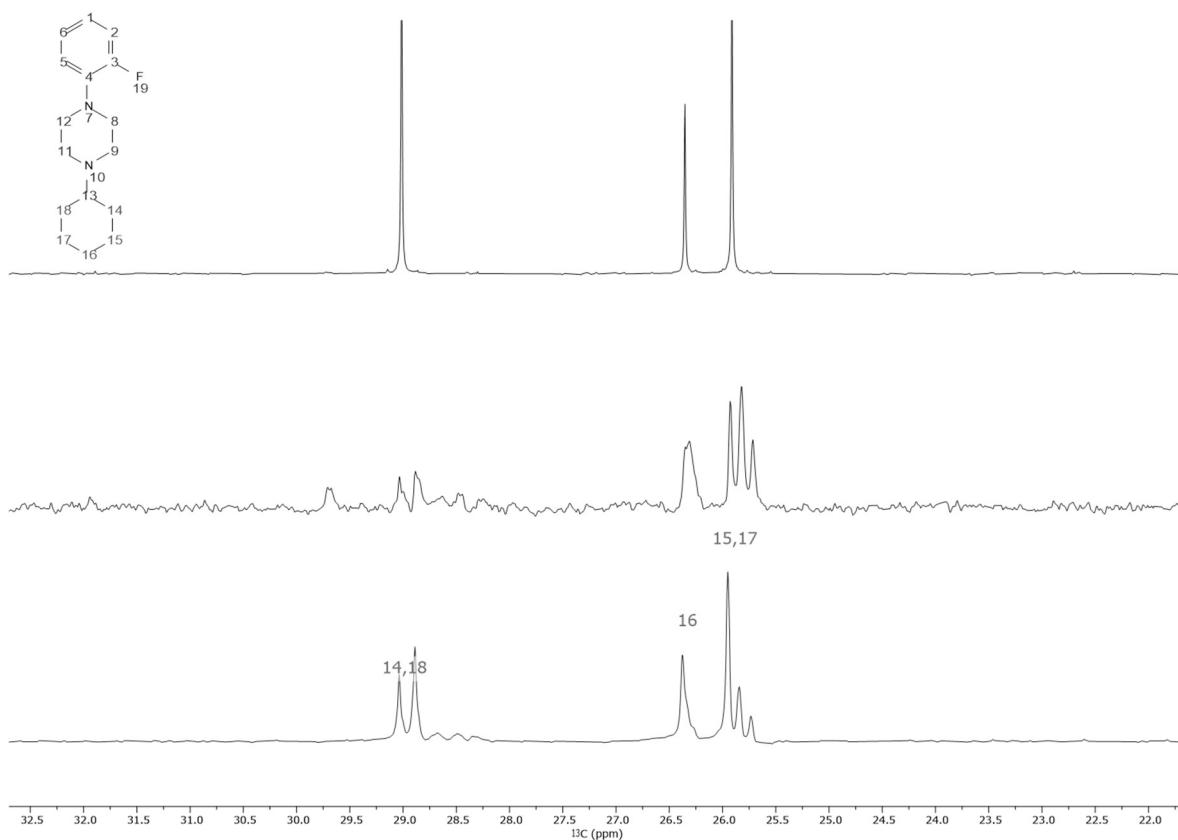


**Figure S4.**  $^1\text{H}$  NMR comparison of 3,  $[{}^2\text{H}] 3$  obtained using  $\text{D}_2$  and  $[{}^2\text{H}] 3$  obtained using  $\text{H}_2$  in  $\text{MeOH-d}_4$ .

## SUPPORTING INFORMATION



**Figure S5.**  $^{13}\text{C}\{^1\text{H}\}$  NMR comparison of **3** (top),  $[^2\text{H}]$  **3** obtained using  $\text{D}_2$  and  $[^2\text{H}]$  **3** obtained using  $\text{H}_2$  in  $\text{MeOH-d}_4$ .



**Figure S6.** Zoom of aliphatic region of  $^{13}\text{C}\{^1\text{H}\}$  NMR comparison.

## SUPPORTING INFORMATION

### 8.4. Conclusion on deuterium experiments

The formation of predominant species like **SI-1** and **SI-2** in the DRA experiment using D<sub>2</sub> suggests the presence of two distinct mechanism for the hydrogenation, one going through the direct hydrogenation of the iminium species, the other via the hydrogenation of the corresponding enamine. Unfortunately, because of the strong background reaction observed when attempting the reported DRA in MeOH-d<sub>4</sub>, an unequivocal conclusion on the hydrogenation mechanism could not be drawn at this stage. The difference of product distribution between the two transformations could be seen in the MS spectra but also in <sup>13</sup>C NMR (Figure S6) where a superior amount of multiplicity is observed when using D<sub>2</sub>.

**SUPPORTING INFORMATION****9. X-ray crystallography data of 1-TFA (CCDC-2129684).**

(C<sub>10</sub>H<sub>14</sub>FN<sub>2</sub> · C<sub>2</sub>F<sub>3</sub>O<sub>2</sub>);  $M = 294.25$ . A suitable crystal for X-ray diffraction single crystal experiment (colourless prism, dimensions = 0.580 x 0.350 x 0.200 mm) was selected and mounted with a cryoloop on the goniometer head of a APEXII Kappa-CCD (Bruker AXS) diffractometer equipped with a CCD plate detector, using Mo-K <sub>$\alpha$</sub>  radiation ( $\lambda = 0.71073 \text{ \AA}$ , multilayer monochromator) at T = 150(2) K. Crystal structure has been described in triclinic symmetry and P 1 (I.T.#2) centric space group. Cell parameters have been refined as follows:  $a = 5.9498(10)$ ,  $b = 9.4209(18)$ ,  $c = 13.185(2) \text{ \AA}$ ,  $\alpha = 108.898(6)$ ,  $\beta = 95.618(5)$ ,  $\gamma = 104.332(6)^\circ$ ,  $V = 664.5(2) \text{ \AA}^3$ . Number of formula unit Z is equal to 2 and calculated density  $d$  and absorption coefficient  $\mu$  values are 1.471 g.cm<sup>-3</sup> and 0.138 mm<sup>-1</sup> respectively. Crystal structure was solved by dual-space algorithm using *SHELXT* program,<sup>[1]</sup> and then refined with full-matrix least-squares methods based on  $P^2$  (*SHELXL* program).<sup>[2]</sup> All non-Hydrogen atoms were refined with anisotropic atomic displacement parameters. Except Hydrogen atoms linked to Nitrogen atom that were introduced in the structural model through Fourier difference maps analysis, H atoms were finally included in their calculated positions and treated as riding on their parent atom with constrained thermal parameters. A final refinement on  $F^2$  with 3007 unique intensities and 187 parameters converged at  $\omega R(F^2) = 0.1419$  ( $R_F = 0.0506$ ) for 2261 observed reflections with ( $I > 2\sigma$ ).

[1] G. M. Sheldrick, *Acta Cryst.* **2015**, A71, 3-8.

[2] G. M. Sheldrick, *Acta Cryst.* **2015**, C71, 3-8.

**Data collection strategy details.**

Software : BIS 2014.5.0.0/23-May-2014 && APEX2\_2014.11-0

Number of scans : 3

Total number of frames : 570

Total length of scans : 570.00 (deg.)

Rotation speed : 5.00 sec./deg.

Total exposition time : 47.5 min.

Scan	Time(s)	Width	DX(mm)	Frames	Range	2Theta	Omega	Phi	Chi	T(K)
1 Omega	5.0	1.00	35.0	105	105.0	14.9	14.5	0.0	305.3	296.1
2 Phi	5.0	1.00	35.0	360	360.0	14.9	10.4	360.0	337.0	296.1
3 Omega	5.0	1.00	35.0	105	105.0	14.9	14.5	120.0	305.3	296.1

## SUPPORTING INFORMATION

## Structural data.

## Crystal data.

Empirical formula	C <sub>12</sub> H <sub>14</sub> F <sub>4</sub> N <sub>2</sub> O <sub>2</sub>
Extended formula	C <sub>10</sub> H <sub>14</sub> FN <sub>2</sub> , C <sub>2</sub> F <sub>3</sub> O <sub>2</sub>
Formula weight	294.25 g/mol
Temperature	150(2) K
Radiation type	Mo-K <sub>α</sub>
Wavelength	0.71073 Å
Crystal system, space group	triclinic, P1
Unit cell dimensions	a = 5.9498(10) Å b = 9.4209(18) Å c = 13.185(2) Å
	$\alpha$ = 108.898(6) $\beta$ = 95.618(5) $\gamma$ = 104.332(6)
Volume	664.5(2) Å <sup>3</sup>
Z, Calculated density	2, 1.471 g.cm <sup>-3</sup>
Absorption coefficient	0.138 mm <sup>-1</sup>
F(000)	304
Crystal size	0.580 x 0.350 x 0.200 mm
Crystal color	colourless
Crystal description	prism

## Data collection

Diffractometer	APEXII Kappa-CCD (Bruker-AXS)
$\vartheta$ range for data collection	2.371 to 27.541
(sin $\vartheta$ /λ) <sub>max</sub> (Å <sup>-1</sup> )	0.651
h <sub>min</sub> , h <sub>max</sub>	-7, 5
k <sub>min</sub> , k <sub>max</sub>	-12, 12
l <sub>min</sub> , l <sub>max</sub>	-16, 17
Reflections collected / unique	9043 / 3007 [ <sup>a</sup> R(int) = 0.0350]
Reflections [ $ I  > 2\sigma$ ]	2261
Completeness to $\vartheta_{\text{max}}$	0.981
Absorption correction type	multi-scan
Max. and min. transmission	0.973, 0.892

## Refinement

Refinement method	Full-matrix least-squares on $F^2$
H-atom treatment	H-atom parameters treated by a mixture of independant and constrained refinement
Data / restraints / parameters	3007 / 0 / 187
<sup>b</sup> Goodness-of-fit	0.949
Final R indices [ $ I  > 2\sigma$ ]	<sup>c</sup> R <sub>1</sub> = 0.0506, <sup>d</sup> $\omega$ R <sub>2</sub> = 0.1419
R indices (all data)	<sup>c</sup> R <sub>1</sub> = 0.0684, <sup>d</sup> $\omega$ R <sub>2</sub> = 0.1565
$\Delta\rho_{\text{max}}, \Delta\rho_{\text{min}}$	0.714, -0.309 e.Å <sup>-3</sup>

$$^aR_{\text{int}} = \frac{\sum |F_o^2 - \langle F_o^2 \rangle|}{\sum F_o^2}$$

$$^bS = \left\{ \sum \frac{[w(F_o^2 - F_c^2)^2]}{n-p} \right\}^{1/2}$$

$$^cR_1 = \frac{\sum |F_o| - |F_c|}{\sum |F_o|}$$

$$^d\omega R_2 = \left\{ \frac{\sum [w(F_o^2 - F_c^2)^2]}{\sum [w(F_o^2)^2]} \right\}^{1/2}$$

$$w = 1./[\sigma(F_o^2) + (aP)^2 + bP] \text{ with } P = [2F_c^2 + \text{Max}(F_o^2, 0)]/3$$

## SUPPORTING INFORMATION

Fractional atomic coordinates, site occupancy (%) and equivalent isotropic displacement parameters ( $\text{\AA}^2$ ).

$U(\text{eq})$  is defined as one third of the trace of the orthogonalized  $U_{ij}$  tensor.

Atom	x	y	z	occ.	$U(\text{eq})$	adp
F1	0.4041(2)	0.90732(16)	0.58139(10)	1	0.0411(4)	Uani
C2	0.1947(3)	0.8457(2)	0.60437(15)	1	0.0260(4)	Uani
C3	0.1696(4)	0.8883(2)	0.71189(16)	1	0.0327(5)	Uani
H3	0.298887	0.958104	0.768649	1	0.039	Uiso
C4	-0.0457(4)	0.8283(2)	0.73607(17)	1	0.0342(5)	Uani
H4	-0.066317	0.857398	0.809794	1	0.041	Uiso
C5	-0.2313(4)	0.7257(3)	0.65265(17)	1	0.0343(5)	Uani
H5	-0.379180	0.683518	0.669356	1	0.041	Uiso
C6	-0.2033(3)	0.6836(2)	0.54441(16)	1	0.0287(4)	Uani
H6	-0.333221	0.613911	0.487938	1	0.034	Uiso
C7	0.0127(3)	0.7422(2)	0.51748(14)	1	0.0204(4)	Uani
N8	0.0587(3)	0.70390(17)	0.40985(11)	1	0.0192(3)	Uani
C9	-0.0958(3)	0.5553(2)	0.32879(14)	1	0.0227(4)	Uani
H9A	-0.254649	0.565511	0.309673	1	0.027	Uiso
H9B	-0.112897	0.470739	0.359178	1	0.027	Uiso
C10	0.0123(3)	0.5152(2)	0.22819(14)	1	0.0234(4)	Uani
H10A	0.169668	0.502903	0.247338	1	0.028	Uiso
H10B	-0.089314	0.414464	0.172768	1	0.028	Uiso
N11	0.0366(3)	0.64221(19)	0.18253(12)	1	0.0215(3)	Uani
H11A	-0.105(4)	0.651(3)	0.1580(18)	1	0.026	Uiso
H11B	0.107(4)	0.621(3)	0.1214(19)	1	0.026	Uiso
C12	0.1796(3)	0.7974(2)	0.26532(15)	1	0.0238(4)	Uani
H12A	0.181451	0.880859	0.234873	1	0.029	Uiso
H12B	0.344615	0.796610	0.283400	1	0.029	Uiso
C13	0.0758(3)	0.8318(2)	0.36792(15)	1	0.0227(4)	Uani
H13A	0.177308	0.931868	0.424121	1	0.027	Uiso
H13B	-0.083334	0.843193	0.351363	1	0.027	Uiso
C21	0.4971(3)	0.6833(2)	0.05318(15)	1	0.0218(4)	Uani
O22	0.2835(2)	0.6238(2)	0.01474(11)	1	0.0368(4)	Uani
O23	0.6073(2)	0.70125(19)	0.14310(11)	1	0.0339(4)	Uani
C24	0.6451(3)	0.7519(2)	-0.01943(16)	1	0.0277(4)	Uani
F25	0.8673(2)	0.7496(2)	-0.00400(14)	1	0.0616(5)	Uani
F26	0.6562(4)	0.90122(19)	0.00355(15)	1	0.0699(5)	Uani
F27	0.5612(3)	0.6773(2)	-0.12503(11)	1	0.0633(5)	Uani

Anisotropic displacement parameters ( $\text{\AA}^2$ )

The anisotropic displacement factor exponent takes the form:  $-2\pi[h^2a^{*2}U_{11} + \dots + 2hka^*b^*U_{12}]$

Atom	U11	U22	U33	U23	U13	U12
F1	0.0319(7)	0.0467(8)	0.0297(7)	0.0083(6)	0.0026(5)	-0.0059(6)
C2	0.0303(10)	0.0225(9)	0.0223(9)	0.0076(8)	0.0063(8)	0.0031(8)
C3	0.0517(13)	0.0209(10)	0.0178(9)	0.0030(8)	0.0024(9)	0.0046(9)
C4	0.0593(14)	0.0284(11)	0.0212(9)	0.0108(8)	0.0178(9)	0.0177(10)
C5	0.0392(12)	0.0415(13)	0.0312(11)	0.0184(10)	0.0192(9)	0.0159(10)
C6	0.0263(10)	0.0353(11)	0.0246(10)	0.0124(8)	0.0063(8)	0.0067(8)
C7	0.0268(9)	0.0190(9)	0.0185(9)	0.0088(7)	0.0068(7)	0.0086(7)
N8	0.0216(7)	0.0189(8)	0.0148(7)	0.0047(6)	0.0039(6)	0.0037(6)
C9	0.0246(9)	0.0214(9)	0.0193(9)	0.0066(7)	0.0042(7)	0.0031(7)
C10	0.0271(9)	0.0226(9)	0.0171(9)	0.0044(7)	0.0036(7)	0.0053(7)
N11	0.0190(7)	0.0292(9)	0.0161(7)	0.0075(6)	0.0045(6)	0.0073(6)
C12	0.0250(9)	0.0246(10)	0.0215(9)	0.0091(7)	0.0080(7)	0.0048(8)
C13	0.0271(9)	0.0209(9)	0.0212(9)	0.0081(7)	0.0085(7)	0.0070(7)
C21	0.0225(9)	0.0217(9)	0.0198(9)	0.0034(7)	0.0070(7)	0.0086(7)
O22	0.0206(7)	0.0594(11)	0.0199(7)	0.0091(7)	0.0040(5)	0.0004(7)
O23	0.0259(7)	0.0571(10)	0.0243(7)	0.0167(7)	0.0069(6)	0.0187(7)
C24	0.0240(10)	0.0326(11)	0.0250(10)	0.0093(8)	0.0057(7)	0.0069(8)
F25	0.0282(7)	0.1082(14)	0.0757(11)	0.0611(11)	0.0260(7)	0.0242(8)
F26	0.1095(14)	0.0432(9)	0.0823(13)	0.0387(9)	0.0533(11)	0.0319(9)
F27	0.0496(9)	0.0954(13)	0.0215(7)	0.0149(7)	0.0110(6)	-0.0125(8)

**SUPPORTING INFORMATION****Bond length [Å]**

F1 - C2 = 1.346(2)  
 C2 - C3 = 1.377(3)  
 C2 - C7 = 1.395(3)  
 C3 - C4 = 1.378(3)  
 C3 - H3 = 0.9500  
 C4 - C5 = 1.382(3)  
 C4 - H4 = 0.9500  
 C5 - C6 = 1.391(3)  
 C5 - H5 = 0.9500  
 C6 - C7 = 1.395(3)  
 C6 - H6 = 0.9500  
 C7 - N8 = 1.419(2)  
 N8 - C9 = 1.466(2)  
 N8 - C13 = 1.467(2)  
 C9 - C10 = 1.509(2)  
 C9 - H9A = 0.9900  
 C9 - H9B = 0.9900  
 C10 - N11 = 1.488(3)  
 C10 - H10A = 0.9900  
 C10 - H10B = 0.9900  
 N11 - C12 = 1.491(2)  
 N11 - H11A = 0.91(2)  
 N11 - H11B = 0.93(2)  
 C12 - C13 = 1.515(2)  
 C12 - H12A = 0.9900  
 C12 - H12B = 0.9900  
 C13 - H13A = 0.9900  
 C13 - H13B = 0.9900  
 C21 - O22 = 1.234(2)  
 C21 - O23 = 1.236(2)  
 C21 - C24 = 1.547(3)  
 C24 - F26 = 1.323(3)  
 C24 - F27 = 1.318(2)  
 C24 - F25 = 1.324(2)

**Angles [°]**

F1 - C2 - C3 = 118.70(17)  
 F1 - C2 - C7 = 118.11(16)  
 C3 - C2 - C7 = 123.20(19)  
 C2 - C3 - C4 = 119.12(19)  
 C2 - C3 - H3 = 120.4  
 C4 - C3 - H3 = 120.4  
 C3 - C4 - C5 = 119.72(19)  
 C3 - C4 - H4 = 120.1  
 C5 - C4 - H4 = 120.1  
 C4 - C5 - C6 = 120.5(2)  
 C4 - C5 - H5 = 119.7  
 C6 - C5 - H5 = 119.7  
 C5 - C6 - C7 = 121.02(19)  
 C5 - C6 - H6 = 119.5  
 C7 - C6 - H6 = 119.5  
 C6 - C7 - C2 = 116.41(17)  
 C6 - C7 - N8 = 124.96(17)  
 C2 - C7 - N8 = 118.64(16)  
 C7 - N8 - C9 = 116.12(14)  
 C7 - N8 - C13 = 113.31(14)  
 C9 - N8 - C13 = 110.51(14)  
 N8 - C9 - C10 = 108.67(15)  
 N8 - C9 - H9A = 110.0  
 C10 - C9 - H9A = 110.0  
 N8 - C9 - H9B = 110.0  
 C10 - C9 - H9B = 110.0  
 H9A - C9 - H9B = 108.3  
 N11 - C10 - C9 = 109.76(15)  
 N11 - C10 - H10A = 109.7  
 C9 - C10 - H10A = 109.7  
 N11 - C10 - H10B = 109.7  
 C9 - C10 - H10B = 109.7

**SUPPORTING INFORMATION**

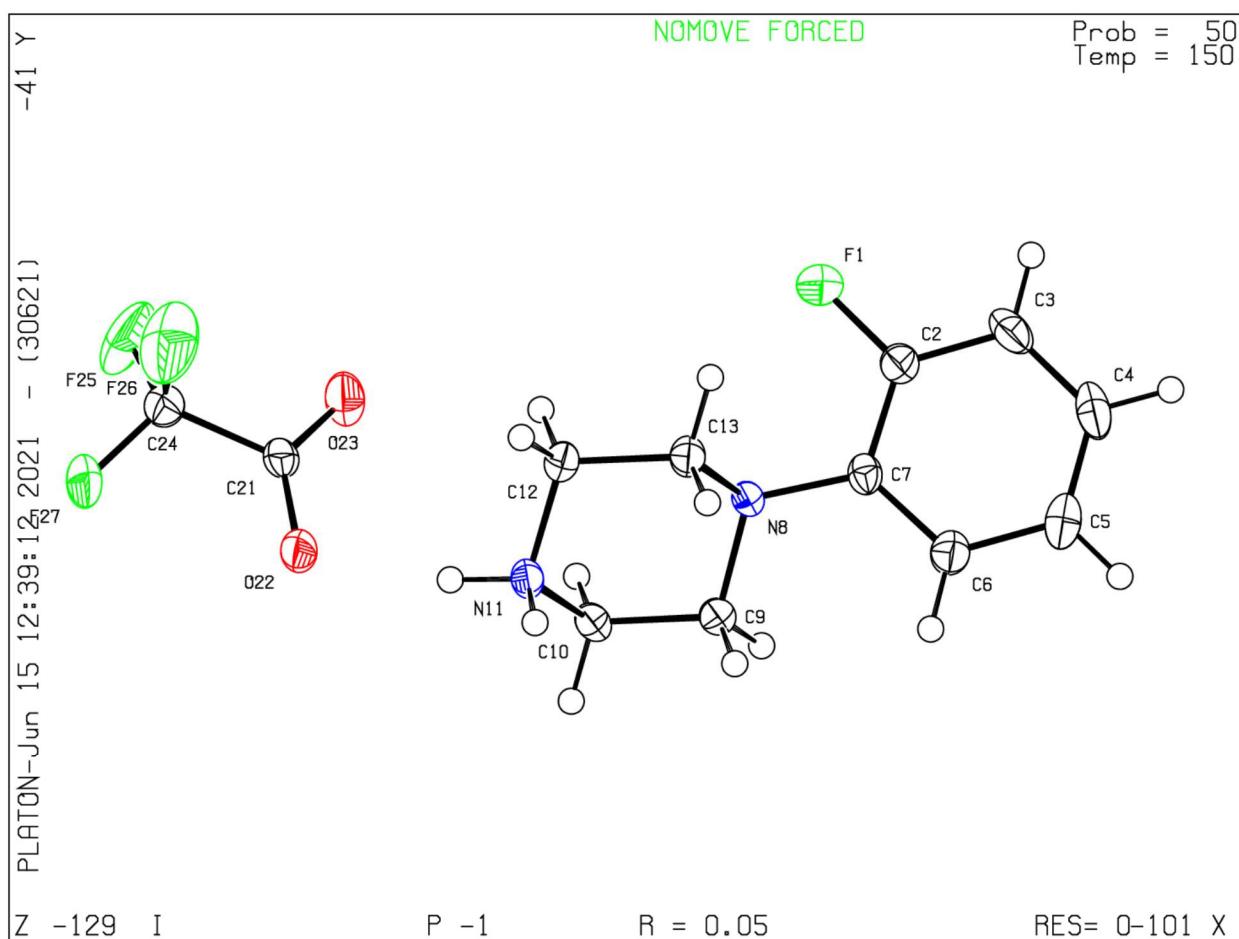
H10A - C10 - H10B = 108.2  
 C10 - N11 - C12 = 111.37(14)  
 C10 - N11 - H11A = 112.3(14)  
 C12 - N11 - H11A = 108.3(14)  
 C10 - N11 - H11B = 111.2(14)  
 C12 - N11 - H11B = 108.9(13)  
 H11A - N11 - H11B = 104.5(19)  
 N11 - C12 - C13 = 110.17(15)  
 N11 - C12 - H12A = 109.6  
 C13 - C12 - H12A = 109.6  
 N11 - C12 - H12B = 109.6  
 C13 - C12 - H12B = 109.6  
 H12A - C12 - H12B = 108.1  
 N8 - C13 - C12 = 110.02(15)  
 N8 - C13 - H13A = 109.7  
 C12 - C13 - H13A = 109.7  
 N8 - C13 - H13B = 109.7  
 C12 - C13 - H13B = 109.7  
 H13A - C13 - H13B = 108.2  
 O22 - C21 - O23 = 129.08(19)  
 O22 - C21 - C24 = 115.24(16)  
 O23 - C21 - C24 = 115.61(16)  
 F26 - C24 - F27 = 107.71(19)  
 F26 - C24 - F25 = 105.66(18)  
 F27 - C24 - F25 = 105.76(18)  
 F26 - C24 - C21 = 110.38(17)  
 F27 - C24 - C21 = 113.68(16)  
 F25 - C24 - C21 = 113.16(17)

**Torsion angles [°]**

F1 - C2 - C3 - C4 = 178.68(18)  
 C7 - C2 - C3 - C4 = -0.9(3)  
 C2 - C3 - C4 - C5 = 0.6(3)  
 C3 - C4 - C5 - C6 = -0.6(3)  
 C4 - C5 - C6 - C7 = 0.8(3)  
 C5 - C6 - C7 - C2 = -0.9(3)  
 C5 - C6 - C7 - N8 = 178.90(18)  
 F1 - C2 - C7 - C6 = -178.57(18)  
 C3 - C2 - C7 - C6 = 1.0(3)  
 F1 - C2 - C7 - N8 = 1.6(3)  
 C3 - C2 - C7 - N8 = -178.85(18)  
 C6 - C7 - N8 - C9 = -22.8(3)  
 C2 - C7 - N8 - C9 = 156.95(17)  
 C6 - C7 - N8 - C13 = 106.7(2)  
 C2 - C7 - N8 - C13 = -73.5(2)  
 C7 - N8 - C9 - C10 = -166.66(15)  
 C13 - N8 - C9 - C10 = 62.50(19)  
 N8 - C9 - C10 - N11 = -59.86(19)  
 C9 - C10 - N11 - C12 = 56.78(19)  
 C10 - N11 - C12 - C13 = -54.5(2)  
 C7 - N8 - C13 - C12 = 166.99(15)  
 C9 - N8 - C13 - C12 = -60.71(19)  
 N11 - C12 - C13 - N8 = 55.79(19)  
 O22 - C21 - C24 - F26 = 90.2(2)  
 O23 - C21 - C24 - F26 = -87.0(2)  
 O22 - C21 - C24 - F27 = -30.9(3)  
 O23 - C21 - C24 - F27 = 151.80(19)  
 O22 - C21 - C24 - F25 = -151.61(19)  
 O23 - C21 - C24 - F25 = 31.1(3)

## SUPPORTING INFORMATION

## Structure visualization



**SUPPORTING INFORMATION****10. X-ray crystallography data of 3 (CCDC-2129685).**

(C<sub>16</sub>H<sub>23</sub>FN<sub>2</sub>);  $M = 262.36$ . A suitable crystal for X-ray diffraction single crystal experiment (colourless prism, dimensions = 0.570 x 0.190 x 0.140 mm) was selected and mounted with a cryoloop on the goniometer head of a APEXII Kappa-CCD (Bruker AXS) diffractometer equipped with a CCD-LDI-APEX2 detector, using Mo-K $\alpha$  radiation ( $\lambda = 0.71073 \text{ \AA}$ , multilayer monochromator) at  $T = 150(2)$  K. Crystal structure has been described in triclinic symmetry and P 1 (I.T.#2) centric space group. Cell parameters have been refined as follows:  $a = 9.2306(14)$ ,  $b = 12.1496(15)$ ,  $c = 14.130(2) \text{ \AA}$ ,  $\alpha = 77.791(6)$ ,  $\beta = 89.882(7)$ ,  $\gamma = 67.955(6)^\circ$ ,  $V = 1430.4(4) \text{ \AA}^3$ . Number of formula unit Z is equal to 4 and calculated density  $d$  and absorption coefficient  $\mu$  values are  $1.218 \text{ g.cm}^{-3}$  and  $0.081 \text{ mm}^{-1}$  respectively. Crystal structure was solved by dual-space algorithm using SHELXT program,<sup>[1]</sup> and then refined with full-matrix least-squares methods based on  $F^2$  (SHELXL program).<sup>[2]</sup> All non-Hydrogen atoms were refined with anisotropic atomic displacement parameters. H atoms were finally included in their calculated positions and treated as riding on their parent atom with constrained thermal parameters. A final refinement on  $F^2$  with 6257 unique intensities and 344 parameters converged at  $\omega R(F^2) = 0.2024$  ( $R_F = 0.0808$ ) for 3771 observed reflections with ( $I > 2\sigma$ ).

[1] G. M. Sheldrick, *Acta Cryst.* **2015**, *A71*, 3-8.

[2] G. M. Sheldrick, *Acta Cryst.* **2015**, *C71*, 3-8.

**Data collection strategy details.**

Software : BIS 2014.5.0.0/23-May-2014 && APEX2\_2014.11-0

Number of scans : 4

Total number of frames : 649

Total length of scans : 649.00 (deg.)

Rotation speed : 16.83 sec./deg.

Total exposition time : 3 h 2.0 min.

Scan	Time(s)	Width	DX(mm)	Frames	Range	2Theta	Omega	Phi	Chi	T(K)
1 Omega	30.0	1.00	35.0	79	79	344.0	254.1	271.6	23.4	150.0
2 Omega	15.0	1.00	35.0	105	105.0	14.1	13.8	60.0	305.3	150.0
3 Omega	15.0	1.00	35.0	105	105.0	14.1	13.8	240.0	305.3	150.0
4 Phi	15.0	1.00	35.0	360	360.0	14.1	13.8	360.0	337.0	150.0

## SUPPORTING INFORMATION

## Structural data.

## Crystal data.

Empirical formula	C <sub>16</sub> H <sub>23</sub> FN <sub>2</sub>
Formula weight	262.36 g/mol
Temperature	150(2) K
Radiation type	Mo-K <sub>α</sub>
Wavelength	0.71073 Å
Crystal system, space group	triclinic, P1
Unit cell dimensions	a = 9.2306(14) Å b = 12.1496(15) Å c = 14.130(2) Å
	$\alpha = 77.791(6)$ $\beta = 89.882(7)$ $\gamma = 67.955(6)$
Volume	1430.4(4) Å <sup>3</sup>
Z, Calculated density	4, 1.218 g.cm <sup>-3</sup>
Absorption coefficient	0.081 mm <sup>-1</sup>
F(000)	568
Crystal size	0.570 x 0.190 x 0.140 mm
Crystal color	colourless
Crystal description	prism

## Data collection

Diffractometer	APEXII Kappa-CCD (Bruker-AXS)
$\vartheta$ range for data collection	1.857 to 27.352
(sin $\vartheta$ /λ) <sub>max</sub> (Å <sup>-1</sup> )	0.646
h <sub>min</sub> , h <sub>max</sub>	-11, 11
k <sub>min</sub> , k <sub>max</sub>	-15, 10
l <sub>min</sub> , l <sub>max</sub>	-18, 18
Reflections collected / unique	21012 / 6257 [ <sup>a</sup> R(int) = 0.0486]
Reflections [I > 2σ]	3771
Completeness to $\vartheta_{\text{max}}$	0.967
Absorption correction type	multi-scan
Max. and min. transmission	0.989 , 0.846

## Refinement

Refinement method	Full-matrix least-squares on $F^2$
H-atom treatment	H-atom parameters constrained
Data / restraints / parameters	6257 / 0 / 344
<sup>b</sup> Goodness-of-fit	1.018
Final R indices [I > 2σ]	<sup>c</sup> R <sub>1</sub> = 0.0808, <sup>d</sup> ωR <sub>2</sub> = 0.2024
R indices (all data)	<sup>c</sup> R <sub>1</sub> = 0.1341, <sup>d</sup> ωR <sub>2</sub> = 0.2504
Δρ <sub>max</sub> , Δρ <sub>min</sub>	0.899, -0.271 e.Å <sup>-3</sup>

$$^a R_{int} = \frac{\sum |F_o^2 - \langle F_o^2 \rangle|}{\sum F_o^2}$$

$$^b S = \left\{ \sum \frac{[w(F_o^2 - F_c^2)^2]}{n-p} \right\}^{1/2}$$

$$^c R_1 = \frac{\sum |F_o| - |F_c|}{\sum |F_o|}$$

$$^d wR_2 = \left\{ \frac{\sum [w(F_o^2 - F_c^2)^2]}{\sum [w(F_o^2)^2]} \right\}^{1/2}$$

$$w = 1./[\sigma(F_o^2) + (aP)^2 + bP] \text{ with } P = [2F_c^2 + \text{Max}(F_o^2, 0)]/3$$

Fractional atomic coordinates, site occupancy (%) and equivalent isotropic displacement parameters (Å<sup>2</sup>).

## SUPPORTING INFORMATION

$U_{\text{eq}}$  is defined as one third of the trace of the orthogonalized  $U_{ij}$  tensor.

Atom	x	y	z	occ.	$U_{\text{eq}}$	adp
F1	0.6170(3)	0.60402(18)	0.74294(15)	1	0.0430(7)	Uani
C2	0.7253(5)	0.4905(3)	0.7787(3)	1	0.0300(9)	Uani
C3	0.7615(5)	0.4534(3)	0.8777(3)	1	0.0372(10)	Uani
H3	0.714414	0.507996	0.918377	1	0.045	Uiso
C4	0.8658(6)	0.3376(4)	0.9172(3)	1	0.0422(11)	Uani
H4	0.891651	0.310505	0.985407	1	0.051	Uiso
C5	0.9331(6)	0.2605(3)	0.8557(3)	1	0.0430(11)	Uani
H5	1.004908	0.179583	0.882322	1	0.052	Uiso
C6	0.8968(5)	0.2999(3)	0.7555(3)	1	0.0341(10)	Uani
H6	0.943480	0.244870	0.715089	1	0.041	Uiso
C7	0.7945(4)	0.4173(3)	0.7135(2)	1	0.0237(8)	Uani
N8	0.7506(4)	0.4633(2)	0.61184(19)	1	0.0244(7)	Uani
C9	0.8034(5)	0.3723(3)	0.5521(2)	1	0.0278(9)	Uani
H9A	0.772643	0.303054	0.579679	1	0.033	Uiso
H9B	0.919149	0.340658	0.552888	1	0.033	Uiso
C10	0.7317(5)	0.4283(3)	0.4490(2)	1	0.0278(9)	Uani
H10A	0.766749	0.365832	0.409765	1	0.033	Uiso
H10B	0.615907	0.458399	0.447920	1	0.033	Uiso
N11	0.7796(4)	0.5308(2)	0.40666(19)	1	0.0226(7)	Uani
C12	0.7228(5)	0.6228(3)	0.4652(2)	1	0.0269(9)	Uani
H12A	0.607008	0.652780	0.463757	1	0.032	Uiso
H12B	0.751584	0.692975	0.437286	1	0.032	Uiso
C13	0.7931(5)	0.5693(3)	0.5688(2)	1	0.0249(8)	Uani
H13A	0.908665	0.542327	0.570616	1	0.030	Uiso
H13B	0.753747	0.632112	0.607405	1	0.030	Uiso
C14	0.7370(5)	0.5835(3)	0.3019(2)	1	0.0248(8)	Uani
H14	0.771793	0.653424	0.285002	1	0.030	Uiso
C15	0.8261(5)	0.4925(3)	0.2413(2)	1	0.0307(9)	Uani
H15A	0.793313	0.422328	0.254732	1	0.037	Uiso
H15B	0.940044	0.461542	0.260175	1	0.037	Uiso
C16	0.7938(6)	0.5530(3)	0.1321(3)	1	0.0386(10)	Uani
H16A	0.835791	0.618154	0.117751	1	0.046	Uiso
H16B	0.848504	0.491582	0.094376	1	0.046	Uiso
C17	0.6209(6)	0.6065(4)	0.1017(3)	1	0.0406(11)	Uani
H17A	0.581634	0.540017	0.108629	1	0.049	Uiso
H17B	0.602939	0.649759	0.032375	1	0.049	Uiso
C18	0.5303(6)	0.6951(3)	0.1629(2)	1	0.0423(11)	Uani
H18A	0.416573	0.724496	0.144111	1	0.051	Uiso
H18B	0.560711	0.766499	0.149979	1	0.051	Uiso
C19	0.5631(5)	0.6343(3)	0.2721(3)	1	0.0360(10)	Uani
H19A	0.506836	0.694913	0.310129	1	0.043	Uiso
H19B	0.523759	0.567592	0.286301	1	0.043	Uiso
F21	0.2927(3)	1.11391(17)	0.72859(15)	1	0.0453(7)	Uani
C22	0.2933(5)	1.0011(3)	0.7676(3)	1	0.0336(10)	Uani
C23	0.2981(6)	0.9664(3)	0.8672(3)	1	0.0412(11)	Uani
H23	0.298013	1.020487	0.906904	1	0.049	Uiso
C24	0.3033(6)	0.8485(4)	0.9089(3)	1	0.0433(12)	Uani
H24	0.305656	0.822739	0.977465	1	0.052	Uiso
C25	0.3048(6)	0.7715(3)	0.8510(3)	1	0.0410(11)	Uani
H25	0.311240	0.691491	0.879633	1	0.049	Uiso
C26	0.2970(5)	0.8088(3)	0.7503(3)	1	0.0353(10)	Uani
H26	0.294967	0.754571	0.711183	1	0.042	Uiso
C27	0.2921(5)	0.9259(3)	0.7051(2)	1	0.0255(8)	Uani
N28	0.2871(4)	0.9696(2)	0.6032(2)	1	0.0242(7)	Uani
C29	0.3236(5)	0.8771(3)	0.5451(2)	1	0.0295(9)	Uani
H29A	0.239501	0.844859	0.547489	1	0.035	Uiso
H29B	0.423372	0.808467	0.572284	1	0.035	Uiso
C30	0.3379(5)	0.9336(3)	0.4400(2)	1	0.0324(10)	Uani
H30A	0.423443	0.964353	0.437446	1	0.039	Uiso
H30B	0.363860	0.870954	0.400966	1	0.039	Uiso
N31	0.1910(4)	1.0331(2)	0.3999(2)	1	0.0261(8)	Uani
C32	0.1574(5)	1.1265(3)	0.4565(2)	1	0.0297(9)	Uani
H32A	0.058327	1.195752	0.429005	1	0.036	Uiso
H32B	0.242795	1.157436	0.453080	1	0.036	Uiso
C33	0.1429(5)	1.0728(3)	0.5618(2)	1	0.0261(9)	Uani
H33A	0.121129	1.136028	0.599893	1	0.031	Uiso

## SUPPORTING INFORMATION

H33B	0.054007	1.045609	0.565289	1	0.031	Uiso
C34	0.1779(6)	1.0856(3)	0.2941(3)	1	0.0347(10)	Uani
H34	0.070981	1.151967	0.279007	1	0.042	Uiso
C35	0.1793(6)	0.9936(3)	0.2354(2)	1	0.0395(11)	Uani
H35A	0.098036	0.961015	0.256282	1	0.047	Uiso
H35B	0.282580	0.924635	0.247998	1	0.047	Uiso
C36	0.1482(7)	1.0524(4)	0.1263(3)	1	0.0532(14)	Uani
H36A	0.159586	0.988530	0.090143	1	0.064	Uiso
H36B	0.038509	1.112351	0.112889	1	0.064	Uiso
C37	0.2551(7)	1.1149(4)	0.0896(3)	1	0.0545(14)	Uani
H37A	0.222628	1.157160	0.020558	1	0.065	Uiso
H37B	0.363357	1.053557	0.093643	1	0.065	Uiso
C38	0.2524(8)	1.2080(4)	0.1491(3)	1	0.0665(19)	Uani
H38A	0.147709	1.275220	0.138591	1	0.080	Uiso
H38B	0.331117	1.243061	0.127341	1	0.080	Uiso
C39	0.2895(7)	1.1446(4)	0.2582(3)	1	0.0593(16)	Uani
H39A	0.397706	1.082045	0.268792	1	0.071	Uiso
H39B	0.284286	1.205610	0.296116	1	0.071	Uiso

**Anisotropic displacement parameters ( $\text{\AA}^2$ )**

The anisotropic displacement factor exponent takes the form:  $-2\pi[h^2a^{*2}U_{11} + \dots + 2hka^*b^*U_{12}]$

Atom	U11	U22	U33	U23	U13	U12
F1	0.0530(16)	0.0292(11)	0.0375(12)	-0.0140(10)	0.0096(11)	-0.0019(11)
C2	0.038(2)	0.0256(17)	0.0244(18)	-0.0064(15)	0.0068(16)	-0.0092(16)
C3	0.049(3)	0.039(2)	0.0249(19)	-0.0162(17)	0.0113(19)	-0.013(2)
C4	0.055(3)	0.050(2)	0.0204(19)	-0.0052(17)	-0.0007(19)	-0.020(2)
C5	0.052(3)	0.035(2)	0.033(2)	-0.0039(17)	0.001(2)	-0.009(2)
C6	0.041(2)	0.0259(18)	0.0291(19)	-0.0087(15)	0.0045(17)	-0.0052(17)
C7	0.0255(19)	0.0223(16)	0.0218(17)	-0.0075(14)	0.0049(15)	-0.0063(15)
N8	0.0358(19)	0.0158(13)	0.0204(15)	-0.0063(11)	0.0049(14)	-0.0077(13)
C9	0.043(2)	0.0124(14)	0.0252(18)	-0.0062(13)	0.0052(17)	-0.0059(16)
C10	0.044(2)	0.0182(15)	0.0229(17)	-0.0075(13)	0.0057(17)	-0.0127(17)
N11	0.0332(18)	0.0160(13)	0.0216(14)	-0.0071(11)	0.0051(13)	-0.0112(13)
C12	0.043(2)	0.0161(15)	0.0219(17)	-0.0086(13)	0.0074(16)	-0.0096(16)
C13	0.039(2)	0.0184(15)	0.0211(16)	-0.0089(13)	0.0068(16)	-0.0127(16)
C14	0.035(2)	0.0203(16)	0.0170(16)	-0.0029(13)	0.0029(15)	-0.0096(16)
C15	0.034(2)	0.0297(18)	0.0274(19)	-0.0133(15)	0.0055(17)	-0.0073(17)
C16	0.055(3)	0.038(2)	0.0231(19)	-0.0142(16)	0.0145(19)	-0.015(2)
C17	0.056(3)	0.039(2)	0.0250(19)	-0.0114(17)	0.0002(19)	-0.015(2)
C18	0.049(3)	0.043(2)	0.024(2)	-0.0095(17)	-0.0041(18)	-0.004(2)
C19	0.041(2)	0.032(2)	0.0284(19)	-0.0103(16)	0.0019(17)	-0.0060(18)
F21	0.0754(19)	0.0263(11)	0.0371(13)	-0.0134(9)	-0.0016(12)	-0.0192(12)
C22	0.045(3)	0.0206(17)	0.030(2)	-0.0094(15)	-0.0006(18)	-0.0050(17)
C23	0.055(3)	0.036(2)	0.025(2)	-0.0143(17)	-0.0056(19)	-0.006(2)
C24	0.052(3)	0.042(2)	0.0181(19)	-0.0025(17)	-0.0019(18)	0.000(2)
C25	0.052(3)	0.0267(19)	0.031(2)	-0.0004(17)	0.002(2)	-0.0037(19)
C26	0.048(3)	0.0218(17)	0.030(2)	-0.0089(15)	-0.0004(18)	-0.0046(17)
C27	0.025(2)	0.0216(16)	0.0229(18)	-0.0052(14)	-0.0022(15)	-0.0015(15)
N28	0.0335(18)	0.0163(13)	0.0213(15)	-0.0086(11)	-0.0009(13)	-0.0055(13)
C29	0.040(2)	0.0175(15)	0.0253(18)	-0.0108(14)	0.0002(17)	-0.0021(16)
C30	0.044(3)	0.0230(18)	0.028(2)	-0.0161(16)	0.0064(18)	-0.0056(18)
N31	0.043(2)	0.0161(13)	0.0205(15)	-0.0085(11)	0.0022(14)	-0.0101(14)
C32	0.048(3)	0.0168(15)	0.0207(17)	-0.0074(14)	0.0041(17)	-0.0075(17)
C33	0.036(2)	0.0155(16)	0.0231(18)	-0.0074(14)	0.0026(16)	-0.0041(16)
C34	0.055(3)	0.0280(18)	0.0221(18)	-0.0084(15)	0.0040(19)	-0.016(2)
C35	0.070(3)	0.0299(18)	0.0214(19)	-0.0101(15)	0.002(2)	-0.020(2)
C36	0.079(4)	0.058(3)	0.030(2)	-0.021(2)	0.003(2)	-0.030(3)
C37	0.091(4)	0.065(3)	0.022(2)	-0.018(2)	0.012(2)	-0.042(3)
C38	0.143(6)	0.062(3)	0.028(2)	-0.018(2)	0.027(3)	-0.072(4)
C39	0.108(5)	0.072(3)	0.032(2)	-0.027(2)	0.021(3)	-0.065(4)

**SUPPORTING INFORMATION****Bond length [Å]**

F1 - C2 = 1.353(4)  
C2 - C3 = 1.376(5)  
C2 - C7 = 1.402(4)  
C3 - C4 = 1.368(5)  
C3 - H3 = 0.9500  
C4 - C5 = 1.387(5)  
C4 - H4 = 0.9500  
C5 - C6 = 1.394(5)  
C5 - H5 = 0.9500  
C6 - C7 = 1.382(5)  
C6 - H6 = 0.9500  
C7 - N8 = 1.426(4)  
N8 - C9 = 1.470(4)  
N8 - C13 = 1.493(4)  
C9 - C10 = 1.507(4)  
C9 - H9A = 0.9900  
C9 - H9B = 0.9900  
C10 - N11 = 1.485(4)  
C10 - H10A = 0.9900  
C10 - H10B = 0.9900  
N11 - C12 = 1.470(4)  
N11 - C14 = 1.473(4)  
C12 - C13 = 1.507(4)  
C12 - H12A = 0.9900  
C12 - H12B = 0.9900  
C13 - H13A = 0.9900  
C13 - H13B = 0.9900  
C14 - C19 = 1.511(6)  
C14 - C15 = 1.531(4)  
C14 - H14 = 1.0000  
C15 - C16 = 1.539(5)  
C15 - H15A = 0.9900  
C15 - H15B = 0.9900  
C16 - C17 = 1.504(7)  
C16 - H16A = 0.9900  
C16 - H16B = 0.9900  
C17 - C18 = 1.524(5)  
C17 - H17A = 0.9900  
C17 - H17B = 0.9900  
C18 - C19 = 1.540(5)  
C18 - H18A = 0.9900  
C18 - H18B = 0.9900  
C19 - H19A = 0.9900  
C19 - H19B = 0.9900  
F21 - C22 = 1.363(4)  
C22 - C23 = 1.377(5)  
C22 - C27 = 1.401(5)  
C23 - C24 = 1.412(6)  
C23 - H23 = 0.9500  
C24 - C25 = 1.364(5)  
C24 - H24 = 0.9500  
C25 - C26 = 1.392(5)  
C25 - H25 = 0.9500  
C26 - C27 = 1.415(5)  
C26 - H26 = 0.9500  
C27 - N28 = 1.419(4)  
N28 - C33 = 1.459(4)  
N28 - C29 = 1.468(4)  
C29 - C30 = 1.527(5)  
C29 - H29A = 0.9900  
C29 - H29B = 0.9900  
C30 - N31 = 1.451(5)  
C30 - H30A = 0.9900  
C30 - H30B = 0.9900  
N31 - C32 = 1.464(4)  
N31 - C34 = 1.483(4)  
C32 - C33 = 1.520(4)  
C32 - H32A = 0.9900  
C32 - H32B = 0.9900

**SUPPORTING INFORMATION**

C33 - H33A = 0.9900  
 C33 - H33B = 0.9900  
 C34 - C39 = 1.494(7)  
 C34 - C35 = 1.522(5)  
 C34 - H34 = 1.0000  
 C35 - C36 = 1.533(5)  
 C35 - H35A = 0.9900  
 C35 - H35B = 0.9900  
 C36 - C37 = 1.488(7)  
 C36 - H36A = 0.9900  
 C36 - H36B = 0.9900  
 C37 - C38 = 1.538(5)  
 C37 - H37A = 0.9900  
 C37 - H37B = 0.9900  
 C38 - C39 = 1.546(6)  
 C38 - H38A = 0.9900  
 C38 - H38B = 0.9900  
 C39 - H39A = 0.9900  
 C39 - H39B = 0.9900

**Angles [°]**

F1 - C2 - C3 = 117.8(3)  
 F1 - C2 - C7 = 118.6(3)  
 C3 - C2 - C7 = 123.6(3)  
 C4 - C3 - C2 = 119.6(3)  
 C4 - C3 - H3 = 120.2  
 C2 - C3 - H3 = 120.2  
 C3 - C4 - C5 = 118.7(3)  
 C3 - C4 - H4 = 120.6  
 C5 - C4 - H4 = 120.6  
 C4 - C5 - C6 = 121.0(4)  
 C4 - C5 - H5 = 119.5  
 C6 - C5 - H5 = 119.5  
 C7 - C6 - C5 = 121.5(3)  
 C7 - C6 - H6 = 119.3  
 C5 - C6 - H6 = 119.3  
 C6 - C7 - C2 = 115.5(3)  
 C6 - C7 - N8 = 124.5(3)  
 C2 - C7 - N8 = 119.9(3)  
 C7 - N8 - C9 = 115.5(2)  
 C7 - N8 - C13 = 113.7(3)  
 C9 - N8 - C13 = 109.6(3)  
 N8 - C9 - C10 = 110.5(3)  
 N8 - C9 - H9A = 109.6  
 C10 - C9 - H9A = 109.6  
 N8 - C9 - H9B = 109.6  
 C10 - C9 - H9B = 109.6  
 H9A - C9 - H9B = 108.1  
 N11 - C10 - C9 = 109.8(3)  
 N11 - C10 - H10A = 109.7  
 C9 - C10 - H10A = 109.7  
 N11 - C10 - H10B = 109.7  
 C9 - C10 - H10B = 109.7  
 H10A - C10 - H10B = 108.2  
 C12 - N11 - C14 = 112.6(2)  
 C12 - N11 - C10 = 108.3(3)  
 C14 - N11 - C10 = 116.0(3)  
 N11 - C12 - C13 = 110.5(3)  
 N11 - C12 - H12A = 109.6  
 C13 - C12 - H12A = 109.6  
 N11 - C12 - H12B = 109.6  
 C13 - C12 - H12B = 109.6  
 H12A - C12 - H12B = 108.1  
 N8 - C13 - C12 = 110.1(3)  
 N8 - C13 - H13A = 109.6  
 C12 - C13 - H13A = 109.6  
 N8 - C13 - H13B = 109.6  
 C12 - C13 - H13B = 109.6  
 H13A - C13 - H13B = 108.2

**SUPPORTING INFORMATION**

N11 - C14 - C19 = 114.6(3)

N11 - C14 - C15 = 111.4(3)

C19 - C14 - C15 = 110.1(3)

N11 - C14 - H14 = 106.7

C19 - C14 - H14 = 106.7

C15 - C14 - H14 = 106.7

C14 - C15 - C16 = 110.9(3)

C14 - C15 - H15A = 109.5

C16 - C15 - H15A = 109.5

C14 - C15 - H15B = 109.5

C16 - C15 - H15B = 109.5

H15A - C15 - H15B = 108.1

C17 - C16 - C15 = 111.0(3)

C17 - C16 - H16A = 109.4

C15 - C16 - H16A = 109.4

C17 - C16 - H16B = 109.4

C15 - C16 - H16B = 109.4

H16A - C16 - H16B = 108.0

C16 - C17 - C18 = 111.3(3)

C16 - C17 - H17A = 109.4

C18 - C17 - H17A = 109.4

C16 - C17 - H17B = 109.4

C18 - C17 - H17B = 109.4

H17A - C17 - H17B = 108.0

C17 - C18 - C19 = 111.4(3)

C17 - C18 - H18A = 109.4

C19 - C18 - H18A = 109.4

C17 - C18 - H18B = 109.4

C19 - C18 - H18B = 109.4

H18A - C18 - H18B = 108.0

C14 - C19 - C18 = 110.5(3)

C14 - C19 - H19A = 109.6

C18 - C19 - H19A = 109.6

C14 - C19 - H19B = 109.6

C18 - C19 - H19B = 109.6

H19A - C19 - H19B = 108.1

F21 - C22 - C23 = 117.7(3)

F21 - C22 - C27 = 118.7(3)

C23 - C22 - C27 = 123.5(3)

C22 - C23 - C24 = 118.4(3)

C22 - C23 - H23 = 120.8

C24 - C23 - H23 = 120.8

C25 - C24 - C23 = 120.0(3)

C25 - C24 - H24 = 120.0

C23 - C24 - H24 = 120.0

C24 - C25 - C26 = 120.8(4)

C24 - C25 - H25 = 119.6

C26 - C25 - H25 = 119.6

C25 - C26 - C27 = 121.2(3)

C25 - C26 - H26 = 119.4

C27 - C26 - H26 = 119.4

C22 - C27 - C26 = 116.0(3)

C22 - C27 - N28 = 119.5(3)

C26 - C27 - N28 = 124.5(3)

C27 - N28 - C33 = 113.9(3)

C27 - N28 - C29 = 115.8(2)

C33 - N28 - C29 = 110.0(3)

N28 - C29 - C30 = 109.7(3)

N28 - C29 - H29A = 109.7

C30 - C29 - H29A = 109.7

N28 - C29 - H29B = 109.7

C30 - C29 - H29B = 109.7

H29A - C29 - H29B = 108.2

N31 - C30 - C29 = 109.6(3)

N31 - C30 - H30A = 109.7

C29 - C30 - H30A = 109.7

N31 - C30 - H30B = 109.7

C29 - C30 - H30B = 109.7

H30A - C30 - H30B = 108.2

C30 - N31 - C32 = 108.9(3)

C30 - N31 - C34 = 116.2(3)

**SUPPORTING INFORMATION**

C32 - N31 - C34 = 111.9(2)

N31 - C32 - C33 = 109.8(3)

N31 - C32 - H32A = 109.7

C33 - C32 - H32A = 109.7

N31 - C32 - H32B = 109.7

C33 - C32 - H32B = 109.7

H32A - C32 - H32B = 108.2

N28 - C33 - C32 = 110.5(3)

N28 - C33 - H33A = 109.5

C32 - C33 - H33A = 109.5

N28 - C33 - H33B = 109.5

C32 - C33 - H33B = 109.5

H33A - C33 - H33B = 108.1

N31 - C34 - C39 = 117.0(4)

N31 - C34 - C35 = 111.4(3)

C39 - C34 - C35 = 110.7(3)

N31 - C34 - H34 = 105.6

C39 - C34 - H34 = 105.6

C35 - C34 - H34 = 105.6

C34 - C35 - C36 = 111.1(3)

C34 - C35 - H35A = 109.4

C36 - C35 - H35A = 109.4

C34 - C35 - H35B = 109.4

C36 - C35 - H35B = 109.4

H35A - C35 - H35B = 108.0

C37 - C36 - C35 = 113.5(4)

C37 - C36 - H36A = 108.9

C35 - C36 - H36A = 108.9

C37 - C36 - H36B = 108.9

C35 - C36 - H36B = 108.9

H36A - C36 - H36B = 107.7

C36 - C37 - C38 = 111.1(4)

C36 - C37 - H37A = 109.4

C38 - C37 - H37A = 109.4

C36 - C37 - H37B = 109.4

C38 - C37 - H37B = 109.4

H37A - C37 - H37B = 108.0

C37 - C38 - C39 = 109.7(3)

C37 - C38 - H38A = 109.7

C39 - C38 - H38A = 109.7

C37 - C38 - H38B = 109.7

C39 - C38 - H38B = 109.7

H38A - C38 - H38B = 108.2

C34 - C39 - C38 = 112.1(4)

C34 - C39 - H39A = 109.2

C38 - C39 - H39A = 109.2

C34 - C39 - H39B = 109.2

C38 - C39 - H39B = 109.2

H39A - C39 - H39B = 107.9

**Torsion angles [°]**

F1 - C2 - C3 - C4 = 177.4(4)

C7 - C2 - C3 - C4 = -2.7(7)

C2 - C3 - C4 - C5 = 0.3(7)

C3 - C4 - C5 - C6 = 0.6(7)

C4 - C5 - C6 - C7 = 0.8(7)

C5 - C6 - C7 - C2 = -3.0(6)

C5 - C6 - C7 - N8 = -179.2(4)

F1 - C2 - C7 - C6 = -176.2(4)

C3 - C2 - C7 - C6 = 4.0(6)

F1 - C2 - C7 - N8 = 0.2(6)

C3 - C2 - C7 - N8 = -179.6(4)

C6 - C7 - N8 - C9 = 8.6(6)

C2 - C7 - N8 - C9 = -167.5(4)

C6 - C7 - N8 - C13 = -119.4(4)

C2 - C7 - N8 - C13 = 64.5(5)

C7 - N8 - C9 - C10 = 172.3(3)

C13 - N8 - C9 - C10 = -57.7(4)

N8 - C9 - C10 - N11 = 60.2(4)

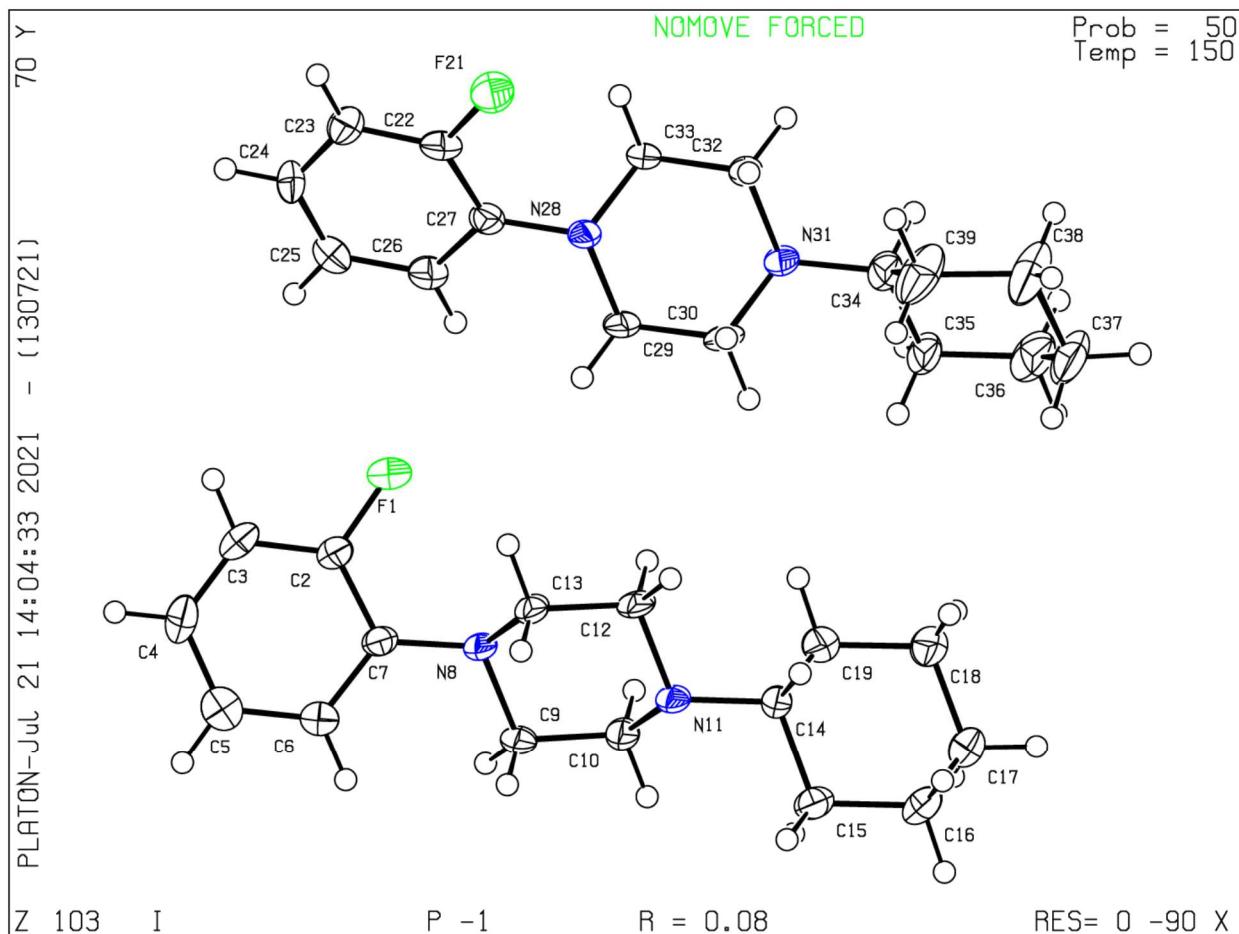
C9 - C10 - N11 - C12 = -60.6(4)

## SUPPORTING INFORMATION

C9 - C10 - N11 - C14 = 171.7(3)  
 C14 - N11 - C12 - C13 = -169.9(3)  
 C10 - N11 - C12 - C13 = 60.5(4)  
 C7 - N8 - C13 - C12 = -172.1(3)  
 C9 - N8 - C13 - C12 = 57.0(4)  
 N11 - C12 - C13 - N8 = -59.2(4)  
 C12 - N11 - C14 - C19 = -66.3(4)  
 C10 - N11 - C14 - C19 = 59.3(4)  
 C12 - N11 - C14 - C15 = 167.8(3)  
 C10 - N11 - C14 - C15 = -66.7(4)  
 N11 - C14 - C15 - C16 = -174.0(3)  
 C19 - C14 - C15 - C16 = 57.6(4)  
 C14 - C15 - C16 - C17 = -56.4(5)  
 C15 - C16 - C17 - C18 = 55.1(4)  
 C16 - C17 - C18 - C19 = -55.3(5)  
 N11 - C14 - C19 - C18 = 176.0(3)  
 C15 - C14 - C19 - C18 = -57.4(4)  
 C17 - C18 - C19 - C14 = 56.5(5)  
 F21 - C22 - C23 - C24 = -178.3(4)  
 C27 - C22 - C23 - C24 = 0.5(7)  
 C22 - C23 - C24 - C25 = 0.6(7)  
 C23 - C24 - C25 - C26 = -1.8(7)  
 C24 - C25 - C26 - C27 = 1.9(7)  
 F21 - C22 - C27 - C26 = 178.4(4)  
 C23 - C22 - C27 - C26 = -0.3(6)  
 F21 - C22 - C27 - N28 = -1.2(6)  
 C23 - C22 - C27 - N28 = -180.0(4)  
 C25 - C26 - C27 - C22 = -0.9(6)  
 C25 - C26 - C27 - N28 = 178.7(4)  
 C22 - C27 - N28 - C33 = -64.9(5)  
 C26 - C27 - N28 - C33 = 115.5(4)  
 C22 - C27 - N28 - C29 = 166.0(4)  
 C26 - C27 - N28 - C29 = -13.6(6)  
 C27 - N28 - C29 - C30 = -171.5(3)  
 C33 - N28 - C29 - C30 = 57.6(5)  
 N28 - C29 - C30 - N31 = -60.1(4)  
 C29 - C30 - N31 - C32 = 61.3(4)  
 C29 - C30 - N31 - C34 = -171.2(3)  
 C30 - N31 - C32 - C33 = -60.5(5)  
 C34 - N31 - C32 - C33 = 169.7(3)  
 C27 - N28 - C33 - C32 = 171.0(3)  
 C29 - N28 - C33 - C32 = -57.1(4)  
 N31 - C32 - C33 - N28 = 58.7(4)  
 C30 - N31 - C34 - C39 = -62.8(4)  
 C32 - N31 - C34 - C39 = 63.1(5)  
 C30 - N31 - C34 - C35 = 65.8(5)  
 C32 - N31 - C34 - C35 = -168.2(4)  
 N31 - C34 - C35 - C36 = 173.9(4)  
 C39 - C34 - C35 - C36 = -54.1(6)  
 C34 - C35 - C36 - C37 = 53.5(6)  
 C35 - C36 - C37 - C38 = -53.9(6)  
 C36 - C37 - C38 - C39 = 54.4(6)  
 N31 - C34 - C39 - C38 = -173.7(3)  
 C35 - C34 - C39 - C38 = 57.3(5)  
 C37 - C38 - C39 - C34 = -57.1(6)

## SUPPORTING INFORMATION

## Structure visualization



**SUPPORTING INFORMATION****11. X-ray crystallography data of 20 (CCDC-2129686).**

(C<sub>16</sub>H<sub>23</sub>NO<sub>2</sub>);  $M = 261.35$ . A suitable crystal for X-ray diffraction single crystal experiment (colourless prism, dimensions = 0.310 x 0.120 x 0.100 mm) was selected and mounted on the goniometer head of a APEXII Kappa-CCD (Bruker AXS) diffractometer equipped with a CCD-LDI-APEX2 detector, using Mo-K $\alpha$  radiation ( $\lambda = 0.71073 \text{ \AA}$ , graphite monochromator) at  $T = 150(2)$  K. Crystal structure has been described in triclinic symmetry and  $P\bar{1}$  (I.T.#2) centric space group. Cell parameters have been refined as follows:  $a = 5.1998(8)$ ,  $b = 10.6245(17)$ ,  $c = 13.555(2) \text{ \AA}$ ,  $\alpha = 101.157(5)$ ,  $\beta = 96.793(5)$ ,  $\gamma = 101.820(5)^\circ$ ,  $V = 709.33(19) \text{ \AA}^3$ . Number of formula unit Z is equal to 2 and calculated density  $d$  and absorption coefficient  $\mu$  values are  $1.224 \text{ g.cm}^{-3}$  and  $0.080 \text{ mm}^{-1}$  respectively. Crystal structure was solved by dual-space algorithm using *SHELXT* program,<sup>[1]</sup> and then refined with full-matrix least-squares methods based on  $F^2$  (*SHELXL* program).<sup>[2]</sup> All non-Hydrogen atoms were refined with anisotropic atomic displacement parameters. H atoms were finally included in their calculated positions and treated as riding on their parent atom with constrained thermal parameters. A final refinement on  $F^2$  with 3204 unique intensities and 173 parameters converged at  $\omega R(F^2) = 0.1435$  ( $R_F = 0.0583$ ) for 2199 observed reflections with ( $I > 2\sigma$ ).

[1] G. M. Sheldrick, *Acta Cryst.* **2015**, *A71*, 3-8.

[2] G. M. Sheldrick, *Acta Cryst.* **2015**, *C71*, 3-8.

## SUPPORTING INFORMATION

## Structural data.

## Crystal data.

Empirical formula	C <sub>16</sub> H <sub>23</sub> NO <sub>2</sub>
Formula weight	261.35 g/mol
Temperature	150(2) K
Radiation type	Mo-K <sub>α</sub>
Wavelength	0.71073 Å
Crystal system, space group	triclinic, P1
Unit cell dimensions	a = 5.1998(8) Å b = 10.6245(17) Å c = 13.555(2) Å
	$\alpha = 101.157(5)$ $\beta = 96.793(5)$ $\gamma = 101.820(5)$
Volume	709.33(19) Å <sup>3</sup>
Z, Calculated density	2, 1.224 g.cm <sup>-3</sup>
Absorption coefficient	0.080 mm <sup>-1</sup>
F(000)	284
Crystal size	0.310 x 0.120 x 0.100 mm
Crystal color	colourless
Crystal description	prism

## Data collection

Diffractometer	APEXII Kappa-CCD (Bruker-AXS)
$\vartheta$ range for data collection	1.802 to 27.509
(sin $\vartheta$ /λ) <sub>max</sub> (Å <sup>-1</sup> )	0.650
h <sub>min</sub> , h <sub>max</sub>	-6, 6
k <sub>min</sub> , k <sub>max</sub>	-8, 13
l <sub>min</sub> , l <sub>max</sub>	-17, 14
Reflections collected / unique	8795 / 3204 [ <sup>a</sup> R(int) = 0.0463]
Reflections [I > 2σ]	2199
Completeness to $\vartheta_{\text{max}}$	0.979
Absorption correction type	multi-scan
Max. and min. transmission	0.992 , 0.851

## Refinement

Refinement method	Full-matrix least-squares on $F^2$
H-atom treatment	H-atom parameters constrained
Data / restraints / parameters	3204 / 0 / 173
<sup>b</sup> Goodness-of-fit	1.078
Final R indices [I > 2σ]	<sup>c</sup> R <sub>1</sub> = 0.0583, <sup>d</sup> ωR <sub>2</sub> = 0.1435
R indices (all data)	<sup>c</sup> R <sub>1</sub> = 0.0897, <sup>d</sup> ωR <sub>2</sub> = 0.1589
Δρ <sub>max</sub> , Δρ <sub>min</sub>	0.273, -0.229 e.Å <sup>-3</sup>

$$^a R_{\text{int}} = \frac{\sum |F_o^2 - \langle F_o^2 \rangle|}{\sum F_o^2}$$

$$^b S = \left\{ \sum \frac{[w(F_o^2 - F_c^2)^2]}{n-p} \right\}^{1/2}$$

$$^c R_1 = \frac{\sum |F_o| - |F_c|}{\sum |F_o|}$$

$$^d wR_2 = \left\{ \frac{\sum [w(F_o^2 - F_c^2)^2]}{\sum [w(F_o^2)^2]} \right\}^{1/2}$$

$$w = 1./[\sigma(F_o^2) + (aP)^2 + bP] \text{ with } P = [2F_c^2 + \text{Max}(F_o^2, 0)]/3$$

## SUPPORTING INFORMATION

Fractional atomic coordinates, site occupancy (%) and equivalent isotropic displacement parameters ( $\text{\AA}^2$ ).

$U(\text{eq})$  is defined as one third of the trace of the orthogonalized  $U_{ij}$  tensor.

Atom	x	y	z	occ.	$U(\text{eq})$	adp
O1	1.1664(3)	0.11311(14)	0.64743(11)	1	0.0281(4)	Uani
O2	0.4719(3)	0.16434(13)	0.41956(10)	1	0.0233(3)	Uani
N1	0.1330(3)	0.27654(16)	0.24618(12)	1	0.0194(4)	Uani
C1	1.3988(4)	0.1635(2)	0.72328(16)	1	0.0269(5)	Uani
H1A	1.518547	0.234887	0.703442	1	0.040	Uiso
H1B	1.490011	0.092709	0.729802	1	0.040	Uiso
H1C	1.347595	0.197547	0.788754	1	0.040	Uiso
C2	1.0330(4)	0.20097(19)	0.61676(14)	1	0.0205(4)	Uani
C3	1.0988(4)	0.33562(19)	0.65983(15)	1	0.0220(4)	Uani
H3	1.241674	0.372682	0.715095	1	0.026	Uiso
C4	0.9508(4)	0.4146(2)	0.62020(16)	1	0.0253(5)	Uani
H4	0.994504	0.506732	0.648920	1	0.030	Uiso
C5	0.7414(4)	0.3627(2)	0.53999(15)	1	0.0234(5)	Uani
H5	0.643864	0.418484	0.513227	1	0.028	Uiso
C6	0.6763(4)	0.22756(19)	0.49927(14)	1	0.0201(4)	Uani
C7	0.8218(4)	0.14620(19)	0.53721(14)	1	0.0202(4)	Uani
H7	0.776908	0.053917	0.508900	1	0.024	Uiso
C8	0.3037(4)	0.24102(19)	0.38368(15)	1	0.0201(4)	Uani
H8	0.230892	0.290886	0.439970	1	0.024	Uiso
C9	0.4030(4)	0.3267(2)	0.31017(15)	1	0.0211(4)	Uani
H9A	0.448140	0.422714	0.340200	1	0.025	Uiso
H9B	0.548033	0.299898	0.276293	1	0.025	Uiso
C10	0.0854(4)	0.16141(19)	0.29542(15)	1	0.0218(4)	Uani
H10A	0.128182	0.081371	0.256735	1	0.026	Uiso
H10B	-0.093759	0.140721	0.314688	1	0.026	Uiso
C11	0.1244(4)	0.24737(19)	0.13610(14)	1	0.0195(4)	Uani
H11	0.245323	0.187342	0.118482	1	0.023	Uiso
C12	0.2188(4)	0.3743(2)	0.10055(15)	1	0.0247(5)	Uani
H12A	0.404731	0.416539	0.133859	1	0.030	Uiso
H12B	0.106276	0.436368	0.121031	1	0.030	Uiso
C13	0.2043(4)	0.3462(2)	-0.01503(16)	1	0.0297(5)	Uani
H13A	0.330255	0.291131	-0.034701	1	0.036	Uiso
H13B	0.258542	0.430364	-0.036402	1	0.036	Uiso
C14	-0.0768(4)	0.2749(2)	-0.07009(16)	1	0.0296(5)	Uani
H14A	-0.199475	0.334010	-0.057203	1	0.036	Uiso
H14B	-0.076765	0.252262	-0.144451	1	0.036	Uiso
C15	-0.1745(4)	0.1494(2)	-0.03344(15)	1	0.0285(5)	Uani
H15A	-0.064674	0.085948	-0.053851	1	0.034	Uiso
H15B	-0.361172	0.108305	-0.066332	1	0.034	Uiso
C16	-0.1587(4)	0.1785(2)	0.08236(15)	1	0.0236(5)	Uani
H16A	-0.281417	0.235276	0.102240	1	0.028	Uiso
H16B	-0.215782	0.094785	0.104162	1	0.028	Uiso

Anisotropic displacement parameters ( $\text{\AA}^2$ )

The anisotropic displacement factor exponent takes the form:  $-2\pi[h^2a^{*2}U_{11} + \dots + 2hka^*b^*U_{12}]$

Atom	U11	U22	U33	U23	U13	U12
O1	0.0302(8)	0.0250(8)	0.0268(8)	0.0081(6)	-0.0085(6)	0.0067(6)
O2	0.0268(8)	0.0215(7)	0.0192(7)	0.0049(6)	-0.0045(6)	0.0051(6)
N1	0.0218(9)	0.0207(8)	0.0147(8)	0.0060(6)	0.0007(7)	0.0018(7)
C1	0.0256(11)	0.0352(12)	0.0198(10)	0.0075(9)	-0.0012(9)	0.0084(9)
C2	0.0220(10)	0.0245(10)	0.0173(10)	0.0097(8)	0.0040(8)	0.0057(8)
C3	0.0215(10)	0.0231(10)	0.0183(10)	0.0034(8)	-0.0001(8)	0.0014(8)
C4	0.0310(12)	0.0193(10)	0.0229(11)	0.0029(8)	0.0010(9)	0.0031(9)
C5	0.0271(11)	0.0221(10)	0.0229(11)	0.0077(8)	0.0027(9)	0.0081(9)
C6	0.0221(10)	0.0236(10)	0.0138(9)	0.0057(8)	0.0029(8)	0.0022(8)
C7	0.0243(11)	0.0184(9)	0.0178(10)	0.0057(8)	0.0036(8)	0.0033(8)
C8	0.0228(10)	0.0229(10)	0.0160(10)	0.0079(8)	0.0025(8)	0.0058(8)
C9	0.0232(10)	0.0221(10)	0.0175(10)	0.0059(8)	0.0012(8)	0.0037(8)
C10	0.0242(11)	0.0233(10)	0.0187(10)	0.0096(8)	0.0022(8)	0.0038(8)
C11	0.0205(10)	0.0225(10)	0.0153(10)	0.0060(8)	0.0012(8)	0.0038(8)

## SUPPORTING INFORMATION

C12	0.0247(11)	0.0279(11)	0.0200(10)	0.0095(9)	0.0008(8)	0.0001(9)
C13	0.0272(12)	0.0404(13)	0.0208(11)	0.0134(10)	0.0032(9)	0.0006(10)
C14	0.0290(12)	0.0406(13)	0.0197(11)	0.0119(9)	0.0004(9)	0.0061(10)
C15	0.0286(12)	0.0315(12)	0.0205(11)	0.0043(9)	-0.0032(9)	0.0019(9)
C16	0.0231(11)	0.0270(11)	0.0202(10)	0.0096(9)	0.0016(8)	0.0015(9)

**Bond length [Å]**

O1 - C2	= 1.368(2)
O1 - C1	= 1.426(2)
O2 - C6	= 1.379(2)
O2 - C8	= 1.418(2)
N1 - C11	= 1.457(2)
N1 - C9	= 1.495(2)
N1 - C10	= 1.495(2)
C1 - H1A	= 0.9800
C1 - H1B	= 0.9800
C1 - H1C	= 0.9800
C2 - C7	= 1.387(3)
C2 - C3	= 1.390(3)
C3 - C4	= 1.388(3)
C3 - H3	= 0.9500
C4 - C5	= 1.383(3)
C4 - H4	= 0.9500
C5 - C6	= 1.390(3)
C5 - H5	= 0.9500
C6 - C7	= 1.390(3)
C7 - H7	= 0.9500
C8 - C10	= 1.526(3)
C8 - C9	= 1.539(3)
C8 - H8	= 1.0000
C9 - H9A	= 0.9900
C9 - H9B	= 0.9900
C10 - H10A	= 0.9900
C10 - H10B	= 0.9900
C11 - C12	= 1.526(3)
C11 - C16	= 1.527(3)
C11 - H11	= 1.0000
C12 - C13	= 1.527(3)
C12 - H12A	= 0.9900
C12 - H12B	= 0.9900
C13 - C14	= 1.529(3)
C13 - H13A	= 0.9900
C13 - H13B	= 0.9900
C14 - C15	= 1.523(3)
C14 - H14A	= 0.9900
C14 - H14B	= 0.9900
C15 - C16	= 1.529(3)
C15 - H15A	= 0.9900
C15 - H15B	= 0.9900
C16 - H16A	= 0.9900
C16 - H16B	= 0.9900

**Angles [°]**

C2 - O1 - C1	= 118.13(16)
C6 - O2 - C8	= 117.36(15)
C11 - N1 - C9	= 116.44(15)
C11 - N1 - C10	= 116.91(15)
C9 - N1 - C10	= 89.76(13)
O1 - C1 - H1A	= 109.5
O1 - C1 - H1B	= 109.5
H1A - C1 - H1B	= 109.5
O1 - C1 - H1C	= 109.5
H1A - C1 - H1C	= 109.5
H1B - C1 - H1C	= 109.5
O1 - C2 - C7	= 114.92(17)
O1 - C2 - C3	= 124.13(18)
C7 - C2 - C3	= 120.94(18)

## SUPPORTING INFORMATION

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C4	- C3	- C2	= 118.43(18)
C4	- C3	- H3	= 120.8
C2	- C3	- H3	= 120.8
C5	- C4	- C3	= 121.79(19)
C5	- C4	- H4	= 119.1
C3	- C4	- H4	= 119.1
C4	- C5	- C6	= 118.79(18)
C4	- C5	- H5	= 120.6
C6	- C5	- H5	= 120.6
O2	- C6	- C5	= 124.18(17)
O2	- C6	- C7	= 115.17(17)
C5	- C6	- C7	= 120.64(18)
C2	- C7	- C6	= 119.39(18)
C2	- C7	- H7	= 120.3
C6	- C7	- H7	= 120.3
O2	- C8	- C10	= 112.95(16)
O2	- C8	- C9	= 117.89(17)
C10	- C8	- C9	= 86.97(14)
O2	- C8	- H8	= 112.2
C10	- C8	- H8	= 112.2
C9	- C8	- H8	= 112.2
N1	- C9	- C8	= 87.76(14)
N1	- C9	- H9A	= 114.0
C8	- C9	- H9A	= 114.0
N1	- C9	- H9B	= 114.0
C8	- C9	- H9B	= 114.0
H9A	- C9	- H9B	= 111.2
N1	- C10	- C8	= 88.23(14)
N1	- C10	- H10A	= 113.9
C8	- C10	- H10A	= 113.9
N1	- C10	- H10B	= 113.9
C8	- C10	- H10B	= 113.9
H10A	- C10	- H10B	= 111.1
N1	- C11	- C12	= 110.18(16)
N1	- C11	- C16	= 109.99(16)
C12	- C11	- C16	= 110.05(15)
N1	- C11	- H11	= 108.9
C12	- C11	- H11	= 108.9
C16	- C11	- H11	= 108.9
C11	- C12	- C13	= 110.95(17)
C11	- C12	- H12A	= 109.4
C13	- C12	- H12A	= 109.4
C11	- C12	- H12B	= 109.4
C13	- C12	- H12B	= 109.4
H12A	- C12	- H12B	= 108.0
C12	- C13	- C14	= 111.49(17)
C12	- C13	- H13A	= 109.3
C14	- C13	- H13A	= 109.3
C12	- C13	- H13B	= 109.3
C14	- C13	- H13B	= 109.3
H13A	- C13	- H13B	= 108.0
C15	- C14	- C13	= 110.75(17)
C15	- C14	- H14A	= 109.5
C13	- C14	- H14A	= 109.5
C15	- C14	- H14B	= 109.5
C13	- C14	- H14B	= 109.5
H14A	- C14	- H14B	= 108.1
C14	- C15	- C16	= 111.29(18)
C14	- C15	- H15A	= 109.4
C16	- C15	- H15A	= 109.4
C14	- C15	- H15B	= 109.4
C16	- C15	- H15B	= 109.4
H15A	- C15	- H15B	= 108.0
C11	- C16	- C15	= 111.06(17)
C11	- C16	- H16A	= 109.4
C15	- C16	- H16A	= 109.4
C11	- C16	- H16B	= 109.4
C15	- C16	- H16B	= 109.4
H16A	- C16	- H16B	= 108.0

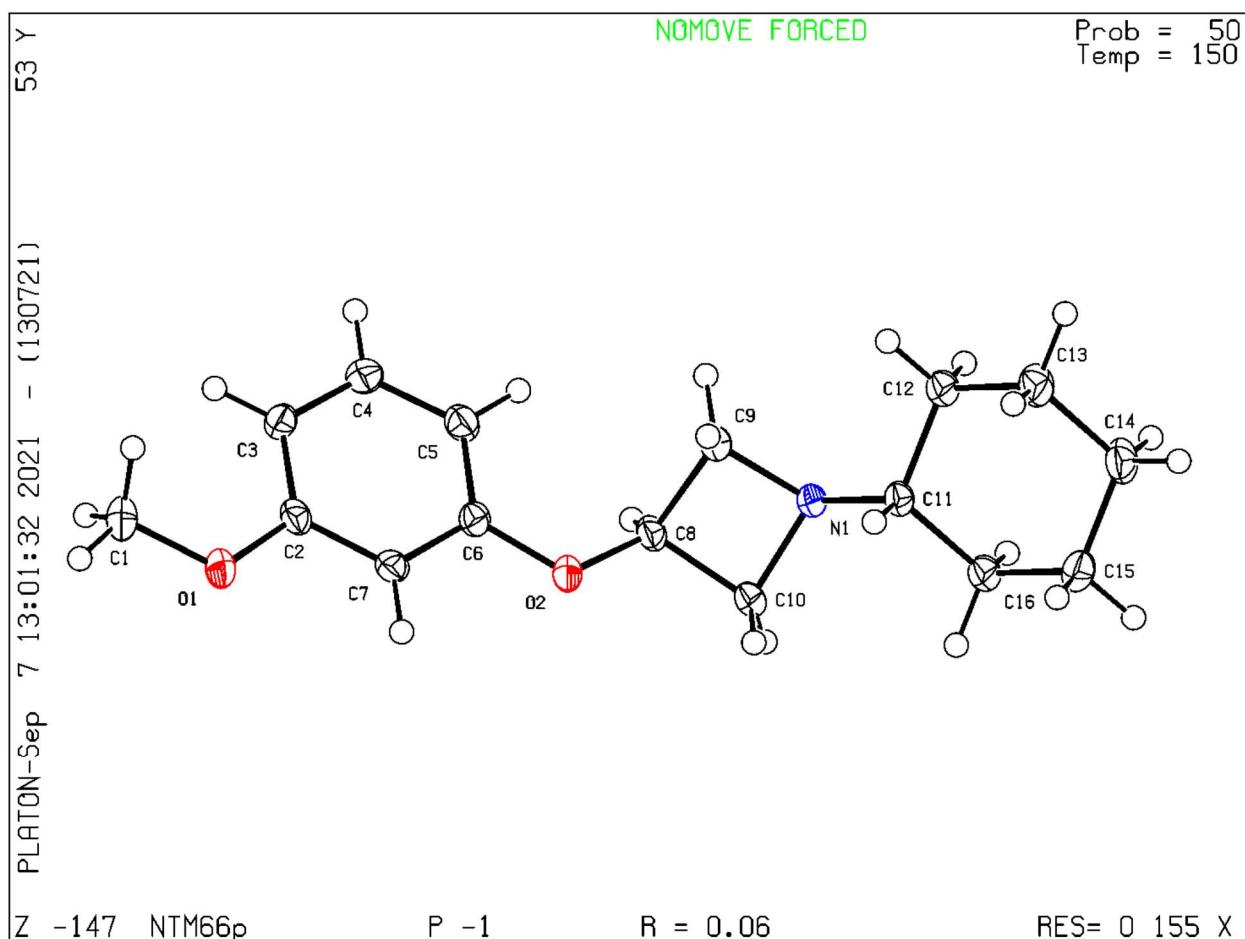
## SUPPORTING INFORMATION

## Torsion angles [°]

C1	- O1	- C2	- C7	= 175.09(17)
C1	- O1	- C2	- C3	= -4.7(3)
O1	- C2	- C3	- C4	= 178.65(19)
C7	- C2	- C3	- C4	= -1.1(3)
C2	- C3	- C4	- C5	= 0.2(3)
C3	- C4	- C5	- C6	= 0.9(3)
C8	- O2	- C6	- C5	= -6.1(3)
C8	- O2	- C6	- C7	= 174.91(16)
C4	- C5	- C6	- O2	= 179.89(19)
C4	- C5	- C6	- C7	= -1.1(3)
O1	- C2	- C7	- C6	= -178.91(17)
C3	- C2	- C7	- C6	= 0.8(3)
O2	- C6	- C7	- C2	= 179.36(17)
C5	- C6	- C7	- C2	= 0.3(3)
C6	- O2	- C8	- C10	= 179.86(16)
C6	- O2	- C8	- C9	= 80.7(2)
C11	- N1	- C9	- C8	= -140.61(16)
C10	- N1	- C9	- C8	= -20.38(15)
O2	- C8	- C9	- N1	= 134.41(17)
C10	- C8	- C9	- N1	= 19.97(14)
C11	- N1	- C10	- C8	= 140.37(17)
C9	- N1	- C10	- C8	= 20.56(15)
O2	- C8	- C10	- N1	= -139.06(16)
C9	- C8	- C10	- N1	= -19.97(14)
C9	- N1	- C11	- C12	= -66.9(2)
C10	- N1	- C11	- C12	= -171.21(16)
C9	- N1	- C11	- C16	= 171.61(16)
C10	- N1	- C11	- C16	= 67.3(2)
N1	- C11	- C12	- C13	= -178.49(17)
C16	- C11	- C12	- C13	= -57.0(2)
C11	- C12	- C13	- C14	= 56.4(2)
C12	- C13	- C14	- C15	= -55.0(3)
C13	- C14	- C15	- C16	= 55.0(3)
N1	- C11	- C16	- C15	= 178.76(16)
C12	- C11	- C16	- C15	= 57.2(2)
C14	- C15	- C16	- C11	= -56.6(2)

## SUPPORTING INFORMATION

## Structure visualization



**SUPPORTING INFORMATION****12. X-ray crystallography data of 23 (CCDC-2129687).**

(C<sub>16</sub>H<sub>26</sub>N<sub>3</sub>O<sub>2</sub>);  $M = 295.42$ . A suitable crystal for X-ray diffraction single crystal experiment (colourless prism, dimensions = 0.540 x 0.310 x 0.130 mm) was selected and mounted on the goniometer head of a APEXII Kappa-CCD (Bruker AXS) diffractometer equipped with a CCD-LDI-APEX2 detector, using Mo-K<sub>α</sub> radiation ( $\lambda = 0.71073 \text{ \AA}$ , graphite monochromator) at  $T = 150(2)$  K. Crystal structure has been described in triclinic symmetry and  $P\bar{1}/c$  (I.T.#14) centric space group. Cell parameters have been refined as follows:  $a = 9.6362(14)$ ,  $b = 6.6206(11)$ ,  $c = 27.615(5) \text{ \AA}$ ,  $\beta = 95.227(8)^\circ$ ,  $V = 1754.4(5) \text{ \AA}^3$ . Number of formula unit  $Z$  is equal to 4 and calculated density  $d$  and absorption coefficient  $\mu$  values are  $1.118 \text{ g.cm}^{-3}$  and  $0.074 \text{ mm}^{-1}$  respectively. Crystal structure was solved by dual-space algorithm using *SHELXT* program,<sup>[1]</sup> and then refined with full-matrix least-squares methods based on  $F^2$  (*SHELXL* program).<sup>[2]</sup> All non-Hydrogen atoms were refined with anisotropic atomic displacement parameters. H atoms were finally included in their calculated positions and treated as riding on their parent atom with constrained thermal parameters. A final refinement on  $F^2$  with 3975 unique intensities and 196 parameters converged at  $\omega R(F^2) = 0.2000$  ( $R_F = 0.0997$ ) for 2533 observed reflections with ( $I > 2\sigma$ ).

[1] G. M. Sheldrick, *Acta Cryst.* **2015**, *A71*, 3-8.

[2] G. M. Sheldrick, *Acta Cryst.* **2015**, *C71*, 3-8.

## SUPPORTING INFORMATION

## Structural data.

## Crystal data.

Empirical formula	C <sub>16</sub> H <sub>29</sub> N <sub>3</sub> O <sub>2</sub>
Formula weight	295.42 g/mol
Temperature	150(2) K
Radiation type	Mo-K <sub>α</sub>
Wavelength	0.71073 Å
Crystal system, space group	triclinic, P 2 <sub>1</sub> /c
Unit cell dimensions	a = 9.6362(14) Å b = 6.6206(11) Å c = 27.615(5) Å
	$\beta = 95.227(8)$
Volume	1754.4(5) Å <sup>3</sup>
Z, Calculated density	4, 1.118 g.cm <sup>-3</sup>
Absorption coefficient	0.074 mm <sup>-1</sup>
F(000)	648
Crystal size	0.540 x 0.310 x 0.130 mm
Crystal color	colourless
Crystal description	prism

## Data collection

Diffractometer	APEXII Kappa-CCD (Bruker-AXS)
$\Theta$ range for data collection	2.475 to 27.482
(sin $\Theta$ / $\lambda$ ) <sub>max</sub> (Å <sup>-1</sup> )	0.649
h <sub>min</sub> , h <sub>max</sub>	-12, 12
k <sub>min</sub> , k <sub>max</sub>	-8, 8
l <sub>min</sub> , l <sub>max</sub>	-35, 35
Reflections collected / unique	3975 / 3975 [ <sup>a</sup> R(int) = ?]
Reflections [ $ I  > 2\sigma$ ]	2533
Completeness to $\Theta_{\text{max}}$	0.986
Absorption correction type	multi-scan
Max. and min. transmission	0.990 , 0.906

## Refinement

Refinement method	Full-matrix least-squares on $F^2$
H-atom treatment	H-atom parameters constrained
Data / restraints / parameters	3975 / 0 / 196
<sup>b</sup> Goodness-of-fit	1.129
Final R indices [ $ I  > 2\sigma$ ]	<sup>c</sup> R <sub>1</sub> = 0.0997, <sup>d</sup> wR <sub>2</sub> = 0.2000
R indices (all data)	<sup>c</sup> R <sub>1</sub> = 0.1418, <sup>d</sup> wR <sub>2</sub> = 0.2151
$\Delta\rho_{\text{max}}, \Delta\rho_{\text{min}}$	0.361, -0.391 e.Å <sup>-3</sup>

$$^a R_{\text{int}} = \frac{\sum |F_o^2 - \langle F_o^2 \rangle|}{\sum F_o^2}$$

$$^b S = \left\{ \frac{\sum [w(F_o^2 - F_c^2)^2]}{n-p} \right\}^{1/2}$$

$$^c R_1 = \frac{\sum |F_o| - |F_c|}{\sum |F_o|}$$

$$^d wR_2 = \left\{ \frac{\sum [w(F_o^2 - F_c^2)^2]}{\sum [w(F_o^2)^2]} \right\}^{1/2}$$

$$w = 1./[\sigma(F_o^2) + (aP)^2 + bP] \text{ with } P = [2F_c^2 + \text{Max}(F_o^2, 0)]/3$$

## SUPPORTING INFORMATION

Fractional atomic coordinates, site occupancy (%) and equivalent isotropic displacement parameters ( $\text{\AA}^2$ ).

$U(\text{eq})$  is defined as one third of the trace of the orthogonalized  $U_{ij}$  tensor.

Atom	x	y	z	occ.	$U(\text{eq})$	adp
O1	0.2193(3)	0.9908(4)	0.39504(10)	1	0.0256(7)	Uani
O2	0.2561(4)	1.2544(5)	0.34345(11)	1	0.0364(9)	Uani
N1	0.2793(4)	0.1440(5)	0.08360(13)	1	0.0266(8)	Uani
N2	0.2636(4)	0.3850(5)	0.16932(12)	1	0.0233(8)	Uani
N3	0.2048(4)	0.9380(5)	0.31613(12)	1	0.0256(8)	Uani
C1	0.2815(5)	-0.0498(7)	0.05867(17)	1	0.0356(11)	Uani
H1A	0.276853	-0.159375	0.082321	1	0.053	Uiso
H1B	0.367918	-0.061667	0.042692	1	0.053	Uiso
H1C	0.201412	-0.058661	0.034226	1	0.053	Uiso
C2	0.1482(5)	0.1685(7)	0.10656(16)	1	0.0298(10)	Uani
H2A	0.139282	0.058750	0.130415	1	0.036	Uiso
H2B	0.068241	0.159376	0.081475	1	0.036	Uiso
C3	0.1460(5)	0.3700(7)	0.13185(16)	1	0.0294(10)	Uani
H3A	0.151883	0.479954	0.107817	1	0.035	Uiso
H3B	0.057400	0.385425	0.146997	1	0.035	Uiso
C4	0.3938(4)	0.3650(7)	0.14665(16)	1	0.0284(10)	Uani
H4A	0.473533	0.373300	0.171860	1	0.034	Uiso
H4B	0.402257	0.476986	0.123344	1	0.034	Uiso
C5	0.3978(5)	0.1634(7)	0.12007(16)	1	0.0321(11)	Uani
H5A	0.485424	0.153275	0.104113	1	0.039	Uiso
H5B	0.396129	0.051592	0.143812	1	0.039	Uiso
C6	0.2585(4)	0.5761(7)	0.19508(15)	1	0.0244(9)	Uani
H6	0.270632	0.691774	0.172572	1	0.029	Uiso
C7	0.1326(4)	0.6126(7)	0.22460(15)	1	0.0264(10)	Uani
H7A	0.089585	0.487337	0.235851	1	0.032	Uiso
H7B	0.061483	0.704511	0.208613	1	0.032	Uiso
C8	0.2338(4)	0.7157(6)	0.26364(15)	1	0.0223(9)	Uani
C9	0.3541(4)	0.6017(7)	0.24276(15)	1	0.0275(10)	Uani
H9A	0.379279	0.473082	0.259592	1	0.033	Uiso
H9B	0.437599	0.685794	0.239338	1	0.033	Uiso
C10	0.2103(5)	0.7158(6)	0.31821(15)	1	0.0263(10)	Uani
H10A	0.121655	0.651980	0.325559	1	0.032	Uiso
H10B	0.289880	0.661956	0.339540	1	0.032	Uiso
C11	0.2376(5)	0.9506(6)	0.26530(15)	1	0.0249(9)	Uani
H11A	0.330352	1.009023	0.261196	1	0.030	Uiso
H11B	0.164095	1.016131	0.243319	1	0.030	Uiso
C12	0.2313(4)	1.0785(6)	0.35124(15)	1	0.0234(9)	Uani
C13	0.2343(5)	1.1151(7)	0.43990(15)	1	0.0280(10)	Uani
C14	0.1230(5)	1.2788(9)	0.43739(19)	1	0.0445(14)	Uani
H14A	0.143996	1.380793	0.413384	1	0.067	Uiso
H14B	0.121597	1.342629	0.469365	1	0.067	Uiso
H14C	0.031727	1.218555	0.427801	1	0.067	Uiso
C15	0.2062(6)	0.9604(9)	0.47848(17)	1	0.0487(15)	Uani
H15A	0.112362	0.904565	0.471353	1	0.073	Uiso
H15B	0.213152	1.025580	0.510473	1	0.073	Uiso
H15C	0.274934	0.851313	0.478497	1	0.073	Uiso
C16	0.3800(5)	1.1996(9)	0.44830(18)	1	0.0427(13)	Uani
H16A	0.447823	1.090273	0.446337	1	0.064	Uiso
H16B	0.392692	1.262074	0.480569	1	0.064	Uiso
H16C	0.394085	1.301330	0.423433	1	0.064	Uiso

Anisotropic displacement parameters ( $\text{\AA}^2$ )

The anisotropic displacement factor exponent takes the form:  $-2\pi[h^2a^{*2}U_{11} + \dots + 2hka^*b^*U_{12}]$

Atom	U11	U22	U33	U23	U13	U12
O1	0.0372(17)	0.0201(15)	0.0196(14)	-0.0008(12)	0.0031(13)	-0.0005(14)
O2	0.058(2)	0.0187(16)	0.0326(18)	0.0014(14)	0.0048(16)	-0.0073(16)
N1	0.0270(19)	0.0239(19)	0.0288(19)	-0.0039(16)	0.0026(16)	0.0056(16)
N2	0.0214(18)	0.0230(19)	0.0260(18)	-0.0045(15)	0.0047(14)	0.0001(15)
N3	0.036(2)	0.0177(18)	0.0236(18)	0.0021(15)	0.0075(16)	0.0005(16)
C1	0.043(3)	0.030(3)	0.032(2)	-0.005(2)	-0.003(2)	0.005(2)

## SUPPORTING INFORMATION

C2	0.022(2)	0.032(3)	0.035(2)	-0.004(2)	0.0026(19)	0.001(2)
C3	0.024(2)	0.031(3)	0.033(2)	-0.006(2)	0.0004(19)	0.000(2)
C4	0.018(2)	0.034(3)	0.034(2)	-0.004(2)	0.0091(18)	-0.0008(19)
C5	0.025(2)	0.037(3)	0.033(2)	-0.004(2)	0.0013(19)	0.007(2)
C6	0.025(2)	0.024(2)	0.025(2)	-0.0022(18)	0.0078(17)	-0.0004(18)
C7	0.0154(19)	0.031(2)	0.034(2)	-0.007(2)	0.0060(17)	-0.0035(18)
C8	0.018(2)	0.023(2)	0.028(2)	-0.0035(18)	0.0067(17)	0.0006(17)
C9	0.020(2)	0.029(2)	0.034(2)	-0.010(2)	0.0049(18)	0.0047(19)
C10	0.033(2)	0.018(2)	0.029(2)	-0.0012(18)	0.0049(19)	-0.0007(19)
C11	0.027(2)	0.024(2)	0.025(2)	-0.0025(18)	0.0045(18)	-0.0024(18)
C12	0.021(2)	0.021(2)	0.027(2)	-0.0016(18)	0.0011(17)	0.0025(18)
C13	0.029(2)	0.033(3)	0.022(2)	-0.0072(19)	0.0014(18)	0.000(2)
C14	0.033(3)	0.054(3)	0.046(3)	-0.022(3)	-0.003(2)	0.004(3)
C15	0.060(4)	0.057(4)	0.029(3)	0.002(3)	0.007(2)	-0.012(3)
C16	0.031(3)	0.057(4)	0.040(3)	-0.013(3)	0.005(2)	-0.008(3)

**Bond length [Å]**

O1 - C12	= 1.356(5)
O1 - C13	= 1.483(5)
O2 - C12	= 1.212(5)
N1 - C1	= 1.457(5)
N1 - C5	= 1.458(5)
N1 - C2	= 1.473(5)
N2 - C6	= 1.454(5)
N2 - C4	= 1.459(5)
N2 - C3	= 1.466(5)
N3 - C12	= 1.351(5)
N3 - C11	= 1.469(5)
N3 - C10	= 1.473(5)
C1 - H1A	= 0.9800
C1 - H1B	= 0.9800
C1 - H1C	= 0.9800
C2 - C3	= 1.507(6)
C2 - H2A	= 0.9900
C2 - H2B	= 0.9900
C3 - H3A	= 0.9900
C3 - H3B	= 0.9900
C4 - C5	= 1.525(6)
C4 - H4A	= 0.9900
C4 - H4B	= 0.9900
C5 - H5A	= 0.9900
C5 - H5B	= 0.9900
C6 - C7	= 1.541(6)
C6 - C9	= 1.546(6)
C6 - H6	= 1.0000
C7 - C8	= 1.545(6)
C7 - H7A	= 0.9900
C7 - H7B	= 0.9900
C8 - C9	= 1.539(5)
C8 - C10	= 1.544(6)
C8 - C11	= 1.556(6)
C9 - H9A	= 0.9900
C9 - H9B	= 0.9900
C10 - H10A	= 0.9900
C10 - H10B	= 0.9900
C11 - H11A	= 0.9900
C11 - H11B	= 0.9900
C13 - C16	= 1.510(6)
C13 - C15	= 1.520(7)
C13 - C14	= 1.522(7)
C14 - H14A	= 0.9800
C14 - H14B	= 0.9800
C14 - H14C	= 0.9800
C15 - H15A	= 0.9800
C15 - H15B	= 0.9800
C15 - H15C	= 0.9800
C16 - H16A	= 0.9800
C16 - H16B	= 0.9800
C16 - H16C	= 0.9800

## SUPPORTING INFORMATION

## Angles [°]

C12	- O1	- C13	=	119.9(3)
C1	- N1	- C5	=	111.1(4)
C1	- N1	- C2	=	110.5(4)
C5	- N1	- C2	=	110.0(3)
C6	- N2	- C4	=	111.0(3)
C6	- N2	- C3	=	110.2(3)
C4	- N2	- C3	=	109.3(3)
C12	- N3	- C11	=	127.2(4)
C12	- N3	- C10	=	131.0(4)
C11	- N3	- C10	=	94.8(3)
N1	- C1	- H1A	=	109.5
N1	- C1	- H1B	=	109.5
H1A	- C1	- H1B	=	109.5
N1	- C1	- H1C	=	109.5
H1A	- C1	- H1C	=	109.5
H1B	- C1	- H1C	=	109.5
N1	- C2	- C3	=	110.2(4)
N1	- C2	- H2A	=	109.6
C3	- C2	- H2A	=	109.6
N1	- C2	- H2B	=	109.6
C3	- C2	- H2B	=	109.6
H2A	- C2	- H2B	=	108.1
N2	- C3	- C2	=	110.1(4)
N2	- C3	- H3A	=	109.6
C2	- C3	- H3A	=	109.6
N2	- C3	- H3B	=	109.6
C2	- C3	- H3B	=	109.6
H3A	- C3	- H3B	=	108.1
N2	- C4	- C5	=	110.2(4)
N2	- C4	- H4A	=	109.6
C5	- C4	- H4A	=	109.6
N2	- C4	- H4B	=	109.6
C5	- C4	- H4B	=	109.6
H4A	- C4	- H4B	=	108.1
N1	- C5	- C4	=	110.9(4)
N1	- C5	- H5A	=	109.5
C4	- C5	- H5A	=	109.5
N1	- C5	- H5B	=	109.5
C4	- C5	- H5B	=	109.5
H5A	- C5	- H5B	=	108.0
N2	- C6	- C7	=	117.3(3)
N2	- C6	- C9	=	117.9(4)
C7	- C6	- C9	=	88.2(3)
N2	- C6	- H6	=	110.5
C7	- C6	- H6	=	110.5
C9	- C6	- H6	=	110.5
C6	- C7	- C8	=	87.8(3)
C6	- C7	- H7A	=	114.0
C8	- C7	- H7A	=	114.0
C6	- C7	- H7B	=	114.0
C8	- C7	- H7B	=	114.0
H7A	- C7	- H7B	=	111.2
C9	- C8	- C10	=	123.3(4)
C9	- C8	- C7	=	88.3(3)
C10	- C8	- C7	=	122.8(4)
C9	- C8	- C11	=	119.0(4)
C10	- C8	- C11	=	88.6(3)
C7	- C8	- C11	=	118.3(4)
C8	- C9	- C6	=	87.8(3)
C8	- C9	- H9A	=	114.0
C6	- C9	- H9A	=	114.0
C8	- C9	- H9B	=	114.0
C6	- C9	- H9B	=	114.0
H9A	- C9	- H9B	=	111.2
N3	- C10	- C8	=	88.3(3)
N3	- C10	- H10A	=	113.9
C8	- C10	- H10A	=	113.9
N3	- C10	- H10B	=	113.9
C8	- C10	- H10B	=	113.9

## SUPPORTING INFORMATION

H10A	- C10	- H10B	= 111.1
N3	- C11	- C8	= 88.0(3)
N3	- C11	- H11A	= 114.0
C8	- C11	- H11A	= 114.0
N3	- C11	- H11B	= 114.0
C8	- C11	- H11B	= 114.0
H11A	- C11	- H11B	= 111.2
O2	- C12	- N3	= 124.2(4)
O2	- C12	- O1	= 127.1(4)
N3	- C12	- O1	= 108.6(4)
O1	- C13	- C16	= 110.6(4)
O1	- C13	- C15	= 101.6(4)
C16	- C13	- C15	= 111.4(4)
O1	- C13	- C14	= 110.0(3)
C16	- C13	- C14	= 112.6(4)
C15	- C13	- C14	= 110.0(4)
C13	- C14	- H14A	= 109.5
C13	- C14	- H14B	= 109.5
H14A	- C14	- H14B	= 109.5
C13	- C14	- H14C	= 109.5
H14A	- C14	- H14C	= 109.5
H14B	- C14	- H14C	= 109.5
C13	- C15	- H15A	= 109.5
C13	- C15	- H15B	= 109.5
H15A	- C15	- H15B	= 109.5
C13	- C15	- H15C	= 109.5
H15A	- C15	- H15C	= 109.5
H15B	- C15	- H15C	= 109.5
C13	- C16	- H16A	= 109.5
C13	- C16	- H16B	= 109.5
H16A	- C16	- H16B	= 109.5
C13	- C16	- H16C	= 109.5
H16A	- C16	- H16C	= 109.5
H16B	- C16	- H16C	= 109.5

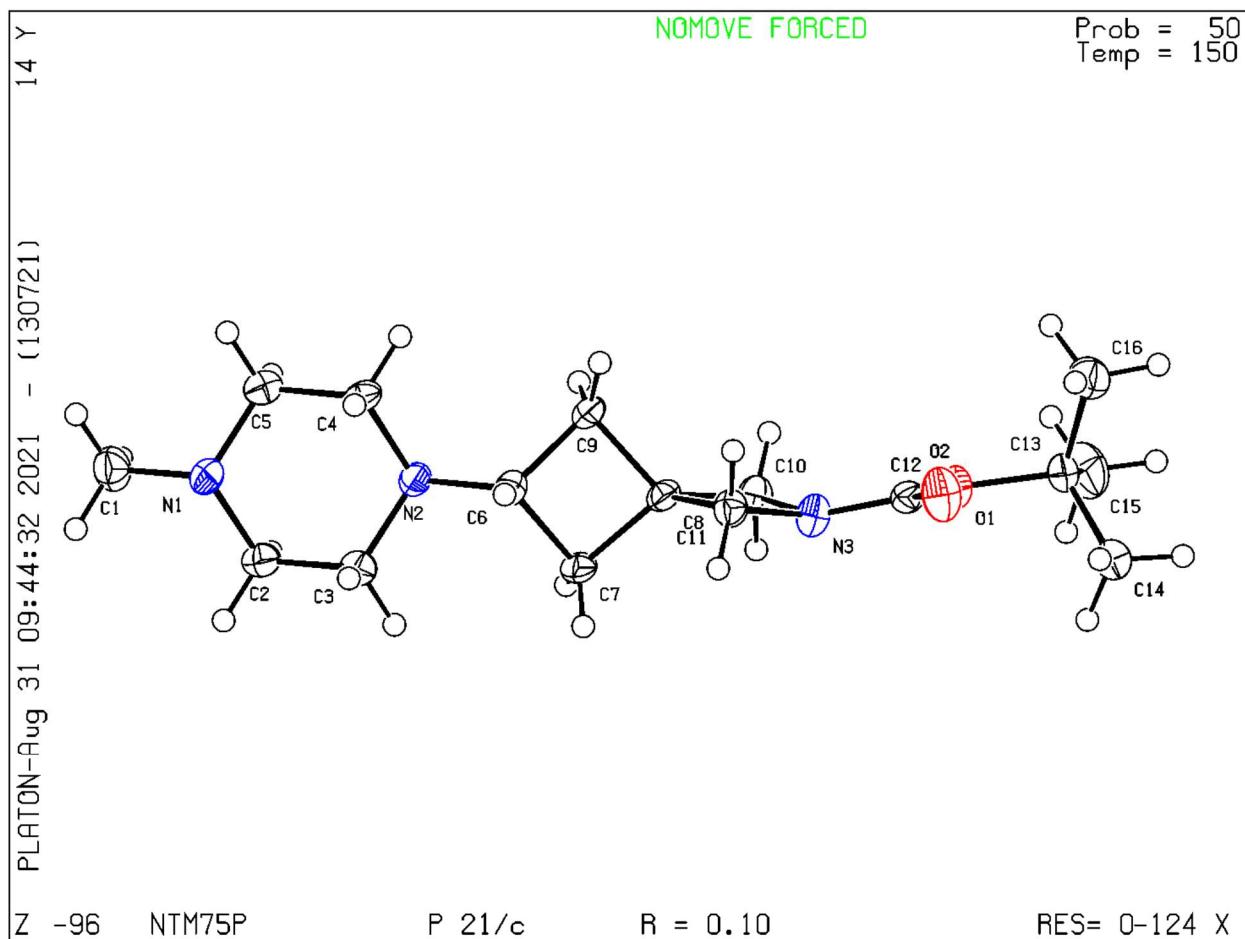
## Torsion angles [°]

C1	- N1	- C2	- C3	= -179.5(3)
C5	- N1	- C2	- C3	= 57.6(5)
C6	- N2	- C3	- C2	= -177.7(3)
C4	- N2	- C3	- C2	= 60.1(5)
N1	- C2	- C3	- N2	= -59.6(5)
C6	- N2	- C4	- C5	= 179.7(3)
C3	- N2	- C4	- C5	= -58.6(5)
C1	- N1	- C5	- C4	= -179.1(4)
C2	- N1	- C5	- C4	= -56.4(5)
N2	- C4	- C5	- N1	= 57.6(5)
C4	- N2	- C6	- C7	= -175.1(4)
C3	- N2	- C6	- C7	= 63.7(5)
C4	- N2	- C6	- C9	= -71.6(5)
C3	- N2	- C6	- C9	= 167.2(4)
N2	- C6	- C7	- C8	= 141.6(4)
C9	- C6	- C7	- C8	= 20.9(3)
C6	- C7	- C8	- C9	= -21.0(3)
C6	- C7	- C8	- C10	= -150.3(4)
C6	- C7	- C8	- C11	= 101.3(4)
C10	- C8	- C9	- C6	= 149.9(4)
C7	- C8	- C9	- C6	= 20.9(3)
C11	- C8	- C9	- C6	= -100.8(4)
N2	- C6	- C9	- C8	= -141.2(4)
C7	- C6	- C9	- C8	= -21.0(3)
C12	- N3	- C10	- C8	= -155.3(5)
C11	- N3	- C10	- C8	= -4.1(4)
C9	- C8	- C10	- N3	= 128.2(4)
C7	- C8	- C10	- N3	= -119.4(4)
C11	- C8	- C10	- N3	= 3.9(3)
C12	- N3	- C11	- C8	= 156.9(4)
C10	- N3	- C11	- C8	= 4.1(4)
C9	- C8	- C11	- N3	= -131.8(4)
C10	- C8	- C11	- N3	= -3.9(3)

## SUPPORTING INFORMATION

C7	- C8	- C11	- N3	= 123.2(4)
C11	- N3	- C12	- O2	= 18.3(7)
C10	- N3	- C12	- O2	= 161.2(5)
C11	- N3	- C12	- O1	= -164.2(4)
C10	- N3	- C12	- O1	= -21.3(6)
C13	- O1	- C12	- O2	= 1.3(7)
C13	- O1	- C12	- N3	= -176.1(3)
C12	- O1	- C13	- C16	= -64.4(5)
C12	- O1	- C13	- C15	= 177.2(4)
C12	- O1	- C13	- C14	= 60.7(5)

## Structure visualization



**SUPPORTING INFORMATION****13. X-ray crystallography data of 24 (CCDC-2129688).**

(C<sub>14</sub>H<sub>20</sub>BrN<sub>3</sub>);  $M = 310.24$ . A suitable crystal for X-ray diffraction single crystal experiment (colourless prism, dimensions = 0.280 x 0.270 x 0.280 mm) was selected and mounted on the goniometer head of a APEXII Kappa-CCD (Bruker AXS) diffractometer equipped with a CCD plate detector, using Mo-K<sub>α</sub> radiation ( $\lambda = 0.71073 \text{ \AA}$ , graphite monochromator) at  $T = 150 \text{ K}$ . Crystal structure has been described in triclinic symmetry and  $P\bar{1}/c$  (I.T.#14) centric space group. Cell parameters have been refined as follows:  $a = 14.2152(7)$ ,  $b = 8.2180(3)$ ,  $c = 12.3724(5) \text{ \AA}$ ,  $\beta = 106.445(2)^\circ$ ,  $V = 1386.34(10) \text{ \AA}^3$ . Number of formula unit  $Z$  is equal to 4 and calculated density  $d$  and absorption coefficient  $\mu$  values are  $1.486 \text{ g.cm}^{-3}$  and  $2.952 \text{ mm}^{-1}$  respectively. Crystal structure was solved by dual-space algorithm using *SHELXT* program,<sup>[1]</sup> and then refined with full-matrix least-squares methods based on  $F^2$  (*SHELXL* program).<sup>[2]</sup> All non-Hydrogen atoms were refined with anisotropic atomic displacement parameters. H atoms were finally included in their calculated positions and treated as riding on their parent atom with constrained thermal parameters. A final refinement on  $F^2$  with 3151 unique intensities and 163 parameters converged at  $\omega R(F^2) = 0.0682$  ( $R_F = 0.0300$ ) for 2464 observed reflections with ( $I > 2\sigma$ ).

[1] G. M. Sheldrick, *Acta Cryst.* **2015**, *A71*, 3-8.

[2] G. M. Sheldrick, *Acta Cryst.* **2015**, *C71*, 3-8.

## SUPPORTING INFORMATION

## Structural data.

## Crystal data.

Empirical formula	C <sub>14</sub> H <sub>20</sub> BrN <sub>3</sub>
Formula weight	310.24 g/mol
Temperature	150 K
Radiation type	Mo-K <sub>α</sub>
Wavelength	0.71073 Å
Crystal system, space group	triclinic, P 2 <sub>1</sub> /c
Unit cell dimensions	a = 14.2152(7) Å b = 8.2180(3) Å c = 12.3734(5) Å
	$\alpha = 90^\circ$ $\beta = 106.445(2)^\circ$ $\gamma = 90^\circ$
Volume	1386.34(10) Å <sup>3</sup>
Z, Calculated density	4, 1.486 g·cm <sup>-3</sup>
Absorption coefficient	2.952 mm <sup>-1</sup>
F(000)	640
Crystal size	0.280 x 0.270 x 0.250 mm
Crystal color	colourless
Crystal description	prism

## Data collection

Diffractometer	APEXII Kappa-CCD (Bruker-AXS)
$\vartheta$ range for data collection	2.894 to 27.474
h <sub>min</sub> , h <sub>max</sub>	-18, 17
k <sub>min</sub> , k <sub>max</sub>	-10, 10
l <sub>min</sub> , l <sub>max</sub>	-16, 15
Reflections collected / unique	9018 / 3151 [ <sup>a</sup> R(int) = 0.0254]
Reflections [ $ I  > 2\sigma$ ]	2464
Completeness to $\vartheta_{\text{max}}$	0.989
Absorption correction type	multi-scan
Max. and min. transmission	0.478, 0.403

## Refinement

Refinement method	Full-matrix least-squares on $F^2$
H-atom treatment	H-atom parameters constrained
Data / restraints / parameters	3151 / 0 / 163
<sup>b</sup> Goodness-of-fit	1.066
Final R indices [ $ I  > 2\sigma$ ]	<sup>c</sup> R <sub>1</sub> = 0.0300, <sup>d</sup> wR <sub>2</sub> = 0.0682
R indices (all data)	<sup>c</sup> R <sub>1</sub> = 0.0442, <sup>d</sup> wR <sub>2</sub> = 0.0717
$\Delta\rho_{\text{max}}, \Delta\rho_{\text{min}}$	0.391, -0.308 e·Å <sup>-3</sup>

$$^aR_{\text{int}} = \frac{\sum |F_o^2 - \langle F_o^2 \rangle|}{\sum F_o^2}$$

$$^bS = \left\{ \frac{\sum [w(F_o^2 - F_c^2)^2]}{n-p} \right\}^{1/2}$$

$$^cR_1 = \frac{\sum |F_o| - |F_c|}{\sum |F_o|}$$

$$^d wR_2 = \left\{ \frac{\sum [w(F_o^2 - F_c^2)^2]}{\sum [w(F_o^2)^2]} \right\}^{1/2}$$

$$w = 1. / [\sigma(F_o^2) + (aP)^2 + bP] \text{ with } P = [2F_c^2 + \text{Max}(F_o^2, 0)] / 3$$

## SUPPORTING INFORMATION

Fractional atomic coordinates, site occupancy (%) and equivalent isotropic displacement parameters ( $\text{\AA}^2$ ).

$U(\text{eq})$  is defined as one third of the trace of the orthogonalized  $U_{ij}$  tensor.

Atom	x	y	z	occ.	$U(\text{eq})$
Br1	0.89270(2)	0.35546(3)	0.99899(2)	1	0.03608(9)
N1	0.61048(12)	0.4264(2)	0.79907(12)	1	0.0222(4)
N2	0.51538(12)	0.33049(17)	0.62618(12)	1	0.0182(3)
N3	0.32155(11)	0.29425(18)	0.47213(12)	1	0.0179(3)
C1	0.77575(15)	0.3400(2)	0.87905(16)	1	0.0226(4)
C2	0.76884(15)	0.2353(2)	0.78934(16)	1	0.0250(4)
H2	0.823184	0.169944	0.786389	1	0.030
C3	0.68231(15)	0.2274(2)	0.70489(16)	1	0.0231(4)
H3	0.676151	0.155894	0.642961	1	0.028
C4	0.60290(15)	0.3254(2)	0.71026(15)	1	0.0179(4)
C5	0.69565(15)	0.4332(2)	0.87987(15)	1	0.0236(4)
H5	0.701148	0.506015	0.940979	1	0.028
C6	0.49357(14)	0.2015(2)	0.54102(14)	1	0.0184(4)
H6A	0.476107	0.100590	0.574589	1	0.022
H6B	0.552722	0.179028	0.516328	1	0.022
C7	0.40974(14)	0.2493(2)	0.43991(14)	1	0.0194(4)
H7A	0.430307	0.342414	0.401174	1	0.023
H7B	0.394199	0.157102	0.386282	1	0.023
C8	0.34783(14)	0.4338(2)	0.54907(15)	1	0.0218(4)
H8A	0.289234	0.470583	0.570469	1	0.026
H8B	0.370189	0.524900	0.510149	1	0.026
C9	0.42806(15)	0.3893(2)	0.65385(15)	1	0.0231(4)
H9A	0.445352	0.485888	0.703296	1	0.028
H9B	0.403893	0.303737	0.695650	1	0.028
C10	0.24021(15)	0.3350(2)	0.37273(16)	1	0.0209(4)
H10	0.260007	0.428887	0.332635	1	0.025
C11	0.20846(16)	0.1940(2)	0.29028(16)	1	0.0258(5)
H11A	0.254999	0.178570	0.244866	1	0.031
H11B	0.203988	0.091524	0.330589	1	0.031
C12	0.10809(16)	0.2459(3)	0.21635(17)	1	0.0317(5)
H12A	0.114545	0.316043	0.153802	1	0.038
H12B	0.067824	0.149762	0.184346	1	0.038
C13	0.0626(2)	0.3387(3)	0.2939(2)	1	0.0564(8)
H13A	0.011407	0.272016	0.312776	1	0.068
H13B	0.032051	0.440273	0.257282	1	0.068
C14	0.14524(17)	0.3780(3)	0.40102(18)	1	0.0343(5)
H14A	0.144269	0.494724	0.420416	1	0.041
H14B	0.138319	0.312262	0.465385	1	0.041

Anisotropic displacement parameters ( $\text{\AA}^2$ )

The anisotropic displacement factor exponent takes the form:  $-2\pi[h^2a^{*2}U_{11} + \dots + 2hka^*b^*U_{12}]$

Atom	U11	U22	U33	U23	U13	U12
Br1	0.02477(14)	0.03907(15)	0.03423(14)	-0.00293(10)	-0.00815(9)	-0.00058(10)
N1	0.0212(9)	0.0267(9)	0.0177(8)	-0.0047(7)	0.0035(7)	0.0011(7)
N2	0.0174(9)	0.0196(8)	0.0163(7)	-0.0047(6)	0.0029(7)	0.0016(6)
N3	0.0176(9)	0.0189(8)	0.0157(7)	-0.0012(6)	0.0022(7)	0.0023(6)
C1	0.0176(10)	0.0238(11)	0.0209(9)	0.0025(8)	-0.0032(8)	-0.0037(8)
C2	0.0201(11)	0.0202(10)	0.0330(11)	-0.0014(9)	0.0047(9)	0.0030(8)
C3	0.0222(11)	0.0198(10)	0.0253(10)	-0.0065(8)	0.0036(9)	0.0000(8)
C4	0.0207(11)	0.0160(9)	0.0171(9)	0.0010(7)	0.0054(8)	-0.0035(7)
C5	0.0251(12)	0.0258(11)	0.0180(9)	-0.0034(8)	0.0029(8)	-0.0029(9)
C6	0.0184(10)	0.0181(9)	0.0183(9)	-0.0052(8)	0.0044(8)	0.0005(8)
C7	0.0225(11)	0.0183(9)	0.0166(9)	-0.0033(8)	0.0042(8)	-0.0002(8)
C8	0.0208(11)	0.0235(10)	0.0202(9)	-0.0018(8)	0.0044(8)	0.0043(8)
C9	0.0229(11)	0.0282(11)	0.0178(9)	-0.0047(8)	0.0053(8)	0.0044(8)
C10	0.0208(11)	0.0211(10)	0.0187(9)	0.0037(8)	0.0022(8)	0.0004(8)
C11	0.0215(12)	0.0308(11)	0.0231(10)	-0.0044(9)	0.0028(9)	0.0010(9)
C12	0.0262(13)	0.0337(12)	0.0290(11)	-0.0007(10)	-0.0022(10)	-0.0021(10)
C13	0.0247(14)	0.087(2)	0.0466(15)	-0.0206(14)	-0.0067(12)	0.0198(13)
C14	0.0251(12)	0.0438(14)	0.0300(11)	-0.0049(10)	0.0014(10)	0.0104(10)

## SUPPORTING INFORMATION

**Bond length [Å]**

Br1 - C1	= 1.894(2)
N1 - C5	= 1.335(2)
N1 - C4	= 1.357(2)
N2 - C4	= 1.378(2)
N2 - C9	= 1.460(3)
N2 - C6	= 1.465(2)
N3 - C7	= 1.466(2)
N3 - C10	= 1.468(2)
N3 - C8	= 1.470(2)
C1 - C5	= 1.375(3)
C1 - C2	= 1.386(3)
C2 - C3	= 1.372(3)
C2 - H2	= 0.9500
C3 - C4	= 1.403(3)
C3 - H3	= 0.9500
C5 - H5	= 0.9500
C6 - C7	= 1.515(2)
C6 - H6A	= 0.9900
C6 - H6B	= 0.9900
C7 - H7A	= 0.9900
C7 - H7B	= 0.9900
C8 - C9	= 1.509(3)
C8 - H8A	= 0.9900
C8 - H8B	= 0.9900
C9 - H9A	= 0.9900
C9 - H9B	= 0.9900
C10 - C11	= 1.525(3)
C10 - C14	= 1.529(3)
C10 - H10	= 1.0000
C11 - C12	= 1.521(3)
C11 - H11A	= 0.9900
C11 - H11B	= 0.9900
C12 - C13	= 1.507(3)
C12 - H12A	= 0.9900
C12 - H12B	= 0.9900
C13 - C14	= 1.536(3)
C13 - H13A	= 0.9900
C13 - H13B	= 0.9900
C14 - H14A	= 0.9900
C14 - H14B	= 0.9900

**Angles [°]**

C5	- N1	- C4	= 118.62(17)
C4	- N2	- C9	= 118.60(15)
C4	- N2	- C6	= 118.90(15)
C9	- N2	- C6	= 112.78(16)
C7	- N3	- C10	= 111.15(13)
C7	- N3	- C8	= 107.01(14)
C10	- N3	- C8	= 111.11(14)
C5	- C1	- C2	= 118.74(18)
C5	- C1	- Br1	= 120.15(14)
C2	- C1	- Br1	= 121.11(15)
C3	- C2	- C1	= 118.97(18)
C3	- C2	- H2	= 120.50
C1	- C2	- H2	= 120.50
C2	- C3	- C4	= 119.79(18)
C2	- C3	- H3	= 120.10
C4	- C3	- H3	= 120.10
N1	- C4	- N2	= 116.15(17)
N1	- C4	- C3	= 120.59(18)
N2	- C4	- C3	= 123.22(16)
N1	- C5	- C1	= 123.28(18)
N1	- C5	- H5	= 118.40
C1	- C5	- H5	= 118.40
N2	- C6	- C7	= 111.30(15)
N2	- C6	- H6A	= 109.40
C7	- C6	- H6A	= 109.40

## SUPPORTING INFORMATION

N2	- C6	- H6B	=	109.40
C7	- C6	- H6B	=	109.40
H6A	- C6	- H6B	=	108.00
N3	- C7	- C6	=	111.96(14)
N3	- C7	- H7A	=	109.20
C6	- C7	- H7A	=	109.20
N3	- C7	- H7B	=	109.20
C6	- C7	- H7B	=	109.20
H7A	- C7	- H7B	=	107.90
N3	- C8	- C9	=	111.03(15)
N3	- C8	- H8A	=	109.40
C9	- C8	- H8A	=	109.40
N3	- C8	- H8B	=	109.40
C9	- C8	- H8B	=	109.40
H8A	- C8	- H8B	=	108.00
N2	- C9	- C8	=	111.38(15)
N2	- C9	- H9A	=	109.40
C8	- C9	- H9A	=	109.40
N2	- C9	- H9B	=	109.40
C8	- C9	- H9B	=	109.40
H9A	- C9	- H9B	=	108.00
N3	- C10	- C11	=	113.63(15)
N3	- C10	- C14	=	113.45(16)
C11	- C10	- C14	=	102.44(17)
N3	- C10	- H10	=	109.00
C11	- C10	- H10	=	109.00
C14	- C10	- H10	=	109.00
C12	- C11	- C10	=	103.82(16)
C12	- C11	- H11A	=	111.00
C10	- C11	- H11A	=	111.00
C12	- C11	- H11B	=	111.00
C10	- C11	- H11B	=	111.00
H11A	- C11	- H11B	=	109.00
C13	- C12	- C11	=	104.90(18)
C13	- C12	- H12A	=	110.80
C11	- C12	- H12A	=	110.80
C13	- C12	- H12B	=	110.80
C11	- C12	- H12B	=	110.80
H12A	- C12	- H12B	=	108.80
C12	- C13	- C14	=	107.13(19)
C12	- C13	- H13A	=	110.30
C14	- C13	- H13A	=	110.30
C12	- C13	- H13B	=	110.30
C14	- C13	- H13B	=	110.30
H13A	- C13	- H13B	=	108.50
C10	- C14	- C13	=	105.25(17)
C10	- C14	- H14A	=	110.70
C13	- C14	- H14A	=	110.70
C10	- C14	- H14B	=	110.70
C13	- C14	- H14B	=	110.70
H14A	- C14	- H14B	=	108.80

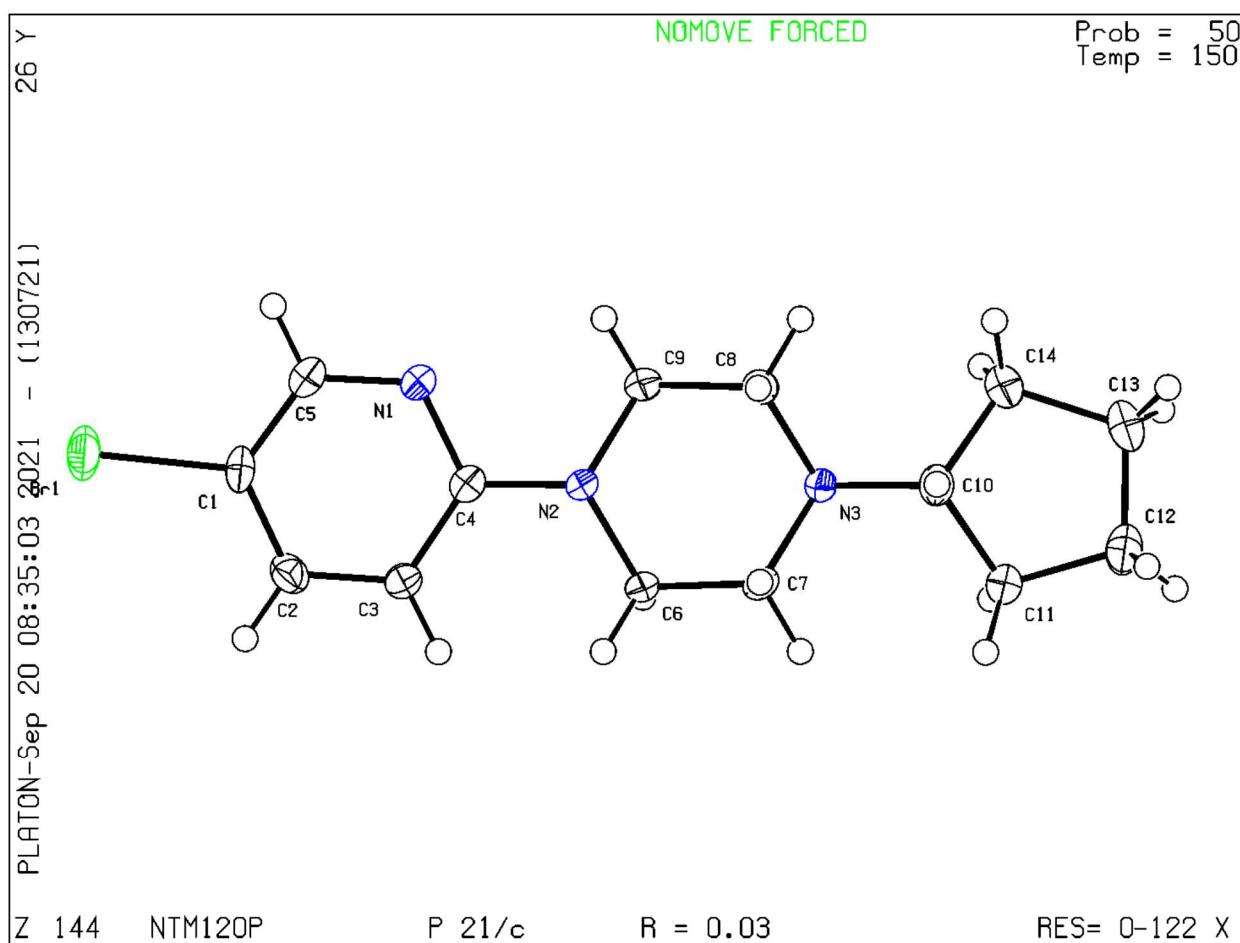
## Torsion angles [°]

C5	- C1	- C2	- C3	=	-0.40(3)
Br1	- C1	- C2	- C3	=	179.48(15)
C1	- C2	- C3	- C4	=	0.30(3)
C5	- N1	- C4	- N2	=	-176.27(16)
C5	- N1	- C4	- C3	=	1.40(3)
C9	- N2	- C4	- N1	=	-23.00(2)
C6	- N2	- C4	- N1	=	-166.62(16)
C9	- N2	- C4	- C3	=	159.34(18)
C6	- N2	- C4	- C3	=	15.80(3)
C2	- C3	- C4	- N1	=	-0.90(3)
C2	- C3	- C4	- N2	=	176.65(17)
C4	- N1	- C5	- C1	=	-1.50(3)
C2	- C1	- C5	- N1	=	1.00(3)
Br1	- C1	- C5	- N1	=	-178.87(15)
C4	- N2	- C6	- C7	=	-164.66(15)
C9	- N2	- C6	- C7	=	49.80(2)

## SUPPORTING INFORMATION

C10	- N3	- C7	- C6	= -178.14(15)
C8	- N3	- C7	- C6	= 60.38(18)
N2	- C6	- C7	- N3	= -55.40(2)
C7	- N3	- C8	- C9	= -61.28(19)
C10	- N3	- C8	- C9	= 177.21(15)
C4	- N2	- C9	- C8	= 163.13(16)
C6	- N2	- C9	- C8	= -51.20(2)
N3	- C8	- C9	- N2	= 57.70(2)
C7	- N3	- C10	- C11	= 61.80(2)
C8	- N3	- C10	- C11	= -179.16(16)
C7	- N3	- C10	- C14	= 178.28(16)
C8	- N3	- C10	- C14	= -62.70(2)
N3	- C10	- C11	- C12	= 163.64(16)
C14	- C10	- C11	- C12	= 40.90(2)
C10	- C11	- C12	- C13	= -34.60(2)
C11	- C12	- C13	- C14	= 14.60(3)
N3	- C10	- C14	- C13	= -154.44(18)
C11	- C10	- C14	- C13	= -31.50(2)
C12	- C13	- C14	- C10	= 10.70(3)

## Structure visualization

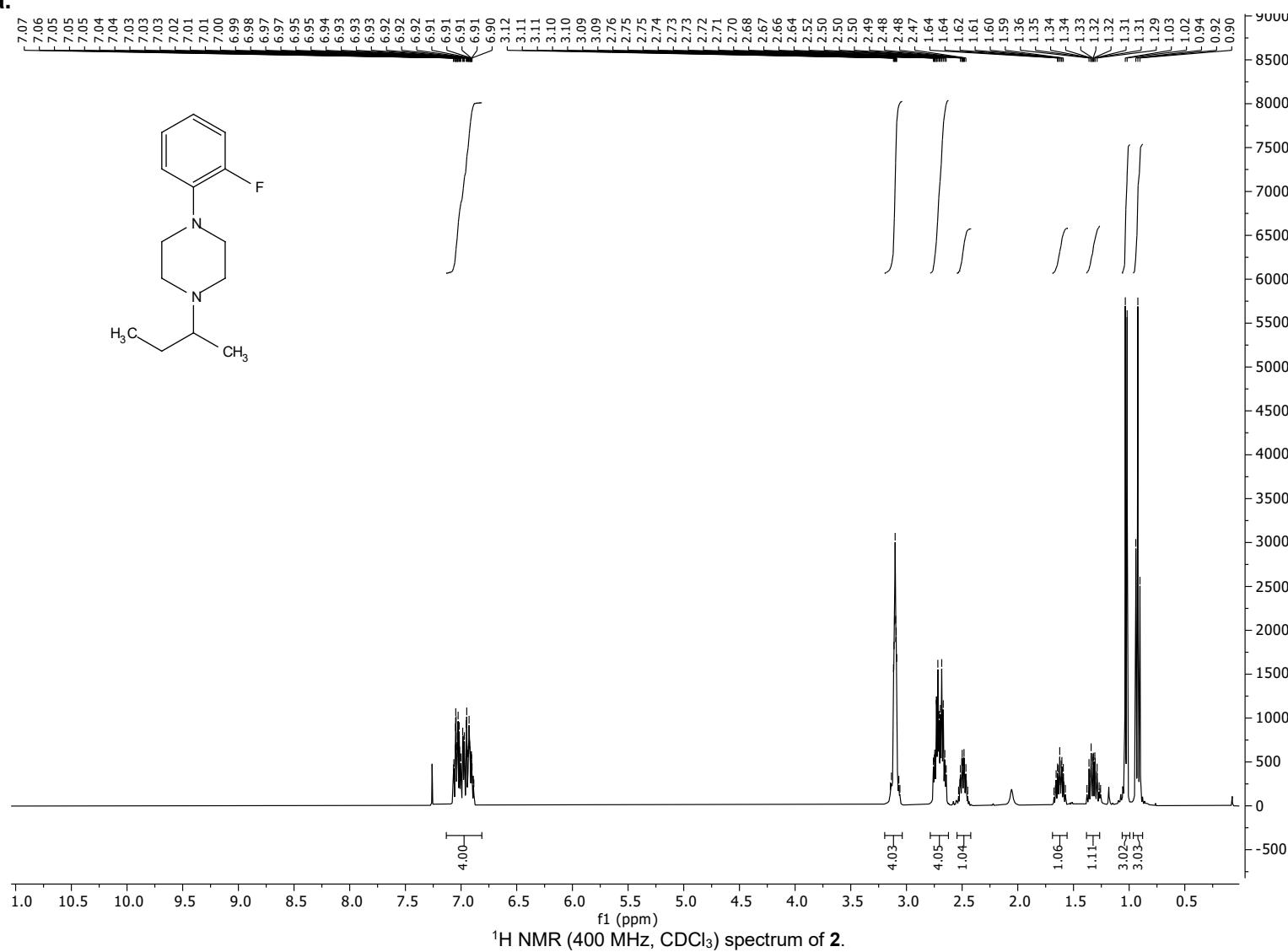


**SUPPORTING INFORMATION****14. References.**

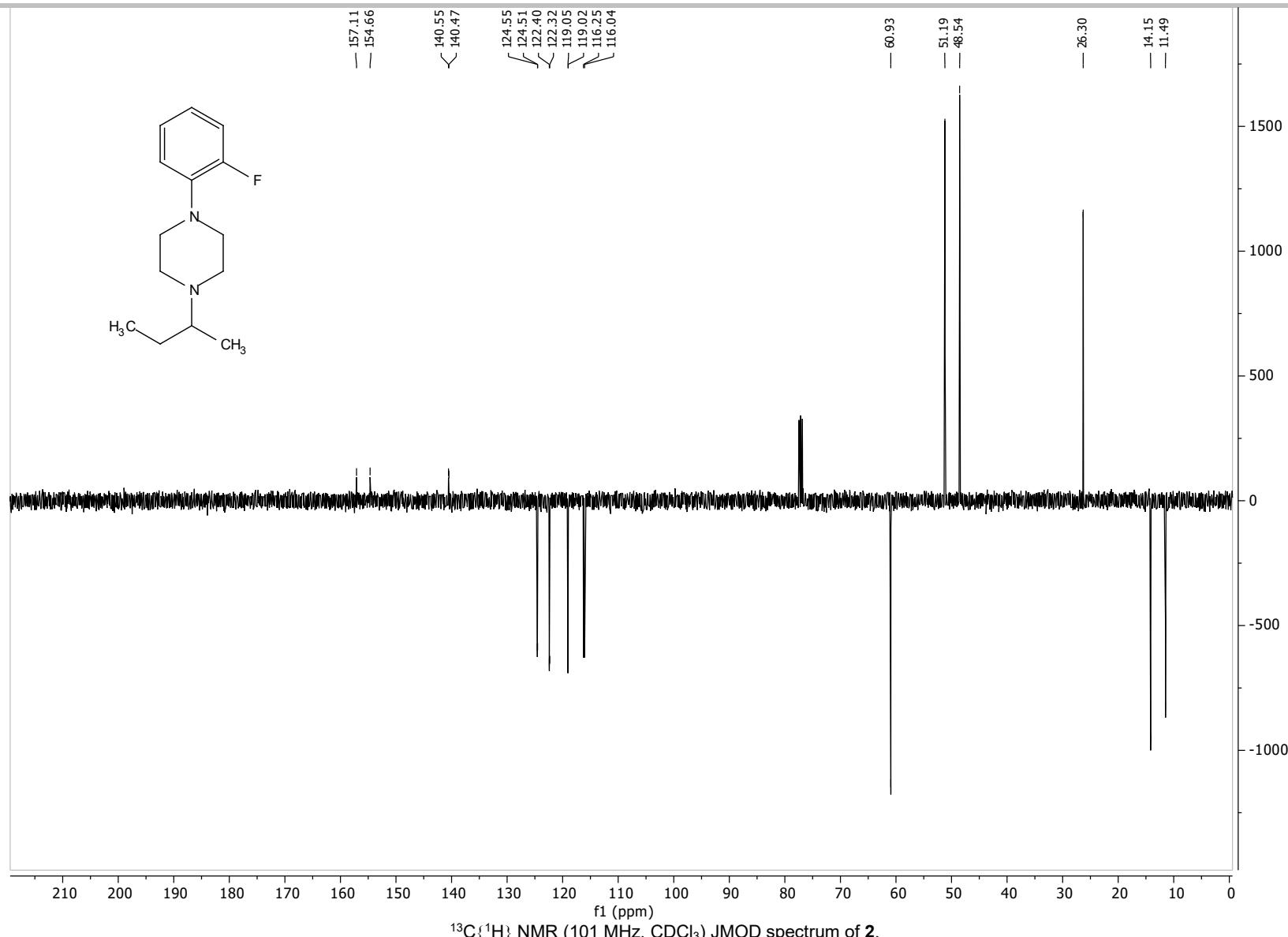
- [1] Z. Chen, H. Zeng, H. Gong, H. Wang, C.-J. Li, *Chem. Sci.* **2015**, *6*, 4174–4178.
- [2] N. Z. Yagafarov, P. N. Kolesnikov, D. L. Usanov, V. V. Novikov, Y. V. Nelyubina, D. Chusov, *Chem. Commun.* **2016**, *52*, 1397–1400.
- [3] H. Reed, T. R. Paul, W. J. Chain, *J. Org. Chem.* **2018**, *83*, 11359–11368.
- [4] Y. Y. Loh, K. Nagao, A. J. Hoover, D. Hesk, N. R. Rivera, S. L. Collettilan, I. W. Davies, D.W.C. Macmillan, *Science* **2017**, *358*, 1182–1187.

## SUPPORTING INFORMATION

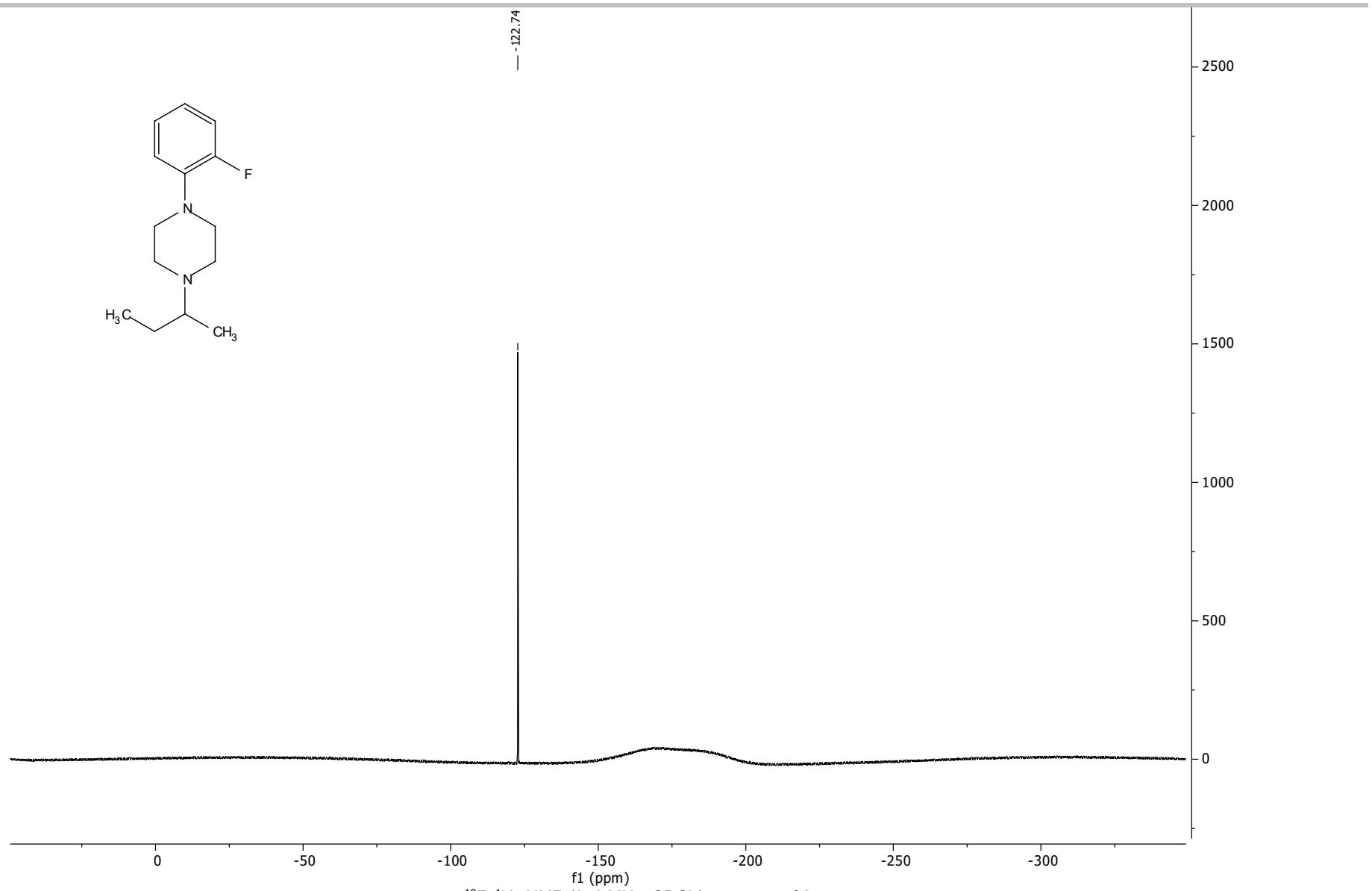
## 15. NMR data.



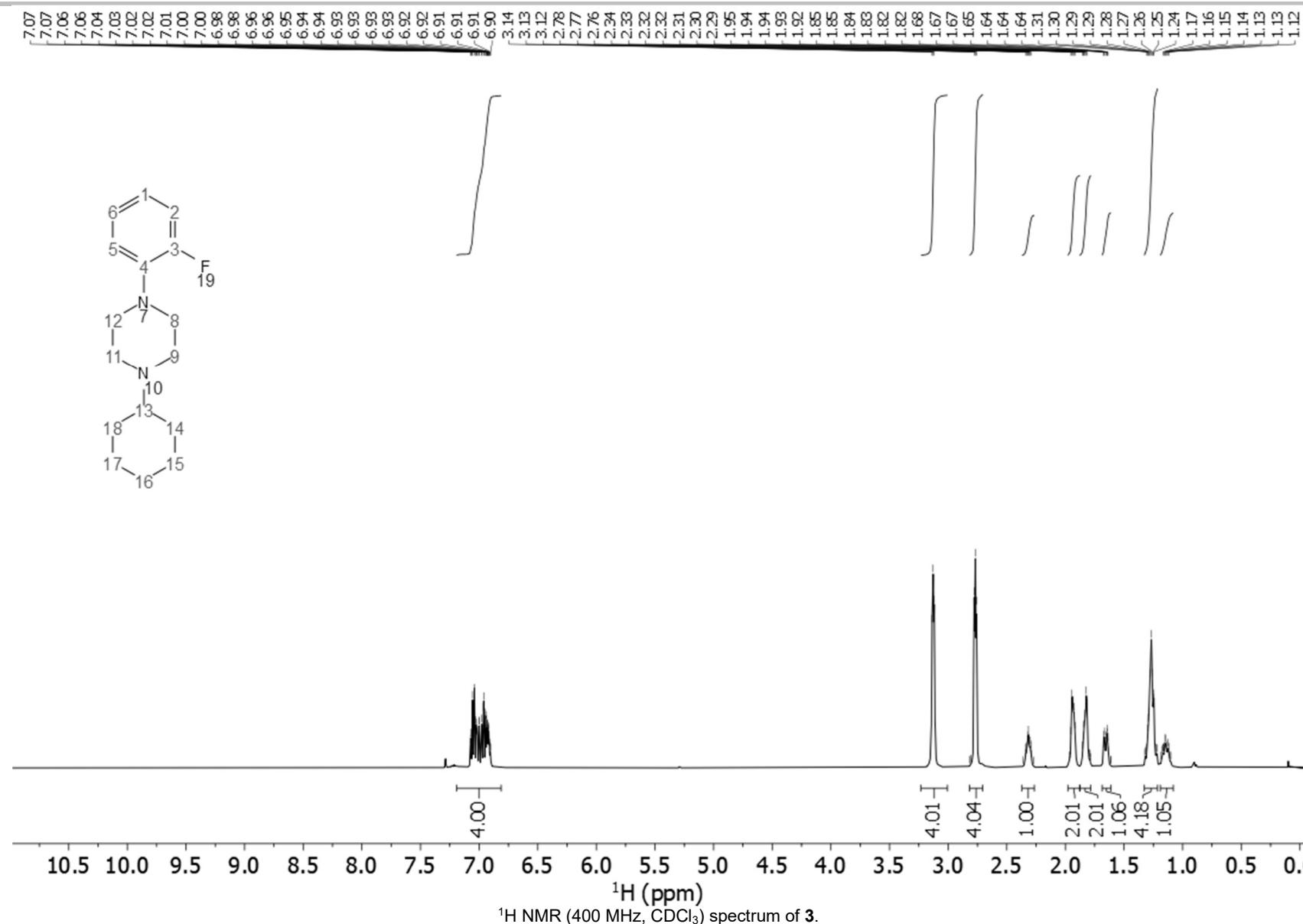
## SUPPORTING INFORMATION

 $^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ) JMOD spectrum of **2**.

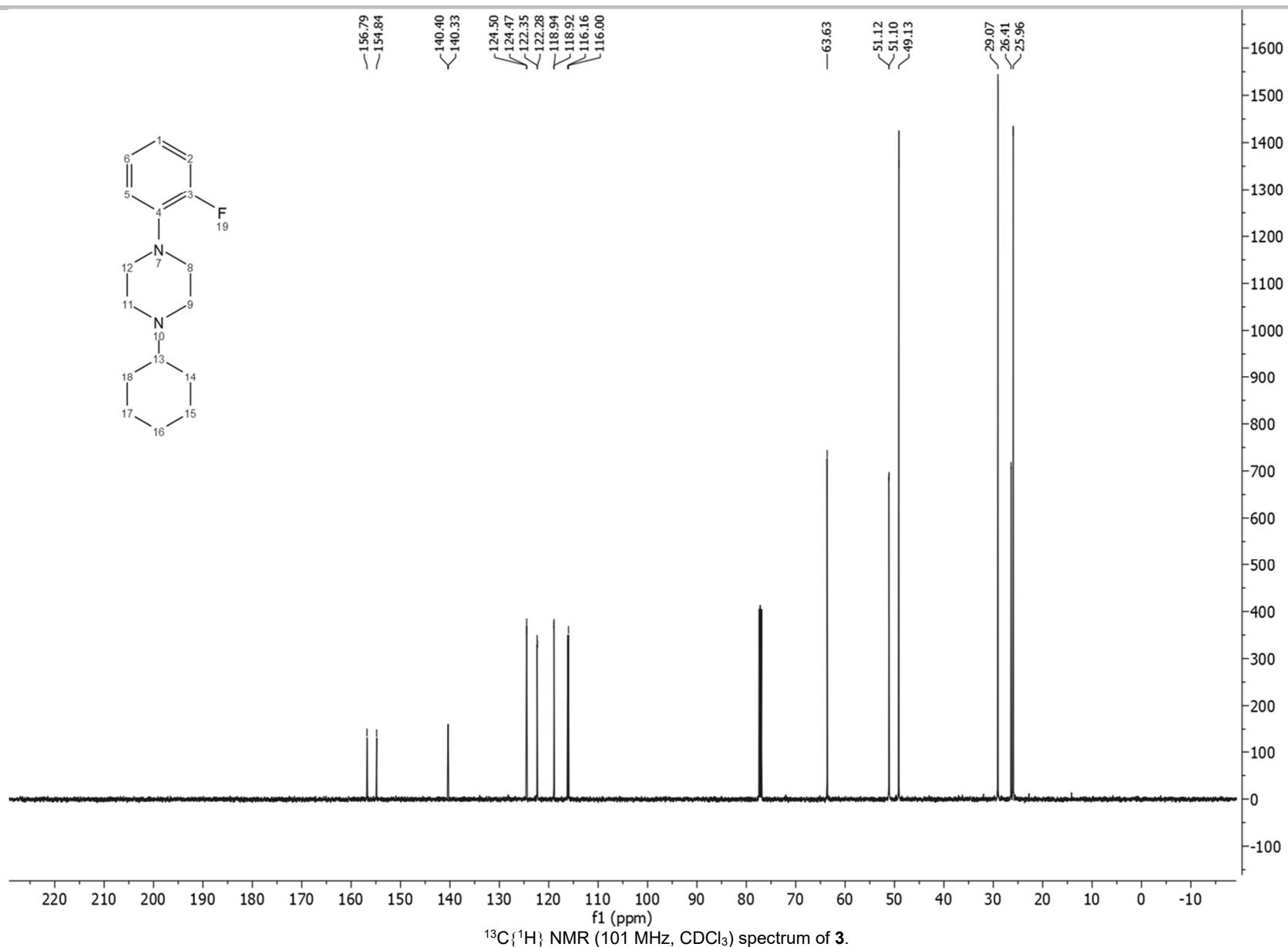
## SUPPORTING INFORMATION

 $^{19}\text{F}\{\text{H}\}$  NMR (376 MHz,  $\text{CDCl}_3$ ) spectrum of **2**.

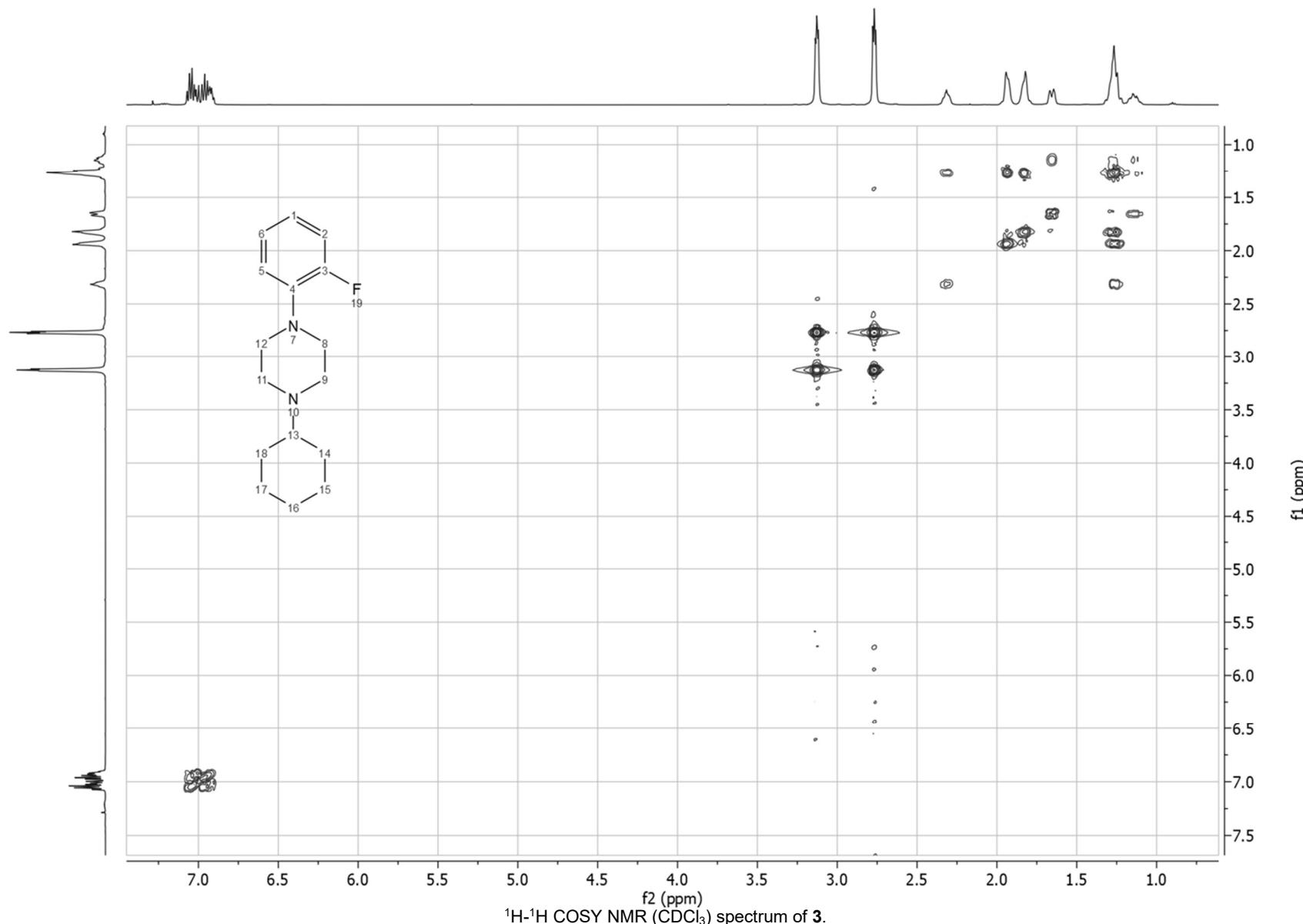
## SUPPORTING INFORMATION



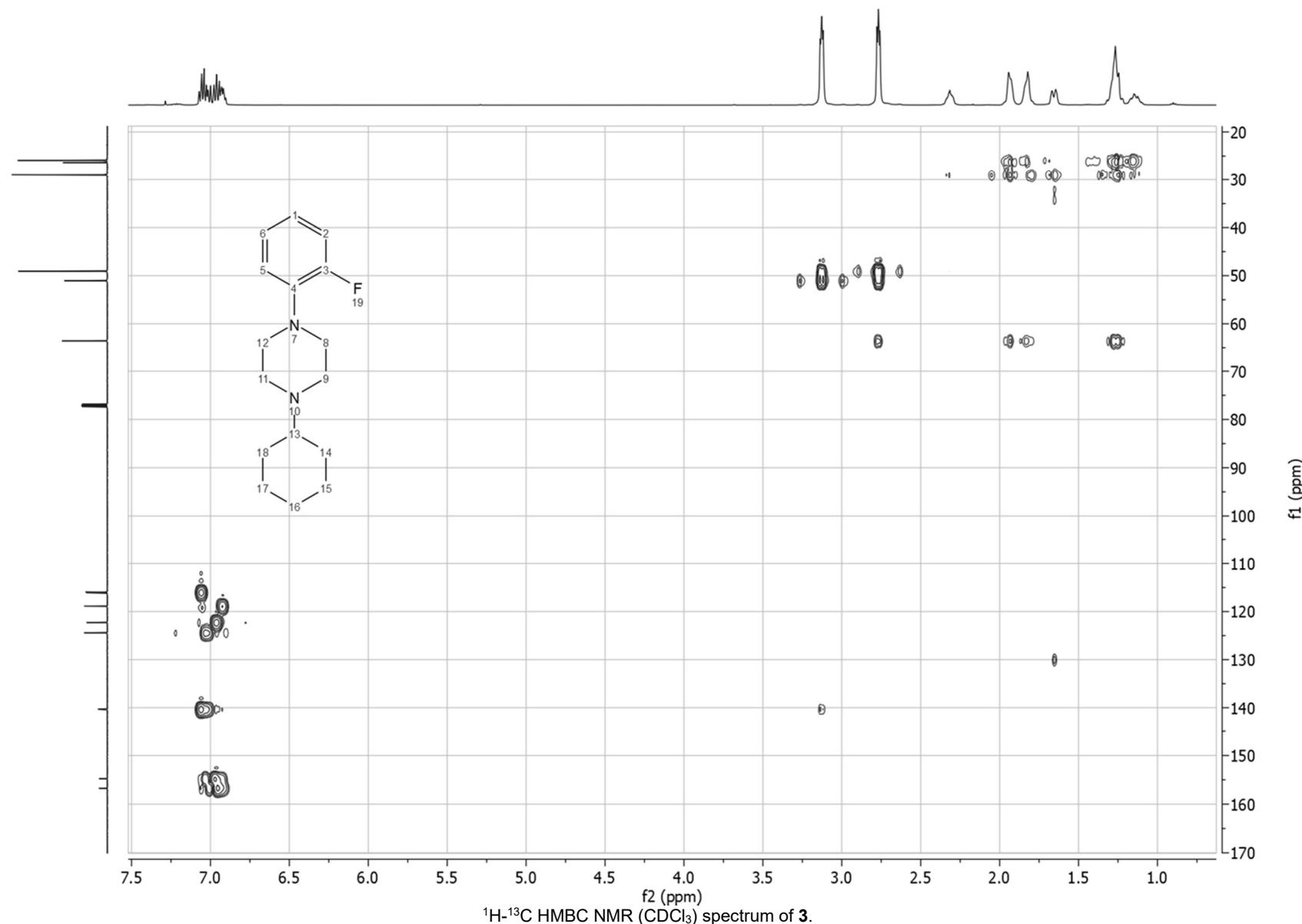
## SUPPORTING INFORMATION



## SUPPORTING INFORMATION

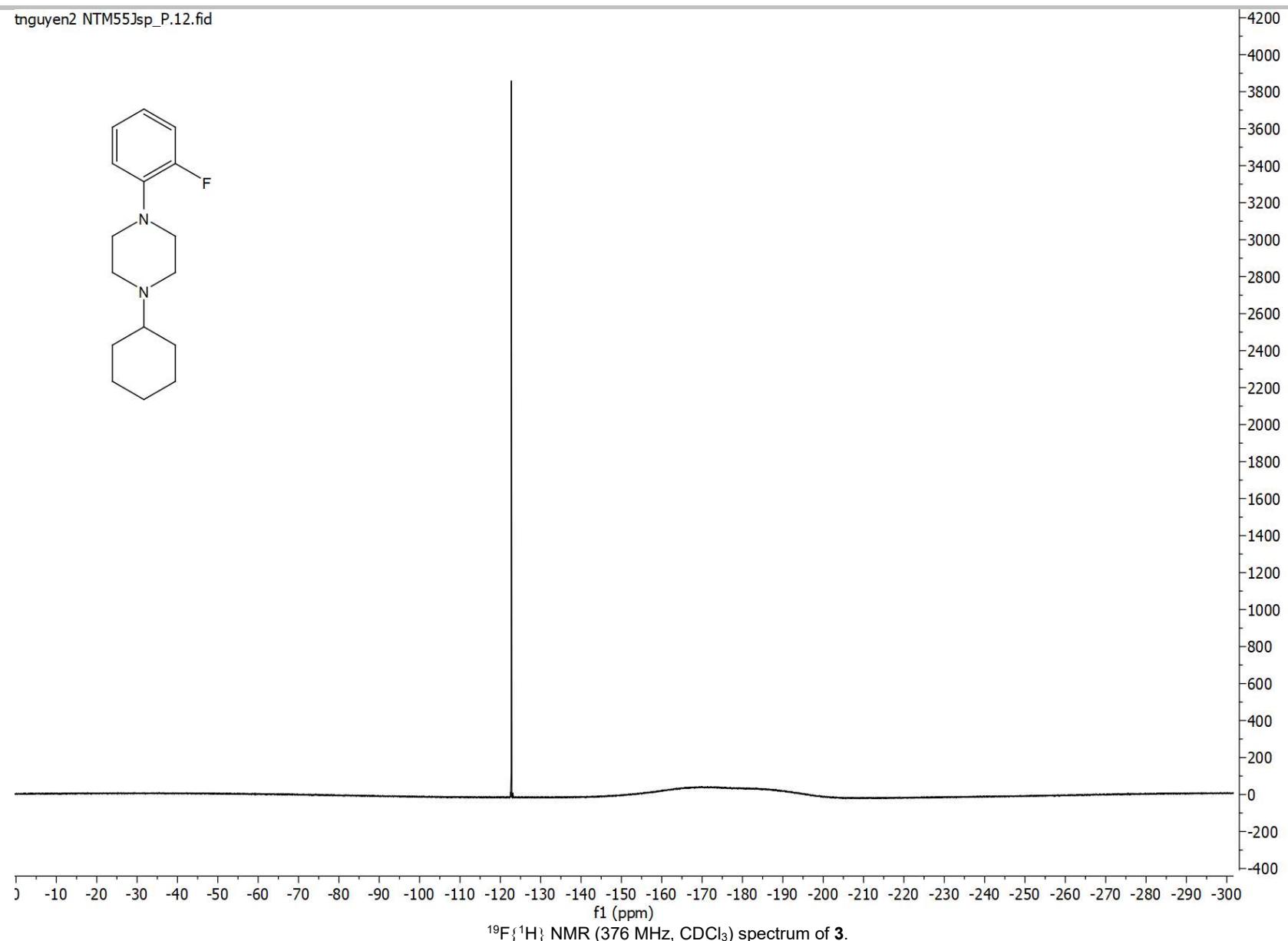
 $^1\text{H}$ - $^1\text{H}$  COSY NMR ( $\text{CDCl}_3$ ) spectrum of **3**.

## SUPPORTING INFORMATION

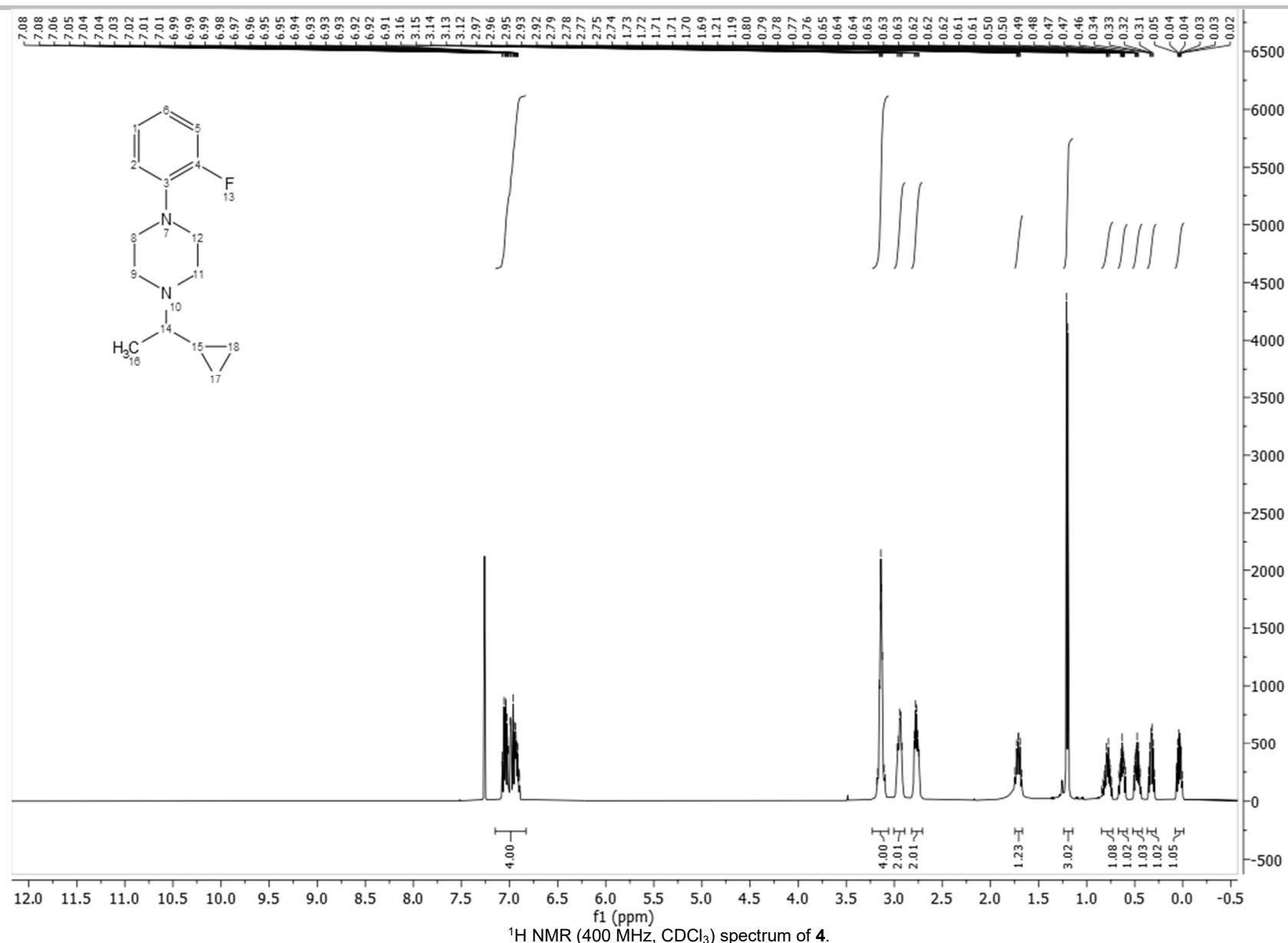


## SUPPORTING INFORMATION

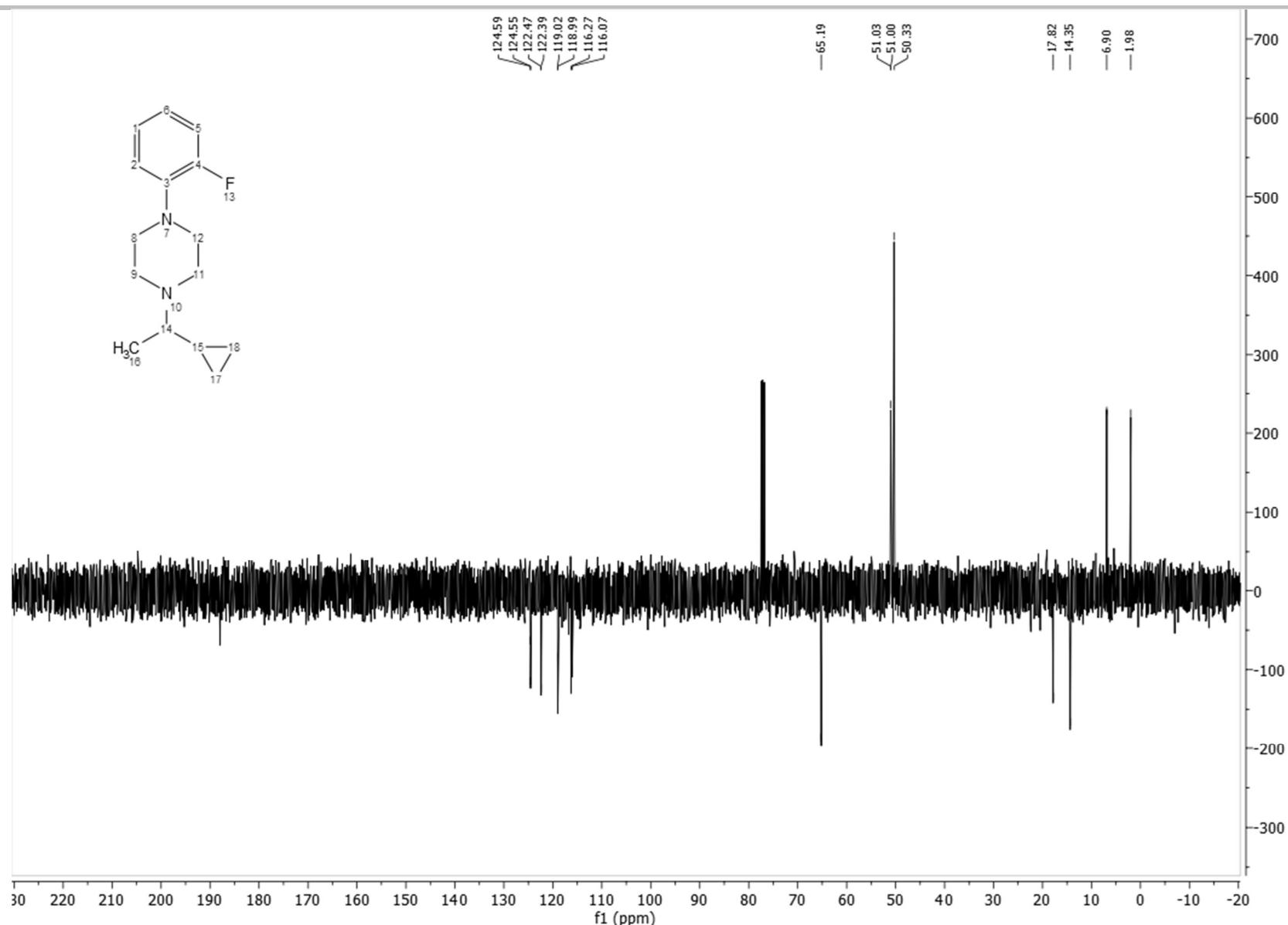
tnguyen2 NTM55Jsp\_P.12.fid



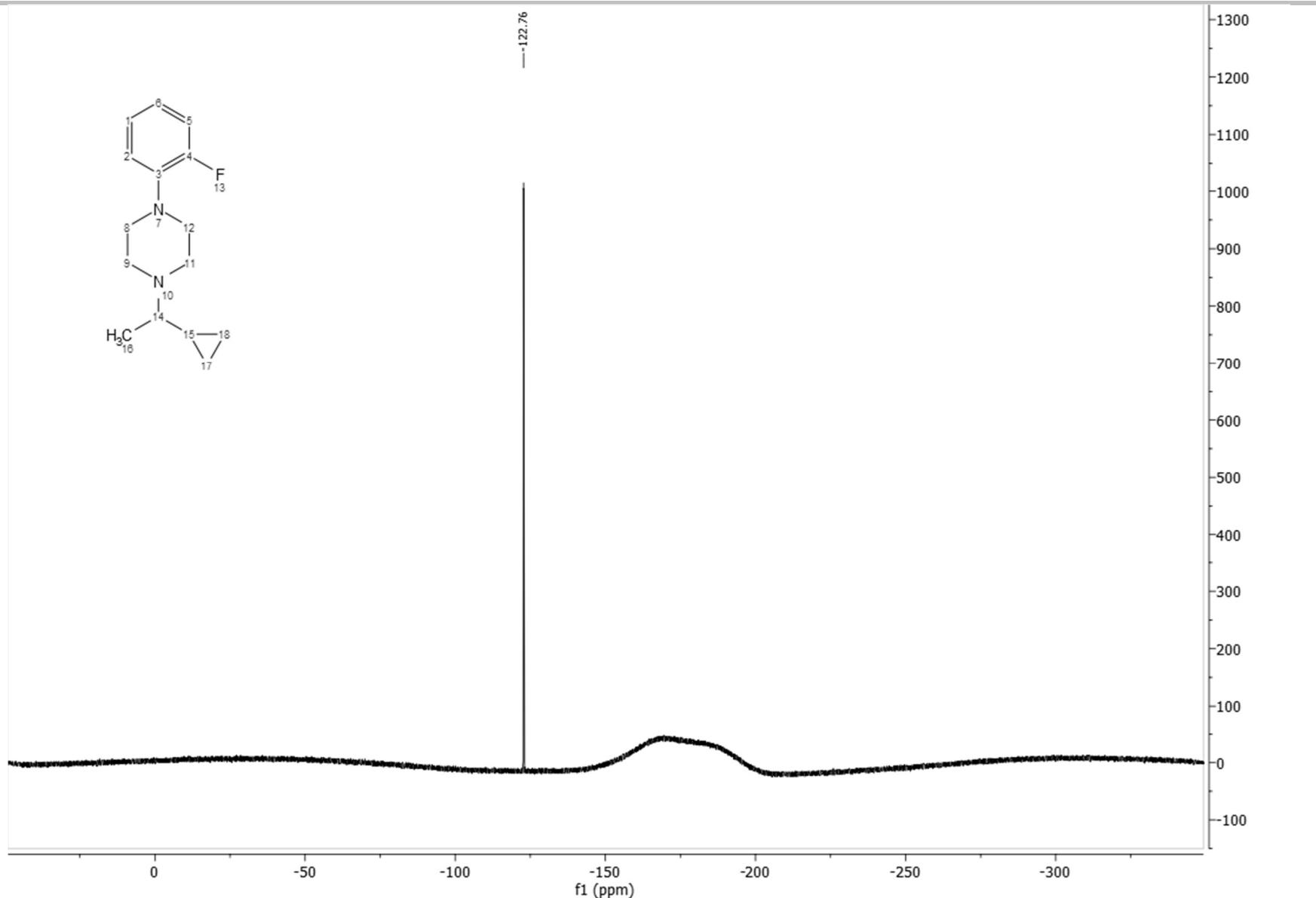
## SUPPORTING INFORMATION



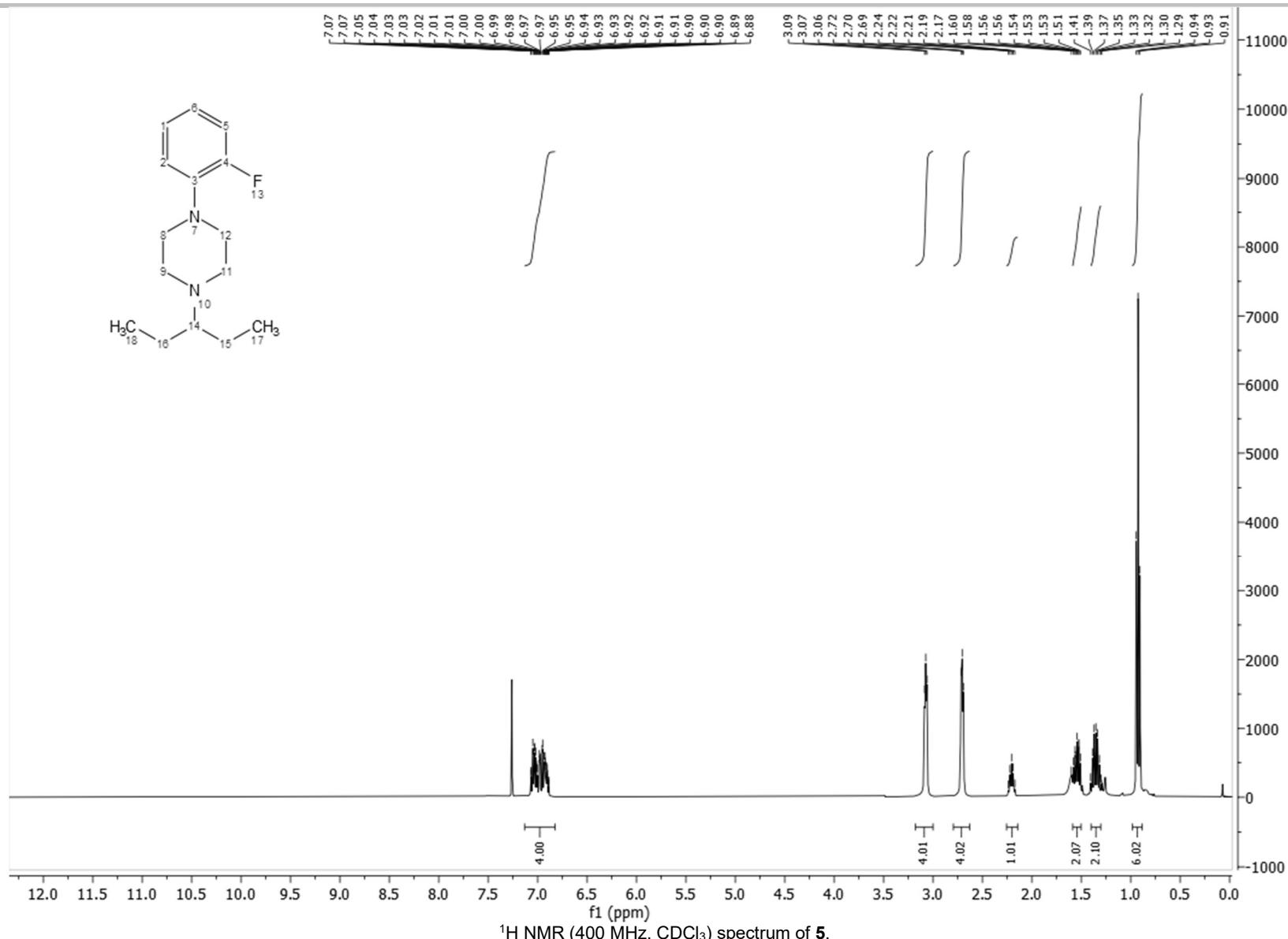
## SUPPORTING INFORMATION

 $^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ) JMOD spectrum of **4**.

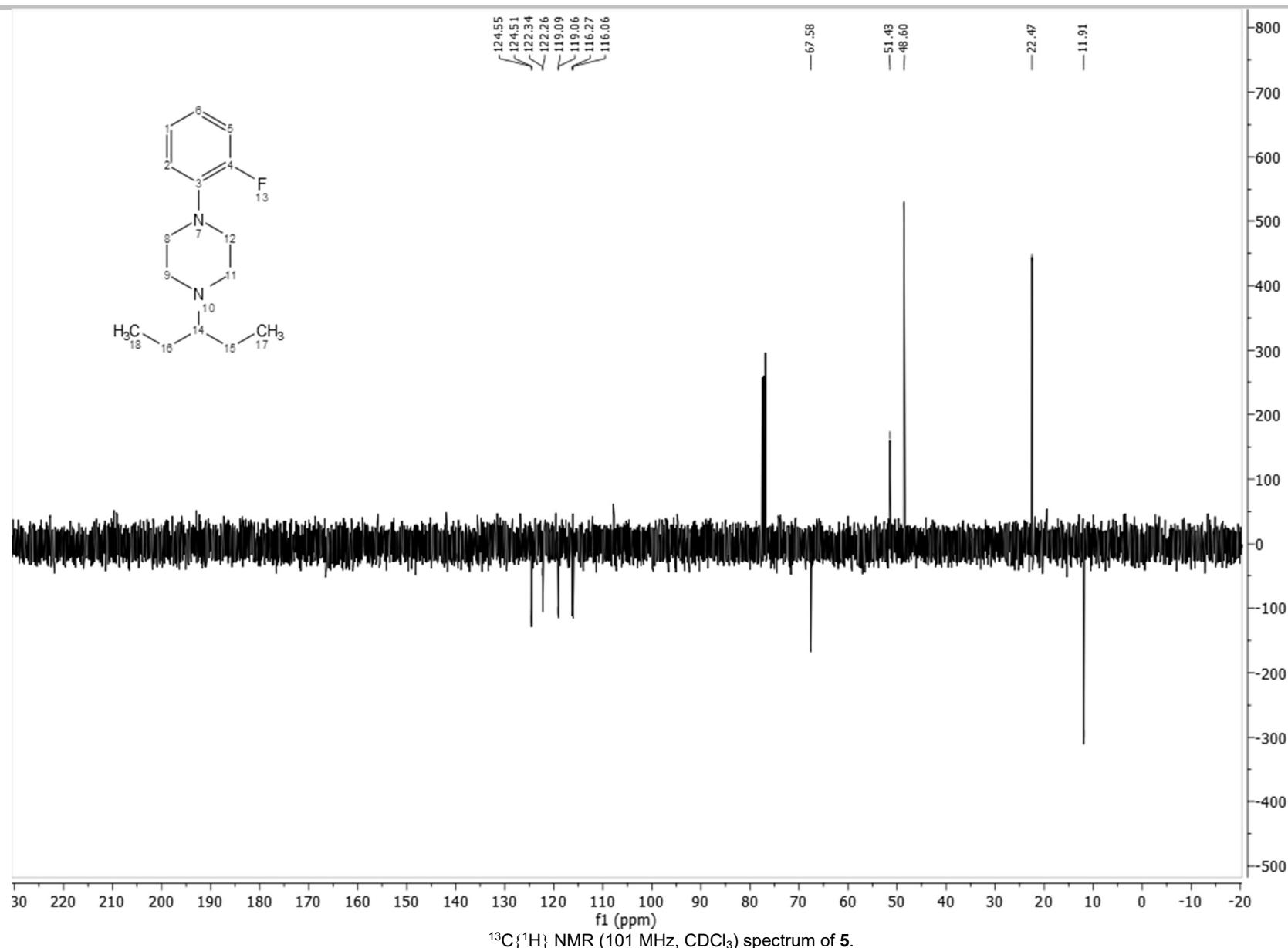
## SUPPORTING INFORMATION

 $^{19}\text{F}\{\text{H}\}$  NMR (376 MHz,  $\text{CDCl}_3$ ) spectrum of **4**.

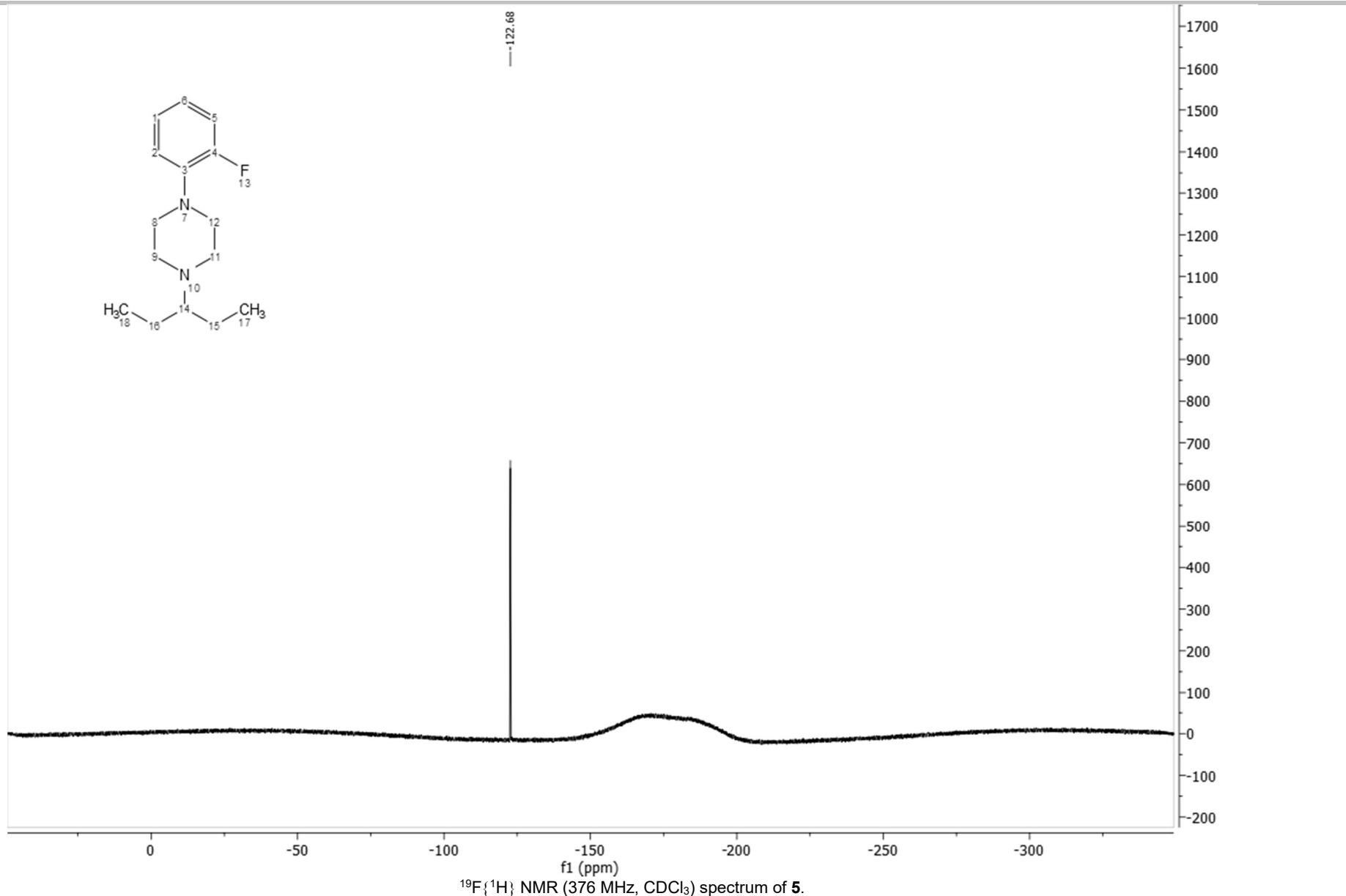
## SUPPORTING INFORMATION



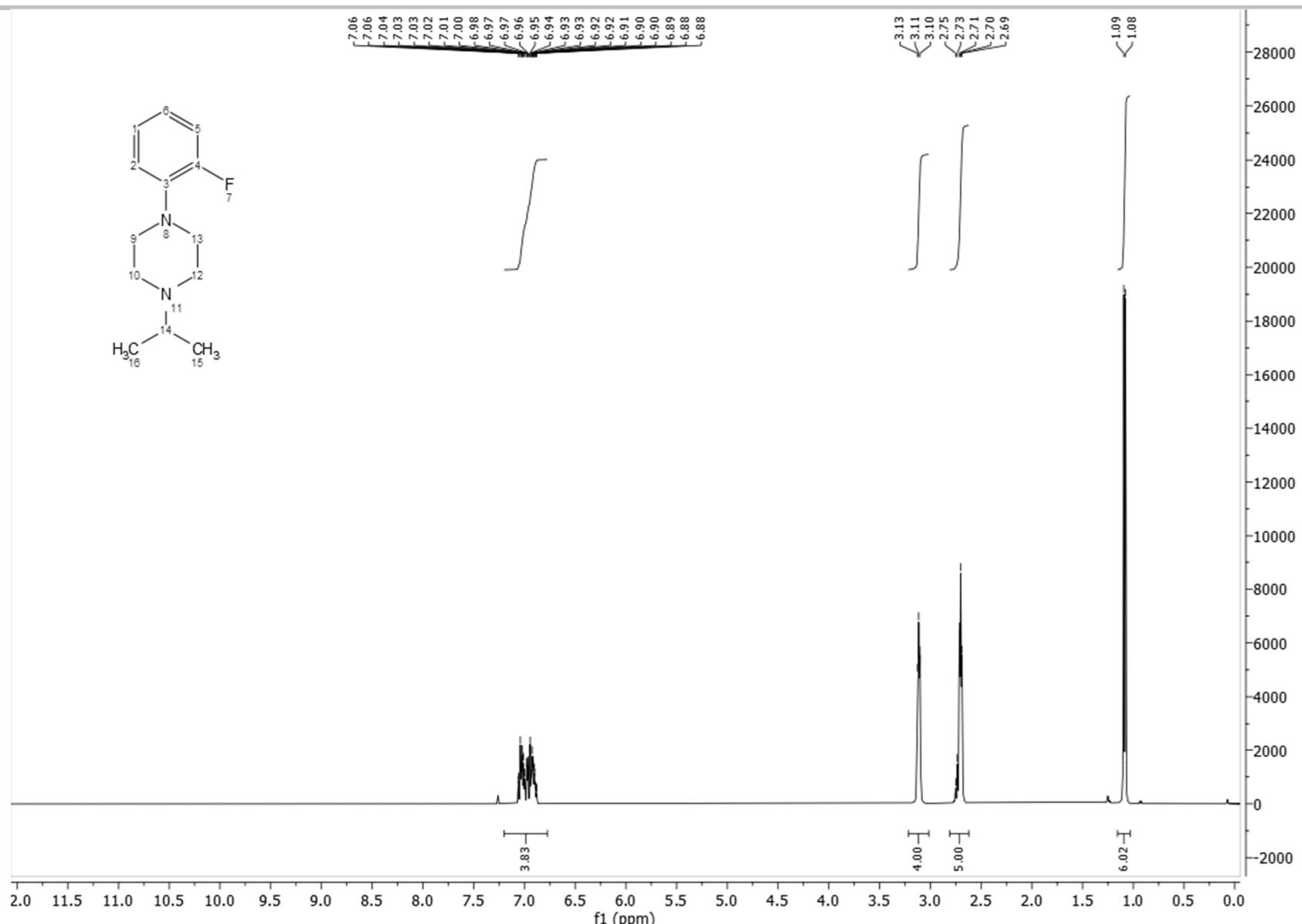
## SUPPORTING INFORMATION



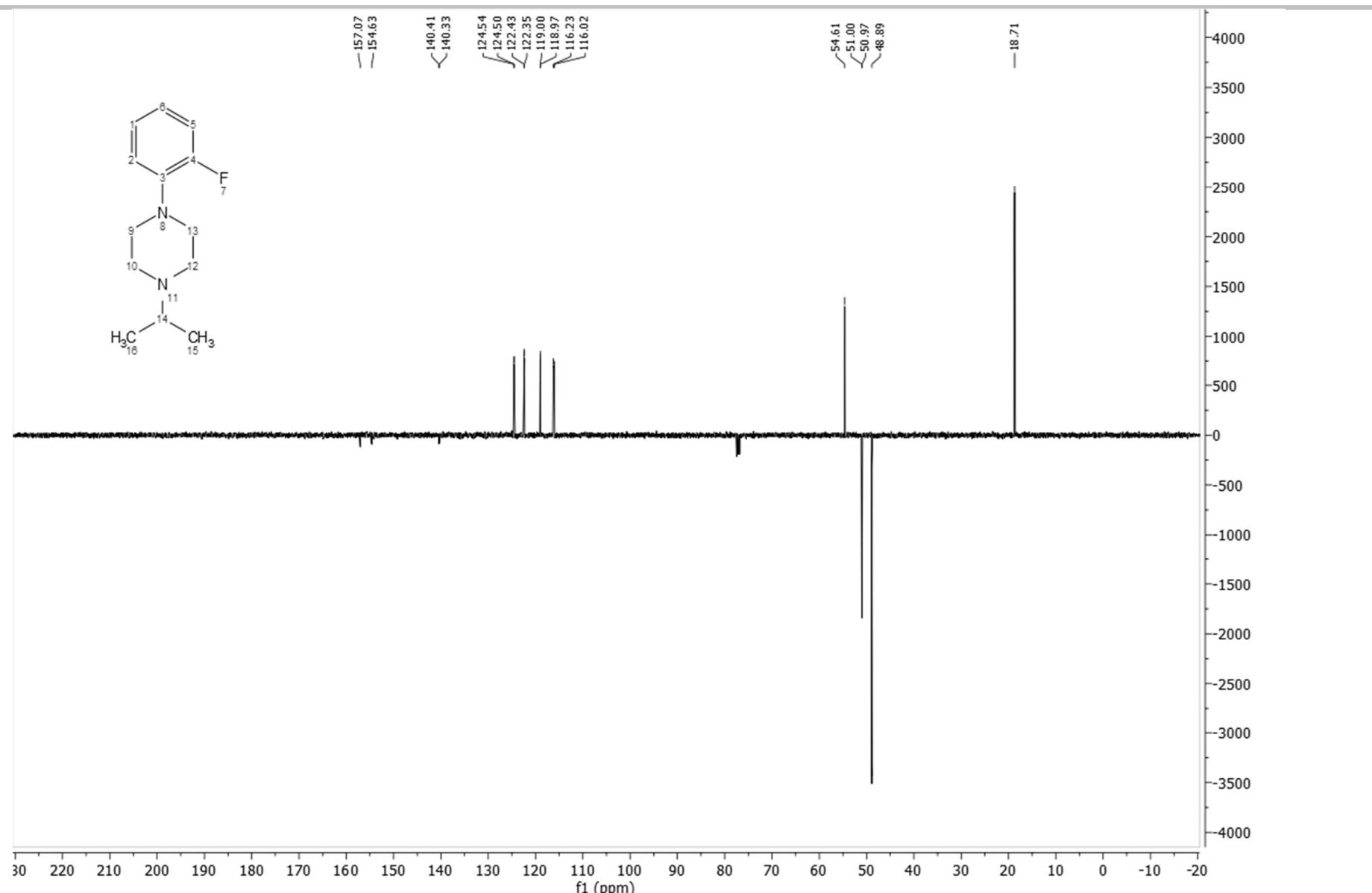
## SUPPORTING INFORMATION

 $^{19}\text{F}\{\text{H}\}$  NMR (376 MHz,  $\text{CDCl}_3$ ) spectrum of **5**.

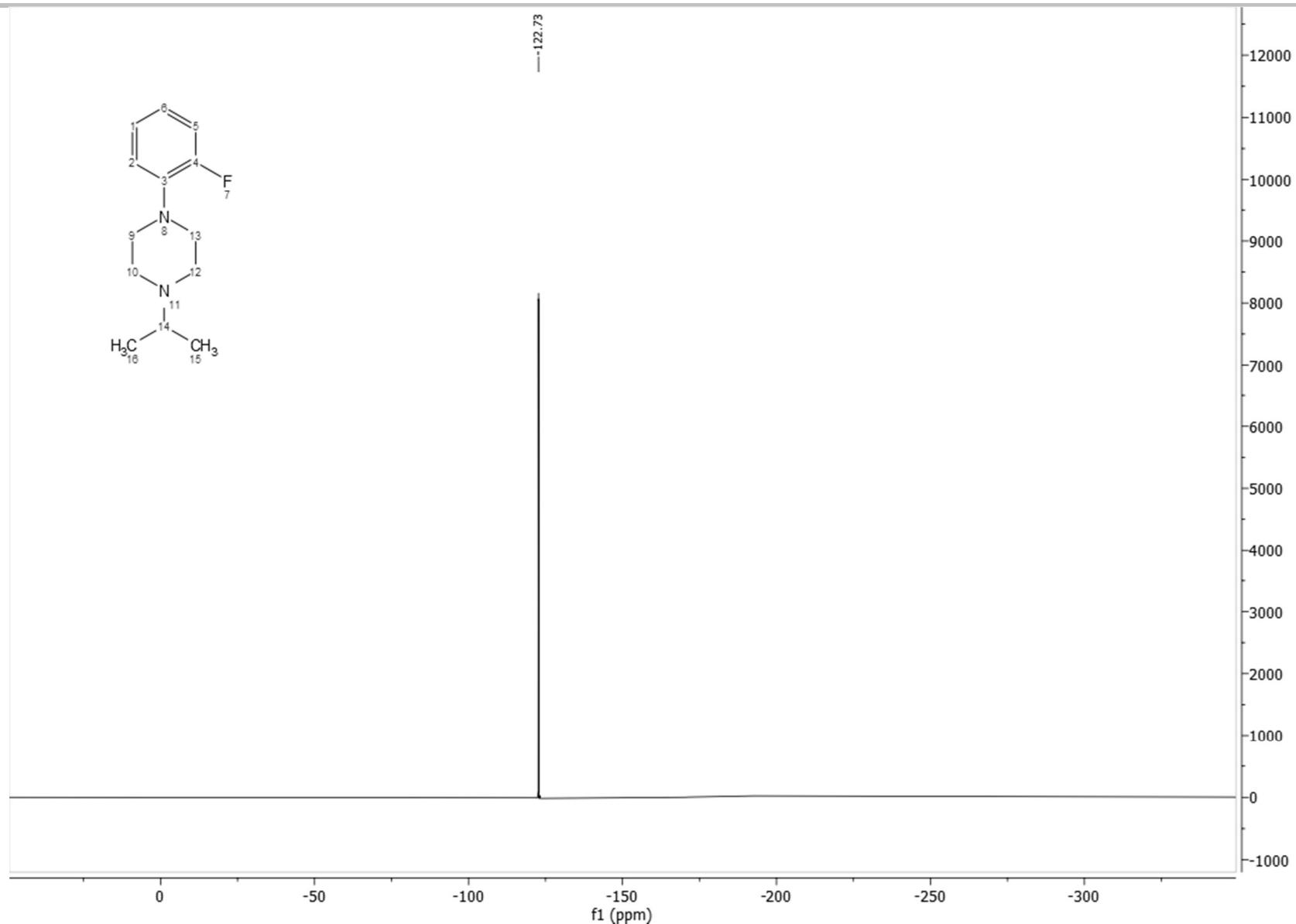
## SUPPORTING INFORMATION

 $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) spectrum of **6**.

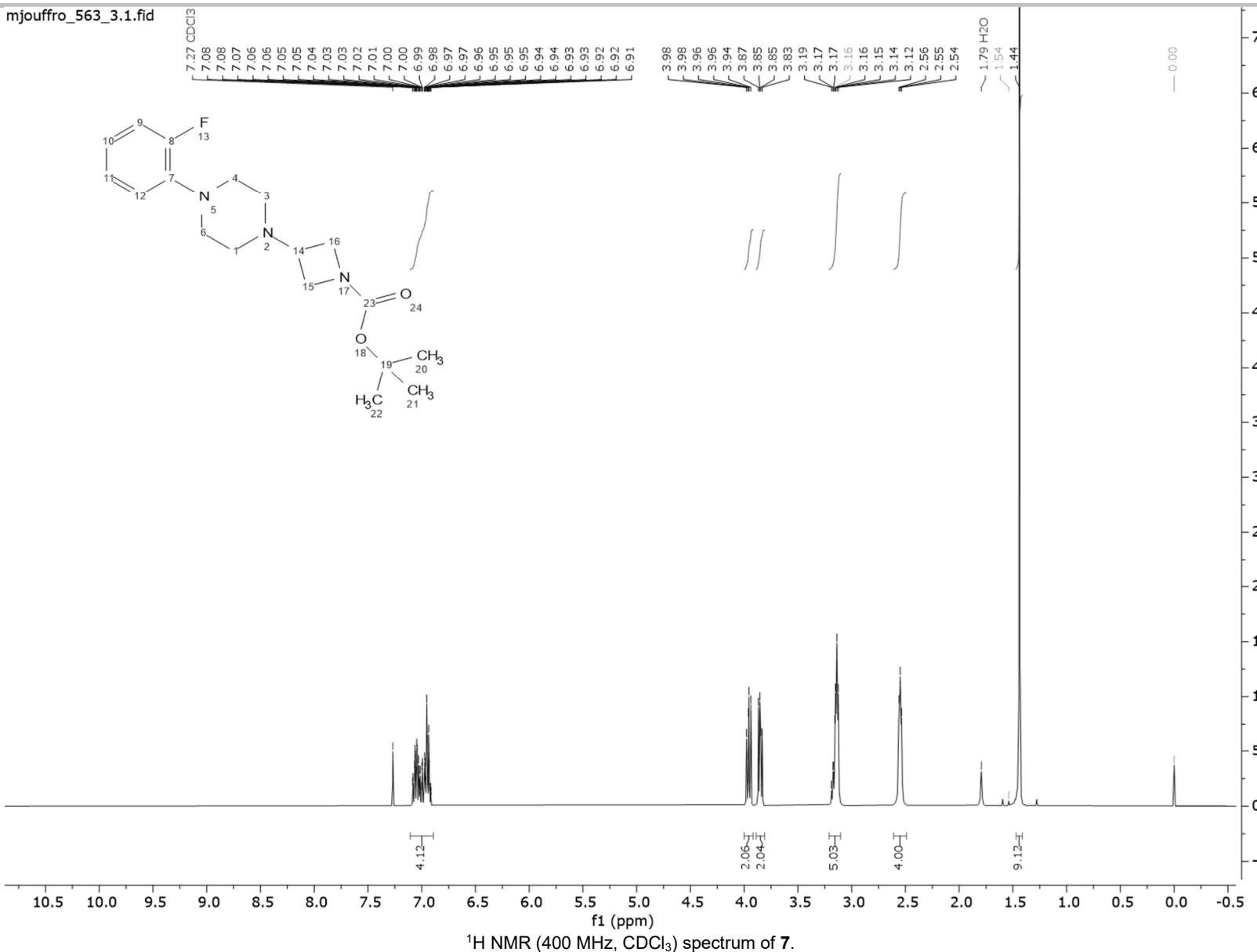
## SUPPORTING INFORMATION

 $^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ) JMOD spectrum of **6**.

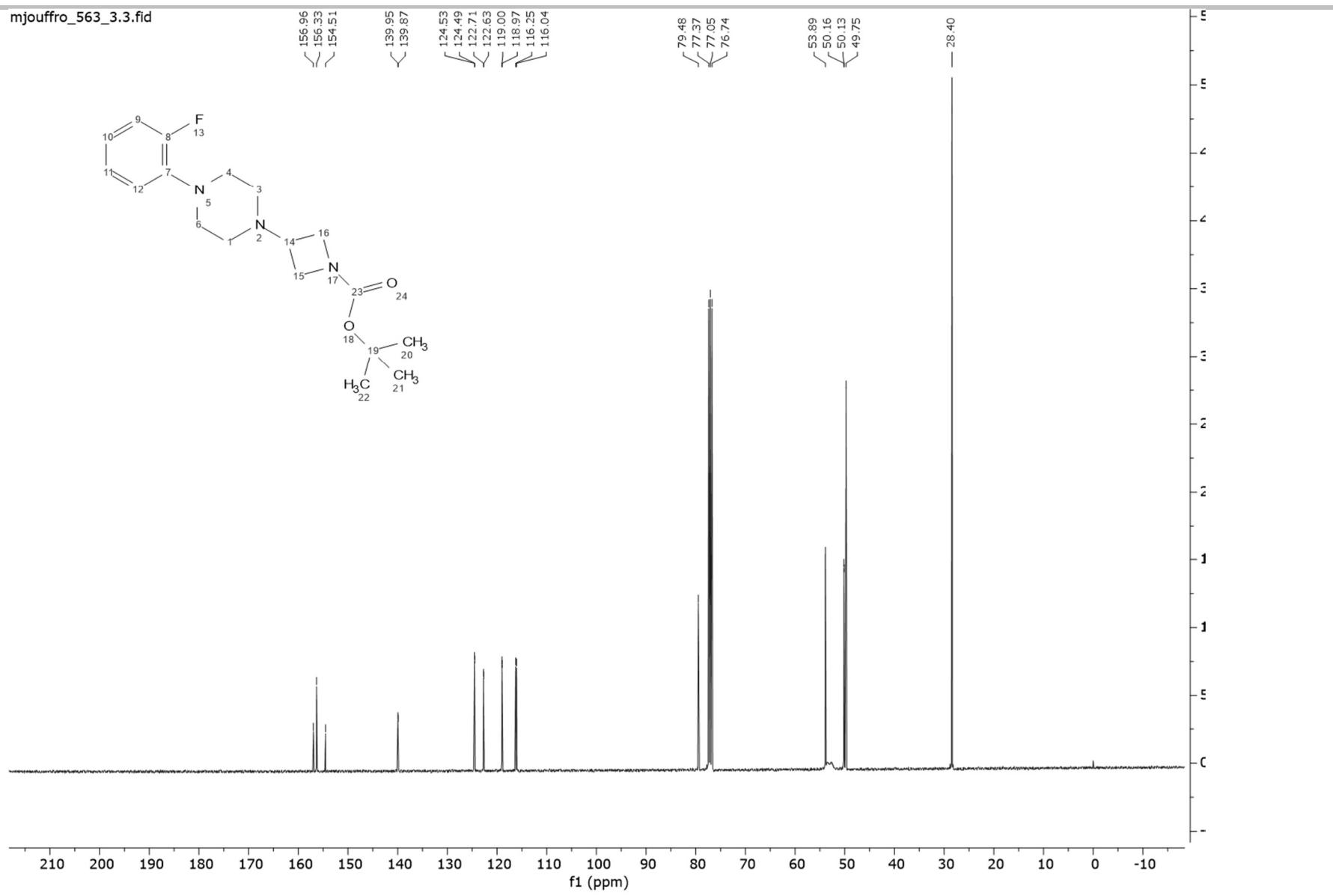
## SUPPORTING INFORMATION

 $^{19}\text{F}\{\text{H}\}$  NMR (376 MHz,  $\text{CDCl}_3$ ) spectrum of **6**.

## SUPPORTING INFORMATION

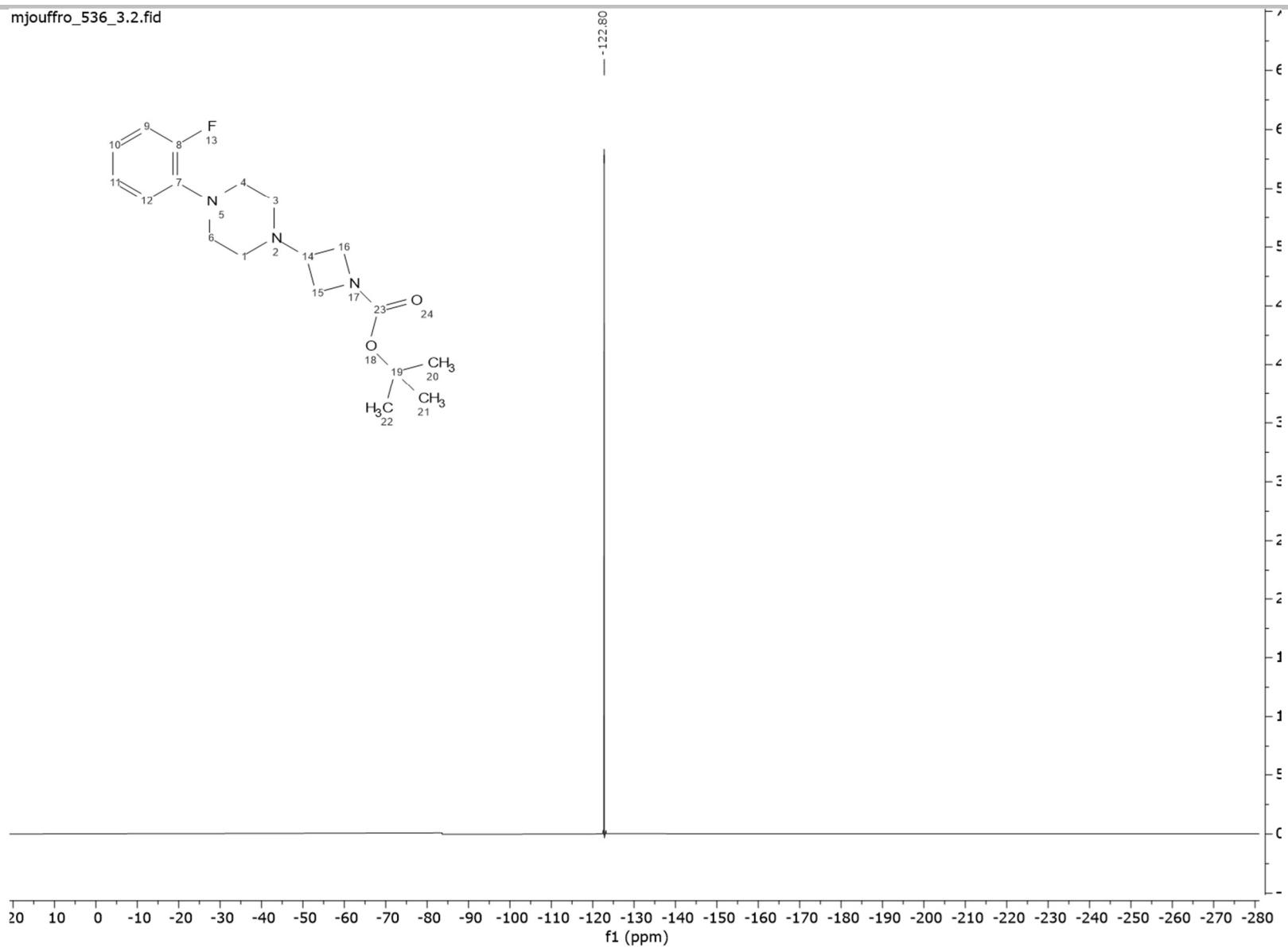


## SUPPORTING INFORMATION

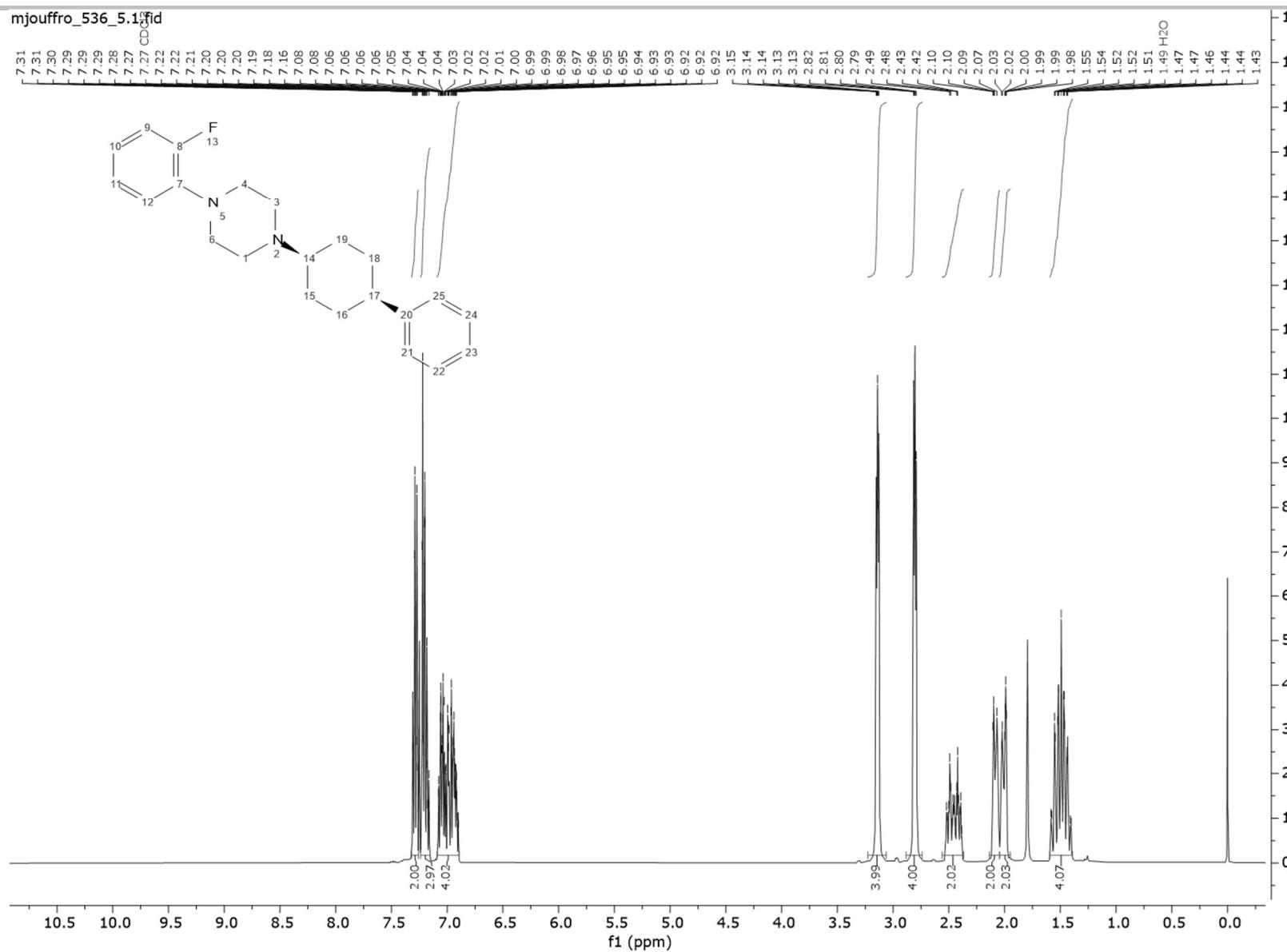


## SUPPORTING INFORMATION

mjouffro\_536\_3.2.fid

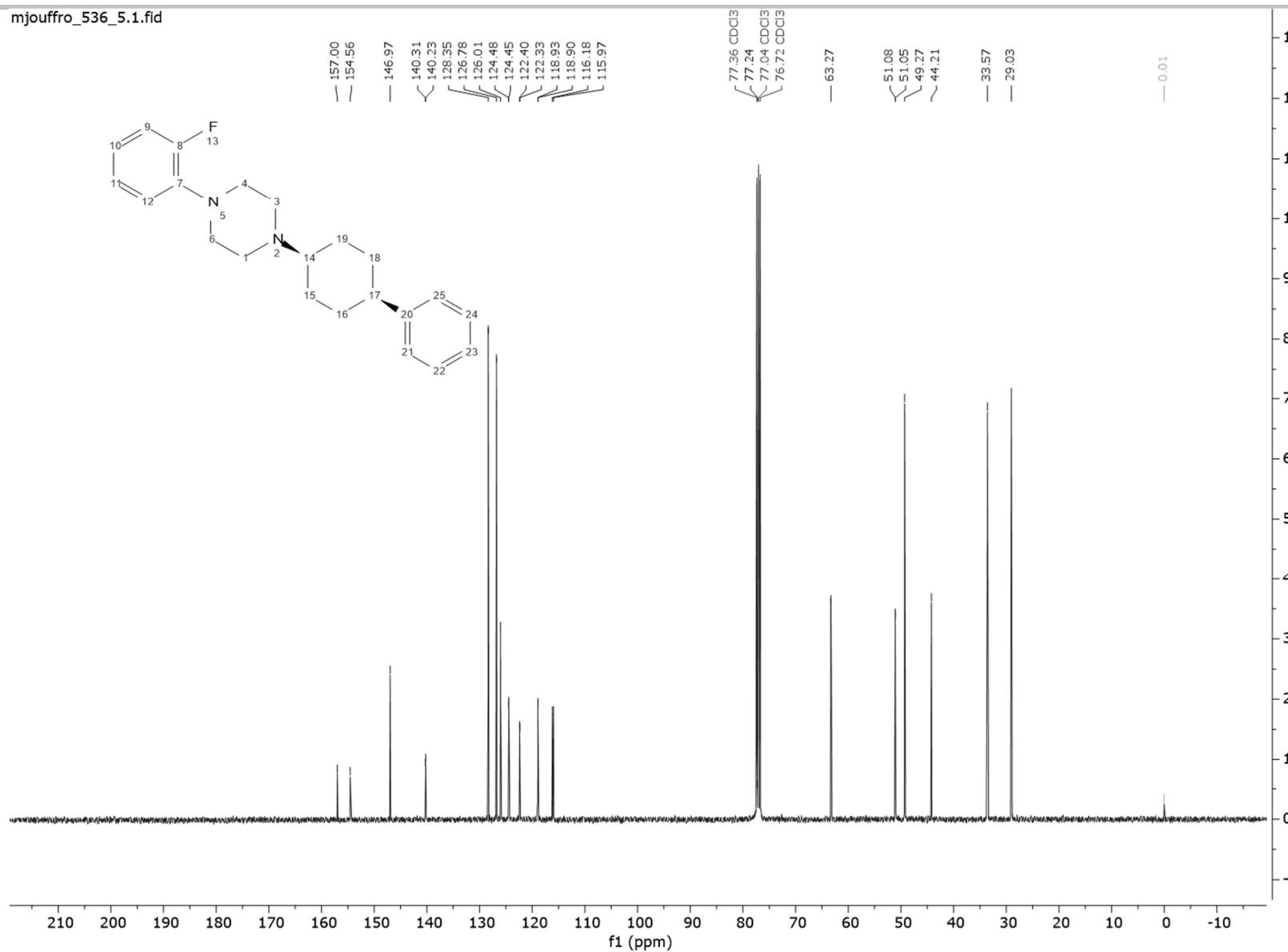
 $^{19}\text{F}\{\text{H}\}$  NMR (376 MHz,  $\text{CDCl}_3$ ) spectrum of 7.

## SUPPORTING INFORMATION



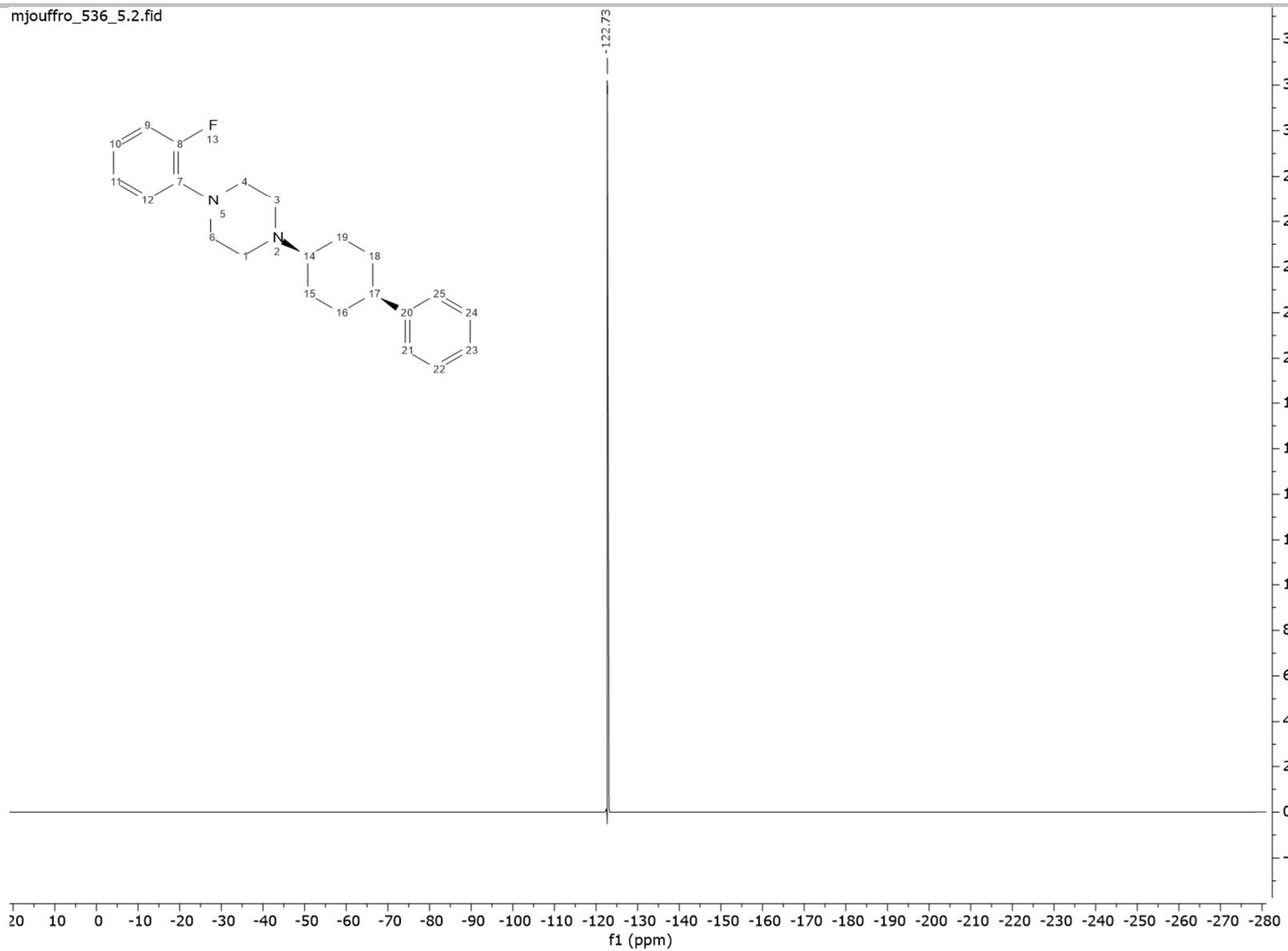
## SUPPORTING INFORMATION

mjouffro\_536\_5.1.fid

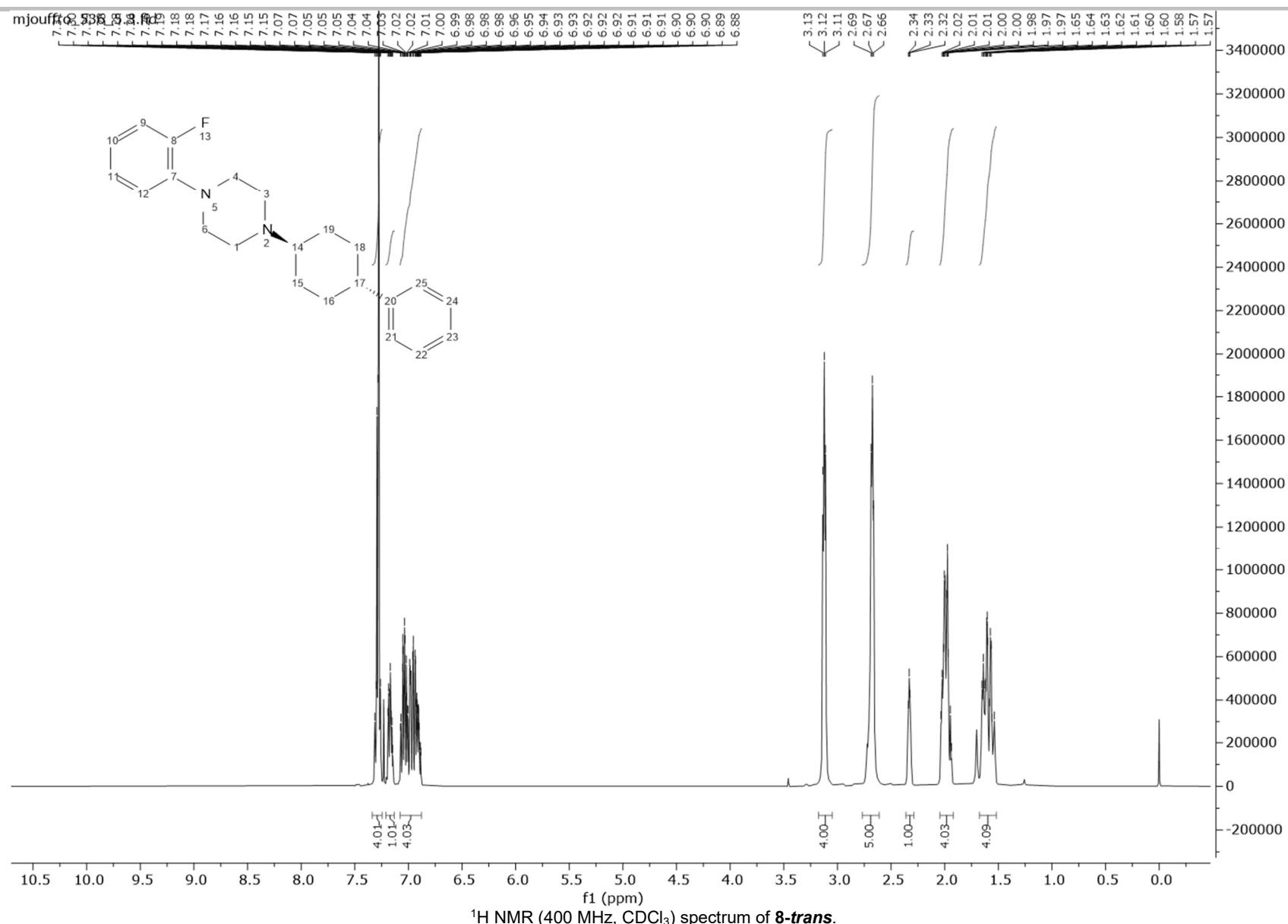


## SUPPORTING INFORMATION

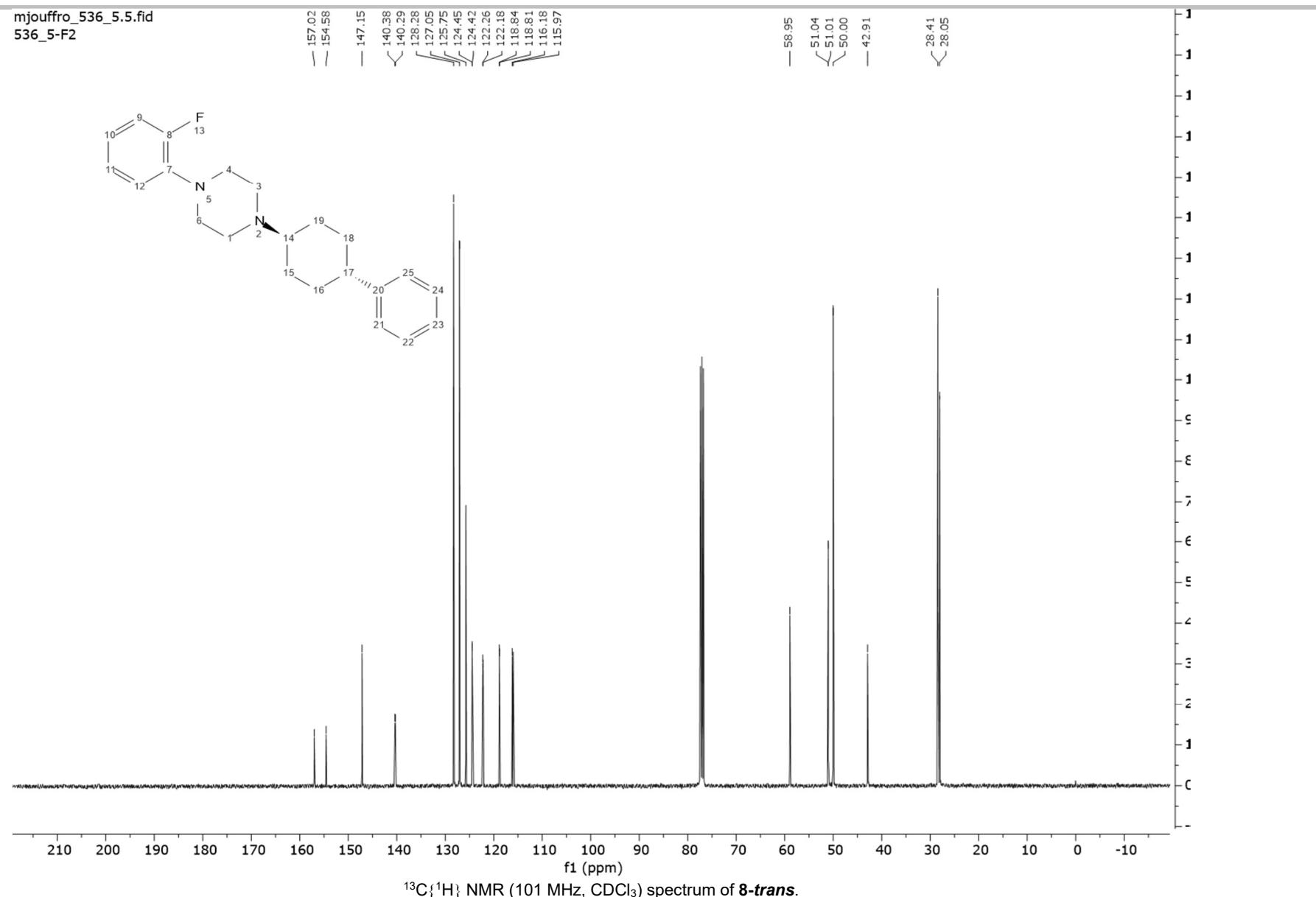
mjouffro\_536\_5.2.fid

 $^{19}\text{F}\{\text{H}\}$  NMR (376 MHz,  $\text{CDCl}_3$ ) spectrum of **8-cis**.

## SUPPORTING INFORMATION

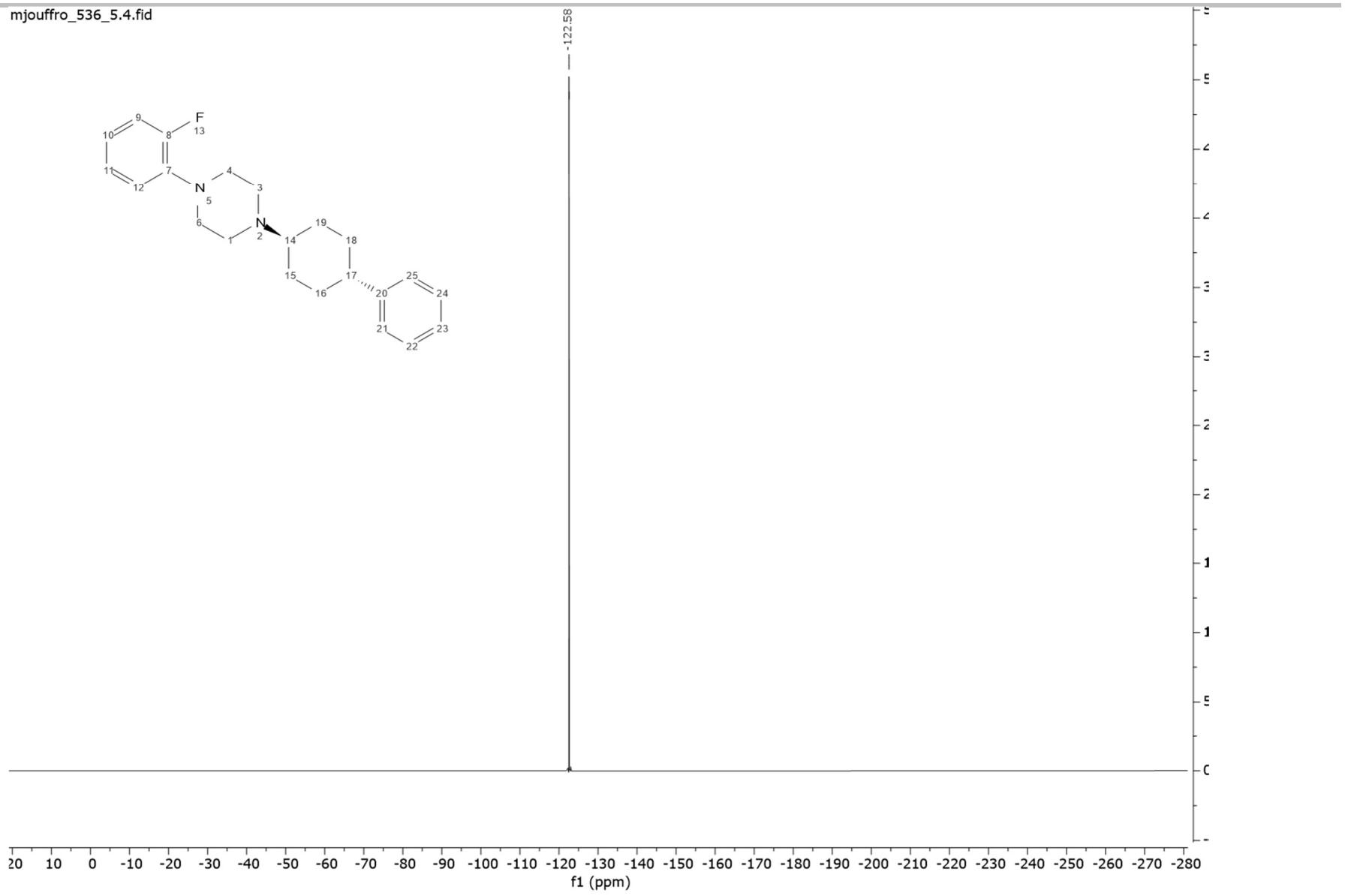


## SUPPORTING INFORMATION



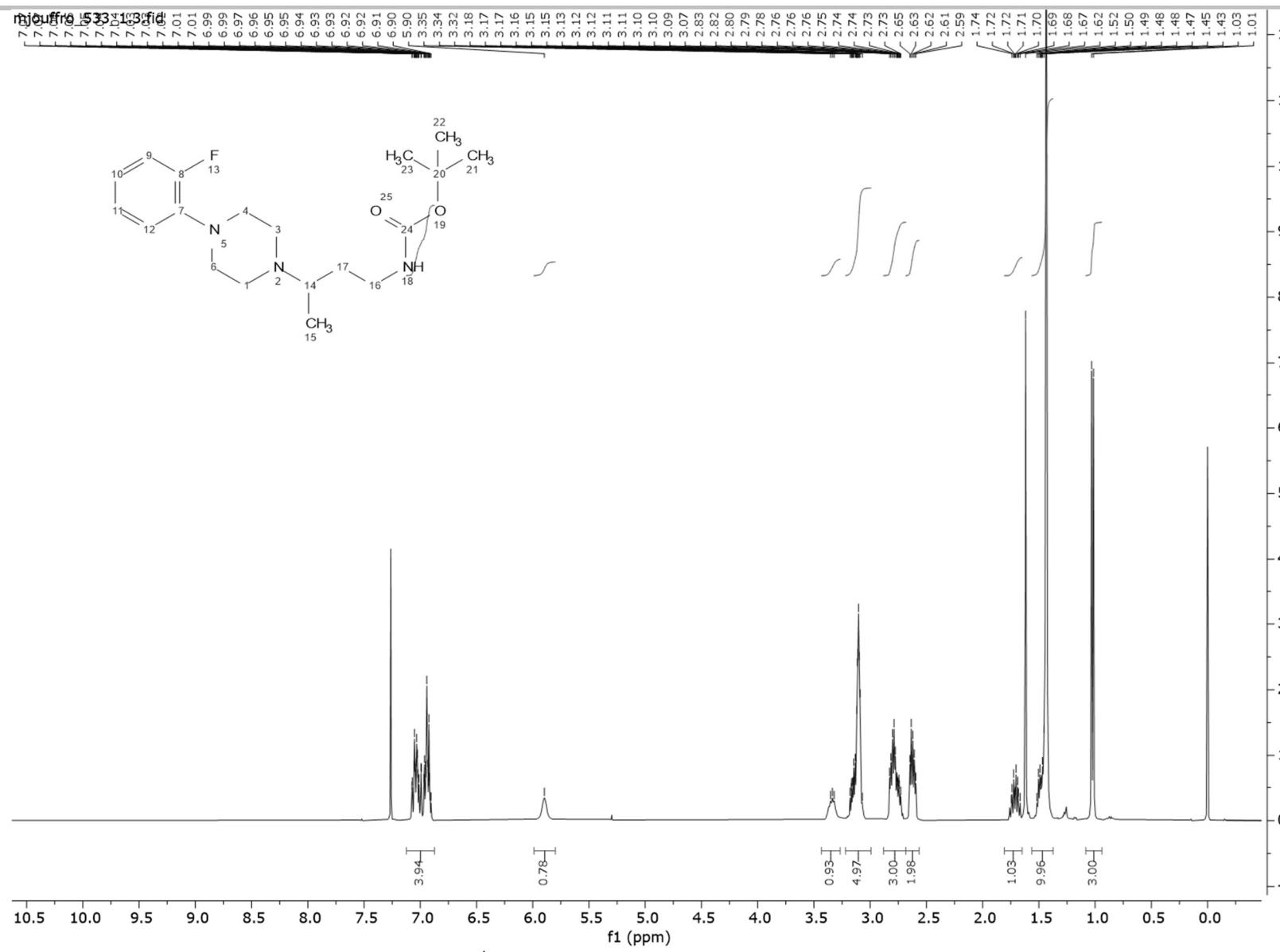
## SUPPORTING INFORMATION

mjouffro\_536\_5.4.fid

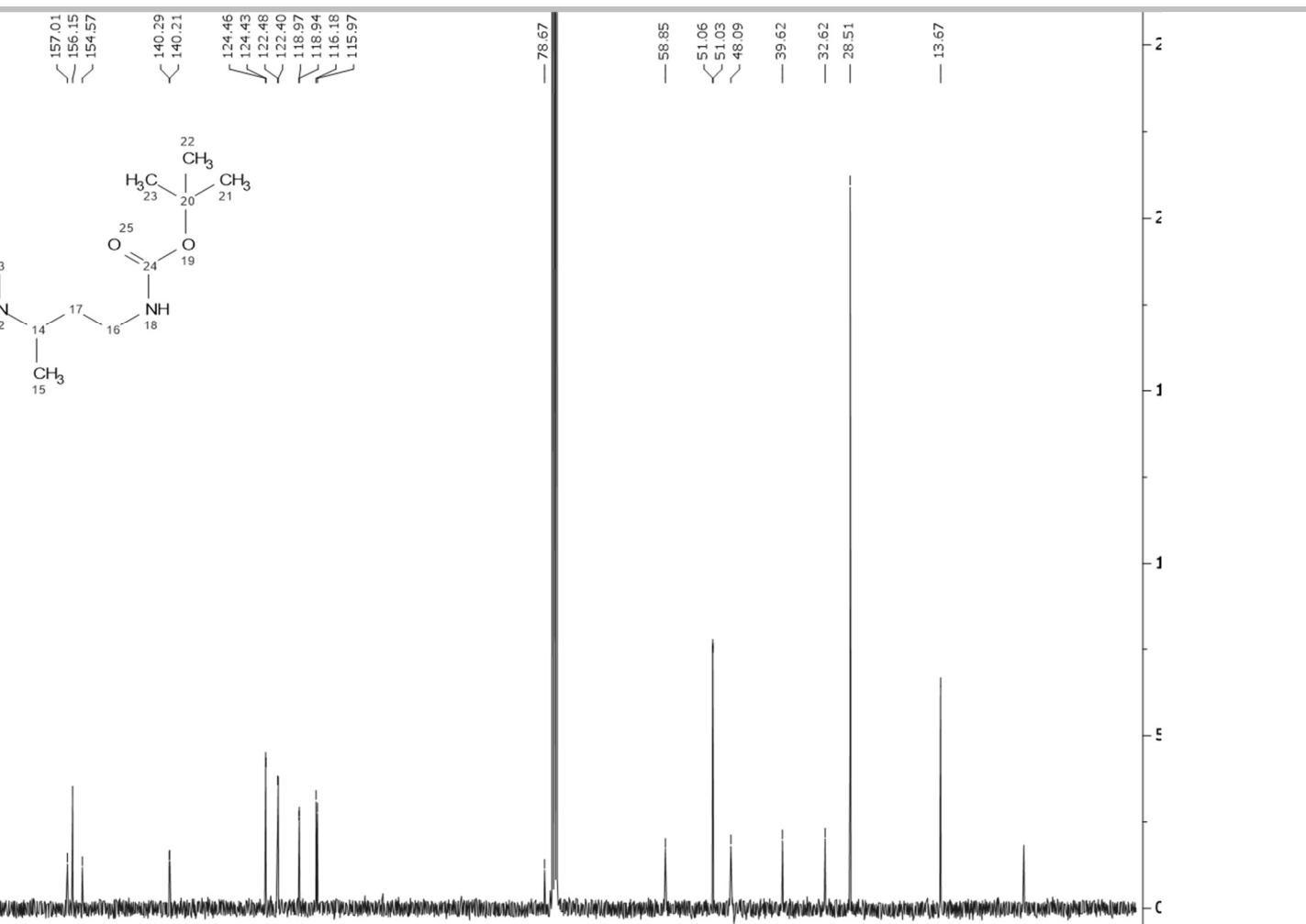


<sup>19</sup>F{<sup>1</sup>H} NMR (376 MHz, CDCl<sub>3</sub>) spectrum of **8-trans**.

## SUPPORTING INFORMATION

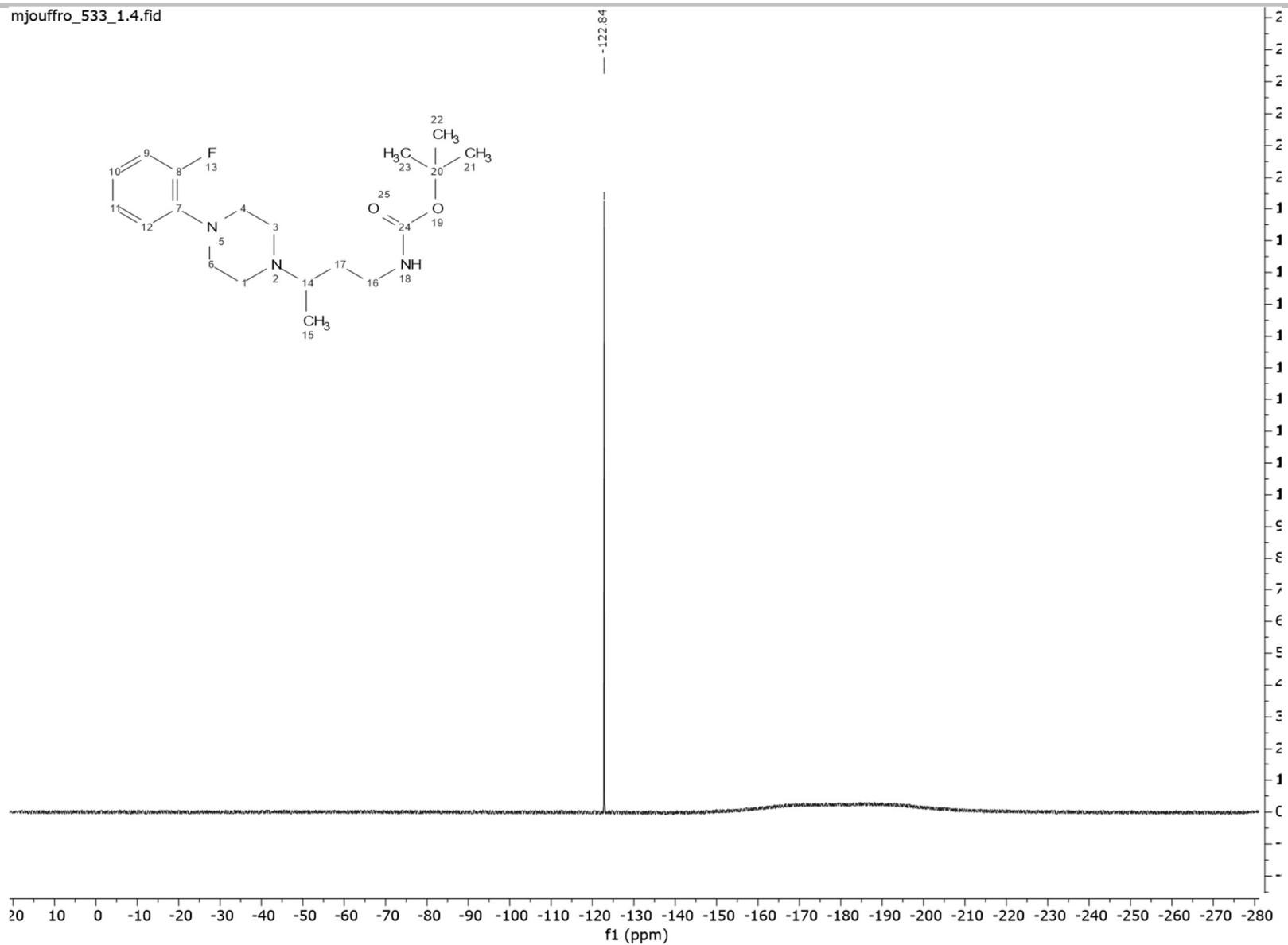


WILEY-VCH

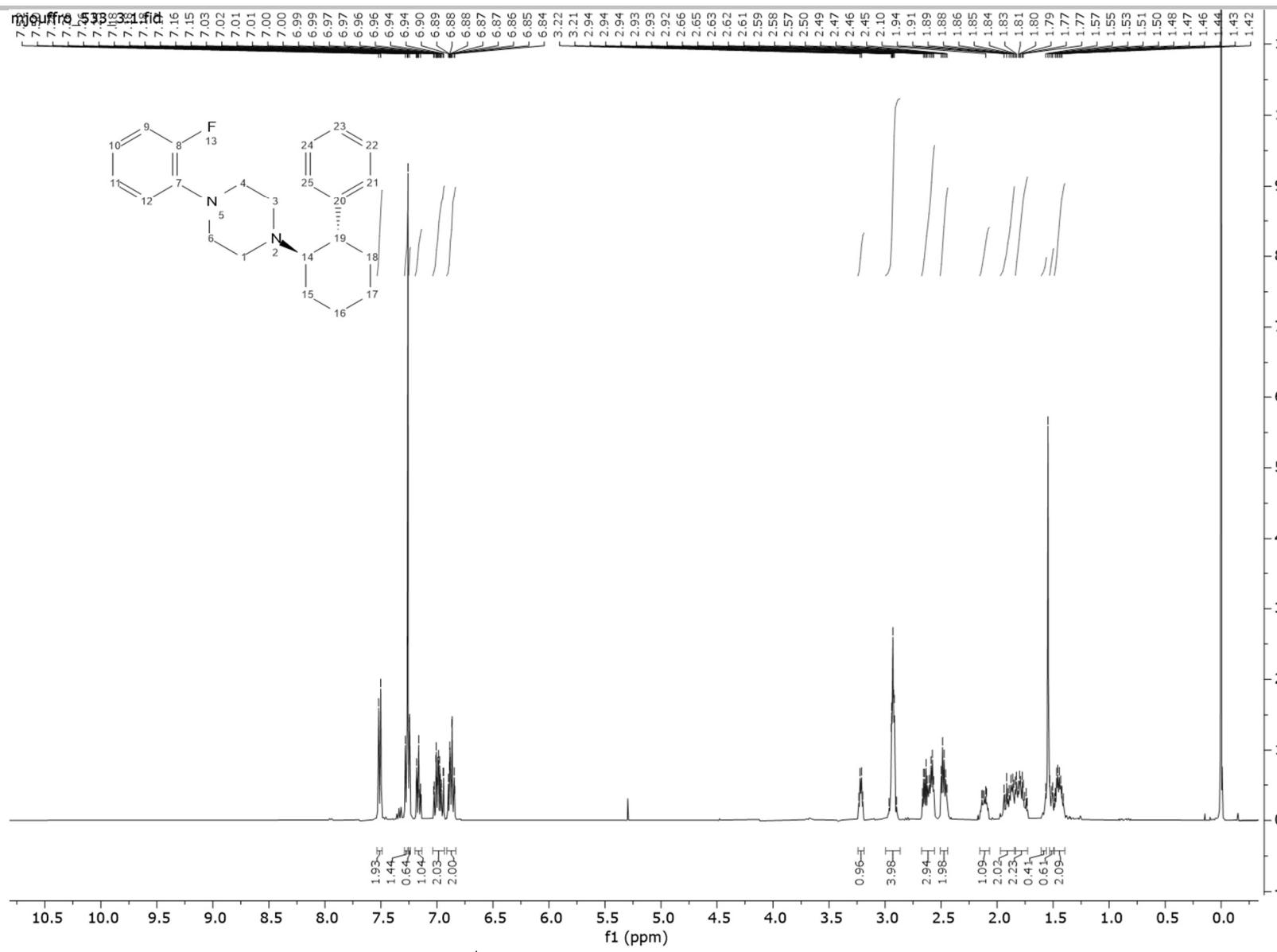


## SUPPORTING INFORMATION

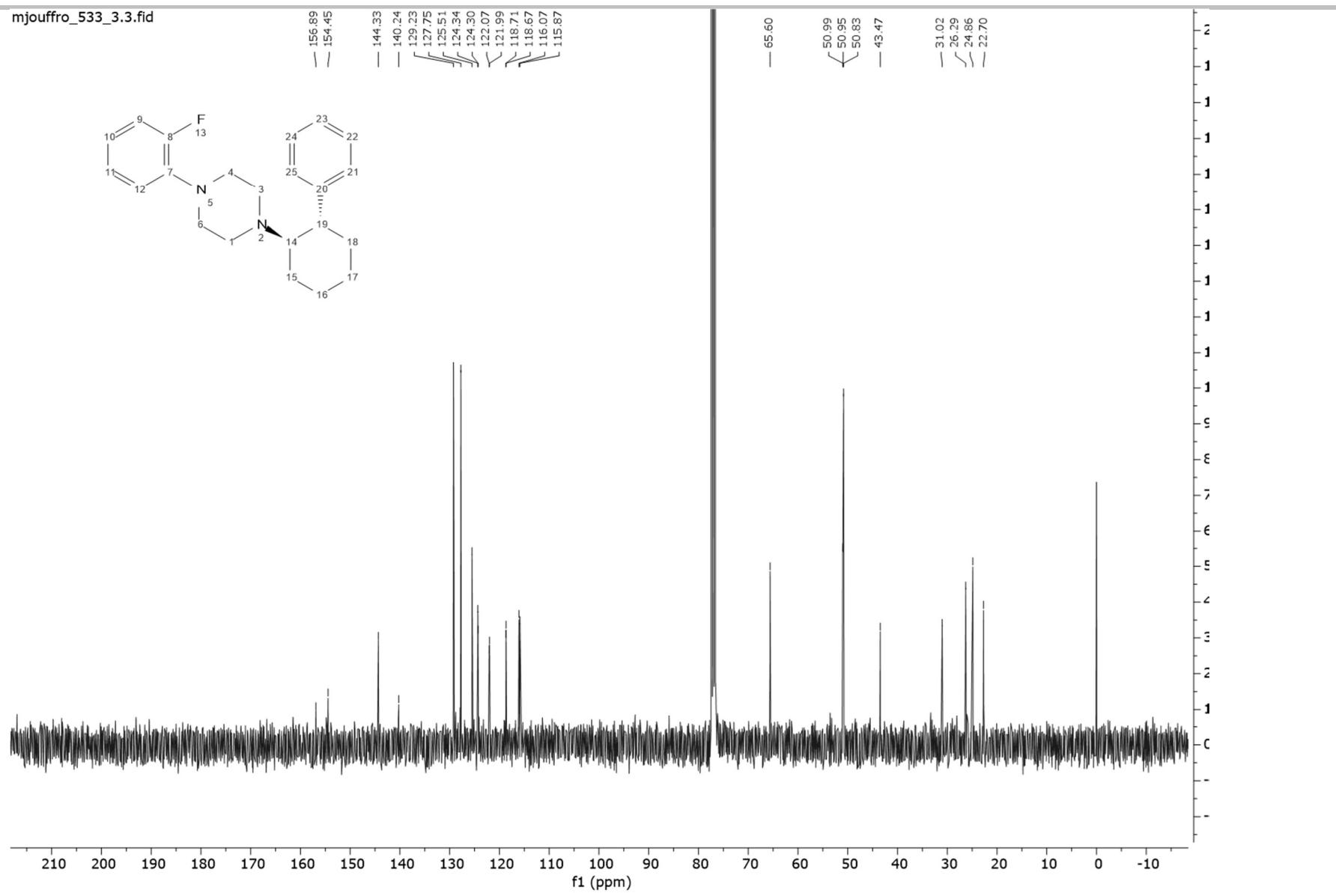
mjouffro\_533\_1.4.fid



## SUPPORTING INFORMATION

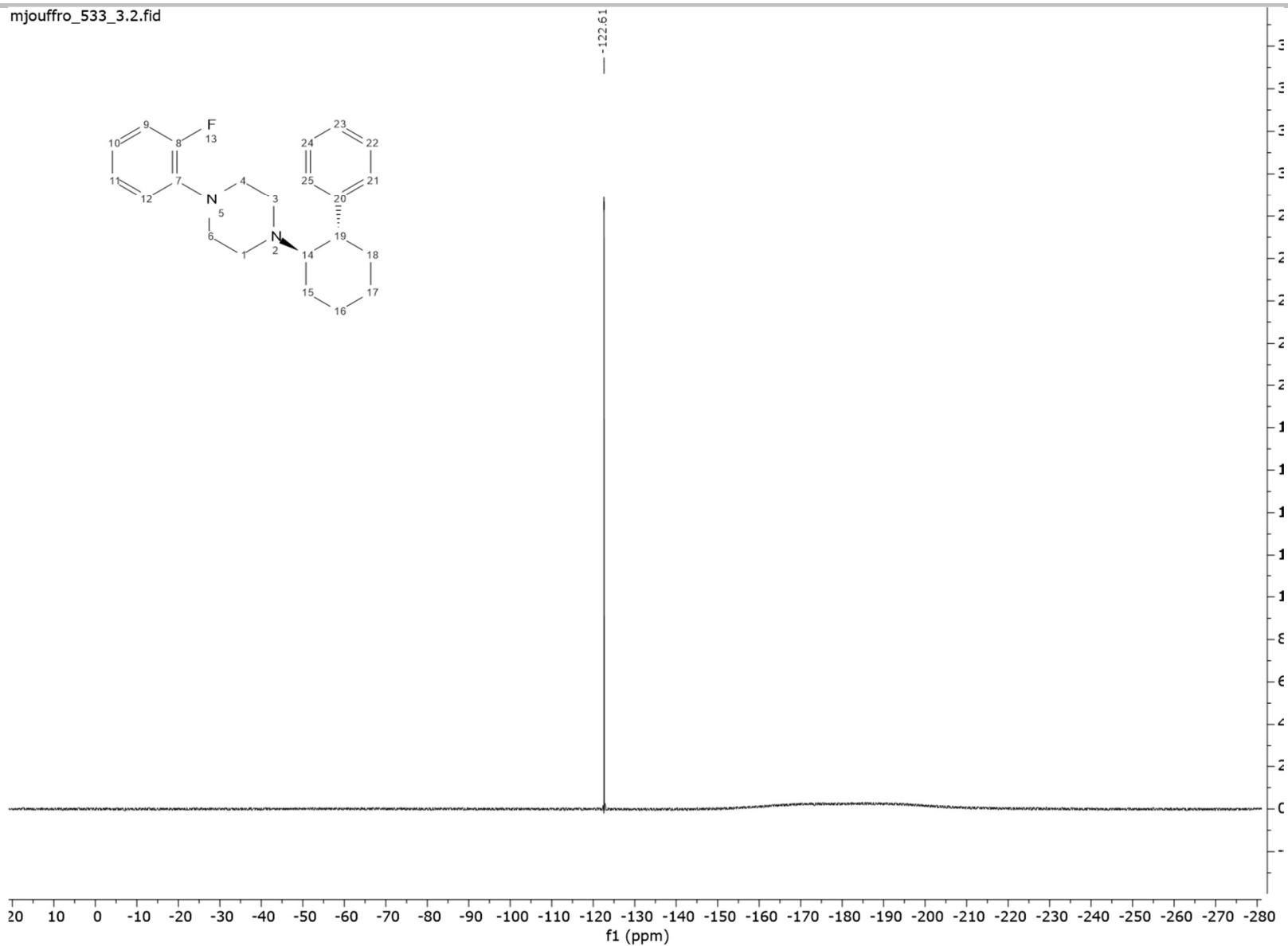


## SUPPORTING INFORMATION

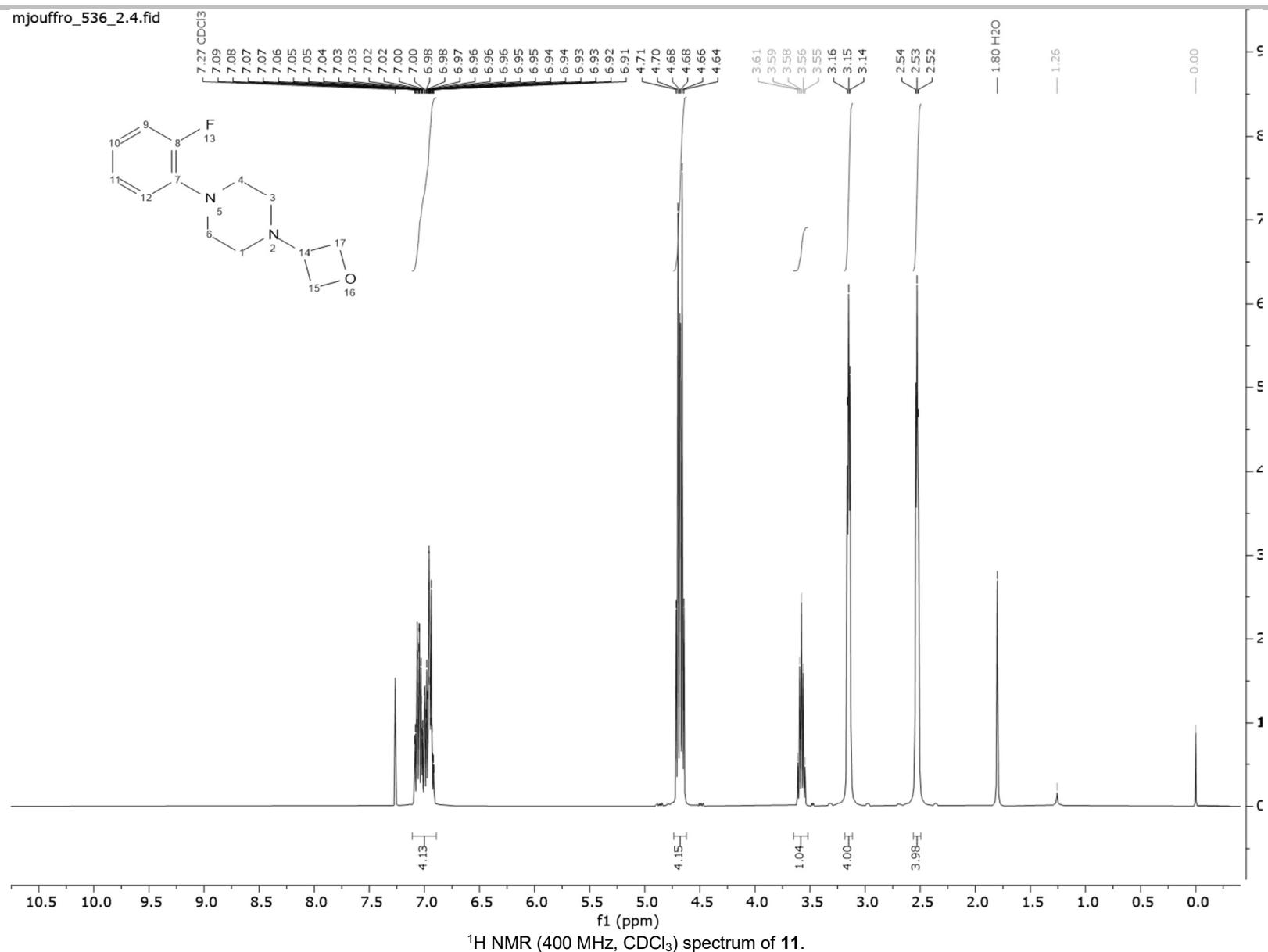


## SUPPORTING INFORMATION

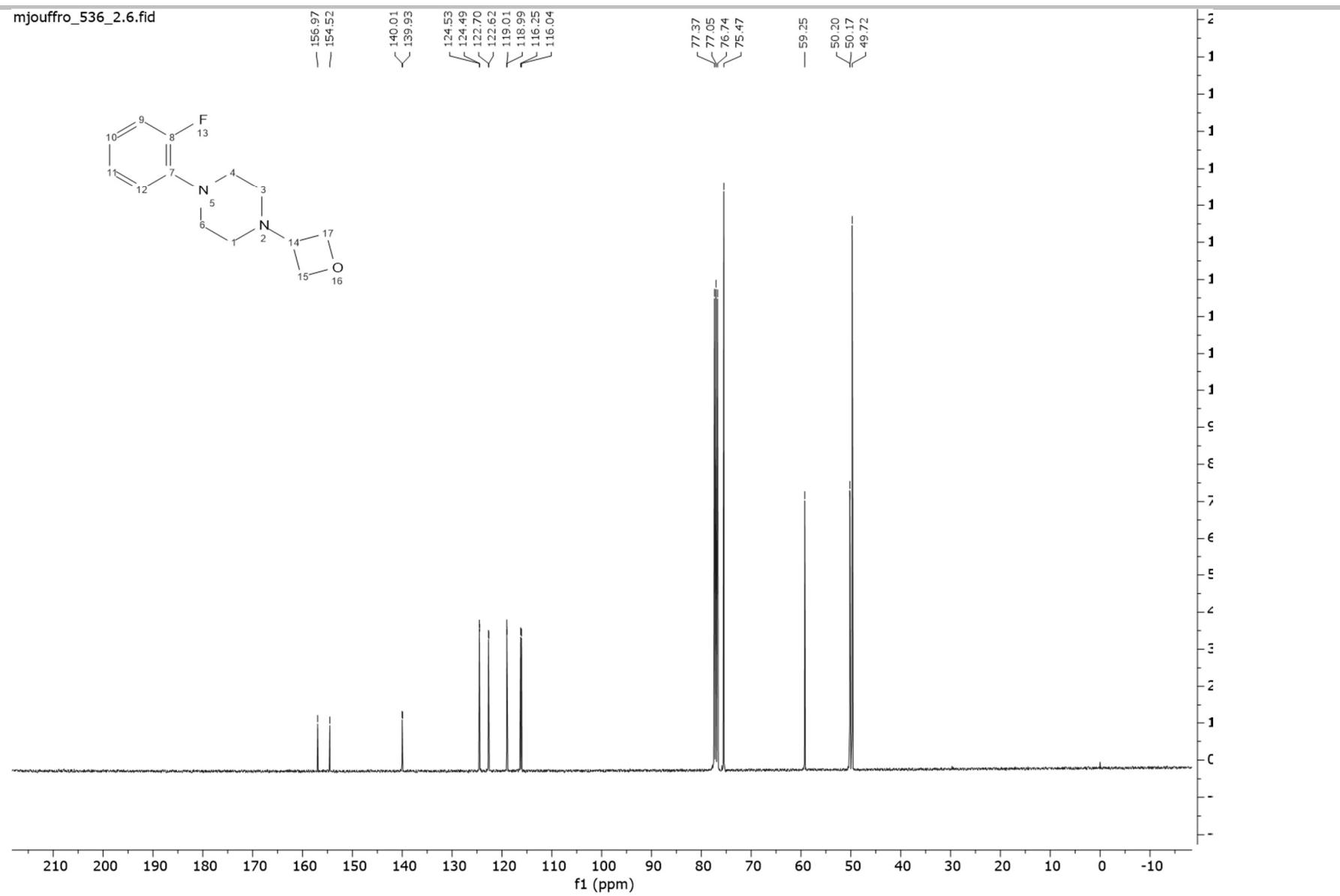
mjouffro\_533\_3.2.fid



## SUPPORTING INFORMATION

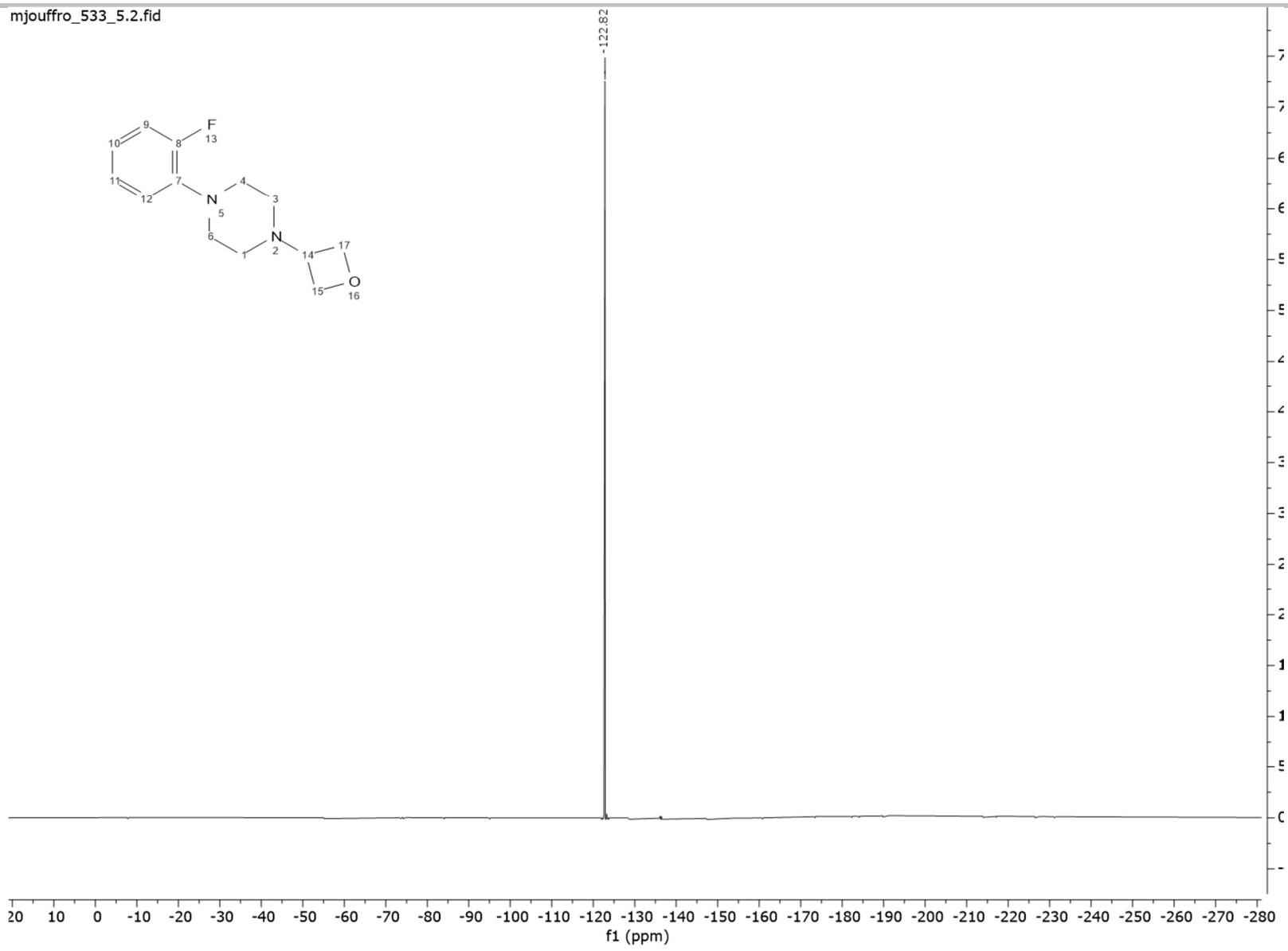


## SUPPORTING INFORMATION

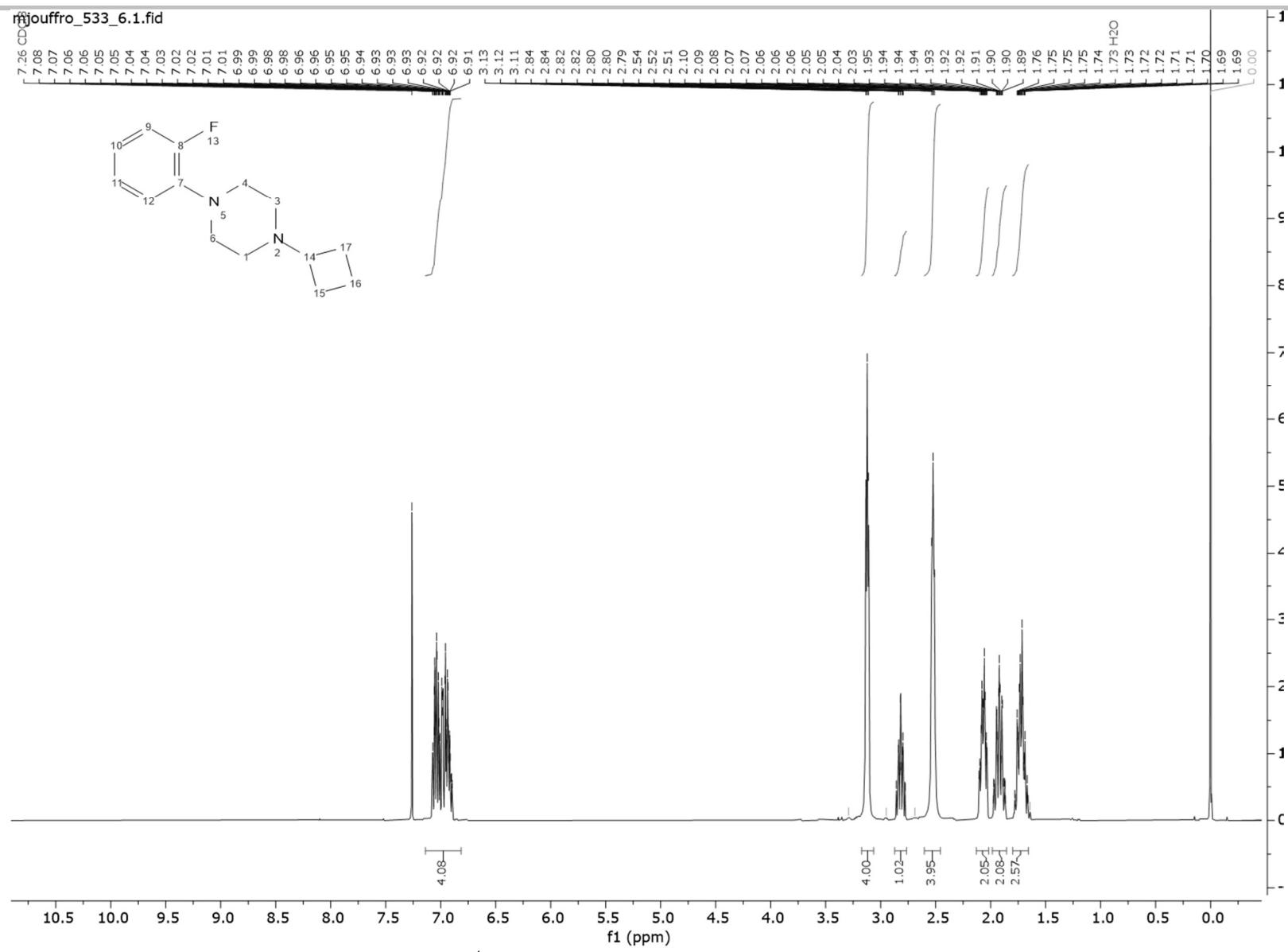


## SUPPORTING INFORMATION

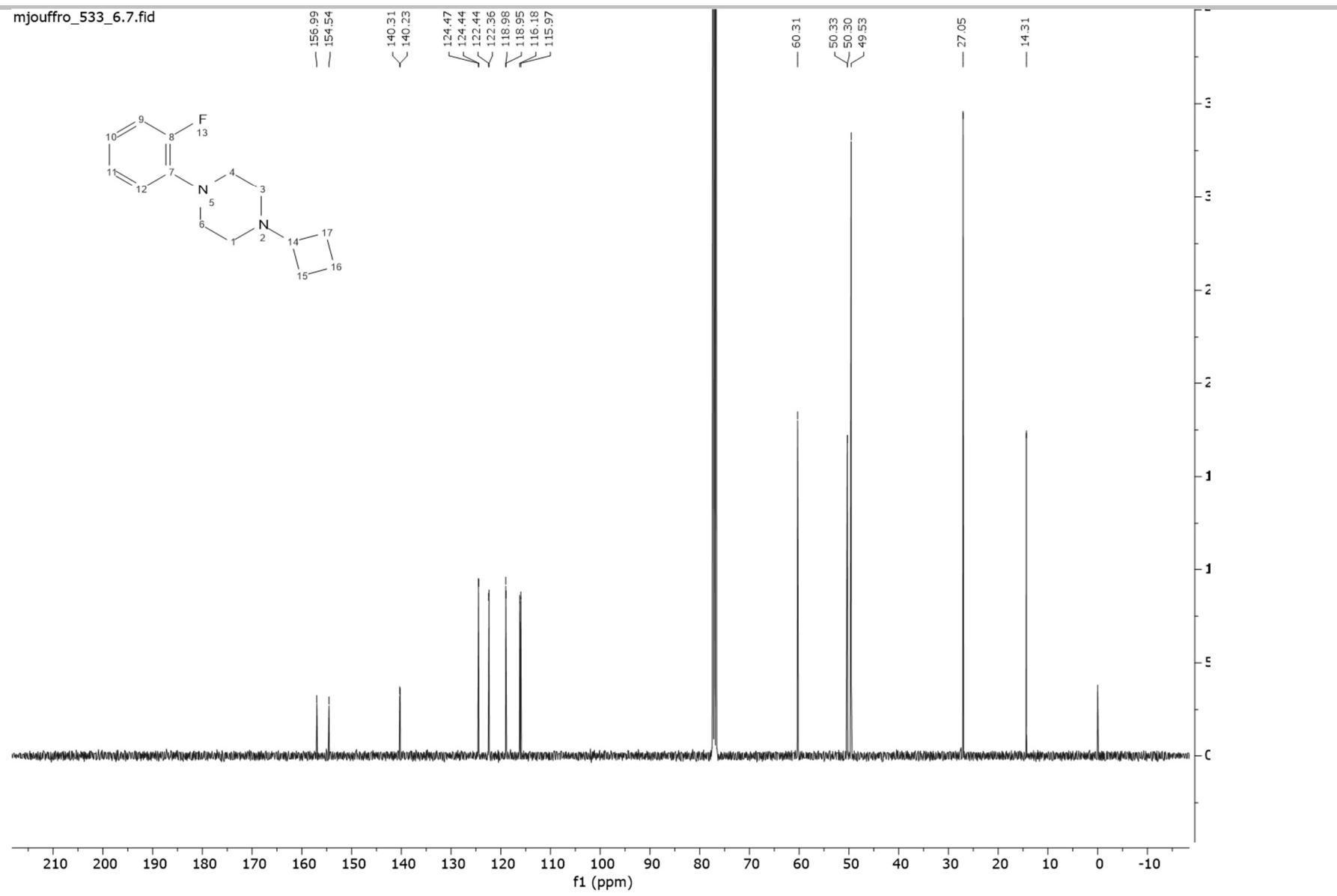
mjouffro\_533\_5.2.fid

 $^{19}\text{F}\{\text{H}\}$  NMR (376 MHz,  $\text{CDCl}_3$ ) spectrum of **11**.

## SUPPORTING INFORMATION

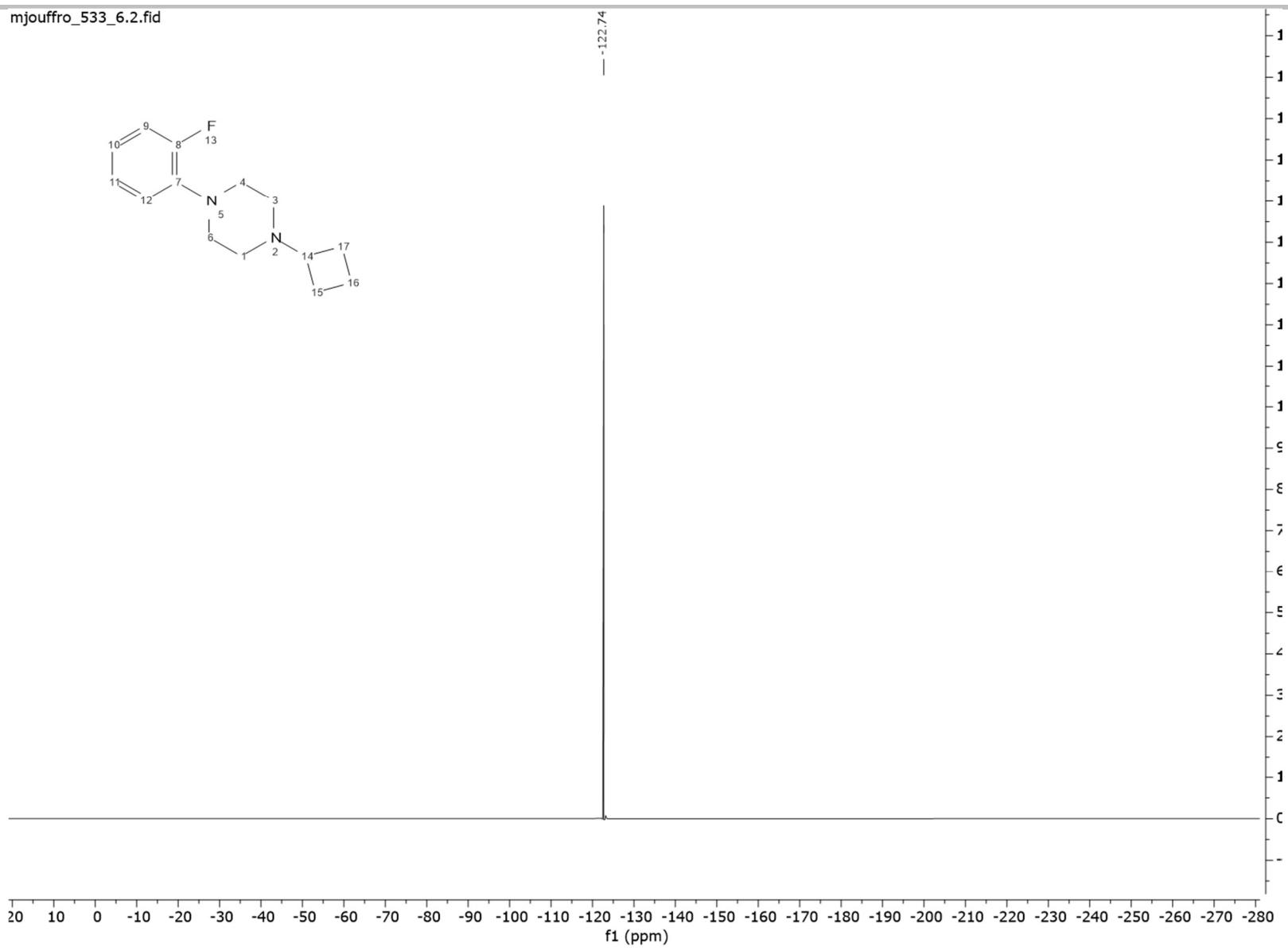


## SUPPORTING INFORMATION

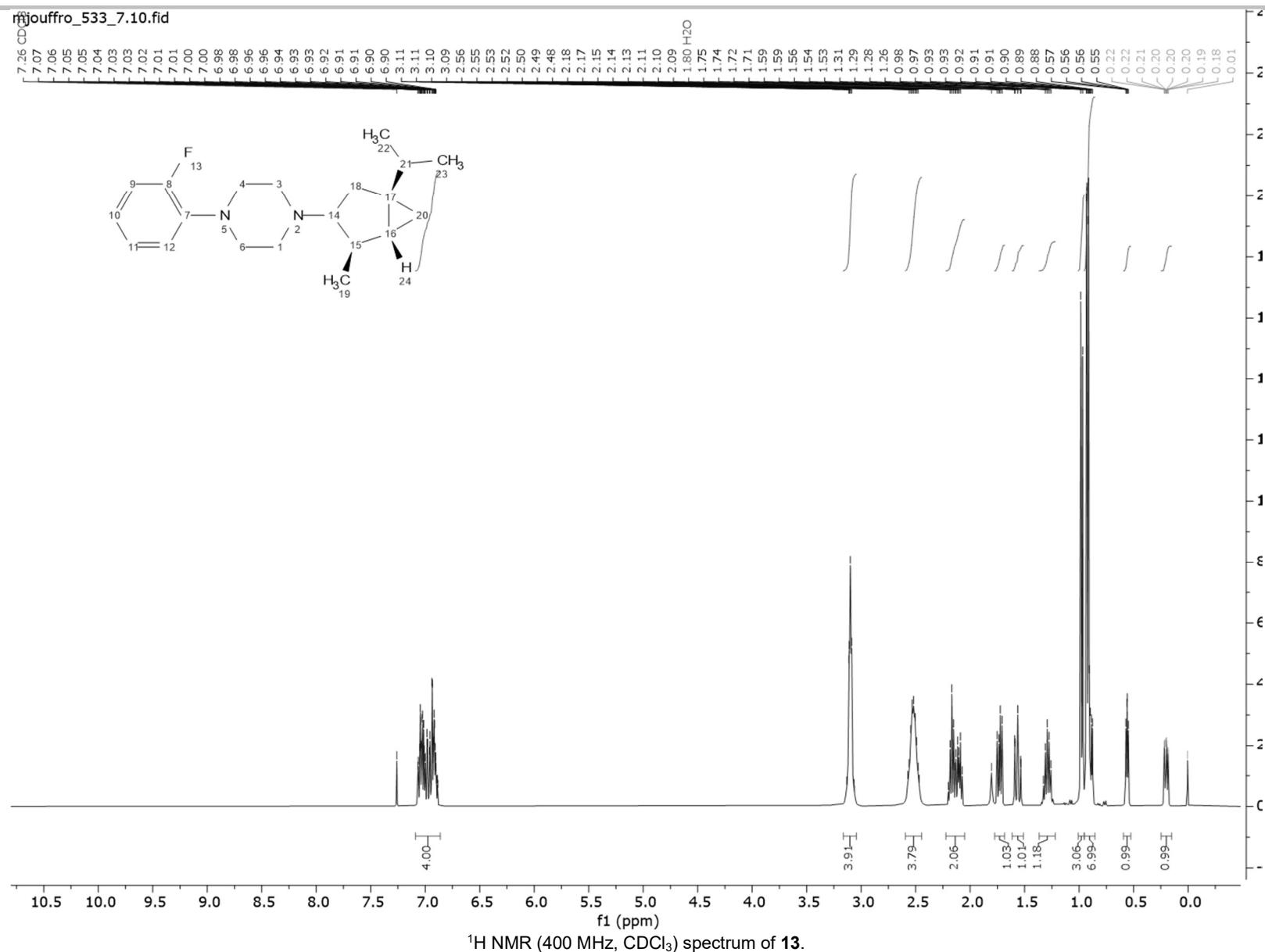
 $^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ) spectrum of **12**.

## SUPPORTING INFORMATION

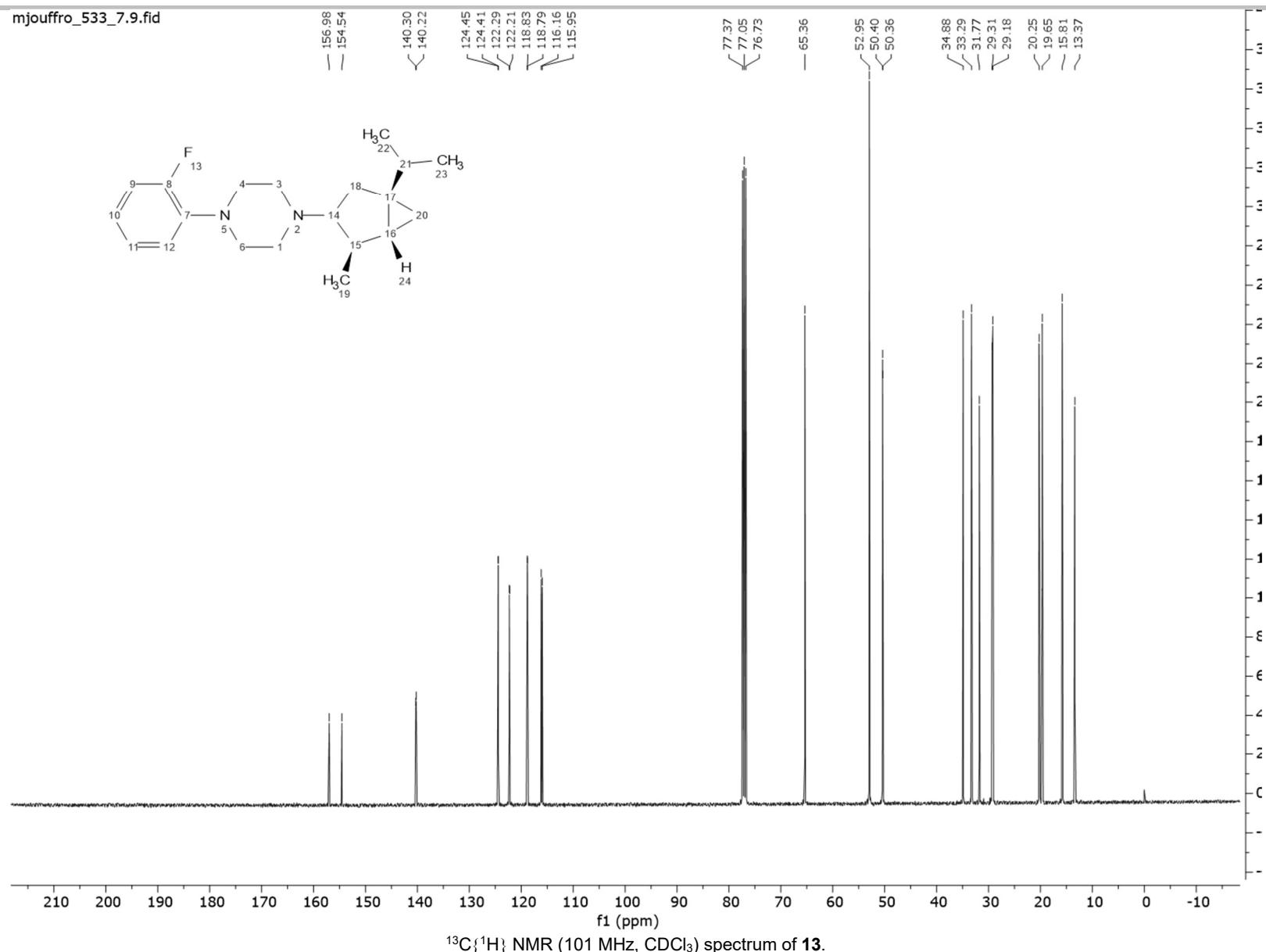
mjouffro\_533\_6.2.fid

 $^{19}\text{F}\{\text{H}\}$  NMR (376 MHz,  $\text{CDCl}_3$ ) spectrum of **12**.

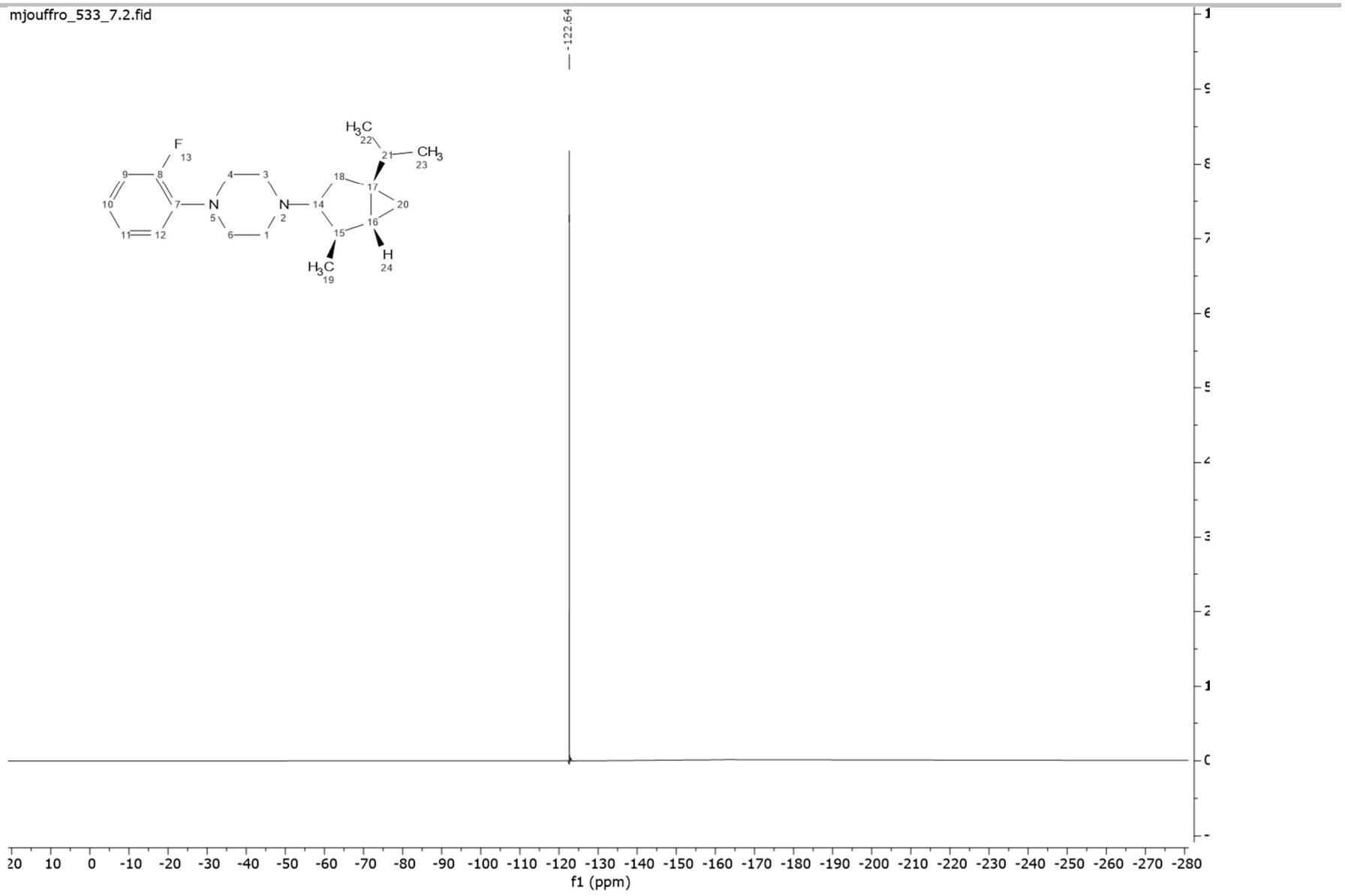
## SUPPORTING INFORMATION



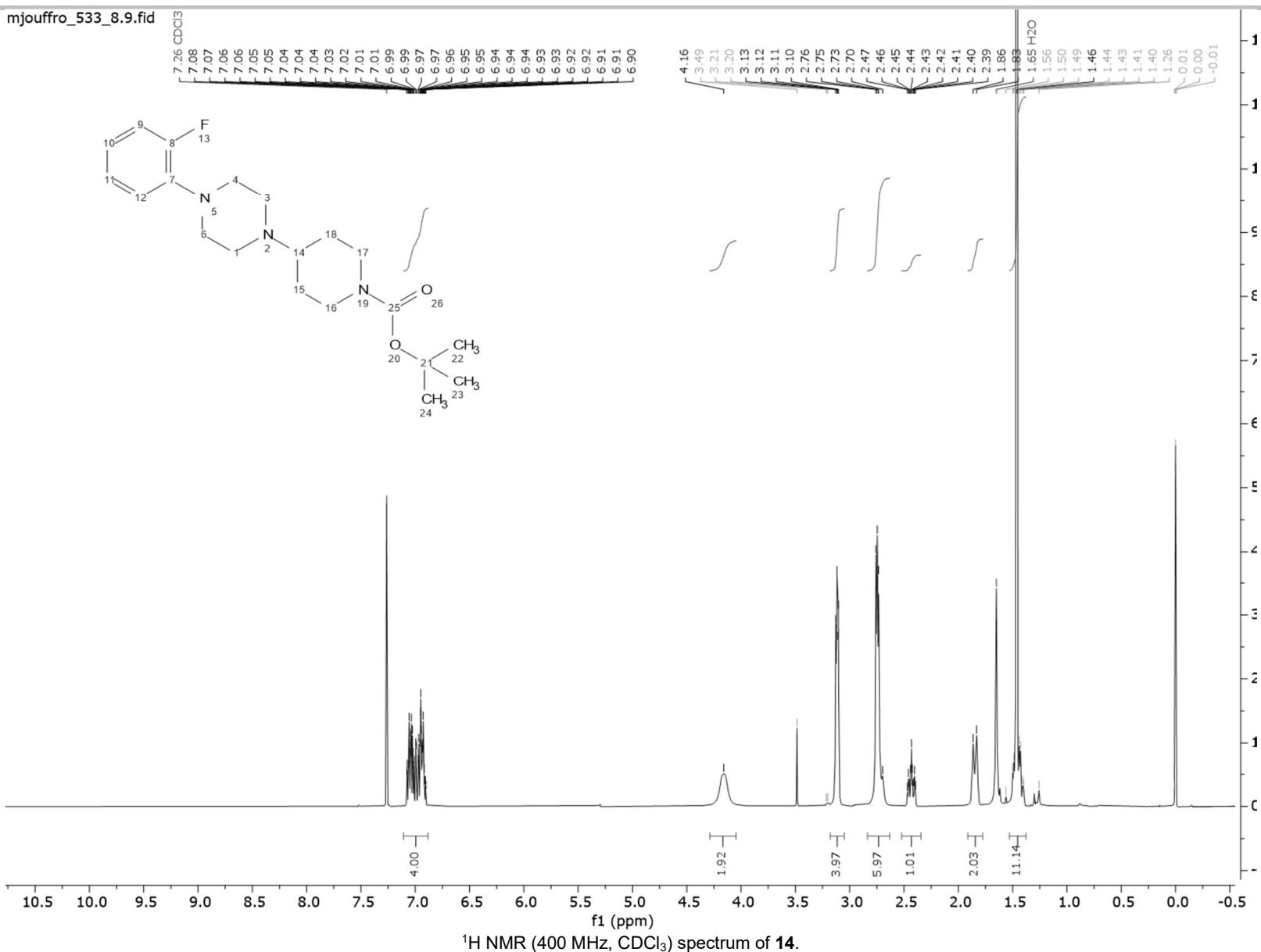
## SUPPORTING INFORMATION



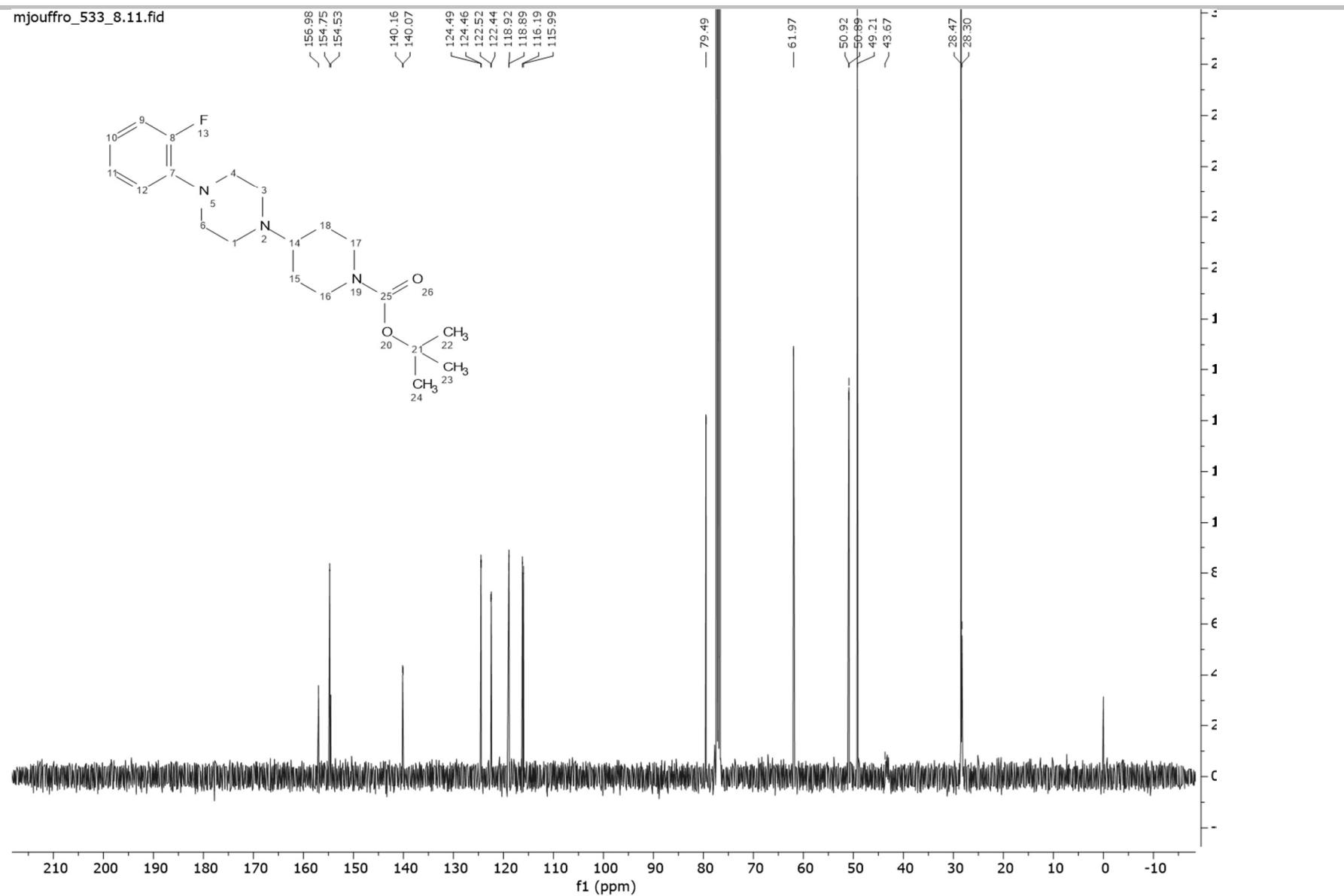
## SUPPORTING INFORMATION



## SUPPORTING INFORMATION

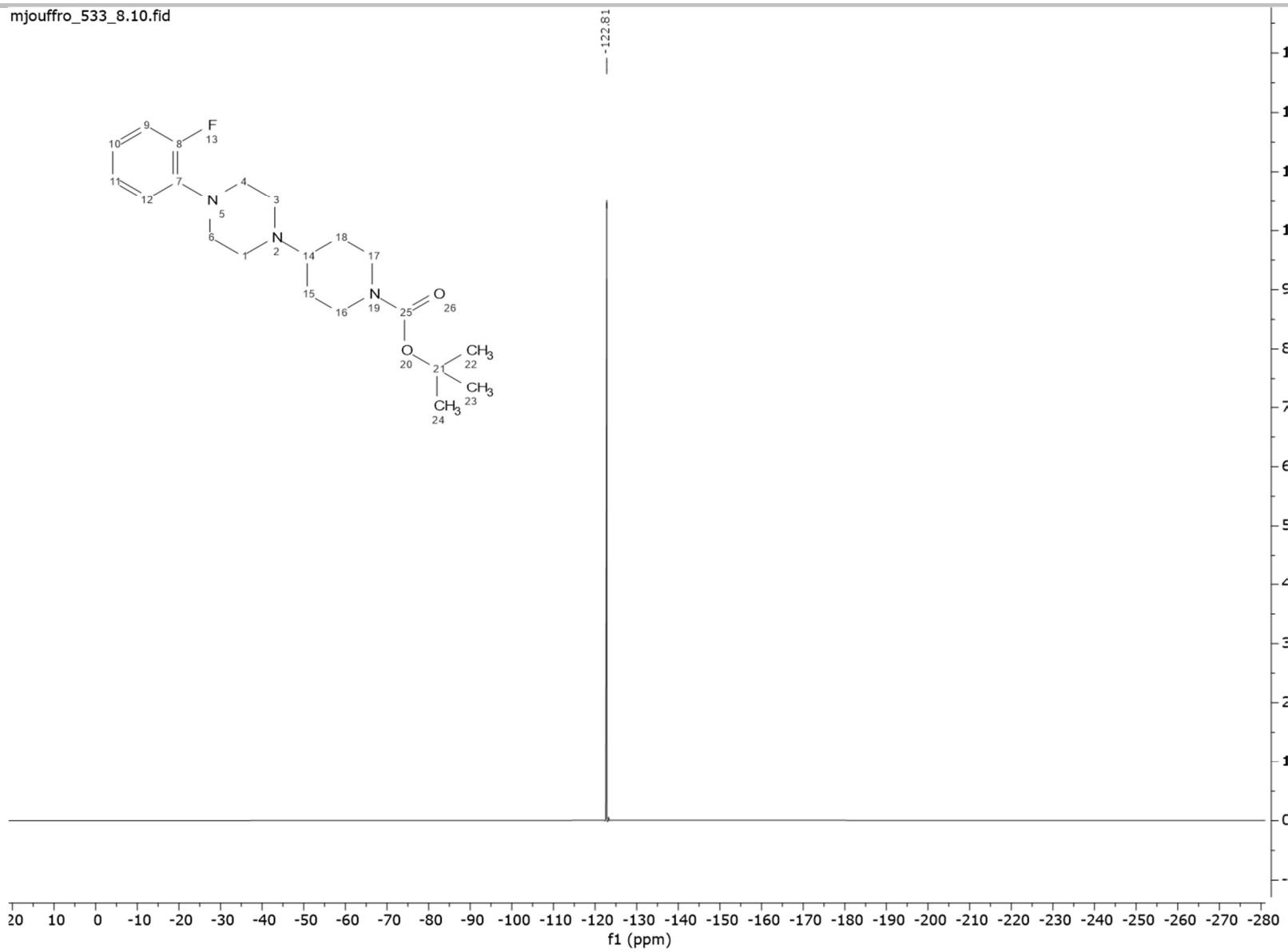


## SUPPORTING INFORMATION



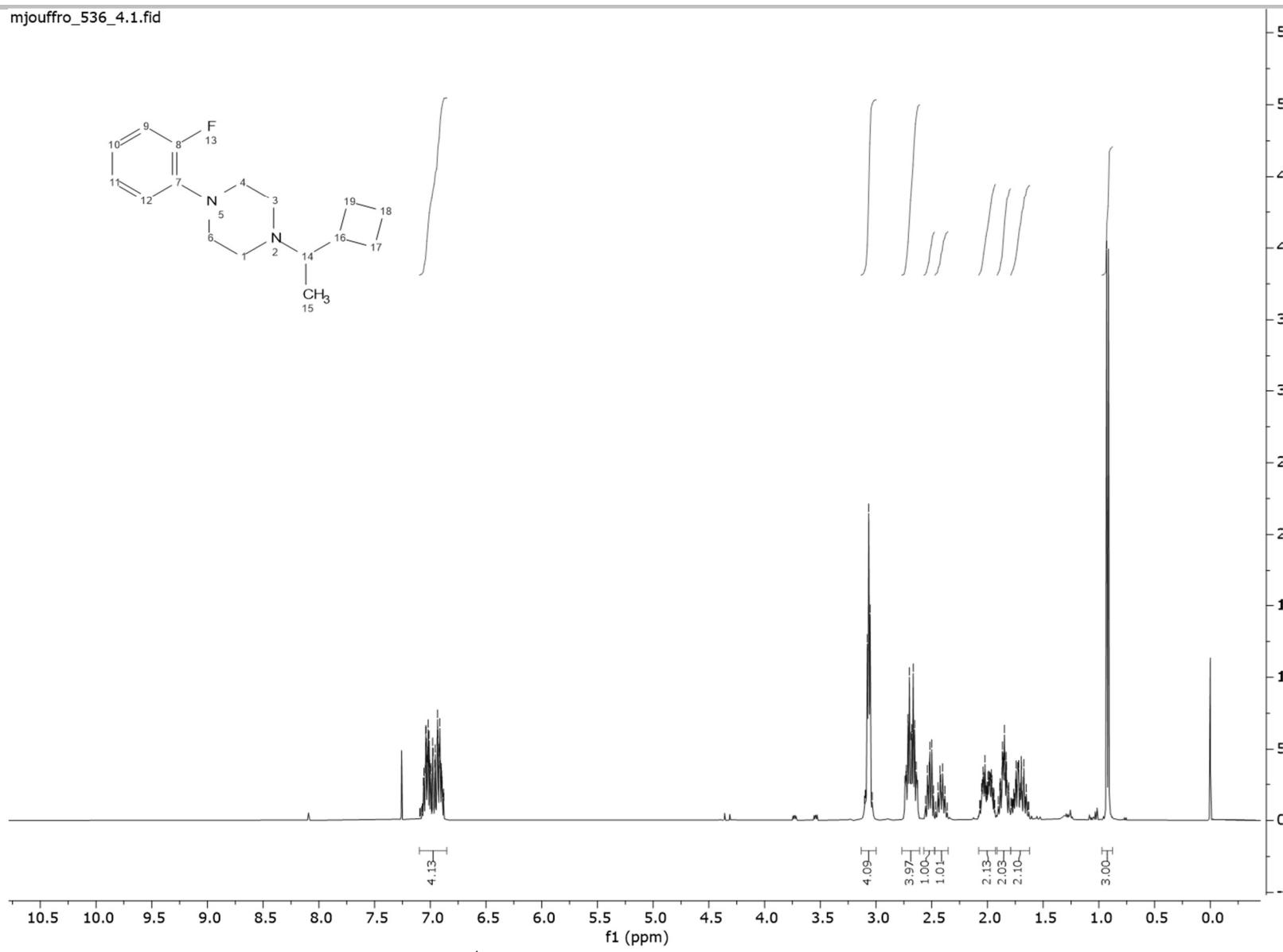
## SUPPORTING INFORMATION

mjouffro\_533\_8.10.fid

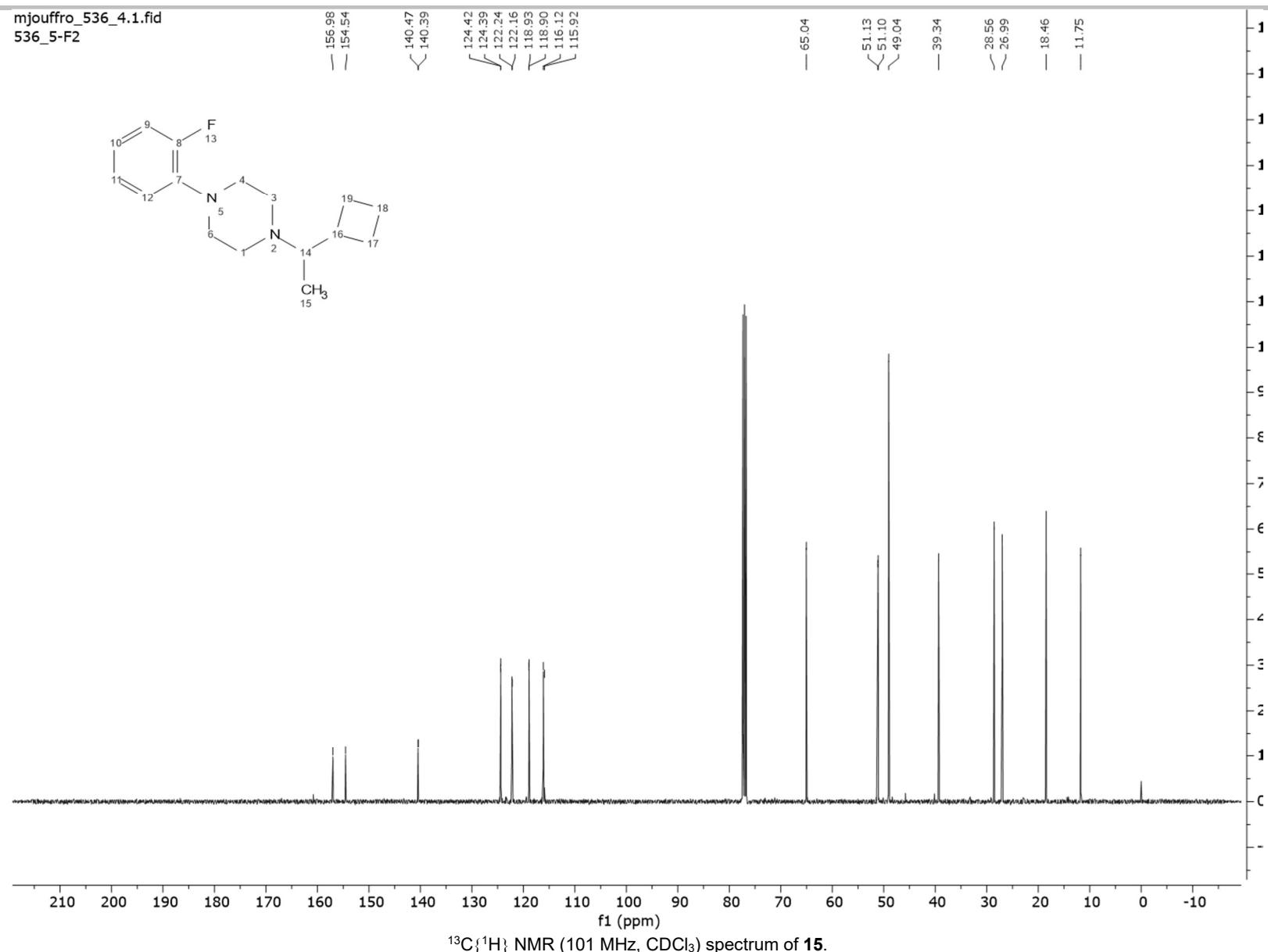
 $^{19}\text{F}\{\text{H}\}$  NMR (376 MHz,  $\text{CDCl}_3$ ) spectrum of **14**.

## SUPPORTING INFORMATION

mjouffro\_536\_4.1.fid

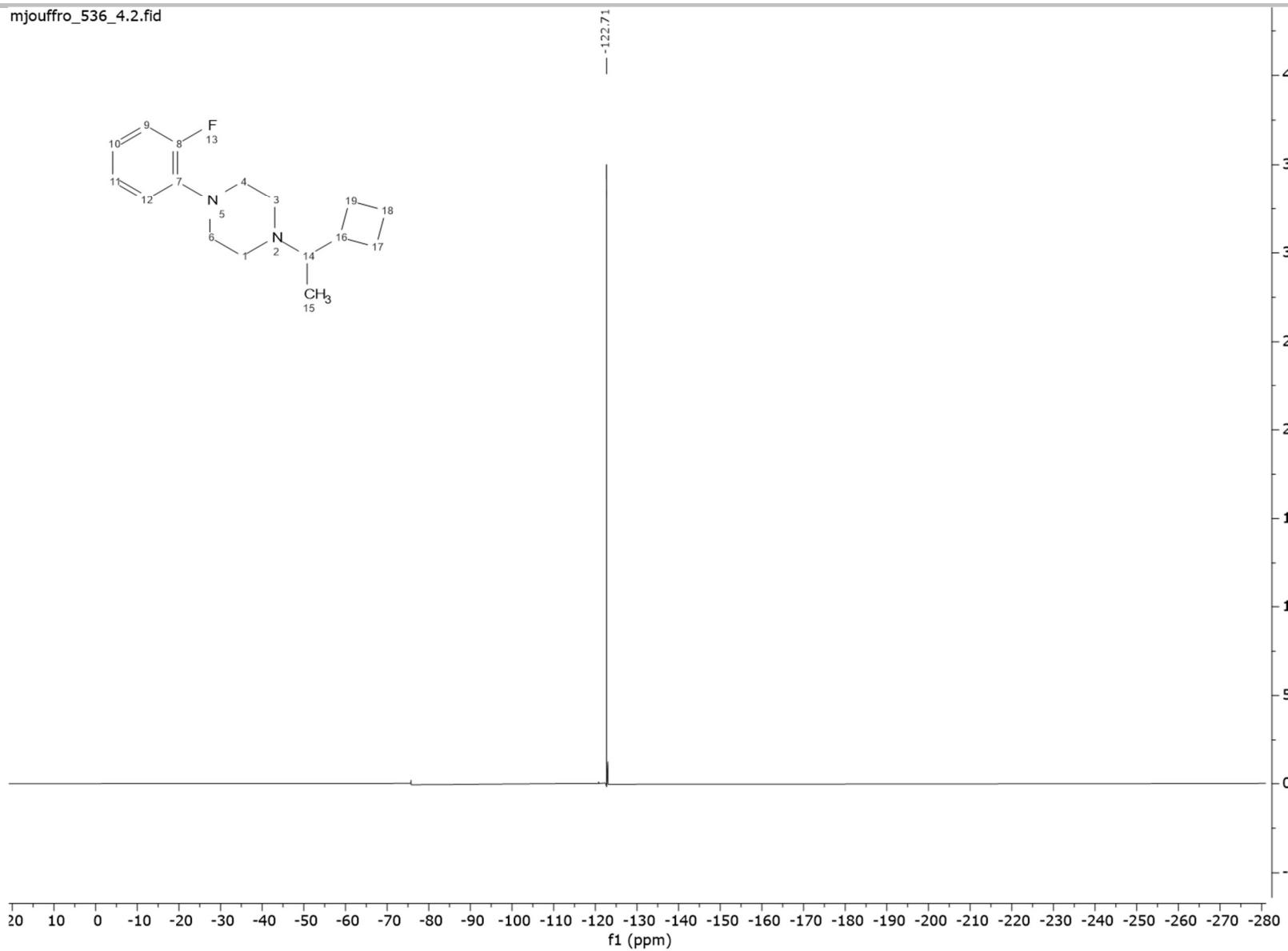
 $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) spectrum of **15**.

## SUPPORTING INFORMATION

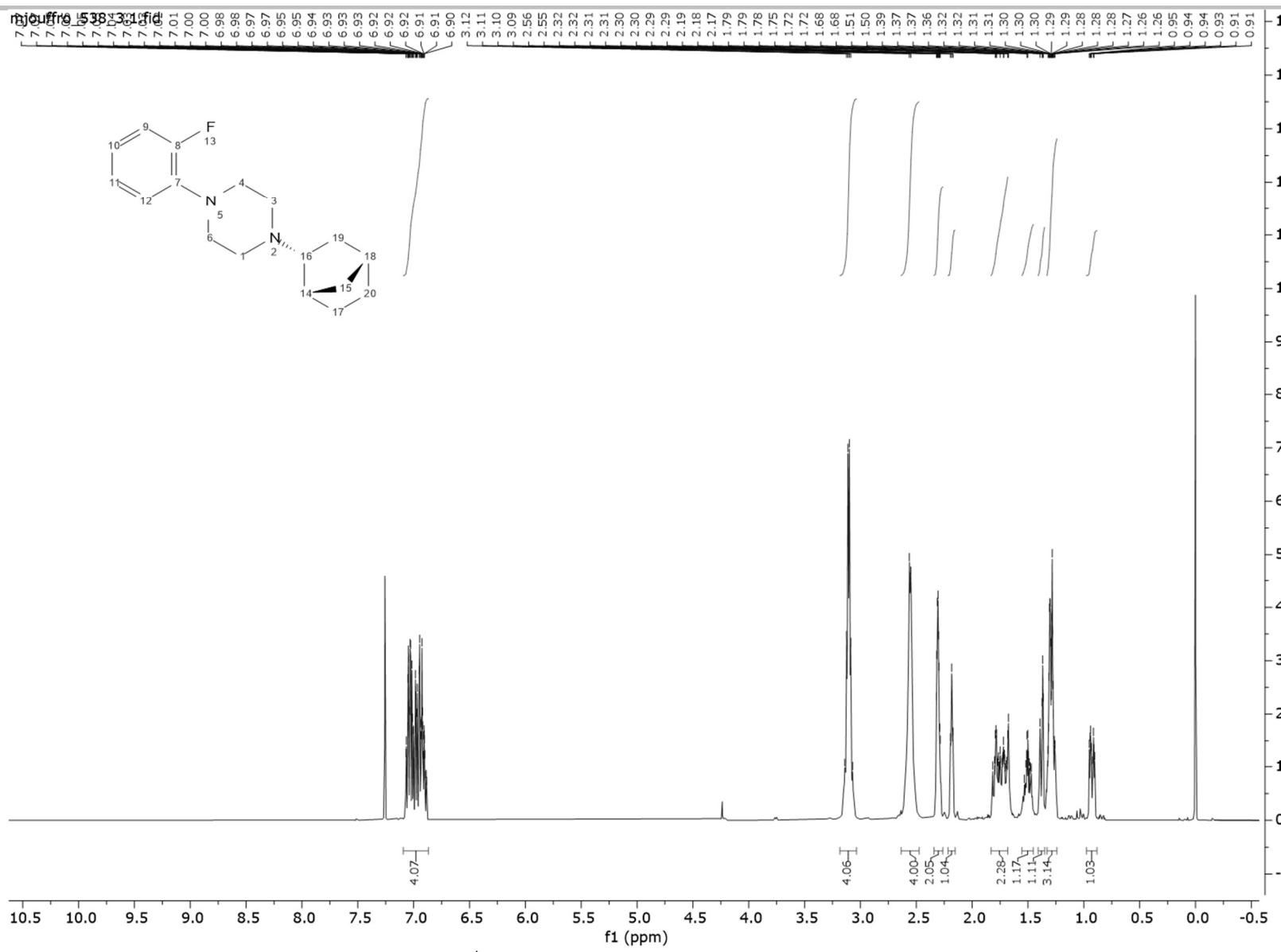


## SUPPORTING INFORMATION

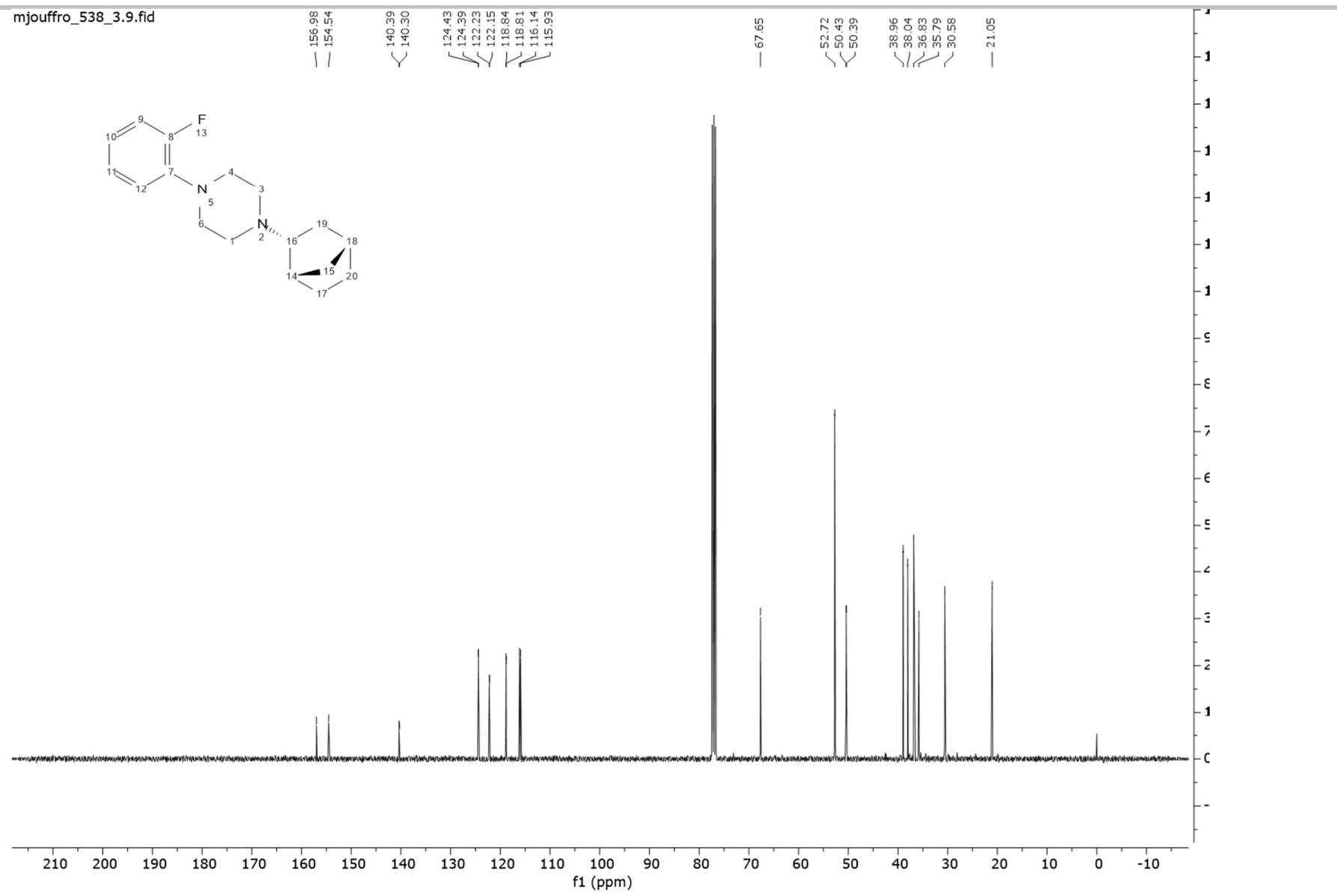
mjouffro\_536\_4.2.fid

 $^{19}\text{F}\{\text{H}\}$  NMR (376 MHz,  $\text{CDCl}_3$ ) spectrum of **15**.

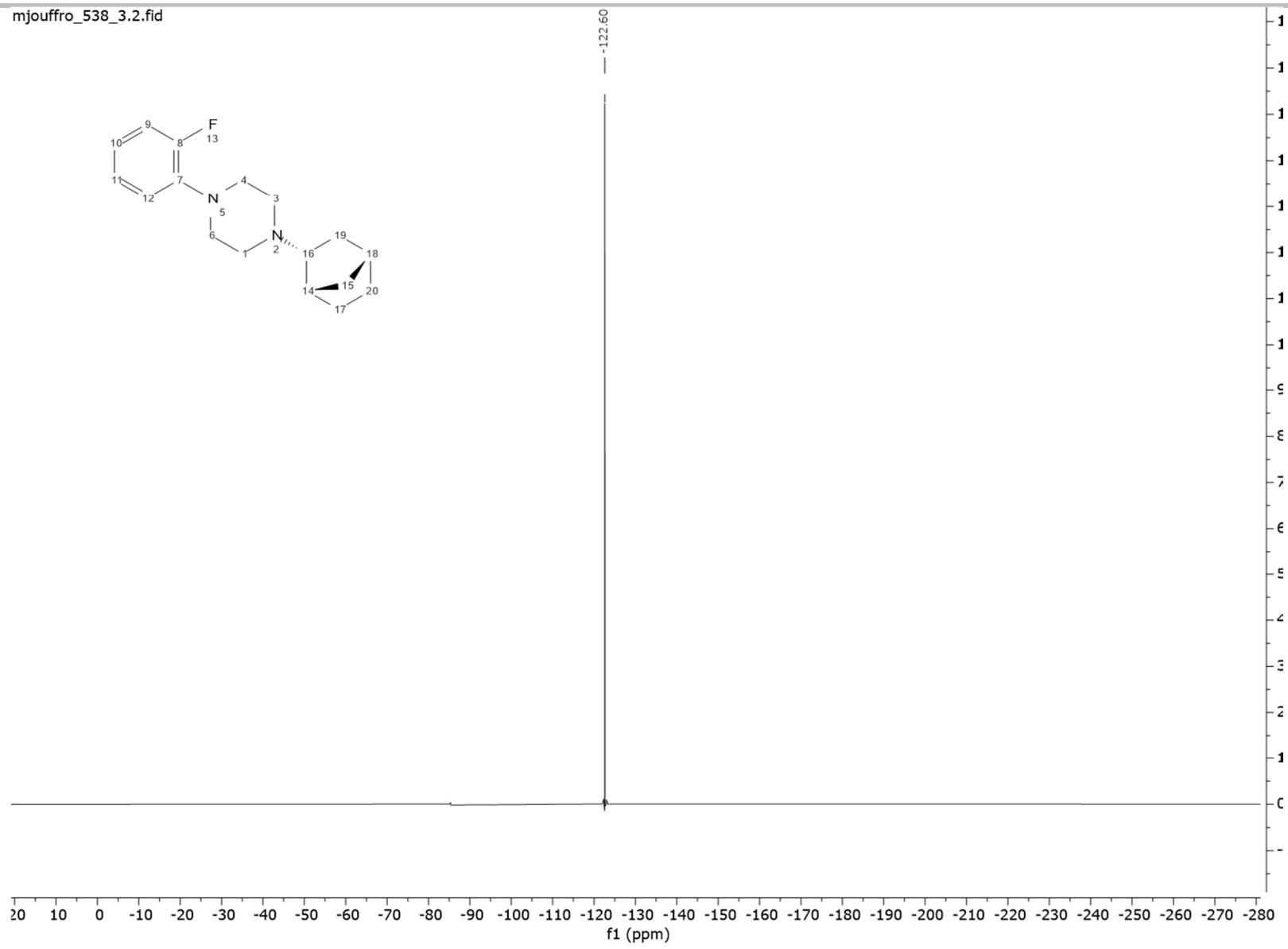
## SUPPORTING INFORMATION



## SUPPORTING INFORMATION

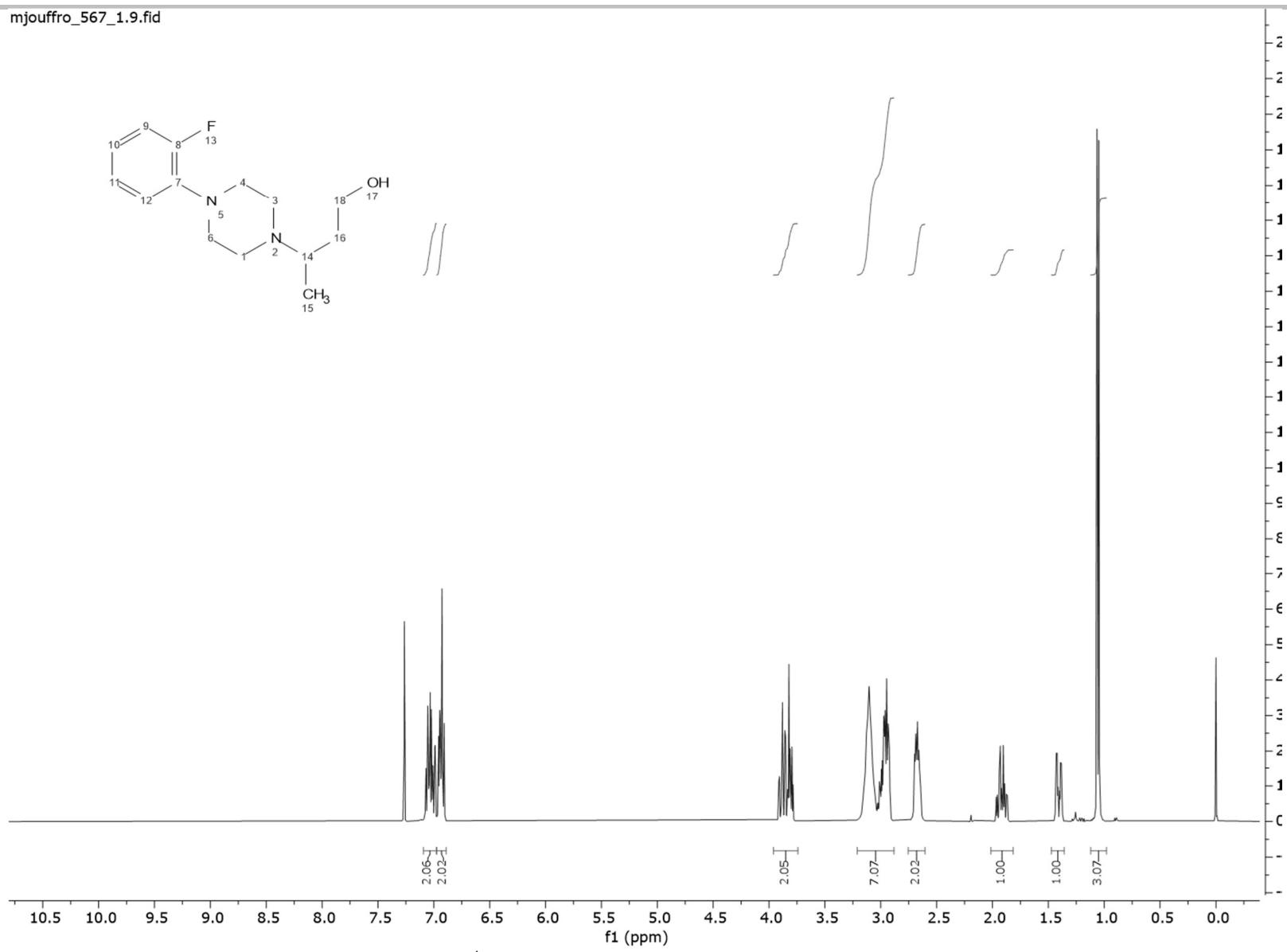


## SUPPORTING INFORMATION

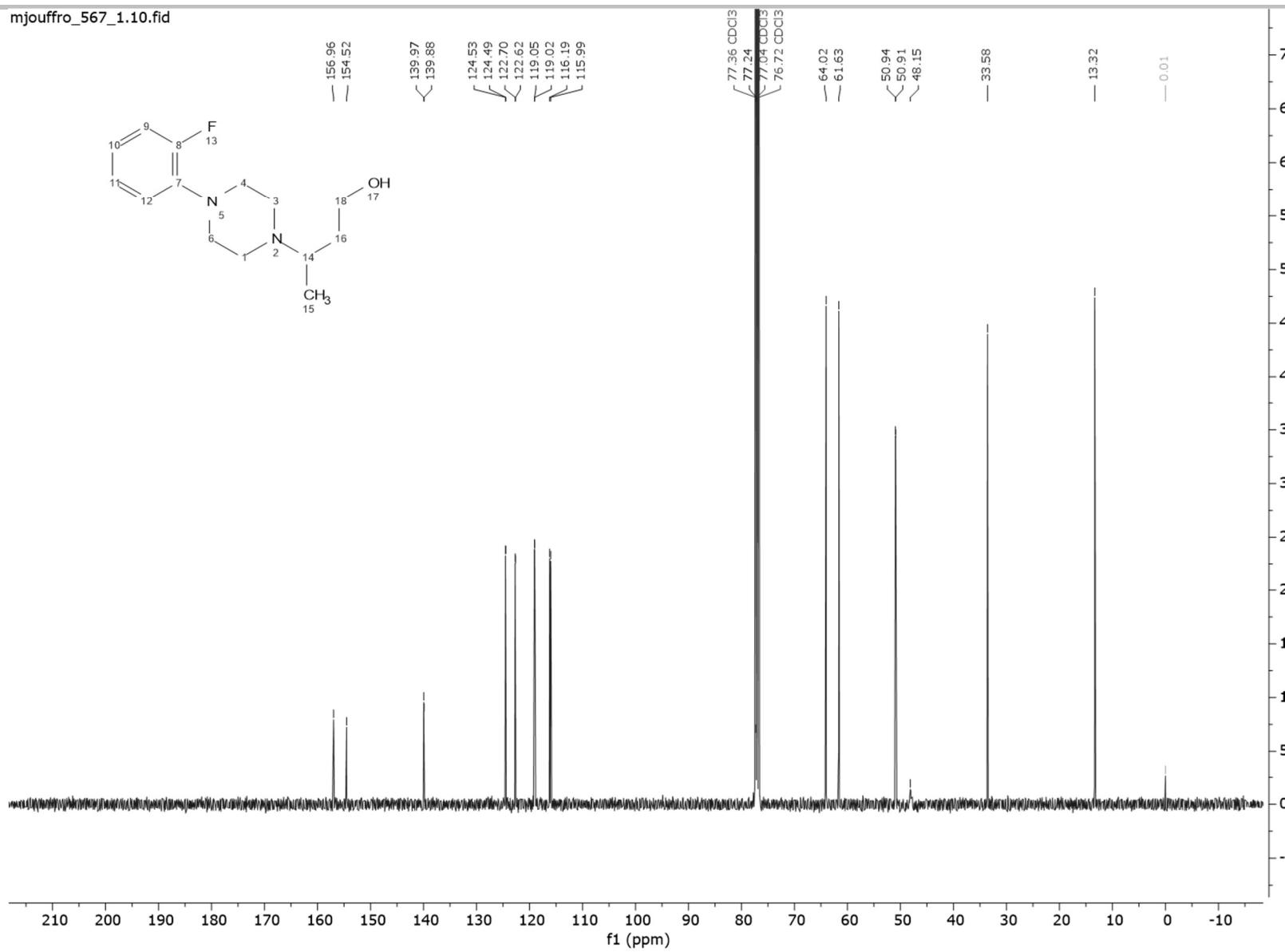


## SUPPORTING INFORMATION

mjouffro\_567\_1.9.fid

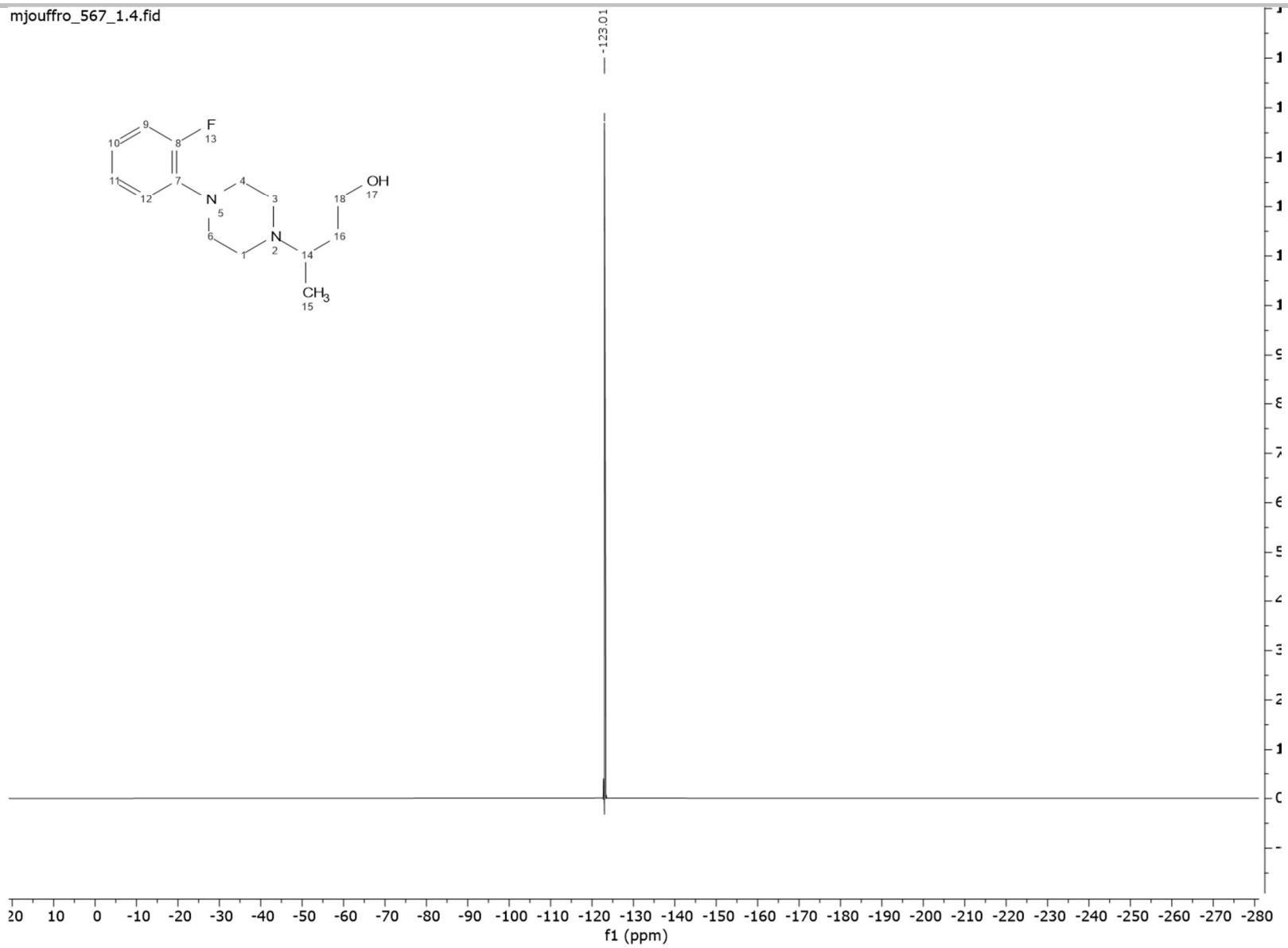
 $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) spectrum of **17**.

## SUPPORTING INFORMATION

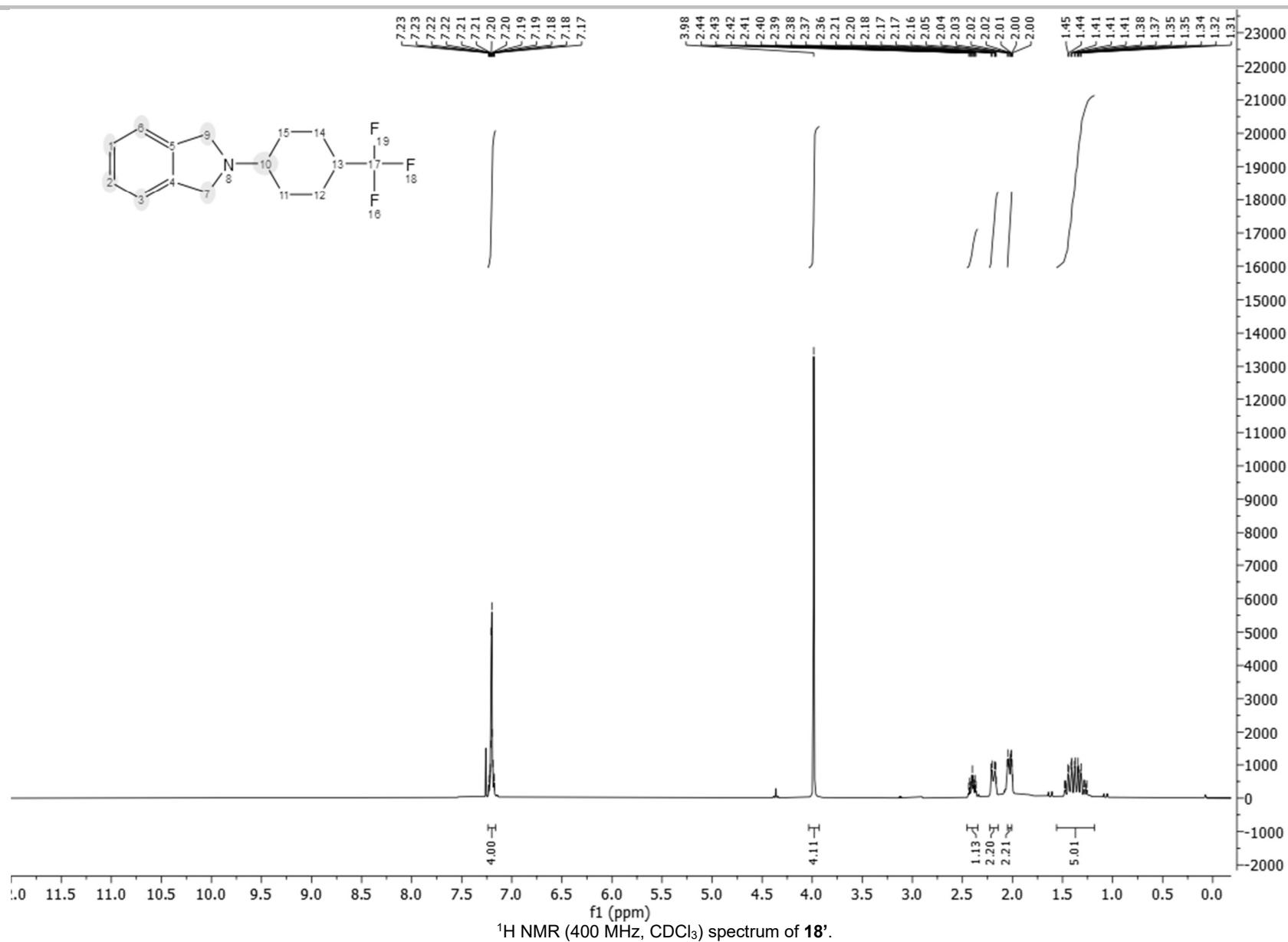


## SUPPORTING INFORMATION

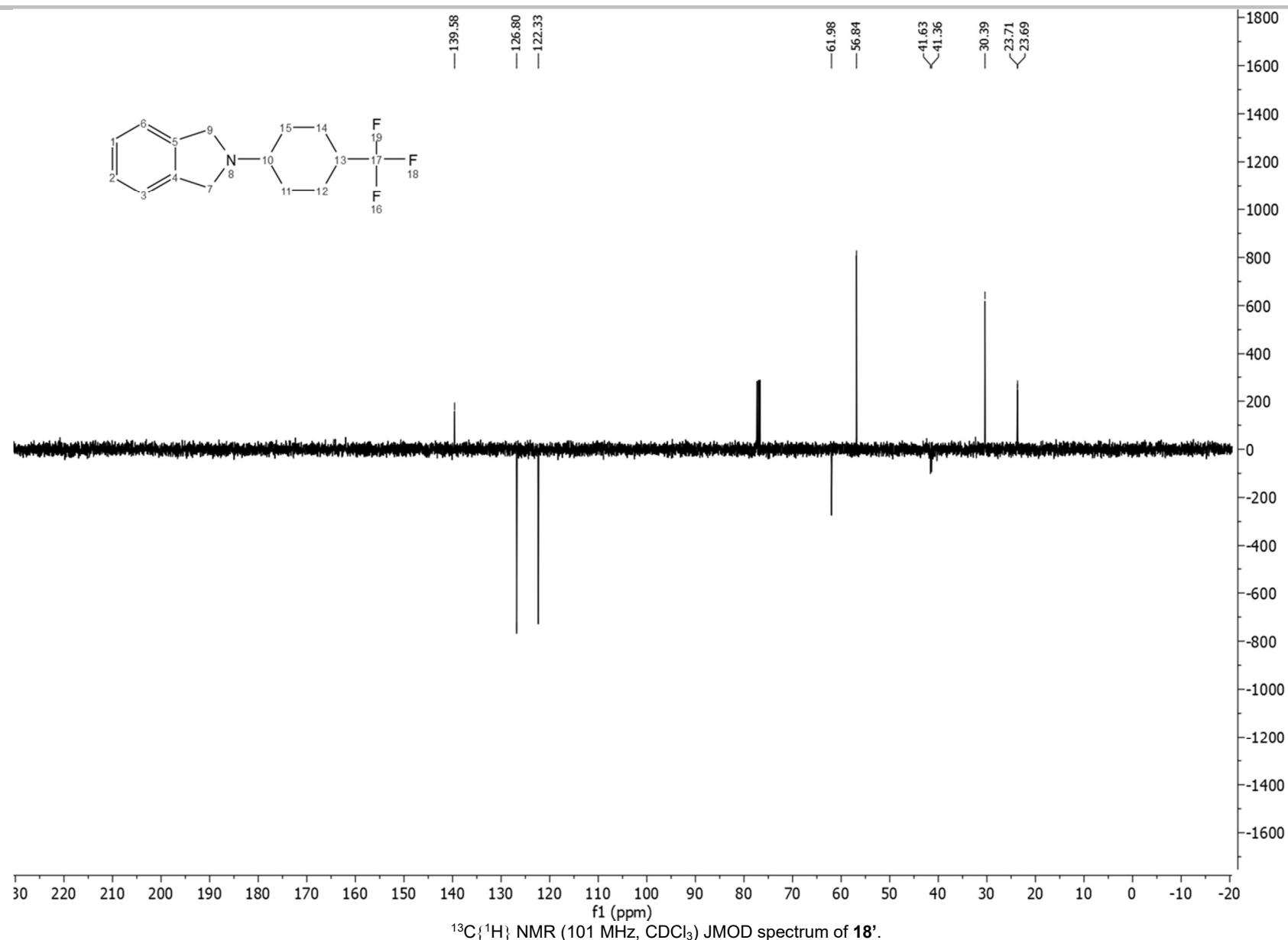
mjouffro\_567\_1.4.fid

 $^{19}\text{F}\{\text{H}\}$  NMR (376 MHz,  $\text{CDCl}_3$ ) spectrum of **17**.

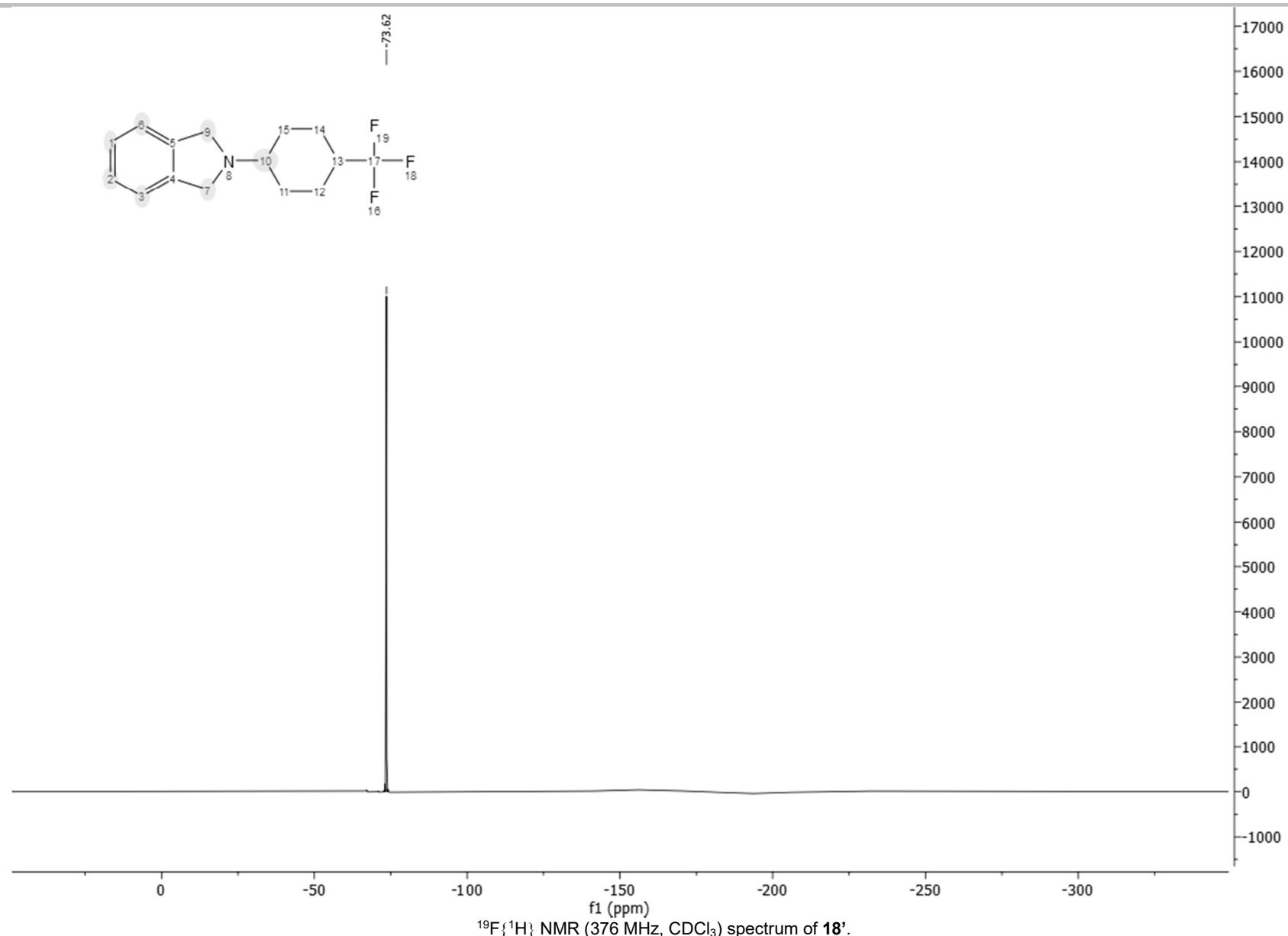
## SUPPORTING INFORMATION



## SUPPORTING INFORMATION

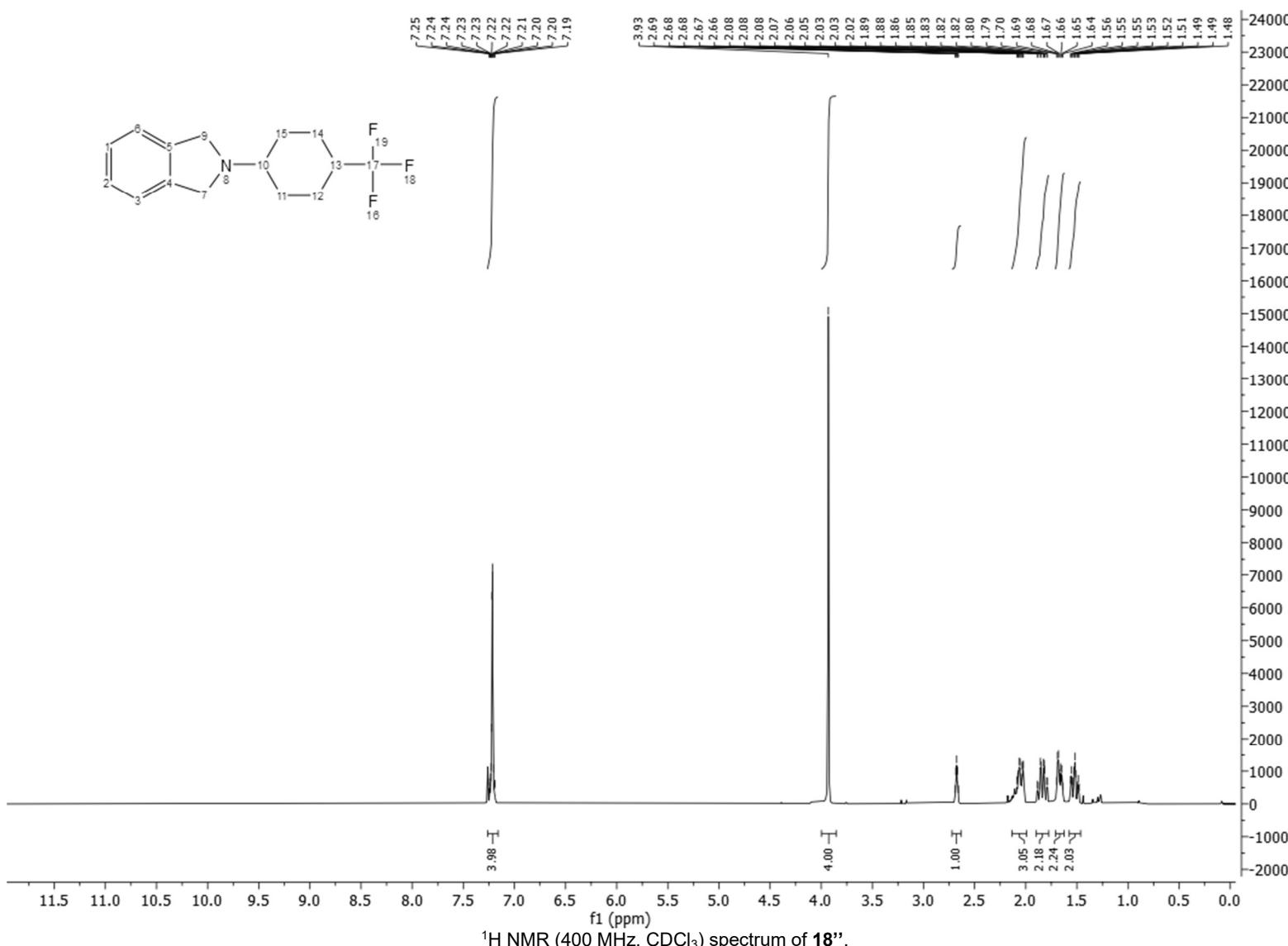
 $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ) JMOD spectrum of **18'**.

## SUPPORTING INFORMATION

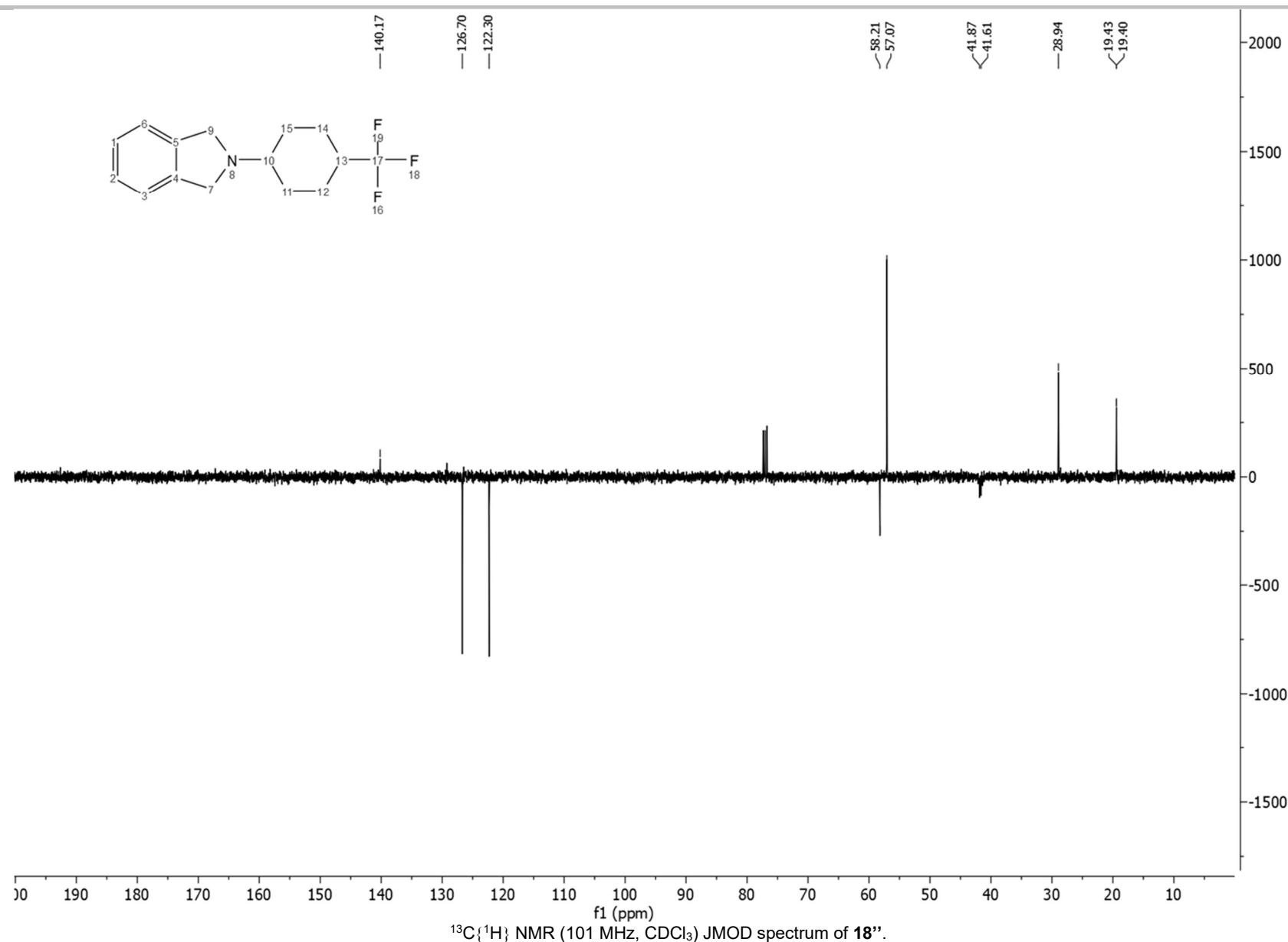


$^{19}\text{F}\{^1\text{H}\}$  NMR (376 MHz,  $\text{CDCl}_3$ ) spectrum of **18'**.

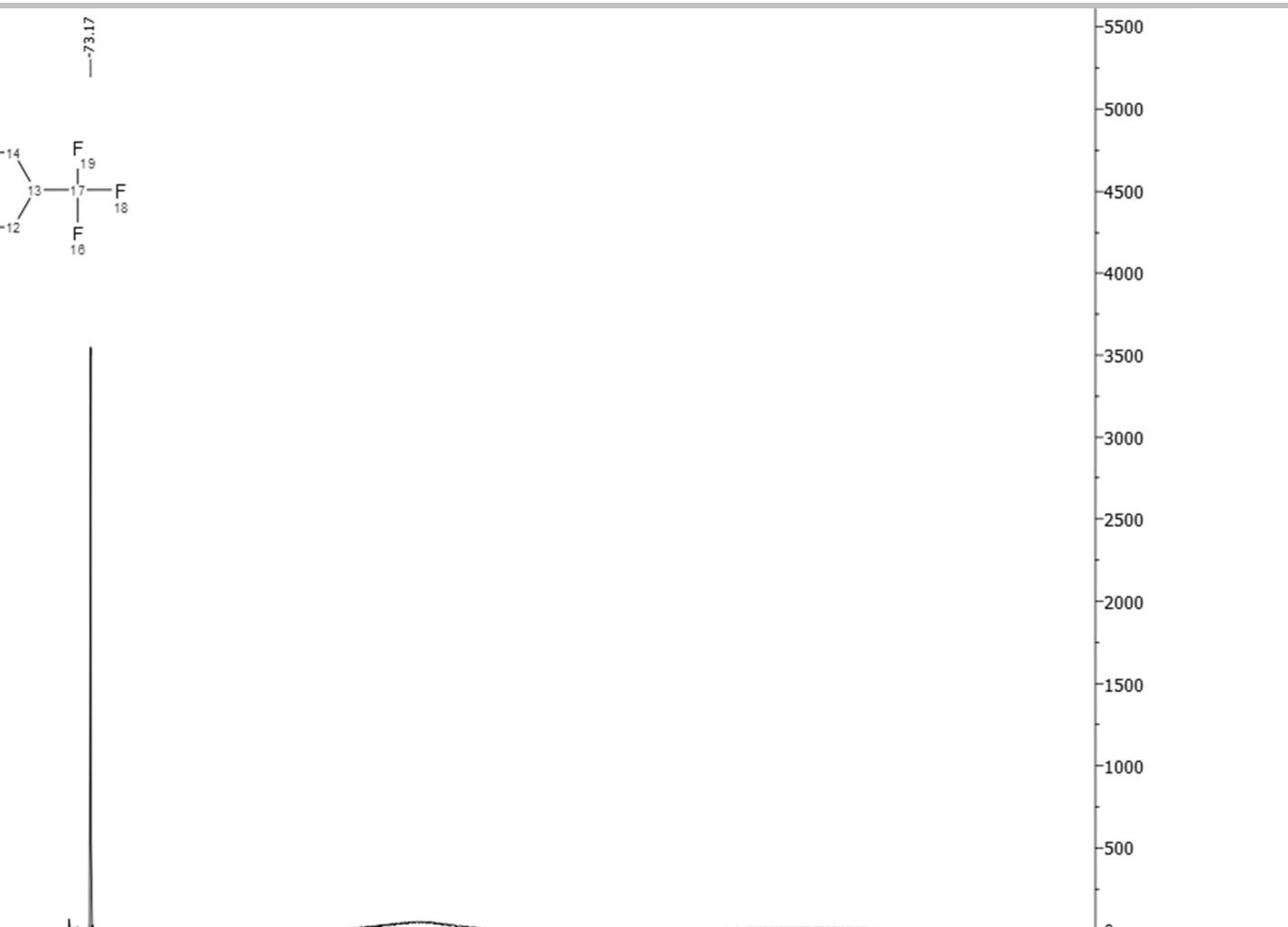
## SUPPORTING INFORMATION



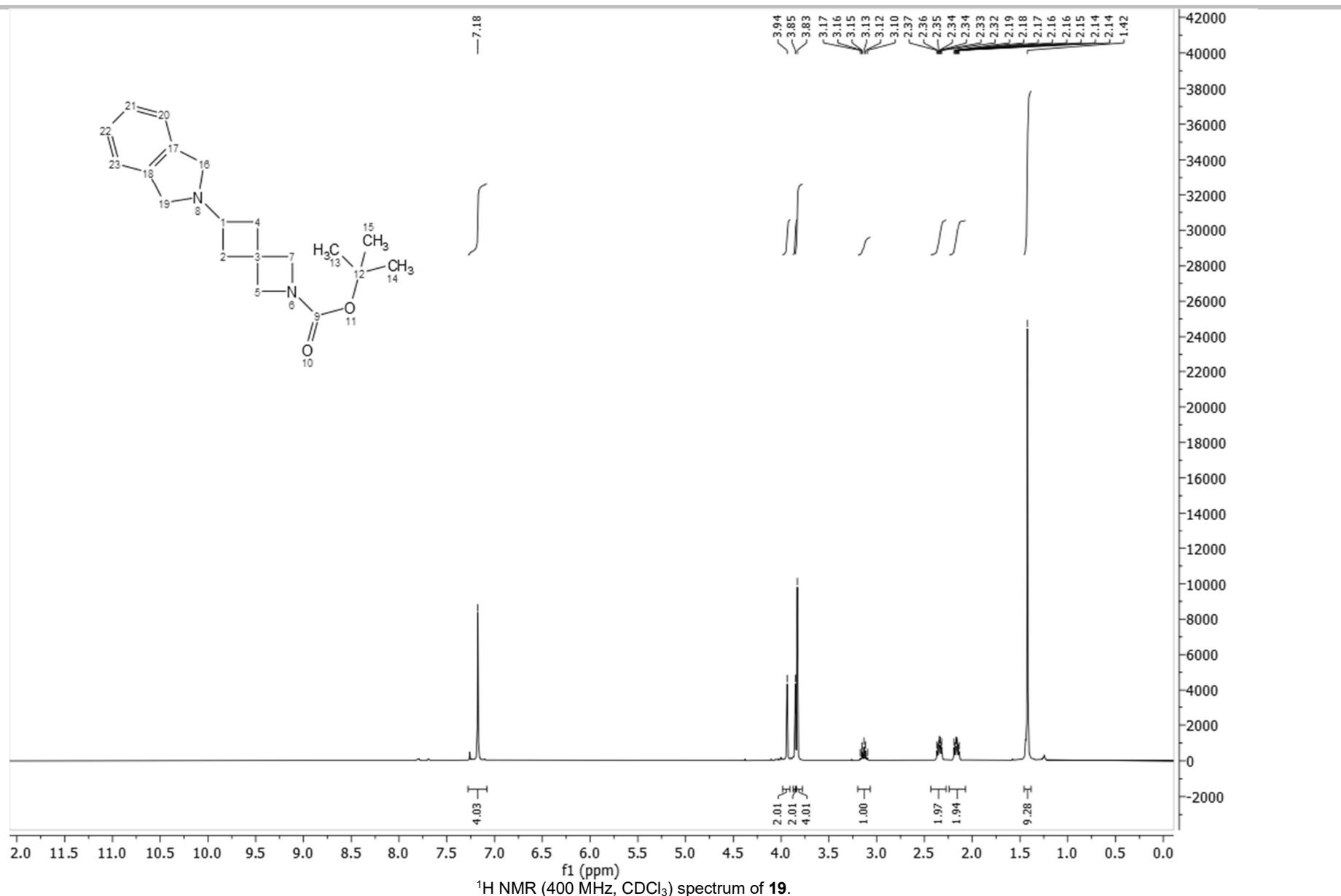
## SUPPORTING INFORMATION



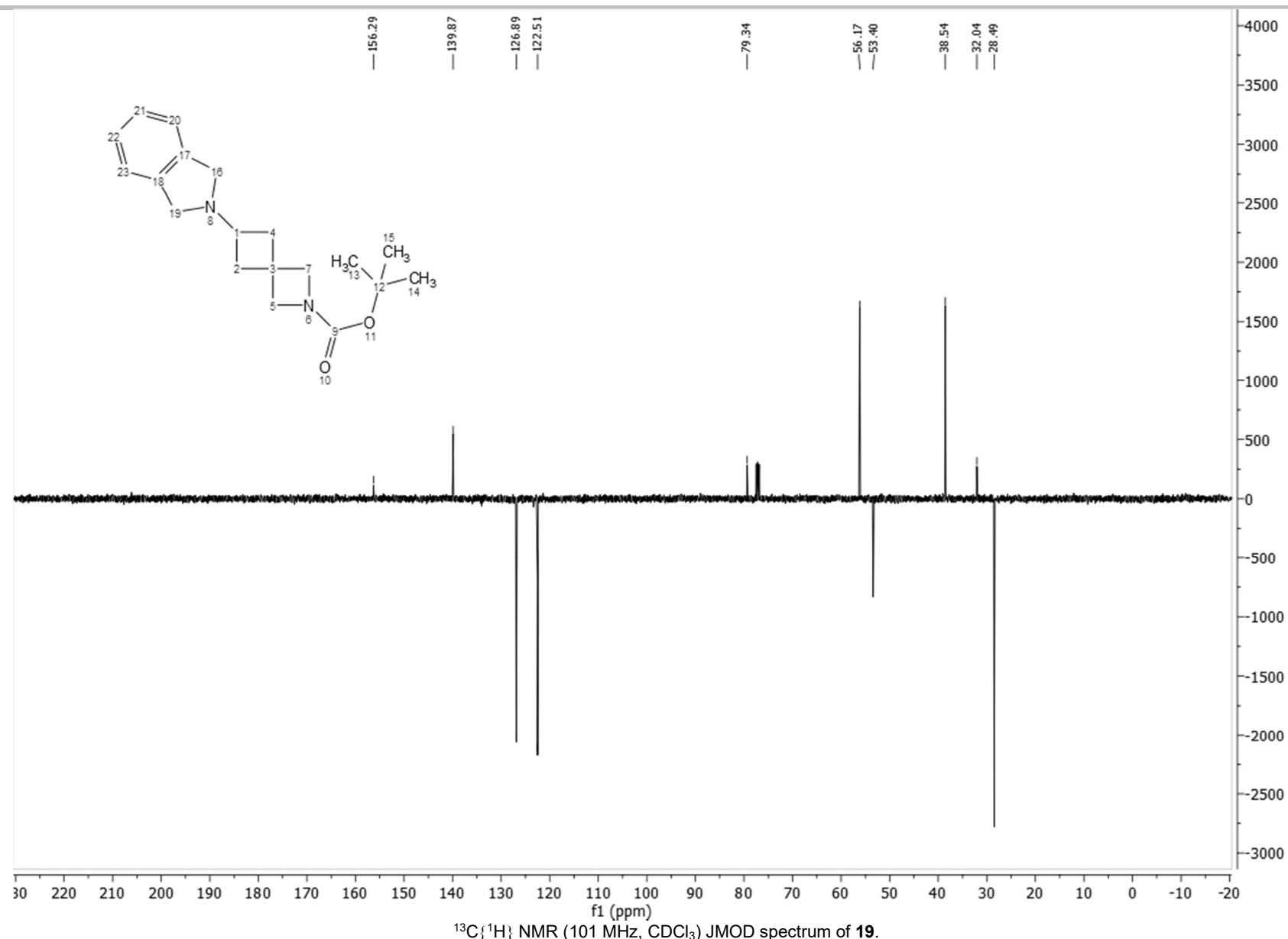
WILEY-VCH



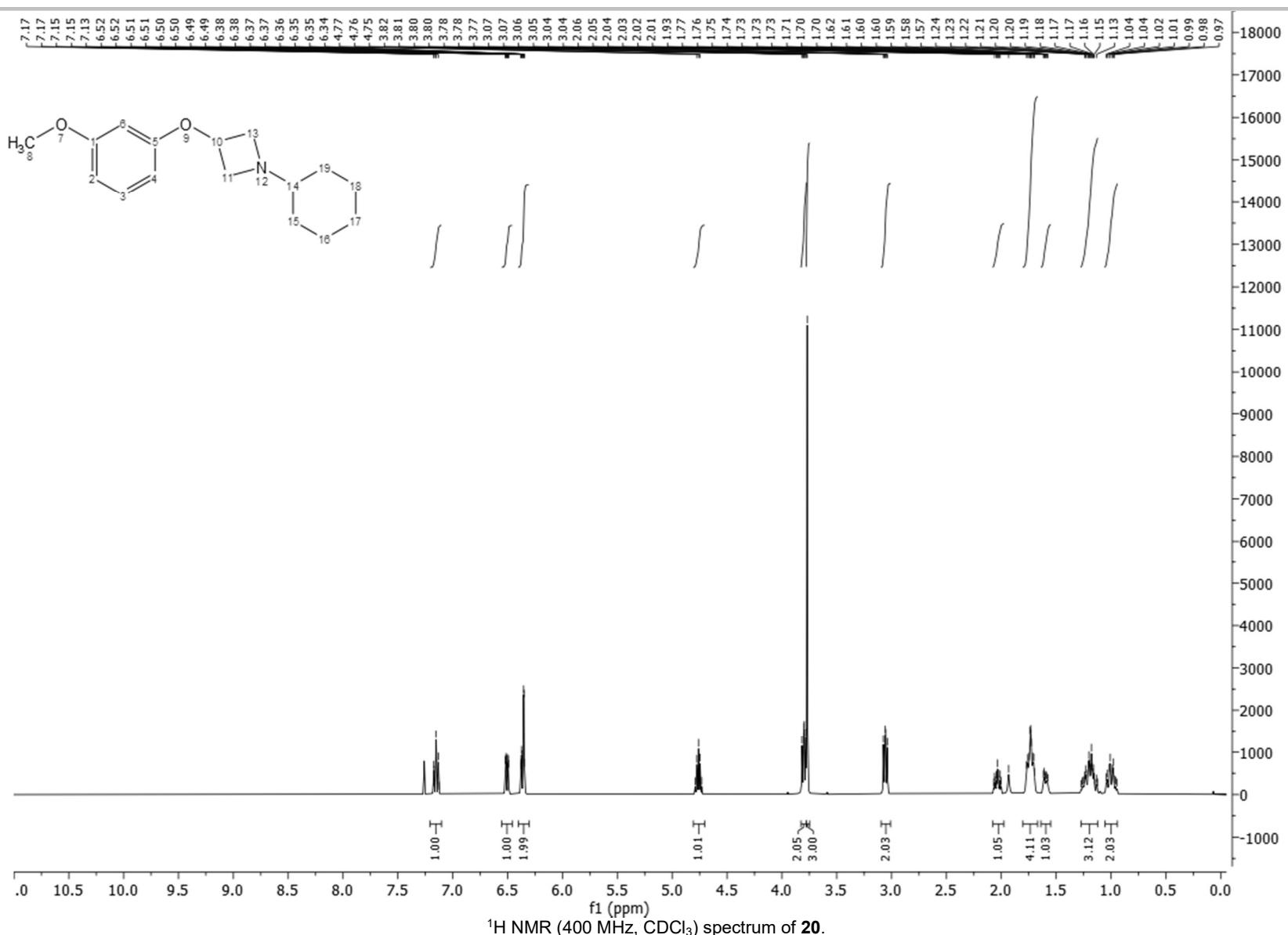
## SUPPORTING INFORMATION

 $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) spectrum of **19**.

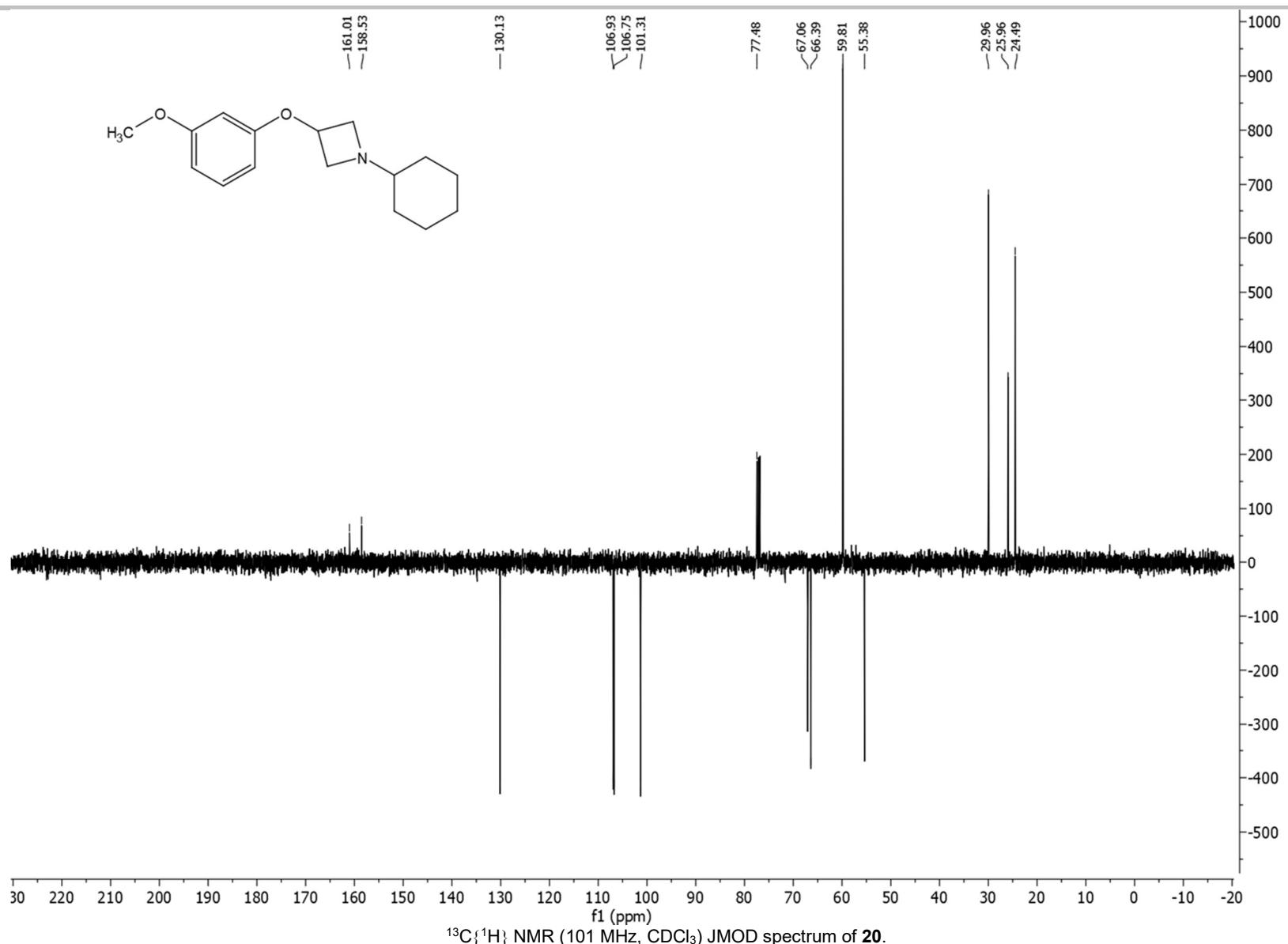
## SUPPORTING INFORMATION



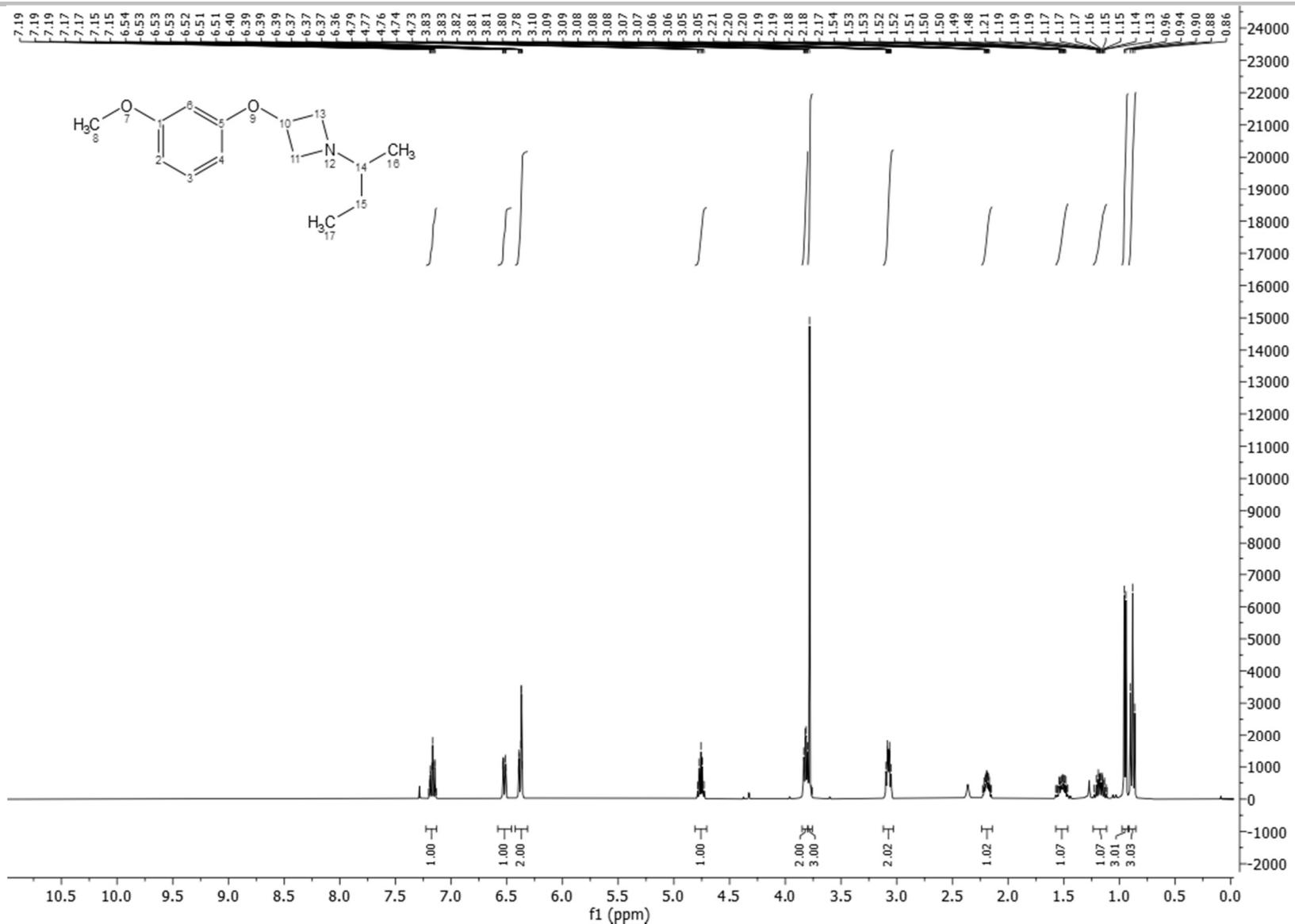
## SUPPORTING INFORMATION



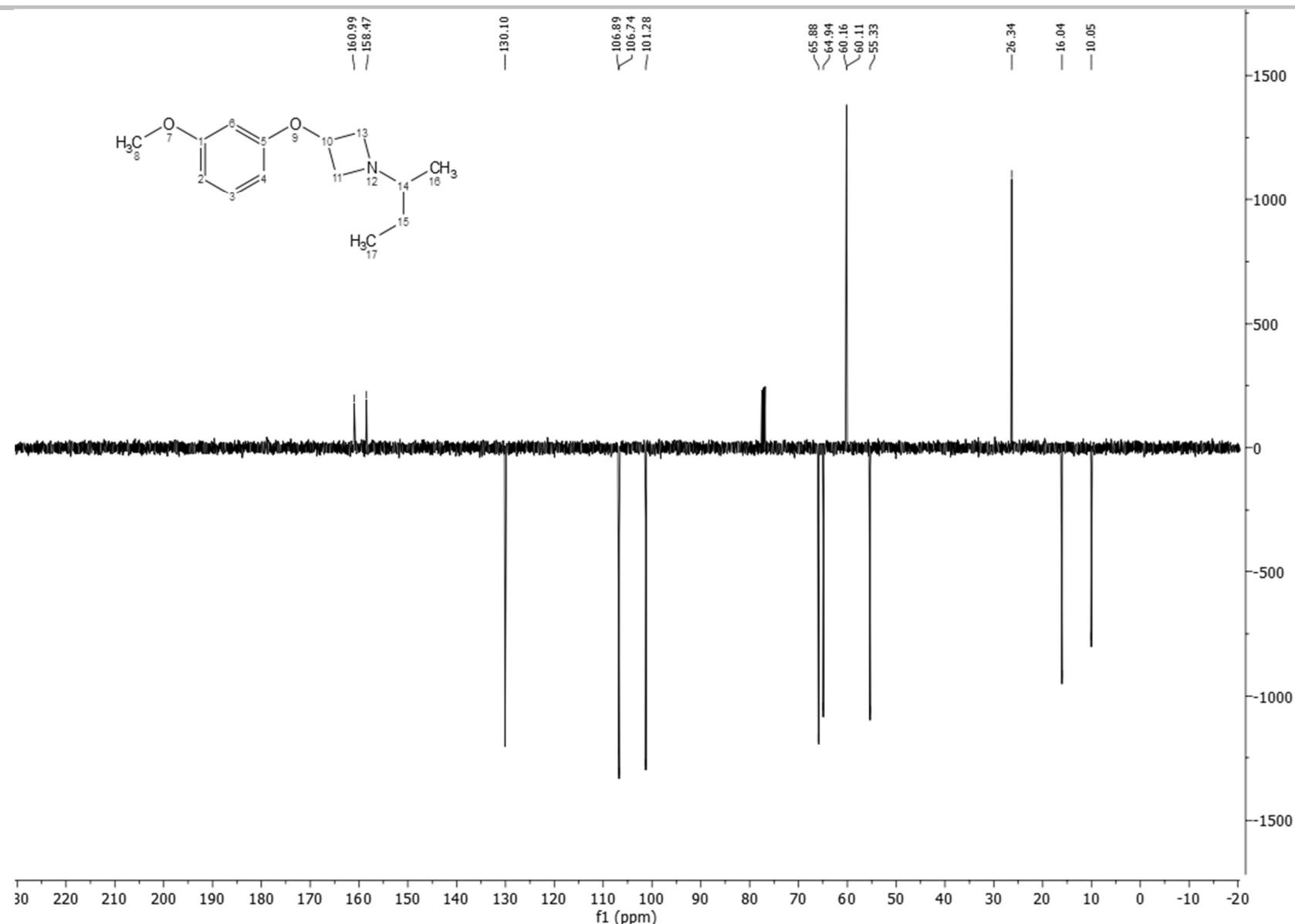
## SUPPORTING INFORMATION



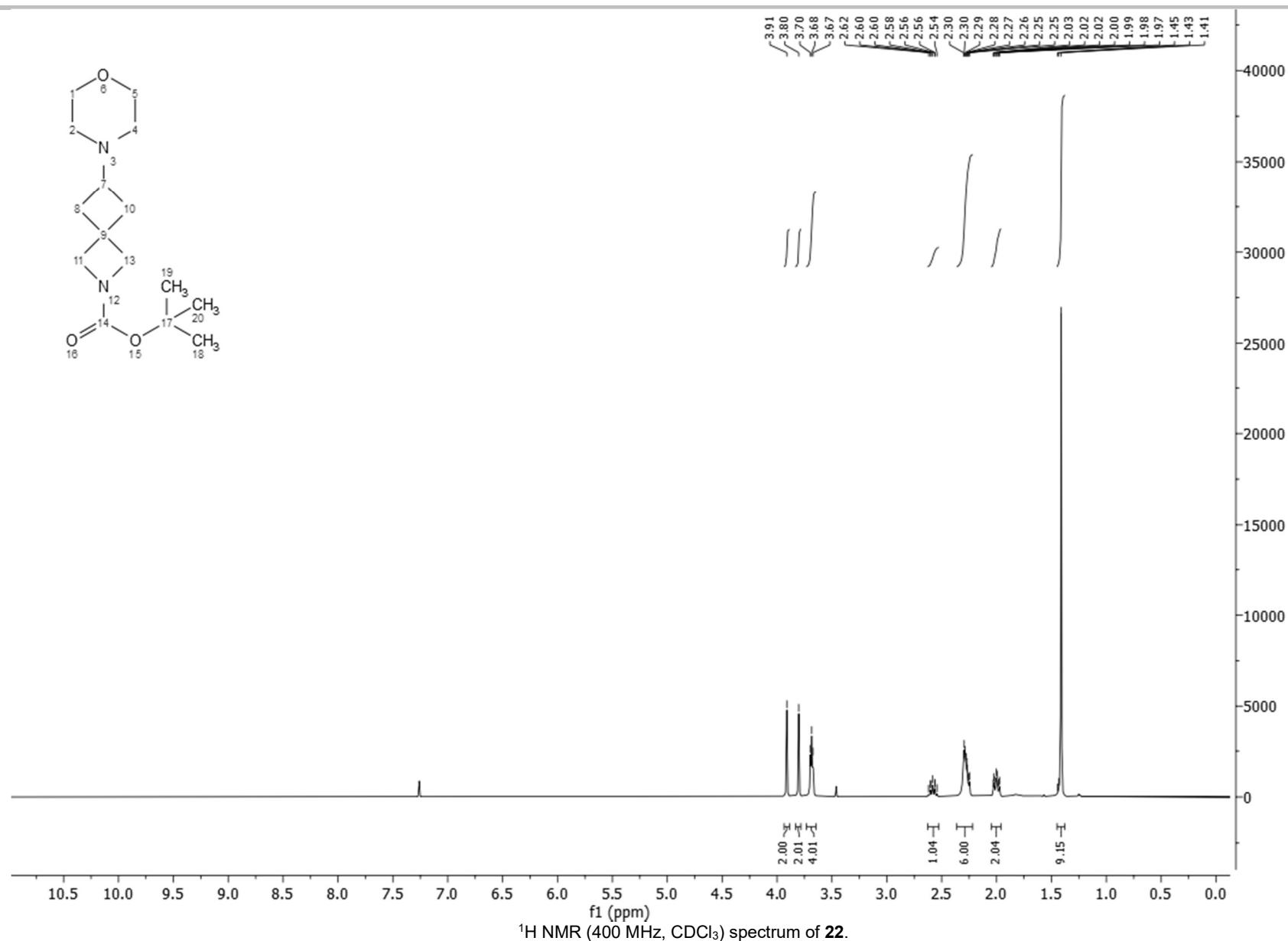
## SUPPORTING INFORMATION



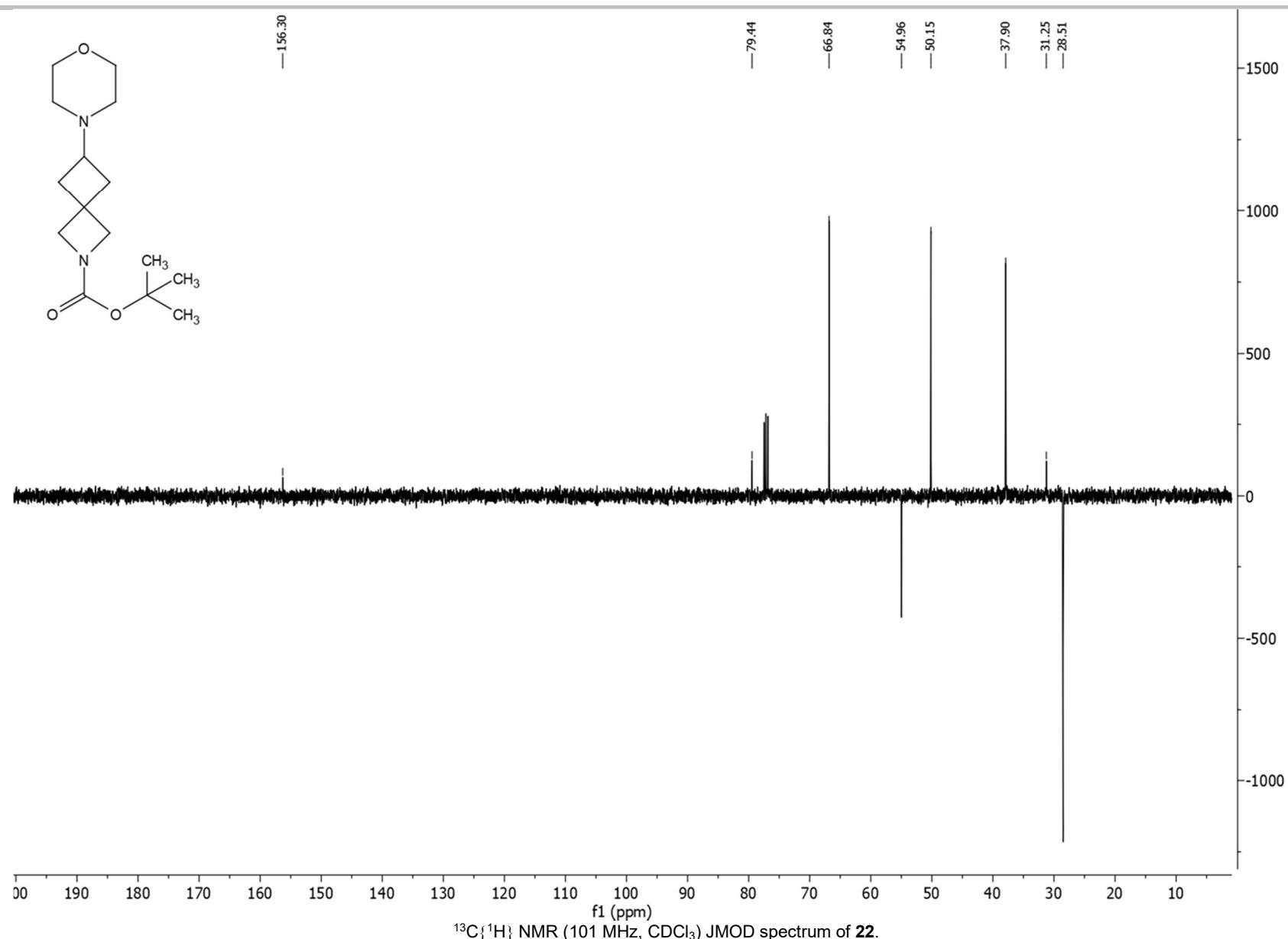
## SUPPORTING INFORMATION

 $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ) JMOD spectrum of **21**.

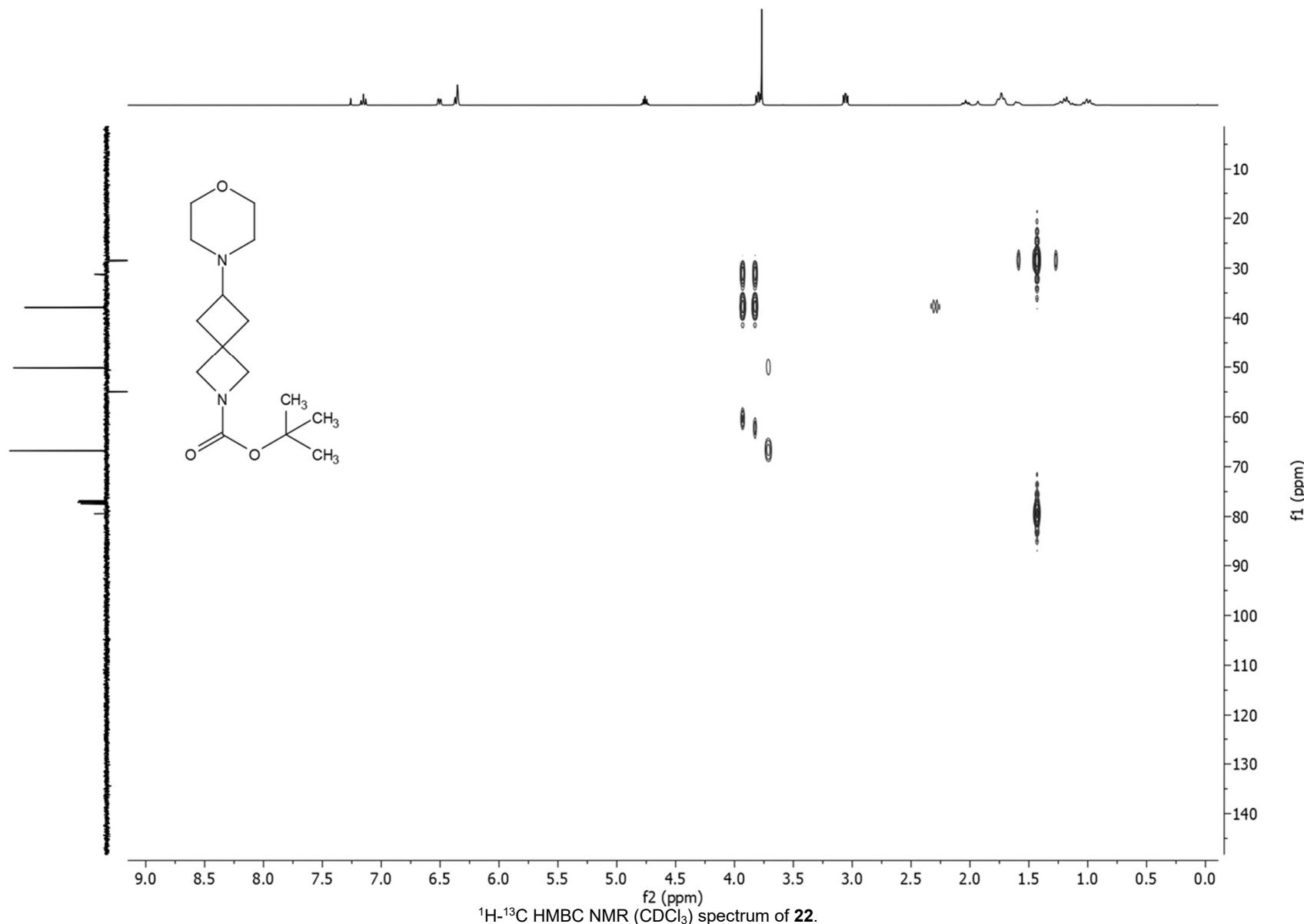
## SUPPORTING INFORMATION



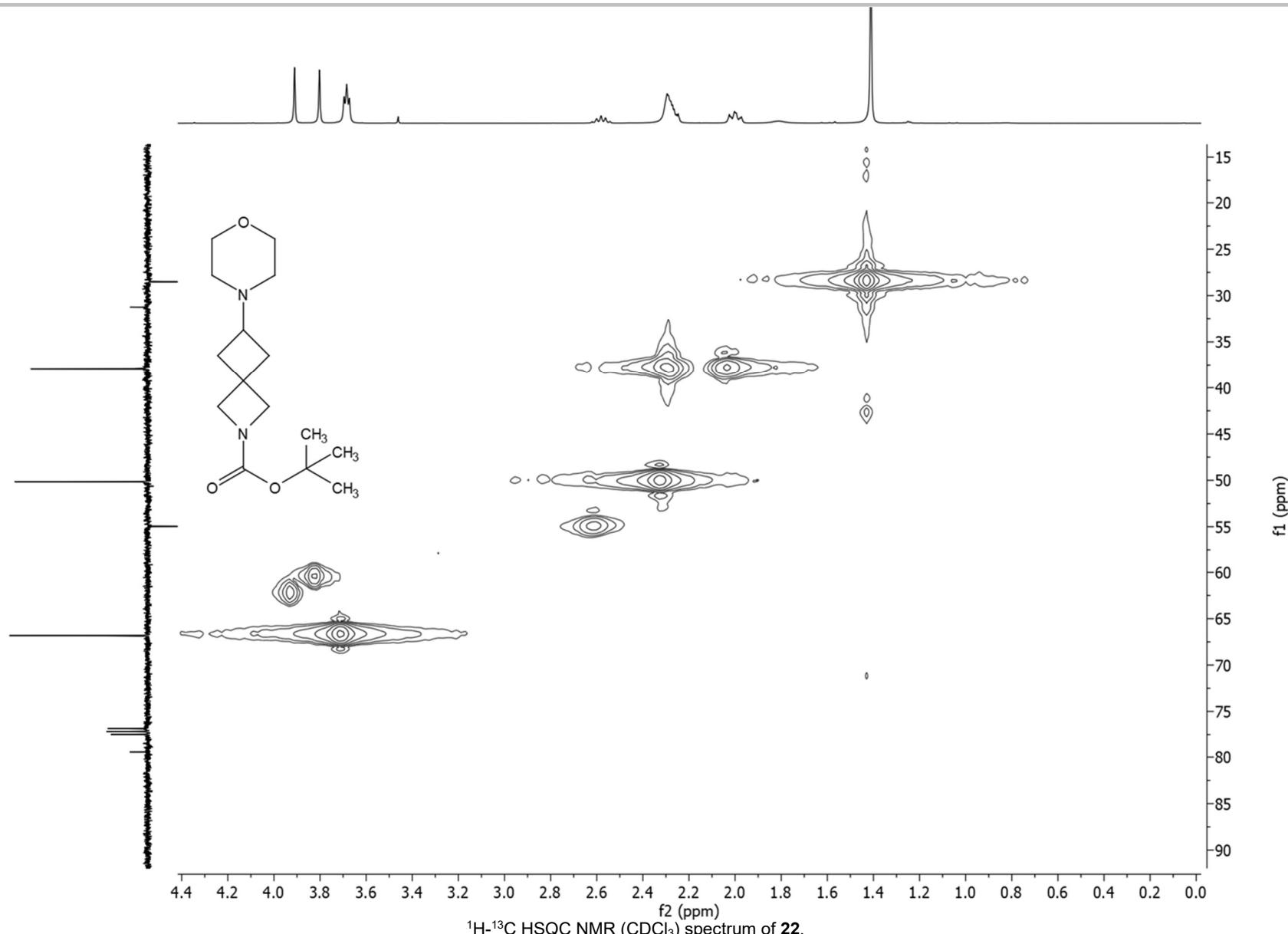
## SUPPORTING INFORMATION



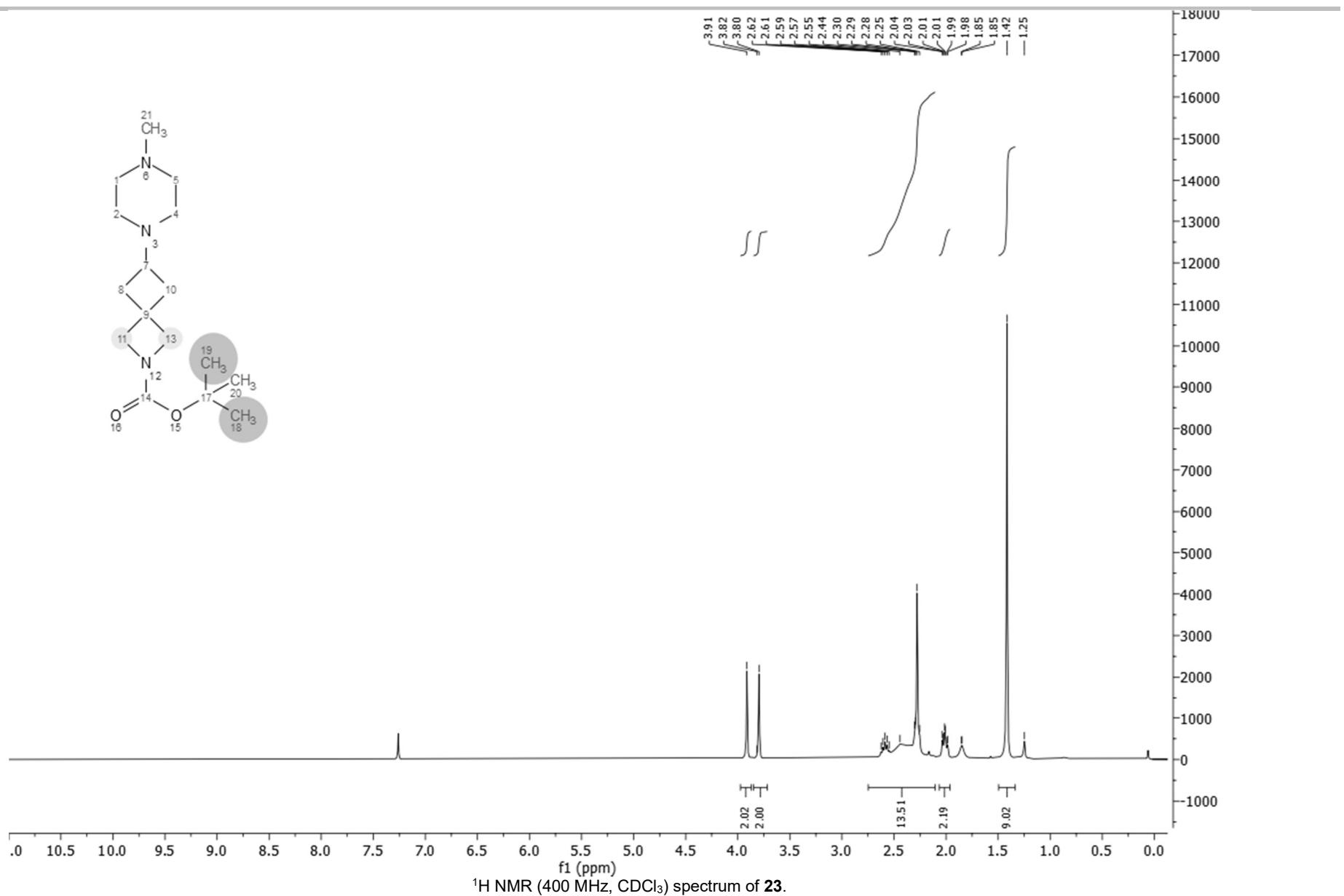
## SUPPORTING INFORMATION



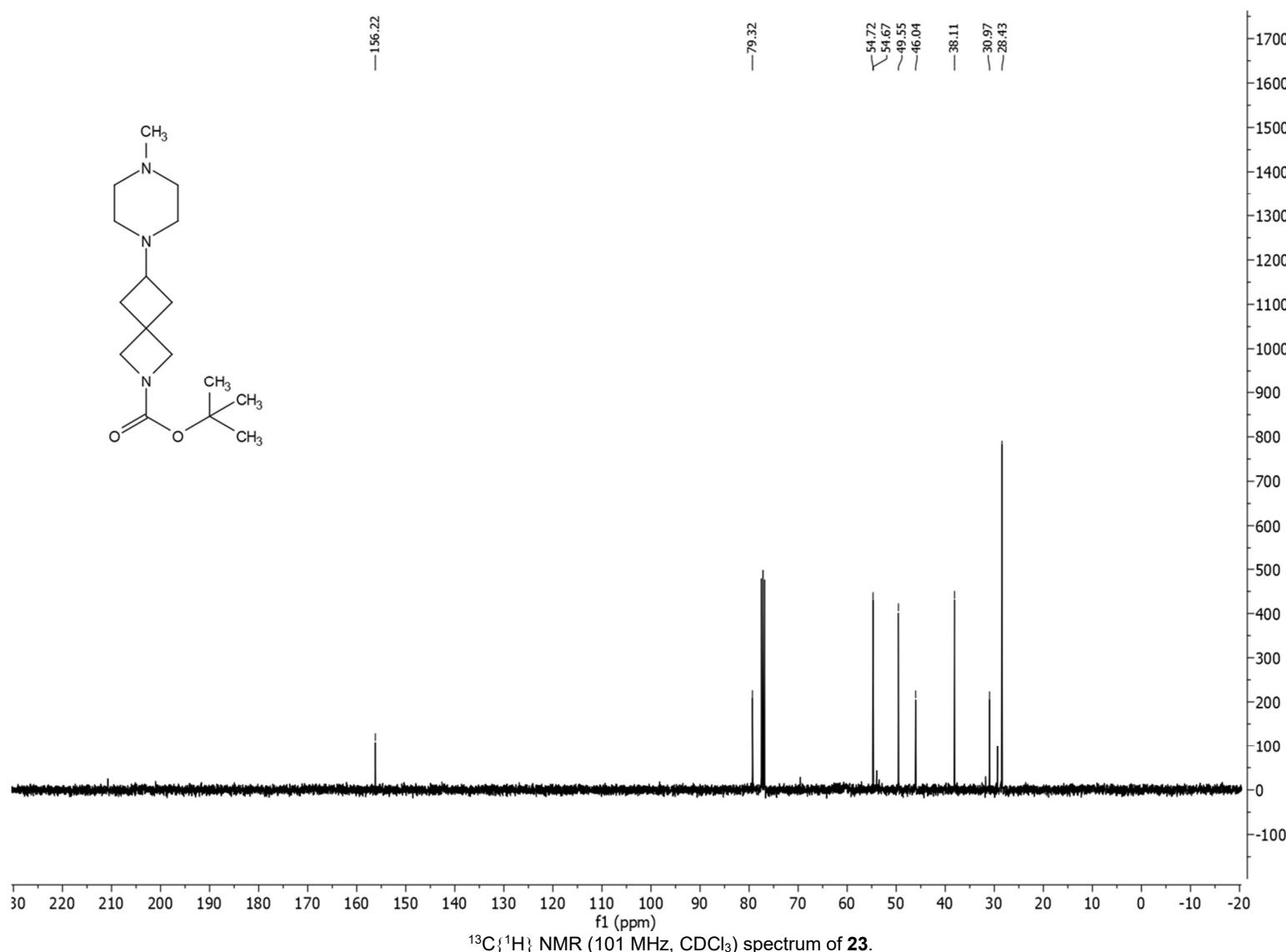
## SUPPORTING INFORMATION



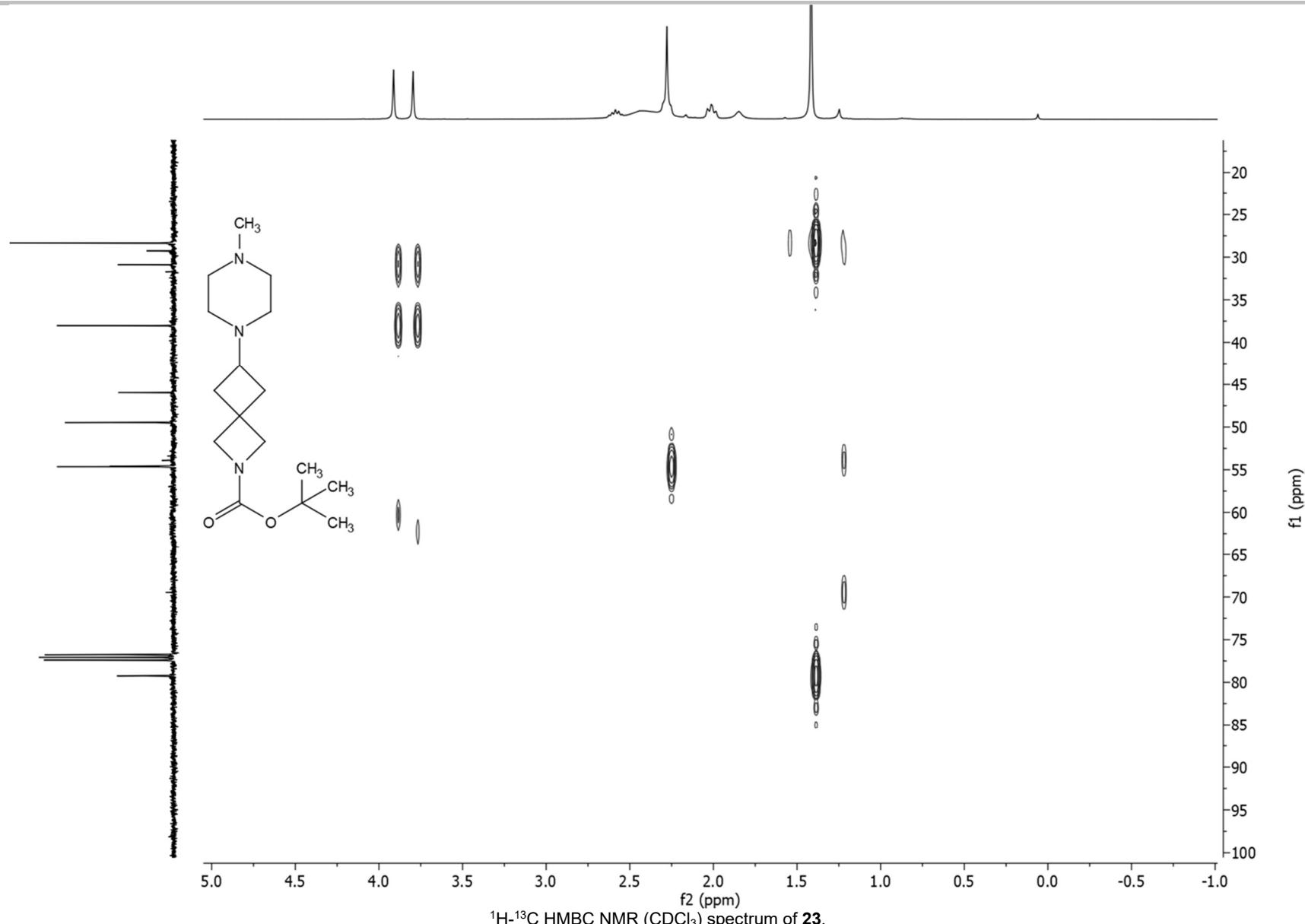
## SUPPORTING INFORMATION

 $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) spectrum of **23**.

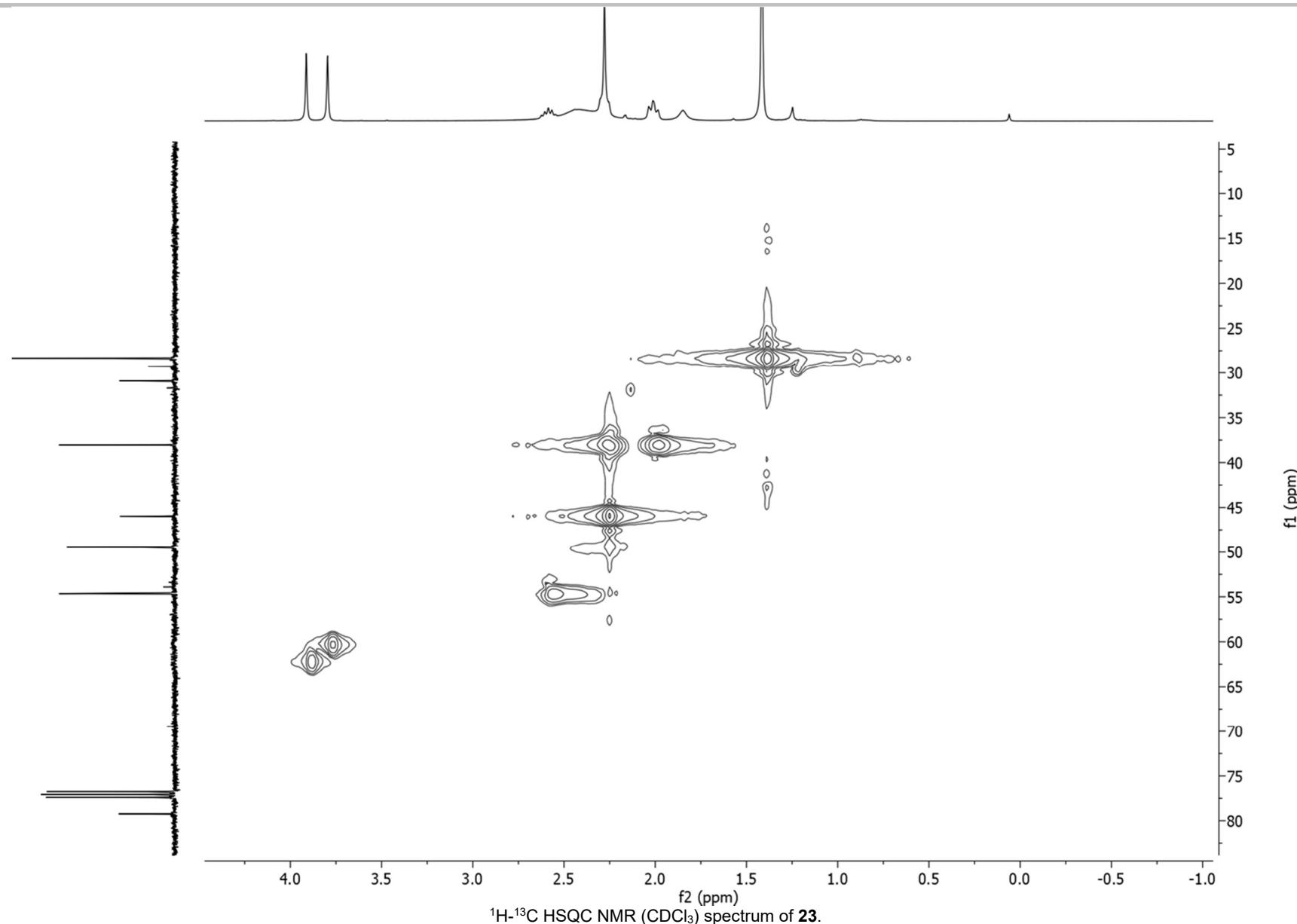
## SUPPORTING INFORMATION

 $^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ) spectrum of **23**.

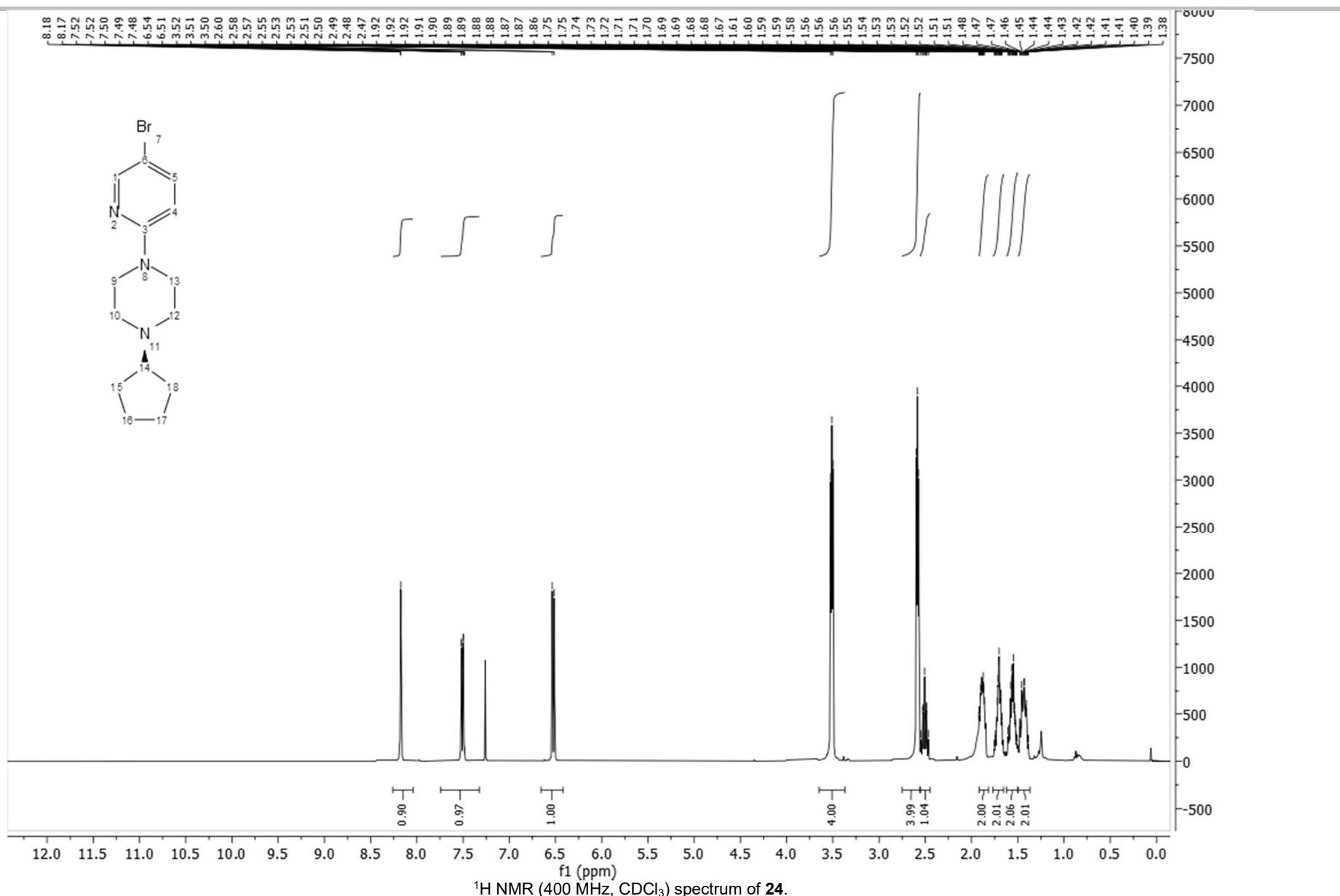
## SUPPORTING INFORMATION



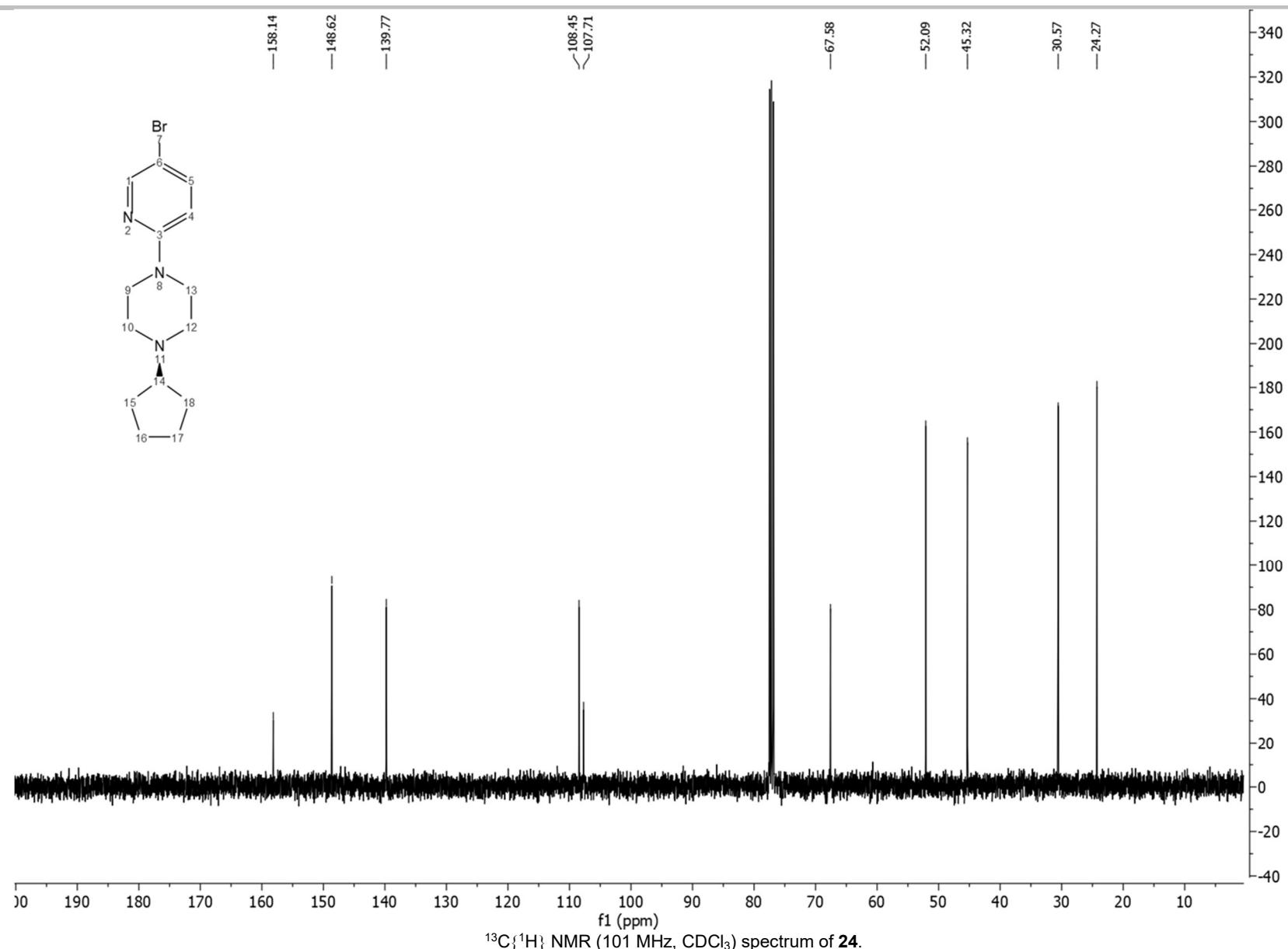
## SUPPORTING INFORMATION



## SUPPORTING INFORMATION

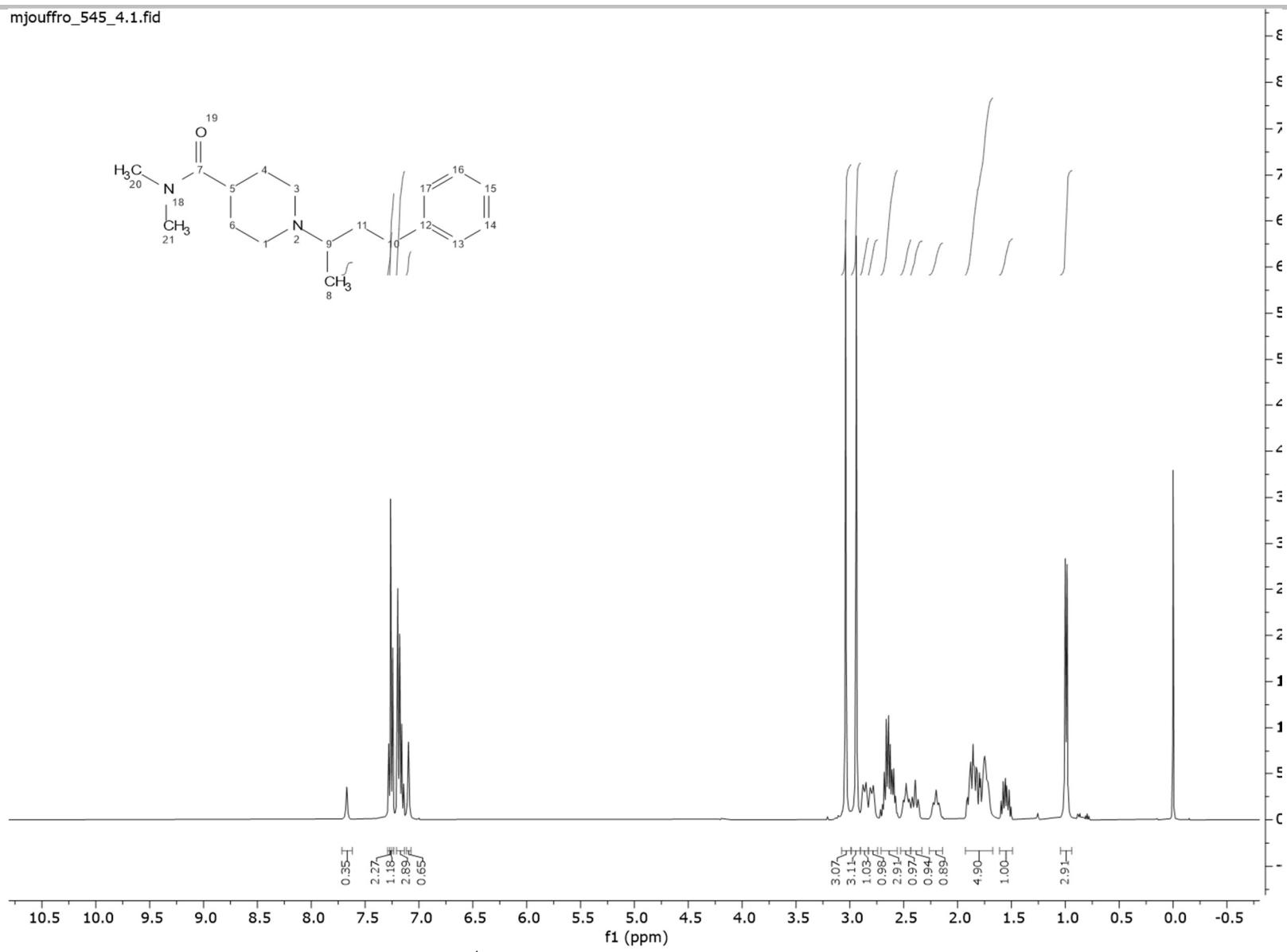
 $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) spectrum of **24**.

## SUPPORTING INFORMATION

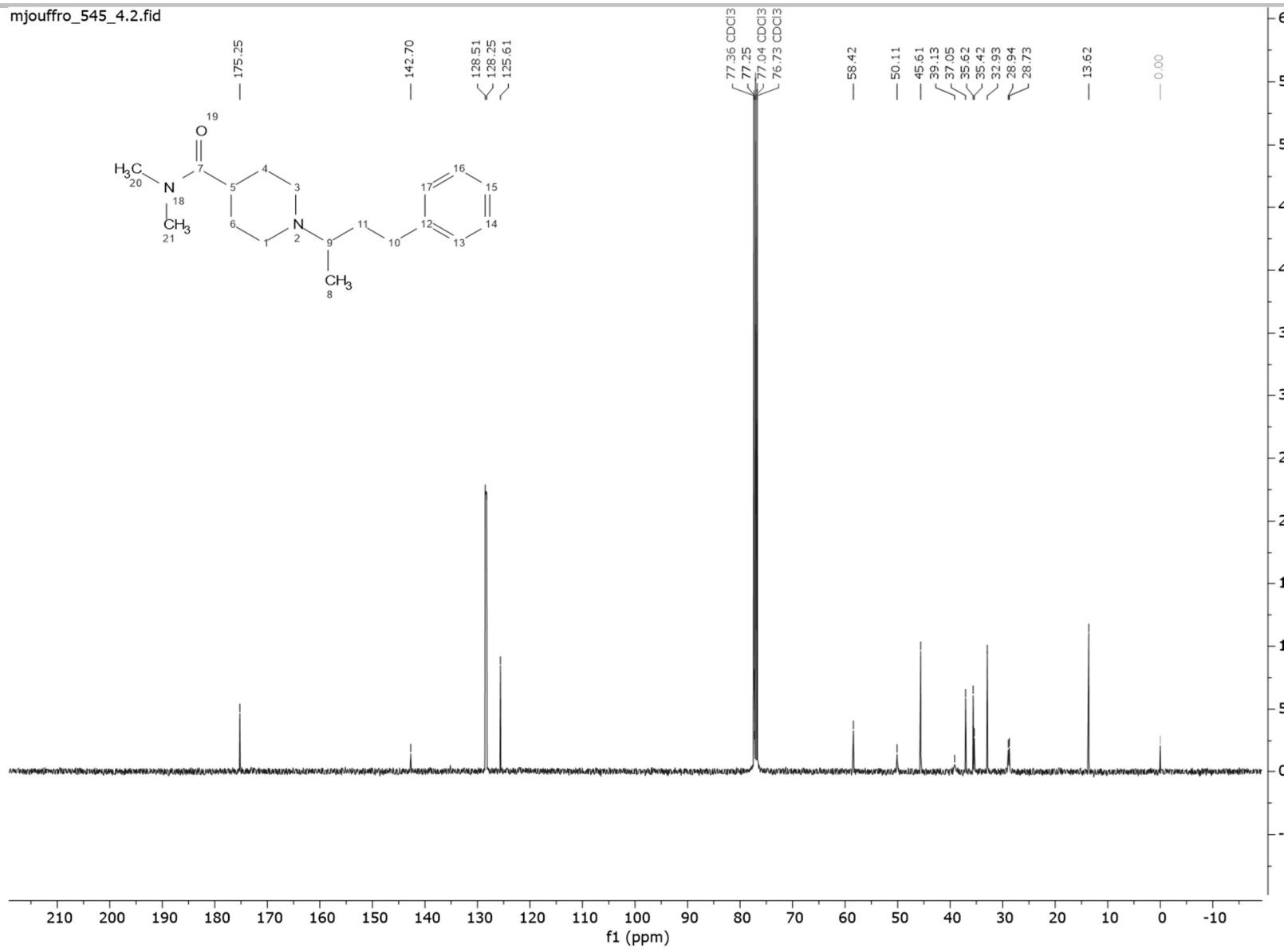
 $^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ) spectrum of **24**.

## SUPPORTING INFORMATION

mjouffro\_545\_4.1.fid

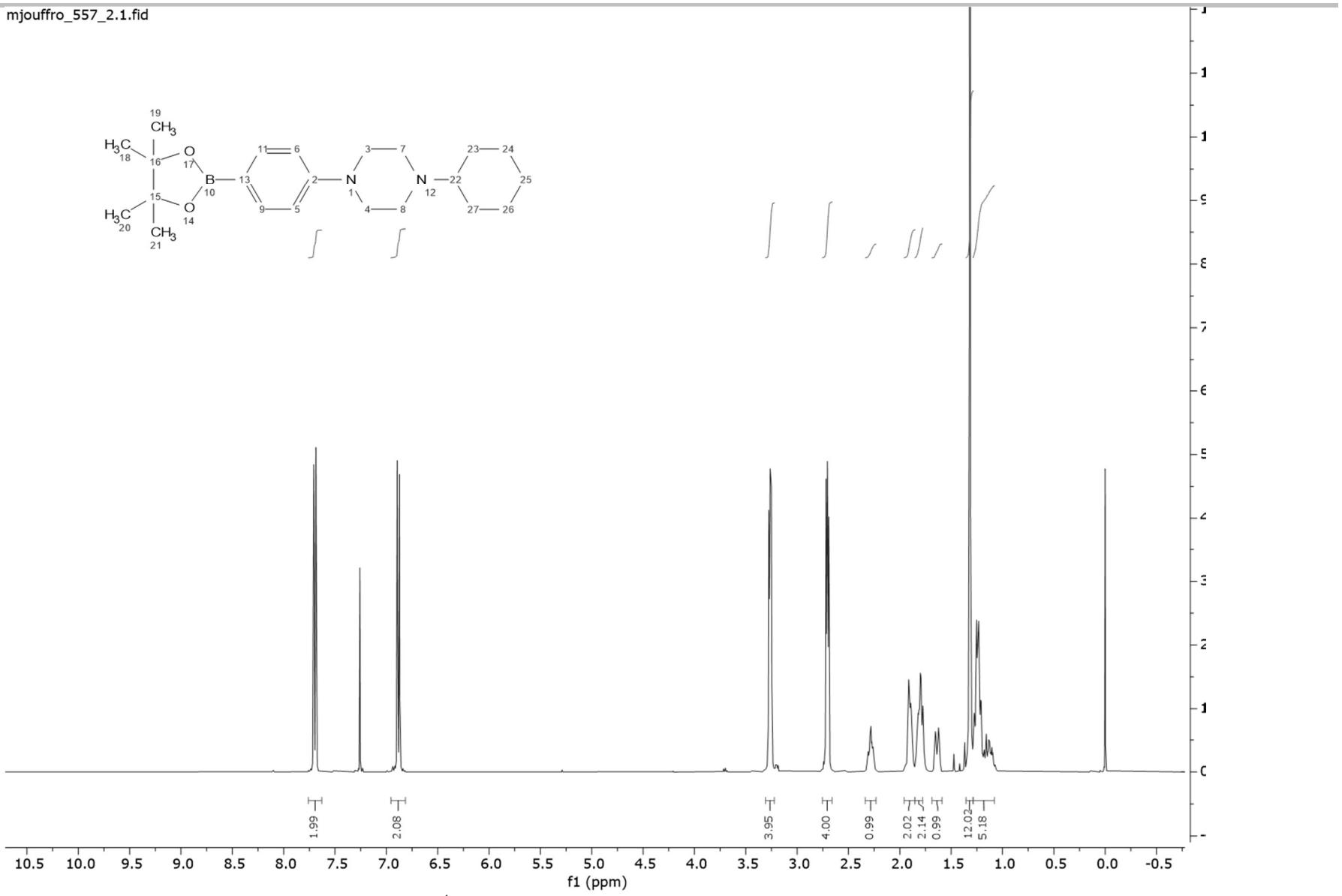
 $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) spectrum of **25**.

## SUPPORTING INFORMATION

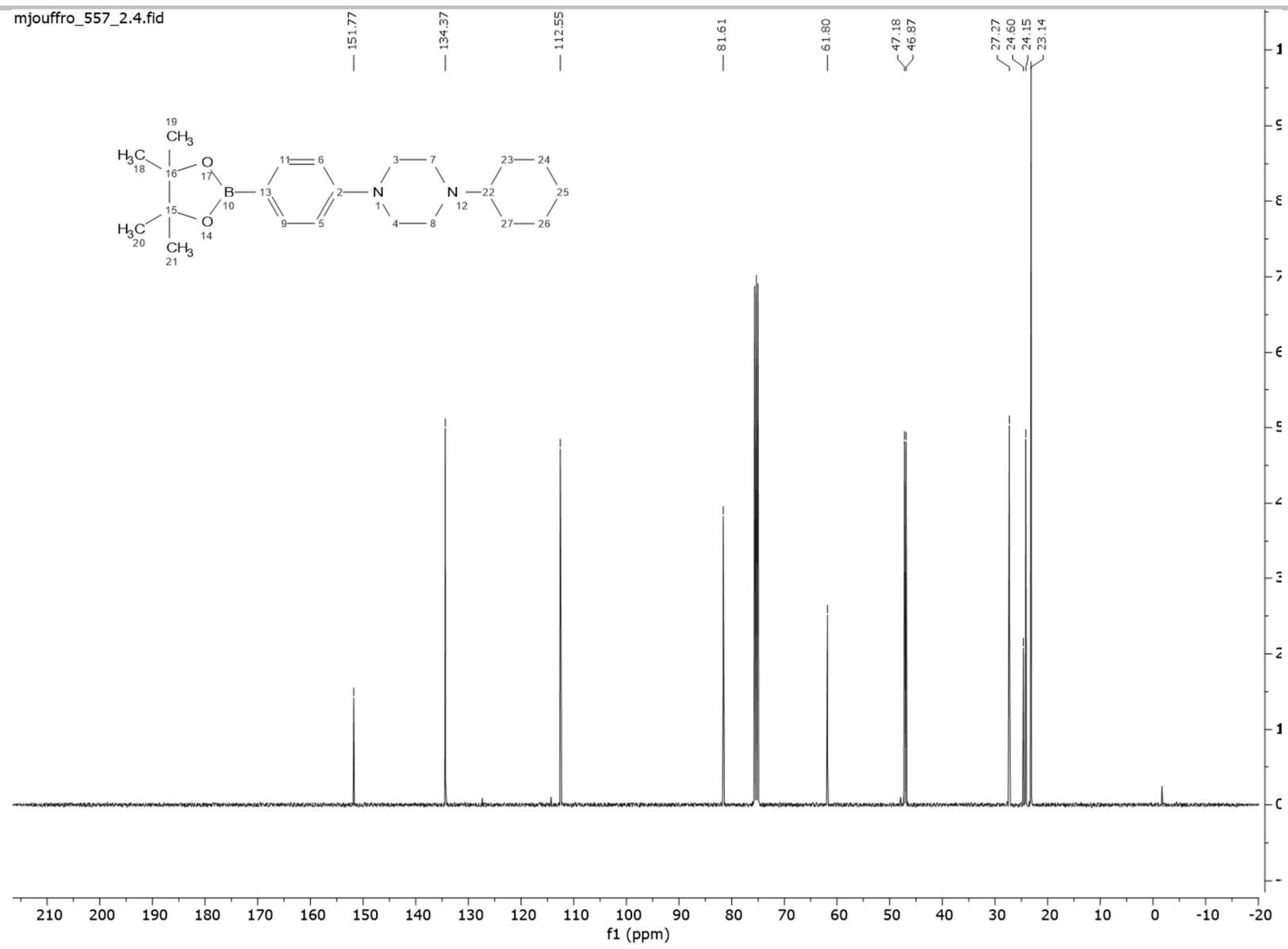


## SUPPORTING INFORMATION

mjouffro\_557\_2.1.fid

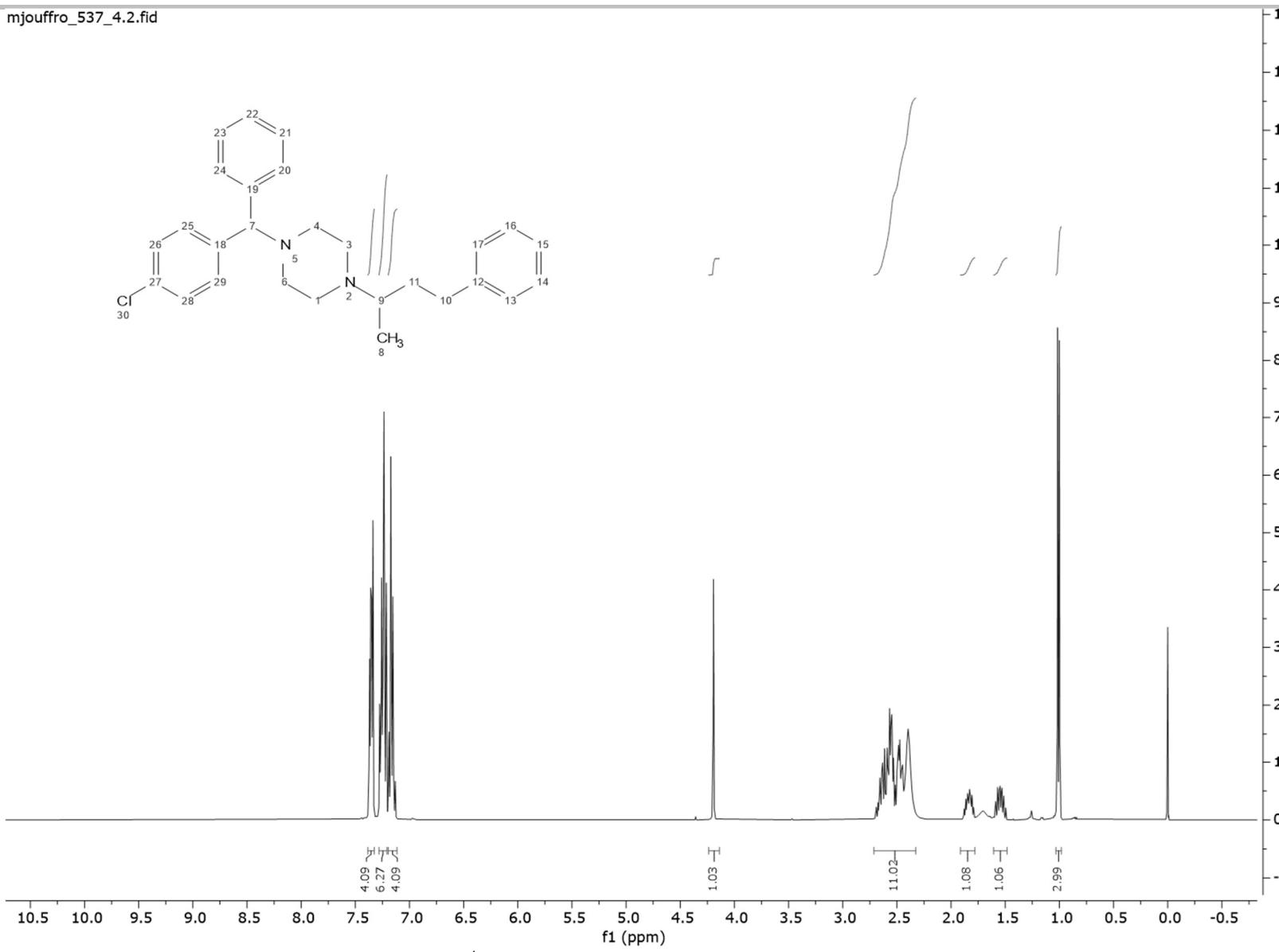
 $^1\text{H}$  NMR (400 MHz, CDCl<sub>3</sub>) spectrum of **26**.

## SUPPORTING INFORMATION



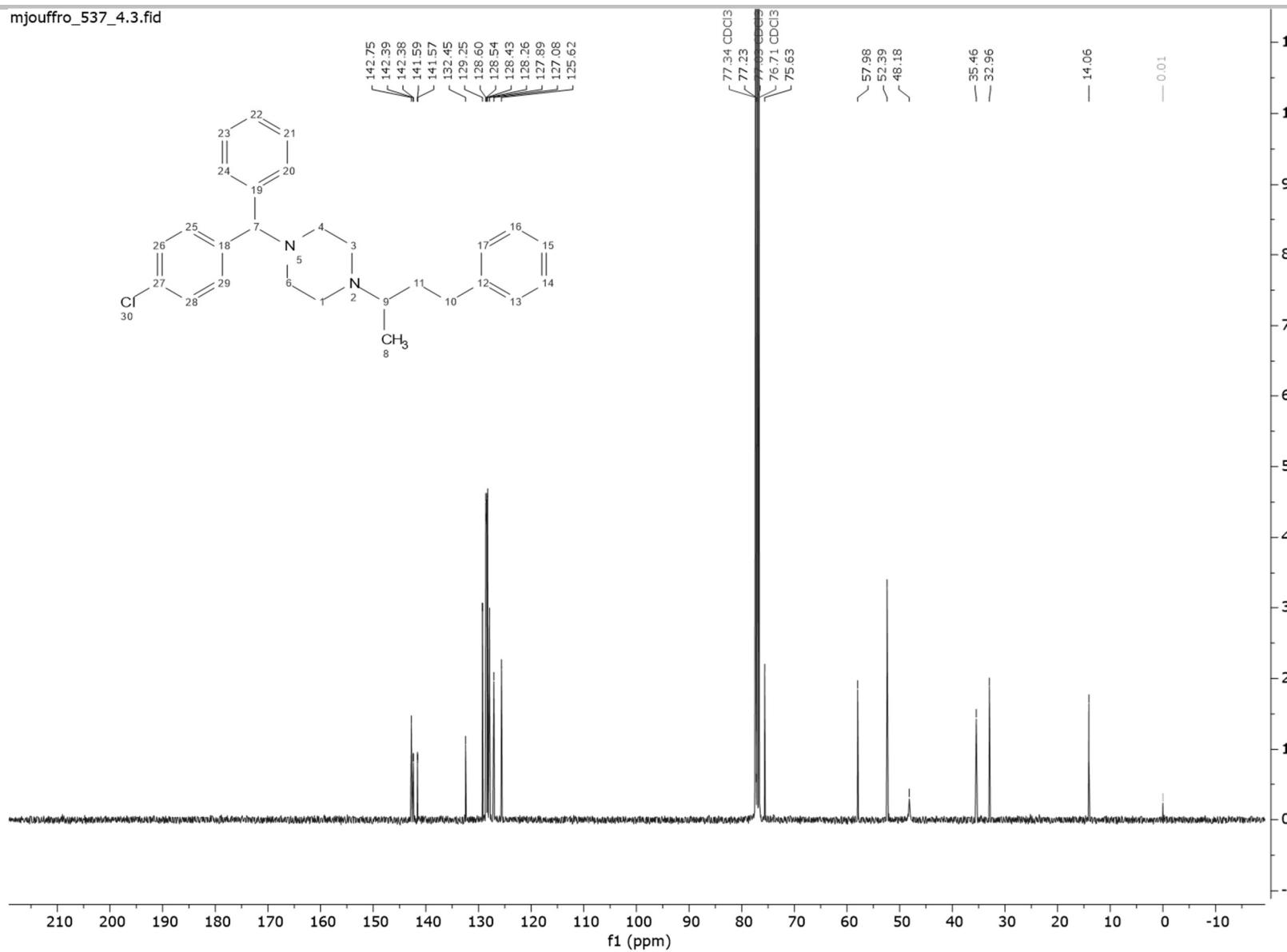
## SUPPORTING INFORMATION

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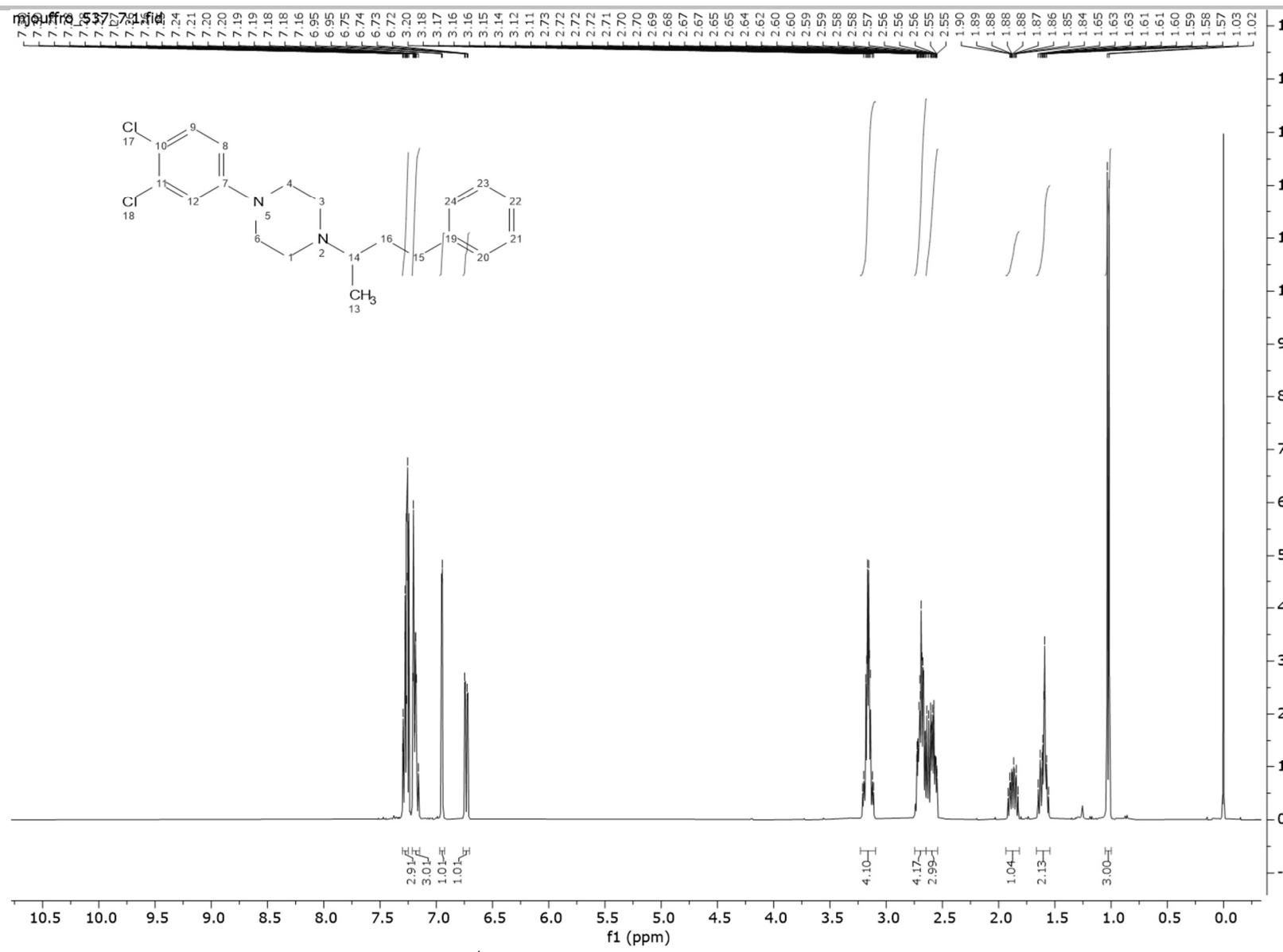


## SUPPORTING INFORMATION

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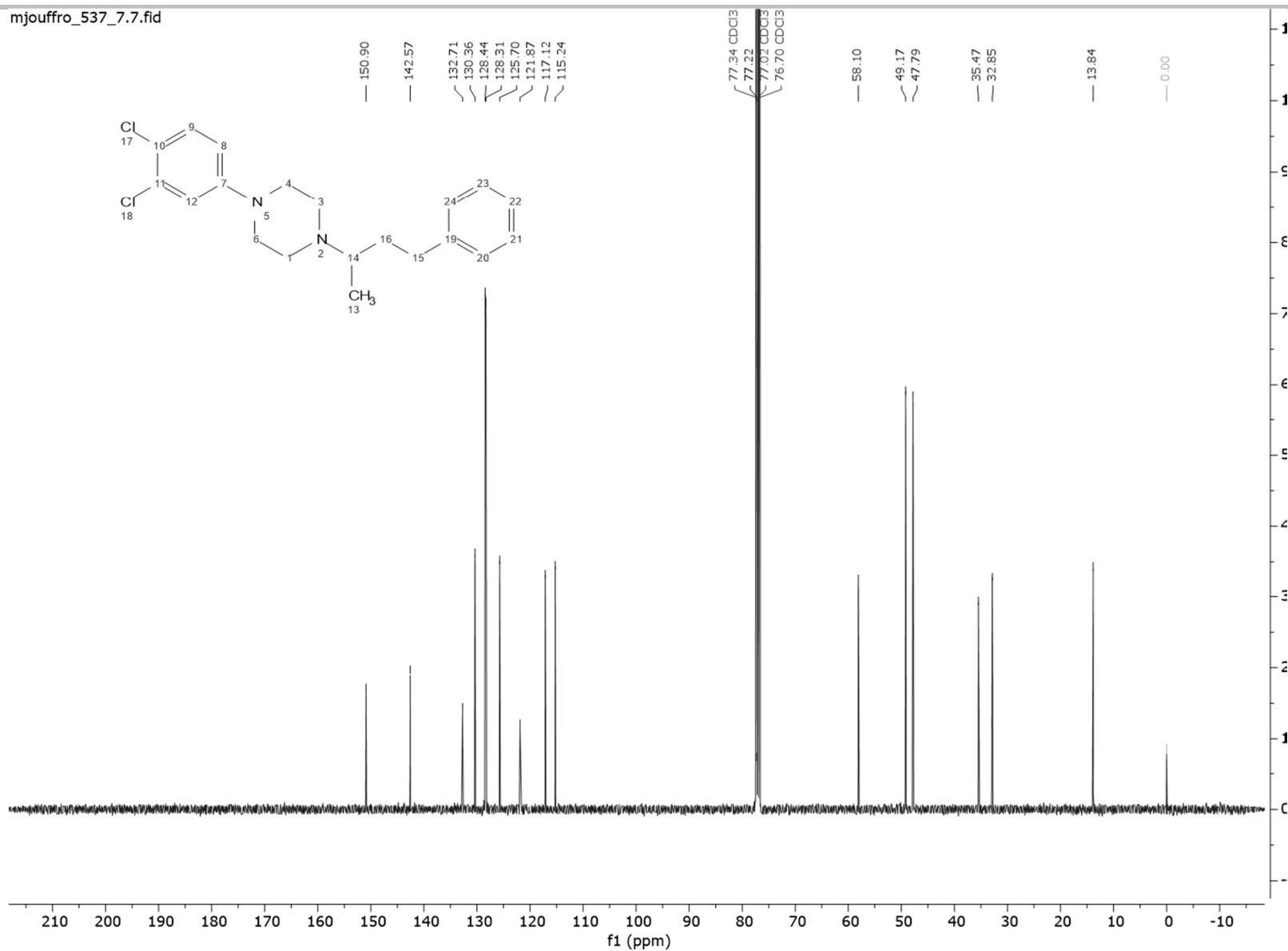
 $^{13}\text{C}\{\text{H}\}$  NMR (101 MHz, CDCl<sub>3</sub>) spectrum of **27**.

## SUPPORTING INFORMATION

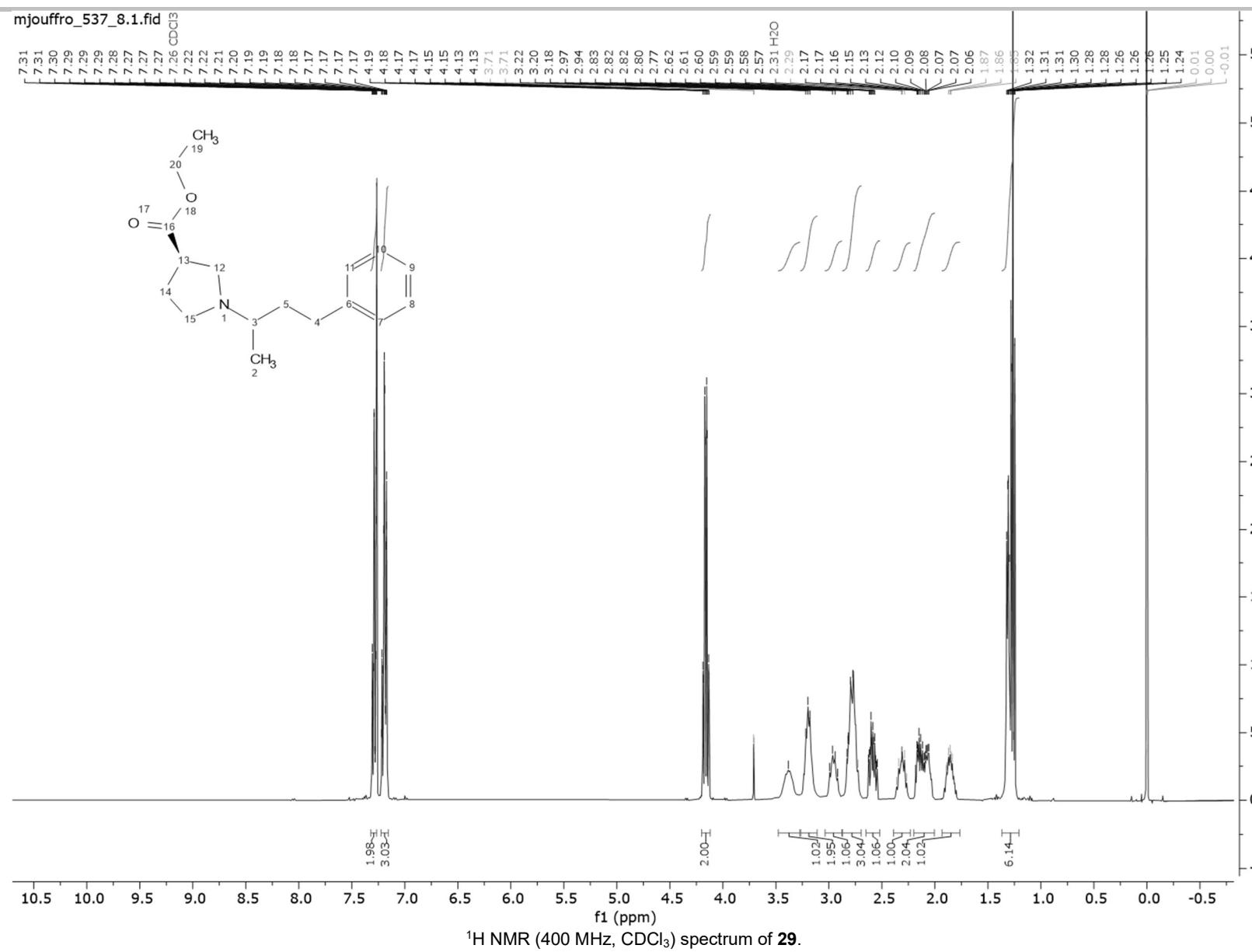


## SUPPORTING INFORMATION

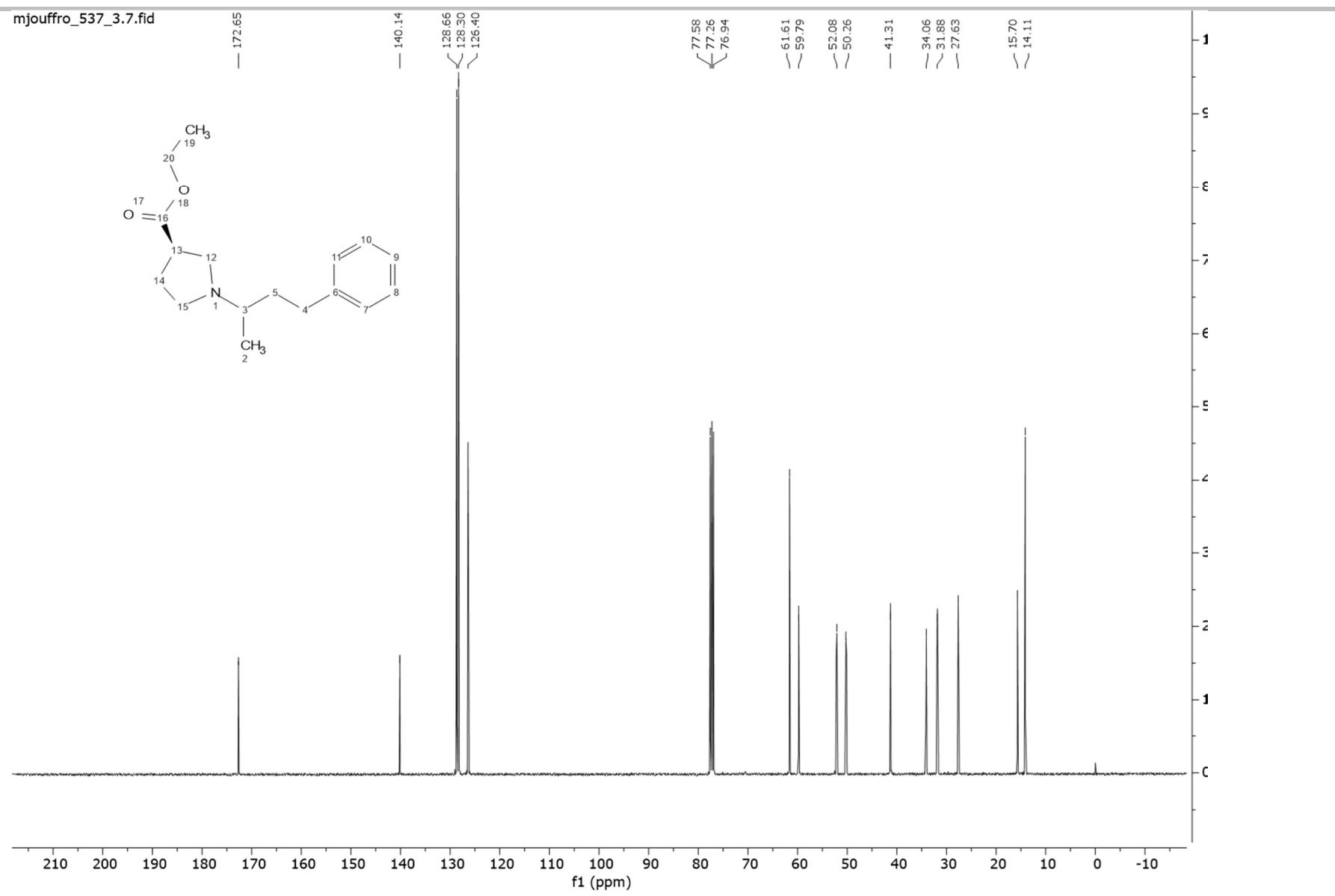
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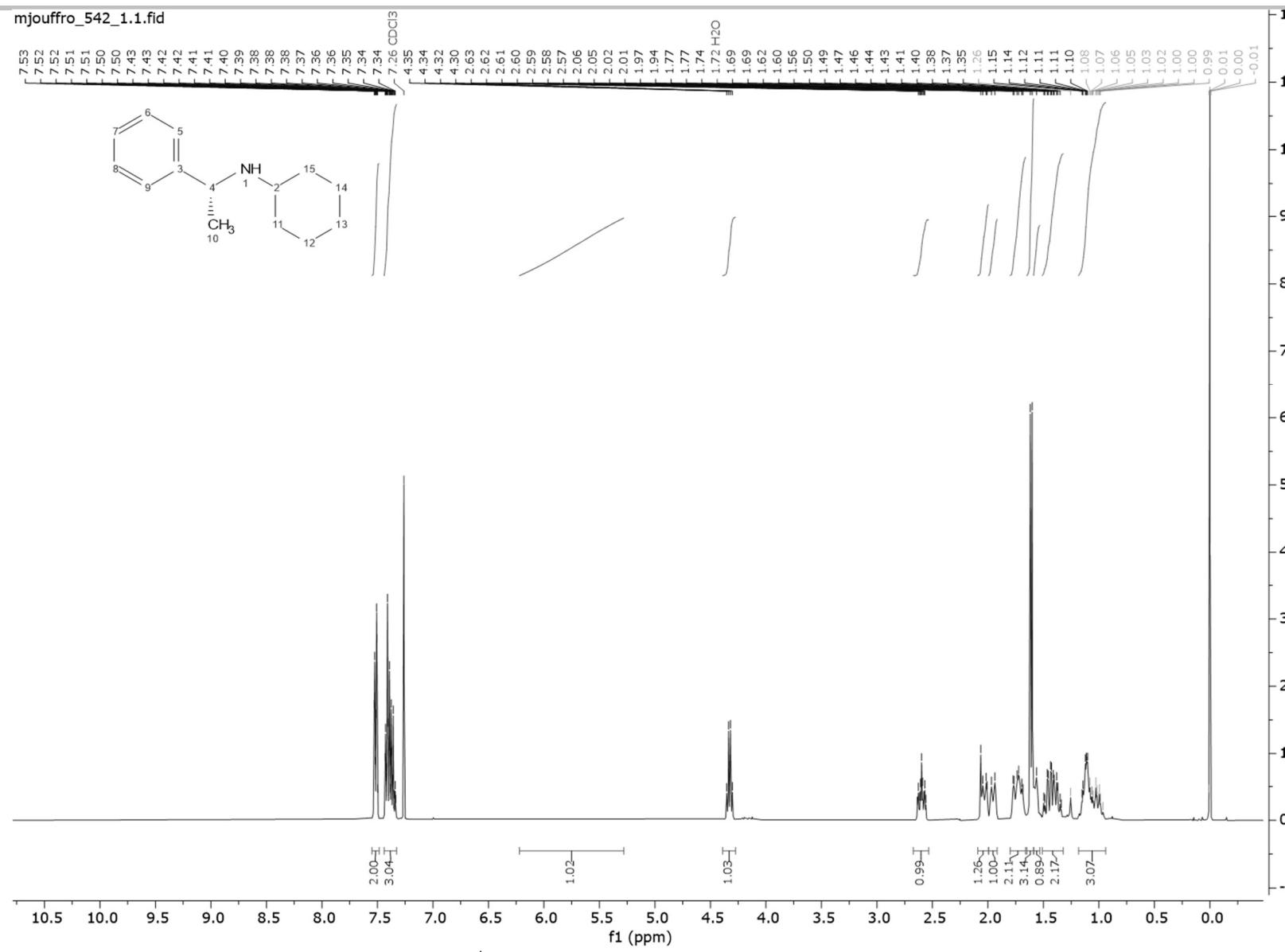
## SUPPORTING INFORMATION



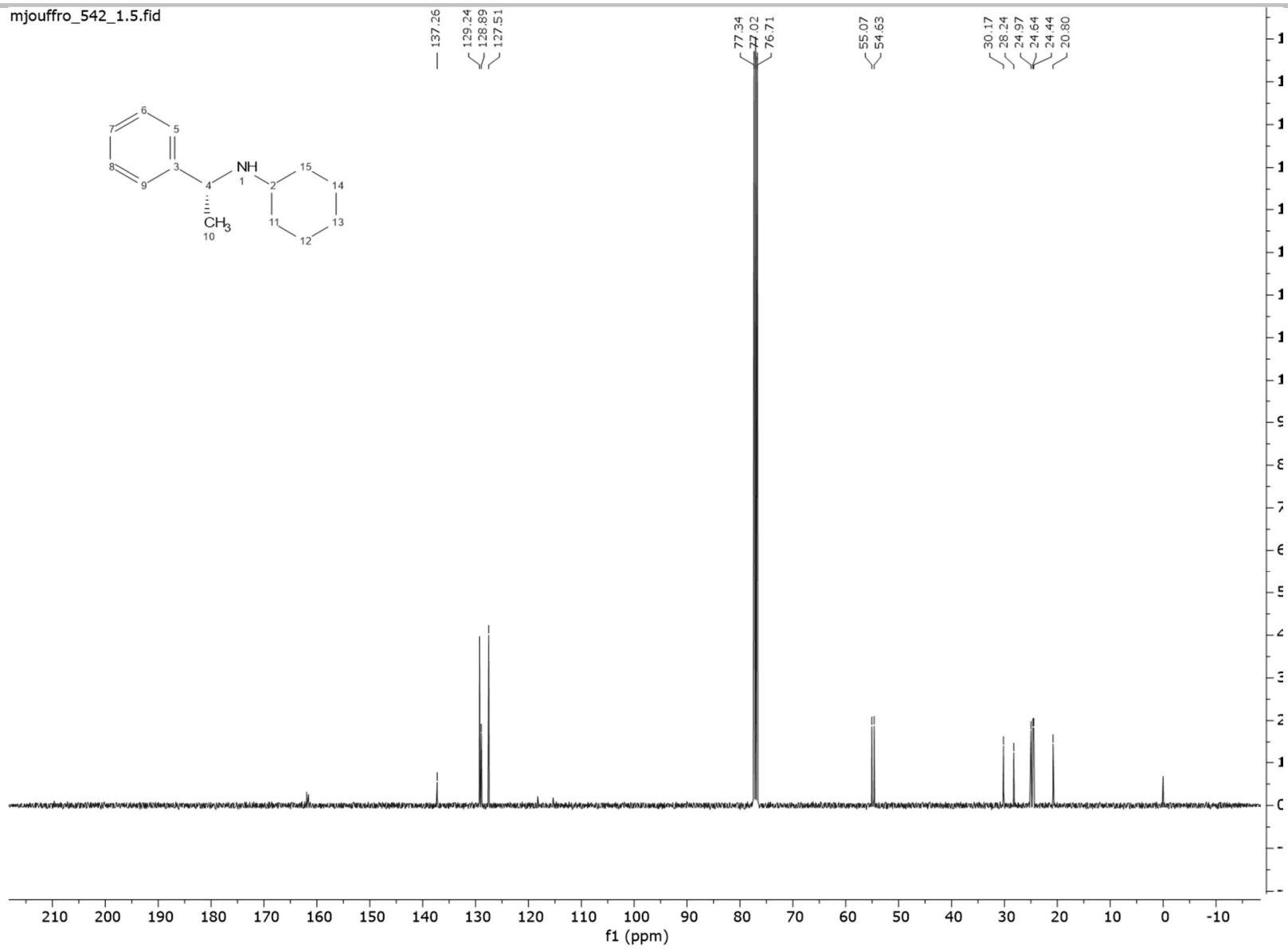
## SUPPORTING INFORMATION



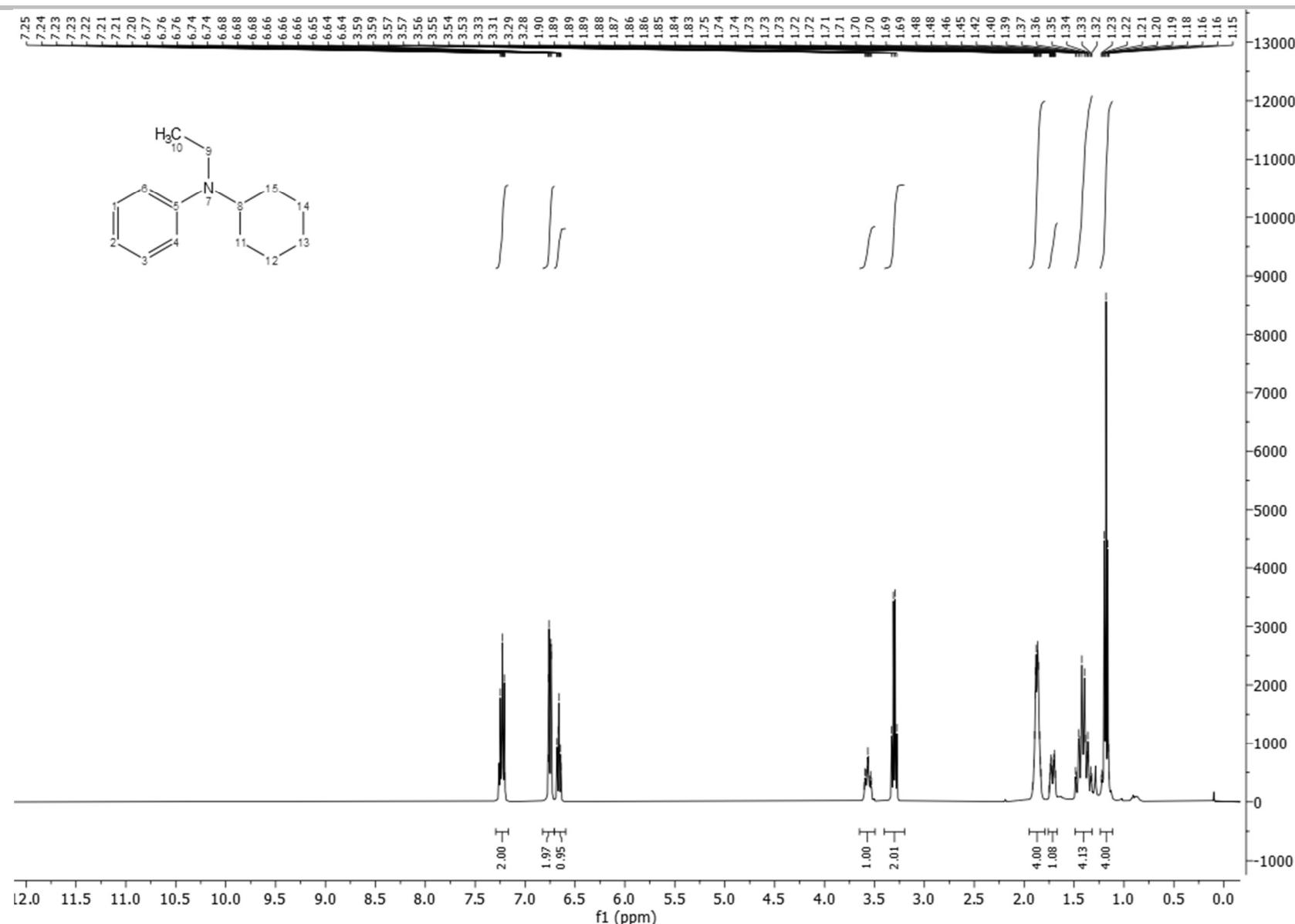
## SUPPORTING INFORMATION



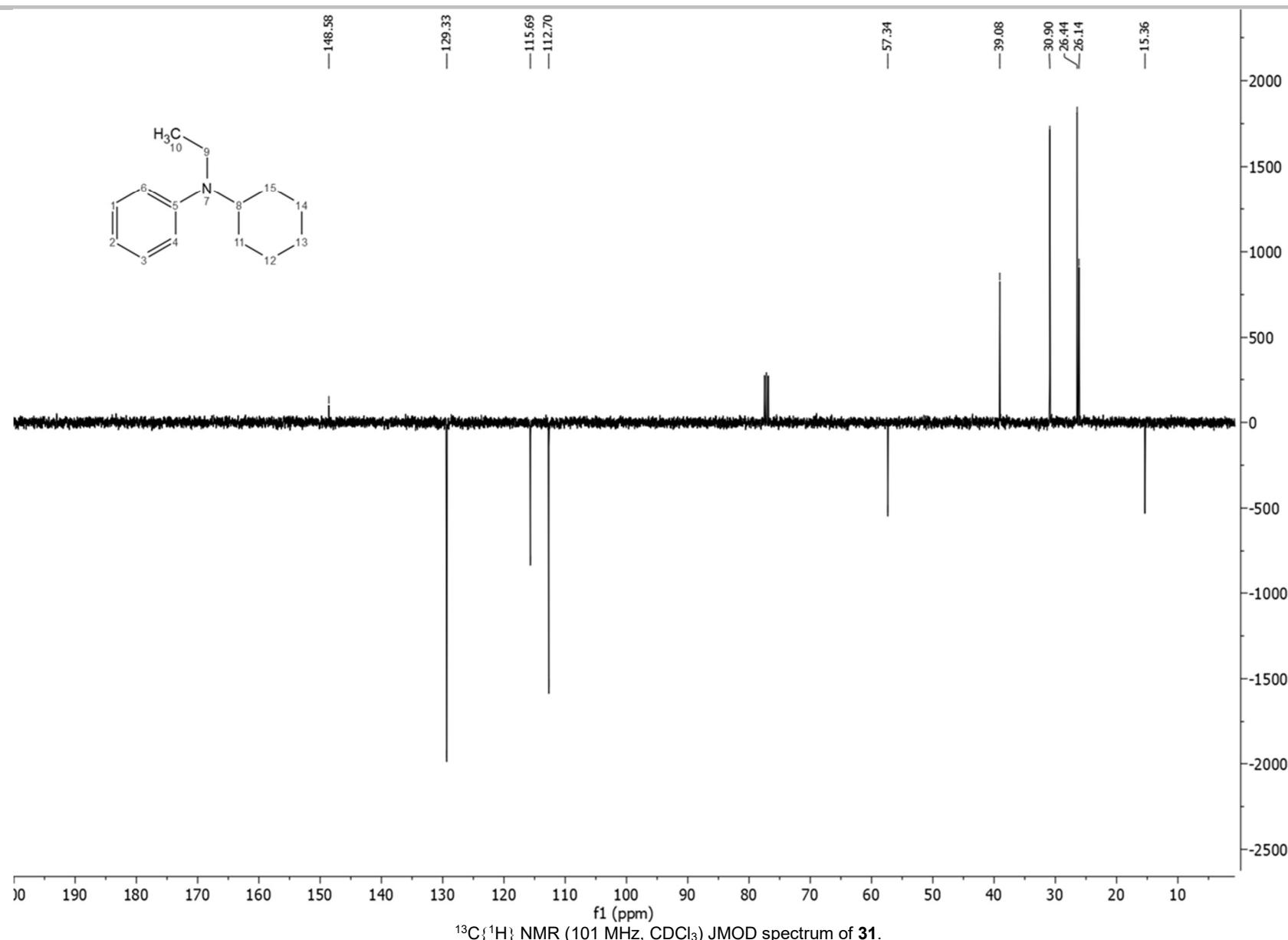
## SUPPORTING INFORMATION



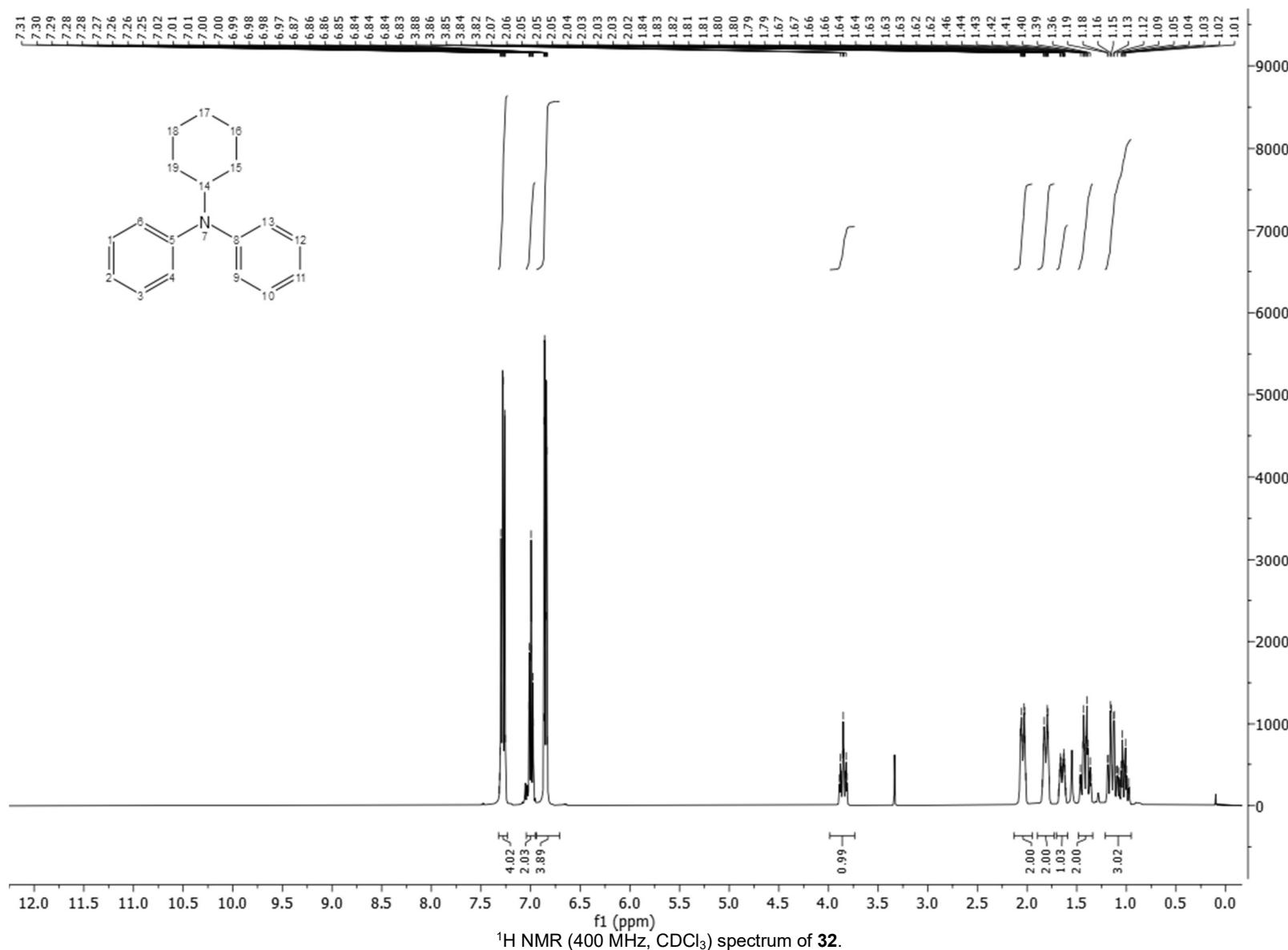
## SUPPORTING INFORMATION



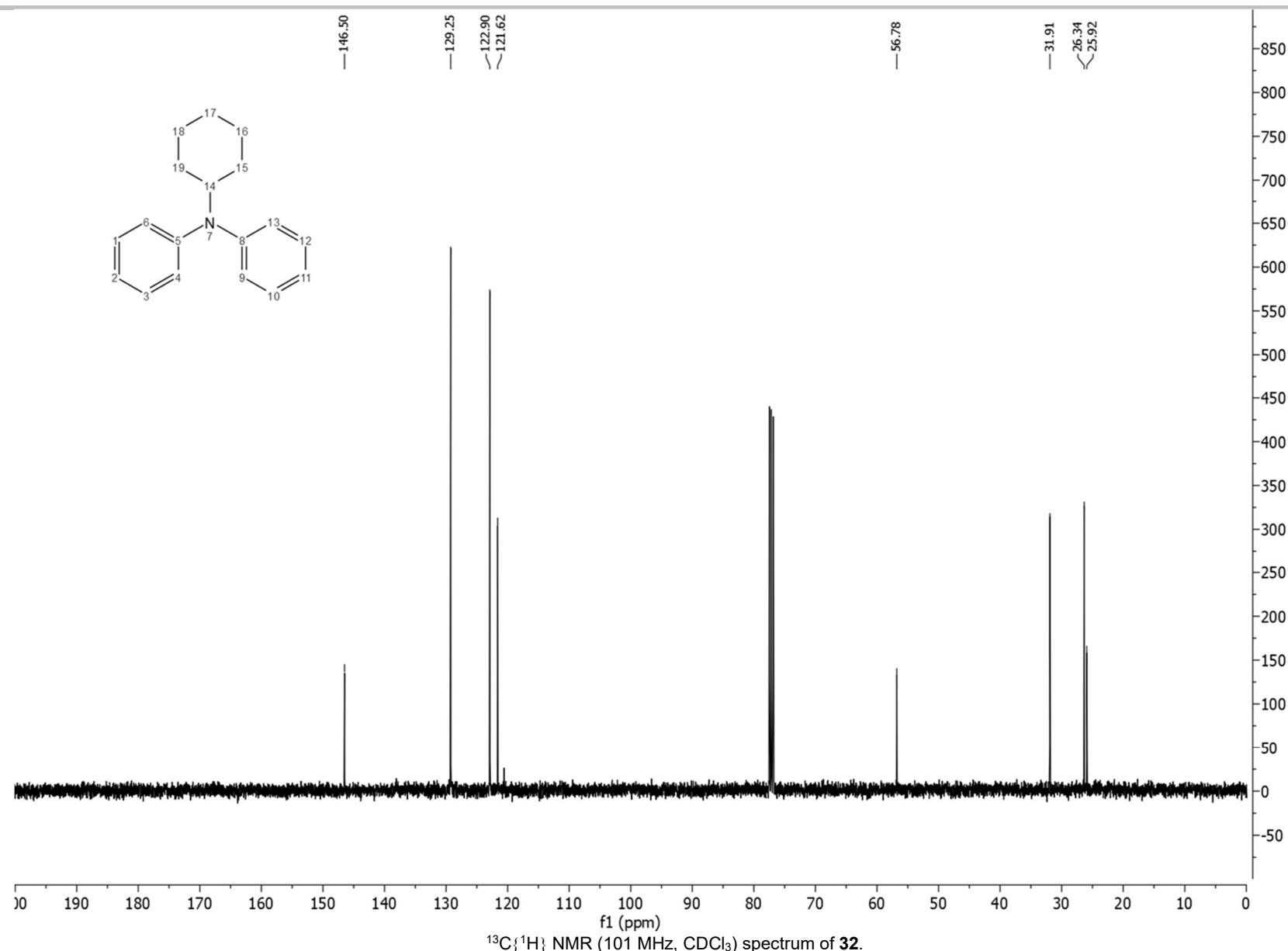
## SUPPORTING INFORMATION



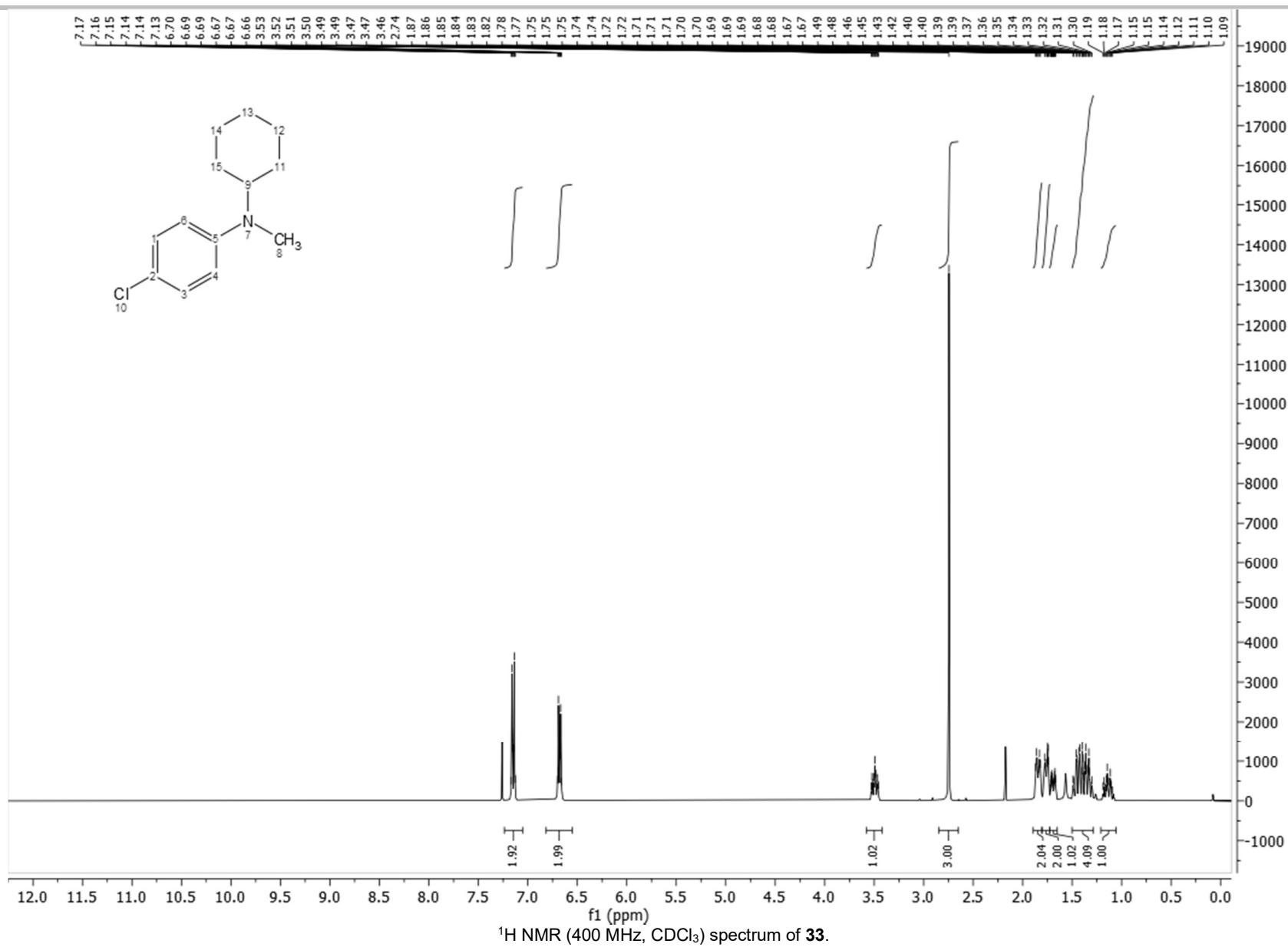
## SUPPORTING INFORMATION



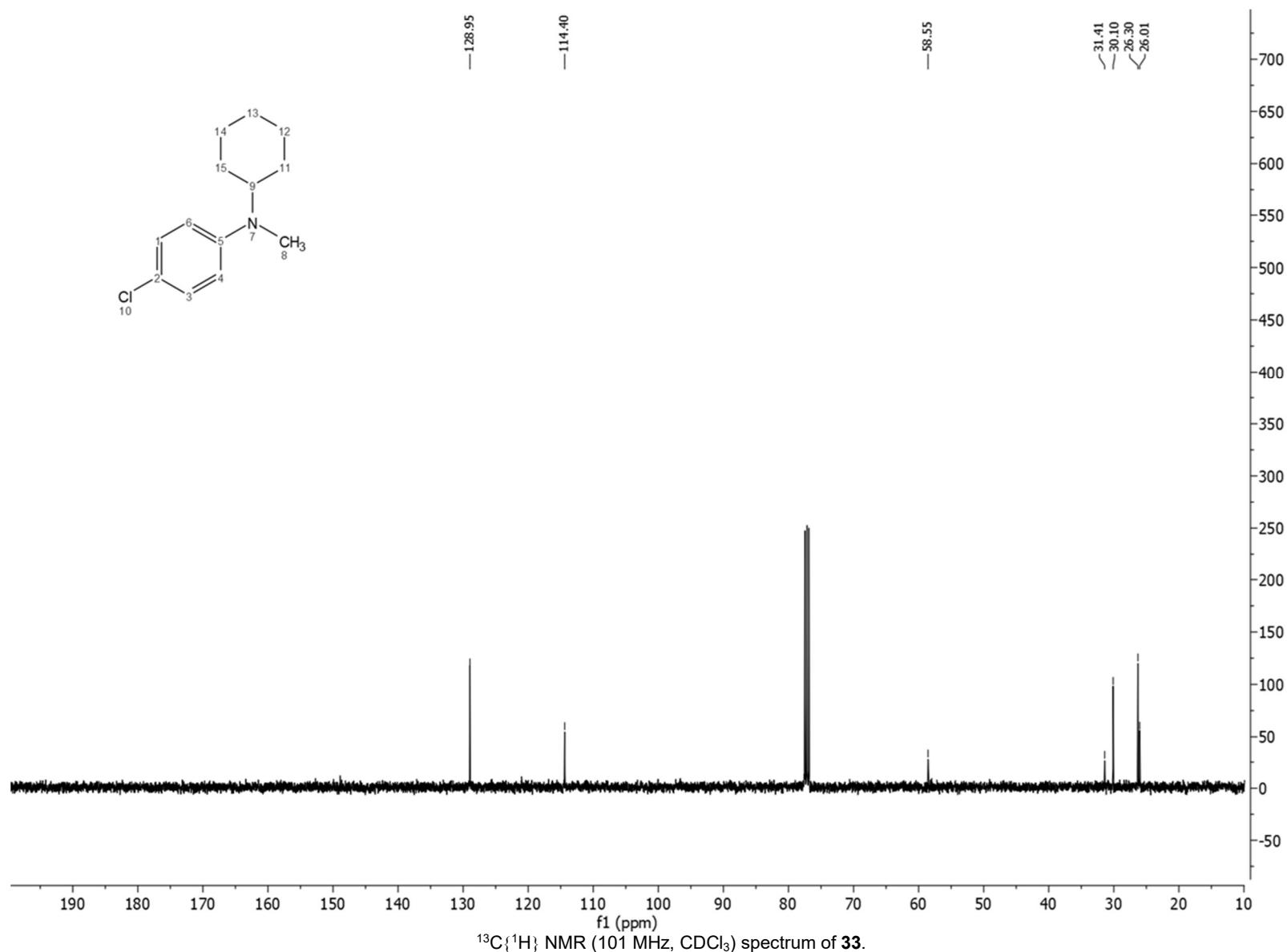
## SUPPORTING INFORMATION

 $^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ) spectrum of **32**.

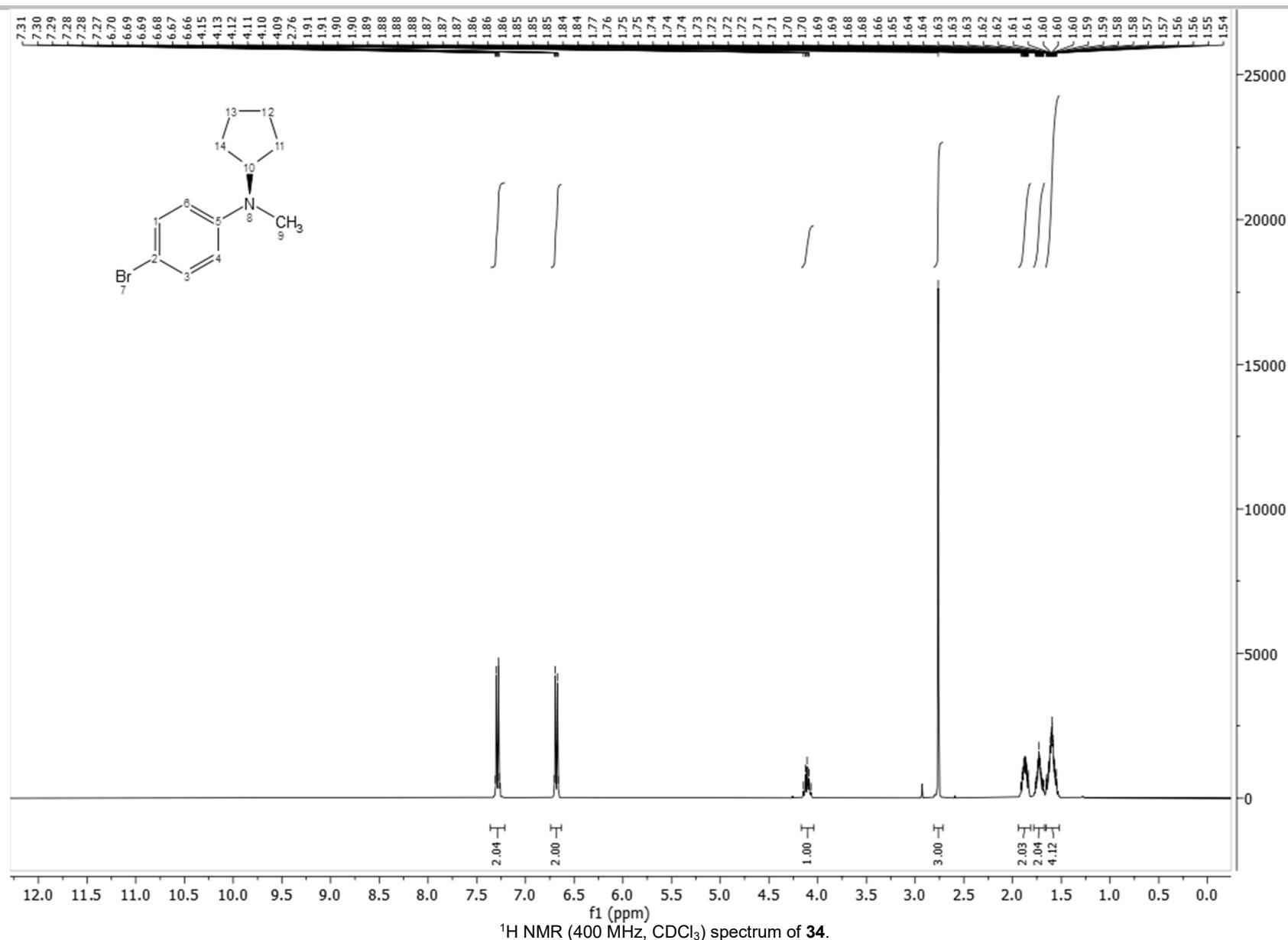
## SUPPORTING INFORMATION



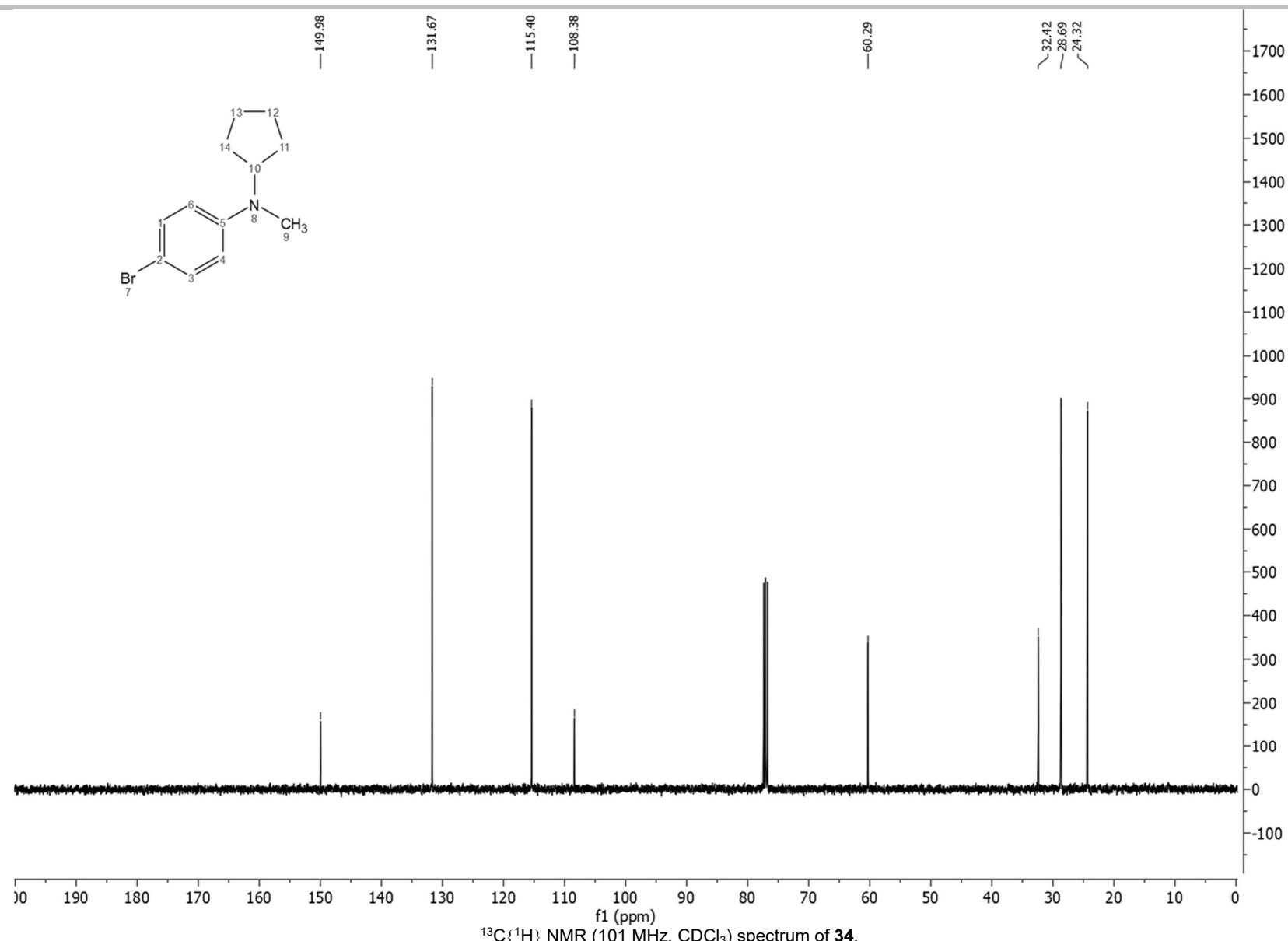
## SUPPORTING INFORMATION

 $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ) spectrum of **33**.

## SUPPORTING INFORMATION

 $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) spectrum of **34**.

## SUPPORTING INFORMATION

 $^{13}\text{C}\{\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ ) spectrum of **34**.