

# Supporting Information

## Silver-Promoted, Palladium-Catalyzed Direct Arylation of Cyclopropanes: Facile Access to Spiro 3,3'-Cyclopropyl Oxindoles

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**General Considerations:** All non-aqueous reactions were run under argon atmosphere with flame-dried glassware using standard techniques for manipulating air-sensitive compounds.<sup>1</sup> Anhydrous solvents were obtained by filtration through drying columns or by distillation over calcium hydride or sodium.

Flash column chromatography was performed using 230-400 mesh silica and Merck type E basic alumina (pH ~ 10-11) by hand or performed on an automatic purification system using the indicated solvent system (Teledyne Isco Combiflash® Rf or Sq16x). Pre-packed normal phase silica gel columns were used for separation of products using Teledyne Isco RediSep® Rf High Performance Gold or Silicycle SiliaSep™ High Performance columns (12g, 24g, 40g, or 80g).

Analytical thin-layer chromatography (TLC) was performed on pre-coated, glass-backed silica gel plates (Merck 60 F254) and visualized by UV absorbance (254 nm), and/or ceric ammonium molybdate (CAM), and potassium permanganate (KMnO<sub>4</sub>).

Nuclear magnetic resonance spectra were recorded on an Avance AV400 MHz, Avance AV 300 MHz, or DRX 400 MHz (<sup>1</sup>H, <sup>13</sup>C, <sup>19</sup>F, 1D NOESY) spectrometer. Chemical shifts for <sup>1</sup>H NMR spectra are recorded in parts per million (ppm) from tetramethylsilane (TMS) with the solvent resonance as the internal standard (CHCl<sub>3</sub>, δ = 7.26 ppm). The data was reported as follows: chemical shift, multiplicity (s = singlet, s (br) = broad singlet, d = doublet, dd = doublet of doublets, dt = doublet of triplets, td = triplet of doublets, ddd = doublet of doublets of doublets, t = triplet, q = quadruplet, m = multiplet, br m = broad multiplet), coupling constant in Hz and integration. Chemical shifts for <sup>13</sup>C NMR spectra were recorded in parts per million from tetramethylsilane using the central peak of CDCl<sub>3</sub> (77.16 ppm) as the internal standard. All <sup>13</sup>C NMR spectra were obtained with complete proton decoupling. The 2-haloanilides were reported as a mixture of rotamers.<sup>2,3</sup>

Infrared spectra were taken on a Bruker Vertex Series FTIR (neat) and are reported in reciprocal centimeters (cm<sup>-1</sup>). Melting points were obtained using a Büchi melting point apparatus and are uncorrected.

High-resolution spectra were performed by the Centre regional de spectroscopie de masse de l'Université de Montréal.

**Reagents:** Commercial reagents were used as supplied or purified by standard techniques where necessary.

<sup>1</sup> Shriver, D.H; Drezdson, M.A. *The Manipulation of Air-Sensitive Compounds*; 2nd Edition; Wiley: New York, **1986**.

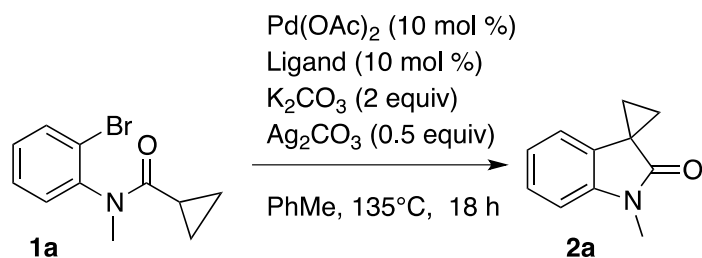
<sup>2</sup> Lipshutz, B.H; McCarthy, K.E; Hungate, R.W, *J.Org. Chem.* **1984**, 49, 1218.

<sup>3</sup> Lewin, A.H.;Frucht, M.; Chen, K.V.J; Benedetti, E.; Di Blasio,B. *Tetrahedron* **1975**, 31, 207.

## Selected Optimization

**Table S1:** Ligand Screenings

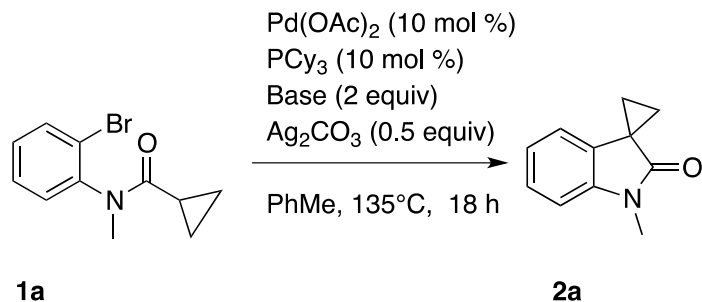
Entry	Ligand	Yield (%)
1	JohnPhos	39%
2	<i>rac</i> -BINAP	25%
3	dppf	20%
4	DavePhos	trace
5	PPh <sub>3</sub>	62%
6	P(tBu) <sub>3</sub> •BF <sub>4</sub>	trace
7	PCy <sub>2</sub> Et	73%



To a 5.0-mL microwave vial in a glovebox was added in the following order: Pd(OAc)<sub>2</sub> (4.5 mg, 0.02 mmol), Ligand (10 mol %, 0.02 mmol), K<sub>2</sub>CO<sub>3</sub> (54.3 mg, 0.4 mmol), Ag<sub>2</sub>CO<sub>3</sub> (27.57 mg, 0.1 mmol). The vial was crimped shut. *N*-(2-bromophenyl)-*N*-methylcyclopropanecarboxamide (**1a**) (50.8 mg, 0.2 mmol) was weighed into a vial, dissolved in 0.2 mL of toluene and added to the reaction vial. The vial containing **1a** was rinsed with 2x's 0.4 mL of toluene for a total volume of 1.0 mL. This yellowish-orange solution was then heated to 135°C in an oil bath for 18 h. The reaction turned black within five minutes. The reaction was cooled to ambient temperature, filtered over a cotton-Celite® plug, and rinsed with 10 mL of ethyl acetate. It was then concentrated *in vacuo* to give the crude product. Trimethoxybenzene was then added as an internal standard and the yields were calculated based on <sup>1</sup>H NMR.

**Table S3:** Base Screenings

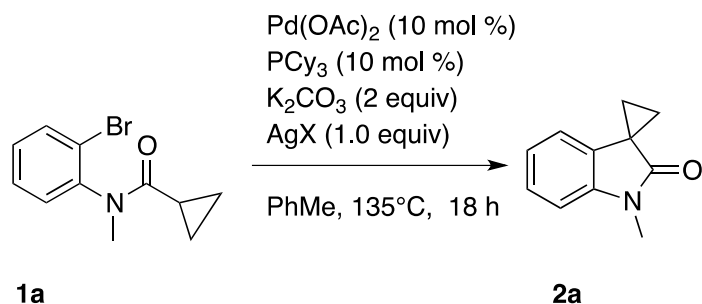
Entry	Base	Yield (%)
1	Cs <sub>2</sub> CO <sub>3</sub>	89
2	NaOAc	68
3	NaOtBu	25
4	K <sub>3</sub> PO <sub>4</sub>	61
5	NEt <sub>3</sub>	57
6	iNHPr <sub>2</sub>	82



To a 5.0-mL microwave vial in a glovebox was added in the following order:  $\text{Pd(OAc)}_2$  (4.5 mg, 0.02 mmol),  $\text{PCy}_3$  (5.61 mg, 0.02 mmol), Base (2.0 equiv, 0.4 mmol),  $\text{Ag}_2\text{CO}_3$  (27.57 mg, 0.1 mmol). The vial was crimped shut. *N*-(2-bromophenyl)-*N*-methylcyclopropanecarboxamide (**1a**) (50.8 mg, 0.2 mmol) was weighed into a vial, dissolved in 0.2 mL of toluene and added to the reaction vial. The vial containing **1a** was rinsed with 2x's 0.4 mL of toluene for a total volume of 1.0 mL. This yellowish-orange solution was then heated to 135 °C in an oil bath for 18 h. The reaction turned black within five minutes. The reaction was cooled to ambient temperature, filtered over a cotton-Celite® plug, and rinsed with 10 mL of ethyl acetate. It was then concentrated *in vacuo* to give the crude product. Trimethoxybenzene was then added as an internal standard and the yields were calculated based on  $^1\text{H}$  NMR.

**Table S4:** Silver Source Screenings

Entry	Silver Source	Yield (%)
1	$\text{AgOAc}$	30
2	$\text{Ag}_2\text{O}$	27
3	$\text{AgOBz}$	49
4	$\text{Ag}_3\text{PO}_4$	90
5	$\text{Ag}_2\text{SO}_4$	79
6	$\text{AgNO}_3$	83
7	$\text{AgBF}_4$	trace
8	$\text{AgOTf}$	trace

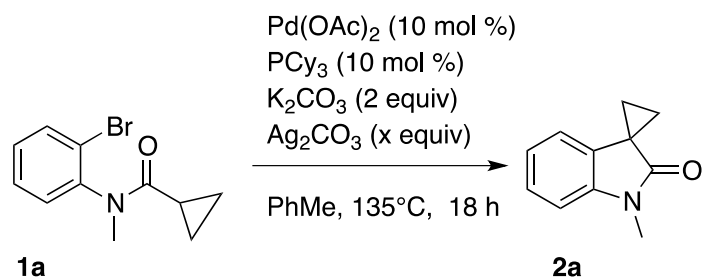


To a 5.0-mL microwave vial in a glovebox was added in the following order:  $\text{Pd(OAc)}_2$  (4.5 mg, 0.02 mmol),  $\text{PCy}_3$  (5.61 mg, 0.02 mmol),  $\text{K}_2\text{CO}_3$  (54.3 mg, 0.4 mmol),  $\text{AgX}$ . The vial was

crimped shut. *N*-(2-bromophenyl)-*N*-methylcyclopropanecarboxamide (**1a**) (50.8 mg, 0.2 mmol) was weighed into a vial, dissolved in 0.2 mL of toluene and added to the reaction vial. The vial containing **1a** was rinsed with 2x's 0.4 mL of toluene for a total volume of 1.0 mL. This yellowish-orange solution was then heated to 135 °C in an oil bath for 18 h. The reaction turned black within five minutes. The reaction was cooled to ambient temperature, filtered over a cotton-Celite® plug, and rinsed with 10 mL of ethyl acetate. It was then concentrated *in vacuo* to give the crude product. Trimethoxybenzene was then added as an internal standard and the yields were calculated based on <sup>1</sup>H NMR.

**Table S5:** Silver Loading Experiments

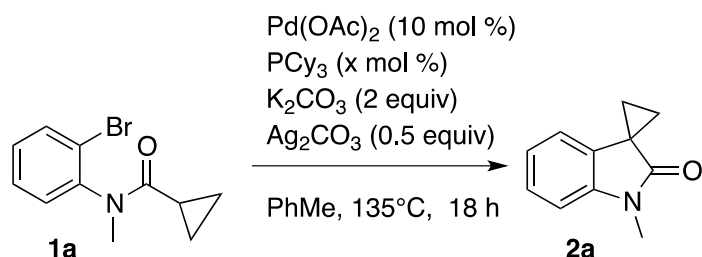
Entry	Equivalences	Yield (%)
1	0.25	63
2	0.5	93
3	0.8	83
4	1.0	77
5	2.0	60
6	3.0	49



To a 5.0-mL microwave vial in a glovebox was added in the following order: Pd(OAc)<sub>2</sub> (4.5 mg, 0.02 mmol), PCy<sub>3</sub> (5.61 mg, 0.02 mmol), K<sub>2</sub>CO<sub>3</sub> (54.3 mg, 0.4 mmol), Ag<sub>2</sub>CO<sub>3</sub>. The vial was crimped shut. *N*-(2-bromophenyl)-*N*-methylcyclopropanecarboxamide (**1a**) (50.8 mg, 0.2 mmol) was weighed into a vial, dissolved in 0.2 mL of toluene and added to the reaction vial. The vial containing **1a** was rinsed with 2x's 0.4 mL of toluene for a total volume of 1.0 mL. This yellowish-orange solution was then heated to 135 °C in an oil bath for 18 h. The reaction turned black within five minutes. The reaction was cooled to ambient temperature, filtered over a cotton-Celite® plug, and rinsed with 10 mL of ethyl acetate. It was then concentrated *in vacuo* to give the crude product. Trimethoxybenzene was then added as an internal standard and the yields were calculated based on <sup>1</sup>H NMR.

**Table S6:** Ligand Loading Experiments

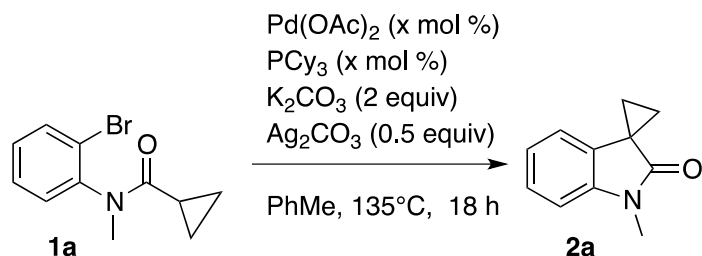
Entry	Ligand (mol %)	Yield (%)
1	20	96
2	15	96
3	10	98
4	5	76



To a 5.0-mL microwave vial in a glovebox was added in the following order:  $\text{Pd}(\text{OAc})_2$  (4.5 mg, 0.02 mmol),  $\text{PCy}_3$ ,  $\text{K}_2\text{CO}_3$  (54.3 mg, 0.4 mmol),  $\text{Ag}_2\text{CO}_3$  (27.57 mg, 0.1 mmol). The vial was crimped shut. *N*-(2-bromophenyl)-*N*-methylcyclopropanecarboxamide (**1a**) (50.8 mg, 0.2 mmol) was weighed into a vial, dissolved in 0.2 mL of toluene and added to the reaction vial. The vial containing **1a** was rinsed with 2x's 0.4 mL of toluene for a total volume of 1.0 mL. This yellowish-orange solution was then heated to  $135^\circ\text{C}$  in an oil bath for 18 h. The reaction turned black within five minutes. The reaction was cooled to ambient temperature, filtered over a cotton-Celite® plug, and rinsed with 10 mL of ethyl acetate. It was then concentrated *in vacuo* to give the crude product. Trimethoxybenzene was then added as an internal standard and the yields were calculated based on  $^1\text{H}$  NMR.

**Table S7:** Catalyst and Ligand Loading Experiments

Entry	Catalyst and Ligand (mol %)	Yield (%)
1	10	89
2	5	84
3	2.5	80
4	1	46



To a 5.0-mL microwave vial in a glovebox was added in the following order: Pd(OAc)<sub>2</sub>, PCy<sub>3</sub>, K<sub>2</sub>CO<sub>3</sub> (54.3 mg, 0.4 mmol), Ag<sub>2</sub>CO<sub>3</sub> (27.57 mg, 0.1 mmol). The vial was crimped shut. *N*-(2-bromophenyl)-*N*-methylcyclopropanecarboxamide (**1a**) (50.8 mg, 0.2 mmol) was weighed into a vial, dissolved in 0.2 mL of toluene and added to the reaction vial. The vial containing **1a** was rinsed with 2x's 0.4 mL of toluene for a total volume of 1.0 mL. This yellowish-orange solution was then heated to 135 °C in an oil bath for 18 h. The reaction turned black within five minutes. The reaction was cooled to ambient temperature, filtered over a cotton-Celite® plug, and rinsed with 10 mL of ethyl acetate. It was then concentrated *in vacuo* to give the crude product. Trimethoxybenzene was then added as an internal standard and the yields were calculated based on <sup>1</sup>H NMR.

**Table S8:** Pd- Catalyst Screenings

Entry	Catalyst	Yield (%)
1	PdBr <sub>2</sub>	81
2	Pd(dba) <sub>2</sub>	92

To a 5.0-mL microwave vial in a glovebox was added in the following order: (Catalyst, 5 mol %, 0.01 mmol), PCy<sub>3</sub> (2.81 mg, 0.01 mmol), K<sub>2</sub>CO<sub>3</sub> (41.44 mg, 0.3 mmol), Ag<sub>2</sub>PO<sub>4</sub> (27.6 mg, 0.066 mmol). The vial was crimped shut. *N*-(2-bromophenyl)-*N*-methylcyclopropanecarboxamide (**1a**) (50.8 mg, 0.2 mmol) was weighed into a vial, dissolved in 0.2 mL of toluene and added to the reaction vial. The vial containing **1a** was rinsed with 2x's 0.4 mL of toluene for a total volume of 1.0 mL. This yellowish-orange solution was then heated to 135 °C in an oil bath for 18 h. The reaction turned black within five minutes. The reaction was cooled to ambient temperature, filtered over a cotton-Celite® plug, and rinsed with 10 mL of ethyl acetate. It was then concentrated *in vacuo* to give the crude product. Trimethoxybenzene was then added as an internal standard and the yields were calculated based on <sup>1</sup>H NMR.

## Synthesis of Starting Materials

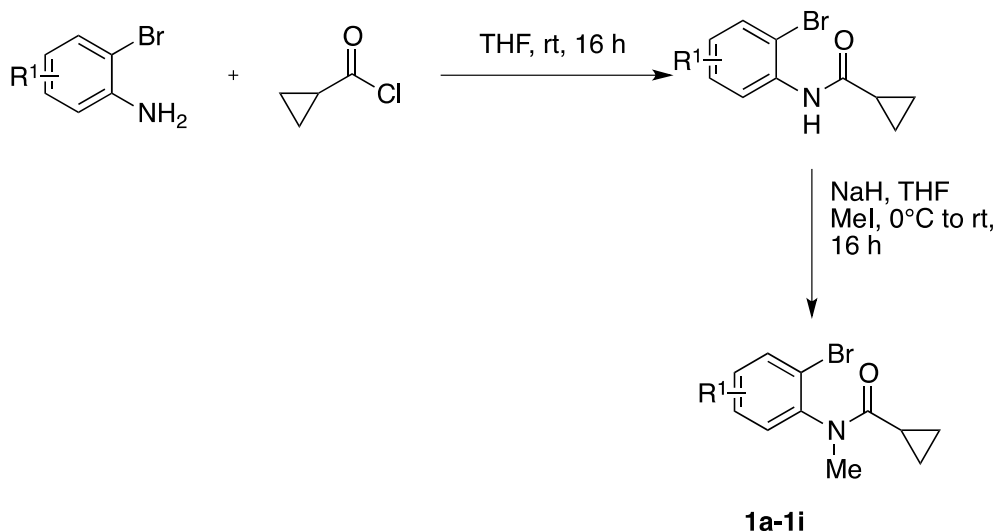
Starting materials not listed below were obtained commercially and the reagents were used without further purification.

### Synthesis of 2-bromoanilines

The following 2-bromoanilines were obtained via bromination from their corresponding anilines according to literature procedure: 2-bromo-4-methylaniline, 4-amino-3-bromobenzaldehyde,<sup>4</sup> 2-bromo-4-(trifluoromethyl)aniline, 4-amino-3-bromobenzonitrile, and 2-bromo-4-chloroaniline,<sup>5</sup> ethyl 4-amino-3-bromobenzoate,<sup>6</sup> 2-bromo-3,4-dimethoxyaniline and 2-bromo-4-methoxyaniline.<sup>7</sup>

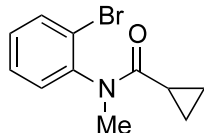
<sup>4</sup> Das, B.; Venkateswarlu, K.; Majhi, A.; Siddaiah, V.; Reddy, K.R. *J. Mol. Cat. A: Chem.* **2007**, 267, 30.

<sup>5</sup> Roche, D.; Prasad, K.; Repic, O.; Blacklock, T.J. *Tetrahedron Lett.* **2000**, 41, 2083.

**General Synthesis of 2-bromoanilides (1a-1i) (example for 1a shown below)**

To a 100-mL round bottom flask flame dried over argon was added 2-bromoaniline (2.47 g, 14.4 mmol) dissolved in 40 mL THF. To this was added cyclopropanecarbonyl chloride (1.4 mL, 15.8 mmol, 1.1 equiv) dropwise, forming a cloudy off-white solution. This mixture was then stirred overnight (16 h) at ambient temperature. 40 mL of EtOAc was then added and the opaque solution was transferred to a 125-mL separatory funnel. The solution was then washed with saturated NaHCO<sub>3</sub> solution (3x's, 40 mL), and brine (2x's 40 mL). The combined organics were then dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated *in vacuo* to give a white solid, which was used crude in the subsequent methylation step.

This intermediate was dissolved in 40 mL of THF, cooled to 0 °C, and NaH (0.52 g, 22.2 mmol, 1.5 equiv) was added, forming a grey solution. After 15 minutes, MeI was added dropwise (0.70 mL, 107 mmol, 7.0 equiv). The reaction was then warmed to ambient temperature and stirred overnight (16 hours). It was then quenched with water (40 mL), EtOAc was added (40 mL), and transferred to a 250-mL separatory funnel. The layers were separated, and the aqueous layer was extracted with EtOAc (3x's, 50 mL). The combined organics were washed with brine (50 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated *in vacuo* to give the desired product as a brown oil. The crude was then purified via column chromatography over silica gel (RediSep® Rf Gold 24g) using a solvent gradient of 10% to 50% ethyl acetate/Hexanes. (*R<sub>f</sub>*: 0.31 (1:1 hexanes: ethyl acetate)). The desired product was isolated as a golden oil (3.30 g, 13 mmol, 90% yield over two steps).



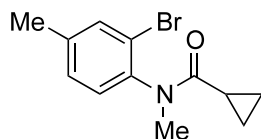
<sup>6</sup> Tobe, Y.; Utsumi, N.; Kawabata, K.; Nagano, A.; Adachi, K.; Araki, S.; Sonoda, M.; Hirose, K.; Naemura, K. *J. Am. Chem. Soc.* **2002**, *124*, 5350.

<sup>7</sup> Peat, A.J.; Buchwald, S.L. *J. Am. Chem. Soc.* **1996**, *118*, 1028.

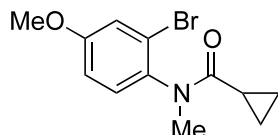


***N*-(2-bromophenyl)-*N*-methylcyclopropanecarboxamide (1a)**

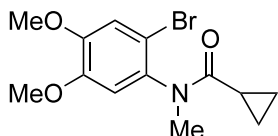
The observed characterization data ( $^1\text{H}$  NMR) was consistent with that previously reported in the literature.<sup>8</sup>  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.71-7.69 (m, 1H), 7.42-7.35 (m, 2H), 7.27-7.22 (m, 1H), 3.21 (s, 3H), 1.23-0.95 (m, 3H), 0.69-0.54 (m, 2H).

***N*-(2-bromo-4-methylphenyl)-*N*-methylcyclopropanecarboxamide (1b)**

The title compound **1b** was prepared by the general synthesis on a 7.07 mmol scale and then purified via column chromatography (20:1 Hex:EtOAc) to give a brown oil in 65% yield (1.23 g, 4.60 mmol) over two steps:  $R_f$ : 0.32 (1:1 hexanes: ethyl acetate);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.53 (s, 1H), 7.27 (d,  $J$  = 7.9 Hz, 1H), 7.23-7.21 (m, 1H), 3.20 (s, 3H), 2.40 (s, 3H), 1.27-1.19 (m, 1H), 1.05-0.96 (m, 2H), 0.65-0.56 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75MHz):  $\delta$  173.1, 139.78, 139.65, 133.7, 129.3, 123.0, 35.6, 20.5, 11.8, 8.1, 7.6; FTIR ( $\text{cm}^{-1}$ ) (neat): 3011, 1655, 1493, 1390, 1283, 1058, 823, 577; HRMS (ESI, Pos) calcd for  $\text{C}_{12}\text{H}_{14}\text{BrNNaO}$  ( $\text{M}+\text{Na}$ )<sup>+</sup>: 290.0151, found: 290.01436  $m/z$ .

***N*-(2-bromo-4-methoxyphenyl)-*N*-methylcyclopropanecarboxamide (1c)**

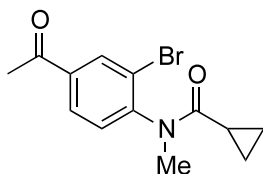
The title compound **1c** was prepared by the general synthesis on a 7.46 mmol scale and then purified via column chromatography (20:1 Hex:EtOAc) to give a dark purple oil in 70% yield (1.49g, 5.25 mmol) over two steps.  $R_f$ : 0.45 (1:1 hexanes: ethyl acetate);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.282-7.279 (m, 1H), 7.23 (d,  $J$  = 2.8 Hz, 1H), 6.92 (dd,  $J$  = 8.7, 2.8 Hz, 1H), 3.85 (s, 3H), 3.20 (s, 3H), 1.24-1.18 (m, 1H), 1.08-0.95 (m, 2H), 0.69-0.55 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75MHz):  $\delta$  173.7, 159.4, 135.5, 130.3, 124.0, 118.5, 114.5, 55.7, 36.1, 12.0, 8.4, 7.9; FTIR ( $\text{cm}^{-1}$ ) (neat): 3009, 1653, 1493, 1390, 1031, 890, 605; HRMS (APPI, Pos) calcd for  $\text{C}_{12}\text{H}_{15}\text{BrNO}_2$  ( $\text{M}+\text{H}$ )<sup>+</sup>: 284.02807, found: 284.02719  $m/z$ .



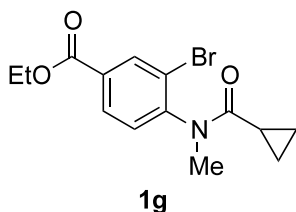
<sup>8</sup> Beckwith, A.L.J.; Storey, J.M.D. *Chem. Commun.* **1995**, 977.

***N*-(2-bromo-4,5-dimethoxyphenyl)-*N*-methylcyclopropanecarboxamide (1d)**

The title compound **1d** was prepared by the general synthesis on a 3.13 mmol scale and then purified via column chromatography (20:1 Hex: EtOAc) to give a dark purple solid in 80% yield (0.782 g, 2.49 mmol) over two steps. **mp**: 75-78°C; **R<sub>f</sub>**: 0.55 (1:1 hexanes: ethyl acetate); **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400MHz): δ 7.06 (s, 1H), 6.81 (s, 1H), 3.86 (s, 3H), 3.84 (s, 3H), 3.14 (s, 3H), 1.22-1.14 (m, 1H), 1.00-0.89 (m, 2H), 0.62-0.52 (m, 2H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100MHz): δ 173.7, 149.16, 149.06, 135.2, 115.3, 113.6, 112.2, 56.23, 56.19, 35.9, 12.0, 8.4, 7.9; **FTIR** (cm<sup>-1</sup>) (neat): 2937, 1648, 1525, 1382, 1070, 898, 875, 637; **HRMS** (ESI, Pos) calcd for C<sub>13</sub>H<sub>16</sub>BrNNaO<sub>3</sub> (M+Na)<sup>+</sup> : 336.02058, found: 336.02066 *m/z*.

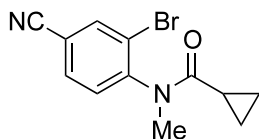
***N*-(4-acetyl-2-bromophenyl)-*N*-methylcyclopropanecarboxamide (1e)**

The title compound **1e** was prepared by the general synthesis on a 5.18 mmol scale and then purified via column chromatography (20:1 Hex: EtOAc) to give an orange oil in 65% yield (1.04 g, 3.39 mmol) over two steps. **R<sub>f</sub>**: 0.35 (1:1 hexanes: ethyl acetate); **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 300MHz): δ 8.27 (d, *J* = 1.9 Hz, 1H), 7.97 (dd, *J* = 8.1, 1.9 Hz, 1H), 7.47 (d, *J* = 8.1 Hz, 1H), 3.22 (s, 3H), 2.63 (s, 3H), 1.13-0.98 (m, 3H), 0.68-0.58 (m, 2H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100MHz): δ 195.6, 173.0, 146.9, 137.9, 133.8, 130.4, 128.7, 124.4, 35.9, 26.7, 12.6, 8.8, 8.4; **FTIR** (cm<sup>-1</sup>) (neat): 3010, 1768, 1687, 1655, 1424, 1264, 1127, 1085, 604; **HRMS** (ESI, Pos) calcd for C<sub>13</sub>H<sub>14</sub>BrNNaO<sub>2</sub> (M+Na)<sup>+</sup> : 318.01001, found: 318.00992 *m/z*.

**Ethyl 3-bromo-4-(*N*-methylcyclopropanecarboxamido)benzoate(1f)**

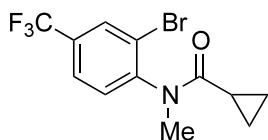
The title compound **1f** was prepared by the general synthesis on a 4.07 mmol scale and then purified via column chromatography over silica gel (RediSep® Rf Gold 24g) using a solvent gradient of 10% to 50% ethyl acetate/hexanes to give a light yellow solid in 66% yield (0.881 g, 2.70 mmol) over two steps. **mp**: 68-72°C; **R<sub>f</sub>**: 0.42 (1:1 hexanes: ethyl acetate); **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400MHz): δ 8.29 (d, *J* = 1.9 Hz, 1H), 8.00 (dd, *J* = 8.1, 1.9 Hz, 1H), 7.39 (d, *J* = 8.1 Hz, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 3.15 (s, 3H), 1.34 (dd, *J* = 9.2, 5.1 Hz, 3H), 1.06-0.89 (m, 3H), 0.61-0.50 (m, 2H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100MHz): δ 172.0, 163.4, 145.7, 133.9, 130.7, 129.11, 128.97, 122.9, 60.6, 34.9, 13.3, 11.5, 7.7, 7.3; **FTIR** (cm<sup>-1</sup>) (neat): 3013, 1715, 1649,

1592, 1471, 1280, 1121, 753; **HRMS** (ESI, Pos) calcd for  $C_{14}H_{16}BrNNaO_3$  ( $M+Na$ )<sup>+</sup>: 348.02058, found: 348.02057  $m/z$ .



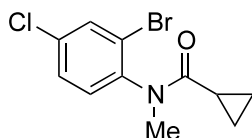
***N*-(2-bromo-4-cyanophenyl)-*N*-methylcyclopropanecarboxamide (1g)**

The title compound **1g** was prepared by the general synthesis on a 4.10 mmol scale and then purified via column chromatography over silica gel (RediSep® Rf Gold 24g) using a solvent gradient of 10% to 50% ethyl acetate/hexanes to give an orange solid in 84% yield (0.949 g, 3.40 mmol) over two steps. **mp**: 210-213°C; **R<sub>f</sub>**: 0.37 (1:1 hexanes: ethyl acetate); **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400MHz): δ 7.99 (s, 1H), 7.69 (dd,  $J$  = 8.1, 1.6 Hz, 1H), 7.48 (d,  $J$  = 8.1 Hz, 1H), 3.18 (s, 3H), 1.07-0.93 (m, 3H), 0.70-0.56 (m, 2H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100MHz): δ 172.9, 147.3, 137.3, 132.6, 131.1, 124.8, 116.6, 113.6, 36.0, 12.7, 9.0, 8.6; **FTIR** (cm<sup>-1</sup>) (neat): 2927, 2229, 1660, 1481, 1425, 1143, 610, 450; **HRMS** (ESI, Pos) calcd for  $C_{12}H_{11}BrN_2NaO$  ( $M+Na$ )<sup>+</sup>: 300.9947, found: 300.99436  $m/z$ .



***N*-(2-bromo-4-(trifluoromethyl)phenyl)-*N*-methylcyclopropanecarboxamide(1h)**

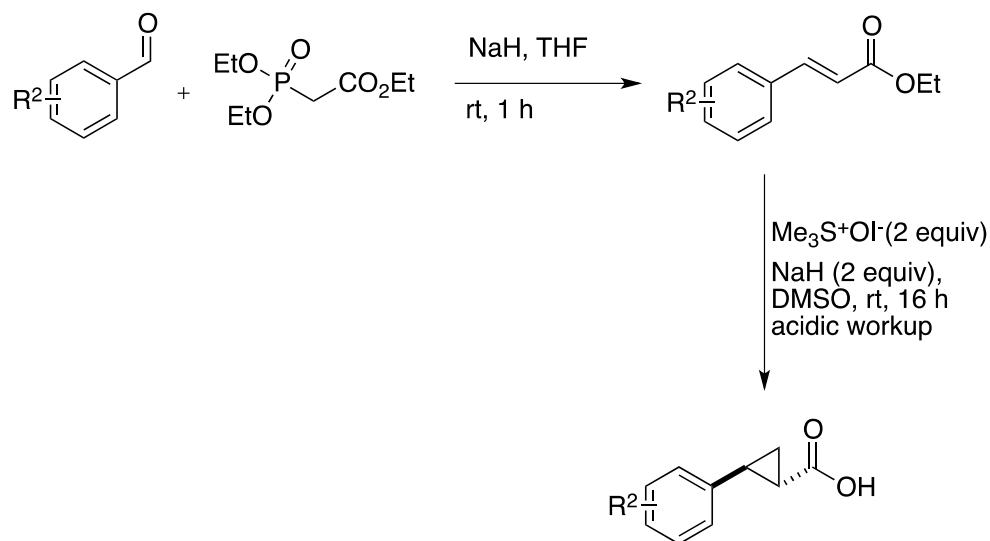
The title compound **1h** was prepared by the general synthesis on a 0.922 mmol scale and then purified via column chromatography over silica gel (RediSep® Rf Gold 24g) using a solvent gradient of 10% to 50% ethyl acetate/hexanes to give a white solid in 72% yield (0.2136 g, 0.663 mmol) over two steps. **mp**: 49-52 °C; **R<sub>f</sub>**: 0.55 (1:1 hexanes: ethyl acetate); **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400MHz): δ 7.95 (s, 1H), 7.66-7.64 (m, 2H), 7.49 (d,  $J$  = 8.0 Hz, 1H), 3.19 (s, 3H), 1.08-0.96 (m, 3H), 0.67-0.57 (m, 2H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 75MHz): 173.1, 146.3, 131.7 (q,  $J$  = 33.5 Hz), 131.1 (q,  $J$  = 3.9 Hz), 130.7, 126.0 (q,  $J$  = 3.5 Hz), 122.8 (q,  $J$  = 273 Hz), 35.9, 12.6, 8.9, 8.4; **<sup>19</sup>F NMR** (282 MHz, CDCl<sub>3</sub>): δ -62.7; **FTIR** (cm<sup>-1</sup>) (neat): 2935, 1783, 1657, 1428, 1157, 935, 680, 648, 484; **HRMS** (ESI, Pos) calcd for  $C_{12}H_{11}BrF_3NNaO$  ( $M+Na$ )<sup>+</sup>: 343.98683, found: 343.98683  $m/z$ .



***N*-(2-bromo-4-chlorophenyl)-*N*-methylcyclopropanecarboxamide(1i)**

The title compound **1i** was prepared by the general synthesis on a 6.55 mmol scale and then purified via column chromatography over silica gel (RediSep® Rf Gold 24g) using a solvent gradient of 10% to 50% ethyl acetate/hexanes to give a light pink solid in 63% yield (1.18 g, 4.08 mmol) over two steps. **mp**: 61-63 °C; **R<sub>f</sub>**: 0.53 (1:1 hexanes: ethyl acetate); **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 300MHz): δ 7.70 (d, *J* = 2.3 Hz, 1H), 7.37 (dd, *J* = 8.4, 2.3 Hz, 1H), 7.30 (d, *J* = 8.4 Hz, 1H), 3.18 (s, 3H), 1.15-0.95 (m, 3H), 0.68-0.57 (m, 2H).; **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 75MHz): δ 173.5, 141.8, 134.8, 133.6, 131.0, 129.3, 124.6, 36.1, 12.5, 8.9, 8.4 ; **FTIR** (cm<sup>-1</sup>) (neat): 2932, 1655, 1556, 1285, 1034, 894, 579; **HRMS** (APPI, Pos) calcd for C<sub>11</sub>H<sub>12</sub>BrClNO (M+H)<sup>+</sup>: 287.97853 , found: 287.97761 *m/z*.

### Synthesis of *trans-rac*-2-arylcyclopropanecarboxylic acids



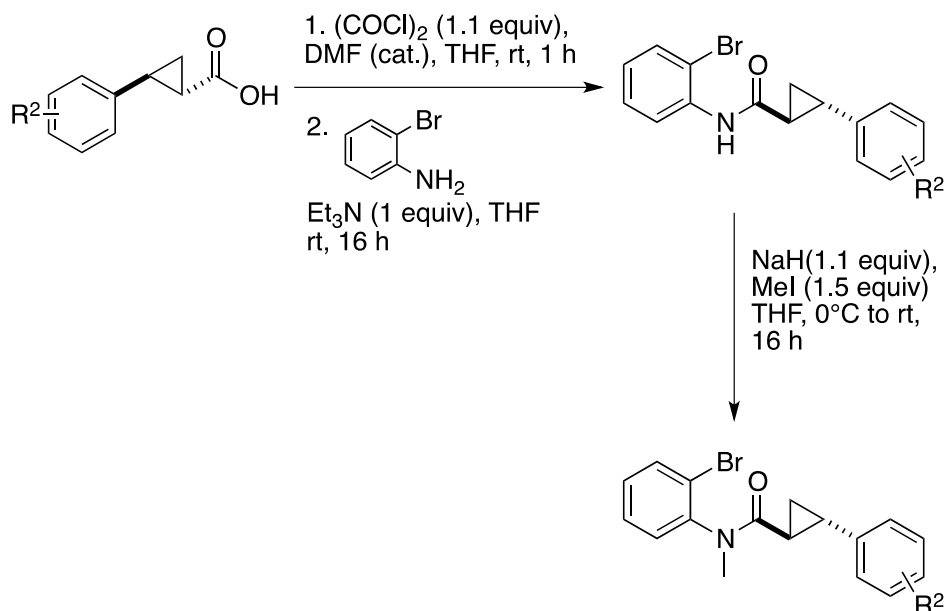
The ethyl-(*E*)-3-arylacrylates were synthesized according to the literature procedure.<sup>9</sup> The Corey-Chaykovsky cyclopropanation was performed as outlined in the literature,<sup>10</sup> except an acidic work up was added to isolate the carboxylic acid. All the intermediates have been previously synthesized and match reported literature data.

<sup>9</sup> Jiang, T.; Livinghouse, T.; Lovick, H.M. *Chem. Commun.* **2011**, 47, 12861-12863.

<sup>10</sup> Corey, E.J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, 87, 1353-1364.

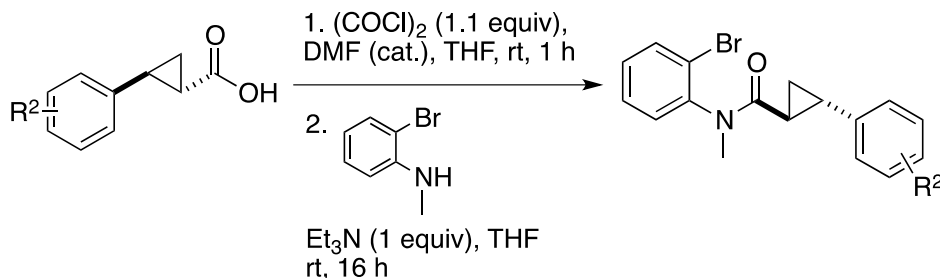
## Synthesis of 2-bromoanilides (1j-1r)

## Route A

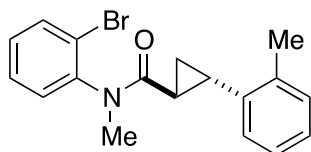


The cyclopropanecarboxylic acid (1 equiv) was dissolved in THF (10 mL) in a 50-mL round-bottomed flask flame-dried and cooled over argon. Catalytic DMF (2-3 drops) was added to the solution. Oxalyl chloride (1.1 equiv) was then added dropwise over 30 min. The reaction was stirred for an additional 30 min at ambient temperature (or until complete by TLC) and then concentrated *in vacuo* to remove excess oxalyl chloride. The residue was re-dissolved in THF (10 mL). 2-bromoaniline (0.95 equiv), then Et<sub>3</sub>N (1.0 equiv) were both added dropwise. The reaction was stirred at ambient temperature for a further 16 h. It was then quenched with water (10 mL), and the aqueous layer was extracted with EtOAc (2x's, 25 mL). The combined organic layers were washed with saturated NaHCO<sub>3</sub> solution (20 mL), brine (10 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated *in vacuo*. The crude was then dissolved in THF (10 mL) in a 25-mL round-bottomed flask under argon and cooled in an ice bath. NaH (60%, 1.1 equiv) was added portionwise. The reaction was stirred for an additional 10 min, then MeI (1.5 equiv) was added. The reaction was allowed to warm up to ambient temperature and stirred for 16 h. Then, the reaction was quenched with water (10 mL) and extracted with EtOAc (3x's, 20 mL). The combined organic layers were washed with brine (10 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated *in vacuo*. The residue was purified by flash chromatography. As indicated, the desired products were *trans*-racemic.

## Route B

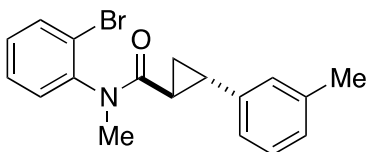


The cyclopropanecarboxylic acid (1.0 equiv) was dissolved in THF (10 mL) in a 50 mL round-bottomed flask, flame-dried and cooled under argon. DMF (2-3 drops) was then added to the solution. Oxalyl chloride (1.1 equiv) was then added dropwise over 30 min. The reaction was stirred for an additional 30 min at ambient temperature (or until complete by TLC). The reaction was then concentrated *in vacuo* to remove excess oxalyl chloride, and the residue was re-dissolved in THF (10 mL). 2-bromo-*N*-methylaniline<sup>11</sup> (0.95 equiv), then  $\text{Et}_3\text{N}$  (1.0 equiv) were both added dropwise. The reaction was stirred at ambient temperature for a further 16 h. It was then quenched with water (10 mL), and the aqueous layer was extracted with  $\text{EtOAc}$  (2x's, 25 mL). The combined organic layers were washed with saturated  $\text{NaHCO}_3$  solution (20 mL) and brine (10 mL), and then dried over anhydrous  $\text{Na}_2\text{SO}_4$ . After filtering and concentrating *in vacuo*, the residue was purified by flash chromatography or re-crystallization to give *trans*-racemic products.

***trans*-rac-*N*-(2-bromophenyl)-*N*-methyl-2-(*o*-tolyl)cyclopropanecarboxamide (1j)**

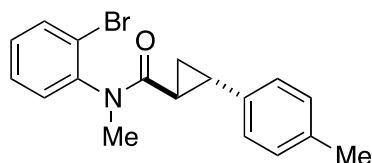
Synthesized according to route B on a 1.9-mmol scale. The residue was purified by flash chromatography (5-20%  $\text{EtOAc}/\text{Hex}$ ), affording the title compound as clear oil in 94% yield (618 mg, 1.80 mmol). Reported as a 1:1 mixture of rotamers. **mp**: 91-93 °C; **R<sub>f</sub>**: 0.44 (1:1 hexanes: ethyl acetate); **<sup>1</sup>H NMR** ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.71-7.66 (m, 1H), 7.40-7.37 (m, 2H), 7.27-7.21 (m, 1H), 7.12-7.06 (m, 2H), 7.02-6.97 (m, 1H), 6.74-6.66 (m, 1H), 3.29 (s, 3H), 2.70-2.56 (m, 1H), 2.39 (d, 3H,  $J = 9.0$  Hz), 1.69-1.53 (m, 1H), 1.46-1.41 (m, 1H), 1.12-0.99 (m, 1H); **<sup>13</sup>C NMR** ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  172.5, 172.4, 142.7, 142.6, 138.4 (2C), 138.3, 137.9, 134.0 (2C), 130.3, 130.1, 129.8, 129.7, 129.0 (2C), 126.4, 126.1, 126.0, 125.5, 123.9, 36.2, 36.1, 24.5, 24.4, 21.4, 19.8, 19.7, 16.3, 15.8; **FTIR** ( $\text{cm}^{-1}$ )(neat): 2939, 1644, 1580, 1477, 1358, 1270, 1059, 1029, 767, 752, 723; **HRMS** (ESI, Pos) calcd for  $\text{C}_{18}\text{H}_{19}\text{BrNO}$   $[\text{M}+\text{H}]^+$ : 344.06445  $m/z$ , found 344.06443  $m/z$ .

<sup>11</sup> Wurtz, S.; Lohre, C.; Frohlich, R.; Bergander, K.; Glorius, F. *J. Am. Chem. Soc.* **2009**, *131*, 8344.



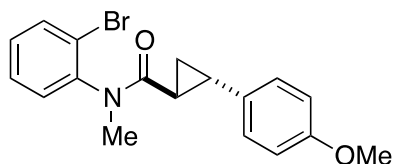
***trans-rac-N-(2-bromophenyl)-N-methyl-2-(m-tolyl)cyclopropanecarboxamide(1k)***

Synthesized according to route A, on a 3.0 mmol scale. The residue was purified by flash chromatography (5-20% EtOAc/Hex), affording the title compound as an off-white solid in 74% yield (764 mg, 2.22 mmol). Reported as a 1:1 mixture of rotamers. **mp**: 87-88 °C; **R<sub>f</sub>**: 0.49 (1:1 hexanes: ethyl acetate); **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz): δ 7.72-7.62 (two br d, 1H, *J* = 7.3 Hz), 7.41-7.40 (m, 1H), 7.32-7.27 (m, 1H), 7.24-7.21 (m, 1H), 7.10-7.07 (m, 1H), 6.97-6.96 (d, 1H, *J* = 7.2 Hz), 6.86-6.71 (m 2H), 3.28 (s, 3H), 2.63-2.50 (m, 1H), 2.27 (s, 3H), 1.72-1.59 (m 1H), 1.47-1.41 (m, 1H), 1.15-1.04 (m, 1H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz): δ 172.2, 172.1, 142.7, 142.6, 140.6, 140.5, 137.8, 137.7, 133.9 (2C), 130.4, 130.1, 129.7 (2C), 129.0, 128.9, 128.2, 128.1, 127.9, 127.3, 126.9, 124.0, 123.8, 123.7, 123.3, 36.2, 36.1, 26.4, 26.1, 23.6, 23.0, 21.4, 17.2, 16.2; **FTIR** (cm<sup>-1</sup>)(neat): 2922, 1650, 1607, 1427, 1363, 1252, 1031, 930, 730, 697, 673; **HRMS** (ESI, Pos) calcd for C<sub>18</sub>H<sub>19</sub>BrNO [M+H]<sup>+</sup>: 344.06445 m/z, found 344.06466 m/z.



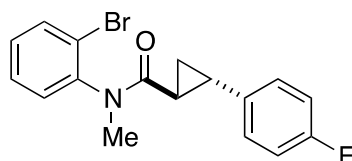
***trans-rac-N-(2-bromophenyl)-N-methyl-2-(p-tolyl)cyclopropanecarboxamide (1l)***

Synthesized according to route B, on a 2.85 mmol scale. The residue was purified by flash chromatography (5-20% EtOAc/Hex), affording the title compound as an off-white solid in 77% yield (769 mg, 2.30 mmol). Reported as a 1:1 mixture of rotamers. **mp**: 98-99 °C; **R<sub>f</sub>**: 0.40 (1:1 hexanes: ethyl acetate); **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz): δ 7.69-7.59 (two d, 1H), 7.38-7.36 (m, 1H), 7.28-7.26 (m, 1H), 7.22-7.17 (m, 1H), 7.00-6.97 (m, 2H), 6.89 (dd, 1H, *J* = 8.0, 1.5 Hz), 6.80 (dd, 1H, *J* = 8.0, 1.5 Hz), 3.25 (s, 3H), 2.60-2.47 (m, 1H), 2.26 (s, 3H), 1.67-1.54 (m 1H), 1.41-1.34 (m, 1H), 1.11-0.99 (m, 1H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz): δ 172.4, 172.2, 142.7, 142.6, 137.6 (2C), 135.7 (2C), 133.9 (2C), 130.4, 130.1, 129.8, 129.7, 129.0 (2C), 128.9, 126.8 (2C), 126.3, 124.0, 123.7, 36.2 (2C), 26.2, 25.9, 23.5, 23.0, 21.1 (2C), 17.2, 16.3; **FTIR** (cm<sup>-1</sup>)(neat): 3082, 3024, 1644, 1581, 1475, 1423, 963, 871, 671, 527; **HRMS** (ESI, Pos) calcd for C<sub>18</sub>H<sub>19</sub>BrNO [M+H]<sup>+</sup>: 344.06465 m/z, found 344.06448 m/z.



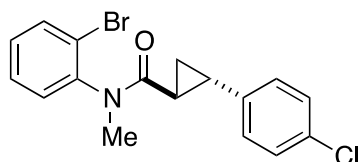
***trans-rac-N-(2-bromophenyl)-2-(4-methoxyphenyl)-N-methylcyclopropanecarboxamide (1m)***

Synthesized according to route B on a 2.37-mmol scale. The residue was purified by flash chromatography (5-20% EtOAc/Hex), affording the title compound as a clear oil in 74% yield (632 mg, 1.75 mmol). Reported as a 1:1 mixture of rotamers. **R<sub>f</sub>**: 0.44 (1:1 hexanes: ethyl acetate); **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz): δ 7.71-7.61 (two br d, 1H), 7.42-7.37 (m, 1H), 7.31-7.27 (m, 1H), 7.23-7.19 (m, 1H), 6.94 (d, 1H, *J* = 8.4 Hz), 6.86 (d, 1H, *J* = 8.5 Hz), 6.73 (dd, 2H, *J* = 8.8, 2.5 Hz), 3.75 (s, 3H), 3.27 (s, 3H), 2.60-2.47 (m, 1H), 1.68-1.55 (m, 1H), 1.39-1.32 (m, 1H), 1.10-0.99 (m, 1H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz): δ 172.4, 172.3, 158.1 (2C), 142.7, 142.6, 133.9 (2C), 132.7, 132.6, 130.4, 130.2, 129.8, 129.7, 129.0, 128.9, 128.0, 127.5 (2C), 124.0, 123.7, 113.8, 55.3 (2C), 36.2, 36.1, 25.9, 25.6, 23.5, 23.0, 17.0, 16.1; **FTIR** (cm<sup>-1</sup>)(neat): 28344, 1651, 1611, 1583, 1514, 1475, 1245, 1119, 1034, 823, 671; **HRMS** (ESI, Pos) calcd for C<sub>18</sub>H<sub>18</sub>BrNNaO<sub>2</sub> [M+Na]<sup>+</sup>: 382.04131 m/z, found 382.04074 m/z.



***trans-rac-N-(2-bromophenyl)-2-(4-fluorophenyl)-N-methylcyclopropanecarboxamide (1n)***

Synthesized according to route B, on a 3.5 mmol scale. The residue was purified by recrystallization from EtOAc/Hex, affording the title compound as a white solid in 78% yield (931 mg, 2.68 mmol). Reported as a 1:1 mixture of rotamers. **mp**: 99-100 °C; **R<sub>f</sub>**: 0.41 (1:1 hexanes: ethyl acetate); **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz): δ 7.67-7.55 (two br d, 1H), 7.37-7.36 (m, 1H), 7.26-7.25 (m, 1H), 7.19-7.15 (m, 1H), 6.93-6.89 (m, 1H), 6.84-6.80 (m, 3H), 3.23 (s, 3H), 2.57-2.45 (m, 1H), 1.68-1.57 (m, 1H), 1.38-1.32 (m, 1H), 1.07-0.97 (m, 1H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz): δ 171.8, 171.7, 162.4, 160.0, 142.4 (2C), 136.2 (d, *J* = 3 Hz), 136.1 (d, *J* = 3 Hz), 133.8, 133.7, 130.1, 130.0, 129.7 (2C), 128.9, 128.8, 128.1, 128.0, 127.6, 127.7, 123.8, 123.5, 115.1, 115.0, 114.9, 114.8, 36.0 (2C), 25.6, 25.2, 23.6, 23.1, 16.9, 16.0; **<sup>19</sup>F NMR** (CDCl<sub>3</sub>, 300 MHz): δ -116.6 (m); **FTIR** (cm<sup>-1</sup>)(neat): 2966, 1650, 1528, 1510, 1475, 1419, 1320, 1211, 1083, 864, 746, 671, 572. **HRMS** (ESI, Pos) calcd for C<sub>17</sub>H<sub>16</sub>BrFNO [M+H]<sup>+</sup>: 348.03938 m/z, found 348.03921 m/z.

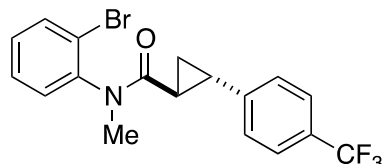


***trans-rac-N-(2-bromophenyl)-2-(4-chlorophenyl)-N-methylcyclopropanecarboxamide (1o)***

Synthesized according to route B, on a 1.9 mmol scale. The residue was purified by flash chromatography (5-20% EtOAc/Hex), affording the title compound as a white solid in 77% yield (533 mg, 1.46 mmol). Reported as a 1:1 mixture of rotamers. **mp**: 80-82 °C; **R<sub>f</sub>**: 0.53 (1:1

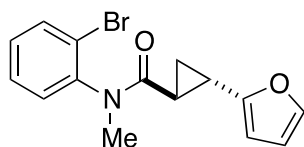


hexanes: ethyl acetate); **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz): δ 7.69-7.57 (two br d, 1H, *J* = 8.3 Hz), 7.41-7.37 (m, 1H), 7.27-7.25 (m, 1H), 7.13-7.11 (m, 2H), 6.98 (d, 1H, *J* = 8.1 Hz), 6.82 (d, 1H, *J* = 8.1 Hz), 3.25 (s, 3H), 2.56-2.46 (m, 1H), 1.72-1.61 (m 1H), 1.40-1.33 (m, 1H), 1.11-1.00 (m, 1H). **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz): δ 171.8, 171.7, 142.5, 142.4, 139.2 (2C), 133.9, 133.8, 131.8 (2C), 130.2, 130.0, 129.8 (2C), 129.0, 128.9, 128.4 (2C), 128.3, 128.0, 127.7, 123.9, 123.6, 36.2, 36.14, 25.8, 25.4, 23.9, 23.5, 17.2, 16.3. **FTIR** (cm<sup>-1</sup>)(neat): 2922, 2866, 1657, 1492, 1477, 1358, 1056, 1012. **HRMS** (ESI, Pos) calcd for C<sub>17</sub>H<sub>16</sub>BrClNO [M+H]<sup>+</sup>: 364.00983 m/z, found 364.00974 m/z.



***trans-rac-N-(2-bromophenyl)-N-methyl-2-(4-(trifluoromethyl)phenyl)cyclopropanecarboxamide(1p)***

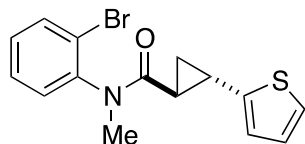
Synthesized according to route B, on a 1.36 mmol scale. The residue was purified by flash chromatography (5-20% EtOAc/Hex), affording the title compound as a yellow solid in 66% yield (356 mg, 0.894 mmol). Reported as a 1:1 mixture of rotamers. **mp**: 74-75 °C; **R<sub>f</sub>**: 0.44 (1:1 hexanes: ethyl acetate); **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz): δ 7.71-7.57 (two br d, 1H), 7.43-7.39 (m, 3H), 7.27-7.26 (m, 1H), 7.23-7.19 (m, 1H), 7.09 (d, 1H, *J* = 7.9 Hz), 6.99 (d, 1H, *J* = 7.9 Hz), 3.26 (s, 3H), 2.69-2.59 (m, 1H), 1.77-1.66 (m 1H), 1.49-1.42 (m, 1H), 1.18-1.06 (m, 1H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz): δ 171.6, 171.5, 145.0 (2C), 142.5, 142.4, 134.0 (2C), 130.2, 130.1, 129.9 (2C), 129.1, 129.0, 126.8, 126.4, 125.3-125.2 (m), 123.9, 123.7, 36.2 (2C), 26.1, 25.7, 24.3, 23.8, 17.6, 16.6; **<sup>19</sup>F NMR** (CDCl<sub>3</sub>, 300 MHz): δ -62.3 (d, *J* = 9.7 Hz). **FTIR** (cm<sup>-1</sup>) (neat): 2931, 1655, 1618, 1476, 1423, 1323, 162, 1116, 1067, 826, 727, 711. **HRMS** (ESI, Pos) calcd for C<sub>18</sub>H<sub>16</sub>BrF<sub>3</sub>NO [M+H]<sup>+</sup>: 398.03619 m/z, found 398.0355 m/z.



***trans-rac-N-(2-bromophenyl)-2-(furan-2-yl)-N-methylcyclopropanecarboxamide(1q)***

Synthesized according to route B, on a 2.85 mmol scale. The residue was purified by flash chromatography (5-20% EtOAc/Hex), affording the title compound as a yellow oil in 77% yield (707 mg, 2.21 mmol). Reported as a 1:1 mixture of rotamers. **R<sub>f</sub>**: 0.48 (1:1 hexanes: ethyl acetate); **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz): δ 7.66-7.59 (two br d, 1H, *J* = 8.0 Hz), 7.39-7.29 (m, 2H), 7.21-7.16 (m, 1H), 7.10-7.08 (m, 1H), 6.15-6.13 (m, 1H), 5.96-5.82 (br d, 1H, *J* = 12.7, 2.6 Hz), 3.21 (s, 3H), 2.54-2.44 (m, 1H), 1.59-1.46 (m, 2H), 1.16-1.06 (m, 1H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz): δ 171.5, 171.4, 154.0 (3C), 142.4, 142.3, 140.8, 140.7, 133.8, 130.2, 130.0, 129.7 (2C), 128.9 (2C), 123.9, 123.5, 110.2, 105.0, 104.8, 36.1 (2C), 32.2, 21.4, 19.5, 19.1, 15.0, 14.4; **FTIR** (cm<sup>-1</sup>) (neat): 3008, 2923, 1650, 1583, 1507, 1422, 1315, 1131, 1119,

1013, 764, 727; **HRMS** (ESI, Pos) calcd for  $C_{15}H_{14}BrNNaO_2$   $[M+Na]^+$ : 342.01001 m/z, found 342.00993 m/z.

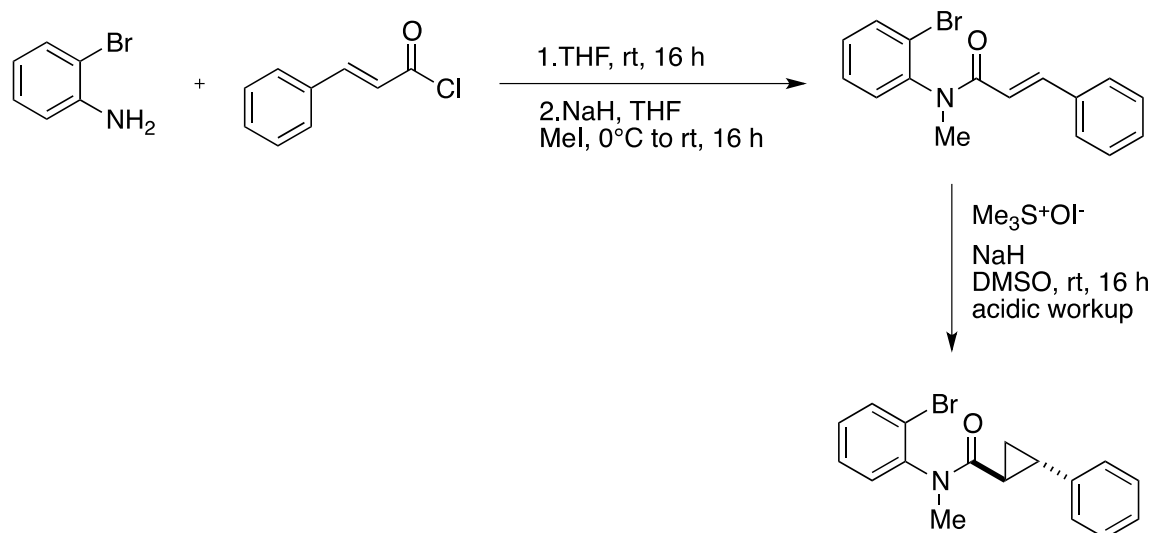


***trans-rac-N-(2-bromophenyl)-N-methyl-2-(thiophen-2-yl)cyclopropanecarboxamide(1r)***

Synthesized according to route A, on a 2.76 mmol scale. The residue was purified by flash chromatography (5-20% EtOAc/Hex), affording the title compound as an off-white solid in 67% yield (622 mg, 1.85 mmol). Reported as a 1:1 mixture of rotamers. **mp**: 119-121 °C; **R<sub>f</sub>**: 0.46 (1:1 hexanes: ethyl acetate); **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz): δ 7.69-7.64 (m, 1H), 7.41-7.31 (m, 2H), 7.24-7.20 (m, 1H), 7.00 (t, 1H, *J* = 4.5 Hz), 6.81-6.79 (m, 1H), 6.66-6.59 (two d, 1H, *J* = 3.2 Hz), 3.25 (s, 3H), 2.72-2.53 (m, 1H), 1.73-1.62 (m 1H), 1.48-1.43 (m, 1H), 1.15-1.04 (m, 1H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz): δ 171.6, 171.5, 144.9, 144.8, 142.6, 142.5, 134.0 (2C), 130.4, 130.1, 129.9, 129.8, 129.1, 129.0, 126.7, 126.6, 124.2, 124.1, 123.7, 123.6, 123.3, 123.1, 36.2 (2C), 24.4, 24.0, 21.5, 21.3, 17.9, 17.1; **FTIR** (cm<sup>-1</sup>) (neat): 2923, 1643, 1582, 1476, 1426, 1203, 1056, 923, 761, 700; **HRMS** (ESI, Pos) calcd for  $C_{15}H_{15}BrNOS$   $[M+H]^+$ : 336.00522 m/z, found 336.005 m/z.

**Synthesis of phenylcyclopropanecarboxamide (1sa)**

***trans-rac-N-(2-bromophenyl)-N-methyl-2-phenylcyclopropanecarboxamide (1sa)***

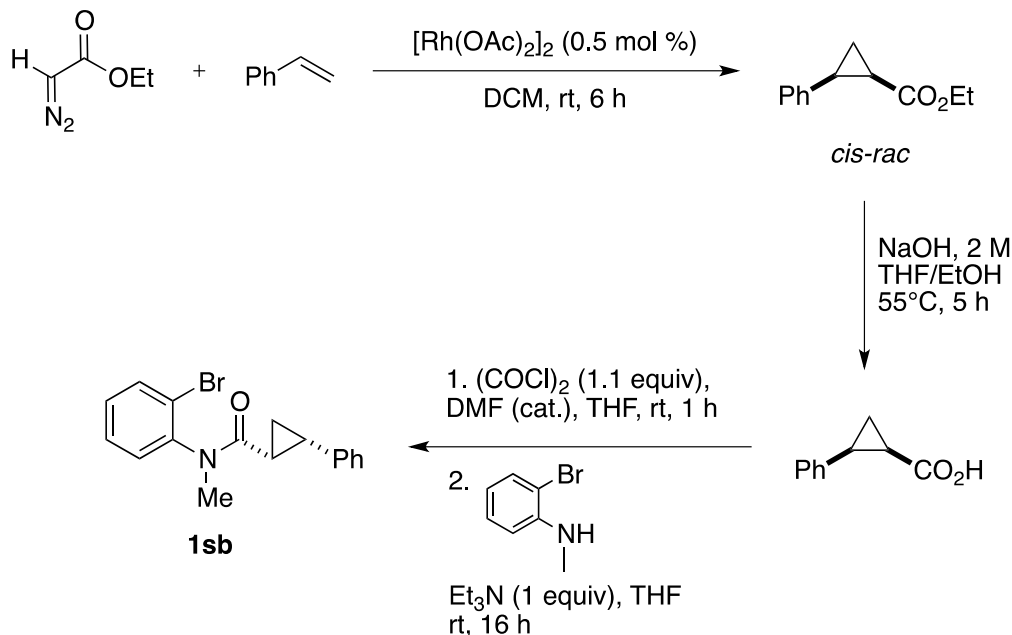


To a solution of 2-bromoaniline (11.6 mmol, 1 equiv) in THF (25 mL) was added cinnamyl chloride (11.9 mmol, 1.1 equiv) under argon. The reaction was stirred at room temperature for 16 h. Then, EtOAc (50 mL) was added and the organic phase was washed with saturated NaHCO<sub>3</sub> solution (2x's, 30 mL) and brine (15 mL). The organic phase was dried over

anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated *in vacuo*. The resulting solid was dried on a vacuum pump, then dissolved in 25 mL of THF, purged with argon, and cooled down in an ice bath. NaH (60%, 15.9 mmol, 1.37 equiv) was added to the solution portionwise over a few minutes. The reaction was stirred for an additional 10 min at 0 °C, then MeI (17.4 mmol, 1.5 equiv) was added to the reaction. The reaction was allowed to warm up to room temperature, and stirred overnight. The reaction was quenched with water (15 mL), and extracted with EtOAc (3x's, 25 mL). The combined organic layers were washed with brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated *in vacuo*. The residue was flashed in 5-30% EtOAc/Hex to give 77% (2.8 g) of *N*-(2-bromophenyl)-*N*-methylcinnamamide as an off-white solid to be used in the subsequent step.

To a solution of trimethylsulfoxonium iodide (2 equiv) in DMSO (100 mL) was added NaH (60%, 2 equiv) portionwise over 15 min. The reaction was allowed to stir for 30 min at room temperature, then a solution of *N*-(2-bromophenyl)-*N*-methylcinnamamide in 5 mL of DMSO was added dropwise. The reaction was allowed to stir for 16 h. Then, the reaction was neutralized with 2.0 M HCl, and extracted with EtOAc (2x's, 25 mL). The combined organic layer was washed with brine (2x's, 30 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. The residue was purified by flash chromatography in 5-10% EtOAc/Hex, affording the title compound as a clear oil in 75% yield and as the *trans*-racemic product.

Reported as a 1:1 mixture of rotamers. **R<sub>f</sub>**: 0.48 (1:1 hexanes: ethyl acetate); **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400 MHz): δ 7.69-7.57 (br d, 1H), 7.39-7.36 (m, 1H), 7.28-7.25 (m, 1H), 7.19-7.11 (m, 4H), 6.97 (d, 1H, *J* = 7.7 Hz), 6.90 (d, 1H, *J* = 7.7 Hz), 3.25 (s, 3H), 2.62-2.49 (m, 1H), 1.70-1.57 (m, 1H), 1.43-1.37 (m, 1H), 1.14-1.02 (m, 1H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 100 MHz): δ 172.3, 172.2, 142.7, 142.6, 140.8, 140.7, 134.0, 133.9, 130.4, 130.2, 129.8 (2C), 129.0 (2C), 128.4, 128.3, 126.9, 126.4, 126.2, 124.0, 123.7, 36.3, 36.2, 26.6, 26.2, 23.8, 23.3, 17.4, 16.4; **FTIR** (cm<sup>-1</sup>) (neat): 3002, 1647, 1583, 1457, 1423, 1358, 1312, 749, 728, 697; **HRMS** (ESI, Pos) calcd for C<sub>17</sub>H<sub>16</sub>BrNNaO [M+Na]<sup>+</sup>: 352.03075 m/z, found 352.03037 m/z.

**Synthesis of *cis-rac*-N-(2-bromophenyl)-N-methyl-2-phenylcyclopropanecarboxamide (1sb)**

To a 250-mL round-bottomed flask flame-dried and cooled under argon was added  $[\text{Rh}(\text{OAc})_2]_2$  (70 mg, 0.324 mmol, 0.5 mol %). Styrene (11.0 mL) was then added, and the reaction was cooled to 0 °C. Ethyl diazoacetate (3.7 g, 32.4 mmol, 1.0 equiv) was then added over 60 min via a syringe pump. The reaction was stirred for 3 h, then filtered through a silica-cotton plug and concentrated in vacuo. The racemic mixture was then flashed in 5-10% EtOAc/Hex and the *cis*-product isolated in 28 % yield (1.7 g, 8.9 mmol).

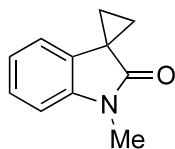
1.42 g (7.5 mmol) of the racemic mixture was then transferred to a 100-mL round-bottomed flask containing 15 mL of THF: 10 mL of MeOH. 2.0 M NaOH (19 mL, 37.4 mmol, 5.0 equiv) was then added and the mixture was heated to 55 °C for 5 hours. The reaction was then cooled to ambient temperature, acidified with 30 mL of 10% HCl. This was transferred to a 250-mL separatory funnel and extracted with benzene (3x's, 25 mL). The combined organics were then washed with brine, dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated *in vacuo* to give the desired *cis-rac*-cyclopropanecarboxylic acid.

**1sb** was then synthesized according to route A from 1.9 mmol of the *cis-rac*-cyclopropanecarboxylic acid. The residue was purified by flash chromatography (5-20% EtOAc/Hex), affording the *cis-racemic* product as a clear oil in 79% yield (494 mg, 1.50 mmol). Reported as a 3:1 mixture of rotamers.  $R_f$ : 0.45;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.72-7.67 (two d, 1H,  $J$  = 8.0, 1.3 Hz), 7.41-7.15 (m, 7H), 6.87 (dd, 1H,  $J$  = 7.8, 1.6 Hz), 3.07 & 3.01 (s, 3H), 2.30 & 2.06 (q, 1H,  $J$  = 8.4 Hz), 1.90-1.86 & 1.81-1.77 (m, 1H), 1.73-1.66 (m, 1H), 1.21-1.14 (m, 1H).  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  169.5, 168.4, 143.0, 142.4, 137.2, 136.6, 133.8, 133.6, 130.6, 130.2, 129.7, 129.6, 129.5, 128.8, 128.6, 128.2, 127.8, 127.4, 126.2, 126.1, 123.7, 123.2, 35.9, 35.8, 26.5, 25.5, 24.4, 21.0, 12.2, 11.2;  $\text{FTIR}$  ( $\text{cm}^{-1}$ ) (neat): 3059,

3008, 1655, 1497, 1476, 1458, 1329, 1068, 1026, 728, 696, 664; **HRMS** (ESI, Pos) calcd for  $C_{17}H_{16}BrNNaO$   $[M+Na]^+$ : 352.03075  $m/z$ , found 352.03049  $m/z$ .

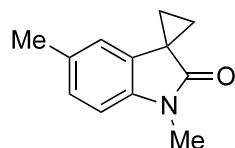
### General Procedure for the Synthesis of Spiro 3,3'-cyclopropyl oxindoles (**2a-2sb**)

To a 5.0-mL microwave vial in a glovebox was added in the following order:  $Pd(OAc)_2$  (5.6 mg, 0.025 mmol),  $PCy_3$  (7.0 mg, 0.025 mmol),  $K_2CO_3$  (104.0 mg, 0.75 mmol) and  $Ag_3PO_4$  (0.17 mmol, 69.1 mg). The vial was crimped shut. The 2-bromoanilide (**1a-1sa**) (0.50 mmol) was weighed into a vial, dissolved in 0.4 mL of toluene and added to the reaction vial. The vial containing 2-bromoanilide was rinsed with 3x's 0.2 mL of toluene for a total volume of 1.0 mL. This yellowish-orange solution was then heated to 130 °C in an oil bath for 3 h as indicated by TLC. The reaction turned black within five minutes. The reaction was cooled to ambient temperature, filtered over a cotton-Celite® plug, and rinsed with 15 mL of ethyl acetate. It was then concentrated *in vacuo* to give the crude product. The crude was then purified via column chromatography over silica gel (RediSep® Rf Gold 24g) using a solvent gradient of 10% to 50% Ethyl Acetate/Hexanes to give **2a-2sb**.



### 1'-methylspiro[cyclopropane-1,3'-indolin]-2'-one (**2a**)

The title compound **2a** was prepared by the general procedure on a 0.464 mmol scale to give an orange solid in 90% yield (72.4 mg, 0.418 mmol). The observed characterization data ( $^1H$  NMR) was consistent with that previously reported in the literature<sup>12,13</sup>.  **$^1H$  NMR** ( $CDCl_3$ , 400 MHz):  $\delta$  7.52-7.47 (m, 1H), 7.28-7.25 (m, 1H), 7.16-7.13 (m, 1H), 7.09-7.06 (m, 1H), 3.54 (s, 3H), 1.98-1.95 (m, 2H), 1.76-1.73 (m, 2H);  **$^{13}C$  NMR** ( $CDCl_3$ , 75 MHz):  $\delta$  177.1, 143.6, 130.9, 126.8, 122.5, 122.0, 118.3, 108.0, 27.1, 26.6, 19.2; **HRMS** (ESI, Pos) calcd for  $C_{11}H_{11}NNaO$   $(M+Na)^+$ : 196.07326, found: 196.07329  $m/z$ .



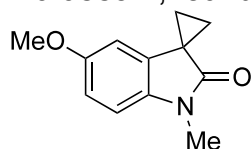
### 1',5'-dimethylspiro[cyclopropane-1,3'-indolin]-2'-one (**2b**)

The title compound **2b** was prepared by the general procedure on a 0.508 mmol scale and then purified via column chromatography over silica gel (RediSep® Rf Gold 24g) using a

<sup>12</sup> Beckwith, A.L.J.; Bowry, V.W.; Bowman, W.R.; Mann, E.; Parr, J.; Storey, J.M.D. *Angew. Chem.* **2004**, 116, 97.

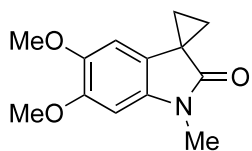
<sup>13</sup> Helan, V.; Mills, A.; Drewry, D.; Grant, D. *J. Org. Chem.* **2010**, 75, 6693.

solvent gradient of 10% to 50% ethyl acetate/hexanes to give a light pink solid in 81% yield (77.2 mg, 0.412 mmol). **mp**: 75-78 °C; **R<sub>f</sub>**: 0.42 (1:1 hexanes: ethyl acetate); **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400MHz): δ 7.06-7.04 (m, 1H), 6.81-6.78 (m, 1H), 6.66 (dd, *J* = 1.0, 0.4 Hz, 1H), 3.28 (s, 3H), 2.35 (s, 3H), 1.74-1.69 (m, 2H), 1.50-1.46 (m, 2H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 75 MHz): δ 177.2, 141.3, 131.6, 131.0, 130.3, 127.1, 119.2, 107.8, 27.1, 26.7, 21.2, 19.1; **FTIR** (cm<sup>-1</sup>) (neat): 2918, 1691, 1493, 1392, 1230, 890, 700, 554; **HRMS** (ESI, Pos) calcd for C<sub>12</sub>H<sub>13</sub>NNaO(M+Na)<sup>+</sup>: 210.08894, found: 210.08811 *m/z*.



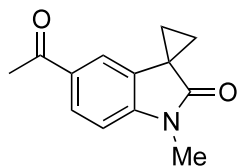
### 5'-methoxy-1'-methylspiro[cyclopropane-1,3'-indolin]-2'-one (2c)

The title compound **2c** was prepared by the general procedure on a 0.506 mmol scale and then purified via column chromatography over silica gel (RediSep® Rf Gold 24g) using a solvent gradient of 10% to 50% ethyl acetate/hexanes to give a cream-coloured solid in 67% yield (69.4 mg, 0.342 mmol). **mp**: 72-75°C; **R<sub>f</sub>**: 0.62(1:1 hexanes: ethyl acetate); **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400MHz): δ 6.80 (d, *J* = 2.1 Hz, 2H), 6.47 (t, *J* = 0.9 Hz, 1H), 3.80 (s, 3H), 3.29 (s, 3H), 1.75 (q, *J* = 3.9 Hz, 2H), 1.49 (q, *J* = 3.9 Hz, 2H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 75 MHz): δ 176.8, 155.9, 137.3, 132.4, 111.0, 108.3, 106.1, 56.0, 27.5, 26.7, 19.3; **FTIR** (cm<sup>-1</sup>) (neat): 2930, 1694, 1370, 1210, 793; **HRMS** (APPI, Pos) calcd for C<sub>12</sub>H<sub>14</sub>NO<sub>2</sub> (M+H)<sup>+</sup>: 204.10191, found: 204.1027 *m/z*.



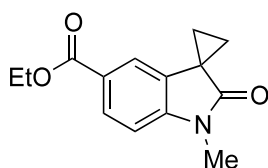
### 5',6'-dimethoxy-1'-methylspiro[cyclopropane-1,3'-indolin]-2'-one (2d)

The title compound **2d** was prepared by the general procedure on a 0.5 mmol scale and then purified via column chromatography over silica gel (RediSep® Rf Gold 24g) using a solvent gradient of 10% to 50% ethyl acetate/hexanes to give a cream-coloured solid in 74% yield (86.3 mg, 0.37 mmol). **mp**: 148-150°C; **R<sub>f</sub>**: 0.52 (1:1 hexanes: ethyl acetate); **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400MHz): δ 6.55 (s, 1H), 6.45 (s, 1H), 3.92 (s, 3H), 3.85 (s, 3H), 3.27 (s, 3H), 1.69-1.66 (m, 2H), 1.45-1.42 (m, 2H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 75 MHz): δ 177.5, 148.9, 145.1, 137.3, 121.6, 104.3, 94.8, 57.1, 56.7, 27.3, 26.7, 18.7; **FTIR** (cm<sup>-1</sup>) (neat): 2932, 1687, 1508, 1285, 1150, 901, 777; **HRMS** (ESI, Pos) calcd for C<sub>13</sub>H<sub>15</sub>NNaO<sub>3</sub> (M+Na)<sup>+</sup>: 256.09441, found: 256.09422 *m/z*.

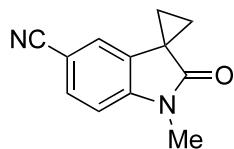


**5'-acetyl-1'-methylspiro[cyclopropane-1,3'-indolin]-2'-one (2e)**

The title compound **2e** was prepared by the general procedure on a 0.412 mmol scale and then purified via column chromatography over silica gel (RediSep® Rf Gold 24g) using a solvent gradient of 10% to 50% ethyl acetate/hexanes to give a cream-coloured solid in 62% yield (54.9 mg, 0.255 mmol). **mp**: 165-167°C; **R<sub>f</sub>**: 0.27 (1:1 hexanes: ethyl acetate); **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400MHz): δ 7.93-7.90 (m, 1H), 7.49 (d, *J* = 1.3 Hz, 1H), 6.93 (dd, *J* = 8.1, 3.3 Hz, 1H), 3.33 (s, 3H), 2.58 (s, 3H), 1.80-1.76 (m, 2H), 1.63-1.61 (m, 2H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 75 MHz): δ 197.1, 177.5, 147.9, 131.8, 131.3, 129.0, 118.2, 107.3, 27.1, 26.9, 26.5, 19.8; **FTIR** (cm<sup>-1</sup>) (neat): 2920, 2851, 1711, 1659, 1616, 1424, 1259, 826, 618, 535; **HRMS** (ESI, Pos) calcd for C<sub>13</sub>H<sub>13</sub>NNaO<sub>2</sub> (M+Na)<sup>+</sup>: 238.08385, found: 238.08336 *m/z*.

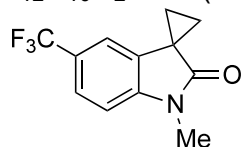
**Ethyl 1'-methyl-2'-oxospiro[cyclopropane-1,3'-indoline]-5'-carboxylate (2f)**

The title compound **2f** was prepared by the general procedure on a 0.432 mmol scale and then purified via column chromatography over silica gel (RediSep® Rf Gold 24g) using a solvent gradient of 10% to 50% ethyl acetate/hexanes to give an orange solid in 99% yield (105 mg, 0.426 mmol). **mp**: 124-126°C; **R<sub>f</sub>**: 0.38 (1:1 hexanes: ethyl acetate); **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400MHz): δ 8.00 (d, *J* = 8.1 Hz, 1H), 7.50 (s, 1H), 6.91 (d, *J* = 8.1 Hz, 1H), 4.35 (q, *J* = 7.0 Hz, 2H), 3.32 (s, 3H), 1.77 (d, *J* = 3.6 Hz, 2H), 1.61-1.60 (m, 2H), 1.38 (t, *J* = 7.0 Hz, 3H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 75 MHz): δ 177.4, 166.6, 147.6, 130.9, 129.5, 124.4, 119.6, 107.5, 61.0, 27.1, 26.9, 19.6, 14.5; **FTIR** (cm<sup>-1</sup>) (neat): 2961, 1701, 1615, 1298, 1104, 1025, 772; **HRMS** (ESI, Pos) calcd for C<sub>14</sub>H<sub>15</sub>NNaO<sub>3</sub> (M+Na)<sup>+</sup>: 268.09441, found: 268.09401 *m/z*.

**1'-methyl-2'-oxospiro[cyclopropane-1,3'-indoline]-5'-carbonitrile (2g)**

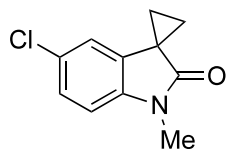
The title compound **2g** was prepared by the general procedure on a 0.524 mmol scale and then purified via column chromatography over silica gel (RediSep® Rf Gold 24g) using a solvent gradient of 10% to 50% ethyl acetate/hexanes to give an orange solid in 78% yield (80.9 mg, 0.409 mmol). **mp**: 124-127°C; **R<sub>f</sub>**: 0.33 (1:1 hexanes: ethyl acetate); **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 400MHz): δ 7.58 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.07 (d, *J* = 1.3 Hz, 1H), 6.95 (d, *J* = 8.1 Hz, 1H), 3.32 (s, 3H), 1.82 (q, *J* = 4.0 Hz, 2H), 1.60 (q, *J* = 4.0 Hz, 2H); **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 75 MHz): δ 176.8, 147.4, 132.16, 132.12, 121.7, 119.5, 108.4, 105.2, 27.0, 26.9, 20.2; **FTIR**

( $\text{cm}^{-1}$ ) (neat): 3053, 2919, 2220, 1711, 1618, 1591, 1253, 829; **HRMS** (ESI, Pos) calcd for  $\text{C}_{12}\text{H}_{10}\text{N}_2\text{NaO}$  ( $\text{M}+\text{Na}$ )<sup>+</sup>: 221.06853, found: 221.06813  $m/z$ .



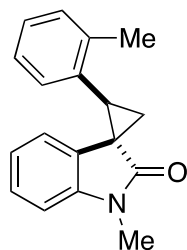
### 1'-methyl-5'-(trifluoromethyl)spiro[cyclopropane-1,3'-indolin]-2'-one (2h)

The title compound **2h** was prepared by the general procedure on a 0.485 mmol scale and then purified via column chromatography over silica gel (RediSep® Rf Gold 24g) using a solvent gradient of 10% to 50% ethyl acetate/hexanes to give an orange solid in 85% yield (99.4 mg, 0.412 mmol). **mp**: 132-134 °C; **R<sub>f</sub>**: 0.56 (1:1 hexanes: ethyl acetate); **<sup>1</sup>H NMR** ( $\text{CDCl}_3$ , 400MHz):  $\delta$  7.53 (d,  $J$  = 8.2 Hz, 1H), 7.05 (dd,  $J$  = 1.2, 0.5 Hz, 1H), 6.96 (d,  $J$  = 8.2 Hz, 1H), 3.32 (s, 3H), 1.82-1.79 (m, 2H), 1.59-1.61 (m, 2H). ; **<sup>13</sup>C NMR** ( $\text{CDCl}_3$ , 75 MHz): 177.1, 146.5, 131.6, 124.6 (q,  $J$  = 271 Hz), 124.6 (q,  $J$  = 4.1 Hz), 124.5 (q,  $J$  = 32.7 Hz), 119.2, 115.5 (q,  $J$  = 3.6 Hz), 114.4, 27.2, 26.9, 19.8; **<sup>19</sup>F NMR** (282 MHz,  $\text{CDCl}_3$ ): -61.3; **FTIR** ( $\text{cm}^{-1}$ ) (neat): 2925, 1708, 1624, 1460, 1163, 954, 520; **HRMS** (ESI, Pos) calcd for  $\text{C}_{12}\text{H}_{10}\text{F}_3\text{NNaO}$  ( $\text{M}+\text{Na}$ )<sup>+</sup>: 264.06067, found: 264.06032  $m/z$ .



### 5'-chloro-1'-methylspiro[cyclopropane-1,3'-indolin]-2'-one (2i)

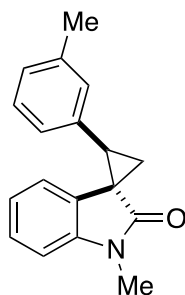
The title compound **2i** was prepared by the general procedure on a 0.491 mmol scale and then purified via column chromatography over silica gel (RediSep® Rf Gold 24g) using a solvent gradient of 10% to 50% ethyl acetate/hexanes to give a pink-colored solid in 89% yield (90.4 mg, 0.437 mmol). **mp**: 130-132°C; **R<sub>f</sub>**: 0.43 (1:1 hexanes: ethyl acetate); **<sup>1</sup>H NMR** ( $\text{CDCl}_3$ , 400MHz):  $\delta$  7.23 (d,  $J$  = 8.3 Hz, 1H), 6.83-6.81 (m, 2H), 3.29 (s, 3H), 1.78-1.77 (m, 2H), 1.54 (td,  $J$  = 3.7, 2.2 Hz, 2H); **<sup>13</sup>C NMR** ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  176.6, 142.2, 132.8, 127.5, 126.7, 118.9, 108.9, 27.3, 26.8, 19.6; **FTIR** ( $\text{cm}^{-1}$ ) (neat): 3058, 2924, 1697, 1612, 1587, 1388, 1085, 802, 666, 545, 458; **HRMS** (APPI, Pos) calcd for  $\text{C}_{11}\text{H}_{11}\text{ClNO}$  ( $\text{M}+\text{H}$ )<sup>+</sup>: 208.05253, found: 208.05237  $m/z$ .



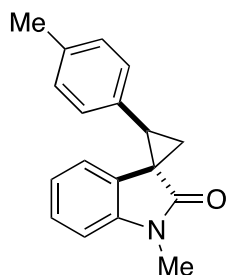


**(1*S*,2*R*)-1'-methyl-2-(*o*-tolyl)spiro[cyclopropane-1,3'-indolin]-2'-one and (1*R*,2*R*)-1'-methyl-2-(*o*-tolyl)spiro[cyclopropane-1,3'-indolin]-2'-one (2j)**

The title compound **2j** was prepared by the general procedure on a 0.471 mmol scale and then purified via column chromatography over silica gel (RediSep® Rf Gold 24g) using a solvent gradient of 10% to 50% ethyl acetate/hexanes to give a yellow oil in 94% yield (90.4 mg, 0.437 mmol) as a mixture of major and minor diastereomers (14:1 dr). Diastereomeric ratios were determined via  $^1\text{H}$  NMR.  $R_f$ : 0.53 (1:1 hexanes: ethyl acetate);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): **Major**:  $\delta$  7.40 (d,  $J$  = 7.4 Hz, 1H), 7.28-7.15 (m, 3H), 7.06-7.05 (m, 1H), 6.89 (d,  $J$  = 7.8 Hz, 1H), 6.69-6.65 (m, 1H), 5.88 (d,  $J$  = 7.5 Hz, 1H), 3.37 (s, 3H), 2.27 (dd,  $J$  = 9.0, 4.5 Hz, 1H), 2.06 (dd,  $J$  = 8.0, 4.5 Hz, 1H), 1.78 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): **Major and Minor**:  $\delta$  176.6, 173.9, 143.7, 143.5, 139.3, 138.0, 133.7, 130.7, 130.1, 130.0, 129.7, 129.1, 128.7, 127.7, 127.6, 127.5, 126.7, 125.9, 125.7, 122.0, 121.6, 119.9, 118.2, 107.9, 107.8, 36.8, 35.1, 33.3, 33.1, 26.8, 26.6, 22.6, 22.5, 19.5, 19.2; **FTIR** ( $\text{cm}^{-1}$ ) (neat): 2938, 1701, 1646, 1493, 1380, 1344, 1133, 748, 728; **HRMS** (ESI, Pos): calcd for  $\text{C}_{18}\text{H}_{18}\text{NO}$   $[\text{M}+\text{H}]^+$ : 264.13829 m/z, found 264.13792 m/z.

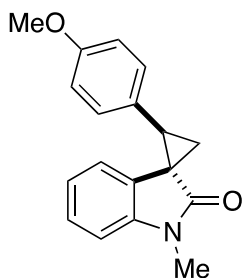
**(1*S*,2*R*)-1'-methyl-2-(*m*-tolyl)spiro[cyclopropane-1,3'-indolin]-2'-one and (1*R*,2*R*)-1'-methyl-2-(*m*-tolyl)spiro[cyclopropane-1,3'-indolin]-2'-one (2k)**

The title compound **2k** was prepared by the general procedure on a 0.485 mmol scale and then purified via column chromatography over silica gel (RediSep® Rf Gold 24g) using a solvent gradient of 10% to 50% ethyl acetate/hexanes to give a yellow oil in 98% yield (126 mg, 0.477 mmol) as a mixture of major and minor diastereomers (11:1 dr). Diastereomeric ratios were determined via  $^1\text{H}$  NMR.  $R_f$ : 0.53, 0.46 (1:1 hexanes: ethyl acetate);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): **Major**:  $\delta$  7.18-7.14 (m, 2H), 7.08-7.06 (m, 1H), 7.03 (br s, 1H), 6.98 (d,  $J$  = 7.6 Hz, 1H), 6.88 (d,  $J$  = 7.8 Hz, 1H), 6.71 (td,  $J$  = 7.6, 1.0 Hz, 1H), 6.03 (dt,  $J$  = 7.5, 0.5 Hz, 1H), 3.34 (s, 3H), 2.31 (s, 3H), 2.18 (dd,  $J$  = 9.1, 4.5 Hz, 1H), 2.00 (dd,  $J$  = 8.0, 4.5 Hz, 1H),  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): **Major and Minor**:  $\delta$  176.5, 143.9, 138.1, 137.4, 135.1, 134.3, 131.0, 130.7, 130.2, 128.2 (2C), 128.1, 127.8, 127.7, 126.9, 126.8, 126.6, 126.3, 121.9, 121.5, 120.8, 118.1, 107.8 (2C), 38.2, 35.9, 33.9, 33.4, 26.7, 26.5, 22.6, 21.5, 21.4; **FTIR** ( $\text{cm}^{-1}$ ) (neat): 2922, 1702, 1650, 1613, 1492, 1346, 1128, 730, 672; **HRMS** (ESI, Pos) calcd for  $\text{C}_{18}\text{H}_{18}\text{NO}$   $[\text{M}+\text{H}]^+$ : 264.13829 m/z, found 264.13796 m/z.



**(1*S*,2*R*)-1'-methyl-2-(*p*-tolyl)spiro[cyclopropane-1,3'-indolin]-2'-one and (1*R*,2*R*)-1'-methyl-2-(*p*-tolyl)spiro[cyclopropane-1,3'-indolin]-2'-one (2l)**

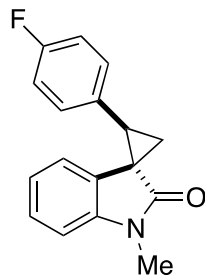
The title compound **2l** was prepared by the general procedure on a 0.496 mmol scale and then purified via column chromatography over silica gel (RediSep® Rf Gold 24g) using a solvent gradient of 10% to 50% ethyl acetate/hexanes to give a yellow oil in 93% yield (121 mg, 0.459 mmol) as a mixture of major and minor diastereomers (8:1 dr). Diastereomeric ratios were determined via  $^1\text{H}$  NMR. **R<sub>f</sub>**: 0.48, 0.38 (1:1 hexanes: ethyl acetate);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): **Major**:  $\delta$  7.34-7.07 (m, 5H), 6.90-6.86 (m, 1H), 6.72 (t, 1H,  $J$  = 7.5 Hz), 6.03 (d, 1H,  $J$  = 7.5 Hz), 3.33 (s, 3H), 3.32 (t, 1H,  $J$  = 8.8 Hz), 2.34 (s, 3H), 2.18 (dd, 1H,  $J$  = 8.9, 4.5 Hz), 1.99 (dd, 1H,  $J$  = 7.8, 4.5 Hz), **Minor**:  $\delta$  7.37-6.86 (m, 8H), 3.19 (s, 3H), 3.13 (t, 1H,  $J$  = 8.9 Hz), 2.42-2.38 (m, 1H), 2.34 (s, 3H), 2.06 (dd, 1H,  $J$  = 9.0, 4.7 Hz);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): **Major**:  $\delta$  176.6, 143.8, 137.0, 132.1, 129.8, 129.1, 127.7, 126.5, 121.5, 120.8, 107.8, 35.7, 33.4, 26.7, 22.6, 21.2, **Minor**:  $\delta$  176.6, 149.3, 136.8, 131.3, 129.4, 126.8, 125.8, 121.9, 118.7, 118.1, 107.8, 36.1, 33.9, 26.5, 22.6, 21.3; **FTIR** ( $\text{cm}^{-1}$ )(neat): 3001, 2922, 1701, 1614, 1517, 1378, 1215, 1158, 748, 585; **HRMS** (ESI, Pos) calcd for  $\text{C}_{18}\text{H}_{17}\text{NNaO}$  [ $\text{M}+\text{Na}$ ] $^+$ : 286.12024 m/z, found 286.11996 m/z.



**(1*S*,2*R*)-2-(4-methoxyphenyl)-1'-methylspiro[cyclopropane-1,3'-indolin]-2'-one and (1*R*,2*R*)-2-(4-methoxyphenyl)-1'-methylspiro[cyclopropane-1,3'-indolin]-2'-one (2m)**

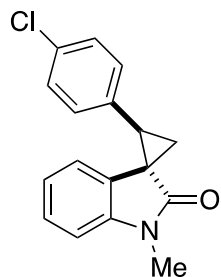
The title compound **2m** was prepared by the general procedure on a 0.496 mmol scale and then purified via column chromatography over silica gel (RediSep® Rf Gold 24g) using a solvent gradient of 10% to 50% ethyl acetate/hexanes to give an off-white in 92% yield (127 mg, 0.456 mmol) as a mixture of major and minor diastereomers (10:1 dr). Diastereomeric ratios were determined via  $^1\text{H}$  NMR. **mp**: 76-74°C; **R<sub>f</sub>**: 0.43, 0.37 (1:1 hexanes: ethyl acetate);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): **Major**:  $\delta$  7.16 (td, 1H,  $J$  = 7.8, 1.1 Hz), 7.10 (d, 2H,  $J$  = 8.3 Hz), 6.88-6.81 (m, 3H), 6.71 (td, 1H,  $J$  = 7.7, 0.6 Hz), 6.00 (dd, 1H,  $J$  = 7.5, 0.6 Hz), 3.79 (s, 3H),

3.32 (s, 3H), 3.29 (t, 1H,  $J = 8.4$  Hz), 2.17 (dd, 1H,  $J = 9.2, 4.5$  Hz), 1.95 (dd, 1H,  $J = 7.9, 4.5$  Hz), **Minor**:  $\delta$  7.37-6.80 (m, 8H), 3.78 (s, 3H), 3.18 (s, 3H), 3.12 (t, 1H,  $J = 8.8$  Hz), 2.37 (dd,  $J = 8.6, 4.8$  Hz), 2.05 (dd, 1H,  $J = 8.6, 4.8$  Hz);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): **Major**:  $\delta$  176.5, 158.8, 143.8, 131.0, 127.7, 127.2, 126.5, 121.5, 120.8, 113.8, 107.8, 55.3, 35.3, 33.4, 26.6, 22.8, **Minor**:  $\delta$  174.0, 158.7, 143.4, 130.3, 128.3, 127.0, 126.7, 122.6, 121.9, 118.0, 113.4, 55.2, 37.8, 33.9, 26.5, 22.7; **FTIR** ( $\text{cm}^{-1}$ )(neat): 2933, 1704, 1613, 1515, 1494, 1346, 1249, 974, 696; **HRMS** (ESI, Pos) calcd for  $\text{C}_{18}\text{H}_{17}\text{NNaO}_2$   $[\text{M}+\text{Na}]^+$ : 302.11515  $m/z$ , found 302.11471  $m/z$ .



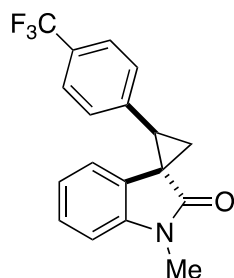
**(1*S*,2*R*)-2-(4-fluorophenyl)-1'-methylspiro[cyclopropane-1,3'-indolin]-2'-one** and **(1*R*,2*R*)-2-(4-fluorophenyl)-1'-methylspiro[cyclopropane-1,3'-indolin]-2'-one (2n)**

The title compound **2n** was prepared by the general procedure on a 0.498 mmol scale and then purified via column chromatography over silica gel (RediSep® Rf Gold 24g) using a solvent gradient of 10% to 50% ethyl acetate/hexanes to give a white solid in 99% yield (132 mg, 0.494 mmol) as a mixture of major and minor diastereomers (8:1 dr). Diastereomeric ratios were determined via  $^1\text{H}$  NMR. The two diastereomers were also separable via flash chromatography (5 to 20% ethyl acetate/hexanes) both yielding white solids. **Major**: mp: 69-70 °C; **R<sub>f</sub>**: 0.46 (1:1 hexanes: ethyl acetate);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.19-7.13 (m, 3H), 7.01-6.96 (m, 2H), 6.89-6.87 (m, 1H), 6.72 (td, 1H,  $J = 7.6, 1.0$  Hz), 5.94 (d, 1H,  $J = 7.8$  Hz), 3.33 (s, 3H), 3.29 (t, 1H,  $J = 7.8$  Hz), 2.19 (dd, 1H,  $J = 9.2, 4.6$  Hz), 1.93 (dd, 1H,  $J = 7.9, 4.3$  Hz);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  176.3, 162.0 (d,  $J = 245$  Hz), 143.9, 131.5 (d,  $J = 8.0$  Hz), 130.6 (d,  $J = 3.2$  Hz), 127.3, 126.8, 121.6, 120.7, 115.3 (d,  $J = 22$  Hz), 107.9, 34.9, 33.2, 26.7, 22.7;  $^{19}\text{F}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  -114.6 (m); **FTIR** ( $\text{cm}^{-1}$ )(neat): 2938, 2844, 1696, 1612, 1510, 1379, 1245, 1090, 1015, 841, 750; **HRMS** (ESI, Pos) calcd for  $\text{C}_{17}\text{H}_{15}\text{FNO}$   $[\text{M}+\text{H}]^+$ : 268.11322  $m/z$ , found 268.11283  $m/z$ . **Minor**: mp: 111-114 °C; **R<sub>f</sub>**: 0.37 (1:1 hexanes: ethyl acetate);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.31-7.27 (m, 3H), 7.08 (td, 1H,  $J = 7.5, 0.9$  Hz), 7.01-6.96 (m, 3H), 6.90 (d, 1H,  $J = 7.8$  Hz), 3.19 (s, 3H), 3.12 (t, 1H,  $J = 8.7$  Hz), 2.36 (dd, 1H,  $J = 8.6, 5.0$  Hz), 2.07 (dd, 1H,  $J = 9.1, 5.0$  Hz);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  173.9, 162.0 (d,  $J = 245$  Hz), 143.6, 130.9 (d,  $J = 8.1$  Hz), 130.7, 130.1 (d,  $J = 3.1$  Hz), 127.0, 122.1, 118.2, 114.9 (d,  $J = 21.5$  Hz), 108.0, 37.3, 33.9, 26.6, 22.8;  $^{19}\text{F}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  -115.2 (m); **FTIR** ( $\text{cm}^{-1}$ ) (neat): 2922, 1704, 1615, 1512, 1469, 1315, 1252, 1230, 1196, 1131, 1102, 908, 730. **HRMS** (ESI, Pos) calcd for  $\text{C}_{17}\text{H}_{15}\text{FNO}$   $[\text{M}+\text{H}]^+$ : 268.11322  $m/z$ , found 268.11297  $m/z$ .



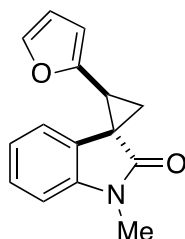
**(1*S*,2*R*)-2-(4-chlorophenyl)-1'-methylspiro[cyclopropane-1,3'-indolin]-2'-one and (1*R*,2*R*)-2-(4-chlorophenyl)-1'-methylspiro[cyclopropane-1,3'-indolin]-2'-one (2o)**

The title compound **2o** was prepared by the general procedure on a 0.348 mmol scale and then purified via column chromatography over silica gel (RediSep® Rf Gold 24g) using a solvent gradient of 10% to 50% ethyl acetate/hexanes to give an orange solid in 95% yield (93.8 mg, 0.331 mmol) as a mixture of major and minor diastereomers (5:1 dr). Diastereomeric ratios were determined via  $^1\text{H}$  NMR. The two diastereomers were also separable via flash chromatography (5 to 20% ethyl acetate/hexanes). **Major**: orange solid; **mp**: 126-128 °C; **R<sub>f</sub>**: 0.58 (1:1 hexanes: ethyl acetate);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.28-7.25 (m, 2H), 7.19 (td, 1H,  $J$  = 7.7, 1.1 Hz), 7.12 (d, 2H,  $J$  = 8.7 Hz), 6.89 (d, 1H,  $J$  = 8.0 Hz), 6.75 (td, 1H,  $J$  = 7.7, 0.9 Hz) 5.98 (d, 1H,  $J$  = 7.5 Hz), 3.34 (s, 3H), 3.27 (t, 1H,  $J$  = 8.5 Hz), 2.19 (dd, 1H,  $J$  = 9.0, 4.5 Hz), 1.94 (dd, 1H,  $J$  = 7.9, 4.5 Hz);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  176.2, 143.9, 133.8, 133.2, 131.3, 128.6, 127.1, 126.4, 121.7, 120.7, 108.0, 35.0, 33.2, 26.7, 22.4. **FTIR** ( $\text{cm}^{-1}$ ) (neat): 2927, 1686, 1610, 1491, 1465, 1292, 1085, 1016, 785, 548. **HRMS** (ESI, Pos) calcd for  $\text{C}_{17}\text{H}_{15}\text{ClNO}$   $[\text{M}+\text{H}]^+$ : 284.08367 m/z, found 284.08341 m/z. **Minor**: off-white solid; **mp**: 110-111 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.56 (td, 1H,  $J$  = 7.8, 1.2 Hz), 7.27-7.24 (m, 4H), 7.08 (td, 1H,  $J$  = 7.5, 0.9 Hz), 6.97 (dd, 1H,  $J$  = 7.5, 0.9 Hz), 6.90 (d, 1H,  $J$  = 7.8, 0.9), 3.19 (s, 3H), 3.10 (t, 1H,  $J$  = 8.8 Hz), 2.35 (dd, 1H,  $J$  = 8.6, 5.0 Hz), 2.07 (dd, 1H,  $J$  = 8.8, 4.9 Hz).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  173.8, 143.6, 133.1, 133.0, 130.7, 130.6, 128.2, 127.1, 122.1, 118.2, 108.0, 37.3, 34.0, 26.6, 22.6. **FTIR** ( $\text{cm}^{-1}$ ) (neat): 2923, 1697, 1614, 1492, 1469, 1345, 1315, 1195, 1109, 975, 746, 530. **HRMS** (ESI, Pos) calcd for  $\text{C}_{17}\text{H}_{15}\text{ClNO}$   $[\text{M}+\text{H}]^+$ : 284.08367 m/z, found 284.08367 m/z.



**(1*S*,2*R*)-1'-methyl-2-(4-(trifluoromethyl)phenyl)spiro[cyclopropane-1,3'-indolin]-2'-one and (1*R*,2*R*)-1'-methyl-2-(4-(trifluoromethyl)phenyl)spiro[cyclopropane-1,3'-indolin]-2'-one (2p)**

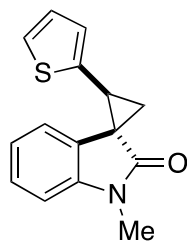
The title compound **2p** was prepared by the general procedure on a 0.30 mmol scale and then purified via column chromatography over silica gel (RediSep® Rf Gold 24g) using a solvent gradient of 10% to 50% ethyl acetate/hexanes to give an orange solid in 85% yield (80.7 mg, 0.254 mmol) as a mixture of major and minor diastereomers (5:1 dr). Diastereomeric ratios were determined via  $^1\text{H}$  NMR. The two diastereomers were also separable via flash chromatography (5 to 20% ethyl acetate/hexanes). **R<sub>f</sub>**: 0.58 (1:1 hexanes: ethyl acetate); **Major**: orange solid; **mp**: 123-125 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.55 (d, 2H,  $J$  = 8.2 Hz), 7.31 (d, 2H,  $J$  = 8.2 Hz), 7.18 (td, 1H,  $J$  = 7.7, 0.9 Hz), 6.89 (d, 1H,  $J$  = 7.9 Hz), 6.72 (td, 1H,  $J$  = 7.6, 0.9 Hz), 5.95 (d, 1H,  $J$  = 7.3 Hz), 3.34 (s, 3H), 3.35-3.31 (m, 1H), 2.13 (dd, 1H,  $J$  = 9.1, 4.7 Hz), 2.00 (dd, 1H,  $J$  = 8.0, 4.7 Hz);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  176.0, 143.9, 139.4, 130.3, 130.0 (q,  $J$  = 32 Hz), 128.2-120.0 (q,  $J$  = 272 Hz), 127.0, 126.8, 125.3 (q,  $J$  = 3.9 Hz), 121.7, 120.5, 108.0, 35.1, 32.3, 26.7, 22.2;  $^{19}\text{F}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  -62.4 (s). **FTIR** ( $\text{cm}^{-1}$ ) (neat): 2934, 1695, 1615, 1496, 1322, 1160, 1112, 1066, 977, 852, 751; **HRMS** (ESI, Pos) calcd for  $\text{C}_{18}\text{H}_{15}\text{F}_3\text{NO}$   $[\text{M}+\text{H}]^+$ : 318.11003 m/z, found 318.10973 m/z. **Minor**: off-white solid; **mp**: 138-139 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.56 (d, 2H,  $J$  = 8.2 Hz), 7.44 (d, 2H,  $J$  = 8.2 Hz), 7.31 (td, 1H,  $J$  = 7.6, 1.2 Hz), 7.10 (td, 1H,  $J$  = 7.5, 0.9 Hz), 6.99 (dd, 1H,  $J$  = 7.5, 0.9), 6.91 (d, 1H,  $J$  = 7.8 Hz), 3.19 (s, 3H), 3.16 (t, 1H,  $J$  = 8.9 Hz), 2.41 (dd, 1H,  $J$  = 8.5, 5.0 Hz), 2.12 (dd, 1H,  $J$  = 9.0, 5.0 Hz);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  173.7, 143.7, 138.5, 130.4, 129.7, 129.5 (q,  $J$  = 32 Hz), 128.4-120.3 (q,  $J$  = 272 Hz), 127.5, 125.0 (q,  $J$  = 3.8 Hz), 122.2, 118.3, 108.2, 37.3, 34.2, 26.6, 22.6;  $^{19}\text{F}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  -62.4 (s). **FTIR** ( $\text{cm}^{-1}$ ) (neat): 2930, 1699, 1615, 1493, 1379, 12544, 1193, 1121, 1069, 744; **HRMS** (ESI, Pos) calcd for  $\text{C}_{18}\text{H}_{15}\text{F}_3\text{NO}$   $[\text{M}+\text{H}]^+$ : 318.11003 m/z, found 318.1097 m/z.



**(1S,2S)-2-(furan-2-yl)-1'-methylspiro[cyclopropane-1,3'-indolin]-2'-one (1S,2S)-2-(furan-2-yl)-1'-methylspiro[cyclopropane-1,3'-indolin]-2'-one and (1R,2S)-2-(furan-2-yl)-1'-methylspiro[cyclopropane-1,3'-indolin]-2'-one (2q)**

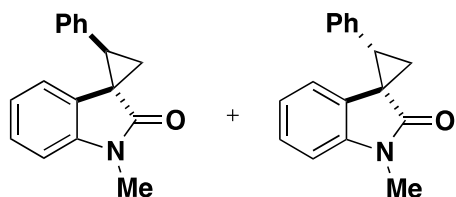
The title compound **2q** was prepared by the general procedure on a 0.494 mmol scale and then purified via column chromatography over silica gel (RediSep® Rf Gold 24g) using a solvent gradient of 10% to 50% ethyl acetate/hexanes to give a yellow oil in 79% yield (92.2 mg, 0.388 mmol) as a mixture of major and minor diastereomers (9:1 dr). Diastereomeric ratios were determined via  $^1\text{H}$  NMR. **R<sub>f</sub>**: 0.53, 0.31 (1:1 hexanes: ethyl acetate); **Major**:  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.32-7.31 (m, 1H), 7.20 (t, 1H,  $J$  = 7.7 Hz), 6.87 (d, 1H,  $J$  = 7.7 Hz), 6.83 (t, 1H,  $J$  = 7.6 Hz), 6.48 (d, 1H,  $J$  = 7.4 Hz), 3.31 (s, 3H), 3.11 (t, 1H,  $J$  = 8.3 Hz), 2.18 (dd, 1H,  $J$  = 9.2, 4.5 Hz), 2.12 (dd, 1H,  $J$  = 7.5, 4.5 Hz);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  175.7, 150.4, 144.0, 142.2, 127.3, 127.1, 122.0, 120.2, 110.7, 109.4, 108.1, 33.9, 28.7, 26.7,

21.3; **FTIR** ( $\text{cm}^{-1}$ ) (neat): 2937, 1699, 1613, 1494, 1421, 1375, 1342, 1329, 1128, 1011, 735, 547; **HRMS** (ESI, Pos) calcd for  $\text{C}_{15}\text{H}_{14}\text{NO}_2$   $[\text{M}+\text{H}]^+$ : 240.10191  $m/z$ , found 240.10158  $m/z$ .



**(1*S*,2*S*)-1'-methyl-2-(thiophen-2-yl)spiro[cyclopropane-1,3'-indolin]-2'-one and (1*R*,2*S*)-1'-methyl-2-(thiophen-2-yl)spiro[cyclopropane-1,3'-indolin]-2'-one (2r)**

The title compound **2m** was prepared by the general procedure on a 0.496 mmol scale and then purified via column chromatography over silica gel (RediSep® Rf Gold 24g) using a solvent gradient of 10% to 50% ethyl acetate/hexanes to give a yellow oil in 92% yield (127 mg, 0.456 mmol) as a mixture of major and minor diastereomers (10:1 dr). Diastereomeric ratios were determined via  $^1\text{H}$  NMR. **R<sub>f</sub>**: 0.56 (1:1 hexanes: ethyl acetate);  **$^1\text{H}$  NMR** ( $\text{CDCl}_3$ , 400 MHz): **Major**:  $\delta$  7.22-7.18 (m, 2H), 6.97-6.96 (m, 1H), 6.91-6.87 (m, 2H), 6.78 t(d, 1H,  $J$  = 7.6, 0.8 Hz), 6.24 (d, 1H,  $J$  = 7.5 Hz), 3.32 (s, 3H), 3.28 (t, 1H,  $J$  = 8.5 Hz), 2.25 (dd, 1H,  $J$  = 9.0, 4.5 Hz), 2.02 (dd, 1H,  $J$  = 7.6, 4.5 Hz); **Minor**:  $\delta$  7.41-6.85 (m, 7H), 3.21 (s, 3H), 3.20-3.18 (m, 1H), 2.35 (dd, 1H,  $J$  = 8.5, 5.0 Hz), 2.14 (dd, 1H,  $J$  = 8.9, 4.6 Hz);  **$^{13}\text{C}$  NMR** ( $\text{CDCl}_3$ , 100 MHz): **Major**:  $\delta$  175.9, 143.9, 139.1, 127.5, 127.0, 126.8, 125.4, 121.8, 120.4, 108.0, 34.2, 30.1, 28.6, 26.7, 23.8, **Minor**:  $\delta$  176.1, 143.5, 137.9, 127.1, 126.9, 126.7, 125.9, 124.7, 122.0, 118.2, 34.3, 32.7, 26.5, 24.0; **FTIR** ( $\text{cm}^{-1}$ ) (neat): 2937, 1699, 1649, 1613, 1493, 1423, 1380, 1028, 749, 696; **HRMS** (ESI, Pos): calcd for  $\text{C}_{15}\text{H}_{14}\text{NOS}$   $[\text{M}+\text{H}]^+$ : 256.07906  $m/z$ , found 256.07874  $m/z$ .



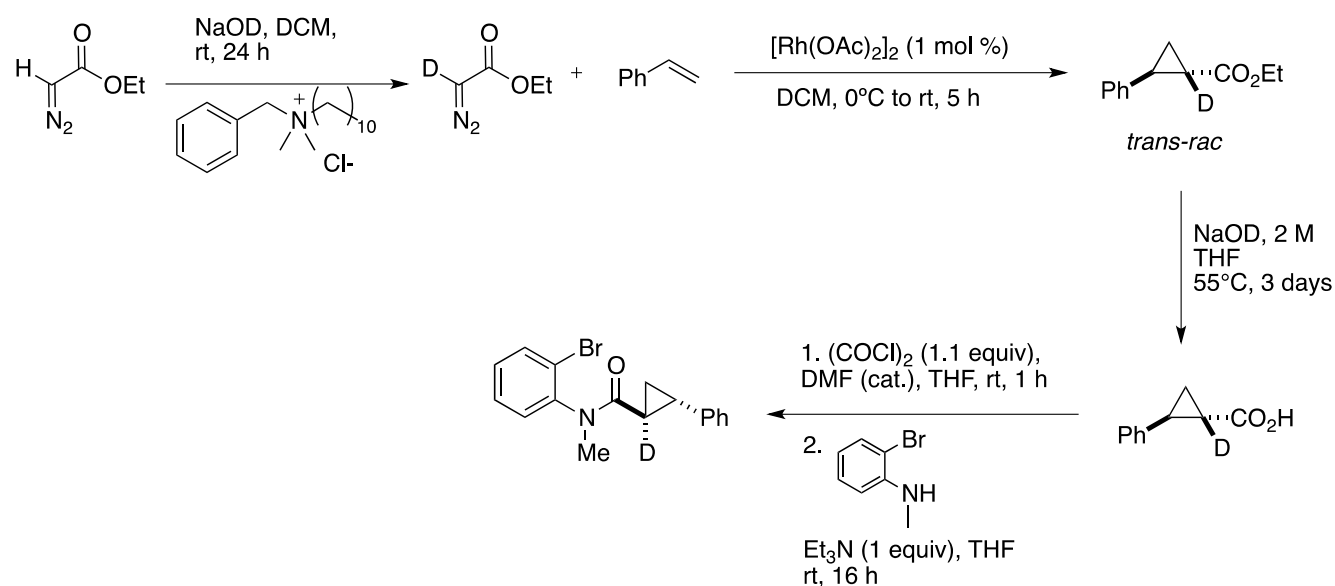
**(1*S*,2*R*)-1'-methyl-2-phenylspiro[cyclopropane-1,3'-indolin]-2'-one and (1*R*,2*R*)-1'-methyl-2-phenylspiro[cyclopropane-1,3'-indolin]-2'-one (2sa and 2sb)**

The title compounds **2s** and **2sb** were prepared by the general procedure from *trans-racemic* **1sa** on a 0.5 mmol scale and then purified via column chromatography over silica gel (RediSep® Rf Gold 24g) using a solvent gradient of 10% to 50% ethyl acetate/hexanes to give a yellow oil in 90% yield (112 mg, 0.449 mmol) as a mixture of major and minor diastereomers (6:1 dr). From *cis-racemic* **1sb** on 0.4 mmol scale: 93% yield, (93 mg, 0.37 mmol) in 1:5 dr. Diastereomeric ratios were determined via  $^1\text{H}$  NMR. **R<sub>f</sub>**: 0.51, 0.44 (1:1 hexanes: ethyl acetate);  **$^1\text{H}$  NMR** ( $\text{CDCl}_3$ , 400 MHz): **Major**:  $\delta$  7.33-7.26 (m, 4H), 7.21-7.14 (m, 3H), 6.99 (d, 1H,  $J$  = 7.9 Hz), 6.70 (t, 1H,  $J$  = 7.5 Hz), 5.98 (d, 1H,  $J$  = 7.6 Hz), 3.34 (s,

3H), 3.38-3.34 (m, 1H), 2.20 (dd, 1H,  $J = 9.1, 4.5$  Hz), 2.0 (dd, 1H,  $J = 8.0, 4.4$  Hz), **Minor**:  $\delta$  7.35-6.87 (m, 9H), 3.16 (s, 3H), 3.18-3.15 (m, 1H), 2.41 (dd,  $J = 8.6, 4.9$  Hz), 2.07 (dd, 1H,  $J = 8.9, 4.6$  Hz);  **$^{13}\text{C}$  NMR** ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  176.5 (2), 143.9, 135.2, 134.4, 130.9, 130.0, 129.3, 128.7, 128.0, 127.6, 127.4, 127.3, 126.9, 126.6, 125.8, 121.9, 121.5, 120.7, 118.1, 107.9, 107.8, 38.2, 35.9, 33.9, 33.4, 26.7, 26.5, 22.6, 22.5; **FTIR** ( $\text{cm}^{-1}$ )(neat): 3056, 3028, 1699, 1614, 1468, 1345, 1128, 747, 696; **HRMS** (ESI, Pos): calcd for  $\text{C}_{17}\text{H}_{16}\text{NO}$   $[\text{M}+\text{H}]^+$ : 250.12264  $m/z$ , found 250.12241  $m/z$ .

## Mechanistic Studies

### Synthesis of *d*-labeled *trans*-*rac*-*N*-(2-bromophenyl)-*N*-methyl-2-phenylcyclopropanecarboxamide



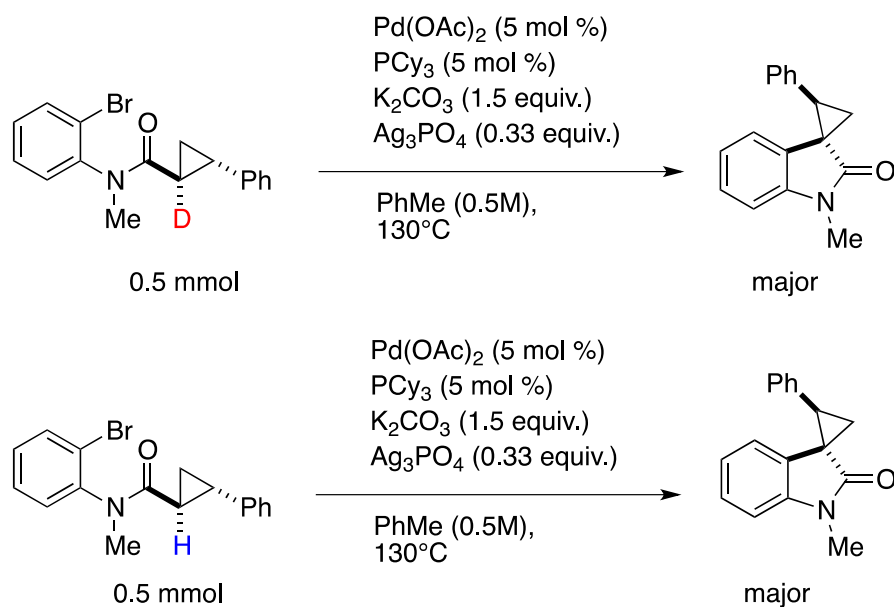
Deuterated ethyl diazoacetate was synthesized according to the literature procedure<sup>14</sup> and then used in the Rh-catalyzed cyclopropanation of styrene as described in the synthesis of **1sb**.

The *trans* product (410 mg, 2.15 mmol) was dissolved in 6 mL of THF and transferred to a 25-mL round-bottom flask. To this was added NaOD (2.0 M, 3.2 mL, 6.45 mmol, 3.0 equiv) and the reaction was heated to 55°C for 3 days. It was then acidified with 10 mL of 2.0 M HCl and extracted with EtOAc (3x's, 10 mL). The combined organics were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and conc *in vacuo* to give a yellow solid in quantitative yield which was used crude in the amide synthesis by Route **B**. The deuterated *trans*-*racemic* product was obtained as a white solid in 70% yield (500 mg, 1.51 mmol) and confirmed by <sup>1</sup>H NMR.

<sup>14</sup> Baldwin, J. E.; Carter, C. G. *J. Am. Chem. Soc.* **1982**, *104*, 1362.

## Kinetic Isotope Effect Studies

Two parallel reactions using *trans-rac-N*-(2-bromophenyl)-*N*-methyl-2-phenylcyclopropanecarboxamide and *d*-labeled *trans-rac-N*-(2-bromophenyl)-*N*-methyl-2-phenylcyclopropanecarboxamide were performed on a 0.5 mmol scale in accordance with the general procedure (Ref. S21). A known amount of internal standard (1,3,6-trimethoxybenzene) was added to each reaction and the formation of the major product was monitored over time using  $^1\text{H}$  NMR. The product concentration for the major product was then graphed vs. time to determine the rate of reaction ( $k_{\text{H}}$  and  $k_{\text{D}}$ ) for both reactions.



Entry	[P] Deuterated	[P] Non-deuterated	Time (min)
1	0.028	0.056	30
2	0.033	0.0714	45
3	0.039	0.11	60
4	0.053	0.1792	90
5	0.07	0.21	120

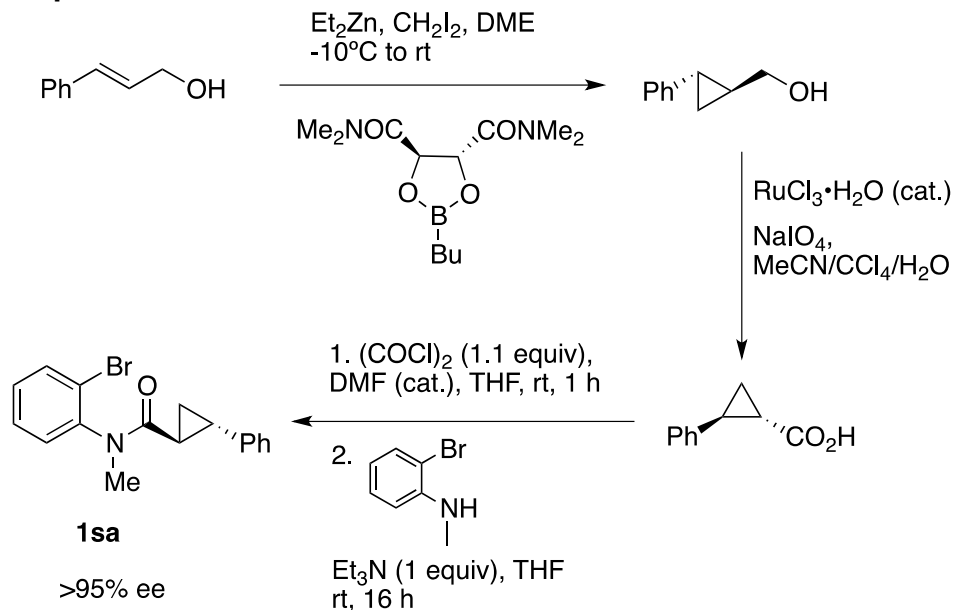
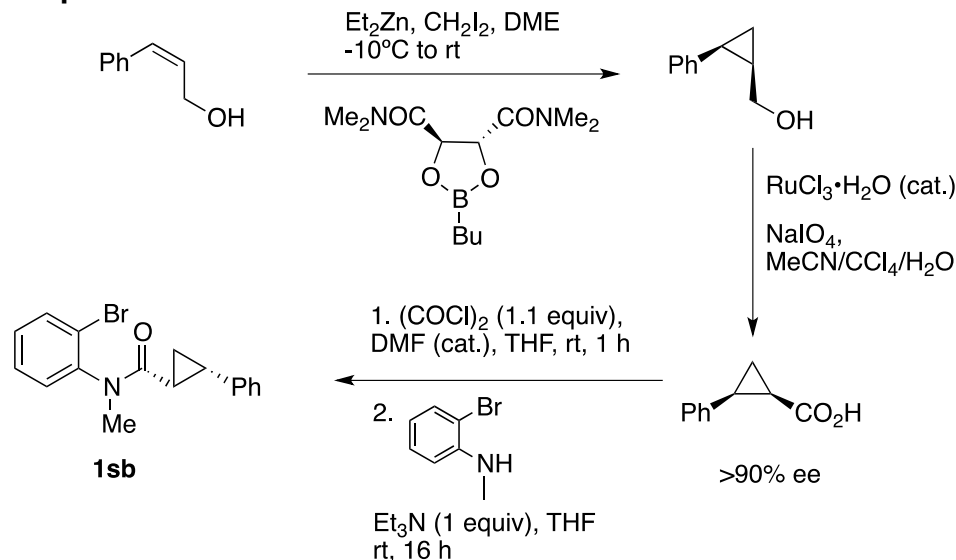
Linear equation for *d*-labeled substrate:  $y = 4.6897\text{E-}04x + 1.2241\text{E-}02$

Linear equation for normal substrate (1sa):  $y = 1.8363\text{E-}03x - 1.3862\text{E-}03$

$$k_{\text{H}}/k_{\text{D}} = 3.9$$



## Epimerization Studies

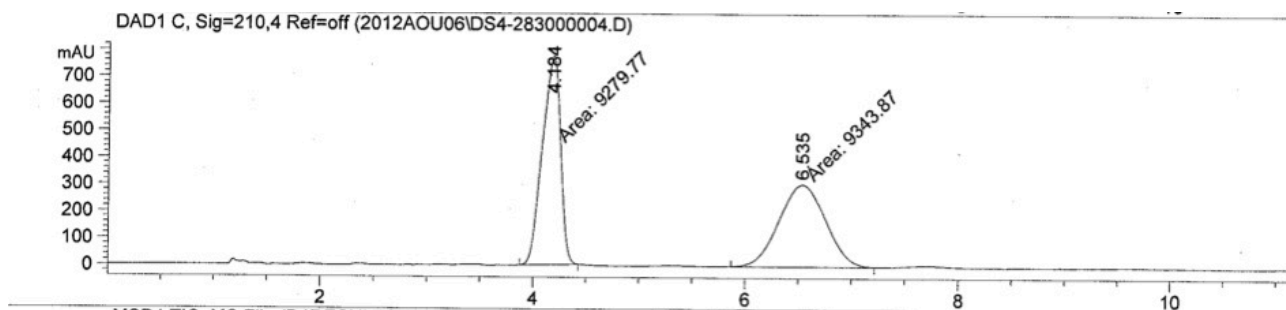
Preparation of enantioenriched **1sa**Preparation of enantioenriched **1sb**

Enantioenriched samples of both *trans*- and *cis*- *N*-(2-bromophenyl)-*N*-methyl-2-phenylcyclopropanecarboxamide were synthesized as shown above, starting from either *trans*- or *cis*- cinnamyl alcohol via an asymmetric Simmons-Smith cyclopropanation according to the literature procedure.<sup>15</sup> The enantioenriched *trans*- or *cis*- cyclopropanes were then oxidized to the corresponding carboxylic acid<sup>16</sup> and then converted to their amide analogues via route B. The enantiomeric excess for both substrates were determined by SFC analysis

<sup>15</sup> Charette, A.B.; Lebel, H. *Org. Synth.* **1999**, 76, 86.

<sup>16</sup> Charette, A. B.; Cote, B. *J. Am. Chem. Soc.* **1995**, 117, 12721.

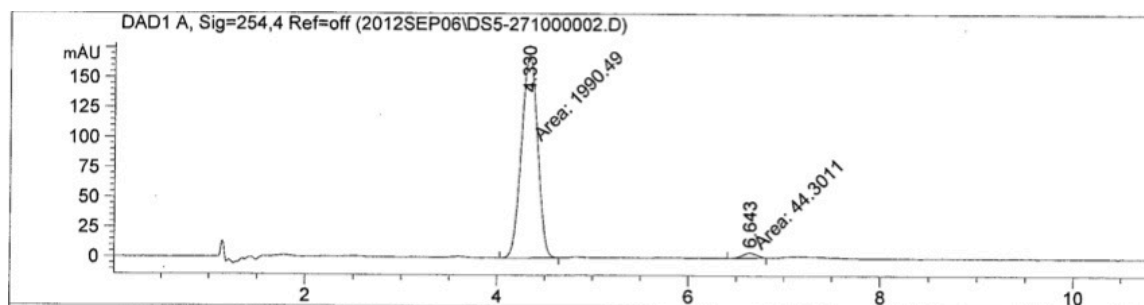
on a chiral stationary phase. Enantioenriched **1sb** could not be separated by SFC; % ee was determined using the *cis*-carboxylic acid. For **1sa**: (Ad-H 25 cm, 5% MeOH, 5mL/min, 35°C, 150 bar, 254 nm, tr (major) 4.3 min, tr (minor) 6.6 min). **SFC trace**:



Signal 2: DAD1 B, Sig=220,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.184	MM	0.1992	7392.40381	618.37195	50.1068
2	6.535	MM	0.5082	7360.90088	241.39609	49.8932

Totals : 1.47533e4 859.76804

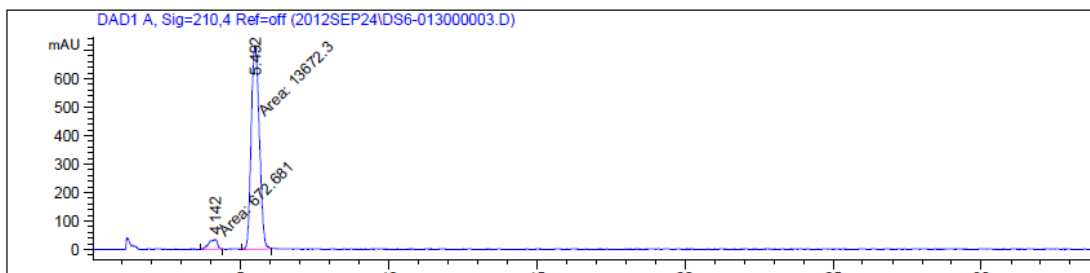


Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.330	MM	0.1959	1990.48682	169.32448	97.8228
2	6.643	MM	0.1718	44.30108	4.29743	2.1772

Totals : 2034.78790 173.62191

For **1sb**: (Ad-H 25 cm, 5% MeOH, 5mL/min, 35 °C, 150 bar, 254 nm, tr (major) 5.49 min, tr (minor) 3.98 min). **SFC trace**:

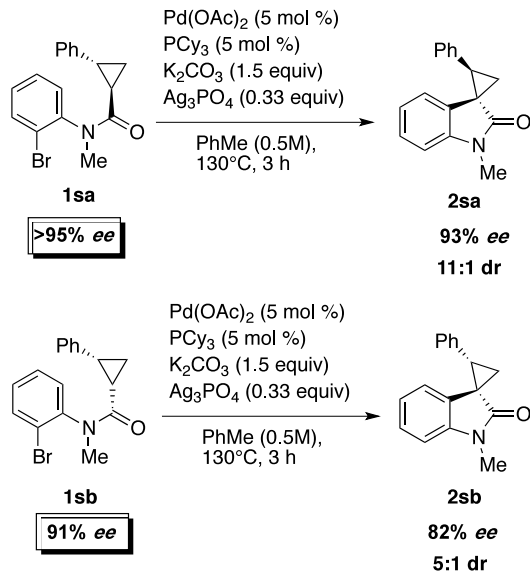


Signal 1: DAD1 A, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.142	MM	0.3360	672.68127	33.36401	4.6893
2	5.492	MM	0.3206	1.36723e4	710.66248	95.3107

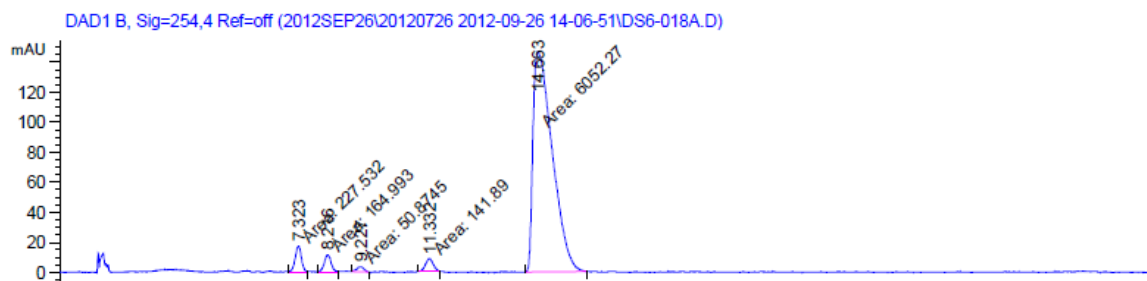
Totals : 1.43450e4 744.02648

Two sets of reactions were set up and carried out in parallel using general procedure C on a 0.4 mmol scale. Samples were taken out of the reactions after 3 hours and analyzed by  $^1\text{H}$  NMR and SFC. The results are tabulated below.



Diastereomeric ratio was determined by  $^1\text{H}$ NMR analysis of the crude mixture. Enantiomeric excess was determined by SFC analysis on chiral stationary phase.

For **2sa**: (Ad-H 25 cm, 5% MeOH, 5mL/min,  $35^\circ\text{C}$ , 150 bar, 254 nm, tr (major) 14.6, 11.3 min, tr (minor) 7.32, 8.22, 9.23 min), **SFC traces**:

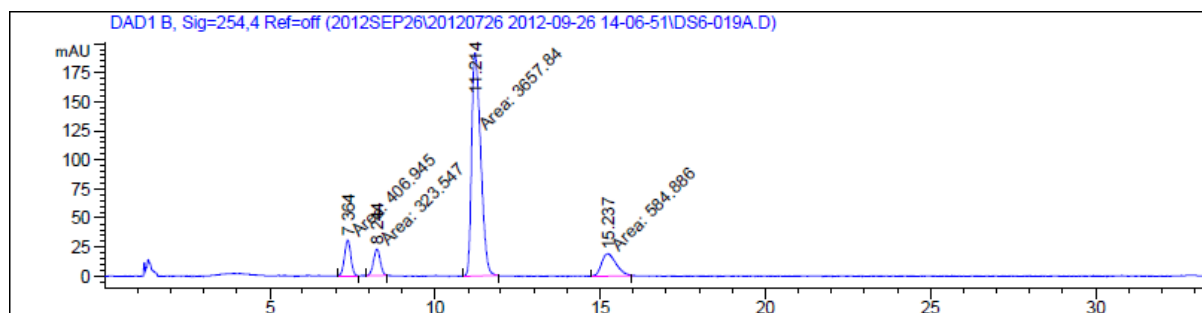


Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.323	MM	0.2207	227.53218	17.18419	3.4280
2	8.216	MM	0.2407	164.99333	11.42589	2.4858
3	9.227	MM	0.2461	50.87452	3.44530	0.7665
4	11.332	MM	0.2778	141.88979	8.51239	2.1377
5	14.663	MM	0.6853	6052.26660	147.18364	91.1821

Totals : 6637.55642 187.75142

For **2sb**: (Ad-H 25 cm, 5% MeOH, 5mL/min, 35°C, 150 bar, 254 nm, tr (major) 11.2, 15.2 min, tr (minor) 7.36, 8.24 min), **SFC traces**:

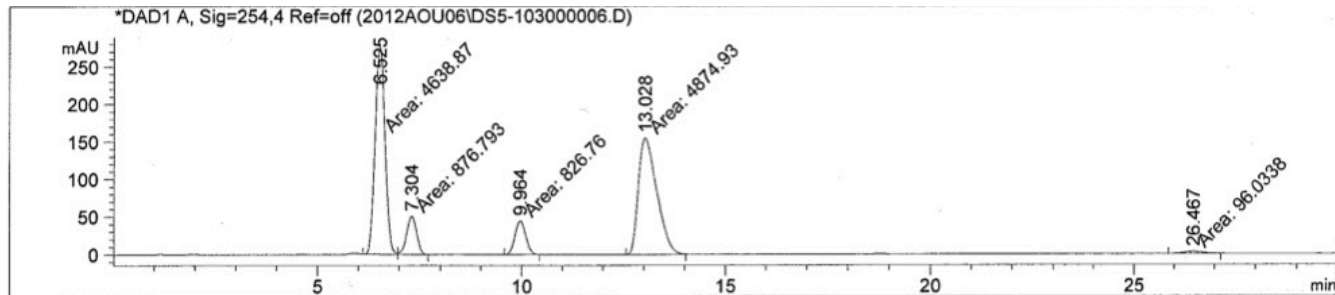


Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.364	MM	0.2212	406.94470	30.65820	8.1827
2	8.244	MM	0.2373	323.54654	22.72843	6.5058
3	11.214	MM	0.3180	3657.83862	191.71494	73.5508
4	15.237	MM	0.5116	584.88580	19.05581	11.7607

Totals : 4973.21567 264.15737

## Racemic SFC trace for 2sa+2sb:

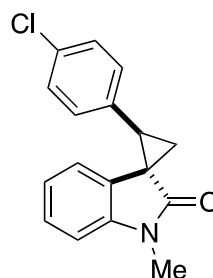
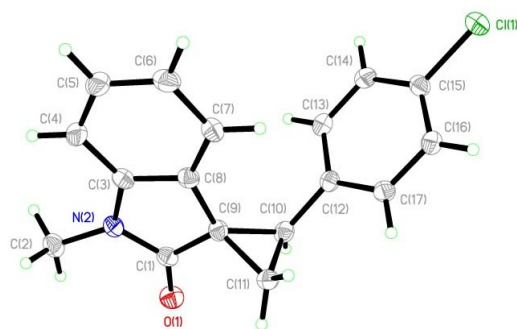


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.525	MF	0.2808	4638.87158	275.32867	41.0034
2	7.304	FM	0.2871	876.79340	50.89171	7.7501
3	9.964	MM	0.3096	826.76001	44.50236	7.3078
4	13.028	MM	0.5237	4874.93115	155.15771	43.0899
5	26.467	MM	0.5554	96.03384	2.88179	0.8489

Totals : 1.13134e4 528.76225

## X-ray Data for Compounds

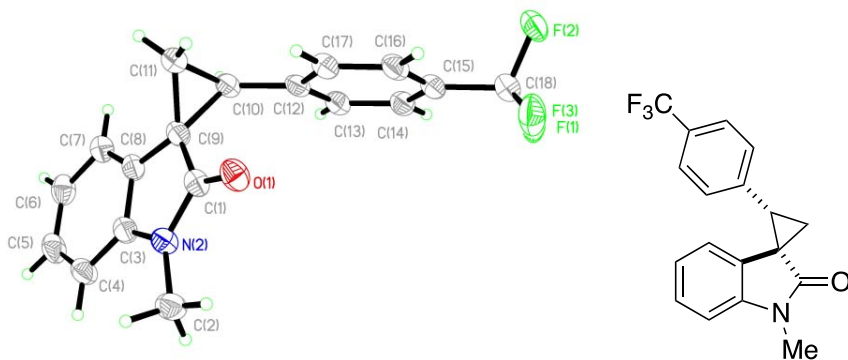
For 2o major:



**Table 1.** Crystal data and structure refinement for C<sub>17</sub> H<sub>14</sub> Cl N O.

Identification code	cha217
Empirical formula	C <sub>17</sub> H <sub>14</sub> Cl N O
Formula weight	283.74
Temperature	150K
Wavelength	1.54178 Å
Crystal system	Orthorhombic
Space group	Pna21
Unit cell dimensions	$a = 12.5875(8) \text{ Å}$ $\alpha = 90^\circ$ $b = 17.8684(12) \text{ Å}$ $\beta = 90^\circ$ $c = 6.0173(4) \text{ Å}$ $\gamma = 90^\circ$
Volume	$1353.40(15) \text{ Å}^3$
Z	4
Density (calculated)	$1.393 \text{ g/cm}^3$
Absorption coefficient	$2.440 \text{ mm}^{-1}$
F(000)	592
Crystal size	0.25 x 0.15 x 0.15 mm

Theta range for data collection	4.30 to 69.70°
Index ranges	$-15 \leq h \leq 15$ , $-21 \leq k \leq 21$ , $-5 \leq l \leq 7$
Reflections collected	39869
Independent reflections	1968 [ $R_{\text{int}} = 0.039$ ]
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.6935 and 0.5640
Refinement method	Full-matrix least-squares on $F^2$
Data / restraints / parameters	1968 / 1 / 183
Goodness-of-fit on $F^2$	1.080
Final R indices [ $I > 2\sigma(I)$ ]	$R_1 = 0.0299$ , $wR_2 = 0.0791$
R indices (all data)	$R_1 = 0.0299$ , $wR_2 = 0.0791$
Absolute structure parameter	0.127(18)
Largest diff. peak and hole	0.254 and $-0.251 \text{ e}/\text{\AA}^3$

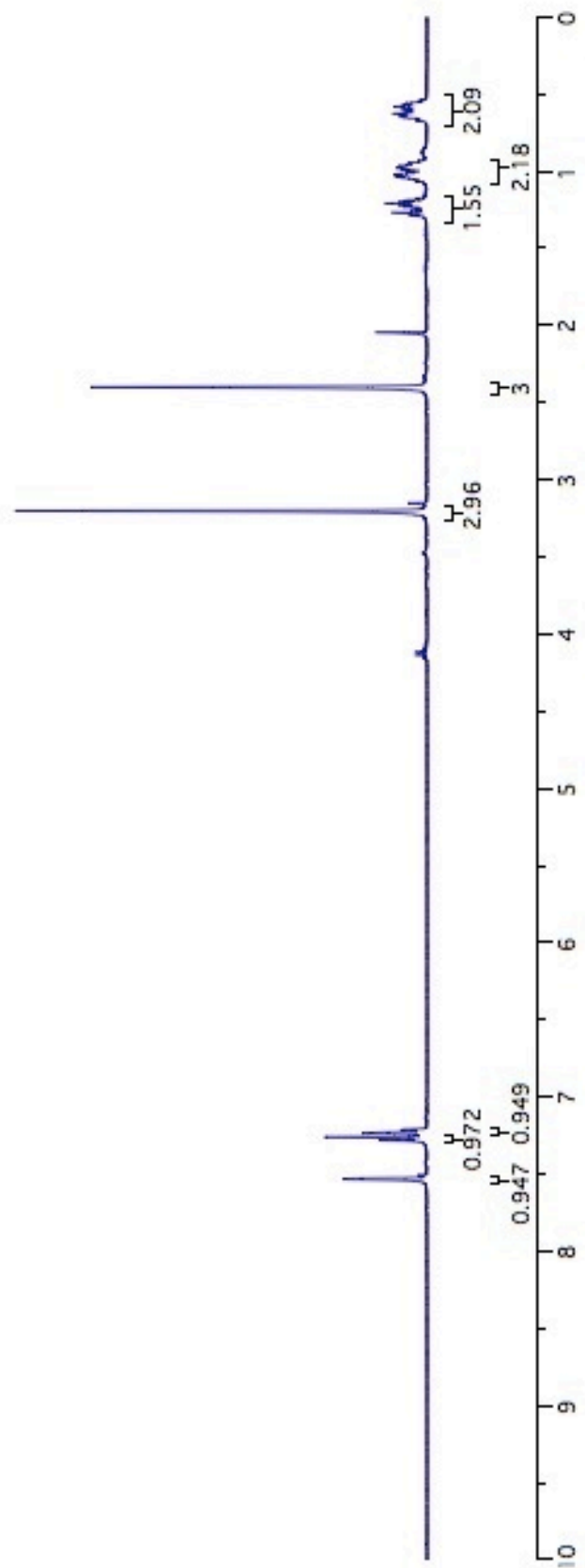
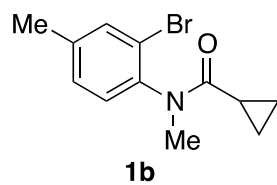
**For 2p minor:****Table 1.** Crystal data and structure refinement for C<sub>18</sub> H<sub>14</sub> F<sub>3</sub> N O.

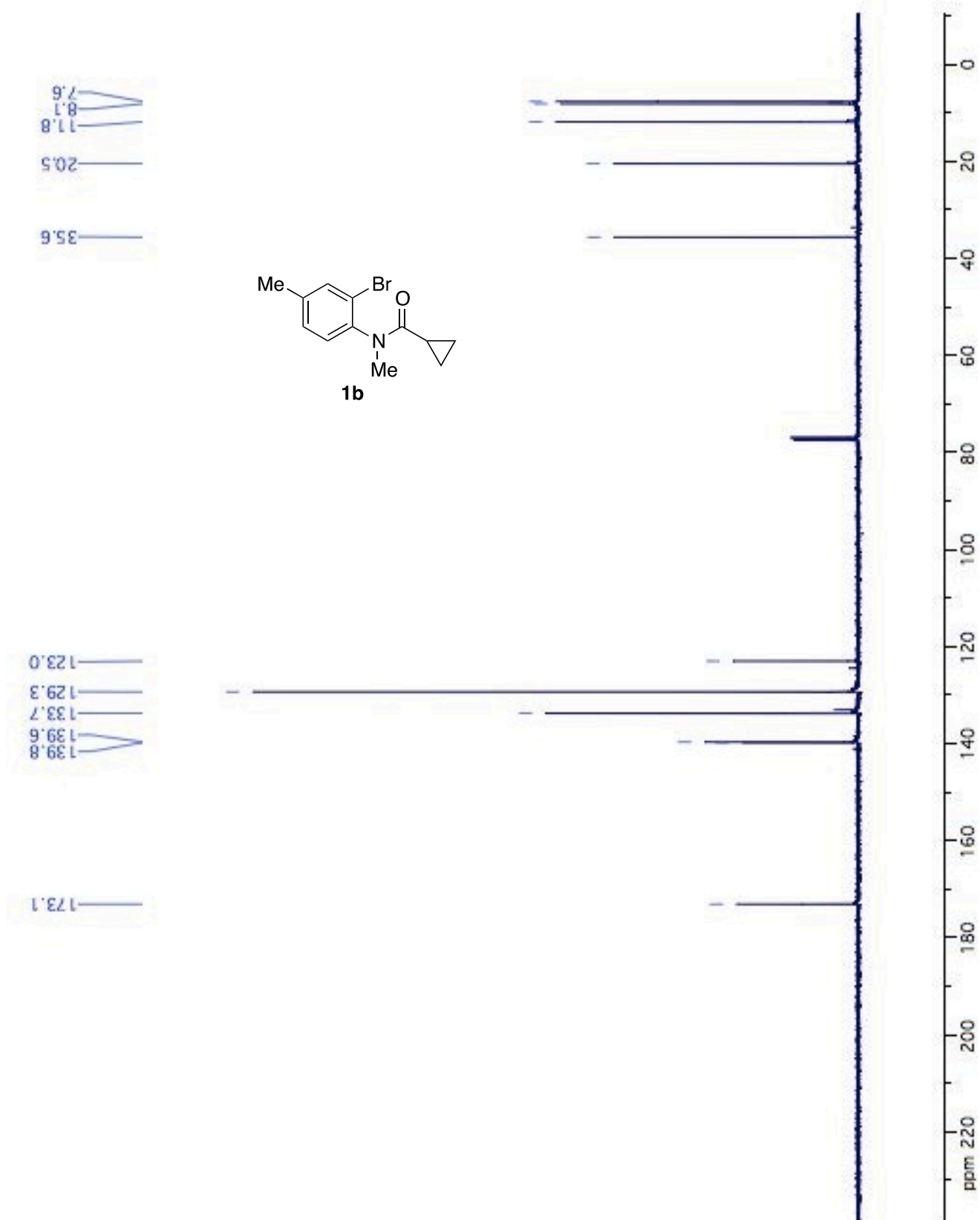
Identification code	cha227
Empirical formula	C <sub>18</sub> H <sub>14</sub> F <sub>3</sub> N O
Formula weight	317.30
Temperature	100K
Wavelength	1.54178 Å

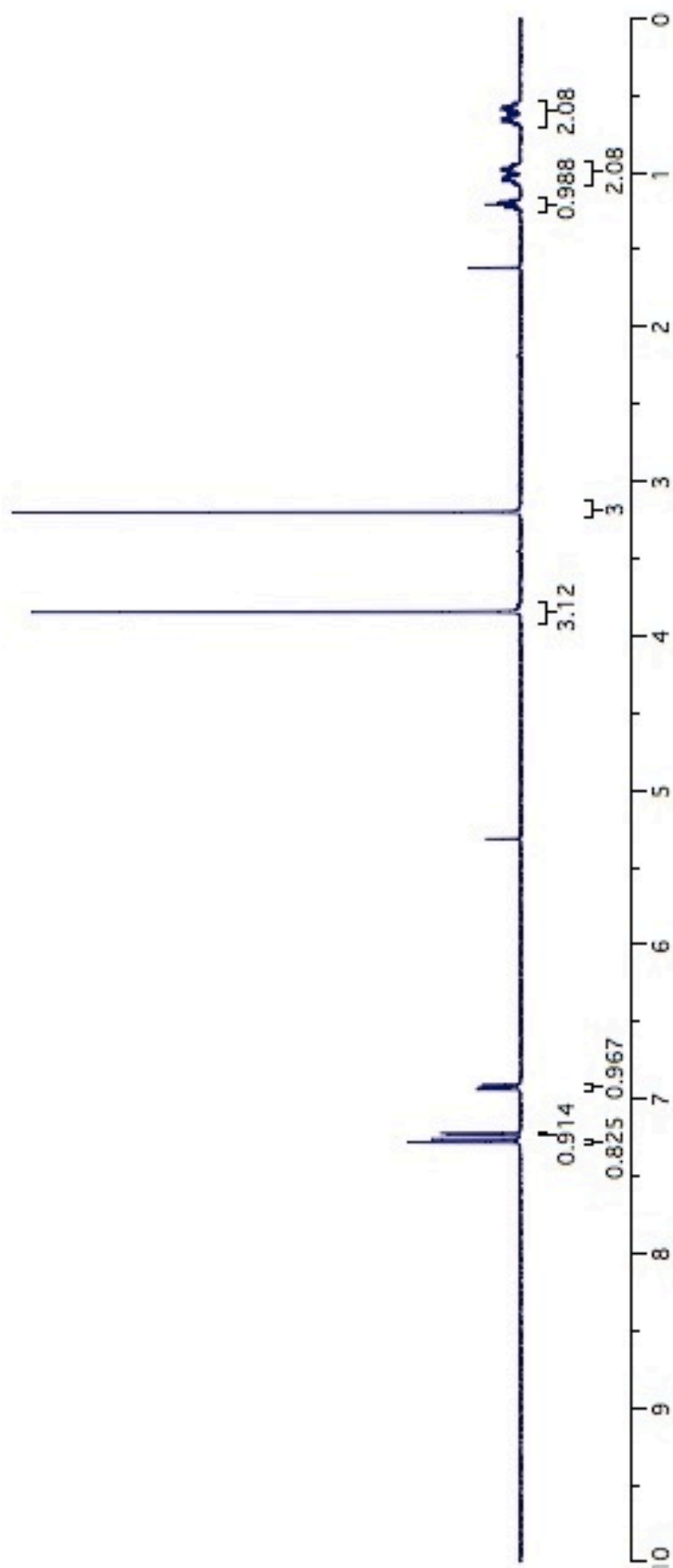
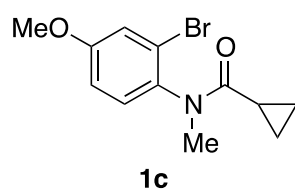
Crystal system	Monoclinic
Space group	P21/n
Unit cell dimensions	$a = 15.2477(7) \text{ \AA}$ $\alpha = 90^\circ$ $b = 5.8321(3) \text{ \AA}$ $\beta = 90.669(3)^\circ$ $c = 16.7963(9) \text{ \AA}$ $\gamma = 90^\circ$
Volume	$1493.53(13) \text{ \AA}^3$
Z	4
Density (calculated)	$1.411 \text{ g/cm}^3$
Absorption coefficient	$0.964 \text{ mm}^{-1}$
F(000)	656
Crystal size	$0.22 \times 0.04 \times 0.02 \text{ mm}$
Theta range for data collection	$3.89 \text{ to } 70.51^\circ$
Index ranges	$-18 \leq h \leq 18, -6 \leq k \leq 7, -20 \leq l \leq 20$
Reflections collected	18994
Independent reflections	2813 [ $R_{\text{int}} = 0.042$ ]
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9809 and 0.7716
Refinement method	Full-matrix least-squares on $F^2$
Data / restraints / parameters	2813 / 84 / 219
Goodness-of-fit on $F^2$	1.112
Final R indices [ $I > 2\sigma(I)$ ]	$R_1 = 0.0453, wR_2 = 0.1269$
R indices (all data)	$R_1 = 0.0515, wR_2 = 0.1323$
Largest diff. peak and hole	$0.358 \text{ and } -0.253 \text{ e/\AA}^3$

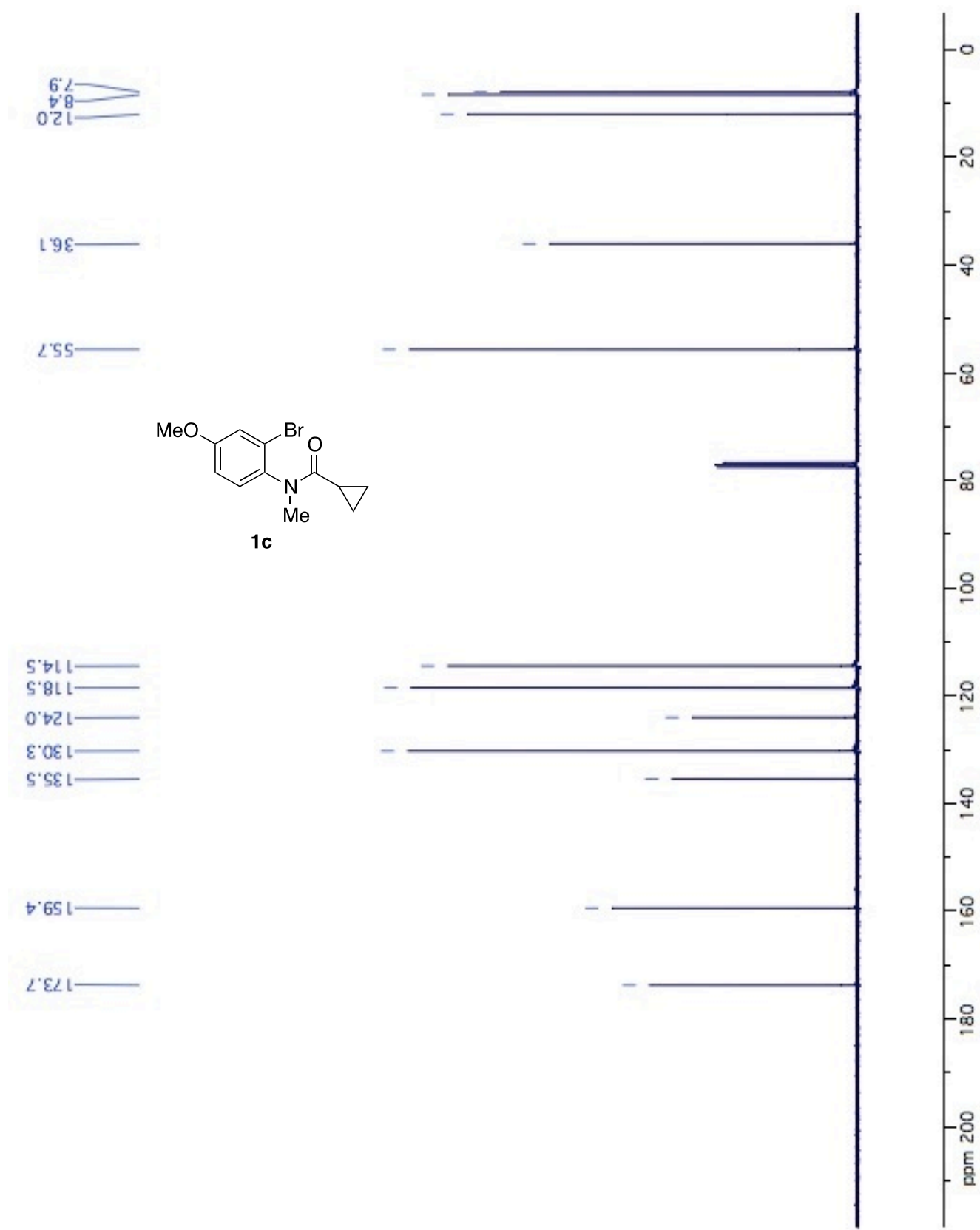


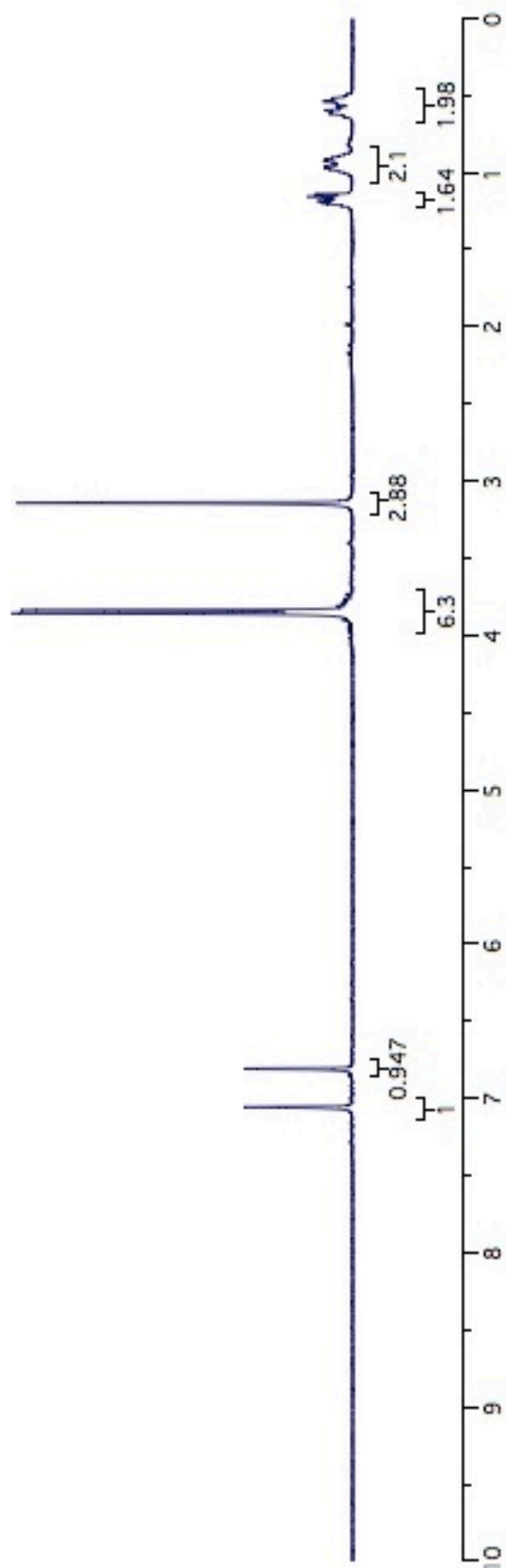
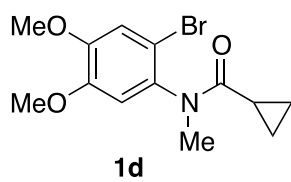
## **$^1\text{H}$ , $^{13}\text{C}$ , and $^{19}\text{F}$ Spectra of Novel Compounds**

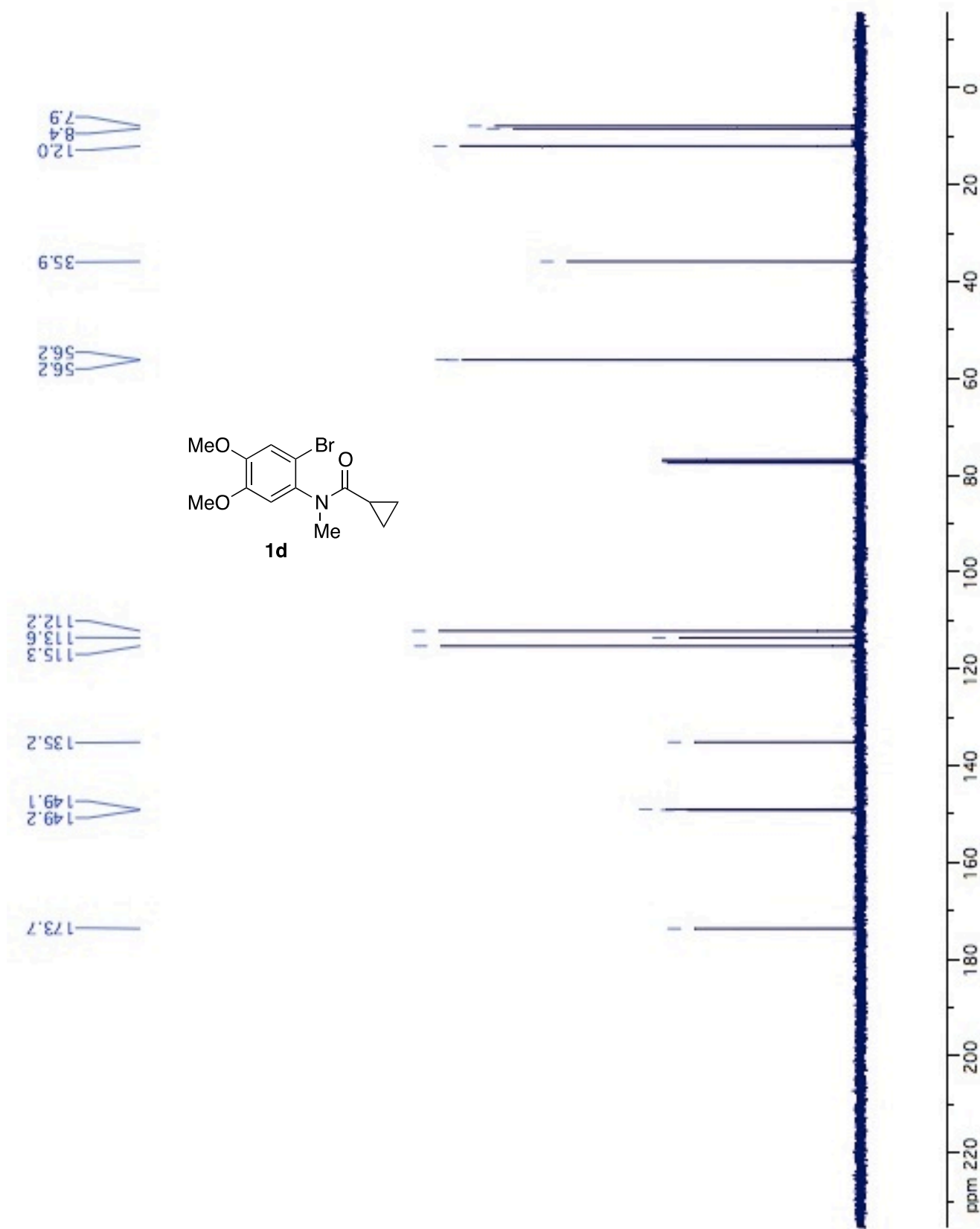


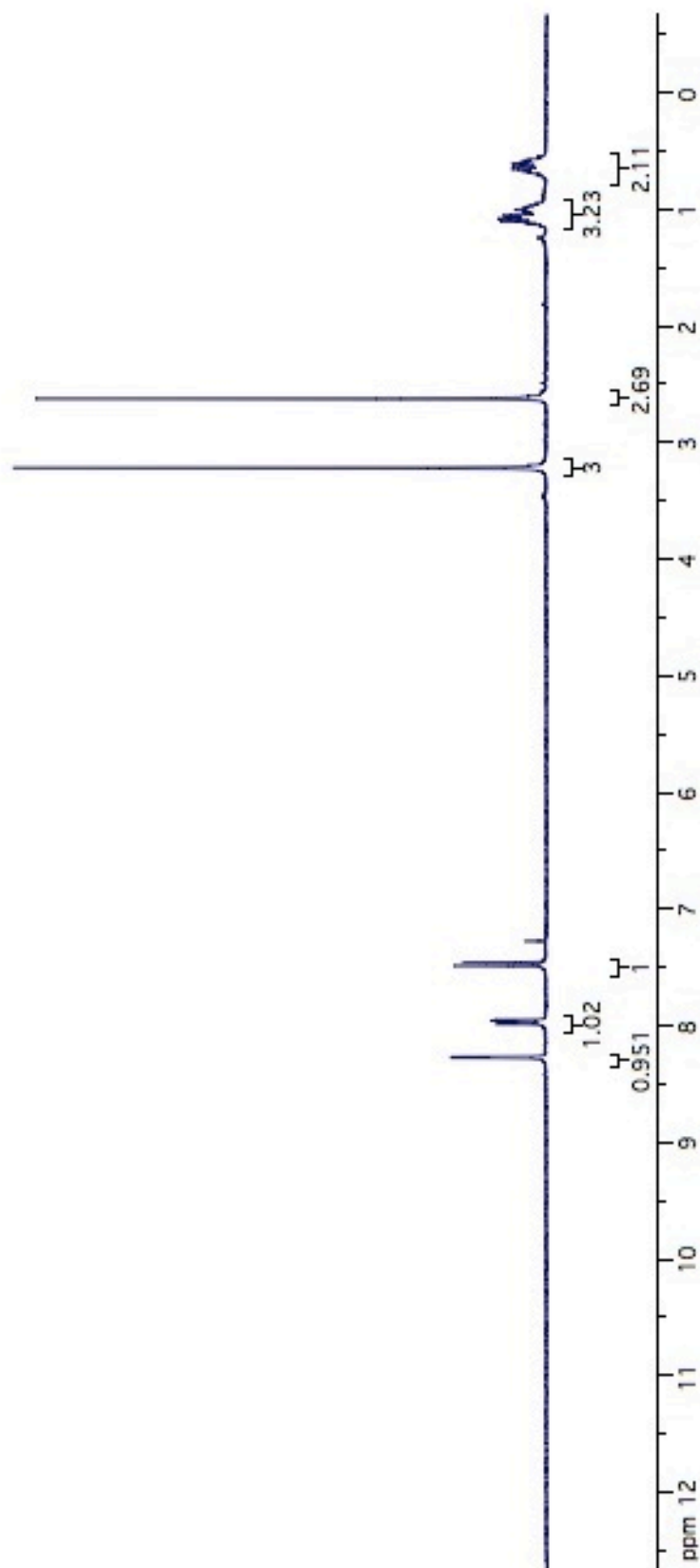
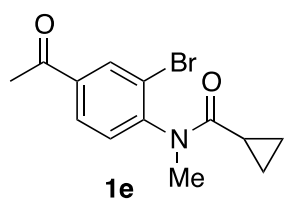




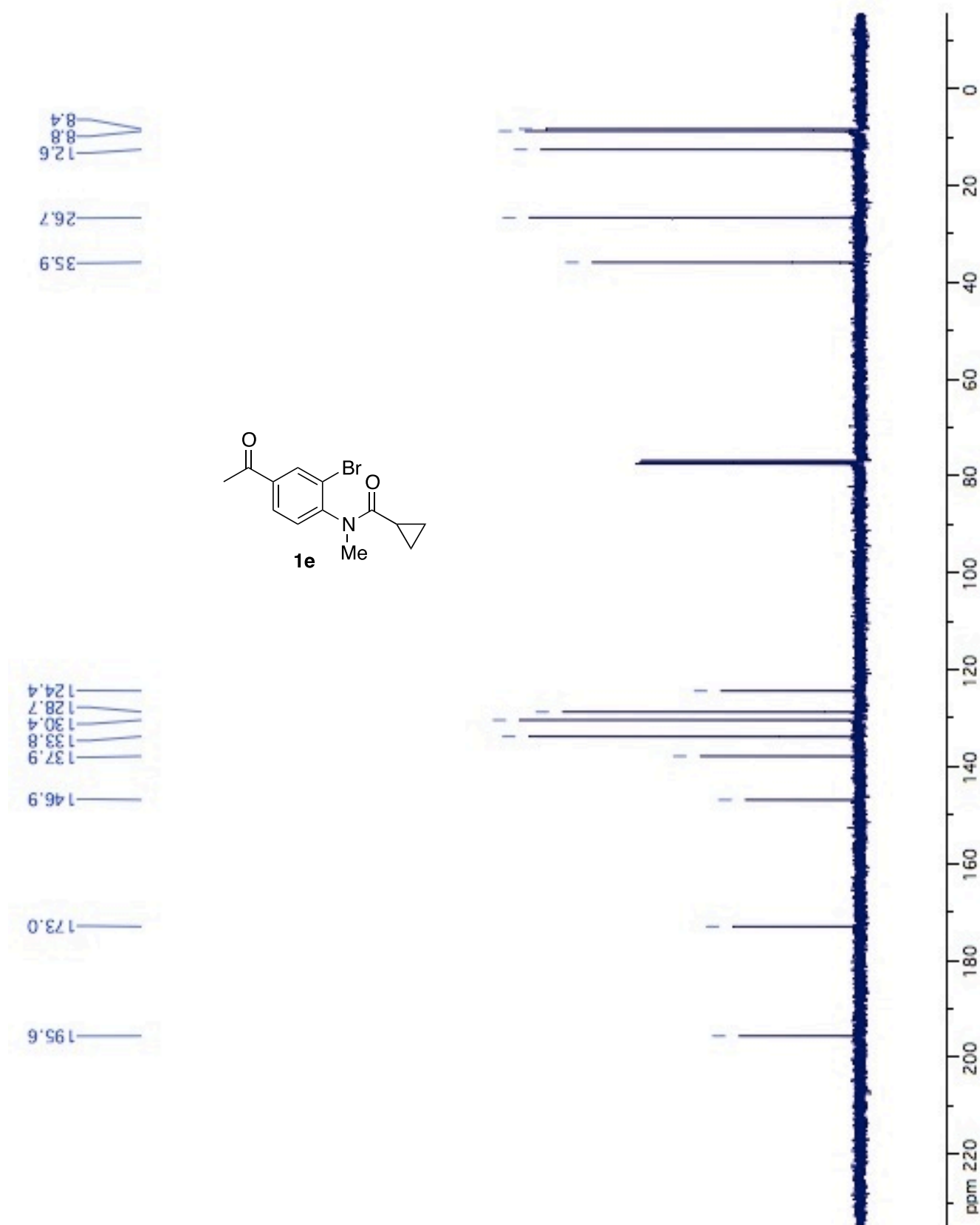


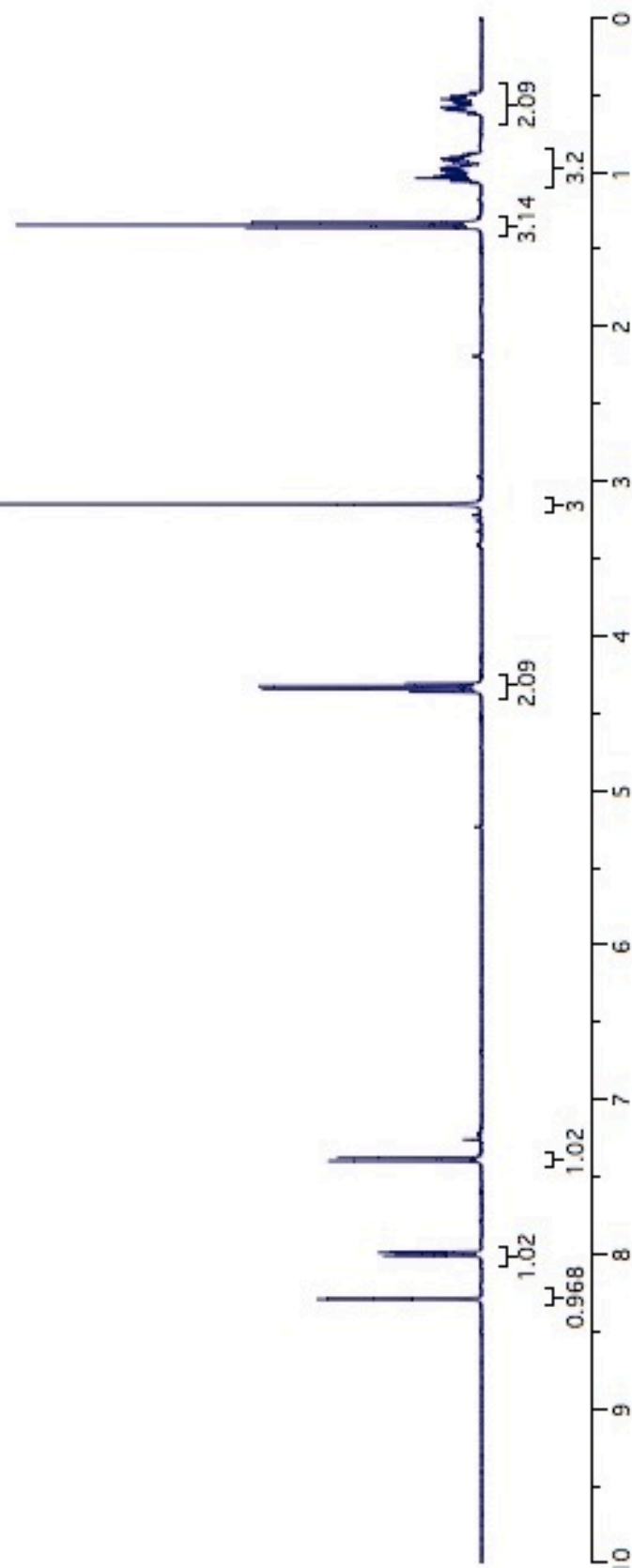
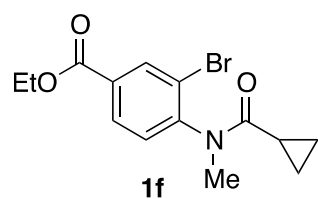


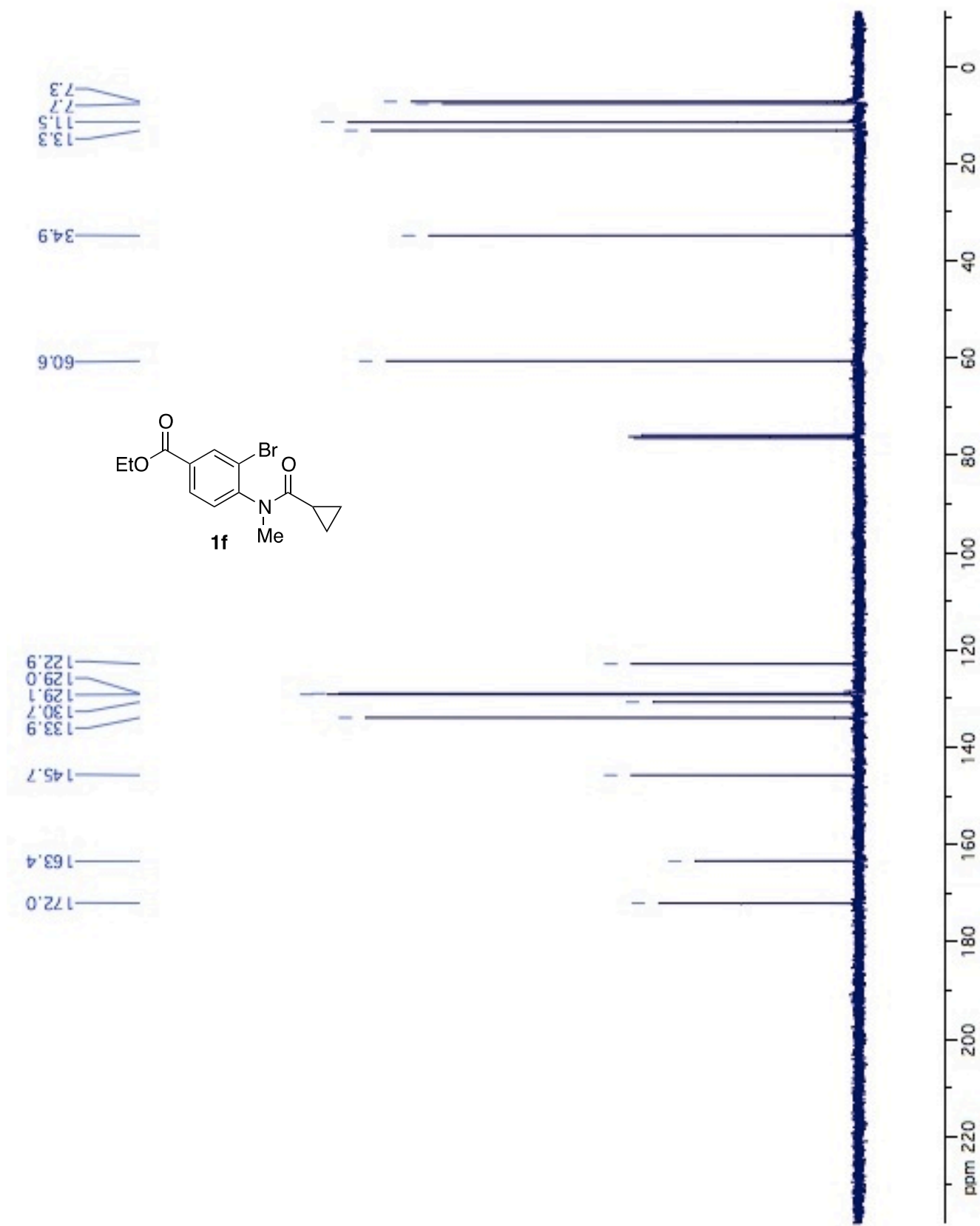


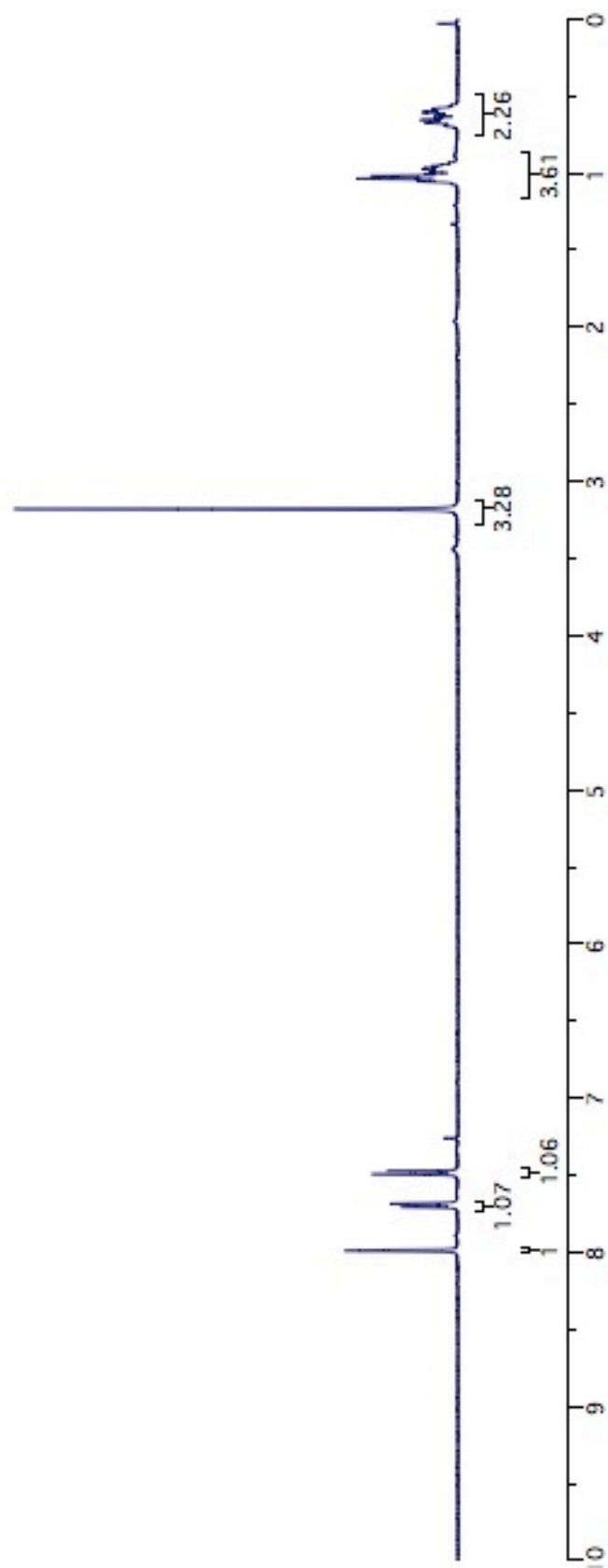
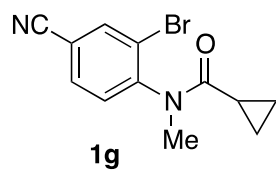


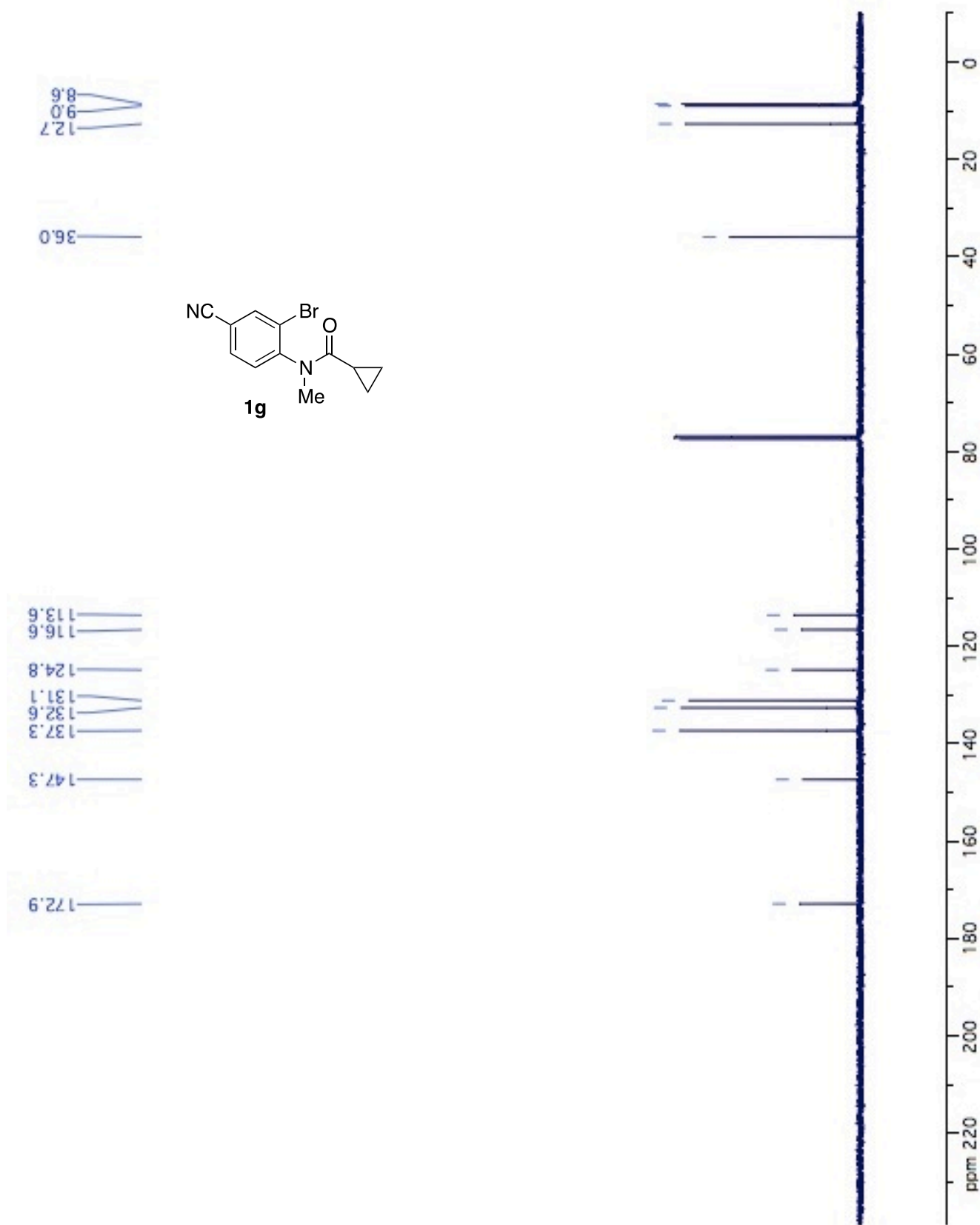


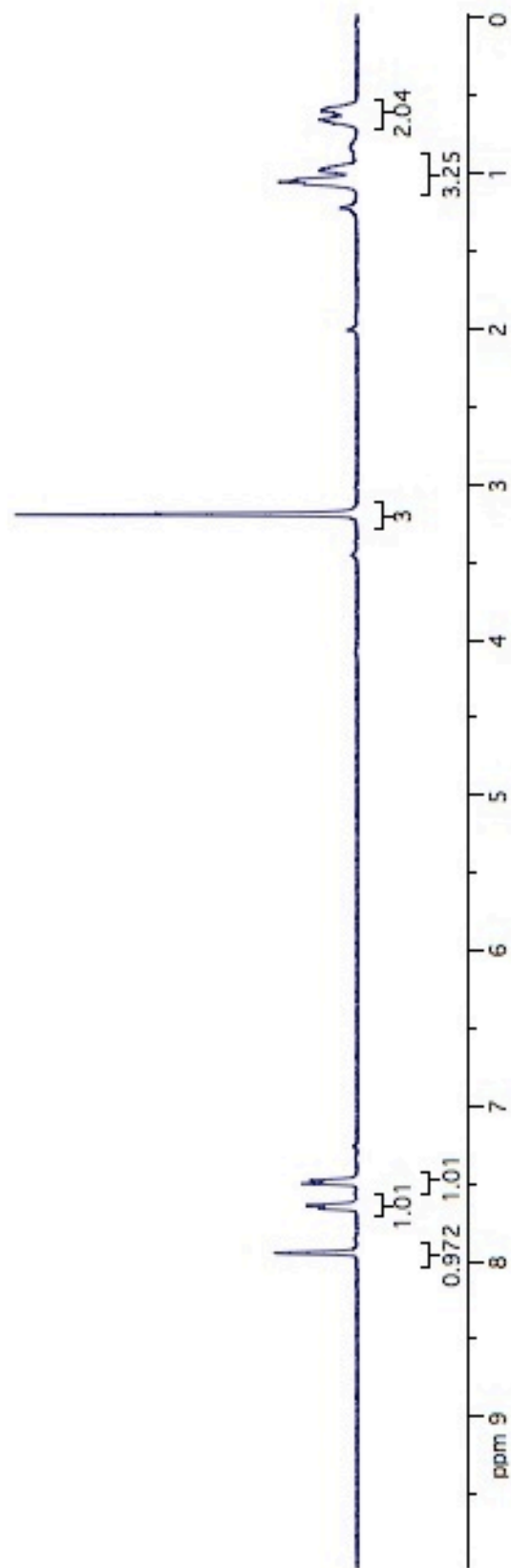
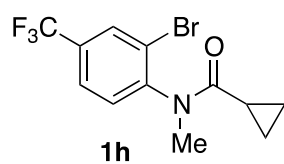


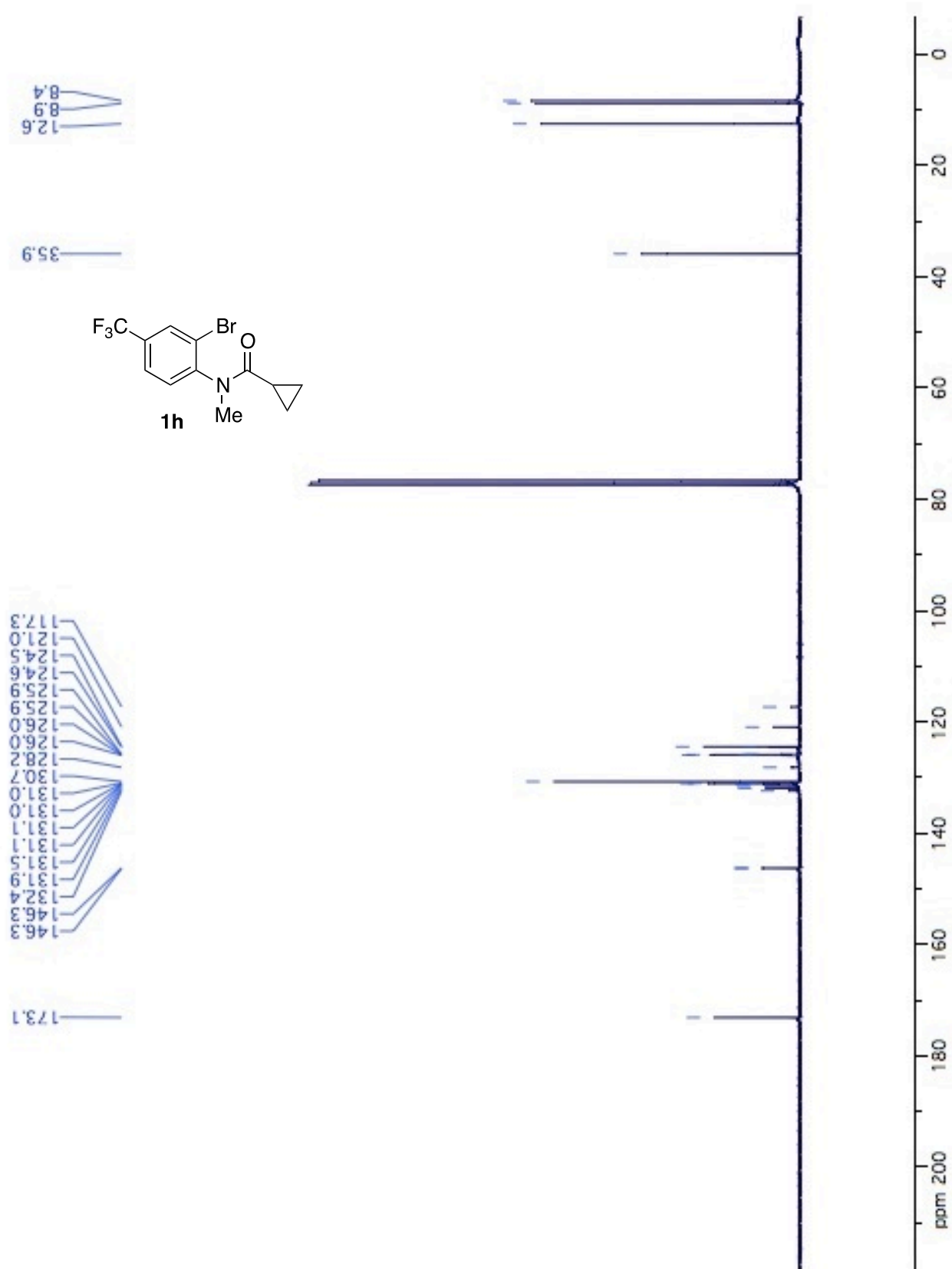


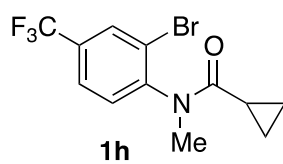










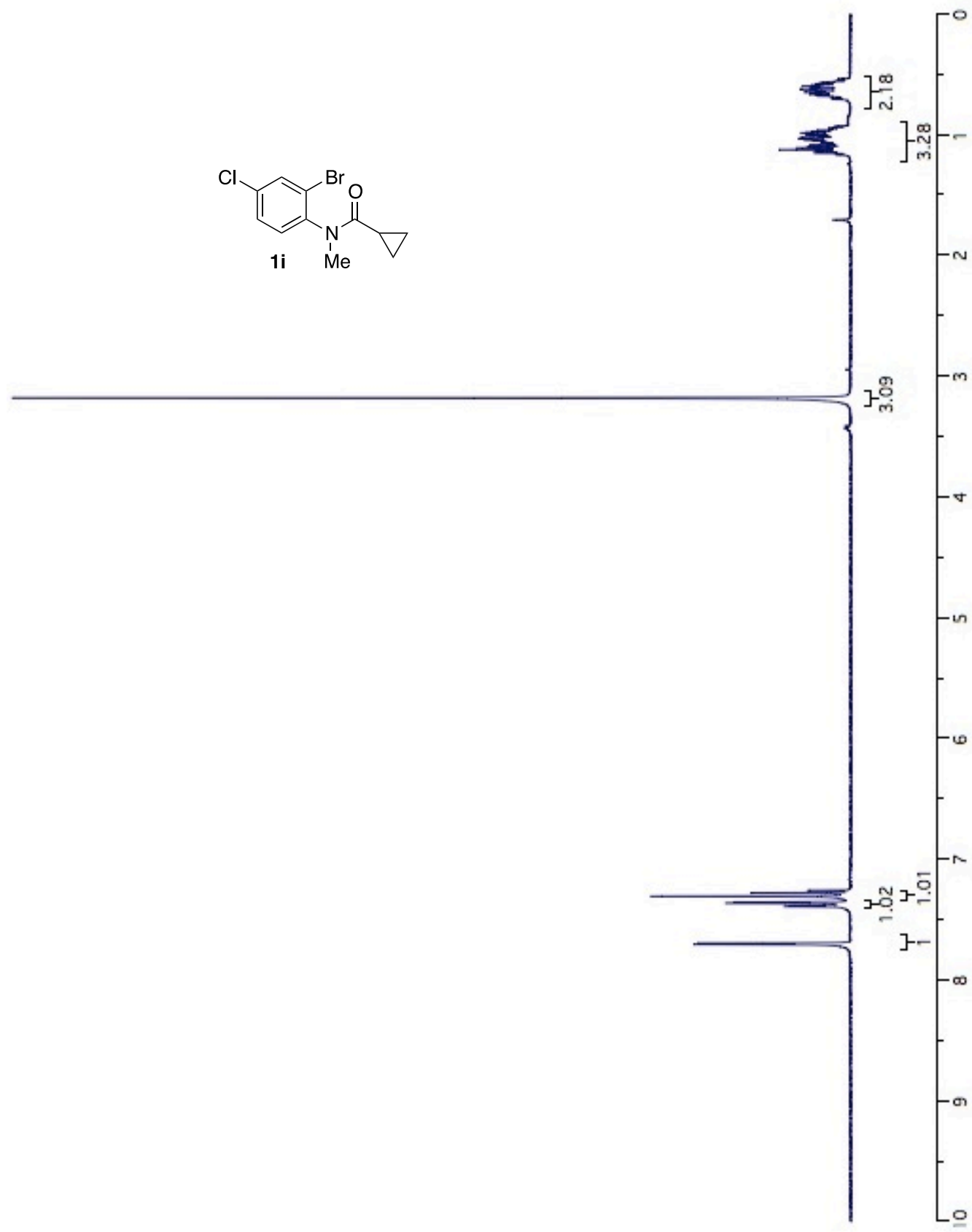


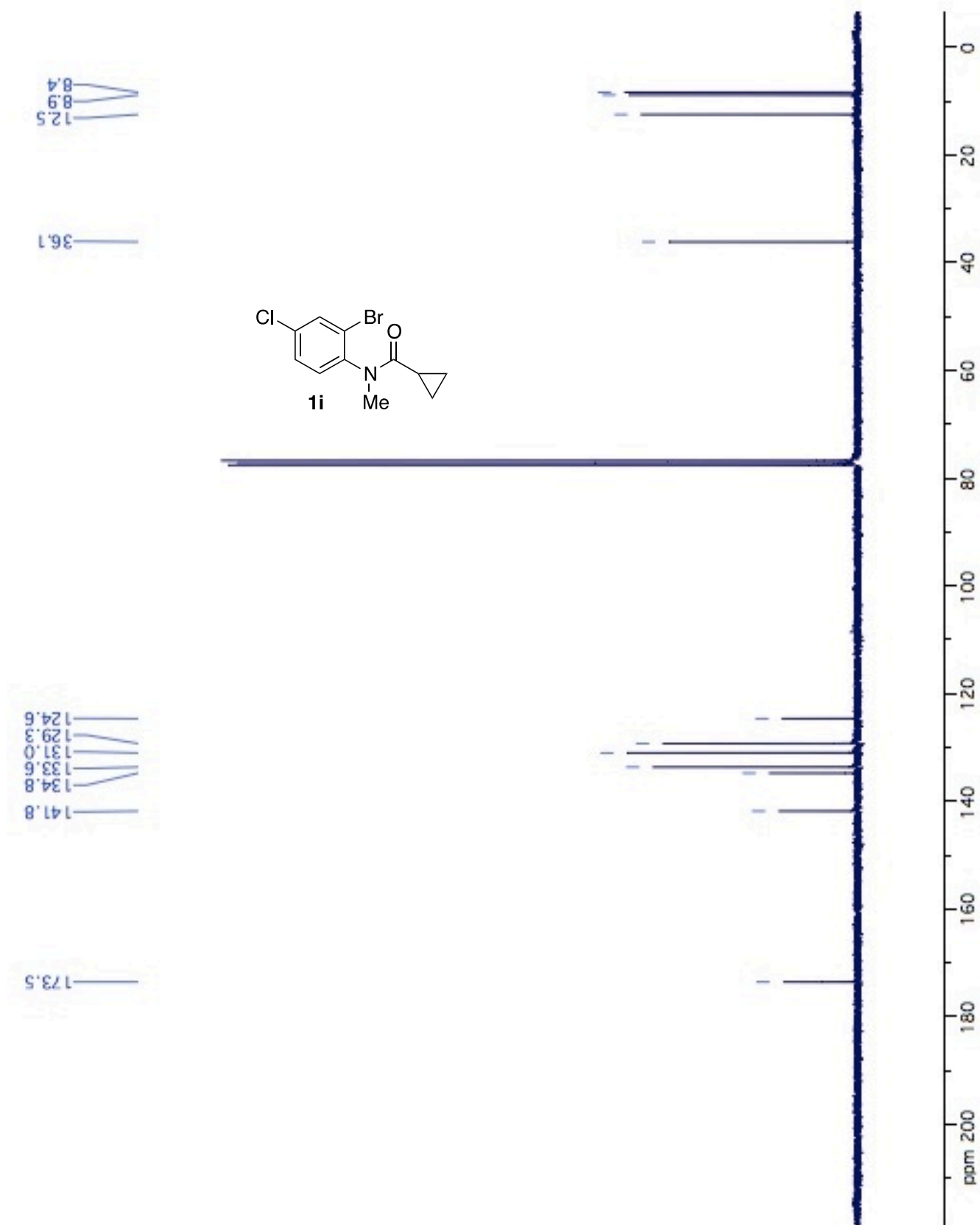
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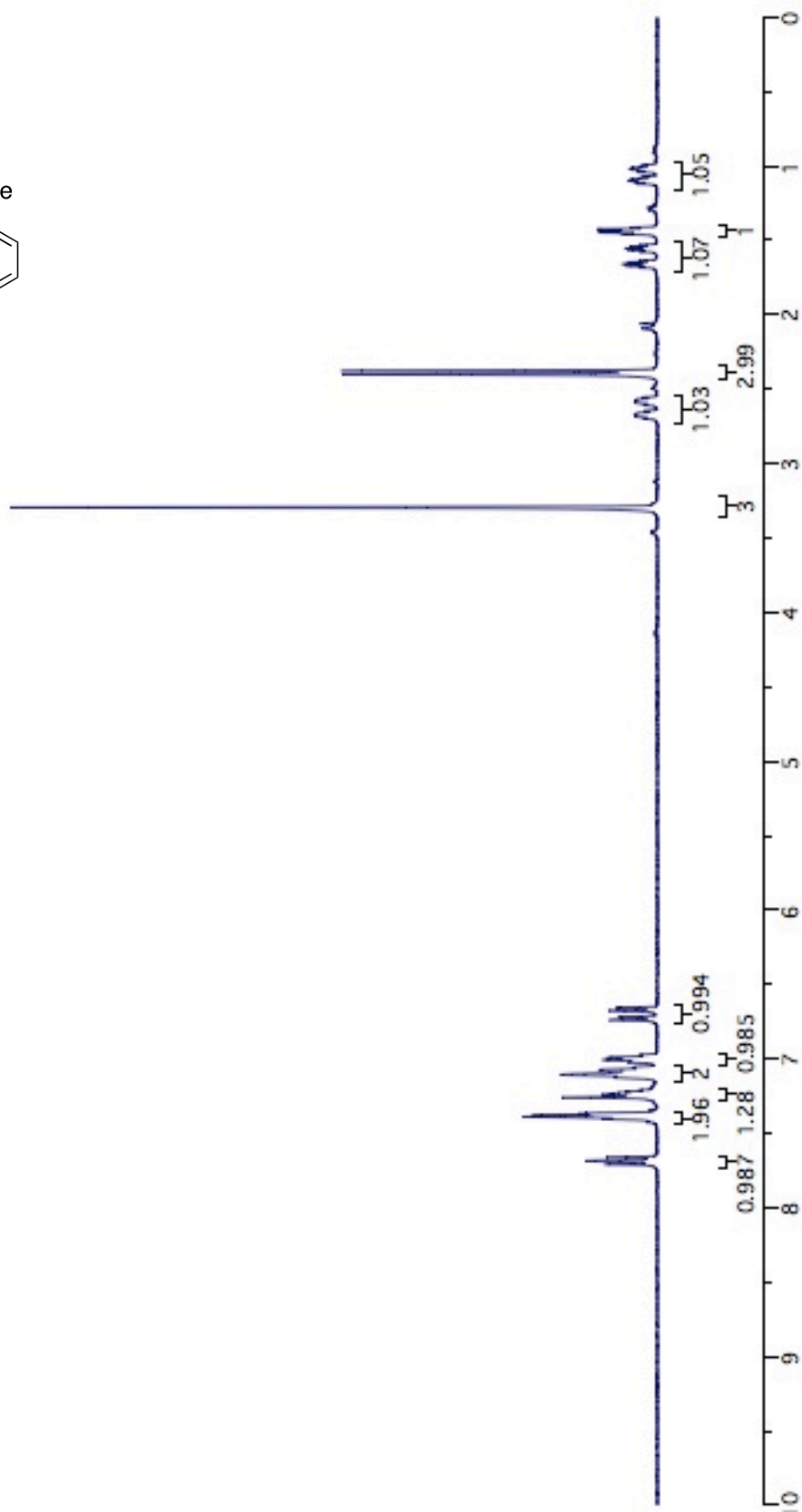
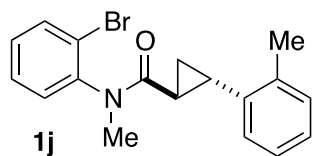
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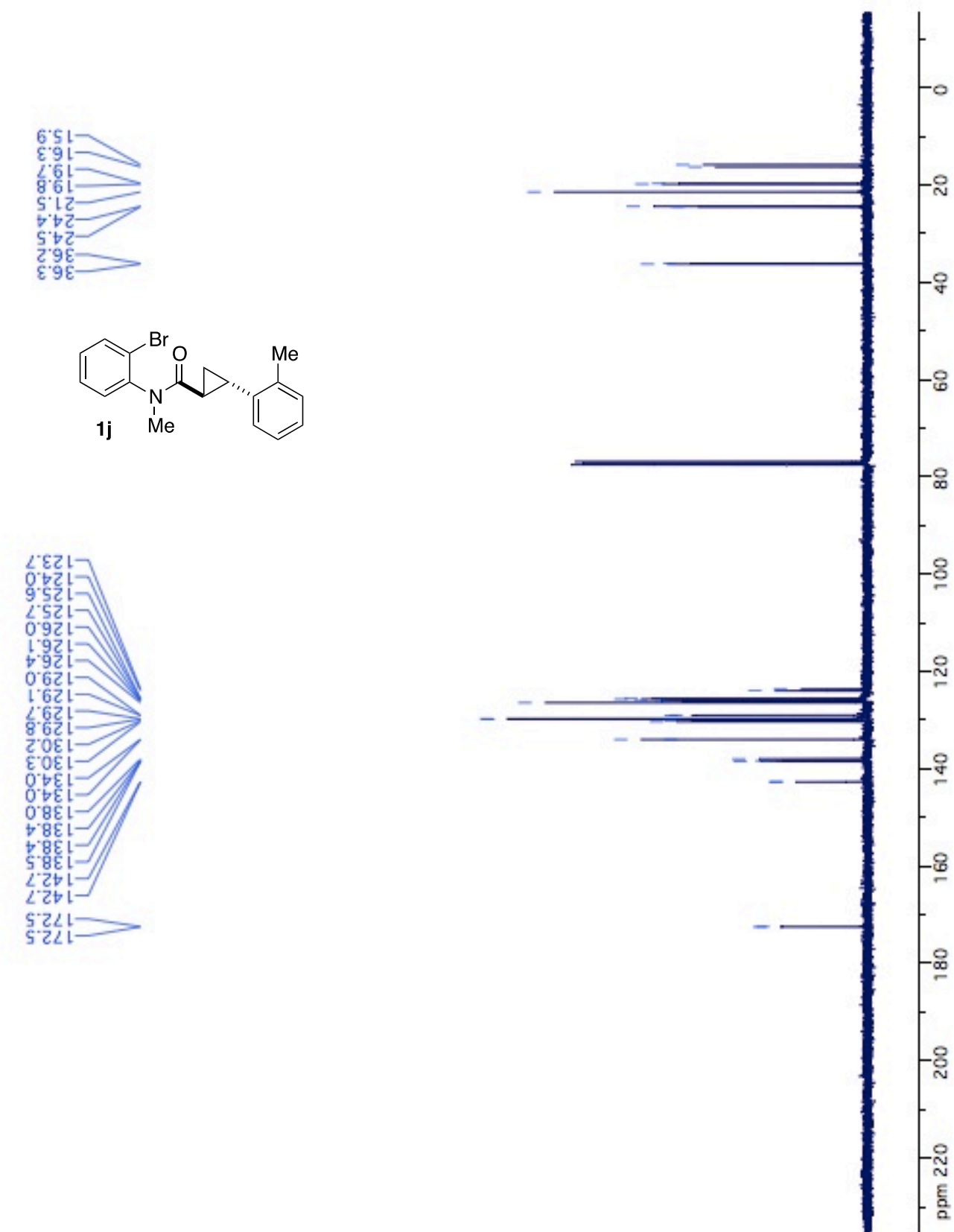
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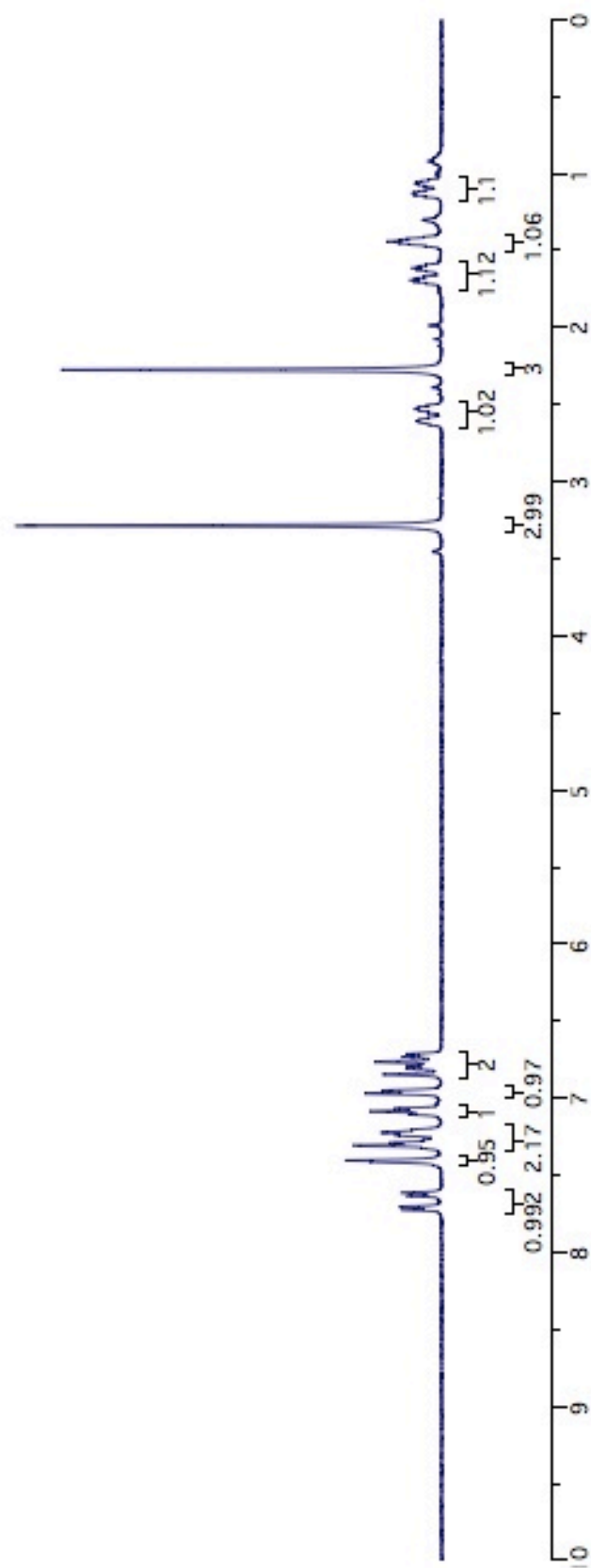
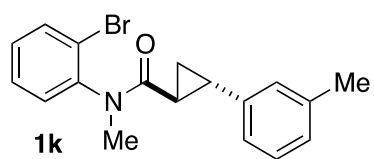


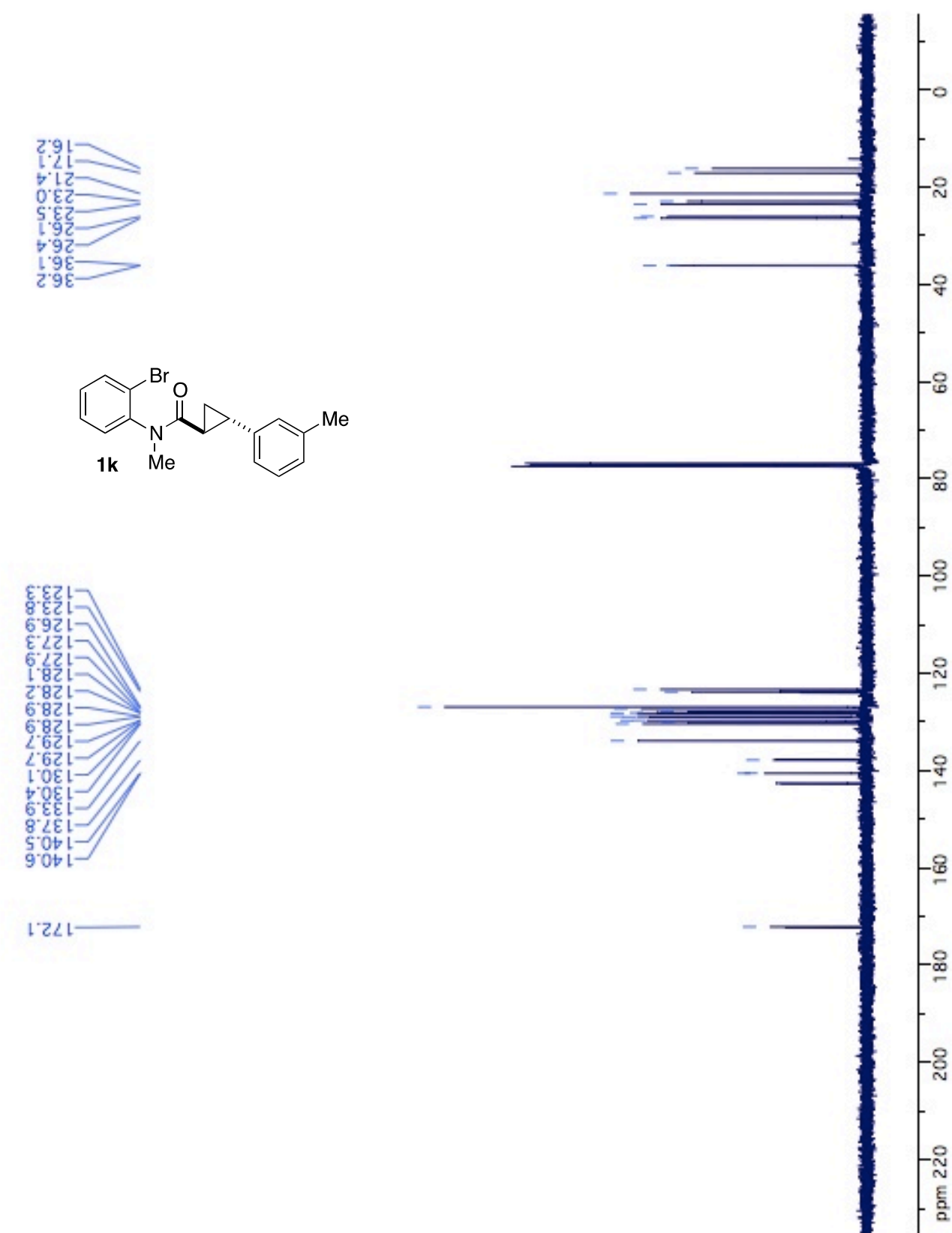


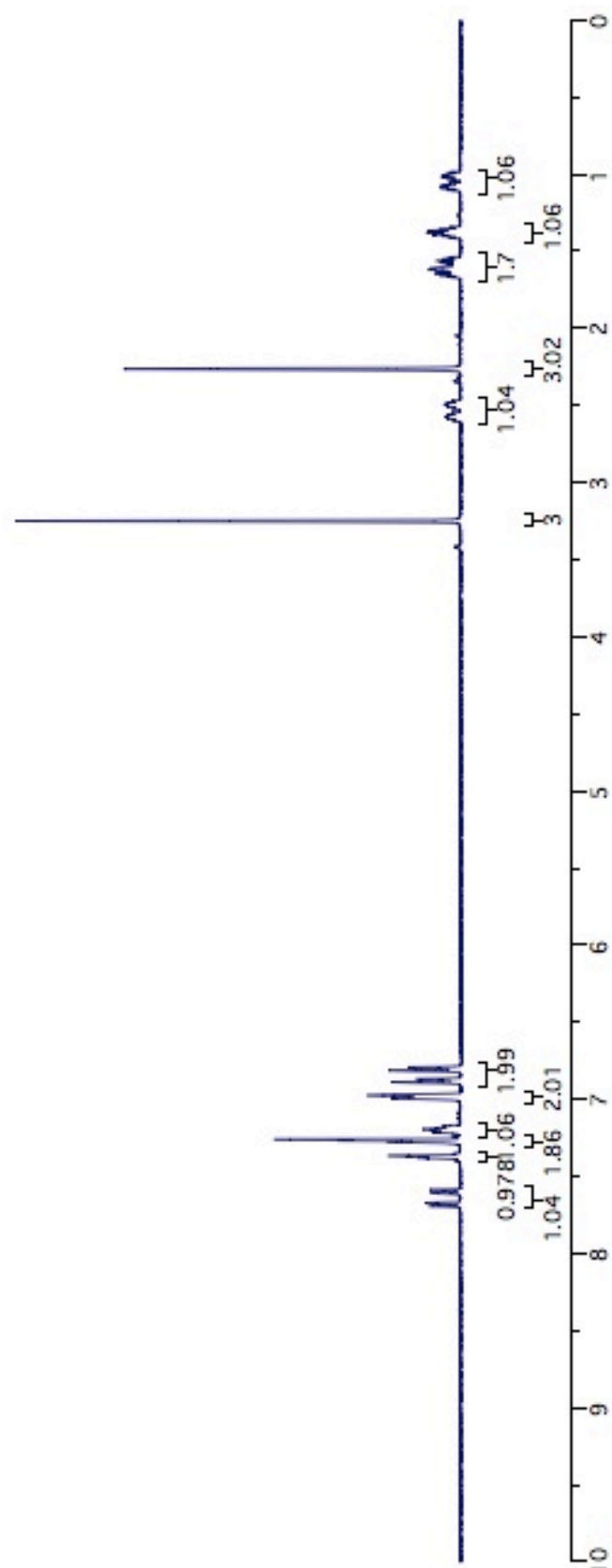
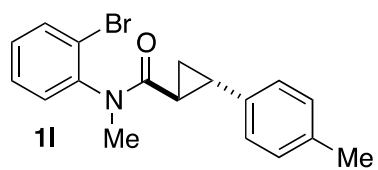


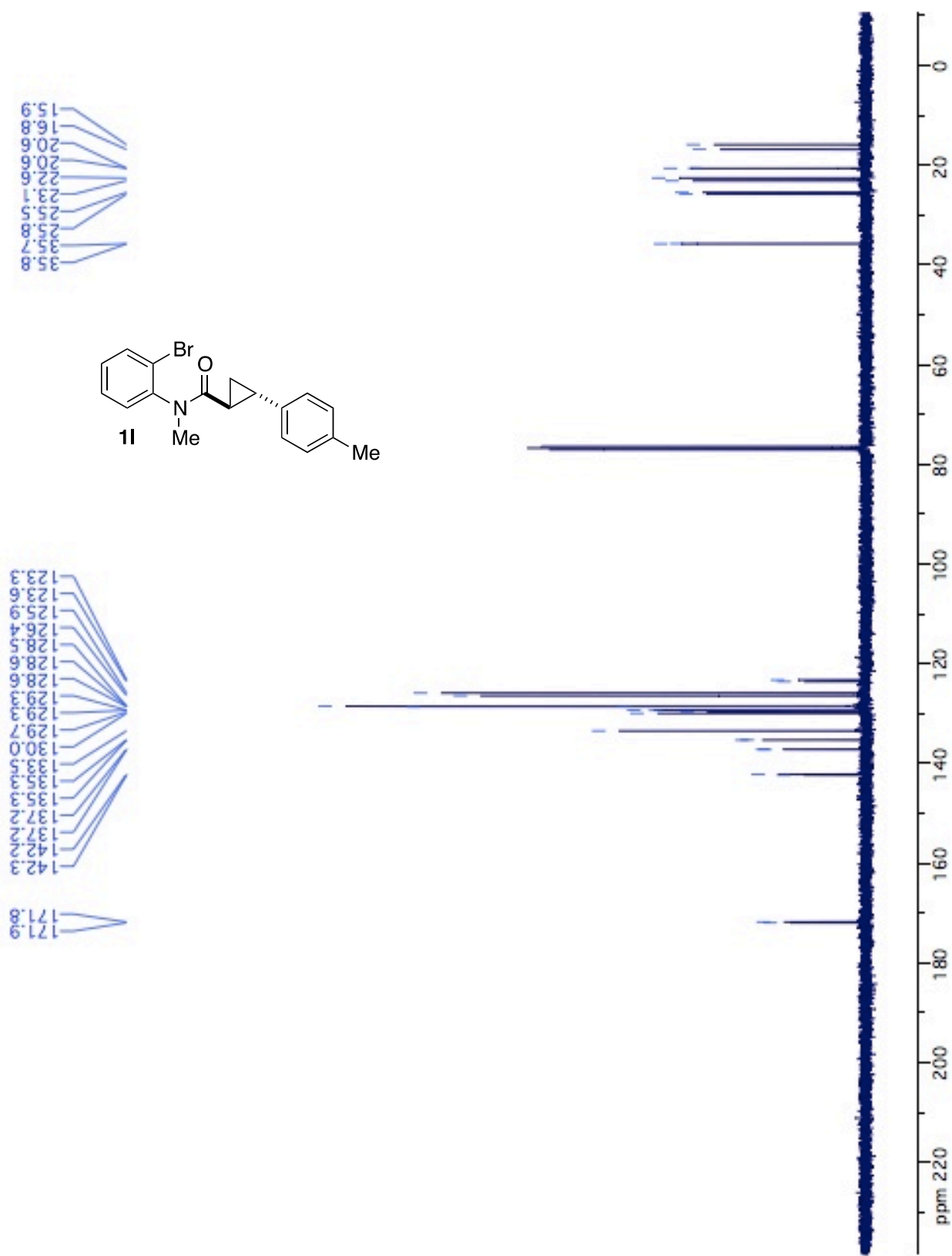




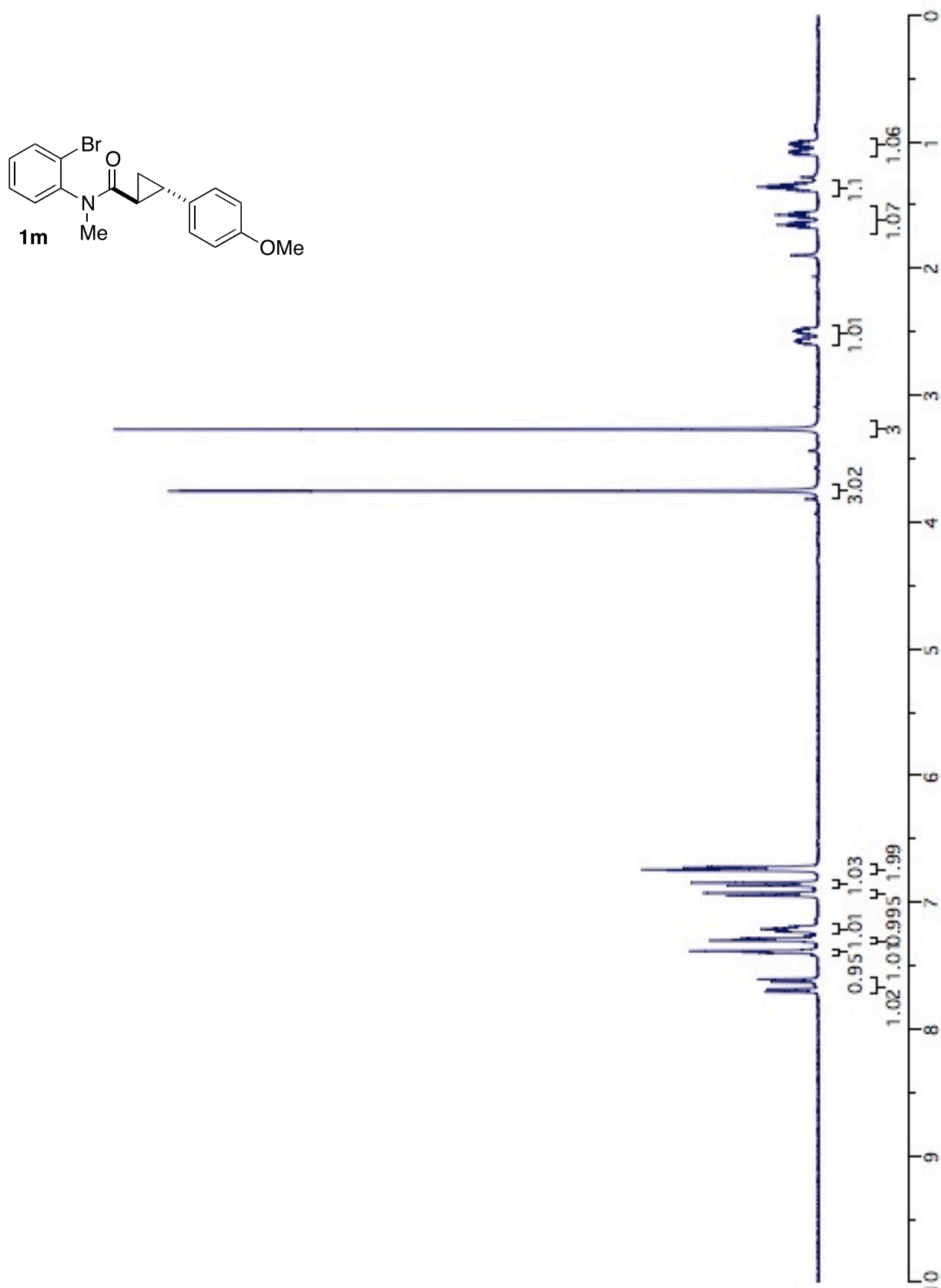


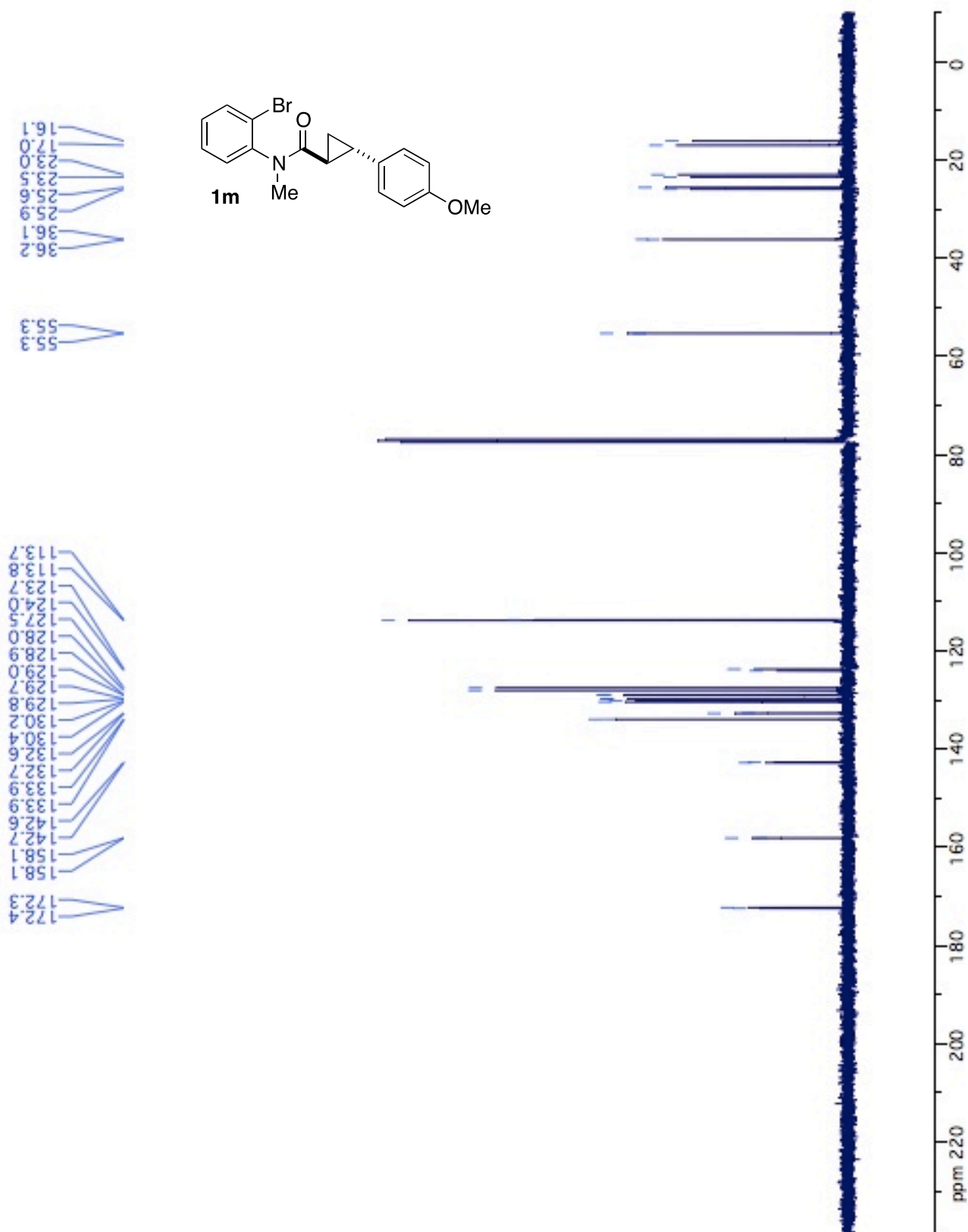


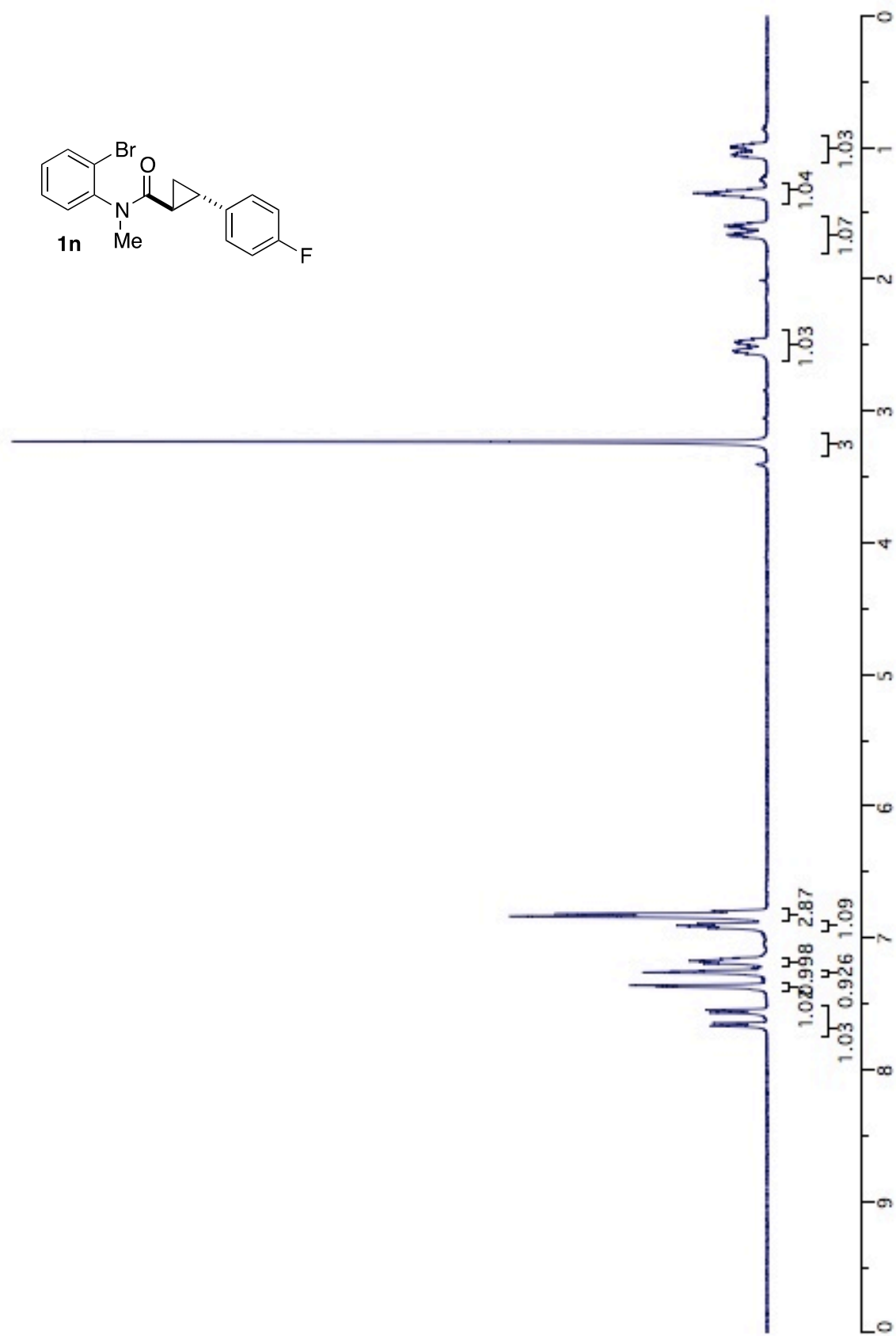


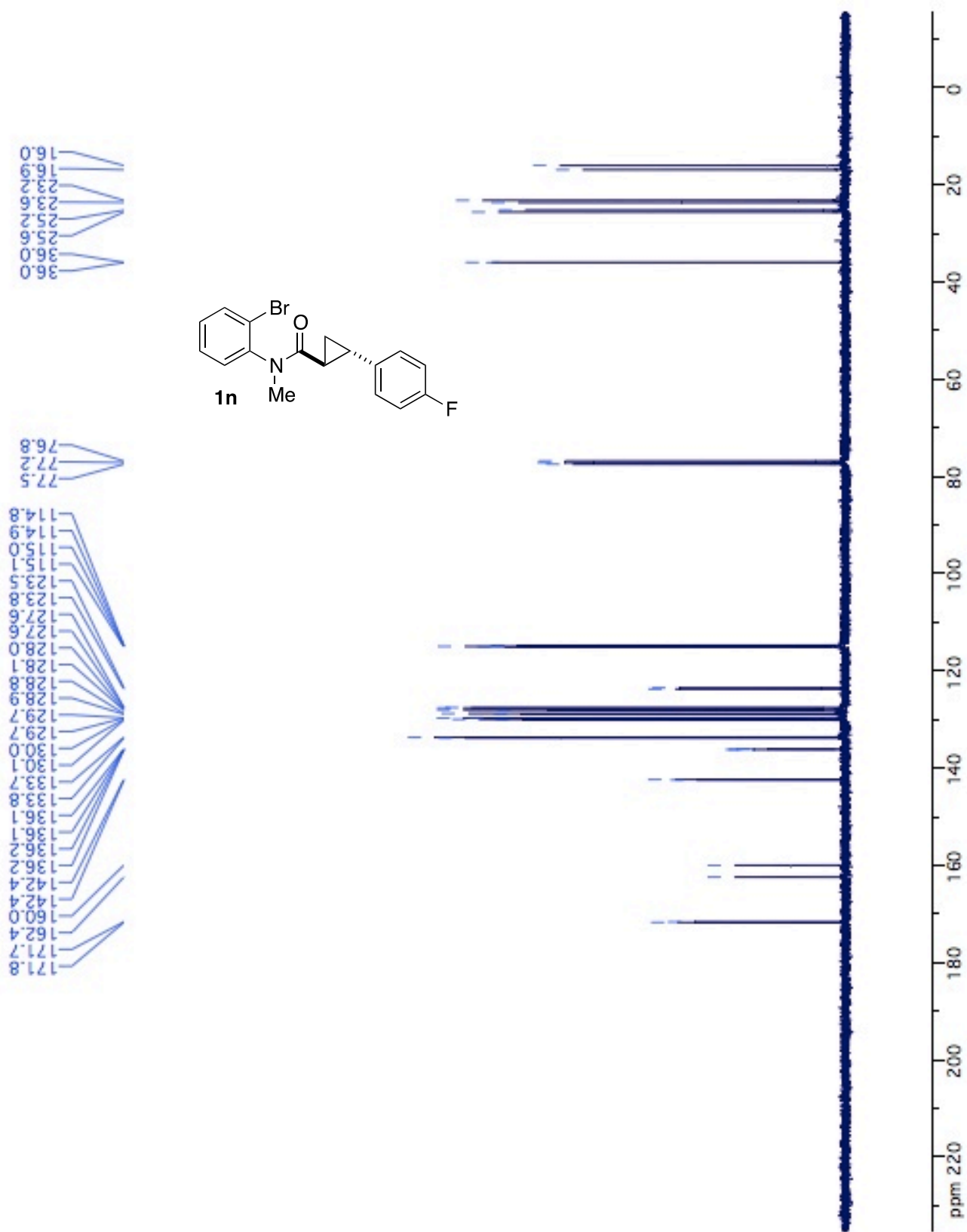


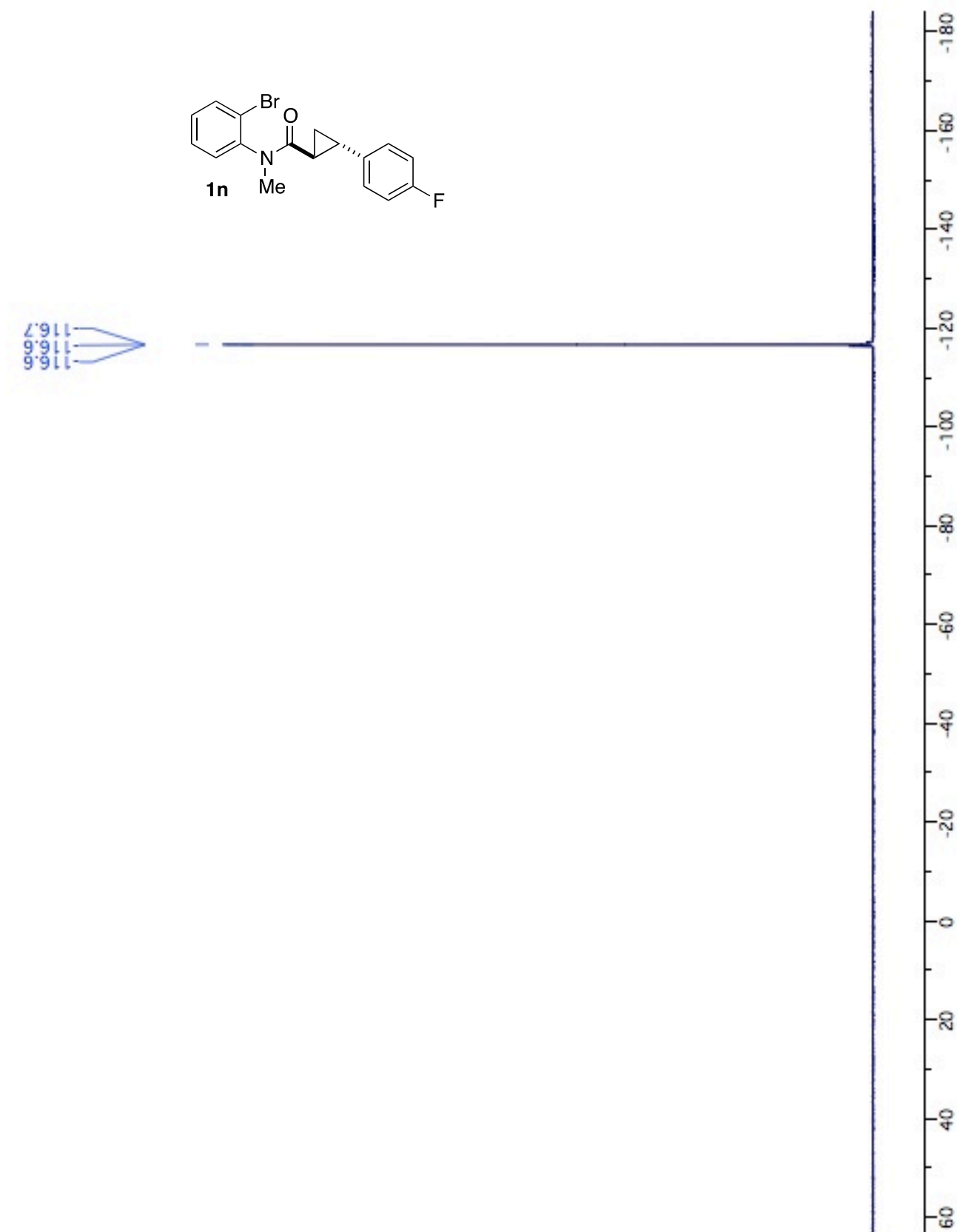


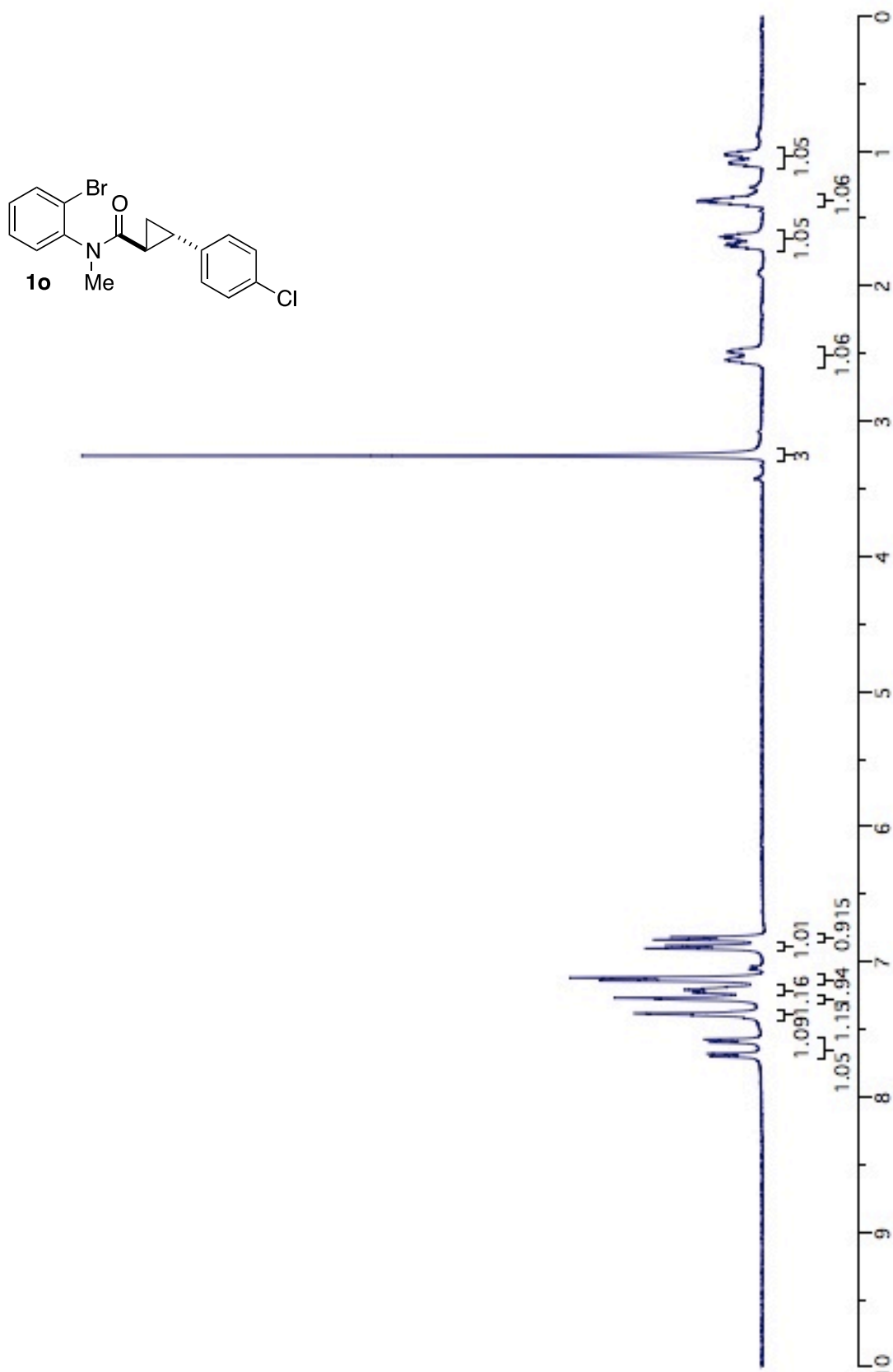


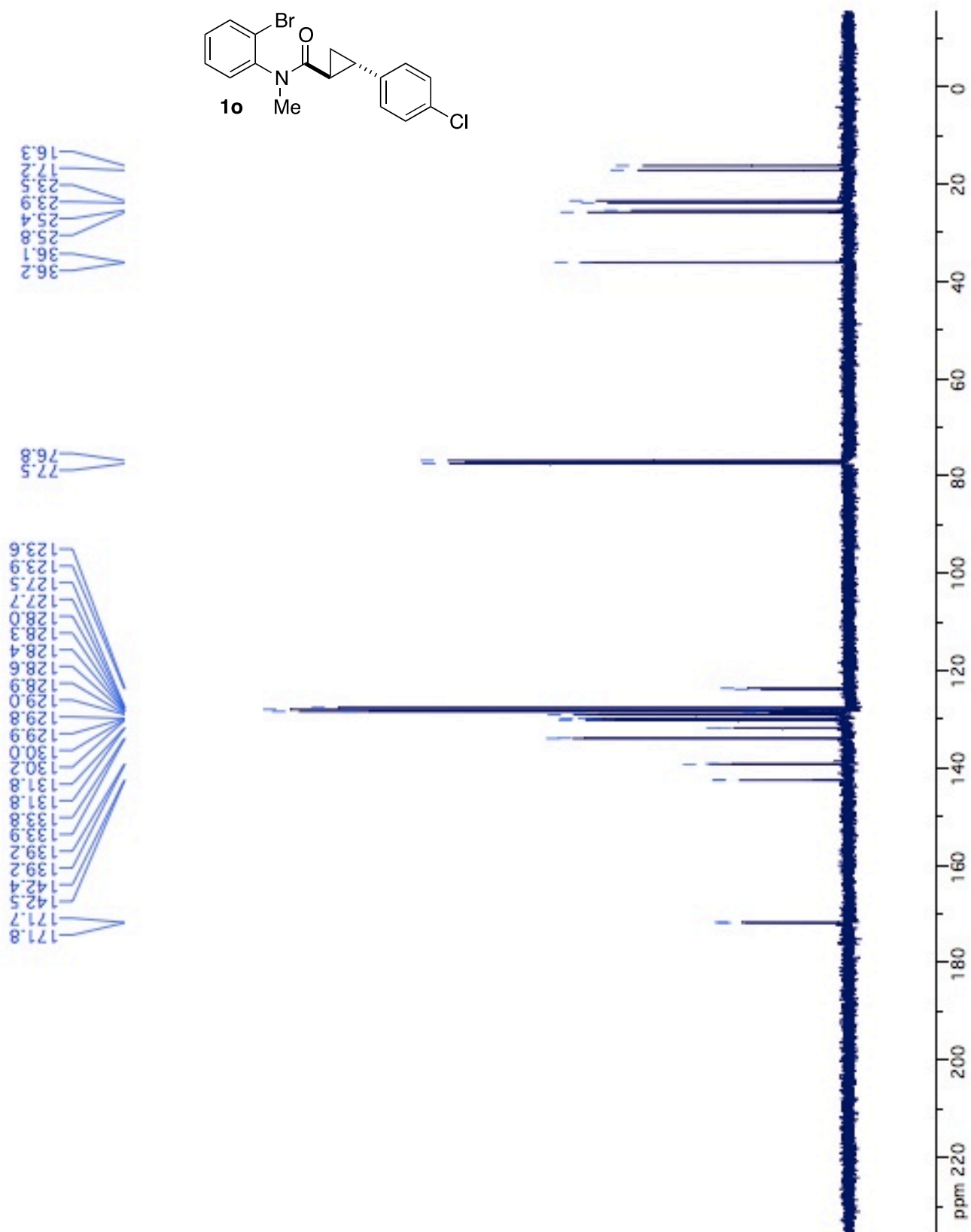


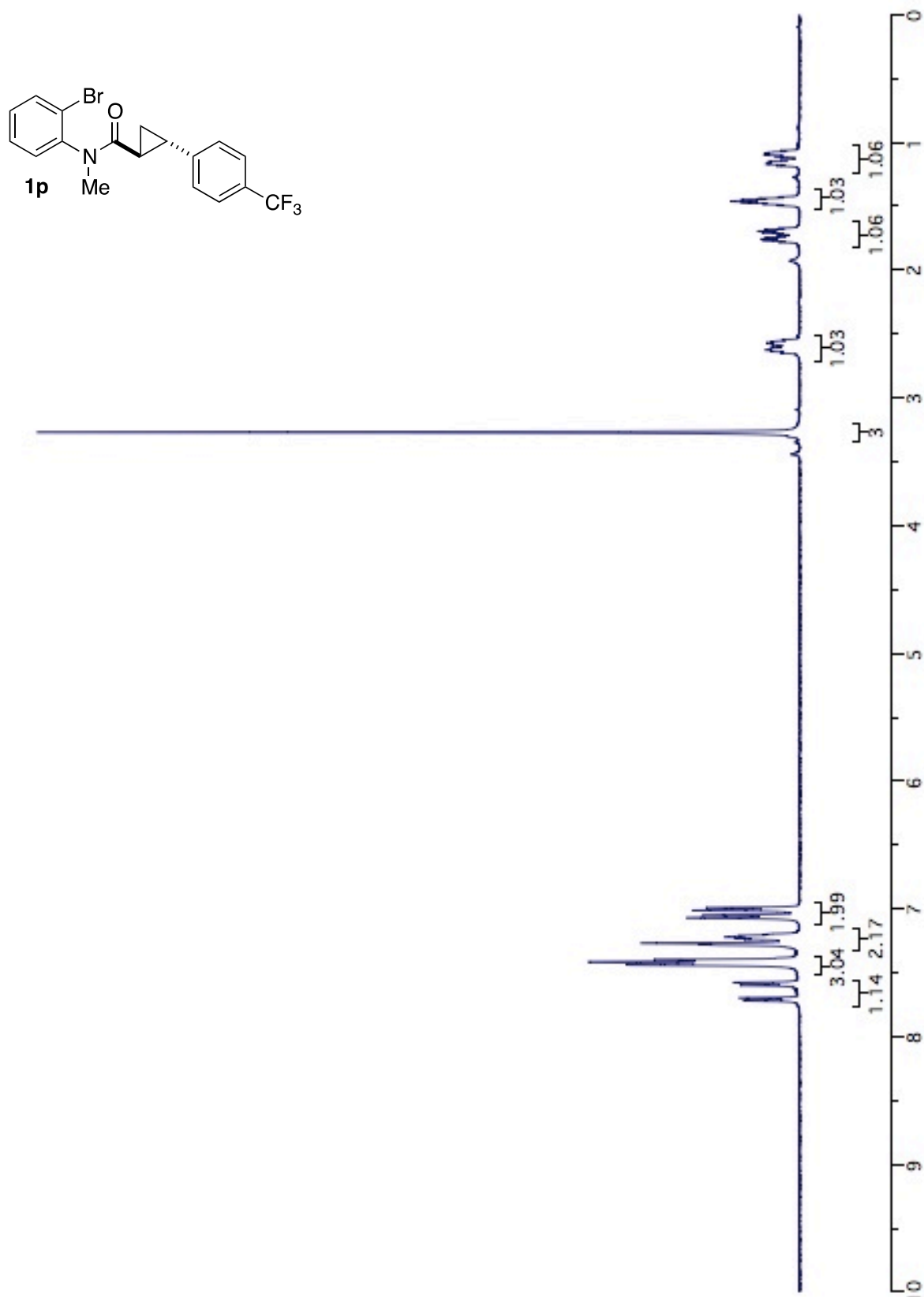




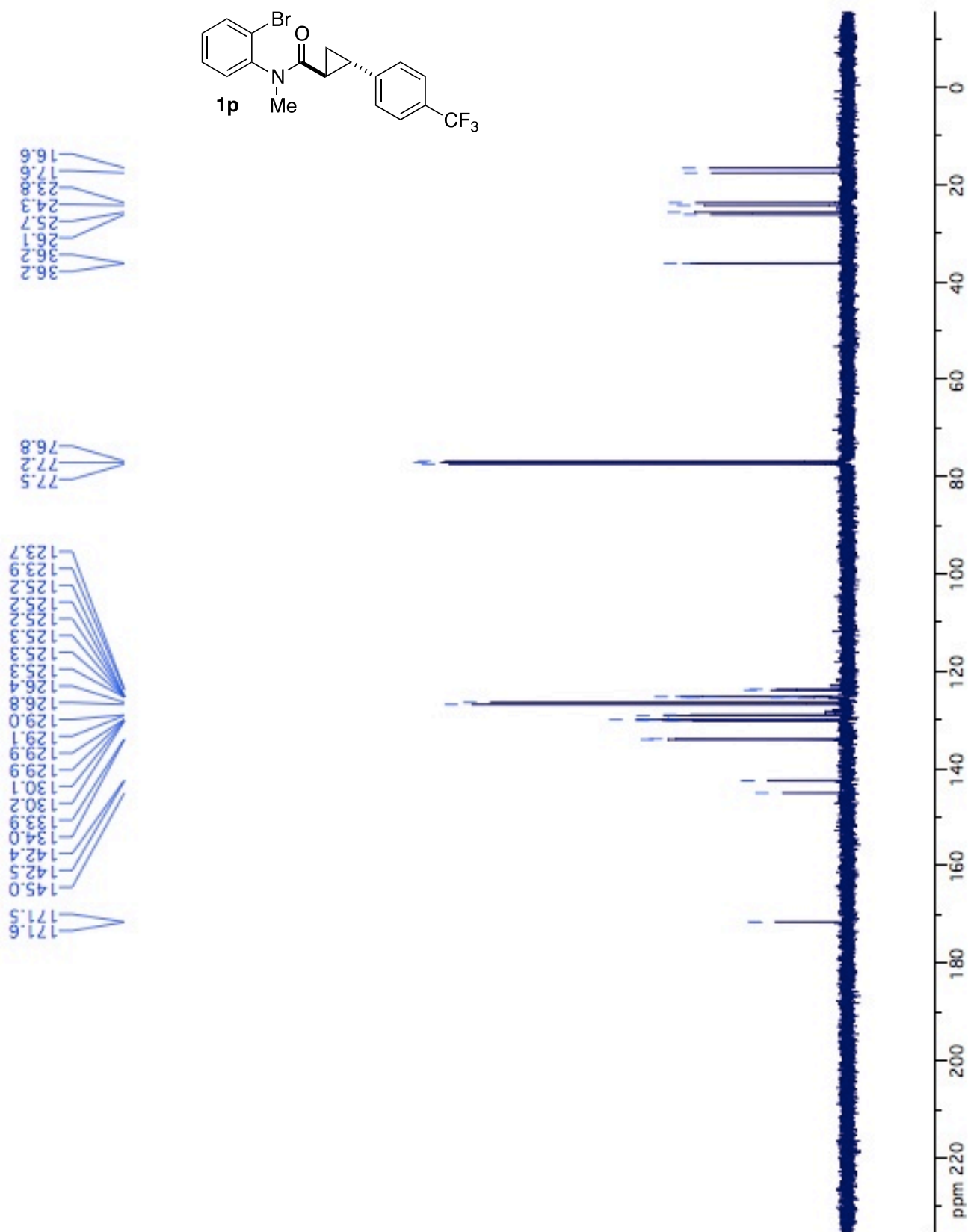


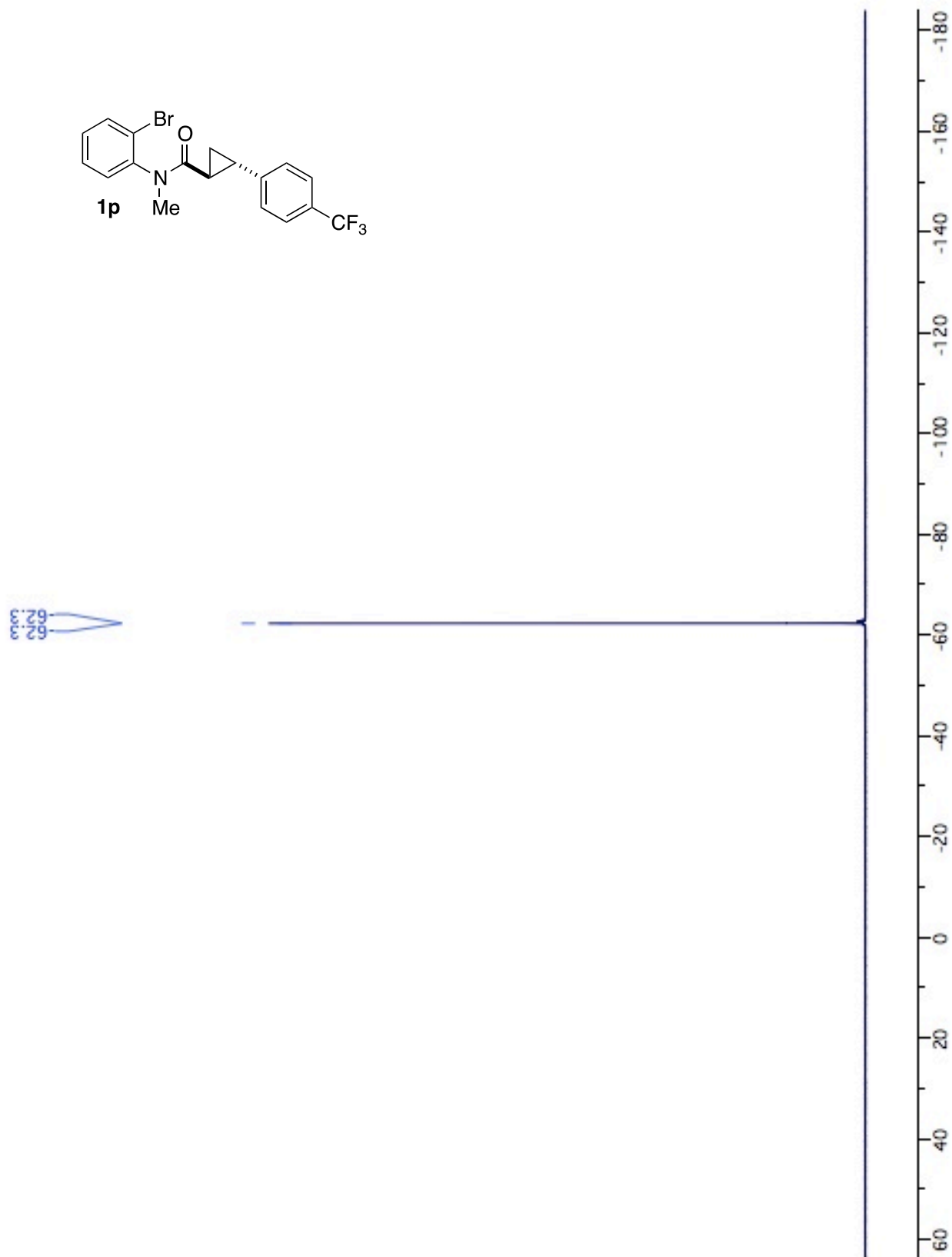


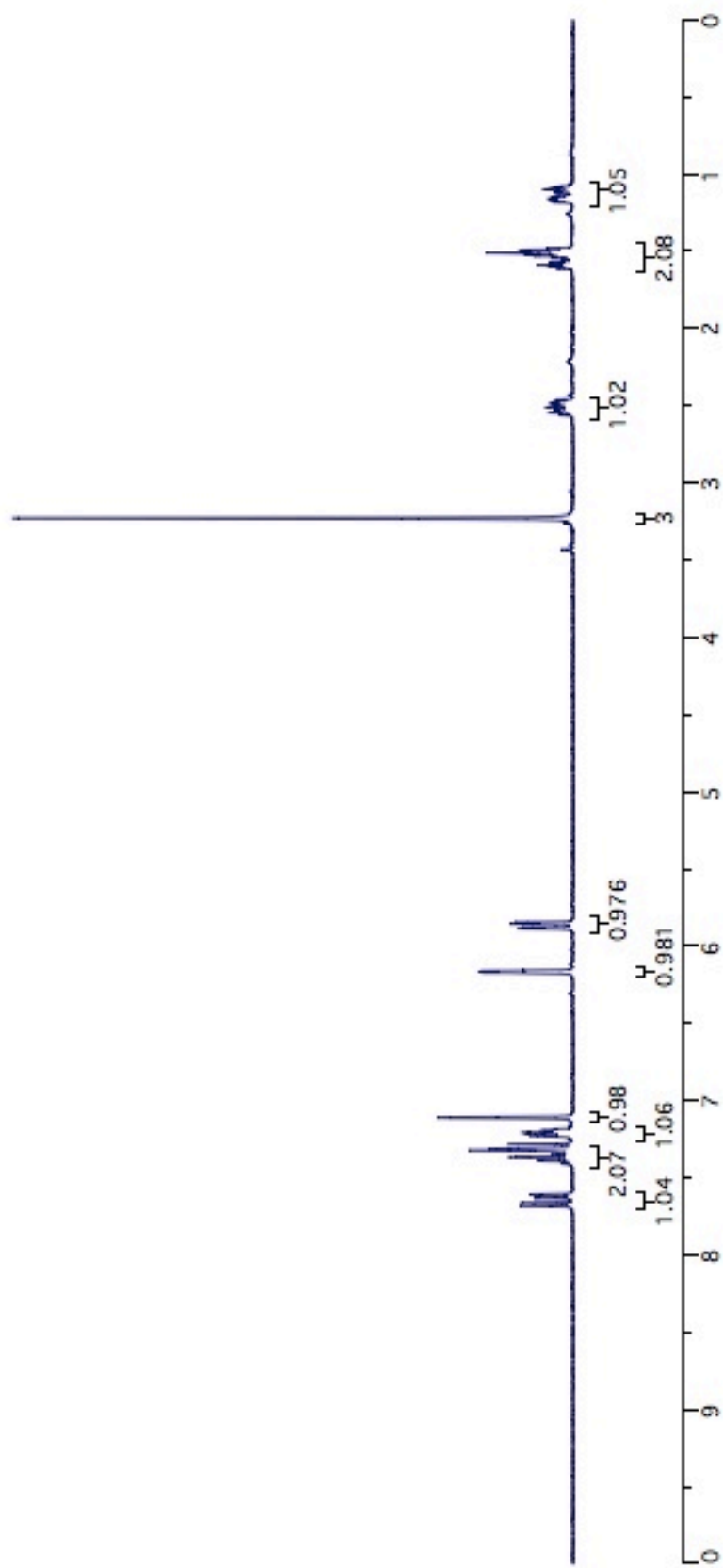
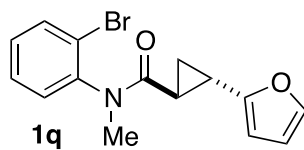


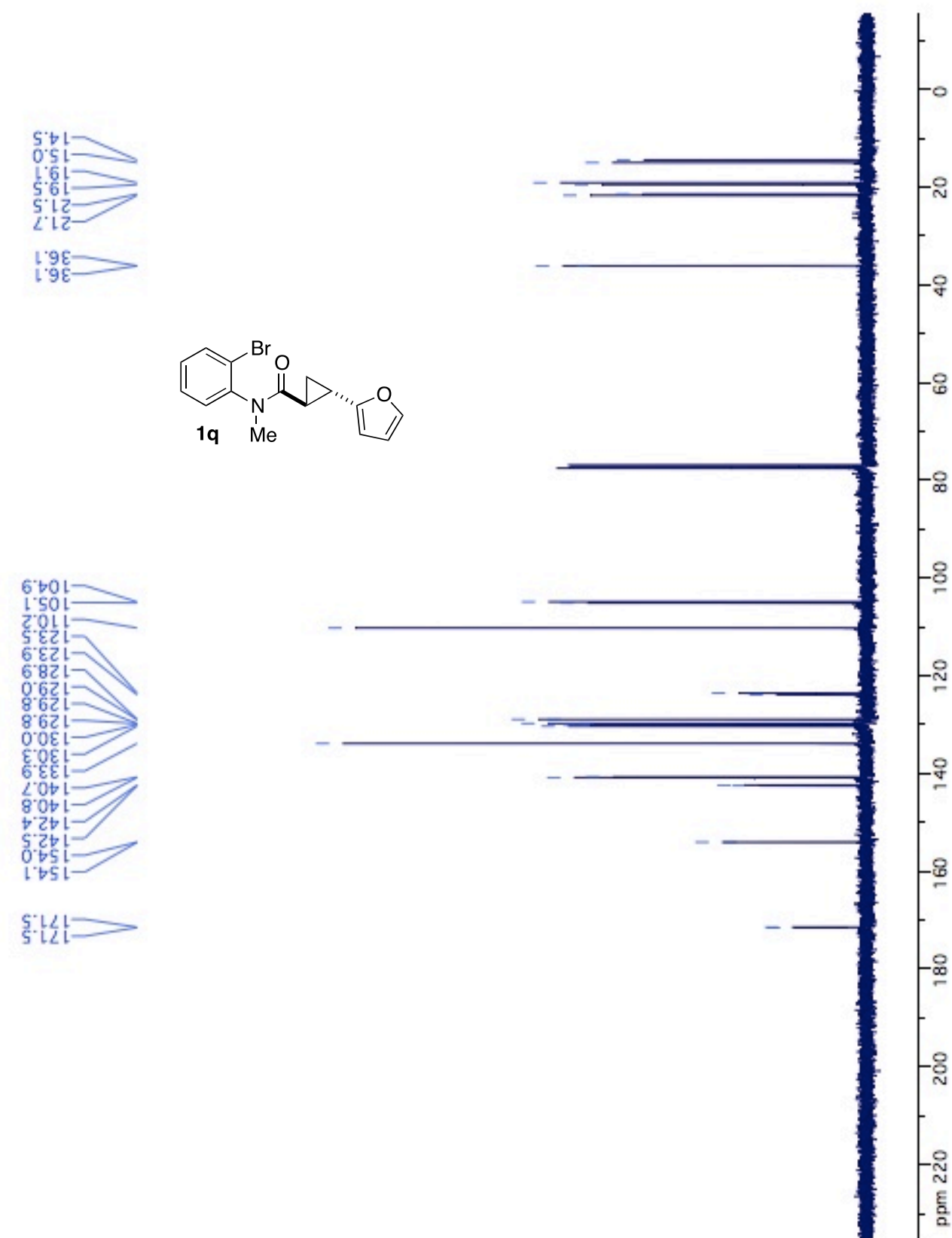


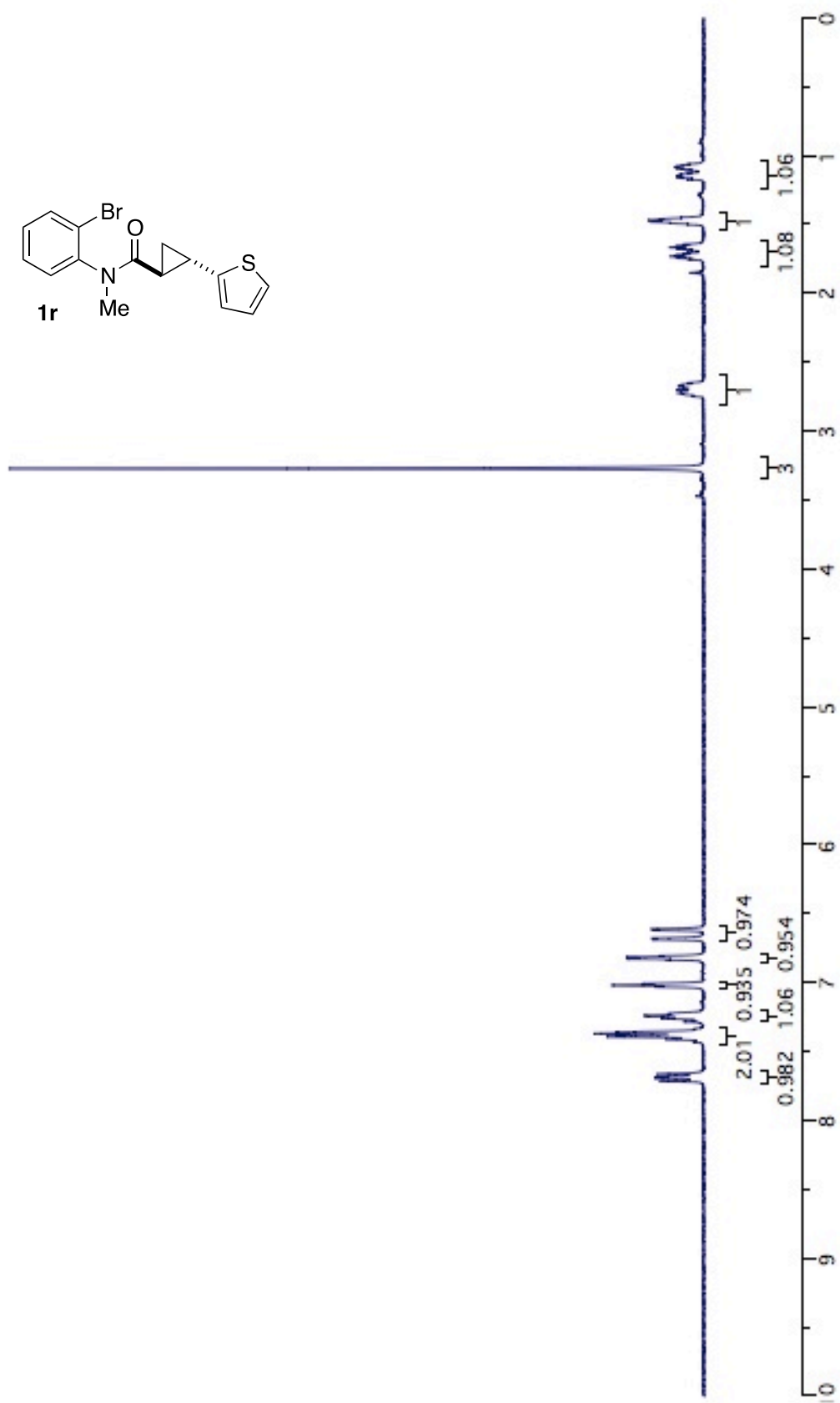


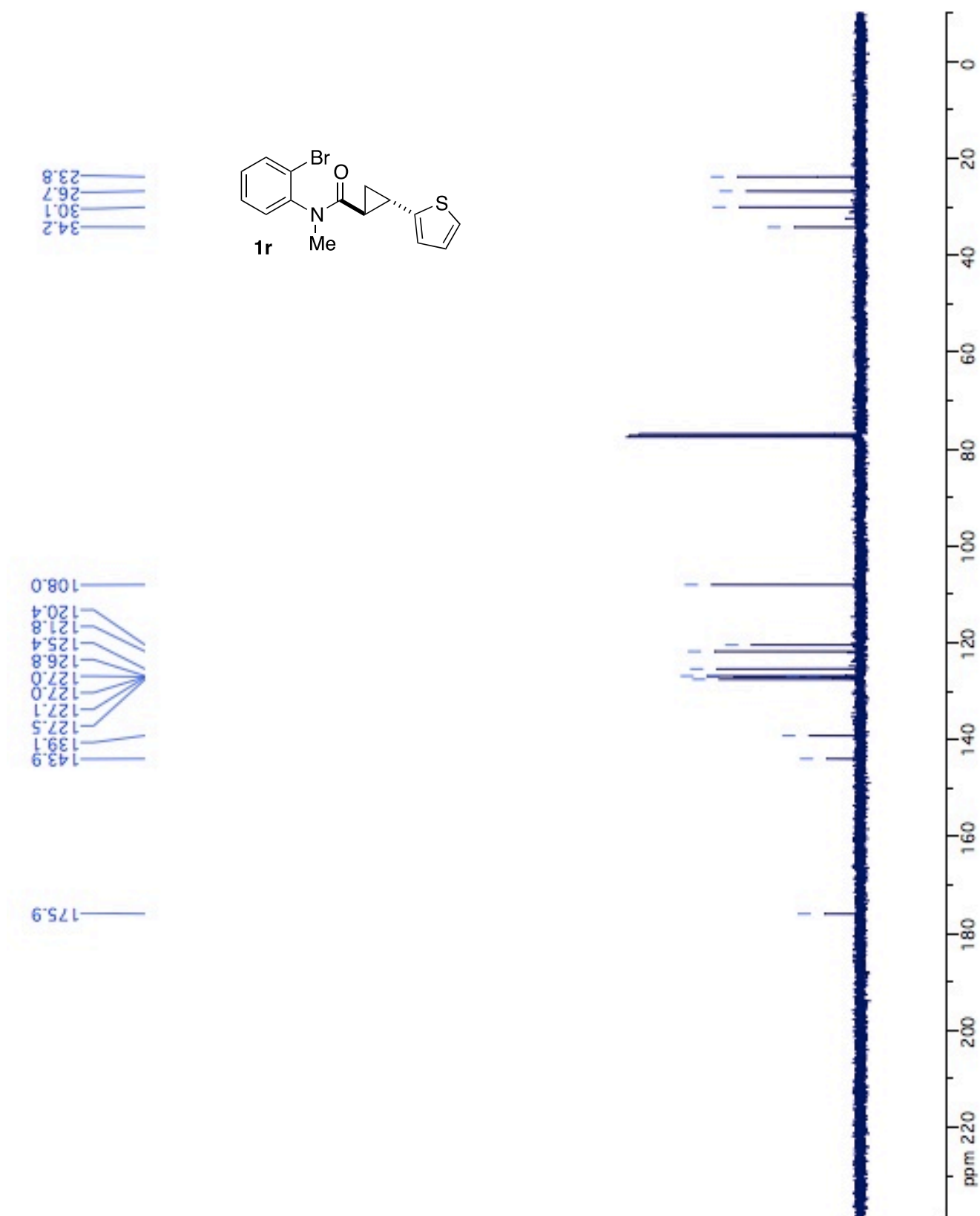


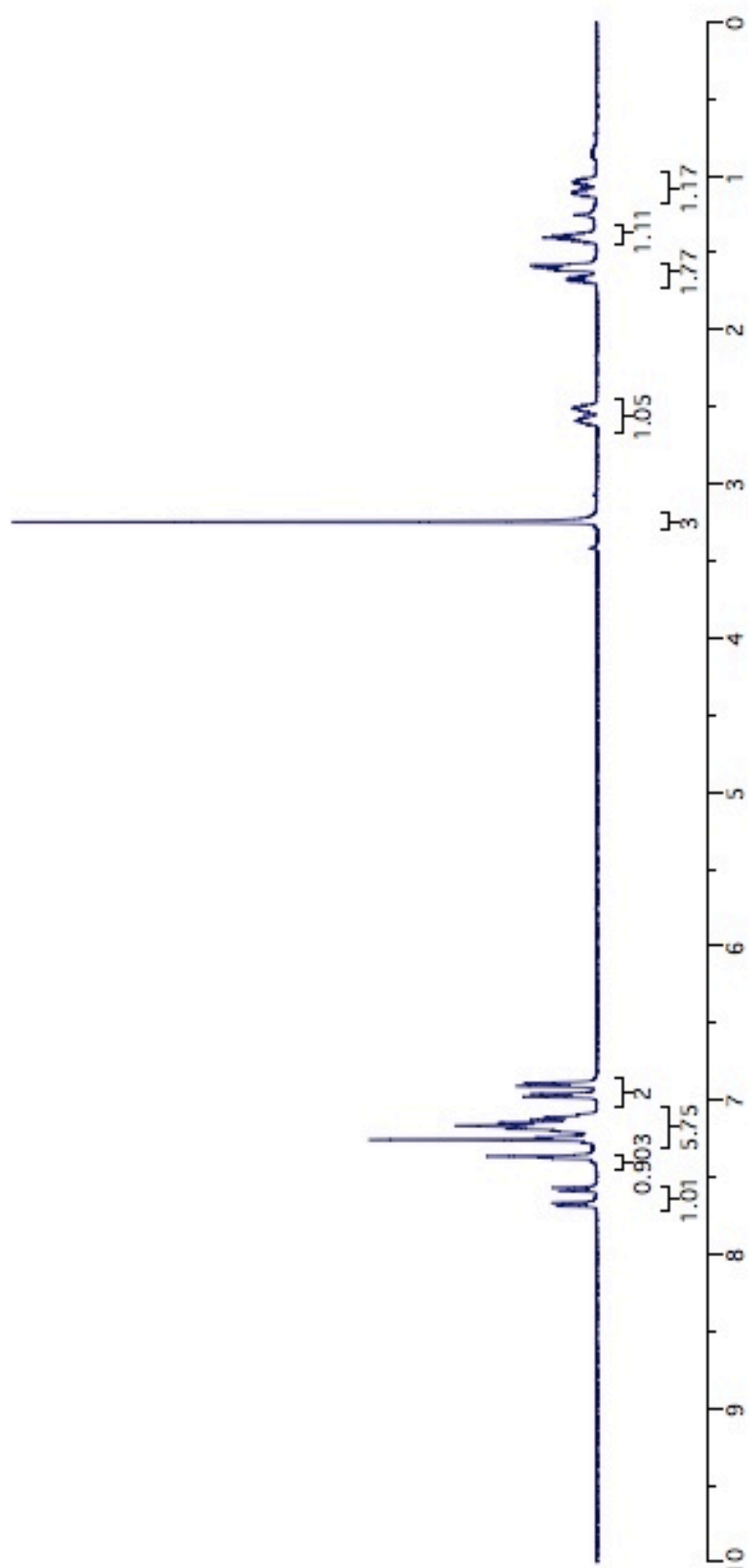
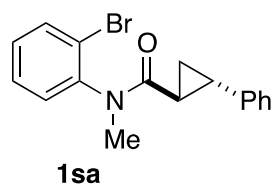


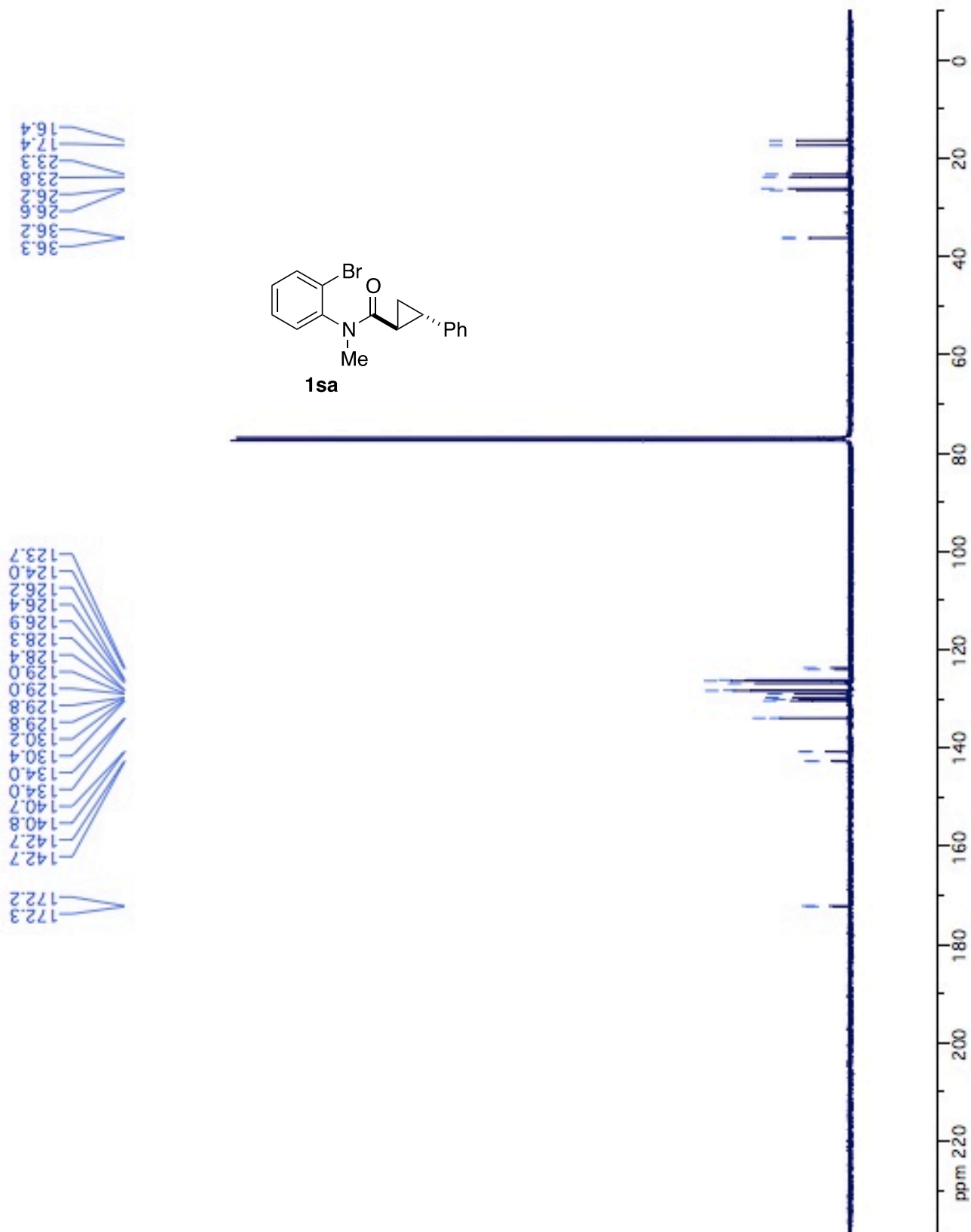




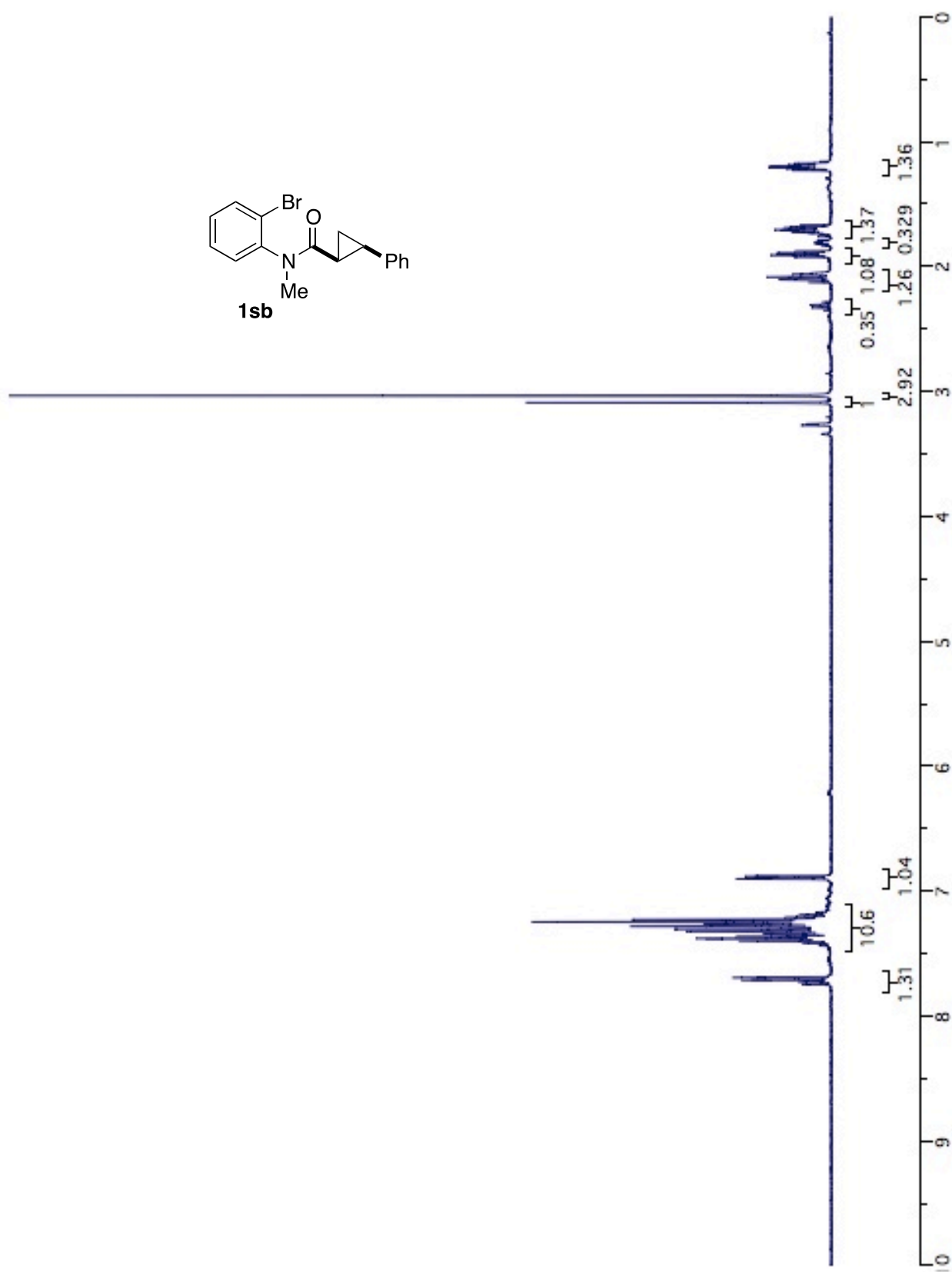


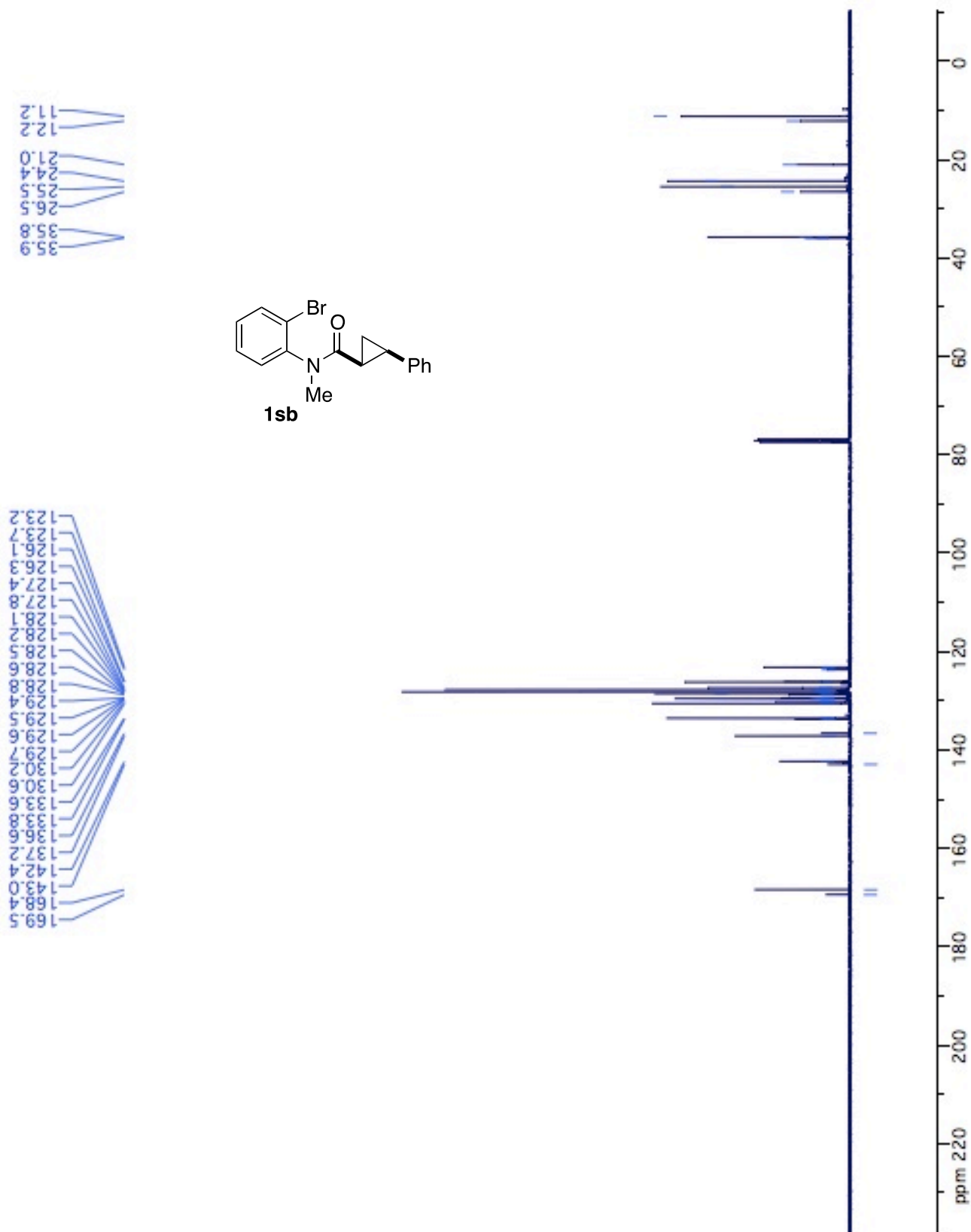


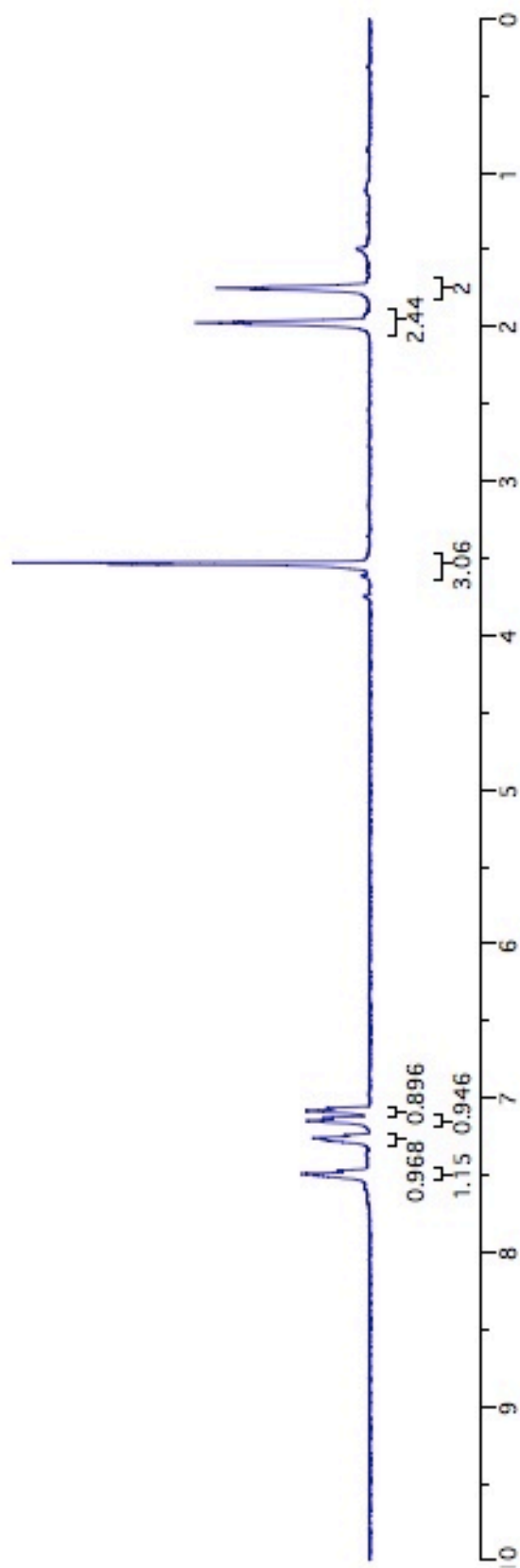
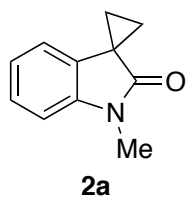


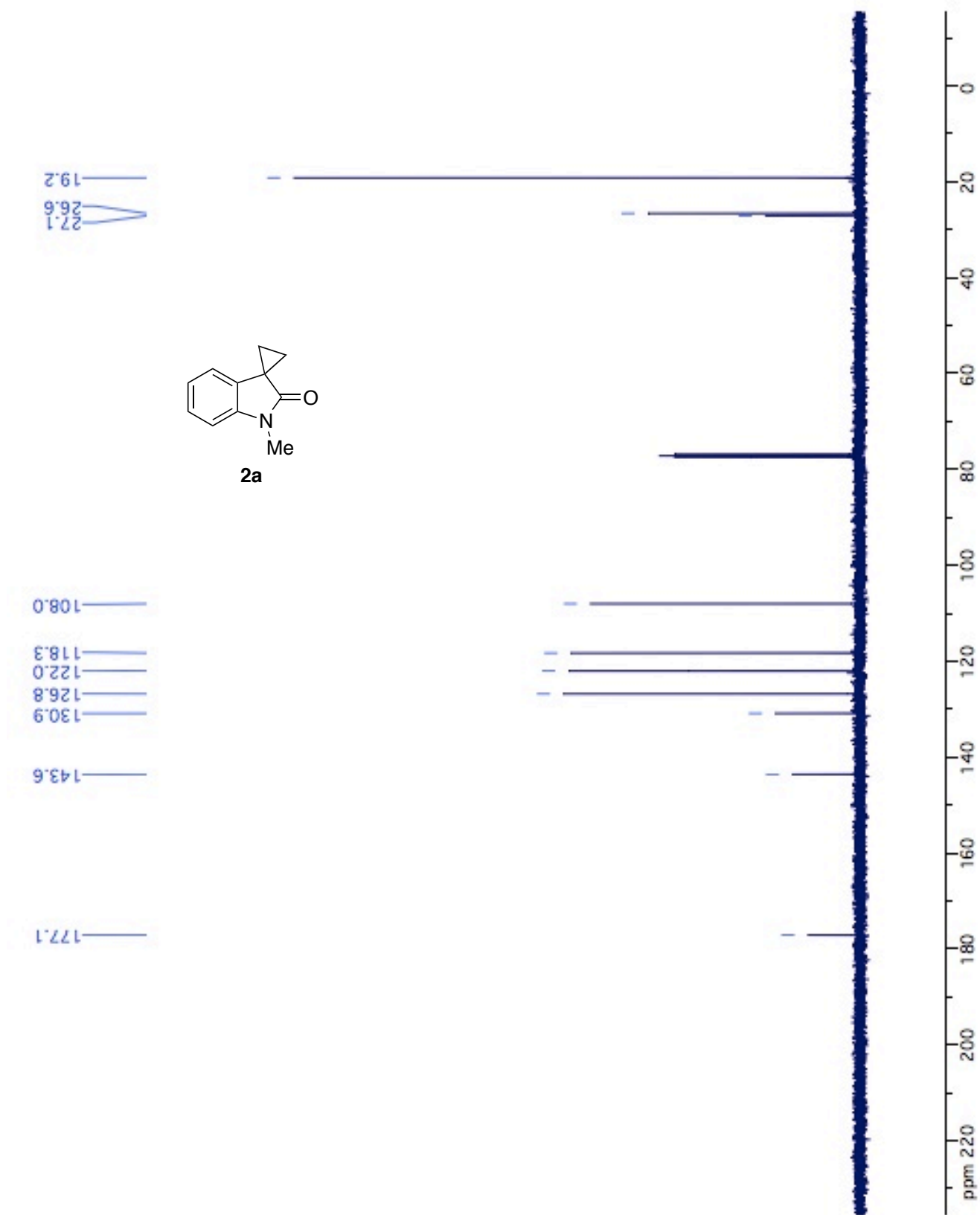


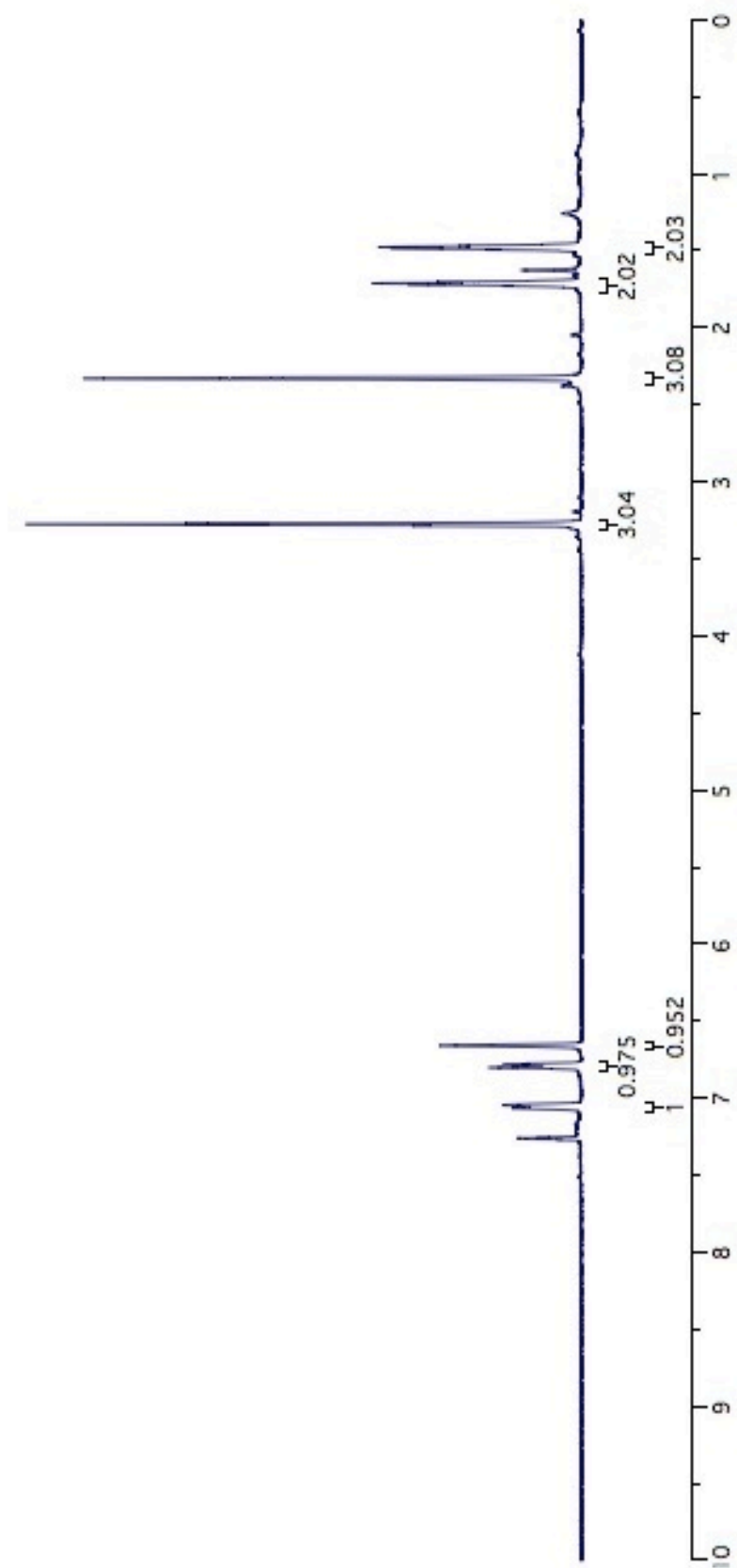
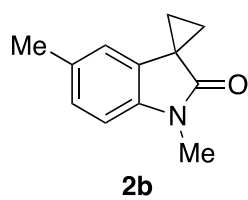


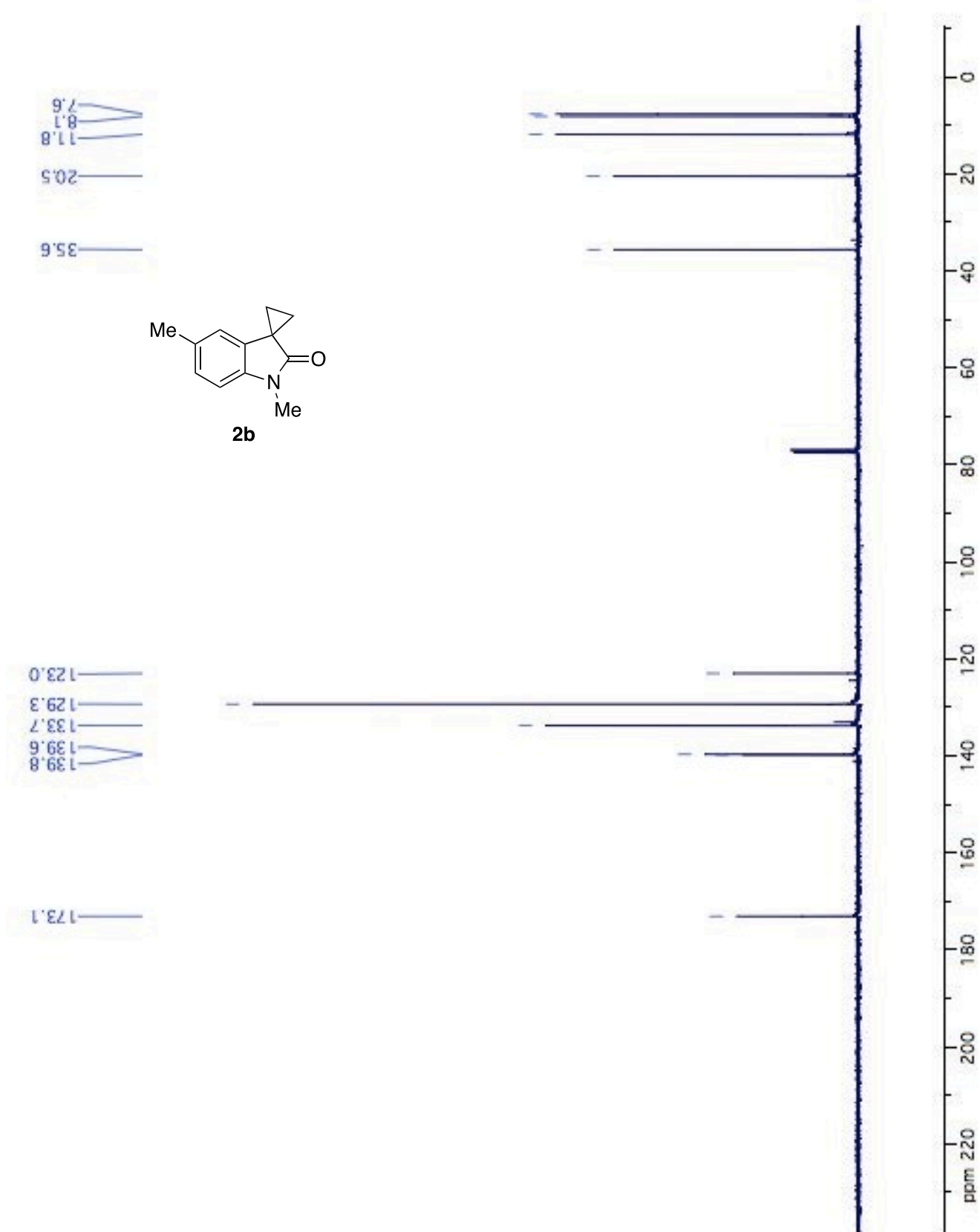


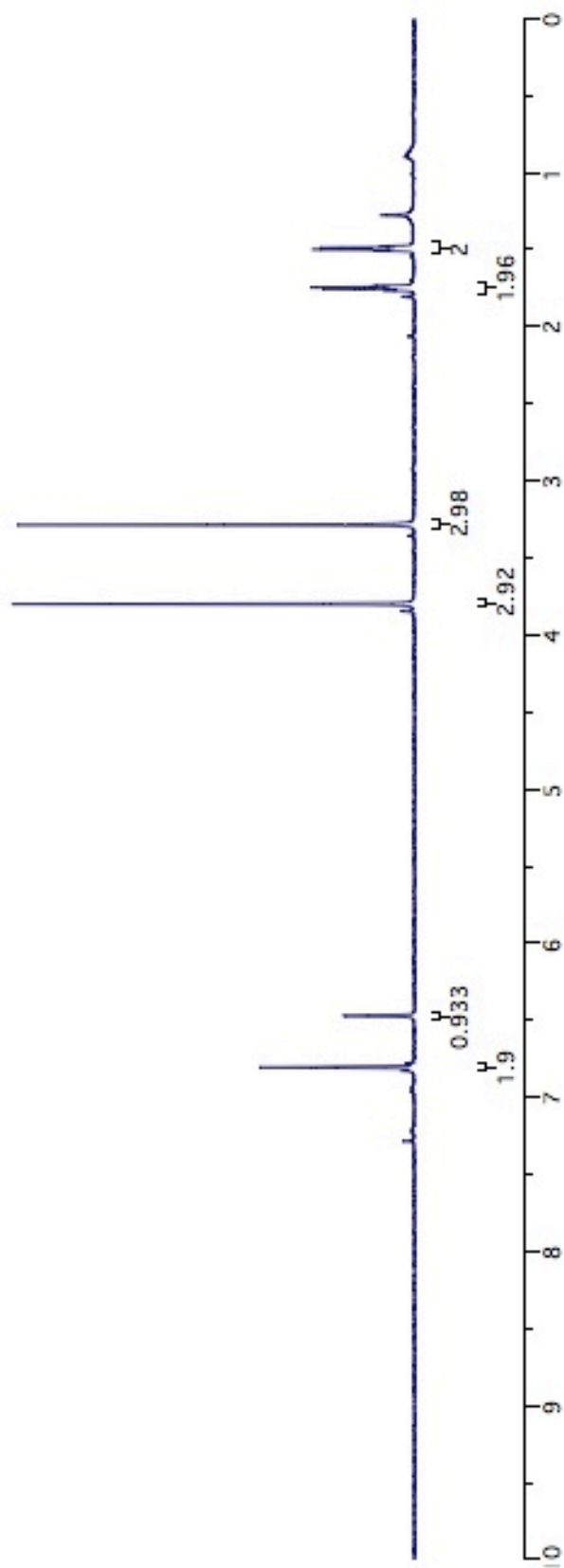
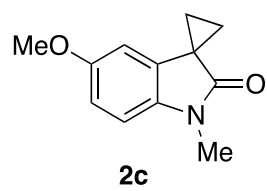


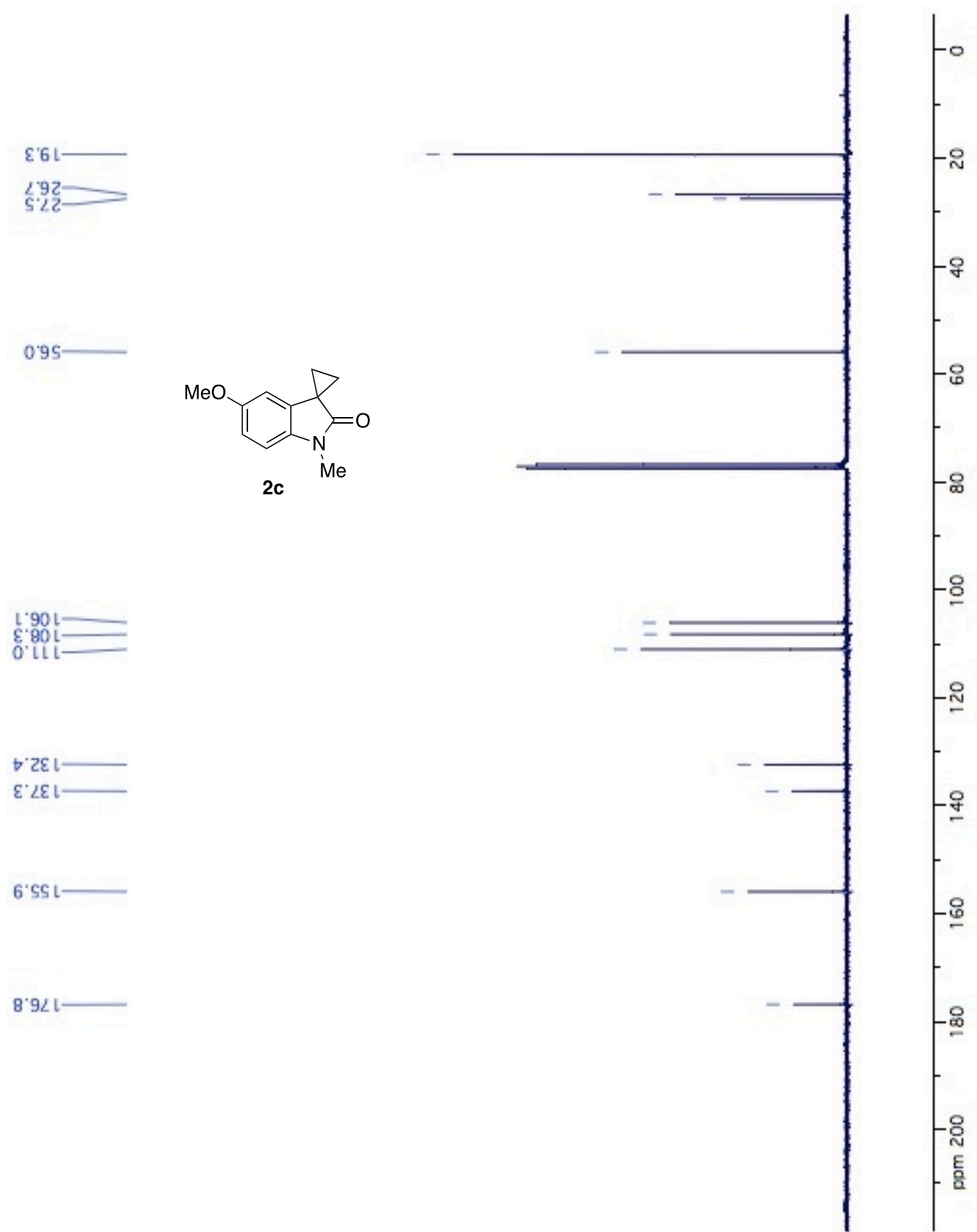




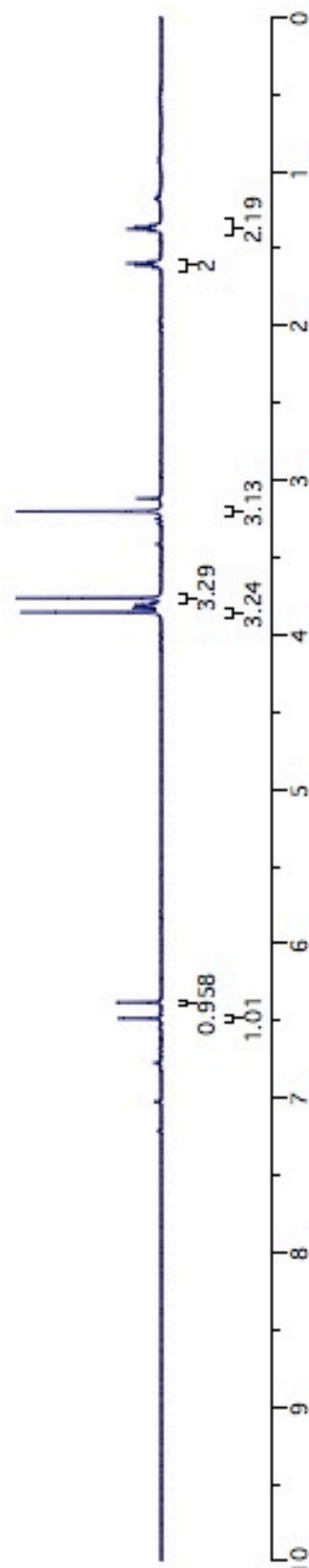
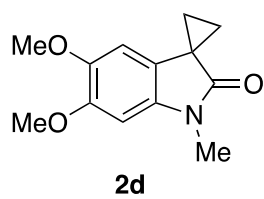


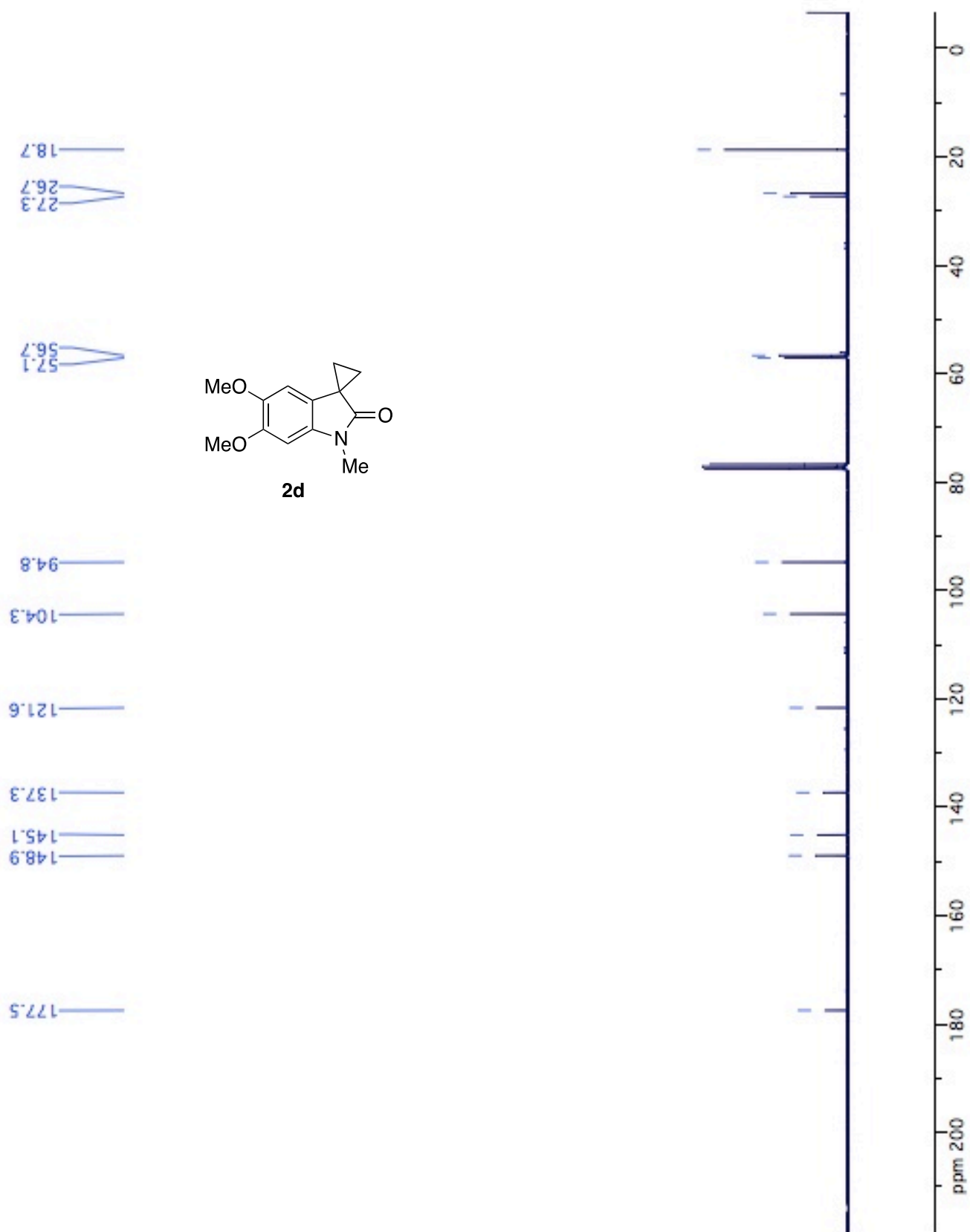


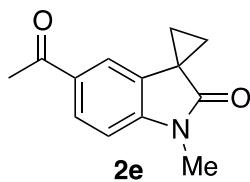


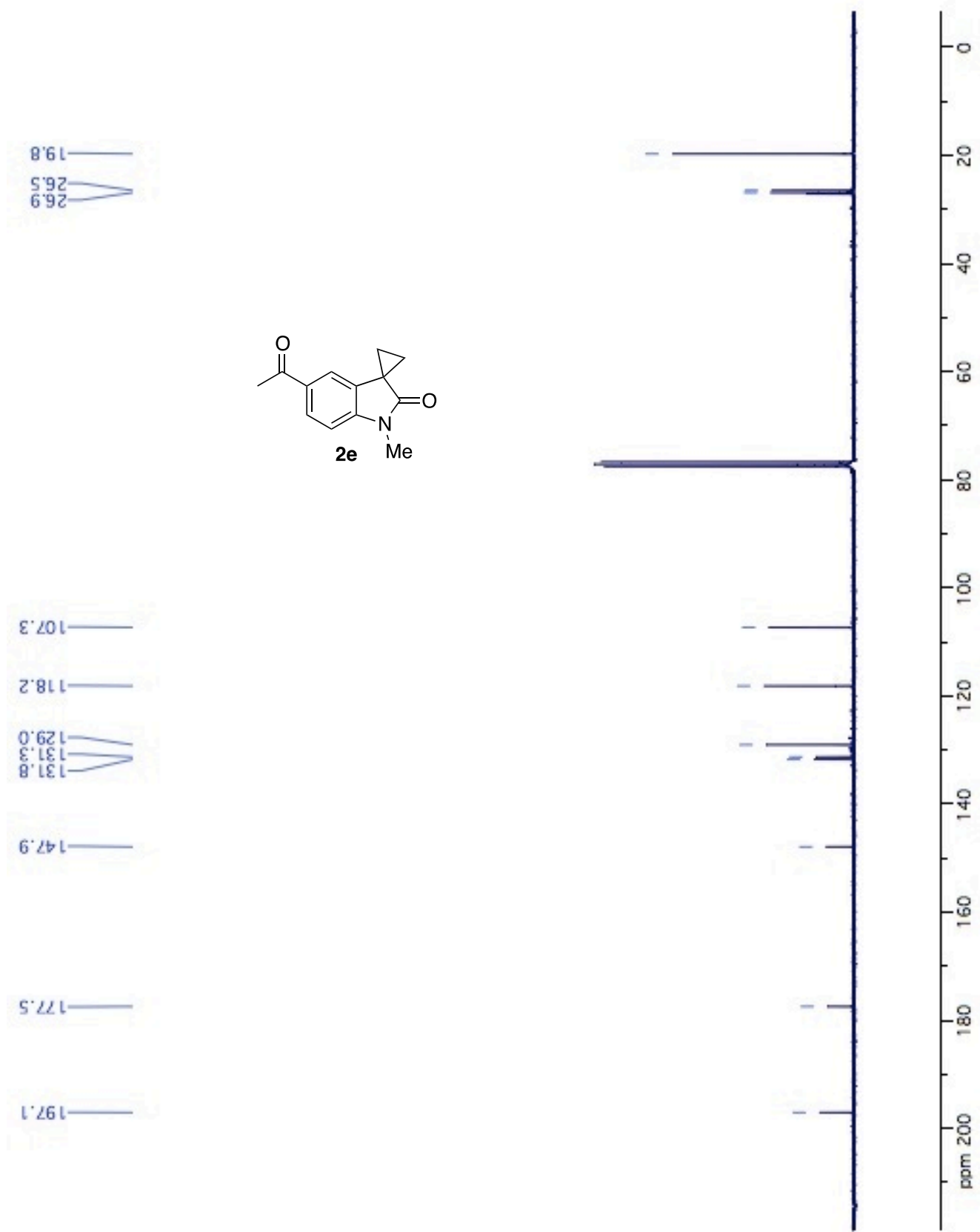


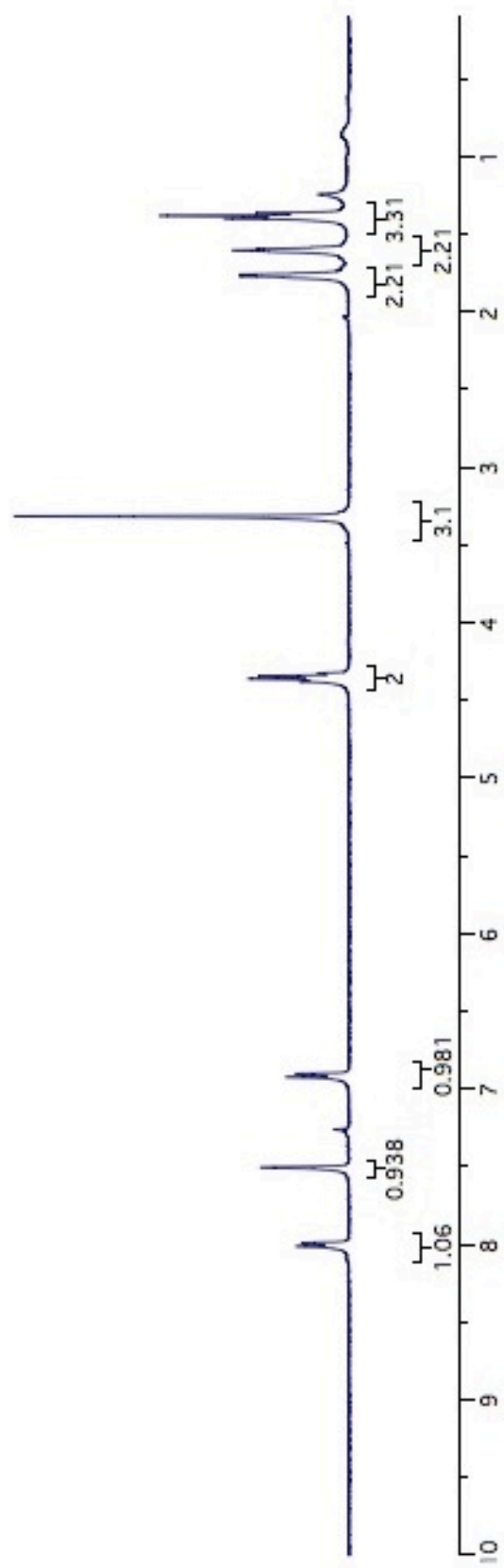
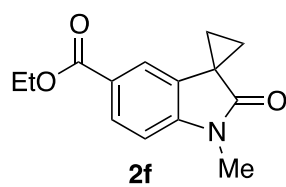


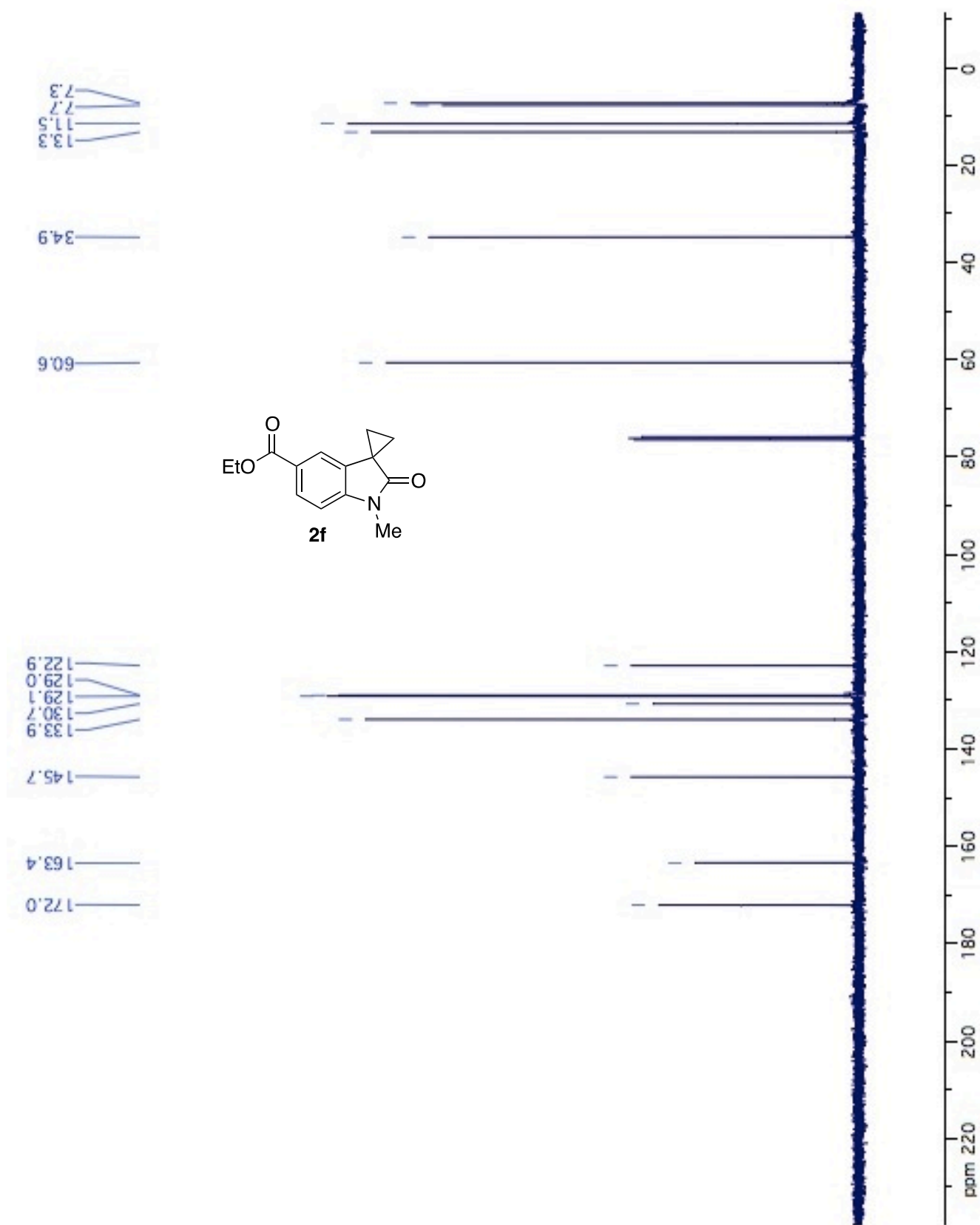


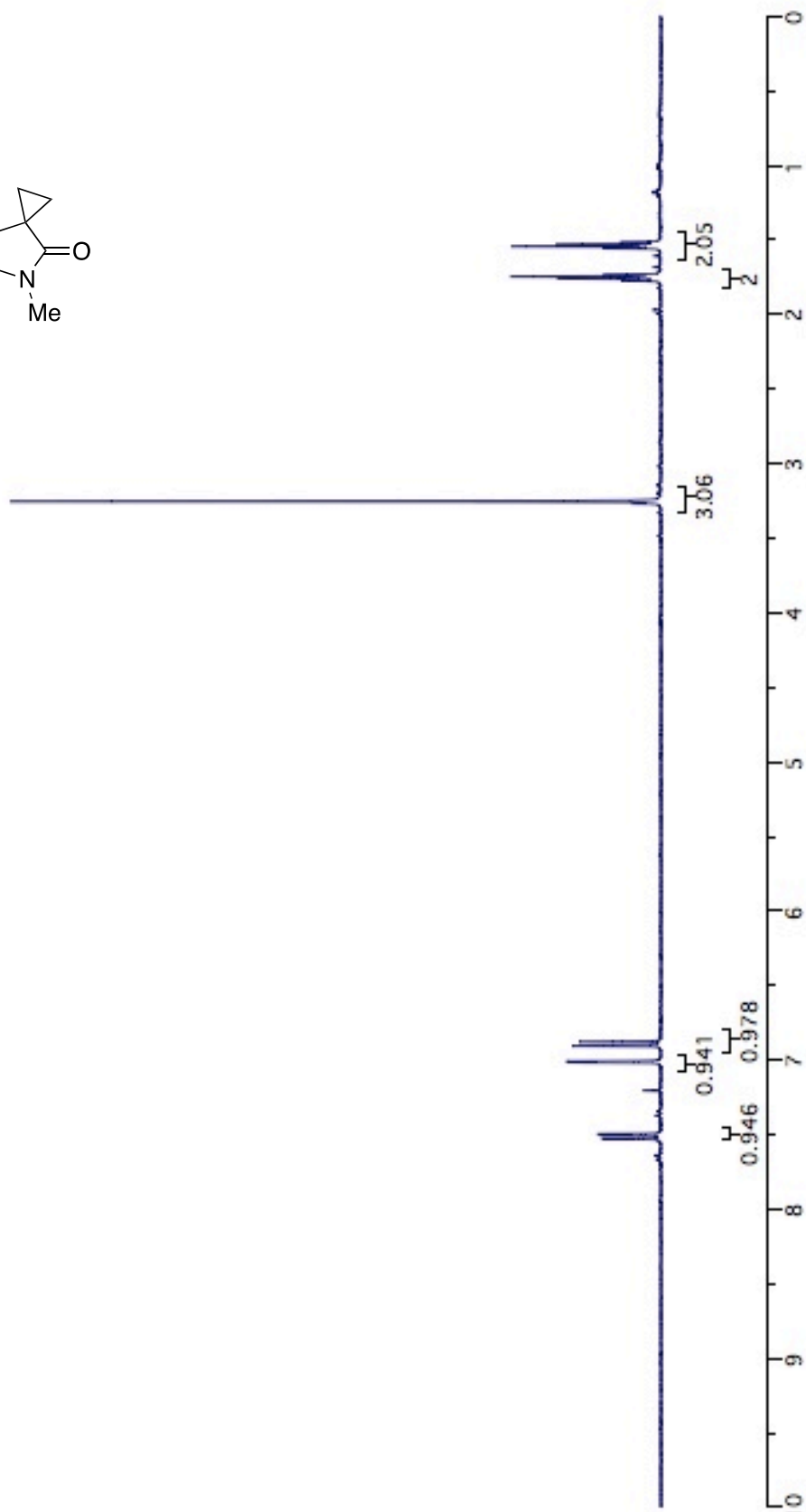
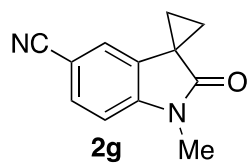


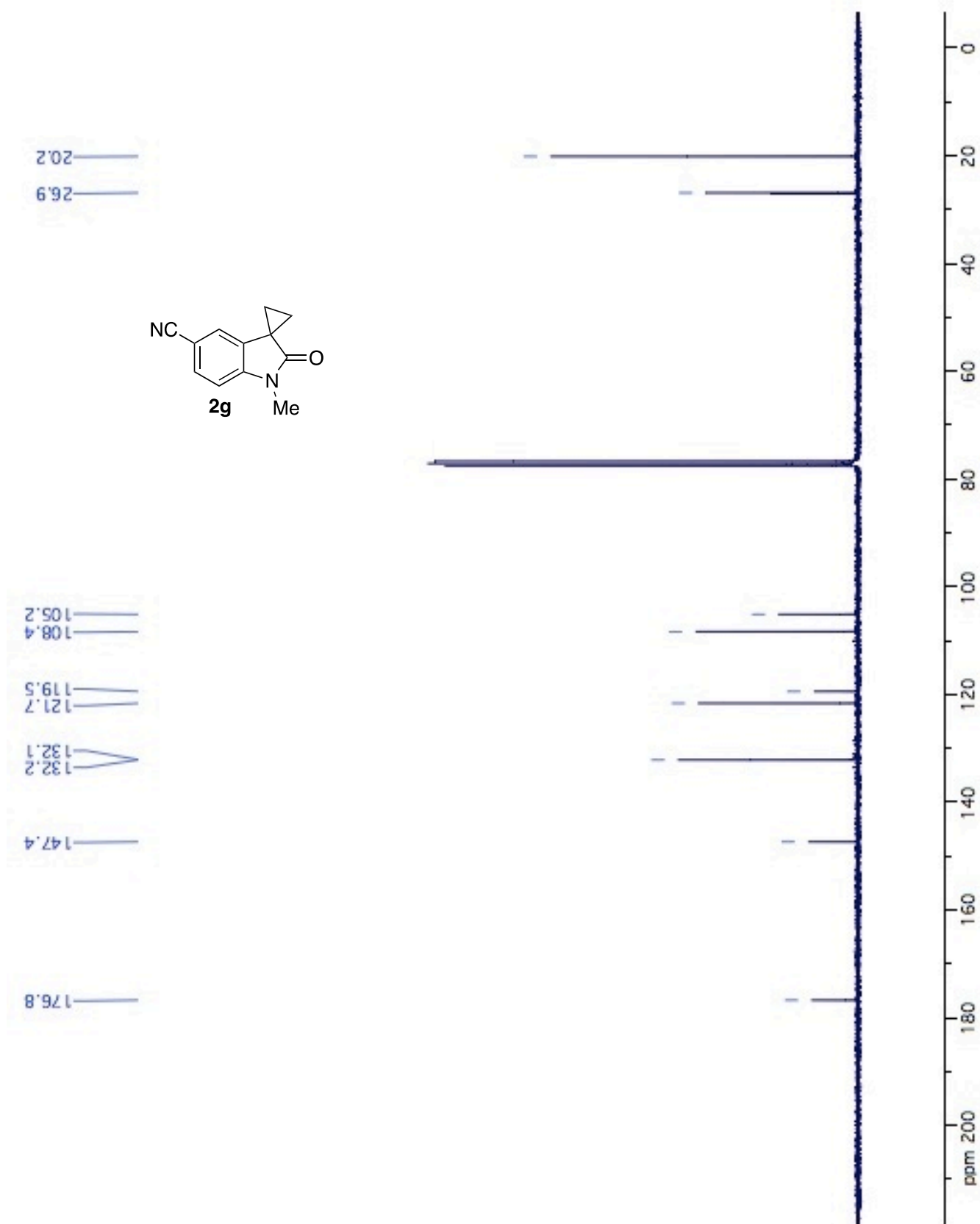




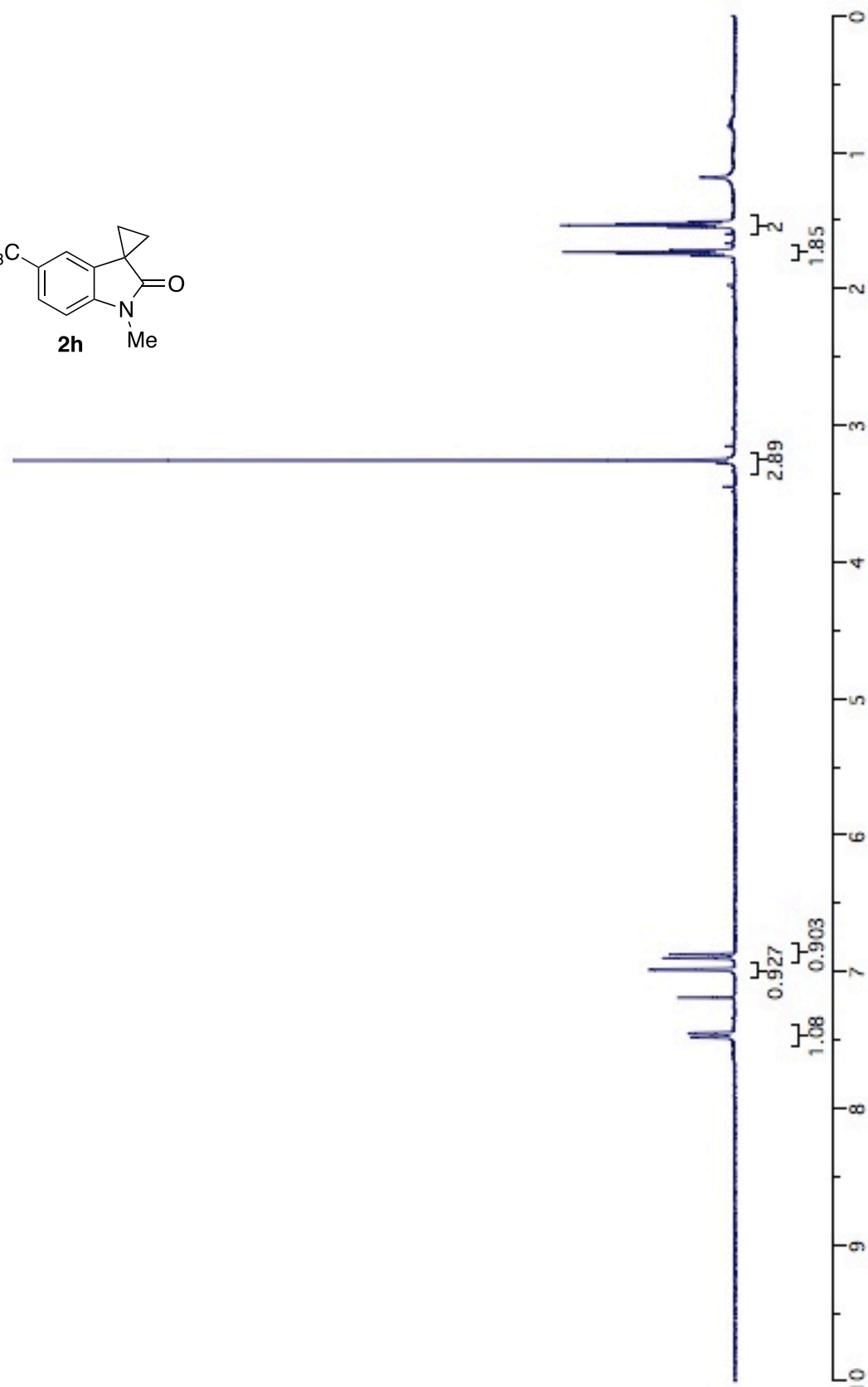
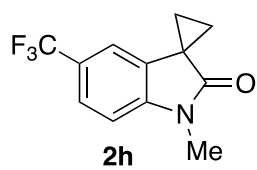


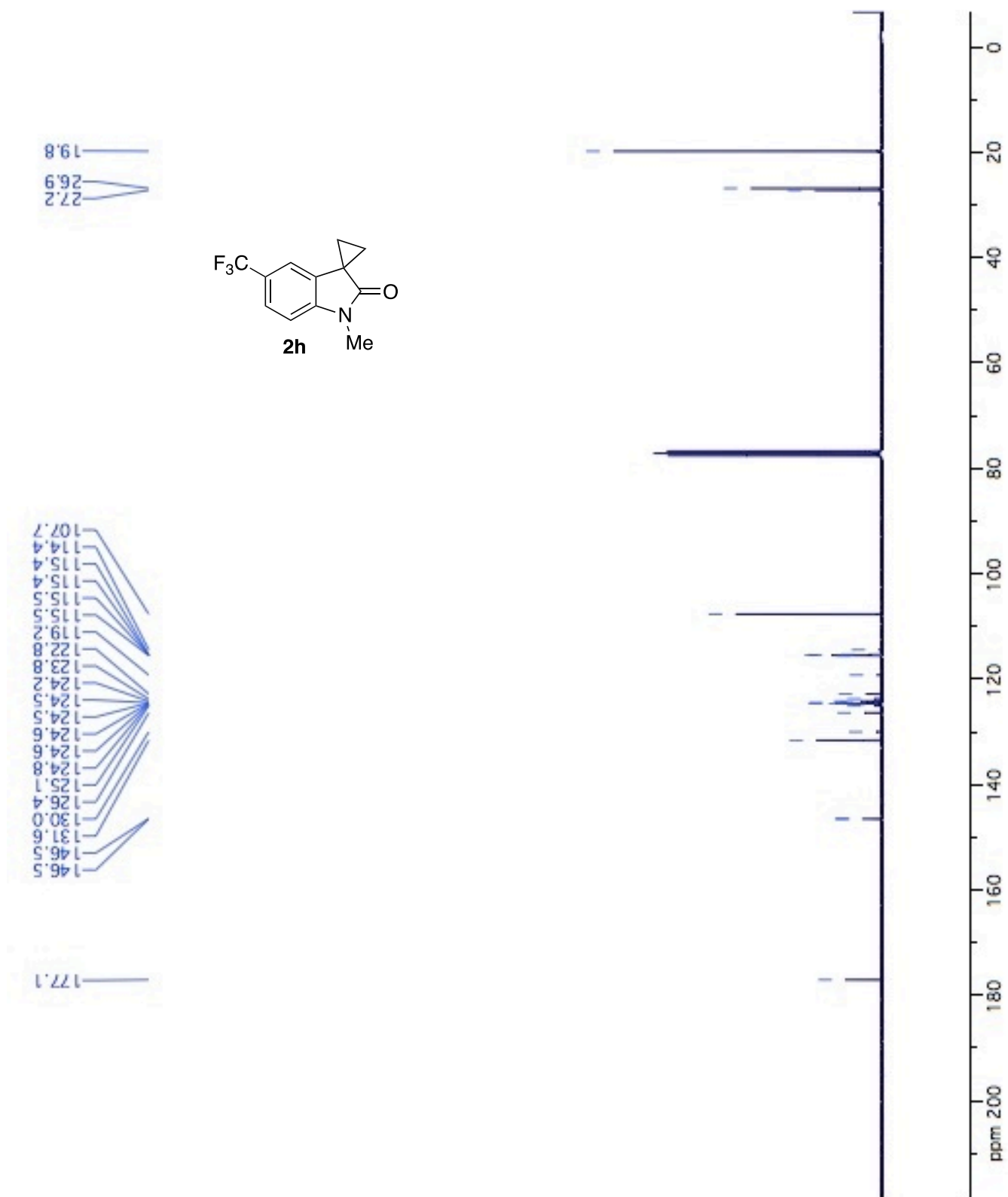


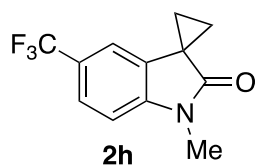






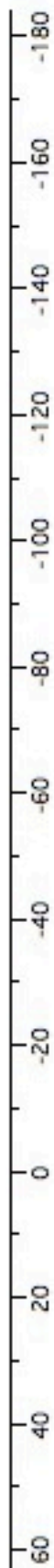


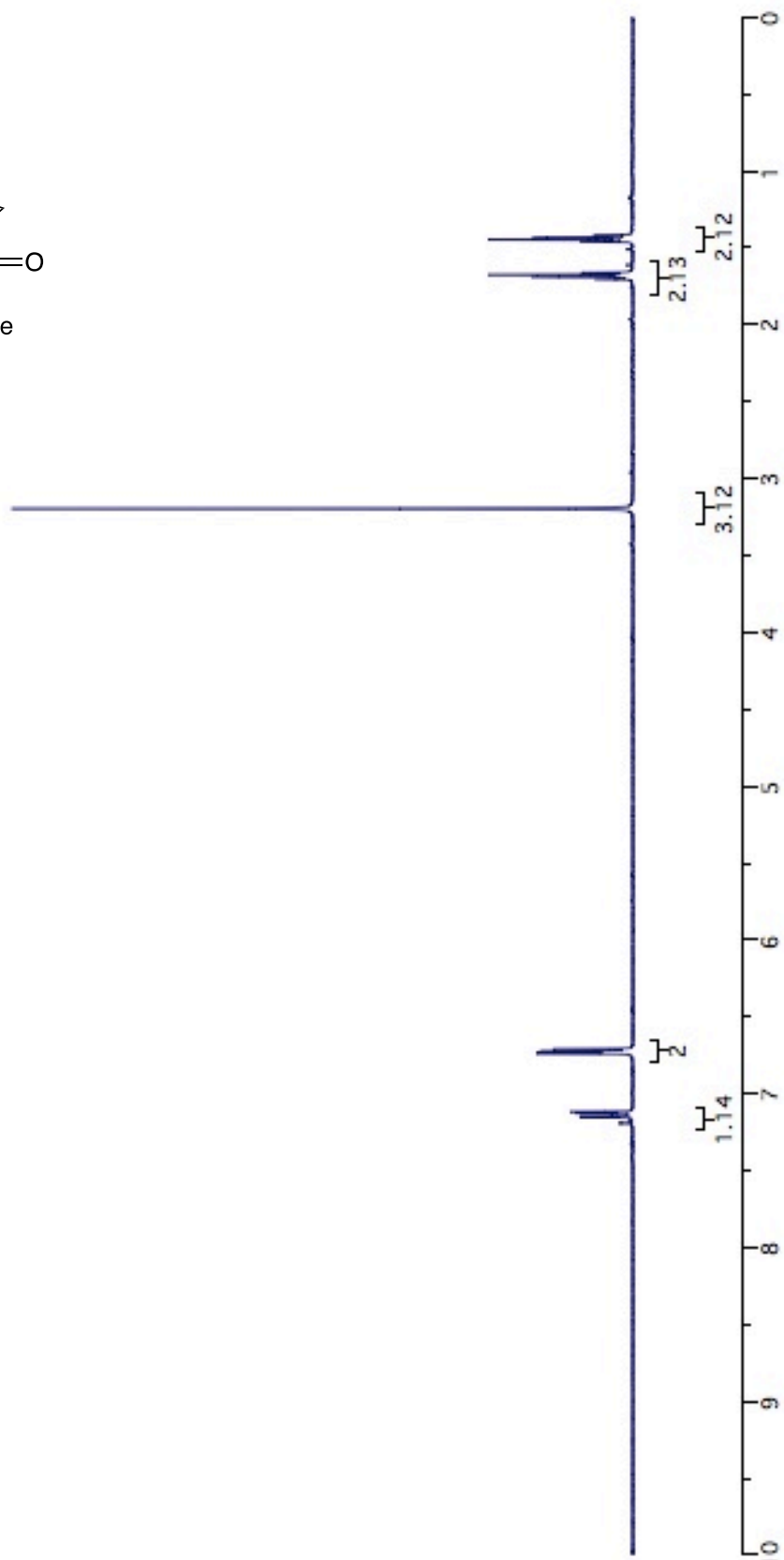
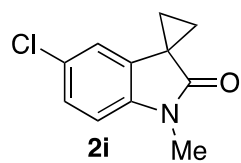


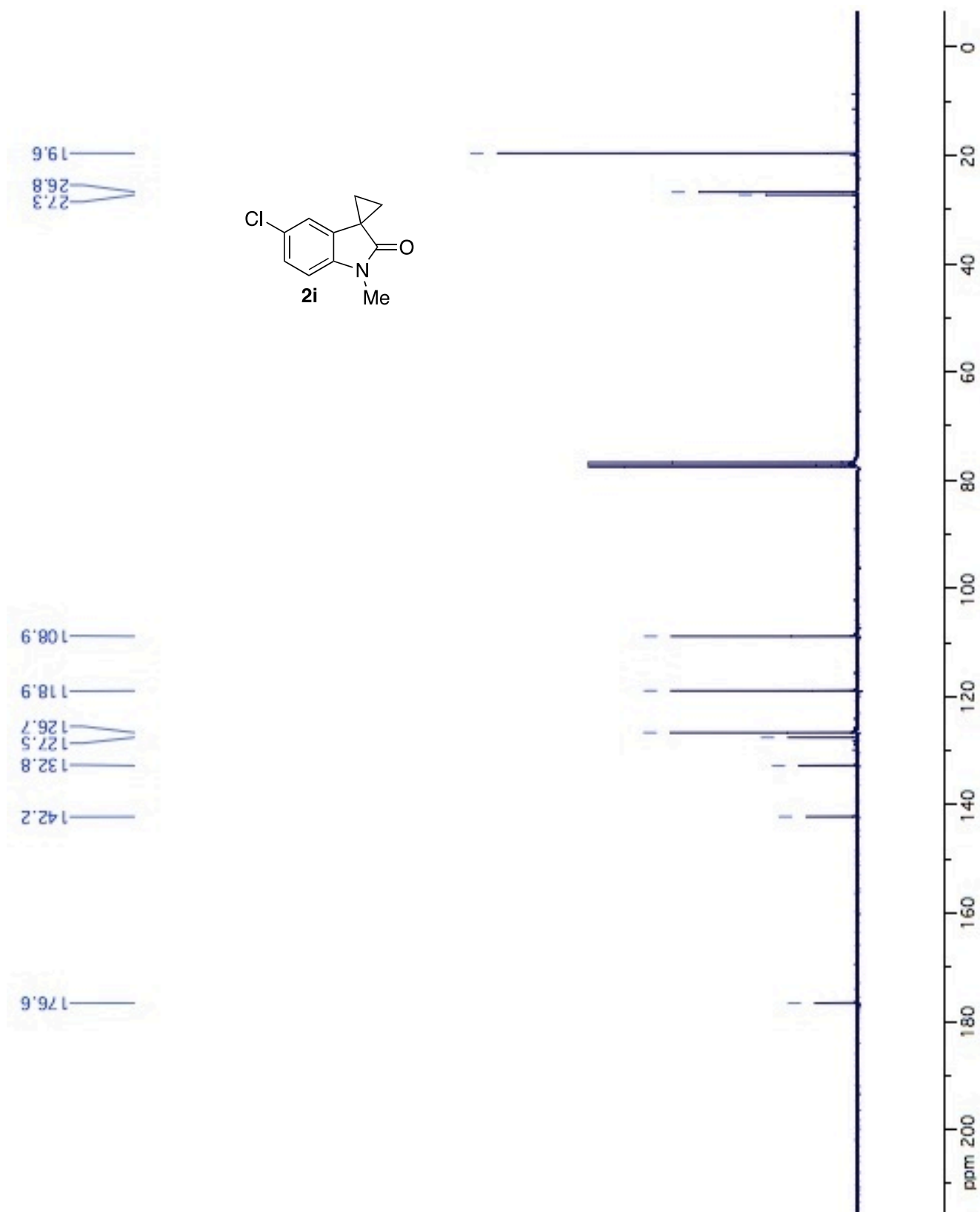


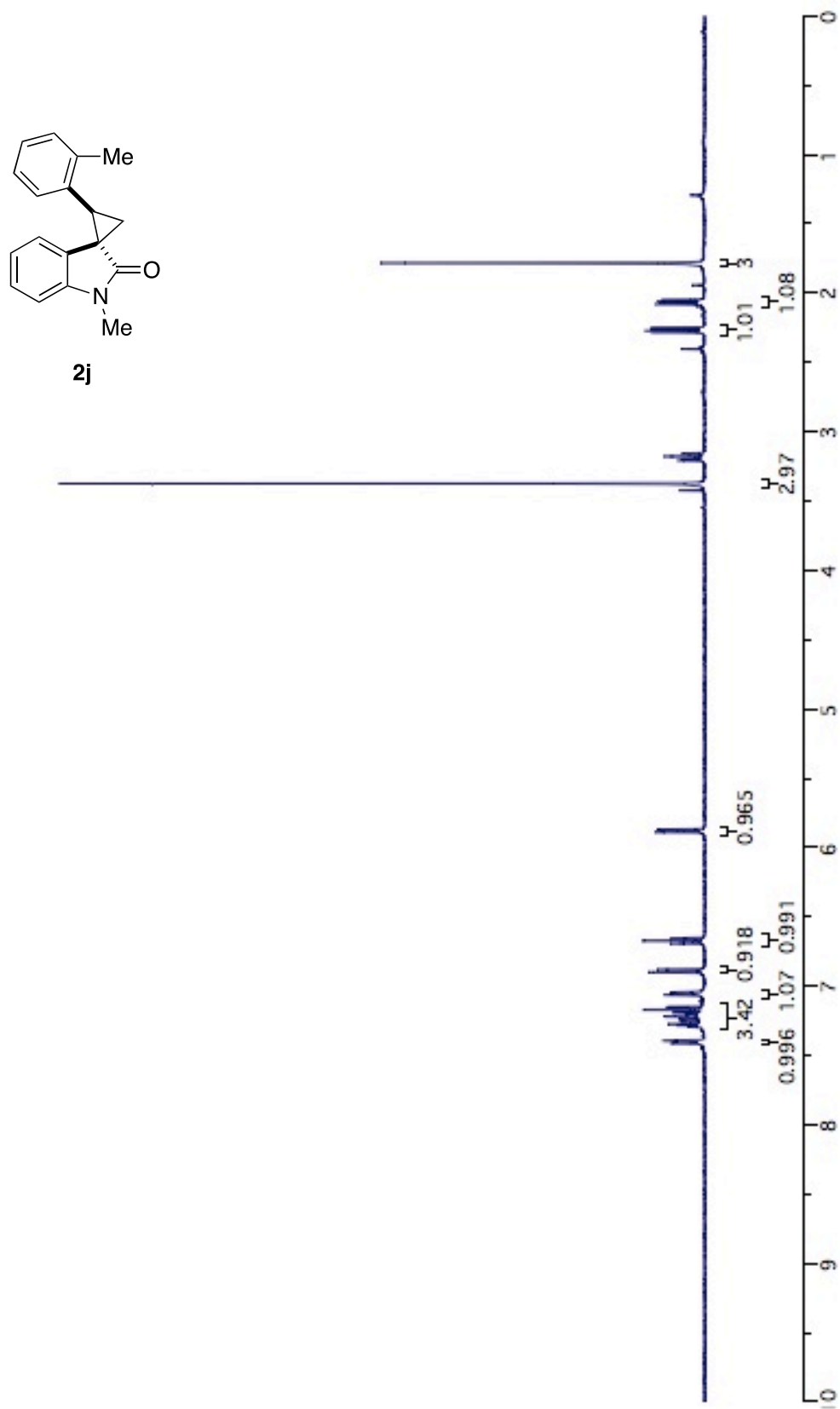
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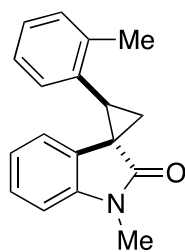




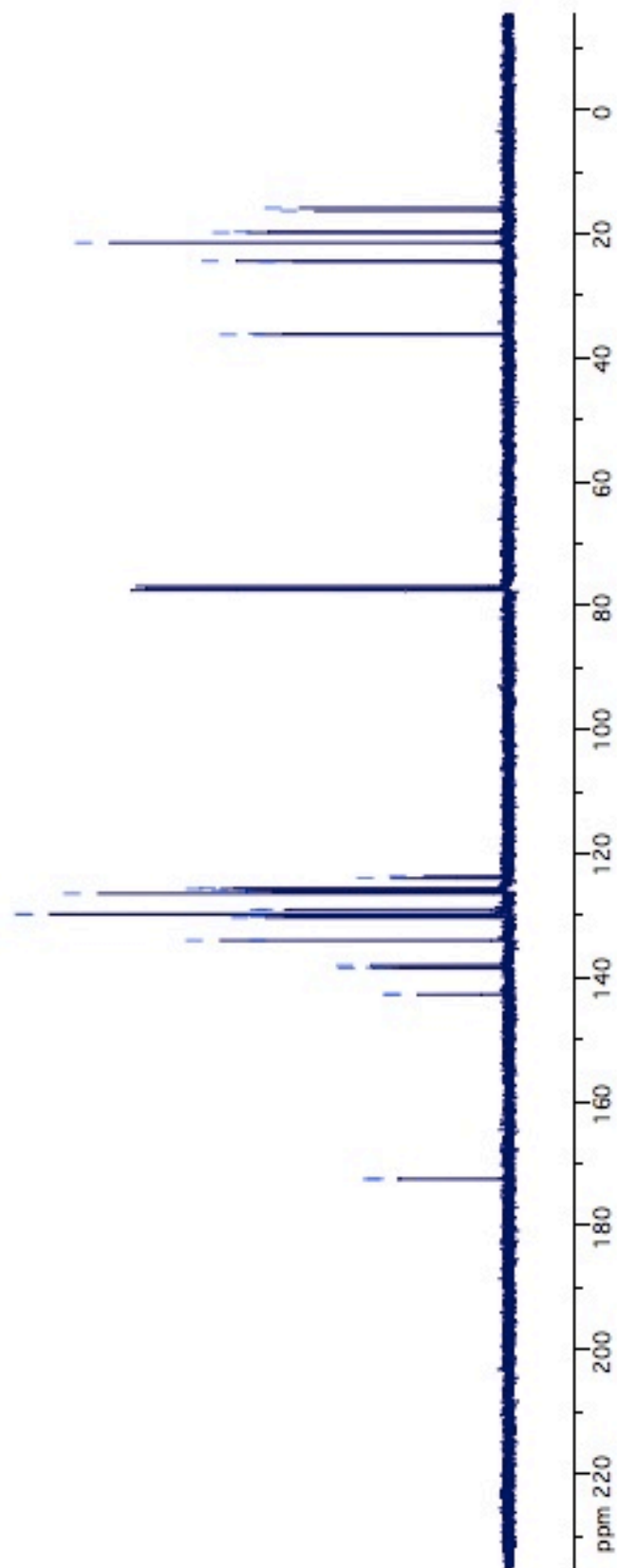


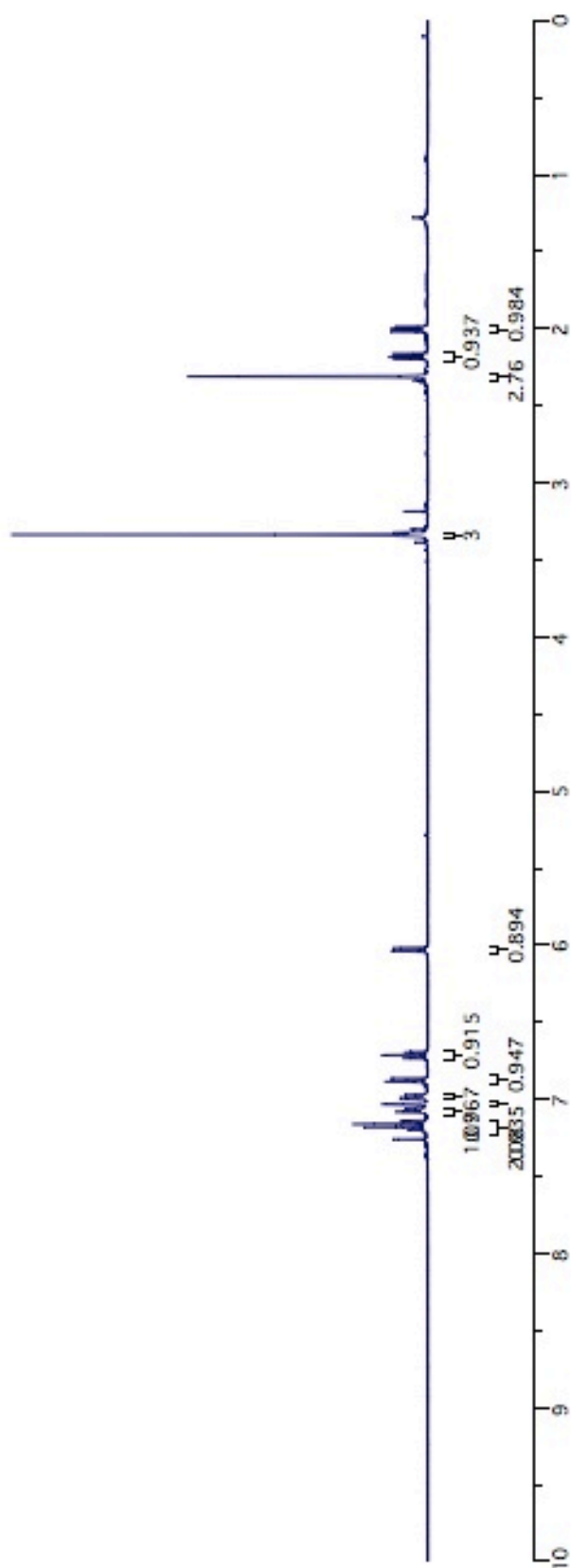
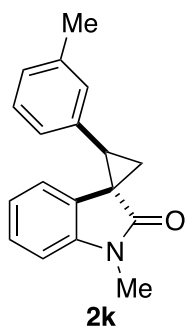


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15.9

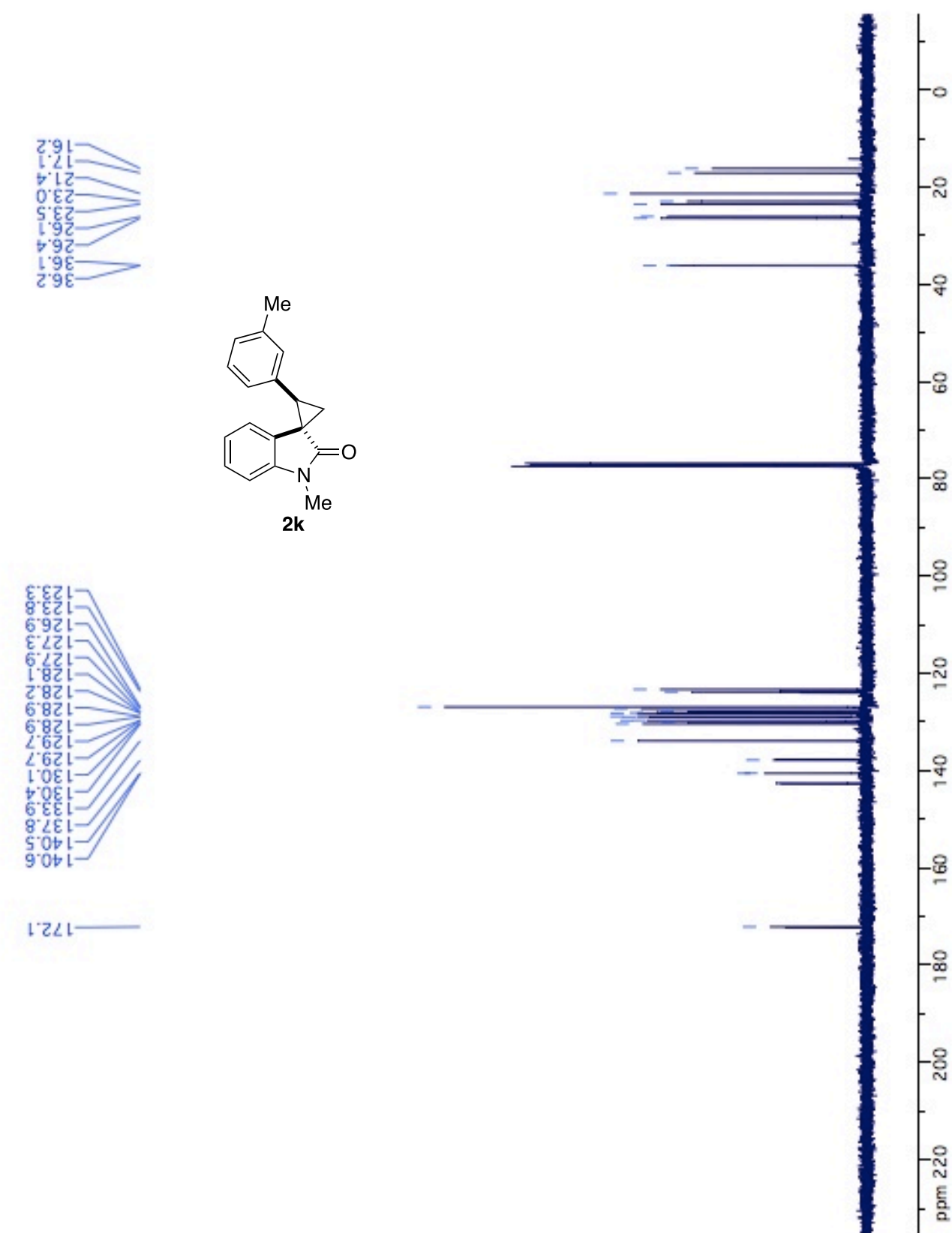
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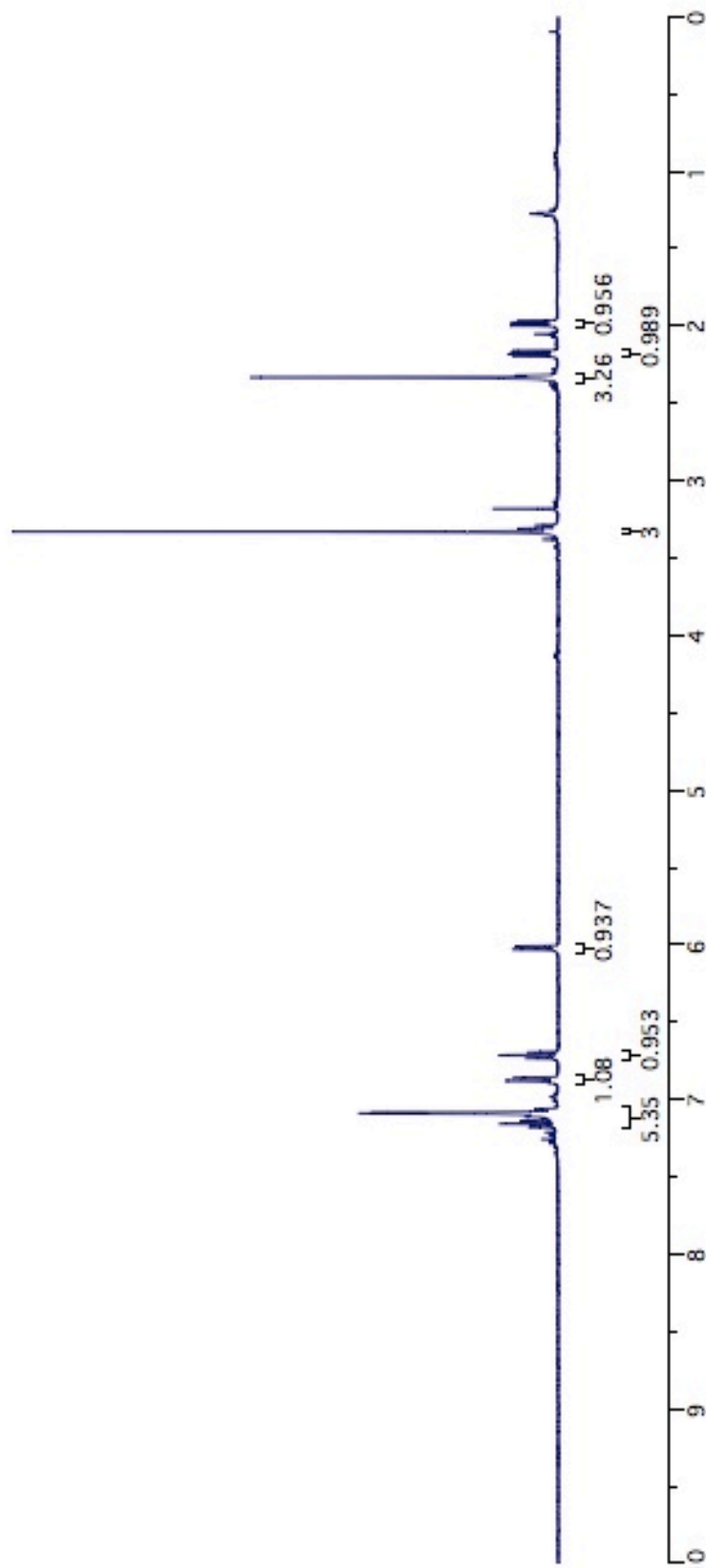
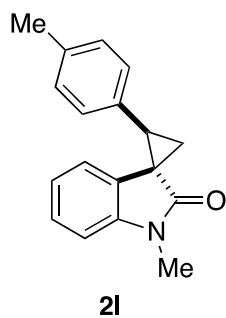
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130.2  
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129.7  
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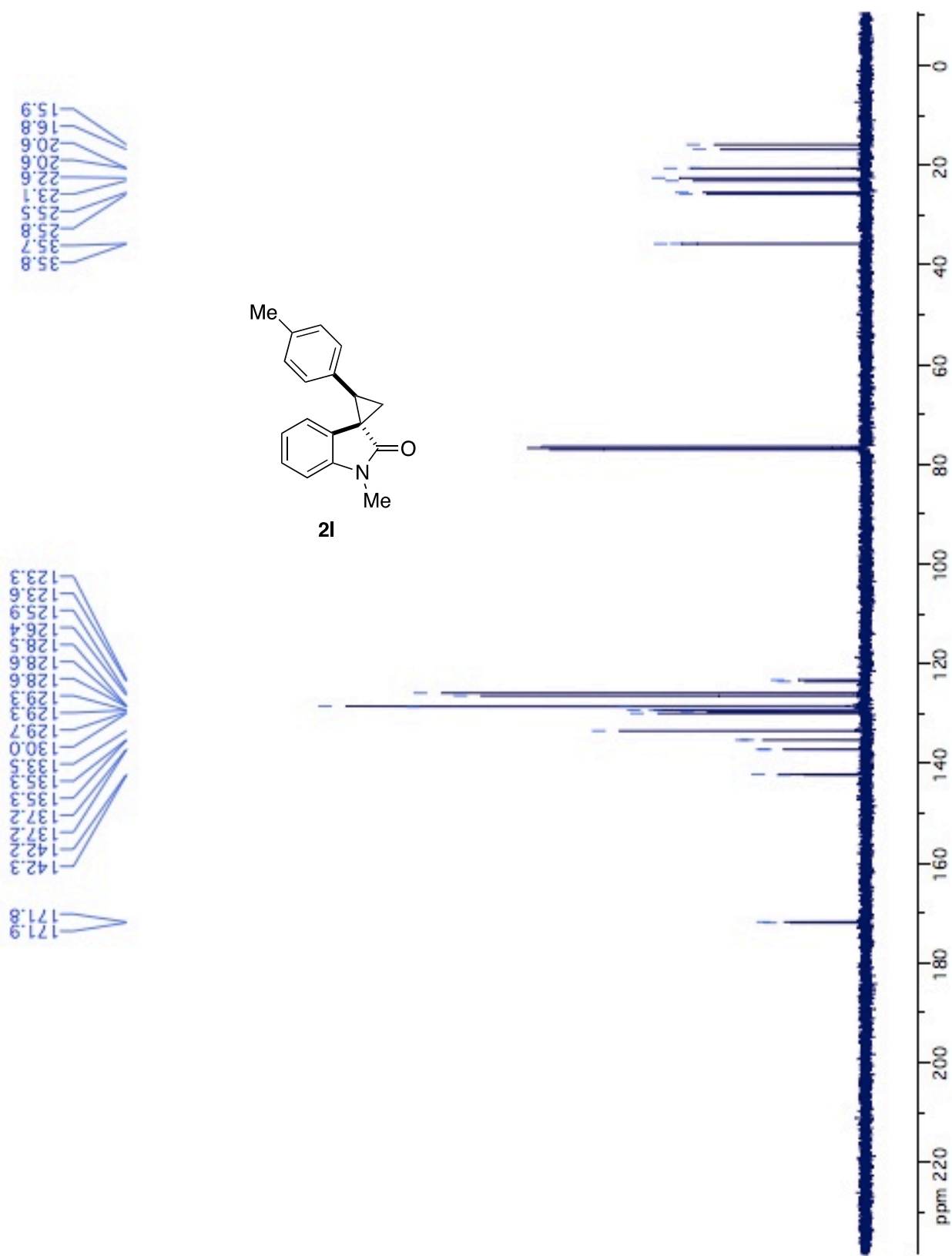


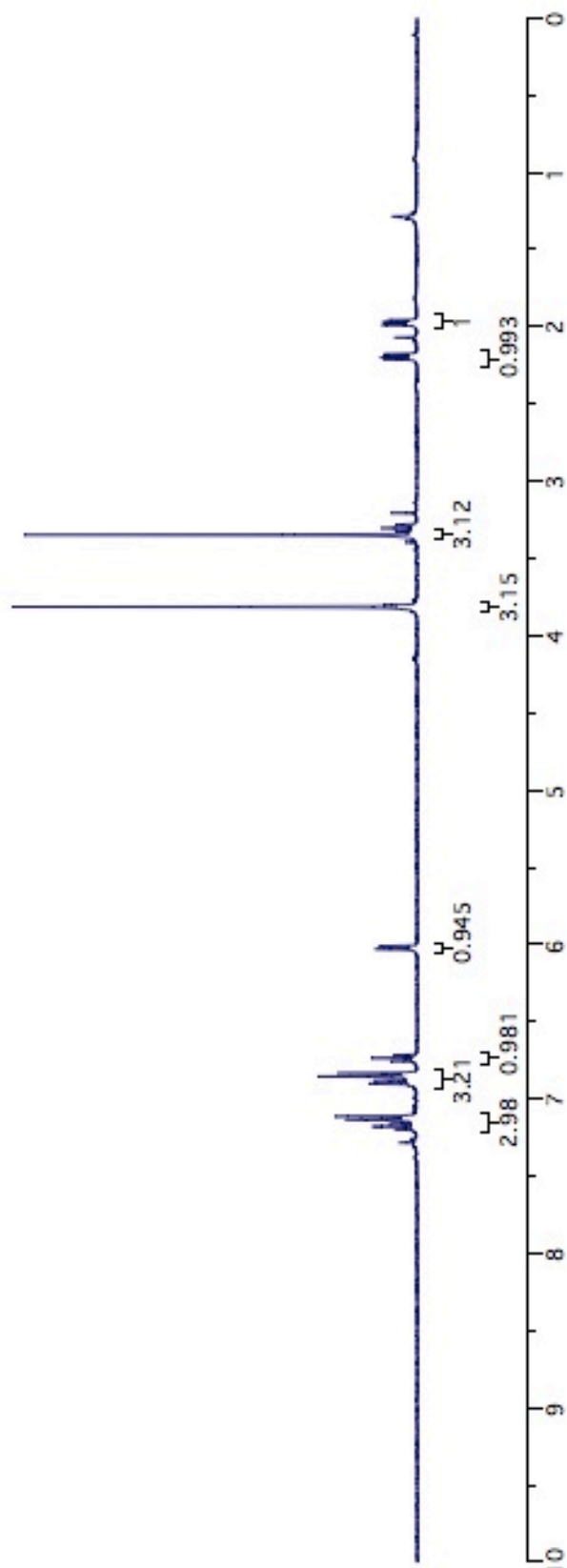
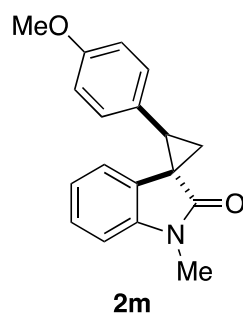


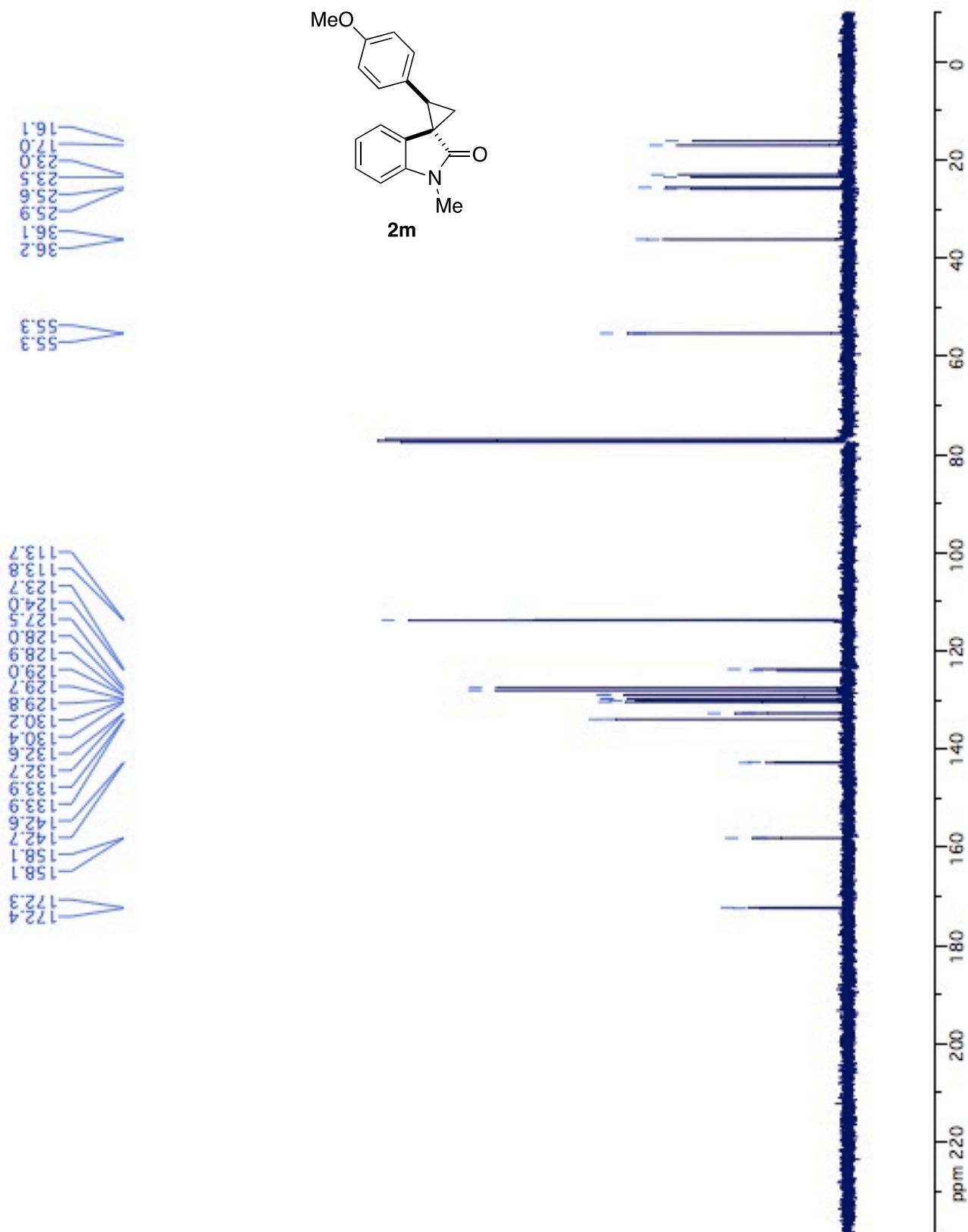


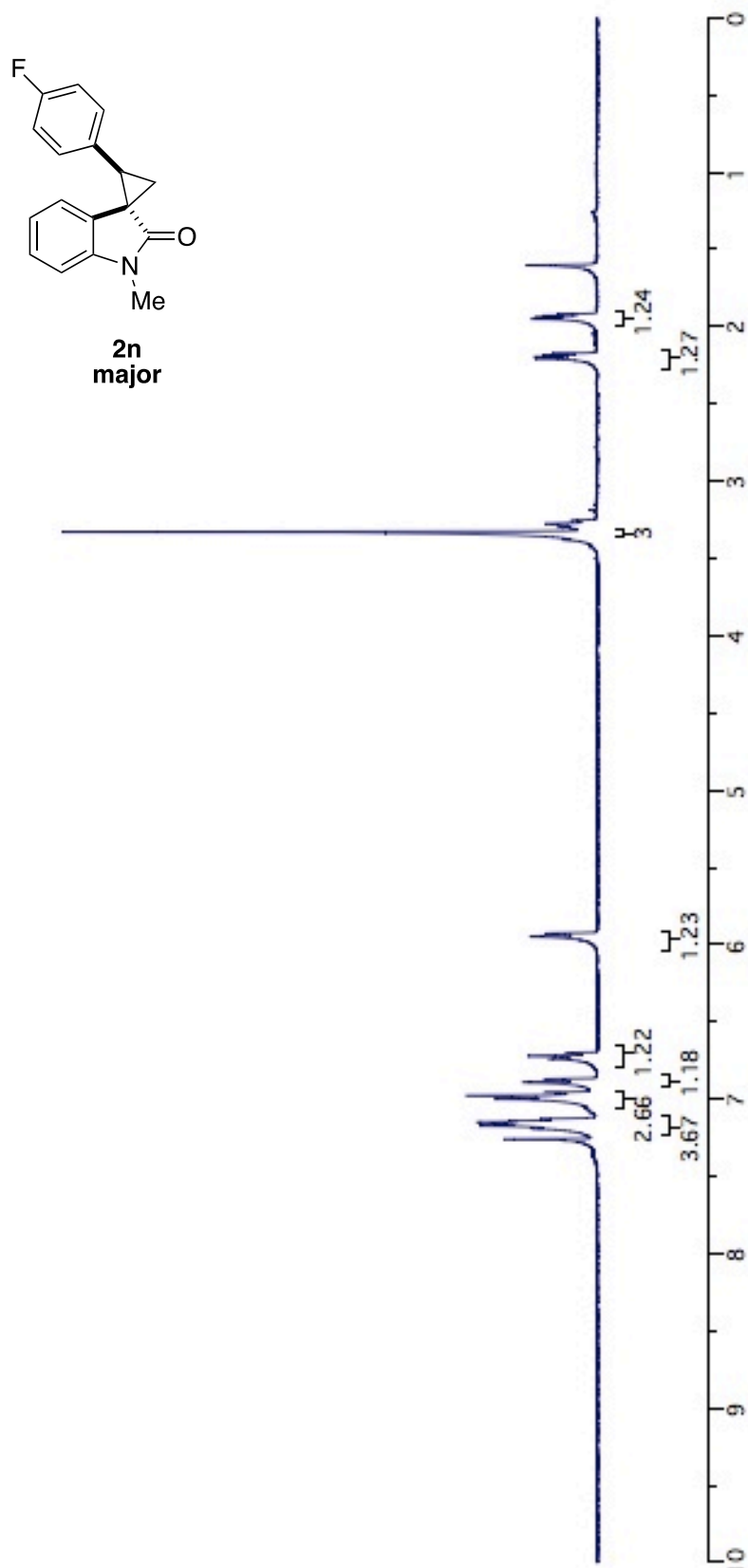


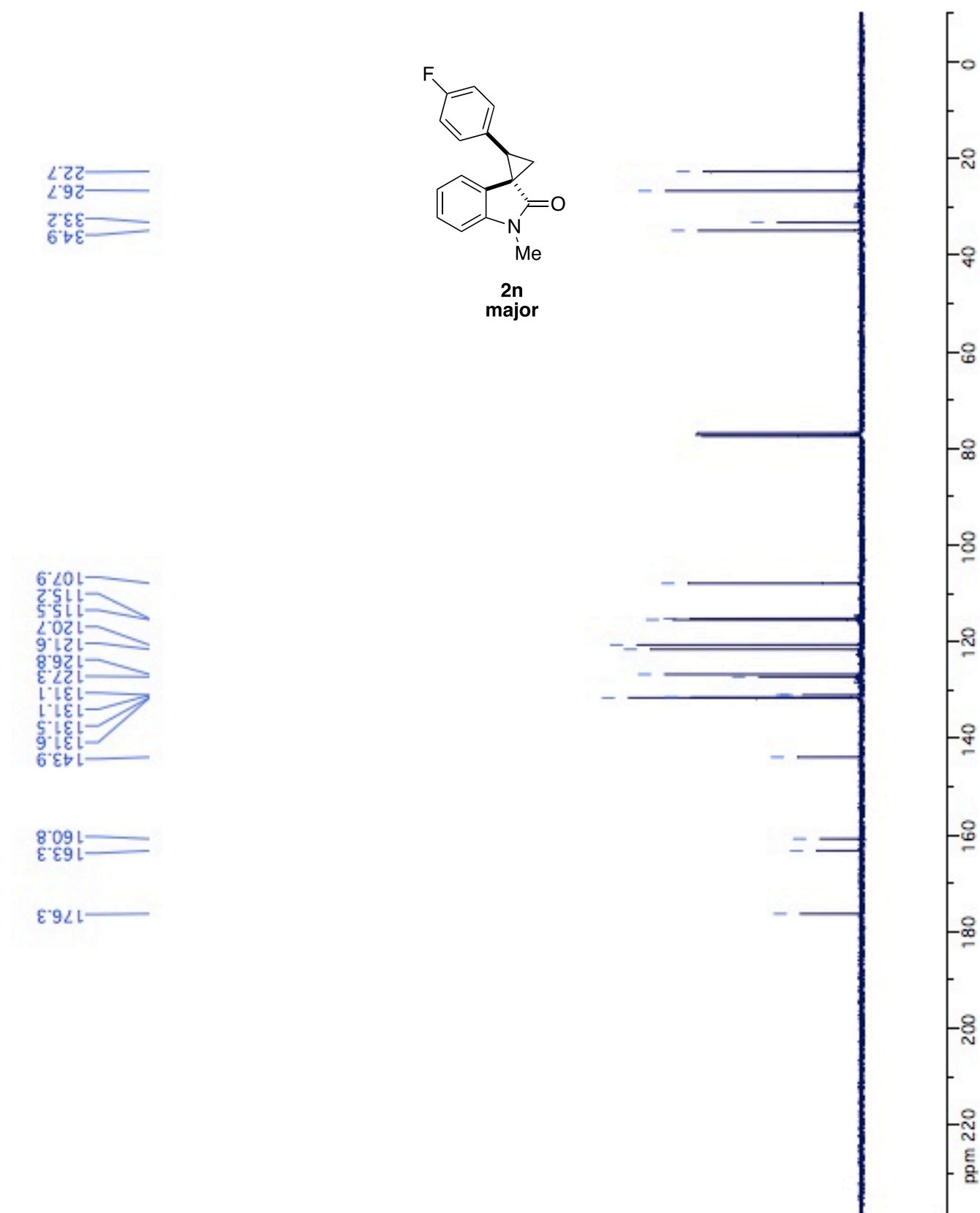




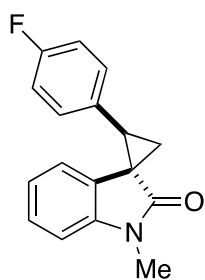








114.6  
114.6  
114.7



**2n**  
**major**

