

## Supporting Information

### IBiox[(-)-menthyl]– a Sterically Demanding Chiral NHC Ligand

Sebastian Würtz, Claudia Lohre, Roland Fröhlich, Klaus Bergander, Frank Glorius\*

*Westfälische Wilhelms-Universität Münster, Organisch-Chemisches Institut, Corrensstraße 40, 48149 Münster*

## Contents

1	General Information .....	2
2	Synthesis of IBiox[(-)-menthyl]·HOTf, the free NHC <b>1</b> and AgBr complex <b>7</b> .....	3
3	Synthesis of Starting Materials for $\alpha$ -Arylation .....	8
3.1	General Procedure for the Amide-Synthesis .....	12
3.2	Characterization of Starting Materials for $\alpha$ -Arylation .....	12
4	Oxindoles .....	17
4.1	General Procedure .....	18
4.2	Characterization of products .....	18
5	NMR Spectra.....	22
5.1	Ligand Synthesis .....	22
5.2	Amide Starting Materials .....	32
5.3	Oxindoles .....	43
6	HPLC Data .....	51
7	Calculation of the Buried Volume of the IBiox-Ligands.....	59
7.1	NHC in conformation <b>6a</b> .....	60
7.2	NHC in conformation <b>6b</b> .....	63
7.3	NHC <b>1</b> in conformation <b>5</b> .....	66
7.4	NHC <b>1</b> in conformation <b>7</b> .....	70
8	X-ray Crystal Structure Analysis.....	74
9	Literature.....	77

## 1 General Information

All reactions were carried out in flame dried reaction vessels with Teflon screw caps under argon. All new compounds were fully characterized.

NMR-spectra were recorded on a Bruker ARX-300, AV-300, AV-400 MHz or on a Varian 600 unity plus or Varian INOVA 500. Chemical shifts ( $\delta$ ) are quoted in ppm downfield of tetramethylsilane. Coupling constants ( $J$ ) are quoted in Hz.

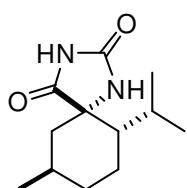
Infrared spectra were recorded on a Varian Associated FT-IR 3100 Excalibur. The wave numbers ( $\nu$ ) of recorded IR-signals are quoted in  $\text{cm}^{-1}$ . ESI-spectra were recorded on a Bruker Daltonics MicroTof.

GC/MS Spectra were recorded with a Agilent Technologies 7890A GC-system with Agilent 5975C VL MSD or 5975 inert Mass Selective Detector and a HP-5MS column (0.25 mm x 30 m, Film: 0.25  $\mu\text{m}$ ).

Optical rotations were measured on a Perkin Elmer 341 polarimeter, using a quartz cell ( $l = 100 \text{ mm}$ ) with a Na high-pressure lamp ( $\lambda = 589 \text{ nm}$ ) or Hg lamp ( $\lambda = 365 \text{ nm}$ ).

## 2 Synthesis of IBiox[(-)-menthyl]·HOTf, the free NHC 1 and AgBr complex 7

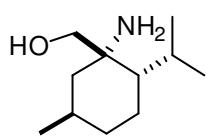
### (5S,6S,9R)-6-Isopropyl-9-methyl-1,3-diazaspiro[4.5]decane-2,4-dione (2) <sup>[1]</sup>



Following a modified procedure of Munday<sup>[2]</sup> and Edwards<sup>[3]</sup>, L-(-)-menthone (15.43 g, 100 mmol, 1 eq), KCN (7.16 g, 110 mmol, 1.1 eq) and  $(\text{NH}_4)_2\text{CO}_3$  (75.0 g, 480 mmol, 4.8 eq) were suspended in EtOH/H<sub>2</sub>O (1:1, 310 mL). While heating the resulting mixture to 60 °C all solids dissolved.

After stirring at 60 °C for 17 h, the reaction mixture was cooled to 0 °C, the resulting precipitate was filtered and washed with H<sub>2</sub>O. The white precipitate was collected and recrystallized from hot EtOH (300 mL) to afford a single diastereomer as colorless needles (19.7 g, 87.8 mmol, 88%). <sup>1</sup>H NMR (400 MHz, d<sub>6</sub>-DMSO):  $\delta$  = 0.78-0.84 (m, 9H, 3xCH<sub>3</sub>), 0.84-0.96 (m, 1H, CH), 1.22-1.30 (m, 2H, 2xCH), 1.36-1.70 (m, 6H, 3xCH<sub>2</sub>), 8.31 (s, 1H, NH), 10.78 (s, 1H, NH); <sup>13</sup>C NMR (400 MHz, d<sub>6</sub>-DMSO):  $\delta$  = 18.1 (CH<sub>3</sub>), 21.3 (CH<sub>2</sub>), 21.8 (CH<sub>3</sub>), 23.1 (CH<sub>3</sub>), 27.2 (CH), 27.8 (CH), 34.0 (CH<sub>2</sub>), 44.2 (CH<sub>2</sub>), 45.6 (CH), 67.0 (C<sub>q</sub>), 156.5 (CO), 178.4 (CO);  $[\alpha]_D^{20}$  +12.6 (c 1.55 in EtOH).

### ((1S,2S,5R)-1-Amino-2-isopropyl-5-methylcyclohexyl)methanol (3)



After a modified procedure of Munday<sup>[2]</sup> (5S, 6S, 9R)-6-isopropyl-9-methyl-1,3-diazaspiro[4.5]decane-2,4-dione (22.5 g, 100.3 mmol) was dissolved in aqueous H<sub>2</sub>SO<sub>4</sub> (60%, 250 mL) and stirred at 150 °C for 96 h.

After cooling to rt the mixture was diluted with H<sub>2</sub>O (65 mL) and filtered. The filtrate was neutralized with NaOH and the water was removed by freeze-drying. The white, solid residue was triturated with MeOH (1.3 L) and filtered again. After concentration of the filtrate in vacuo, the crude amino acid was obtained as a pale solid (11.79 g) that was used without further purification. The crude amino acid (11.79 g) was added slowly to a suspension of NaBH<sub>4</sub> (7.84 g, 207 mmol) in THF (210 mL). A solution of iodine (18.0 g, 71.0 mmol) in THF (75 mL) is added dropwise to the reaction mixture. After ceasing of the gas formation, the mixture was heated under reflux for 18 h. The mixture was cooled to rt and quenched with MeOH (caution, vigorous gas formation). After evaporation of the volatiles the residue was dissolved in aqueous KOH solution (20%, 210 mL), heated under reflux for 3 h, cooled to rt and extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 210 mL). The combined organic layers were dried over MgSO<sub>4</sub> and the solvents evaporated under reduced pressure. After purification by bulb to bulb distillation (125 °C, 0.2 mbar) the pure product was obtained as colorless needles (12.1 g,

65.3 mmol, 65%). **<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** δ = 0.84-0.92 (m, 10H), 0.99-1.03 (m, 1H, CH), 1.14-1.20 (m, 1H, CH), 1.34 (dq, *J* = 3.4 Hz, *J* = 12.9 Hz, 1H, CH), 1.49-1.66 (m, 6H, 3xCH<sub>2</sub>), 1.72-1.79 (m, 1H, CH), 1.98-2.12 (m, 1H, CH), 3.30 (d, *J* = 10.4 Hz, 1H, CH), 3.50 (d, *J* = 10.4 Hz, 1H, CH); **<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** δ = 18.6 (CH<sub>3</sub>), 21.1 (CH<sub>2</sub>), 22.5 (CH<sub>3</sub>), 24.4 (CH<sub>3</sub>), 25.7 (CH), 27.8 (CH), 35.2 (CH<sub>2</sub>), 46.5 (CH<sub>2</sub>), 47.7 (CH), 56.0 (C<sub>q</sub>), 70.5 (CH<sub>2</sub>); **ESI-MS:** calculated for [C<sub>11</sub>H<sub>23</sub>NOH]<sup>+</sup>: 186.1852, found: 186.1865; **ATR-FTIR [cm<sup>-1</sup>]:** 3366.5, 2949.7, 2921.1, 2867.7, 1455.5, 1049.4. [α]<sub>D</sub><sup>20</sup> -18 (c 1.33 in CHCl<sub>3</sub>).

### N,N'-Bis((1S,2S,5R)-1-(hydroxymethyl)-2-isopropyl-5-methylcyclohexyl)oxalamide

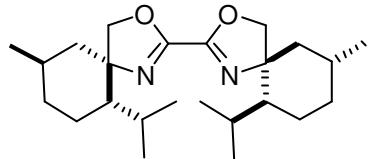
((1S,2S,5R)-1-amino-2-isopropyl-5-methylcyclohexyl)methanol (5.0 g, 27 mmol, 2.1 eq) was dissolved in toluene (65 mL) and treated with diethyloxalate (1.88 g, 12.9 mmol, 1.0 eq). The mixture was stirred at 90 °C for 18 h. During cooling to 0 °C the product crystallized as colorless needles, that were filtered and washed with a small amount of cold toluene and hexane. The product (4.43 g, 10.4 mmol, 81%) was obtained in very good purity and was carried on without further purification. **<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ = 0.86-0.94 (m, 22 H), 1.29-1.37 (m, 4H), 1.14-1.51 (m, 2H), 1.68-1.71 (m, 2H), 1.79-1.82 (d, *J* = 13.1 Hz, 2H), 2.00 (sept, *J* = 6.8 Hz, 2H, 2xCH), 2.36 (d, *J* = 13.6 Hz, 2H), 3.49 (d, *J* = 12.0 Hz, 2H), 4.07 (bs, 2H, 2xOH), 4.19 (d, *J* = 12.0 Hz, 2H), 7.91 (s, 2H, NH); **<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):** δ = 17.8 (CH<sub>3</sub>), 20.9 (CH<sub>2</sub>), 22.2 (CH<sub>3</sub>), 24.1 (CH<sub>3</sub>), 25.5 (CH), 27.5 (CH), 34.4 (CH<sub>2</sub>), 40.4 (CH<sub>2</sub>), 49.6 (CH), 61.6 (C<sub>q</sub>), 69.4 (CH<sub>2</sub>), 159.7 (CO); **ESI-MS:** calculated for [C<sub>24</sub>H<sub>44</sub>N<sub>2</sub>O<sub>4</sub>Na]<sup>+</sup>: 447.3193, found: 447.3185; **ATR -FTIR [cm<sup>-1</sup>]:** 3415.7, 3383.9, 2955.1, 2926.0, 1670.5, 1501.7, 1053.6; [α]<sub>D</sub><sup>20</sup> +66.8 (c 1.03 in CHCl<sub>3</sub>).

### N,N'-Bis((1S,2S,5R)-1-(chloromethyl)-2-isopropyl-5-methylcyclohexyl)oxalamide

((1S,2S,5R)-1-amino-2-isopropyl-5-methylcyclohexyl)methanol (2.95 g, 6.9 mmol, 1.0 eq) was dissolved in toluene (70 mL) and treated with SOCl<sub>2</sub> (1.50 mL, 20.1 mmol, 2.9 eq) and stirred at 60 °C for 45 min and additional 3.5 h at 90 °C. After that time all gas formation ceased and the mixture was cooled to rt and all volatile materials were evaporated under reduced pressure. The yellowish solid product was used without further purification. **<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ = 0.90 (d, *J* = 6.4 Hz, 7H), 0.95 (d, *J* = 6.9 Hz, 7H), 0.98 (d, *J* = 6.9 Hz, 7H), 1.29-1.39 (m, 4H), 1.43-1.53 (m, 2H), 1.64-1.70 (m, 4H), 1.77-1.80 (m, 2H), 2.05-2.16 (m, 2H), 2.40-2.44 (m, 2H), 3.69 (d, *J* = 11.1 Hz, 2H), 4.28 (d, *J* =

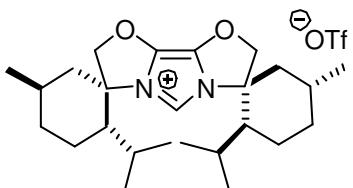
11.2 Hz, 2H), 7.68 (s, 2H); **<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)**: δ = 18.0 (CH<sub>3</sub>), 20.6 (CH<sub>2</sub>), 22.0 (CH<sub>3</sub>), 24.0 (CH<sub>3</sub>), 25.2 (CH), 27.7 (CH), 34.5 (CH<sub>2</sub>), 39.0 (CH<sub>2</sub>), 45.5 (CH), 47.6 (CH<sub>2</sub>), 60.9 (C<sub>q</sub>), 159.2 (C<sub>q</sub>); **ESI-MS**: calculated for [C<sub>24</sub>H<sub>42</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>2</sub>Na]<sup>+</sup>: 483.2516, found: 483.2521; **ATR -FTIR [cm<sup>-1</sup>]**: 3382.1, 2951.3, 2931.6, 1685.1, 1493.1;  $[\alpha]_D^{20} +54$  (c 0.985 in CHCl<sub>3</sub>).

### Bioxazoline 4



*N,N'*-bis((1*S*,2*S*,5*R*)-1-(chloromethyl)-2-isopropyl-5-methylcyclohexyl)oxalamide (2.9 g, 6.3 mmol, 1.0 eq) was dissolved in THF (130 mL) and treated with a solution of NaOH (529 mg, 13.23 mmol, 2.1 eq) in EtOH (26 mL). The mixture is stirred under reflux for 19 h. After cooling to rt, the solvents are evaporated and the residue was suspended in MTBE and washed with Na<sub>2</sub>CO<sub>3</sub>-solution (10%). The organic phase was dried over MgSO<sub>4</sub> and the solvents were evaporated under reduced pressure. The product was obtained as a white solid that was carried on without further purification (2.37 g, 6.1 mmol, 97%). **<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**: δ = 0.75 (d, *J* = 6.8 Hz, 6H, 2xCH<sub>3</sub>), 0.85 (d, *J* = 6.6 Hz, 6H, 2xCH<sub>3</sub>), 0.89-0.97 (m, 8H), 1.10-1.18 (m, 4H), 1.47-1.54 (m, 2H, 2xCH), 1.61-1.82 (m, 8H), 1.96-2.10 (m, 2H, 2xCH), 3.85 (d, *J* = 8.6 Hz, 2H, CH<sub>2</sub>), 4.33 (d, *J* = 8.5 Hz, 2H, CH<sub>2</sub>); **<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)**: δ = 18.0 (CH<sub>3</sub>), 22.0 (CH<sub>2</sub>), 22.2 (CH<sub>3</sub>), 24.1 (CH<sub>3</sub>), 26.4 (CH), 28.5 (CH), 35.1 (CH<sub>2</sub>), 49.4 (CH<sub>2</sub>), 50.8 (CH), 75.7 (C<sub>q</sub>), 78.1 (CH<sub>2</sub>), 153.1 (CO); **ESI-MS**: calculated for [C<sub>24</sub>H<sub>40</sub>N<sub>2</sub>O<sub>2</sub>H]<sup>+</sup>: 389.3163, found: 389.3138; **ATR -FTIR [cm<sup>-1</sup>]**: 2921.8, 2868.1, 1617.8, 1108.6, 939.2, 668.84;  $[\alpha]_D^{20} -26$  (c 1.075 in CHCl<sub>3</sub>).

### IBiox[(-)-menthyl]-HOTf (5)



AgOTf (500 mg, 1.55 mmol, 1.2 eq) was weighed in a Schlenk flask and suspended in CH<sub>2</sub>Cl<sub>2</sub> (6.4 mL). After addition of chloromethyl pivalate (0.22 mL, 1.55 mmol, 1.2 eq) the mixture was stirred at 20 °C (water bath) for 45 min in the dark.

Precipitation of AgCl is observed in 5 min. The supernatant was transferred to another flask filled with the bioxazoline 4 (500 mg, 1.29 mmol, 1.0 eq). The resulting clear solution was stirred at 60 °C for 12 h, when another 0.6 eq. of reagent were added and stirring continued for additional 6 h in the dark. The solution was cooled to rt and quenched with MeOH. The solvents were evaporated under reduced pressure and after purification by flash chromatography (silica, CH<sub>2</sub>Cl<sub>2</sub>/MeOH 90:1-10:1) and recrystallization with CH<sub>2</sub>Cl<sub>2</sub>/Et<sub>2</sub>O the

pure product was obtained as colorless crystals (508 mg, 0.91 mmol, 71%).  $R_f$  ( $\text{CH}_2\text{Cl}_2/\text{MeOH}$  20:1): 0.29;  **$^1\text{H NMR}$**  (400 MHz,  $\text{d}_6\text{-DMSO}$ ):  $\delta$  = 0.22 (d,  $J$  = 6.8 Hz, 6H, 2x $\text{CH}_3$ ), 0.89-1.05 (m, 14H), 1.36-1.57 (m, 4H), 1.63-1.72 (m, 4H), 1.83-2.03 (m, 8H), 4.82 (d,  $J$  = 9.4 Hz, 2H,  $\text{CH}_2$ ), 5.15 (d,  $J$  = 9.4 Hz, 2H,  $\text{CH}_2$ ), 9.10 (s, 1H, CH);  **$^{13}\text{C NMR}$**  (100 MHz,  $\text{d}_6\text{-DMSO}$ ):  $\delta$  = 15.6 ( $\text{CH}_3$ ), 20.9 ( $\text{CH}_2$ ), 21.7 ( $\text{CH}_3$ ), 23.4 ( $\text{CH}_3$ ), 25.3 (CH), 27.4 (CH), 33.2 ( $\text{CH}_2$ ), 44.1 ( $\text{CH}_2$ ), 47.2 (CH), 71.1 ( $\text{CH}_2$ ), 86.9 ( $\text{C}_q$ ), 114.8 (CH), 126.1 ( $\text{C}_q$ ); **ESI-MS**: calculated for  $[\text{C}_{25}\text{H}_{41}\text{N}_2\text{O}_2]^+$ : 401.3163, found: 401.3173; **Elemt. Anal.** calcd. for  $\text{C}_{26}\text{H}_{41}\text{F}_3\text{N}_2\text{O}_5\text{S}$ : C, 56.71; H, 7.50; N, 5.09. found: C, 56.60; H, 7.44; N, 5.01. **ATR -FTIR** [ $\text{cm}^{-1}$ ]: 3094.5, 2964.1, 1731.5, 1496.9, 1256.4, 1139.5, 1029.8, 635.8;  $[\alpha]_D^{20}$  + 27.4 (c 0.96 in  $\text{CHCl}_3$ ).

### High and low temperature NMR experiments of IBiox[(-)-menthyl]·HOTf (5):

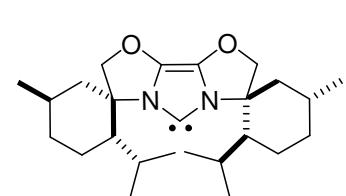
IBiox[(-)-menthyl]·HOTf only exists in one conformation:

**$^1\text{H NMR}$**  (600 MHz,  $\text{CD}_2\text{Cl}_2$ , 298K):  $\delta$  = 0.29 (d,  $J$  = 6.8 Hz, 6H, 2x $\text{CH}_3$ ), 0.97-1.00 (m, 14H), 1.46-1.54 (m, 6H), 1.80-2.16 (m, 10H), 4.68 (d,  $J$  = 9.4 Hz, 2H,  $\text{CH}_2$ ), 4.99 (d,  $J$  = 9.4 Hz, 2H,  $\text{CH}_2$ ), 8.62 (s, 1H, CH);

**$^1\text{H NMR}$**  (600 MHz,  $\text{CD}_2\text{Cl}_2$ , 193K):  $\delta$  = 0.03 (d,  $J$  = 6.2 Hz, 6H, 2x $\text{CH}_3$ ), 0.87-0.89 (m, 14H), 1.25-1.42 (m, 6H), 1.67-1.99 (m, 10H), 4.63 (d,  $J$  = 9.1 Hz, 2H,  $\text{CH}_2$ ), 4.91 (d,  $J$  = 9.1 Hz, 2H,  $\text{CH}_2$ ), 8.61 (s, 1H, CH);

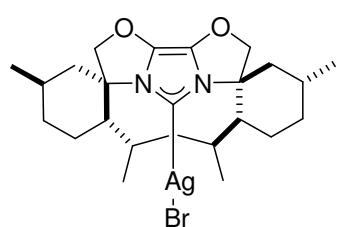
**$^1\text{H NMR}$**  (500 MHz,  $\text{d}_6\text{-DMSO}$ , 373K):  $\delta$  = 0.32 (d,  $J$  = 6.2 Hz, 6H, 2x $\text{CH}_3$ ), 0.93-0.99 (m, 14H), 1.49-1.59 (m, 4H), 1.68-1.76 (m, 4 H), 1.89-2.06 (m, 8H), 4.80 (d,  $J$  = 9.4 Hz, 2H,  $\text{CH}_2$ ), 5.13 (d,  $J$  = 9.4 Hz, 2H,  $\text{CH}_2$ ), 9.00 (s, 1H, CH).

### IBiox[(-)-menthyl] (1)



IBiox·HOTf (40 mg, 0.073 mmol, 1.0 eq.) was treated with  $\text{NaOtBu}$  (7 mg, 0.073 mmol, 1.0 eq.) in  $\text{d}_8\text{-THF}$  (0.8 mL) in a standard NMR tube to afford the free carbene in solution.  **$^1\text{H NMR}$**  (300 MHz,  $\text{d}_8\text{-THF}$ ):  $\delta$  = 0.88 (d,  $J$  = 6.8 Hz, 6H, 2x $\text{CH}_3$ ), 1.33-1.57 (m, 21H), 1.76-2.10 (m, 7H), 2.28-2.96 (m, 11), 4.88 (d,  $J$  = 8.7 Hz, 2H,  $\text{CH}_2$ ), 5.25 (d,  $J$  = 8.7 Hz, 2H,  $\text{CH}_2$ );  **$^{13}\text{C NMR}$**  (75 MHz,  $\text{d}_8\text{-THF}$ ):  $\delta$  = 17.2 ( $\text{CH}_3$ ), 22.0 ( $\text{CH}_2$ ), 23.1 ( $\text{CH}_3$ ), 24.8 ( $\text{CH}_3$ ), 27.3 (CH), 28.3 (CH), 36.6 ( $\text{CH}_2$ ), 48.5 ( $\text{CH}_2$ ), 51.5 (CH), 64.6 ( $\text{CH}_2$ ), 88.0 ( $\text{C}_q$ ), 126.6 ( $\text{C}_q$ ), 194.6 ( $\text{C}_q$ ).

**Ag-IBiox[(-)-menthyl] (7)<sup>[4]</sup>**

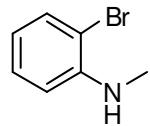


A Schlenk flask was charged with IBiox[(-)-menthyl]·HOTf salt (150mg, 0.27 mmol, 1.0 eq.), Ag<sub>2</sub>O (63 mg, 0.27 mmol, 1.0 eq.), NaBr (139 mg, 1.35 mmol, 5 eq.), and then CH<sub>2</sub>Cl<sub>2</sub> (6 mL) was added. The resulting solution was stirred in the dark at rt for 12 h.

The resulting precipitate was filtered over Celite and washed with CH<sub>2</sub>Cl<sub>2</sub> (3 x 20 mL). The combined filtrates were collected, and the solvent was evaporated under reduced pressure. After crystallization from CH<sub>2</sub>Cl<sub>2</sub>/hexane the pure product was obtained as colorless crystals (151 mg, 0.26 mmol, 96%). R<sub>f</sub> (CH<sub>2</sub>Cl<sub>2</sub>/MeOH 10:1): 0.87; **<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**: 0.30 (d, *J* = 6.8 Hz, 6H, 2xCH<sub>3</sub>), 0.93-0.95 (m, 14H), 1.21-1.39 (m, 4H), 1.67-1.73 (m, 2H), 1.89-1.95 (m, 2H), 2.03-2.15 (m, 4H), 2.20-2.35 (m, 2H), 3.16-3.32 (m, 2H, CH<sub>2</sub>), 4.42 (d, *J* = 9.4 Hz, 2H, CH<sub>2</sub>), 4.65 (d, *J* = 9.4 Hz, 2H, CH<sub>2</sub>); **<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)**: δ = 16.6 (CH<sub>3</sub>), 22.7 (CH<sub>3</sub>), 22.8 (CH<sub>2</sub>), 24.4 (CH<sub>3</sub>), 30.5 (CH), 34.1 (CH), 45.8 (CH<sub>2</sub>), 51.5 (CH), 67.8 (C<sub>q</sub>), 88.3 (CH<sub>2</sub>), 127.5 (C<sub>q</sub>); 156.9 (dd, *J* (<sup>13</sup>C, <sup>109</sup>Ag) = 275.9 Hz, *J* (<sup>13</sup>C, <sup>107</sup>Ag) = 240.2 Hz, C<sub>q</sub>); **ESI-MS**: calculated for [C<sub>25</sub>H<sub>40</sub>N<sub>2</sub>O<sub>2</sub>AgBrN<sub>2</sub>O<sub>2</sub>Na]<sup>+</sup>: 611.1199, found: 611.1193; **Elemt. Anal.** calcd. for C<sub>25</sub>H<sub>40</sub>AgBrN<sub>2</sub>O<sub>2</sub>: C, 51.03; H, 6.85; N, 4.76. found: C, 51.01; H, 6.92; N, 4.82. **ATR - FTIR [cm<sup>-1</sup>]**: 2958, 2924, 2857, 1754, 1433, 1297, 976, 937, 806, 741, 686, 655, 602, 596; **[α]<sub>D</sub><sup>20</sup>** +71 (c 0.284 in CHCl<sub>3</sub>).

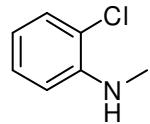
### 3 Synthesis of Starting Materials for $\alpha$ -Arylation

#### 2-Bromo-N-methylaniline<sup>[5]</sup>



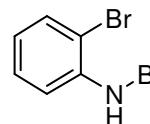
Following a procedure of Barluenga,<sup>[6]</sup> 2-bromoaniline (5g, 29.1 mmol, 2 eq) was dissolved in THF (30 mL). A solution of *n*-BuLi (1.6 M in hexane, 9.1 mL, 14.55 mmol, 1.0 eq) was added slowly at -40 °C and the resulting red mixture was stirred for 15 min at the same temperature. After cooling to -60 °C, iodomethane (0.91 mL, 14.6 mmol, 1.0 eq) was added slowly and the mixture was allowed to warm to rt and stirred for additional 14 h at rt. The mixture was quenched by adding H<sub>2</sub>O (20 ml) and the organic phase was separated. The aqueous phase was extracted with EtOAc (3 x 30 mL) and the combined organic phases were washed with sat. NaHCO<sub>3</sub>-solution dried over MgSO<sub>4</sub> and the solvents were evaporated under reduced pressure. After purification by flash chromatography (silica, pentane/EtOAc = 50:1) the pure product was obtained as a yellow liquid (2.41 g, 13.0 mmol, 89%). R<sub>f</sub> (pentane/EtOAc 20:1): 0.38; **1H NMR (300 MHz, CDCl<sub>3</sub>)**: δ = 0.22 (s, 3H, CH<sub>3</sub>), 4.32 (bs, 1H, NH), 6.47-6.57 (m, 2H, CH<sub>ar</sub>); **13C NMR (75 MHz, CDCl<sub>3</sub>)**: δ = 30.6 (CH<sub>3</sub>), 109.6 (C<sub>q</sub>), 110.8, 117.6, 128.5, 132.2 (CH<sub>ar</sub>), 145.9 (C<sub>q</sub>).

#### 2-Chloro-N-methylaniline<sup>[7]</sup>



Prepared from 2-chloroaniline (5g, 39.2 mmol, 2 eq) following the procedure described above gave the title compound after purification by flash chromatography (silica, pentane/EtOAc = 50:1) as colorless oil (2.02 g, 14.3 mmol, 73 %). R<sub>f</sub> (pentane/EtOAc 20:1): 0.63; **1H NMR (400 MHz, CDCl<sub>3</sub>)**: δ = 2.93 (s, 3H, CH<sub>3</sub>), 4.41 (bs, 1H, NH), 6.71 (td, *J* = 7.5 Hz, *J* = 1.2 Hz, 1H, CH<sub>ar</sub>), 6.78 (d, *J* = 8.0 Hz, 1H, CH<sub>ar</sub>), 7.17-7.21 (m, 1H, CH<sub>ar</sub>), 7.26-7.28 (m, 1H, CH<sub>ar</sub>).

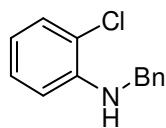
#### 2-Bromo-N-benzylaniline<sup>[8]</sup>



Following the procedure of Barluenga,<sup>[6]</sup> 2-bromoaniline (3.8 mL, 35 mmol, 2.0 eq) was dissolved in THF (40 mL), a solution of *n*-BuLi (1.6 M in hexane, 10.9 mL, 17.5 mmol, 1.0 eq) was added slowly at -40 °C and the resulting mixture was stirred for 15 min at the same temperature. After cooling to -60 °C benzyl bromide (2.1 mL, 17.5 mmol, 1.0 eq) was added. The mixture was stirred at rt overnight and quenched with H<sub>2</sub>O (40 mL). After extraction with EtOAc (3 x 30 mL), the combined organic phases were washed with sat. NaHCO<sub>3</sub>-solution (100 mL), dried over Na<sub>2</sub>SO<sub>4</sub> and the solvents are evaporated under reduced pressure. After purification by flash chromatography

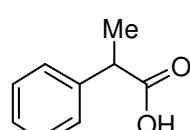
(silica, pentane/EtOAc = 50:1) the pure product was obtained as colorless crystals (4.59 g, 17.5 mmol, 100%).  $R_f$  (pentane/EtOAc 50:1): 0.23; **1H NMR (300 MHz, CDCl<sub>3</sub>)**:  $\delta$  = 4.39 (d,  $J$  = 5.5 Hz, 2H, CH<sub>2</sub>), 4.75 (bs, 1H, NH), 6.54-6.61 (m, 2H, CH<sub>ar</sub>), 7.09-7.14 (m, 1H, CH<sub>ar</sub>), 7.25-7.36 (m, 5H, CH<sub>ar</sub>), 7.43 (dd,  $J$  = 1.5 Hz,  $J$  = 7.8 Hz, 1H, CH<sub>ar</sub>).

### **2-Chloro-N-benzylaniline<sup>[9]</sup>**



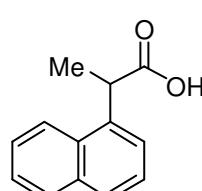
Prepared from 2-chloroaniline (3.7 mL, 35 mmol, 2 eq) following the procedure described above gave the title compound after purification by flash chromatography (silica, pentane/EtOAc = 50:1) as colorless oil (2.91 g, 77%).  $R_f$  (pentane/EtOAc 50:1): 0.19; **1H NMR (300 MHz, CDCl<sub>3</sub>)**:  $\delta$  = 4.40 (d,  $J$  = 5.6 Hz, 2H, CH<sub>2</sub>), 4.76 (bs, 1H, NH), 6.61-6.66 (m, 2H, CH<sub>ar</sub>), 7.06-7.11 (ddd,  $J$  = 1.5 Hz,  $J$  = 7.4 Hz,  $J$  = 8.2 Hz, 1H, CH<sub>ar</sub>), 7.25-7.36 (m, 6H, CH<sub>ar</sub>).

### **2-Phenylpropionic acid<sup>[10]</sup>**



Following a procedure of A. Bruggink and B. Zwanenburg,<sup>[10]</sup> a solution of NaClO<sub>2</sub> (17.9 g, 197 mmol) in H<sub>2</sub>O (75 mL) was added to a mixture of hydratropaldehyde (15.0 mL, 113 mmol, 1 eq) in MeCN (75 mL), aqueous H<sub>2</sub>O<sub>2</sub> (30%, 13.3 mL, 130 mmol, 1.15 eq) and NaH<sub>2</sub>PO<sub>4</sub>·12H<sub>2</sub>O (9.14 g, 27 mmol) in H<sub>2</sub>O (30 mL) while keeping the temperature between 0-10 °C. The mixture was stirred at the same temperature for 1.5 h until the gas formation (O<sub>2</sub>) ceased. To the stirred solution was added Na<sub>2</sub>SO<sub>3</sub> (2 g) to destroy unreacted HOCl and H<sub>2</sub>O<sub>2</sub>, followed by the addition of NaHCO<sub>3</sub> until a pH 9–10 was reached. The resulting mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (4x), acidified with concentrated hydrochloride until pH=1–2 and extracted with dichloromethane (4x). The combined organic layers from the acidic extraction were dried over MgSO<sub>4</sub> and concentrated under reduced pressure to obtain the pure product as yellowish oil (15.1 g, 100.6 mmol, 89 %). **1H NMR (300 MHz, CDCl<sub>3</sub>)**:  $\delta$  = 1.51 (d,  $J$  = 7.2 Hz, 3H, CH<sub>3</sub>), 3.73 (q,  $J$  = 7.2 Hz, 1H, CH), 7.36-7.23 (m, 5H, CH<sub>ar</sub>), 11.18 (br, 1H, OH).

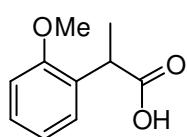
### **2-(Naphthalen-1-yl)propanoic acid<sup>[11]</sup>**



Following a modified procedure of Thompson,<sup>[11]</sup> *n*-BuLi (1.6 M in hexane, 68.8 mL, 110 mmol, 2.2 eq) was added dropwise to a solution of diisopropylamin (17.1 mL, 110 mmol, 2.2 eq) in THF (250 mL) at -78 °C. After stirring for additional 40 min at the same temperature a solution of 1-naphthylacetic acid (9.31 g, 50 mmol, 1.0 eq) in THF (50 mL) was added dropwise at -78 °C.

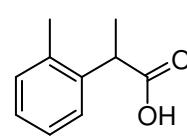
The mixture was warmed to 0 °C and stirred for additional 1 h. After cooling to –78 °C, iodomethane (4.7 mL, 75 mmol, 1.5 eq) was added in one portion. The mixture was allowed to warm to rt overnight, quenched by adding of H<sub>2</sub>O (25 mL) to obtain a clear yellow solution that was concentrated under reduced pressure. The residue is taken up in H<sub>2</sub>O, acidified with HCl (1M) and extracted with Et<sub>2</sub>O (6x, altogether 1 L). The combined organic phases were dried over MgSO<sub>4</sub> and the solvents evaporated under reduced pressure. After purification by flash chromatography (silica, pentane/EtOAc = 5:1-1:1) the pure product was obtained as a colorless solid (8.44 g, 42.2 mmol, 84%). R<sub>f</sub> (pentane/EtOAc 2:1): 0.1; **1H NMR (300 MHz, CDCl<sub>3</sub>)**: δ = 1.72 (d, *J* = 7.1 Hz, 3H, CH<sub>3</sub>), 4.55 (q, *J* = 7.1 Hz, 1H, CH), 7.45-7.58 (m, 4H, CH<sub>ar</sub>), 7.79-7.81 (m, 1H, CH<sub>ar</sub>), 7.87-7.90 (m, 1H, CH<sub>ar</sub>), 8.10 (d, *J* = 8.3 Hz, 1H, CH<sub>ar</sub>), 11.0 (bs, 1H, COOH).

### **2-(2-Methoxyphenyl)propanoic acid<sup>[12]</sup>**



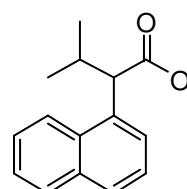
Prepared from 2-(2-methoxyphenyl)acetic (2.49 g, 15 mmol) acid following the procedure described above gave the title compound after purification by flash chromatography (silica, pentane/EtOAc = 5:1-2:1) as colorless solid (2.51 g, 13.9 mmol, 93%). R<sub>f</sub> (pentane/EtOAc 50:1): 0.19; **1H NMR (300 MHz, CDCl<sub>3</sub>)**: δ = 1.49 (d, *J* = 7.2 Hz, 3H), 3.84 (s, 3H), 4.10 (q, *J* = 7.2 Hz, 1H), 6.90 (d, *J* = 8.3 Hz, 1H), 6.96 (t, *J* = 7.5 Hz, 1H), 7.24-7.30 (m, 2H), 10.2 (bs, 1H); **13C NMR (75 MHz, CDCl<sub>3</sub>)**: δ = 16.8, 39.1, 55.5, 110.7, 120.8, 128.0, 128.3, 128.7, 156.6, 181.0.

### **2-*o*-Tolylpropanoic acid<sup>[13]</sup>**



Prepared from 2-*o*-tolylacetic acid (2.25 g, 15 mmol) following the procedure described above gave the title compound after purification by flash chromatography (silica, pentane/EtOAc = 5:1-1:1) as colorless solid ((2.03 g, 12.4 mmol, 82%). R<sub>f</sub> (pentane/EtOAc 50:1): 0.19; **1H NMR (300 MHz, CDCl<sub>3</sub>)**: δ = 1.41 (d, *J* = 7.1 Hz, 3H), 2.30 (s, 3H), 3.90 (q, *J* = 7.1 Hz, 1H), 7.09-7.16 (m, 3H), 7.20-7.22 (m, 1H), 10.96 (bs, 1H); **13C NMR (75 MHz, CDCl<sub>3</sub>)**: δ = 17.5, 19.6, 41.1, 126.4, 126.5, 127.2, 130.5, 135.9, 138.3, 181.2.

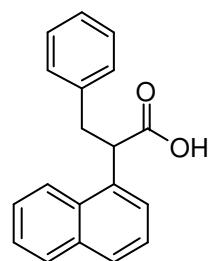
### **3-Methyl-2-(naphthalen-1-yl)butanoic acid<sup>[14]</sup>**



Following a modified procedure of Thompson<sup>[11]</sup> *n*-BuLi (1.6 M in hexane, 34.4 mL, 55 mmol, 2.2 eq) was added dropwise to a solution of diisopropylamin (8.5 mL, 60 mmol, 2.4 eq) in THF (60 mL) at –78 °C. After

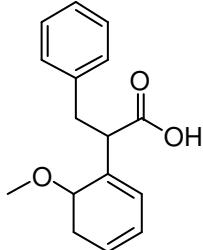
stirring for additional 40 min at the same temperature a solution of 1-naphthylacetic acid (4.66 g, 25 mmol, 1.0 eq) in THF (25 mL) was added dropwise at  $-78^{\circ}\text{C}$ . The mixture was warmed to  $0^{\circ}\text{C}$  and stirred for additional 1 h. After cooling to  $-78^{\circ}\text{C}$ , 2-bromopropane (3.5 mL, 37.5 mmol, 1.5 eq) was added in one portion. The mixture was allowed to warm to rt overnight, quenched by adding of  $\text{H}_2\text{O}$  (13 mL) to obtain a clear yellow solution that was concentrated under reduced pressure. The residue was taken up in  $\text{HCl}$  (1M, 40 mL) and extracted with  $\text{Et}_2\text{O}$  (3 x 20 mL). The combined organic phases were dried over  $\text{MgSO}_4$  and the solvents evaporated under reduced pressure. After purification by flash chromatography (silica, pentane/EtOAc = 10:3) the pure product was obtained as an off-white solid (3.21 g, 14 mmol, 56%).  $R_f$  (pentane/EtOAc 10:3): 0.16; **GC-MS**  $t_{\text{R}}$  (method 50\_40): 8.76 min; **MS-EI**: m/z(%) = 228 (79), 186 (91), 168 (63), 141 (100);  **$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**:  $\delta$  = 0.70 (d,  $J$  = 6.8 Hz, 2H), 1.19 (d,  $J$  = 6.4 Hz, 3H), 2.52-2.62 (m, 1H), 4.10 (d,  $J$  = 10.4 Hz, 1H), 7.44-7.56 (m, 4H), 7.63-7.65 (d,  $J$  = 6.4 Hz, 1H), 7.77 (d,  $J$  = 8.0 Hz,  $J$  = 7.2 Hz, 1H), 7.85-7.87 (m, 1H), 8.20 (d,  $J$  = 8.5 Hz, 1H), 10.5 (bs, 1H);  **$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )**:  $\delta$  = 20.0, 21.7, 31.2, 53.5, 123.2, 125.3, 125.5, 126.3, 127.9, 128.9, 132.3, 133.9, 134.0, 180.0; **ESI-MS**: calculated for  $[\text{C}_{15}\text{H}_{16}\text{O}_2\text{Na}]^+$ : 251.1043, found: 251.1036; **ATR -FTIR [cm $^{-1}$ ]**: 2969, 1698, 1414, 1301, 1217, 926, 797, 772, 737.

### 3- (4, 8-Dihydro-naphthalen-1-yl)-4-phenyl-butrylic acid



Prepared from 1-naphthylacetic acid (4.66 g, 25 mmol) acid following the procedure described above gave the title compound after purification by flash chromatography (silica, pentane/EtOAc = 10:1-5:1) as colorless solid (6.85 g, 24.8 mmol, 99%).  $R_f$  (pentane/EtOAc 5:1): 0.20;  **$^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )**:  $\delta$  = 3.23 (dd,  $J$  = 13.9 Hz,  $J$  = 5.8 Hz, 1H), 3.66 (dd,  $J$  = 13.9 Hz,  $J$  = 9.1 Hz, 1H), 4.77 (dd,  $J$  = 9.0 Hz,  $J$  = 5.8 Hz, 1H), 7.23 (m, 3 H,  $\text{CH}_{\text{ar}}$ ), 7.57 (m, 6 H,  $\text{CH}_{\text{ar}}$ ), 7.86 (d,  $J$  = 8.1 Hz, 1H,  $\text{CH}_{\text{ar}}$ ), 7.94 (dd,  $J$  = 7.2 Hz,  $J$  = 2.2 Hz, 1 H,  $\text{CH}_{\text{ar}}$ ), 8.19 (d,  $J$  = 8.1 Hz, 1 H,  $\text{CH}_{\text{ar}}$ ), 11.15 (bs, 1H, COOH );  **$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )**:  $\delta$  = 38.8, 48.7, 123.0, 125.2, 125.5, 125.7, 126.5, 126.6, 128.2, 128.4, 128.8, 129.0, 131.3, 134.0, 134.3, 139.0, 179.7; **ESI-MS**: calculated for  $[\text{C}_{19}\text{H}_{16}\text{O}_2\text{Na}]^+$ : 299.1043, found: 299.1029; **ATR -FTIR [cm $^{-1}$ ]**: 3062, 2636, 1416, 1314, 1250, 1229, 1080, 959, 761, 701, 665.

## 2-(2-Methoxyphenyl)-3-phenyl-propionic acid



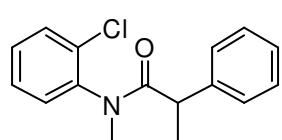
Prepared from 2-(2-methoxyphenyl)acetic acid (4.0 g, 24.1 mmol) following the procedure described above gave the title compound after purification by flash chromatography (silica, pentane/EtOAc = 50:1-20:1) as colorless solid (4.03 g, 15.7 mmol, 65%).  $R_f$  (pentane/EtOAc 5:1): 0.22;  **$^1H$  NMR (300 MHz, CDCl<sub>3</sub>)**:  $\delta$  = 3.06 (dd,  $J$  = 13.8 Hz,  $J$  = 7.2 Hz, 1H), 3.42 (dd,  $J$  = 13.7 Hz,  $J$  = 7.9 Hz, 1H), 3.80 (s, 3H), 4.38 (t,  $J$  = 7.5 Hz, 1 H), 6.94 (m, 3 H, CH<sub>ar</sub>), 7.23 (m, 6H, CH<sub>ar</sub>), 11.84 (bs, 1H, COOH);  **$^{13}C$  NMR (100 MHz, CDCl<sub>3</sub>)**:  $\delta$  = 38.0, 46.4, 55.5, 110.9, 120.7, 126.1, 126.9, 128.1, 128.5, 129.0, 139.3, 156.7, 179.9; **ESI-MS**: calculated for [C<sub>16</sub>H<sub>16</sub>O<sub>3</sub>Na]<sup>+</sup>: 279.0992, found: 279.0992; **ATR -FTIR [cm<sup>-1</sup>]**: 3024, 2941, 2841, 2619, 1697, 1601, 1492, 1414, 1339, 1300, 1237, 1017, 936, 820, 743, 695, 585.

### 3.1 General Procedure for the Amide-Synthesis

The carboxyl acid (1.2 eq) was heated with SOCl<sub>2</sub> (2.4 eq) under reflux for 2 h. After ceasing of the gas evolution, the mixture was cooled to rt and excess SOCl<sub>2</sub> was removed under reduced pressure. The resulting crude carbonyl chloride (1.2 eq) was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (0.28 M), treated with NEt<sub>3</sub> (2.0 eq) and the 2-haloaniline derivative (1.0 eq). The resulting mixture was stirred at rt for 12-24 h, diluted with Et<sub>2</sub>O (100 mL) and quenched with saturated NH<sub>4</sub>Cl-solution (100 mL). The organic layer was separated, washed with brine, dried over MgSO<sub>4</sub> and the solvents were evaporated under reduced pressure. The crude product was purified by flash chromatography (silica, pentane/EtOAc).

### 3.2 Characterization of Starting Materials for $\alpha$ -Arylation

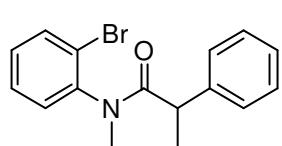
#### N-(2-Chlorophenyl)-N-methyl-2-phenylpropanamide (Table 2, entry 1)



Following the general procedure 3.1, 2-chloro-N-methylaniline was converted with 2-phenylpropanoyl chloride to the title compound after flash chromatography (silica, pentane/EtOAc = 10:1-2:1) as a yellow viscous oil (1.87 g, 6.83 mmol, 65%).  $R_f$  (pentane/EtOAc = 20:1): 0.11;  **$^1H$  NMR (400 MHz, CDCl<sub>3</sub>)**:  $\delta$  = 1.40-1.42 (m, 3H), 3.16 (s, 2H), 3.19 (s, 0.87H), 3.34 (q,  $J$  = 6.9 Hz, 0.71H), 3.55 (q,  $J$  = 7.0 Hz, 0.30H), 6.71 (dd,  $J$  = 7.8 Hz,  $J$  = 1.6 Hz, 0.68H), 6.95-6.97 (m, 2H), 7.12 (dd,  $J$  = 7.6 Hz,  $J$  = 1.4 Hz, 0.55 H), 7.15-7.20 (m, 3H), 7.30 (dt,  $J$  = 1.59 Hz,  $J$  = 7.97 Hz, 0.89H), 7.33-7.40 (m, 1.25H), 7.52 (dd,  $J$  = 8.0 Hz,  $J$  = 1.4 Hz, 0.68H);  **$^{13}C$  NMR (100 MHz, CDCl<sub>3</sub>)**:  $\delta$  = 38.0, 46.4, 55.5, 110.9, 120.7, 126.1, 126.9, 128.1, 128.5, 129.0, 139.3, 156.7, 179.9; **ESI-MS**: calculated for [C<sub>16</sub>H<sub>16</sub>ClNO]<sup>+</sup>: 294.1018, found: 294.1018; **ATR -FTIR [cm<sup>-1</sup>]**: 3024, 2941, 2841, 2619, 1697, 1601, 1492, 1414, 1339, 1300, 1237, 1017, 936, 820, 743, 695, 585.

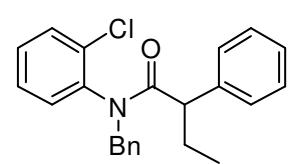
**MHz, CDCl<sub>3</sub>):** δ = 20.0, 20.5, 36.0, 36.1, 43.3, 43.8, 126.6, 127.4, 127.7, 127.8, 127.9, 128.1, 128.4, 129.4, 129.5, 130.0, 130.3, 130.8, 133.0, 133.9, 140.6, 140.7, 140.9, 141.7, 173.9, 174.0; **ESI-MS:** calculated for [C<sub>16</sub>H<sub>16</sub>ClONa]<sup>+</sup>: 296.0813, found: 296.0825; **ATR-FTIR [cm<sup>-1</sup>]:** 3029, 2933, 1666, 1482, 1378, 1131, 1056, 632.

**N-(2-Bromophenyl)-N-methyl-2-phenylpropanamide** (Table 2, entry 2)<sup>[15]</sup>



Following the general procedure 3.1, 2-bromo-N-methylaniline was converted with 2-phenylpropanoyl chloride to the title compound after flash chromatography (silica, pentane/EtOAc = 10:1-7:1) as a yellow viscous oil (1.74 g, 5.47 mmol, 68%). R<sub>f</sub> (pentane/EtOAc = 20:1): 0.15; **¹H NMR (400 MHz, CDCl<sub>3</sub>):** δ = 1.41 (d, J = 7.0 Hz, 0.91H, CH<sub>3</sub>), 1.43 (d, 6.9 Hz, 2.1H, CH<sub>3</sub>), 3.61 (s, 2.17H, CH<sub>3</sub>), 3.81 (s, 0.81H, CH<sub>3</sub>), 3.34 (q, J = 6.9 Hz, 0.75H, CH), 3.53 (q, J = 6.9 Hz, 0.25H, CH), 6.70 (dd, J = 7.7 Hz, J = 1.8 Hz, 0.75H, CH<sub>ar</sub>), 6.94-6.96 (m, 1.44H, CH<sub>ar</sub>), 7.00-7.02 (m, 0.53H, CH<sub>ar</sub>), 7.14-7.28 (m, 5H, CH<sub>ar</sub>), 7.35 (dd, J = 7.8 Hz, J = 1.7 Hz, 0.34H, CH<sub>ar</sub>), 7.43 (dt, J = 1.4 Hz, J = 7.4 Hz, 0.30H, CH<sub>ar</sub>), 7.57 (dd, J = 8.0 Hz, J = 1.4 Hz, 0.3H, CH<sub>ar</sub>), 7.70 (dd, J = 7.9 Hz, J = 1.5 Hz, 0.70H, CH<sub>ar</sub>); **¹³C NMR (100 MHz, CDCl<sub>3</sub>):** δ = 20.0, 20.6, 2x 36.1, 43.2, 44.0, 123.6, 124.2, 126.6, 126.7, 127.4, 128.0, 128.2, 2x 128.4, 128.6, 129.6, 129.7, 130.1, 130.8, 133.5, 134.0, 140.6, 141.7, 142.2, 173.7, 173.9.

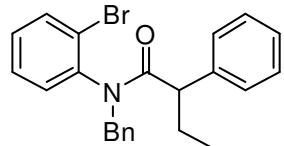
**N-Benzyl-N-(2-chlorophenyl)-2-phenylbutanamide** (Table 2, entry 3)



Following the general procedure 3.1, 2-chloro-N-benzylaniline (1.07 g, 5.0 mmol) was converted with 2-phenylbutanoyl chloride (1.09 g, 6.0 mmol) to the title compound after flash chromatography (silica, pentane/EtOAc = 40:1-10:1) as colorless solid (690 mg, 1.9 mmol, 38%). R<sub>f</sub> (pentane/EtOAc = 10:1): 0.29; **¹H NMR (400 MHz, CDCl<sub>3</sub>):** δ = 0.88 (t, J = 7.4 Hz, 0.9H), 0.95 (t, J = 7.4 Hz, 2.1H), 1.71-1.88 (m, 1H), 2.19-2.30 (m, 1H), 3.12 (d, J = 6.8 Hz, 0.33H), 3.14 (d, J = 6.8 Hz, 0.33H), 3.21 (t, J = 7.5 Hz, 0.30H), 3.96 (d, J = 14.3 Hz, 0.3H), 4.17, (d, J = 14.4 Hz, 0.7 H), 5.69 (d, J = 14.4 Hz, 0.7H), 5.87 (d, J = 14.3 Hz, 0.3H), 6.21 (dd, J = 1.6 Hz, 7.9 Hz, 0.7H), 6.93 (dd, J = 1.6 Hz, J = 7.8 Hz, 0.31H), 6.97 (dt, J = 1.4 Hz, J = 7.7 Hz, 0.7H), 7.01-7.40 (m, 7.71H), 7.48 (dd, J = 1.4 Hz, J = 8.0 Hz, 0.7H); **¹³C NMR (100 MHz, CDCl<sub>3</sub>):** δ = 12.6, 12.7, 28.5, 28.6, 2x 51.4, 51.7, 52.4, 124.9, 127.0, 127.1, 127.4, 127.4, 127.6, 128.1, 128.3, 2x 128.4, 2x 128.5, 129.1, 129.4, 129.6, 129.7, 130.4, 130.8, 132.3, 132.5, 133.3, 134.4, 137.3, 137.5, 138.8, 139.0, 139.3, 140.4, 173.1, 173.3. **ESI-MS:** calculated for: [C<sub>23</sub>H<sub>22</sub>ClONa]<sup>+</sup>

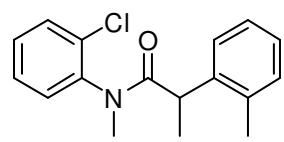
386.1282, found: 386.1282. **ATR-FTIR [cm<sup>-1</sup>]:** 3066, 2962, 1656, 1478, 1454, 1393, 1286, 1220, 1014, 763, 793, 697.

**N-Benzyl-N-(2-bromophenyl)-2-phenylbutanamide** (Table 2, entry 4)



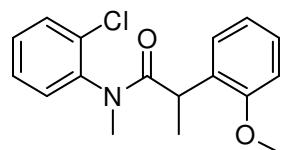
Following the general procedure 3.1, 2-bromo-*N*-benzylaniline (1.35 g, 5.2 mmol) was converted with 2-phenylbutanoyl chloride (1.27 g, 7.0 mmol) to the title compound after flash chromatography (silica, pentane/EtOAc = 30:1-10:1) as colorless solid (1.15 g, 2.8 mmol, 54 %).  $R_f$  (pentane/EtOAc = 50:1): 0.04; **<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):**  $\delta$  = 0.88 (t,  $J$  = 7.5 Hz, 0.9H), 0.97 (t,  $J$  = 7.4 Hz, 2.13H), 1.72-1.88 (m, 1H), 2.18-2.34 (m, 1H), 3.13 (t,  $J$  = 7.2 Hz, 0.7H), 3.31 (t,  $J$  = 7.2 Hz, 0.28H), 3.96 (d,  $J$  = 14.4 Hz, 0.7H), CH), 4.08 (d,  $J$  = 14.3 Hz, 0.3H), 5.77 (d,  $J$  = 14.4 Hz, 0.7H), 5.90 (d,  $J$  = 14.3 Hz, 0.3H), 6.15 (dd,  $J$  = 1.6 Hz,  $J$  = 7.9 Hz, 0.7H), 6.90-7.38 (m, 12.53H), 7.69-7.72 (m, 0.3H), 7.80 (dd,  $J$  = 1.4 Hz,  $J$  = 8.0 Hz, 0.7H); **<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):**  $\delta$  = 12.6, 12.8, 28.6, 28.7, 51.3, 51.5, 51.6, 52.5, 124.1, 124.9, 126.9, 127.0, 127.5, 127.6, 127.7, 128.1, 128.3, 2x 128.4, 128.6, 128.7, 129.2, 129.4, 2x 129.9, 132.4, 132.8, 133.6, 134.1, 137.3, 137.5, 139.2, 140.2, 140.3, 140.5, 173.0, 173.2; **ESI-MS:** calculated for [C<sub>23</sub>H<sub>22</sub>BrNONa]<sup>+</sup>: 432.0759, found: 432.0767; **ATR-FTIR [cm<sup>-1</sup>]:** 3064, 2959, 2929, 1653, 1471, 1394, 1286, 1015, 762, 726, 696.

**N-(2-Chlorophenyl)-N-methyl-2-*o*-tolylpropanamide** (Table 2, entry 5)



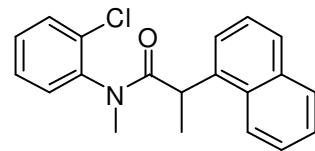
Following the general procedure 3.1, 2-chloro-*N*-methylaniline was converted with *o*-methylphenylpropanoyl chloride to the title compound after flash chromatography (silica, pentane/EtOAc = 10:1-5:1) as a pale oil.  $R_f$  (pentane/EtOAc = 10:1): 0.08; **<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):**  $\delta$  = 1.32 (d,  $J$  = 6.8 Hz, 2.24H), 1.33 (d,  $J$  = 6.8 Hz, 0.76 H), 1.47 (s, 2.34H), 1.51 (s, 0.64H), 3.17 (s, 2.27H), 3.19 (s, 0.62H), 3.50 (q,  $J$  = 6.8 Hz, 0.80H), 3.85 (q,  $J$  = 6.8 Hz, 0.20H), 6.31 (dd,  $J$  = 1.6 Hz,  $J$  = 7.9 Hz, 0.78H), 6.89-6.91 (m, 0.91 H), 6.94 (dt,  $J$  = 1.4Hz,  $J$  = 7.7 Hz, 0.85H), 7.03-7.09 (m, 1.12H), 7.14 (dt,  $J$  = 1.0 Hz,  $J$  = 7.4 Hz, 0.86H), 7.20-7.26 (m, 1.72H), 7.32-7.35 (m, 1.39H), 7.49 (dd,  $J$  = 1.4 Hz,  $J$  = 8.0 Hz, 0.79H); **<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):**  $\delta$  = 18.2, 19.2, 19.7, 36.0, 36.2, 39.2, 40.1, 126.3, 2x 126.4, 127.4, 127.7, 127.9, 129.2, 129.3, 129.8, 130.0, 130.1, 130.3, 130.7, 130.8, 133.2, 134.9, 140.4, 140.6, 174.2; **ESI-MS:** calculated for [C<sub>17</sub>H<sub>18</sub>ClNONa]<sup>+</sup>: 310.0969, found: 310.0975; **ATR-FTIR [cm<sup>-1</sup>]:** 3062, 2966, 2927, 1649, 1586, 1484, 1379, 1134, 1058, 754, 727.

**N-(2-Chlorophenyl)-2-(2-methoxyphenyl)-N-methylpropanamide** (Table 2, entry 6)



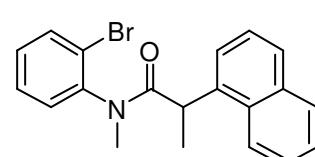
Following the general procedure 3.1, 2-chloro-N-methylaniline was converted with *o*-methoxyphenylpropanoyl chloride to the title compound after flash chromatography (silica, pentane/EtOAc = 10:1) as a pale oil (1.14 g, 3.8 mmol, 81%).  $R_f$  (pentane/EtOAc = 5:1): 0.23; **1H NMR (300 MHz, CDCl<sub>3</sub>)**:  $\delta$  = 1.29 (d,  $J$  = 6.6 Hz, 1.25H), 1.34 (d,  $J$  = 6.9 Hz, 1.89H), 3.16 (s, 2.07H), 3.17 (s, 0.89H), 3.38 (s, 0.83H), 3.39 (s, 2.18H), 3.88 (q,  $J$  = 6.9 Hz, 1H), 6.52 (dq,  $J$  = 1.6 Hz,  $J$  = 7.9 Hz, 0.72H), 6.58-6.62 (m, 1H), 6.82-6.92 (m, 1H), 6.98 (dq,  $J$  = 1.6 Hz,  $J$  = 7.9 Hz, 0.8H), 7.08-7.16 (m, 1H), 7.19-7.26 (m, 1.58H), 7.32-7.36 (m, 1.53H), 7.48 (dd,  $J$  = 1.4 Hz,  $J$  = 7.4 Hz, 0.74H); **13C NMR (75 MHz, CDCl<sub>3</sub>)**:  $\delta$  = 18.8, 19.4, 34.8, 35.8, 35.9, 36.1, 54.6, 54.7, 109.3, 109.7, 120.6, 127.2, 127.5, 127.6, 128.6, 128.8, 128.9, 130.0, 2x 130.2, 130.3, 133.1, 140.6, 155.6, 174.7, 174.8; **ESI-MS**: calculated for [C<sub>17</sub>H<sub>18</sub>CINO<sub>2</sub>Na]<sup>+</sup>: 326.0918, found: 326.0923; **ATR-FTIR [cm<sup>-1</sup>]**: 3064, 2932, 1660, 1482, 1330, 1132, 1054, 1033, 754.

**N-(2-Chlorophenyl)-N-methyl-2-(naphthalen-1-yl)propanamide**<sup>[15]</sup> (Table 2, entry 7)



Following the general procedure 3.1, 2-chloro-N-methylaniline was converted with 2-(naphthalen-1-yl)propanoyl chloride to the title compound after flash chromatography (silica, pentane/EtOAc = 10:1) as colorless solid (777 mg, 2.40 mmol, 83%).  $R_f$  (pentane/EtOAc = 10:1): 0.24; **1H NMR (400 MHz, CDCl<sub>3</sub>)**:  $\delta$  = 1.52 (t,  $J$  = 6.9 Hz, 3H), 3.20 (s, 3H), 4.16 (q,  $J$  = 6.9 Hz, 0.77H), 4.47 (q,  $J$  = 6.9 Hz, 0.23H), 6.08 (dd,  $J$  = 7.9 Hz,  $J$  = 1.6 Hz, 0.73H), 6.45 (dt,  $J$  = 7.6 Hz,  $J$  = 1.4 Hz, 0.74H), 6.79 (dd,  $J$  = 8.1 Hz,  $J$  = 1.4 Hz, 0.22H), 6.96 (dt,  $J$  = 7.6 Hz,  $J$  = 1.6 Hz, 0.74H), 7.02-7.06 (m, 0.25H), 7.13-7.19 (m, 1H), 7.22-7.24 (m, 1H), 7.28-7.44 (m, 3.58H), 7.49 (dd,  $J$  = 7.2 Hz,  $J$  = 1.1 Hz, 0.81H), 7.64-7.69 (m, 1H), 7.75 (d,  $J$  = 8.2 Hz, 1H); **13C NMR (75 MHz, CDCl<sub>3</sub>)**:  $\delta$  = 19.9, 20.1, 36.1, 36.2, 39.4, 121.9, 122.0, 124.4, 124.9, 125.2, 125.4, 125.5, 2x 125.7, 127.0, 127.1, 127.4, 127.8, 2x 128.6, 2x 129.0, 2x 129.1, 129.8, 130.0, 130.4, 130.5, 130.6, 132.6, 133.6, 138.5, 140.2, 174.1, 174.3.

**N-(2-Bromophenyl)-N-methyl-2-(naphthalen-1-yl)propanamide**<sup>[15]</sup> (Table 1, entry 8)



Following the general procedure 3.1, 2-bromo-N-methylaniline was converted with 2-(naphthalen-1-yl)propanoyl chloride to the title compound after flash chromatography (silica, pentane/EtOAc = 10:1) as colorless solid (1.45 g, 3.92 mmol, 69%).  $R_f$

(pentane/EtOAc = 10:1): 0.16; **<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**: δ = 1.51-1.54 (m, 3H), 3.19 (s, 2.32H), 3.20 (s, 0.59H), 4.16 (q, *J* = 6.9 Hz, 0.86H), 4.46 (q, *J* = 6.9 Hz, 0.19H), 6.08 (dd, *J* = 7.9 Hz, *J* = 1.6 Hz, 0.76 H), 6.47 (dt, *J* = 1.4 Hz, *J* = 7.7 Hz, 0.79H), 6.88 (dt, *J* = 1.6 Hz, *J* = 7.9 Hz, 0.78H), 7.01-7.03 (m, 0.38H), 7.12-7.22 (m, 2H), 7.32-7.40 (m, 2.43H), 7.45 (d, *J* = 6.9 Hz, 0.24H), 7.49 (dd, *J* = 7.2 Hz, *J* = 1.1 Hz, 0.87H), 7.60 (dd, *J* = 8.0 Hz, *J* = 1.4 Hz, 0.84H), 7.65-7.69 (m, 1.06H), 7.74-7.76 (m, 1H); **<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)**: δ = 20.0, 20.3, 36.2, 39.6, 121.9, 122.0, 123.3, 124.4, 125.9, 125.2, 125.5, 125.6, 2x 125.7, 127.1, 128.0, 128.5, 128.6, 129.2, 129.3, 130.0, 130.5, 130.6, 133.2, 133.6, 133.9, 138.5, 141.7, 174.0, 174.1.

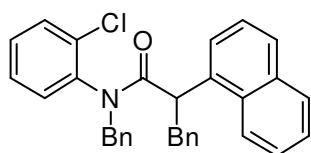
**N-Benzyl-N-(2-bromophenyl)-2-(naphthalen-1-yl)propanamide** (Table 2, entries 9,10)

Following the general procedure 3.1, 2-chloro-*N*-benzylaniline (675 mg, 3.1 mmol) was converted with 2-phenylpropanoyl chloride (810 mg, 3.7 mmol) to the title compound after flash chromatography (silica, pentane/EtOAc = 30:1-5:1) as colorless solid (870 mg, 2.2 mmol, 70%). R<sub>f</sub> (pentane/EtOAc = 10:1): 0.22; **<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)**: δ = 1.53 (d, *J* = 6.9 Hz, 3H), 3.84 (d, *J* = 14.3 Hz, 0.2H), 4.06 (d, *J* = 14.3 Hz, 0.8H), 4.15 (q, *J* = 6.9 Hz, 0.8H), 4.41 (q, *J* = 6.9 Hz, 0.2H), 5.55 (m, 0.7H), 5.59 (d, *J* = 14.3 Hz, 0.8H), 5.77 (d, *J* = 14.3 Hz, 0.2H), 6.19 (td, *J* = 1.4 Hz, *J* = 7.7 Hz, 0.8H), 7.74-6.75 (m, 14.5H); **<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)**: δ = 20.1, 20.5, 39.1, 39.9, 51.4, 52.0, 122.1, 122.1, 124.5, 125.1, 125.4, 125.6, 125.7, 125.8, 125.9, 125.9, 126.9, 127.3, 127.3, 127.4, 127.5, 127.6, 128.4, 128.5, 128.7, 128.8, 129.2, 129.4, 129.5, 130.1, 130.6, 130.7, 130.9, 131.9, 133.0, 133.8, 134.0, 136.8, 137.3, 137.3, 138.5, 138.6, 174.1, 174.3; **ESI-MS**: calculated for: [C<sub>26</sub>H<sub>22</sub>ClNONa]<sup>+</sup> 422.1282, found: 422.1282. **ATR-FTIR [cm<sup>-1</sup>]**: 3062, 2930, 1664, 1479, 1391, 1254, 1205, 1069, 1011, 804, 777, 732, 699.

**N-Benzyl-N-(2-chlorophenyl)-2-(naphthalen-1-yl)propanamide**<sup>[15]</sup> (Table 2, entry 11)

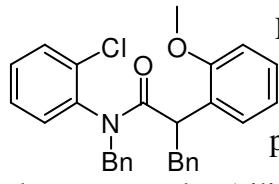
Following the general procedure 3.1, 2-bromo-*N*-benzylaniline (1.05 g, 4.0 mmol) was converted with 2-phenylpropanoyl chloride (1.05 g, 4.2 mmol) to the title compound after flash chromatography (silica, pentane/EtOAc = 30:1-10:1) as colorless solid (748 mg, 1.7 mmol, 42%). R<sub>f</sub> (pentane/EtOAc = 10:1): 0.24.

**N-Benzyl-N-(2-chlorophenyl)-2-(naphthalen-1-yl)-3-phenyl-propionamide** (Table 2, entry 12)



Following the general procedure 3.1, 2-chloro-*N*-benzylaniline (1.50 g, 6.9 mmol) was converted with 3- (4, 8-Dihydro-naphthalen-1-yl)-4-phenyl-butrylic acid (2.0 g, 7.2 mmol) to the title compound after flash chromatography (silica, pentane/EtOAc = 50:1-30:1) as colorless solid (783 mg, 1.64 mmol, 24%).  $R_f$  (pentane/EtOAc = 5:1): 0.40;  **$^1H$  NMR (300 MHz, CDCl<sub>3</sub>)**:  $\delta$  = 2.89 (ddd,  $J$  = 17.1 Hz,  $J$  = 13.4 Hz,  $J$  = 4.7 Hz, 1 H), 3.65 (t,  $J$  = 6.6 Hz, 0.85 H), 3.71 (d,  $J$  = 14.3 Hz, 0.52 H), 3.97 (d,  $J$  = 14.4 Hz, 0.57 H), 4.26 (dd,  $J$  = 8.4 Hz,  $J$  = 5.6 Hz, 0.56 H) 4.56 (dd,  $J$  = 10.7 Hz,  $J$  = 3.7 Hz, 0.37 H), 5.49 (dd,  $J$  = 7.9 Hz,  $J$  = 1.5 Hz, 0.54 H), 5.59 (d,  $J$  = 14.3 Hz, 0.54 H), 5.78 (d,  $J$  = 14.5 Hz, 0.39 H) 6.12 (m, 1 H), 7.00 (m, 11.51 H) 7.35 (m, 5.14 H), 7.72 (m, 2.62 H), 7.93 (d,  $J$  = 6.5 Hz, 0.5 H);  **$^{13}C$  NMR (75 MHz, CDCl<sub>3</sub>)**:  $\delta$  = 40.8, 41.8, 51.2, 51.7, 121.6, 121.8, 125.0, 125.1, 125.3, 125.6, 126.0, 126.3, 126.6, 127.1, 127.2, 127.4, 128.1, 128.2, 128.8, 128.8, 128.9, 129.2, 129.9, 130.5, 130.8, 130.9, 131.8, 131.9, 132.8, 133.6, 133.8, 133.9, 134.9, 136.3, 136.8, 137.0, 138.0, 138.5, 140.1, 140.2, 172.2, 172.7; **ESI-MS**: calculated for: [C<sub>32</sub>H<sub>26</sub>BrNONa]<sup>+</sup> 542.1090, found: 542.1078. **ATR-FTIR [cm<sup>-1</sup>]**: 3064, 2924, 1660, 1479, 1393, 1272, 1241, 1206, 1072, 1035, 983, 909, 792, 774, 731, 700, 632, 550.

**N-Benzyl-N-(2-chlorophenyl)-2-(2-methoxyphenyl)-3-phenyl-propionamide** (Table 2, entry 13)



Following the general procedure 3.1, 2-chloro-*N*-benzylaniline (1.60 g, 7.3 mmol) was converted with 2-(2-Methoxyphenyl)-3-phenyl-propionic acid (2.0 g, 7.8 mmol) to the title compound after flash chromatography (silica, pentane/EtOAc = 50:1-20:1) as colorless solid (1.30 g, 2.85 mmol, 39%).  $R_f$  (pentane/EtOAc = 5:1): 0.58;  **$^1H$  NMR (300 MHz, CDCl<sub>3</sub>)**:  $\delta$  = 2.85 (ddd,  $J$  = 16.9 Hz,  $J$  = 13.1 Hz,  $J$  = 5.1 Hz, 1 H), 3.28 (s, 1.41 H), 3.50 (s, 1.64 H), 3.81 (d,  $J$  = 14.4 Hz, 0.67 H), 4.02 (t,  $J$  = 8.3 Hz, 0.59 H), 4.13 (dd,  $J$  = 8.1 Hz,  $J$  = 6.2 Hz, 0.53 H), 4.37 (dd,  $J$  = 11.0 Hz,  $J$  = 4.0 Hz, 0.57 H), 5.67 (d,  $J$  = 14.4 Hz, 0.49 H), 5.79 (d,  $J$  = 14.5 Hz, 0.53 H), 5.90 (dd,  $J$  = 7.9 Hz,  $J$  = 1.5 Hz, 0.45 H), 5.98 (dd,  $J$  = 7.9 Hz,  $J$  = 1.6 Hz, 0.49 H), 6.60 (m, 0.56 H), 6.78 (m, 1.19 H), 7.02 (m, 3.05 H), 7.21 (m, 5 H), 7.32 (m, 6.20 H), 7.51 (ddd,  $J$  = 8.1 Hz,  $J$  = 6.5 Hz,  $J$  = 1.6 Hz, 14 H), 7.86 (dd,  $J$  = 7.6 Hz,  $J$  = 1.7 Hz, 0.52 H);  **$^{13}C$  NMR (75 MHz, CDCl<sub>3</sub>)**:  $\delta$  = 39.9, 41.1, 41.9, 44.2, 51.1, 54.5, 54.6, 109.5, 109.7, 120.4, 120.6, 125.6, 126.1, 126.4, 126.8, 127.1, 127.2, 127.5, 127.7, 127.8, 127.8, 127.9, 128.0, 128.1, 128.1, 128.4, 128.8, 128.9, 128.9, 129.0, 129, 129.3, 129.6, 129.7, 129.9, 131.9, 132.2, 133.3, 133.8, 136.8, 127.3, 138.3, 138.6, 140.2, 155.9, 155.9, 172.9, 173.1; **ESI-MS**: calculated for:

$[C_{29}H_{26}ClNO_2Na]^+$  478.1544, found: 478.1542; **ATR-FTIR [cm<sup>-1</sup>]:** 3060, 2937, 2838, 1734, 1657, 1599, 1492, 1265, 1394, 1265, 1247, 1031, 910, 733, 701, 630, 550.

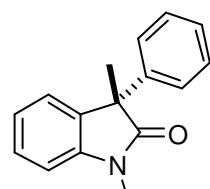
## 4 Oxindoles

### 4.1 General Procedure

$[Pd(allyl)Cl]_2$  (2.7 mg,  $7.5 \cdot 10^{-4}$  mmol, 2.5 mol%), IBiox·HOTf (8 mg,  $1.5 \cdot 10^{-3}$  mmol, 5 mol%), NaOtBu (43 mg, 0.45 mmol, 1.5 eq) and the starting material (0.3 mmol) were combined with DME (3 mL) and stirred at 50 °C until all starting material was consumed (GC/MS). After completion the mixture was filtered through a short plug of silica, diluted with EtOAc (50 mL) and the solvents were evaporated. The crude material was dissolved in a small amount of  $CH_2Cl_2$ , adsorbed on silica and purified by flash chromatography (silica, pentane/EtOAc).

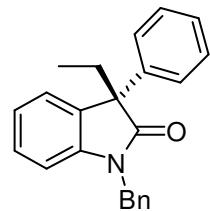
### 4.2 Characterization of products

**(S)-1,3-Dimethyl-3-phenylindolin-2-one<sup>[16]</sup>** (Table 2, entries 1,2)



Following the general procedure 4.1, the title compound was obtained after flash chromatography (silica, pentane/EtOAc = 10:1) as pale oil (65 mg, 0.27 mmol, 91%).  $R_f$  (pentane/EtOAc = 5:1): 0.26;  **$^1H$  NMR (400 MHz,  $CDCl_3$ ):**  $\delta$  = 1.81 (s, 3H), 3.25 (s, 3H), 6.93 (d,  $J$  = 7.8 Hz, 1H), 7.11 (dt,  $J$  = 7.5 Hz,  $J$  = 1.0 Hz, 1H), 7.19-7.36 (m, 7H);  **$^{13}C$  NMR (100 MHz,  $CDCl_3$ ):**  $\delta$  = 23.7, 26.4, 52.1, 108.2, 122.7, 124.1, 126.6, 127.1, 128.0, 128.4, 134.7, 140.7, 143.2, 179.3; **GC-MS**  $t_R$  (method 50\_40): 9.2 min; **MS-EI:** m/z(%) = 237 (96), 222 (100), 207 (12), 194 (20), 165 (12), 152 (9); **ESI-MS:** calculated for:  $[C_{16}H_{15}NONa]^+$ : 260.1046, found: 260.1042; 84% ee (Chiracel AS-H column, n-hexane/i-PrOH = 99:1, 1.0 mL/min, 254 nm;  $t_R$  = 10.98 min (major) and 13.45 min);  $[\alpha]_D^{20}$  −87 (c 0.97 in  $CH_2Cl_2$ ).

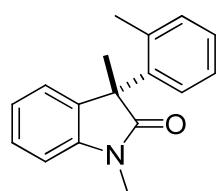
**(S)-1-Benzyl-3-ethyl-3-phenylindolin-2-one** (Table 2, entries 3,4)



Following the general procedure 4.1, the title compound was obtained after flash chromatography (silica, pentane/EtOAc = 20:1) as pale oil (98 mg, 0.30 mmol, 100%).  $R_f$  (pentane/EtOAc = 5:1): 0.53;  **$^1H$  NMR (400 MHz,  $CDCl_3$ ):**  $\delta$  = 0.65 (t,  $J$  = 7.4 Hz, 3H), 2.16-2.25 (m, 1H), 2.39-2.48 (m, 1H), 4.81 (d,  $J$  = 15.6 Hz, 1H), 4.88 (d,  $J$  = 15.6 Hz, 1H), 6.70 (d,  $J$  = 7.7 Hz, 1H), 6.98 (dt,  $J$  =

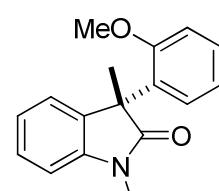
1.0 Hz,  $J = 7.4$  Hz, 1H), 7.09-7.24 (m, 10H), 7.29-7.31 (m, 2H);  **$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):**  $\delta = 9.1, 30.8, 43.9, 57.2, 109.2, 122.6, 124.8, 126.9, 127.2, 127.3, 127.5, 127.9, 128.5, 128.7, 132.1, 136.0, 140.3, 143.2, 178.6$ ; **GC-MS  $t_R$**  (method 50\_40): 11.4 min; **MS-EI:** m/z(%) = 327 (100), 298 (100), 270 (7), 91 (75); **ESI-MS:** calculated for:  $[\text{C}_{23}\text{H}_{21}\text{NONa}]^+$ : 350.1515, found: 350.1491; 87% ee (Chiracel AS-H column, *n*-hexane/*i*-PrOH = 99:1, 1.0 mL/min, 254 nm;  $t_R$  = 12.47 min (major) and 15.34 min);  $[\alpha]_D^{20} -68$  (c 0.845 in  $\text{CH}_2\text{Cl}_2$ ); **ATR-FTIR [cm<sup>-1</sup>]:** 3059, 2968, 2933, 1708, 1610, 1487, 1465, 1352, 1172, 1078, 750, 696, 634.

**(S)-1,3-Dimethyl-3-*o*-tolylindolin-2-one<sup>[16]</sup> (Table 2, entry 5)**



Following the general procedure 4.1, the title compound was obtained after flash chromatography (silica, pentane/EtOAc = 5:1) as a white solid (67 mg, 0.27 mmol, 89%).  $R_f$  (pentane/EtOAc = 5:1): 0.20;  **$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):**  $\delta = 1.53$  (s, 3H), 1.69 (s, 3H), 3.24 (s, 3H), 6.77 (d,  $J = 6.8$  Hz, 1H), 6.83 (d,  $J = 7.8$  Hz, 1H), 6.89-6.96 (m, 2H), 7.11 (dt,  $J = 0.8$  Hz,  $J = 7.3$  Hz, 1H), 7.17-7.23 (m, 2H), 7.57 (d,  $J = 7.6$  Hz, 1H);  **$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):**  $\delta = 19.2, 25.8, 26.4, 52.3, 108.0, 2x 122.9, 126.0, 127.4, 127.6, 127.8, 131.7, 135.1, 136.8, 137.9, 143.0, 180.0$ ; **GC-MS  $t_R$**  (method 50\_40): 9.4 min; **MS-EI:** m/z(%) = 251 (100), 250 (44), 236 (11), 208 (24), 193 (45), 165 (25), 160 (23); **ESI-MS:** calculated for:  $[\text{C}_{17}\text{H}_{17}\text{NONa}]^+$ : 274.1202, found: 274.1209; 95% ee (Chiracel AS-H column, *n*-hexane/*i*-PrOH = 98:2, 1.0 mL/min, 254 nm;  $t_R$  = 18.3 (major) and 29.1;  $[\alpha]_D^{20} +53$  (c 0.99 in  $\text{CH}_2\text{Cl}_2$ ).

**(R)-3-(2-Methoxyphenyl)-1,3-dimethylindolin-2-one<sup>[16]</sup> (Table 2, entry 6)**



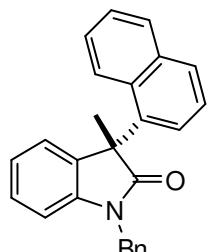
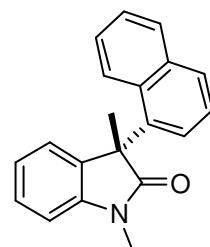
Following the general procedure 4.1, the title compound was obtained after stirring at 80 °C for 14 h after flash chromatography (silica, pentane/EtOAc = 3:1) as a pale solid (66 mg, 0.25 mmol, 82%).  $R_f$  (pentane/EtOAc = 3:1): 0.16;  **$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):**  $\delta = 1.62$  (s, 3H), 3.24 (s, 3H), 3.33 (s, 3H), 6.67 (d,  $J = 8.0$  Hz, 1H), 6.76-6.87 (m, 3H), 6.97 (t,  $J = 7.5$  Hz, 1H), 7.12-7.20 (m, 2H), 7.51 (dd,  $J = 7.7$  Hz,  $J = 1.3$  Hz, 1H);  **$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):**  $\delta = 23.3, 26.4, 49.8, 55.8, 107.3, 112.1, 120.9, 122.1, 122.2, 127.3, 127.6, 128.7, 130.0, 135.7, 143.6, 157.0, 181.0$ ; **GC-MS  $t_R$**  (method 50\_40): 9.6 min; **MS-EI:** m/z(%) = 267 (100), 252 (43), 234 (8), 224 (24), 222 (14); **ESI-MS:** calculated for:  $[\text{C}_{17}\text{H}_{17}\text{NO}_2\text{Na}]^+$ : 290.1151, found: 290.1150; 95% ee (Chiracel AS-H column, *n*-hexane/*i*-PrOH = 98:2, 1.0 mL/min, 254 nm;  $t_R$  = 16.4 (major) and 29.0;  $[\alpha]_D^{20} +73$  (c 0.965 in  $\text{CH}_2\text{Cl}_2$ ).

**(S)-1,3-Dimethyl-3-(naphthalen-1-yl)indolin-2-one<sup>[15]</sup>** (Table 2, entries 7,8)

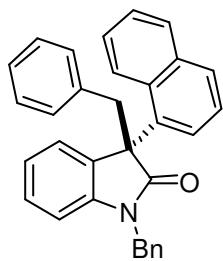
Following the general procedure 4.1, the title compound was obtained after flash chromatography (silica, pentane/EtOAc = 10:1.5) as colorless solid (85 mg, 0.296 mmol, 96%).  $R_f$  (pentane/EtOAc = 5:1): 0.20; **1H NMR (400 MHz, CDCl<sub>3</sub>)**:  $\delta$  = 1.91 (s, 3H), 3.45 (s, 3H), 6.84 (dd,  $J$  = 0.8 Hz,  $J$  = 7.4 Hz, 1H), 6.88 (dd,  $J$  = 0.6 Hz,  $J$  = 8.7 Hz, 1H), 6.94 (dt,  $J$  = 0.9 Hz,  $J$  = 7.5 Hz, 1H), 7.05 (d,  $J$  = 7.8 Hz, 1H), 7.14-7.18 (m, 1H), 7.29-7.35 (m, 2H), 7.53-7.57 (m, 1H), 7.79-7.87 (m, 3H); **13C NMR (100 MHz, CDCl<sub>3</sub>)**:  $\delta$  = 26.7, 26.8, 52.5, 108.6, 122.9, 123.1, 123.5, 125.1, 125.2, 2x 126.3, 2x 127.9, 2x 129.1, 131.4, 134.4, 135.1, 136.8, 142.2, 180.5 (some carbon signals not fully resolved); **GC-MS**  $t_R$  (method 50\_40): 10.9 min; **MS-EI**: m/z(%) = 315 (23), 273 (100), 256 (8), 244 (17), 215 (13); **ESI-MS**: calculated for: [C<sub>20</sub>H<sub>17</sub>NONa]<sup>+</sup>: 310.1202, found: 310.1194; 96% ee (Chiracel AS-H column, *n*-hexane/*i*-PrOH = 99:1, 1.0 mL/min, 254 nm;  $t_R$  = 20.06 min (major) and 37.89 min);  $[\alpha]_D^{20}$  + 1.2,  $[\alpha]_{365}^{20}$  -78 (c 1.04 in CH<sub>2</sub>Cl<sub>2</sub>).

**(S)-1-Benzyl-3-methyl-3-(naphthalen-1-yl)indolin-2-one<sup>[15]</sup>** (Table 2, entries 9-11)

Following the general procedure 4.1, the title compound was obtained after flash chromatography (silica, pentane/EtOAc = 15:1) as colorless solid (94 mg, 0.26 mmol, 86%).  $R_f$  (pentane/EtOAc = 5:1): 0.33; **1H NMR (400 MHz, CDCl<sub>3</sub>)**:  $\delta$  = 1.96 (s, 3H), 5.00 (d,  $J$  = 15.2 Hz, 1H), 5.23 (d,  $J$  = 15.2 Hz, 1H), 6.82-6.86 (m, 2H), 6.89 (dt,  $J$  = 0.9 Hz,  $J$  = 7.5 Hz, 1H), 6.94-6.98 (m, 1H), 7.02 (d,  $J$  = 7.8 Hz, 1H), 7.21 (dt,  $J$  = 1.3 Hz,  $J$  = 7.7 Hz, 1H), 7.30-7.42 (m, 4H), 7.51-7.58 (m, 3H), 7.80 (d,  $J$  = 8.1 Hz, 1H), 7.84 (d,  $J$  = 8.2 Hz, 1H), 7.88 (d,  $J$  = 7.3 Hz, 1H); **13C NMR (100 MHz, CDCl<sub>3</sub>)**:  $\delta$  = 27.1, 43.3, 52.4, 109.6, 122.9, 123.0, 124.0, 125.1, 125.3, 126.1, 126.3, 127.7, 127.9, 128.3, 128.8, 129.0, 129.1, 131.3, 134.3, 135.1, 136.1, 136.8, 141.3, 180.3; **MS-EI**: m/z(%) = 363 (100), 348 (11), 272 (95), 254 (15), 116 (22), 91 (37); **ESI-MS**: calculated for: [C<sub>26</sub>H<sub>21</sub>NONa]<sup>+</sup>: 386.1515, found: 386.1498; 97% ee (Chiracel AS-H column, *n*-hexane/*i*-PrOH = 99:1, 1.0 mL/min, 254 nm;  $t_R$  = 27.22 min (major) and 34.45 min);  $[\alpha]_D^{20}$  + 45.1 (c 0.51 in CH<sub>2</sub>Cl<sub>2</sub>).

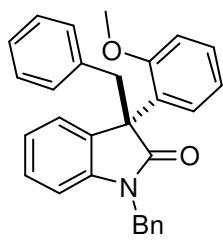


**(S)-1,3-Dibenzyl-3-naphthalen-1-yl-1,3-dihydro-indol-2-one** (Table 2, entry 12)



Following the general procedure 4.1, the title compound was obtained after stirring at 90 °C for 16 h after flash chromatography (silica, pentane/EtOAc = 30:1) as a pale solid (109 mg, 0.25 mmol, 83%).  $R_f$  (pentane/EtOAc = 5:1): 0.40; **1H NMR (400 MHz, CDCl<sub>3</sub>)**:  $\delta$  = 3.72 (d,  $J$  = 11.5 Hz, 1 H), 3.94 (dd,  $J$  = 22.4 Hz,  $J$  = 13.3 Hz, 2 H), 5.01 (d,  $J$  = 15.4 Hz, 1 H), 6.52 (d,  $J$  = 7.8 Hz, 1 H), 6.76 (d,  $J$  = 7.5 Hz, 2 H), 7.13 (m, 14 H), 7.61 (t,  $J$  = 7.8 Hz, 1 H), 7.85 (dd,  $J$  = 19.6 Hz,  $J$  = 8.1 Hz, 2 H), 8.05 (d,  $J$  = 7.3 Hz, 1 H); **13C NMR (100 MHz, CDCl<sub>3</sub>)**:  $\delta$  = 44.0, 44.9, 57.6, 109.1, 122.8, 123.5, 124.2, 125.1, 125.3, 125.8, 126.1, 126.8, 127.3, 127.6, 128.0, 128.1, 128.6, 129.0, 129.2, 130.2, 131.5, 133.7, 134.5, 134.6, 135.5, 135.8, 142.6, 178.1; **ESI-MS**: calculated for: [C<sub>32</sub>H<sub>25</sub>NONa]<sup>+</sup>: 462.1828, found: 462.1836; 92% ee (Chiracel OD-H column, *n*-hexane/*i*-PrOH = 97:3, 1.0 mL/min, 230 nm;  $t_R$  = 26.83 min (major) and 43.85 min);  $[\alpha]_D^{20}$  + 43 (c 1.04 in CHCl<sub>3</sub>). **ATR-FTIR [cm<sup>-1</sup>]**: 3057, 2927, 1711, 1610, 1486, 1466, 1343, 1197, 1170, 1080, 1029, 973, 933, 793, 775, 750, 695, 587.

**(R)-1,3-Dibenzyl-3-(2-methoxyphenyl)-1,3-dihydro-indol-2-one** (Table 2, entry 13)

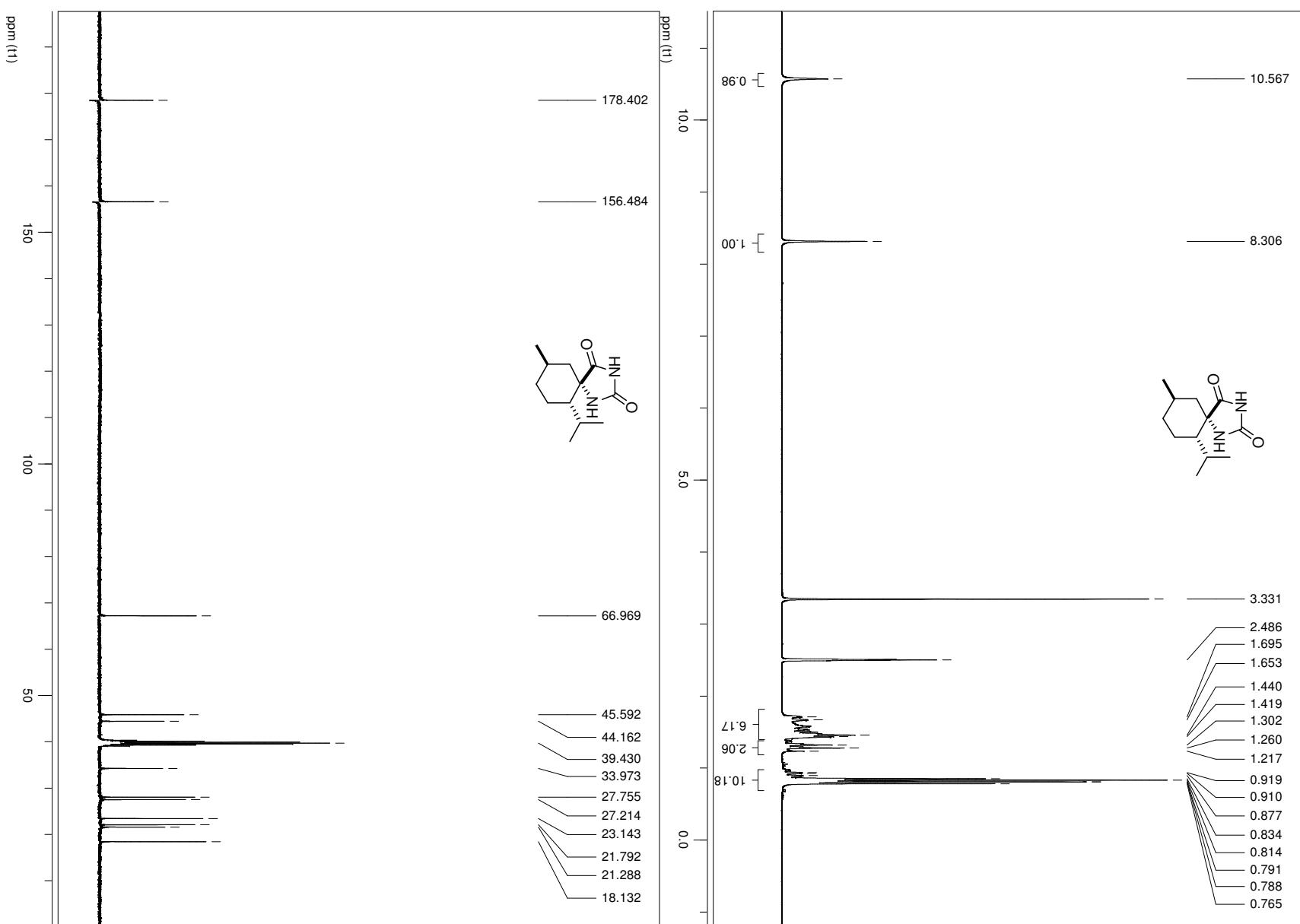


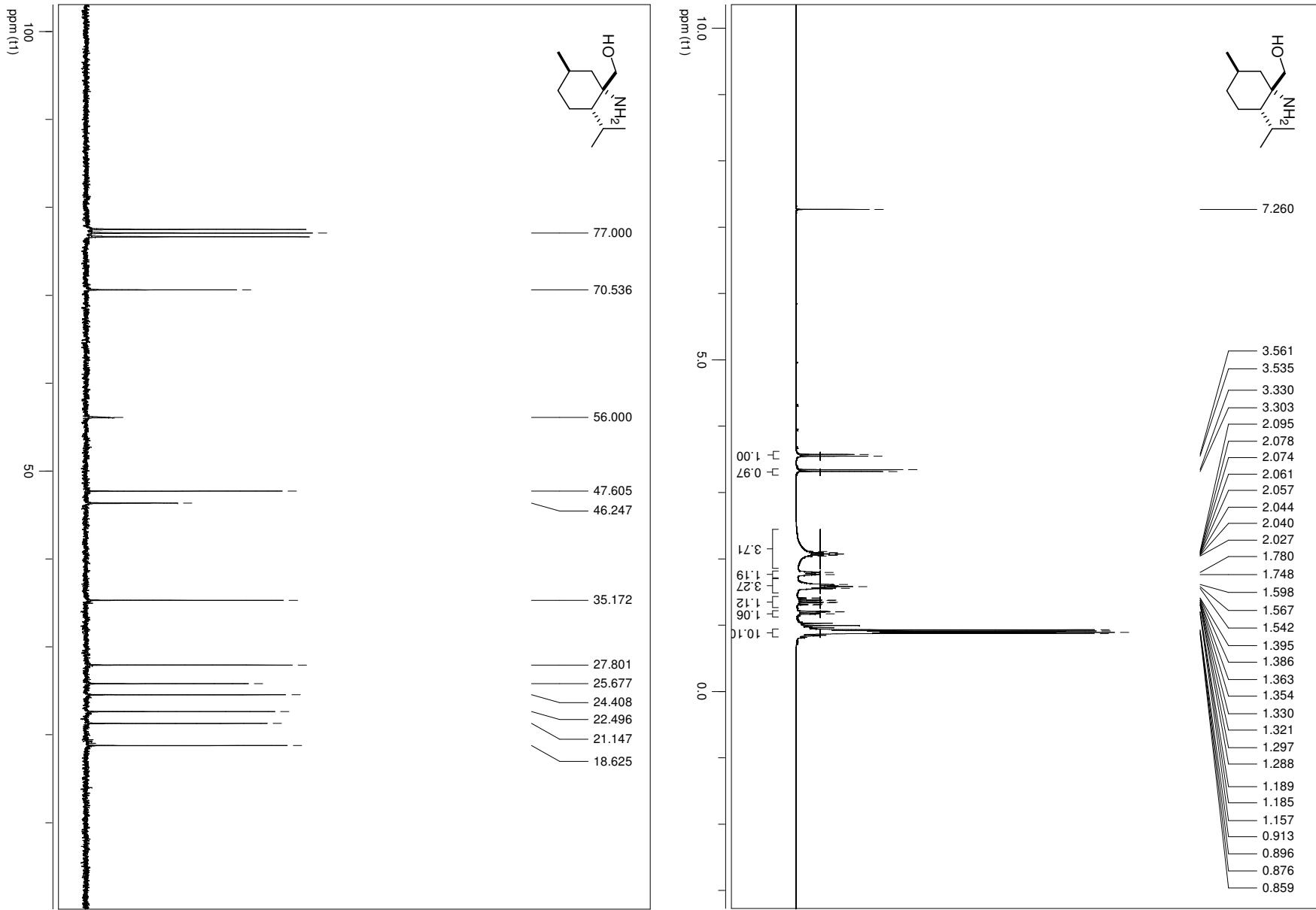
Following the general procedure 4.1, the title compound was obtained after stirring at 90 °C for 24 h after flash chromatography (silica, pentane/EtOAc = 30:1) as a pale solid (101 mg, 0.24 mmol, 80%).  $R_f$  (pentane/EtOAc = 5:1): 0.41; **1H NMR (400 MHz, CDCl<sub>3</sub>)**:  $\delta$  = 3.36 (s, 3 H), 3.71 (d,  $J$  = 1.9 Hz, 2 H), 4.62 (q,  $J$  = 15.8 Hz, 2 H), 6.41 (d,  $J$  = 7.6 Hz, 1 H), 6.89 (m, 5 H), 7.15 (m, 1 H), 7.36 (dd,  $J$  = 10.2 Hz,  $J$  = 9.0 Hz, 1 H), 7.83 (d,  $J$  = 7.7 Hz, 1 H); **13C NMR (100 MHz, CDCl<sub>3</sub>)**:  $\delta$  = 42.3, 43.9, 55.2, 55.6, 108.2, 112.3, 120.9, 121.9, 122.8, 126.5, 127.0, 127.2, 127.3, 127.4, 127.5, 128.3, 128.7, 130.0, 130.3, 132.8, 135.0, 136.1, 143.9, 157.0, 178.; **ESI-MS**: calculated for: [C<sub>29</sub>H<sub>25</sub>NO<sub>2</sub>Na]<sup>+</sup>: 478.1544, found: 478.1541; 92% ee (Chiracel OD-H column, *n*-hexane/*i*-PrOH = 97:3, 1.0 mL/min, 254 nm;  $t_R$  = 39.04 min (major) and 62.27 min);  $[\alpha]_D^{20}$  + 116 (c 0.96 in CHCl<sub>3</sub>). **ATR-FTIR [cm<sup>-1</sup>]**: 3055, 2935, 2837, 1719, 1609, 1490, 1465, 1361, 1253, 1026, 949, 751, 728, 698, 652, 594, 523, 556.

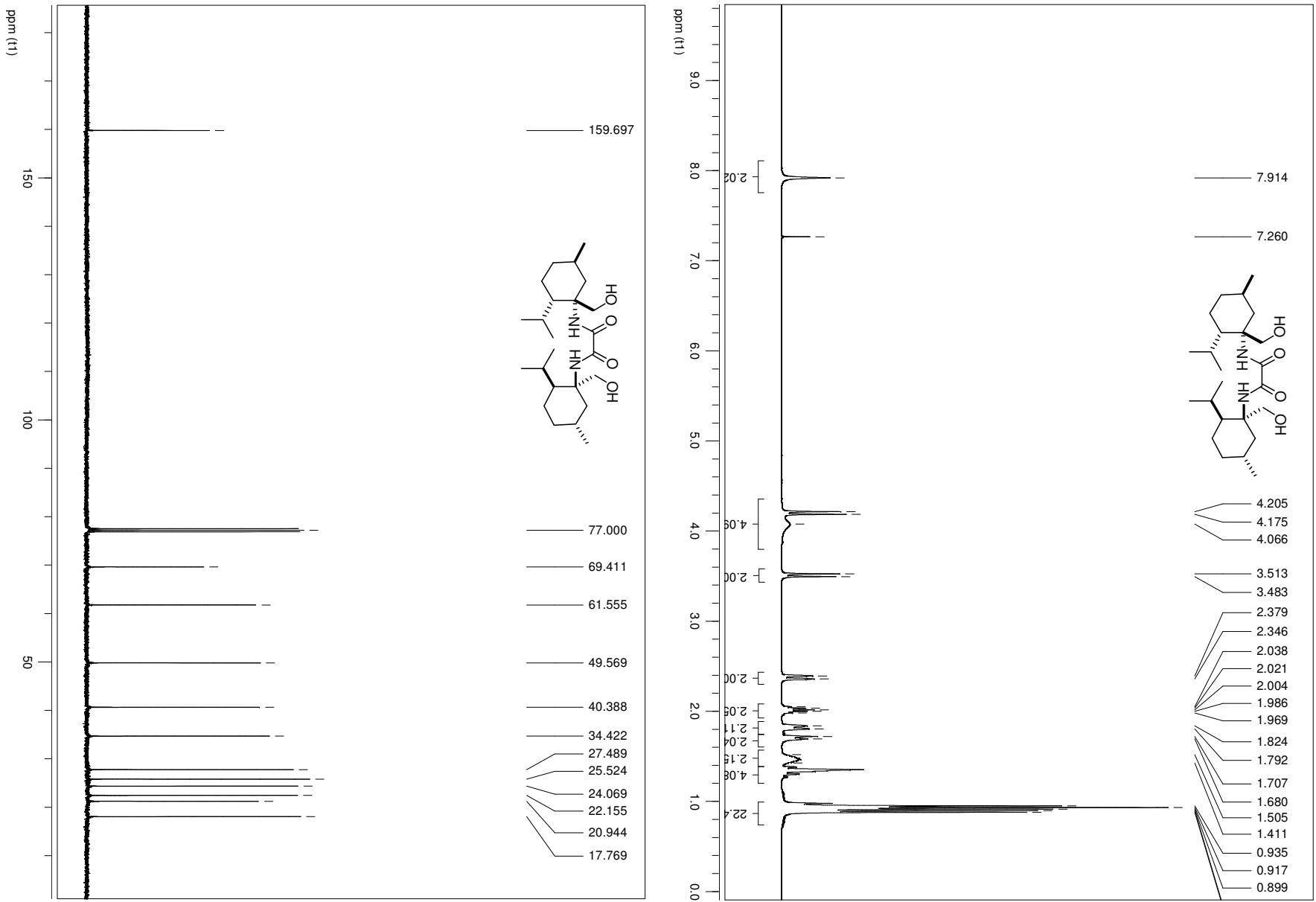
The title compound was obtained after stirring at 80 °C for 24 h in 37% (46 mg, 0.11 mmol) with an ee of 99%.

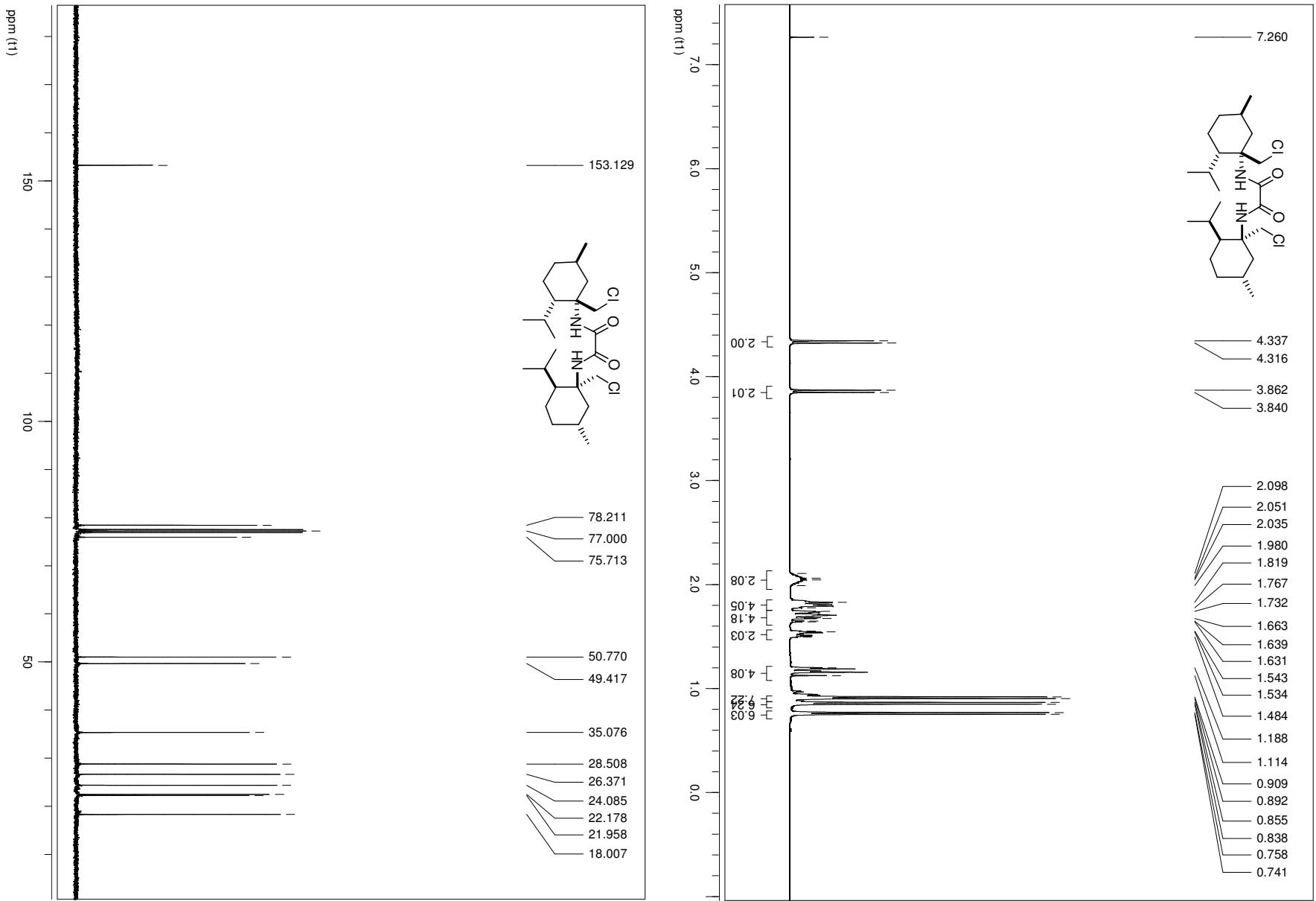
## 5 NMR Spectra

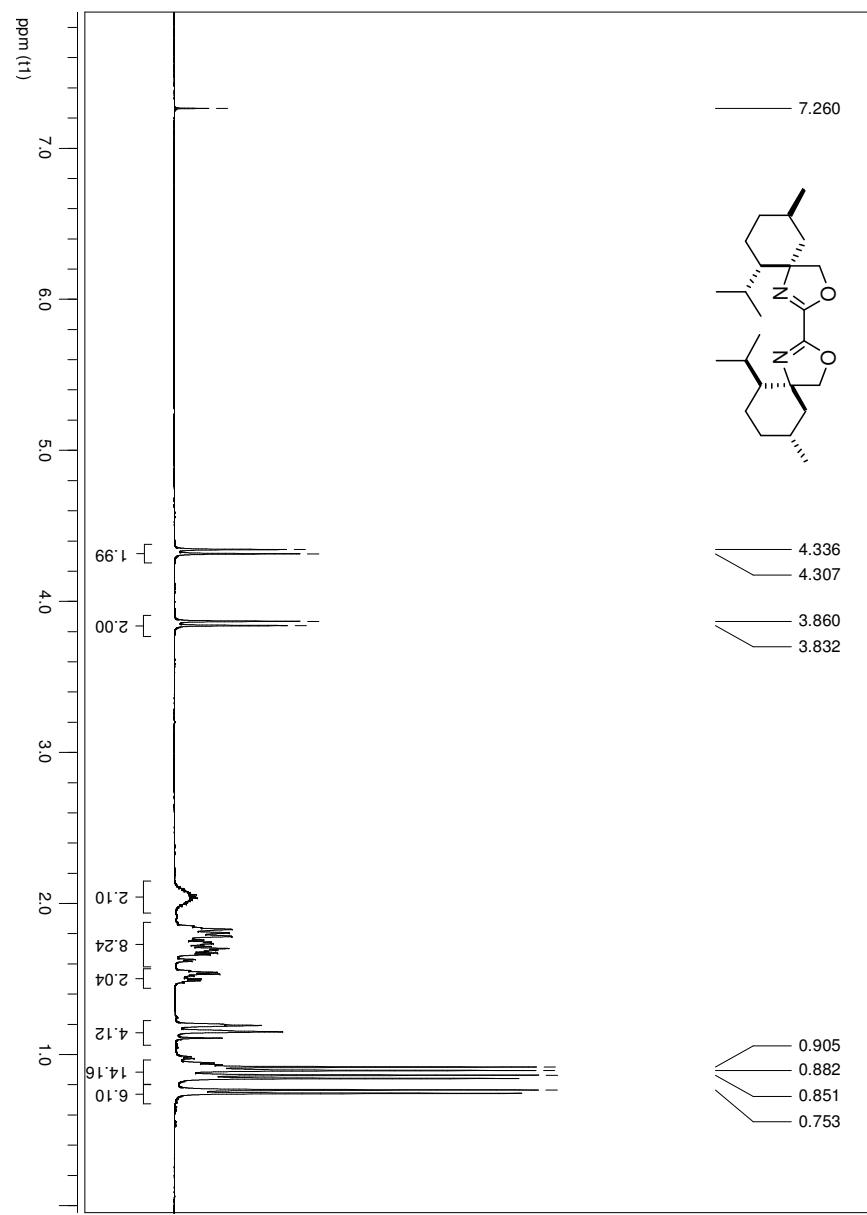
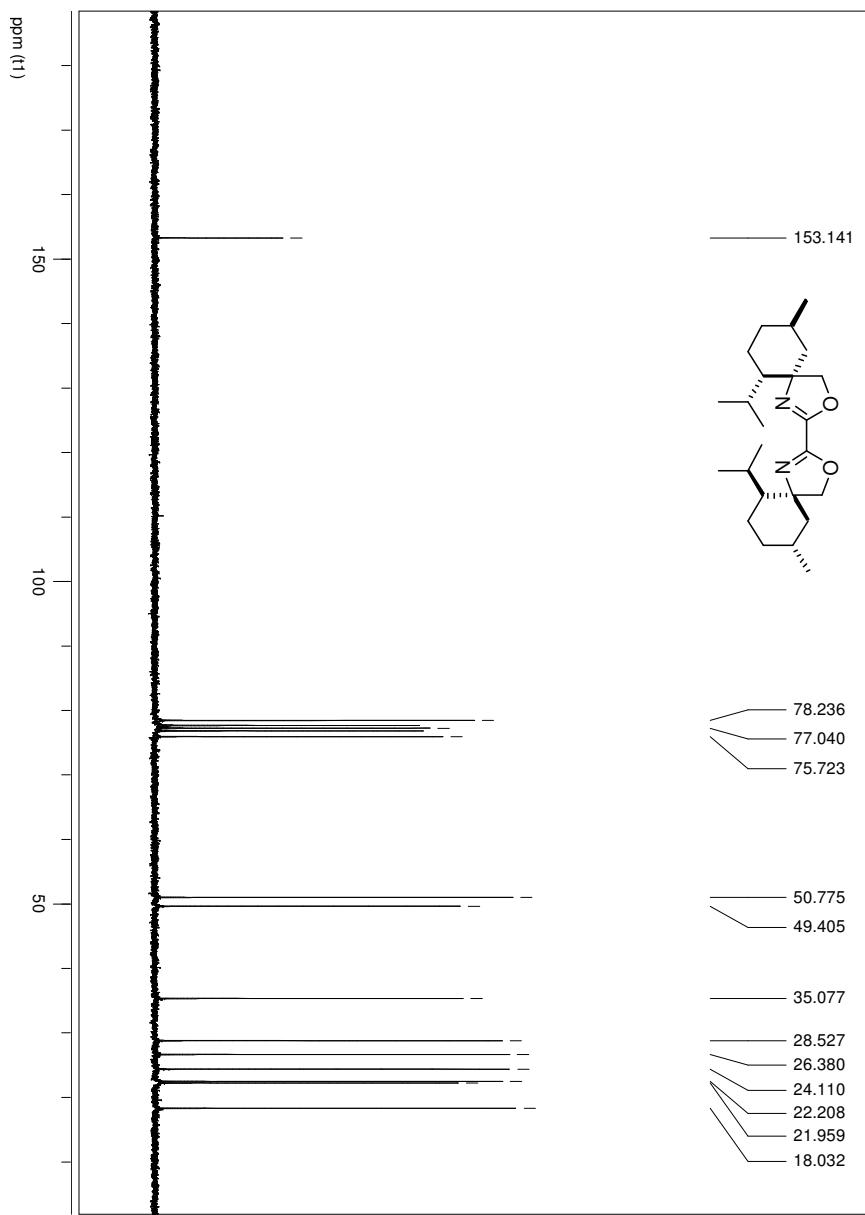
### 5.1 Ligand Synthesis

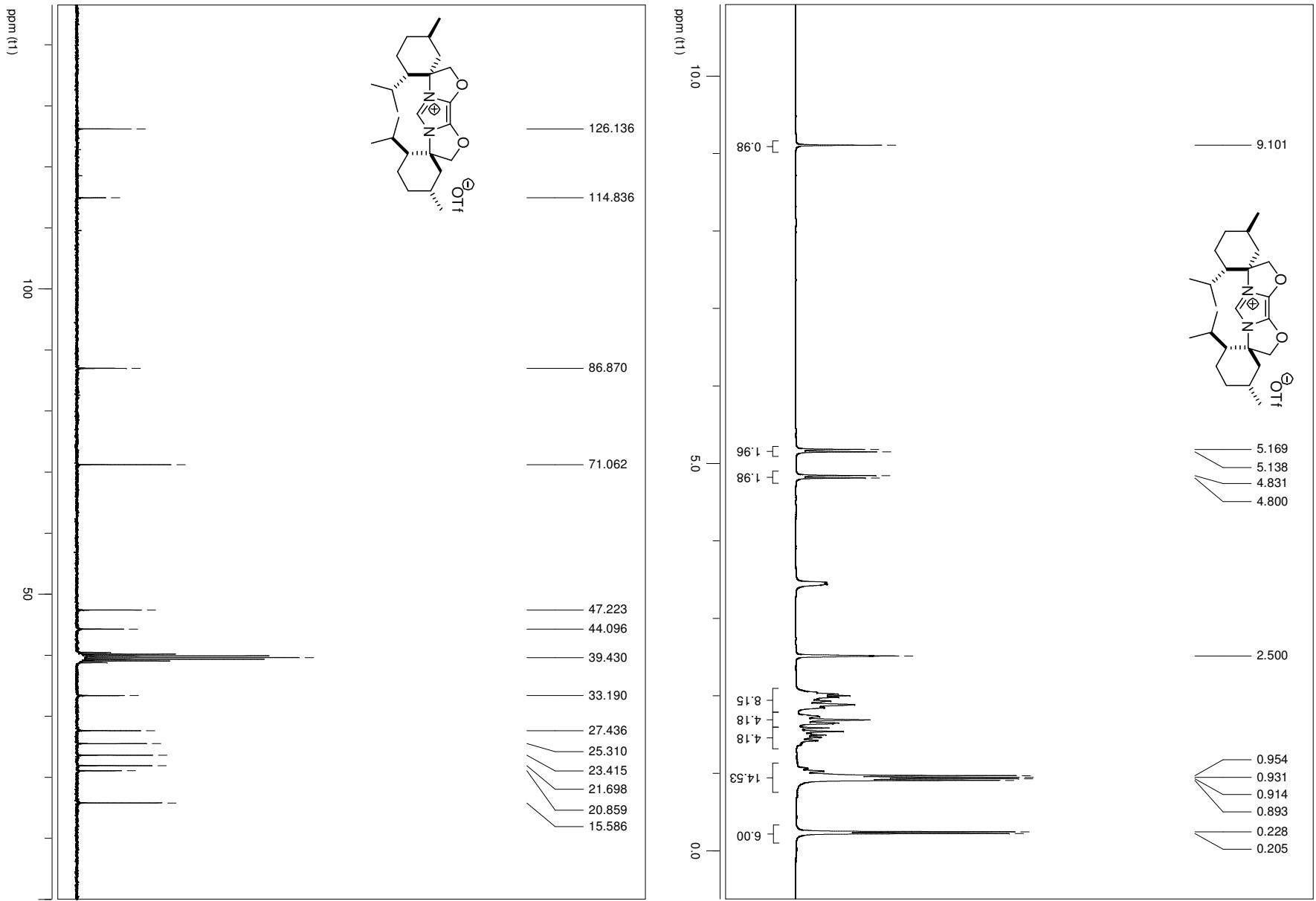




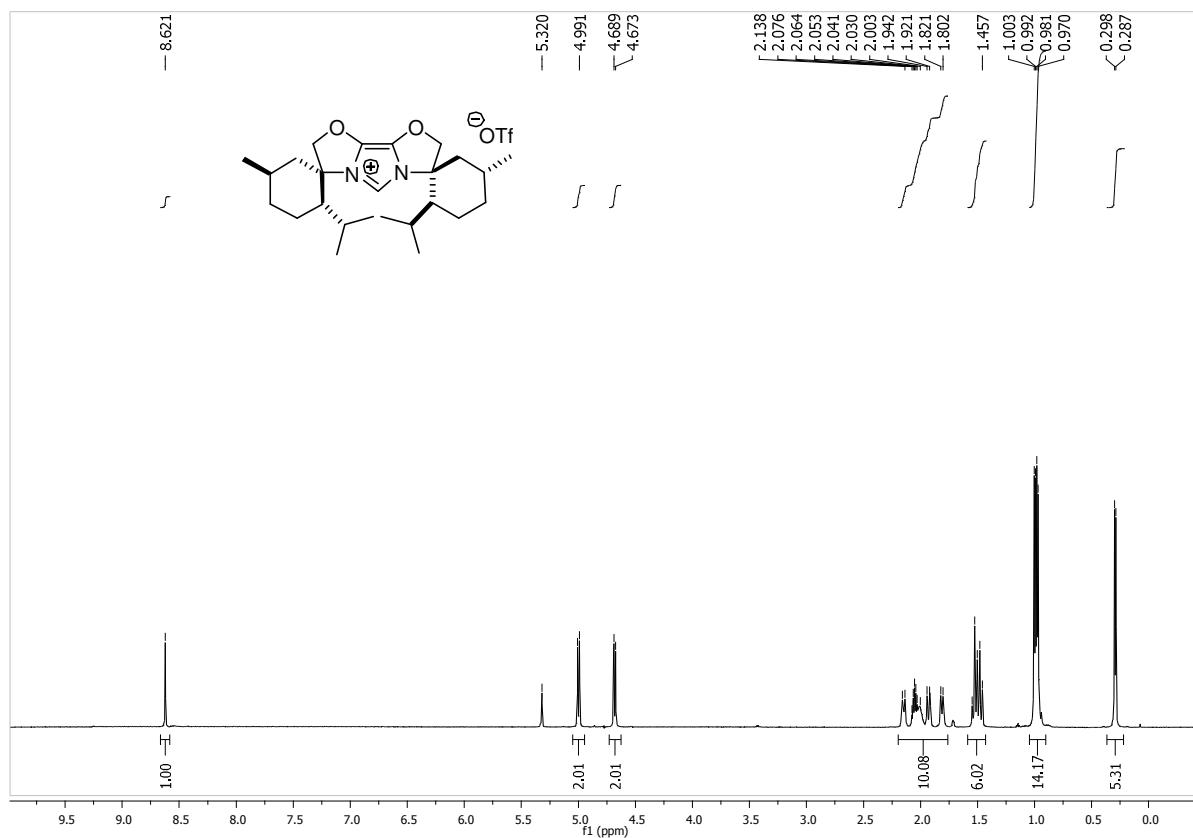




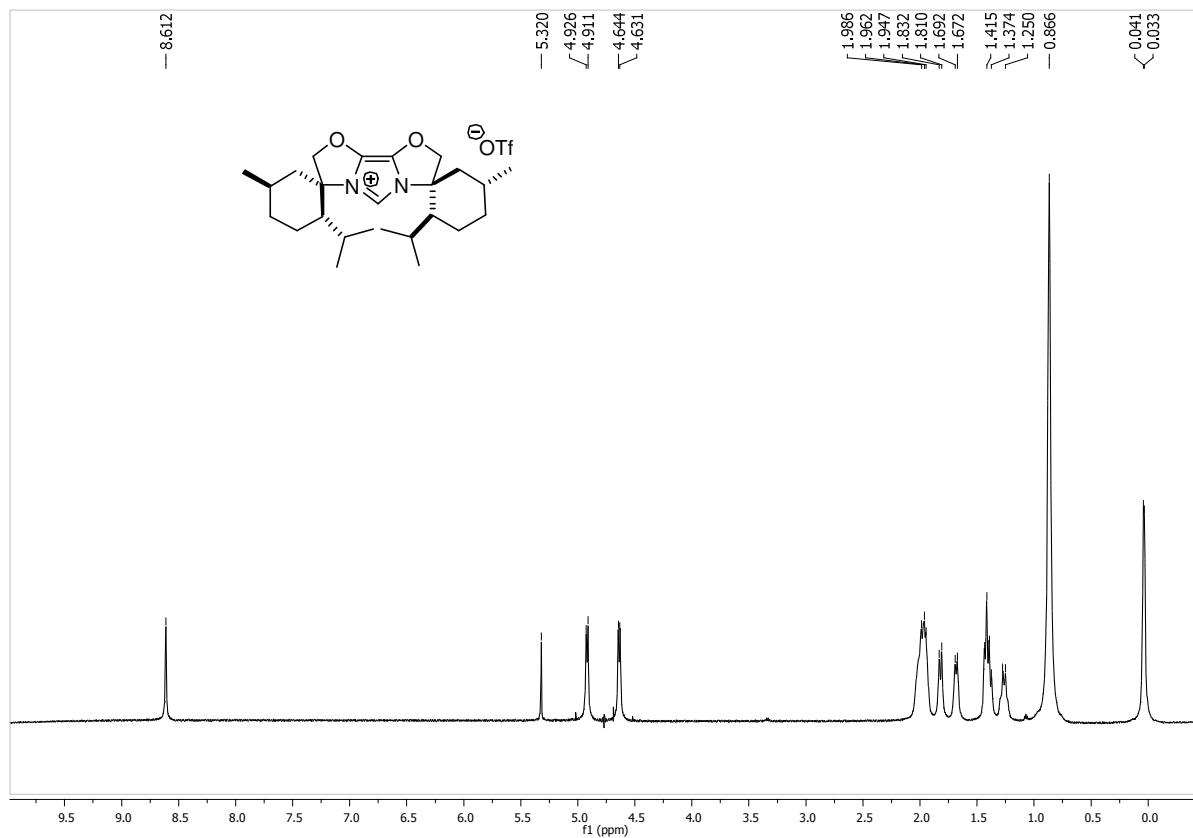




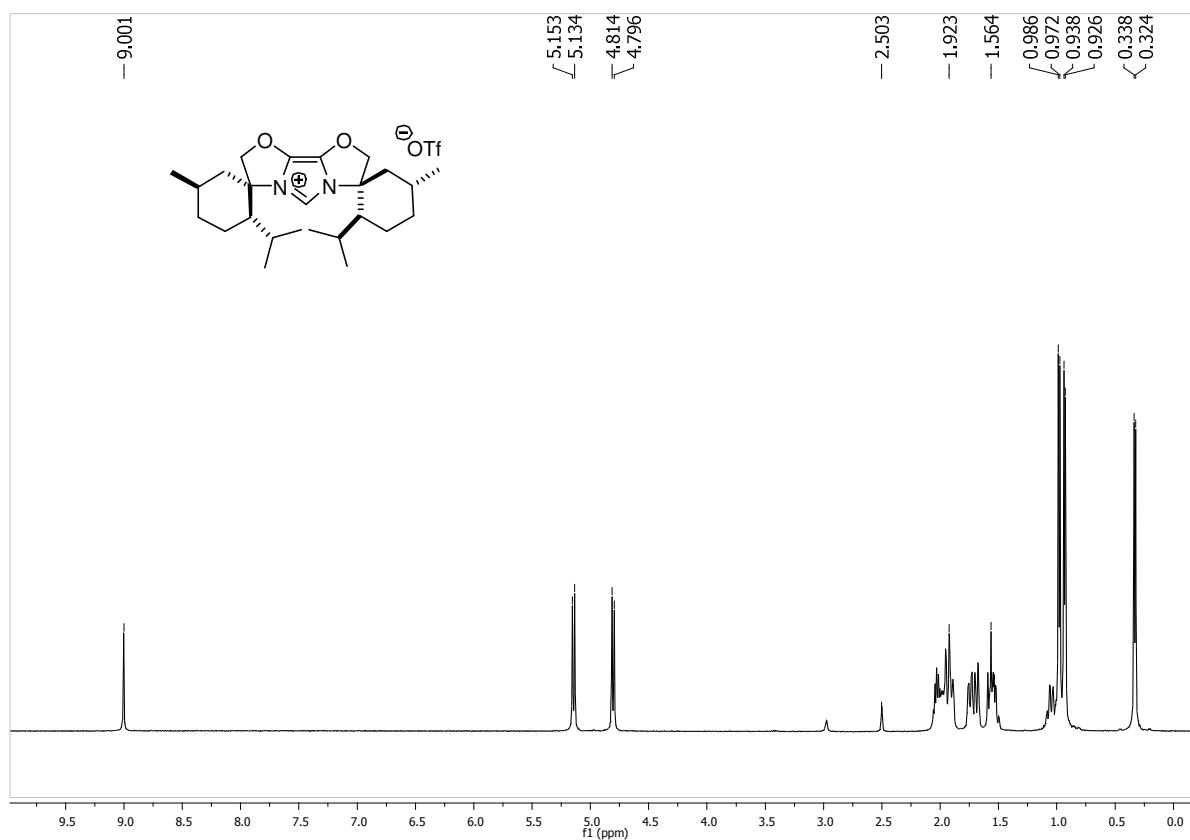
600 MHz, CD<sub>2</sub>Cl<sub>2</sub>, 298K

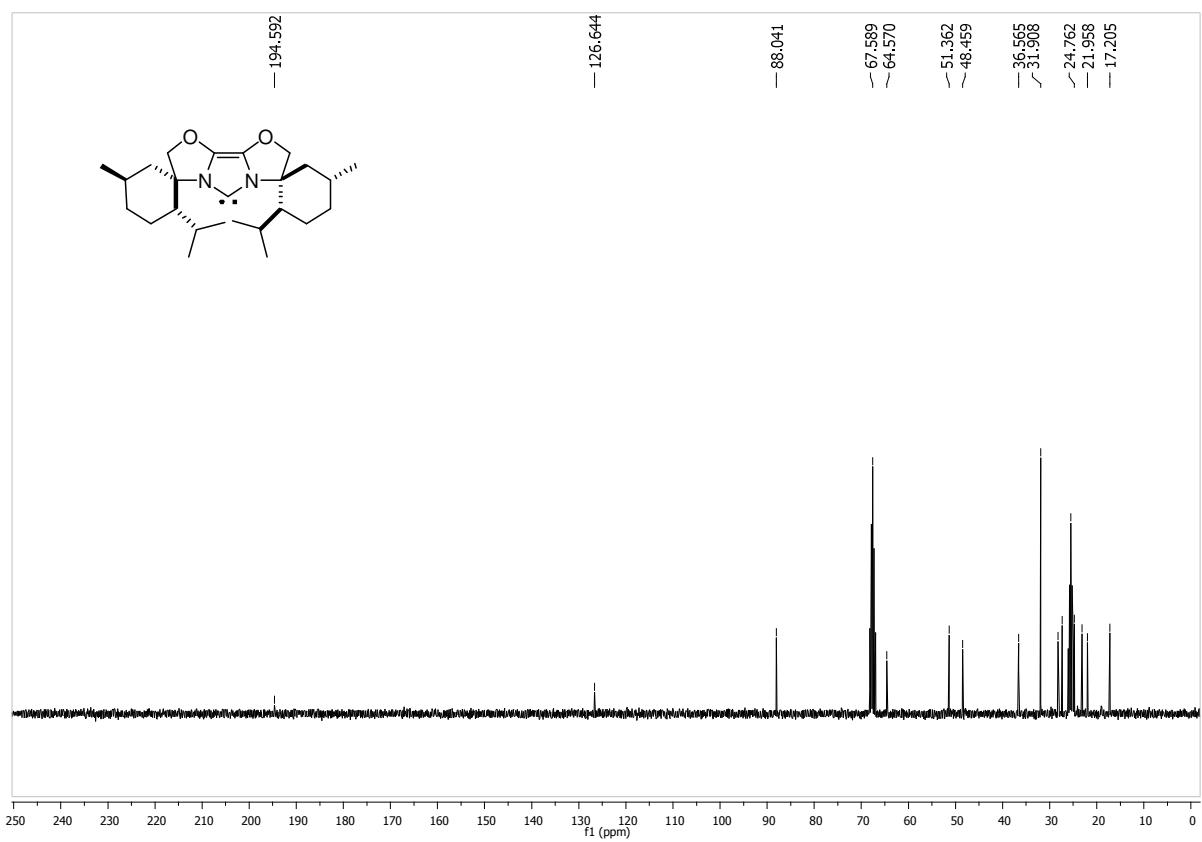
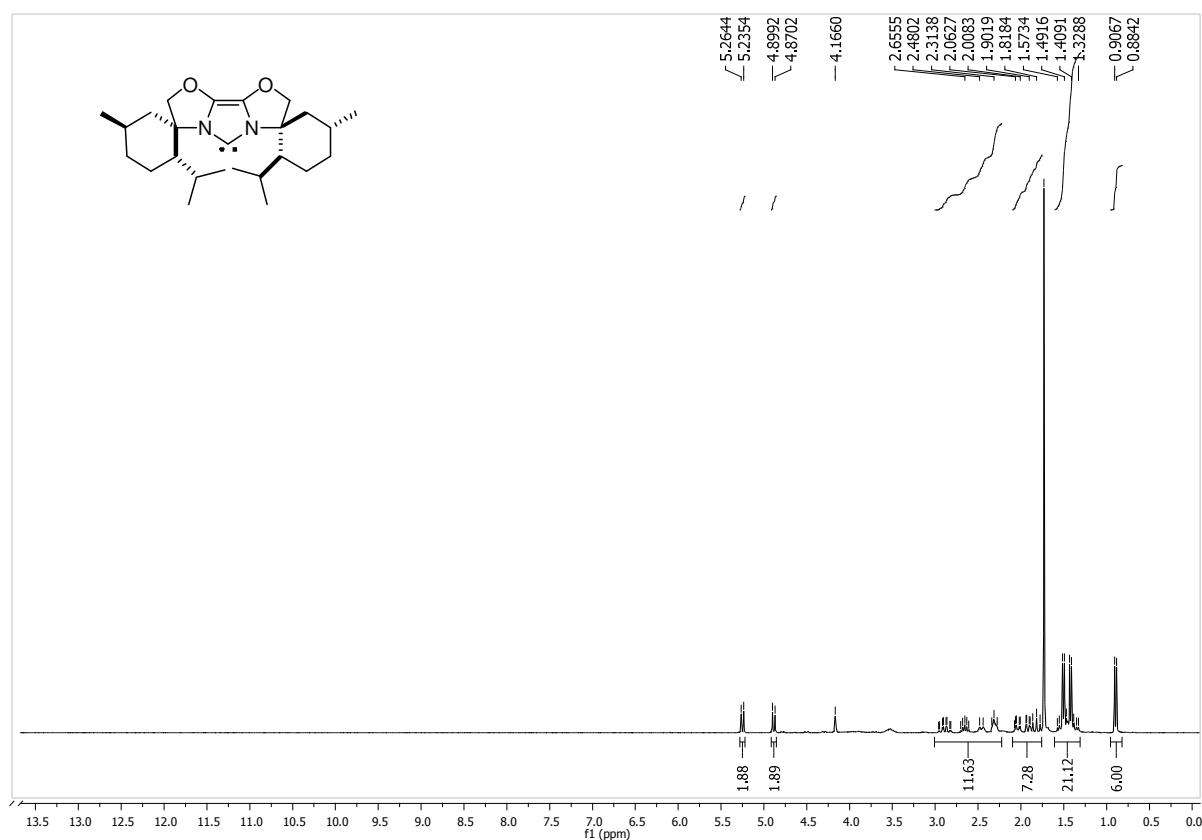


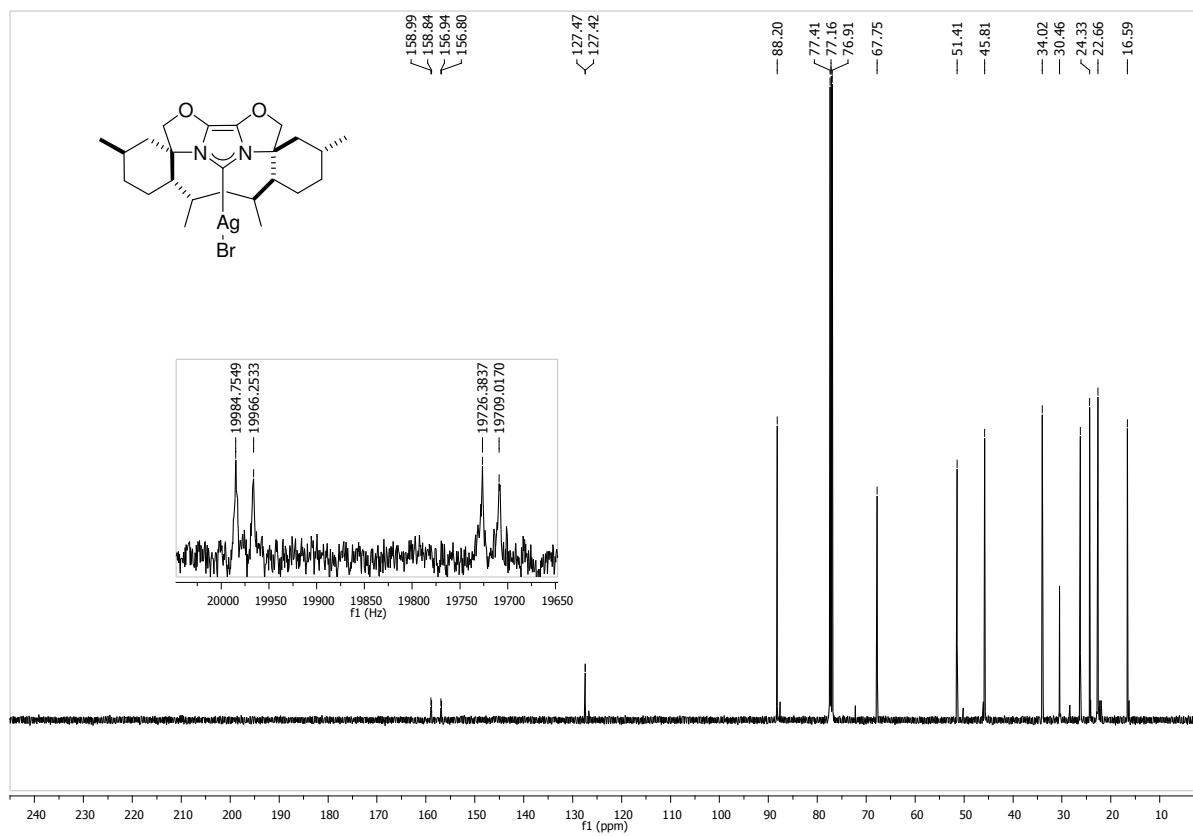
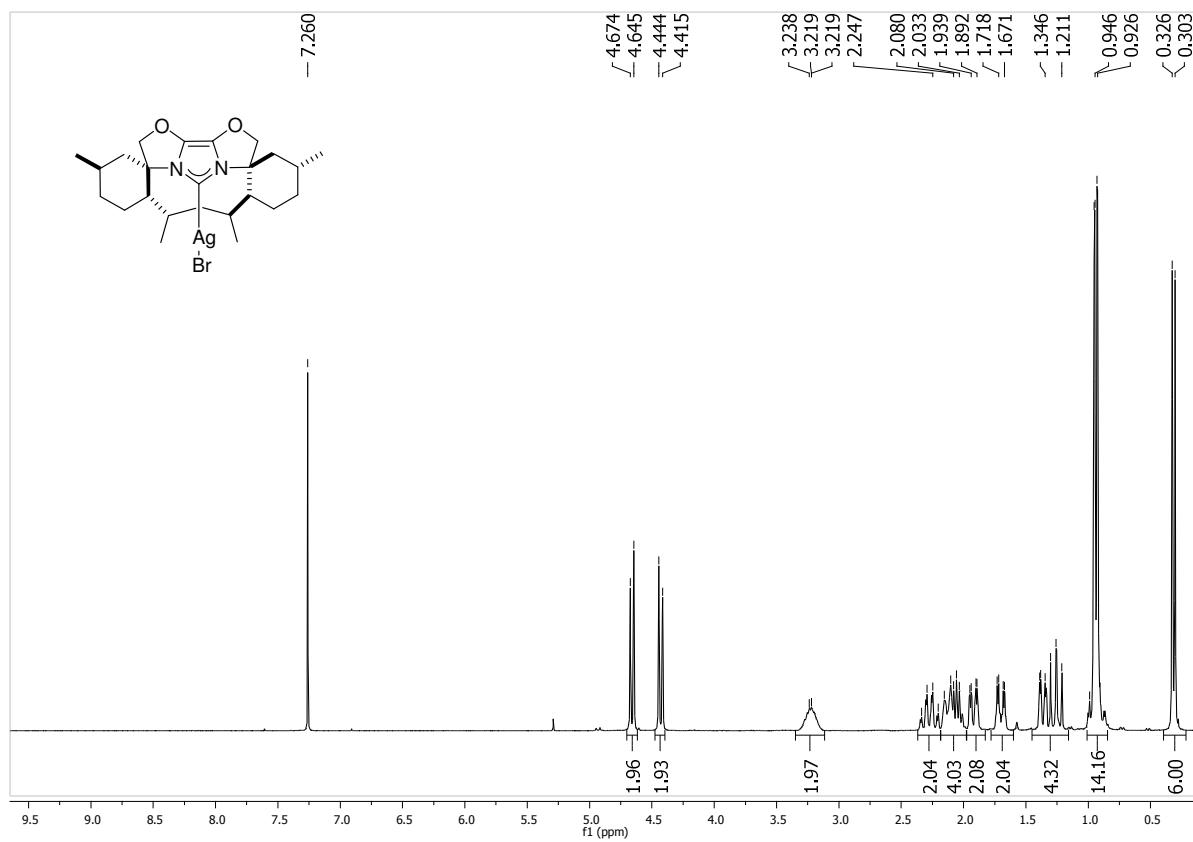
600 MHz, CD<sub>2</sub>Cl<sub>2</sub>, 193K



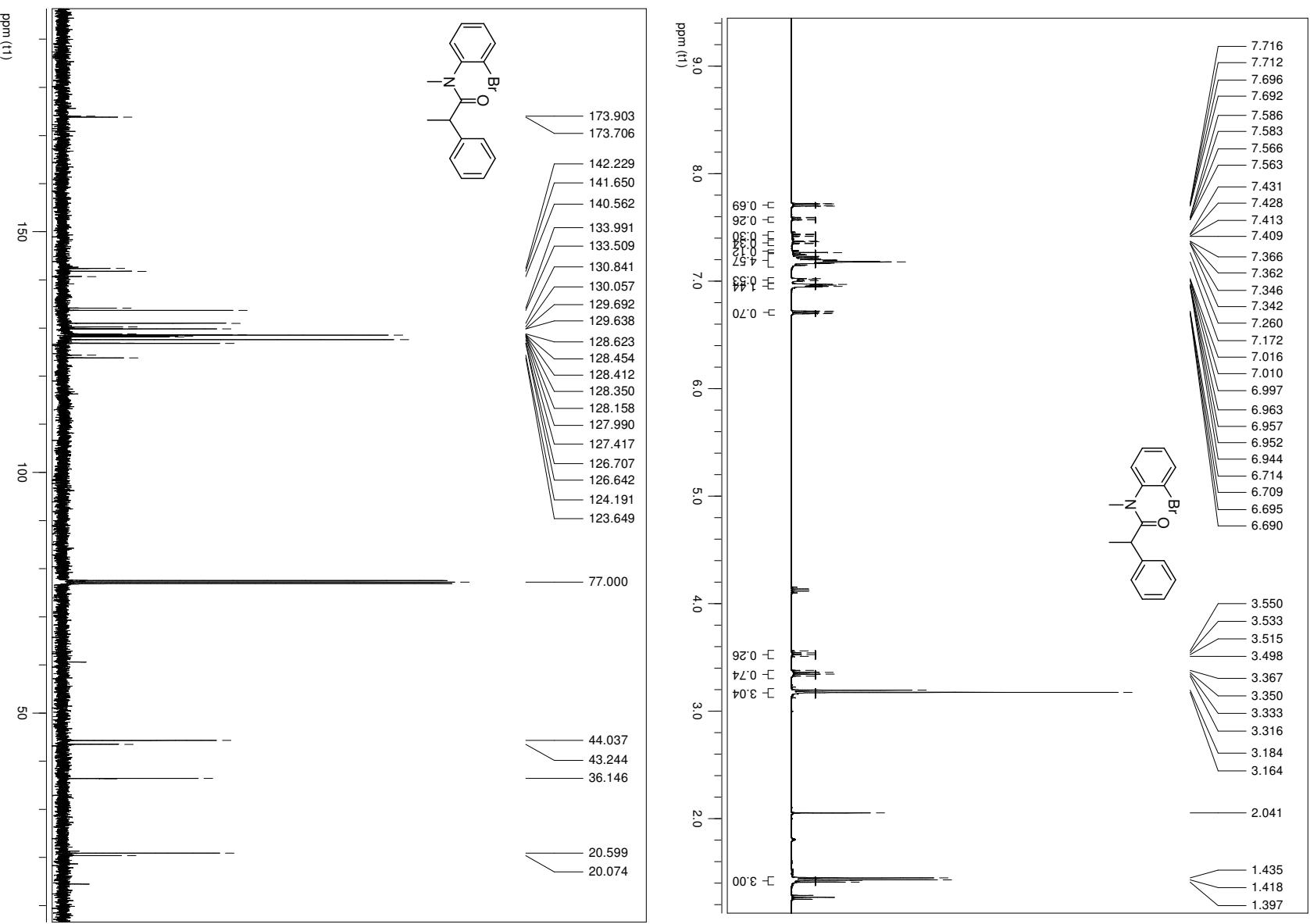
600 MHz, d<sub>6</sub>-DMSO, 373K

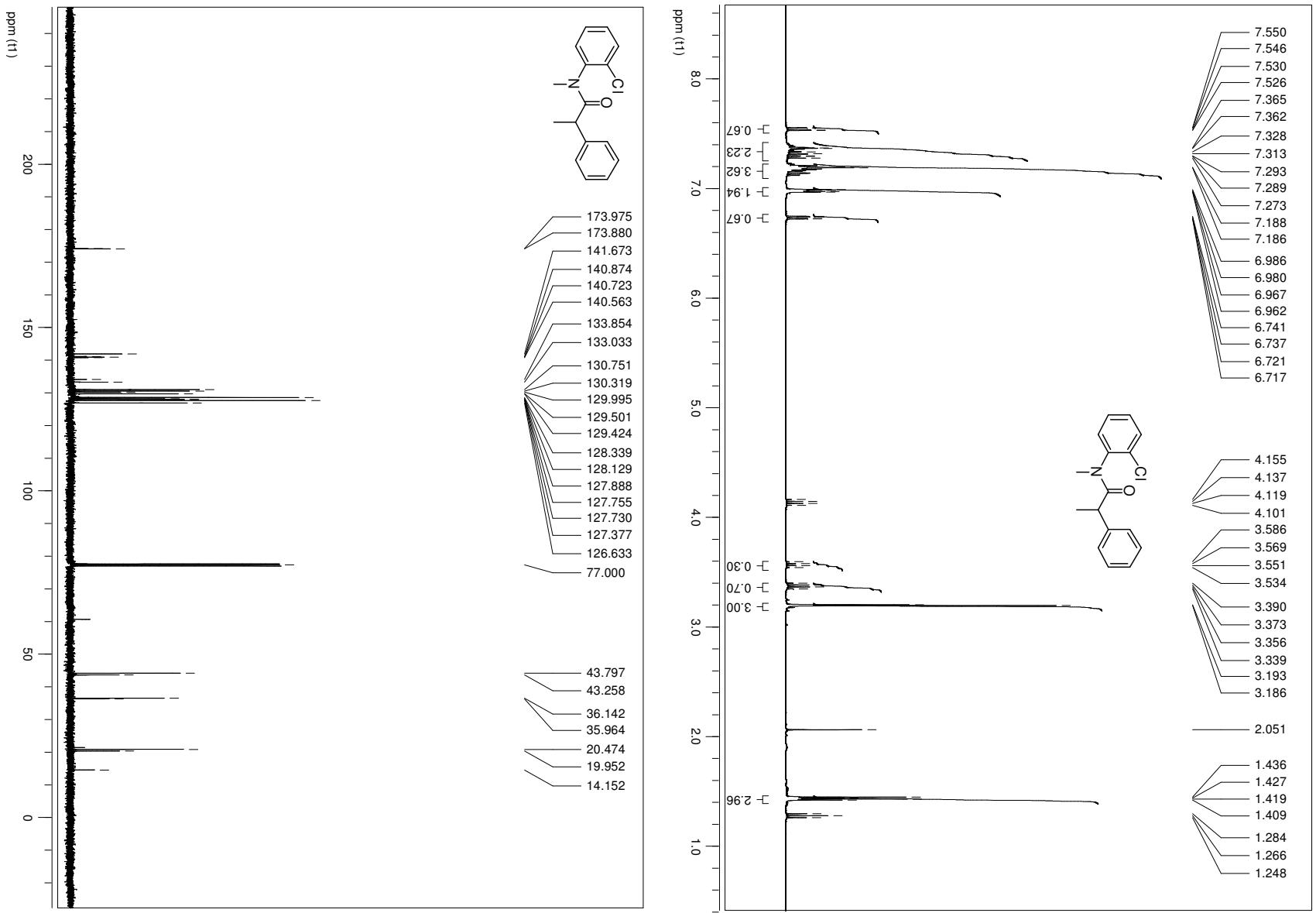


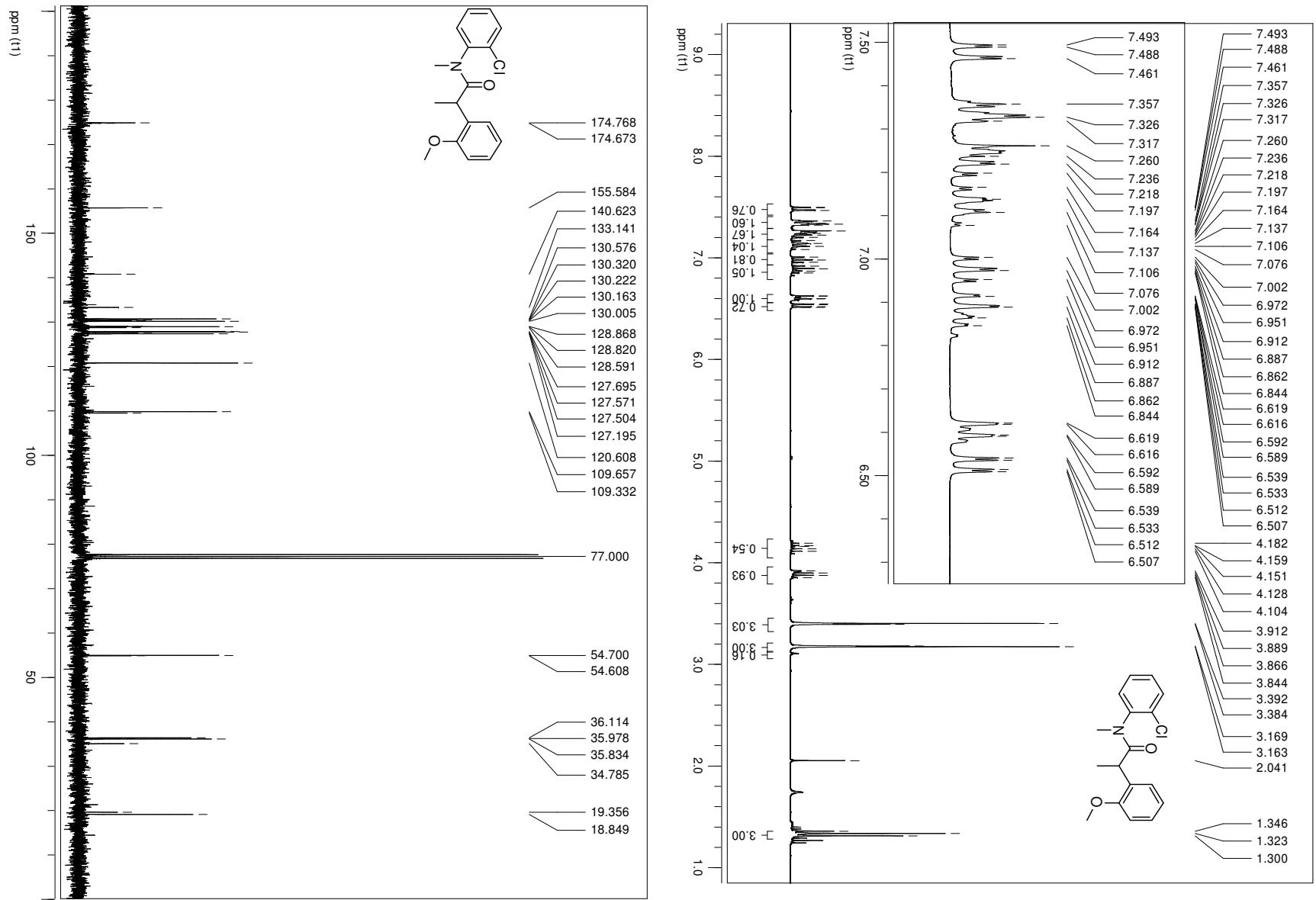


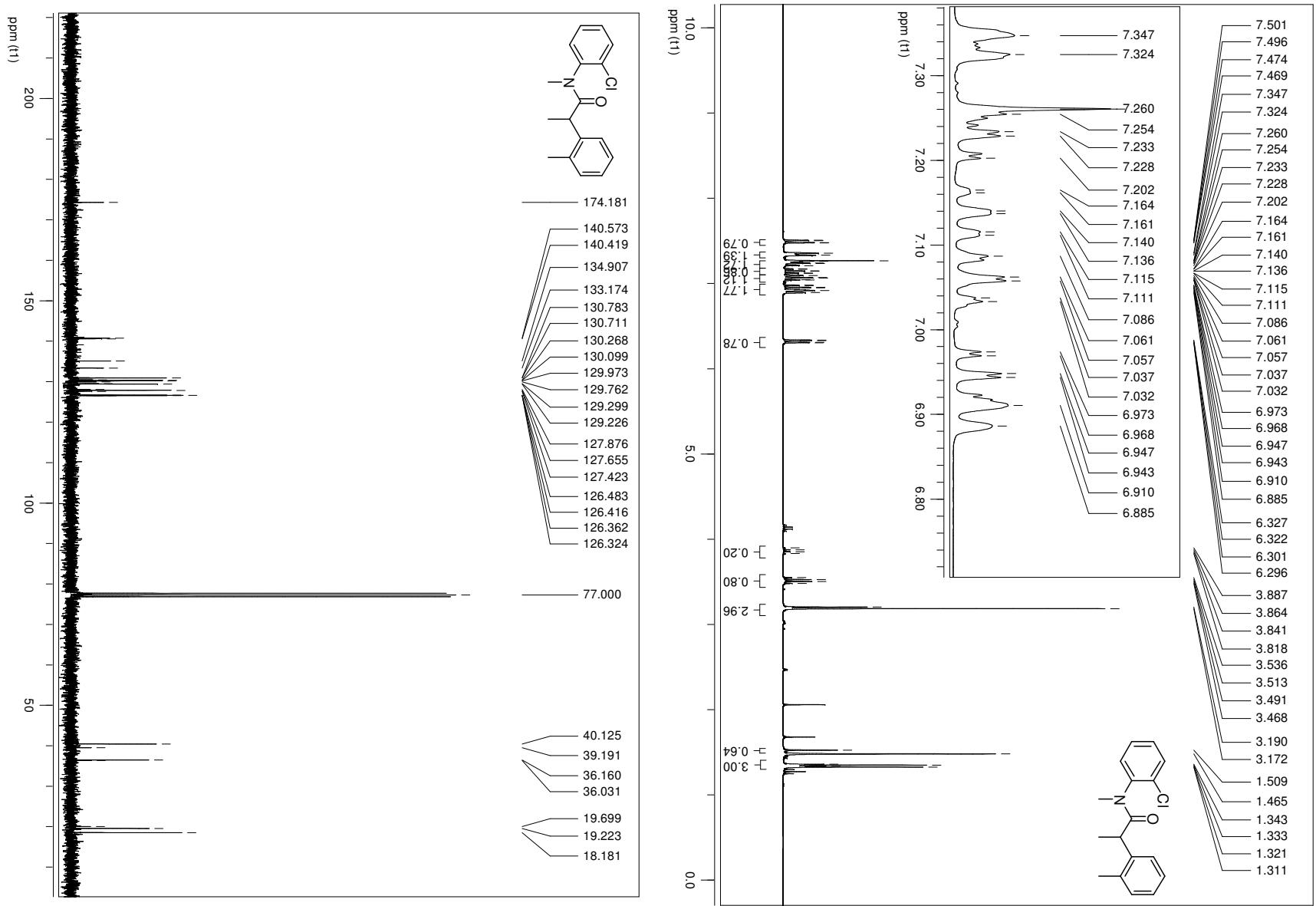


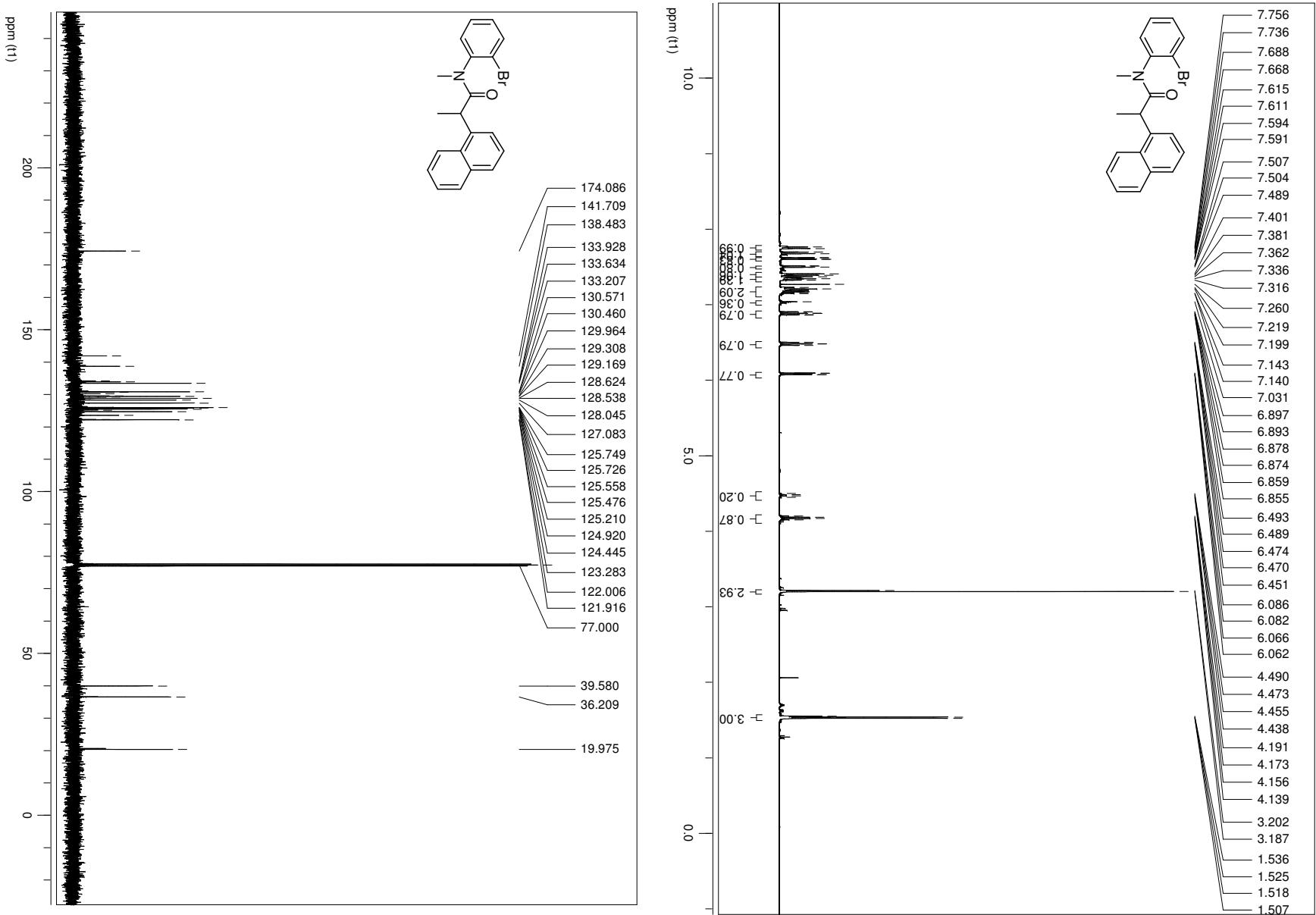
## 6.2 Amide Starting Materials

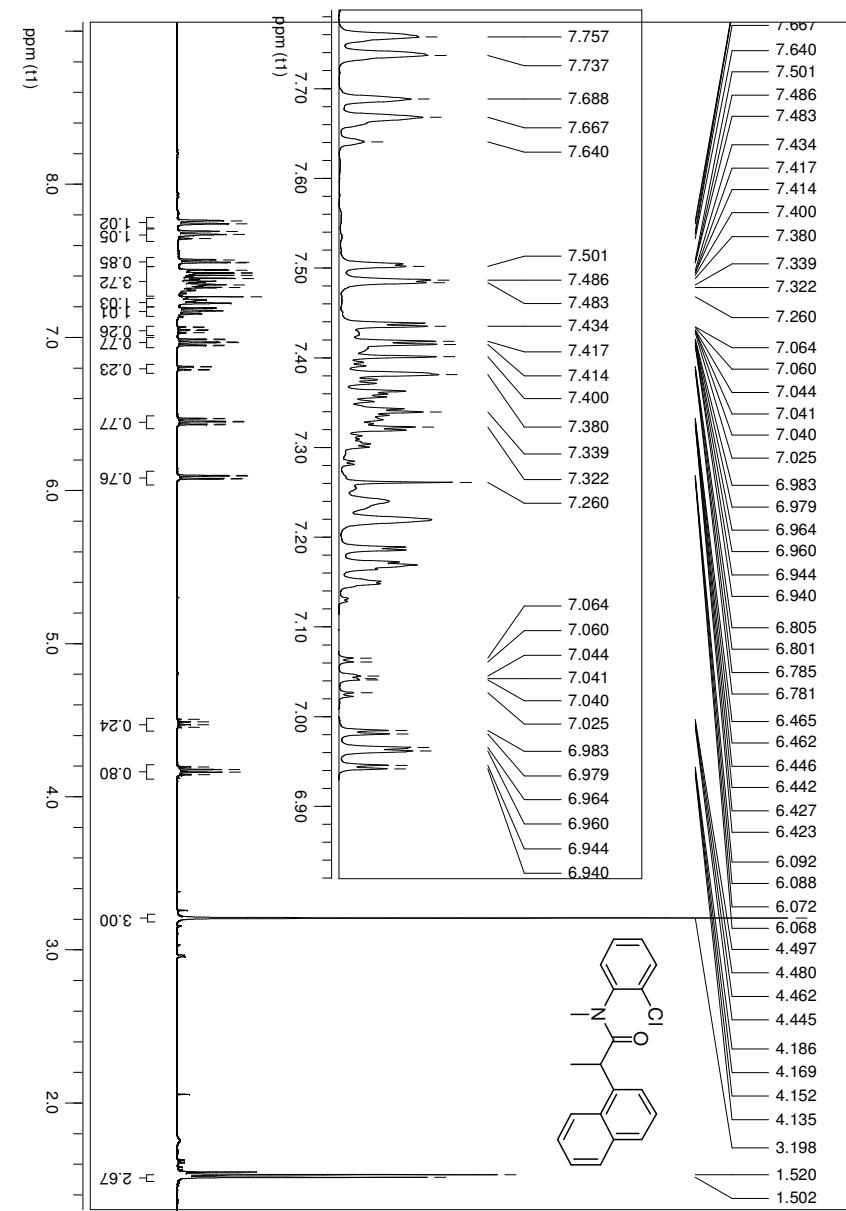
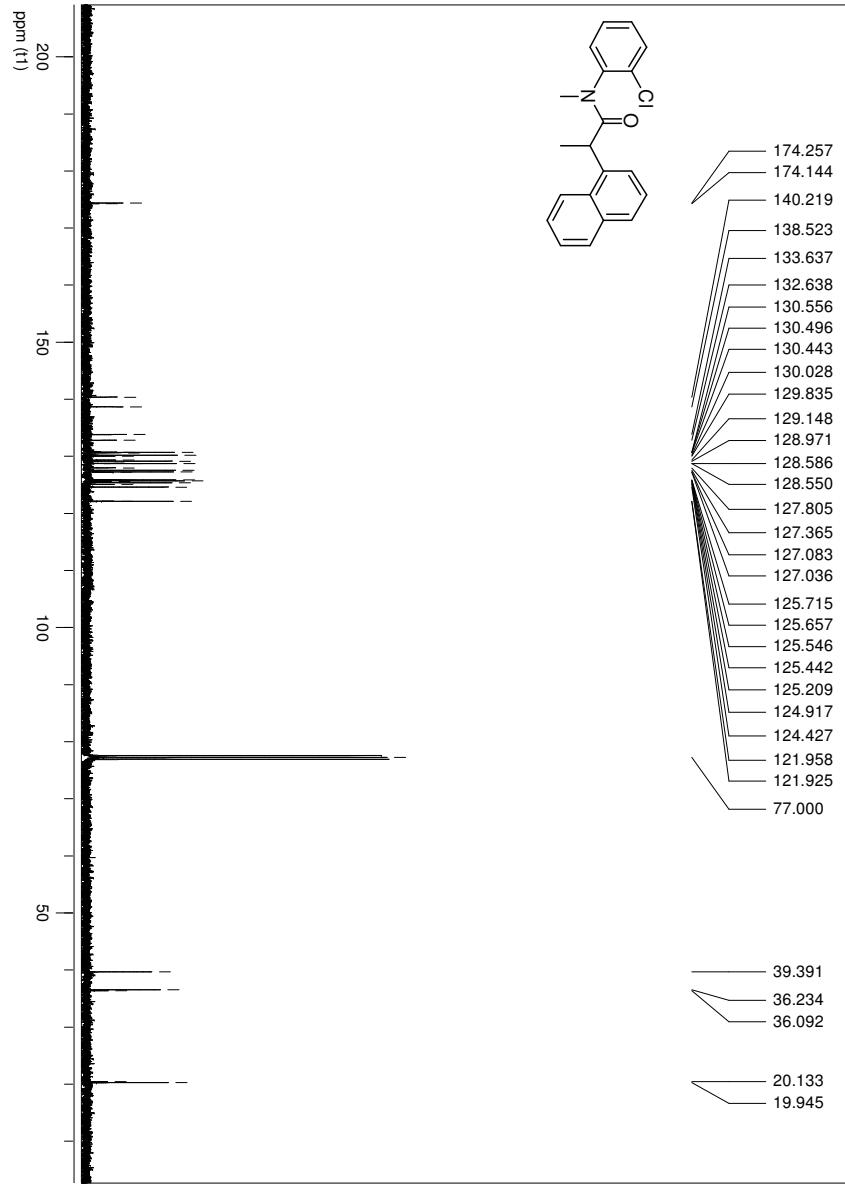


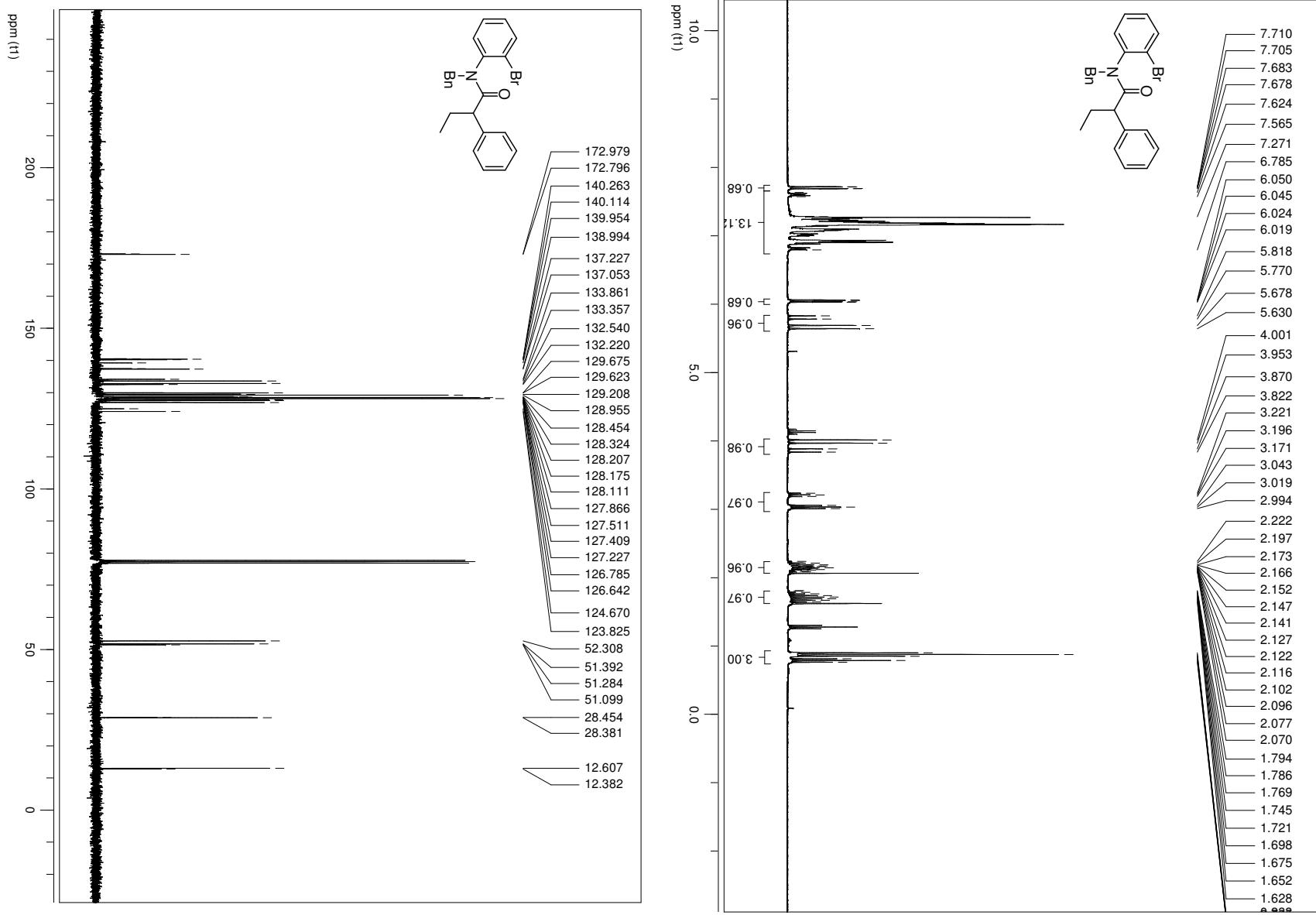


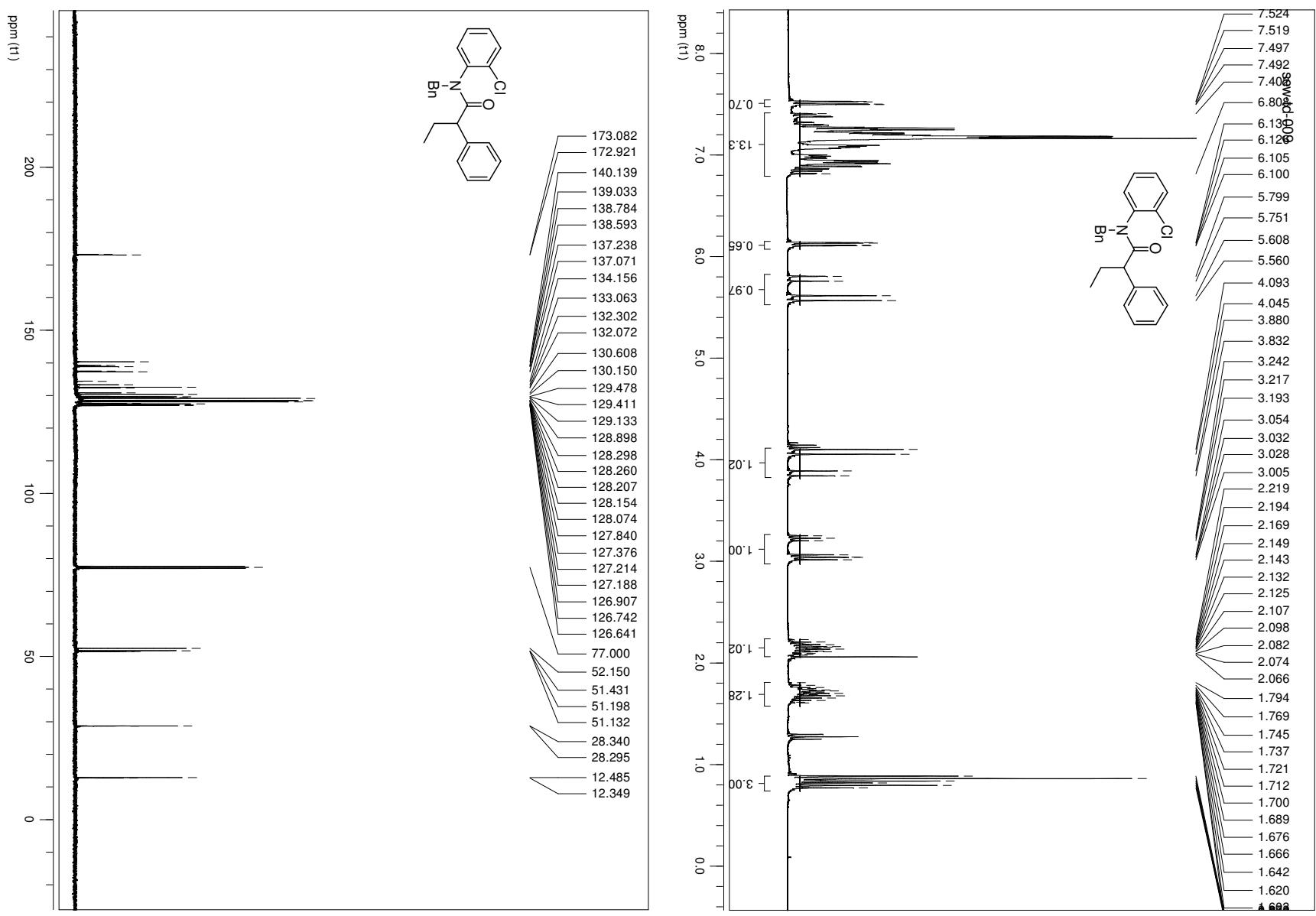


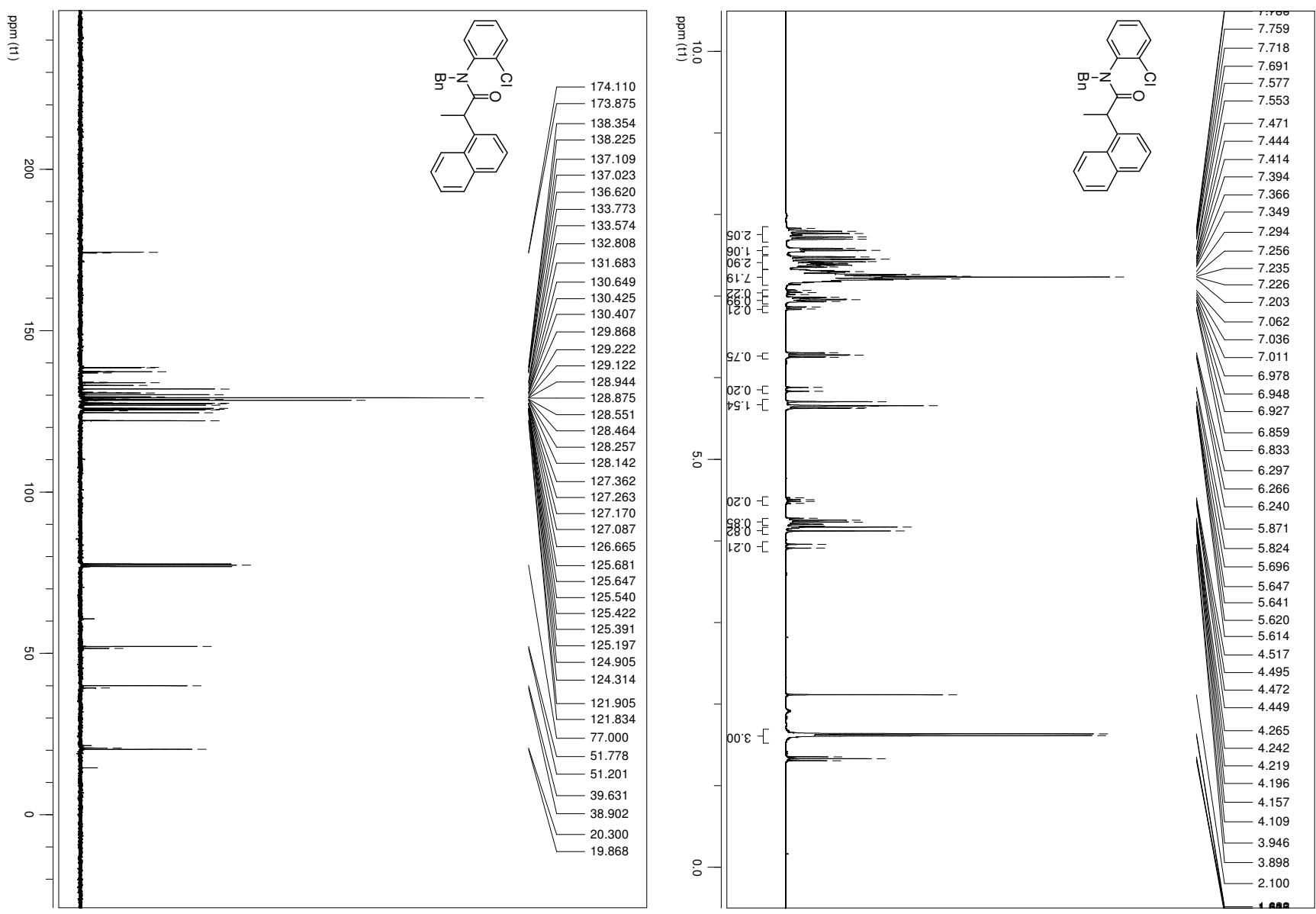


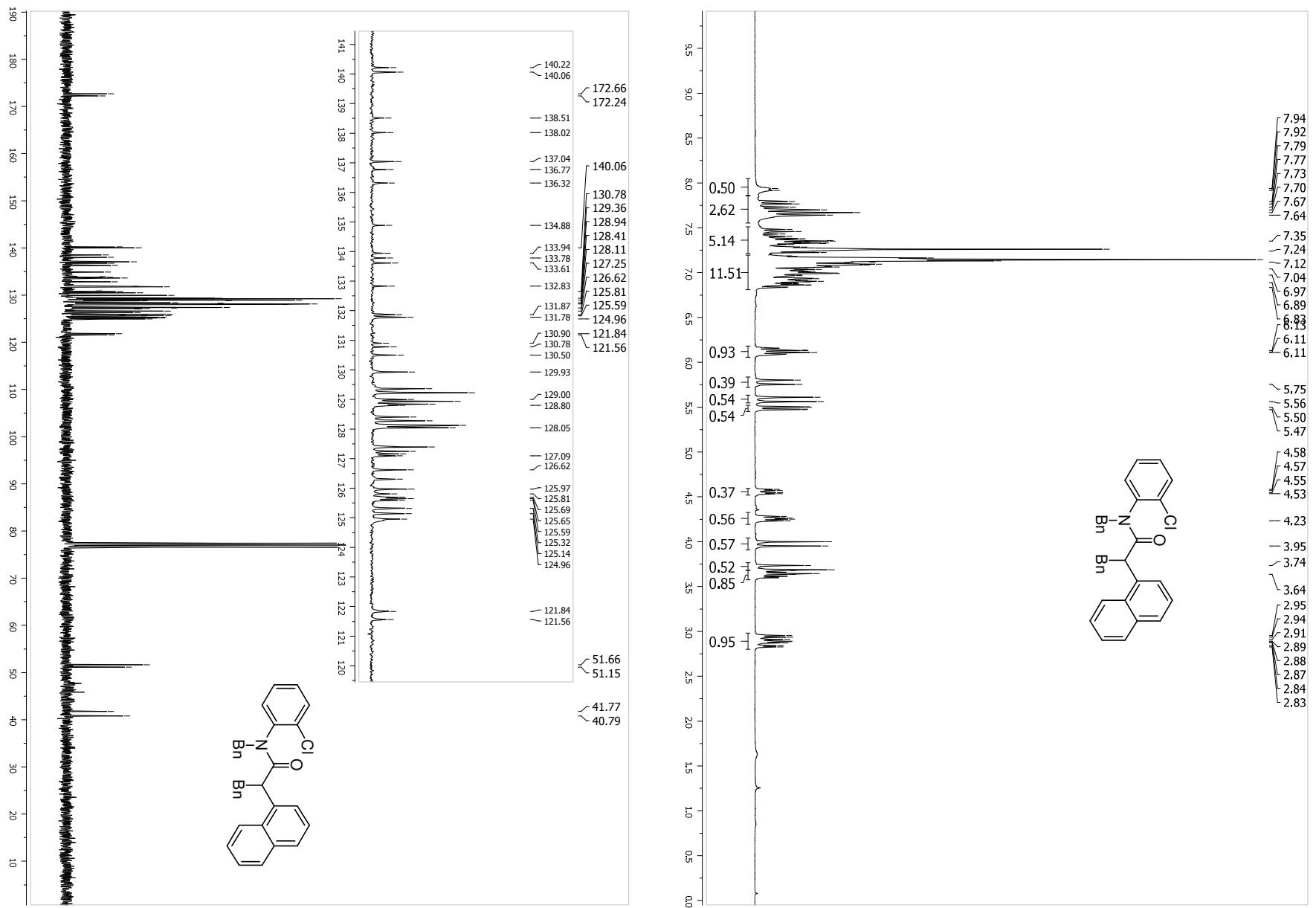


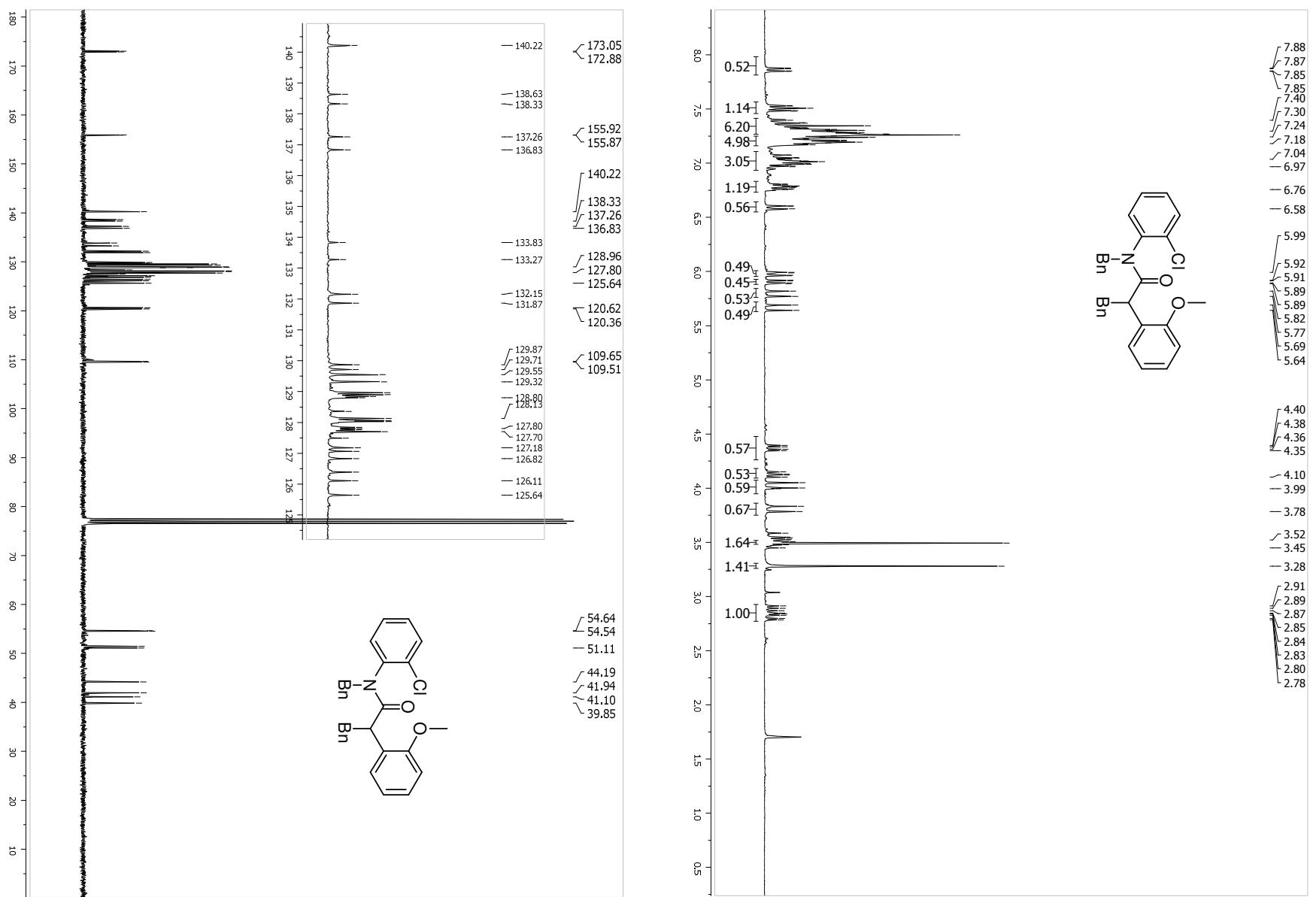




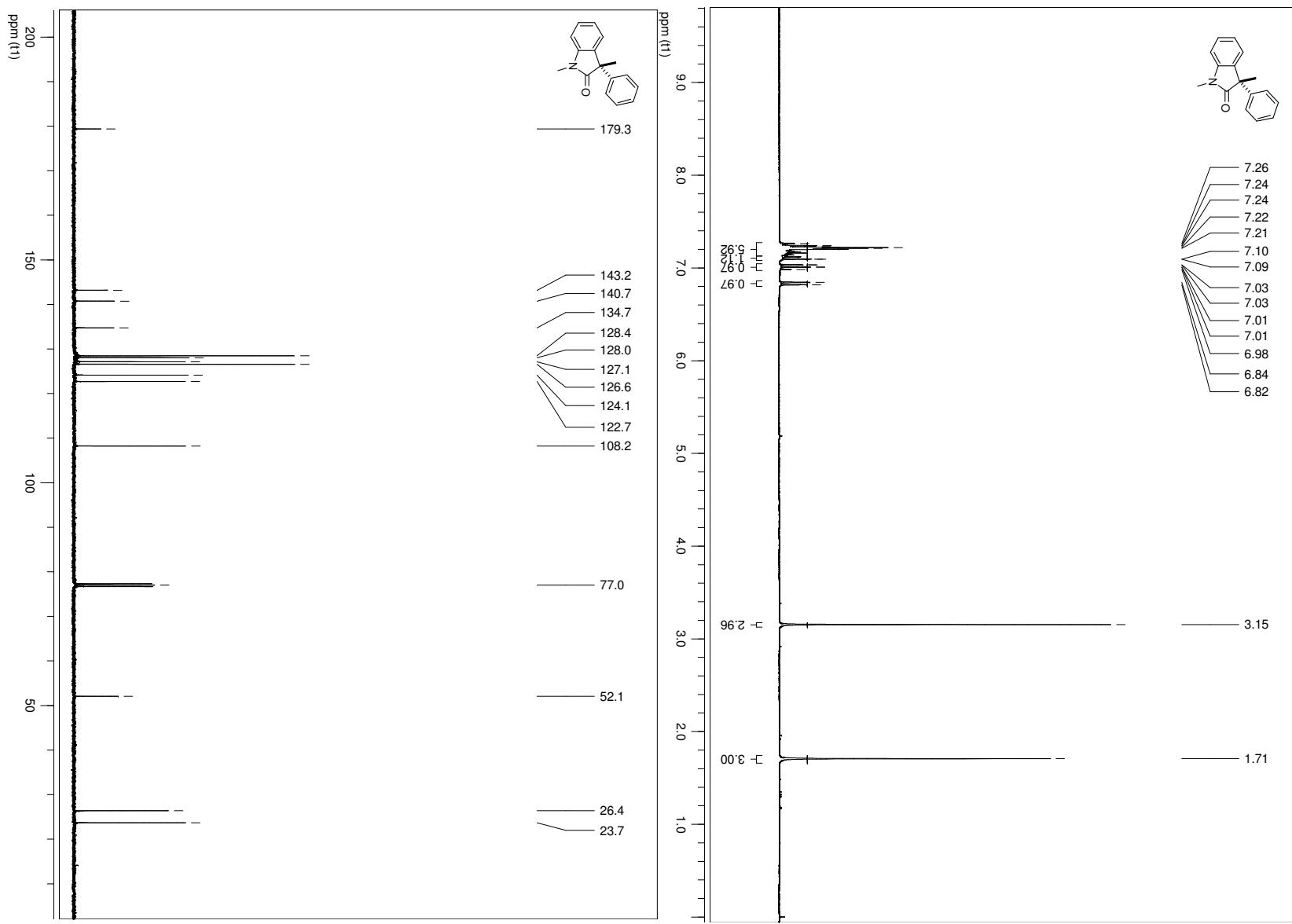


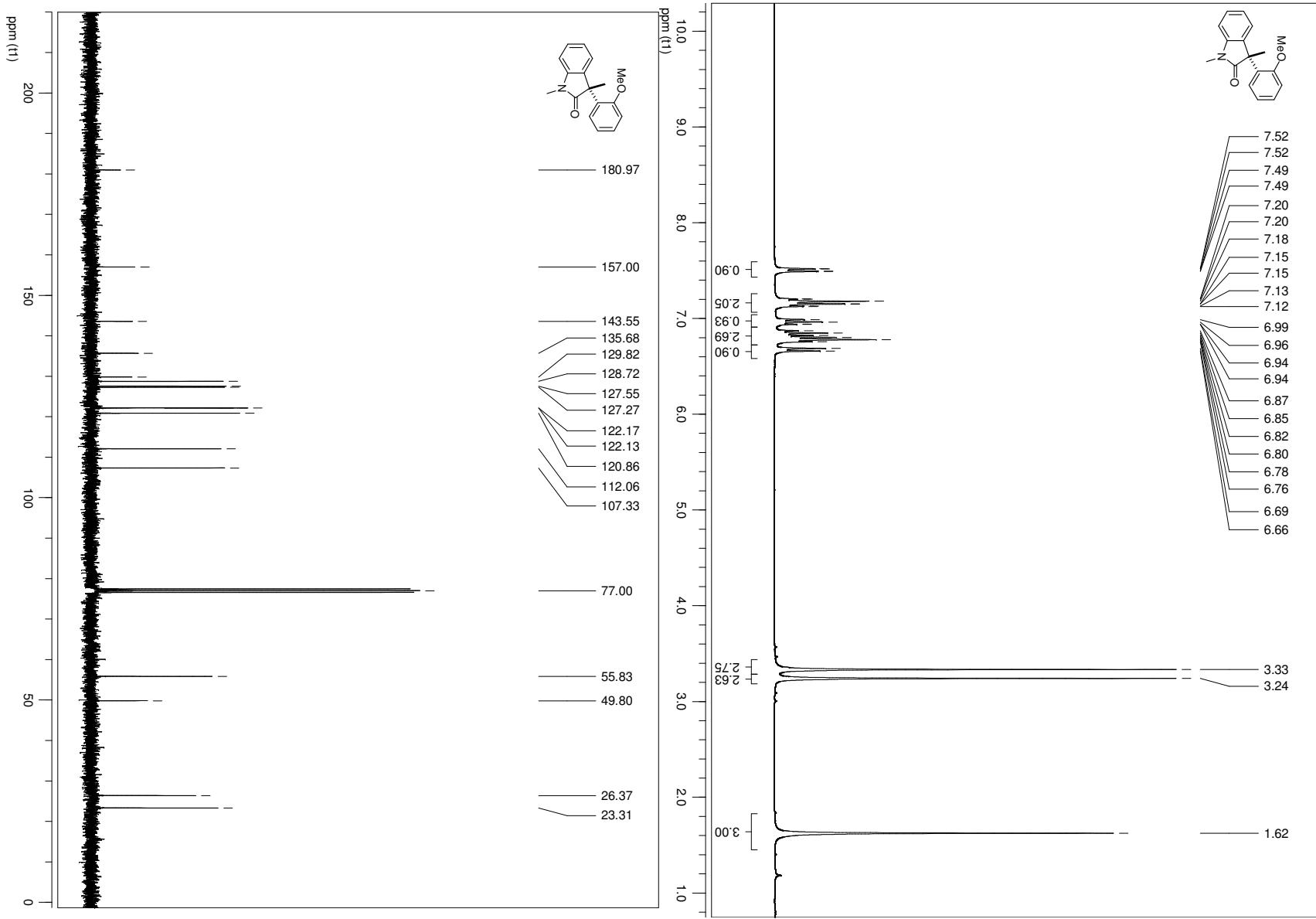


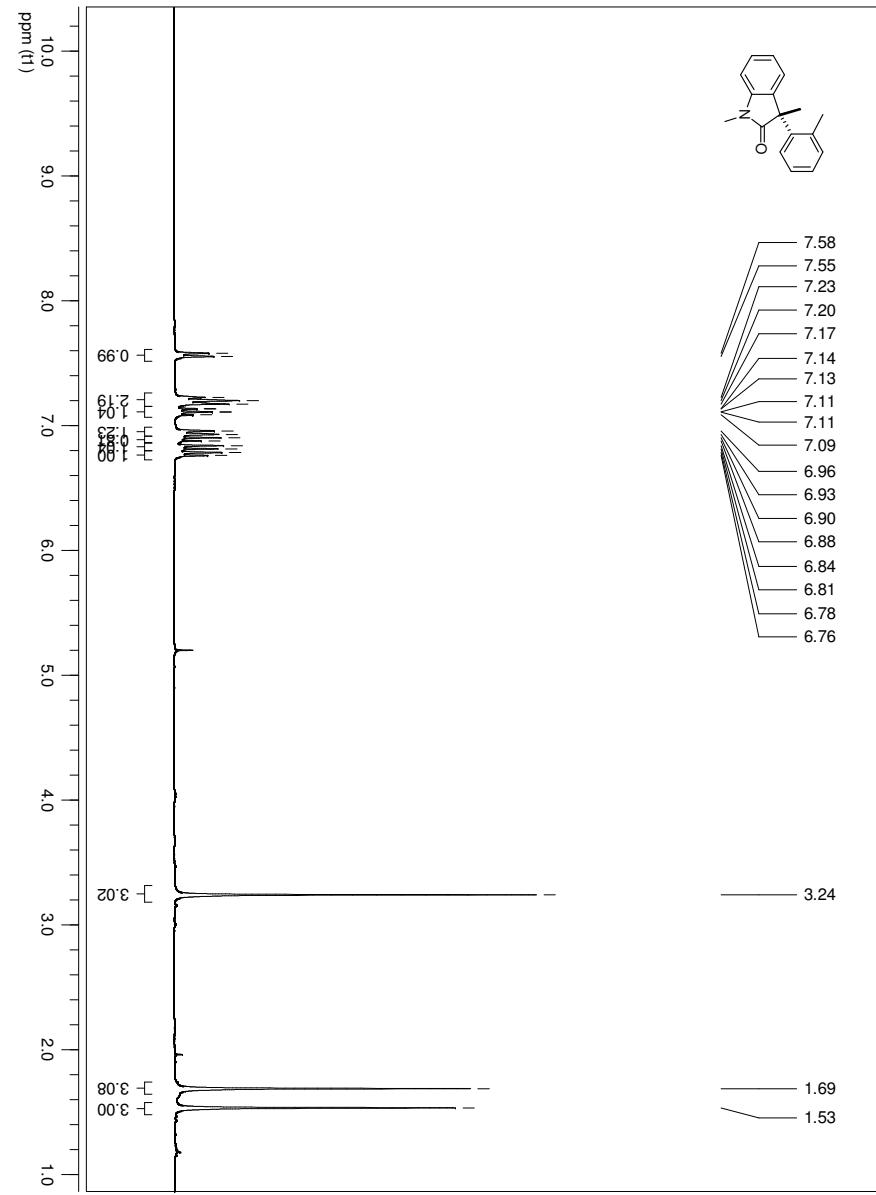
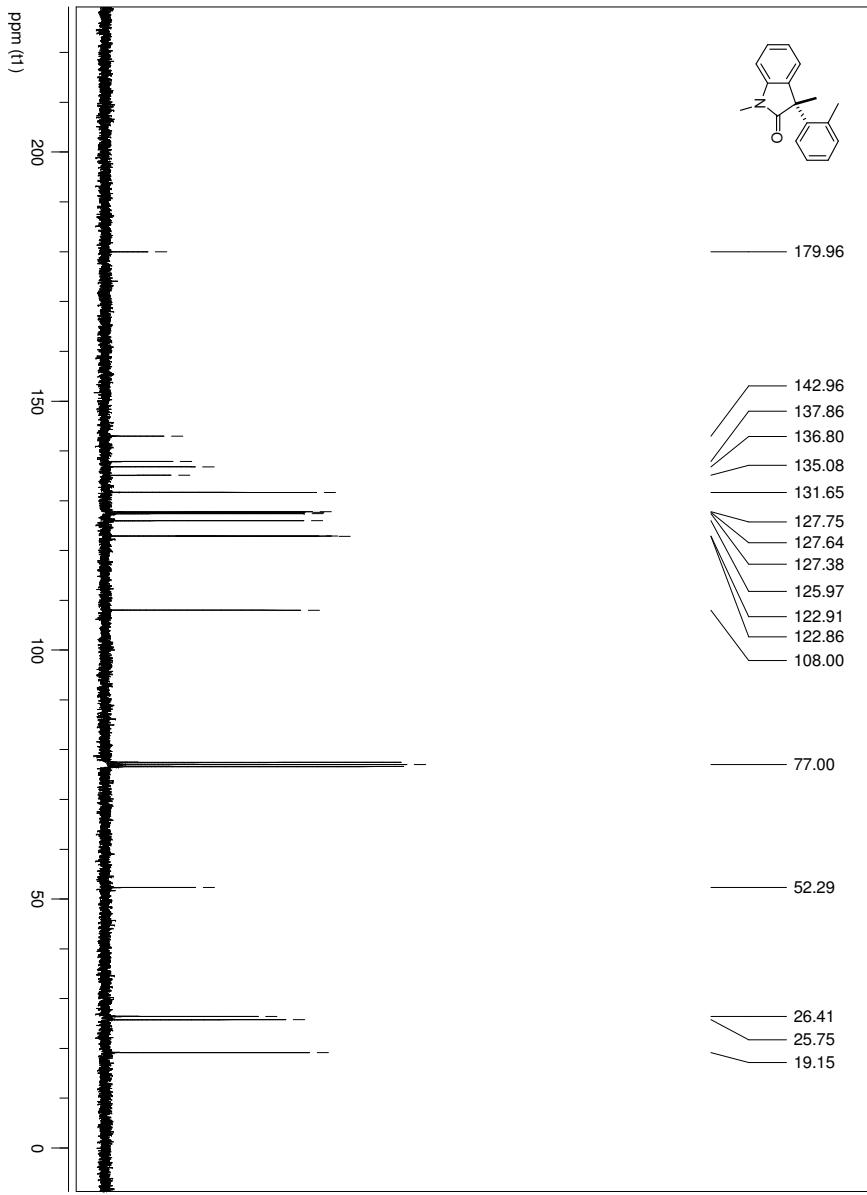


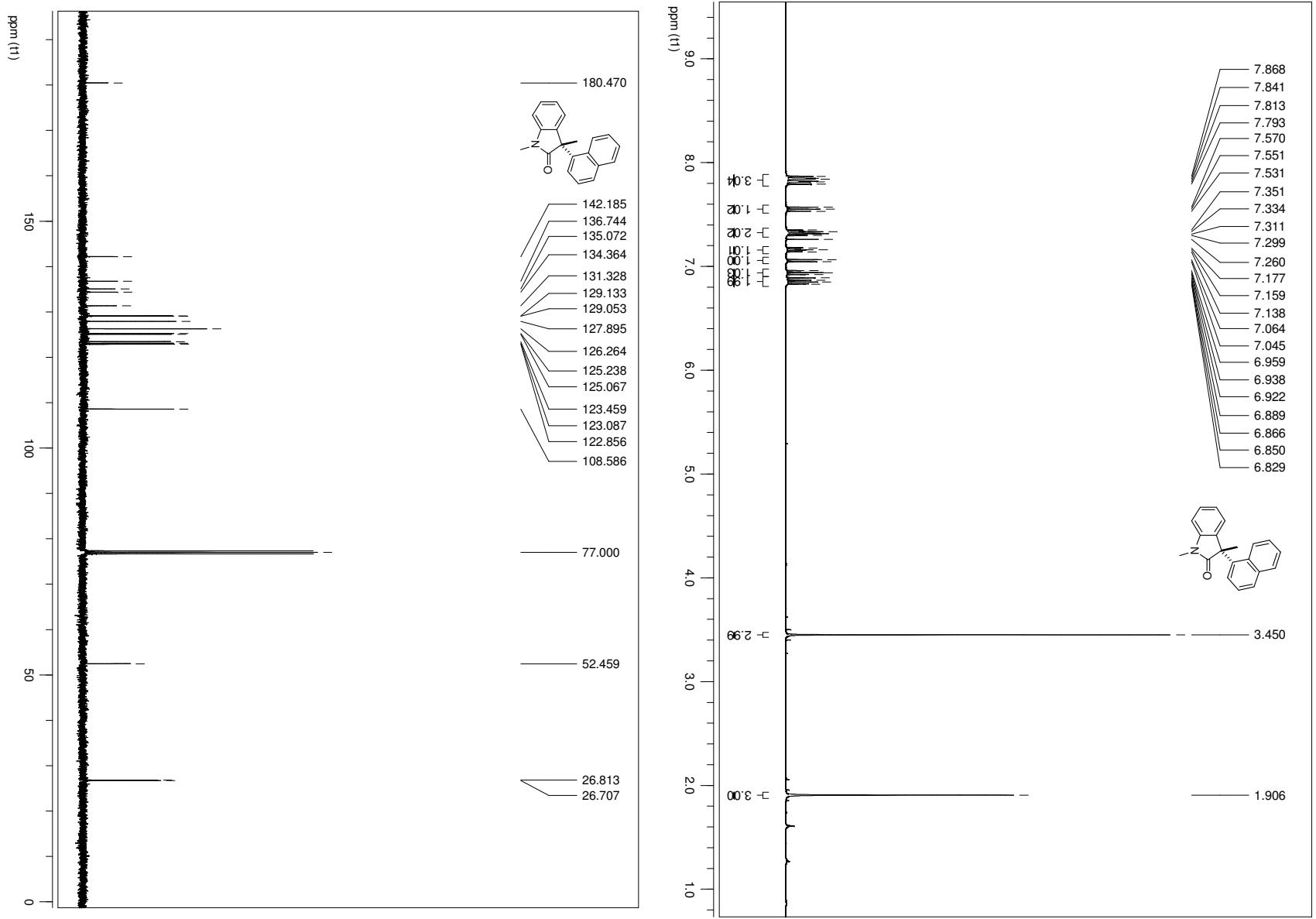


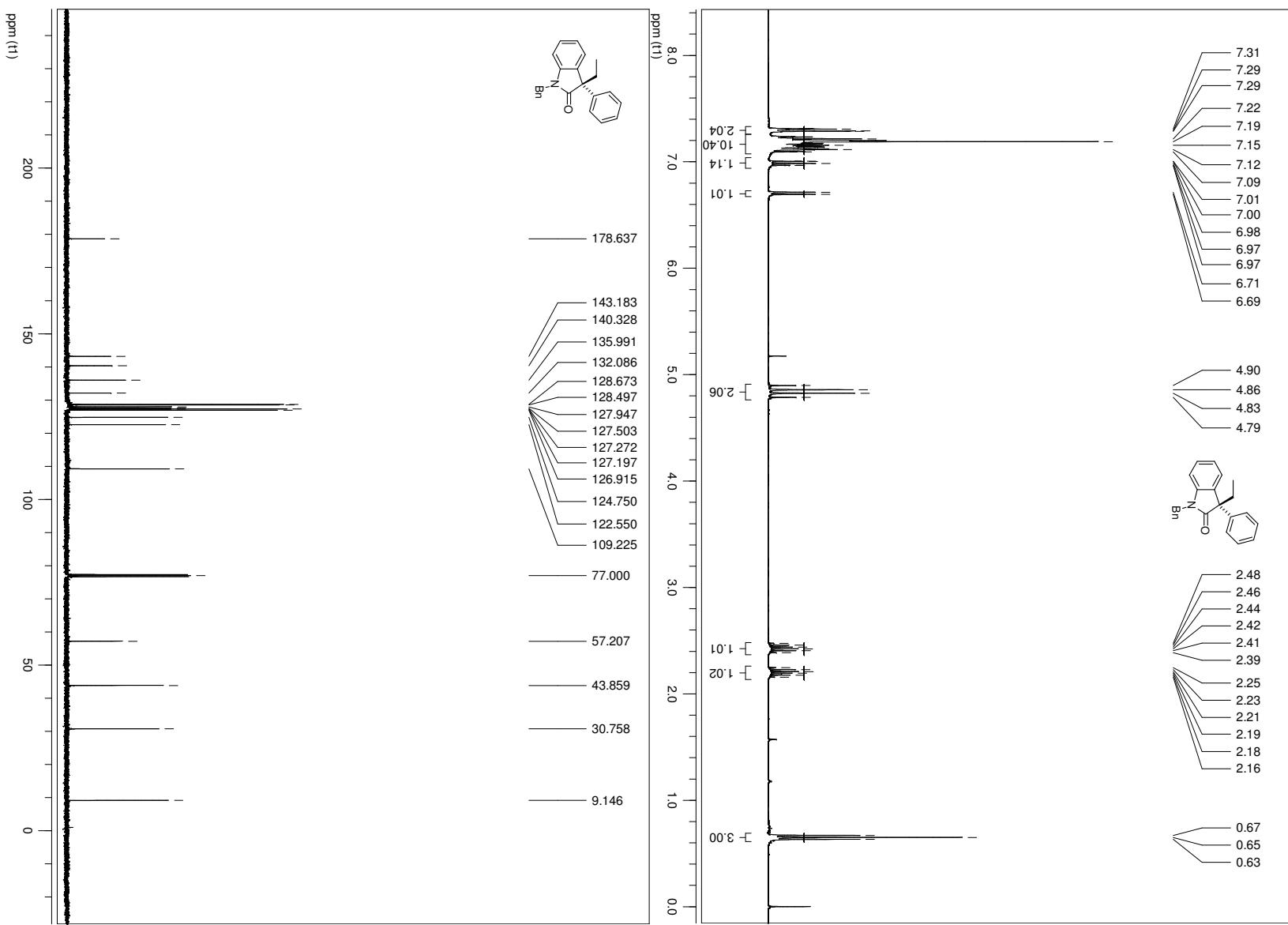
### 6.3 Oxindoles

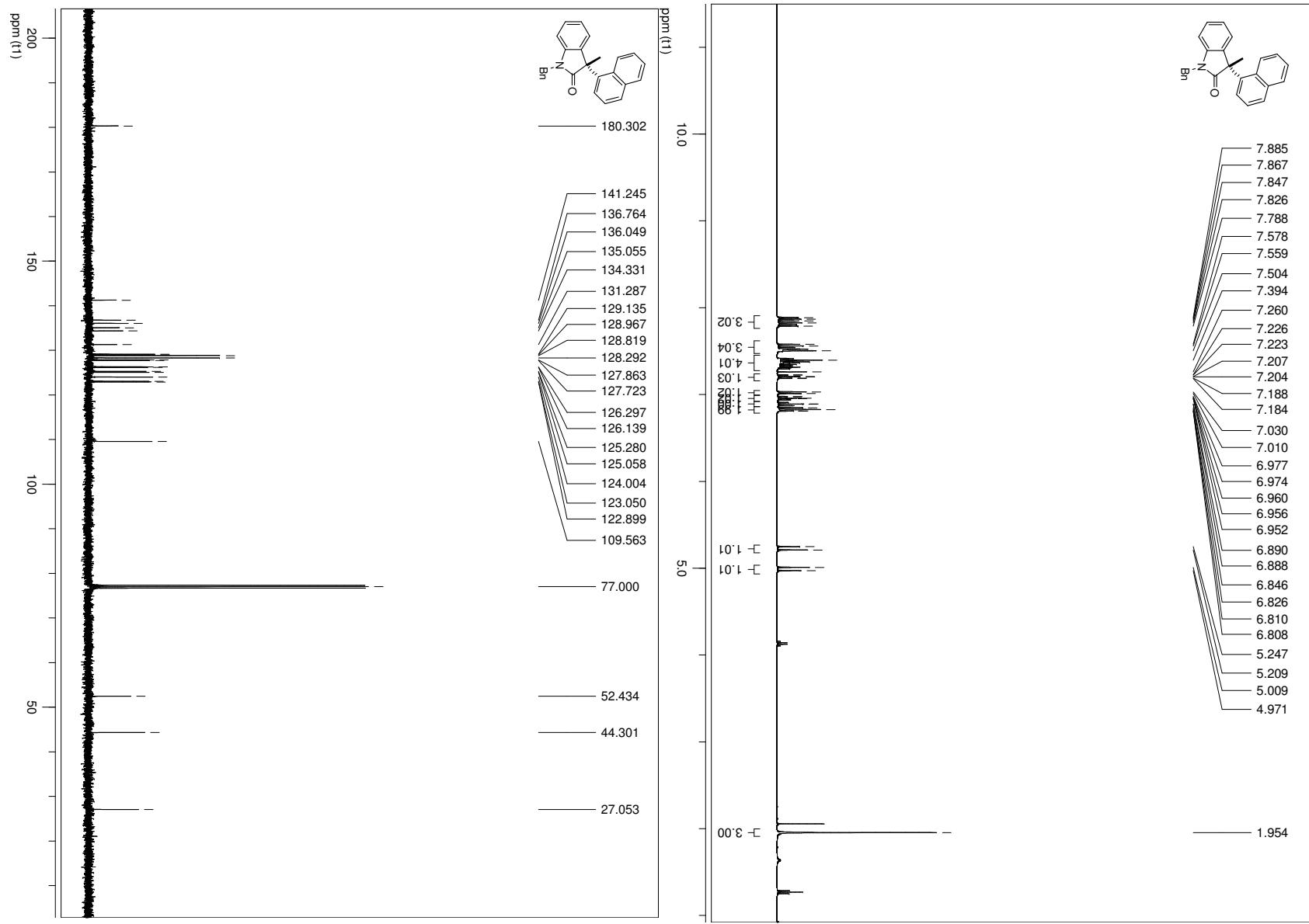


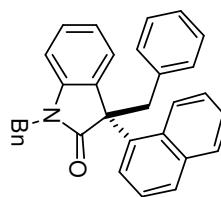
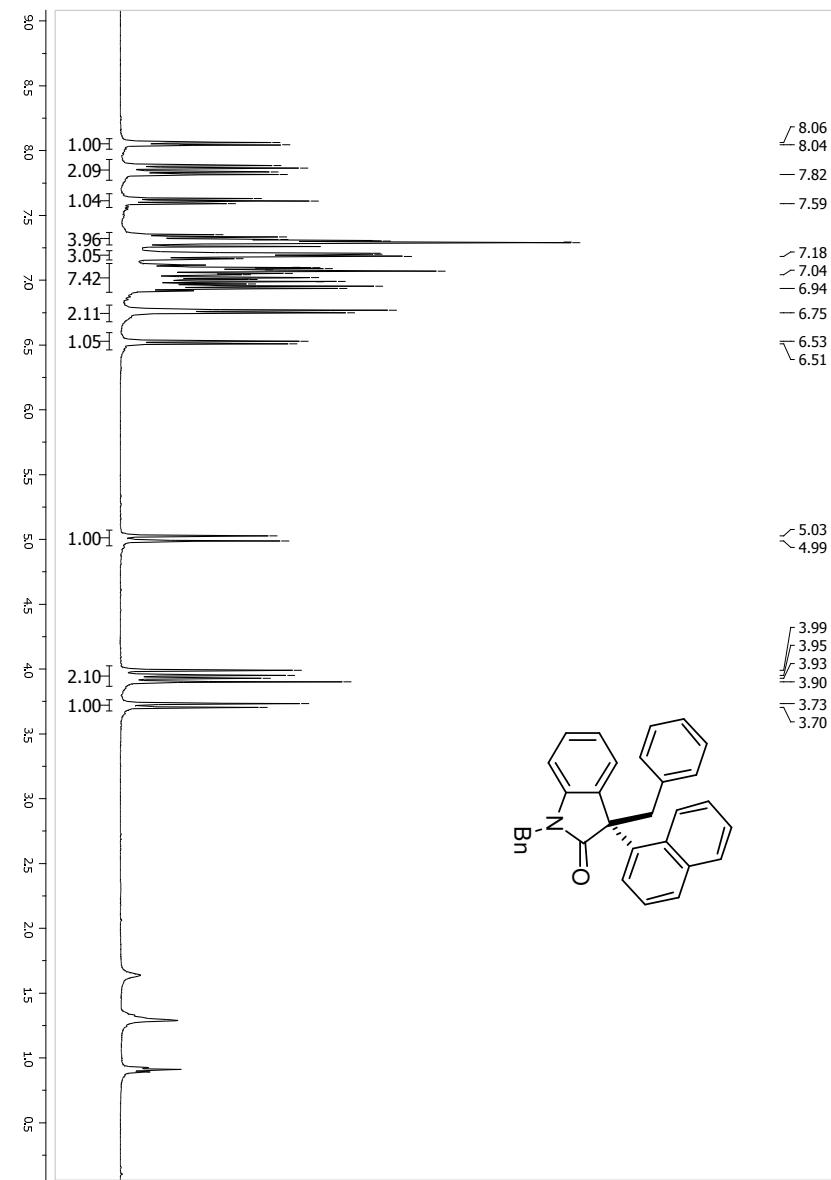
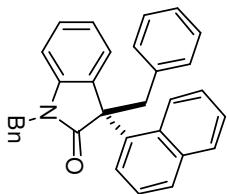
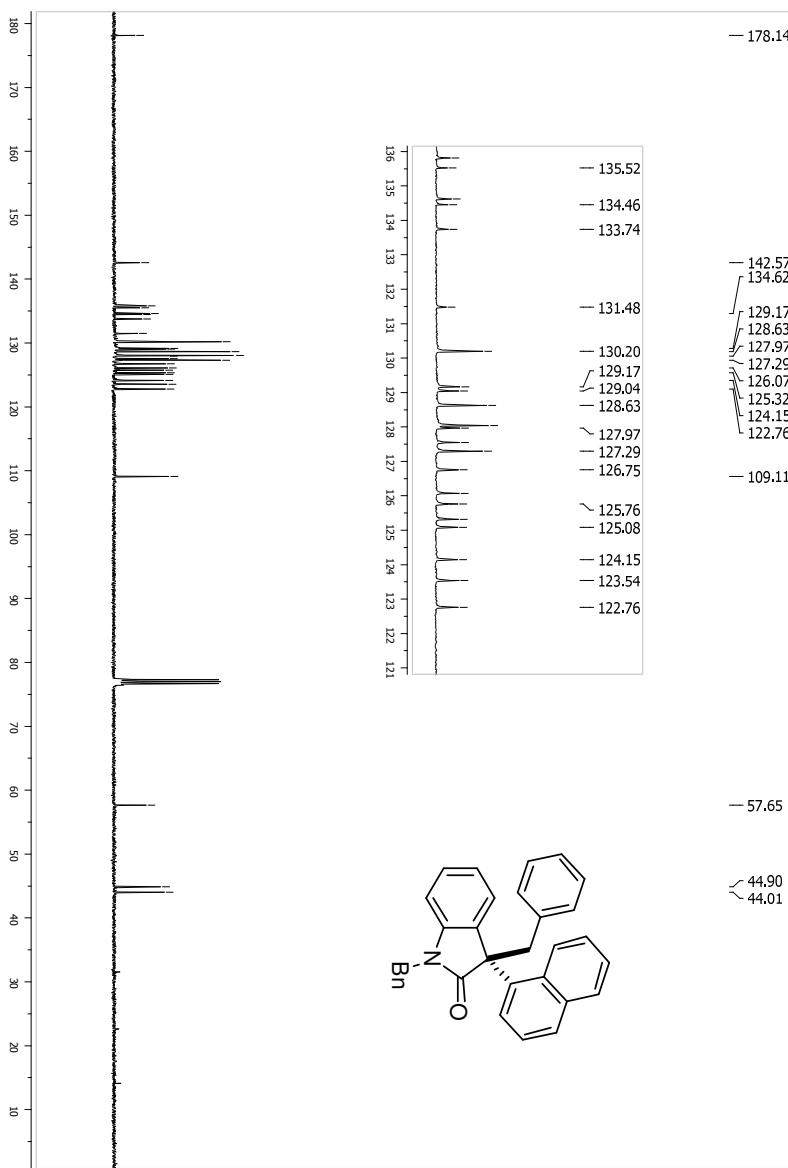


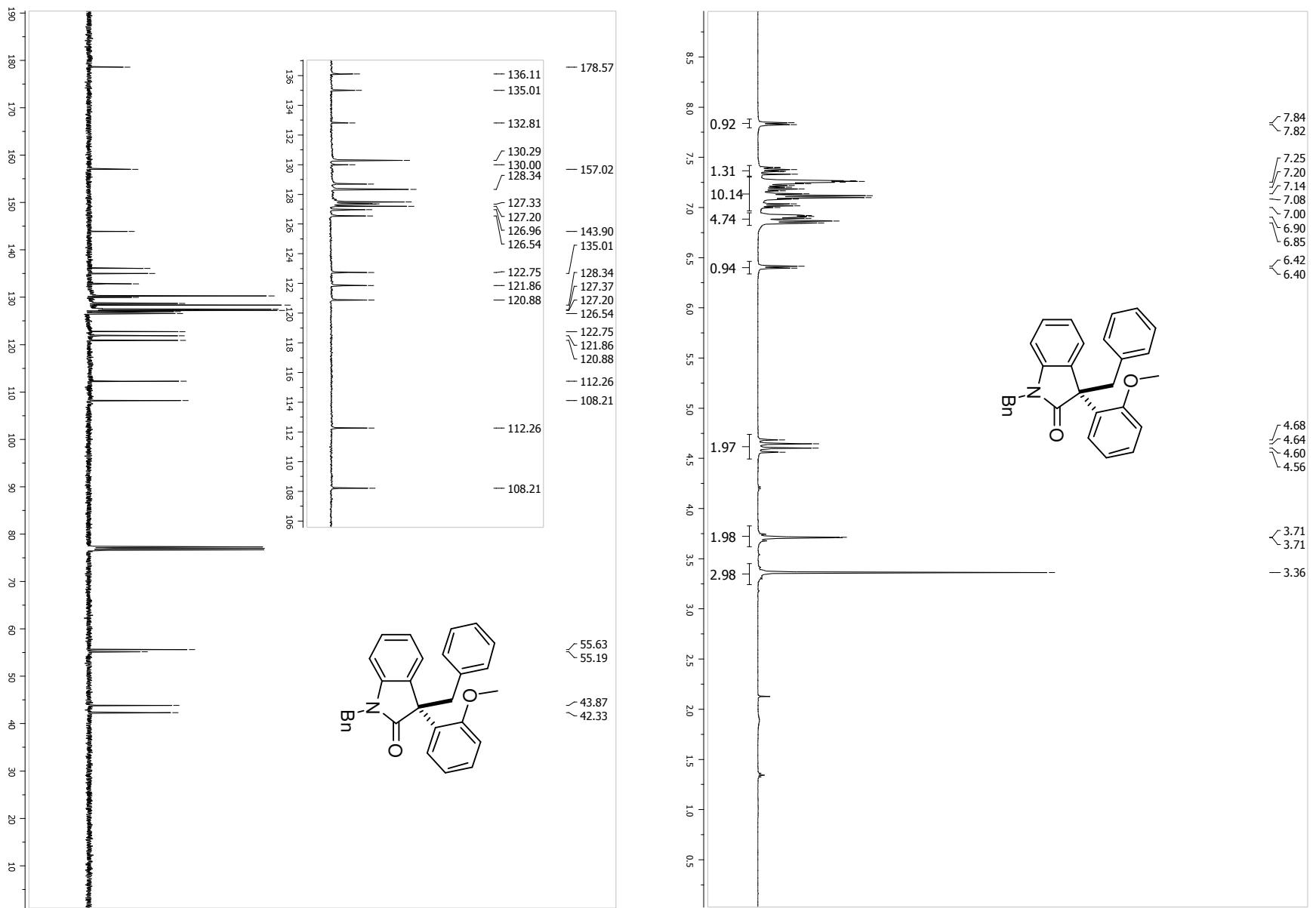




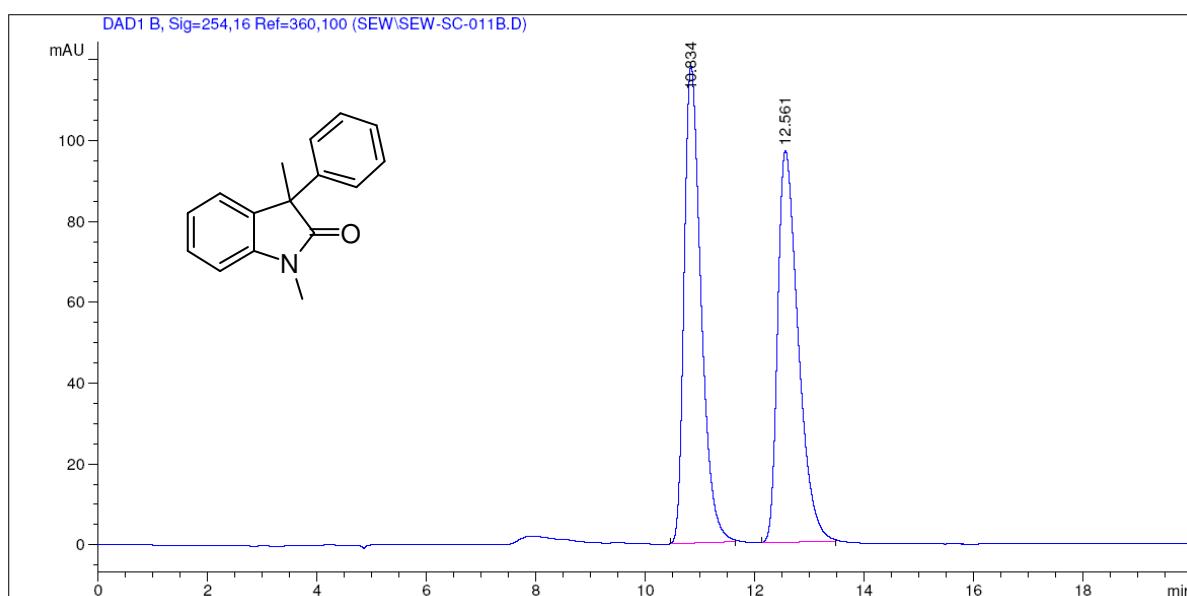
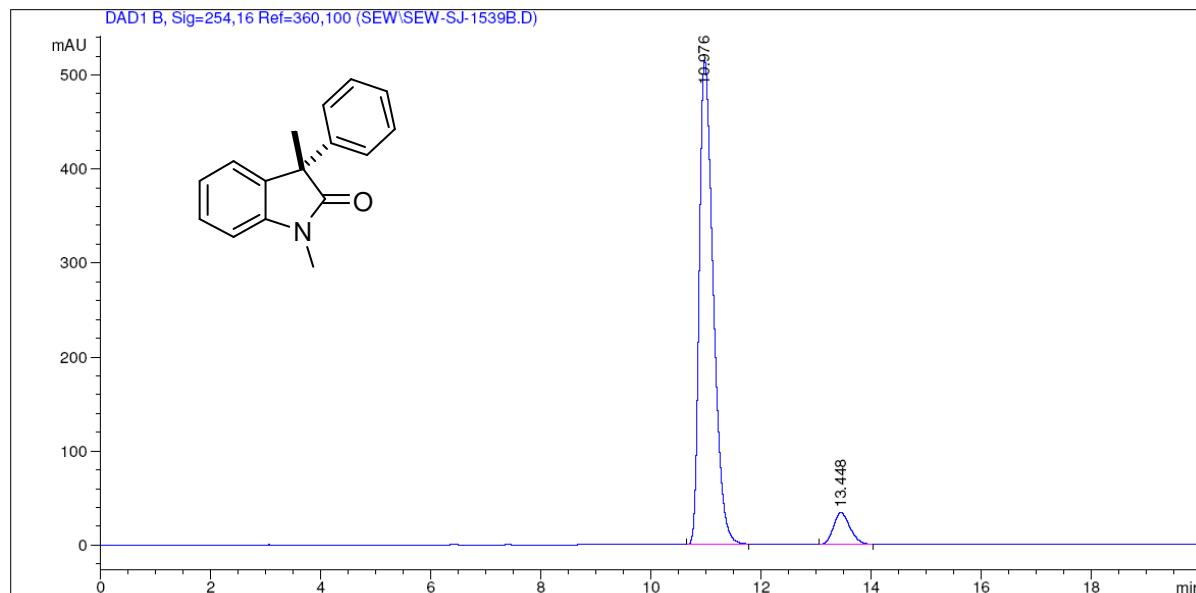








## 6 HPLC Data



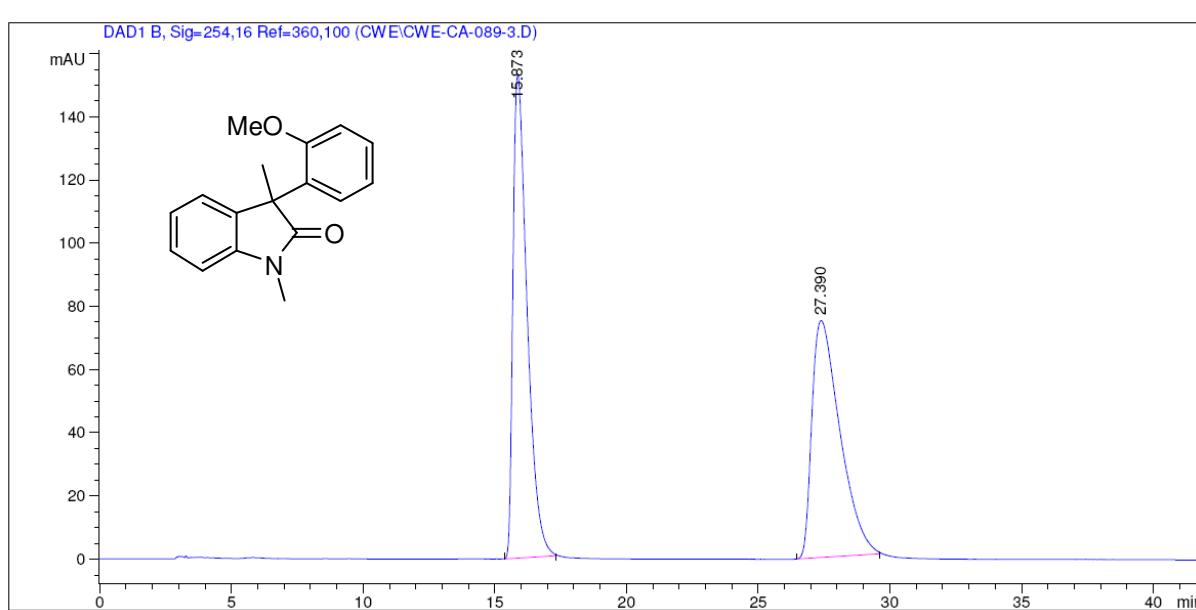
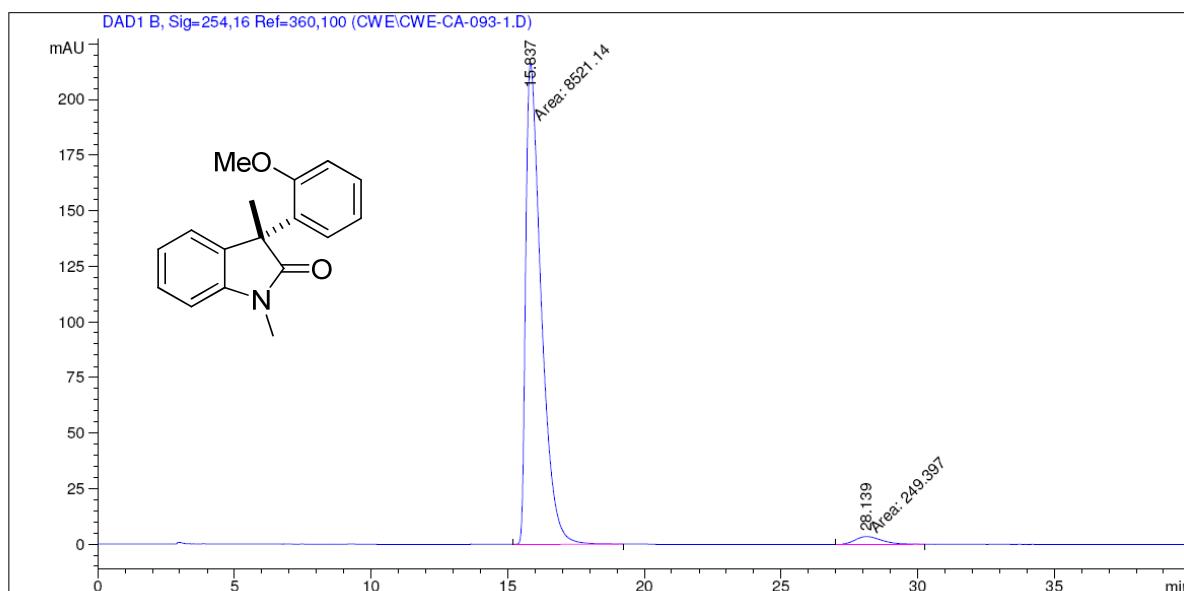
---

=====  
Area Percent Report  
=====

Sorted By : Signal  
Multiplier : 1.0000  
Dilution : 1.0000  
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.976	BB	0.2712	9063.28125	515.24048	92.8140
2	13.448	BB	0.3233	701.71283	33.64147	7.1860



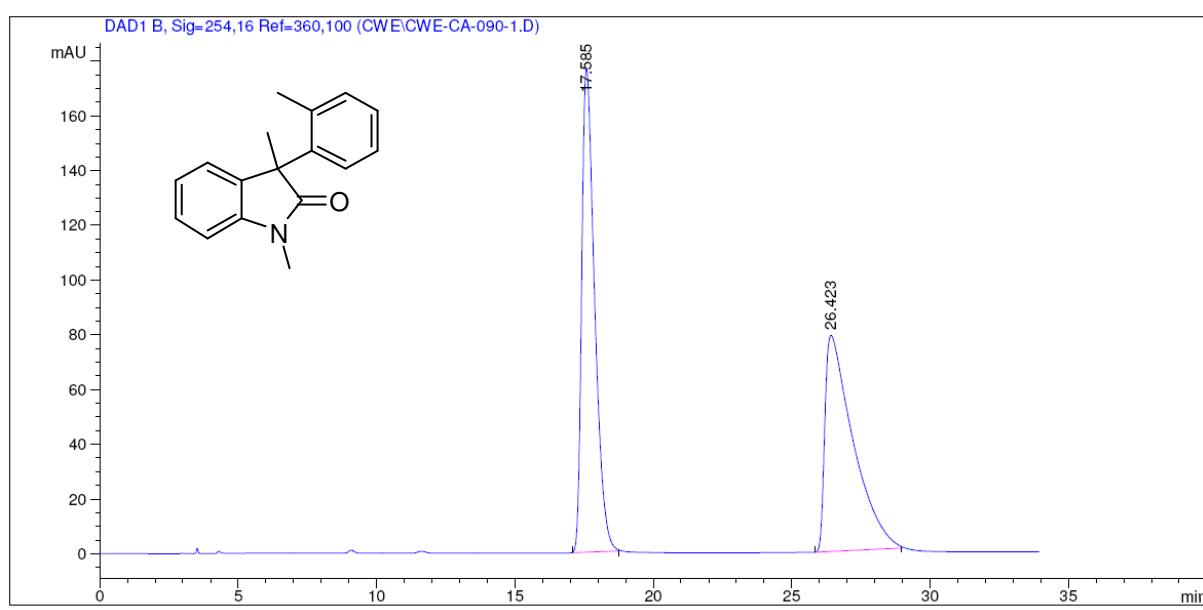
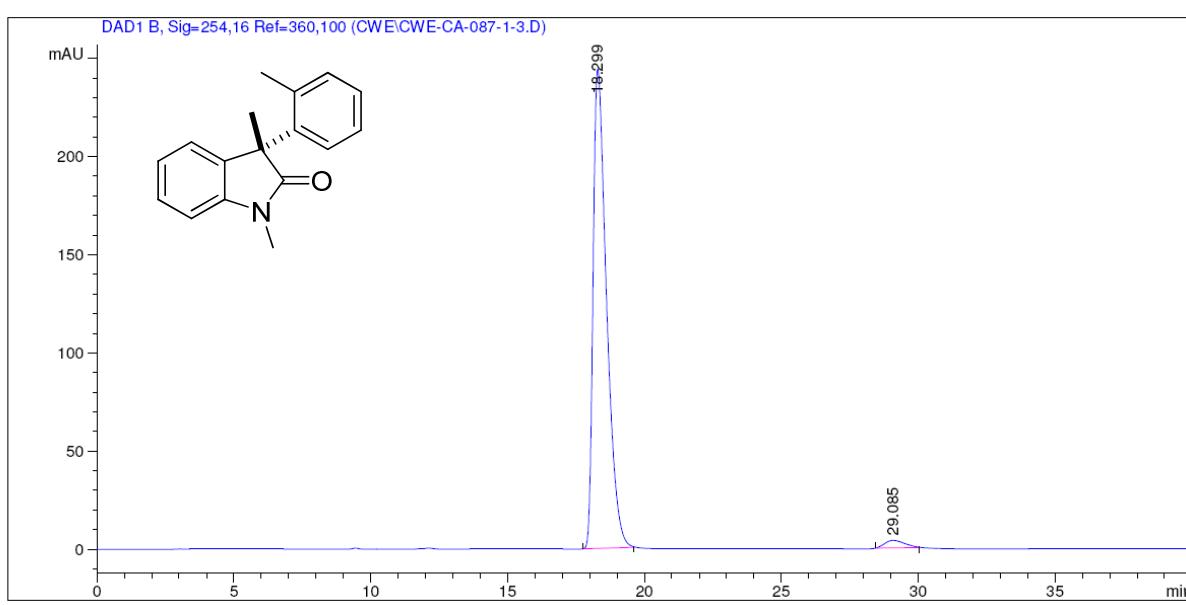
## Area Percent Report

Sorted By : Signal  
Multiplier : 1.0000  
Dilution : 1.0000  
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 B, Sig=254, 16 Ref=360, 100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.837	MM	0.6561	8521.14258	216.47548	97.1564
2	28.139	MM	1.1608	249.39680	3.58076	2.8436

Totals : 8770.53938 220.05624

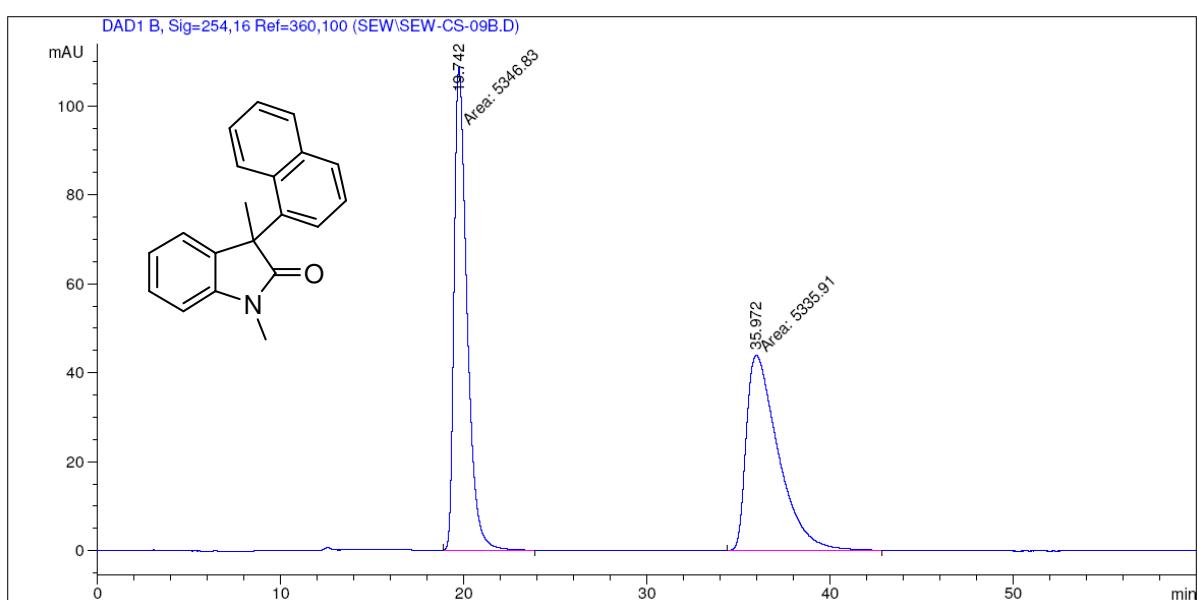
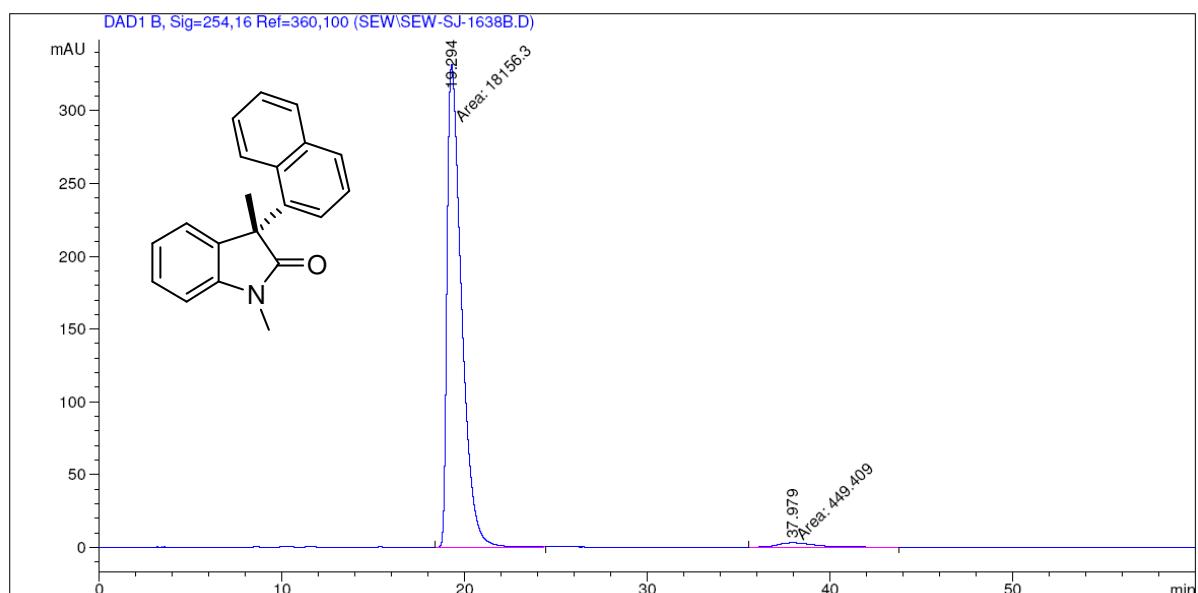


=====  
Area Percent Report  
=====

Sorted By : Signal  
 Multiplier : 1.0000  
 Dilution : 1.0000  
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.299	BB	0.5131	8318.59961	244.37587	97.6964
2	29.085	BB	0.7033	196.14159	3.83087	2.3036



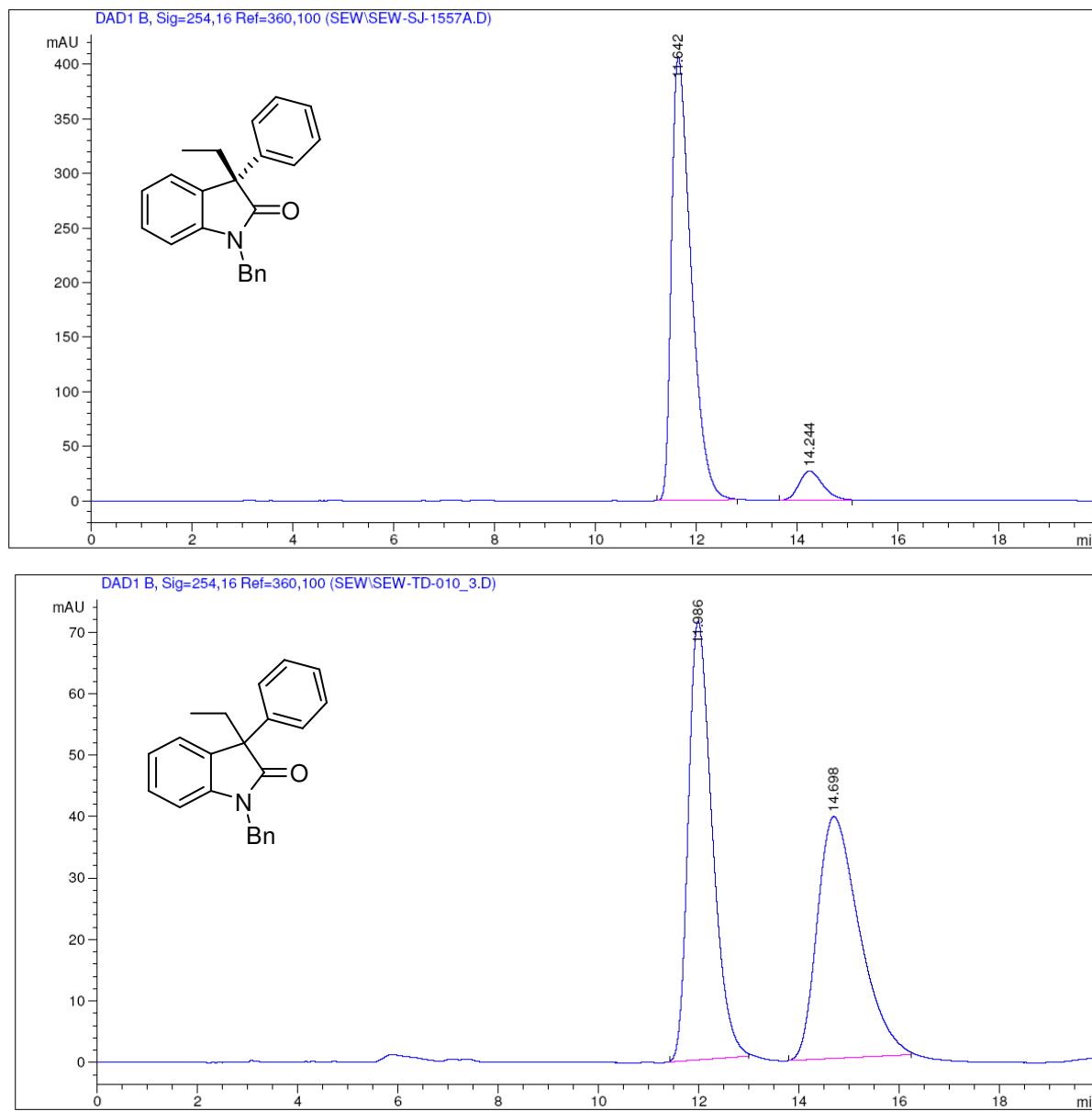

---

=====  
Area Percent Report  
=====

Sorted By : Signal  
 Multiplier : 1.0000  
 Dilution : 1.0000  
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.294	MM	0.9117	1.81563e4	331.92889	97.5846
2	37.979	MM	2.4872	449.40912	3.01147	2.4154



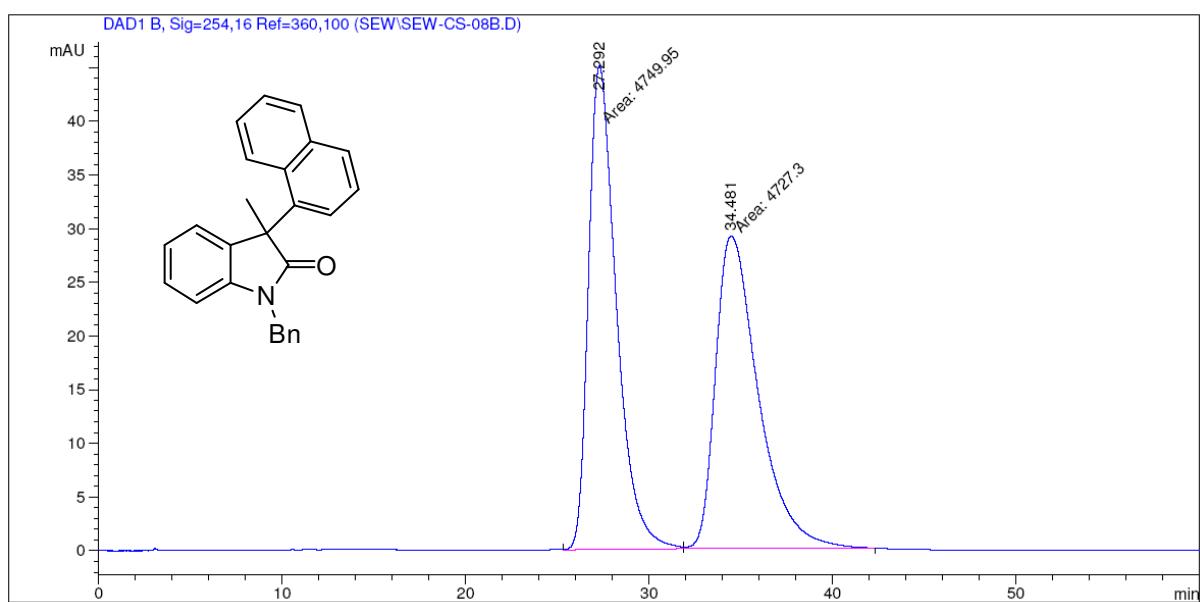
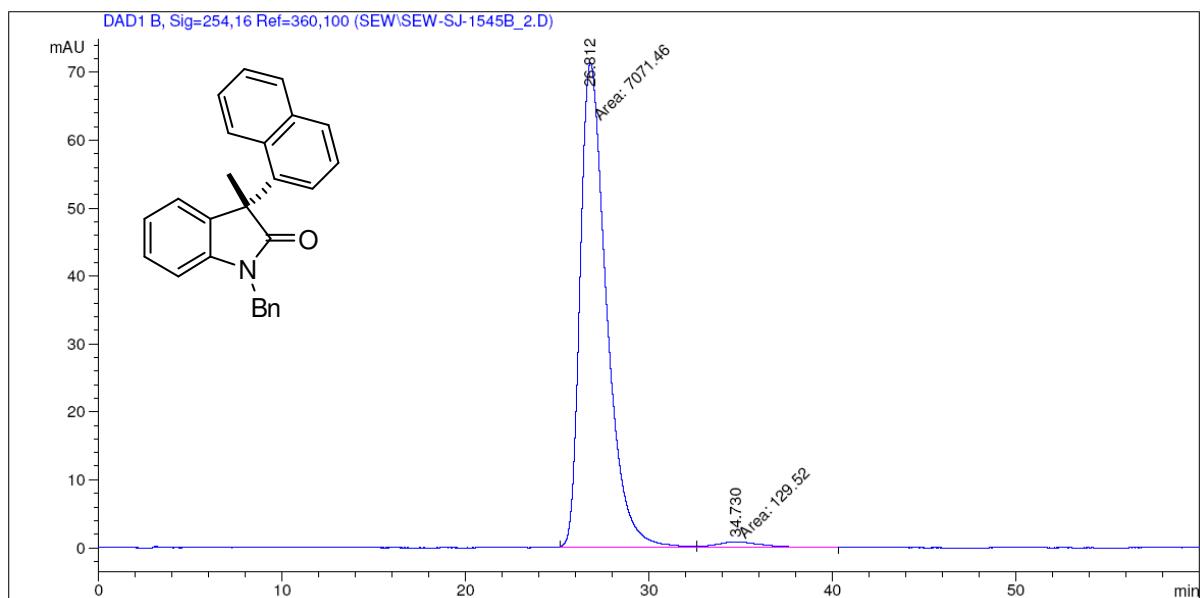

---

=====  
Area Percent Report  
=====

Sorted By : Signal  
 Multiplier : 1.0000  
 Dilution : 1.0000  
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.642	BB	0.4112	1.09819e4	406.52167	92.6438
2	14.244	BB	0.5032	872.00110	26.68465	7.3562

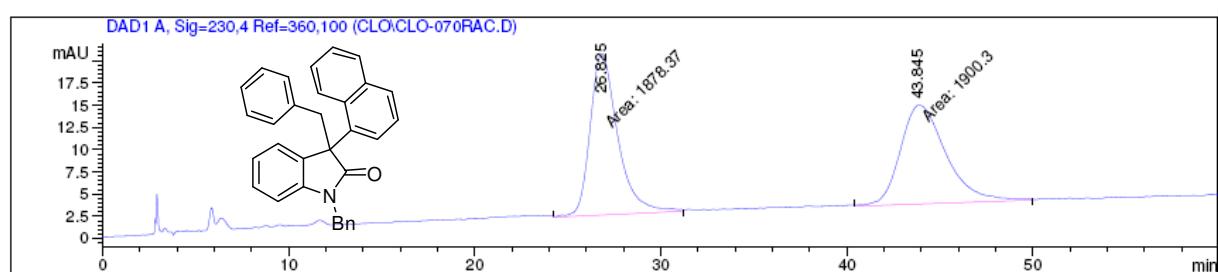
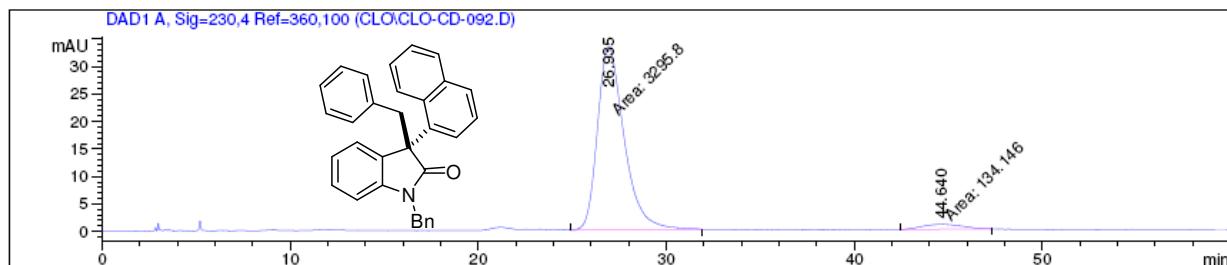


=====  
Area Percent Report  
=====

Sorted By : Signal  
 Multiplier : 1.0000  
 Dilution : 1.0000  
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.812	MM	1.6539	7071.46191	71.26247	98.2014
2	34.730	MM	2.7097	129.52017	7.96645e-1	1.7986




---

=====  
Area Percent Report  
=====

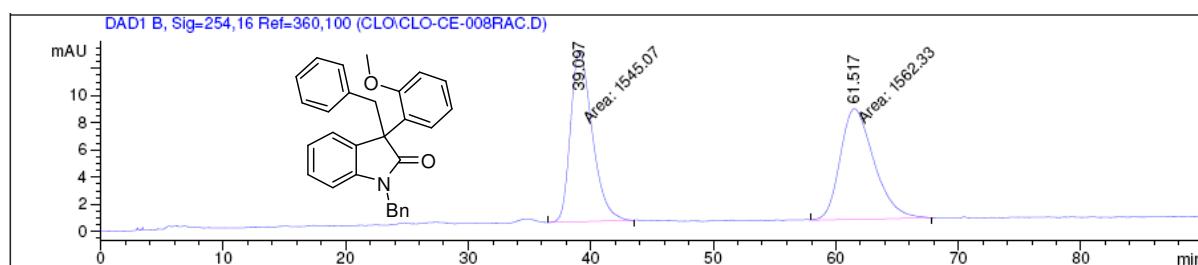
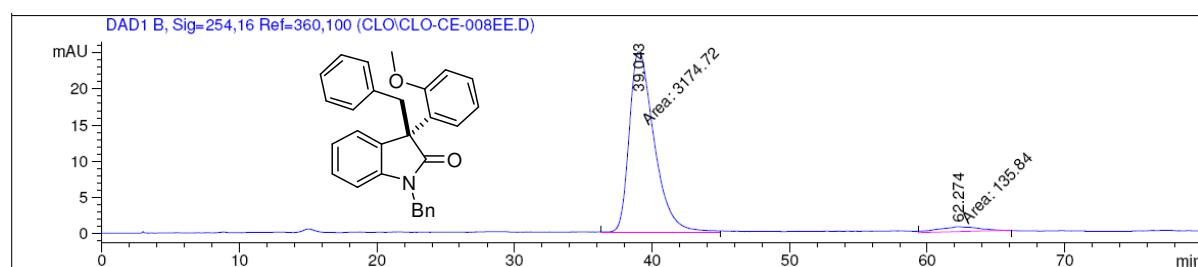
Sorted By : Signal  
 Multiplier : 1.0000  
 Dilution : 1.0000  
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.935	MM	1.6506	3295.80273	33.27854	96.0890
2	44.640	MM	2.3839	134.14584	9.37842e-1	3.9110

Totals : 3429.94858 34.21638

at 90 °C:



=====  
Area Percent Report  
=====

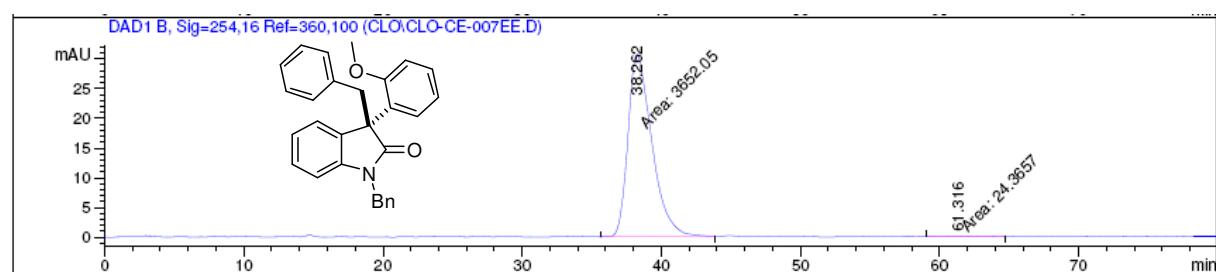
Sorted By : Signal  
Multiplier : 1.0000  
Dilution : 1.0000  
Use Multiplier & Dilution Factor with ISTDs

Signal 2: DAD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	39.043	MM	2.1110	3174.72046	25.06464	95.8968
2	62.274	MM	3.3604	135.83981	6.73721e-1	4.1032

Totals : 3310.56027 25.73837

at 80 °C:



=====  
Area Percent Report  
=====

Sorted By : Signal  
Multiplier : 1.0000  
Dilution : 1.0000  
Use Multiplier & Dilution Factor with ISTDs

Signal 2: DAD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	38.262	MM	1.9913	3652.04712	30.56676	99.3372
2	61.316	MM	3.1676	24.36568	1.28202e-1	0.6628
Totals :				3676.41280	30.69496	

## 7 Calculation of the Buried Volume of the IBiox-Ligands<sup>[17,18]</sup>

The buried volume (%V<sub>Bur</sub>; the fraction of the space buried by the NHC ligand of a sphere around the metal) of the IBiox-ligands was calculated by using the web application SambVca<sup>[18]</sup> developed by Cavallo et al.<sup>[17b]</sup> for the calculation of the buried volume of any type of ligands. As an input file for this computer program, only the coordinates of the ligand must be supplied. This program positions the putative metal atom at 2.10 Å from the coordinating atom of the ligand; a value of 3.5 Å is taken for the radius of the sphere around this metal atom. For our calculations of the buried volumes, we have used two different methods. Either we took the coordinates from the crystal structure analyses of the imidazolium salts **6a**,<sup>[19]</sup> **6b**<sup>[19]</sup> and **5** from which the proton at C2 and the triflate anion were deleted (7.1 to 7.3). Alternatively, the coordinates from the crystal structure analyses of **7**, the AgBr complex of **1**, were taken, from which the AgBr moiety was deleted (7.4).

## 7.1 NHC in conformation 6a

```
-----  
|  
|          S A M B V C A  
|  
|          Buried Volume in Salerno  
|  
|      http://www.molnac.unisa.it/OM-tools/SambVca  
|  
|      L. Cavallo et al. email: lcavall@unisa.it  
|  
-----
```

### Molecule from input :

NHC in conformation 6a

```
Number of atoms          :    45  
Atom that is coordinated :     1  
Atoms that define the axis :     2  
ID of these atoms        :   2   3  
  
Radius of sphere (Angs)   :  3.500  
Distance from sphere (Angs) :  2.100  
Mesh step (Angs)          :  0.050  
H atoms omitted in the V_bur calculation
```

### Cartesian coordinates from input :

C	-7.78128	5.02293	1.39164
N	-7.65532	4.91172	2.71534
N	-7.04265	4.02787	0.87224
C	-8.12479	5.59339	3.94700
C	-7.03174	5.06192	4.90690
H	-6.28146	5.66126	4.92662
H	-7.37932	4.97382	5.79667
O	-6.63052	3.74914	4.37654
C	-6.81237	3.86612	3.04188
C	-6.42234	3.31011	1.87159
O	-5.62966	2.32949	1.39383
C	-5.98083	2.21251	-0.02849
H	-6.63817	1.52363	-0.15560
H	-5.20432	1.99444	-0.54789
C	-6.55220	3.59606	-0.45804
C	-9.52364	5.09803	4.31956
H	-10.11669	5.22945	3.57662
H	-9.48860	4.15785	4.50804
C	-10.07202	5.84323	5.54683
H	-10.97316	5.55873	5.71339
H	-9.54457	5.61794	6.31607
C	-10.04963	7.35387	5.34521
H	-10.65052	7.59216	4.63515
H	-10.34560	7.79001	6.14732
C	-8.63685	7.82323	4.99894

H	-8.64437	8.77063	4.84334
H	-8.05295	7.64848	5.73969
C	-8.10429	7.10691	3.74976
H	-7.20600	7.39575	3.57224
H	-8.64529	7.33942	2.99148
C	-7.69646	3.50652	-1.46615
H	-8.32691	2.84507	-1.17468
H	-8.15104	4.35137	-1.50998
C	-7.17708	3.13680	-2.85779
H	-6.81724	2.24718	-2.84026
H	-7.90377	3.15269	-3.48677
C	-6.08988	4.12030	-3.30706
H	-5.75993	3.86035	-4.17054
H	-6.46592	4.99982	-3.38377
C	-4.93806	4.14341	-2.30771
H	-4.53399	3.27400	-2.26388
H	-4.27006	4.76730	-2.60138
C	-5.43630	4.54634	-0.91826
H	-5.76964	5.44608	-0.94456
H	-4.70773	4.51457	-0.29367

### Atoms and radius in the parameter file

C2	1.99
C3	1.99
C	1.99
N2	1.81
N3	1.81
N	1.81
O	1.78
P	2.11
H	1.40
F	1.72

### Coordinates scaled to put the metal at the origin

C	1.12208	-1.43574	1.04384
N	1.24804	-1.54695	2.36754
N	1.86071	-2.43080	0.52444
C	0.77857	-0.86528	3.59920
C	1.87162	-1.39675	4.55910
H	2.62190	-0.79741	4.57882
H	1.52404	-1.48485	5.44887
O	2.27284	-2.70953	4.02874
C	2.09099	-2.59255	2.69408
C	2.48102	-3.14856	1.52379
O	3.27370	-4.12918	1.04603
C	2.92253	-4.24616	-0.37629
H	2.26519	-4.93504	-0.50340
H	3.69904	-4.46423	-0.89569
C	2.35116	-2.86261	-0.80584
C	-0.62028	-1.36064	3.97176
H	-1.21333	-1.22922	3.22882
H	-0.58524	-2.30082	4.16024
C	-1.16866	-0.61544	5.19903
H	-2.06980	-0.89994	5.36559
H	-0.64121	-0.84073	5.96827
C	-1.14627	0.89520	4.99741
H	-1.74716	1.13349	4.28735
H	-1.44224	1.33134	5.79952

C	0.26651	1.36456	4.65114
H	0.25899	2.31196	4.49554
H	0.85041	1.18981	5.39189
C	0.79907	0.64824	3.40196
H	1.69736	0.93708	3.22444
H	0.25807	0.88075	2.64368
C	1.20690	-2.95215	-1.81395
H	0.57645	-3.61360	-1.52248
H	0.75232	-2.10730	-1.85778
C	1.72628	-3.32187	-3.20559
H	2.08612	-4.21149	-3.18806
H	0.99959	-3.30598	-3.83457
C	2.81348	-2.33837	-3.65486
H	3.14343	-2.59832	-4.51834
H	2.43744	-1.45885	-3.73157
C	3.96530	-2.31526	-2.65551
H	4.36937	-3.18467	-2.61168
H	4.63330	-1.69137	-2.94918
C	3.46706	-1.91233	-1.26606
H	3.13372	-1.01259	-1.29236
H	4.19563	-1.94410	-0.64147
XX	0.00000	0.00000	0.00000

### **Results : Volumes in Angs^3**

N of voxels examined : 1436277  
 Volume of voxel : 0.125E-03

V Free	V Buried	V Total	V Exact
123.63	55.90	179.53	179.59

%V_Free	%V_Bur	% Tot/Ex
68.86	31.14	99.97

## 7.2 NHC in conformation 6b

```
-----  
|  
|          S A M B V C A  
|  
|          Buried Volume in Salerno  
|  
|          http://www.molnac.unisa.it/OM-tools/SambVca  
|  
|          L. Cavallo et al. email: lcavall@unisa.it  
|  
-----
```

### Molecule from input :

NHC in conformation 6b

```
Number of atoms          : 45  
Atom that is coordinated : 1  
Atoms that define the axis : 2  
ID of these atoms        : 2   3  
  
Radius of sphere (Angs)    : 3.500  
Distance from sphere (Angs) : 2.100  
Mesh step (Angs)          : 0.050  
H atoms omitted in the V_bur calculation
```

### Cartesian coordinates from input :

C	-13.77833	16.80327	1.47711
N	-13.41447	16.61696	2.75260
N	-12.96261	17.75211	1.00154
C	-13.80887	15.81110	3.95357
C	-12.49263	15.97718	4.74692
H	-12.66432	15.95408	5.69148
H	-11.87785	15.27242	4.52995
O	-11.94000	17.28419	4.35463
C	-12.35941	17.44305	3.07914
C	-12.07312	18.15215	1.96802
O	-11.20750	19.09521	1.51437
C	-11.83008	19.60501	0.29148
H	-11.15697	19.86930	-0.33969
H	-12.38083	20.36611	0.48872
C	-12.69208	18.45110	-0.28709
C	-14.99536	16.47399	4.66583
H	-15.07751	16.10572	5.54903
H	-14.82319	17.41416	4.75568
C	-16.30615	16.27613	3.91851
H	-17.02365	16.66174	4.42695
H	-16.26402	16.72961	3.07256
C	-16.58619	14.79005	3.68620
H	-16.69901	14.34957	4.53214
H	-17.40008	14.69040	3.18653
C	-15.43639	14.14016	2.92135

H	-15.60540	13.19854	2.83588
H	-15.39338	14.51421	2.03815
C	-14.09223	14.34813	3.62045
H	-13.39186	14.01596	3.05503
H	-14.08013	13.83544	4.43133
C	-13.98502	18.95513	-0.92922
H	-14.57960	18.21714	-1.08482
H	-14.42147	19.57180	-0.33750
C	-13.66689	19.64834	-2.25511
H	-14.48411	19.94151	-2.66493
H	-13.12500	20.42243	-2.08855
C	-12.93372	18.71539	-3.20187
H	-13.49811	17.97018	-3.41883
H	-12.72931	19.18042	-4.01713
C	-11.64332	18.20848	-2.56851
H	-11.22454	17.58025	-3.16023
H	-11.04058	18.94502	-2.44359
C	-11.90932	17.53259	-1.21412
H	-11.07285	17.30152	-0.80211
H	-12.40572	16.72239	-1.35438

### Atoms and radius in the parameter file

C2	1.99
C3	1.99
C	1.99
N2	1.81
N3	1.81
N	1.81
O	1.78
P	2.11
H	1.40
F	1.72

### Coordinates scaled to put the metal at the origin

C	1.53250	0.99067	1.03925
N	1.89636	0.80436	2.31474
N	2.34822	1.93951	0.56368
C	1.50196	-0.00150	3.51571
C	2.81820	0.16458	4.30906
H	2.64651	0.14148	5.25362
H	3.43298	-0.54018	4.09209
O	3.37083	1.47159	3.91677
C	2.95142	1.63045	2.64128
C	3.23771	2.33955	1.53016
O	4.10333	3.28261	1.07651
C	3.48075	3.79241	-0.14638
H	4.15386	4.05670	-0.77755
H	2.93000	4.55351	0.05086
C	2.61875	2.63850	-0.72495
C	0.31547	0.66139	4.22797
H	0.23332	0.29312	5.11117
H	0.48764	1.60156	4.31782
C	-0.99532	0.46353	3.48065
H	-1.71282	0.84914	3.98909

H	-0.95319	0.91701	2.63470
C	-1.27536	-1.02255	3.24834
H	-1.38818	-1.46303	4.09428
H	-2.08925	-1.12220	2.74867
C	-0.12556	-1.67244	2.48349
H	-0.29457	-2.61406	2.39802
H	-0.08255	-1.29839	1.60029
C	1.21860	-1.46447	3.18259
H	1.91897	-1.79664	2.61717
H	1.23070	-1.97716	3.99347
C	1.32581	3.14253	-1.36708
H	0.73123	2.40454	-1.52268
H	0.88936	3.75920	-0.77536
C	1.64394	3.83574	-2.69297
H	0.82672	4.12891	-3.10279
H	2.18583	4.60983	-2.52641
C	2.37711	2.90279	-3.63973
H	1.81272	2.15758	-3.85669
H	2.58152	3.36782	-4.45499
C	3.66751	2.39588	-3.00637
H	4.08629	1.76765	-3.59809
H	4.27025	3.13242	-2.88145
C	3.40151	1.71999	-1.65198
H	4.23798	1.48892	-1.23997
H	2.90511	0.90979	-1.79224
XX	0.00000	0.00000	0.00000

### Results : Volumes in Angs^3

N of voxels examined :	1436277		
Volume of voxel :	0.125E-03		
V Free	V Buried	V Total	V Exact
109.01	70.53	179.53	179.59
%V_Free	%V_Bur	% Tot/Ex	
60.72	39.28	99.97	

### 7.3 NHC 1 in conformation 5

```
-----  
|  
|          S A M B V C A  
|  
|          Buried Volume in Salerno  
|  
|      http://www.molnac.unisa.it/OM-tools/SambVca  
|  
|      L. Cavallo et al. email: lcavallo@unisa.it  
|  
-----
```

#### Molecule from input :

NHC 1 in conformation 5

```
Number of atoms          : 69  
Atom that is coordinated : 1  
Atoms that define the axis : 2  
ID of these atoms       : 2   3  
  
Radius of sphere (Angs)    : 3.500  
Distance from sphere (Angs) : 2.100  
Mesh step (Angs)          : 0.050  
H atoms omitted in the V_bur calculation
```

#### Cartesian coordinates from input :

C	-0.53115	0.15144	16.68969
N	-0.44404	0.08834	18.03225
N	-1.83780	0.11638	16.39348
C	-1.70713	-0.00421	18.56889
O	-1.71669	-0.17528	19.90376
C	-0.34206	0.07291	20.33461
H	-0.26239	0.97735	20.70006
H	-0.08817	-0.56790	21.03282
C	0.58852	-0.08834	19.09399
C	1.25671	-1.47375	19.02859
H	1.80699	-1.52983	19.84990
C	2.26272	-1.51721	17.87837
H	1.78362	-1.43168	17.02821
H	2.71739	-2.38519	17.88222
C	3.29529	-0.41506	17.98224
H	3.90930	-0.47676	17.22056
H	3.81901	-0.54126	18.80163
C	2.66852	0.96333	18.00340
H	2.22342	1.11197	17.13208
C	1.60728	1.03625	19.09399
H	1.12817	1.88600	19.00359
H	2.05876	1.04466	19.96338
C	0.32294	-2.70350	19.09207

H	-0.36331	-2.51560	19.78065
C	1.09630	-3.94588	19.54984
H	1.59134	-3.73975	20.35769
H	0.47273	-4.66803	19.72872
H	1.71351	-4.21791	18.85356
C	-0.41536	-3.04985	17.79182
H	0.22946	-3.20971	17.08592
H	-0.95077	-3.84772	17.92838
H	-0.99326	-2.31228	17.54177
C	3.70746	2.07249	18.19767
H	4.36503	2.02903	17.48599
H	3.26660	2.93627	18.17843
H	4.14938	1.95471	19.05360
C	-2.57398	0.01963	17.54370
O	-3.90505	-0.00561	17.34174
C	-4.04209	-0.28746	15.91262
H	-4.18231	-1.24658	15.77221
H	-4.81439	0.19491	15.54909
C	-2.74182	0.17247	15.19710
C	-2.84062	1.57751	14.59699
H	-3.52474	1.50599	13.88531
C	-1.54991	1.92666	13.87185
H	-1.63489	2.81708	13.47177
H	-0.81373	1.95471	14.51813
C	-1.22272	0.91145	12.77549
H	-0.36968	1.15123	12.35618
H	-1.91747	0.94510	12.08497
C	-1.13136	-0.49359	13.32559
H	-0.34737	-0.53004	13.92955
C	-2.34983	-0.84695	14.13921
H	-3.10726	-0.96474	13.52755
H	-2.19048	-1.70651	14.57968
C	-3.34521	2.70350	15.52985
H	-4.03784	2.31368	16.12035
C	-4.01128	3.80705	14.70470
H	-3.33459	4.28662	14.20076
H	-4.65079	3.41303	14.09304
H	-4.46914	4.42403	15.29904
C	-2.27865	3.32188	16.42041
H	-1.62321	3.77761	15.87030
H	-2.69189	3.95849	17.02437
H	-1.84204	2.62497	16.93397
C	-0.89765	-1.51581	12.19269
H	-1.64658	-1.49057	11.57526
H	-0.08180	-1.29145	11.71952
H	-0.82010	-2.40483	12.56968

### Atoms and radius in the parameter file

C2	1.99
C3	1.99
C	1.99
N2	1.81
N3	1.81
N	1.81
O	1.78
P	2.11
H	1.40
F	1.72

**Coordinates scaled to put the metal at the origin**

C	-1.59081	-0.12804	1.36489
N	-1.50370	-0.19114	2.70745
N	-2.89746	-0.16310	1.06868
C	-2.76679	-0.28369	3.24409
O	-2.77635	-0.45476	4.57896
C	-1.40172	-0.20657	5.00981
H	-1.32205	0.69787	5.37526
H	-1.14783	-0.84738	5.70802
C	-0.47114	-0.36782	3.76919
C	0.19705	-1.75323	3.70379
H	0.74733	-1.80931	4.52510
C	1.20306	-1.79669	2.55357
H	0.72396	-1.71116	1.70341
H	1.65773	-2.66467	2.55742
C	2.23563	-0.69454	2.65744
H	2.84964	-0.75624	1.89576
H	2.75935	-0.82074	3.47683
C	1.60886	0.68385	2.67860
H	1.16376	0.83249	1.80728
C	0.54762	0.75677	3.76919
H	0.06851	1.60652	3.67879
H	0.99910	0.76518	4.63858
C	-0.73672	-2.98298	3.76727
H	-1.42297	-2.79508	4.45585
C	0.03664	-4.22536	4.22504
H	0.53168	-4.01923	5.03289
H	-0.58693	-4.94751	4.40392
H	0.65385	-4.49739	3.52876
C	-1.47502	-3.32933	2.46702
H	-0.83020	-3.48919	1.76112
H	-2.01043	-4.12720	2.60358
H	-2.05292	-2.59176	2.21697
C	2.64780	1.79301	2.87287
H	3.30537	1.74955	2.16119
H	2.20694	2.65679	2.85363
H	3.08972	1.67523	3.72880
C	-3.63364	-0.25985	2.21890
O	-4.96471	-0.28509	2.01694
C	-5.10175	-0.56694	0.58782
H	-5.24197	-1.52606	0.44741
H	-5.87405	-0.08457	0.22429
C	-3.80148	-0.10701	-0.12770
C	-3.90028	1.29803	-0.72781
H	-4.58440	1.22651	-1.43949
C	-2.60957	1.64718	-1.45295
H	-2.69455	2.53760	-1.85303
H	-1.87339	1.67523	-0.80667
C	-2.28238	0.63197	-2.54931
H	-1.42934	0.87175	-2.96862
H	-2.97713	0.66562	-3.23983
C	-2.19102	-0.77307	-1.99921
H	-1.40703	-0.80952	-1.39525
C	-3.40949	-1.12643	-1.18559
H	-4.16692	-1.24422	-1.79725
H	-3.25014	-1.98599	-0.74512
C	-4.40487	2.42402	0.20505
H	-5.09750	2.03420	0.79555
C	-5.07094	3.52757	-0.62010
H	-4.39425	4.00714	-1.12404

H	-5.71045	3.13355	-1.23176
H	-5.52880	4.14455	-0.02576
C	-3.33831	3.04240	1.09561
H	-2.68287	3.49813	0.54550
H	-3.75155	3.67901	1.69957
H	-2.90170	2.34549	1.60917
C	-1.95731	-1.79529	-3.13211
H	-2.70624	-1.77005	-3.74954
H	-1.14146	-1.57093	-3.60528
H	-1.87976	-2.68431	-2.75512
XX	0.00000	0.00000	0.00000

### **Results : Volumes in Angs^3**

N of voxels examined : 1436277  
 Volume of voxel : 0.125E-03

V Free	V Buried	V Total	V Exact
86.92	92.61	179.53	179.59

%V_Free	%V_Bur	% Tot/Ex
48.42	51.58	99.97

## 7.4 NHC 1 in conformation 7

```
-----  
|  
|          S A M B V C A  
|  
|          Buried Volume in Salerno  
|  
|      http://www.molnac.unisa.it/OM-tools/SambVca  
|  
|      L. Cavallo et al. email: lcavall@unisa.it  
|  
-----
```

### Molecule from input :

NHC 1 in conformation 7

```
Number of atoms          : 69  
Atom that is coordinated : 1  
Atoms that define the axis : 2  
ID of these atoms       : 2   3  
  
Radius of sphere (Angs)    : 3.500  
Distance from sphere (Angs) : 2.100  
Mesh step (Angs)          : 0.050  
H atoms omitted in the V_bur calculation
```

### Cartesian coordinates from input :

C	-11.03088	6.85538	16.08018
N	-12.38227	6.77668	15.86327
N	-10.97222	6.92375	17.44105
C	-13.09690	6.80378	17.04529
O	-14.44617	6.71476	16.85843
C	-14.59122	6.24260	15.51083
H	-14.70855	5.26989	15.50896
H	-15.38052	6.65026	15.09827
C	-13.31236	6.62446	14.70252
C	-13.51075	7.91839	13.88862
H	-14.24458	7.71456	13.25579
C	-12.30121	8.19059	13.01685
H	-11.52259	8.35056	13.58994
H	-12.46014	9.00333	12.49229
C	-11.99189	7.04889	12.07414
H	-12.71292	6.97148	11.41518
H	-11.16314	7.24885	11.59065
C	-11.83617	5.71626	12.80030
H	-10.98928	5.75367	13.31366
C	-12.95291	5.46985	13.78408
H	-13.75500	5.21958	13.27819
H	-12.70759	4.70098	14.33851
C	-14.00032	9.15426	14.69132
H	-14.57522	8.82530	15.42682

C	-14.85894	10.04957	13.79528
H	-14.31817	10.39272	13.06725
H	-15.59704	9.53225	13.43500
H	-15.20772	10.78877	14.31797
C	-12.88251	9.97087	15.31108
H	-13.26223	10.70750	15.81511
H	-12.36094	9.40712	15.90471
H	-12.30974	10.31919	14.61105
C	-11.72098	4.56036	11.79599
H	-12.52520	4.52037	11.25464
H	-10.95195	4.70614	11.22290
H	-11.61218	3.72440	12.27575
C	-12.22228	6.88505	18.02534
O	-12.19882	6.86957	19.37761
C	-10.82076	7.12371	19.72781
H	-10.70983	8.06287	19.98543
H	-10.56157	6.56382	20.48945
C	-9.92587	6.80248	18.50883
C	-9.32857	5.37955	18.60030
H	-8.80486	5.37826	19.44220
C	-8.30036	5.15379	17.50078
H	-7.91211	4.25978	17.59785
H	-8.74300	5.19894	16.62714
C	-7.18575	6.20003	17.55865
H	-6.55432	6.03748	16.82689
H	-6.69831	6.10456	18.40242
C	-7.71799	7.60877	17.45038
H	-8.09770	7.71327	16.54127
C	-8.83686	7.85775	18.44349
H	-8.44115	7.94548	19.33580
H	-9.25604	8.71693	18.22321
C	-10.34185	4.22366	18.76644
H	-11.04261	4.53843	19.38993
C	-11.04795	3.75278	17.50265
H	-10.38985	3.43414	16.86422
H	-11.65911	3.03293	17.72292
H	-11.54285	4.49070	17.11623
C	-9.64215	3.03293	19.43660
H	-9.00432	2.64333	18.81871
H	-9.17818	3.33738	20.23183
H	-10.30345	2.36726	19.68301
C	-6.62578	8.65243	17.61092
H	-6.14901	8.49633	18.44162
H	-6.00608	8.59051	16.86609
H	-7.02363	9.53741	17.62772

#### Atoms and radius in the parameter file

C2	1.99
C3	1.99
C	1.99
N2	1.81
N3	1.81
N	1.81
O	1.78
P	2.11
H	1.40
F	1.72

**Coordinates scaled to put the metal at the origin**

C	-1.57263	-0.01257	1.39165
N	-2.92402	-0.09127	1.17474
N	-1.51397	0.05580	2.75252
C	-3.63865	-0.06417	2.35676
O	-4.98792	-0.15319	2.16990
C	-5.13297	-0.62535	0.82230
H	-5.25030	-1.59806	0.82043
H	-5.92227	-0.21769	0.40974
C	-3.85411	-0.24349	0.01399
C	-4.05250	1.05044	-0.79991
H	-4.78633	0.84661	-1.43274
C	-2.84296	1.32264	-1.67168
H	-2.06434	1.48261	-1.09859
H	-3.00189	2.13538	-2.19624
C	-2.53364	0.18094	-2.61439
H	-3.25467	0.10353	-3.27335
H	-1.70489	0.38090	-3.09788
C	-2.37792	-1.15169	-1.88823
H	-1.53103	-1.11428	-1.37487
C	-3.49466	-1.39810	-0.90445
H	-4.29675	-1.64837	-1.41034
H	-3.24934	-2.16697	-0.35002
C	-4.54207	2.28631	0.00279
H	-5.11697	1.95735	0.73829
C	-5.40069	3.18162	-0.89325
H	-4.85992	3.52477	-1.62128
H	-6.13879	2.66430	-1.25353
H	-5.74947	3.92082	-0.37056
C	-3.42426	3.10292	0.62255
H	-3.80398	3.83955	1.12658
H	-2.90269	2.53917	1.21618
H	-2.85149	3.45124	-0.07748
C	-2.26273	-2.30759	-2.89254
H	-3.06695	-2.34758	-3.43389
H	-1.49370	-2.16181	-3.46563
H	-2.15393	-3.14355	-2.41278
C	-2.76403	0.01710	3.33681
O	-2.74057	0.00162	4.68908
C	-1.36251	0.25576	5.03928
H	-1.25158	1.19492	5.29690
H	-1.10332	-0.30413	5.80092
C	-0.46762	-0.06547	3.82030
C	0.12968	-1.48840	3.91177
H	0.65339	-1.48969	4.75367
C	1.15789	-1.71416	2.81225
H	1.54614	-2.60817	2.90932
H	0.71525	-1.66901	1.93861
C	2.27250	-0.66792	2.87012
H	2.90393	-0.83047	2.13836
H	2.75994	-0.76339	3.71389
C	1.74026	0.74082	2.76185
H	1.36055	0.84532	1.85274
C	0.62139	0.98980	3.75496
H	1.01710	1.07753	4.64727
H	0.20221	1.84898	3.53468
C	-0.88360	-2.64429	4.07791
H	-1.58436	-2.32952	4.70140
C	-1.58970	-3.11517	2.81412
H	-0.93160	-3.43381	2.17569

H	-2.20086	-3.83502	3.03439
H	-2.08460	-2.37725	2.42770
C	-0.18390	-3.83502	4.74807
H	0.45393	-4.22462	4.13018
H	0.28007	-3.53057	5.54330
H	-0.84520	-4.50069	4.99448
C	2.83247	1.78448	2.92239
H	3.30924	1.62838	3.75309
H	3.45217	1.72256	2.17756
H	2.43462	2.66946	2.93919
XX	0.00000	0.00000	0.00000

### **Results : Volumes in Angs^3**

N of voxels examined : 1436277  
 Volume of voxel : 0.125E-03

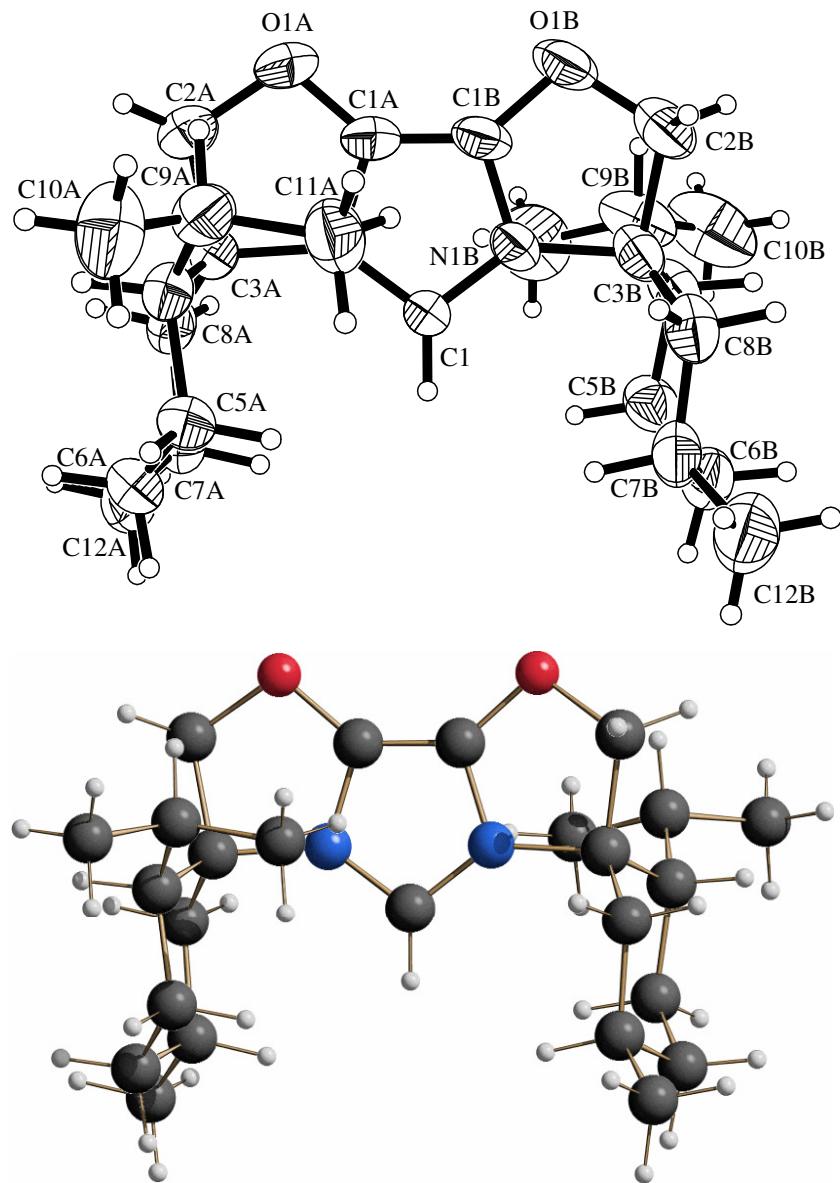
V Free	V Buried	V Total	V Exact
93.75	85.79	179.53	179.59

%V_Free	%V_Bur	% Tot/Ex
52.22	47.78	99.97

## 8 X-ray Crystal Structure Analysis

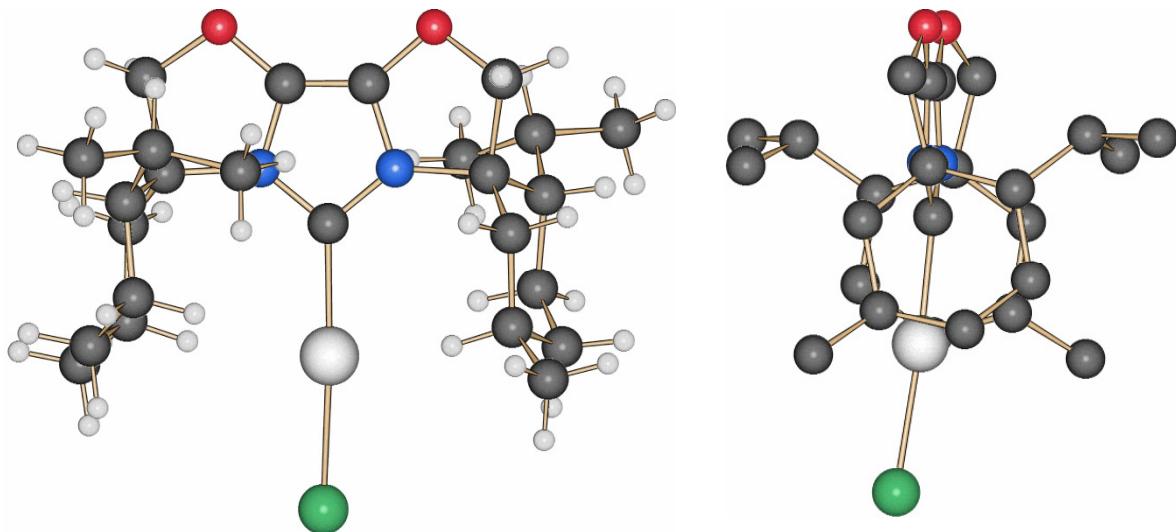
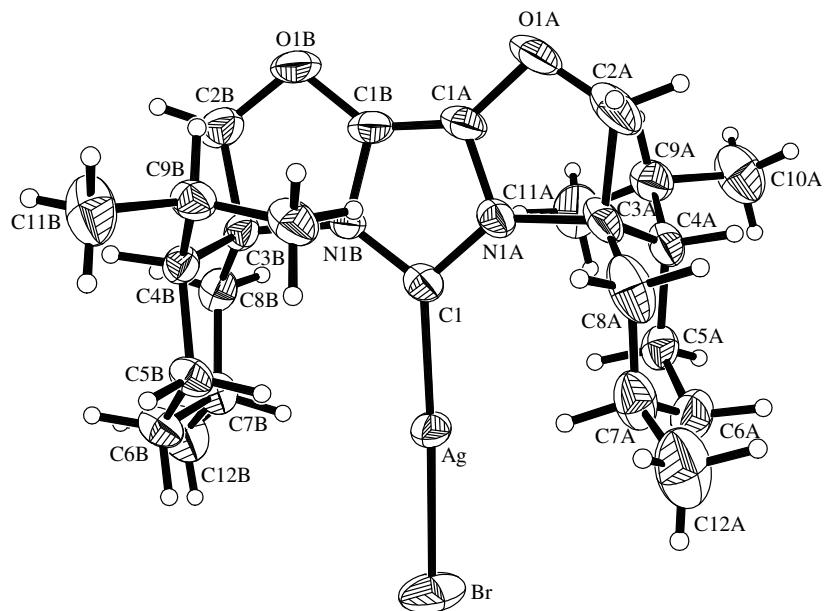
### X-ray Crystal Structure Analysis of 5

X-ray crystal structure analysis of **5**: formula  $C_{26}H_{41}F_3N_2O_5S$ ,  $M = 550.67$ , colorless crystal  $0.30 \times 0.15 \times 0.05$  mm,  $a = 10.6231(3)$ ,  $b = 14.0223(5)$ ,  $c = 19.2344(9)\text{\AA}$ ,  $V = 2865.16(19)$   $\text{\AA}^3$ ,  $\rho_{\text{calc}} = 1.277$  g  $\text{cm}^{-3}$ ,  $\mu = 1.493$  mm $^{-1}$ , empirical absorption correction ( $0.663 \leq T \leq 0.929$ ),  $Z = 4$ , orthorhombic, space group  $P2_12_12_1$  (No. 19),  $\lambda = 1.54178$   $\text{\AA}$ ,  $T = 223(2)$  K,  $\omega$  and  $\phi$  scans, 14433 reflections collected ( $\pm h, \pm k, \pm l$ ),  $[(\sin\theta)/\lambda] = 0.60$   $\text{\AA}^{-1}$ , 4920 independent ( $R_{\text{int}} = 0.064$ ) and 3988 observed reflections [ $I \geq 2 \sigma(I)$ ], 340 refined parameters,  $R = 0.052$ ,  $wR^2 = 0.125$ , Flack parameter 0.00(3), max. (min.) residual electron density 0.19 (-0.26) e  $\text{\AA}^{-3}$ , hydrogen atoms calculated and refined as riding atoms.



## X-ray Crystal Structure Analysis of 7

X-ray crystal structure analysis of **7**: formula  $C_{25}H_{40}AgBrN_2O_2$ ,  $M = 588.37$ , colorless crystal  $0.20 \times 0.05 \times 0.05$  mm,  $a = 10.6661(2)$ ,  $b = 12.9006(2)$ ,  $c = 18.6675(4)\text{\AA}$ ,  $V = 2568.63(8) \text{\AA}^3$ ,  $\rho_{\text{calc}} = 1.521 \text{ g cm}^{-3}$ ,  $\mu = 2.363 \text{ mm}^{-1}$ , empirical absorption correction ( $0.649 \leq T \leq 0.891$ ),  $Z = 4$ , orthorhombic, space group  $P2_12_12_1$  (No. 19),  $\lambda = 0.71073 \text{ \AA}$ ,  $T = 223(2) \text{ K}$ ,  $\omega$  and  $\varphi$  scans, 19164 reflections collected ( $\pm h, \pm k, \pm l$ ),  $[(\sin\theta)/\lambda] = 0.66 \text{ \AA}^{-1}$ , 6082 independent ( $R_{\text{int}} = 0.063$ ) and 4556 observed reflections [ $I \geq 2 \sigma(I)$ ], 286 refined parameters,  $R = 0.046$ ,  $wR^2 = 0.0.078$ , Flack parameter -0.001(11), max. (min.) residual electron density  $0.54$  (- $0.80$ )  $e \text{ \AA}^{-3}$ , hydrogen atoms calculated and refined as riding atoms.



Data sets were collected with Nonius KappaCCD diffractometers, in case of Mo-radiation a rotating anode generator was used. Programs used: data collection COLLECT (Nonius B.V., 1998), data reduction Denzo-SMN (Z. Otwinowski, W. Minor, *Methods in Enzymology*, **1997**, 276, 307-326), absorption correction SORTAV (R.H. Blessing, *Acta Cryst.* **1995**, A51, 33-37; R.H. Blessing, *J. Appl. Cryst.* **1997**, 30, 421-426) and Denzo (Z. Otwinowski, D. Borek, W. Majewski, W. Minor, *Acta Cryst.* **2003**, A59, 228-234), structure solution SHELXS-97 (G.M. Sheldrick, *Acta Cryst.* **1990**, A46, 467-473), structure refinement SHELXL-97 (G.M. Sheldrick, *Acta Cryst.* **2008**, A64, 112-122), graphics XP (BrukerAXS, 2000), graphics SCHAKAL (E. Keller, Universität Freiburg, 1997).

## 9 Literature

---

- [1] Cremlyn, R. J. W.; Chrisholm, M. *J. Chem. Soc. (C)* **1967**, 1762.
- [2] Munday, L. *J. Chem. Soc.* **1961**, 4372.
- [3] Sacripante, G.; Edwards, J.T. *Can. J. Chem.* **1982**, 60, 1982.
- [4] Iglesias, M.; Beetstra, D. J.; Knight, J. C.; Ooi, L.-L.; Stasch, A.; Coles, S.; Male, L.; Hursthouse, M. B.; Cavell, K. J.; Dervisi, A.; Fallis, I. A. *Organometallics*, **2008**, 27, 3279.
- [5] Sørensen, U. S.; Pombo-Villar, E. *Helv. Chim. Acta* **2004**, 87, 1, 82.
- [6] Barluenga, J. M.; *Chem. Eur. J.* **2001**, 7, 13, 2896.
- [7] Barluenga, J.; Fañanás, F. J.; Sanz, R.; Fernández, Y. *Chem. Eur. J.* **2002**, 8, 9, 2034.
- [8] Kessler, A.; Coleman, C. M.; Charoenying, P.; O'Shea, D. F. *J. Org. Chem.* **2004**, 69, 7836.
- [9] Bedford, R. B.; Cazin, C. S. *J. Chem. Commun.* **2002**, 2310.
- [10] Ebbers, E. J.; Ariaans, G. J. A.; Bruggink, A.; Zwanenburg, B. *Tetrahedron: Asymmetry* **1999**, 10, 3701.
- [11] Thompson, H. W.; Rashid, S. Y. *J. Org. Chem.* **2002**, 67, 2813.
- [12] Mutti, S.; Daubie, C.; Decalogne, F.; Fournier, R.; Montouri, O.; Rossi, P. *Synth. Commun.* **1996**, 26, 2349.
- [13] Schultz, A. G.; Kirincich, S. *J. J. Org. Chem.* **1996**, 61, 5631.
- [14] Piccolo, O.; Menicagli, R.; Lardicci, L. *Tetrahedron* **1979**, 35, 1751.
- [15] Lee, S.; Hartwig, J. F. *J. Org. Chem.* **2001**, 66, 3402.
- [16] Kündig, E. P.; Seidel, T. M.; Jia, Y. X.; Bernadinelli, G. *Angew. Chem. Int. Ed.* **2007**, 46, 8484.
- [17] (a) Scott, N. M.; Nolan, S. P. *Eur. J. Inorg. Chem.* **2005**, 1815; (b) Poater, A.; Cosenza, B.; Correa, A.; Giudice, S.; Ragone, F.; Scarano, V.; Cavallo, L. *Eur. J. Inorg. Chem.* **2009**, 1759.
- [18] The web application can be found at: <http://www.molnac.unisa.it/OMtools.php>
- [19] Altenhoff, G.; Goddard, R.; Lehmann, C. W.; Glorius, F. *Angew. Chem. Int. Ed.* **2003**, 42, 3690.