

# DIASTEREOSELECTIVE SYNTHESIS OF AMINO-BRIDGED AXIALLY CHIRAL BIARYLS THROUGH POINT-TO-AXIAL ASYMMETRIC C-H ARYLATION

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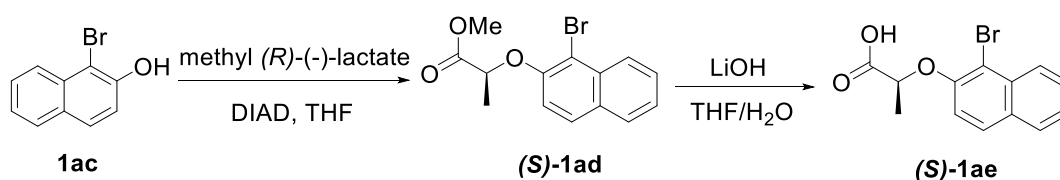
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## 1. General information

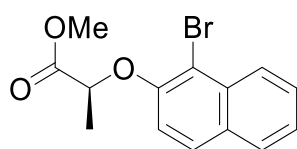
Unless otherwise noted, all experiments were carried out under an atmosphere of nitrogen using standard Schlenk techniques or in a nitrogen-filled glovebox.  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were recorded on Bruker Model Avance DMX 300 Spectrometer ( $^1\text{H}$  400 MHz and  $^{13}\text{C}$  100 MHz, respectively), Bruker Model Avance DMX 400 Spectrometer ( $^1\text{H}$  500 MHz and  $^{13}\text{C}$  125 MHz, respectively). Chemical shifts ( $\delta$ ) were given in ppm and were referenced to residual solvent or TMS peaks. Optical rotations were measured with Rudolph Autopl VI polarimeter. High resolution mass spectra (P-ESI HRMS) were obtained on P-SIMS-Gly of Bruker Daltonics Inc. All organic solvents were dried using standard, published methods and were distilled before use. All other chemicals were used as received from Aldrich or Acros without further purification.

## 2. General procedure for the synthesis of substrates

### 2.1 General procedure for the synthesis of **1ae** and **1be**.<sup>1-3</sup>



A stirred suspension of **1ac** (10.0 g, 44.8 mmol),  $\text{Ph}_3\text{P}$  (29.4 g, 112.1 mmol) and methyl (S)-(-)-lactate (4.67 g, 44.8 mmol) in THF (120 mL) was placed in an ice-water bath for 10 min. Then diisopropyl azodicarboxylate (DIAD) (23.1 mL, 112.1 mmol) was added dropwise via syringe. After the addition of DIAD, the homogenic mixture was stirred at 0°C for 20 min, then at r.t. overnight. The solvent was removed in vacuo and the crude product was isolated by column chromatography, giving (S)-**1ad** as a yellow oil.

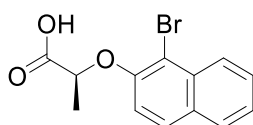


**(S)-1ad:** (new compound). White solid; isolated yield 89%; mp 250-251°C.  $[\alpha]_D^{24} = -17.6$  (*c* 0.5 in CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ (ppm) 8.26 (d, *J* = 10.0 Hz, 1H), 7.76-7.72

**(S)-1ad** (m, 2H), 7.58-7.55 (m, 1H), 7.41 (t, *J* = 5.0 Hz, 1H), 7.16 (d,

*J* = 10.0 Hz, 1H), 4.92 (q, *J* = 6.7 Hz, 1H), 3.77 (s, 3H), 1.76 (d, *J* = 5.0 Hz, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ (ppm) 172.1, 152.3, 133.2, 130.5, 128.9, 128.0, 127.7, 126.5, 124.9, 116.6, 111.2, 75.2, 52.3, 18.7. HRMS (ESI) *m/z* calcd. for C<sub>14</sub>H<sub>14</sub>BrO<sub>3</sub><sup>+</sup> (M+H)<sup>+</sup> 309.0121, found 309.0111.

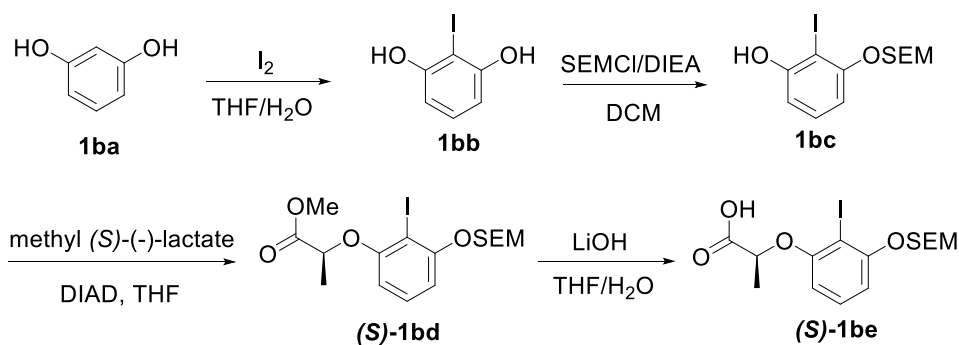
To a solution of **(S)-1ad** (13.9 g, 44.8 mmol) in THF-H<sub>2</sub>O (4:1, 250 mL) at room temperature was added LiOH (4.3 g, 179.3 mmol). The reaction was stirred at room temperature overnight. 1M HCl was added to reach a pH of 5, then the solution was extracted with EtOAc for several times. The combined organic layer was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, filtrated, and concentrated to afford **(S)-1ae**. The product **(S)-1ae** was directly used without further purification.



**(S)-1ae**

**(S)-1ae:** (new compound). White solid; isolated yield 99%; mp 240-241°C.  $[\alpha]_D^{24} = -8.6$  (*c* 0.5 in CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (500 MHz, d<sub>6</sub>-DMSO): δ (ppm) 8.10 (d, *J* = 10.0 Hz, 1H), 7.96-7.91 (m, 2H), 7.65-7.62 (m, 1H), 7.48-7.45 (m, 1H), 7.34 (d, *J* = 10.0 Hz, 1H),

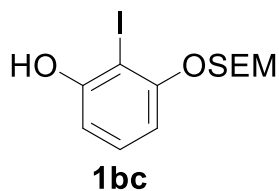
5.11 (q, *J* = 6.7 Hz, 1H), 3.34 (s, 1H), 2.50 (s, 4H), 1.60 (d, *J* = 5.0 Hz, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ (ppm) 172.9, 152.4, 132.4, 130.5, 129.5, 128.9, 128.2, 128.0, 125.3, 124.4, 115.6, 107.9, 73.6, 18.4. HRMS (ESI) *m/z* calcd. for C<sub>13</sub>H<sub>12</sub>BrO<sub>3</sub><sup>+</sup> (M+H)<sup>+</sup> 294.9965, found 294.9970.



To a solution of resorcinol (1.1g, 10 mmol) and NaHCO<sub>3</sub> (924 mg, 11 mmol) in

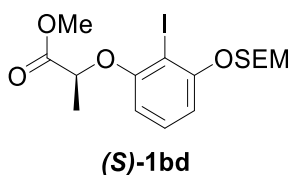
THF-H<sub>2</sub>O (1:1, 20 mL) at room temperature was added I<sub>2</sub> (2.66 g, 10.5 mmol). The reaction was stirred at room temperature overnight. 10% Aqueous Na<sub>2</sub>SO<sub>3</sub> was added and it was extracted with EtOAc. The combined organic layer was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, filtrated, and concentrated. Flash column chromatography afforded 2-iodobenzene-1,3-diol **1bb** as a white solid with 70% yield (known compound, see: J. Shi, H. Xu, D. Qiu, J. He, Y. Li, *J. Am. Chem. Soc.* 2017, 139, 623).

A solution of 2-iodobenzene-1,3-diol (5.3g, 22.5 mmol) and SEMCl (4.0 mL, 22.5 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (25 mL) was cooled to 0°C, Then N, N-Diisopropylethylamine (DIEA) (7.4 mL, 45.0 mmol) was added dropwise via syringe. After the addition of DIEA, the mixture was stirred from 0°C to r.t overnight. The solvent was removed in vacuo and the crude product was purified by silica gel chromatography, providing **1bc** as a yellow oil.



**1bc**: (new compound). Yellow oil; isolated yield 35%; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ (ppm) 7.20 (t, *J* = 10.0 Hz, 1H), 6.74-6.68 (m, 2H), 5.77 (s, 1H), 5.34 (s, 2H), 3.88-3.83 (m, 2H), 1.02(t, *J* = 12.5 Hz 2H), -0.06(s, 9H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ (ppm) 157.0, 156.3, 130.3, 108.7, 106.8, 93.6, 79.7, 66.9, 18.2, -1.3. HRMS (ESI) *m/z* calcd. for C<sub>12</sub>H<sub>20</sub>IO<sub>3</sub>Si<sup>+</sup>(M+H)<sup>+</sup> 367.0148, found 367.0140.

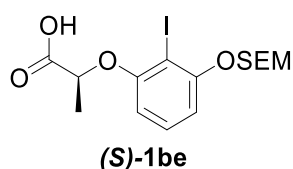
A stirred suspension of **1bc** (1.75g, 4.8 mmol), Ph<sub>3</sub>P (3.13 g, 12.0 mmol) and methyl (*S*)-(-)-lactate (498mg, 4.8 mmol) in THF (20 mL) was placed in an ice-water bath for 10 min. Then DIAD (2.5 mL, 12.0 mmol) was added dropwise via syringe. after the addition of DIAD, the homogenic mixture was stirred at 0°C for 20 min, then at r.t. overnight. The solvent was removed in vacuo and the crude product was isolated by column chromatography, giving (*S*)-**1bd** as a yellow oil.



**(S)-1bd**: (new compound). Yellow oil; isolated yield 92%; [α]<sub>D</sub><sup>24</sup> = -7.9 (c 0.5 in CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ (ppm) 7.18-7.15 (m, 1H), 6.75 (d, *J* = 10.0 Hz, 1H), 6.45 (d, *J* = 5.0 Hz, 1H), 5.28 (s, 2H), 4.77 (q, *J* = 6.7 Hz, 1H), 3.81-3.75 (m, 5H), 1.70 (d, *J* = 5.0 Hz, 3H), 0.95 (t, *J* = 10.0 Hz, 2H), 0.00 (s, 9H). <sup>13</sup>C NMR

(125 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 172.3, 158.1, 158.0, 129.7, 108.8, 107.1, 93.6, 80.9, 74.4, 66.8, 52.4, 18.7, 18.1, -1.3. HRMS (ESI)  $m/z$  calcd. for C<sub>16</sub>H<sub>15</sub>IO<sub>5</sub>SiNa<sup>+</sup> (M+Na)<sup>+</sup> 475.0408, found 475.0417.

To a solution of (**S**)-**1bd** (1.43g, 3.16 mmol) in THF-H<sub>2</sub>O (4:1, 50 mL) at room temperature was added LiOH (150mg, 6.32 mmol). The reaction was stirred at room temperature overnight. 1M HCl was added to reach a pH of 5, then the solution was extracted with EtOAc for several times. The combined organic layer was washed with brine (10 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtrated, and concentrated to afford (**S**)-**1be**. The product (**S**)-**1be** was directly used without further purification.

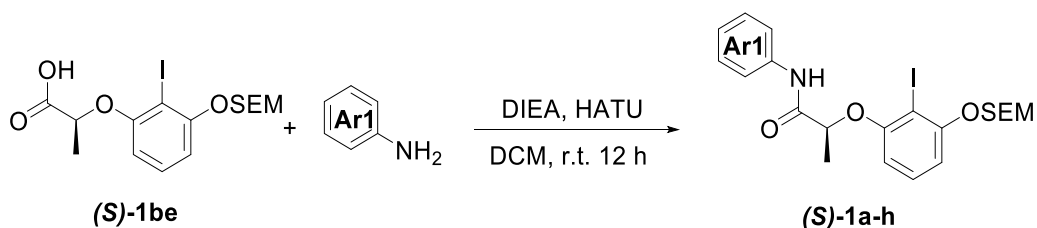


(**S**)-**1be**: (new compound). Yellow oil; isolated yield 95%;

$[\alpha]_D^{24} = -9.9$  (*c* 0.5 in CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 7.22-7.19 (m, 1H), 6.79 (d, *J* = 10.0 Hz, 1H), 6.45 (d, *J* = 5.0 Hz, 1H), 5.30 (s, 2H), 4.83 (q, *J* = 6.7 Hz, 1H), 3.80 (t,

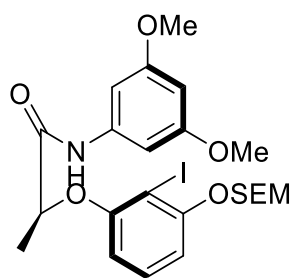
*J* = 10.0 Hz, 2H), 1.74 (d, *J* = 5.0 Hz, 3H), 0.96 (t, *J* = 7.5 Hz, 2H), 0.00 (s, 9H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 175.1, 158.2, 157.3, 130.0, 109.3, 107.2, 93.6, 81.0, 74.1, 66.9, 18.4, 18.1, -1.3. HRMS (ESI)  $m/z$  calcd. for C<sub>15</sub>H<sub>23</sub>IO<sub>5</sub>SiNa<sup>+</sup> (M+Na)<sup>+</sup> 461.0251, found 461.0256.

## 2.2 General procedure for the synthesis of 1a-h.



Using (**S**)-**1a** as an example. A stirred solution of (**S**)-**1be** (0.65 g, 1.5 mmol), 3,5-Dimethoxyaniline (0.28 g, 1.8 mmol) and *N,N*-diisopropylethylamine (0.5 mL, 3.0 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (50 mL) was stirred under room temperature for 30 min. Then 2-(7-Azabenzotriazol-1-yl)-*N,N,N',N'*-tetramethyluronium hexafluorophosphate (HATU) (0.68 g, 1.8 mmol) was added dropwise via syringe. After the addition of HATU, the homogenic mixture was stirred at Room temperature overnight. The solvent was

removed in vacuo and the crude product was isolated by column chromatography, giving **(S)-1a** as a yellow oil.



**(S)-1a**

**(S)-1a:** (new compound). Light yellow oil; isolated yield 96%;

$[\alpha]^{24}_{\text{D}} = -48.6$  (*c* 0.5 in  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):

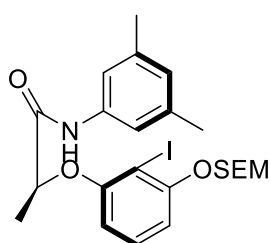
$\delta$  (ppm) 8.95 (s, 1H), 7.33-7.29 (m, 2H), 6.97(s, 2H), 6.86 (d,

$J = 10.0$  Hz, 1H), 6.58 (d,  $J = 10.0$  Hz, 1H), 6.32 (t,  $J = 5.0$ Hz,

1H), 5.37 (s, 2H), 4.95 (q,  $J = 8.3$ Hz, 1H), 3.88-3.84 (m, 8H),

1.77 (d,  $J = 10.0$  Hz, 3H), 1.01 (t,  $J = 12.5$  Hz, 2H), -0.06 (s,

9H).  $^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 169.4, 161.3, 158.2, 156.5, 139.3, 130.3, 109.1, 106.9, 98.4, 97.1, 93.6, 80.9, 76.2, 67.0, 55.6, 27.1, 18.4, 18.1, -1.3. HRMS (ESI)  $m/z$  calcd. for  $\text{C}_{23}\text{H}_{33}\text{INO}_6\text{Si}^+$  ( $\text{M}+\text{H}$ ) $^+$  574.1117, found 574.1118.



**(S)-1b**

**(S)-1b:** (new compound). Light yellow oil; isolated yield 95%;

$[\alpha]^{24}_{\text{D}} = -76.0$  (*c* 1.0 in acetone);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$

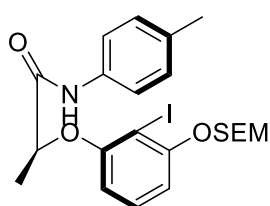
(ppm) 8.73 (s, 1H), 7.25 – 7.21 (m, 2H), 6.80 – 6.75 (m, 2H),

6.51 (d,  $J = 8.1$  Hz, 1H), 5.30 (s, 2H), 4.87 (q,  $J = 6.7$  Hz, 1H),

3.82 – 3.77 (m, 2H), 2.29 (s, 6H), 1.69 (d,  $J = 6.7$  Hz, 3H), 0.97

– 0.92 (m, 2H), -0.01 (s, 9H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ ):  $\delta$

(ppm) 169.17, 158.02, 156.50, 138.78, 137.24, 130.18, 126.40, 117.68, 108.93, 106.83, 93.52, 80.83, 76.10, 66.85, 21.41, 18.39, 18.04, -1.36. HRMS (ESI)  $m/z$  calcd. for  $\text{C}_{23}\text{H}_{33}\text{INO}_4\text{Si}^+$  ( $\text{M}+\text{H}$ ) $^+$  542.1120, found 542.1121.



**(S)-1c**

**(S)-1c:** (new compound). Yellow oil; isolated yield 92%;  $[\alpha]^{24}_{\text{D}}$

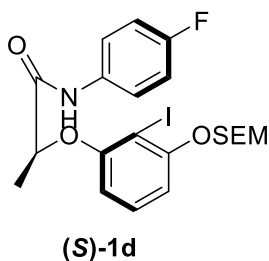
= -109 (*c* 1.0 in acetone);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm)

7.53 (d,  $J = 10.0$  Hz, 2H), 7.25-7.13 (m, 4H), 6.80 (d,  $J = 10.0$

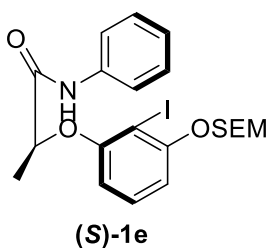
Hz, 1H), 6.53 (d,  $J = 10.0$  Hz, 1H), 5.31 (s, 2H), 4.90 (t,  $J = 5$

Hz, 1H), 3.81 (t,  $J = 7.5$  Hz, 2H), 2.32 (s, 4H), 1.72 (d,  $J = 5.0$

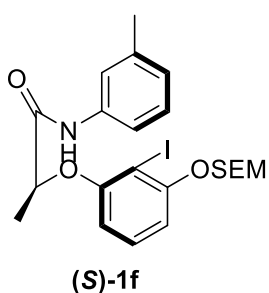
Hz, 4H), 0.96 (t,  $J = 10.0$  Hz, 3H), 0.00 (s, 9H).  $^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 169.2, 158.2, 156.7, 135.1, 134.4, 130.4, 129.8, 128.7, 120.1, 109.1, 107.0, 93.7, 81.9, 76.2, 67.0, 21.1, 18.6, 18.2, -1.2. HRMS (ESI)  $m/z$  calcd. for  $\text{C}_{22}\text{H}_{31}\text{INO}_4\text{Si}^+$  ( $\text{M}+\text{H}$ ) $^+$  528.1062, found 528.1062.



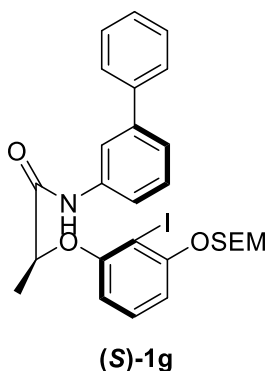
**(S)-1d:** (new compound). Light yellow oil; isolated yield 93%;  $[\alpha]_D^{24} = -44.7$  (*c* 0.5 in  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.93 (s, 1H), 7.64-7.61 (m, 2H), 7.27-7.24 (m, 1H), 7.03 (t,  $J = 10.0$  Hz, 2H), 6.81 (d,  $J = 10.0$  Hz, 1H), 6.53 (d,  $J = 10.0$  Hz, 1H), 5.31 (s, 2H), 4.91 (q,  $J = 5.0$  Hz, 1H), 3.81 (t,  $J = 7.5$  Hz, 2H), 1.72 (d,  $J = 5.0$  Hz, 3H), 0.96 (t,  $J = 10.0$  Hz, 2H), 0.00 (s, 9H).  $^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 169.2, 160.6, 158.7, 158.1, 156.5, 133.6, 133.6, 130.4, 121.7, 121.6, 115.9, 115.7, 109.1, 106.8, 93.6, 80.9, 76.1, 67.0, 18.4, 18.1, -1.3. HRMS (ESI)  $m/z$  calcd. for  $\text{C}_{21}\text{H}_{28}\text{FINO}_4\text{Si}^+$  ( $\text{M}+\text{H}$ ) $^+$  532.0811, found 532.0819.



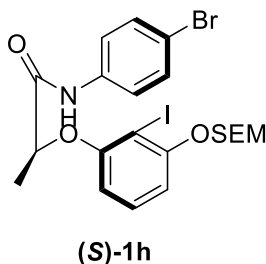
**(S)-1e:** (new compound). Light yellow oil; isolated yield 89%;  $[\alpha]_D^{24} = -40.3$  (*c* 0.5 in  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.91 (s, 1H), 7.66 (d,  $J = 10.0$  Hz, 2H), 7.35 (t,  $J = 10.0$  Hz, 2H), 7.28-7.25 (m, 1H), 7.15-7.12 (m, 1H), 6.81 (d,  $J = 5.0$  Hz, 1H), 6.54 (d,  $J = 5.0$  Hz, 1H), 5.31 (s, 2H), 4.92 (q,  $J = 6.7$  Hz, 1H), 3.81 (t,  $J = 7.5$  Hz, 2H), 1.72 (d,  $J = 10.0$  Hz, 3H), 0.97 (t,  $J = 10.0$  Hz, 2H), 0.00 (s, 9H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 169.21, 158.03, 156.44, 137.46, 130.24, 129.09, 124.63, 119.87, 108.93, 106.74, 93.51, 80.77, 66.87, 18.34, 18.04, -1.36. HRMS (ESI)  $m/z$  calcd. for  $\text{C}_{21}\text{H}_{29}\text{INO}_4\text{Si}^+$  ( $\text{M}+\text{H}$ ) $^+$  514.0832, found 514.0835.



**(S)-1f:** (new compound). Light yellow oil; isolated yield 90%;  $[\alpha]_D^{24} = -30.1$  (*c* 0.5 in  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.84 (s, 1H), 7.53 (s, 1H), 7.43-7.41 (m, 1H), 7.28-7.22 (m, 2H), 6.96-6.95 (m, 1H), 6.82-6.81 (m, 1H), 6.55-6.53 (m, 1H), 5.32-5.26 (m, 2H), 4.93-4.89 (m, 1H), 3.83-3.80 (m, 2H), 2.36 (s, 3H), 1.73 (m, 3H), 0.96 (t,  $J = 10$  Hz, 1H), 0.00 (s, 9H).  $^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 169.3, 158.1, 156.6, 139.1, 137.5, 130.3, 129.0, 125.6, 120.6, 117.1, 109.0, 106.9, 93.6, 80.9, 76.1, 67.0, 29.8, 21.7, 18.5, 18.1, -1.3. HRMS (ESI)  $m/z$  calcd. for  $\text{C}_{22}\text{H}_{31}\text{INO}_4\text{Si}^+$  ( $\text{M}+\text{H}$ ) $^+$  528.1062, found 528.1054.

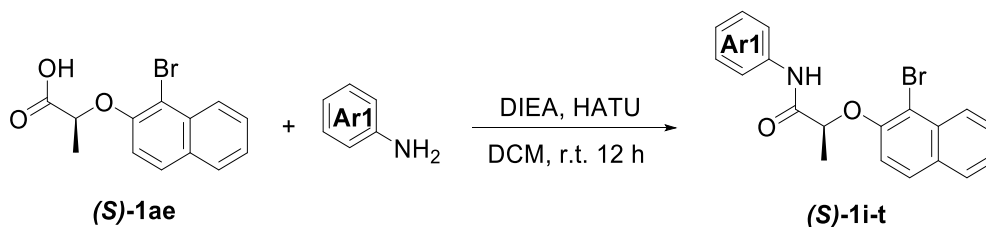


**(S)-1g:** (new compound). Yellow oil; isolated yield 85%;  $[\alpha]^{24}_D = -54.0$  (*c* 1.0 in acetone);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.98 (s, 1H), 7.93 (s, 1H), 7.60 (d,  $J = 10.0$  Hz, 2H), 7.43 (t,  $J = 5.0$  Hz, 3H), 7.38 – 7.34 (m, 2H), 7.25 (s, 1H), 6.81 (d,  $J = 10.0$  Hz, 1H), 6.55 (d,  $J = 10.0$  Hz, 1H), 5.31 (s, 2H), 4.93 (q,  $J = 6.7$  Hz, 1H), 3.81 (t,  $J = 10.0$  Hz, 2H), 1.74 (d,  $J = 10.0$  Hz, 3H), 0.96 (t,  $J = 10.0$  Hz, 2H), -0.00 (s, 9H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 169.34, 158.08, 156.52, 142.33, 140.77, 137.91, 130.26, 129.45, 128.81, 127.56, 127.28, 123.50, 118.79, 118.70, 109.02, 106.86, 93.56, 76.16, 66.90, 18.38, 18.07, -1.34. HRMS (ESI)  $m/z$  calcd. for  $\text{C}_{27}\text{H}_{33}\text{INO}_4\text{Si}^+$  ( $\text{M}+\text{H}$ ) $^+$  590.1145, found 590.1147.



**(S)-1h:** (new compound). Yellow oil; isolated yield 96%;  $[\alpha]^{24}_D = -75.0$  (*c* 1.0 in acetone);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.96 (s, 1H), 7.57 (d,  $J = 10.0$  Hz, 2H), 7.45 (d,  $J = 5.0$  Hz, 2H), 6.81 (d,  $J = 5.0$  Hz, 1H), 6.53 (d,  $J = 5.0$  Hz, 1H), 5.31 (s, 2H), 4.90 (q,  $J = 6.6$  Hz, 1H), 3.81 (t,  $J = 5.0$  Hz, 2H), 1.71 (d,  $J = 5.0$  Hz, 3H), 0.96 (t,  $J = 10.0$  Hz, 2H), 0.00 (s, 9H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 169.26, 158.05, 156.34, 136.57, 132.07, 130.29, 121.40, 117.24, 109.03, 106.74, 93.53, 76.00, 66.90, 18.28, 18.06, -1.35. HRMS (ESI)  $m/z$  calcd. for  $\text{C}_{21}\text{H}_{28}\text{BrINO}_4\text{Si}^+$  ( $\text{M}+\text{H}$ ) $^+$  591.9937, found 591.9937.

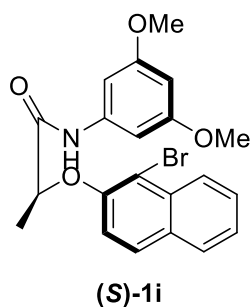
### 2.3 General procedure for the synthesis of 1i-t.



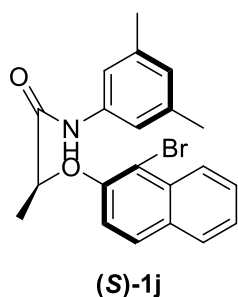
Using **(S)-1i** as an example. A stirred solution of **(S)-1ae** (0.5 g, 1.7 mmol), 3,5-Dimethoxyaniline (0.31 g, 2.04 mmol) and *N,N*-diisopropylethylamine (DIEA) (0.6 mL, 3.4 mmol) in  $\text{CH}_2\text{Cl}_2$  (50 mL) was stirred under room temperature for 30 min. Then 2-



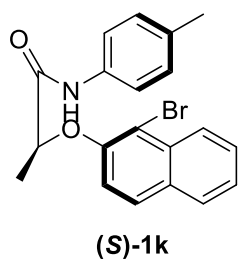
(7-Azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (HATU) (0.78 g, 2.04 mmol) was added dropwise via syringe. After the addition of HATU, the homogenic mixture was stirred at Room temperature overnight. The solvent was removed in vacuo and the crude product was isolated by column chromatography, giving **(S)-1i** as a white solid.



**(S)-1i:** (new compound). White solid; isolated yield 96%; mp 132-133°C.  $[\alpha]_D^{24} = -39.0$  (*c* 1.0 in acetone);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.90 (s, 1H), 8.23 (d,  $J = 5.0$  Hz, 1H), 7.84-7.80 (m, 2H), 7.61-7.46 (m, 2H), 7.25-7.24 (m, 1H), 6.90 (s, 2H), 5.01-4.98 (m, 1H), 3.79 (s, 6H), 1.76 (d,  $J = 5.0$  Hz, 3H).  $^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 169.5, 161.3, 151.1, 139.2, 133.2, 130.8, 129.7, 128.3, 126.5, 125.5, 115.9, 111.0, 98.3, 97.2, 77.3, 55.6, 18.9. HRMS (ESI)  $m/z$  calcd. for  $\text{C}_{21}\text{H}_{21}\text{BrNO}_4^+$  ( $\text{M}+\text{H}$ ) $^+$  430.0649, found 430.0646.

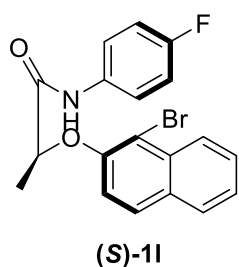


**(S)-1j:** (new compound). White solid; isolated yield 97%; mp 120-121°C.  $[\alpha]_D^{24} = -34.0$  (*c* 1.0 in acetone);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.78 (s, 1H), 8.22 (d,  $J = 5.0$  Hz, 1H), 7.80 (t,  $J = 10.0$  Hz, 2H), 7.61 – 7.56 (m, 1H), 7.44 (t,  $J = 10.0$  Hz, 1H), 7.23 (d,  $J = 5.0$  Hz, 1H), 7.21 (s, 1H), 6.77 (s, 1H), 4.97 (q,  $J = 6.7$  Hz, 1H), 2.30 (s, 6H), 1.74 (d,  $J = 15.0$  Hz, 3H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  169.30, 151.05, 138.83, 137.15, 133.10, 130.64, 129.53, 128.22, 128.17, 126.46, 126.40, 125.29, 117.66, 115.78, 110.89, 77.20, 21.40, 18.86. HRMS (ESI)  $m/z$  calcd. for  $\text{C}_{21}\text{H}_{21}\text{BrNO}_2^+$  ( $\text{M}+\text{H}$ ) $^+$  398.0677, found 398.0670.



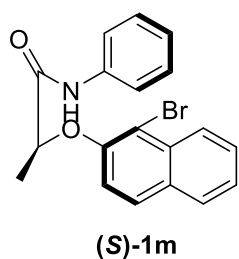
**(S)-1k:** (new compound). White solid. Isolated yield 93%; mp 170-171°C.  $[\alpha]_D^{24} = -80.0$  (*c* 1.0 in acetone);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.89 (s, 1H), 8.24 (d,  $J = 10.0$  Hz, 1H), 7.83 (t,  $J = 10.0$  Hz, 2H), 7.64-7.60 (m, 1H), 7.52-7.47 (m, 2H), 7.24 (s, 1H), 7.16 (m, 2H), 5.02 (q,  $J = 8.3$  Hz, 1H), 2.33 (s, 3H), 1.78 (d,  $J = 5.0$  Hz, 3H).  $^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 169.3, 151.2, 134.9, 134.4, 133.2, 130.7, 129.7, 129.7, 128.3, 128.3, 126.5, 125.4, 120.0, 115.9, 110.9, 77.3, 21.0, 19.0

HRMS (ESI)  $m/z$  calcd. for  $C_{20}H_{19}BrNO_2^+$  ( $M+H$ ) $^+$  384.0594, found 384.0615.



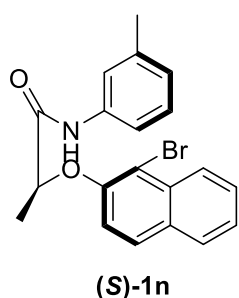
**(S)-11:** (new compound). White solid; isolated yield 94%; mp 165-166°C.  $[\alpha]^{24}_D = -41.0$  ( $c$  1.0 in acetone);  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  (ppm) 8.98 (s, 1H), 8.26 (d,  $J = 8.0$  Hz, 1H), 7.89-7.84 (m, 2H), 7.65-7.63 (m, 3H), 7.52-7.48 (m, 1H), 7.28-7.26 (m, 2H), 7.07(t,  $J = 10.0$  Hz, 2H), 5.05 (q,  $J = 6.7$  Hz, 1H), 1.80 (d,  $J = 8.0$

Hz, 3H).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  (ppm) 169.4, 160.7, 158.8, 151.1, 133.5, 133.2, 130.8, 129.8, 128.4, 128.4, 126.5, 125.5, 121.7, 121.7, 116.0, 115.9, 115.8, 111.0, 77.2, 18.9. HRMS (ESI)  $m/z$  calcd. for  $C_{19}H_{16}BrFNO_2^+$  ( $M+H$ ) $^+$  388.0348, found 388.0343.



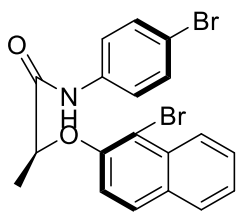
**(S)-1m:** (new compound). White solid; isolated yield 90%; mp 166-167°C.  $[\alpha]^{24}_D = -84.0$  ( $c$  1.0 in acetone);  $^1H$  NMR (500 MHz,  $CDCl_3$ ):  $\delta$  (ppm) 8.95 (s, 1H), 8.23 (d,  $J = 5.0$  Hz, 1H), 7.83-7.79 (m, 2H), 7.65 (d,  $J = 5.0$  Hz, 1H), 7.45 (s, 1H), 7.36-7.33 (m, 2H), 7.23 (t,  $J = 5.0$  Hz, 2H), 7.14 (s, 1H), 5.01 (q,  $J = 6.7$  Hz, 1H), 1.77

(d,  $J = 5.0$  Hz, 3H).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  (ppm) 169.5, 151.1, 137.4, 133.2, 130.7, 129.7, 129.2, 128.3, 128.3, 126.5, 125.4, 124.8, 120.0, 115.8, 110.9, 77.2, 18.9. HRMS (ESI)  $m/z$  calcd. for  $C_{19}H_{17}BrNO_2^+$  ( $M+H$ ) $^+$  370.0437, found 370.0448.



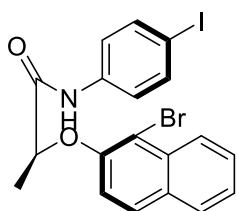
**(S)-1n:** (new compound). White solid; isolated yield 92%; mp 142-143°C.  $[\alpha]^{24}_D = -95.0$  ( $c$  1.0 in acetone);  $^1H$  NMR (500 MHz,  $CDCl_3$ ):  $\delta$  (ppm) 8.87 (s, 1H), 8.23 (d,  $J = 10.0$  Hz, 1H), 7.83-7.79 (m, 2H), 7.60 (m, 1H), 7.50-7.42 (m, 3H), 7.25-7.21 (m, 2H), 7.07(t,  $J = 10.0$  Hz, 2H), 5.00 (q,  $J = 6.7$  Hz, 1H), 2.36 (s, 2H),

1.76 (d,  $J = 10.0$  Hz, 3H).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  (ppm) 169.4, 151.2, 139.2, 137.4, 133.2, 130.8, 129.7, 129.0, 128.3, 128.3, 126.5, 125.6, 125.4, 120.6, 117.1, 115.9, 111.0, 77.3, 21.6, 19.0. HRMS (ESI)  $m/z$  calcd. for  $C_{20}H_{18}BrNO_2^+$  ( $M+H$ ) $^+$  384.0594, found 384.0612.



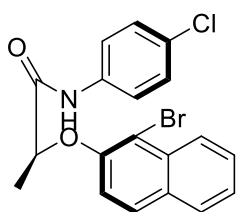
**(S)-1o**

**(S)-1o:** (new compound). White solid; isolated yield 87%; mp 173-174°C.  $[\alpha]^{24}_{\text{D}} = -38.0$  (*c* 1.0 in actone);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.98 (s, 1H), 8.23 (d,  $J = 10.0$  Hz, 1H), 7.85 – 7.81 (m, 2H), 7.62 (t,  $J = 10.0$  Hz, 1H), 7.56 (d,  $J = 10.0$  Hz, 2H), 7.47 (t,  $J = 10.0$  Hz, 3H), 7.23 (d,  $J = 5.0$  Hz, 1H), 5.01 (q,  $J = 6.8$  Hz, 1H), 1.77 (d,  $J = 10.0$  Hz, 3H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 169.40, 150.90, 136.45, 133.06, 132.09, 130.69, 129.65, 128.29, 128.25, 126.38, 125.43, 121.40, 117.30, 115.73, 110.90, 77.16, 18.77. HRMS (ESI) *m/z* calcd. for  $\text{C}_{19}\text{H}_{16}\text{Br}_2\text{NO}_2^+$  ( $\text{M}+\text{H}$ ) $^+$  447.9470, found 447.9474.



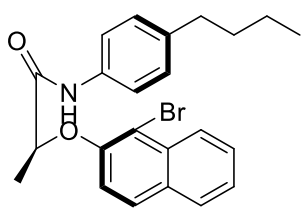
**(S)-1p**

**(S)-1p:** (new compound). White solid; isolated yield 90%; mp 177-178°C.  $[\alpha]^{24}_{\text{D}} = -39.0$  (*c* 1.0 in actone);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.96 (s, 1H), 8.23 (d,  $J = 8.6$  Hz, 1H), 7.87 – 7.80 (m, 2H), 7.64 (t,  $J = 8.0$  Hz, 3H), 7.45 (t,  $J = 7.9$  Hz, 3H), 7.23 (s, 1H), 5.01 (q,  $J = 6.7$  Hz, 1H), 1.77 (d,  $J = 6.8$  Hz, 3H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 169.44, 150.91, 138.07, 137.16, 133.08, 130.71, 129.67, 128.26, 126.40, 125.45, 121.71, 115.76, 110.93, 87.92, 18.78. HRMS (ESI) *m/z* calcd. for  $\text{C}_{19}\text{H}_{16}\text{IBrNO}_2^+$  ( $\text{M}+\text{H}$ ) $^+$  495.9331, found 495.9330.



**(S)-1q**

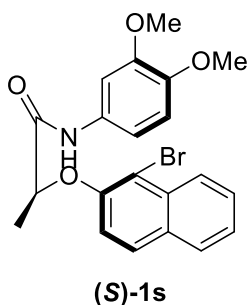
**(S)-1q:** (new compound). White solid; isolated yield 95%; mp 168-169°C.  $[\alpha]^{24}_{\text{D}} = -39.0$  (*c* 1.0 in actone);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.99 (s, 1H), 8.23 (d,  $J = 10.0$  Hz, 1H), 7.85-7.81 (m, 2H), 7.64-7.61 (m, 2H), 7.49-7.46 (m, 3H), 7.32-7.31 (m, 2H), 7.26-7.23 (m, 1H), 5.02 (q,  $J = 6.7$  Hz, 1H), 1.77 (d,  $J = 10.0$  Hz, 3H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 169.39, 150.91, 135.96, 133.06, 130.69, 129.69, 129.65, 129.14, 128.29, 128.25, 126.38, 125.42, 121.08, 115.73, 110.89, 77.14, 18.79. HRMS (EI) *m/z* calcd. for  $\text{C}_{19}\text{H}_{16}\text{BrClNO}_2^+$  ( $\text{M}+\text{H}$ ) $^+$  403.9975, found 403.9980.



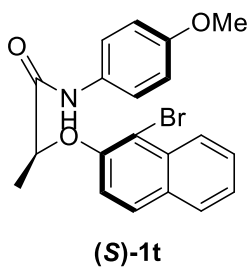
**(S)-1r**

**(S)-1r:** (new compound). White solid; isolated yield 91%; mp 121-122°C.  $[\alpha]^{24}_{\text{D}} = -47.3$  (*c* 0.5 in  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.88 (s, 1H), 8.24 (d,  $J = 10.0$  Hz, 1H), 7.84-7.81 (m, 2H), 7.62-7.47 (m, 4H), 7.26-7.24 (m, 1H),

7.17(d,  $J = 5.0$  Hz, 2H), 5.04-5.00 (m, 1H), 2.61-2.58 (m, 2H), 1.78 (d,  $J = 5.0$  Hz, 3H), 1.61-1.55(m, 2H), 1.37-1.32(m, 2H), 0.94-0.91(m, 3H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 169.3, 151.2, 139.6, 135.1, 133.2, 130.7, 129.7, 129.1, 128.3, 128.3, 126.5, 125.4, 120.0, 115.9, 110.9, 77.3, 35.2, 33.8, 22.4, 19.0, 14.0. HRMS (ESI)  $m/z$  calcd. for  $\text{C}_{23}\text{H}_{24}\text{BrNO}_2^+$  ( $\text{M}+\text{H}$ ) $^+$  426.1063, found 426.1061.

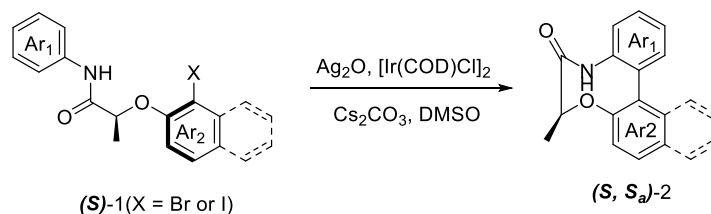


**(S)-1s:** (new compound). White solid; isolated yield 96%; mp 175-176°C.  $[\alpha]_{\text{D}}^{24} = -43.0$  ( $c$  0.5 in  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.85 (s, 1H), 8.23 (d,  $J = 10.0$  Hz, 1H), 7.85-7.81 (m, 2H), 7.62 (m, 1H), 7.49-7.47 (m, 2H), 7.24 (s, 1H), 7.01-6.99 (m, 1H), 6.83 (d,  $J = 10.0$  Hz, 1H), 5.01 (q,  $J = 6.7$  Hz, 1H), 3.88(d,  $J = 15.0$  Hz, 6H), 1.78 (d,  $J = 5.0$  Hz, 3H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 169.2, 151.2, 149.4, 146.3, 130.8, 129.7, 128.3, 126.5, 125.5, 116.0, 112.0, 111.6, 111.0, 104.9, 56.3, 56.1, 19.0. HRMS (EI)  $m/z$  calcd. for  $\text{C}_{21}\text{H}_{21}\text{BrNO}_4^+$  ( $\text{M}+\text{H}$ ) $^+$  430.0649, found 430.0646.

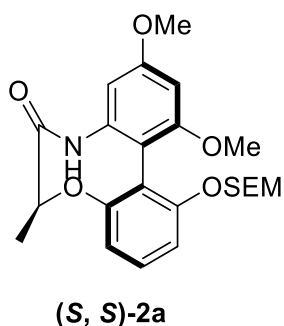


**(S)-1t:** (new compound). White solid; isolated yield 95%; mp 190-191°C.  $[\alpha]_{\text{D}}^{24} = -46.0$  ( $c$  1.0 in acetone);  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.83 (s, 1H), 8.24 (d,  $J = 10.0$  Hz, 1H), 7.85-7.81 (m, 2H), 7.62-7.47 (m, 4H), 7.25 (m, 1H), 6.89 (d,  $J = 10.0$  Hz, 1H), 5.02 (q,  $J = 6.7$  Hz, 1H), 3.80(s, 3H), 1.78 (d,  $J = 5.0$  Hz, 3H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 169.2, 156.8, 151.2, 133.2, 130.7, 130.6, 129.7, 128.3, 128.3, 126.5, 125.4, 121.7, 115.9, 114.4, 110.9, 77.3, 55.7, 19.0. HRMS (ESI)  $m/z$  calcd. for  $\text{C}_{20}\text{H}_{19}\text{BrNO}_3^+$  ( $\text{M}+\text{H}$ ) $^+$  400.0543, found 400.0541.

### 3. General procedure for construction of axially chiral biaryl compounds catalyzed by iridium

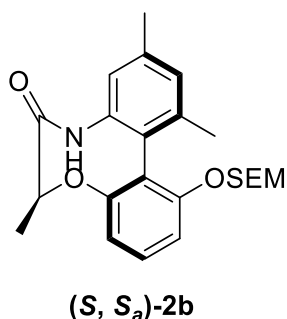


Using **(S, Sa)-2a** as an example. An oven dried Schlenk tube was charged with a magnetic stir bar, **(S)-1a** (57.3 mg, 0.10 mmol), [Ir(COD)Cl]<sub>2</sub> (5.0 mol %), Ag<sub>2</sub>O (0.2 mmol), Cs<sub>2</sub>CO<sub>3</sub> (2.0 equiv.). The Schlenk tube was capped, and then evacuated and backfilled with nitrogen (3 times). Under a positive pressure of nitrogen, DMSO (4 mL) was added via syringe and Schlenk tube was sealed and allowed to stir at 130°C for 16 h. The reaction mixture was directly passed through celite and rinsed with an additional 10 mL of EtOAc. The combined filtrate was concentrated and purified by column chromatography on silica gel to give the corresponding product.



**(S, Sa)-2a:** (new compound). Light yellow oil; isolated yield 80%;  $[\alpha]^{24}_{\text{D}} = -32.0$  (*c* 1.0 in acetone); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ (ppm) 8.15 (s, 1H), 7.21 (t, *J* = 10.0 Hz, 1H), 6.79 (s, 2H), 6.70 (t, *J* = 5.0 Hz, 1H), 6.25 (s, 1H), 5.21 (s, 2H), 4.76 (q, *J* = 6.7 Hz, 1H), 3.78 (s, 6H), 3.74 (d, *J* = 5.0 Hz, 2H), 1.64 (d, *J* = 10.0 Hz, 3H), 0.96 (t, *J* = 5.0 Hz, 2H), -0.00 (s, 9H). <sup>13</sup>C

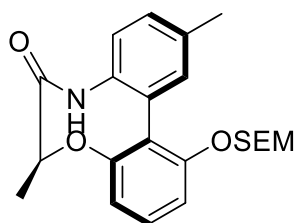
NMR (126 MHz, CDCl<sub>3</sub>): δ (ppm) 170.17, 161.17, 158.98, 157.80, 138.88, 130.39, 110.42, 108.70, 104.77, 98.28, 97.26, 92.98, 75.62, 66.42, 55.46, 18.63, 18.11, -1.39. HRMS (EI) *m/z* calcd. for C<sub>23</sub>H<sub>32</sub>NO<sub>4</sub>Si<sup>+</sup> (M+H)<sup>+</sup> 446.1994, found 446.1998.



**(S, Sa)-2b:** (new compound). Light yellow oil; isolated yield 38%;  $[\alpha]^{24}_{\text{D}} = -23.0$  (*c* 1.0 in acetone); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 8.17 (s, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 6.84 – 6.78 (m, 3H), 6.67 (d, *J* = 8.0 Hz, 1H), 5.28 (s, 2H), 4.83 (q, *J* = 8.6, 7.9 Hz, 1H), 3.82 (t, *J* = 12.0 Hz, 2H), 2.37 (s, 6H), 1.72 (d, *J* = 4.0 Hz, 3H), 1.03 (t, *J* = 8.0 Hz, 2H), 0.07 (s, 9H). <sup>13</sup>C

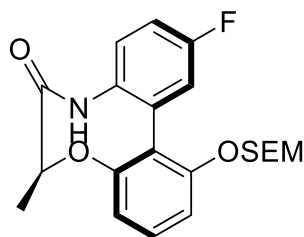
NMR (126 MHz, CDCl<sub>3</sub>) δ 170.08, 158.94, 157.87, 138.79, 136.96, 130.35, 126.42, 117.72, 110.29, 108.58, 104.66, 92.96, 75.57, 66.40, 21.35, 18.74, 18.09, -1.39. HRMS

(EI)  $m/z$  calcd. for  $C_{23}H_{32}NO_6Si^+$  ( $M+H$ )<sup>+</sup> 414.2022, found 414.2025.



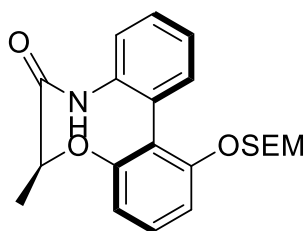
**(S, Sa)-2c**

**(S, Sa)-2c:** (new compound). Light yellow oil; isolated yield 34%;  $[\alpha]^{24}_D = -27.0$  ( $c$  1.0 in acetone);  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  (ppm) 8.86 (s, 1H), 7.54 (d,  $J = 8.0$  Hz, 2H), 7.15 (d,  $J = 8.0$  Hz, 2H), 6.81 (d,  $J = 8.0$  Hz, 1H), 6.54 (d,  $J = 8.0$  Hz, 1H), 5.32 (s, 2H), 4.91 (q,  $J = 7.4, 7.0$  Hz, 1H), 3.81 (t,  $J = 8.0$  Hz, 2H), 2.33 (s, 3H), 1.72 (d,  $J = 8.0$  Hz, 3H), 0.97 (t,  $J = 8.0$  Hz, 2H), 0.01 (s, 9H).  $^{13}C$  NMR (126 MHz,  $CDCl_3$ ):  $\delta$  (ppm) 169.06, 158.02, 156.50, 134.90, 134.26, 130.22, 129.56, 119.90, 108.90, 106.76, 93.52, 80.78, 76.06, 66.87, 20.93, 18.37, 18.05, 0.03, -1.35. HRMS (ESI)  $m/z$  calcd. for  $C_{22}H_{30}NO_4Si^+$  ( $M+H$ )<sup>+</sup> 400.1939, found 400.1941.



**(S, Sa)-2d**

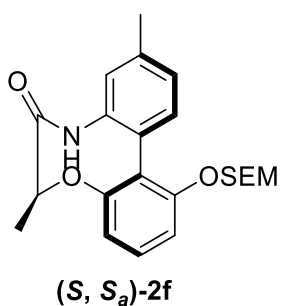
**(S, Sa)-2d:** (new compound). Red oil; isolated yield 41%;  $[\alpha]^{24}_D = -30.0$  ( $c$  1.0 in acetone);  $^1H$  NMR (500 MHz,  $CDCl_3$ ):  $\delta$  (ppm) 8.18 (s, 1H), 7.50 (dd,  $J = 9.0, 4.8$  Hz, 2H), 7.21 (t,  $J = 10.0$  Hz, 1H), 7.02 (t,  $J = 5.0$  Hz, 2H), 6.70 (s, 1H), 5.21 (s, 2H), 4.78 (q,  $J = 6.7$  Hz, 1H), 3.75 (t,  $J = 10.0$  Hz, 2H), 1.65 (d,  $J = 5.0$  Hz, 3H), 0.95 (t,  $J = 10.0$  Hz, 3H), -0.00 (s, 9H).  $^{13}C$  NMR (126 MHz,  $CDCl_3$ ):  $\delta$  (ppm) 170.15, 158.98, 157.77, 130.41, 121.85, 115.81, 110.43, 108.64, 104.69, 92.97, 75.49, 66.43, 29.73, 18.65, 18.12, -1.39. HRMS (EI)  $m/z$  calcd. for  $C_{21}H_{27}FNO_4Si^+$  ( $M+H$ )<sup>+</sup> 404.1688, found 404.1686.



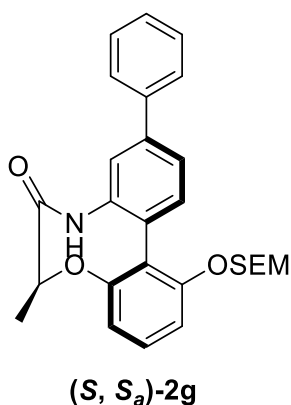
**(S, Sa)-2e**

**(S, Sa)-2e:** (new compound). Light yellow oil; isolated yield 20%;  $[\alpha]^{24}_D = -25.0$  ( $c$  1.0 in acetone);  $^1H$  NMR (500 MHz,  $CDCl_3$ ):  $\delta$  (ppm) 8.19 (s, 1H), 7.55 (d,  $J = 5.0$  Hz, 2H), 7.33 (t,  $J = 5.0$  Hz, 2H), 7.21 (t,  $J = 10.0$  Hz, 1H), 7.13 (t,  $J = 5.0$  Hz, 1H), 6.61 (dd,  $J = 8.2, 2.2$  Hz, 1H), 5.21 (s, 2H), 4.78 (q,  $J = 6.7$  Hz, 1H), 3.72 (t,  $J = 10.0$  Hz, 2H), 1.65 (d,  $J = 10.0$  Hz, 3H), 0.96 (t,  $J = 5.0$  Hz, 2H), 0.00 (s, 9H).  $^{13}C$  NMR (126 MHz,  $CDCl_3$ ):  $\delta$  (ppm) 170.16, 158.96, 157.83, 137.13, 130.38, 129.06, 124.71, 120.05, 110.36, 108.65, 104.69, 92.97, 75.57, 66.41, 18.70, 18.11, -1.38. HRMS (EI)  $m/z$  calcd. for  $C_{21}H_{28}NO_4Si^+$

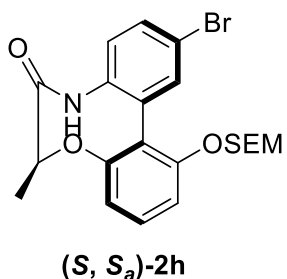
(M+H)<sup>+</sup> 386.1782, found 386.1774.



**(S, Sa)-2f:** (new compound). White oil; isolated yield 30%;  $[\alpha]^{24}_{\text{D}} = -32.0$  (*c* 1.0 in acetone); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 8.13 (s, 1H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.21 (t, *J* = 8.0 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 2H), 6.60 (dd, *J* = 8.2, 2.2 Hz, 1H), 5.21 (s, 2H), 4.77 (q, *J* = 6.9 Hz, 1H), 3.75 (t, *J* = 8.0 Hz, 2H), 2.31 (s, 3H), 1.65 (d, *J* = 8.0 Hz, 3H), 0.96 (t, *J* = 8.0 Hz, 2H), -0.00 (s, 9H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 170.03, 158.95, 157.88, 134.37, 130.37, 129.54, 120.11, 110.32, 108.65, 104.69, 92.98, 75.56, 66.41, 20.90, 18.71, 18.11, 0.03, -1.38. HRMS (EI) *m/z* calcd. for C<sub>22</sub>H<sub>29</sub>NO<sub>4</sub>Si<sup>+</sup> (M+H)<sup>+</sup> 400.1939, found 400.1941.

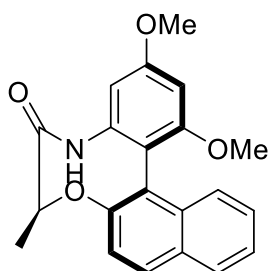


**(S, Sa)-2g:** (new compound). Light yellow oil; isolated yield 22%;  $[\alpha]^{24}_{\text{D}} = -34.0$  (*c* 1.0 in acetone); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 8.27 (s, 1H), 7.79 (s, 1H), 7.59 (d, *J* = 10.0 Hz, 2H), 7.41-7.37 (m, 5H), 7.22 (t, *J* = 10.0 Hz, 1H), 6.73 (s, 2H), 5.21 (s, 2H), 4.80 (q, *J* = 6.7 Hz, 1H), 3.75 (t, *J* = 5.0 Hz, 2H), 1.67 (d, *J* = 10.0 Hz, 3H), 0.95 (t, *J* = 5.0 Hz, 2H), -0.00 (s, 9H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 170.27, 159.00, 157.85, 142.33, 140.64, 137.59, 130.42, 129.45, 128.78, 127.58, 127.26, 123.54, 118.87, 110.41, 108.68, 104.75, 93.00, 75.62, 66.43, 18.72, 18.12, 0.04, -1.37. HRMS (EI) *m/z* calcd. for C<sub>27</sub>H<sub>32</sub>NO<sub>4</sub>Si<sup>+</sup> (M+H)<sup>+</sup> 462.2022, found 462.2020.



**(S, Sa)-2h:** (new compound). Light red oil; isolated yield 51%;  $[\alpha]^{24}_{\text{D}} = -28.0$  (*c* 1.0 in acetone); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 8.88 (s, 1H), 8.00 (d, *J* = 10.0 Hz, 1H), 7.42 (d, *J* = 10.0 Hz, 2H), 6.92 (d, *J* = 10.0 Hz, 2H), 6.86 (d, *J* = 10.0 Hz, 1H), 5.28 (s, 2H), 4.78 (dd, *J* = 6.6, 3.2 Hz, 1H), 3.82 – 3.73 (m, 2H), 1.70 (d, *J* = 5.0 Hz, 3H), 0.96 (t, *J* = 5.0 Hz, 2H), -0.00 (s, 9H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 170.05, 156.54, 155.96, 138.83, 132.77, 129.83, 117.49, 114.83, 110.85, 93.54, 83.69, 75.73, 66.83, 29.74, 18.73, 18.04, -1.36. HRMS (EI) *m/z* calcd.

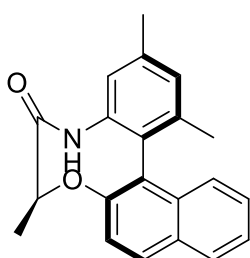
for  $C_{21}H_{27}BrNO_4Si^+$  ( $M+H$ )<sup>+</sup> 464.0814, found 464.0816.



**(S, Sa)-2i**

**(S, Sa)-2i:** (new compound). Yellow oil; isolated yield 55%;  $[\alpha]_D^{24} = -35.0$  (*c* 1.0 in acetone);  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  (ppm) 8.19 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.53 (t, *J* = 8.0 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 6.75 (d, *J* = 12.0 Hz, 1H), 6.56 (s, 1H), 6.46 (s, 2H), 4.95 (q, *J* = 6.8 Hz, 1H), 3.80 (s, 6H), 1.74 (d, *J* = 8.0 Hz, 3H).  $^{13}C$

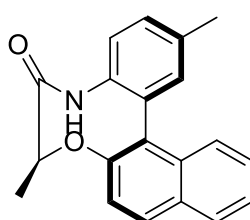
NMR (126 MHz,  $CDCl_3$ ):  $\delta$  (ppm) 166.27, 161.78, 138.32, 138.26, 130.83, 127.61, 126.44, 125.57, 125.36, 125.08, 122.08, 121.19, 116.65, 106.92, 101.32, 74.55, 55.60, 16.28. HRMS (EI) *m/z* calcd. for  $C_{21}H_{20}NO_4^+$  ( $M+H$ )<sup>+</sup> 350.1387, found 350.1380.



**(S, Sa)-2j**

**(S, Sa)-2j:** (new compound). Light yellow oil; isolated yield 80%;  $[\alpha]_D^{24} = -27.0$  (*c* 1.0 in acetone);  $^1H$  NMR (500 MHz,  $CDCl_3$ ):  $\delta$  (ppm) 8.21 (d, *J* = 10.0 Hz, 1H), 7.76 (d, *J* = 10.0 Hz, 1H), 7.53 (t, *J* = 5.0 Hz, 1H), 7.44 (t, *J* = 5.0 Hz, 1H), 7.37 (d, *J* = 10.0 Hz, 1H), 7.11 (s, 1H), 6.94 (s, 2H), 6.70 (d, *J* = 5.0 Hz, 1H), 4.97 (q, *J* = 6.8 Hz, 1H), 2.38 (s, 6H), 1.74 (d, *J* = 10.0 Hz, 3H).  $^{13}C$  NMR

(126 MHz,  $CDCl_3$ ):  $\delta$  (ppm) 166.45, 139.74, 138.24, 136.40, 130.74, 130.44, 127.57, 126.36, 126.30, 125.57, 125.46, 125.09, 121.90, 121.17, 116.68, 113.10, 74.50, 26.96, 21.26, 16.29. HRMS (EI) *m/z* calcd. for  $C_{21}H_{20}NO_2^+$  ( $M+H$ )<sup>+</sup> 318.1416, found 318.1414.

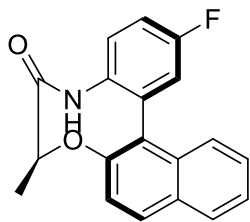


**(S, Sa)-2k**

**(S, Sa)-2k:** (new compound). White oil; isolated yield 55%;  $[\alpha]_D^{24} = -35.0$  (*c* 1.0 in acetone);  $^1H$  NMR (500 MHz,  $CDCl_3$ ):  $\delta$  (ppm) 8.21 (d, *J* = 5.0 Hz, 1H), 7.76 (d, *J* = 5.0 Hz, 1H), 7.53 (t, *J* = 10.0 Hz, 1H), 7.44 (t, *J* = 5.0 Hz, 1H), 7.35 (t, *J* = 10.0 Hz, 3H), 7.20 (d, *J* = 10.0 Hz, 2H), 6.70 (d, *J* = 10.0 Hz, 1H), 4.97 (q,

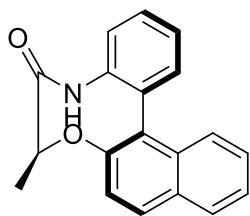
*J* = 6.8 Hz, 1H), 2.45 (s, 3H), 1.74 (d, *J* = 10.0 Hz, 3H).  $^{13}C$  NMR (126 MHz,  $CDCl_3$ ):  $\delta$  (ppm) 166.54, 138.61, 138.35, 133.95, 130.76, 130.57, 128.50, 127.59, 126.40, 125.60, 125.49, 125.13, 121.95, 121.17, 116.57, 74.54, 21.26, 16.31. HRMS (EI) *m/z* calcd. for  $C_{20}H_{18}NO_2^+$  ( $M+H$ )<sup>+</sup> 304.1332, found 304.1329.





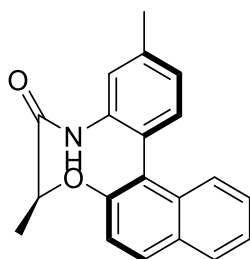
**(S, S<sub>a</sub>)-2l**

**(S, S<sub>a</sub>)-2l:** (new compound). Light red oil; isolated yield 43%;  $[\alpha]_D^{24} = -22.0$  (*c* 1.0 in acetone);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.20 (d,  $J = 10.0$  Hz, 1H), 7.76 (d,  $J = 10.0$  Hz, 1H), 7.54 (t,  $J = 5.0$  Hz, 1H), 7.45 (t,  $J = 5.0$  Hz, 1H), 7.38 (d,  $J = 5.0$  Hz, 1H), 7.31 – 7.29 (m, 2H), 7.25–7.21 (m, 2H), 6.66 (d,  $J = 10.0$  Hz, 1H), 4.95 (q,  $J = 6.8$  Hz, 1H), 1.74 (d,  $J = 10.0$  Hz, 3H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 166.64, 163.35, 161.37, 138.58, 130.87, 130.64, 130.57, 127.65, 126.58, 125.70, 125.37, 125.15, 122.18, 121.21, 117.02, 116.83, 116.27, 74.56, 16.26. HRMS (EI)  $m/z$  calcd. for  $\text{C}_{19}\text{H}_{15}\text{FNO}_2^+$  ( $\text{M}+\text{H}$ ) $^+$  308.1081, found 308.1075.



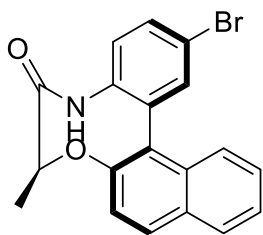
**(S, S<sub>a</sub>)-2m**

**(S, S<sub>a</sub>)-2m:** (new compound). White oil; isolated yield 80%;  $[\alpha]_D^{24} = -27.0$  (*c* 1.0 in acetone);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 9.25 (s, 1H), 8.56 (d,  $J = 5.0$  Hz, 1H), 8.15 (d,  $J = 5.0$  Hz, 1H), 7.84 – 7.80 (m, 2H), 7.57 (t,  $J = 10.0$  Hz, 1H), 7.46 (t,  $J = 10.0$  Hz, 1H), 7.36 – 7.33 (m, 2H), 7.06 (d,  $J = 10.0$  Hz, 2H), 4.90 (q,  $J = 6.8$  Hz, 1H), 1.75 (d,  $J = 10.0$  Hz, 3H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 170.67, 156.85, 133.73, 132.08, 131.75, 129.95, 128.44, 128.21, 127.83, 126.71, 125.70, 122.49, 120.43, 115.75, 112.18, 75.50, 18.84. HRMS (EI)  $m/z$  calcd. for  $\text{C}_{19}\text{H}_{16}\text{NO}_2^+$  ( $\text{M}+\text{H}$ ) $^+$  290.1175, found 290.1168.



**(S, S<sub>a</sub>)-2n**

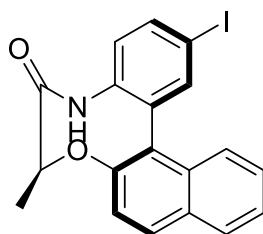
**(S, S<sub>a</sub>)-2n:** (new compound). Light yellow oil; isolated yield 58%;  $[\alpha]_D^{24} = -35.0$  (*c* 1.0 in acetone);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.18 (d,  $J = 10.0$  Hz, 1H), 7.73 (d,  $J = 10.0$  Hz, 1H), 7.50 (t,  $J = 7.5$  Hz, 1H), 7.40 (t,  $J = 7.5$  Hz, 2H), 7.34 (d,  $J = 10.0$  Hz, 1H), 7.24 (d,  $J = 5.0$  Hz, 1H), 7.11 – 7.08 (m, 2H), 6.66 (d,  $J = 10.0$  Hz, 1H), 4.94 (q,  $J = 6.8$  Hz, 1H), 2.39 (s, 3H), 1.72 (d,  $J = 5.0$  Hz, 3H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 166.47, 140.03, 138.37, 136.56, 130.78, 129.70, 129.48, 129.33, 127.60, 126.42, 125.75, 125.53, 125.13, 124.93, 121.97, 121.19, 116.63, 74.54, 29.73, 21.37, 16.30. HRMS (EI)  $m/z$  calcd. for  $\text{C}_{20}\text{H}_{18}\text{NO}_2^+$  ( $\text{M}+\text{H}$ ) $^+$  304.1332, found 304.1331.



**(S, S<sub>a</sub>)-2o**

**(S, S<sub>a</sub>)-2o:** (new compound). Light white solid; isolated yield 75%; mp 188-189°C.  $[\alpha]^{24}_{\text{D}} = -28.0$  (*c* 1.0 in acetone); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ (ppm) 9.14 (s, 1H), 8.53 (d, *J* = 10.0 Hz, 1H), 8.14 (d, *J* = 5.0 Hz, 1H), 7.82 (t, *J* = 10.0 Hz, 2H), 7.58 (t, *J* = 5.0 Hz, 1H), 7.44 (d, *J* = 10.0 Hz, 2H), 6.94 (d, *J* = 10.0 Hz, 2H), 4.83 (q, *J* = 6.8 Hz, 1H), 1.74 (d, *J* = 10.0 Hz, 3H). <sup>13</sup>C

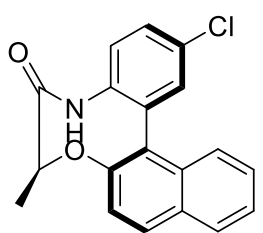
NMR (126 MHz, CDCl<sub>3</sub>): δ (ppm) 170.15, 155.93, 132.84, 132.03, 131.78, 128.51, 128.22, 127.90, 126.69, 125.79, 120.36, 117.49, 114.86, 112.25, 75.86, 18.76. HRMS (EI) *m/z* calcd. for C<sub>19</sub>H<sub>15</sub>BrNO<sub>2</sub><sup>+</sup> (*M*+H)<sup>+</sup> 368.0208, found 368.0211.



**(S, S<sub>a</sub>)-2p**

**(S, S<sub>a</sub>)-2p:** (new compound). Light white solid; isolated yield 49%; mp 180-181°C.  $[\alpha]^{24}_{\text{D}} = -17.0$  (*c* 1.0 in acetone); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ (ppm) 9.13 (s, 1H), 8.53 (d, *J* = 10.0 Hz, 1H), 8.14 (d, *J* = 10.0 Hz, 1H), 7.82 (t, *J* = 10.0 Hz, 2H), 7.62 (d, *J* = 10.0 Hz, 2H), 7.57 (t, *J* = 5.0 Hz, 1H), 7.47 (t, *J* = 10.0 Hz, 1H), 6.83 (d, *J* = 10.0 Hz, 2H), 4.83 (q, *J* = 6.8 Hz, 1H), 1.74 (d,

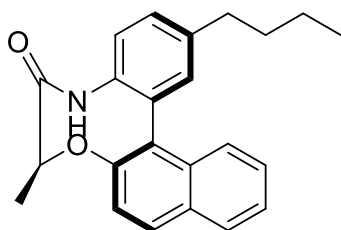
*J* = 10.0 Hz, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>): δ (ppm) 170.10, 156.70, 138.79, 133.51, 132.01, 131.76, 128.49, 128.21, 127.88, 126.68, 125.77, 120.34, 117.96, 112.23, 84.89, 75.67, 18.73. HRMS (EI) *m/z* calcd. for C<sub>19</sub>H<sub>15</sub>INO<sub>2</sub><sup>+</sup> (*M*+H)<sup>+</sup> 416.0069, found 416.0065.



**(S, S<sub>a</sub>)-2q**

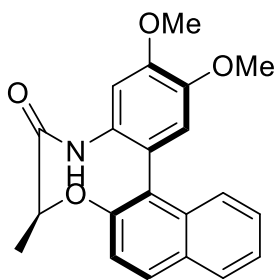
**(S, S<sub>a</sub>)-2q:** (new compound). Light white solid; isolated yield 85%; mp 175-176°C.  $[\alpha]^{24}_{\text{D}} = -24.0$  (*c* 1.0 in acetone); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ (ppm) 9.15 (s, 1H), 8.53 (d, *J* = 10.0 Hz, 1H), 8.14 (d, *J* = 5.0 Hz, 1H), 7.82 (t, *J* = 10.0 Hz, 2H), 7.58 (t, *J* = 5.0 Hz, 1H), 7.30 (d, *J* = 10.0 Hz, 2H), 6.99 (d, *J* = 10.0 Hz,

2H), 4.83 (q, *J* = 6.8 Hz, 1H), 1.74 (d, *J* = 10.0 Hz, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>): δ (ppm) 170.20, 155.42, 133.54, 132.04, 131.78, 129.89, 128.51, 128.23, 127.90, 126.69, 125.79, 120.37, 117.03, 112.24, 75.95, 18.78. HRMS (EI) *m/z* calcd. for C<sub>19</sub>H<sub>15</sub>ClNO<sub>2</sub><sup>+</sup> (*M*+H)<sup>+</sup> 324.0786, found 324.0775.



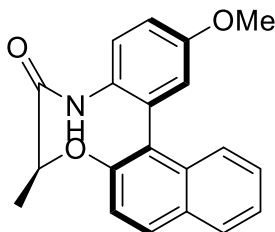
**(S, S<sub>a</sub>)-2r**

**(S, Sa)-2r:** (new compound). Light yellow oil; isolated yield 46%;  $[\alpha]^{24}_{\text{D}} = -30.0$  (*c* 1.0 in acetone);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.20 (d,  $J = 10.0$  Hz, 1H), 7.75 (d,  $J = 10.0$  Hz, 1H), 7.53 (t,  $J = 5.0$  Hz, 1H), 7.43 (t,  $J = 5.0$  Hz, 1H), 7.35 (t,  $J = 10.0$  Hz, 3H), 7.21 (d,  $J = 5.0$  Hz, 2H), 6.69 (d,  $J = 10.0$  Hz, 1H), 4.96 (q,  $J = 6.8$  Hz, 1H), 2.70 (t,  $J = 5.0$  Hz, 2H), 1.73 (d,  $J = 5.0$  Hz, 3H), 1.70-1.64 (m, 2H), 1.46-1.42 (m, 2H), 0.97 (t,  $J = 10.0$  Hz, 3H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 166.56, 143.53, 138.39, 134.06, 130.76, 129.87, 128.45, 127.61, 126.41, 125.64, 125.50, 125.14, 121.96, 121.18, 116.64, 74.56, 35.42, 33.46, 22.46, 16.32, 13.98. HRMS (EI) *m/z* calcd. for  $\text{C}_{23}\text{H}_{24}\text{NO}_2^+$  ( $\text{M}+\text{H}$ ) $^+$  346.1801, found 346.1806.



**(S, S<sub>a</sub>)-2s**

**(S, Sa)-2s:** (new compound). Light yellow oil; isolated yield 62%;  $[\alpha]^{24}_{\text{D}} = -35.0$  (*c* 1.0 in acetone);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.20 (d,  $J = 5.0$  Hz, 1H), 7.76 (d,  $J = 10.0$  Hz, 1H), 7.53 (t,  $J = 10.0$  Hz, 1H), 7.44 (t,  $J = 5.0$  Hz, 1H), 7.38 (d,  $J = 10.0$  Hz, 1H), 7.00 (d,  $J = 5.0$  Hz, 1H), 6.89 (d,  $J = 10.0$  Hz, 1H), 6.78 (s, 1H), 6.71 (d,  $J = 10.0$  Hz, 1H), 4.96 (q,  $J = 6.8$  Hz, 1H), 3.95 (s, 3H), 3.86 (s, 3H), 1.74 (d,  $J = 10.0$  Hz, 3H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 166.68, 150.12, 149.27, 138.33, 130.79, 129.29, 127.62, 126.46, 125.71, 125.55, 125.10, 122.04, 121.18, 121.11, 116.55, 111.85, 74.60, 56.13, 29.74, 16.33. HRMS (EI) *m/z* calcd. for  $\text{C}_{21}\text{H}_{20}\text{NO}_4^+$  ( $\text{M}+\text{H}$ ) $^+$  350.1387, found 350.1386.

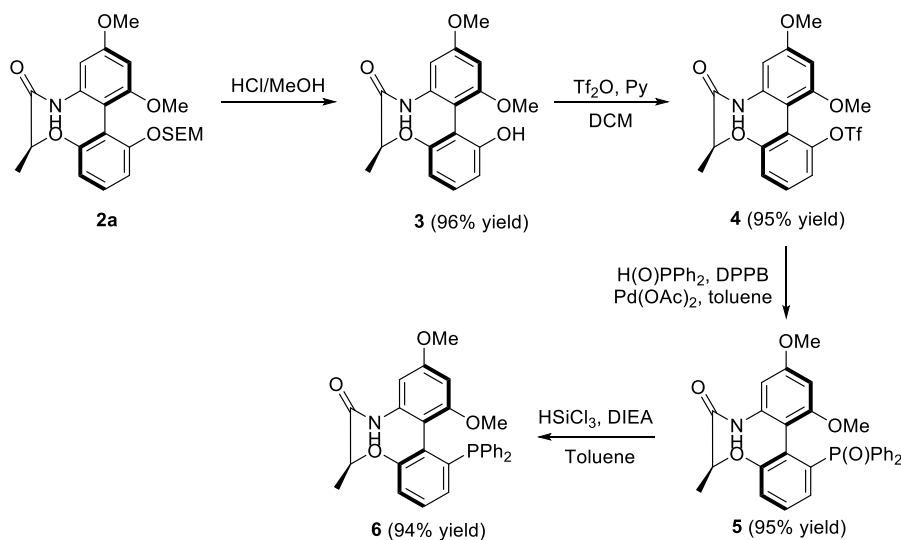


**(S, S<sub>a</sub>)-2t**

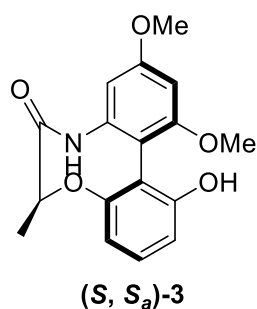
**(S, Sa)-2t:** (new compound). Yellow oil; isolated yield 73%;  $[\alpha]^{24}_{\text{D}} = -28.0$  (*c* 1.0 in acetone);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.20 (d,  $J = 10.0$  Hz, 1H), 7.75 (d,  $J = 5.0$  Hz, 1H), 7.53 (t,  $J = 5.0$  Hz, 1H), 7.43 (t,  $J = 10.0$  Hz, 1H), 7.37 (d,  $J = 10.0$  Hz, 1H), 7.23 (d,  $J = 10.0$  Hz, 2H), 7.05 (d,  $J = 10.0$  Hz, 2H), 6.71 (d,  $J = 10.0$  Hz, 1H), 4.96 (q,  $J = 6.8$  Hz, 1H), 3.88 (s, 3H), 1.74 (d,  $J = 5.0$  Hz, 3H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 166.70, 159.58, 138.32, 130.75, 129.83, 129.13, 127.60, 126.41, 125.74, 125.49, 125.12, 121.97,

121.16, 116.50, 115.22, 74.55, 55.56, 16.32. HRMS (EI)  $m/z$  calcd. for  $C_{20}H_{18}NO_3^+$  ( $M+H$ )<sup>+</sup> 320.1281, found 320.1277.

#### 4. Derivatization of (*S*, *Sa*)-2a<sup>4</sup>



To a mixture of (*S*, *Sa*)-2a (0.405g 0.91 mmol) in MeOH was added 1M HCl (20 equiv.) and stirred at room temperature for 1 h. The resulting mixture was concentrated under reduced pressure to give a residue, which was washed with water (100 mL) and extracted with EtOAc. The combined organic layers were washed with brine (50 mL), dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated under reduced pressure, giving the desired pure product (*S*, *Sa*)-3.

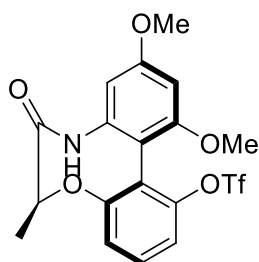


**(*S*, *Sa*)-3:** (new compound). Colorless oil; isolated yield 96%;  $[\alpha]_D^{24} = -33.0$  ( $c$  1.0 in acetone);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.18 (s, 1H), 7.14 (t,  $J = 5.0$  Hz, 1H), 6.76 (d,  $J = 2.1$  Hz, 2H), 6.52 – 6.49 (m, 2H), 6.25 (s, 1H), 4.72 (q,  $J = 6.6$  Hz, 1H), 3.75 (s, 6H), 1.63 (d,  $J = 5.0$  Hz, 3H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 170.78, 161.14, 157.94, 157.59, 138.59, 130.63,

109.87, 107.82, 103.34, 98.51, 97.48, 94.75, 75.52, 55.46, 18.72. HRMS (EI)  $m/z$  calcd. for  $C_{17}H_{17}NO_5^+$  ( $M+H$ )<sup>+</sup> 316.1180, found 316.1189.

Trifluoromethanesulfonic anhydride (1.38 g, 4.90 mmol) was added dropwise to a solution of (*S*, *Sa*)-3 (0.287 g, 0.91 mmol) in pyridine (10 mL) at 0 °C. Then the mixture

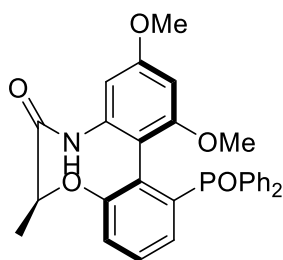
was allowed to warm to room temperature and stirred for 12 h. After removal of the solvent *in vacuo*, the residue was diluted with EtOAc and was then washed successively with aqueous 1M HCl, saturated NaHCO<sub>3</sub> and brine. The organic layer was dried with Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to give compound **(S, Sa)-4**.



**(S, Sa)-4**

**(S, Sa)-4**: (new compound). Light yellow oil; isolated yield 95%;  $[\alpha]_D^{24} = -27.0$  (*c* 1.0 in acetone); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 8.09 (s, 1H), 7.40 (t, *J* = 8.0 Hz, 1H), 6.96 (s, 1H), 6.83 (s, 1H), 6.41 (d, *J* = 8.0 Hz, 2H), 4.82 – 4.76 (m, 1H), 3.77 (s, 6H), 1.67 (d, *J* = 4.0 Hz, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 169.30, 150.24, 137.49, 131.26, 120.42, 115.30, 114.95, 112.50, 110.21, 96.67, 76.19, 55.81, 29.73, 27.49, 18.46. HRMS (EI) *m/z* calcd. for C<sub>18</sub>H<sub>17</sub>F<sub>3</sub>NO<sub>7</sub>S<sup>+</sup> (M+H)<sup>+</sup> 448.0600, found 448.0606.

Under nitrogen atmosphere, **(S, Sa)-4** (150 mg, 0.335 mmol), diphenylphosphine (135.6 mg, 0.67 mmol), dppd (14.5 mg, 0.034 mmol), Pd<sub>2</sub>(dba)<sub>3</sub> (7.6 mg, 0.034 mmol) were added to Schleck tube, then add 0.38 mL DIEA, 3-4 mL DMSO, and heat the reaction at 110°C for 24 hours. After the reaction, it was extracted several times with ethyl acetate, washed with 1M HCl, saturated sodium bicarbonate solution, and saturated brine. The residue was purified by silica gel column chromatography to give compound **(S, Sa)-5**.

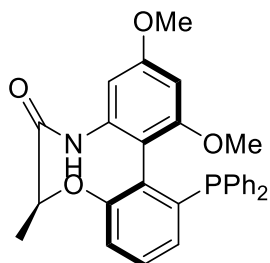


**(S, Sa)-5**

**(S, Sa)-5**: (new compound). White oil; isolated yield 95%;  $[\alpha]_D^{24} = -34.0$  (*c* 1.0 in acetone); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 8.36 (s, 1H), 7.68 – 7.62 (m, 4H), 7.56 – 7.41 (m, 9H), 6.84 (s, 1H), 6.41 (d, *J* = 8.3 Hz, 1H), 4.77 (t, *J* = 5.7 Hz, 1H), 3.75 (s, 6H), 1.60 (d, *J* = 8.0 Hz, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 167.06, 159.27, 150.54, 139.92, 131.49, 131.07, 130.72, 128.33, 127.71, 123.90, 120.33, 100.09, 75.17, 60.38, 15.18, 14.22. HRMS (EI) *m/z* calcd. for C<sub>29</sub>H<sub>26</sub>NO<sub>5</sub>PNa<sup>+</sup> (M+Na)<sup>+</sup> 522.1441, found 522.1454.

**(S, Sa)-5** (100 mg, 0.20 mmol) was added to the bottle, DIEA (1.15 mL, 6.35

mmol) was added under nitrogen atmosphere, the solution was cooled to 0 °C, then trichlorosilane (0.22 mL, 2.13 mmol) was added by syringe, and the temperature was raised to 110 °C, refluxed for 12 h. After the reaction, ethyl acetate was added for extraction and purified by silica gel flash chromatography to obtain (*S, Sa*)-6.



(*S, Sa*)-6

(*S, Sa*)-6: (new compound). White oil; isolated yield 94%;  $[\alpha]_D^{24} = -28.0$  (*c* 1.0 in acetone);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.13 (s, 1H), 7.34-7.30 (m, 9H), 6.95 (d,  $J = 10.0$  Hz, 2H), 6.80 (s, 2H), 6.43 (d,  $J = 10.0$  Hz, 2H), 4.69 (q,  $J = 6.7$  Hz, 1H), 3.77 (s, 6H), 1.58 (d,  $J = 5.0$  Hz, 3H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 170.05, 159.04, 152.94, 139.51, 137.75,

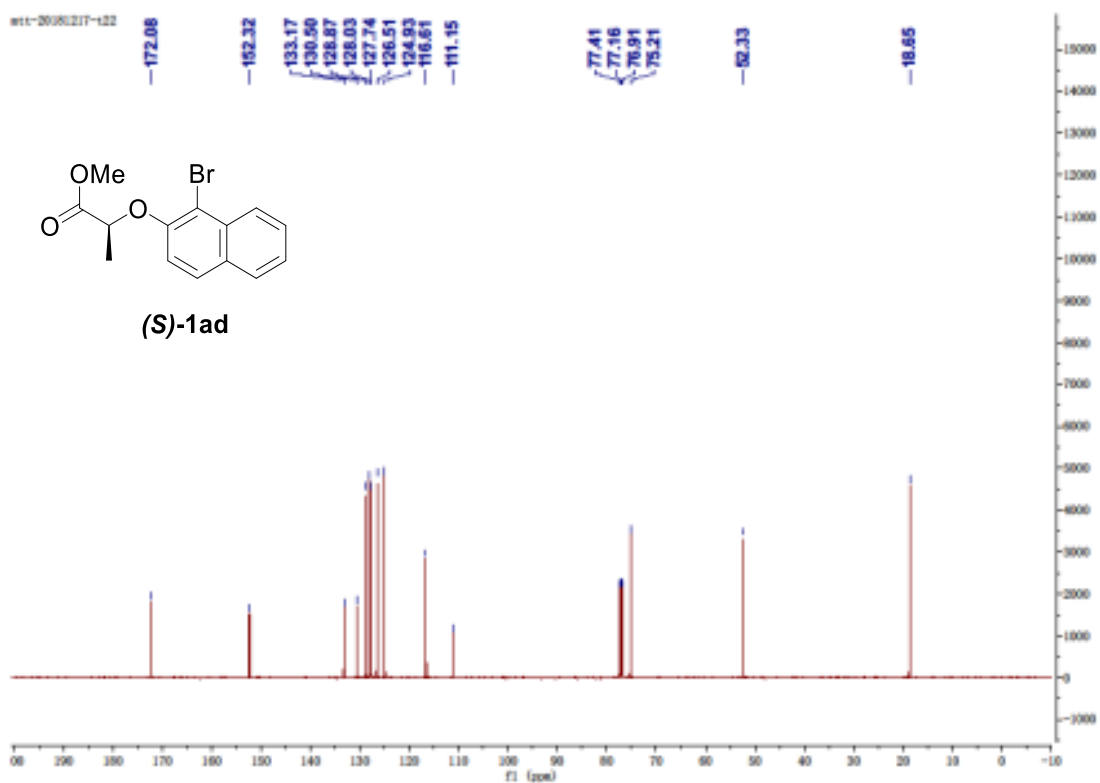
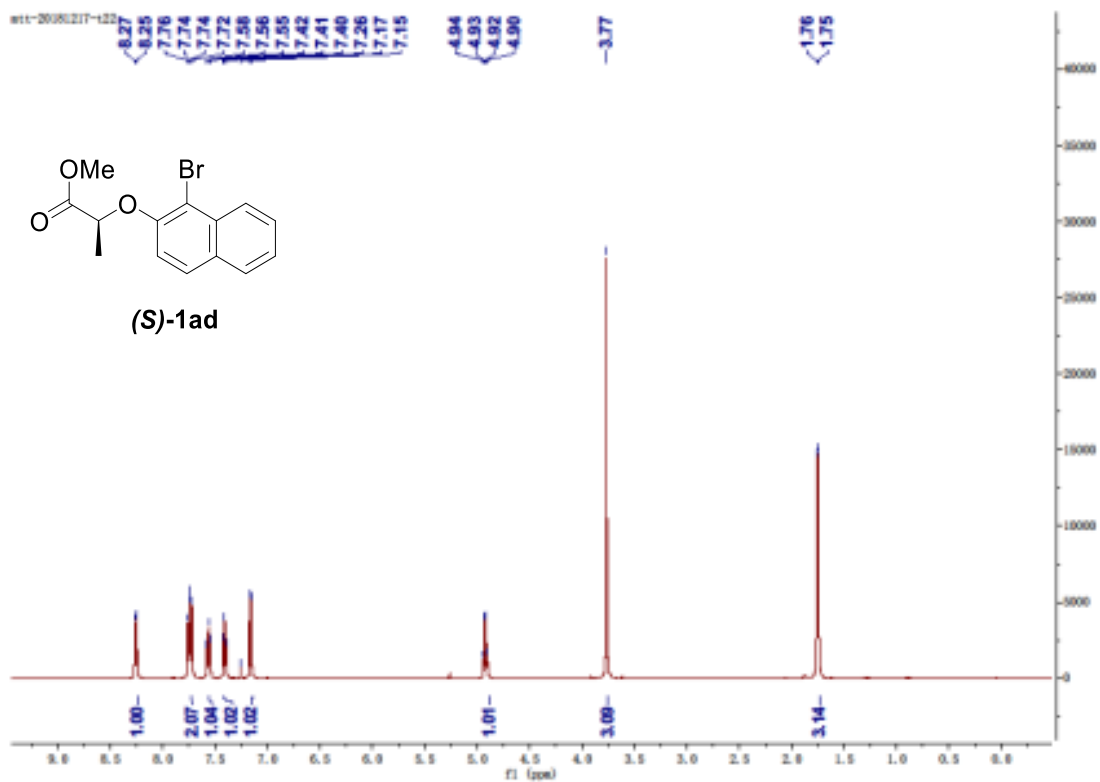
136.39, 133.71, 130.04, 129.40, 129.01, 128.66, 127.91, 121.04, 120.40, 116.02, 114.65, 112.57, 96.51, 75.62, 55.80, 27.47, 18.47. HRMS (EI)  $m/z$  calcd. for  $\text{C}_{29}\text{H}_{27}\text{NO}_4\text{P}^+$  ( $\text{M}+\text{H}$ ) $^+$  484.1672, found 484.1670.

## 5. References

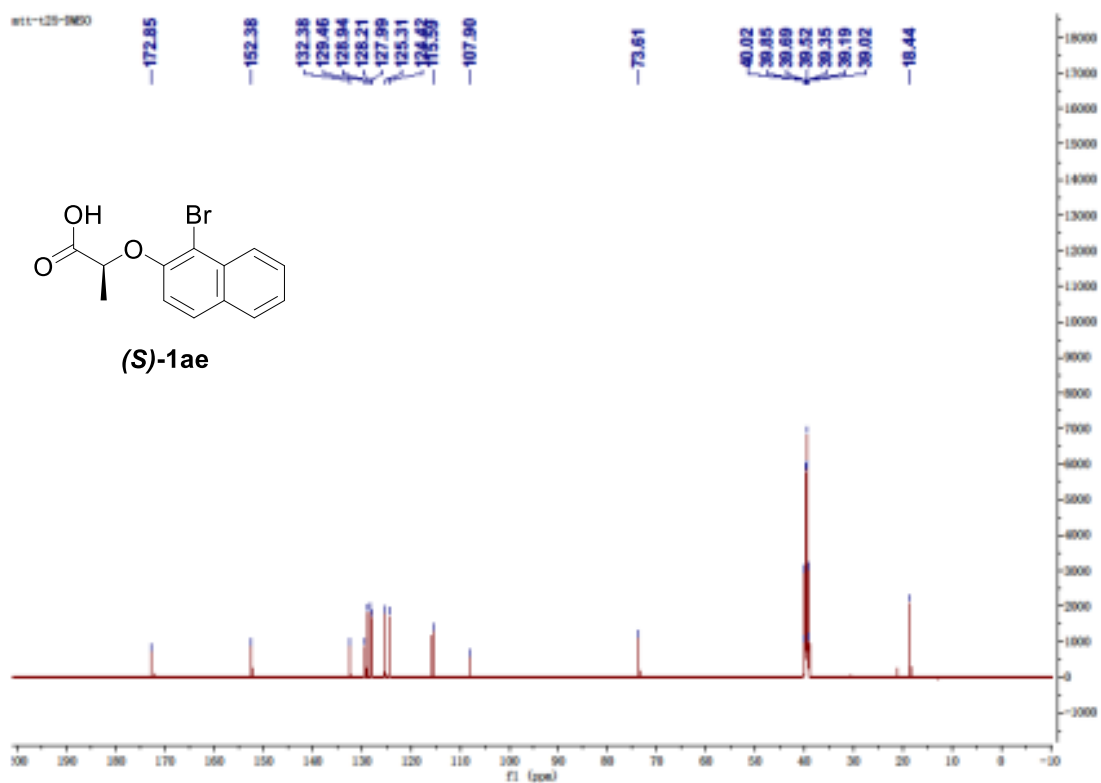
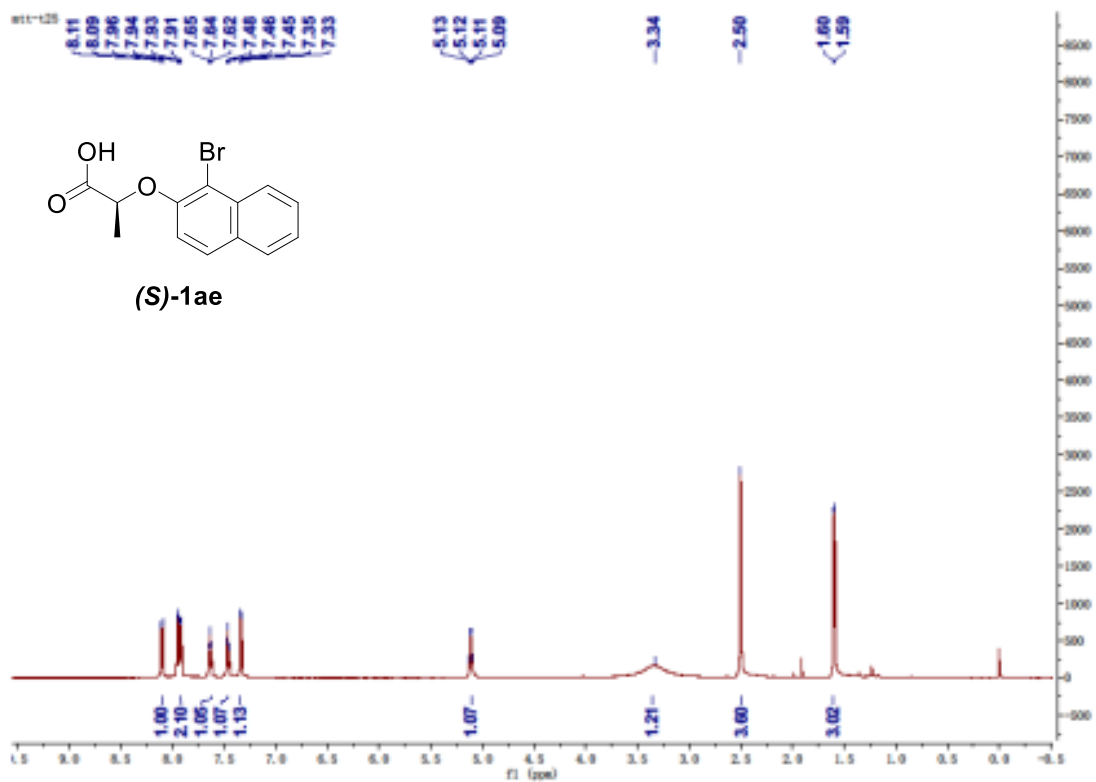
- 1 J. Shi, H. Xu, D. Qiu, J. He, and Y. Li, *J. Am. Chem. Soc.*, 2017, **139**, 623.
- 2 D. R. Brandt, K. M. Pannone, J. J. Romano, and E. G. Casillas, *Tetrahedron*, 2013, **69**, 9994.
- 3 Ł. Sidorowicz and J. Skarzewski, *Synthesis*, 2011, **5**, 708.
- 4 S. Wang, J. Li, T. Miao, W. Wu, Q. Li, Y. Zhuang, Z. Zhou, and L. Qiu, *Org. Lett.*, 2012, **14**, 1966.

## 6. Copy of NMR spectra

Compound (*S*)-1ad

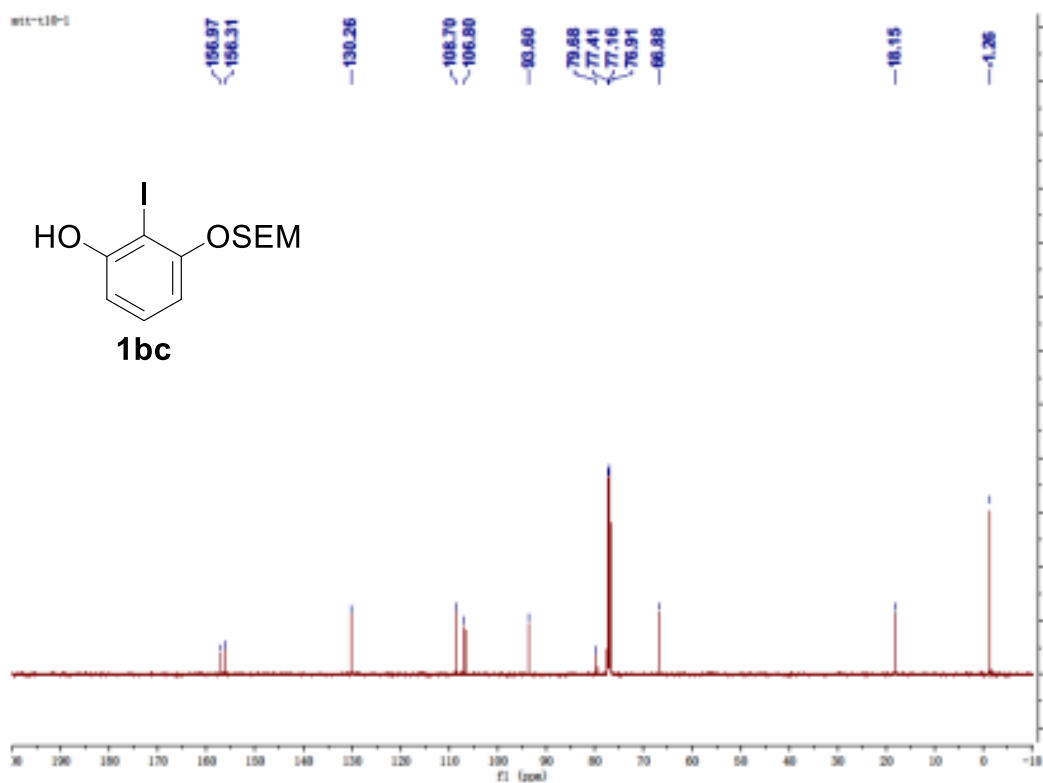
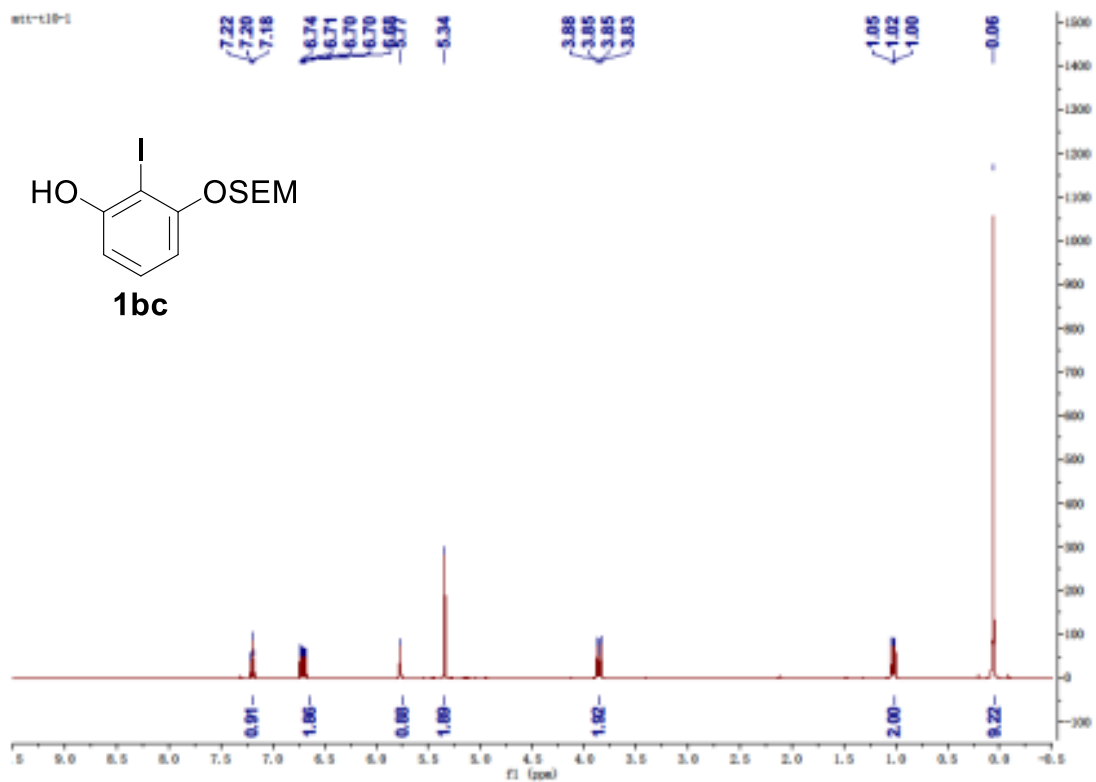


Compound (S)-1ae

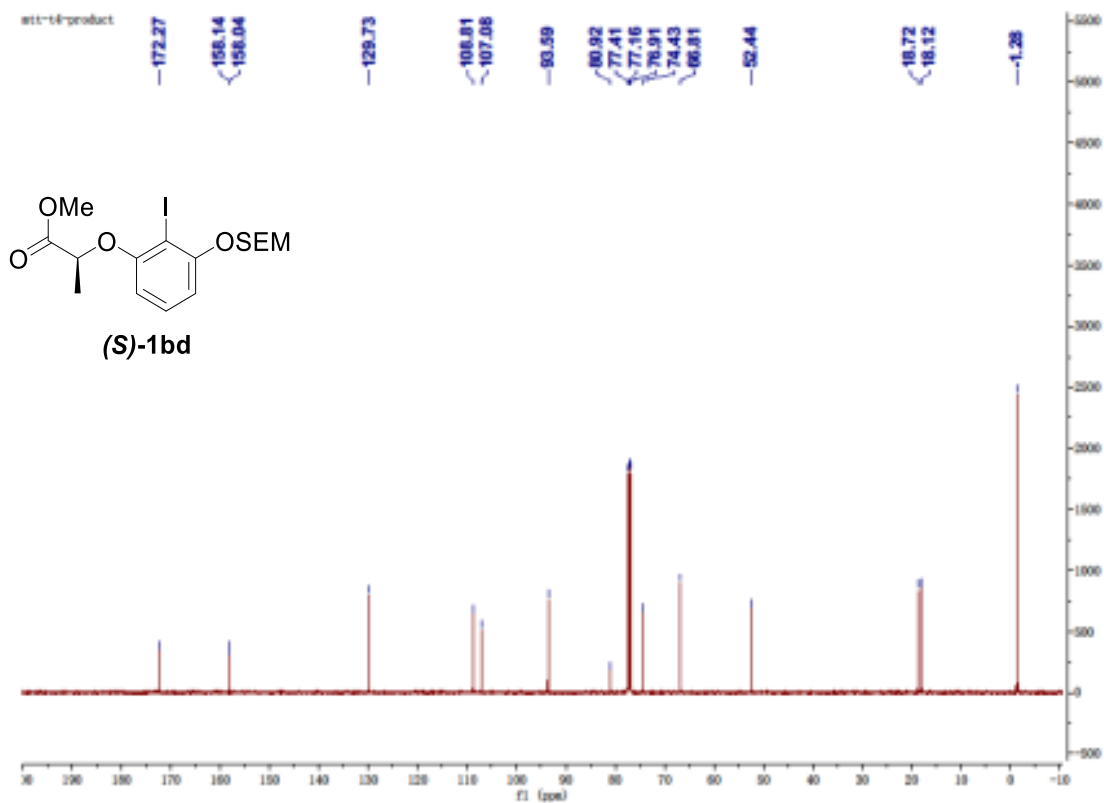
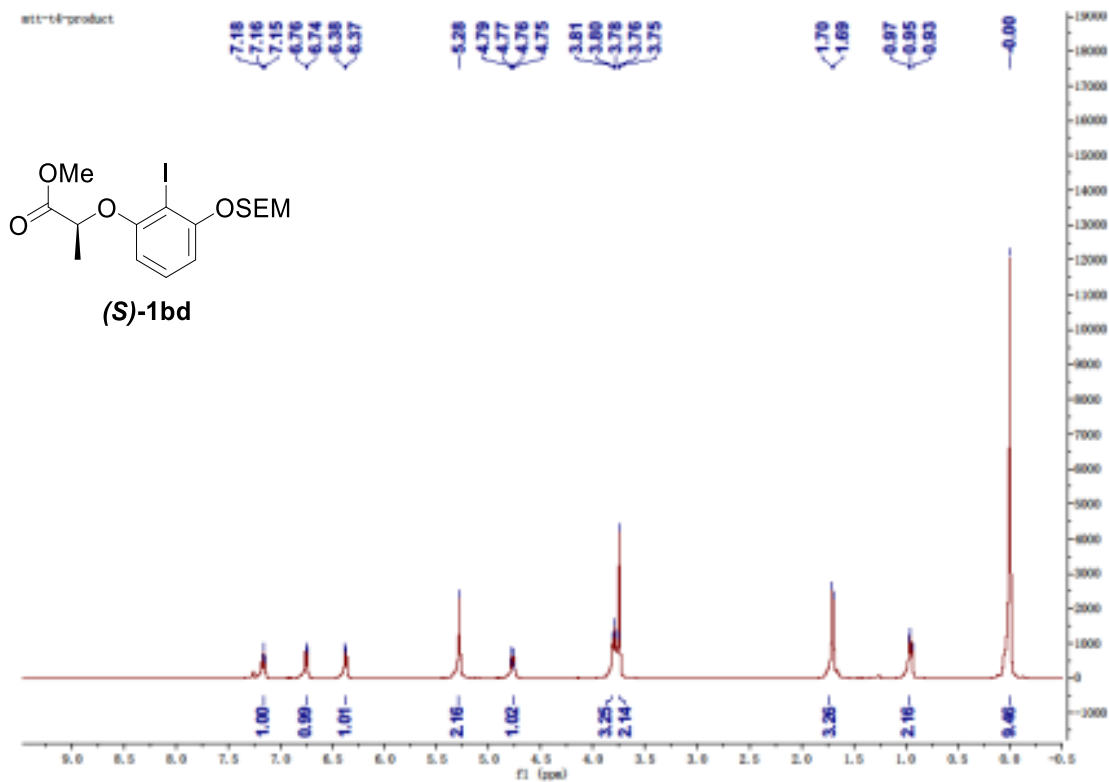


Compound **1bc**

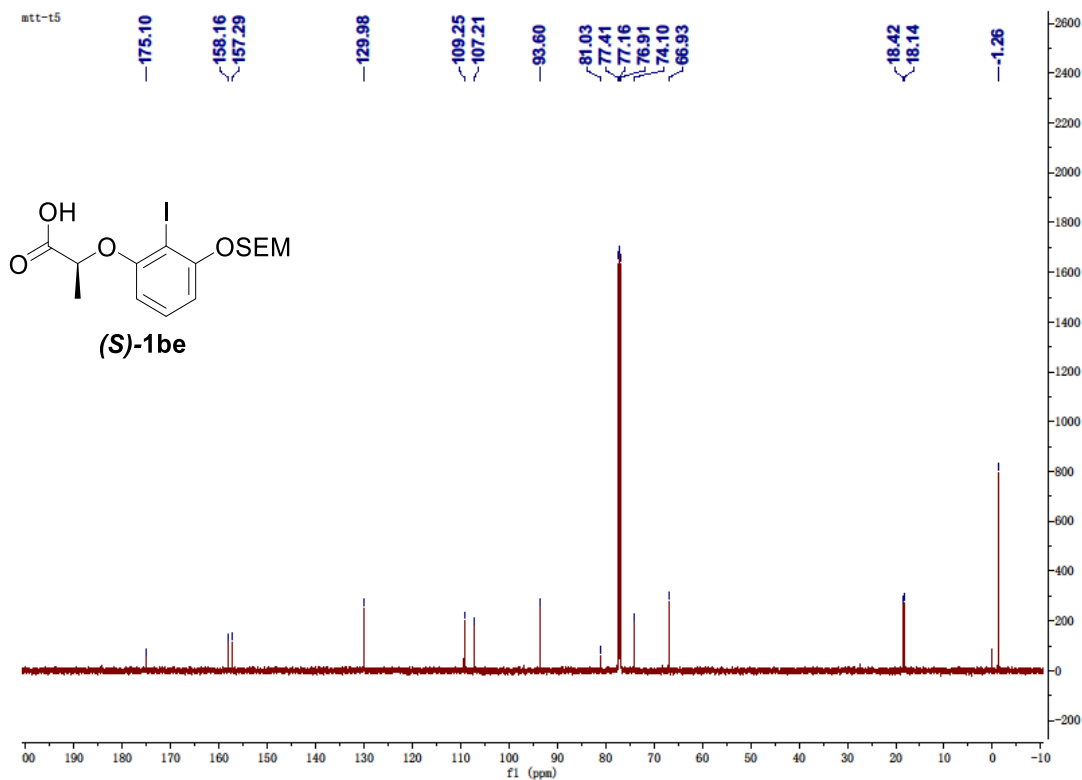
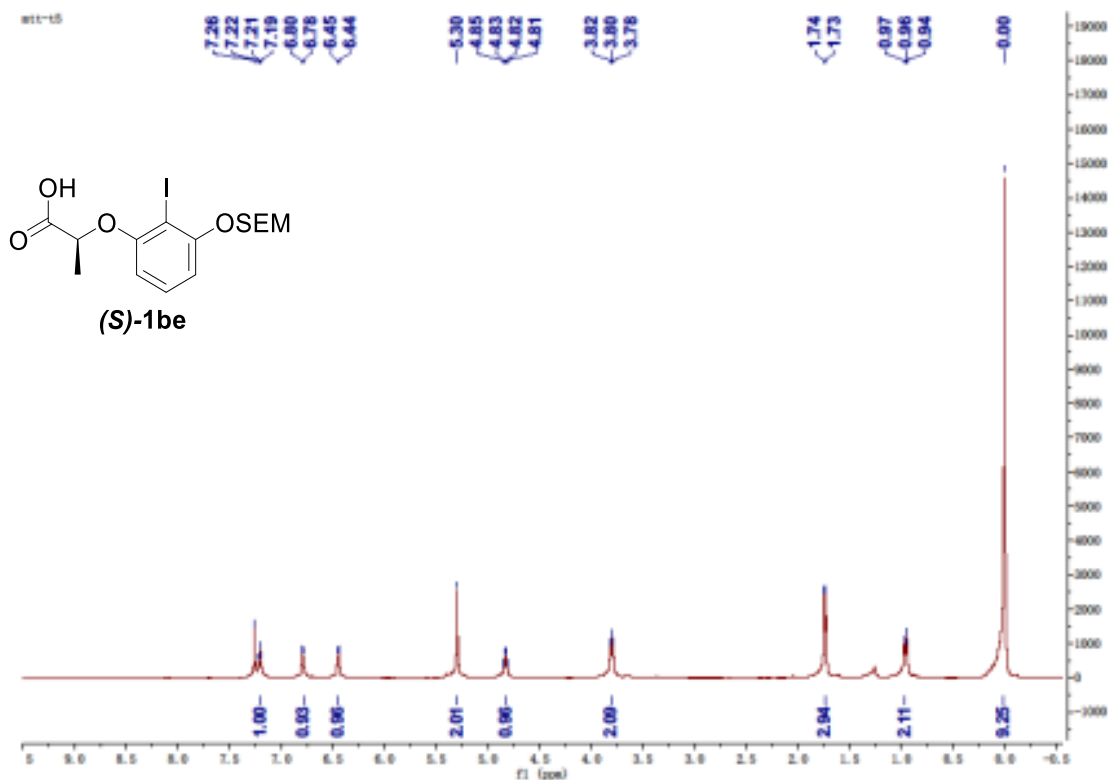




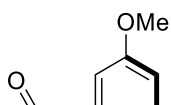
Compound (*S*)-**1bd**

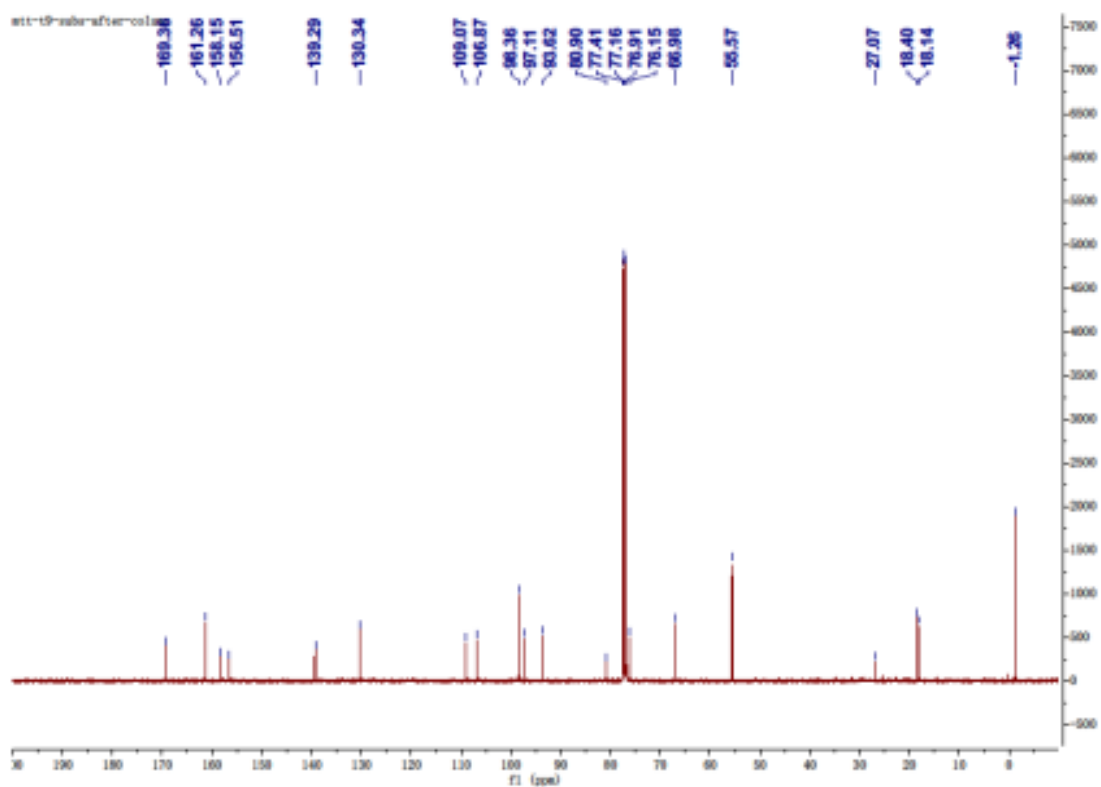
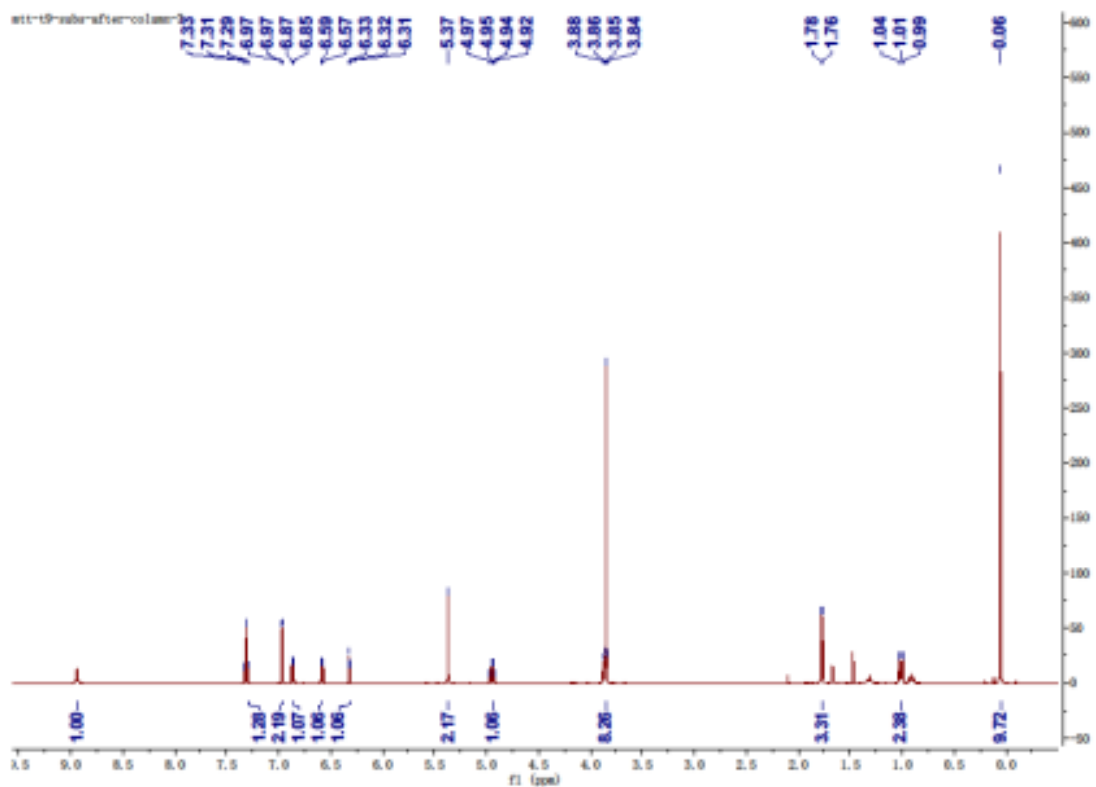


Compound (S)-1be

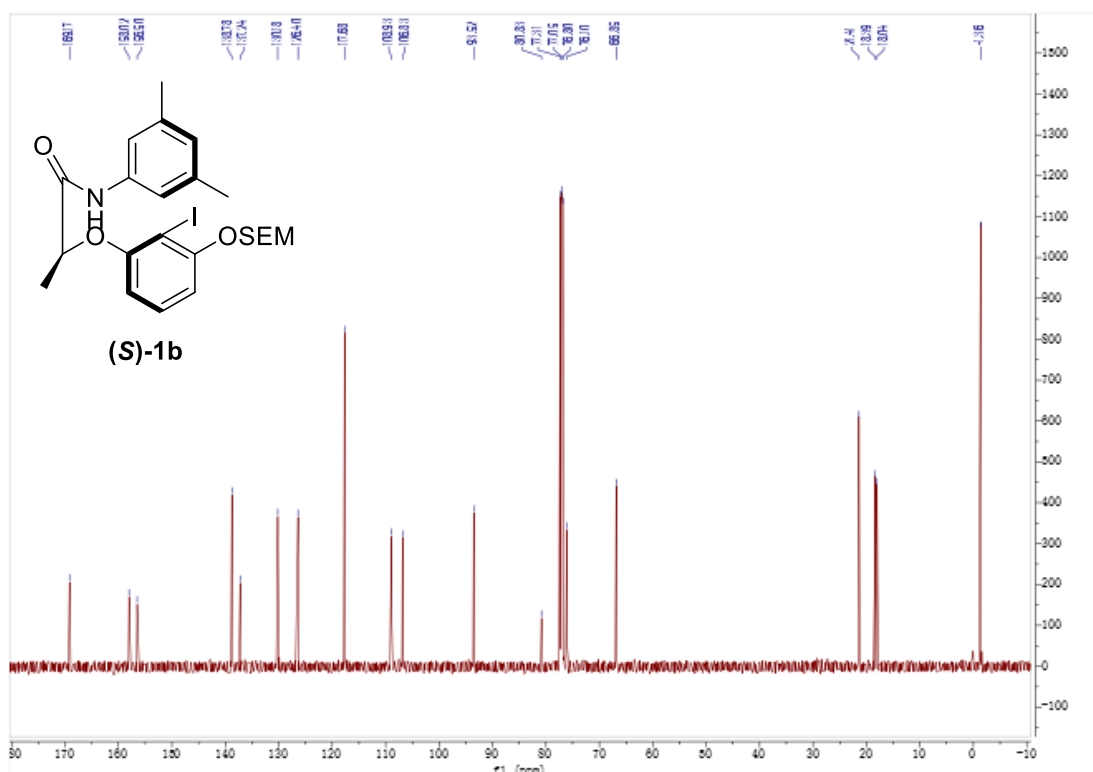
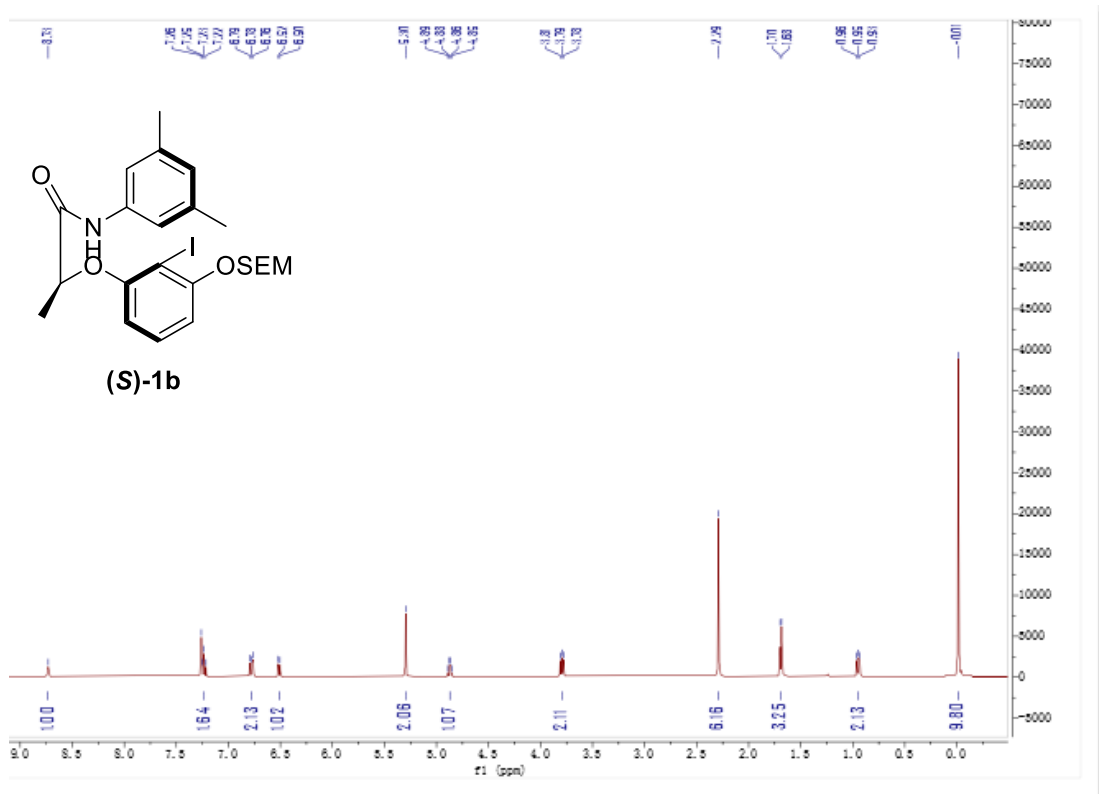


Compound (S)-1a

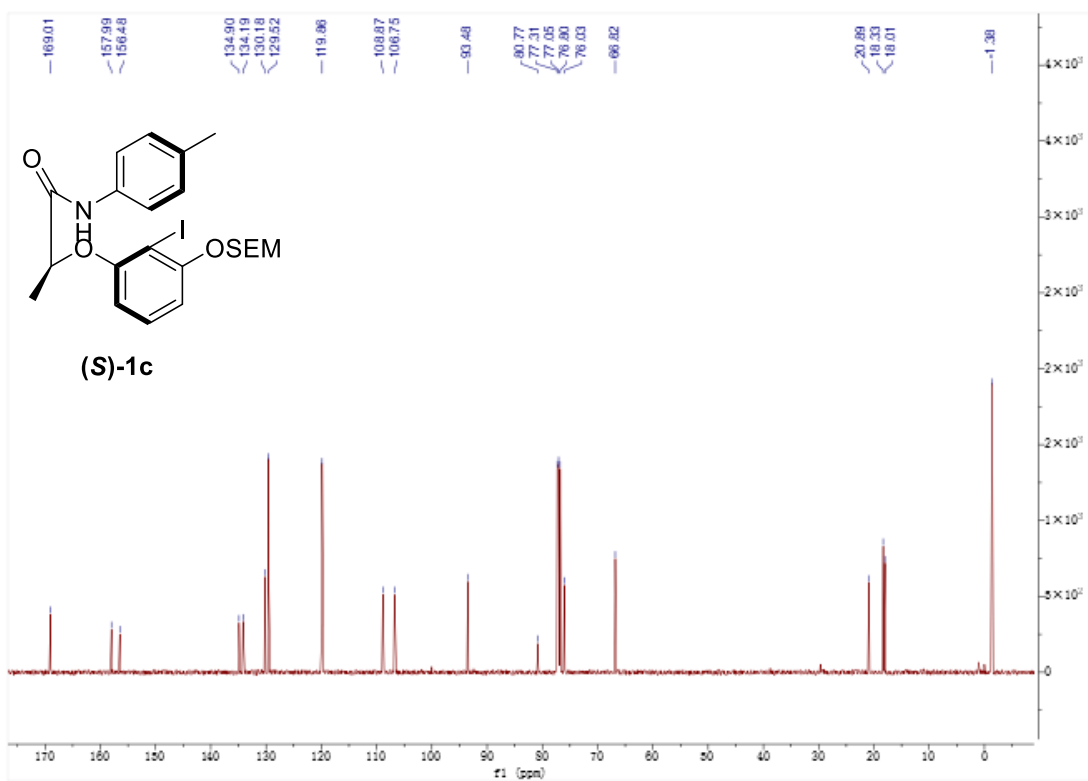
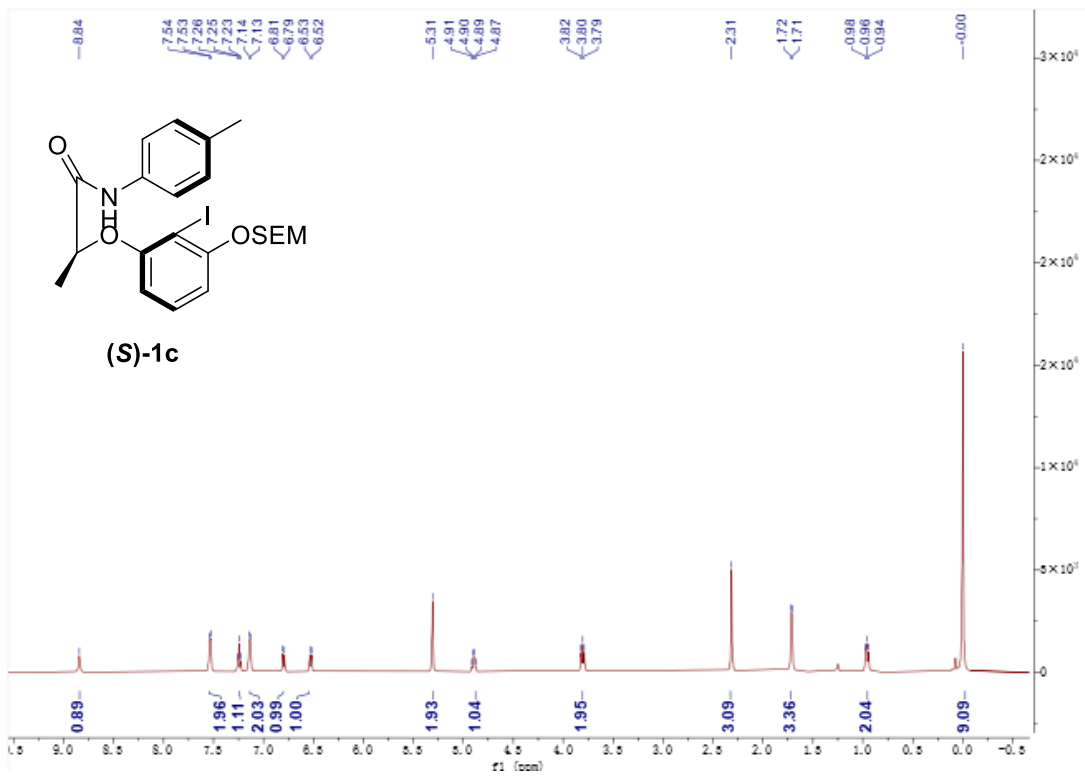




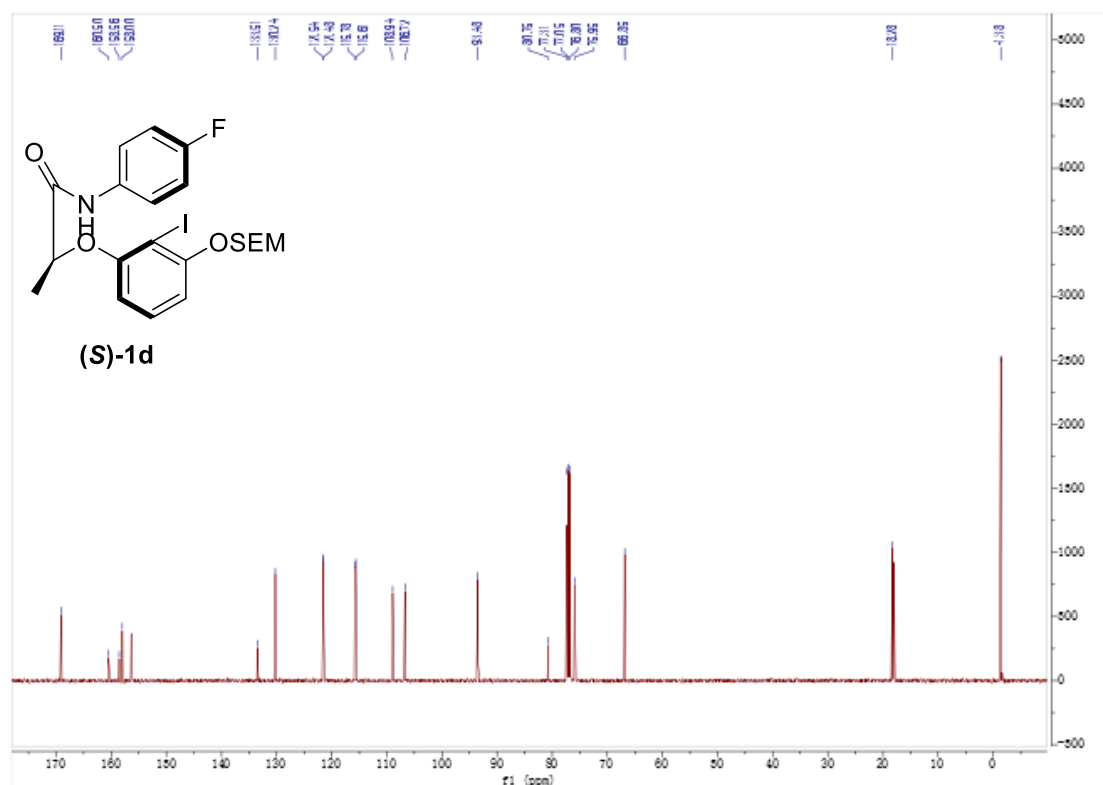
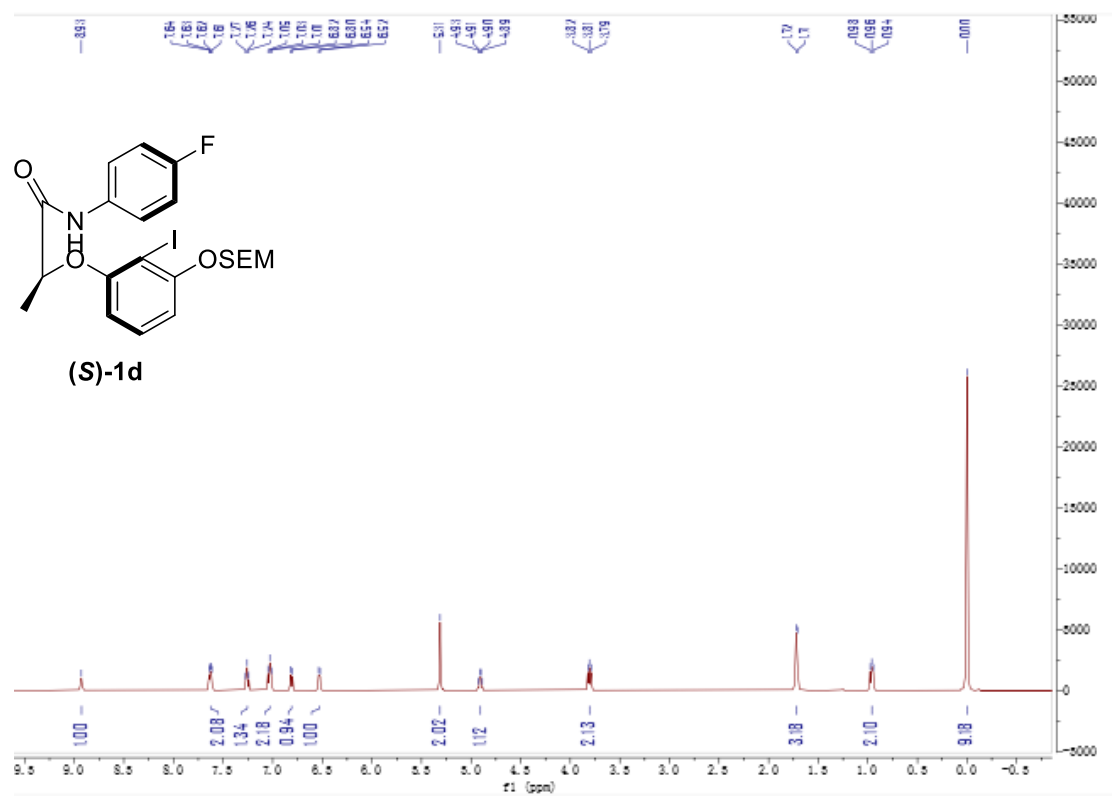
Compound (S)-1b



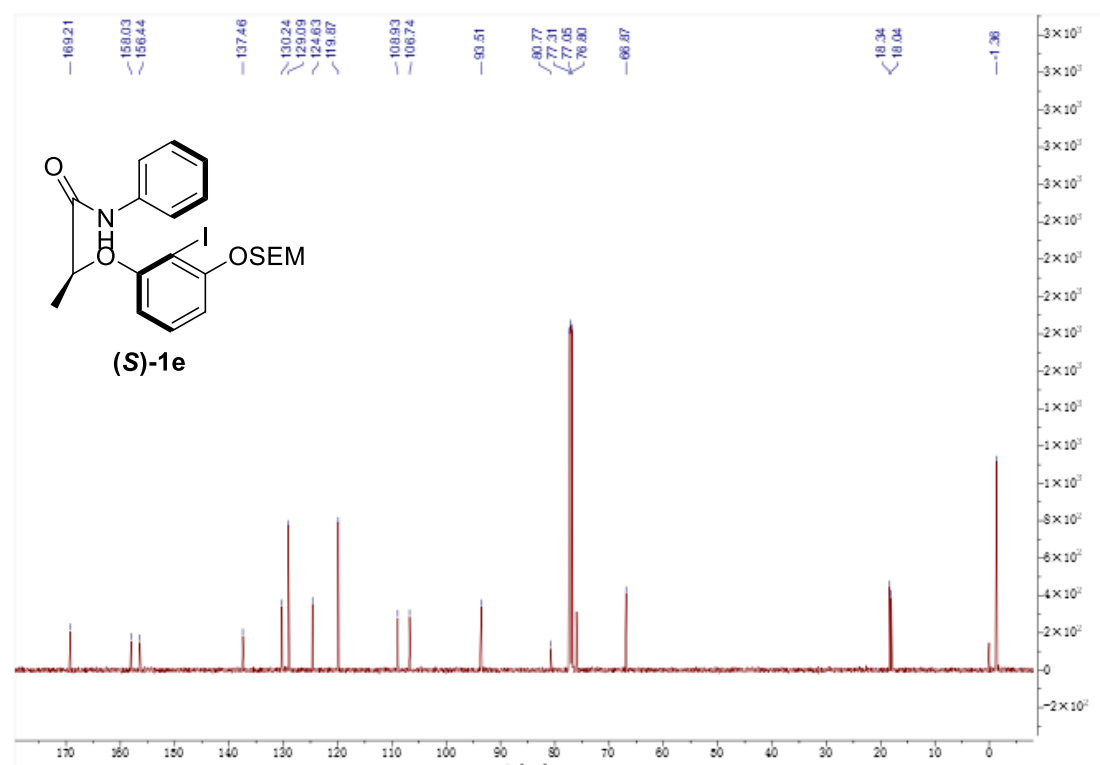
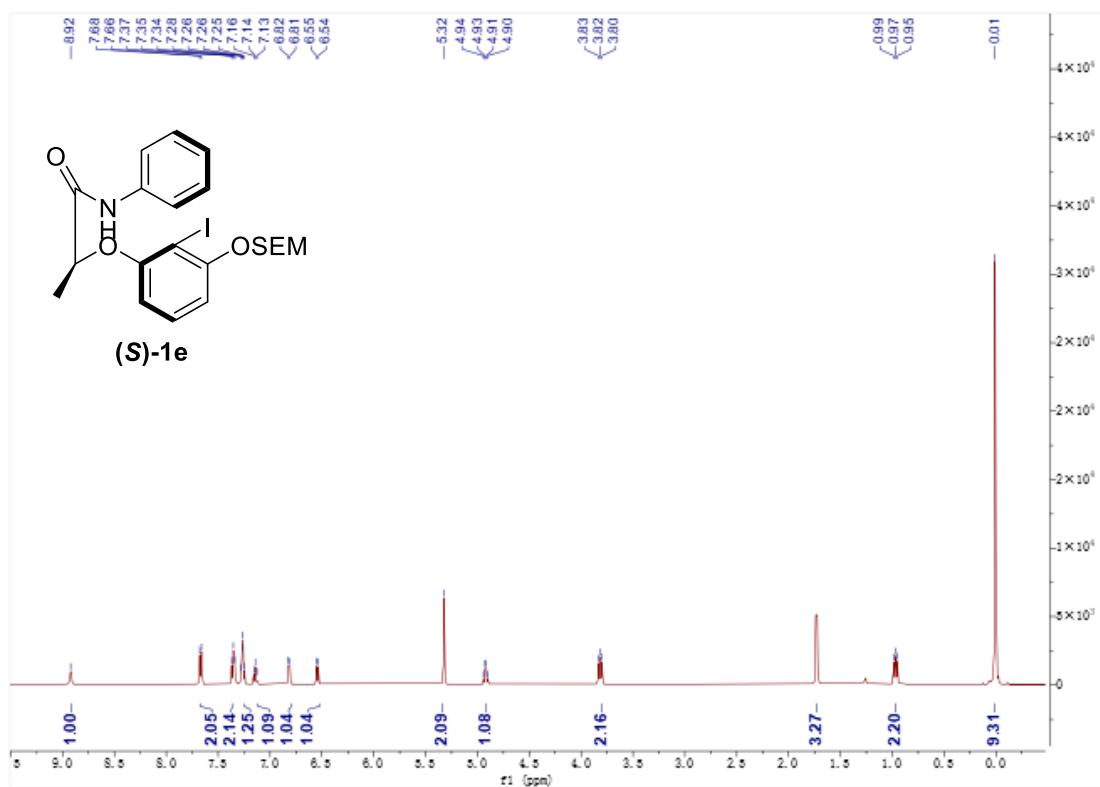
Compound **(S)-1c**



Compound (S)-1d

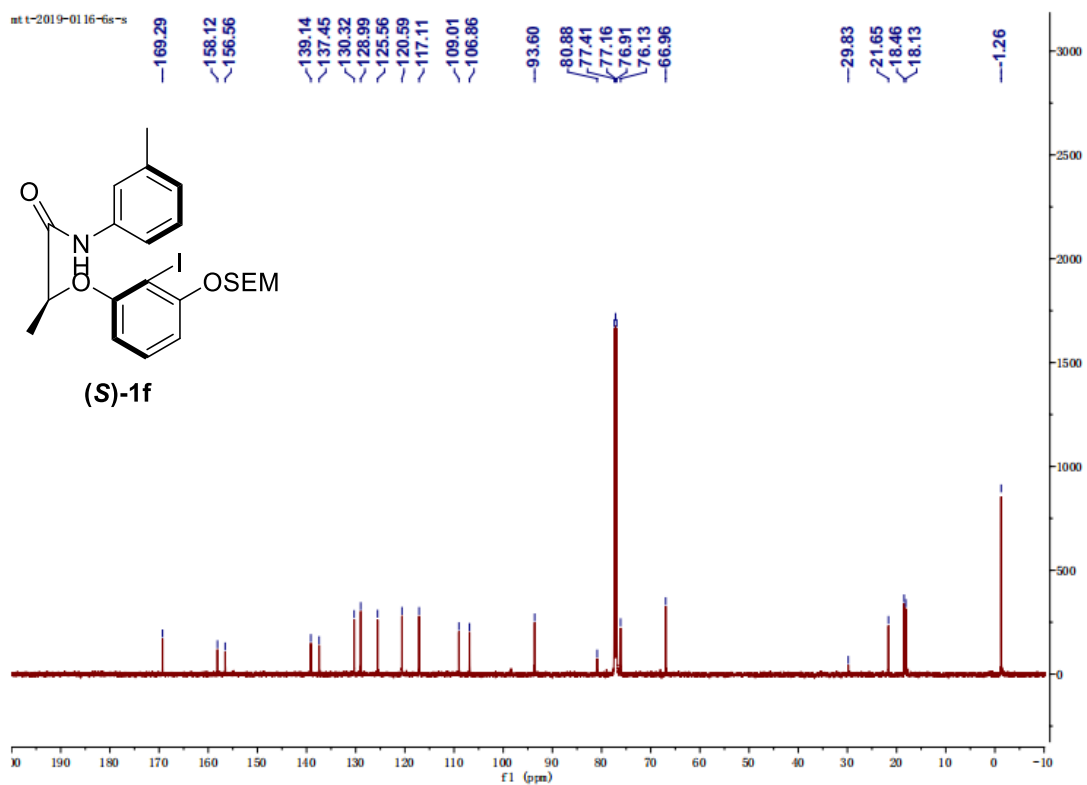
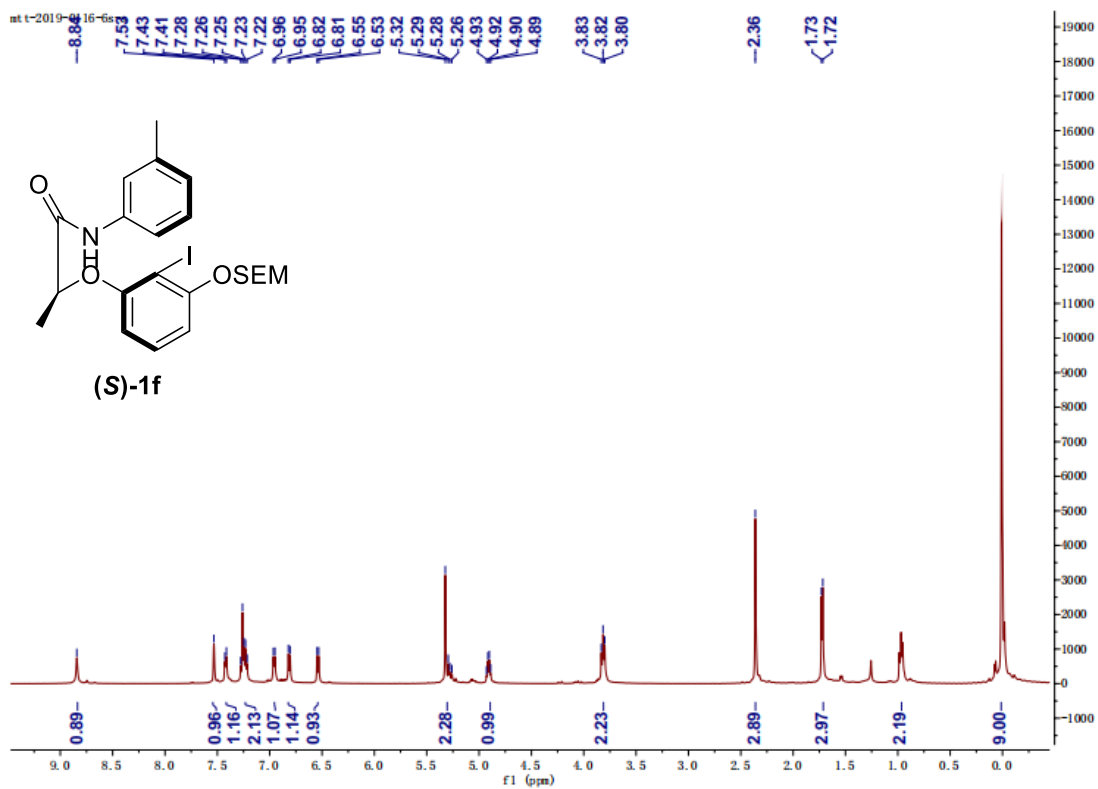


Compound **(S)-1e**

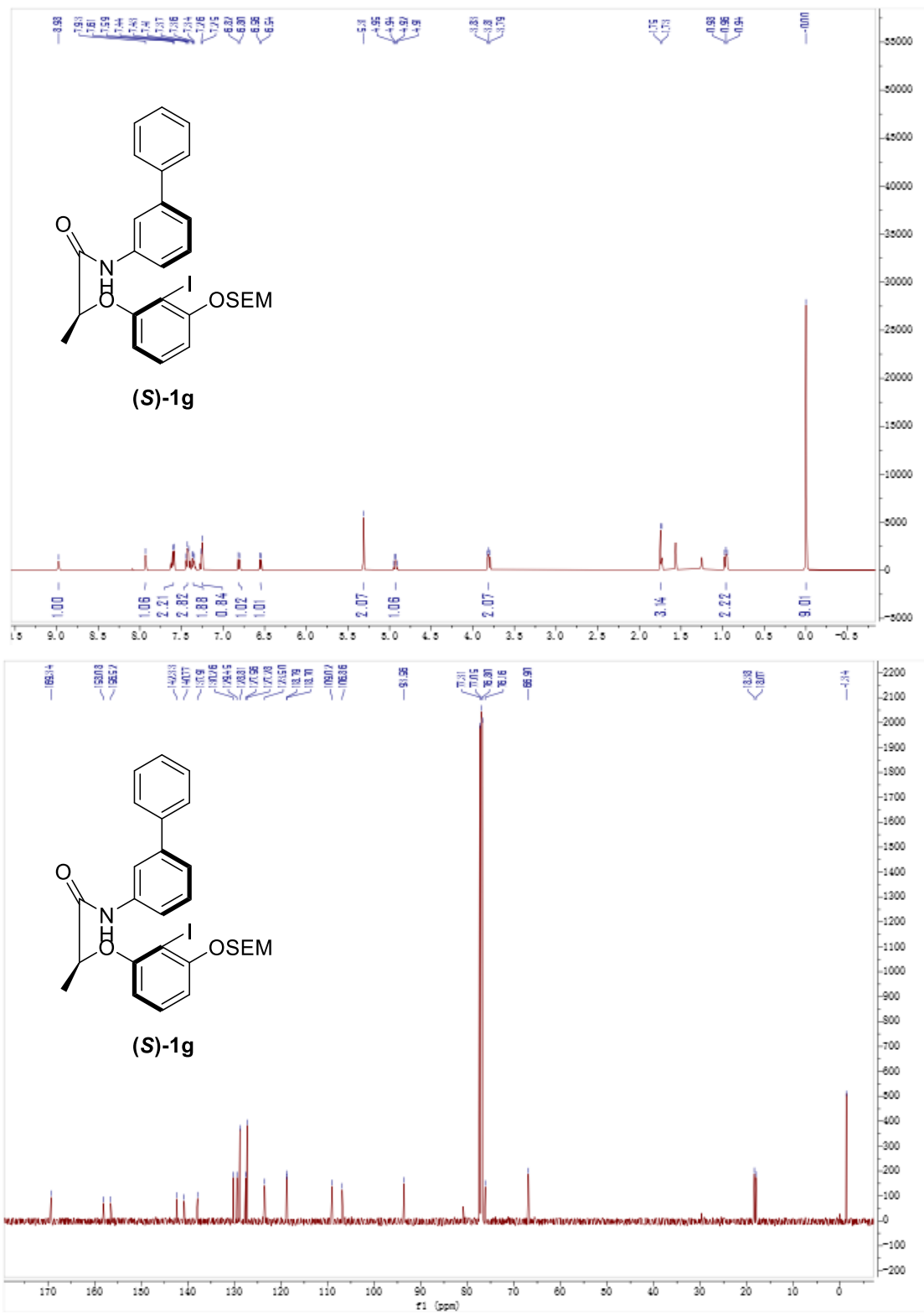


Compound **(S)-1f**

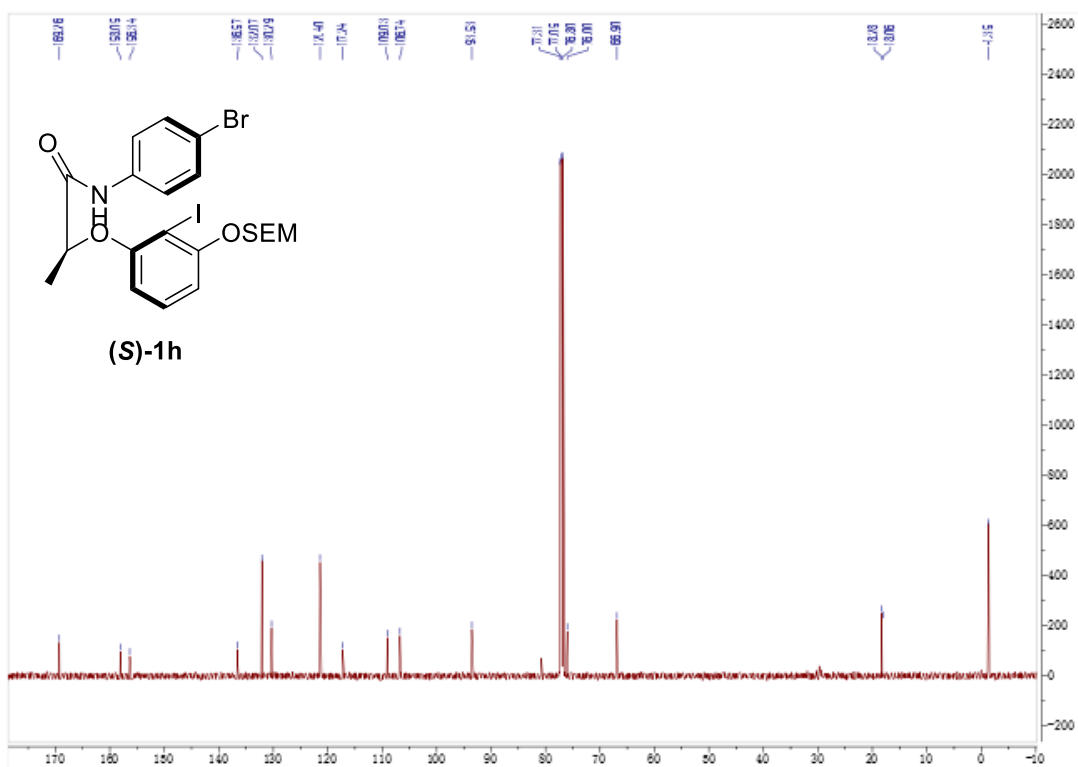
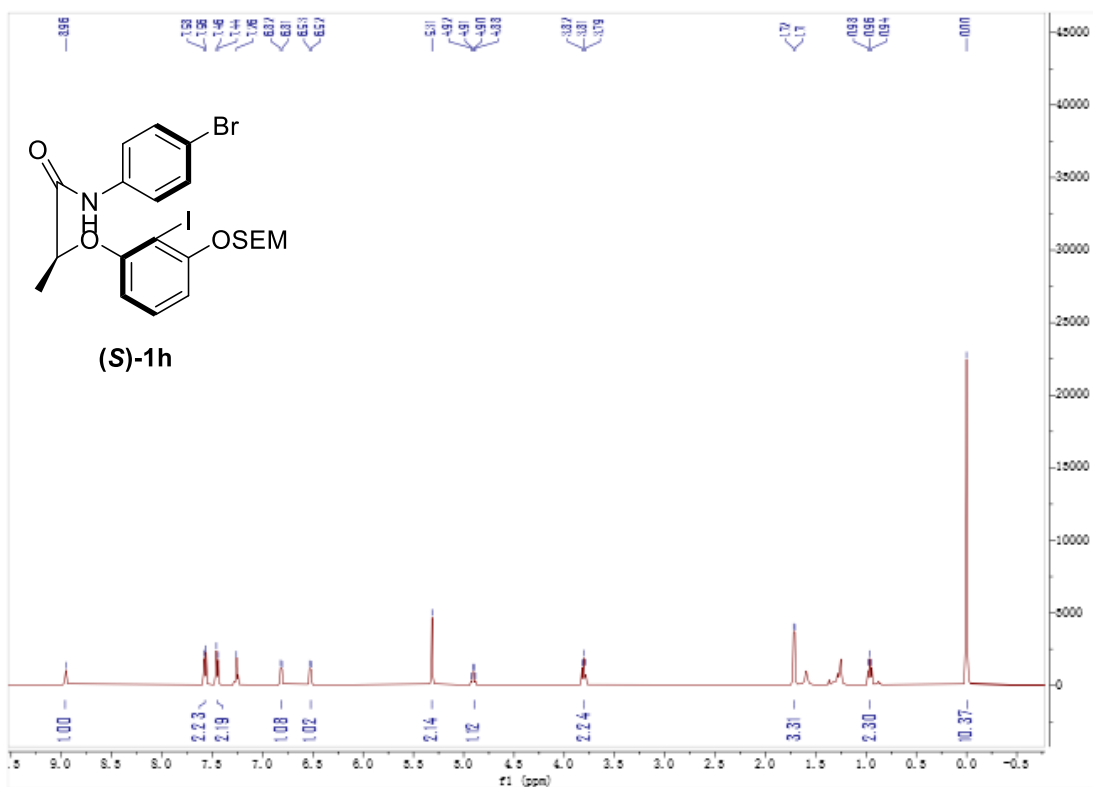




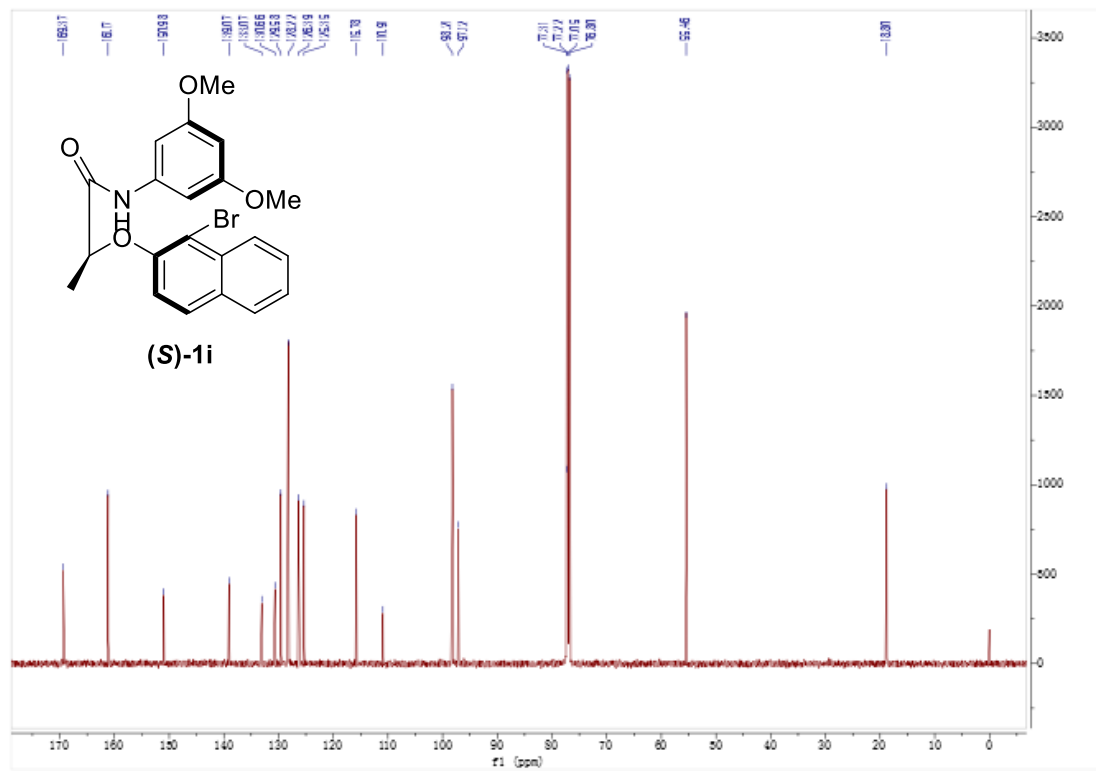
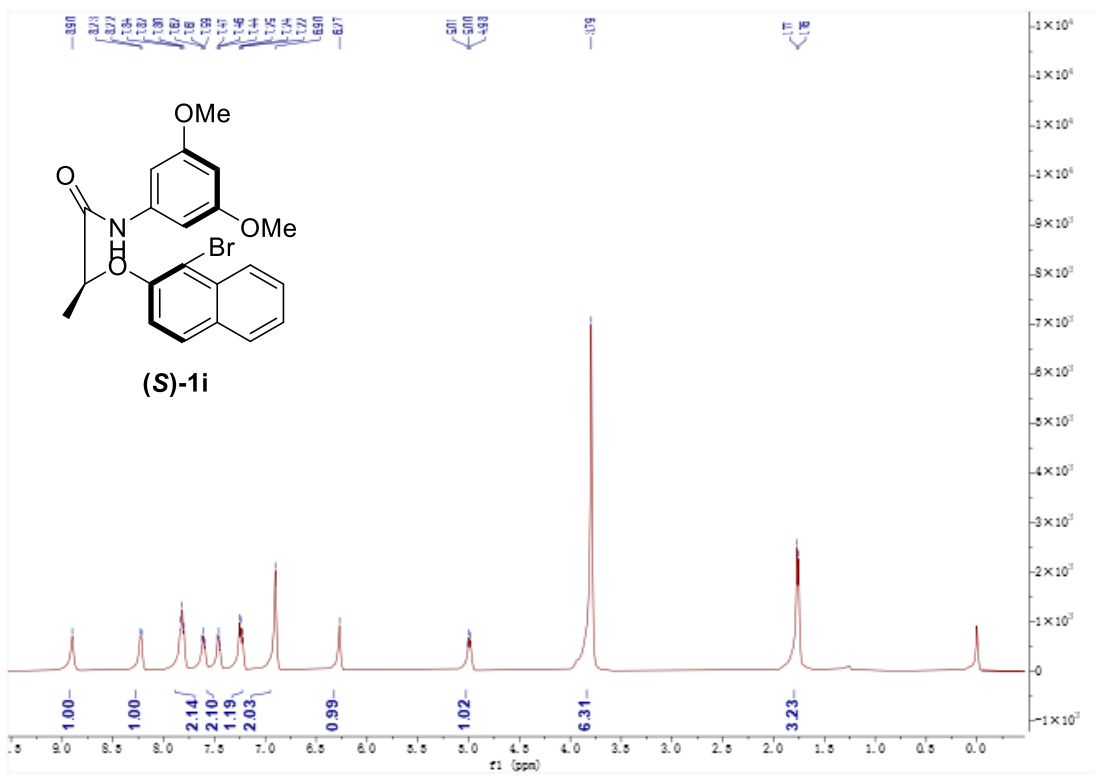
Compound (S)-1g



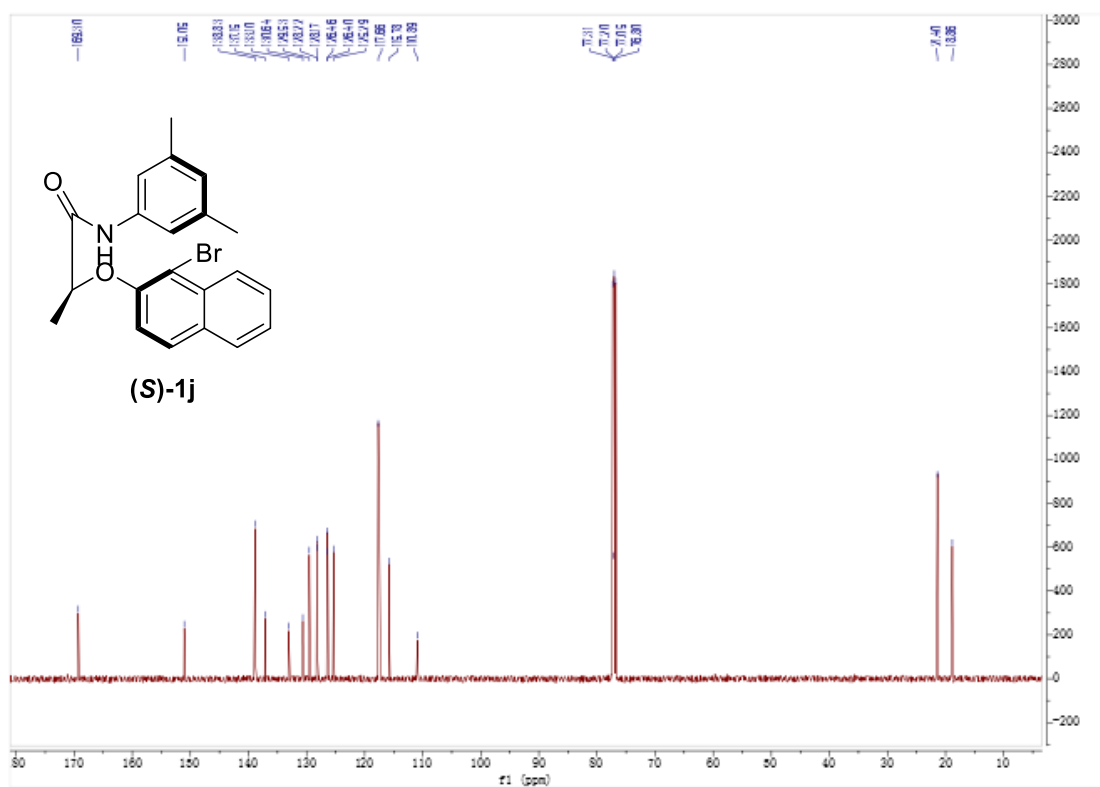
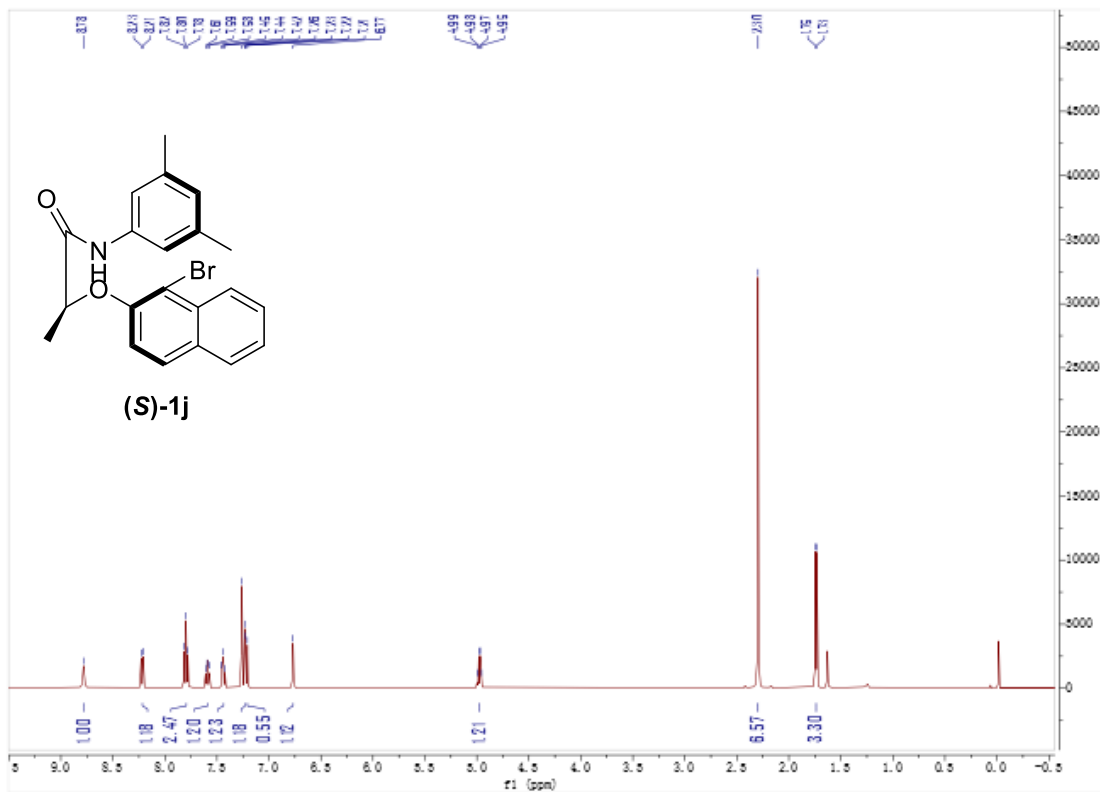
Compound **(S)-1h**



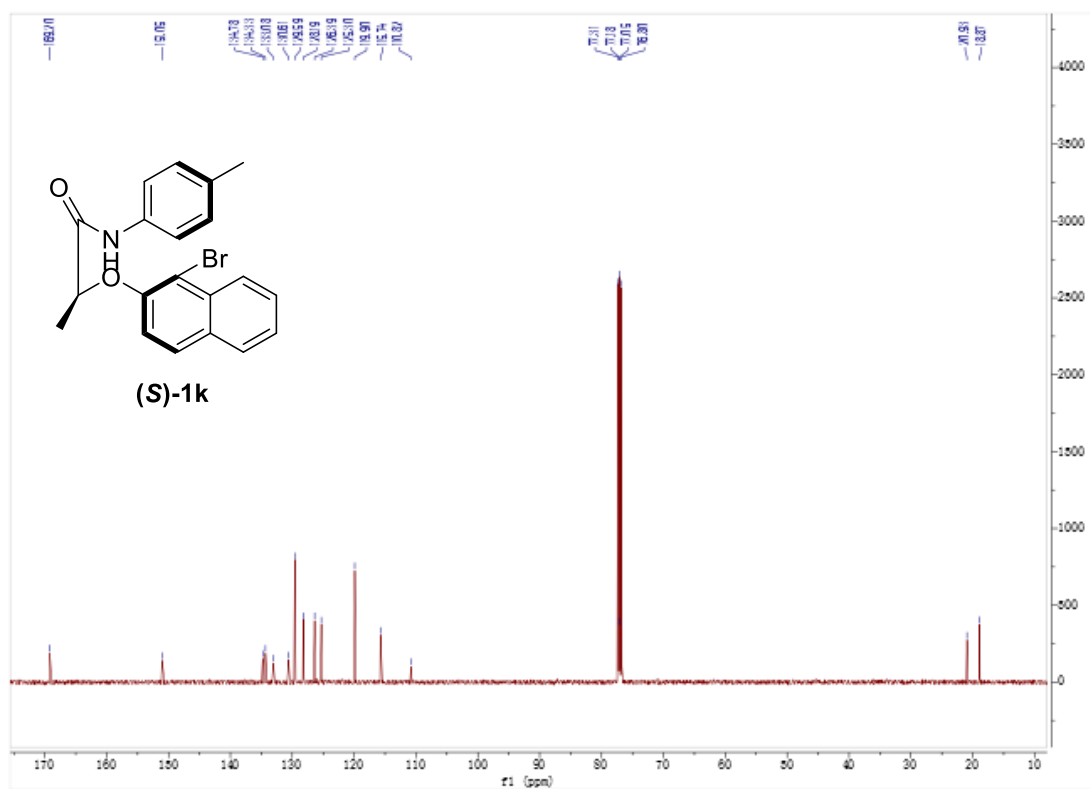
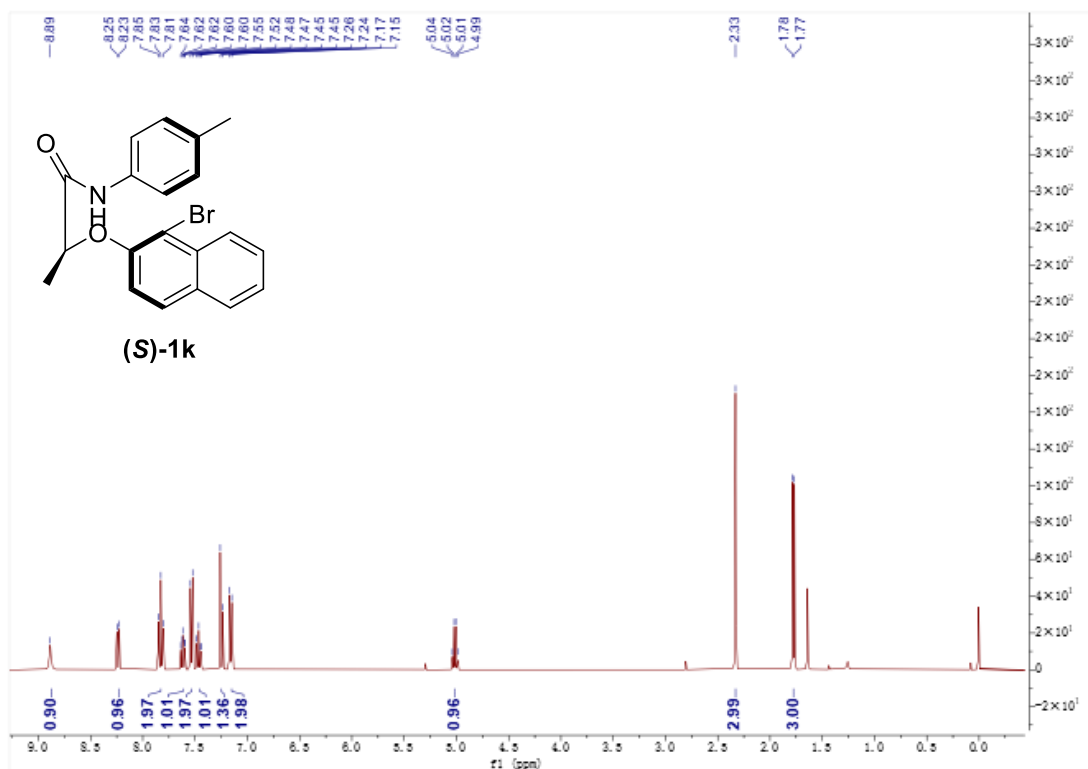
Compound **(S)-1i**



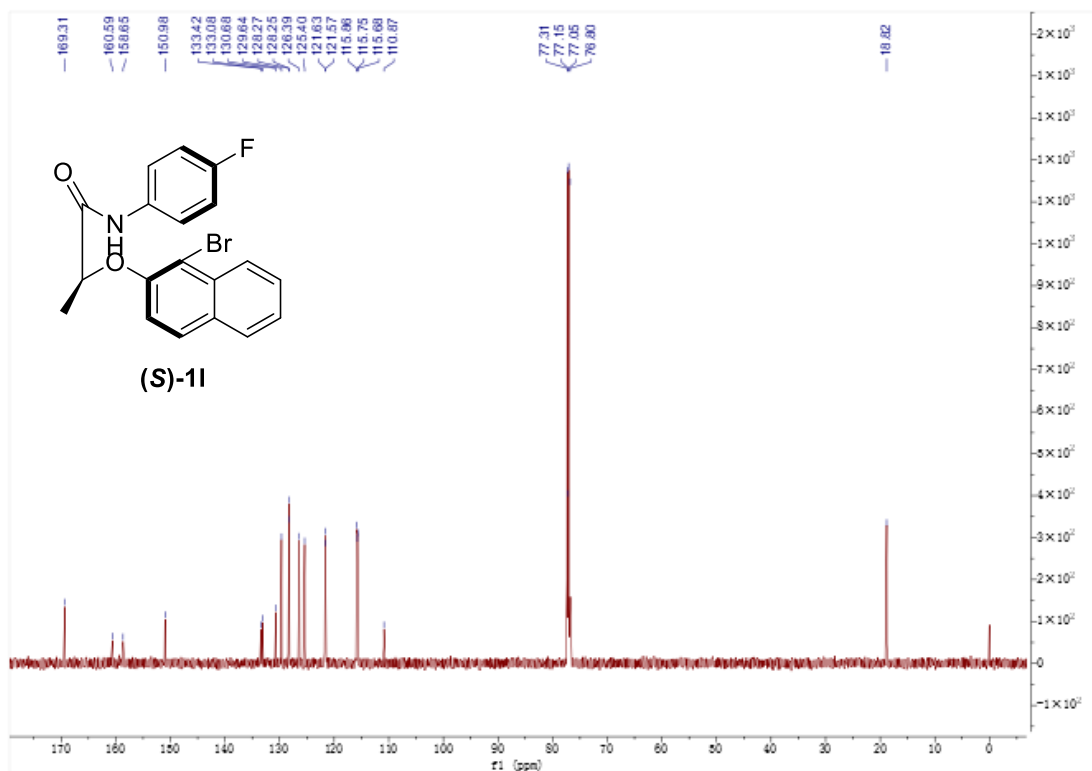
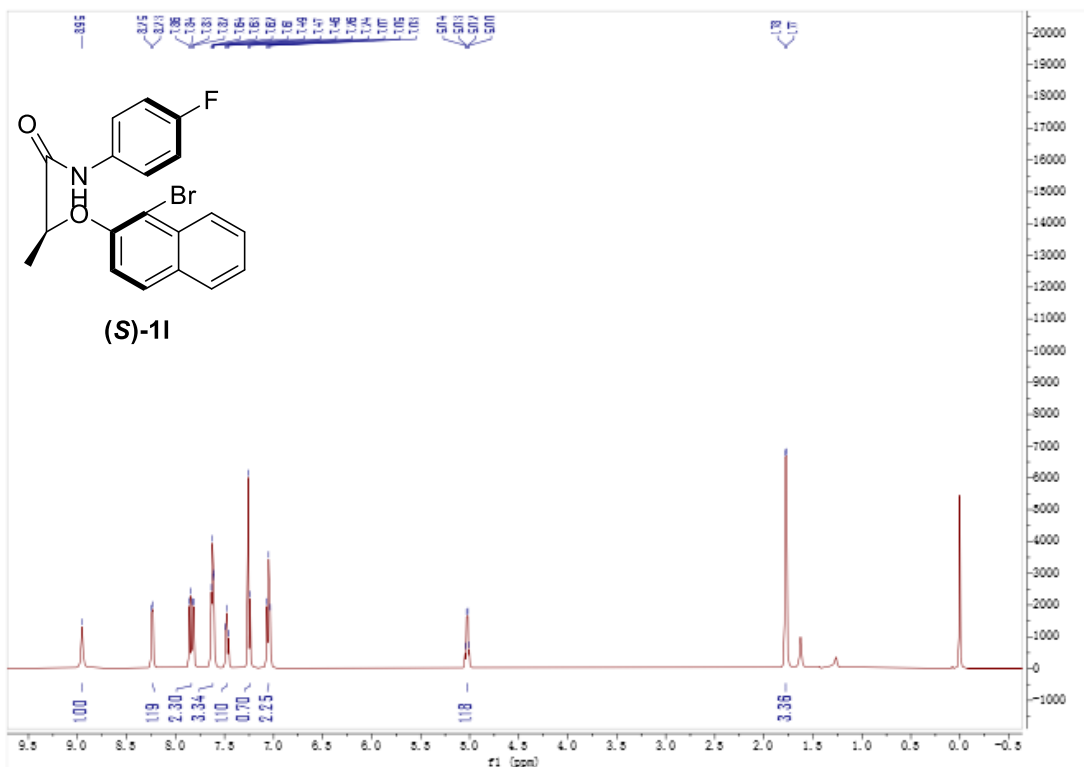
Compound **(S)-1j**



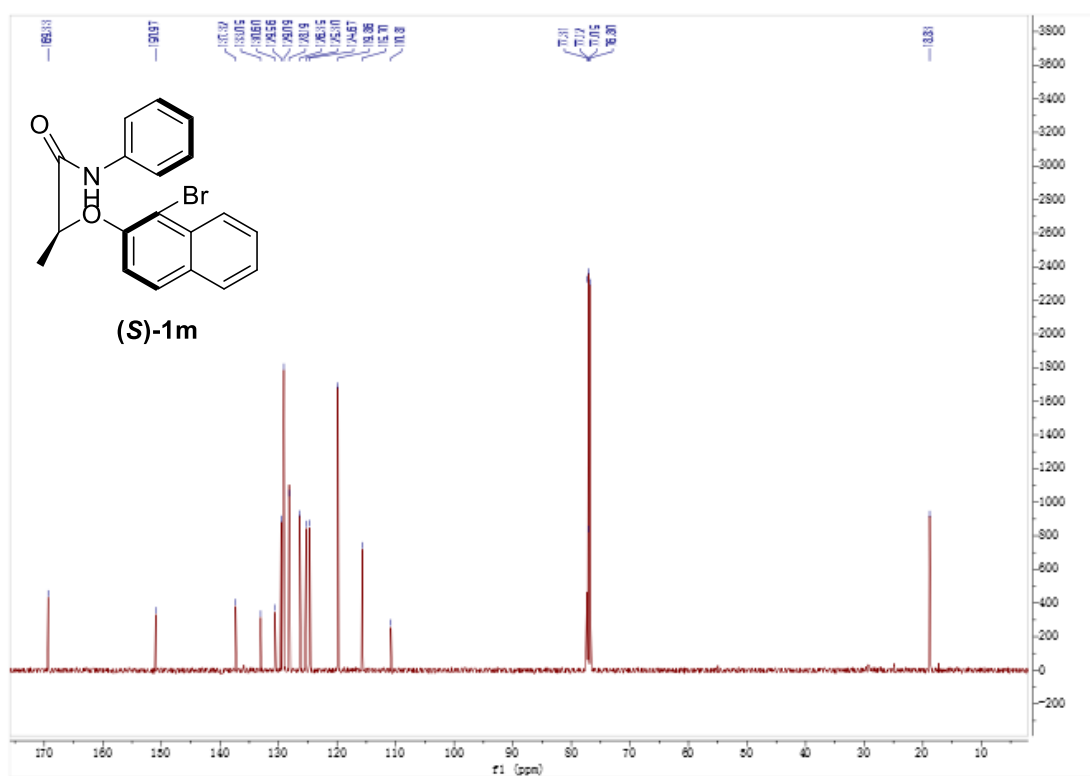
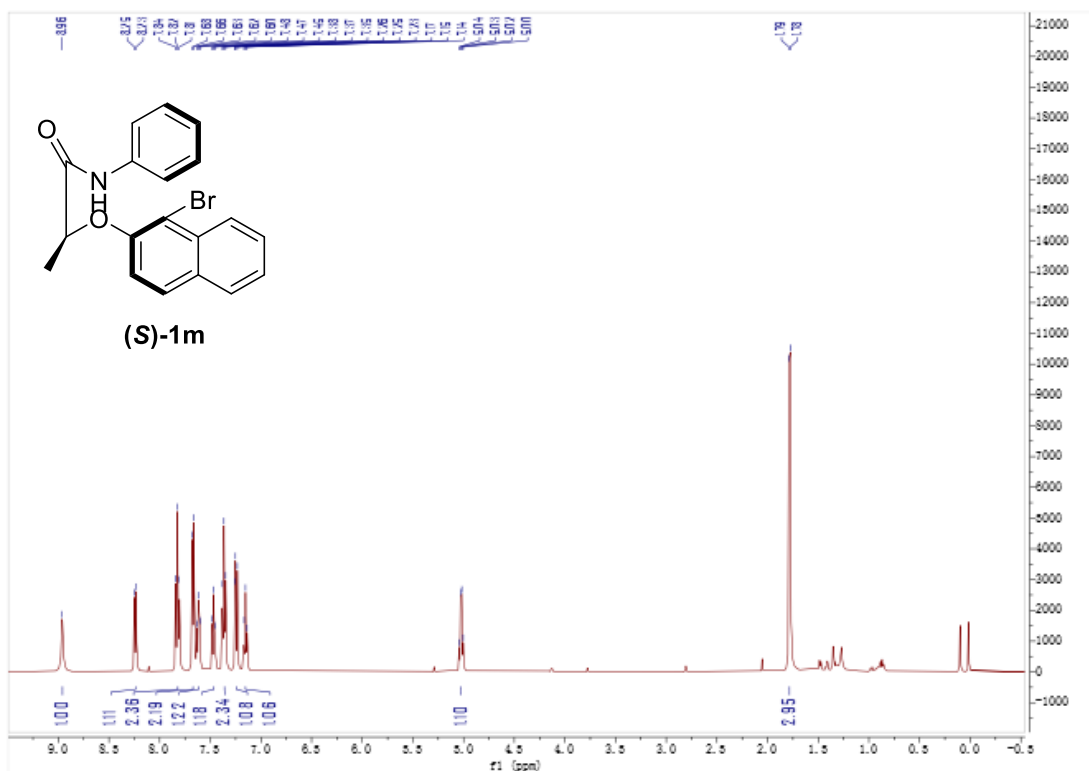
Compound (S)-1k



Compound (S)-11

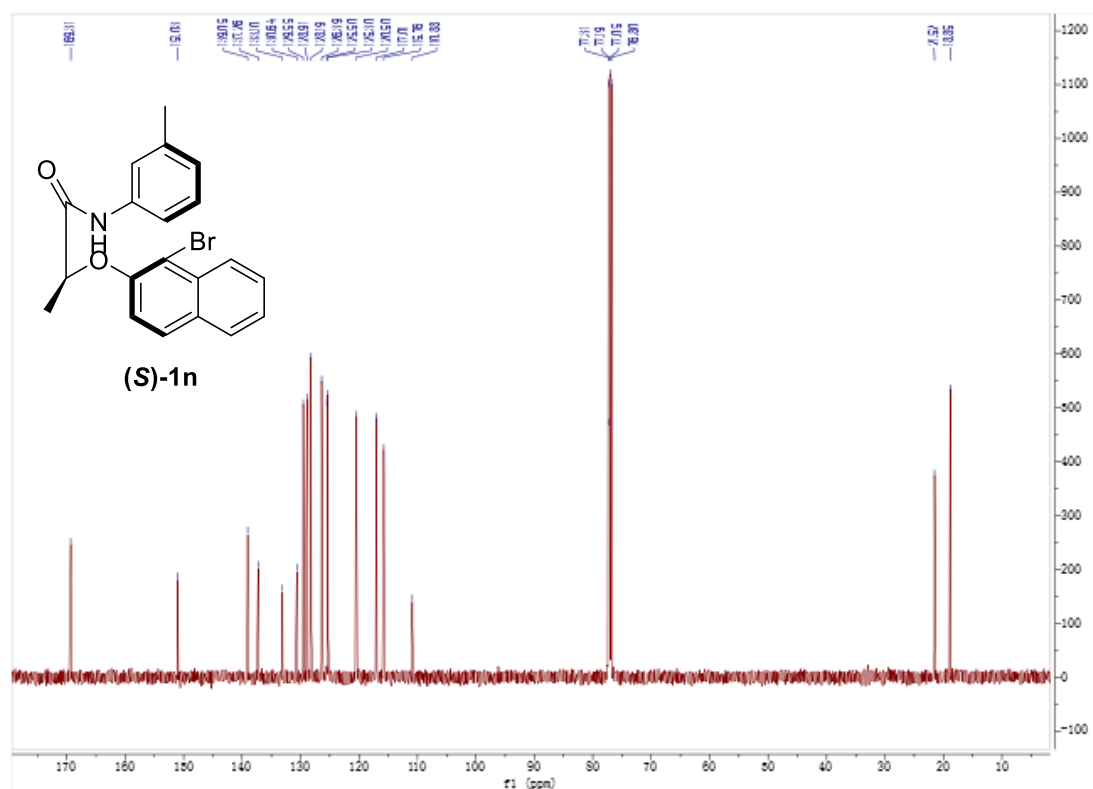
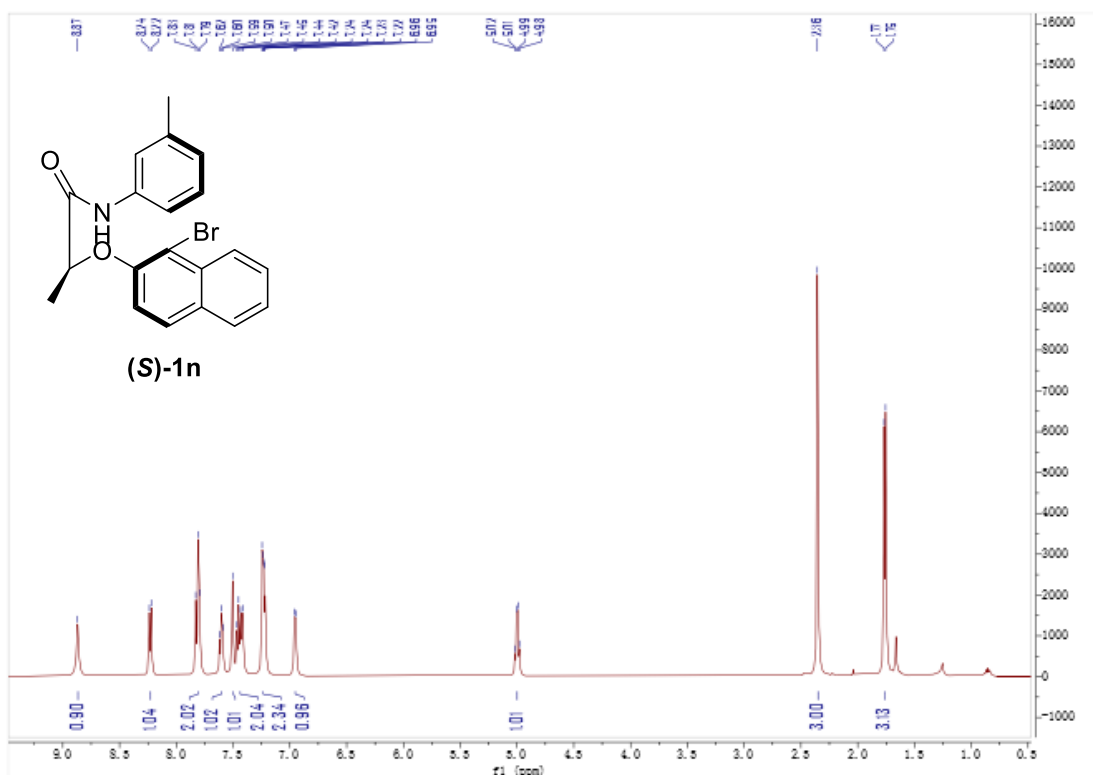


Compound (S)-1m

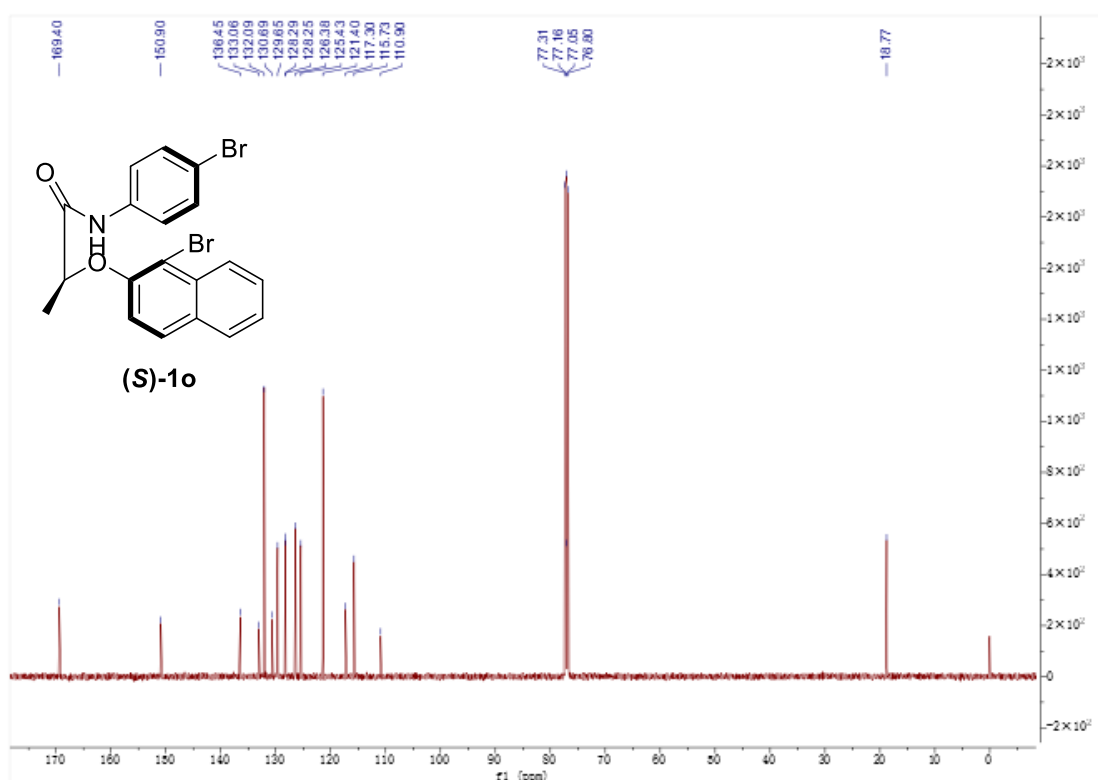
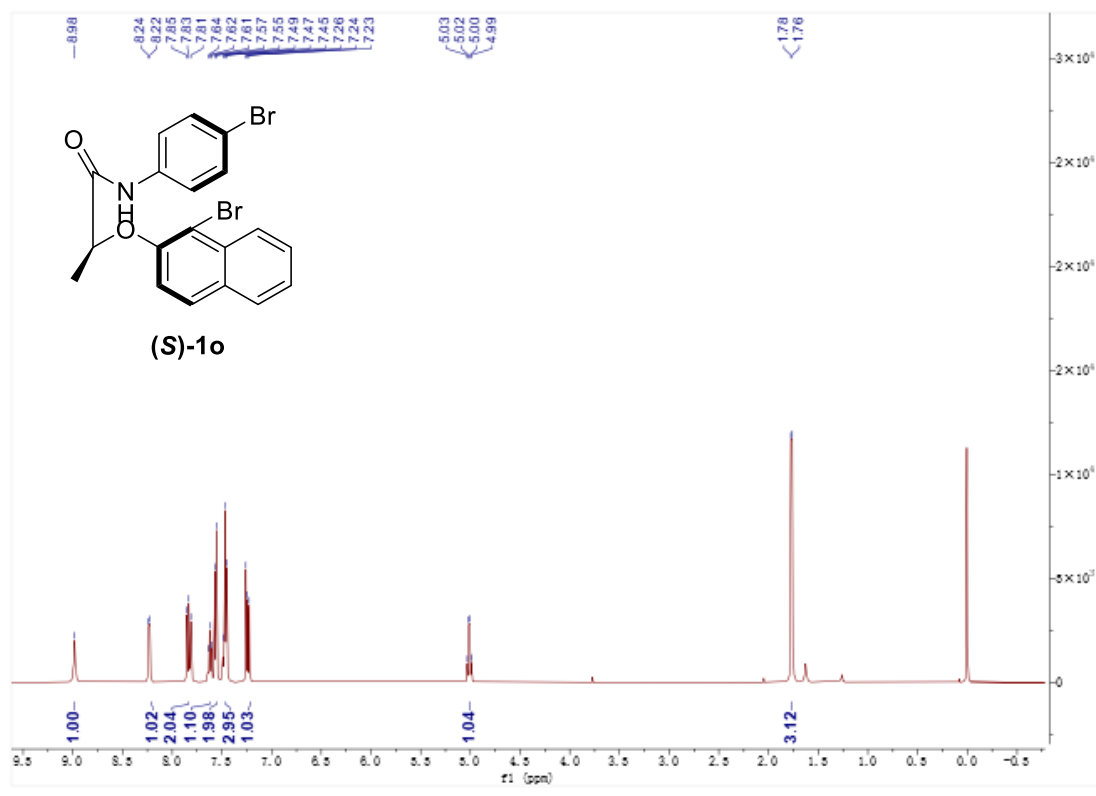


Compound **(S)-1n**

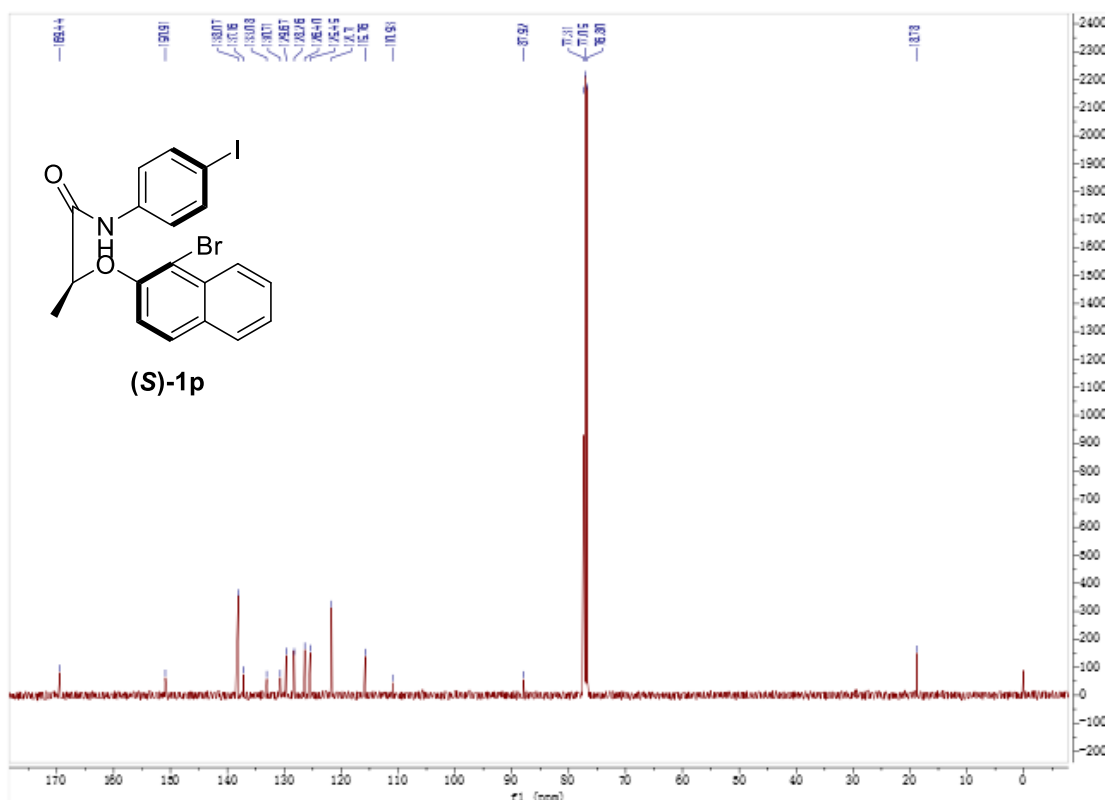
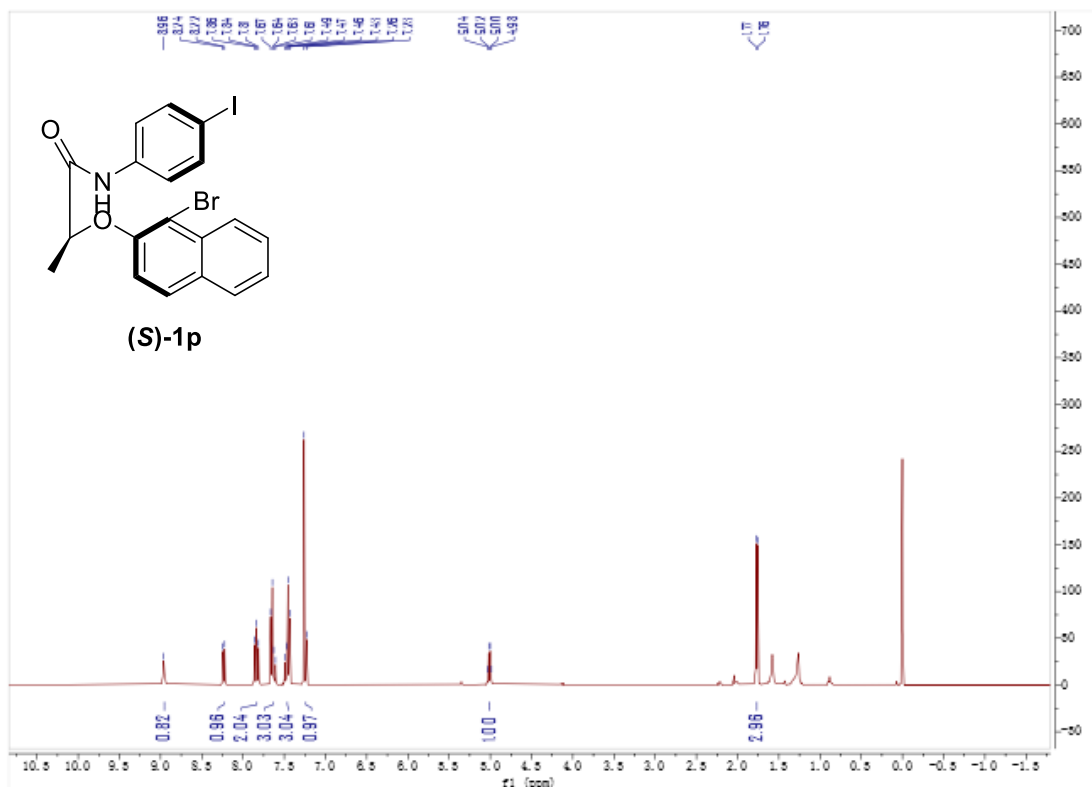




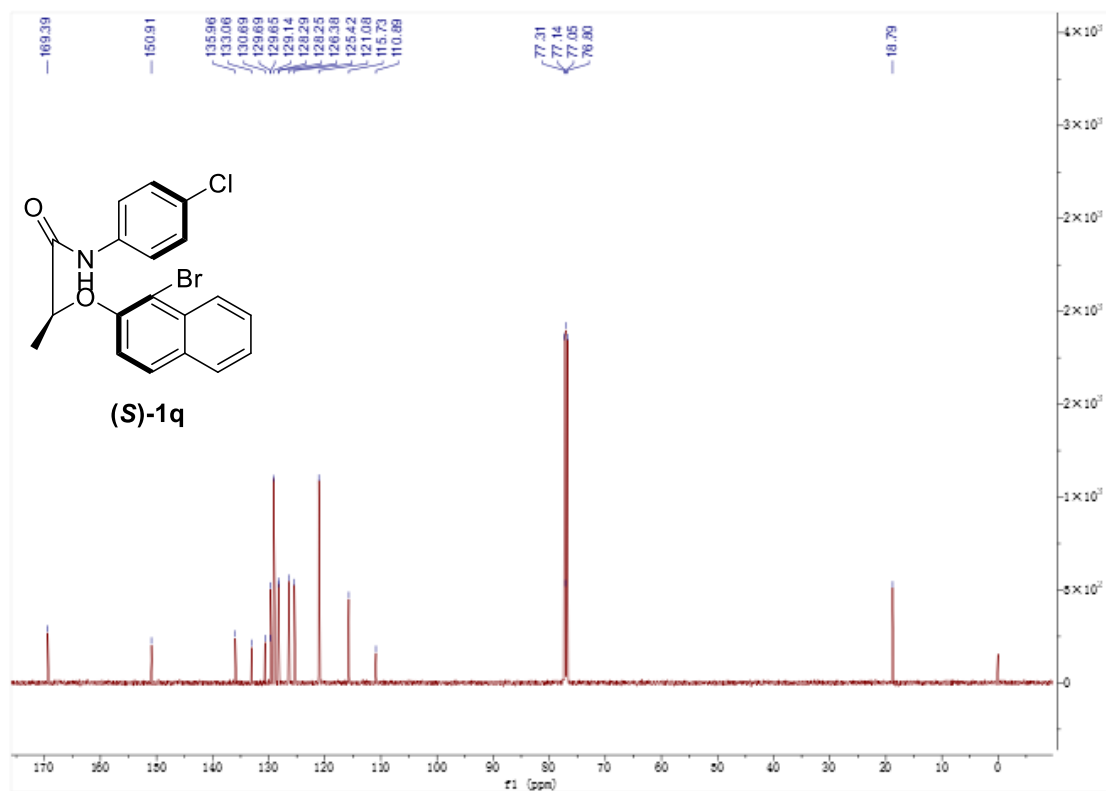
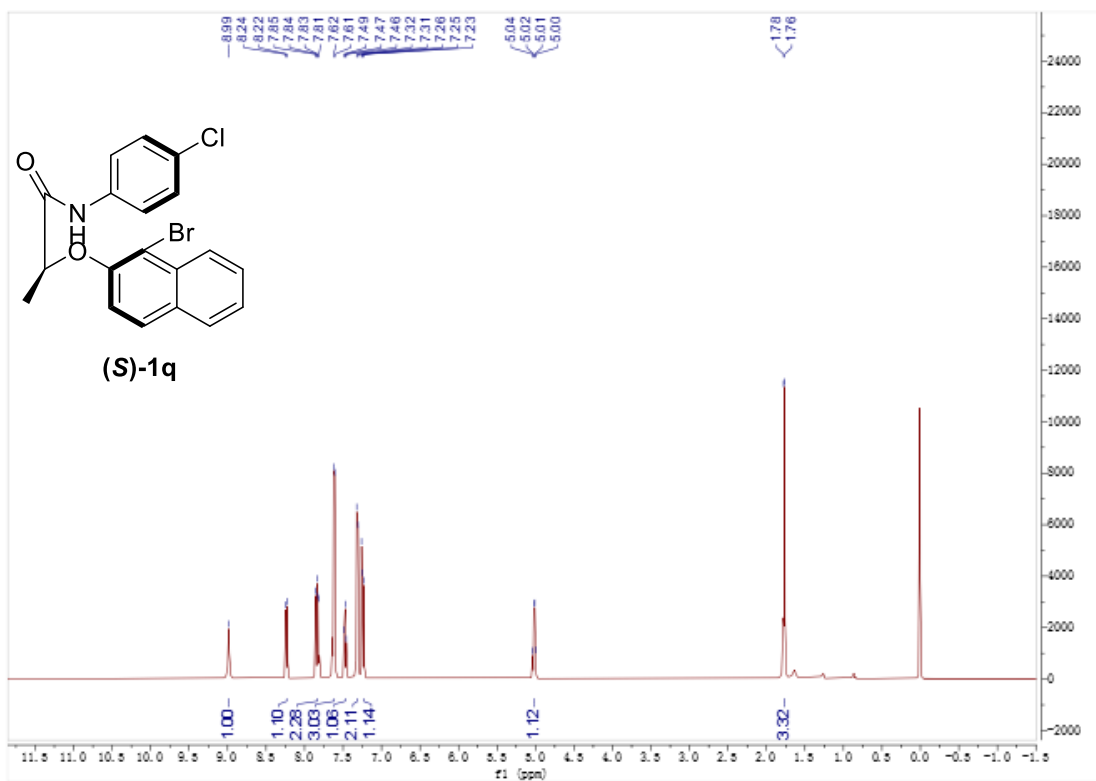
Compound **(S)-1o**



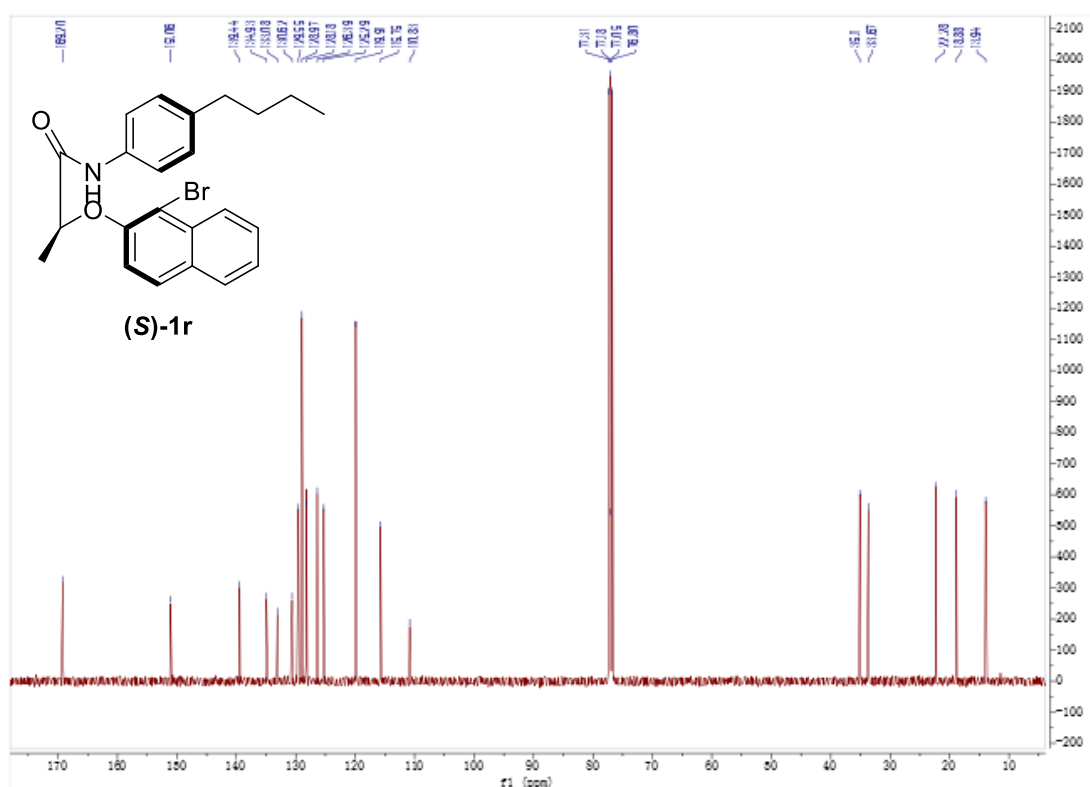
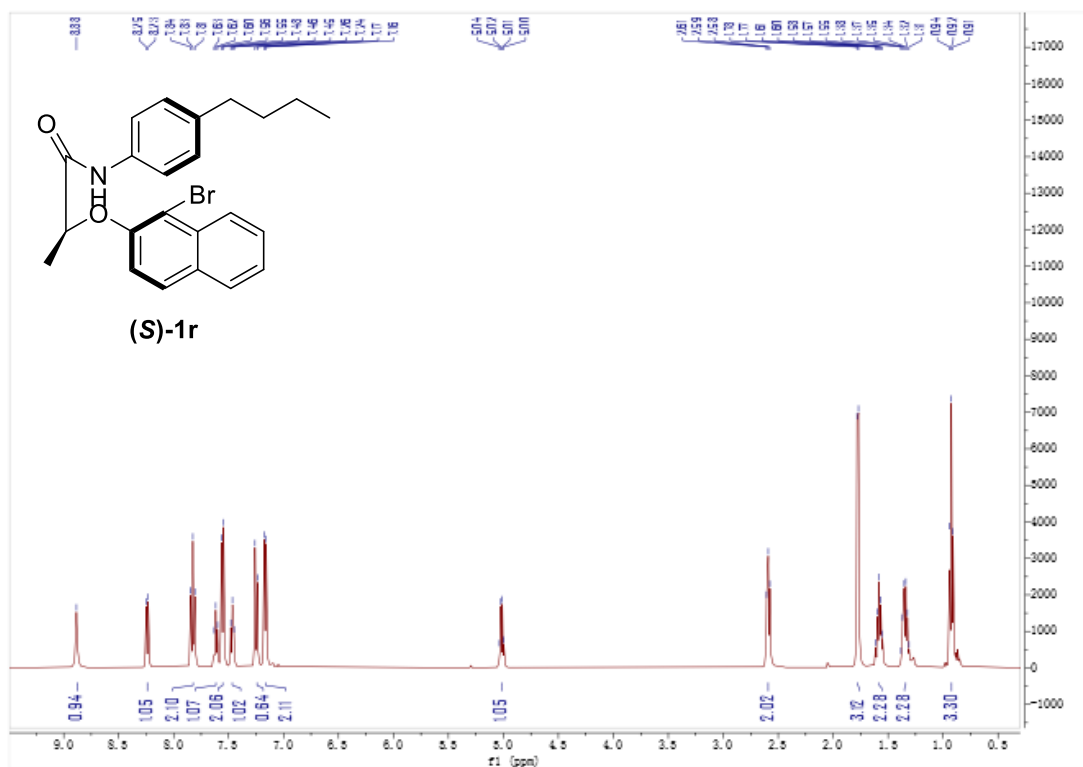
Compound **(S)-1p**



Compound **(S)-1q**

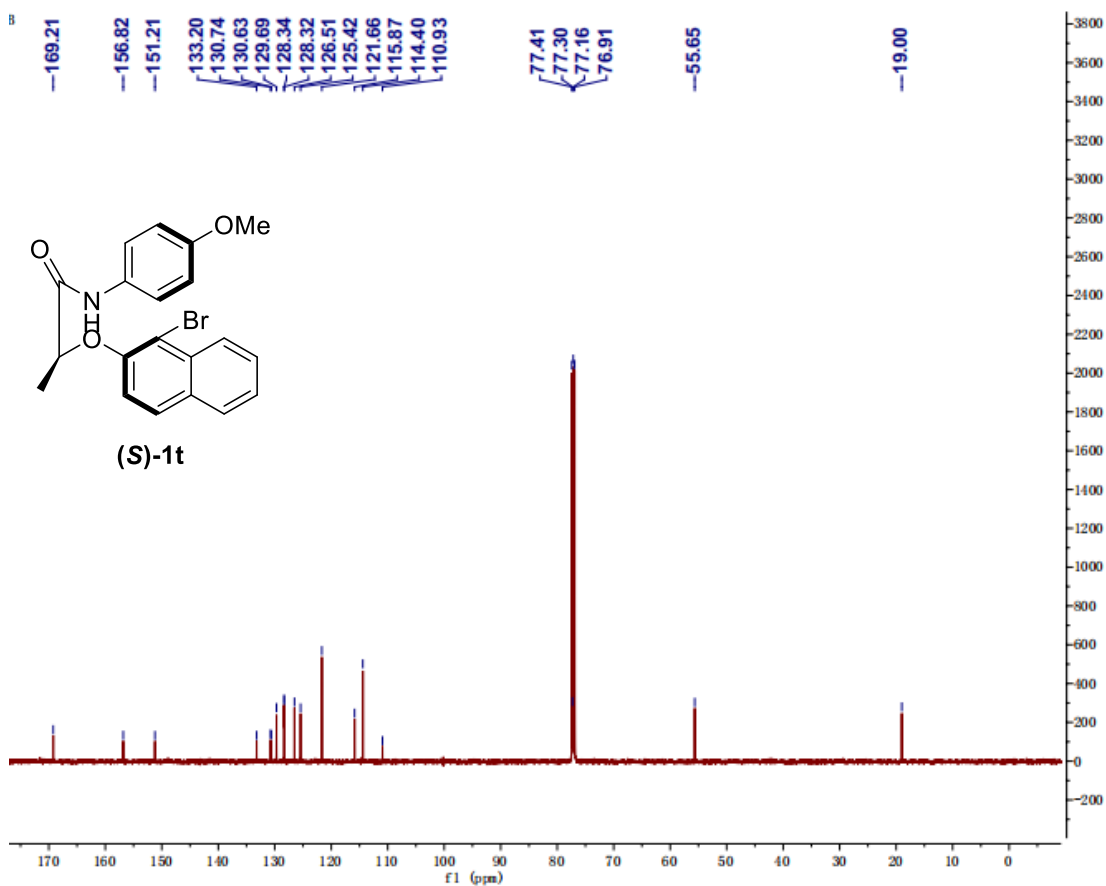
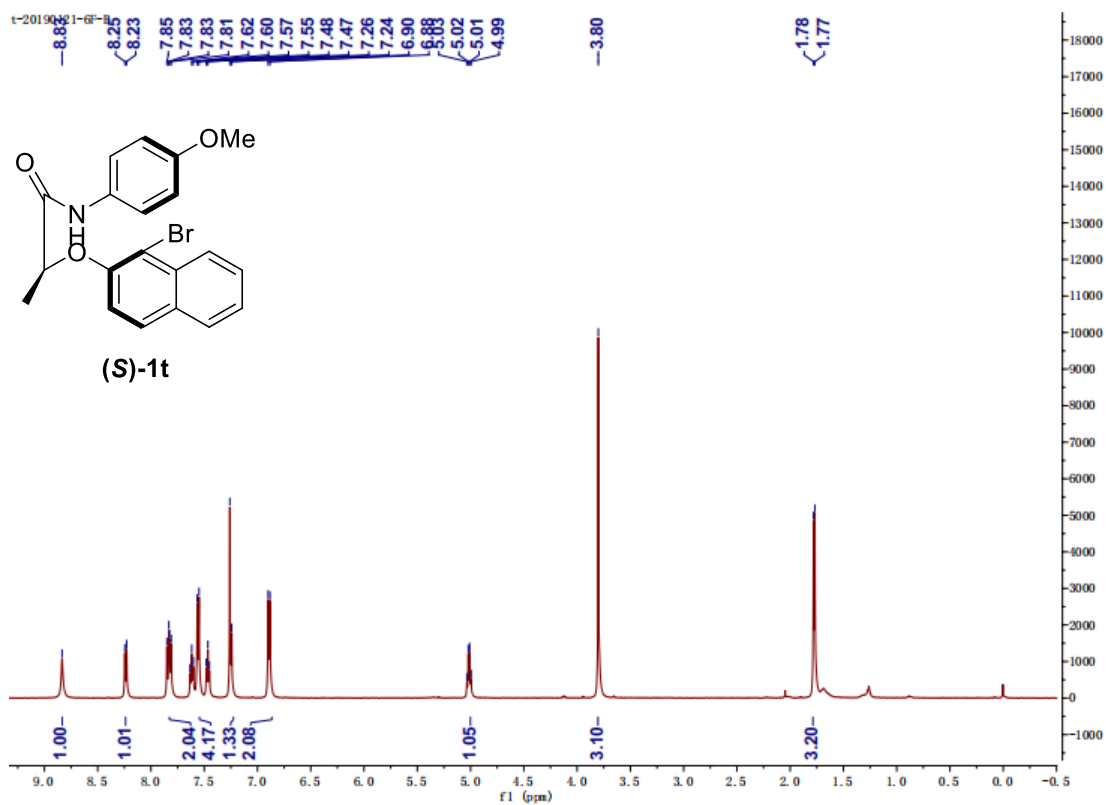


Compound **(S)-1r**

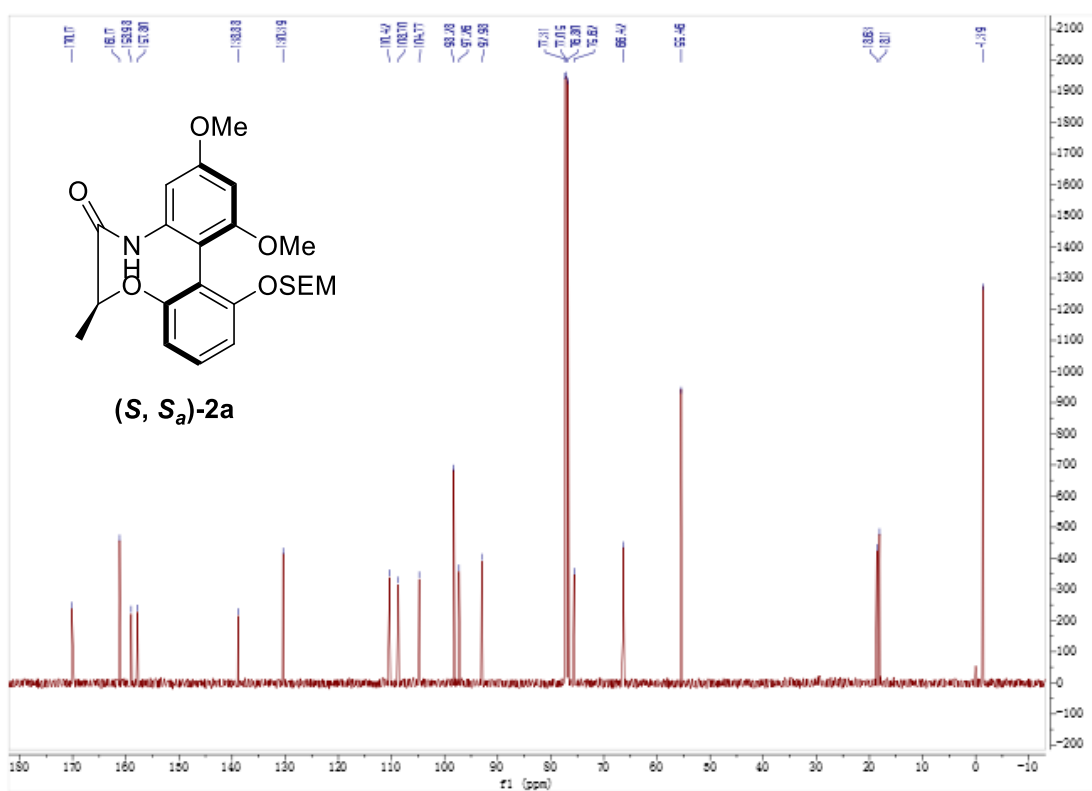
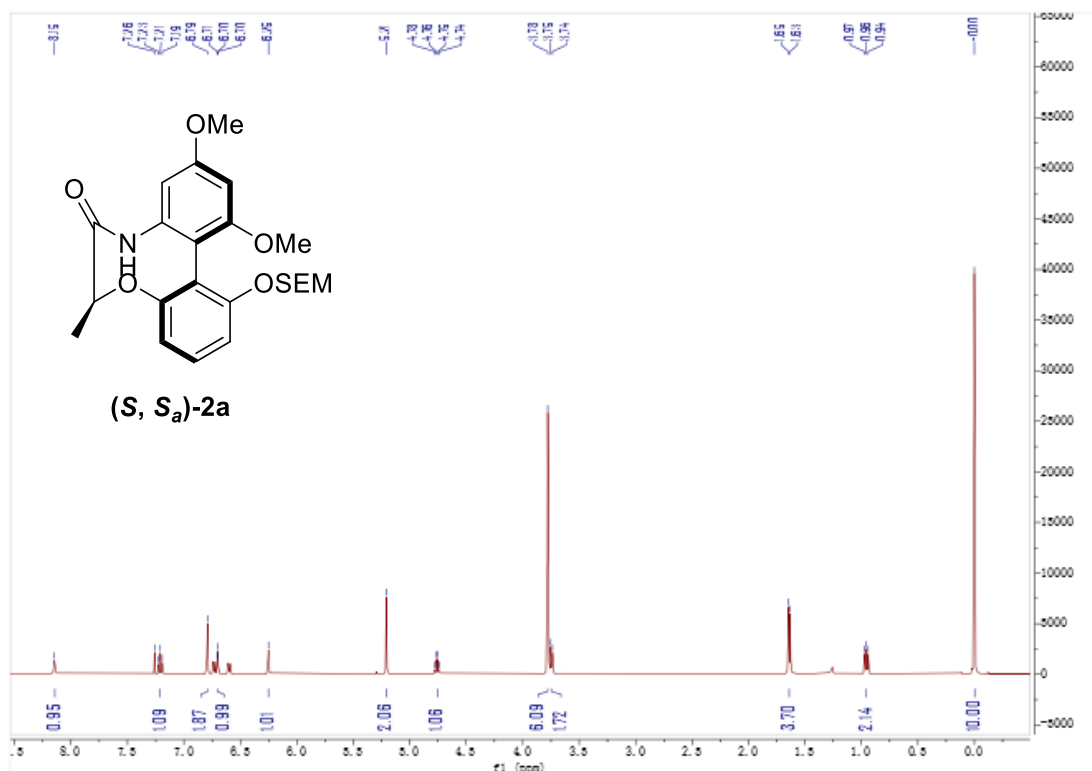


Compound **(S)-1s**



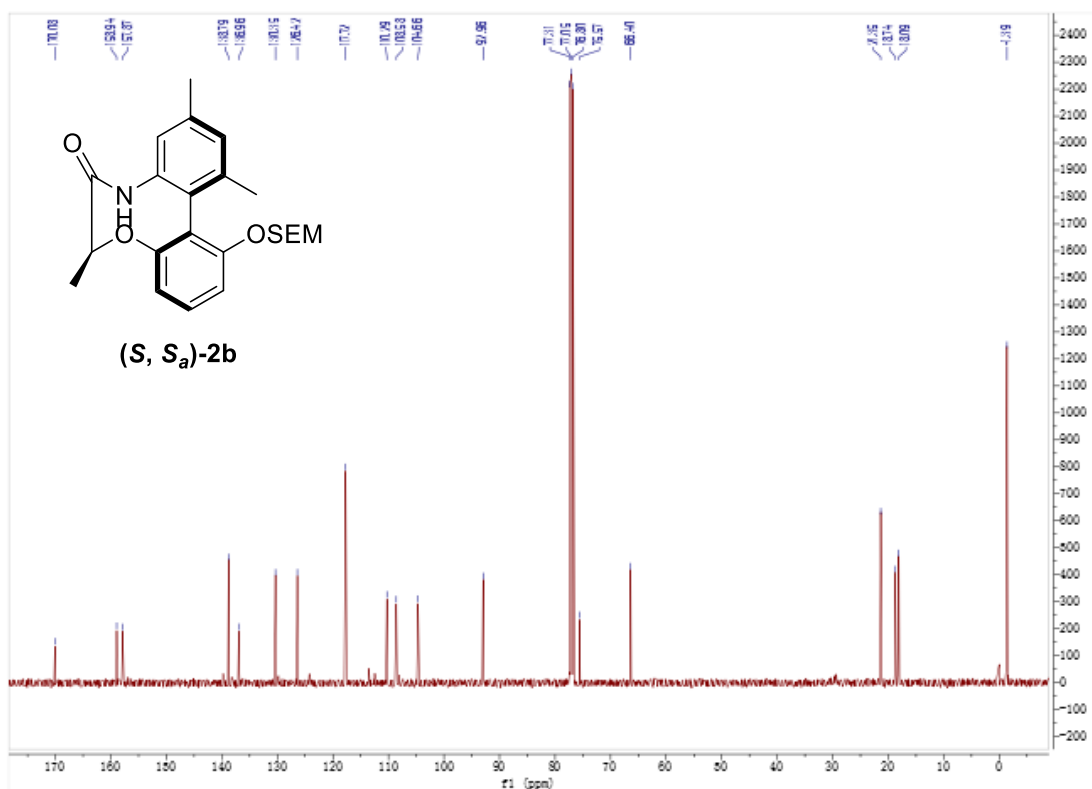
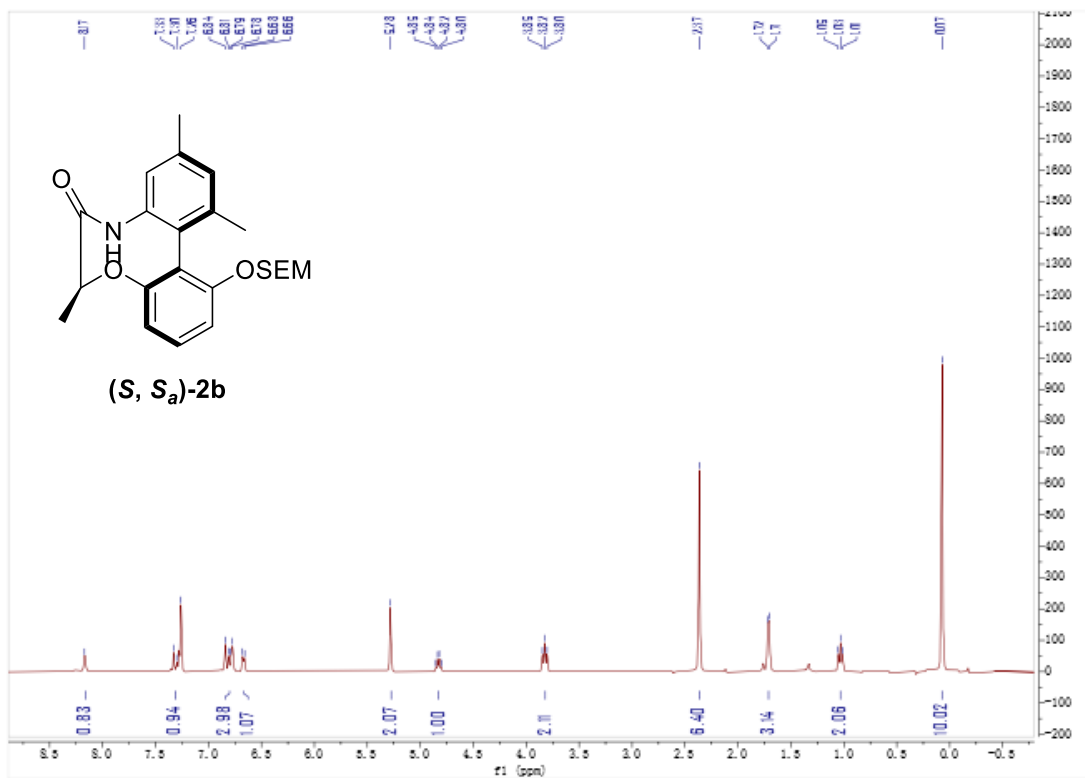


Compound (S, Sa)-2a

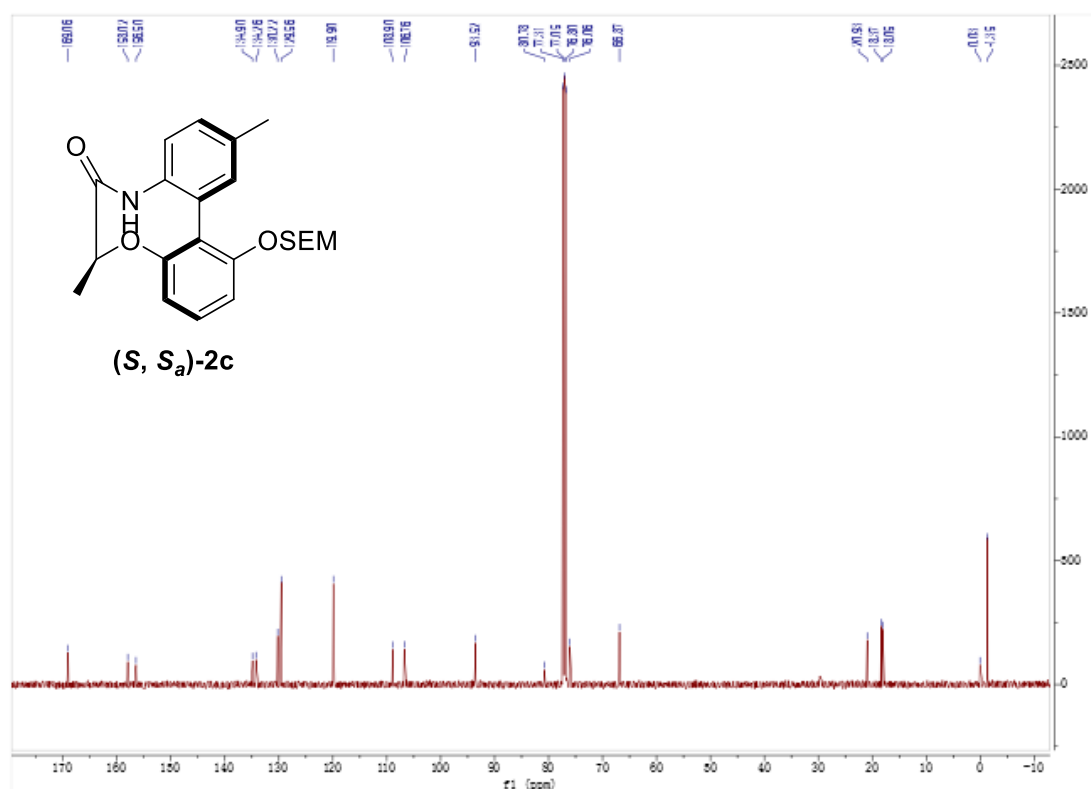
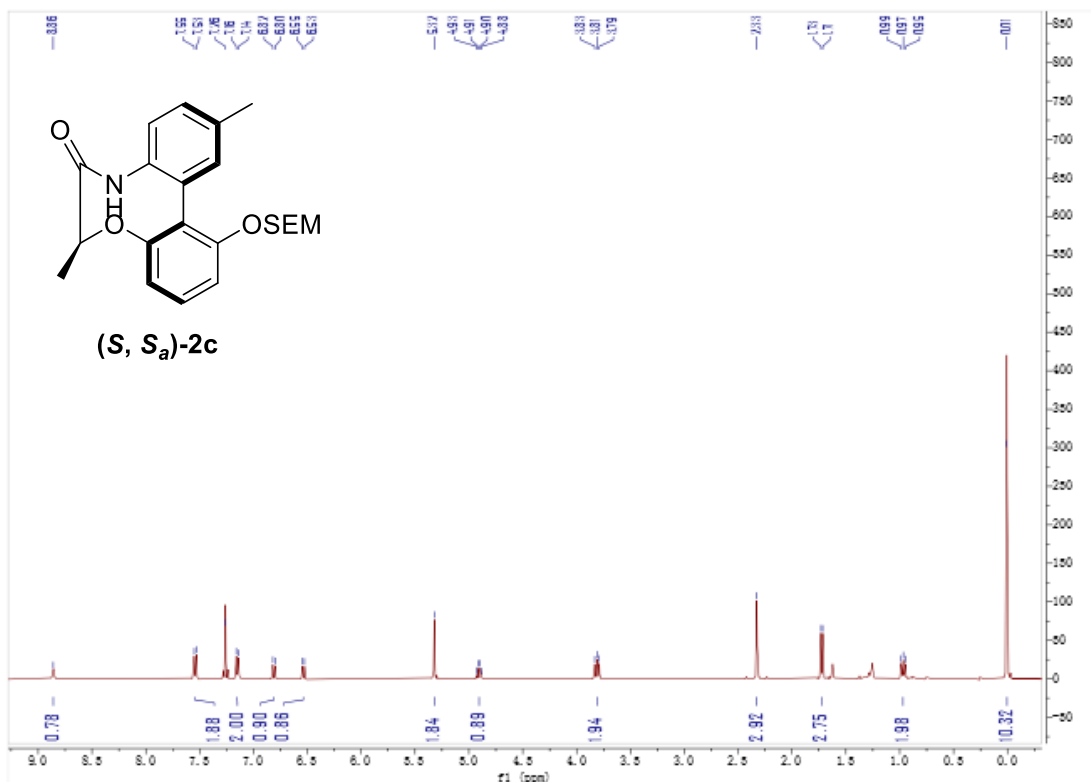


Compound **(S, S<sub>a</sub>)-2b**

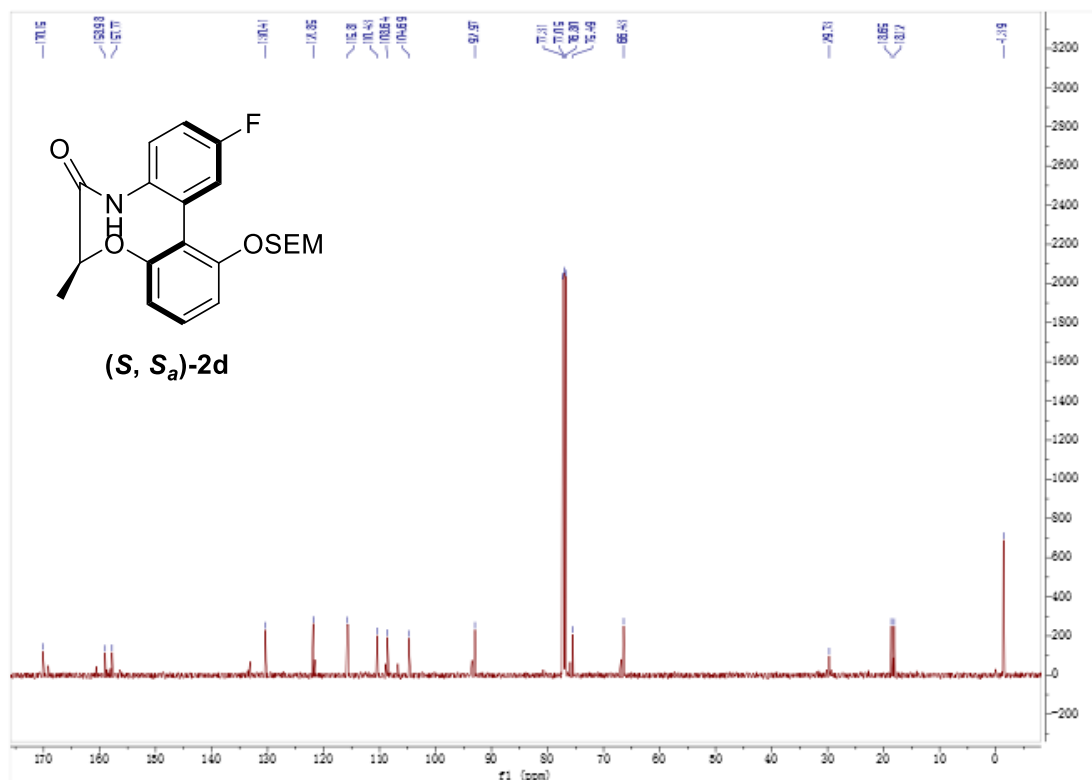
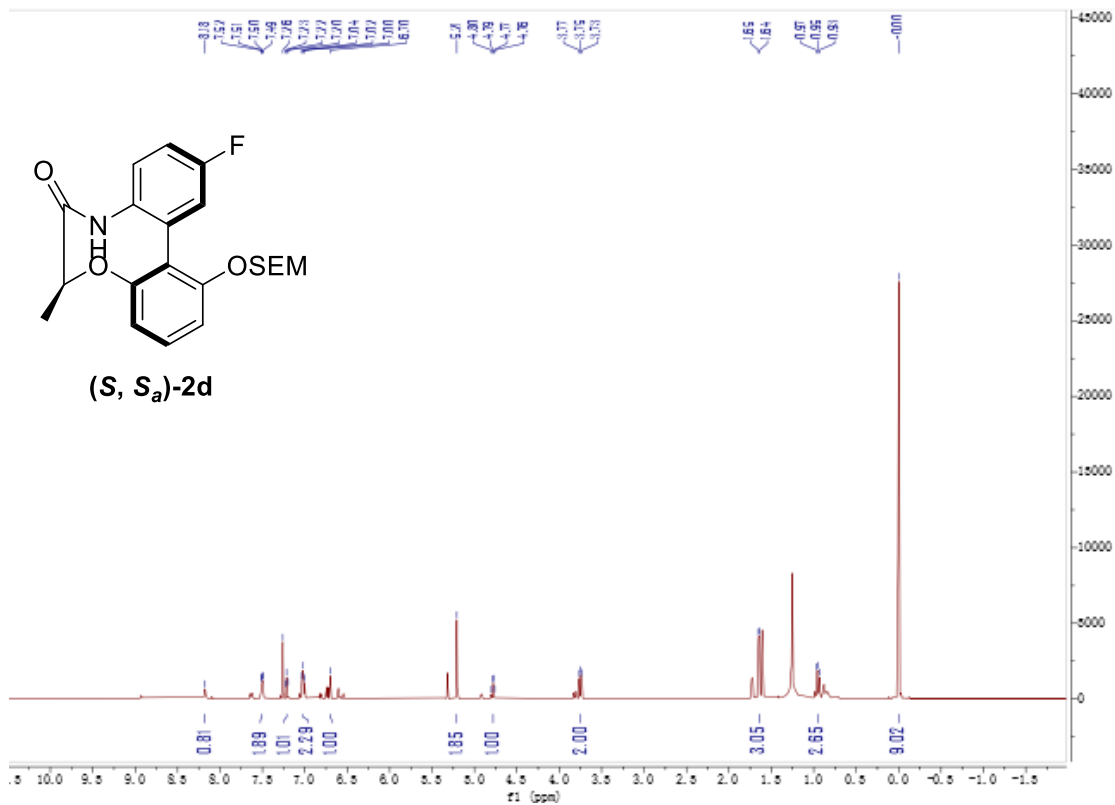




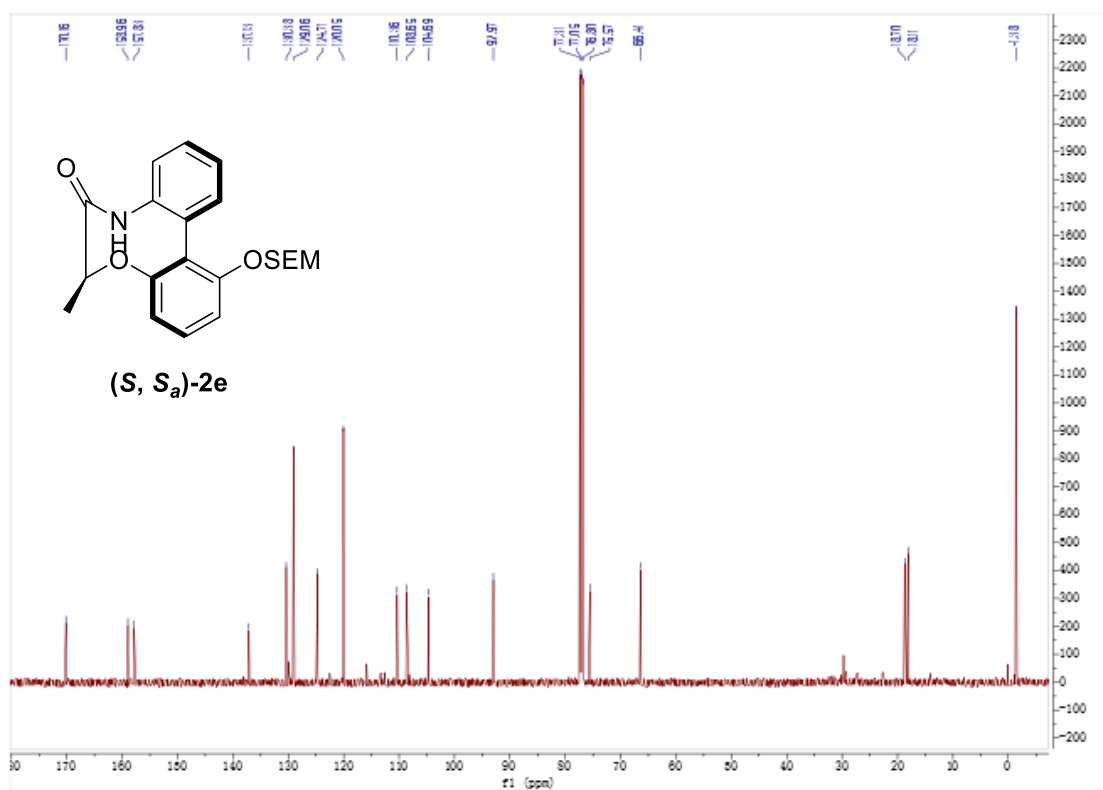
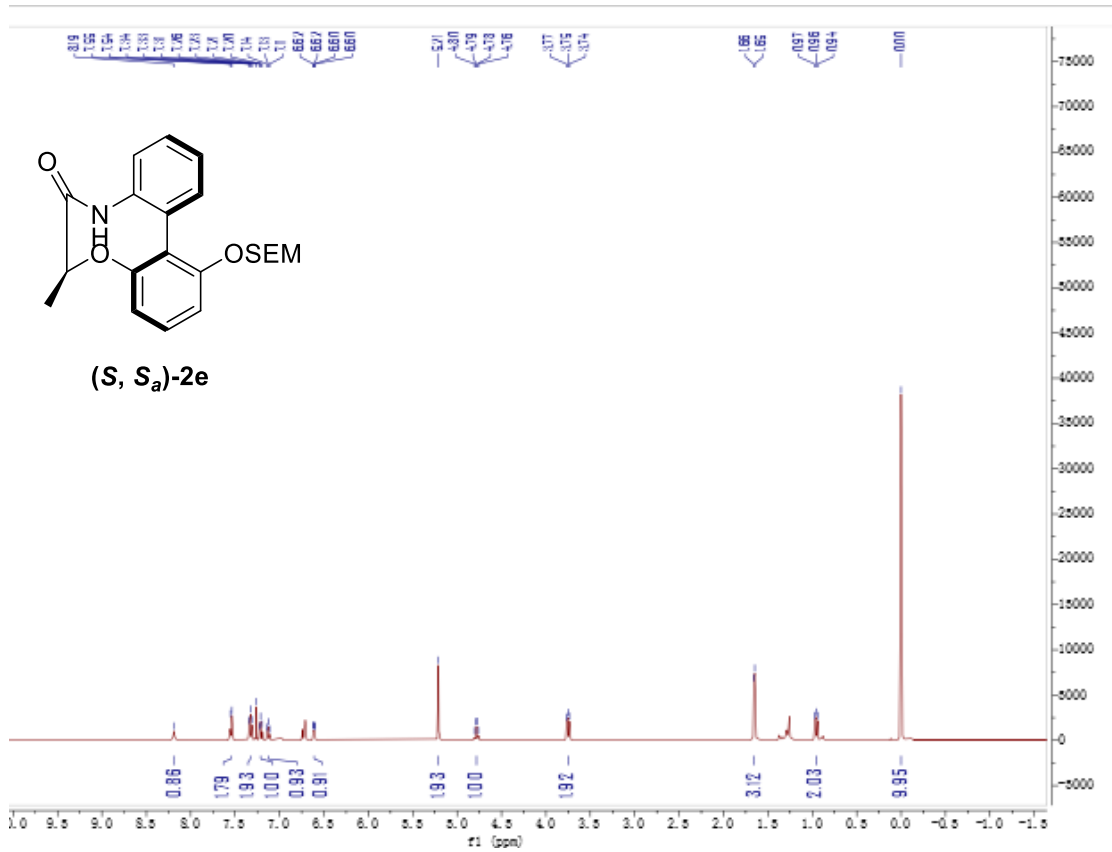
Compound (S, S<sub>a</sub>)-2c



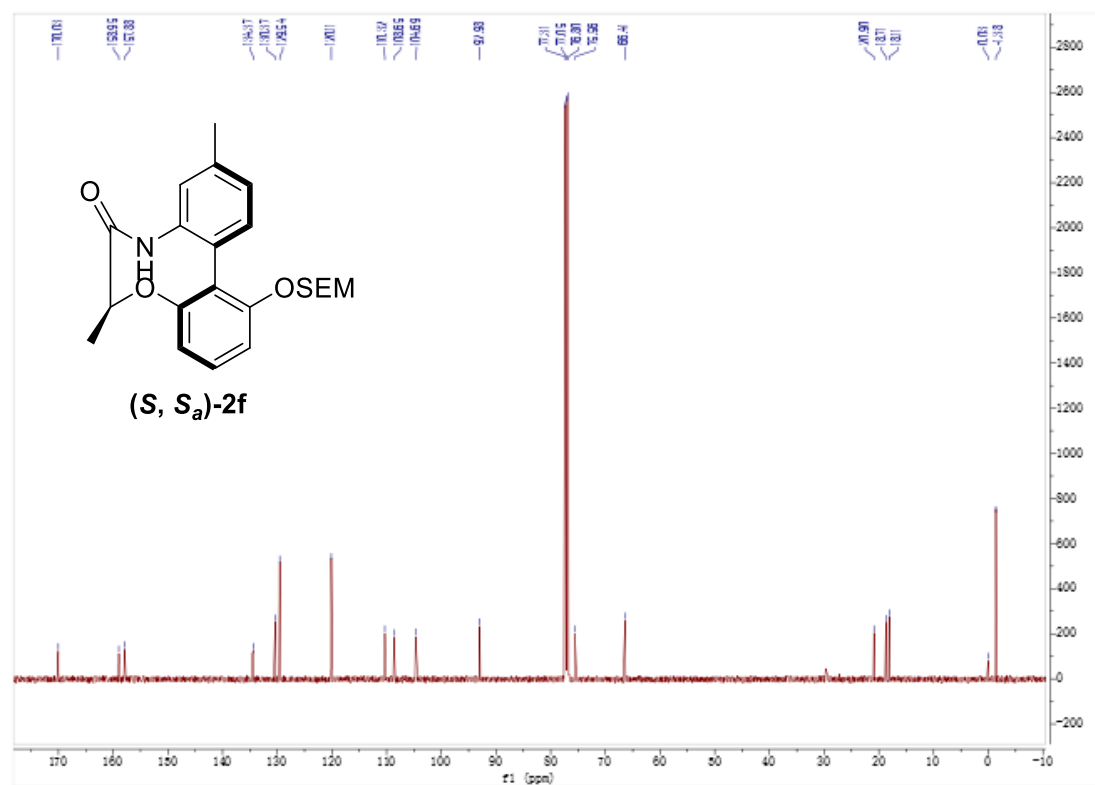
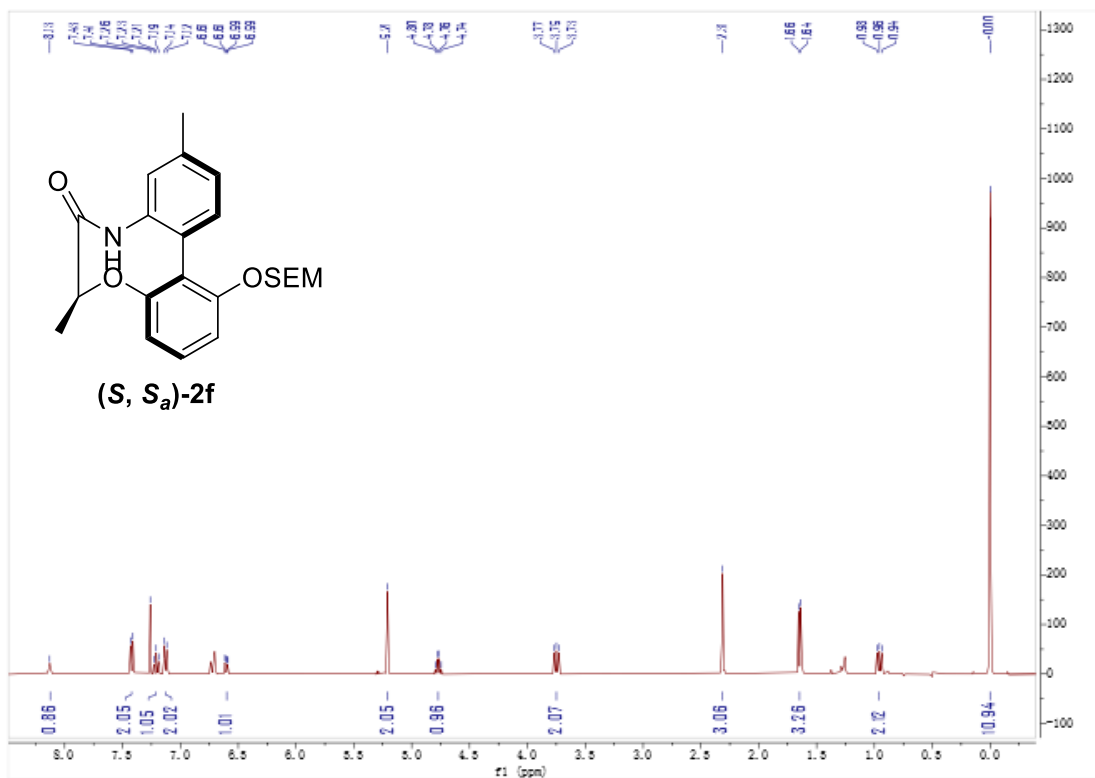
Compound **(S, S<sub>a</sub>)-2d**



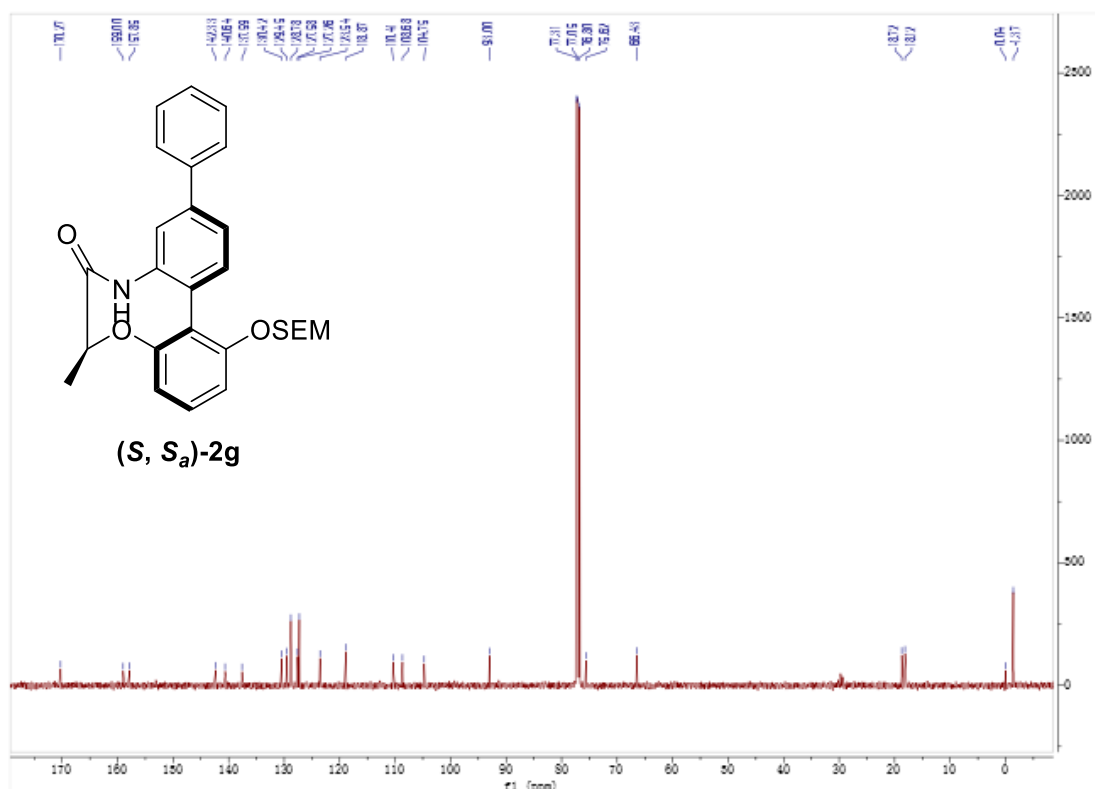
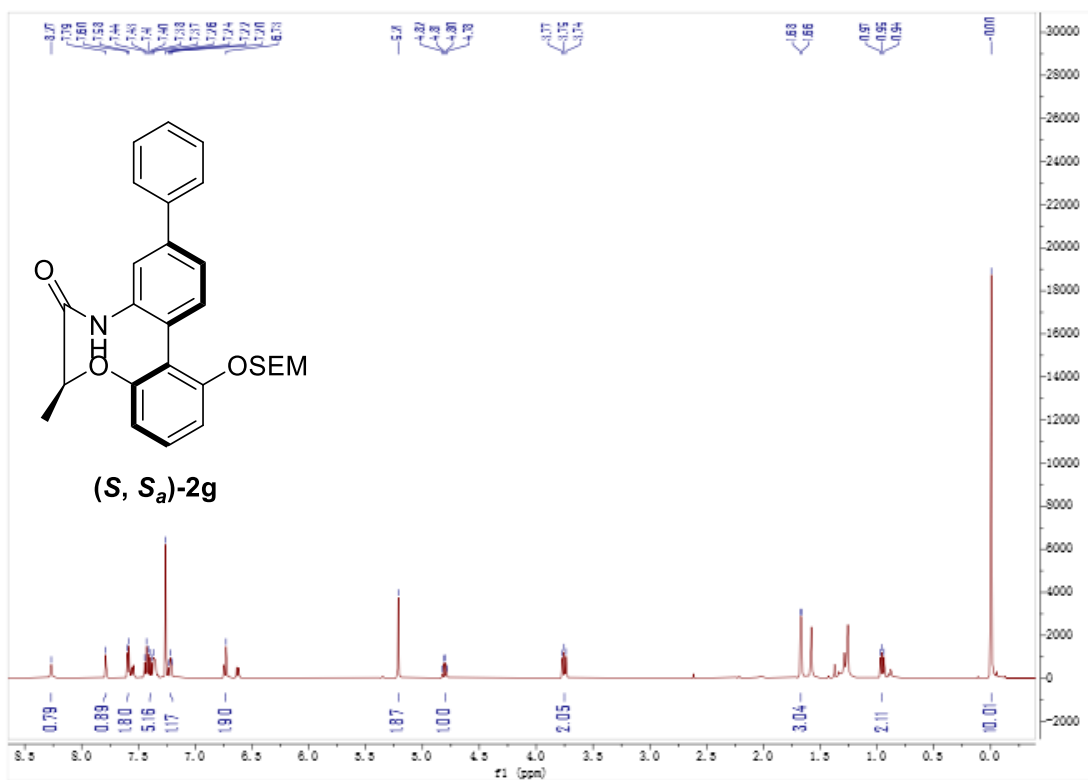
Compound (S, S<sub>a</sub>)-2e



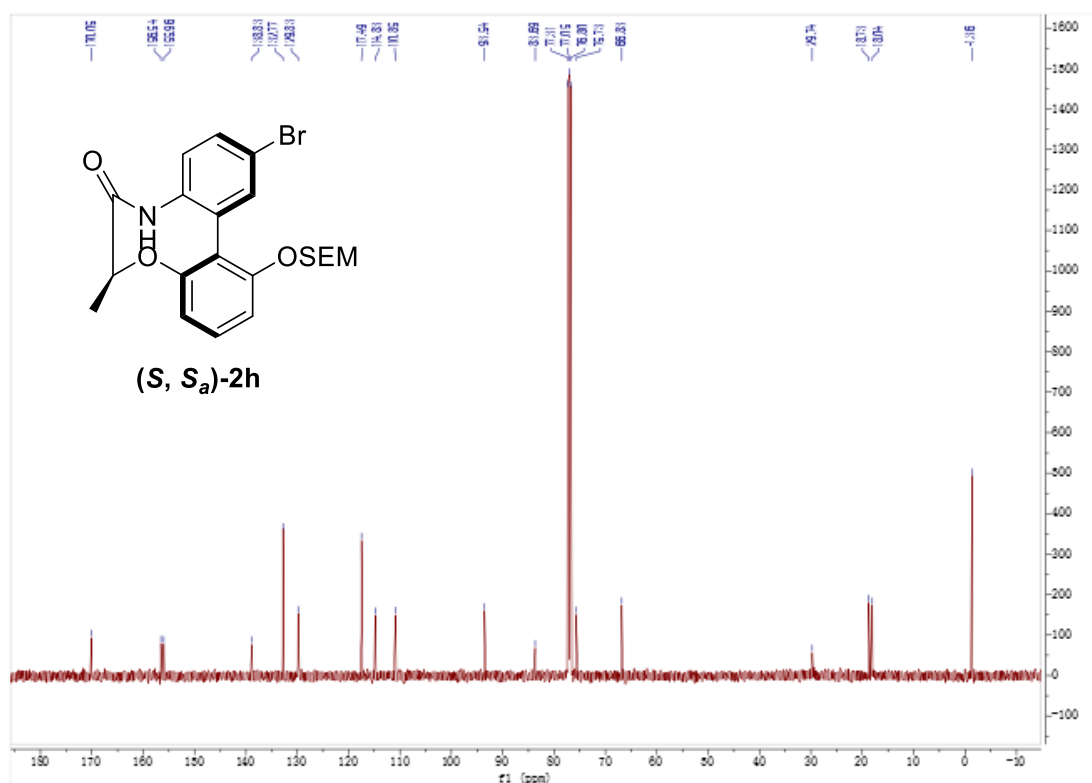
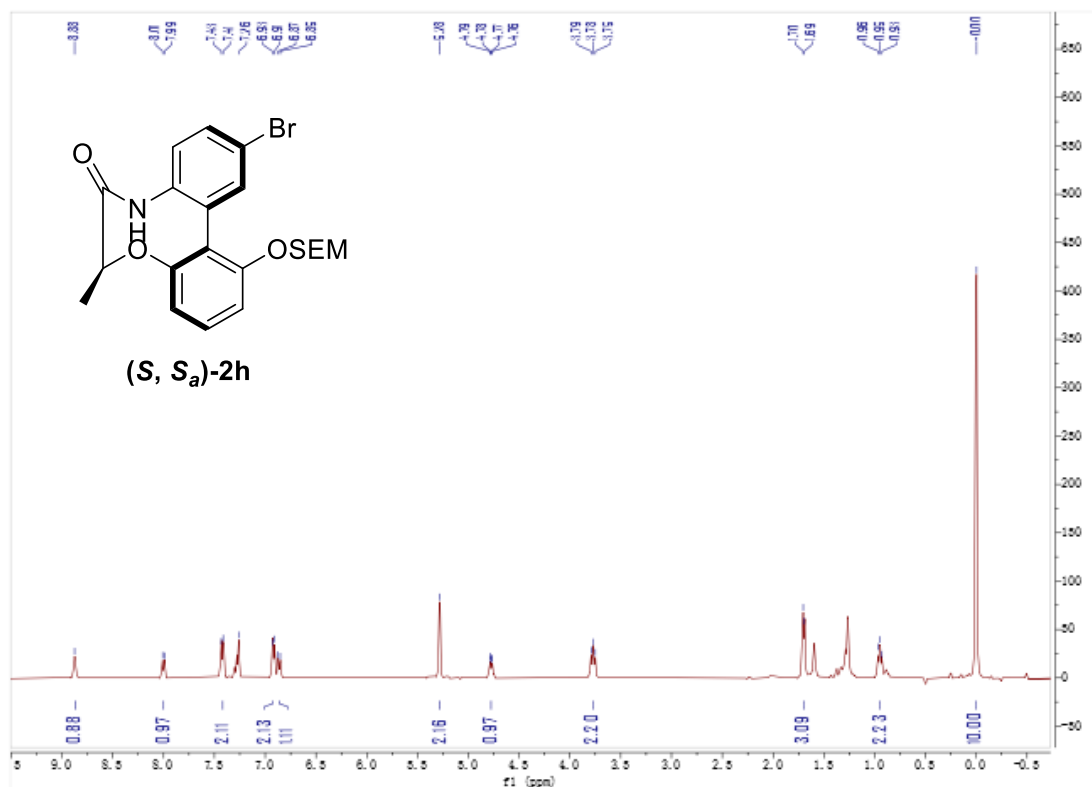
Compound (S, S<sub>a</sub>)-2f



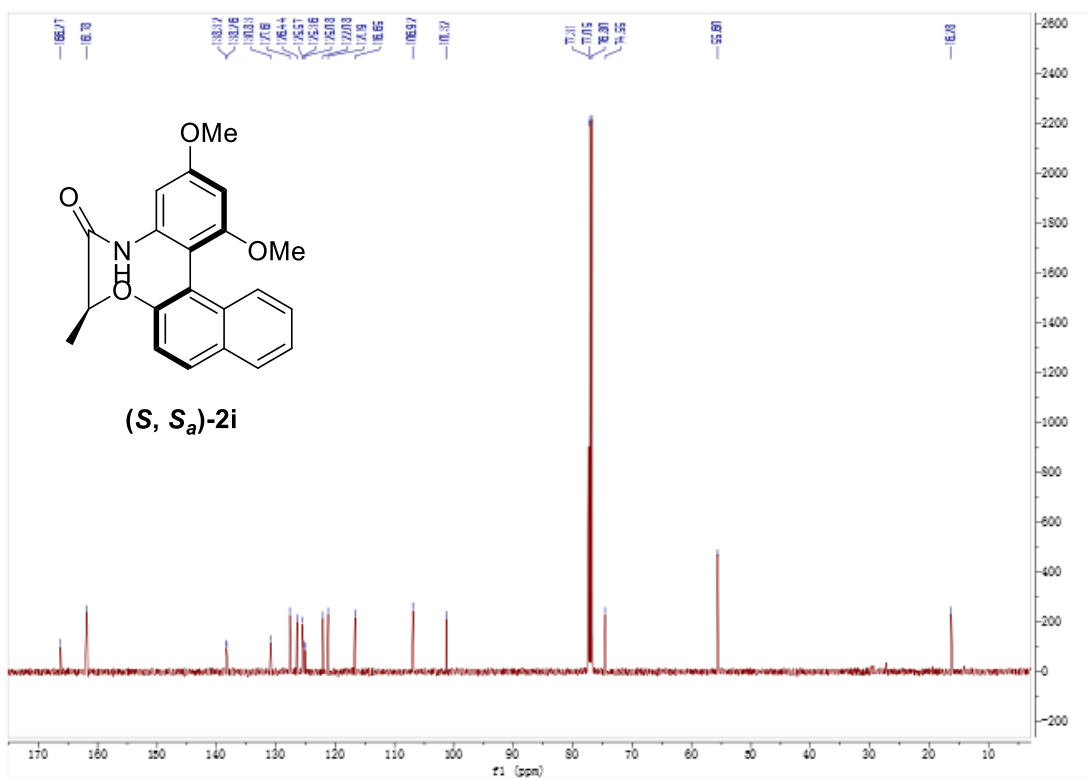
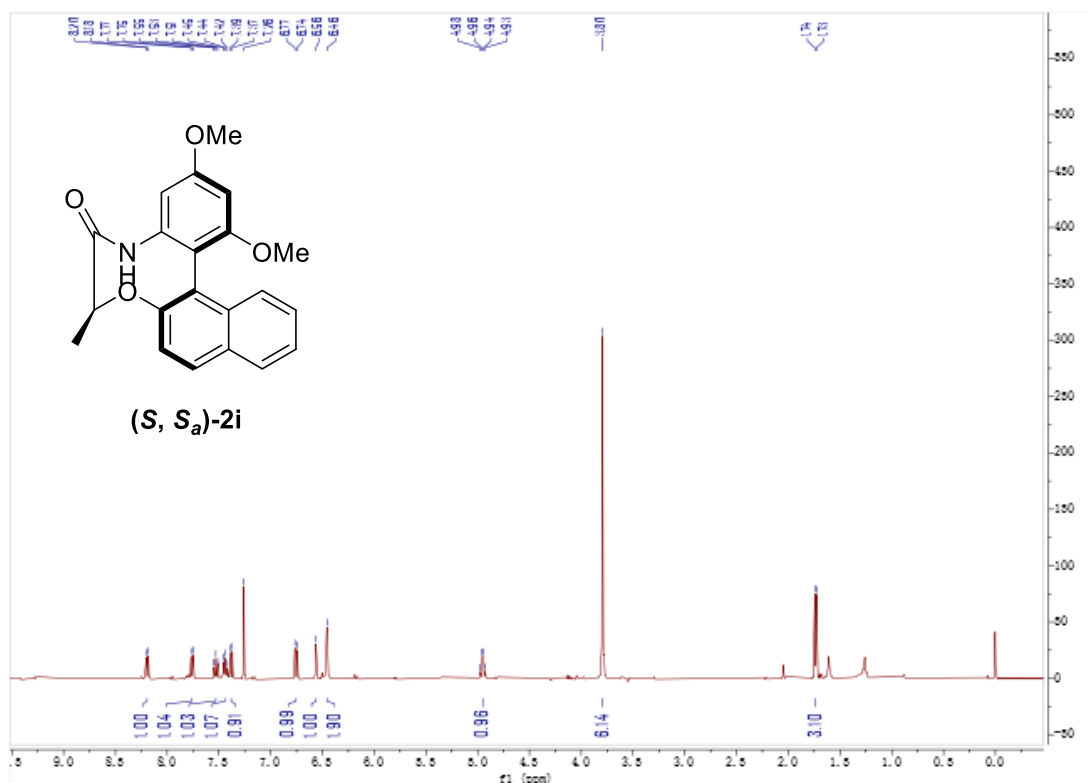
Compound **(S, S<sub>a</sub>)-2g**



Compound (S, S<sub>a</sub>)-2h

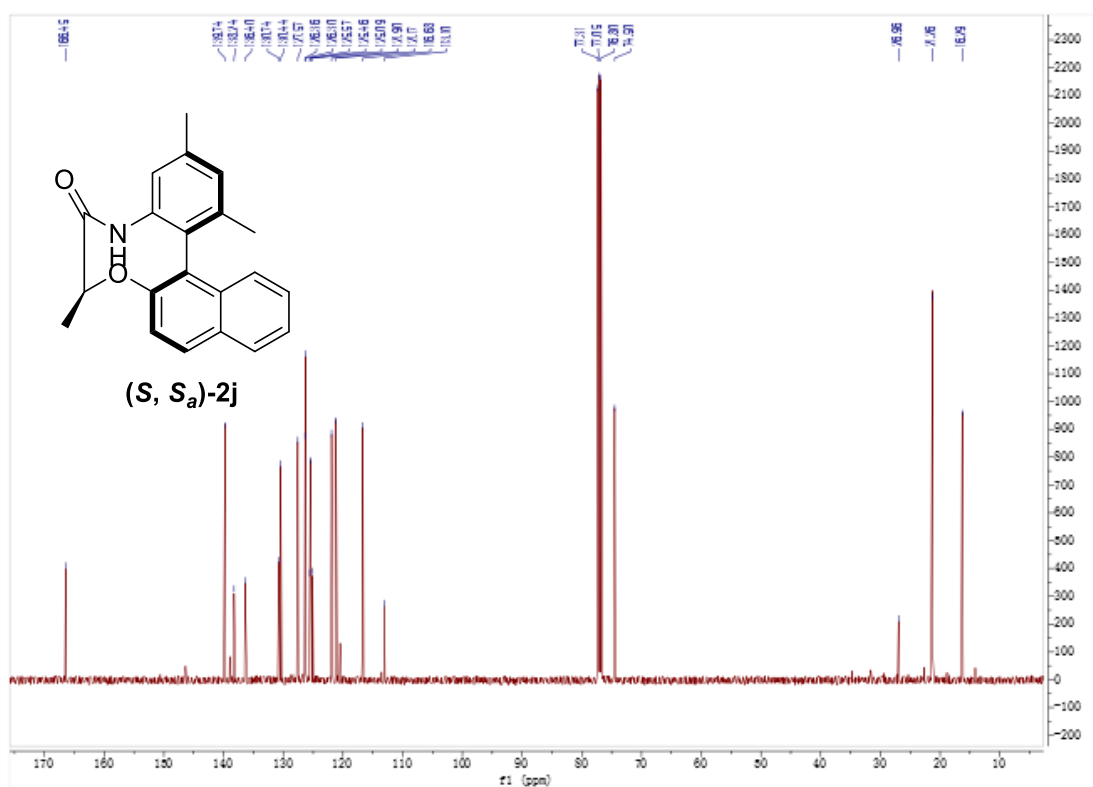
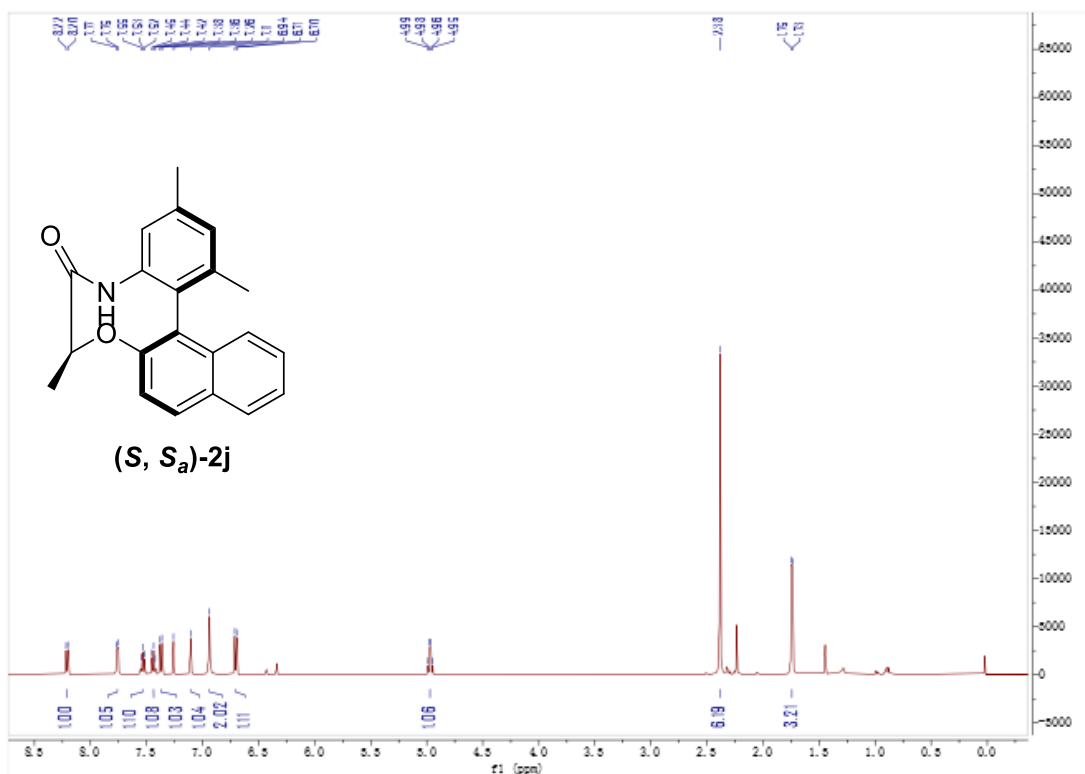


Compound (S, S<sub>a</sub>)-2i

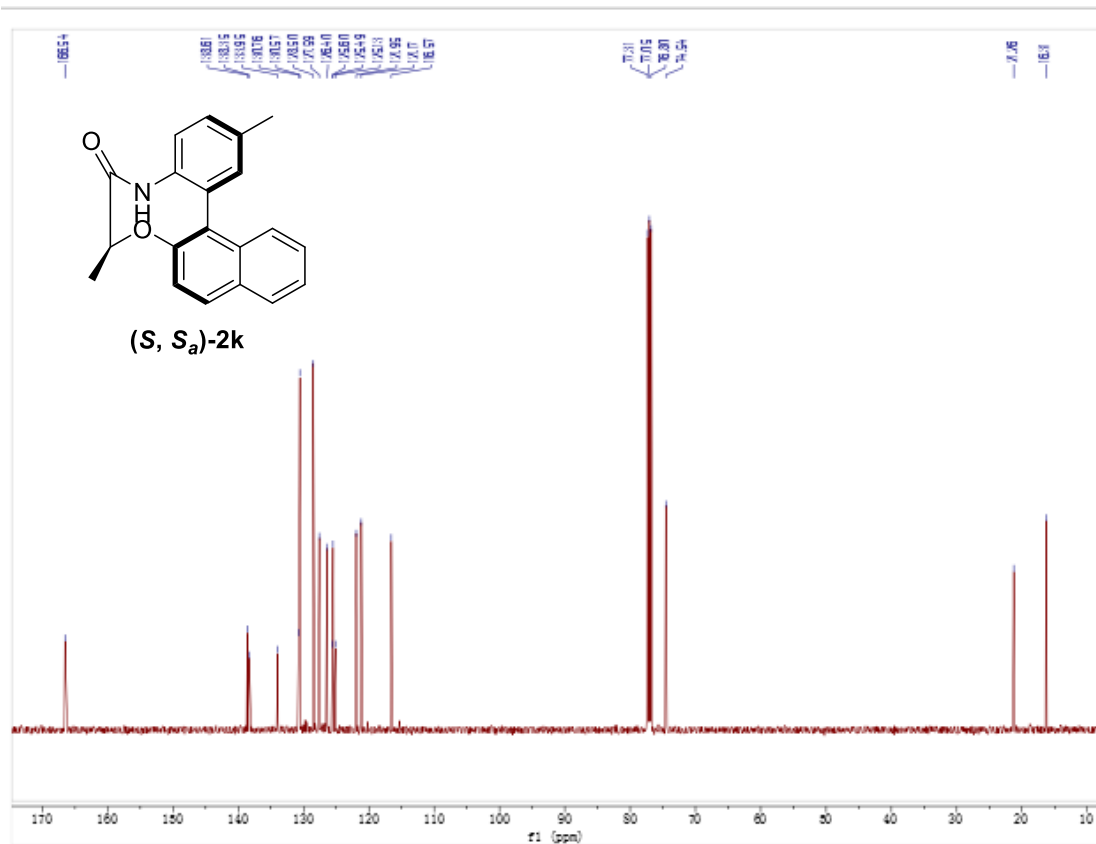
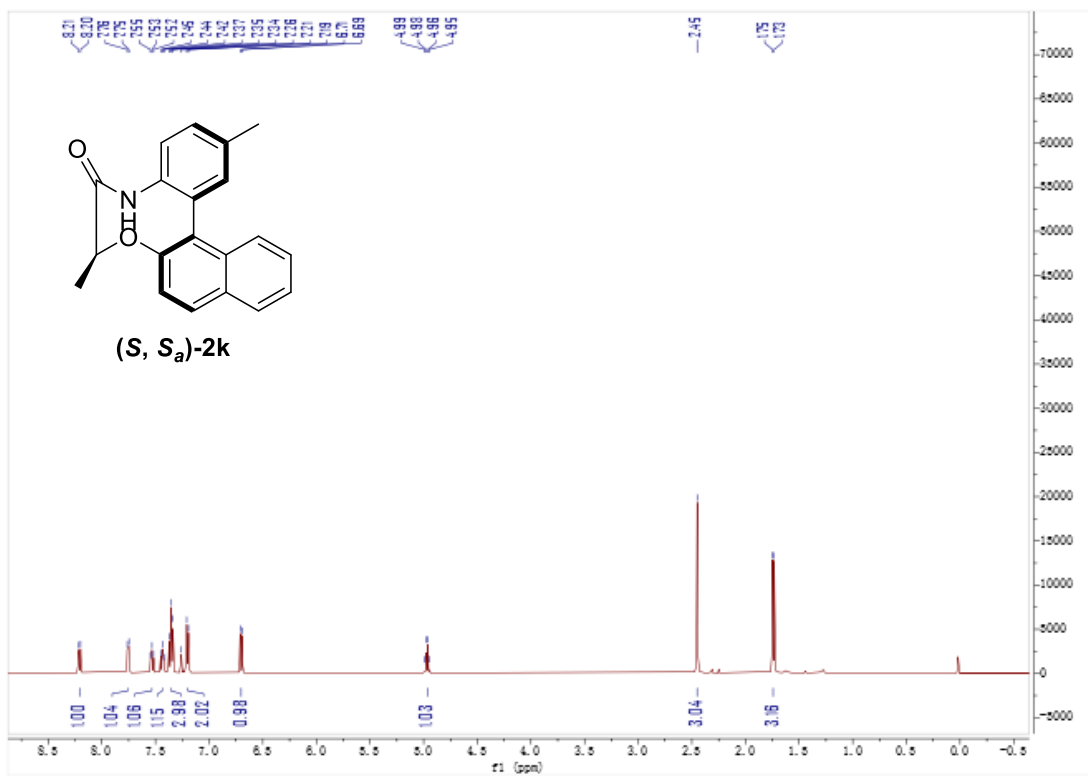


Compound **(S, S<sub>a</sub>)-2j**

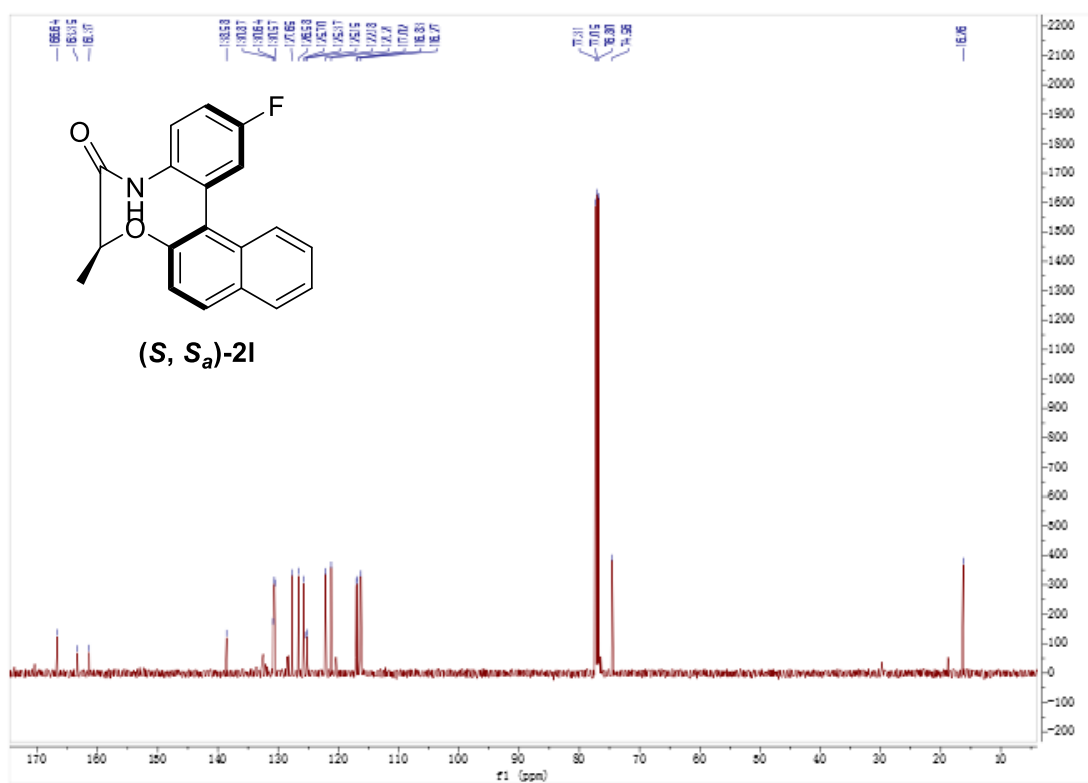
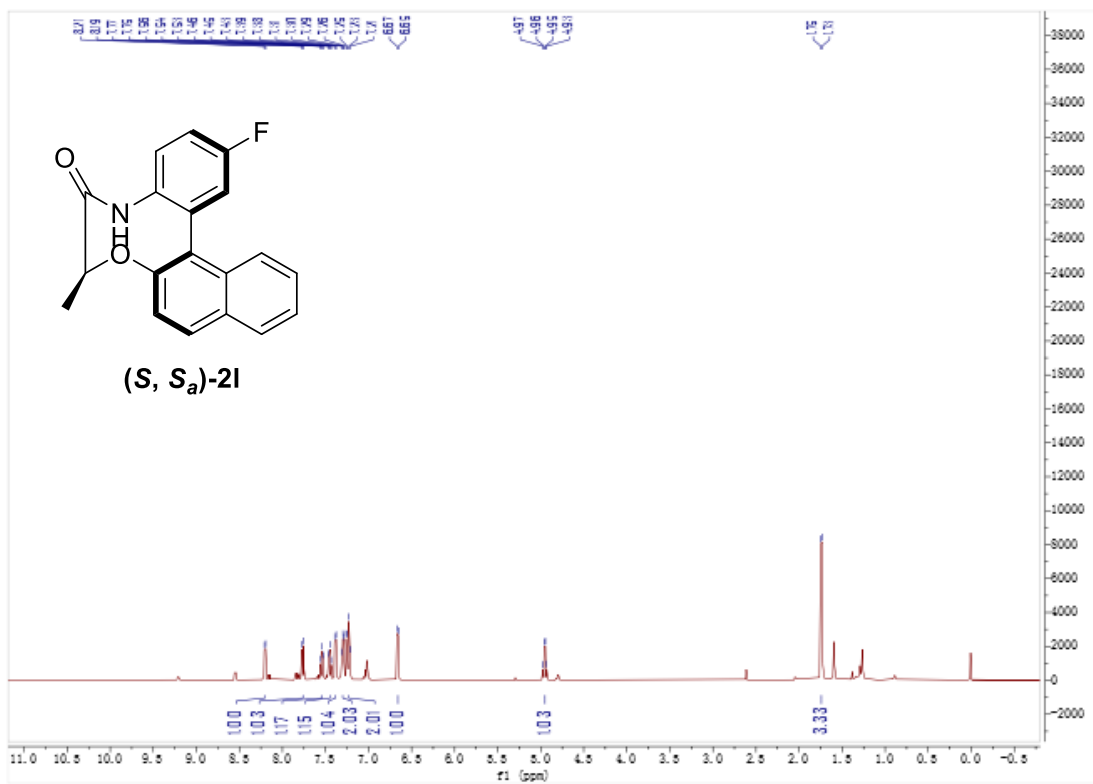


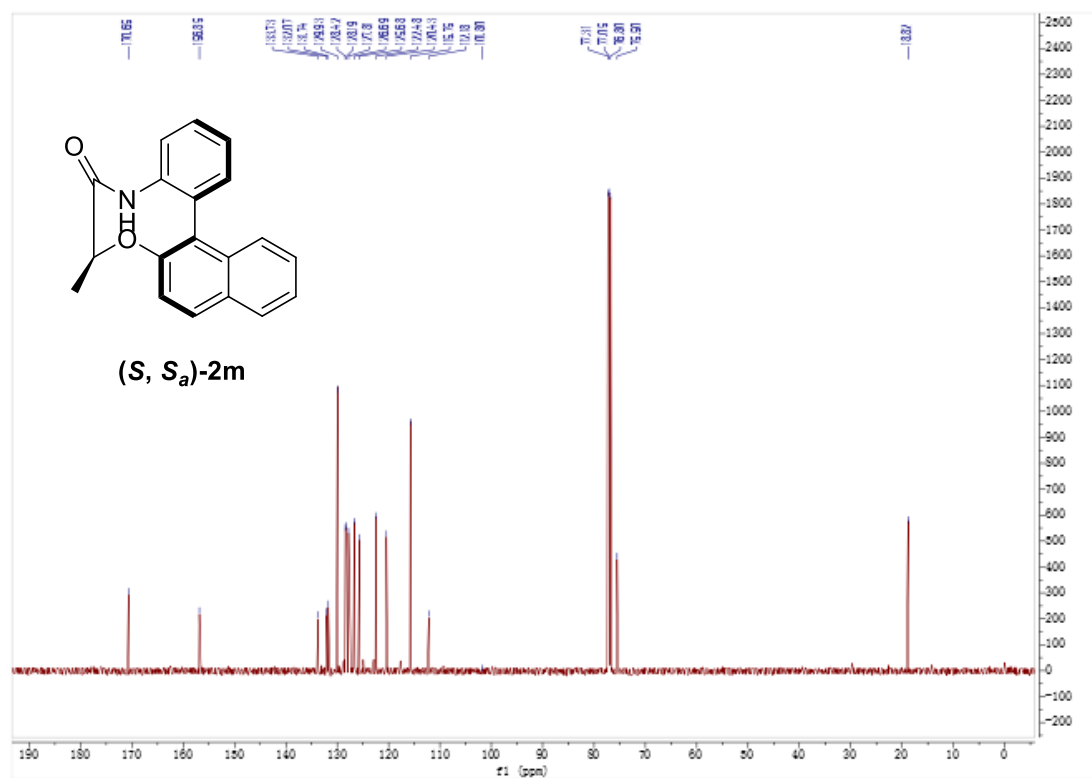
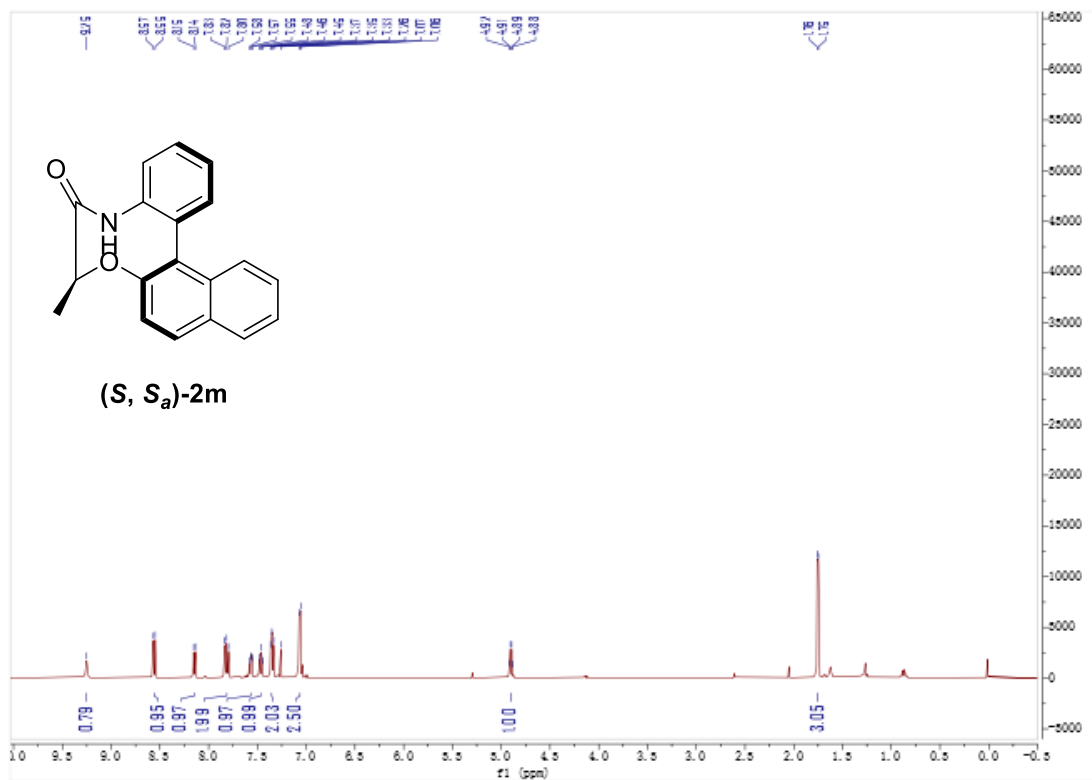


Compound (S, S<sub>a</sub>)-2k



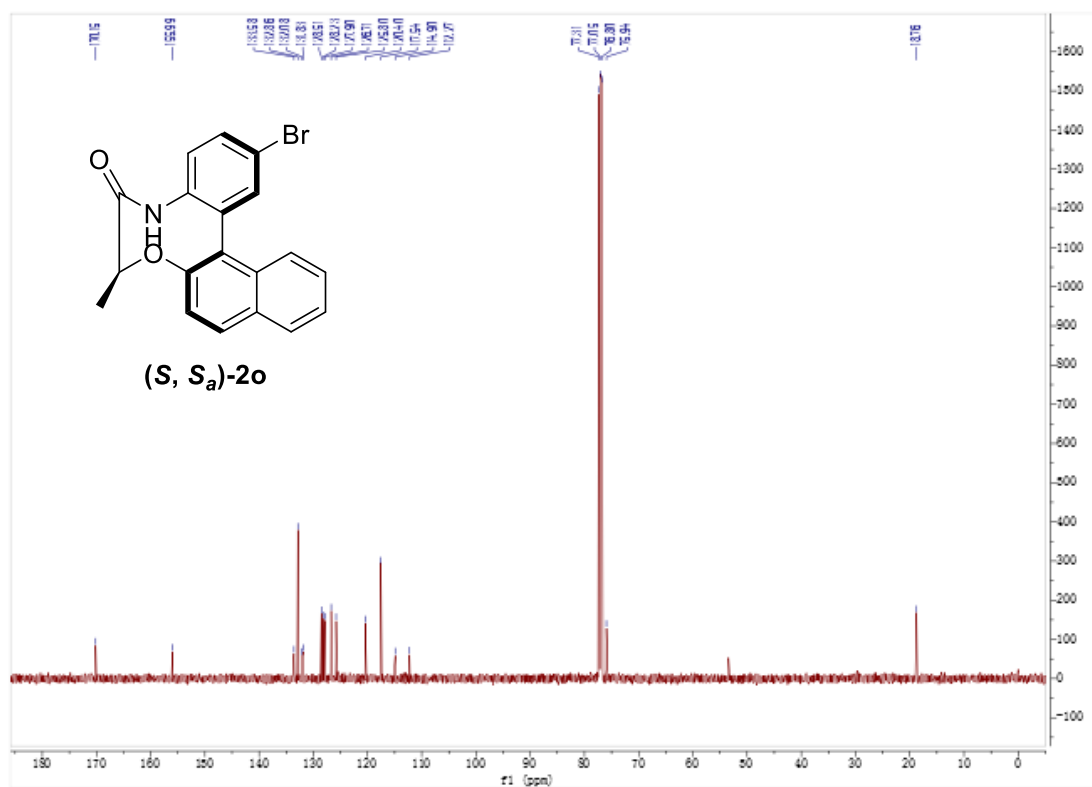
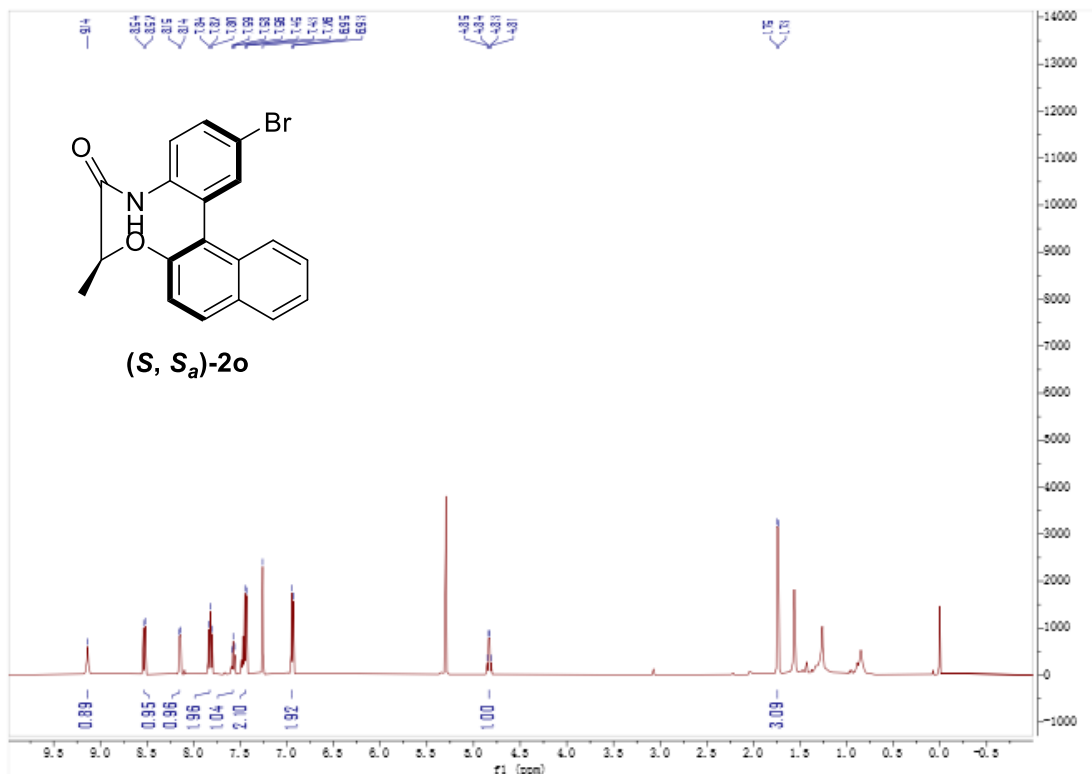
Compound (S, S<sub>a</sub>)-21



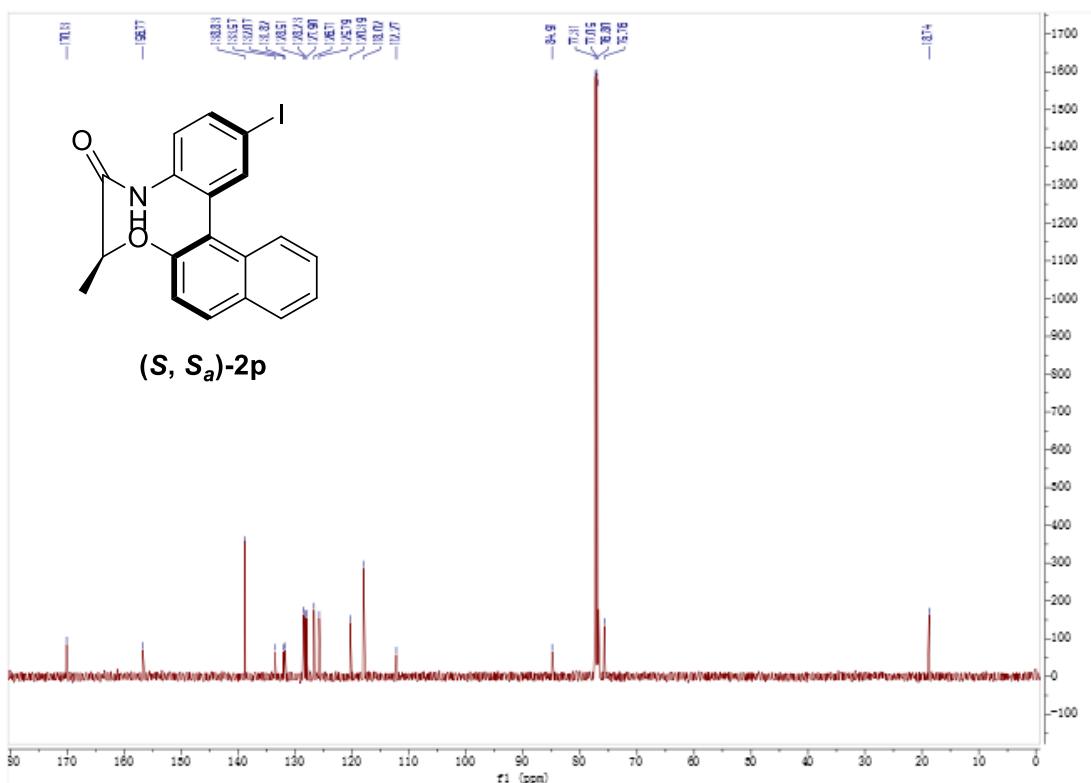
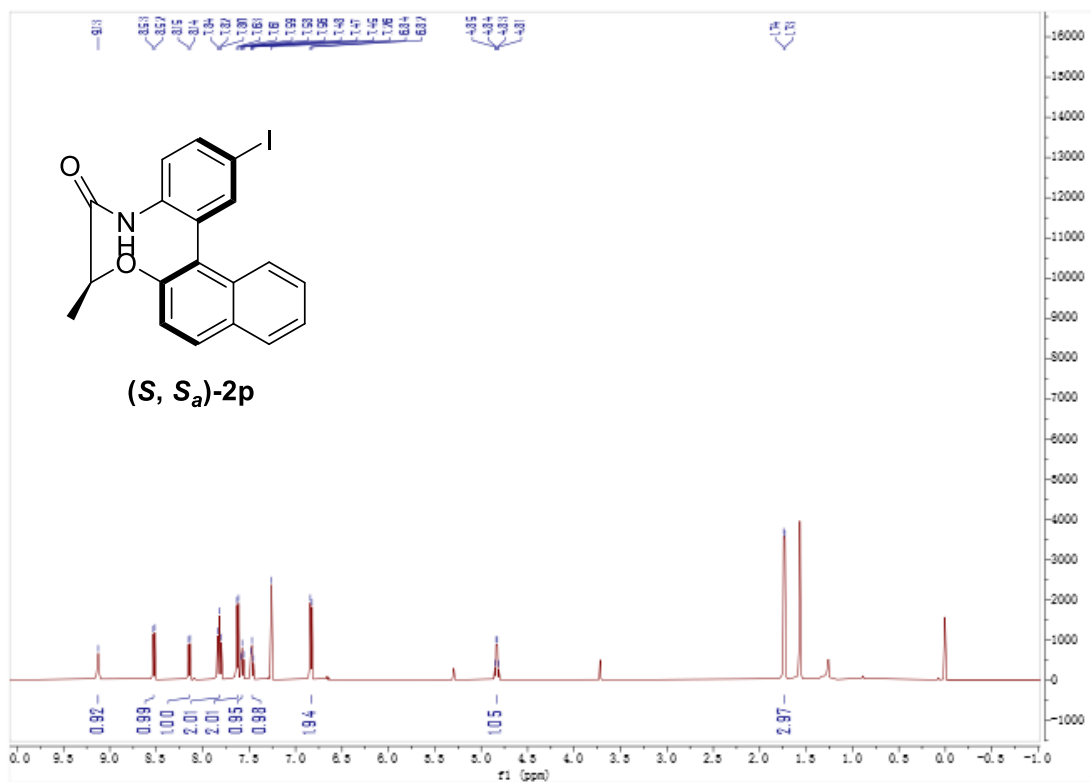


Compound **(S, S<sub>a</sub>)-2n**

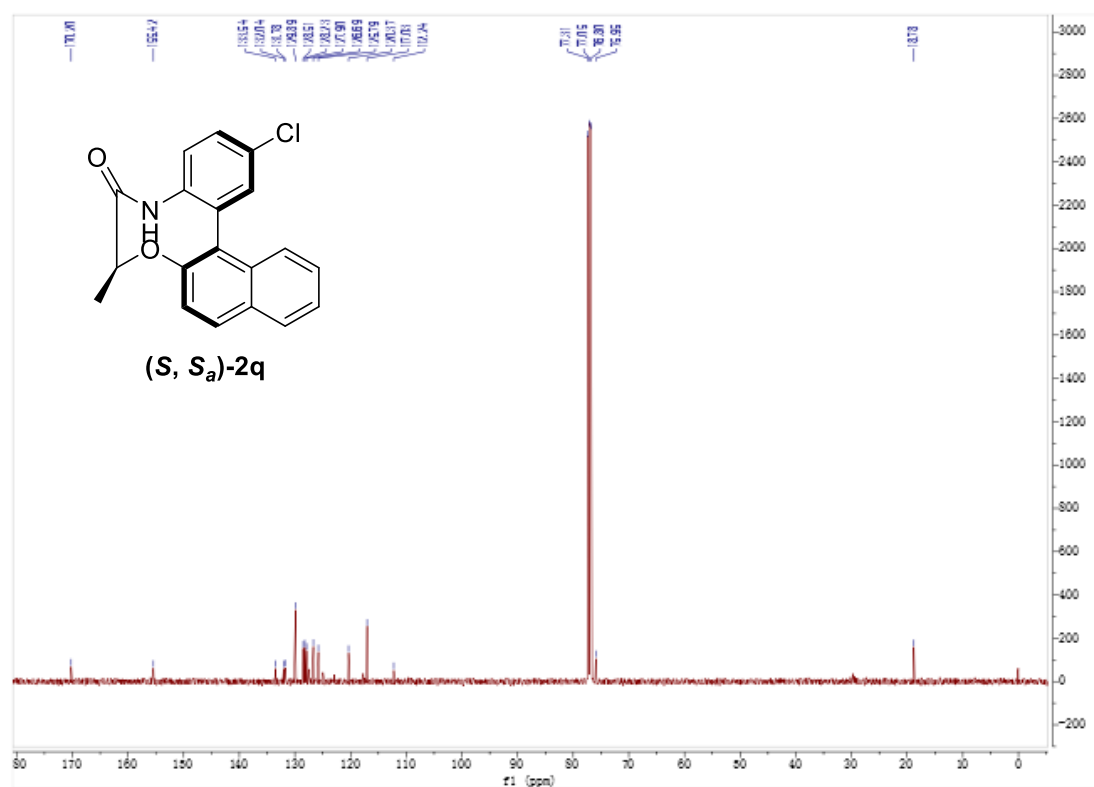
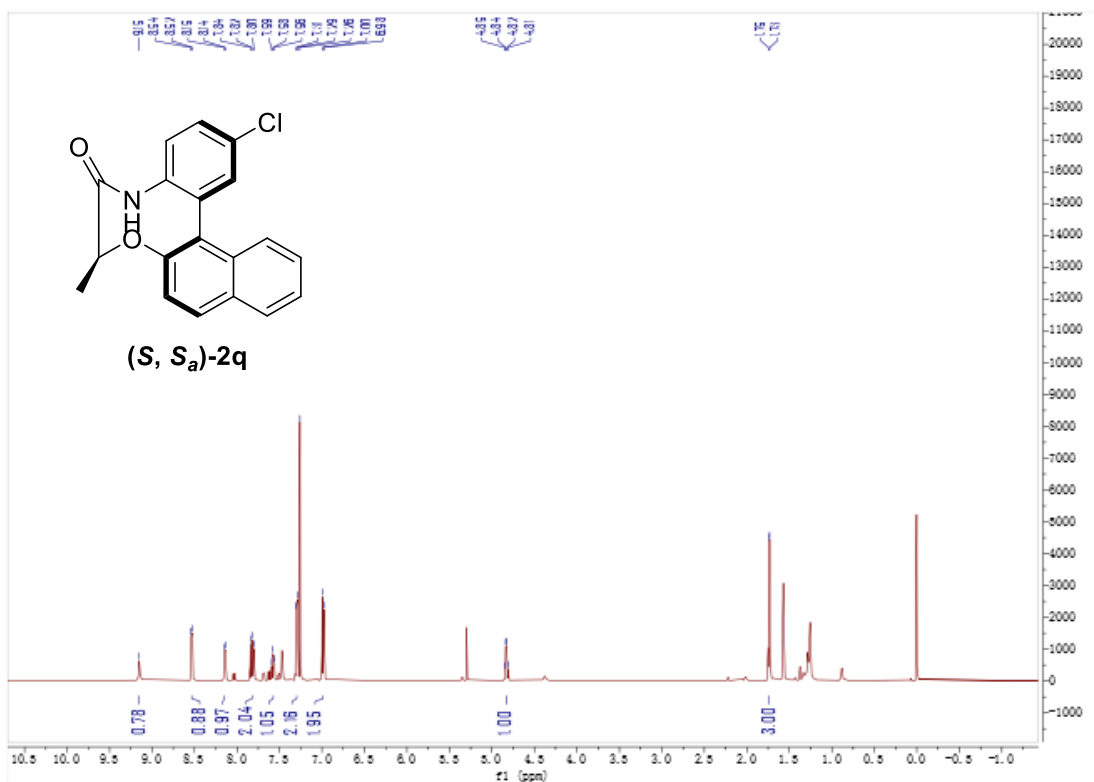




Compound (S, S<sub>a</sub>)-2p

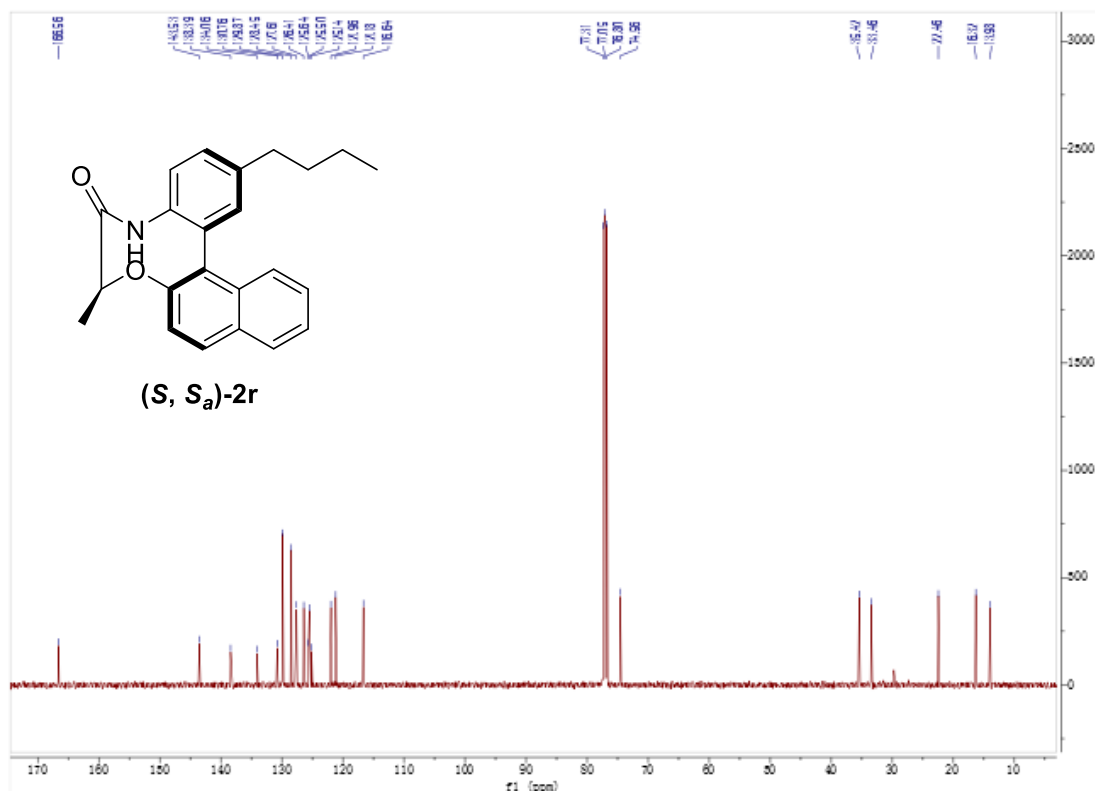
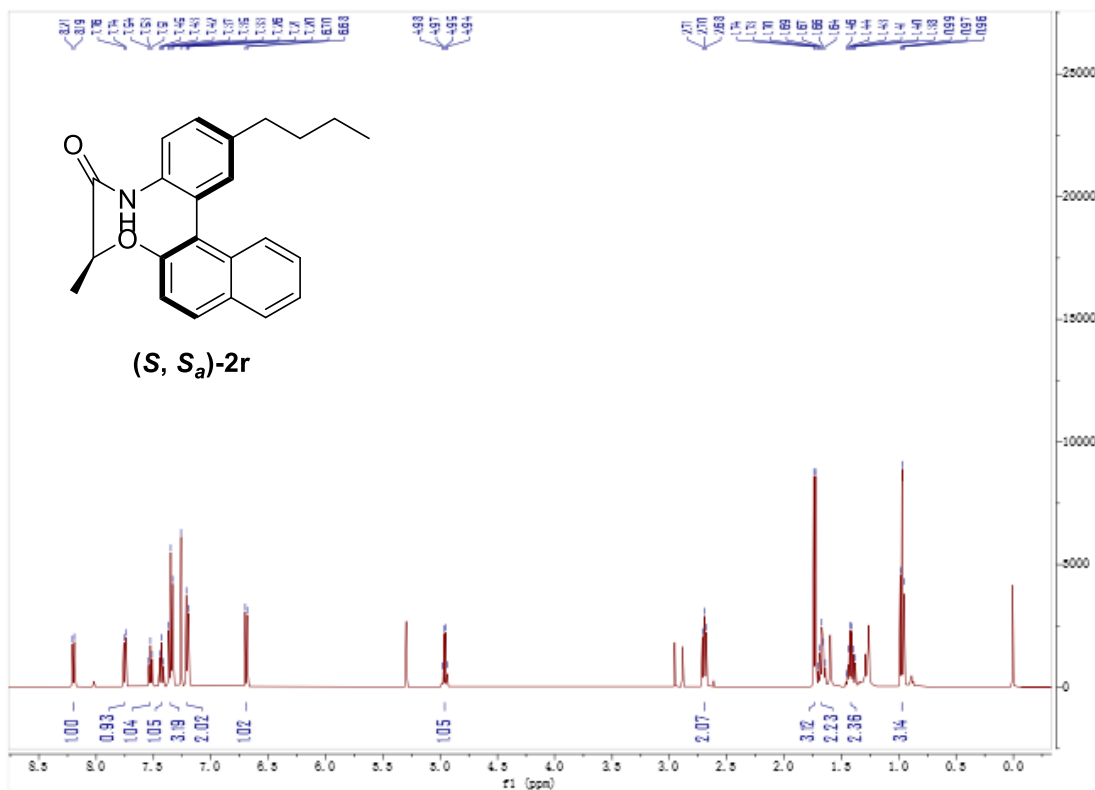


Compound (S, S<sub>a</sub>)-2q

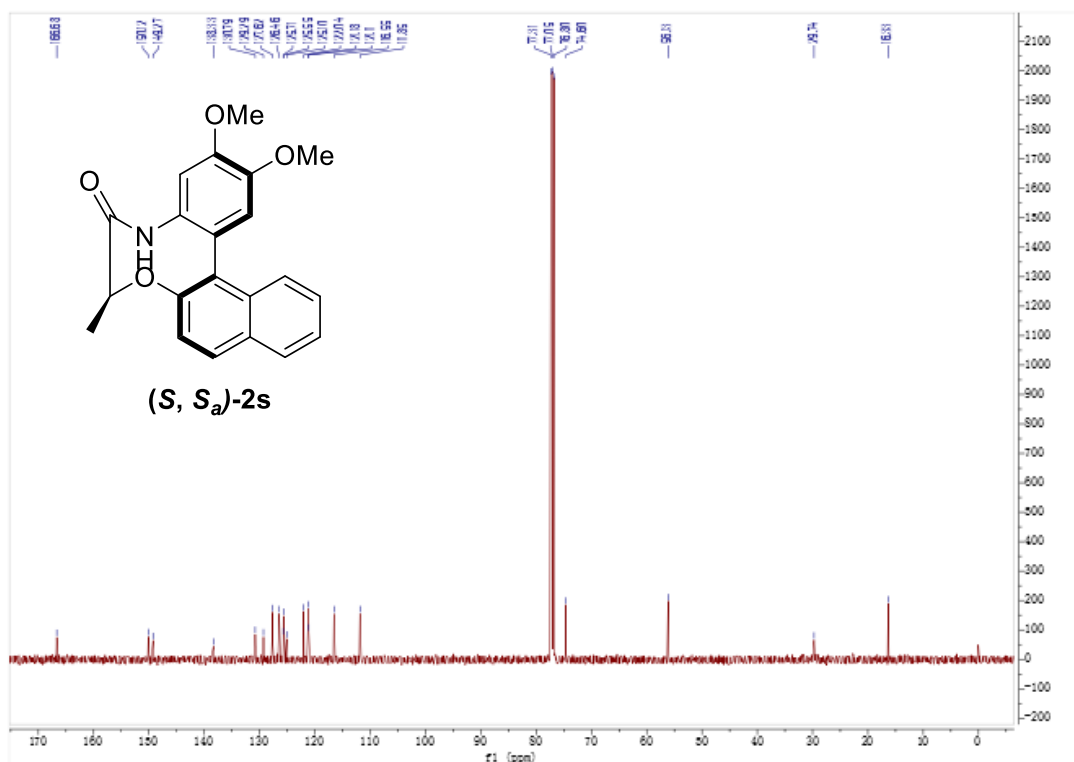
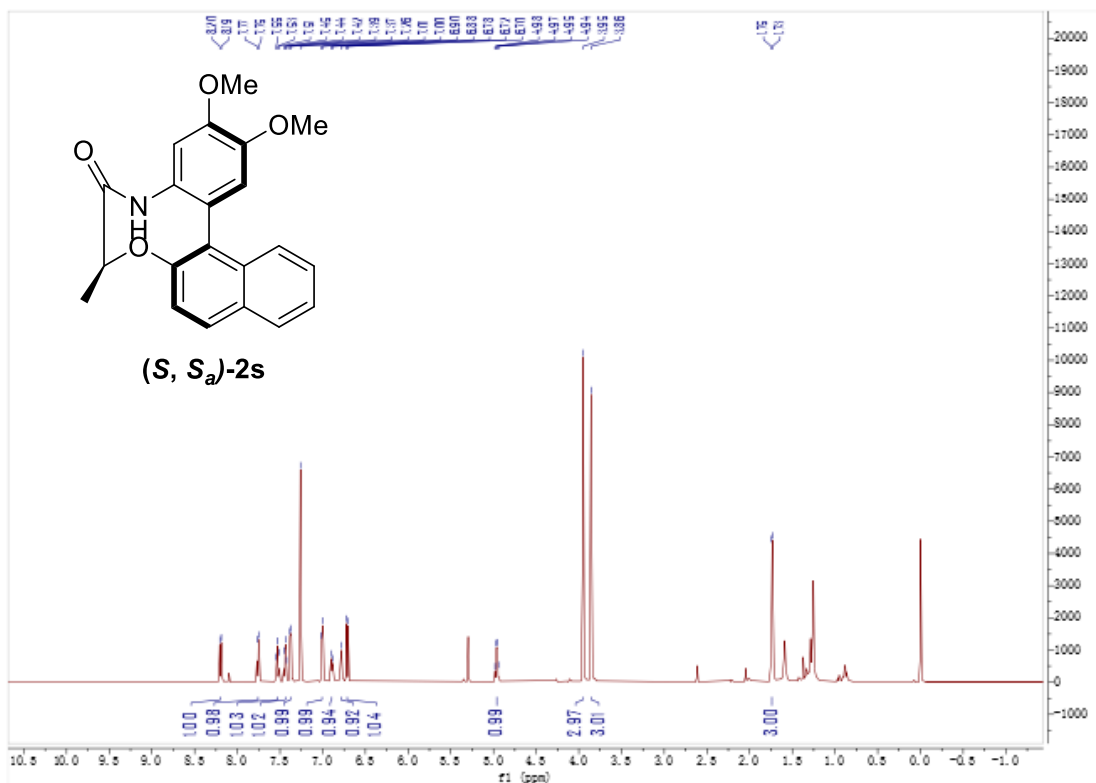


Compound **(S, S<sub>a</sub>)-2r**

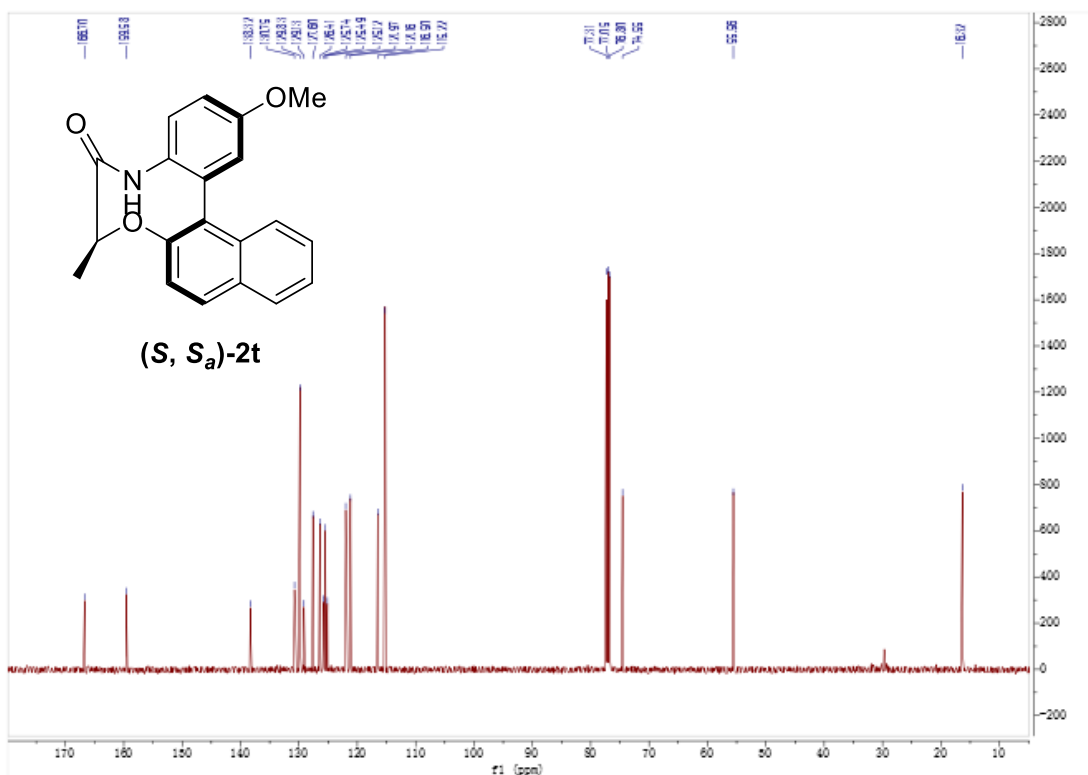
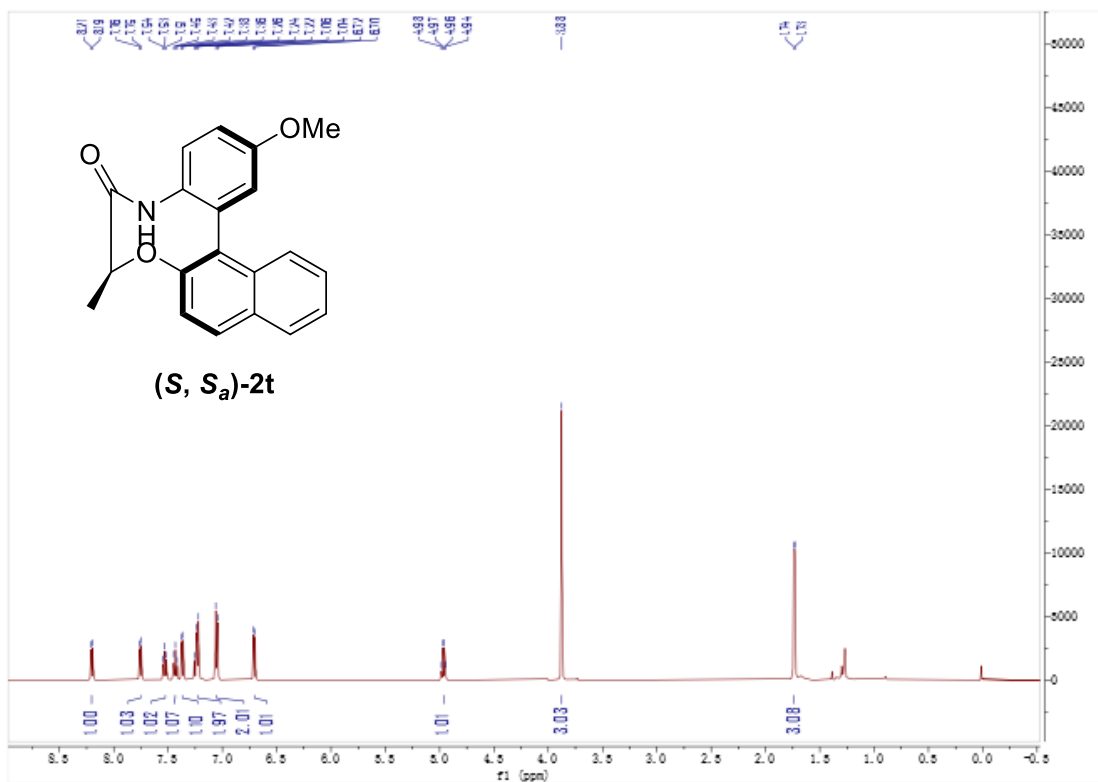




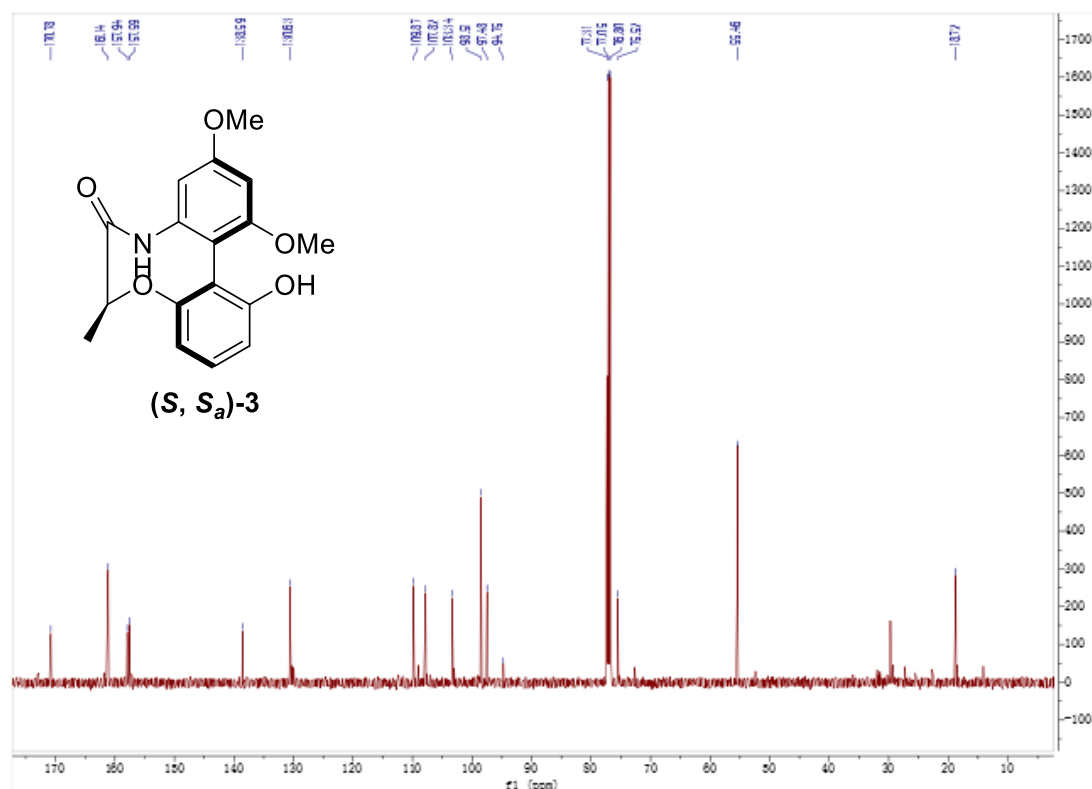
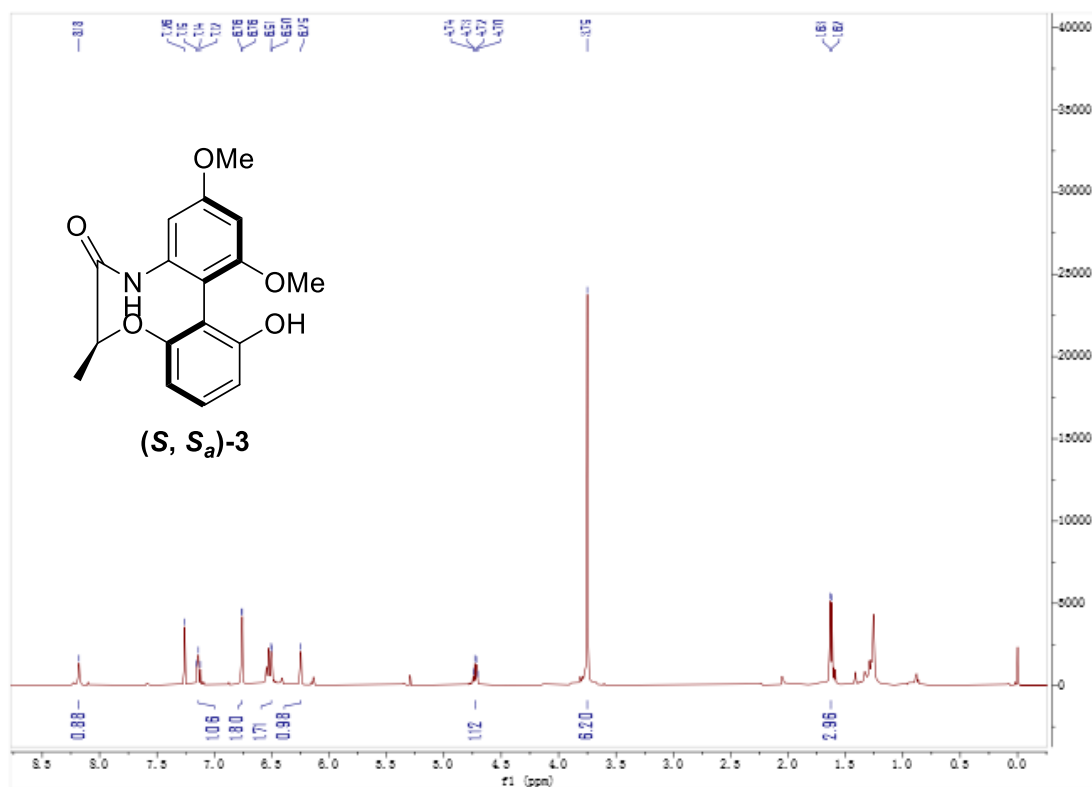
Compound (S, S<sub>a</sub>)-2s



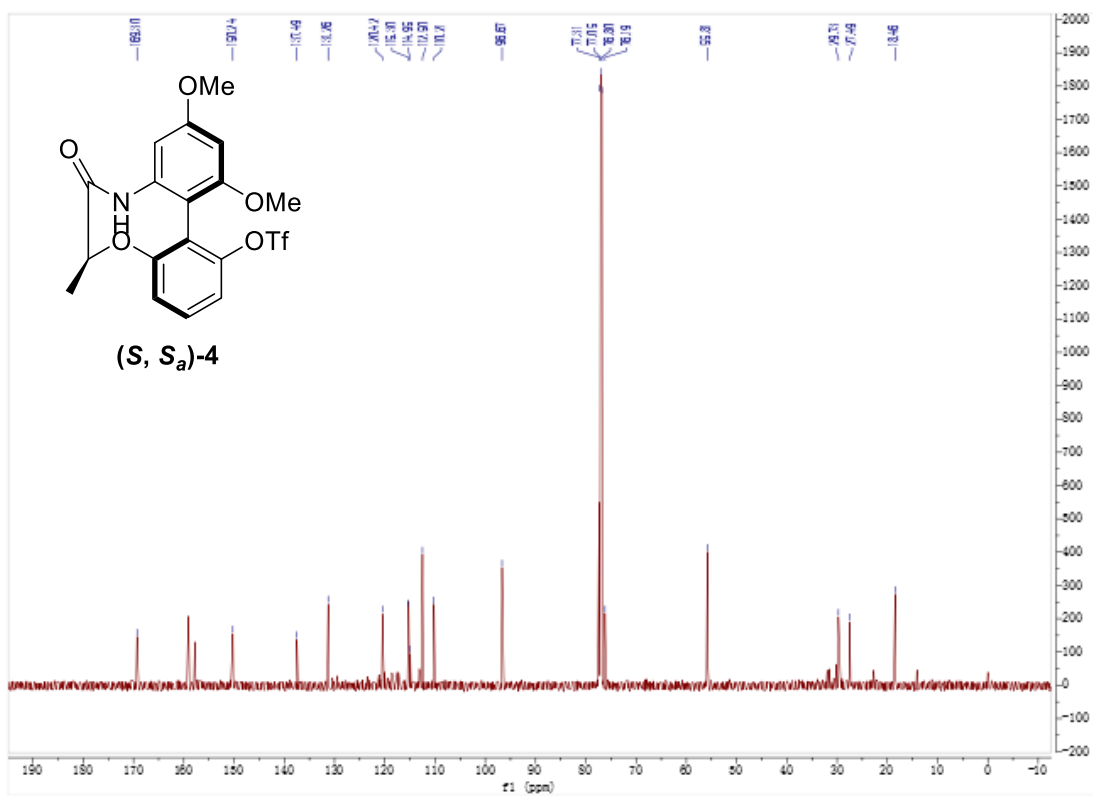
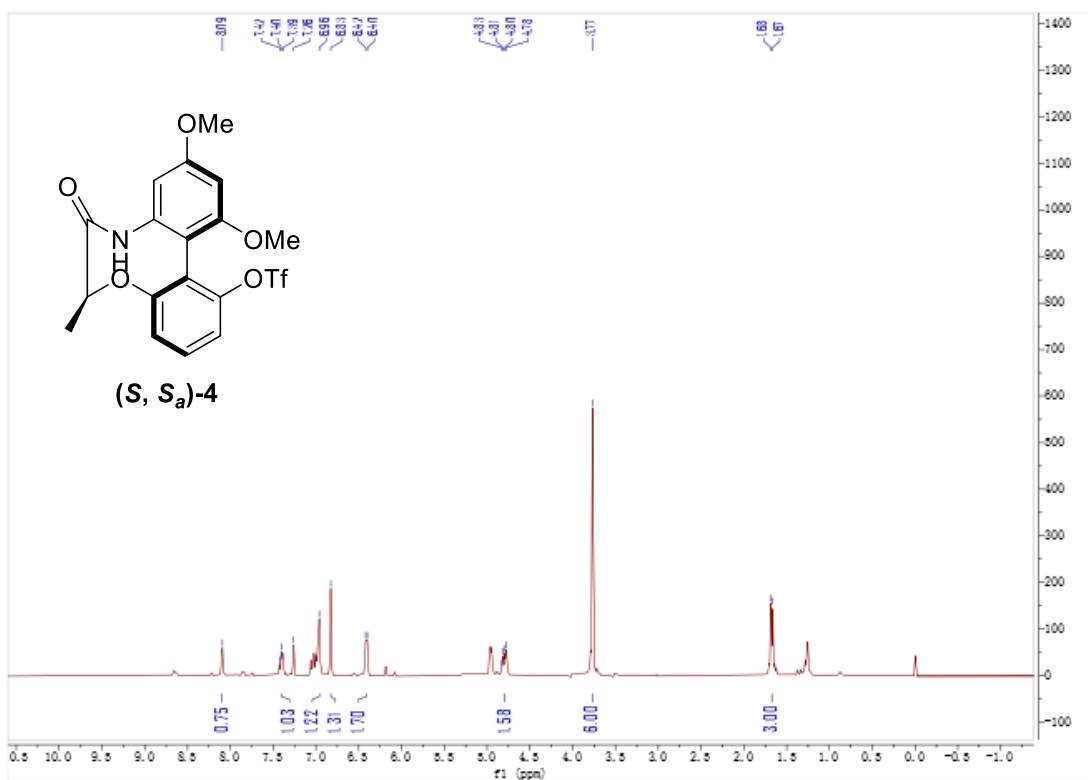
Compound (S, S<sub>a</sub>)-2t



Compound (S, S<sub>a</sub>)-3



Compound **(S, S<sub>a</sub>)-4**



Compound (S, S<sub>a</sub>)-5



