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# Design of Oxa-Spirocyclic PHOX Ligands for the Asymmetric Synthesis of Lorcaserin via Iridium-Catalyzed Asymmetric Hydrogenation

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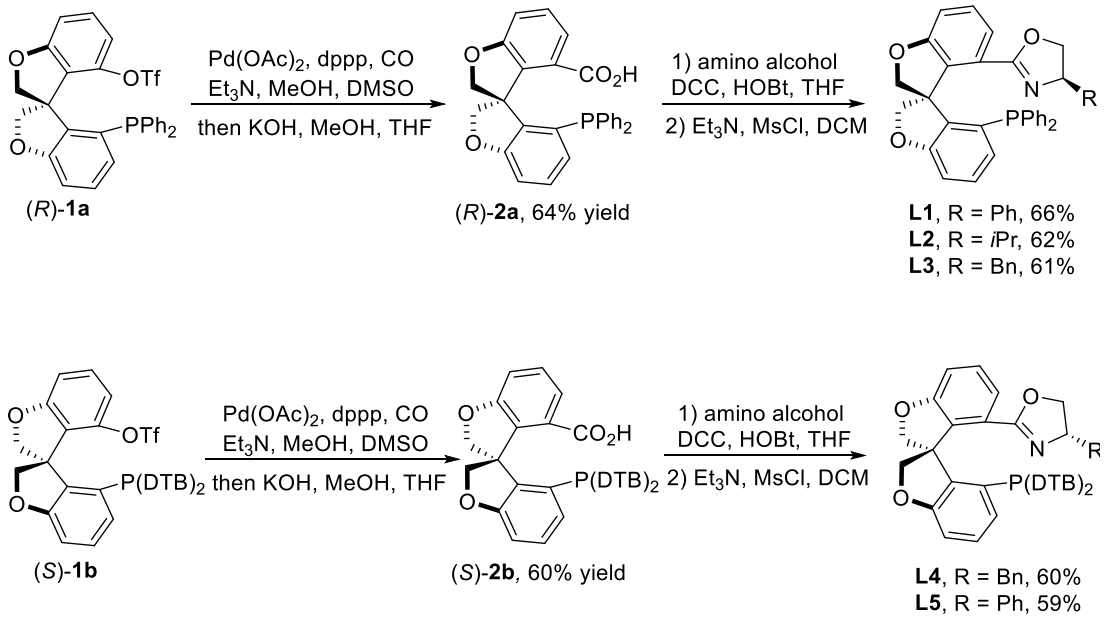
## Content

# 1. General Information

Unless otherwise mentioned, all experiments were carried out under an atmosphere of argon in a glovebox or using standard Schlenk techniques. Solvents were dried with standard procedures and degassed with Ar. Flash column chromatography was performed using Tsingdao silica gel (60, particle size 300-400 mesh). NMR spectra were recorded on a Bruker DPX 400 spectrometer at 400 MHz for $^{1}H$ NMR, 101 MHz for $^{13}C$ NMR and 162 MHz for $^{31}P$ NMR or a Bruker DPX 600 spectrometer at 600 MHz for $^{1}H$ NMR, 151 MHz for $^{13}C$ NMR and 243 MHz for $^{31}P$ NMR in $CDCl_3$ with tetramethylsilane (TMS) as internal standard. Chemical shifts are reported in ppm and coupling constants are given in Hz. Chemical shifts were reported relative to TMS (0.00 ppm) for $^{1}H$ NMR and relative to $CDCl_3$ (77.0 ppm) for $^{13}C$ NMR.

## 2. Preparation and Analytical Data of Ligands

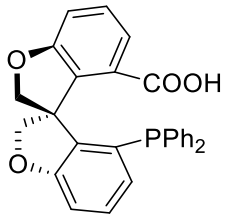
Ligands **L1**-**L5** were synthesized according to a reported procedure:[1, 2]




**Scheme S1**. Synthesis of **L1**-**L5**

Synthesis of compound (*R*)**-2a** and (*S*)**-2b**:

**(*R*)-4'-(diphenylphosphanyl)-2*H*,2'*H*-3,3'-spirobi[benzofuran]-4-carboxylic acid ((*R*)-2a):**

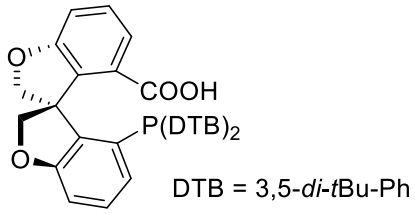


Chemical Formula: $C_{28}H_{21}O_4P$
Exact Mass: 452.1177

**Typical procedure:** To a solution of triflates (*R*)**-1a** (3.90 g, 7.0 mmol) in MeOH (42 mL), $Pd(OAc)_2$ (259 mg, 1.16 mmol), 1,3-bis(diphenylphosphino)propane (dppp, 478 mg, 1.16 mmol), DMSO (60 mL) and $Et_3N$ (11.6 mL) were successively added. The resulting mixture was saturated with CO and stirred under a CO atmosphere at 70°C. The reaction mixture was monitored by TLC until full conversion of (*R*)**-1a**. After cooling to room temperature, the mixture was concentrated under reduced pressure. The

residue was subjected to KOH hydrolysis. The product (*R*)-**2a** was afforded as white solid after purification by column chromatography (2.02 g, yield = 64%), $[\alpha]^{25}_{D}$ = +23.40 (c = 0.5, methanol), mp: 182 – 184 °C. $^{1}$H NMR (400 MHz, Chloroform-*d*) : δ 7.32 – 7.22 (m, 4H), 7.22 – 7.14 (m, 3H), 7.13 – 7.01 (m, 4H), 6.90 – 6.79 (m, 2H), 6.69 – 6.64 (m, 1H), 6.29 (dd, *J* = 8.0, 0.8 Hz, 1H), 5.73 (dd, *J* = 8.0, 0.8 Hz, 1H), 5.01 (dd, *J* = 9.2, 2.6 Hz, 1H), 4.67 (d, *J* = 9.3 Hz, 1H), 4.62 (dd, *J* = 9.2, 1.3 Hz, 1H), 4.53 (d, *J* = 9.3 Hz, 1H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 161.3, 160.2 (d, *J*(P,C) = 10.1 Hz, 2C), 143.5, 137.0 (d, *J*(P,C) = 11.0 Hz), 135.8 (d, *J*(P,C) = 20.8 Hz), 135.0 (d, *J*(P,C) = 10.9 Hz), 134.0 (d, *J*(P,C) = 17.3 Hz, 2C), 133.2 (d, *J*(P,C) = 19.0 Hz, 2C), 132.5, 132.2, 130.4, 129.9, 128.7, 128.3 (2C), 128.2 (d, *J*(P,C) = 1.8 Hz, 2C), 128.1 (d, *J*(P,C) = 7.5 Hz), 127.8 (d, *J*(P,C) = 2.5 Hz, 2C), 110.9, 108.8, 83.3 (d, *J*(P,C) = 6.4 Hz), 80.7, 56.1 (d, *J*(P,C) = 2.9 Hz). $^{31}$P NMR (162 MHz, Chloroform-*d*): δ -22.55. HRMS (ESI) calcd. for $C_{28}H_{20}O_4P$ $[M-H]^-$: 451.1105. Found: 451.1104.

**(*S*)-4'-(bis(3,5-di-tert-butylphenyl)phosphanyl)-2*H*,2'*H*-3,3'-spirobi[benzofuran]-4-carboxylic acid ((*S*)-2b):**



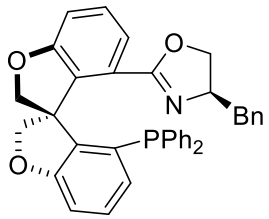

Chemical Formula: $C_{44}H_{53}O_4P$
Exact Mass: 676.3681

2.84 g, yield = 60% (7.0 mmol scale), $[\alpha]^{25}_{D}$ = -32.00 (c = 0.5, acetone), white solid, mp: 210 – 212 °C. $^{1}$H NMR (400 MHz, Chloroform-*d*) : δ 7.36-7.17 (m, 4H), 7.17-7.00 (m, 2H), 6.94 (d, *J* = 6.5 Hz, 1H), 6.76 (d, *J* = 8.5 Hz, 4H), 6.54 (s, 1H), 4.98 (d, *J* = 8.4 Hz, 1H), 4.74 (d, *J* = 8.3 Hz, 2H), 4.61 (d, *J* = 8.5 Hz, 1H), 1.15 (s, 18H), 1.13 (s, 18H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 169.7, 162.3, 160.8 (d, *J*(P,C) = 10.3 Hz), 150.1 (d, *J*(P,C) = 6.4 Hz, 2C), 150.0 (d, *J*(P,C) = 7.0 Hz, 2C), 136.4 (d, *J*(P,C) = 8.9 Hz), 135.2 (d, *J*(P,C) = 26.0 Hz, 3C), 133.9, 133.7, 132.3 (d, *J*(P,C) = 3.7 Hz), 129.4, 128.6, 127.7 (d, *J*(P,C) = 9.8 Hz), 127.5 (d, *J*(P,C) = 10.9 Hz), 126.9, 126.8 (d, *J*(P,C) = 2.4 Hz), 124.0, 122.6, 121.8, 114.6, 109.7, 85.3, 83.4, 58.0 (d, *J*(P,C) = 3.1 Hz), 34.7

(2C), 34.6 (2C), 31.3 (6C), 31.2 (6C). $^{31}$P NMR (162 MHz, Chloroform-*d*): δ -20.01. HRMS (ESI) calcd. for $C_{44}H_{54}O_4P$ $[M+H]^-$: 677.3754. Found: 677.3745.

Synthesis of compound **L1-L5**:

**(*R*)-4-benzyl-2-((*R*)-4'-(diphenylphosphanyl)-2*H*,2'*H*-3,3'-spirobi[benzofuran]-4-yl)-4,5-dihydrooxazole (L3):**

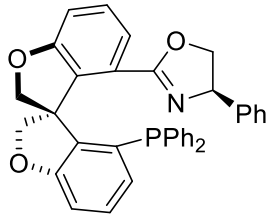



Chemical Formula: $C_{37}H_{30}NO_3P$
Exact Mass: 567.1963

**Typical procedure:** To a mixture of (*R*)-**2a** (669 mg, 1.48 mmol), D-phenylalaninol (702 mg, 4.65 mmol), 1-hydroxybenzotriazole (HOBt, 504 mg, 3.29 mmol) and dicyclohexylcarbodiimide (DCC, 881 mg, 4.27 mmol), 80 mL THF was added with stirring at 0 °C under Ar. The resulting mixture was heated at 40 °C for 24 h. After cooling to rt, the mixture was concentrated under reduced pressure. The product was afforded as white solid after purification by column chromatography (607 mg, yield = 70%). To a solution of the afforded product (1.04 mmol), triethylamine (0.32 mL), and 4-dimethylaminopyridine (DMAP, 5 mg, 0.04 mmol) in 65 mL dichloromethane was added MsCl (methane sulfonyl chloride, 120 μL, 1.55 mmol) at 0 °C. The mixture was stirred for 30 min, then another portion of triethylamine (1.35 mL) was added. The resulting mixture was warmed to room temperature. The reaction was monitored with TLC for a complete conversion. The crude product was purified by chromatography on a silica gel column to afford **L3** (512 mg, yield = 87%), $[\alpha]^{25}_D$ = +228.10 (c = 1.0, $CH_2Cl_2$), mp: 110 – 112 °C. $^1$H NMR (400 MHz, Chloroform-*d*): δ 7.34 – 7.14 (m, 11H), 7.12 – 6.95 (m, 8H), 6.76 (d, *J* = 7.9 Hz, 1H), 6.63 - 6.55 (m, 1H), 5.04 (d, *J* = 8.4 Hz, 1H), 4.82 – 4.62 (m, 3H), 4.24 - 4.12 (m, 1H), 3.68 – 3.52 (m, 2H), 2.62 (dd, *J* = 13.9, 4.4 Hz, 1H), 1.82 (dd, *J* = 13.9, 10.2 Hz, 1H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 161.8 (d, *J*(P,C) = 1.9 Hz), 161.7, 161.3, 138.2 (2C), 137.5 (d, *J*(P,C) = 10.5 Hz), 136.0 (d, *J*(P,C) = 27.5 Hz), 135.7 (d, *J*(P,C) = 11.6 Hz), 134.0 (d, *J*(P,C) = 19.0 Hz, 2C),

133.4 (d, *J*(P,C) = 18.4 Hz), 133.1 (d, *J*(P,C) = 18.8 Hz, 2C), 129.7 (d, *J*(P,C) = 3.3 Hz), 129.3, 129.0 (2C), 128.8 (d, *J*(P,C) = 16.3 Hz, 2C), 128.5 (2C), 128.2 (d, *J*(P,C) = 6.1 Hz, 2C), 128.1 (d, *J*(P,C) = 7.2 Hz, 2C), 127.0 (d, *J*(P,C) = 2.6 Hz), 126.3, 125.6 (d, *J*(P,C) = 2.3 Hz), 122.6, 112.5, 109.6, 84.9 (d, *J*(P,C) = 5.5 Hz), 83.3, 70.7, 67.5, 58.1 (d, *J*(P,C) = 3.6 Hz), 40.9. $^{31}$P NMR (162 MHz, Chloroform-*d*): δ -23.15. HRMS (ESI) calcd for $C_{37}H_{31}NO_3P^+$: 568.2036. Found: 568.2040.

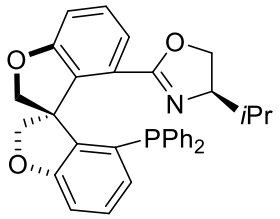
**(*R*)-2-((*R*)-4'-(diphenylphosphanyl)-2*H*,2'*H*-3,3'-spirobi[benzofuran]-4-yl)-4-phenyl-4,5-dihydrooxazole (L1):**




Chemical Formula: $C_{36}H_{28}NO_3P$
Exact Mass: 553.1807

540 mg, yield = 66% (1.48 mmol scale), $[\alpha]^{25}_D$ = +236.80 (c = 0.5, $CH_2Cl_2$), white solid, mp: 105 – 107 ℃. $^1$H NMR (400 MHz, Chloroform-*d*): δ 7.38 – 7.30 (m, 1H), 7.30 – 7.15 (m, 8H), 7.15 – 6.94 (m, 8H), 6.86 – 6.76 (m, 2H), 6.70 (d, *J* = 7.9 Hz, 1H), 6.59 (dd, *J* = 7.6, 4.3 Hz, 1H), 5.10 – 4.95 (m, 2H), 4.83 (dd, *J* = 9.0, 2.0 Hz, 1H), 4.73 (dd, *J* = 9.1, 1.2 Hz, 1H), 4.68 – 4.62 (m, 1H), 4.03 (dd, *J* = 10.3, 8.2 Hz, 1H), 3.75 – 3.68 (m, 1H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 162.8, 162.0 (d, *J*(P,C) = 2.1 Hz), 161.0, 141.8 (2C), 137.4 (d, *J*(P,C) = 10.7 Hz), 136.1 (d, *J*(P,C) = 27.0 Hz), 135.3 (d, *J*(P,C) =10.8 Hz), 134.1 (d, *J*(P,C) = 19.0 Hz, 2C), 133.6, 133.4, 133.2 (d, *J*(P,C) = 18.9 Hz, 2C), 129.5 (d, *J*(P,C) = 3.5 Hz), 129.4, 128.8, 128.6, 128.4 (2C), 128.3, 128.2 (d, *J*(P,C) = 2.7 Hz, 2C), 128.0 (d, *J*(P,C) = 7.4 Hz, 2C), 127.0 (d, *J*(P,C) = 2.4 Hz), 126.4, 125.4 (d, *J*(P,C) = 1.9 Hz), 123.0, 112.7, 109.9, 85.1 (d, *J*(P,C) = 5.3 Hz), 83.1, 73.4, 69.8, 58.2 (d, *J*(P,C) = 3.6 Hz). $^{31}$P NMR (243 MHz, Chloroform-*d*): δ -22.18. HRMS (ESI) calcd for $C_{36}H_{29}NO_3P^+$: 554.1880. Found: 554.1867.

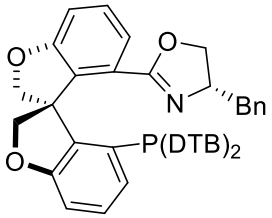
**(*R*)-2-((*R*)-4'-(diphenylphosphanyl)-2*H*,2'*H*-3,3'-spirobi[benzofuran]-4-yl)-4-isopropyl-4,5-dihydrooxazole (L2):**




Chemical Formula: $C_{33}H_{30}NO_3P$
Exact Mass: 519.1963

476 mg, yield = 62% (1.48 mmol scale), $[\alpha]^{25}_D$ = +188.20 (c = 0.5, $CH_2Cl_2$), white solid, mp: 90 – 92 °C. $^1$H NMR (400 MHz, Chloroform-*d*): δ 7.27 – 7.16 (m, 8H), 7.11 – 6.98 (m, 5H), 6.99 – 6.91 (m, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.53 (dd, *J* = 7.6, 4.3 Hz, 1H), 5.04 (d, *J* = 8.4 Hz, 1H), 4.72 – 4.57 (m, 3H), 3.72 – 3.57 (m, 3H), 1.64 (s, 1H), 0.78 (d, *J* = 6.7 Hz, 3H), 0.68 (d, *J* = 6.7 Hz, 3H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 168.4, 161.9, 160.9 (d, *J*(P,C) = 2.5 Hz), 137.7, 135.8, 135.7, 135.5, 134.9 (d, *J*(P,C) = 22.4 Hz), 133.9, 132.7 (d, *J*(P,C) = 18.1 Hz, 2C), 130.3, 129.8 (2C), 129.1, 128.2 (d, *J*(P,C) = 5.7 Hz, 2C), 128.1 (d, *J*(P,C) = 7.9 Hz, 2C), 128.0 (2C), 127.0 (d, *J*(P,C) = 2.5 Hz), 119.8, 112.0, 110.6, 86.6 (d, *J*(P,C) = 7.7 Hz), 85.4, 63.1, 59.2, 57.0 (d, *J*(P,C) = 3.2 Hz), 28.3, 19.6, 19.1. $^{31}$P NMR (162 MHz, Chloroform-*d*): δ -22.33. HRMS (ESI) calcd for $C_{33}H_{31}NO_3P^+$: 520.2036. Found: 520.2023.

**(*S*)-4-benzyl-2-((*S*)-4'-(bis(3,5-di-tert-butylphenyl)phosphanyl)-2*H*,2'*H*-3,3'-spirobi[benzofuran]-4-yl)-4,5-dihydrooxazole (L4):**

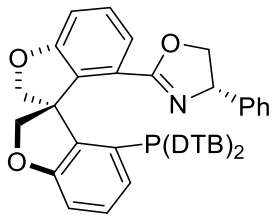



Chemical Formula: $C_{53}H_{62}NO_3P$
Exact Mass: 791.4467

702 mg, yield = 60% (1.48 mmol scale), $[\alpha]^{25}_D$ = (c = 166.00, $CH_2Cl_2$), white solid, mp: 94 – 96 °C. $^1$H NMR (400 MHz, Chloroform-*d*): δ 7.38 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.31 – 7.26 (m, 3H), 7.23 (d, *J* = 7.5 Hz, 2H), 7.17 (s, 1H), 7.12 – 6.99 (m, 3H), 6.98 – 6.82 (m, 5H), 6.74 (dd, *J* = 8.0, 0.9 Hz, 1H), 6.65 – 6.58 (m, 1H), 5.05 (d, *J* = 8.4 Hz, 1H),

4.61 (d, *J* = 8.4 Hz, 1H), 4.50 (d, *J* = 9.1 Hz, 1H), 4.31 (d, *J* = 9.1 Hz, 1H), 4.27 – 4.15 (m, 1H), 3.73 – 3.59 (m, 2H), 2.74 (dd, *J* = 14.0, 4.6 Hz, 1H), 2.04 (dd, *J* = 14.1, 9.5 Hz, 1H), 1.19 (s, 18H), 1.18 (s, 18H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 168.8, 161.8, 160.8 (d, *J*(P,C) = 10.1 Hz), 150.6 (d, *J*(P,C) = 7.6 Hz, 2C), 150.2 (d, *J*(P,C) = 6.0 Hz, 2C), 138.3, 137.0 (d, *J*(P,C) = 7.5 Hz), 135.6 (d, *J*(P,C) = 20.8 Hz), 135.3 (d, *J*(P,C) = 11.6 Hz), 134.8 (d, *J*(P,C) = 26.5 Hz), 134.1 (d, *J*(P,C) = 2.0 Hz), 129.7, 129.6, 129.1 (2C), 128.9 (2C), 128.7 (2C), 128.4 (2C), 127.3 (d, *J*(P,C) = 18.8 Hz, 2C), 126.8 (d, *J*(P,C) = 3.3 Hz), 126.4, 123.5, 122.0, 119.9, 111.8, 110.5, 85.3 (d, *J*(P,C) = 5.5 Hz), 84.6, 63.7, 60.4, 57.2 (d, *J*(P,C) = 3.3 Hz), 35.5, 34.9 (2C), 34.7 (2C), 31.3 (12C). $^{31}$P NMR (162 MHz, Chloroform-*d*): δ -19.23. HRMS (ESI) calcd for $C_{53}H_{63}NO_3P^+$: 792.4540. Found: 792.4518.

**(*S*)-2-((*S*)-4'-(bis(3,5-di-tert-butylphenyl)phosphanyl)-2*H*,2'*H*-3,3'-spirobi[benzofuran]-4-yl)-4-phenyl-4,5-dihydrooxazole (L5):**




Chemical Formula: $C_{52}H_{60}NO_3P$
Exact Mass: 777.4311

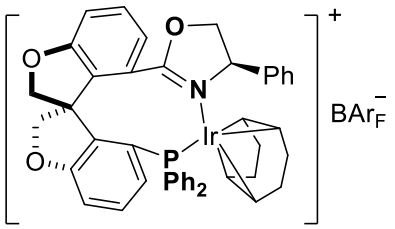
678 mg, yield = 59% (1.48 mmol scale), $[\alpha]^{25}_D$ = -154.40 (c = 0.5, $CH_2Cl_2$), white solid, mp: 82 – 84 °C. $^1$H NMR (400 MHz, Chloroform-*d*): δ 7.44 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.22 – 7.17 (m, 3H), 7.09 – 6.99 (m, 4H), 6.91 (dd, *J* = 8.0, 1.0 Hz, 1H), 6.84 (d, *J* = 1.8 Hz, 1H), 6.82 (d, *J* = 1.8 Hz, 1H), 6.80 (d, *J* = 1.8 Hz, 1H), 6.78 (d, *J* = 1.8 Hz, 1H), 6.76 – 6.72 (m, 2H), 6.67 – 6.59 (m, 2H), 5.05 – 4.88 (m, 2H), 4.52 (dd, *J* = 18.2, 8.7 Hz, 2H), 4.36 (d, *J* = 9.0 Hz, 1H), 3.98 (dd, *J* = 10.1, 8.2 Hz, 1H), 3.66 – 3.57 (m, 1H), 1.11 (s, 18H), 1.07 (s, 18H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 163.5, 162.0 (d, *J*(P,C) = 1.9 Hz), 160.7, 150.2 (d, *J*(P,C) = 6.4 Hz, 2C), 150.0 (d, *J*(P,C) = 6.9 Hz, 2C), 141.9, 136.4 (d, *J*(P,C) = 9.3 Hz), 135.3 (d, *J*(P,C) = 16.6 Hz), 135.1 (d, *J*(P,C) = 15.3 Hz), 129.3 (2C), 128.9 (d, *J*(P,C) = 3.0 Hz), 128.5 (2C), 128.1 (d, *J*(P,C) = 2.3 Hz, 2C),

127.9 (d, *J*(P,C) = 3.1 Hz, 2C), 127.0 (2C), 126.9 (d, *J*(P,C) = 2.3 Hz), 126.4 (2C), 126.2 (d, *J*(P,C) = 3.1 Hz), 122.9, 122.5, 122.0, 112.6, 109.6, 83.9 (d, *J*(P,C) = 4.1 Hz), 82.8, 73.7, 69.9, 58.3 (d, *J*(P,C) = 3.6 Hz), 34.8 (2C), 34.7 (2C), 31.3 (12C). $^{31}$P NMR (162 MHz, Chloroform-*d*): δ -19.31. HRMS (ESI) calcd for $C_{52}H_{61}NO_3P^+$: 778.4384. Found: 778.4358.

## 3. Preparation and Analytical Data of Iridium Complexes

**Typical procedure:** iridium complexes were synthesized according to a reported procedure:[1] Ligand (0.085 mmol), $[Ir(cod)Cl]_2$ (32 mg, 0.047 mmol) and $NaBArF \cdot 3H_2O$ (100 mg, 0.107 mmol) were added to 2 mL of $CH_2Cl_2$ in a Schlenk tube under argon atmosphere. The mixture was heated to reflux for 0.5 hours. The TLC analysis revealed no free ligand existed. After cooling to room temperature, the mixture was concentrated under reduced pressure and the residue was purified by a flash column chromatography on silica gel with $CH_2Cl_2$/petroleum ether (1:1) to offer an orange-yellow solid.

**Cat 1**:

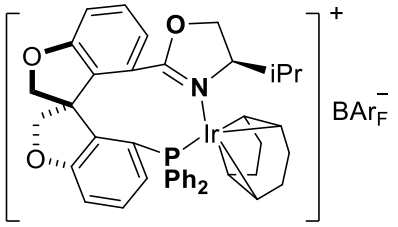



Chemical Formula: $C_{76}H_{52}BF_{24}IrNO_3P$
Exact Mass: 1717.3024

432.7 mg, yield = 84% for one step (0.3 mmol scale), $[\alpha]^{25}_D$ = -160.00 (c = 0.1, $CH_2Cl_2$), orange-yellow solid, mp: 160 – 162 ℃. $^1$H NMR (400 MHz, Chloroform-*d*): δ 7.80 – 7.67 (m, 10H), 7.66 – 7.39 (m, 15H), 7.38 – 7.30 (m, 3H), 7.25 – 7.19 (m, 1H), 7.13 – 7.01 (m, 4H), 4.55 – 4.40 (m, 4H), 4.25 – 4.16 (m, 1H), 4.06 (d, *J* = 9.2 Hz, 1H), 3.88 – 3.80 (m, 1H), 3.73 - 3.64 (m, 1H), 3.50 – 3.36 (m, 1H), 2.73 – 2.65 (m, 1H), 2.20 – 2.03 (m, 1H), 2.00 (dd, *J* = 9.2, 1.6 Hz, 1H), 1.97 – 1.85 (m, 1H), 1.76 – 1.63 (m, 1H), 1.54 (s, 2H), 1.40 – 1.28 (m, 3H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 168.2, 163.3, 163.2, 162.4, 161.9, 161.4, 160.9, 136.9, 136.1, 136.0, 133.7, 133.6, 133.3, 133.2, 131.5, 131.4, 131.3, 131.2, 130.8, 130.7, 130.2, 130.0, 129.9, 129.7, 129.4, 129.0, 128.9, 128.8, 128.7, 128.6, 128.4, 127.1, 126.8, 126.7, 126.6, 126.2, 126.1, 125.9, 124.9, 123.2, 123.1, 120.5, 119.9, 114.4, 86.5, 86.4, 83.6, 83.4, 83.1, 79.4, 71.6, 71.0, 67.8, 57.8, 31.0 , 30.6, 29.1, 29.0, 28.8. $^{31}$P NMR (162 MHz, Chloroform-*d*): δ 14.12. HRMS (ESI) calcd for

$C_{44}H_{40}IrNO_3P^+$: 854.2370. Found: 854.2371.

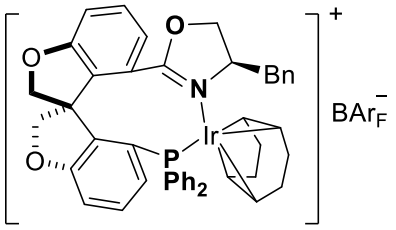
**Cat 2**:




Chemical Formula: $C_{73}H_{54}BF_{24}IrNO_3P$
Exact Mass: 1683.3180

378.6 mg, yield = 75% for one step (0.3 mmol scale), $[\alpha]^{25}_D$ = -90.00 (c = 0.1, $CH_2Cl_2$), orange-yellow solid, mp: 172 – 174 °C. $^1$H NMR (400 MHz, Chloroform-*d*): δ 7.72 (d, *J* = 2.8 Hz, 8H), 7.68 – 7.34 (m, 14H), 7.29 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.16 (d, *J* = 1.0 Hz, 1H), 7.10 (d, *J* = 8.0 Hz, 1H), 7.07 – 6.93 (m, 3H), 4.71 – 4.61 (m, 1H), 4.47 – 4.36 (m, 3H), 4.27 (dd, *J* = 9.3, 6.1 Hz, 1H), 4.04 (d, *J* = 9.2 Hz, 1H), 3.76 – 3.67 (m, 1H), 3.50 – 3.40 (m, 1H), 3.29 – 3.24 (m, 1H), 2.89 – 2.80 (m, 1H), 2.32 – 2.16 (m, 1H), 2.13 – 1.94 (m, 3H), 1.91 – 1.69 (m, 2H), 1.56 (s, 2H), 1.49 – 1.37 (m, 2H), 1.02 (d, *J* = 6.9 Hz, 3H), 0.89 (d, *J* = 6.7 Hz, 3H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 169.5, 163.1, 163.0, 162.4, 161.9, 161.5, 161.4, 160.9, 136.0, 135.8, 133.4, 133.3, 133.2, 131.3, 131.1, 131.0, 130.6, 130.2, 130.0, 129.9, 129.7, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 127.2, 127.1, 126.9, 126.7, 126.1, 126.0, 125.9, 124.9, 123.2, 120.5, 119.5, 117.5, 117.4, 114.7, 114.3, 83.1, 82.3, 82.2, 79.8, 79.6, 72.7, 71.0, 70.9, 68.7, 57.6, 31.0, 30.9, 30.5, 29.6, 29.5, 29.2, 20.1, 14.9. $^{31}$P NMR (162 MHz, Chloroform-*d*): δ 14.48. HRMS (ESI) calcd for $C_{41}H_{42}IrNO_3P^+$: 820.2526. Found: 818.2495.

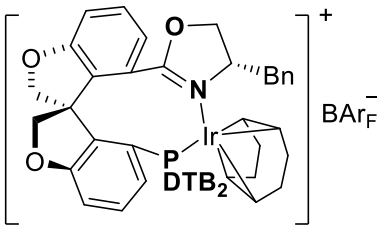
**Cat 3:**




Chemical Formula: $C_{77}H_{54}BF_{24}IrNO_3P$
Exact Mass: 1731.3180

709.7 mg, yield = 82% for one step (0.5 mmol scale), $[\alpha]^{25}_D$ = -84.00 (c = 0.1, $CH_2Cl_2$), orange-yellow solid, mp: 178 – 180 °C. $^1$H NMR (400 MHz, Chloroform-*d*): δ 7.75 – 7.61 (m, 10H), 7.60 – 7.44 (m, 10H), 7.39 – 7.15 (m, 9H), 7.10 – 7.00 (m, 3H), 6.96 (dd, *J* = 7.7, 1.6 Hz, 1H), 4.79 - 4.65 (m, 2H), 4.36 (d, *J* = 8.9 Hz, 1H), 4.28 (dd, *J* = 8.9, 1.7 Hz, 1H), 4.22 – 4.16 (m, 1H), 3.98 (d, *J* = 9.2 Hz, 1H), 3.79 – 3.67 (m, 2H), 3.62 – 3.47 (m, 2H), 2.83 (dd, *J* = 13.2, 11.5 Hz, 1H), 2.78 - 2.68 (m, 1H), 2.23 – 1.91 (m, 4H), 1.87 – 1.75 (m, 1H), 1.68 – 1.58 (m, 2H), 1.55 (s, 2H). $^{13}$C NMR (400 MHz, Chloroform-*d*): δ 168.6, 163.4, 163.3, 162.4, 161.9, 161.5, 160.9, 136.4, 136.3, 134.3, 133.7, 133.6, 133.4, 133.3, 131.6, 131.1, 131.0, 130.8, 130.1, 130.0, 129.6, 129.1, 129.0, 128.7, 128.6, 128.5, 128.3, 128.2, 128.1, 127.1, 126.6, 126.4, 125.9, 125.8, 125.7, 125.2, 123.5, 123.2, 120.5, 119.5, 117.5, 117.4, 114.6, 114.2, 87.3, 87.2, 85.9, 85.8, 82.6, 79.0, 74.7, 73.2, 69.2, 66.6, 58.1, 40.8, 31.2, 30.9, 29.2, 29.1, 28.9. $^{31}$P NMR (162 MHz, Chloroform-*d*): δ 15.00. HRMS (ESI) calcd for $C_{45}H_{42}IrNO_3P^+$: 868.2526. Found: 866.2497.

**Cat 4**:

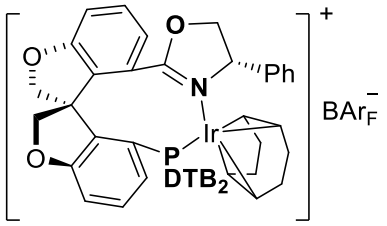



Chemical Formula: $C_{93}H_{86}BF_{24}IrNO_3P$
Exact Mass: 1955.5684

475.3 mg, yield = 81% for one step (0.3 mmol scale), $[\alpha]^{25}_D$ = +59.00 (c = 0.1, $CH_2Cl_2$), orange-yellow solid, mp: 223 – 225 °C. $^1$H NMR (400 MHz, Chloroform-*d*): δ 7.78 –

7.62 (m, 9H), 7.62 – 7.44 (m, 7H), 7.43 – 7.26 (m, 7H), 7.11 – 7.02 (m, 3H), 6.98 (dd, *J* = 7.1, 2.1 Hz, 1H), 6.87 (dd, *J* = 11.7, 1.8 Hz, 2H), 4.80 – 4.70 (m, 1H), 4.59 – 4.48 (m, 1H), 4.39 (d, *J* = 8.9 Hz, 1H), 4.28 – 4.18 (m, 2H), 3.92 (d, *J* = 9.0 Hz, 1H), 3.87-3.75 (m, 2H), 3.56 (dd, *J* = 13.4, 3.8 Hz, 1H), 3.41- 3.36 (m, 1H), 2.99 - 2.88 (m, 1H), 2.80 (dd, *J* = 13.5, 11.9 Hz, 1H), 2.38 – 2.23 (m, 1H), 2.16 – 2.04 (m, 1H), 1.94 (dd, *J* = 9.0, 1.7 Hz, 1H), 1.79 – 1.65 (m, 2H), 1.55 (s, 4H), 1.40 – 1.09 (m, 36H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 169.5, 163.3, 163.1, 162.5, 162.0, 161.5, 161.0, 160.9, 153.1, 153.0, 133.9, 130.1, 129.5, 129.1, 129.0, 128.7, 128.6, 128.4, 128.1, 127.8, 125.9, 125.8, 124.9, 124.7, 123.2, 122.8, 120.2, 117.5, 114.8, 114.2, 82.8, 78.2, 74.6, 71.4, 68.1, 67.2, 57.9, 40.6, 35.1, 31.8, 31.2, 31.1, 30.6, 30.1, 29.7, 28.4. $^{31}$P NMR (162 MHz, Chloroform-*d*): δ 16.37. HRMS (ESI) calcd for $C_{61}H_{74}IrNO_3P^+$: 1092.5030. Found: 1092.5018.

**Cat 5**:



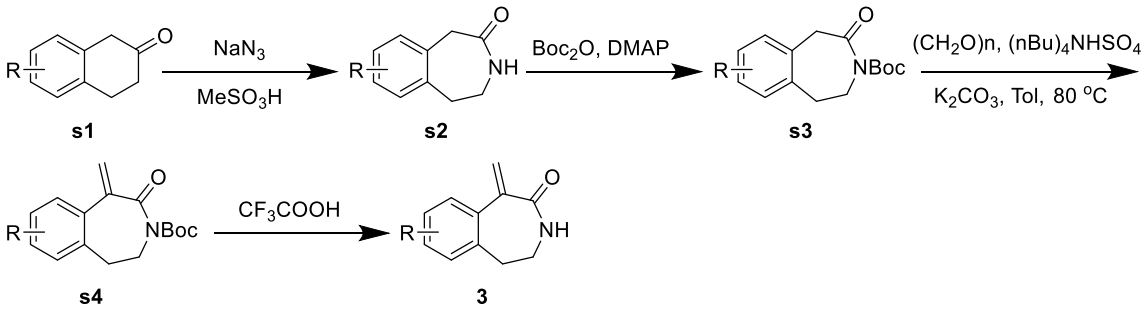

Chemical Formula: $C_{92}H_{84}BF_{24}IrNO_3P$
Exact Mass: 1941.5528

786.5 mg, yield = 81% for one step (0.5 mmol scale), $[\alpha]^{25}_D$ = +70.00 (c = 0.1, $CH_2Cl_2$), orange-yellow solid, mp: 240 – 242 °C. $^1$H NMR (400 MHz, Chloroform-*d*): δ 7.80 – 7.61 (m, 9H), 7.60 – 7.30 (m, 15H), 7.14 – 6.98 (m, 3H), 6.83 (dd, *J* = 11.7, 1.8 Hz, 2H), 4.61 (dd, *J* = 10.2, 4.8 Hz, 1H), 4.50 – 4.44 (m, 2H), 4.37 (dd, *J* = 8.9, 1.8 Hz, 1H), 4.12 (d, *J* = 7.2 Hz, 1H), 3.96 (d, *J* = 9.0 Hz, 1H), 3.90 – 3.86 (m, 1H), 3.65 – 3.52 (m, 2H), 2.82 (d, *J* = 6.7 Hz, 1H), 2.25 – 2.12 (m, 1H), 1.56 (s, 8H), 1.41 – 1.13 (m, 36H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 162.2, 161.9, 145.7, 144.0, 138.1, 134.8, 132.2, 130.4, 130.3, 129.8, 129.0, 128.8, 128.1, 128.0, 127.3, 126.6, 126.3, 125.9, 125.5, 124.0, 123.7, 121.8, 120.7, 117.5, 117.4, 79.1, 76.2, 69.9, 69.7, 69.6, 69.4, 68.1, 62.9, 41.5, 35.1, 35.0, 33.5, 31.2, 31.0, 30.7, 30.4, 29.9, 28.7. $^{31}$P NMR (162 MHz, Chloroform-*d*):

δ 16.82. HRMS (ESI) calcd for $C_{60}H_{72}IrNO_3P^+$: 1078.4874. Found: 1076.4835.

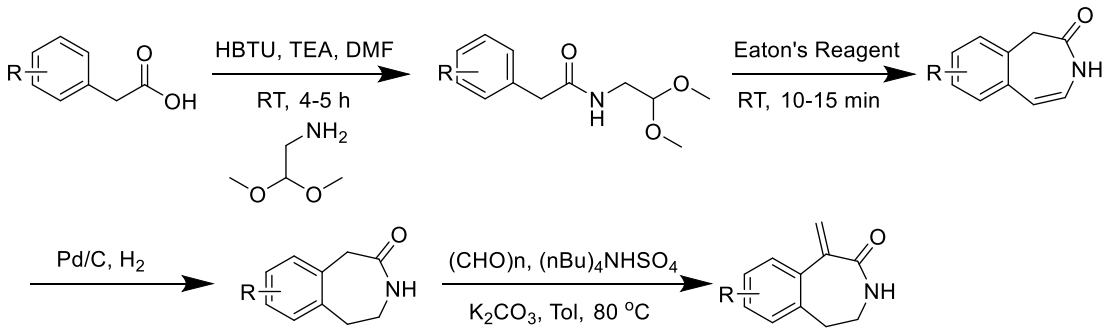
## 4. Representative Procedures for the Synthesis of Substrates

The synthetic pathway of the substrate **3a-3h** is outlined as follow[3-7]:




**Scheme S2**. Synthesis of substrate **3a-3h**

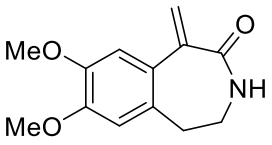
The substrate **3a-3b** can also be synthesized by another procedure[8]:




**Scheme S3**. Synthesis of substrate **3a-3b**

Synthesis of substrate **3a-3h**[3-7]**:**

**7,8-dimethoxy-1-methylene-1,3,4,5-tetrahydro-2*H*-benzo[*d*]azepin-2-one (3a):**

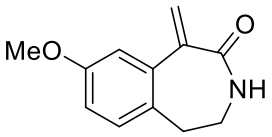



Chemical Formula: $C_{13}H_{15}NO_3$
Exact Mass: 233.1052

**Typical procedure:** A solution of 6,7-dimethoxy-3,4-dihydronaphthalen-2(1*H*)-one (2.06 g, 10.0 mmol) in $MeSO_3H$ (10.0 mL) was cooled in an ice bath and treated with sodium azide (0.85 g, 13.0 mmol) with stirring (**caution: sodium azide is a highly toxic and explosive compound, please add slowly and carefully**). The reaction

mixture was allowed to warm to room temperature and stirred for a further 2 h then poured into a cold solution of 1 M aqueous KOH (200 mL) and extracted thoroughly with ethyl acetate. The extracts were washed with brine and the mixture was concentrated under reduced pressure. Then, the residue was purified by a flash column chromatography on silica gel to afford a white solid **s2a** (1.33 g, yield = 60%). The afforded **s2a** (6.0 mmol) and *N*, *N*-dimethylaminopyridine (73.2 mg, 0.6 mmol) dissolved in 0.5 M $CH_2Cl_2$, di-*tert*-butyl dicarbonate (1.57 g, 7.2 mmol) was added under vigorous stirring at 0 °C. The reaction was then allowed to stir at room temperature overnight. Brine (30 mL) and $CH_2Cl_2$ (20 mL) were added to the reaction mixture and the organic layer extracted. The aqueous layer was further extracted with $CH_2Cl_2$ (2 x 30 mL). The combined organic layers were dried over $MgSO_4$ concentrated in vacuum and the crude was directly submitted to a flash column chromatography on silica gel to afford a white solid **s3a** (1.62 g, yield = 84%). **s3a** (5 mmol), $(CHO)_n$ (15.0 mmol), $(n\text{Bu})_4NHSO_4$ (0.50 mmol) and $K_2CO_3$ (15.0 mmol) was added in toluene (80 mL) and stirred at 80 °C. The reaction was followed by TLC until it was completed. Water (100 mL) was added and the resulting mixture was extracted with $Et_2O$ (3 x 150 mL). Removal of the solvent under vacuum and purification of the residue by a flash column chromatography on silica gel afforded the desired product **s4a** (1.58 g, yield = 95%). Finally, TFA (5.0 mL) was added cautiously to a stirred solution of **s4a** (4.75 mmol) in DCM (5.0 mL). After 1h the reaction mixture was diluted with DCM (15 mL) and washed with water (2 x 15 mL) and brine. The organic layer was dried (anhydrous $Na_2SO_4$) and concentrated in vacuo to give **3a** (1.09 g, yield = 98%) as a white solid, mp: 166 – 168 °C. $^1$H NMR (400 MHz, Chloroform-*d*): δ 7.15 (br, 1H), 6.81 (s, 1H), 6.60 (s, 1H), 5.89 (s, 1H), 5.64 (s, 1H), 3.88 (s, 6H), 3.63 – 3.45 (m, 2H), 3.12 – 2.94 (m, 2H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 173.7, 149.2, 147.6, 145.7, 128.5, 126.3, 122.4, 112.5, 112.2, 55.94, 55.91, 41.0, 34.0. HRMS (ESI) calcd for $C_{13}H_{16}NO_3^+$: 234.1125. Found: 234.1124.

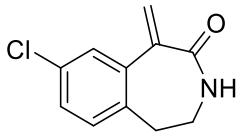
**8-methoxy-1-methylene-1,3,4,5-tetrahydro-2*H*-benzo[*d*]azepin-2-one (3b):**




Chemical Formula: $C_{12}H_{13}NO_2$
Exact Mass: 203.0946

591.6 mg, yield = 29% for 4 steps (10 mmol scale), white solid, mp: 76 – 78 °C. $^1$H NMR (600 MHz, Chloroform-*d*): δ 8.06 (br, 1H), 7.06 (d, *J* = 8.3 Hz, 1H), 6.86 (dd, *J* = 8.3, 2.7 Hz, 1H), 6.84 (d, *J* = 2.7 Hz, 1H), 6.12 (s, 1H), 5.79 (s, 1H), 3.81 (s, 3H), 3.62 – 3.54 (m, 2H), 3.09 – 2.99 (m, 2H). $^{13}$C NMR (151 MHz, Chloroform-*d*): δ 173.3, 158.6, 144.1, 135.4, 130.3, 128.3, 126.6, 114.9, 114.4, 55.4, 42.9, 32.5. HRMS (ESI) calcd for $C_{12}H_{14}NO_2^+$: 204.1019. Found: 204.1020.

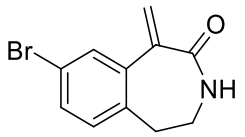
**8-chloro-1-methylene-1,3,4,5-tetrahydro-2*H*-benzo[*d*]azepin-2-one (3c):**




Chemical Formula: $C_{11}H_{10}ClNO$
Exact Mass: 207.0451

769.7 mg, yield = 37% for 4 steps (10 mmol scale), white solid, mp: 179 – 181 °C. $^1$H NMR (400 MHz, Chloroform-*d*): δ 7.37 (br, 1H), 7.29 (d, *J* = 2.3 Hz, 1H), 7.22 (dd, *J* = 8.2, 2.3 Hz, 1H), 7.06 (d, *J* = 8.2 Hz, 1H), 6.00 (s, 1H), 5.67 (s, 1H), 3.63 – 3.53 (m, 2H), 3.23 – 2.92 (m, 2H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 172.0, 145.3, 136.4, 134.8, 132.4, 130.8, 129.0, 128.3, 124.6, 41.2, 33.6. HRMS (ESI) calcd for $C_{11}H_{11}ClNO^+$: 208.0524. Found: 208.0525.

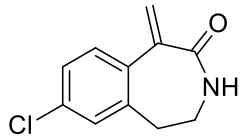
**8-bromo-1-methylene-1,3,4,5-tetrahydro-2*H*-benzo[*d*]azepin-2-one (3d):**




Chemical Formula: $C_{11}H_{10}BrNO$
Exact Mass: 250.9946

226.7 mg, yield = 18% for 4 steps (5 mmol scale), white solid, mp: 173 – 175 °C. $^{1}$H NMR (600 MHz, Chloroform-*d*): δ 7.46 (d, *J* = 2.1 Hz, 1H), 7.38 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.01 (d, *J* = 8.2 Hz, 1H), 6.19 (br, 1H), 6.05 (s, 1H), 5.67 (s, 1H), 3.58 – 3.52 (m, 2H), 3.09 – 3.00 (m, 2H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 171.2, 145.0, 137.0, 135.3, 132.0, 131.3, 131.0, 125.2, 120.5, 41.5, 33.7. HRMS (ESI) calcd for $C_{11}H_{11}BrNO^{+}$: 252.0019. Found: 252.0019.

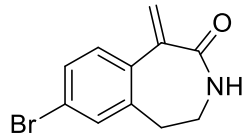
**7-chloro-1-methylene-1,3,4,5-tetrahydro-2*H*-benzo[*d*]azepin-2-one (3e):**




Chemical Formula: $C_{11}H_{10}ClNO$
Exact Mass: 207.0451

239.2 mg, yield = 23% for 4 steps (5 mmol scale), white solid, mp: 175 – 177 °C. $^{1}$H NMR (400 MHz, Chloroform-*d*): δ 7.29 – 7.17 (m, 2H), 7.13 (d, *J* = 2.1 Hz, 1H), 6.84 (br, 1H), 5.99 (d, *J* = 1.2 Hz, 1H), 5.64 (s, 1H), 3.74 – 3.45 (m, 2H), 3.27 – 3.00 (m, 2H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 172.2, 145.5, 138.0, 134.1, 133.4, 130.9, 129.3, 127.1, 124.1, 41.0, 34.1. HRMS (ESI) calcd for $C_{11}H_{11}ClNO^{+}$: 208.0524. Found: 208.0524.

**7-bromo-1-methylene-1,3,4,5-tetrahydro-2*H*-benzo[*d*]azepin-2-one (3f):**

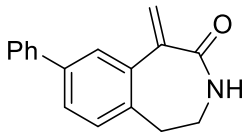



Chemical Formula: $C_{11}H_{10}BrNO$
Exact Mass: 250.9946

529.2 mg, yield = 21% for 4 steps (10 mmol scale), white solid, mp: 170 – 172 °C. $^{1}$H NMR (400 MHz, Chloroform-*d*): δ 7.45 (br, 1H), 7.35 (dd, *J* = 8.3, 2.1 Hz, 1H), 7.28 (d, *J* = 2.1 Hz, 1H), 7.17 (d, *J* = 8.3 Hz, 1H), 5.97 (s, 1H), 5.64 (s, 1H), 3.57 – 3.49 (m, 2H), 3.17 – 2.93 (m, 2H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 172.0, 145.4, 138.3, 133.9, 132.2, 131.1, 130.0, 124.3, 122.3, 41.1, 34.0. HRMS (ESI) calcd for

$C_{11}H_{11}BrNO^+$: 252.0019. Found: 252.0019.

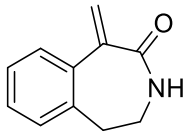
**1-methylene-8-phenyl-1,3,4,5-tetrahydro-2*H*-benzo[*d*]azepin-2-one (3g):**




Chemical Formula: $C_{17}H_{15}NO$
Exact Mass: 249.1154

500.2 mg, yield = 20% for 4 steps (10 mmol scale), white solid, mp: 143 – 145 °C. $^1$H NMR (400 MHz, Chloroform-*d*): δ 7.62 – 7.53 (m, 3H), 7.52 – 7.40 (m, 3H), 7.39 – 7.31 (m, 1H), 7.21 (d, *J* = 7.9 Hz, 1H), 6.72 (br, 1H), 6.03 (s, 1H), 5.72 (s, 1H), 3.68 – 3.54 (m, 2H), 3.21 – 3.03 (m, 2H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 172.2, 146.4, 140.3, 140.0, 135.4, 135.3, 130.0, 128.8 (2C), 128.2, 127.4, 127.2, 127.0 (2C), 124.0, 41.5, 33.9. HRMS (ESI) calcd for $C_{17}H_{16}NO^+$: 250.1224. Found: 250.1223.

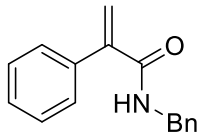
**1-methylene-1,3,4,5-tetrahydro-2*H*-benzo[*d*]azepin-2-one (3h):**




Chemical Formula: $C_{11}H_{11}NO$
Exact Mass: 173.0841

300.9 mg, yield = 17% for 4 steps (10 mmol scale), white solid, mp: 174 – 176 °C. $^1$H NMR (400 MHz, Chloroform-*d*): δ 7.38 – 7.29 (m, 2H), 7.30 – 7.20 (m, 2H), 7.17 – 7.09 (m, 1H), 5.97 (d, *J* = 1.5 Hz, 1H), 5.64 (s, 1H), 3.64 – 3.48 (m, 2H), 3.18 – 2.98 (m, 2H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 172.6, 146.5, 136.4, 135.0, 129.5, 129.4, 128.4, 126.8, 123.6, 41.3, 34.2. HRMS (ESI) calcd for $C_{11}H_{12}NO^+$: 174.0913. Found: 174.0914.

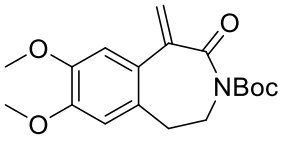
***N*-benzyl-2-phenylacrylamide (3i)**:




Chemical Formula: $C_{16}H_{15}NO$
Exact Mass: 237.1154

This is a known compound.[9] Substrate **3i** was synthesized according to a reported procedure:[9] EDC·HCl (1.15 g, 6.00 mmol) was added at ambient temperature to a stirred mixture of 2-phenylacrylic acid (5.00 mmol), HOBt·$H_2O$ (230 mg, 1.50 mmol) and phenylmethanamine (5.25 mmol) in anhydrous MeCN (6.00 mL). After 5 min, $Et_3N$ (0.73 mL, 5.25 mmol) was added, and the reaction mixture was allowed to stir for 6 hours at the room temperature. Thereafter, water was added, and the mixture was extracted with EtOAc. The combined organic phase was washed with brine (30.0 mL) and dried over anhydrous $Na_2SO_4$. After removal of the solvents in reduced pressure, the crude product was purified by column chromatography on silica gel (EtOAc/Hexane) to yield light yellow solid **3i** (605.2 mg, yield = 51%), mp: 80 – 82 °C. $^1$H NMR (400 MHz, Chloroform-*d*): δ 7.47 – 7.16 (m, 10H), 6.17 (d, *J* = 1.3 Hz, 1H), 6.08 (br, 1H), 5.63 (d, *J* = 1.3 Hz, 1H), 4.52 (d, *J* = 5.9 Hz, 2H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 167.1, 144.5, 138.0, 136.9, 128.7 (2C), 128.6 (2C), 128.5, 128.1 (2C), 127.6 (2C), 127.4, 122.4, 43.8. HRMS (ESI) calcd for $C_{16}H_{16}NO^+$: 238.1226. Found: 238.1224.

***tert*-butyl-7,8-dimethoxy-1-methylene-2-oxo-1,2,4,5-tetrahydro-3*H*-benzo[*d*]azepine-3-carboxylate (3j)**:

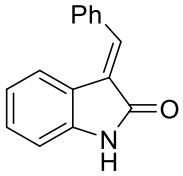



Chemical Formula: $C_{18}H_{23}NO_5$
Exact Mass: 333.1576

The afforded **3a** (140.0 mg, 0.6 mmol) and *N*, *N*-dimethylaminopyridine (7.3 mg, 0.06 mmol) dissolved in $CH_2Cl_2$ (7 mL), di-*tert*-butyl dicarbonate (157 mg, 0.72 mmol) was added under vigorous stirring at 0 °C. The reaction was then allowed to stir at room

temperature overnight. Brine (10 mL) and $CH_2Cl_2$ (10 mL) were added to the reaction mixture and the organic layer extracted. The aqueous layer was further extracted with $CH_2Cl_2$ (2 x 10 mL). The combined organic layers were dried over $MgSO_4$ concentrated in vacuum and the crude was directly submitted to a flash column chromatography on silica gel to afford a white solid **3j** (143.9 mg, yield = 72%), mp: 140 – 142 °C. $^1$H NMR (400 MHz, Chloroform-*d*): δ 6.73 (s, 1H), 6.61 (s, 1H), 5.82 (d, *J* = 1.0 Hz, 1H), 5.59 (d, *J* = 1.0 Hz, 1H), 4.16 – 4.08 (m, 2H), 3.87 (s, 6H), 3.15 – 3.07 (m, 2H), 1.54 (s, 9H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 170.9, 151.5, 149.4, 148.2, 147.6, 127.4, 125.4, 122.2, 113.2, 112.3, 83.2, 56.0, 55.9, 43.5, 33.1, 28.0 (3C). HRMS (ESI) calcd for $C_{18}H_{24}NO_5^+$: 334.1649. Found: 334.1647.

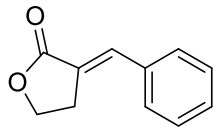
**(*E*)-3-benzylideneindolin-2-one (3k)**:




Chemical Formula: $C_{15}H_{11}NO$
Exact Mass: 221.0841

This is a known compound and it was synthesized according to a reported procedure. [12] Yellow solid. $^1$H NMR (600 MHz, Chloroform-*d*): δ 8.25 (br, 1H), 7.84 (s, 1H), 7.69 – 7.65 (m, 2H), 7.64 (d, *J* = 7.7 Hz, 1H), 7.51 – 7.46 (m, 2H), 7.46 – 7.42 (m, 1H), 7.24 – 7.20 (m, 1H), 6.92 – 6.84 (m, 2H). $^{13}$C NMR (151 MHz, Chloroform-*d*): δ 170.6, 141.8, 137.5, 134.8, 129.9, 129.6, 129.3 (2C), 128.6 (2C), 127.7, 123.0, 121.8, 121.6, 110.4.

**(*E*)-3-benzylidenedihydrofuran-2(3*H*)-one (3l)**:




Chemical Formula: $C_{11}H_{10}O_2$
Molecular Weight: 174.1990

This is a known compound and it was synthesized according to a reported procedure.

[13] Yellow solid. $^{1}$H NMR (400 MHz, Chloroform-*d*): 7.57 (t, *J* = 3.0 Hz, 1H), 7.53 – 7.47 (m, 2H), 7.47 – 7.37 (m, 3H), 4.46 (t, *J* = 7.3 Hz, 2H), 3.28 – 3.24 (m, 2H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 172.5, 136.5, 134.5, 129.9 (2C), 129.8, 128.8 (2C), 123.5, 65.4, 27.3.

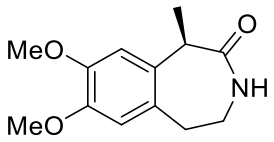
## 5. Representative Procedures for Asymmetric Hydrogenation

Representative procedures for asymmetric hydrogenation, as exemplified with **3a**:

To a 5 mL vial was added **3a** (70.8 mg, 0.3 mmol) and a stir bar. **Cat 5** (5.8 mg, 1 mol%) and 3 mL toluene (degassed) were added to the vial in an argon-filled glovebox. The vial was placed in an autoclave and the autoclave was pressurized with $H_2$ (40 atm). The reaction mixture was allowed to stir at room temperature for 24 h before carefully releasing $H_2$. The resulting reaction residue was passed through a short column of silicon (acetone as the eluent) to give the **4a**.

According to a reported procedure[10], the Lorcaserin (**5c**) can be synthesized from **4c**.

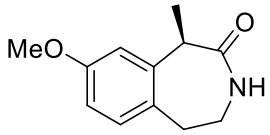
**(*R*)-7,8-dimethoxy-1-methyl-1,3,4,5-tetrahydro-2*H*-benzo[*d*]azepin-2-one (4a):**




Chemical Formula: $C_{13}H_{17}NO_3$
Exact Mass: 235.1208

70.3 mg, yield = 99%, 98% ee, $[\alpha]^{25}_D$ = -144.00 (c = 0.1, $CH_2Cl_2$), light yellow solid, mp: 140 – 142 °C. $^1$H NMR (400 MHz, Chloroform-*d*): δ 6.76 (s, 1H), 6.64 (s, 1H), 5.81 (br, 1H), 4.15 (q, *J* = 7.0 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.82 – 3.73 (m, 1H), 3.47 – 3.35 (m, 1H), 3.30 – 3.20 (m, 1H), 3.04 – 2.94 (m, 1H), 1.56 (d, *J* = 7.0 Hz, 3H). $^{13}$C NMR (151 MHz, Chloroform-*d*): δ 175.7, 147.6, 147.6, 129.5, 128.9, 113.0, 109.8, 56.01, 55.97, 41.7, 40.4, 32.8, 15.0. HRMS (ESI) calcd for $C_{13}H_{18}NO_3^+$ $[M+H]^+$: 236.1281. Found: 236.1280. The enantiomeric excess of **4a** was determined by HPLC analysis on Chiralpak IA column. Conditions: hexane/isopropanol = 80/20, flow rate = 1.0 mL/min, uv-vis detection at λ = 210 nm, $t_R$ = 17.838 min (minor), 19.254 min (major).

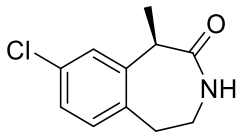
**(*R*)-8-methoxy-1-methyl-1,3,4,5-tetrahydro-2*H*-benzo[*d*]azepin-2-one (4b):**




Chemical Formula: $C_{12}H_{15}NO_2$
Exact Mass: 205.1103

This is a known compound.[10] 61.1 mg, yield = 99%, 98% ee, $[\alpha]^{25}_D$ = +12.00 (c = 0.1, $CH_2Cl_2$), light yellow solid, mp: 101 – 103 °C. $^1$H NMR (400 MHz, Chloroform-*d*): δ 7.06 (d, *J* = 8.3 Hz, 1H), 6.81 (d, *J* = 2.6 Hz, 1H), 6.74 (dd, *J* = 8.3, 2.6 Hz, 1H), 5.77 (br, 1H), 4.16 (q, *J* = 7.0 Hz, 1H), 3.79 (s, 3H), 3.78 – 3.70 (m, 1H), 3.43 – 3.35 (m, 1H), 3.33 – 3.24 (m, 1H), 3.04 – 2.93 (m, 1H), 1.56 (d, *J* = 7.0 Hz, 3H). $^{13}$C NMR (101 MHz, Chloroform-*d*): 174.9, 158.6, 139.1, 130.3, 129.1, 112.0, 111.8, 55.3, 42.4, 40.9, 31.9, 14.5. HRMS (ESI) calcd for $C_{12}H_{16}NO_2^+$ $[M+H]^+$: 206.1176. Found: 206.1176. The enantiomeric excess of **4b** was determined by HPLC analysis on Chiralpak IA column. Conditions: hexane/isopropanol = 80/20, flow rate = 1.0 mL/min, uv-vis detection at λ = 230 nm, $t_R$ = 9.891 min (major), 14.454 min (minor).

**(*R*)-8-chloro-1-methyl-1,3,4,5-tetrahydro-2*H*-benzo[*d*]azepin-2-one (4c):**

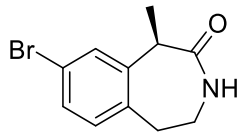



Chemical Formula: $C_{11}H_{12}ClNO$
Exact Mass: 209.0607

This is a known compound.[10] 62.8 mg, yield = 99%, 99% ee, $[\alpha]^{24}_D$ = -1.60 (c = 0.5, $CH_2Cl_2$), light yellow solid, mp: 167 – 169 °C. $^1$H NMR (400 MHz, Chloroform-*d*): δ 7.21 (d, *J* = 2.4 Hz, 1H), 7.15 (dd, *J* = 8.0, 2.4 Hz, 1H), 7.05 (d, *J* = 8.0 Hz, 1H), 6.35 (br, 1H), 4.17 (q, *J* = 7.0 Hz, 1H), 3.88 – 3.78 (m, 1H), 3.50 – 3.33 (m, 1H), 3.32 – 3.19 (m, 1H), 3.12 – 2.92 (m, 1H), 1.53 (d, *J* = 6.8 Hz, 3H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 174.8, 139.3, 135.3, 132.6, 130.9, 126.9, 126.0, 41.5, 40.3, 32.3, 14.2. HRMS (ESI) calcd for $C_{11}H_{13}ClNO^+$ $[M+H]^+$: 210.0680. Found: 210.0680. The enantiomeric excess of **4c** was determined by HPLC analysis on Chiralpak IA column.

Conditions: hexane/isopropanol = 90/10, flow rate = 1.0 mL/min, uv-vis detection at λ = 210 nm, $t_R$ = 14.554 min (major), 18.217 min (minor).

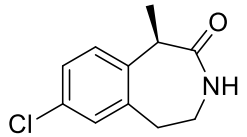
**(*R*)-8-bromo-1-methyl-1,3,4,5-tetrahydro-2*H*-benzo[*d*]azepin-2-one (4d):**




Chemical Formula: $C_{11}H_{12}BrNO$
Exact Mass: 253.0102

This is a known compound.[10] 75.5 mg, yield = 99%, 98% ee, $[\alpha]^{24}_D$ = +4.30 (c = 0.5, $CH_2Cl_2$), white solid, mp: 120 – 122 °C. $^1$H NMR (400 MHz, Chloroform-*d*): δ 7.36 (d, *J* = 2.1 Hz, 1H), 7.32 (dd, *J* = 8.0, 2.1 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 5.95 (br, 1H), 4.18 (q, *J* = 7.0 Hz, 1H), 3.84 - 3.72 (m, 1H), 3.44 – 3.34 (m, 1H), 3.33 – 3.20 (m, 1H), 3.07 – 2.94 (m, 1H), 1.55 (d, *J* = 7.0 Hz, 3H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 174.5, 139.7, 135.9, 131.2, 130.0, 128.9, 120.8, 41.6, 40.4, 32.4, 14.3. HRMS (ESI) calcd for $C_{11}H_{13}BrNO^+$ $[M+H]^+$: 254.0175. Found: 254.0174. The enantiomeric excess of **4d** was determined by HPLC analysis on Chiralpak IA column. Conditions: hexane/isopropanol = 80/20, flow rate = 1.0 mL/min, uv-vis detection at λ = 210 nm, $t_R$ = 9.471min (major), 11.319 min (minor).

**(*R*)-7-chloro-1-methyl-1,3,4,5-tetrahydro-2*H*-benzo[*d*]azepin-2-one (4e):**

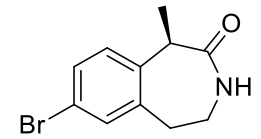



Chemical Formula: $C_{11}H_{12}ClNO$
Exact Mass: 209.0607

This is a known compound.[10] 62.1 mg, yield = 99%, 97% ee, $[\alpha]^{24}_D$ = -88.20 (c = 0.5, $CH_2Cl_2$), yellow solid, mp: 164 – 166 °C. $^1$H NMR (600 MHz, Chloroform-*d*): δ 7.22 – 7.15 (m, 2H), 7.14 (d, *J* = 2.1 Hz, 1H), 5.86 (br, 1H), 4.16 (q, *J* = 7.0 Hz, 1H), 3.85 – 3.75 (m, 1H), 3.46 – 3.36 (m, 1H), 3.34 – 3.26 (m, 1H), 3.08 – 2.96 (m, 1H), 1.55 (d, *J* = 7.0 Hz, 3H). $^{13}$C NMR (151 MHz, Chloroform-*d*): δ 174.7, 138.8, 136.1, 132.6, 129.4,

127.3, 126.9, 41.6, 40.3, 32.8, 14.6. HRMS (ESI) calcd for $C_{11}H_{13}ClNO^+$ $[M+H]^+$: 210.0680. Found: 210.0679. The enantiomeric excess of **4e** was determined by HPLC analysis on Chiralpak IA column. Conditions: hexane/isopropanol = 90/10, flow rate = 1.0 mL/min, uv-vis detection at λ = 210 nm, $t_R$ = 16.199min (major), 20.358 min (minor).

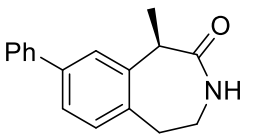
**(*R*)-7-bromo-1-methyl-1,3,4,5-tetrahydro-2*H*-benzo[*d*]azepin-2-one (4f):**




Chemical Formula: $C_{11}H_{12}BrNO$
Exact Mass: 253.0102

75.6 mg, yield = 99%, 98% ee, $[\alpha]^{24}_D$ = -85.20 (c = 0.5, $CH_2Cl_2$), yellow solid, mp: 111 – 113 °C. $^1$H NMR (400 MHz, Chloroform-*d*): δ 7.35 (dd, *J* = 8.3, 2.2 Hz, 1H), 7.29 (d, *J* = 2.2 Hz, 1H), 7.11 (d, *J* = 8.3 Hz, 1H), 5.85 (br, 1H), 4.14 (q, *J* = 7.0 Hz, 1H), 3.84 – 3.71 (m, 1H), 3.50 – 3.35 (m, 1H), 3.34 – 3.25 (m, 1H), 3.06 – 2.95 (m, 1H), 1.54 (d, *J* = 7.0 Hz, 3H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 174.6, 139.1, 136.7, 132.3, 129.9, 127.6, 120.7, 41.6, 40.4, 32.7, 14.5. HRMS (ESI) calcd for $C_{11}H_{13}BrNO^+$ $[M+H]^+$: 254.0175. Found: 254.0175. The enantiomeric excess of **4f** was determined by HPLC analysis on Chiralpak IA column. Conditions: hexane/isopropanol = 80/20, flow rate = 1.0 mL/min, uv-vis detection at λ = 230 nm, $t_R$ = 10.064 min (major), 11.931 min (minor).

**(*R*)-1-methyl-8-phenyl-1,3,4,5-tetrahydro-2*H*-benzo[*d*]azepin-2-one (4g):**

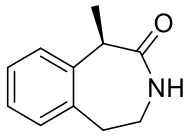



Chemical Formula: $C_{17}H_{17}NO$
Exact Mass: 251.1310

74.5mg, yield = 99%, 99% ee, $[\alpha]^{24}_D$ = +25.00 (c = 0.5, $CH_2Cl_2$), light yellow solid, mp: 164 – 166 °C. $^1$H NMR (400 MHz, Chloroform-*d*): δ 7.57 (dd, *J* = 7.7, 1.6 Hz, 2H),

7.53 – 7.39 (m, 4H), 7.39 – 7.31 (m, 1H), 7.22 (d, $J$ = 7.7 Hz, 1H), 5.69 (br, 1H), 4.26 (q, $J$ = 7.0 Hz, 1H), 3.88 – 3.76 (m, 1H), 3.52 – 3.31 (m, 2H), 3.18- 3.04 (m, 1H), 1.64 (d, $J$ = 7.0 Hz, 3H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 175.2, 140.9, 140.0, 138.0, 136.0, 130.1, 128.8 (2C), 127.3, 127.1 (2C), 125.7, 124.8, 42.0, 41.0, 32.6, 14.7. HRMS (ESI) calcd for $C_{17}H_{18}NO^+$ $[M+H]^+$: 252.1383. Found: 252.1382. The enantiomeric excess of **4g** was determined by HPLC analysis on Chiralpak OD-3 column. Conditions: hexane/isopropanol = 80/20, flow rate = 1.0 mL/min, uv-vis detection at λ = 210 nm, $t_R$ = 11.481min (minor), 25.034 min (major).

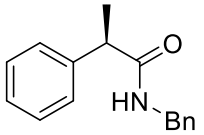
**(*R*)-1-methyl-1,3,4,5-tetrahydro-2*H*-benzo[*d*]azepin-2-one (4h):**




Chemical Formula: $C_{11}H_{13}NO$
Exact Mass: 175.0997

This is a known compound.[10] 52.4 mg, yield = 99%, 97% ee, $[\alpha]^{24}_D$ = -66.20 (c = 0.5, $CH_2Cl_2$), light yellow solid, mp: 161 – 163 °C. $^1$H NMR (400 MHz, Chloroform-*d*): δ 7.29 – 7.17 (m, 3H), 7.14 (d, $J$ = 6.6 Hz, 1H), 5.89 (br, 1H), 4.20 (q, $J$ = 7.0 Hz, 1H), 3.84 – 3.69 (m, 1H), 3.46 – 3.26 (m, 2H), 3.10 – 3.00 (m, 1H), 1.57 (d, $J$ = 7.0 Hz, 3H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 175.2, 137.7, 137.1, 129.5, 126.96, 126.95, 125.8, 42.1, 40.9, 32.9, 14.6. HRMS (ESI) calcd for $C_{11}H_{14}NO^+$ $[M+H]^+$: 176.1070. Found: 176.1069. The enantiomeric excess of **4h** was determined by HPLC analysis on Chiralpak IA column. Conditions: hexane/isopropanol = 90/10, flow rate = 1.0 mL/min, uv-vis detection at λ = 230 nm, $t_R$ = 16.246 min (major), 19.042 min (minor).

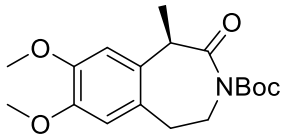
**(*R*)-*N*-benzyl-2-phenylpropanamide (4i):**




Chemical Formula: $C_{16}H_{17}NO$
Exact Mass: 239.1310

This is a known compound.[11] 71.6 mg, yield = 99%, 77% ee, $[\alpha]^{24}_D$ = -2.20 (c = 0.5, $CH_2Cl_2$), yellow solid, mp: 75 – 77 °C. $^1$H NMR (400 MHz, Chloroform-*d*): δ 7.51 – 7.18 (m, 8H), 7.19 – 7.07 (m, 2H), 5.69 (s, 1H), 4.55 – 4.23 (m, 2H), 3.60 (q, *J* = 7.2 Hz, 1H), 1.55 (d, *J* = 7.1 Hz, 3H). $^{13}$C NMR (151 MHz, Chloroform-*d*): δ 174.0, 141.2, 138.3, 128.9 (2C), 128.6 (2C), 127.6 (2C), 127.4 (2C), 127.31, 127.28, 47.1, 43.5, 18.5. HRMS (ESI) calcd for $C_{16}H_{18}NO^+$ $[M+H]^+$: 240.1383. Found: 240.1381. The enantiomeric excess of **4i** was determined by HPLC analysis on Chiralpak IA column. Conditions: hexane/isopropanol = 80/20, flow rate = 1.0 mL/min, uv-vis detection at λ = 230 nm, $t_R$ = 5.314 min (minor), 6.697 min (major).

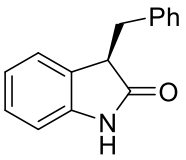
**_tert_-butyl-(_R_)-7,8-dimethoxy-1-methyl-2-oxo-1,2,4,5-tetrahydro-3_H_-benzo[_d_]azepine-3-carboxylate (4j):**




Chemical Formula: $C_{18}H_{25}NO_5$
Exact Mass: 335.1733

99.4 mg, yield = 99%, 95% ee, $[\alpha]^{21}_D$ = -28.20 (c = 1.0, $CH_2Cl_2$), light yellow solid, mp: 123 – 125 °C. $^1$H NMR (400 MHz, Chloroform-*d*): 6.75 (s, 1H), 6.59 (s, 1H), 4.52 – 4.33 (m, 2H), 4.14 – 4.05 (m, 1H), 3.86 (s, 6H), 3.24 – 3.18 (m, 2H), 1.56 (d, *J* = 6.8 Hz, 3H), 1.50 (s, 9H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 173.9, 152.7, 147.9, 147.4, 127.5, 127.0, 113.4, 109.4, 83.1, 56.0, 55.9, 42.9, 41.4, 32.8, 28.0 (3C), 14.4. HRMS (ESI) calcd for $C_{18}H_{26}NO_5^+$ $[M+H]^+$: 336.1805. Found: 336.1803. The enantiomeric excess of **4j** was determined by HPLC analysis on Chiralpak AD-3 column. Conditions: hexane/isopropanol = 80/20, flow rate = 1.0 mL/min, uv-vis detection at λ = 208 nm, $t_R$ = 6.897 min (major), 8.396 min (minor).

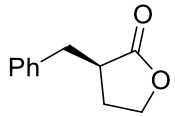
**(*R*)-3-benzylindolin-2-one (4k):**




Chemical Formula: $C_{15}H_{13}NO$
Exact Mass: 223.0997

65.5 mg, yield = 98%, 8% ee (60 °C, 60 atm $H_2$, THF, **Cat 4**), $[\alpha]^{21}_D$ = 7.40 (c = 1.0, $CH_2Cl_2$), yellow solid, mp: 130 – 132 °C. $^1$H NMR (400 MHz, Chloroform-*d*): δ 8.39 (br, 1H), 7.30 – 7.13 (m, 6H), 6.93 – 6.87 (m, 1H), 6.83 (d, *J* = 7.7 Hz, 1H), 6.75 (d, *J* = 7.4 Hz, 1H), 3.75 (dd, *J* = 9.2, 4.6 Hz, 1H), 3.49 (dd, *J* = 13.7, 4.6 Hz, 1H), 2.94 (dd, *J* = 13.7, 9.2 Hz, 1H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 179.4, 141.3, 137.7, 129.4 (2C), 128.9, 128.3 (2C), 127.9, 126.7, 124.9, 122.0, 109.6, 47.5, 36.6. HRMS (ESI) calcd for $C_{15}H_{14}NO^+$ $[M+H]^+$: 224.1070. Found: 224.1069. The enantiomeric excess of **4k** was determined by HPLC analysis on Chiralpak AD-3 column. Conditions: hexane/isopropanol = 80/20, flow rate = 1.0 mL/min, uv-vis detection at λ = 210 nm, $t_R$ = 5.760 min (minor), 6.603 min (major).

**(*R*)-3-benzyldihydrofuran-2(3*H*)-one (4l):**

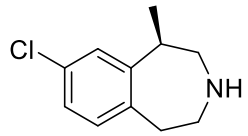



Chemical Formula: $C_{11}H_{12}O_2$
Exact Mass: 176.0837

This is a known compound.[13] 52.3 mg, yield = 99%, 42% ee (60 °C, 60 atm $H_2$, 1,4-dioxane, **Cat 4**), $[\alpha]^{21}_D$ = -12.20 (c = 1.0, $CH_2Cl_2$), white solid, mp: 94 – 96 °C. $^1$H NMR (400 MHz, Chloroform-*d*): 7.36 – 7.16 (m, 5H), 4.29 – 4.07 (m, 2H), 3.26 (dd, *J* = 13.6, 4.0 Hz, 1H), 2.92 – 2.69 (m, 2H), 2.32 – 2.18 (m, 1H), 2.06 – 1.93 (m, 1H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 178.7, 138.4, 128.9 (2C), 128.7 (2C), 126.7, 66.5, 41.1, 36.1, 28.0. HRMS (ESI) calcd for $C_{11}H_{13}O_2^+$ $[M+H]^+$: 177.0910. Found: 177.0910. The enantiomeric excess of **4l** was determined by HPLC analysis on Chiralpak AD-3

column. Conditions: hexane/isopropanol = 95/5, flow rate = 1.0 mL/min, uv-vis detection at λ = 210 nm, $t_R$ = 11.621 min (minor), 13.176 min (major).

**Lorcaserin (5c):**

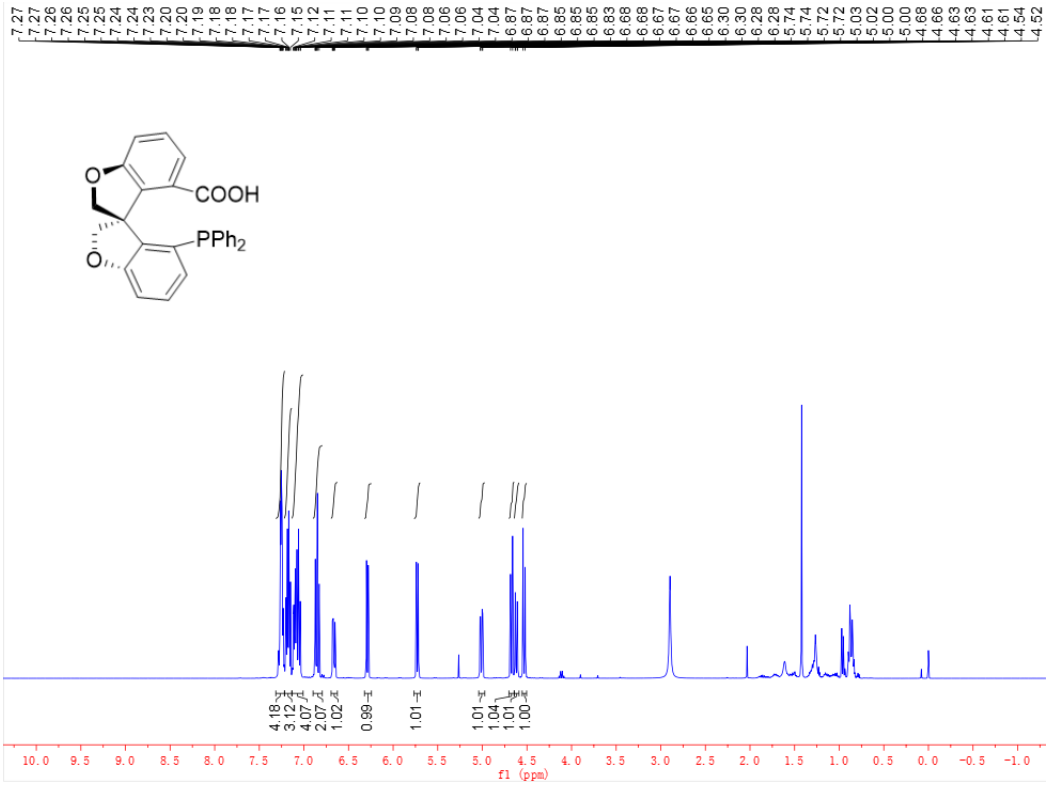



Chemical Formula: $C_{11}H_{14}ClN$
Exact Mass: 195.0815

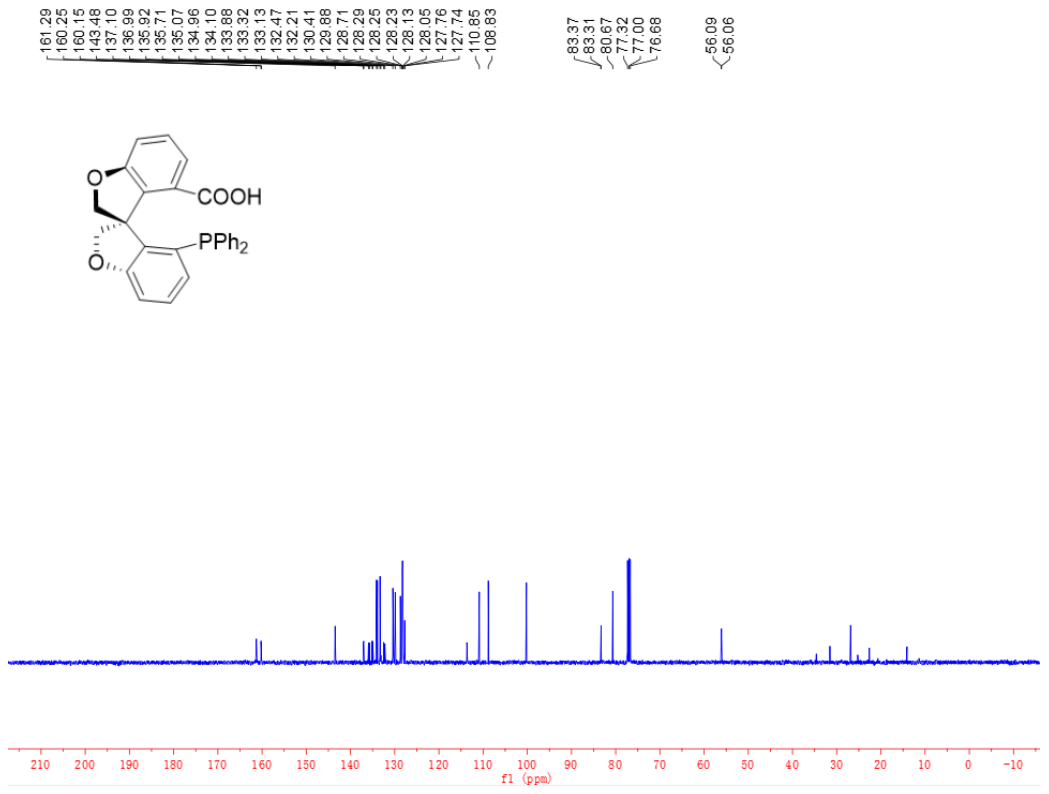
This is a known compound.[10] Lorcaserin (**5c)** was synthesized according to a reported procedure:[10] a mixture of **4c** (41.8 mg, 0.2 mmol) was dissolved in THF (2 mL). The mixture was cooled to 0 ℃, then borane-tetrahydrofuran complex (1M, 0.3 mL, 1.50 equiv) was added dropwise with stirring. The reaction mixture was stirred for 24 h at 24 ℃. The reaction was quenched by addition of methanol (0.5 mL). The pH was adjusted to 6.0 with 1N HCl aqueous solution and stirred for 30 minutes at 24 ℃. It was then neutralized with saturated aqueous $Na_2CO_3$ and the pH was adjusted to 8.0. The solution was extracted with EtOAc, then the organic phase was washed with brine, dried over anhydrous $Na_2SO_4$, filtered and concentrated under vacuum to provide **5c** as a light-yellow solid (35.9 mg, yield = 92%). The material was used without further purification. 99% ee, $[\alpha]^{23}_D$ = -205.60 (c = 0.5, $CH_2Cl_2$), mp: 86 – 88 ℃. $^1$H NMR (400 MHz, Chloroform-*d*): δ 7.06 (d, *J* = 2.2 Hz, 1H), 7.00 (dd, *J* = 8.0, 2.2 Hz, 1H), 6.93 (d, *J* = 8.0 Hz, 1H), 3.06 – 2.74 (m, 6H), 2.64 (q, *J* = 7.5 Hz, 1H), 2.19 (br, 1H), 1.25 (d, *J* = 7.1 Hz, 3H). $^{13}$C NMR (101 MHz, Chloroform-*d*): δ 147.3, 139.6, 131.8, 130.9, 126.6, 125.8, 54.5, 47.8, 41.5, 38.9, 17.6. HRMS (ESI) calcd for $C_{11}H_{15}ClN^+$ $[M+H]^+$: 196.0888. Found: 196.0888. The enantiomeric excess of **5c** was determined by HPLC analysis on Chiralpak OJ-3 column. Conditions: hexane/isopropanol = 97/3, flow rate = 0.8 mL/min, uv-vis detection at λ = 220 nm, $t_R$ = 5.674 min (major), 6.675 min (minor).

## 6. Spectroscopic Data

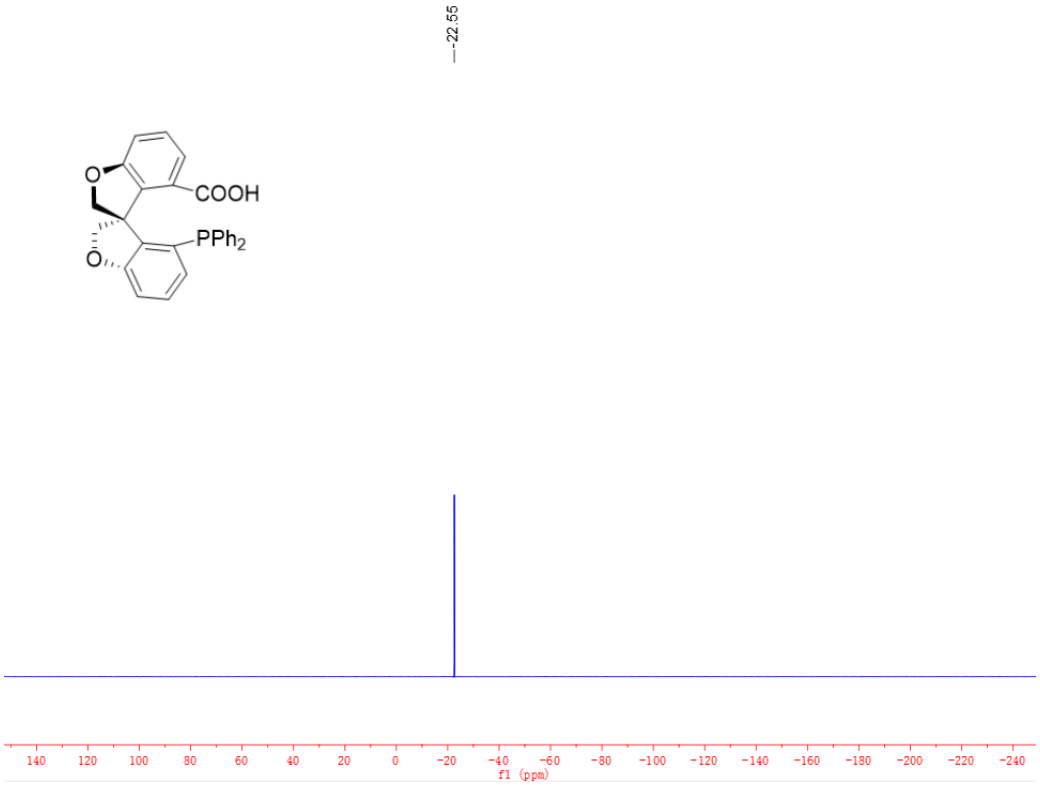
$^{1}$H NMR (400 MHz, Chloroform-*d*) of (*R*)-**2a:**



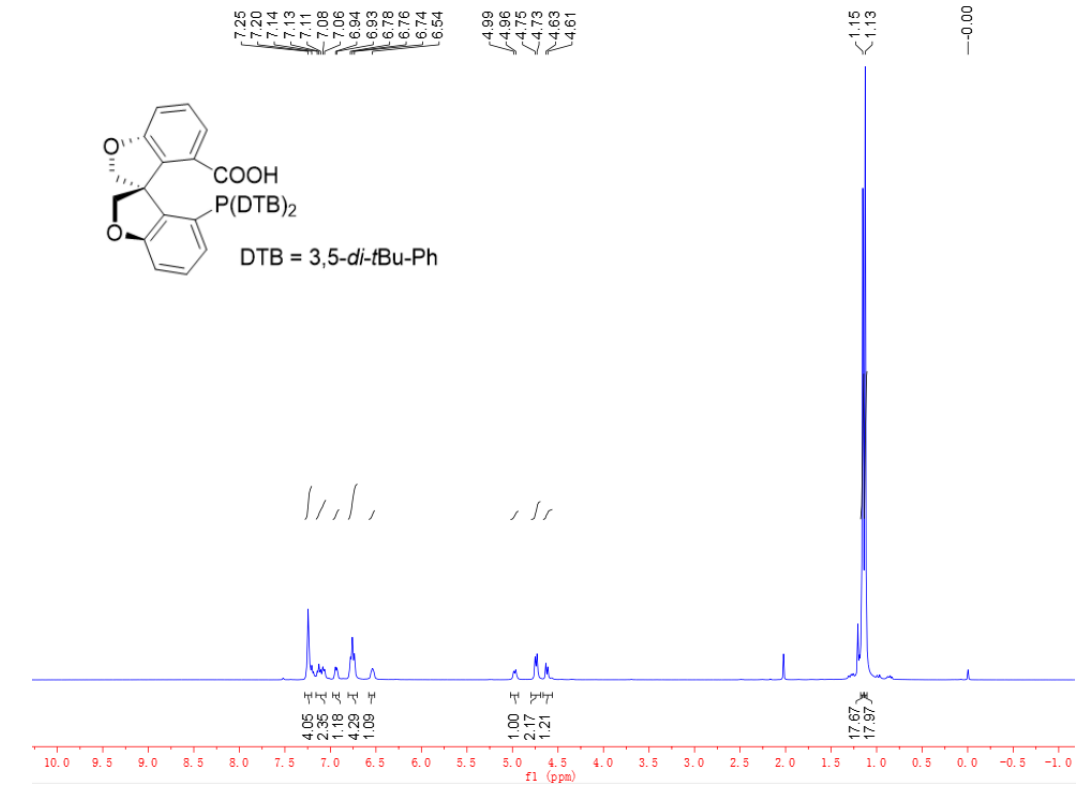

$^{13}$C NMR (101 MHz, Chloroform-*d*) of (*R*)-**2a**:



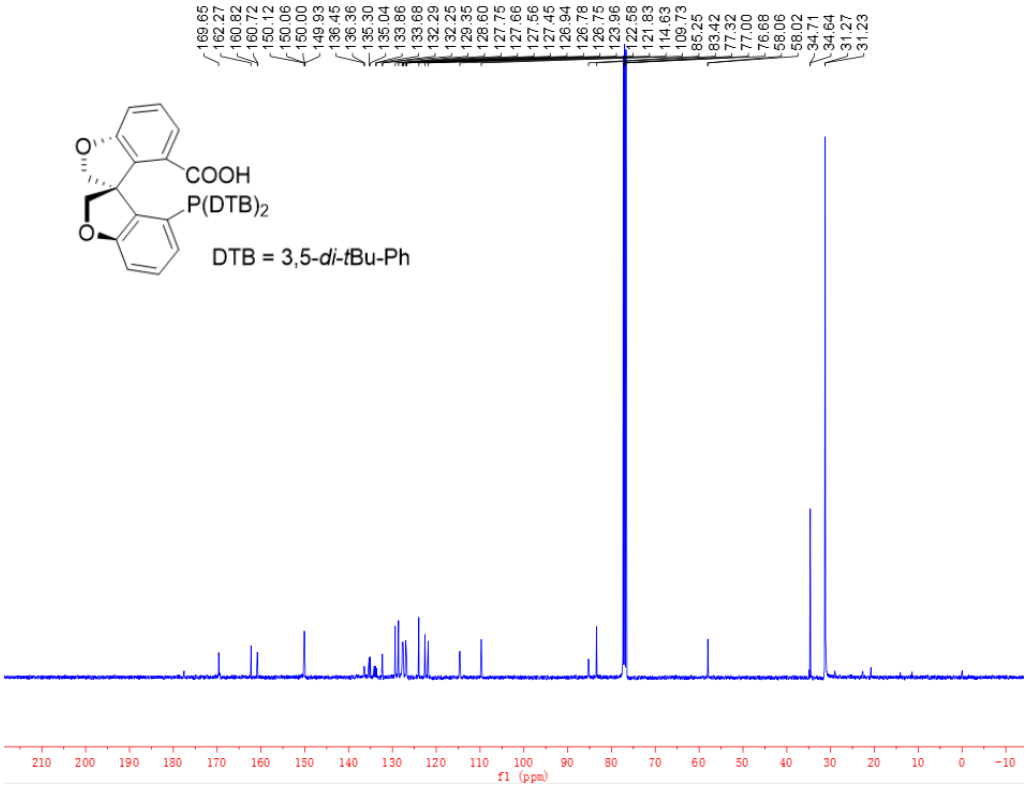
$^{31}$P NMR (162 MHz, Chloroform-*d*) of (*R*)-**2a**:



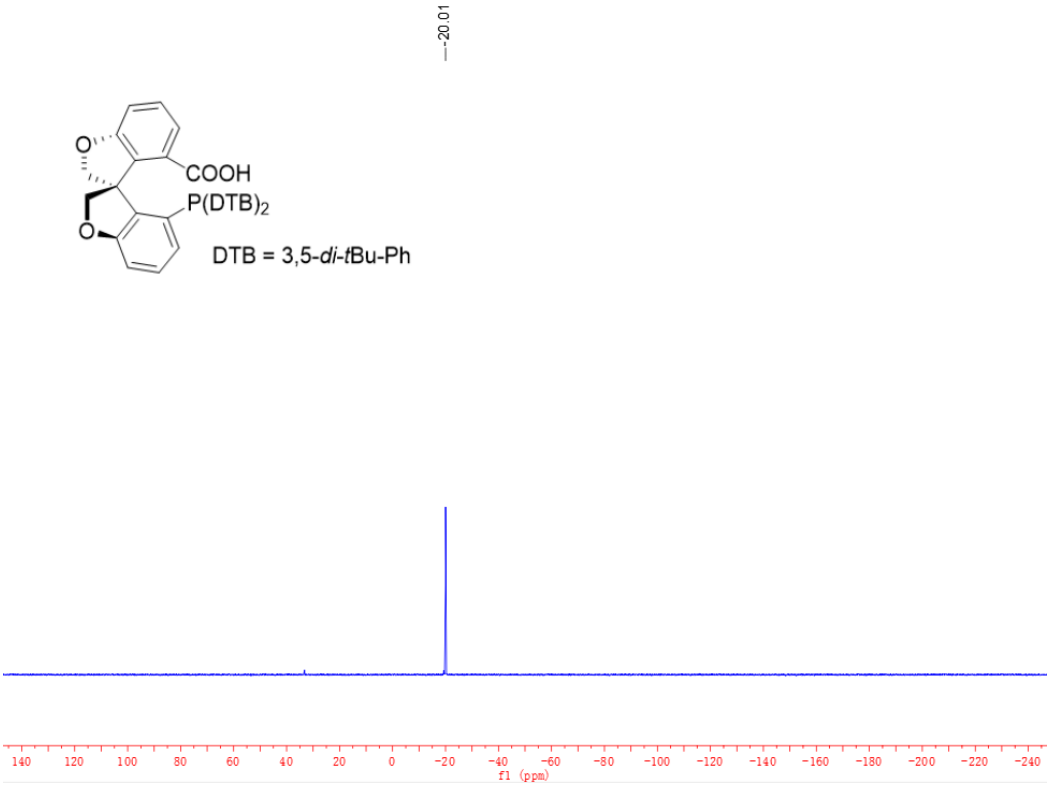

$^{1}$H NMR (400 MHz, Chloroform-*d*) of (*S*)-**2b:**



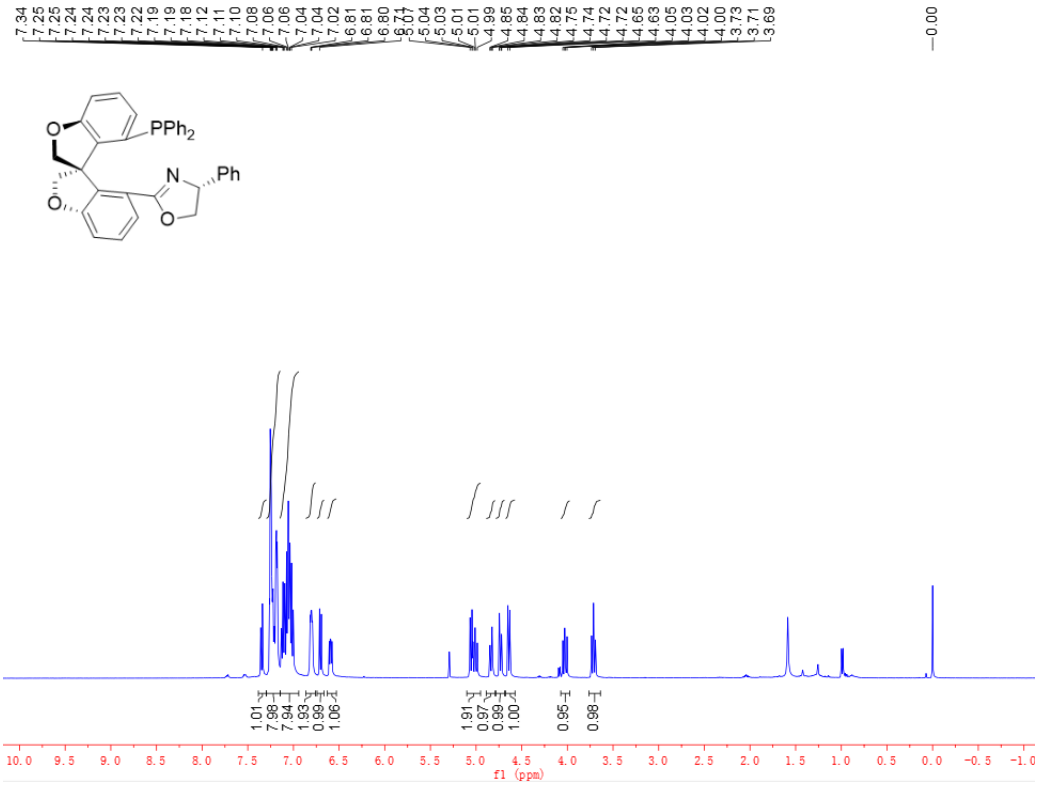
$^{13}$C NMR (101 MHz, Chloroform-*d*) of (*S*)-**2b**:



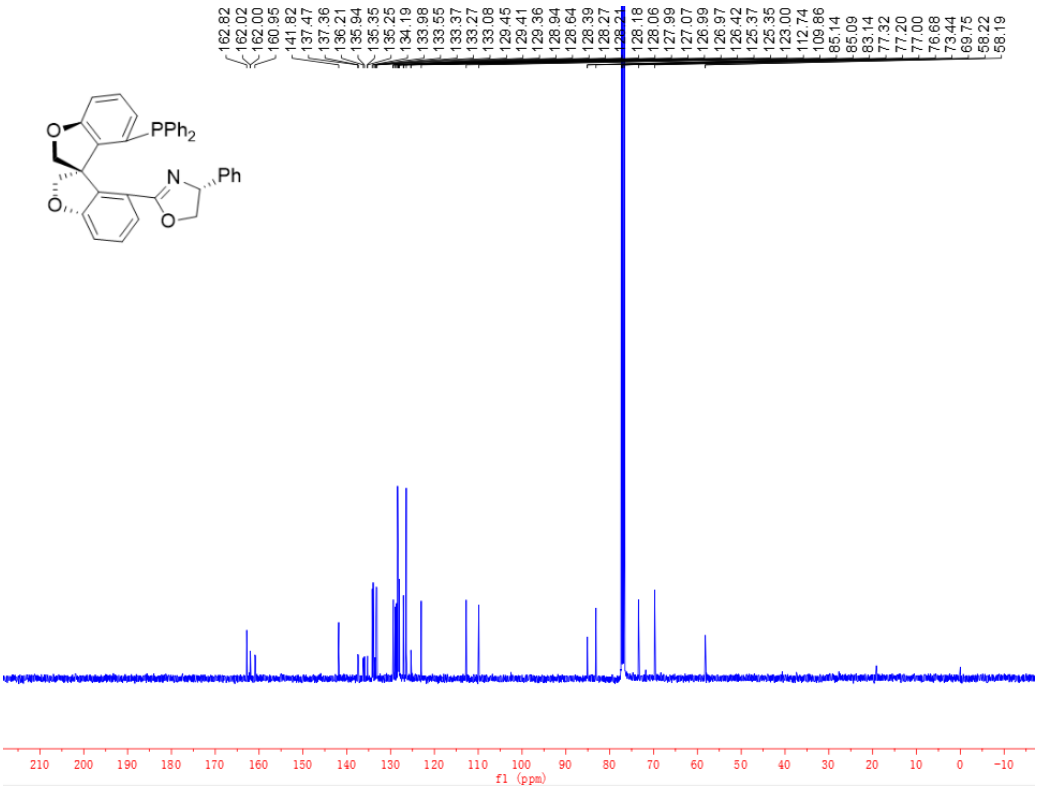

$^{31}$P NMR (162 MHz, Chloroform-*d*) of (*S*)-**2b**:



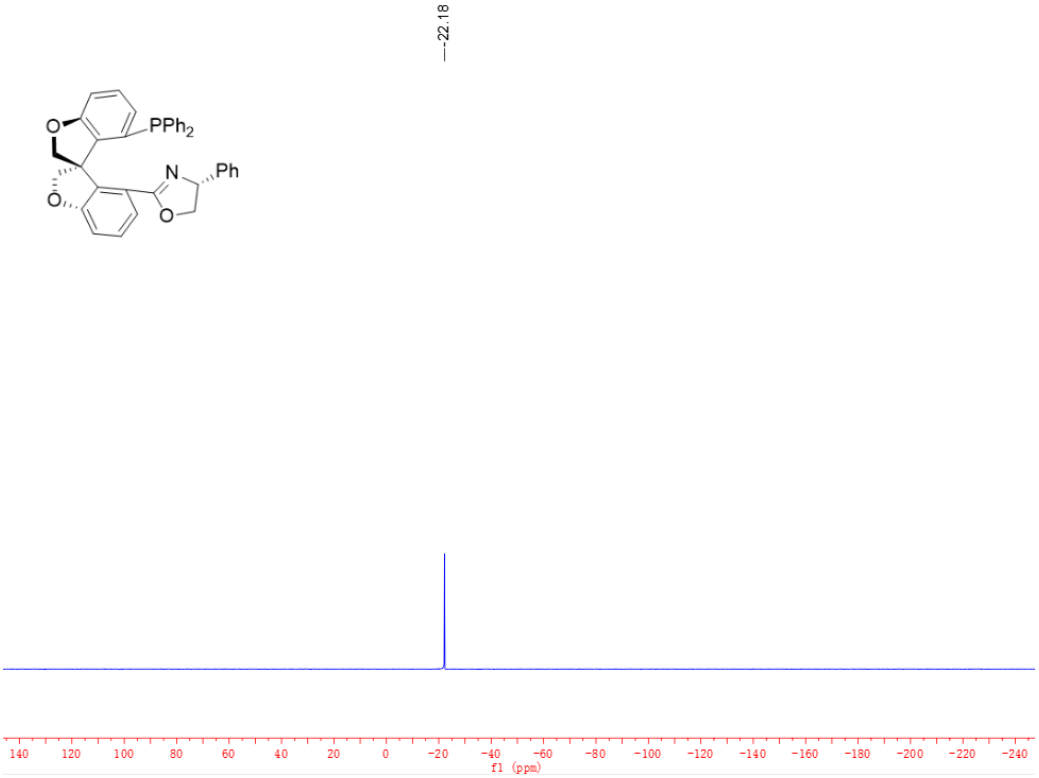
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **L1:**



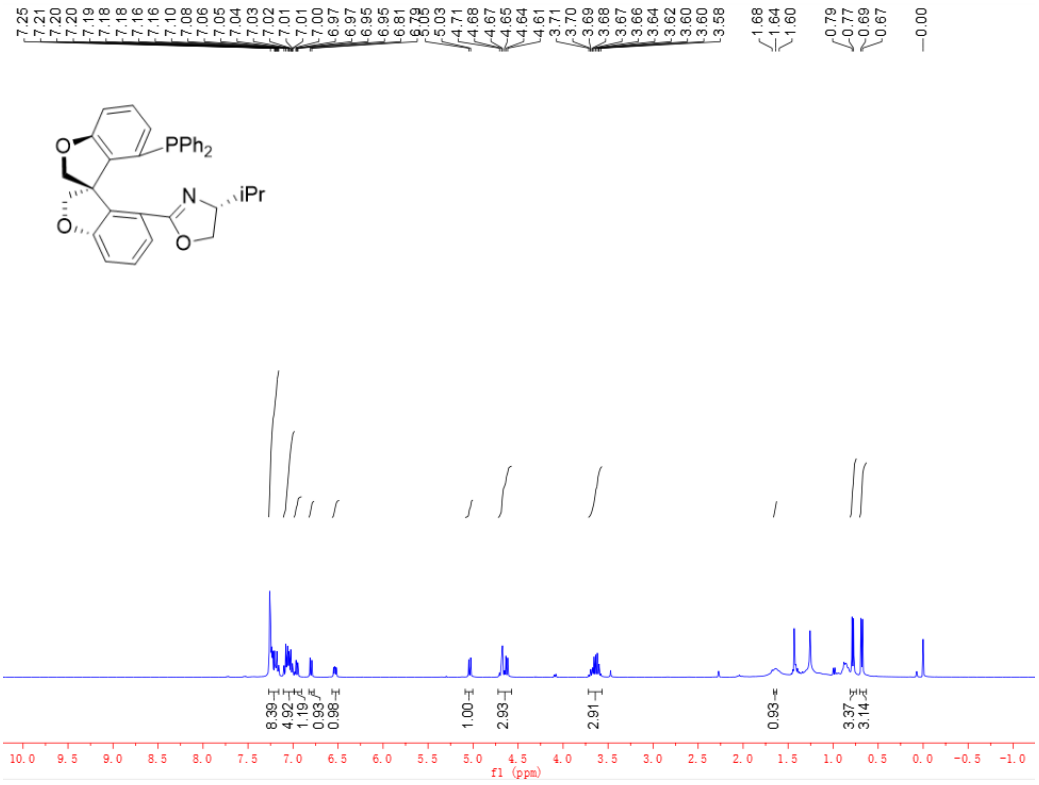

$^{13}$C NMR (101 MHz, Chloroform-*d*) of **L1**:



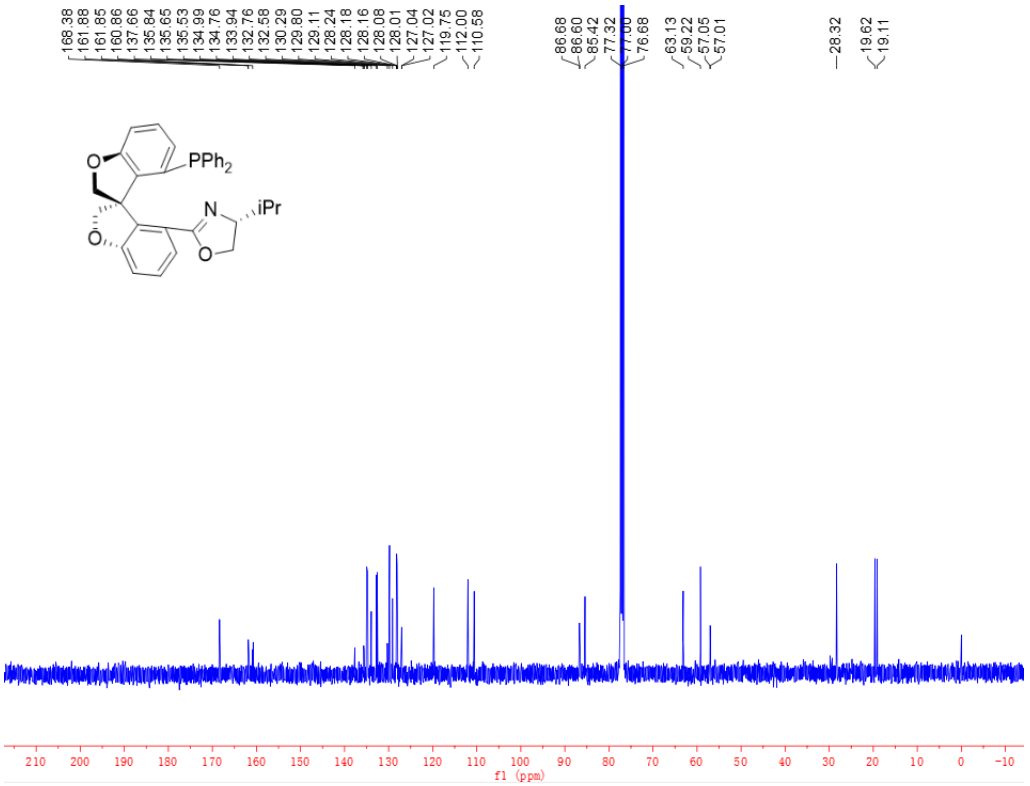
$^{31}$P NMR (243 MHz, Chloroform-*d*) of **L1**:



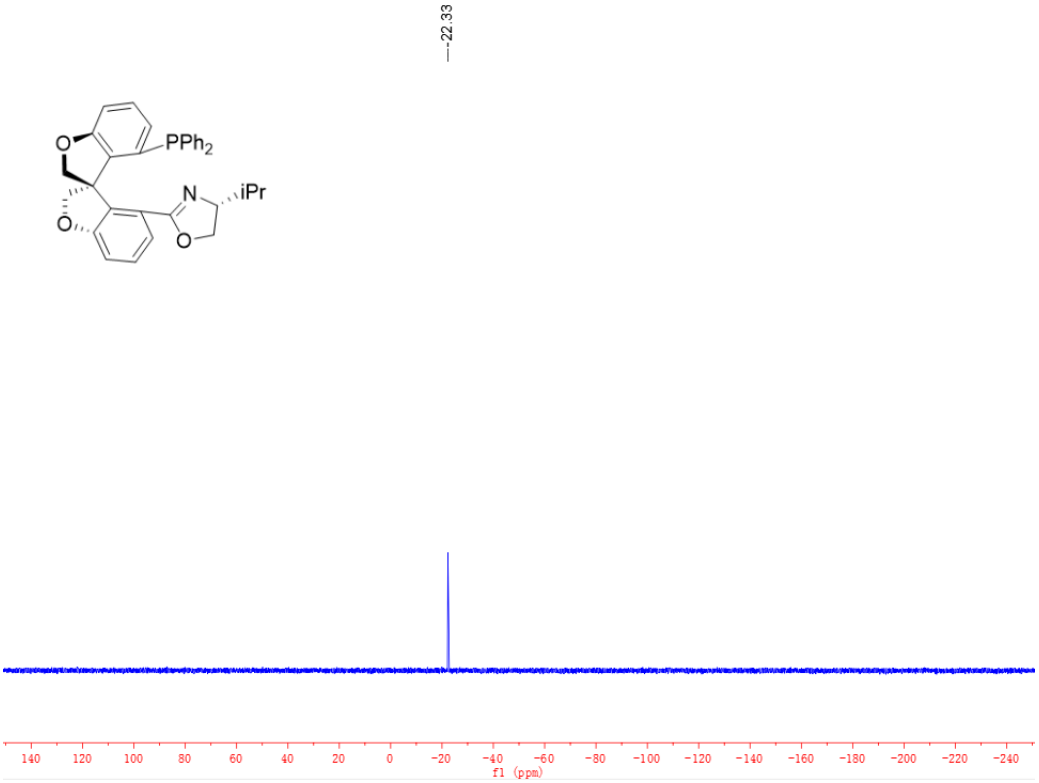

$^{1}$H NMR (400 MHz, Chloroform-*d*) of **L2:**



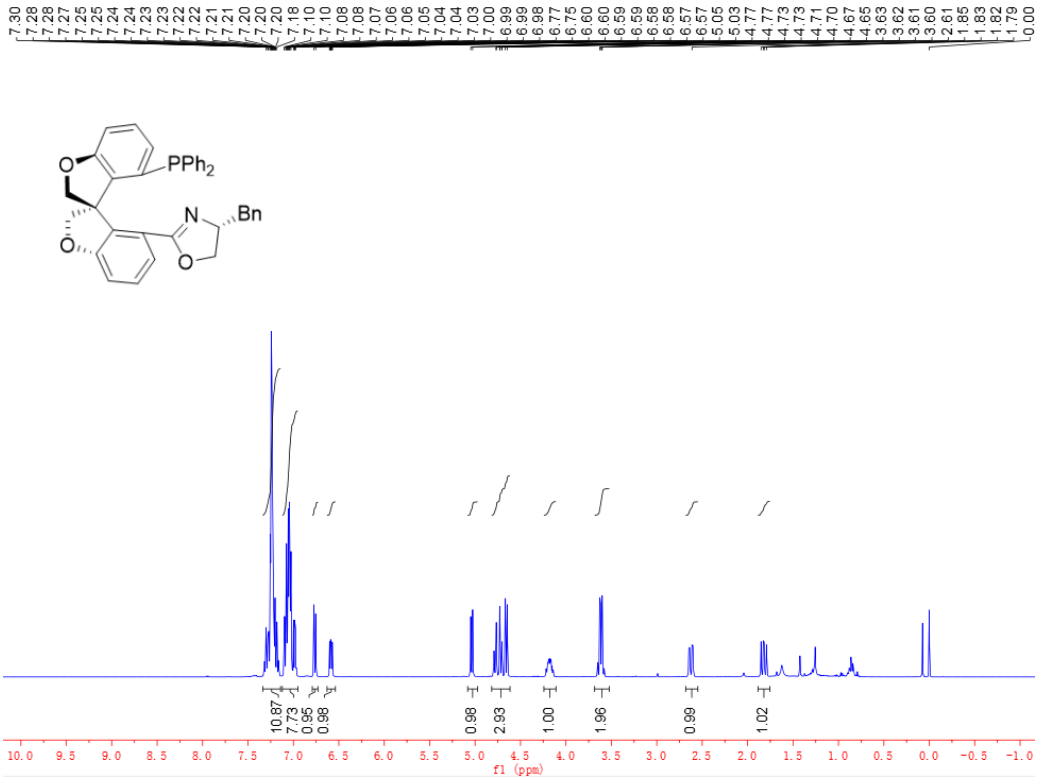
$^{13}$C NMR (101 MHz, Chloroform-*d*) of **L2**:



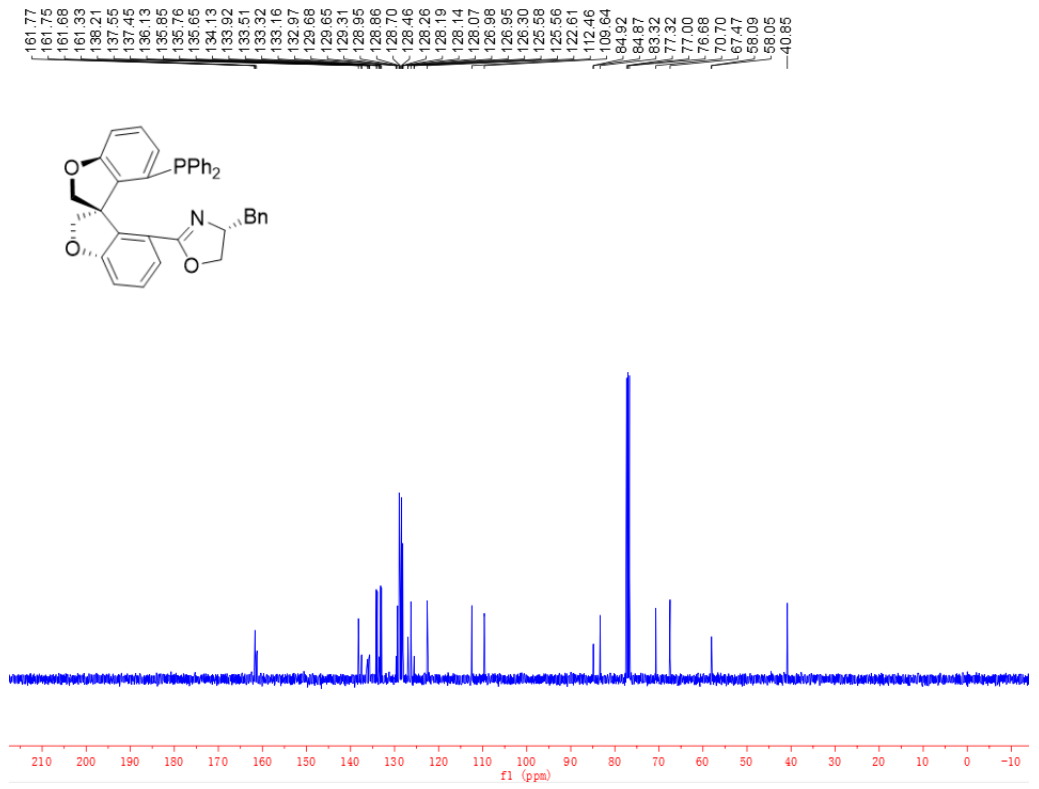

$^{31}$P NMR (162 MHz, Chloroform-*d*) of **L2**:



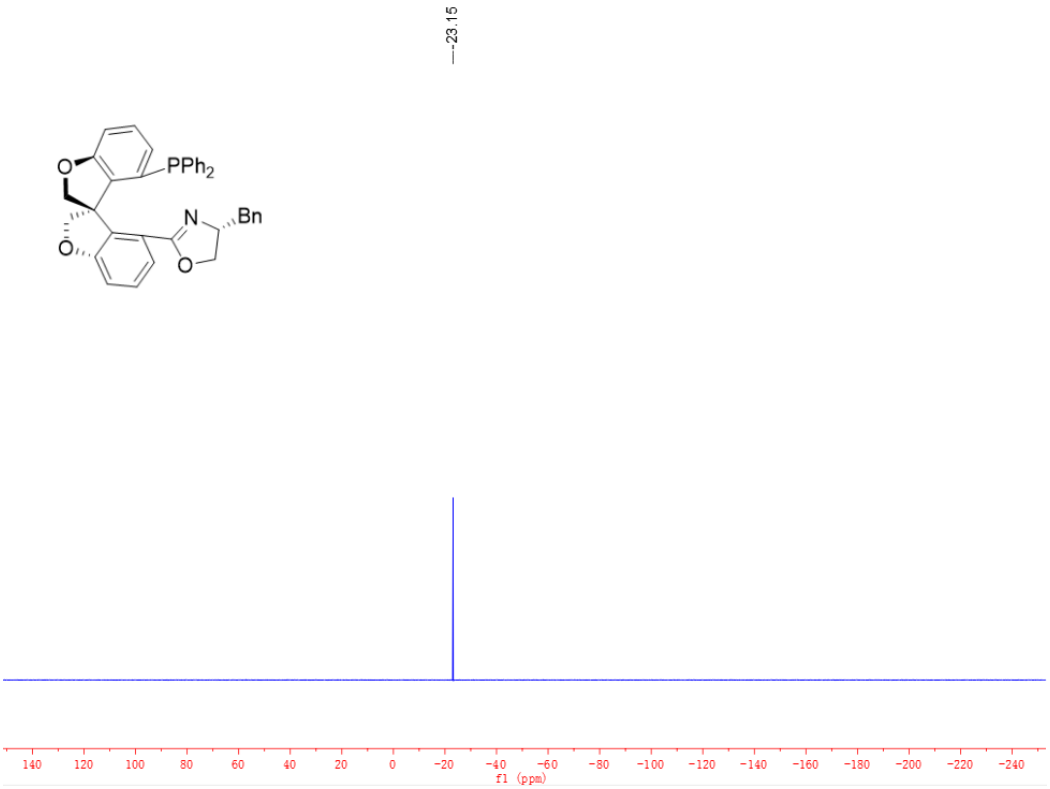
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **L3:**



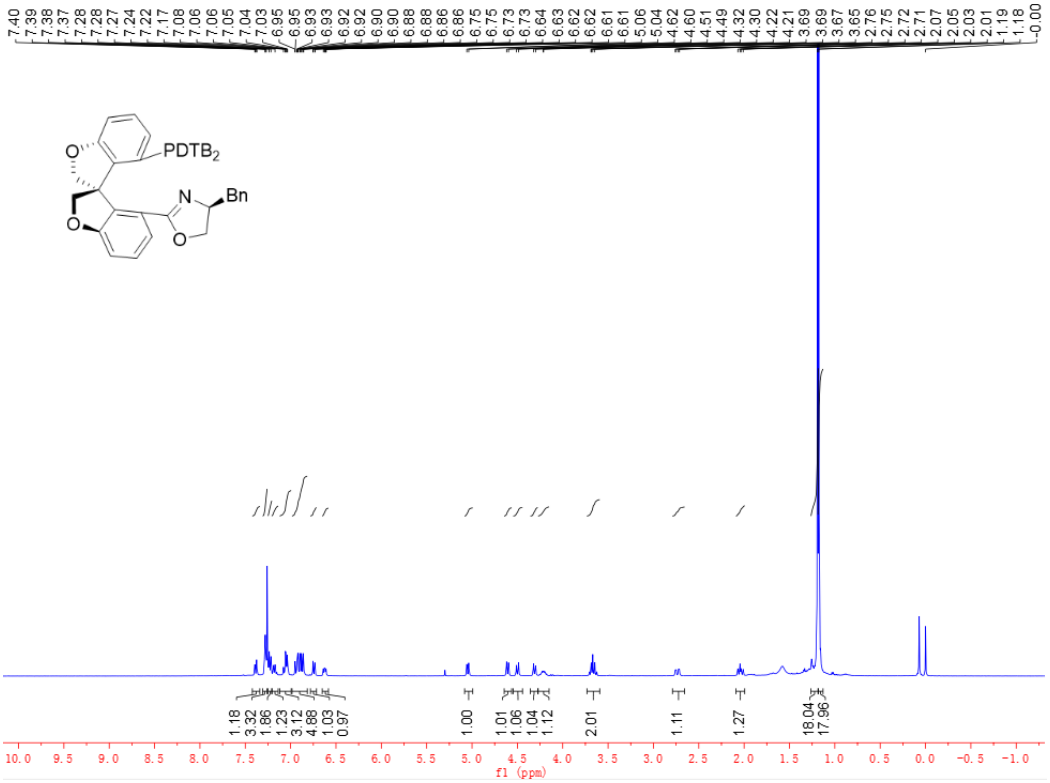

$^{13}$C NMR (101 MHz, Chloroform-*d*) of **L3**:



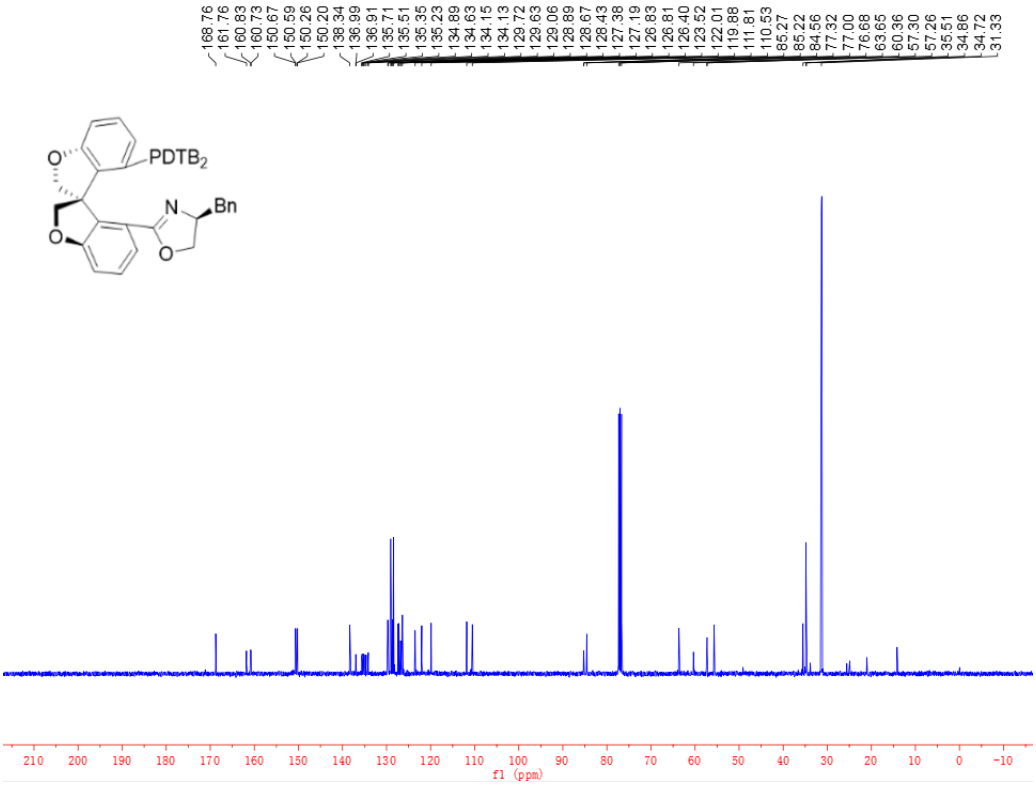
$^{31}$P NMR (162 MHz, Chloroform-*d*) of **L3**:



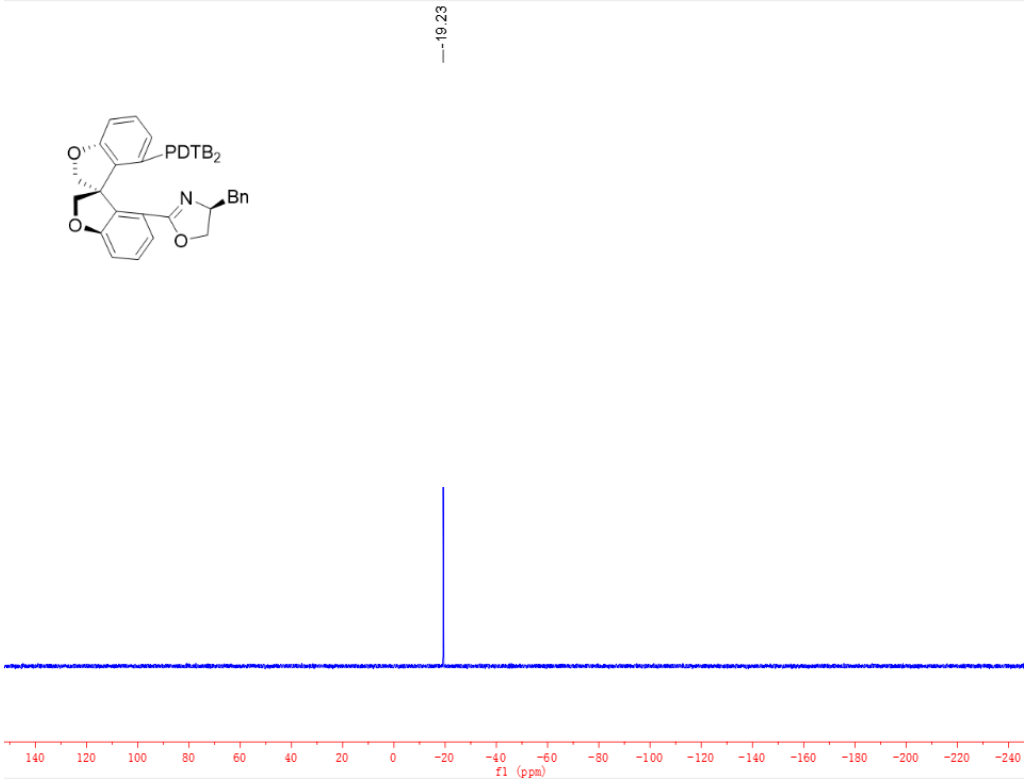

$^{1}$H NMR (400 MHz, Chloroform-*d*) of **L4:**



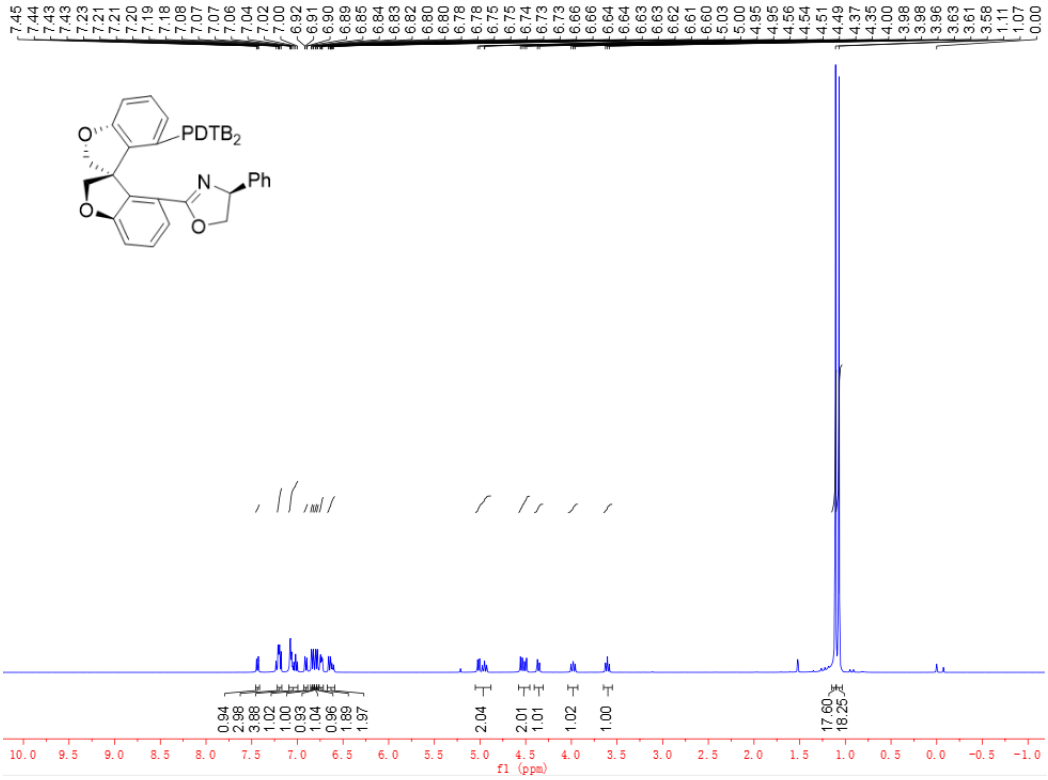
$^{13}$C NMR (101 MHz, Chloroform-*d*) of **L4**:



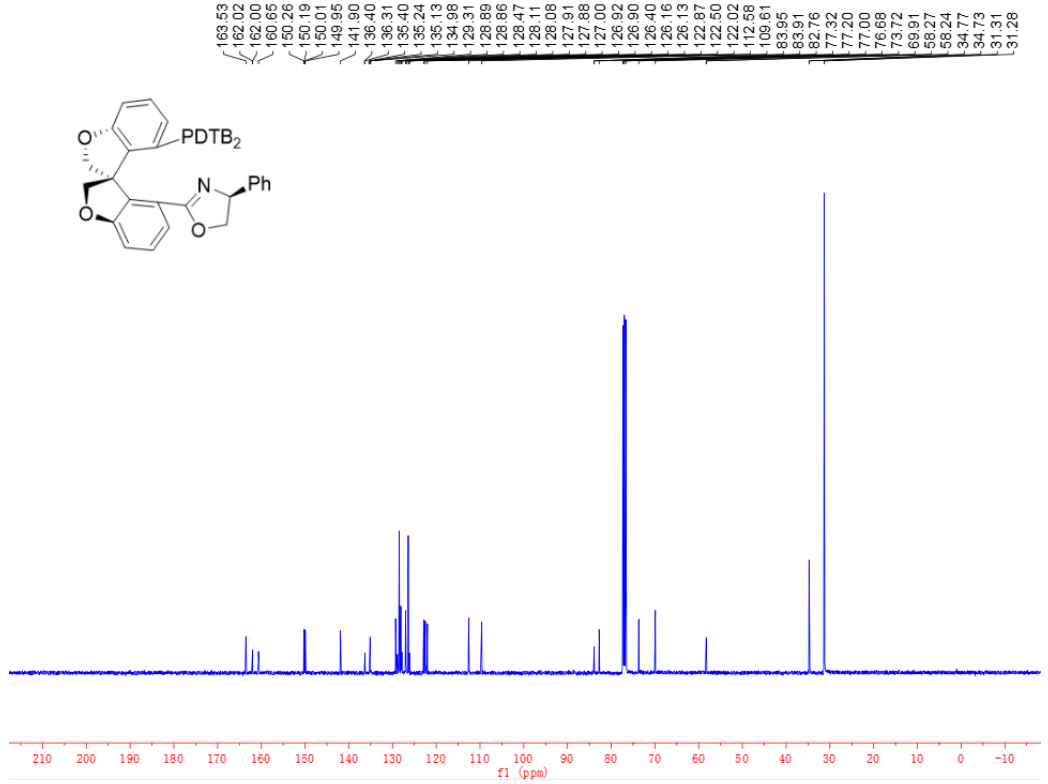

$^{31}$P NMR (162 MHz, Chloroform-*d*) of **L4**:



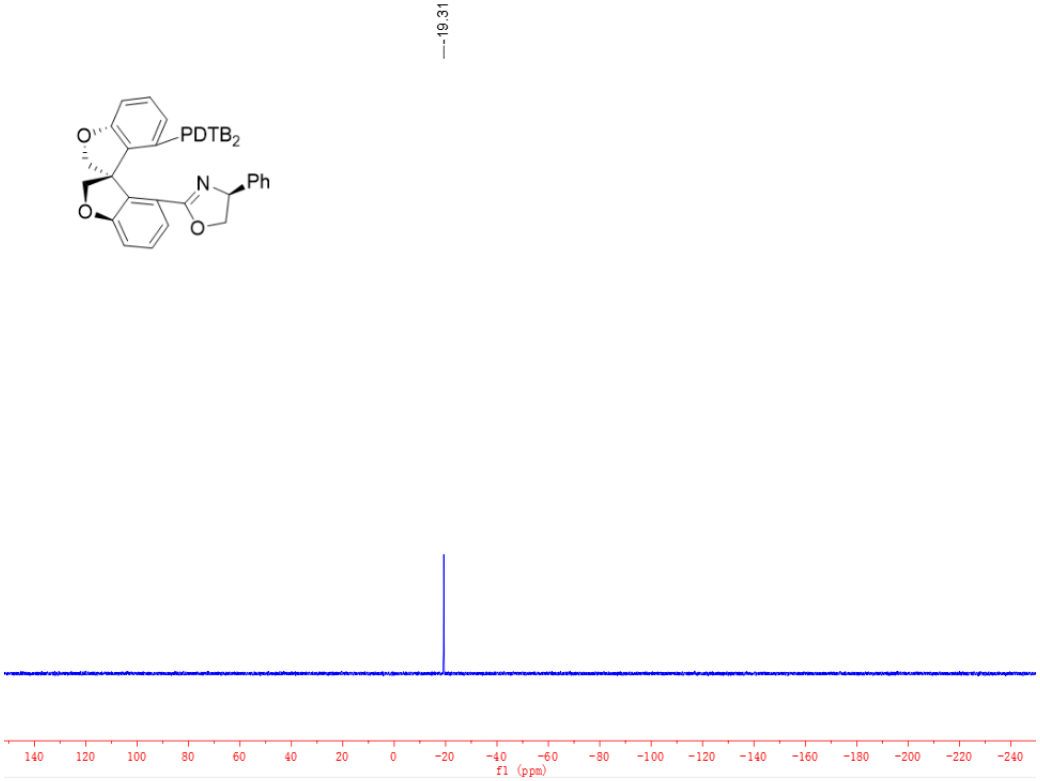
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **L5:**



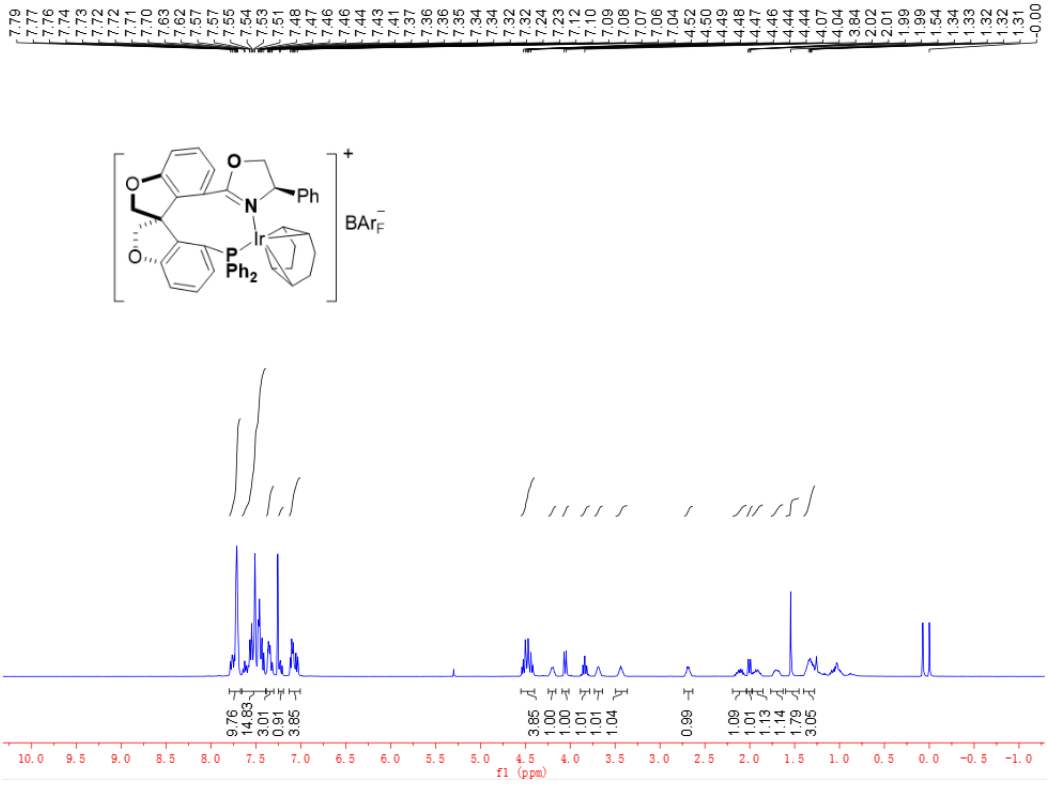

$^{13}$C NMR (101 MHz, Chloroform-*d*) of **L5**:



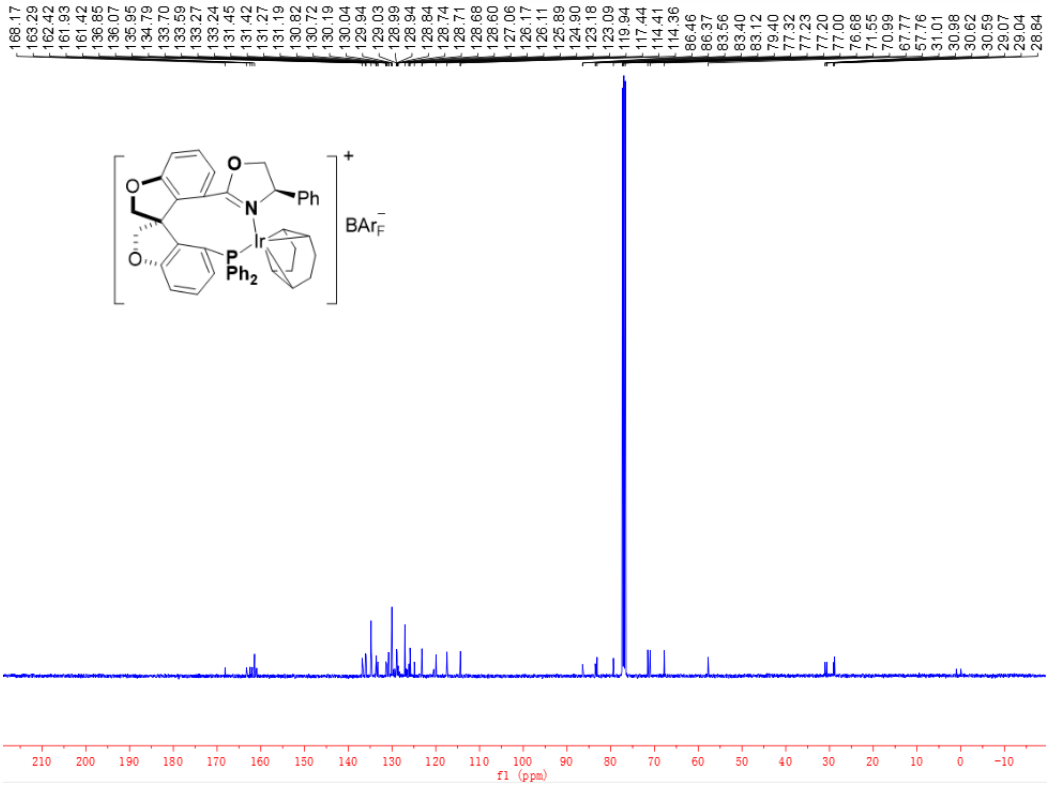
$^{31}$P NMR (162 MHz, Chloroform-*d*) of **L5**:



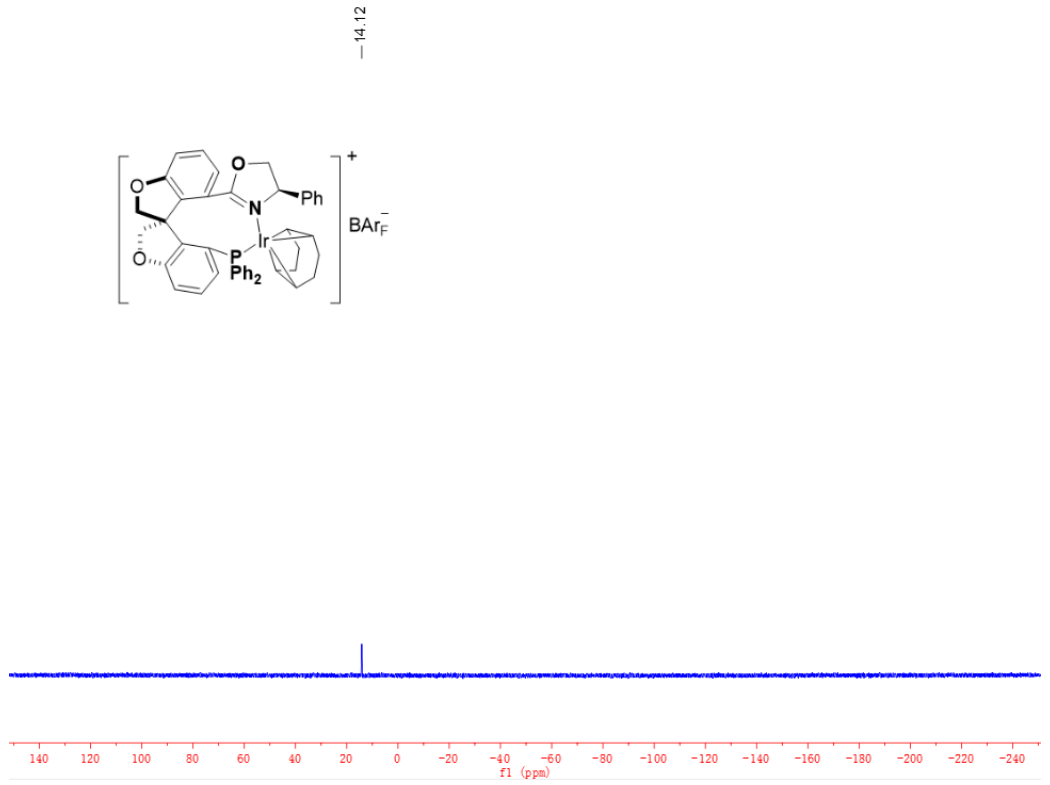

$^{1}$H NMR (400 MHz, Chloroform-*d*) of **Cat 1**:



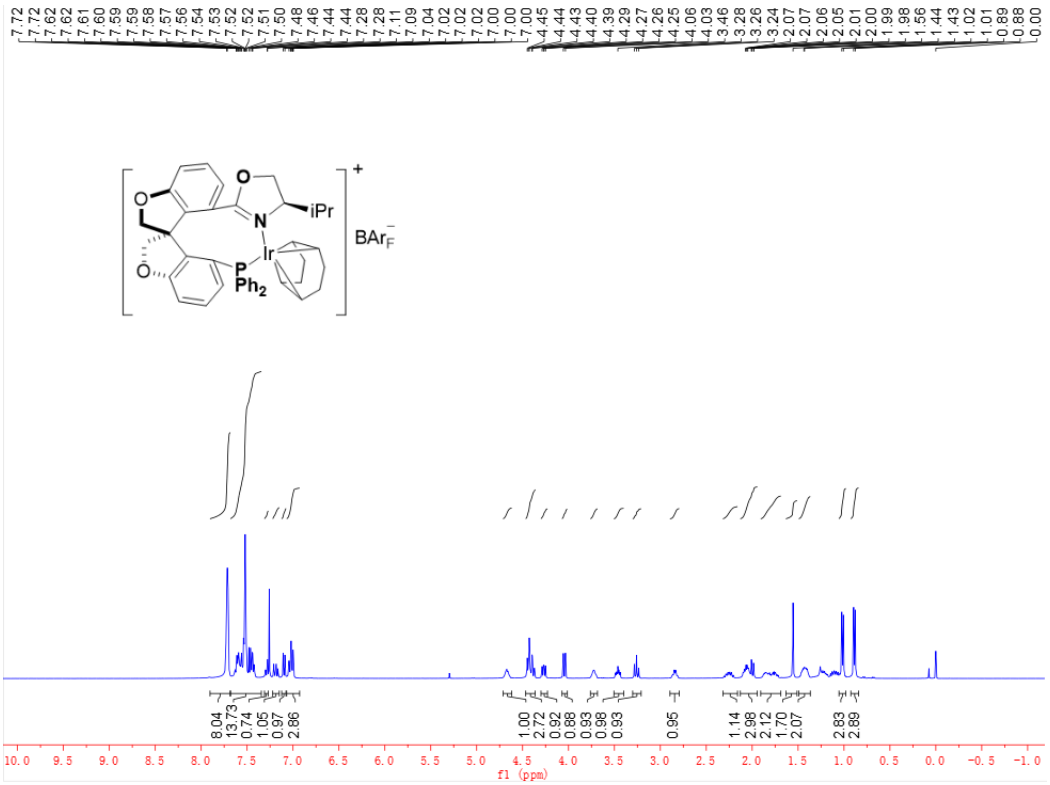
$^{13}$C NMR (101 MHz, Chloroform-*d*) of **Cat 1**:



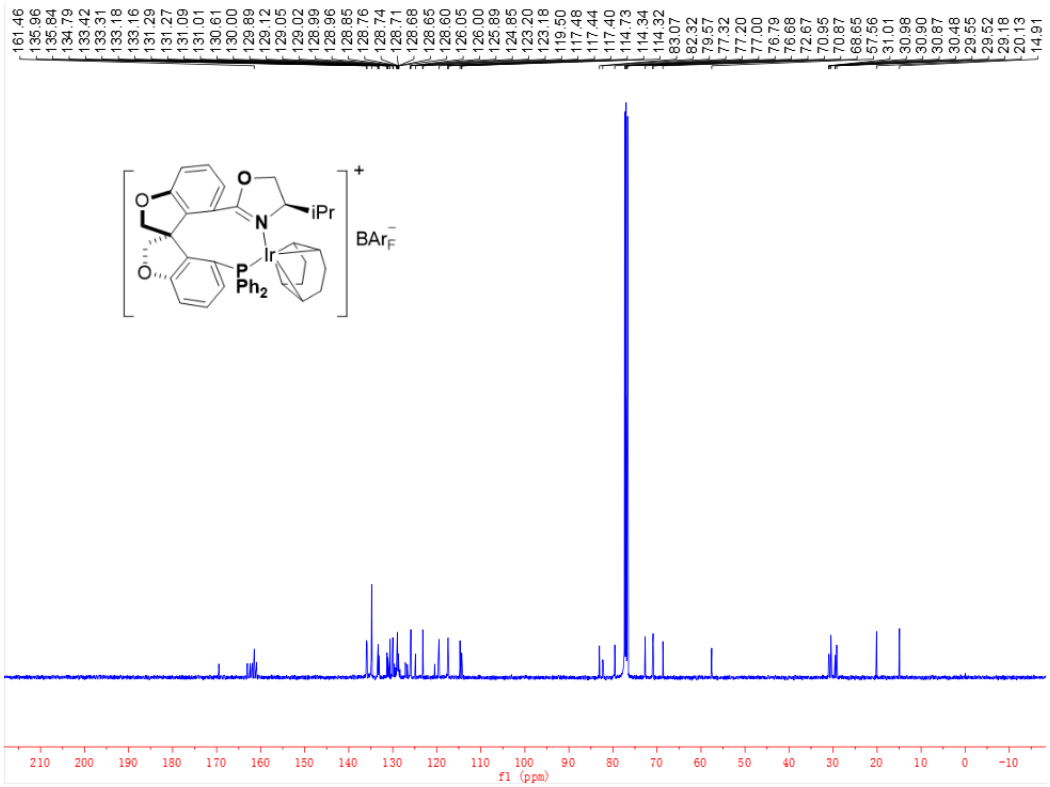

$^{31}$P NMR (162 MHz, Chloroform-*d*) of **Cat 1**:



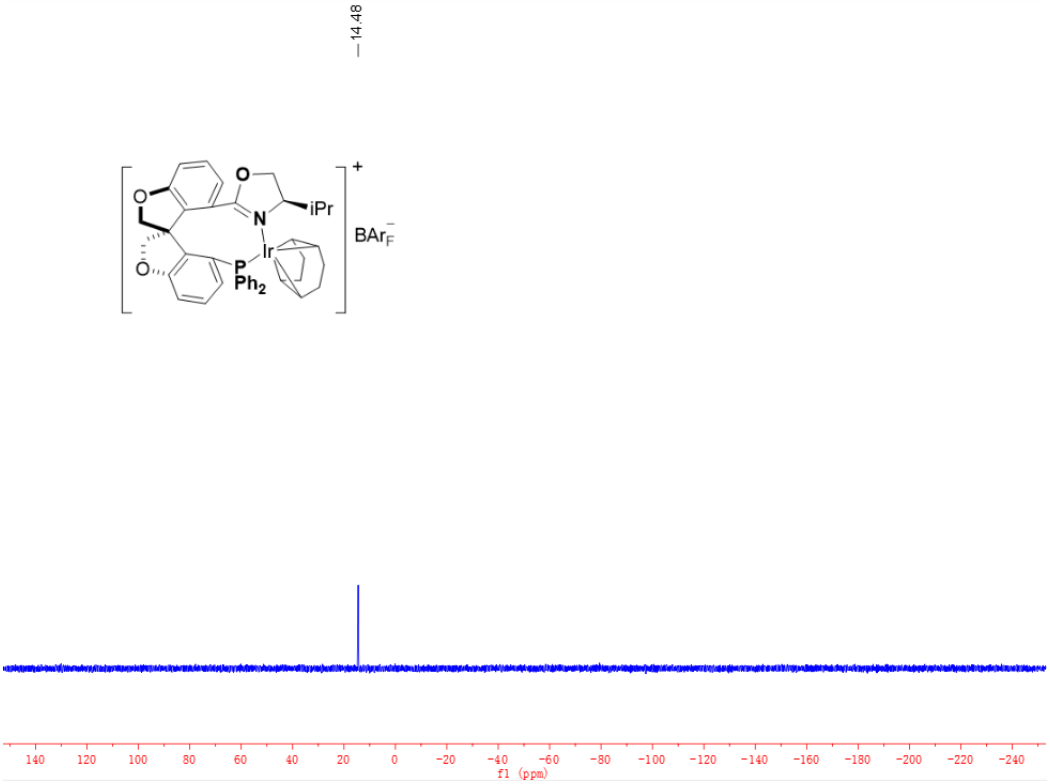
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **Cat 2**:



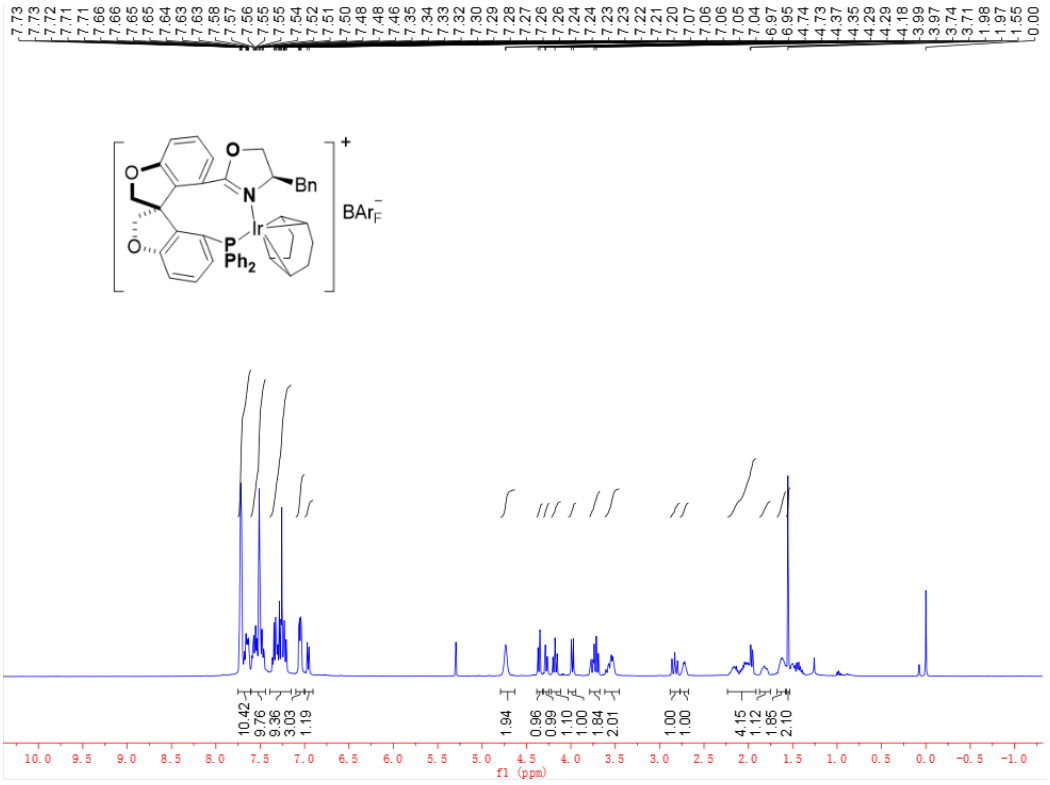

$^{13}$C NMR (101 MHz, Chloroform-*d*) of **Cat 2**:



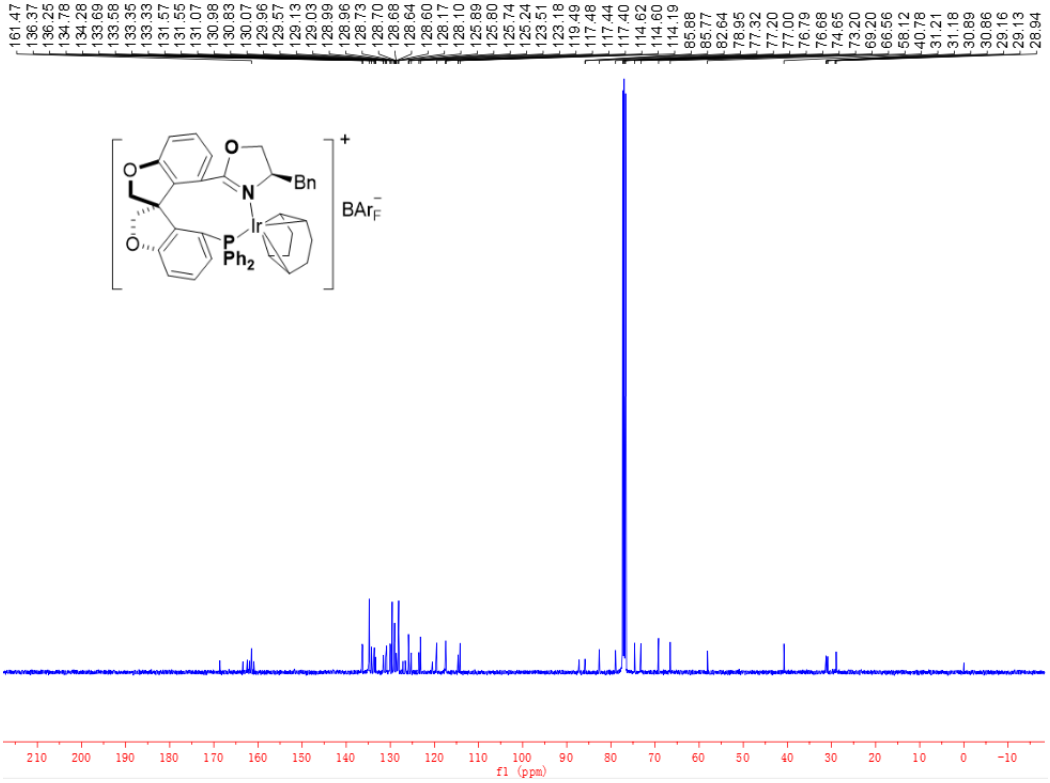
$^{31}$P NMR (162 MHz, Chloroform-*d*) of **Cat 2**:



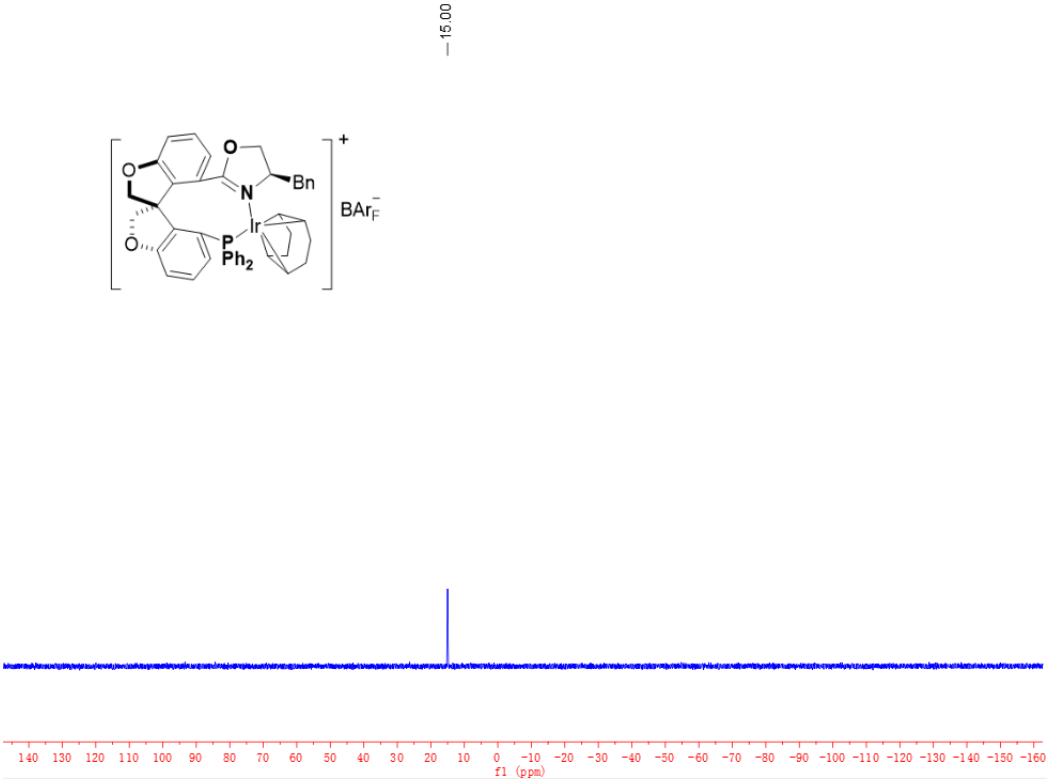

$^{1}$H NMR (400 MHz, Chloroform-*d*) of **Cat 3**:



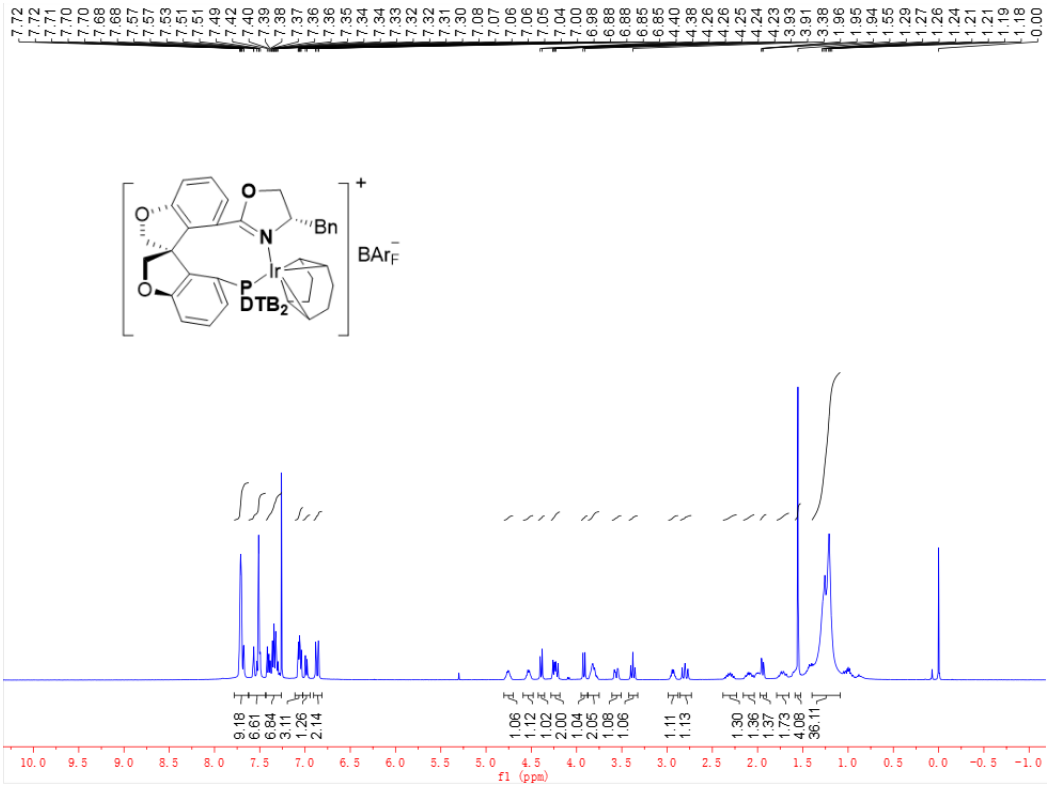
$^{13}$C NMR (101 MHz, Chloroform-*d*) of **Cat 3**:



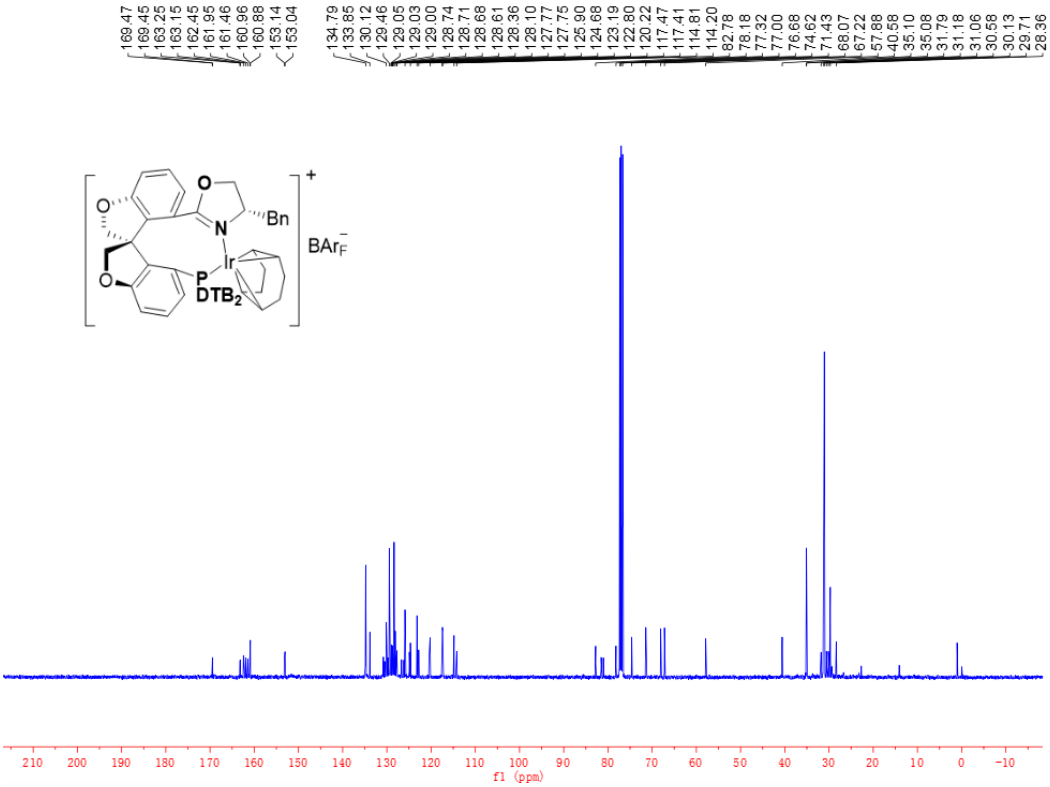

$^{31}$P NMR (162 MHz, Chloroform-*d*) of **Cat 3**:



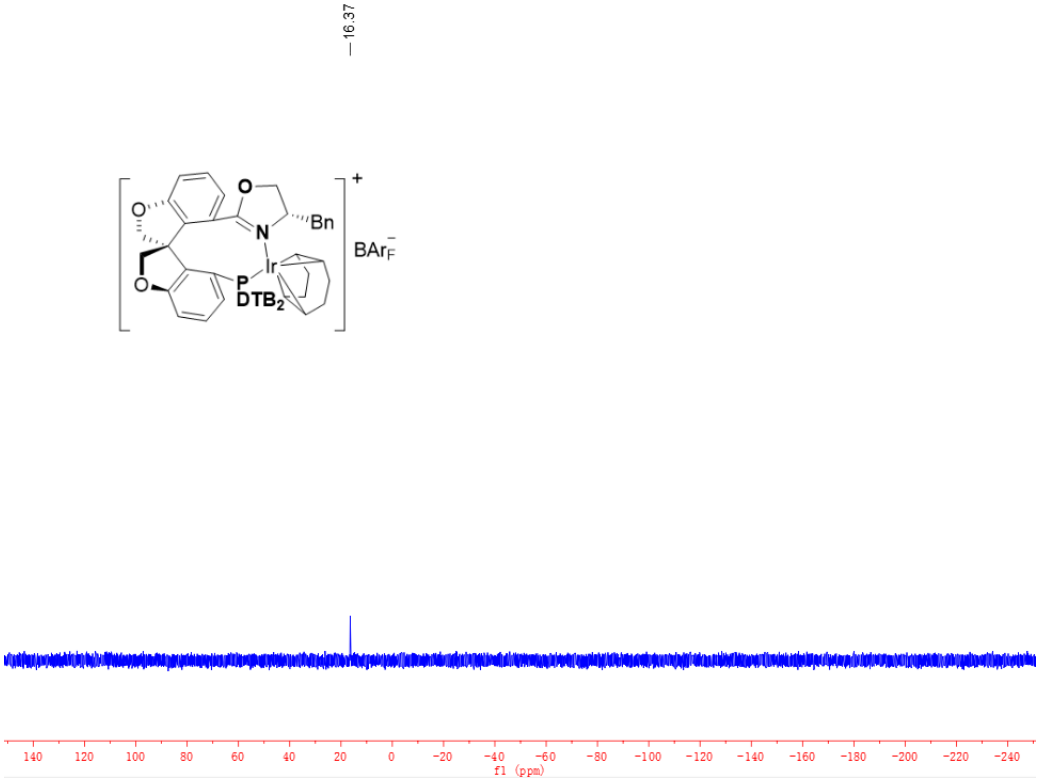
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **Cat 4**:



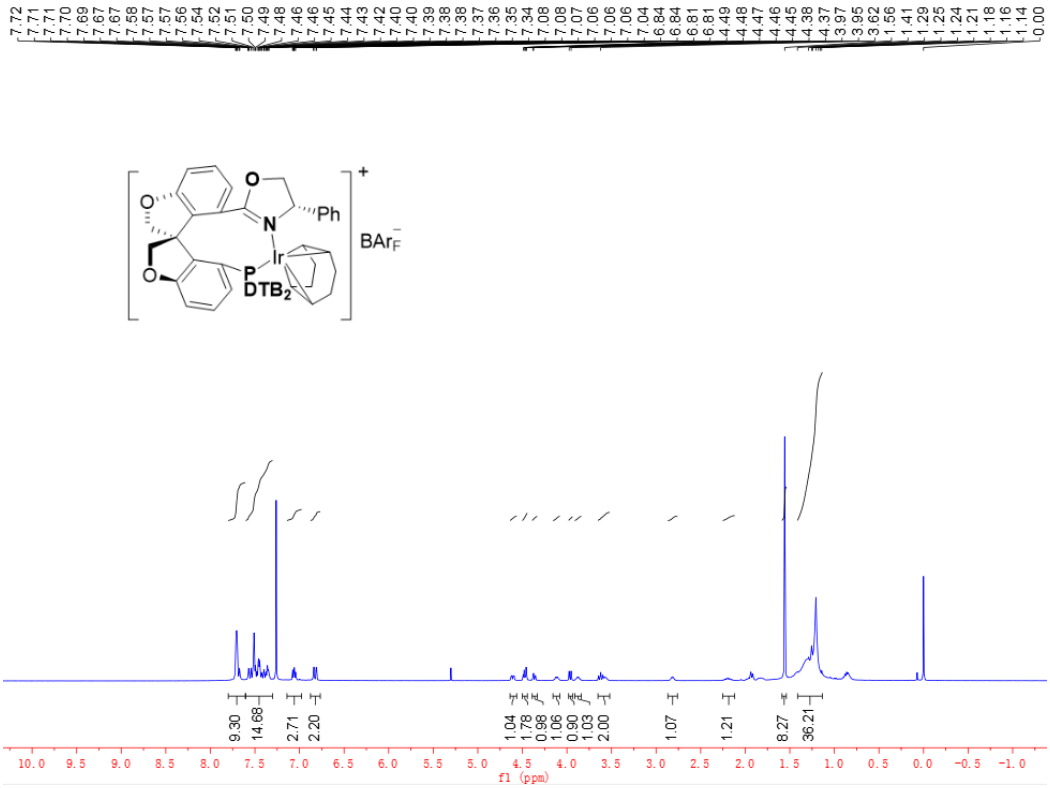

$^{13}$C NMR (101 MHz, Chloroform-*d*) of **Cat 4**:



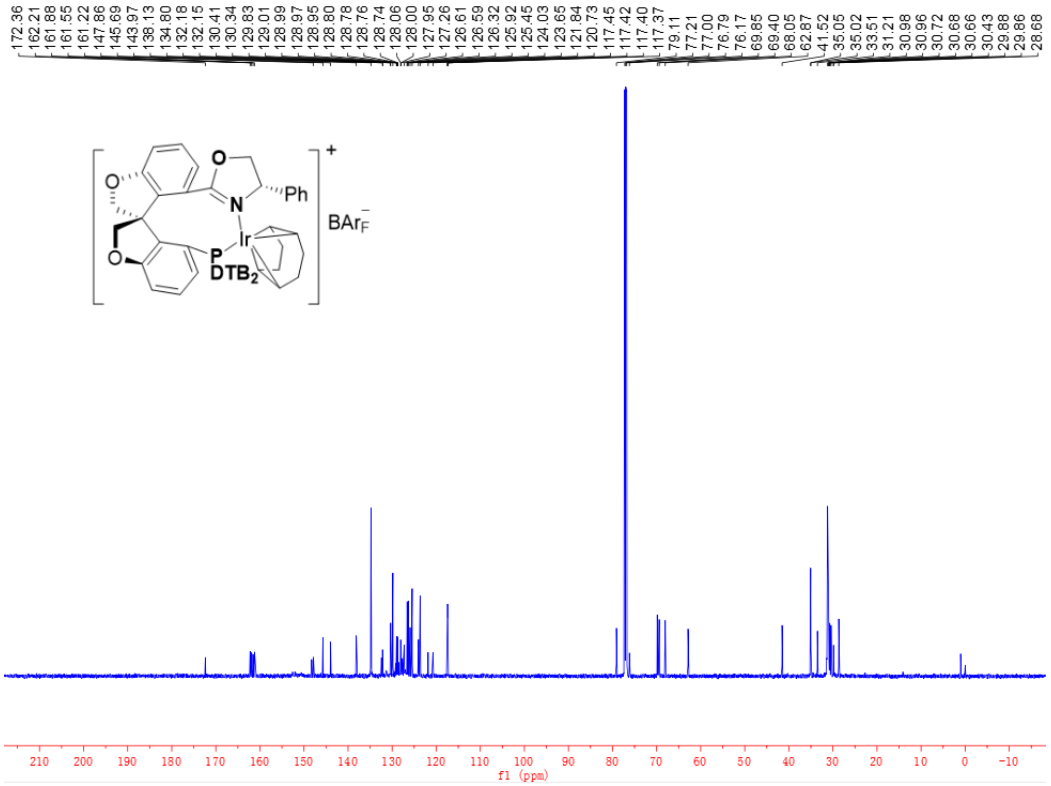
$^{31}$P NMR (162 MHz, Chloroform-*d*) of **Cat 4**:



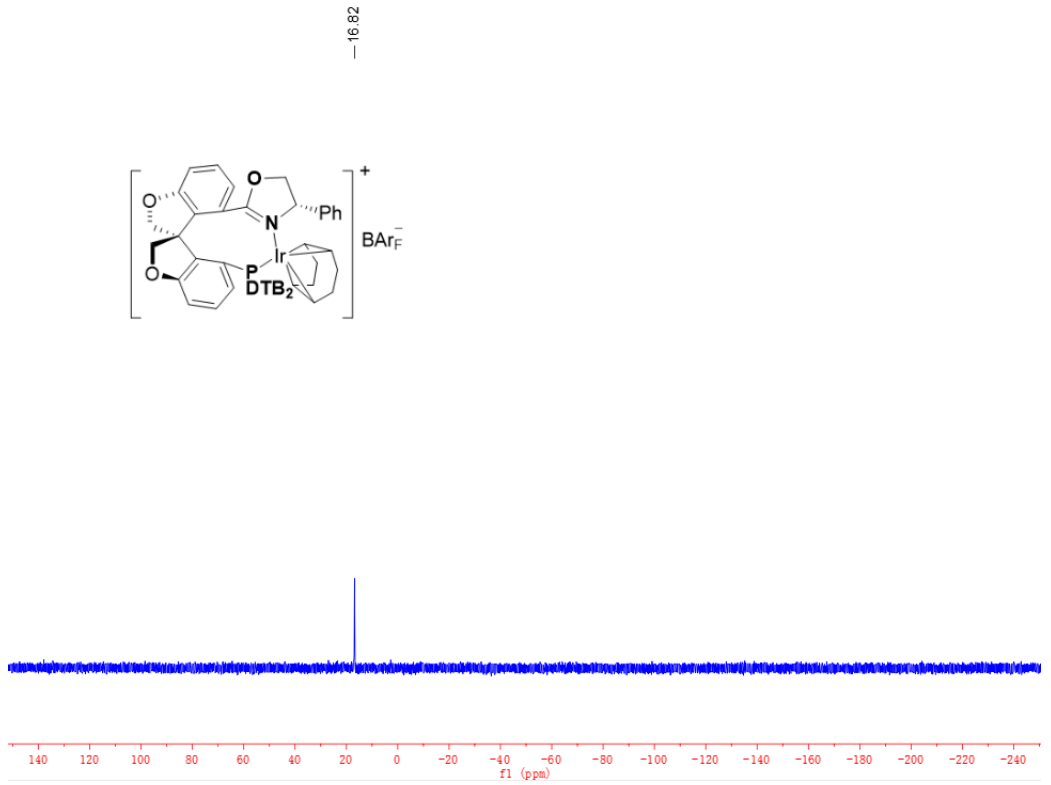

$^{1}$H NMR (400 MHz, Chloroform-*d*) of **Cat 5**:



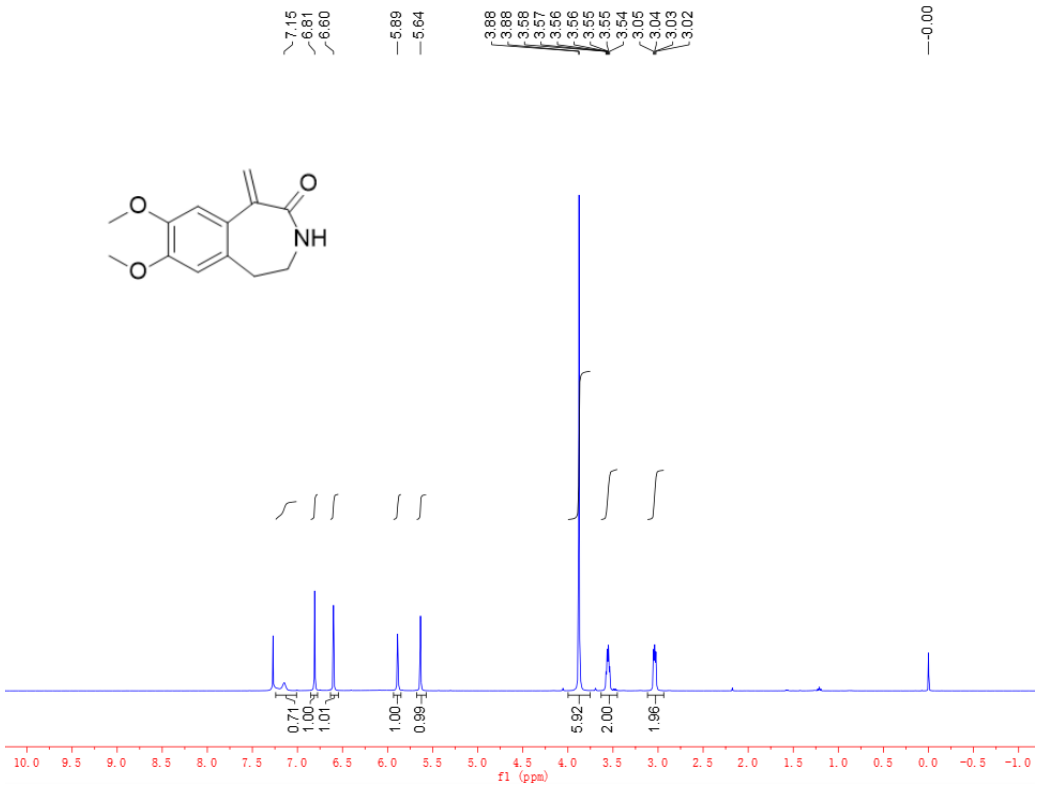
$^{13}$C NMR (101 MHz, Chloroform-*d*) of **Cat 5**:



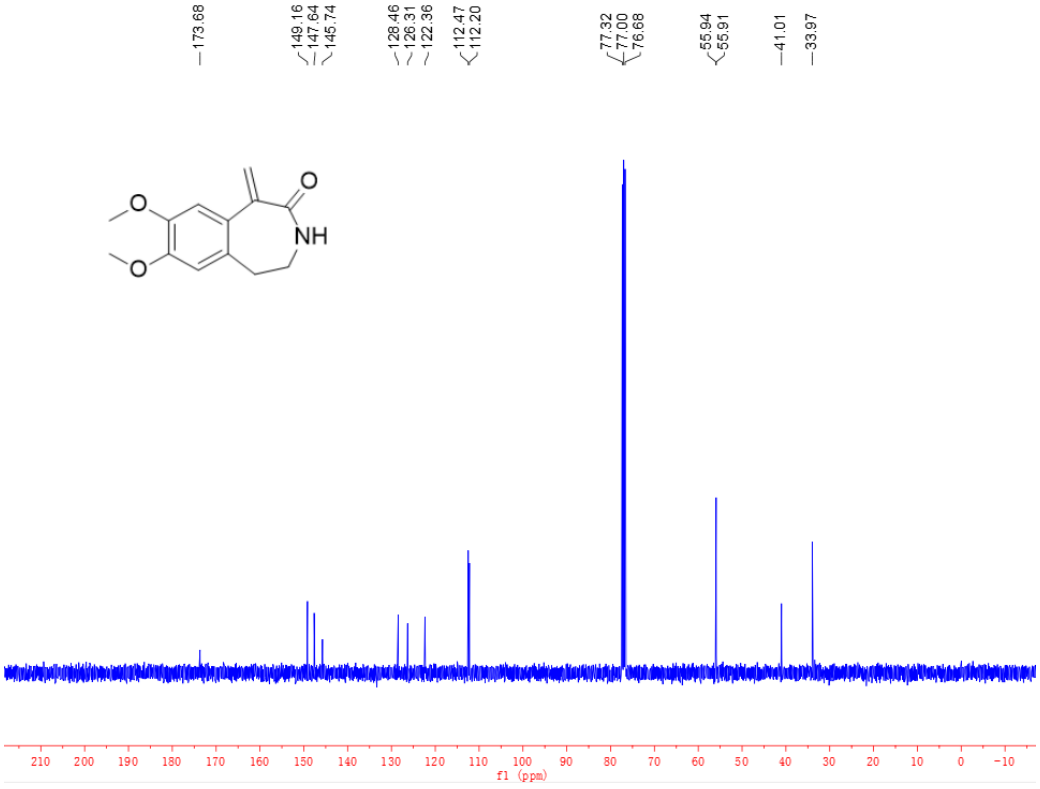

$^{31}$P NMR (162 MHz, Chloroform-*d*) of **Cat 5**:



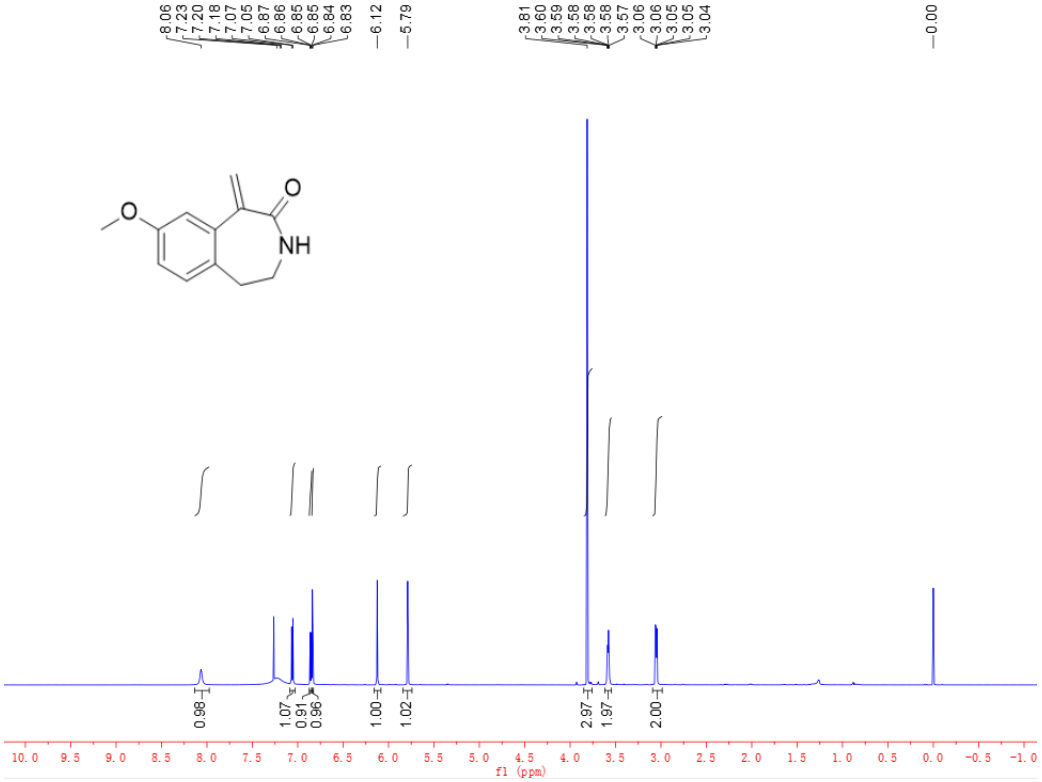
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **3a**:



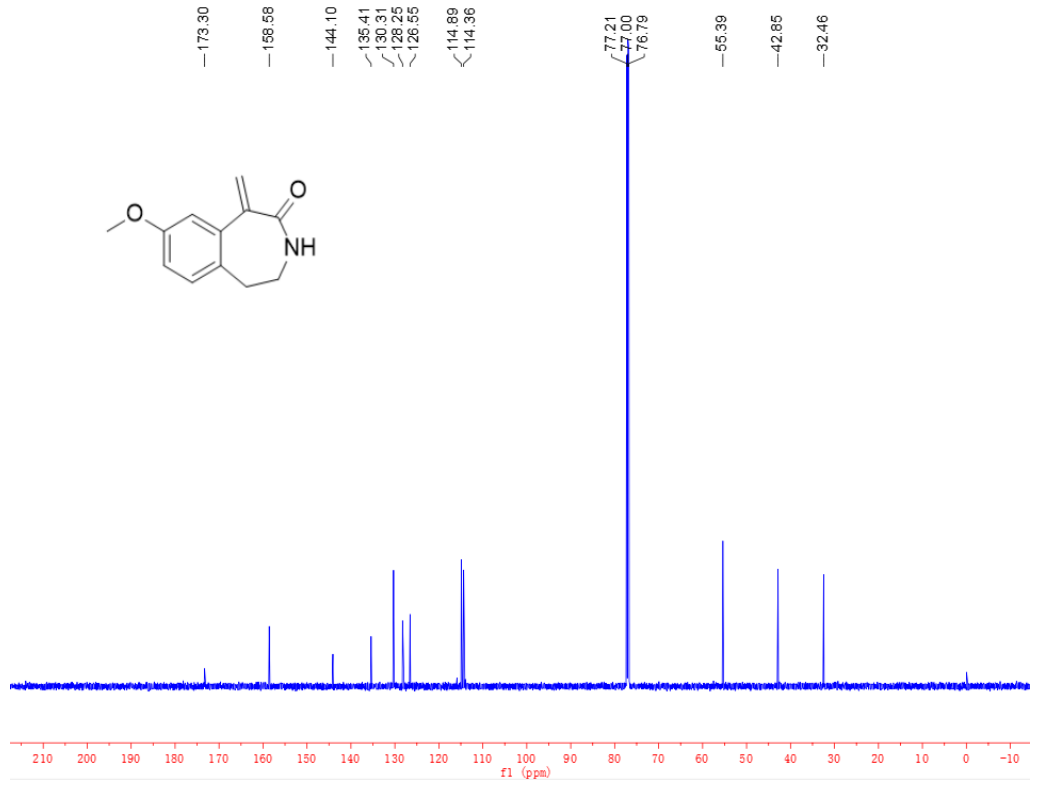

$^{13}$C NMR (101 MHz, Chloroform-*d*) of **3a**:



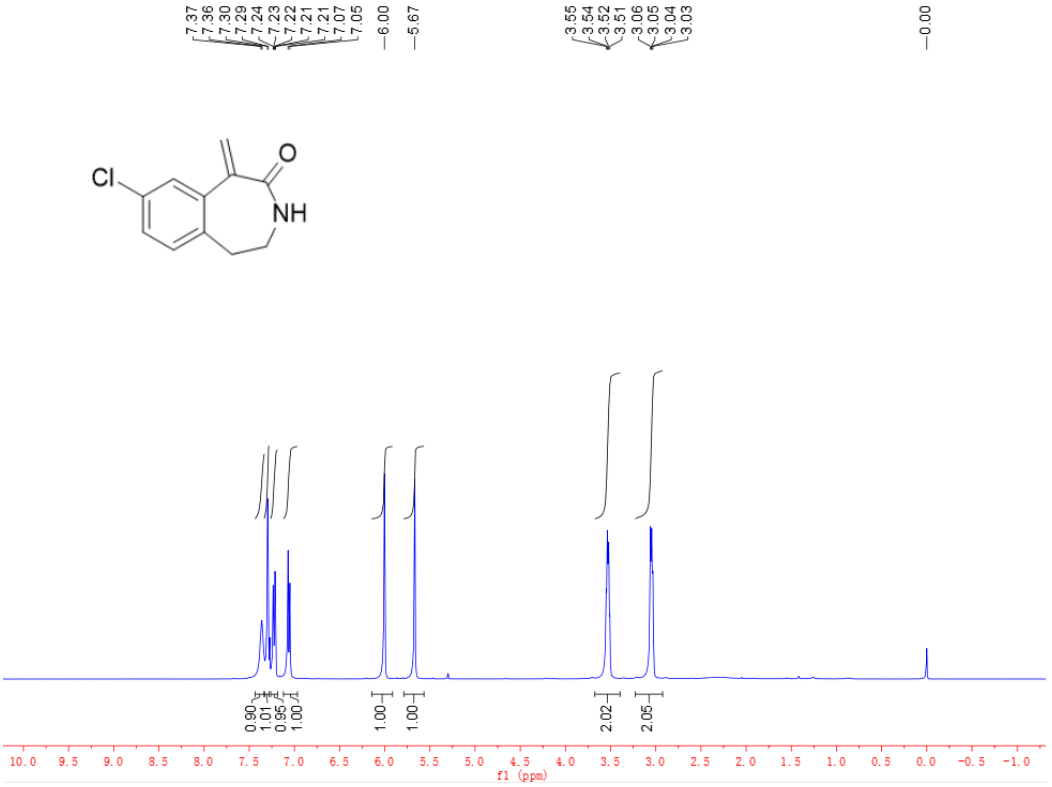
$^{1}$H NMR (600 MHz, Chloroform-*d*) of **3b**:



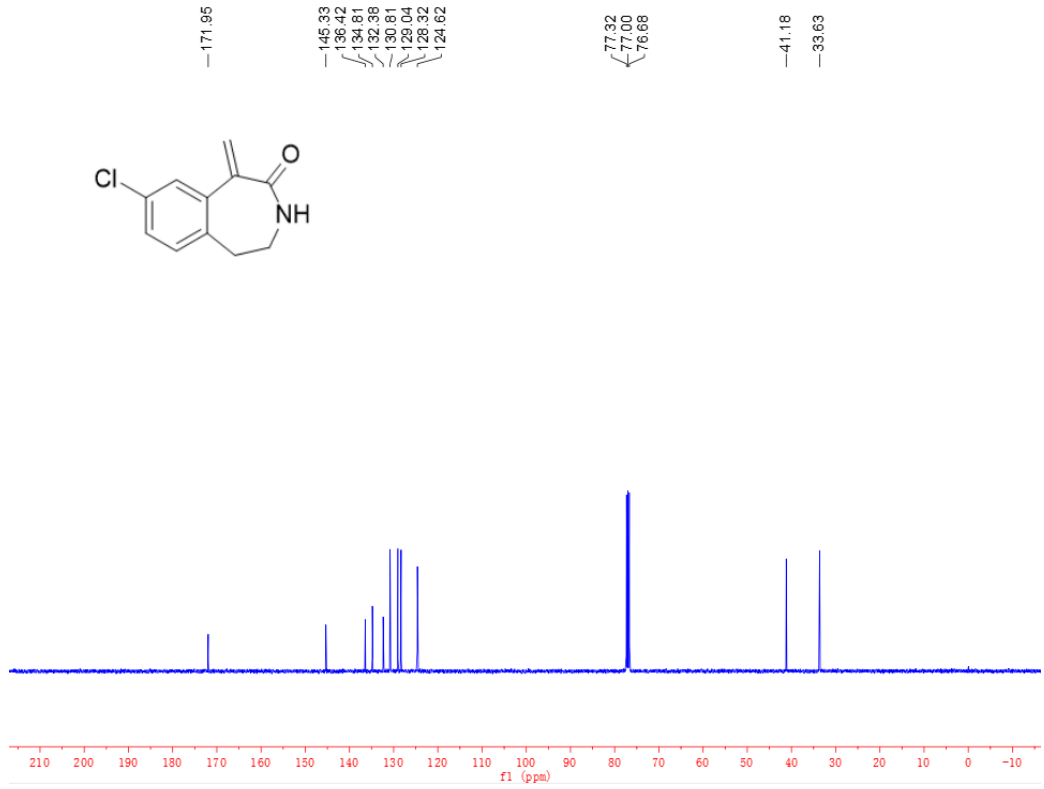

$^{13}$C NMR (151 MHz, Chloroform-*d*) of **3b**:



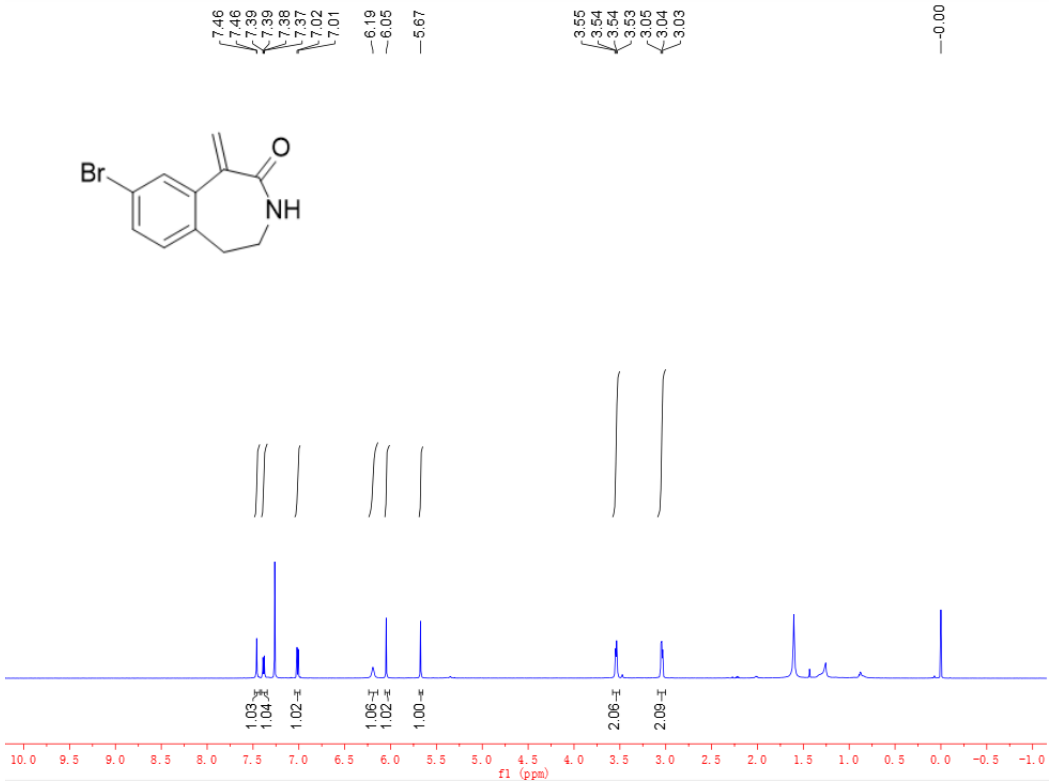
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **3c**:



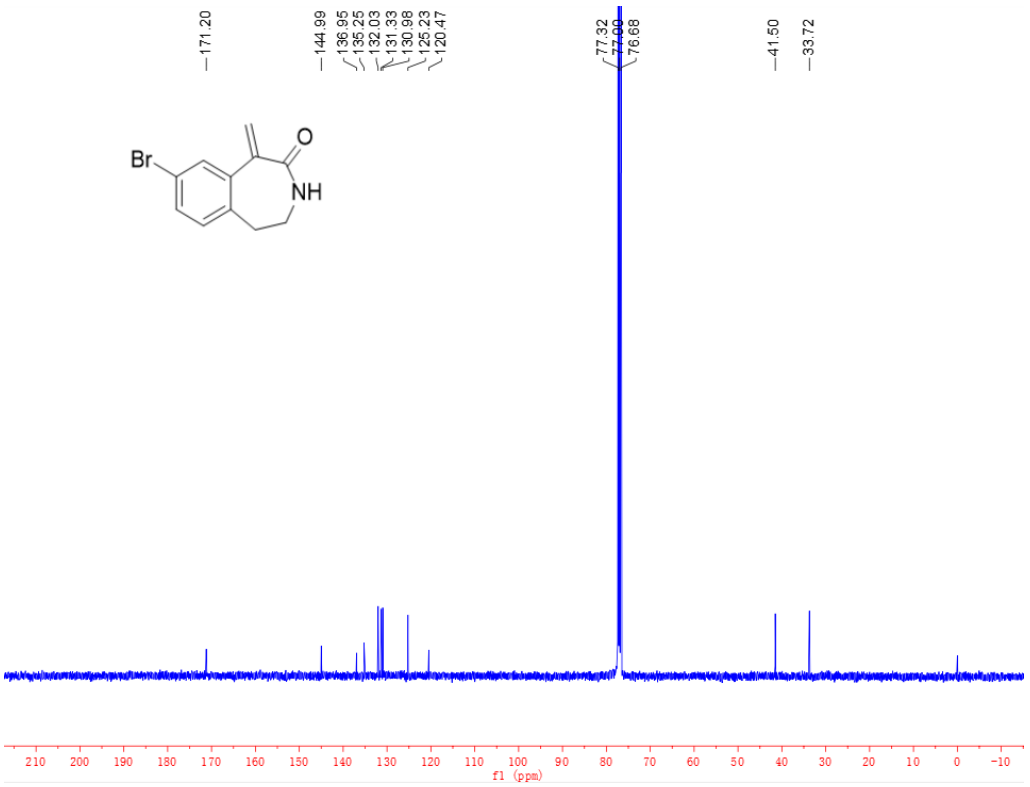

$^{13}$C NMR (101 MHz, Chloroform-*d*) of **3c**:



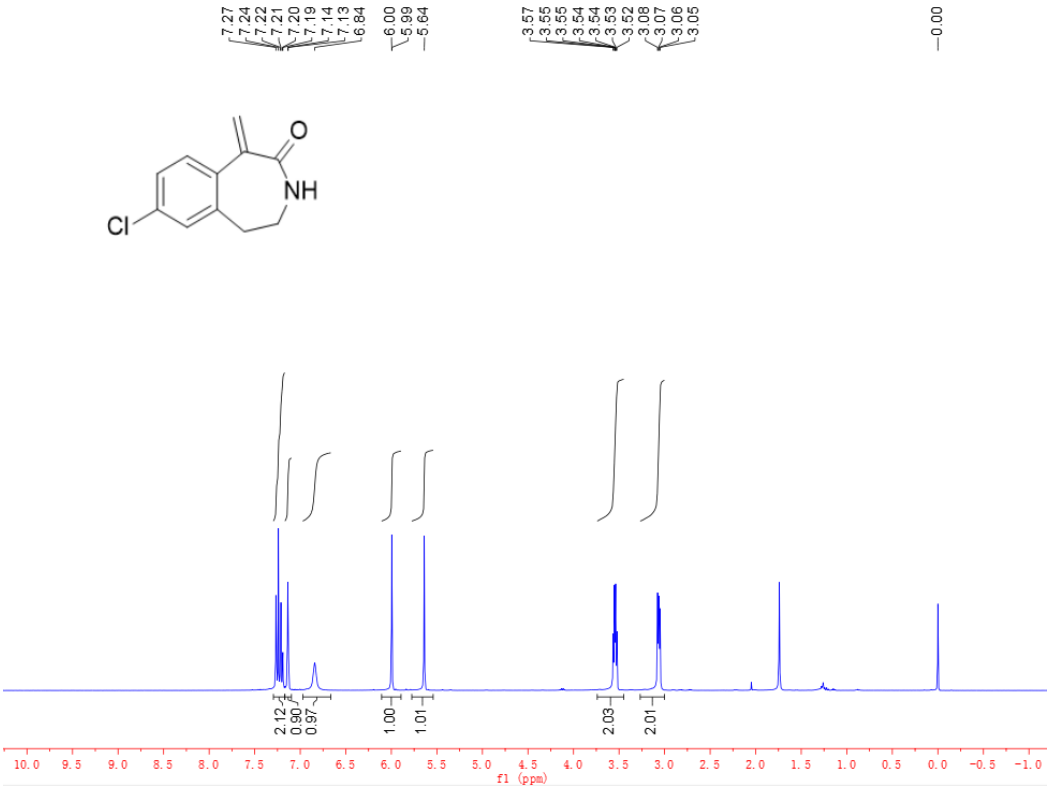
$^{1}$H NMR (600 MHz, Chloroform-*d*) of **3d**:



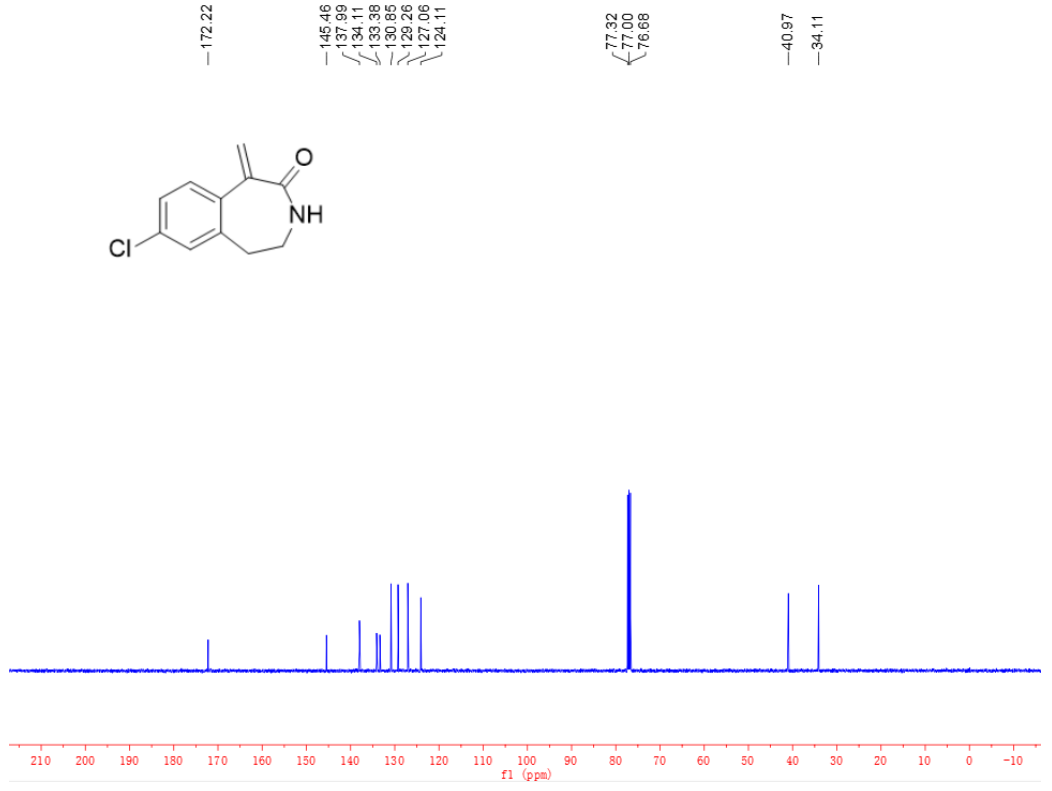

$^{13}$C NMR (101 MHz, Chloroform-*d*) of **3d**:



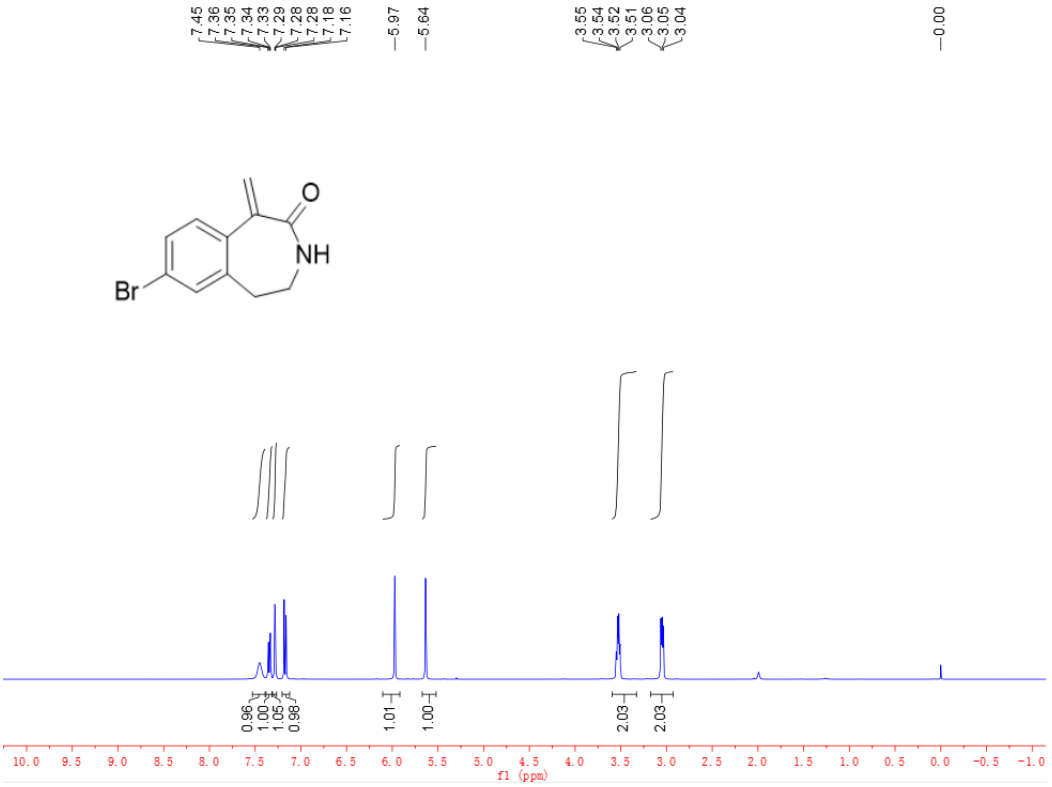
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **3e**:



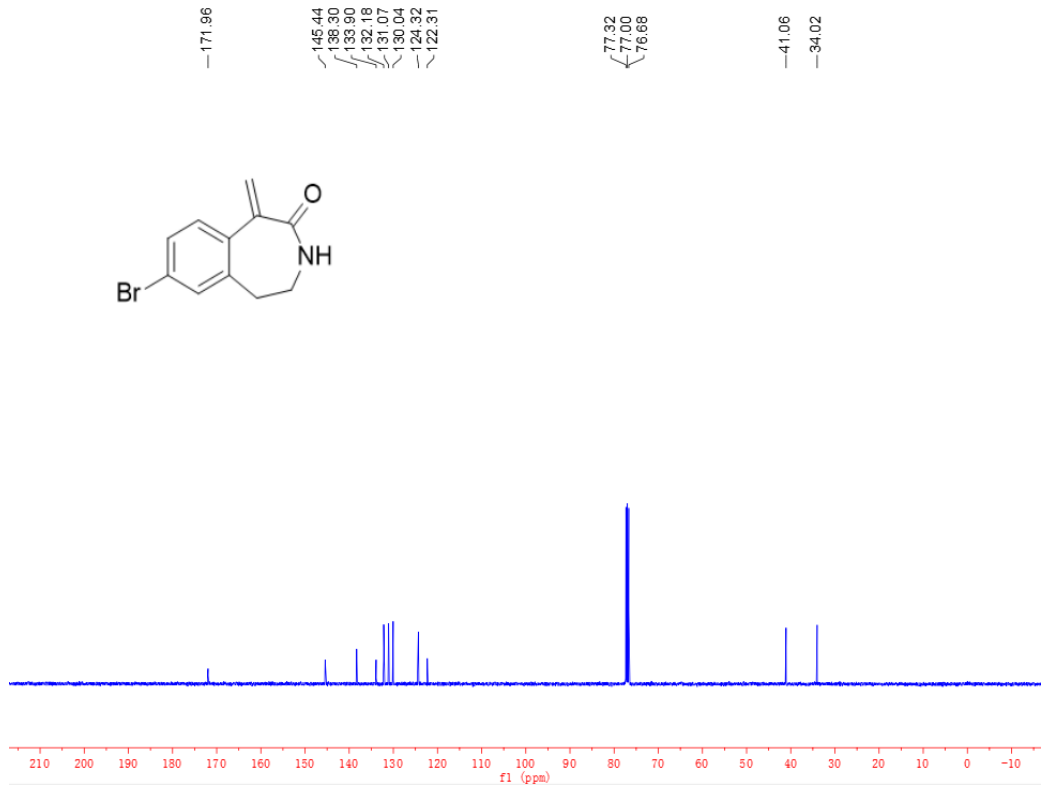

$^{13}$C NMR (101 MHz, Chloroform-*d*) of **3e**:



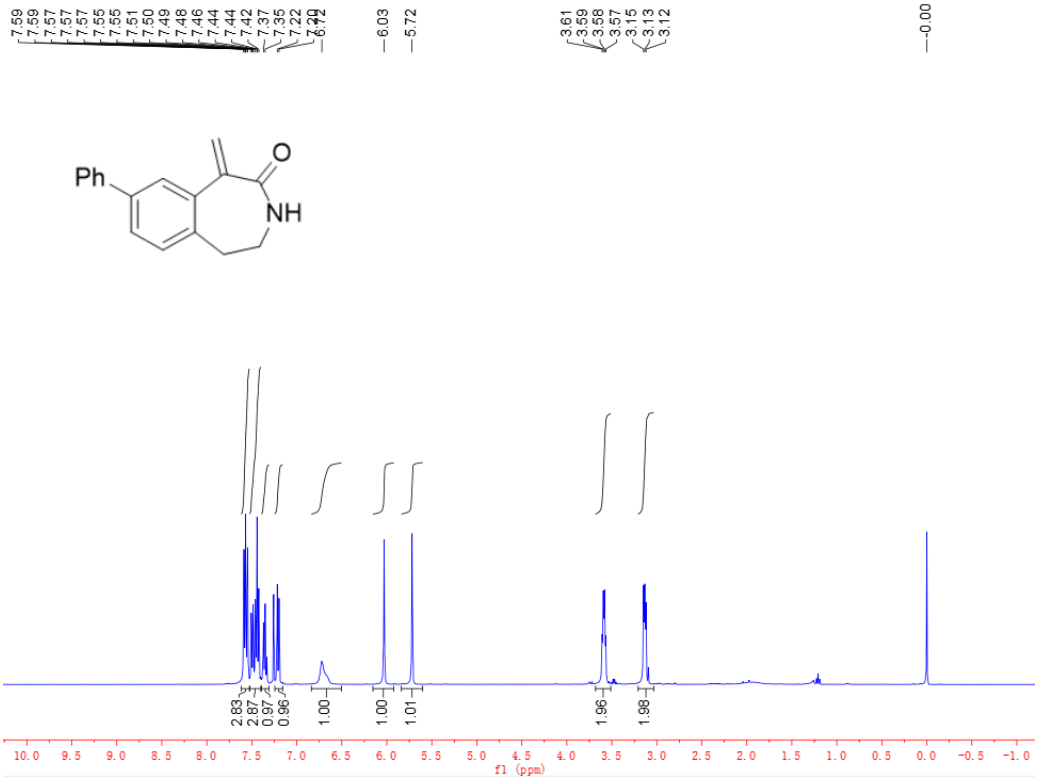
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **3f**:



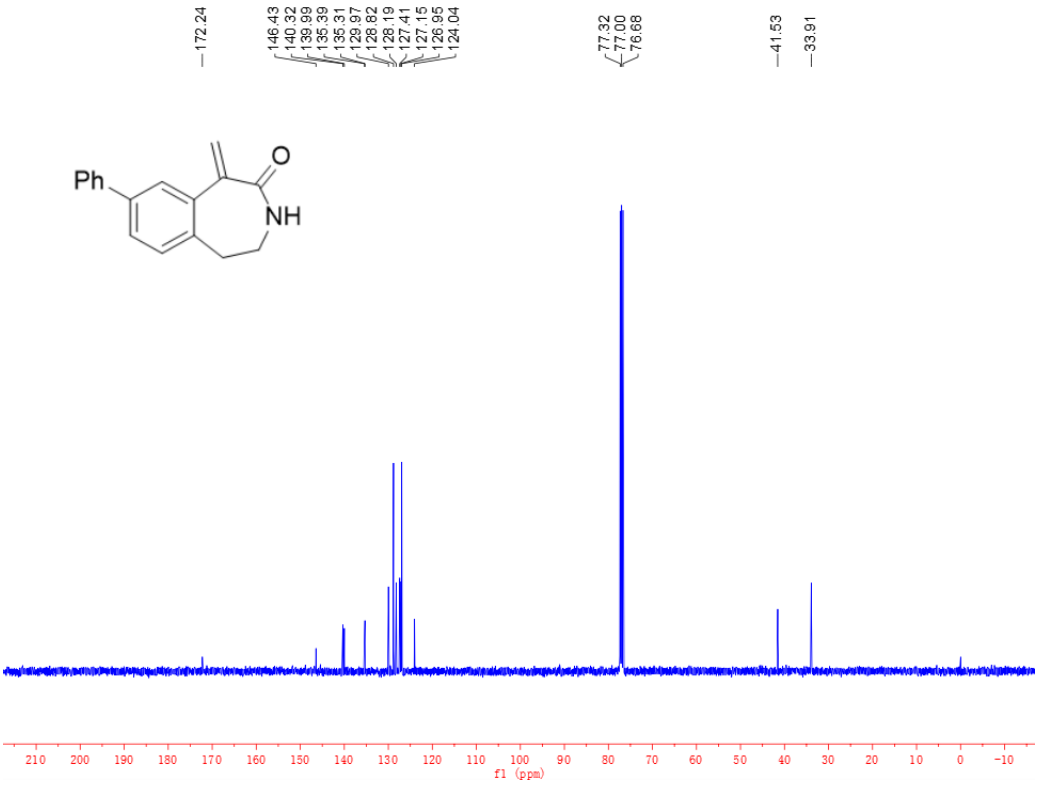

$^{13}$C NMR (101 MHz, Chloroform-*d*) of **3f**:



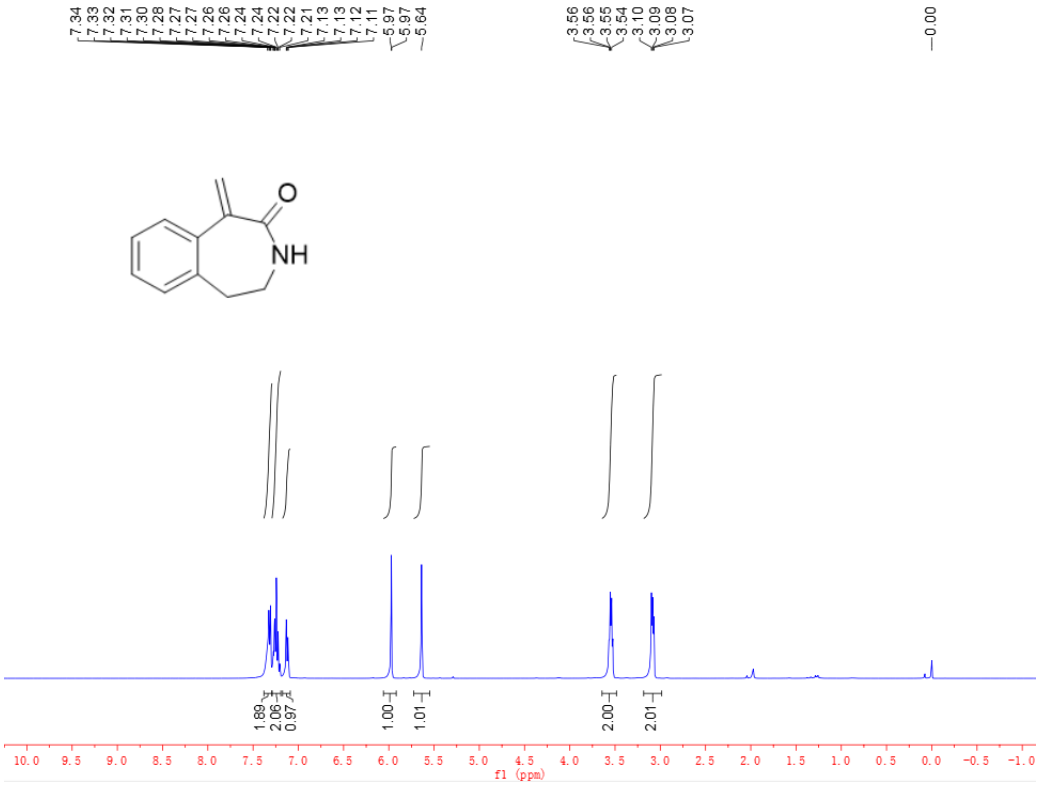
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **3g**:



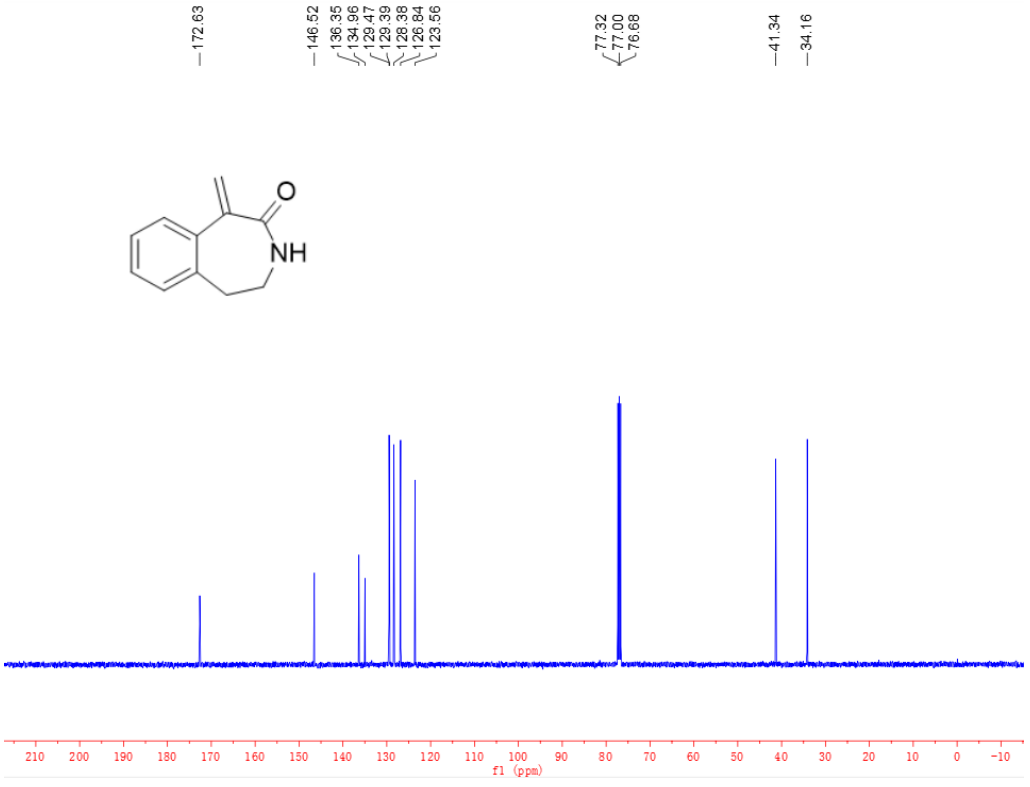

$^{13}$C NMR (101 MHz, Chloroform-*d*) of **3g**:



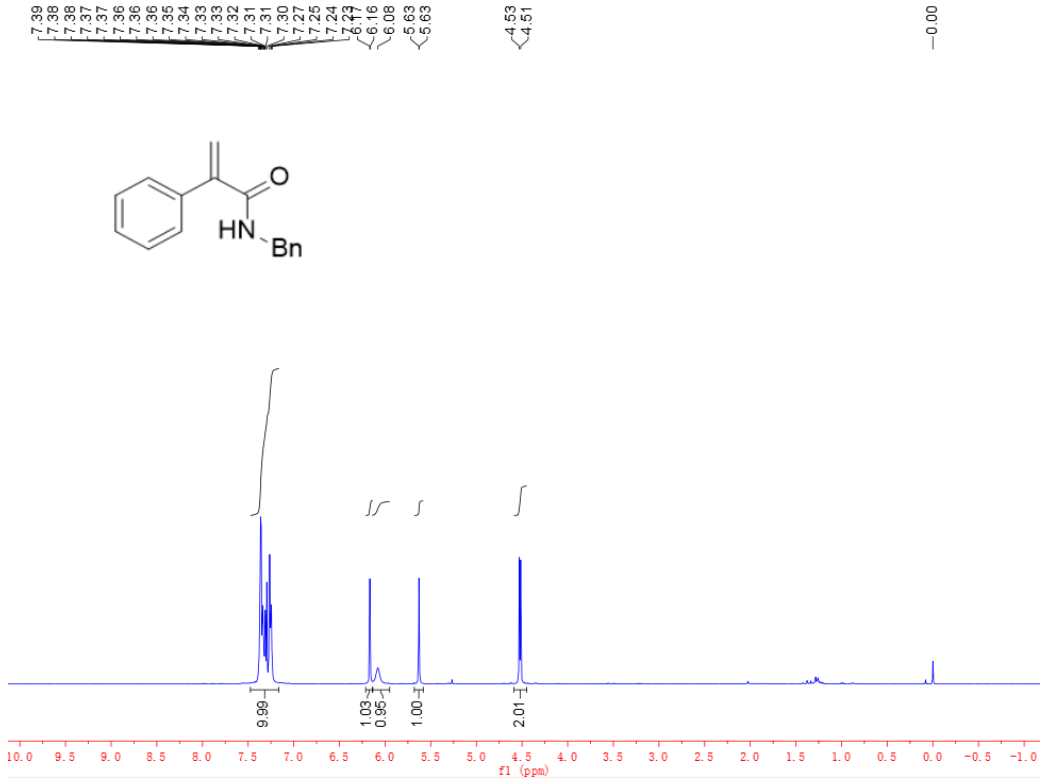
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **3h**:



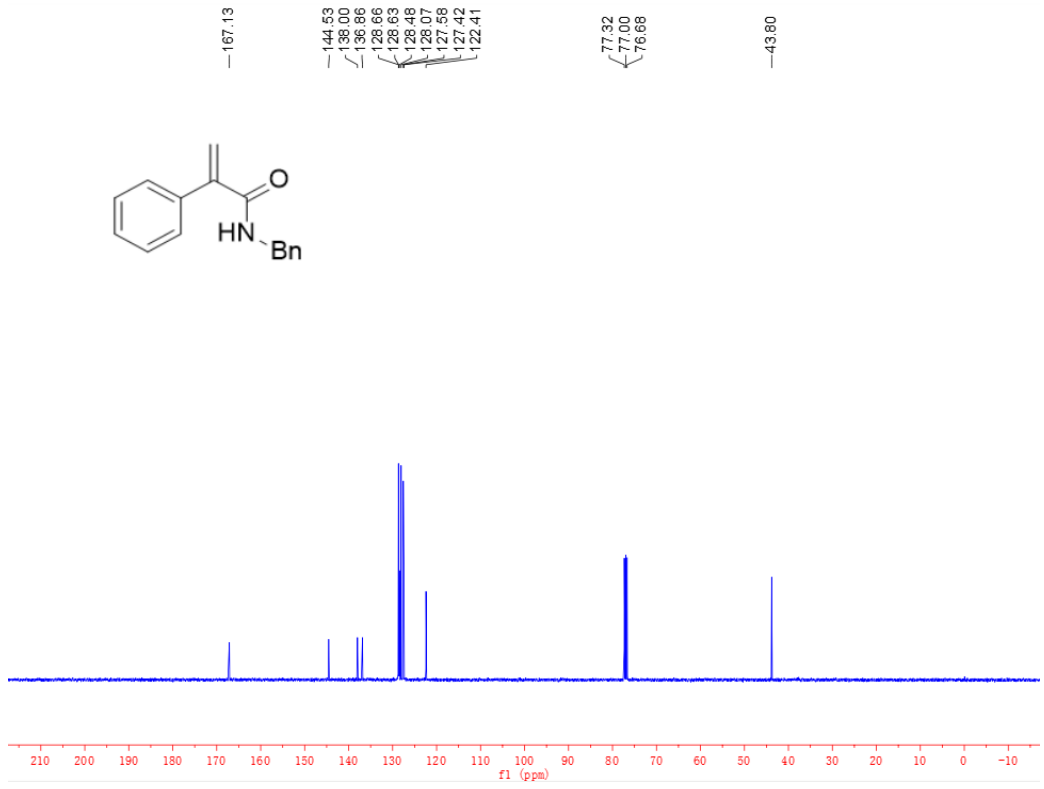

$^{13}$C NMR (101 MHz, Chloroform-*d*) of **3h**:



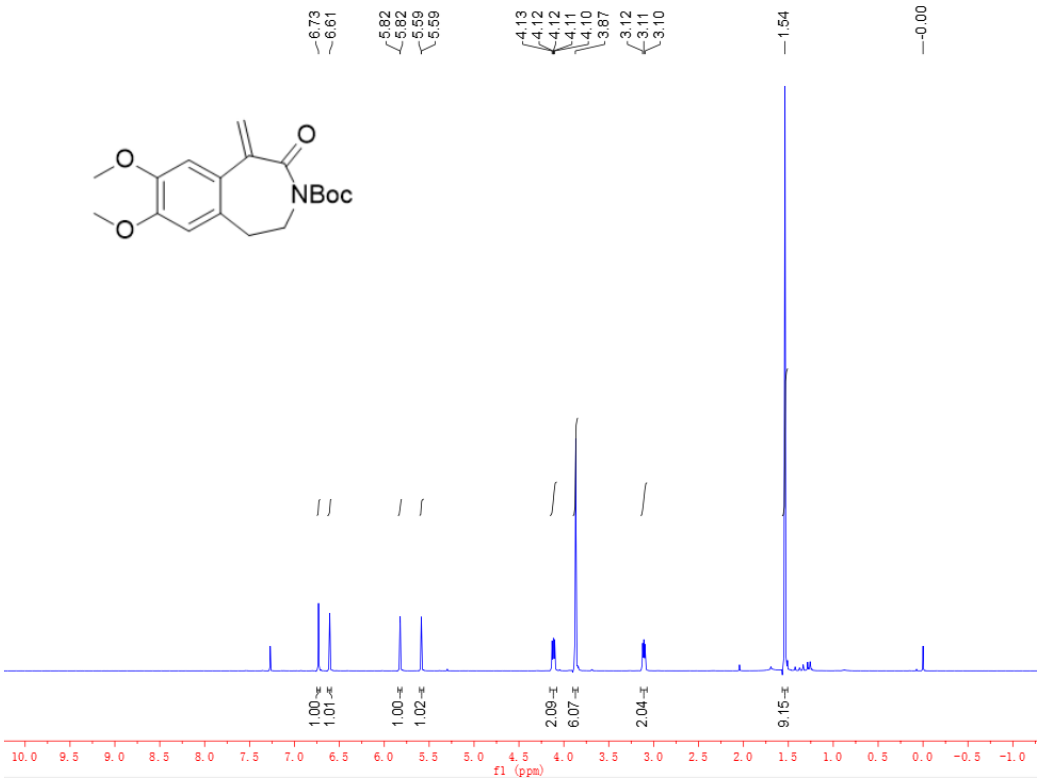
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **3i**:



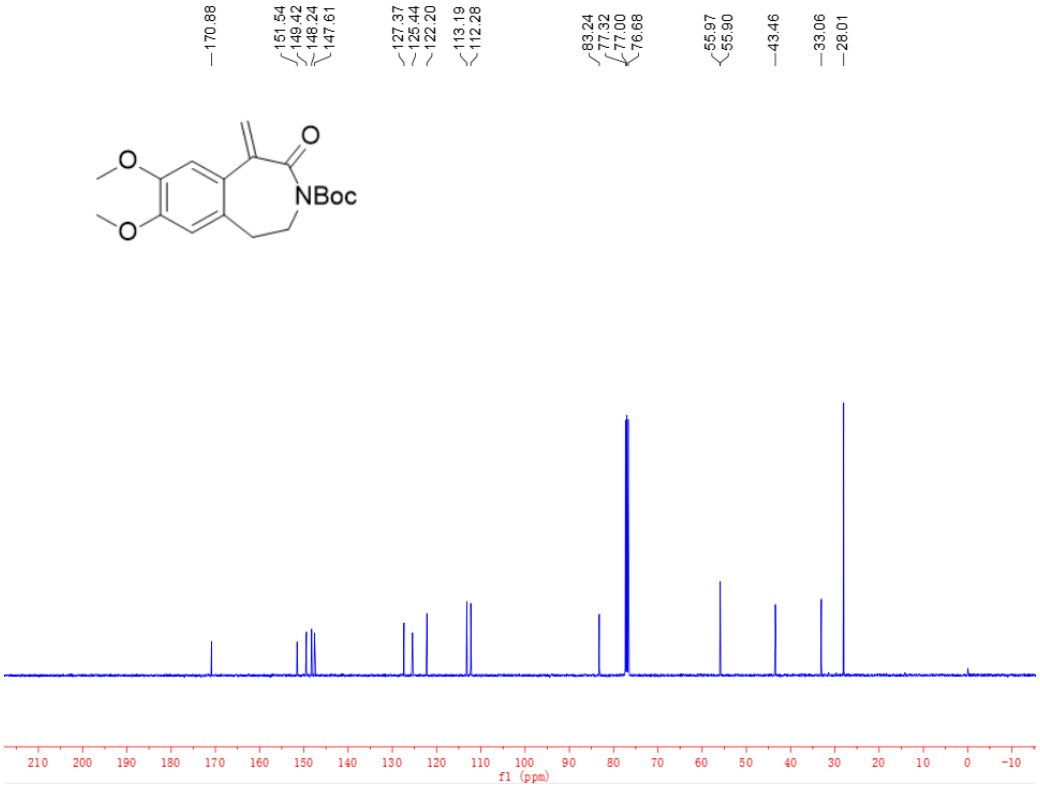

$^{13}$C NMR (101 MHz, Chloroform-*d*) of **3i**:



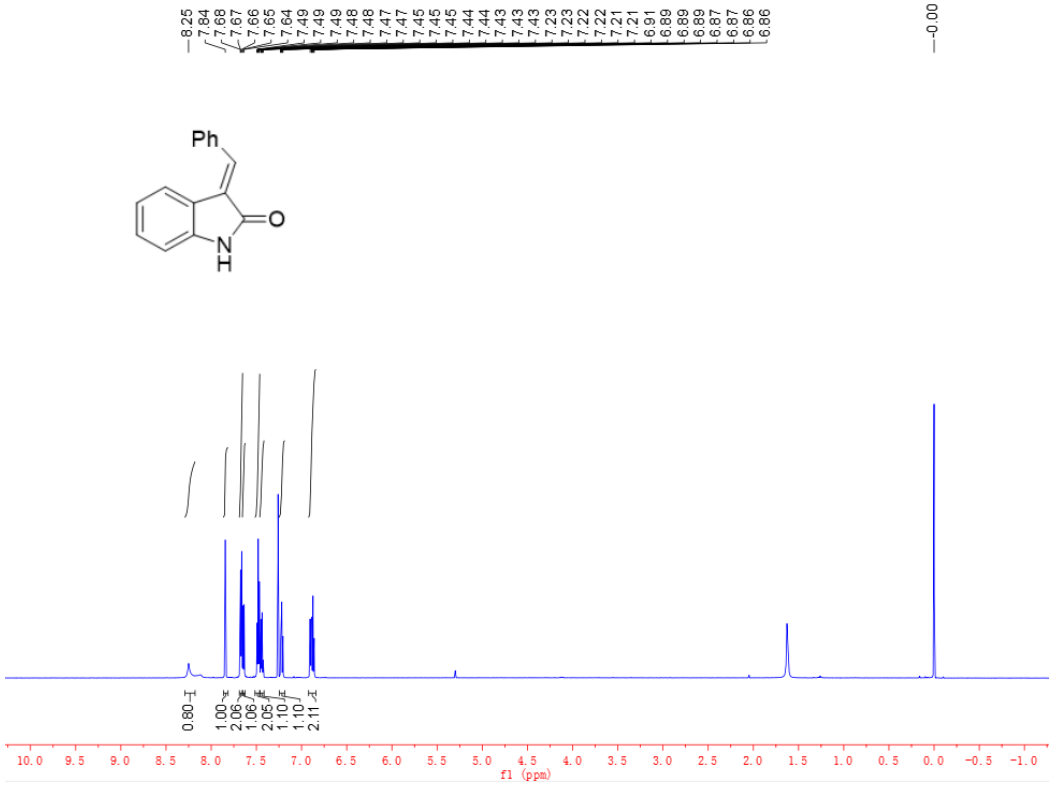
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **3j**:



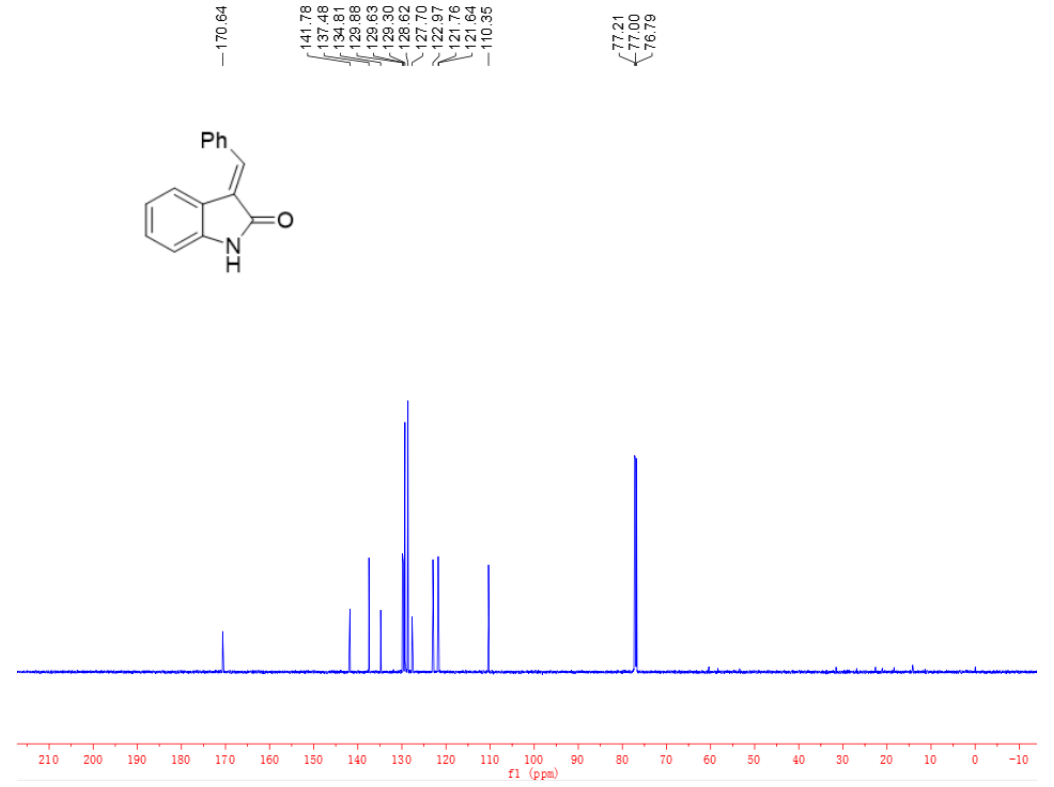

$^{13}$C NMR (101 MHz, Chloroform-*d*) of **3j**:



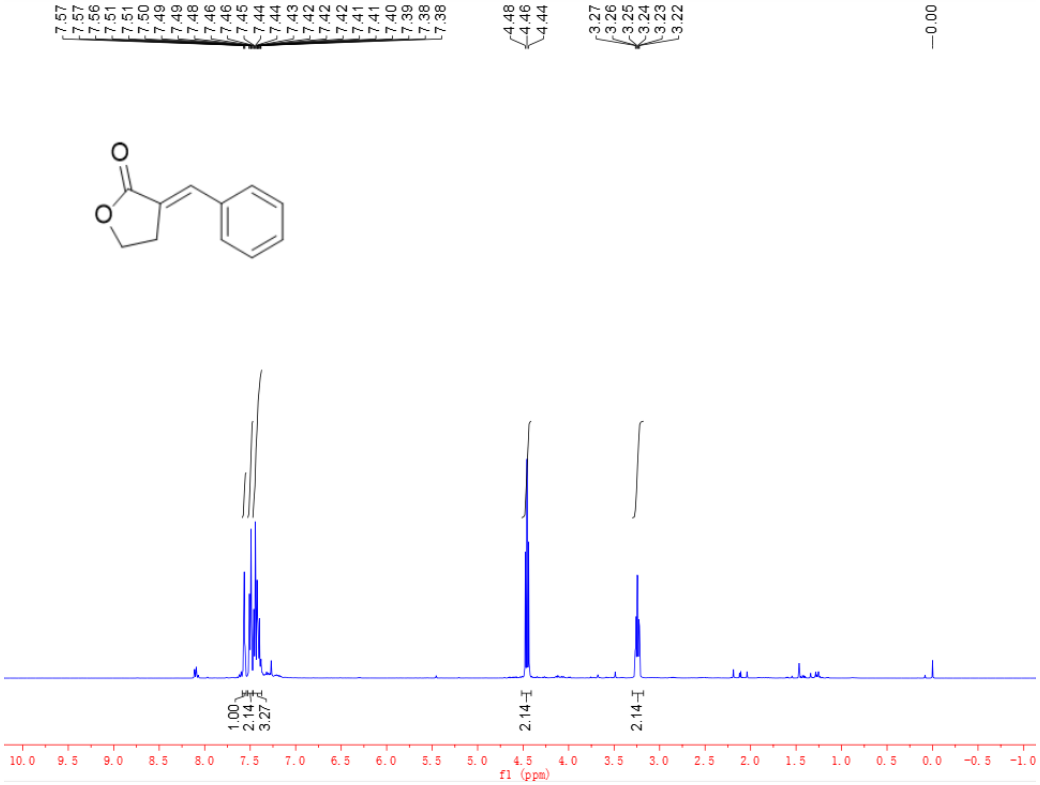
$^{1}$H NMR (600 MHz, Chloroform-*d*) of **3k**:



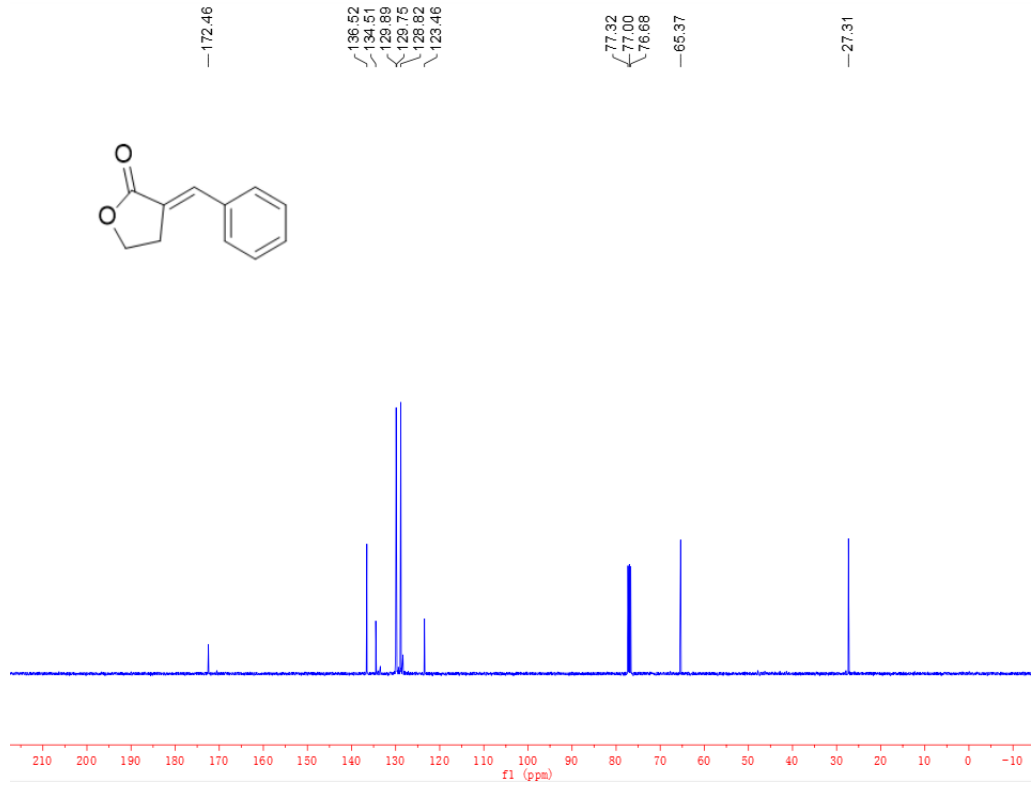

$^{13}$C NMR (151 MHz, Chloroform-*d*) of **3k**:



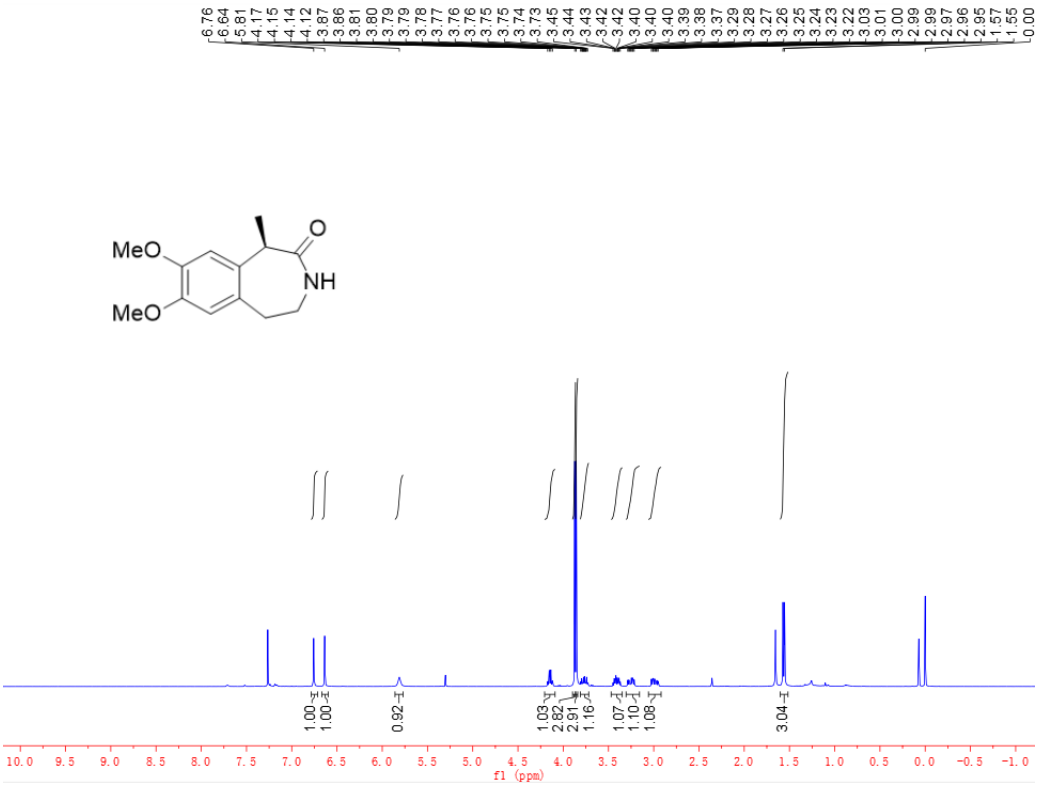
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **3l**:



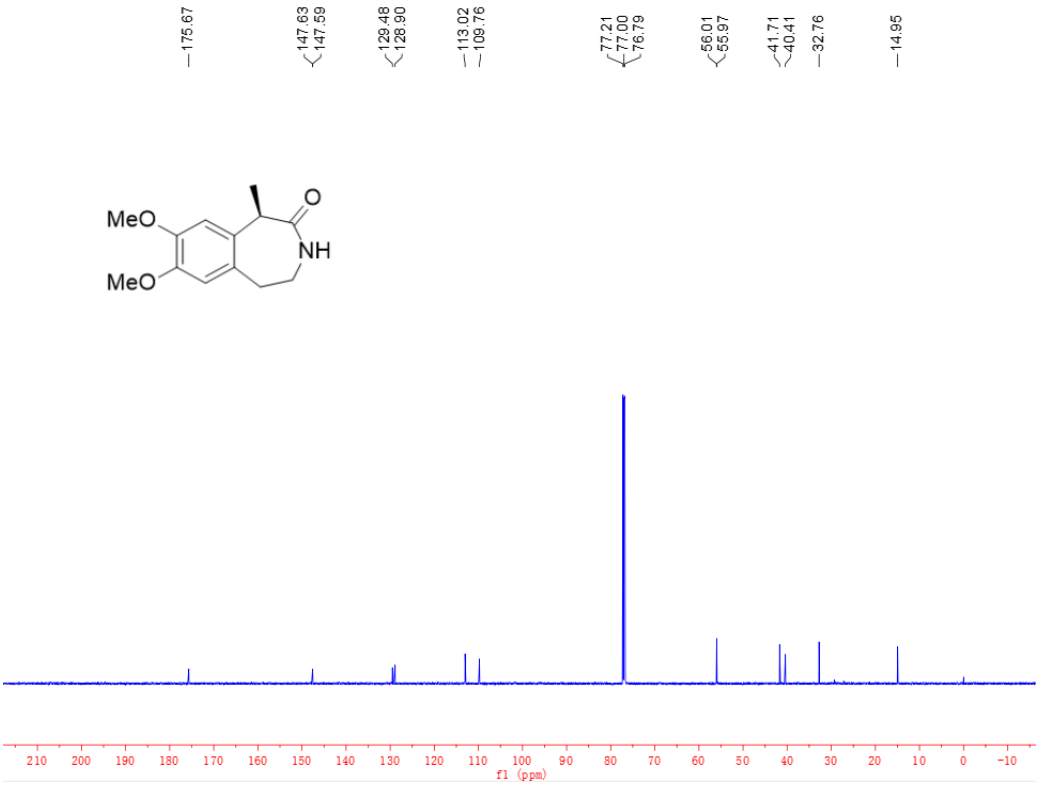

$^{13}$C NMR (101 MHz, Chloroform-*d*) of **3l**:



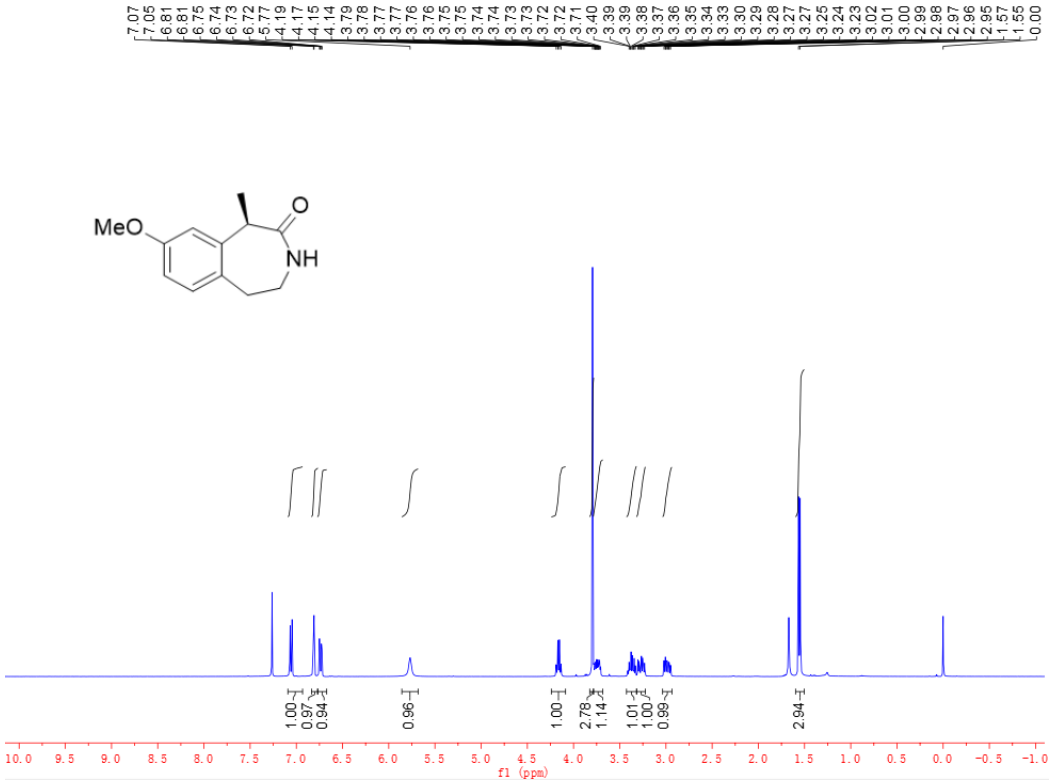
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **4a**:



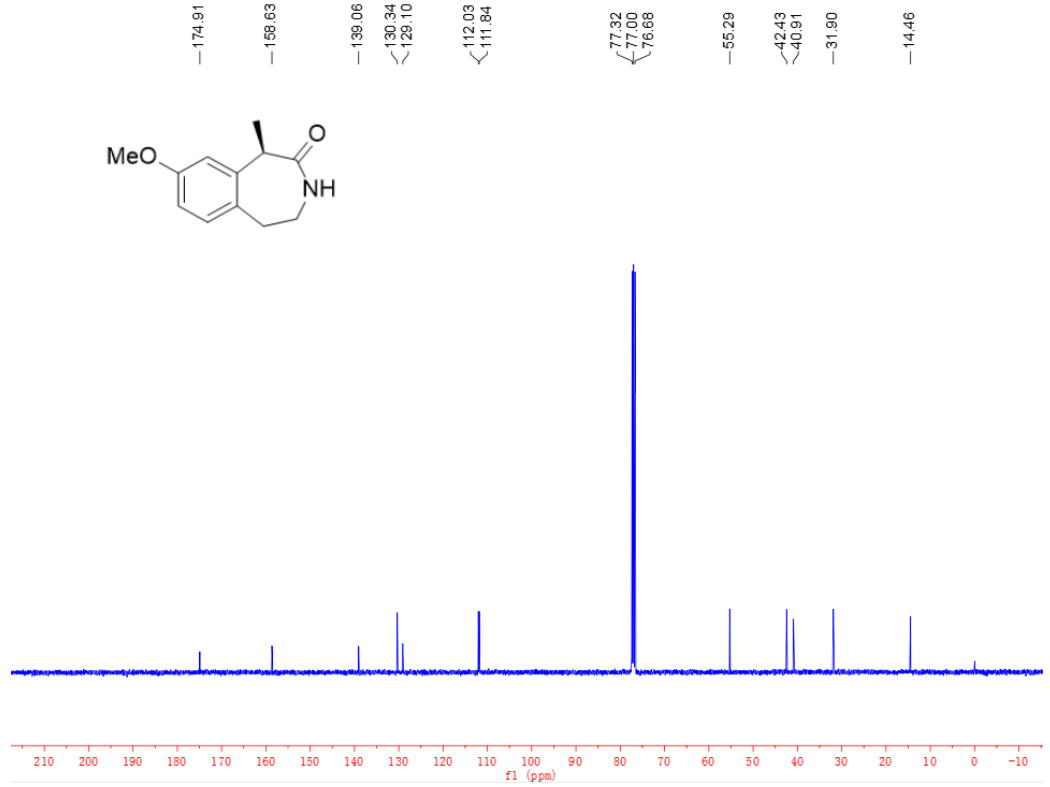

$^{13}$C NMR (151 MHz, Chloroform-*d*) of **4a**:



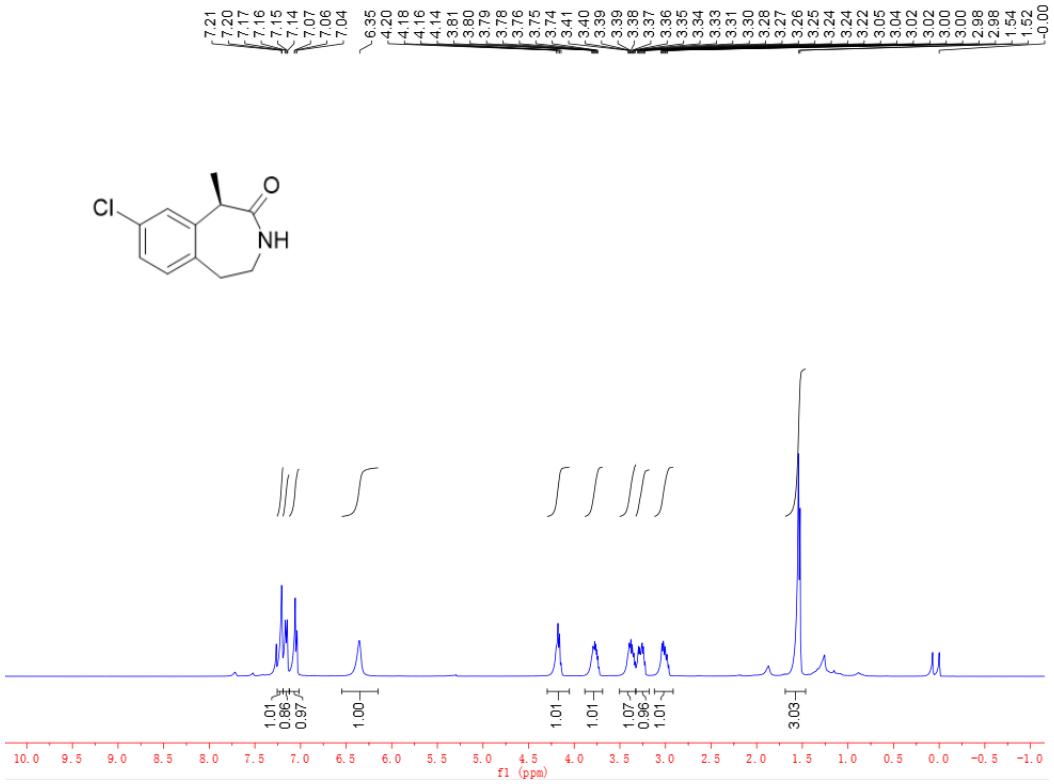
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **4b**:



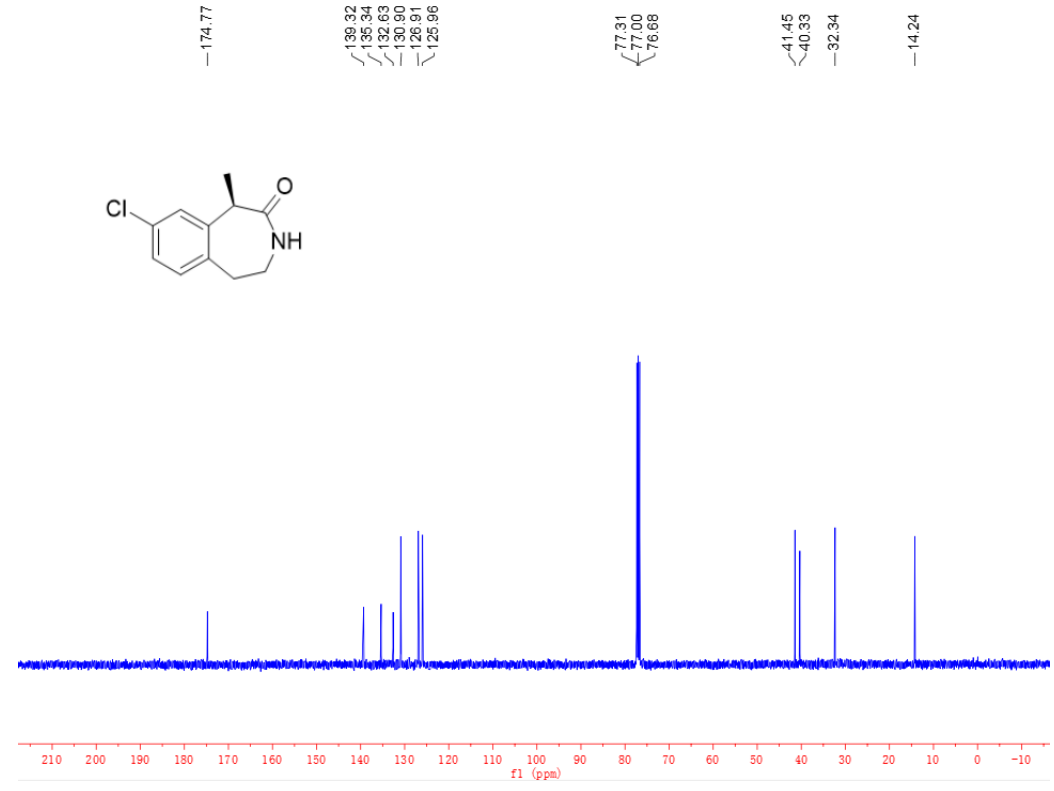

$^{13}$C NMR (101 MHz, Chloroform-*d*) of **4b**:



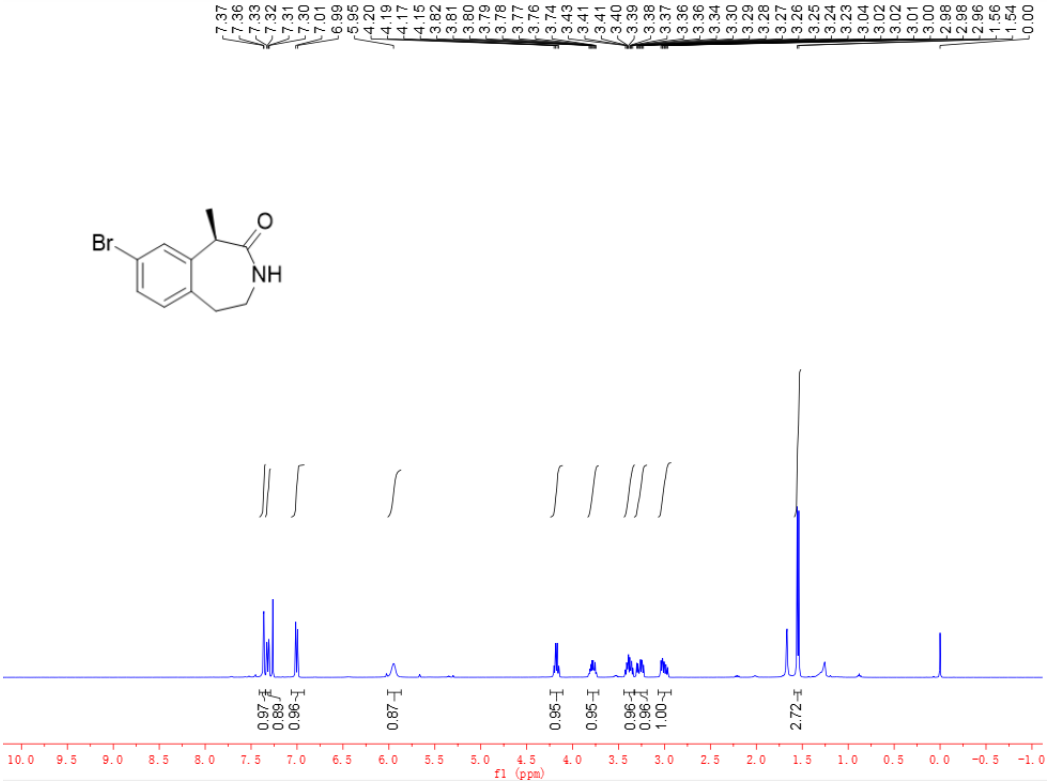
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **4c**:



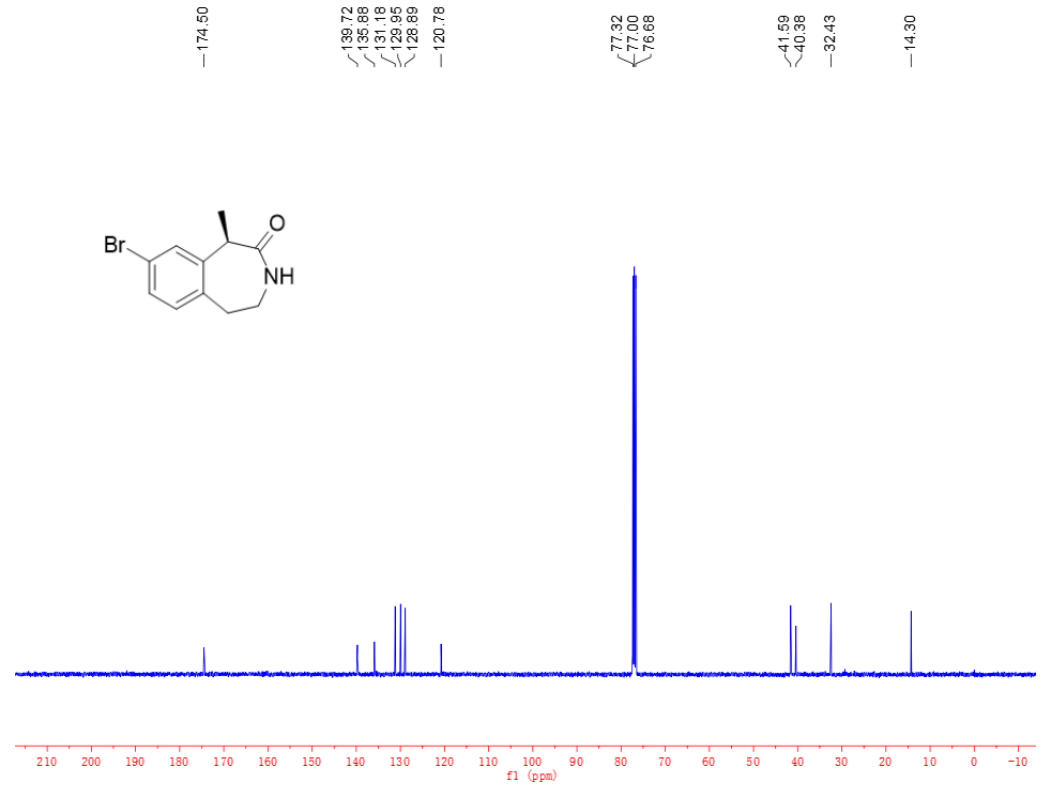

$^{13}$C NMR (101 MHz, Chloroform-*d*) of **4c**:



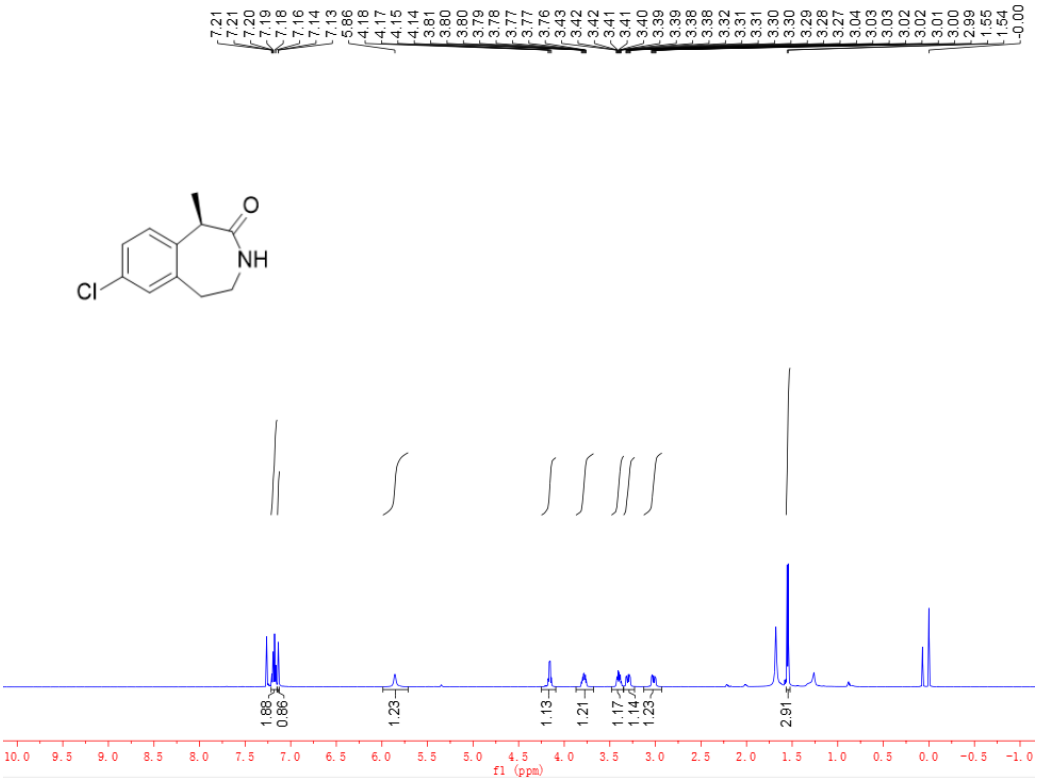
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **4d**:



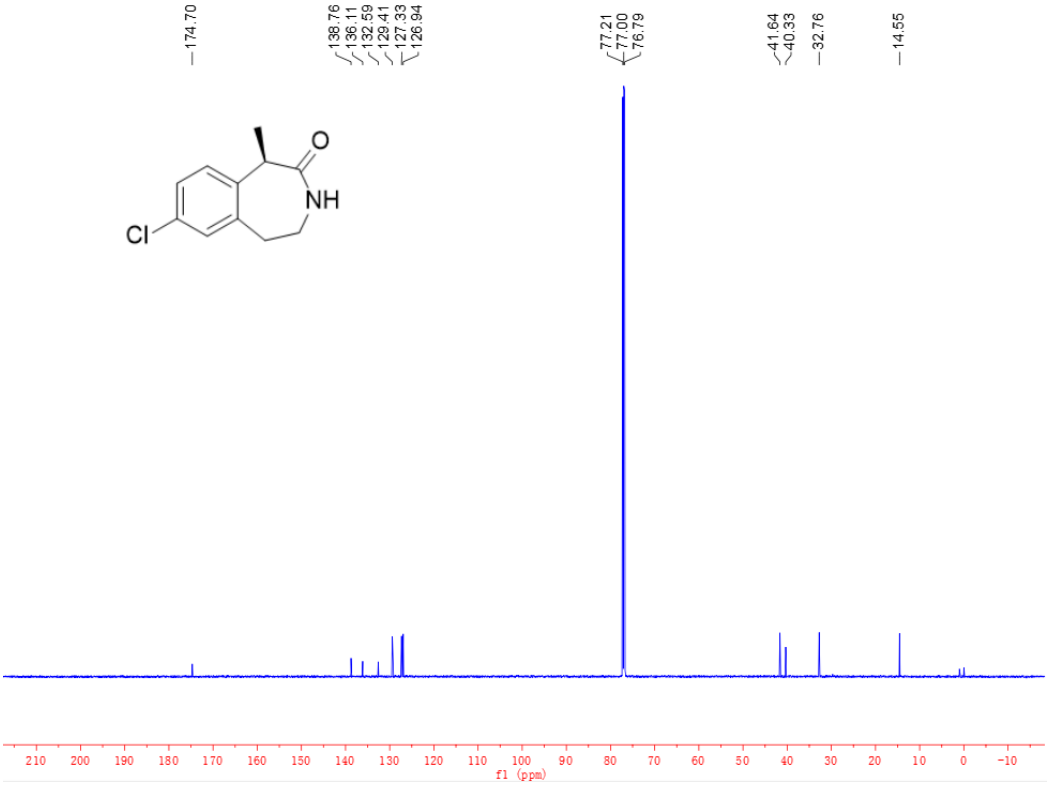

$^{13}$C NMR (101 MHz, Chloroform-*d*) of **4d**:



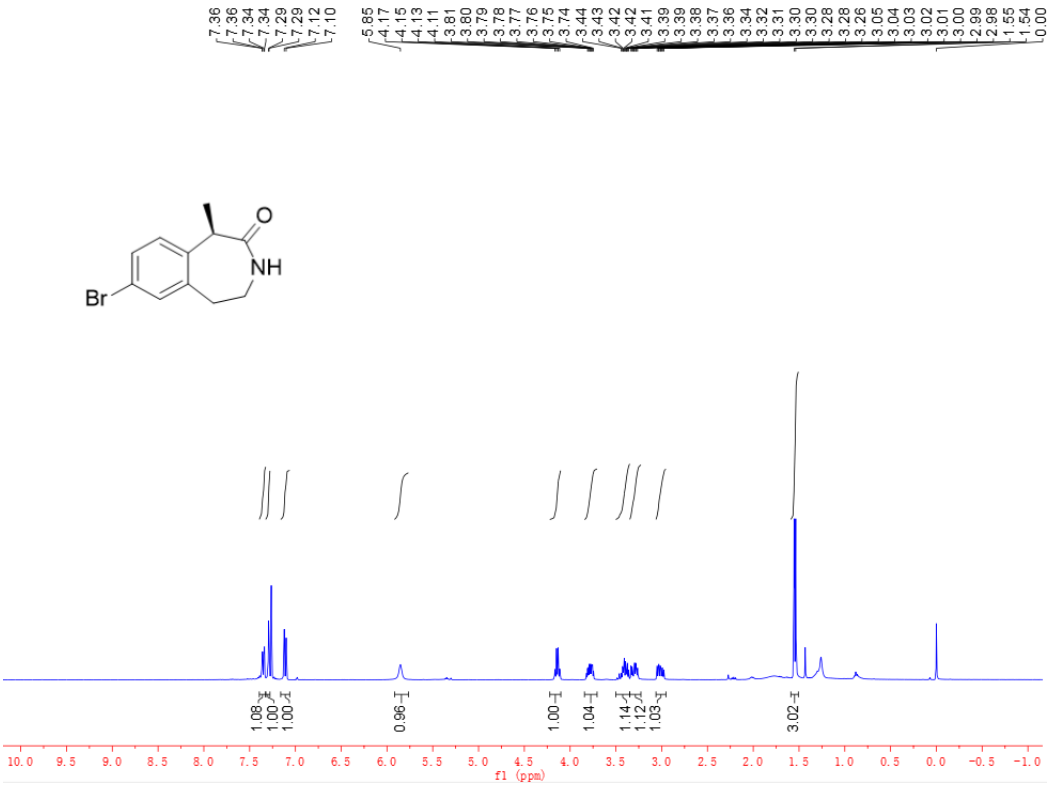
$^{1}$H NMR (600 MHz, Chloroform-*d*) of **4e**:



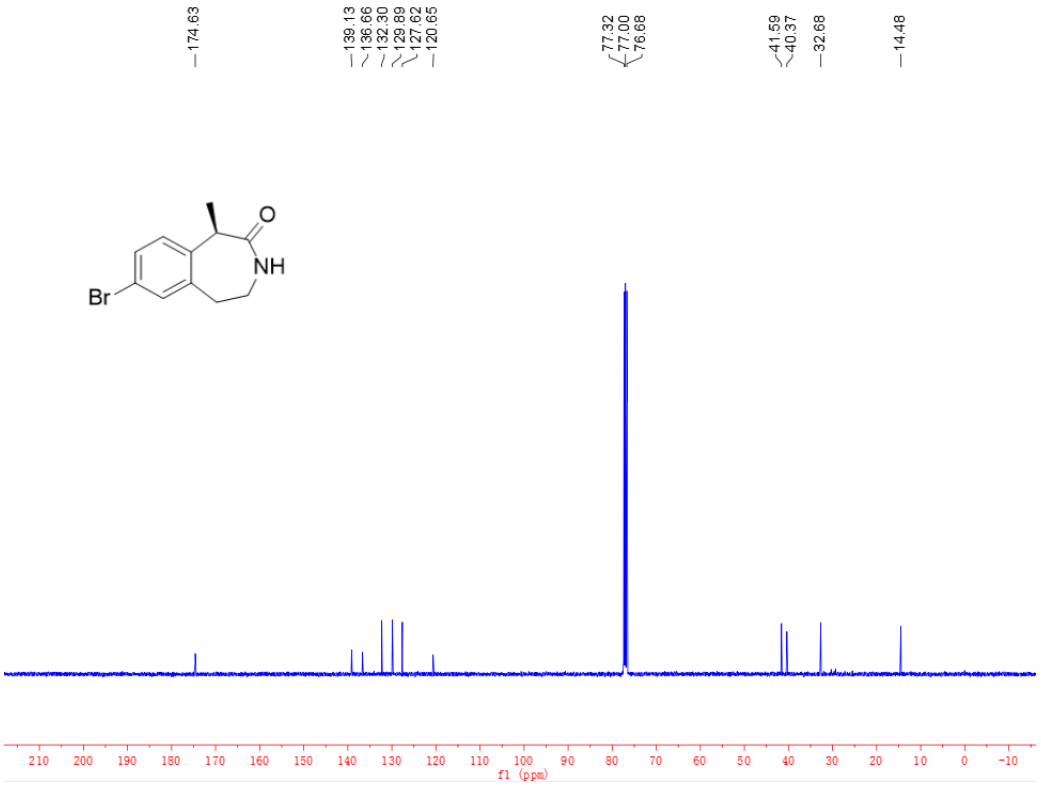

$^{13}$C NMR (151 MHz, Chloroform-*d*) of **4e**:



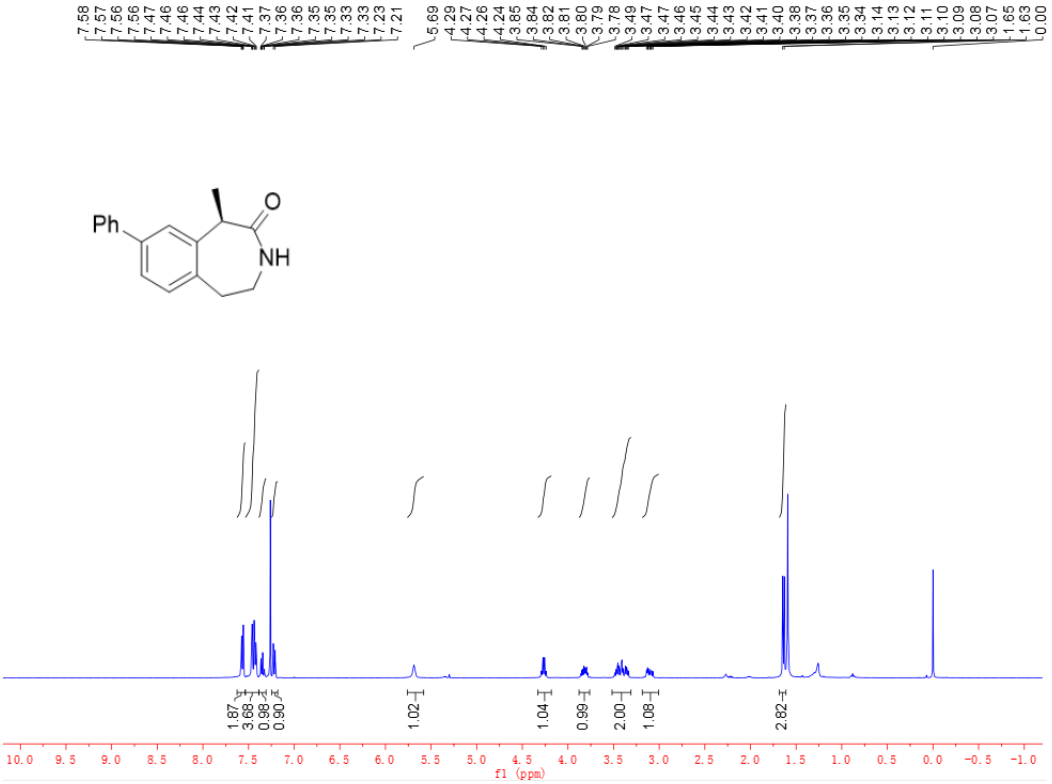
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **4f**:



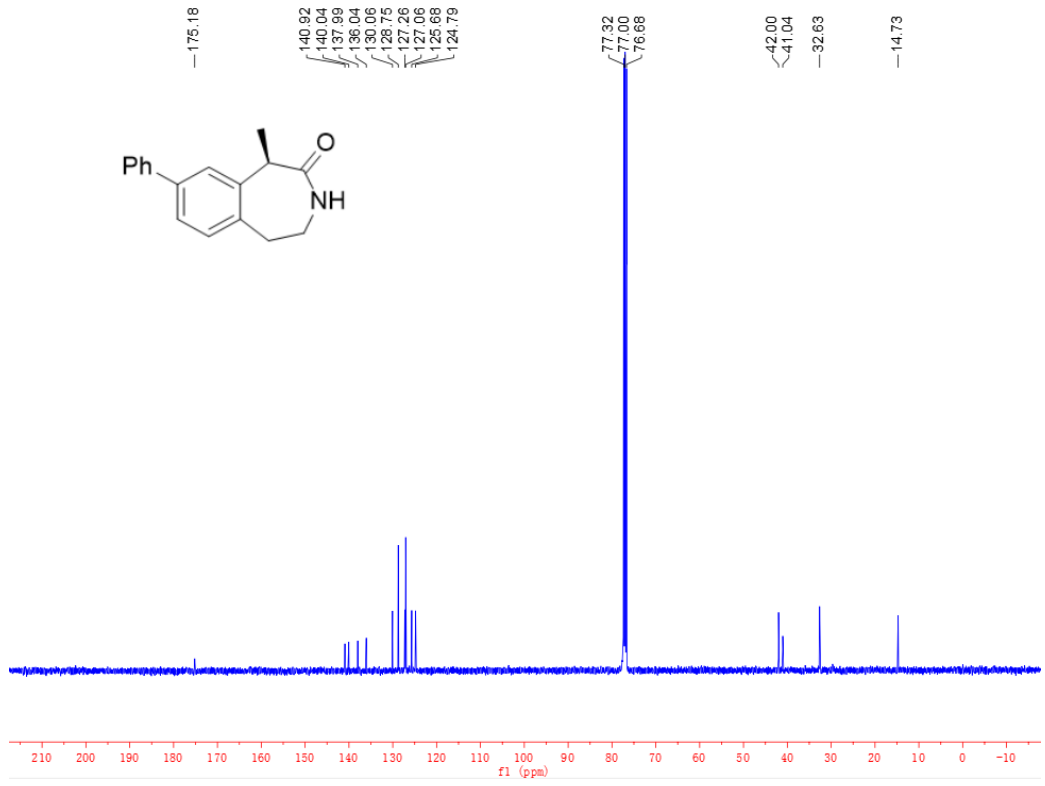

$^{13}$C NMR (101 MHz, Chloroform-*d*) of **4f**:



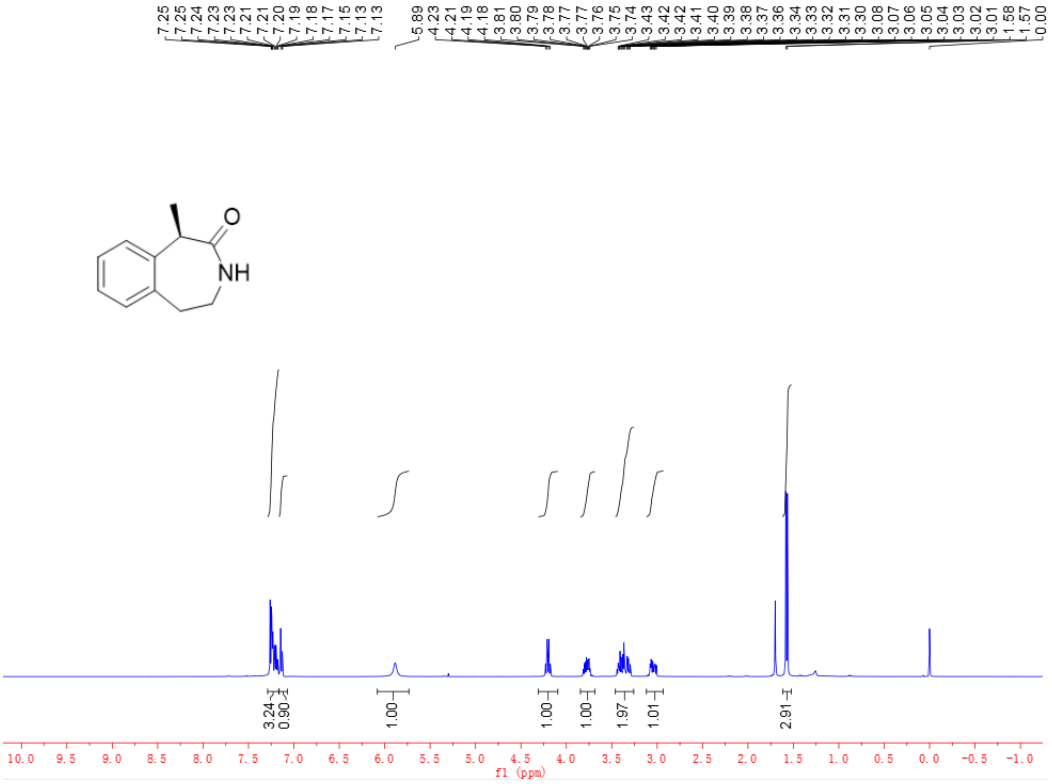
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **4g**:



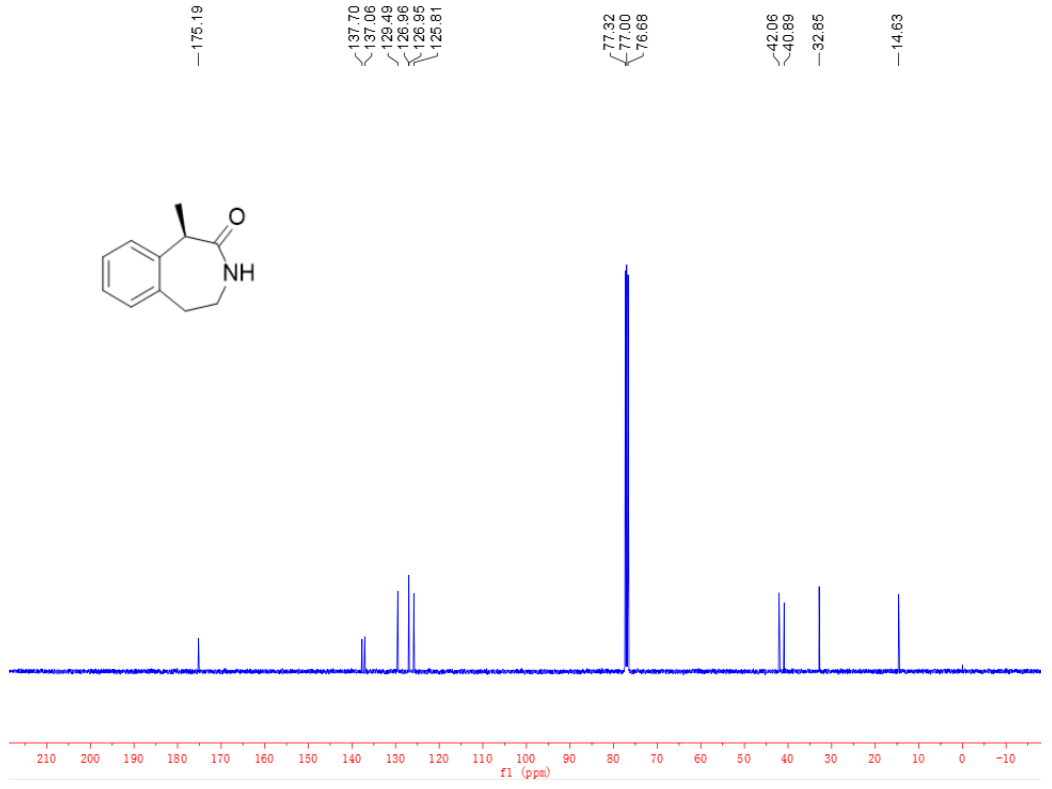

$^{13}$C NMR (101 MHz, Chloroform-*d*) of **4g**:



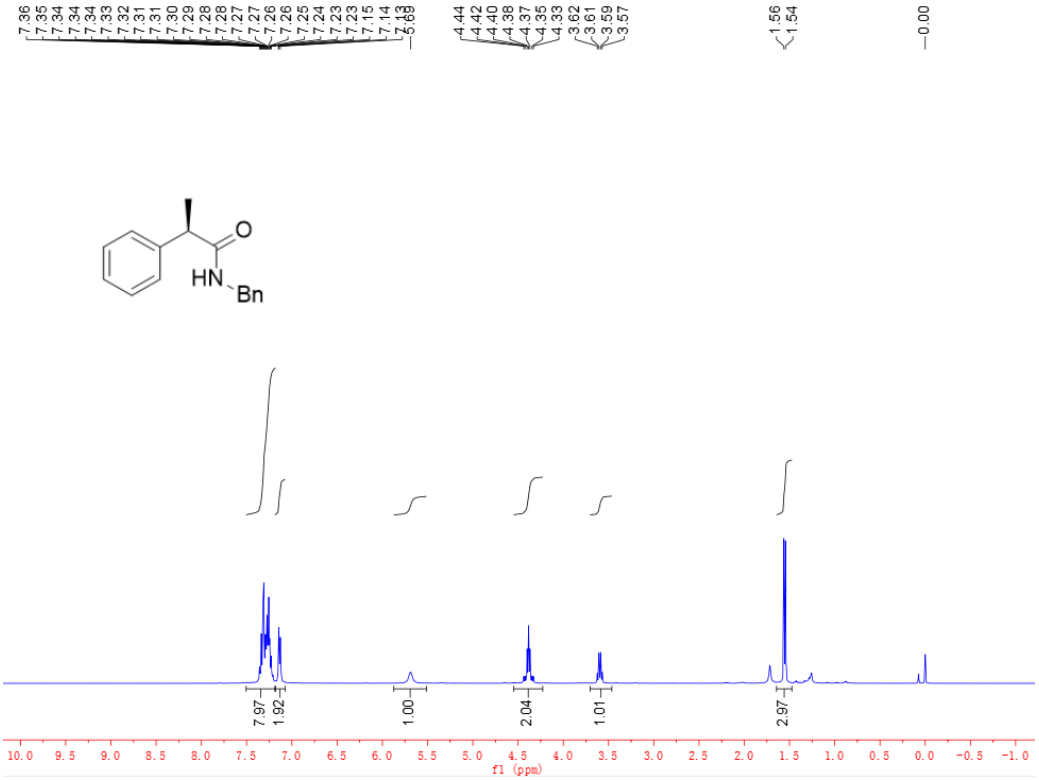
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **4h**:



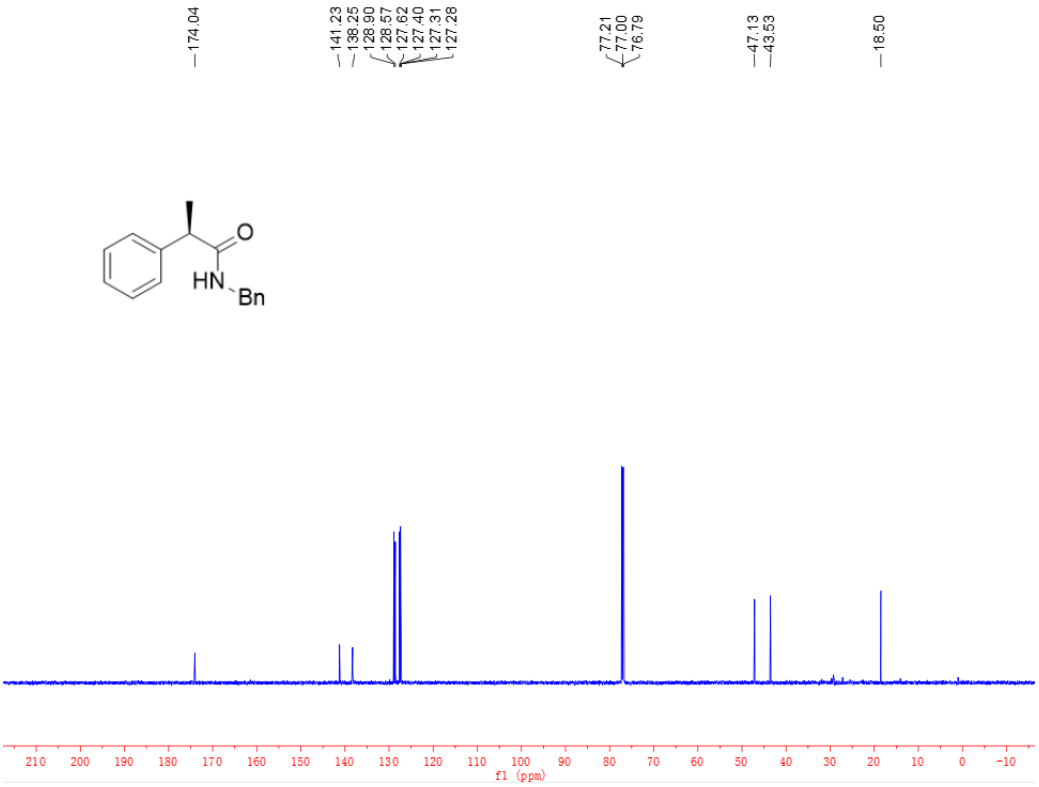

$^{13}$C NMR (101 MHz, Chloroform-*d*) of **4h**:



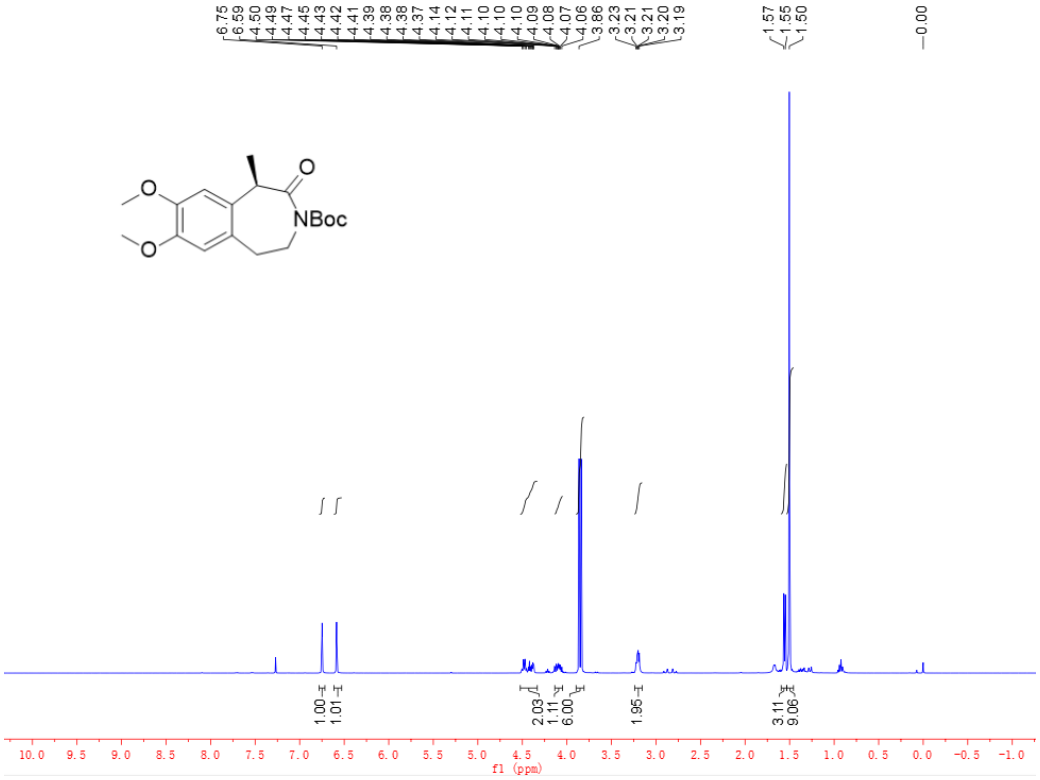
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **4i**:



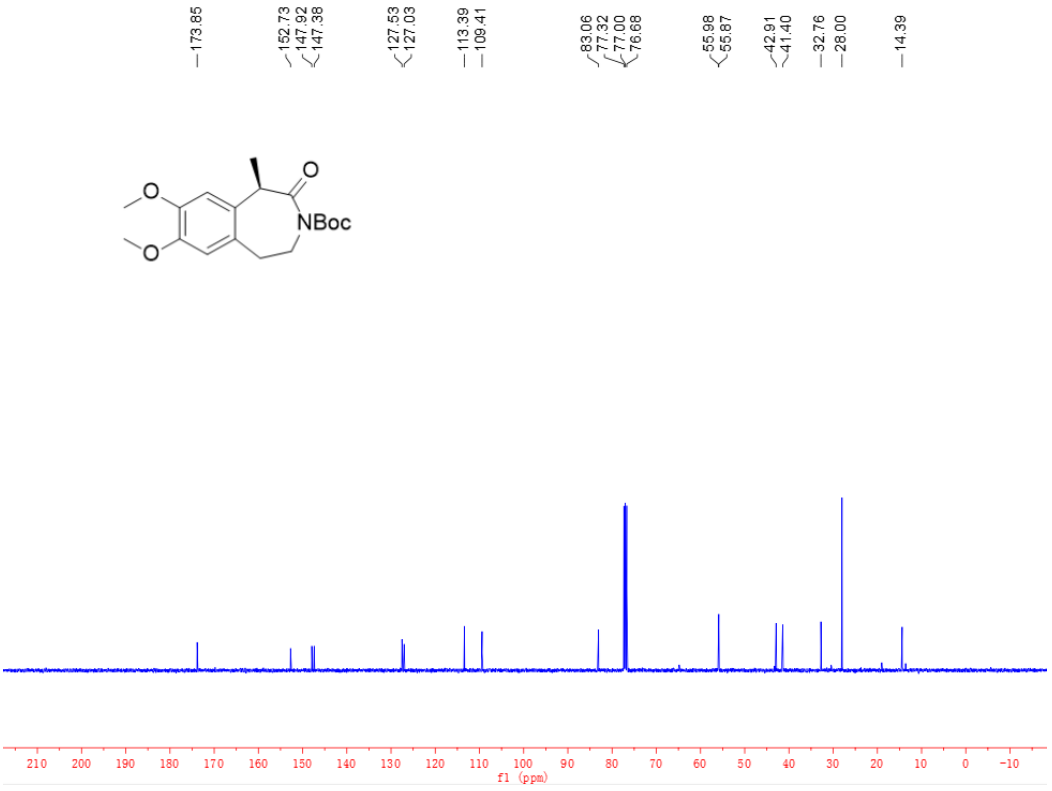

$^{13}$C NMR (151 MHz, Chloroform-*d*) of **4i**:



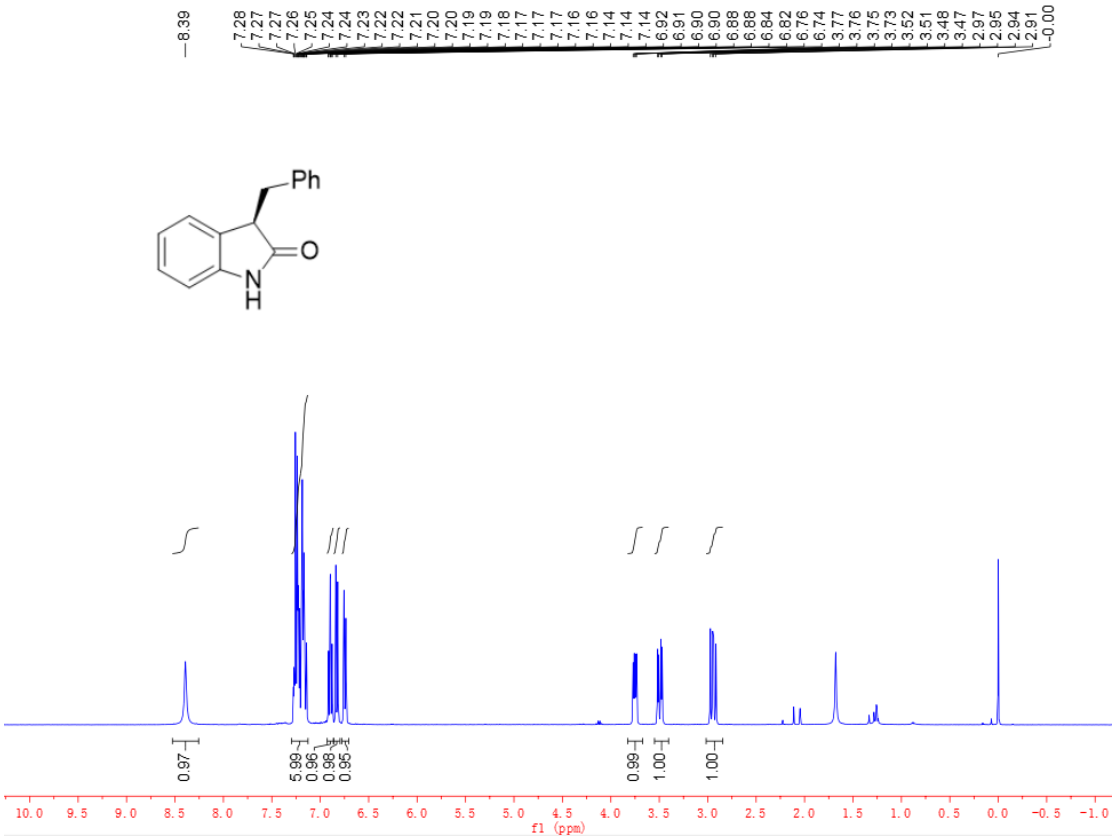
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **4j**:



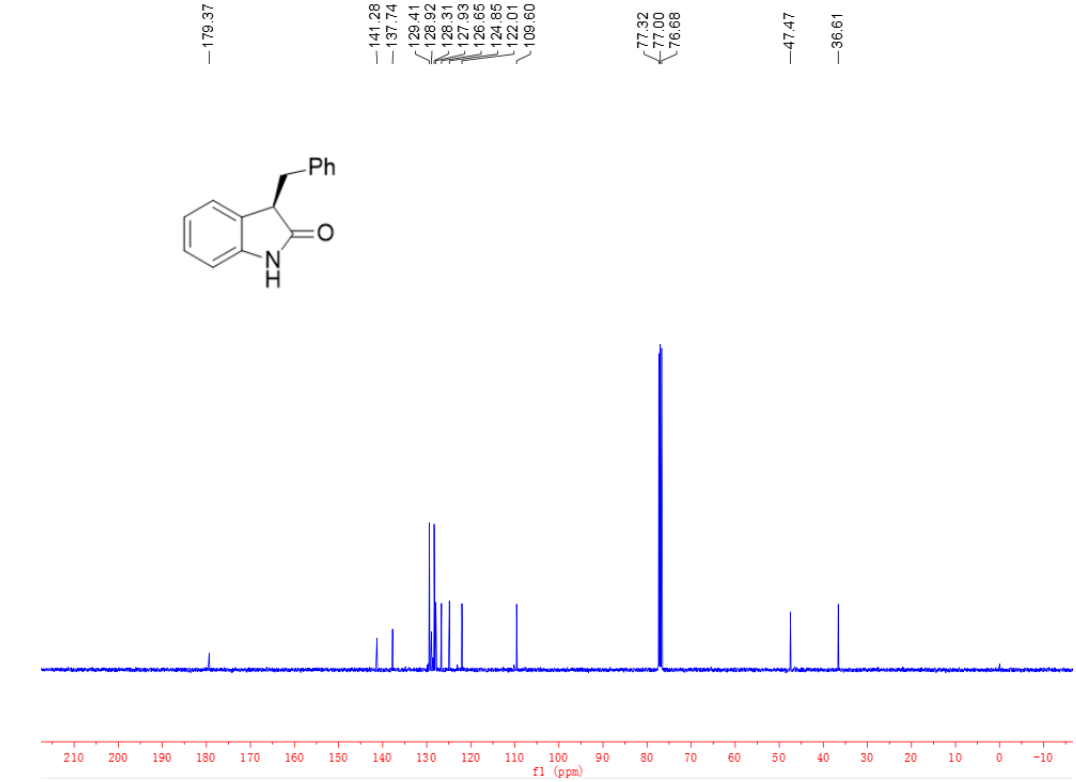

$^{13}$C NMR (101 MHz, Chloroform-*d*) of **4j**:



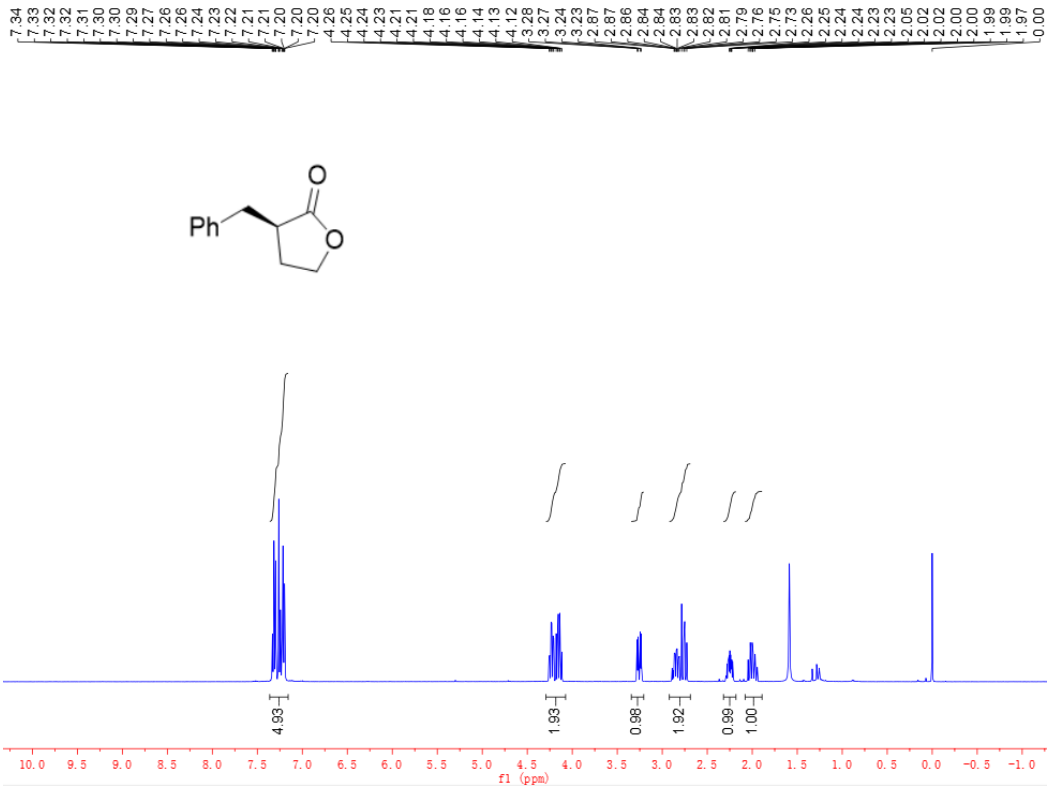
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **4k**:



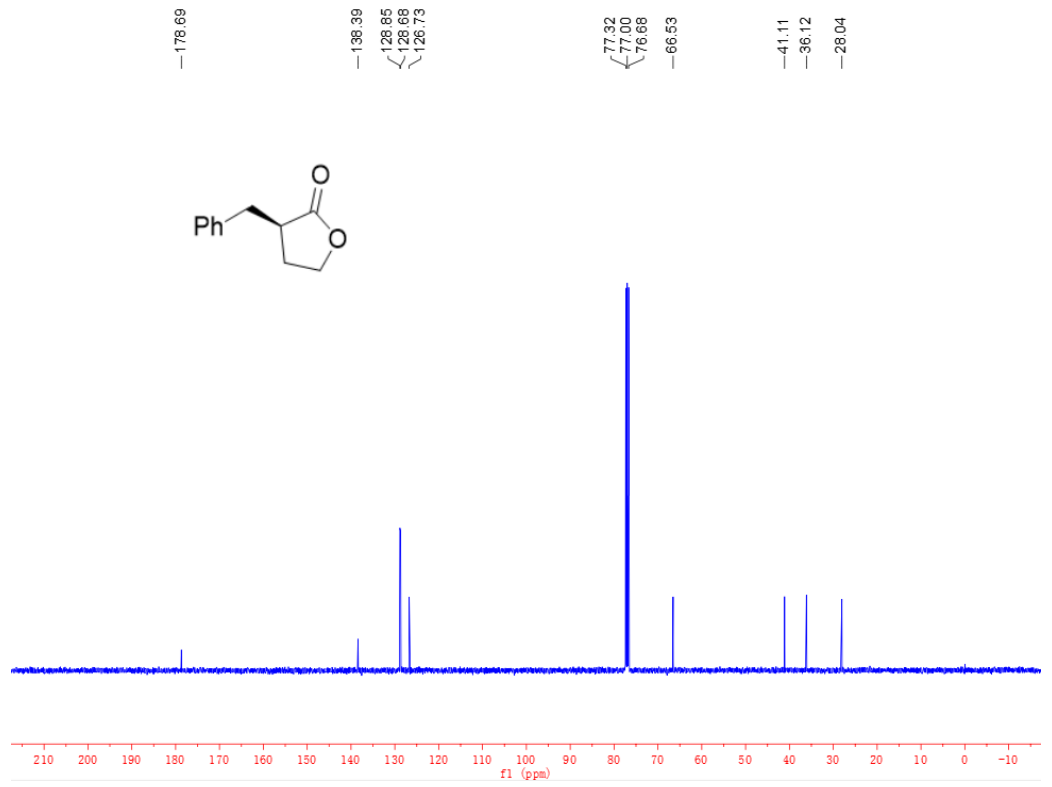

$^{13}$C NMR (101 MHz, Chloroform-*d*) of **4k**:



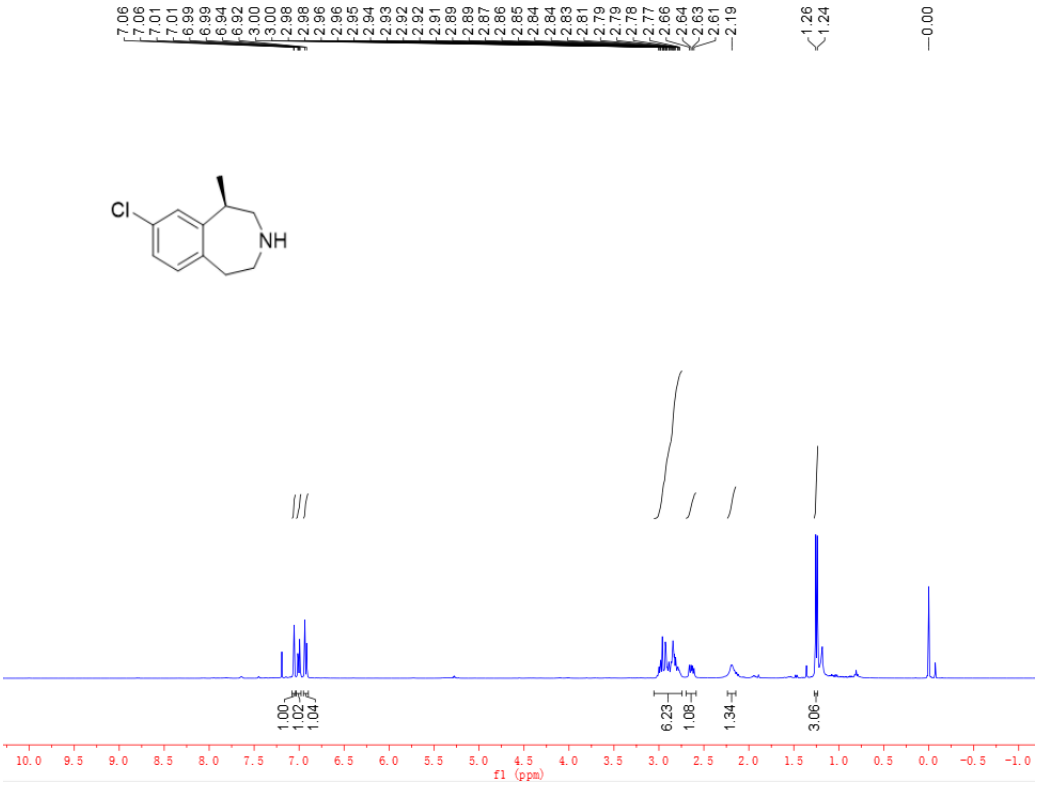
$^{1}$H NMR (400 MHz, Chloroform-*d*) of **4l**:



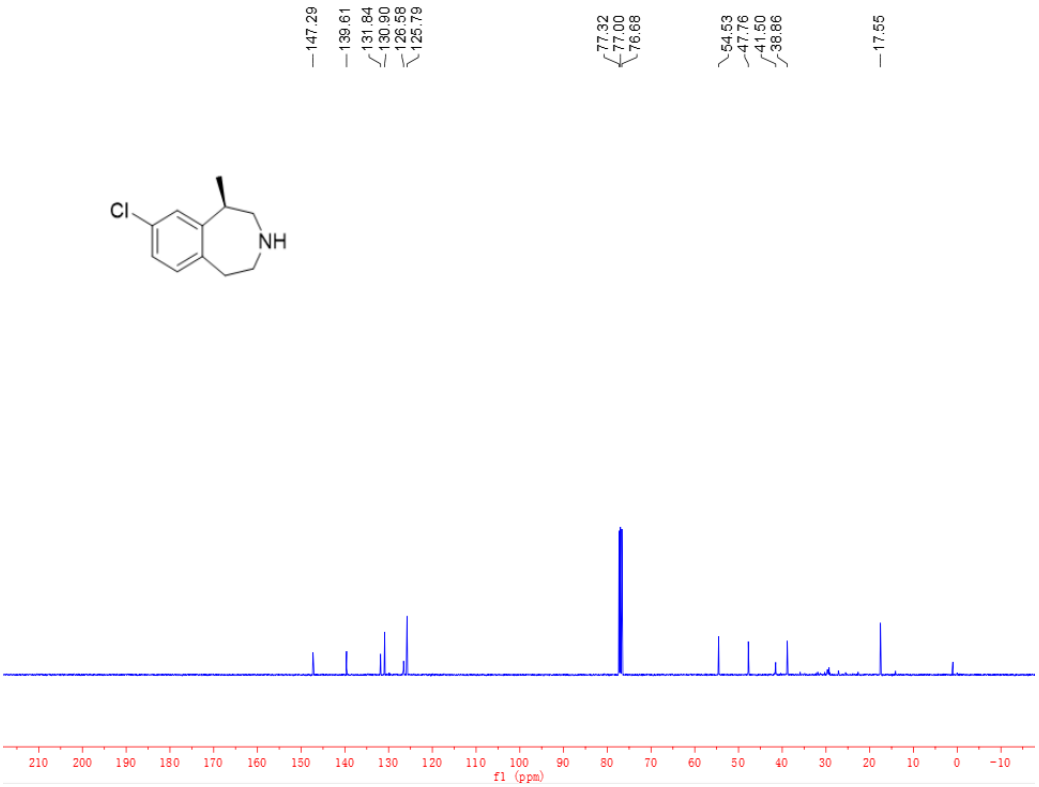

$^{13}$C NMR (101 MHz, Chloroform-*d*) of **4l**:



$^{1}$H NMR (400 MHz, Chloroform-*d*) of **5c**:

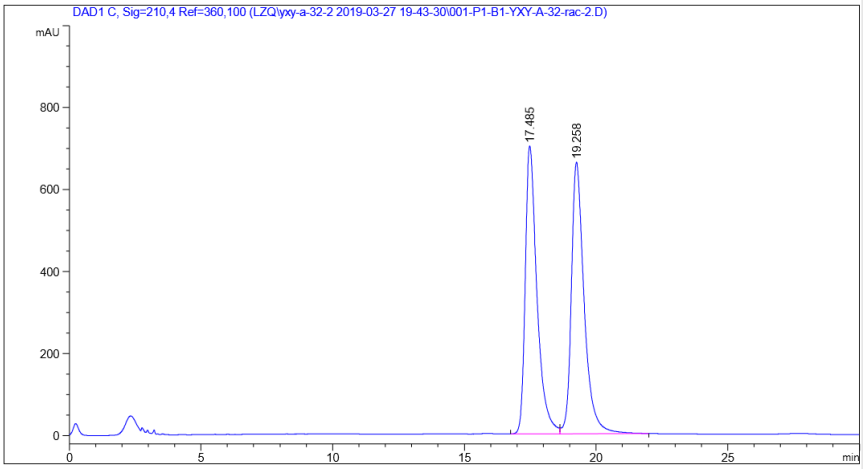



$^{13}$C NMR (101 MHz, Chloroform-*d*) of **5c**:



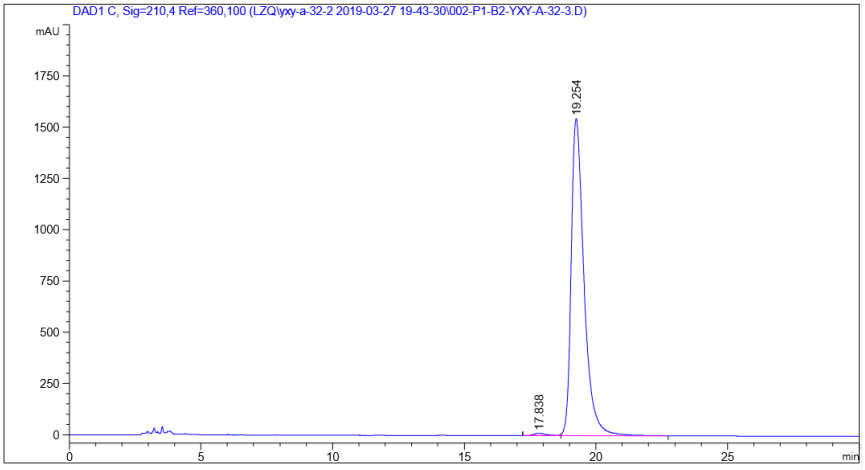
# 7. HPLC Spectra

(*R*)-7,8-dimethoxy-1-methyl-1,3,4,5-tetrahydro-2*H*-benzo[*d*]azepin-2-one **4a**:




Signal 1: DAD1 C, Sig=210,4 Ref=360,100

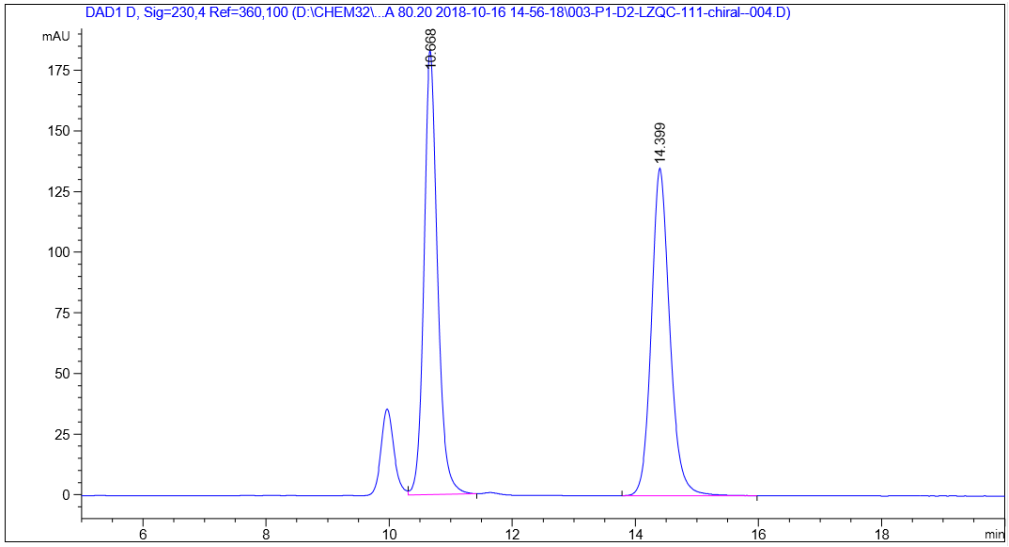
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 17.485 | BV | 0.4591 | 2.17438e4 | 702.48987 | 49.2402 |
| 2 | 19.258 | VB | 0.5067 | 2.24148e4 | 662.50220 | 50.7598 |
| Totals : | | | | 4.41587e4 | 1364.99207 | |




Signal 1: DAD1 C, Sig=210,4 Ref=360,100

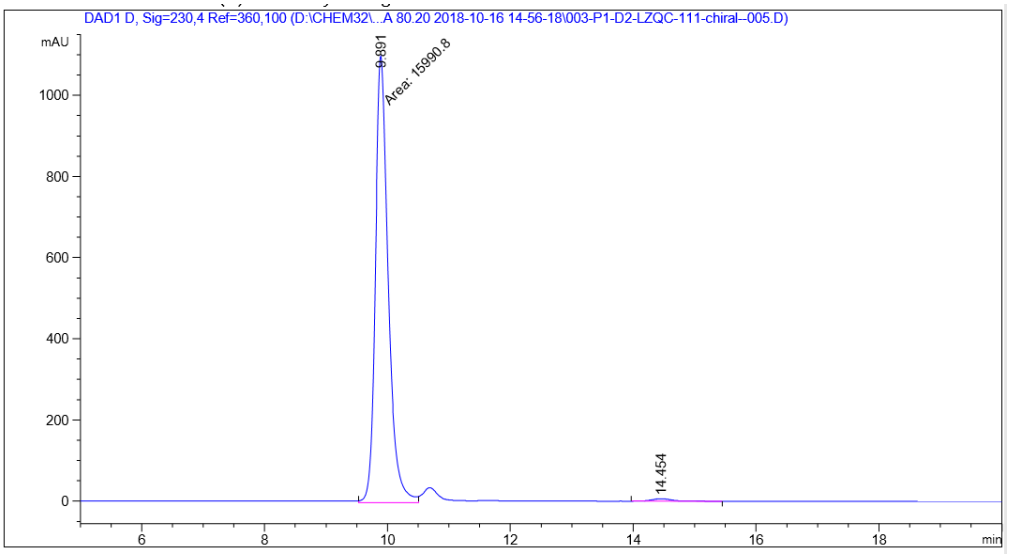
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 17.838 | BV E | 0.4563 | 391.45914 | 11.88425 | 0.7440 |
| 2 | 19.254 | VB R | 0.5062 | 5.22273e4 | 1545.68237 | 99.2560 |
| Totals : | | | | 5.26187e4 | 1557.56662 | |

(*R*)-8-methoxy-1-methyl-1,3,4,5-tetrahydro-2*H*-benzo[*d*]azepin-2-one **4b**:




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

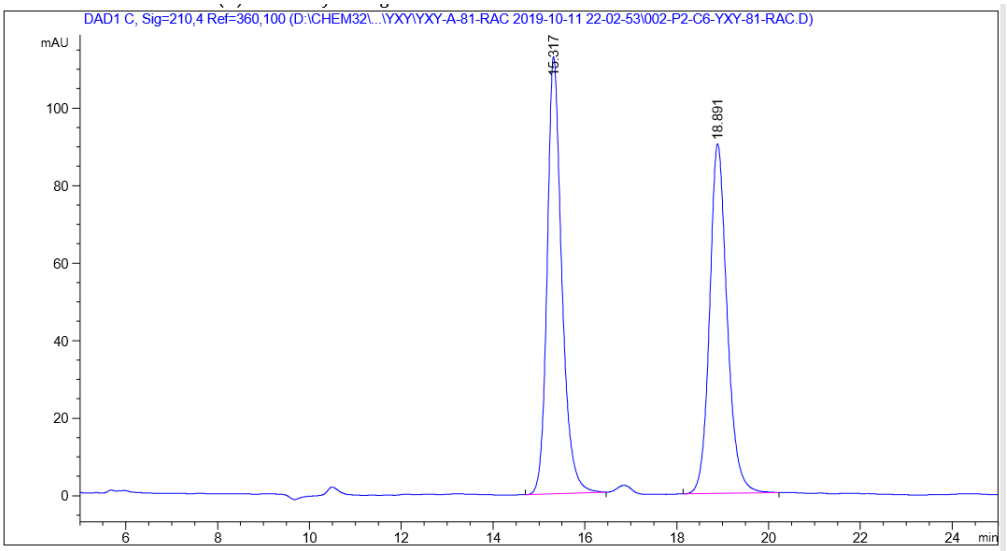
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 10.668 | VB | 0.2325 | 2802.12061 | 183.15195 | 49.9300 |
| 2 | 14.399 | BB | 0.3146 | 2809.98242 | 135.12183 | 50.0700 |
| Totals : | | | | 5612.10303 | 318.27377 | |




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

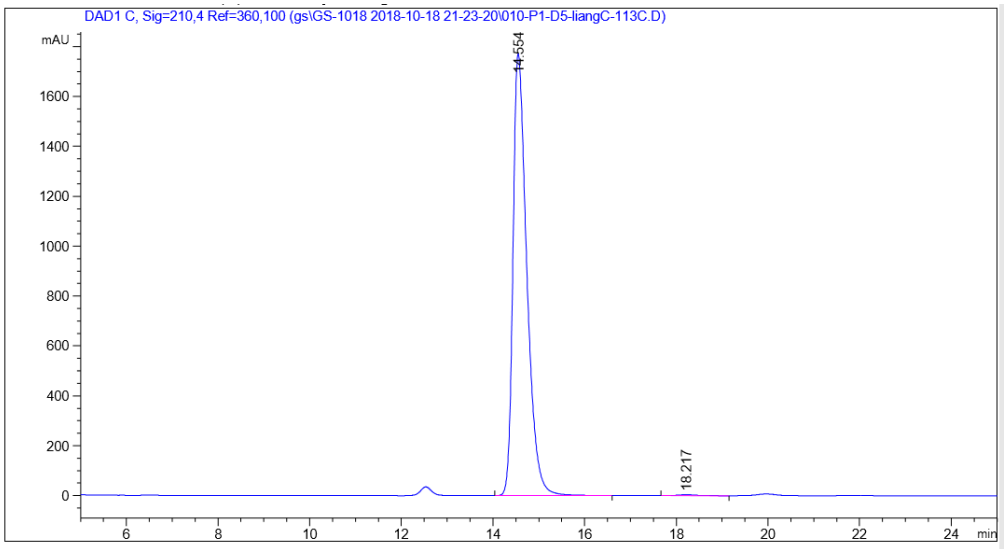
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 9.891 | MM | 0.2421 | 1.59908e4 | 1101.01648 | 99.1717 |
| 2 | 14.454 | BB | 0.3283 | 133.55370 | 6.22604 | 0.8283 |
| Totals : | | | | 1.61243e4 | 1107.24252 | |

(*R*)-8-chloro-1-methyl-1,3,4,5-tetrahydro-2*H*-benzo[*d*]azepin-2-one **4c**:




Signal 1: DAD1 C, Sig=210,4 Ref=360,100

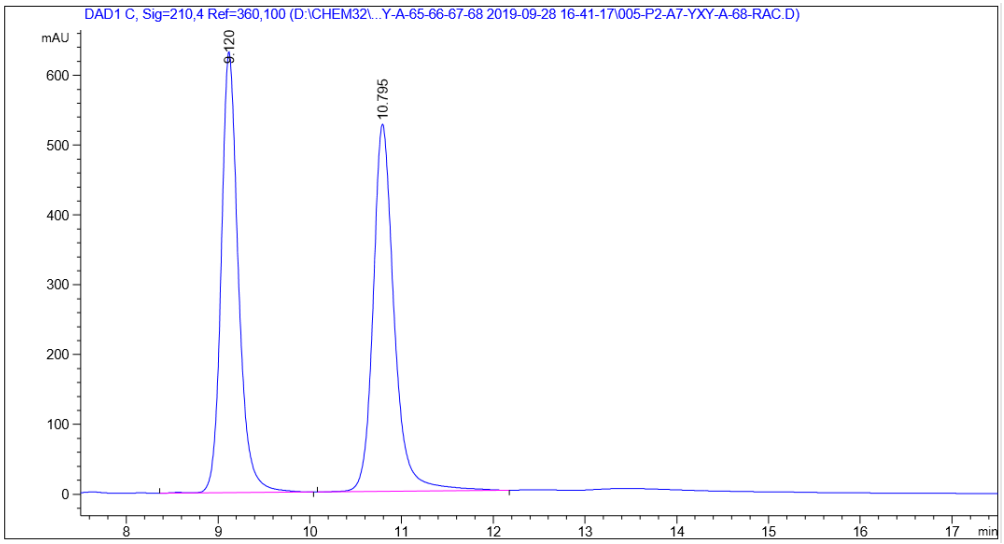
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 15.317 | BB | 0.3326 | 2499.38330 | 112.77146 | 51.0664 |
| 2 | 18.891 | BB | 0.3998 | 2394.99146 | 90.20644 | 48.9336 |
| Totals : | | | | 4894.37476 | 202.97791 | |




Signal 1: DAD1 C, Sig=210,4 Ref=360,100

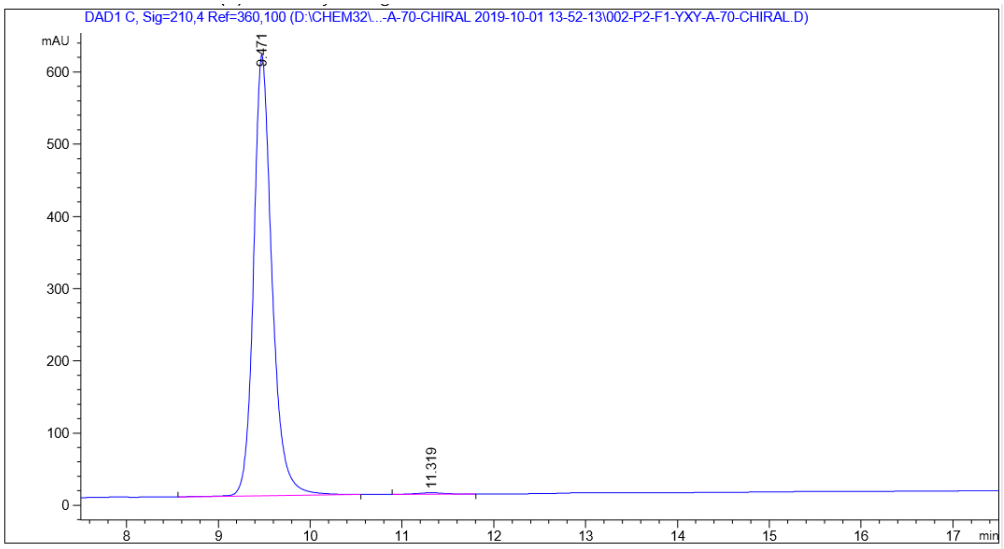
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 14.554 | BB | 0.3171 | 3.72118e4 | 1771.34985 | 99.7073 |
| 2 | 18.217 | BB | 0.3782 | 109.22614 | 4.08166 | 0.2927 |
| Totals : | | | | 3.73211e4 | 1775.43152 | |

(*R*)-8-bromo-1-methyl-1,3,4,5-tetrahydro-2*H*-benzo[*d*]azepin-2-one **4d**:




Signal 1: DAD1 C, Sig=210,4 Ref=360,100

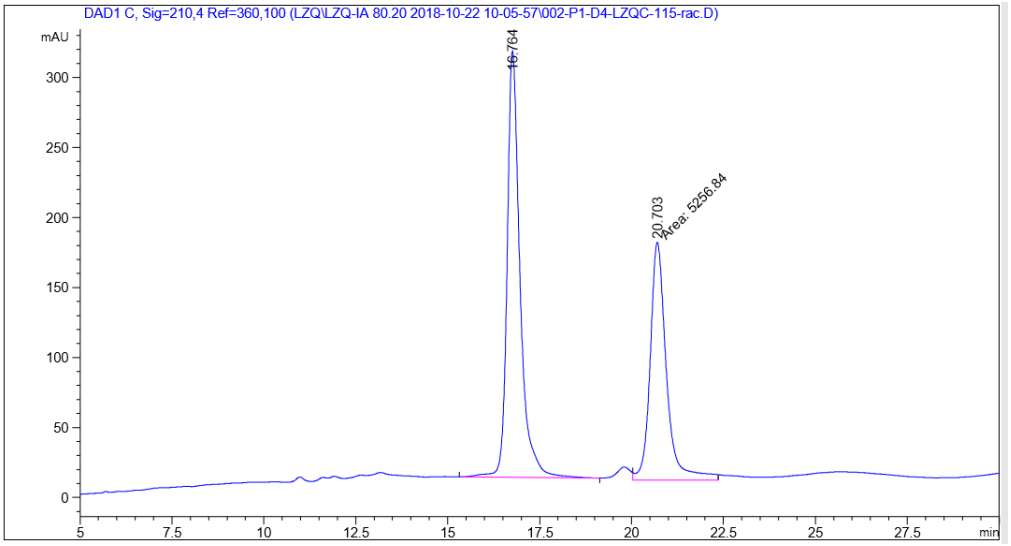
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 9.120 | VB R | 0.1979 | 8223.95215 | 631.45380 | 49.4867 |
| 2 | 10.795 | BB | 0.2401 | 8394.54590 | 526.26166 | 50.5133 |
| Totals : | | | | 1.66185e4 | 1157.71545 | |




Signal 1: DAD1 C, Sig=210,4 Ref=360,100

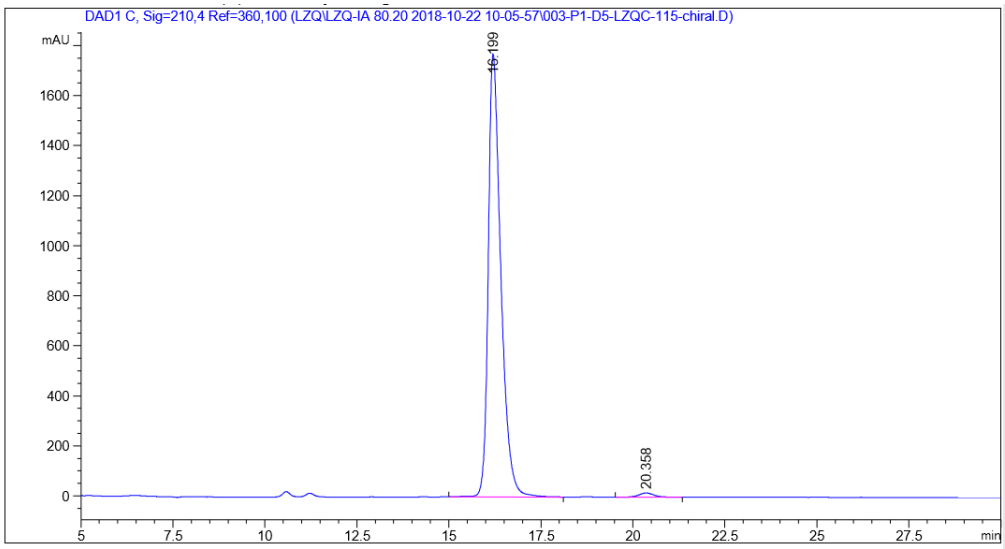
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 9.471 | BB | 0.2092 | 8539.21387 | 610.55475 | 99.4958 |
| 2 | 11.319 | BB | 0.2978 | 43.27232 | 2.12335 | 0.5042 |
| Totals : | | | | 8582.48619 | 612.67810 | |

(*R*)-7-chloro-1-methyl-1,3,4,5-tetrahydro-2*H*-benzo[*d*]azepin-2-one **4e**:




Signal 1: DAD1 C, Sig=210,4 Ref=360,100

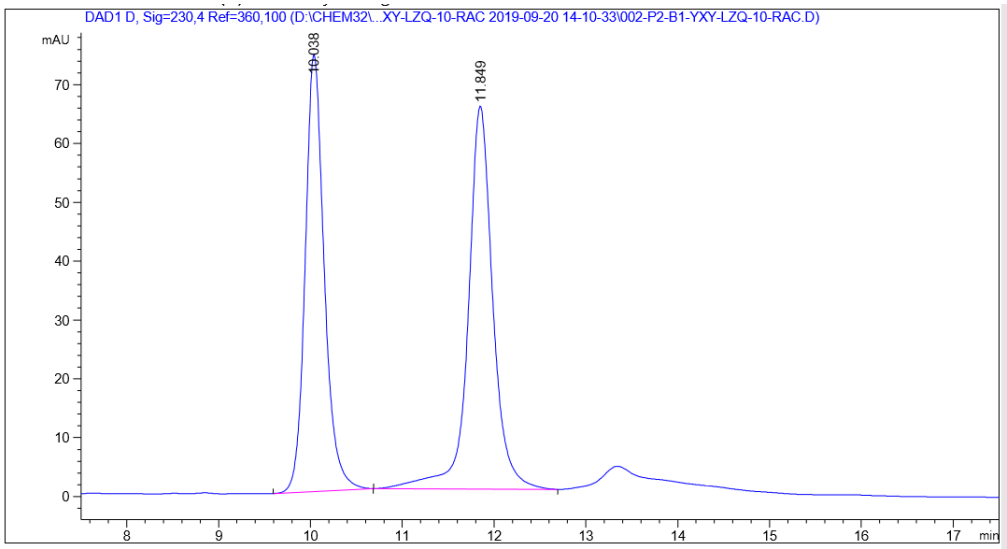
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 16.764 | BB | 0.3631 | 7440.10400 | 304.47150 | 58.5976 |
| 2 | 20.703 | MM | 0.5157 | 5256.83984 | 169.89113 | 41.4024 |
| Totals : | | | | 1.26969e4 | 474.36263 | |




Signal 1: DAD1 C, Sig=210,4 Ref=360,100

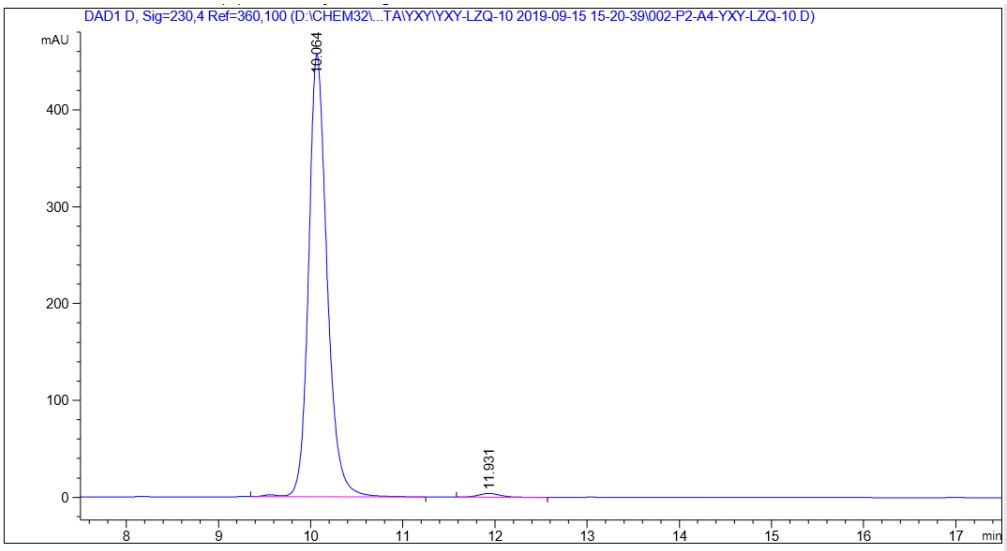
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 16.199 | BB | 0.3550 | 4.20209e4 | 1769.95740 | 98.8777 |
| 2 | 20.358 | BB | 0.4314 | 476.94000 | 16.58888 | 1.1223 |
| Totals : | | | | 4.24978e4 | 1786.54628 | |

(*R*)-7-bromo-1-methyl-1,3,4,5-tetrahydro-2*H*-benzo[*d*]azepin-2-one **4f**:




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

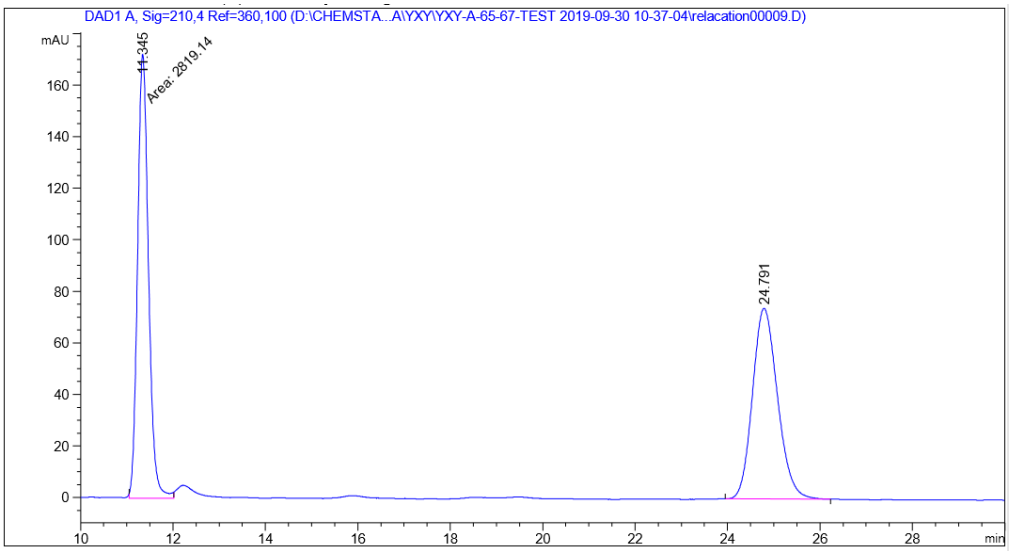
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 10.038 | BB | 0.2184 | 1071.46021 | 74.25084 | 46.7254 |
| 2 | 11.849 | BB | 0.2790 | 1221.64001 | 65.06683 | 53.2746 |
| Totals : | | | | 2293.10022 | 139.31767 | |




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

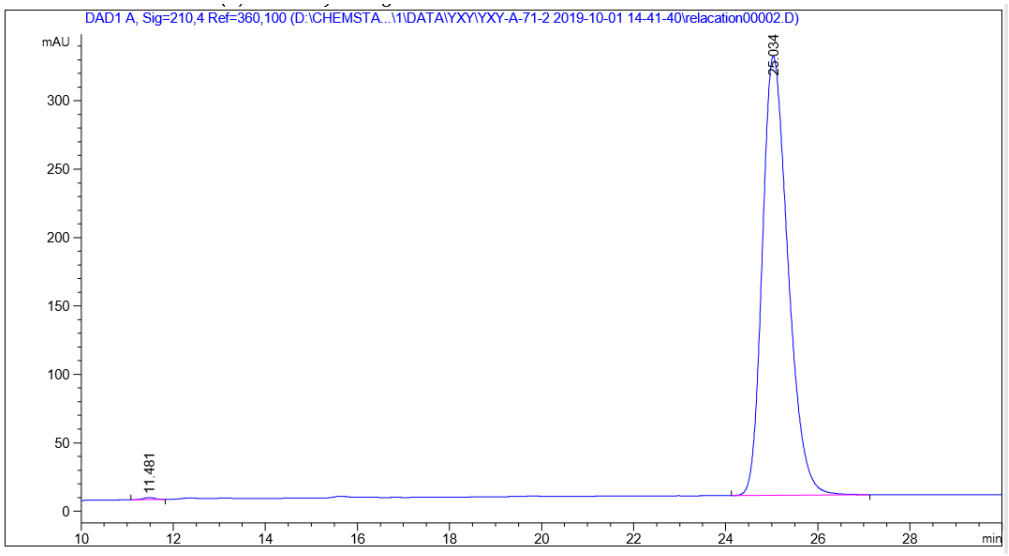
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 10.064 | VB R | 0.2102 | 6375.16016 | 456.92630 | 99.0227 |
| 2 | 11.931 | BB | 0.2538 | 62.91971 | 3.82704 | 0.9773 |
| Totals : | | | | 6438.07987 | 460.75334 | |

(*R*)-1-methyl-8-phenyl-1,3,4,5-tetrahydro-2*H*-benzo[*d*]azepin-2-one **4g**:




Signal 1: DAD1 A, Sig=210,4 Ref=360,100

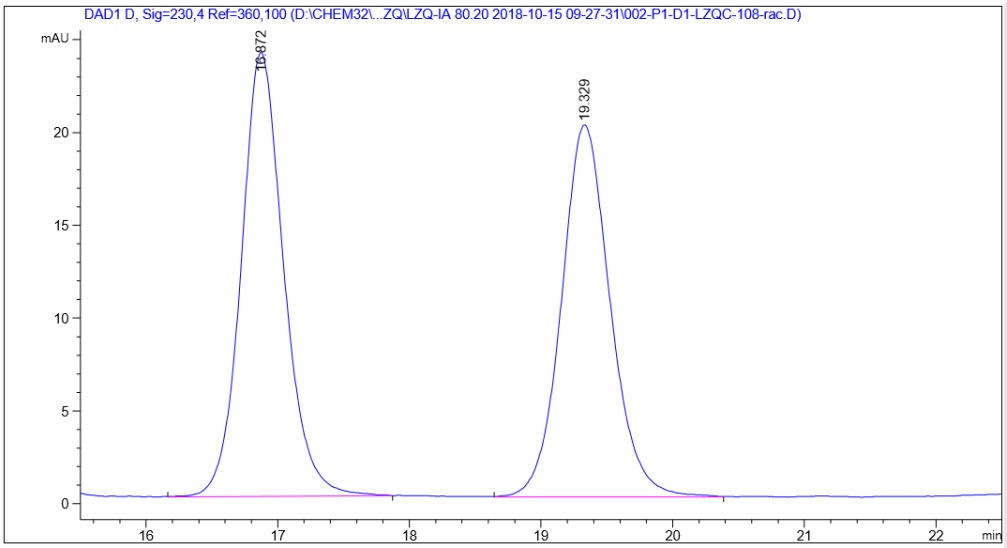
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 11.345 | MM | 0.2729 | 2819.14185 | 172.16219 | 50.3629 |
| 2 | 24.791 | BB | 0.5807 | 2778.50879 | 73.89603 | 49.6371 |
| Totals : | | | | 5597.65063 | 246.05821 | |




Signal 1: DAD1 A, Sig=210,4 Ref=360,100

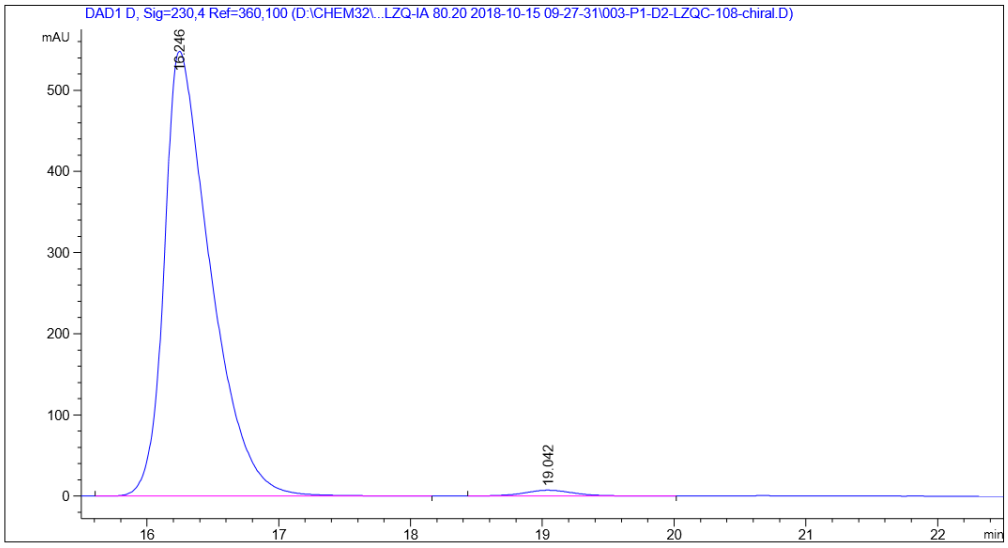
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 11.481 | BB | 0.2496 | 23.85749 | 1.45293 | 0.1917 |
| 2 | 25.034 | BB | 0.5956 | 1.24231e4 | 320.95847 | 99.8083 |
| Totals : | | | | 1.24470e4 | 322.41140 | |

(*R*)-1-methyl-1,3,4,5-tetrahydro-2*H*-benzo[*d*]azepin-2-one **4h**:




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

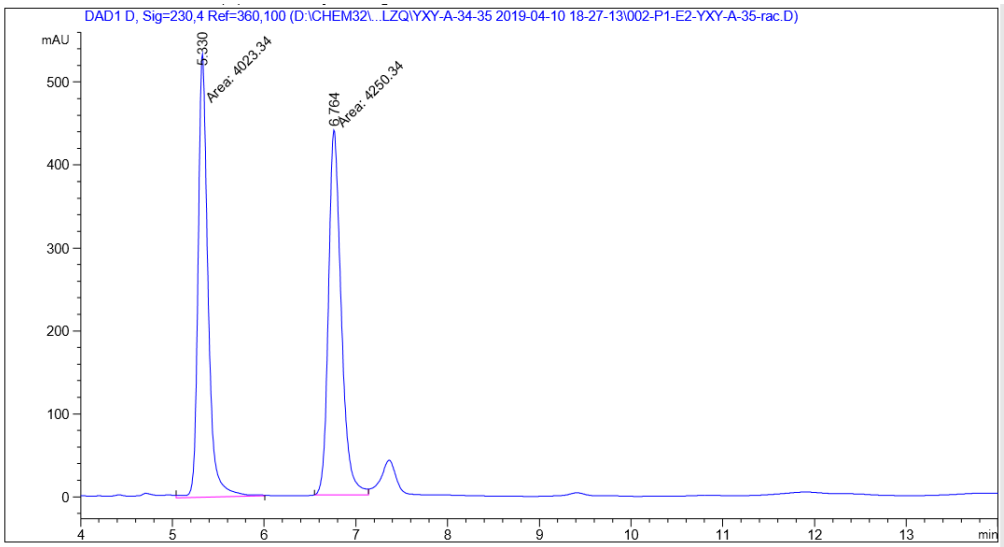
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 16.872 | BB | 0.3376 | 536.46466 | 23.92044 | 51.0156 |
| 2 | 19.329 | BB | 0.3879 | 515.10468 | 20.03985 | 48.9844 |
| Totals : | | | | 1051.56934 | 43.96029 | |




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

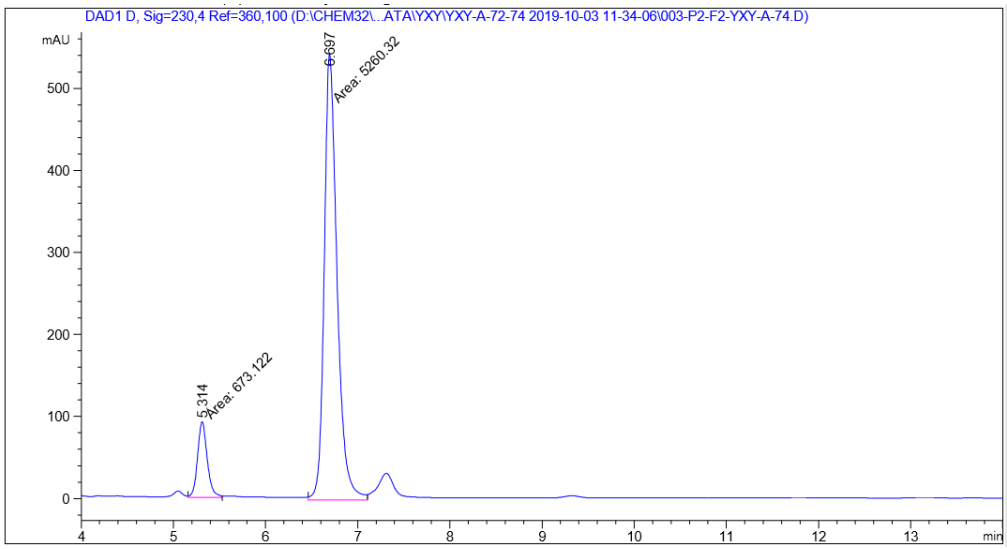
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 16.246 | BB | 0.3592 | 1.33946e4 | 547.87103 | 98.6624 |
| 2 | 19.042 | BB | 0.3901 | 181.59720 | 7.06007 | 1.3376 |
| Totals : | | | | 1.35762e4 | 554.93110 | |

(*R*)-*N*-benzyl-2-phenylpropanamide **4i**:




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

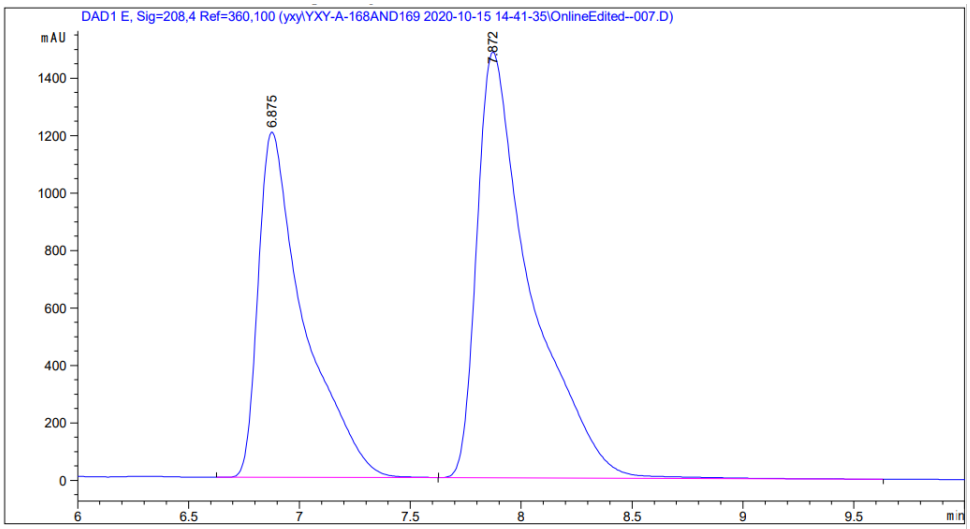
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 5.330 | MM | 0.1254 | 4023.33936 | 534.83826 | 48.6282 |
| 2 | 6.764 | MM | 0.1611 | 4250.33594 | 439.75070 | 51.3718 |
| Totals : | | | | 8273.67529 | 974.58896 | |




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

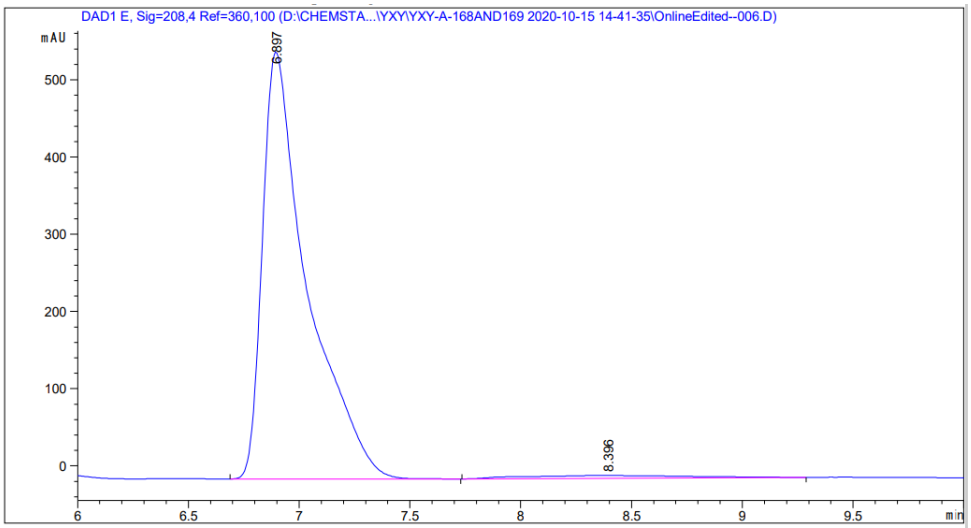
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 5.314 | MM | 0.1220 | 673.12250 | 91.97347 | 11.3446 |
| 2 | 6.697 | MM | 0.1612 | 5260.31934 | 543.87115 | 88.6554 |
| Totals : | | | | 5933.44183 | 635.84463 | |

*tert*-butyl-(*R*)-7,8-dimethoxy-1-methyl-2-oxo-1,2,4,5-tetrahydro-3*H*-benzo[*d*]azepine-3-carboxylate **4j:**




Signal 1: DAD1 E, Sig=208,4 Ref=360,100

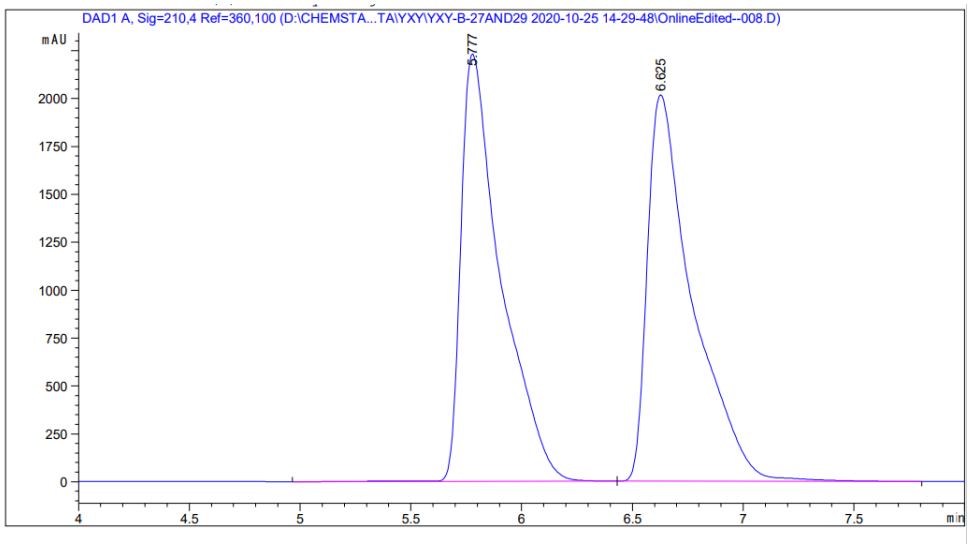
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 6.875 | BB | 0.2029 | 1.72093e4 | 1202.79529 | 40.9004 |
| 2 | 7.872 | BB | 0.2378 | 2.48668e4 | 1481.77356 | 59.0996 |
| Totals : | | | | 4.20761e4 | 2684.56885 | |




Signal 1: DAD1 E, Sig=208,4 Ref=360,100

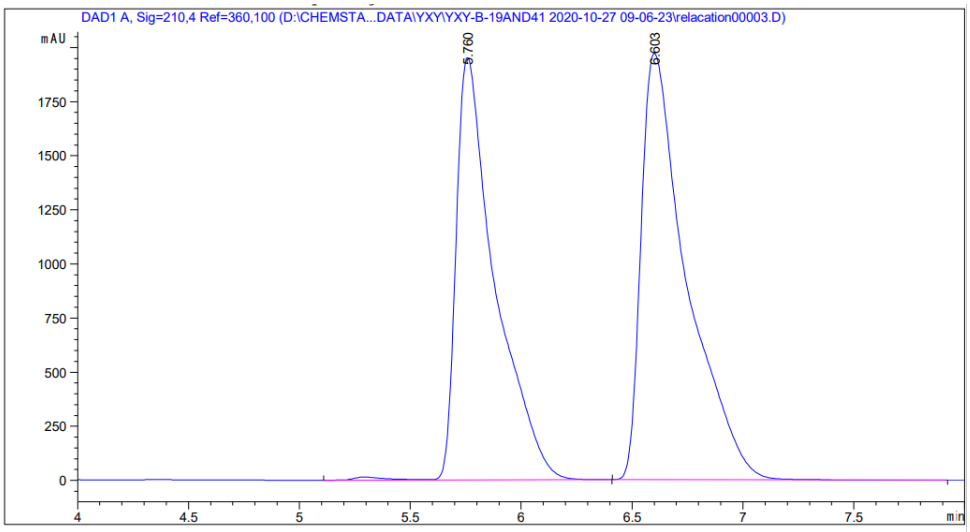
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 6.897 | BB | 0.1978 | 7765.42334 | 552.96527 | 97.6408 |
| 2 | 8.396 | BB | 0.6214 | 187.62727 | 3.59178 | 2.3592 |
| Totals : | | | | 7953.05061 | 556.55705 | |

(*R*)-3-benzylindolin-2-one **4k:**




Signal 1: DAD1 A, Sig=210,4 Ref=360,100

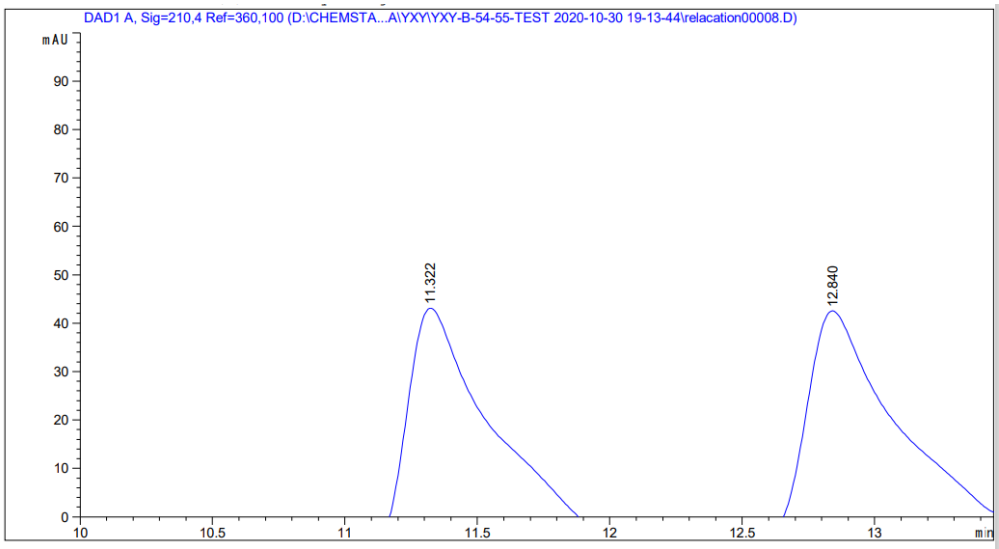
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 5.777 | BB | 0.1797 | 2.78564e4 | 2231.26343 | 49.3879 |
| 2 | 6.625 | BB | 0.2031 | 2.85469e4 | 2017.11914 | 50.6121 |
| Totals : | | | | 5.64033e4 | 4248.38257 | |




Signal 1: DAD1 A, Sig=210,4 Ref=360,100

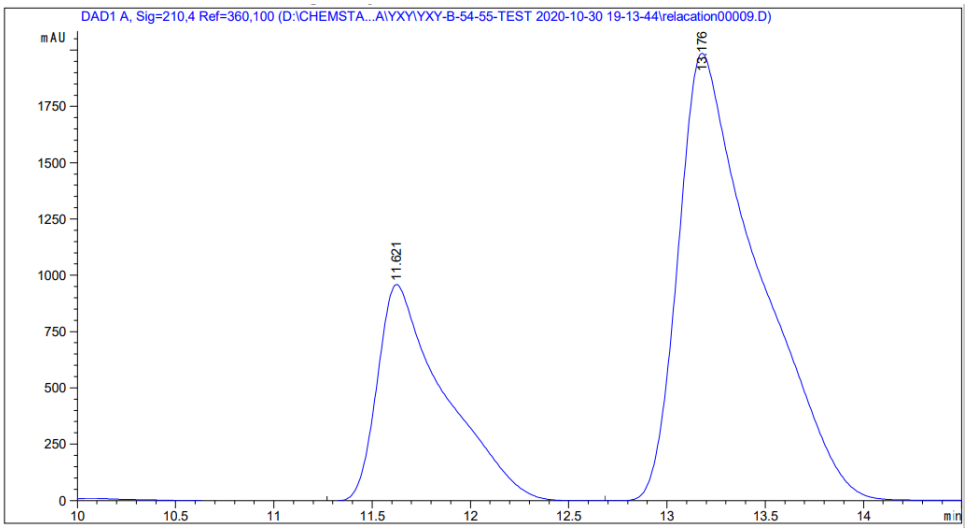
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 5.760 | VB R | 0.1733 | 2.38037e4 | 1952.85767 | 45.8861 |
| 2 | 6.603 | BB | 0.2041 | 2.80719e4 | 1971.34717 | 54.1139 |
| Totals : | | | | 5.18756e4 | 3924.20483 | |

(*S*)-3-benzyldihydrofuran-2(3*H*)-one **4l:**




Signal 1: DAD1 A, Sig=210,4 Ref=360,100

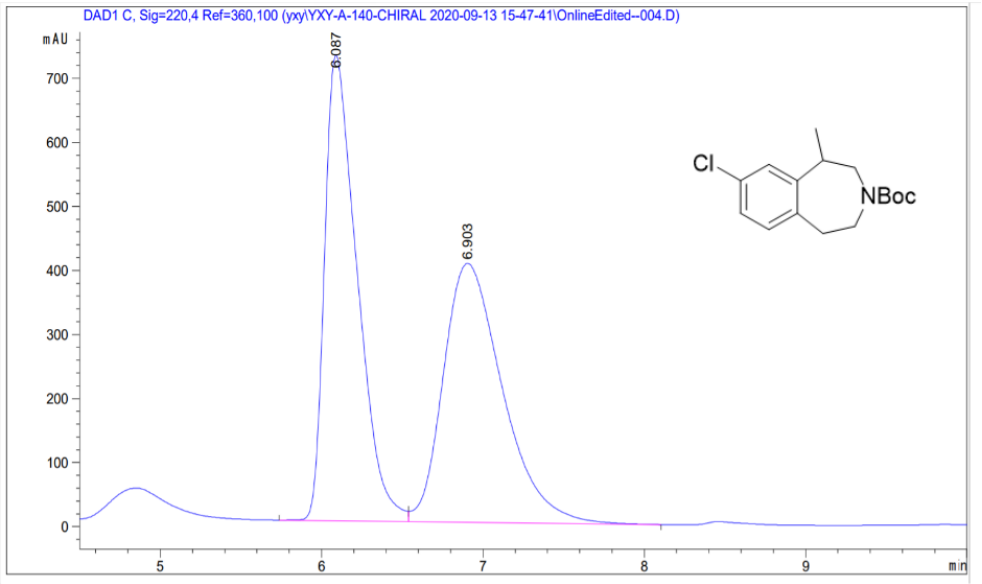
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 11.322 | BB | 0.3179 | 1155.51746 | 49.94479 | 49.0161 |
| 2 | 12.840 | BV | 0.3397 | 1201.90674 | 48.40458 | 50.9839 |
| Totals : | | | | 2357.42419 | 98.34937 | |




Signal 1: DAD1 A, Sig=210,4 Ref=360,100

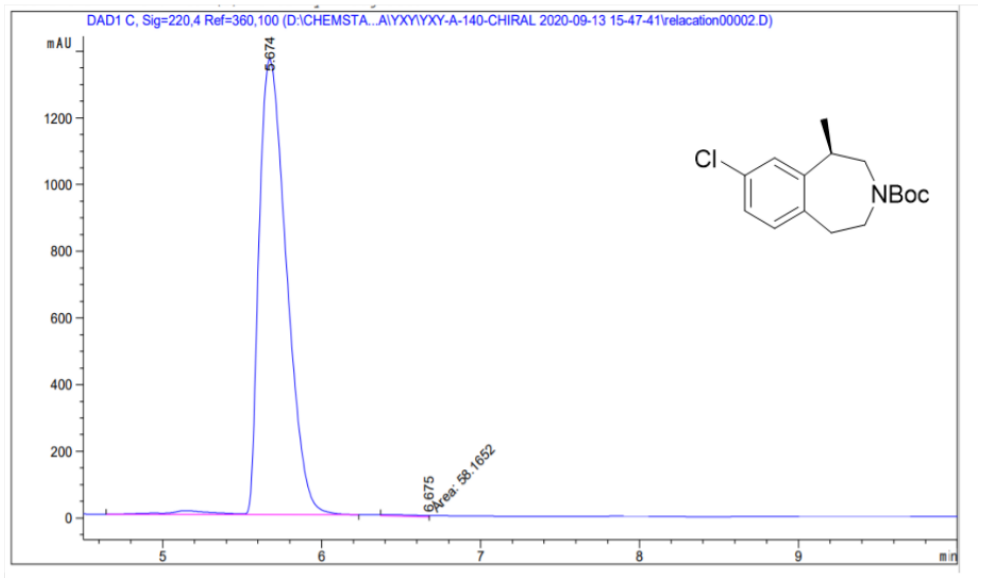
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 11.621 | BB | 0.3277 | 2.28862e4 | 961.58057 | 28.7496 |
| 2 | 13.176 | BB | 0.3909 | 5.67193e4 | 1987.74976 | 71.2504 |
| Totals : | | | | 7.96055e4 | 2949.33032 | |

Lorcaserin **5c**:




Signal 1: DAD1 C, Sig=220,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 6.087 | BV | 0.2060 | 1.02219e4 | 727.31104 | 49.7892 |
| 2 | 6.903 | VB | 0.3914 | 1.03085e4 | 404.32211 | 50.2108 |
| Totals : | | | | 2.05304e4 | 1131.63315 | |

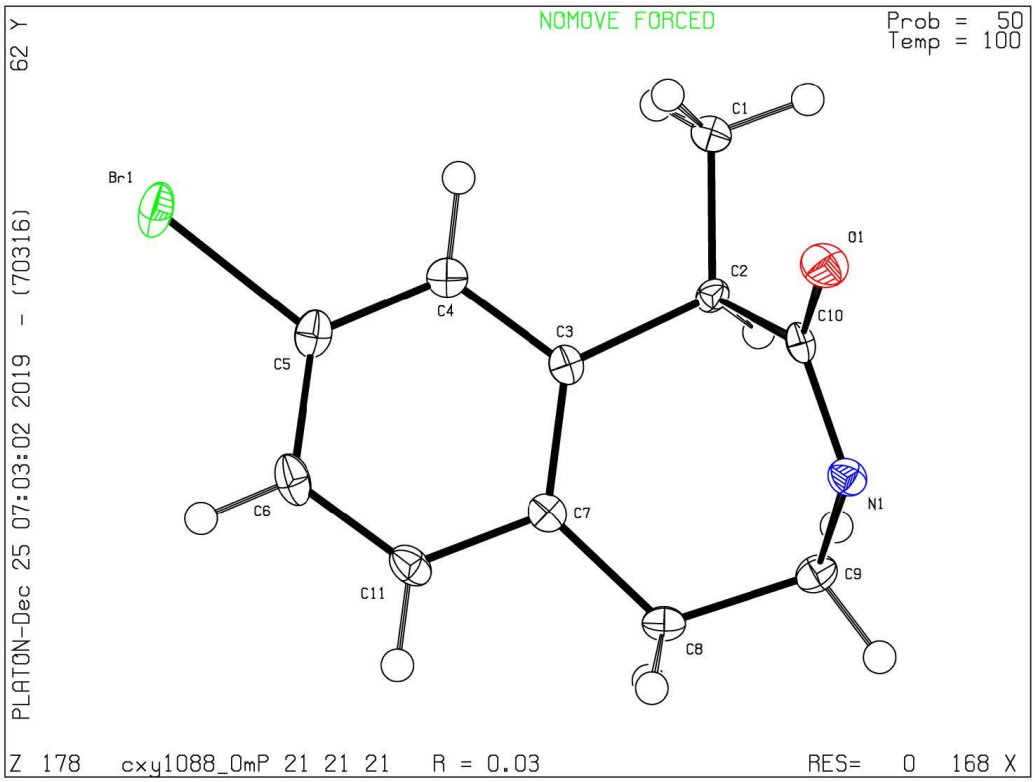



Signal 1: DAD1 C, Sig=220,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 5.674 | VB R | 0.1887 | 1.64731e4 | 1366.42114 | 99.6482 |
| 2 | 6.675 | MM | 0.2647 | 58.16516 | 3.66224 | 0.3518 |
| Totals : | | | | 1.65313e4 | 1370.08339 | |

## 8. Crystalgraphic Information

The crystal data of compound **4d** has been deposited in cxy1088_0m.




| **Table S1 Crystal data and structure refinement for cxy1088_0m.** | |
|---|---|
| Identification code | cxy1088_0m |
| Empirical formula | $C_{11}H_{11}NOBr$ |
| Formula weight | 253.12 |
| Temperature/K | 100 |
| Crystal system | orthorhombic |
| Space group | $P2_12_12_1$ |
| a/Å | 4.2604(2) |
| b/Å | 7.8580(4) |
| c/Å | 30.3127(14) |
| α/° | 90 |
| β/° | 90 |
| γ/° | 90 |
| Volume/Å$^3$ | 1014.82(8) |
| Z | 4 |
| $\rho_{calc}$g/cm$^3$ | 1.657 |
| μ/mm$^{-1}$ | 4.015 |
| F(000) | 508.0 |

| | |
|---|---|
| Crystal size/mm$^3$ | 0.42 × 0.38 × 0.36 |
| Radiation | MoKα (λ = 0.71073) |
| 2Θ range for data collection/° | 5.356 to 61.358 |
| Index ranges | -5 ≤ h ≤ 6, -11 ≤ k ≤ 11, -43 ≤ l ≤ 42 |
| Reflections collected | 13812 |
| Independent reflections | 3143 [Rint = 0.0485, Rsigma = 0.0365] |
| Data/restraints/parameters | 3143/0/128 |
| Goodness-of-fit on $F^2$ | 1.076 |
| Final R indexes [I>=2σ (I)] | $R_1$ = 0.0304, $wR_2$ = 0.0706 |
| Final R indexes [all data] | $R_1$ = 0.0326, $wR_2$ = 0.0714 |
| Largest diff. peak/hole / e Å$^{-3}$ | 0.81/-1.13 |
| Flack parameter | 0.010(5) |

**Table S2. Fractional Atomic Coordinates (×10$^4$) and Equivalent Isotropic Displacement Parameters (Å$^2$×10$^3$) for cxy1088_0m.** $U_{eq}$ is defined as 1/3 of of the trace of the orthogonalised $U_{IJ}$ tensor.

| **Atom** | ***x*** | ***y*** | ***z*** | **U(eq)** |
|---|---|---|---|---|
| Br1 | 8210.2(8) | 6030.4(4) | 4660.3(2) | 20.74(9) |
| O1 | 4916(6) | 3434(3) | 2639.4(7) | 19.3(5) |
| N1 | 2679(5) | 1023(3) | 2885.5(8) | 13.3(5) |
| C1 | 1420(8) | 5541(4) | 3190.5(10) | 17.2(6) |
| C2 | 1639(7) | 3640(3) | 3291.8(9) | 11.1(5) |
| C3 | 3419(7) | 3189(3) | 3715.7(9) | 11.3(5) |
| C4 | 4783(7) | 4512(4) | 3960.8(10) | 13.2(5) |
| C5 | 6451(7) | 4180(4) | 4341.9(9) | 14.9(5) |
| C6 | 6848(9) | 2522(4) | 4492.8(10) | 17.3(6) |
| C7 | 3763(7) | 1502(4) | 3868.4(9) | 11.7(5) |
| C8 | 2430(7) | -85(4) | 3648.2(10) | 14.3(6) |
| C9 | 788(7) | 105(4) | 3204.5(10) | 14.0(6) |
| C10 | 3210(8) | 2707(3) | 2906.3(9) | 11.7(5) |
| C11 | 5487(7) | 1220(4) | 4253.2(9) | 15.4(6) |

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