Umpolung *α*-regioselective 1,3-dipolar cycloaddition and internal recycle of byproduct as two key strategies: access to diverse chiral bipyridines

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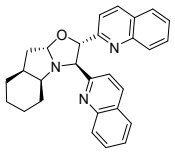
1. General information

Reactions were monitored by thin layer chromatography using UV light to visualize the course of reaction. Purification of reaction products was carried out by flash chromatography on silica gel or just by simple filtration and washing. ^{1}H and ^{13}CNMR spectra were obtained using a Bruker DPX-400 spectrometer. ^{1}H NMR chemical shifts are reported in ppm (δ) relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constants (Hz) and integration. ^{13}C NMR chemical shifts are reported in ppm (δ) from tetramethylsilane (TMS) with the solvent resonance as the internal standard. Melting points were measured on an electrothermal digital melting point apparatus.

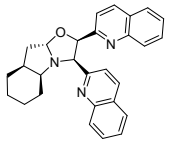
2. The synthesis of perhydroindole-bipyridines 3

In a sealed tube equipped with a magnetic stirring bar, a mixture of optically pure perhydroindole-2-carboxylic acid **1** (0.6 mmol) and pyridinecarboxaldehyde **2** (0.4 mmol) in 2.0 mL of toluene was stirred at 80 ^{o}C for 1 h, and then was directly loaded onto a silica gel and purified by flash chromatography to give the desired product **3**, using hexane/EtOAc (7/1, v/v) as the eluent.

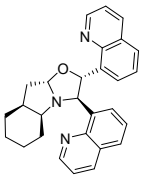
3. Characterization data of compounds 3



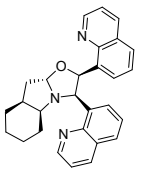
3a-1: Light yellow oil; 27.8 mg, yield 33%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.07-1.13 (m, 1H), 1.18-1.20 (m, 1H), 1.36-1.44 (m, 3H), 1.52-1.59 (m, 3H), 1.92-1.96 (m, 1H), 2.16-2.23 (m, 2H), 3.22 (d, J = 3.6 Hz, 1H), 4.68 (d, J = 6.0 Hz, 1H), 5.41-5.43 (m, 1H), 5.49 (d, J = 7.2 Hz, 1H), 7.36-7.41 (m, 2H), 7.51-7.57 (m, 2H), 7.69-7.73 (m, 3H), 7.78 (d, J = 7.6 Hz, 1H), 7.85 (d, J = 8.4 Hz, 1H), 7.90 (d, J = 8.8 Hz, 1H), 8.08 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.1, 23.8, 26.5, 28.2, 36.5, 37.9, 62.0, 73.1, 86.1, 98.1, 118.0, 118.7, 124.7, 124.9, 126.2, 126.4, 127.9, 128.0, 128.2, 135.4, 135.5, 146.2, 146.3, 159.2, 161.3; HRMS (ESI-TOF) m/z: Calcd. for $C_{28}H_{28}N_3O$ $[M+H]^+$: 422.2227; Found: 422.2231.



3a-2: Light yellow oil; 31.2 mg, yield 37%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.12-1.24 (m, 3H), 1.40-1.59 (m, 4H), 1.72 (d, J = 11.6 Hz, 1H), 1.99-2.10 (m, 2H), 2.16-2.20 (m, 1H), 3.30 (d, J = 4.0 Hz, 1H), 4.92 (d, J = 6.8 Hz, 1H), 5.73 (d, J = 6.8 Hz, 1H), 5.99-6.02 (m, 1H), 6.81 (d, J = 8.4 Hz, 1H), 7.22-7.30 (m, 2H), 7.32-7.36 (m, 3H), 7.40-7.43 (m, 2H), 7.47-7.53 (m, 2H), 7.72 (d, J = d, J = 8.4 Hz, 1H), 7.89 (d, J = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 18.4, 23.3, 26.8, 27.1, 36.6, 37.6, 61.7, 70.8, 80.0, 98.0, 117.4, 118.5, 123.9, 124.0, 125.3, 125.4, 126.9, 127.0, 127.1, 127.2, 133.1, 133.7, 145.0, 145.3, 157.7, 158.7; HRMS (ESI-TOF) m/z: Calcd. for $C_{28}H_{28}N_3O$ $[M+H]^+$: 422.2227; Found: 422.2225.

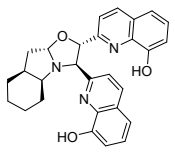


3b-1: Light yellow solid; 17.7 mg, yield 21%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.07-1.12 (m, 2H), 1.33-1.46 (m, 3H), 1.53-1.56 (m, 3H), 2.01-2.05 (m, 1H), 2.24-2.27 (m, 2H), 3.44 (d, J = 2.8 Hz, 1H), 5.30 (d, J = 7.6 Hz, 1H), 5.57-5.58 (m, 1H), 6.01 (d, J = 7.6 Hz, 1H), 6.77-6.80 (m, 1H), 6.84-6.88 (m, 1H), 7.53-7.57 (m, 3H), 7.60-7.64 (m, 2H), 7.77-7.83 (m, 3H), 8.18 (d, J = 6.4 Hz, 1H), 8.24-8.26 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.5, 24.2, 26.9, 28.6, 36.7, 38.5, 63.6, 69.1, 83.3, 97.4, 118.8, 119.0, 125.4, 125.5, 125.6, 134.1, 134.3, 138.2, 141.1, 145.2, 145.3, 146.3, 146.9; HRMS (ESI-TOF) m/z: Calcd. for $C_{28}H_{28}N_3O$ $[M+H]^+$: 422.2227; Found: 422.2224.

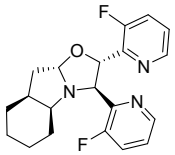


3b-2: Light yellow solid; 32.0 mg, yield 38%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.17-1.22 (m, 3H), 1.43-1.59 (m, 4H), 1.84 (d, J = 7.2 Hz, 1H), 1.99-2.10 (m, 2H), 2.15-2.19 (m, 1H), 3.59 (s, 1H), 5.84-5.87 (m, 2H), 6.60-6.68 (m, 2H), 6.80 (d, J = 5.6 Hz, 2H), 7.03-7.06 (m, 1H), 7.19-7.25 (m, 1H), 7.33-7.38 (m, 2H), 7.57-7.61 (m, 2H), 7.73-7.77 (m, 2H), 8.93 (s, 1H); ^{13}C NMR ($CDCl_3$,

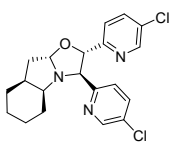
100 MHz) δ: 19.2, 24.4, 27.9, 28.2, 37.0, 38.9, 62.8, 64.3, 73.1, 96.9, 118.4, 119.1, 123.6, 124.8, 124.9, 125.0, 125.5, 125.8, 125.9, 127.4, 133.9, 134.5, 135.6, 144.6, 145.6, 145.8, 147.9; HRMS (ESI-TOF) m/z: Calcd. for $C_{28}H_{28}N_3O$ $[M+H]^+$: 422.2227; Found: 422.2229.



3c: Light yellow solid; 37.1 mg, yield 41%, 17:1 dr; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.12-1.18 (m, 1H), 1.27-1.30 (m, 1H), 1.35-1.48 (m, 2H), 1.54-1.60 (m, 3H), 1.75 (d, J = 13.2 Hz, 1H), 1.98-2.11 (m, 2H), 2.18-2.22 (m, 1H), 3.28 (d, J = 2.8 Hz, 1H), 4.88 (d, J = 6.4 Hz, 1H), 5.68 (d, J = 6.8 Hz, 1H), 5.84-5.86 (m, 1H), 6.83 (d, J = 7.2 Hz, 1H), 6.98-7.04 (m, 4H), 7.15-7.24 (m, 3H), 7.40 (d, J = 8.4 Hz, 1H), 7.61 (d, J = 8.8 Hz, 1H), 7.80 (d, J = 8.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.2, 24.1, 27.7, 28.0, 37.4, 38.4, 62.4, 70.8, 80.1, 98.5, 108.5, 108.8, 116.3, 116.6, 119.0, 120.1, 126.0, 126.1, 134.6, 135.0, 135.7, 135.9, 150.5, 150.6, 156.5, 157.2; HRMS (ESI-TOF) m/z: Calcd. for $C_{28}H_{28}N_3O_3$ $[M+H]^+$: 454.2125; Found: 454.2115.

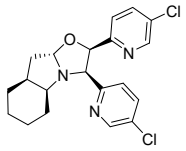


3d: Light yellow oil; 24.3 mg, yield 34%, 12:1 dr; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.06-1.18 (m, 2H), 1.27-1.34 (m, 2H), 1.41-1.48 (m, 3H), 1.63-1.67 (m, 1H), 1.81-1.85 (m, 1H), 2.09-2.16 (m, 2H), 3.32-3.35 (m, 1H), 4.86 (d, J = 6.8 Hz, 1H), 5.43-5.45 (m, 1H), 5.76 (d, J = 6.8 Hz, 1H), 7.08-7.16 (m, 2H), 7.20-7.27 (m, 2H), 8.33-8.37 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.2, 23.9, 26.8, 28.2, 36.0, 37.7, 62.6, 65.5, 78.5, 98.7, 121.9, 122.1 (d, J_{CF} = 4.2 Hz), 122.3 (d, J_{CF} = 2.4 Hz), 123.3 (d, J_{CF} = 4.1 Hz), 144.0 (d, J_{CF} = 5.2 Hz), 144.3 (d, J_{CF} = 5.3 Hz), 145.0 (d, J_{CF} = 12.3 Hz), 148.6 (d, J_{CF} = 13.1 Hz), 156.6 (d, J_{CF} = 257.0 Hz), 157.5 (d, J_{CF} = 258.2 Hz); HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{22}F_2N_3O$ $[M+H]^+$: 358.1725; Found: 358.1721.

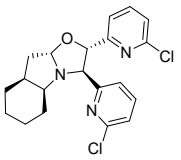


3e-1: Light yellow oil; 19.5 mg, yield 25%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.09-1.15 (m, 1H),

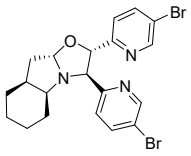
1.25-1.27 (m, 1H), 1.34-1.42 (m, 3H), 1.48-1.57 (m, 3H), 1.87-1.92 (m, 1H), 2.08-2.13 (m, 2H), 3.07 (d, J = 2.8 Hz, 1H), 4.39 (d, J = 6.0 Hz, 1H), 5.06 (d, J = 5.6 Hz, 1H), 5.24-5.26 (m, 1H), 7.43 (d, J = 8.4 Hz, 1H), 7.56-7.59 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.4, 24.0, 26.6, 28.5, 36.8, 37.9, 61.8, 71.7, 85.4, 98.1, 121.1, 121.2, 129.3, 129.7, 135.3, 135.4, 147.1, 147.2, 157.5, 159.6; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{22}Cl_2N_3O$ $[M+H]^+$: 390.1134 and 392.1105; Found: 390.1132 and 392.1108.



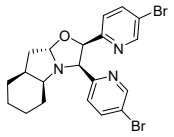
3e-2: Light yellow oil; 16.3 mg, yield 21%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.11-1.18 (m, 1H), 1.24-1.30 (m, 1H), 1.33-1.42 (m, 2H), 1.45-1.51 (m, 1H), 1.53-1.57 (m, 2H), 1.64-1.68 (m, 1H), 1.87-1.93 (m, 1H), 1.99-2.04 (m, 1H), 2.09-2.16 (m, 1H), 3.16 (d, J = 4.0 Hz, 1H), 4.59 (d, J = 6.4 Hz, 1H), 5.40 (d, J = 6.4 Hz, 1H), 5.72-5.75 (m, 1H), 6.83 (d, J = 8.4 Hz, 1H), 7.17-7.20 (m, 1H), 7.25-7.28 (m, 1H), 7.37-7.40 (m, 1H), 8.05 (d, J = 2.4 Hz, 1H), 8.28 (d, J = 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.1, 24.1, 27.6, 27.8, 37.1, 38.3, 62.4, 70.0, 79.1, 98.2, 121.0, 122.0, 128.6, 129.0, 134.4, 134.6, 145.9, 146.3, 155.8, 157.1; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{22}Cl_2N_3O$ $[M+H]^+$: 390.1134 and 392.1105; Found: 390.1134 and 392.1104.



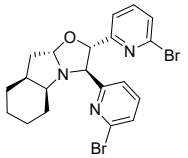
3f: Light yellow oil; 17.9 mg, yield 23%, 5:1 dr; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.10-1.16 (m, 1H), 1.24-1.28 (m, 1H), 1.34-1.43 (m, 3H), 1.50-1.56 (m, 3H), 1.85-1.89 (m, 1H), 2.08-2.16 (m, 2H), 3.17 (d, J = 2.8 Hz, 1H), 4.35 (d, J = 6.0 Hz, 1H), 5.02 (d, J = 5.6 Hz, 1H), 5.23-5.25 (m, 1H), 7.10-7.16 (m, 2H), 7.41 (d, J = 7.6 Hz, 1H), 7.52-7.59 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.4, 24.1, 26.5, 28.5, 36.6, 37.9, 61.7, 71.7, 85.3, 98.2, 118.7, 119.1, 121.5, 122.2, 138.1, 138.2, 149.5, 149.8, 159.9, 162.5; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{22}Cl_2N_3O$ $[M+H]^+$: 390.1134 and 392.1105; Found: 390.1137 and 392.1102.



3g-1: Light yellow solid; 20.0 mg, yield 21%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.10-1.16 (m, 1H), 1.25-1.27 (m, 1H), 1.34-1.42 (m, 3H), 1.48-1.54 (m, 3H), 1.88-1.92 (m, 1H), 2.09-2.15 (m, 2H), 3.07 (d, J = 3.2 Hz, 1H), 4.37 (d, J = 6.0 Hz, 1H), 5.05 (d, J = 6.0 Hz, 1H), 5.24-5.26 (m, 1H), 7.39 (d, J = 8.4 Hz, 1H), 7.53 (d, J = 8.4 Hz, 1H), 7.71-7.74 (m, 2H), 8.51 (d, J = 2.4 Hz, 1H), 8.57 (d, J = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.4, 24.1, 26.6, 28.5, 36.8, 37.9, 61.8, 71.7, 85.4, 98.1, 117.8, 118.4, 121.7, 138.2, 149.2, 149.4, 157.9, 160.0; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{22}Br_2N_3O$ $[M+H]^+$: 478.0124 and 480.0104; Found: 478.0123 and 480.0107.

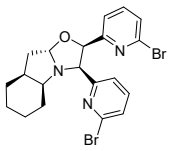


3g-2: Light yellow solid; 28.6 mg, yield 30%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.11-1.18 (m, 1H), 1.24-1.27 (m, 1H), 1.32-1.42 (m, 2H), 1.45-1.58 (m, 3H), 1.63-1.67 (m, 1H), 1.86-1.92 (m, 1H), 1.99-2.04 (m, 1H), 2.10-2.14 (m, 1H), 3.15 (d, J = 3.6 Hz, 1H), 4.56 (d, J = 6.4 Hz, 1H), 5.37 (d, J = 6.4 Hz, 1H), 5.71-5.74 (m, 1H), 6.78 (d, J = 8.4 Hz, 1H), 7.13 (d, J = 8.4 Hz, 1H), 7.41-7.43 (m, 1H), 7.52-7.54 (m, 1H), 8.16 (d, J = 2.0 Hz, 1H), 8.38 (d, J = 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.1, 24.1, 27.6, 27.8, 37.1, 38.3, 62.4, 70.0, 79.1, 98.2, 117.4, 117.6, 121.6, 122.6, 137.3, 137.5, 148.1, 148.5, 156.2, 157.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{22}Br_2N_3O$ $[M+H]^+$: 478.0124 and 480.0104; Found: 478.0127 and 480.0107.

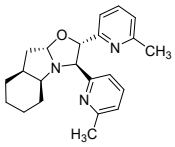


3h-1: Light yellow solid; 19.1 mg, yield 20%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.10-1.16 (m, 1H), 1.24-1.28 (m, 1H), 1.33-1.43 (m, 3H), 1.50-1.56 (m, 3H), 1.84-1.89 (m, 1H), 2.07-2.16 (m, 2H), 3.18 (d, J = 3.2 Hz, 1H), 4.35 (d, J = 5.6 Hz, 1H), 5.01 (d, J = 5.6 Hz, 1H), 5.21-5.23 (m, 1H), 7.25-7.31 (m, 2H), 7.43-7.48 (m, 3H), 7.56 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.2, 23.8, 26.3, 28.2, 36.3, 37.6, 61.4, 71.4, 85.1, 97.9, 118.7, 119.1, 125.0, 125.7, 137.6, 137.7,

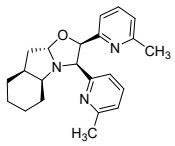
140.0, 140.3, 160.1, 162.7; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{22}Br_2N_3O$ $[M+H]^+$: 478.0124 and 480.0104; Found: 478.0127 and 480.0099.



3h-2: Light yellow solid; 30.5 mg, yield 32%; ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.12-1.17 (m, 1H), 1.25-1.31 (m, 1H), 1.33-1.50 (m, 3H), 1.52-1.58 (m, 2H), 1.65-1.68 (m, 1H), 1.89-2.02 (m, 2H), 2.09-2.15 (m, 1H), 3.12-3.14 (m, 1H), 4.64 (d, J = 6.4 Hz, 1H), 5.40 (d, J = 6.8 Hz, 1H), 5.71-5.74 (m, 1H), 6.86 (d, J = 7.6 Hz, 1H), 7.00-7.02 (m, 1H), 7.09-7.11 (m, 1H), 7.15-7.20 (m, 1H), 7.23-7.30 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 20.2, 25.2, 28.4, 29.0, 38.3, 39.2, 63.0, 70.8, 80.3, 99.5, 120.1, 121.0, 125.5, 126.2, 137.8, 138.1, 140.3, 140.7, 160.3, 161.3; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{22}Br_2N_3O$ $[M+H]^+$: 478.0124 and 480.0104; Found: 478.0126 and 480.0101.

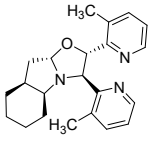


3i-1: Light yellow oil; 23.0 mg, yield 33%; ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.09-1.15 (m, 1H), 1.18-1.24 (m, 1H), 1.35-1.42 (m, 3H), 1.51-1.55 (m, 3H), 1.86-1.90 (m, 1H), 2.09-2.15 (m, 2H), 2.38 (s, 3H), 2.44 (s, 3H), 3.19 (d, J = 2.4 Hz, 1H), 4.36 (d, J = 6.0 Hz, 1H), 5.00 (d, J = 6.0 Hz, 1H), 5.27-5.29 (m, 1H), 6.90 (d, J = 7.2 Hz, 1H), 6.94 (d, J = 7.6 Hz, 1H), 7.31 (d, J = 7.6 Hz, 1H), 7.41-7.49 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.5, 23.4, 23.5, 24.1, 26.7, 28.5, 36.8, 38.0, 61.8, 72.4, 86.8, 97.9, 117.0, 117.4, 120.3, 121.0, 135.6, 135.7, 156.4, 156.7, 158.5, 161.1; HRMS (ESI-TOF) m/z: Calcd. for $C_{22}H_{28}N_3O$ $[M+H]^+$: 350.2227; Found: 350.2228.

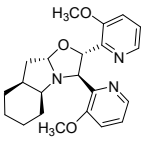


3i-2: Light yellow oil; 28.6 mg, yield 41%; ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.11-1.18 (m, 1H), 1.24-1.26 (m, 1H), 1.35-1.48 (m, 3H), 1.55 (d, J = 12.0 Hz, 2H), 1.69-1.71 (m, 1H), 1.89-1.94 (m, 1H), 1.97-2.02 (m, 1H), 2.06 (s, 3H), 2.09-2.13 (m, 1H), 2.36 (s, 3H), 3.19 (d, J = 1.6 Hz, 1H), 4.61 (d, J = 6.4 Hz, 1H), 5.41 (d, J = 6.4 Hz, 1H), 5.74-5.77 (m, 1H), 5.52 (d, J = 7.6 Hz, 1H),

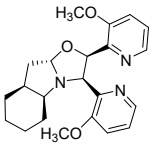
6.63 (d, J = 7.6 Hz, 1H), 6.90 (d, J = 7.6 Hz, 1H), 7.05-7.08 (m, 2H), 7.25-7.29 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 20.2, 23.9, 24.3, 25.3, 28.6, 29.0, 38.2, 39.5, 63.2, 71.6, 81.2, 99.2, 118.1, 118.9, 120.3, 120.9, 135.3, 135.8, 156.2, 156.7, 158.3, 159.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{22}H_{28}N_3O$ $[M+H]^+$: 350.2227; Found: 350.2229.



3j: Light yellow oil; 16.1 mg, yield 23%, 12:1 dr; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.07-1.10 (m, 2H), 1.26-1.32 (m, 1H), 1.40-1.45 (m, 5H), 1.84-1.90 (m, 1H), 2.01 (s, 3H), 2.06-2.09 (m, 1H), 2.16-2.19 (m, 4H), 3.24-3.27 (m, 1H), 4.84 (d, J = 7.6 Hz, 1H), 5.48 (d, J = 7.6 Hz, 1H), 5.53-5.55 (m, 1H), 6.91-6.94 (m, 1H), 6.97-7.00 (m, 1H), 7.21-7.27 (m, 2H), 8.39-8.43 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 17.2, 17.7, 19.5, 23.7, 27.5, 28.0, 36.0, 37.8, 63.7, 68.8, 83.8, 98.5, 120.5, 121.8, 130.2, 131.6, 136.9, 137.1, 145.9, 146.3, 153.9, 158.5; HRMS (ESI-TOF) m/z: Calcd. for $C_{22}H_{28}N_3O$ $[M+H]^+$: 350.2227; Found: 350.2228.

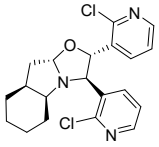


3k-1: Light yellow oil; 25.9 mg, yield 34%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.09-1.17 (m, 1H), 1.27-1.31 (m, 1H), 1.37-1.65 (m, 6H), 1.80-1.84 (m, 1H), 2.08-2.16 (m, 2H), 3.40-3.43 (m, 1H), 3.66 (s, 3H), 3.80 (s, 3H), 4.45 (d, J = 5.6 Hz, 1H), 4.99 (d, J = 5.6 Hz, 1H), 5.17-5.19 (m, 1H), 6.47 (d, J = 8.4 Hz, 1H), 6.54 (d, J = 8.8 Hz, 1H), 6.97 (d, J = 7.2 Hz, 1H), 7.16 (d, J = 7.6 Hz, 1H), 7.41-7.46 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.6, 24.3, 26.5, 28.8, 36.5, 37.7, 51.9, 52.1, 60.7, 70.8, 85.6, 98.0, 107.5, 108.7, 112.0, 114.0, 137.7, 137.8, 156.8, 159.8, 162.4, 162.8; HRMS (ESI-TOF) m/z: Calcd. for $C_{22}H_{28}N_3O_3$ $[M+H]^+$: 382.2125; Found: 382.2126.

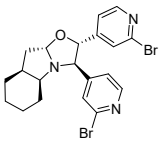


3k-2: Light yellow oil; 16.8 mg, yield 22%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.15 (m, 1H), 1.25-1.28 (m, 1H), 1.36-1.40 (m, 1H), 1.47-1.58 (m, 4H), 1.70-1.73 (m, 1H), 1.92-1.96 (m, 2H), 2.09-

2.14 (m, 1H), 3.15-3.16 (m, 1H), 3.43 (s, 3H), 3.69 (s, 3H), 4.50 (d, J = 6.8 Hz, 1H), 5.31 (d, J = 6.8 Hz, 1H), 5.74-5.77 (m, 1H), 6.25 (d, J = 8.0 Hz, 1H), 6.30 (d, J = 8.0 Hz, 1H), 6.50 (d, J = 7.6 Hz, 1H), 6.89 (d, J = 6.8 Hz, 1H), 7.14-7.17 (m, 1H), 7.25-7.29 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.3, 24.2, 27.5, 28.2, 37.3, 38.2, 51.7, 52.1, 61.9, 69.8, 79.9, 98.0, 106.8, 107.1, 113.2, 113.6, 137.0, 137.1, 156.1, 157.1, 161.3, 161.8; HRMS (ESI-TOF) m/z: Calcd. for $C_{22}H_{28}N_3O_3$ $[M+H]^+$: 382.2125; Found: 382.2127.



3l: Light yellow oil; 33.5 mg, 43% yield, 6:1 dr; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.11-1.22 (m, 3H), 1.32-1.38 (m, 3H), 1.50-1.59 (m, 2H), 1.96-2.01 (m, 1H), 2.07-2.13 (m, 1H), 2.19-2.24 (m, 1H), 3.14-3.17 (m, 1H), 4.18 (d, J = 7.6 Hz, 1H), 5.02 (d, J = 8.0 Hz, 1H), 5.36-5.39 (m, 1H), 7.20-7.25 (m, 2H), 7.93-7.95 (m, 1H), 8.06-8.09 (m, 1H), 8.22-8.28 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 18.9, 24.0, 27.4, 28.0, 36.7, 38.3, 63.2, 64.6, 73.3, 97.3, 120.6, 121.2, 130.0, 132.8, 135.9, 137.8, 147.0, 147.7, 149.1, 149.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{22}Cl_2N_3O$ $[M+H]^+$: 390.1134 and 392.1105; Found: 390.1137 and 392.1106.



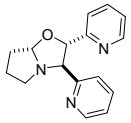
3m: Light yellow oil; 48.7 mg, 51% yield, 12:1 dr; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.18-1.22 (m, 2H), 1.25-1.31 (m, 2H), 1.35-1.42 (m, 2H), 1.56-1.57 (m, 2H), 1.96-2.01 (m, 1H), 2.08-2.14 (m, 1H), 2.18-2.25 (m, 1H), 3.05-3.07 (m, 1H), 3.61 (d, J = 7.6 Hz, 1H), 4.45 (d, J = 7.6 Hz, 1H), 5.27-5.30 (m, 1H), 6.99-7.03 (m, 2H), 7.39-7.42 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 20.3, 24.6, 27.8, 29.2, 37.2, 39.4, 65.1, 74.5, 86.9, 99.5, 120.4, 121.1, 125.3, 126.1, 142.8, 142.9, 150.4, 150.5, 150.6, 153.6; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{22}Br_2N_3O$ $[M+H]^+$: 478.0124 and 480.0104; Found: 478.0121 and 480.0100.

4. The synthesis of pyrrolidine-bipyridines 4

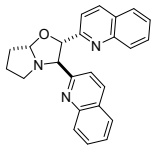
In a sealed tube equipped with a magnetic stirring bar, a mixture of *L*-proline (0.6 mmol) and

pyridinecarboxaldehyde **2** (0.4 mmol) in 2.0 mL of toluene was stirred at 80 °C for 1 h, and then was directly loaded onto a silica gel and purified by flash chromatography to give the desired product **4**, using hexane/EtOAc (6/1, v/v) as the eluent.

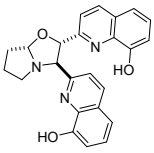
5. Characterization data of compounds 4



4a: Light yellow oil; 21.9 mg, yield 41%, 10:1 dr; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.74-1.80 (m, 1H), 1.89-1.99 (m, 1H), 2.09-2.13 (m, 2H), 2.79-2.85 (m, 1H), 3.11-3.16 (m, 1H), 4.49 (d, J = 6.0 Hz, 1H), 5.17 (d, J = 5.6 Hz, 1H), 5.30 (d, J = 1.2 Hz, 1H), 7.04-7.08 (m, 2H), 7.39-7.46 (m, 2H), 7.53-7.59 (m, 2H), 8.47-8.51 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 21.4, 28.6, 52.6, 73.7, 83.5, 97.0, 118.3, 119.5, 119.6, 119.9, 134.1, 134.2, 146.8, 147.1, 157.8, 159.1; HRMS (ESI-TOF) m/z: Calcd. for $C_{16}H_{18}N_3O$ $[M+H]^+$: 268.1444; Found: 268.1445.

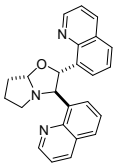


4b: Light yellow oil; 52.1 mg, yield 71%, 19:1 dr; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.78-1.86 (m, 1H), 1.94-2.04 (m, 1H), 2.12-2.22 (m, 2H), 2.88-2.95 (m, 1H), 3.18-3.24 (m, 1H), 4.83 (d, J = 5.6 Hz, 1H), 5.43-5.44 (m, 1H), 5.54 (d, J = 6.0 Hz, 1H), 7.38-7.43 (m, 2H), 7.55-7.58 (m, 2H), 7.66-7.72 (m, 4H), 7.91-7.96 (m, 2H), 8.07-8.10 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 22.9, 30.2, 54.3, 75.7, 85.0, 98.8, 117.8, 119.5, 125.1, 125.2, 126.4, 126.5, 126.6, 128.2, 128.3, 128.4, 128.5, 135.7, 135.8, 146.6, 146.7, 159.7, 160.8; HRMS (ESI-TOF) m/z: Calcd. for $C_{24}H_{22}N_3O$ $[M+H]^+$: 368.1757; Found: 368.1754.

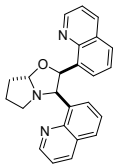


4c: Light yellow oil; 48.7 mg, yield 61%, 15:1 dr; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.79-1.88 (m, 1H), 1.96-2.06 (m, 1H), 2.13-2.19 (m, 2H), 2.86-2.92 (m, 1H), 3.21-3.26 (m, 1H), 4.67 (d, J = 6.0 Hz, 1H), 5.31-5.32 (m, 1H), 5.49 (d, J = 6.0 Hz, 1H), 7.05-7.08 (m, 2H), 7.21-7.24 (m, 2H), 7.30-

7.35 (m, 2H), 7.63-7.67 (m, 2H), 7.90 (br s, 2H), 8.07-8.11 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 24.1, 31.1, 55.8, 76.8, 86.0, 99.7, 110.3, 110.4, 117.7, 117.8, 120.9, 127.5, 127.7, 137.0, 137.2, 137.5, 137.6, 152.0, 152.1, 158.5, 159.9; HRMS (ESI-TOF) m/z: Calcd. for $C_{24}H_{22}N_3O_3$ $[M+H]^+$: 400.1656; Found: 400.1656.

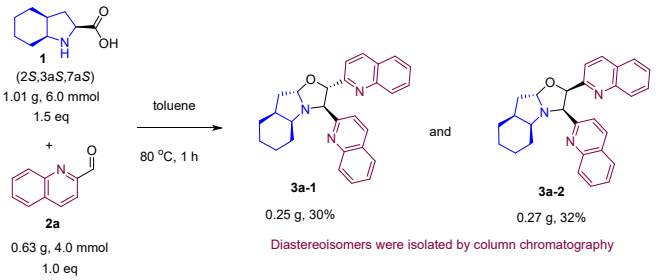


4d-1: Light yellow oil; 27.2 mg, yield 37%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.850-1.87 (m, 1H), 2.13-2.27 (m, 3H), 3.11-3.22 (m, 2H), 5.53-5.55 (m, 2H), 6.21 (d, J = 7.6 Hz, 1H), 6.92-6.97 (m, 2H), 7.51-7.60 (m, 4H), 7.84-7.88 (m, 2H), 7.99-8.00 (m, 1H), 8.07-8.08 (m, 1H), 8.15 (d, J = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 21.8, 29.2, 53.7, 69.1, 80.0, 96.3, 117.8, 117.9, 124.1, 124.2, 124.3, 133.1, 133.2, 136.6, 138.8, 143.8, 144.1, 145.7, 145.9; HRMS (ESI-TOF) m/z: Calcd. for $C_{24}H_{22}N_3O$ $[M+H]^+$: 368.1757; Found: 368.1760.



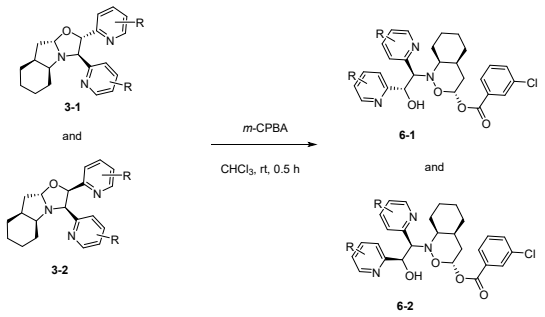
4d-2: Light yellow oil; 29.4 mg, yield 40%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.84-1.89 (m, 1H), 1.97-2.08 (m, 3H), 2.27-2.33 (m, 1H), 3.31-3.37 (m, 1H), 3.48-3.52 (m, 1H), 5.79-5.81 (m, 1H), 6.17 (d, J = 6.0 Hz, 1H), 6.75-6.80 (m, 2H), 7.07-7.12 (m, 2H), 7.18-7.21 (m, 1H), 7.29-7.36 (m, 2H), 7.62-7.68 (m, 2H), 7.73-7.76 (m, 1H), 7.86-7.88 (m, 1H), 8.85-8.86 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 23.0, 32.1, 54.6, 65.8, 73.7, 96.9, 118.6, 119.1, 123.7, 124.6, 124.8, 125.0, 125.4, 125.8, 125.9, 126.8, 134.0, 134.3, 137.6, 144.4, 145.0, 146.1, 147.5; HRMS (ESI-TOF) m/z: Calcd. for $C_{24}H_{22}N_3O$ $[M+H]^+$: 368.1757; Found: 368.1758.

6. Preparative scale synthesis of two diastereoisomers 3a-1 and 3a-2



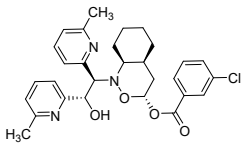
In a sealed tube equipped with a magnetic stirring bar, a mixture of optically pure perhydroindole-2-carboxylic acid **1** (1.01 g, 6.0 mmol, 1.5 eq) and pyridinecarboxaldehyde **2** (0.63 g, 4.0 mmol, 1.0 eq) in 2.0 mL of toluene was stirred at 80 °C for 1 h, and then was directly loaded onto a silica gel and purified by flash chromatography (hexane/EtOAc, 8/1, v/v) to give the desired diastereoisomers **3a-1** (0.25 g, 30%) and **3a-2** (0.27 g, 32%) respectively.

7. The further chemical transformations of the compounds 3 into compounds 6

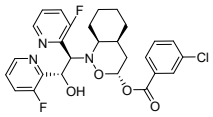


In a sealed tube equipped with a magnetic stirring bar, a mixture of 0.2 mmol of compound **3**, *m*-CPBA (2.0 eq) in 2.0 mL of $CHCl_3$ was stirred at rt for 0.5 h, and then was directly loaded onto a silica gel and purified by flash chromatography to give the desired product **6**, using hexane/EtOAc (1/2, v/v) as the eluent.

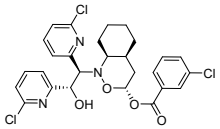
8. Characterization data of compounds 6



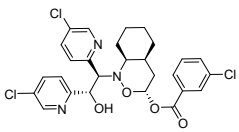
6a-1: Light yellow solid; 64.6 mg, yield 62%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.16-1.21 (m, 4H), 1.28-1.35 (m, 1H), 1.46-1.52 (m, 4H), 2.05-2.13 (m, 1H), 2.15 (s, 3H), 2.35 (s, 3H), 2.59-2.65 (m, 1H), 3.21-3.24 (m, 1H), 4.33 (d, J = 6.8 Hz, 1H), 4.54 (br s, 1H), 4.90 (d, J = 6.8 Hz, 1H), 6.32 (d, J = 4.0 Hz, 1H), 6.79-6.82 (m, 3H), 7.20-7.27 (m, 3H), 7.30-7.34 (m, 1H), 7.44-7.47 (m, 1H), 7.91-7.93 (m, 1H), 7.97 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.9, 23.7, 24.2, 24.7, 27.5, 29.7, 30.2, 30.3, 61.4, 73.3, 74.4, 94.0, 119.1, 121.7, 122.0, 122.3, 128.0, 129.8, 131.9, 133.2, 134.6, 136.0, 136.1, 156.5, 157.2, 158.0, 158.8, 164.0; HRMS (ESI-TOF) m/z: Calcd. for $C_{29}H_{33}ClN_3O_4$ $[M+H]^+$: 522.2154 and 524.2125; Found: 522.2151 and 524.2127.



6b-1: Light yellow solid; 64.5 mg, yield 61%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.05-1.13 (m, 1H), 1.18-1.27 (m, 3H), 1.32-1.36 (m, 1H), 1.50-1.59 (m, 4H), 2.09-2.17 (m, 1H), 2.65-2.68 (m, 1H), 3.33-3.37 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 18.7, 19.1, 23.9, 26.5, 29.2, 29.6, 61.2, 64.6, 65.2, 94.1, 121.5 (d, J_{CF} = 20.3 Hz), 121.9 (d, J_{CF} = 20.2 Hz), 122.8 (d, J_{CF} = 4.3 Hz), 123.0 (d, J_{CF} = 4.1 Hz), 126.9, 128.8 (d, J_{CF} = 5.1 Hz), 130.9, 132.1, 133.5, 143.6 (d, J_{CF} = 5.1 Hz), 144.1 (d, J_{CF} = 5.0 Hz), 145.1 (d, J_{CF} = 13.4 Hz), 145.7 (d, J_{CF} = 13.1 Hz), 156.2 (d, J_{CF} = 259.2 Hz), 157.7 (d, J_{CF} = 257.4 Hz), 163.1; HRMS (ESI-TOF) m/z: Calcd. for $C_{27}H_{27}ClF_2N_3O_4$ $[M+H]^+$: 530.1653 and 532.1623; Found: 530.1655 and 532.1620.

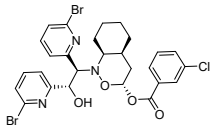


6c-1: Light yellow solid; 71.8 mg, yield 64%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.96-1.03 (m, 1H), 1.10-1.22 (m, 2H), 1.31-1.41 (m, 2H), 1.51-1.56 (m, 4H), 2.08-2.16 (m, 1H), 2.63-2.67 (m, 1H), 3.14-3.19 (m, 1H), 4.14 (d, J = 8.4 Hz, 1H), 4.85 (d, J = 8.0 Hz, 1H), 6.39 (d, J = 3.6 Hz, 1H), 7.00 (d, J = 8.0 Hz, 1H), 7.04-7.08 (m, 2H), 7.32-7.37 (m, 2H), 7.44-7.47 (m, 2H), 7.50 (d, J = 7.6 Hz, 1H), 7.90-7.94 (m, 1H), 7.99-8.01 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 18.7, 20.0, 23.7, 26.4, 29.1, 29.3, 61.2, 72.9, 73.4, 93.1, 119.3, 122.0, 122.2, 126.9, 127.3, 128.8, 128.9, 129.2, 132.4, 132.7, 137.4, 137.8, 148.6, 149.2, 157.7, 159.3, 163.0; HRMS (ESI-TOF) m/z: Calcd. for $C_{27}H_{27}Cl_3N_3O_4$ $[M+H]^+$: 562.1062 and 564.1032; Found: 562.1063 and 564.1037.

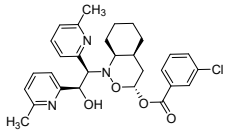


6d-1: Light yellow solid; 67.3 mg, yield 60%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.96-1.03 (m, 2H), 1.16-1.24 (m, 1H), 1.31-1.35 (m, 2H), 1.50-1.57 (m, 4H), 2.07-2.15 (m, 1H), 2.64-2.67 (m, 1H), 3.14-3.19 (m, 1H), 4.23 (d, J = 8.4 Hz, 1H), 4.85 (d, J = 8.4 Hz, 1H), 6.40 (d, J = 4.0 Hz, 1H), 7.00 (d, J = 8.4 Hz, 1H), 7.31-7.38 (m, 2H), 7.45-7.49 (m, 3H), 7.93 (d, J = 8.0 Hz, 1H), 8.00-8.01 (m, 1H), 8.12 (d, J = 2.0 Hz, 1H), 8.26 (d, J = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 18.6,

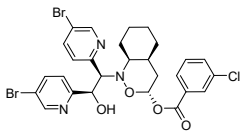
19.8, 23.7, 26.4, 29.1, 29.4, 61.3, 72.8, 73.3, 93.2, 122.1, 125.2, 126.9, 128.8, 128.9, 129.8, 130.1, 130.6, 132.4, 133.7, 134.6, 134.9, 146.2, 146.7, 154.9, 156.4, 163.0; HRMS (ESI-TOF) m/z: Calcd. for $C_{27}H_{27}Cl_3N_3O_4$ $[M+H]^+$: 562.1062 and 564.1032; Found: 562.1065 and 564.1026.



6e-1: Light yellow solid; 73.9 mg, yield 57%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.96-1.03 (m, 1H), 1.12-1.22 (m, 2H), 1.30-1.42 (m, 2H), 1.51-1.55 (m, 4H), 2.07-2.15 (m, 1H), 2.63-2.66 (m, 1H), 3.13-3.18 (m, 1H), 4.12 (d, J = 8.0 Hz, 1H), 4.84 (d, J = 8.0 Hz, 1H), 6.38 (d, J = 3.6 Hz, 1H), 7.11-7.15 (m, 2H), 7.20 (d, J = 8.0 Hz, 1H), 7.25 (d, J = 8.0 Hz, 1H), 7.30-7.35 (m, 2H), 7.44-7.48 (m, 1H), 7.53 (d, J = 7.6 Hz, 1H), 7.91-7.94 (m, 1H), 7.98-7.99 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 18.7, 20.0, 23.7, 26.5, 29.1, 29.3, 61.1, 72.9, 73.3, 93.1, 119.5, 123.7, 125.8, 126.0, 126.9, 128.8, 128.9, 130.6, 132.4, 133.7, 137.0, 137.5, 139.1, 139.7, 158.3, 159.9, 163.0; HRMS (ESI-TOF) m/z: Calcd. for $C_{27}H_{27}Br_2ClN_3O_4$ $[M+H]^+$: 650.0051 and 652.0031; Found: 650.0051 and 652.0027.

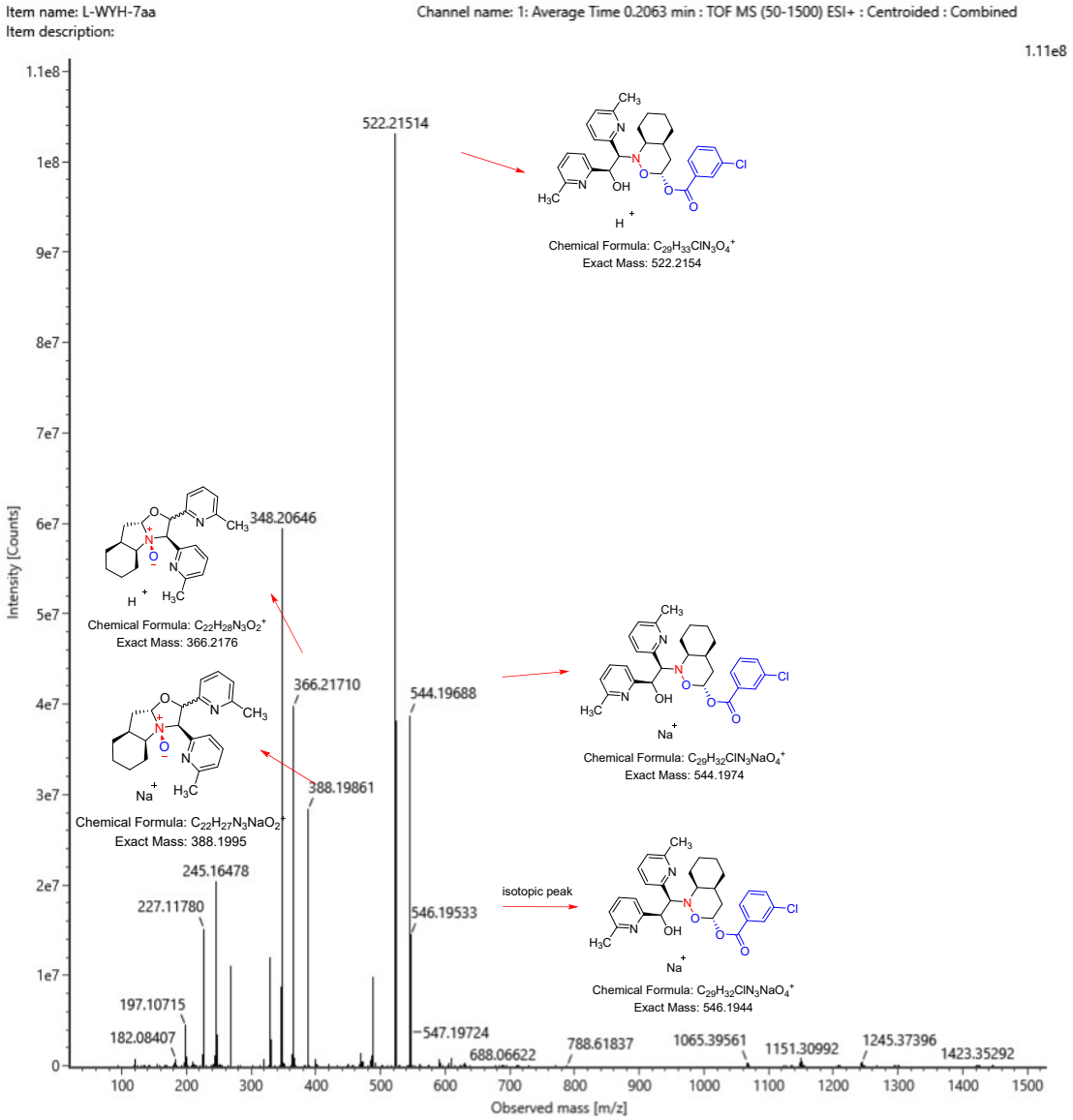


6a-2: Light yellow solid; 61.5 mg, yield 59%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.25-1.37 (m, 2H), 1.43-1.47 (m, 2H), 1.56-1.59 (m, 1H), 1.63-1.69 (m, 1H), 1.78 (s, 3H), 1.79-1.82 (m, 1H), 1.84-1.92 (m, 1H), 2.01-2.14 (m, 2H), 2.36 (s, 3H), 2.72-2.74 (m, 1H), 3.60-3.63 (m, 1H), 4.37 (d, J = 2.8 Hz, 1H), 5.19 (d, J = 2.8 Hz, 1H), 6.03 (d, J = 4.0 Hz, 1H), 6.63 (d, J = 7.6 Hz, 1H), 6.73 (d, J = 7.6 Hz, 1H), 6.78 (d, J = 7.6 Hz, 1H), 7.08-7.12 (m, 1H), 7.17-7.21 (m, 1H), 7.29-7.34 (m, 1H), 7.44-7.47 (m, 1H), 7.77-7.80 (m, 1H), 7.82-7.83 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 17.2, 19.3, 22.1, 22.9, 23.9, 26.4, 28.6, 29.3, 56.9, 66.7, 71.9, 92.3, 116.9, 120.3, 120.6, 121.4, 127.0, 128.5, 128.8, 131.3, 131.7, 133.3, 135.1, 135.4, 155.0, 155.6, 157.1, 159.7, 162.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{29}H_{32}ClN_3NaO_4$ $[M+Na]^+$: 544.1974 and 546.1944; Found: 544.1969 and 546.1953.

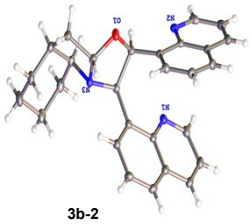


6f-2: Light yellow solid; 82.9 mg, yield 64%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.25-1.38 (m, 2H), 1.45-1.52 (m, 2H), 1.58-1.69 (m, 2H), 1.81-1.92 (m, 3H), 2.06-2.14 (m, 1H), 2.69-2.71 (m, 1H), 3.55-3.59 (m, 1H), 4.00 (d, J = 2.8 Hz, 1H), 5.15 (d, J = 2.8 Hz, 1H), 6.02 (d, J = 4.0 Hz, 1H), 6.73 (d, J = 8.4 Hz, 1H), 6.96 (d, J = 8.4 Hz, 1H), 7.33-7.37 (m, 2H), 7.46-7.52 (m, 2H), 7.65 (d, J = 2.0 Hz, 1H), 7.75-7.79 (m, 1H), 7.85-7.86 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 17.5, 19.3, 23.8, 26.4, 28.7, 29.2, 57.0, 66.0, 71.5, 92.3, 117.8, 118.2, 121.2, 125.6, 127.1, 128.6, 128.9, 131.0, 132.0, 133.4, 137.5, 138.0, 147.7, 148.3, 156.2, 158.8, 162.5; HRMS (ESI-TOF) m/z: Calcd. for $C_{27}H_{27}Br_2ClN_3O_4$ $[M+H]^+$: 650.0051 and 652.0031; Found: 650.0053 and 652.0035.

9. Figure S1: reaction solution detected by ESI-MS analysis.

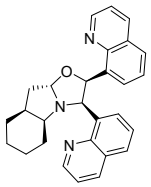


10. X-ray crystal data for compounds 3b-2, 3g-2, 4d-1 and 6c-1



3b-2

CCDC 2258768

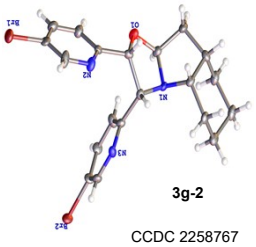


3b-2

Table S1 Crystal data and structure refinement for 3b-2

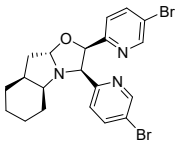
Identification code	**3b-2**
Empirical formula	$C_{28}H_{27}N_3O$
Formula weight	421.52
Temperature/K	99.95(19)
Crystal system	monoclinic
Space group	$P2_1$
a/Å, b/Å, c/Å	7.5239(7), 9.0245(8), 16.1748(14)
α/°, β/°, γ/°,	90, 90.02(2), 90
Volume/Å^3	1098.26(17)
Z	2
ρ_{calc}g/cm^3	1.275
μ/mm^{-1}	0.611
F(000)	448.0
Radiation	Cu Kα (λ = 1.54184)
Crystal size/mm^3	0.14 × 0.12 × 0.11
2Θ range for data collection/°	5.464 to 144.366
Index ranges	-9 ≤ h ≤ 8, -10 ≤ k ≤ 10, -19 ≤ l ≤ 14
Reflections collected	11455
Independent reflections	3946 [R_{int} = 0.0312, R_{sigma} = 0.0302]
Data/restraints/parameters	3946/1/289
Goodness-of-fit on F^2	1.077
Final R indexes [I>=2σ (I)]	R_1 = 0.0331, wR_2 = 0.0871
Final R indexes [all data]	R_1 = 0.0344, wR_2 = 0.0880
Largest diff. peak/hole / e Å^{-3}	0.39/-0.23
Flack parameter	-0.03(12)/-0.01(12)

Crystal Data for $C_{28}H_{27}N_3O$ (M =421.52 g/mol): monoclinic, space group $P2_1$ (no. 4), a = 7.5239(7) Å, b = 9.0245(8) Å, c = 16.1748(14) Å, β = 90.02(2)°, V = 1098.26(17) Å^3, Z = 2, T = 99.95(19) K, μ(Cu Kα) = 0.611 mm^{-1}, *Dcalc* = 1.275 g/cm^3, 11455 reflections measured (5.464° ≤ 2Θ ≤ 144.366°), 3946 unique (R_{int} = 0.0312, R_{sigma} = 0.0302) which were used in all calculations. The final R_1 was 0.0331 (I > 2σ(I)) and wR_2 was 0.0880 (all data).



3g-2

CCDC 2258767

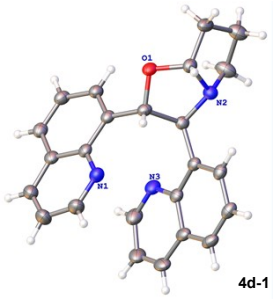


3g-2

Table S2 Crystal data and structure refinement for 3g-2

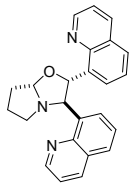
Identification code	**3g-2**
Empirical formula	$C_{20}H_{21}Br_2N_3O$
Formula weight	479.22
Temperature/K	169.99(10)
Crystal system	monoclinic
Space group	$P2_1$
a/Å, b/Å, c/Å	6.02540(14), 17.1860(4), 9.4103(2)
α/°, β/°, γ/°,	90, 99.742(2), 90
Volume/Å^3	960.41(4)
Z	2
ρ_{calc}g/cm^3	1.657
μ/mm^{-1}	5.463
F(000)	480.0
Radiation	Cu Kα (λ = 1.54184)
Crystal size/mm^3	0.16 × 0.13 × 0.12
2Θ range for data collection/°	9.536 to 147.002
Index ranges	$-7 \le h \le 6$, $-20 \le k \le 14$, $-11 \le l \le 11$
Reflections collected	4451
Independent reflections	2900 [R_{int} = 0.0706, R_{sigma} = 0.0603]
Data/restraints/parameters	2900/1/235
Goodness-of-fit on F^2	1.186
Final R indexes [I>=2σ (I)]	R_1 = 0.0868, wR_2 = 0.2504
Final R indexes [all data]	R_1 = 0.0883, wR_2 = 0.2544
Largest diff. peak/hole / e Å^{-3}	1.71/-2.42
Flack parameter	-0.09(5)/-0.053(15)

Crystal Data for $C_{20}H_{21}Br_2N_3O$ (M =479.22 g/mol): monoclinic, space group $P2_1$ (no. 4), a = 6.02540(14) Å, b = 17.1860(4) Å, c = 9.4103(2) Å, β = 99.742(2)°, V = 960.41(4) Å^3, Z = 2, T = 169.99(10) K, μ(Cu Kα) = 5.463 mm^{-1}, *Dcalc* = 1.657 g/cm^3, 4451 reflections measured (9.536° ≤ 2Θ ≤ 147.002°), 2900 unique (R_{int} = 0.0706, R_{sigma} = 0.0603) which were used in all calculations. The final R_1 was 0.0868 (I > 2σ(I)) and wR_2 was 0.2544 (all data).



4d-1

CCDC 2258770

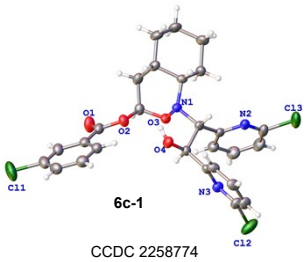


4d-1

Table S3 Crystal data and structure refinement for 4d-1

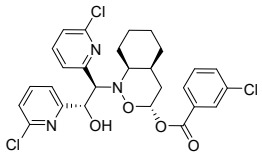
Identification code	**4d-1**
Empirical formula	$C_{24}H_{21}N_3O$
Formula weight	367.44
Temperature/K	170.00(10)
Crystal system	orthorhombic
Space group	Pccn
a/Å, b/Å, c/Å	21.3764(18), 11.6397(10), 15.2354(10)
α/°, β/°, γ/°,	90, 90, 90
Volume/Å^3	3790.8(5)
Z	8
ρ_{calc}g/cm^3	1.288
μ/mm^{-1}	0.632
F(000)	1552.0
Radiation	Cu Kα (λ = 1.54184)
Crystal size/mm^3	0.13 × 0.12 × 0.11
2Θ range for data collection/°	8.272 to 144.2
Index ranges	-23 ≤ h ≤ 26, -13 ≤ k ≤ 11, -18 ≤ l ≤ 15
Reflections collected	18443
Independent reflections	3680 [R_{int} = 0.1115, R_{sigma} = 0.1137]
Data/restraints/parameters	3680/0/253
Goodness-of-fit on F^2	1.037
Final R indexes [I>=2σ (I)]	R_1 = 0.1003, wR_2 = 0.2458
Final R indexes [all data]	R_1 = 0.1320, wR_2 = 0.2740
Largest diff. peak/hole / e Å^{-3}	0.46/-0.27

Crystal Data for $C_{24}H_{21}N_3O$ (*M* =367.44 g/mol): orthorhombic, space group Pccn (no. 56), *a* = 21.3764(18) Å, *b* = 11.6397(10) Å, *c* = 15.2354(10) Å, *V* = 3790.8(5) Å^3, *Z* = 8, *T* = 170.00(10) K, μ(Cu Kα) = 0.632 mm^{-1}, *Dcalc* = 1.288 g/cm^3, 18443 reflections measured (8.272° ≤ 2Θ ≤ 144.2°), 3680 unique (R_{int} = 0.1115, R_{sigma} = 0.1137) which were used in all calculations. The final R_1 was 0.1003 (I > 2σ(I)) and wR_2 was 0.2740 (all data).



6c-1

CCDC 2258774



6c-1

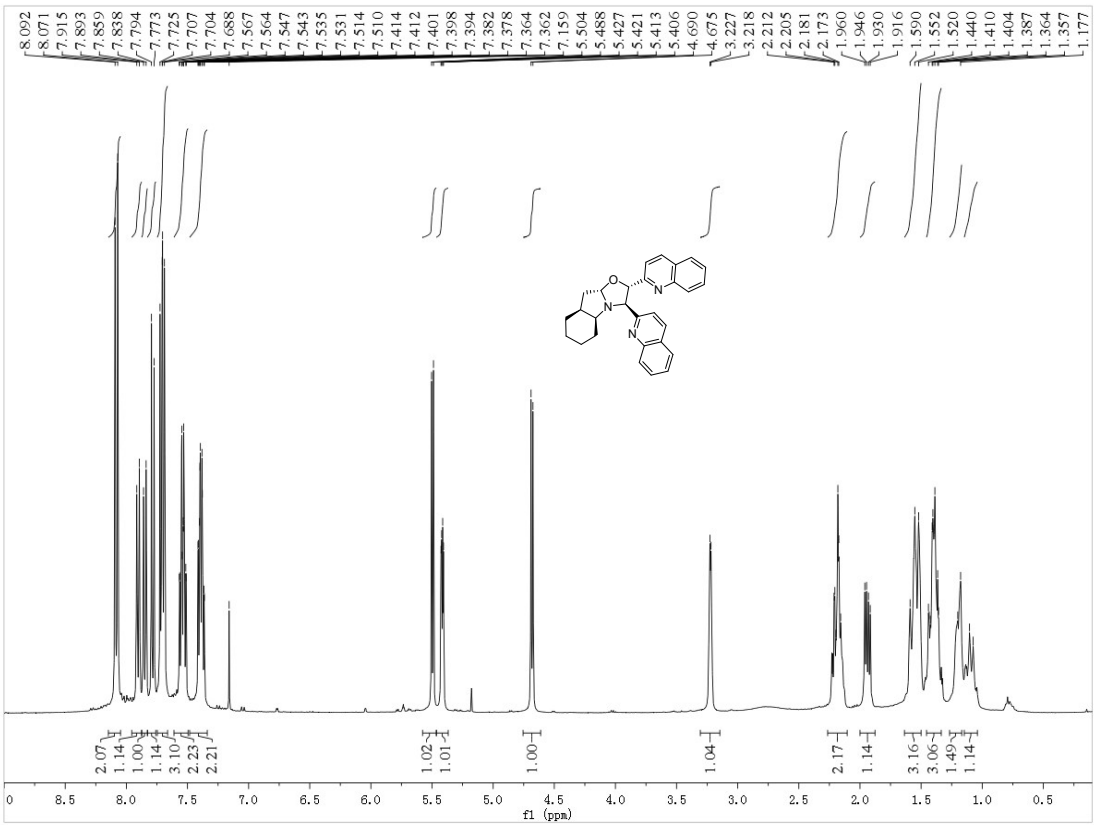
Table S4 Crystal data and structure refinement for 6c-1

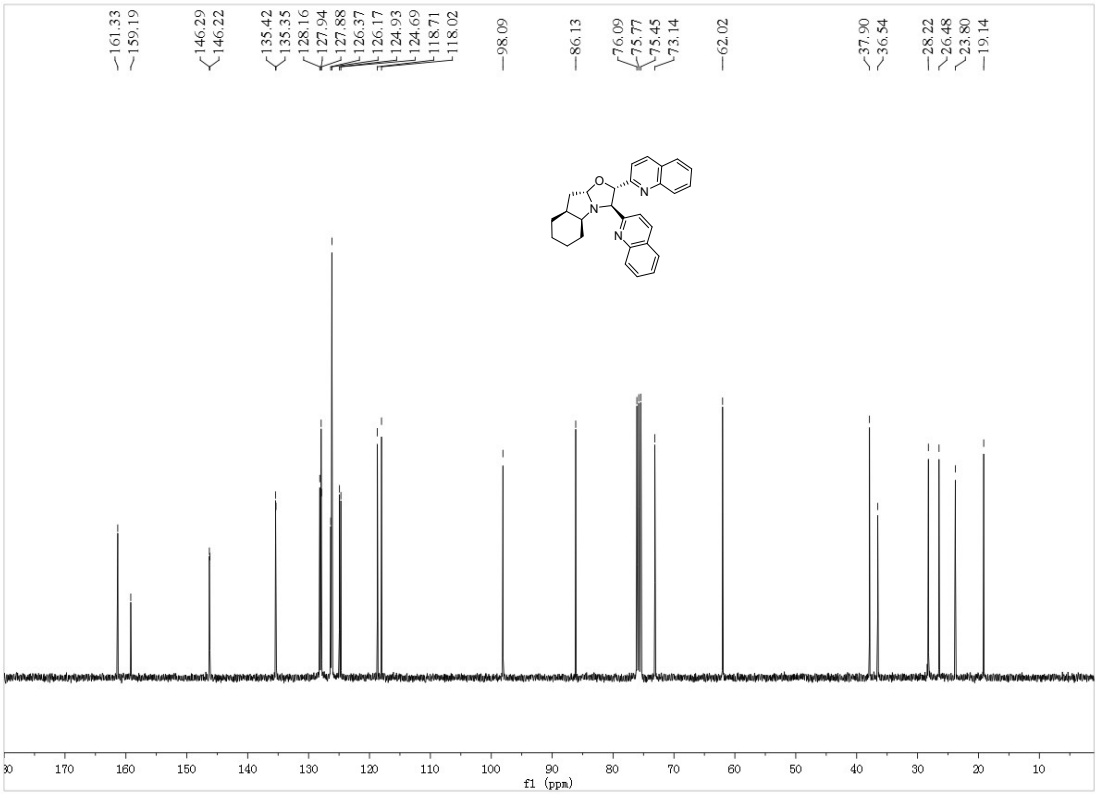
Identification code	**6c-1**
Empirical formula	$C_{27}H_{26}Cl_3N_3O_4$
Formula weight	562.86
Temperature/K	169.98(10)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å, b/Å, c/Å	6.0111(2), 12.8027(4), 34.2524(12)
α/°, β/°, γ/°,	90, 90, 90
Volume/Å^3	2636.01(15)
Z	4
ρ_{calc}g/cm^3	1.418
μ/mm^{-1}	3.475
F(000)	1168.0
Radiation	Cu Kα (λ = 1.54184)
Crystal size/mm^3	0.13 × 0.1 × 0.08
2Θ range for data collection/°	5.16 to 147.44
Index ranges	$-5 \le h \le 7$, $-15 \le k \le 15$, $-42 \le l \le 41$
Reflections collected	10170
Independent reflections	5202 [R_{int} = 0.0374, R_{sigma} = 0.0540]
Data/restraints/parameters	5202/0/336
Goodness-of-fit on F^2	1.027
Final R indexes [I>=2σ (I)]	R_1 = 0.0424, wR_2 = 0.1013
Final R indexes [all data]	R_1 = 0.0481, wR_2 = 0.1060
Largest diff. peak/hole / e Å^{-3}	0.21/-0.21
Flack parameter	-0.004(11)/-0.001(10)

Crystal Data for $C_{27}H_{26}Cl_3N_3O_4$ (*M* =562.86 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), *a* = 6.0111(2) Å, *b* = 12.8027(4) Å, *c* = 34.2524(12) Å, *V* = 2636.01(15) Å^3, *Z* = 4, *T* = 169.98(10) K, μ(Cu Kα) = 3.475 mm^{-1}, *Dcalc* = 1.418 g/cm^3, 10170 reflections measured (5.16° ≤ 2Θ ≤ 147.44°), 5202 unique (R_{int} = 0.0374, R_{sigma} = 0.0540) which were used in all calculations. The final R_1 was 0.0424 (I > 2σ(I)) and wR_2 was 0.1060 (all data).

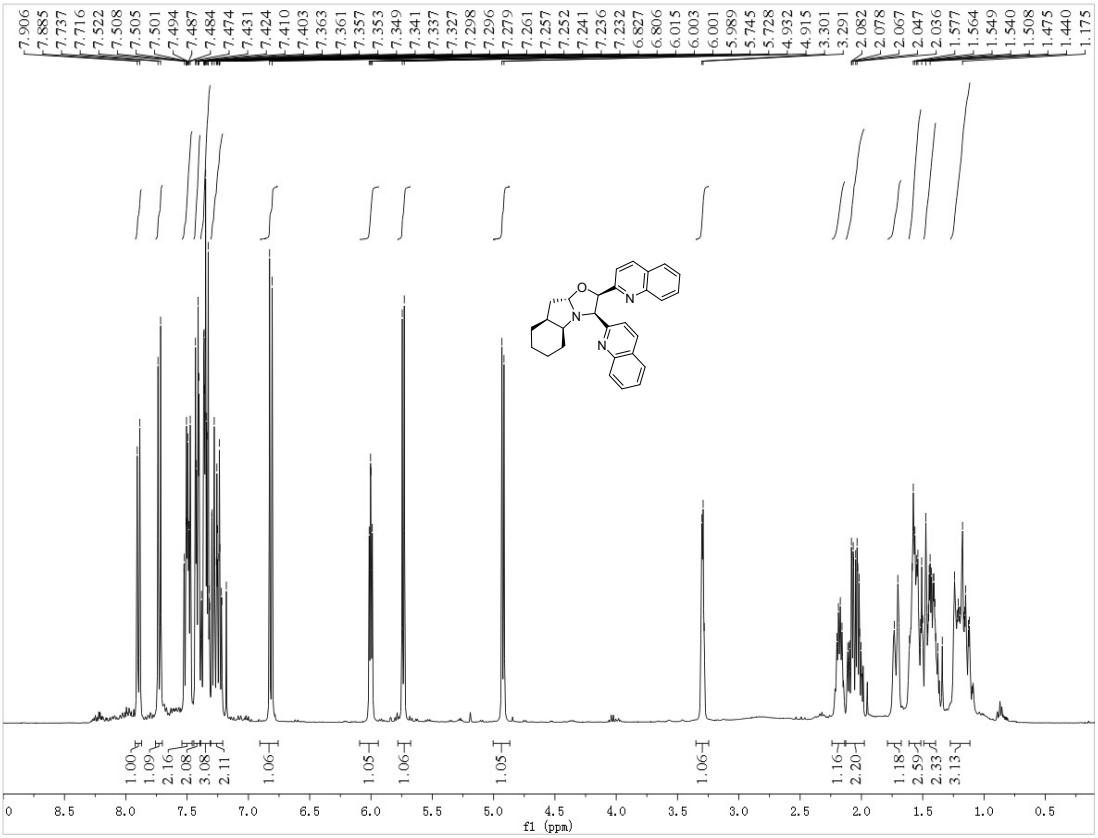
11. The copies of ^{1}H NMR and ^{13}C NMR spectra for compounds 3, 4 and 6

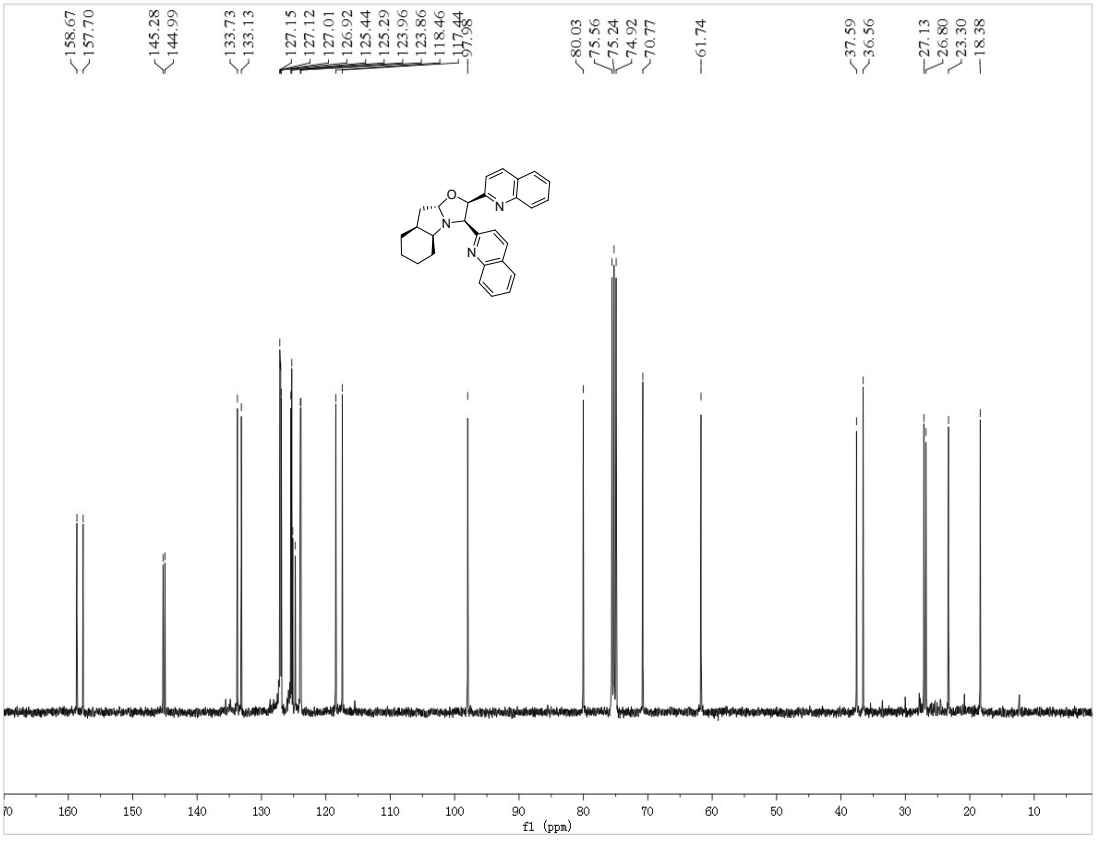
^{1}H and ^{13}C NMR of 3a-1



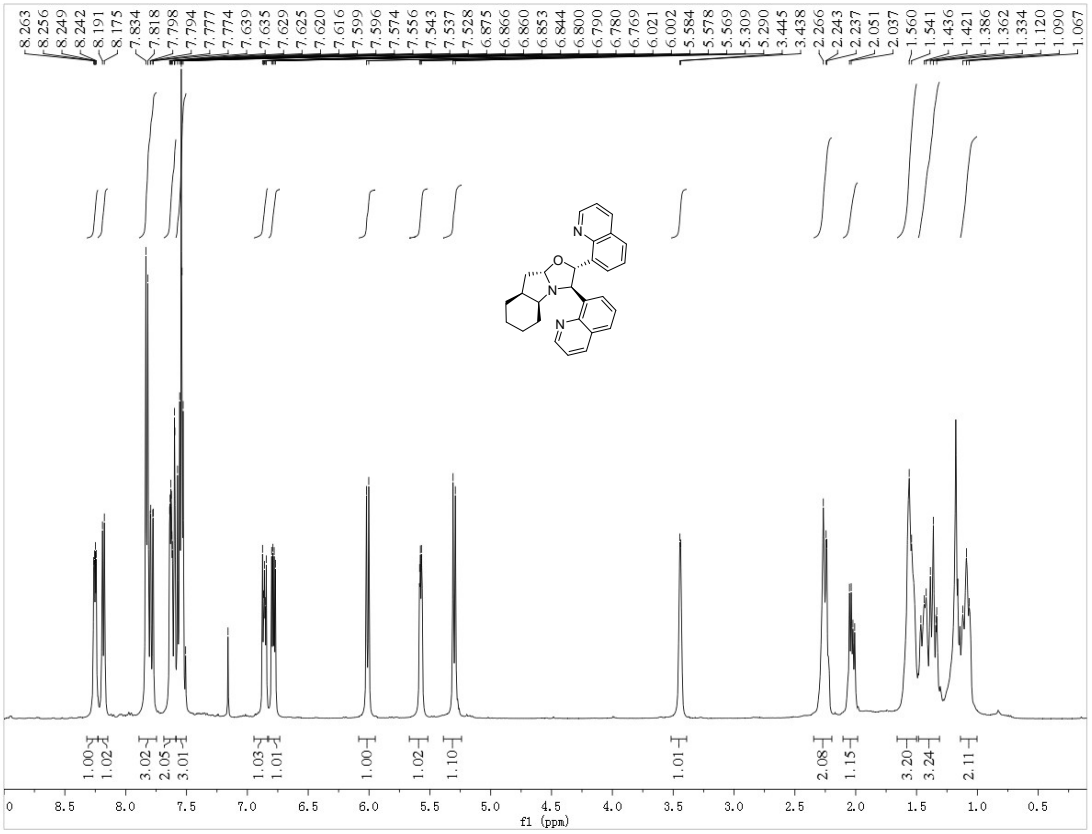


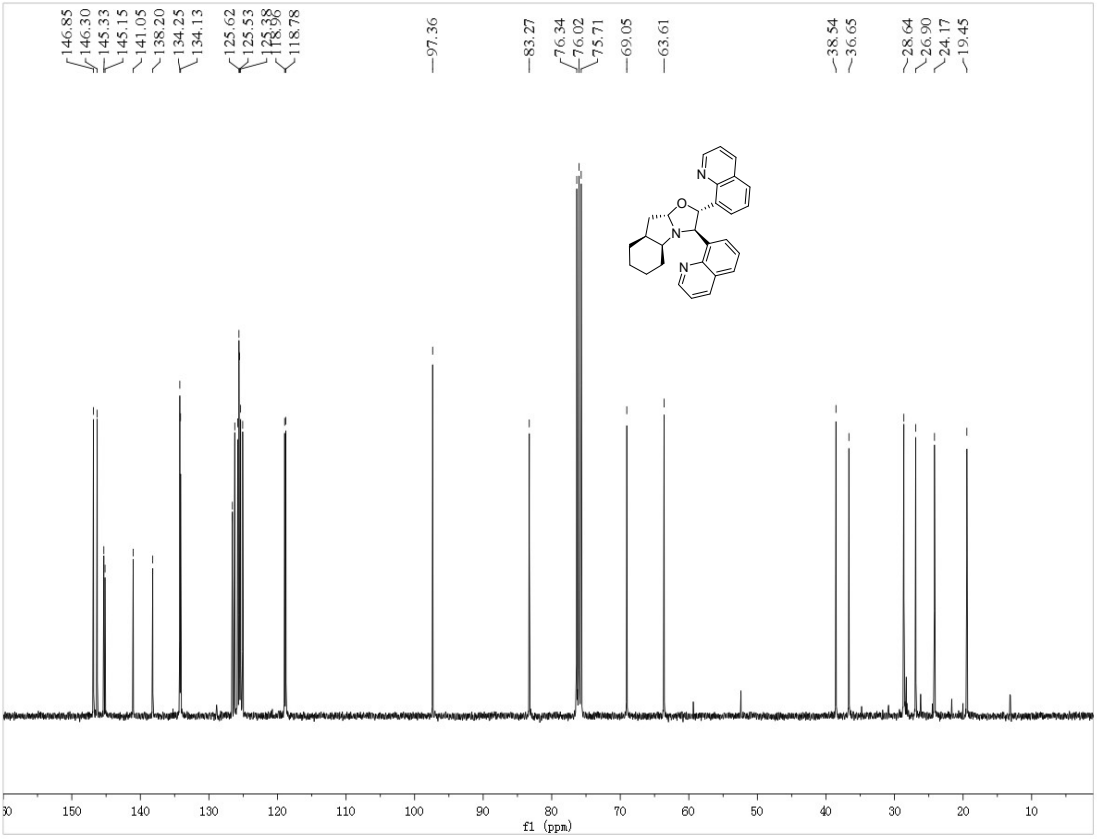
^{1}H and ^{13}C NMR of 3a-2



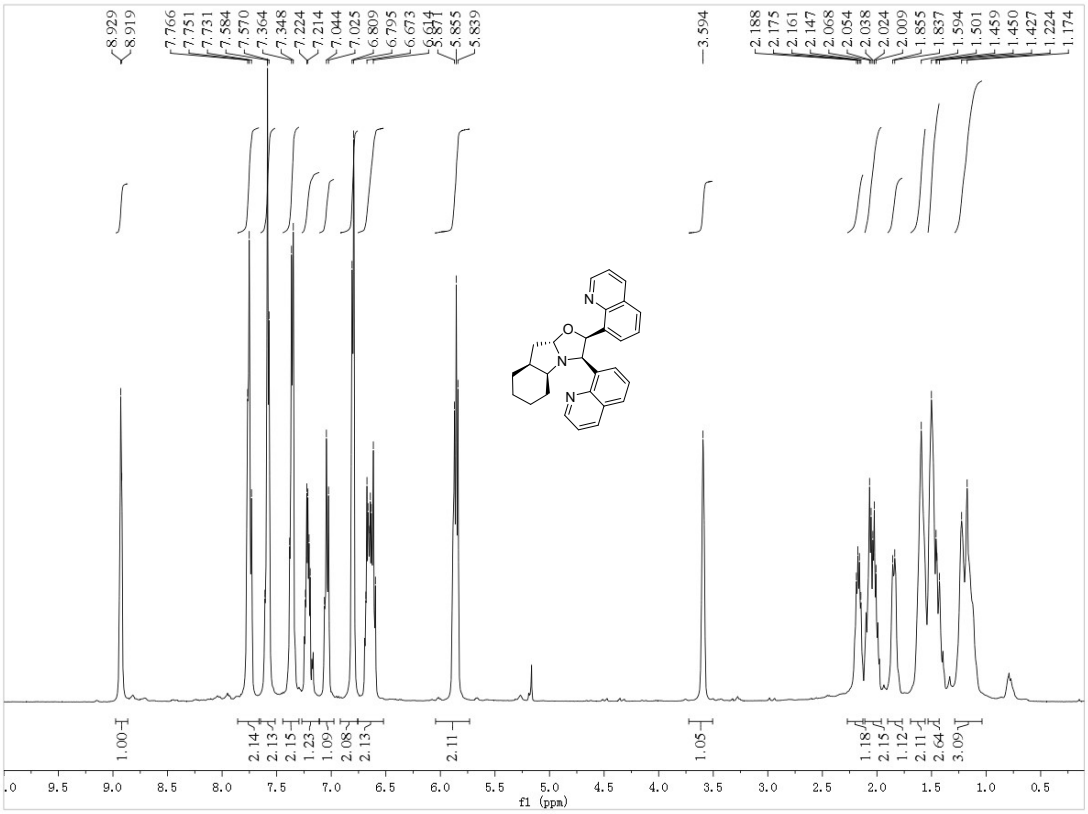


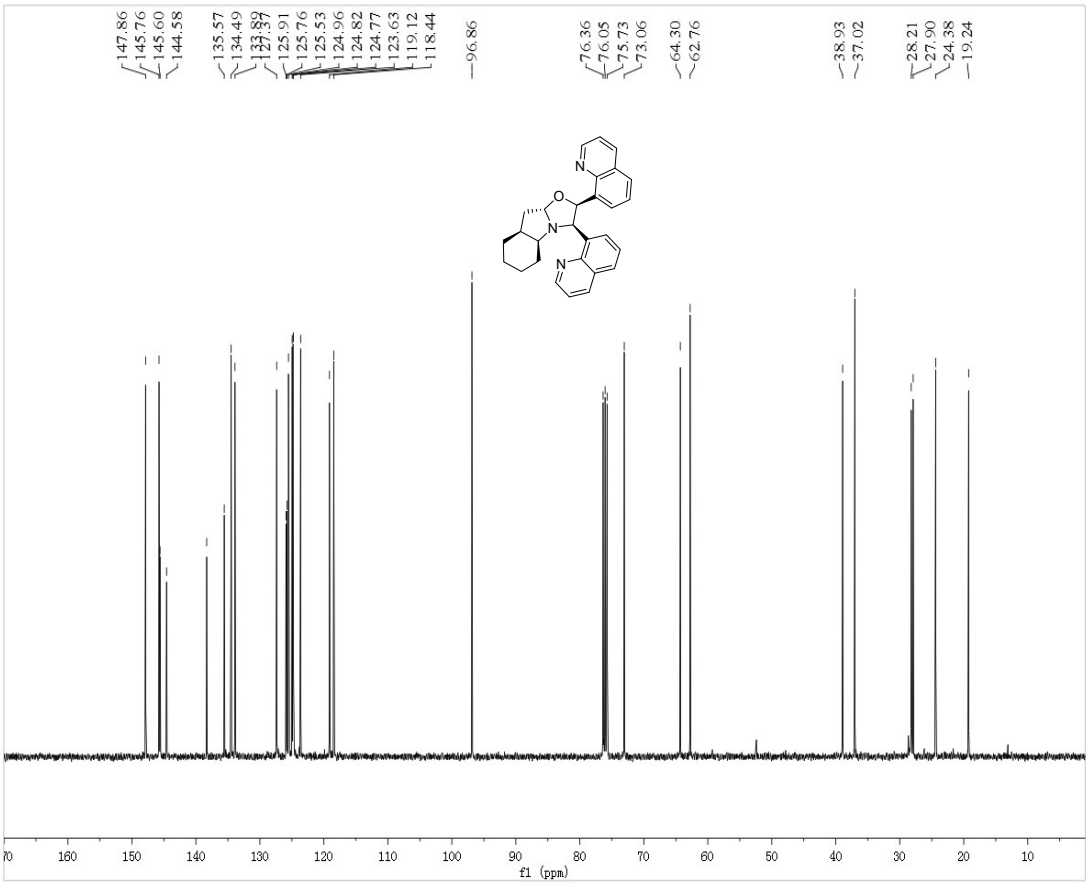
^{1}H and ^{13}C NMR of 3b-1



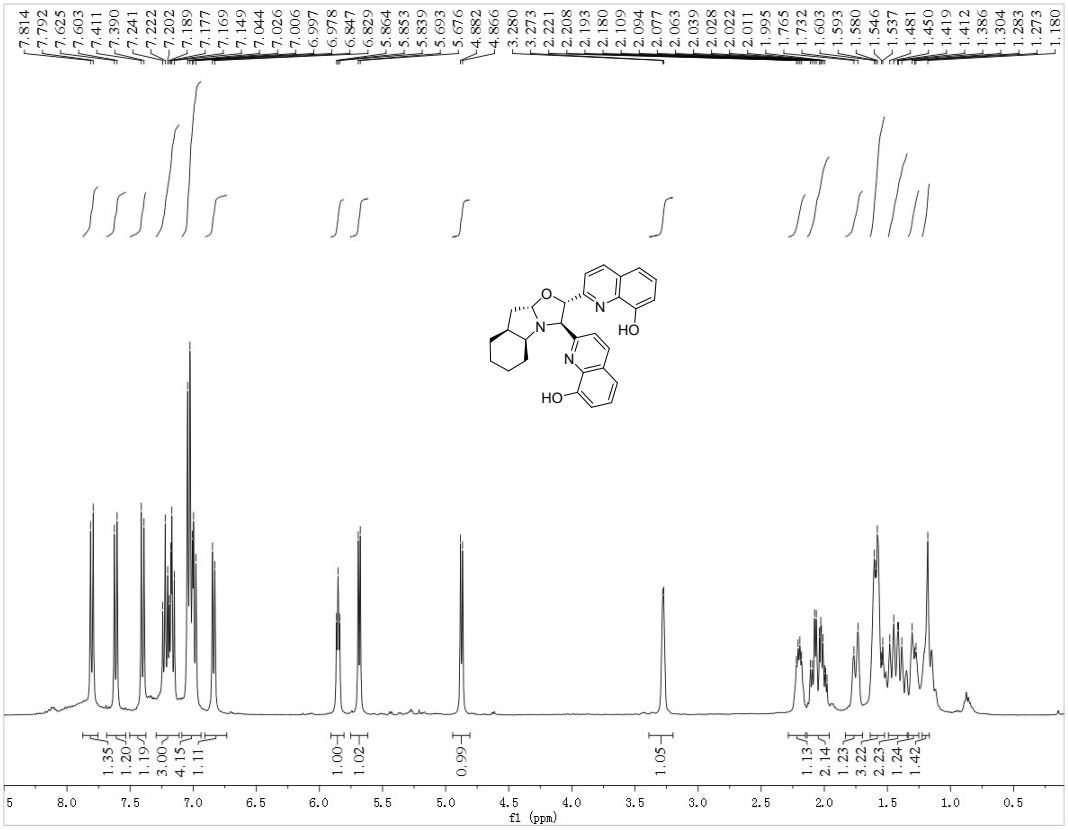


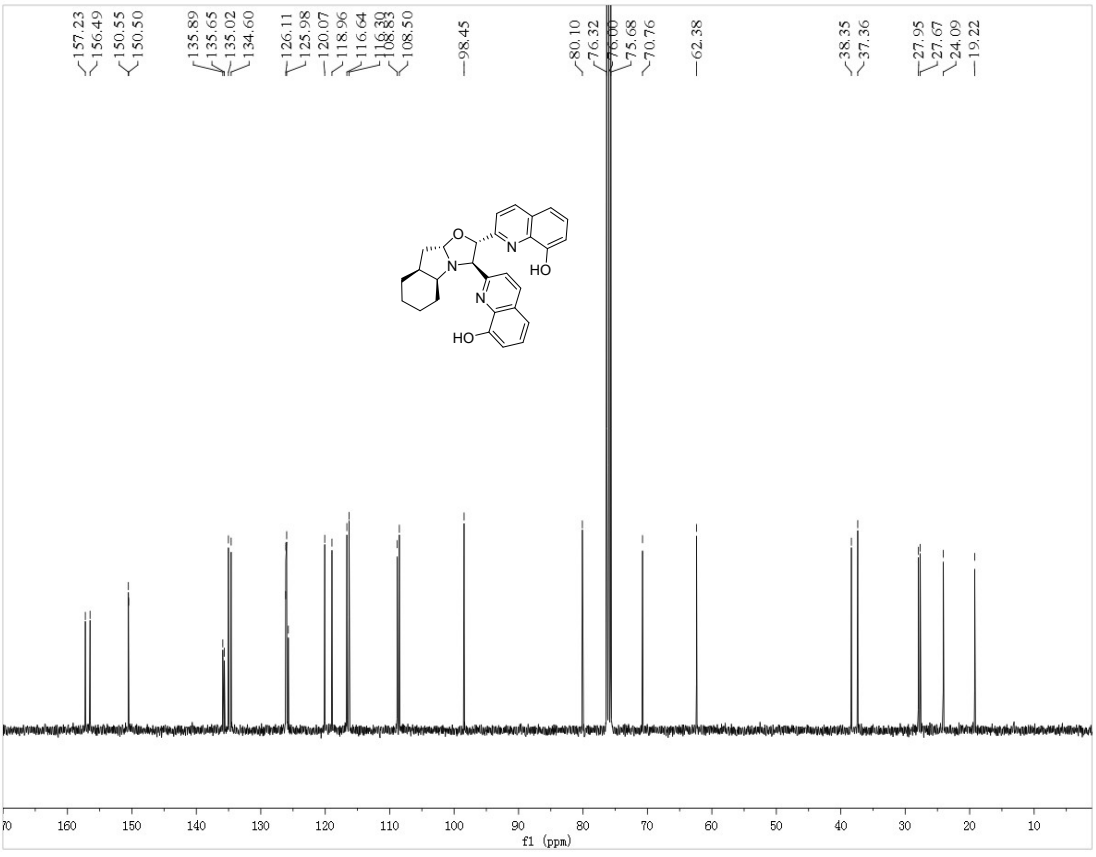
^{1}H and ^{13}C NMR of 3b-2



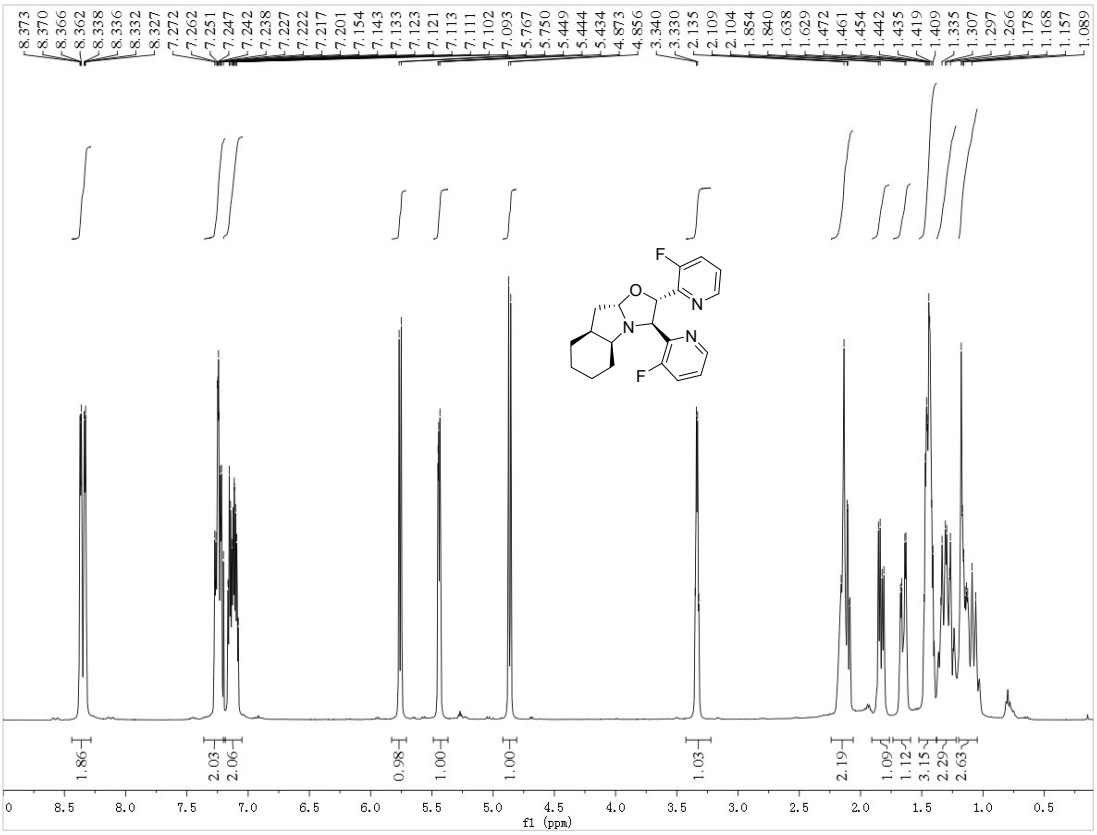


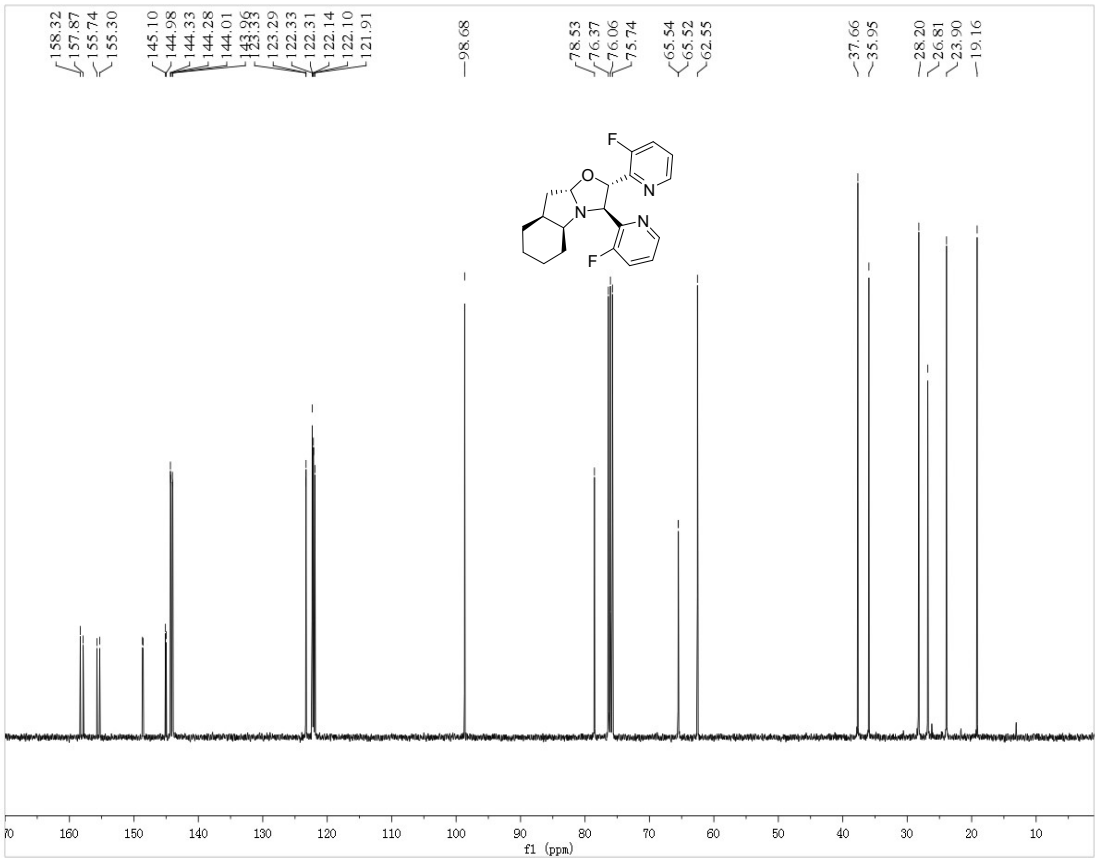
^{1}H and ^{13}C NMR of 3c



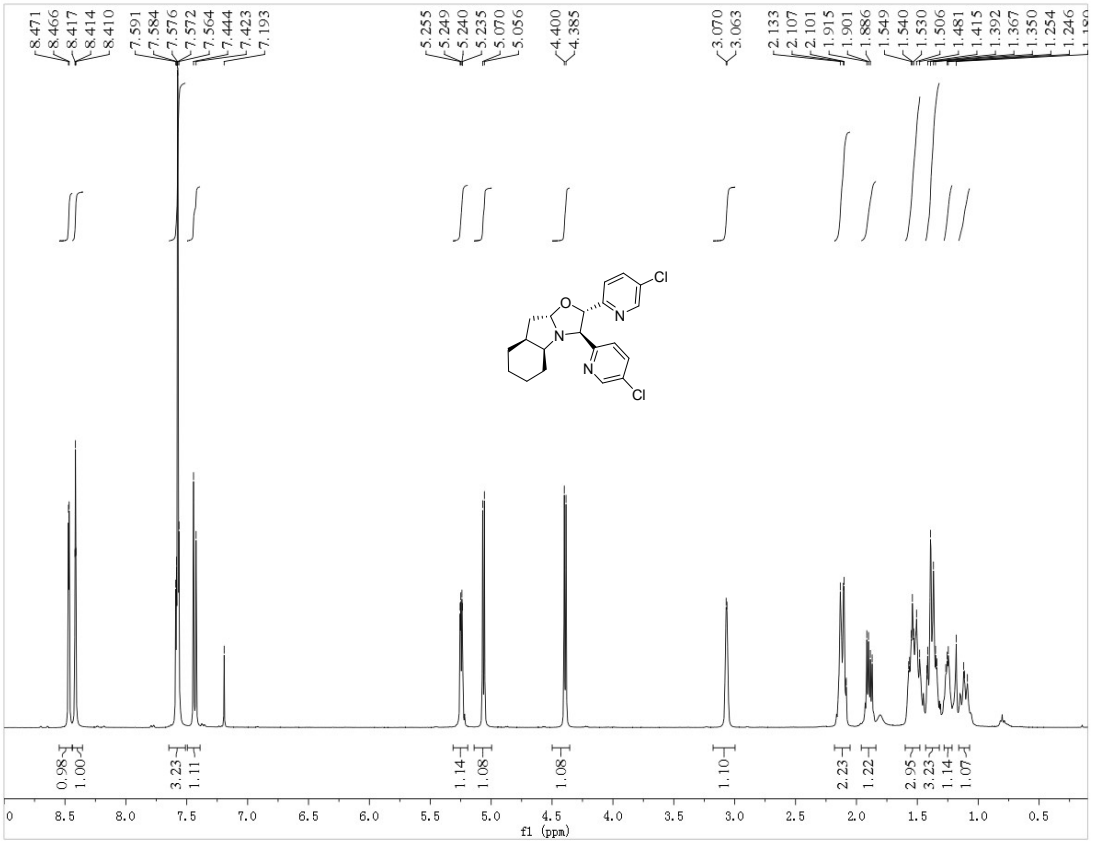


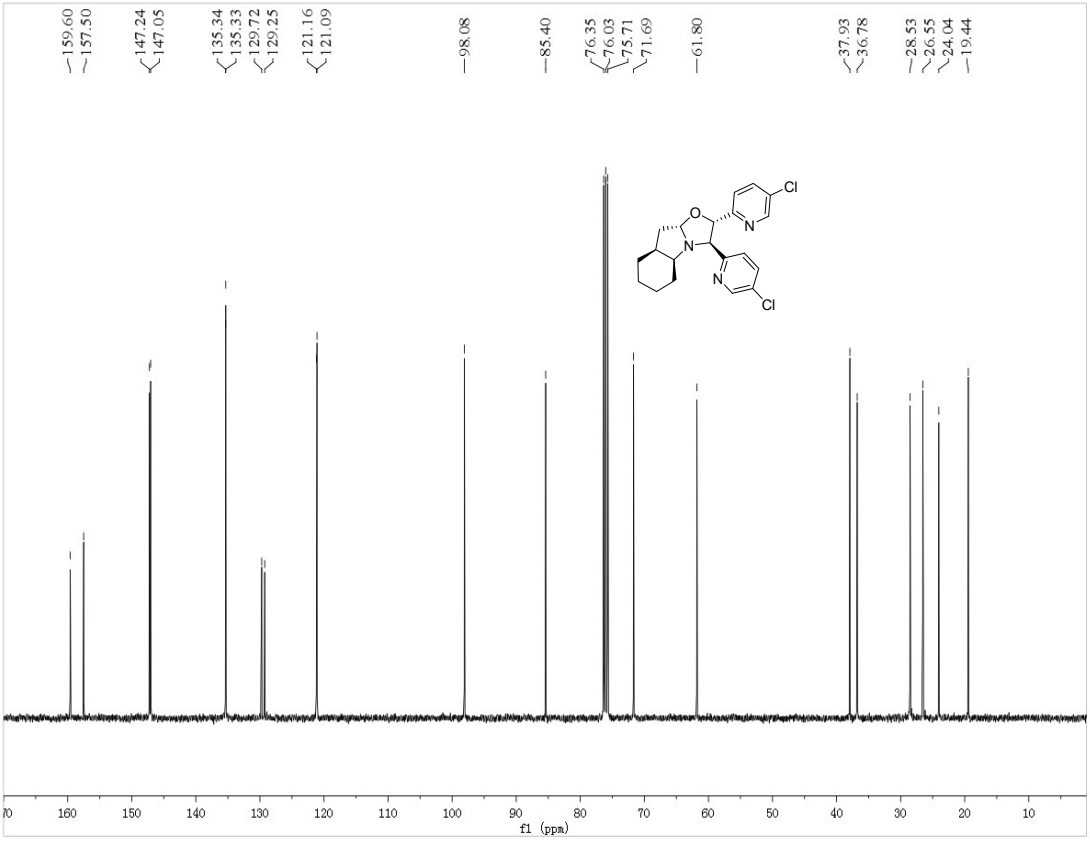
^{1}H and ^{13}C NMR of 3d



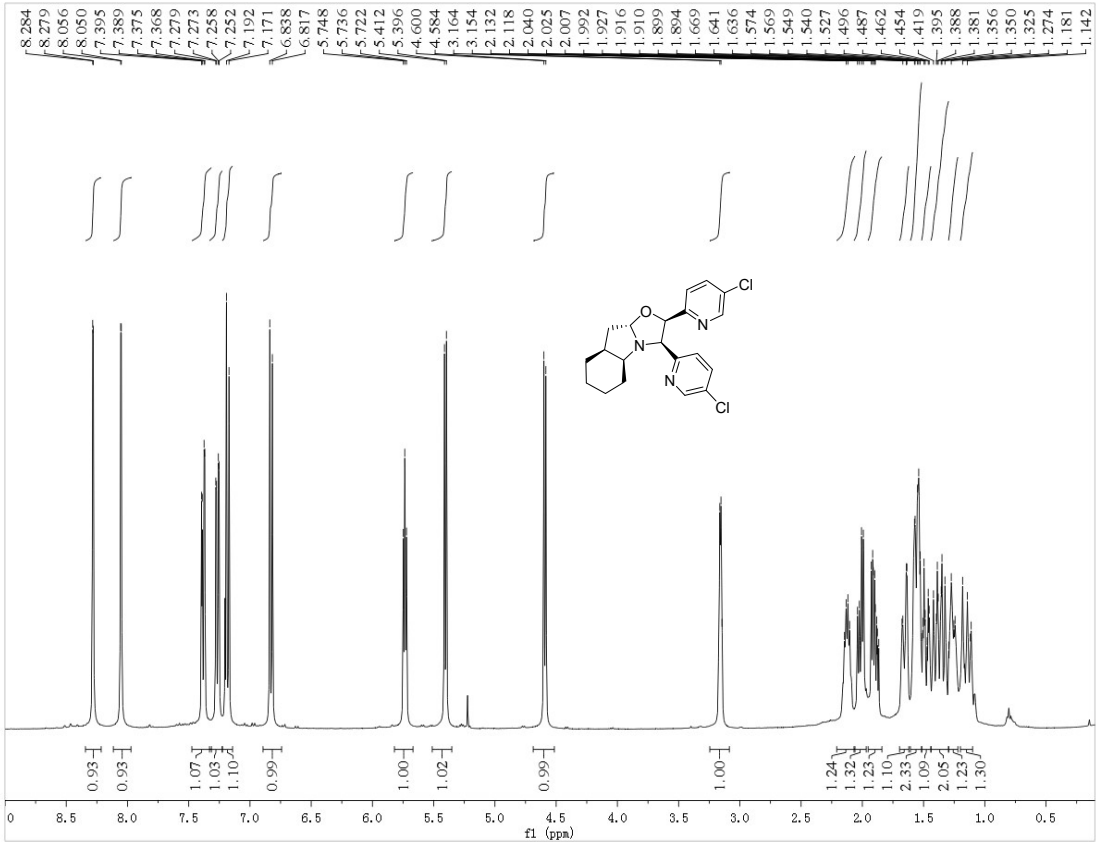


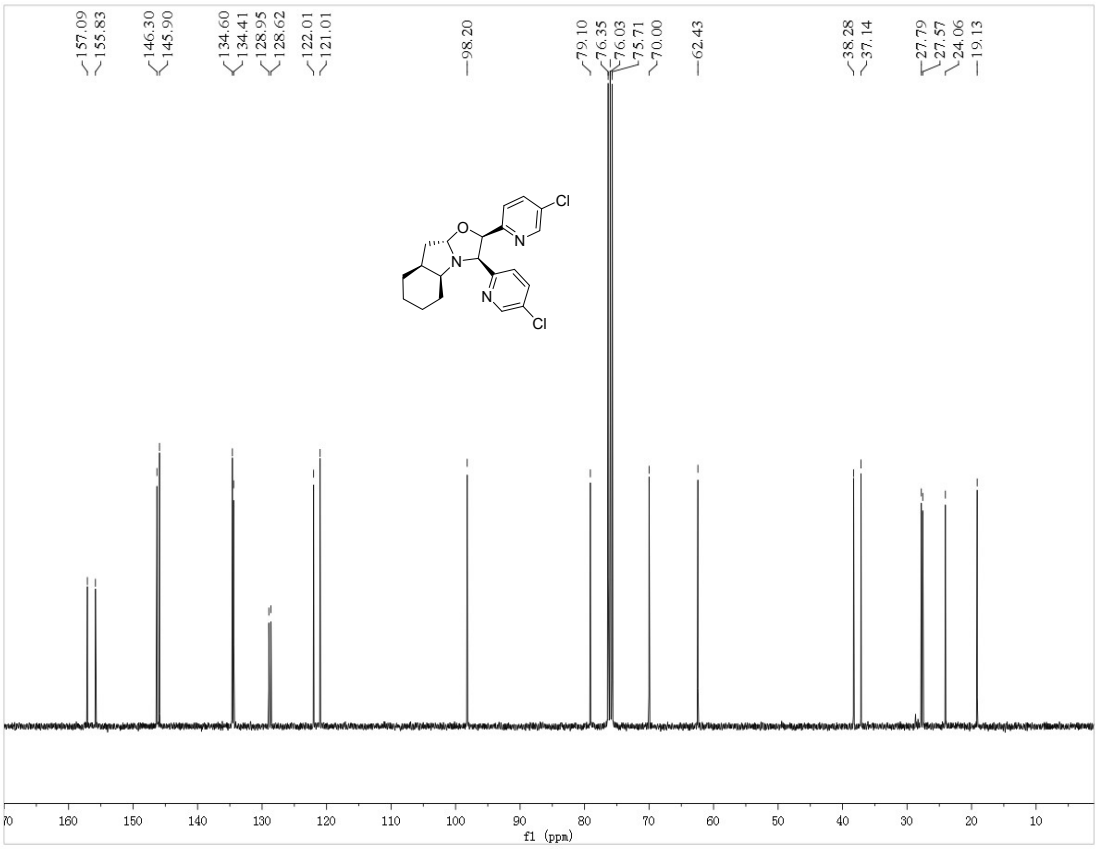
^{1}H and ^{13}C NMR of 3e-1



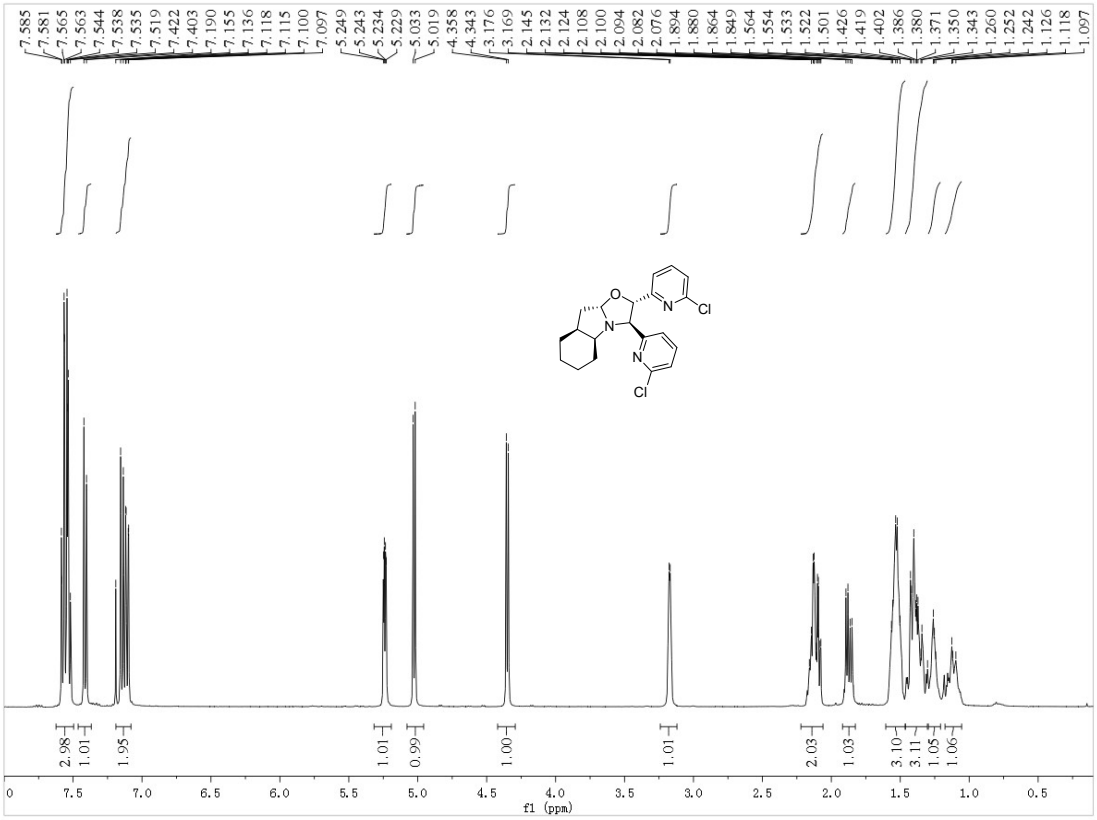


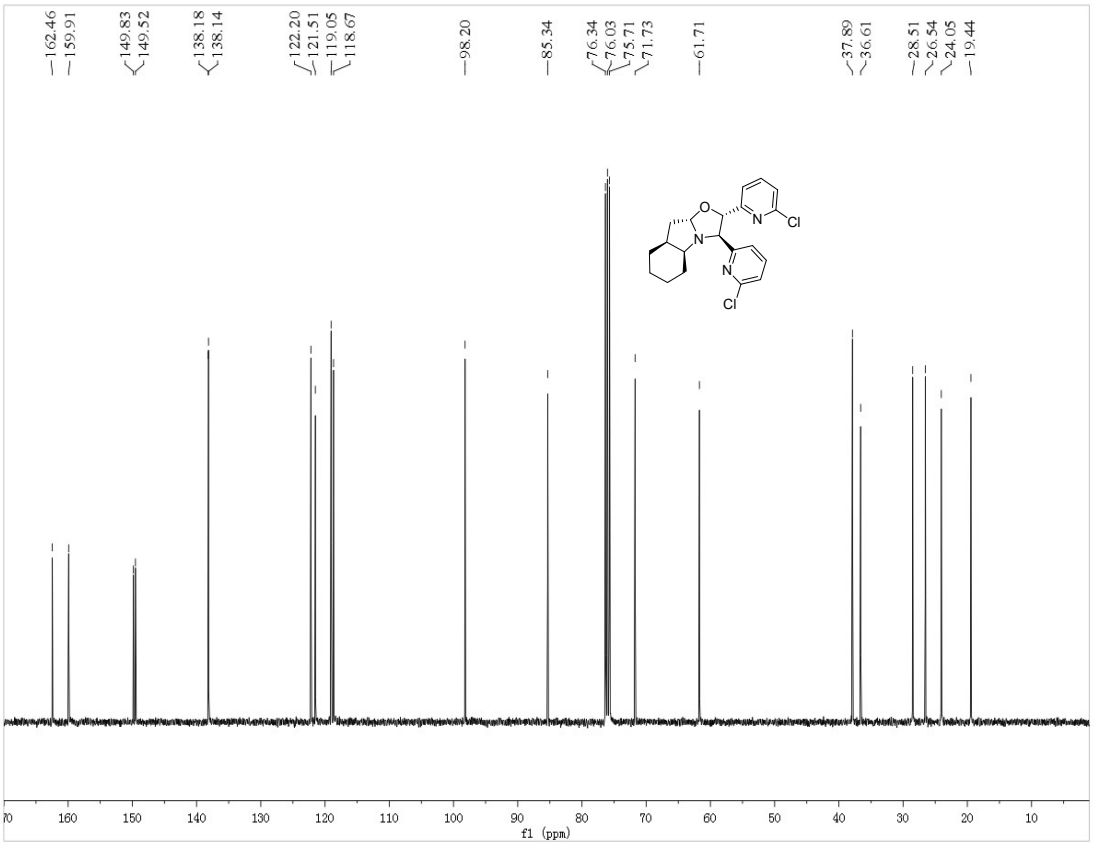
^{1}H and ^{13}C NMR of 3e-2



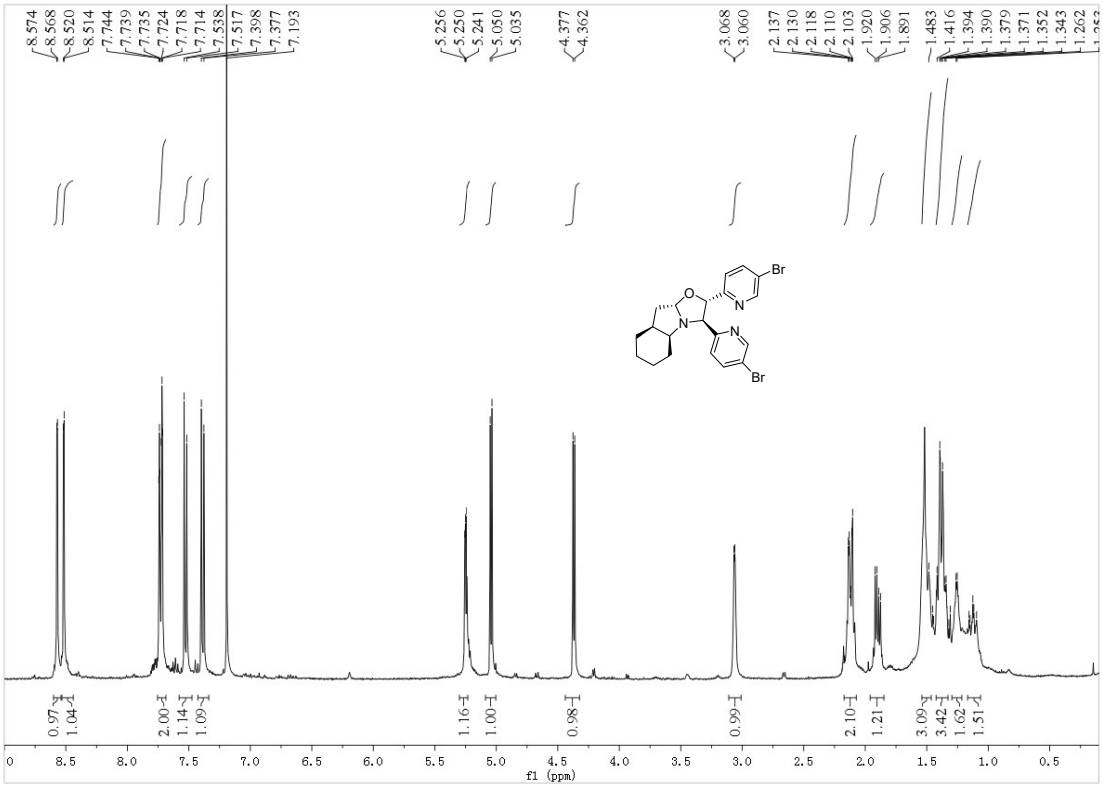


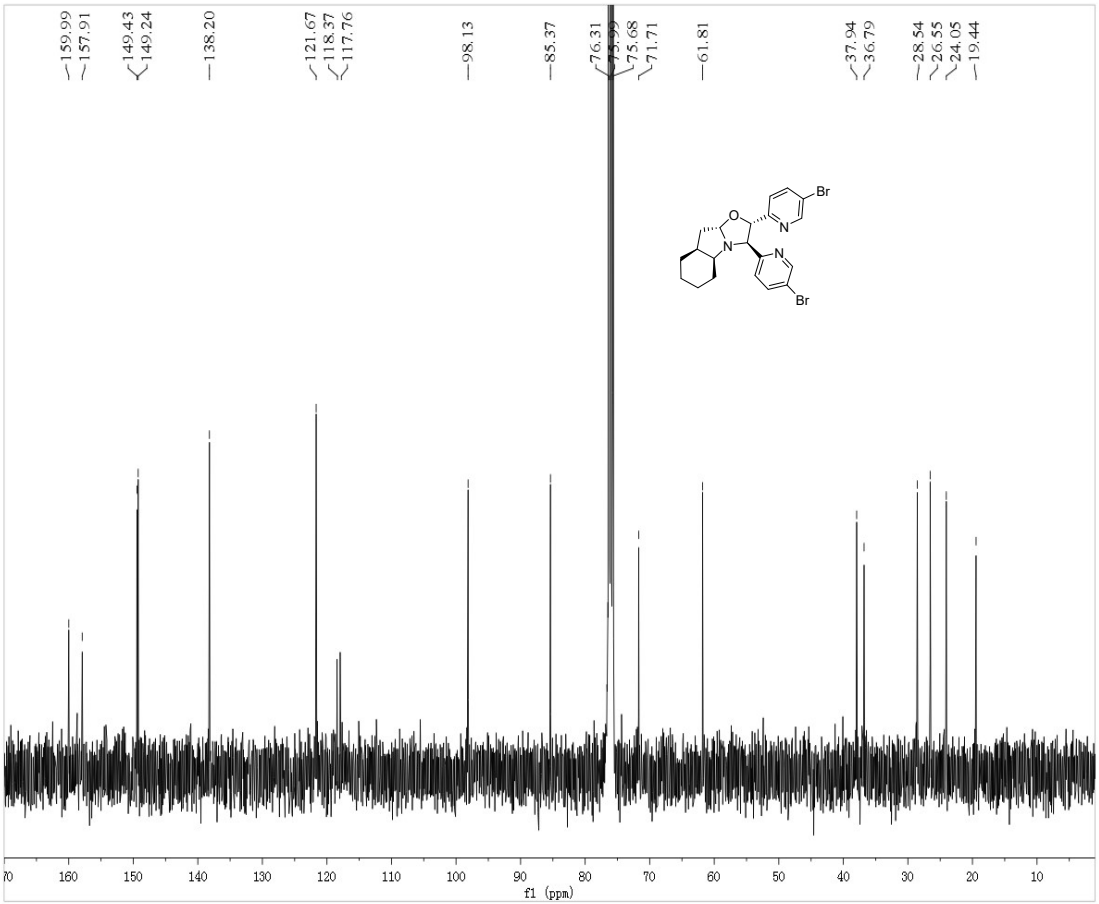
^{1}H and ^{13}C NMR of 3f



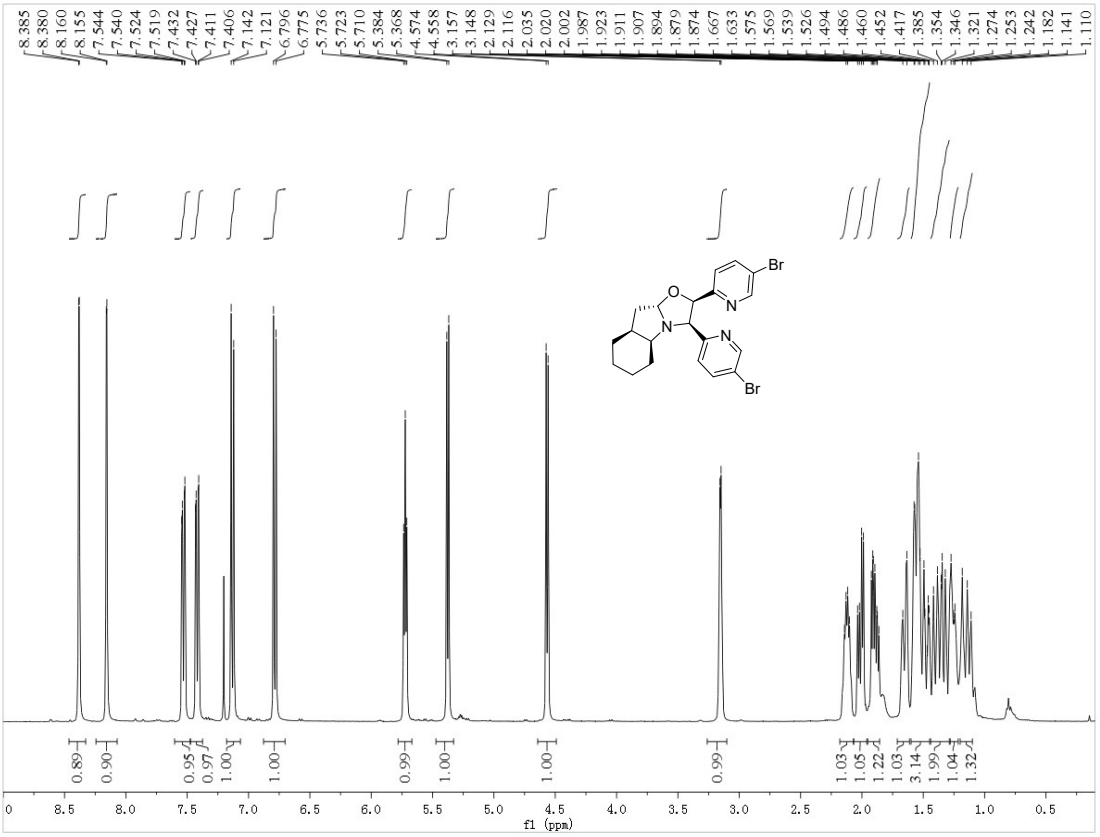


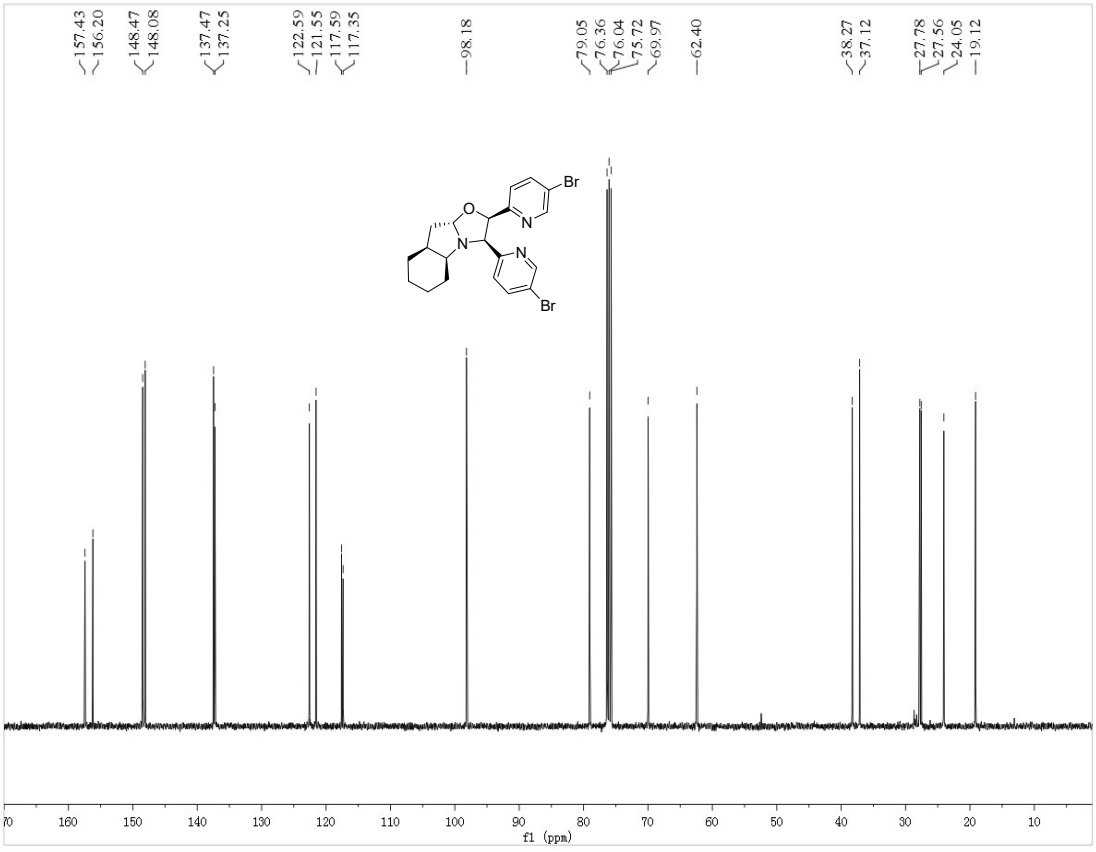
^{1}H and ^{13}C NMR of 3g-1



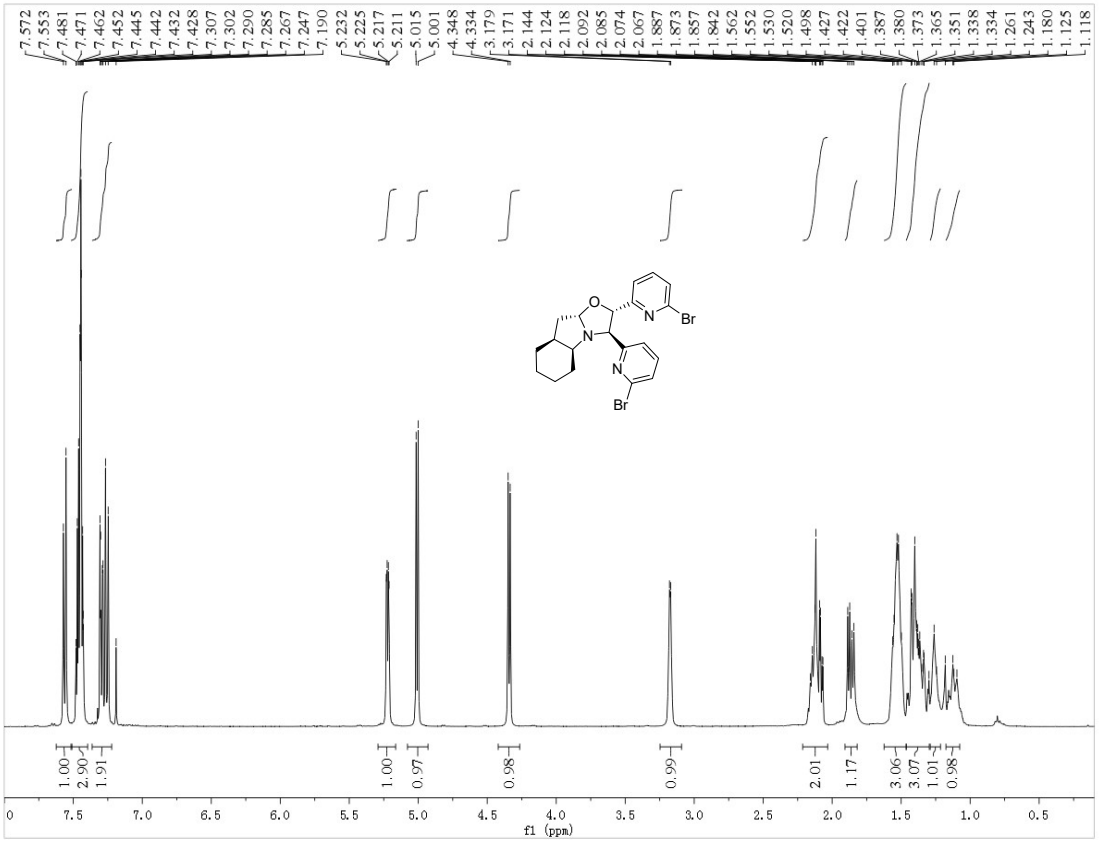


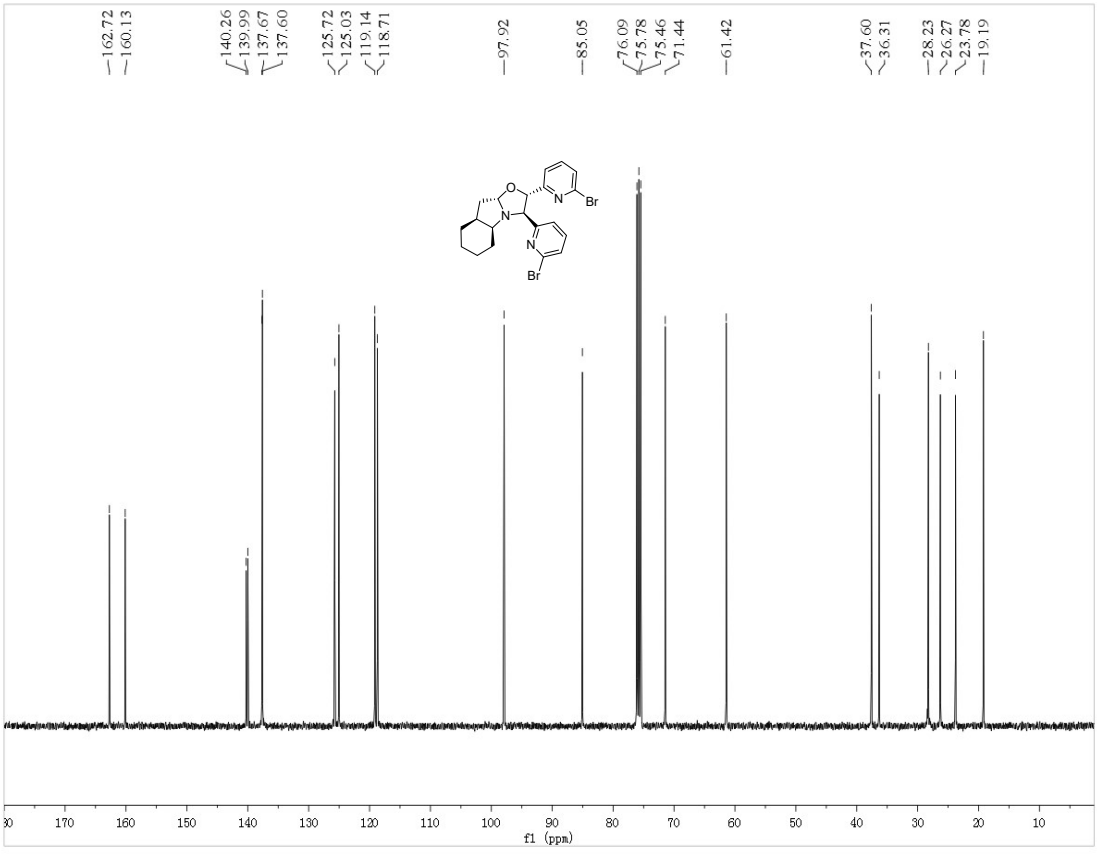
^{1}H and ^{13}C NMR of 3g-2



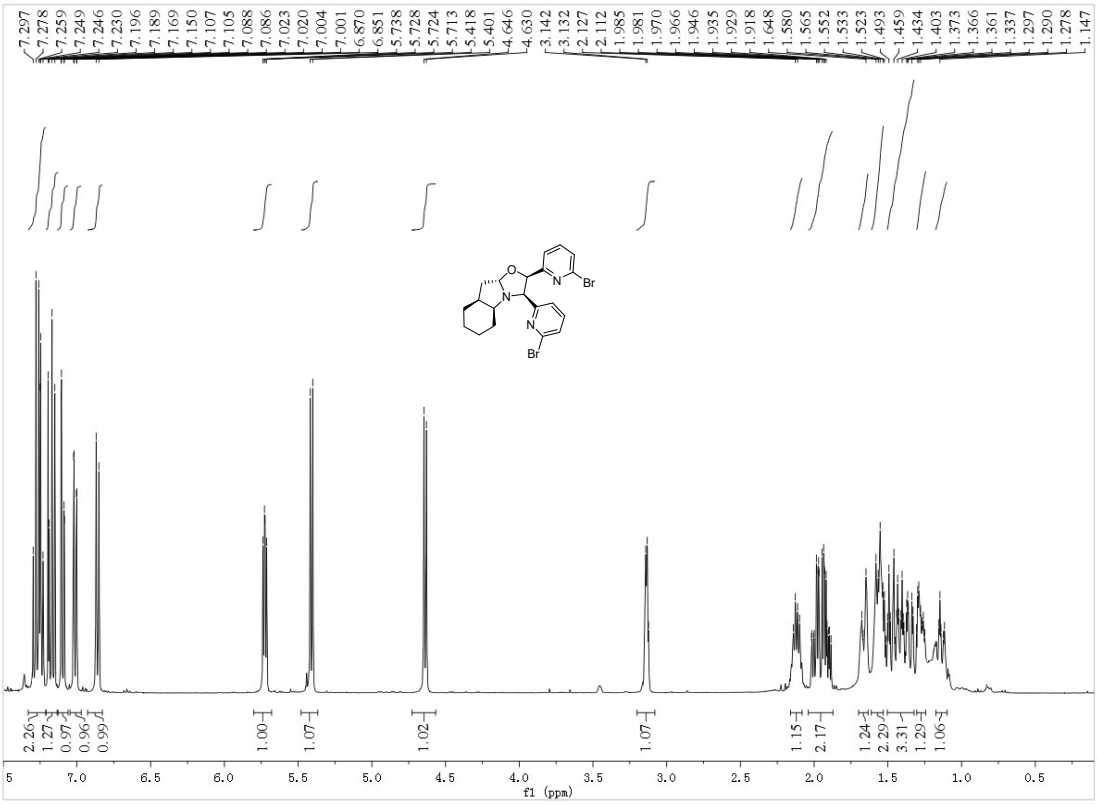


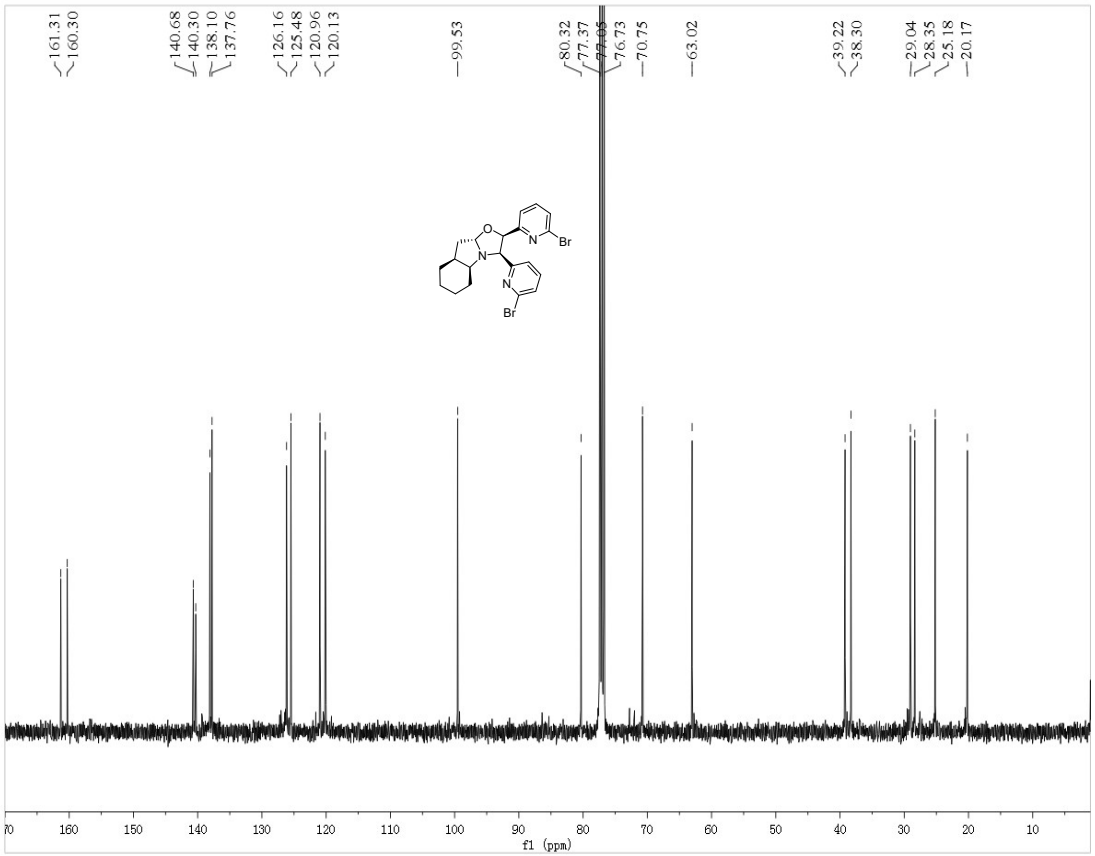
^{1}H and ^{13}C NMR of 3h-1



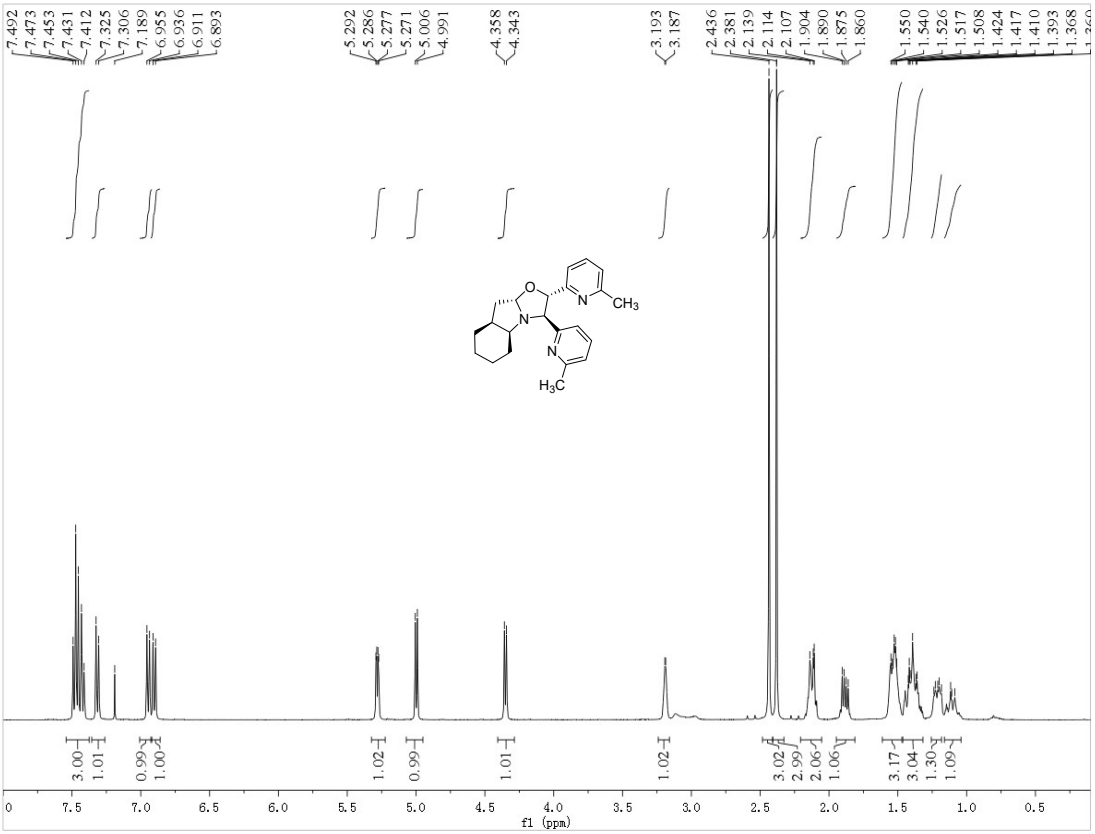


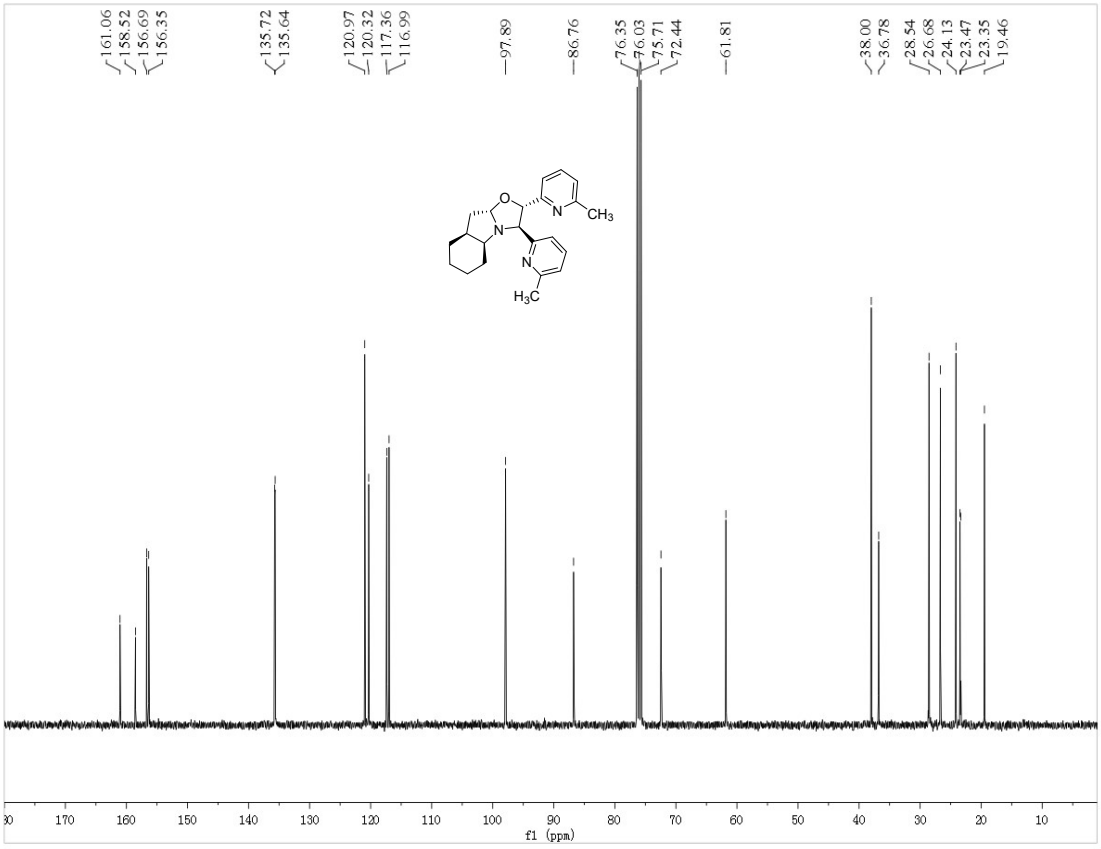
^{1}H and ^{13}C NMR of 3h-2



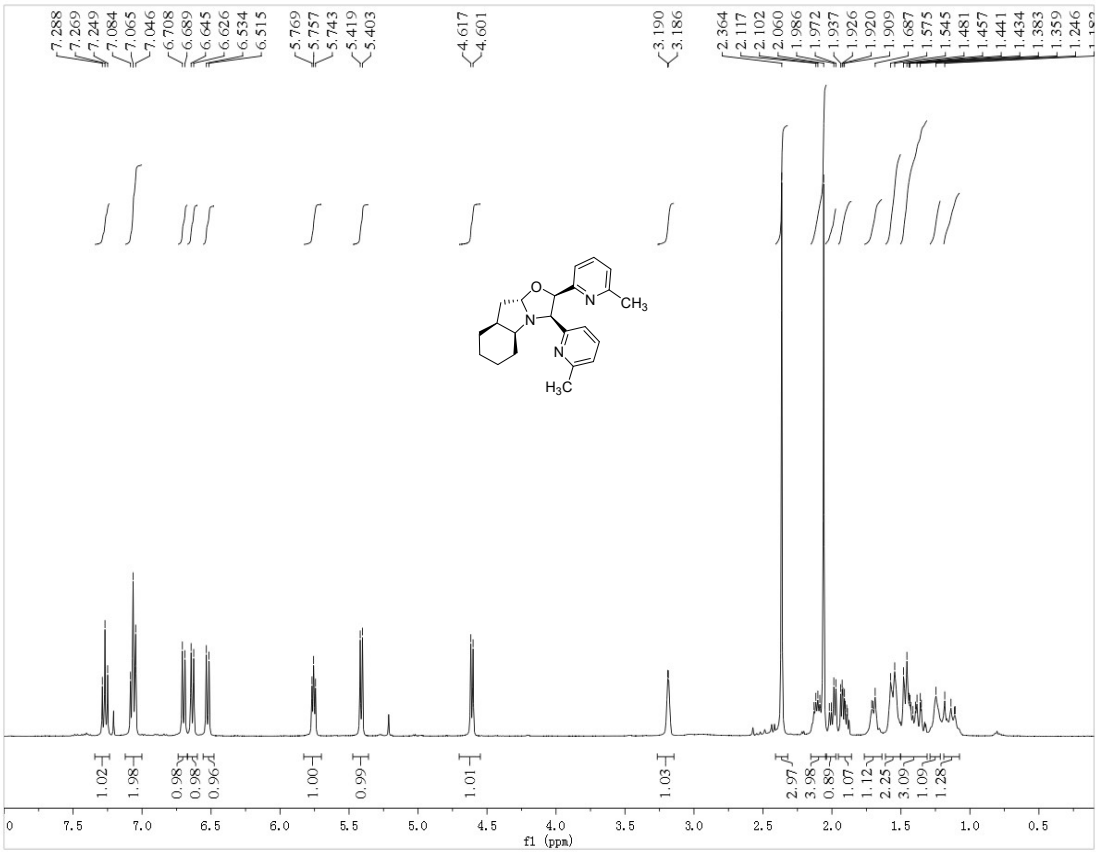


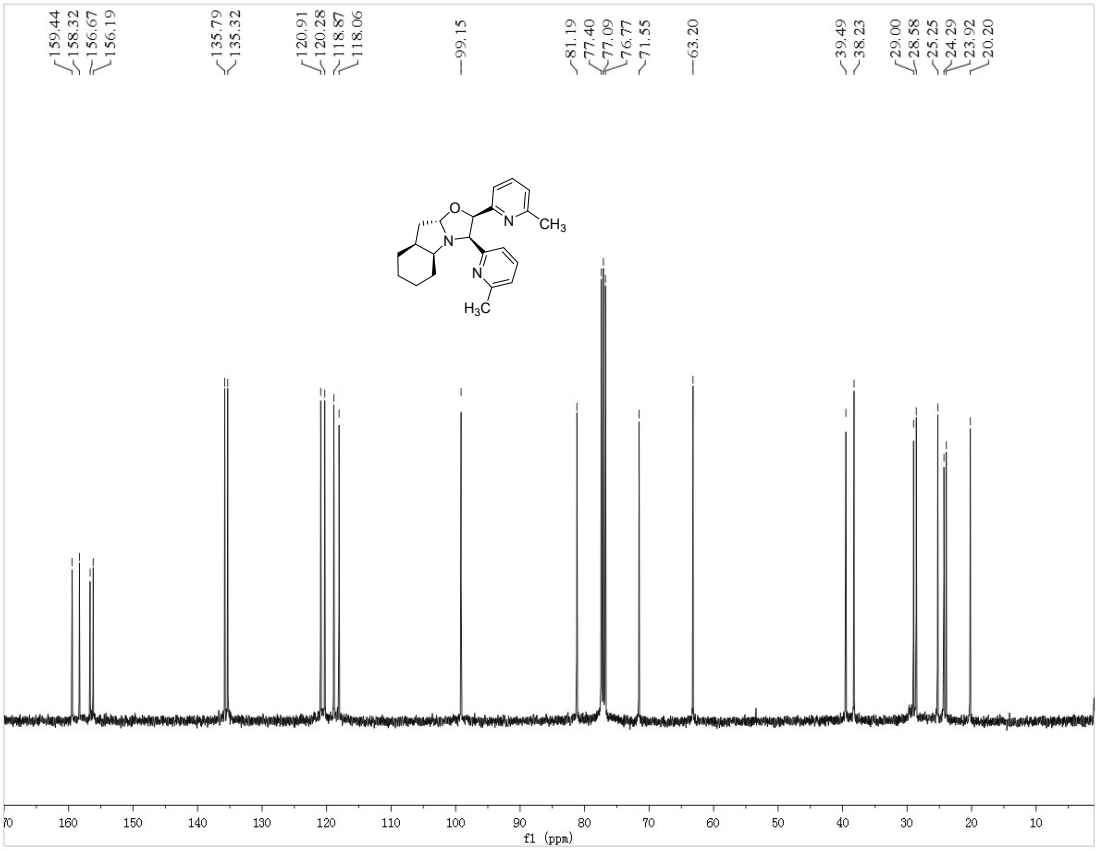
^{1}H and ^{13}C NMR of 3i-1



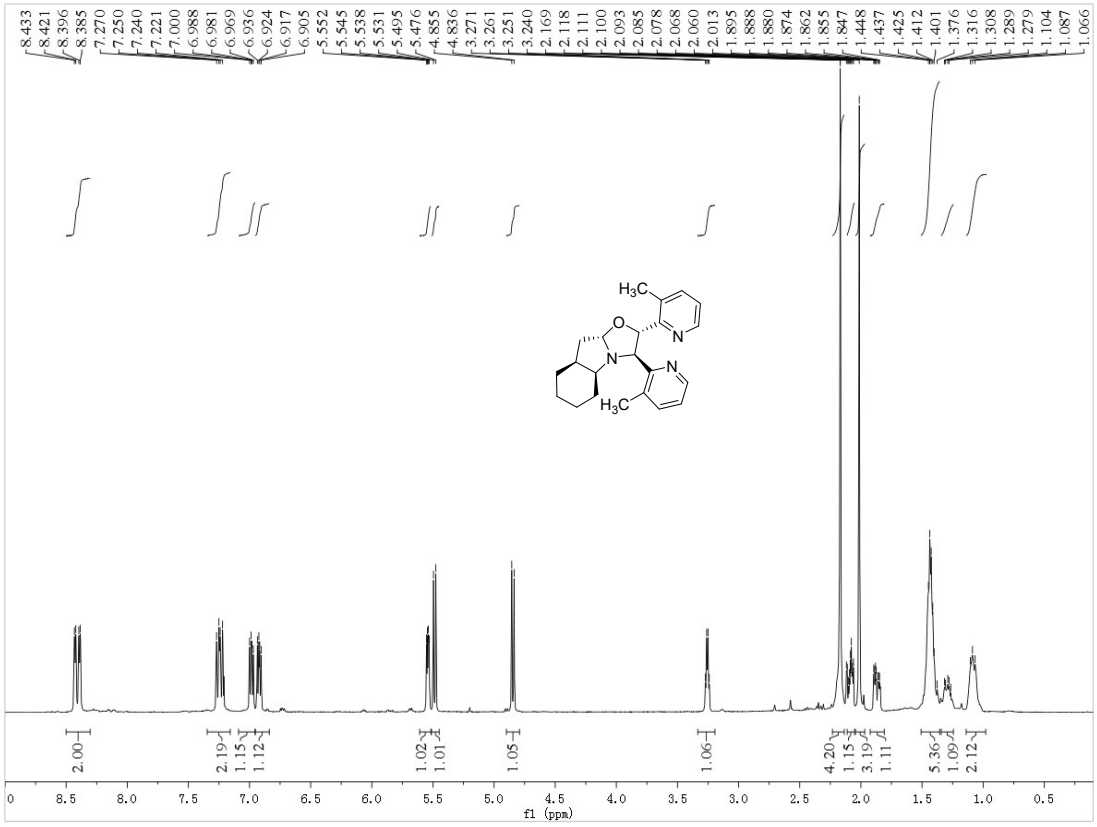


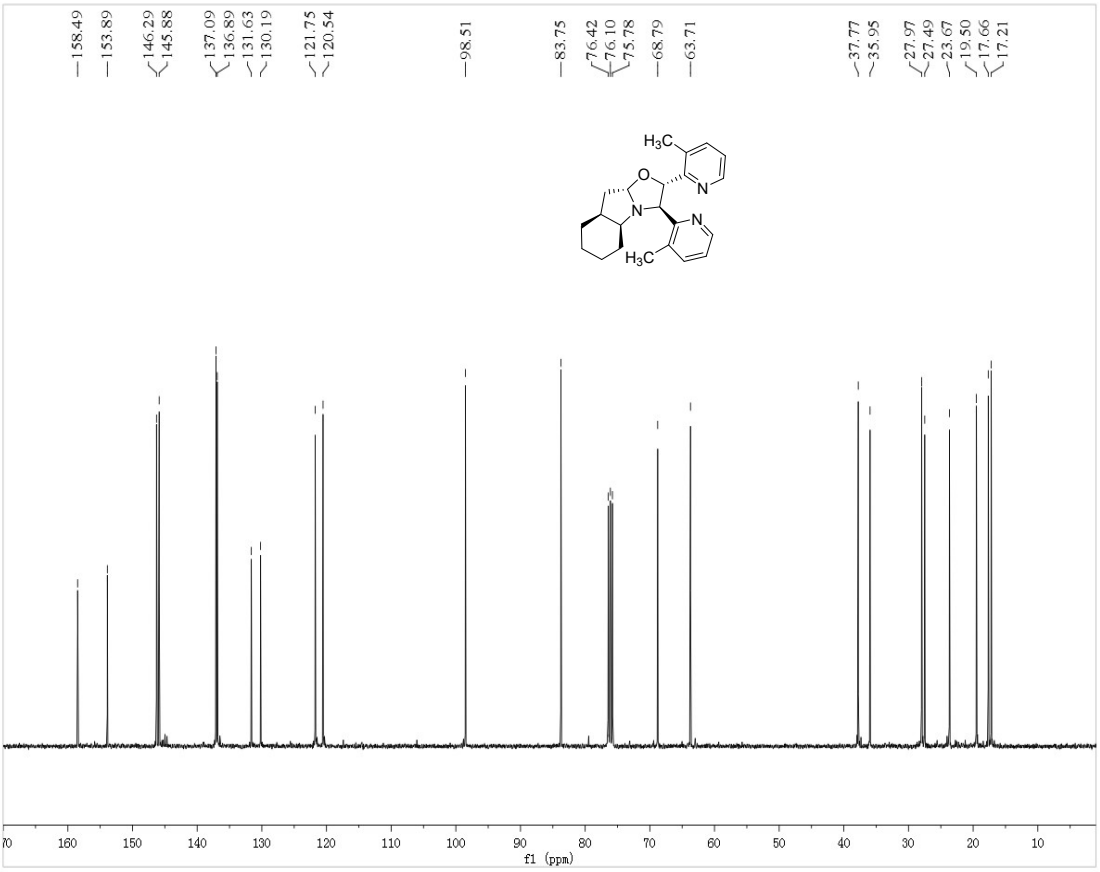
^{1}H and ^{13}C NMR of 3i-2



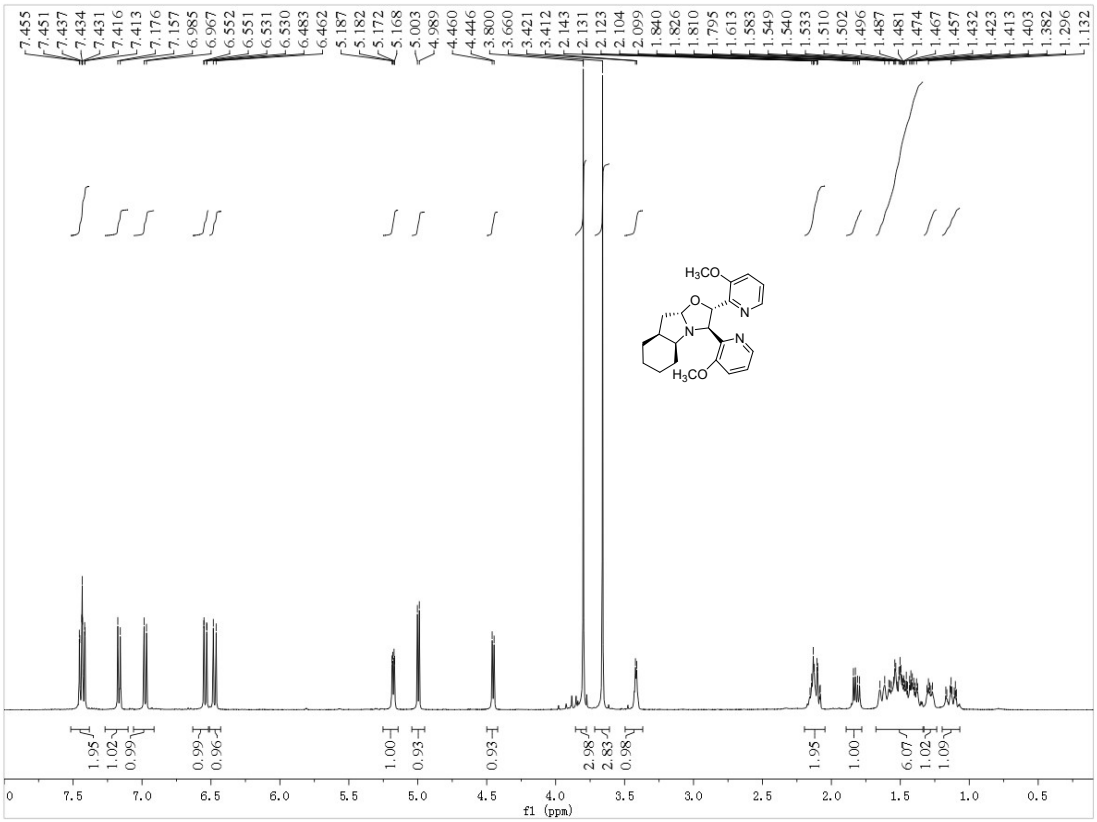


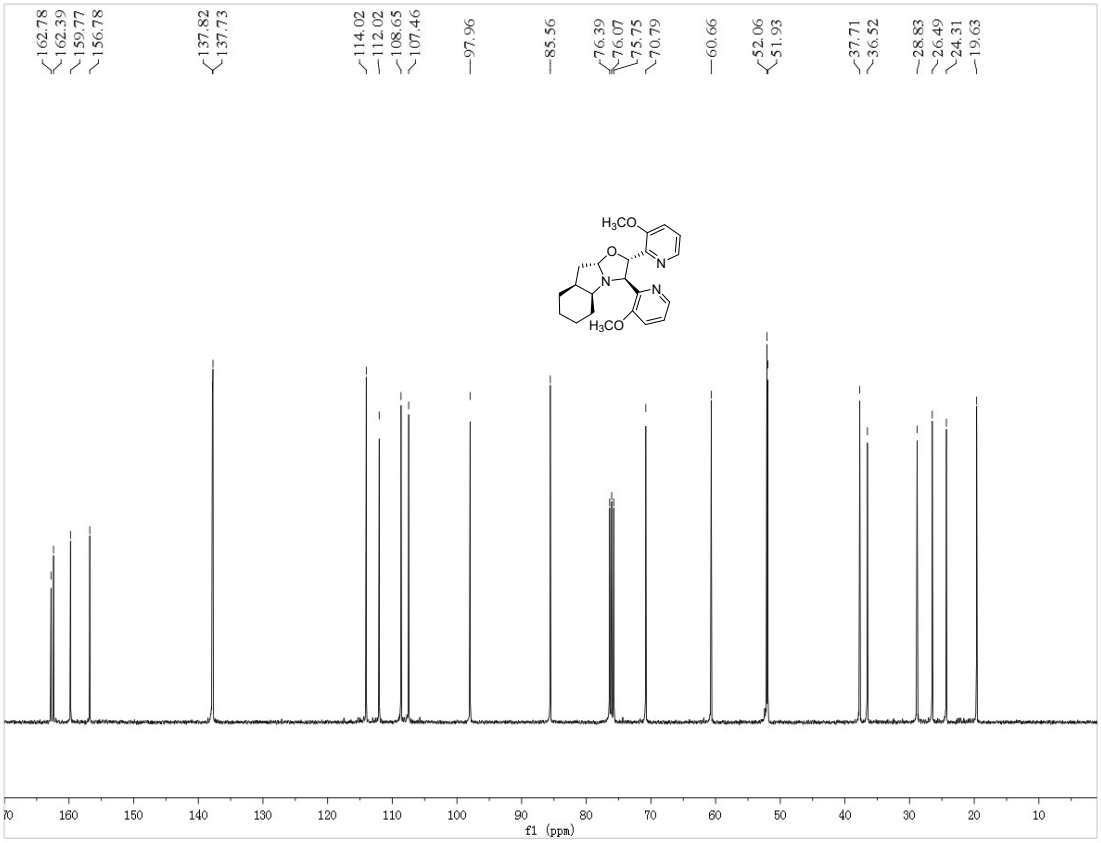
^{1}H and ^{13}C NMR of 3j



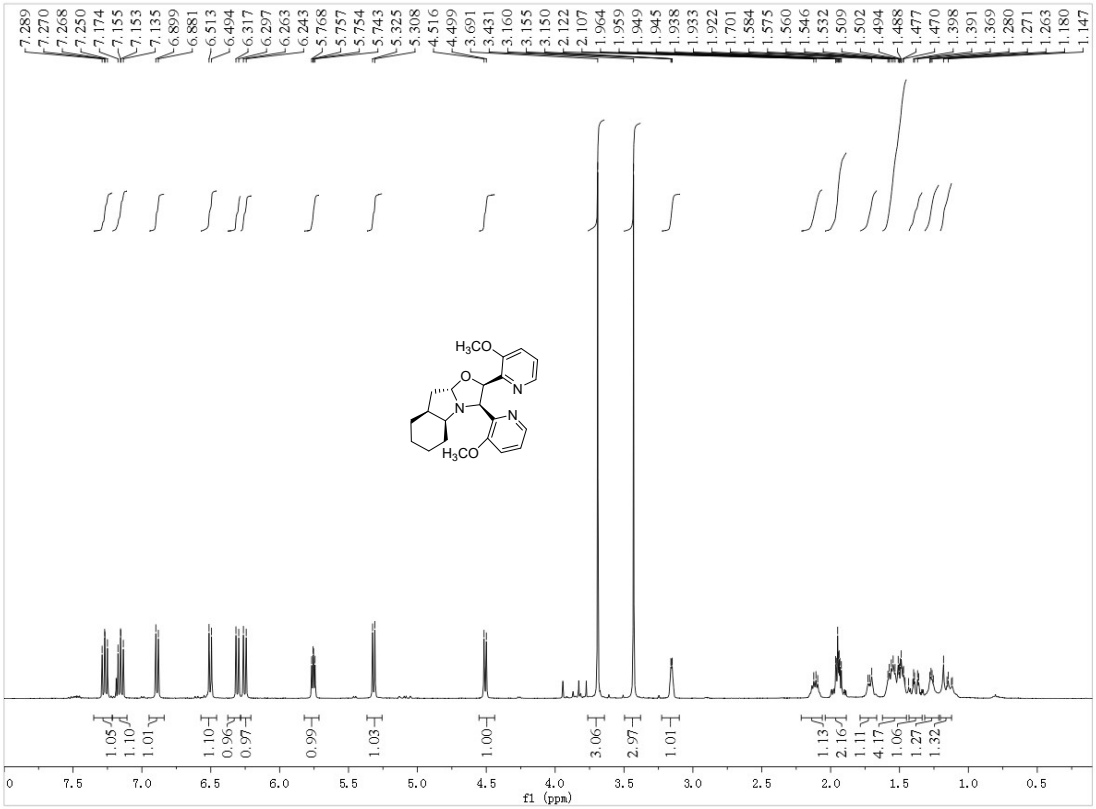


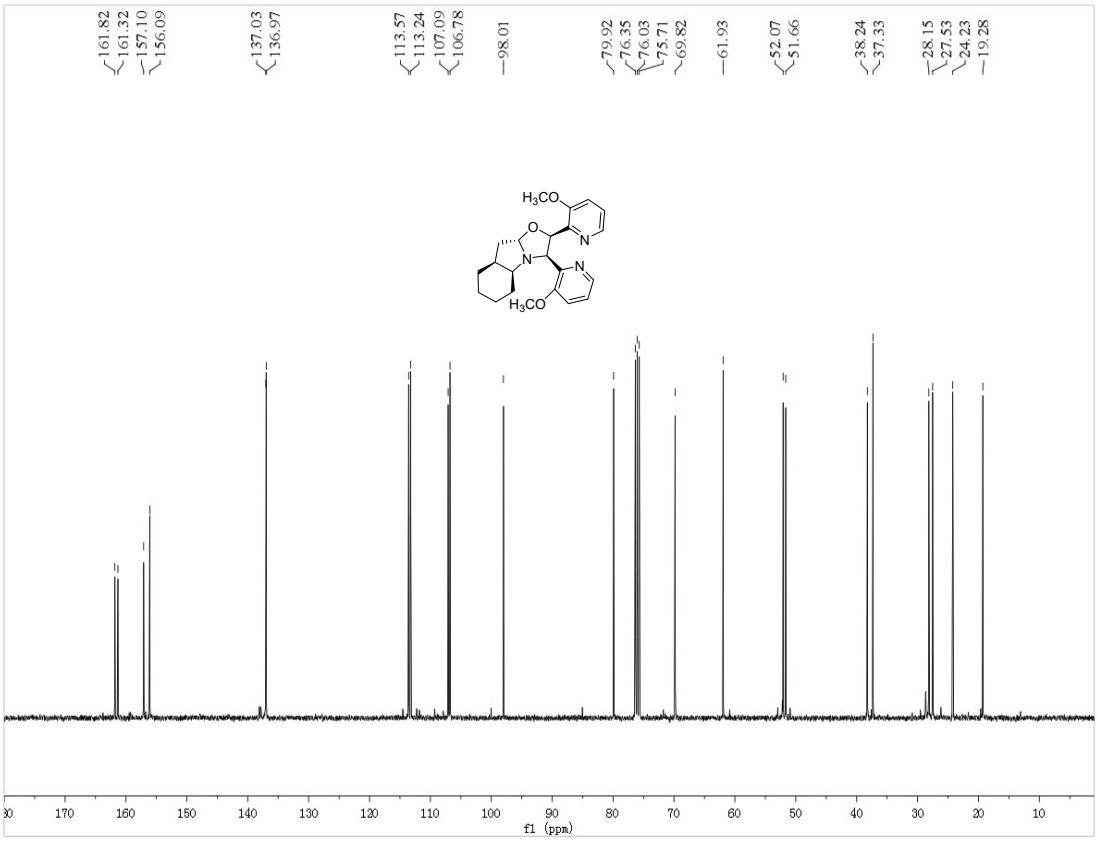
^{1}H and ^{13}C NMR of 3k-1



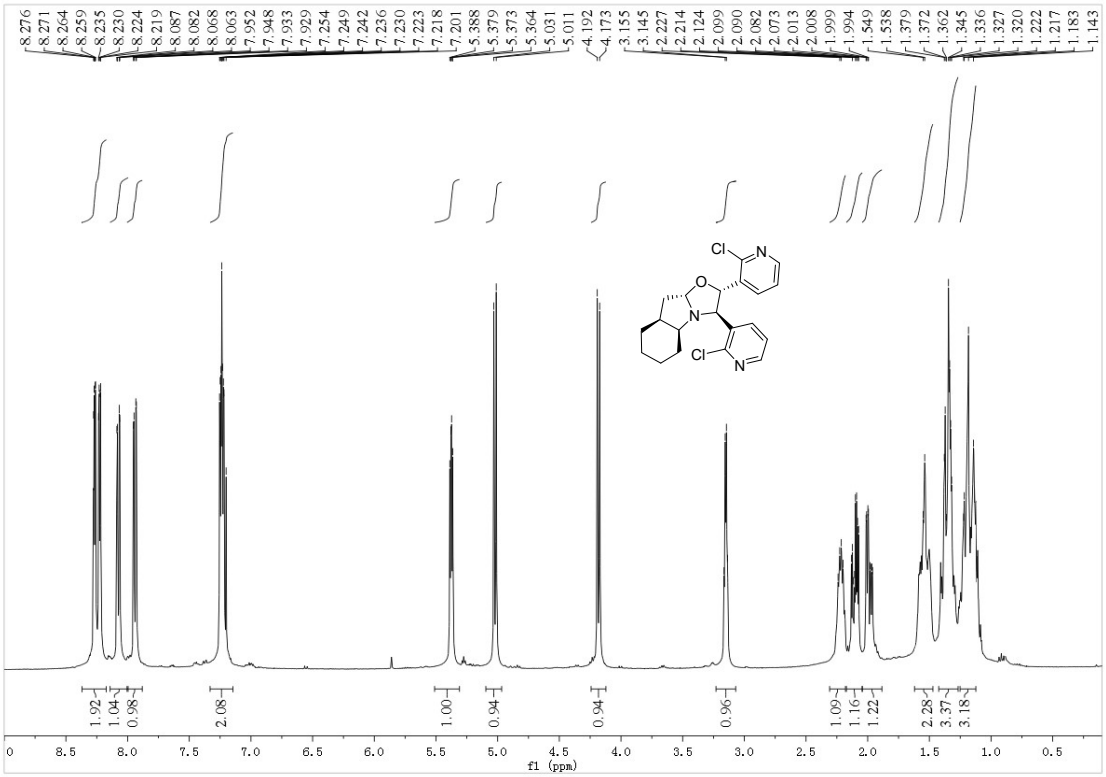


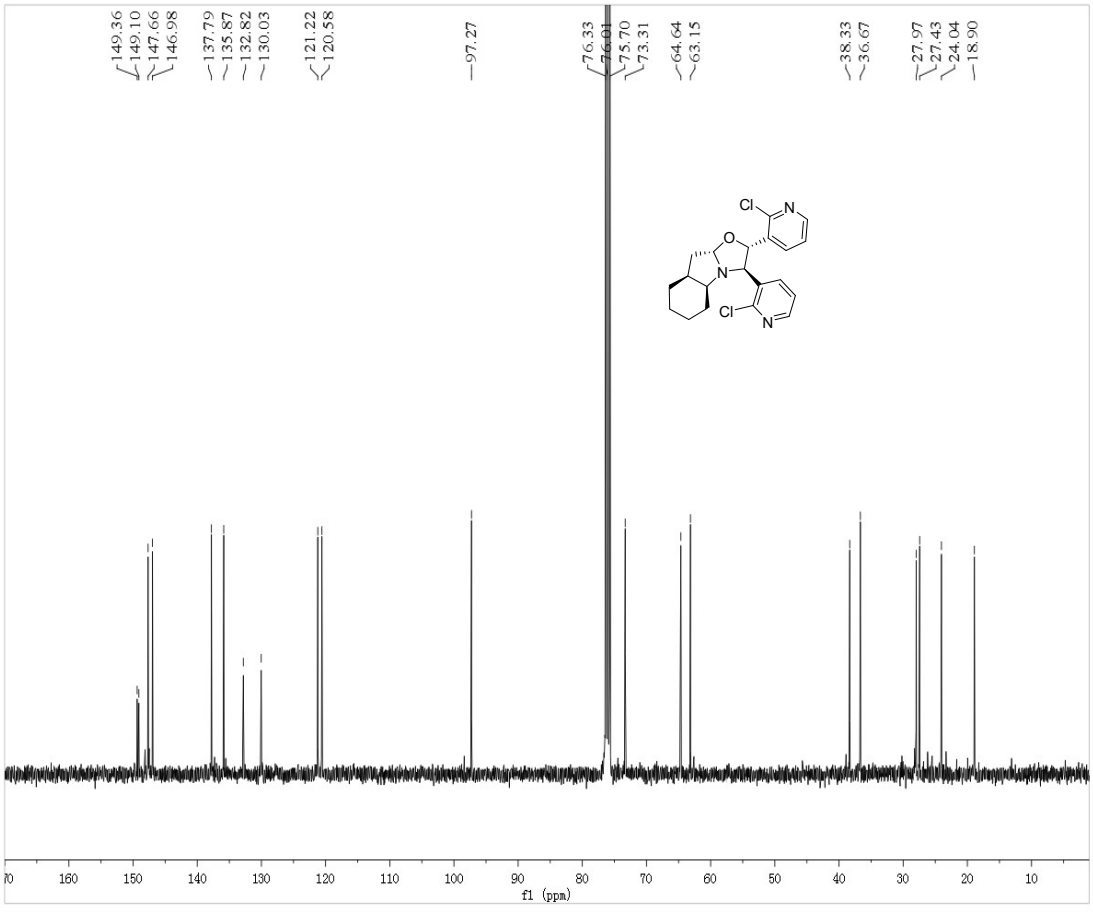
^{1}H and ^{13}C NMR of 3k-2



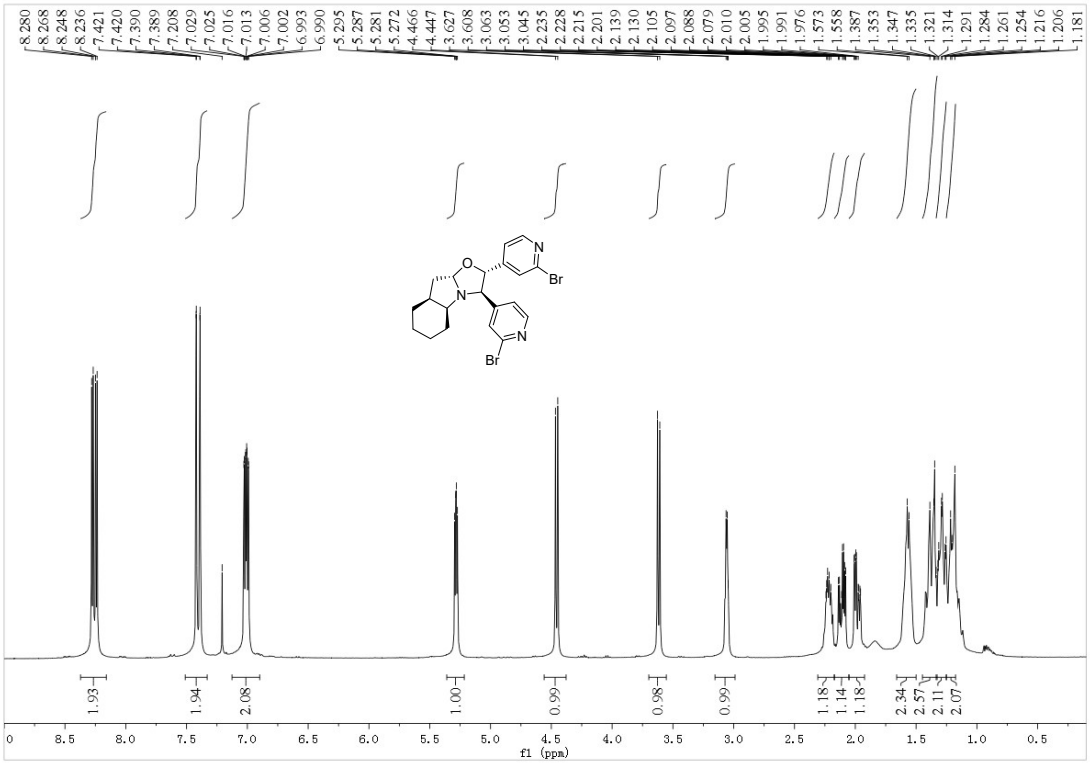


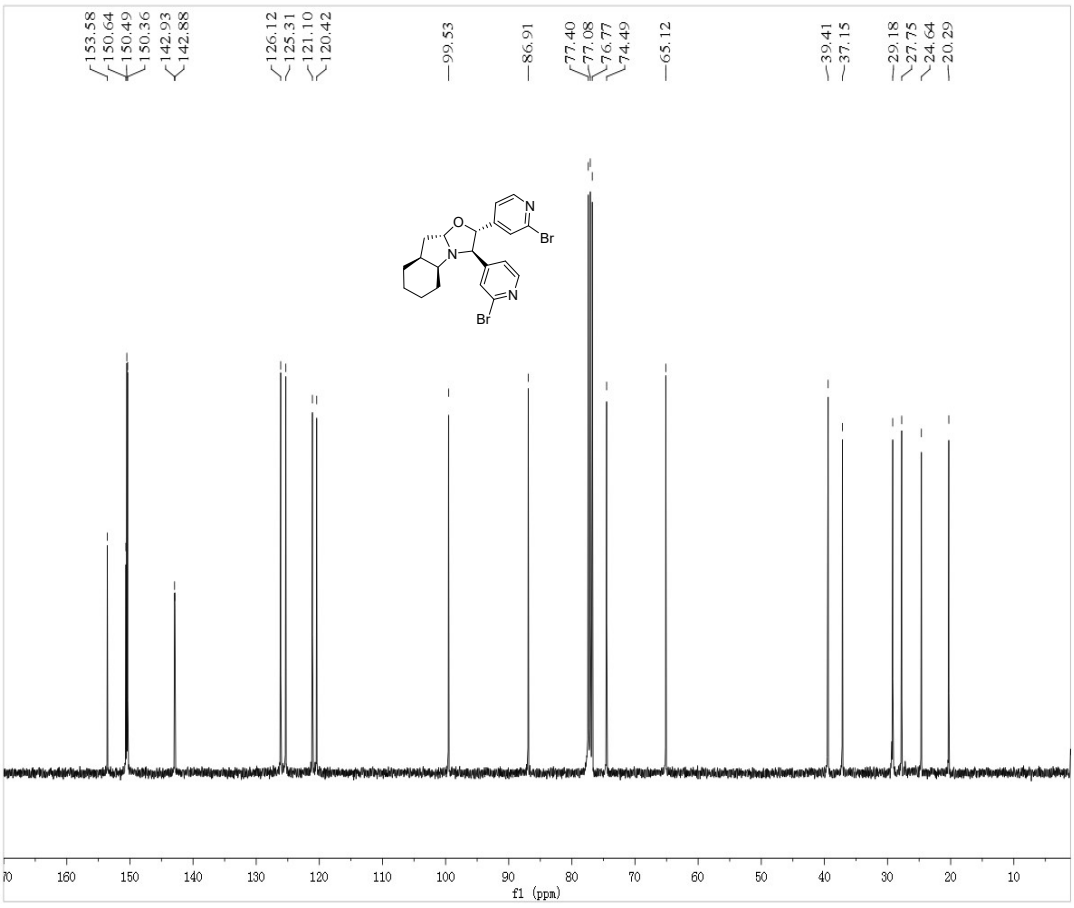
^{1}H and ^{13}C NMR of 3l



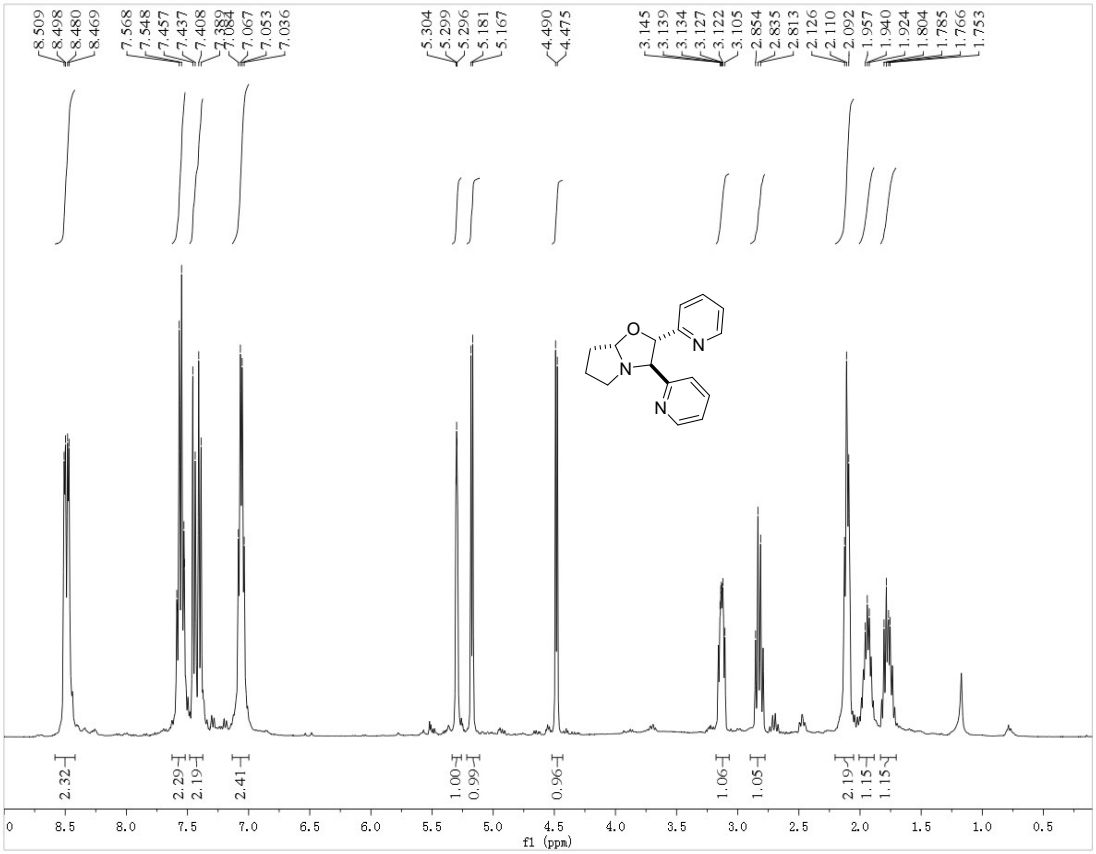


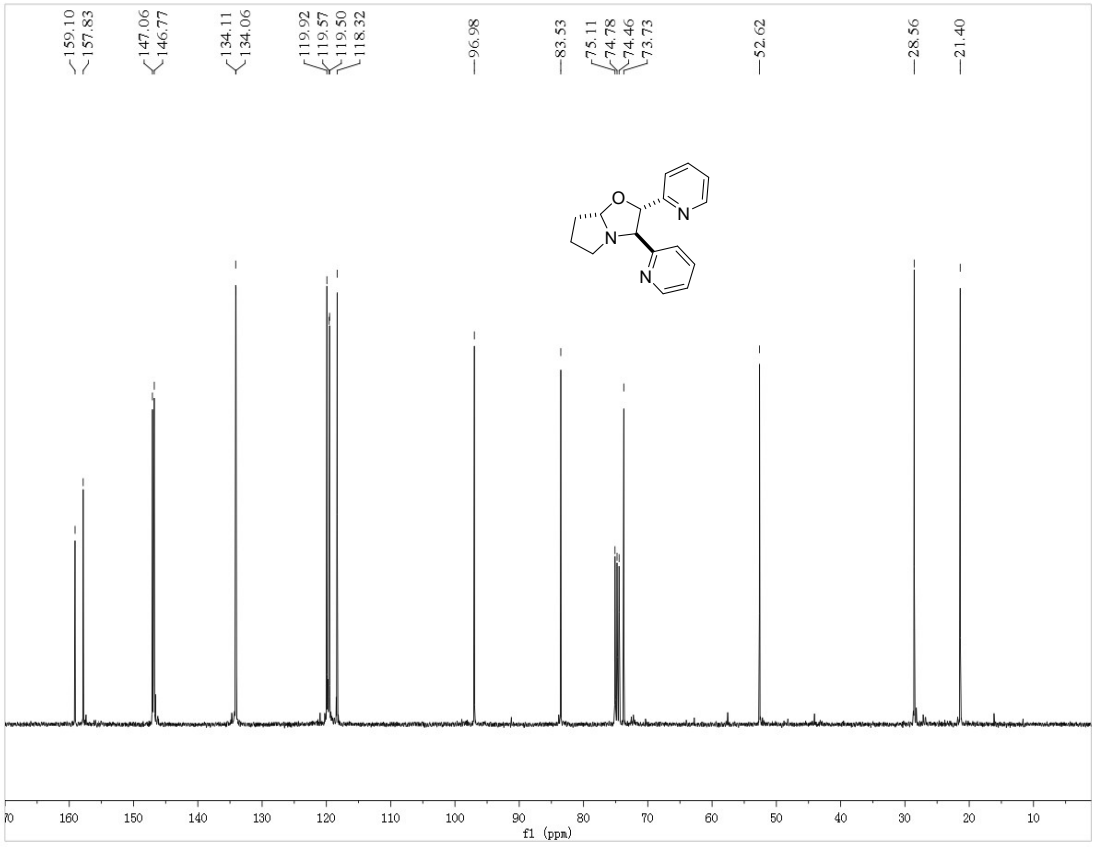
^{1}H and ^{13}C NMR of 3m



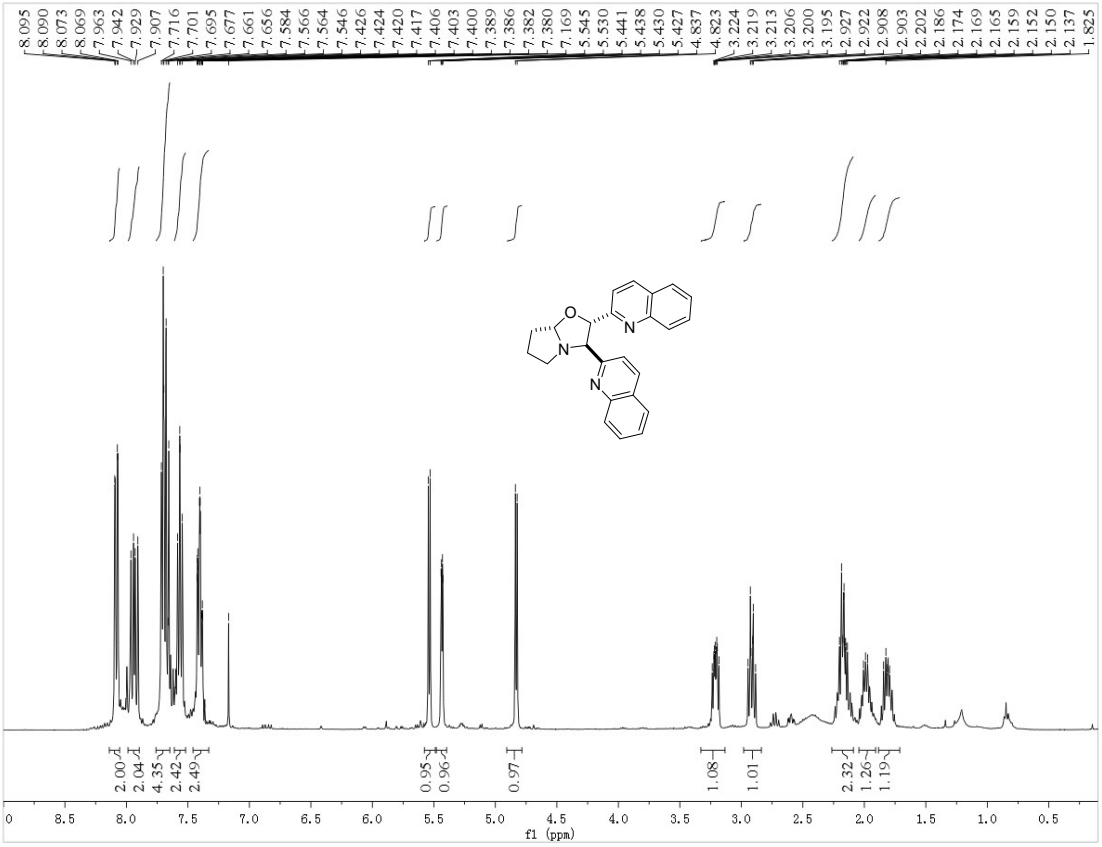


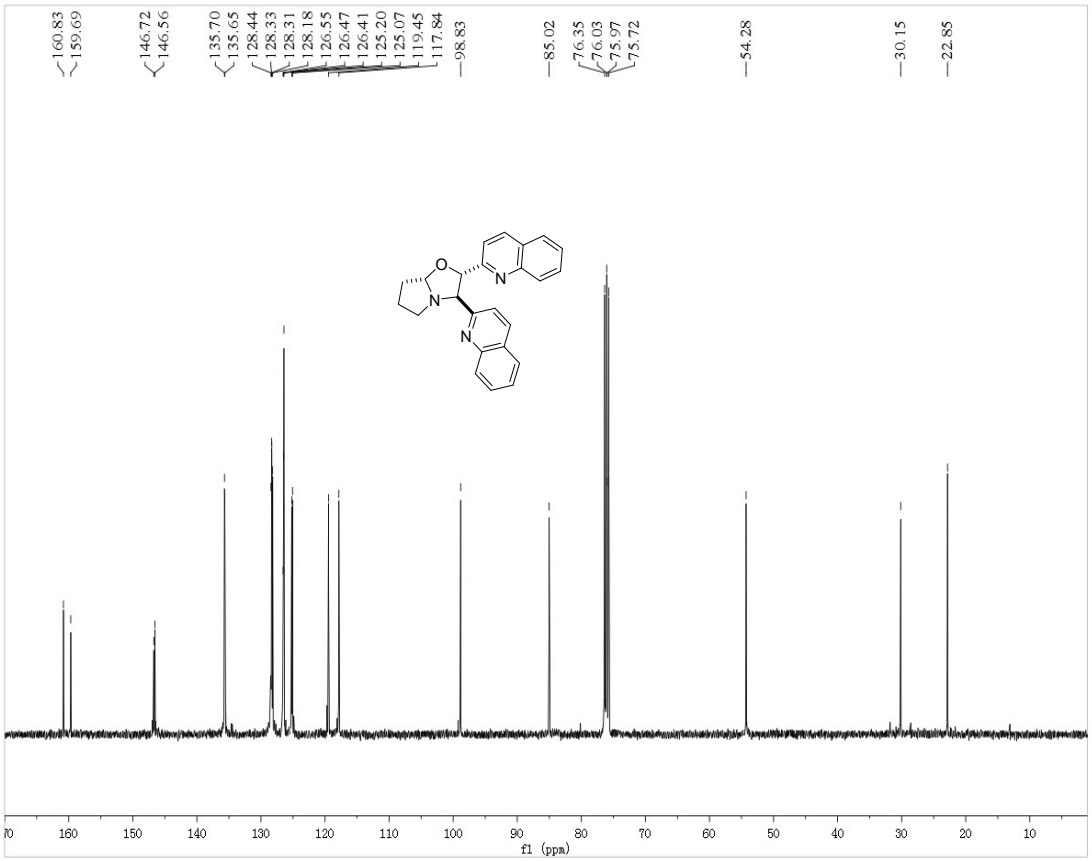
^{1}H and ^{13}C NMR of 4a



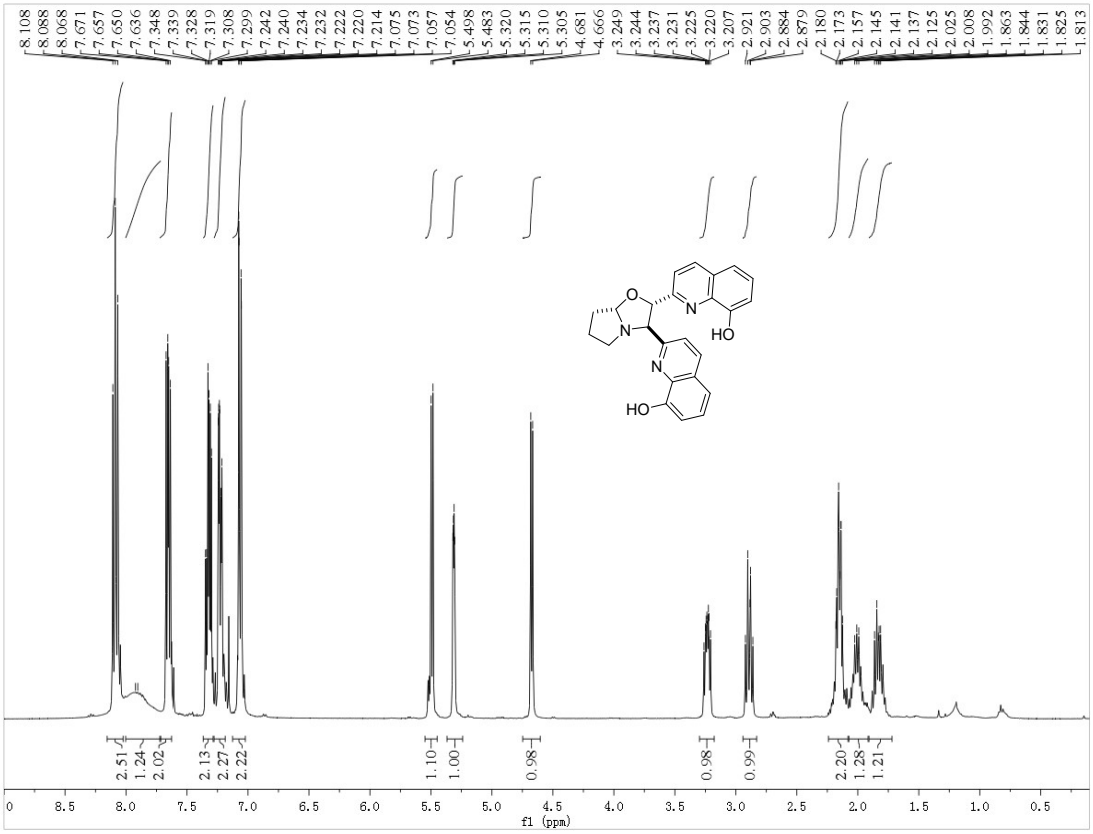


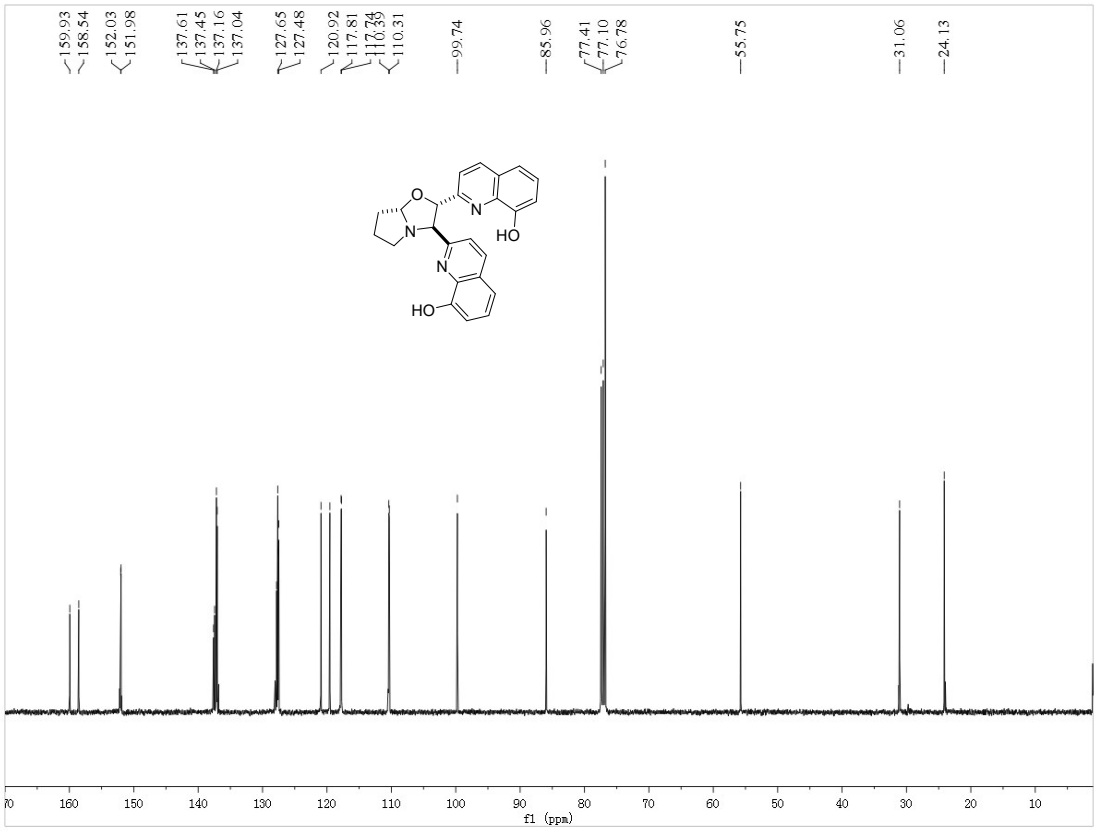
^{1}H and ^{13}C NMR of 4b



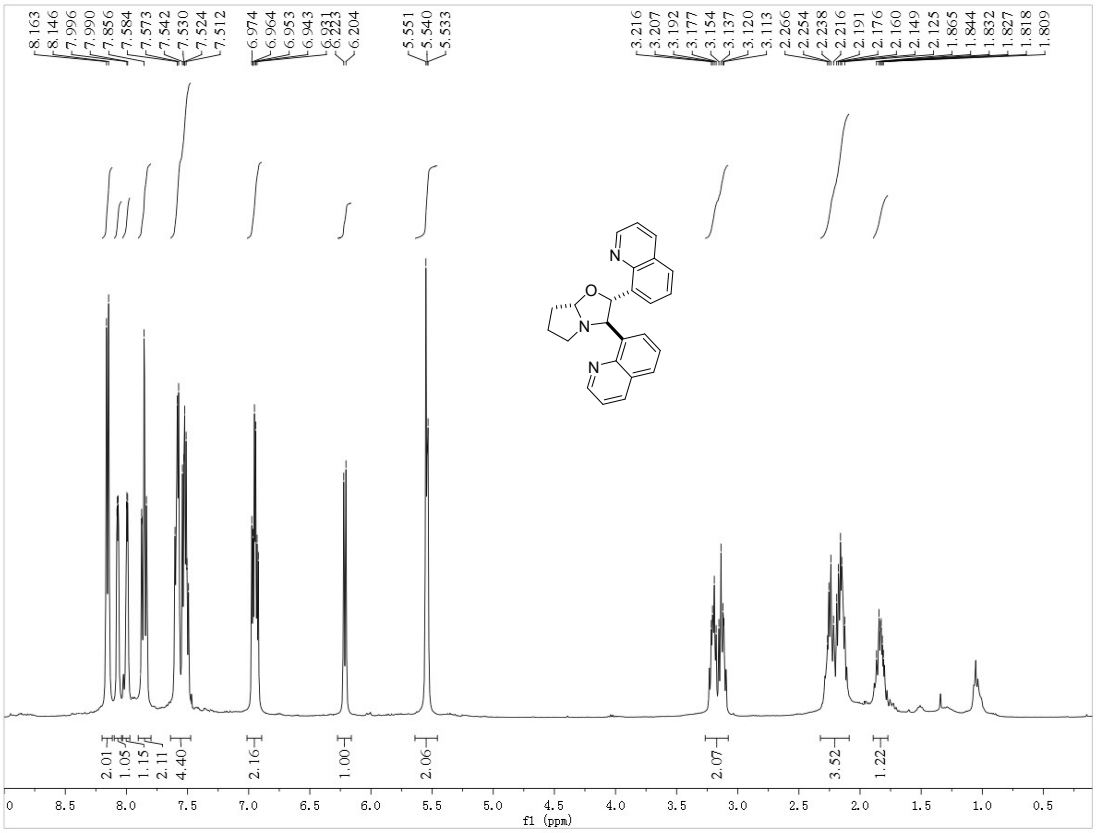


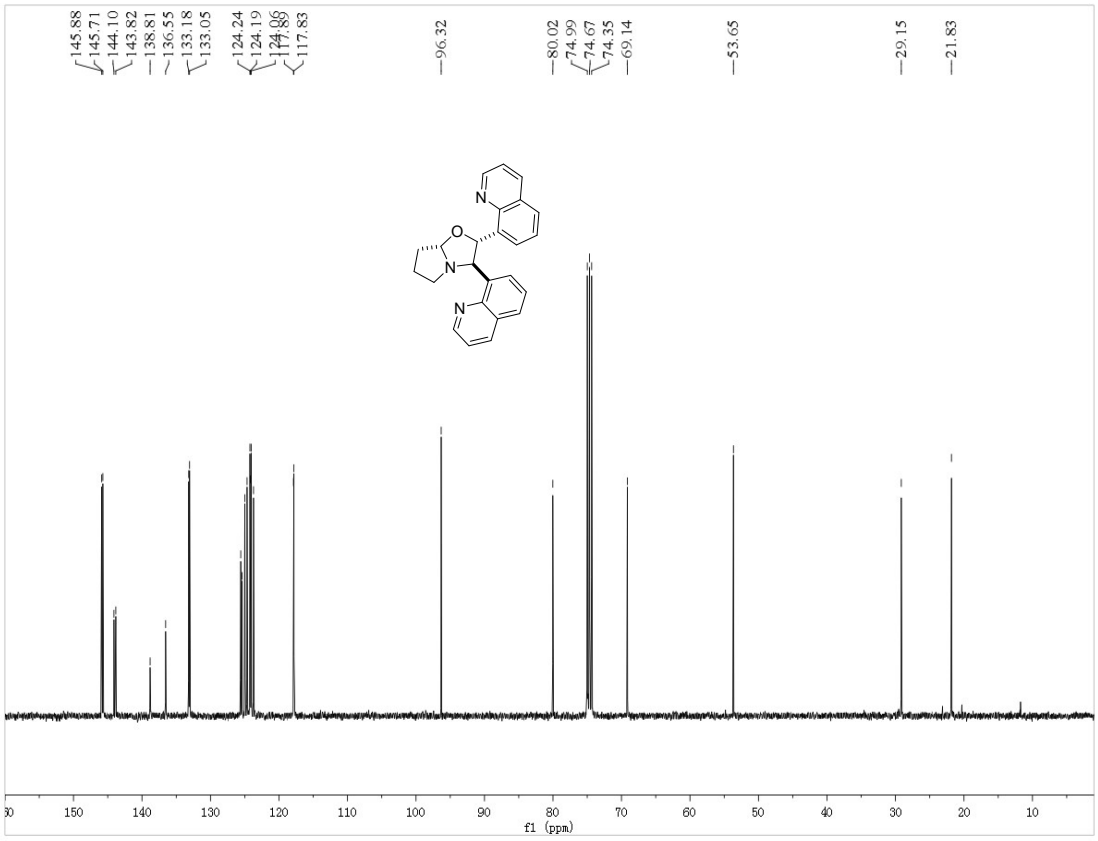
^{1}H and ^{13}C NMR of 4c



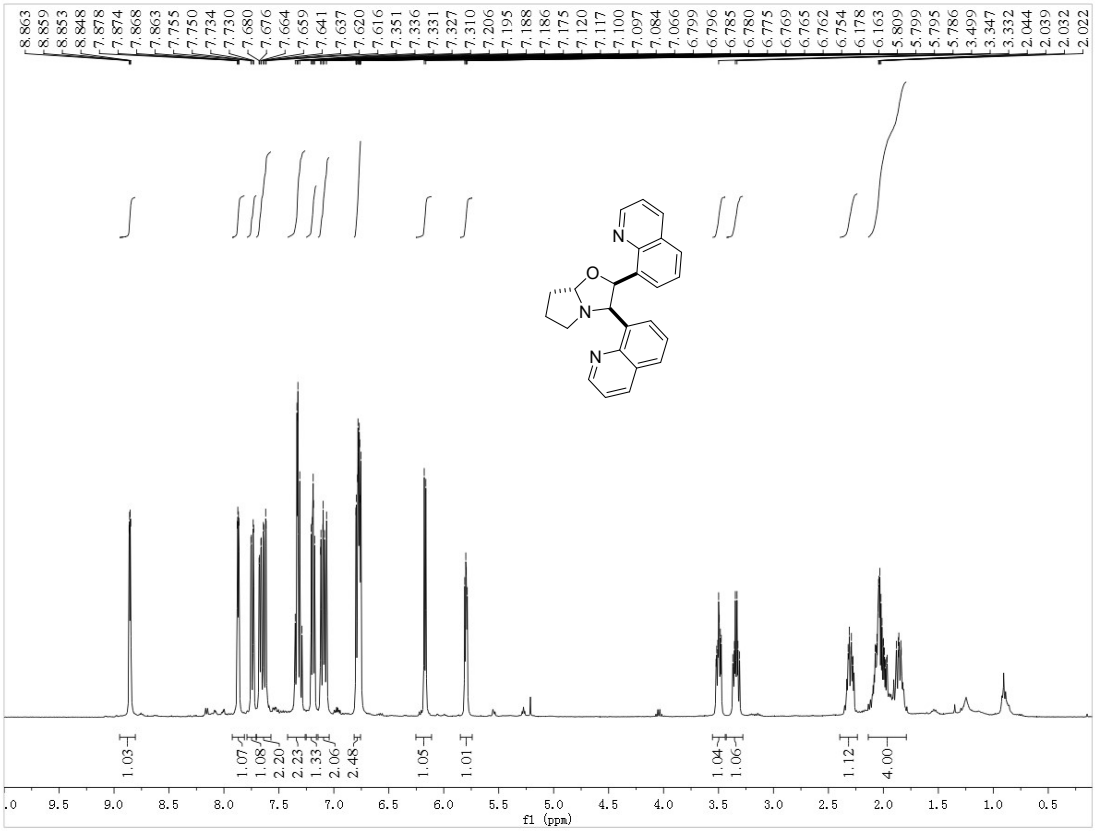


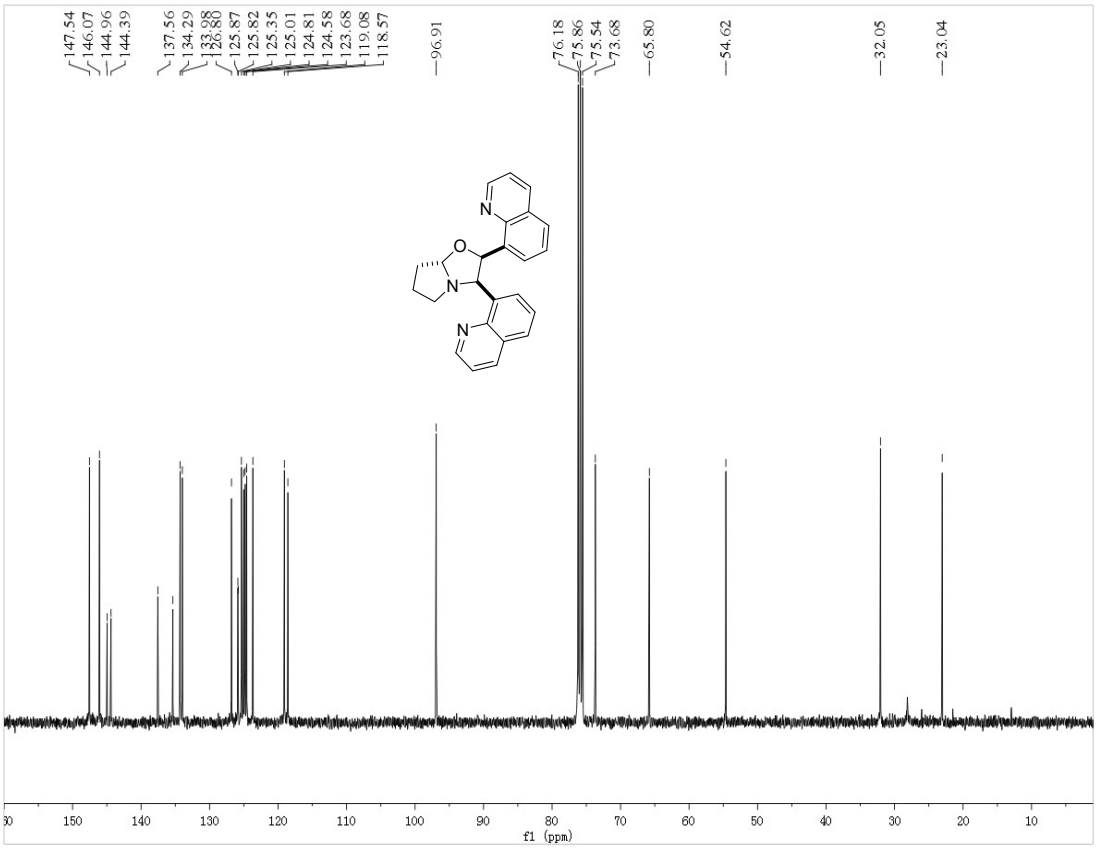
^{1}H and ^{13}C NMR of 4d-1



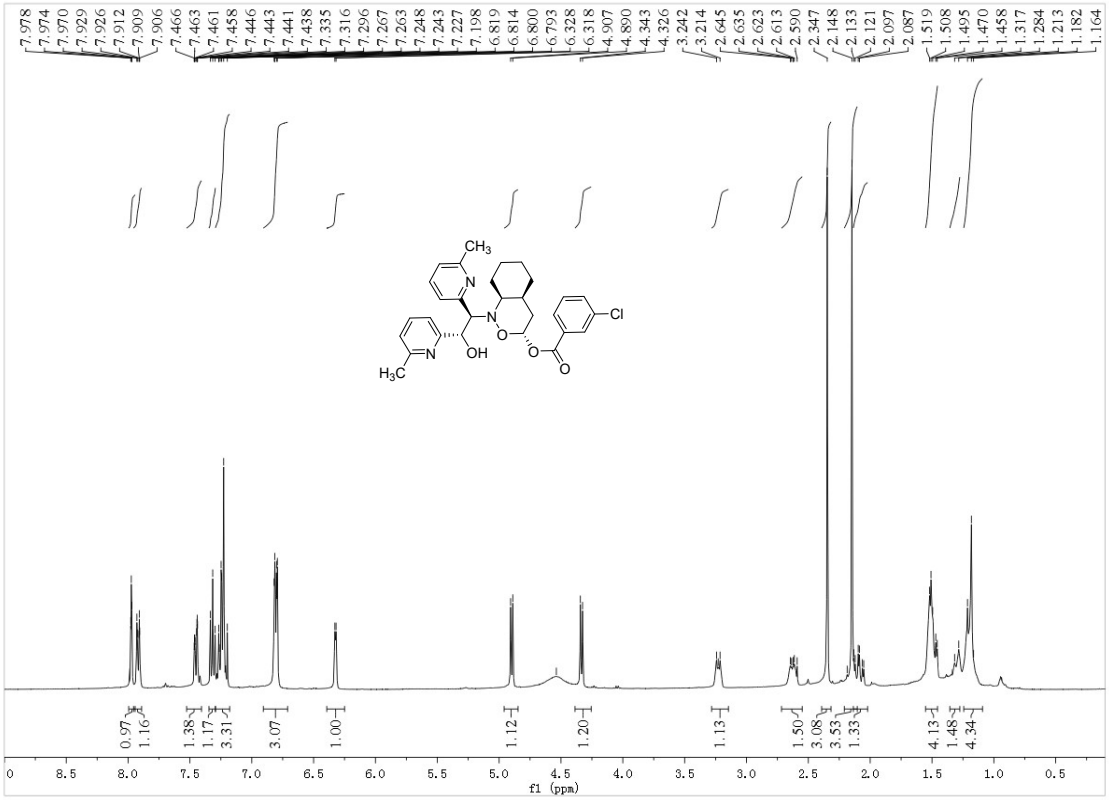


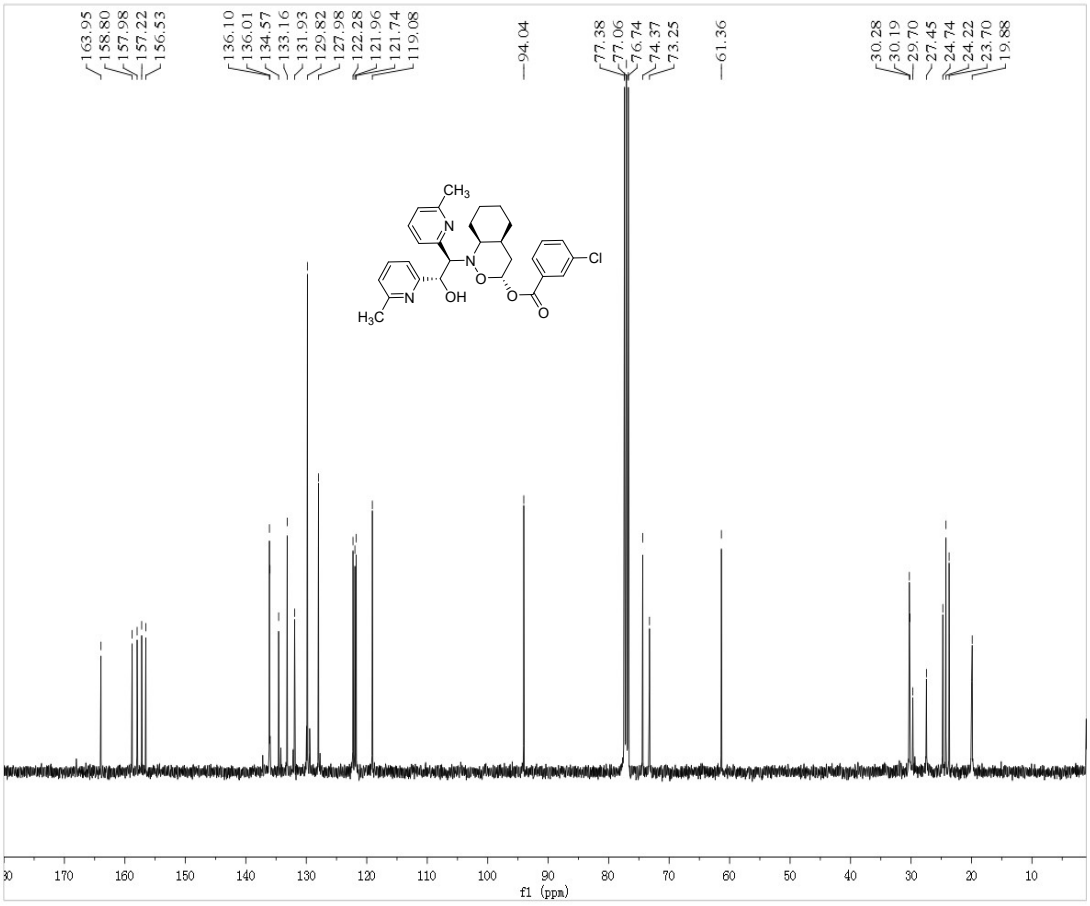
^{1}H and ^{13}C NMR of 4d-2



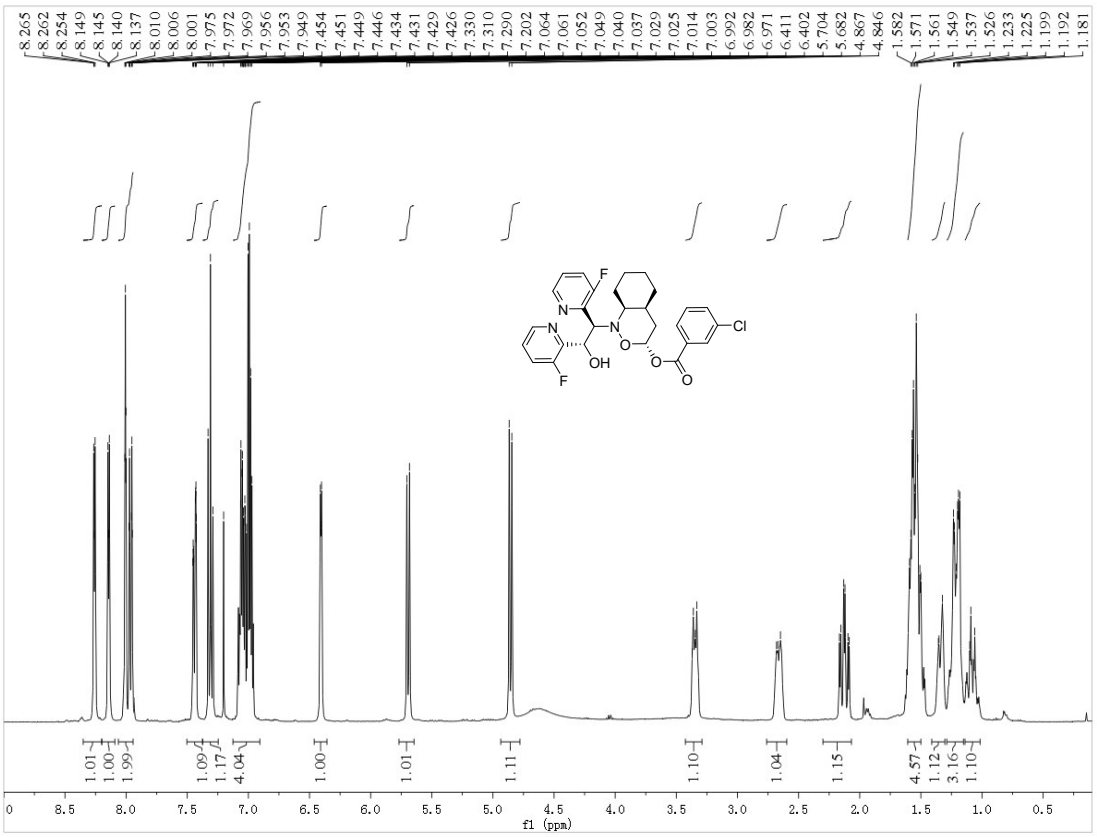


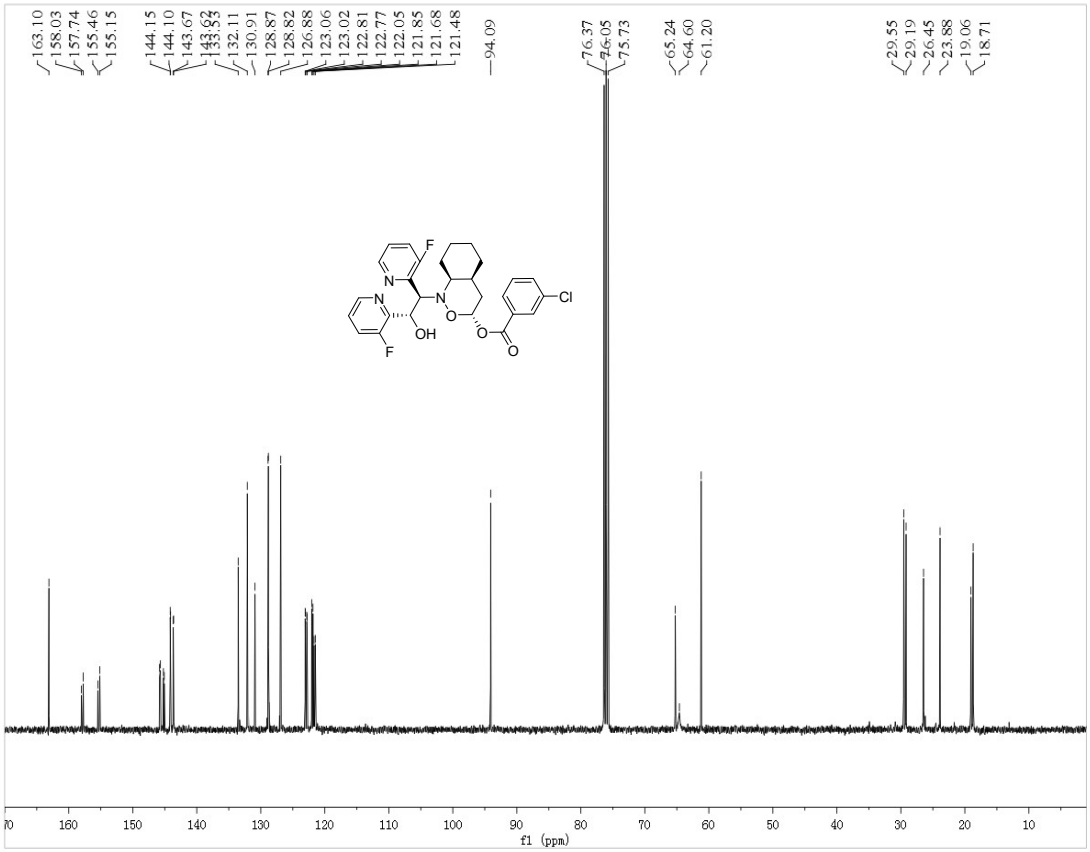
^{1}H and ^{13}C NMR of 6a-1



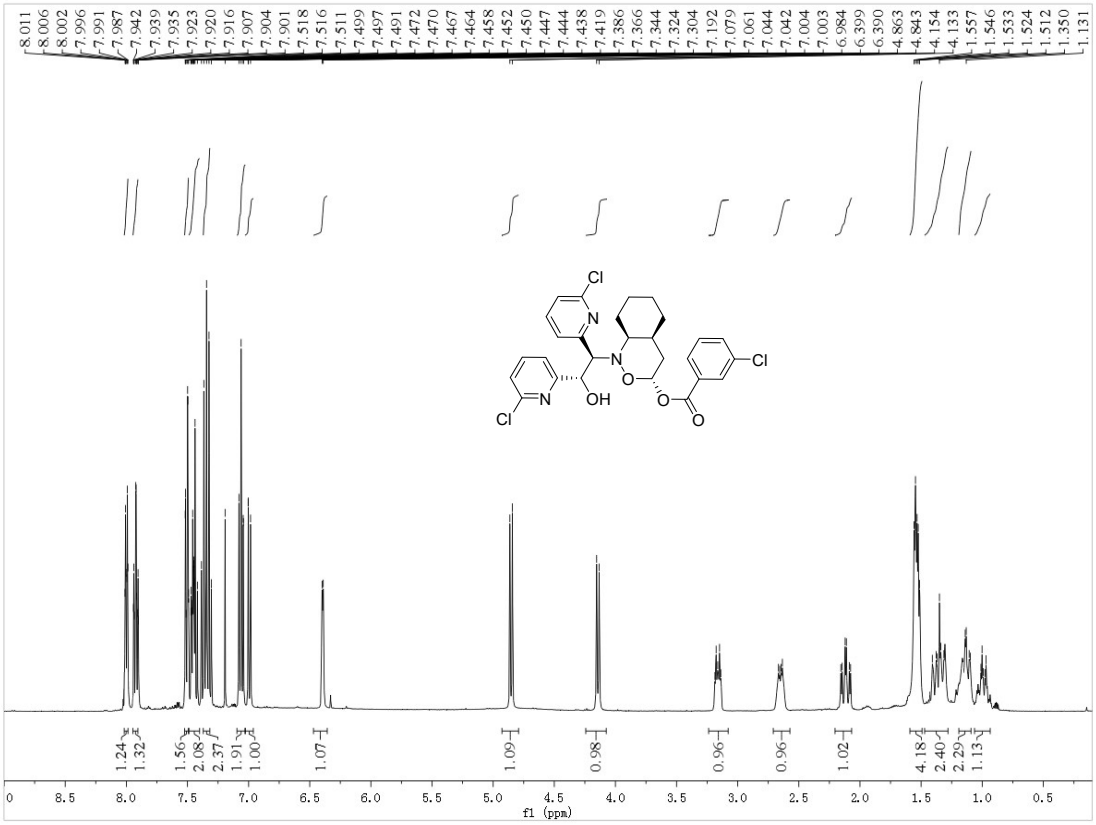


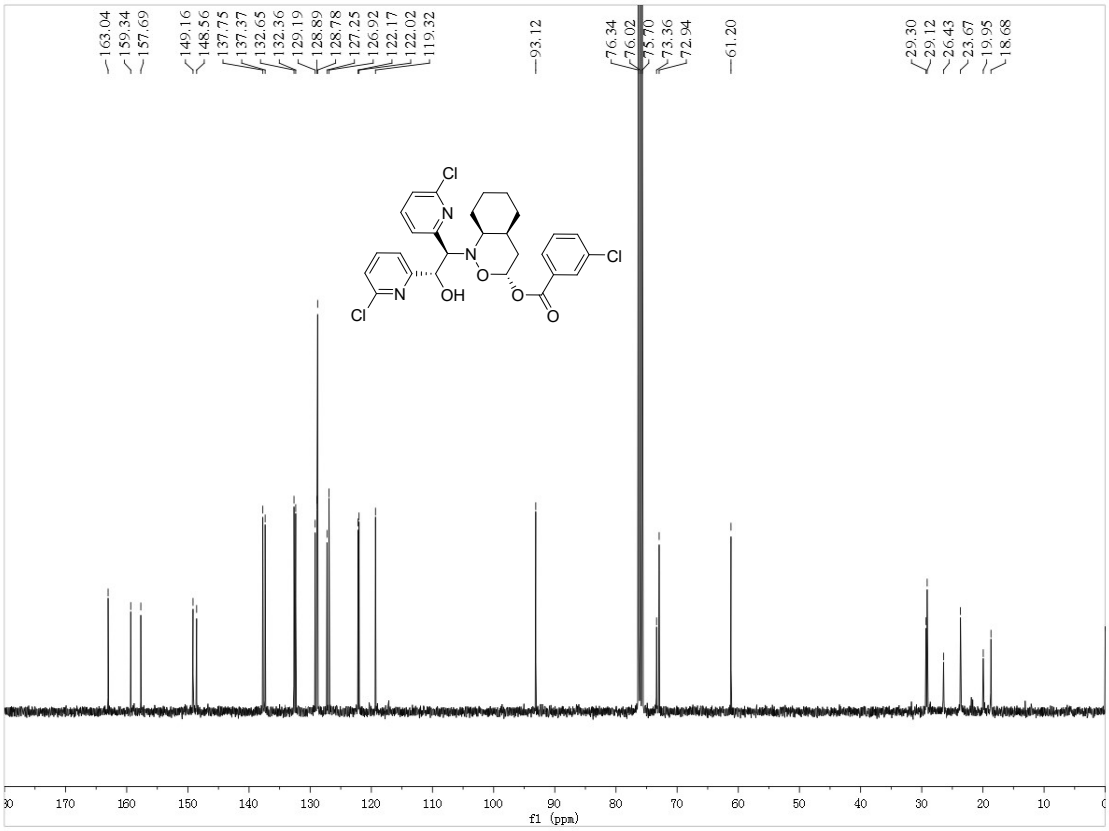
^{1}H and ^{13}C NMR of 6b-1



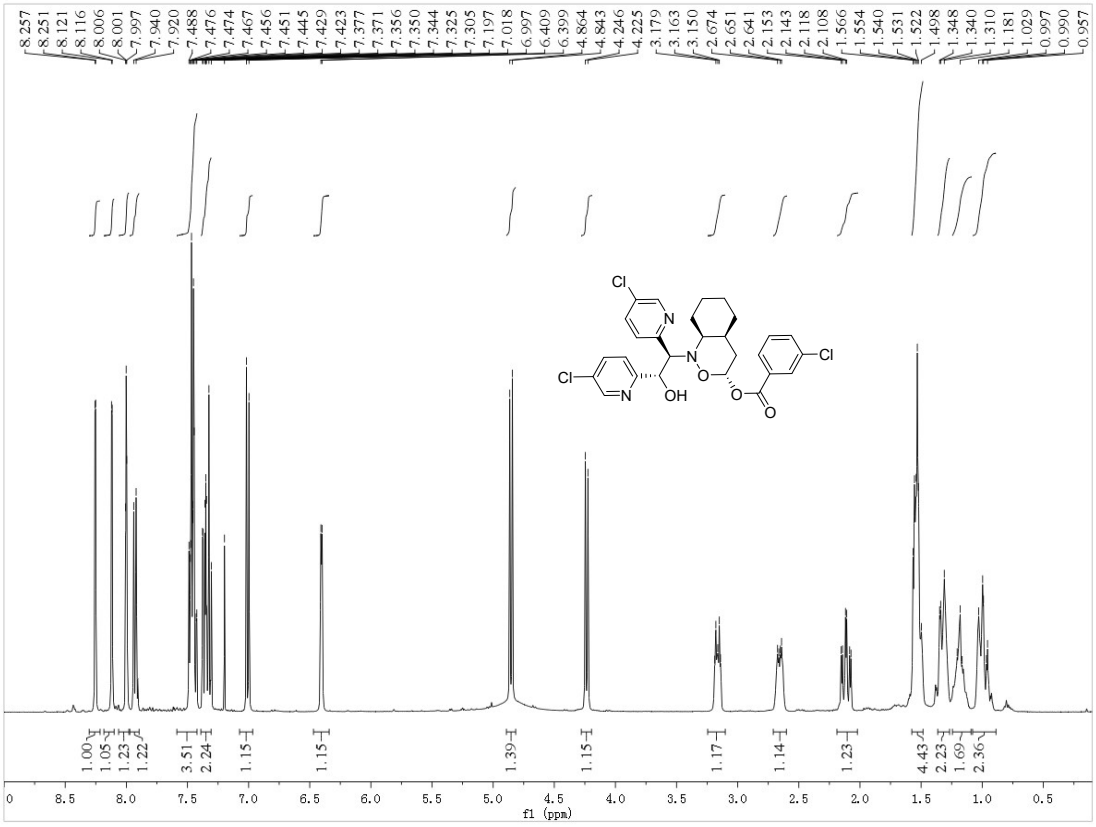


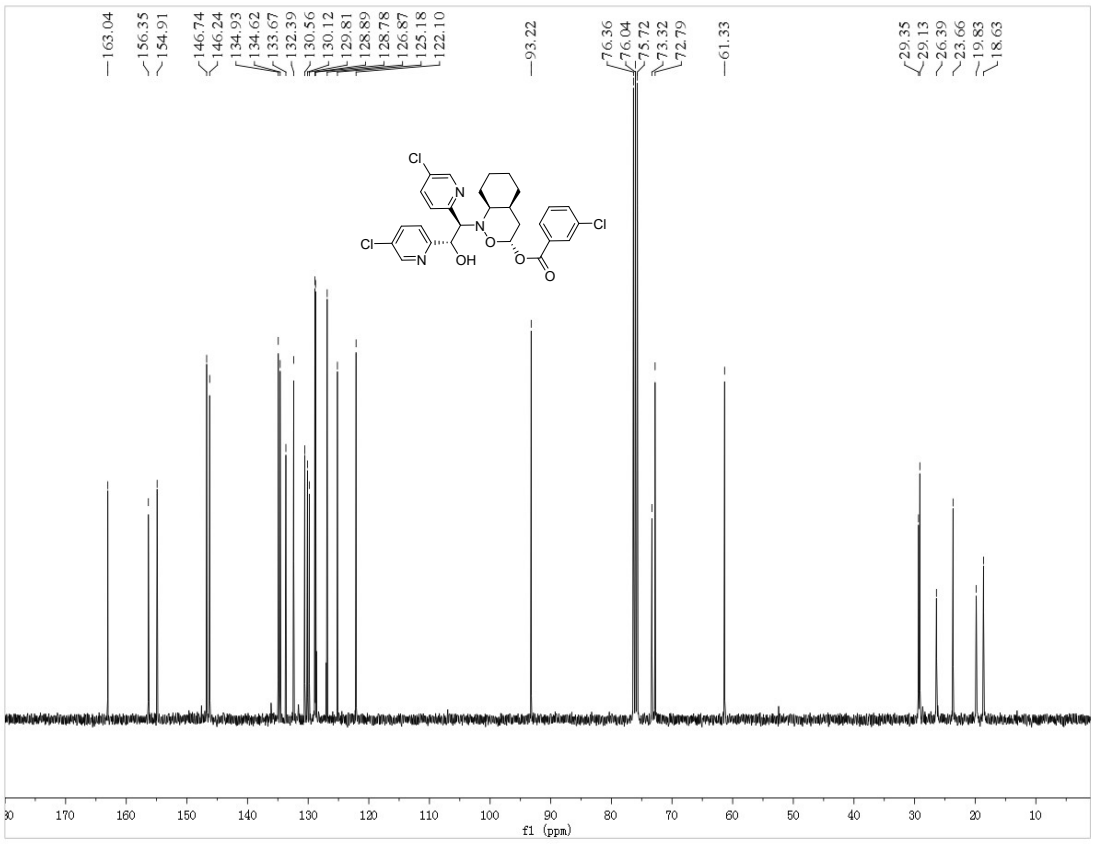
^{1}H and ^{13}C NMR of 6c-1



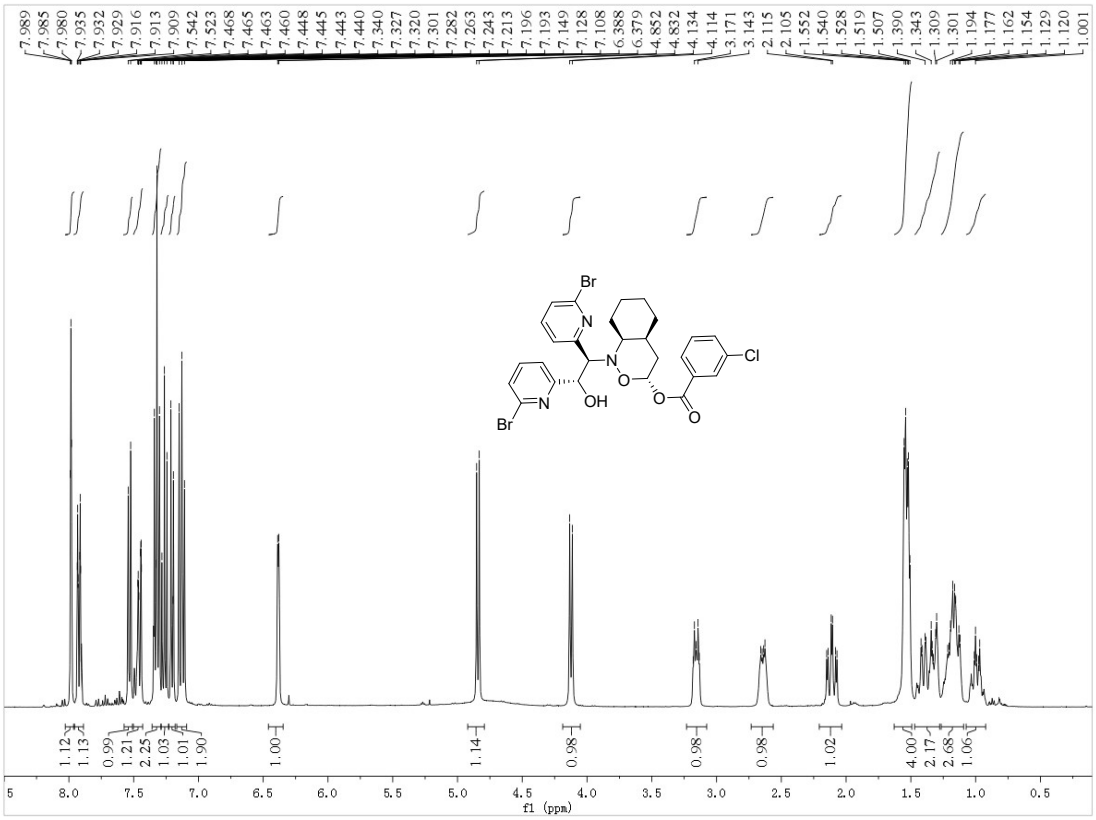


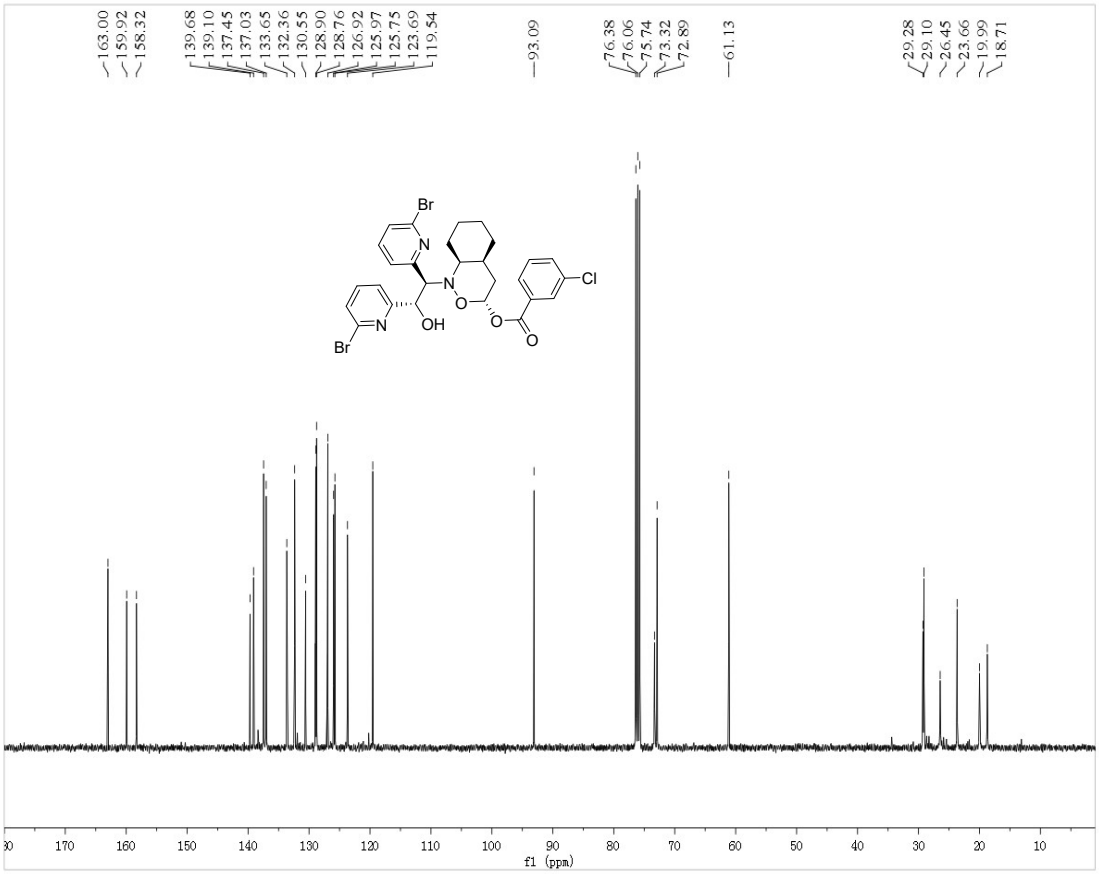
^{1}H and ^{13}C NMR of 6d-1



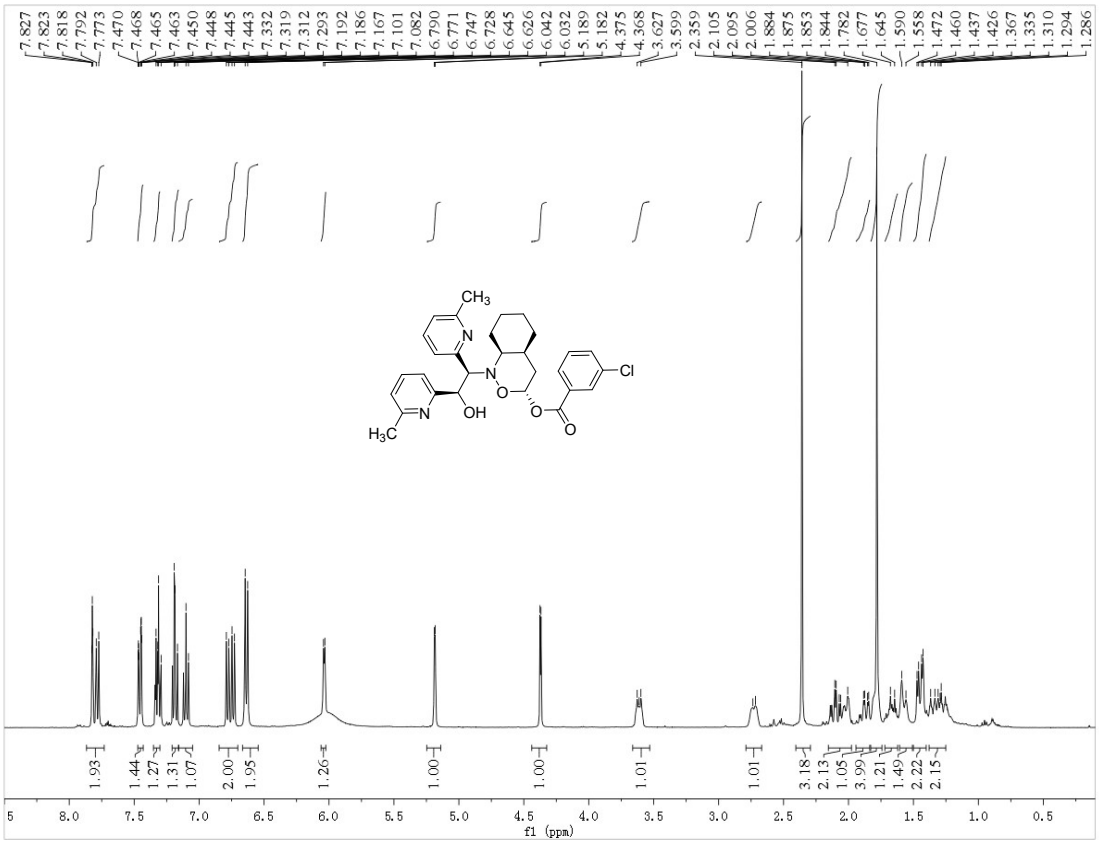


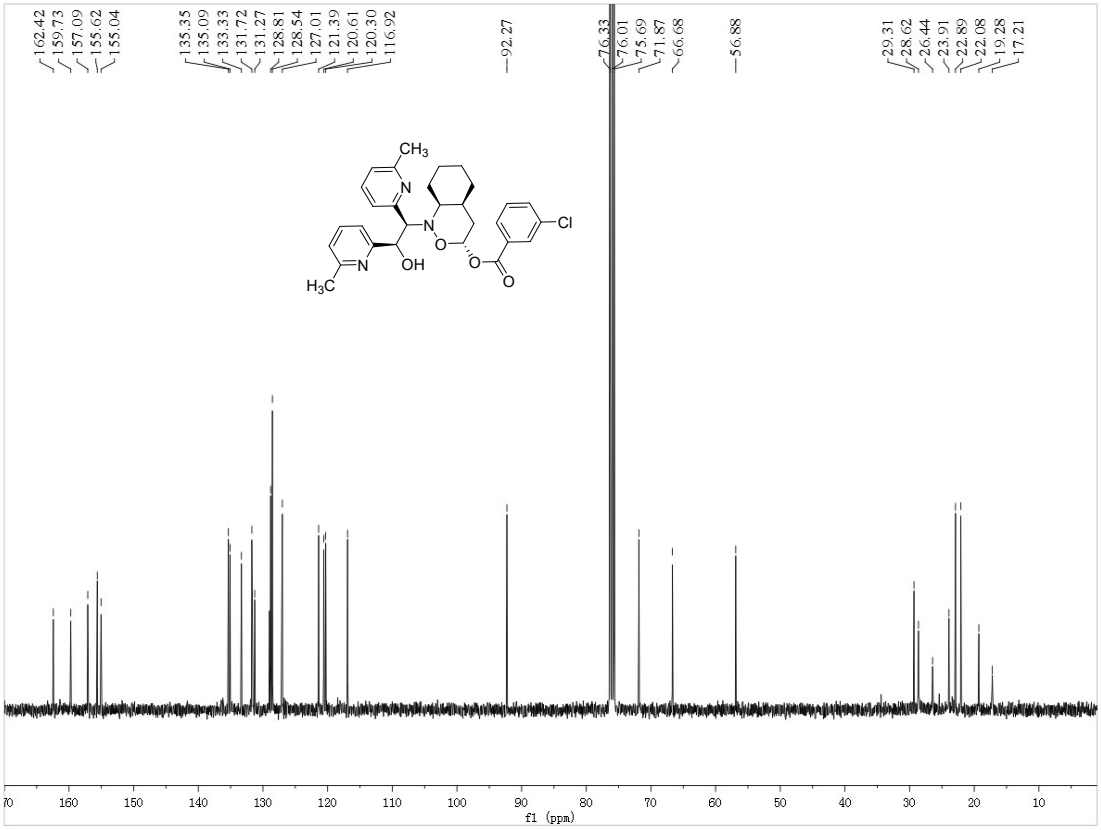
^{1}H and ^{13}C NMR of 6e-1





^{1}H and ^{13}C NMR of 6a-2





^{1}H and ^{13}C NMR of 6f-2