Phen-2NO, a new C_2-symmetric rigid-featured tetradentate ligand and its application in asymmetric alkylation reaction of indoles

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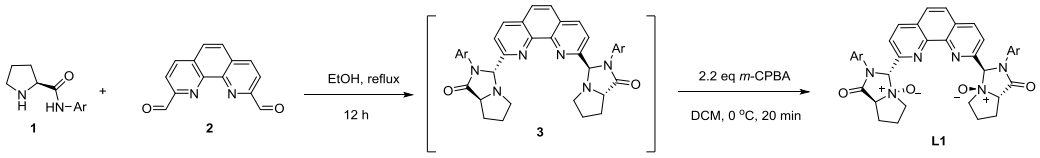
1. General information

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. ^{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.

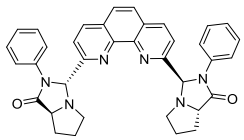
2. General procedure for preparation of chiral Phen-2NO ligands L1



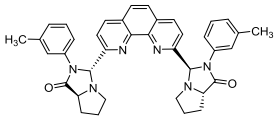
General procedure A-In a sealed tube equipped with a magnetic stirring bar, phenanthroline-dicarbaldehyde **2** (1.0 mmol) and optically pure prolinamide **1** (2.4 mmol, 2.4 equiv) were added. Then, ethanol (6.0 mL) was added and the reaction was heated with stirring at reflux for 12 h. After completion of the reaction, as indicated by TLC, the aftertreatment residue was purified by flash column chromatography to give the intermediate **3**.

For the oxidation step, see: X. Liu, L. Lin and X. Feng, Chiral *N,N'*-dioxide ligands: synthesis, coordination chemistry and asymmetric catalysis, *Org. Chem. Front.*, 2014, **1**, 298-302. In a sealed tube equipped with a magnetic stirring bar, to the intermediate **3** was added 3.0 mL of DCM and *m*-CPBA (2.2 eq). The reaction mixture was stirred at 0 ^{o}C for 20 min. After completion of the reaction, as indicated by TLC, the aftertreatment residue was purified by flash column chromatography to furnish the Phen-2NO ligand **L1**.

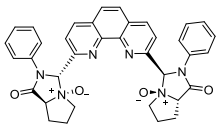
3. Characterization data of compounds 3 and ligands L



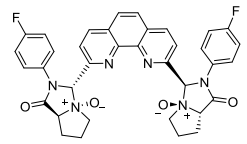
3a: Light yellow solid, yield 73%, >20:1 dr; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.84-1.89 (m, 4H), 2.18-2.23 (m, 4H), 3.04-3.10 (m, 2H), 3.47-3.52 (m, 2H), 4.23-4.26 (m, 2H), 6.15 (s, 2H), 6.95-6.99 (m, 2H), 7.14-7.18 (m, 4H), 7.47 (d, J = 8.0 Hz, 2H), 7.58-7.61 (m, 6H), 8.09 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 23.7, 26.9, 55.3, 63.8, 83.6, 118.3, 120.0, 123.9, 125.3, 127.3, 127.8, 136.2, 136.4, 144.5, 157.5, 173.9; HRMS (ESI-TOF) m/z: Calcd. for $C_{36}H_{32}N_6NaO_2$ $[M+Na]^+$: 603.2479; Found: 603.2467.



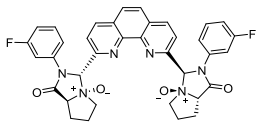
3i: Light yellow solid, yield 74%, >20:1 dr; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.84-1.90 (m, 4H), 2.17-2.22 (m, 10H), 3.04-3.11 (m, 2H), 3.48-3.54 (m, 2H), 4.20-4.23 (m, 2H), 6.16 (s, 2H), 6.79 (d, J = 7.2 Hz, 2H), 7.01-7.05 (m, 2H), 7.25-7.28 (m, 2H), 7.46 (d, J = 8.4 Hz, 2H), 7.52 (s, 2H), 7.62 (s, 2H), 8.10 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.5, 22.9, 26.1, 54.5, 63.0, 82.8, 116.4, 117.5, 119.9, 124.1, 124.5, 126.5, 126.8, 135.4, 135.6, 136.9, 143.8, 156.8, 173.1; HRMS (ESI-TOF) m/z: Calcd. for $C_{38}H_{36}N_6NaO_2$ $[M+Na]^+$: 631.2792; Found: 631.2787.



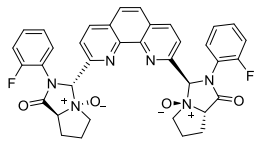
L1a (Prepared according to general procedure A): Light yellow solid, M.p. 256.3-256.9 ^{o}C, overall yield 42%, >20:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 2.24-2.26 (m, 2H), 2.50-2.58 (m, 2H), 2.64-2.82 (m, 4H), 3.97-4.01 (m, 2H), 4.19-4.27 (m, 2H), 5.43 (d, J = 7.6 Hz, 2H), 6.92 (s, 2H), 7.09-7.13 (m, 2H), 7.22-7.26 (m, 4H), 7.44-7.46 (m, 4H), 7.80-7.83 (m, 2H), 7.97 (d, J = 8.0 Hz, 2H), 8.38-8.40 (m, 2H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 22.0, 24.8, 71.0, 77.4, 87.4, 122.6, 126.0, 126.4, 127.3, 128.9, 129.7, 135.7, 137.2, 145.8, 151.7, 169.5; HRMS (ESI-TOF) m/z: Calcd. for $C_{36}H_{32}N_6NaO_4$ $[M+Na]^+$: 635.2371; Found: 635.2363.



L1b (Prepared according to general procedure A): Light yellow solid, M.p. 243.5-244.4 ^{o}C, overall yield 38%, 20:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 2.25-2.27 (m, 2H), 2.54-2.56 (m, 2H), 2.62-2.67 (m, 2H), 2.76-2.78 (m, 2H), 4.02 (s, 2H), 4.27 (d, J = 9.6 Hz, 2H), 5.44 (s, 2H), 6.90-6.93 (m, 2H), 6.97-7.03 (m, 4H), 7.46-7.51 (m, 4H), 7.81-7.87 (m, 2H), 7.95-7.99 (m, 2H), 8.41-8.45 (m, 2H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 22.1, 24.7, 71.1, 77.2, 87.7, 115.6 (d, J_{CF} = 23.0 Hz), 125.5 (d, J_{CF} = 9.3 Hz), 126.1, 127.3, 129.8, 131.6 (d, J_{CF} = 3.3 Hz), 137.3, 145.9, 151.6, 161.5 (d, J_{CF} = 244.1 Hz), 169.6; HRMS (ESI-TOF) m/z: Calcd. for $C_{36}H_{30}F_2N_6NaO_4$ $[M+Na]^+$: 671.2189; Found: 671.2177.

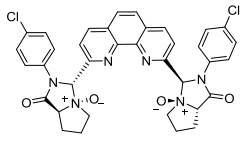


L1c (Prepared according to general procedure A): Light yellow solid, M.p. 231.1-232.2 ^{o}C, overall yield 35%, 15:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 2.25-2.27 (m, 2H), 2.51-2.61 (m, 2H), 2.66-2.75 (m, 2H), 2.76-2.85 (m, 2H), 3.95-4.00 (m, 2H), 4.17-4.25 (m, 2H), 5.39 (d, J = 6.4 Hz, 2H), 6.83-6.88 (m, 2H), 6.99 (s, 2H), 7.17-7.26 (m, 4H), 7.49-7.53 (m, 2H), 7.87 (s, 2H), 8.04 (d, J = 8.0 Hz, 2H), 8.46 (d, J = 8.0 Hz, 2H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 22.0, 24.9, 71.1, 77.3, 86.8, 108.9 (d, J_{CF} = 26.3 Hz), 112.7 (d, J_{CF} = 21.4 Hz), 117.0, 126.0, 127.3, 129.8, 130.4 (d, J_{CF} = 10.1 Hz), 137.3 (d, J_{CF} = 8.4 Hz), 145.8, 151.4, 162.6 (d, J_{CF} = 243.4 Hz), 169.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{36}H_{30}F_2N_6NaO_4$ $[M+Na]^+$: 671.2189; Found: 671.2186.

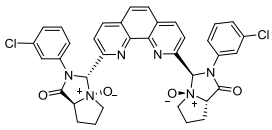


L1d (Prepared according to general procedure A): Light yellow solid, M.p. 263.1-264.0 ^{o}C, overall yield 32%, 13:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 2.25-2.31 (m, 2H), 2.50-2.62 (m, 4H), 2.67-2.73 (m, 2H), 4.03-4.07 (m, 2H), 4.32-4.39 (m, 2H), 5.43-5.45 (m, 2H), 6.73 (s, 2H), 6.91-6.95 (m, 2H), 7.00-7.10 (m, 2H), 7.19-7.29 (m, 4H), 7.89-7.94 (m, 4H), 8.43-8.46 (m, 2H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 22.1, 24.7, 71.3, 76.7, 87.6, 116.1 (d, J_{CF} = 20.3 Hz), 121.9 (d,

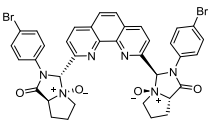
J_{CF} = 12.1 Hz), 124.8 (d, J_{CF} = 4.4 Hz), 126.1, 127.4, 129.5, 129.9, 130.2 (d, J_{CF} = 8.5 Hz), 137.2, 146.0, 151.5, 158.4 (d, J_{CF} = 248.2 Hz), 170.1; HRMS (ESI-TOF) m/z: Calcd. for $C_{36}H_{30}F_2N_6NaO_4$ [M+Na]$^+$: 671.2184; Found: 671.2170.



L1e (Prepared according to general procedure A): Light yellow solid, M.p. 255.7-256.5 ^{o}C, overall yield 36%, 13:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 2.25-2.27 (m, 2H), 2.55-2.58 (m, 2H), 2.68-2.71 (m, 2H), 2.77-2.83 (m, 2H), 4.00-4.02 (m, 2H), 4.22-4.27 (m, 2H), 5.43 (s, 2H), 6.95-6.99 (m, 2H), 7.23-7.28 (m, 4H), 7.47-7.54 (m, 4H), 7.76-7.85 (m, 2H), 7.99-8.03 (m, 2H), 8.39-8.44 (m, 2H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 22.1, 24.8, 71.1, 77.3, 87.2, 124.1, 126.1, 127.3, 129.0, 129.8, 131.7, 134.4, 137.4, 145.8, 151.5, 169.5; HRMS (ESI-TOF) m/z: Calcd. for $C_{36}H_{30}Cl_2N_6NaO_4$ [M+Na]$^+$: 703.1578; Found: 703.1566.

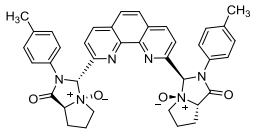


L1f (Prepared according to general procedure A): Light yellow solid, M.p. 257.1-258.3 ^{o}C, overall yield 32%, 12:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 2.25-2.27 (m, 2H), 2.51-2.59 (m, 2H), 2.67-2.74 (m, 2H), 2.76-2.82 (m, 2H), 3.95-3.99 (m, 2H), 4.17-4.25 (m, 2H), 5.38 (d, J = 6.8 Hz, 2H), 6.99 (s, 2H), 7.11-7.13 (m, 2H), 7.17-7.21 (m, 2H), 7.31-7.33 (m, 2H), 7.68 (d, J = 2.0 Hz, 2H), 7.85 (s, 2H), 8.04 (d, J = 8.4 Hz, 2H), 8.45 (d, J = 8.4 Hz, 2H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 22.0, 24.9, 71.1, 77.3, 86.8, 120.0, 121.6, 126.0, 126.1, 127.4, 129.8, 130.2, 134.3, 137.1, 137.4, 145.8, 151.4, 169.5; HRMS (ESI-TOF) m/z: Calcd. for $C_{36}H_{30}Cl_2N_6NaO_4$ [M+Na]$^+$: 703.1589; Found: 703.1577.

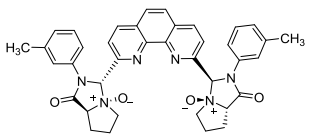


L1g (Prepared according to general procedure A): Light yellow solid, M.p. 257.7-258.9 ^{o}C, overall yield 35%, 15:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 2.25-2.27 (m, 2H), 2.53-2.57 (m, 2H), 2.66-2.68 (m, 2H), 2.74-2.79 (m, 2H), 3.97-4.01 (m, 2H), 4.20-4.27 (m, 2H), 5.38 (d, J = 8.4 Hz,

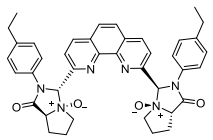
2H), 6.95 (s, 2H), 7.37-7.44 (m, 8H), 7.87-7.89 (m, 2H), 8.00 (d, *J* = 8.4 Hz, 2H), 8.44-8.47 (m, 2H); ^{13}C NMR (CD_3OD, 100 MHz) *δ*: 22.0, 24.8, 71.1, 77.2, 87.1, 119.4, 124.2, 126.1, 127.4, 129.8, 131.9, 134.8, 137.4, 145.8, 151.4, 169.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{36}H_{30}Br_2N_6NaO_4$ $[M+Na]^+$: 791.0569; Found: 791.0550.



L1h (Prepared according to general procedure A): Light yellow solid, M.p. 264.9-265.5 ^{o}C, overall yield 32%, 12:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) *δ*: 2.17 (s, 3H), 2.23-2.24 (m, 2H), 2.52-2.57 (m, 2H), 2.66-2.70 (m, 2H), 2.74-2.79 (m, 2H), 3.97-4.01 (m, 2H), 4.19-4.27 (m, 2H), 5.44 (d, *J* = 11.6 Hz, 2H), 6.88 (s, 2H), 7.05 (d, *J* = 8.4 Hz, 4H), 7.28-7.34 (m, 4H), 7.71 (s, 2H), 7.94 (d, *J* = 8.0 Hz, 2H), 8.31 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (CD_3OD, 100 MHz) *δ*: 23.5, 25.9, 28.7, 75.0, 81.3, 91.6, 126.7, 129.9, 131.2, 133.3, 133.6, 137.0, 140.6, 141.1, 149.8, 155.7, 173.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{38}H_{36}N_6NaO_4$ $[M+Na]^+$: 663.2682; Found: 663.2675.

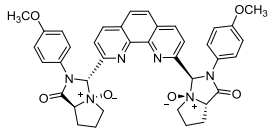


L1i (Prepared according to general procedure A): Light yellow solid, M.p. 262.1-263.3 ^{o}C, overall yield 31%, 11:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) *δ*: 2.22-2.26 (m, 8H), 2.50-2.57 (m, 2H), 2.65-2.80 (m, 4H), 3.96-4.00 (m, 2H), 4.18-4.25 (m, 2H), 5.44 (s, 2H), 6.90-6.94 (m, 4H), 7.07-7.12 (m, 2H), 7.18-7.22 (m, 2H), 7.31-7.33 (m, 2H), 7.71-7.78 (m, 2H), 7.98 (d, *J* = 8.0 Hz, 2H), 8.32-8.38 (m, 2H); ^{13}C NMR (CD_3OD, 100 MHz) *δ*: 20.0, 22.0, 24.8, 71.0, 77.4, 87.4, 119.5, 122.6, 125.9, 127.1, 127.2, 128.7, 129.7, 135.7, 137.2, 139.1, 145.8, 151.8, 169.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{38}H_{36}N_6NaO_4$ $[M+Na]^+$: 663.2682; Found: 663.2679.

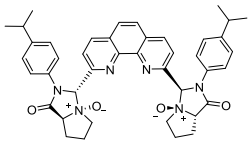


L1j (Prepared according to general procedure A): Light yellow solid, M.p. 238.4-239.5 ^{o}C, overall yield 38%, 18:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) *δ*: 1.03-1.06 (m, 6H), 2.23-2.25 (m, 2H),

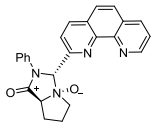
2.44-2.50 (m, 4H), 2.53-2.59 (m, 2H), 2.64-2.81 (m, 4H), 3.98-4.02 (m, 2H), 4.20-4.27 (m, 2H), 6.90 (s, 2H), 7.08 (d, J = 8.4 Hz, 4H), 7.37 (d, J = 8.4 Hz, 4H), 7.63 (s, 2H), 7.95 (d, J = 8.0 Hz, 2H), 8.26 (d, J = 8.0 Hz, 2H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 14.7, 22.0, 24.7, 27.9, 71.1, 77.4, 87.6, 122.8, 126.0, 127.2, 128.3, 129.6, 133.3, 137.1, 143.0, 145.8, 151.7, 169.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{40}H_{40}N_6NaO_4$ $[M+Na]^+$: 691.2989; Found: 691.2975.



L1k (Prepared according to general procedure A): Light yellow solid, M.p. 258.9-259.4 ^{o}C, overall yield 35%, 13:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 2.23-2.28 (m, 2H), 2.50-2.57 (m, 2H), 2.62-2.65 (m, 2H), 2.70-2.75 (m, 2H), 3.64 (s, 6H), 3.97-4.01 (m, 2H), 4.23-4.30 (m, 2H), 5.41-5.44 (m, 2H), 6.76-6.81 (m, 6H), 7.28-7.32 (m, 4H), 7.81-7.87 (m, 2H), 7.91 (d, *J* = 8.0 Hz, 2H), 8.37-8.43 (m, 2H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 22.0, 24.6, 54.5, 71.0, 77.3, 88.1, 114.1, 125.3, 126.0, 127.3, 128.0, 129.7, 137.1, 145.9, 151.8, 158.6, 169.6; HRMS (ESI-TOF) m/z: Calcd. for $C_{38}H_{36}N_6NaO_6$ $[M+Na]^+$: 695.2589; Found: 695.2589.



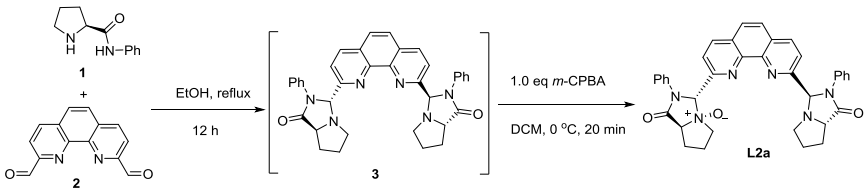
L1l (Prepared according to general procedure A): Light yellow solid, M.p. 248.8-249.7 ^{o}C, overall yield 33%, 12:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 1.08-1.10 (m, 12H), 2.24-2.26 (m, 2H), 2.52-2.55 (m, 2H), 2.67-2.79 (m, 6H), 3.99 (s, 2H), 4.20-4.27 (m, 2H), 5.42 (s, 2H), 6.88 (d, *J* = 4.0 Hz, 2H), 7.11 (d, *J* = 6.8 Hz, 4H), 7.35-7.37 (m, 4H), 7.71-7.81 (m, 2H), 7.95 (d, *J* = 8.0 Hz, 2H), 8.32-8.39 (m, 2H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 22.0, 22.8, 24.7, 33.5, 71.0, 77.3, 87.6, 122.8, 126.0, 126.8, 127.2, 129.7, 133.3, 137.2, 145.8, 147.6, 151.8, 169.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{42}H_{44}N_6NaO_4$ $[M+Na]^+$: 719.3304; Found: 719.3290.



L6a (Prepared according to general procedure A): White solid, overall yield 35%, 10:1 dr; ^{1}H

NMR (DMSO-d_6, 400 MHz) δ: 2.13-2.18 (m, 1H), 2.27-2.34 (m, 1H), 2.38-2.51 (m, 2H), 3.75-3.79 (m, 1H), 4.11-4.18 (m, 1H), 4.73-7.76 (m, 1H), 7.07 (s, 1H), 7.11-7.14 (m, 1H), 7.28-7.32 (m, 2H), 7.60 (d, J = 8.0 Hz, 2H), 7.75-7.78 (m, 1H), 7.94-8.05 (m, 3H), 8.45-8.50 (m, 2H), 9.14-9.16 (m, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 23.0, 24.8, 71.7, 77.8, 88.0, 123.2, 123.9, 126.0, 126.6, 126.7, 127.9, 129.1, 129.3, 129.4, 136.6, 136.7, 136.8, 145.2, 145.7, 150.8, 152.9, 169.8; HRMS (ESI-TOF) m/z: Calcd. for $C_{24}H_{20}N_4NaO_2$ $[M+Na]^+$: 419.1478; Found: 419.1470.

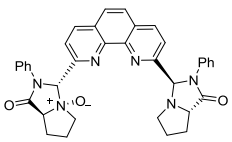
4. General procedure for preparation of chiral ligand L2a



In a sealed tube equipped with a magnetic stirring bar, phenanthroline-dicarbaldehyde **2** (1.0 mmol) and optically pure prolinamide **1** (2.4 mmol, 2.4 equiv) were added. Then, ethanol (6.0 mL) was added and the reaction was heated with stirring at reflux for 12 h. After completion of the reaction, as indicated by TLC, the aftertreatment residue was purified by flash column chromatography to give the intermediate **3**.

In a sealed tube equipped with a magnetic stirring bar, to the intermediate **3** was added 3.0 mL of DCM and *m*-CPBA (1.0 eq). The reaction mixture was stirred at 0 ^{o}C for 20 min. After completion of the reaction, as indicated by TLC, the aftertreatment residue was purified by flash column chromatography to furnish the chiral ligand **L2a**.

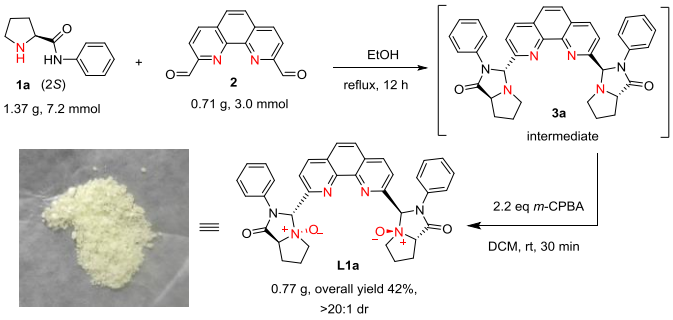
5. Characterization data of chiral ligand L2a



L2a: White solid; yield 37%, >20:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 1.82-1.87 (m, 1H), 1.92-1.95 (m, 1H), 2.22-2.31 (m, 2H), 2.40-2.48 (m, 1H), 2.53-2.60 (m, 1H), 2.68-2.78 (m, 2H), 3.08-3.14 (m, 1H), 3.45-3.50 (m, 1H), 3.97-4.02 (m, 1H), 4.22-4.30 (m, 1H), 4.99 (d, J = 4.4 Hz,

1H), 5.40 (d, *J* = 6.8 Hz, 1H), 6.23 (s, 1H), 6.94 (s, 1H), 7.00-7.04 (m, 1H), 7.08-7.12 (m, 1H), 7.17-7.24 (m, 4H), 7.45-7.52 (m, 4H), 7.64-7.76 (m, 3H), 7.92 (d, *J* = 8.0 Hz, 1H), 8.19-8.35 (m, 2H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 22.1, 24.3, 24.4, 27.5, 56.0, 65.5, 70.9, 77.2, 84.2, 87.8, 122.0, 122.5, 123.0, 125.4, 125.7, 126.4, 126.6, 127.2, 128.6, 128.8, 128.9, 129.5, 137.0, 137.1, 137.3, 145.7, 145.9, 151.2, 158.3, 169.4, 175.8; HRMS (ESI-TOF) m/z: Calcd. for $C_{36}H_{32}N_6NaO_3$ $[M+Na]^+$: 619.2420; Found: 619.2428.

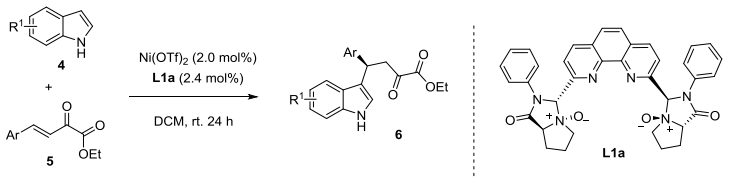
6. The gram scale synthesis of the Phen-2NO ligand L1a



In a sealed tube equipped with a magnetic stirring bar, phenanthroline-dicarbaldehyde **2** (0.71 g, 3.0 mmol) and optically pure prolinamide **1a** (1.37 g, 7.2 mmol) were added. Then, anhydrous ethanol (30.0 mL) was added and the reaction was heated with stirring at reflux for 12 h. After completion of the reaction, as indicated by TLC, the aftertreatment residue was purified by flash column chromatography to give the intermediate **3a**.

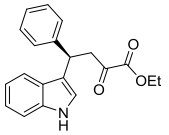
For the oxidation step, see: X. Liu, L. Lin and X. Feng, Chiral *N,N'*-dioxide ligands: synthesis, coordination chemistry and asymmetric catalysis, *Org. Chem. Front.*, 2014, **1**, 298-302. In a sealed tube equipped with a magnetic stirring bar, to the intermediate **3** was added 20.0 mL of DCM and *m*-CPBA (2.2 eq). The reaction mixture was stirred at 0 ^{o}C for 30 min. After completion of the reaction, as indicated by TLC, the aftertreatment residue was purified by flash column chromatography to furnish the Phen-2NO ligand **L1a** (0.77 g, 42% overall yield, >20:1 dr).

7. Catalytic asymmetric synthesis of compounds 6

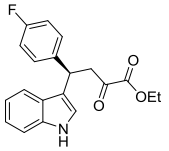


In a sealed tube equipped with a magnetic stirring bar, to the mixture of $Ni(OTf)_2$ (2.0 mol %), **L1a** (2.4 mol %) in 2.0 mL of CH_2Cl_2 was added **4** (0.30 mmol), and **5** (0.20 mmol). The reaction mixture was stirred at room temperature for 24 h and was directly loaded onto a silica gel and purified by flash chromatography to give the desired product **6**, using hexane/EtOAc (10/1, v/v) as the eluent.

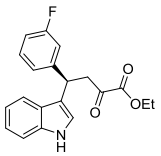
8. Characterization data of compounds 6



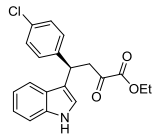
6a: Product in accordance with literature characterization data[10a,c]. 91% yield, 99% ee, $[\alpha]_D^{20}$ = -27.2 (*c* 0.70, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IA column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 33.63 min; τ_{minor} = 42.85 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.16-1.19 (m, 3H), 3.48-3.62 (m, 2H), 4.09-4.15 (m, 2H), 4.81-4.85 (m, 1H), 6.90-6.95 (m, 2H), 7.04-7.11 (m, 2H), 7.15-7.25 (m, 5H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.96 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 12.9, 36.8, 44.6, 61.5, 110.2, 118.4, 120.6, 121.2, 125.5, 126.7, 127.5, 135.5, 142.2, 159.9, 192.1.



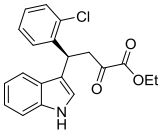
6b: Product in accordance with literature characterization data[10c]. 89% yield, 93% ee, $[\alpha]_D^{20}$ = -22.7 (*c* 0.45, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IA column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 15.26 min; τ_{minor} = 22.01 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.18-1.22 (m, 3H), 3.45-3.60 (m, 2H), 4.11-4.17 (m, 1H), 4.80-4.83 (m, 1H), 6.83-6.88 (m, 2H), 6.92-6.96 (m, 2H), 7.05-7.09 (m, 1H), 7.18-7.24 (m, 3H), 7.29 (d, *J* = 7.6 Hz, 1H), 8.00 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 13.9, 37.1, 45.7, 62.6, 111.3, 115.3 (d, J_{CF} = 22.3 Hz), 118.2, 119.5 (d, J_{CF} = 29.1 Hz), 121.5, 122.4, 126.3, 129.3 (d, J_{CF} = 8.4 Hz), 136.6, 139.0, 161.0, 161.5 (d, J_{CF} = 243.3 Hz), 193.0; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{18}FNNaO_3$ $[M+Na]^+$: 362.1163; Found: 362.1168.



6c: Product in accordance with literature characterization data[10b]. 87% yield, 90% ee; The ee was determined by HPLC analysis using a Chiralpak IA column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 20.86 min; τ_{minor} = 24.62 min); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.16-1.20 (m, 3H), 3.45-3.61 (m, 2H), 4.10-4.16 (m, 2H), 4.80-4.84 (m, 1H), 6.74-6.79 (m, 1H), 6.90-6.96 (m, 3H), 7.02-7.15 (m, 3H), 7.20 (d, *J* = 8.0 Hz, 1H), 7.31 (d, *J* = 7.6 Hz, 1H), 8.02 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 12.8, 36.4, 44.4, 61.6, 110.3, 112.5 (d, J_{CF} = 21.2 Hz), 113.7 (d, J_{CF} = 22.3 Hz), 116.5, 118.1, 118.5, 120.6, 121.3, 122.6 (d, J_{CF} = 2.4 Hz), 125.2, 128.9 (d, J_{CF} = 8.1 Hz), 129.1, 135.5, 145.0 (d, J_{CF} = 6.4 Hz), 159.8, 161.8 (d, J_{CF} = 247.3 Hz), 191.8.

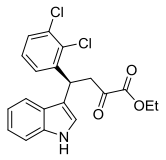


6d: Product in accordance with literature characterization data[10b]. 92% yield, 99% ee; The ee was determined by HPLC analysis using a Chiralpak IA column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 20.18 min; τ_{minor} = 25.48 min); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.18-1.21 (m, 3H), 3.45-3.60 (m, 2H), 4.11-4.17 (m, 2H), 4.78-4.82 (m, 1H), 6.91-6.96 (m, 2H), 7.05-7.09 (m, 1H), 7.12-7.18 (m, 4H), 7.23 (d, *J* = 8.0 Hz, 1H), 7.28 (d, *J* = 8.0 H, 1H), 8.00 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 12.9, 36.1, 44.4, 61.6, 110.3, 116.7, 118.2, 118.6, 120.5, 121.4, 125.2, 127.6, 128.2, 131.2, 135.6, 140.8, 159.8, 191.8.

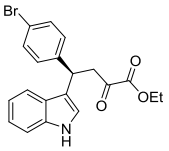


6e: Product in accordance with literature characterization data[10b,c]. 89% yield, 97% ee, $[\alpha]_D^{20}$ = -22.1 (*c* 0.43, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IA column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 27.09 min; τ_{minor} = 33.78 min); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.18-1.21 (m, 3H), 3.36-3.42 (m, 1H), 3.59-3.66 (m, 1H), 4.13-4.18 (m, 2H), 5.34-5.38 (m, 1H), 6.92-6.96 (m, 2H), 7.00-7.06 (m, 3H), 7.10-7.12 (m, 1H),

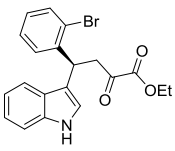
7.21 (d, J = 8.4 Hz, 1H), 7.28-7.30 (m, 1H), 7.35 (d, J = 8.0 Hz, 1H), 8.03 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 12.9, 33.2, 43.6, 61.5, 110.2, 115.8, 118.3, 118.5, 121.1, 121.3, 125.4, 126.0, 126.9, 128.0, 128.7, 132.4, 135.5, 139.5, 159.9, 191.7.



6f: 87% yield, 98% ee; The ee was determined by HPLC analysis using a Chiralpak IA column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 30.33 min; τ_{minor} = 38.88 min); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.19-1.22 (m, 3H), 3.34-3.40 (m, 1H), 3.59-3.66 (m, 1H), 4.14-4.19 (m, 2H), 5.37-5.40 (m, 1H), 6.92-6.97 (m, 3H), 7.00-7.03 (m, 1H), 7.05-7.09 (m, 1H), 7.20-7.22 (m, 2H), 7.31 (d, J = 7.6 Hz, 1H), 8.05 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 12.2, 33.4, 42.6, 60.9, 109.5, 114.8, 117.5, 118.0, 120.4, 120.8, 124.6, 125.4, 125.6, 127.0, 130.1, 131.6, 134.8, 141.3, 159.1, 190.6; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{17}Cl_2NNaO_3$ $[M+Na]^+$: 412.0478; Found: 412.0484.

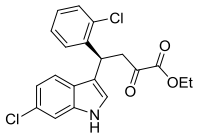


6g: Product in accordance with literature characterization data[10b,c]. 90% yield, 95% ee, $[\alpha]_D^{20}$ = -27.9 (*c* 0.50, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IA column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 16.04 min; τ_{minor} = 25.17 min); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.18-1.21 (m, 3H), 3.44-3.60 (m, 2H), 4.11-4.17 (m, 2H), 4.76-4.80 (m, 1H), 6.90-6.96 (m, 2H), 7.05-7.12 (m, 3H), 7.21 (d, J = 8.0 Hz, 1H), 7.27-7.29 (m, 3H), 8.01 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 11.7, 35.0, 43.1, 60.4, 109.1, 115.4, 117.0, 117.4, 118.1, 119.3, 120.2, 124.0, 127.4, 129.4, 134.3, 140.1, 158.6, 190.6.

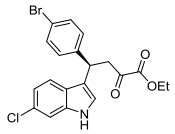


6h: Product in accordance with literature characterization data[10c]. 88% yield, 98% ee, $[\alpha]_D^{20}$ = -28.2 (*c* 0.43, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IA column

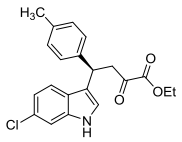
(95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 15.51 min; τ_{minor} = 18.78 min); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.18-1.22 (m, 3H), 3.34-3.39 (m, 1H), 3.58-3.65 (m, 1H), 4.13-4.19 (m, 2H), 5.32-5.35 (m, 1H), 6.93-6.97 (m, 3H), 7.03-7.11 (m, 3H), 7.21 (d, *J* = 8.4 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.48-7.50 (m, 1H), 8.03 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 14.0, 37.1, 44.8, 62.6, 111.3, 117.0, 119.5, 119.6, 122.2, 122.4, 124.3, 126.5, 127.8, 128.3, 129.2, 133.1, 136.6, 142.2, 161.0, 192.7; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{18}BrNNaO_3$ $[M+Na]^+$: 422.0362; Found: 422.0365.



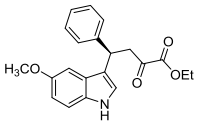
6i: 82% yield, 95% ee; The ee was determined by HPLC analysis using a Chiralpak IA column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 15.40 min; τ_{minor} = 13.50 min); ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.21-1.24 (m, 3H), 3.35-3.41 (m, 1H), 3.58-3.64 (m, 1H), 4.16-4.21 (m, 2H), 5.29-5.33 (m, 1H), 6.90-6.96 (m, 2H), 7.03-7.09 (m, 3H), 7.21-7.24 (m, 2H), 7.29-7.32 (m, 1H), 8.05 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 14.2, 33.6, 44.7, 62.3, 111.6, 116.6, 119.4, 120.1, 124.6, 125.4, 126.5, 127.9, 128.5, 129.7, 129.8, 132.9, 137.2, 141.5, 160.8, 192.6; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{17}Cl_2NNaO_3$ $[M+Na]^+$: 412.0478; Found: 412.0479.



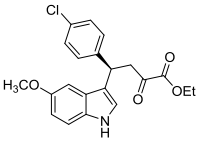
6j: 85% yield, 91% ee; The ee was determined by HPLC analysis using a Chiralpak IA column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 19.42 min; τ_{minor} = 16.17 min); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.20-1.23 (m, 3H), 3.43-3.58 (m, 2H), 4.14-4.19 (m, 2H), 4.73-4.76 (m, 1H), 6.89-6.94 (m, 2H), 7.08-7.10 (m, 2H), 7.15 (d, *J* = 8.4 Hz, 1H), 7.22 (d, *J* = 1.6 Hz, 1H), 7.29-7.31 (m, 2H), 8.04 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 12.9, 36.0, 44.2, 61.7, 110.2, 116.9, 119.1, 119.4, 119.5, 121.1, 123.8, 127.4, 128.5, 130.7, 135.9, 141.0, 159.8, 191.6; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{17}BrClNNaO_3$ $[M+Na]^+$: 455.9973; Found: 455.9977.



6k: 83% yield, 91% ee; The ee was determined by HPLC analysis using a Chiralpak IA column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 17.61 min; τ_{minor} = 15.15 min); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.18-1.22 (m, 3H), 2.20 (s, 3H), 3.44-3.59 (m, 2H), 4.12-4.17 (m, 2H), 4.74-4.77 (m, 1H), 6.88-6.94 (m, 2H), 6.99 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 7.20-7.22 (m, 2H), 7.97 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 12.9, 36.0, 44.2, 61.7, 110.2, 116.9, 119.1, 119.4, 119.5, 121.1, 123.8, 127.4, 128.5, 130.7, 135.9, 141.0, 159.8, 191.6; HRMS (ESI-TOF) m/z: Calcd. for $C_{21}H_{20}ClNNaO_3$ $[M+Na]^+$: 392.1024; Found: 392.1024.

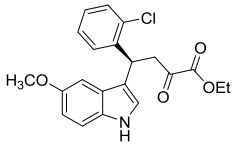


6l: Product in accordance with literature characterization data[10b,c]. 91% yield, 93% ee, $[\alpha]_D^{20}$ = -55.2 (*c* 0.57, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IA column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 31.16 min; τ_{minor} = 36.82 min); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.23-1.27 (m, 3H), 3.54-3.68 (m, 2H), 3.73 (s, 3H), 4.17-4.22 (m, 2H), 4.83-4.87 (m, 1H), 6.77-6.83 (m, 2H), 6.94 (d, *J* = 2.4 Hz, 1H), 7.14-7.18 (m, 2H), 7.22-7.27 (m, 2H), 7.31-7.33 (m, 2H), 7.99 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 13.9, 37.8, 45.6, 55.9, 62.6, 101.4, 112.0, 112.3, 117.9, 122.4, 126.6, 126.9, 127.8, 128.6, 131.8, 143.3, 153.9, 161.0, 193.3.

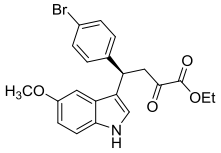


6m: Product in accordance with literature characterization data[10c]. 92% yield, 95% ee, $[\alpha]_D^{20}$ = -34.4 (*c* 0.37, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IA column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 13.75 min; τ_{minor} = 19.70 min); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.19-1.23 (m, 3H), 3.44-3.57 (m, 2H), 3.67 (s, 3H), 4.13-4.18 (m, 2H), 4.73-4.77 (m, 1H), 6.70-6.76 (m, 2H), 6.91 (d, *J* = 2.4 Hz, 1H), 7.11-7.19 (m, 5H), 7.91 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 13.9, 37.1, 45.4, 55.9, 62.6, 101.3, 111.9, 112.4, 117.6, 122.2,

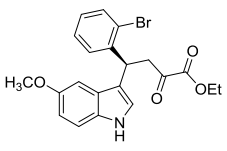
126.7, 128.7, 129.2, 131.7, 132.3, 141.8, 154.0, 160.9, 192.8; HRMS (ESI-TOF) m/z: Calcd. for $C_{21}H_{20}ClNNaO_4$ $[M+Na]^+$: 408.0973; Found: 408.0969.



6n: Product in accordance with literature characterization data[10c]. 92% yield, 97% ee, $[\alpha]_D^{20}$ = -37.2 (*c* 0.36, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IA column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 9.40 min; τ_{minor} = 16.28 min); ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.21-1.25 (m, 3H), 3.49-3.55 (m, 1H), 3.68 (s, 3H), 3.76-3.83 (m, 1H), 4.17-4.23 (m, 2H), 5.16-5.19 (m, 1H), 6.71-6.74 (m, 1H), 6.88 (d, *J* = 2.4 Hz, 1H), 7.17-7.25 (m, 4H), 7.38-7.44 (m, 2H), 10.81 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 14.2, 33.7, 44.7, 55.7, 62.3, 100.9, 111.5, 112.7, 116.2, 123.8, 127.8, 128.3, 129.7, 129.8, 132.0, 141.7, 153.5, 160.8, 192.8; HRMS (ESI-TOF) m/z: Calcd. for $C_{21}H_{20}ClNNaO_4$ $[M+Na]^+$: 408.0973; Found: 408.0974.

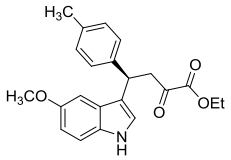


6o: Product in accordance with literature characterization data[10c]. 93% yield, 96% ee, $[\alpha]_D^{20}$ = -45.0 (*c* 0.24, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IA column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 36.32 min; τ_{minor} = 53.68 min); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.16-1.20 (m, 3H), 3.42-3.57 (m, 2H), 3.65 (s, 3H), 4.10-4.16 (m, 2H), 4.70-4.74 (m, 1H), 6.69-6.73 (m, 2H), 6.85 (s, 1H), 7.06-7.10 (m, 3H), 7.26 (d, *J* = 8.8 Hz, 2H), 7.99 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 12.2, 35.4, 43.5, 54.1, 60.9, 99.5, 110.2, 110.6, 115.7, 118.6, 120.5, 124.9, 127.8, 129.8, 130.0, 140.5, 152.2, 159.1, 191.0; HRMS (ESI-TOF) m/z: Calcd. for $C_{21}H_{20}BrNNaO_4$ $[M+Na]^+$: 452.0468; Found: 452.0474.

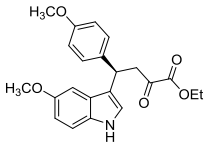


6p: Product in accordance with literature characterization data[10c]. 91% yield, 97% ee, $[\alpha]_D^{20}$ =

-42.5 (*c* 0.37, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IA column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 9.64 min; τ_{minor} = 15.29 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.90-1.23 (m, 3H), 3.34-3.39 (m, 1H), 3.57-3.64 (m, 1H), 3.68 (s, 3H), 4.14-4.19 (m, 2H), 5.27-5.31 (m, 1H), 6.71-6.74 (m, 1H), 6.82 (d, *J* = 2.4 Hz, 1H), 6.92-6.97 (m, 2H), 7.05-7.13 (m, 3H), 7.48-7.50 (m, 1H), 7.95 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 12.9, 35.9, 43.7, 54.8, 61.5, 100.3, 110.8, 111.5, 121.6, 123.2, 125.9, 126.7, 127.2, 128.2, 130.6, 132.0, 141.1, 152.9, 159.9, 191.6; HRMS (ESI-TOF) m/z: Calcd. for $C_{21}H_{20}BrNNaO_4$ $[M+Na]^+$: 452.0468; Found: 452.0462.

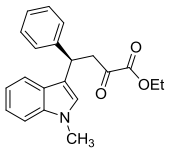


6q: 88% yield, 95% ee; The ee was determined by HPLC analysis using a Chiralpak IA column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 21.54 min; τ_{minor} = 18.18 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.14-1.18 (m, 3H), 2.18 (s, 3H), 3.44-3.58 (m, 2H), 3.65 (s, 3H), 4.08-4.13 (m, 2H), 4.71-4.75 (m, 1H), 6.68-6.71 (m, 1H), 6.76 (d, *J* = 2.4 Hz, 1H), 6.84 (d, *J* = 2.4 Hz, 1H), 6.97 (d, *J* = 8.0 Hz, 2H), 7.05 (d, *J* = 8.8 Hz, 1H), 7.12 (d, *J* = 8.8 Hz, 2H), 7.91 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 12.4, 19.5, 35.9, 44.1, 54.3, 60.9, 99.9, 110.3, 110.7, 116.7, 120.7, 125.3, 126.1, 127.7, 130.2, 134.5, 138.6, 152.3, 159.5, 191.8; HRMS (ESI-TOF) m/z: Calcd. for $C_{22}H_{23}NNaO_4$ $[M+Na]^+$: 388.1519; Found: 388.1527.



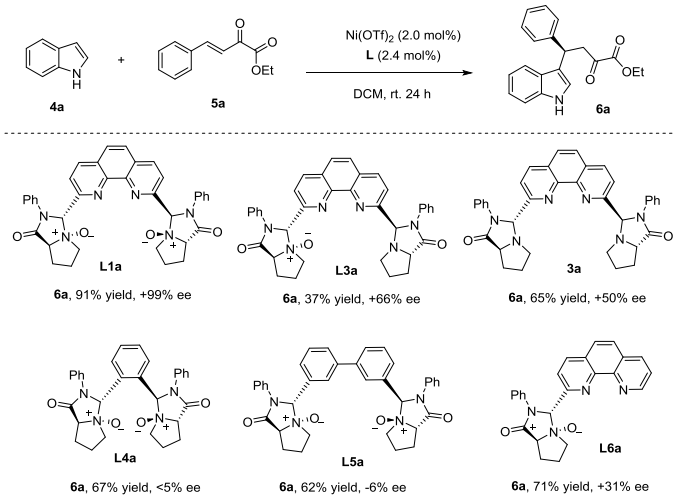
6r: 90% yield, 98% ee; The ee was determined by HPLC analysis using a Chiralpak IA column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 58.96 min; τ_{minor} = 73.92 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.17-1.20 (m, 3H), 3.43-3.57 (m, 2H), 3.66 (s, 3H), 3.67 (s, 3H), 4.10-4.16 (m, 2H), 4.71-4.75 (m, 1H), 6.70-6.76 (m, 4H), 6.87 (d, *J* = 2.0 Hz, 1H), 7.08 (d, *J* = 8.8 Hz, 1H), 7.15 (d, *J* = 9.6 Hz, 2H), 7.91 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 12.9, 36.0, 44.7, 54.2, 54.8, 61.5, 100.4, 110.8, 111.2, 112.9, 117.2, 121.2, 125.8, 127.7, 130.7, 134.3, 152.8, 157.1, 160.0, 192.3; HRMS (ESI-TOF) m/z: Calcd. for $C_{22}H_{23}NNaO_5$ $[M+Na]^+$: 404.1468; Found:

404.1474.

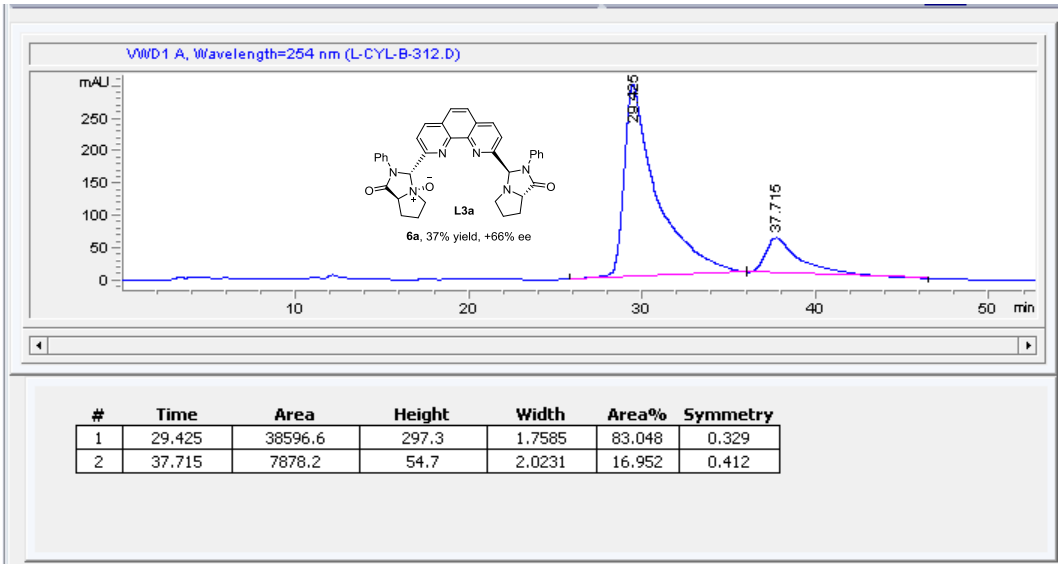


6s: Product in accordance with literature characterization data[10a,c]. 71% yield, 50% ee, $[\alpha]_D^{20}$ = -12.4 (*c* 0.38, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IA column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 16.07 min; τ_{minor} = 15.24 min); ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.20-1.23 (m, 3H), 3.55-3.62 (m, 1H), 3.68-3.74 (m, 4H), 4.15-4.21 (m, 2H), 4.70-4.74 (m, 1H), 6.92-6.95 (m, 1H), 7.08-7.14 (m, 2H), 7.22-7.25 (m, 3H), 7.33-7.36 (m, 3H), 7.42 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 14.2, 32.8, 37.4, 45.5, 62.3, 110.1, 117.0, 118.9, 119.3, 121.7, 126.6, 126.9, 127.0, 128.1, 128.7, 137.2, 144.8, 161.0, 193.0.

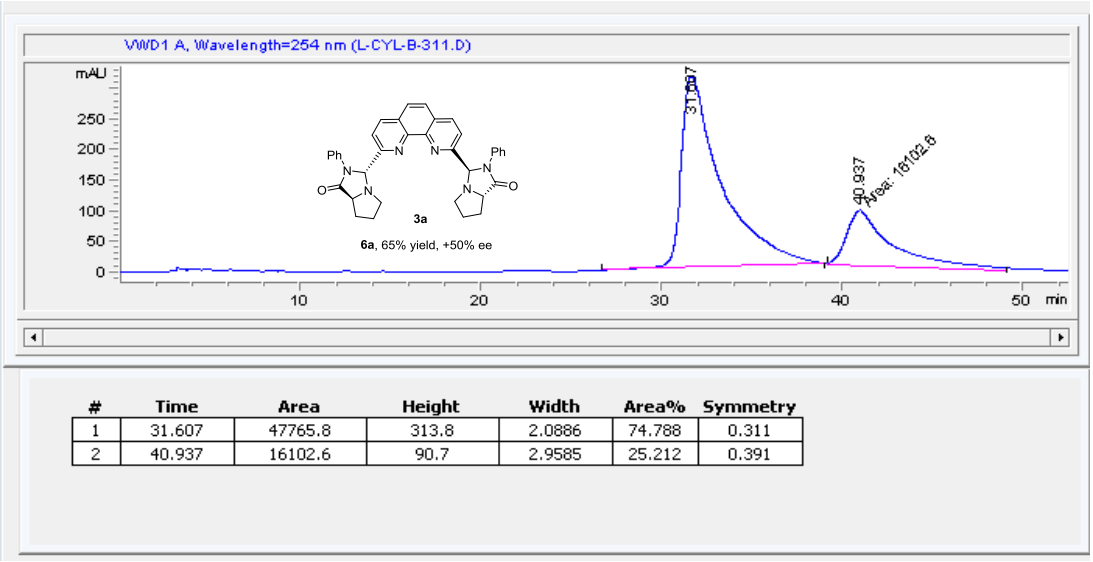
9. Control experiments and HPLC spectra for compound 6a



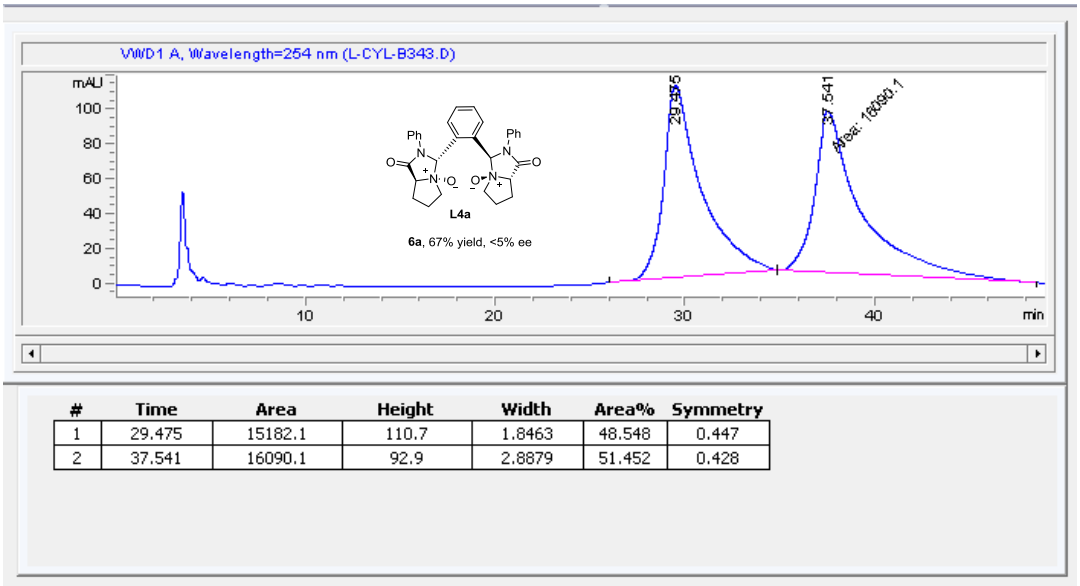
In a sealed tube equipped with a magnetic stirring bar, to the mixture of $Ni(OTf)_2$ (2.0 mol %), **L** (2.4 mol %) in 2.0 mL of CH_2Cl_2 was added **4** (0.30 mmol), and **5** (0.20 mmol). The reaction mixture was stirred at room temperature for 24 h and was directly loaded onto a silica gel and purified by flash chromatography to give the desired product **6a**, using hexane/EtOAc (10/1, v/v) as the eluent.



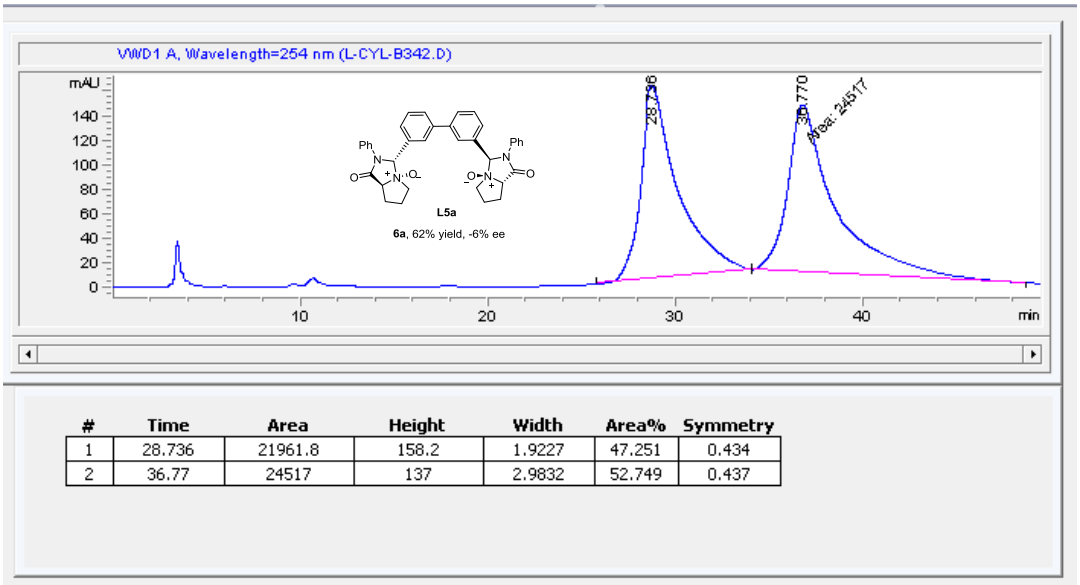
#	Time	Area	Height	Width	Area%	Symmetry
1	29.425	38596.6	297.3	1.7585	83.048	0.329
2	37.715	7878.2	54.7	2.0231	16.952	0.412



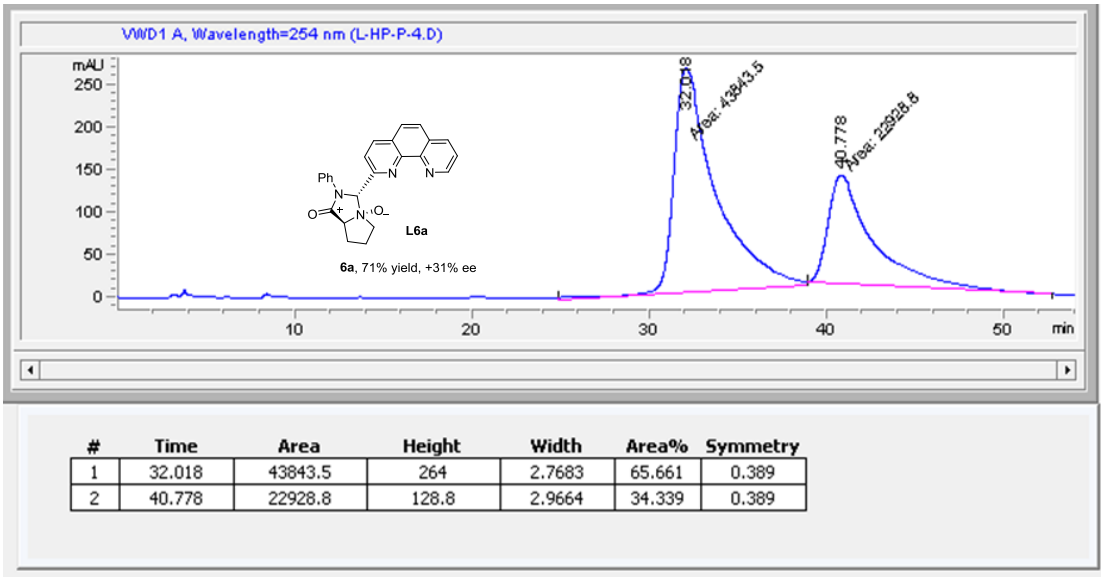
#	Time	Area	Height	Width	Area%	Symmetry
1	31.607	47765.8	313.8	2.0886	74.788	0.311
2	40.937	16102.6	90.7	2.9585	25.212	0.391



#	Time	Area	Height	Width	Area%	Symmetry
1	29.475	15182.1	110.7	1.8463	48.548	0.447
2	37.541	16090.1	92.9	2.8879	51.452	0.428



#	Time	Area	Height	Width	Area%	Symmetry
1	28.736	21961.8	158.2	1.9227	47.251	0.434
2	36.77	24517	137	2.9832	52.749	0.437

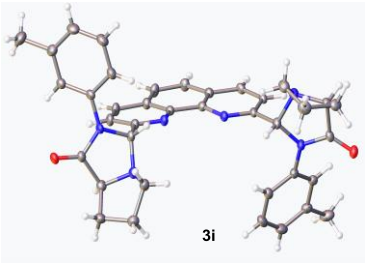


#	Time	Area	Height	Width	Area%	Symmetry
1	32.018	43843.5	264	2.7683	65.661	0.389
2	40.778	22928.8	128.8	2.9664	34.339	0.389

10. References

(a) Y. Liu, D. Shang, X. Zhou, Y. Zhu, L. Lin, X. Liu and X. Feng, *Org. Lett.*, 2010, **12**, 180-183; *(b)* S. Yu, Q. Cai, C. Wang, J. Hou, J. Liang, Z. Jiao, C. Yao and Y. M. Li, *J. Org. Chem.*, 2023, **88**, 3046-3053; *(c)* Y. H. Wang, P. Hu, X. R. Wang, K. L. Xu, Q. L. Wang, H. J. Wang and X. L. Liu, *Org. Chem. Front.*, 2024, DOI: 10.1039/D3QO01748F.

11. X-ray crystal data for compounds 3i



CCDC 2297366

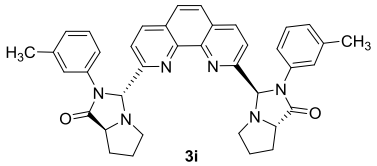


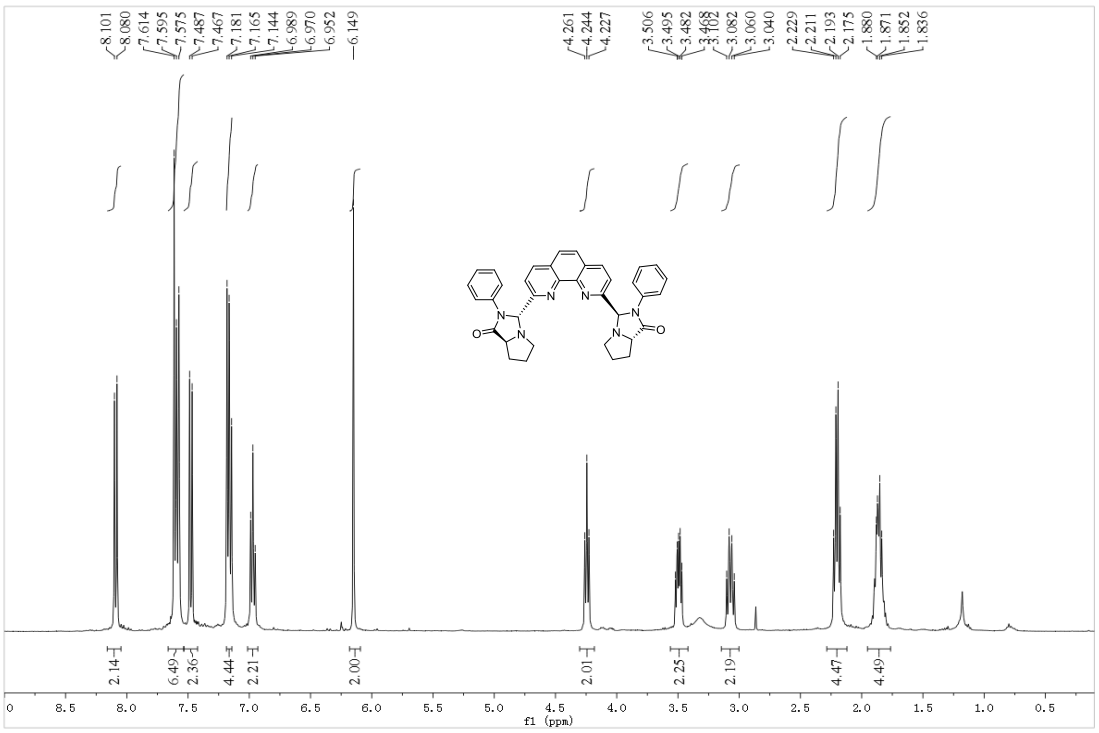
Table S1 Crystal data and structure refinement for 3i

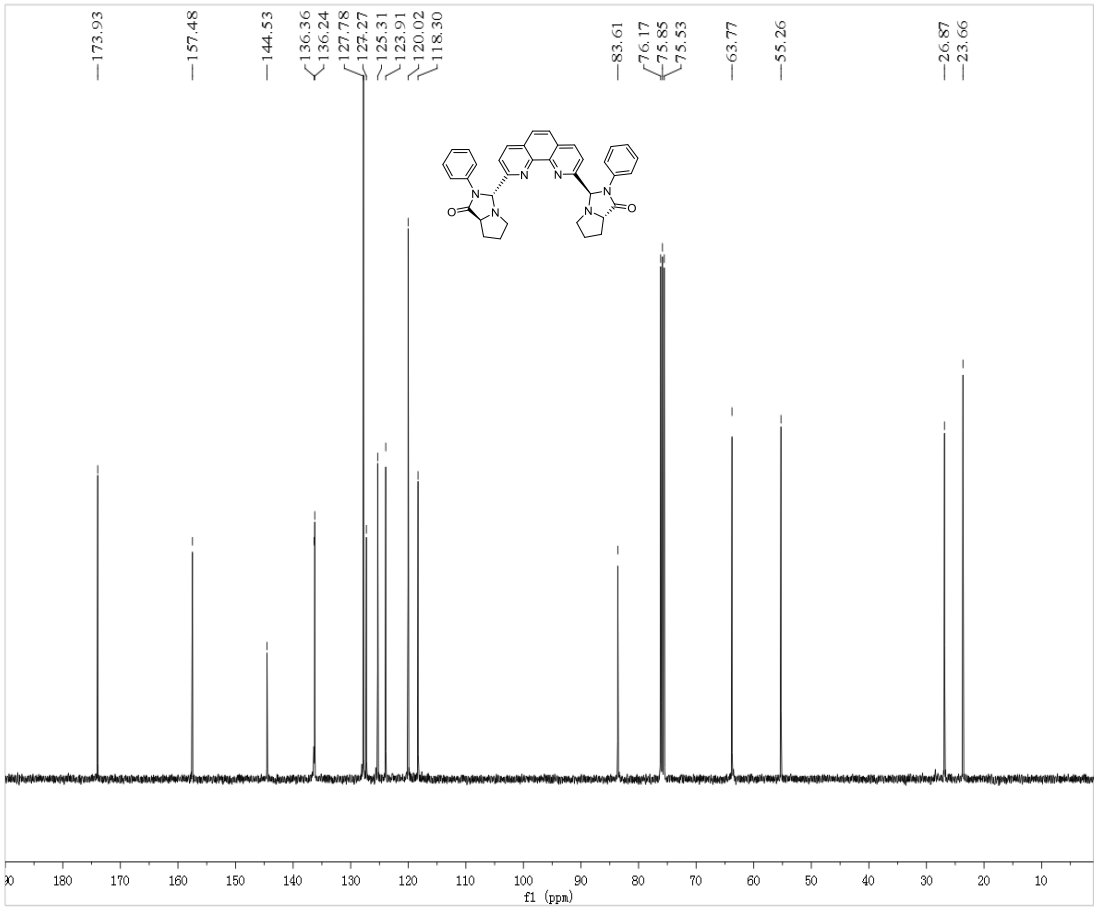
Identification code	**3i**
Empirical formula	$C_{38}H_{40}N_6O_4$
Formula weight	644.76
Temperature/K	99.97(13)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å, b/Å, c/Å	9.32674(13), 13.9964(2), 25.3147(3)
α/°, β/°, γ/°,	90, 90, 90
Volume/Å^3	3304.59(8)
Z	4
ρ_{calc}g/cm^3	1.296
μ/mm^{-1}	0.690
F(000)	1368.0
Radiation	Cu Kα (λ = 1.54184)
Crystal size/mm^3	0.15 × 0.13 × 0.12
2Θ range for data collection/°	6.984 to 148.426
Index ranges	-8 ≤ h ≤ 11, -17 ≤ k ≤ 13, -31 ≤ l ≤ 30
Reflections collected	16596
Independent reflections	6509 [R_{int} = 0.0389, R_{sigma} = 0.0407]
Data/restraints/parameters	6509/3/446
Goodness-of-fit on F^2	1.026
Final R indexes [I>=2σ (I)]	R_1 = 0.0446, wR_2 = 0.1248
Final R indexes [all data]	R_1 = 0.0463, wR_2 = 0.1264
Largest diff. peak/hole / e Å^{-3}	0.39/-0.36
Flack parameter	0.01(13)/0.01(10)

Crystal Data for $C_{38}H_{40}N_6O_4$ (*M* =644.76 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), *a* = 9.32674(13) Å, *b* = 13.9964(2) Å, *c* = 25.3147(3) Å, *V* = 3304.59(8) Å^3, *Z* = 4, *T* = 99.97(13) K, μ(Cu Kα) = 0.690 mm^{-1}, *Dcalc* = 1.296 g/cm^3, 16596 reflections measured (6.984° ≤ 2Θ ≤ 148.426°), 6509 unique (R_{int} = 0.0389, R_{sigma} = 0.0407) which were used in all calculations. The final R_1 was 0.0446 (I > 2σ(I)) and wR_2 was 0.1264 (all data).

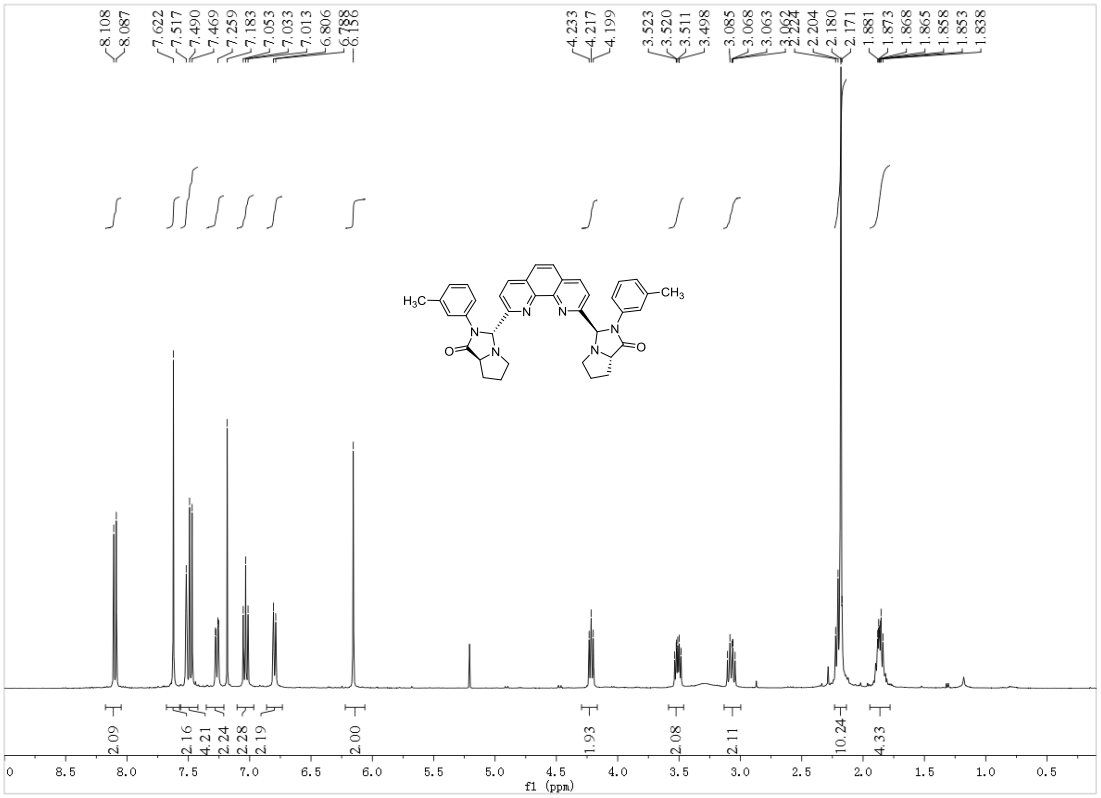
12. The copies of ^{1}H NMR, ^{13}C NMR and HPLC spectra for compounds 3, L and 6

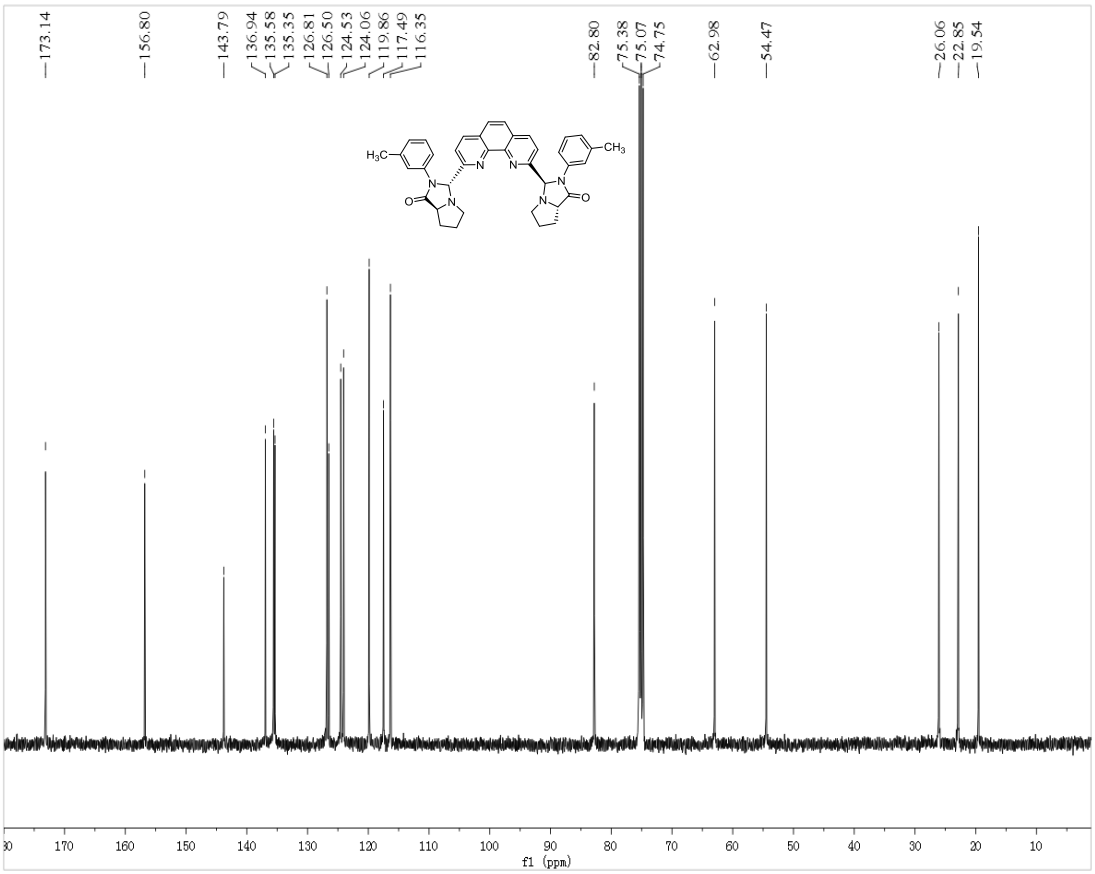
^{1}H and ^{13}C NMR of 3a



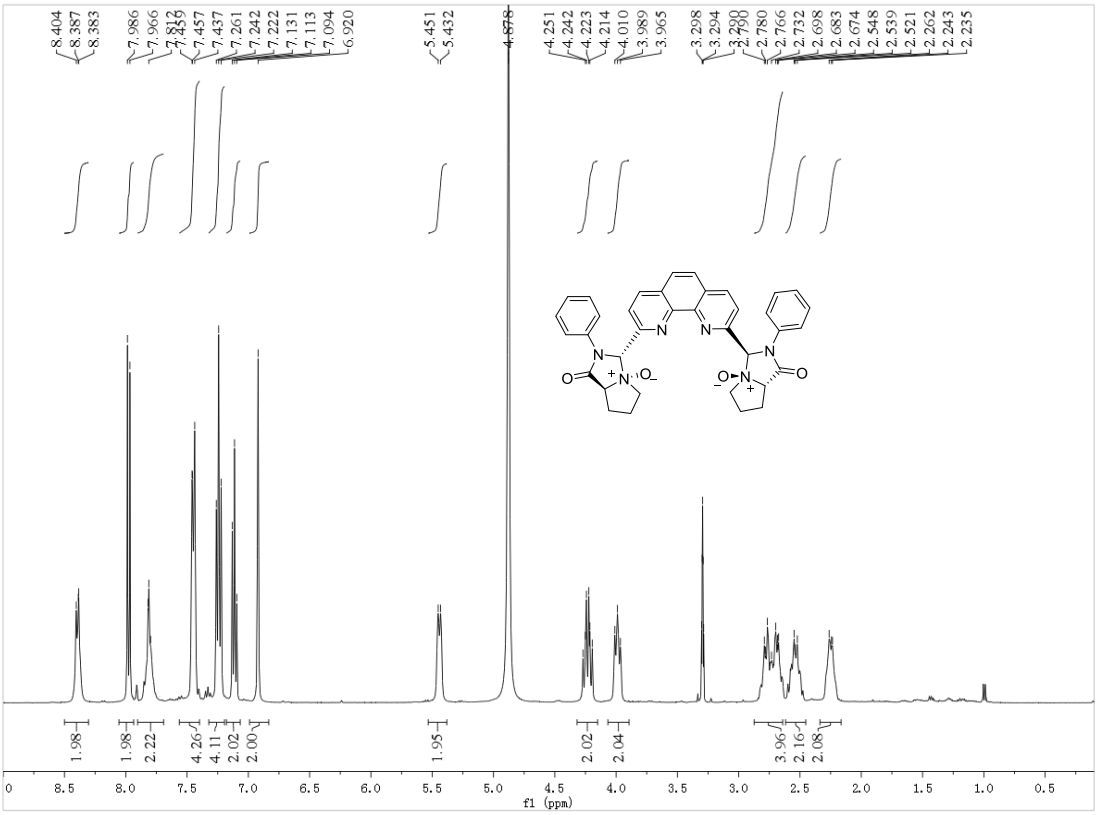


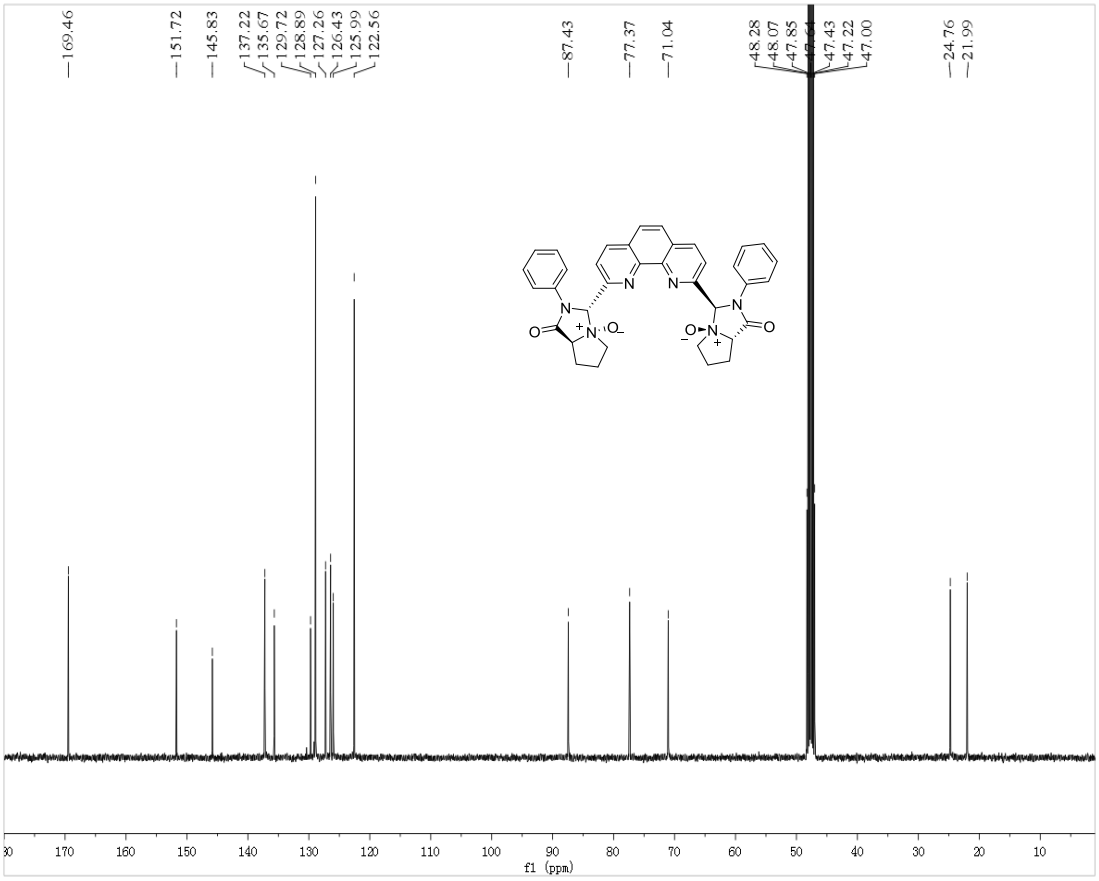
^{1}H and ^{13}C NMR of 3i



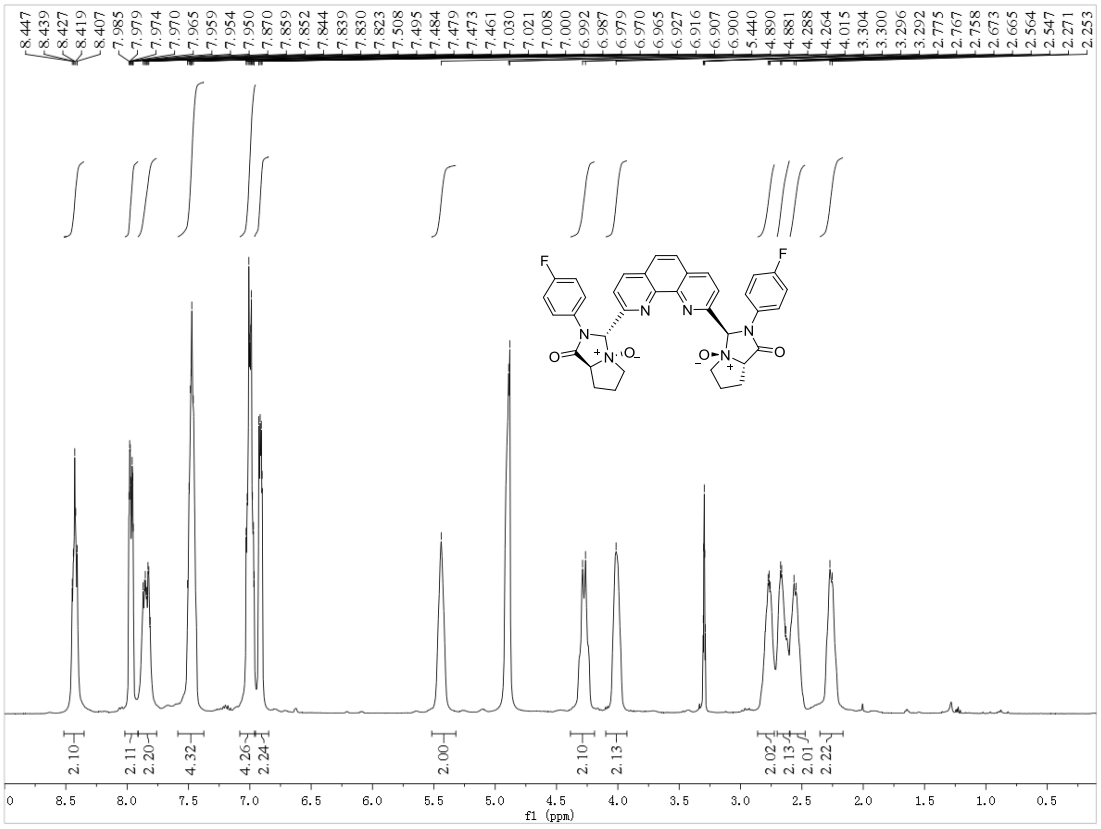


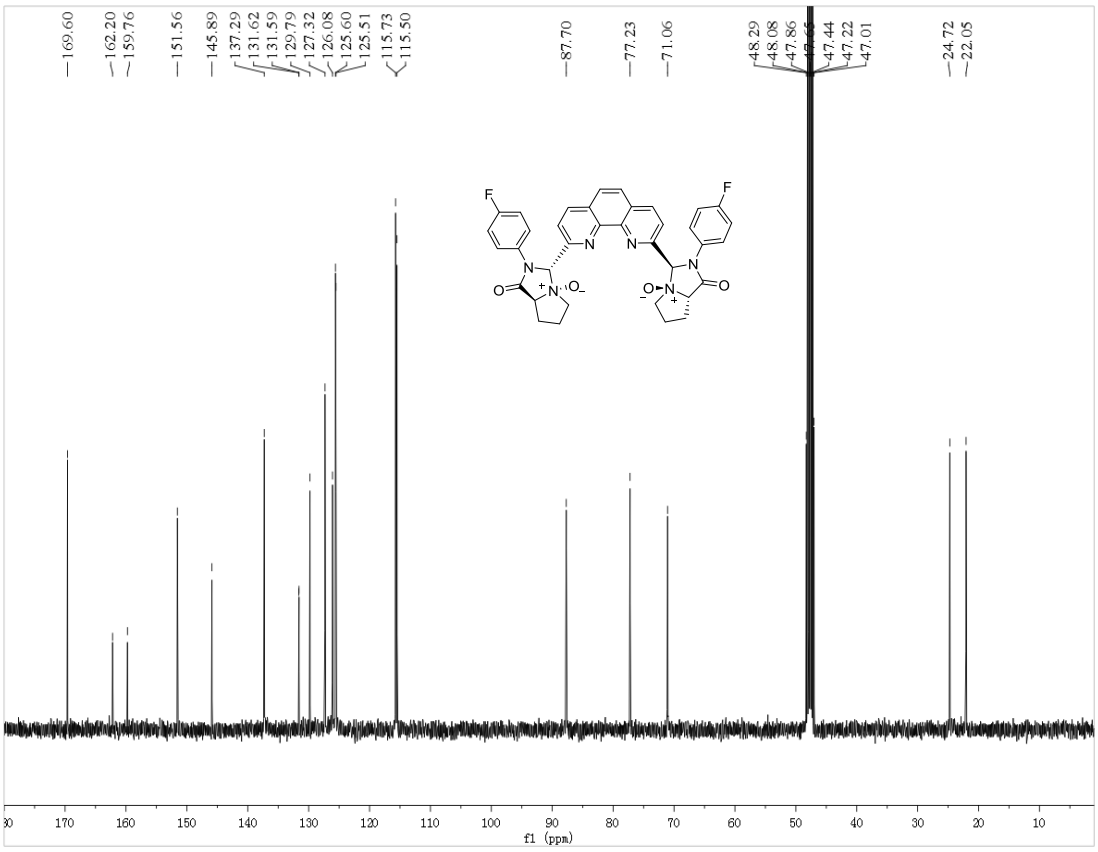
^{1}H and ^{13}C NMR of L1a



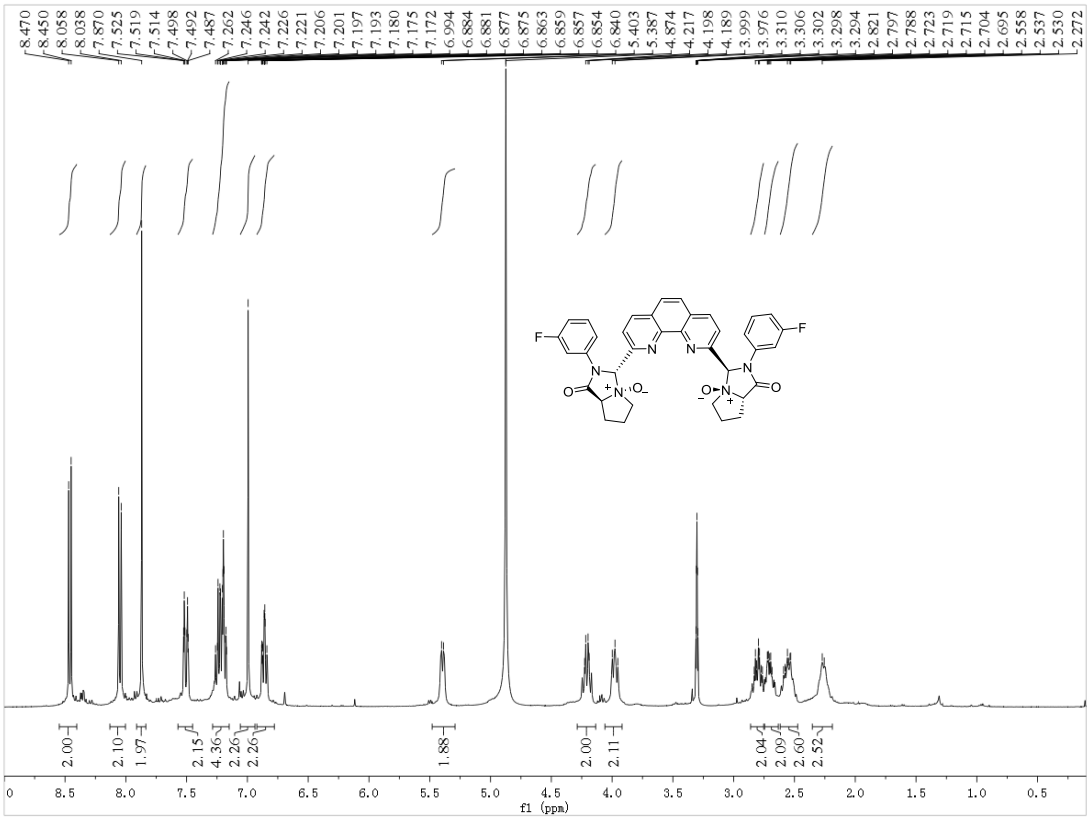


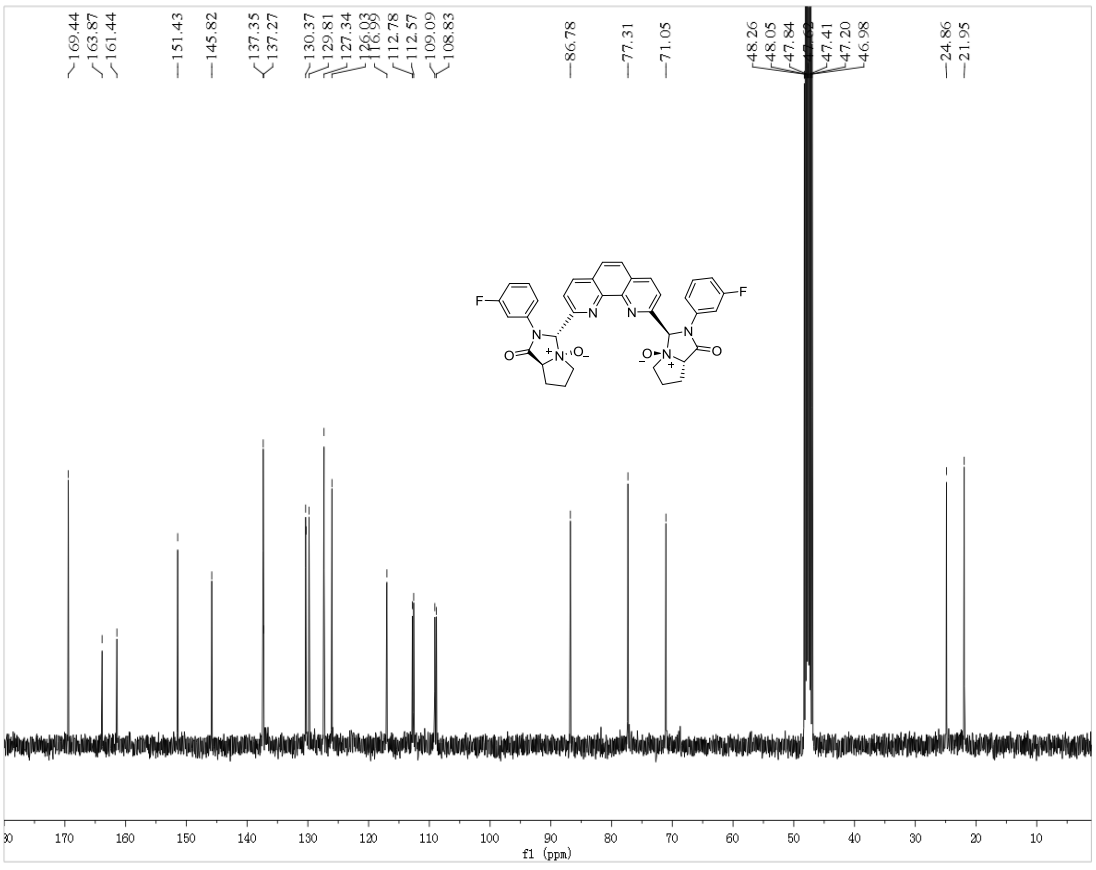
^{1}H and ^{13}C NMR of L1b



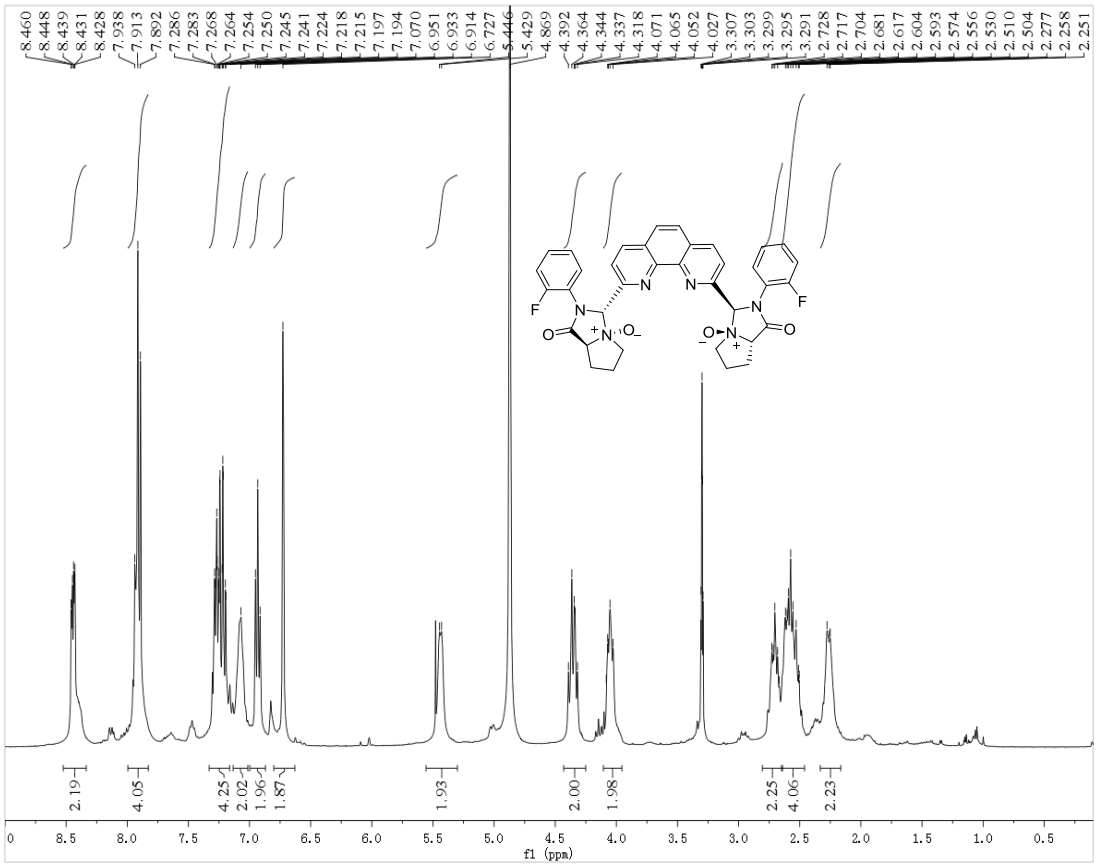


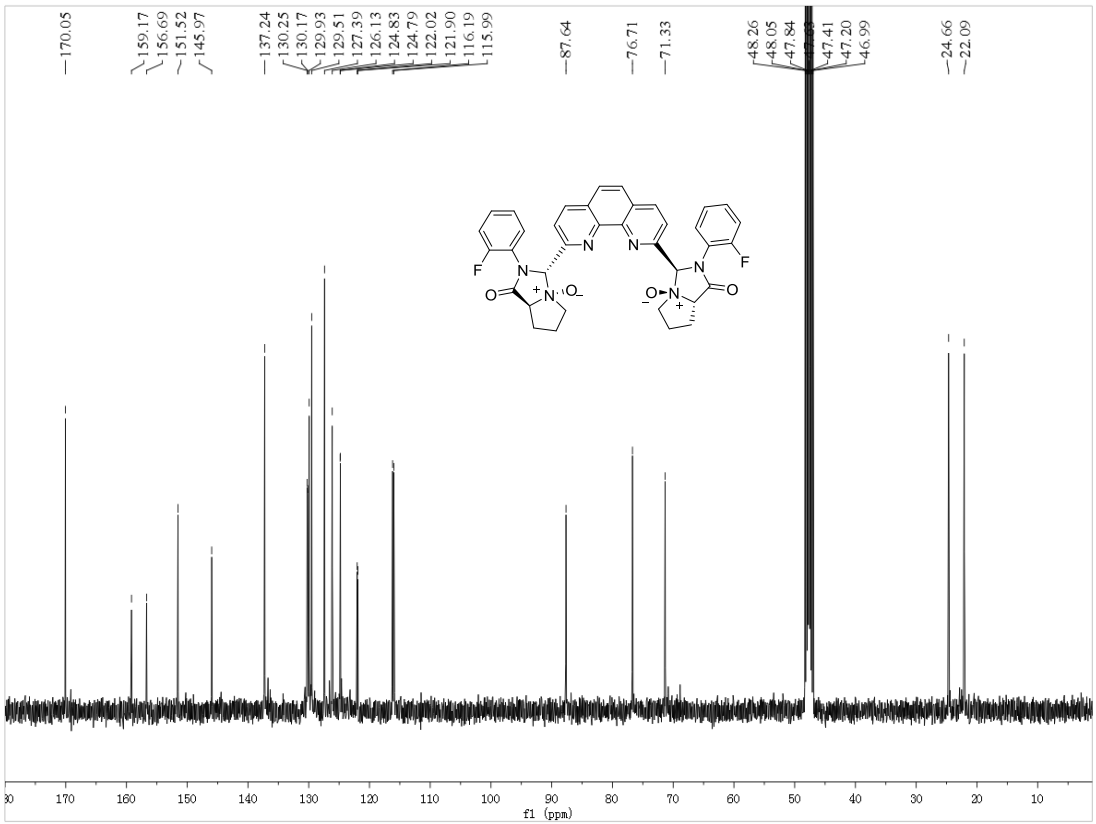
^{1}H and ^{13}C NMR of L1c



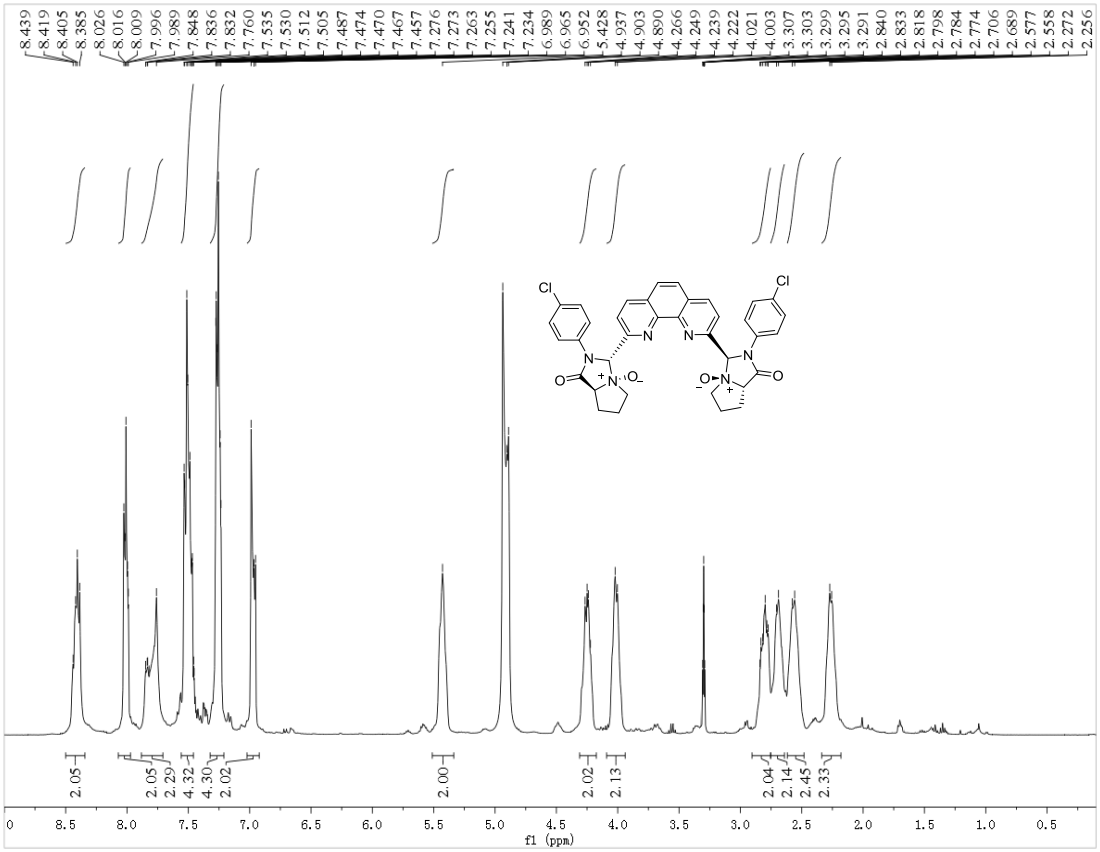


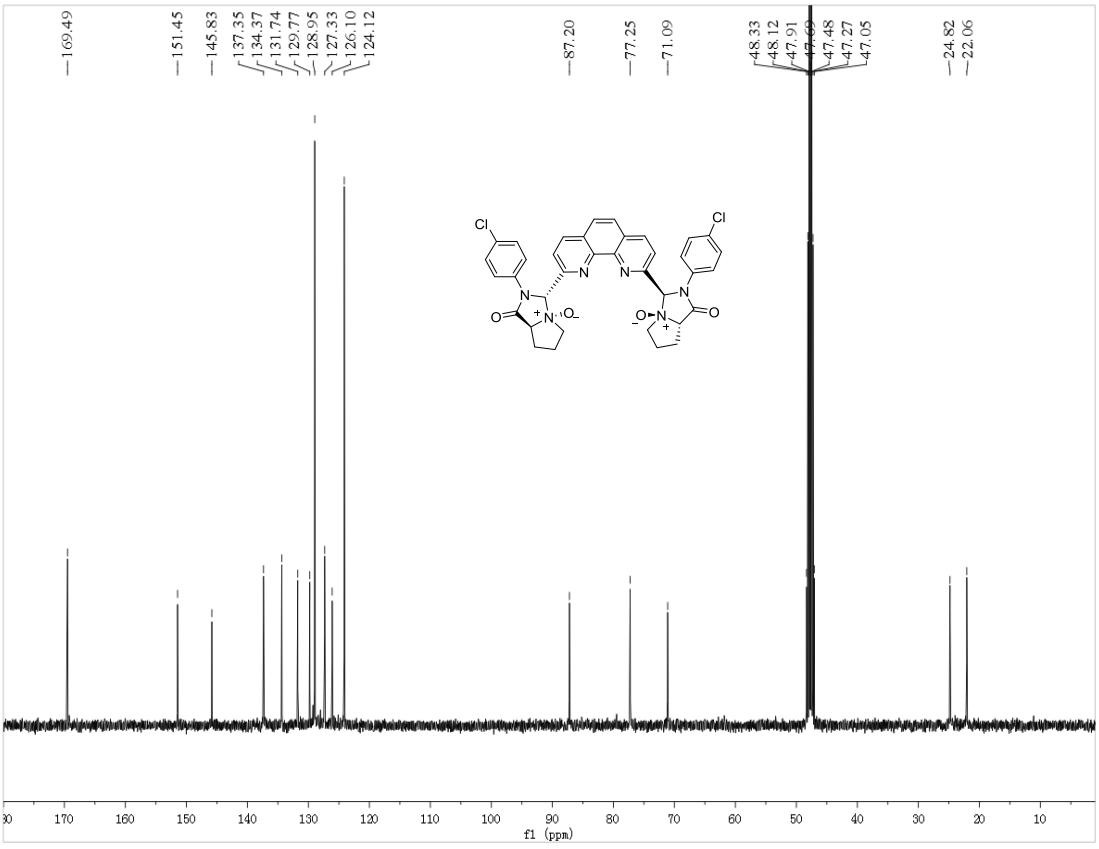
^{1}H and ^{13}C NMR of L1d



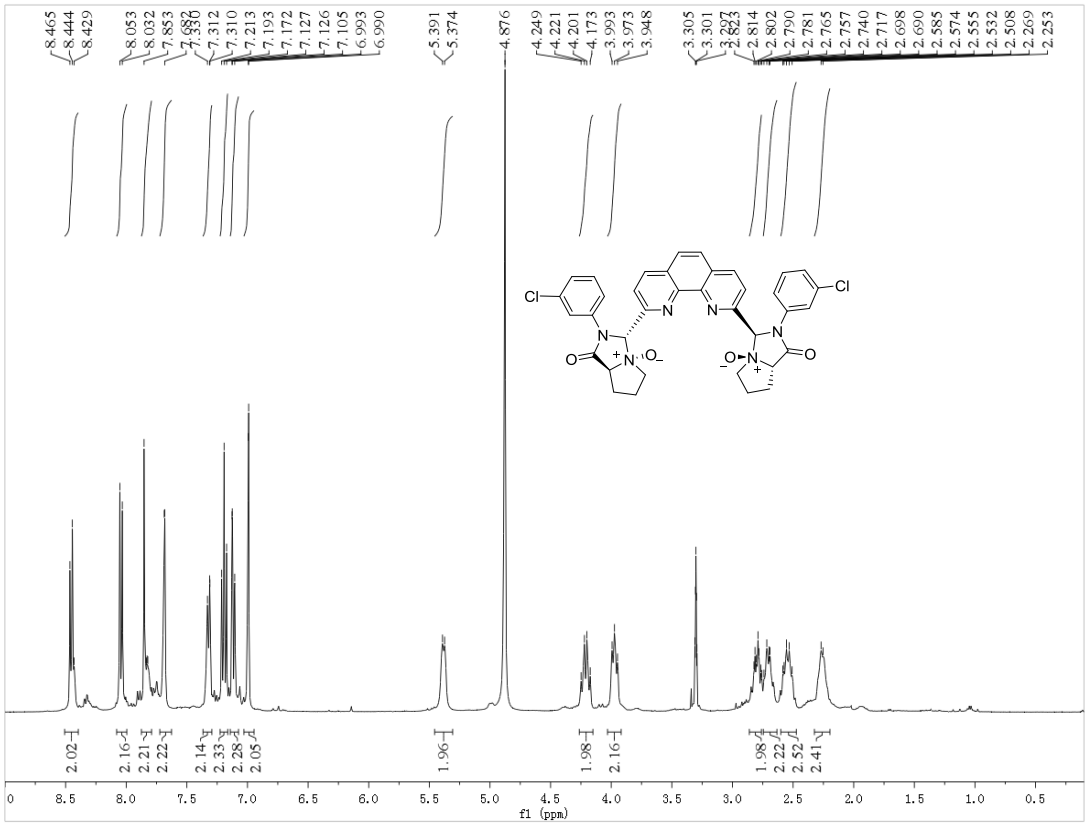


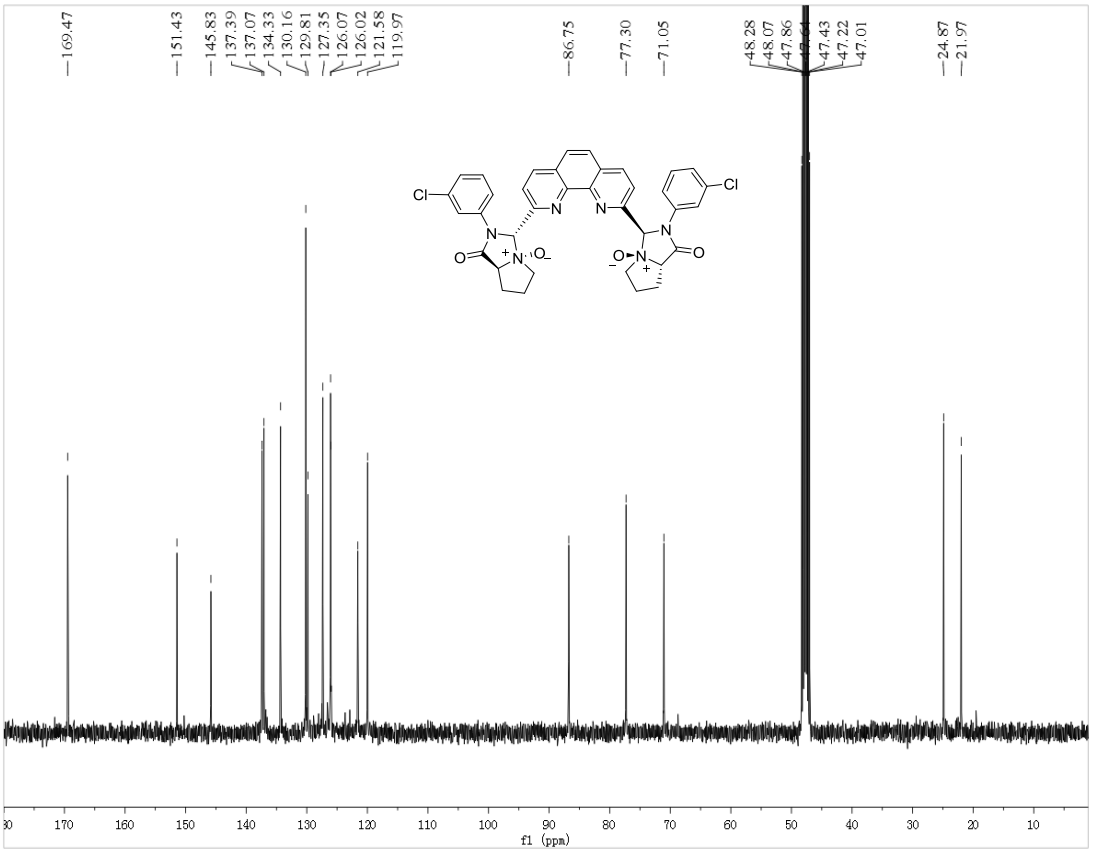
^{1}H and ^{13}C NMR of L1e



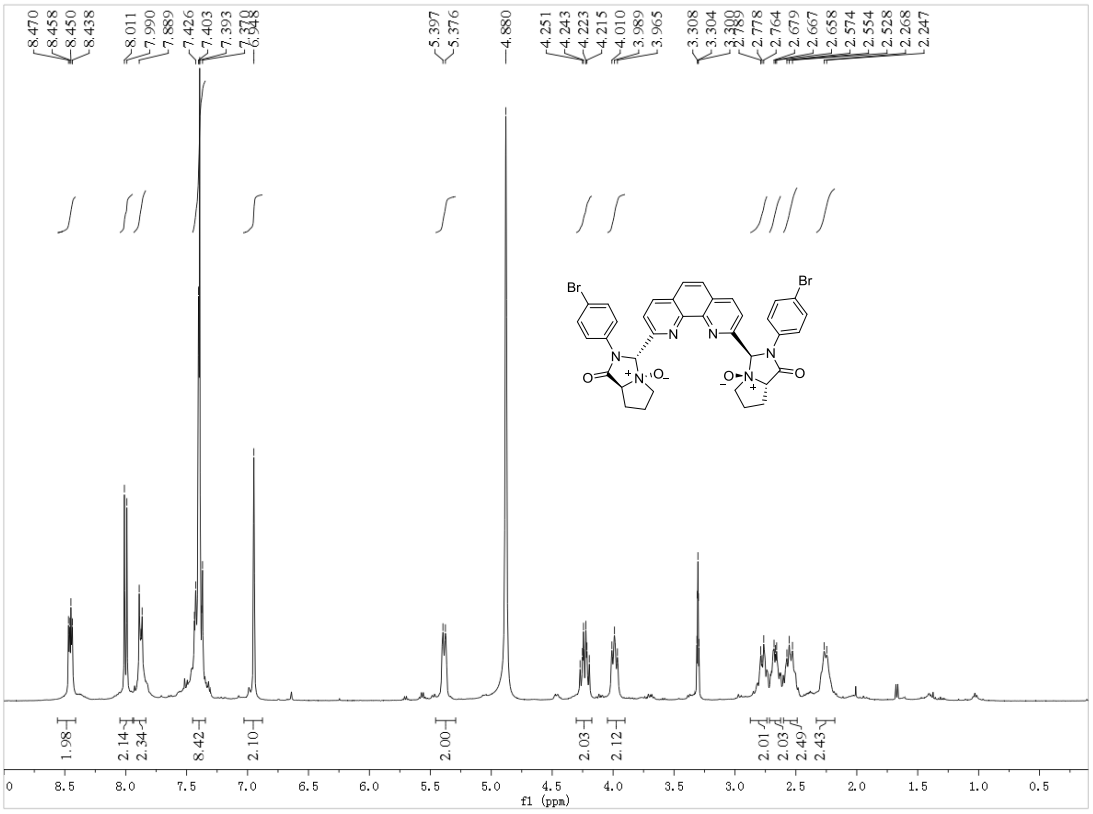


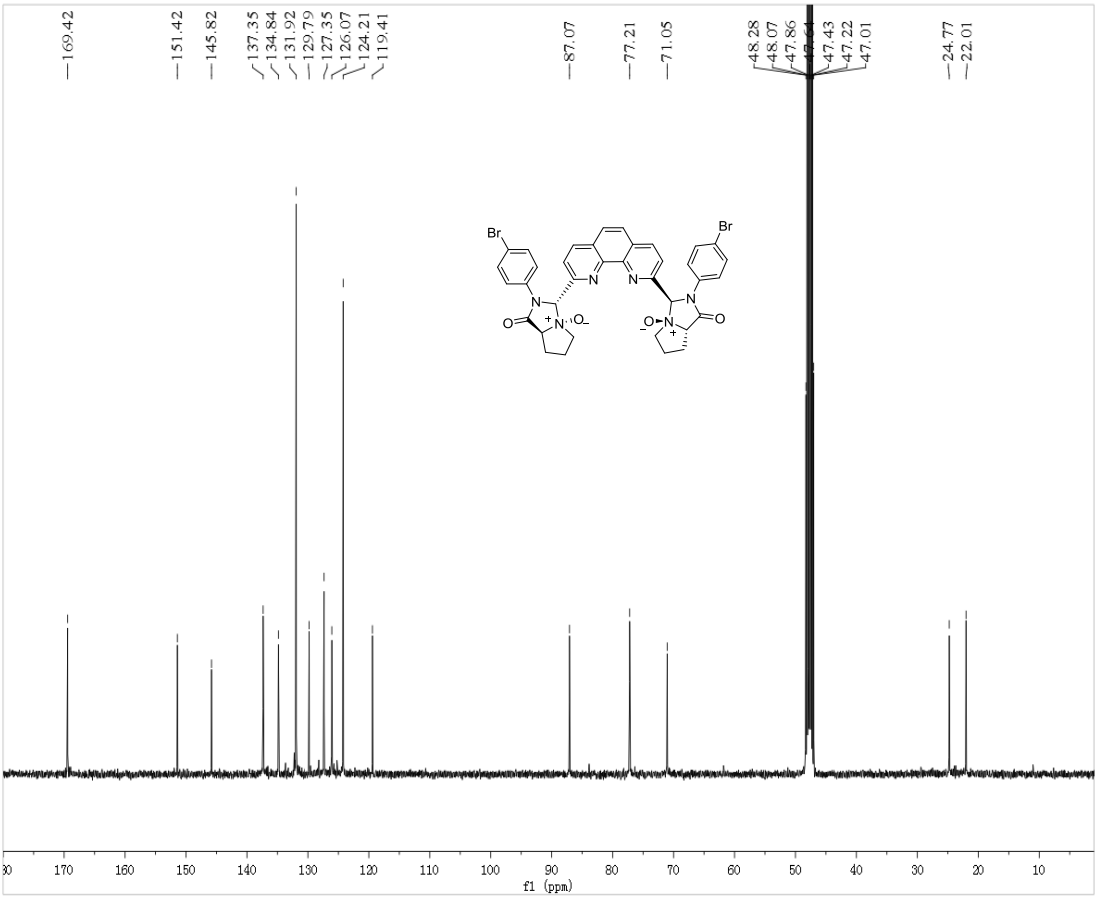
^{1}H and ^{13}C NMR of L1f



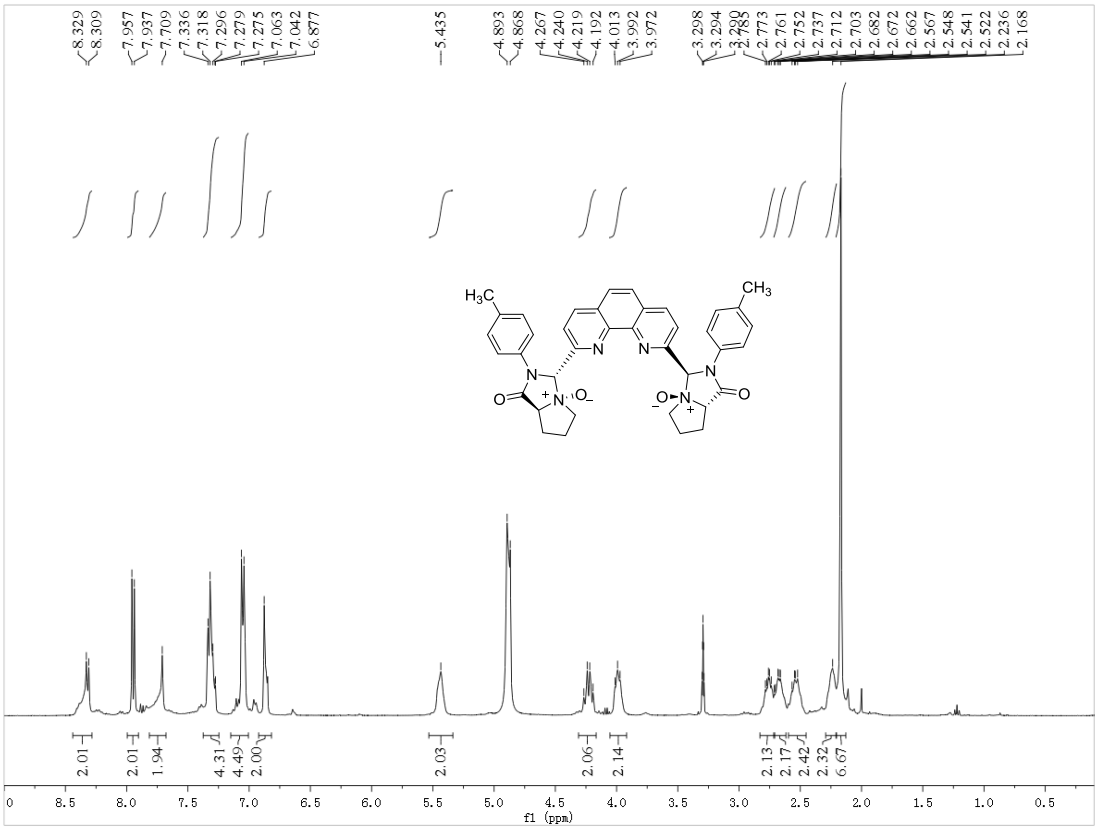


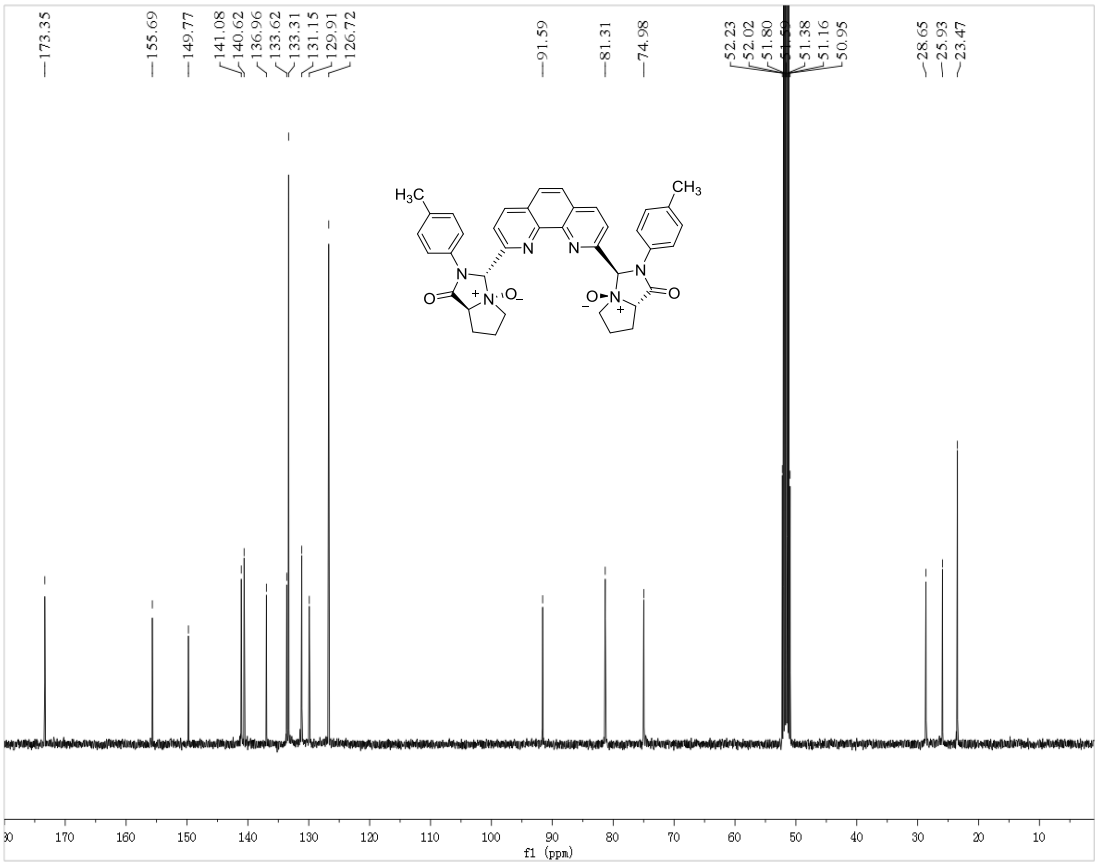
^{1}H and ^{13}C NMR of L1g



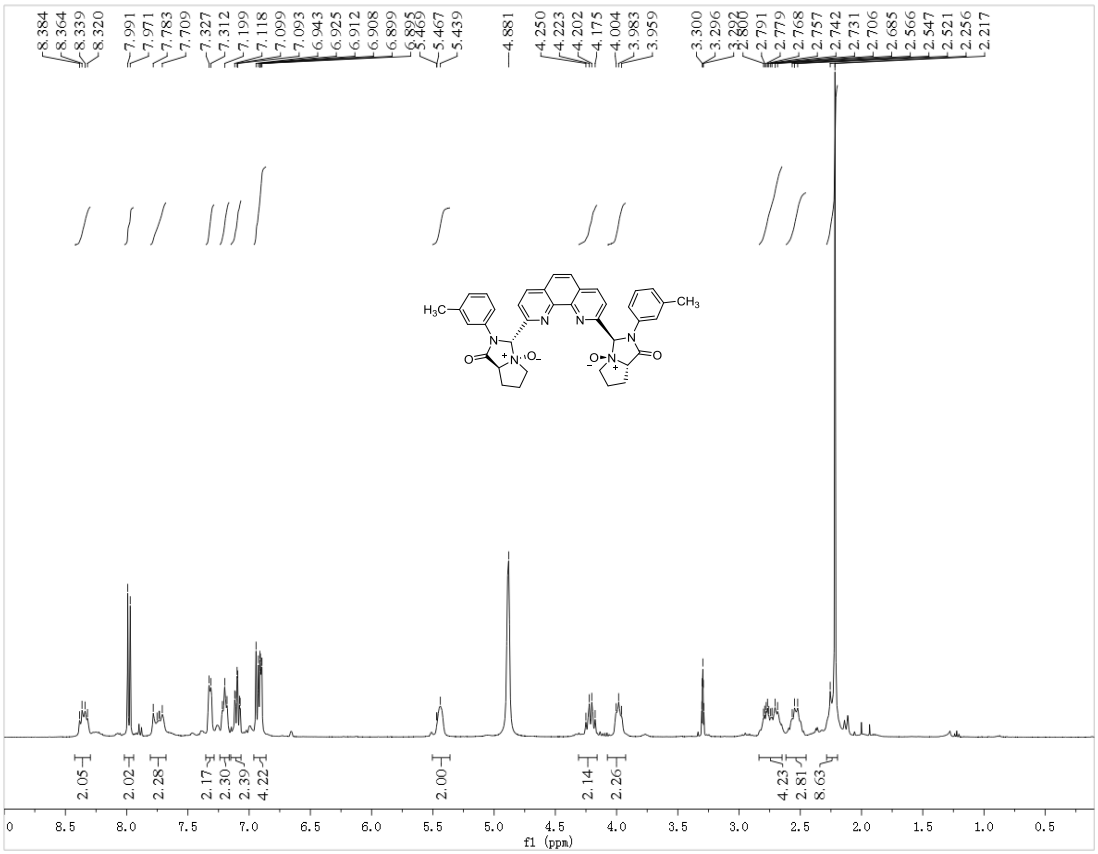


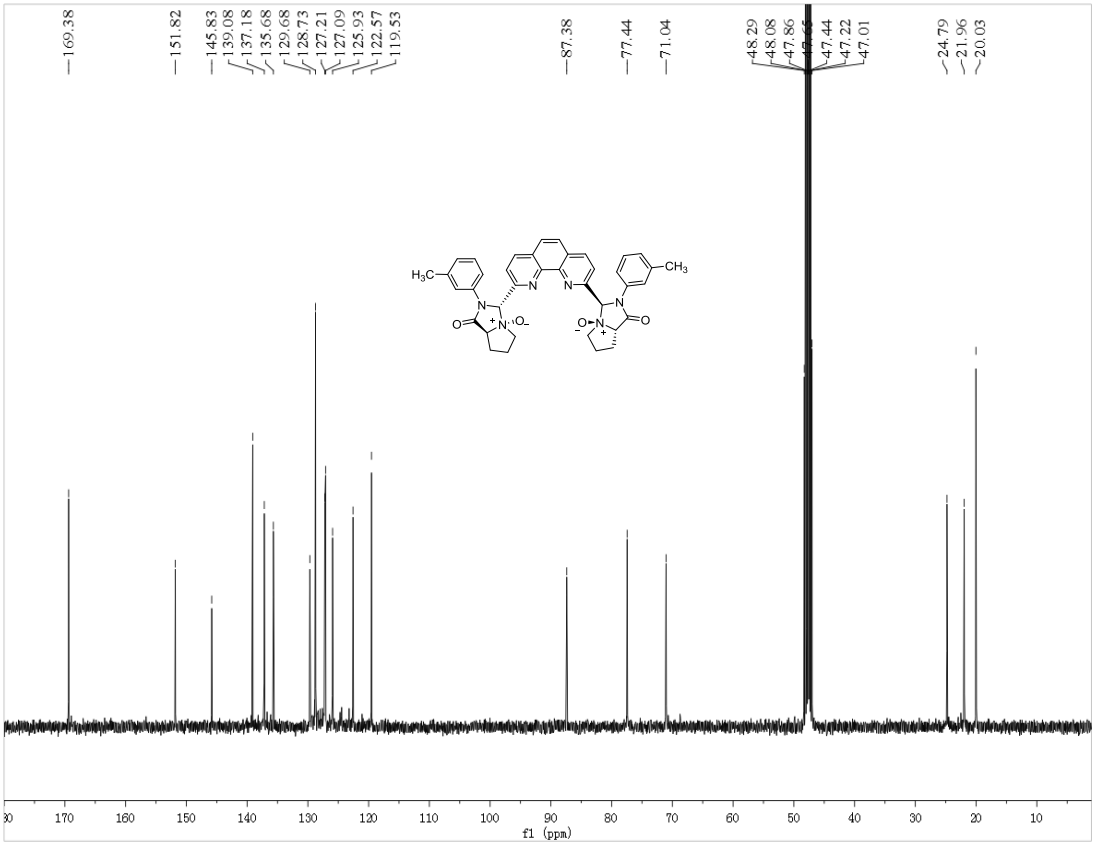
^{1}H and ^{13}C NMR of L1h



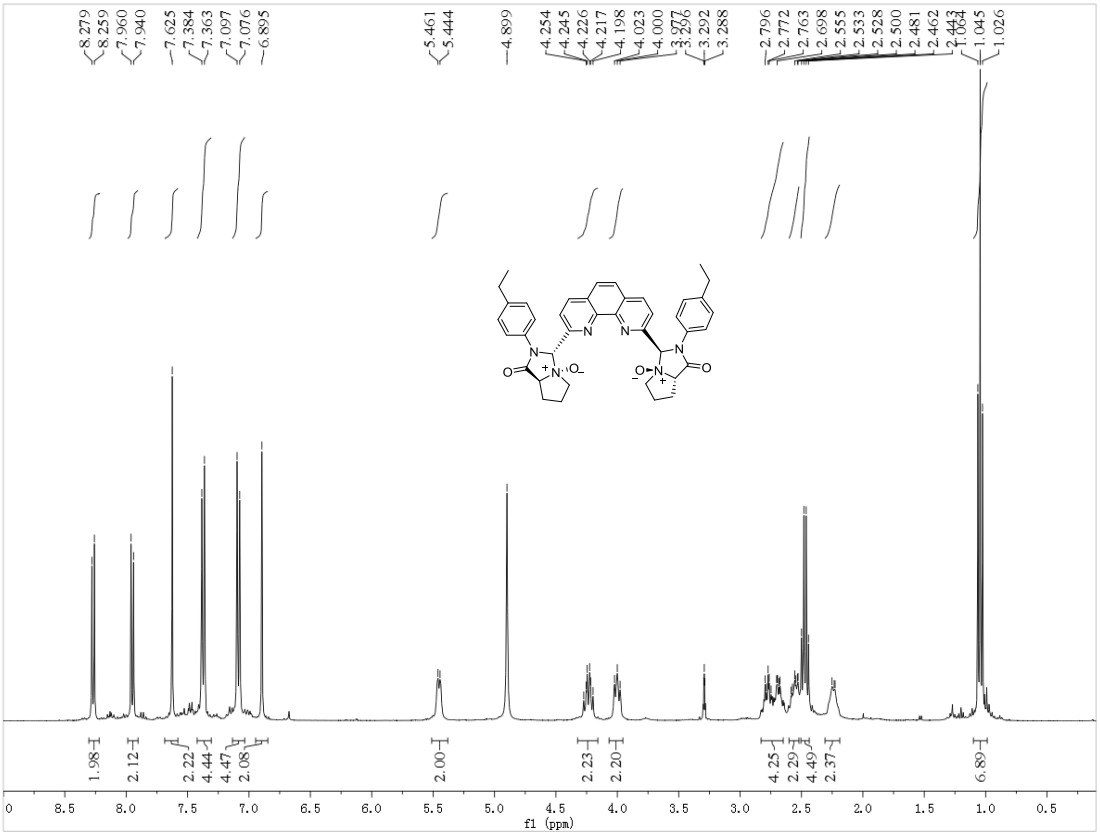


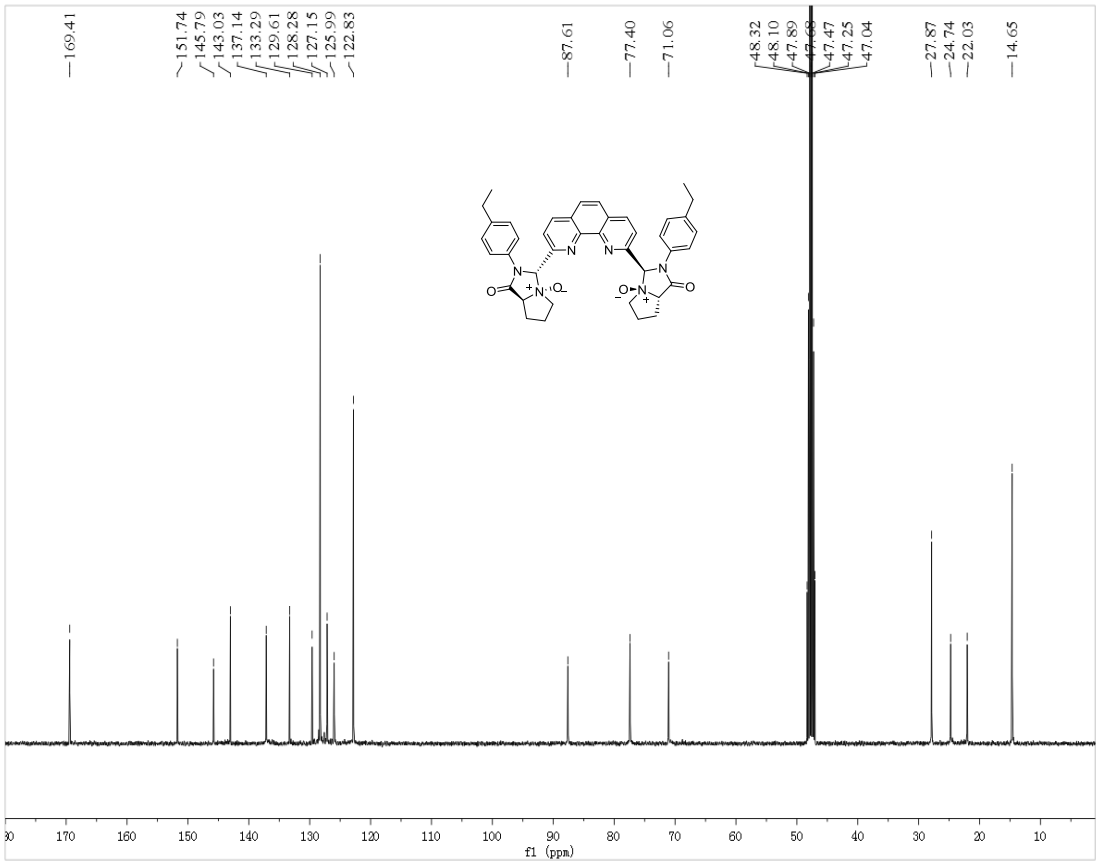
^{1}H and ^{13}C NMR of L1i



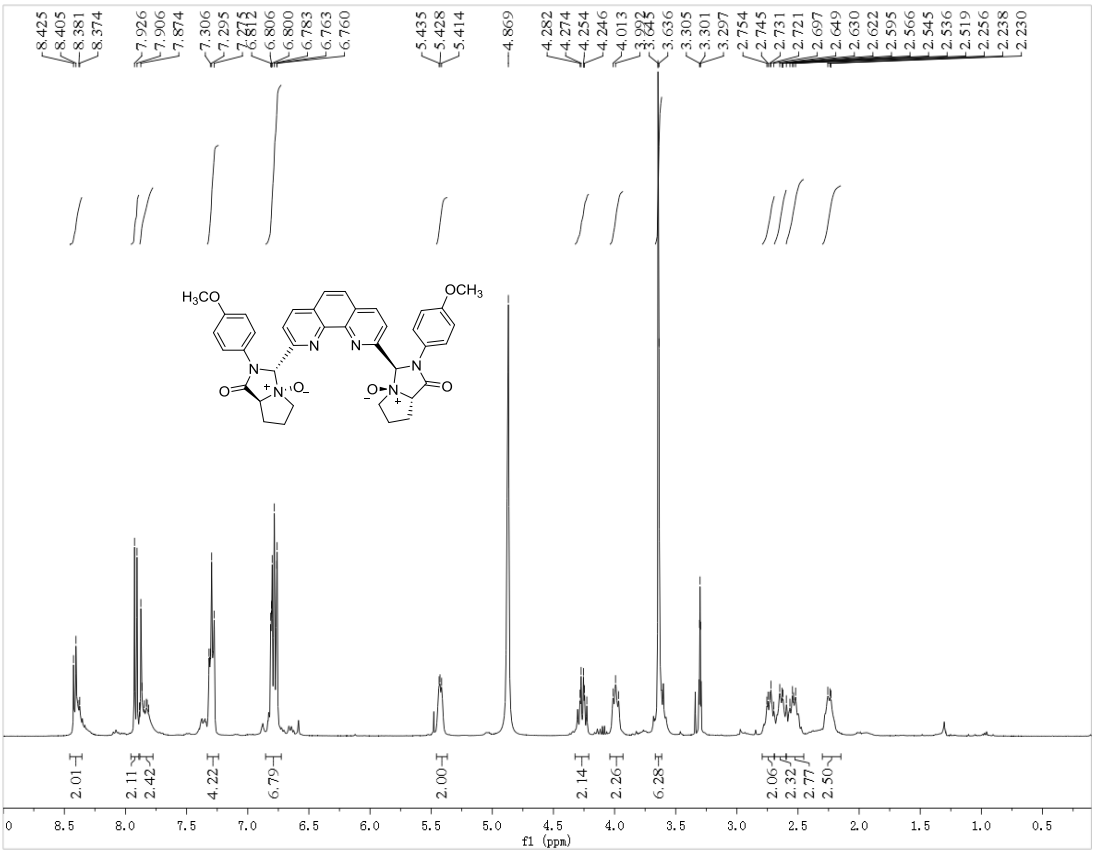


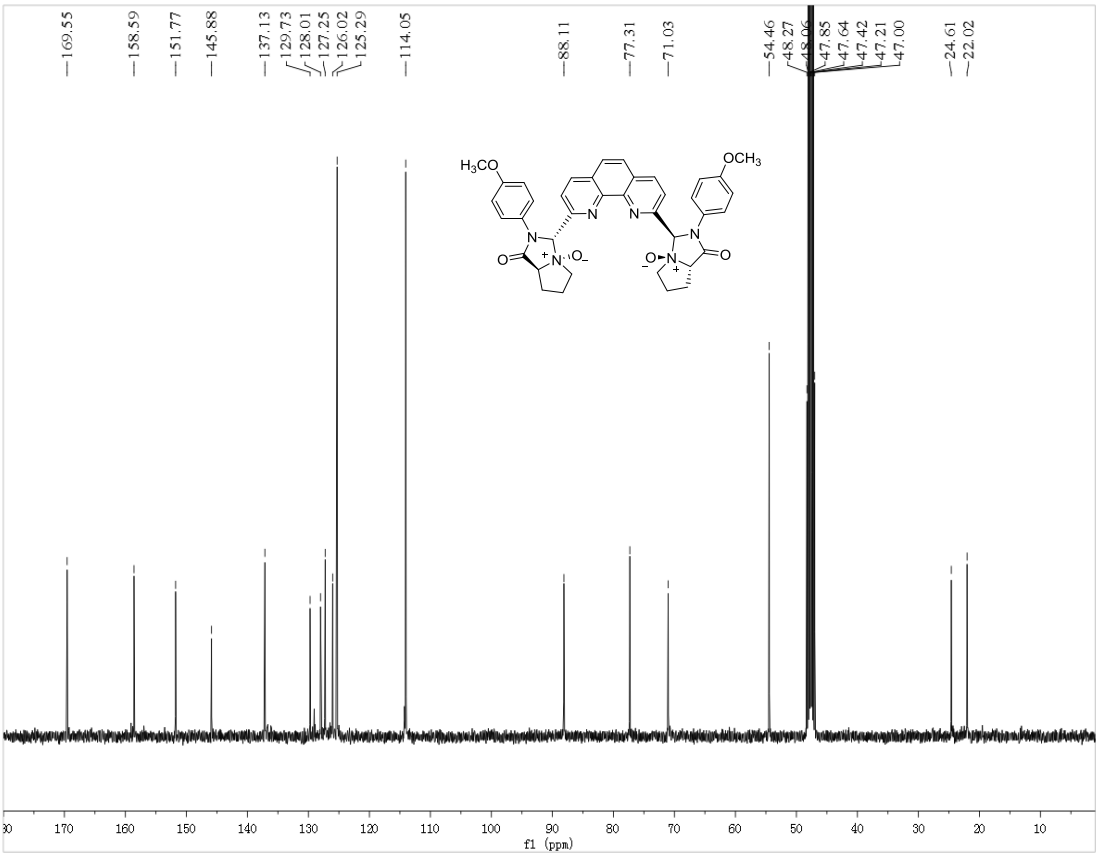
^{1}H and ^{13}C NMR of L1j



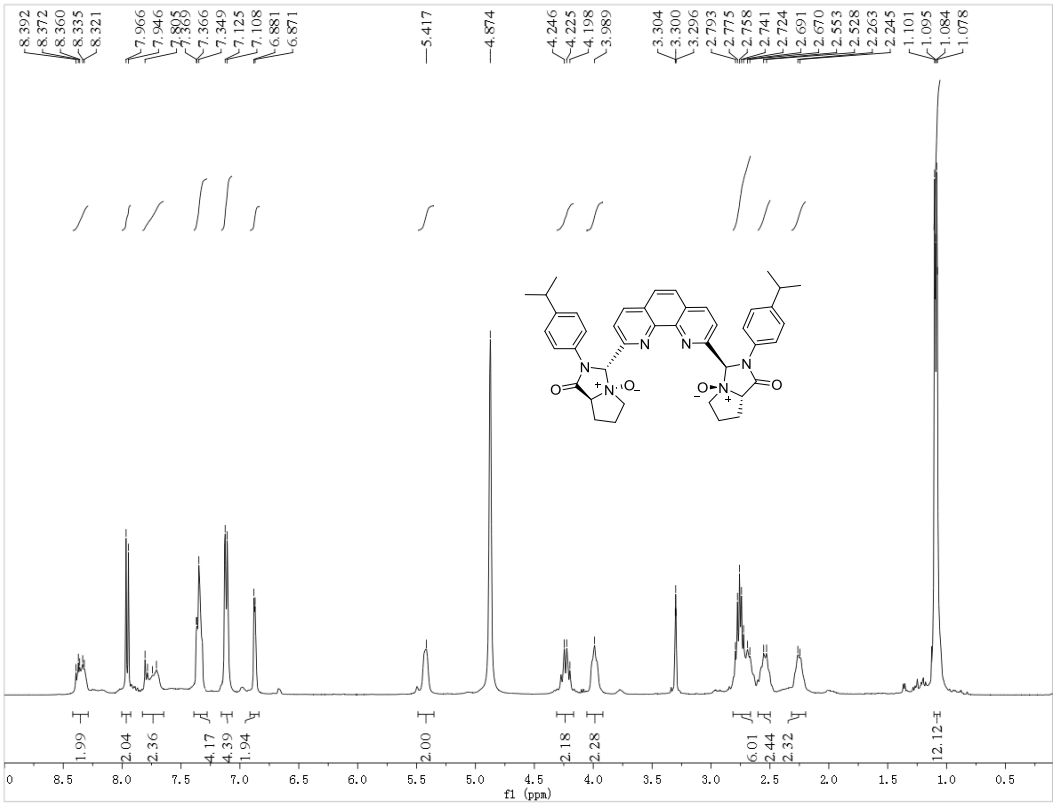


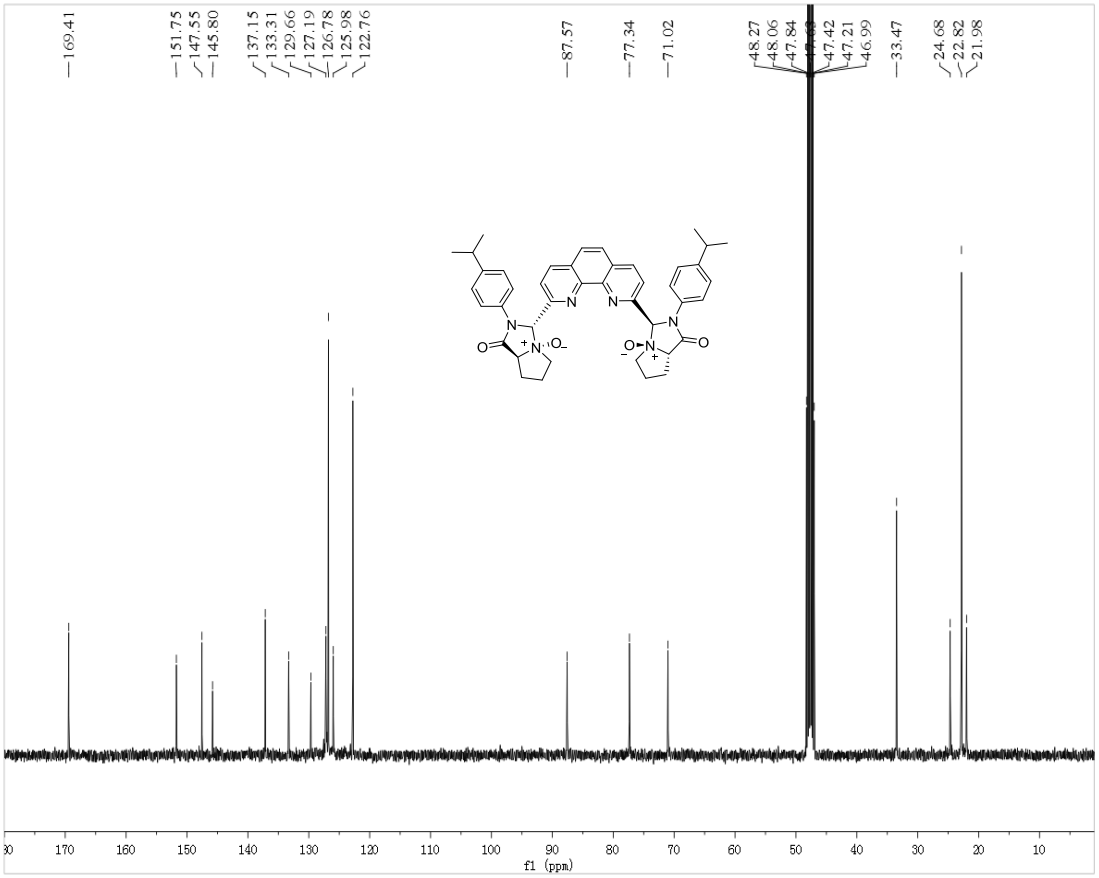
^{1}H and ^{13}C NMR of L1k



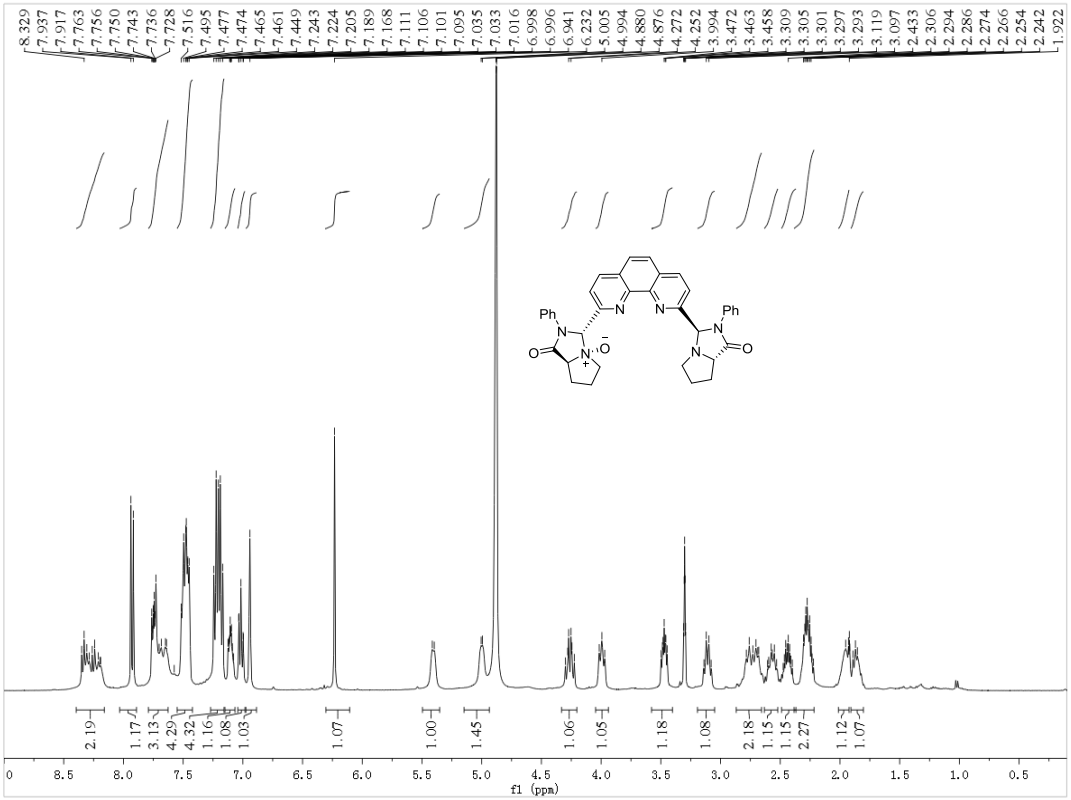


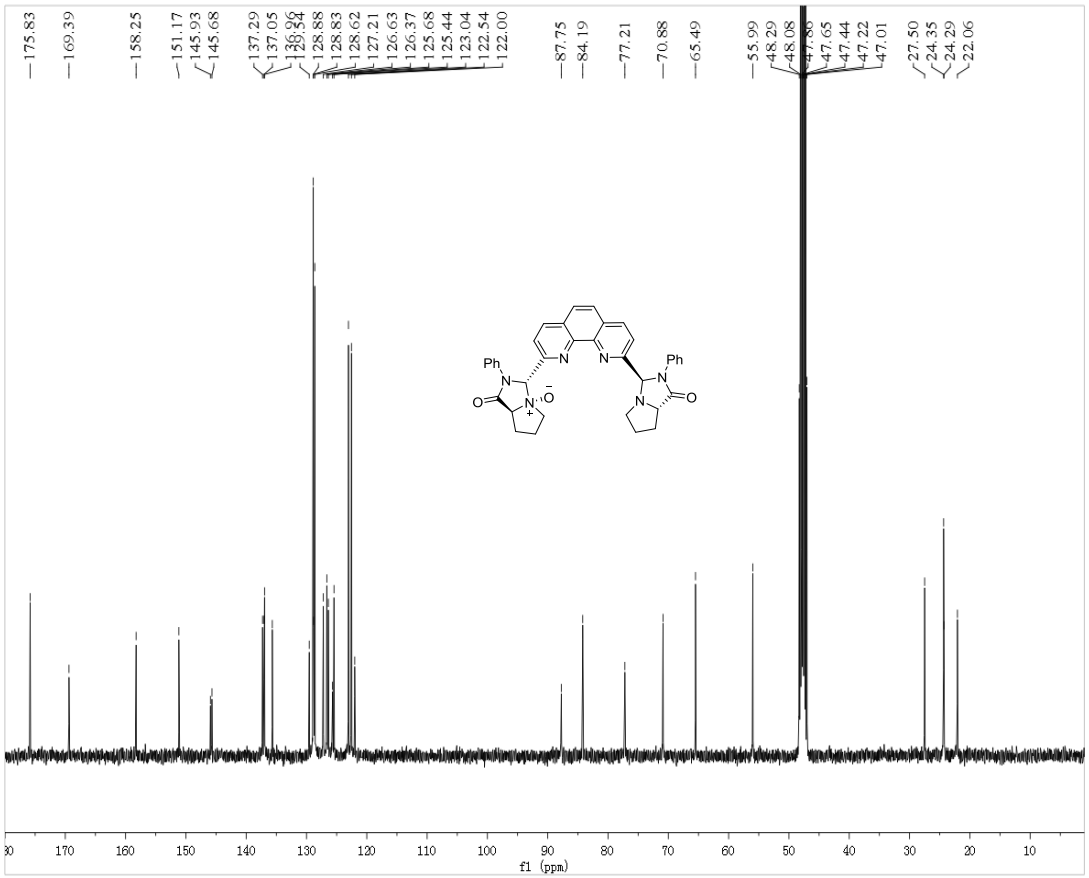
^{1}H and ^{13}C NMR of L1l



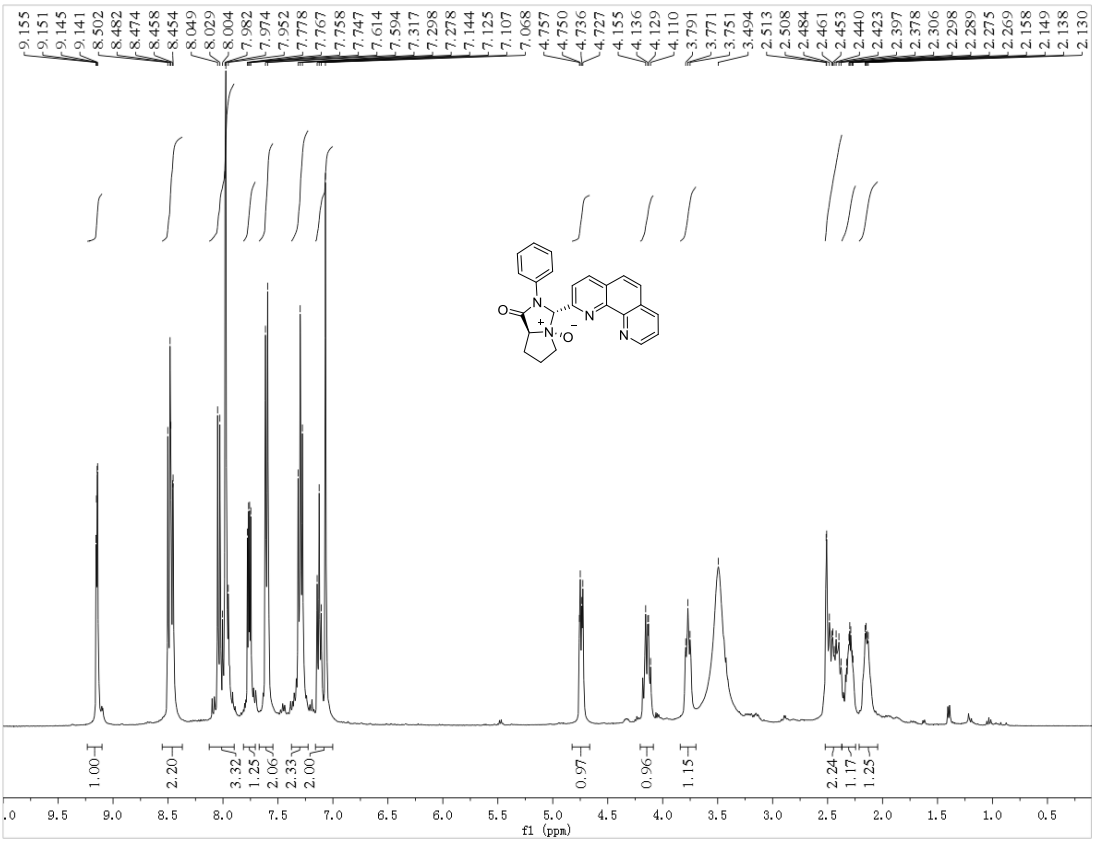


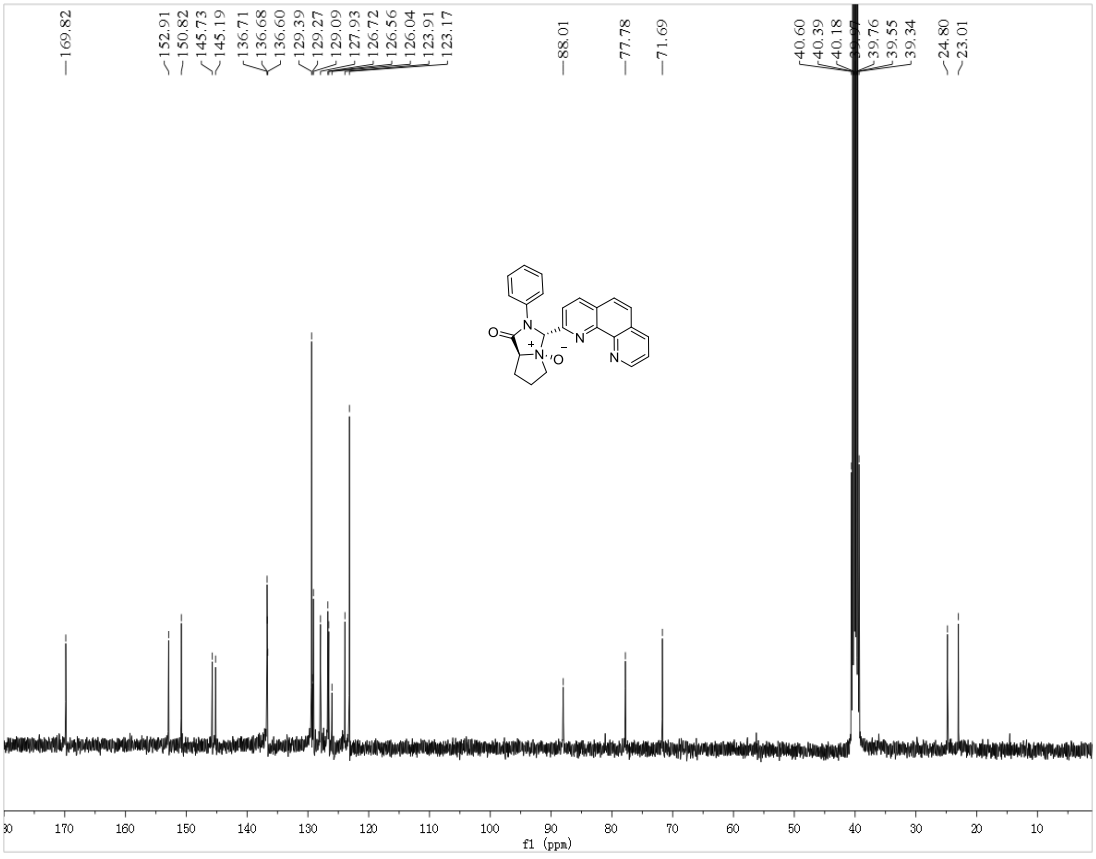
^{1}H and ^{13}C NMR of L2a



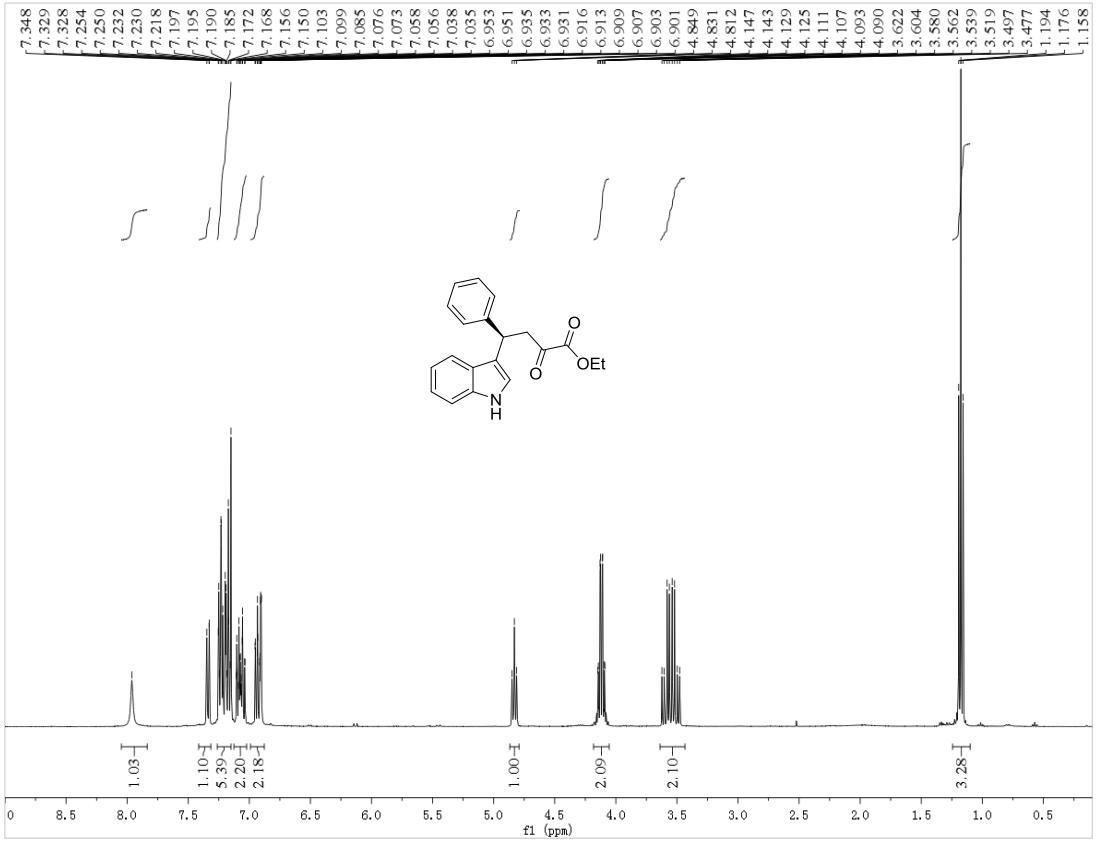


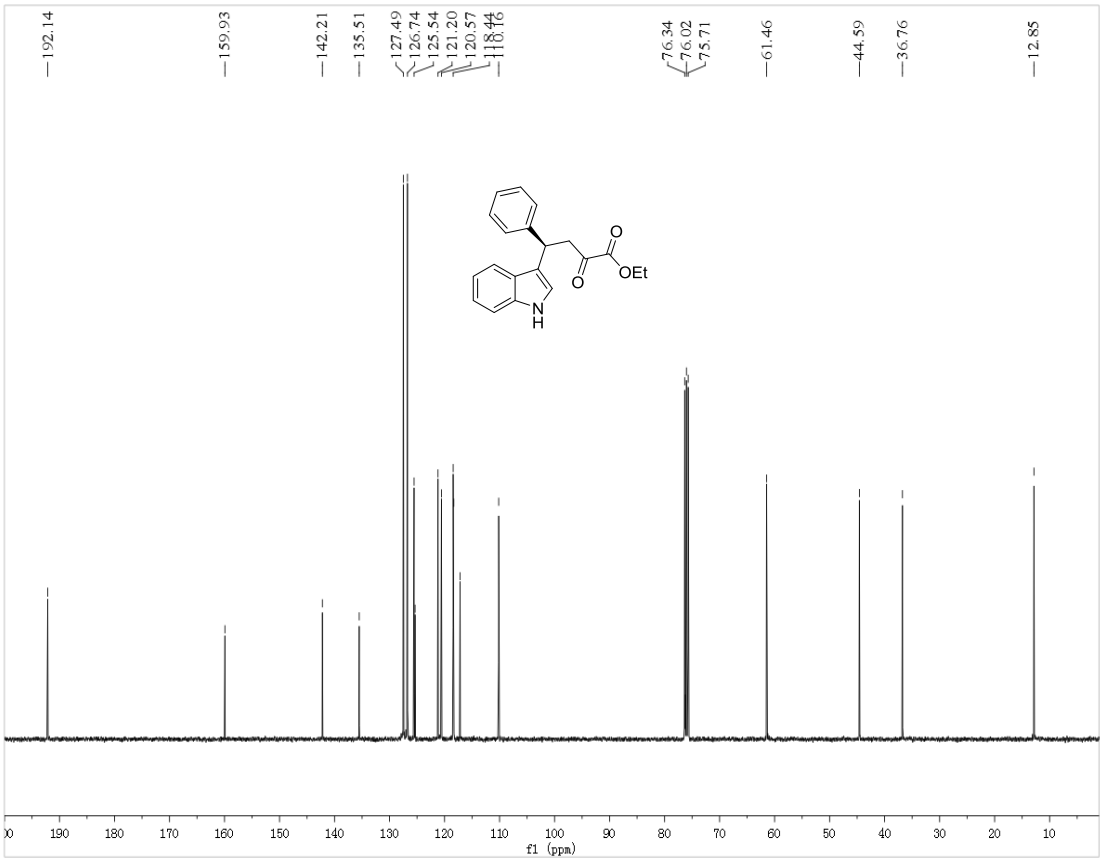
^{1}H and ^{13}C NMR of L6a



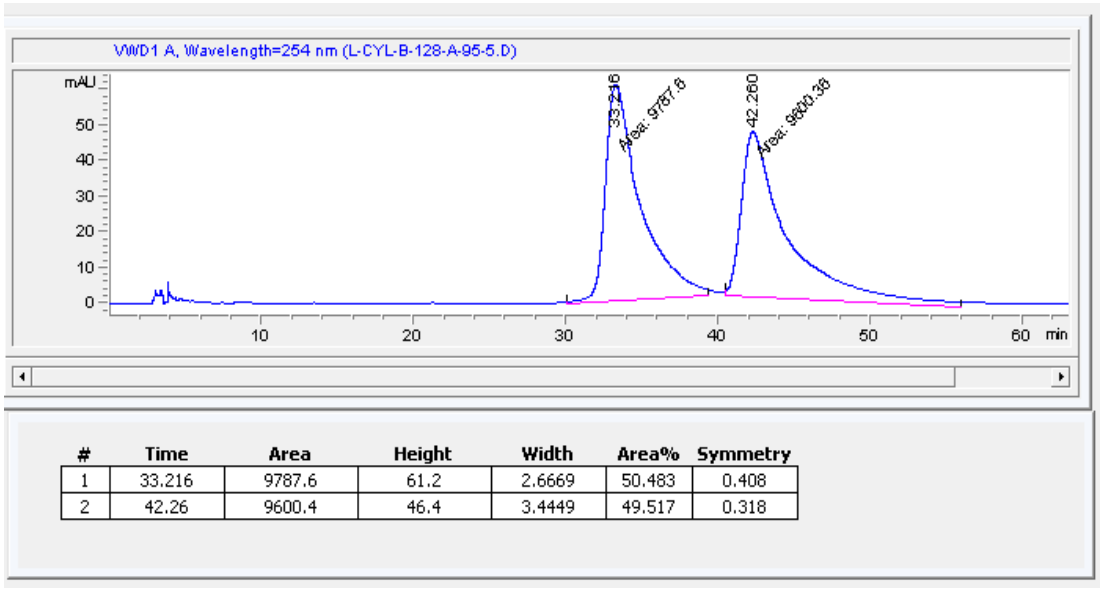


^{1}H and ^{13}C NMR of 6a

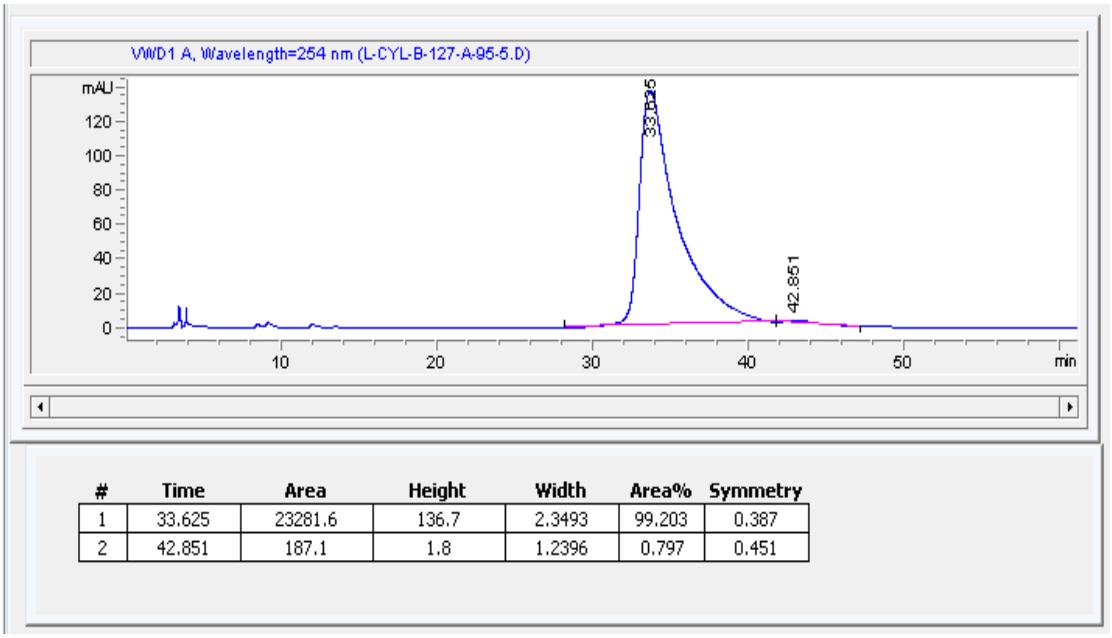




HPLC of 6a

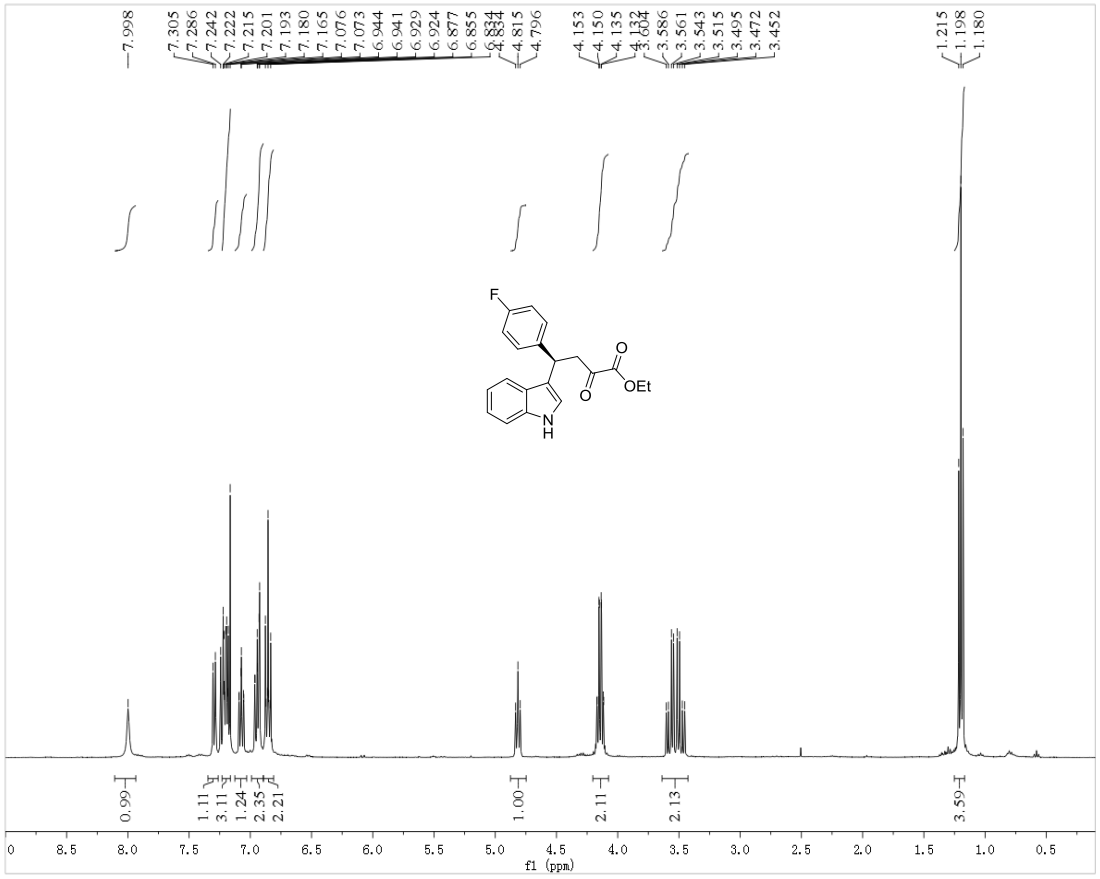


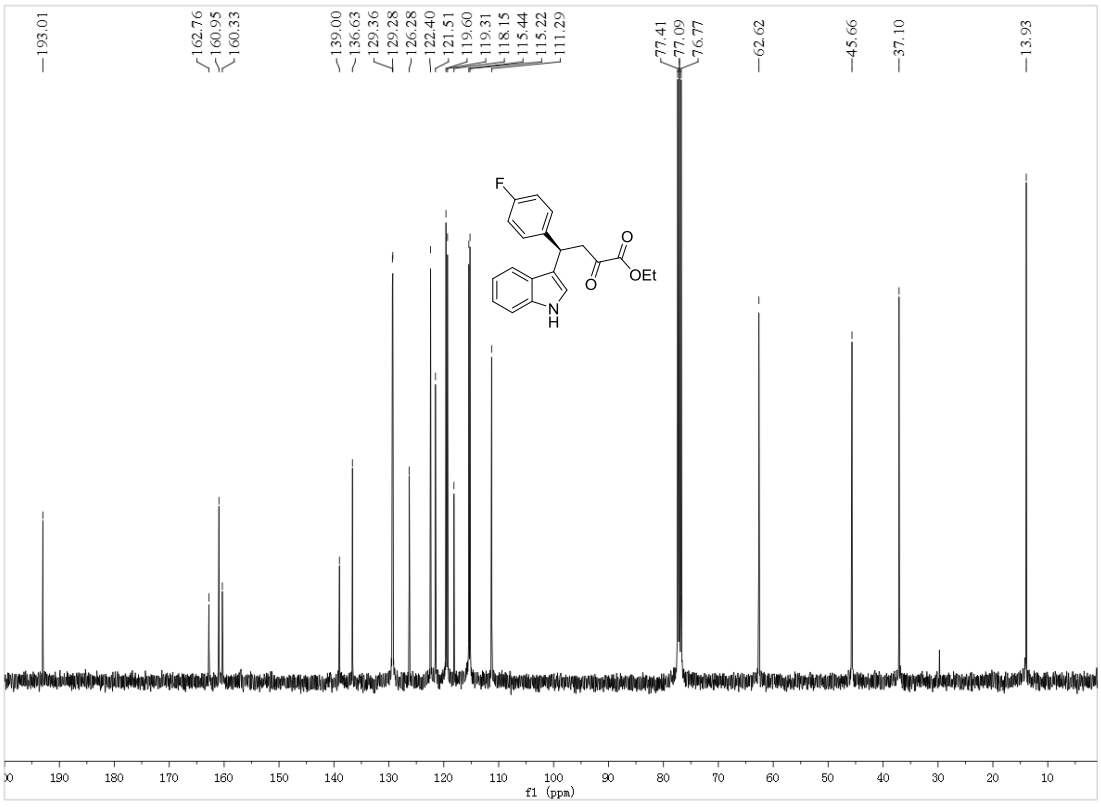
#	Time	Area	Height	Width	Area%	Symmetry
1	33.216	9787.6	61.2	2.6669	50.483	0.408
2	42.26	9600.4	46.4	3.4449	49.517	0.318



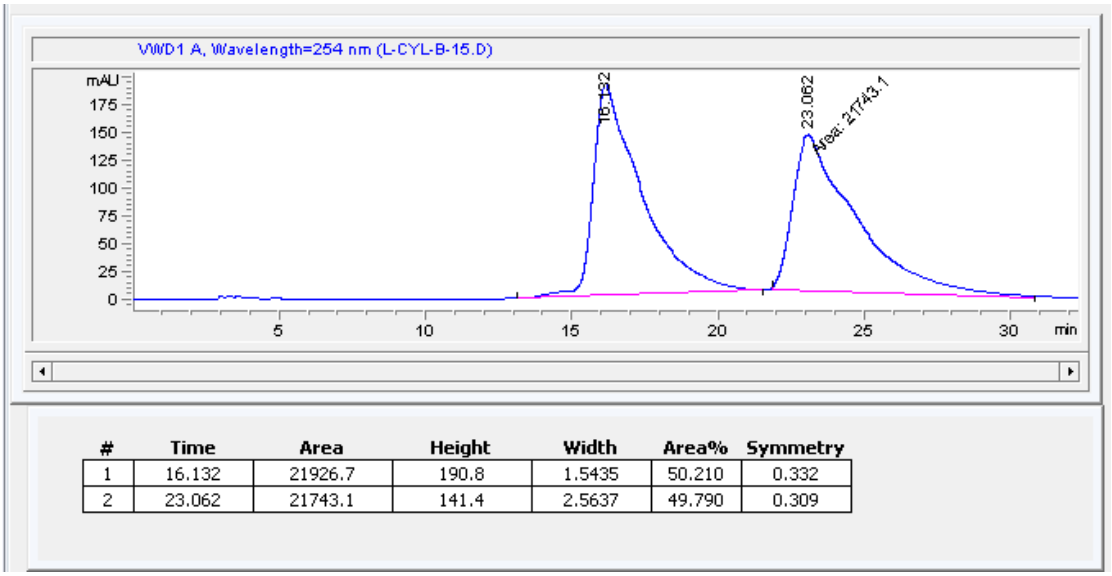
#	Time	Area	Height	Width	Area%	Symmetry
1	33.625	23281.6	136.7	2.3493	99.203	0.387
2	42.851	187.1	1.8	1.2396	0.797	0.451

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

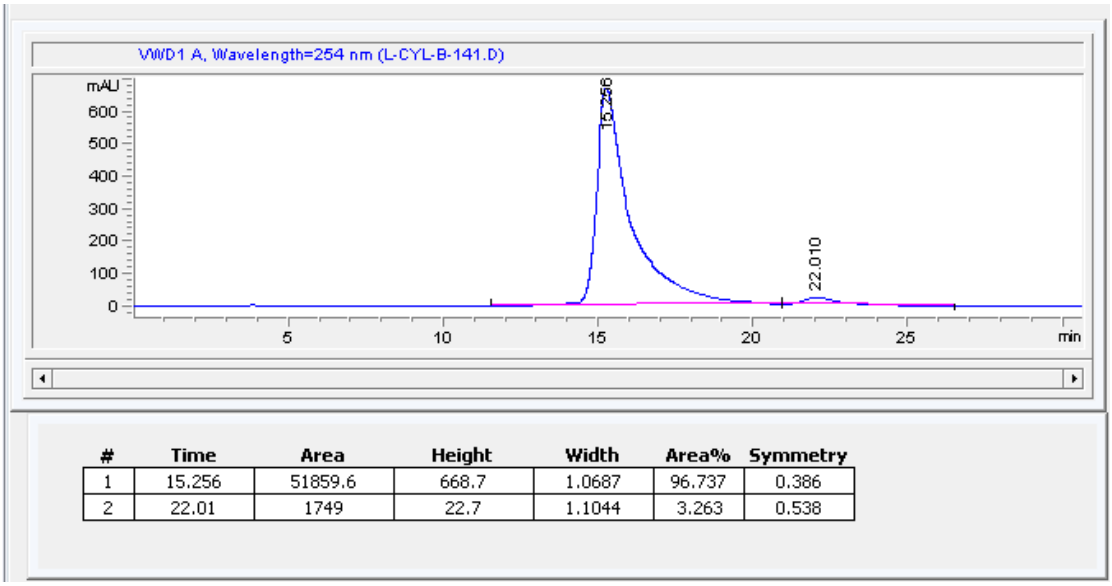




HPLC of 6b

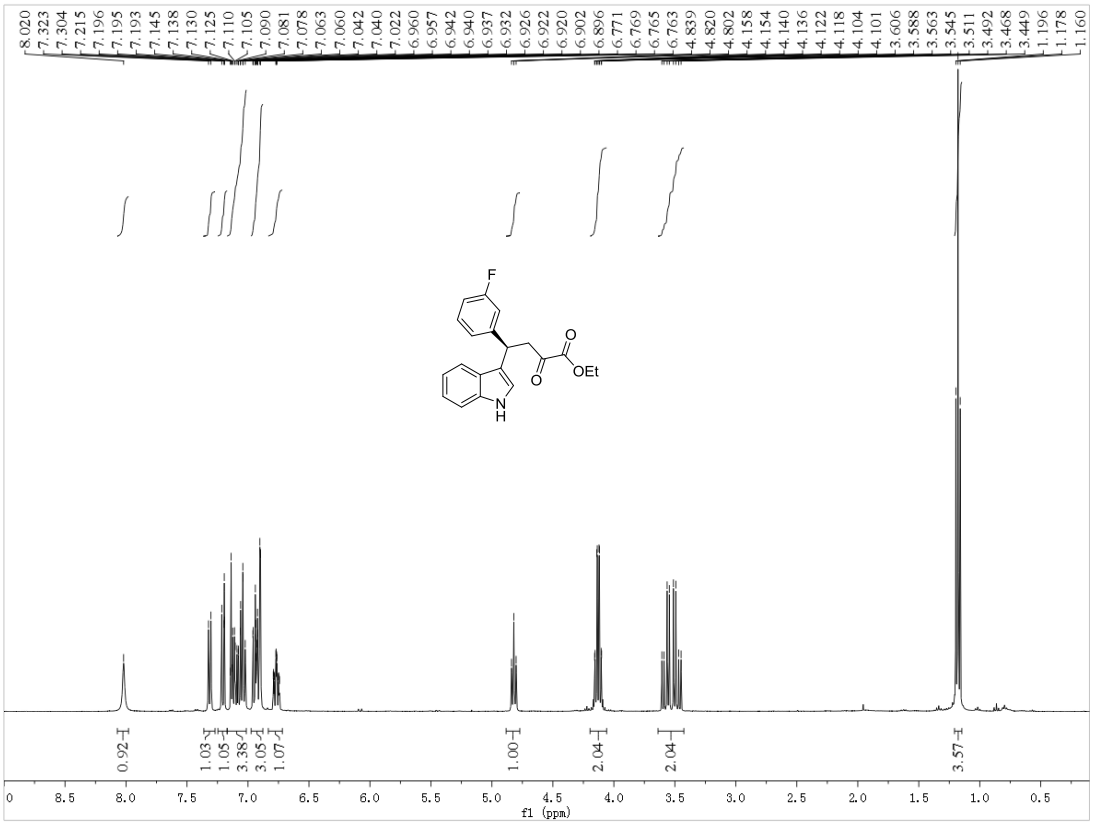


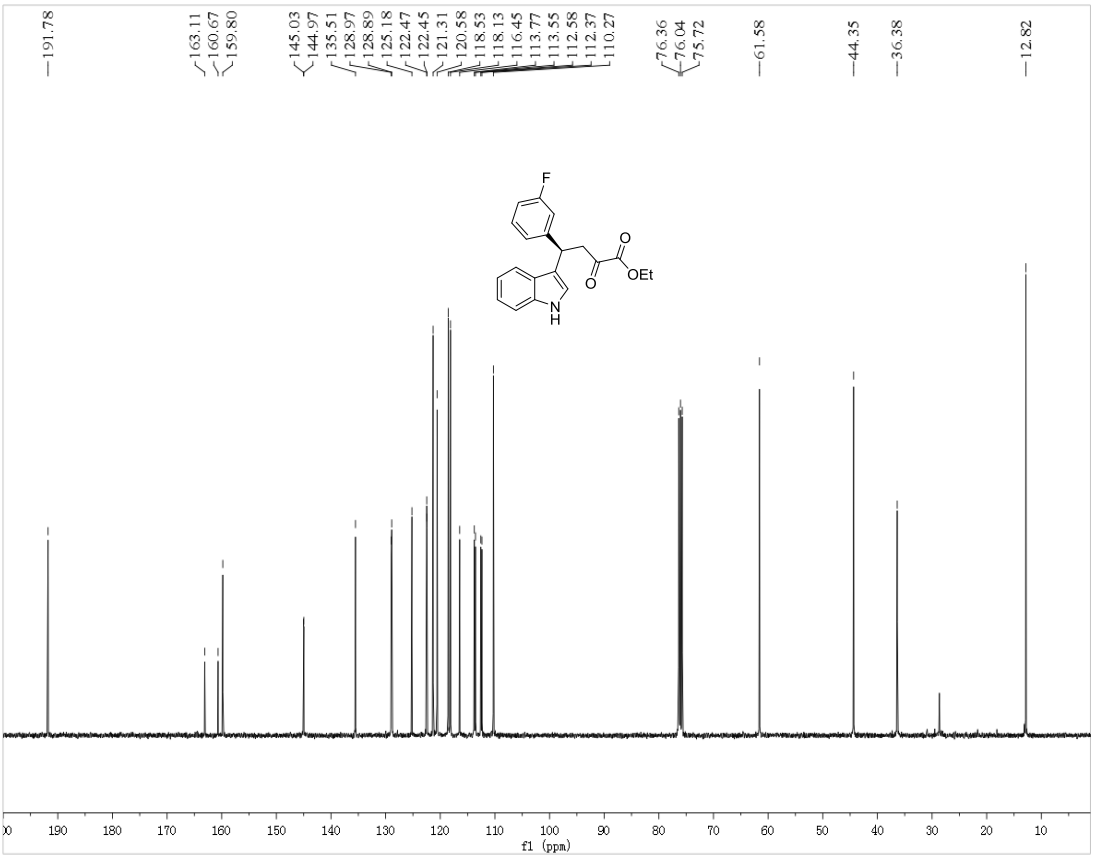
#	Time	Area	Height	Width	Area%	Symmetry
1	16.132	21926.7	190.8	1.5435	50.210	0.332
2	23.062	21743.1	141.4	2.5637	49.790	0.309



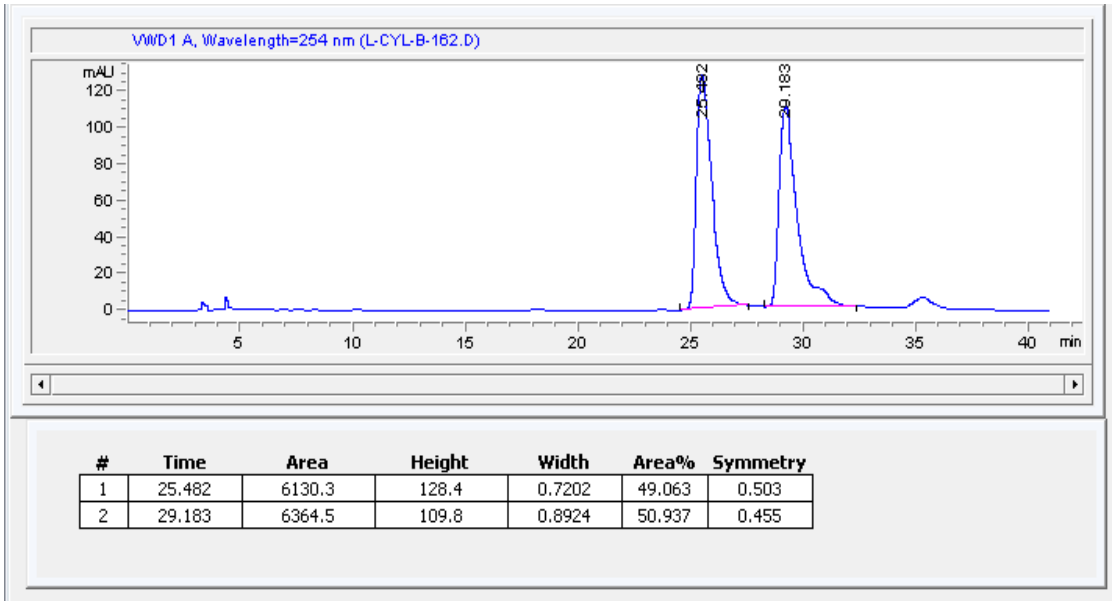
#	Time	Area	Height	Width	Area%	Symmetry
1	15.256	51859.6	668.7	1.0687	96.737	0.386
2	22.01	1749	22.7	1.1044	3.263	0.538

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

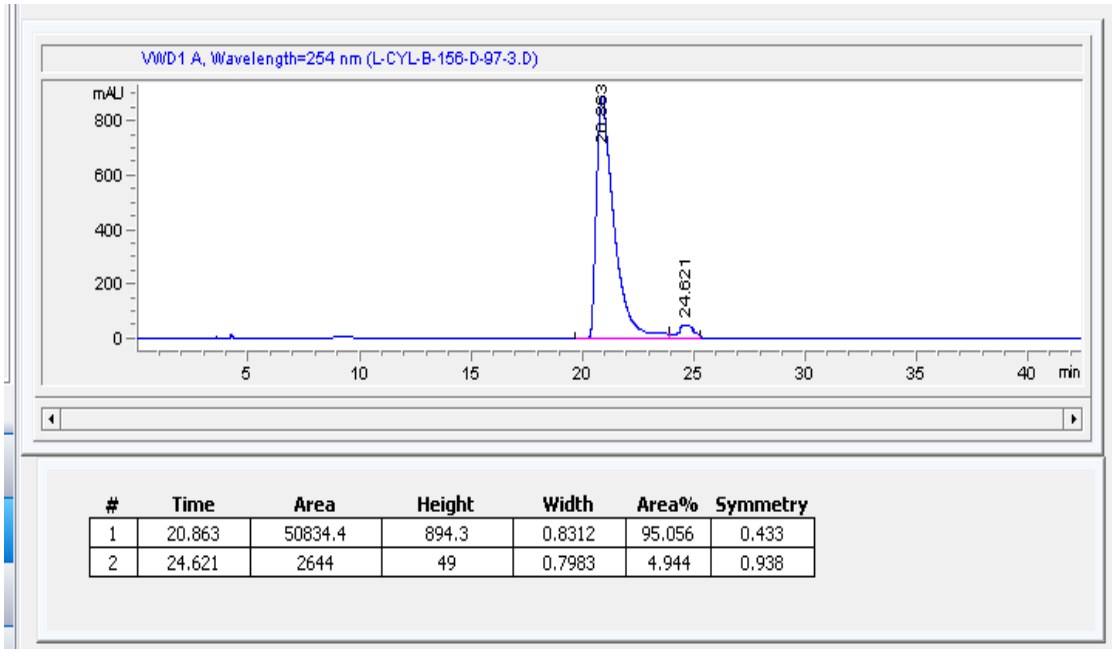




HPLC of 6c

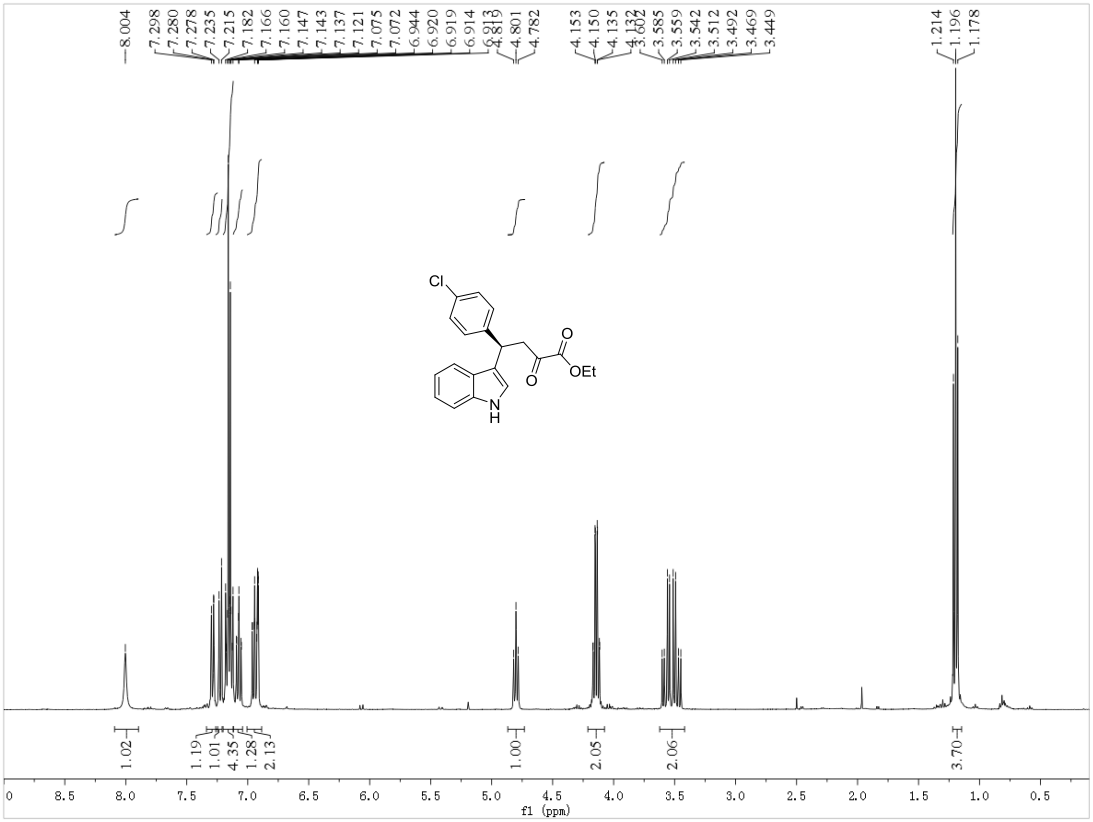


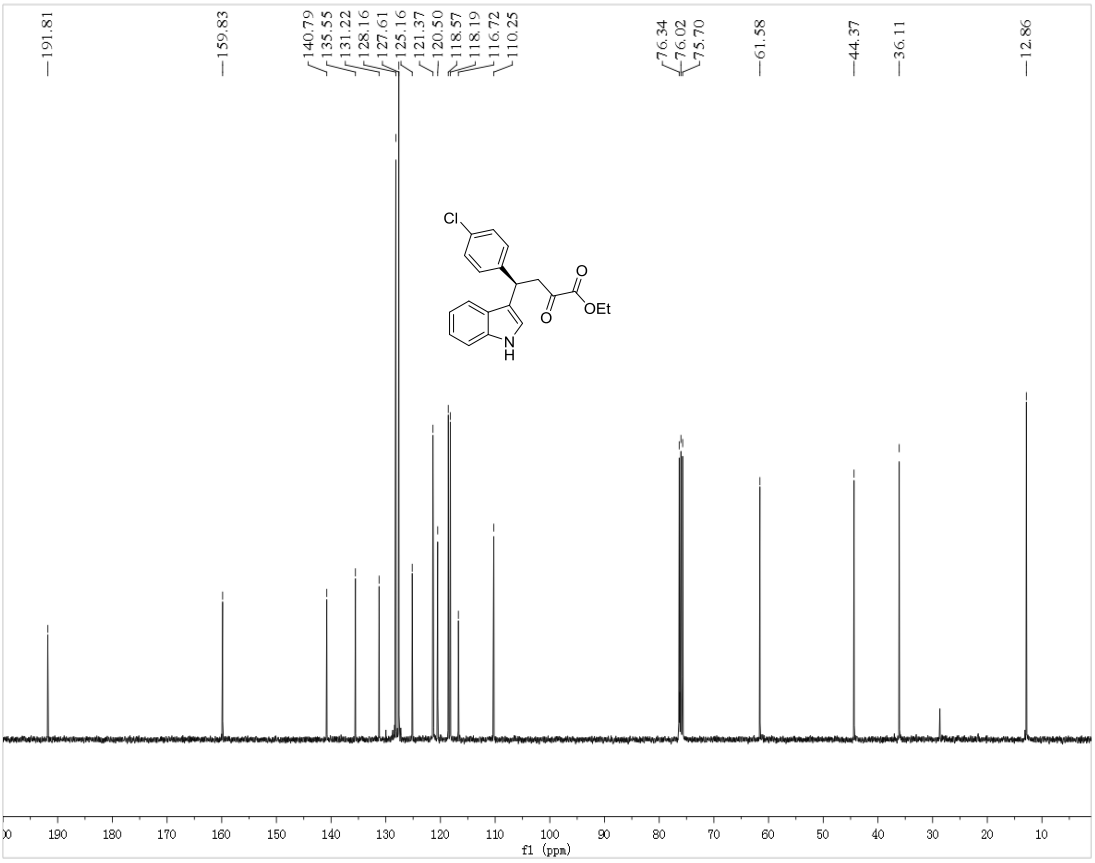
#	Time	Area	Height	Width	Area%	Symmetry
1	25.482	6130.3	128.4	0.7202	49.063	0.503
2	29.183	6364.5	109.8	0.8924	50.937	0.455



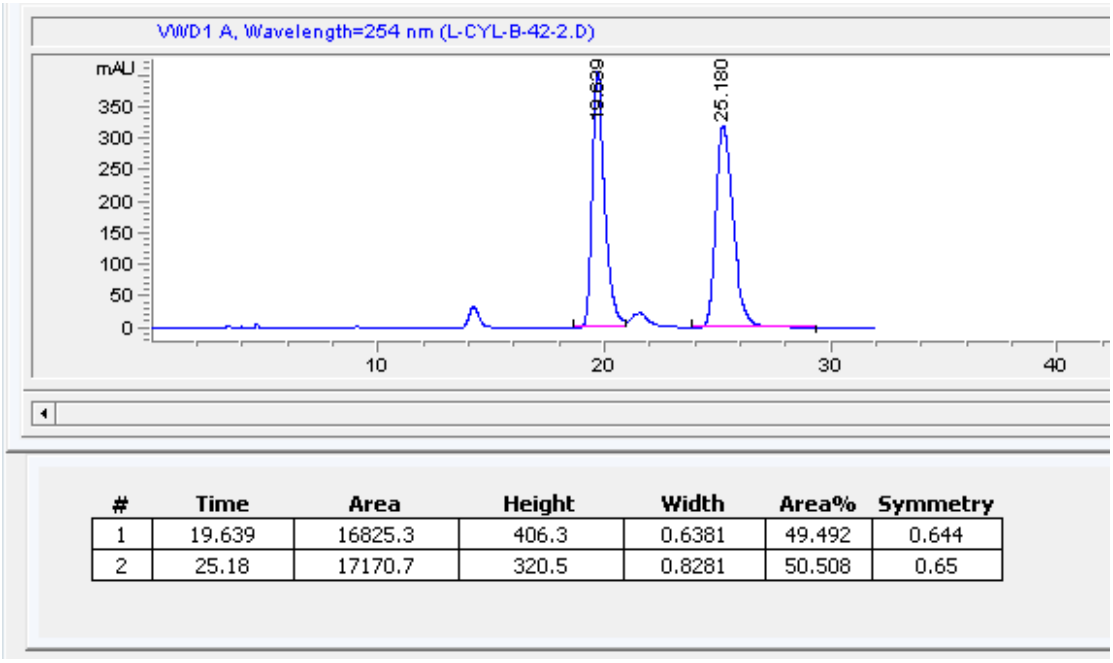
#	Time	Area	Height	Width	Area%	Symmetry
1	20.863	50834.4	894.3	0.8312	95.056	0.433
2	24.621	2644	49	0.7983	4.944	0.938

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

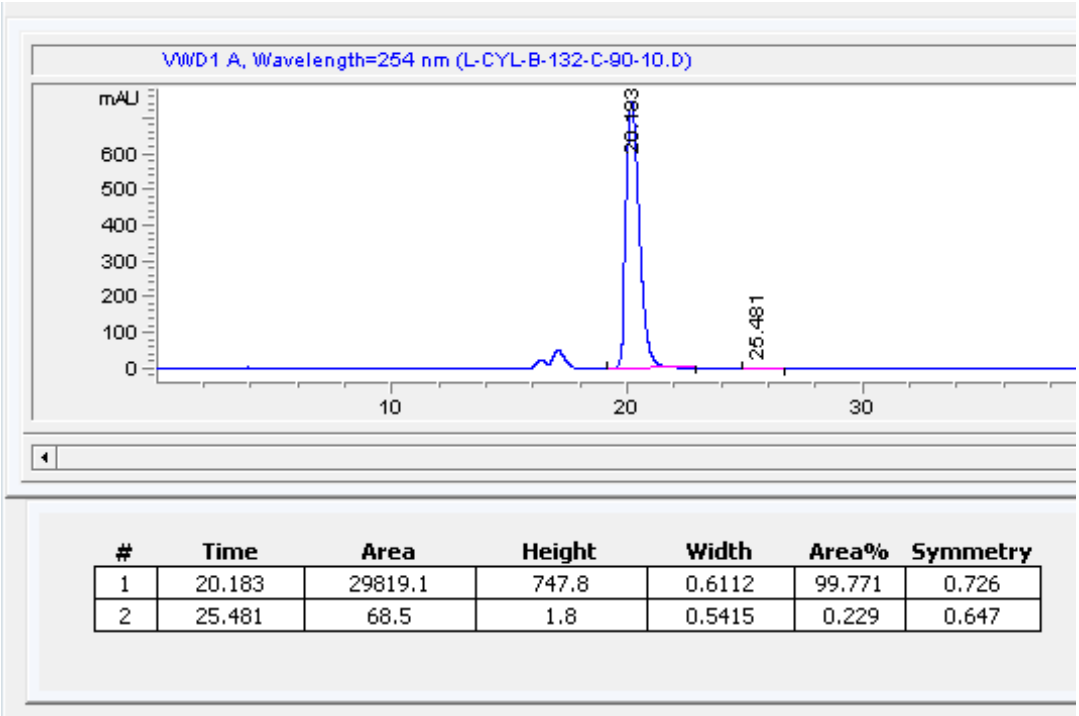




HPLC of 6d

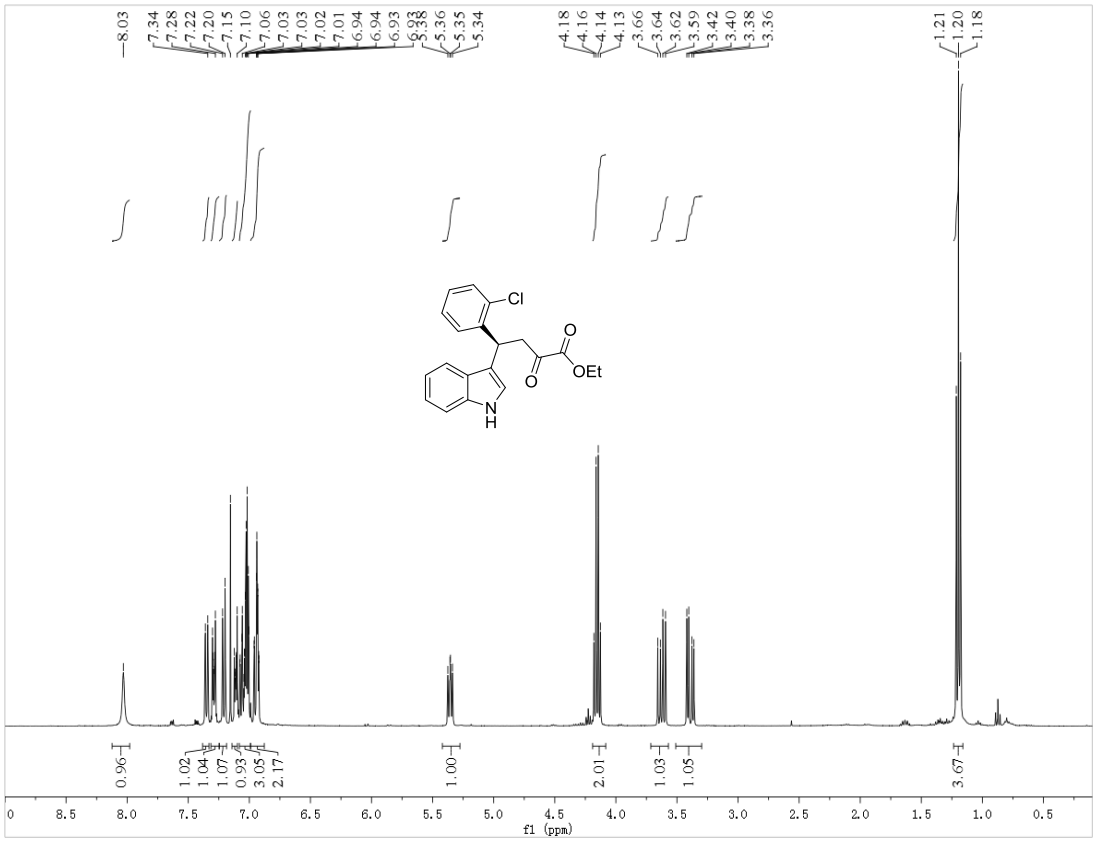


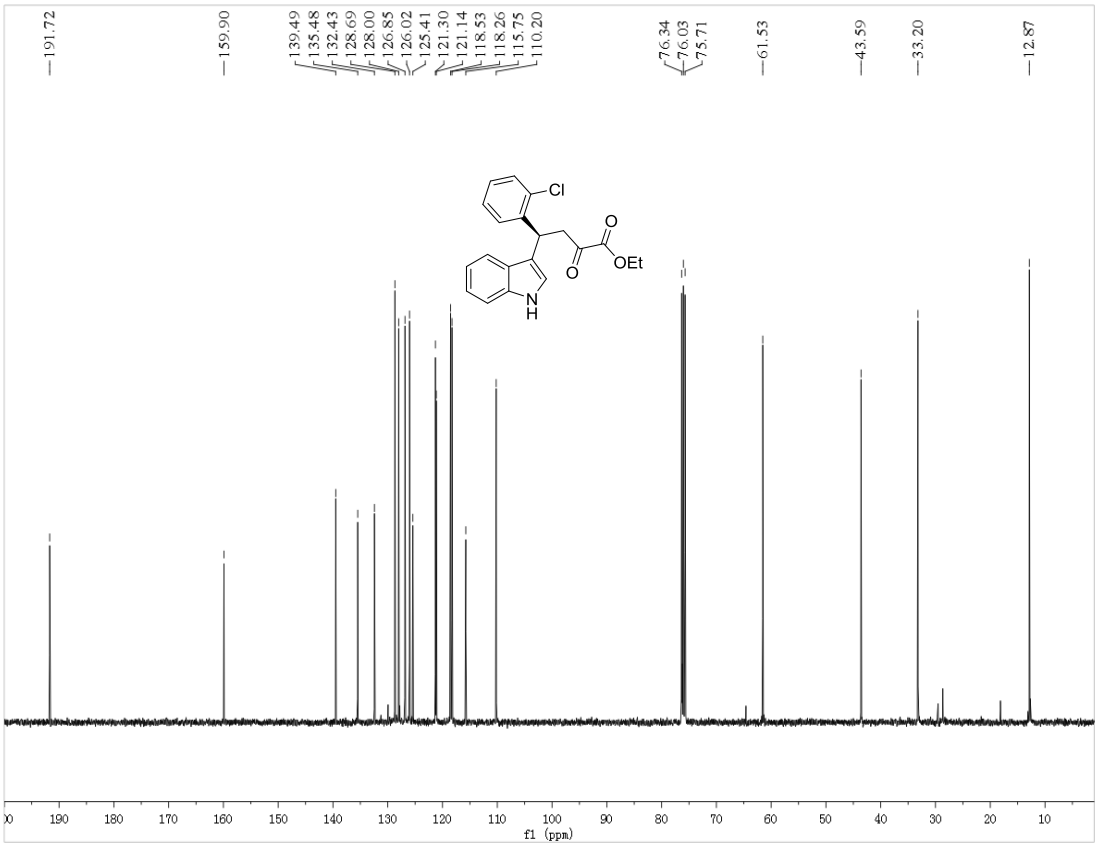
#	Time	Area	Height	Width	Area%	Symmetry
1	19.639	16825.3	406.3	0.6381	49.492	0.644
2	25.18	17170.7	320.5	0.8281	50.508	0.65



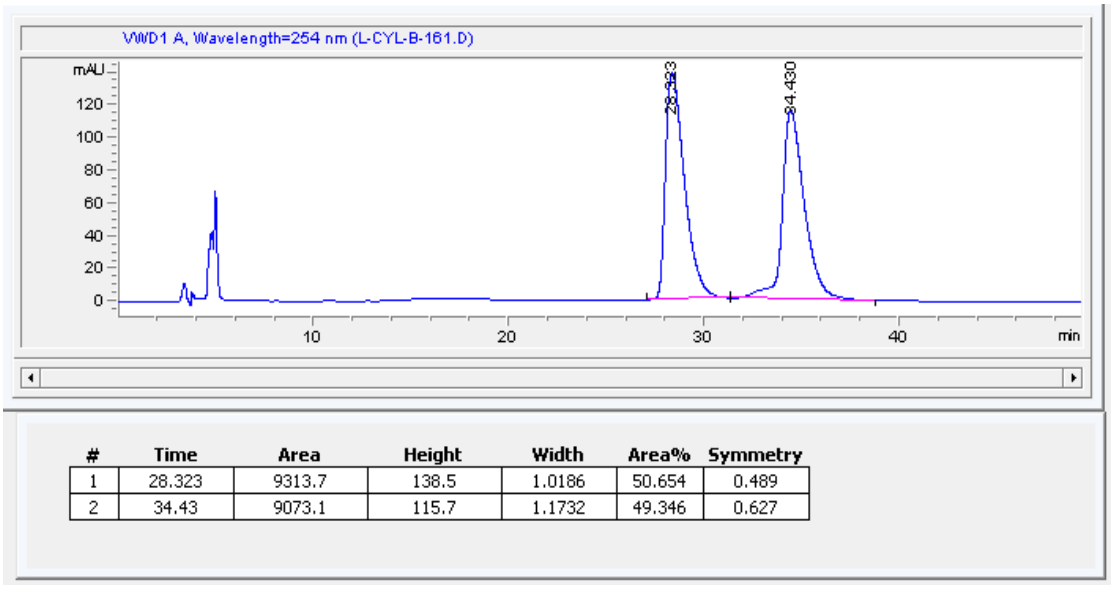
#	Time	Area	Height	Width	Area%	Symmetry
1	20.183	29819.1	747.8	0.6112	99.771	0.726
2	25.481	68.5	1.8	0.5415	0.229	0.647

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

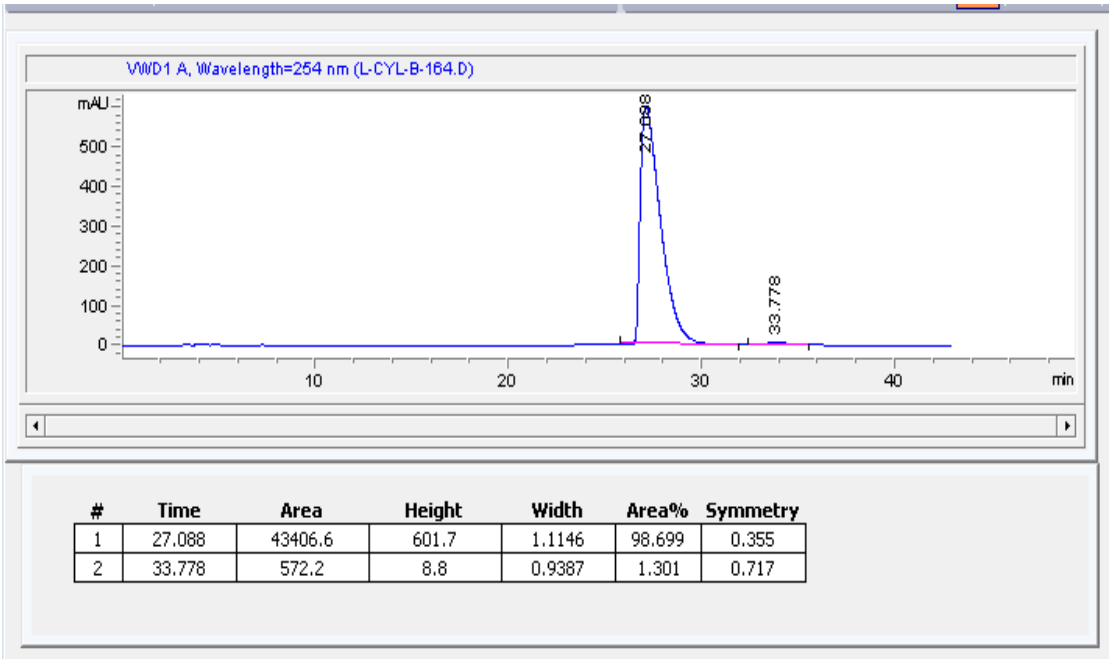




HPLC of 6e

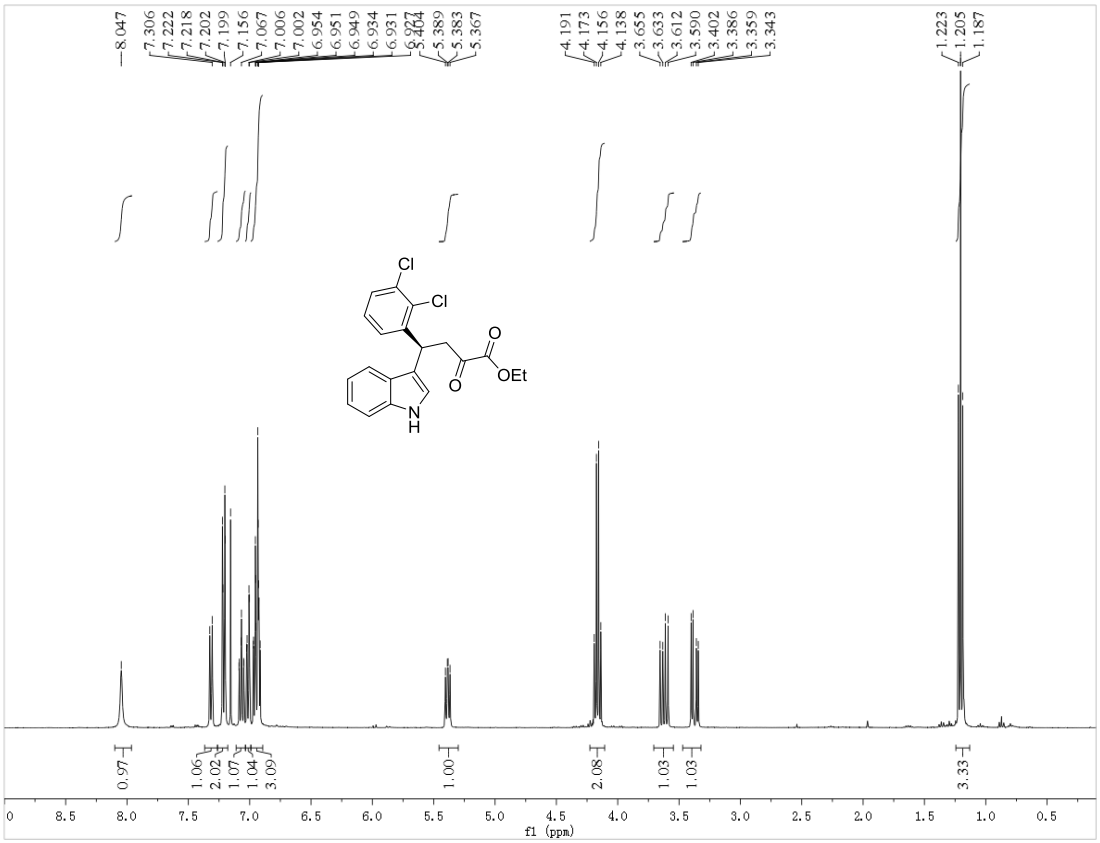


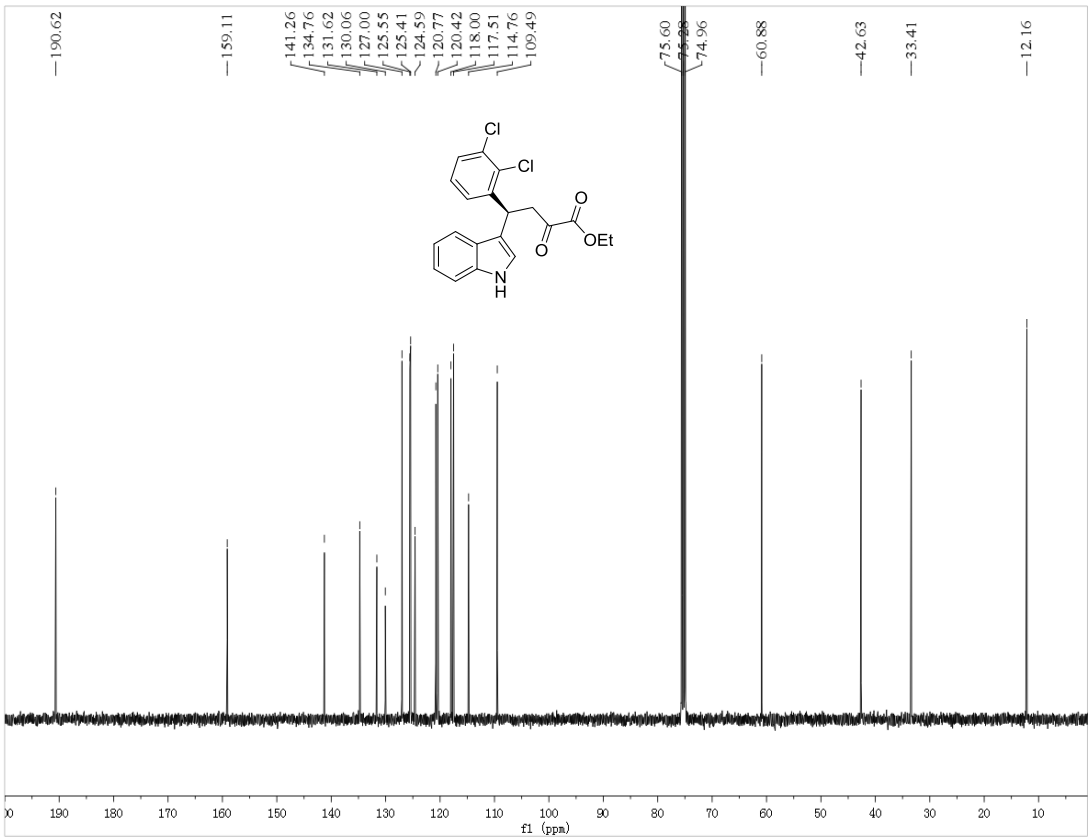
#	Time	Area	Height	Width	Area%	Symmetry
1	28.323	9313.7	138.5	1.0186	50.654	0.489
2	34.43	9073.1	115.7	1.1732	49.346	0.627



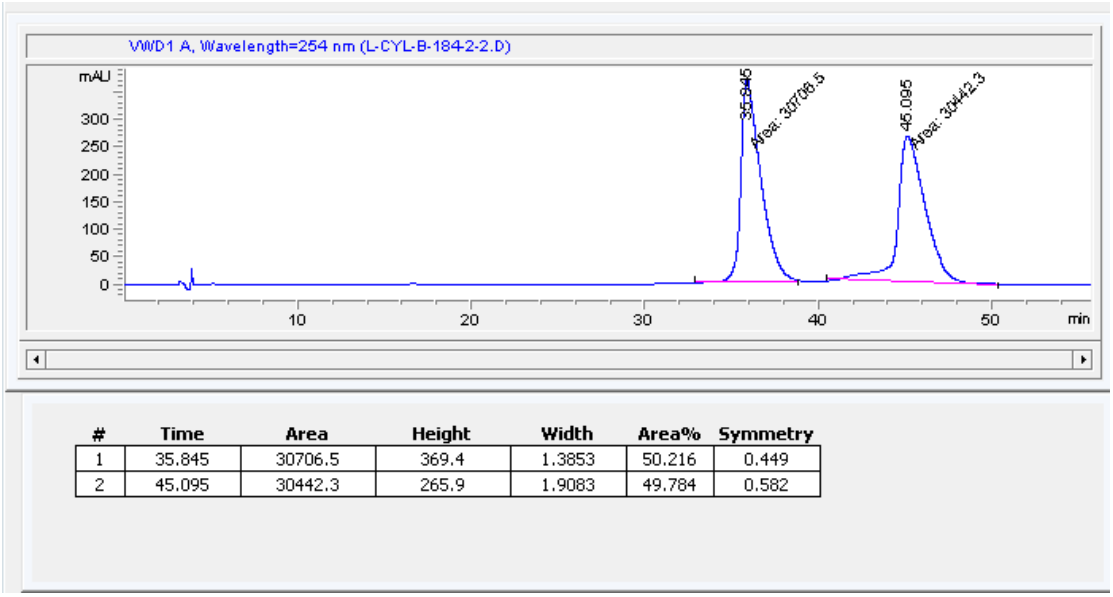
#	Time	Area	Height	Width	Area%	Symmetry
1	27.088	43406.6	601.7	1.1146	98.699	0.355
2	33.778	572.2	8.8	0.9387	1.301	0.717

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

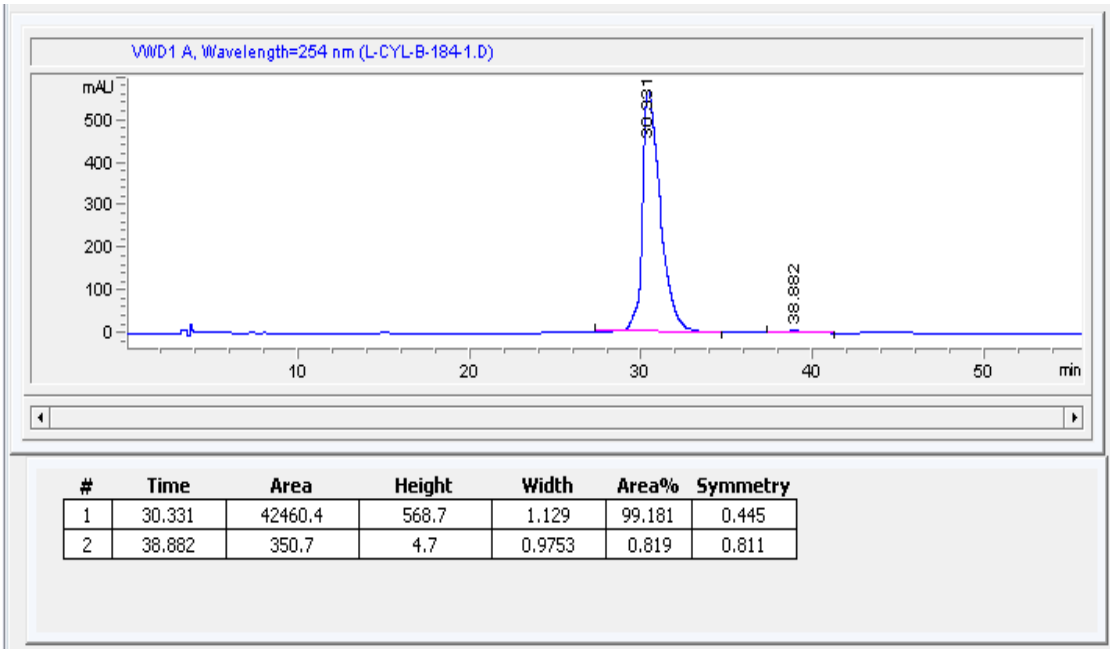




HPLC of 6f

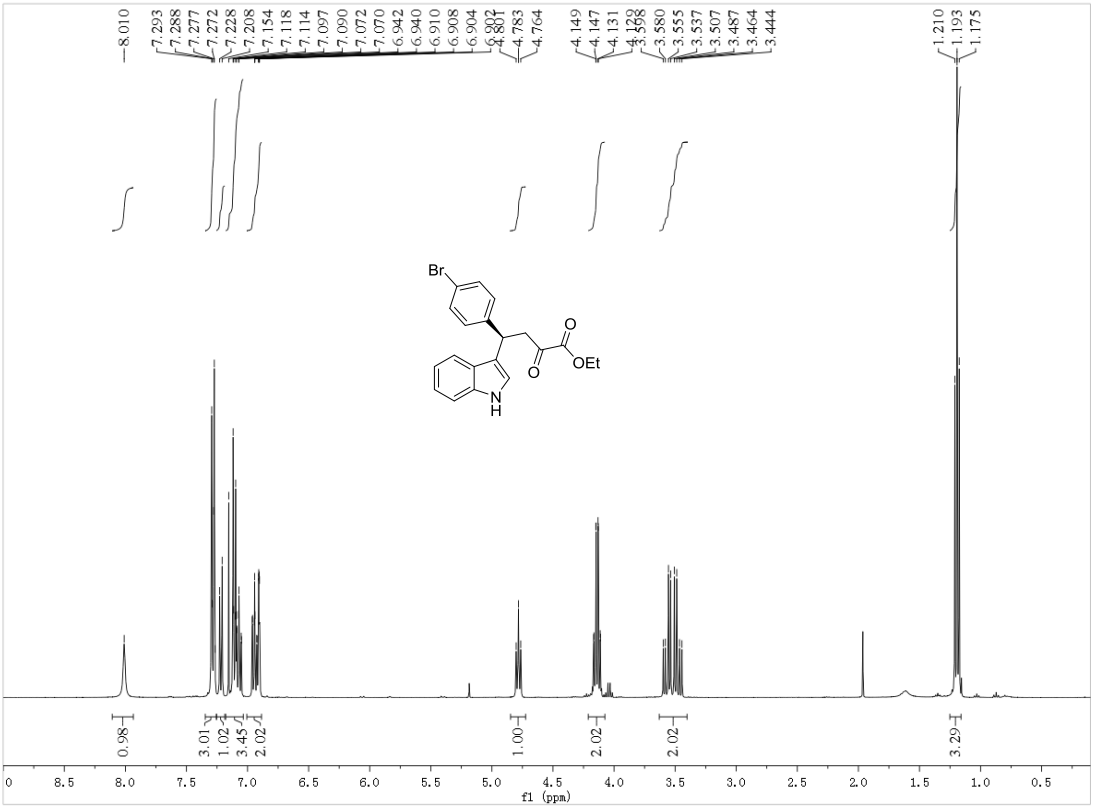


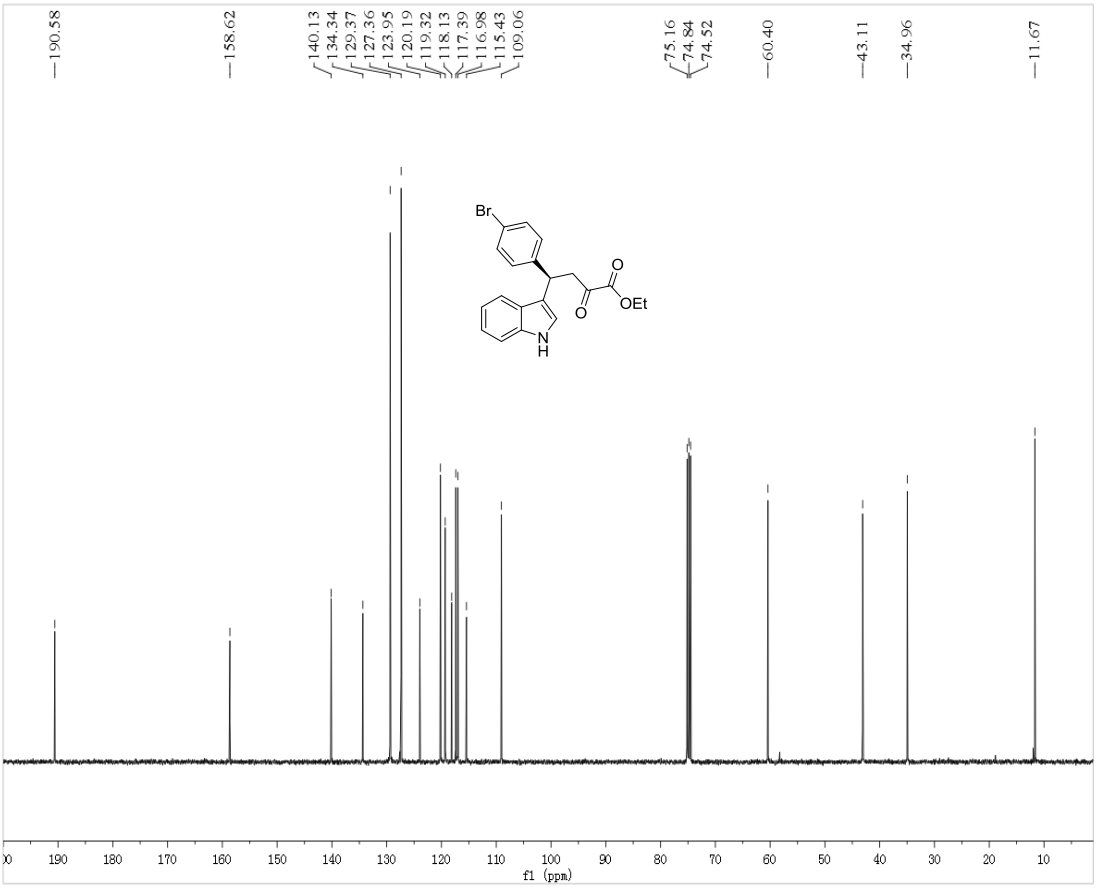
#	Time	Area	Height	Width	Area%	Symmetry
1	35.845	30706.5	369.4	1.3853	50.216	0.449
2	45.095	30442.3	265.9	1.9083	49.784	0.582



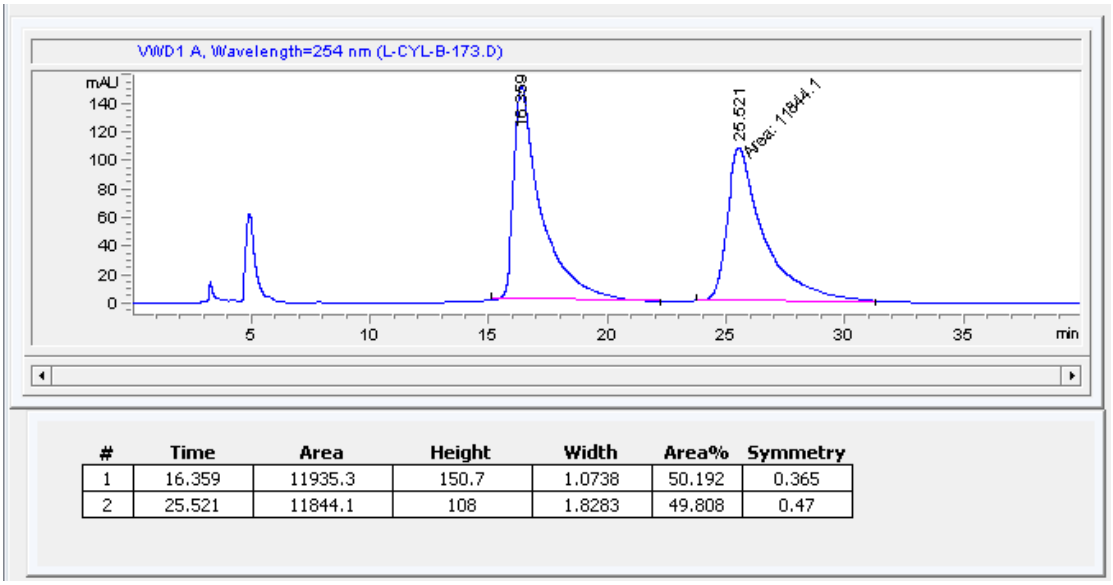
#	Time	Area	Height	Width	Area%	Symmetry
1	30.331	42460.4	568.7	1.129	99.181	0.445
2	38.882	350.7	4.7	0.9753	0.819	0.811

^{1}H and ^{13}C NMR of 6g





HPLC of 6g



#	Time	Area	Height	Width	Area%	Symmetry
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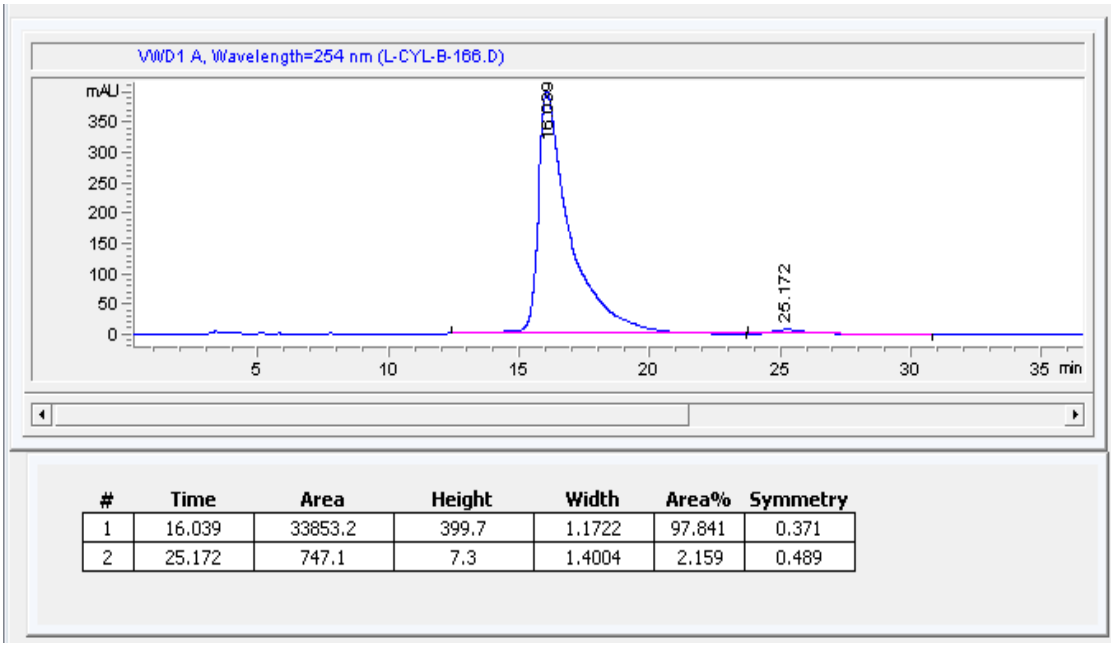
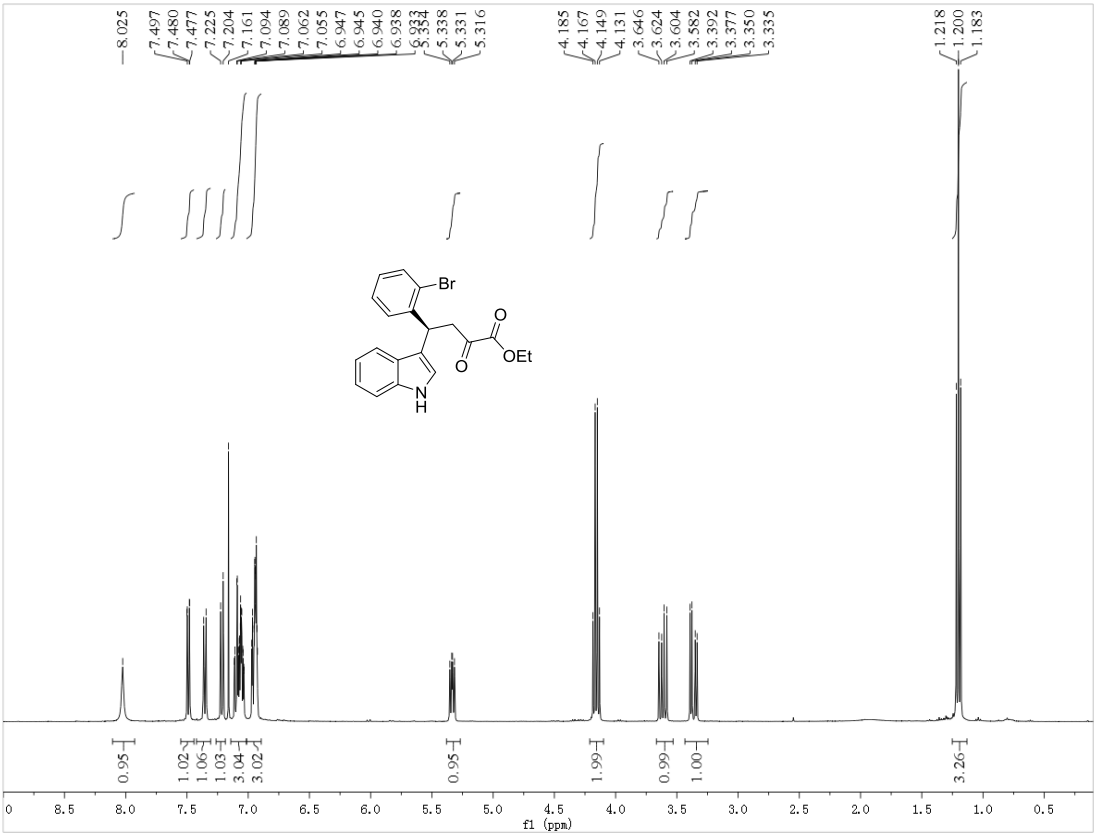
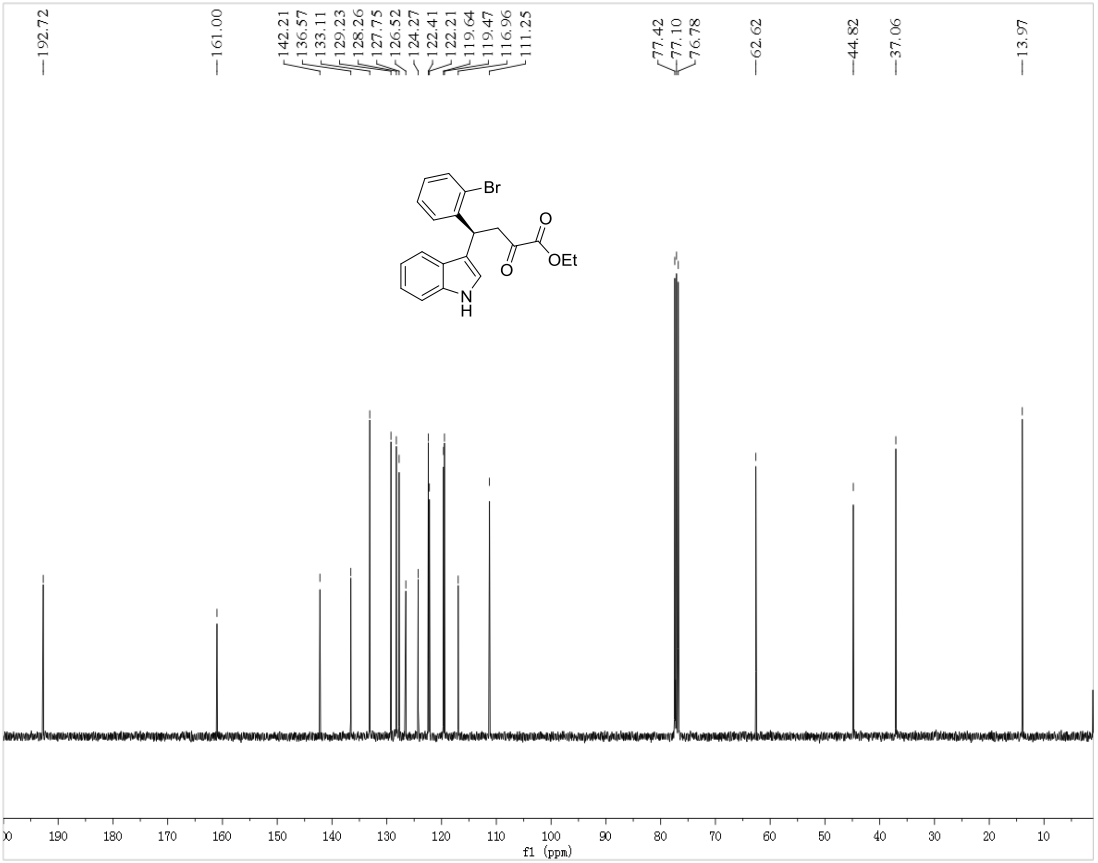
2	25.521	11844.1	108	1.8283	49.808	0.47



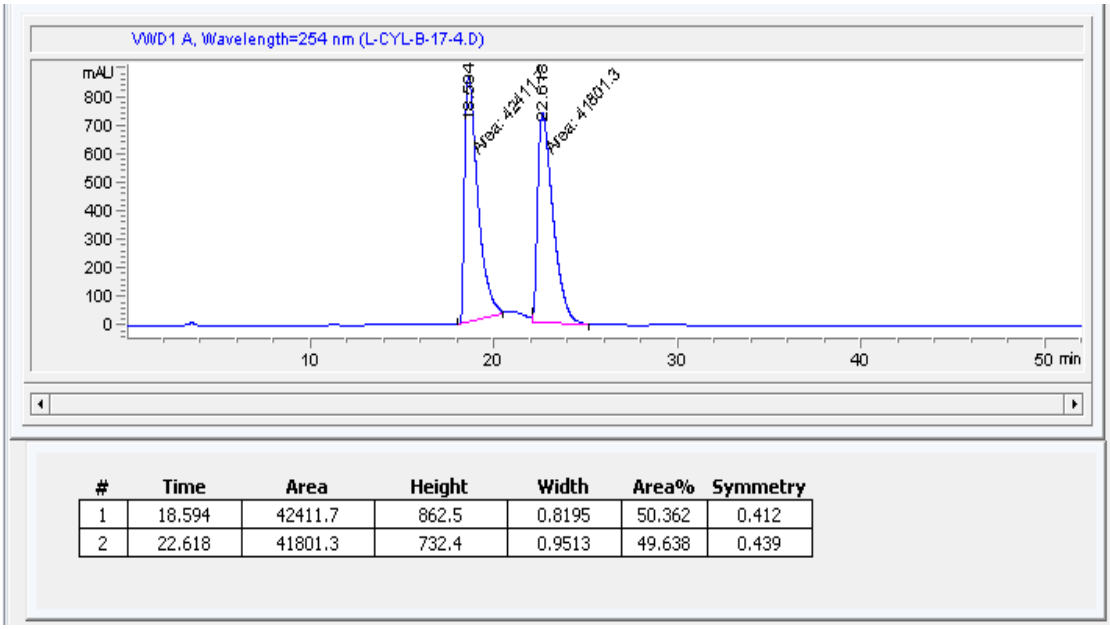
#	Time	Area	Height	Width	Area%	Symmetry
1	16.039	33853.2	399.7	1.1722	97.841	0.371
2	25.172	747.1	7.3	1.4004	2.159	0.489

^{1}H and ^{13}C NMR of 6h

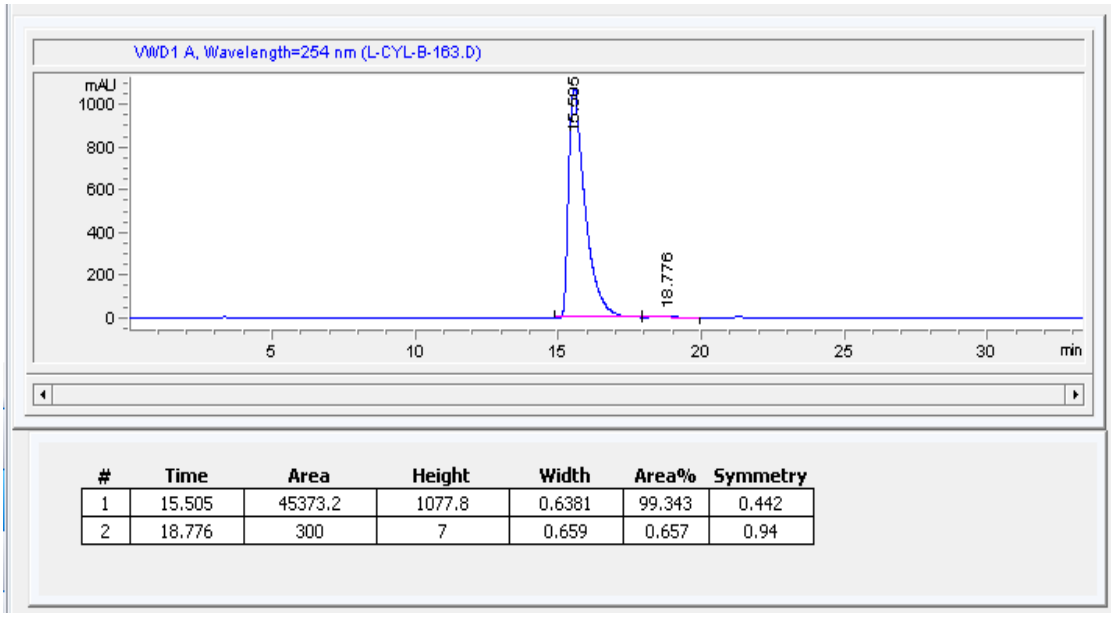




HPLC of 6h

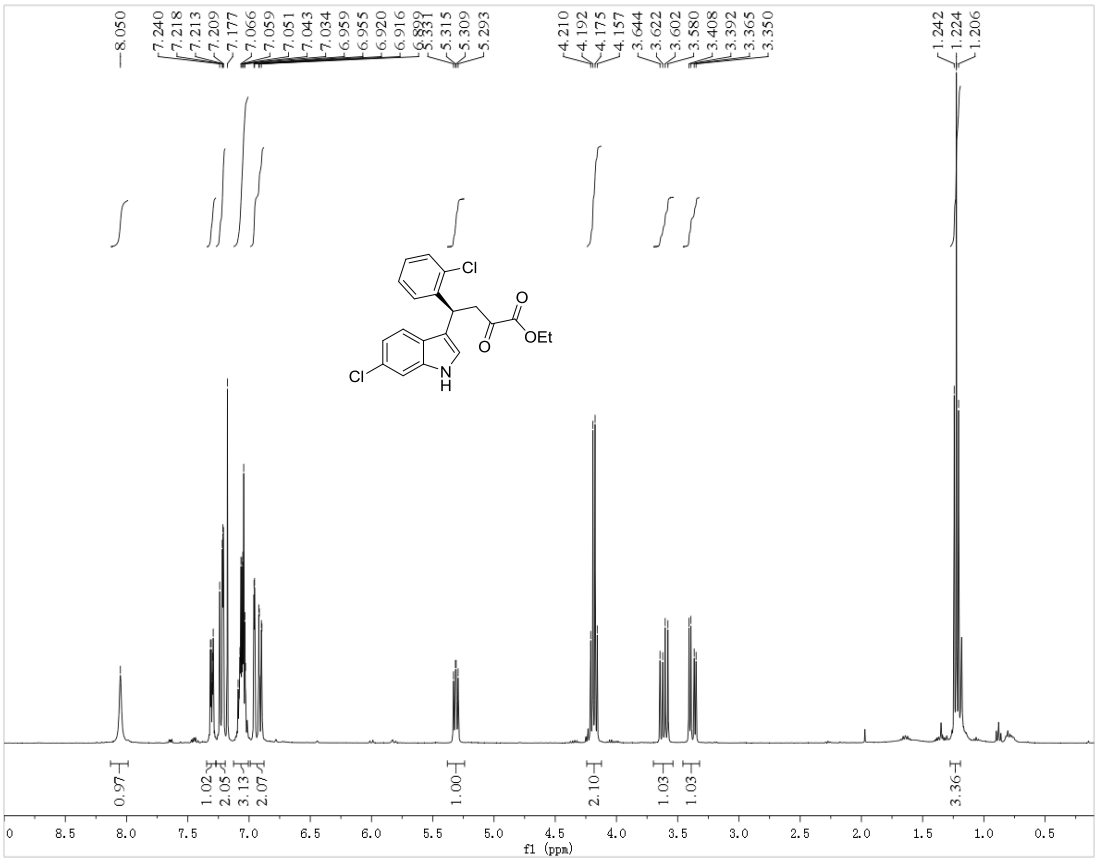


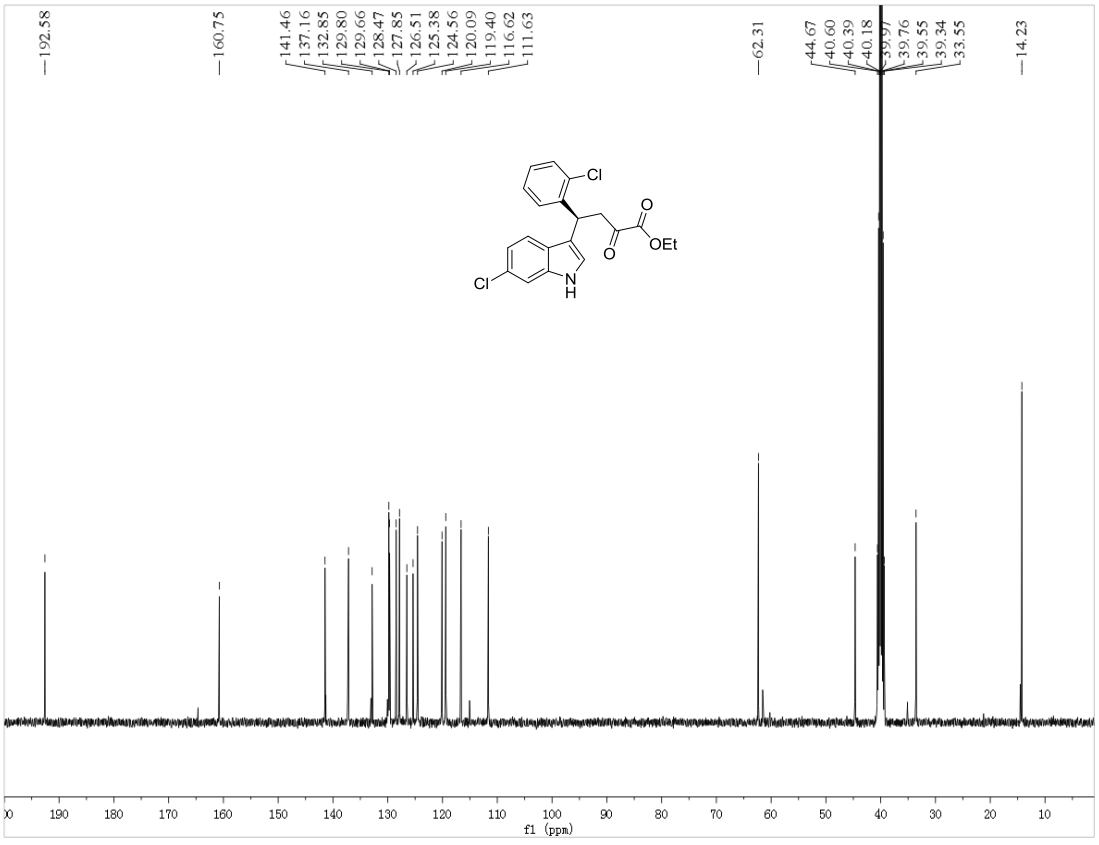
#	Time	Area	Height	Width	Area%	Symmetry
1	18.594	42411.7	862.5	0.8195	50.362	0.412
2	22.618	41801.3	732.4	0.9513	49.638	0.439



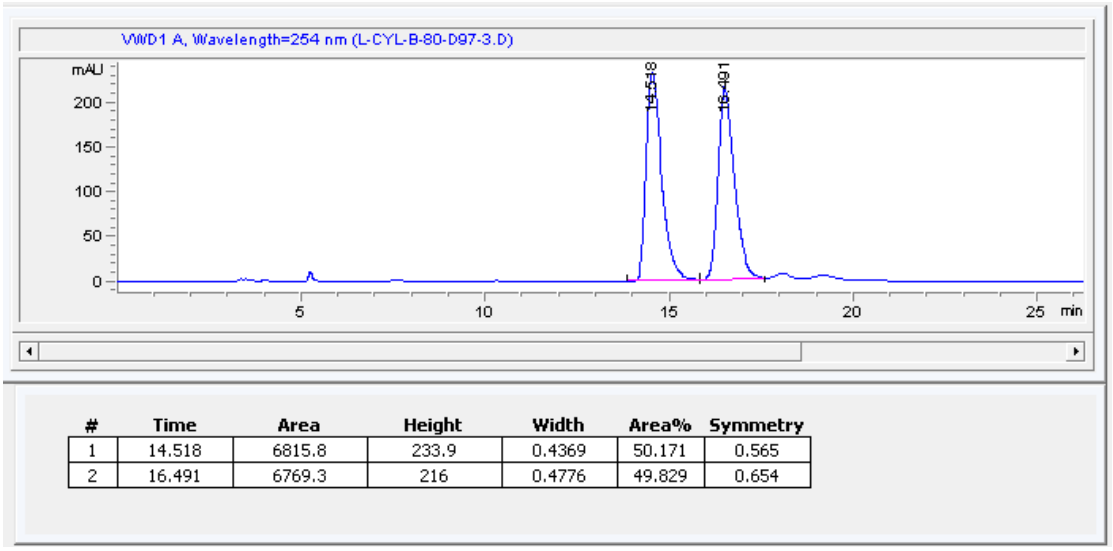
#	Time	Area	Height	Width	Area%	Symmetry
1	15.505	45373.2	1077.8	0.6381	99.343	0.442
2	18.776	300	7	0.659	0.657	0.94

^{1}H and ^{13}C NMR of 6i

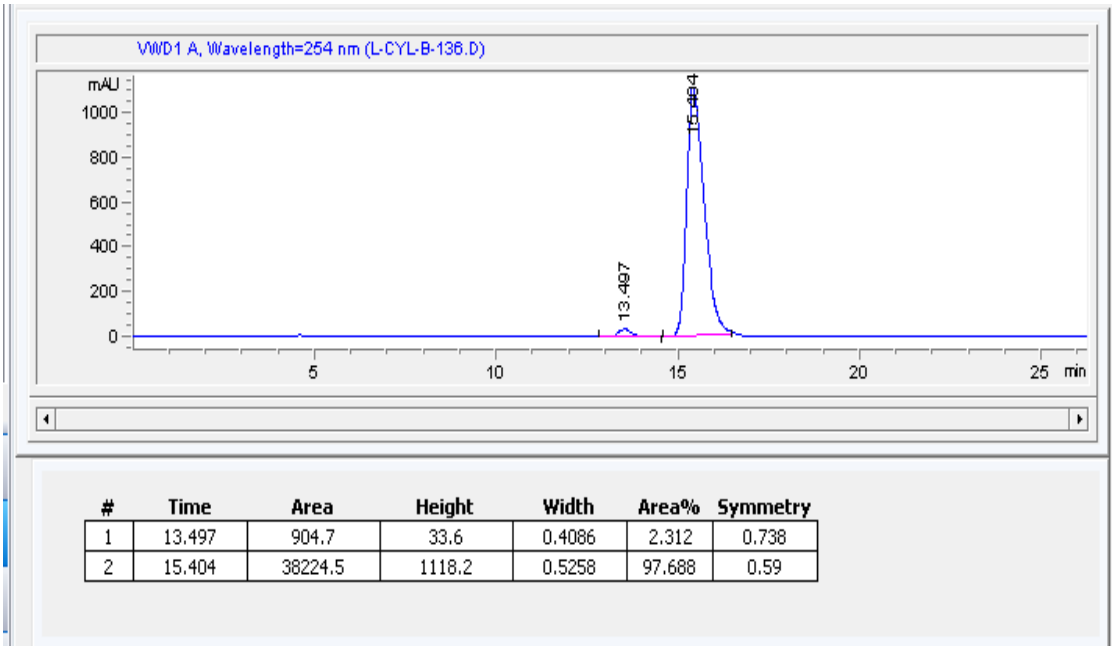




HPLC of 6i

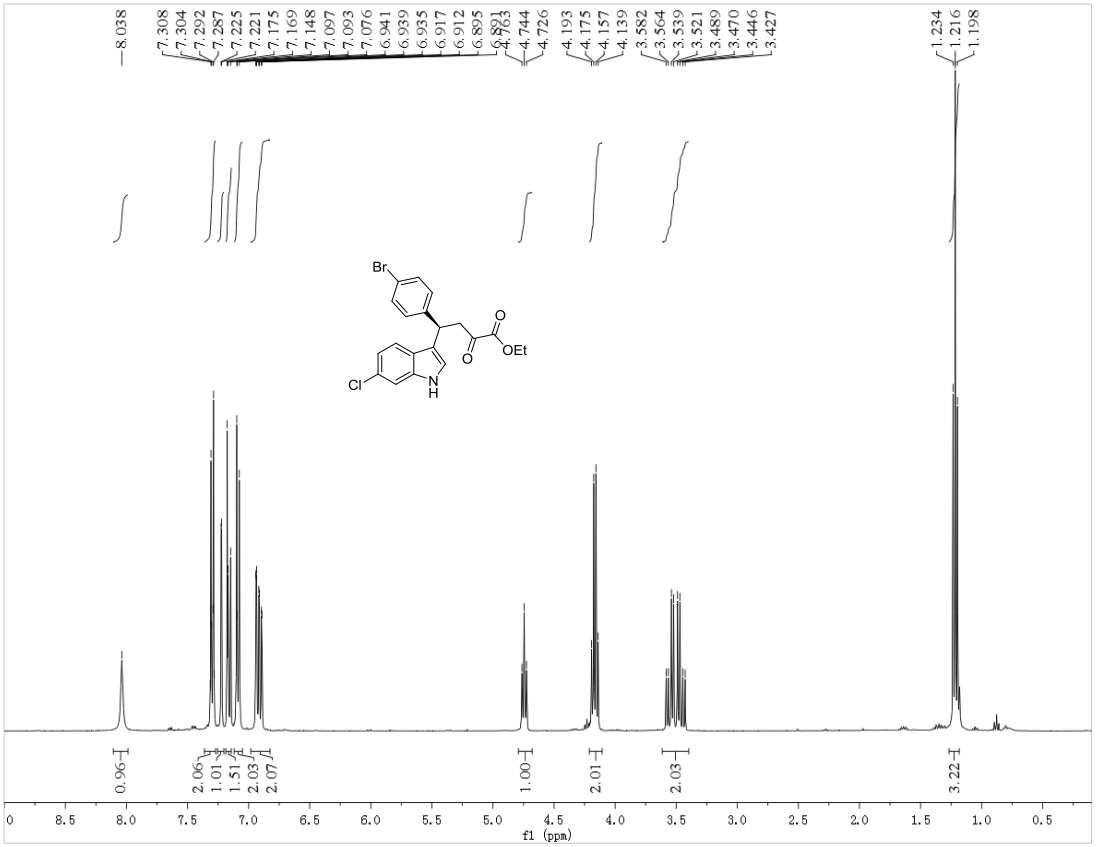


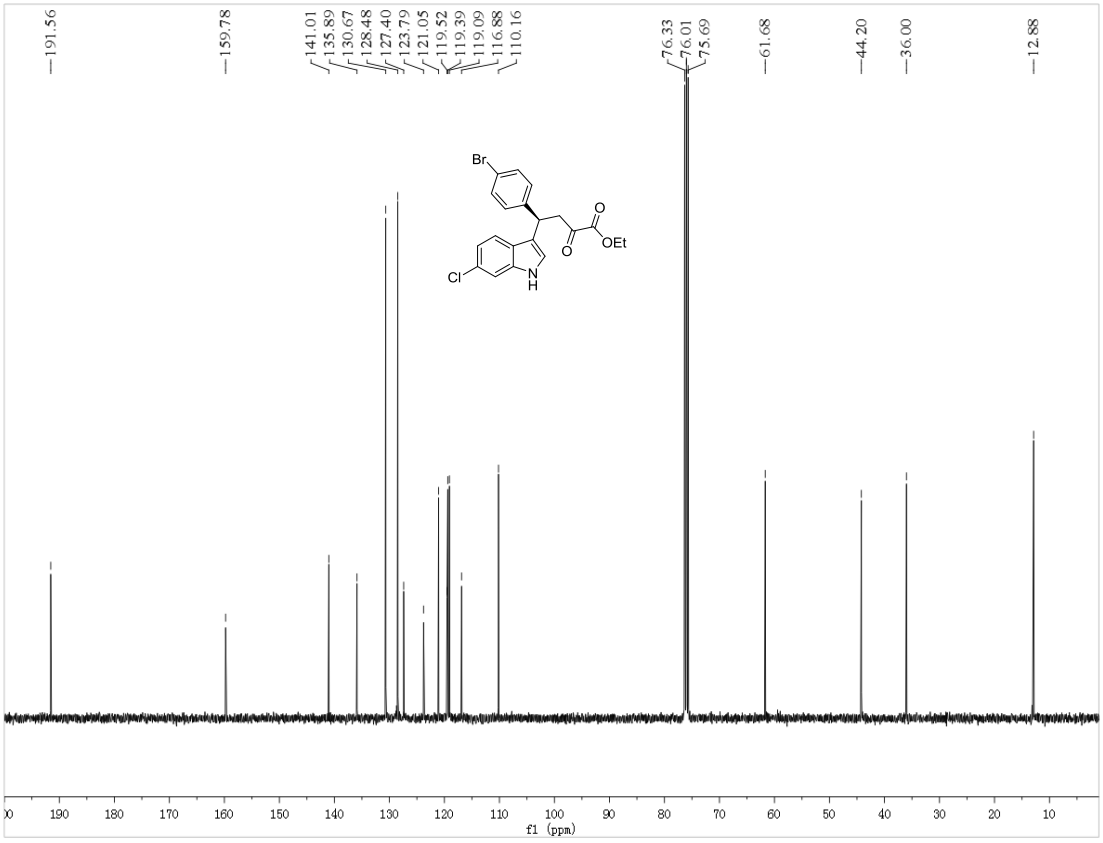
#	Time	Area	Height	Width	Area%	Symmetry
1	14.518	6815.8	233.9	0.4369	50.171	0.565
2	16.491	6769.3	216	0.4776	49.829	0.654



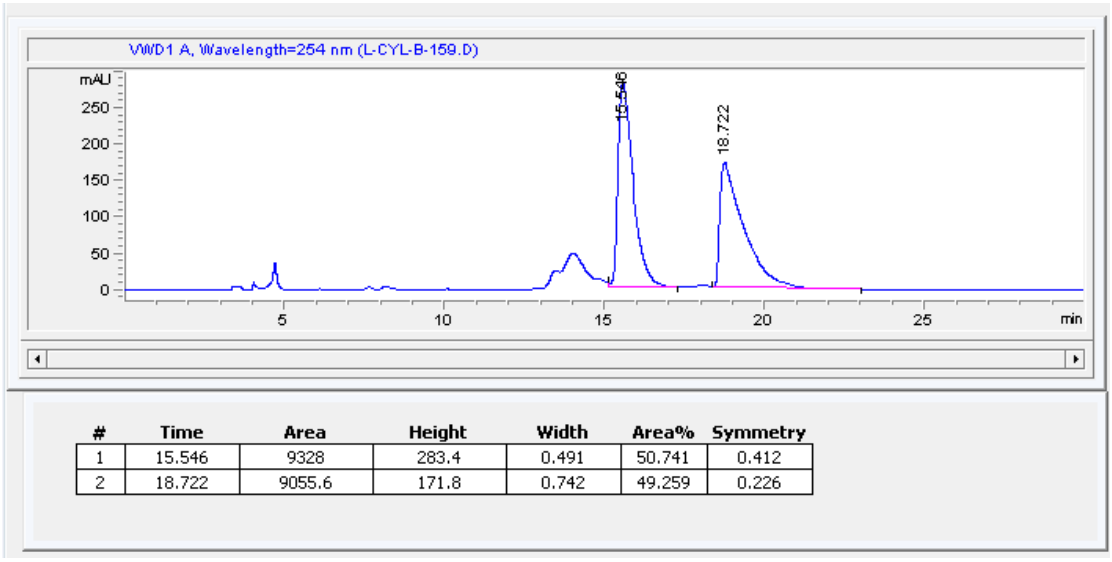
#	Time	Area	Height	Width	Area%	Symmetry
1	13.497	904.7	33.6	0.4086	2.312	0.738
2	15.404	38224.5	1118.2	0.5258	97.688	0.59

^{1}H and ^{13}C NMR of 6j

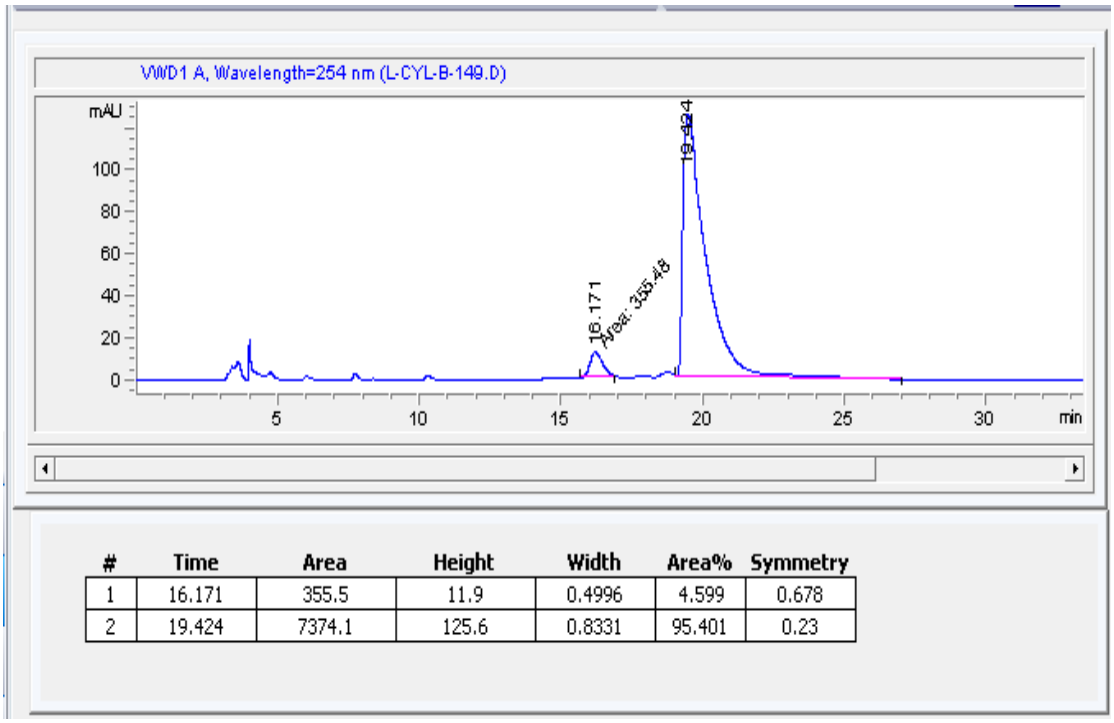




HPLC of 6j

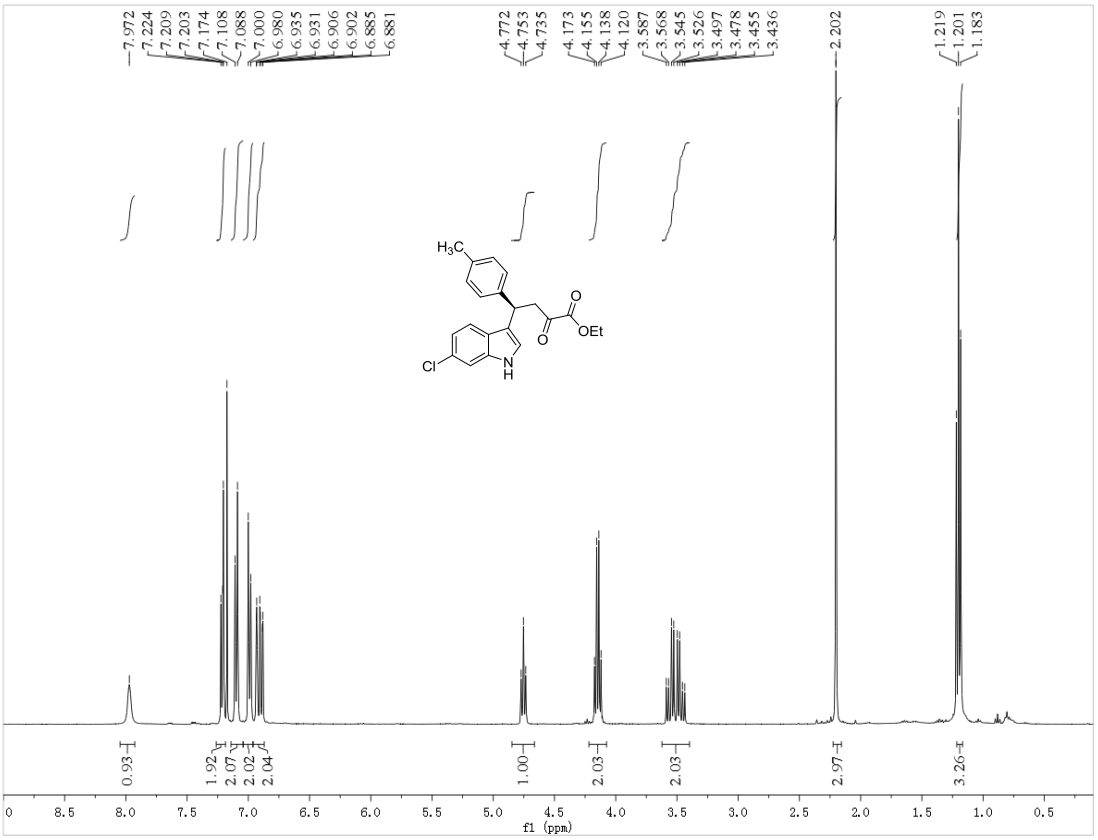


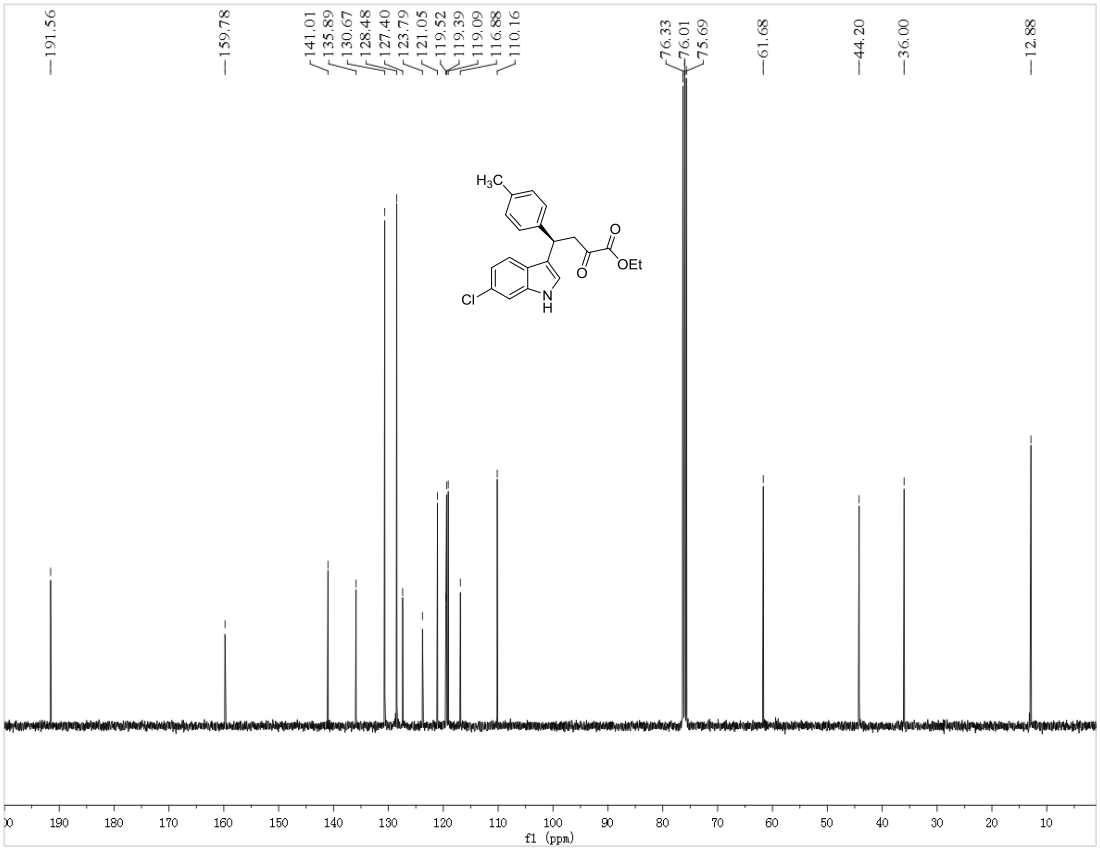
#	Time	Area	Height	Width	Area%	Symmetry
1	15.546	9328	283.4	0.491	50.741	0.412
2	18.722	9055.6	171.8	0.742	49.259	0.226



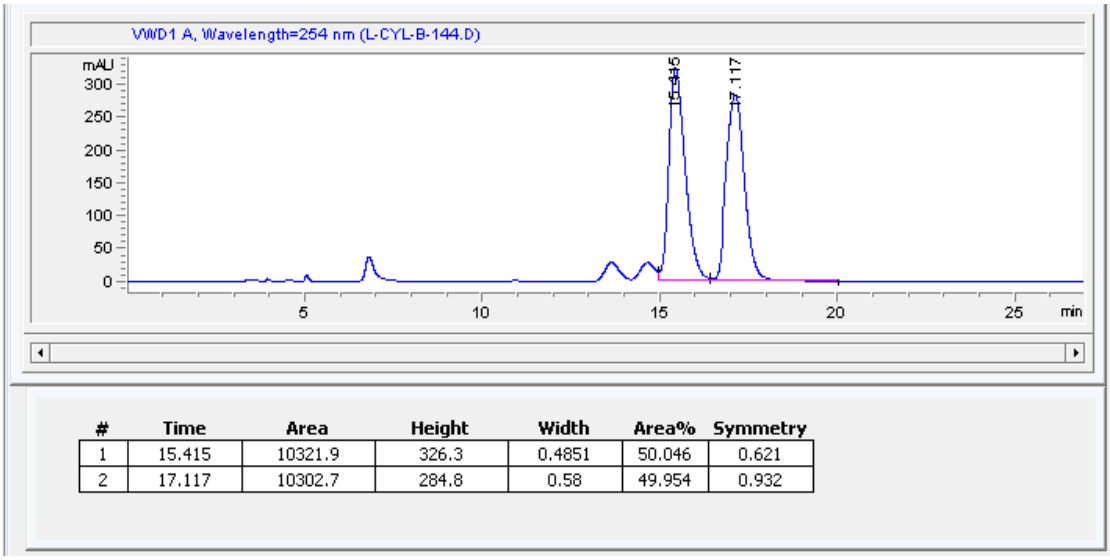
#	Time	Area	Height	Width	Area%	Symmetry
1	16.171	355.5	11.9	0.4996	4.599	0.678
2	19.424	7374.1	125.6	0.8331	95.401	0.23

^{1}H and ^{13}C NMR of 6k

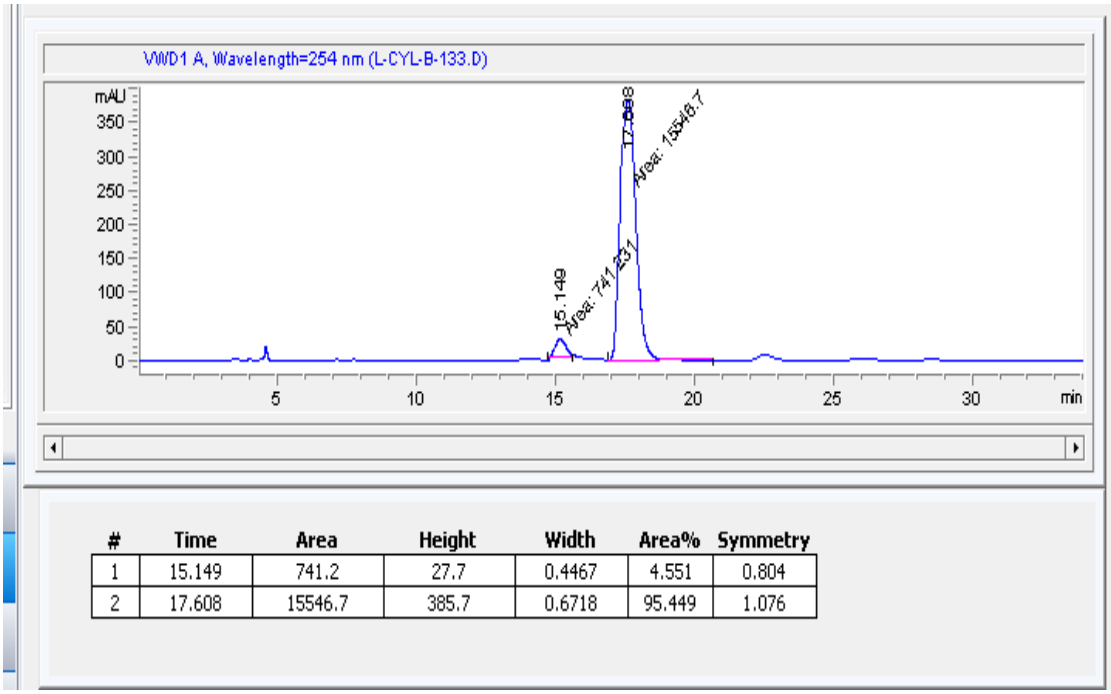




HPLC of 6k

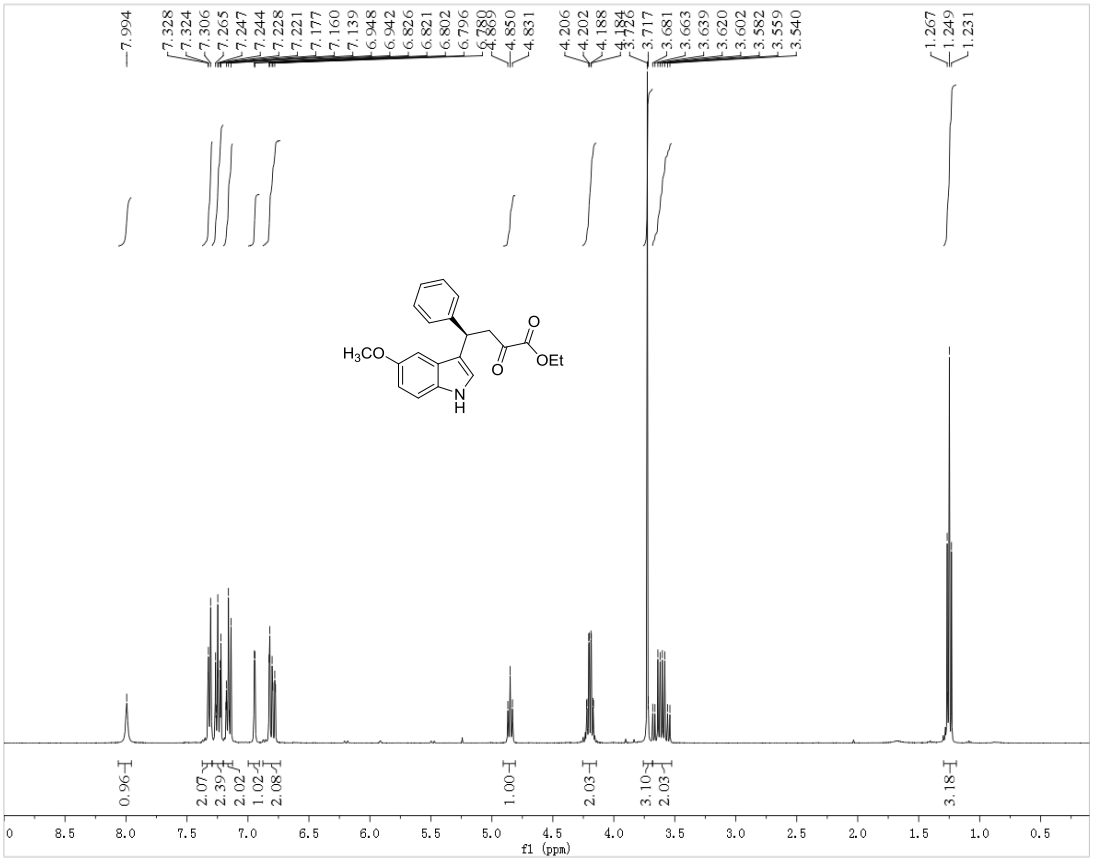


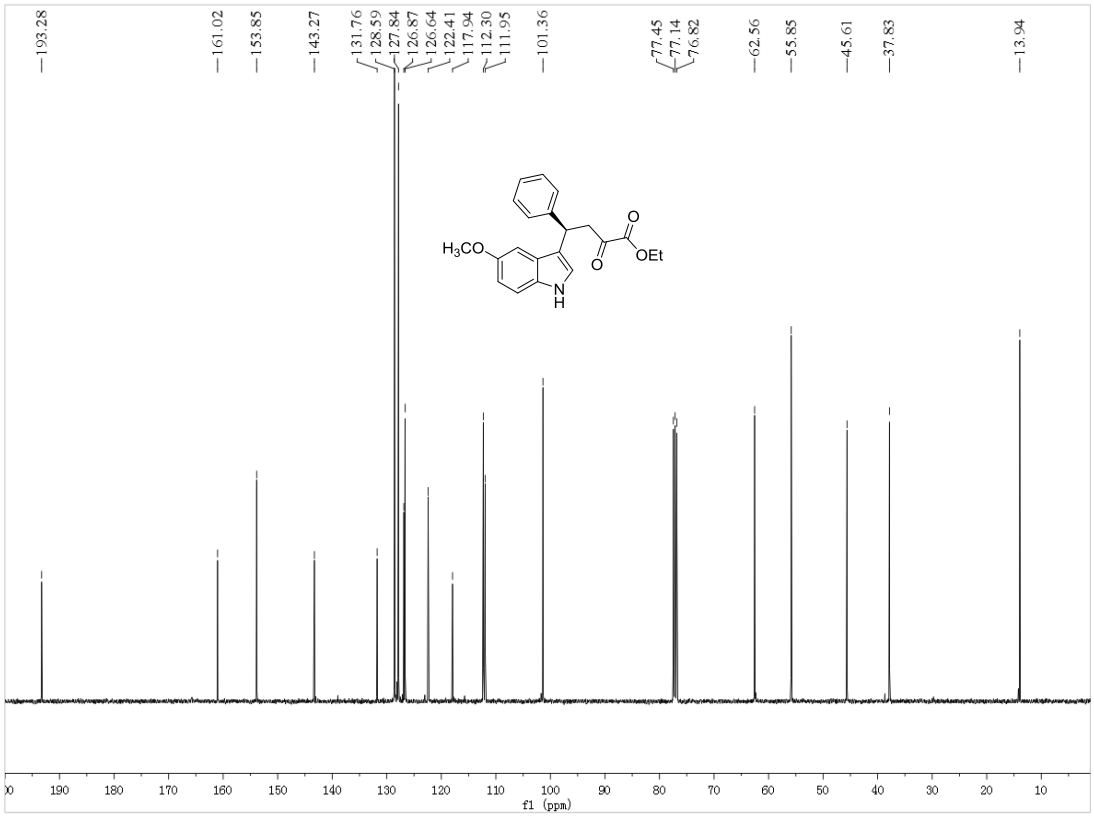
#	Time	Area	Height	Width	Area%	Symmetry
1	15.415	10321.9	326.3	0.4851	50.046	0.621
2	17.117	10302.7	284.8	0.58	49.954	0.932



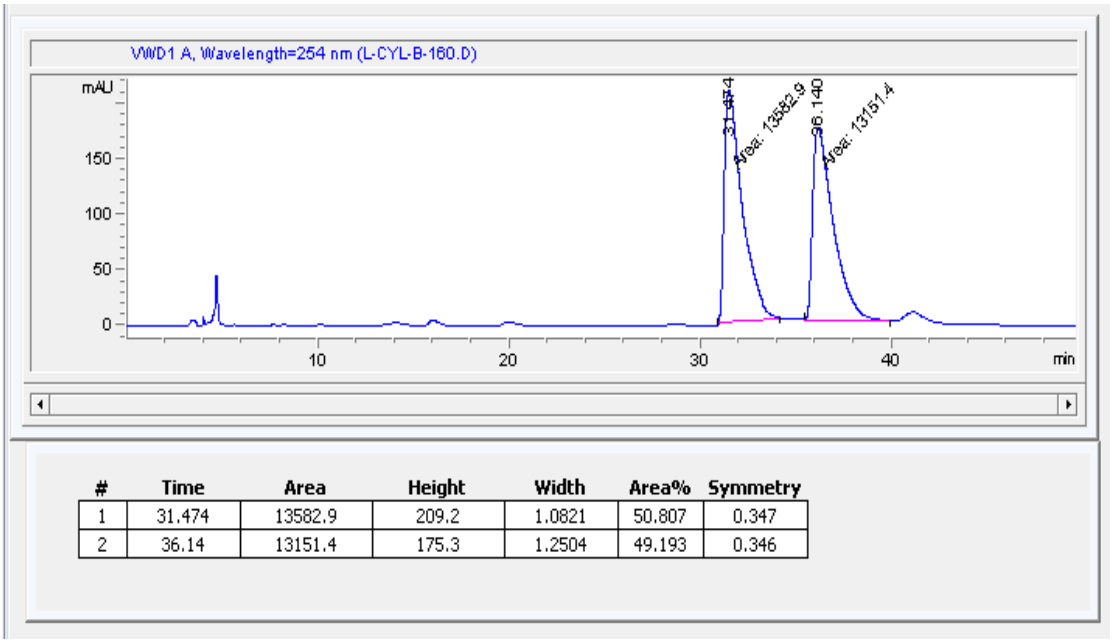
#	Time	Area	Height	Width	Area%	Symmetry
1	15.149	741.2	27.7	0.4467	4.551	0.804
2	17.608	15546.7	385.7	0.6718	95.449	1.076

^{1}H and ^{13}C NMR of 6l

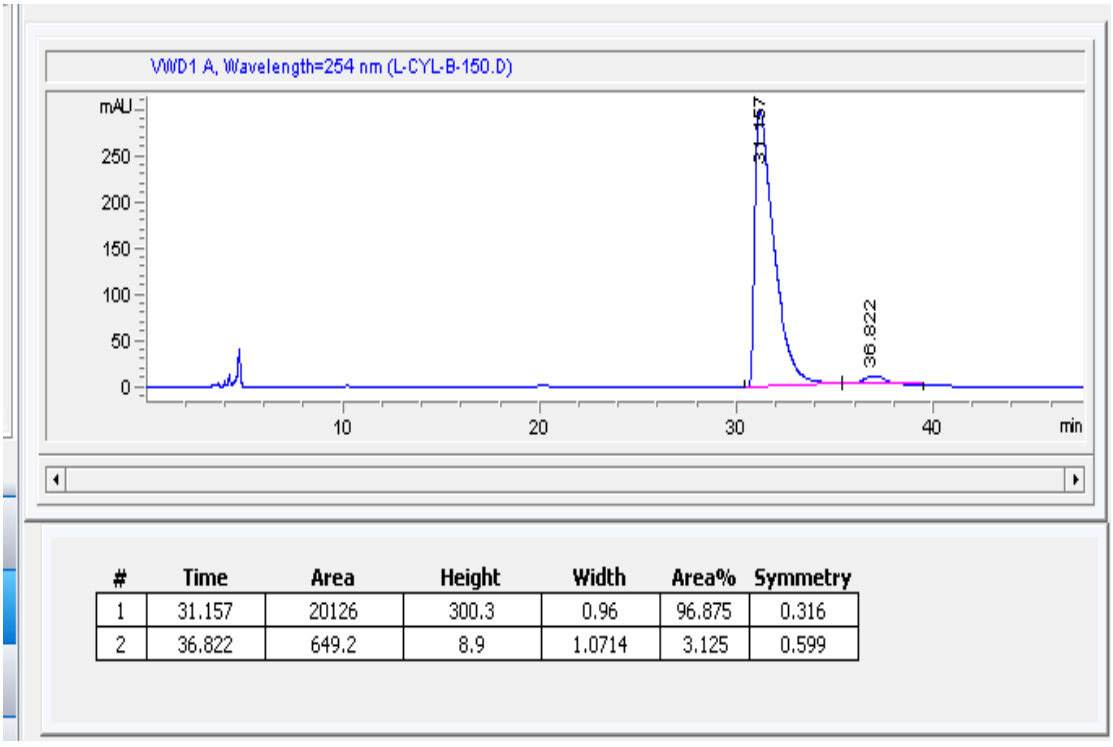




HPLC of 6l

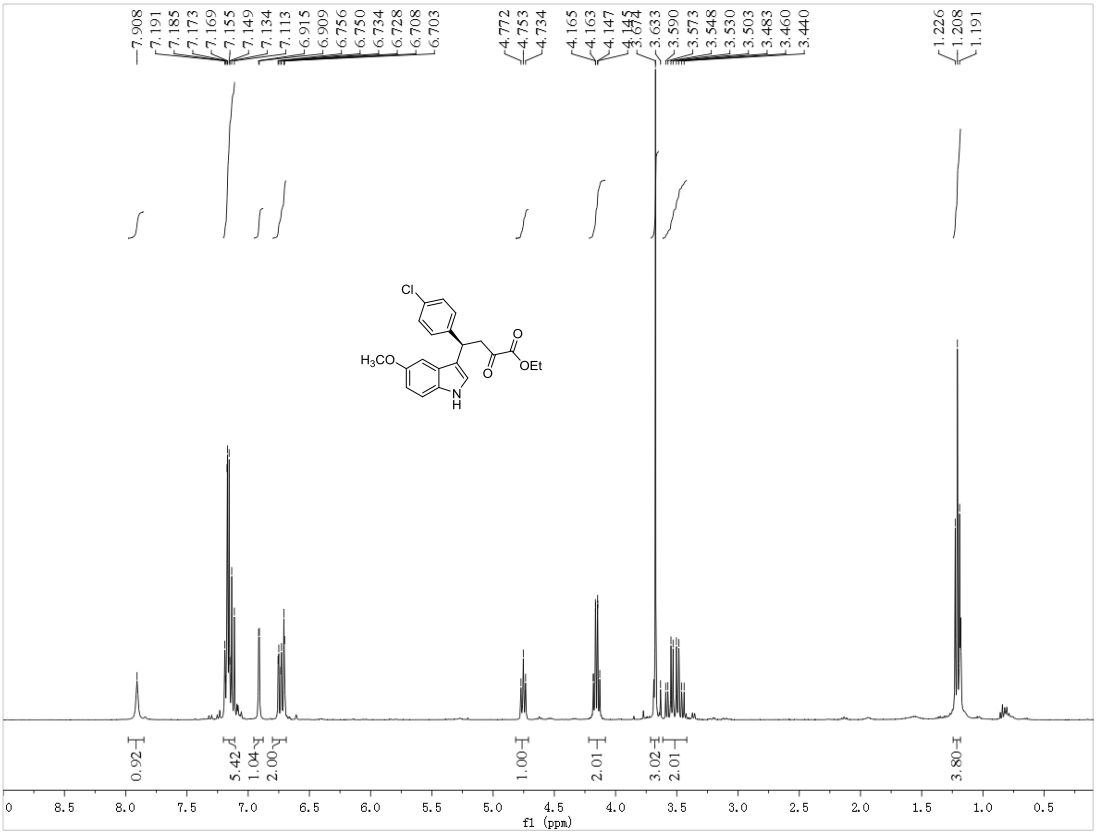


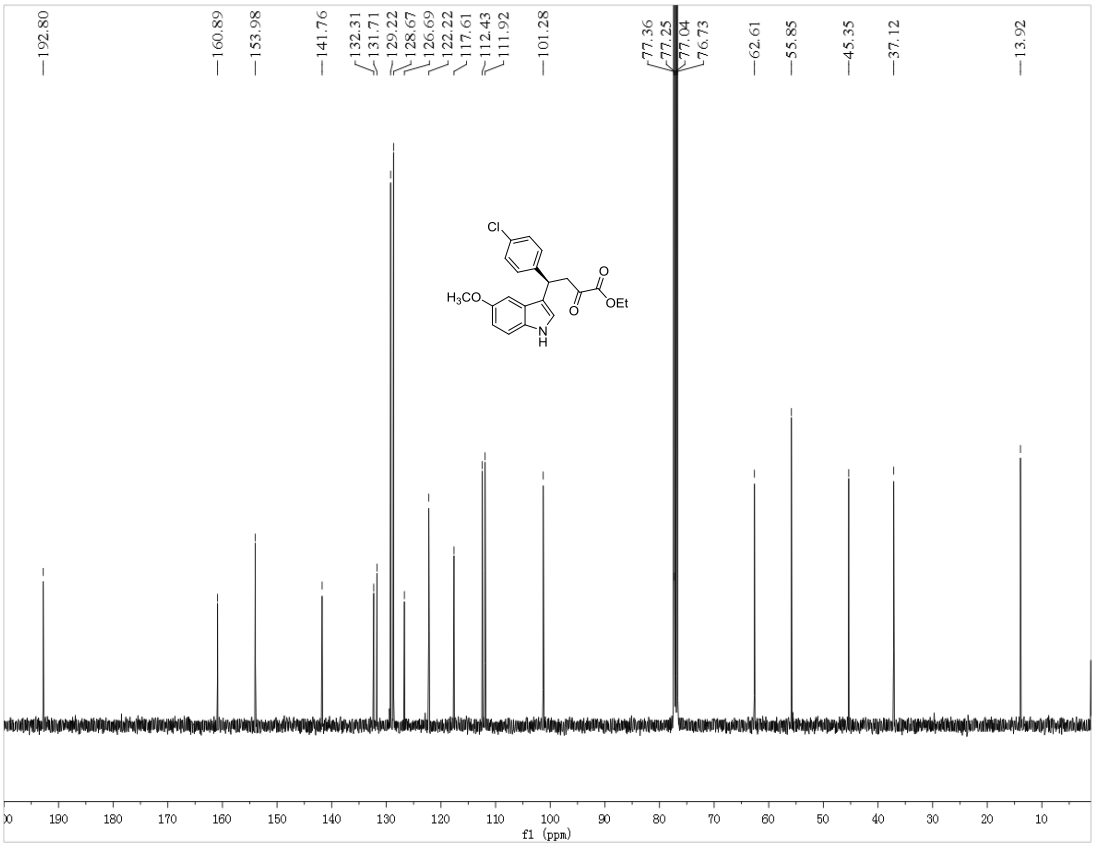
#	Time	Area	Height	Width	Area%	Symmetry
1	31.474	13582.9	209.2	1.0821	50.807	0.347
2	36.14	13151.4	175.3	1.2504	49.193	0.346



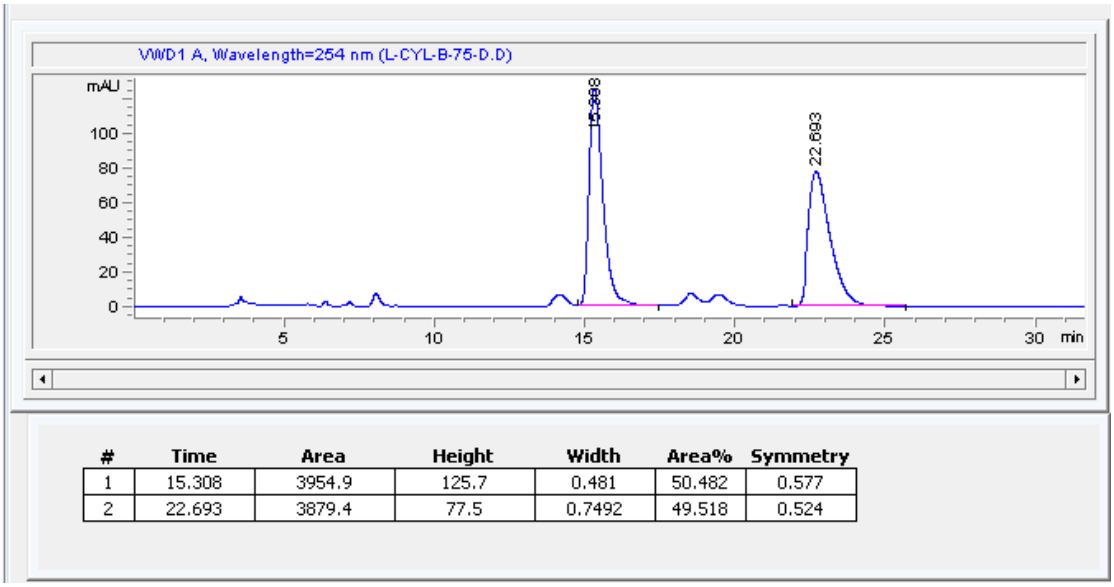
#	Time	Area	Height	Width	Area%	Symmetry
1	31.157	20126	300.3	0.96	96.875	0.316
2	36.822	649.2	8.9	1.0714	3.125	0.599

^{1}H and ^{13}C NMR of 6m

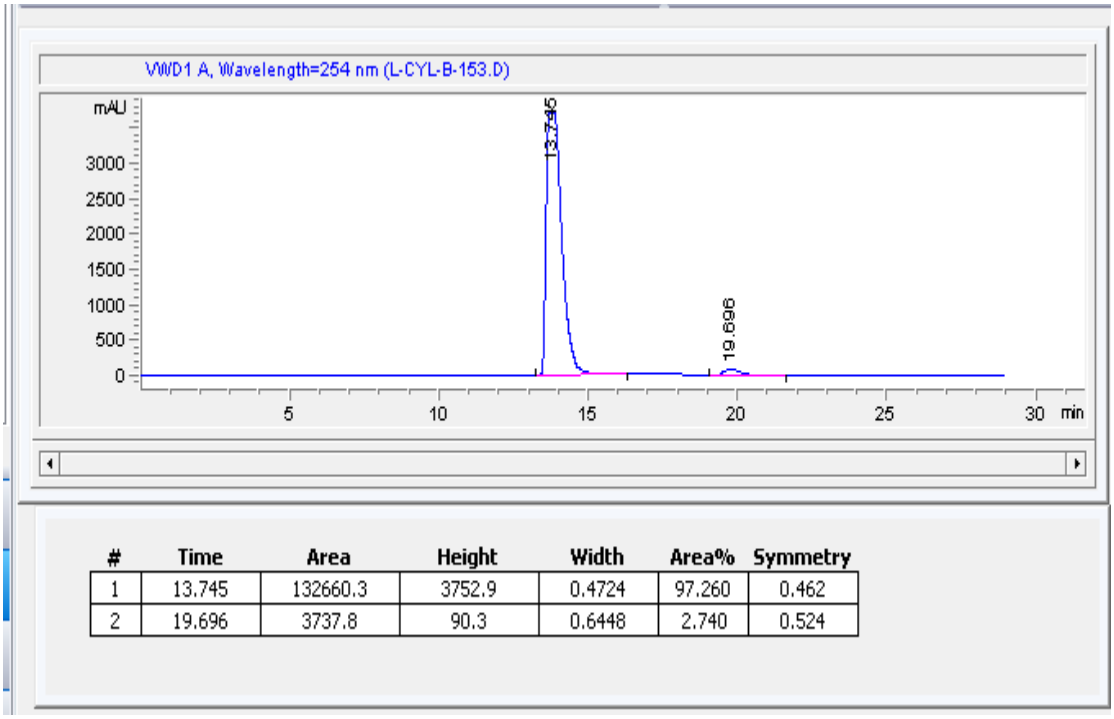




HPLC of 6m

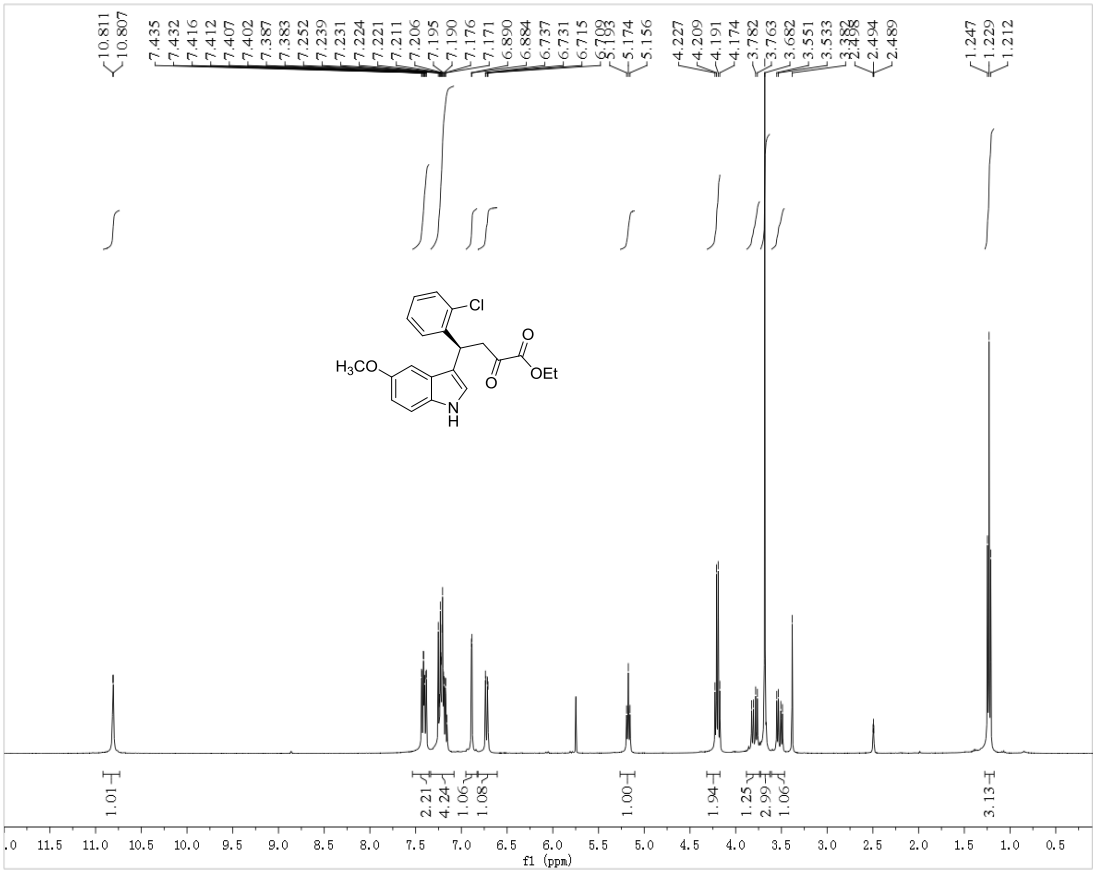


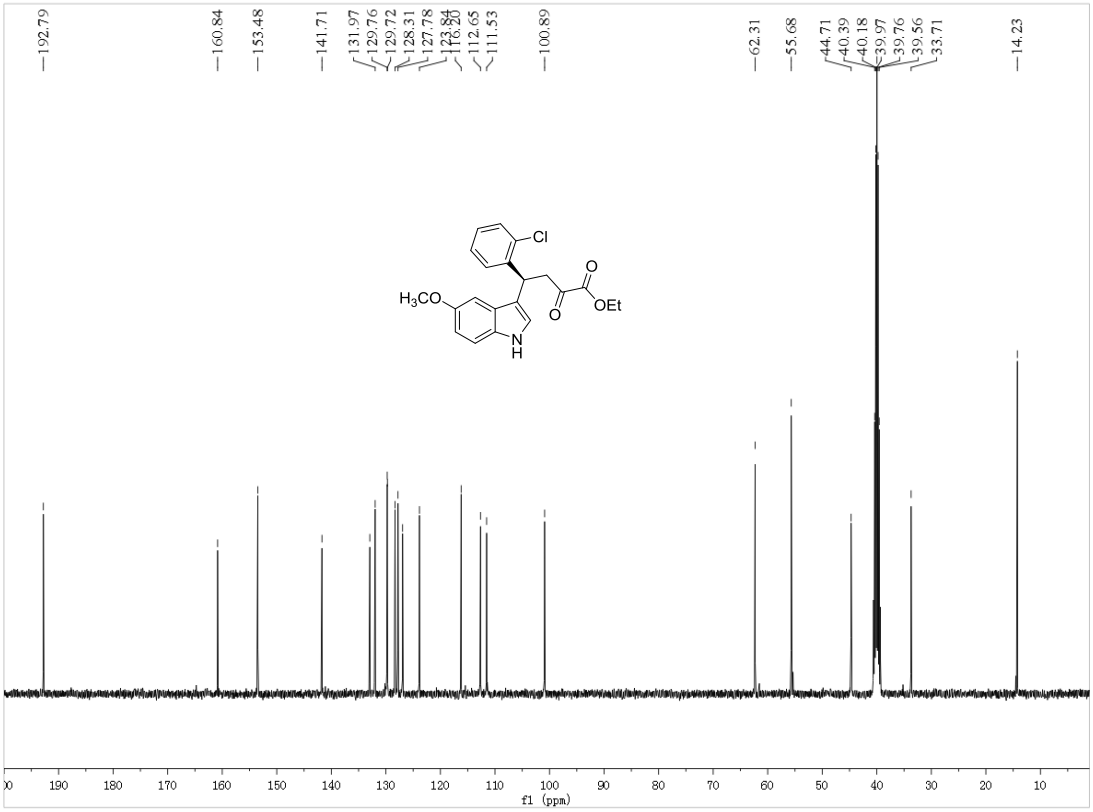
#	Time	Area	Height	Width	Area%	Symmetry
1	15.308	3954.9	125.7	0.481	50.482	0.577
2	22.693	3879.4	77.5	0.7492	49.518	0.524



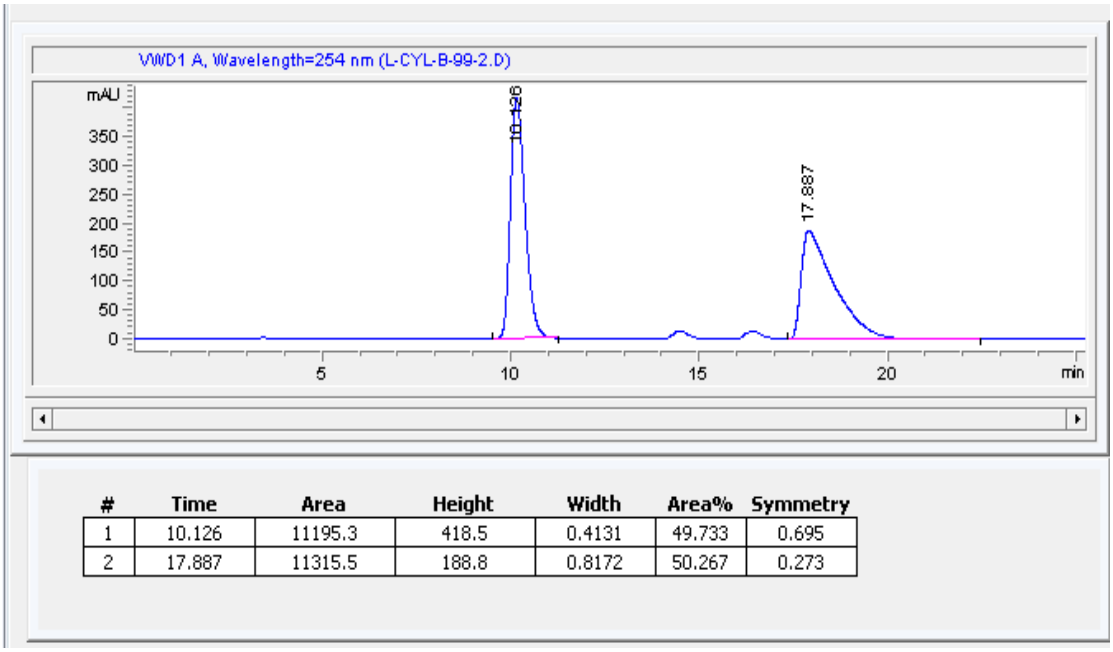
#	Time	Area	Height	Width	Area%	Symmetry
1	13.745	132660.3	3752.9	0.4724	97.260	0.462
2	19.696	3737.8	90.3	0.6448	2.740	0.524

^{1}H and ^{13}C NMR of 6n

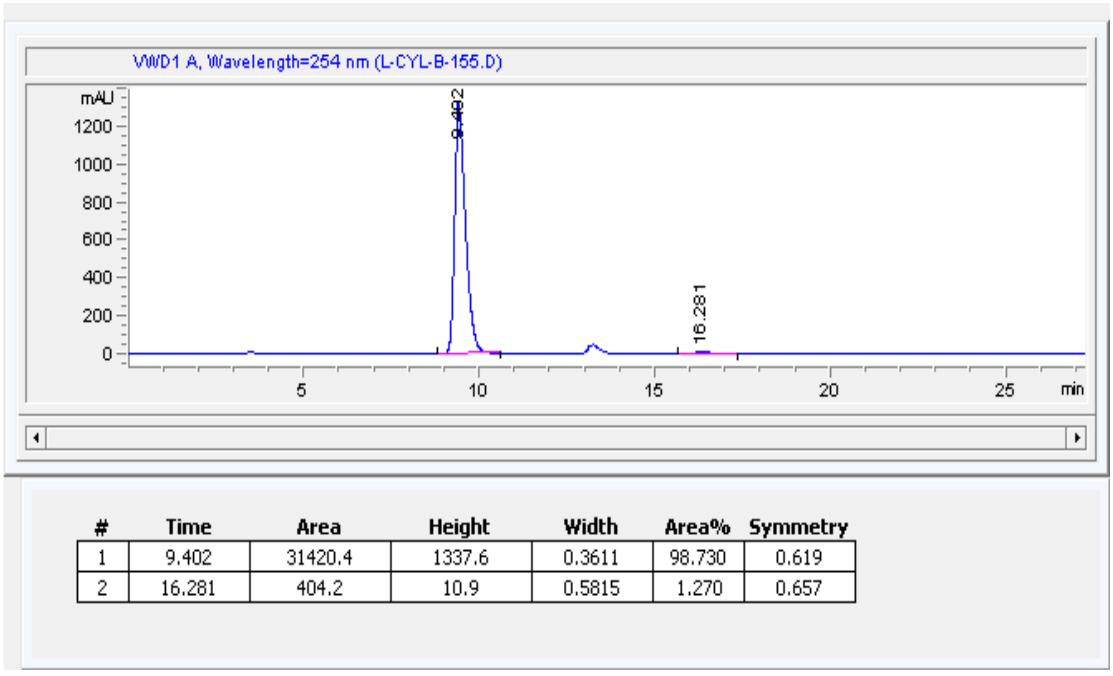




HPLC of 6n

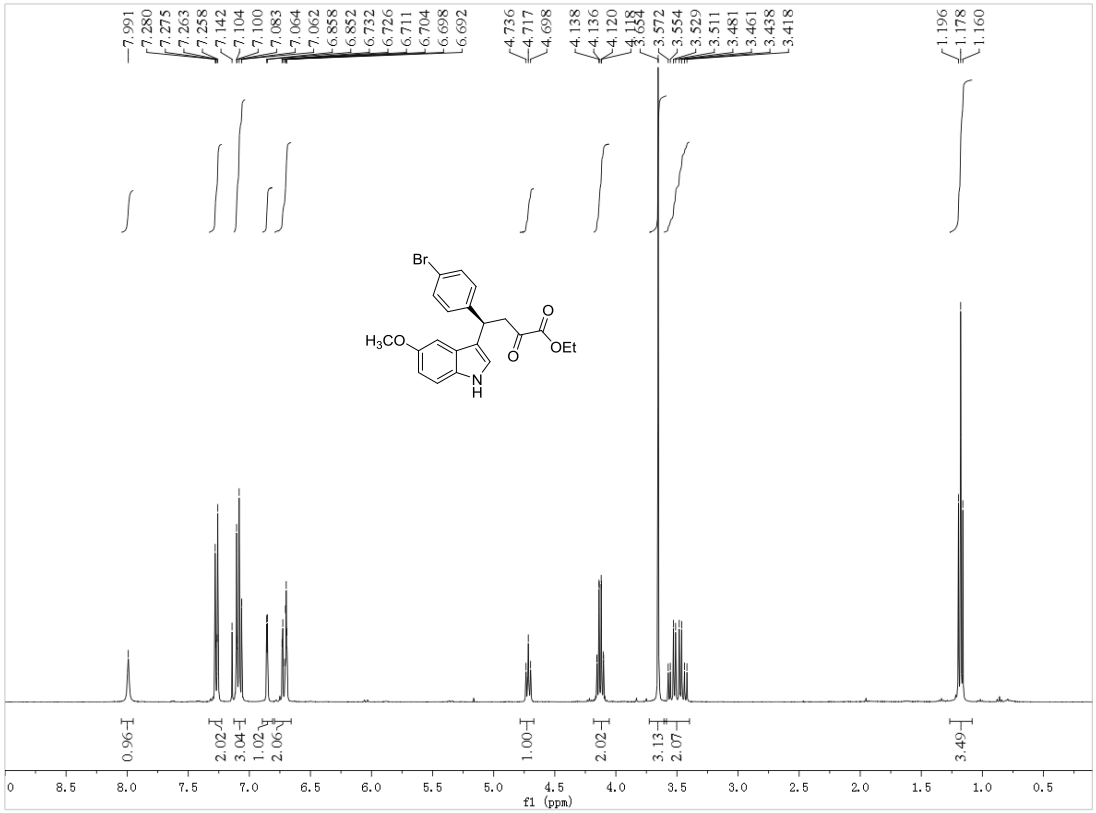


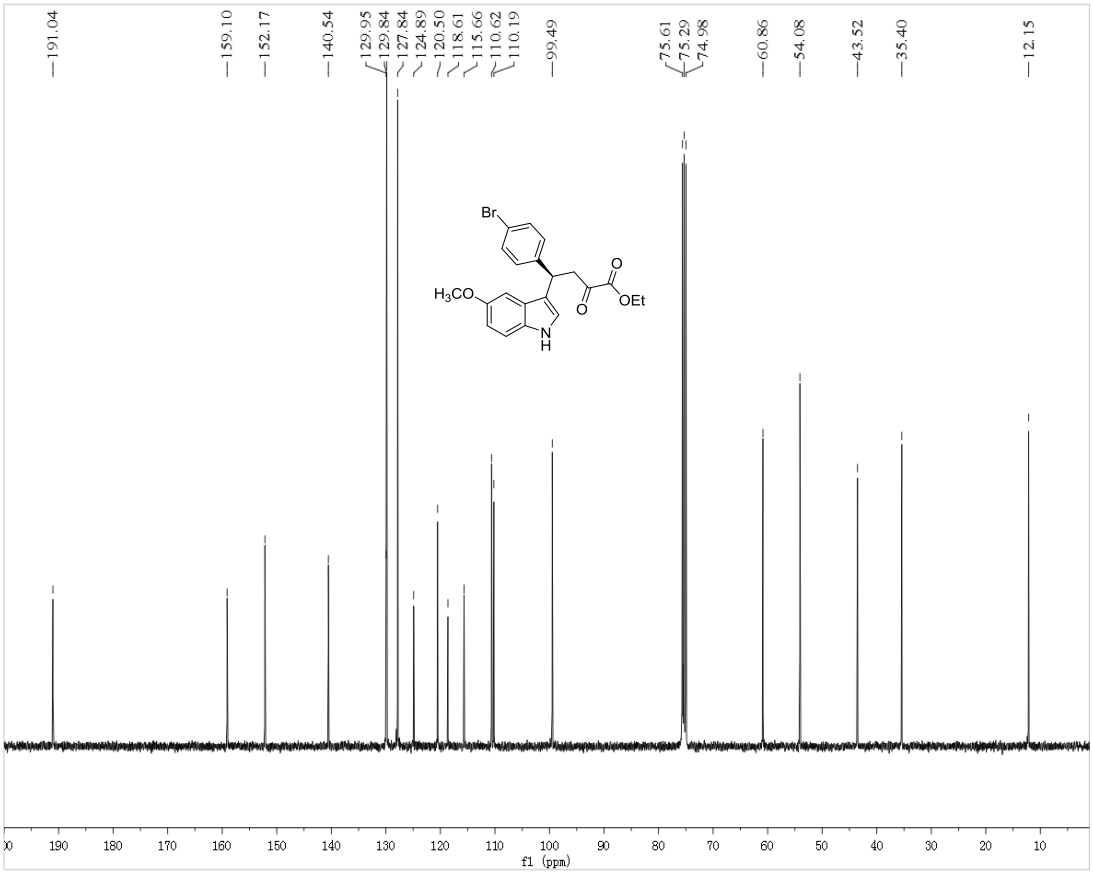
#	Time	Area	Height	Width	Area%	Symmetry
1	10.126	11195.3	418.5	0.4131	49.733	0.695
2	17.887	11315.5	188.8	0.8172	50.267	0.273



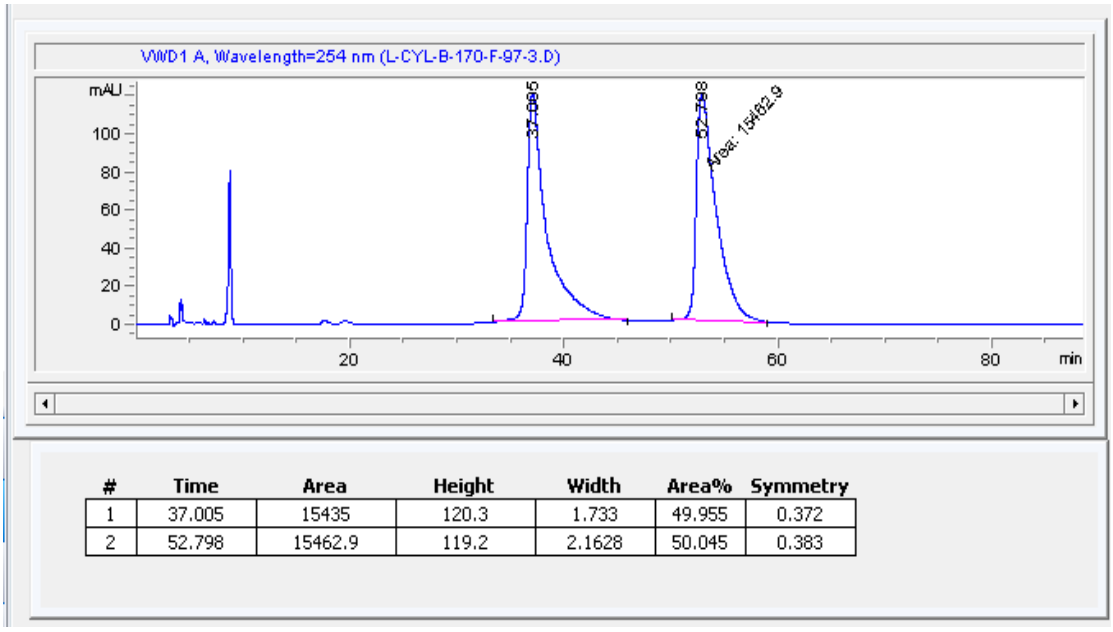
#	Time	Area	Height	Width	Area%	Symmetry
1	9.402	31420.4	1337.6	0.3611	98.730	0.619
2	16.281	404.2	10.9	0.5815	1.270	0.657

^{1}H and ^{13}C NMR of 6o

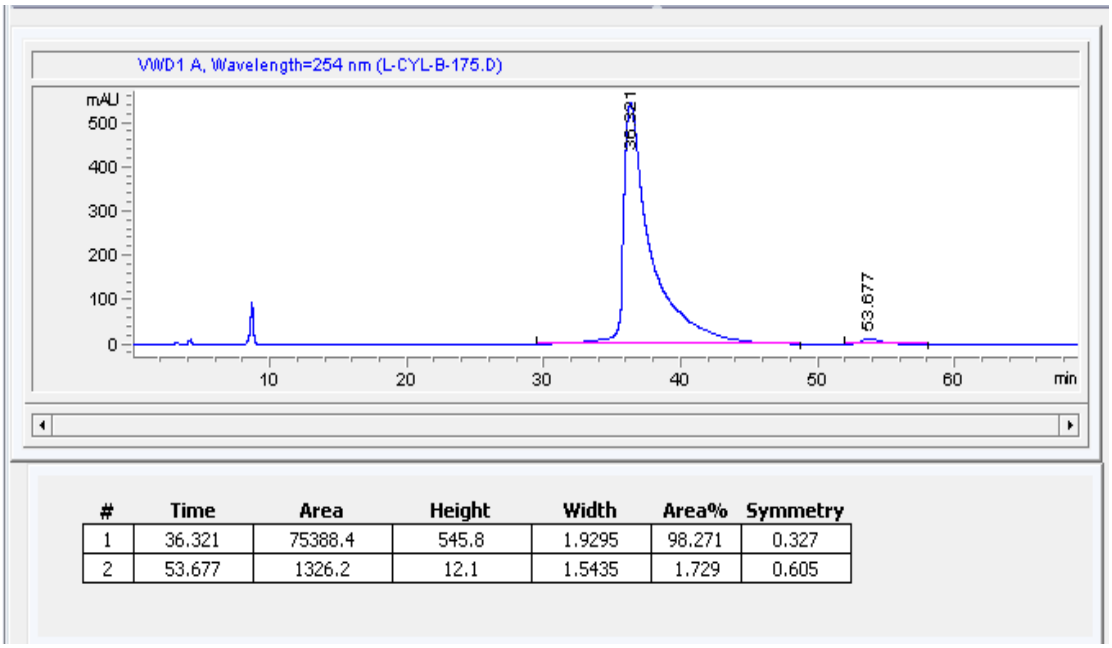




HPLC of 6o

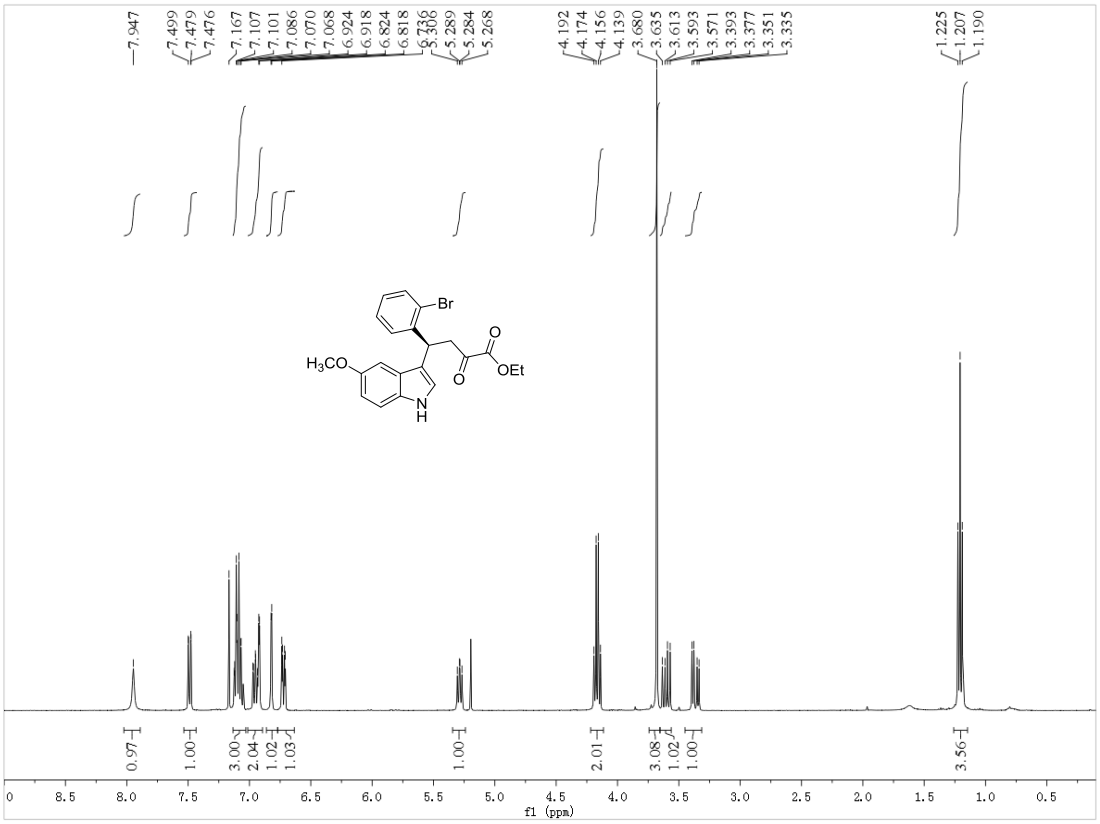


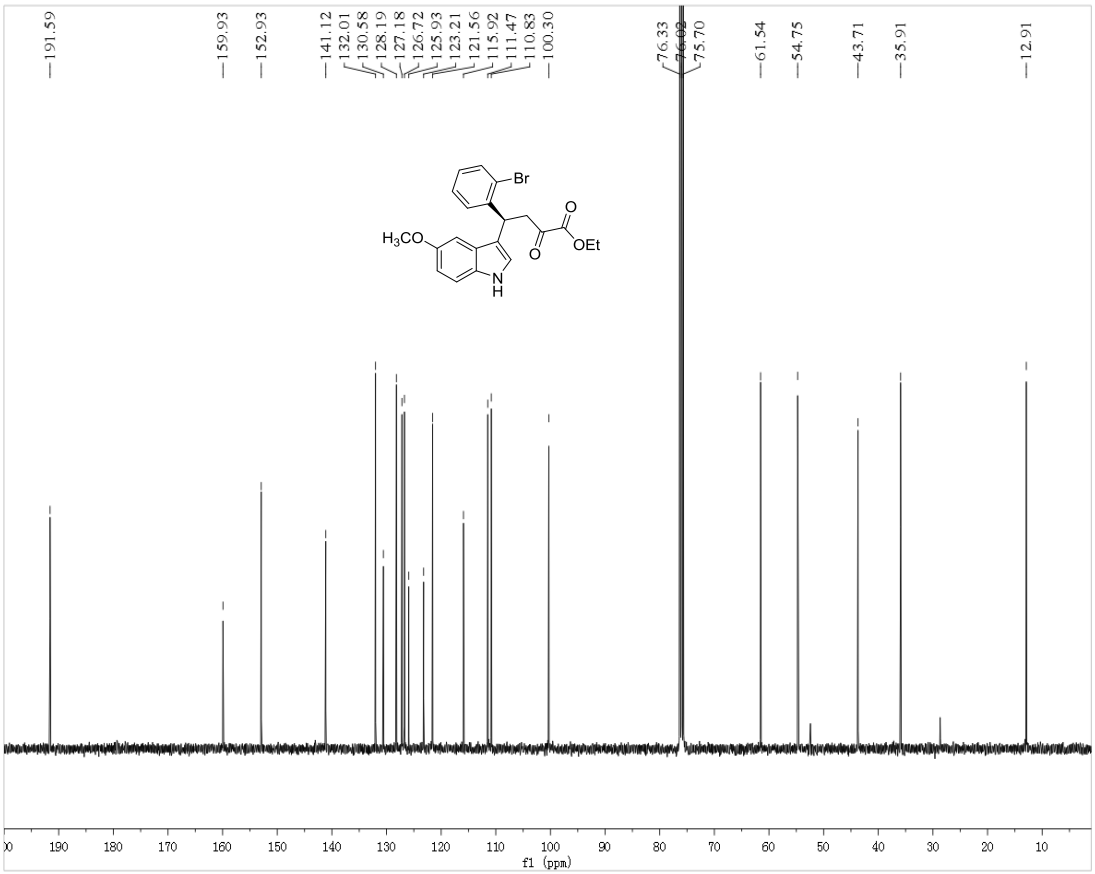
#	Time	Area	Height	Width	Area%	Symmetry
1	37.005	15435	120.3	1.733	49.955	0.372
2	52.798	15462.9	119.2	2.1628	50.045	0.383



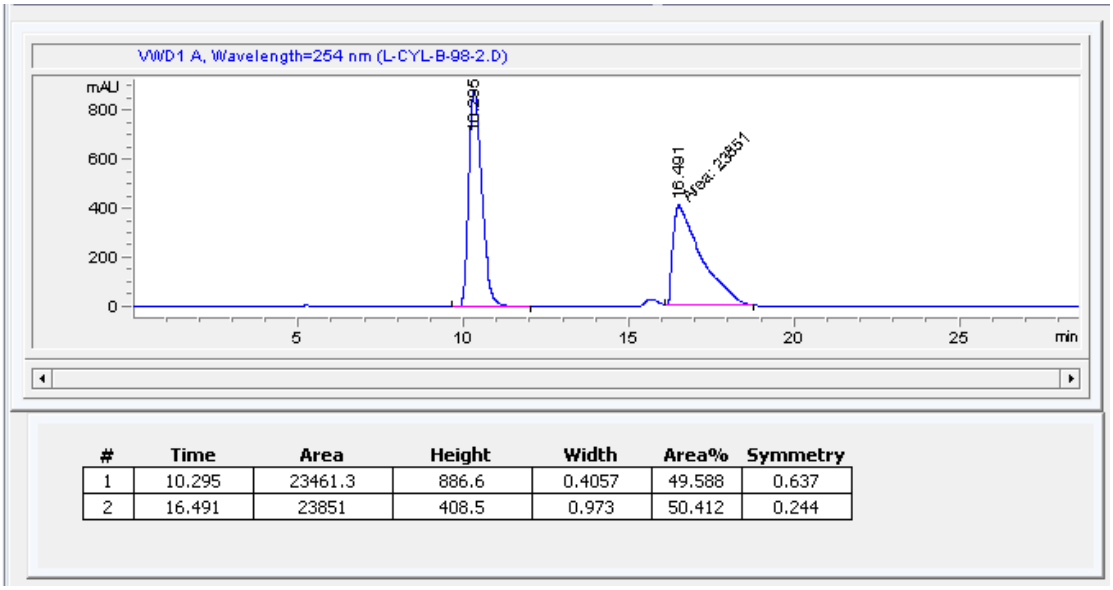
#	Time	Area	Height	Width	Area%	Symmetry
1	36.321	75388.4	545.8	1.9295	98.271	0.327
2	53.677	1326.2	12.1	1.5435	1.729	0.605

^{1}H and ^{13}C NMR of 6p

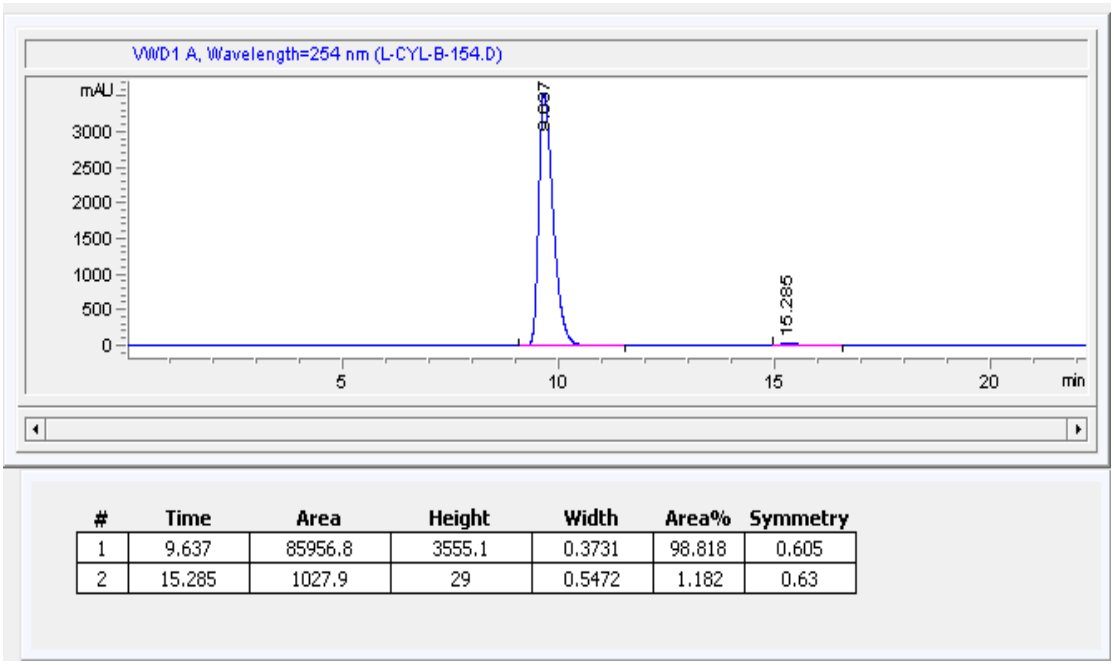




HPLC of 6p

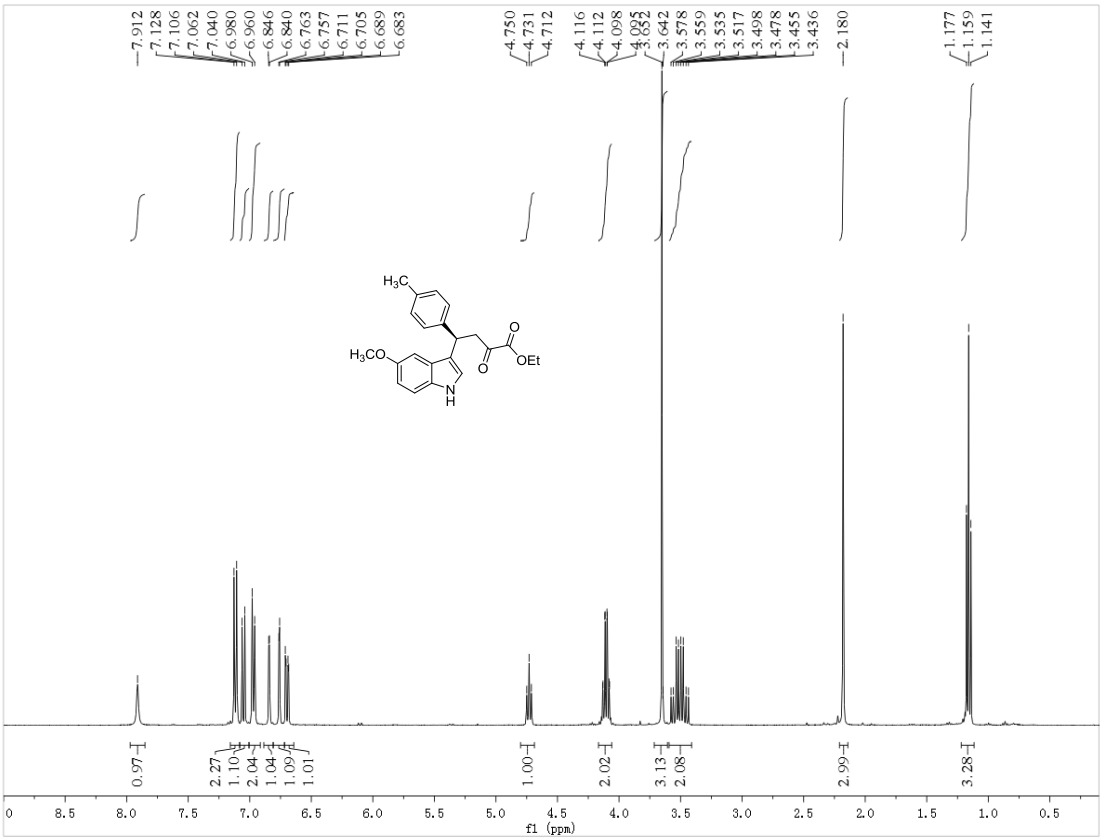


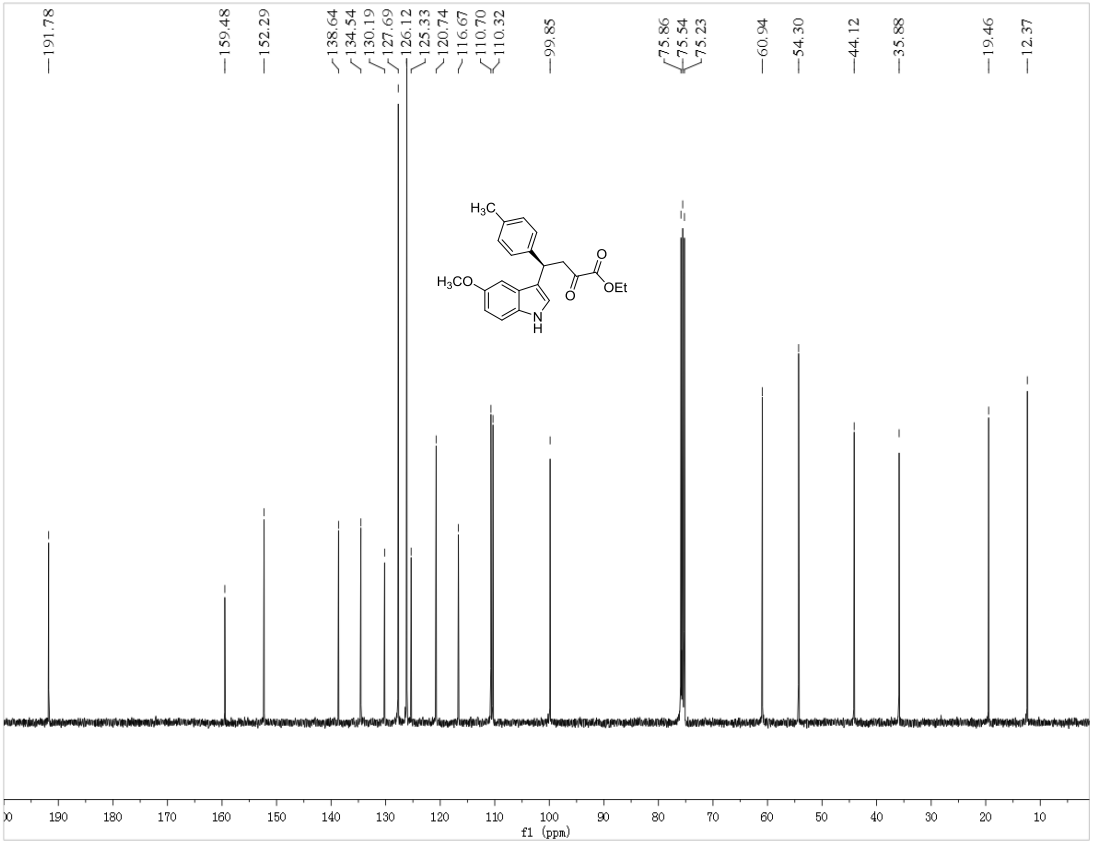
#	Time	Area	Height	Width	Area%	Symmetry
1	10.295	23461.3	886.6	0.4057	49.588	0.637
2	16.491	23851	408.5	0.973	50.412	0.244



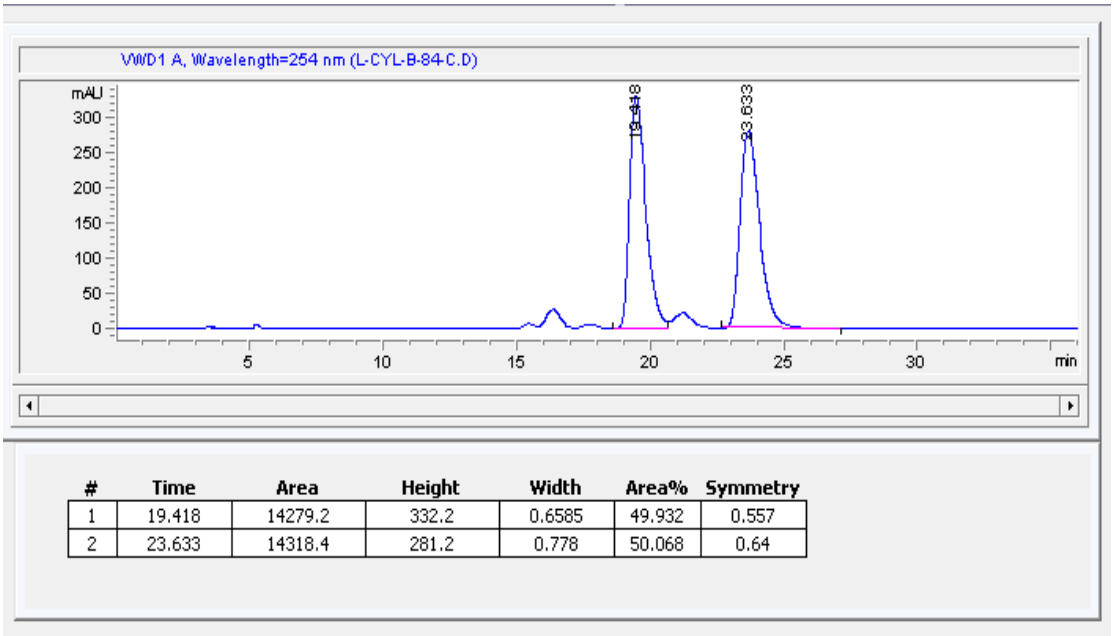
#	Time	Area	Height	Width	Area%	Symmetry
1	9.637	85956.8	3555.1	0.3731	98.818	0.605
2	15.285	1027.9	29	0.5472	1.182	0.63

^{1}H and ^{13}C NMR of 6q

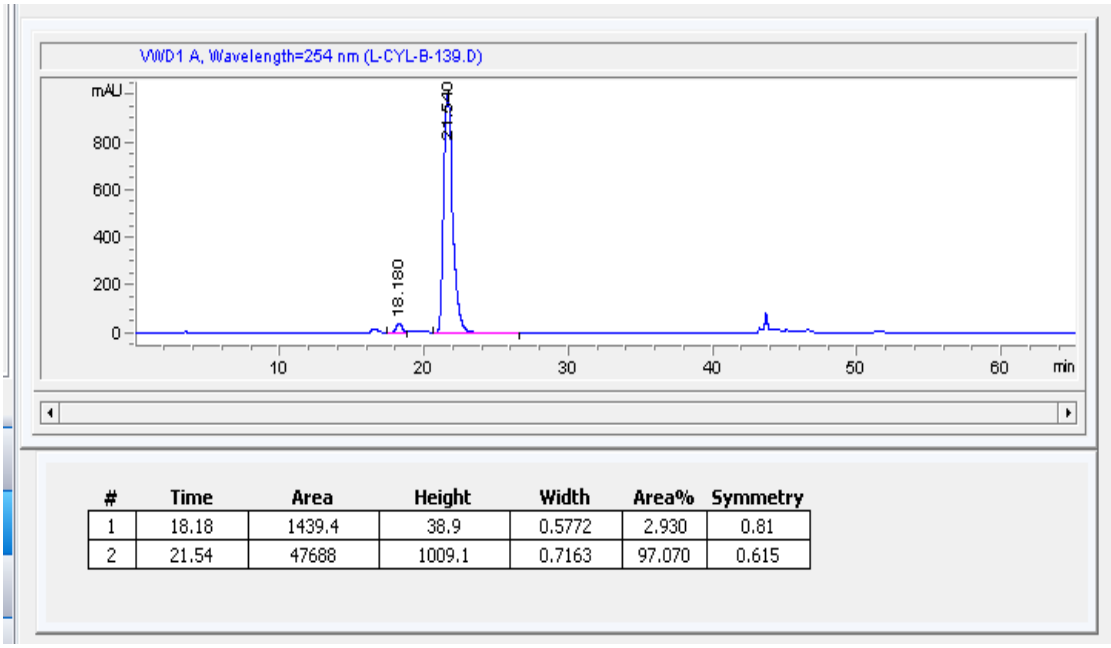




HPLC of 6q

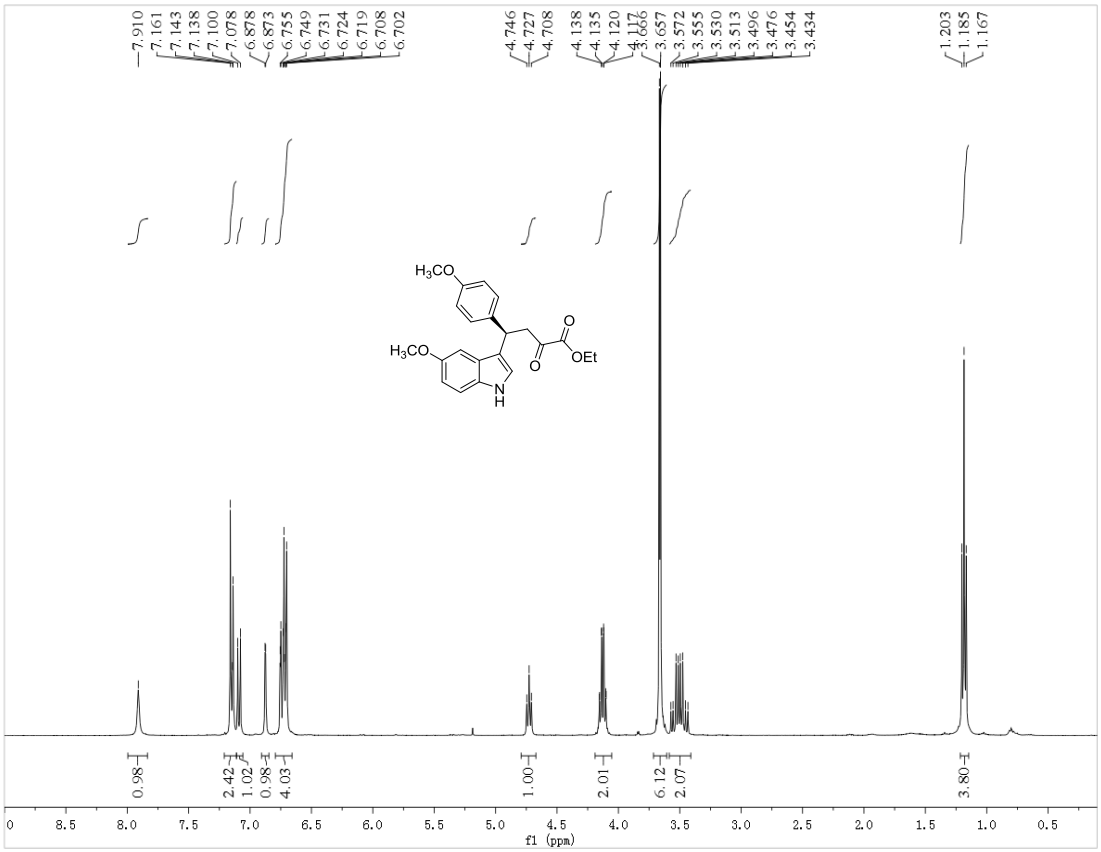


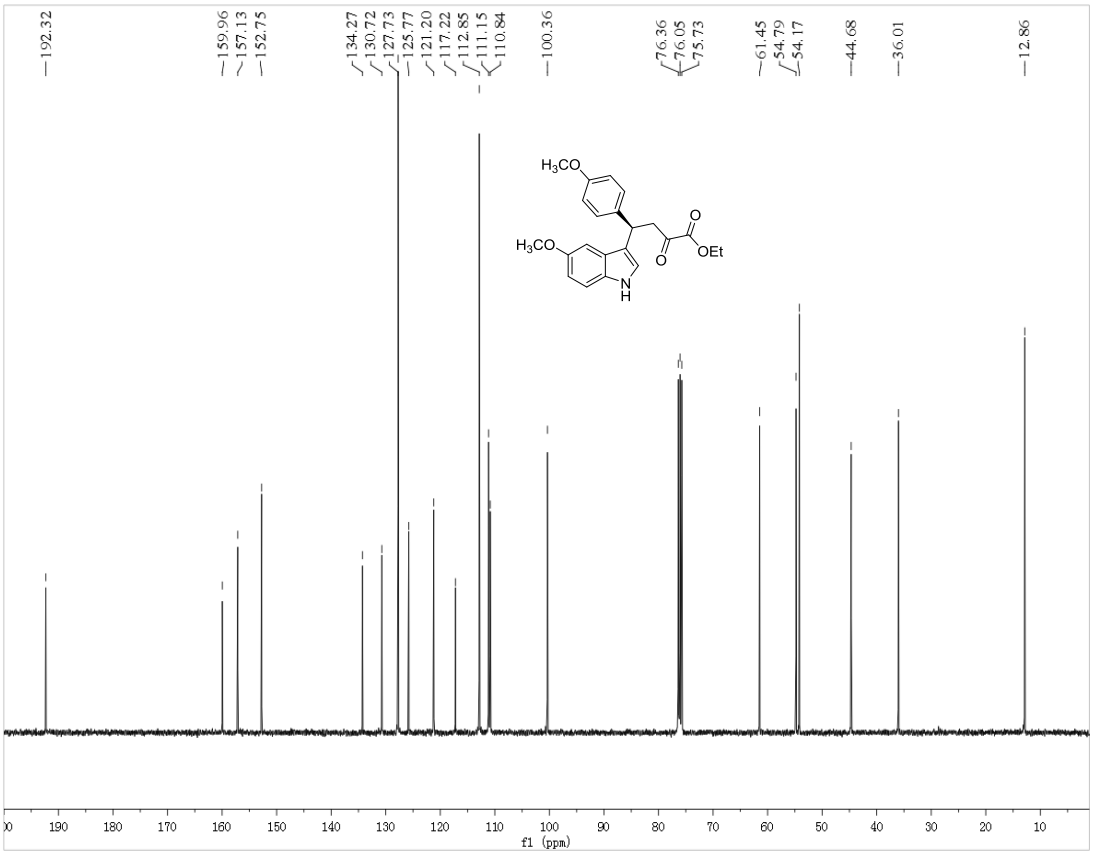
#	Time	Area	Height	Width	Area%	Symmetry
1	19.418	14279.2	332.2	0.6585	49.932	0.557
2	23.633	14318.4	281.2	0.778	50.068	0.64



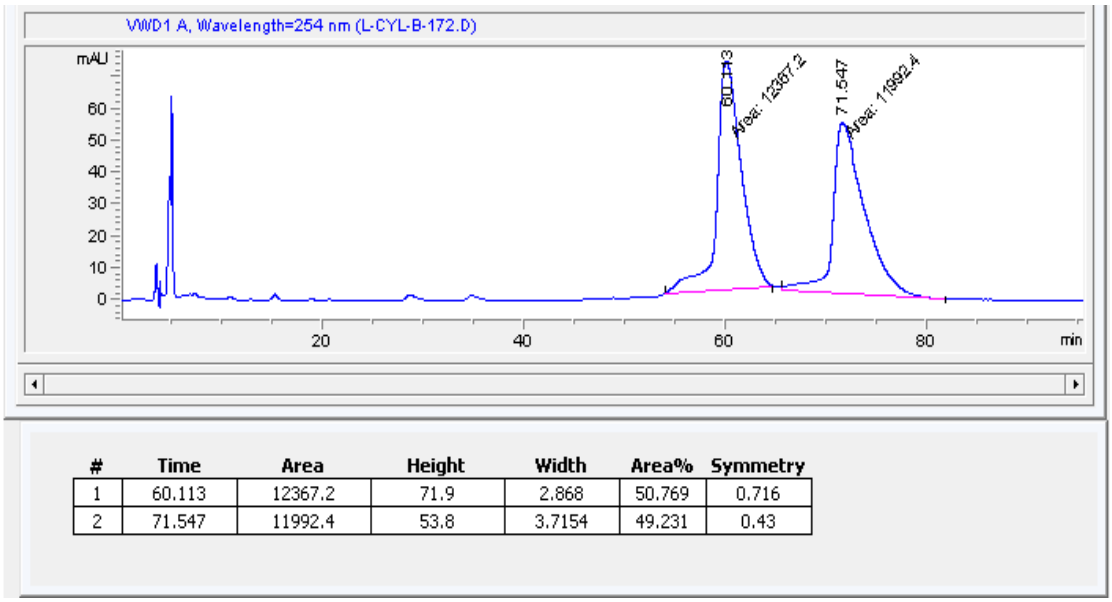
#	Time	Area	Height	Width	Area%	Symmetry
1	18.18	1439.4	38.9	0.5772	2.930	0.81
2	21.54	47688	1009.1	0.7163	97.070	0.615

^{1}H and ^{13}C NMR of 6r

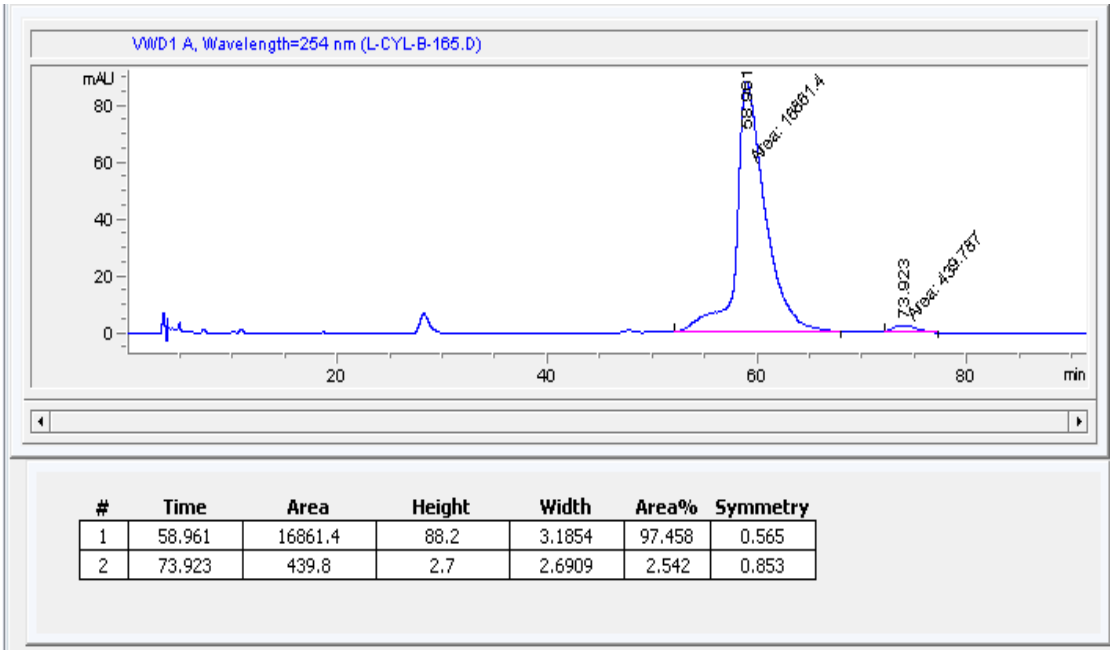




HPLC of 6r

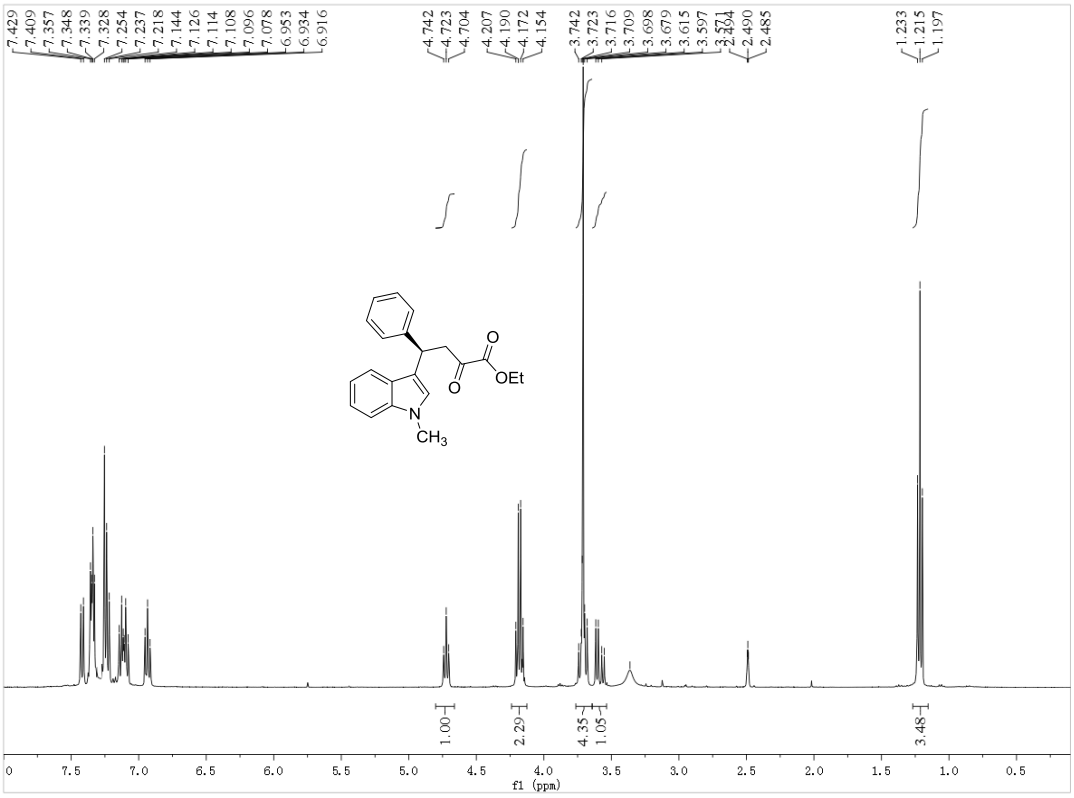


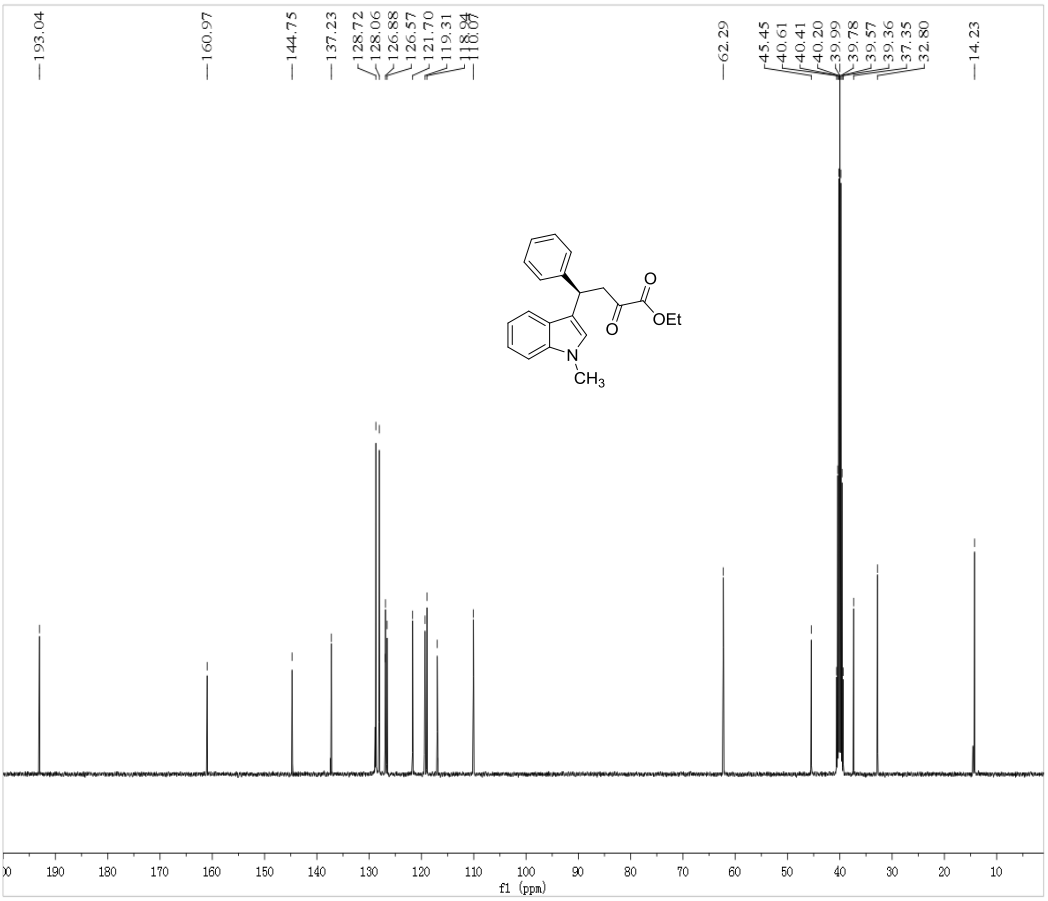
#	Time	Area	Height	Width	Area%	Symmetry
1	60.113	12367.2	71.9	2.868	50.769	0.716
2	71.547	11992.4	53.8	3.7154	49.231	0.43



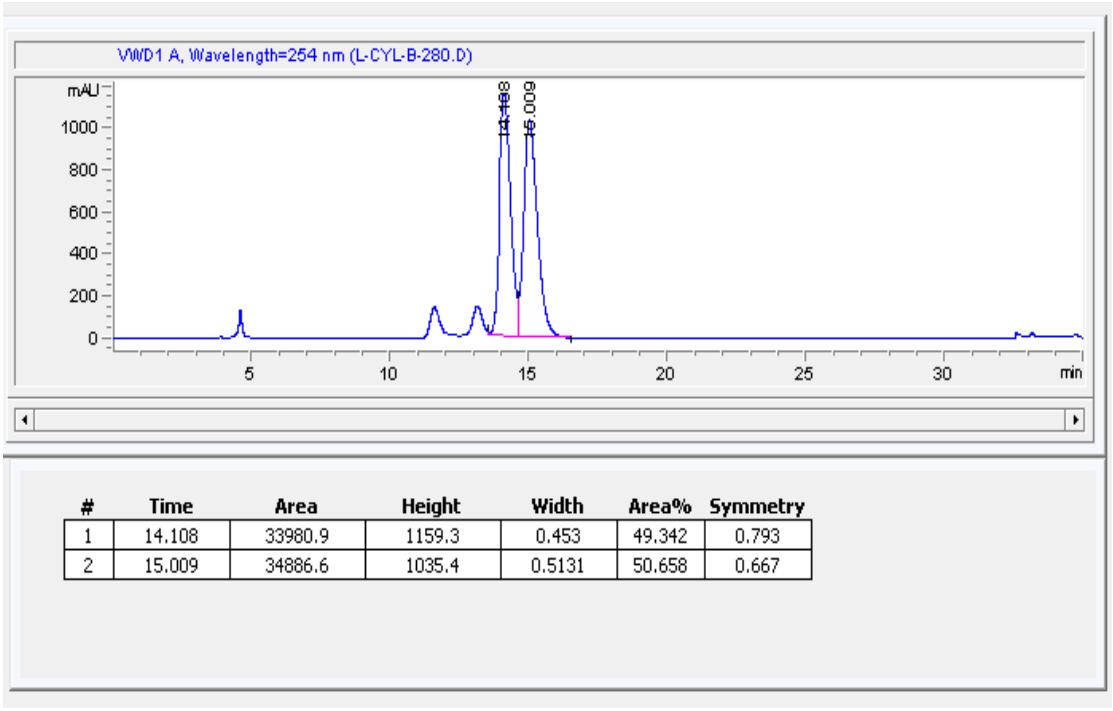
#	Time	Area	Height	Width	Area%	Symmetry
1	58.961	16861.4	88.2	3.1854	97.458	0.565
2	73.923	439.8	2.7	2.6909	2.542	0.853

^{1}H and ^{13}C NMR of 6s

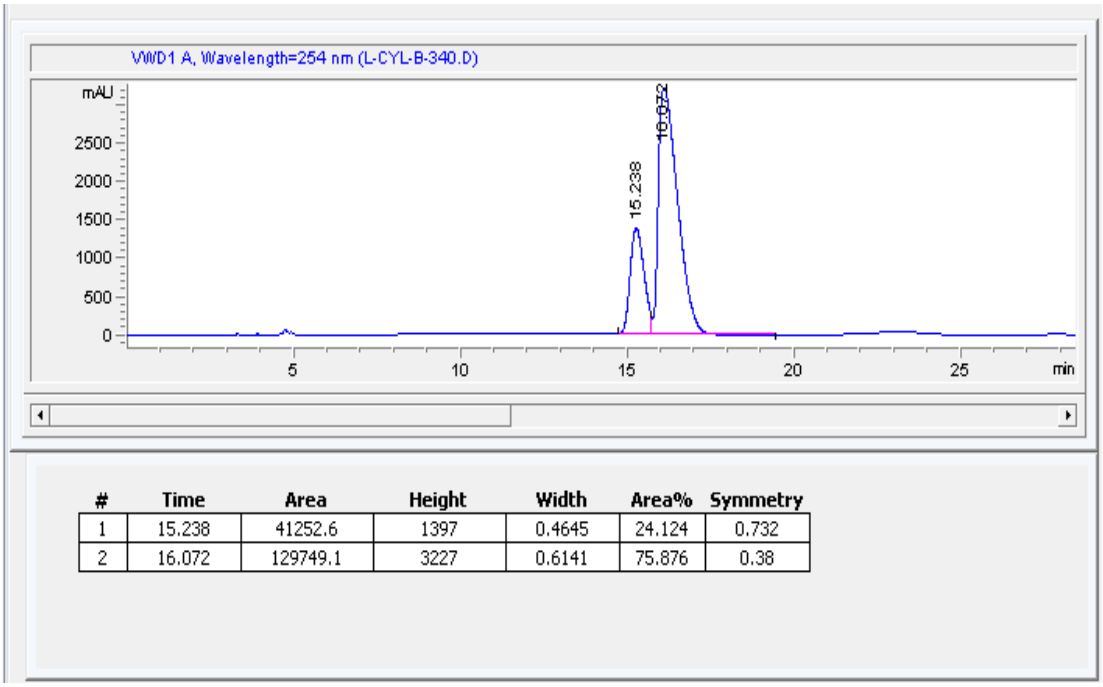




HPLC of 6s



#	Time	Area	Height	Width	Area%	Symmetry
1	14.108	33980.9	1159.3	0.453	49.342	0.793
2	15.009	34886.6	1035.4	0.5131	50.658	0.667



#	Time	Area	Height	Width	Area%	Symmetry
1	15.238	41252.6	1397	0.4645	24.124	0.732
2	16.072	129749.1	3227	0.6141	75.876	0.38