Design rigid-featured chiral bipyridine-2NO tetradentate ligands: application in asymmetric catalysis

Yu-Heng Wang[a,c], Pan Hu[a,c], Xi-Rui Wang[a,c], Ke-Lan Xu[a,c], Qi-Lin Wang[b], Hui-Juan Wang[a], and Xiong-Li Liu[a,*]

[a] National & Local Joint Engineering Research Center for the Exploitation of Homology Resources of Southwest Medicine and Food, Guizhou University, Guiyang 550025, Guizhou, China.

[b] Institute of Functional Organic Molecular Engineering, College of Chemistry and Chemical Engineering, Henan University, Kaifeng 475004, China.

[c] These four authors contributed equally to this work.

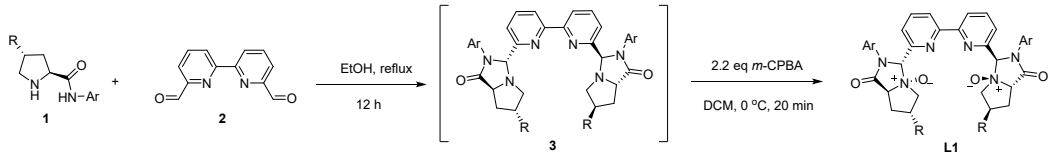
*E-mail address: xlliu1@gzu.edu.cn

Table of Contents

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.

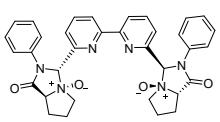
2. General procedure for preparation of chiral bipyridine-2NO ligands L1



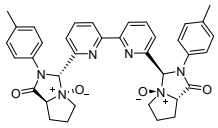
General procedure A-In a sealed tube equipped with a magnetic stirring bar, bipyridine-dicarbaldehyde **2** (1.0 mmol) and optically pure 4-hydroxyprolinamide or prolinamide **1** (2.4 mmol, 2.4 equiv) were added. Then, ethanol (6.0 mL) was added and the reaction was heated with stirring at reflux for 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 °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 bipyridine-2NO ligand **L1**.

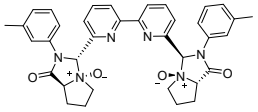
3. Characterization data of bipyridine-2NO ligands L1



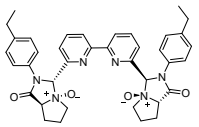
L1a (Prepared according to general procedure A): White solid, M.p. 263.1-263.9 °C, $[\alpha]_D^{20}$ = -40.6 (*c* 0.60, $CHCl_3$); overall yield 53%, >20:1 dr; ^1H NMR (CD_3OD, 400 MHz) δ: 2.23-2.28 (m, 2H), 2.45-2.66 (m, 6H), 3.91-3.95 (m, 2H), 4.16-4.24 (m, 2H), 4.73-4.76 (m, 2H), 6.79 (s, 2H), 7.12-7.16 (m, 2H), 7.23-7.27 (m, 4H), 7.40-7.43 (m, 4H), 7.70-7.72 (m, 2H), 7.97-8.01 (m, 2H), 8.38-8.40 (m, 2H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 35.5, 70.0, 76.3, 76.7, 88.1, 122.2, 122.9, 126.8, 127.7, 128.9, 135.3, 138.2, 149.8, 155.2, 168.7; HRMS (ESI-TOF) m/z: Calcd. for $C_{34}H_{32}N_6NaO_4$ $[M+Na]^+$: 611.2376; Found: 611.2372.



L1b (Prepared according to general procedure A): White solid, M.p. 223.2-224.9 °C, $[\alpha]_D^{20}$ = -84.3 (*c* 0.60, $CHCl_3$); overall yield 52%, >20:1 dr; ^1H NMR (CD_3OD, 400 MHz) δ: 2.10 (s, 6H), 2.22-2.26 (m, 2H), 2.43-2.66 (m, 6H), 3.92-3.96 (m, 2H), 4.14-4.22 (m, 2H), 4.75-4.78 (m, 2H), 6.74 (s, 2H), 6.98 (d, *J* = 8.8 Hz, 4H), 7.26 (d, *J* = 8.8 Hz, 4H), 7.71 (d, *J* = 7.2 Hz, 2H), 7.97-8.01 (m, 2H), 8.41 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 19.6, 22.5, 24.6, 71.0, 76.9, 87.9, 121.9, 122.9, 127.6, 129.4, 132.8, 136.9, 138.2, 150.3, 155.1, 169.3; HRMS (ESI-TOF) m/z: Calcd. for $C_{36}H_{36}N_6NaO_4$ $[M+Na]^+$: 639.2687; Found: 639.2676.

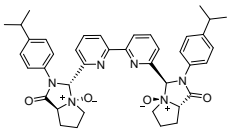


L1c (Prepared according to general procedure A): White solid, M.p. 257.9-258.6 °C, $[\alpha]_D^{20}$ = -64.3 (*c* 0.60 $CHCl_3$); overall yield 50%, >20:1 dr; ^1H NMR (CD_3OD, 400 MHz) δ: 2.16 (s, 6H), 2.22-2.26 (m, 2H), 2.45-2.65 (m, 6H), 3.91-3.95 (m, 2H), 4.16-4.23 (m, 2H), 4.73-4.76 (m, 2H), 6.78 (s, 2H), 6.95 (d, *J* = 7.6 Hz, 2H), 7.09-7.17 (m, 4H), 7.28 (s, 2H), 7.70-7.72 (m, 2H), 7.98-8.02 (m, 2H), 8.39-8.41 (m, 2H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 20.0, 22.4, 24.6, 70.9, 77.0, 87.9, 119.9, 121.9, 123.5, 127.5, 128.7, 135.3, 138.1, 139.2, 150.3, 155.1, 169.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{36}H_{36}N_6NaO_4$ $[M+Na]^+$: 639.2690; Found: 639.2689.

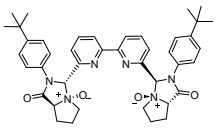


L1d (Prepared according to general procedure A): White solid, M.p. 258.9-259.7 °C, $[\alpha]_D^{20}$ = -

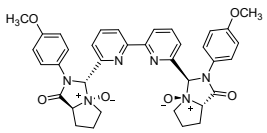
89.5 (*c* 0.60 $CHCl_3$); overall yield 48%, >20:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 1.00-1.04 (m, 6H), 2.23-2.28 (m, 2H), 2.41-2.65 (m, 10H), 3.92-3.96 (m, 2H), 4.15-4.22 (m, 2H), 4.75-4.78 (m, 2H), 6.74 (s, 2H), 7.01 (d, J = 8.8 Hz, 4H), 7.29 (d, J = 8.4 Hz, 4H), 7.69-7.71 (m, 2H), 7.98-8.02 (m, 2H), 8.40-8.43 (m, 2H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 14.5, 22.4, 24.6, 27.8, 71.0, 77.0, 87.9, 121.9, 123.0, 127.6, 128.3, 133.0, 138.2, 143.3, 150.3, 155.1, 169.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{38}H_{40}N_6NaO_4$ $[M+Na]^+$: 667.3001; Found: 667.2991.



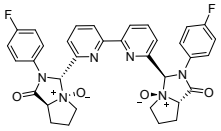
L1e (Prepared according to general procedure A): White solid, M.p. 257.2-258.3 °C, $[\alpha]_D^{20}$ = -66.1 (*c* 0.60 $CHCl_3$); overall yield 50%, >20:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 1.05 (s, 6H), 1.07 (s, 6H), 2.23-2.28 (m, 2H), 2.46-2.65 (m, 6H), 2.69-2.76 (m, 2H), 3.92-3.96 (m, 2H), 4.15-4.22 (m, 2H), 4.75-4.78 (m, 2H), 6.75 (s, 2H), 7.07 (d, J = 8.4 Hz, 4H), 7.31 (d, J = 8.4 Hz, 4H), 7.70-7.72 (m, 2H), 7.97-8.01 (m, 2H), 8.41-8.43 (m, 2H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 22.4, 22.9, 24.6, 33.5, 71.0, 76.9, 87.9, 122.0, 123.0, 126.9, 127.5, 133.1, 138.2, 147.8, 150.4, 155.2, 169.3; HRMS (ESI-TOF) m/z: Calcd. for $C_{40}H_{44}N_6NaO_4$ $[M+Na]^+$: 695.3312; Found: 695.3294.



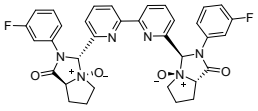
L1f (Prepared according to general procedure A): White solid, M.p. 247.0-247.9 °C, $[\alpha]_D^{20}$ = -86.7 (*c* 0.60 $CHCl_3$); overall yield 53%, >20:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 1.11 (s, 18H), 2.23-2.28 (m, 2H), 2.47-2.66 (m, 6H), 3.95-3.99 (m, 2H), 4.14-4.22 (m, 2 H), 4.77-4.80 (m, 2H), 6.77 (s, 2H), 7.21 (d, J = 8.8 Hz, 4H), 7.34 (d, J = 8.8 Hz, 4H), 7.75 (d, J = 7.6 Hz, 2H), 7.99-8.03 (m, 2H), 8.44 (d, J = 7.6 Hz, 2H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 22.5, 24.7, 30.3, 34.0, 71.0, 76.9, 87.8, 122.0, 122.4, 125.9, 127.6, 132.9, 138.3, 149.8, 150.4, 155.2, 169.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{42}H_{48}N_6NaO_4$ $[M+Na]^+$: 723.3629; Found: 723.3629.



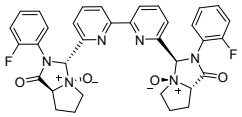
L1g (Prepared according to general procedure A): White solid, M.p. 257.1-258.2 °C, $[\alpha]_D^{20}$ = -110.6 (*c* 0.60 $CHCl_3$); overall yield 53%, 15:1 dr; ^1H NMR (CD_3OD, 400 MHz) δ: 2.24-2.27 (m, 2H), 2.46-2.63 (m, 6H), 3.66 (s, 6H), 3.91-3.95 (m, 2H), 4.18-4.25 (m, 2H), 4.74 (d, J = 9.2 Hz, 2H), 6.68 (s, 2H), 6.77-6.79 (m, 4H), 7.26-7.28 (m, 4H), 7.66 (d, J = 7.6 Hz, 2H), 7.98-8.02 (m, 2H), 8.42 (d, J = 7.6 Hz, 2H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 22.4, 24.5, 54.5, 71.0, 76.9, 88.4, 114.1, 121.8, 125.2, 127.6, 127.8, 138.1, 150.3, 155.1, 158.7, 169.5; HRMS (ESI-TOF) m/z: Calcd. for $C_{36}H_{36}N_6NaO_6$ $[M+Na]^+$: 671.2581; Found: 671.2565.



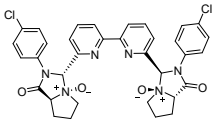
L1h (Prepared according to general procedure A): White solid, M.p. 248.7-249.3 °C, $[\alpha]_D^{20}$ = -30.7 (*c* 0.60 $CHCl_3$); overall yield 48%, >20:1 dr; ^1H NMR (CD_3OD, 400 MHz) δ: 2.23-2.30 (m, 2H), 2.44-2.67 (m, 6H), 3.92-3.96 (m, 2H), 4.19-4.26 (m, 2H), 4.73-4.76 (m, 2H), 6.78 (s, 2H), 7.00-7.04 (m, 4H), 7.42-7.46 (m, 4H), 7.70-7.72 (m, 2H), 8.00-8.04 (m, 2H), 8.39-8.41 (m, 2H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 22.4, 24.6, 71.0, 76.8, 87.9, 115.6 (d, J_{CF} = 23.1 Hz), 122.0, 125.3 (d, J_{CF} = 8.3 Hz), 127.7, 131.5 (d, J_{CF} = 3.4 Hz), 138.2, 150.1, 155.1, 161.6 (d, J_{CF} = 245.3 Hz), 169.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{34}H_{30}F_2N_6NaO_4$ $[M+Na]^+$: 647.2189; Found: 647.2189.



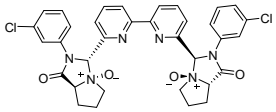
L1i (Prepared according to general procedure A): White solid, M.p. 255.0-255.9 °C, $[\alpha]_D^{20}$ = -15.9 (*c* 0.60 $CHCl_3$); overall yield 49%, >20:1 dr; ^1H NMR (CD_3OD, 400 MHz) δ: 2.27-2.32 (m, 2H), 2.50-2.60 (m, 4H), 2.65-2.70 (m, 2H), 3.98-4.02 (m, 2H), 4.19-4.26 (m, 2H), 4.79-4.82 (m, 2H), 6.83-6.88 (m, 2H), 6.92 (s, 2H), 7.20-7.27 (m, 4H), 7.47-7.51 (m, 2H), 7.81 (d, J = 7.6 Hz, 2H), 8.05-8.09 (m, 2H), 8.41-8.43 (m, 2H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 22.4, 24.7, 71.1, 76.9, 87.3, 109.5 (d, J_{CF} = 26.0 Hz), 113.0 (d, J_{CF} = 22.1 Hz), 117.5 (d, J_{CF} = 3.1 Hz), 122.1, 127.7, 130.4 (d, J_{CF} = 9.0 Hz), 137.1 (d, J_{CF} = 10.0 Hz), 138.3, 150.0, 155.2, 162.8 (d, J_{CF} = 244.3 Hz), 169.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{34}H_{30}F_2N_6NaO_4$ $[M+Na]^+$: 647.2186; Found: 647.2173.



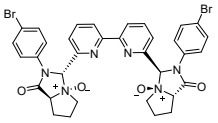
L1j (Prepared according to general procedure A): White solid, M.p. 252.0-252.5 °C, $[\alpha]_D^{20}$ = -318.6 (*c* 0.60 $CHCl_3$); overall yield 46%, 20:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) *δ*: 2.23-2.30 (m, 2H), 2.43-2.68 (m, 6H), 3.98-4.02 (m, 2H), 4.26-4.33 (m, 2H), 4.80-4.83 (m, 2H), 6.63 (s, 2H), 7.03-7.07 (m, 2H), 7.17-7.25 (m, 4H), 7.29-7.35 (m, 2H), 7.67-7.69 (m, 2H), 7.99-8.03 (m, 2H), 8.50-8.52 (m, 2H); ^{13}C NMR (CD_3OD, 100 MHz) *δ*: 22.5, 24.6, 71.2, 76.4, 88.0, 116.4 (d, J_{CF} = 20.2 Hz), 121.8 (d, J_{CF} = 11.1 Hz), 122.1, 124.7 (d, J_{CF} = 4.3 Hz), 127.7, 128.6, 130.4 (d, J_{CF} = 8.2 Hz), 138.3, 150.1, 155.2, 158.7 (d, J_{CF} = 249.1 Hz), 169.7; HRMS (ESI-TOF) m/z: Calcd. for $C_{34}H_{30}F_2N_6NaO_4$ $[M+Na]^+$: 647.2189; Found: 647.2187.



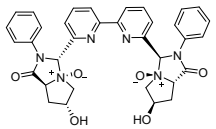
L1k (Prepared according to general procedure A): White solid, M.p. 258.2-258.9 °C, $[\alpha]_D^{20}$ = -20.2 (*c* 0.20 $CHCl_3$); overall yield 50%, >20:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) *δ*: 2.25-2.30 (m, 2H), 2.46-2.70 (m, 6H), 3.95-3.99 (m, 2H), 4.17-4.24 (m, 2H), 4.75-4.78 (m, 2H), 6.83 (s, 2H), 7.11-7.15 (m, 4H), 7.39-7.43 (m, 4H), 7.76 (d, *J* = 7.6 Hz, 2H), 8.02-8.06 (m, 2H), 8.40 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (CD_3OD, 100 MHz) *δ*: 22.5, 24.7, 71.0, 76.8, 87.4, 122.1, 123.9, 127.8, 128.9, 131.7, 134.2, 138.3, 150.0, 155.1, 169.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{34}H_{30}Cl_2N_6NaO_4$ $[M+Na]^+$: 679.1593; Found: 679.1582.



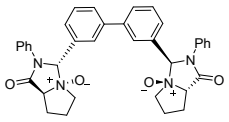
L1l (Prepared according to general procedure A): White solid, M.p. 260.5-261.7 °C, $[\alpha]_D^{20}$ = +97.6 (*c* 0.20 $CHCl_3$); overall yield 49%, 18:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) *δ*: 2.25-2.30 (m, 2H), 2.46-2.69 (m, 6H), 3.93-3.97 (m, 2H), 4.17-4.24 (m, 2H), 4.75-4.78 (m, 2H), 6.88 (d, *J* = 2H), 7.06-7.09 (m, 2H), 7.15-7.19 (m, 2H), 7.28-7.30 (m, 2H), 7.66-7.67 (m, 2H), 7.77 (d, *J* = 7.6 Hz, 2H), 8.02-8.06 (m, 2H), 8.38 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR (CD_3OD, 100 MHz) *δ*: 22.4, 24.7, 71.0, 76.8, 87.2, 120.4, 122.1, 122.5, 126.4, 127.7, 130.2, 134.4, 136.8, 138.3, 150.0, 155.2, 169.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{34}H_{30}Cl_2N_6NaO_4$ $[M+Na]^+$: 679.1598; Found: 679.1595.



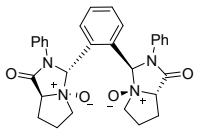
L1m (Prepared according to general procedure A): White solid, M.p. 260.9-261.6 °C, $[\alpha]_D^{20}$ = -80.2 (*c* 0.60 $CHCl_3$); overall yield 51%, >20:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) *δ*: 2.23-2.28 (m, 2H), 2.44-2.68 (m, 6H), 3.92-3.96 (m, 2H), 4.15-4.22 (m, 2H), 4.72-4.75 (m, 2H), 6.81 (s, 2H), 7.25-7.28 (m, 4H), 7.32-7.35 (m, 4H), 7.74 (d, *J* = 8.1 Hz, 2H), 8.01-8.04 (m, 2H), 8.37 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (CD_3OD, 100 MHz) *δ*: 22.4, 24.7, 71.0, 76.8, 87.3, 119.5, 122.1, 124.0, 127.7, 131.9, 134.7, 138.3, 150.1, 155.1, 169.2; HRMS (ESI-TOF) m/z: Calcd. for $C_{34}H_{30}Br_2N_6NaO_4$ $[M+Na]^+$: 767.0579; Found: 767.0561.



L1n (Prepared according to general procedure A): White solid, M.p. 248.2-248.8 °C, $[\alpha]_D^{20}$ = -21.9 (*c* 0.20 $CHCl_3$); overall yield 51%, >20:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) *δ*: 2.65-2.72 (m, 2H), 2.84-2.91 (m, 2H), 3.95 (d, *J* = 12.0 Hz, 2H), 4.42-4.46 (m, 2H), 4.65 (d, *J* = 6.0 Hz, 2H), 4.97-5.00 (m, 2H), 6.80 (s, 2H), 7.13-7.17 (m, 2H), 7.24-7.28 (m, 4H), 7.39-7.42 (m, 4H), 7.70 (d, *J* = 7.2 Hz, 2H), 7.97-8.01 (m, 2H), 8.37 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (CD_3OD, 100 MHz) *δ*: 35.5, 70.0, 76.3, 76.7, 88.1, 122.2, 122.9, 126.8, 127.7, 128.9, 135.3, 138.2, 149.8, 155.2, 168.7; HRMS (ESI-TOF) m/z: Calcd. for $C_{34}H_{32}N_6NaO_6$ $[M+Na]^+$: 643.2271; Found: 643.2262.

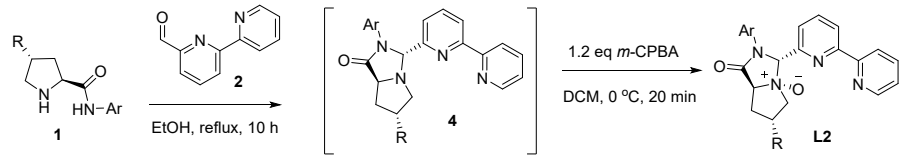


L4a (Prepared according to general procedure A): White solid, M.p. 195.8-196.2 °C, $[\alpha]_D^{20}$ = +6.8 (*c* 0.60, $CHCl_3$); overall yield 37%, >20:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) *δ*: 2.20-2.25 (m, 2H), 2.42-2.59 (m, 6H), 3.83-3.87 (m, 2H), 3.99-4.06 (m, 2H), 4.48-4.51 (m, 2H), 6.76 (s, 2H), 7.14-7.18 (m, 2H), 7.29-7.33 (m, 4H), 7.50-7.57 (m, 8H), 7.72 (d, *J* = 7.2 Hz, 2H), 7.77 (s, 2H); ^{13}C NMR (CD_3OD, 100 MHz) *δ*: 22.4, 24.2, 70.6, 76.4, 88.5, 122.6, 126.6, 128.8, 129.0, 129.1, 131.3, 135.6, 140.6, 167.7; HRMS (ESI-TOF) m/z: Calcd. for $C_{36}H_{34}N_4NaO_4$ $[M+Na]^+$: 609.2472; Found: 609.2467.



L6a (Prepared according to general procedure A): White solid, M.p. 180.6-181.2 °C, $[\alpha]_D^{20}$ = +26.8 (*c* 0.60, $CHCl_3$); overall yield 41%, 12:1 dr; ^1H NMR (CD_3OD, 400 MHz) δ: 2.33-2.39 (m, 2H), 2.48-2.64 (m, 6H), 4.18-4.33 (m, 4H), 4.89-4.93 (m, 2H), 7.21-7.25 (m, 2H), 7.33-7.40 (m, 5H), 7.50-7.59 (m, 8H), 7.84-7.86 (m, 1H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 22.1, 24.3, 69.3, 73.4, 85.7, 121.7, 126.6, 126.7, 129.0, 130.0, 130.8, 131.3, 165.9; HRMS (ESI-TOF) m/z: Calcd. for $C_{30}H_{30}N_4NaO_4$ $[M+Na]^+$: 533.2159; Found: 533.2156.

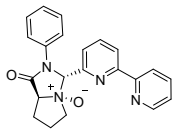
4. General procedure for preparation of chiral bipyridine-NO ligands L2



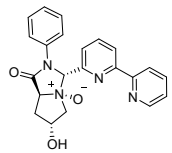
In a sealed tube equipped with a magnetic stirring bar, bipyridine-carbaldehyde **2** (1.0 mmol) and optically pure 4-hydroxyprolinamide or prolinamide **1** (1.2 mmol, 1.2 equiv) were added. Then, anhydrous ethanol (8.0 mL) was added and the reaction was heated with stirring at reflux for 12 h. After completion of the reaction, as indicated by TLC, the aftertreatment residue was purified by flash column chromatography to give the intermediate **4**.

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 **4** was added 3.0 mL of DCM and *m*-CPBA (1.2 eq). The reaction mixture was stirred at 0 °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 bipyridine-NO ligand **L2**.

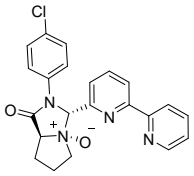
5. Characterization data of bipyridine-NO ligands L2



L2a: White solid, M.p. 181.9-182.2 °C, $[\alpha]_D^{20}$ = -40.9 (*c* 0.60, $CHCl_3$); overall yield 52%, >20:1 dr; ^1H NMR (CD_3OD, 400 MHz) *δ*: 2.23-2.29 (m, 1H), 2.45-2.65 (m, 3H), 3.93-3.97 (m, 1H), 4.18-4.25 (m, 1H), 4.77-4.80 (m, 1H), 6.81 (s, 1H), 7.15-7.20 (m, 1H), 7.27-7.32 (m, 2H), 7.39-7.42 (m, 1H), 7.44-7.47 (m, 2H), 7.68-7.70 (m, 1H), 7.88-7.93 (m, 1H), 7.97-8.00 (m, 1H), 8.34 (d, *J* = 8.0 Hz, 1H), 8.43-8.45 (m, 1H), 8.61-8.63 (m, 1H); ^{13}C NMR (CD_3OD, 100 MHz) *δ*: 22.4, 24.5, 70.9, 76.8, 87.8, 120.9, 121.8, 122.9, 124.3, 126.8, 127.2, 129.0, 135.5, 137.4, 137.9, 148.9, 150.0, 155.0, 155.8, 169.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{22}H_{20}N_4NaO_2$ $[M+Na]^+$: 395.1478; Found: 395.1478.

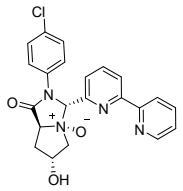


L2b: White solid, M.p. 183.1-183.9 °C, $[\alpha]_D^{20}$ = -113.6 (*c* 0.60, $CHCl_3$); overall yield 50%, >20:1 dr; ^1H NMR (CD_3OD, 400 MHz) *δ*: 2.64-2.71 (m, 1H), 2.85-2.92 (m, 1H), 3.98-4.01 (m, 1H), 4.44-4.48 (m, 1H), 4.66-4.69 (m, 1H), 5.00-5.03 (m, 1H), 6.81 (s, 1H), 7.16-7.20 (m, 1H), 7.27-7.32 (m, 2H), 7.40-7.45 (m, 3H), 7.68-7.70 (m, 1H), 7.89-7.94 (m, 1H), 7.97-8.01 (m, 1H), 8.33-8.36 (m, 1H), 8.44-8.46 (m, 1H), 8.62-8.64 (m, 1H); ^{13}C NMR (CD_3OD, 100 MHz) *δ*: 35.5, 70.0, 76.4, 76.6, 88.2, 120.9, 122.0, 123.0, 124.3, 126.8, 127.4, 128.9, 135.3, 137.4, 138.0, 148.9, 149.5, 155.0, 155.9, 168.7; HRMS (ESI-TOF) m/z: Calcd. for $C_{22}H_{20}N_4NaO_3$ $[M+Na]^+$: 411.1428; Found: 411.1427.

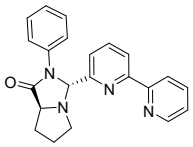


L2c: White solid, M.p. 185.7-186.6 °C, $[\alpha]_D^{20}$ = -87.5 (*c* 0.60, $CHCl_3$); overall yield 52%, >20:1 dr; ^1H NMR (CD_3OD, 400 MHz) *δ*: 2.25-2.30 (m, 1H), 2.46-2.65 (m, 3H), 3.93-3.97 (m, 1H), 4.18-4.25 (m, 1H), 4.76-4.79 (m, 1H), 6.83 (s, 1H), 7.28-7.31 (m, 2H), 7.38-7.42 (m, 1H), 7.47-7.51 (m, 2H), 7.71-7.74 (m, 1H), 7.88-7.92 (m, 1H), 7.99-8.03 (m, 1H), 8.30-8.33 (m, 1H), 8.44-8.46 (m, 1H), 8.61-8.63 (m, 1H); ^{13}C NMR (CD_3OD, 100 MHz) *δ*: 22.4, 24.6, 70.9, 76.7, 87.5, 120.9, 122.0, 124.1, 124.3, 127.3, 129.0, 132.0, 134.3, 137.4, 138.0, 149.0, 149.8, 154.9, 155.9,

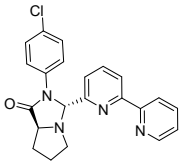
169.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{22}H_{19}ClN_4NaO_2$ $[M+Na]^+$: 429.1089; Found: 429.1095.



L2d: White solid, M.p. 187.6-188.0 °C, $[\alpha]_D^{20}$ = -51.2 (*c* 0.60, $CHCl_3$); overall yield 51%, >20:1 dr; ^1H NMR (CD_3OD, 400 MHz) *δ*: 2.66-2.73 (m, 1H), 2.86-2.92 (m, 1H), 3.98-4.01 (m, 1H), 4.43-4.48 (m, 1H), 4.66-4.70 (m, 1H), 5.00-5.03 (m, 1H), 6.83 (s, 1H), 7.27-7.31 (m, 2H), 7.39-7.42 (m, 1H), 7.44-7.48 (m, 2H), 7.71-7.73 (m, 1H), 7.88-7.92 (m, 1H), 7.99-8.03 (m, 1H), 8.30-8.33 (m, 1H), 8.45-8.47 (m, 1H), 8.62-8.63 (m, 1H); ^{13}C NMR (CD_3OD, 100 MHz) *δ*: 35.5, 70.0, 76.4, 76.5, 87.9, 120.9, 122.1, 124.2, 124.4, 127.5, 129.0, 132.0, 134.1, 137.4, 138.1, 149.0, 149.3, 154.9, 156.0, 168.6; HRMS (ESI-TOF) m/z: Calcd. for $C_{22}H_{19}ClN_4NaO_3$ $[M+Na]^+$: 445.1038; Found: 445.1039.



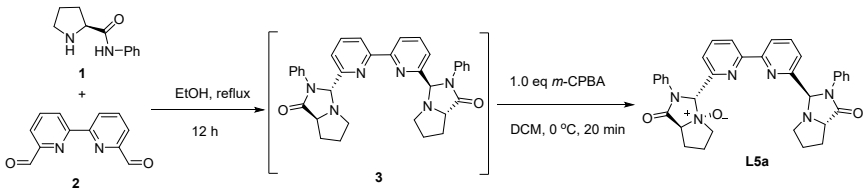
4a: White solid, M.p. 183.9-185.0 °C, $[\alpha]_D^{20}$ = +39.3 (*c* 0.60, $CHCl_3$); yield 81%, >20:1 dr; ^1H NMR (CD_3OD, 400 MHz) *δ*: 1.82-1.90 (m, 1H), 1.91-1.97 (m, 1H), 2.13-2.30 (m, 2H), 3.05-3.12 (m, 1H), 3.44-3.49 (m, 1H), 4.34-4.37 (m, 1H), 6.11 (s, 1H), 7.09-7.13 (m, 1H), 7.25-7.29 (m, 2H), 7.38-7.41 (m, 1H), 7.46-7.49 (m, 3H), 7.87-7.91 (m, 2H), 8.25-8.31 (m, 2H), 8.59-8.61 (m, 1H); ^{13}C NMR (CD_3OD, 100 MHz) *δ*: 24.4, 27.4, 55.8, 65.1, 84.1, 120.3, 121.1, 121.9, 122.6, 124.1, 125.7, 128.7, 137.0, 137.4, 138.3, 148.8, 155.4, 155.6, 157.0, 175.9; HRMS (ESI-TOF) m/z: Calcd. for $C_{22}H_{20}N_4NaO$ $[M+Na]^+$: 379.1529; Found: 379.1532.



4c: White solid, M.p. 186.4-187.9 °C, $[\alpha]_D^{20}$ = +47.0 (*c* 0.60, $CHCl_3$); yield 81%, >20:1 dr; ^1H NMR ($CDCl_3$, 400 MHz) *δ*: 1.79-1.88 (m, 2H), 2.14-2.20 (m, 2H), 2.87-2.93 (m, 1H), 3.41-3.46 (m, 1H), 4.19-4.22 (m, 1H), 5.71 (s, 1H), 7.13-7.16 (m, 2H), 7.19-7.24 (m, 2H), 7.36-7.40 (m, 2H),

7.68-7.75 (m, 2H), 8.21 (d, J = 8.0 Hz, 1H), 8.28-8.30 (m, 1H), 8.55-8.57 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 23.9, 26.7, 55.4, 63.8, 83.3, 119.6, 119.7, 120.3, 121.6, 123.0, 128.0, 129.3, 135.3, 136.0, 137.3, 148.0, 154.4, 155.3, 155.8, 174.5; HRMS (ESI-TOF) m/z: Calcd. for $C_{22}H_{19}ClN_4NaO$ $[M+Na]^+$: 413.1140; Found: 413.1135.

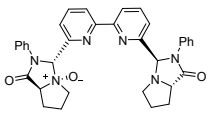
6. General procedure for preparation of chiral ligand L5a



In a sealed tube equipped with a magnetic stirring bar, bipyridine-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 (1.0 eq). The reaction mixture was stirred at 0 °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 **L5a**.

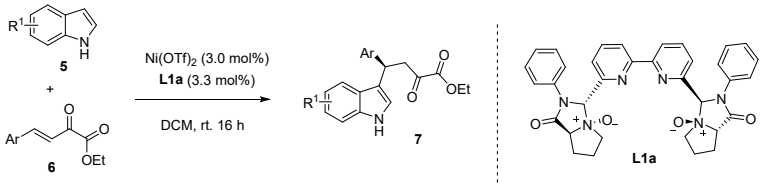
7. Characterization data of chiral ligand L5a



L5a: White solid, M.p. 238.2-238.8 °C, $[\alpha]_D^{20}$ = -56.4 (*c* 0.60, $CHCl_3$); yield 36%, 12:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 1.84-1.87 (m, 1H), 1.92-1.96 (m, 1H), 2.13-2.28 (m, 3H), 2.46-2.61 (m, 3H), 3.03-3.09 (m, 1H), 3.41-3.47 (m, 1H), 3.91-3.95 (m, 1H), 4.16-4.21 (m, 1H), 4.29-4.32 (m, 1H), 4.72 (d, *J* = 8.8 Hz, 1H), 6.10 (s, 1H), 6.77 (s, 1H), 7.06-7.10 (m, 1H), 7.13-7.17 (m, 1H), 7.22-7.28 (m, 4H), 7.40-7.50 (m, 5H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.87-7.91 (m, 1H), 7.93-7.97 (m,

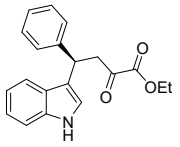
1H), 8.24 (d, J = 8.0 Hz, 1H), 8.36 (d, J = 8.0 Hz, 1H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 22.4, 24.4, 24.5, 27.4, 55.7, 65.0, 70.9, 76.8, 84.1, 87.8, 120.2, 121.9, 122.2, 122.5, 123.0, 125.6, 126.8, 127.3, 128.6, 128.9, 135.4, 137.1, 137.9, 138.5, 150.0, 154.9, 155.5, 157.2, 169.4, 175.8; HRMS (ESI-TOF) m/z: Calcd. for $C_{34}H_{32}N_6NaO_3$ $[M+Na]^+$: 595.2481; Found: 595.2492.

8. Catalytic asymmetric synthesis of compounds 7

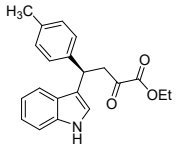


In a sealed tube equipped with a magnetic stirring bar, to the mixture of $Ni(OTf)_2$ (3.0 mol %), **L1a** (3.3 mol %) in 3.0 mL of CH_2Cl_2 was added **5** (0.30 mmol), and **6** (0.20 mmol). The reaction mixture was stirred at room temperature for 16 h and was directly loaded onto a silica gel and purified by flash chromatography to give the desired product **7**, using hexane/EtOAc (10/1, v/v) as the eluent.

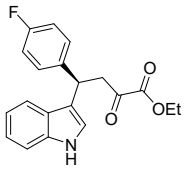
9. Characterization data of compounds 7



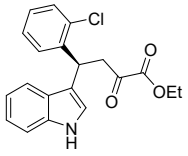
7a: Product in accordance with literature characterization data[1]. Light yellow solid, M.p. 94.6-95.2 ^{o}C, 93% yield, 99% ee, $[\alpha]_D^{20}$ = -26.0 (c 0.71, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IA column (95/5 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 30.64 min; τ_{minor} = 39.17 min); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.16-1.20 (m, 3H), 3.48-3.63 (m, 2H), 4.09-4.15 (m, 2H), 4.81-4.85 (m, 1H), 6.91-6.96 (m, 2H), 7.04-7.11 (m, 2H), 7.16-7.26 (m, 5H), 7.34 (d, J = 8.0 Hz, 1H), 7.97 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 12.9, 36.8, 44.6, 61.5, 110.2, 118.3, 118.4, 121.2, 125.5, 126.7, 127.5, 135.5, 142.2, 159.9, 192.1.



7b: Product in accordance with literature characterization data[1]. Light yellow solid, M.p. 111.7-112.2 °C, 85% yield, 94% ee, $[\alpha]_D^{20}$ = -76.0 (*c* 0.57, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IA column (90/10 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 14.98 min; τ_{minor} = 19.82 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.15-1.19 (m, 3H), 2.19 (s, 3H), 3.45-3.60 (m, 2H), 4.08-4.14 (m, 2H), 4.77-4.81 (m, 1H), 6.88-6.99 (m, 4H), 7.03-7.07 (m, 1H), 7.11 (s, 1H), 7.13 (d, *J* = 3.2 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.94 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 12.8, 19.9, 36.4, 44.7, 61.4, 110.1, 118.3, 118.4, 121.1, 126.6, 128.2, 135.0, 135.5, 139.2, 160.0, 192.3.

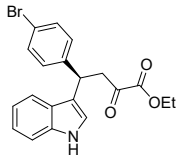


7c: Light yellow solid, M.p. 109.7-110.3 °C, 85% yield, 94% ee, $[\alpha]_D^{20}$ = -23.0 (*c* 0.51, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IA column (90/10 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 15.28 min; τ_{minor} = 22.12 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.17-1.21 (m, 3H), 3.45-3.60 (m, 2H), 4.11-4.16 (m, 2H), 4.79-4.83 (m, 1H), 6.83-6.87 (m, 3H), 6.90-6.96 (m, 1H), 7.05-7.09 (m, 1H), 7.17-7.23 (m, 3H), 7.29 (d, *J* = 8.0 Hz, 1H), 8.01 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 12.8, 36.0, 44.6, 61.5, 110.2, 114.3 (d, J_{CF} = 21.3 Hz), 117.0, 118.3 (d, J_{CF} = 28.0 Hz), 120.5, 121.3, 125.2, 128.2 (d, J_{CF} = 8.3 Hz), 135.6, 137.9, 138.0, 159.9, 160.6 (d, J_{CF} = 243.3 Hz), 192.0; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{18}FNNaO_3$ $[M+Na]^+$: 362.1163; Found: 362.1158.

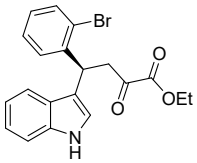


7d: Product in accordance with literature characterization data[1]. Light yellow solid, M.p. 110.5-111.1 °C, 92% yield, 97% ee, $[\alpha]_D^{20}$ = -21.1 (*c* 0.40, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IB column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 27.59 min; τ_{minor} = 34.96 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.17-1.21 (m, 3H), 3.36-3.42 (m, 1H), 3.59-3.65 (m, 1H), 4.12-4.18 (m, 1H), 5.34-5.37 (m, 1H), 6.92-6.96 (m, 2H), 7.00-

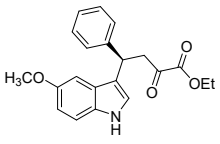
7.12 (m, 4H), 7.19 (d, J = 8.4 Hz, 1H), 7.27-7.30 (m, 1H), 7.35 (d, J = 8.4 Hz, 1H), 8.02 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 12.9, 33.2, 43.6, 61.5, 110.2, 115.7, 118.3, 118.5, 121.2, 121.3, 125.4, 126.0, 126.9, 128.0, 128.7, 132.4, 135.5, 139.5, 159.9, 191.8.



7e: Product in accordance with literature characterization data[1]. Light yellow solid, M.p. 103.6-104.2 °C, 93% yield, 99% ee, $[\alpha]_D^{20}$ = -28.2 (c 0.60, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IB column (90/10 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 23.16 min; τ_{minor} = 12.46 min); ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.21-1.24 (m, 3H), 3.55-3.62 (m, 1H), 3.70-3.76 (m, 1H), 4.16-4.21 (m, 2H), 4.70-4.73 (m, 1H), 6.89-6.92 (m, 1H), 7.02-7.06 (m, 1H), 7.30-7.44 (m, 7H), 10.94 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 14.2, 36.9, 45.1, 62.3, 111.9, 117.1, 118.9, 119.0, 119.5, 121.6, 122.6, 126.5, 130.4, 131.5, 136.9, 144.4, 161.0, 193.0.

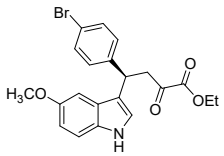


7f: Light yellow solid, M.p. 91.7-92.9 °C, 90% yield, 97% ee, $[\alpha]_D^{20}$ = -25.7 (c 0.30, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IB column (90/10 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 15.01 min; τ_{minor} = 18.49 min); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.19-1.22 (m, 3H), 3.34-3.40 (m, 1H), 3.59-3.65 (m, 1H), 4.14-4.19 (m, 2H), 5.32-5.36 (m, 1H), 6.93-6.98 (m, 3H), 7.04-7.12 (m, 3H), 7.22 (d, J = 8.0 Hz, 1H), 7.36 (d, J = 7.6 Hz, 1H), 7.48-7.51 (m, 1H), 8.01 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 12.9, 36.0, 43.7, 61.5, 110.2, 115.9, 118.4, 118.6, 121.1, 121.4, 123.2, 125.5, 126.7, 127.2, 128.2, 132.0, 135.5, 141.1, 159.9, 191.6; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{18}BrNNaO_3$ $[M+Na]^+$: 422.0362; Found: 422.0362.

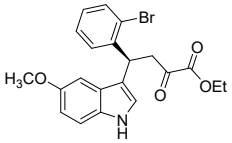


7g: Product in accordance with literature characterization data[1]. Light yellow solid, M.p. 87.9-

88.7 °C, 90% yield, 95% ee, $[\alpha]_D^{20}$ = -51.3 (*c* 0.60, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IE column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 32.24 min; τ_{minor} = 39.12 min); ^{1}H NMR (DMSO-d_6, 400 MHz) *δ*: 1.19-1.23 (m, 3H), 3.53-3.60 (m, 1H), 3.64-3.75 (m, 4H), 4.15-4.20 (m, 2H), 4.67-4.71 (m, 1H), 6.68-6.71 (m, 1H), 6.86 (d, *J* = 2.4 Hz, 1H), 7.11-7.15 (m, 1H), 7.20-7.26 (m, 4H), 7.36 (d, *J* = 7.2 Hz, 2H), 10.74 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) *δ*: 14.2, 37.5, 45.4, 55.8, 62.3, 101.2, 111.4, 112.5, 117.4, 123.2, 126.5, 127.0, 128.1, 128.7, 132.0, 144.8, 153.4, 161.1, 193.3.

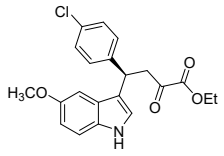


7h: Light yellow solid, M.p. 103.8-104.6 °C, 93% yield, 96% ee, $[\alpha]_D^{20}$ = -46.0 (*c* 0.27, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IF column (97/3 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 42.95 min; τ_{minor} = 59.98 min); ^{1}H NMR (DMSO-d_6, 400 MHz) *δ*: 1.21-1.24 (m, 3H), 3.54-3.60 (m, 1H), 3.66-3.75 (m, 4H), 4.16-4.22 (m, 2H), 4.65-4.69 (m, 1H), 6.69-6.72 (m, 1H), 6.86 (d, *J* = 2.4 Hz, 1H), 7.21-7.23 (m, 2H), 7.32-7.34 (m, 2H), 7.41-7.45 (m, 2H), 10.77 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) *δ*: 14.2, 36.8, 45.1, 55.8, 62.3, 101.2, 111.5, 112.6, 116.9, 119.5, 123.3, 126.8, 130.4, 131.5, 132.0, 144.3, 153.4, 161.0, 193.1; HRMS (ESI-TOF) m/z: Calcd. for $C_{21}H_{20}BrNNaO_4$ $[M+Na]^+$: 452.0468; Found: 452.0474.

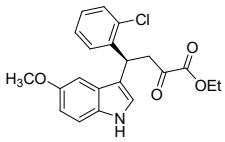


7i: Light yellow solid, M.p. 101.7-102.9 °C, 93% yield, 92% ee, $[\alpha]_D^{20}$ = -40.3 (*c* 0.35, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak ID column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 9.84 min; τ_{minor} = 14.91 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.18-1.22 (m, 3H), 3.33-3.39 (m, 1H), 3.57-3.63 (m, 1H), 3.67 (s, 3H), 4.13-4.19 (m, 2H), 5.26-5.30 (m, 1H), 6.70-6.73 (m, 1H), 6.82 (d, *J* = 2.4 Hz, 1H), 6.91-6.96 (m, 2H), 7.04-7.12 (m, 3H), 7.47-7.49 (m, 1H), 7.97 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 12.6, 35.6, 43.5, 54.5, 61.3, 100.0, 110.6, 111.1, 115.5, 121.4, 122.9, 125.6, 126.5, 126.9, 127.9, 130.3, 131.7, 140.9, 152.6, 159.6, 191.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{21}H_{20}BrNNaO_4$ $[M+Na]^+$: 452.0468;

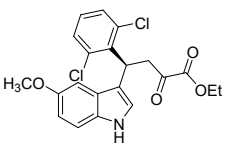
Found: 452.0464.



7j: Light yellow solid, M.p. 90.9-91.6 °C, 92% yield, 91% ee, $[\alpha]_D^{20}$ = -34.1 (*c* 0.40, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak ID column (90/10 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 14.46 min; τ_{minor} = 21.64 min); ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.21-1.24 (m, 3H), 3.54-3.60 (m, 1H), 3.66-3.75 (m, 4H), 4.16-4.22 (m, 2H), 4.67-4.70 (m, 1H), 6.69-6.72 (m, 1H), 6.86 (d, *J* = 2.4 Hz, 1H), 6.69-6.72 (m, 1H), 6.86 (d, *J* = 2.4 Hz, 1H), 7.21-7.23 (m, 2H), 7.29-7.31 (m, 2H), 7.38-7.41 (m, 2H), 10.77 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 14.2, 36.8, 45.1, 55.8, 62.3, 101.2, 111.5, 112.5, 117.0, 123.3, 126.8, 128.6, 130.0, 131.0, 132.0, 143.9, 153.4, 161.0, 193.1; HRMS (ESI-TOF) m/z: Calcd. for $C_{21}H_{20}ClNNaO_4$ $[M+Na]^+$: 408.0973; Found: 408.0973.

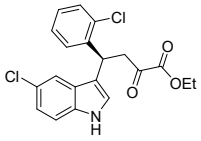


7k: Light yellow solid, M.p. 89.9-90.6 °C, 93% yield, 92% ee, $[\alpha]_D^{20}$ = -36.1 (*c* 0.24, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak ID column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 9.59 min; τ_{minor} = 13.82 min); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.19-1.22 (m, 3H), 3.36-3.42 (m, 1H), 3.59-3.65 (m, 1H), 3.67 (s, 3H), 4.14-4.19 (m, 1H), 5.29-5.32 (m, 1H), 6.71-6.73 (m, 1H), 6.81 (d, *J* = 2.4 Hz, 1H), 6.92 (d, *J* = 2.4 Hz, 1H), 7.02-7.04 (m, 2H), 7.10-7.14 (m, 2H), 7.28-7.30 (m, 1H), 7.93 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 12.9, 33.1, 43.5, 54.7, 61.5, 100.2, 110.9, 111.4, 121.6, 125.9, 126.1, 126.9, 128.0, 128.7, 130.6, 132.4, 139.5, 152.9, 159.9, 191.7; HRMS (ESI-TOF) m/z: Calcd. for $C_{21}H_{20}ClNNaO_4$ $[M+Na]^+$: 408.0973; Found: 408.0973.

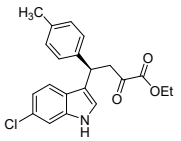


7l: Light yellow solid, M.p. 91.3-92.2 °C, 87% yield, 95% ee, $[\alpha]_D^{20}$ = -50.2 (*c* 0.27, $CHCl_3$);

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} = 10.91 min; τ_{minor} = 18.15 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.20-1.23 (m, 3H), 3.35-3.41 (m, 1H), 3.58-3.65 (m, 1H), 3.69 (s, 3H), 4.15-4.20 (m, 2H), 5.32-5.35 (m, 1H), 6.72-6.77 (m, 2H), 6.92-6.98 (m, 2H), 7.03-7.05 (m, 1H), 7.11 (d, *J* = 8.8 Hz, 1H), 7.21-7.23 (m, 1H), 7.97 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 12.7, 33.8, 43.1, 54.6, 61.4, 99.9, 110.7, 111.3, 115.0, 121.5, 125.5, 125.9, 126.1, 127.5, 130.4, 130.5, 132.1, 141.8, 152.8, 159.6, 191.2; HRMS (ESI-TOF) m/z: Calcd. for $C_{21}H_{19}Cl_2NNaO_4$ $[M+Na]^+$: 442.0583; Found: 442.0586.

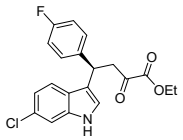


7m: Light yellow solid, M.p. 111.3-112.9 °C, 93% yield, 92% ee, $[\alpha]_D^{20}$ = -39.2 (*c* 0.31, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IC column (97/3 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 16.49 min; τ_{minor} = 18.34 min); ^{1}H NMR (DMSO-d_6, 400 MHz) *δ*: 1.22-1.25 (m, 3H), 3.49-3.55 (m, 1H), 3.77-3.83 (m, 1H), 4.18-4.24 (m, 2H), 5.18-5.22 (m, 1H), 6.95-6.98 (m, 1H), 7.17-7.24 (m, 2H), 7.33-7.44 (m, 5H), 11.14 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) *δ*: 19.0, 38.3, 49.3, 67.1, 116.4, 121.4, 124.2, 124.9, 129.3, 130.1, 131.3, 132.6, 133.2, 134.4, 134.6, 137.6, 141.9, 146.2, 165.5, 197.3; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{17}Cl_2NNaO_3$ $[M+Na]^+$: 412.0478; Found: 412.0477.

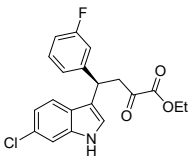


7n: Light yellow solid, M.p. 98.1-99.5 °C, 89% yield, 91% ee, $[\alpha]_D^{20}$ = -30.2 (*c* 0.19, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IC column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 19.28 min; τ_{minor} = 17.69 min); ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 1.18-1.22 (m, 3H), 2.20 (s, 3H), 3.43-3.59 (m, 2H), 4.12-4.17 (m, 2H), 4.73-4.77 (m, 1H), 6.88-6.93 (m, 2H), 6.98 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 8.0 Hz, 2H), 7.17-7.20 (m, 2H), 7.98 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 11.8, 18.9, 35.2, 43.5, 60.5, 109.0, 118.1, 118.2, 120.0, 125.5, 127.2, 134.2, 134.8, 137.9, 158.9, 191.0; HRMS (ESI-TOF) m/z: Calcd. for

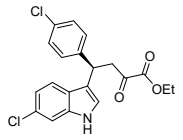
$C_{21}H_{20}ClNNaO_3$ $[M+Na]^+$: 392.1024; Found: 392.1027.



7o: Light yellow solid, M.p. 100.6-101.9 °C, 88% yield, 90% ee, $[\alpha]_D^{20}$ = -37.5 (*c* 0.17, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IE column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 15.85 min; τ_{minor} = 14.34 min); ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.21-1.25 (m, 3H), 3.54-3.60 (m, 1H), 3.69-3.76 (m, 1H), 4.17-4.22 (m, 2H), 4.70-4.74 (m, 1H), 6.92-6.94 (m, 1H), 7.04-7.09 (m, 2H), 7.36-7.40 (m, 5H), 11.08 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 19.0, 41.2, 50.1, 67.0, 116.3, 120.1 (d, J_{CF} = 21.0 Hz), 122.6, 123.9, 125.2, 128.5, 130.1, 131.2, 134.6 (d, J_{CF} = 7.8 Hz), 142.0, 145.6, 165.7, 165.9 (d, J_{CF} = 240.1 Hz), 197.7; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{17}ClFNNaO_3$ $[M+Na]^+$: 396.0773; Found: 396.0780.

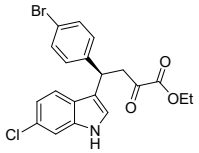


7p: Light yellow solid, M.p. 101.6-102.7 °C, 92% yield, 91% ee, $[\alpha]_D^{20}$ = -41.2 (*c* 0.32, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IC column (97/3 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 17.17 min; τ_{minor} = 14.59 min); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.20-1.23 (m, 3H), 3.44-3.50 (m, 1H), 3.54-3.60 (m, 1H), 4.14-4.20 (m, 2H), 4.77-4.81 (m, 1H), 6.77-6.82 (m, 1H), 6.87-6.96 (m, 3H), 7.01 (d, J = 8.0 Hz, 1H), 7.12-7.23 (m, 3H), 8.06 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 12.9, 36.2, 44.3, 61.7, 110.2, 112.7 (d, J_{CF} = 21.2 Hz), 113.6 (d, J_{CF} = 20.2 Hz), 116.8, 119.1, 119.4, 121.1, 122.4, 123.8, 127.4, 129.0 (d, J_{CF} = 8.1 Hz), 135.9, 144.6, 144.7, 159.8, 161.9 (d, J_{CF} = 241.3 Hz), 191.6; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{17}ClFNNaO_3$ $[M+Na]^+$: 396.0773; Found: 396.0770.

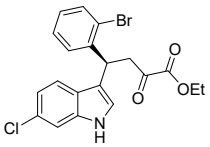


7q: Light yellow solid, M.p. 102.4-103.5 °C, 89% yield, 91% ee, $[\alpha]_D^{20}$ = -43.3 (*c* 0.47, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IE column (95/5 hexane/*i*-PrOH; flow

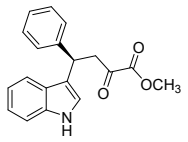
rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 17.26 min; τ_{minor} = 15.02 min); ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.22-1.25 (m, 3H), 3.55-3.62 (m, 1H), 3.70-3.77 (m, 1H), 4.17-4.23 (m, 2H), 4.70-4.74 (m, 1H), 6.92-6.95 (m, 1H), 7.29 (d, J = 8.4 Hz, 2H), 7.36-7.40 (m, 5H), 11.10 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 19.0, 41.3, 49.9, 67.1, 116.3, 122.3, 124.0, 125.1, 128.6, 130.1, 131.2, 133.4, 134.8, 135.9, 142.0, 148.4, 165.6, 197.6; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{17}Cl_2NNaO_3$ $[M+Na]^+$: 396.0773; Found: 396.0780.



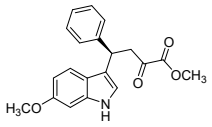
7r: Light yellow solid, M.p. 107.1-108.9 °C, 92% yield, 91% ee, $[\alpha]_D^{20}$ = -21.0 (*c* 0.15, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IE column (95/5 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 19.41 min; τ_{minor} = 16.46 min); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.22-1.25 (m, 3H), 3.55-3.62 (m, 1H), 3.70-3.76 (m, 1H), 4.17-4.22 (m, 2H), 4.68-4.72 (m, 1H), 6.92-6.95 (m, 1H), 7.30-7.44 (m, 7H), 11.10 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 14.2, 36.6, 45.1, 62.3, 111.5, 117.5, 119.3, 119.6, 120.4, 123.8, 125.3, 126.5, 130.4, 131.6, 137.2, 144.1, 160.9, 192.8; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{17}BrClNNaO_3$ $[M+Na]^+$: 455.9973; Found: 455.9978.



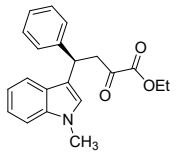
7s: Light yellow solid, M.p. 110.7-111.6 °C, 89% yield, 97% ee, $[\alpha]_D^{20}$ = -17.2 (*c* 0.20, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IC column (97/3 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 14.39 min; τ_{minor} = 16.20 min); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.20-1.24 (m, 3H), 3.32-3.38 (m, 1H), 3.56-3.63 (m, 1H), 4.16-4.21 (m, 2H), 5.27-5.31 (m, 1H), 6.89-6.99 (m, 3H), 7.05-7.07 (m, 2H), 7.19-7.24 (m, 2H), 7.48-7.50 (m, 1H), 8.10 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 12.9, 35.8, 43.6, 61.7, 110.1, 116.1, 119.2, 119.3, 121.7, 123.1, 124.0, 126.7, 127.3, 127.4, 128.0, 132.1, 135.8, 140.8, 159.9, 191.6; HRMS (ESI-TOF) m/z: Calcd. for $C_{20}H_{17}BrClNNaO_3$ $[M+Na]^+$: 455.9973; Found: 455.9971.



7t: Product in accordance with literature characterization data[1]. Light yellow solid, M.p. 101.7-102.5 °C, 89% yield, 90% ee, $[\alpha]_D^{20}$ = -23.0 (*c* 0.15, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IC column (90/10 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 9.50 min; τ_{minor} = 8.82 min); ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.55-3.61 (m, 1H), 3.70-3.76 (m, 4H), 4.69-4.73 (m, 1H), 6.87-6.91 (m, 1H), 7.00-7.04 (m, 1H), 7.10-7.15 (m, 1H), 7.22-7.39 (m, 7H), 10.89 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 37.4, 45.5, 53.1, 111.9, 117.7, 118.8, 119.1, 121.5, 122.5, 126.5, 126.6, 128.1, 128.7, 136.8, 144.9, 161.4, 192.8.



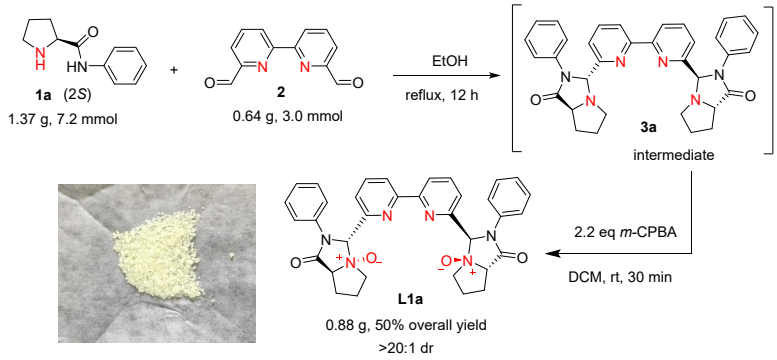
7u: Product in accordance with literature characterization data[1]. Light yellow solid, M.p. 121.3-122.8 °C, 90% yield, 94% ee, $[\alpha]_D^{20}$ = -23.5 (*c* 0.25, $CHCl_3$); The ee was determined by HPLC analysis using a Chiralpak IC column (97/3 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 25.10 min; τ_{minor} = 20.79 min); ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.54-3.61 (m, 1H), 3.67-3.76 (m, 7H), 4.66-4.70 (m, 1H), 6.68-6.71 (m, 1H), 6.85 (d, *J* = 1.2 Hz, 1H), 7.11-7.15 (m, 1H), 7.20-7.26 (m, 4H), 7.36 (d, *J* = 7.6 Hz, 2H), 10.73 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 37.4, 45.4, 53.1, 55.8, 101.2, 111.4, 112.5, 117.4, 123.2, 126.5, 127.0, 128.1, 128.7, 132.0, 144.8, 153.3, 161.5, 192.8.



7w: Product in accordance with literature characterization data[1]. Light yellow solid, M.p. 80.0-81.7 °C, 68% yield, 52% ee, $[\alpha]_D^{20}$ = -15.6 (*c* 4.0, $CHCl_3$); 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} = 15.67 min; τ_{minor} = 14.84 min); ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.20-1.24 (m, 3H), 3.55-3.61 (m, 1H), 3.67-3.74 (m, 4H), 4.16-4.21 (m, 2H), 4.70-4.73 (m, 1H), 6.91-6.95 (m, 1H), 7.08-7.15 (m, 2H), 7.22-7.26 (m, 3H), 7.33-7.36 (m, 3H), 7.41 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (DMSO-

d_6, 100 MHz) δ: 14.2, 32.8, 37.3, 45.4, 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, 160.9, 193.0.

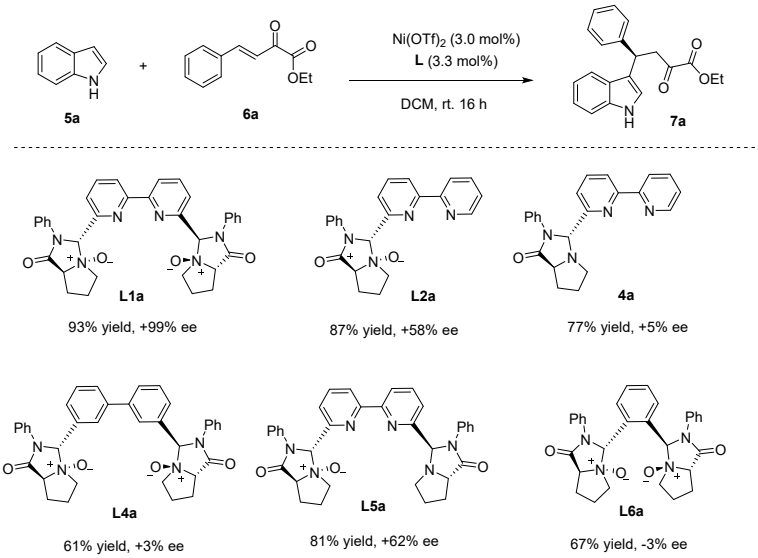
10. The gram scale synthesis of the bipyridine-2NO ligand L1a



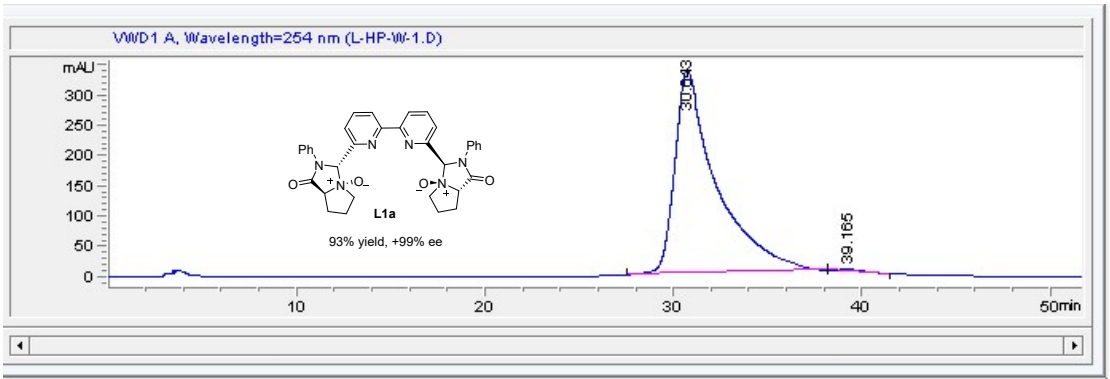
In a sealed tube equipped with a magnetic stirring bar, bipyridine-dicarbaldehyde **2** (0.64 g, 3.0 mmol) and optically pure prolinamide **1a** (1.37 g, 7.2 mmol) were added. Then, anhydrous ethanol (30.0 mL) was added and the reaction was heated with stirring at reflux for 12 h. After completion of 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 °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 bipyridine-2NO ligand **L1a** (0.88 g, 50% overall yield, >20:1 dr).

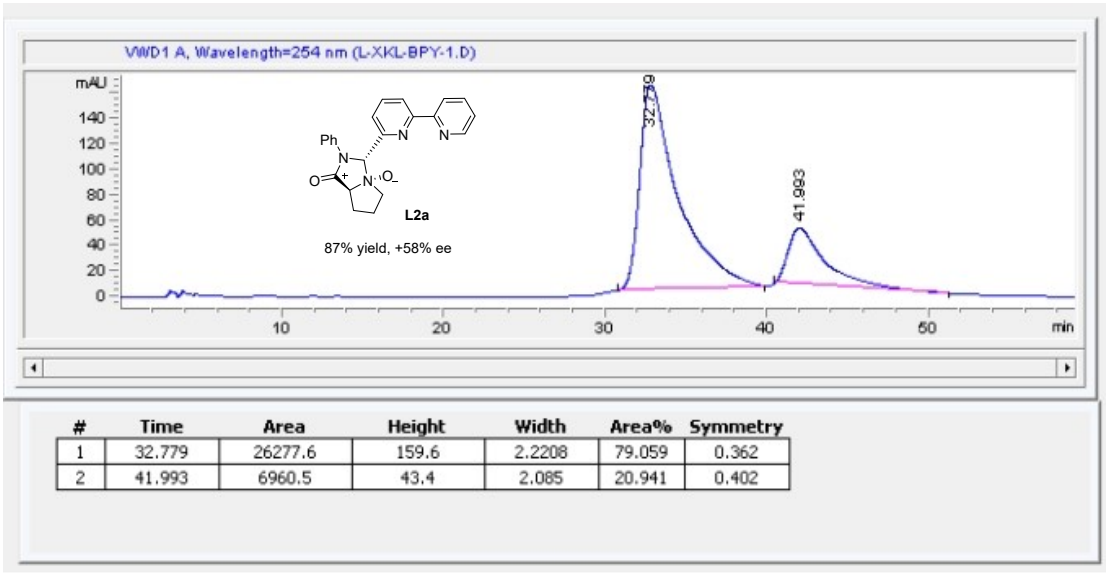
11. Control experiments and HPLC spectra for compound 7a



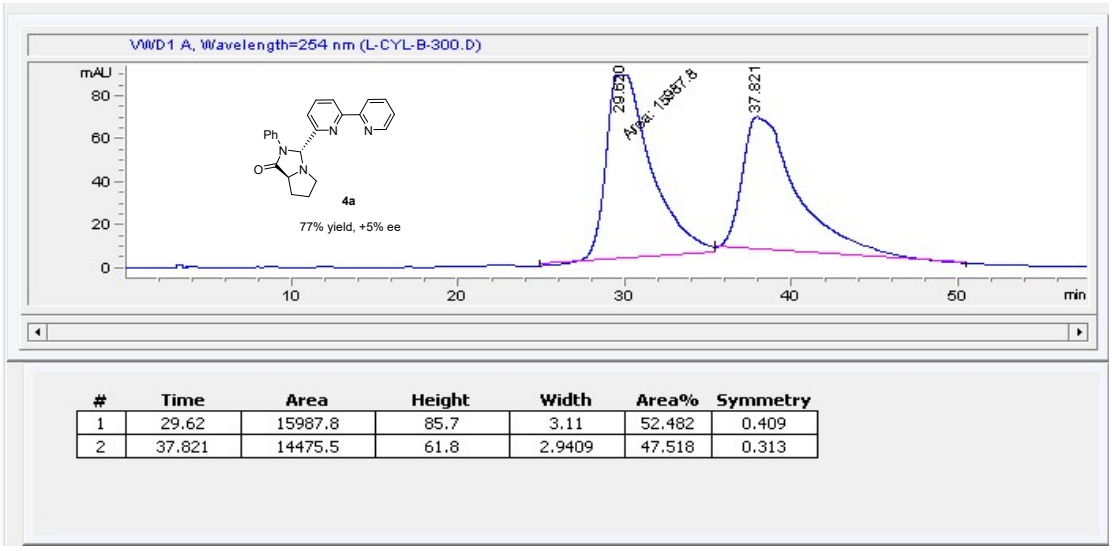
In a sealed tube equipped with a magnetic stirring bar, to the mixture of $Ni(OTf)_2$ (3.0 mol %), **L** (3.3 mol %) in 3.0 mL of CH_2Cl_2 was added **5** (0.30 mmol), and **6** (0.20 mmol). The reaction mixture was stirred at room temperature for 16 h and was directly loaded onto a silica gel and purified by flash chromatography to give the desired product **7a**, using hexane/EtOAc (10/1, v/v) as the eluent.



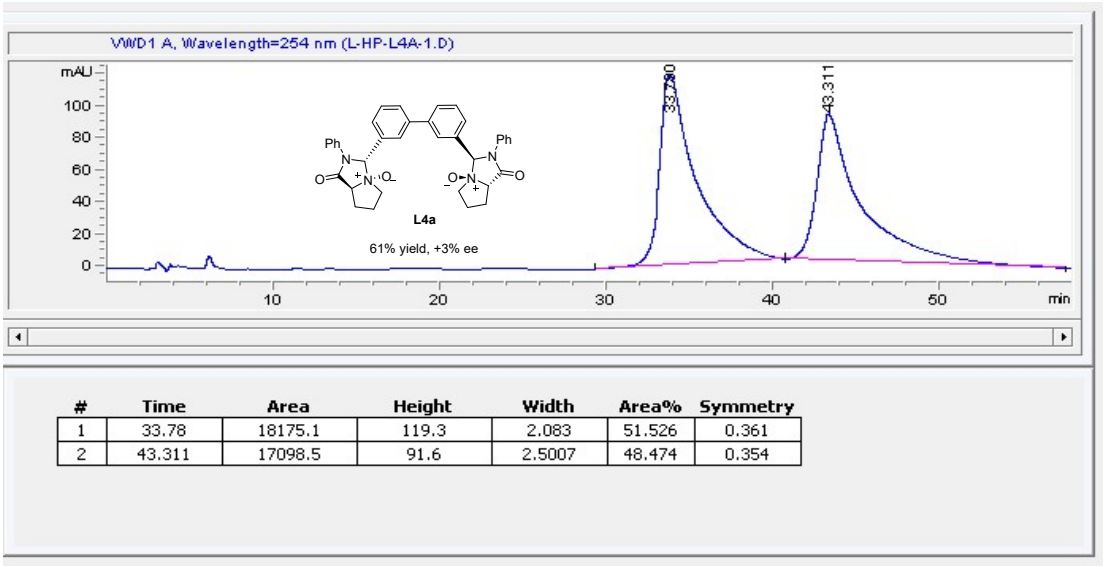
#	Time	Area	Height	Width	Area%	Symmetry
1	30.643	52184.3	335.8	2.0832	99.455	0.373
2	39.165	286.2	3.3	1.0783	0.545	0.49



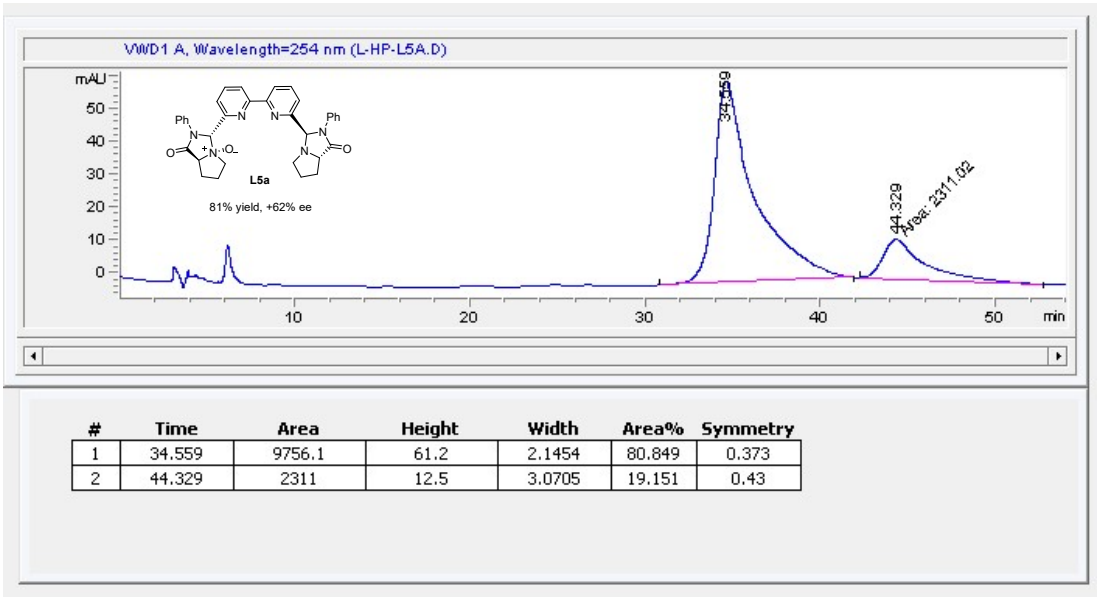
#	Time	Area	Height	Width	Area%	Symmetry
1	32.779	26277.6	159.6	2.2208	79.059	0.362
2	41.993	6960.5	43.4	2.085	20.941	0.402



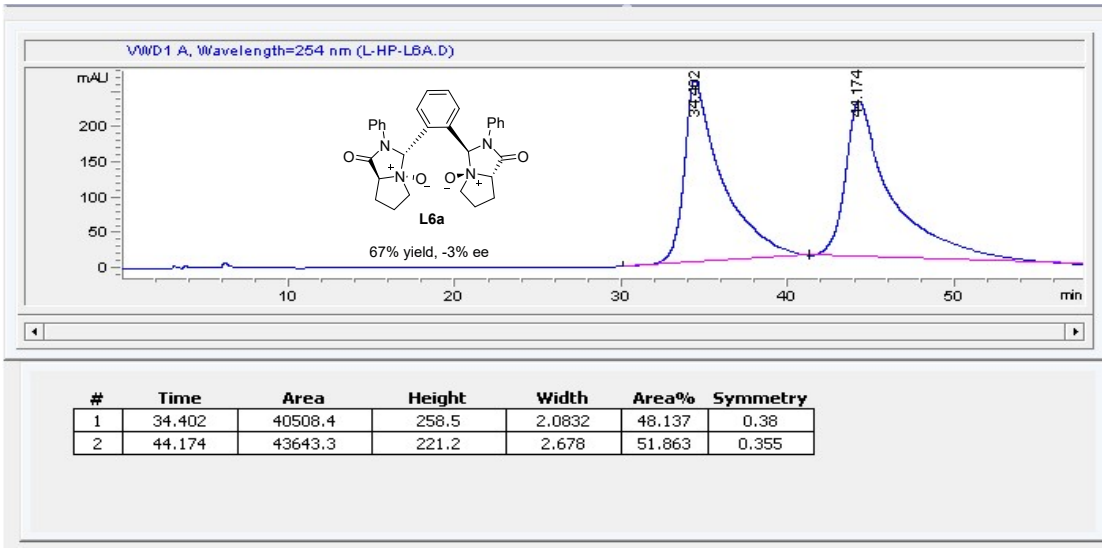
#	Time	Area	Height	Width	Area%	Symmetry
1	29.62	15987.8	85.7	3.11	52.482	0.409
2	37.821	14475.5	61.8	2.9409	47.518	0.313



#	Time	Area	Height	Width	Area%	Symmetry
1	33.78	18175.1	119.3	2.083	51.526	0.361
2	43.311	17098.5	91.6	2.5007	48.474	0.354



#	Time	Area	Height	Width	Area%	Symmetry
1	34.559	9756.1	61.2	2.1454	80.849	0.373
2	44.329	2311	12.5	3.0705	19.151	0.43

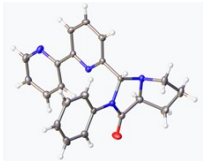


#	Time	Area	Height	Width	Area%	Symmetry
1	34.402	40508.4	258.5	2.0832	48.137	0.38
2	44.174	43643.3	221.2	2.678	51.863	0.355

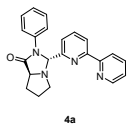
12. References

1 *(a)* Y. Liu, D. Shang, X. Zhou, Y. Zhu, L. Lin, X. Liu and X. Feng, $AgAsF_6/Sm(OTf)_3$ promoted reversal of enantioselectivity for the asymmetric Friedel-Crafts alkylations of indoles with *β*,*γ*-unsaturated α-ketoesters, *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, Enantioselective Friedel-Crafts alkylation of indoles with *β*,*γ*-unsaturated α-ketoesters catalysed by new copper(I) catalysts, *J. Org. Chem.*, 2023, **88**, 3046-3053; *(c)* V. Juste-Navarro, E. Marqués-López and R. P. Herrera, Thiourea-catalyzed addition of indoles to aliphatic *β*,*γ*-unsaturated *α*-ketoesters, *Asian J. Org. Chem.*, 2015, **4**, 884-889.

13. X-ray crystal data for compounds 4a, 4c and 7e



CCDC 2295226

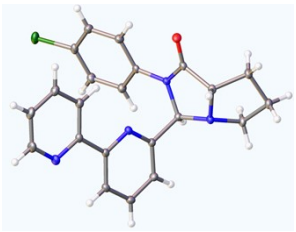


4a

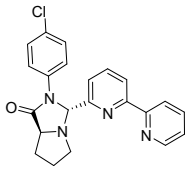
Table S1 Crystal data and structure refinement for 4a

Identification code	**4a**
Empirical formula	$C_{22}H_{20}N_4O$
Formula weight	356.42
Temperature/K	126(10)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å, b/Å, c/Å	6.83171(10), 16.1053(2), 16.2446(2)
α/°, β/°, γ/°,	90, 90, 90
Volume/Å^3	1787.34(4)
Z	4
ρ_{calc}g/cm^3	1.325
μ/mm^{-1}	0.668
F(000)	752.0
Radiation	Cu Kα (λ = 1.54184)
Crystal size/mm^3	0.15 × 0.13 × 0.11
2Θ range for data collection/°	7.73 to 154.122
Index ranges	-8 ≤ h ≤ 6, -20 ≤ k ≤ 17, -20 ≤ l ≤ 20
Reflections collected	15544
Independent reflections	3620 [R_{int} = 0.0266, R_{sigma} = 0.0133]
Data/restraints/parameters	3620/0/245
Goodness-of-fit on F^2	1.063
Final R indexes [I>=2σ (I)]	R_1 = 0.0283, wR_2 = 0.0711
Final R indexes [all data]	R_1 = 0.0285, wR_2 = 0.0712
Largest diff. peak/hole / e Å^{-3}	0.18/-0.15
Flack parameter	0.04(11)/-0.01(5)

Crystal Data for $C_{22}H_{20}N_4O$ (*M* =356.42 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), *a* = 6.83171(10) Å, *b* = 16.1053(2) Å, *c* = 16.2446(2) Å, *V* = 1787.34(4) Å^3, *Z* = 4, *T* = 126(10) K, μ(Cu Kα) = 0.668 mm^{-1}, *Dcalc* = 1.325 g/cm^3, 15544 reflections measured (7.73° ≤ 2Θ ≤ 154.122°), 3620 unique (R_{int} = 0.0266, R_{sigma} = 0.0133) which were used in all calculations. The final R_1 was 0.0283 (I > 2σ(I)) and wR_2 was 0.0712 (all data).



CCDC 2288367

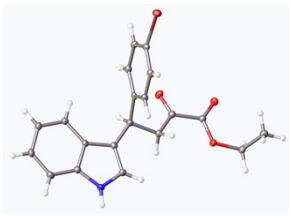


4c

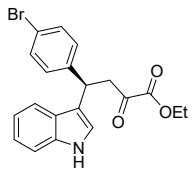
Table S2 Crystal data and structure refinement for 4c

Identification code	**4c**
Empirical formula	$C_{22}H_{19}ClN_4O$
Formula weight	390.86
Temperature/K	120.01(11)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å, b/Å, c/Å	6.01670(10), 16.8651(2), 18.0753(2)
α/°, β/°, γ/°,	90, 90, 90
Volume/Å^3	1834.14(4)
Z	4
ρ_{calc}g/cm^3	1.415
μ/mm^{-1}	2.012
F(000)	816.0
Radiation	Cu Kα (λ = 1.54184)
Crystal size/mm^3	0.15 × 0.1 × 0.08
2Θ range for data collection/°	7.168 to 148.652
Index ranges	-3 ≤ h ≤ 7, -21 ≤ k ≤ 20, -22 ≤ l ≤ 22
Reflections collected	9702
Independent reflections	3654 [R_{int} = 0.0319, R_{sigma} = 0.0346]
Data/restraints/parameters	3654/0/253
Goodness-of-fit on F^2	1.042
Final R indexes [I>=2σ (I)]	R_1 = 0.0288, wR_2 = 0.0754
Final R indexes [all data]	R_1 = 0.0301, wR_2 = 0.0763
Largest diff. peak/hole / e Å^{-3}	0.20/-0.26
Flack parameter	0.018(7)/0.014(70)

Crystal Data for $C_{22}H_{19}ClN_4O$ (*M* =390.86 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), *a* = 6.01670(10) Å, *b* = 16.8651(2) Å, *c* = 18.0753(2) Å, *V* = 1834.14(4) Å^3, *Z* = 4, *T* = 120.01(11) K, μ(Cu Kα) = 2.012 mm^{-1}, *Dcalc* = 1.415 g/cm^3, 9702 reflections measured (7.168° ≤ 2Θ ≤ 148.652°), 3654 unique (R_{int} = 0.0319, R_{sigma} = 0.0346) which were used in all calculations. The final R_1 was 0.0288 (I > 2σ(I)) and wR_2 was 0.0763 (all data).



CCDC 2292424



7e

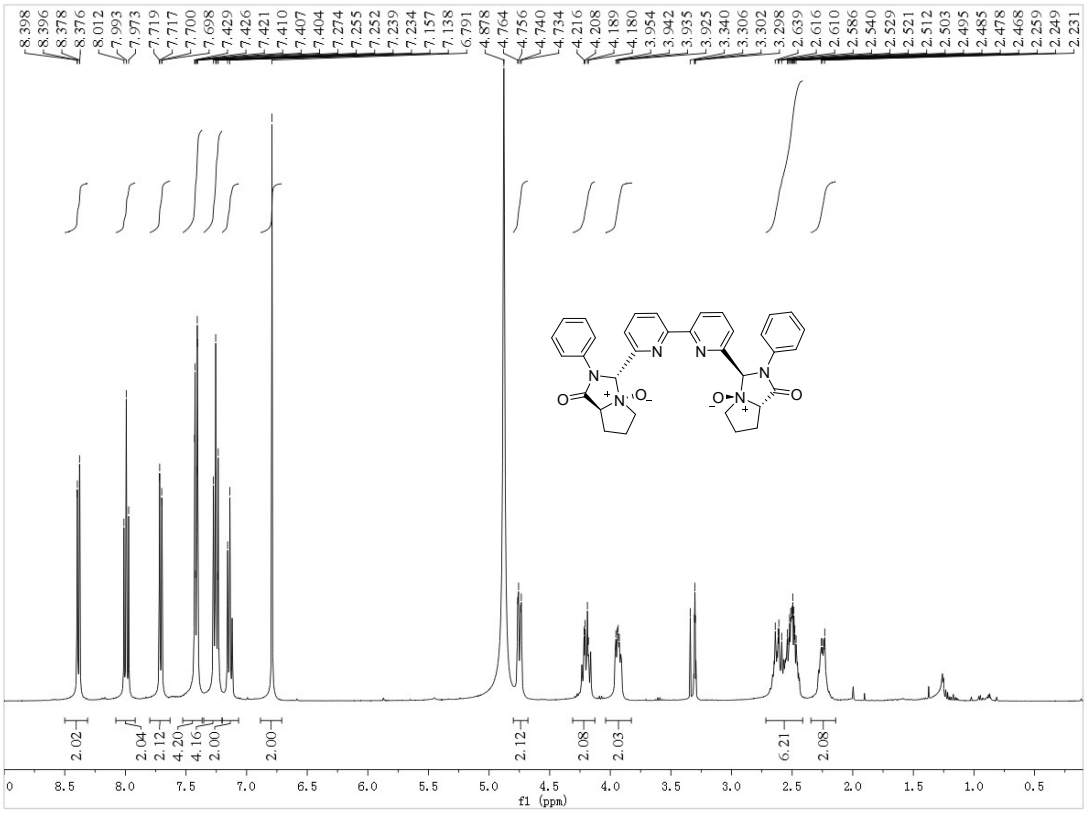
Table S3 Crystal data and structure refinement for 7e

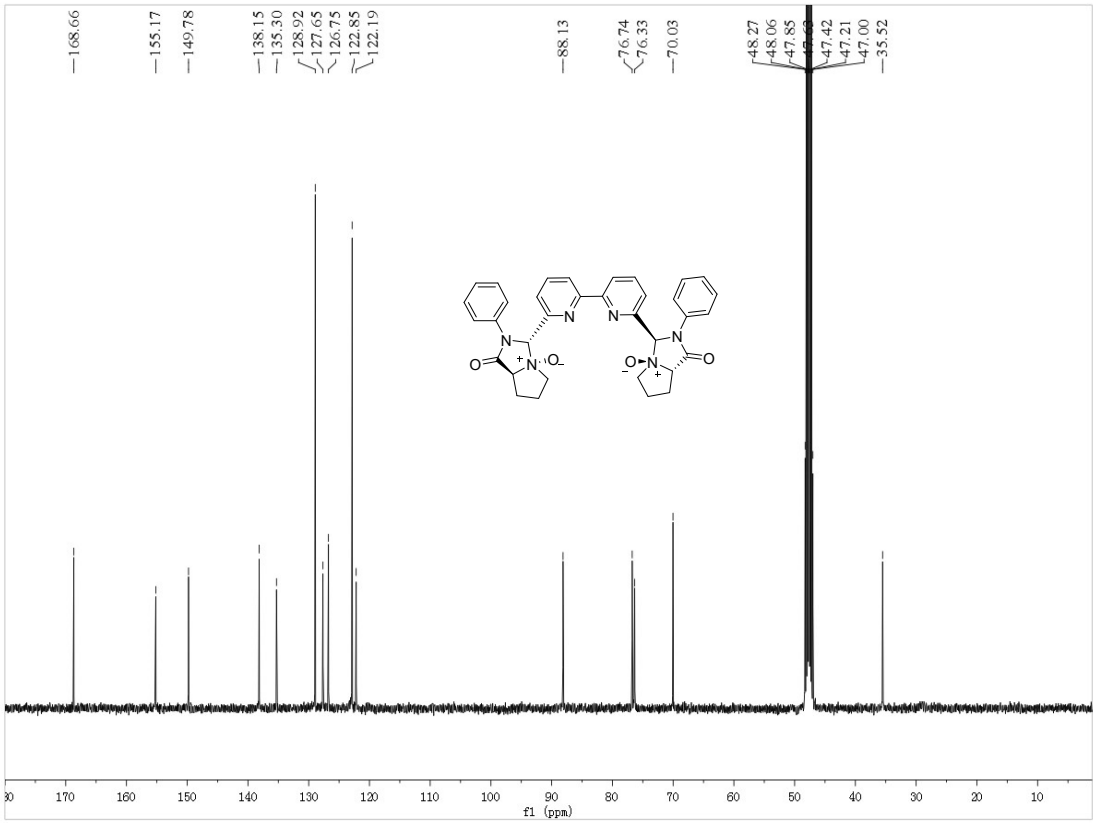
Identification code	**7e**
Empirical formula	$C_{20}H_{18}BrNO_3$
Formula weight	400.26
Temperature/K	99.99(10)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å, b/Å, c/Å	9.49786(7), 12.22987(9), 14.93872(11)
α/°, β/°, γ/°,	90, 90, 90
Volume/Å^3	1735.25(2)
Z	4
ρ_{calc}g/cm^3	1.532
μ/mm^{-1}	3.387
F(000)	816.0
Radiation	Cu Kα (λ = 1.54184)
Crystal size/mm^3	0.15 × 0.12 × 0.11
2Θ range for data collection/°	9.346 to 143.776
Index ranges	-8 ≤ h ≤ 11, -15 ≤ k ≤ 14, -17 ≤ l ≤ 18
Reflections collected	8067
Independent reflections	3324 [R_{int} = 0.0191, R_{sigma} = 0.0217]
Data/restraints/parameters	3324/5/231
Goodness-of-fit on F^2	1.063
Final R indexes [I>=2σ (I)]	R_1 = 0.0209, wR_2 = 0.0560
Final R indexes [all data]	R_1 = 0.0211, wR_2 = 0.0561
Largest diff. peak/hole / e Å^{-3}	0.40/-0.36
Flack parameter	-0.015(6)/-0.006(5)

Crystal Data for $C_{20}H_{18}BrNO_3$ (*M* =400.26 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), *a* = 9.49786(7) Å, *b* = 12.22987(9) Å, *c* = 14.93872(11) Å, *V* = 1735.25(2) Å^3, *Z* = 4, *T* = 99.99(10) K, μ(Cu Kα) = 3.387 mm^{-1}, *Dcalc* = 1.532 g/cm^3, 8067 reflections measured (9.346° ≤ 2Θ ≤ 143.776°), 3324 unique (R_{int} = 0.0191, R_{sigma} = 0.0217) which were used in all calculations. The final R_1 was 0.0209 (I > 2σ(I)) and wR_2 was 0.0561 (all data).

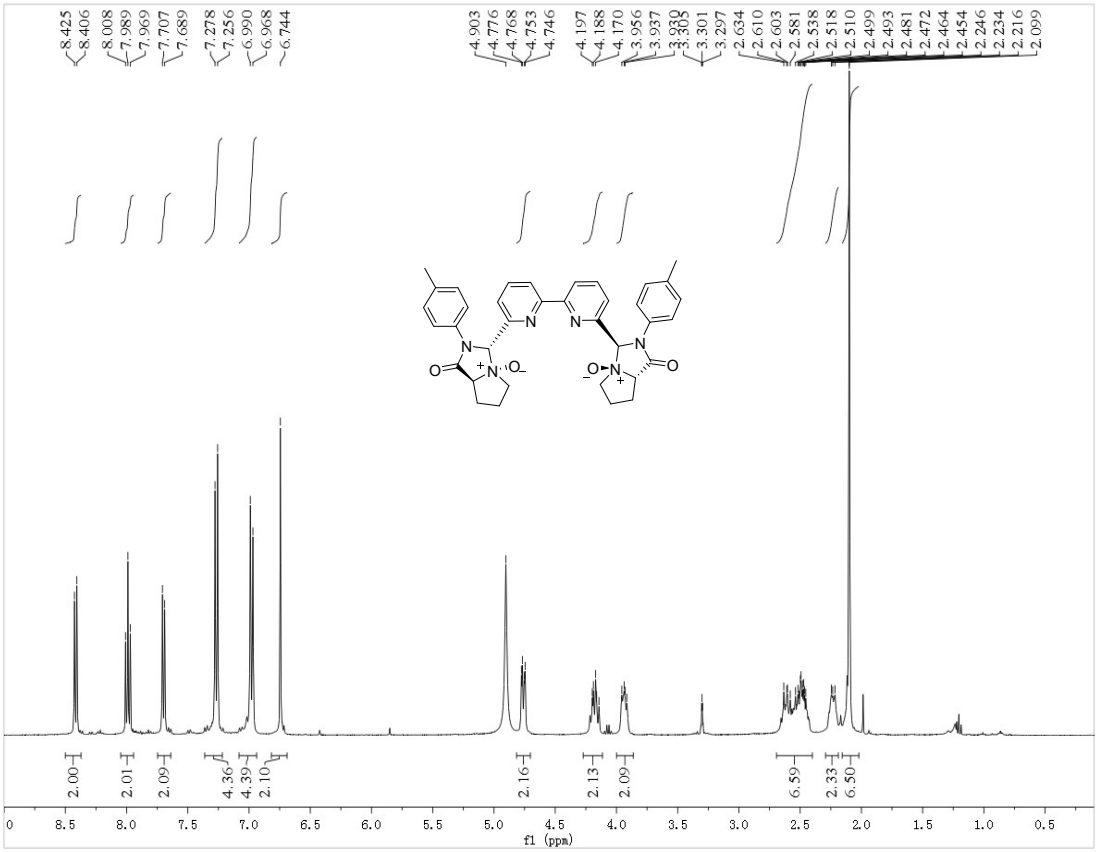
14. The copies of ^{1}H NMR, ^{13}C NMR and HPLC spectra for compounds L, 4 and 7

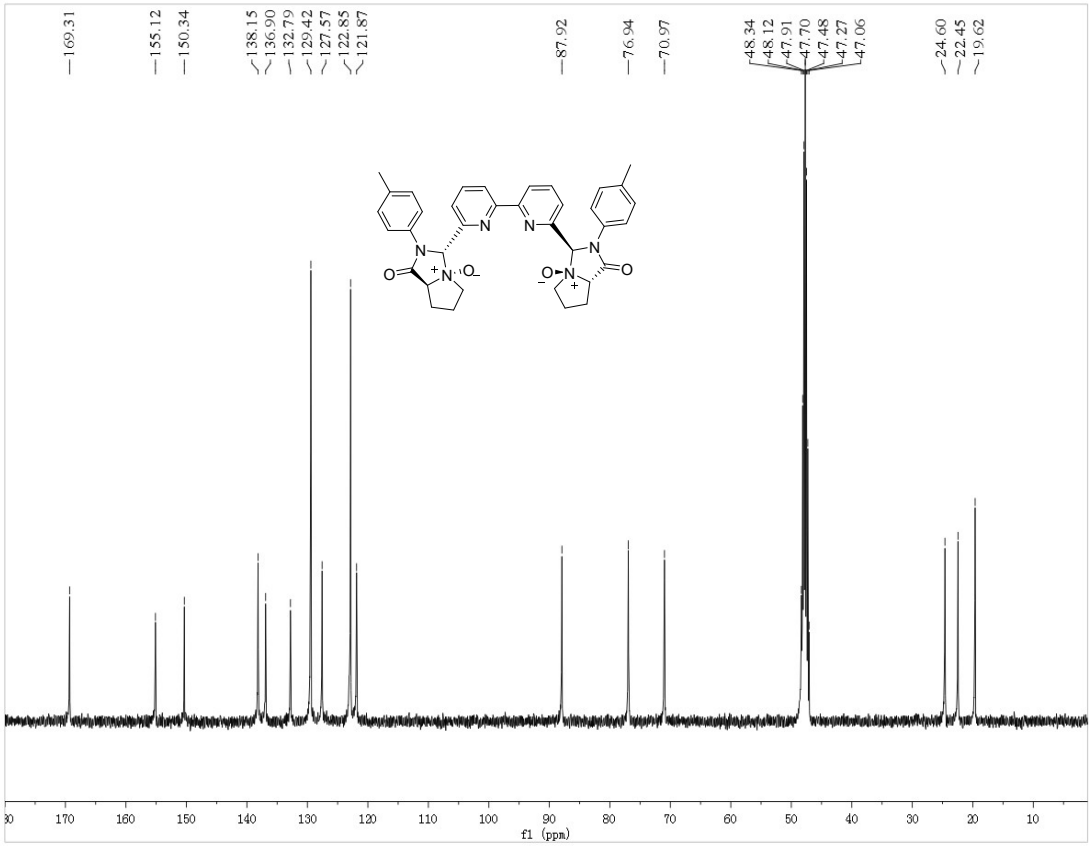
^{1}H and ^{13}C NMR of L1a



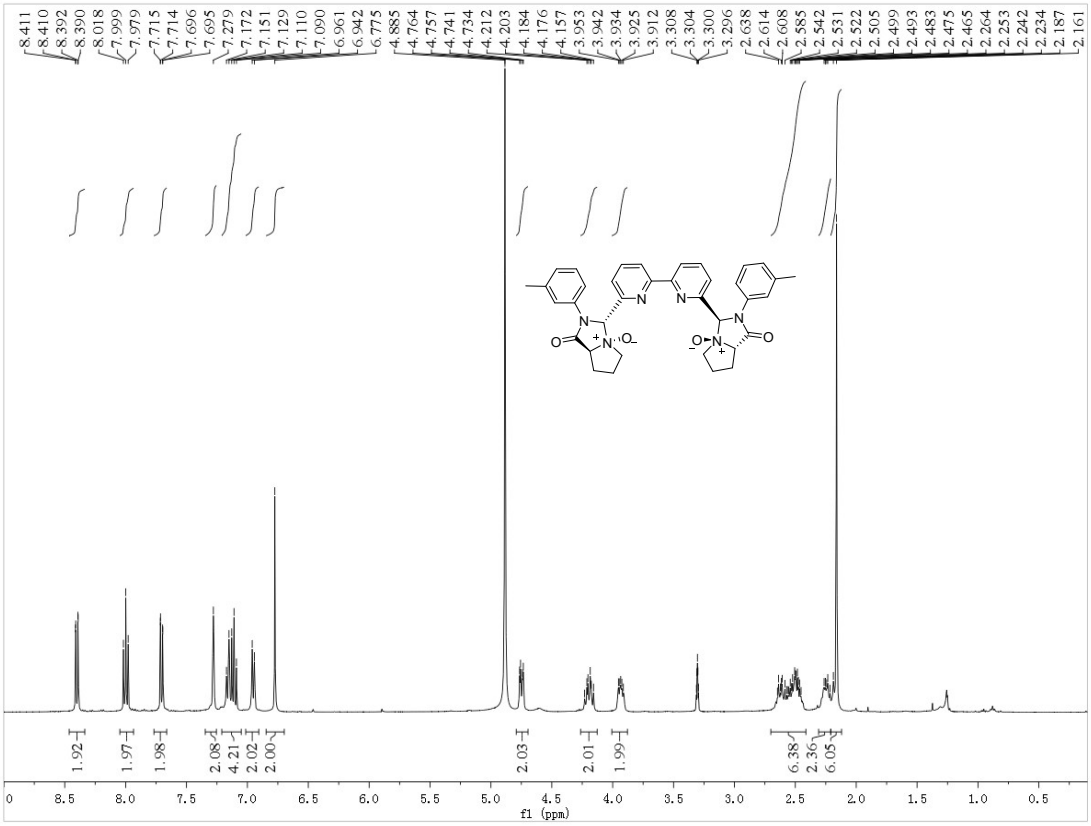


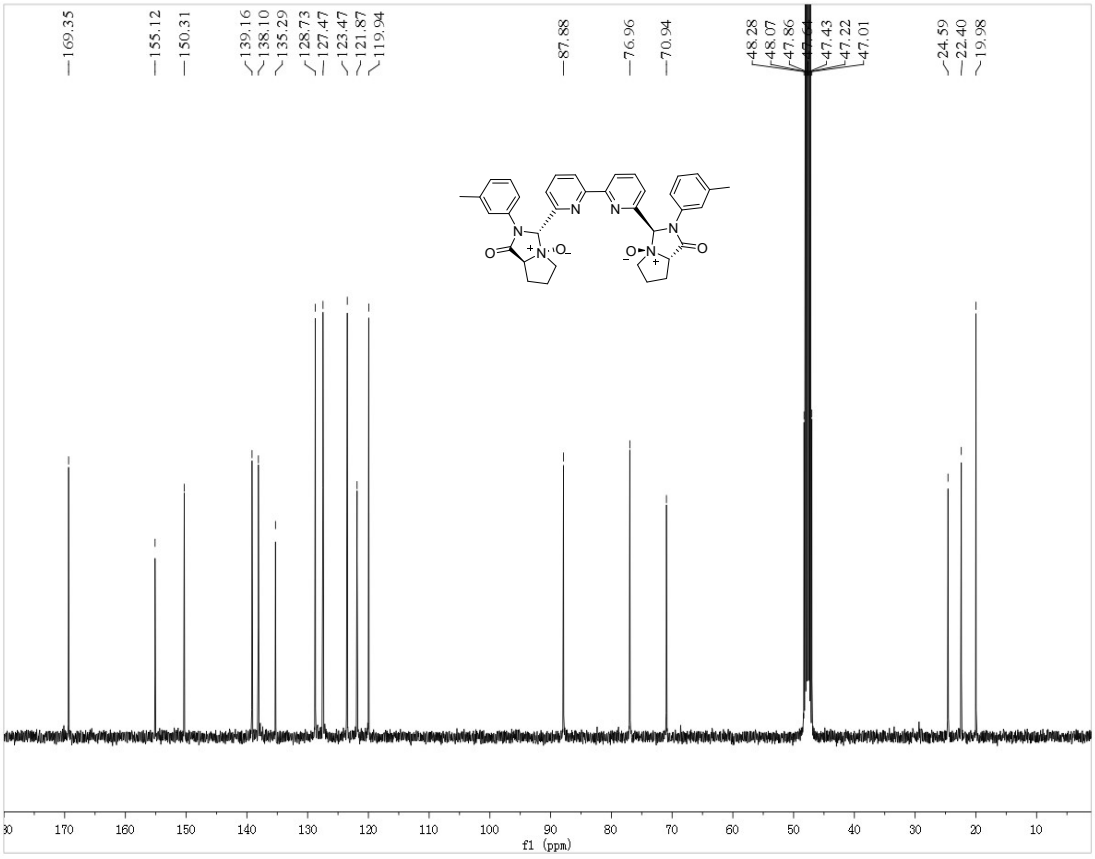
^{1}H and ^{13}C NMR of L1b



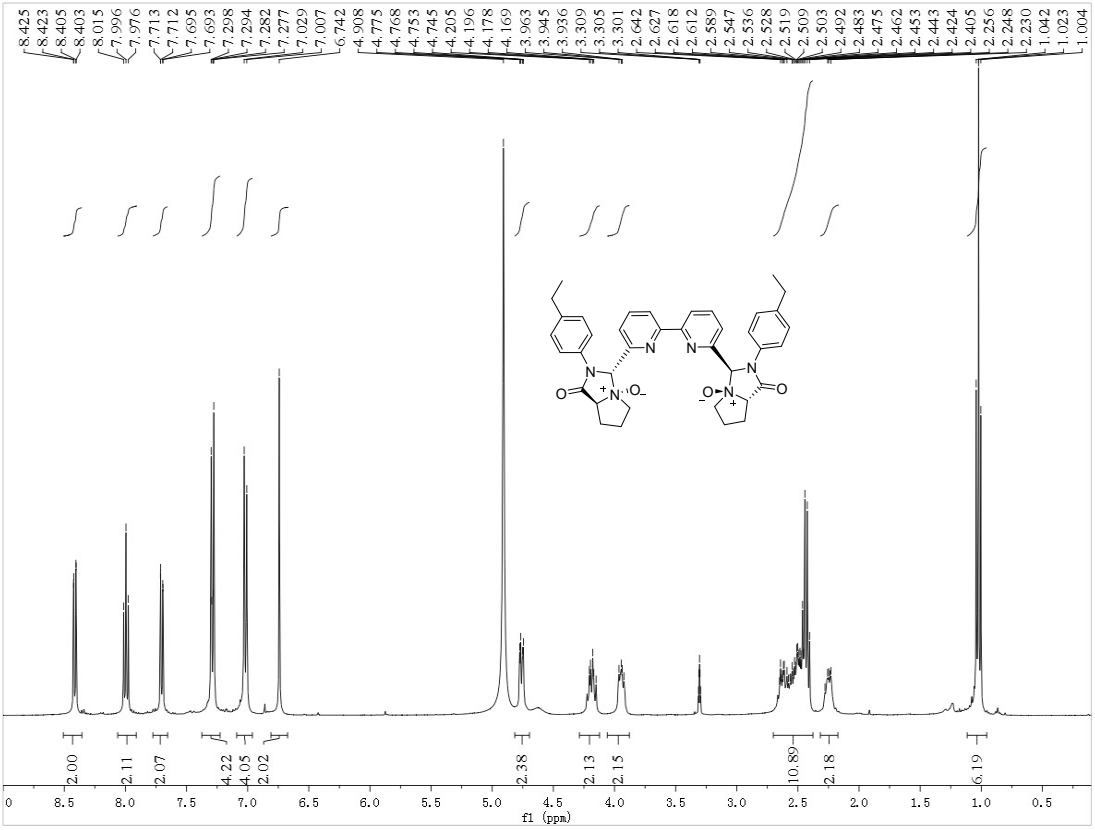


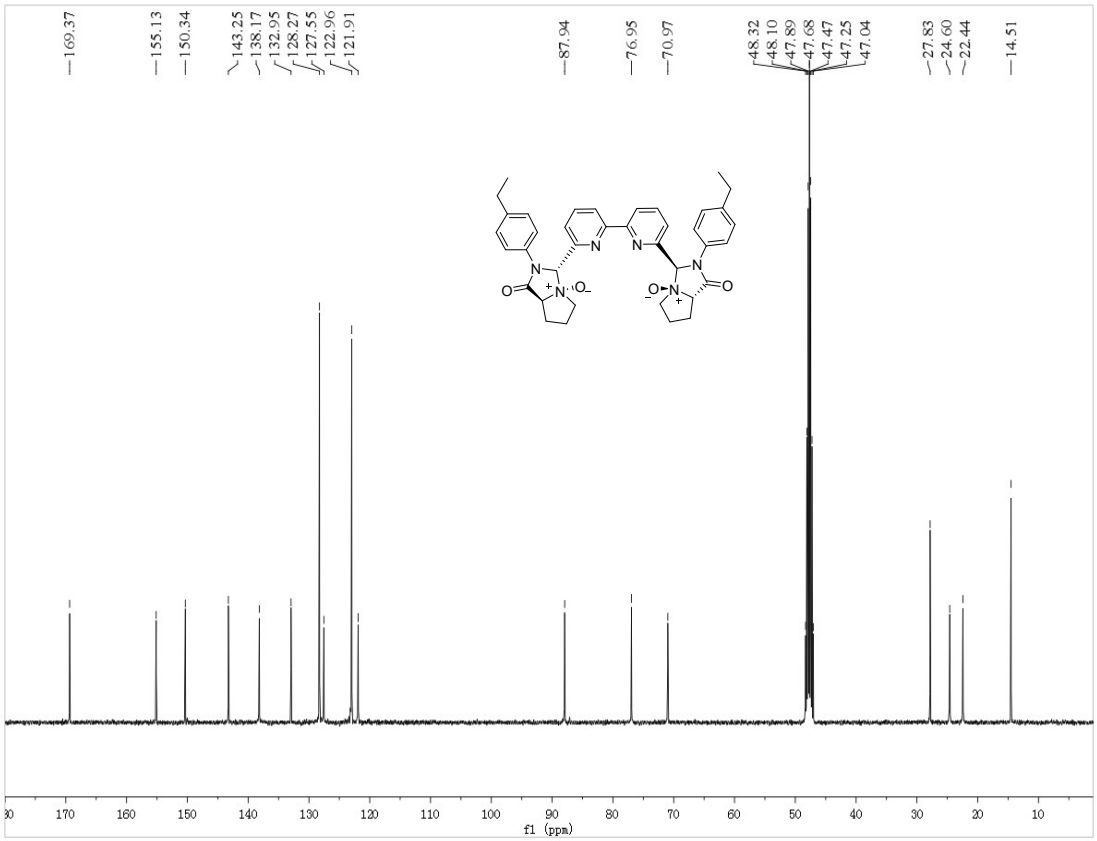
^{1}H and ^{13}C NMR of L1c



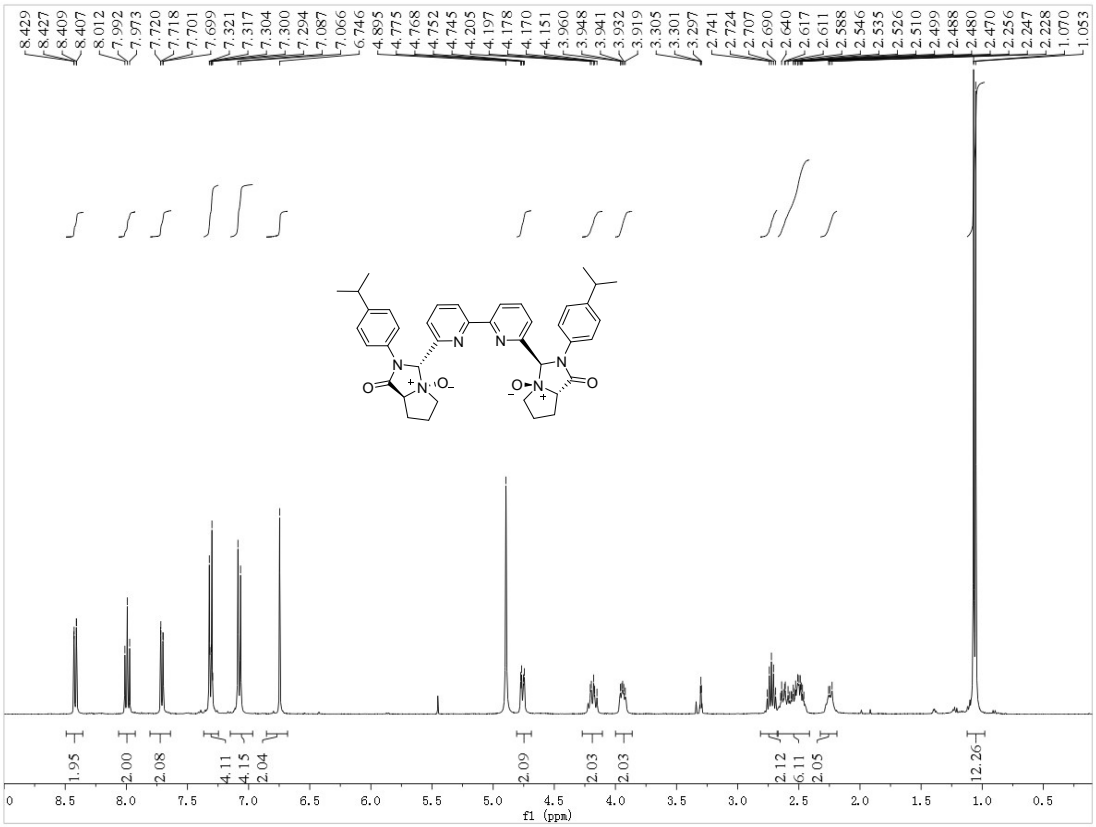


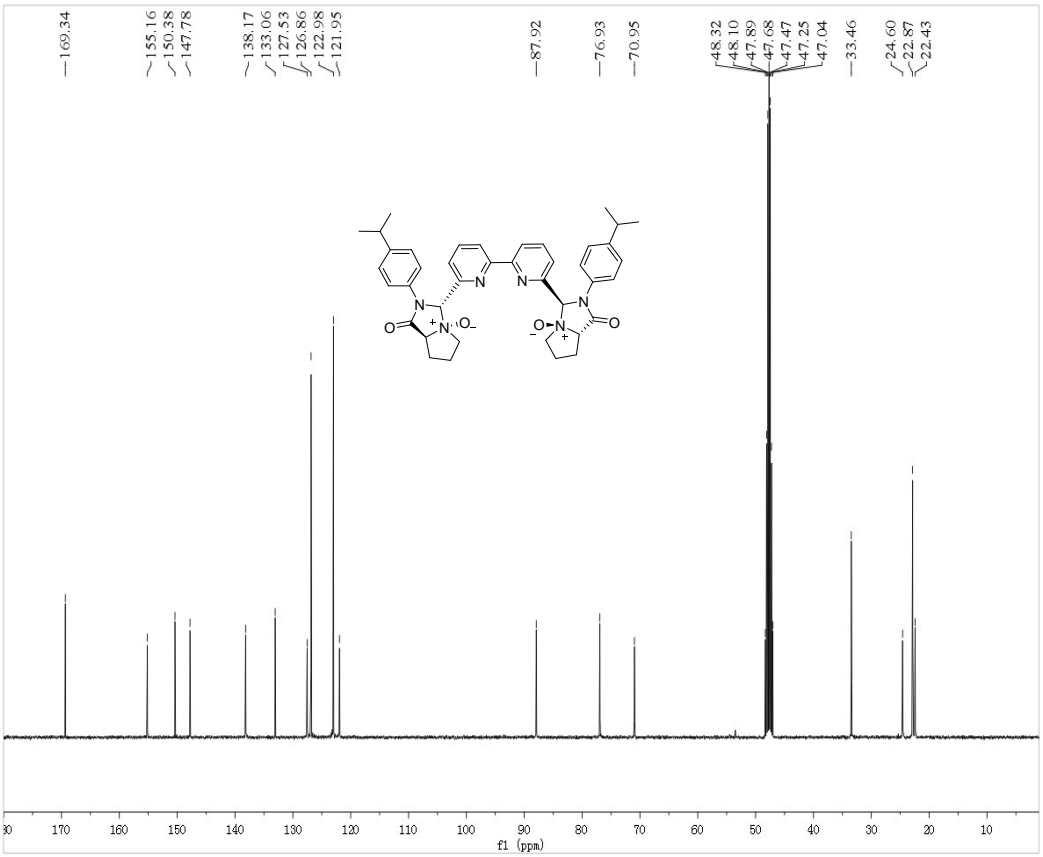
^{1}H and ^{13}C NMR of L1d



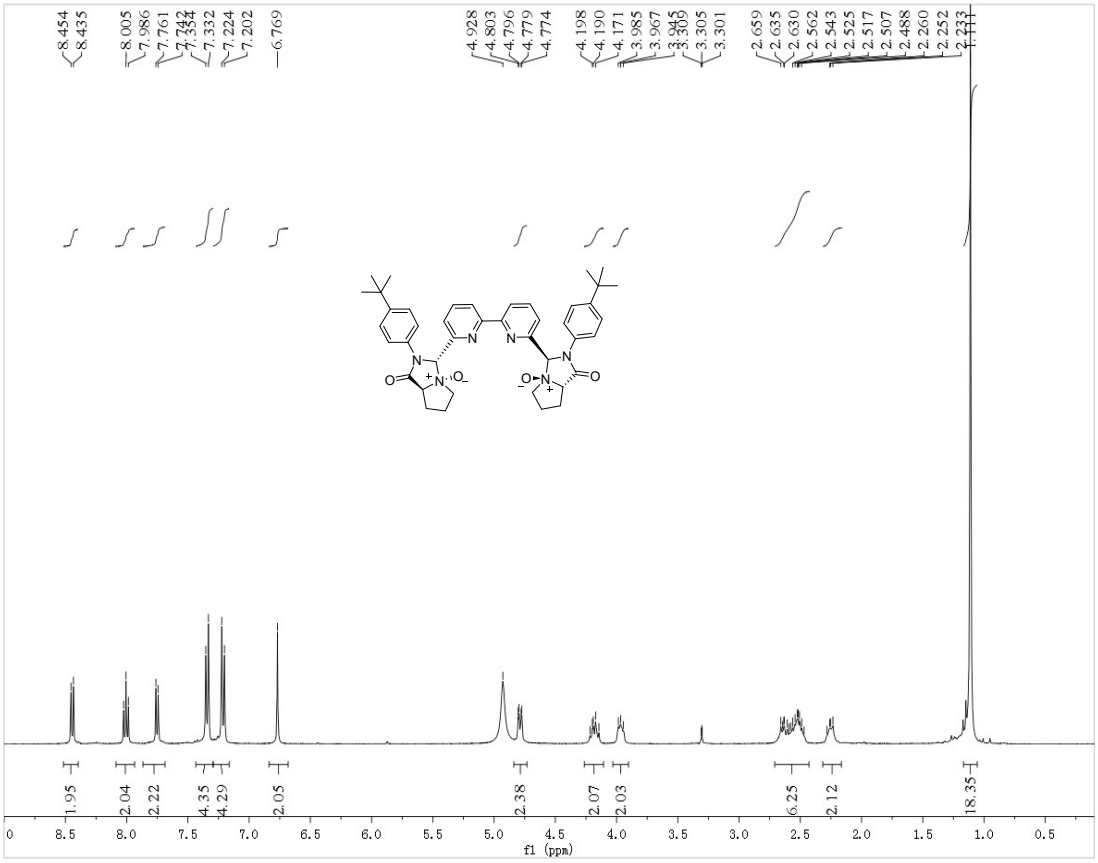


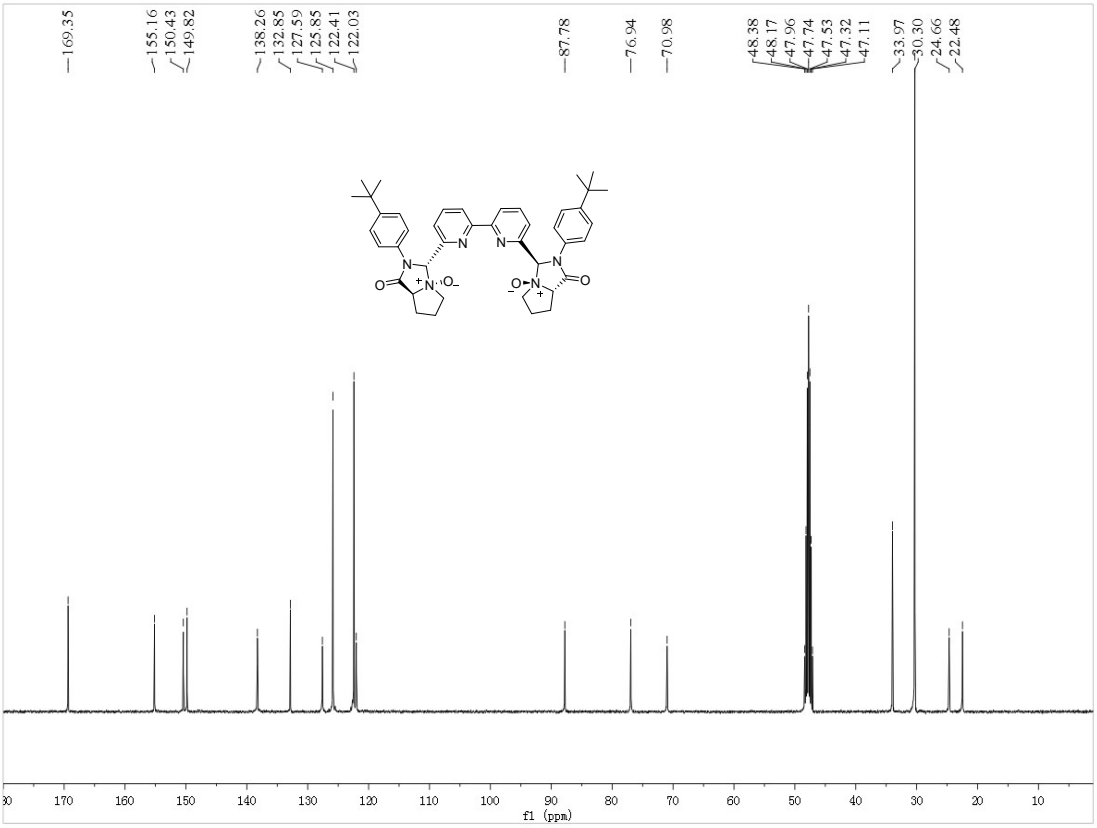
^{1}H and ^{13}C NMR of L1e



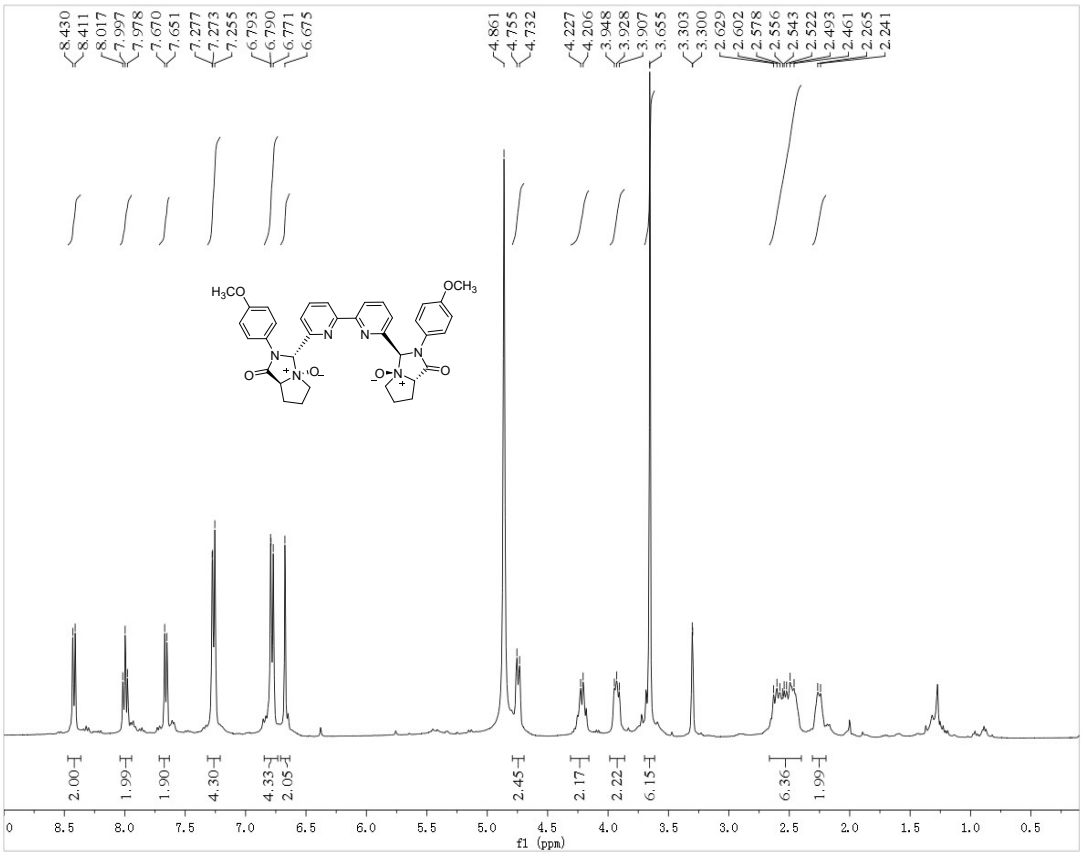


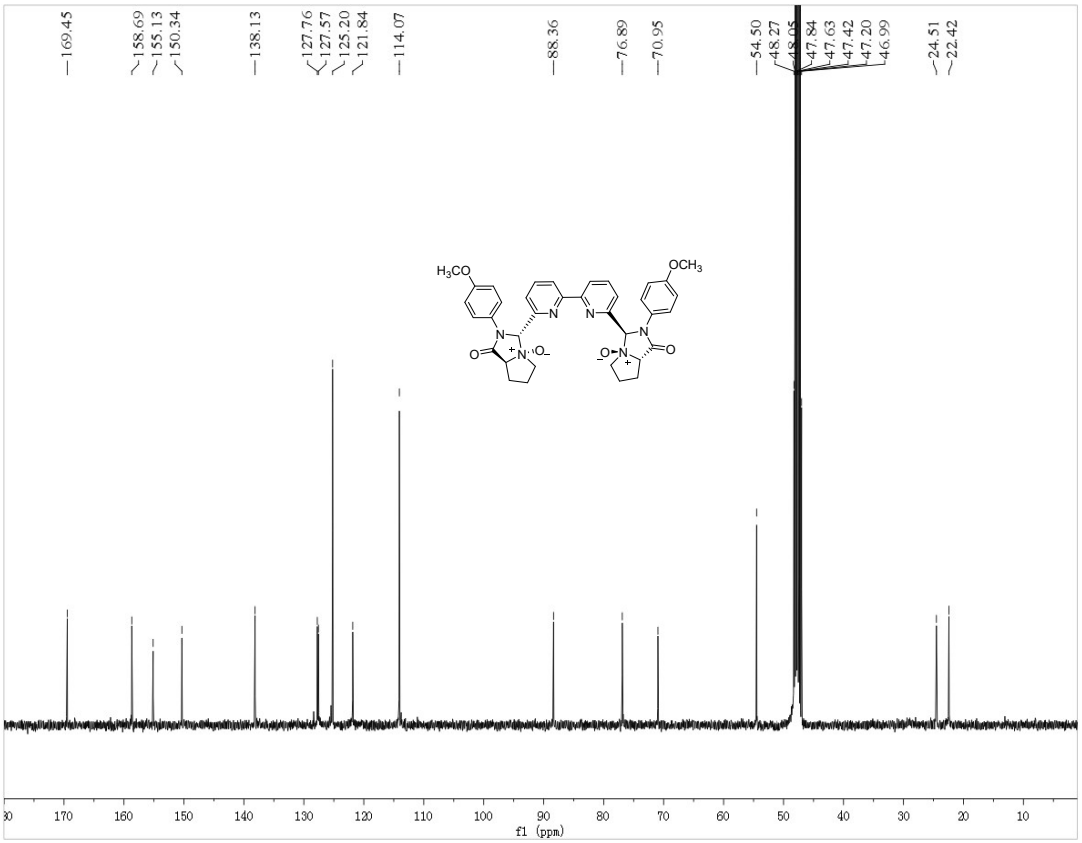
^{1}H and ^{13}C NMR of L1f



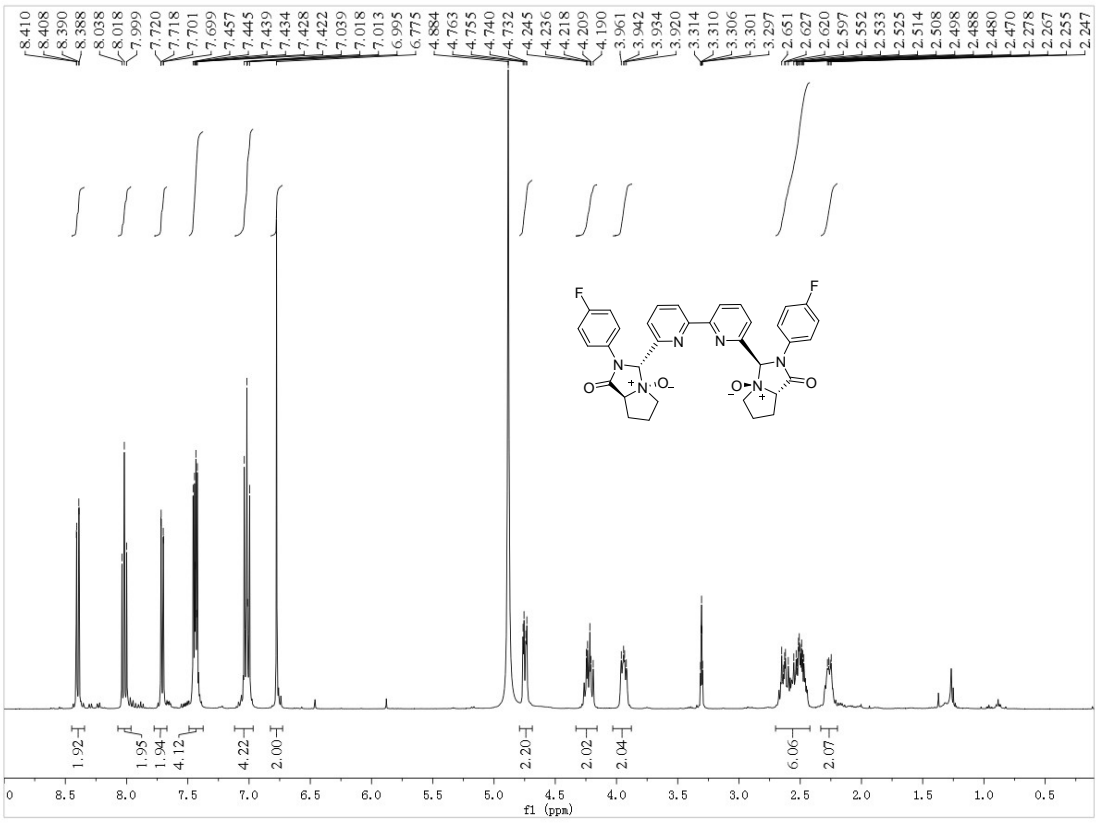


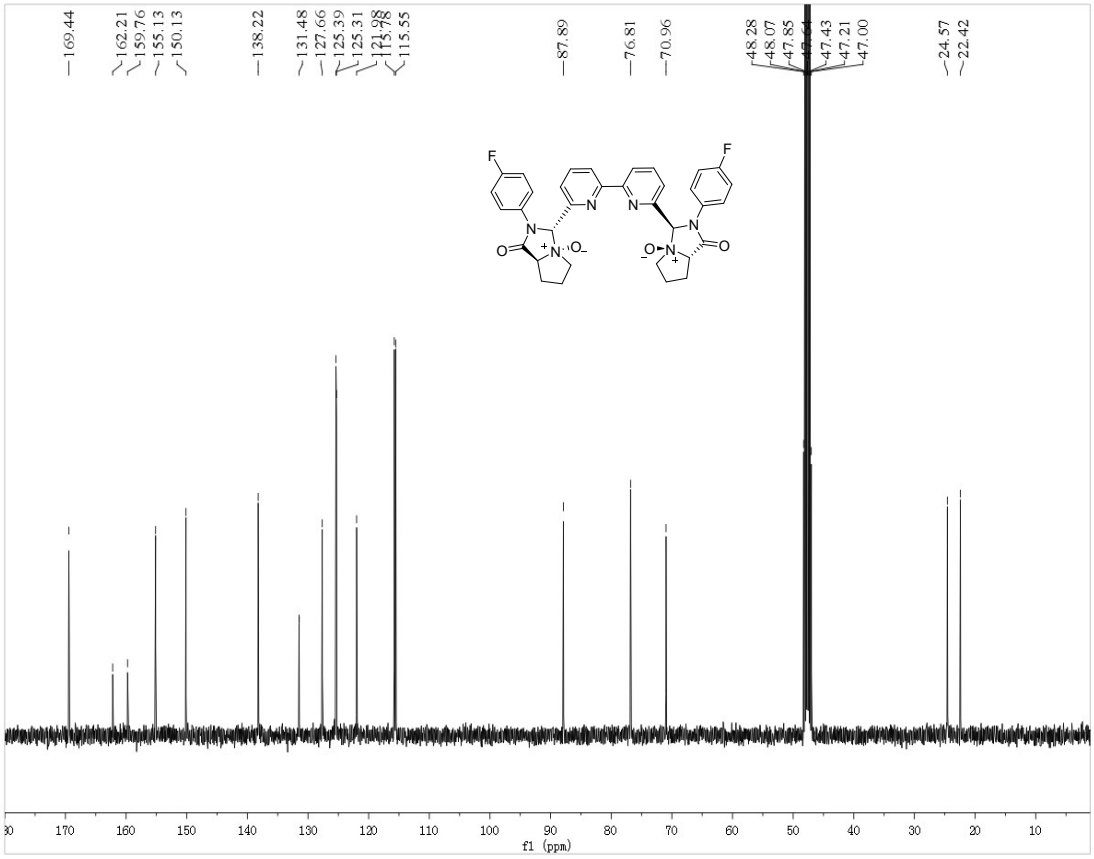
^{1}H and ^{13}C NMR of L1g



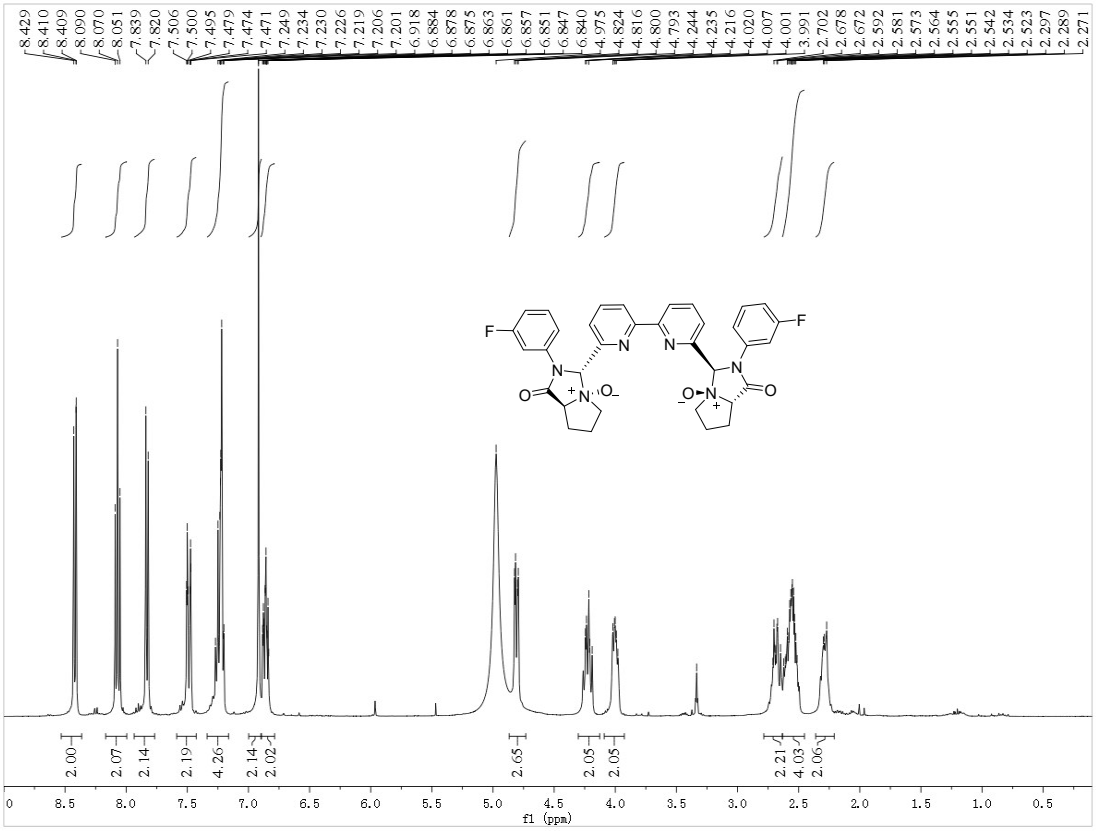


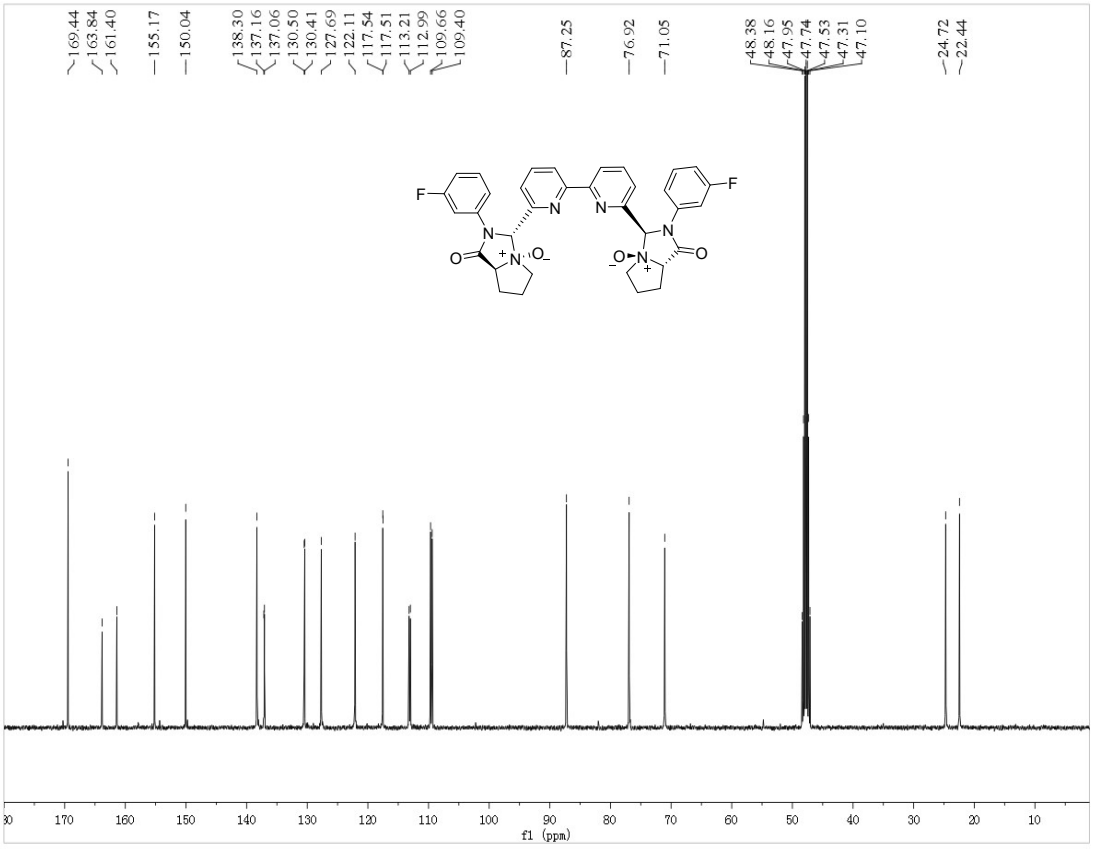
^{1}H and ^{13}C NMR of L1h



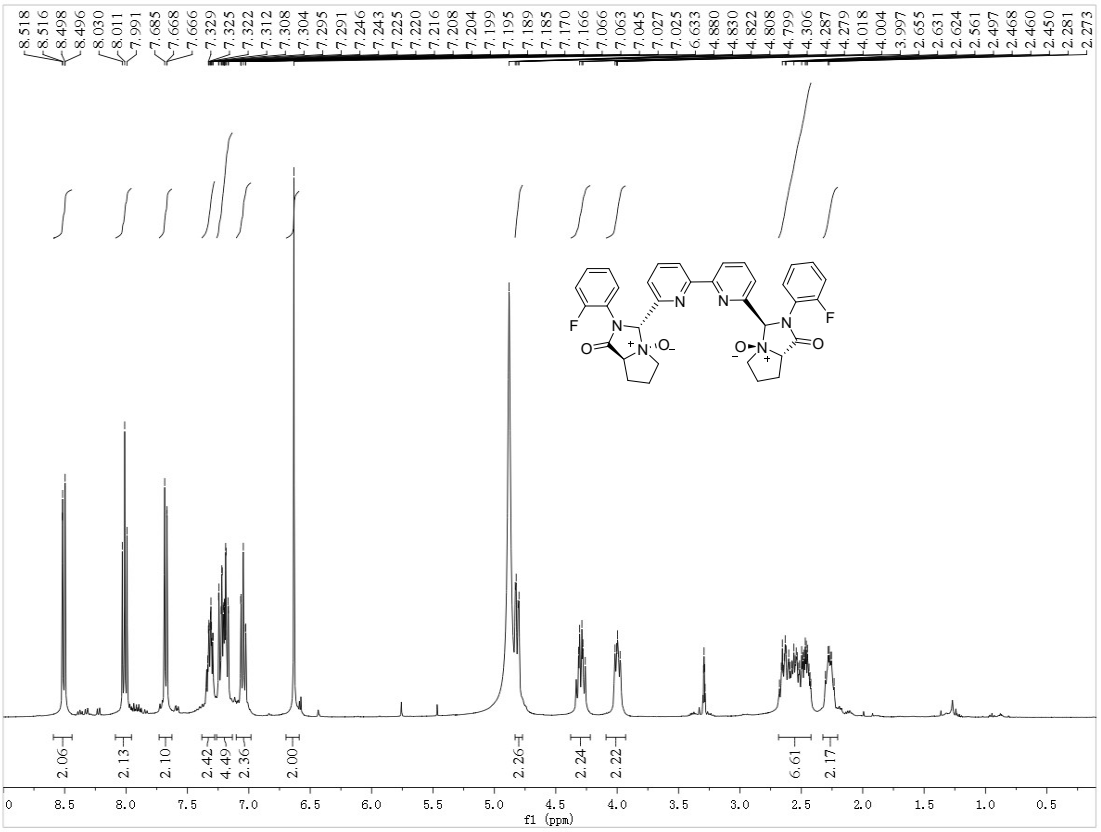


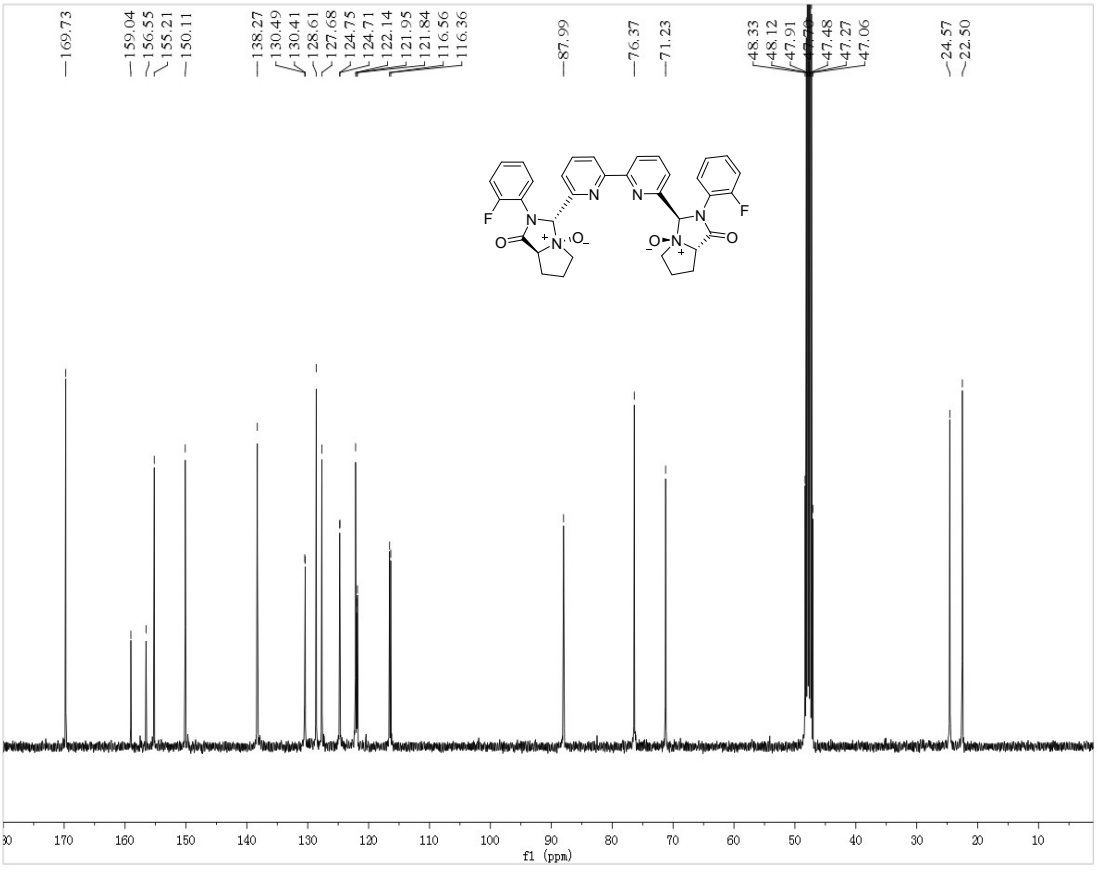
^{1}H and ^{13}C NMR of L1i



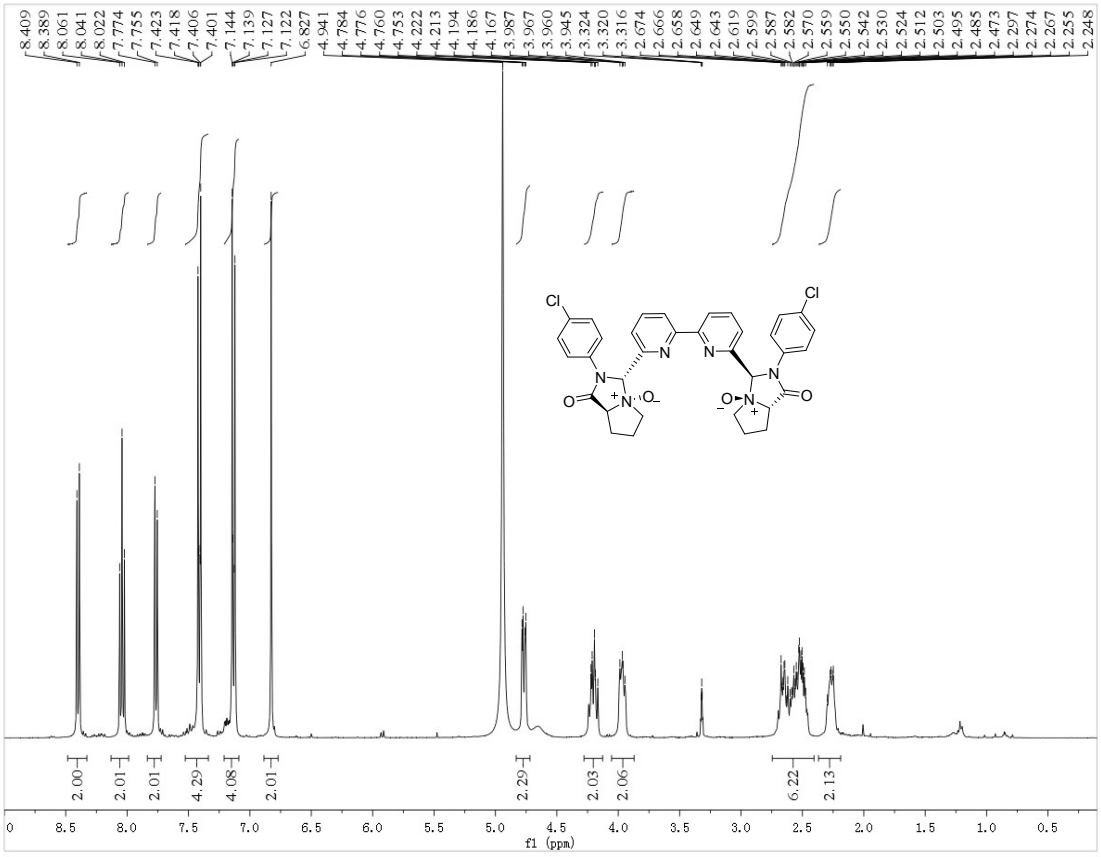


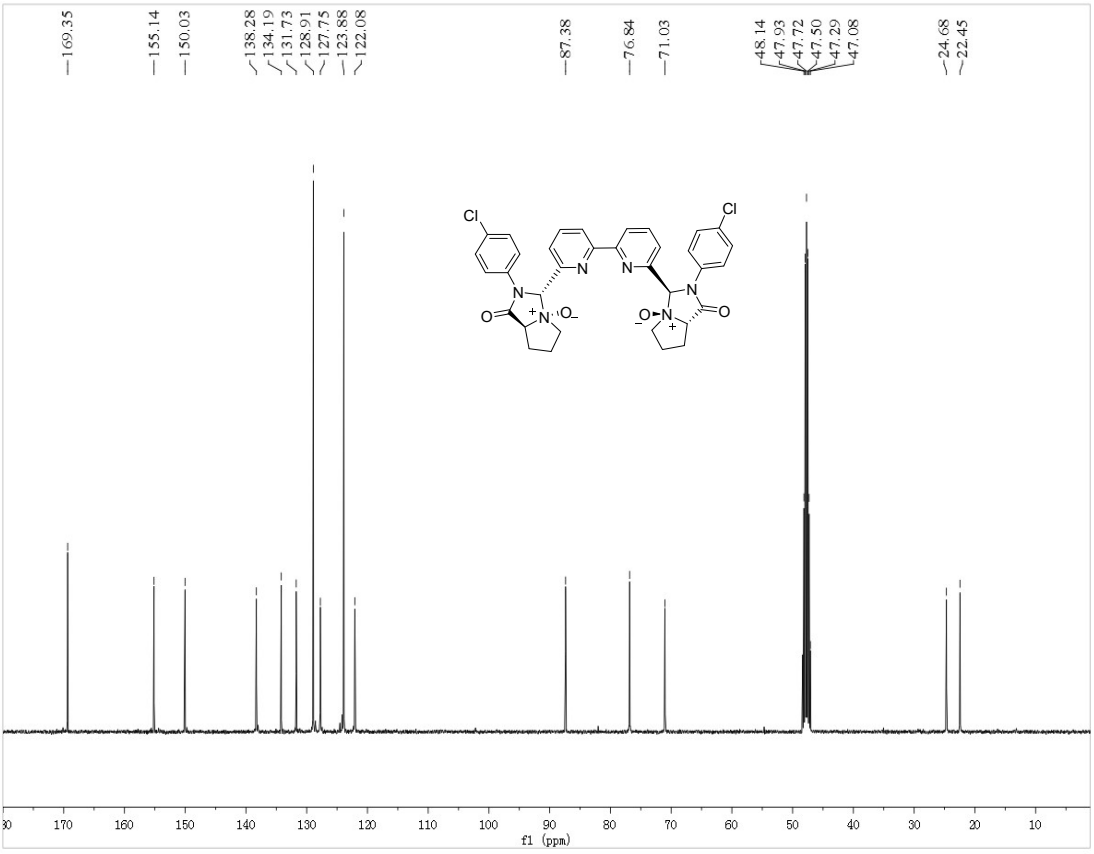
^{1}H and ^{13}C NMR of L1j



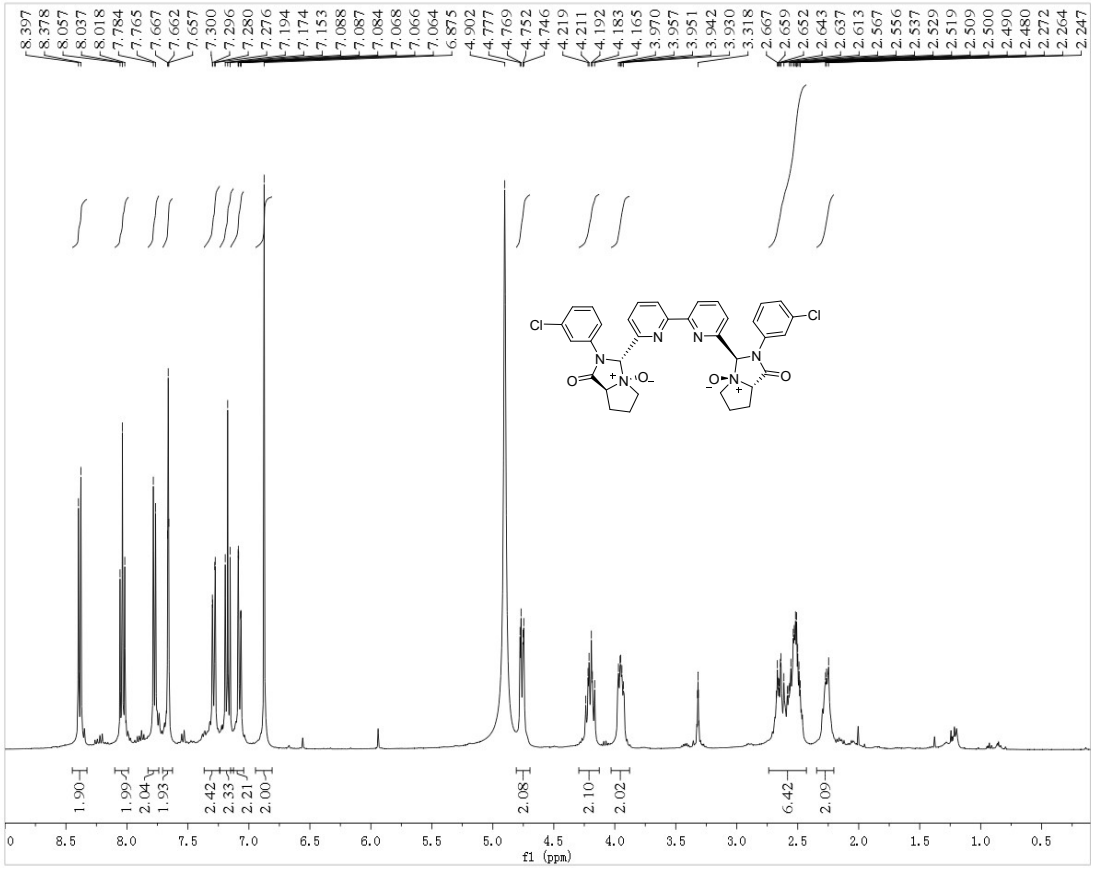


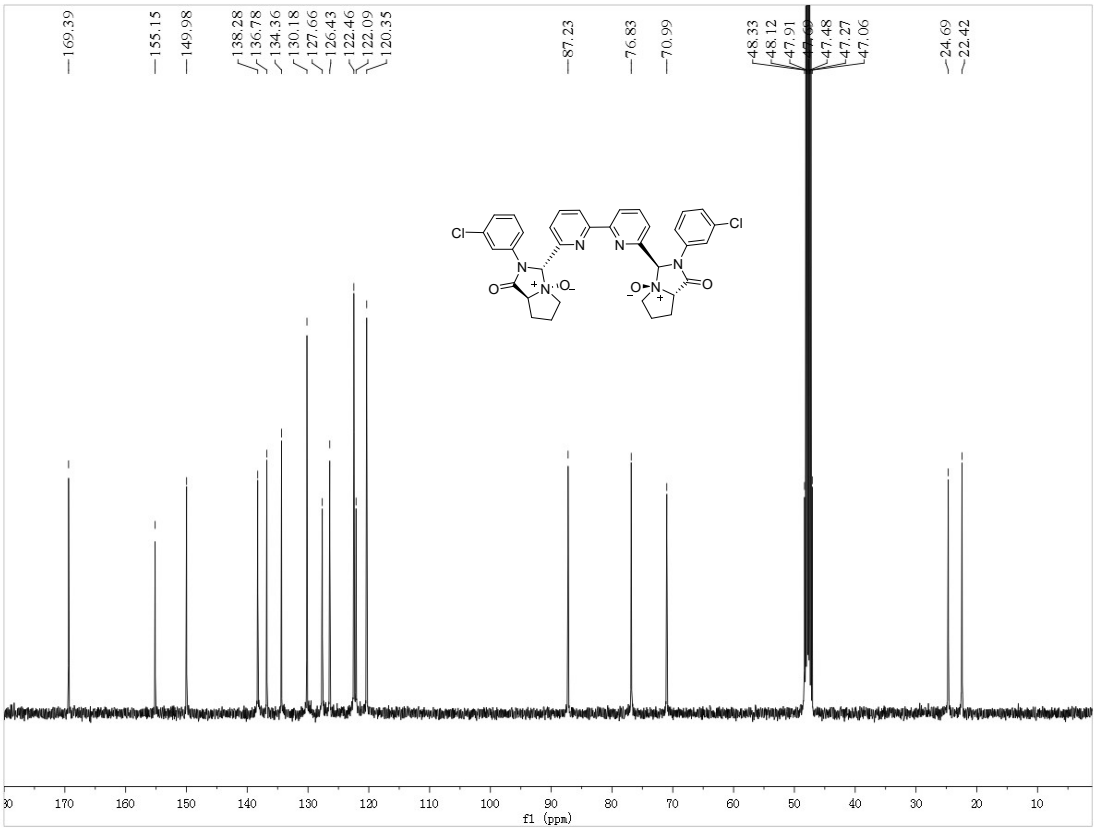
^{1}H and ^{13}C NMR of L1k



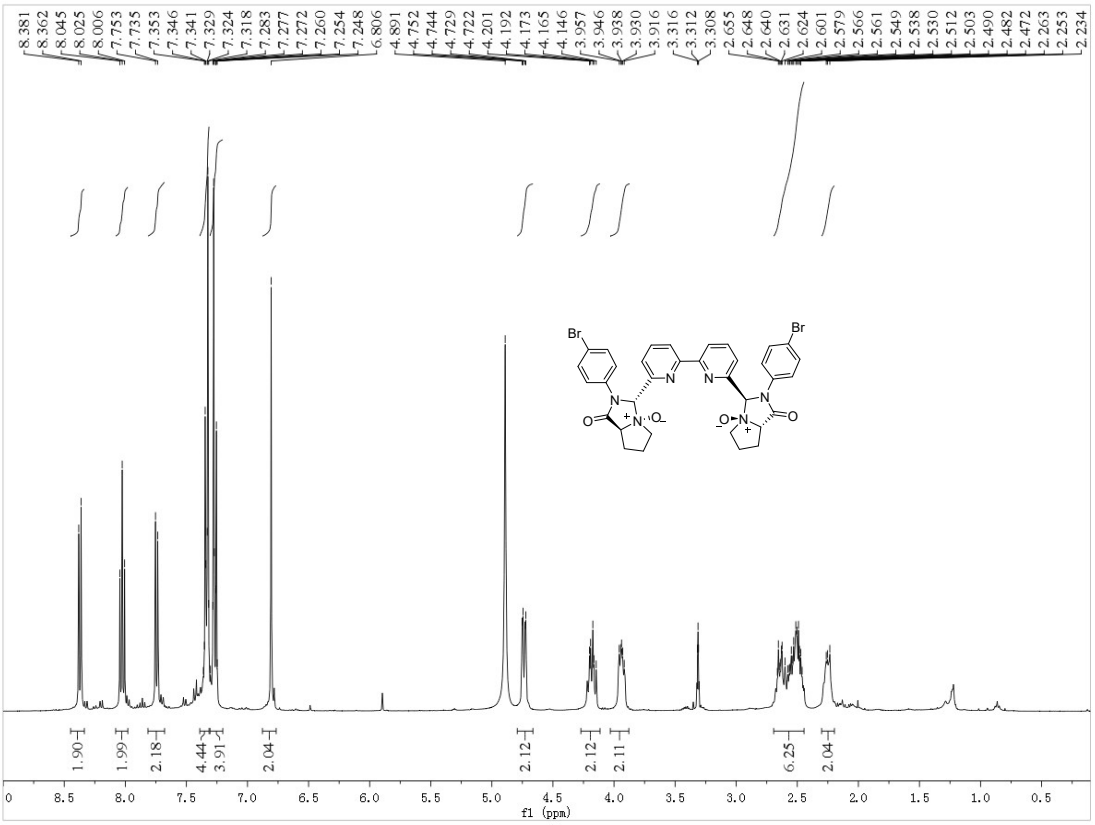


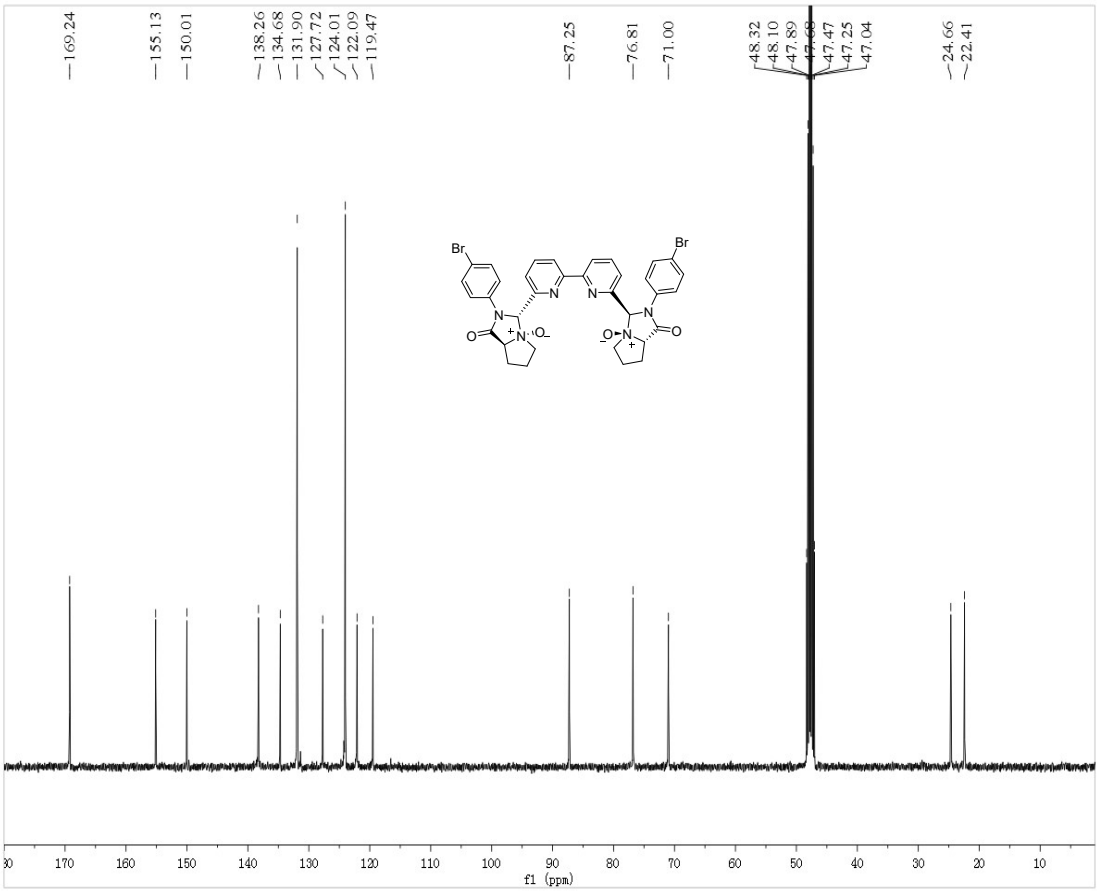
^{1}H and ^{13}C NMR of L1l



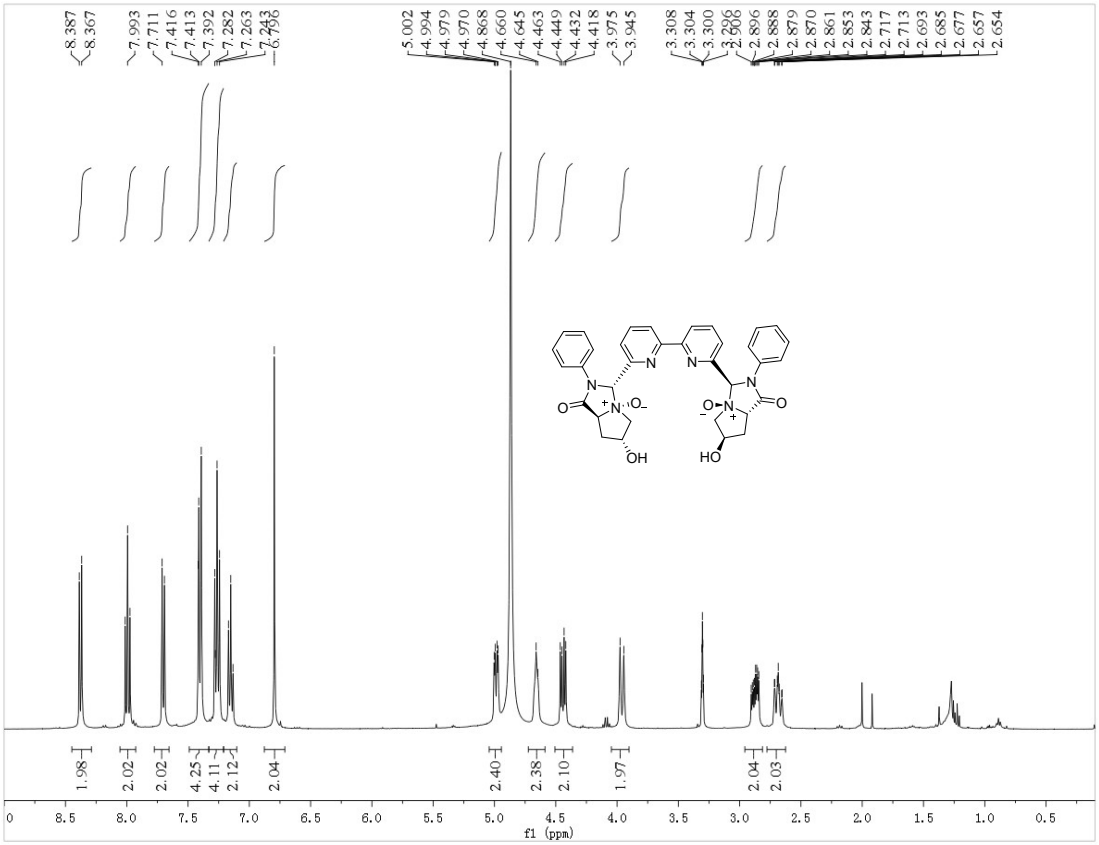


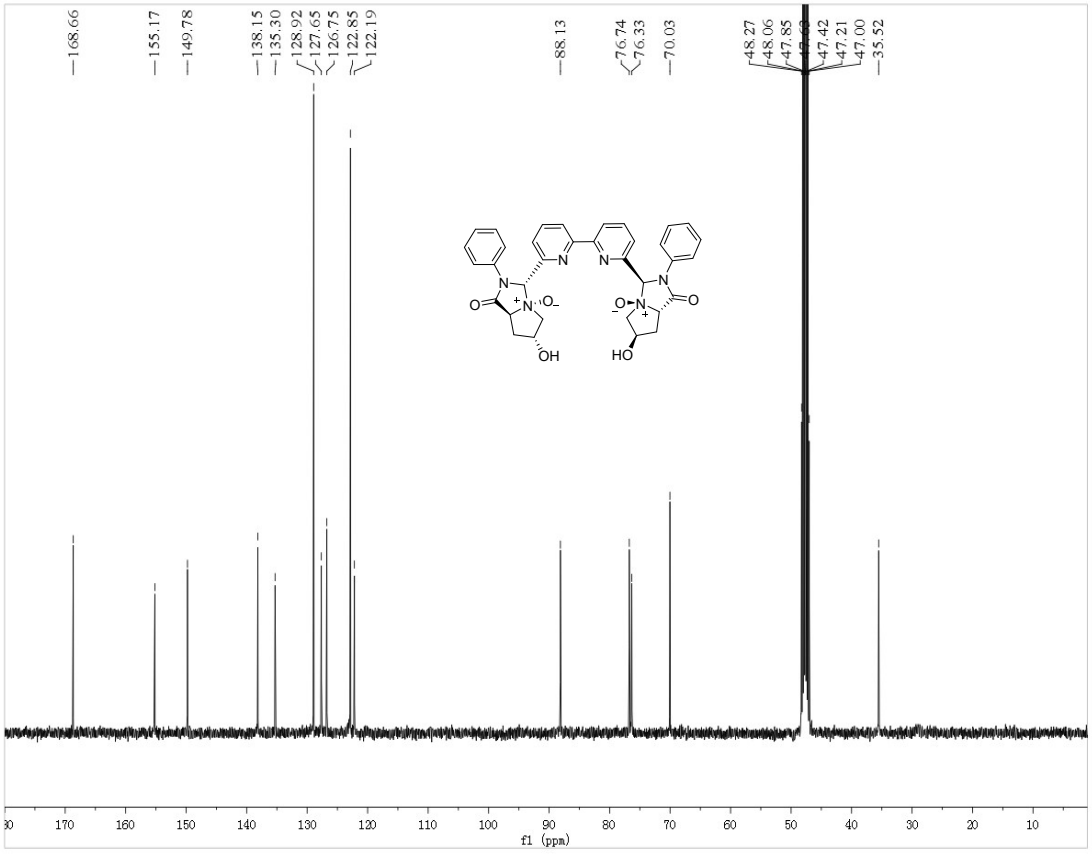
^{1}H and ^{13}C NMR of L1m



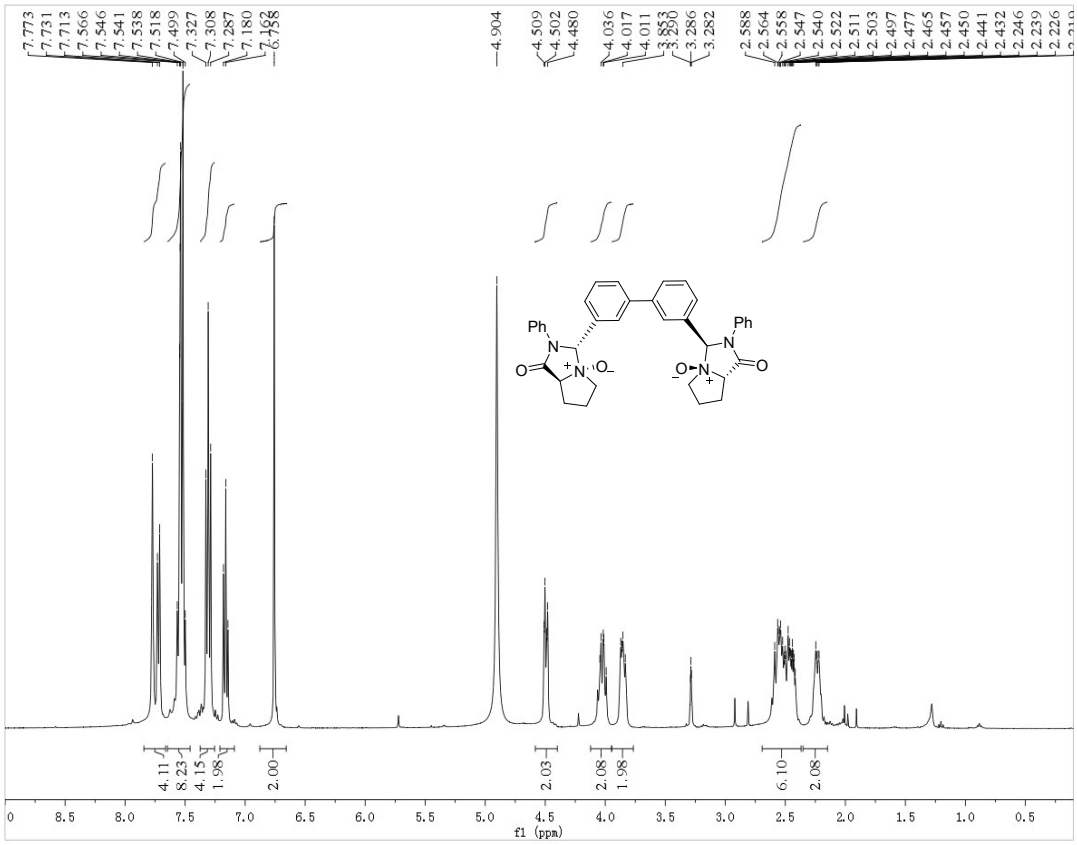


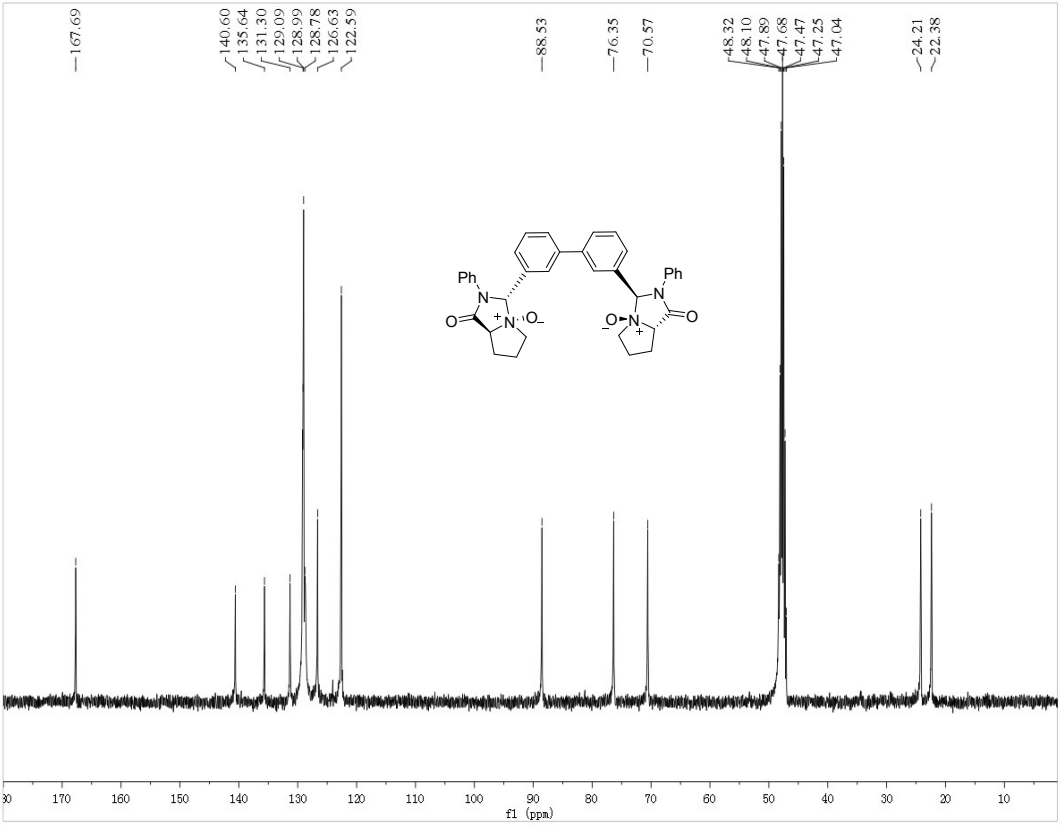
^{1}H and ^{13}C NMR of L1n



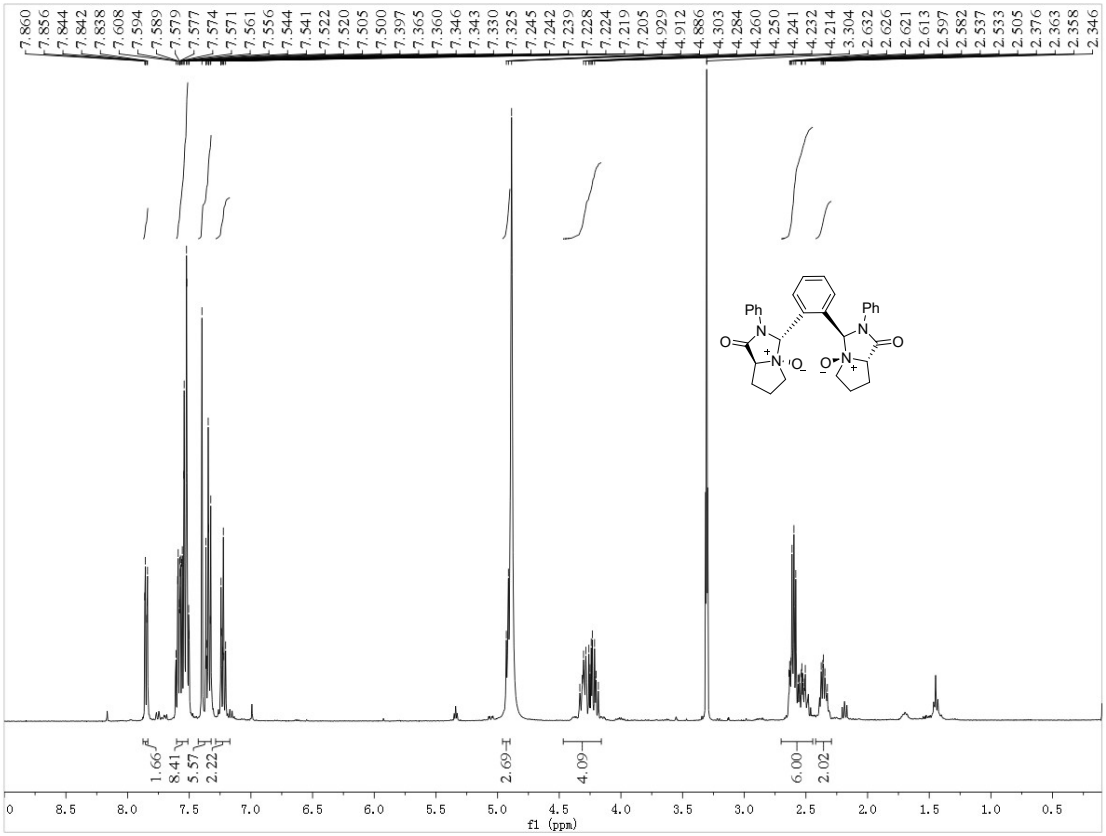


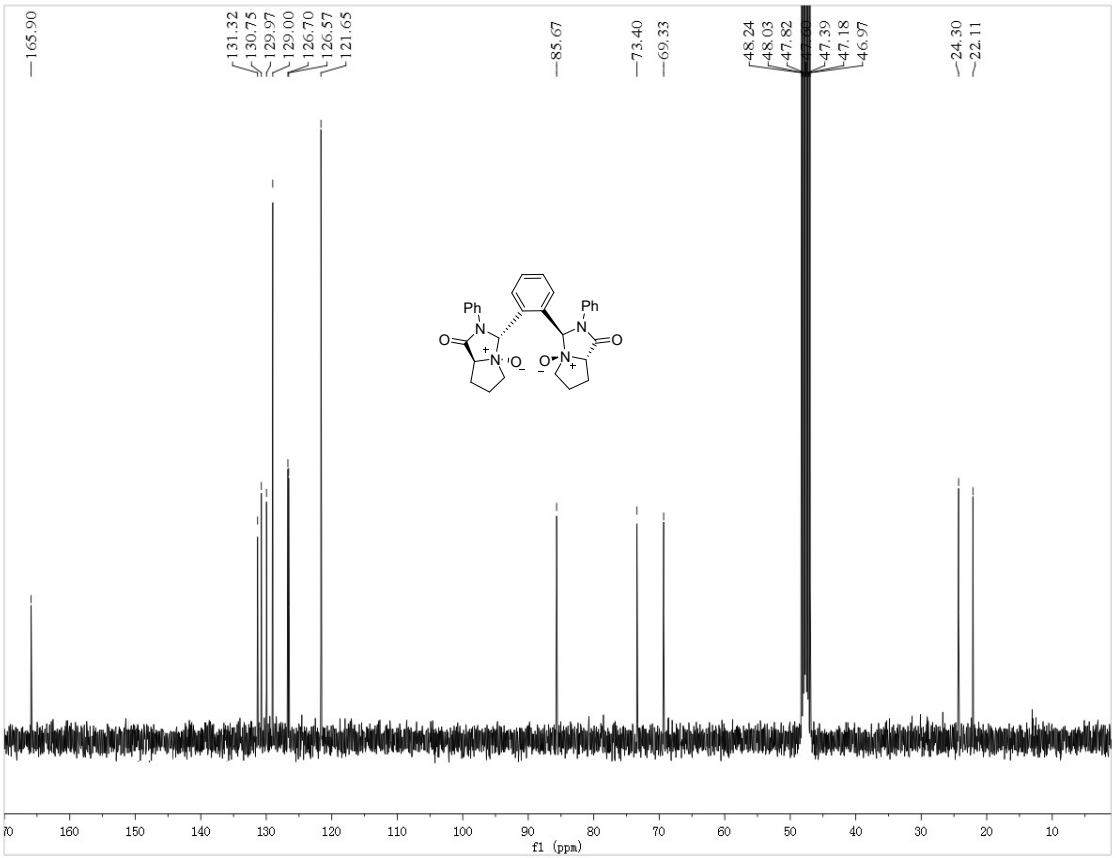
^{1}H and ^{13}C NMR of L4a



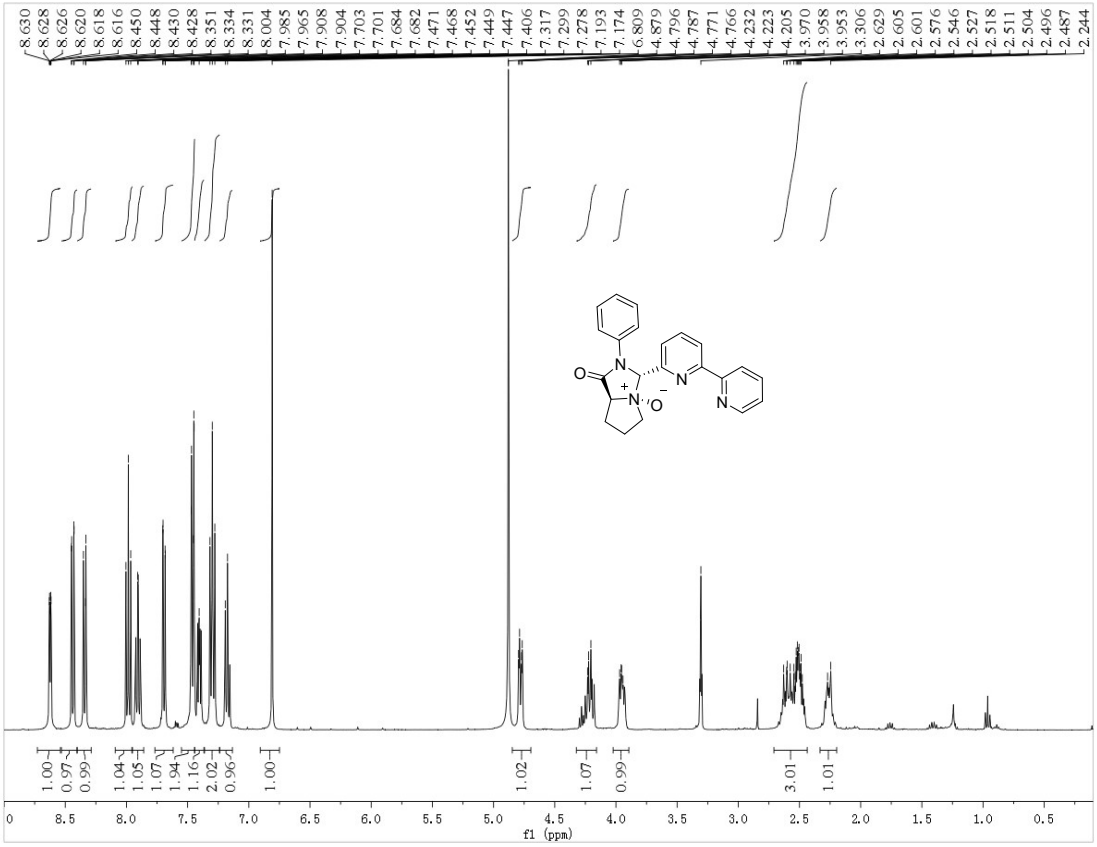


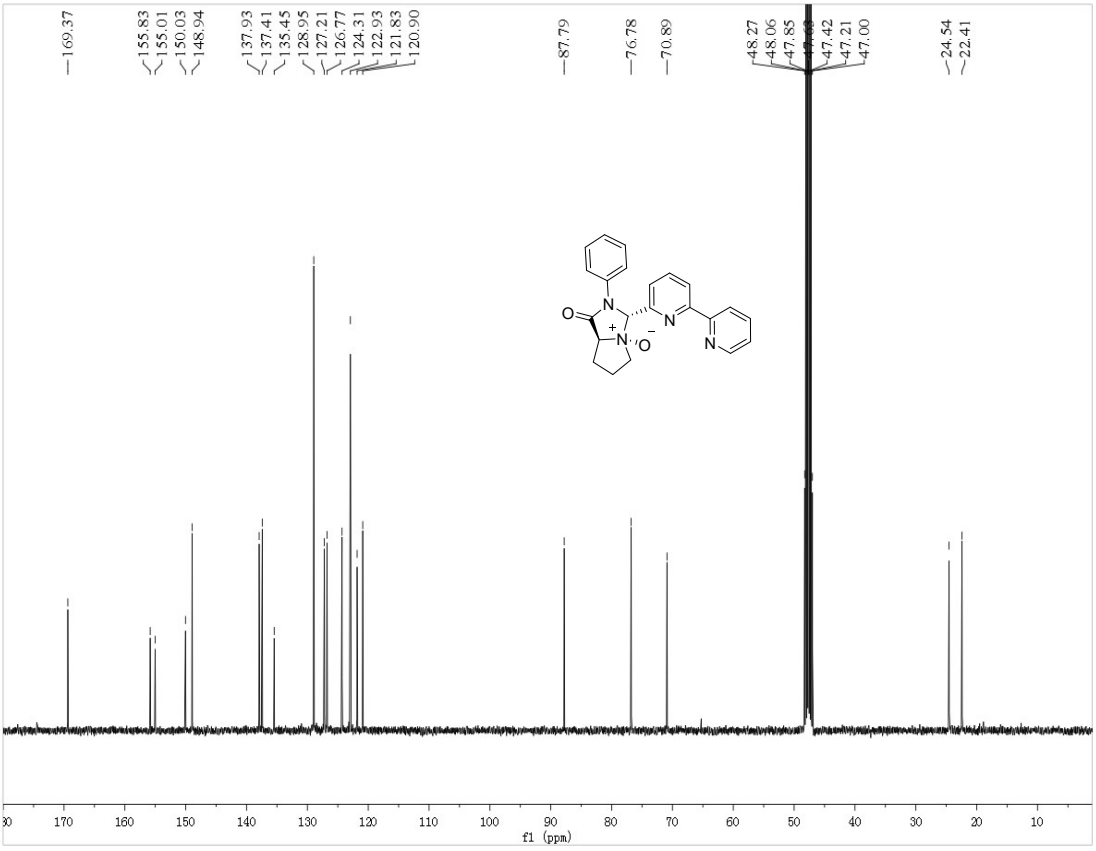
^{1}H and ^{13}C NMR of L6a



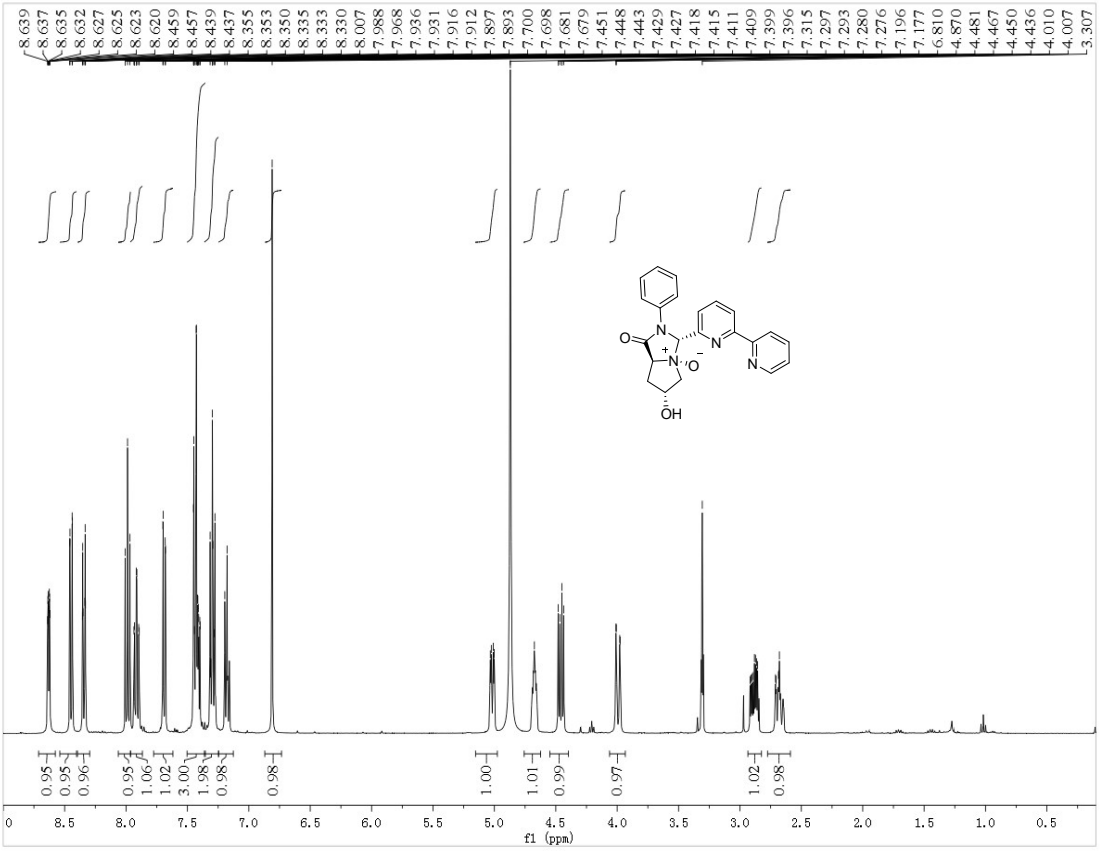


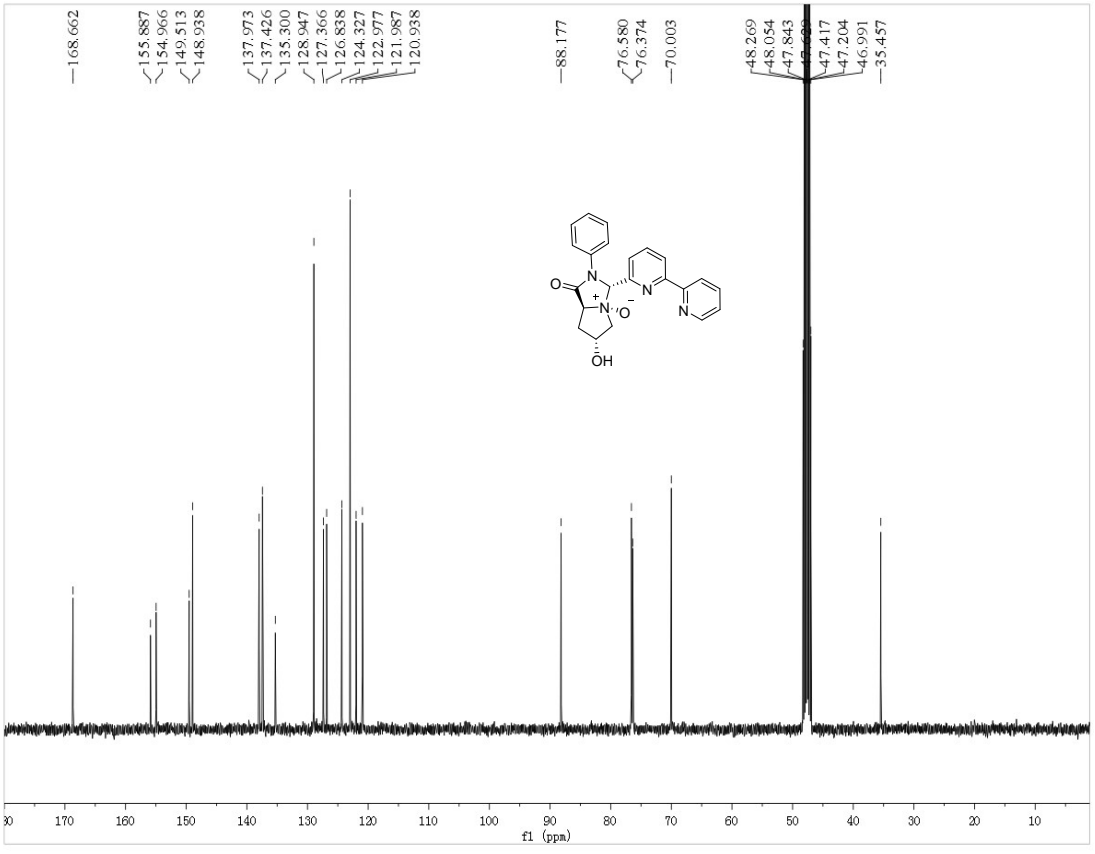
^{1}H and ^{13}C NMR of L2a



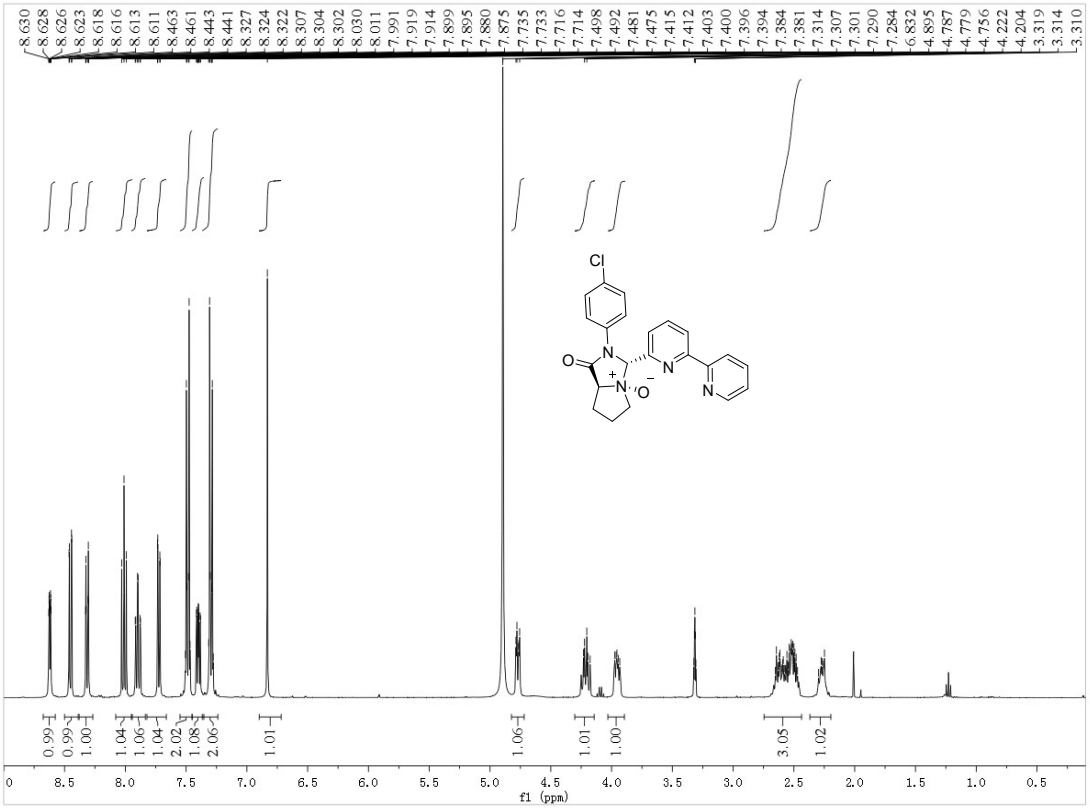


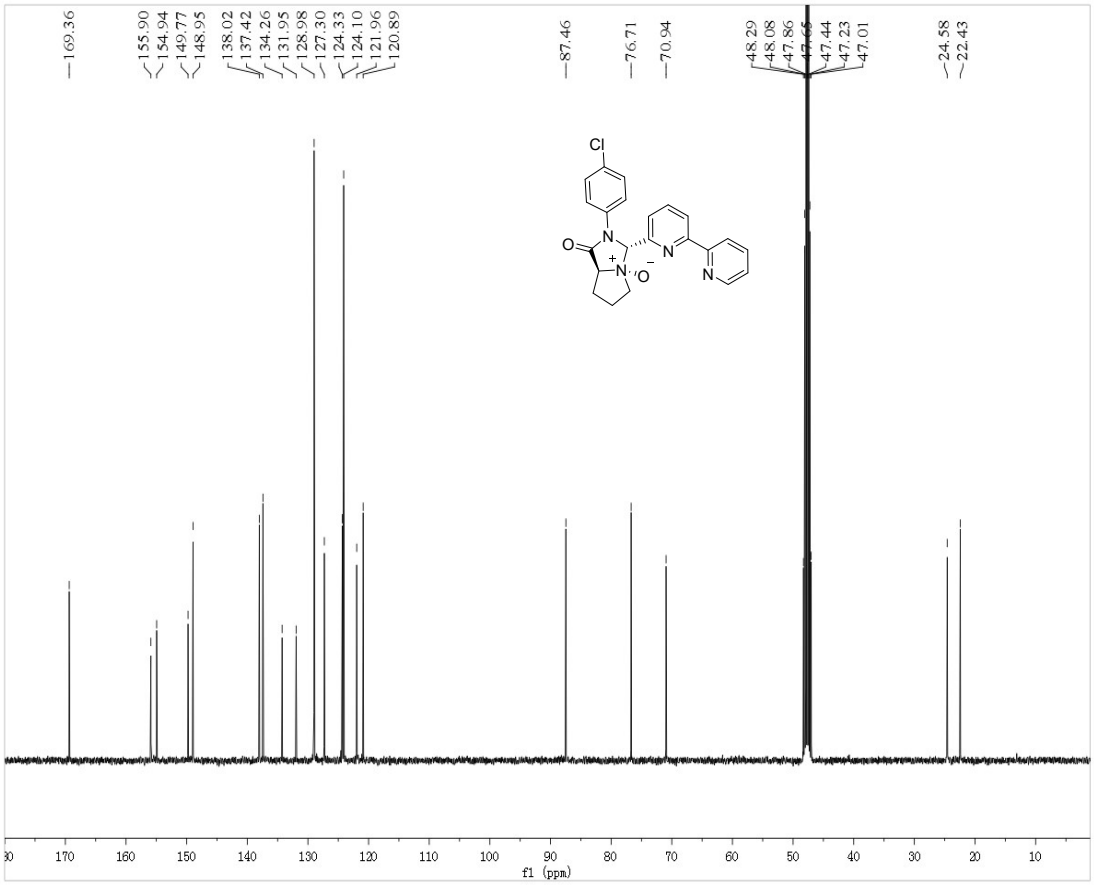
^{1}H and ^{13}C NMR of L2b



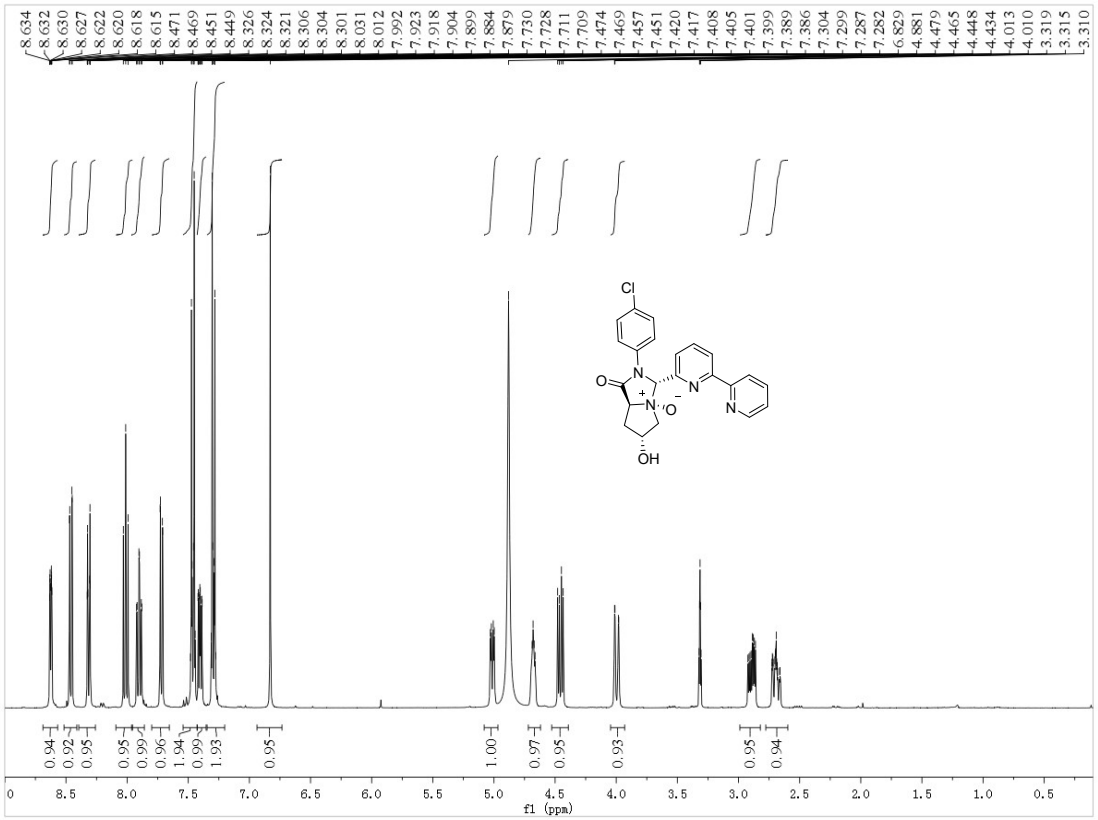


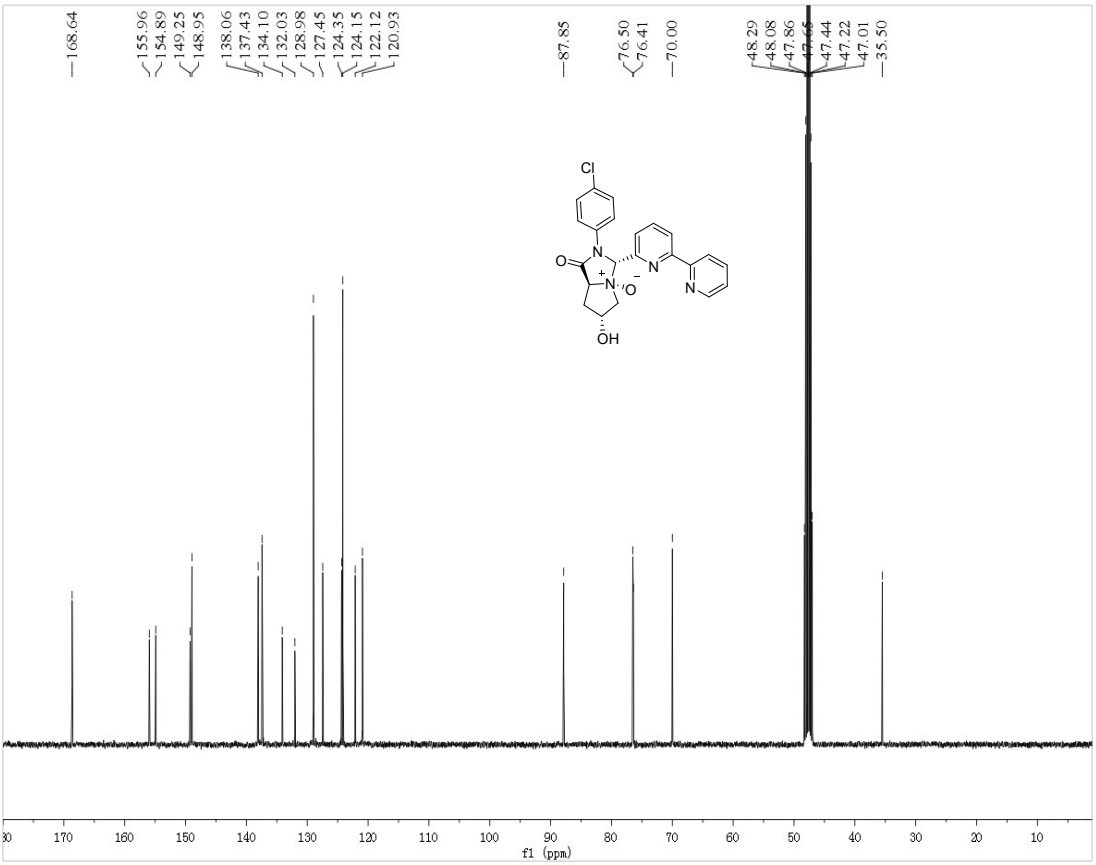
^{1}H and ^{13}C NMR of L2c



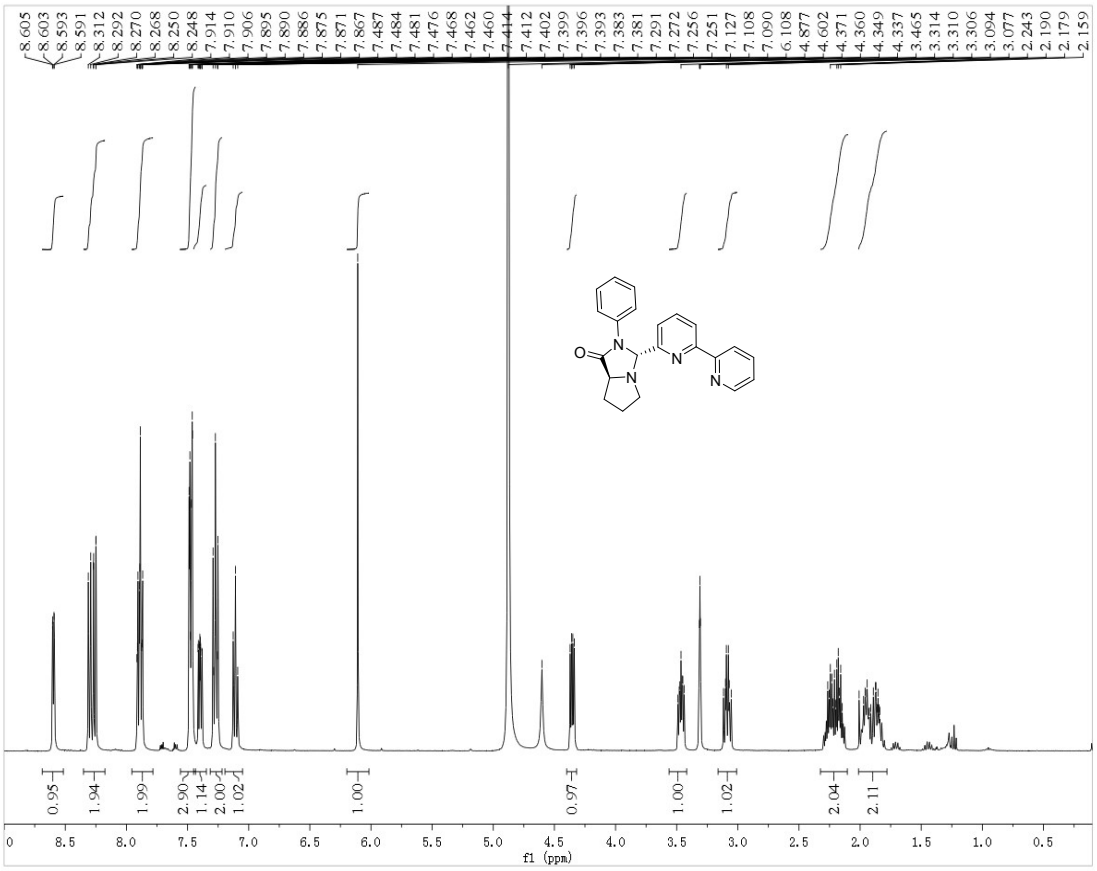


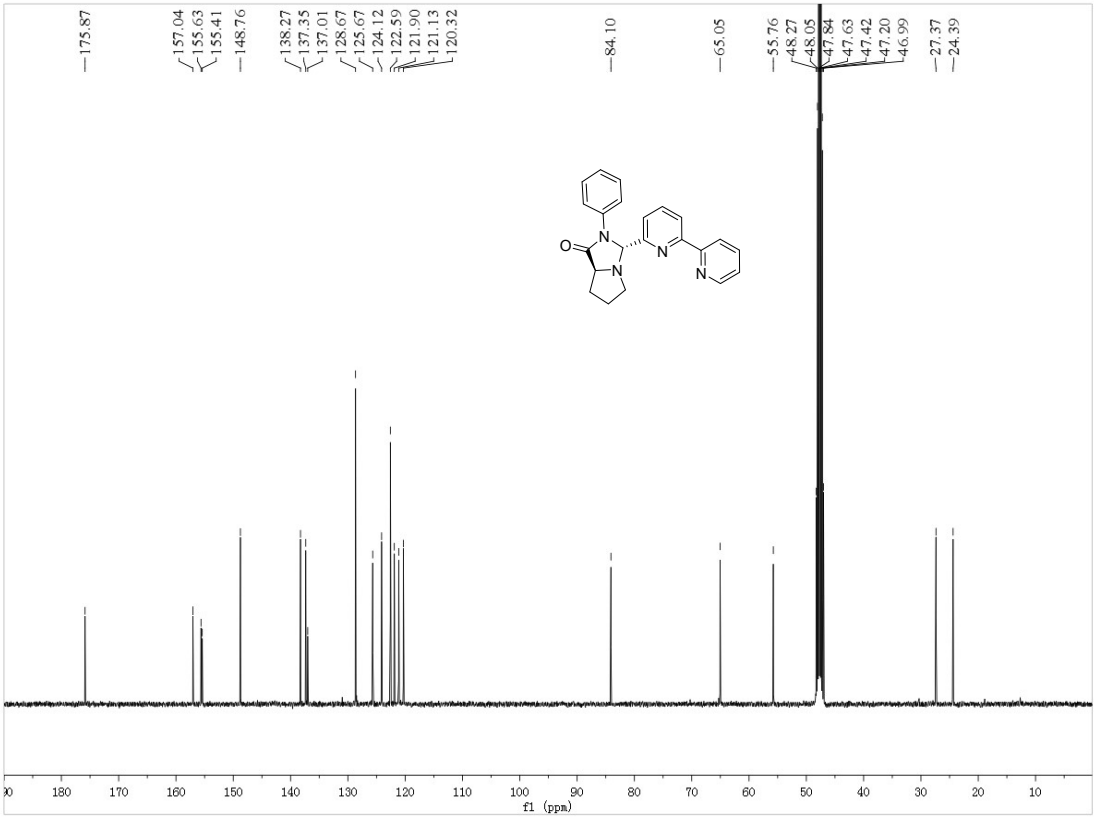
^{1}H and ^{13}C NMR of L2d



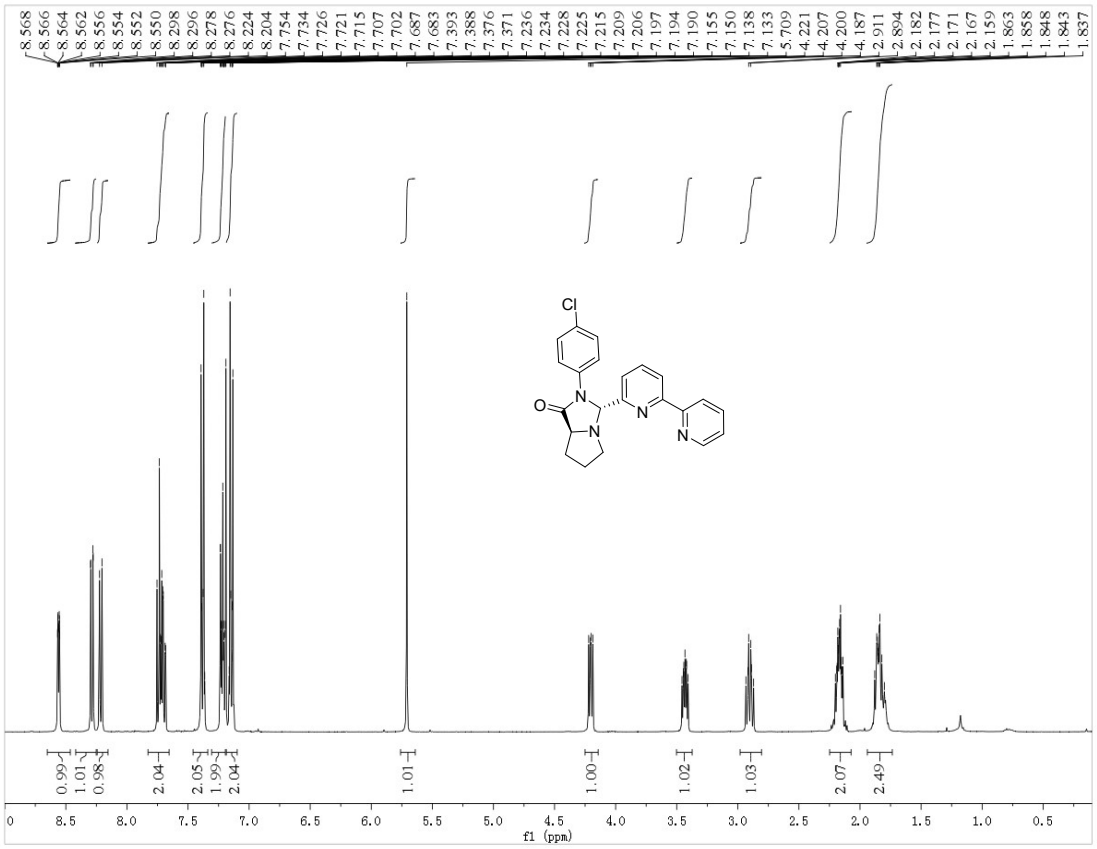


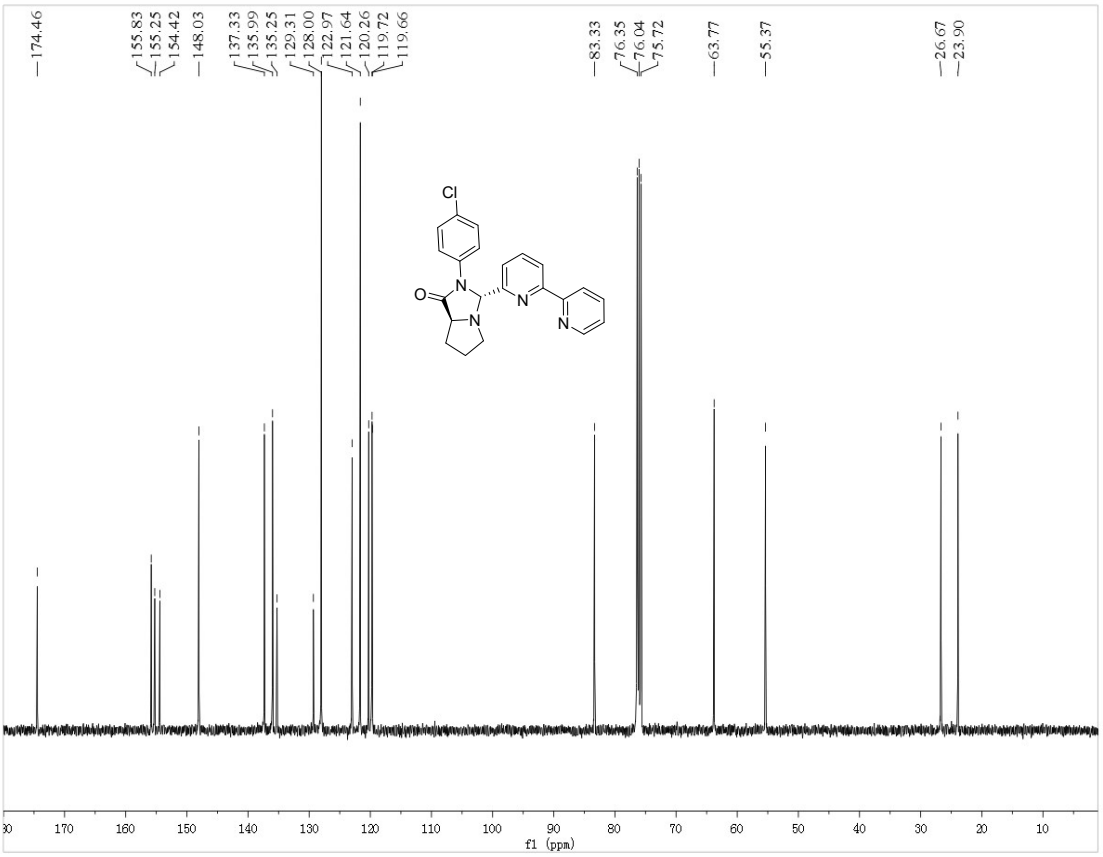
^{1}H and ^{13}C NMR of 4a



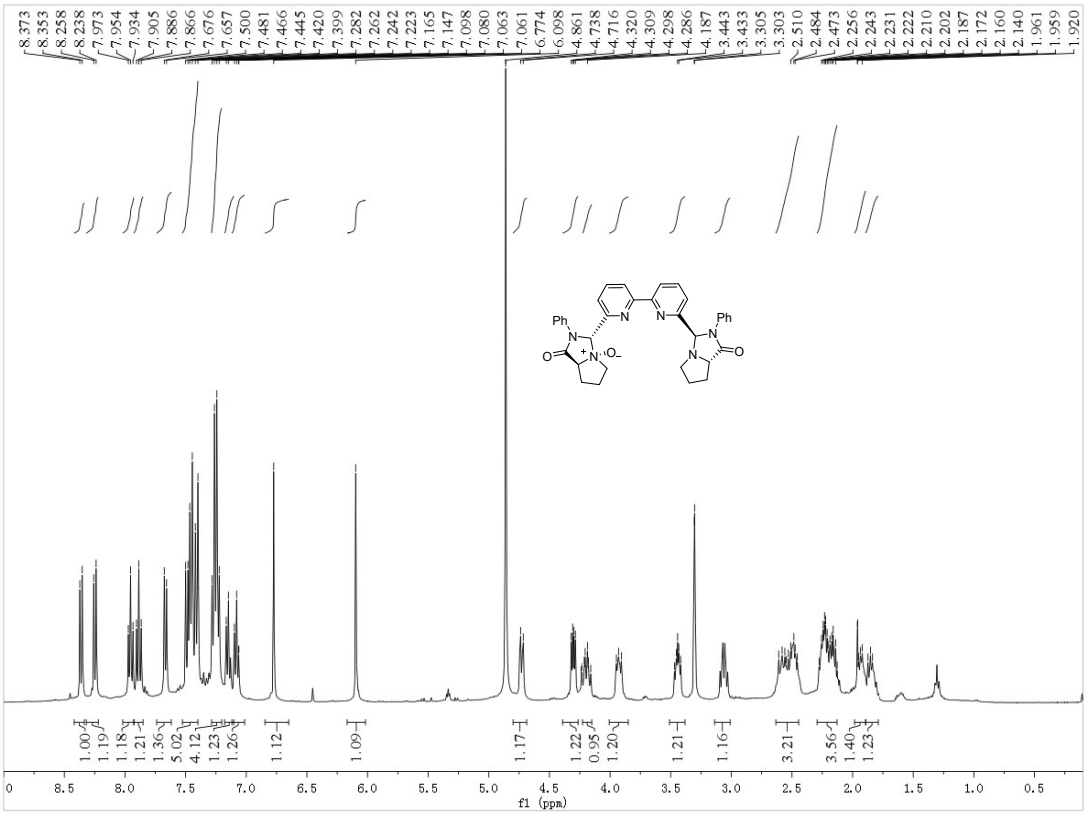


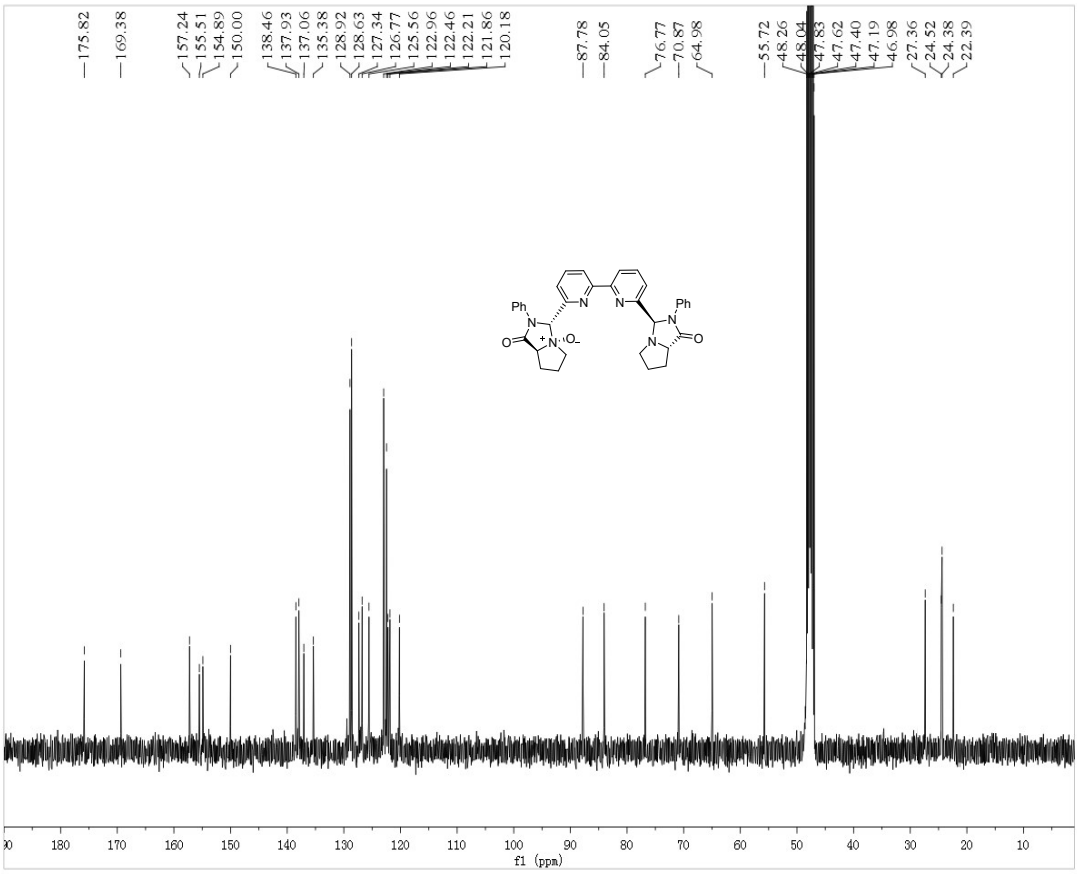
^{1}H and ^{13}C NMR of 4c



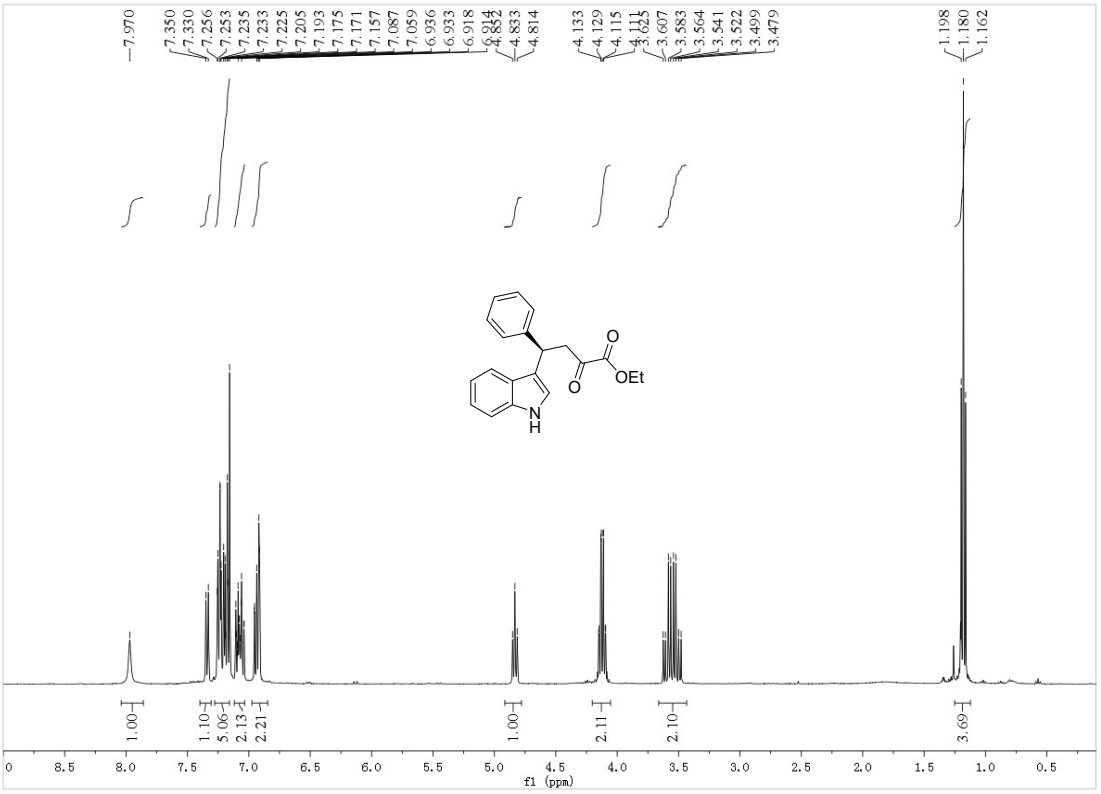


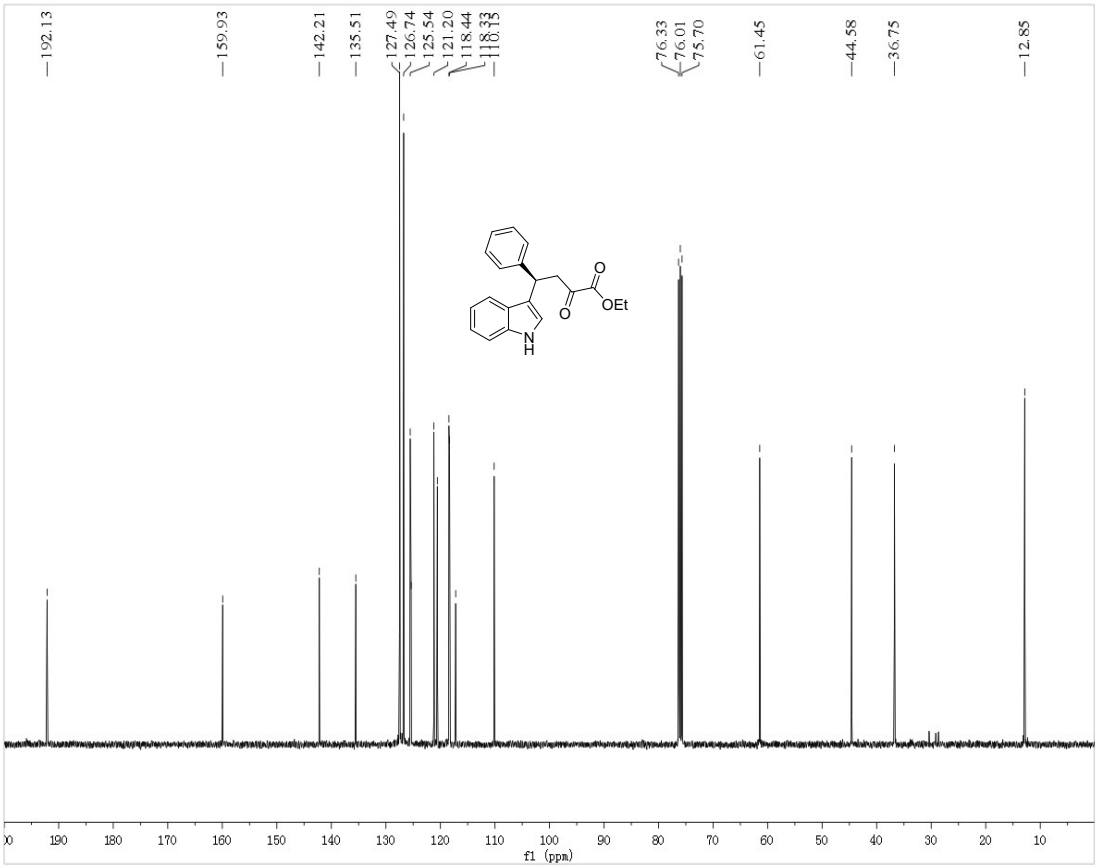
^{1}H and ^{13}C NMR of L5a



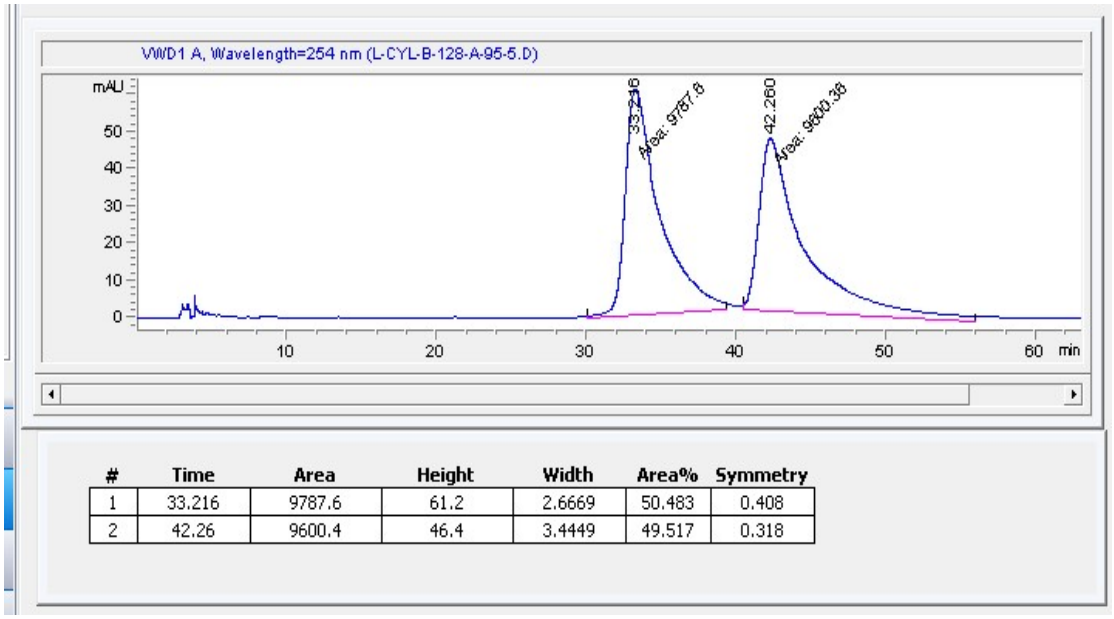


^{1}H and ^{13}C NMR of 7a



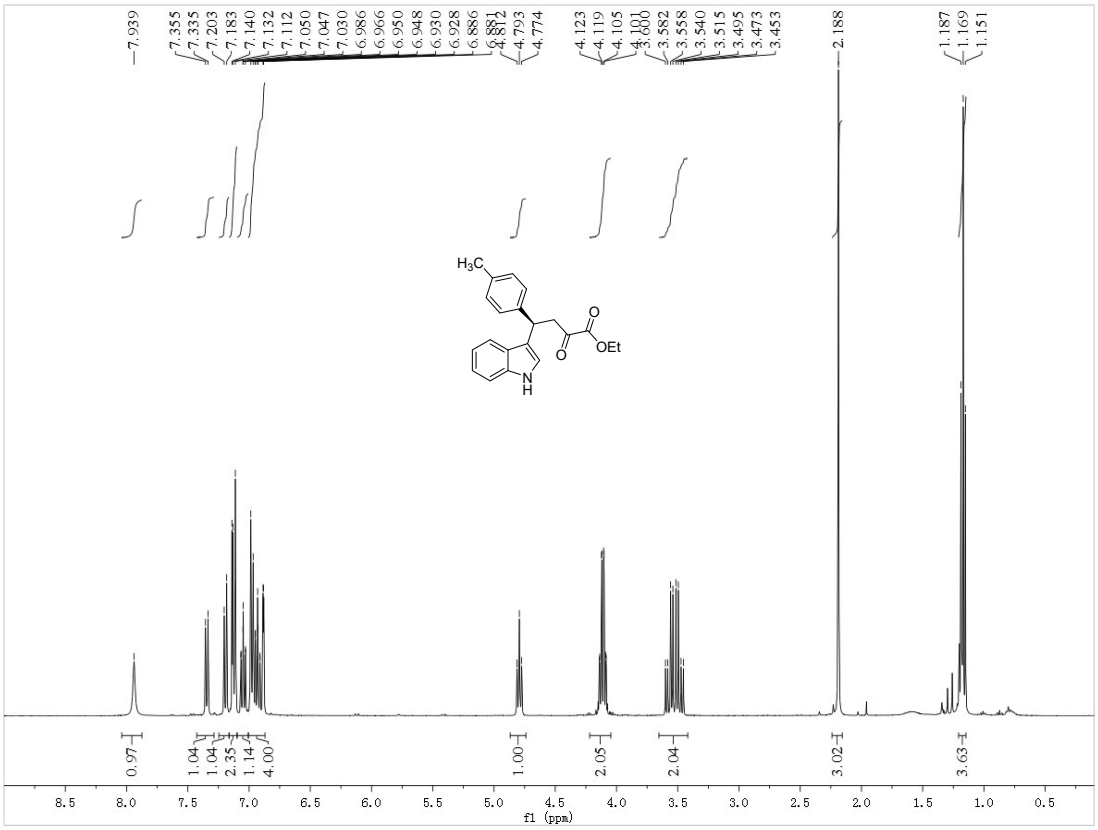


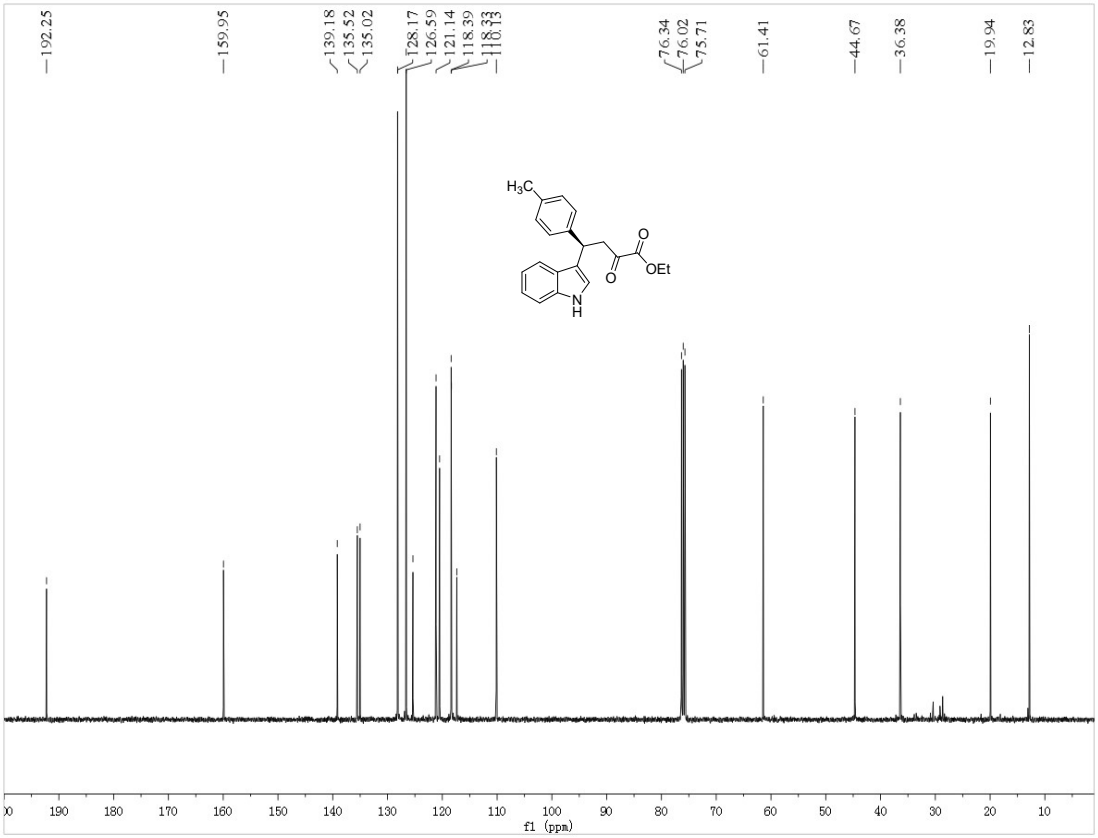
HPLC of 7a



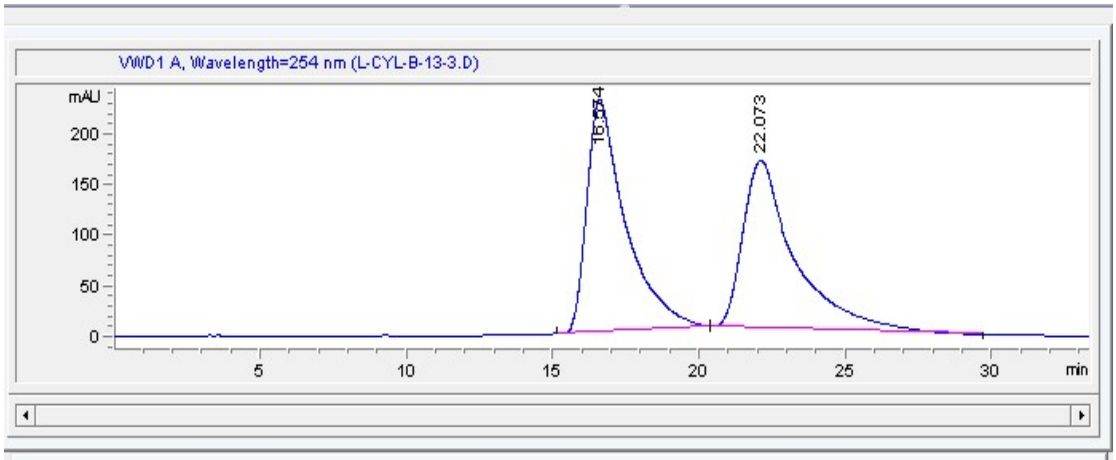
#	Time	Area	Height	Width	Area%	Symmetry
1	33.216	9787.6	61.2	2.6669	50.483	0.408
2	42.26	9600.4	46.4	3.4449	49.517	0.318

^{1}H and ^{13}C NMR of 7b

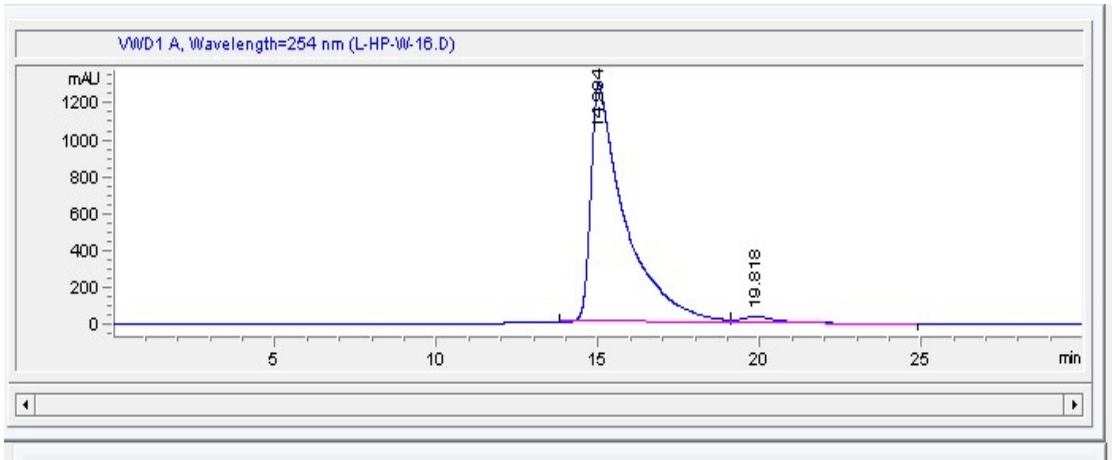




HPLC of 7b

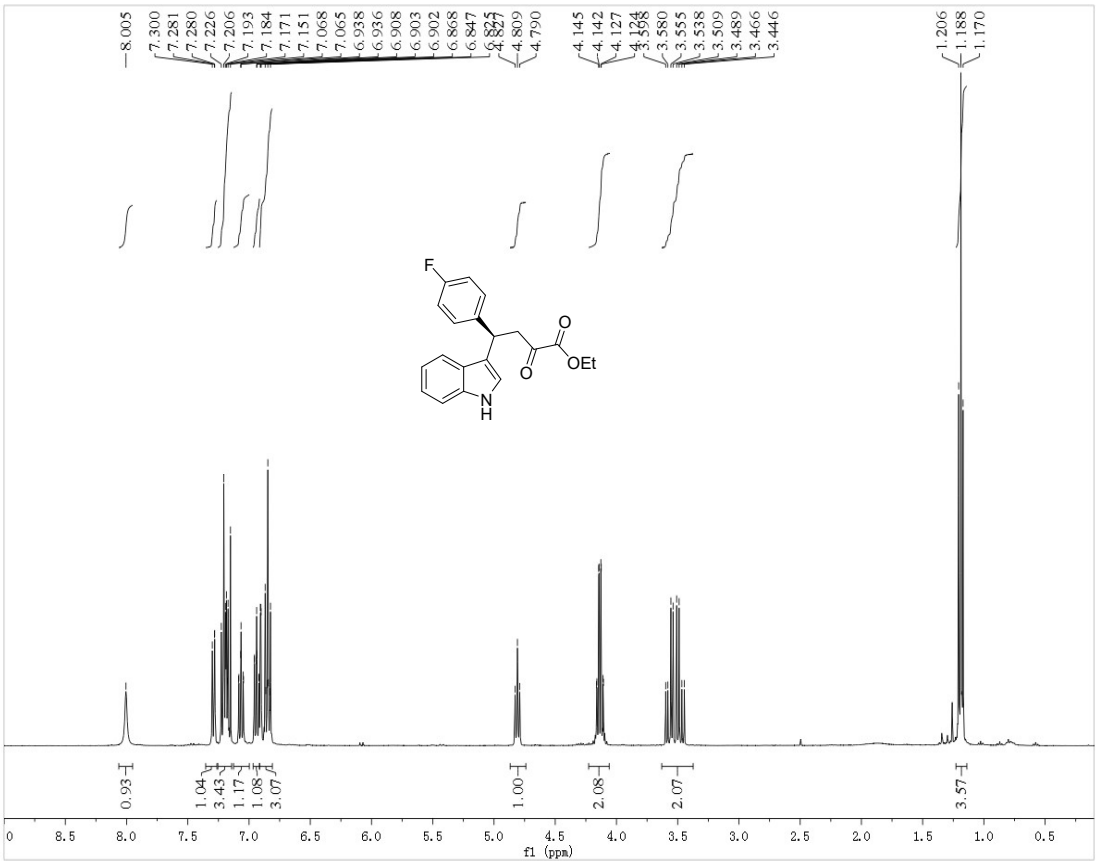


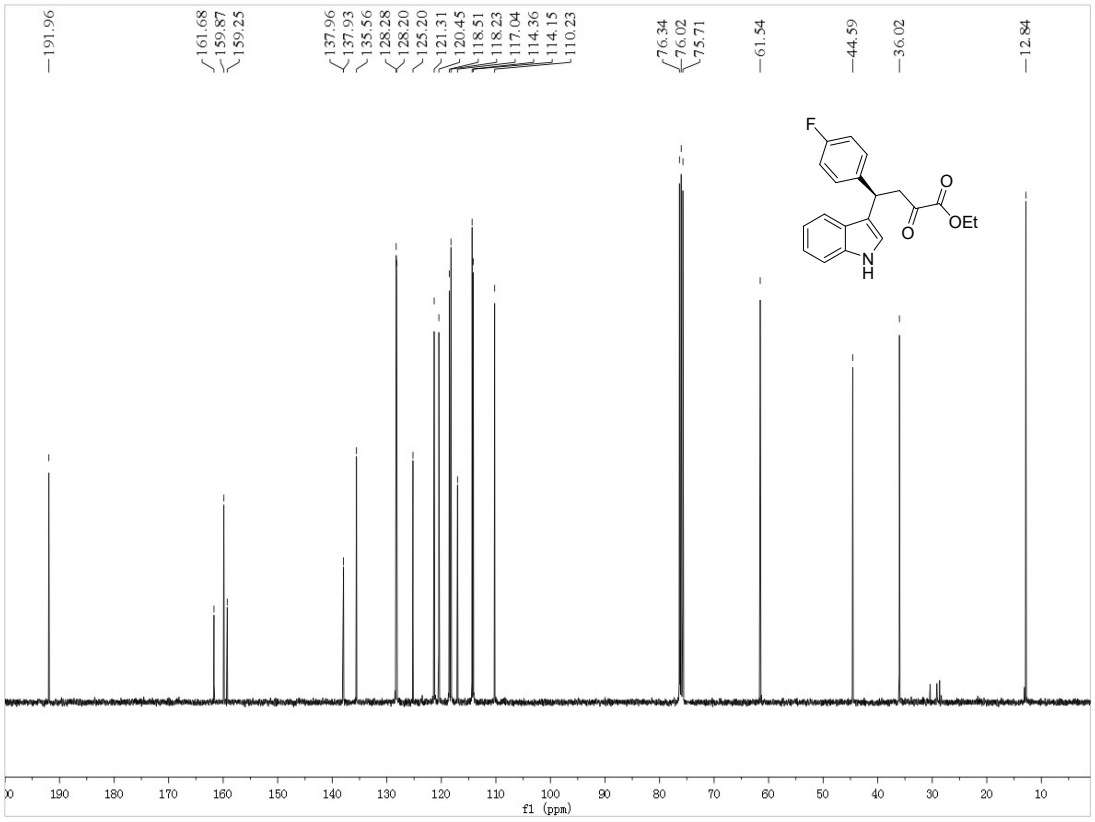
#	Time	Area	Height	Width	Area%	Symmetry
1	16.574	20801.7	229.6	1.2619	50.580	0.445
2	22.073	20325	165.4	1.7342	49.420	0.469



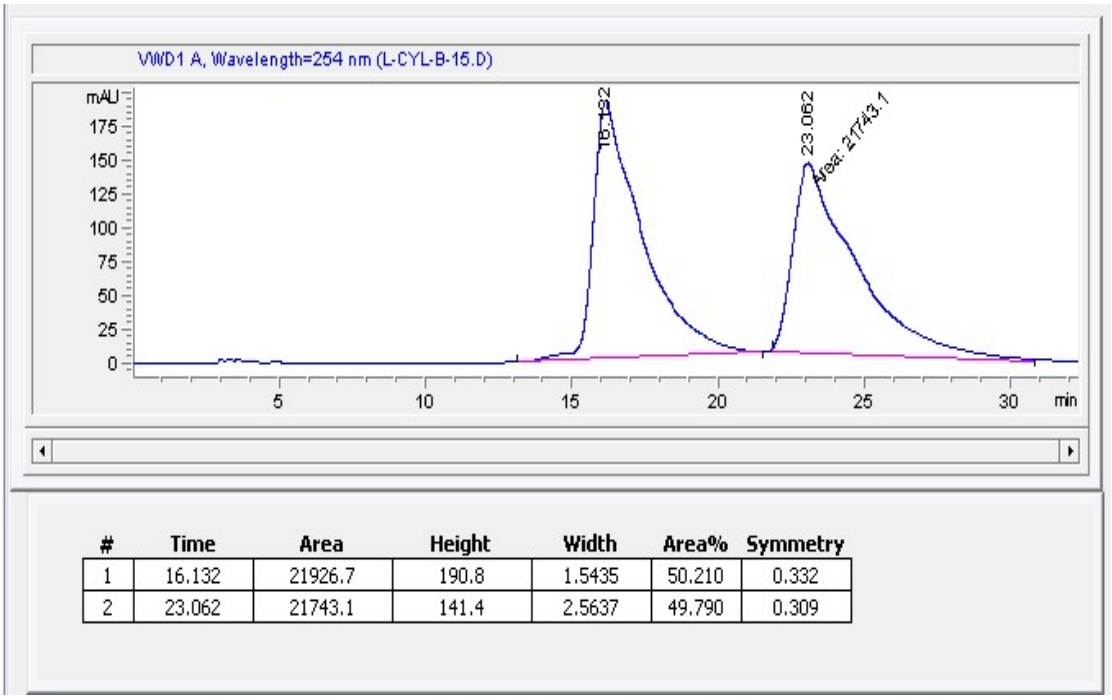
#	Time	Area	Height	Width	Area%	Symmetry
1	14.984	96729.3	1309.9	1.0075	96.757	0.273
2	19.818	3242.5	37.5	1.1959	3.243	0.527

^{1}H and ^{13}C NMR of 7c

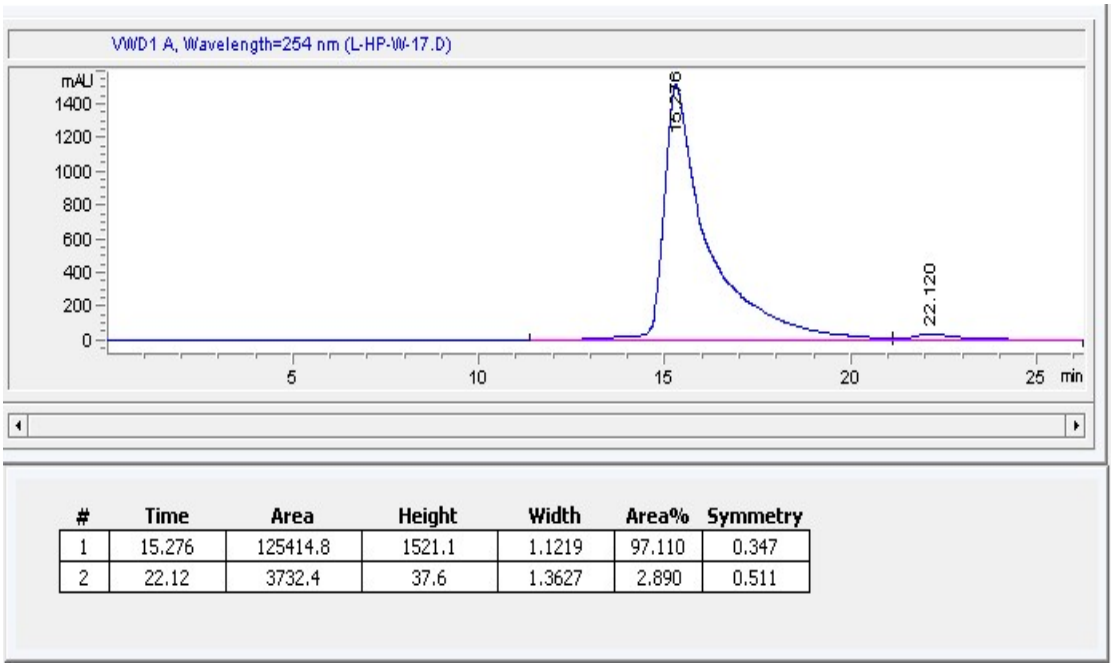




HPLC of 7c

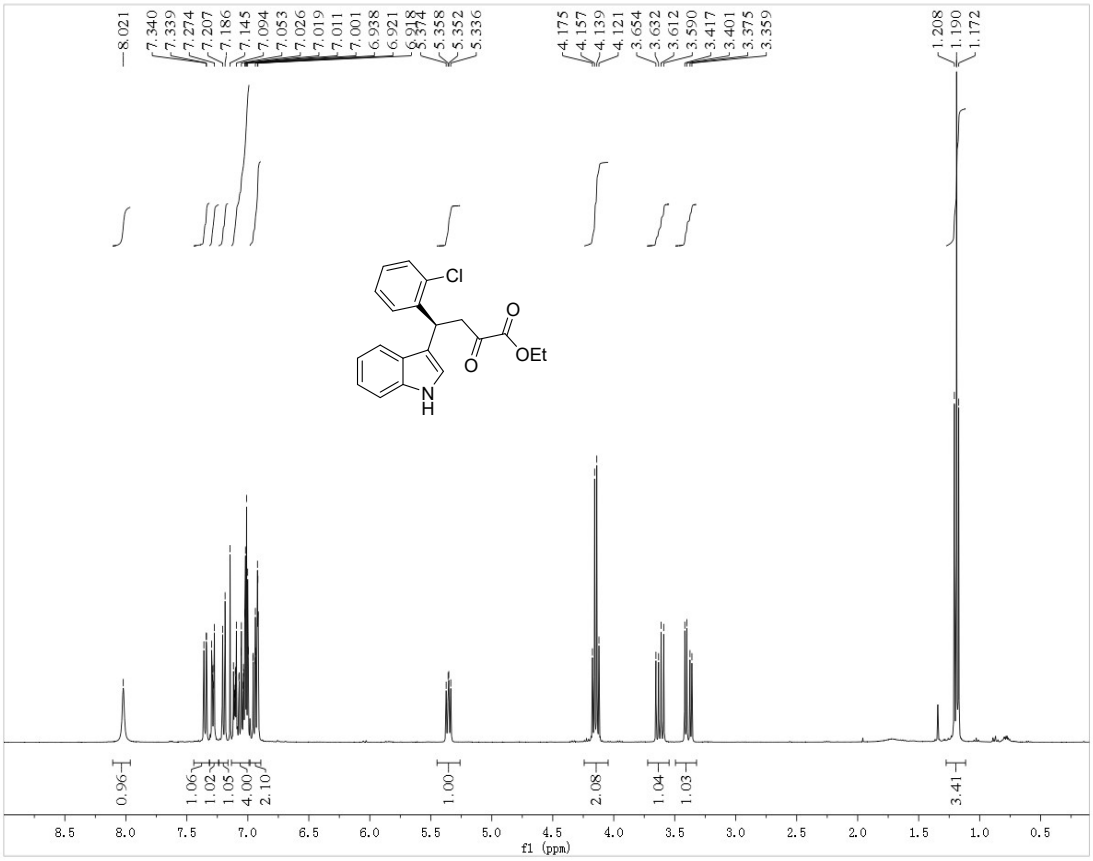


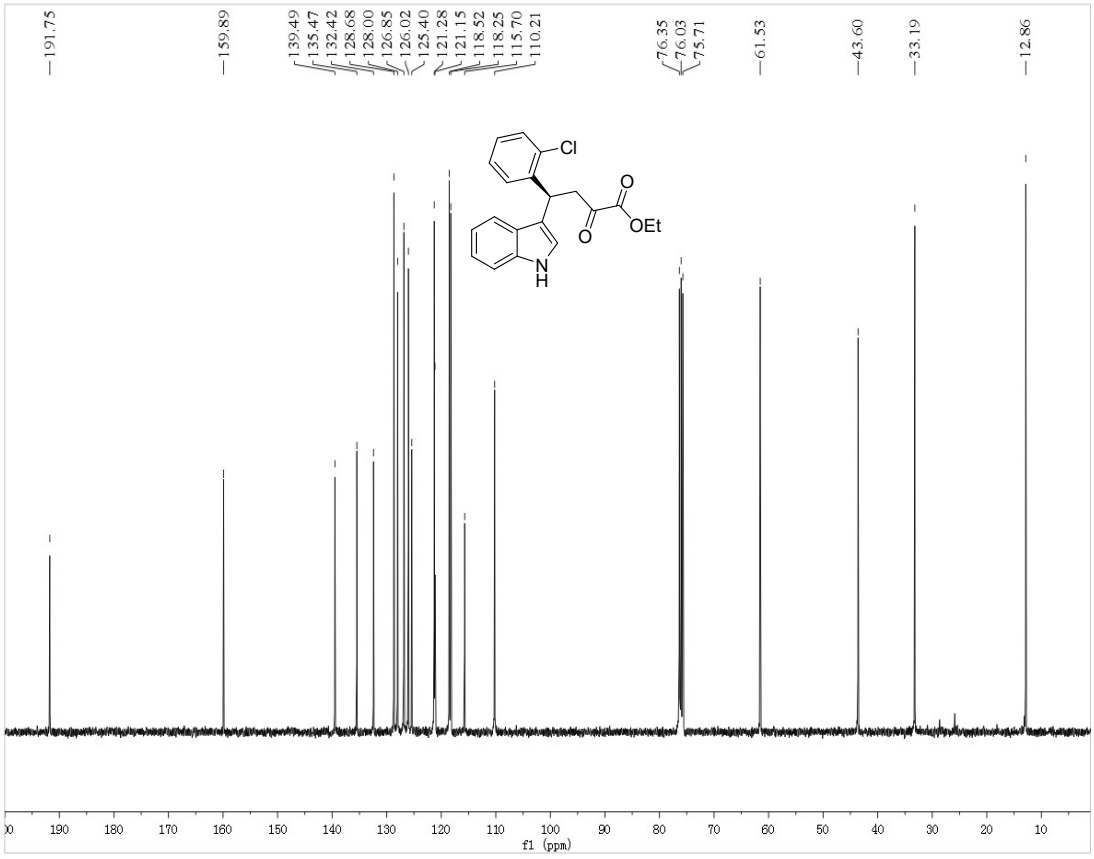
#	Time	Area	Height	Width	Area%	Symmetry
1	16.132	21926.7	190.8	1.5435	50.210	0.332
2	23.062	21743.1	141.4	2.5637	49.790	0.309



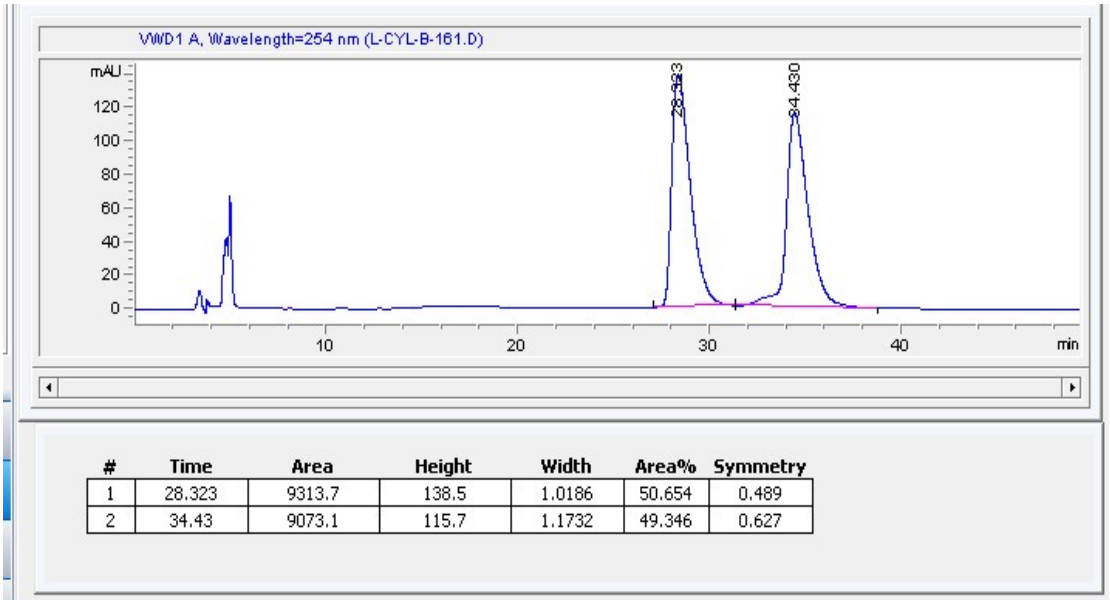
#	Time	Area	Height	Width	Area%	Symmetry
1	15.276	125414.8	1521.1	1.1219	97.110	0.347
2	22.12	3732.4	37.6	1.3627	2.890	0.511

^{1}H and ^{13}C NMR of 7d

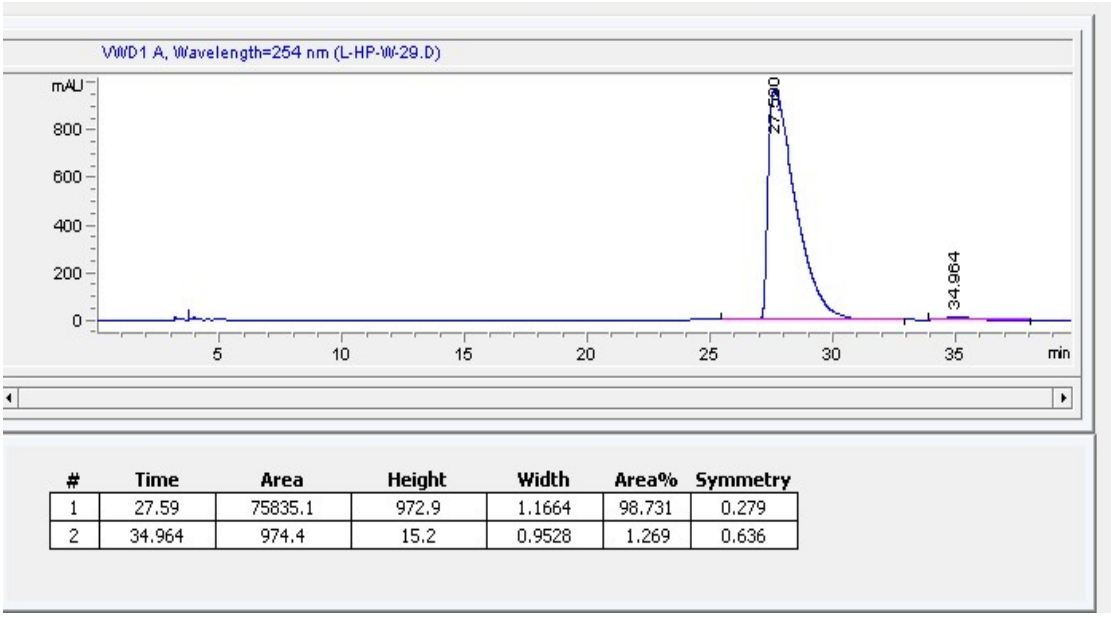




HPLC of 7d

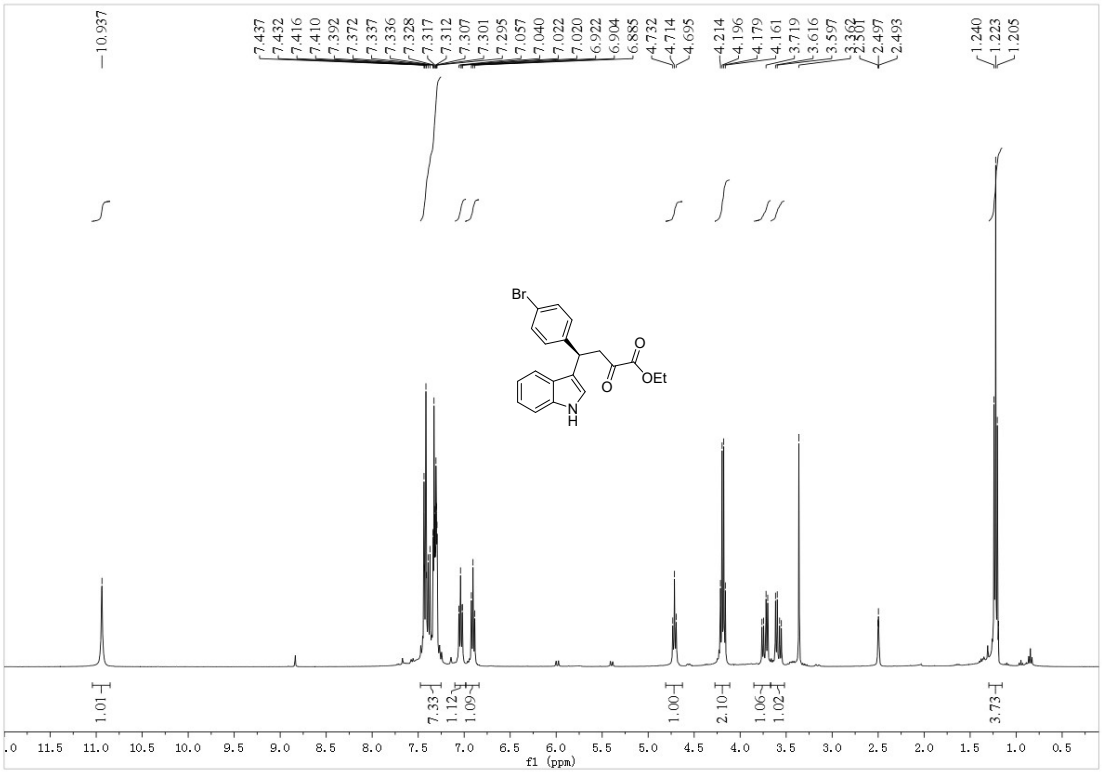


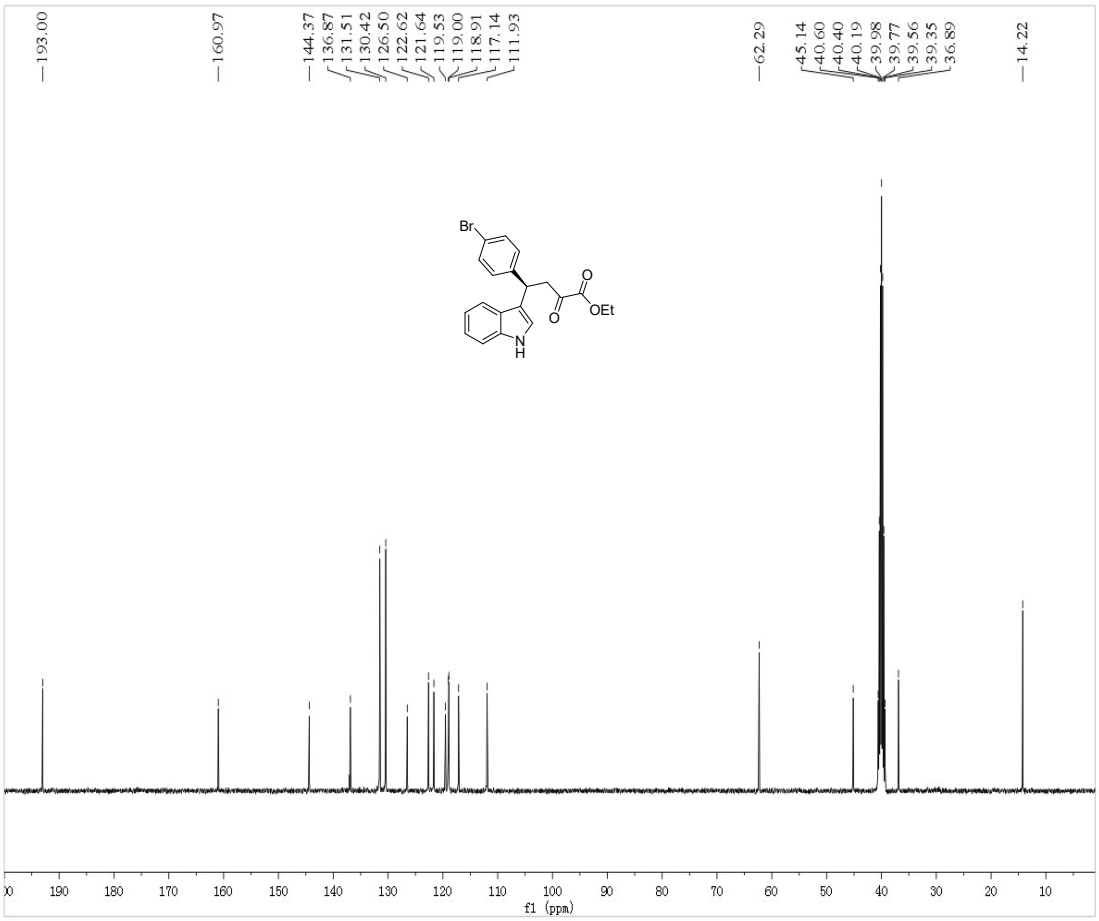
#	Time	Area	Height	Width	Area%	Symmetry
1	28.323	9313.7	138.5	1.0186	50.654	0.489
2	34.43	9073.1	115.7	1.1732	49.346	0.627



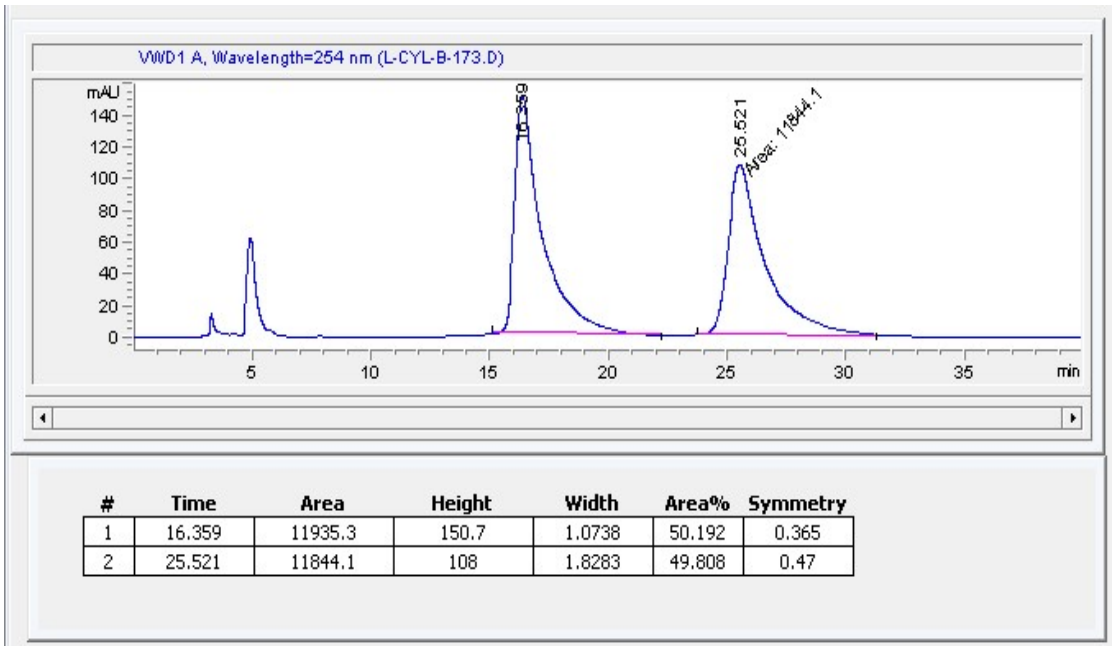
#	Time	Area	Height	Width	Area%	Symmetry
1	27.59	75835.1	972.9	1.1664	98.731	0.279
2	34.964	974.4	15.2	0.9528	1.269	0.636

^{1}H and ^{13}C NMR of 7e

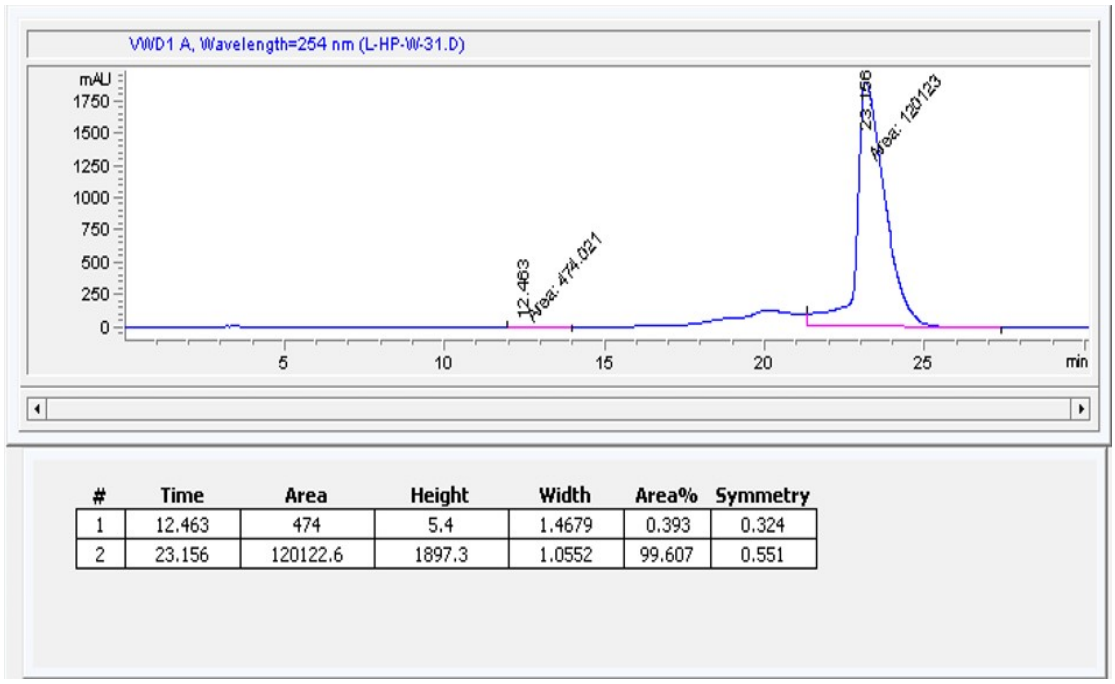




HPLC of 7e

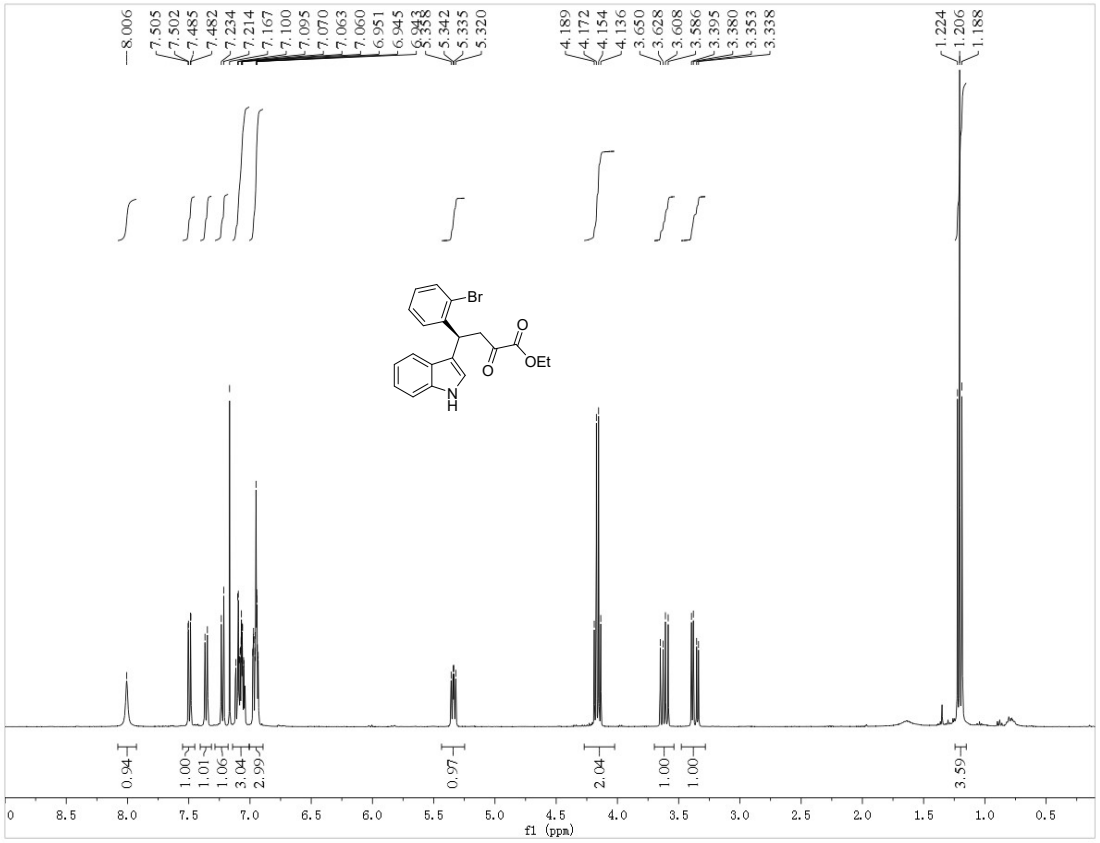


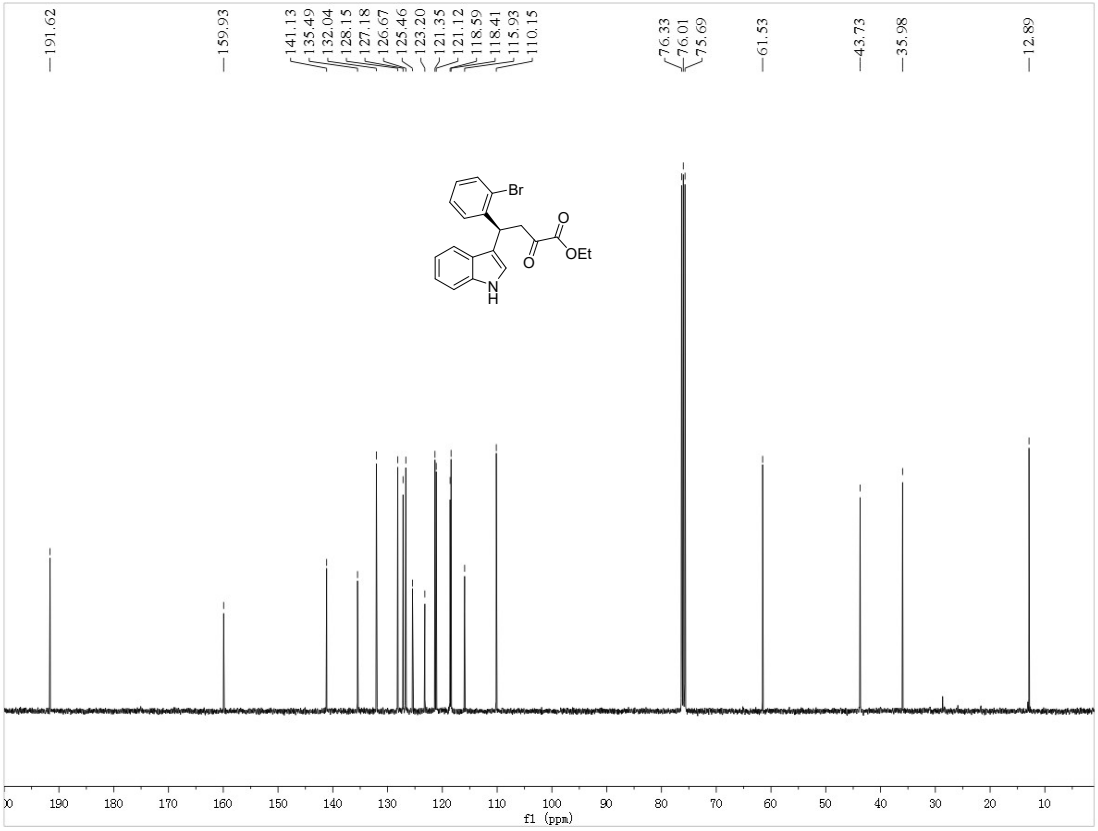
#	Time	Area	Height	Width	Area%	Symmetry
1	16.359	11935.3	150.7	1.0738	50.192	0.365
2	25.521	11844.1	108	1.8283	49.808	0.47



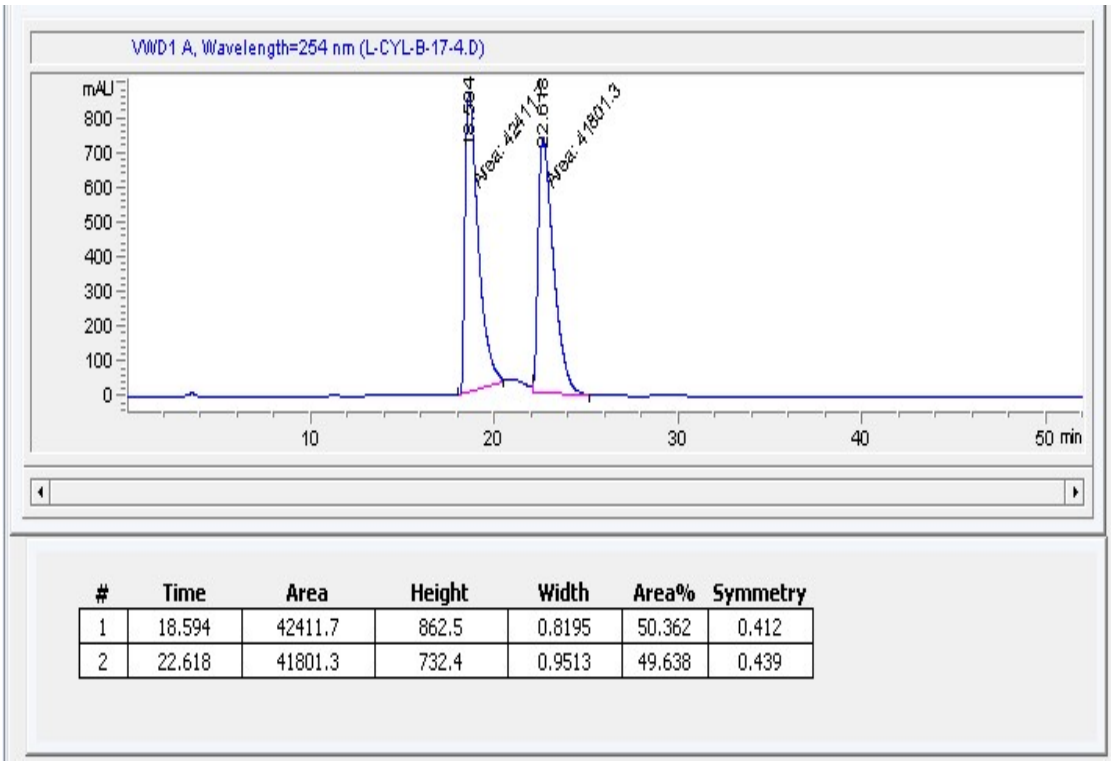
#	Time	Area	Height	Width	Area%	Symmetry
1	12.463	474	5.4	1.4679	0.393	0.324
2	23.156	120122.6	1897.3	1.0552	99.607	0.551

^{1}H and ^{13}C NMR of 7f

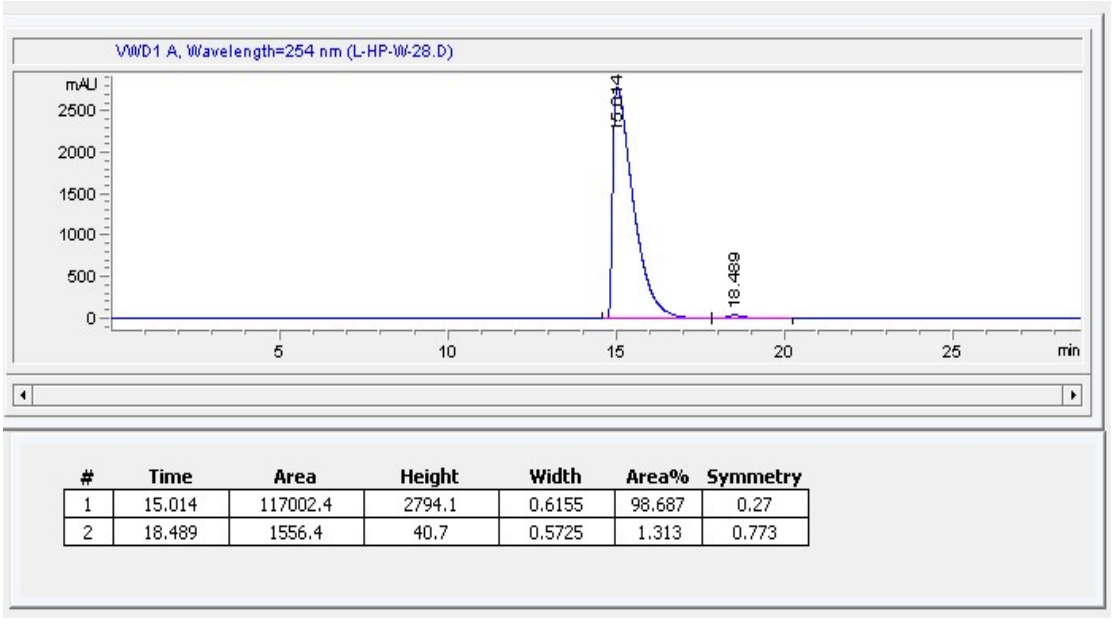




HPLC of 7f

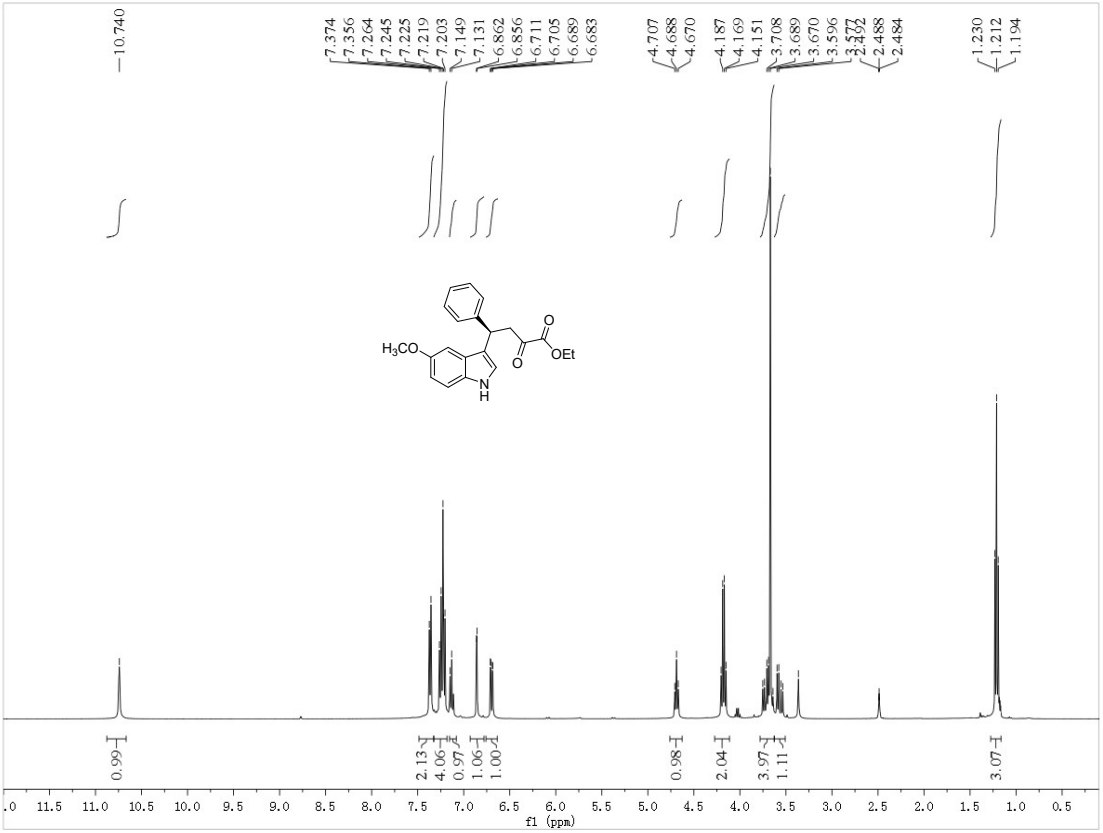


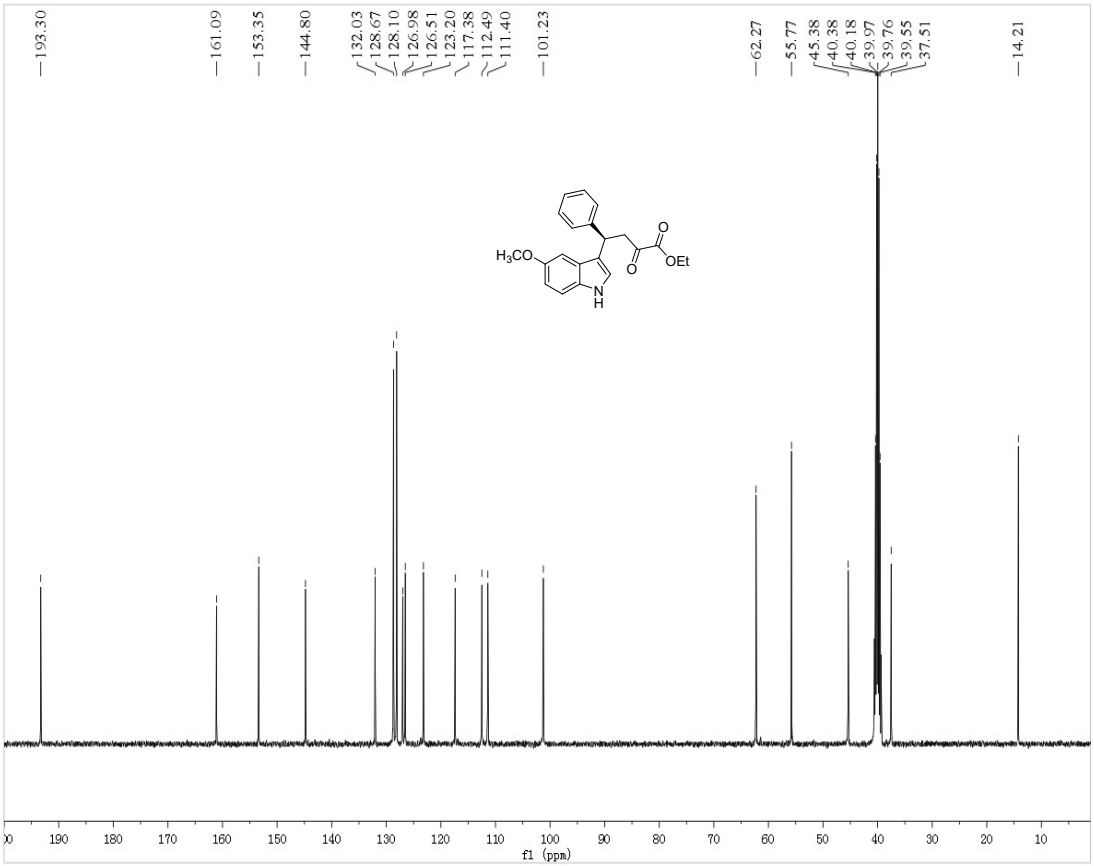
#	Time	Area	Height	Width	Area%	Symmetry
1	18.594	42411.7	862.5	0.8195	50.362	0.412
2	22.618	41801.3	732.4	0.9513	49.638	0.439



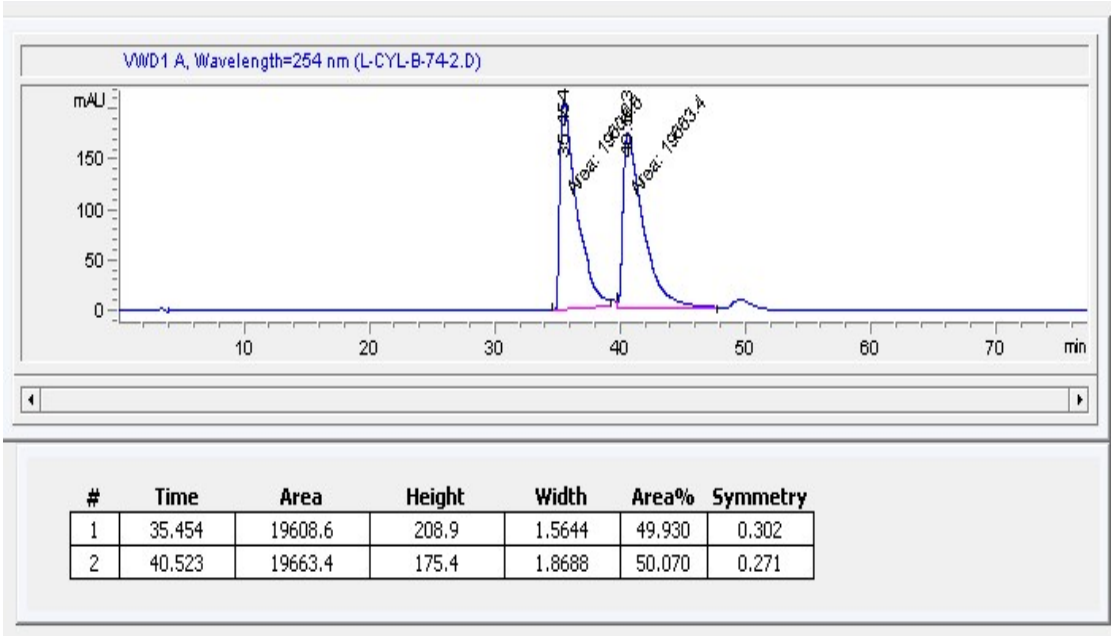
#	Time	Area	Height	Width	Area%	Symmetry
1	15.014	117002.4	2794.1	0.6155	98.687	0.27
2	18.489	1556.4	40.7	0.5725	1.313	0.773

^{1}H and ^{13}C NMR of 7g

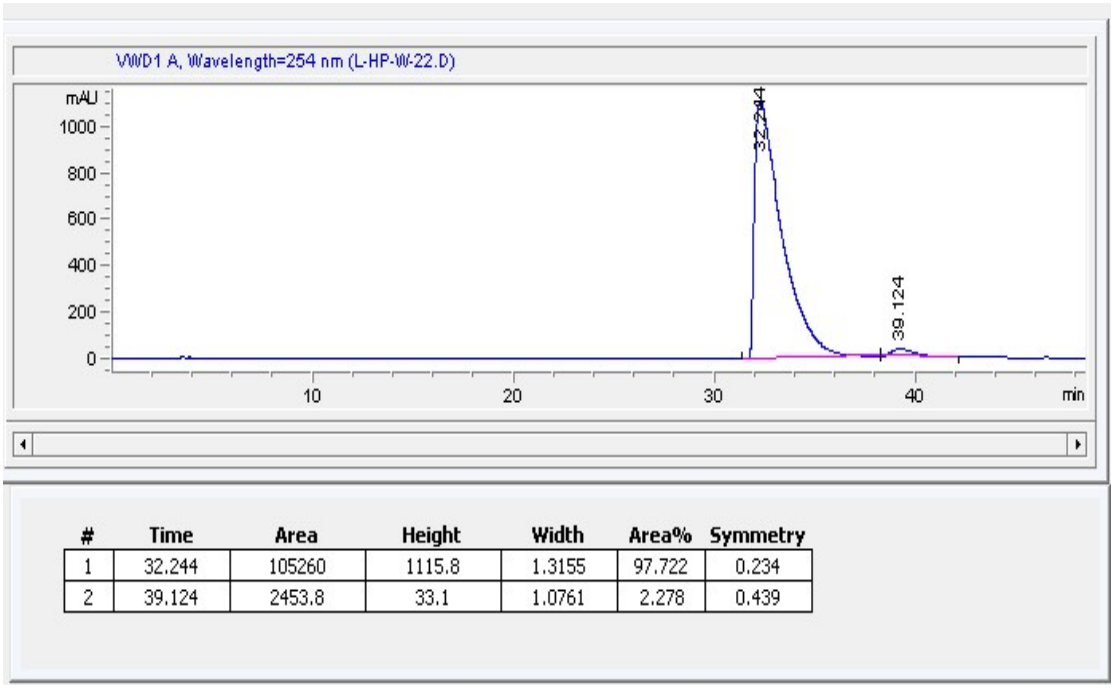




HPLC of 7g

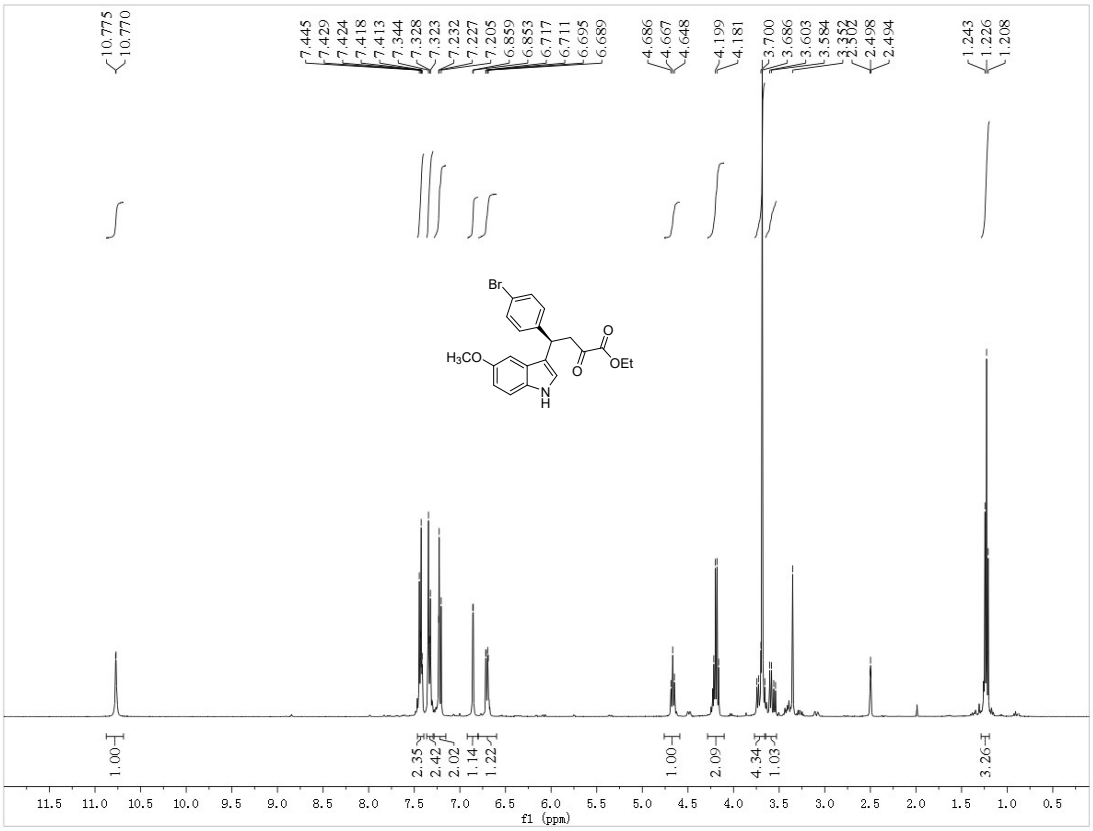


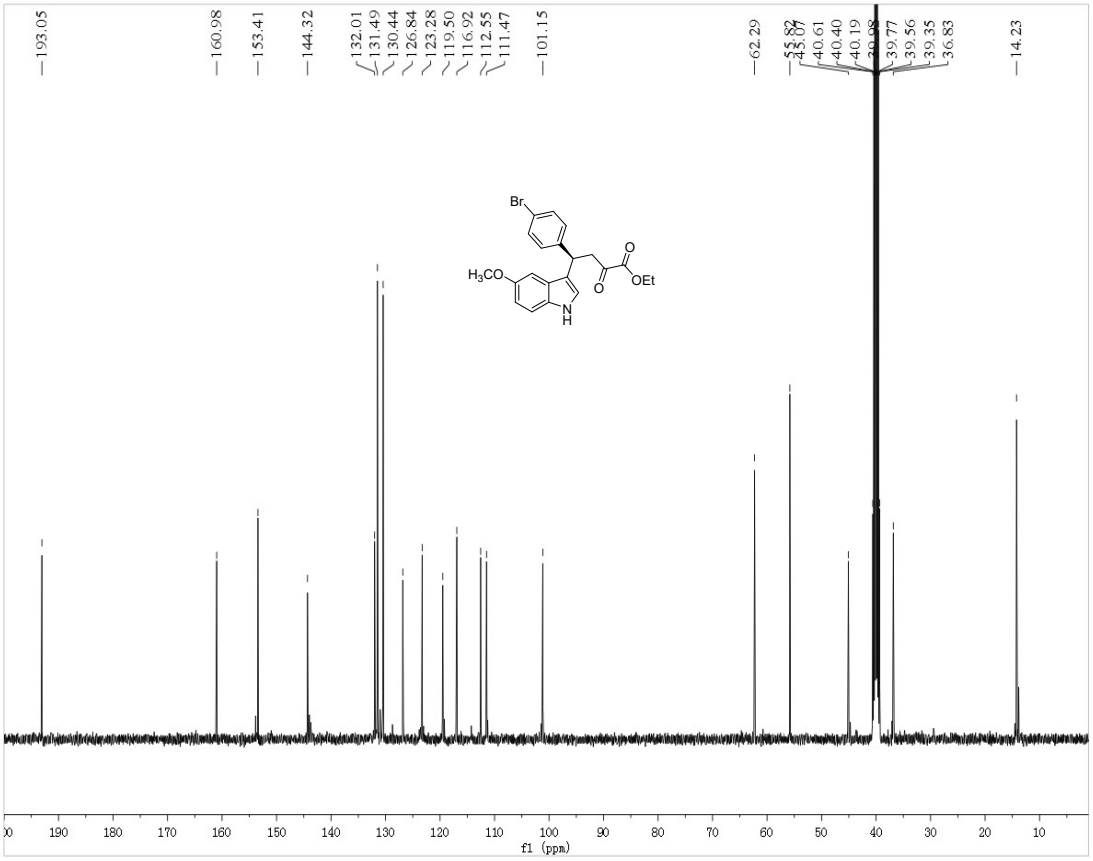
#	Time	Area	Height	Width	Area%	Symmetry
1	35.454	19608.6	208.9	1.5644	49.930	0.302
2	40.523	19663.4	175.4	1.8688	50.070	0.271



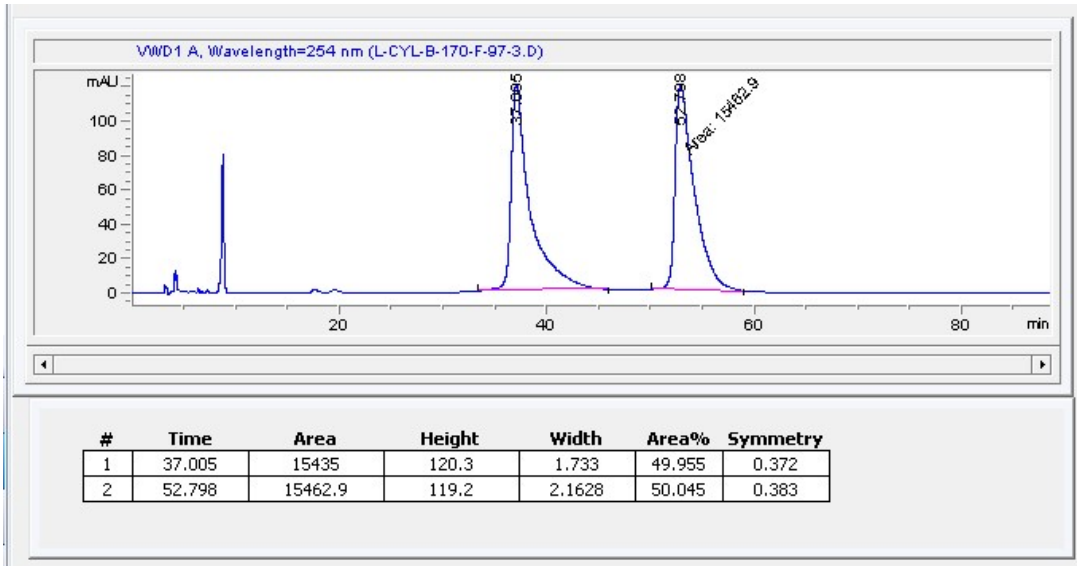
#	Time	Area	Height	Width	Area%	Symmetry
1	32.244	105260	1115.8	1.3155	97.722	0.234
2	39.124	2453.8	33.1	1.0761	2.278	0.439

^{1}H and ^{13}C NMR of 7h

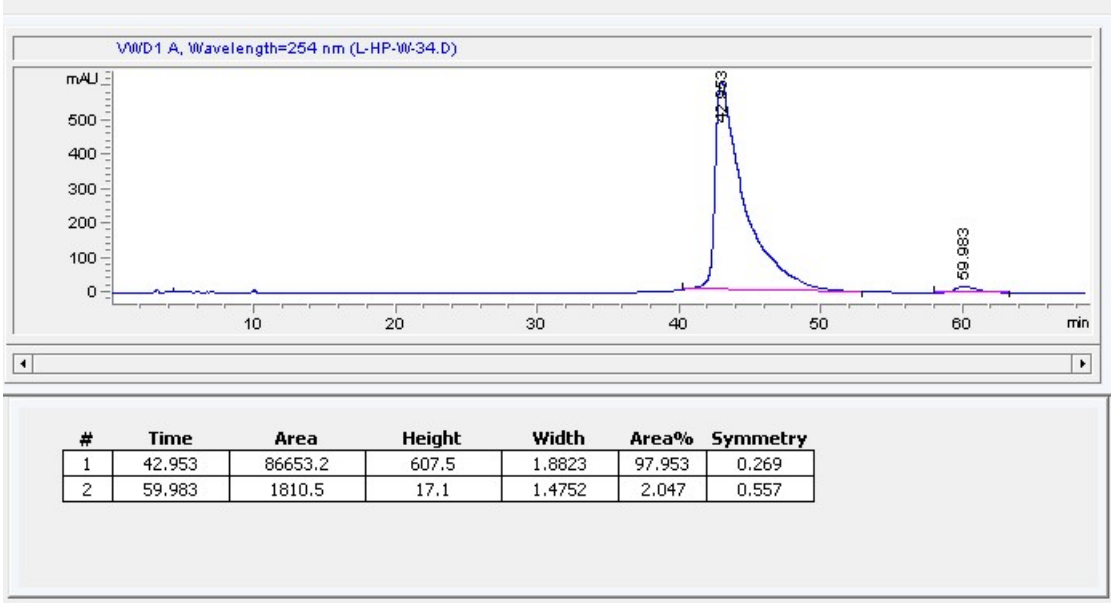




HPLC of 7h

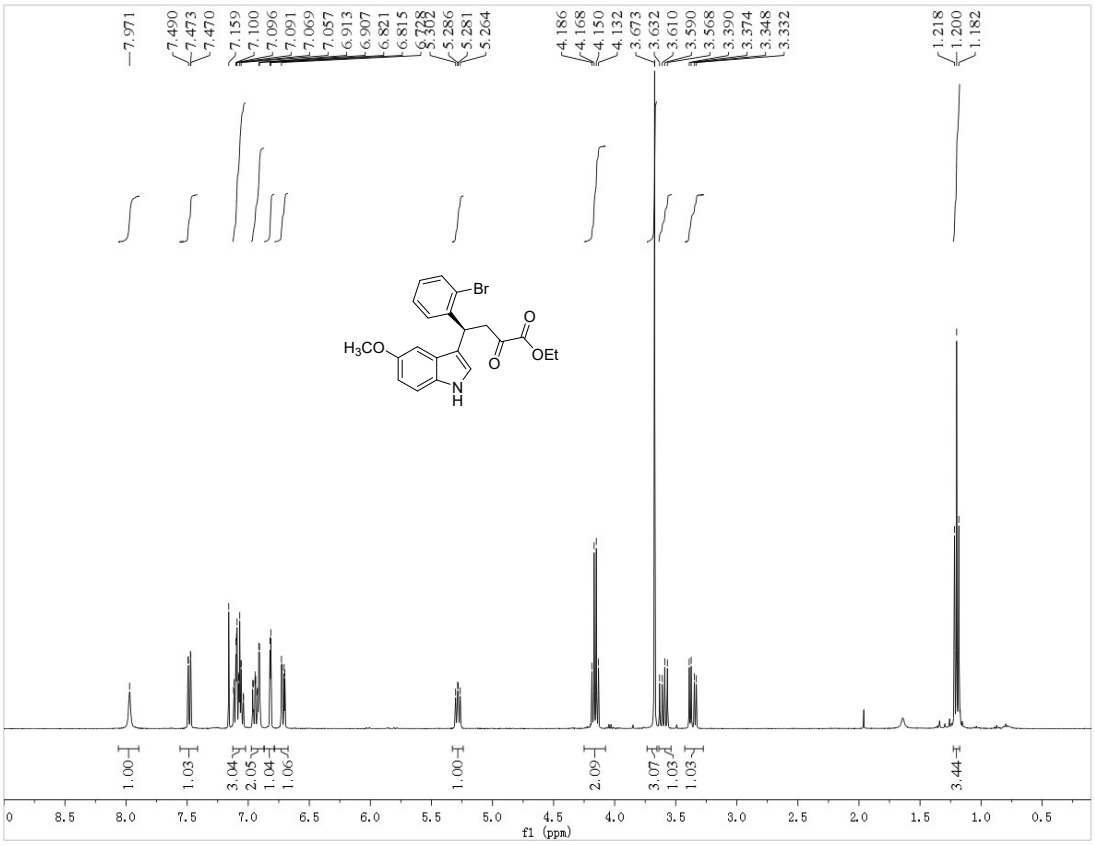


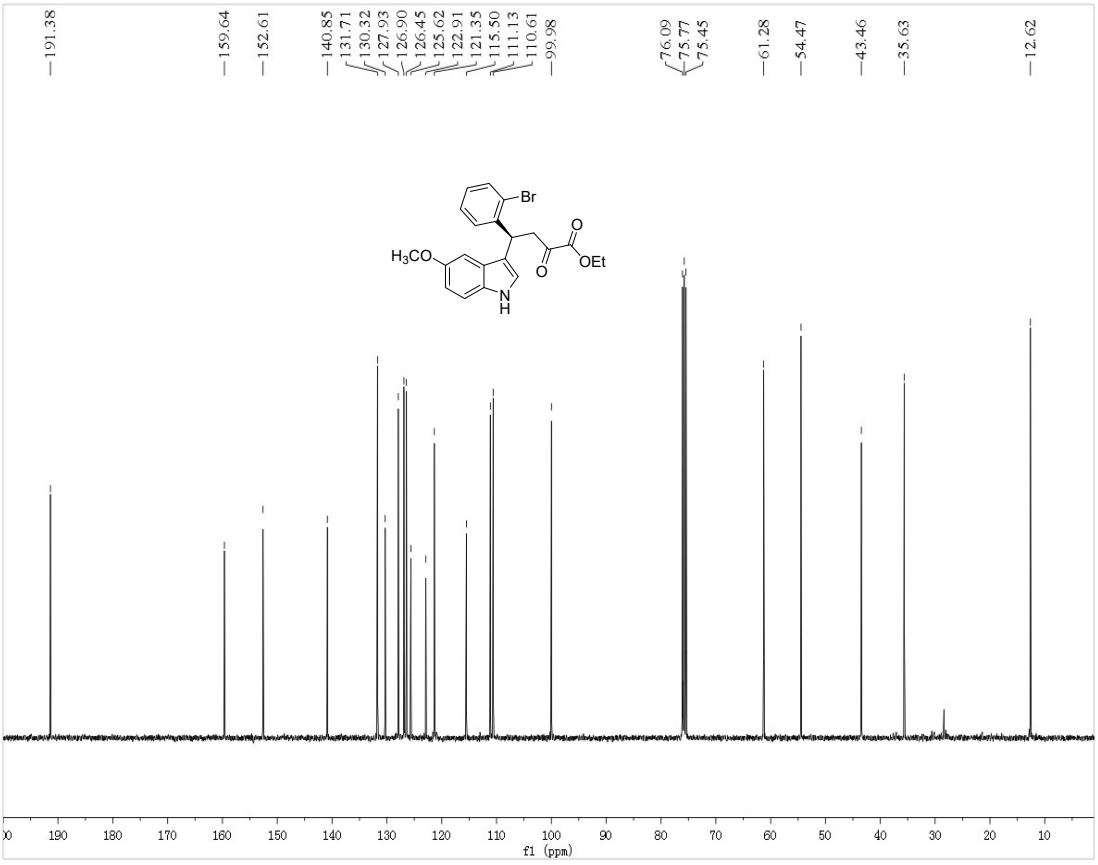
#	Time	Area	Height	Width	Area%	Symmetry
1	37.005	15435	120.3	1.733	49.955	0.372
2	52.798	15462.9	119.2	2.1628	50.045	0.383



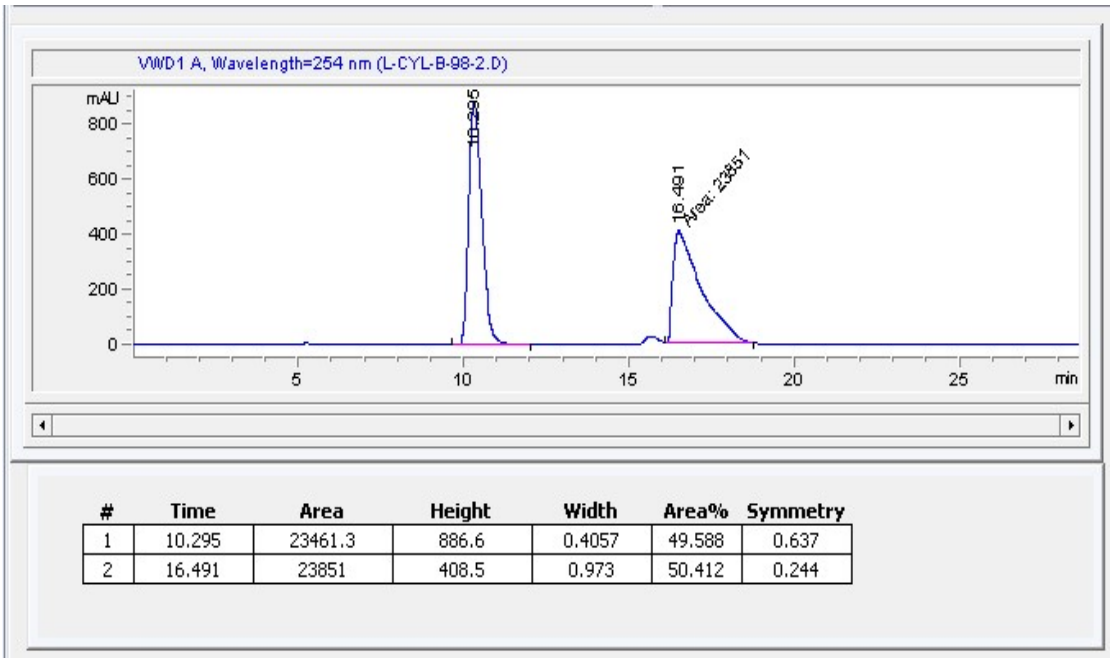
#	Time	Area	Height	Width	Area%	Symmetry
1	42.953	86653.2	607.5	1.8823	97.953	0.269
2	59.983	1810.5	17.1	1.4752	2.047	0.557

^{1}H and ^{13}C NMR of 7i

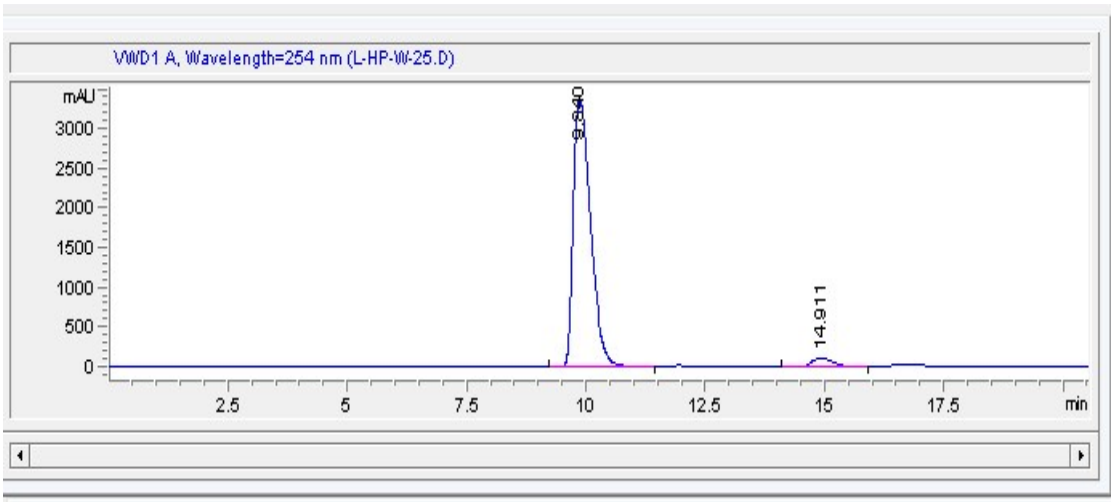




HPLC of 7i

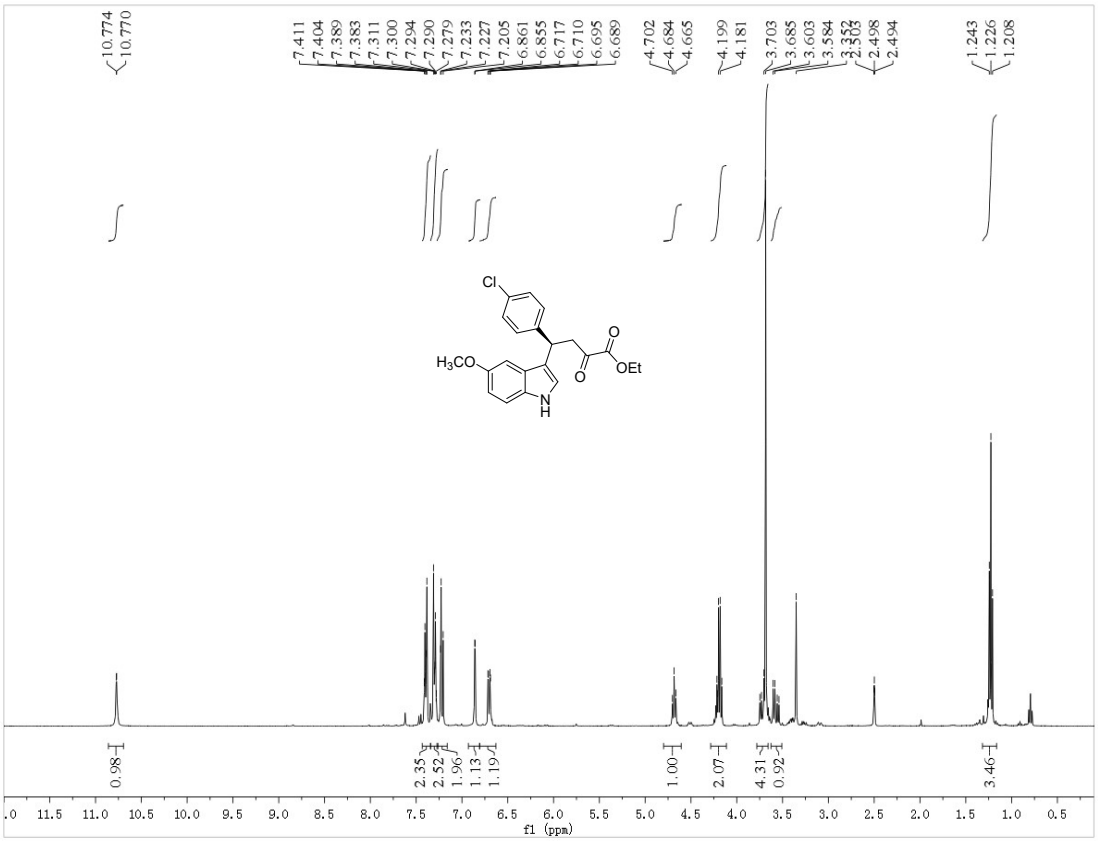


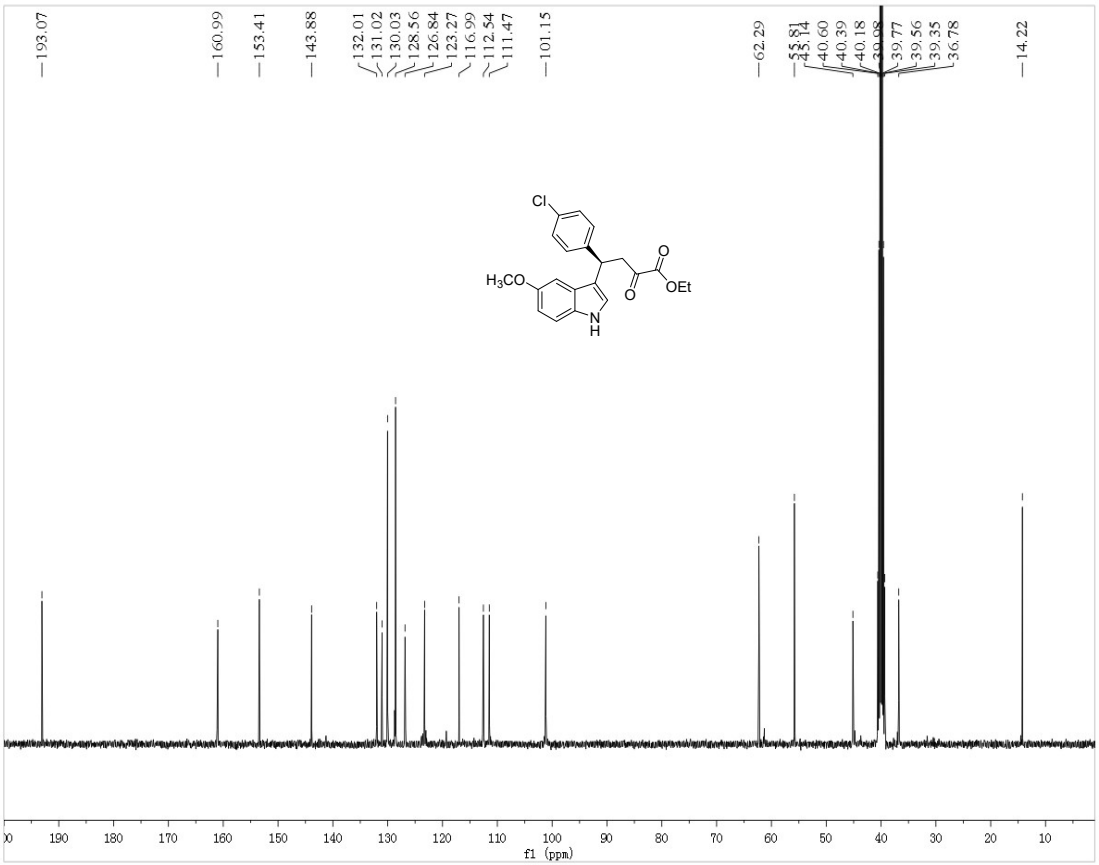
#	Time	Area	Height	Width	Area%	Symmetry
1	10.295	23461.3	886.6	0.4057	49.588	0.637
2	16.491	23851	408.5	0.973	50.412	0.244



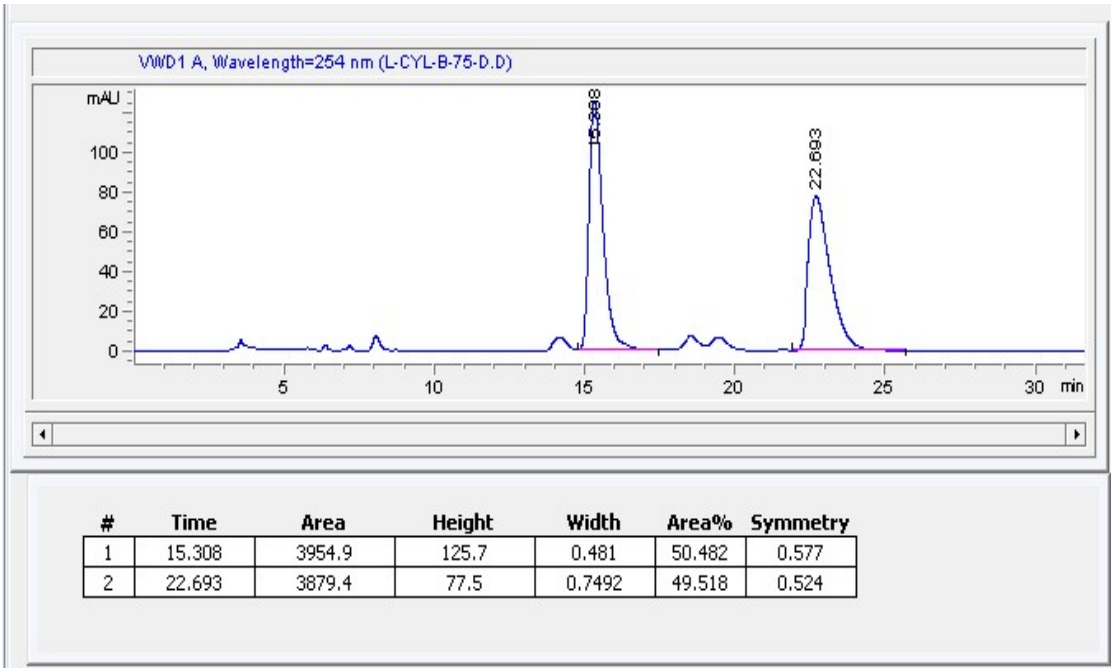
#	Time	Area	Height	Width	Area%	Symmetry
1	9.84	86286.8	3379.5	0.3929	96.232	0.535
2	14.911	3379	113.1	0.4586	3.768	0.699

^{1}H and ^{13}C NMR of 7j

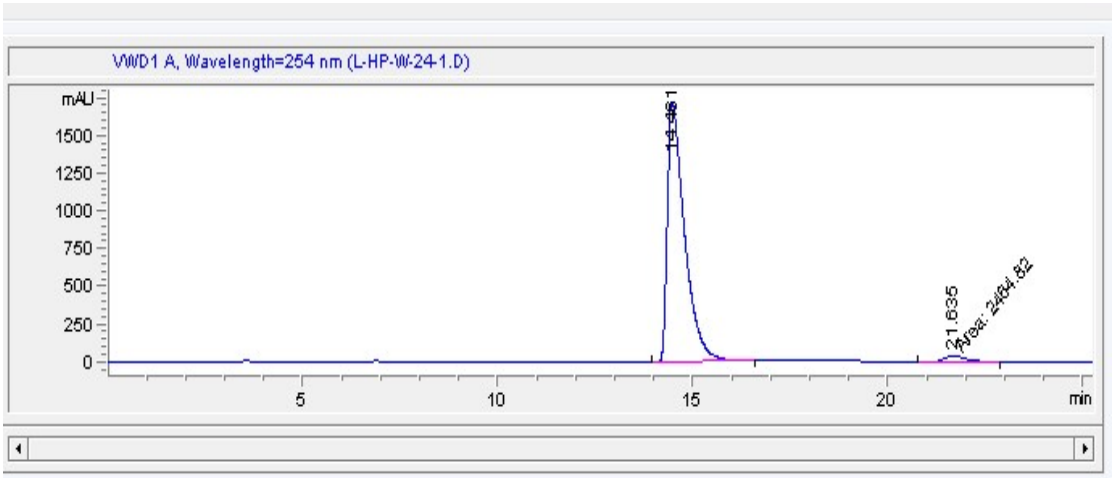




HPLC of 7j

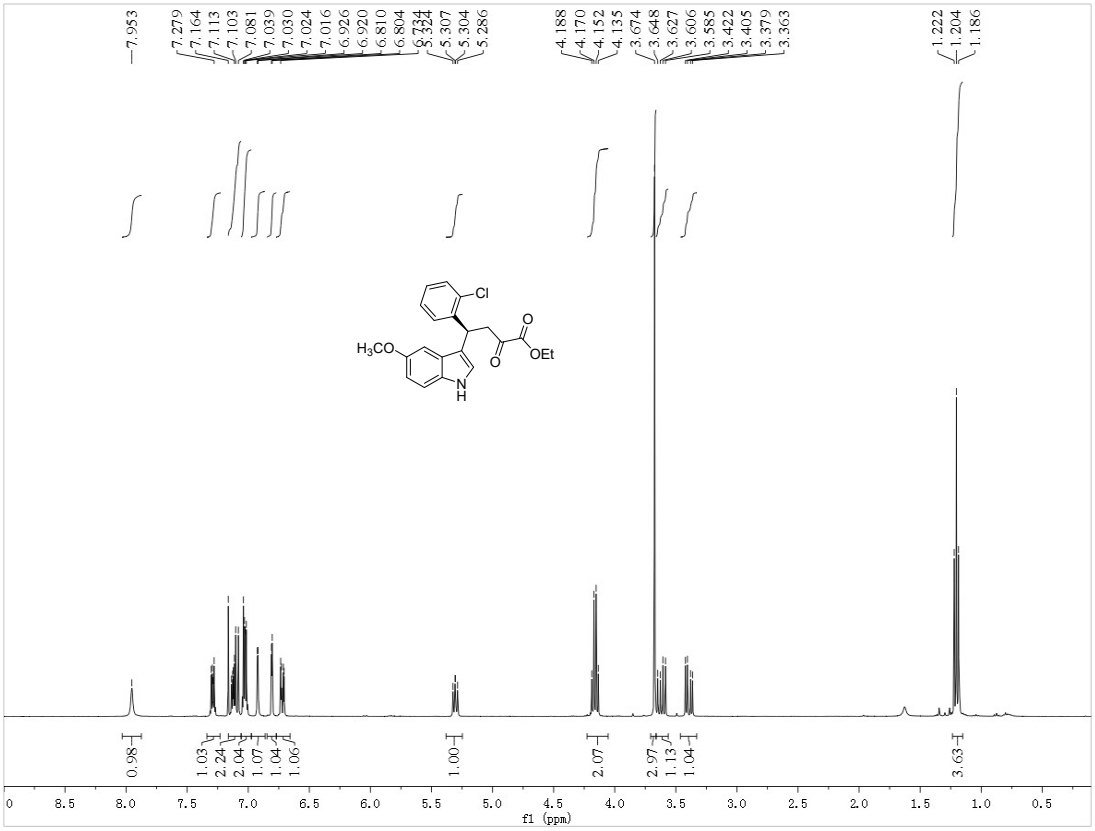


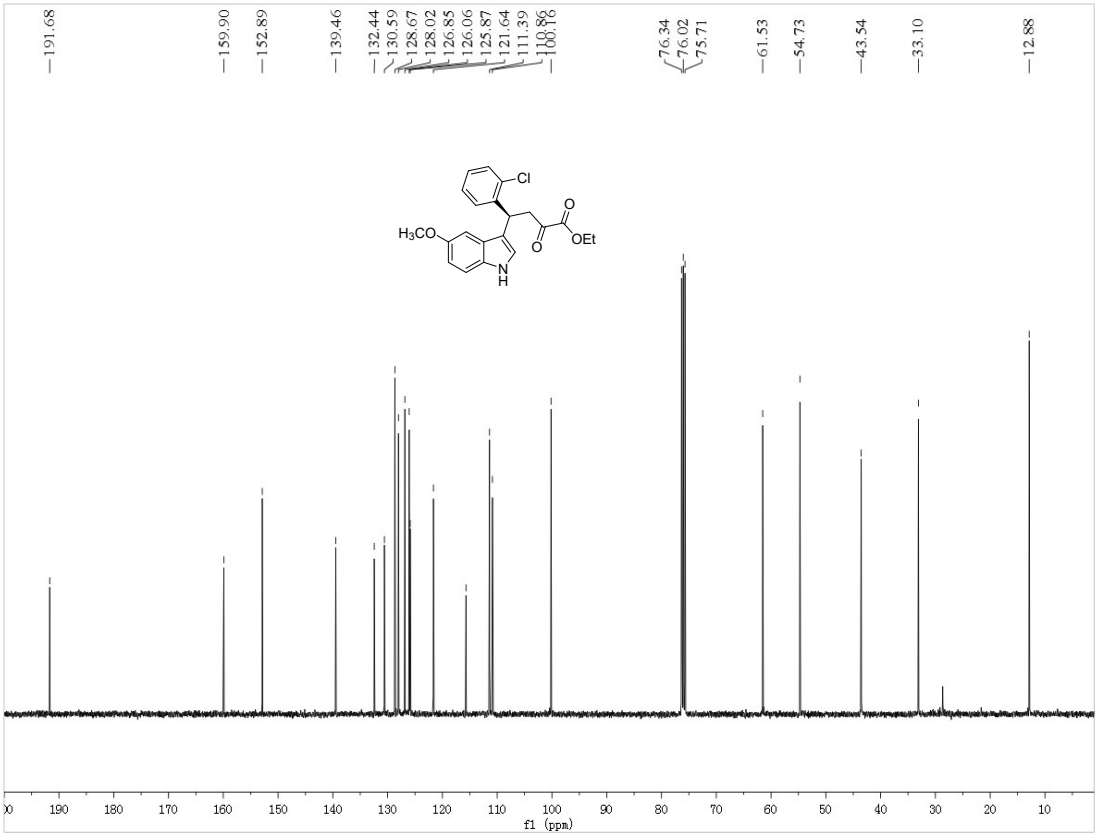
#	Time	Area	Height	Width	Area%	Symmetry
1	15.308	3954.9	125.7	0.481	50.482	0.577
2	22.693	3879.4	77.5	0.7492	49.518	0.524



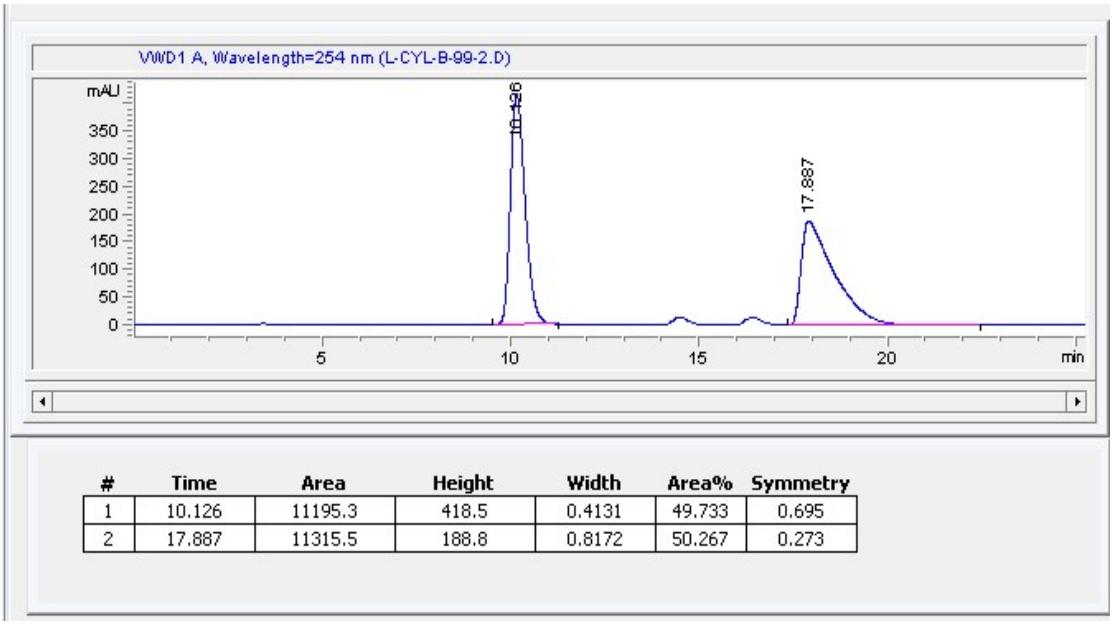
#	Time	Area	Height	Width	Area%	Symmetry
1	14.461	54900.7	1725.2	0.4783	95.703	0.427
2	21.635	2464.8	44	0.9344	4.297	0.578

^{1}H and ^{13}C NMR of 7k

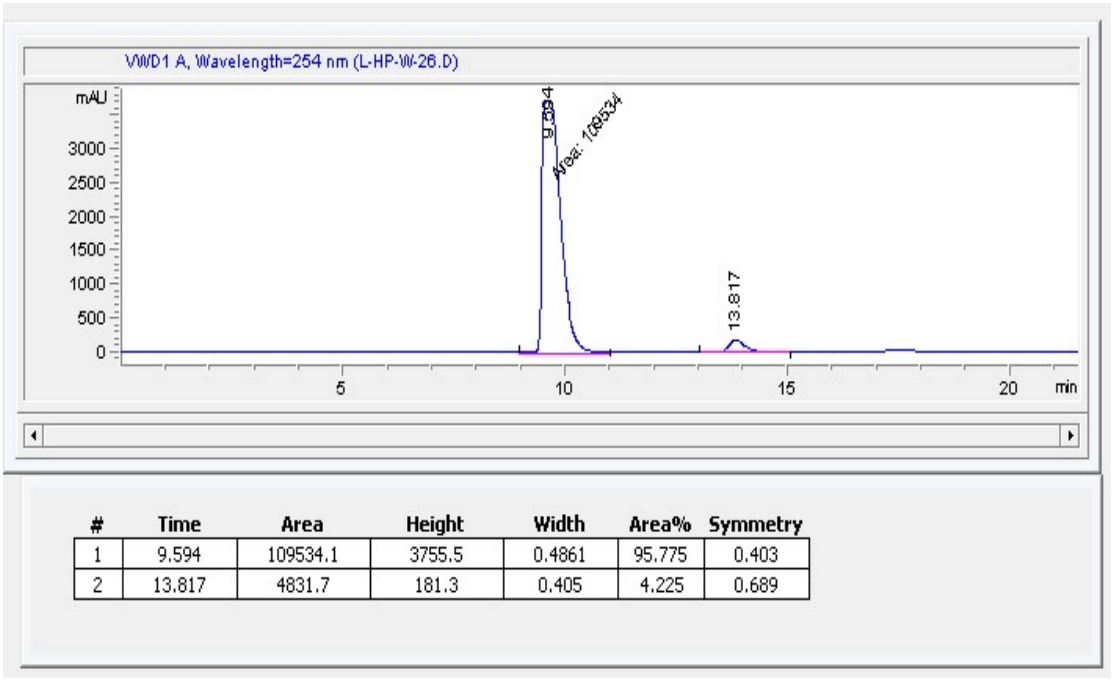




HPLC of 7k

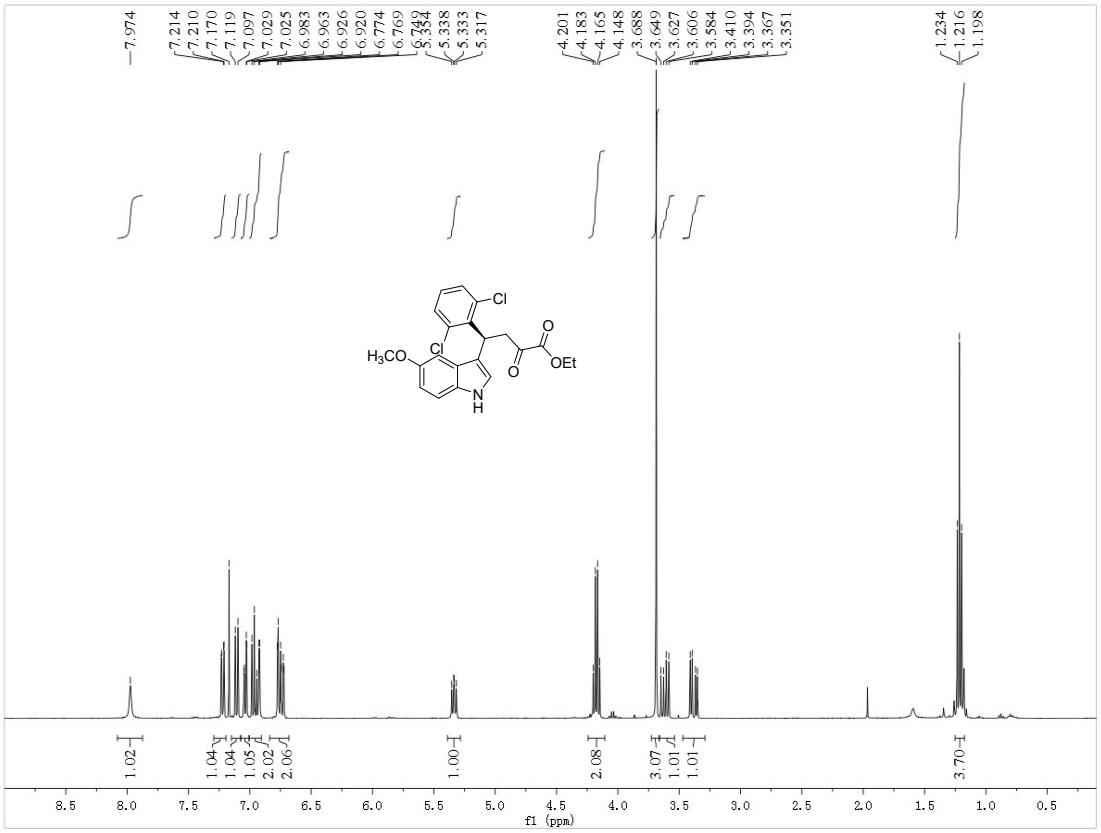


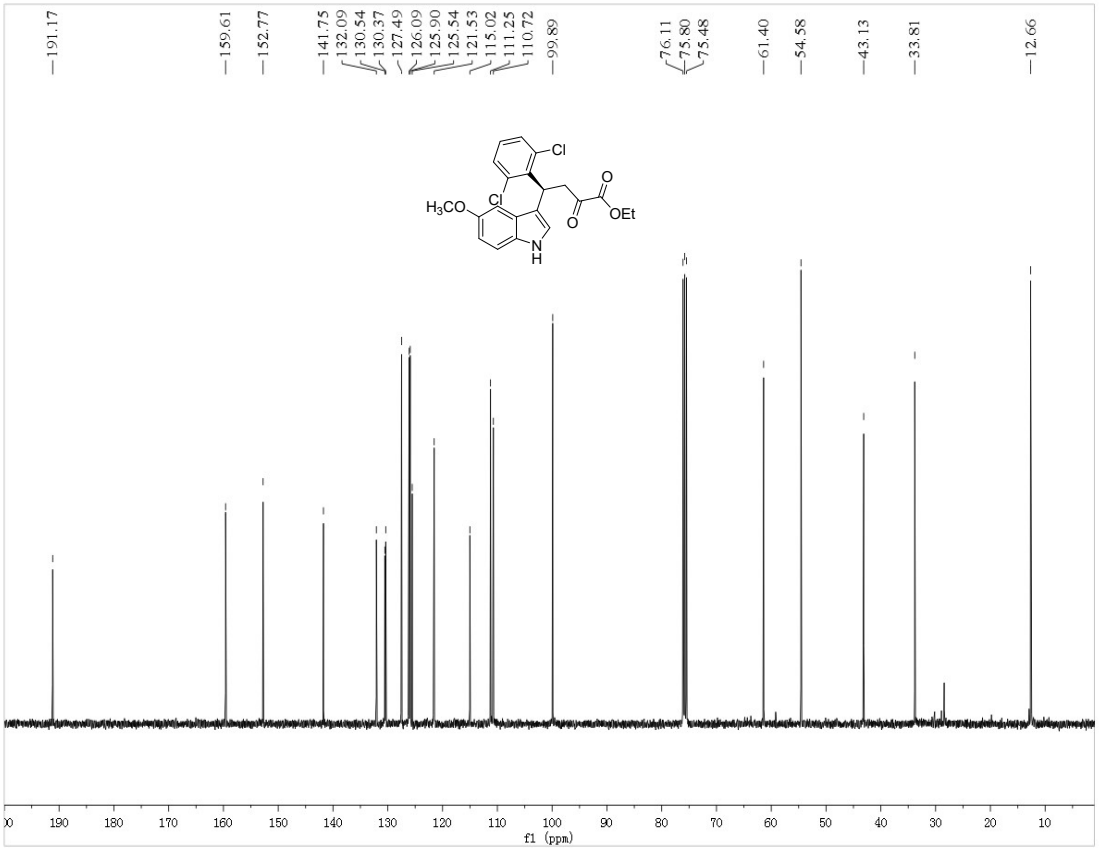
#	Time	Area	Height	Width	Area%	Symmetry
1	10.126	11195.3	418.5	0.4131	49.733	0.695
2	17.887	11315.5	188.8	0.8172	50.267	0.273



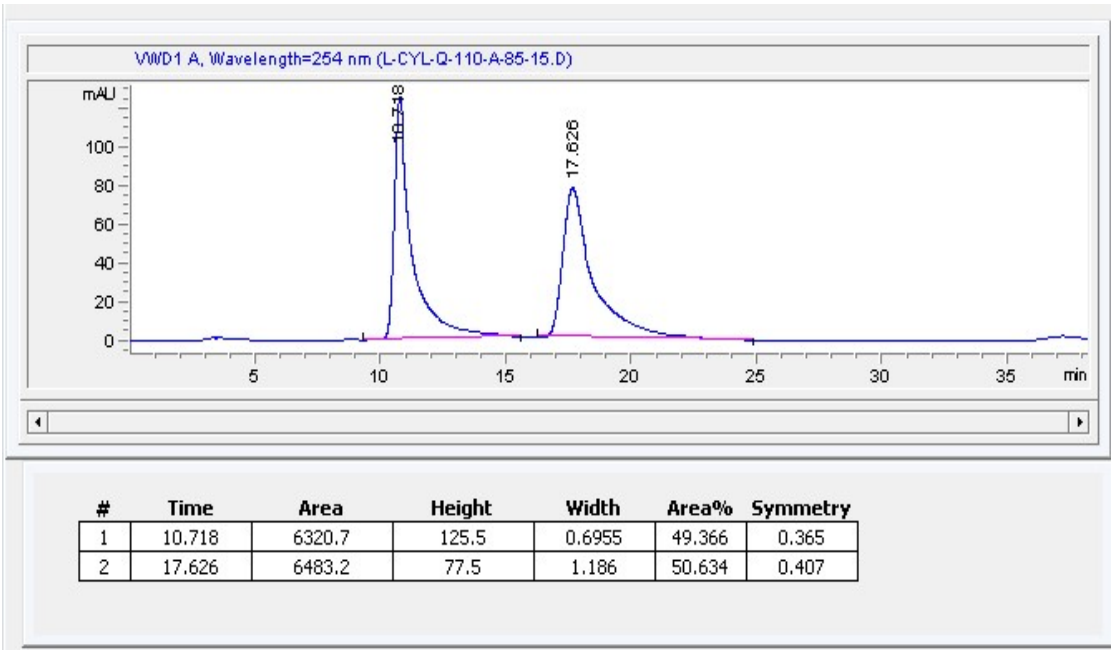
#	Time	Area	Height	Width	Area%	Symmetry
1	9.594	109534.1	3755.5	0.4861	95.775	0.403
2	13.817	4831.7	181.3	0.405	4.225	0.689

^{1}H and ^{13}C NMR of 7l

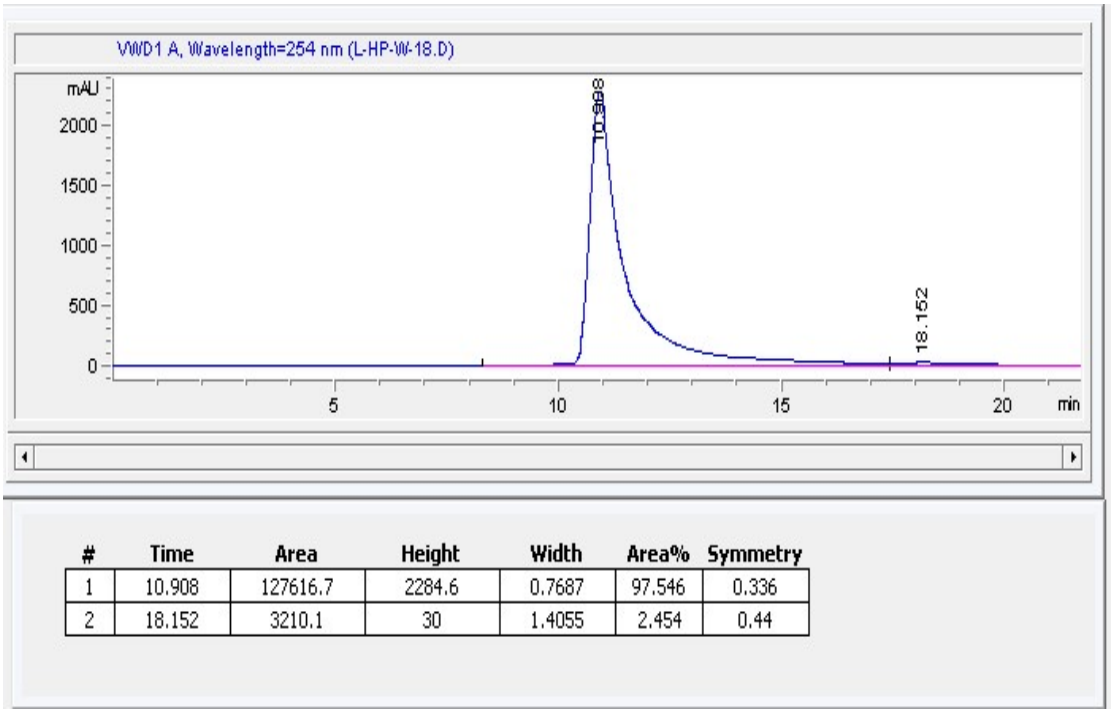




HPLC of 7l

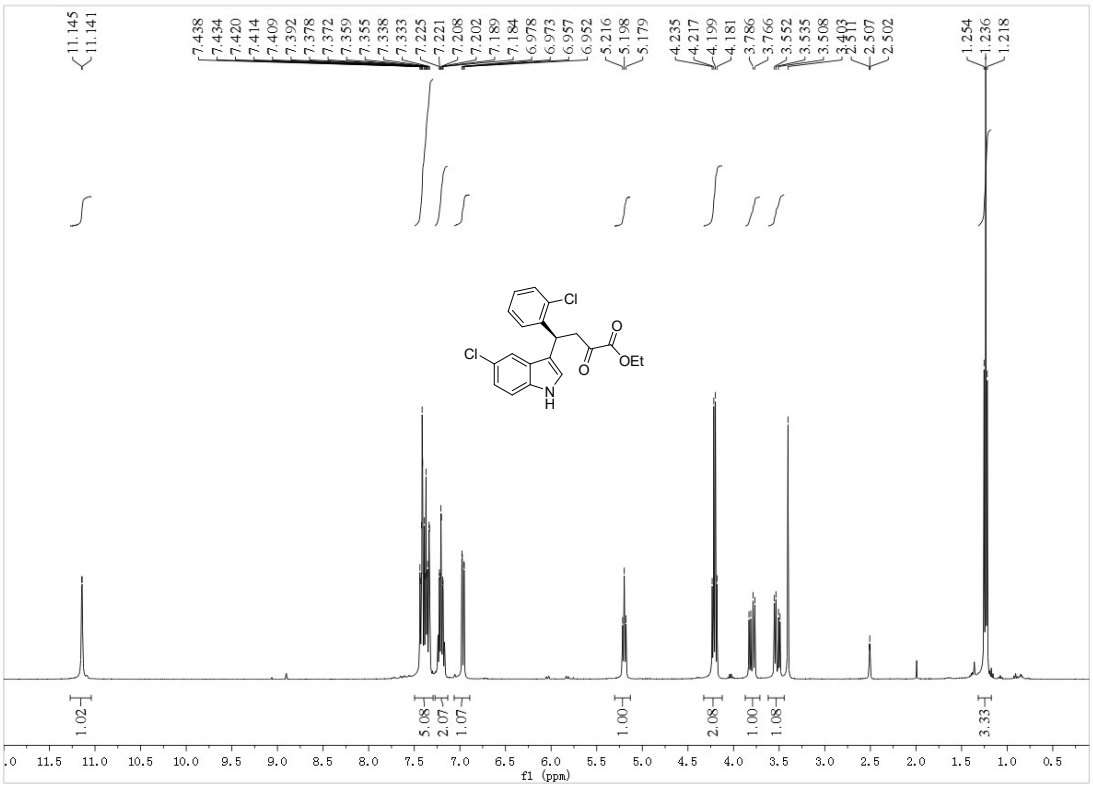


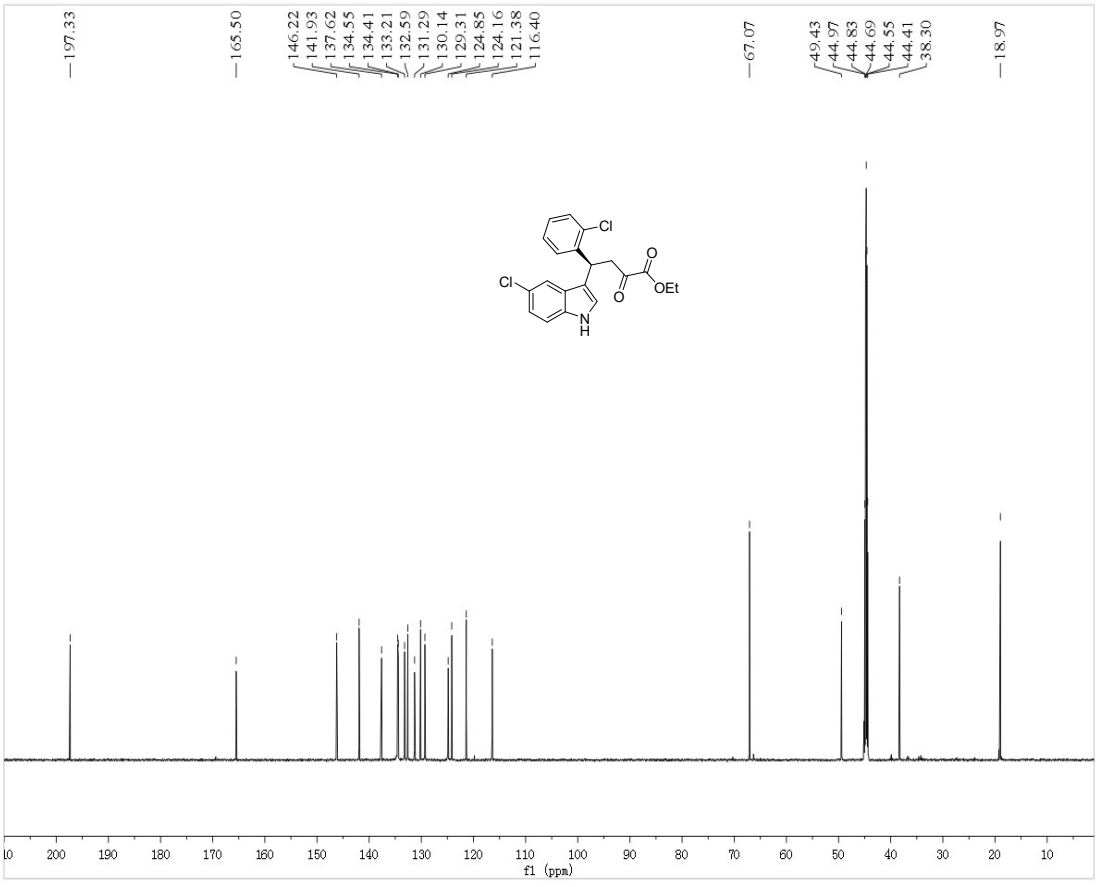
#	Time	Area	Height	Width	Area%	Symmetry
1	10.718	6320.7	125.5	0.6955	49.366	0.365
2	17.626	6483.2	77.5	1.186	50.634	0.407



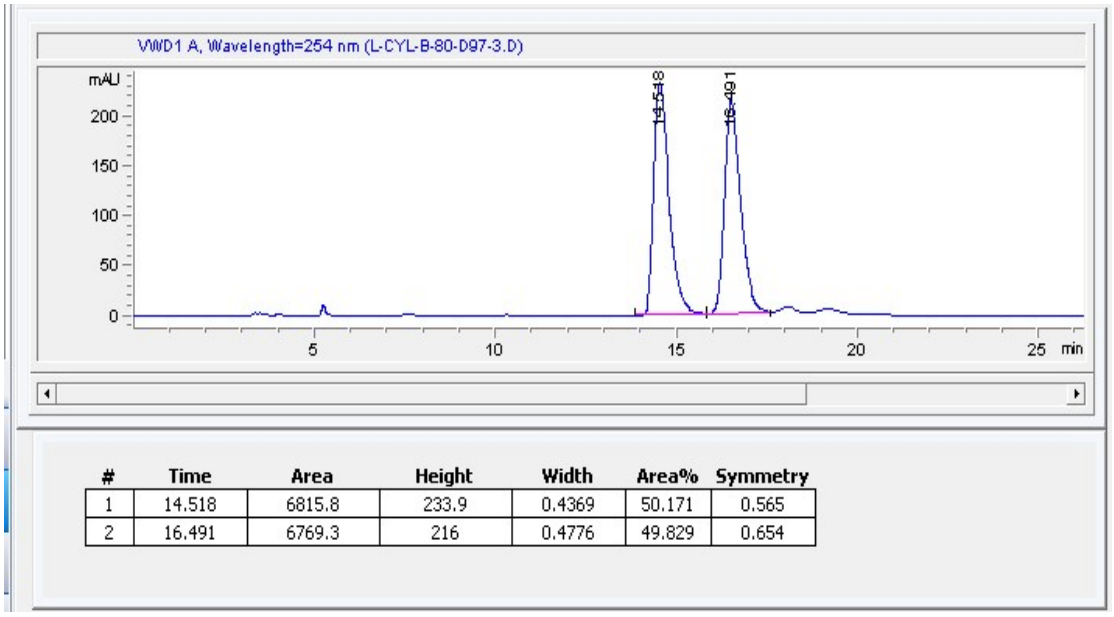
#	Time	Area	Height	Width	Area%	Symmetry
1	10.908	127616.7	2284.6	0.7687	97.546	0.336
2	18.152	3210.1	30	1.4055	2.454	0.44

^{1}H and ^{13}C NMR of 7m

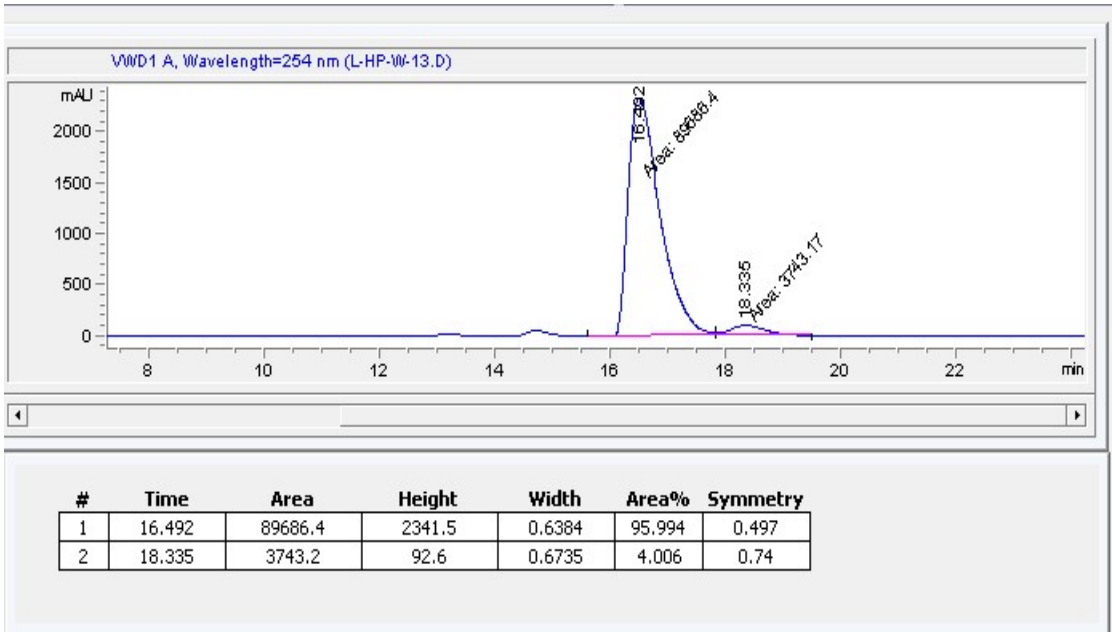




HPLC of 7m

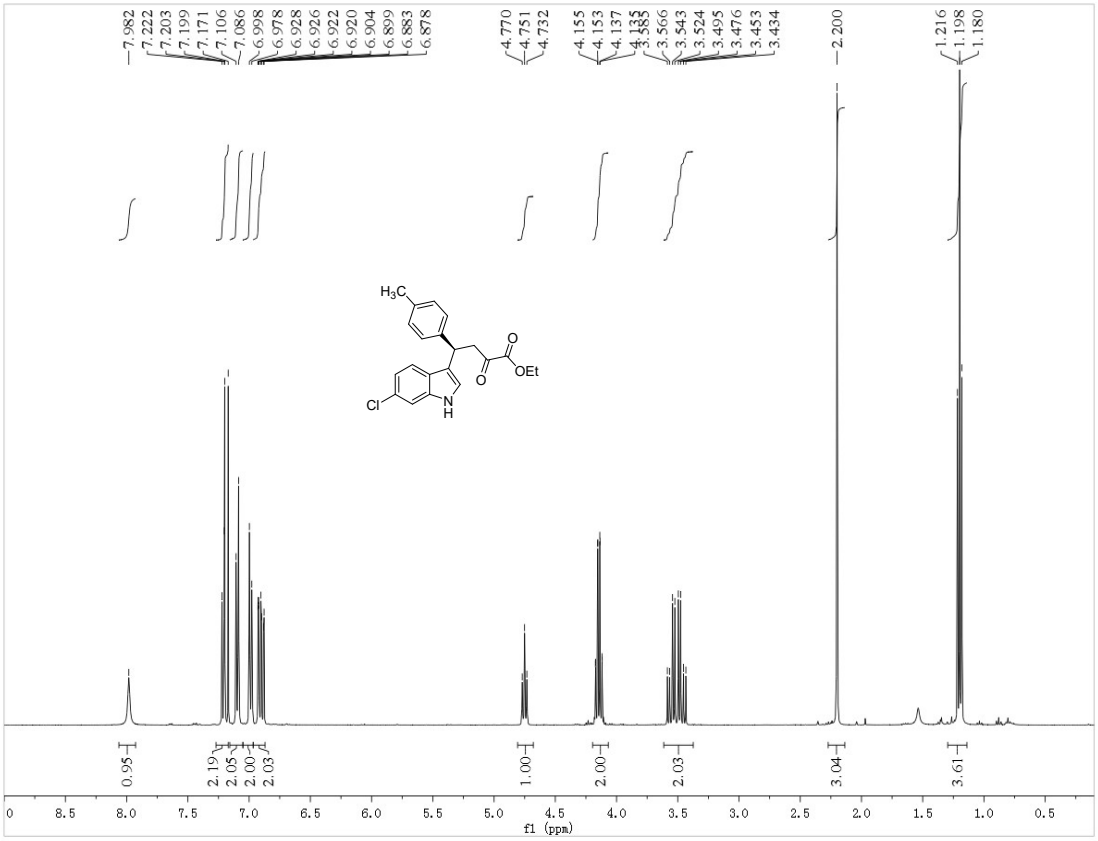


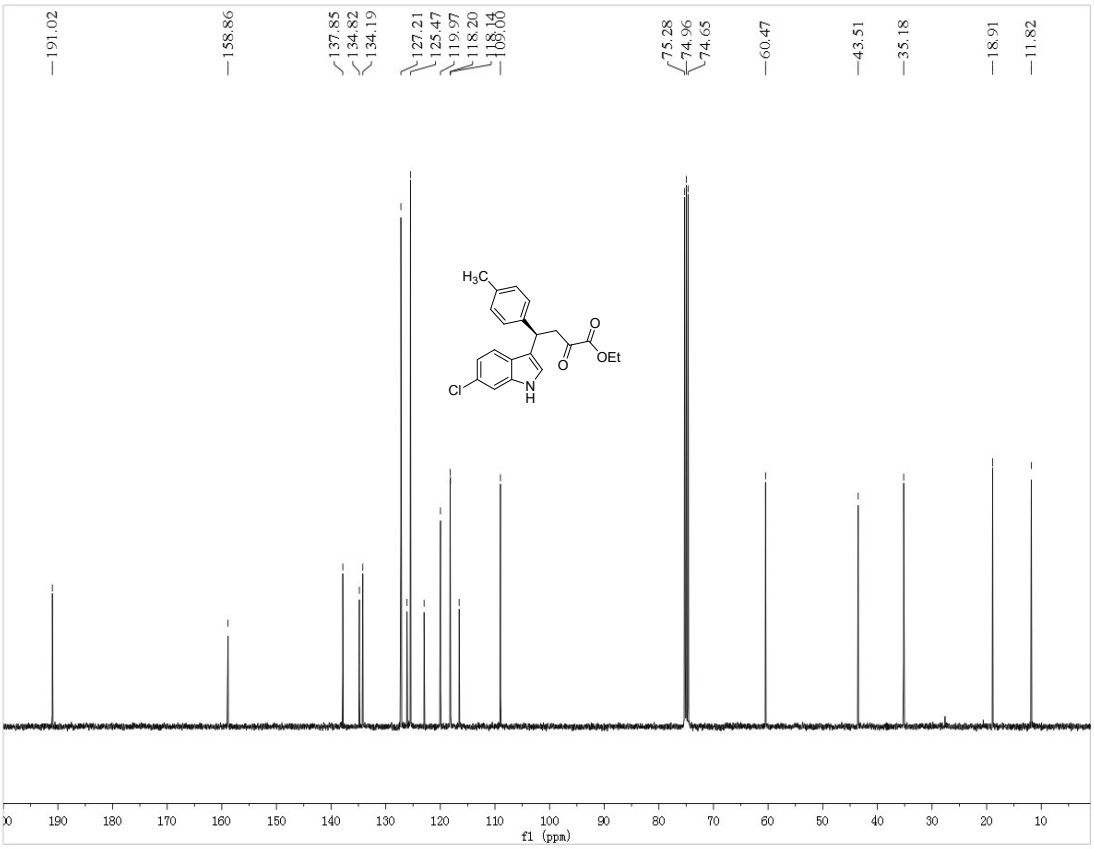
#	Time	Area	Height	Width	Area%	Symmetry
1	14.518	6815.8	233.9	0.4369	50.171	0.565
2	16.491	6769.3	216	0.4776	49.829	0.654



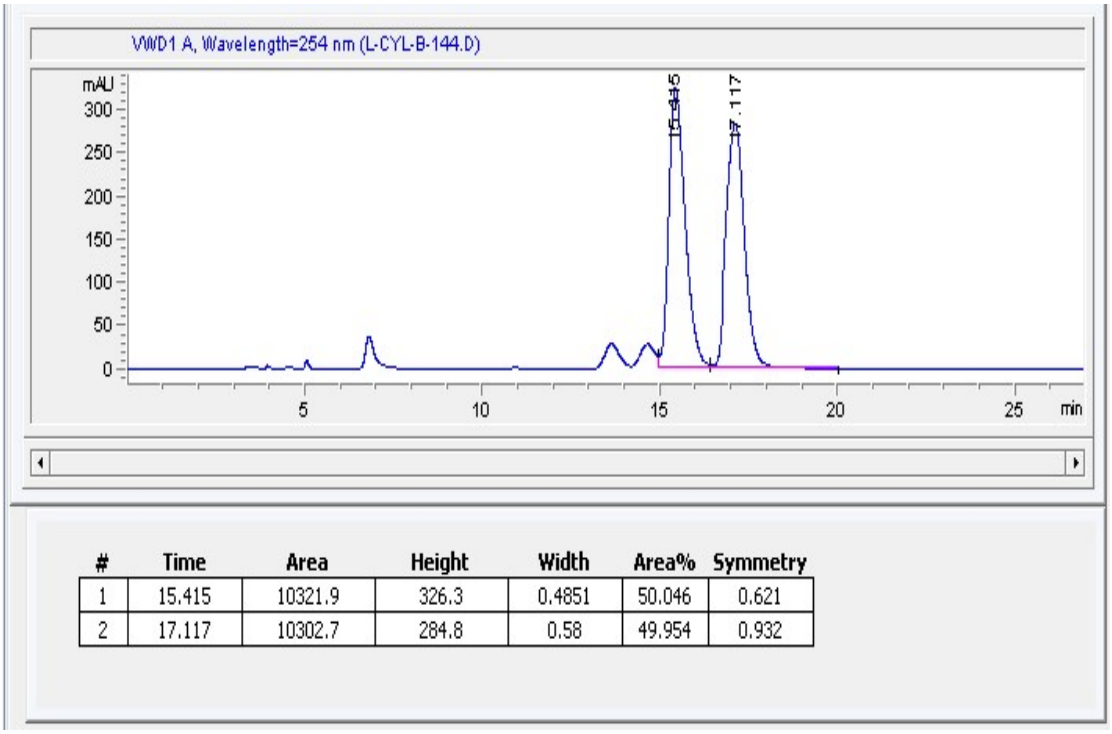
#	Time	Area	Height	Width	Area%	Symmetry
1	16.492	89686.4	2341.5	0.6384	95.994	0.497
2	18.335	3743.2	92.6	0.6735	4.006	0.74

^{1}H and ^{13}C NMR of 7n

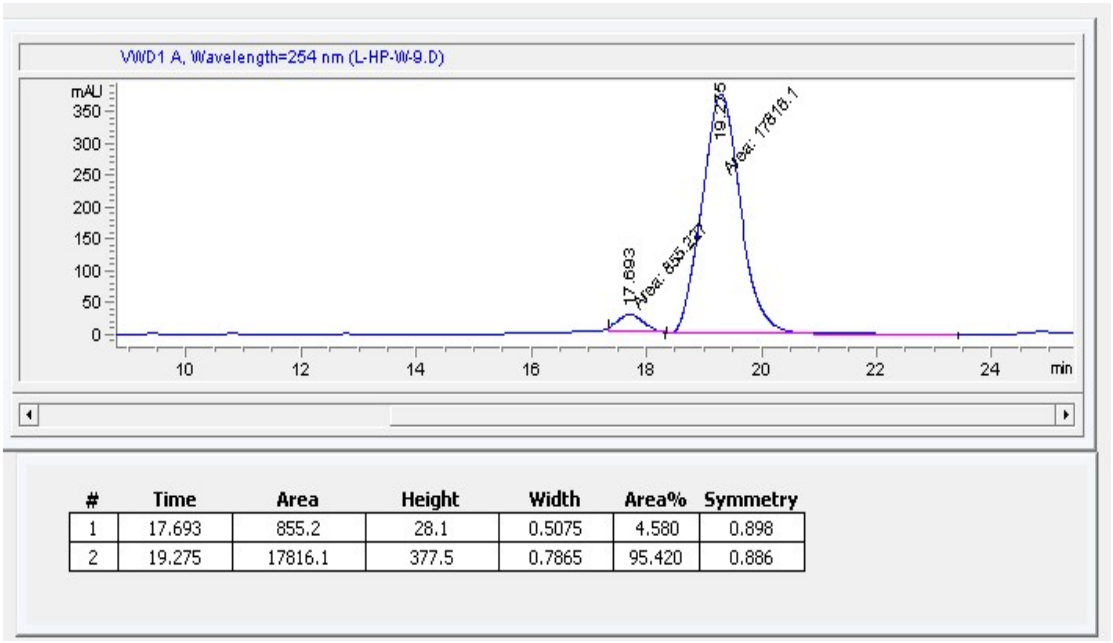




HPLC of 7n

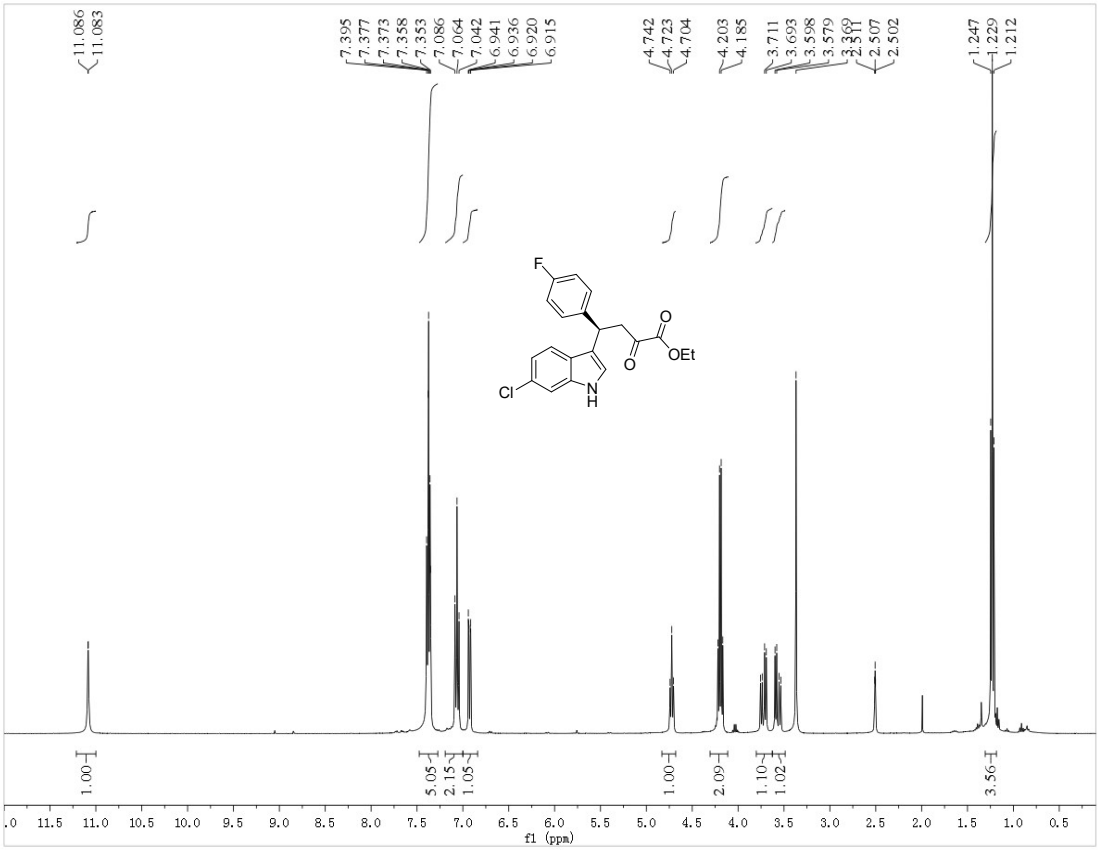


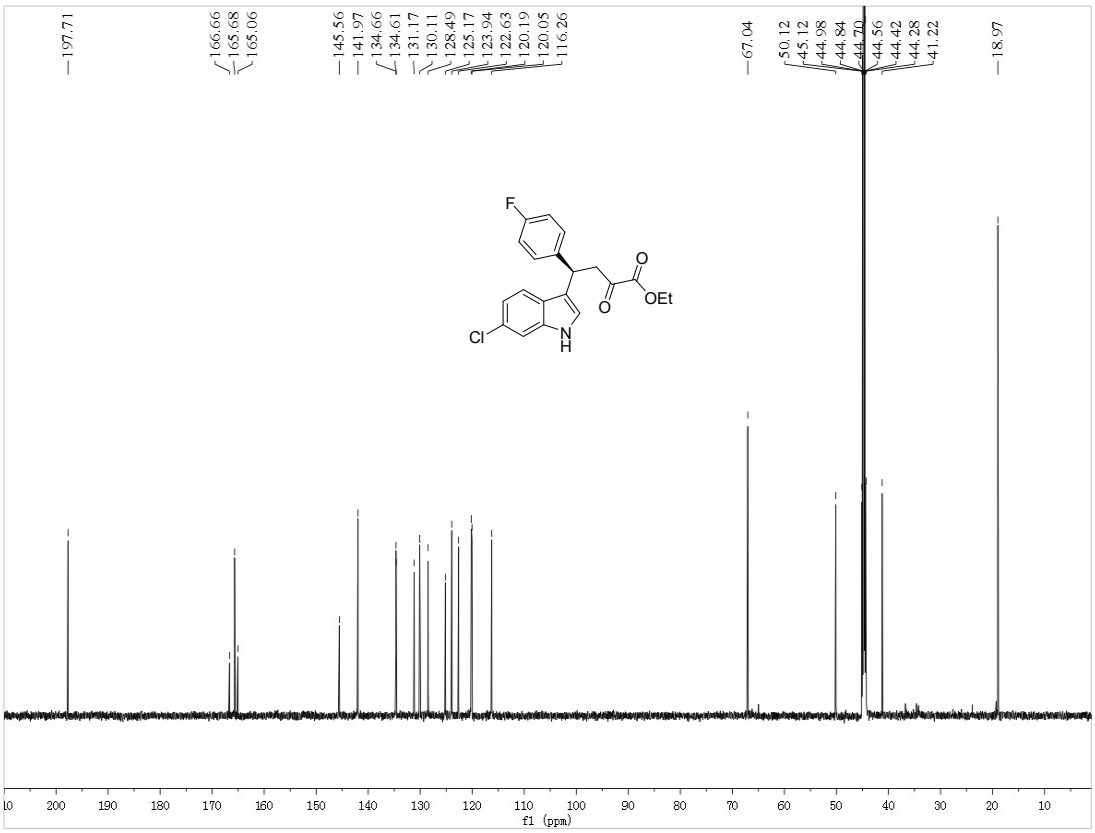
#	Time	Area	Height	Width	Area%	Symmetry
1	15.415	10321.9	326.3	0.4851	50.046	0.621
2	17.117	10302.7	284.8	0.58	49.954	0.932



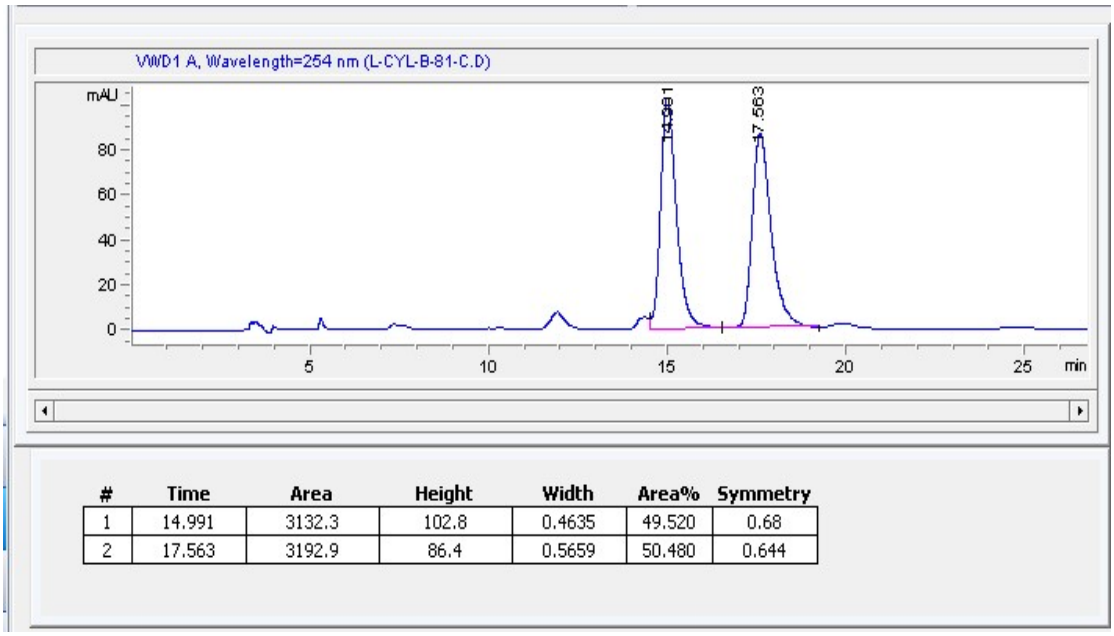
#	Time	Area	Height	Width	Area%	Symmetry
1	17.693	855.2	28.1	0.5075	4.580	0.898
2	19.275	17816.1	377.5	0.7865	95.420	0.886

^{1}H and ^{13}C NMR of 7o

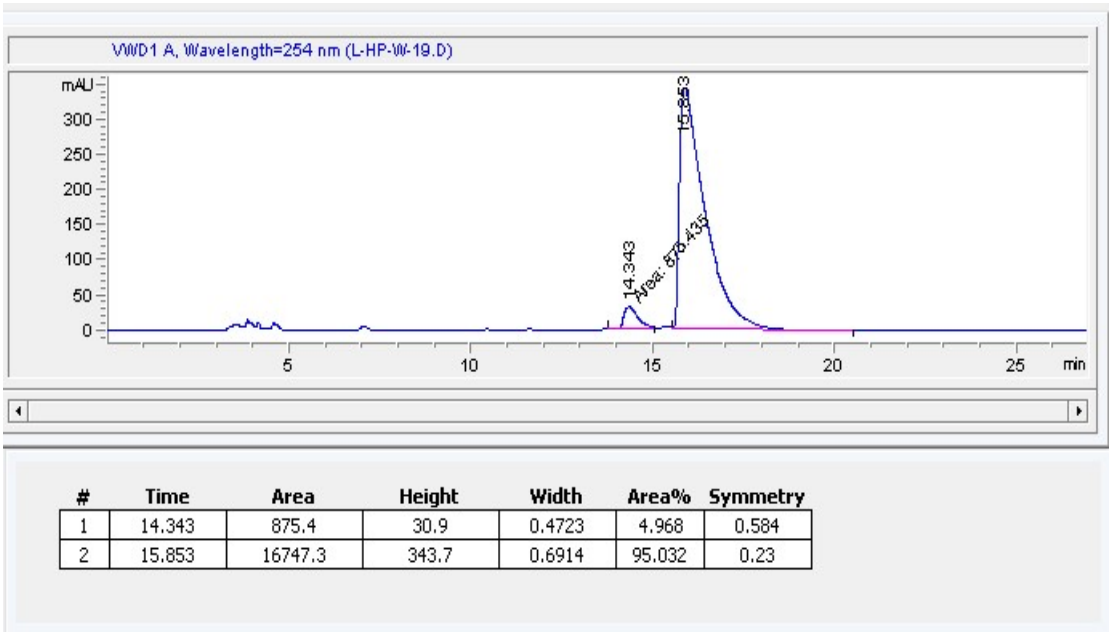




HPLC of 7o

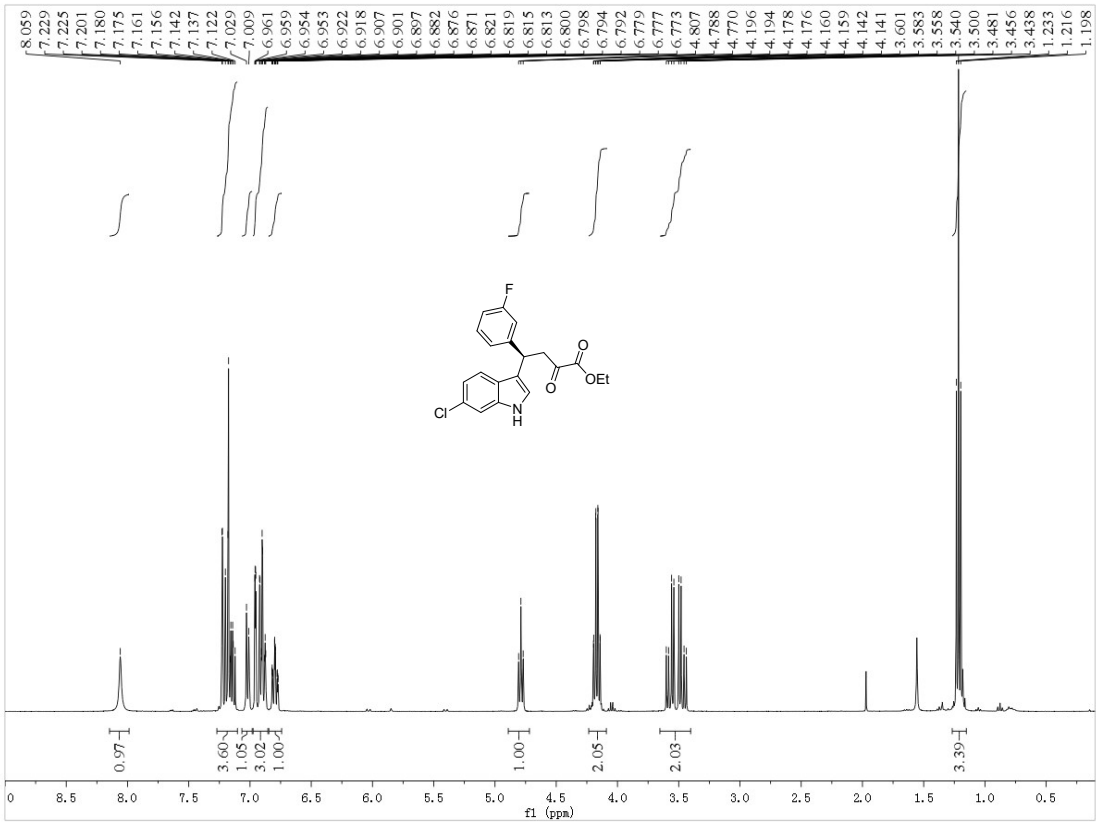


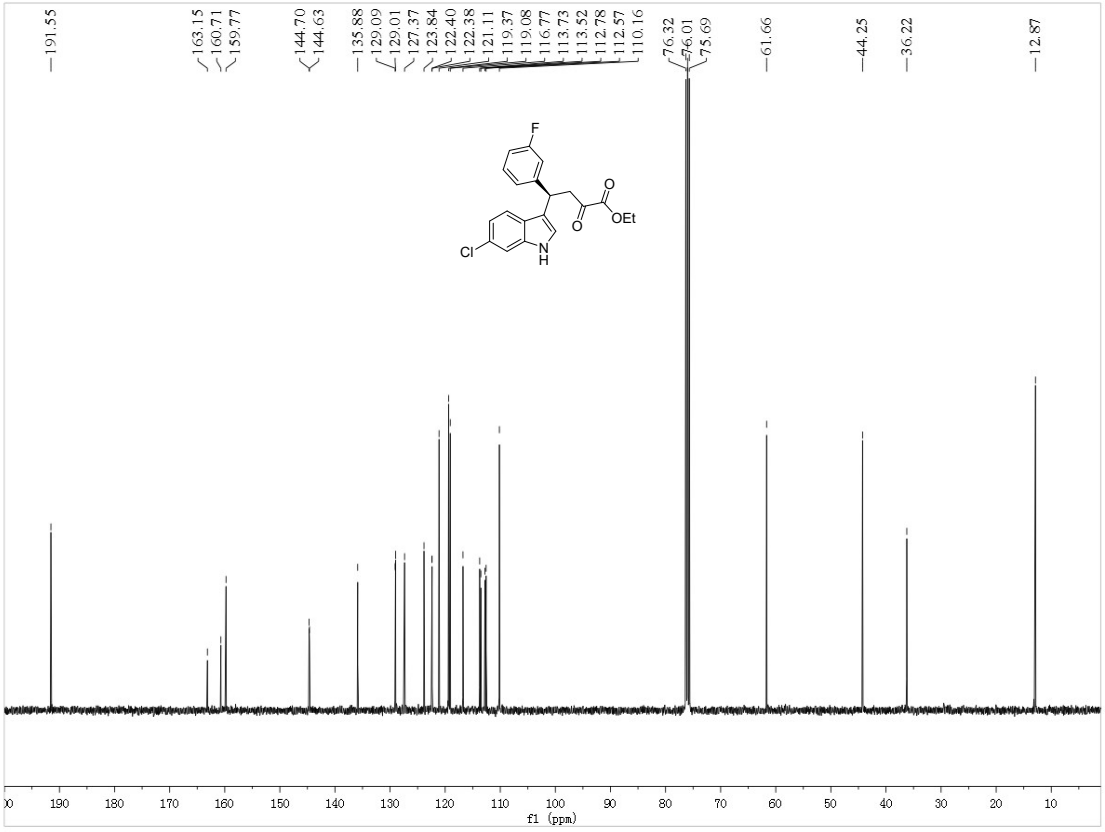
#	Time	Area	Height	Width	Area%	Symmetry
1	14.991	3132.3	102.8	0.4635	49.520	0.68
2	17.563	3192.9	86.4	0.5659	50.480	0.644



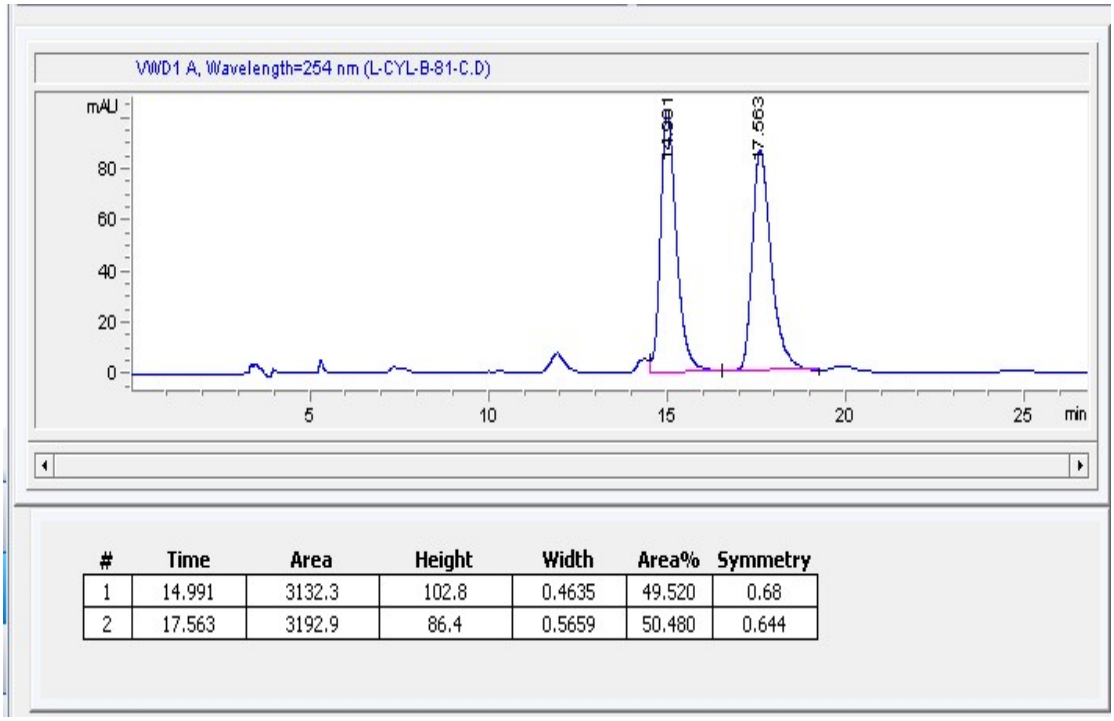
#	Time	Area	Height	Width	Area%	Symmetry
1	14.343	875.4	30.9	0.4723	4.968	0.584
2	15.853	16747.3	343.7	0.6914	95.032	0.23

^{1}H and ^{13}C NMR of 7p

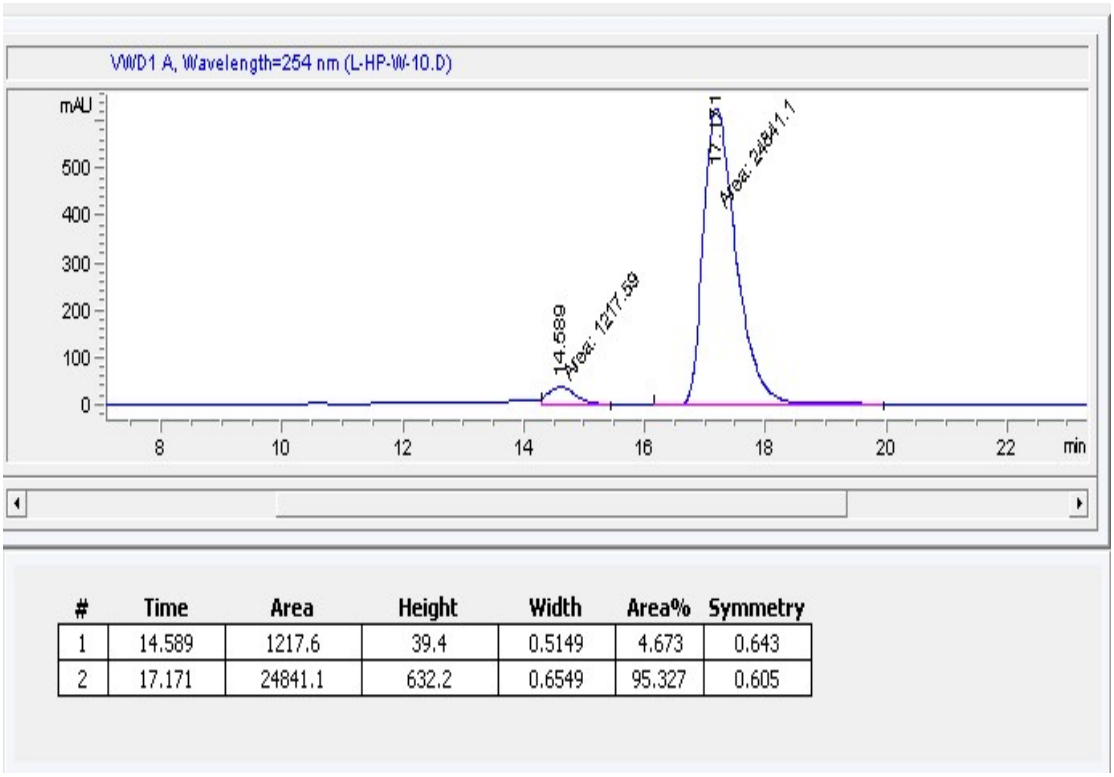




HPLC of 7p

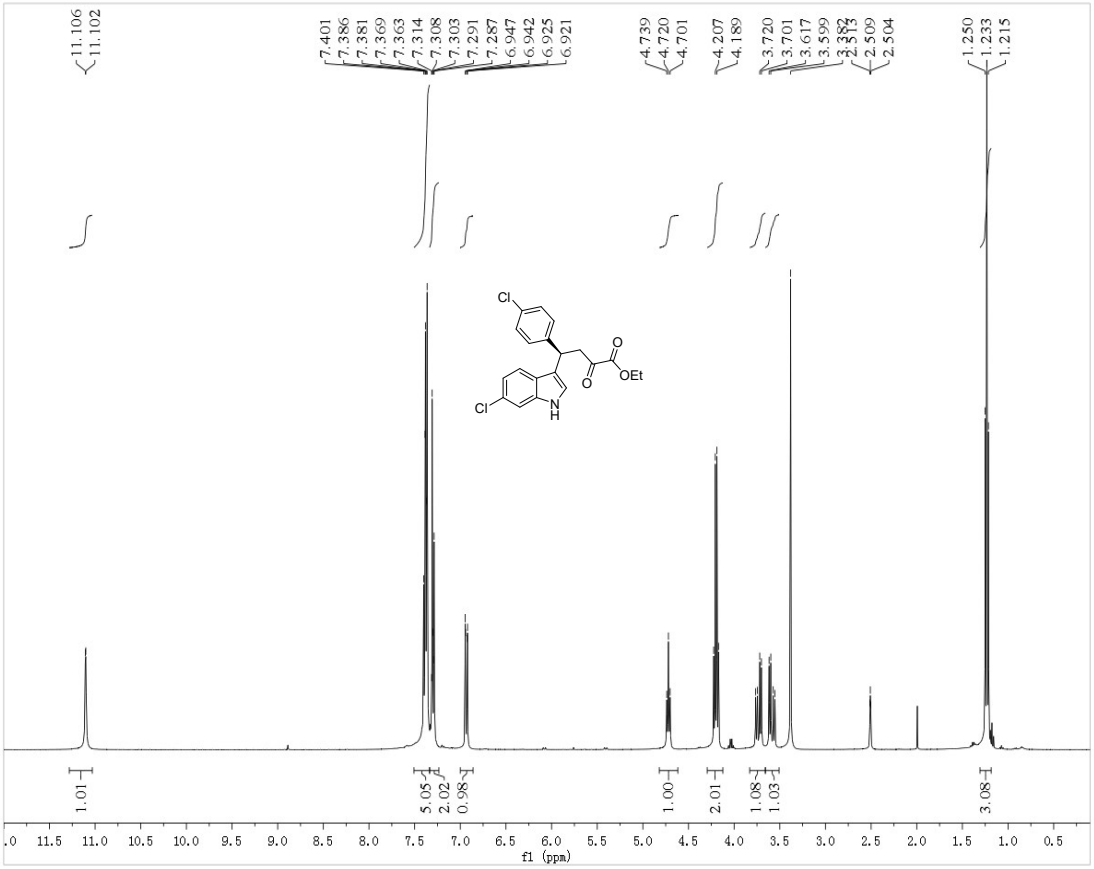


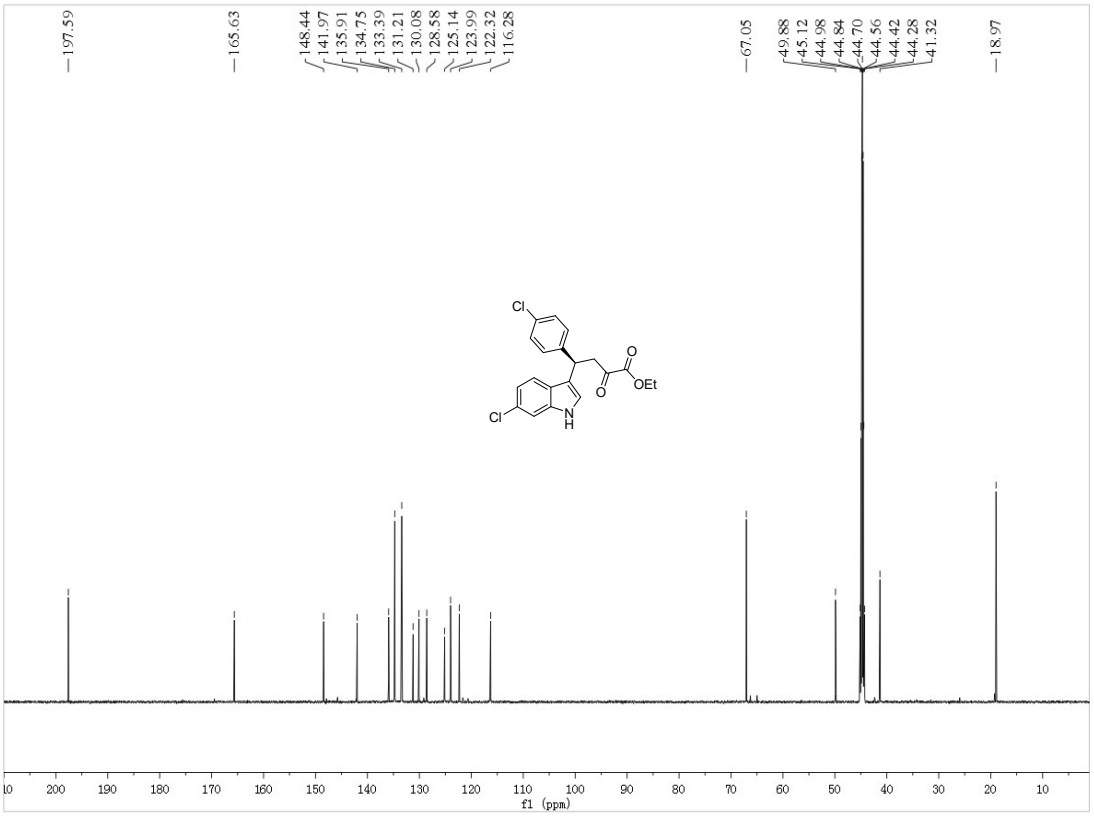
#	Time	Area	Height	Width	Area%	Symmetry
1	14.991	3132.3	102.8	0.4635	49.520	0.68
2	17.563	3192.9	86.4	0.5659	50.480	0.644



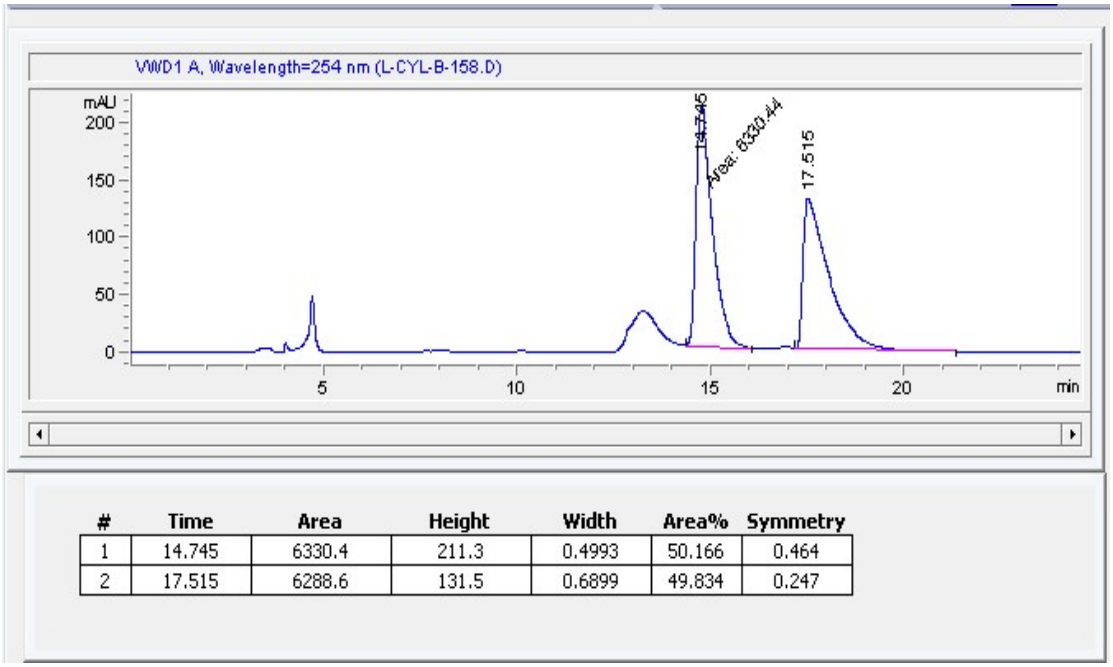
#	Time	Area	Height	Width	Area%	Symmetry
1	14.589	1217.6	39.4	0.5149	4.673	0.643
2	17.171	24841.1	632.2	0.6549	95.327	0.605

^{1}H and ^{13}C NMR of 7q

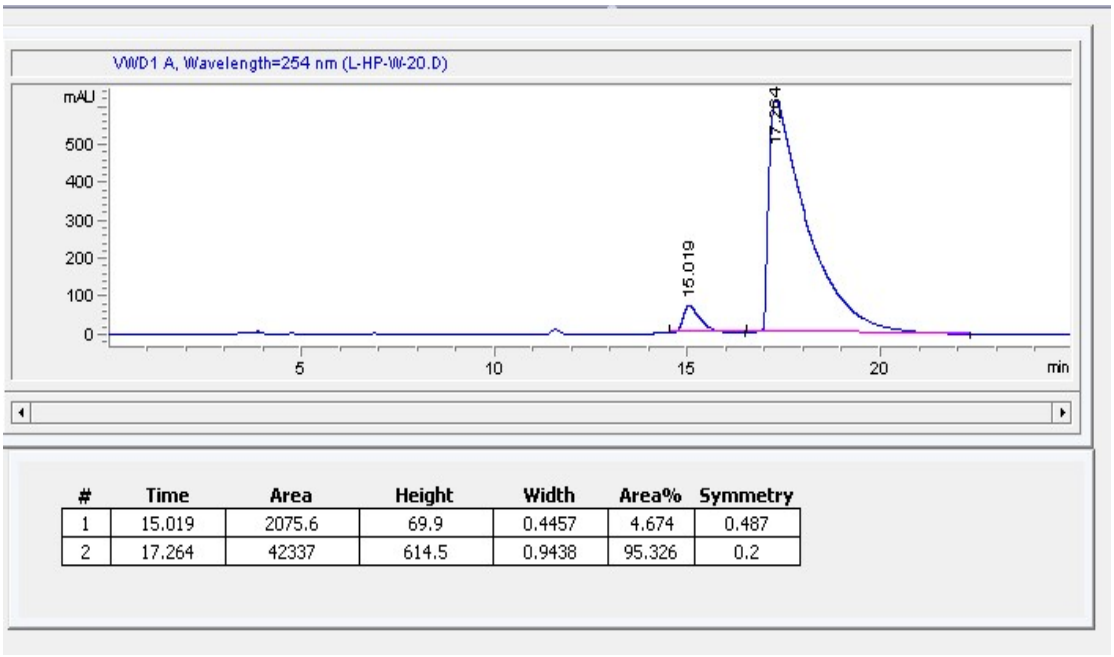




HPLC of 7q

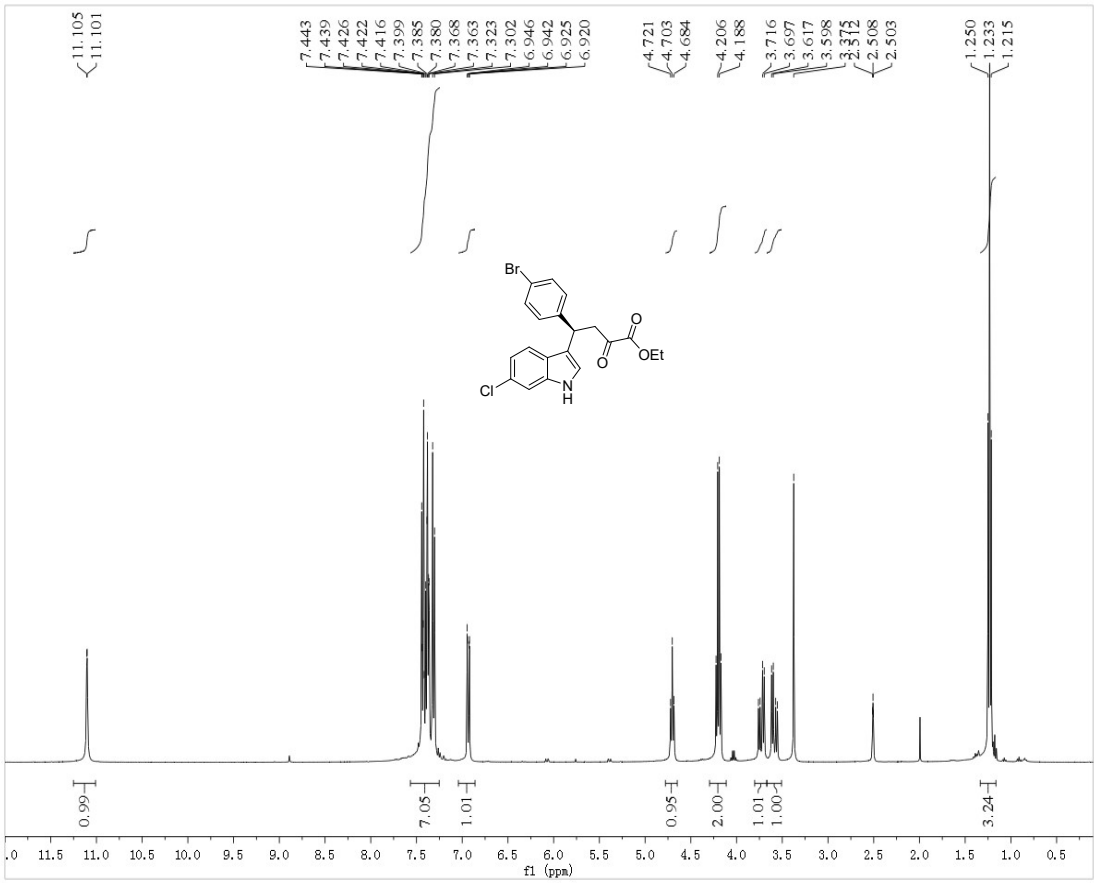


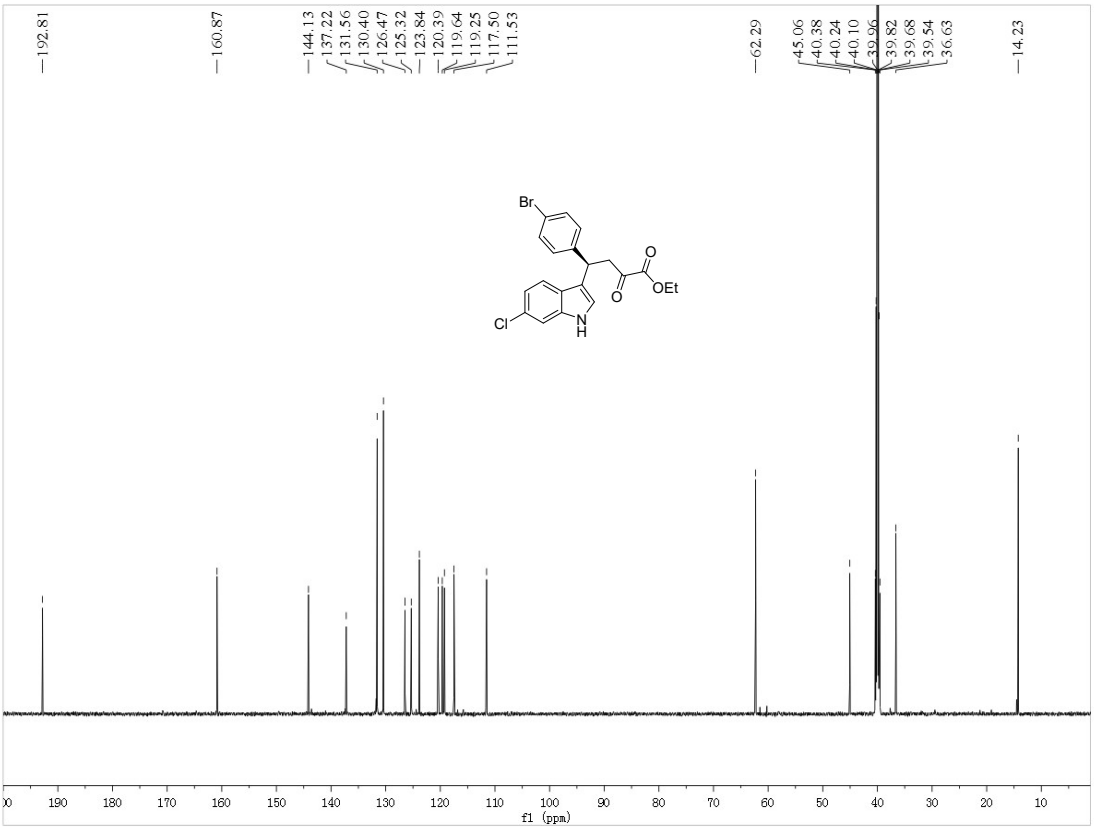
#	Time	Area	Height	Width	Area%	Symmetry
1	14.745	6330.4	211.3	0.4993	50.166	0.464
2	17.515	6288.6	131.5	0.6899	49.834	0.247



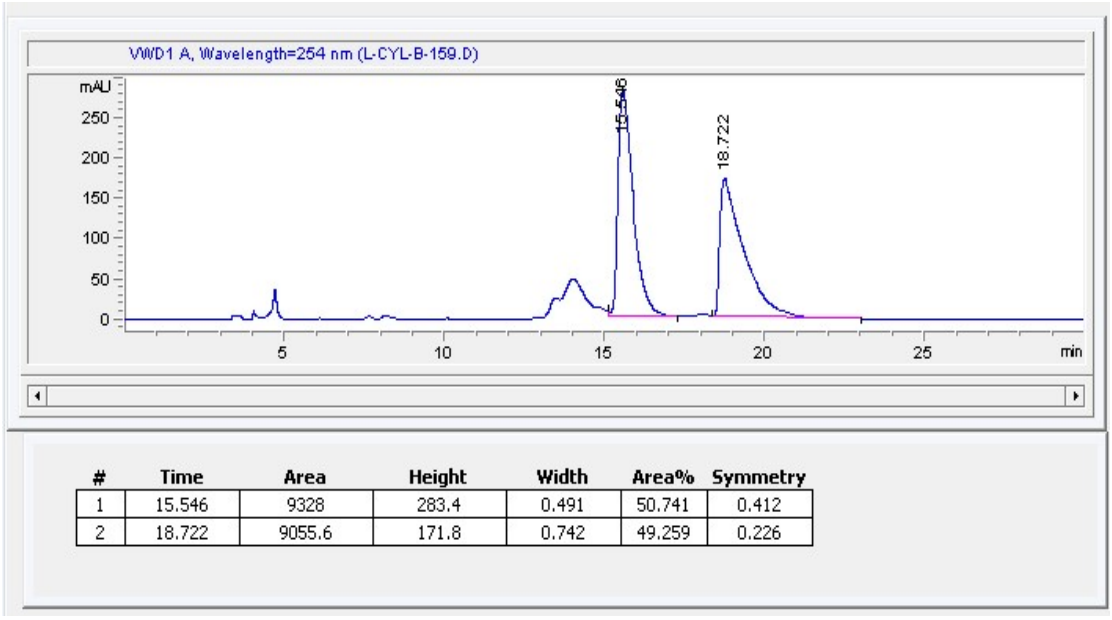
#	Time	Area	Height	Width	Area%	Symmetry
1	15.019	2075.6	69.9	0.4457	4.674	0.487
2	17.264	42337	614.5	0.9438	95.326	0.2

^{1}H and ^{13}C NMR of 7r

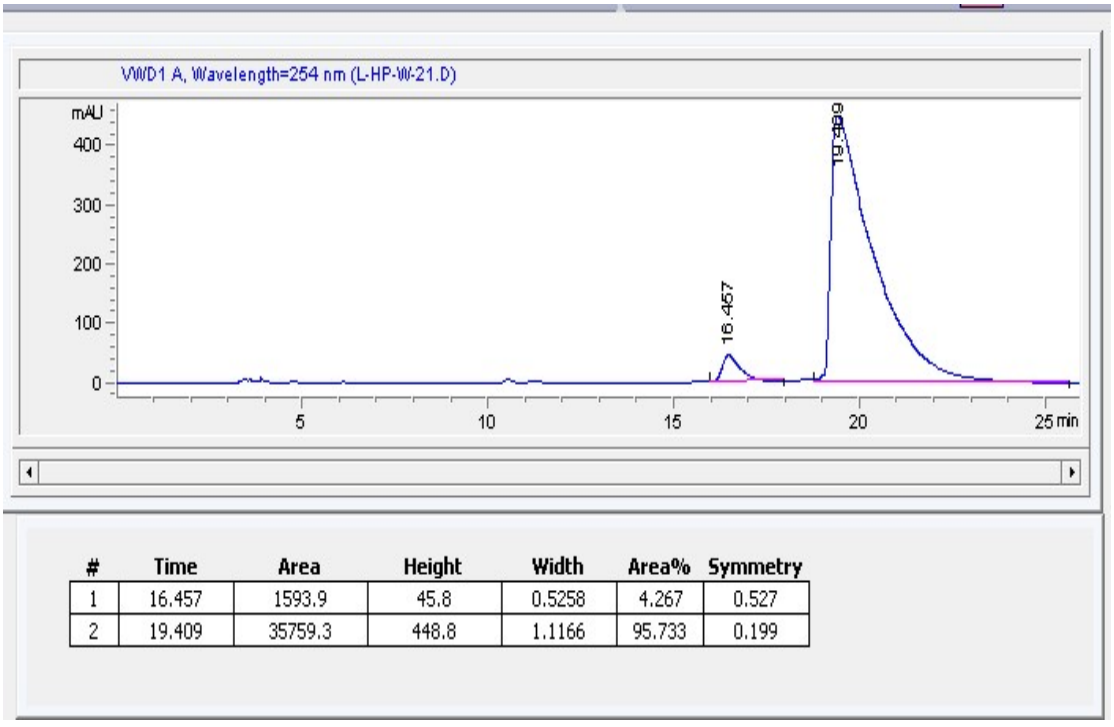




HPLC of 7r

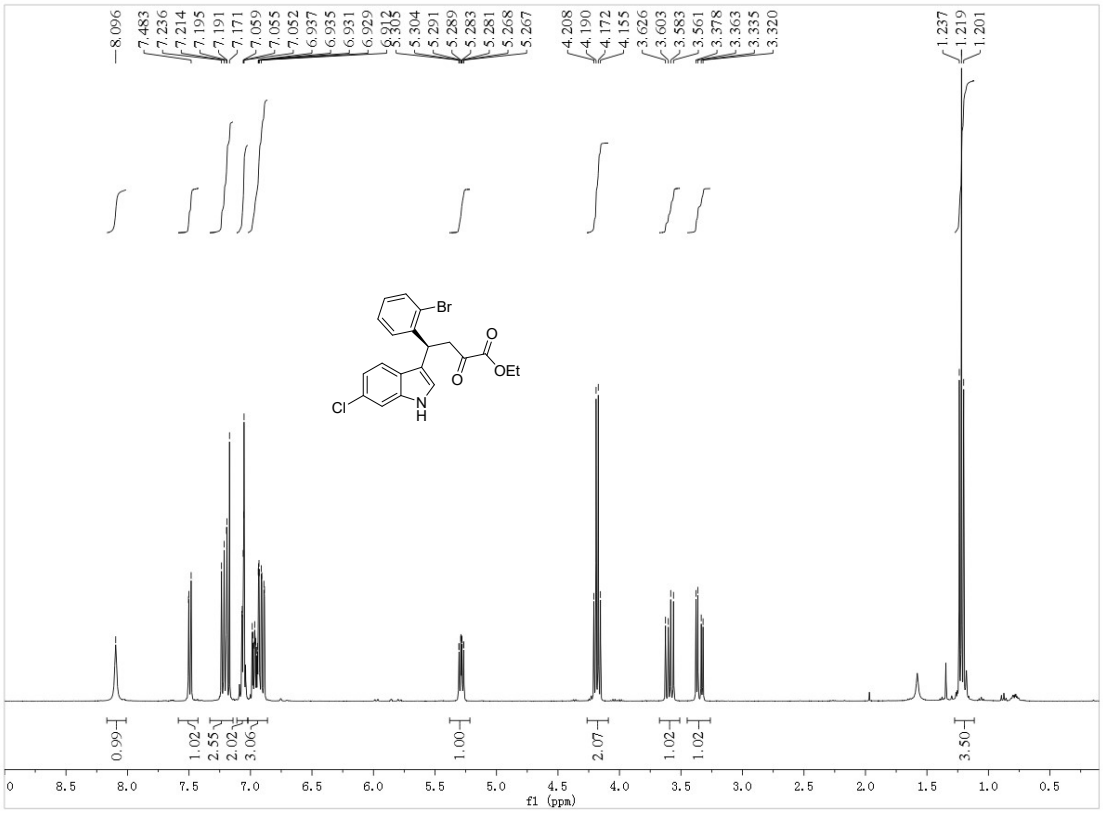


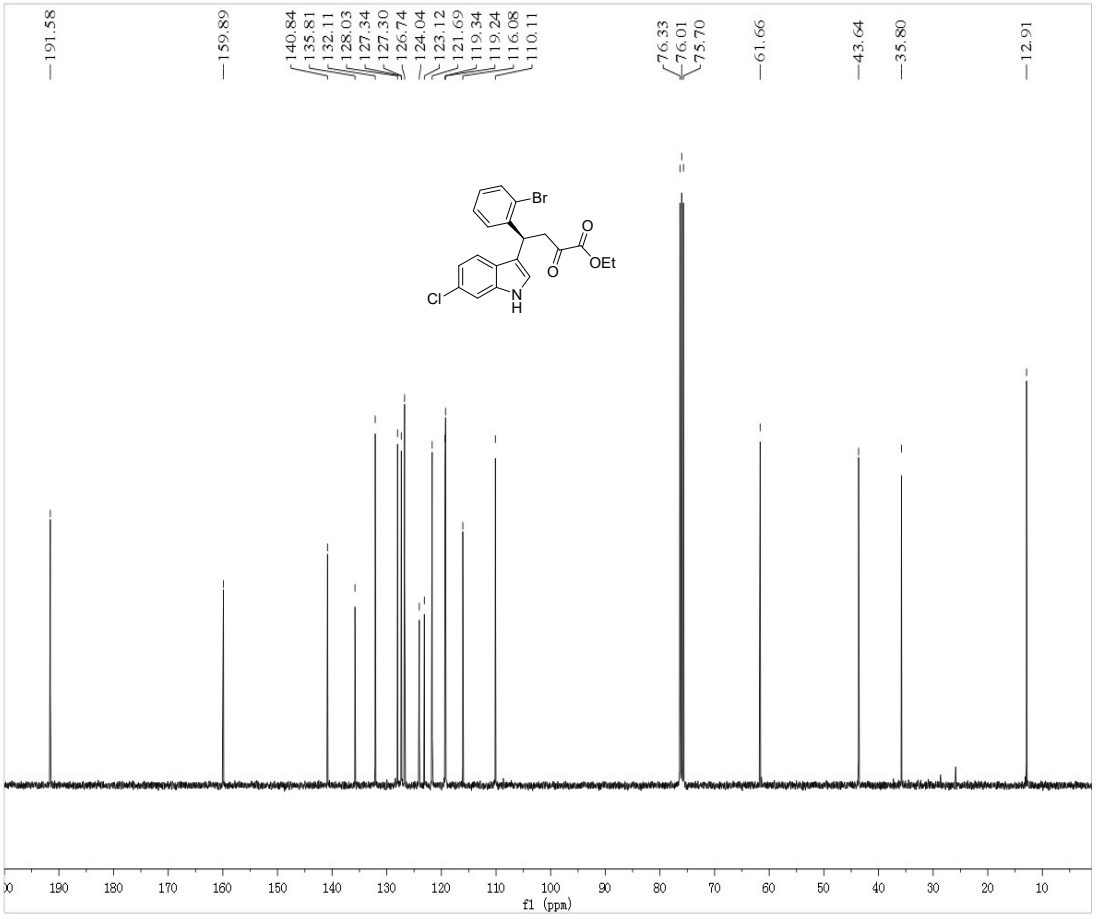
#	Time	Area	Height	Width	Area%	Symmetry
1	15.546	9328	283.4	0.491	50.741	0.412
2	18.722	9055.6	171.8	0.742	49.259	0.226



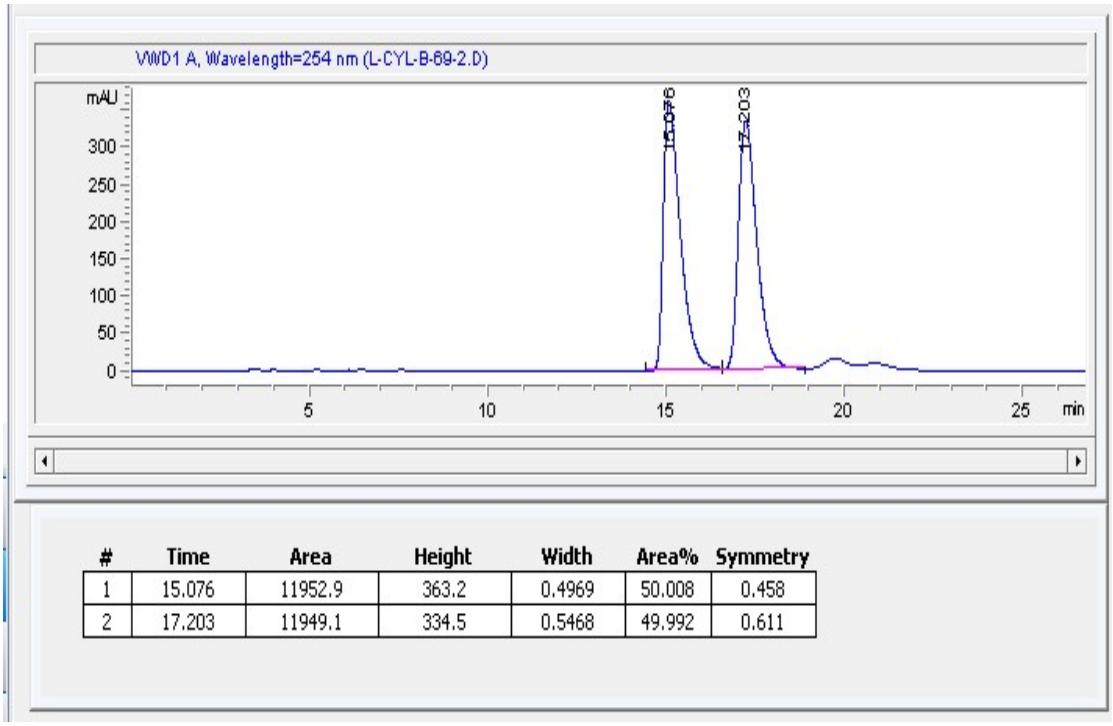
#	Time	Area	Height	Width	Area%	Symmetry
1	16.457	1593.9	45.8	0.5258	4.267	0.527
2	19.409	35759.3	448.8	1.1166	95.733	0.199

^{1}H and ^{13}C NMR of 7s

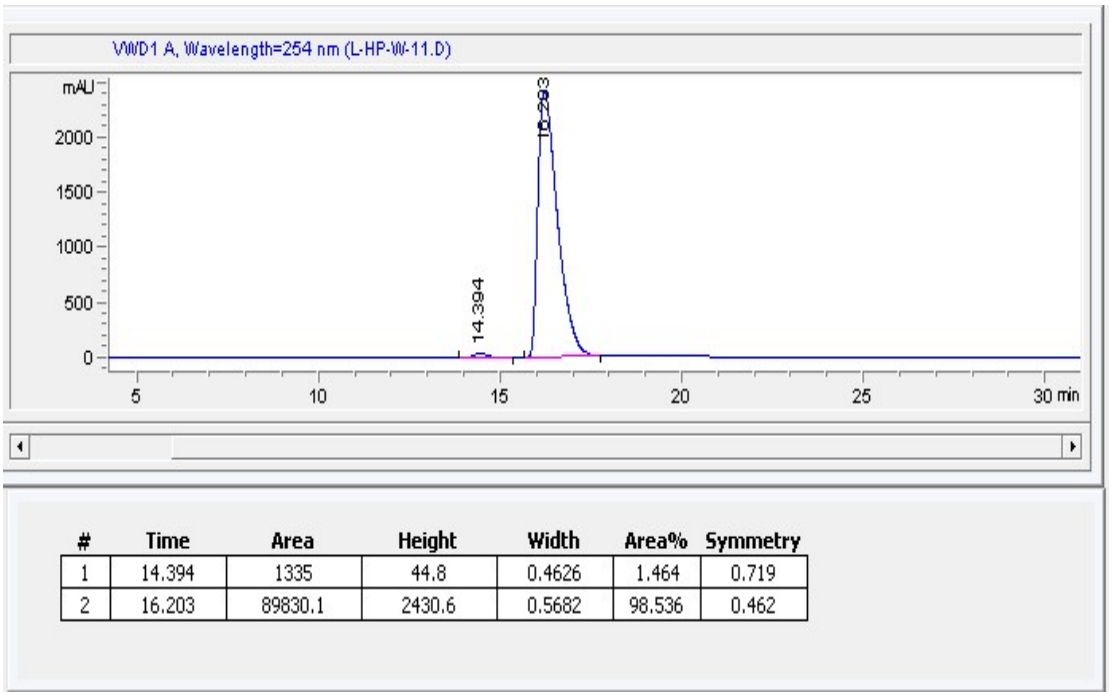




HPLC of 7s

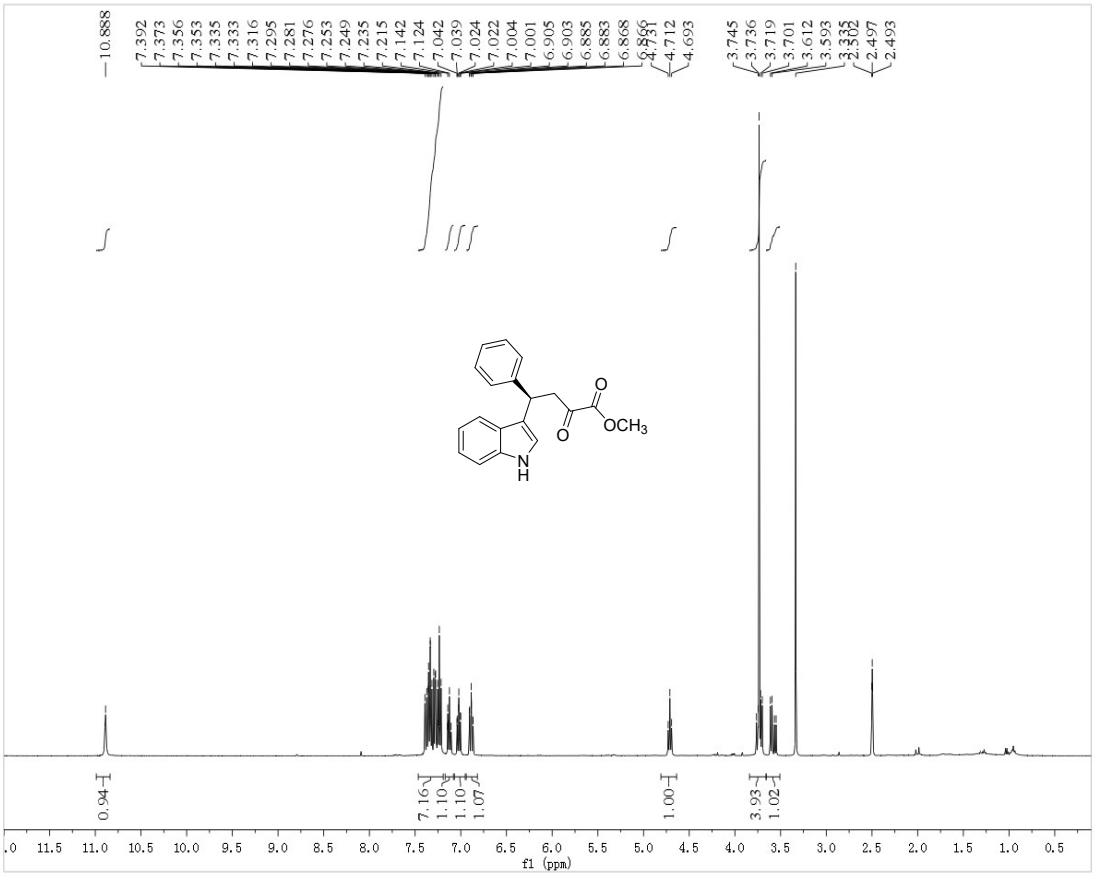


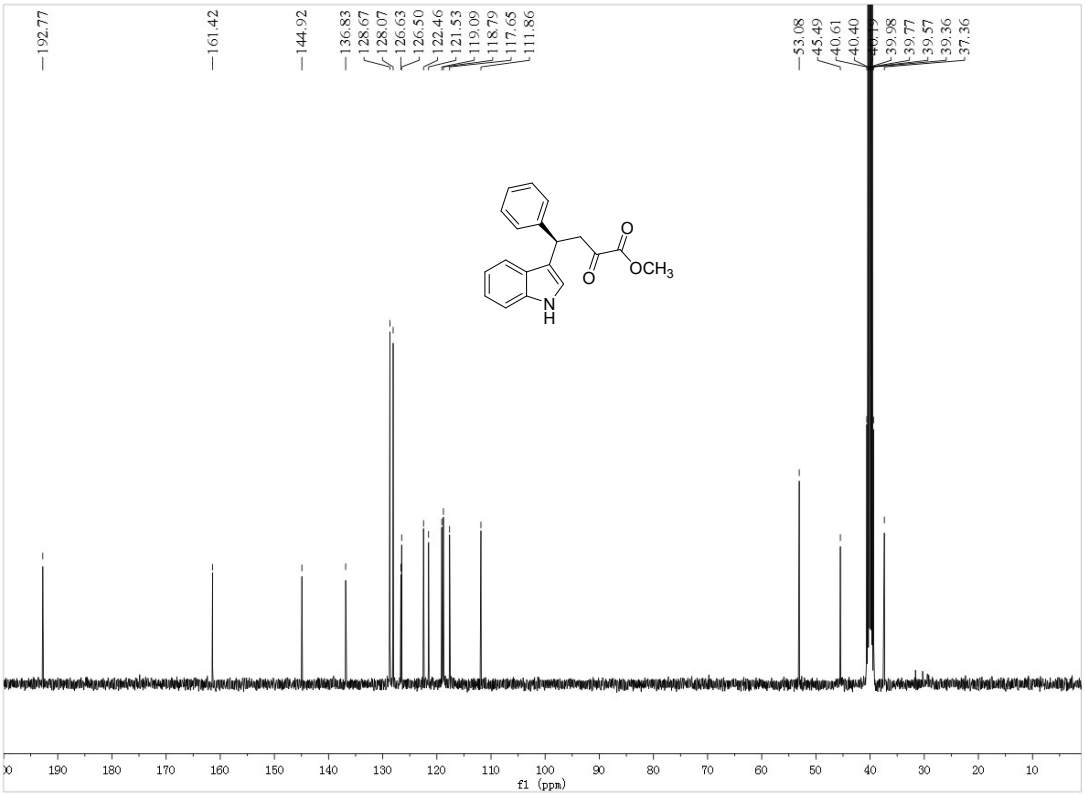
#	Time	Area	Height	Width	Area%	Symmetry
1	15.076	11952.9	363.2	0.4969	50.008	0.458
2	17.203	11949.1	334.5	0.5468	49.992	0.611



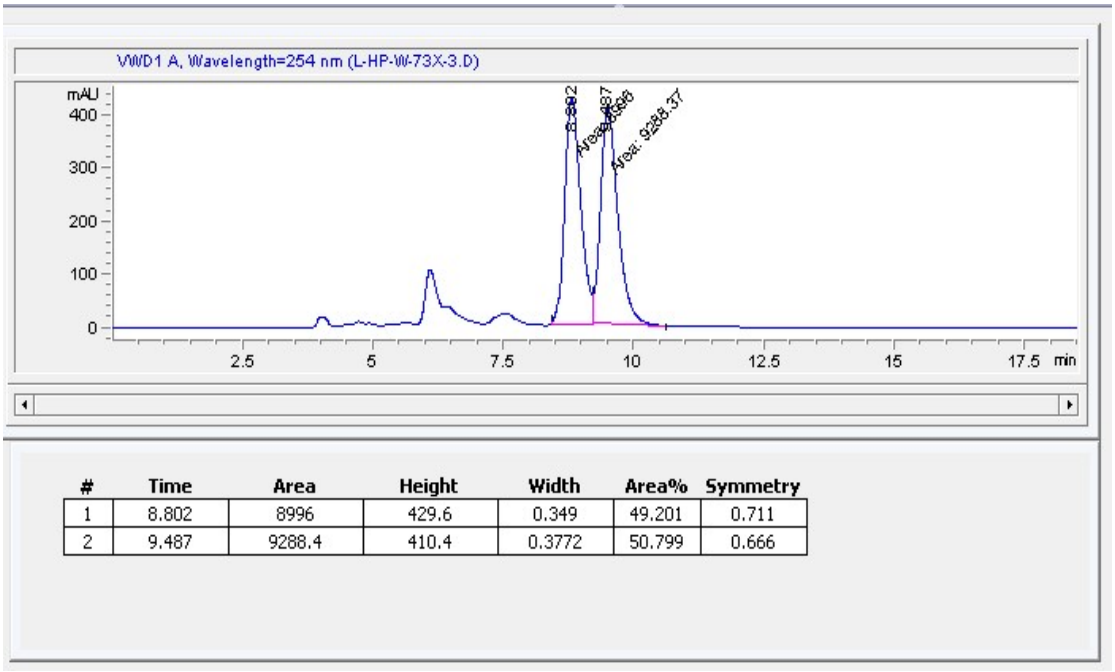
#	Time	Area	Height	Width	Area%	Symmetry
1	14.394	1335	44.8	0.4626	1.464	0.719
2	16.203	89830.1	2430.6	0.5682	98.536	0.462

^{1}H and ^{13}C NMR of 7t

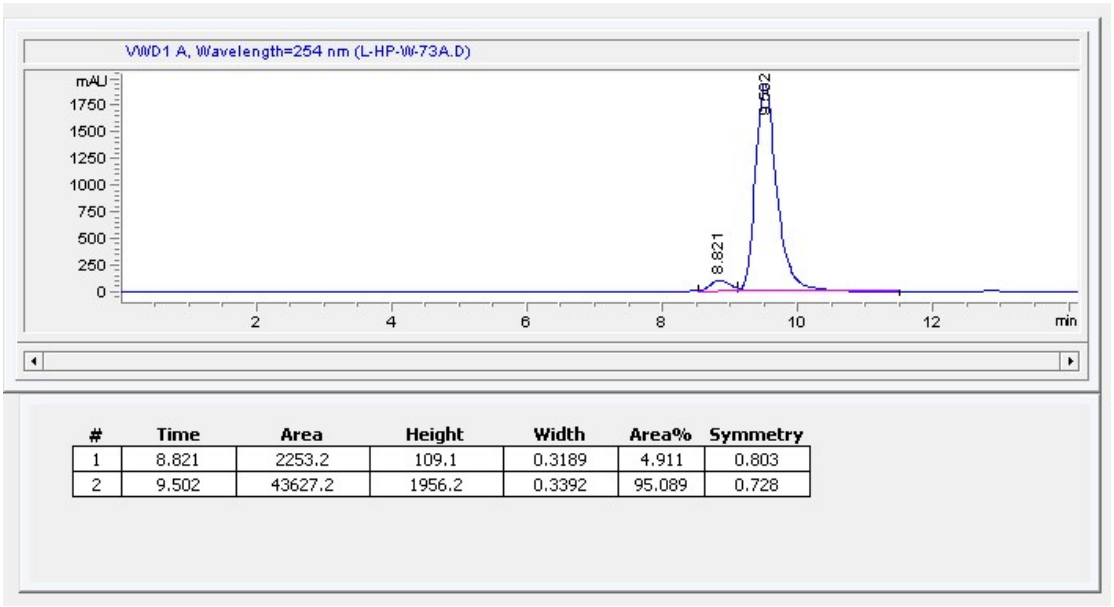




HPLC of 7t

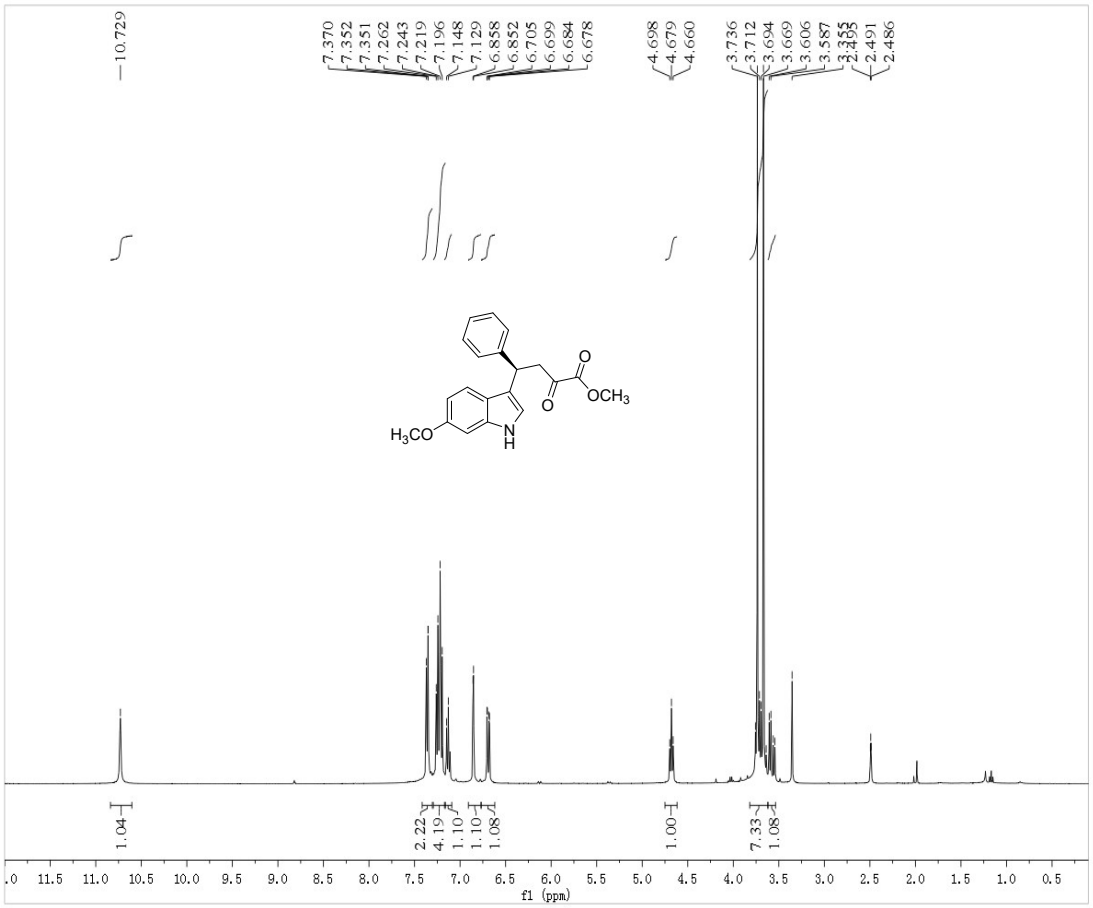


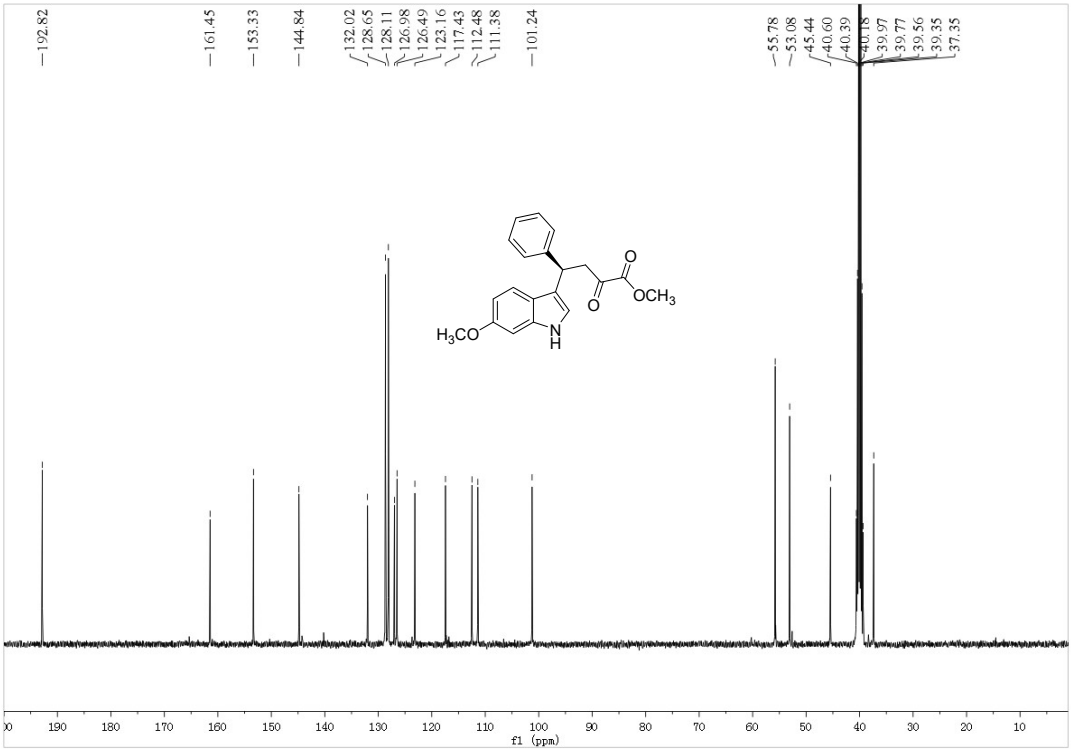
#	Time	Area	Height	Width	Area%	Symmetry
1	8.802	8996	429.6	0.349	49.201	0.711
2	9.487	9288.4	410.4	0.3772	50.799	0.666



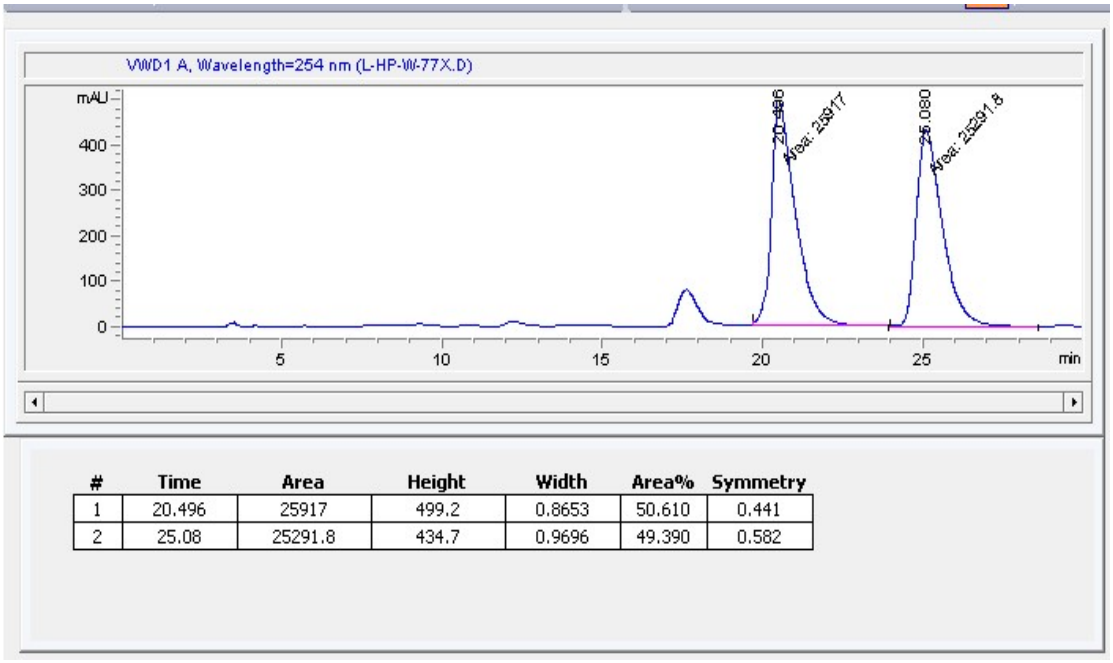
#	Time	Area	Height	Width	Area%	Symmetry
1	8.821	2253.2	109.1	0.3189	4.911	0.803
2	9.502	43627.2	1956.2	0.3392	95.089	0.728

^{1}H and ^{13}C NMR of 7u

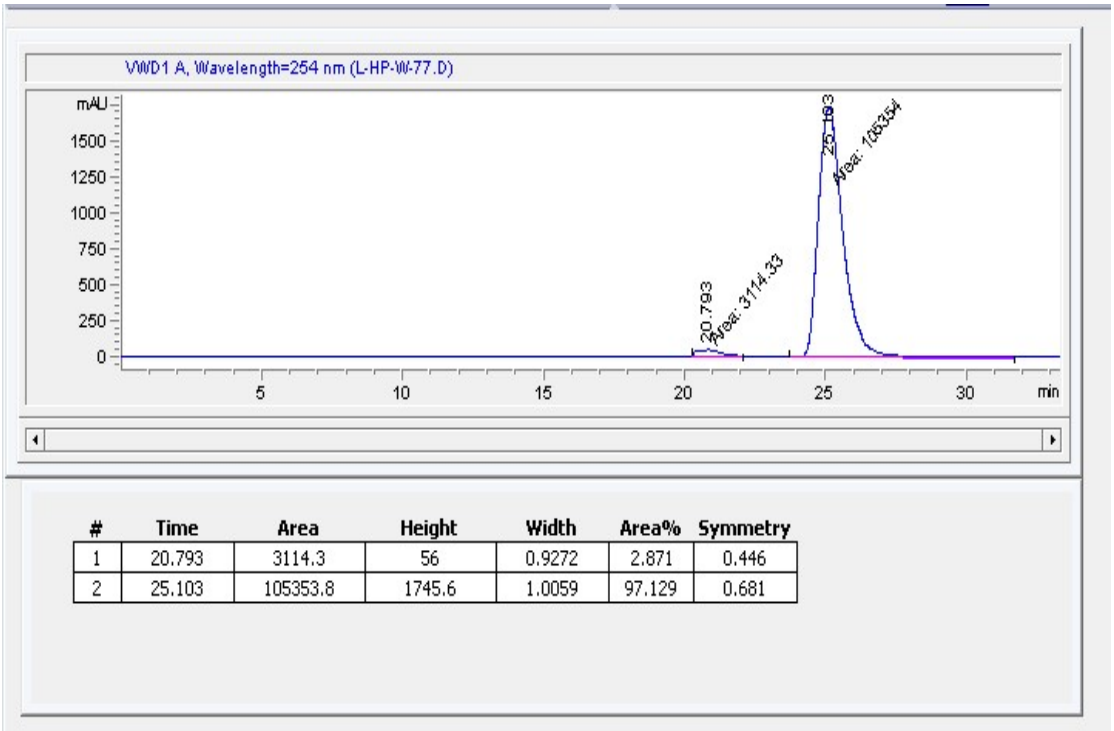




HPLC of 7u

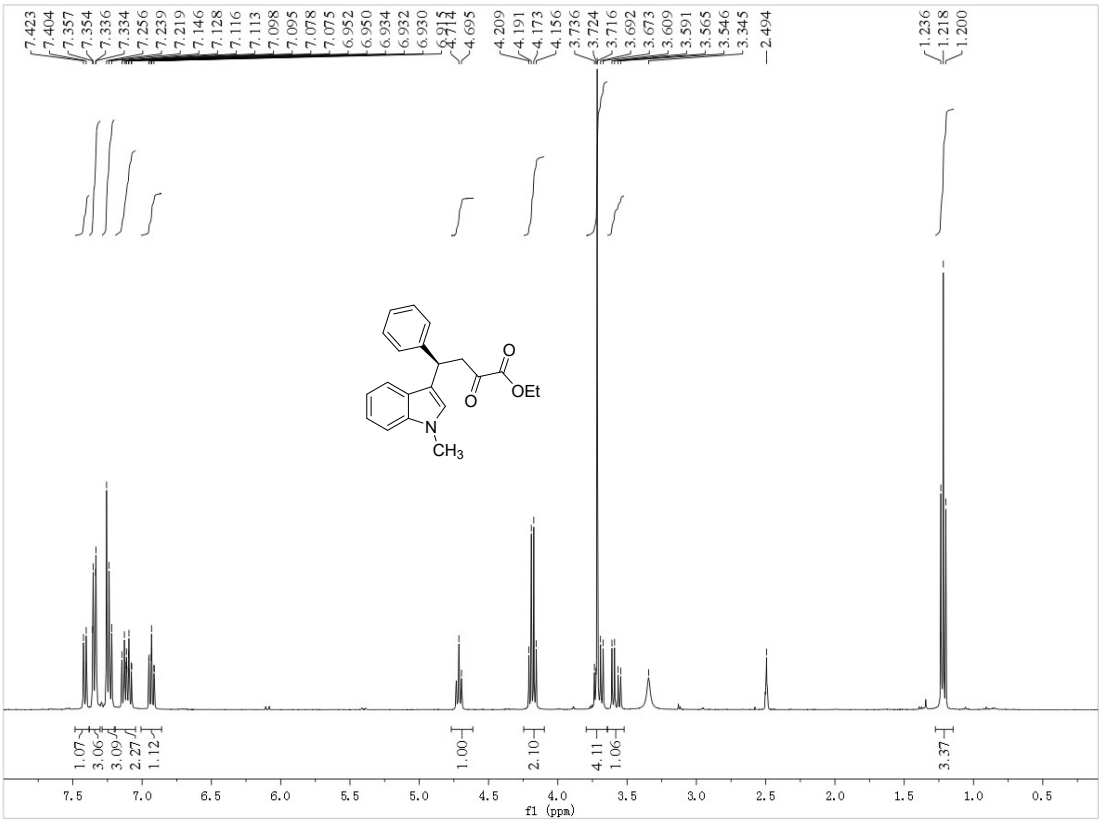


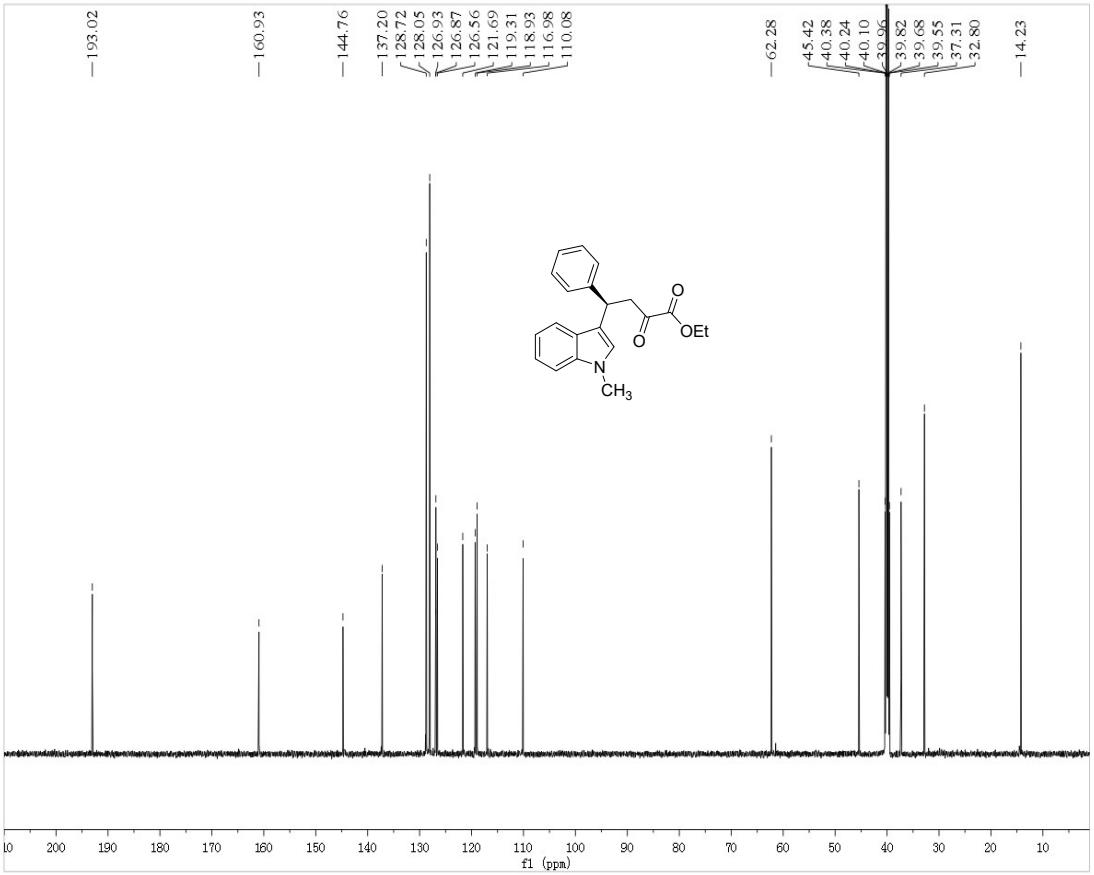
#	Time	Area	Height	Width	Area%	Symmetry
1	20.496	25917	499.2	0.8653	50.610	0.441
2	25.08	25291.8	434.7	0.9696	49.390	0.582



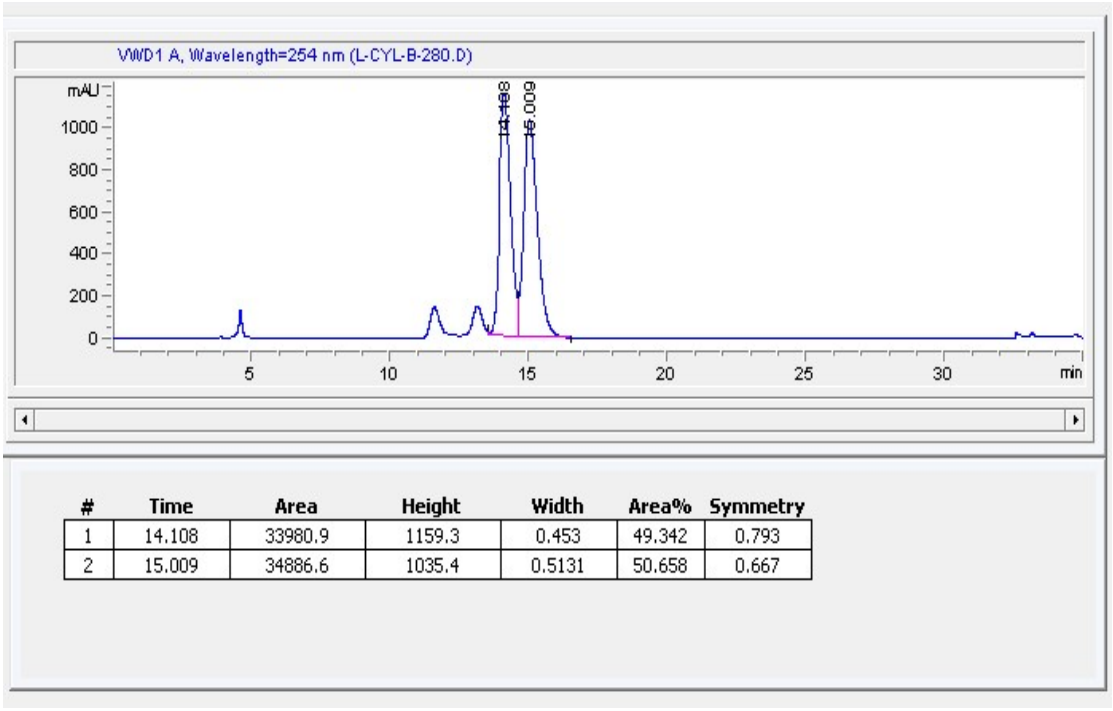
#	Time	Area	Height	Width	Area%	Symmetry
1	20.793	3114.3	56	0.9272	2.871	0.446
2	25.103	105353.8	1745.6	1.0059	97.129	0.681

^{1}H and ^{13}C NMR of 7w

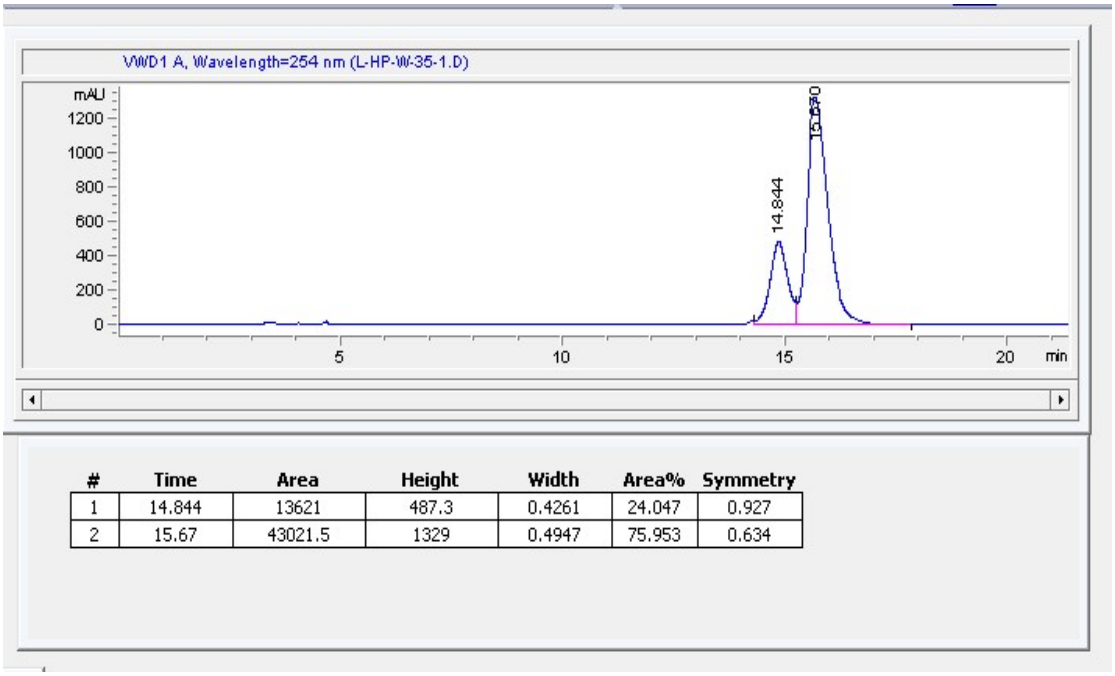




HPLC of 7w



#	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	14.844	13621	487.3	0.4261	24.047	0.927
2	15.67	43021.5	1329	0.4947	75.953	0.634