Mantis-shaped chiral pyridine-*N*-oxides: a new class of ligands in asymmetric palladium(II)-catalysed Friedel-Crafts alkylation

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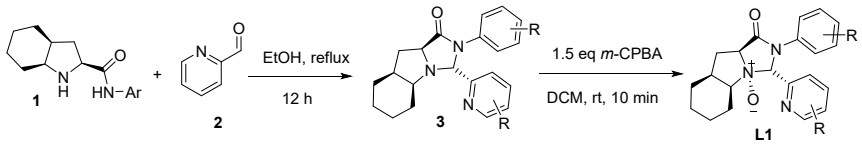
1. General information

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

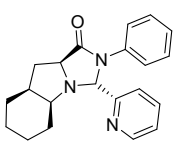
2. General procedure for preparation of chiral ligands L1



In a sealed tube equipped with a magnetic stirring bar, bicyclic prolinamides **1** (1.2 mmol, 1.2 equiv) and pyridinecarboxaldehydes **2** (1.0 mmol) were added. Then, 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 **3**.

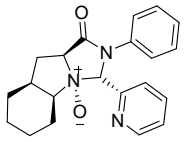
In a sealed tube equipped with a magnetic stirring bar, to the intermediate **3** was added 3.0 mL of DCM and *m*-CPBA (1.5 eq). The reaction mixture was stirred at rt for 10 min. After completion of the reaction, as indicated by TLC, the aftertreatment residue was purified by flash column chromatography to furnish the pyridine-NO ligands **L1**.

3. Characterization data of 3a and ligands L

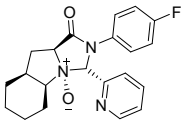


(3R,4aS,8aS,9aS)-2-phenyl-3-(pyridin-2-yl)decahydro-1H-imidazo[1,5-a]indol-1-one ***(3a)***: White

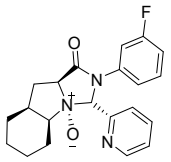
solid, yield 82%, >20:1 dr; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.06-1.29 (m, 3H), 1.36-1.40 (m, 1H), 1.55-1.65 (m, 3H), 1.96-2.00 (m, 3H), 2.31-2.36 (m, 1H), 3.25-3.30 (m, 1H), 4.21-4.25 (m, 1H), 6.08 (s, 1H), 6.97-7.01 (m, 1H), 7.14-7.19 (m, 3H), 7.29 (d, J = 7.6 Hz, 1H), 7.35 (d, J = 8.0 Hz, 2H), 7.62-7.66 (m, 1H), 8.41 (d, J = 4.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 20.3, 22.8, 23.9, 25.4, 27.8, 38.3, 62.6, 63.5, 78.0, 121.4, 121.6, 123.5, 125.4, 128.7, 136.6, 137.5, 149.4, 158.2, 176.9; HRMS (ESI-TOF) m/z: Calcd. for $C_{21}H_{24}N_3O$ $[M+H]^+$: 334.1914; Found: 334.1917.



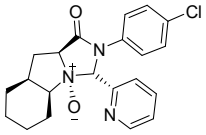
*(3S,4R,4aS,8aS,9aS)-1-oxo-2-phenyl-3-(pyridin-2-yl)decahydroimidazo[1,5-a]indole 4(1H)-oxide (**L1a**)*: White solid, m.p. 198.1-198.9 ^{o}C, overall yield 62%, >20:1 dr; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.08-1.15 (m, 1H), 1.22-1.32 (m, 1H), 1.40-1.51 (m, 2H), 1.57-1.64 (m, 1H), 1.73-1.76 (m, 2H), 2.05-2.08 (m, 2H), 2.19-2.27 (m, 1H), 2.36-2.44 (m, 1H), 3.45-3.46 (m, 1H), 3.93-3.99 (m, 1H), 4.67-4.71 (m, 1H), 6.28 (s, 1H), 7.06-7.09 (m, 1H), 7.16-7.23 (m, 3H), 7.30 (d, J = 8.4 Hz, 2H), 7.46 (d, J = 7.6 Hz, 1H), 7.60-7.64 (m, 1H), 8.55 (d, J = 4.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.1, 23.0, 23.4, 23.9, 26.7, 34.6, 75.4, 83.3, 84.0, 120.6, 123.4, 124.8, 125.4, 128.3, 134.2, 135.5, 148.8, 150.8, 168.6; HRMS (ESI-TOF) m/z: Calcd. for $C_{21}H_{24}N_3O_2$ $[M+H]^+$: 350.1863; Found: 350.1864.



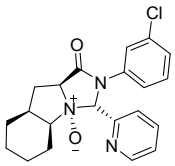
*(3S,4R,4aS,8aS,9aS)-2-(4-fluorophenyl)-1-oxo-3-(pyridin-2-yl)decahydroimidazo[1,5-a]indole 4(1H)-oxide (**L1b**)*: White solid, m.p. 191.2-191.8 ^{o}C, overall yield 57%, >20:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 1.13-1.20 (m, 1H), 1.27-1.37 (m, 2H), 1.47-1.50 (m, 1H), 1.64-1.84 (m, 3H), 2.18-1.42 (m, 3H), 3.28-3.34 (m, 1H), 3.79-3.85 (m, 1H), 4.63-4.67 (m, 1H), 6.71 (s, 1H), 6.92-6.96 (m, 2H), 7.25-7.28 (m, 1H), 7.32-7.36 (m, 2H), 7.50 (d, J = 7.6 Hz, 1H), 7.69-7.73 (m, 1H), 8.54 (d, J = 4.4 Hz, 1H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 19.7, 23.8, 24.0, 24.5, 26.9, 35.7, 75.5, 84.2, 84.5, 115.6 (d, J_{CF} = 23.4 Hz), 124.6, 126.7, 130.2, 131.1, 136.5, 149.7, 151.3, 160.8 (d, J_{CF} = 239.2 Hz), 169.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{21}H_{23}FN_3O_2$ $[M+H]^+$: 368.1763; Found: 368.1756.



*(3S,4R,4aS,8aS,9aS)-2-(3-fluorophenyl)-1-oxo-3-(pyridin-2-yl)decahydroimidazo[1,5-a]indole 4(1H)-oxide (**L1c**)*: White solid, m.p. 206.3-206.8 °C, overall yield 57%, >20:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 1.21-1.29 (m, 1H), 1.37-1.47 (m, 2H), 1.56-1.59 (m, 1H), 1.74-1.91 (m, 3H), 2.30-2.38 (m, 2H), 2.45-2.53 (m, 1H), 3.38-3.42 (m, 1H), 3.90-3.96 (m, 1H), 4.73-4.77 (m, 1H), 6.88-6.93 (m, 2H), 7.23-7.33 (m, 2H), 7.36-7.39 (m, 1H), 7.44-7.48 (m, 1H), 7.68 (d, J = 7.6 Hz, 1H), 7.82-7.86 (m, 1H), 8.62 (d, J = 4.4 Hz, 1H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 19.8, 23.7, 23.9, 24.5, 27.1, 35.7, 75.5, 83.8, 84.3, 108.6 (d, J_{CF} = 26.2 Hz), 112.7 (d, J_{CF} = 21.4 Hz), 116.6, 122.3, 124.6, 126.7, 130.4 (d, J_{CF} = 10.1 Hz), 136.6, 149.7, 151.2, 162.8 (d, J_{CF} = 243.1 Hz), 169.3; HRMS (ESI-TOF) m/z: Calcd. for $C_{21}H_{22}FN_3NaO_2$ $[M+Na]^+$: 390.1586; Found: 390.1579.

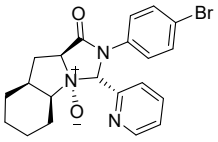


*(3S,4R,4aS,8aS,9aS)-2-(4-chlorophenyl)-1-oxo-3-(pyridin-2-yl)decahydroimidazo[1,5-a]indole 4(1H)-oxide (**L1d**)*: White solid, m.p. 197.6-197.9 °C, overall yield 60%, >20:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 1.23-1.29 (m, 1H), 1.39-1.46 (m, 2H), 1.57-1.60 (m, 1H), 1.77-1.91 (m, 3H), 2.29-2.37 (m, 2H), 2.44-2.52 (m, 1H), 3.37-3.42 (m, 1H), 3.90-3.95 (m, 1H), 4.72-4.76 (m, 1H), 6.86 (s, 1H), 7.29-7.31 (m, 2H), 7.37-7.40 (m, 1H), 7.46 (d, J = 8.4 Hz, 2H), 7.64 (d, J = 7.6 Hz, 1H), 7.81-7.85 (m, 1H), 8.63 (d, J = 4.0 Hz, 1H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 19.7, 23.8, 23.9, 24.5, 27.0, 35.7, 75.4, 84.1, 84.3, 123.3, 124.6, 126.7, 128.9, 131.6, 133.7, 136.6, 149.7, 151.1, 169.3; HRMS (ESI-TOF) m/z: Calcd. for Calcd. for $C_{21}H_{23}ClN_3O_2$ $[M+H]^+$: 384.1473; Found: 384.1466.

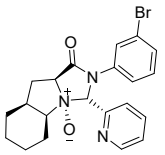


*(3S,4R,4aS,8aS,9aS)-2-(3-chlorophenyl)-1-oxo-3-(pyridin-2-yl)decahydroimidazo[1,5-a]indole 4(1H)-oxide (**L1e**)*: White solid, m.p. 190.9-191.2 °C, overall yield 60%, >20:1 dr; ^{1}H NMR

(CD_3OD, 400 MHz) δ: 1.21-1.28 (m, 1H), 1.37-1.47 (m, 2H), 1.55-1.58 (m, 1H), 1.73-1.90 (m, 3H), 2.29-2.37 (m, 2H), 2.44-2.52 (m, 1H), 3.35-3.41 (m, 1H), 3.90-3.96 (m, 1H), 4.72-4.76 (m, 1H), 6.93 (s, 1H), 7.14-7.16 (m, 1H), 7.24-7.28 (m, 1H), 7.36-7.39 (m, 2H), 7.68-7.69 (m, 2H), 7.82-7.86 (m, 1H), 8.62 (d, J = 4.4 Hz, 1H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 19.8, 23.8, 23.9, 24.5, 27.1, 35.7, 75.4, 83.7, 84.3, 119.4, 121.5, 124.7, 126.1, 126.8, 130.2, 134.4, 136.4, 136.6, 149.7, 151.1, 169.3; HRMS (ESI-TOF) m/z: Calcd. for $C_{21}H_{23}ClN_3O_2$ $[M+H]^+$: 384.1473; Found: 384.1466.

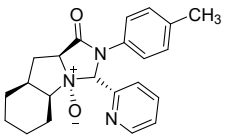


*(3S,4R,4aS,8aS,9aS)-2-(4-bromophenyl)-1-oxo-3-(pyridin-2-yl)decahydroimidazo[1,5-a]indole 4(1H)-oxide (**L1f**)*: White solid, m.p. 191.3-191.7 °C, overall yield 59%, >20:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 1.22-1.29 (m, 1H), 1.37-1.46 (m, 2H), 1.56-1.59 (m, 1H), 1.77-1.91 (m, 3H), 2.29-2.37 (m, 2H), 2.45-2.53 (m, 1H), 3.38-3.42 (m, 1H), 3.89-3.95 (m, 1H), 4.72-4.76 (m, 1H), 6.86 (s, 1H), 7.36-7.45 (m, 5H), 7.64 (d, J = 7.6 Hz, 1H), 7.81-7.85 (m, 1H), 8.61 (d, J = 4.0 Hz, 1H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 19.8, 23.8, 24.0, 24.5, 27.1, 35.7, 75.5, 84.0, 84.3, 119.3, 123.5, 124.6, 126.7, 132.0, 134.3, 136.6, 149.7, 151.2, 169.3; HRMS (ESI-TOF) m/z: Calcd. for $C_{21}H_{23}BrN_3O_2$ $[M+H]^+$: 428.0958; Found: 428.0959.

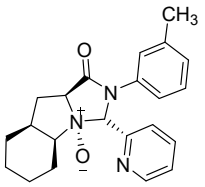


*(3S,4R,4aS,8aS,9aS)-2-(3-bromophenyl)-1-oxo-3-(pyridin-2-yl)decahydroimidazo[1,5-a]indole 4(1H)-oxide (**L1g**)*: White solid, m.p. 195.9-196.3 °C, overall yield 58%, >20:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 1.23-1.29 (m, 1H), 1.38-1.45 (m, 2H), 1.57-1.60 (m, 1H), 1.77-1.91 (m, 3H), 2.29-2.37 (m, 2H), 2.44-2.52 (m, 1H), 3.37-3.40 (m, 1H), 3.89-3.95 (m, 1H), 4.71-4.75 (m, 1H), 6.91 (d, J = 2.0 Hz, 1H), 7.19-7.23 (m, 1H), 7.29-7.34 (m, 1H), 7.37-7.42 (m, 2H), 7.64-7.68 (m, 1H), 7.79-7.86 (m, 2H), 8.62-8.63 (m, 1H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 19.7, 23.7, 23.9, 24.5, 27.1, 35.7, 75.4, 83.8, 84.3, 119.9, 122.2, 124.4, 124.7, 126.7, 129.1, 130.4, 136.4, 136.6, 149.7, 151.1, 169.4; HRMS (ESI-TOF) m/z: Calcd. for $C_{21}H_{23}BrN_3O_2$ $[M+H]^+$: 428.0958; Found:

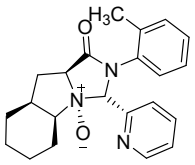
428.0945.



*(3S,4R,4aS,8aS,9aS)-1-oxo-3-(pyridin-2-yl)-2-(p-tolyl)decahydroimidazo[1,5-a]indole 4(1H)-oxide (**L1h**)*: White solid, m.p. 220.6-220.9 °C, overall yield 59%, >20:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 1.19-1.25 (m, 1H), 1.33-1.37 (m, 1H), 1.45-1.55 (m, 2H), 1.73-1.87 (m, 3H), 2.20 (s, 3H), 2.30-2.46 (m, 3H), 3.37-3.41 (m, 1H), 3.90-3.96 (m, 1H), 4.74-4.78 (m, 1H), 6.82 (s, 1H), 7.07 (d, J = 8.8 Hz, 2H), 7.31-7.34 (m, 3H), 7.63 (d, J = 7.6 Hz, 1H), 7.76-7.80 (m, 1H), 8.61 (d, J = 4.8 Hz, 1H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 19.7, 19.8, 23.8, 24.0, 24.6, 27.1, 35.7, 75.6, 84.2, 84.5, 122.1, 124.5, 126.7, 127.7, 129.5, 130.0, 132.5, 136.5, 136.6, 149.6, 151.6, 169.2; HRMS (ESI-TOF) m/z: Calcd. for $C_{22}H_{26}N_3O_2$ $[M+H]^+$: 364.2020; Found: 364.2014.

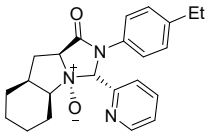


*(3S,4R,4aS,8aS,9aS)-1-oxo-3-(pyridin-2-yl)-2-(m-tolyl)decahydroimidazo[1,5-a]indole 4(1H)-oxide (**L1i**)*: White solid, m.p. 220.1-220.4 °C, overall yield 57%, >20:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 1.23-1.29 (m, 1H), 1.38-1.49 (m, 2H), 1.57-1.60 (m, 1H), 1.74-1.91 (m, 3H), 2.24 (s, 3H), 2.32-2.38 (m, 2H), 2.43-2.51 (m, 1H), 3.36-3.42 (m, 1H), 3.89-3.95 (m, 1H), 4.73-4.77 (m, 1H), 6.84 (s, 1H), 6.98 (d, J = 7.2 Hz, 1H), 7.14-7.22 (m, 2H), 7.31 (s, 1H), 7.34-7.37 (m, 1H), 7.62 (d, J = 7.6 Hz, 1H), 7.78-7.83 (m, 1H), 8.62-8.63 (m, 1H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 20.0, 20.1, 23.8, 24.0, 24.5, 27.0, 35.7, 75.6, 84.2, 84.4, 119.0, 122.5, 124.5, 126.6, 127.1, 128.7, 134.9, 136.5, 139.1, 149.6, 151.5, 169.3; HRMS (ESI-TOF) m/z: Calcd. for $C_{22}H_{26}N_3O_2$ $[M+H]^+$: 364.2020; Found: 364.2014.

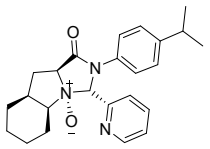


(3S,4R,4aS,8aS,9aS)-1-oxo-3-(pyridin-2-yl)-2-(o-tolyl)decahydroimidazo[1,5-a]indole 4(1H)-

*oxide (**L1j**)*: White solid, m.p. 230.5-230.9 °C, overall yield 55%, >20:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 1.19-1.31 (m, 2H), 1.43-1.50 (m, 2H), 1.63-1.70 (m, 1H), 1.78-1.89 (m, 2H), 2.15 (s, 3H), 2.21-2.26 (m, 1H), 2.29-2.37 (m, 1H), 2.61-2.64 (m, 1H), 3.31-3.35 (m, 1H), 3.82-3.88 (m, 1H), 4.81-4.85 (m, 1H), 6.74 (s, 1H), 7.02-7.09 (m, 3H), 7.20-7.23 (m, 1H), 7.27-7.29 (m, 1H), 7.33 (d, J = 8.0 Hz, 1H), 7.57-7.61 (m, 1H), 8.56 (d, J = 4.4 Hz, 1H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 18.0, 19.6, 23.7, 24.1, 24.6, 26.2, 35.8, 75.6, 84.4, 86.4, 124.5, 125.0, 126.3, 128.2, 131.6, 132.9, 136.2, 136.5, 149.4, 151.4, 168.0; HRMS (ESI-TOF) m/z: Calcd. for $C_{22}H_{26}N_3O_2$ $[M+H]^+$: 364.2020; Found: 364.2014.

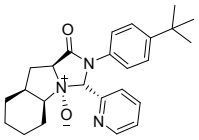


*(3S,4R,4aS,8aS,9aS)-2-(4-ethylphenyl)-1-oxo-3-(pyridin-2-yl)decahydroimidazo[1,5-a]indole 4(1H)-oxide (**L1k**)*: White solid, m.p. 200.0-200.7 °C, overall yield 58%, >20:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 1.00-1.04 (m, 3H), 1.11-1.18 (m, 1H), 1.27-1.39 (m, 2H), 1.45-1.48 (m, 1H), 1.65-1.80 (m, 3H), 2.18-2.28 (m, 2H), 2.32-2.46 (m, 3H), 3.27-3.30 (m, 1H), 3.79-3.84 (m, 1H), 4.63-4.67 (m, 1H), 6.70 (s, 1H), 7.01 (d, J = 8.4 Hz, 2H), 7.22-7.26 (m, 3H), 7.51 (d, J = 7.6 Hz, 1H), 7.67-7.71 (m, 1H), 8.51 (d, J = 4.4 Hz, 1H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 14.6, 19.8, 23.8, 24.0, 24.6, 27.0, 27.9, 35.7, 75.6, 84.2, 84.5, 122.2, 124.5, 126.6, 128.3, 132.6, 136.5, 143.0, 149.6, 151.5, 169.3; HRMS (ESI-TOF) m/z: Calcd. for $C_{23}H_{27}N_3NaO_2$ $[M+Na]^+$: 400.1992; Found: 400.1985.

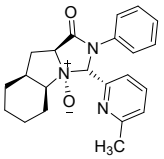


*(3S,4R,4aS,8aS,9aS)-2-(4-isopropylphenyl)-1-oxo-3-(pyridin-2-yl)decahydroimidazo[1,5-a]indole 4(1H)-oxide (**L1l**)*: White solid, m.p. 210.7-211.3 °C, overall yield 60%, >20:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 1.14 (s, 3H), 1.15 (s, 3H), 1.21-1.28 (m, 1H), 1.36-1.49 (m, 2H), 1.55-1.59 (m, 1H), 1.56-1.91 (m, 3H), 2.32-2.38 (m, 2H), 2.43-2.51 (m, 1H), 2.77-2.84 (m, 1H), 3.38-3.42 (m, 1H), 3.89-3.95 (m, 1H), 4.77-4.78 (m, 1H), 6.81 (s, 1H), 7.15 (d, J = 8.4 Hz, 2H), 7.33-7.36 (m, 3H), 7.62 (d, J = 8.0 Hz, 1H), 7.78-7.82 (m, 1H), 8.62-8.63 (m, 1H); ^{13}C NMR (CD_3OD, 100

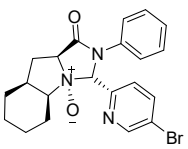
MHz) δ: 19.8, 22.9, 23.8, 24.0, 24.6, 27.0, 33.5, 35.7, 75.6, 84.2, 84.4, 122.1, 124.5, 126.6, 126.8, 132.7, 136.5, 147.5, 149.6, 151.6, 169.3; HRMS (ESI-TOF) m/z: Calcd. for $C_{24}H_{29}N_3NaO_2$ $[M+Na]^+$: 414.2147; Found: 414.2140.



*(3S,4R,4aS,8aS,9aS)-2-(4-(tert-butyl)phenyl)-1-oxo-3-(pyridin-2-yl)decahydroimidazo[1,5-a]indole 4(1H)-oxide (**L1m**)*: White solid, m.p. 226.6-227.2 °C, overall yield 61%, >20:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 1.18-1.28 (m, 10H), 1.35-1.49 (m, 2H), 1.56-1.59 (m, 1H), 1.56-1.91 (m, 3H), 2.29-2.37 (m, 2H), 2.44-2.52 (m, 1H), 3.38-3.43 (m, 1H), 3.89-3.95 (m, 1H), 4.74-4.78 (m, 1H), 6.82 (s, 1H), 7.31-7.38 (m, 5H), 7.63 (d, J = 7.6 Hz, 1H), 7.78-7.82 (m, 1H), 8.61 (d, J = 4.4 Hz, 1H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 19.8, 23.8, 24.0, 24.6, 27.0, 30.2, 34.0, 35.7, 75.6, 84.2, 84.3, 121.6, 124.5, 125.8, 126.6, 132.4, 136.5, 149.6, 149.7, 151.6, 169.3; HRMS (ESI-TOF) m/z: Calcd. for $C_{25}H_{32}N_3O_2$ $[M+H]^+$: 406.2486; Found: 406.2474.



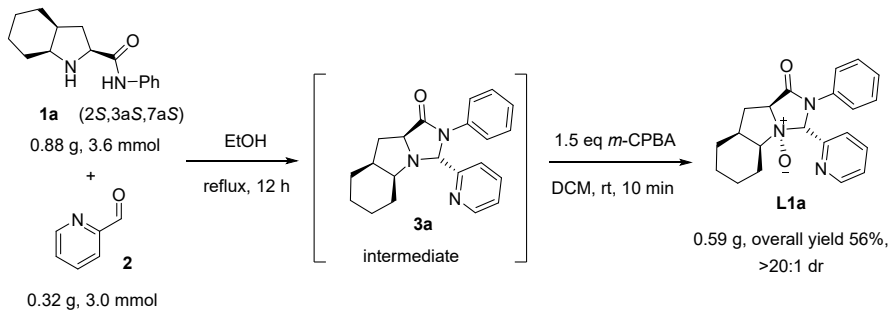
*(3S,4R,4aS,8aS,9aS)-3-(6-methylpyridin-2-yl)-1-oxo-2-phenyldecahydroimidazo[1,5-a]indole 4(1H)-oxide (**L1n**)*: White solid, overall yield 56%, >20:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 1.25-1.29 (m, 1H), 1.39-1.50 (m, 2H), 1.58-1.61 (m, 1H), 1.75-1.92 (m, 3H), 2.32-2.36 (m, 2H), 2.42-2.47 (m, 1H), 2.52 (s, 3H), 3.37-3.41 (m, 1H), 3.88-3.94 (m, 1H), 4.76-4.81 (m, 1H), 6.76 (s, 1H), 7.15-7.19 (m, 1H), 7.22 (d, J = 7.6 Hz, 1H), 7.28-7.32 (m, 2H), 7.40-7.44 (m, 3H), 7.66-7.69 (m, 1H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 19.8, 23.2, 23.8, 24.0, 24.5, 27.0, 35.7, 75.5, 84.2, 84.5, 122.2, 123.5, 124.0, 126.4, 128.9, 135.1, 136.7, 150.6, 159.0, 169.5; HRMS (ESI-TOF) m/z: Calcd. for $C_{22}H_{26}N_3O_2$ $[M+H]^+$: 364.2020; Found: 364.2017.



(3S,4R,4aS,8aS,9aS)-3-(5-bromopyridin-2-yl)-1-oxo-2-phenyldecahydroimidazo[1,5-a]indole

*4(1H)-oxide (**L1o**)*: White solid, overall yield 58%, >20:1 dr; ^{1}H NMR (CD_3OD, 400 MHz) δ: 1.09-1.17 (m, 1H), 1.24-1.47 (m, 3H), 1.62-1.79 (m, 3H), 2.17-2.25 (m, 2H), 2.33-2.41 (m, 1H), 3.26-3.30 (m, 1H), 3.78-3.84 (m, 1H), 4.58-4.62 (m, 1H), 6.80 (s, 1H), 7.04-7.07 (m, 1H), 7.17-7.21 (m, 2H), 7.33-7.35 (m, 2H), 7.47 (d, J = 8.4 Hz, 1H), 7.87-7.90 (m, 1H), 8.59 (d, J = 2.4 Hz, 1H); ^{13}C NMR (CD_3OD, 100 MHz) δ: 19.8, 23.8, 24.0, 24.5, 27.1, 35.7, 75.6, 83.8, 84.3, 121.5, 122.0, 126.5, 127.9, 129.1, 134.9, 139.2, 150.4, 150.8, 169.2; HRMS (ESI-TOF) m/z: Calcd. for $C_{21}H_{23}BrN_3O_2$ $[M+H]^+$: 428.0968; Found: 428.0971.

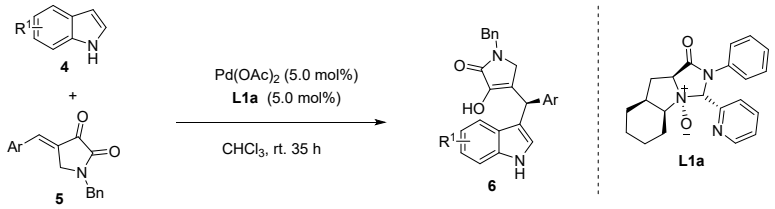
4. The gram scale synthesis of the ligand L1a



In a sealed tube equipped with a magnetic stirring bar, optically pure bicyclic prolinamide **1a** (0.88 g, 3.6 mmol) and pyridinecarboxaldehyde **2** (0.32 g, 3.0 mmol) were added. Then, ethanol (20.0 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**.

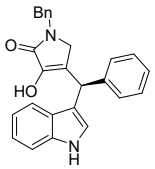
In a sealed tube equipped with a magnetic stirring bar, to the intermediate **3a** was added 20.0 mL of DCM and *m*-CPBA (3.0 eq). The reaction mixture was stirred at rt for 10 min. After completion of the reaction, as indicated by TLC, the aftertreatment residue was purified by flash column chromatography to furnish the pyridine-NO ligand **L1a** (0.59 g, overall yield 56%, >20:1 dr).

5. Catalytic asymmetric synthesis of compounds 6

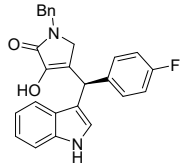


In a sealed tube equipped with a magnetic stirring bar, to the mixture of $Pd(AcO)_2$ (5.0 mol %), 5.0 mol % of **L1a** in 1.0 mL of $CHCl_3$ was added **4** (0.30 mmol), and **5** (0.20 mmol). The reaction mixture was stirred at room temperature for 35 h and was directly loaded onto a silica gel and purified by flash chromatography to give the desired product **6**, using hexane/EtOAc (10/1, v/v) as the eluent.

6. Characterization data of compounds 6

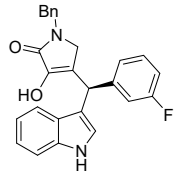


(S)-4-((1H-indol-3-yl)(phenyl)methyl)-1-benzyl-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one ***(6a)***: Product in accordance with literature characterization data[8]. 90%, 93% ee, $[\alpha]_D^{20} = +18.3$ (*c* 0.50, $CHCl_3$). The ee was determined by HPLC analysis using a Chiralpak IA column (60/40 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 10.55 min; τ_{minor} = 19.49 min). ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 3.54-3.67 (m, 2H), 4.51 (s, 2H), 5.58 (s, 1H), 6.85-6.89 (m, 1H), 6.95 (d, *J* = 2.0 Hz, 1H), 7.02-7.05 (m, 1H), 7.11-7.16 (m, 3H), 7.19-7.35 (m, 9H), 9.52 (br s, 1H), 10.92 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 39.0, 45.9, 48.1, 112.0, 115.6, 118.9, 119.1, 121.6, 123.4, 123.8, 126.8, 126.9, 127.6, 127.7, 128.5, 128.8, 129.0, 136.9, 138.2, 142.5, 142.8, 167.3.

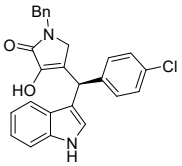


(S)-1-benzyl-4-((4-fluorophenyl)(1H-indol-3-yl)methyl)-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one ***(6b)***: Product in accordance with literature characterization data[8]. 90%, 98% ee. The ee was determined by HPLC analysis using a Chiralpak IA column (60/40 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 9.03 min; τ_{minor} = 16.33 min). ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 3.55-3.67 (m, 2H), 4.47-4.56 (m, 2H), 5.58 (s, 1H), 6.87-6.91 (m, 1H), 6.97 (d, *J* = 2.0 Hz, 1H), 7.03-7.17 (m, 6H), 7.22-7.36 (m, 6H), 9.55 (br s, 1H), 10.95 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 38.3, 46.0, 48.2, 112.1, 115.3, 115.4 (d, J_{CF} = 21.4 Hz), 119.0 (d, J_{CF} = 4.4 Hz), 121.6, 123.1,

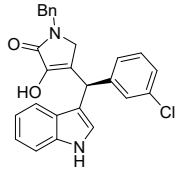
123.9, 126.7, 127.6, 127.7, 129.1, 130.2 (d, J_{CF} = 8.2 Hz), 137.0, 138.1, 139.0, 142.6, 161.8 (d, J_{CF} = 226.3 Hz), 167.3.



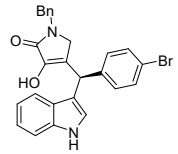
(S)-1-benzyl-4-((3-fluorophenyl)(1H-indol-3-yl)methyl)-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one ***(6c)***: Product in accordance with literature characterization data[8]. 89%, 94% ee. The ee was determined by HPLC analysis using a Chiralpak IA column (60/40 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 8.83 min; τ_{minor} = 14.93 min). ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 3.58-3.69 (m, 2H), 4.47-4.57 (m, 2H), 5.59 (s, 1H), 6.88-6.92 (m, 1H), 7.02-7.07 (m, 4H), 7.10-7.19 (m, 4H), 7.23 (d, *J* = 6.8 Hz, 1H), 7.28-7.36 (m, 4H), 9.58 (br s, 1H), 10.97 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 38.8, 46.0, 48.2, 112.1, 113.5 (d, J_{CF} = 21.2 Hz), 114.9, 115.1 (d, J_{CF} = 21.3 Hz), 119.0 (d, J_{CF} = 8.4 Hz), 121.7, 122.6, 124.0, 124.6, 126.7, 127.7, 127.8, 129.1, 130.6 (d, J_{CF} = 8.4 Hz), 136.9, 138.1, 142.8, 145.8 (d, J_{CF} = 7.1 Hz), 162.8 (d, J_{CF} = 241.4 Hz), 167.2.



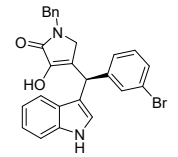
(S)-1-benzyl-4-((4-chlorophenyl)(1H-indol-3-yl)methyl)-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one ***(6d)***: Product in accordance with literature characterization data[8]. 88%, 92% ee, $[\alpha]_D^{20}$ = +67.1 (*c* 0.50, $CHCl_3$). The ee was determined by HPLC analysis using a Chiralpak IA column (60/40 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 9.13 min; τ_{minor} = 16.98 min). ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 3.55-3.66 (m, 2H), 4.46-4.56 (m, 2H), 5.56 (s, 1H), 6.86-6.90 (m, 1H), 6.98 (d, *J* = 2.0 Hz, 1H), 7.02-7.06 (m, 1H), 7.12-7.16 (m, 3H), 7.23-7.35 (m, 8H), 9.56 (br s, 1H), 10.96 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 38.5, 46.0, 48.2, 112.1, 115.1, 119.0, 121.6, 122.7, 124.0, 126.7, 127.7, 127.8, 128.7, 129.1, 130.3, 131.3, 136.9, 138.1, 141.8, 142.7, 167.3.



(S)-1-benzyl-4-((3-chlorophenyl)(1H-indol-3-yl)methyl)-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one ***(6e)***: Product in accordance with literature characterization data[8]. 89%, 95% ee. The ee was determined by HPLC analysis using a Chiralpak IA column (60/40 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 8.66 min; τ_{minor} = 16.34 min). ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 3.57-3.68 (m, 2H), 4.47-4.56 (m, 2H), 5.57 (s, 1H), 6.88-6.91 (m, 1H), 7.01-7.07 (m, 2H), 7.12-7.17 (m, 2H), 7.17 (d, *J* = 8.0 Hz, 1H), 7.21-7.31 (m, 7H), 7.35 (d, *J* = 8.0 Hz, 1H), 9.59 (br s, 1H), 10.97 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 38.8, 46.0, 48.3, 112.1, 114.8, 118.9, 119.1, 121.7, 122.5, 124.1, 126.7, 126.8, 127.2, 127.7, 127.8, 128.2, 129.1, 130.6, 133.4, 136.9, 138.1, 142.8, 145.5, 167.2.

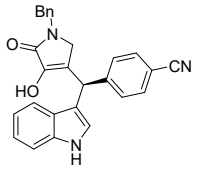


(S)-1-benzyl-4-((4-bromophenyl)(1H-indol-3-yl)methyl)-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one ***(6f)***: Product in accordance with literature characterization data[8]. 91%, 99% ee, $[\alpha]_D^{20}$ = +36.7 (*c* 0.50, $CHCl_3$). The ee was determined by HPLC analysis using a Chiralpak IA column (60/40 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 9.15 min; τ_{minor} = 15.92 min). ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 3.55-3.67 (m, 2H), 4.46-4.57 (m, 2H), 5.55 (s, 1H), 6.87-6.91 (m, 1H), 6.99 (d, *J* = 2.0 Hz, 1H), 7.03-7.06 (m, 1H), 7.12-7.16 (m, 3H), 7.19-7.24 (m, 3H), 7.27-7.31 (m, 2H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.45 (d, *J* = 8.4 Hz, 2H), 9.57 (br s, 1H), 10.96 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 38.5, 46.0, 48.2, 112.1, 115.0, 119.0, 119.8, 121.7, 122.7, 124.0, 126.7, 127.7, 127.8, 129.1, 130.7, 131.6, 136.9, 138.1, 142.3, 142.8, 167.3.

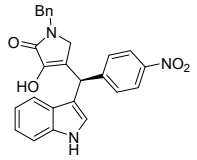


(S)-1-benzyl-4-((3-bromophenyl)(1H-indol-3-yl)methyl)-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one ***(6g)***: Product in accordance with literature characterization data[8]. 91%, 97% ee. The ee was determined by HPLC analysis using a Chiralpak IA column (60/40 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 8.85 min; τ_{minor} = 17.52 min). ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 3.57-3.68 (m, 2H), 4.48-4.57 (m, 2H), 5.57 (s, 1H), 6.88-6.92 (m, 1H), 7.02-7.08 (m, 2H), 7.12-7.19 (m,

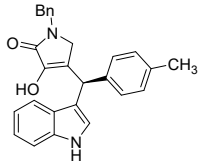
3H), 7.23-7.32 (m, 5H), 7.35 (d, *J* = 8.4 Hz, 1H), 7.39-7.40 (m, 2H), 9.59 (br s, 1H), 10.98 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 38.7, 46.0, 48.2, 112.1, 114.8, 118.9, 119.1, 121.7, 122.1, 122.5, 124.1, 126.7, 127.6, 127.7, 129.1, 129.7, 131.0, 131.1, 136.9, 138.1, 142.8, 145.7, 167.2.



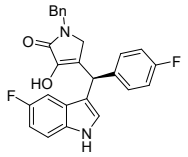
(S)-4-((1-benzyl-4-hydroxy-5-oxo-2,5-dihydro-1H-pyrrol-3-yl)(1H-indol-3-yl)methyl)benzonitrile ***(6h)***: Product in accordance with literature characterization data[8]. 90%, 99% ee. The ee was determined by HPLC analysis using a Chiralpak IA column (60/40 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 10.74 min; τ_{minor} = 14.94 min). ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 3.58-3.68 (m, 2H), 4.46-4.58 (m, 2H), 5.64 (s, 1H), 6.88-6.91 (m, 1H), 7.03-7.07 (m, 2H), 7.12-7.17 (m, 3H), 7.21-7.25 (m, 1H), 7.28-7.32 (m, 2H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.44 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 9.63 (br s, 1H), 11.01 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 39.3, 46.0, 48.3, 109.6, 112.1, 114.4, 118.9, 119.1, 119.4, 121.7, 121.9, 124.2, 126.6, 127.7, 127.8, 129.1, 129.6, 132.8, 136.9, 138.1, 143.1, 148.7, 167.2.



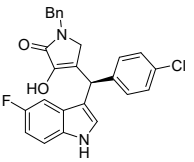
(S)-4-((1H-indol-3-yl)(4-nitrophenyl)methyl)-1-benzyl-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one ***(6i)***: Product in accordance with literature characterization data[8]. 89%, 92% ee, $[\alpha]_D^{20}$ = +12.2 (*c* 0.50, $CHCl_3$). The ee was determined by HPLC analysis using a Chiralpak IA column (60/40 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 11.84 min; τ_{minor} = 16.38 min). ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 3.61-3.71 (m, 2H), 4.46-4.59 (m, 2H), 5.70 (s, 1H), 6.88-6.92 (m, 1H), 7.04-7.08 (m, 2H), 7.13-7.19 (m, 3H), 7.21-7.25 (m, 1H), 7.28-7.32 (m, 2H), 7.36 (d, *J* = 8.4 Hz, 1H), 7.52 (d, *J* = 8.8 Hz, 2H), 9.68 (br s, 1H), 11.04 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 39.1, 46.0, 48.4, 112.2, 114.3, 118.9, 119.2, 121.7, 121.8, 124.0, 124.3, 126.6, 127.7, 127.8, 127.9, 128.7, 129.1, 129.8, 136.9, 138.1, 143.2, 146.5, 150.9, 167.1.



(S)-4-((1H-indol-3-yl)(p-tolyl)methyl)-1-benzyl-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one ***(6j)***: Product in accordance with literature characterization data[8]. 92%, 94% ee, $[\alpha]_D^{20}$ = +6.7 (*c* 0.47, $CHCl_3$). The ee was determined by HPLC analysis using a Chiralpak IA column (60/40 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 9.17 min; τ_{minor} = 17.31 min). ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 3.50-3.62 (m, 2H), 4.43-4.51 (m, 2H), 5.51 (s, 1H), 6.84-6.90 (m, 2H), 7.01-7.13 (m, 8H), 7.18-7.22 (m, 1H), 7.24-7.28 (m, 2H), 7.33 (d, *J* = 8.0 Hz, 1H), 9.56 (br s, 1H), 10.83 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 21.0, 38.6, 45.9, 48.1, 112.0, 115.7, 119.0, 121.7, 123.7, 124.1, 126.7, 127.7, 127.8, 128.3, 129.1, 129.4, 135.9, 136.8, 137.9, 139.5, 142.1, 167.5.

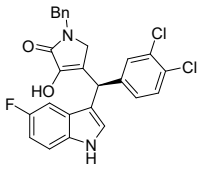


(S)-1-benzyl-4-((5-fluoro-1H-indol-3-yl)(4-fluorophenyl)methyl)-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one ***(6k)***: Product in accordance with literature characterization data[8]. 87%, 94% ee. The ee was determined by HPLC analysis using a Chiralpak IA column (60/40 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 7.44 min; τ_{minor} = 11.24 min). ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 3.56-3.68 (m, 2H), 4.48-4.58 (m, 2H), 5.53 (s, 1H), 6.85-6.93 (m, 2H), 7.08-7.15 (m, 5H), 7.21-7.37 (m, 6H), 9.58 (br s, 1H), 11.08 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 38.3, 46.0, 48.1, 103.5 (d, J_{CF} = 23.2 Hz), 109.7 (d, J_{CF} = 25.1 Hz), 113.1 (d, J_{CF} = 9.2 Hz), 115.5 (d, J_{CF} = 21.3 Hz), 115.8 (d, J_{CF} = 5.2 Hz), 122.8, 126.0, 127.7 (d, J_{CF} = 5.4 Hz), 129.0, 130.2 (d, J_{CF} = 8.2 Hz), 133.6, 138.1, 138.6 (d, J_{CF} = 3.3 Hz), 142.7, 156.8 (d, J_{CF} = 230.3 Hz), 161.6 (d, J_{CF} = 241.2 Hz), 167.3.

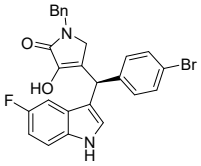


(S)-1-benzyl-4-((4-chlorophenyl)(5-fluoro-1H-indol-3-yl)methyl)-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one ***(6l)***: Product in accordance with literature characterization data[8]. 89%, 96% ee. The

ee was determined by HPLC analysis using a Chiralpak IA column (60/40 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 7.61 min; τ_{minor} = 11.74 min). ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 3.58-3.69 (m, 2H), 4.48-4.59 (m, 2H), 5.54 (s, 1H), 6.88-6.94 (m, 2H), 7.11-7.15 (m, 3H), 7.23-7.39 (m, 8H), 9.63 (br s, 1H), 11.11 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 38.5, 46.0, 48.2, 103.6 (d, J_{CF} = 24.2 Hz), 109.8 (d, J_{CF} = 26.1 Hz), 113.1 (d, J_{CF} = 9.2 Hz), 115.4 (d, J_{CF} = 5.1 Hz), 122.4, 126.1 (d, J_{CF} = 9.0 Hz), 126.9, 127.7 (d, J_{CF} = 4.2 Hz), 129.0, 130.3, 131.4, 133.6, 138.1, 141.5, 142.8, 156.9 (d, J_{CF} = 230.3 Hz), 167.3.

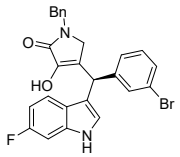


*(S)-1-benzyl-4-((3,4-dichlorophenyl)(5-fluoro-1H-indol-3-yl)methyl)-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one (**6m**)*: Product in accordance with literature characterization data[8]. 84%, 96% ee. The ee was determined by HPLC analysis using a Chiralpak IA column (60/40 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 6.65 min; τ_{minor} = 9.13 min). ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 3.60-3.70 (m, 2H), 4.47-4.59 (m, 2H), 5.51 (s, 1H), 6.89-6.96 (m, 2H), 7.14-7.15 (m, 3H), 7.22-7.26 (m, 2H), 7.29-7.32 (m, 2H), 7.34-7.37 (m, 1H), 7.47 (d, *J* = 2.0 Hz, 1H), 7.53 (d, *J* = 8.4 Hz, 1H), 9.62 (br s, 1H), 11.13 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) *δ*: 38.3, 46.0, 48.4, 103.3, 103.7 (d, J_{CF} = 23.3 Hz), 109.7 (d, J_{CF} = 27.0 Hz), 113.2 (d, J_{CF} = 10.0 Hz), 114.8, 121.7, 126.3, 126.9 (d, J_{CF} = 9.2 Hz), 127.7, 128.9, 129.0, 129.4, 130.4, 130.9, 131.3, 133.5, 138.1, 143.0, 143.8, 157.6 (d, J_{CF} = 230.2 Hz), 167.2.

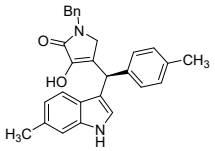


*(S)-1-benzyl-4-((4-bromophenyl)(5-fluoro-1H-indol-3-yl)methyl)-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one (**6n**)*: Product in accordance with literature characterization data[8]. 87%, 98% ee. The ee was determined by HPLC analysis using a Chiralpak IA column (60/40 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 7.62 min; τ_{minor} = 11.40 min). ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 3.57-3.68 (m, 2H), 4.48-4.59 (m, 2H), 5.52 (s, 1H), 6.88-6.94 (m, 2H), 7.10-7.15 (m, 3H), 7.21-

7.25 (m, 3H), 7.28-7.32 (m, 2H), 7.35-7.38 (m, 1H), 7.47 (d, J = 8.4 Hz, 2H), 9.62 (br s, 1H), 11.10 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 38.5, 46.0, 48.2, 103.5 (d, J_{CF} = 23.1 Hz), 109.8 (d, J_{CF} = 26.0 Hz), 113.2 (d, J_{CF} = 10.1 Hz), 115.4 (d, J_{CF} = 5.3 Hz), 119.9, 122.3, 126.1, 126.8 (d, J_{CF} = 10.1 Hz), 127.7 (d, J_{CF} = 4.4 Hz), 129.0, 130.7, 131.7, 133.6, 138.1, 141.9, 142.8, 156.8 (d, J_{CF} = 230.2 Hz), 167.2.



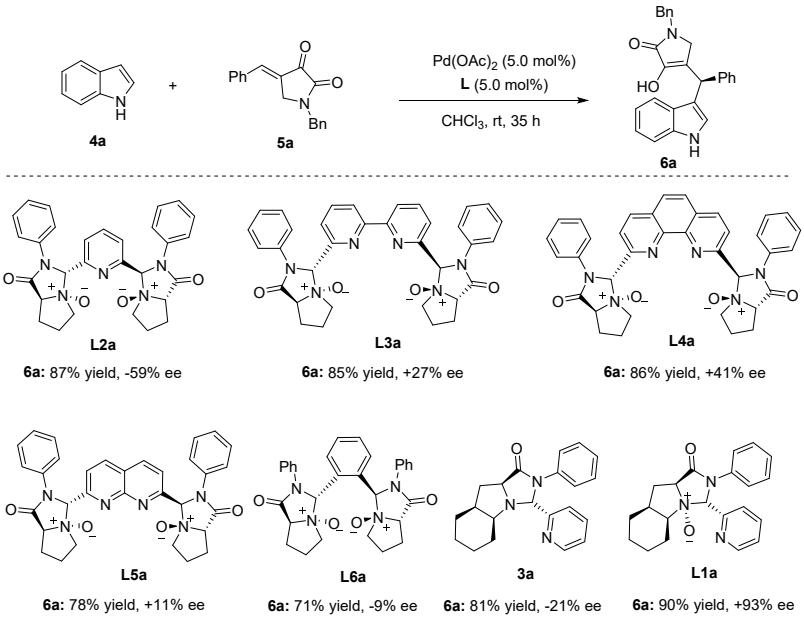
*(S)-1-benzyl-4-((3-bromophenyl)(6-fluoro-1H-indol-3-yl)methyl)-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one (**6o**)*: Product in accordance with literature characterization data[8]. 85%, 95% ee. The ee was determined by HPLC analysis using a Chiralpak IA column (60/40 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 7.21 min; τ_{minor} = 12.68 min). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.57-3.68 (m, 2H), 4.49-4.57 (m, 2H), 5.56 (s, 1H), 6.76-6.81 (m, 1H), 7.02 (d, J = 2.0 Hz, 1H), 7.13-7.17 (m, 4H), 7.24-7.32 (m, 5H), 7.39-7.41 (m, 2H), 9.62 (br s, 1H), 11.06 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 38.7, 46.0, 48.2, 98.0 (d, J_{CF} = 25.0 Hz), 107.6 (d, J_{CF} = 25.1 Hz), 115.1, 119.9 (d, J_{CF} = 11.0 Hz), 122.2 (d, J_{CF} = 7.3 Hz), 123.5, 124.7, 127.6, 127.7, 129.1, 129.8, 131.0 (d, J_{CF} = 6.2 Hz), 136.7 (d, J_{CF} = 13.2 Hz), 138.1, 142.9, 145.5, 159.6 (d, J_{CF} = 233.0 Hz), 167.2.

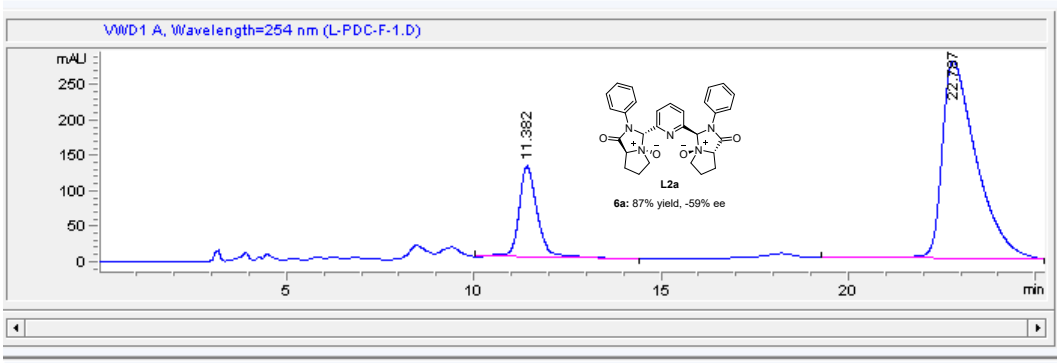


*(S)-1-benzyl-3-hydroxy-4-((6-methyl-1H-indol-3-yl)(p-tolyl)methyl)-1,5-dihydro-2H-pyrrol-2-one (**6p**)*: Product in accordance with literature characterization data[8]. 88%, 94% ee. The ee was determined by HPLC analysis using a Chiralpak IC column (60/40 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 6.79 min; τ_{minor} = 9.65 min). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.24 (s, 3H), 2.34 (s, 3H), 3.51-3.65 (m, 2H), 4.51 (s, 2H), 5.52 (s, 1H), 6.70 (d, J = 8.0 Hz, 1H), 6.85 (d, J = 1.6 Hz, 1H), 7.00-7.13 (m, 8H), 7.23-7.31 (m, 3H), 9.48 (br s, 1H), 10.74 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 21.1, 21.8, 38.7, 45.9, 48.1, 111.8, 115.5, 118.9, 120.7, 123.1, 123.8, 124.8, 127.6, 127.7, 128.3, 129.1, 129.3, 130.6, 135.7, 137.4, 138.2, 139.8, 142.3, 167.4.

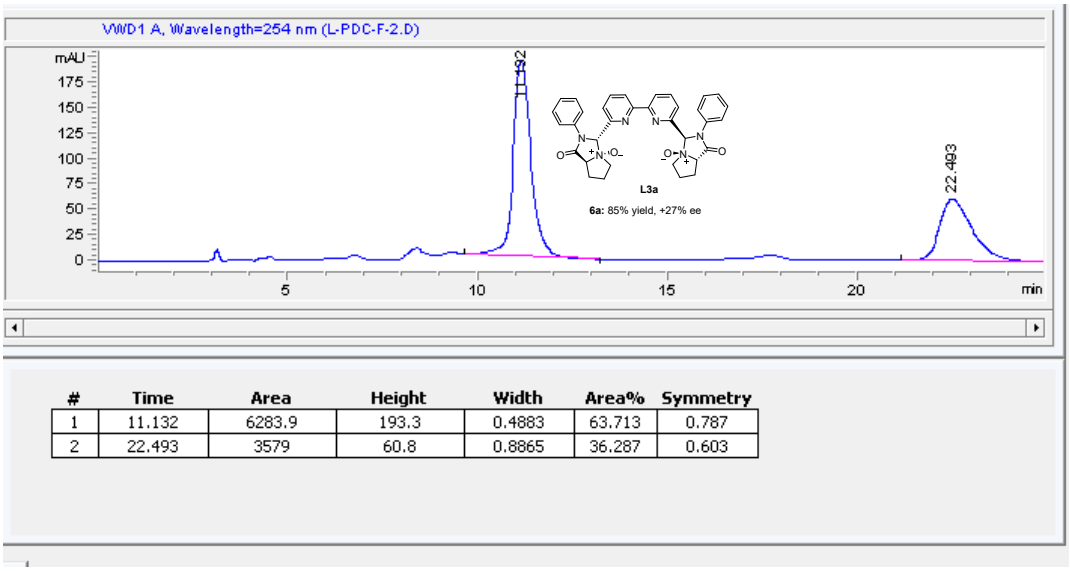
7. Compared experiments using different ligands

In a sealed tube equipped with a magnetic stirring bar, to the mixture of $Pd(AcO)_2$ (5.0 mol %), 5.0 mol % of **L** in 1.0 mL of $CHCl_3$ was added **4a** (0.30 mmol), and **5a** (0.20 mmol). The reaction mixture was stirred at room temperature for 35 h and was directly loaded onto a silica gel and purified by flash chromatography to give the desired product **6a**, using hexane/EtOAc (10/1, v/v) as the eluent.

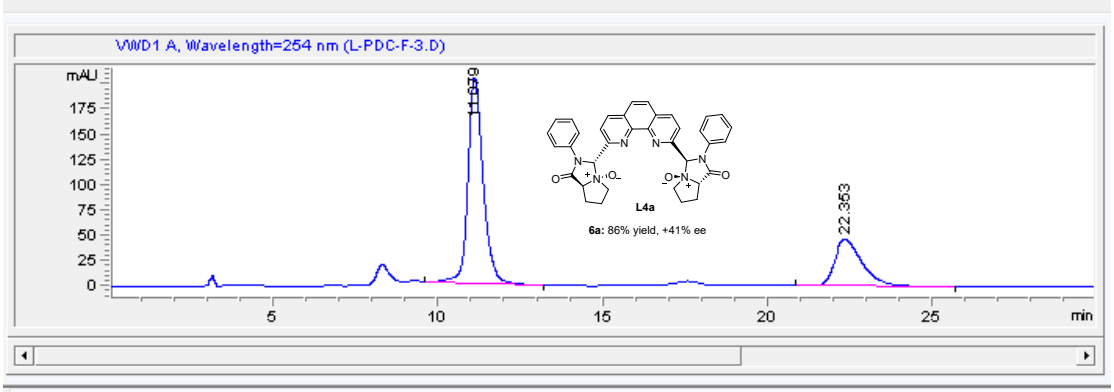




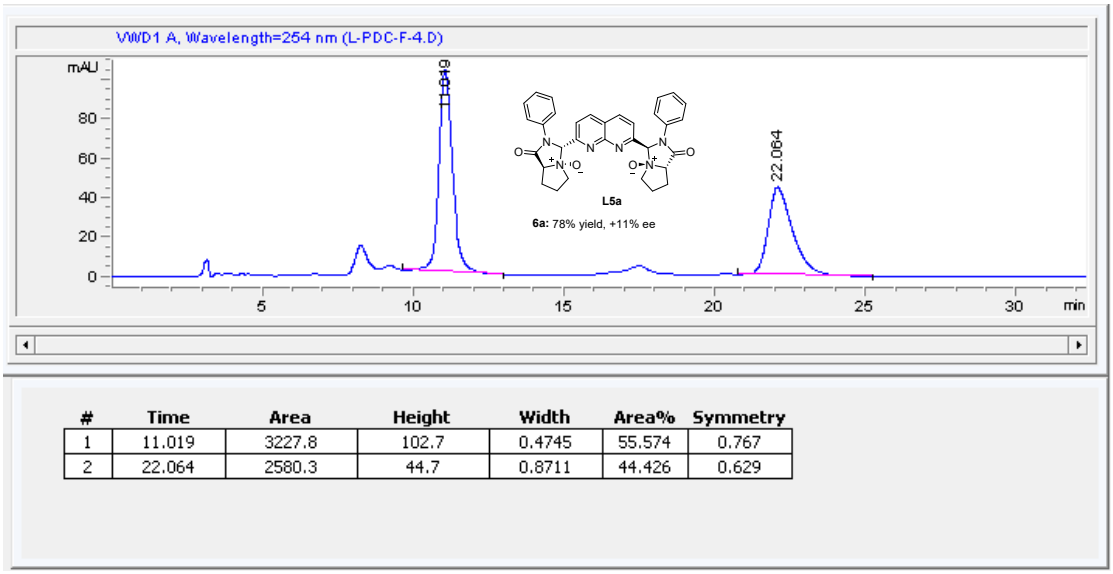
#	Time	Area	Height	Width	Area%	Symmetry
1	11.382	4518.1	129.1	0.5233	20.239	0.719
2	22.787	17806.1	279.5	0.9422	79.761	0.467



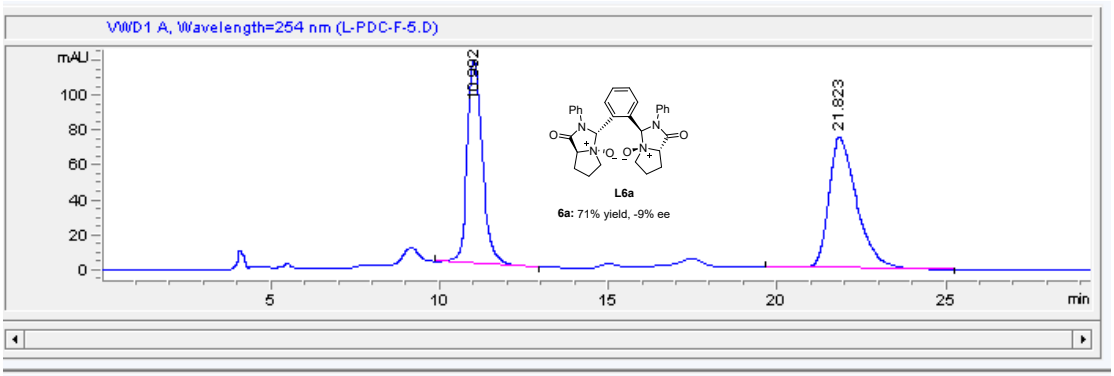
#	Time	Area	Height	Width	Area%	Symmetry
1	11.132	6283.9	193.3	0.4883	63.713	0.787
2	22.493	3579	60.8	0.8865	36.287	0.603



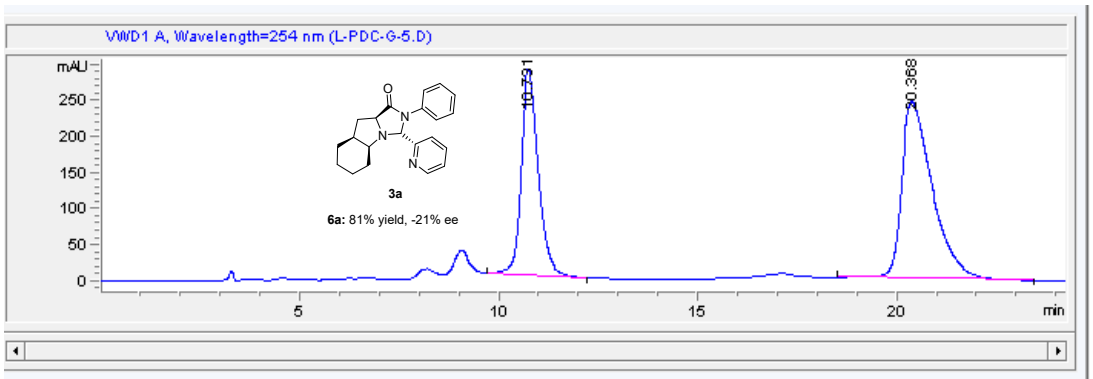
#	Time	Area	Height	Width	Area%	Symmetry
1	11.079	6462.4	203.7	0.4772	70.461	0.749
2	22.353	2709.2	45.9	0.8916	29.539	0.62



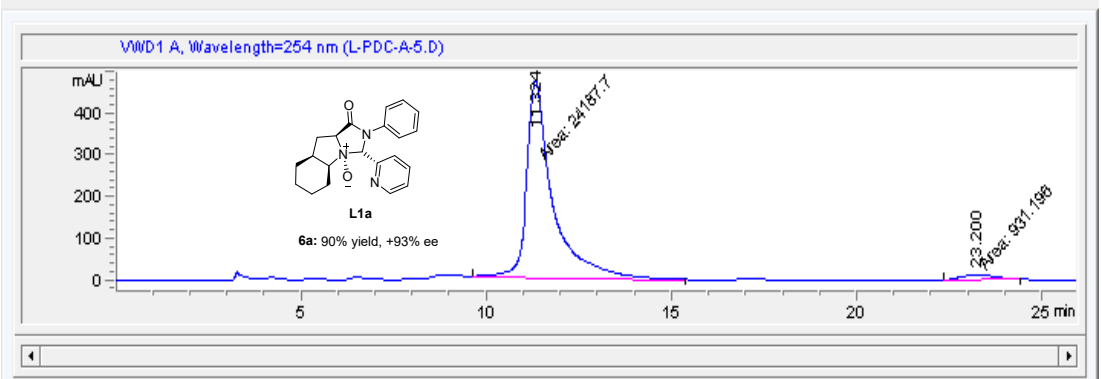
#	Time	Area	Height	Width	Area%	Symmetry
1	11.019	3227.8	102.7	0.4745	55.574	0.767
2	22.064	2580.3	44.7	0.8711	44.426	0.629



#	Time	Area	Height	Width	Area%	Symmetry
1	10.992	3611.7	116.8	0.4688	45.364	0.759
2	21.823	4349.8	75	0.8725	54.636	0.593



#	Time	Area	Height	Width	Area%	Symmetry
1	10.731	8579.9	285.9	0.4571	39.373	0.751
2	20.368	13211.6	245.3	0.7984	60.627	0.5



#	Time	Area	Height	Width	Area%	Symmetry
1	11.324	24187.7	474.3	0.85	96.293	0.52
2	23.2	931.2	13.4	1.1579	3.707	0.789

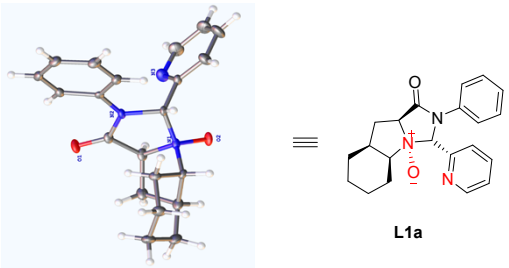
8. References

(a) J. K. Mansaray, Y. Huang, K. Li, X. Sun, Z. Zha and Z. *Org. Biomol. Chem.*, 2022, **20**, 5510-5514; *(b)* R. M. Liu, Y. H. Wang, Z. Y. Chen, L. Zhang, Q. H. Shi, Y. Zhou, Y. P. Tian and X. L. Liu, *Org. Chem. Front.*, 2022, **9**, 6881-6887; *(c)* K.-L. Xu, Y.-H. Wang, X.-R. Wang, P. Hu, B.-W. Pan, W.-J. Zhang, Z.-Y. Chen, Y. Zhou and X.-L. Liu*, Chin. J. Chem.*, 2024, **42**, 1474-1480; *(d)* X. Q. Zhu, W. W. Li, L. L. Liu, K. L. Xu, L. J. Peng, M. Zhang, X. L. Liu, and W. J. Zhang, *Adv. Synth. Catal.,* 2024, DOI: 10.1002adsc.202401348.

9. General experimental procedures for in vitro cytotoxicity assay

The human cancer cell line K562 was purchased from Chinese Academy of Sciences. All the cells were cultured in RPMI-1640 medium (GIBICO, USA), supplemented with 10% fetal bovine serum (Hyclone, USA) and Penicillin-Streptomycin (respectively 100 U/mL) in 5% CO_2 at 37°C. The cytotoxicity assay was performed according to the MTT (3-(4,5-dimethylthiazol-2-yl)-2, 5-diphenyl tetrazolium bromide) method in 96-well microplates. Briefly, 5000 cells were seeded into each well of 96-well cell culture plates and allowed to grow for 24 h before drug addition. The K562 tumor cell line was exposed to test compounds **6g**, **6l** and **6m** at the concentrations of 10, 20, 40, 80, and 100 μmol·L^{-1} in triplicates for 48 h, comparable to cisplatin (Aladdin, China). Then the MTT reagent was added to reaction with the cancer cells for 4 hours. At least, measure the OD value at 490 wavelengths. IC_{50} of all the compounds were calculated by IBM SPSS Statistics (version 19).

10. X-ray crystal data for compound L1a



L1a

CCDC 2412333

Table S1 Crystal data and structure refinement for L1a

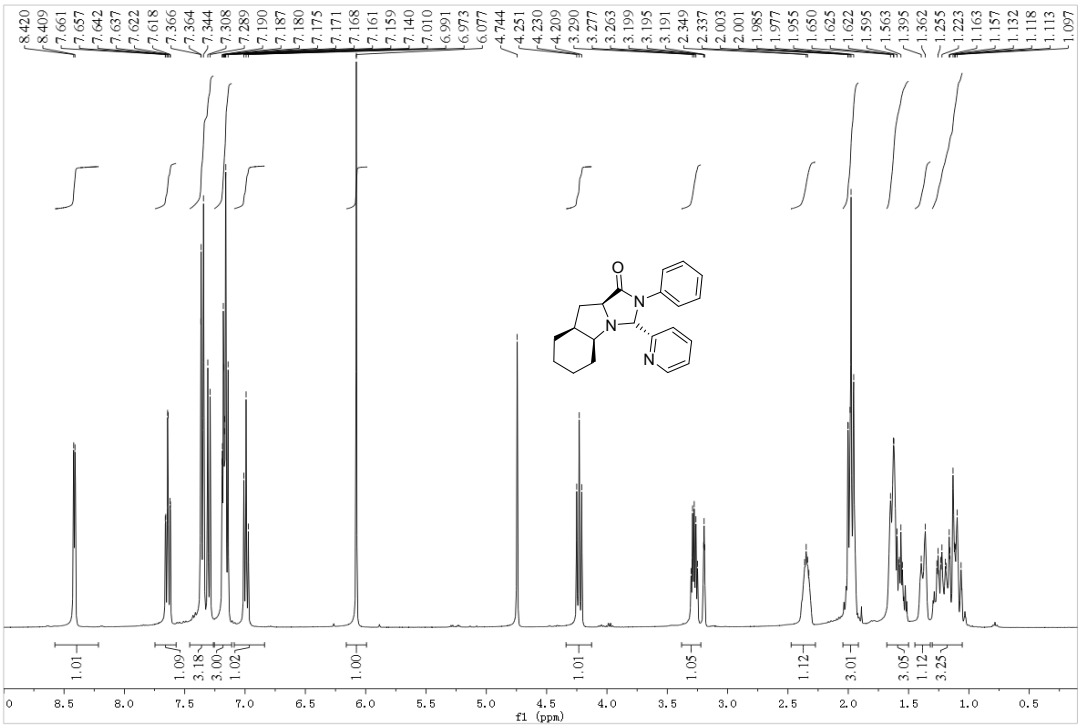
Identification code	**L1a**
Empirical formula	$C_{21}H_{25}N_3O_3$
Formula weight	367.44

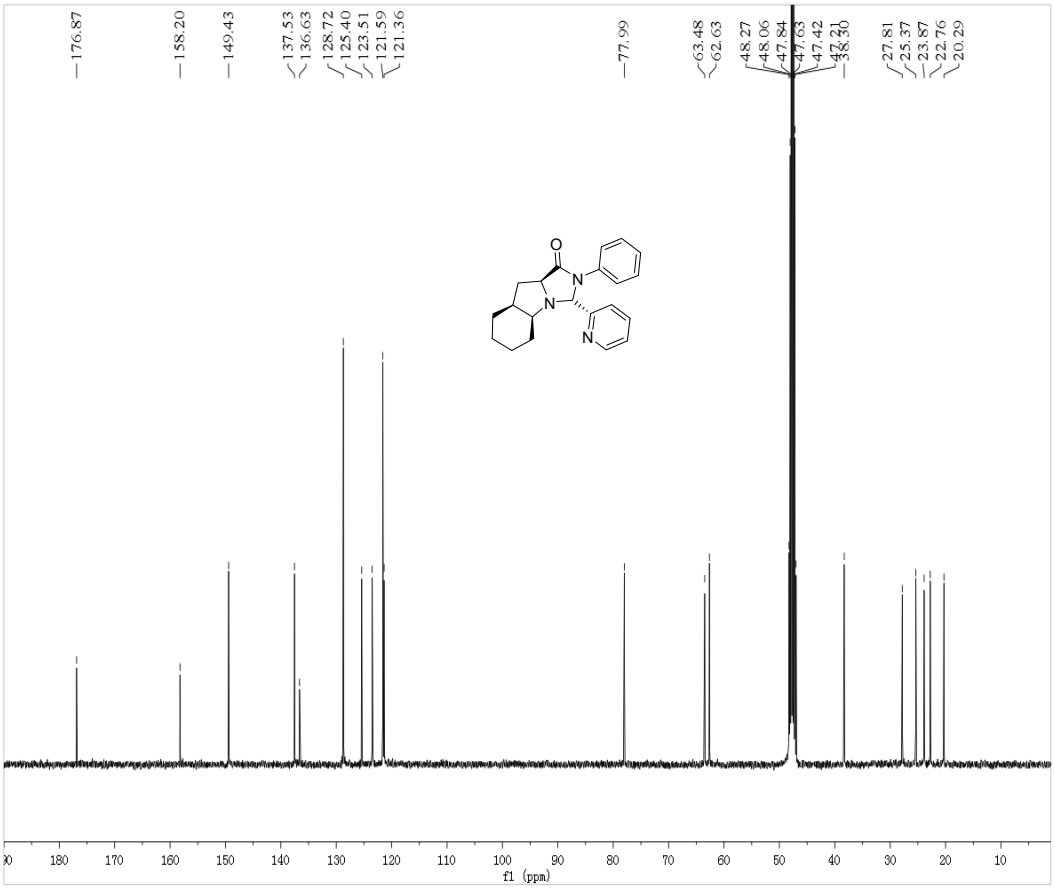
Temperature/K	150.00
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å, b/Å, c/Å	7.1170(3), 16.0841(7), 16.6316(7)
α/°, β/°, γ/°,	90, 90, 90
Volume/Å^3	1903.83(14)
Z	4
ρ_{calc}g/cm^3	1.282
μ/mm^{-1}	0.701
F(000)	784.0
Radiation	CuKα (λ = 1.54178)
Crystal size/mm^3	0.16 × 0.13 × 0.09
2Θ range for data collection/°	7.646 to 137.416
Index ranges	$-8 \le h \le 7$, $-19 \le k \le 19$, $-20 \le l \le 20$
Reflections collected	39237
Independent reflections	3504 [R_{int} = 0.0874, R_{sigma} = 0.0370]
Data/restraints/parameters	3504/0/247
Goodness-of-fit on F^2	1.151
Final R indexes [I>=2σ (I)]	R_1 = 0.0477, wR_2 = 0.1211
Final R indexes [all data]	R_1 = 0.0510, wR_2 = 0.1232
Largest diff. peak/hole / e Å^{-3}	0.23/-0.22
Flack parameter	0.05(9)/0.07(10)

Crystal Data for $C_{21}H_{25}N_3O_3$ (*M* =367.44 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), *a* = 7.1170(3) Å, *b* = 16.0841(7) Å, *c* = 16.6316(7) Å, *V* = 1903.83(14) Å^3, *Z* = 4, *T* = 150.00 K, μ(CuKα) = 0.701 mm^{-1}, *Dcalc* = 1.282 g/cm^3, 39237 reflections measured (7.646° ≤ 2Θ ≤ 137.416°), 3504 unique (R_{int} = 0.0874, R_{sigma} = 0.0370) which were used in all calculations. The final R_1 was 0.0477 (I > 2σ(I)) and wR_2 was 0.1232 (all data).

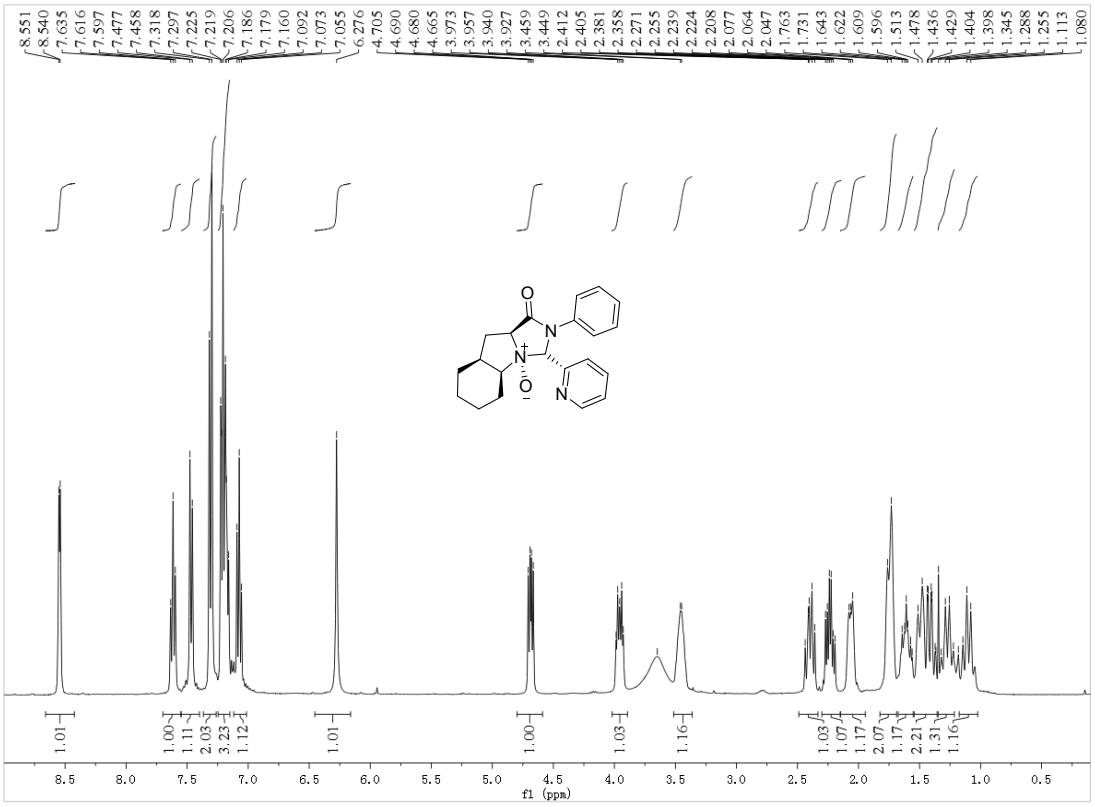
11. The copies of ^{1}H NMR, ^{13}C NMR and HPLC spectra for compounds 3a, L and 6

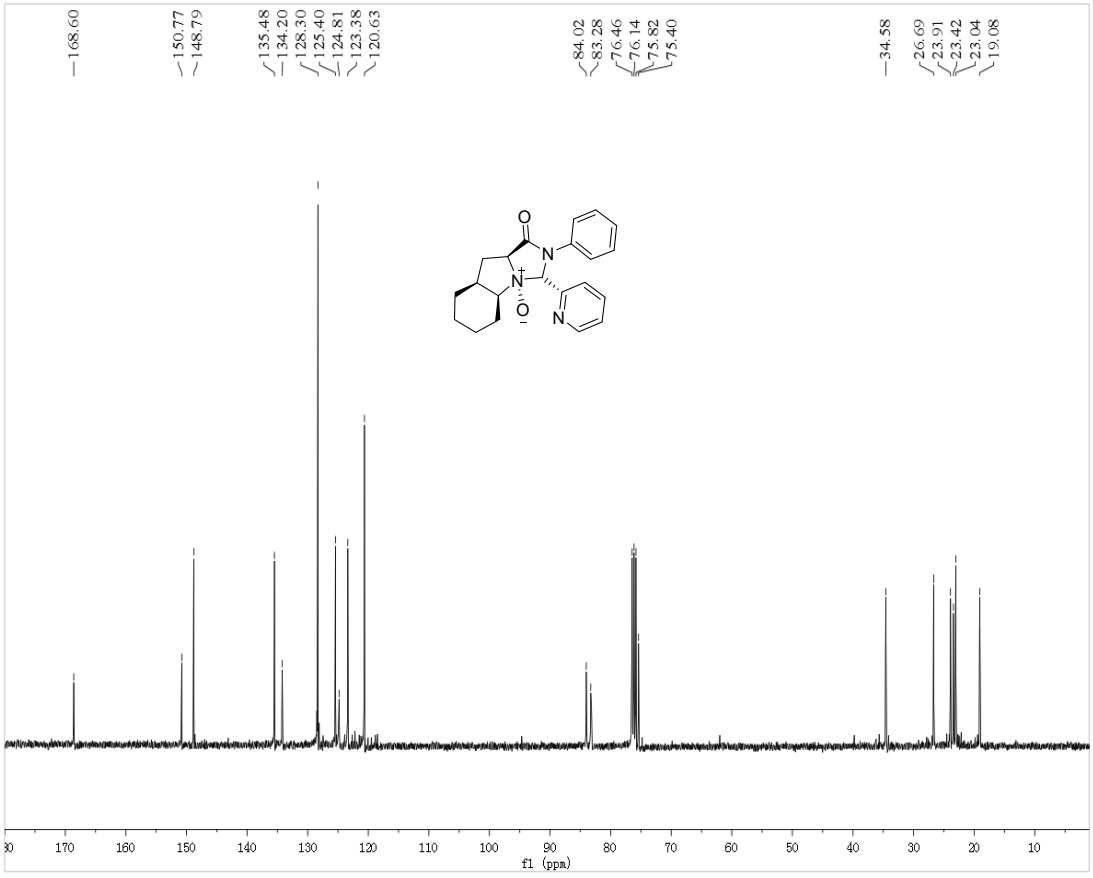
^{1}H and ^{13}C NMR of 3a



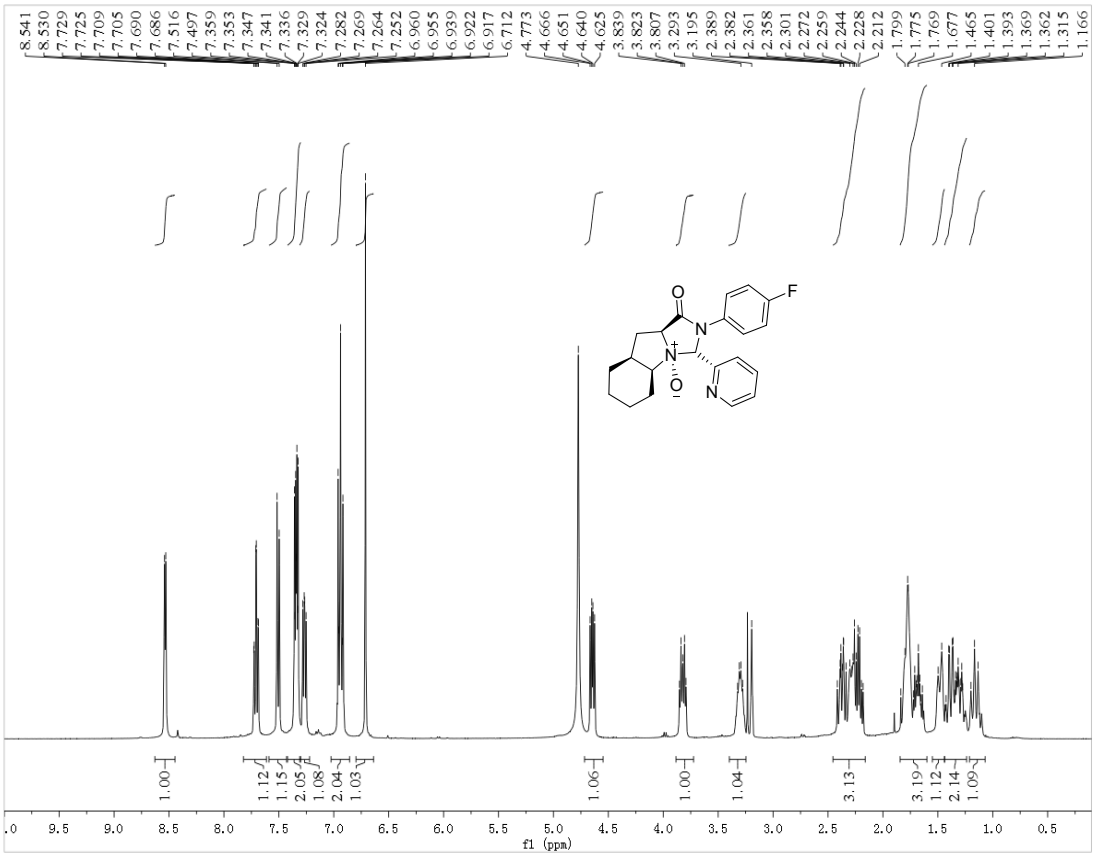


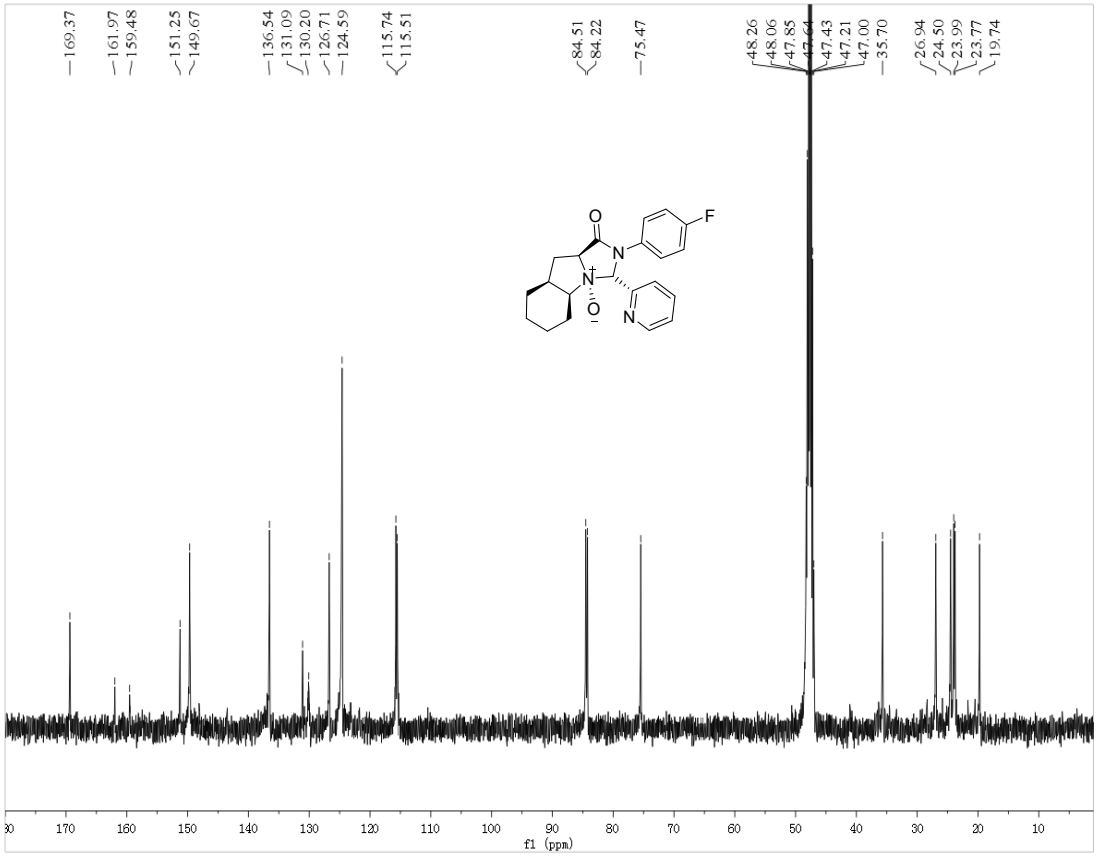
^{1}H and ^{13}C NMR of L1a



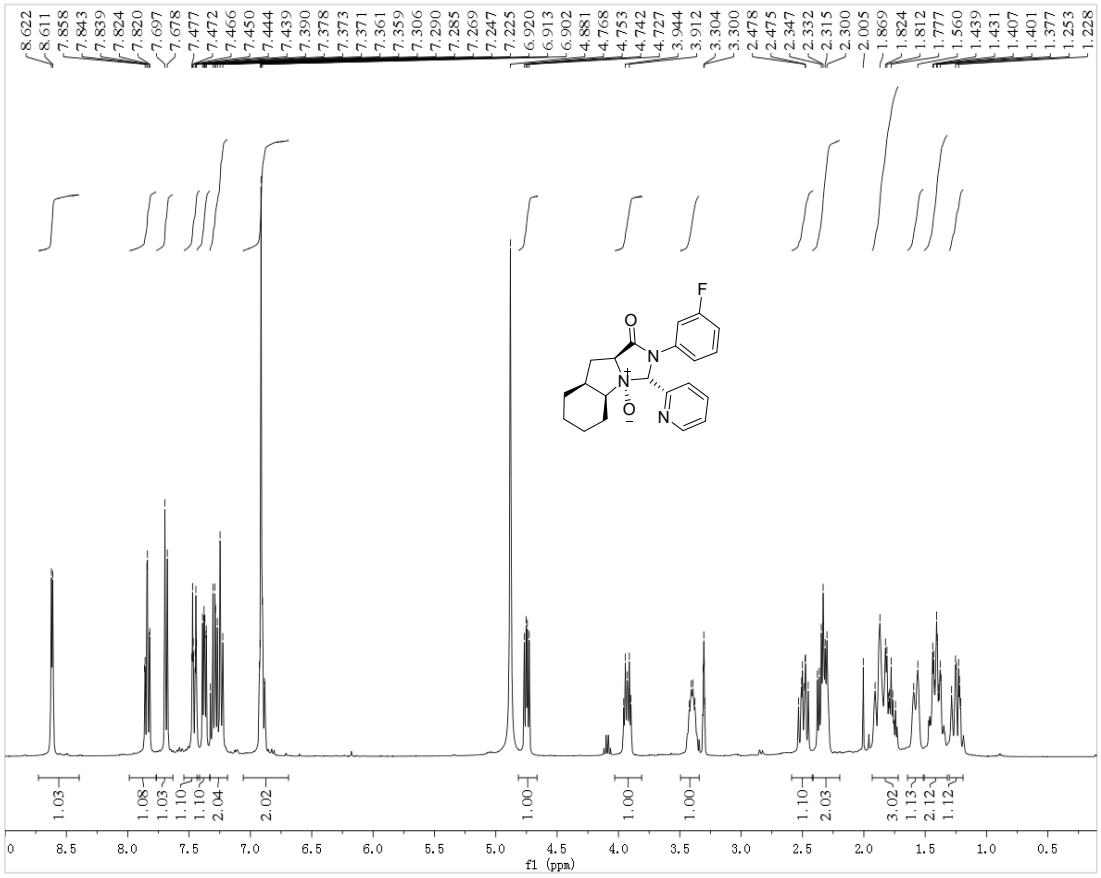


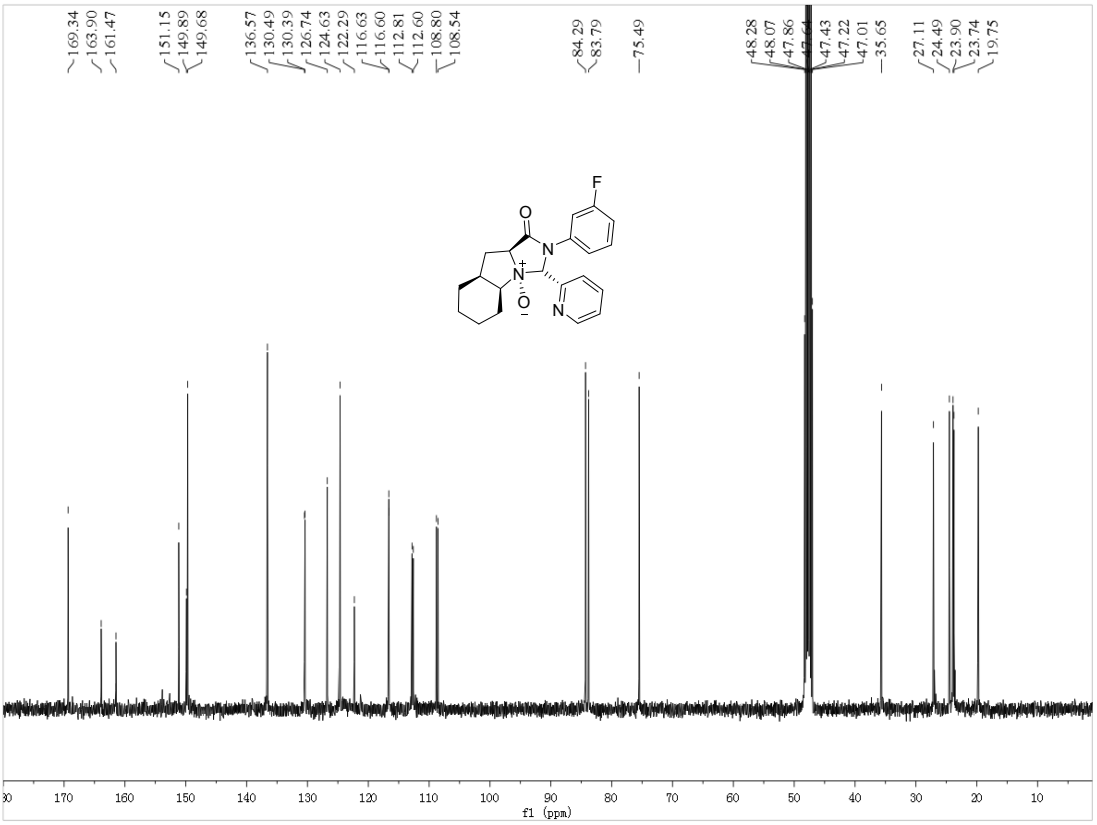
^{1}H and ^{13}C NMR of L1b



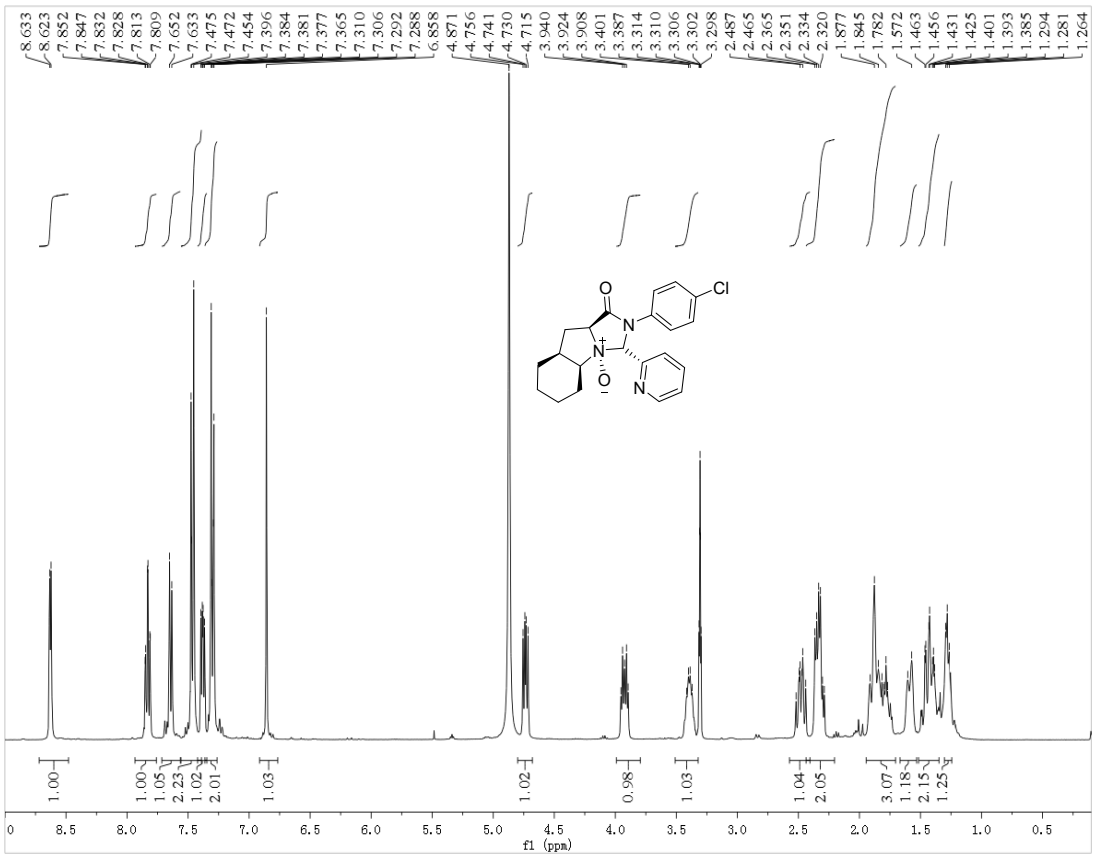


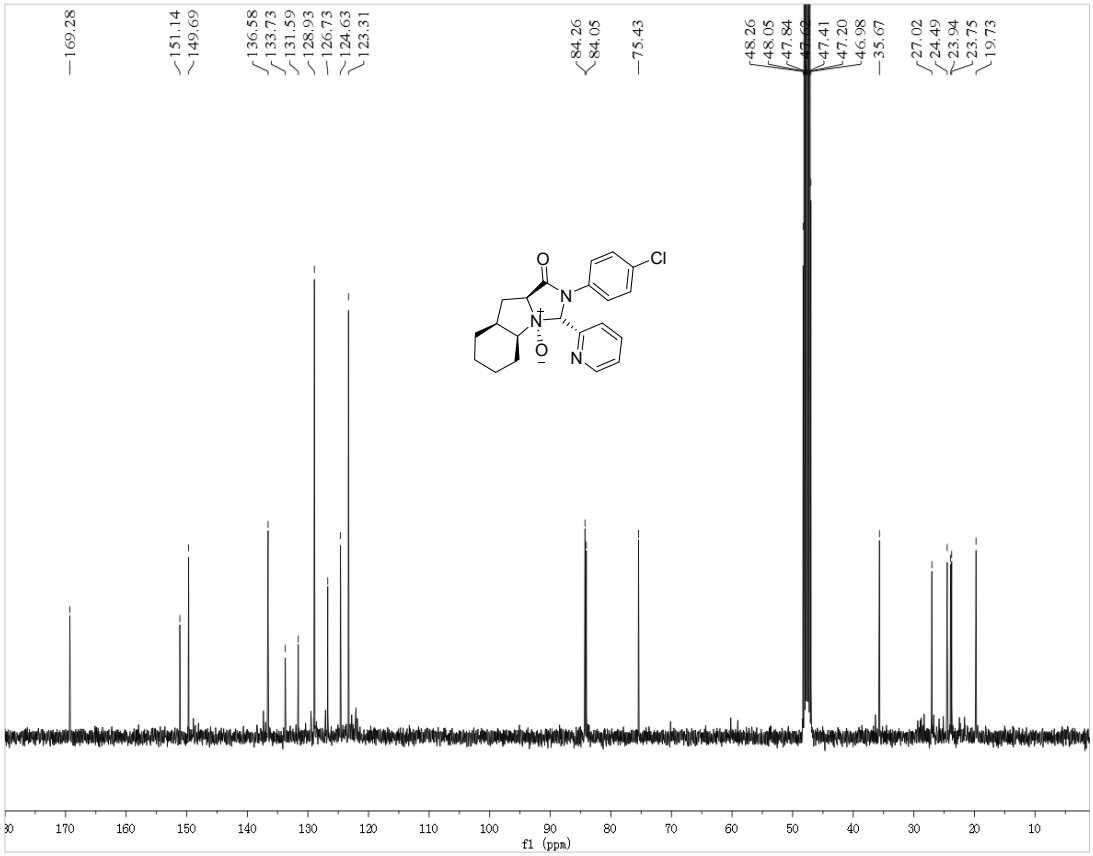
^{1}H and ^{13}C NMR of L1c



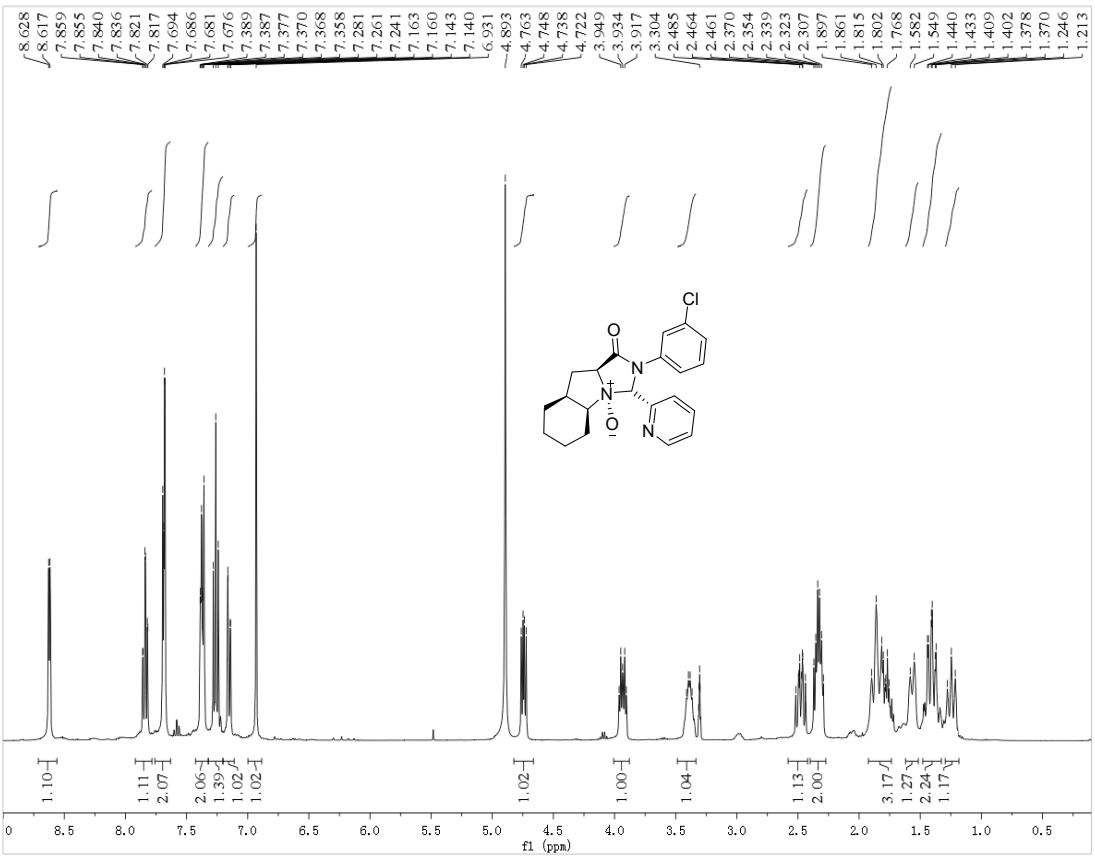


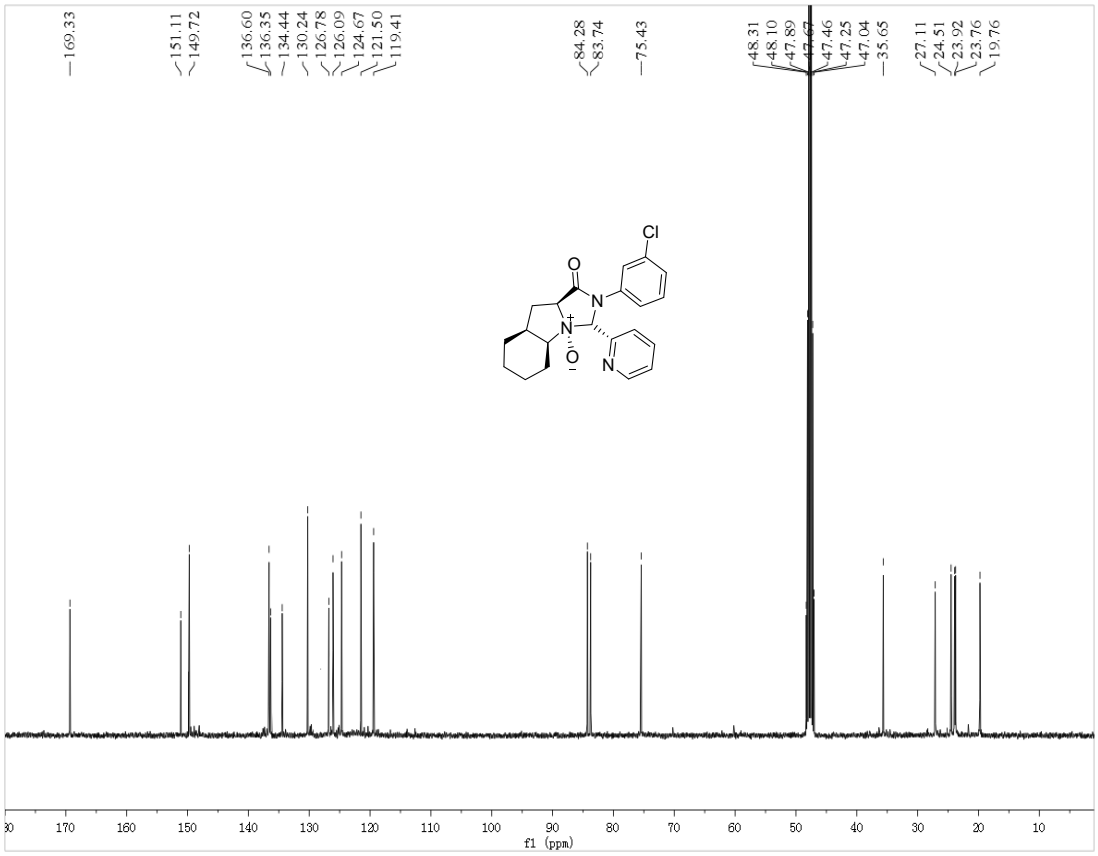
^{1}H and ^{13}C NMR of L1d



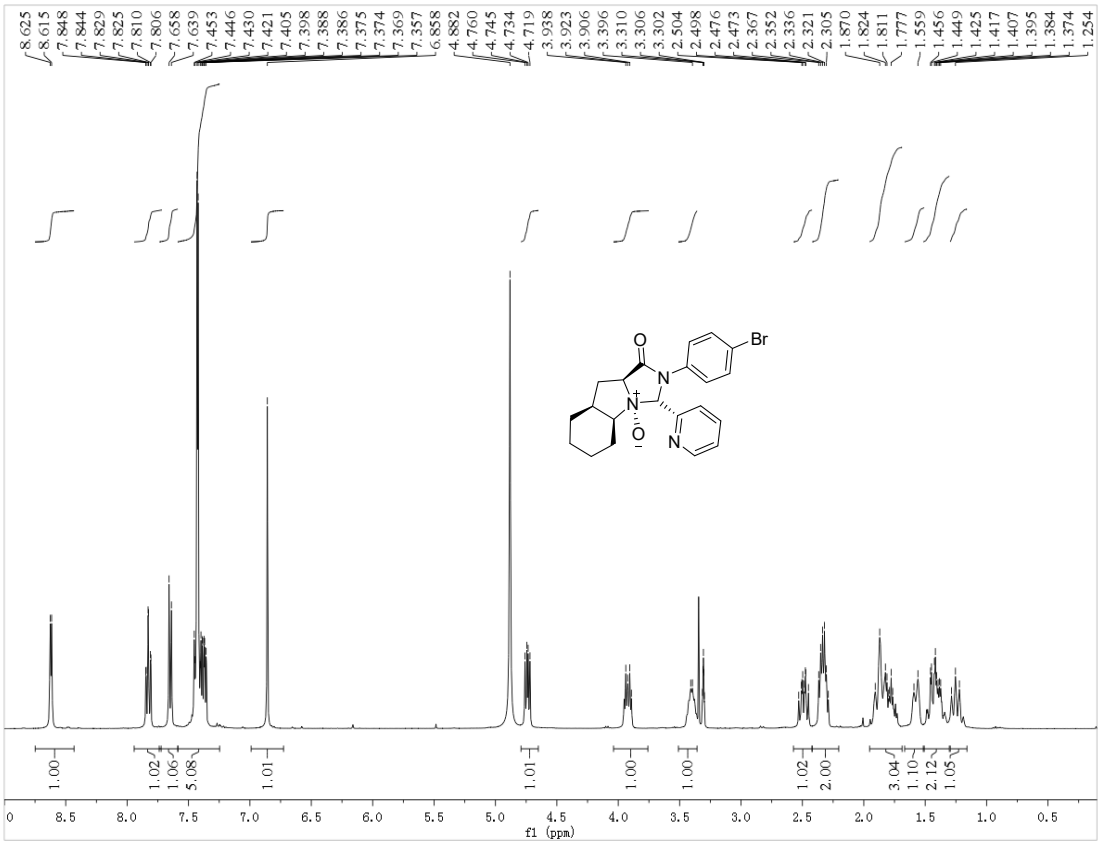


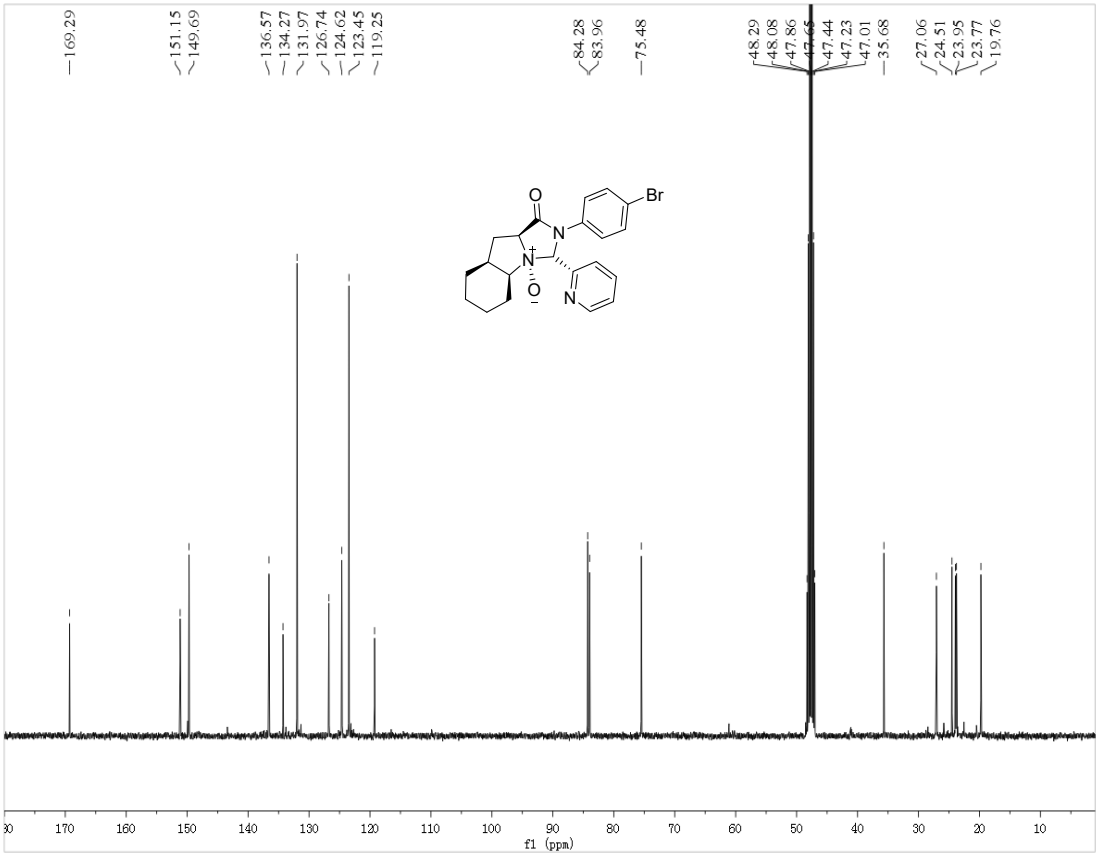
^{1}H and ^{13}C NMR of L1e



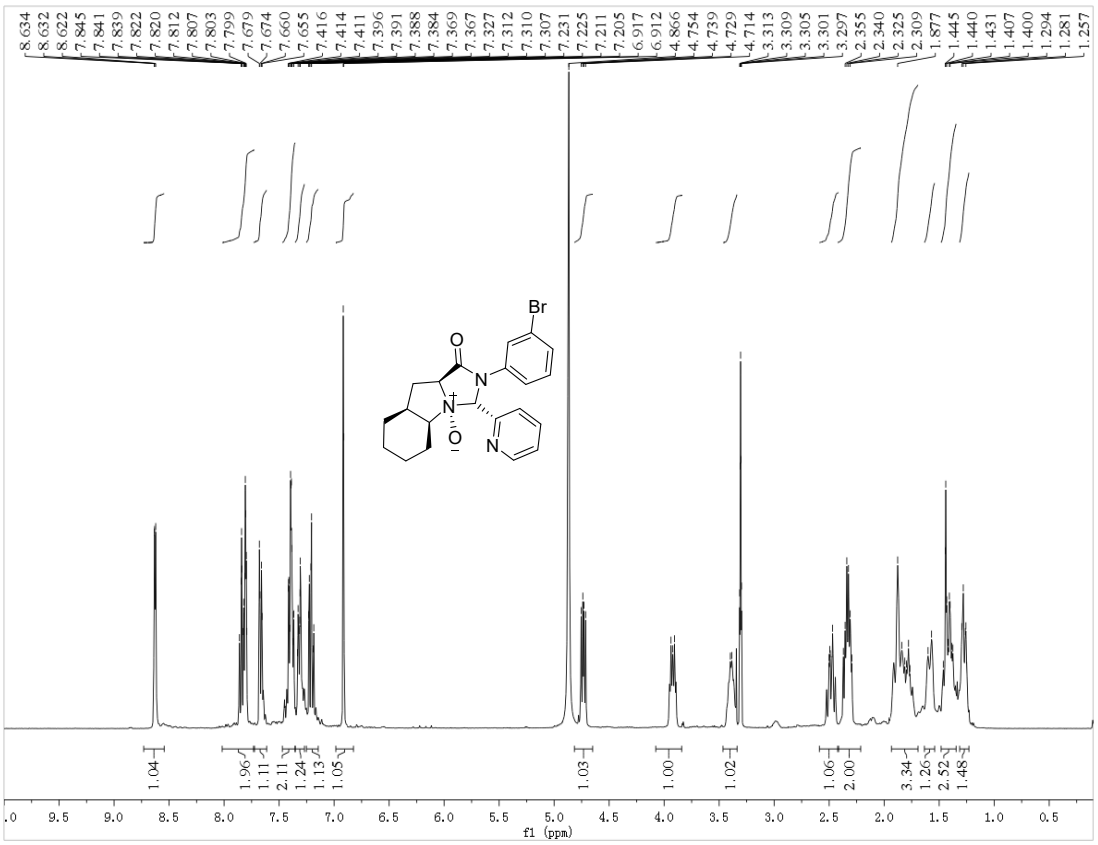


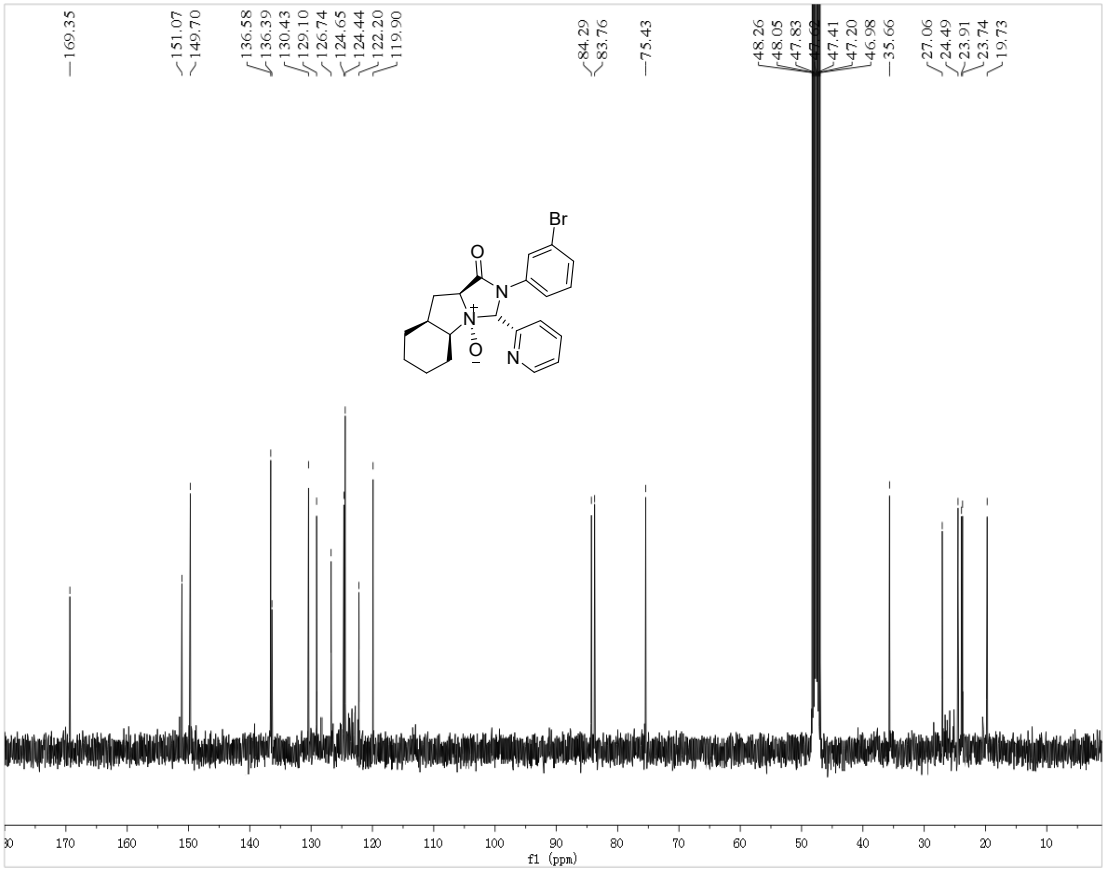
^{1}H and ^{13}C NMR of L1f



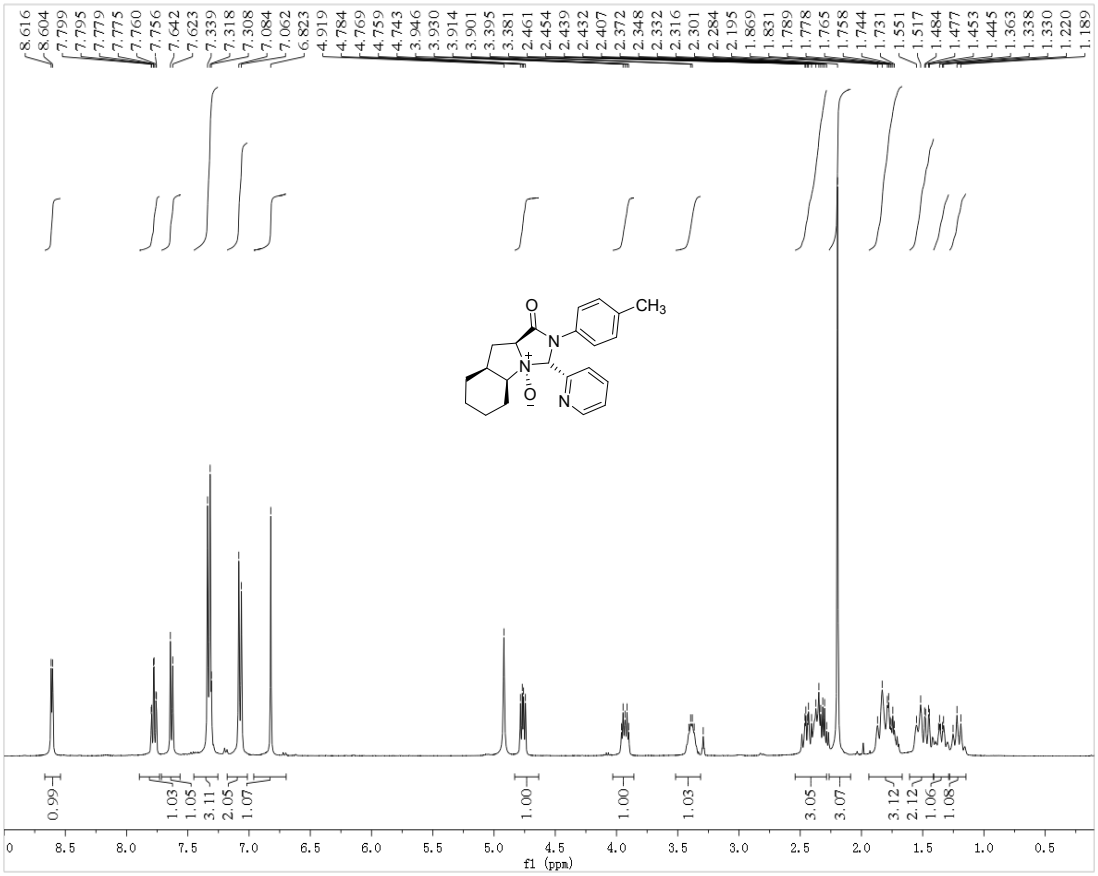


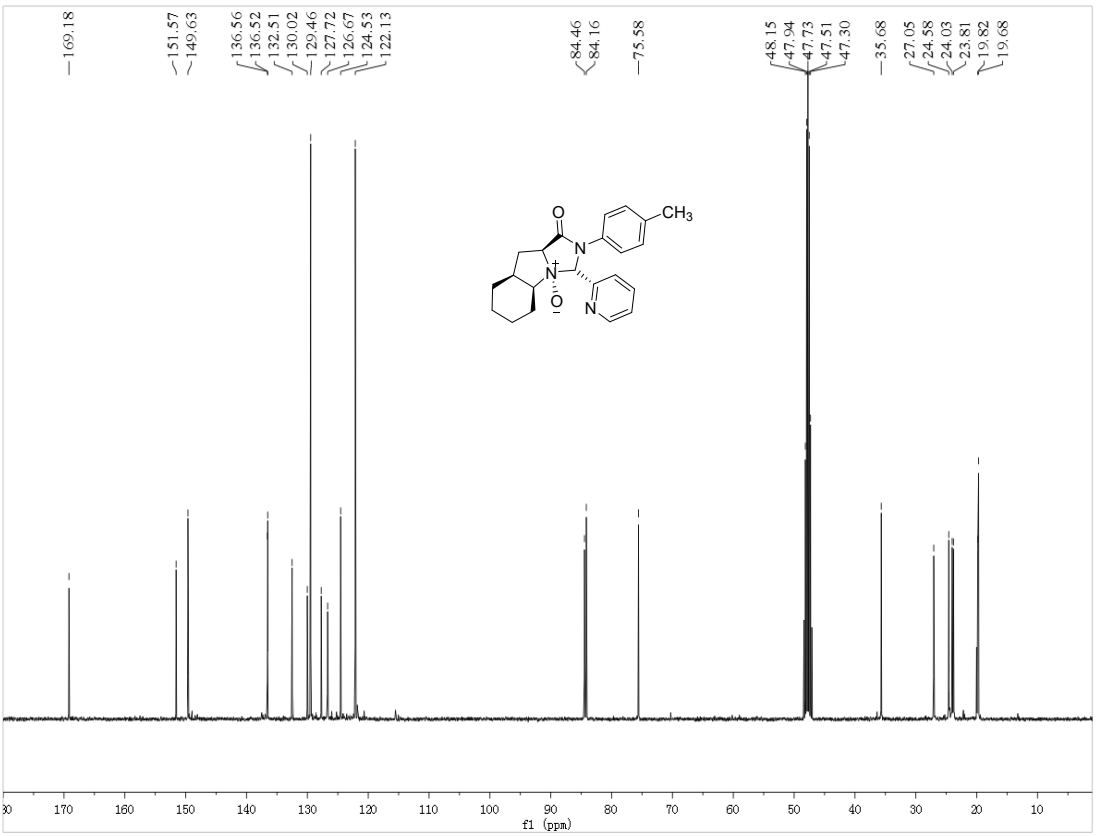
^{1}H and ^{13}C NMR of L1g



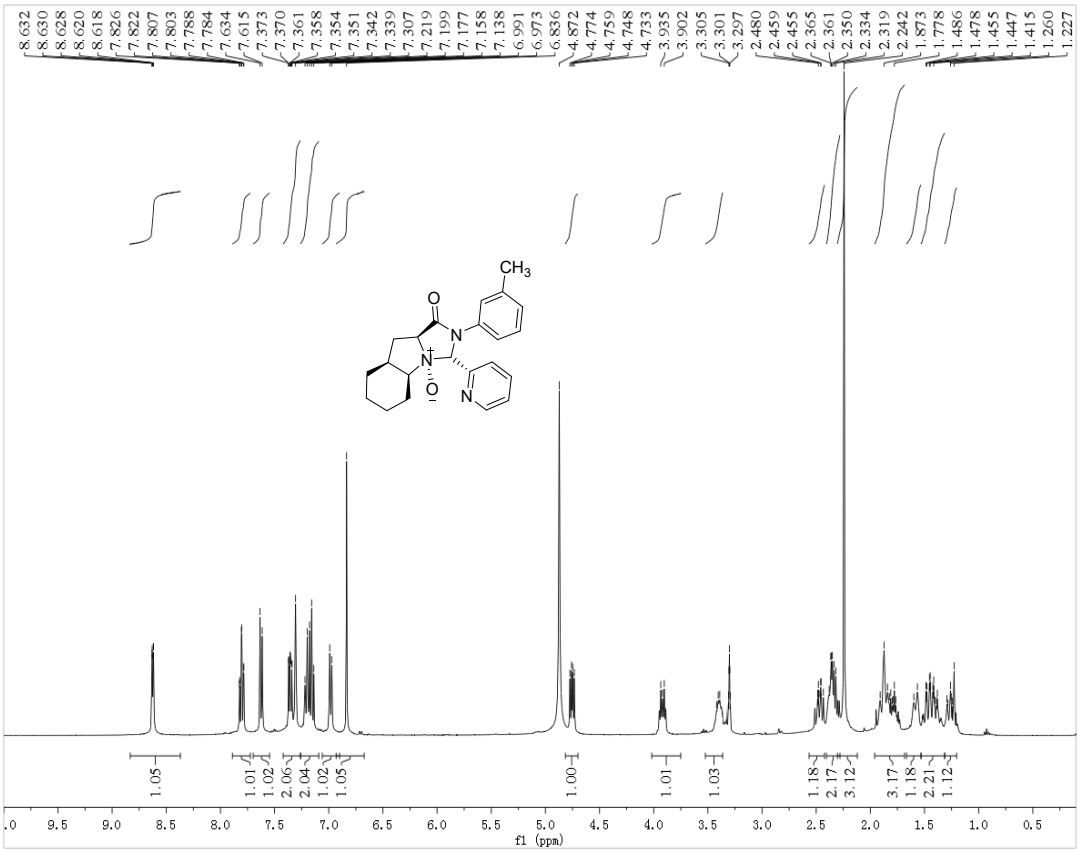


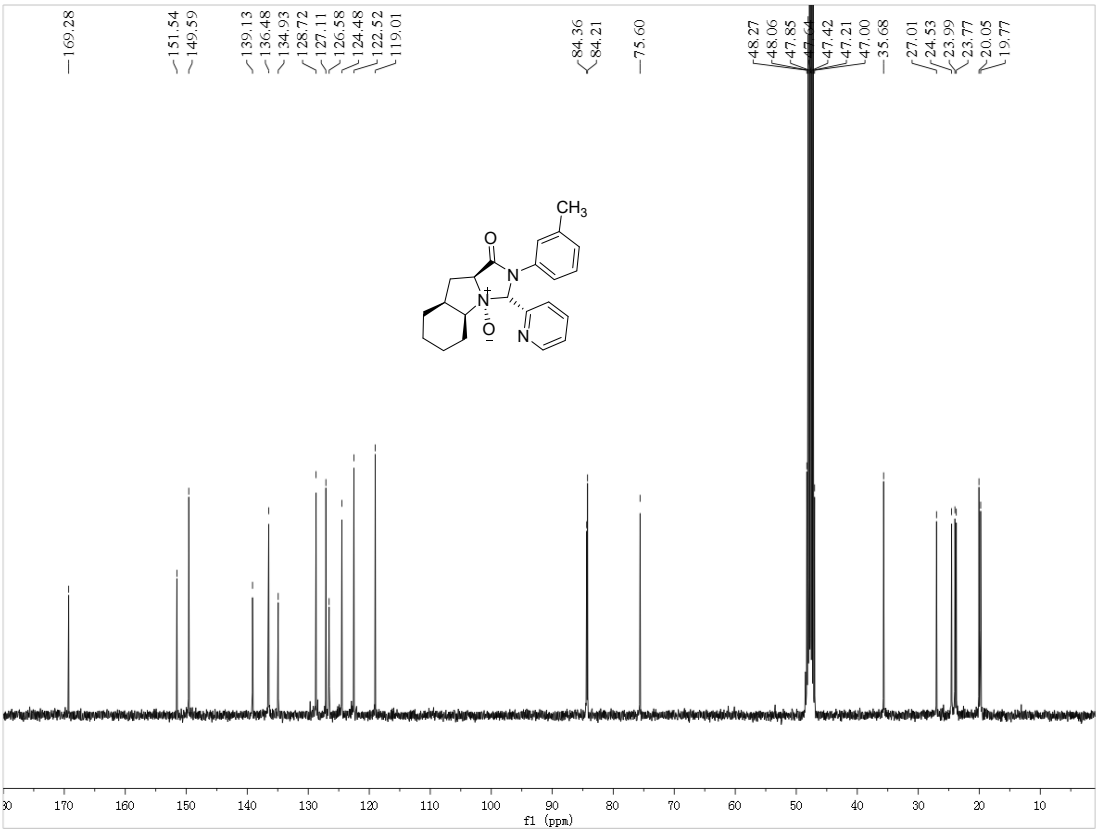
^{1}H and ^{13}C NMR of L1h


8.616
8.604
7.799
7.795
7.779
7.775
7.760
7.756
7.642
7.623
7.339
7.318
7.308
7.084
7.062
6.823
4.919
4.784
4.769
4.759
4.743
3.946
3.930
3.914
3.901
3.395
3.381
2.461
2.454
2.439
2.432
2.407
2.372
2.348
2.332
2.316
2.301
2.284
2.195
1.869
1.831
1.789
1.778
1.765
1.758
1.744
1.731
1.551
1.517
1.484
1.477
1.453
1.445
1.363
1.338
1.330
1.220
1.189
CH3
O
N
N
O
0.99
1.03
1.05
3.11
2.05
1.07
1.00
1.00
1.03
3.05
3.07
3.12
2.12
1.06
1.08
f1 (ppm)

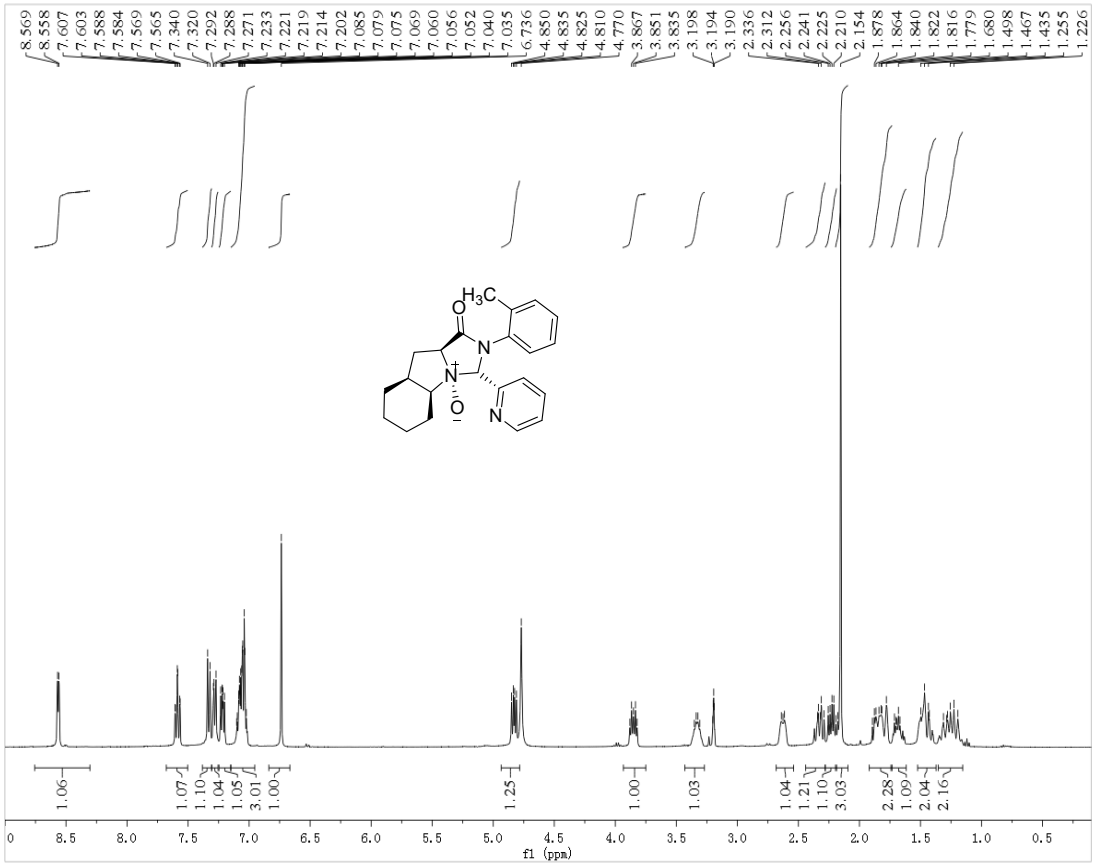

169.18
151.57
149.63
136.56
136.52
132.51
130.02
129.46
127.72
126.67
124.53
122.13
84.46
84.16
75.58
48.15
47.94
47.73
47.51
47.30
35.68
27.05
24.58
24.03
23.81
19.82
19.68
CH3
O
N
N
O
f1 (ppm)

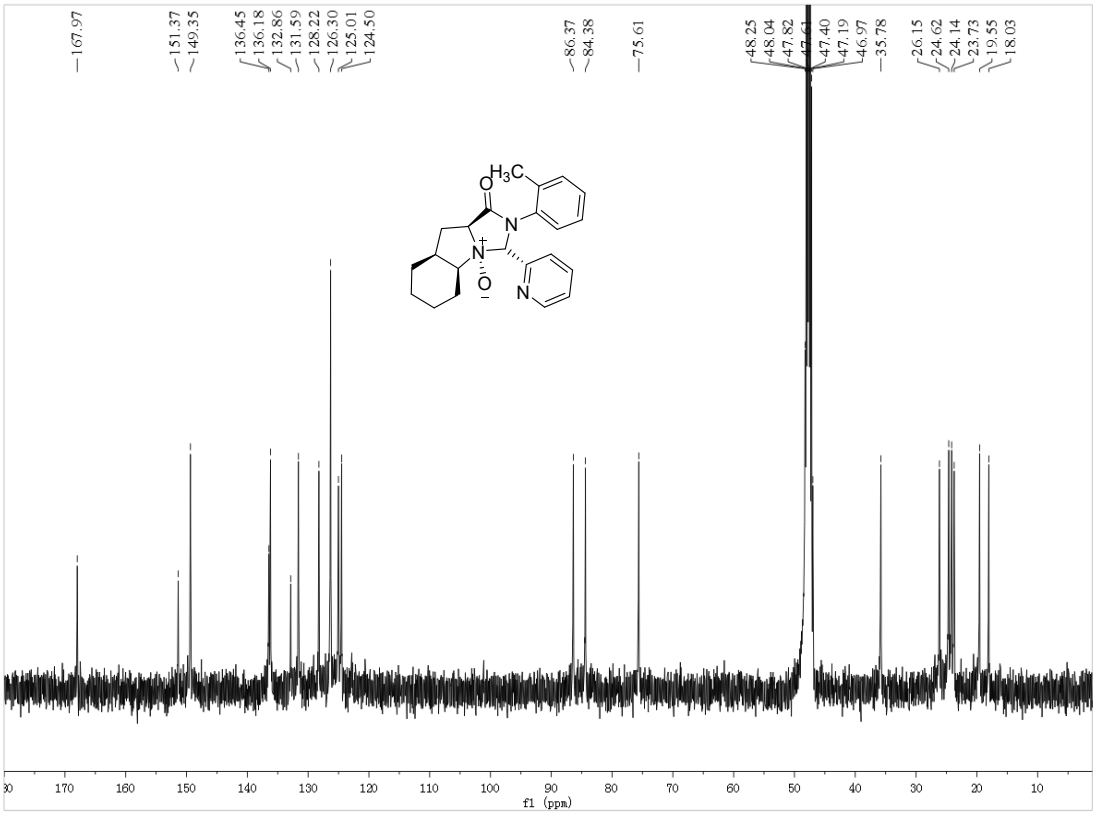
^{1}H and ^{13}C NMR of L1i



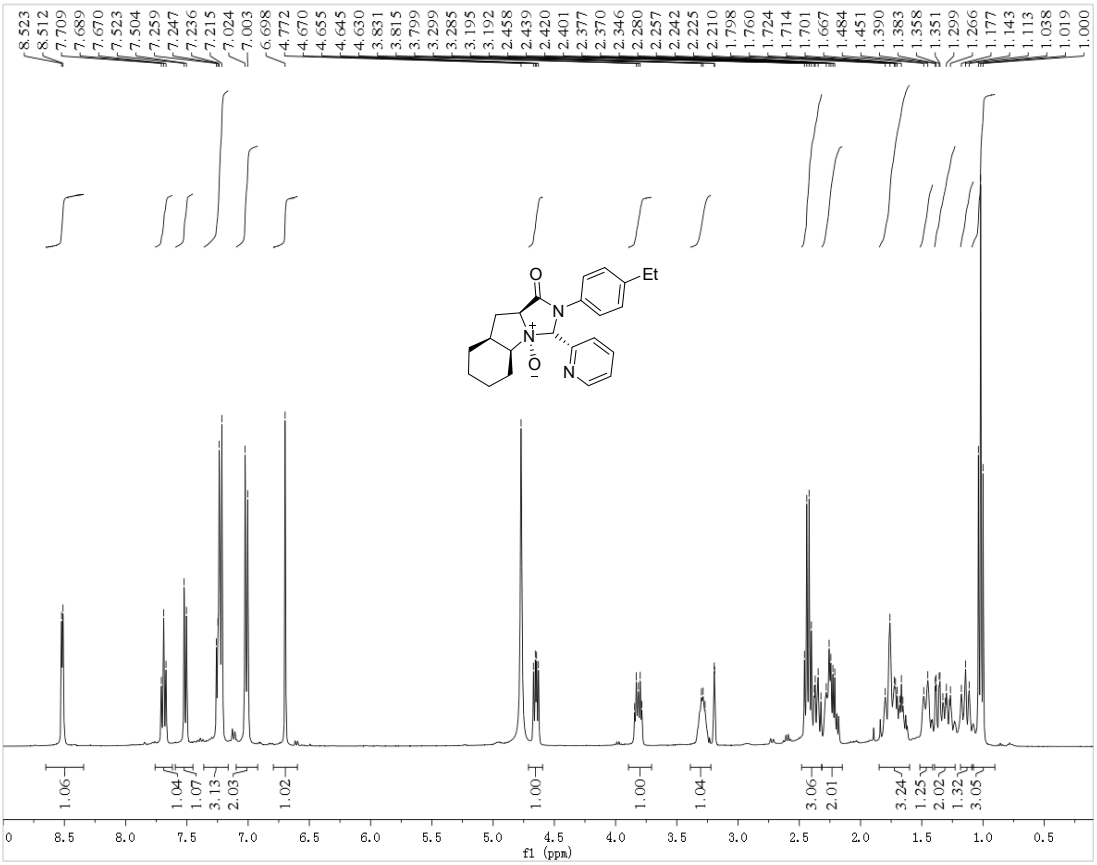


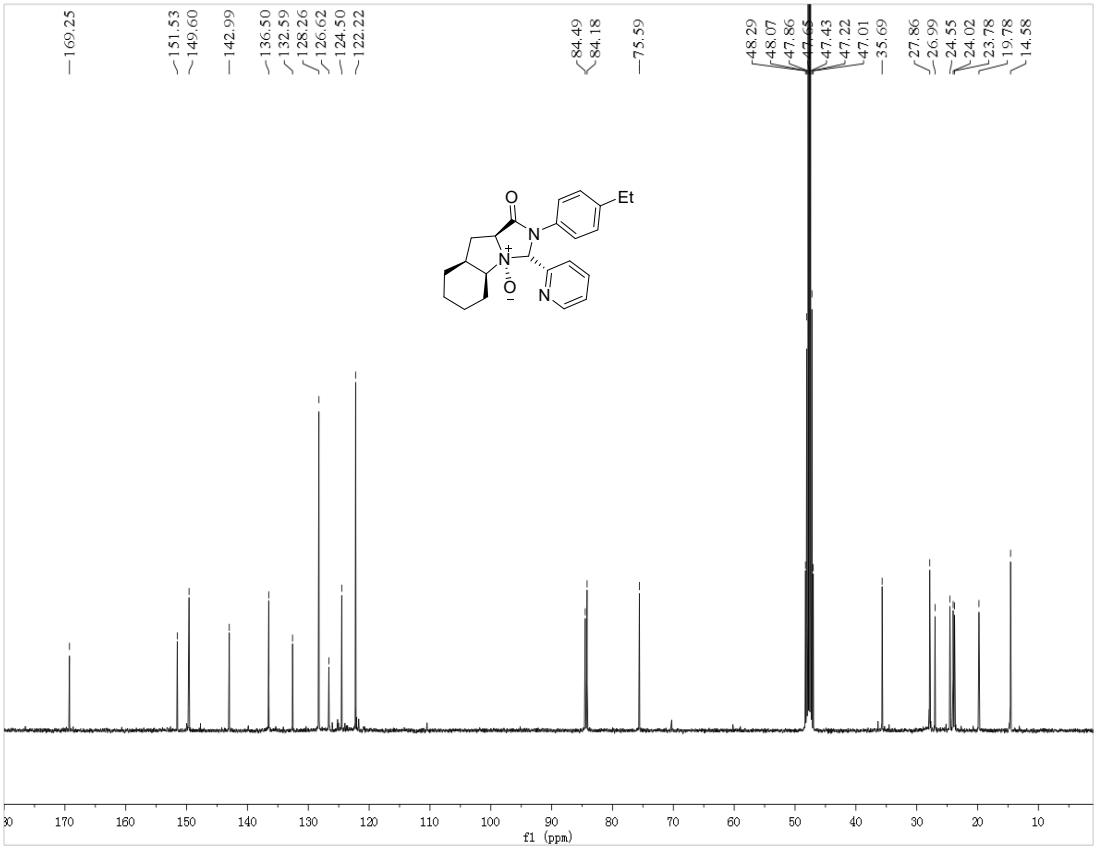
^{1}H and ^{13}C NMR of L1j



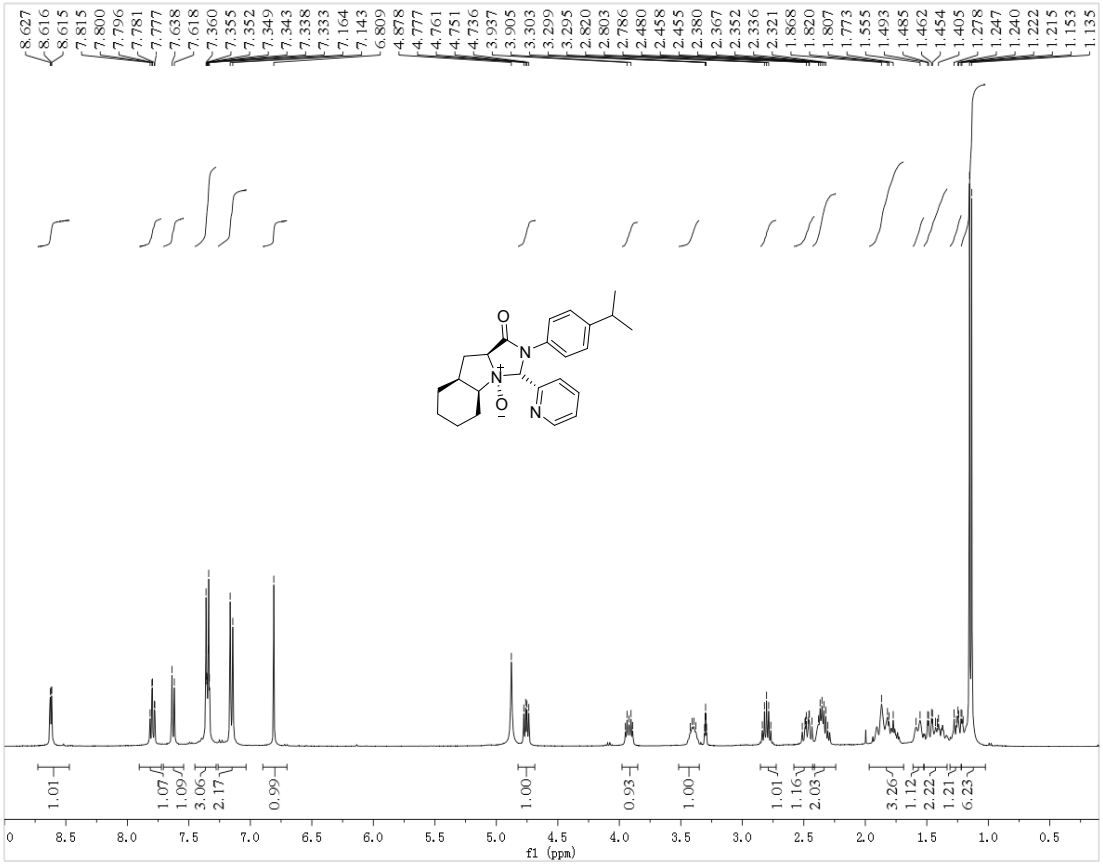


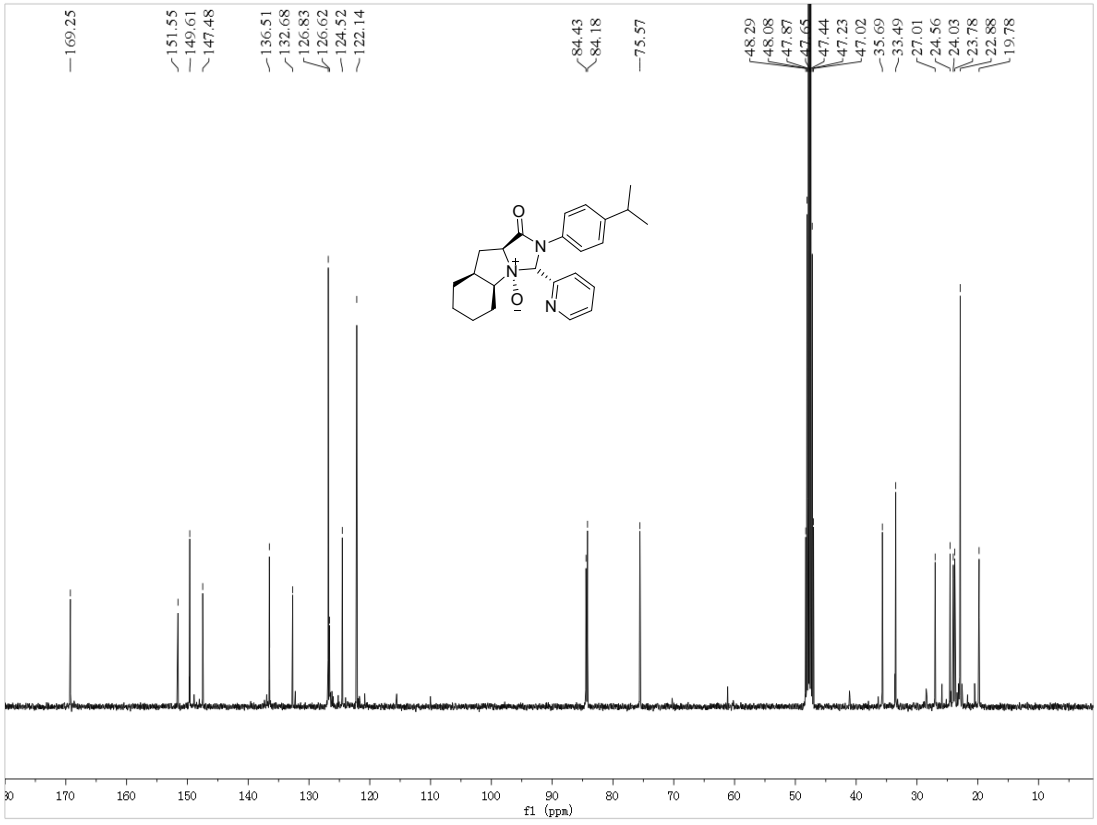
^{1}H and ^{13}C NMR of L1k



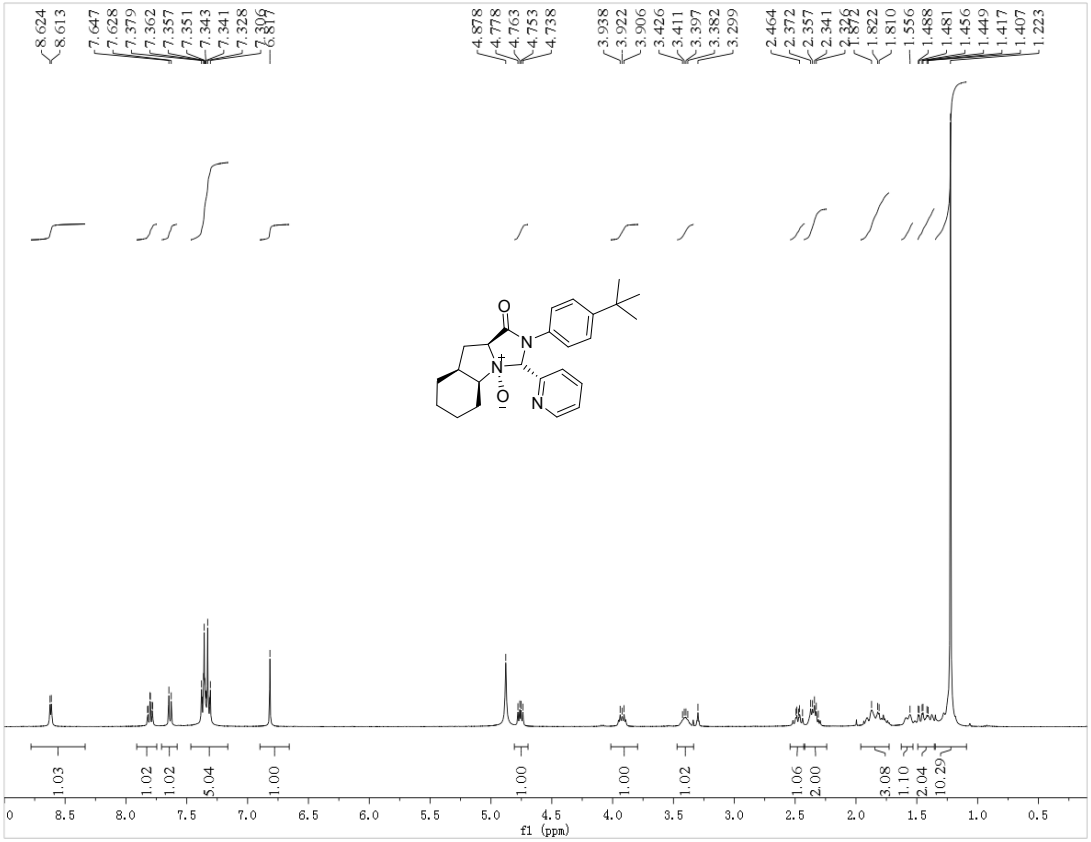


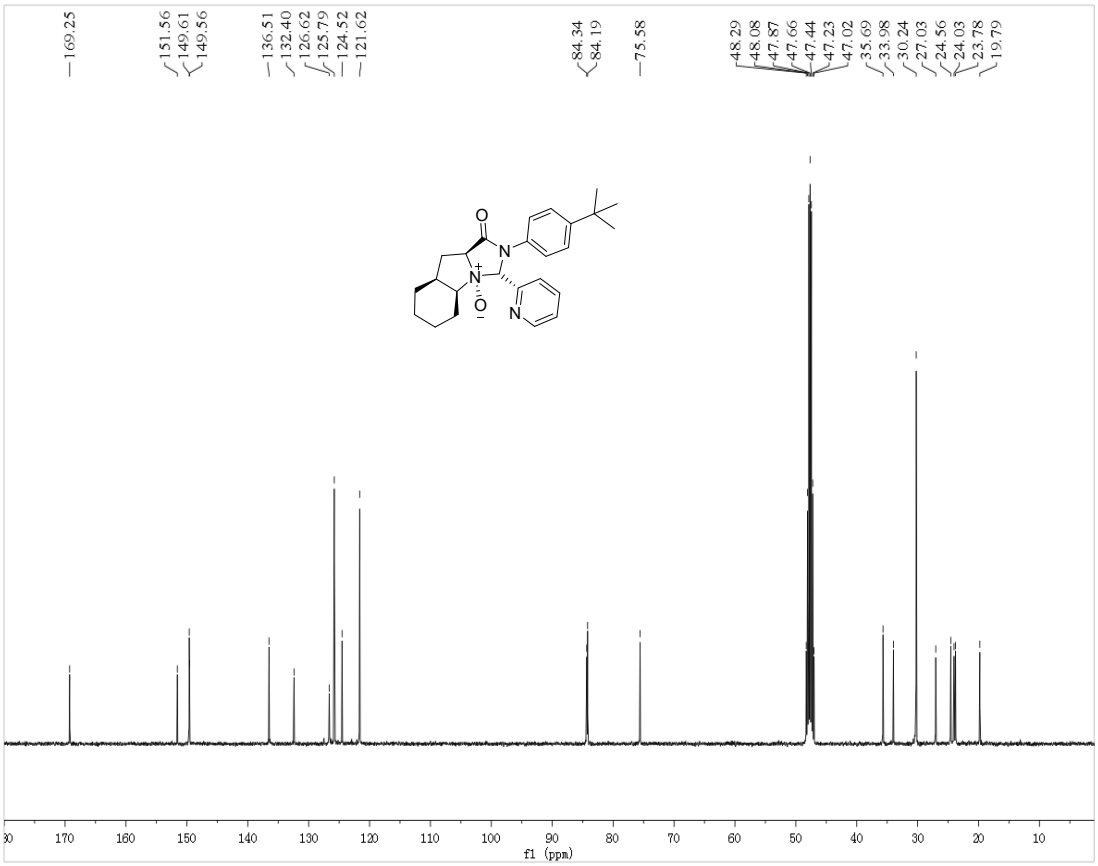
^{1}H and ^{13}C NMR of L1l



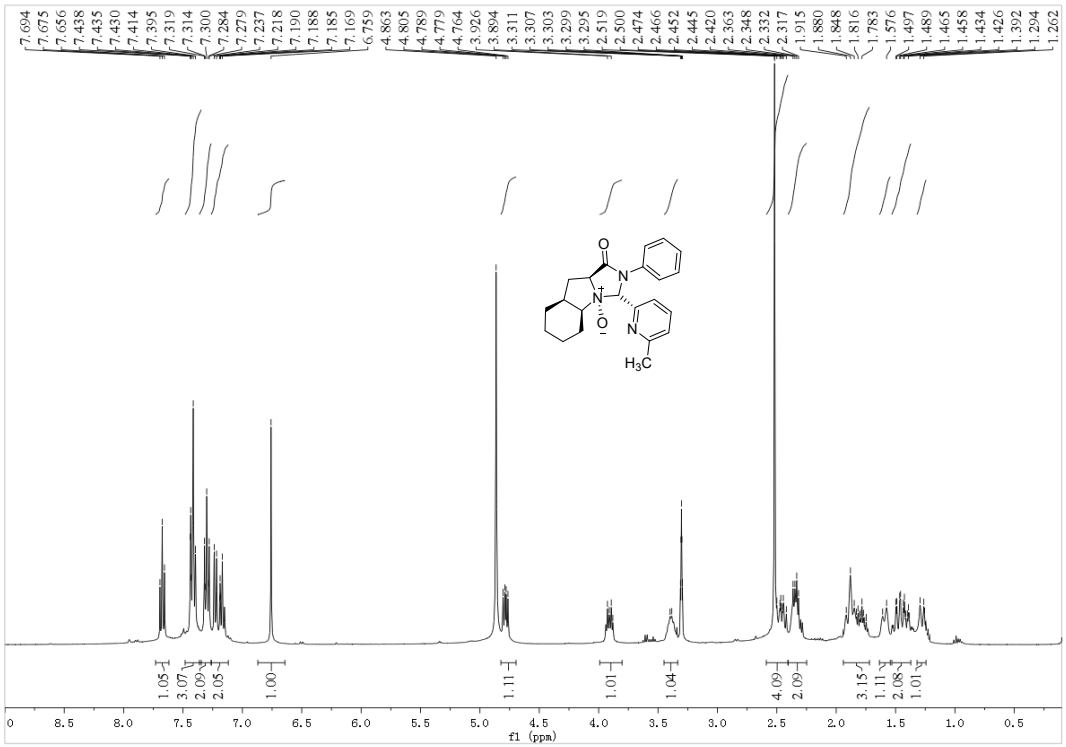


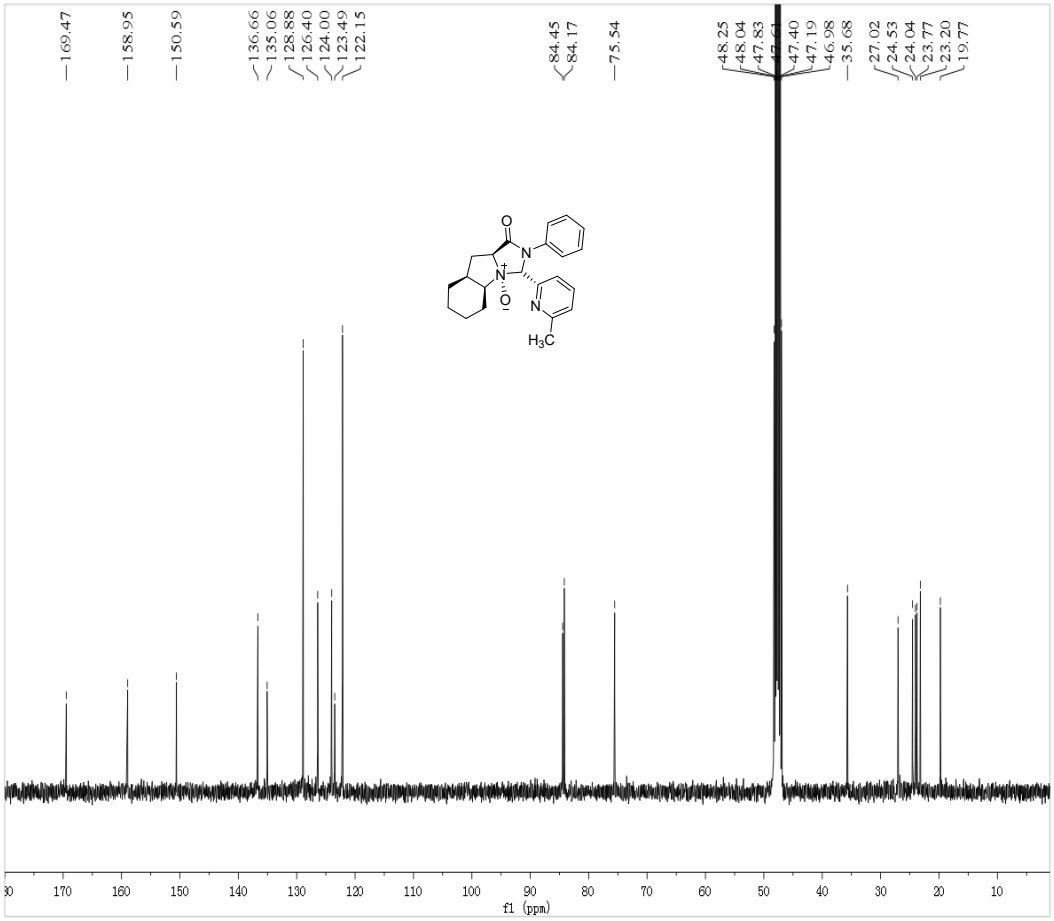
^{1}H and ^{13}C NMR of L1m



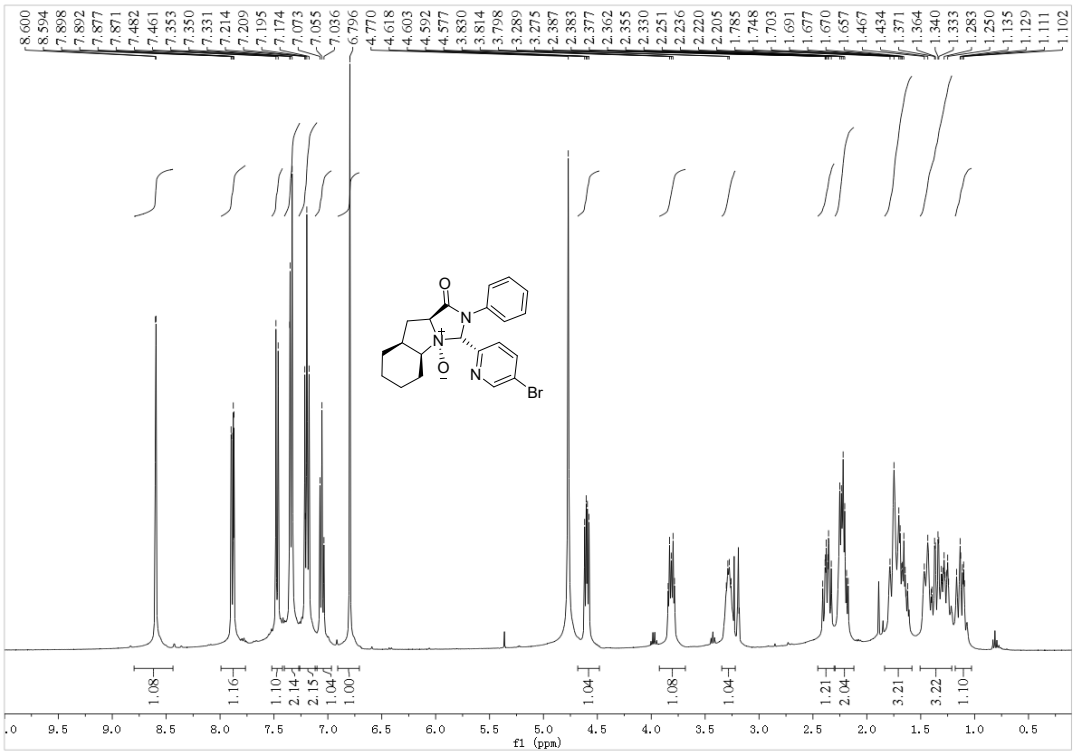


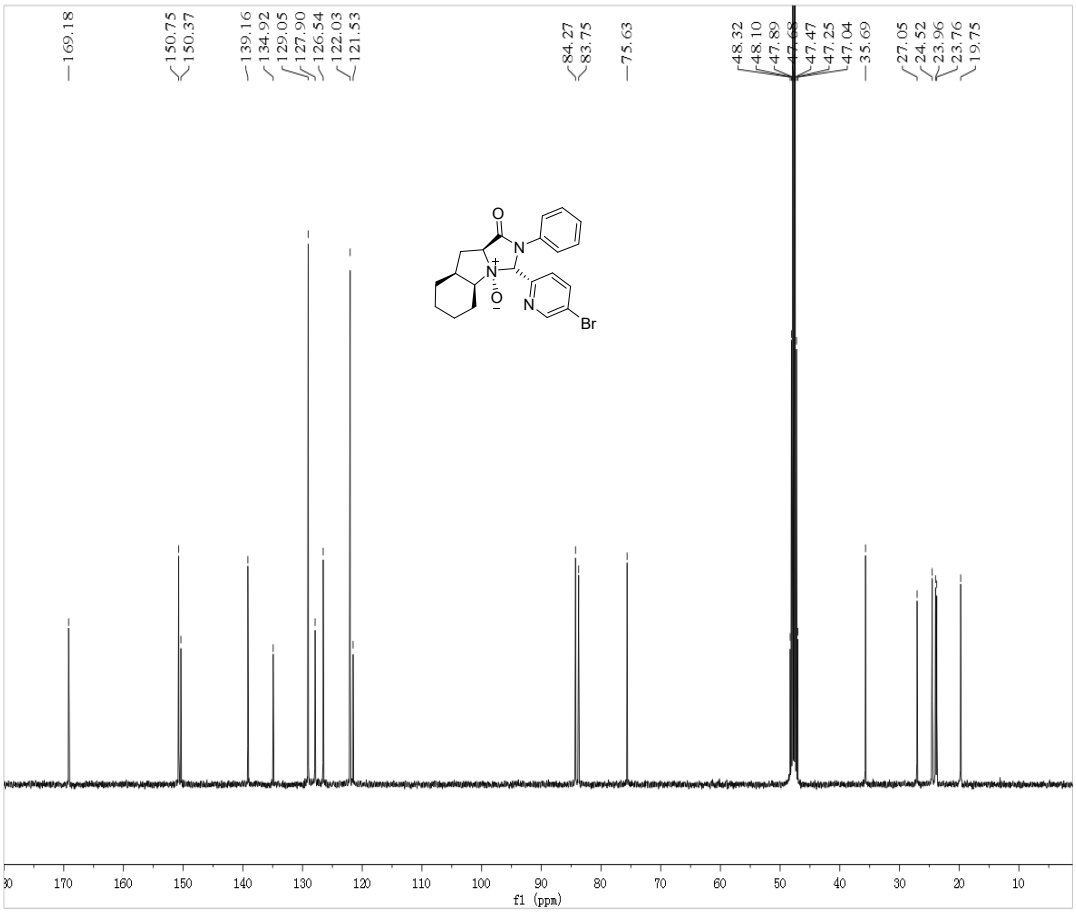
^{1}H and ^{13}C NMR of L1n



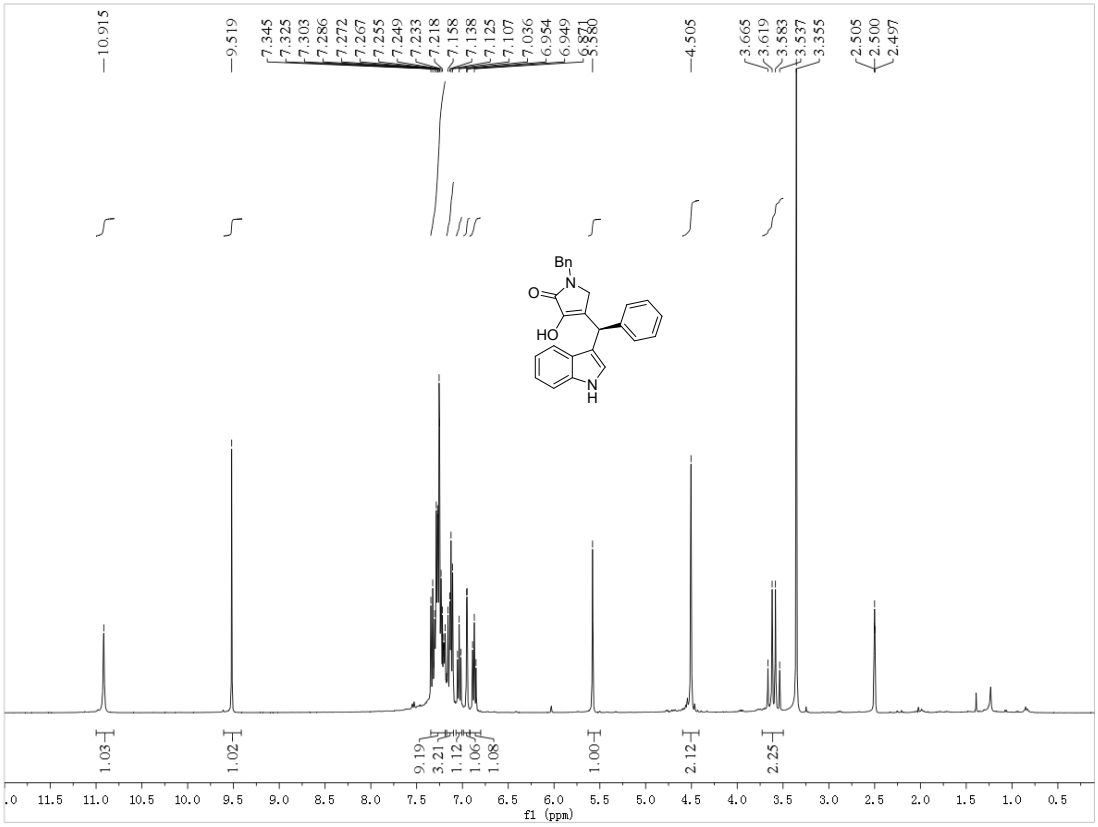


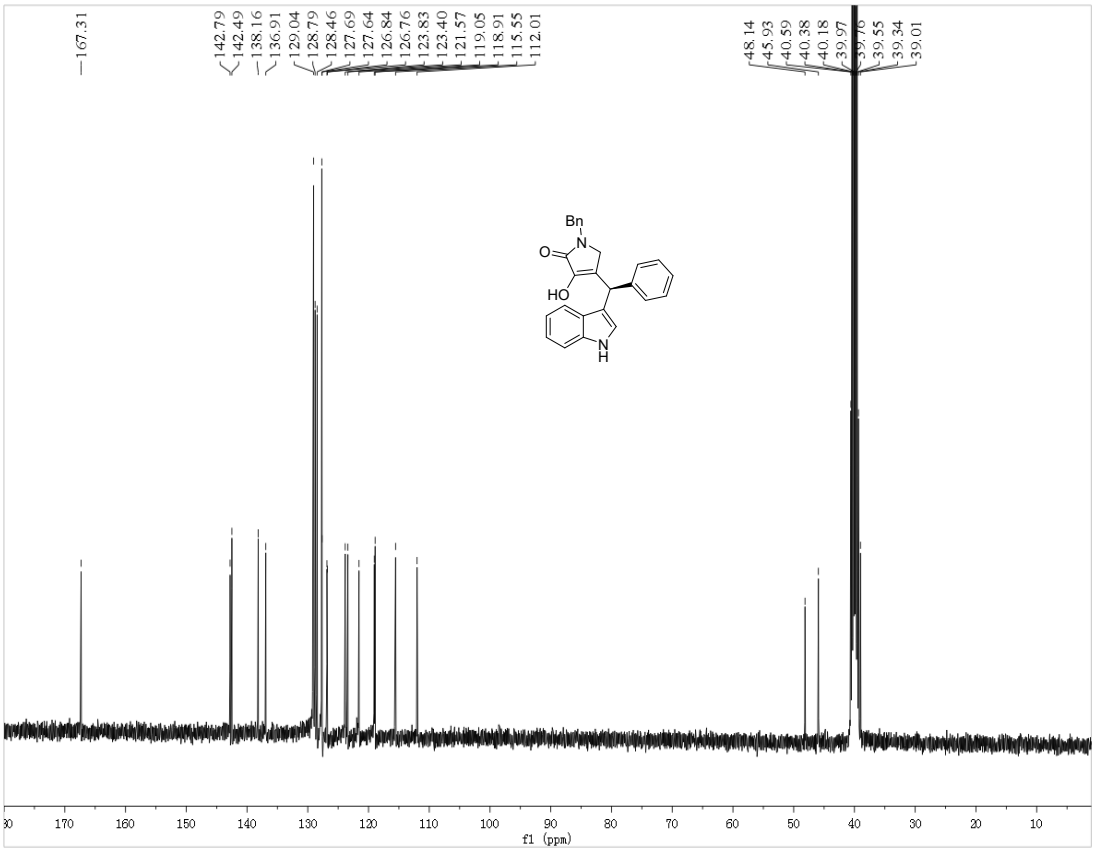
^{1}H and ^{13}C NMR of L1o



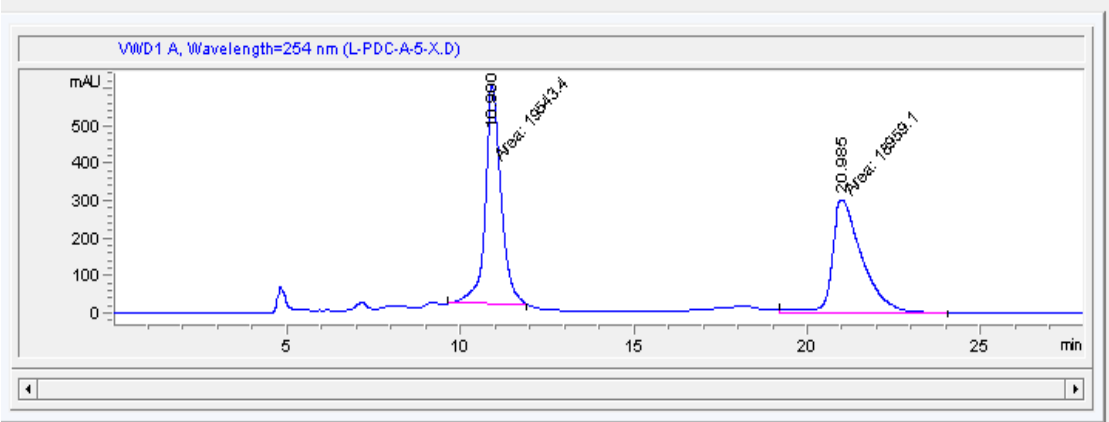


^{1}H and ^{13}C NMR of 6a





HPLC of 6a



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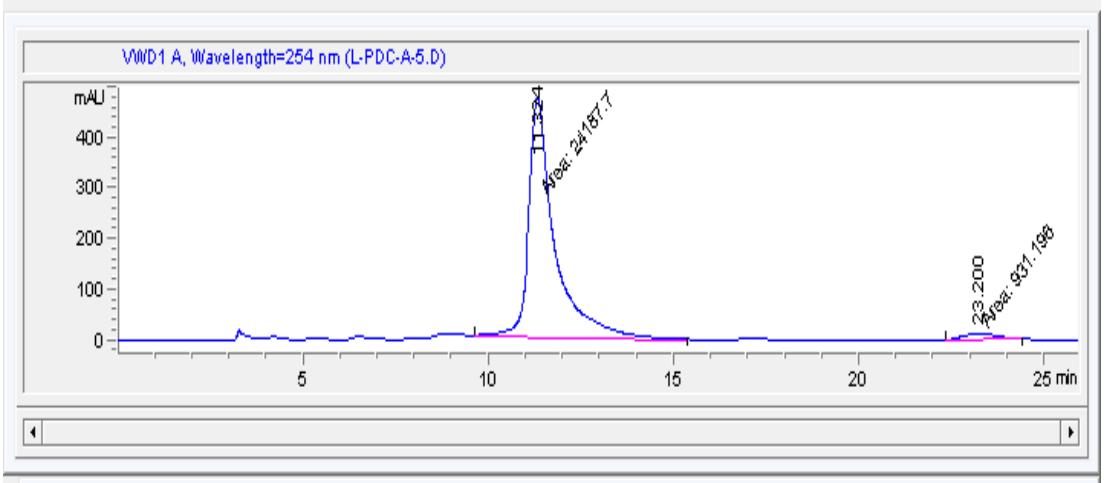
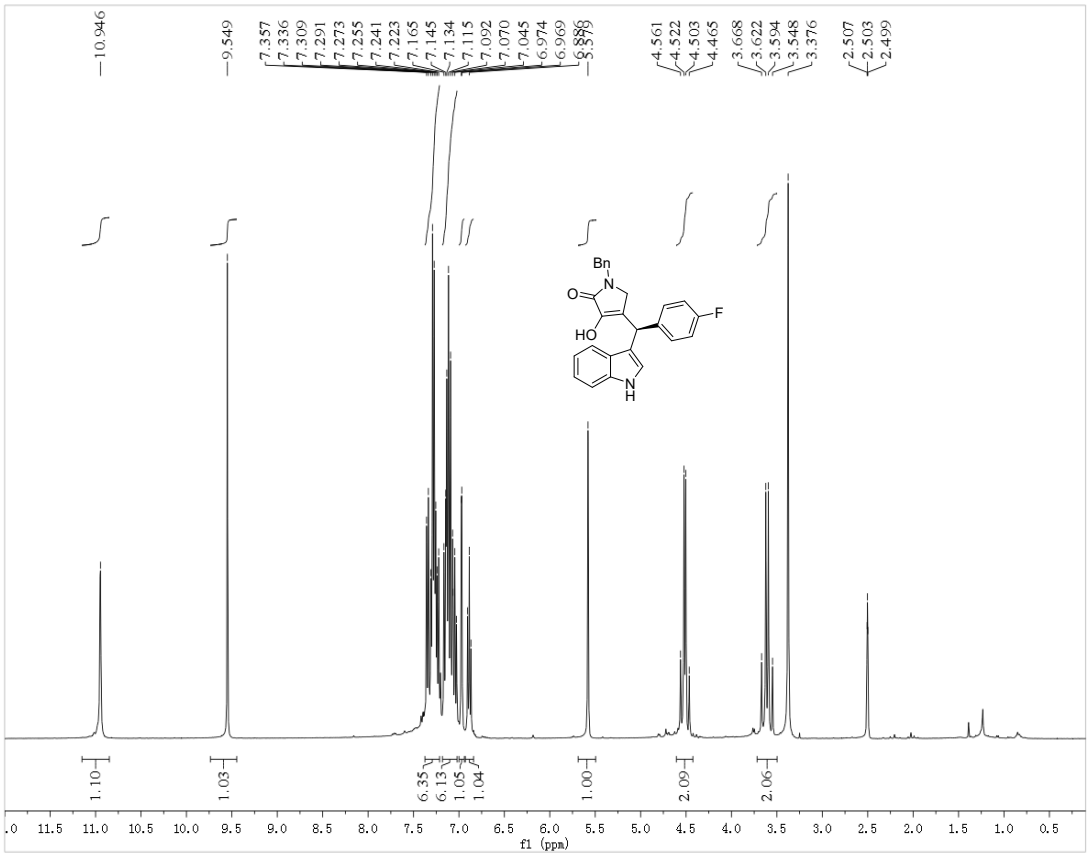
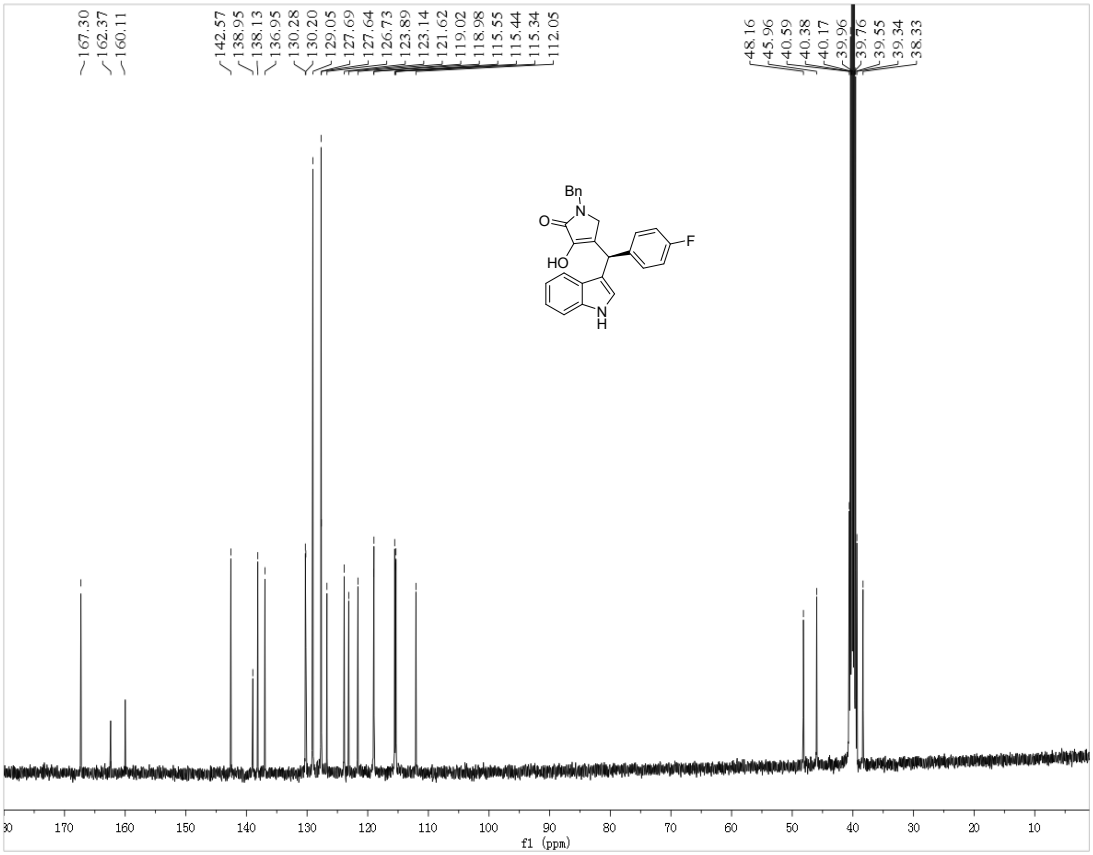
2	20.985	18959.1	304.8	1.0368	49.241	0.534



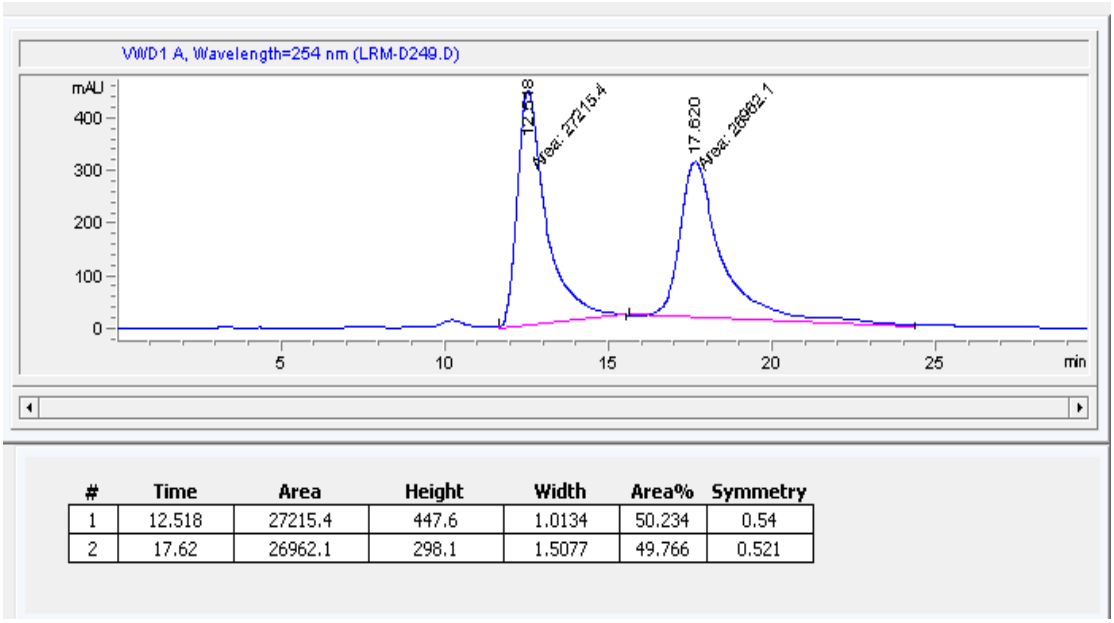
#	Time	Area	Height	Width	Area%	Symmetry
1	11.324	24187.7	474.3	0.85	96.293	0.52
2	23.2	931.2	13.4	1.1579	3.707	0.789

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

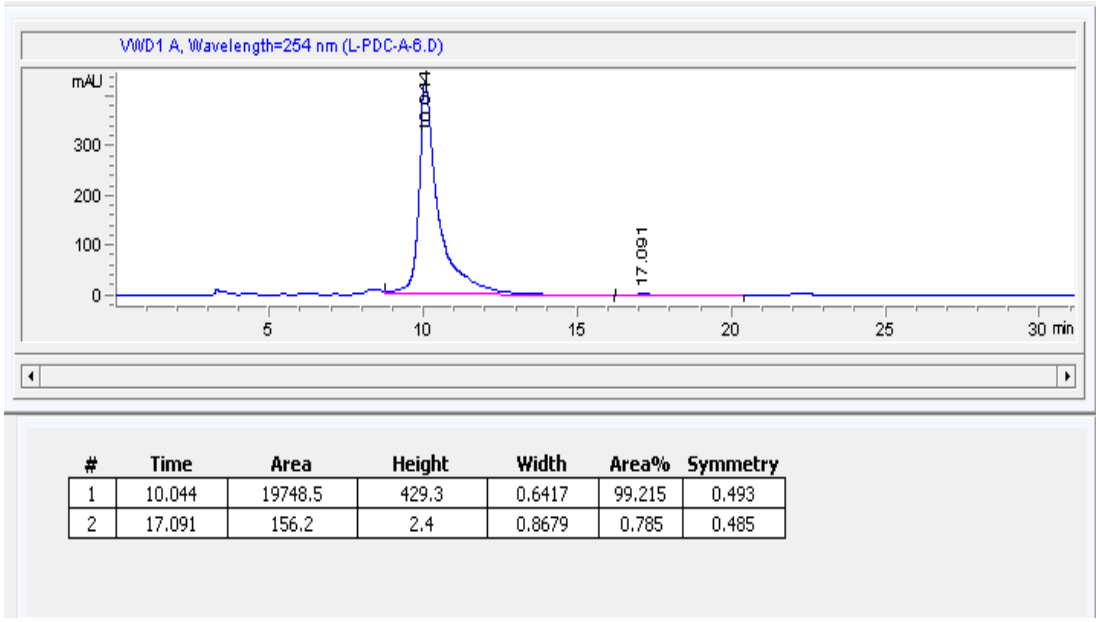




HPLC of 6b

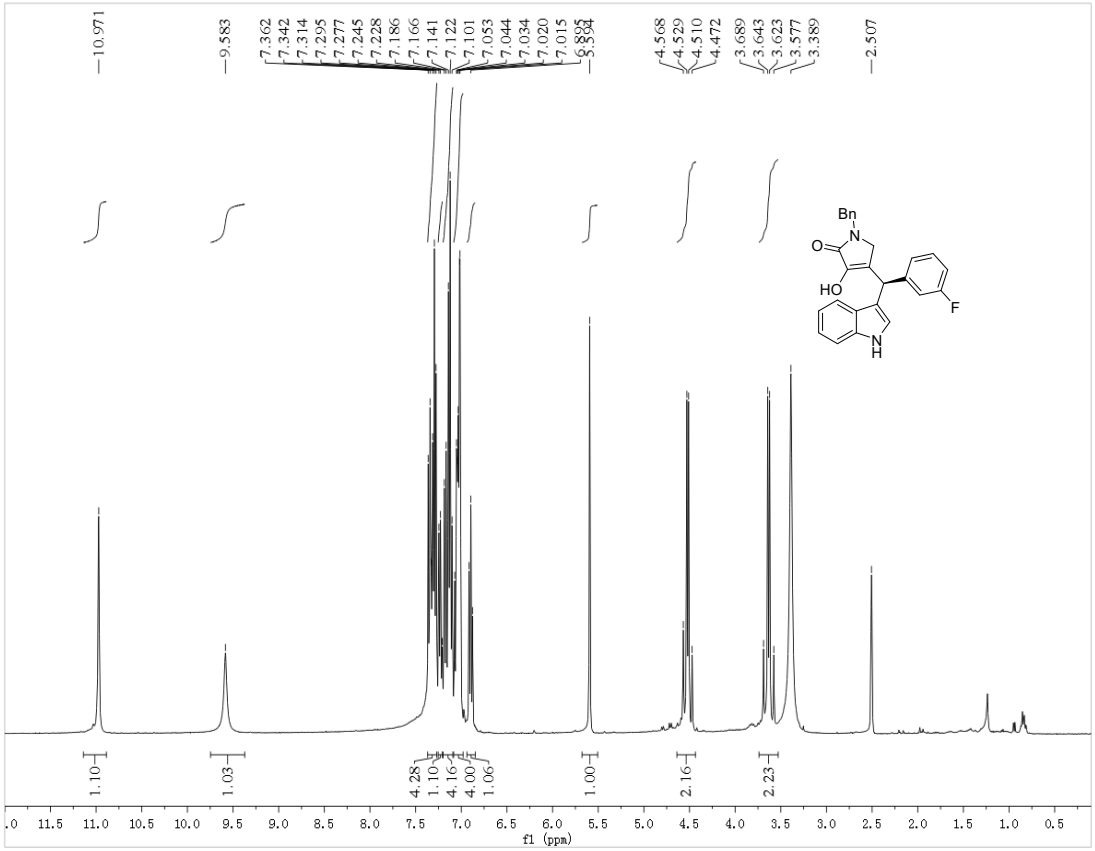


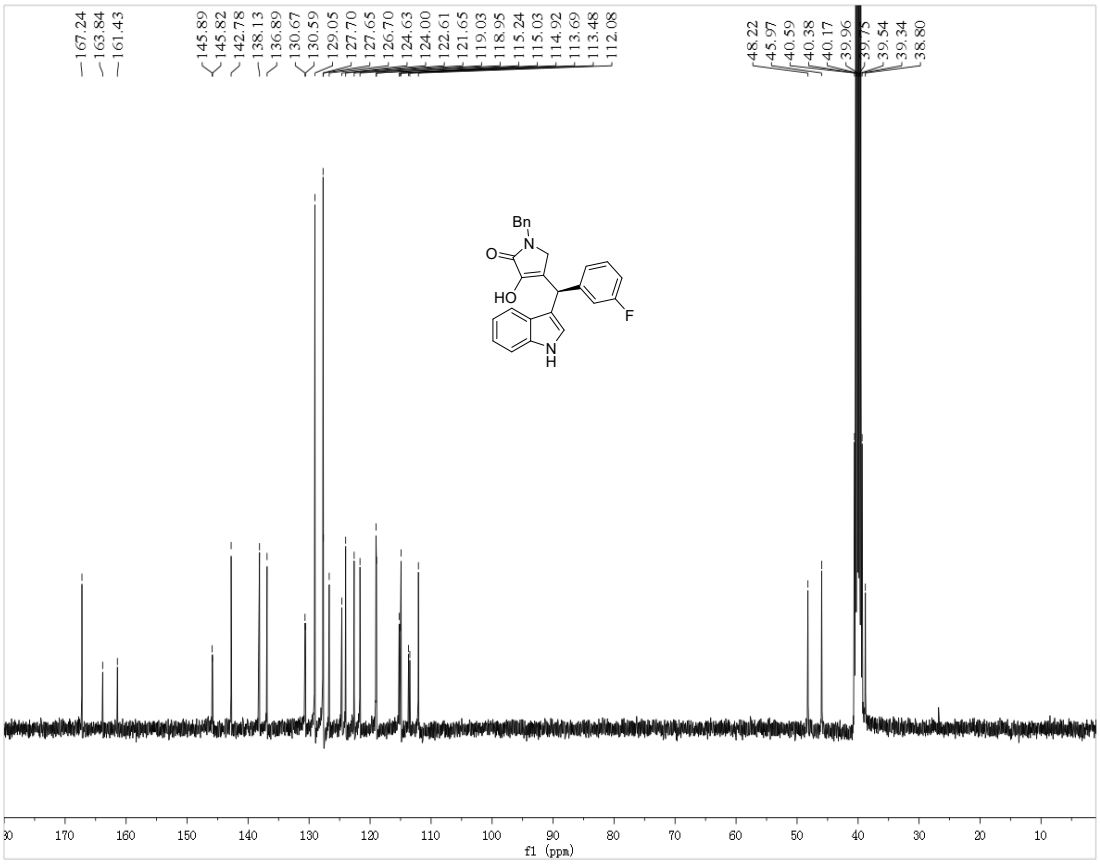
#	Time	Area	Height	Width	Area%	Symmetry
1	12.518	27215.4	447.6	1.0134	50.234	0.54
2	17.62	26962.1	298.1	1.5077	49.766	0.521



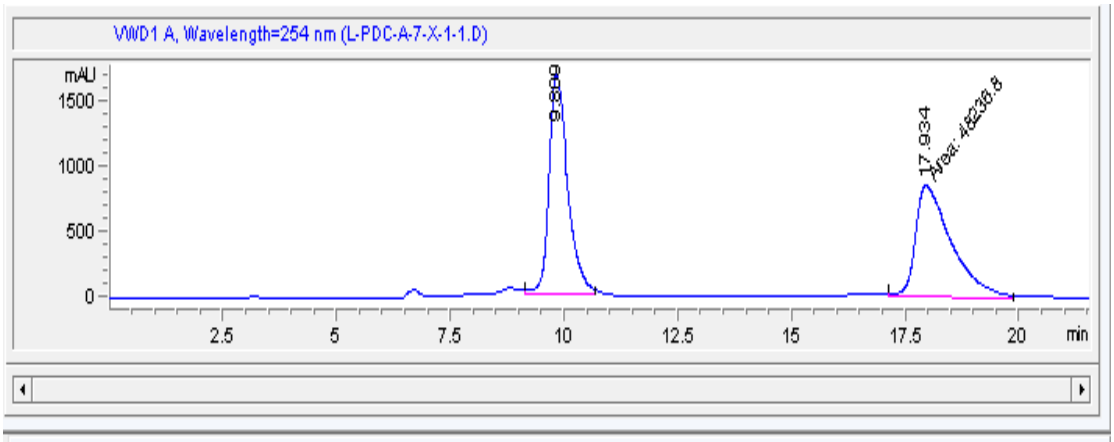
#	Time	Area	Height	Width	Area%	Symmetry
1	10.044	19748.5	429.3	0.6417	99.215	0.493
2	17.091	156.2	2.4	0.8679	0.785	0.485

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

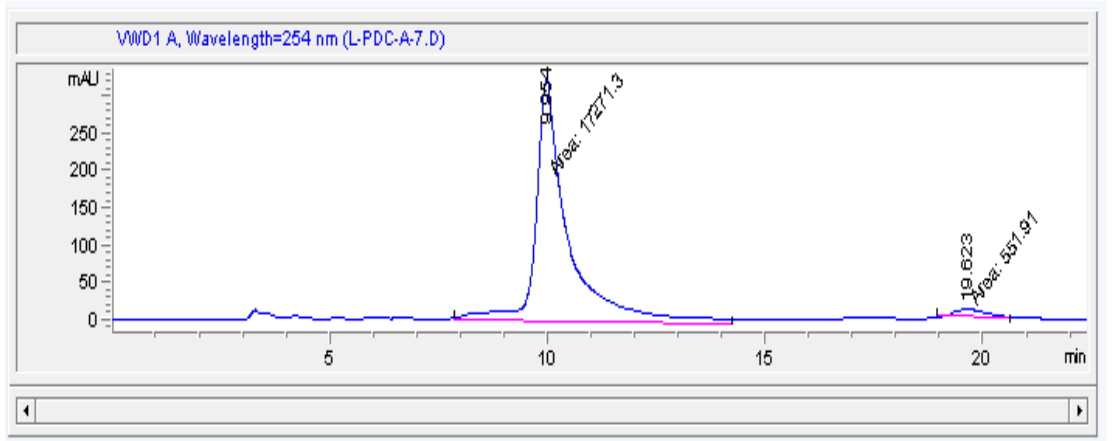




HPLC of 6c

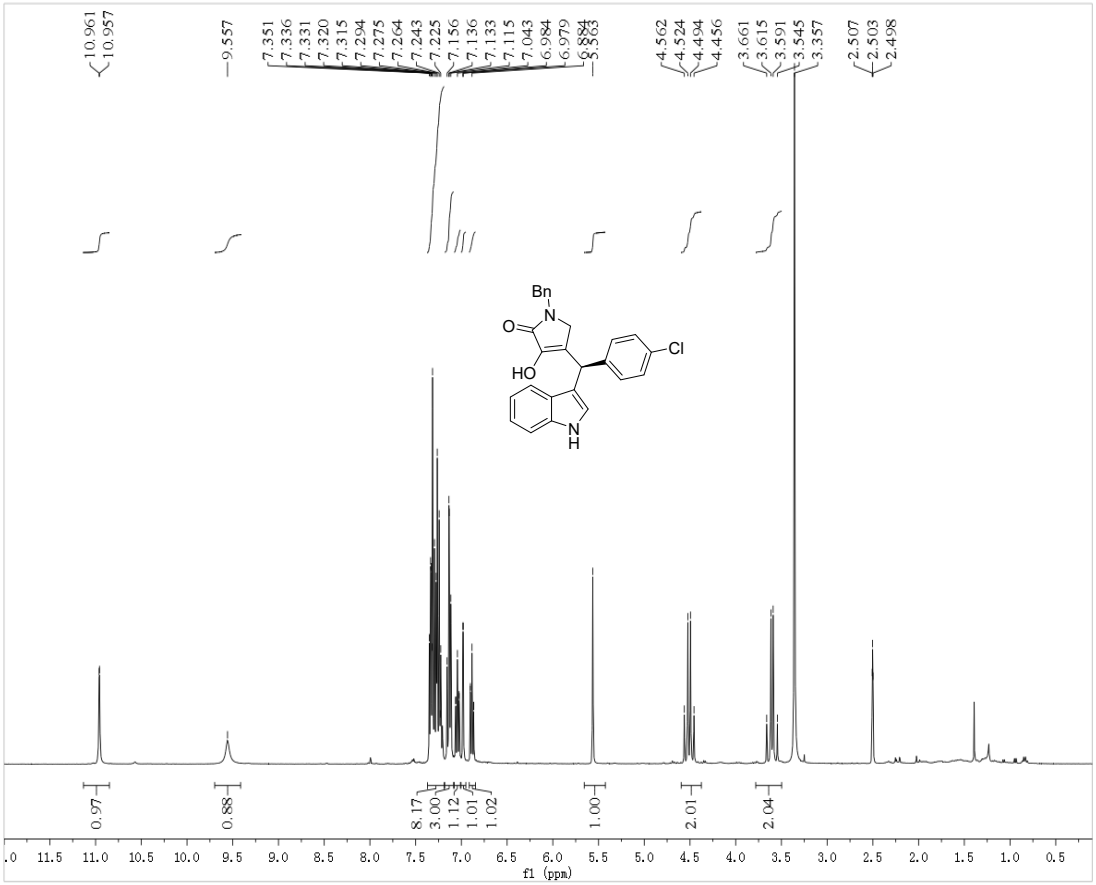


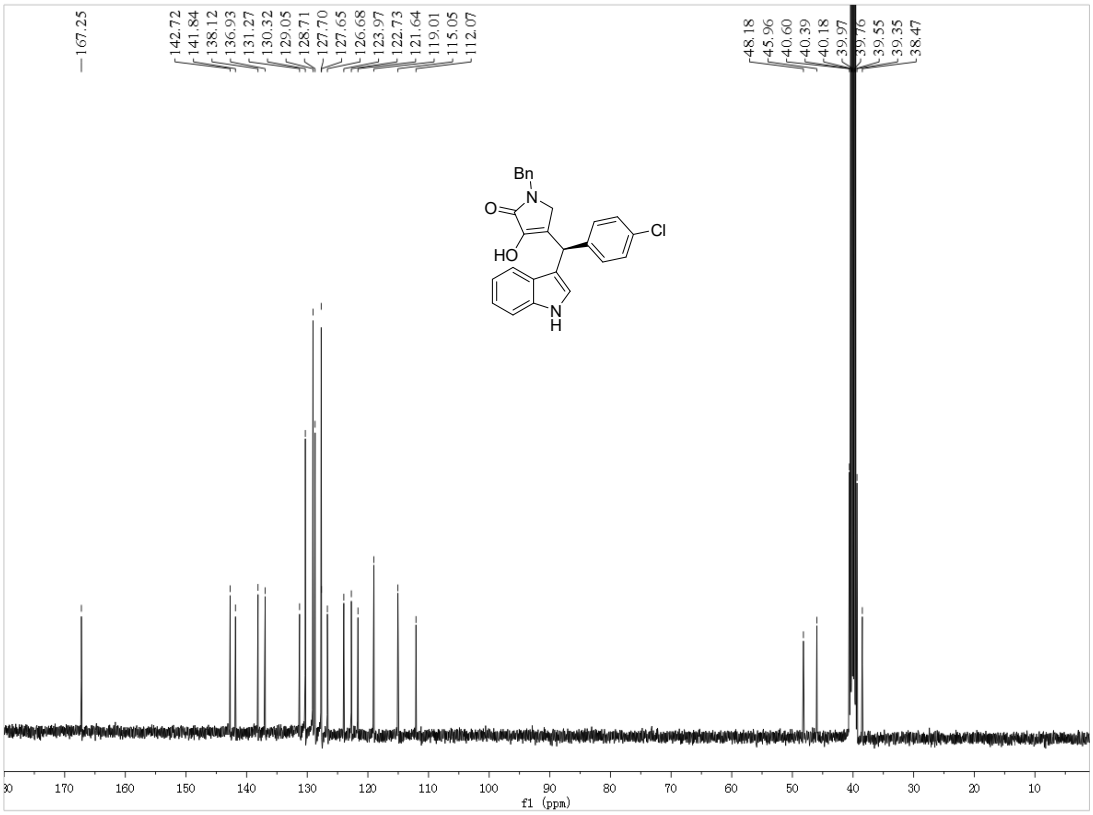
#	Time	Area	Height	Width	Area%	Symmetry
1	9.809	49928.2	1687.9	0.4461	50.861	0.612
2	17.934	48236.8	856.7	0.9384	49.139	0.391



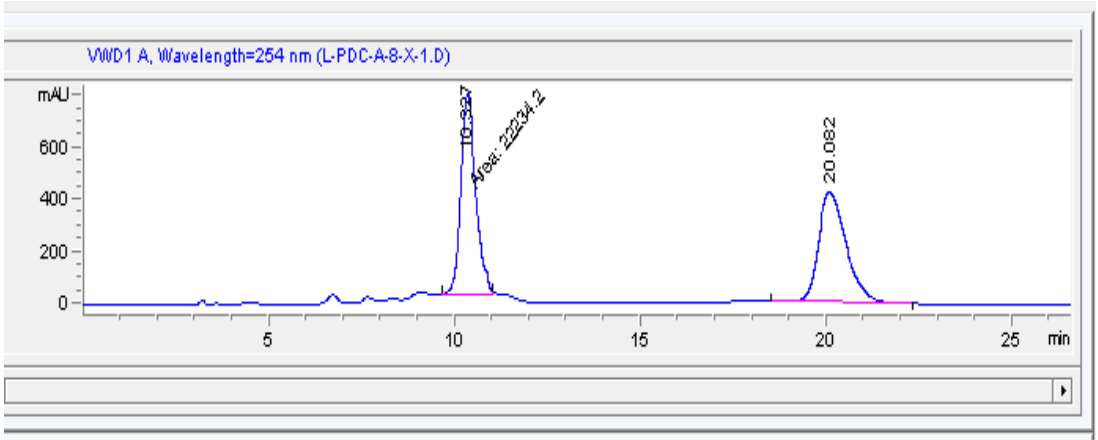
#	Time	Area	Height	Width	Area%	Symmetry
1	9.954	17271.3	325.6	0.8842	96.903	0.489
2	19.623	551.9	10.6	0.8687	3.097	0.665

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





HPLC of 6d



#	Time	Area	Height	Width	Area%	Symmetry
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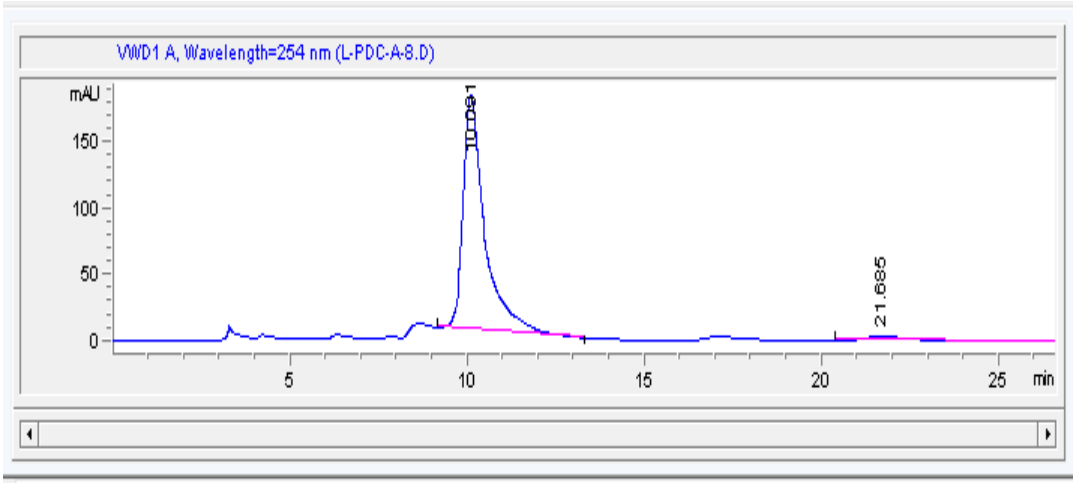
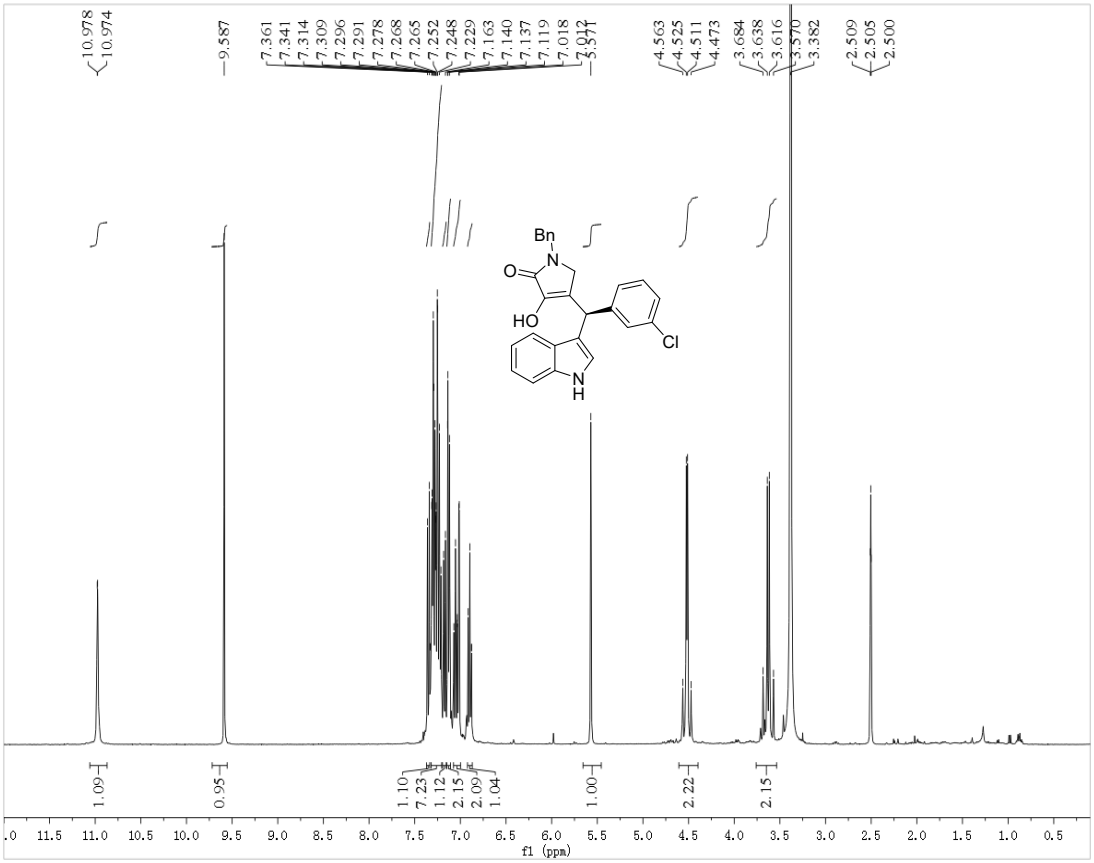
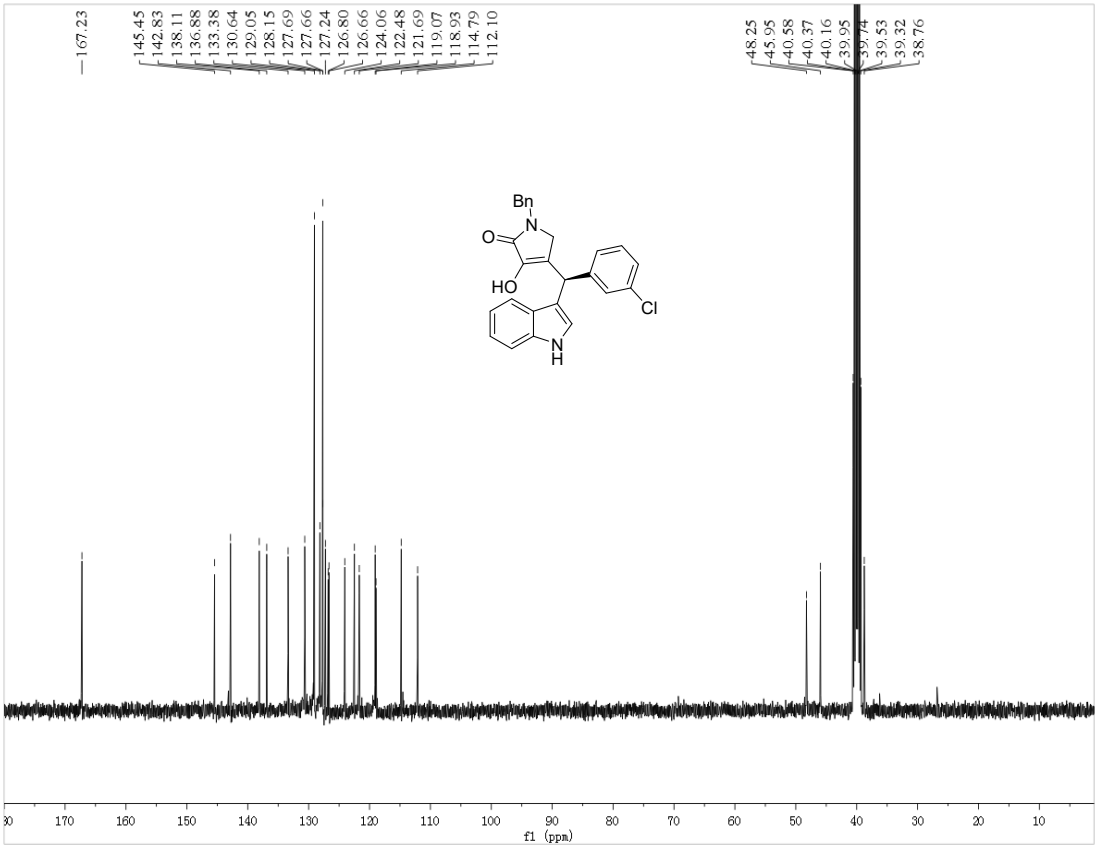


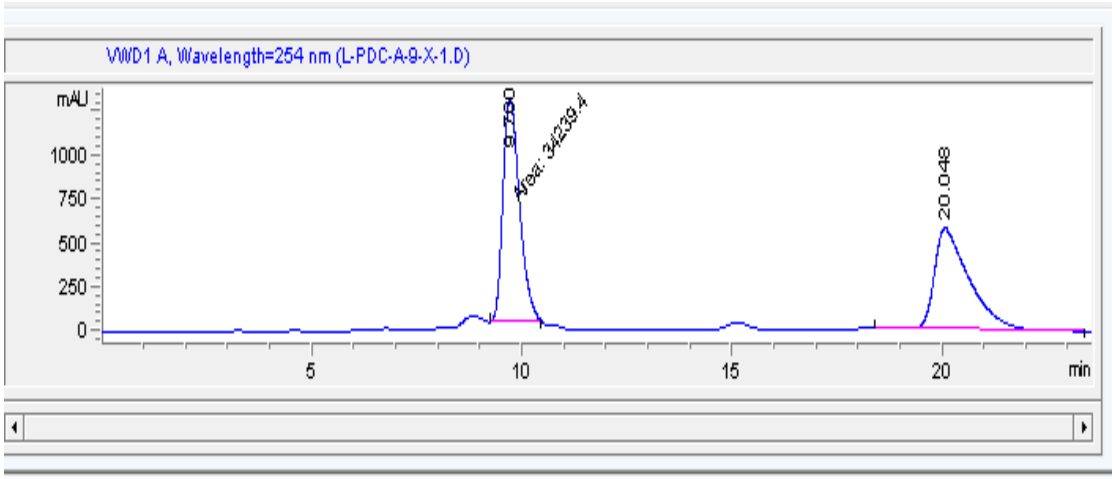
#	Time	Area	Height	Width	Area%	Symmetry
1	10.091	7529.2	177.4	0.6013	96.155	0.494
2	21.685	301	3.6	1.077	3.845	0.543

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

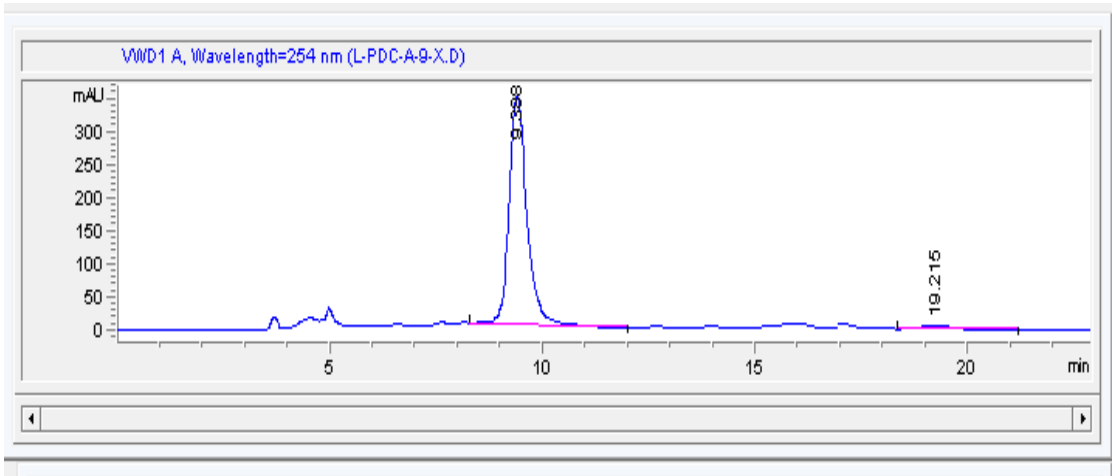




HPLC of 6e

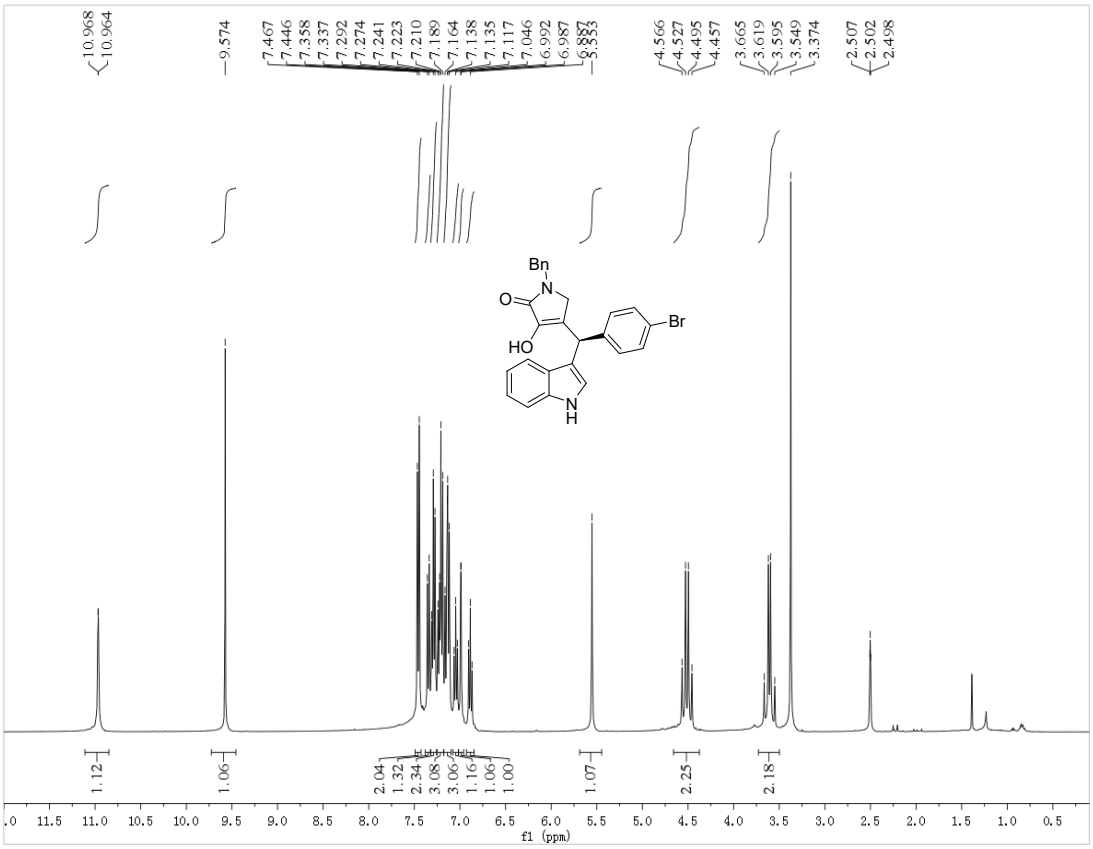


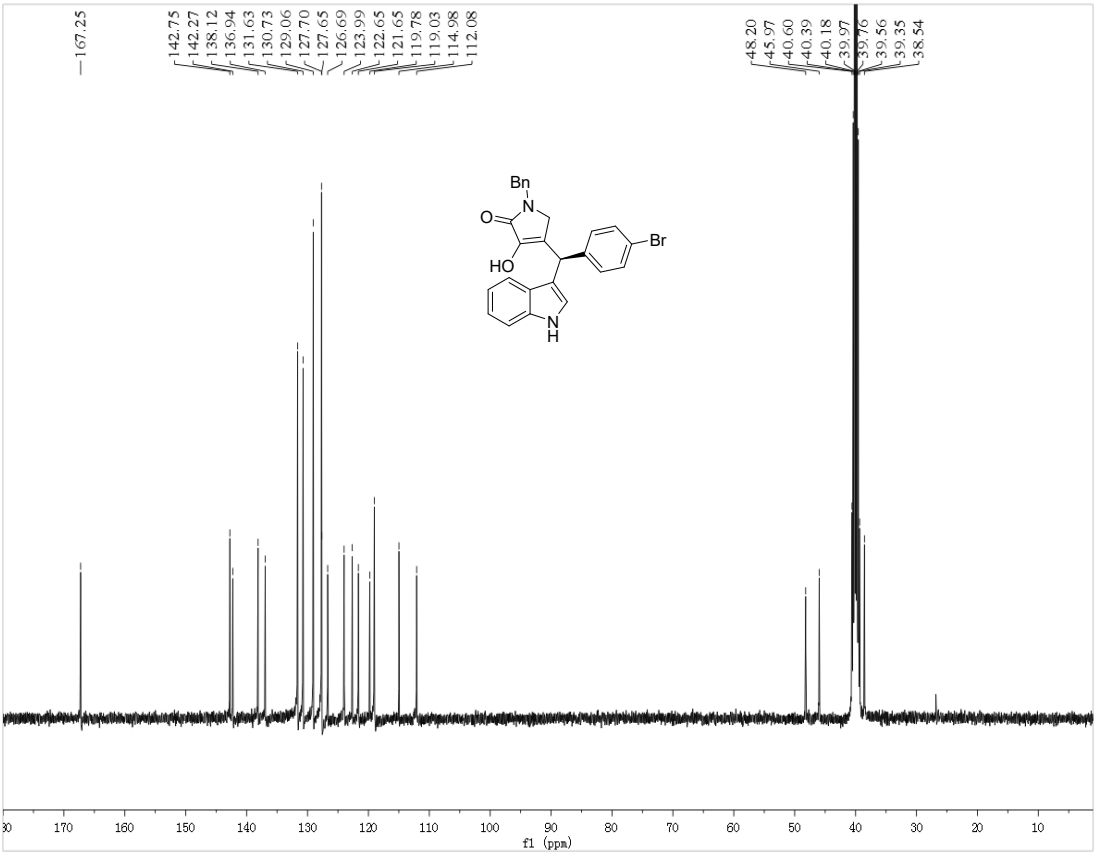
#	Time	Area	Height	Width	Area%	Symmetry
1	9.7	34239.4	1270.8	0.4491	50.353	0.709
2	20.048	33759.4	577.6	0.8559	49.647	0.418



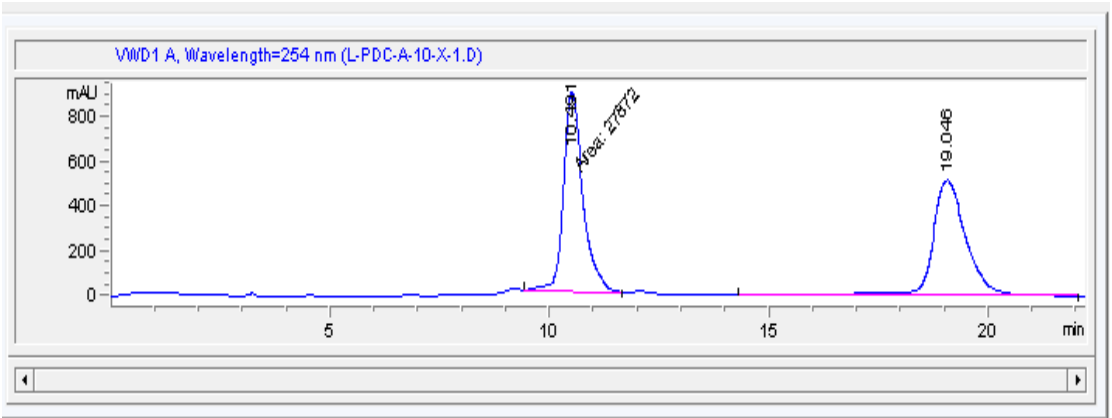
#	Time	Area	Height	Width	Area%	Symmetry
1	9.388	11057.9	347.9	0.4669	97.443	0.89
2	19.215	290.2	6.3	0.7029	2.557	0.852

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

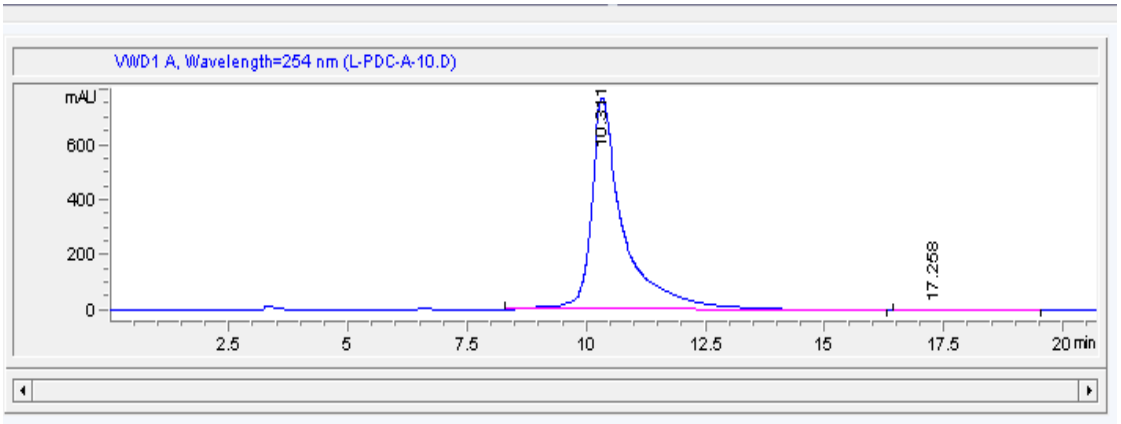




HPLC of 6f

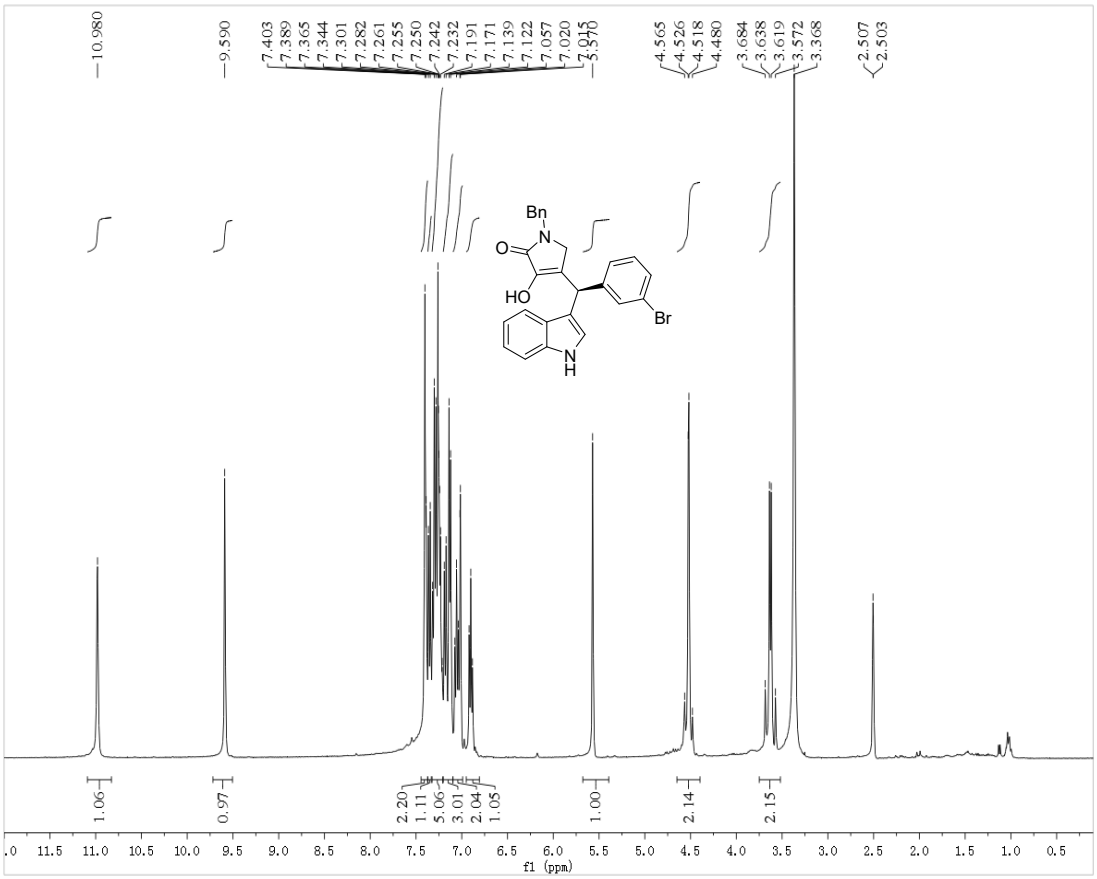


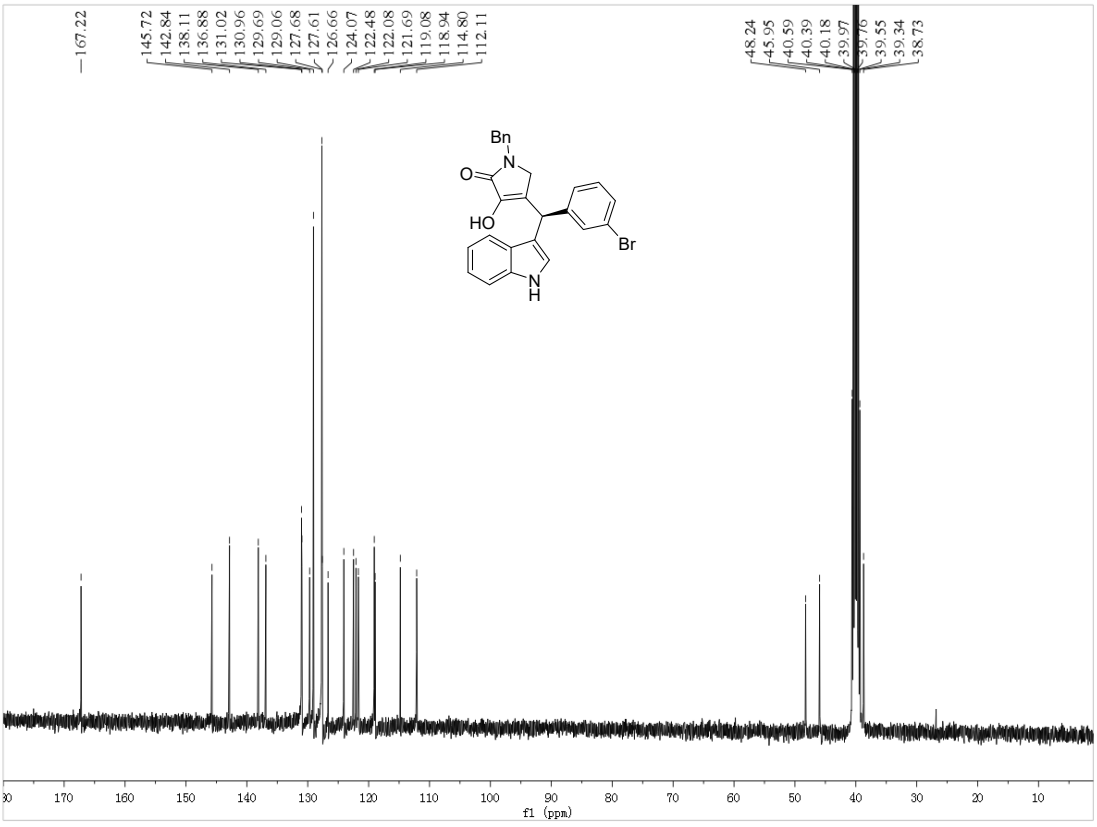
#	Time	Area	Height	Width	Area%	Symmetry
1	10.491	27872	894.3	0.5194	50.471	0.71
2	19.046	27352.1	514.3	0.7975	49.529	0.755



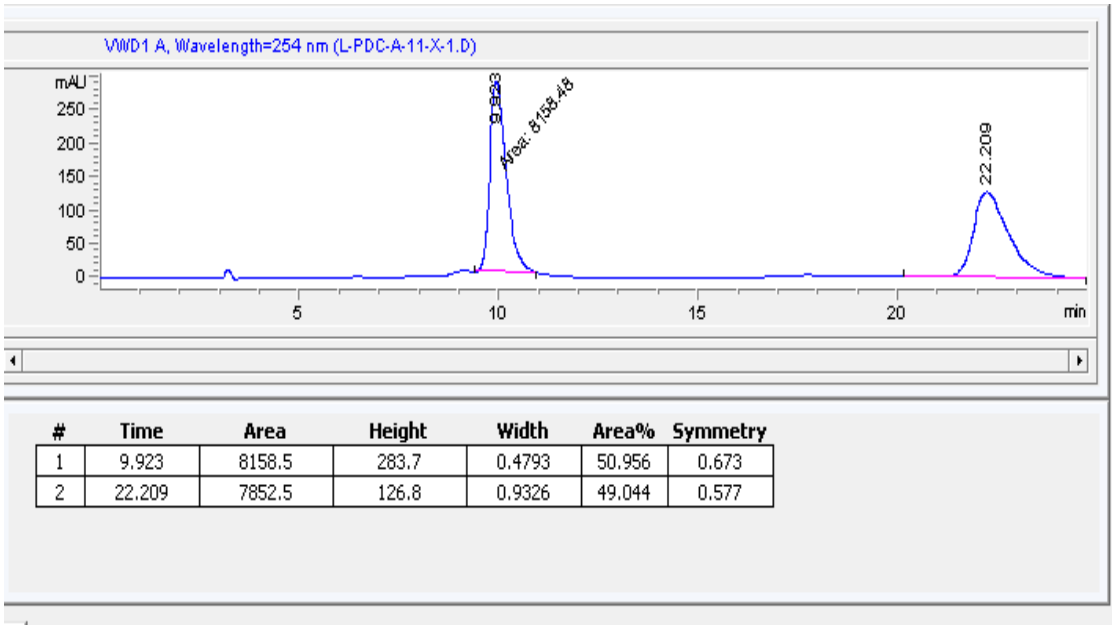
#	Time	Area	Height	Width	Area%	Symmetry
1	10.311	36566.9	769.3	0.6616	99.455	0.476
2	17.258	200.2	3.1	0.9021	0.545	0.474

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

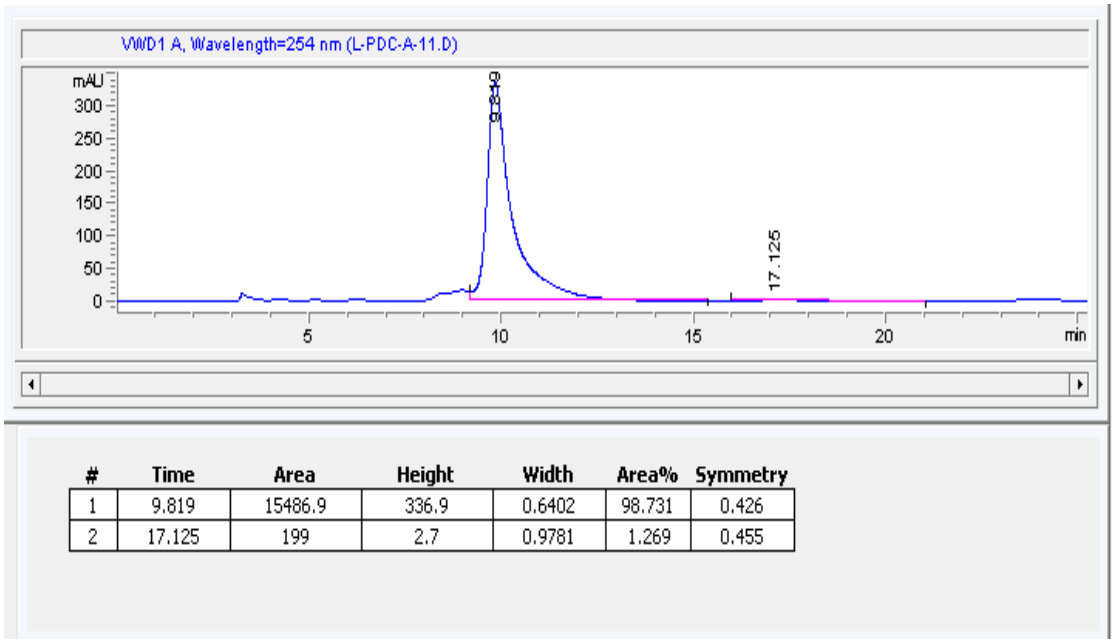




HPLC of 6g

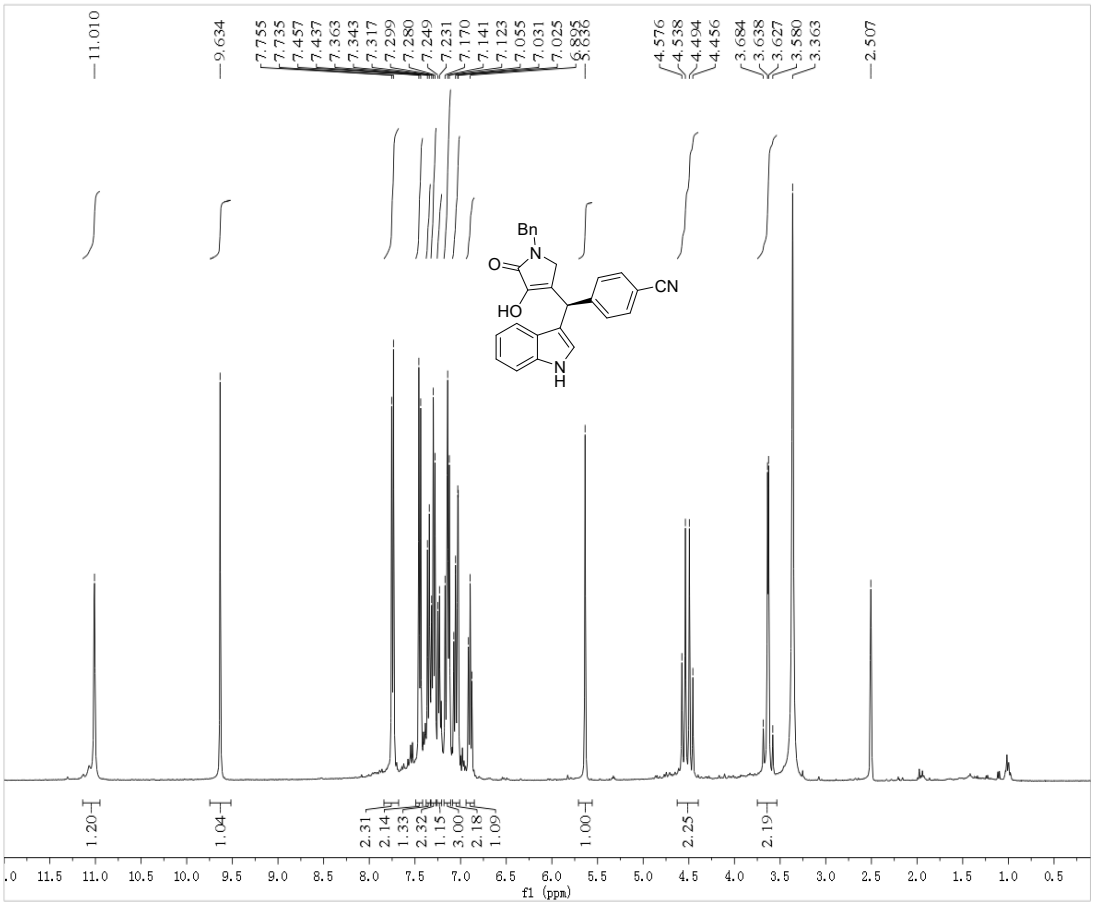


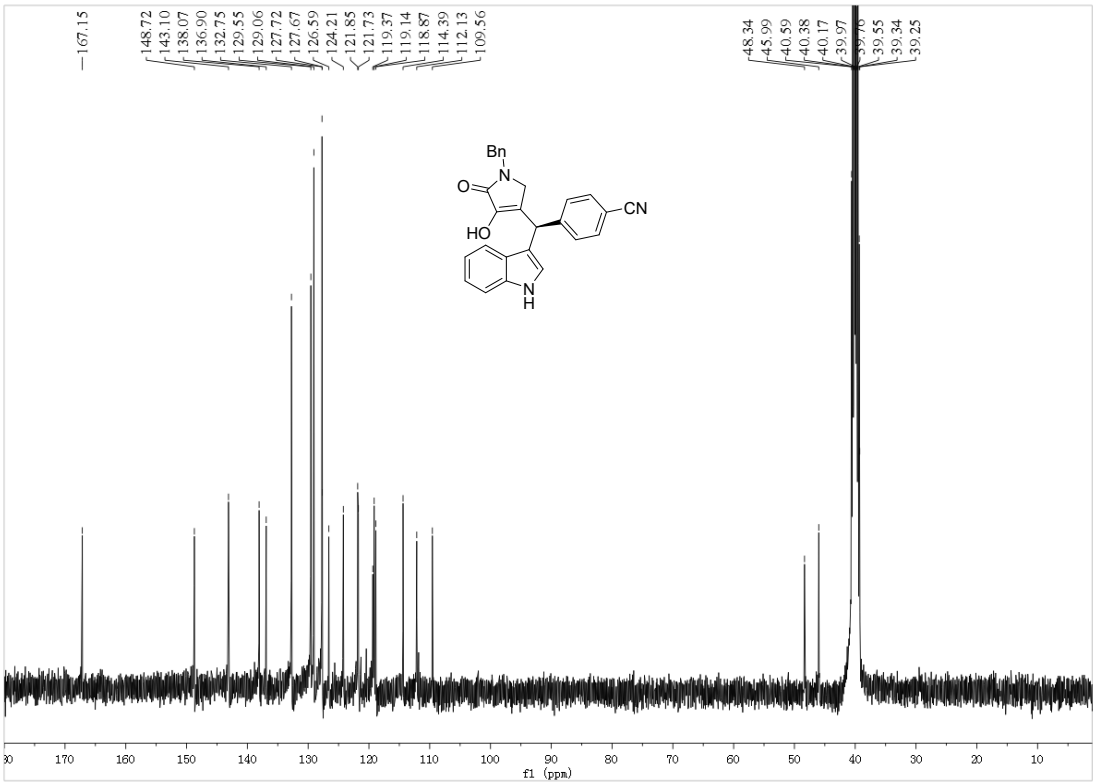
#	Time	Area	Height	Width	Area%	Symmetry
1	9.923	8158.5	283.7	0.4793	50.956	0.673
2	22.209	7852.5	126.8	0.9326	49.044	0.577



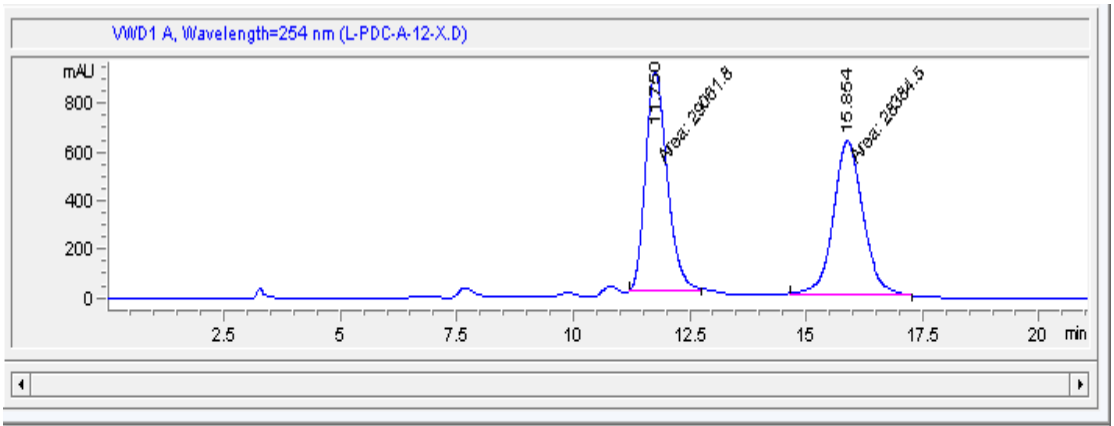
#	Time	Area	Height	Width	Area%	Symmetry
1	9.819	15486.9	336.9	0.6402	98.731	0.426
2	17.125	199	2.7	0.9781	1.269	0.455

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

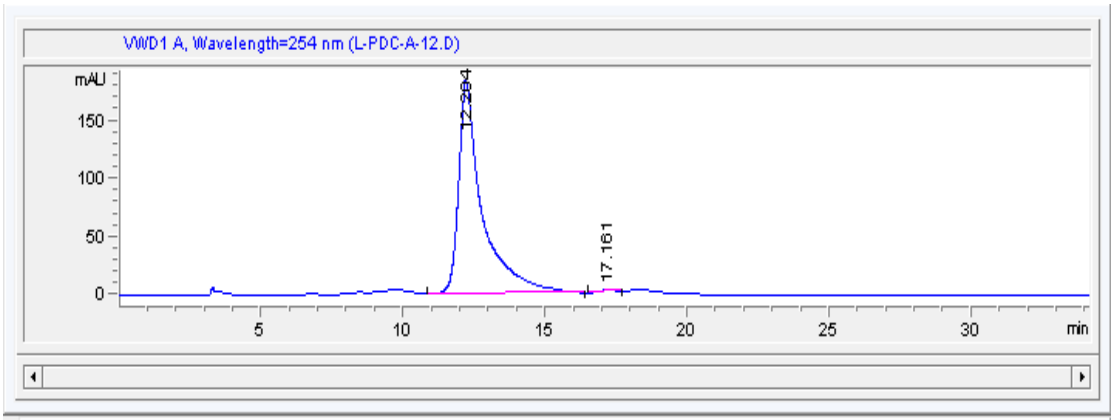




HPLC of 6h

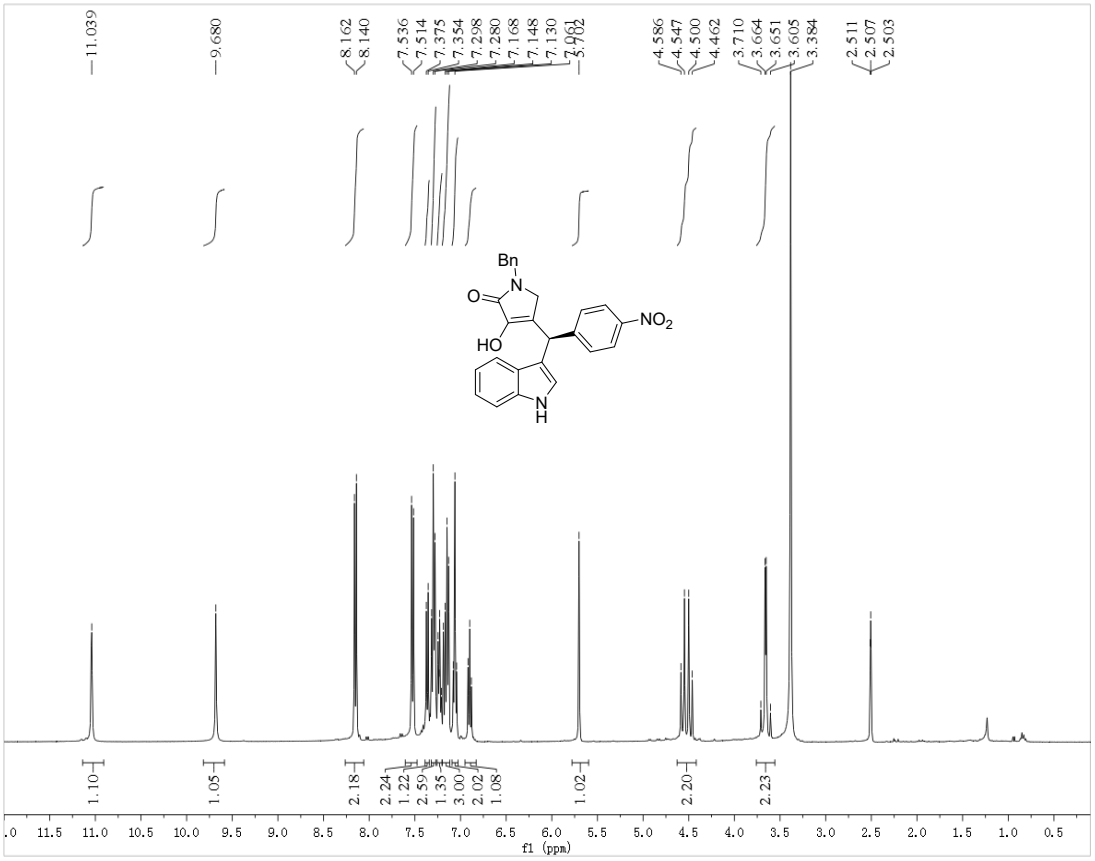


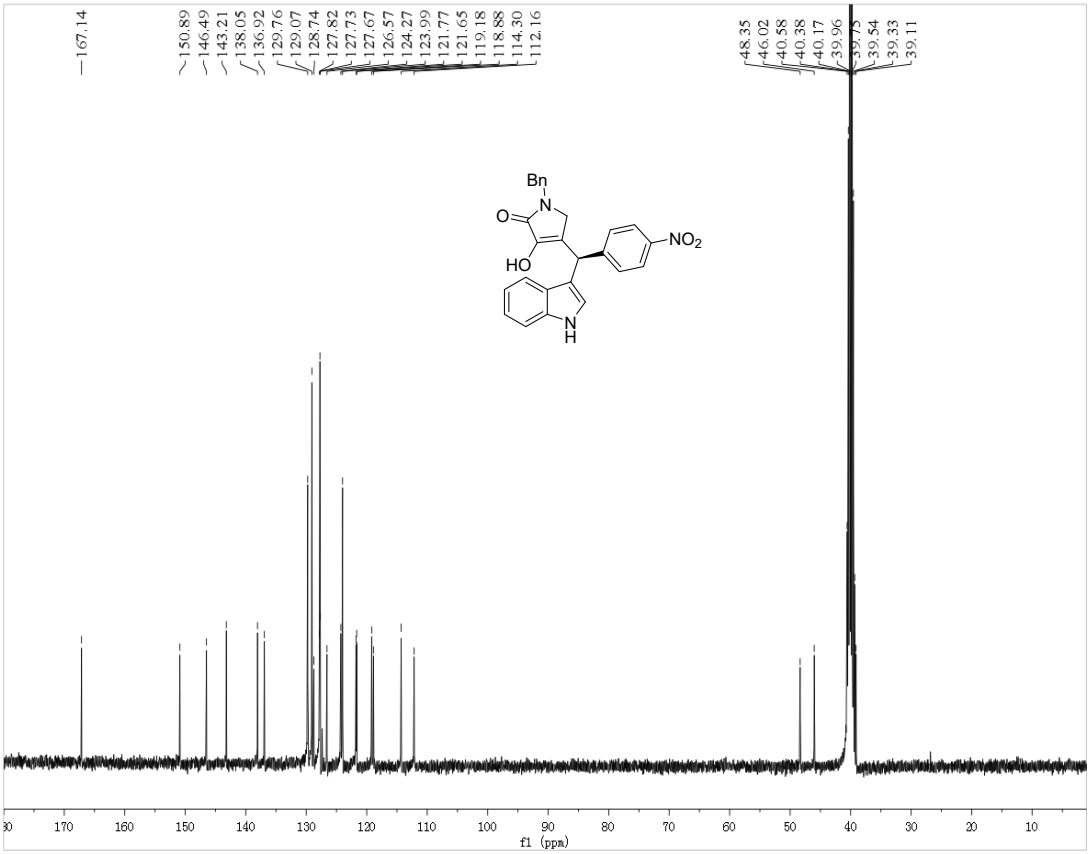
#	Time	Area	Height	Width	Area%	Symmetry
1	11.75	29061.8	899.6	0.5384	50.590	0.779
2	15.854	28384.5	633.3	0.747	49.410	0.878



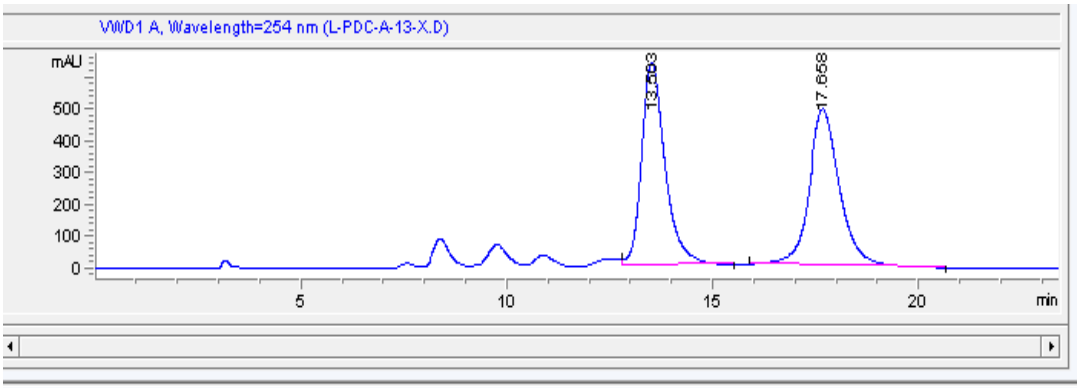
#	Time	Area	Height	Width	Area%	Symmetry
1	12.204	10928.7	183.6	0.8386	99.436	0.441
2	17.161	62	1.8	0.5248	0.564	1.183

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

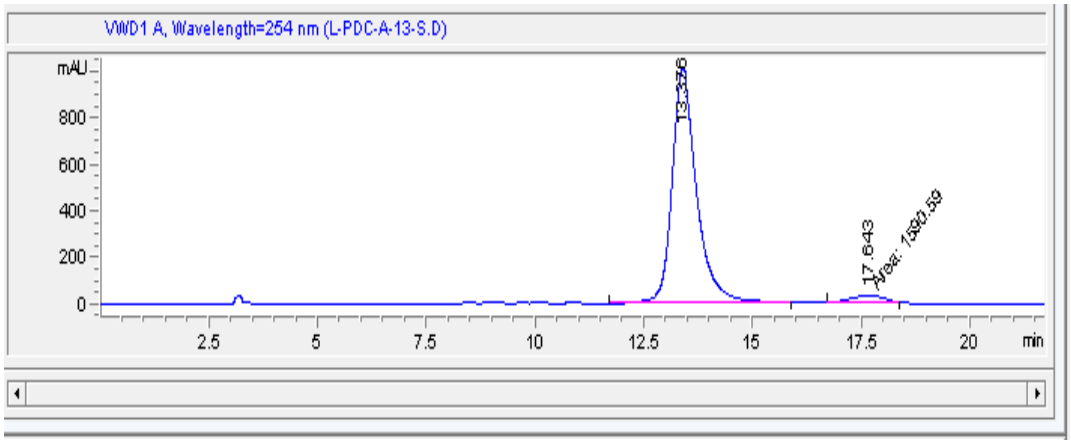




HPLC of 6i

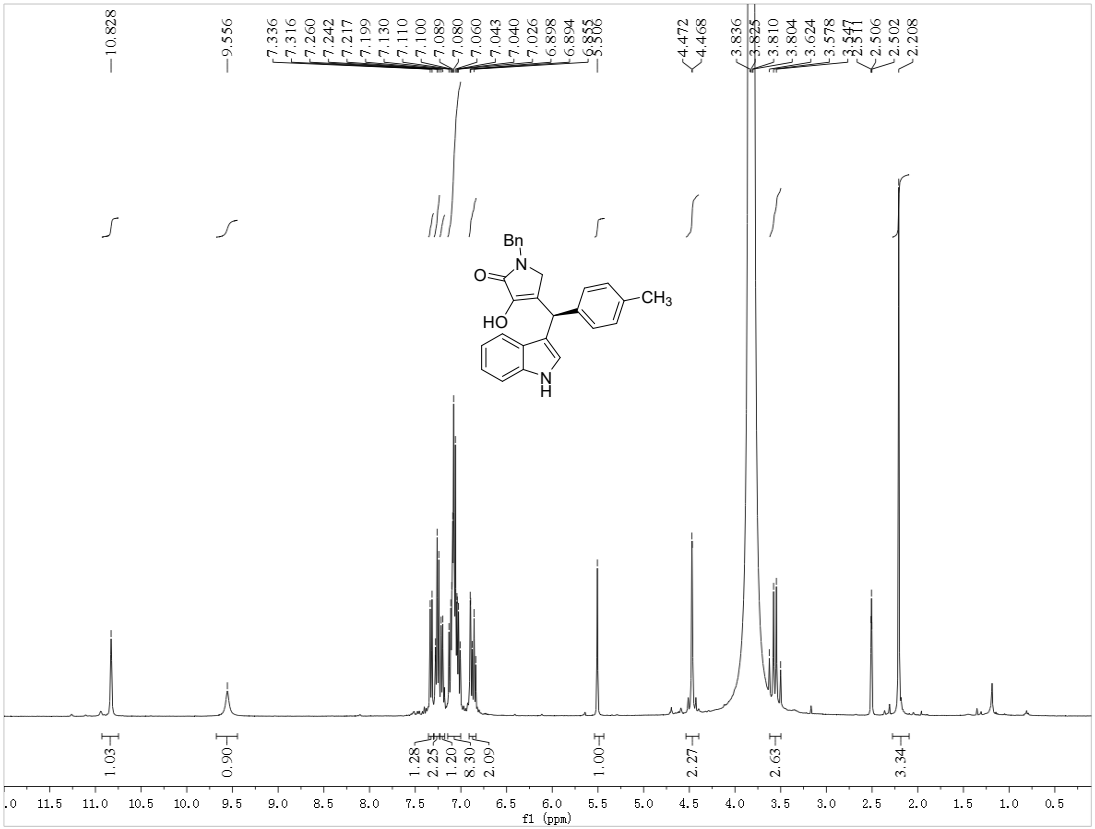


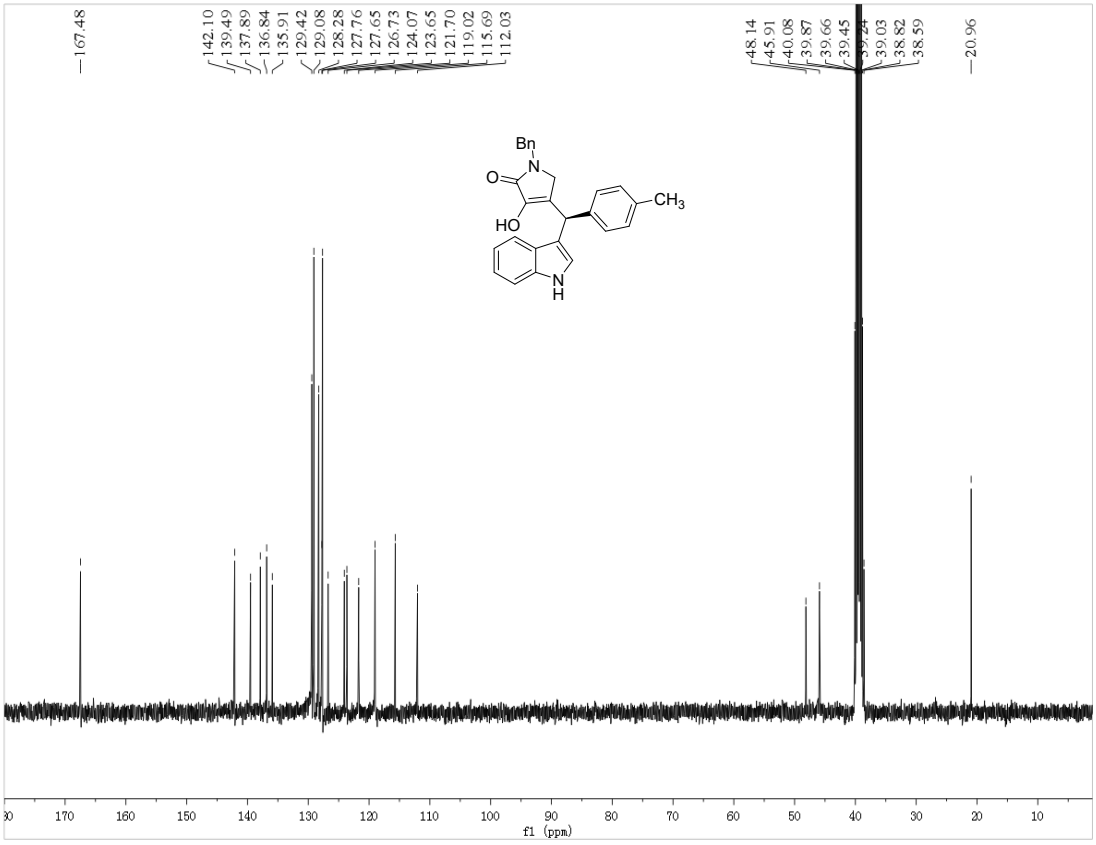
#	Time	Area	Height	Width	Area%	Symmetry
1	13.503	25092.4	637.9	0.5929	49.531	0.705
2	17.658	25567.7	489.5	0.7833	50.469	0.821



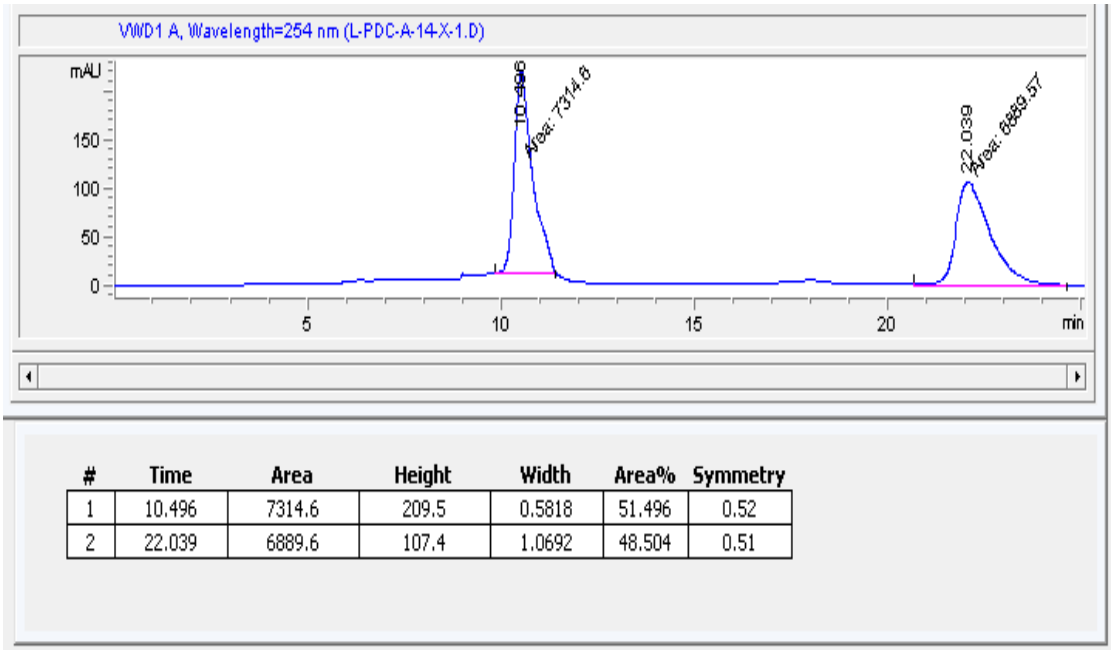
#	Time	Area	Height	Width	Area%	Symmetry
1	13.376	40263.5	1009.5	0.5973	96.200	0.708
2	17.643	1590.6	31.1	0.8532	3.800	1.075

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

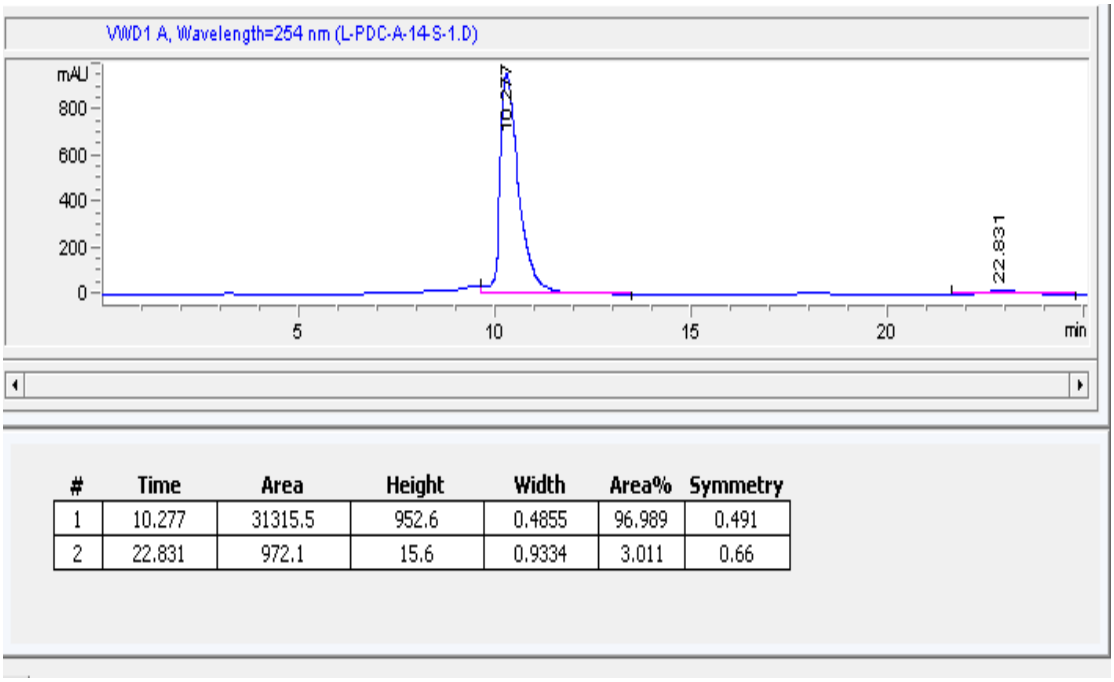




HPLC of 6j

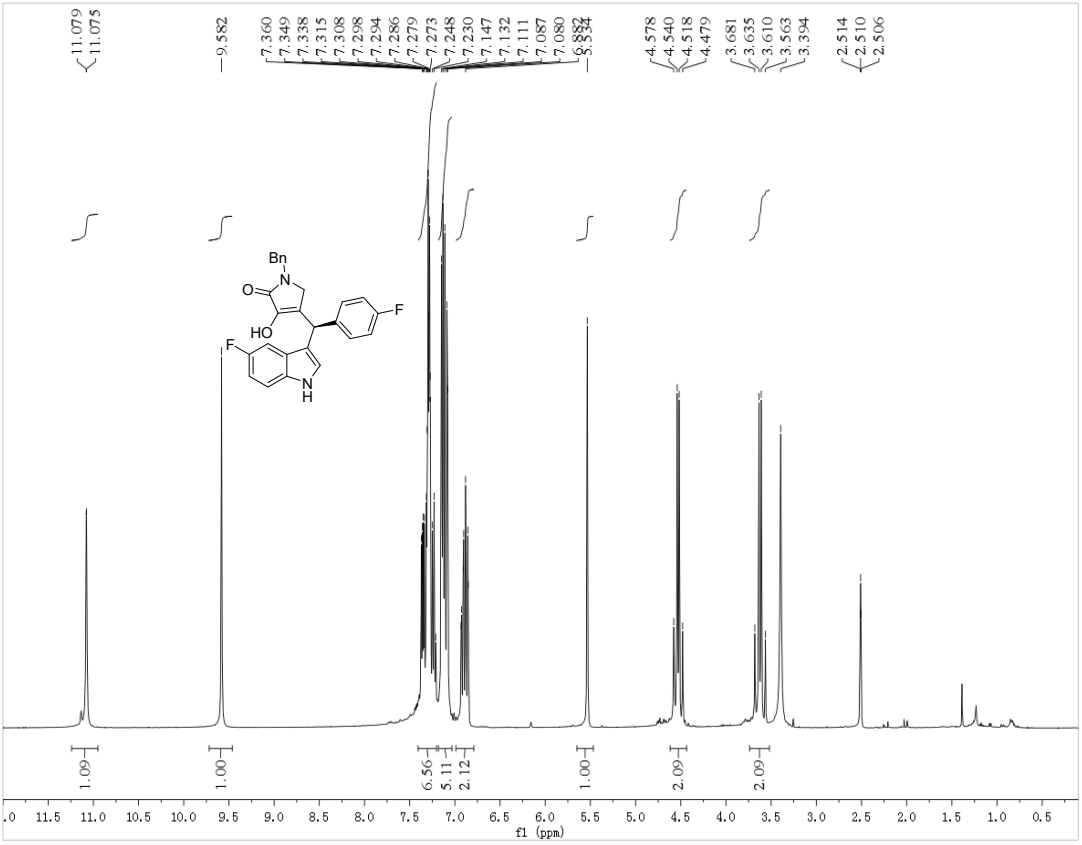


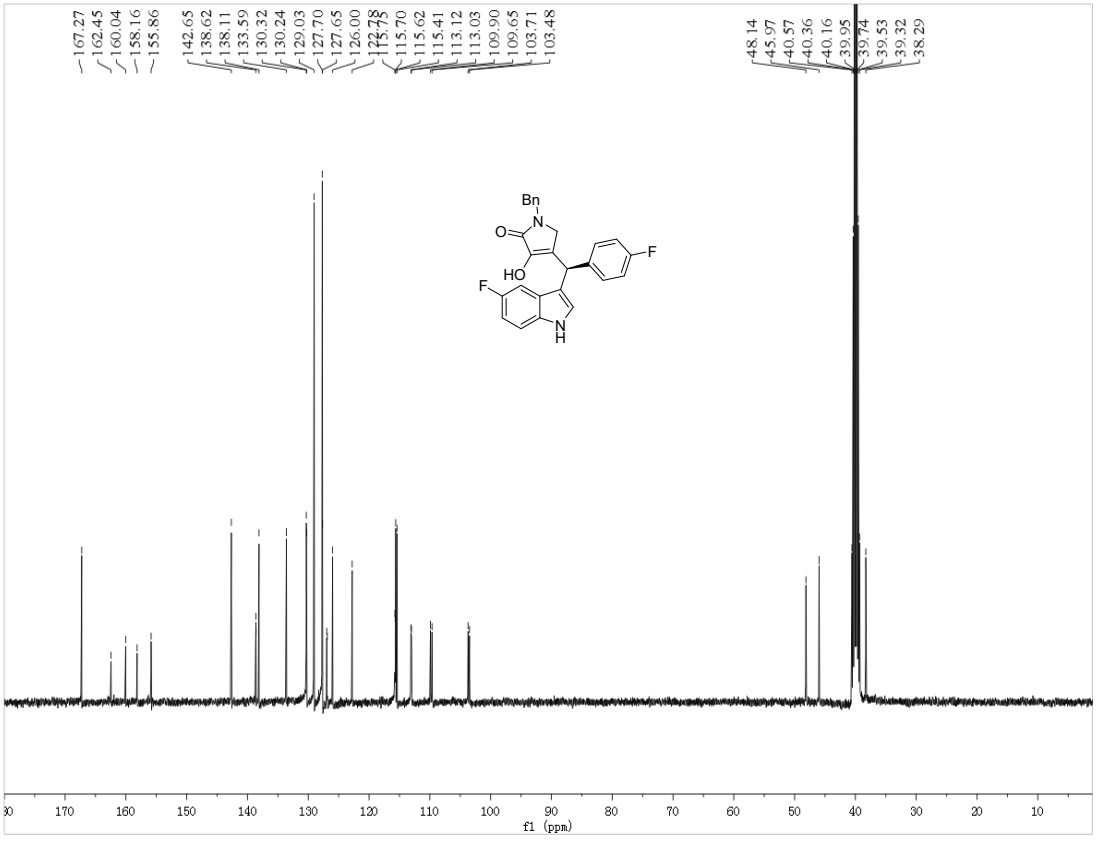
#	Time	Area	Height	Width	Area%	Symmetry
1	10.496	7314.6	209.5	0.5818	51.496	0.52
2	22.039	6889.6	107.4	1.0692	48.504	0.51



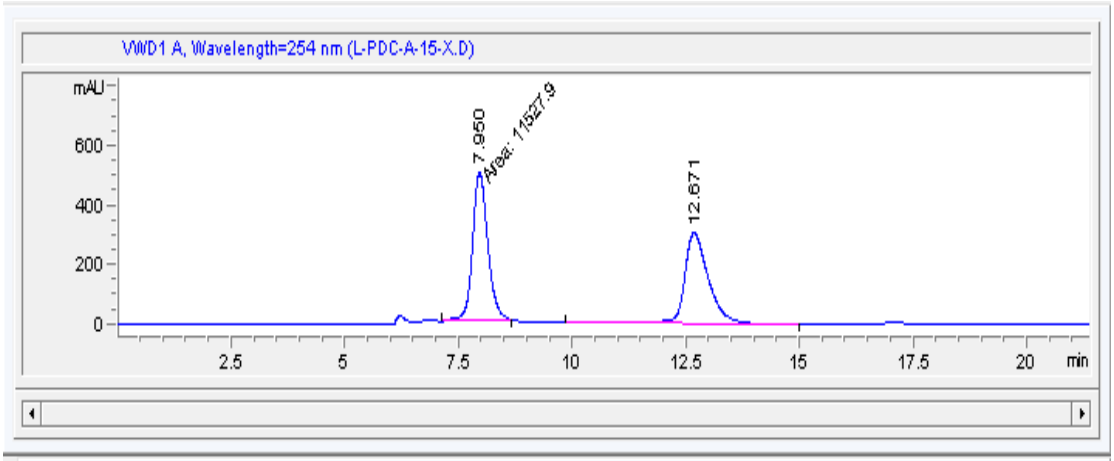
#	Time	Area	Height	Width	Area%	Symmetry
1	10.277	31315.5	952.6	0.4855	96.989	0.491
2	22.831	972.1	15.6	0.9334	3.011	0.66

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

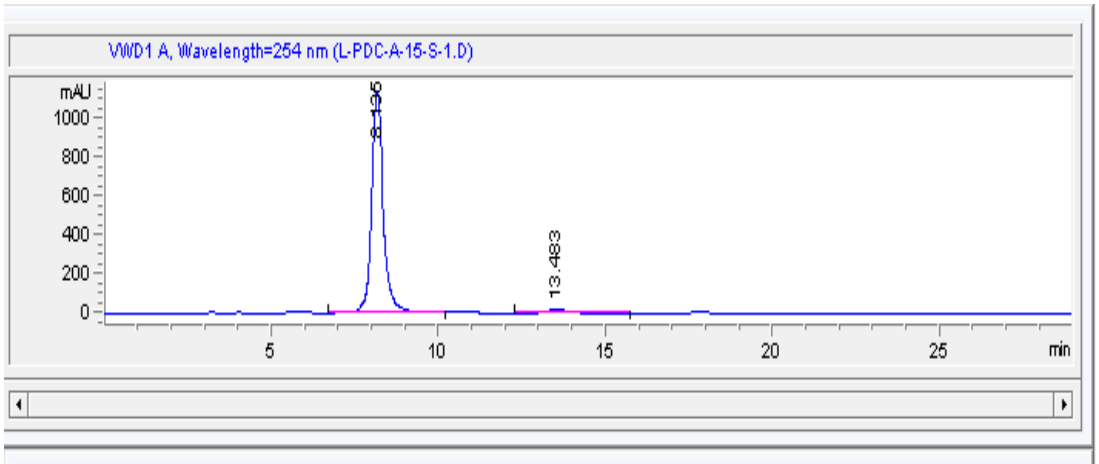




HPLC of 6k

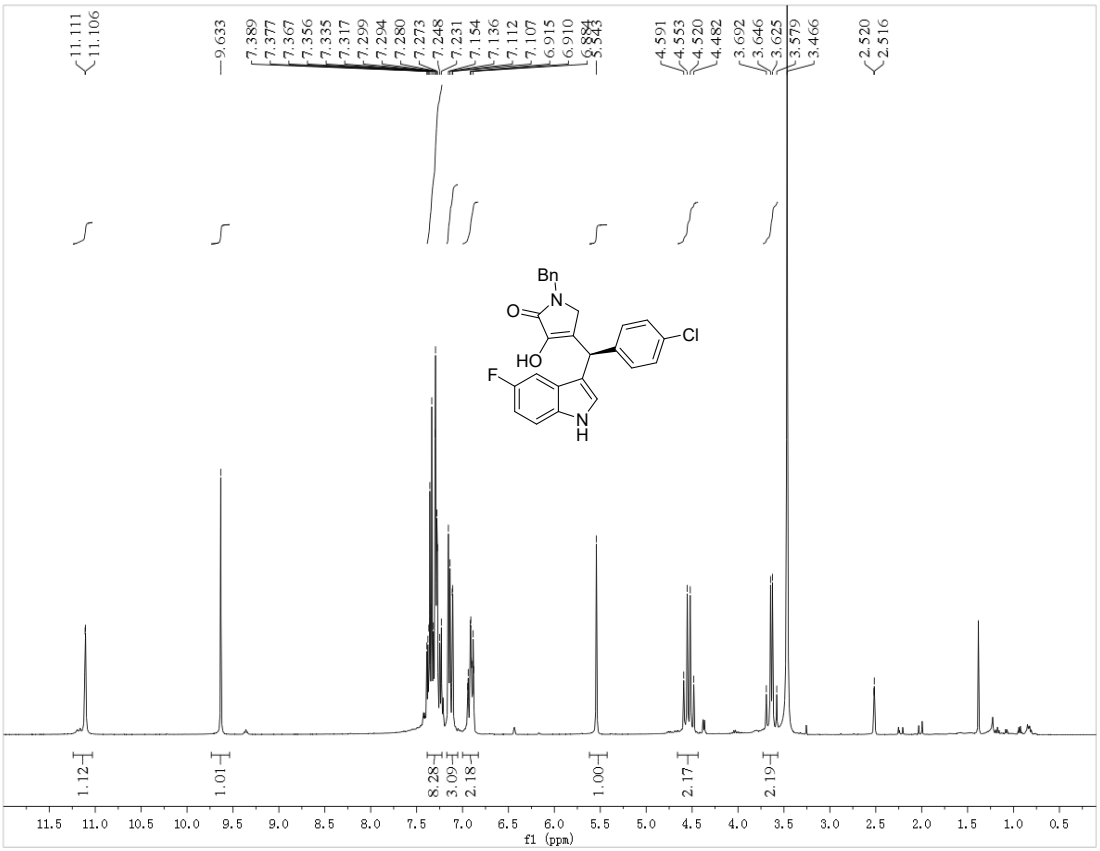


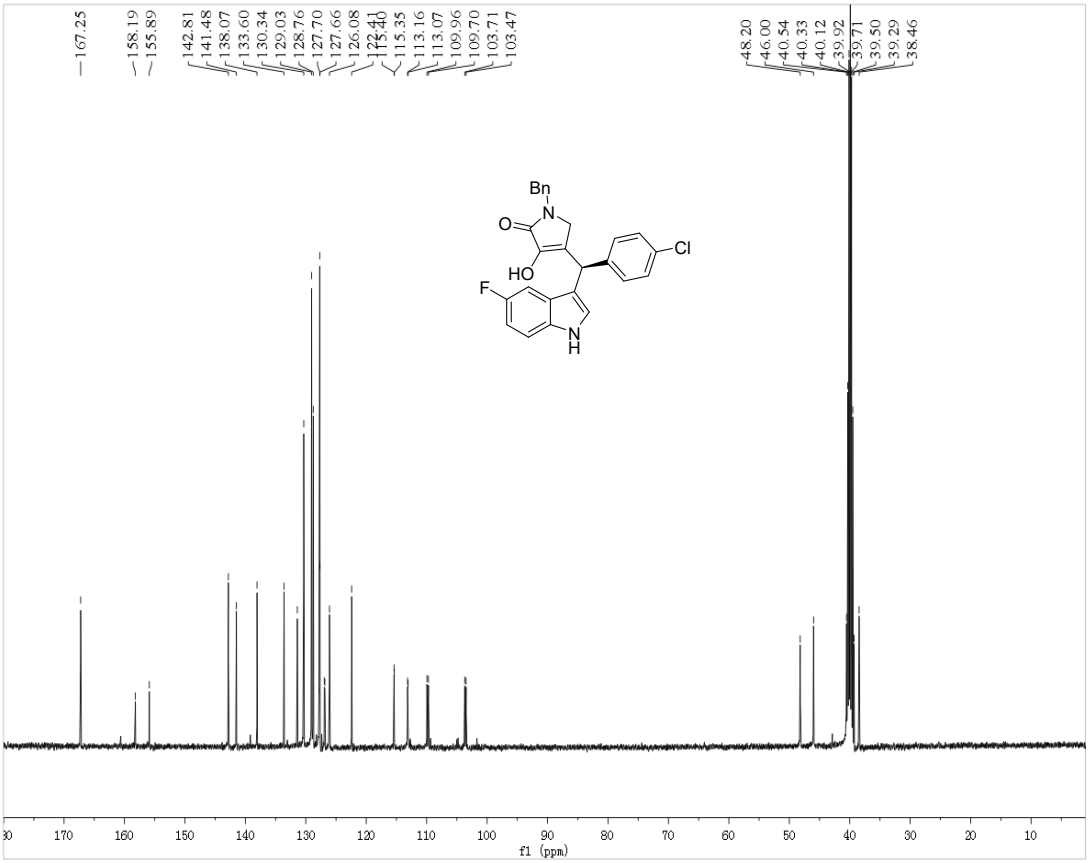
#	Time	Area	Height	Width	Area%	Symmetry
1	7.95	11527.9	500	0.3843	50.762	0.819
2	12.671	11181.8	305.6	0.5459	49.238	0.682



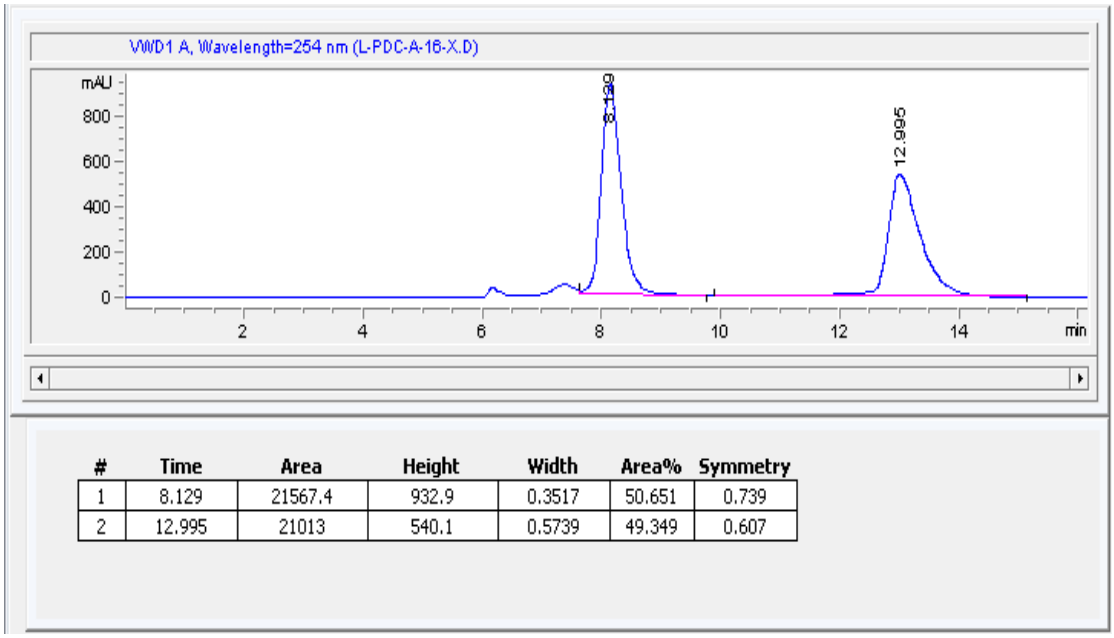
#	Time	Area	Height	Width	Area%	Symmetry
1	8.135	27966.1	1136.9	0.37	97.075	0.752
2	13.483	842.5	21.4	0.5904	2.925	0.73

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

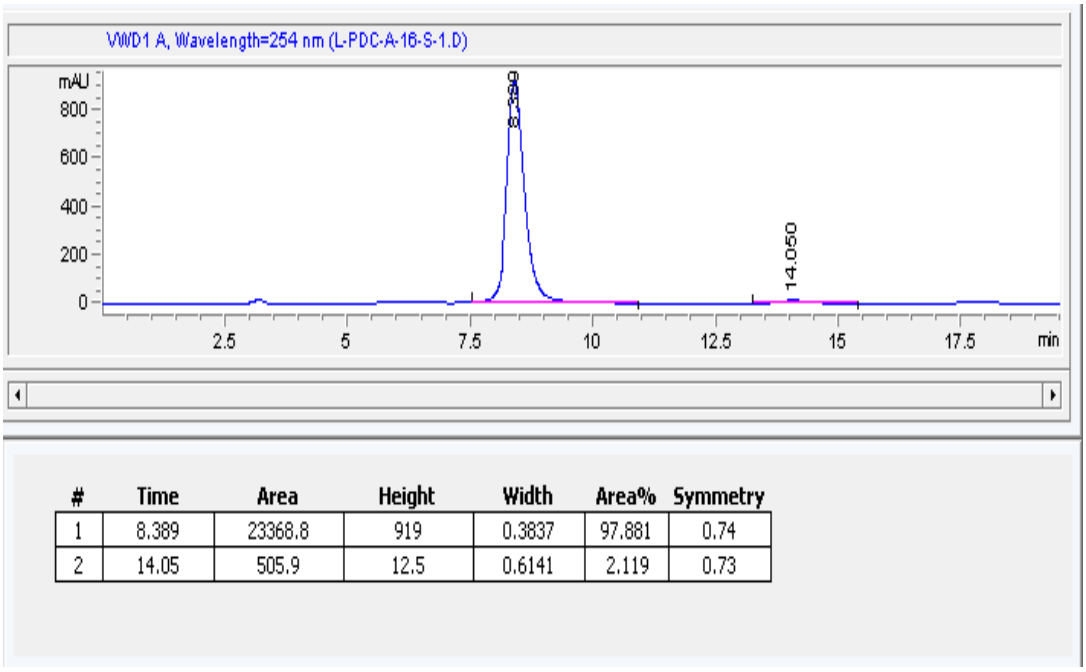




HPLC of 6l

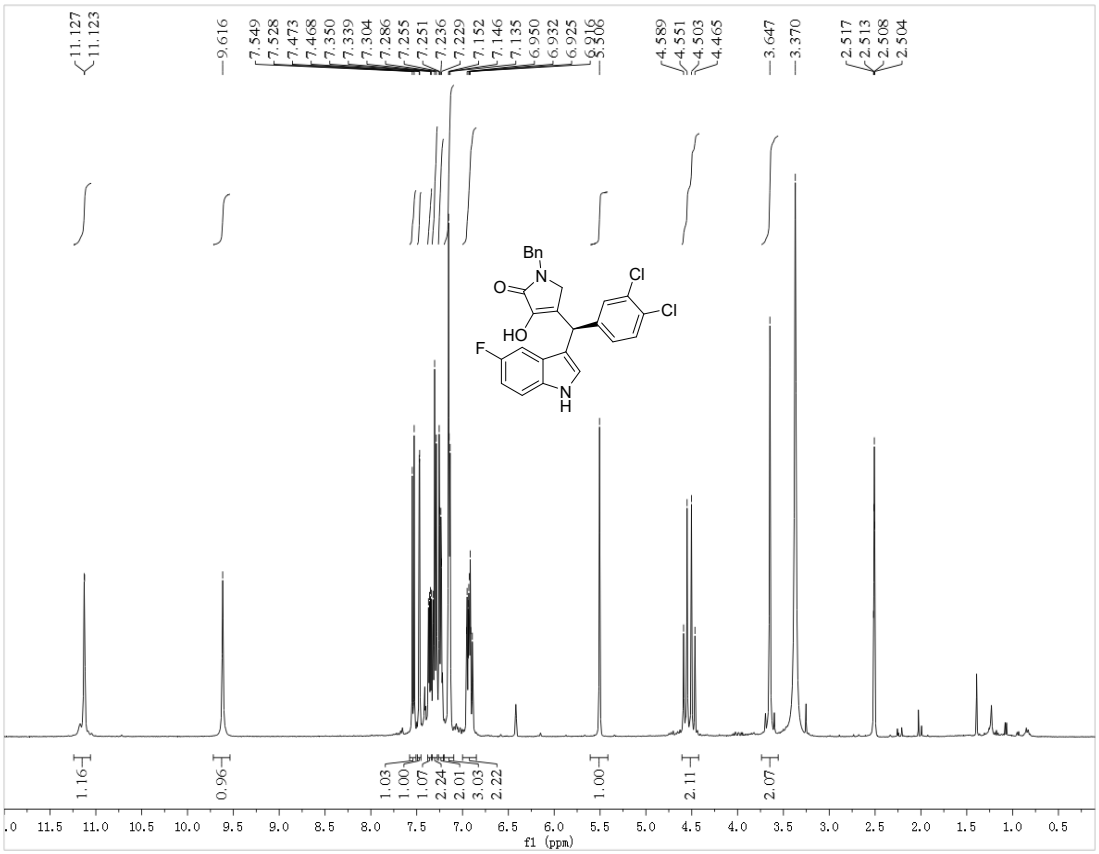


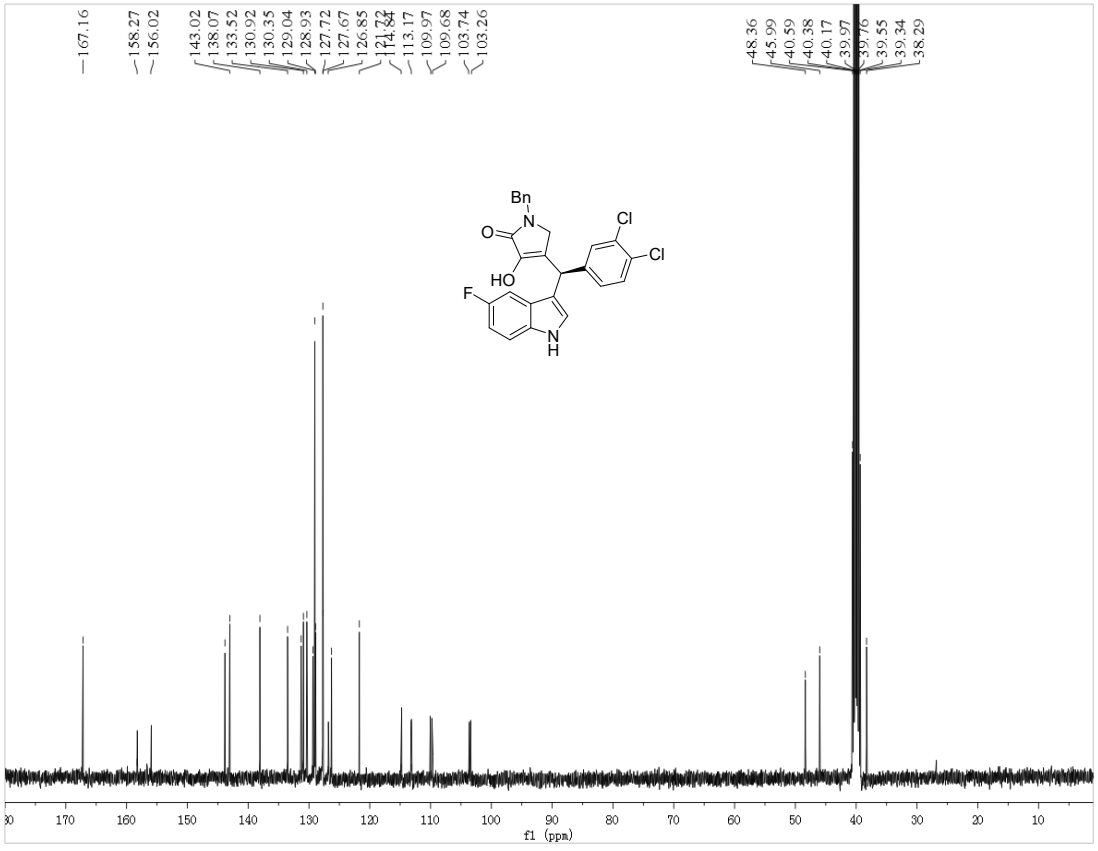
#	Time	Area	Height	Width	Area%	Symmetry
1	8.129	21567.4	932.9	0.3517	50.651	0.739
2	12.995	21013	540.1	0.5739	49.349	0.607



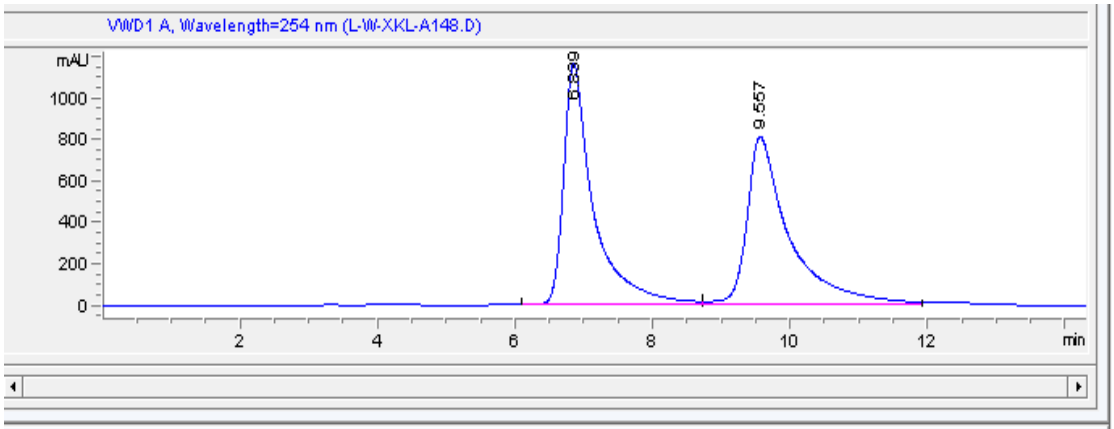
#	Time	Area	Height	Width	Area%	Symmetry
1	8.389	23368.8	919	0.3837	97.881	0.74
2	14.05	505.9	12.5	0.6141	2.119	0.73

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

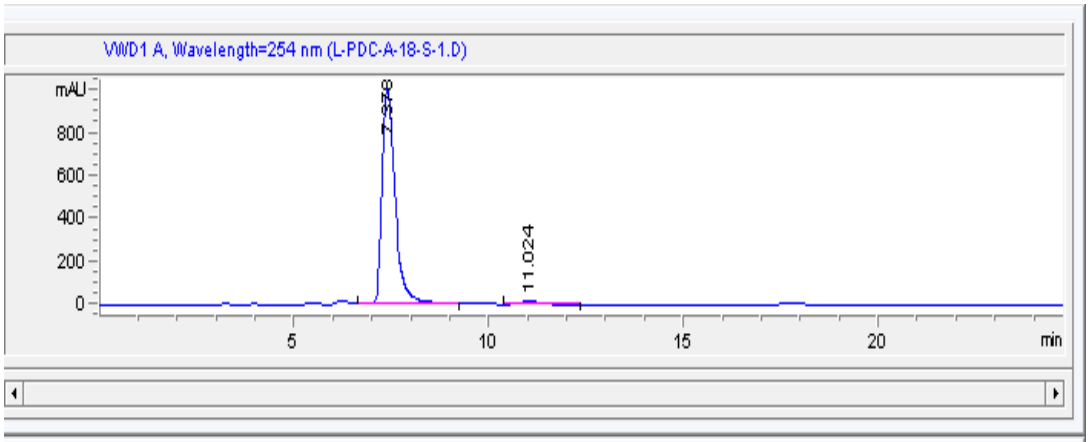




HPLC of 6m

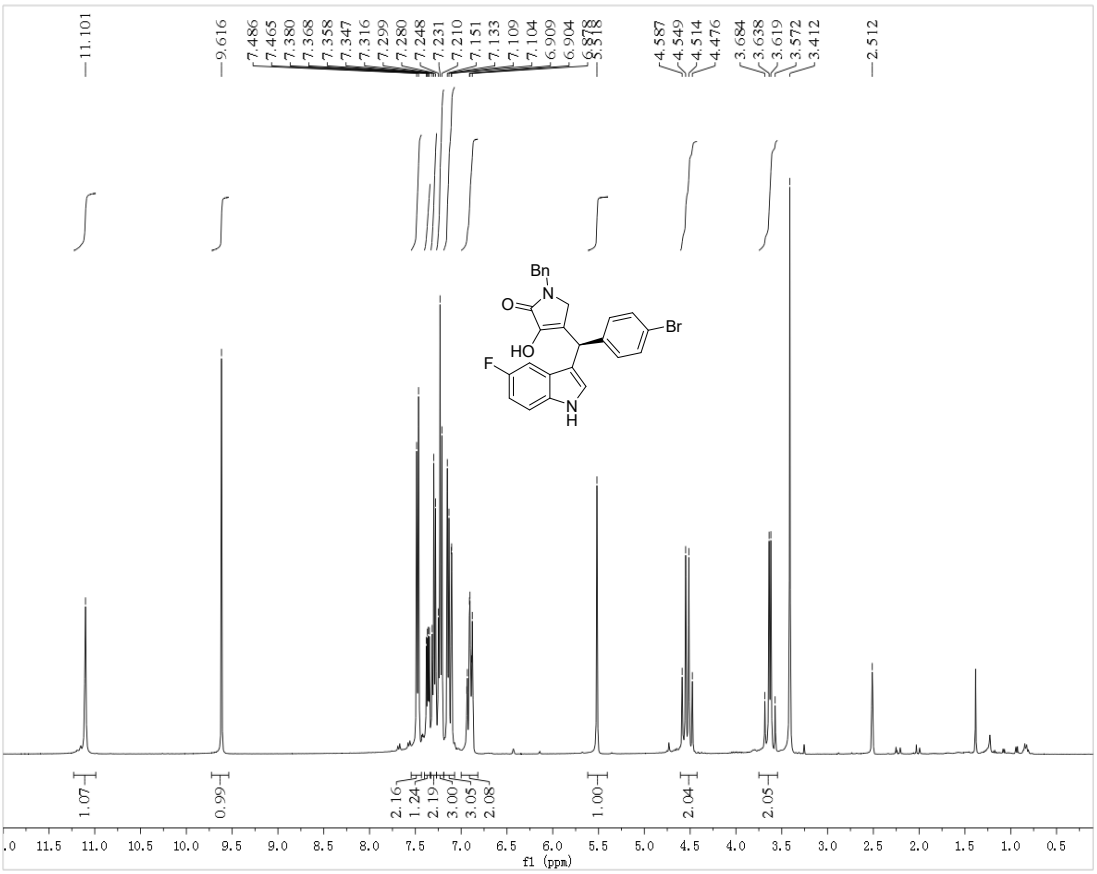


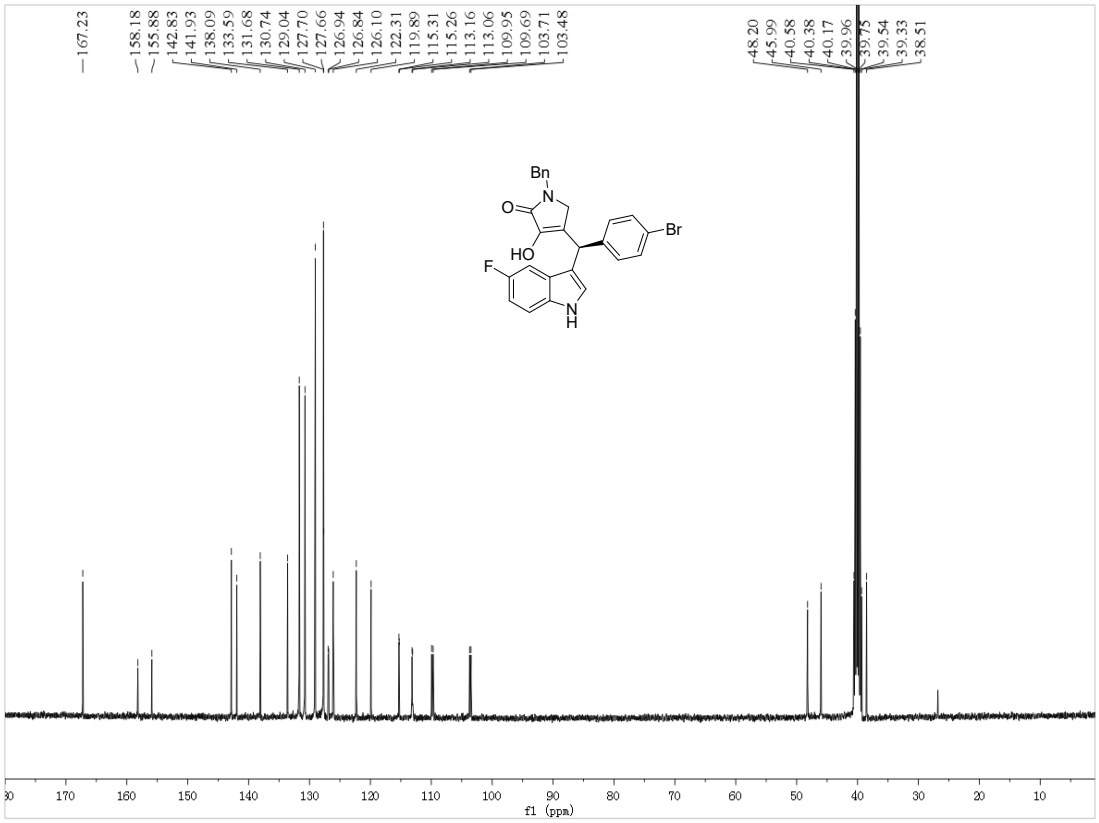
#	Time	Area	Height	Width	Area%	Symmetry
1	6.839	35691.9	1169.8	0.429	50.104	0.447
2	9.557	35543.3	815.1	0.6048	49.896	0.417



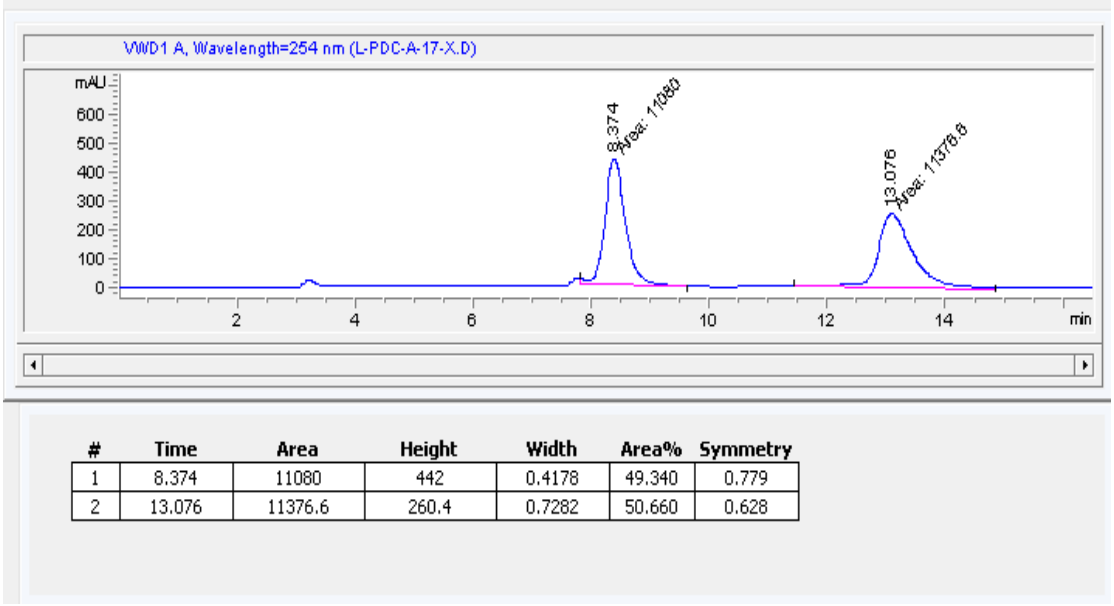
#	Time	Area	Height	Width	Area%	Symmetry
1	7.378	22873.1	1000.9	0.3426	97.978	0.597
2	11.024	472	14.5	0.4961	2.022	0.779

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

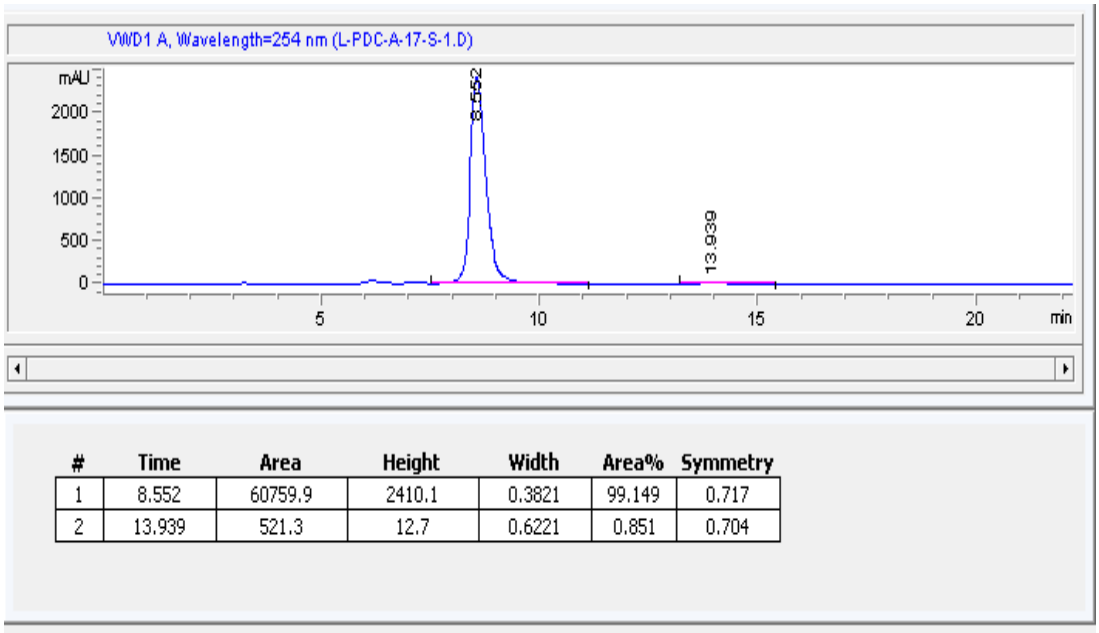




HPLC of 6n

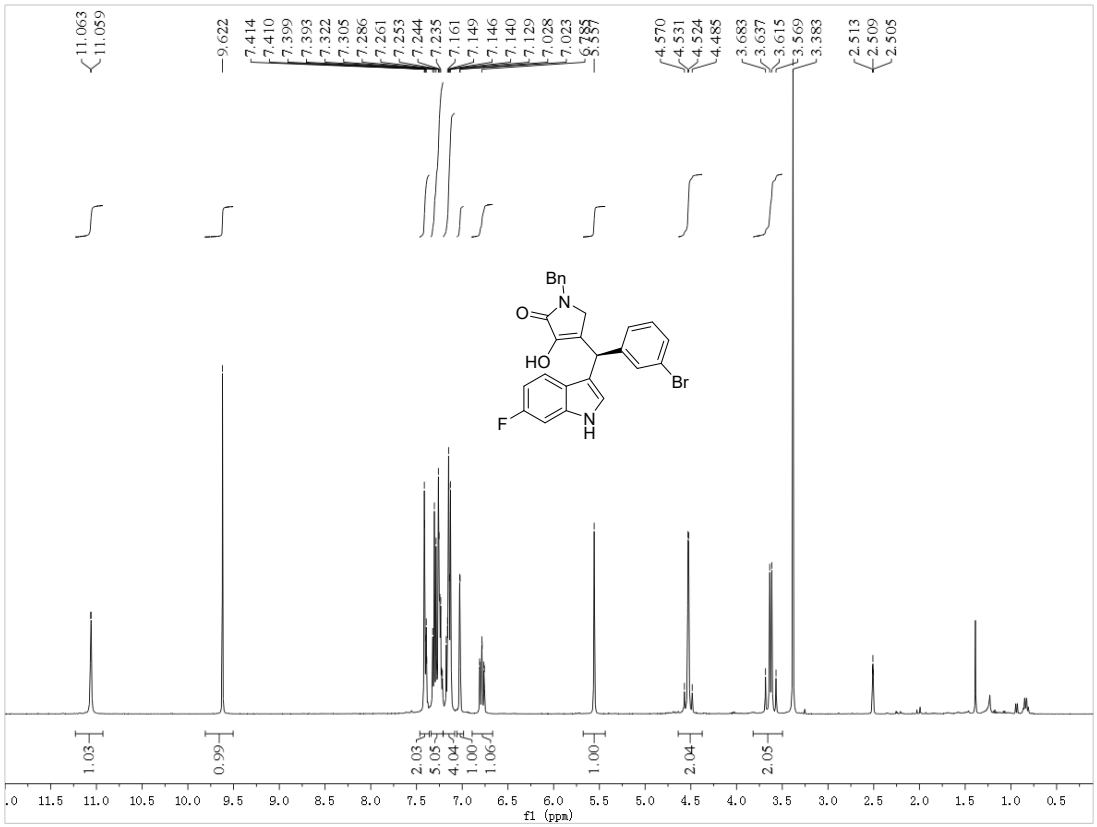


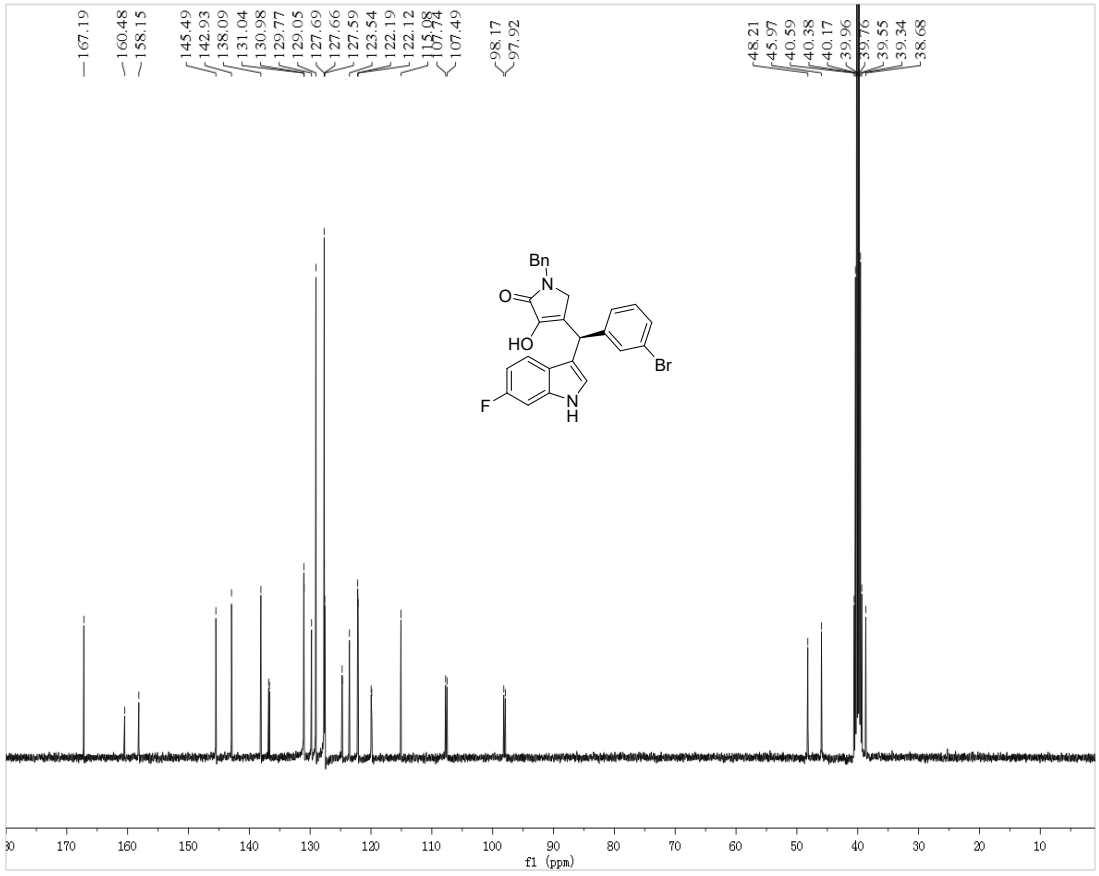
#	Time	Area	Height	Width	Area%	Symmetry
1	8.374	11080	442	0.4178	49.340	0.779
2	13.076	11376.6	260.4	0.7282	50.660	0.628



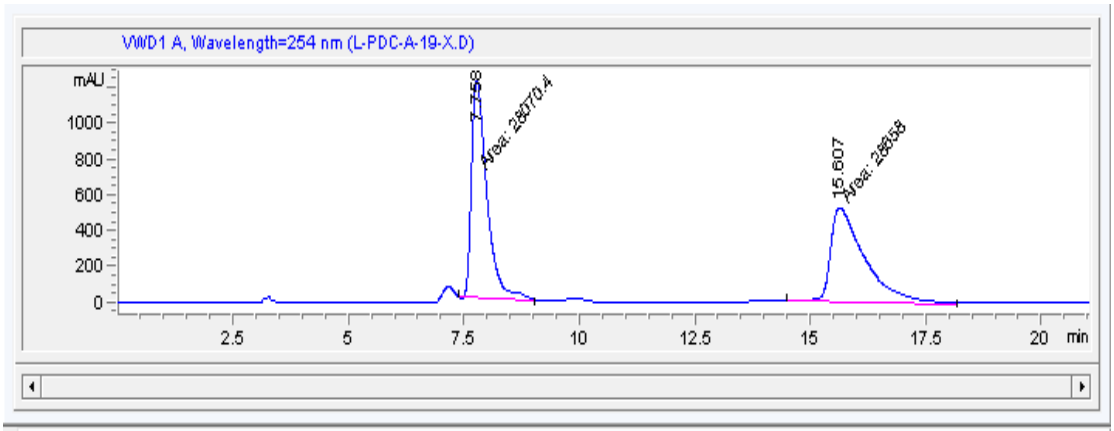
#	Time	Area	Height	Width	Area%	Symmetry
1	8.552	60759.9	2410.1	0.3821	99.149	0.717
2	13.939	521.3	12.7	0.6221	0.851	0.704

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

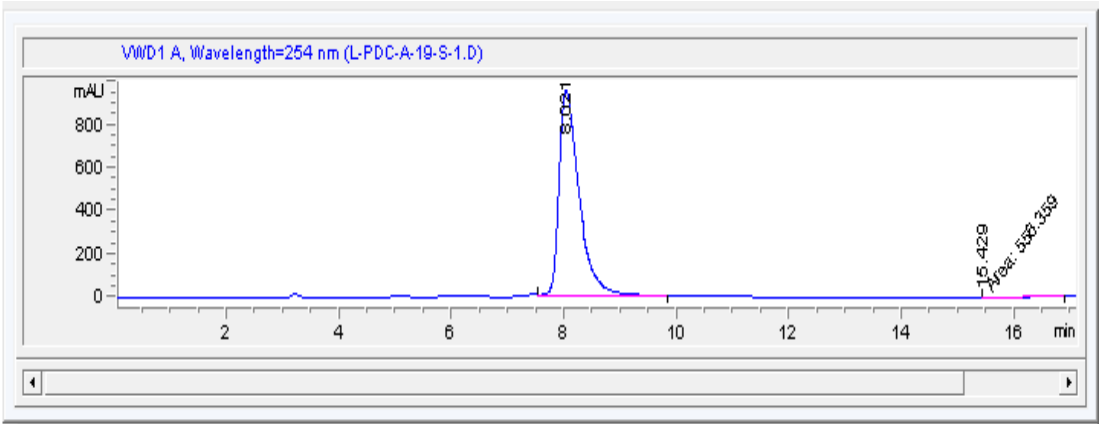




HPLC of 6o

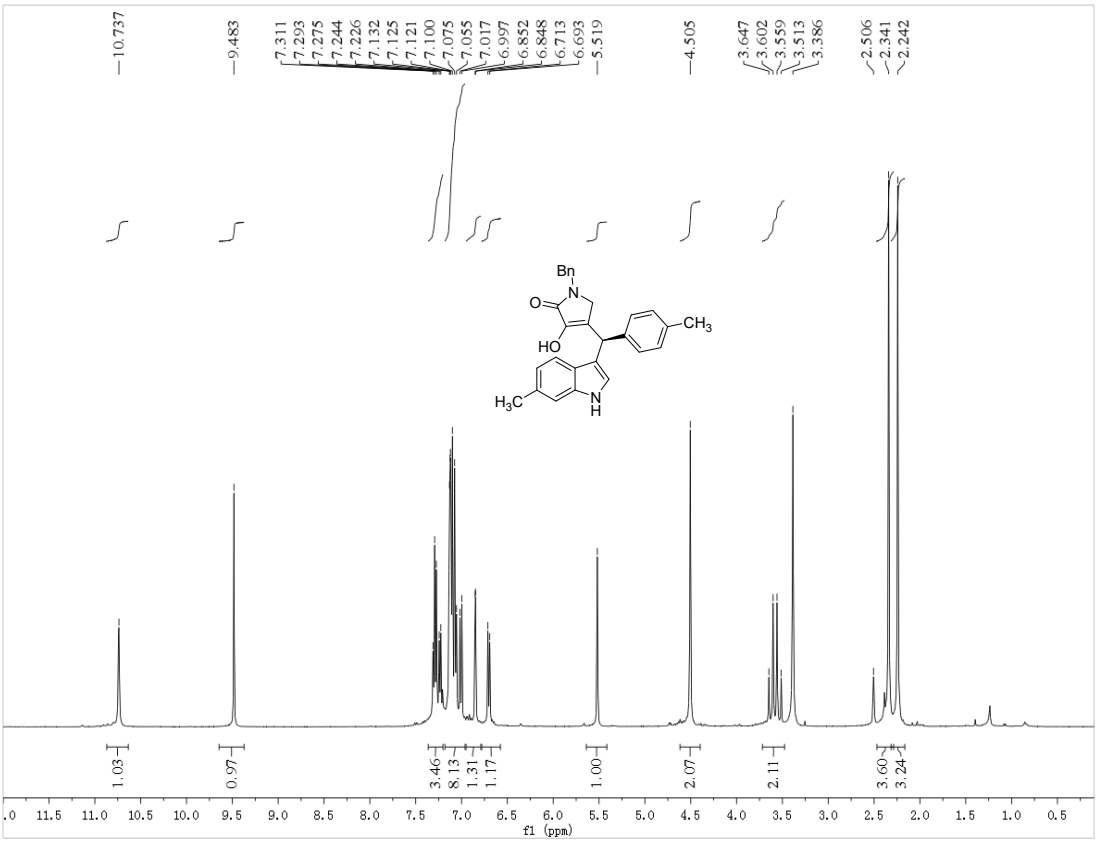


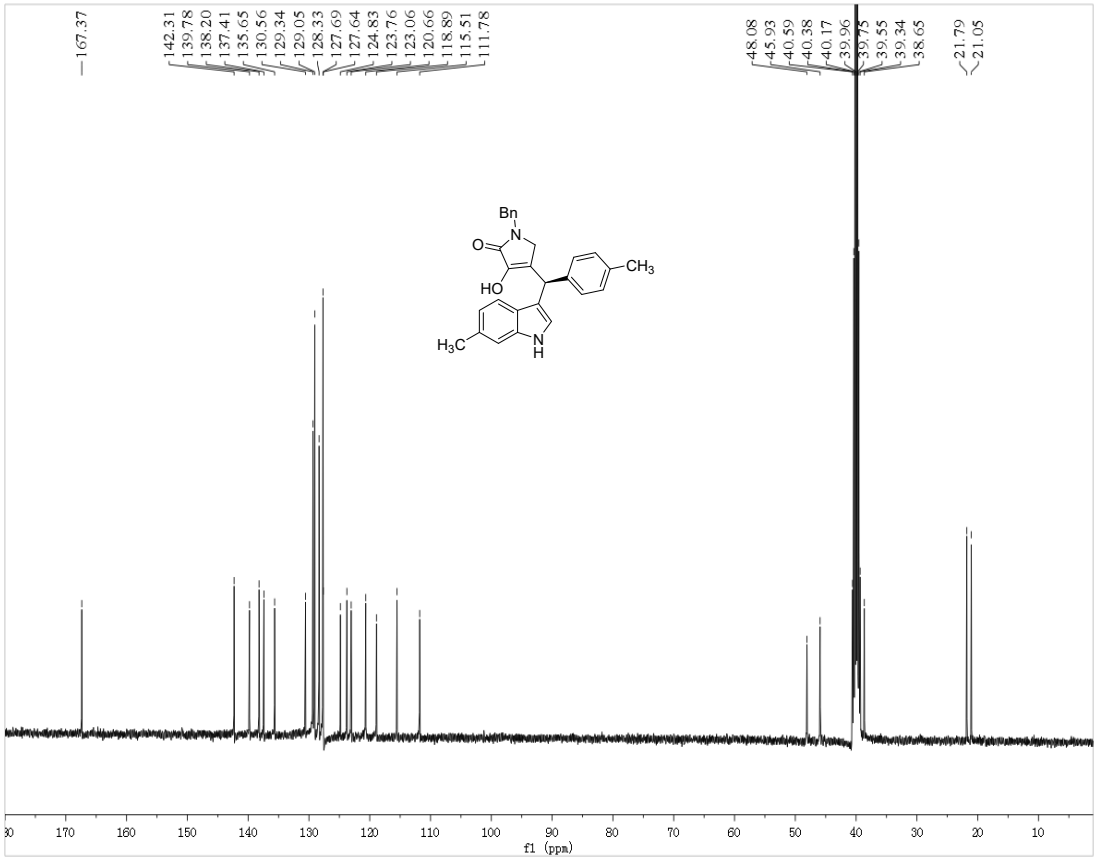
#	Time	Area	Height	Width	Area%	Symmetry
1	7.758	28070.4	1213.2	0.3856	49.482	0.494
2	15.607	28658	530.9	0.8997	50.518	0.364



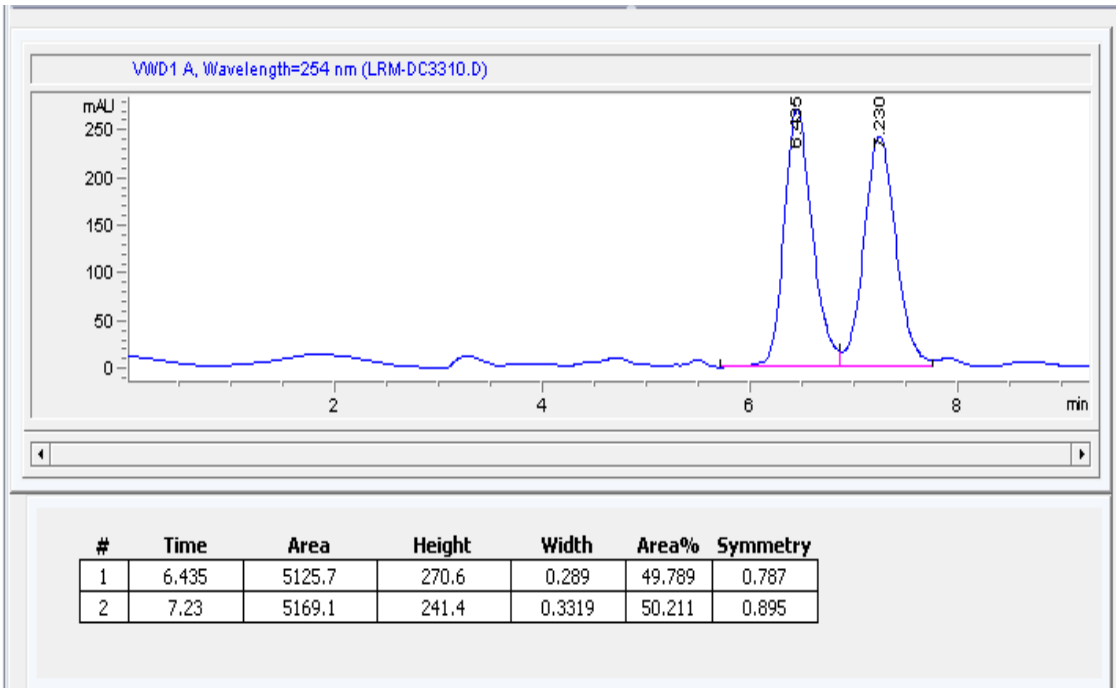
#	Time	Area	Height	Width	Area%	Symmetry
1	8.021	23984.9	955.9	0.3727	97.733	0.486
2	15.429	556.4	8.7	1.0649	2.267	0

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

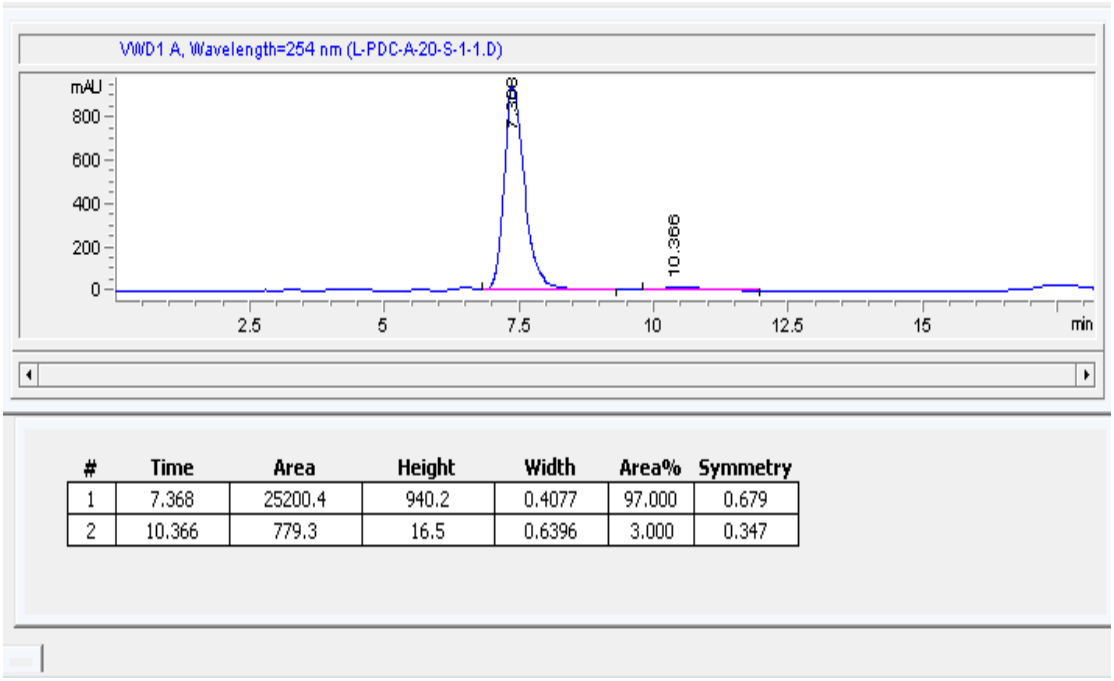




HPLC of 6p



#	Time	Area	Height	Width	Area%	Symmetry
1	6.435	5125.7	270.6	0.289	49.789	0.787
2	7.23	5169.1	241.4	0.3319	50.211	0.895



#	Time	Area	Height	Width	Area%	Symmetry
1	7.368	25200.4	940.2	0.4077	97.000	0.679
2	10.366	779.3	16.5	0.6396	3.000	0.347