Enantioselective Synthesis of Isoquinoline-1,3(2*H*,4*H*)-dione Derivatives via Chiral Phosphoric Acid Catalyzed aza-Friedel−Crafts Reaction

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Supporting Information

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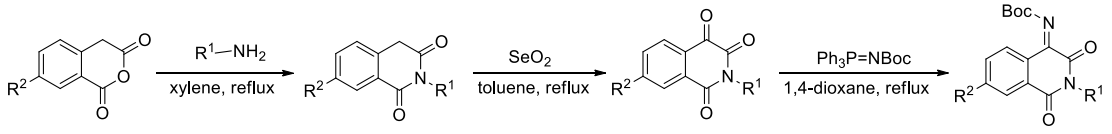
1. General Information

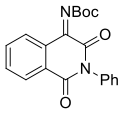
Reagents were purchased from commercial sources and were used as received unless mentioned otherwise. Reactions were monitored by TLC. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded in $CDCl_3$ and DMSO-d_6. ^{1}H NMR chemical shifts are reported in ppm relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard ($CDCl_3$ at 7.26 ppm, DMSO-d_6 at 2.50 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration. ^{13}C NMR chemical shifts are reported in ppm from tetramethylsilane (TMS) with the solvent resonance as the internal standard ($CDCl_3$ at 77.20 ppm, DMSO-d_6 at 39.51 ppm). The enantiomeric excesses were determined by chiral HPLC analysis. HPLC analysis was performed on Shimadzu SCL-10A*VP* HPLC systems consisting of the followings: pump, LC-10AD; detector, SPD-10A measured at 254 nm. HRMS was recorded on Bruker Q TOF. Optical rotations were measured with a Perkin-Elmer-341 polarimeter. Melting points were recorded on a Büchi Melting Point B-545.

2. General procedure for the synthesis of ketimines 1

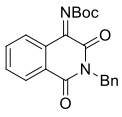


A mixture of homophthalic anhydride (1 equiv), amine (1.2 equiv) in dry xylene (0.5 M) was refluxed using a Dean–Stark apparatus for 6-10 h. After completion of the reaction, monitored by TLC, the solvent was evaporated. The residue was recrystallized with methanol to produce the homophthalimide.

To a solution of homophthalimide (1equiv) in toluene (0.2 M) was added SeO_2 (1.5 equiv), and then, the mixture was refluxed until the homophthalimide disappeared, monitored by TLC. The mixture was filtered through a Celite plug, and the filtrate was concentrated in vacuo. The residue and aza-Wittig reagent (1.5 equiv) were placed in an oven-dried Schlenk flask under argon atmosphere. After an injection of anhydrous 1,4-dioxane (0.2 M), the mixture was heated under reflux until complete disappearance of the starting materials. Then the reaction was cooled to room temperature. After an evaporation of the volatile organic solvents, the crude residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) and afforded the resulting ketimine as described below.

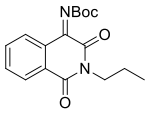


***tert*-butyl (1,3-dioxo-2-phenyl-2,3-dihydroisoquinolin-4(1*H*)-ylidene)carbamate (1a):** White solid; 46% yield; mp 228.7-230.5 ℃; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.29-8.21 (m, 1H), 8.21-8.12 (m, 1H), 7.94-7.82 (m, 2H), 7.59-7.41 (m, 3H), 7.41-7.29 (m, 2H), 1.50 (s, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 162.6, 160.2, 155.8, 146.5, 135.0, 134.2, 133.4, 131.4, 128.9, 128.7, 128.6, 128.5, 125.5, 82.0, 27.8; HRMS (ESI-TOF) calcd. for $C_{20}H_{18}N_2NaO_4$ $[M + Na]^+$ 373.1159; found: 373.1158.

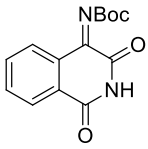


***tert*-butyl (2-benzyl-1,3-dioxo-2,3-dihydroisoquinolin-4(1*H*)-ylidene)carbamate (1b):** White solid; 35% yield; mp 166.8-168.5 ℃; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.27-8.08 (m, 2H), 7.95-7.77 (m, 2H), 7.44-7.15 (m, 5H), 5.07 (s, 2H), 1.53 (s, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 162.5, 160.1, 156.0, 146.3, 136.3, 134.2, 133.4, 131.3, 128.6,

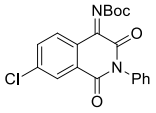
128.2, 128.1, 127.6, 127.1, 125.4, 82.0, 43.6, 27.8; HRMS (ESI-TOF) calcd. for $C_{21}H_{20}N_2NaO_4$ $[M + Na]^+$ 387.1315; found: 387.1316.



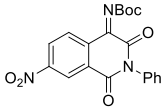
***tert*-butyl (1,3-dioxo-2-propyl-2,3-dihydroisoquinolin-4(1*H*)-ylidene)carbamate (1c):** White solid; 40% yield; mp 149.4-150.9 ℃; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.25-8.07 (m, 2H), 7.94-7.75 (m, 2H), 3.83 (t, *J* = 7.4 Hz, 2H), 1.65-1.50 (m, 11H), 0.89 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 162.4, 160.2, 155.8, 146.2, 134.0, 133.3, 131.1, 128.5, 128.3, 125.4, 81.9, 41.9, 27.8, 20.5, 11.3; HRMS (ESI-TOF) calcd. for $C_{17}H_{20}N_2NaO_4$ $[M + Na]^+$ 339.1315; found: 339.1311.



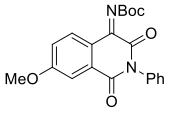
***tert*-butyl (1,3-dioxo-2,3-dihydroisoquinolin-4(1*H*)-ylidene)carbamate (1d)：** White solid; 31% yield; mp 225.7-227.5 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.72 (s, 1H), 8.42-8.16 (m, 2H), 7.92-7.64 (m, 2H), 1.63 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3, 160.7, 155.0, 146.2, 134.9, 133.8, 132.1, 129.2, 127.6, 127.1, 83.9, 28.2; HRMS (ESI-TOF) calcd. for $C_{14}H_{14}N_2NaO_4$ $[M + Na]^+$ 297.0846; found: 297.0855.



***tert*-butyl (7-chloro-1,3-dioxo-2-phenyl-2,3-dihydroisoquinolin-4(1*H*)-ylidene)carbamate (1e):** White solid; 18% yield; mp 226.5-228.3 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.37-8.17 (m, 2H), 7.75 (d, *J* = 8.5 Hz, 1H), 7.61-7.40 (m, 3H), 7.30-7.14 (m, 2H), 1.58 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.8, 160.4, 155.4, 145.2, 140.7, 134.9, 133.8, 129.9, 129.6, 129.5, 129.4, 128.5, 128.4, 84.0, 28.2; HRMS (ESI-TOF) calcd. for $C_{20}H_{17}ClN_2NaO_4$ $[M + Na]^+$ 407.0769; found: 407.0780.



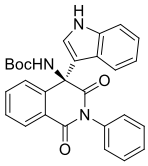
***tert*-butyl (7-nitro-1,3-dioxo-2-phenyl-2,3-dihydroisoquinolin-4(1*H*)-ylidene)carbamate (1f):** White solid; 21% yield; mp 225.0-226.3 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.10 (d, *J* = 2.2 Hz, 1H), 8.59 (dd, *J* = 8.7, 2.3 Hz, 1H), 8.53 (d, *J* = 8.6 Hz, 1H), 7.61-7.46 (m, 3H), 7.30-7.16 (m, 2H), 1.57 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.1, 159.9, 154.9, 151.0, 144.7, 136.2, 133.4, 129.7, 128.6, 128.2, 124.9, 84.7, 28.2; HRMS (ESI-TOF) calcd. for $C_{20}H_{17}N_3NaO_6$ $[M + Na]^+$ 418.1010; found: 418.1015.



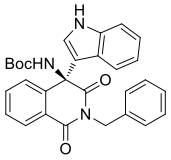
***tert*-butyl (7-methoxy-1,3-dioxo-2-phenyl-2,3-dihydroisoquinolin-4(1*H*)-ylidene)carbamate (1g):** White solid; 10% yield; mp 227.5-229.4 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.8 Hz, 1H), 7.72 (d, *J* = 2.7 Hz, 1H), 7.56-7.42 (m, 3H), 7.29 (dd, *J* = 8.8, 2.7 Hz, 1H), 7.25-7.17 (m, 2H), 3.95 (s, 3H), 1.58 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.1, 162.9, 161.0, 155.9, 145.3, 134.1, 130.0, 129.5, 129.2, 129.0, 128.4, 124.4, 122.3, 112.3, 83.3, 56.2, 28.2; HRMS (ESI-TOF) calcd. for $C_{21}H_{20}N_2NaO_5$ $[M + Na]^+$ 403.1264; found: 403.1259.

3. General procedure for the synthesis of compounds 3

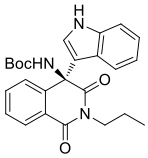
In an ordinary vial equipped with a magnetic stirring bar, the ketimines **1** (0.05 mmol, 1.0 equiv) were added to a solution of indoles **2** (0.055 mmol, 1.1 equiv or 0.1 mmol, 2.0 equiv) and catalyst **D** (2 mol %) in toluene (1.0 or 0.5 mL) at 60 ^{o}C. And then, the mixture was stirred at the same temperature for specified time. After completion of the reaction, as indicated by TLC, the products **3** were isolated by flash chromatography on silica gel (petroleum ether/ethyl acetate = 10/1～3/1).



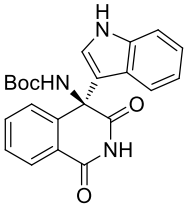
(*S*)-*tert*-butyl (4-(1*H*-indol-3-yl)-1,3-dioxo-2-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3aa): White solid; 22.7 mg, 97% yield; >99% ee; $[\alpha]_D^{20}$ = -50.8 (*c* 1.15, CH_2Cl_2); mp 235.2-237.0 ℃; The ee was determined by HPLC (Chiralpak AD-H, EtOH/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 8.3 min, t_{major} = 5.6 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.23 (s, 1H), 8.64 (br s , 1H), 8.16 (d, *J* = 7.8 Hz, 1H), 7.83 (br s , 1H), 7.77-7.51 (m, 3H), 7.48-7.28 (m, 4H), 7.11 (t, *J* = 7.2 Hz, 1H), 6.99 (t, *J* = 7.5 Hz, 1H), 6.87 (br s , 2H), 6.56 (d, *J* = 2.8 Hz, 1H), 1.40-1.04 (m, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.8, 163.6, 155.0, 143.4, 136.7, 135.8, 134.3, 128.9, 128.3, 128.2, 128.0, 127.5, 126.3, 125.5, 125.1, 124.4, 121.6, 120.7, 119.2, 113.6, 111.9, 79.0, 61.5, 28.0; HRMS (ESI-TOF) calcd. for $C_{28}H_{25}N_3NaO_4$ $[M + Na]^+$ 490.1737; found: 490.1727.



(*S*)-*tert*-butyl (2-benzyl-4-(1*H*-indol-3-yl)-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3ba): White solid; 23.3 mg, 97% yield; 98% ee; $[\alpha]_D^{20}$ = -48.4 (*c* 1.59, CH_2Cl_2); mp 145.0-146.9 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 4.5 min, t_{major} = 6.0 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.18 (s, 1H), 8.63 (br s , 1H), 8.12 (d, *J* = 6.9 Hz, 1H), 7.82-7.76 (m, 1H), 7.69-7.57 (m, 3H), 7.38 (d, *J* = 8.1 Hz, 1H), 7.13-6.96 (m, 7H), 6.39 (s, 1H), 5.04-4.90 (m, 2H), 1.35-0.82 (m, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 171.0, 163.2, 155.0, 143.3, 136.9, 136.7, 134.1, 128.1, 127.8, 127.4, 126.9, 126.7, 126.1, 125.4, 124.9, 124.5, 121.6, 120.9, 119.2, 113.7, 111.8, 79.0, 61.4, 43.2, 28.1; HRMS (ESI-TOF) calcd. for $C_{29}H_{27}N_3NaO_4$ $[M + Na]^+$ 504.1894; found: 504.1889.

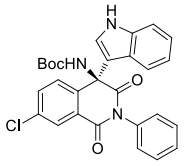


(*S*)-*tert*-butyl (4-(1*H*-indol-3-yl)-1,3-dioxo-2-propyl-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3ca): White solid; 21.2 mg, 98% yield; >99% ee; $[\alpha]_D^{20}$ = -59.0 (*c* 1.52, CH_2Cl_2); mp 229.2-231.0 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 4.3 min, t_{major} = 5.7 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.13 (s, 1H), 8.49 (br s , 1H), 8.15 (d, *J* = 7.7 Hz, 1H), 7.79-7.74 (m, 1H), 7.65-7.57 (m, 3H), 7.34 (d, *J* = 8.1 Hz, 1H), 7.08 (t, *J* = 7.3 Hz, 1H), 6.99 (t, *J* = 7.2 Hz, 1H), 6.37 (s, 1H), 3.88-3.55 (m, 2H), 1.38-1.23 (m, 9H), 0.98 (br s , 2H), 0.61 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.8, 163.4, 154.9, 143.2, 136.6, 133.9, 128.0, 127.3, 126.1, 125.3, 125.1, 124.4, 121.5, 120.9, 119.1, 113.9, 111.8, 78.8, 61.1, 41.5, 28.0, 20.6, 10.7; HRMS (ESI-TOF) calcd. for $C_{29}H_{27}N_3NaO_4$ $[M + Na]^+$ 456.1894; found: 456.1884.



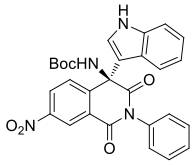
(*S*)-*tert*-butyl (4-(1*H*-indol-3-yl)-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3da):White solid; 19.3 mg, 99% yield; >99% ee; $[\alpha]_D^{20}$ = -107.9 (*c* 1.90, CH_2Cl_2); mp 179.2-180.8 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 7.4 min, t_{major} = 10.3 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.14 (s, 2H), 8.48 (s, 1H), 8.10 (d, *J* = 7.8 Hz, 1H), 7.87-7.71 (m, 1H), 7.71-7.48 (m, 3H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.99 (t, *J* = 7.5 Hz, 1H), 6.34 (s, 1H), 1.17 (d, *J* = 86.8 Hz, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 171.0, 164.2, 155.0, 144.5, 136.6, 134.0, 128.0, 126.7, 126.5, 125.3, 124.6, 121.6, 121.2, 119.0, 114.1, 111.8, 78.8, 60.8, 28.2, 27.5; HRMS (ESI-TOF) calcd. for $C_{22}H_{21}N_3NaO_4$ $[M + Na]^+$ 414.1424; found: 414.1426.

(*S*)-*tert*-butyl



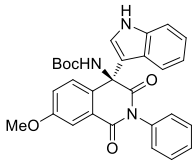
(7-chloro-4-(1*H*-indol-3-yl)-1,3-dioxo-2-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3ea): White solid; 24.6 mg, 98% yield; >99% ee; $[\alpha]_D^{20}$ = -92.1 (*c* 2.38, CH_2Cl_2); mp 174.8-176.5 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 4.9 min, t_{major} = 5.6 min); ^{1}H NMR (300 MHz, Chloroform-*d*) δ 11.28 (s, 1H), 8.49 (d, *J* = 146.1 Hz, 1H), 8.09 (s, 1H), 7.92 (d, *J* = 8.4 Hz, 1H), 7.74-7.53 (m, 2H), 7.43-7.25 (m, 4H), 7.11 (t, *J* = 7.6 Hz, 1H), 7.01 (t, *J* = 7.4 Hz, 1H), 6.87 (brs, 2H), 6.63 (s, 1H), 1.42-1.22 (m, 7H), 1.10 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.3, 162.4, 155.2, 142.2, 136.8, 135.5, 134.3, 133.0, 129.0, 128.7, 128.2, 126.7, 125.7, 124.3, 123.3, 121.7, 120.7, 119.3, 118.4, 113.1, 112.0, 79.3, 61.2, 28.0; HRMS (ESI-TOF) calcd. for $C_{28}H_{24}ClN_3NaO_4$ $[M + Na]^+$ 524.1348; found: 524.1345.

(*S*)-*tert*-butyl



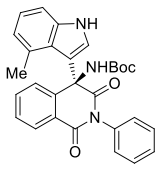
(4-(1*H*-indol-3-yl)-7-nitro-1,3-dioxo-2-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3fa): Yellow solid; 24.6 mg, 96% yield; >99% ee; $[\alpha]_D^{20}$ = -80.0 (*c* 1.17, CH_2Cl_2); mp 173.2-175.0 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 5.9 min, t_{major} = 6.6 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.37 (s, 1H), 8.93 (s, 1H), 8.84 (s, 1H), 8.80-8.62 (m, 1H), 7.97 (d, *J* = 8.7 Hz, 1H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.53-7.32 (m, 4H), 7.14 (t, *J* = 7.5 Hz, 1H), 7.05 (t, *J* = 7.6 Hz, 1H), 6.91 (brs, 2H), 6.73-6.55 (m, 1H), 1.45-1.04 (m, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.9, 162.0, 155.3, 149.5, 147.5, 136.8, 135.3, 129.1, 128.7, 128.4, 128.2, 126.2, 126.0, 124.3, 122.8, 121.9, 120.8, 119.5, 112.4, 112.0, 79.5, 61.7, 28.1; HRMS (ESI-TOF) calcd. for $C_{28}H_{24}N_4NaO_6$ $[M + Na]^+$ 535.1588; found: 535.1594.

(*S*)-*tert*-butyl



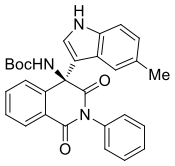
(4-(1*H*-indol-3-yl)-7-methoxy-1,3-dioxo-2-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3ga): White solid; 24.6 mg, 99% yield; >99% ee; $[\alpha]_D^{20}$ = -127.5 (*c* 1.24, CH_2Cl_2); mp 168.5-170.2 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 6.4 min, t_{major} = 7.4 min); ^{1}H NMR (300 MHz, Chloroform-*d*) δ 11.22 (s, 1H), 8.34 (d, *J* = 140.1 Hz, 1H), 7.70-7.47 (m, 3H), 7.45-7.16 (m, 5H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.98 (t, *J* = 7.5 Hz, 1H), 6.93-6.70 (m, 2H), 6.68-6.46 (m, 1H), 3.89 (s, 3H), 1.44-1.01 (m, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) ^{13}C NMR (75 MHz, DMSO) δ 170.8, 163.4, 158.8, 154.9, 136.8, 135.9, 128.9, 128.3, 128.1, 128.0, 126.1, 125.5, 124.4, 121.7, 121.6, 120.7, 119.1, 115.9, 114.0, 111.9, 110.2, 79.0, 61.0, 55.5, 28.0; HRMS (ESI-TOF) calcd. for $C_{29}H_{27}N_3NaO_5$ $[M + Na]^+$ 520.1843; found: 520.1840.

(*S*)-*tert*-butyl

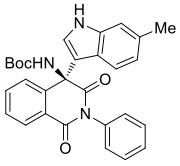


(4-(4-methyl-1*H*-indol-3-yl)-1,3-dioxo-2-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3ab): White solid; 20.9 mg, 87% yield; >99% ee; $[\alpha]_D^{20}$ = -20.7 (*c* 1.04, CH_2Cl_2); mp 183.8-185.4 ℃; The ee was determined by HPLC (Chiralpak AD-H, EtOH/hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 11.5 min, t_{major} = 14.9 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.19 (s, 1H), 8.59 (br s , 1H), 8.14 (d, *J* = 7.8 Hz, 1H), 7.83 (t, *J* = 7.5 Hz, 1H), 7.71-7.61 (m, 2H), 7.42-7.34 (m, 3H), 7.24 (d, *J* = 8.0 Hz, 1H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.88-6.82 (m, 3H), 6.23 (d, *J* = 2.3 Hz, 1H), 2.89 (s, 3H), 1.25 (s, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 171.4, 163.6, 154.0, 145.0, 138.1, 136.0, 134.5, 131.4,

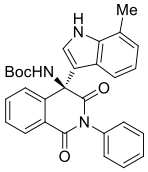
129.0, 128.4, 128.1, 127.1, 127.0, 126.9, 125.4, 124.1, 122.7, 121.8, 115.3, 109.8, 79.0, 61.7, 28.1, 23.2; HRMS (ESI-TOF) calcd. for $C_{29}H_{27}N_3NaO_4$ [M + Na]$^+$ 504.1894; found: 504.1895.



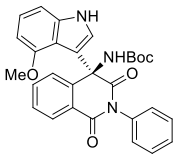
(*S*)-*tert*-butyl (4-(5-methyl-1*H*-indol-3-yl)-1,3-dioxo-2-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3ac): White solid; 23.8 mg, 99% yield; >99% ee; $[\alpha]_D^{20}$ = -118.3 (*c* 1.07, CH_2Cl_2); mp 165.9-167.6 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 4.9 min, t_{major} = 6.8 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.11 (s, 1H), 8.64 (br s , 1H), 8.17 (d, *J* = 7.6 Hz, 1H), 7.83 (br s , 1H), 7.77-7.57 (m, 2H), 7.57-7.33 (m, 4H), 7.29 (d, *J* = 8.3 Hz, 1H), 7.04-6.72 (m, 3H), 6.45 (br s , 1H), 2.33 (s, 3H), 1.45-0.97 (m, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.8, 163.6, 155.2, 143.5, 135.9, 135.2, 134.4, 129.0, 128.4, 128.2, 128.1, 127.6, 126.4, 125.6, 125.1, 124.7, 123.3, 120.4, 113.2, 111.7, 79.1, 61.5, 28.2, 21.5; HRMS (ESI-TOF) calcd. for $C_{29}H_{27}N_3NaO_4$ [M + Na]$^+$ 504.1894; found: 504.1889.



(*S*)-*tert*-butyl (4-(6-methyl-1*H*-indol-3-yl)-1,3-dioxo-2-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3ad): White solid; 23.6 mg, 98% yield; >99% ee; $[\alpha]_D^{20}$ = -70.0 (*c* 1.20, CH_2Cl_2); mp 166.5-168.2 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 5.3 min, t_{major} = 7.3 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.08 (s, 1H), 8.57 (br s , 1H), 8.16 (d, *J* = 7.8 Hz, 1H), 7.82 (br s , 1H), 7.76-7.56 (m, 2H), 7.54-7.31 (m, 4H), 7.18 (s, 1H), 7.02-6.74 (m, 3H), 6.50 (s, 1H), 2.36 (s, 3H), 1.44-1.00 (m, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.8, 163.6, 155.0, 143.4, 137.2, 135.8, 134.2, 130.8, 128.9, 128.3, 128.1, 128.0, 127.5, 126.3, 125.1, 124.8, 122.3, 121.0, 120.3, 113.5, 111.6, 79.0, 61.5, 28.0, 21.2; HRMS (ESI-TOF) calcd. for $C_{29}H_{27}N_3NaO_4$ [M + Na]$^+$ 504.1894; found: 504.1895.

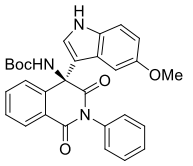


(*S*)-*tert*-butyl (4-(7-methyl-1*H*-indol-3-yl)-1,3-dioxo-2-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3ae): White solid; 23.8 mg, 99% yield; >99% ee; $[\alpha]_D^{20}$ = -43.6 (*c* 1.15, CH_2Cl_2); mp 176.7-178.5 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 5.6 min, t_{major} = 7.2 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.25 (s, 1H), 8.63 (s, 1H), 8.16 (d, *J* = 7.9 Hz, 1H), 7.82 (brs, 1H), 7.75-7.56 (m, 2H), 7.50-7.25 (m, 4H), 7.04-6.74 (m, 4H), 6.62 (s, 1H), 2.42 (s, 3H), 1.49-0.94 (m, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.9, 163.6, 155.1, 143.4, 136.2, 135.8, 134.3, 128.9, 128.3, 128.2, 128.1, 127.5, 126.4, 125.1, 125.0, 124.0, 122.1, 121.0, 119.4, 118.1, 114.1, 79.1, 61.4, 28.0, 16.7; HRMS (ESI-TOF) calcd. for $C_{29}H_{27}N_3NaO_4$ [M + Na]$^+$ 504.1894; found: 504.1896.

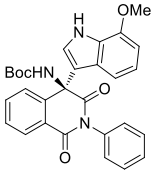


(*S*)-*tert*-butyl (4-(4-methoxy-1*H*-indol-3-yl)-1,3-dioxo-2-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3af): White solid; 24.6 mg, 99% yield; >99% ee; $[\alpha]_D^{20}$ = -38.1 (*c* 1.08, CH_2Cl_2); mp 173.7-175.3 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 21.2 min, t_{major} = 18.6 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.36 (d, *J* = 2.8 Hz, 1H), 8.44 (s, 1H), 8.12 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.63-7.31 (m, 7H), 7.12 (d, *J* = 7.0 Hz, 2H), 7.00 (d, *J* = 3.8 Hz, 2H), 6.41 (t, *J* = 4.4 Hz, 1H), 3.59 (s, 3H), 1.31 (s, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 172.5, 164.6, 155.1, 152.2, 144.1, 138.6, 136.4, 133.5, 128.9, 128.4, 128.0, 127.3, 127.2, 126.5,

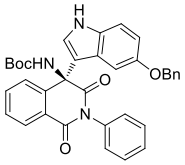
126.0, 124.0, 122.5, 114.7, 113.9, 105.4, 100.0, 79.3, 60.4, 54.9, 27.9; HRMS (ESI-TOF) calcd. for $C_{29}H_{27}N_3NaO_5$ [M + Na]$^+$ 520.1843; found: 520.1850.



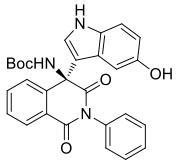
(*S*)-*tert*-butyl (4-(5-methoxy-1*H*-indol-3-yl)-1,3-dioxo-2-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3ag): White solid; 24.6 mg, 99% yield; >99% ee; $[\alpha]_D^{20}$ = -138.2 (*c* 1.24, CH_2Cl_2); mp 212.9-214.5 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 11.8 min, t_{major} = 29.5 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.12 (s, 1H), 8.60 (br s , 1H), 8.17 (d, *J* = 7.8 Hz, 1H), 7.83 (br s , 1H), 7.77-7.53 (m, 2H), 7.49-7.32 (m, 3H), 7.28 (d, *J* = 8.8 Hz, 1H), 7.09-6.80 (m, 3H), 6.77 (dd, *J* = 8.8, 2.5 Hz, 1H), 6.66-6.49 (m, 1H), 3.63 (s, 3H), 1.45-0.95 (m, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.8, 163.6, 155.0, 153.1, 143.3, 135.8, 134.3, 131.8, 128.9, 128.3, 128.1, 127.5, 126.4, 126.2, 125.2, 124.8, 112.8, 112.5, 111.3, 102.8, 79.1, 61.4, 55.2, 28.0; HRMS (ESI-TOF) calcd. for $C_{29}H_{27}N_3NaO_5$ [M + Na]$^+$ 520.1843; found: 520.1832.



(*S*)-*tert*-butyl (4-(7-methoxy-1*H*-indol-3-yl)-1,3-dioxo-2-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3ah): White solid; 23.4 mg, 94% yield; >99% ee; $[\alpha]_D^{20}$ = -45.4 (*c* 1.16, CH_2Cl_2); mp 170.8-172.4 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 7.2 min, t_{major} = 10.5 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.40 (s, 1H), 8.64 (s, 1H), 8.15 (d, *J* = 7.9 Hz, 1H), 7.82 (br s, 1H), 7.76-7.57 (m, 2H), 7.48-7.31 (m, 3H), 7.13 (d, *J* = 8.1 Hz, 1H), 7.02-6.74 (m, 3H), 6.67 (d, *J* = 7.7 Hz, 1H), 6.43 (s, 1H), 3.88 (s, 3H), 1.42-0.98 (m, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.8, 163.7, 155.2, 146.2, 143.4, 135.9, 134.4, 129.0, 128.3, 128.2, 127.6, 127.0, 126.4, 125.9, 125.2, 124.9, 119.9, 114.4, 113.4, 102.1, 79.1, 61.4, 55.2, 28.2; HRMS (ESI-TOF) calcd. for $C_{29}H_{27}N_3NaO_5$ [M + Na]$^+$ 520.1843; found: 520.1837.

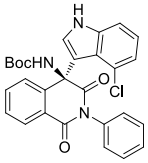


(*S*)-*tert*-butyl (4-(5-(benzyloxy)-1*H*-indol-3-yl)-1,3-dioxo-2-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3ai): White solid; 27.8 mg, 97% yield; >99% ee; $[\alpha]_D^{20}$ = -161.6 (*c* 1.31, CH_2Cl_2); mp 147.4-149.0 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 5.4 min, t_{major} = 7.7 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.09 (d, *J* = 46.7 Hz, 1H), 8.65 (s, 1H), 8.19 (d, *J* = 7.9 Hz, 1H), 8.02-7.52 (m, 3H), 7.52-7.24 (m, 9H), 7.25-7.02 (m, 1H), 7.00-6.70 (m, 3H), 6.67-6.49 (m, 1H), 5.11-4.76 (m, 2H), 1.61-0.93 (m, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.8, 163.6, 155.2, 152.2, 143.3, 137.4, 135.9, 134.4, 132.1, 129.0, 128.4, 128.3, 128.2, 127.8, 127.6, 127.1, 126.5, 125.7, 125.2, 124.9, 115.1, 113.0, 112.6, 111.9, 104.7, 79.1, 69.9, 61.4, 28.2; HRMS (ESI-TOF) calcd. for $C_{35}H_{31}N_3NaO_5$ [M + Na]$^+$ 596.2156; found: 596.2161.

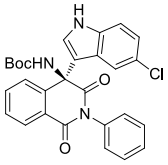


(*S*)-*tert*-butyl (4-(5-hydroxy-1*H*-indol-3-yl)-1,3-dioxo-2-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3aj): White solid; 23.4 mg, 97% yield; 99% ee; $[\alpha]_D^{20}$ = -132.9 (*c* 1.72, CH_2Cl_2); mp 190.3-191.0 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 6.9 min, t_{major} = 10.3 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.26-10.63 (m, 1H), 8.78 (s, 1H), 8.49 (br s , 1H), 8.24-8.03 (m, 1H), 7.90-7.73 (m, 1H), 7.73-7.49 (m, 2H), 7.49-7.32 (m, 3H),

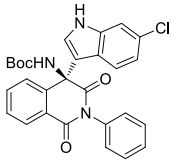
7.27-7.00 (m, 2H), 6.98-6.72 (m, 2H), 6.63 (dd, *J* = 8.7, 2.4 Hz, 1H), 6.35 (s, 1H), 1.44-1.22 (m, 7H), 1.09 (br s , 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.6, 163.5, 155.2, 150.6, 146.9, 143.5, 142.8, 135.9, 134.2, 131.2, 128.9, 128.3, 128.1, 128.0, 127.5, 126.2, 125.6, 125.2, 112.7, 112.2, 104.9, 79.0, 61.5, 27.9; HRMS (ESI-TOF) calcd. for $C_{28}H_{25}N_3NaO_5$ $[M + Na]^+$ 506.1686; found: 506.1695.



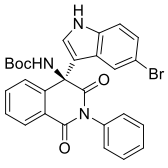
(*S*)-*tert*-butyl (4-(4-chloro-1*H*-indol-3-yl)-1,3-dioxo-2-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3ak): White solid; 16.8 mg, 37% yield; 98% ee; $[\alpha]_D^{20}$ = +9.7 (*c* 0.58, CH_2Cl_2); mp 169.1-170.9 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 27.4 min, t_{major} = 18.1 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.72 (d, *J* = 2.9 Hz, 1H), 8.23 (s, 1H), 8.07 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.70 (d, *J* = 2.8 Hz, 1H), 7.65-7.55 (m, 1H), 7.56-7.44 (m, 3H), 7.44-7.34 (m, 2H), 7.24 (d, *J* = 7.8 Hz, 1H), 7.17 (d, *J* = 7.2 Hz, 2H), 7.04 (t, *J* = 7.9 Hz, 1H), 6.91 (d, *J* = 7.5 Hz, 1H), 1.39-1.21 (m, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 171.4, 164.5, 154.4, 142.8, 139.0, 136.4, 133.7, 128.9, 128.4, 128.1, 127.7, 127.0, 126.4, 123.6, 122.2, 121.4, 120.7, 113.5, 111.2, 79.3, 60.5, 28.0; HRMS (ESI-TOF) calcd. for $C_{28}H_{24}ClN_3NaO_4$ $[M + Na]^+$ 524.1348; found: 524.1328.



(*S*)-*tert*-butyl (4-(5-chloro-1*H*-indol-3-yl)-1,3-dioxo-2-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3al): White solid; 24.8 mg, 99% yield; 99% ee; $[\alpha]_D^{20}$ = -103.0 (*c* 1.39, CH_2Cl_2); mp 205.7-207.3 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 4.7 min, t_{major} = 5.9 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.42 (s, 1H), 8.61 (d, *J* = 137.1 Hz, 1H), 8.16 (d, *J* = 7.6 Hz, 1H), 7.98-7.82 (m, 1H), 7.82-7.58 (m, 3H), 7.49-7.32 (m, 4H), 7.14 (dd, *J* = 8.7, 2.1 Hz, 1H), 6.87 (brs, 2H), 6.44 (d, *J* = 2.7 Hz, 1H), 1.41-0.99 (m, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.6, 163.4, 155.1, 143.0, 135.7, 135.3, 134.5, 129.0, 128.4, 128.3, 128.1, 127.7, 127.5, 126.2, 125.6, 125.1, 123.8, 121.7, 120.5, 113.6, 79.2, 61.2, 28.1; HRMS (ESI-TOF) calcd. for $C_{28}H_{24}ClN_3NaO_4$ $[M + Na]^+$ 524.1348; found: 524.1330.

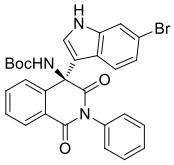


(*S*)-*tert*-butyl (4-(6-chloro-1*H*-indol-3-yl)-1,3-dioxo-2-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3am): White solid; 24.8 mg, 99% yield; >99% ee; $[\alpha]_D^{20}$ = -83.5 (*c* 1.34, CH_2Cl_2); mp 187.6-189.4 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 4.5 min, t_{major} = 6.6 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.32 (s, 1H), 8.71 (br s , 1H), 8.15 (d, *J* = 7.5 Hz, 1H), 7.99-7.78 (m, 1H), 7.78-7.53 (m, 3H), 7.53-7.20 (m, 4H), 7.06-6.85 (m, 1H), 6.86 (br s , 2H), 6.50 (d, *J* = 2.5 Hz, 1H), 1.45-0.95 (m, 9H); 13C NMR (75 MHz, DMSO-d_6) δ 170.7, 163.5, 155.1, 143.0, 137.3, 135.8, 134.5, 129.0, 128.4, 128.2, 128.1, 127.7, 126.8, 126.5, 126.3, 125.1, 123.3, 122.5, 119.6, 114.1, 111.5, 79.2, 61.3, 28.1; HRMS (ESI-TOF) calcd. for $C_{28}H_{24}ClN_3NaO_4$ $[M + Na]^+$ 524.1348; found: 524.1350.

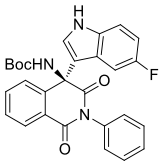


(*S*)-*tert*-butyl (4-(5-bromo-1*H*-indol-3-yl)-1,3-dioxo-2-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3an): White solid; 26.2 mg, 96% yield; >99% ee; $[\alpha]_D^{20}$ = -167.0 (*c* 1.32, CH_2Cl_2); mp 206.6-208.3 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 15/85, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} =

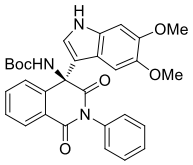
5.7 min, t_{major} = 7.7 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.42 (s, 1H), 8.62 (d, *J* = 136.4 Hz, 1H), 8.16 (d, *J* = 7.6 Hz, 1H), 8.02-7.77 (m, 2H), 7.76-7.60 (m, 2H), 7.48-7.32 (m, 4H), 7.29-7.18 (m, 1H), 6.88 (brs, 2H), 6.42 (d, *J* = 2.7 Hz, 1H), 1.50-0.94 (m, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.6, 163.4, 155.2, 153.2, 143.0, 135.7, 135.5, 134.5, 129.0, 128.4, 128.3, 128.2, 127.7, 127.3, 126.2, 125.1, 124.2, 123.5, 114.0, 113.4, 111.9, 79.2, 61.2, 28.1; HRMS (ESI-TOF) calcd. for $C_{28}H_{24}BrN_3NaO_4$ $[M + Na]^+$ 568.0842; found: 568.0848.



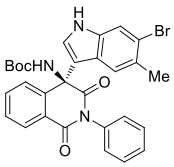
(*S*)-*tert*-butyl (4-(6-bromo-1*H*-indol-3-yl)-1,3-dioxo-2-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3ao): White solid; 27.0 mg, 99% yield; >99% ee; $[\alpha]_D^{20}$ = -84.6 (*c* 1.06, CH_2Cl_2); mp 180.7-182.6 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 4.6 min, t_{major} = 6.4 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.32 (s, 1H), 8.71 (br s , 1H), 8.15 (d, *J* = 7.7 Hz, 1H), 7.84 (br s , 1H), 7.77-7.50 (m, 4H), 7.48-7.28 (m, 3H), 7.22-7.08 (m, 1H), 6.86 (br s , 2H), 6.49 (d, *J* = 2.7 Hz, 1H), 1.48-0.90 (m, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.6, 163.5, 155.1, 143.0, 137.7, 135.8, 134.5, 129.0, 128.4, 128.3, 128.2, 127.7, 126.7, 126.3, 125.1, 123.6, 122.8, 122.2, 114.6, 114.5, 114.1, 79.2, 61.3, 28.1; HRMS (ESI-TOF) calcd. for $C_{28}H_{24}BrN_3NaO_4$ $[M + Na]^+$ 568.0842; found: 568.0845.



(*S*)-*tert*-butyl (4-(5-fluoro-1*H*-indol-3-yl)-1,3-dioxo-2-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3ap): White solid; 19.4 mg, 80% yield; 99% ee; $[\alpha]_D^{20}$ = -76.7 (*c* 1.00, CH_2Cl_2); mp 174.8-176.7 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 4.9 min, t_{major} = 6.2 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.33 (s, 1H), 8.72 (br s , 1H), 8.17 (d, *J* = 7.8 Hz, 1H), 7.96-7.78 (m, 1H), 7.78-7.58 (m, 2H), 7.48-7.27 (m, 5H), 7.04-6.94 (m, 1H), 6.94-6.61 (m, 2H), 6.50 (d, *J* = 2.8 Hz, 1H), 1.51-0.91 (m, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.6, 163.4, 158.2, 155.1, 143.0, 135.7, 134.4, 133.4, 129.0, 128.4, 128.3, 128.1, 127.7, 126.2, 125.1, 124.7 (d, *J* = 10.4 Hz, 1C), 113.7, 113.0 (d, *J* = 9.7 Hz, 1C), 110.0 (d, *J* = 26.1 Hz, 1C), 105.8 (d, *J* = 24.5 Hz, 1C), 79.1, 61.3, 28.1; HRMS (ESI-TOF) calcd. for $C_{28}H_{24}FN_3NaO_4$ $[M + Na]^+$ 508.1643; found: 508.1623.

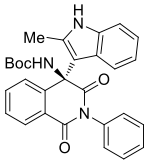


(*S*)-*tert*-butyl (4-(5,6-dimethoxy-1*H*-indol-3-yl)-1,3-dioxo-2-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3aq): White solid; 25.3 mg, 96% yield; >99% ee; $[\alpha]_D^{20}$ = -61.3 (*c* 1.45, CH_2Cl_2); mp 169.0-170.7 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 6.4 min, t_{major} = 15.3 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.95 (s, 1H), 8.54 (br s , 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 7.92-7.76 (m, 1H), 7.75-7.60 (m, 2H), 7.45-7.35 (m, 3H), 7.03-6.72 (m, 4H), 6.52-6.32 (m, 1H), 3.74 (s, 3H), 3.59 (s, 3H), 1.41-1.26 (m, 6H), 1.05 (br s , 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.9, 163.7, 155.2, 146.8, 144.2, 143.3, 135.8, 134.3, 131.3, 129.0, 128.3, 128.2, 127.6, 126.4, 125.2, 123.9, 117.3, 113.1, 103.2, 95.2, 79.1, 61.5, 55.9, 55.6, 28.2; HRMS (ESI-TOF) calcd. for $C_{30}H_{29}N_3NaO_6$ $[M + Na]^+$ 550.1949; found: 550.1954.



(*S*)-*tert*-butyl (4-(6-bromo-5-methyl-1*H*-indol-3-yl)-1,3-dioxo-2-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3ar): White solid; 23.2 mg, 83% yield; >99% ee;

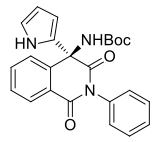
$[\alpha]_D^{20}$ = -92.5 (*c* 1.16, CH_2Cl_2); mp 173.5-175.3 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 4.6 min, t_{major} = 5.9 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.21 (s, 1H), 8.50 (d, *J* = 137.8 Hz, 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 7.97-7.77 (m, 1H), 7.76-7.49 (m, 4H), 7.48-7.31 (m, 3H), 7.00-6.71 (m, 2H), 6.43 (s, 1H), 2.36 (s, 3H), 1.42-1.21 (m, 6H), 1.05 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.6, 163.5, 155.1, 143.1, 136.2, 135.7, 134.4, 129.0, 128.7, 128.4, 128.1, 127.6, 126.9, 126.7, 126.3, 125.0, 124.2, 122.3, 117.7, 115.0, 113.3, 79.2, 61.3, 28.1, 23.1; HRMS (ESI-TOF) calcd. for $C_{29}H_{26}BrN_3NaO_4$ [M + Na]$^+$ 582.0999; found: 582.0990.



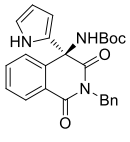
(*S*)-*tert*-butyl (4-(2-methyl-1*H*-indol-3-yl)-1,3-dioxo-2-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (3as): White solid; 23.6 mg, 98% yield; 99% ee; $[\alpha]_D^{20}$ = -23.5 (*c* 2.52, CH_2Cl_2); mp 160.5-162.3 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 4.5 min, t_{major} = 6.6 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.21 (s, 1H), 8.70 (s, 1H), 8.18 (d, *J* = 7.7 Hz, 1H), 7.95-7.73 (m, 2H), 7.68 (brs, 1H), 7.47-7.30 (m, 3H), 7.25 (d, *J* = 8.0 Hz, 1H), 7.03-6.93 (m, 1H), 6.89 (brs, 2H), 6.81-6.65 (m, 2H), 1.94 (s, 3H), 1.42-0.98 (m, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.5, 163.6, 154.9, 143.7, 135.9, 135.6, 135.0, 134.7, 134.5, 128.9, 128.5, 128.4, 128.0, 127.4, 126.3, 125.9, 120.4, 119.9, 118.8, 110.6, 106.5, 79.0, 61.8, 28.0, 13.2; HRMS (ESI-TOF) calcd. for $C_{29}H_{27}N_3NaO_4$ [M + Na]$^+$ 504.1894; found: 504.1903.

4. General procedure for the synthesis of compounds 5

In an ordinary vial equipped with a magnetic stirring bar, the ketimines **1** (0.05 mmol, 1.0 equiv) were added to a solution of pyrrole **4** (0.1 mmol, 2.0 equiv) and catalyst **D** (2 mol %) in toluene (0.5 mL) at 60 ^{o}C. And then, the mixture was stirred at the same temperature for specified time. After completion of the reaction, as indicated by TLC, the products **5** were isolated by flash chromatography on silica gel (petroleum ether/ethyl acetate = 10/1～3/1).

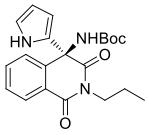


(*R*)-*tert*-butyl (1,3-dioxo-2-phenyl-4-(1*H*-pyrrol-2-yl)-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (5a): White solid; 20.5 mg, 98% yield; 93% ee; $[\alpha]_D^{20}$ = -14.5 (*c* 1.15, CH_2Cl_2); mp 102.7-104.2 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 5.4 min, t_{major} = 6.7 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.92 (s, 1H), 8.42 (d, *J* = 136.8 Hz, 1H), 8.10 (d, *J* = 7.7 Hz, 1H), 7.92-7.76 (m, 1H), 7.75-7.67 (m, 1H), 7.66-7.55 (m, 1H), 7.54-7.31 (m, 3H), 6.99 (d, *J* = 7.3 Hz, 2H), 6.75 (s, 1H), 5.89 (s, 1H), 5.53-5.25 (m, 1H), 1.43-0.95 (m, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 171.0, 163.4, 155.1, 142.4, 135.8, 134.4, 129.1, 128.5, 128.3, 127.8, 127.6, 126.2, 124.8, 120.6, 108.5, 107.4, 79.3, 61.1, 28.1; HRMS (ESI-TOF) calcd. for $C_{24}H_{23}N_3NaO_4$ [M + Na]$^+$ 440.1586; found: 440.1583.

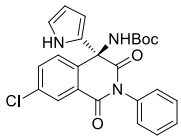


(*R*)-*tert*-butyl (2-benzyl-1,3-dioxo-4-(1*H*-pyrrol-2-yl)-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (5b): White solid; 21.4 mg, 99% yield; 88% ee; $[\alpha]_D^{20}$ = -5.7 (*c* 1.48, CH_2Cl_2); mp 114.9-116.5 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 4.5 min, t_{major} = 5.4 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.91 (d, *J* = 17.8 Hz, 1H), 8.40 (d, *J* = 147.6 Hz, 1H), 8.07 (d, *J* = 7.7 Hz, 1H), 7.77

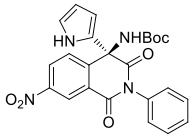
(t, *J* = 7.2 Hz, 1H), 7.68 (d, *J* = 7.7 Hz, 1H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.23-6.96 (m, 5H), 6.73 (s, 1H), 5.83 (s, 1H), 5.27-5.09 (m, 1H), 5.09-4.93 (m, 2H), 1.39-1.22 (m, 7H), 0.79 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 171.4, 163.1, 155.1, 142.3, 136.9, 134.1, 128.2, 128.1, 127.6, 127.5, 126.7, 126.5, 126.0, 124.6, 120.5, 108.8, 107.1, 79.2, 60.8, 43.2, 28.0; HRMS (ESI-TOF) calcd. for $C_{25}H_{25}N_3NaO_4$ [M + Na]$^+$ 454.1743; found: 454.1738.



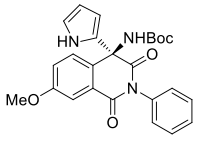
(*R*)-*tert*-butyl (1,3-dioxo-2-propyl-4-(1*H*-pyrrol-2-yl)-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (5c): White solid; 18.2 mg, 95% yield; 90% ee; $[\alpha]_D^{20}$ = -28.2 (*c* 0.91, CH_2Cl_2); mp 203.2-205.0 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 4.3 min, t_{major} = 4.8 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.86 (s, 1H), 8.51 (s, 1H), 8.09 (d, *J* = 7.8 Hz, 1H), 7.73 (t, *J* = 7.4 Hz, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 6.69 (s, 1H), 5.79 (s, 1H), 5.14 (d, *J* = 34.2 Hz, 1H), 3.90-3.67 (m, 2H), 1.52-1.37 (m, 2H), 1.28 (s, 7H), 0.92 (s, 2H), 0.77-0.61 (m, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 171.2, 163.3, 155.0, 142.2, 133.9, 128.1, 127.7, 127.5, 126.0, 124.8, 120.4, 108.4, 107.1, 79.1, 60.4, 41.5, 28.1, 20.6, 10.8; HRMS (ESI-TOF) calcd. for $C_{21}H_{25}N_3NaO_4$ [M + Na]$^+$ 406.1743; found: 406.1757.



(*R*)-*tert*-butyl (7-chloro-1,3-dioxo-2-phenyl-4-(1*H*-pyrrol-2-yl)-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (5d): White solid; 22.3 mg, 99% yield; 93% ee; $[\alpha]_D^{20}$ = -33.3 (*c* 1.13, CH_2Cl_2); mp 124.4-126.0 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 3/97, flow rate 0.8 mL/min, λ = 254 nm, t_{minor} = 18.6 min, t_{major} = 20.3 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.95 (s, 1H), 8.48 (d, *J* = 141.9 Hz, 1H), 8.05 (s, 1H), 7.89 (d, *J* = 8.6 Hz, 1H), 7.71 (d, *J* = 8.6 Hz, 1H), 7.55-7.39 (m, 3H), 6.99 (d, *J* = 7.4 Hz, 2H), 6.76 (s, 1H), 5.91 (s, 1H), 5.48 (s, 1H), 1.31 (s, 7H), 1.06 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.5, 162.3, 155.1, 141.2, 135.5, 134.2, 133.1, 129.1, 128.6, 128.4, 128.3, 126.9, 126.5, 120.7, 108.6, 107.5, 79.5, 60.8, 28.0; HRMS (ESI-TOF) calcd. for $C_{24}H_{22}ClN_3NaO_4$ [M + Na]$^+$ 474.1197; found: 474.1206.



(*R*)-*tert*-butyl (7-nitro-1,3-dioxo-2-phenyl-4-(1*H*-pyrrol-2-yl)-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (5e): White solid; 18.9 mg, 82% yield; 97% ee; $[\alpha]_D^{20}$ = -38.8 (*c* 0.89, CH_2Cl_2); mp 125.8-127.5 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 18.2 min, t_{major} = 21.8 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.03 (s, 1H), 8.90 (s, 1H), 8.76 (s, 1H), 8.63 (d, *J* = 7.5 Hz, 1H), 7.97 (d, *J* = 8.9 Hz, 1H), 7.58-7.39 (m, 3H), 7.03 (d, *J* = 7.3 Hz, 2H), 6.78 (s, 1H), 5.92 (s, 1H), 5.56 (s, 1H), 1.32 (s, 7H), 1.05 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.2, 161.8, 155.3, 148.4, 147.4, 135.2, 129.2, 128.6, 128.3, 128.2, 126.1, 125.9, 122.8, 120.9, 108.8, 107.6, 79.8, 61.2, 28.0; HRMS (ESI-TOF) calcd. for $C_{24}H_{22}N_4NaO_6$ [M + Na]$^+$ 485.1437; found: 485.1458.



(*R*)-*tert*-butyl (7-methoxy-1,3-dioxo-2-phenyl-4-(1*H*-pyrrol-2-yl)-1,2,3,4-tetrahydroisoquinolin-4-yl)carbamate (5f): White solid; 14.5 mg, 65% yield; 86% ee; $[\alpha]_D^{20}$ = -18.5 (*c* 0.72, CH_2Cl_2); mp 116.8-118.3 ℃; The ee was determined by HPLC (Chiralpak IA, EtOH/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 10.7 min, t_{major} = 11.5 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.88 (s, 1H), 8.57 (s, 1H), 7.60 (d, *J* = 8.6 Hz, 1H),

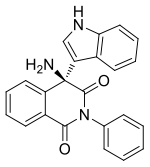
7.57-7.27 (m, 5H), 6.97 (d, J = 7.3 Hz, 2H), 6.73 (s, 1H), 5.88 (s, 1H), 5.39 (brs, 1H), 3.87 (s, 3H), 1.45-0.92 (m, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 171.0, 163.2, 158.8, 154.9, 135.8, 134.5, 129.0, 128.4, 128.2, 127.9, 125.8, 121.6, 120.4, 110.4, 108.4, 107.3, 79.1, 60.6, 55.5, 28.0; HRMS (ESI-TOF) calcd. for $C_{25}H_{25}N_3NaO_5$ $[M + Na]^+$ 470.1692; found: 470.1691.

5. Procedure for the Scale-up Experiment

In a 100 mL dry round bottom flask equipped with a magnetic stirring bar, the ketimines **1** (2.80 mmol, 1.0 equiv) were added to a solution of indoles **2** (3.08 mmol, 1.1 equiv) and catalyst **D** (1 mol %) in toluene (56 mL) at 60 ^{o}C. And then, the mixture was stirred at the same temperature for 96 h. After completion of the reaction, as indicated by TLC, the toluene were evaporated under vacuum, and the residues were isolated by flash chromatography on silica gel (petroleum ether/ethyl acetate = 10/1～3/1) to obtain product **3aa** as a white solid; 1.22 g, 94% yield, >99 ee.

6. Procedure for the deprotection of 3aa to prepare primary amine 6

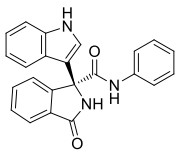
To a suspension of compound **3aa** (0.25 mmol, 1.0 equiv, >99 ee) in ethyl acetate (5 mL) was added concentrated hydrochloric acid (0.5 mL) at room temperature and the mixture was stirred at room temperature for 5 h, after which the mixture was quenched with $NaHCO_3$ (sat.) solution and adjusted the pH to 9. The mixture was extracted with EtOAc (5 mL×2). The combined organic layers were washed with brine and dried over Na_2SO_4. After filtered, it was concentrated under vacuum and the residues were isolated by flash chromatography on silica gel (petroleum ether/ethyl acetate = 5/1~1/1) to obtain product **6**.



(*S*)-4-amino-4-(1*H*-indol-3-yl)-2-phenylisoquinoline-1,3(2*H*,4*H*)-dione (6): White solid; 79.5 mg, 87% yield; 99% ee; $[\alpha]_D^{20}$ = +137.1 (*c* 1.04, CH_2Cl_2); mp 173.6-175.3 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 11.0 min, t_{major} = 9.1 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.18 (s, 1H), 8.15 (d, J = 7.7 Hz, 1H), 7.77 (d, J = 7.8 Hz, 1H), 7.69 (t, J = 7.5 Hz, 1H), 7.55 (t, J = 7.5 Hz, 1H), 7.51-7.34 (m, 4H), 7.32-7.21 (m, 2H), 7.14 (d, J = 7.1 Hz, 2H), 7.06 (t, J = 7.5 Hz, 1H), 6.92 (t, J = 7.5 Hz, 1H), 3.42 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 176.1, 164.0, 143.9, 136.8, 136.0, 134.0, 129.0, 128.6, 128.3, 128.2, 128.0, 127.5, 124.4, 124.1, 123.8, 121.3, 119.1, 119.0, 118.6, 112.0, 59.7; HRMS (ESI-TOF) calcd. for $C_{23}H_{17}N_3NaO_2$ $[M + Na]^+$ 390.1213; found: 390.1233.

7. Procedure for the synthesis of isoindolinone derivative 7

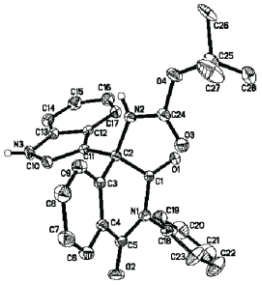
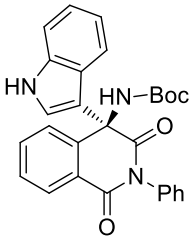
To a suspension of compound **3aa** (0.1 mmol, 1.0 equiv, >99 ee) in MeOH/DMSO (4 mL, v/v = 1:1) was added KOH (1 mmol, 10 equiv) at room temperature and the mixture was stirred at 65 ^{o}C for 0.5 h, after which the mixture was cooled to room temperature, quenched with H_2O (5 mL), extracted with EtOAc (5 mL×2). The combined organic layers were washed with brine and dried over Na_2SO_4. After filtered, it was concentrated under vacuum and the residues were isolated by flash chromatography on silica gel (petroleum ether/ethyl acetate = 3/1~1/1) to obtain product **7**.



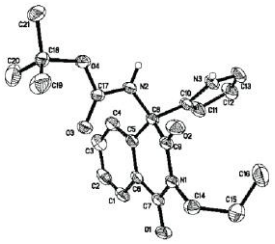
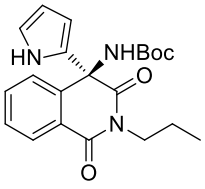
(*S*)-1-(1*H*-indol-3-yl)-3-oxo-*N*-phenylisoindoline-1-carboxamide (7): White solid; 30.8 mg, 84% yield; >99% ee; $[\alpha]_D^{20}$ = +77.4 (*c* 0.86, $CHCl_3$); mp 263.9-265.6 ℃; The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 36.9 min, t_{major} = 32.0 min);

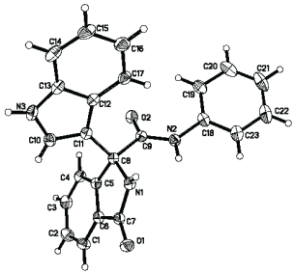
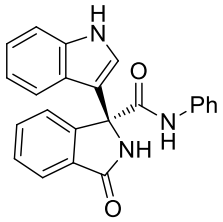
^{1}H NMR (300 MHz, DMSO-d_6) δ 11.20 (s, 1H), 9.76 (s, 1H), 9.25 (s, 1H), 7.85 (d, *J* = 7.2 Hz, 1H), 7.78 (d, *J* = 7.5 Hz, 1H), 7.68-7.53 (m, 4H), 7.40 (d, *J* = 8.8 Hz, 1H), 7.32 (t, *J* = 7.9 Hz, 2H), 7.24 (d, *J* = 2.6 Hz, 1H), 7.15-6.99 (m, 3H), 6.89 (t, *J* = 7.5 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 168.9, 168.3, 146.7, 138.2, 136.6, 132.1, 131.0, 129.0, 128.7, 125.0, 124.8, 124.4, 124.2, 122.9, 121.4, 120.5, 119.1, 118.8, 112.8, 111.9, 67.6; HRMS (ESI-TOF) calcd. for $C_{23}H_{17}N_3NaO_2$ $[M + Na]^+$ 390.1213; found: 390.1206.

8. X-ray crystal data for compound 3aa, 5c and 7.

	 **3aa**
Identification code	**3aa**
Empirical formula	$C_{28}H_{25}N_3O_4$
Formula weight	467.51
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1$
a/Å	8.0685(2)
b/Å	18.8284(6)
c/Å	8.1393(2)
α/°	90
β/°	95.576(2)
γ/°	90
Volume/Å^3	1230.64(6)
Z	2
ρ_{calc}g/cm^3	1.262
μ/mm^{-1}	0.694
F(000)	492.0
Crystal size/mm^3	0.2 ×0.16 ×0.15
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/ °	9.394 to 134.15
Index ranges	-9 ≤ h ≤ 9, -22 ≤ k ≤ 22, -9 ≤ l ≤ 6
Reflections collected	10206
Independent reflections	4407 [R_{int} = 0.0206, R_{sigma} = 0.0257]
Data/restraints/parameters	4407/4/341
Goodness-of-fit on F^2	1.029
Final R indexes [I>=2σ (I)]	R_1 = 0.0345, wR_2 = 0.0902
Final R indexes [all data]	R_1 = 0.0365, wR_2 = 0.0924
Largest diff. peak/hole / e Å^{-3}	0.14/-0.13

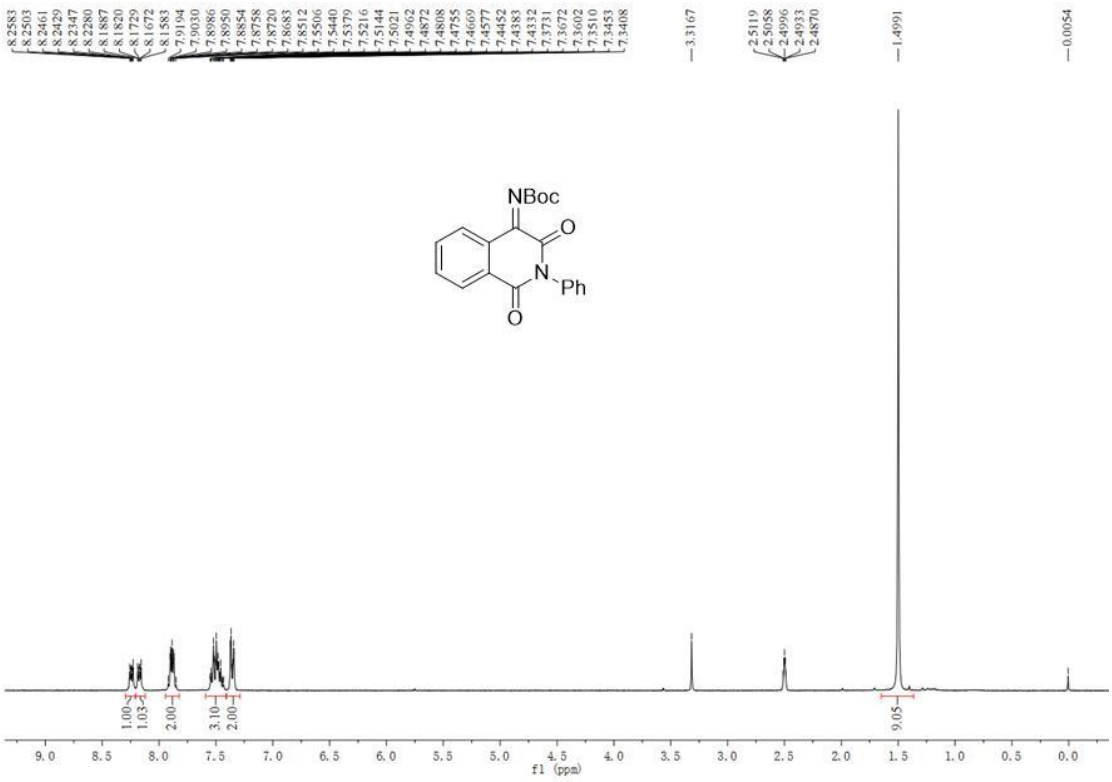
Flack parameter	0.09(10)

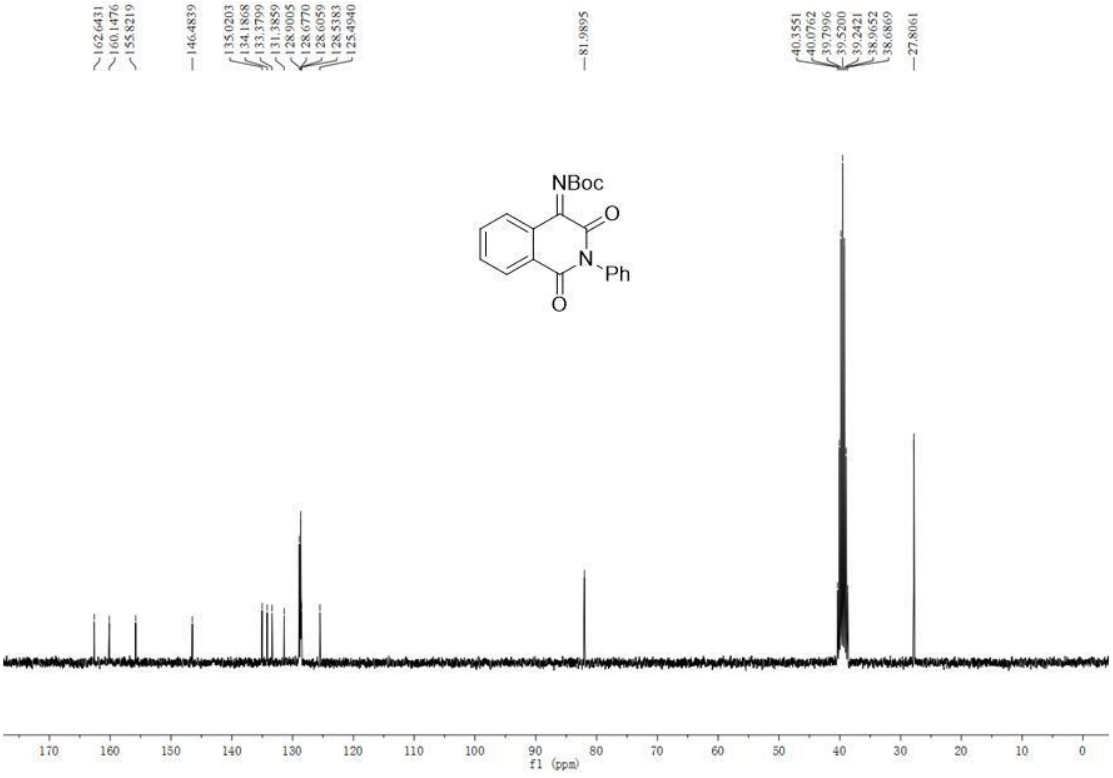
	 **5c**
Identification code	**5c**
Empirical formula	$C_{21}H_{25}N_3O_4$
Formula weight	383.44
Temperature/K	293(2)
Crystal system	tetragonal
Space group	$P4_12_12$
a/Å	10.81497(10)
b/Å	10.81497(10)
c/Å	37.0777(4)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	4336.74(9)
Z	8
ρ_{calc}g/cm^3	1.175
μ/mm^{-1}	0.671
F(000)	1632.0
Crystal size/mm^3	0.16 ×0.13 ×0.11
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.516 to 141.784
Index ranges	$-13 \leq h \leq 12$, $-13 \leq k \leq 9$, $-44 \leq l \leq 38$
Reflections collected	18060
Independent reflections	4153 [R_{int} = 0.0302, R_{sigma} = 0.0207]
Data/restraints/parameters	4153/5/276
Goodness-of-fit on F^2	1.043
Final R indexes [I>=2σ (I)]	R_1 = 0.0423, wR_2 = 0.1131
Final R indexes [all data]	R_1 = 0.0471, wR_2 = 0.1178
Largest diff. peak/hole / e Å^{-3}	0.12/-0.20
Flack parameter	-0.20(11)

	 **7**
Identification code	**7**
Empirical formula	$C_{23}H_{17}N_3O_2$
Formula weight	367.39
Temperature/K	293(2)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	8.05116(14)
b/Å	10.41903(19)
c/Å	21.8099(4)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	1829.53(6)
Z	4
ρ_{calc}g/cm^3	1.334
μ/mm^{-1}	0.701
F(000)	768.0
Crystal size/mm^3	0.15 ×0.12 ×0.09
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.108 to 141.838
Index ranges	$-9 \le h \le 9$, $-12 \le k \le 7$, $-25 \le l \le 26$
Reflections collected	13473
Independent reflections	3496 [R_{int} = 0.0393, R_{sigma} = 0.0296]
Data/restraints/parameters	3496/0/265
Goodness-of-fit on F^2	1.032
Final R indexes [I>=2σ (I)]	R_1 = 0.0378, wR_2 = 0.0993
Final R indexes [all data]	R_1 = 0.0410, wR_2 = 0.1033
Largest diff. peak/hole / e Å^{-3}	0.16/-0.17
Flack parameter	-0.06(13)

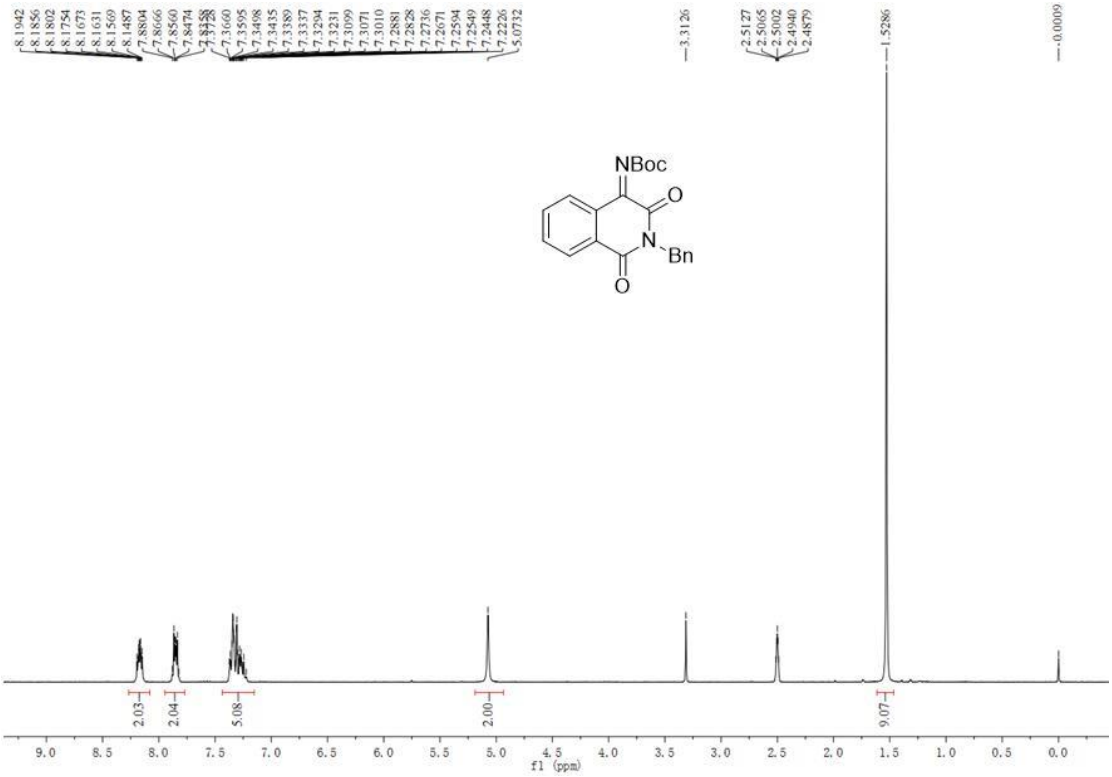
9. The copies of ^{1}H NMR, ^{13}C NMR for ketimines 1

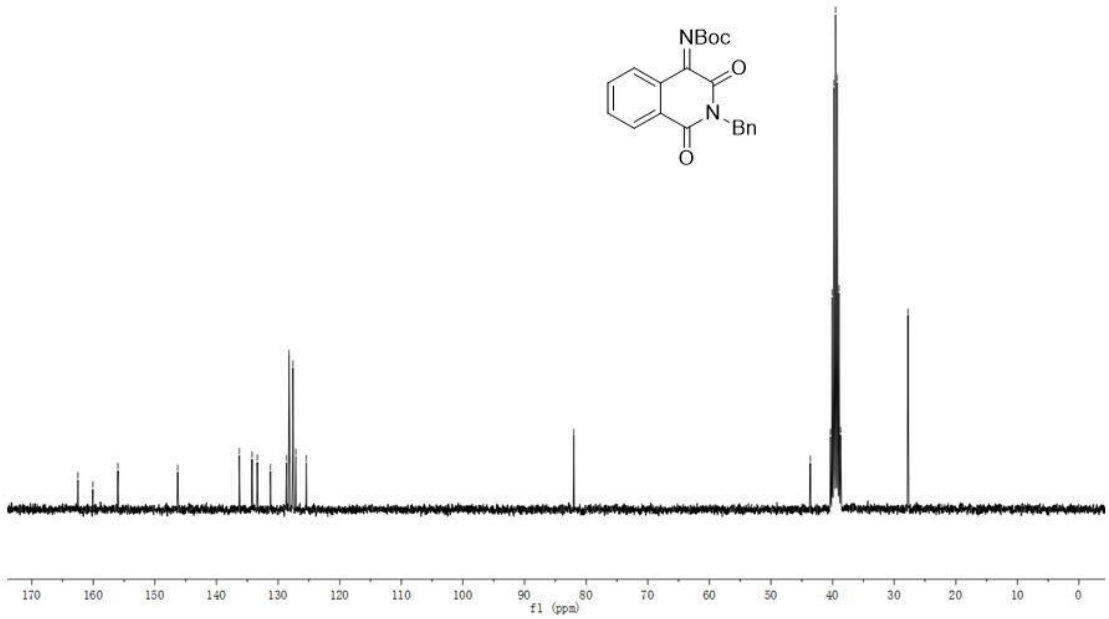
^{1}H NMR, ^{13}C NMR of 1a


NBoc
O
N
Ph
O
1.00
1.03
2.00
3.10
2.00
9.05
f1 (ppm)

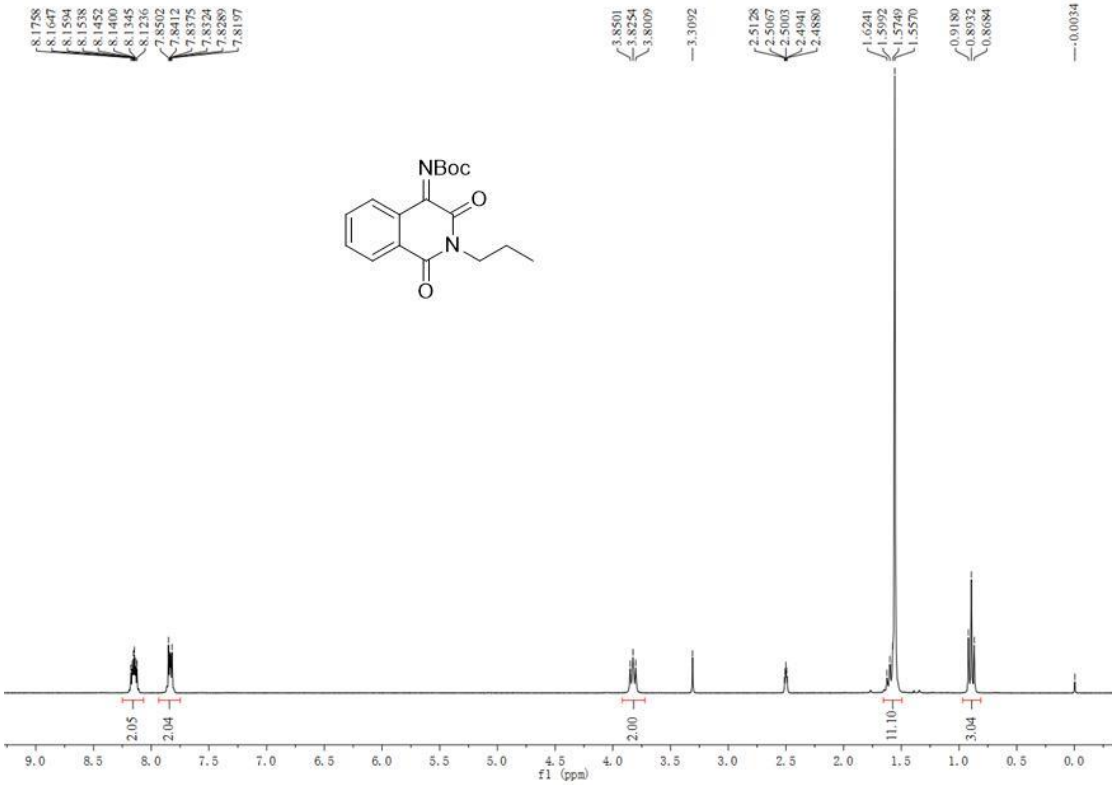

NBoc
O
N
Ph
O
f1 (ppm)

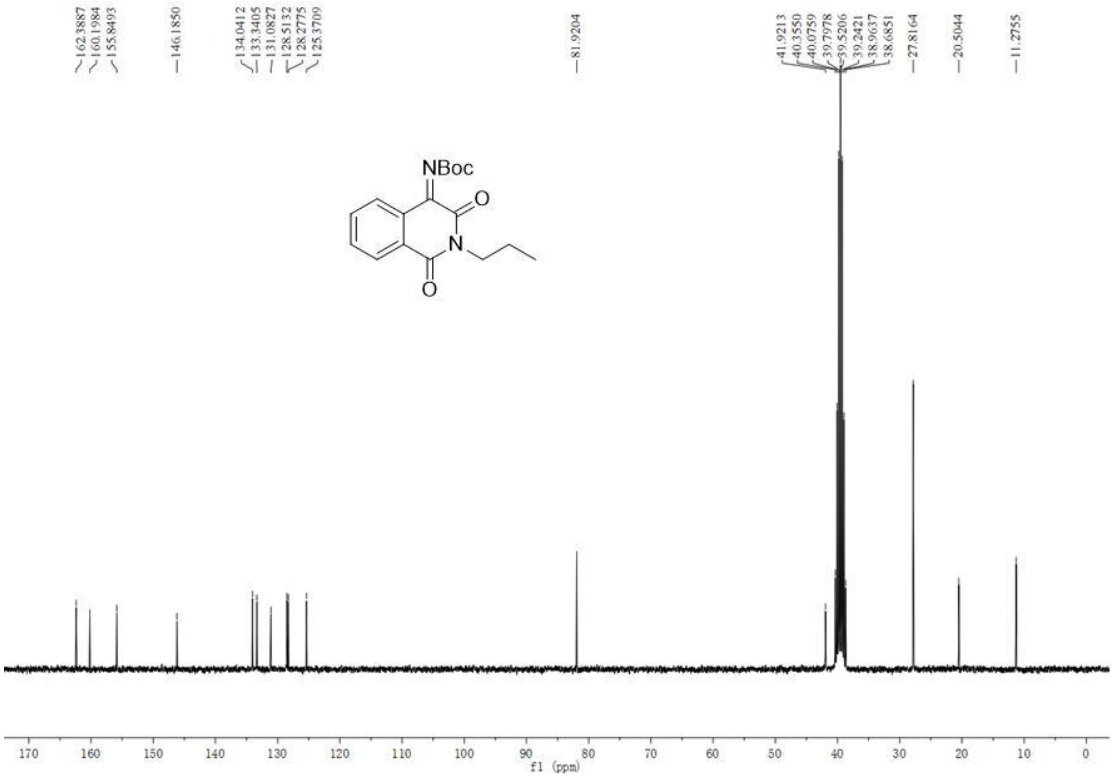
^{1}H NMR, ^{13}C NMR of 1b



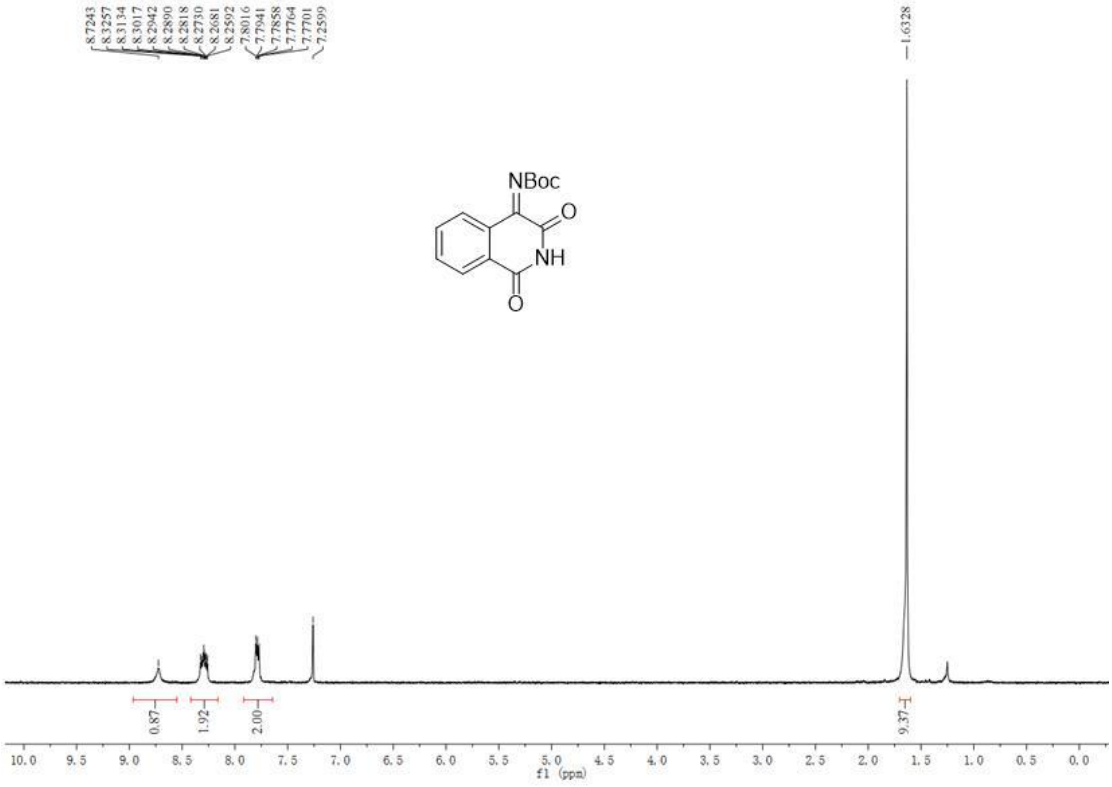


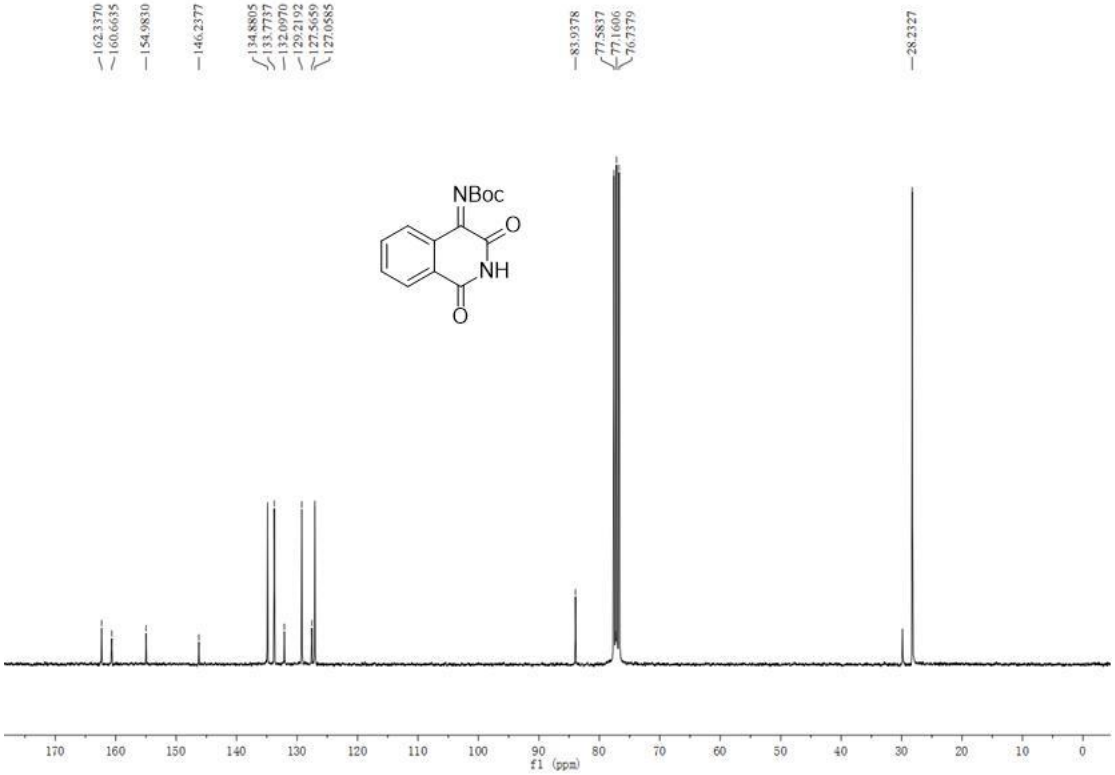
^{1}H NMR, ^{13}C NMR of 1c



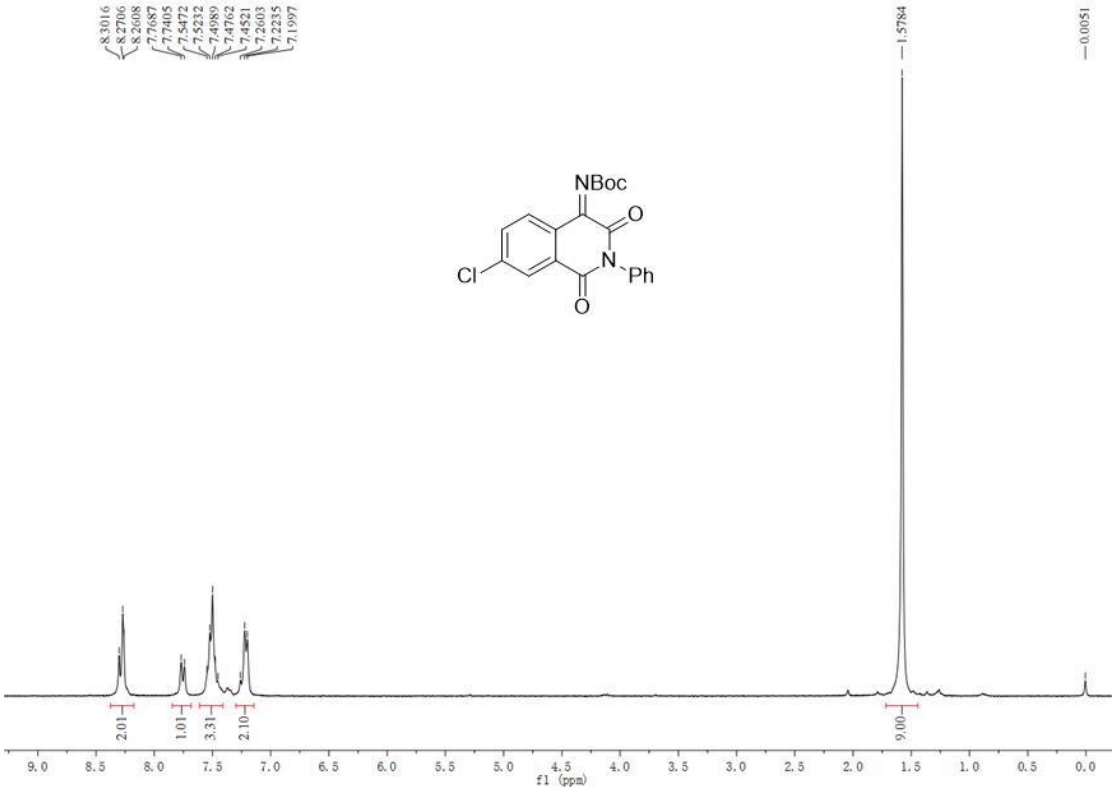


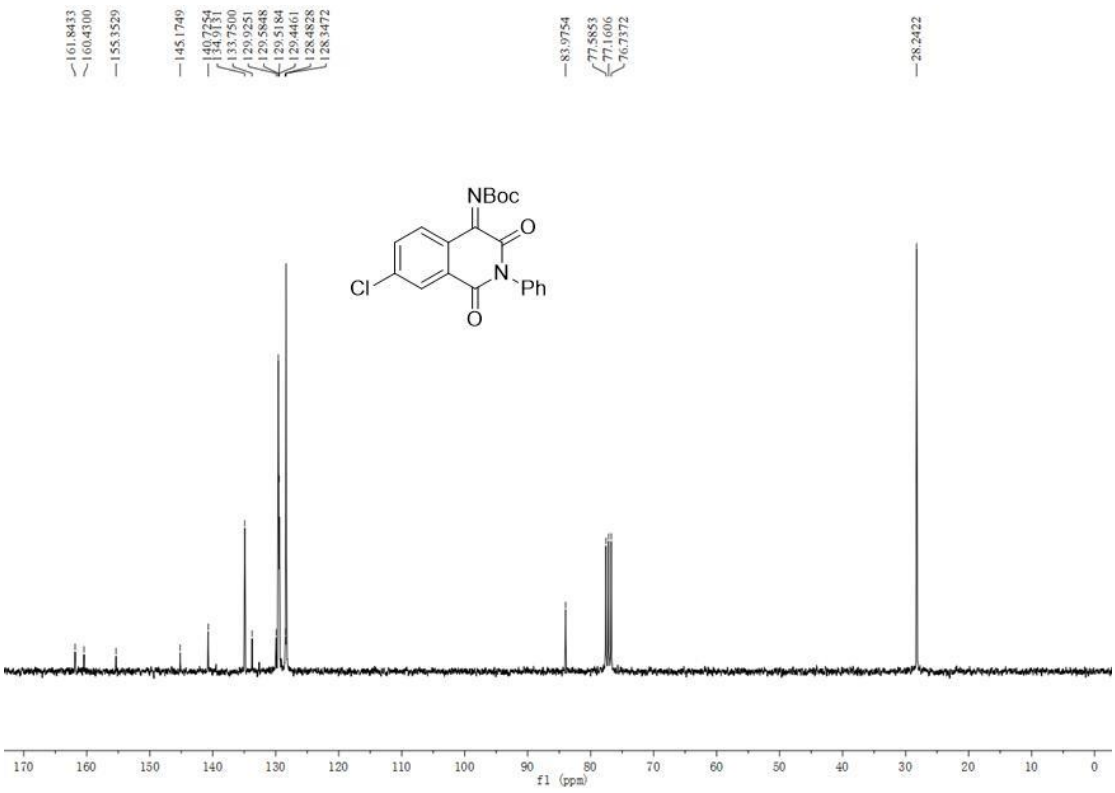
^{1}H NMR, ^{13}C NMR of 1d



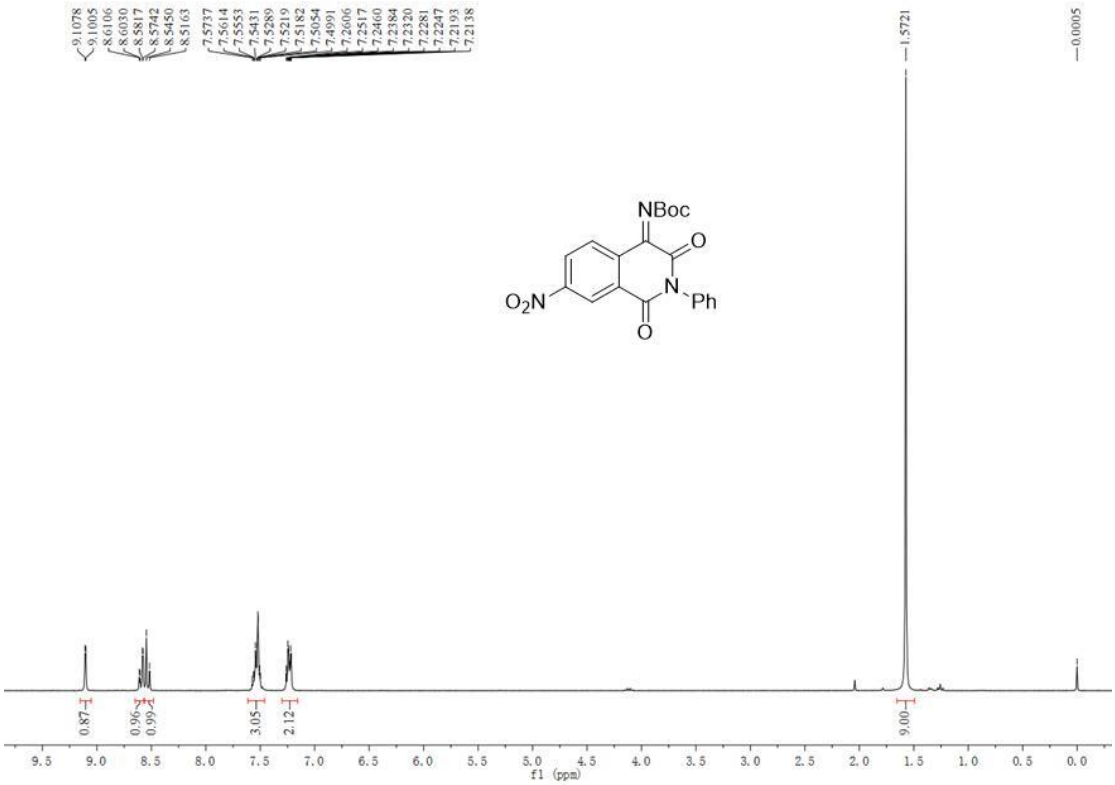


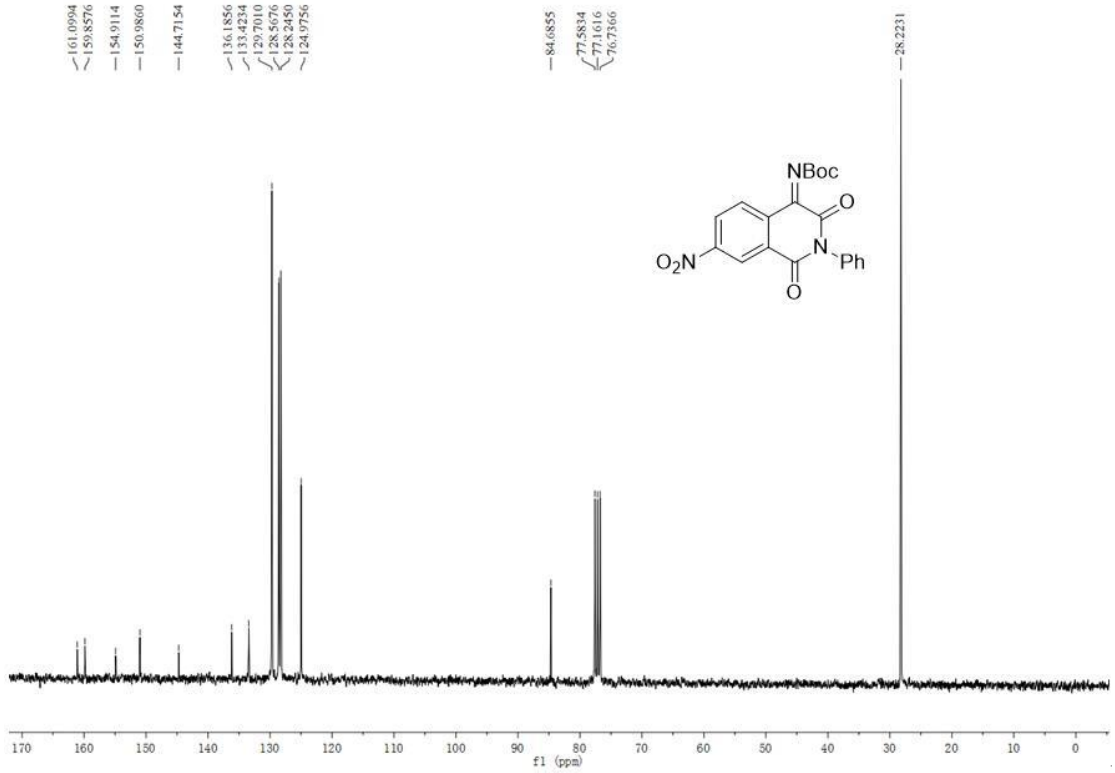
^{1}H NMR, ^{13}C NMR of 1e



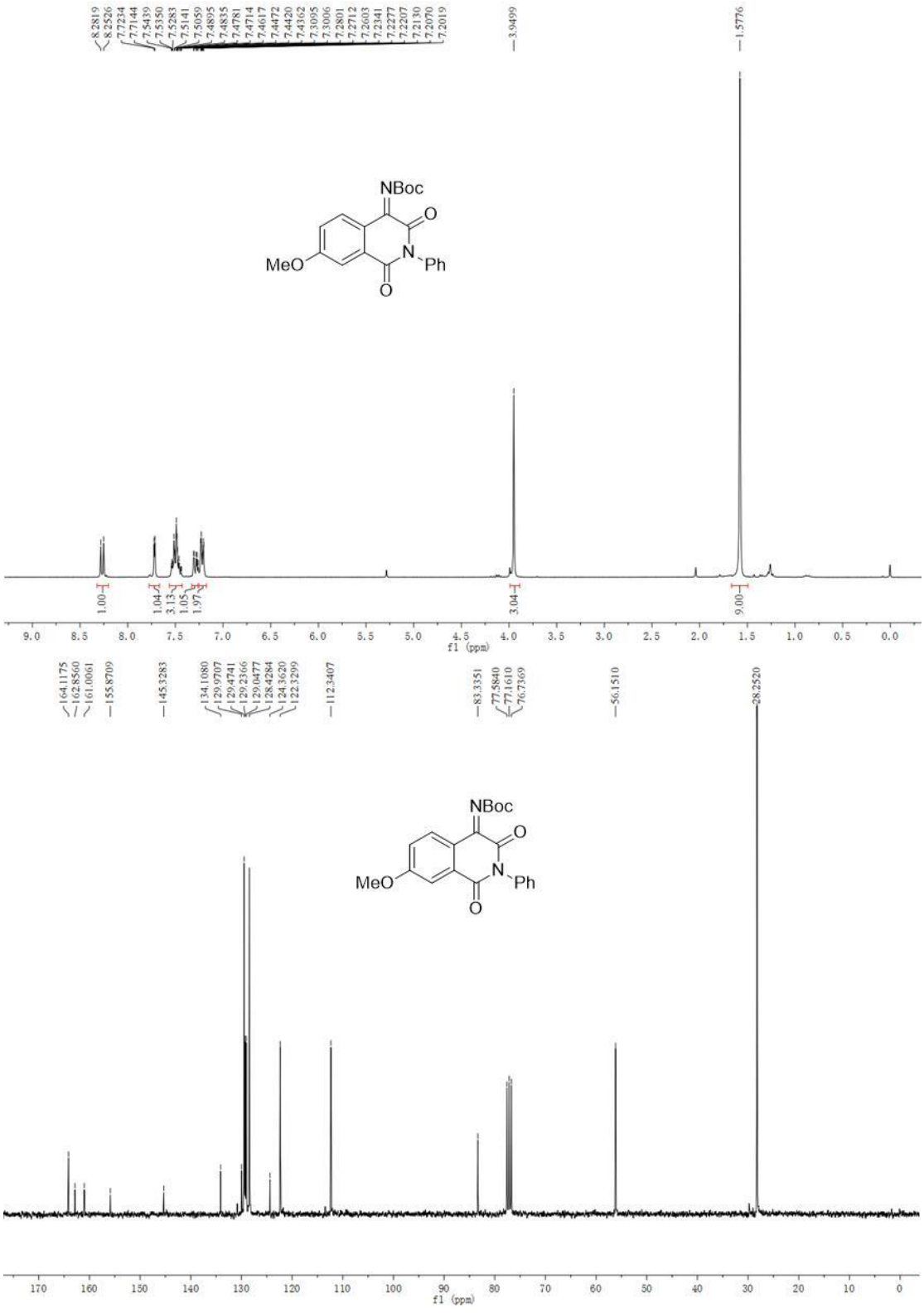


^{1}H NMR, ^{13}C NMR of 1f



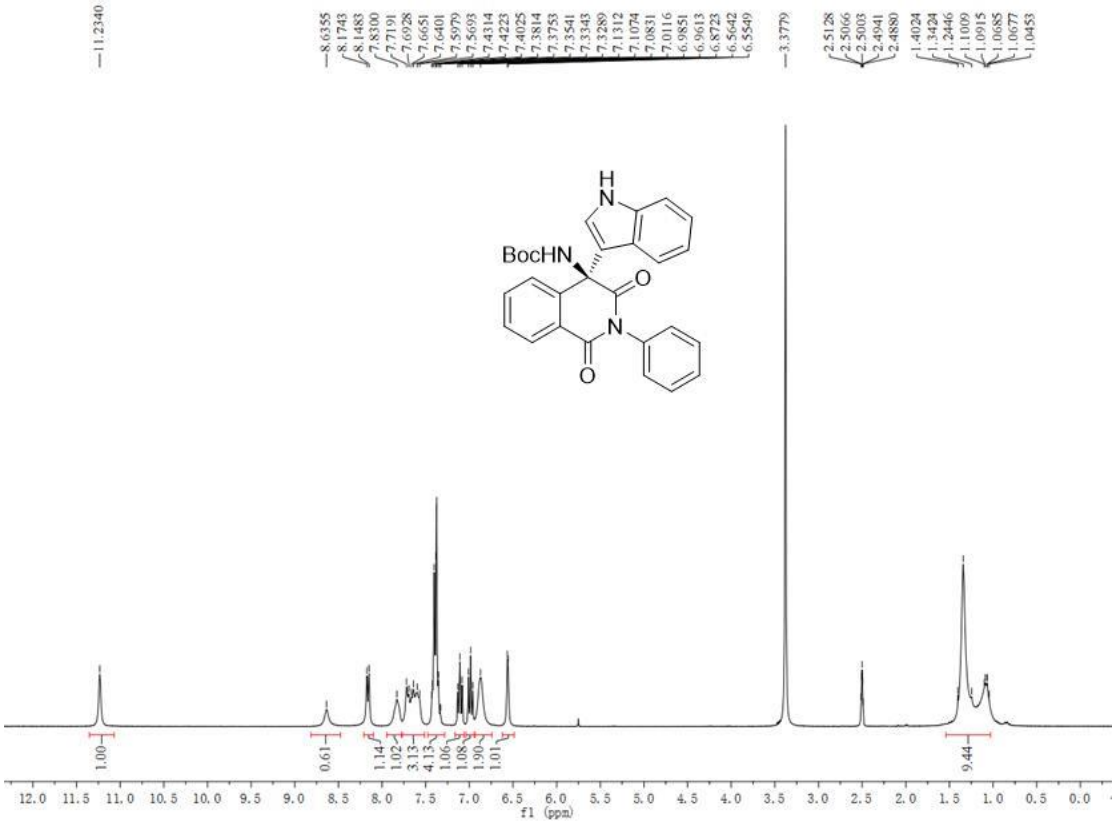


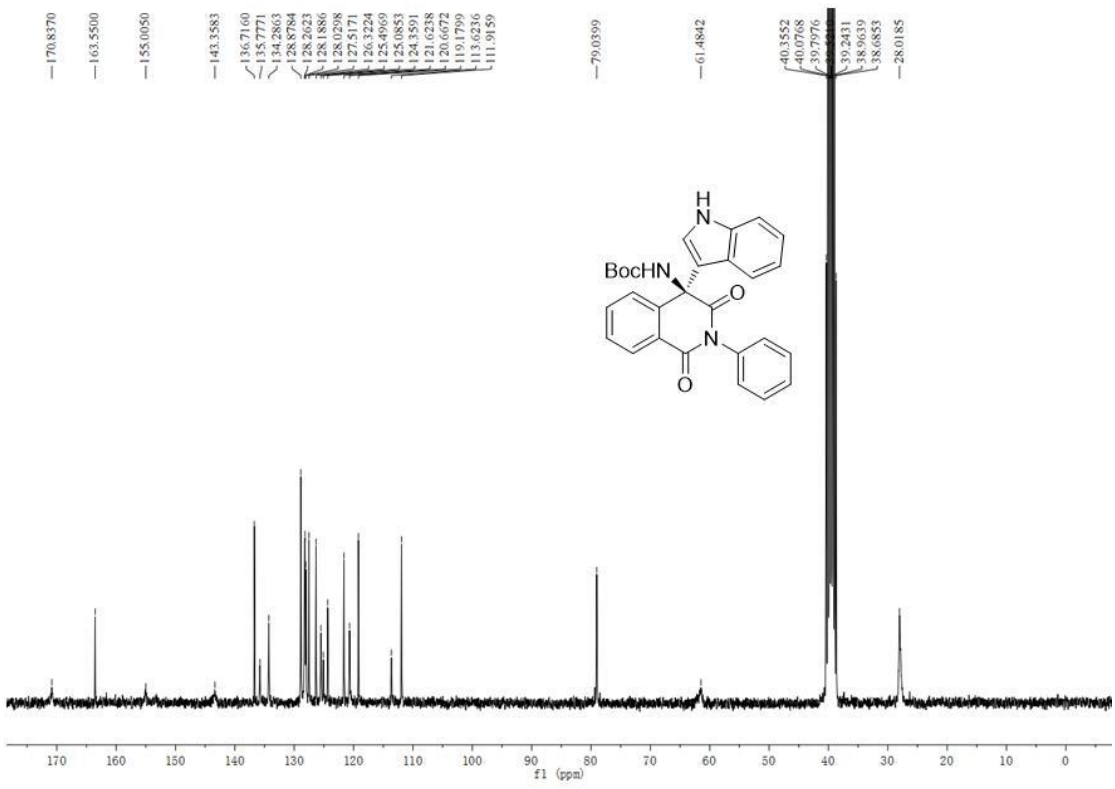
^{1}H NMR, ^{13}C NMR of 1g

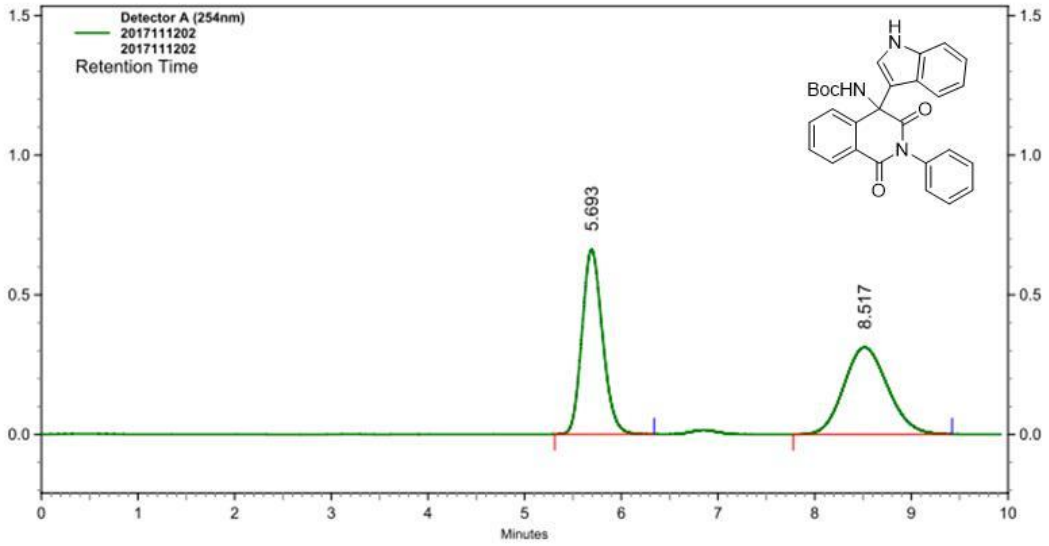


10. The copies of ^{1}H NMR, ^{13}C NMR and HPLC spectra for compounds 3, 5, 6 and 7

^{1}H NMR, ^{13}C NMR and HPLC spectra of 3aa

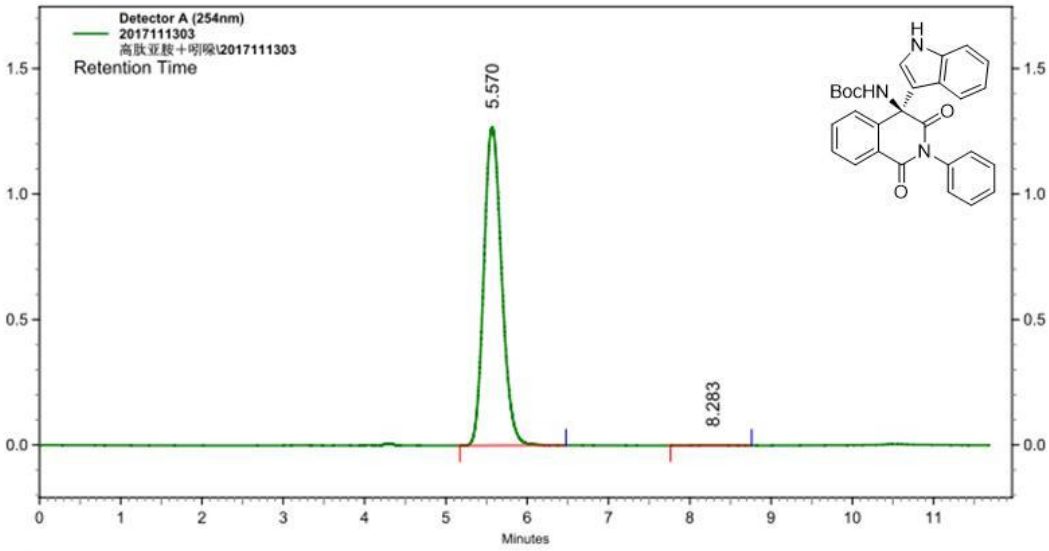






Detector A (254nm)

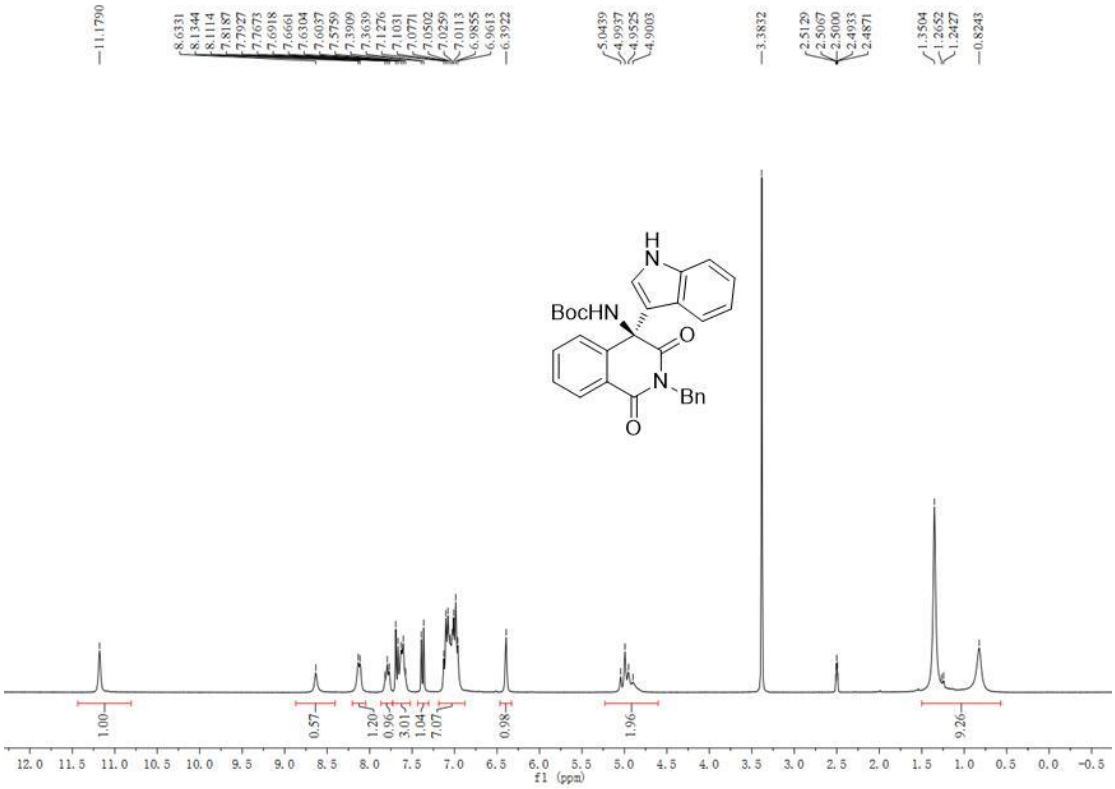
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	5.693	661619	68.00	9757103	49.84
2	8.517	311304	32.00	9820028	50.16
Totals		972923	100.00	19577131	100.00

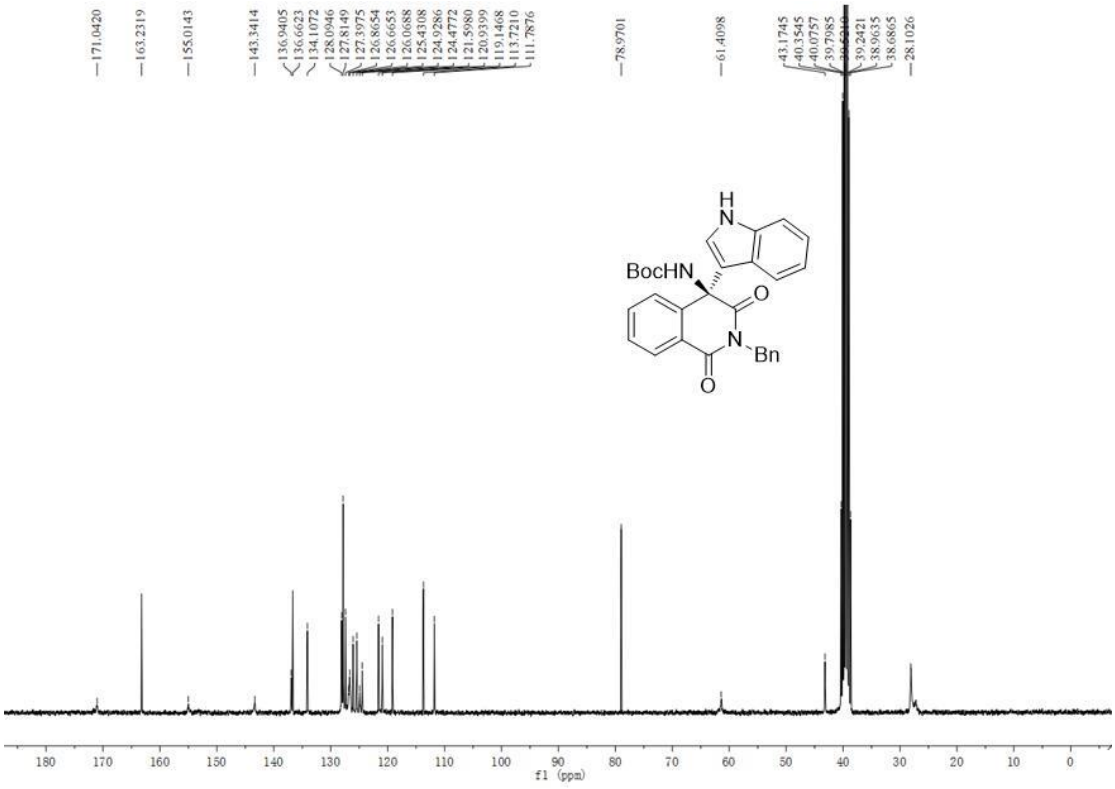


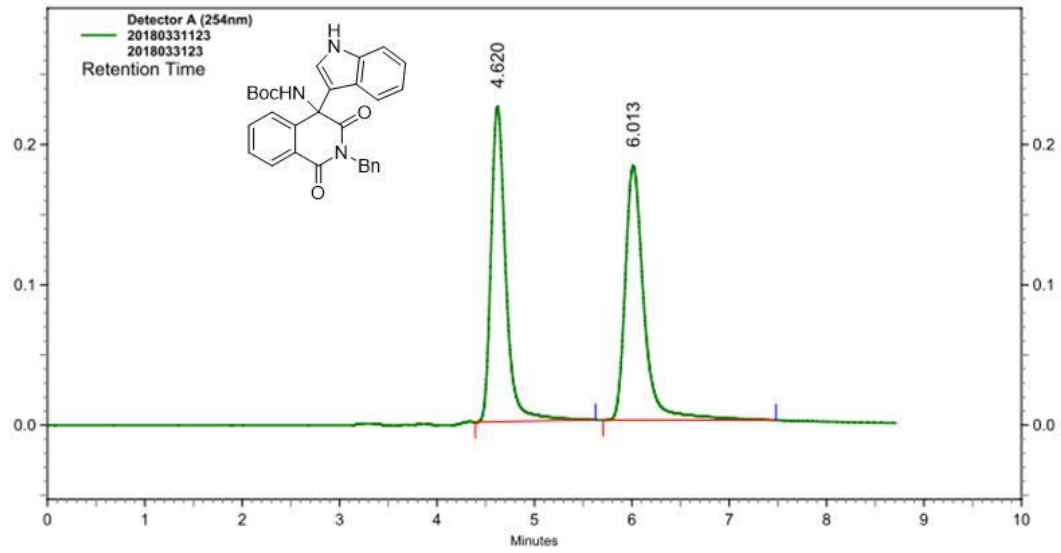
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	5.570	1267550	99.89	19324051	99.78
2	8.283	1432	0.11	42335	0.22
Totals		1268982	100.00	19366386	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 3ba

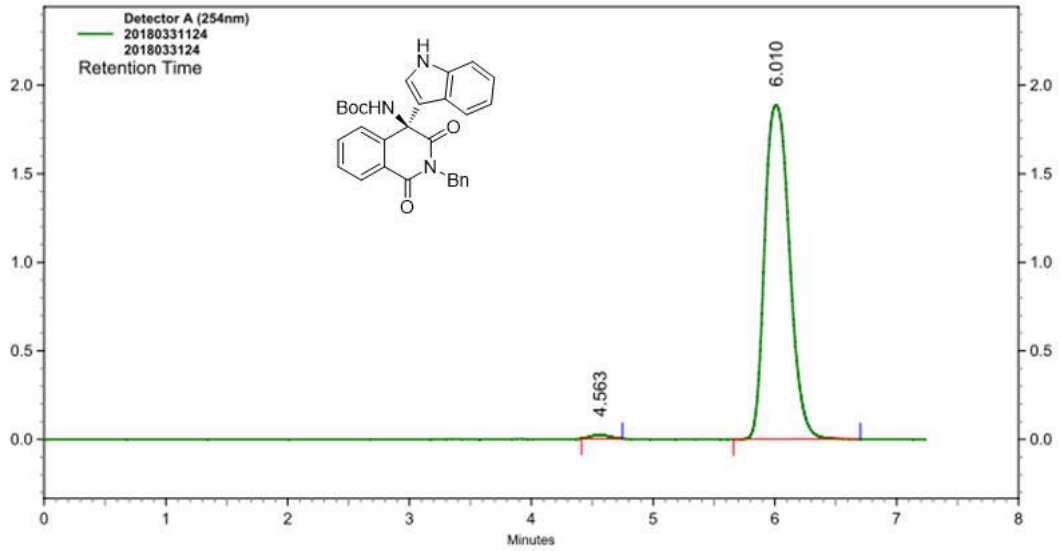






Detector A (254nm)

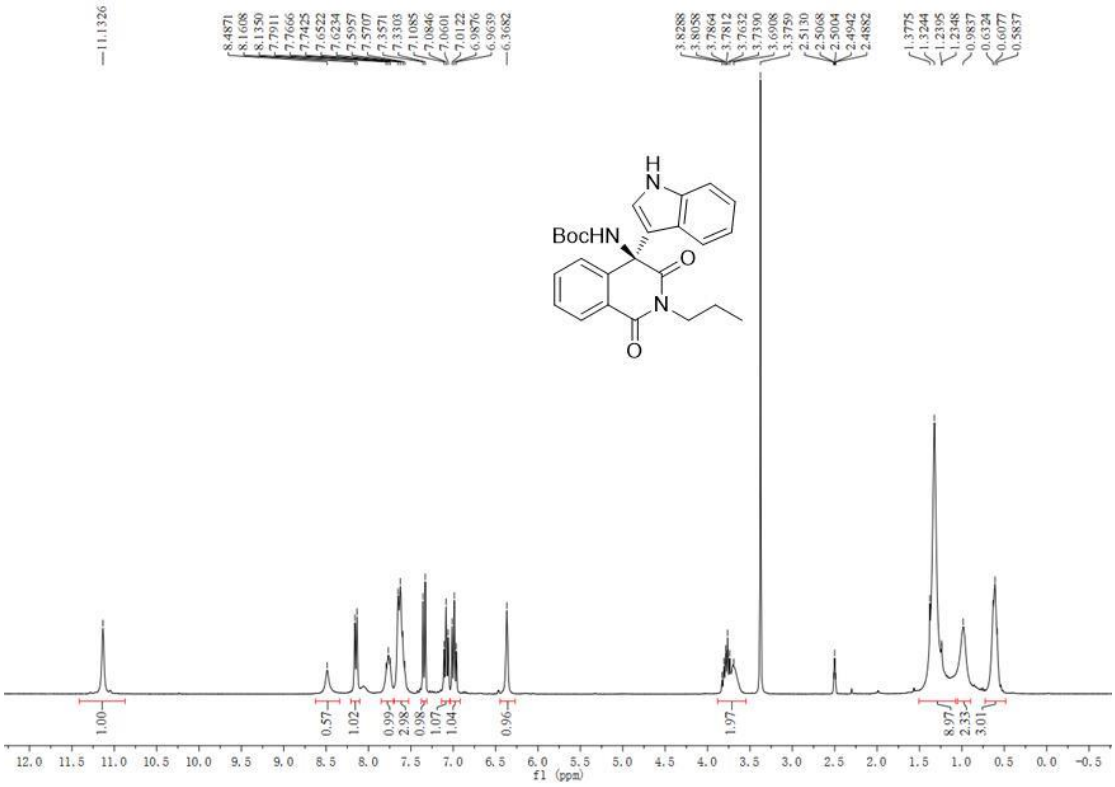
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	4.620	224824	55.35	2372258	49.41
2	6.013	181363	44.65	2428572	50.59
Totals		406187	100.00	4800830	100.00

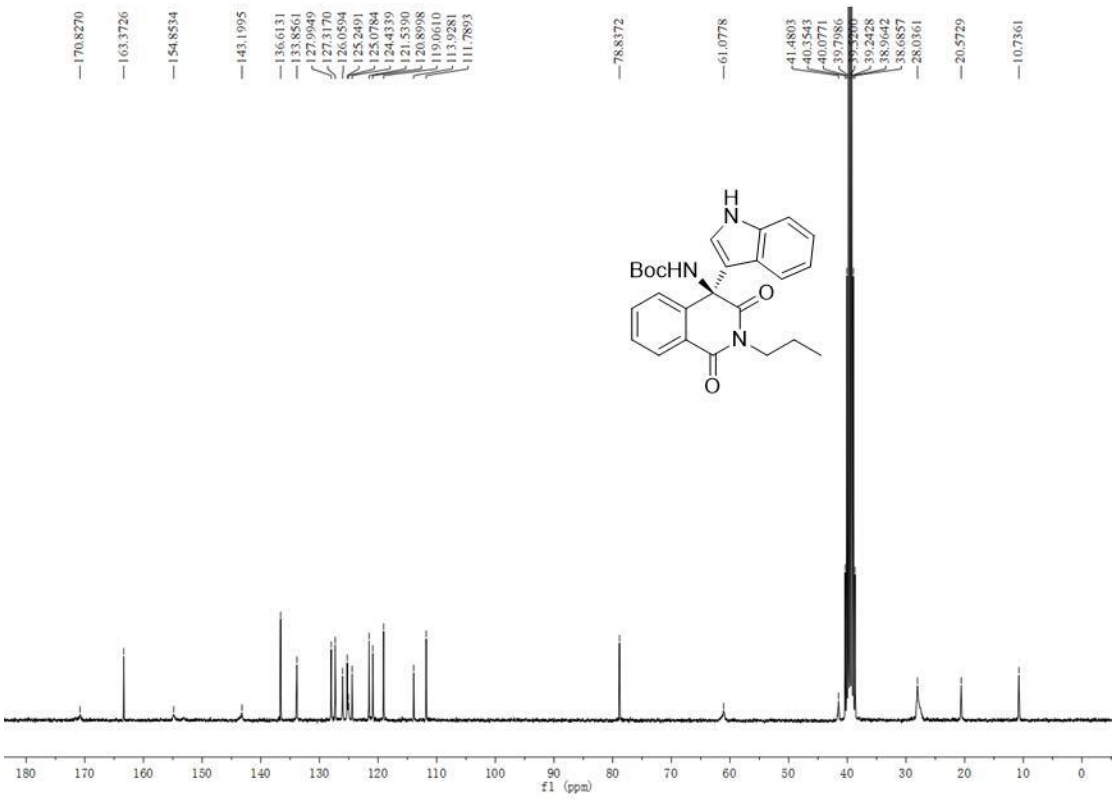


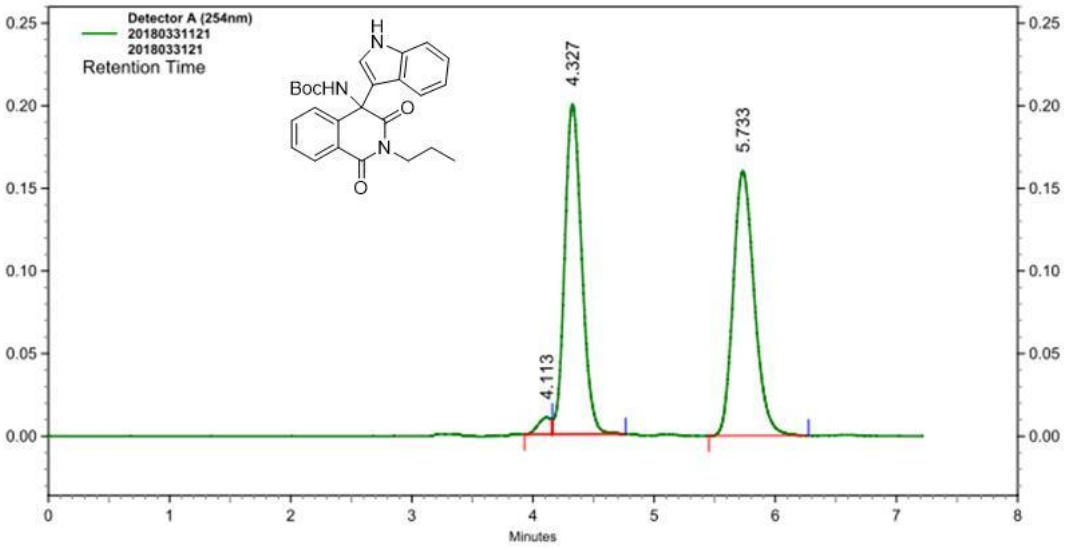
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	4.563	20944	1.10	225795	0.84
2	6.010	1887149	98.90	26721317	99.16
Totals		1908093	100.00	26947112	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 3ca

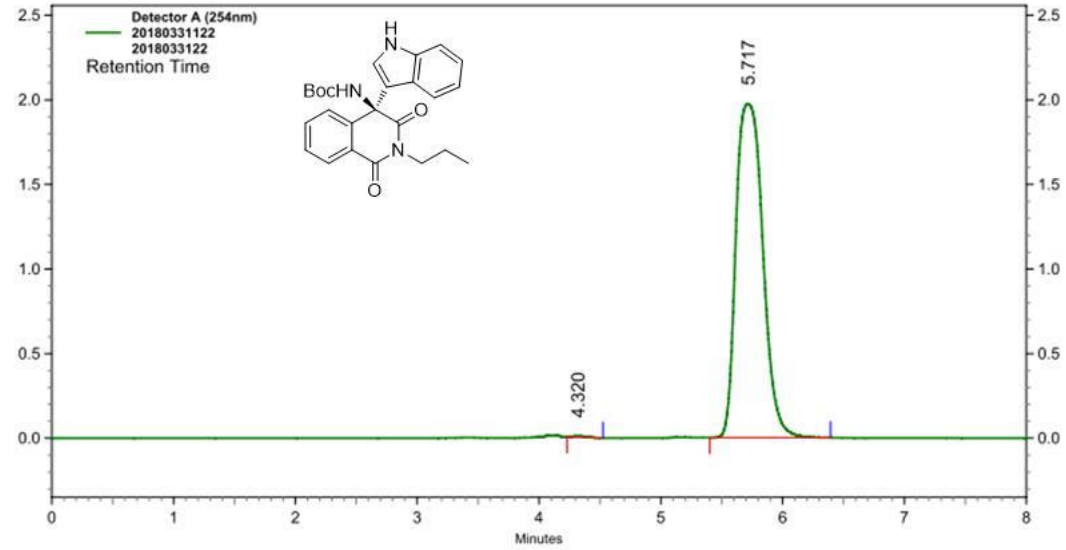






Detector A (254nm)

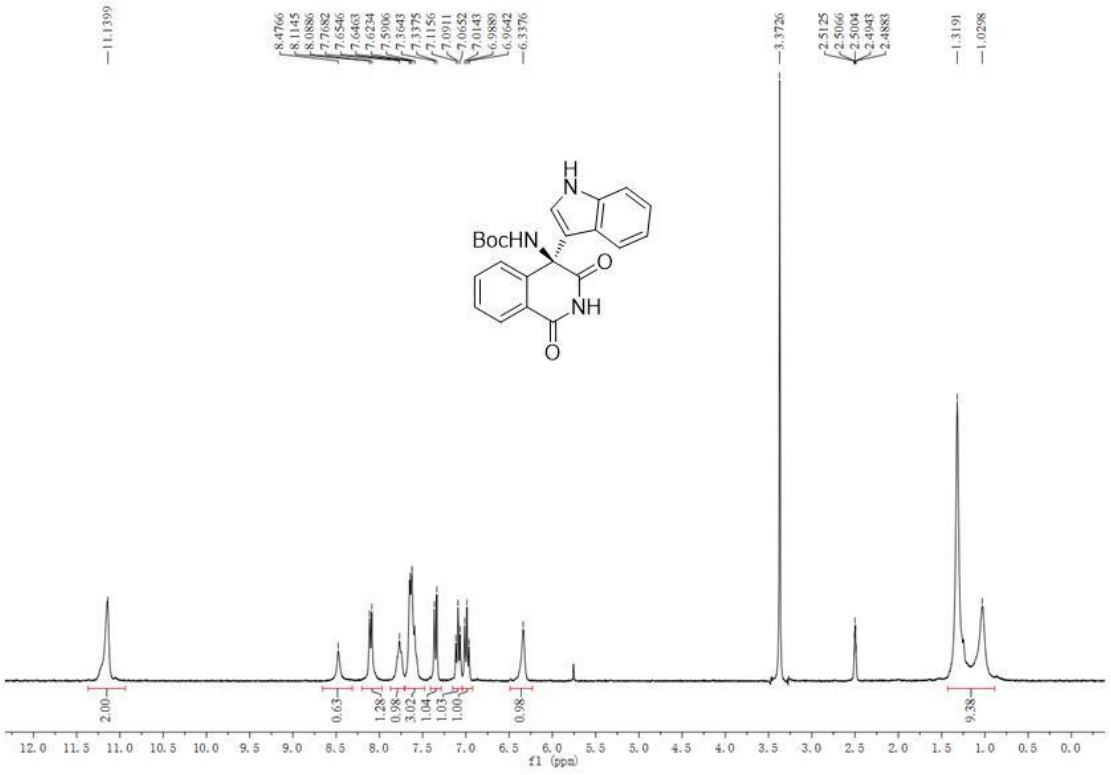
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	4.113	10070	2.72	75562	1.90
2	4.327	199673	53.97	1952156	49.18
3	5.733	160197	43.30	1941302	48.91
Totals		369940	100.00	3969020	100.00

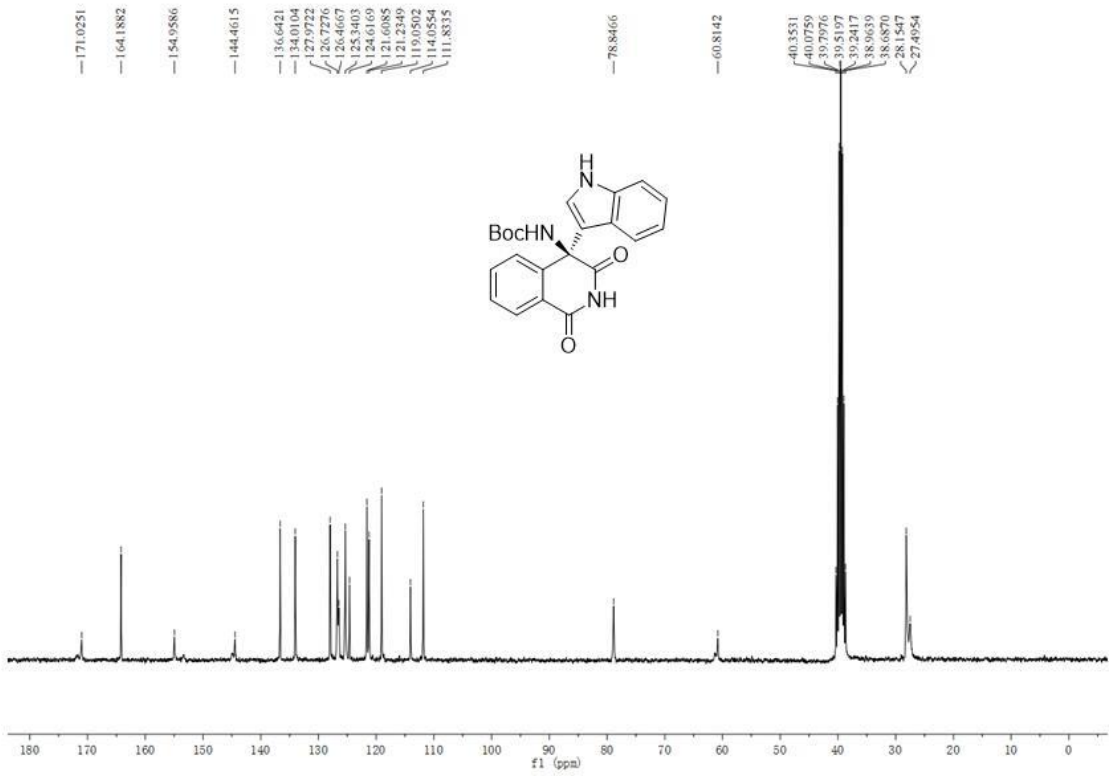


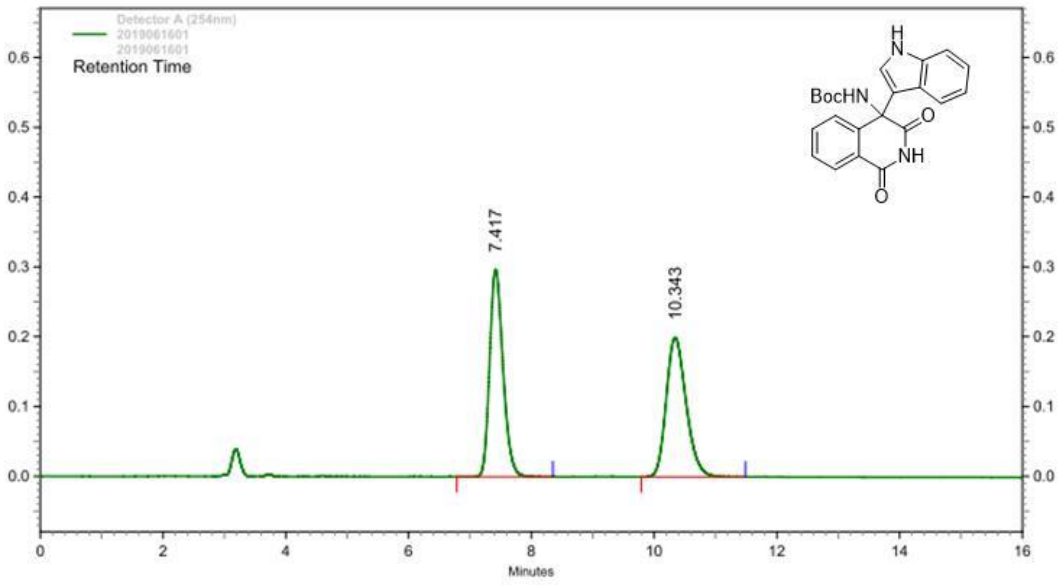
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	4.320	7084	0.36	52666	0.17
2	5.717	1973100	99.64	30244883	99.83
Totals		1980184	100.00	30297549	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 3da

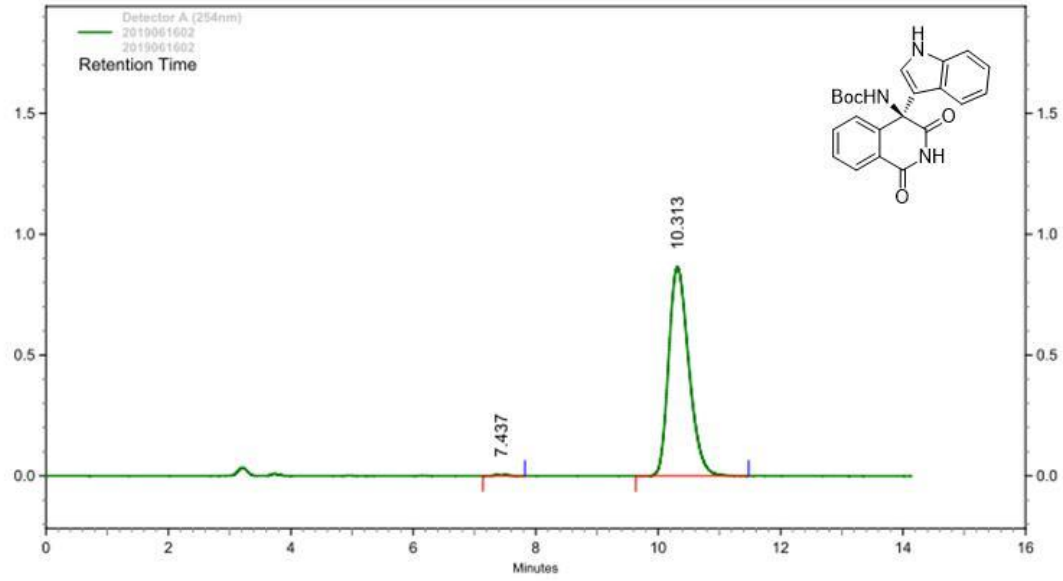






Detector A (254nm)

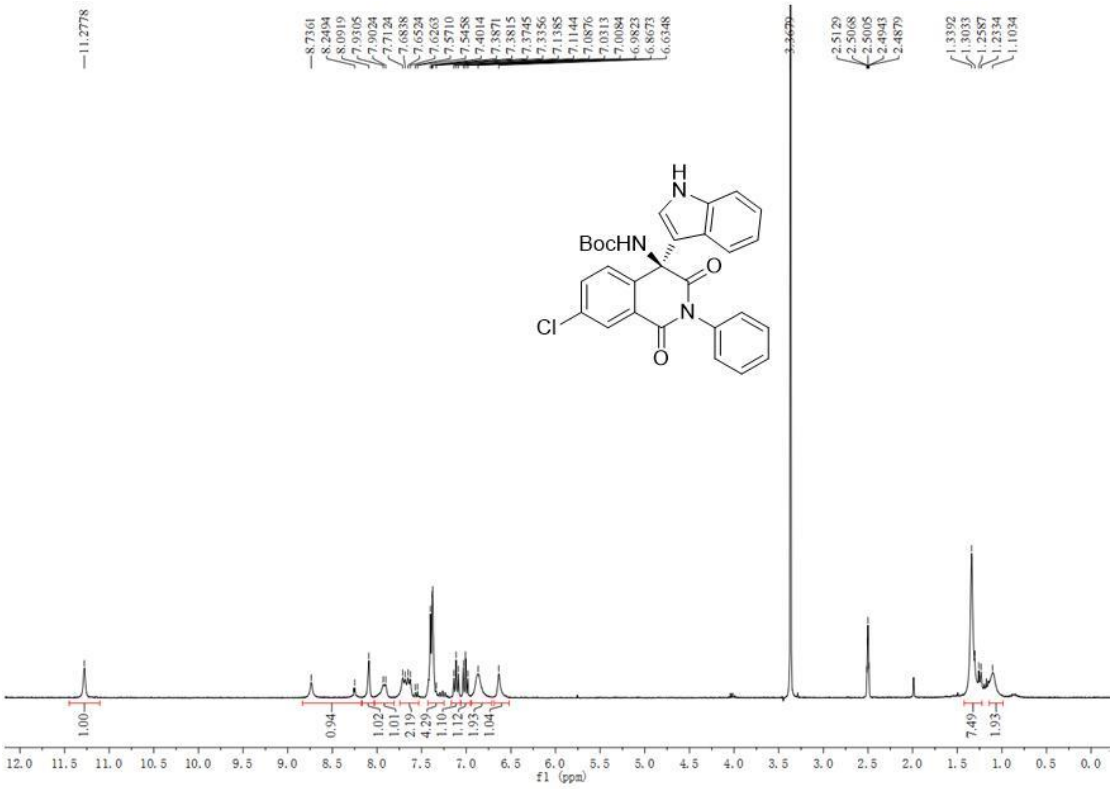
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	7.417	296213	59.76	4494521	49.96
2	10.343	199429	40.24	4502361	50.04
Totals		495642	100.00	8996882	100.00

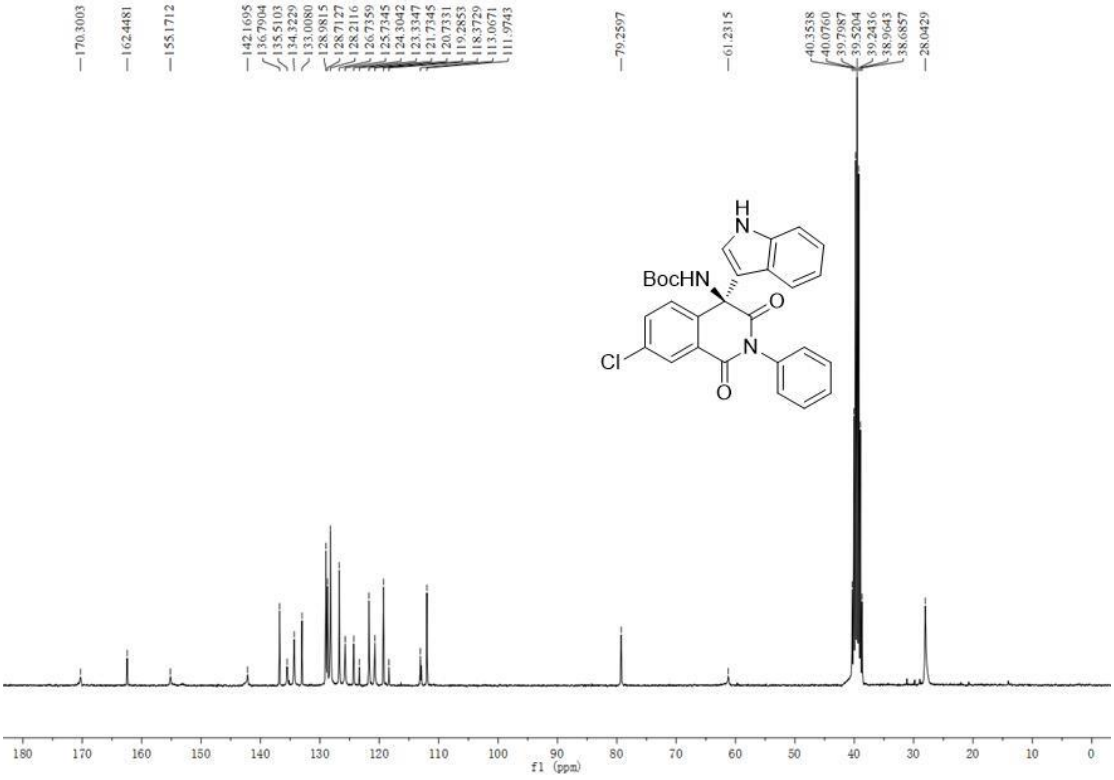


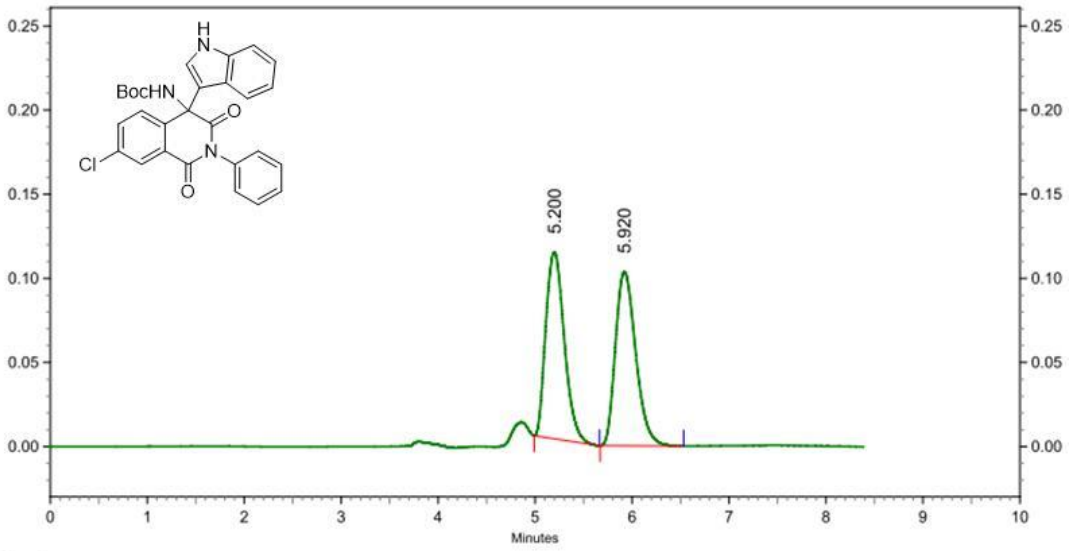
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	7.437	4353	0.50	64743	0.33
2	10.313	863381	99.50	19733103	99.67
Totals		867734	100.00	19797846	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 3ea

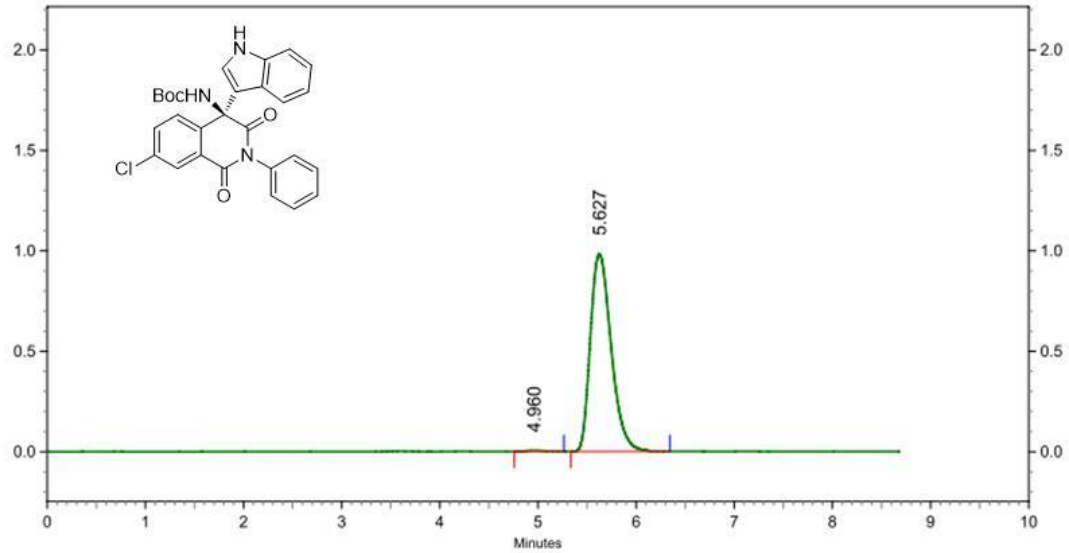






Detector A (254nm)

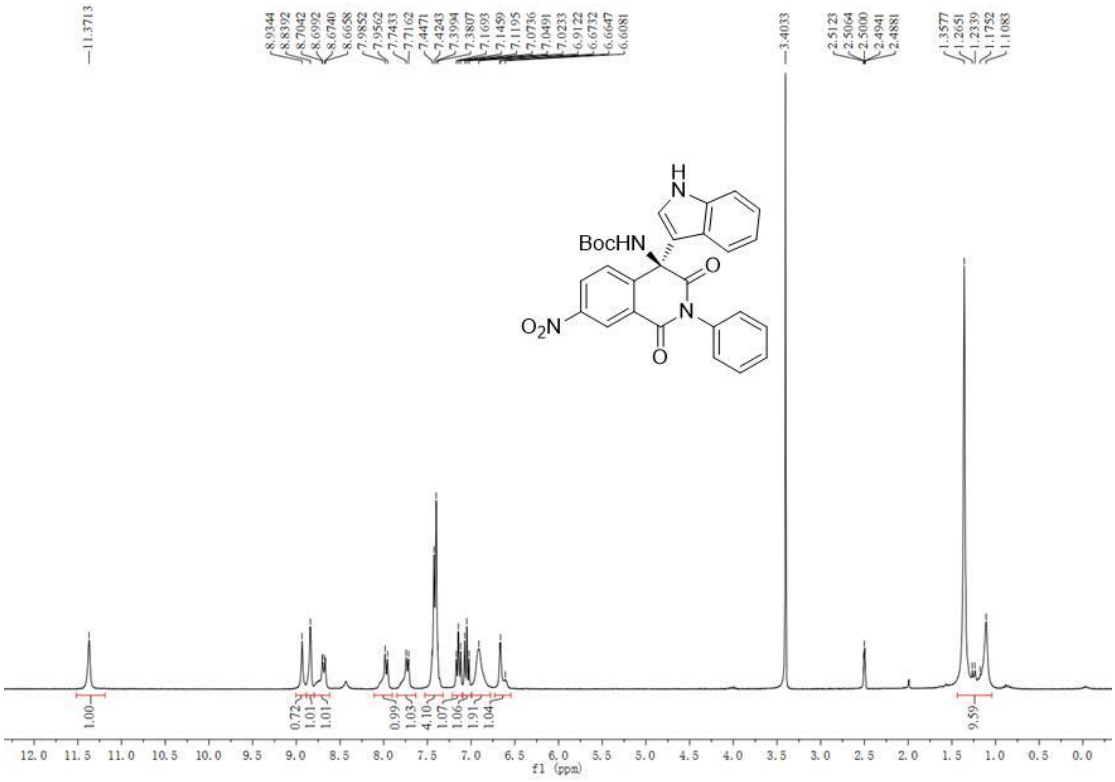
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	5.200	110983	51.75	1472819	49.43
2	5.920	103471	48.25	1507074	50.57
Totals		214454	100.00	2979893	100.00

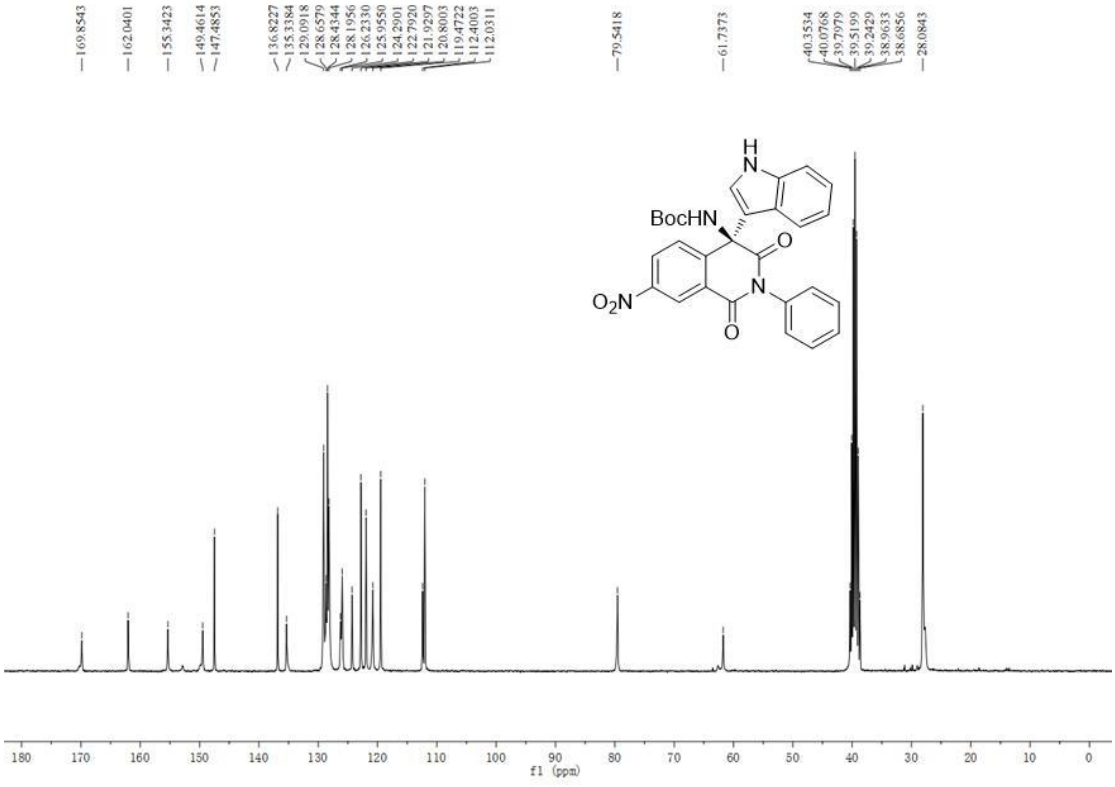


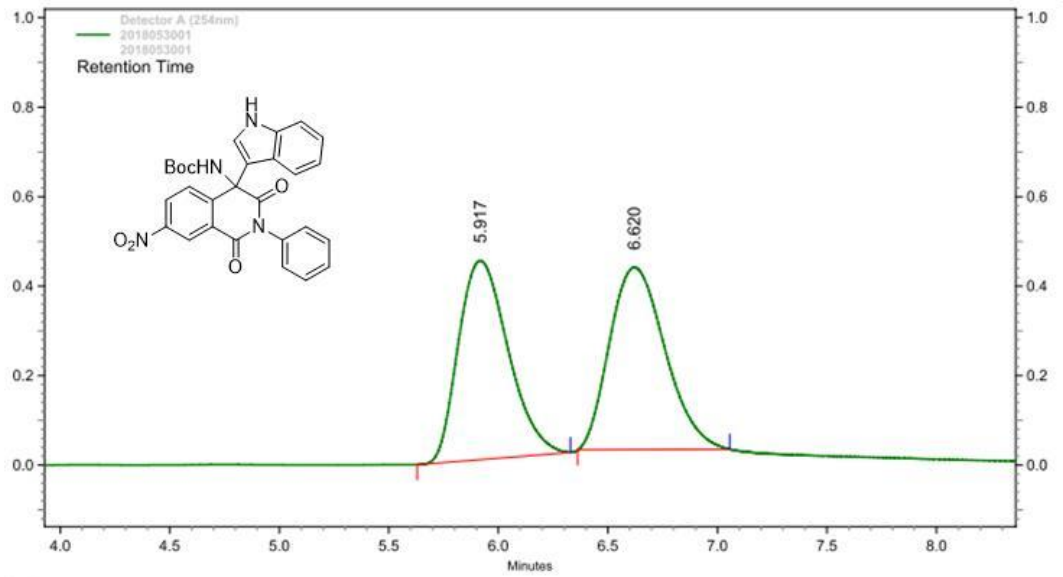
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	4.960	4529	0.46	67448	0.46
2	5.627	982726	99.54	14472249	99.54
Totals		987255	100.00	14539697	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 3fa

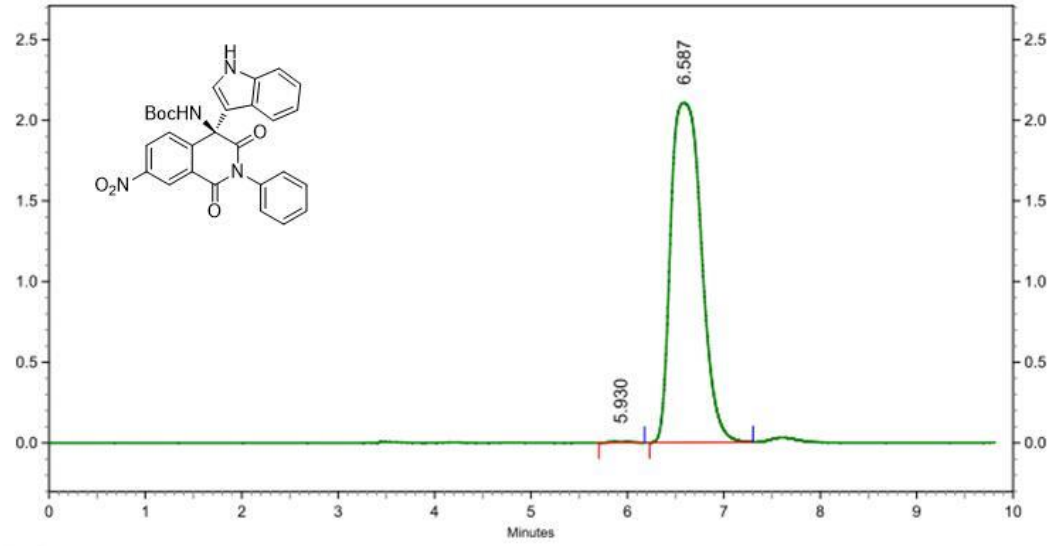






Detector A (254nm)

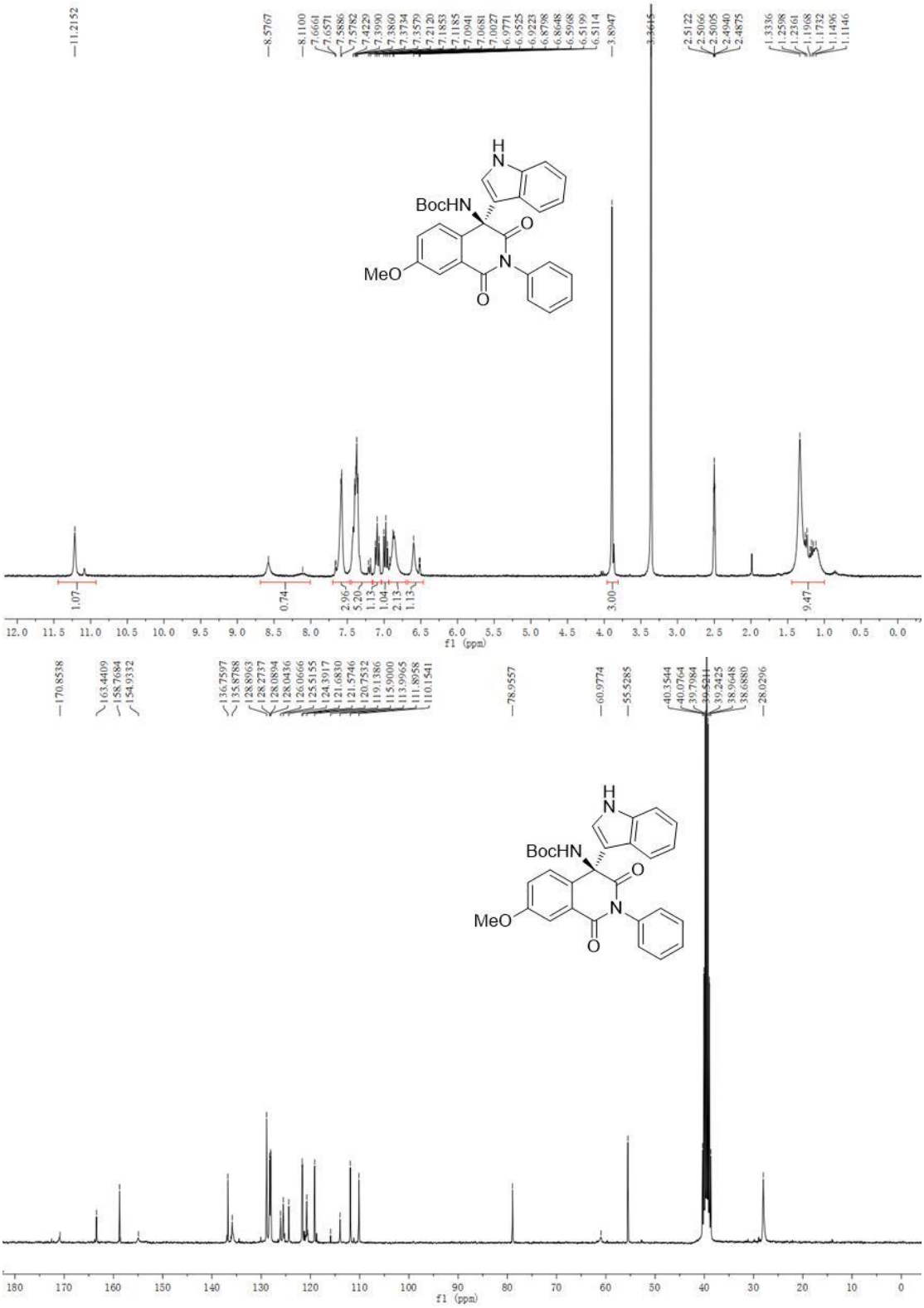
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	5.917	444985	52.21	7017856	49.41
2	6.620	407347	47.79	7185950	50.59
Totals		852332	100.00	14203806	100.00

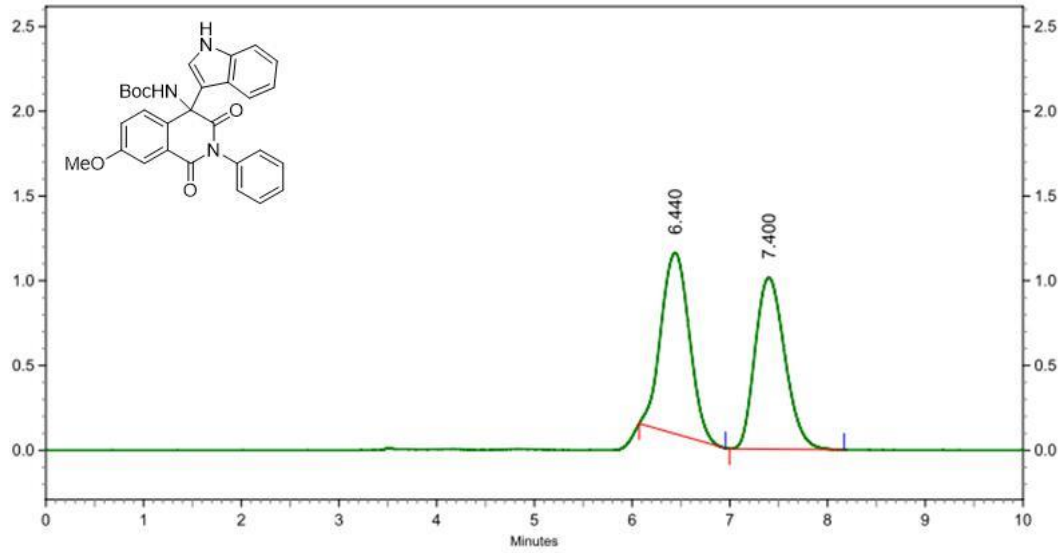


Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	5.930	6666	0.32	95453	0.20
2	6.587	2105649	99.68	46481008	99.80
Totals		2112315	100.00	46576461	100.00

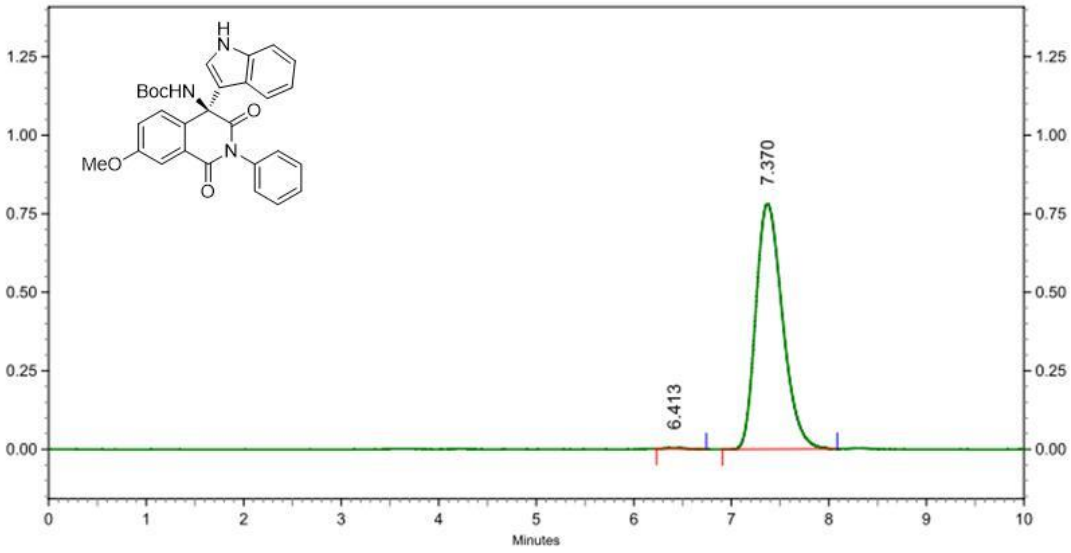
^{1}H NMR, ^{13}C NMR and HPLC spectra of 3ga





Detector A (254nm)

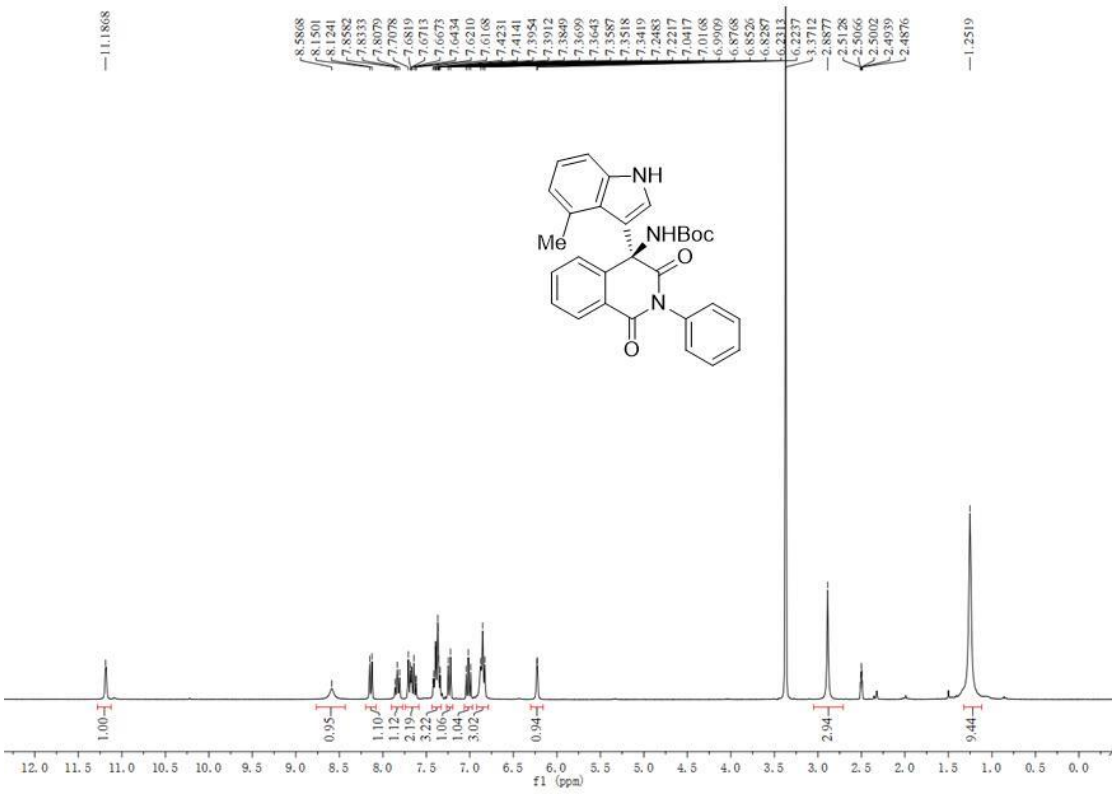
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	6.440	1066111	51.30	21534357	50.10
2	7.400	1011937	48.70	21451870	49.90
Totals		2078048	100.00	42986227	100.00

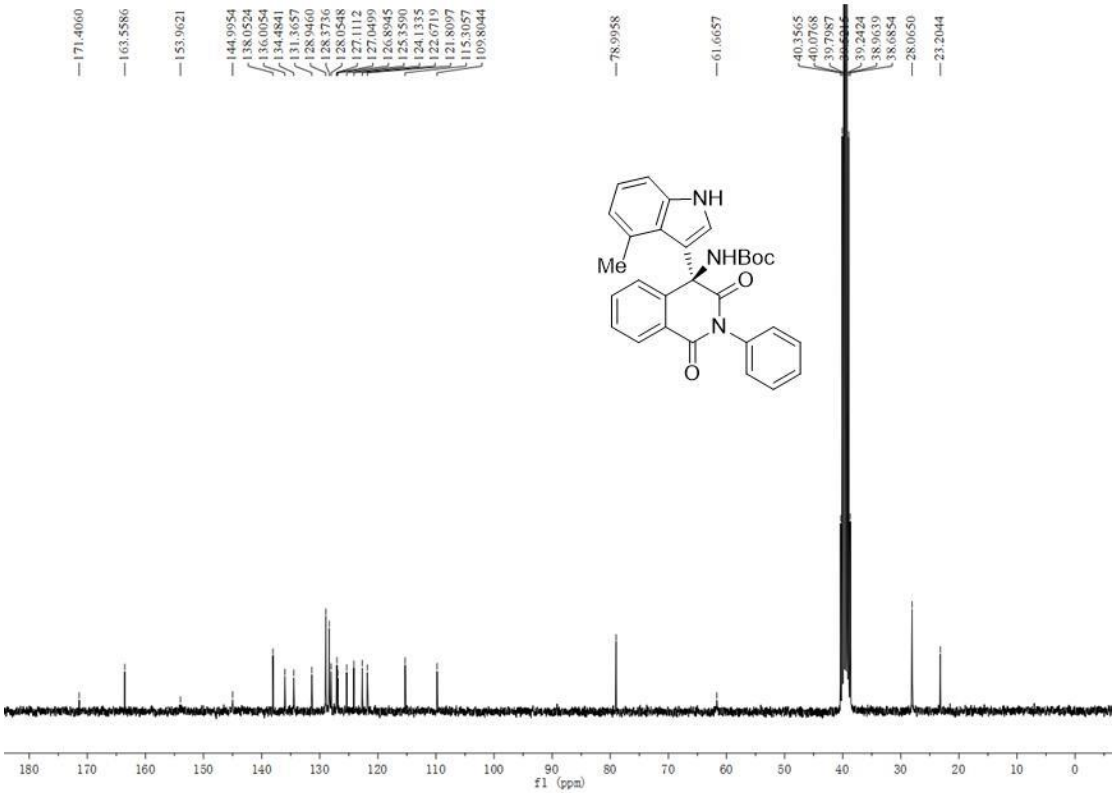


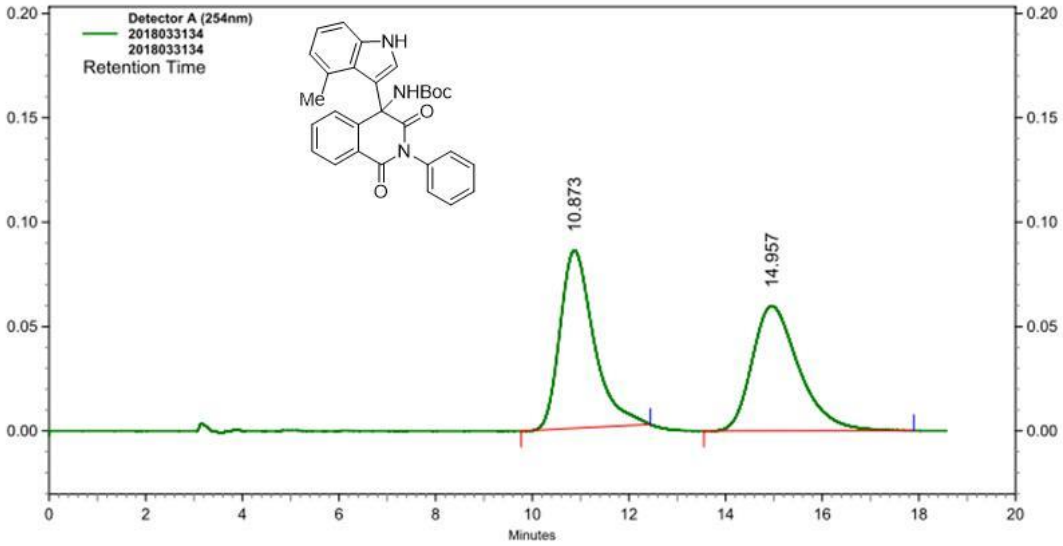
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	6.413	3004	0.38	44078	0.30
2	7.370	781836	99.62	14867098	99.70
Totals		784840	100.00	14911176	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 3ab

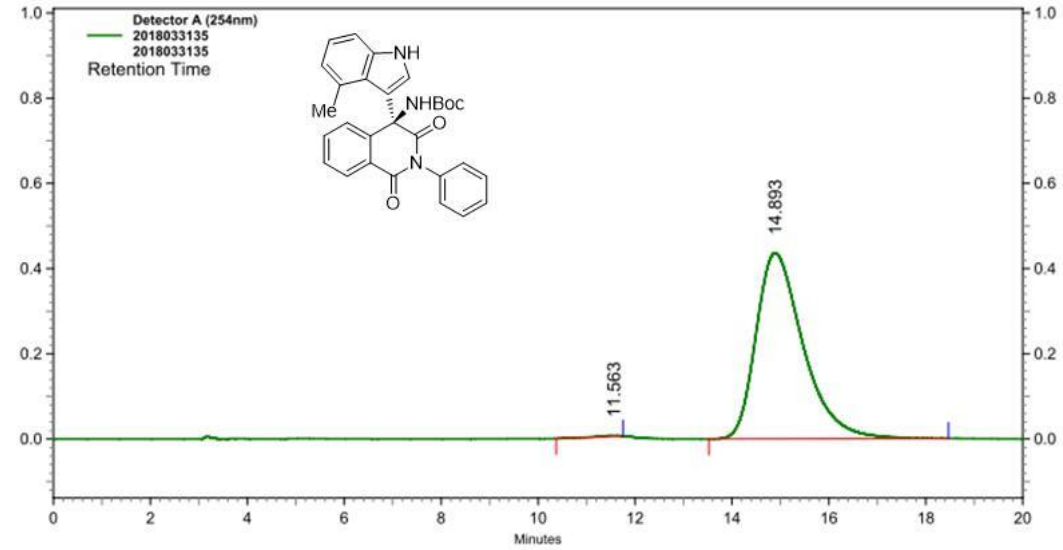






Detector A (254nm)

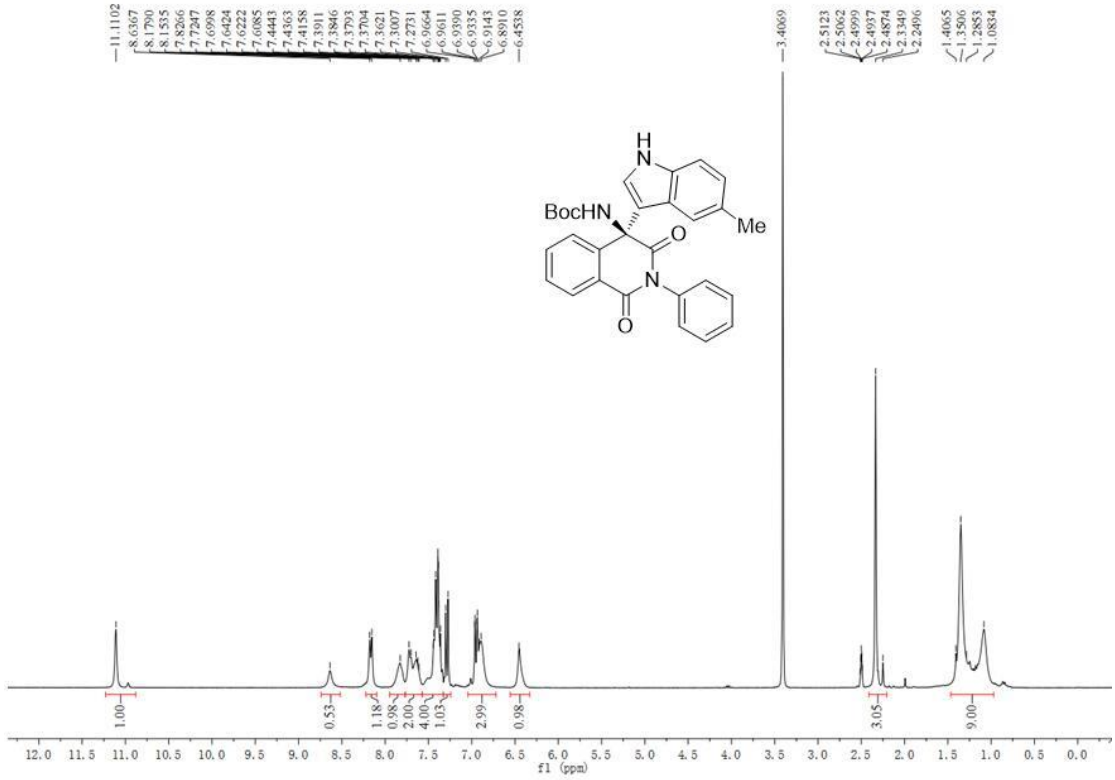
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	10.873	85180	58.72	4145965	50.72
2	14.957	59877	41.28	4028007	49.28
Totals		145057	100.00	8173972	100.00

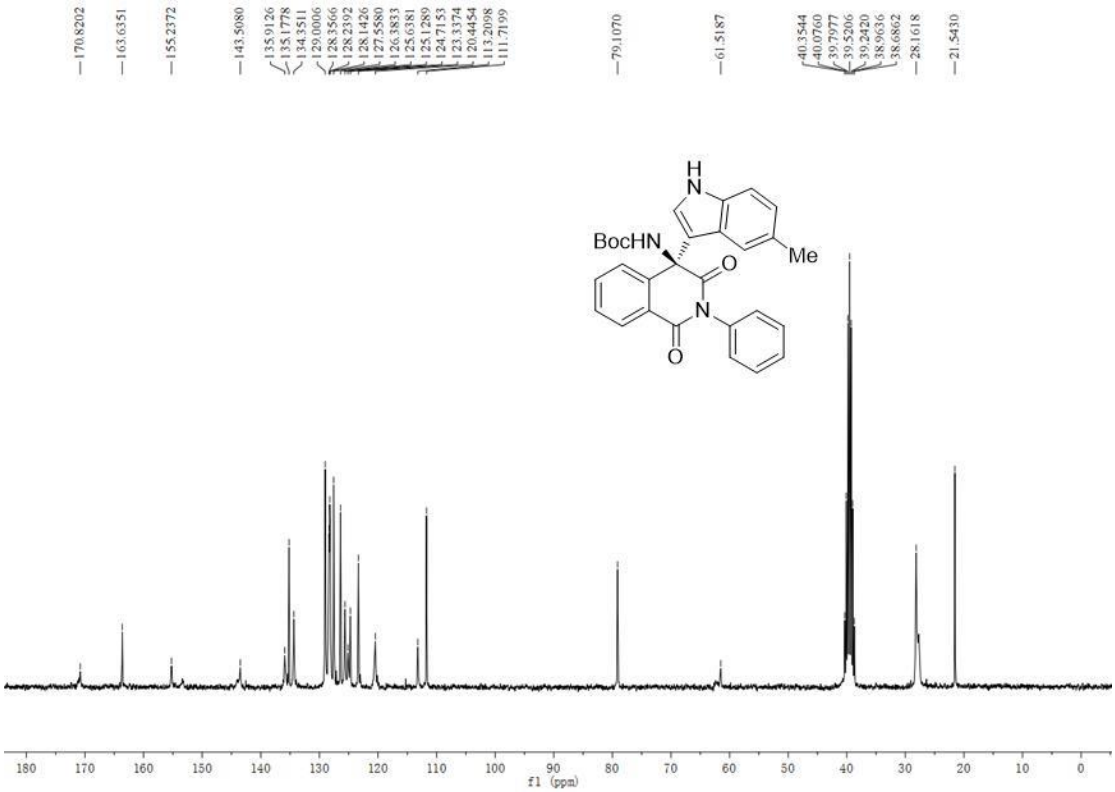


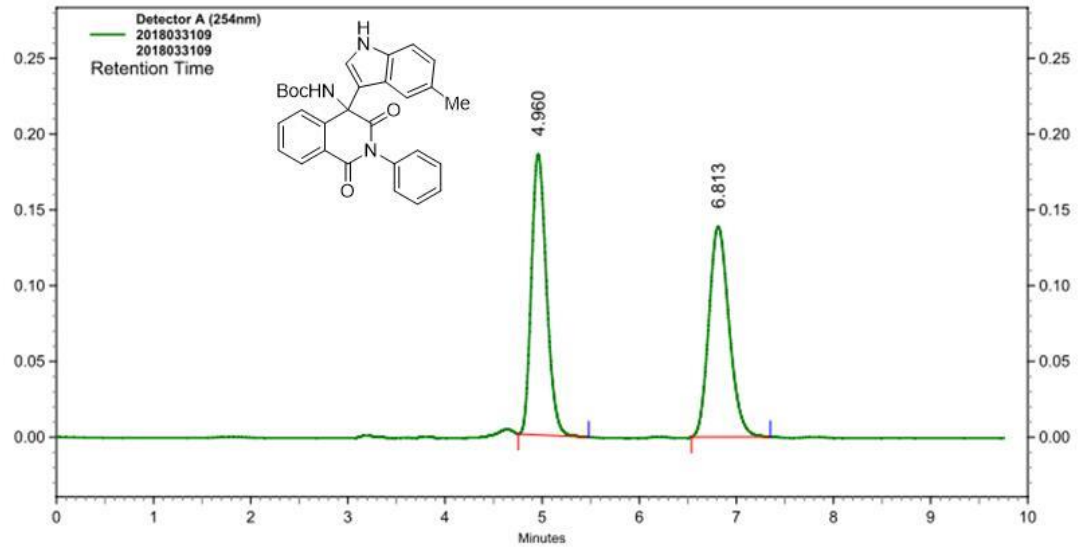
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	11.563	1970	0.45	57718	0.20
2	14.893	435638	99.55	29438525	99.80
Totals		437608	100.00	29496243	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 3ac

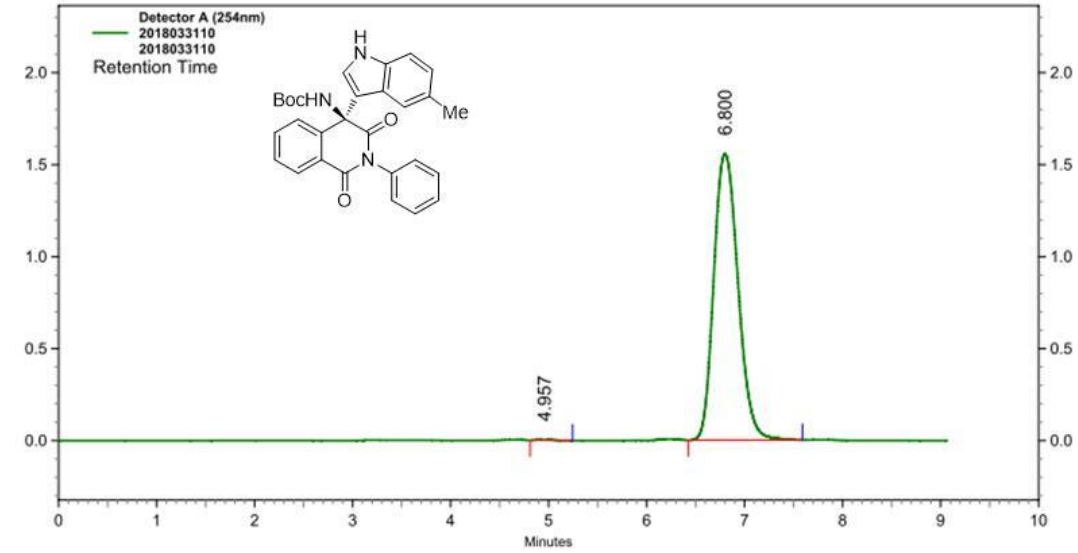






Detector A (254nm)

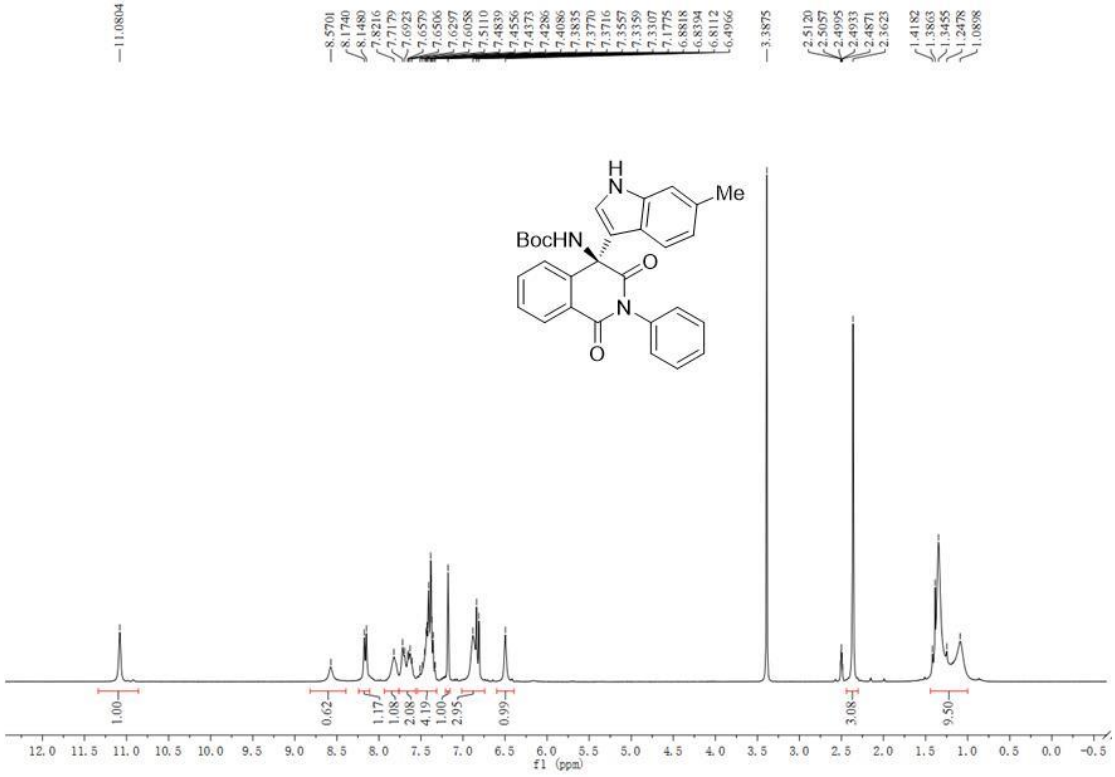
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	4.960	185250	57.16	1994348	49.78
2	6.813	138829	42.84	2011983	50.22
Totals		324079	100.00	4006331	100.00

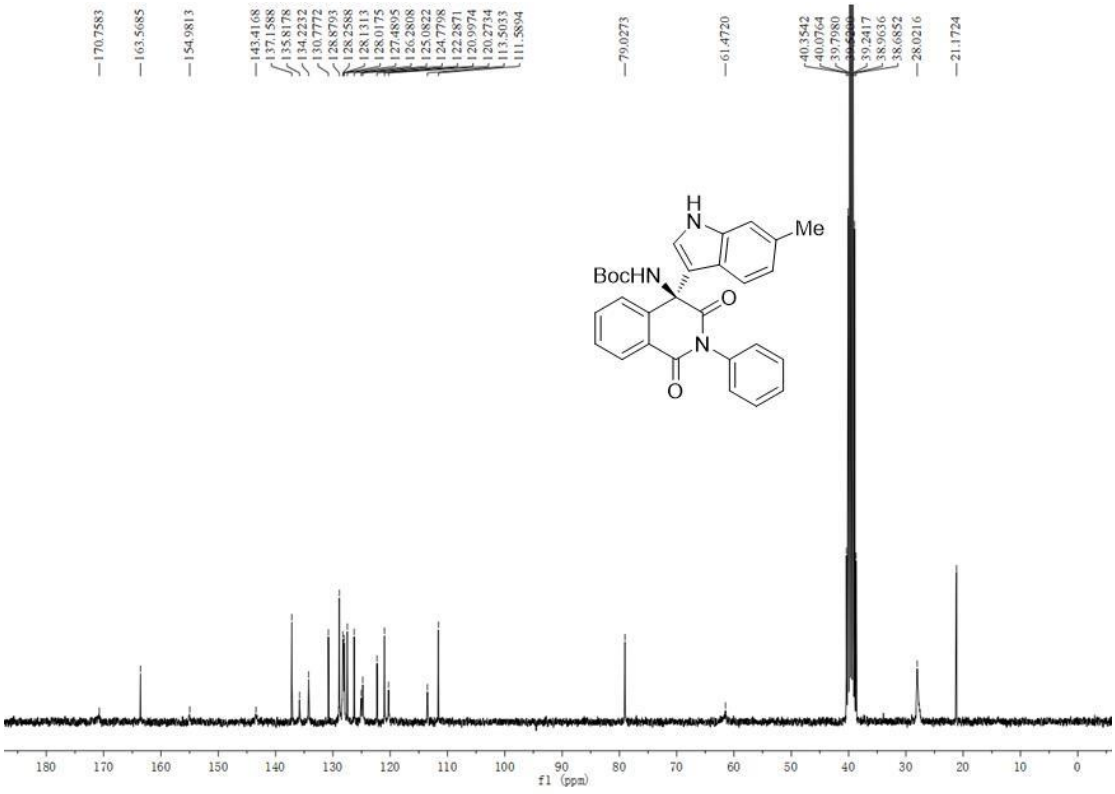


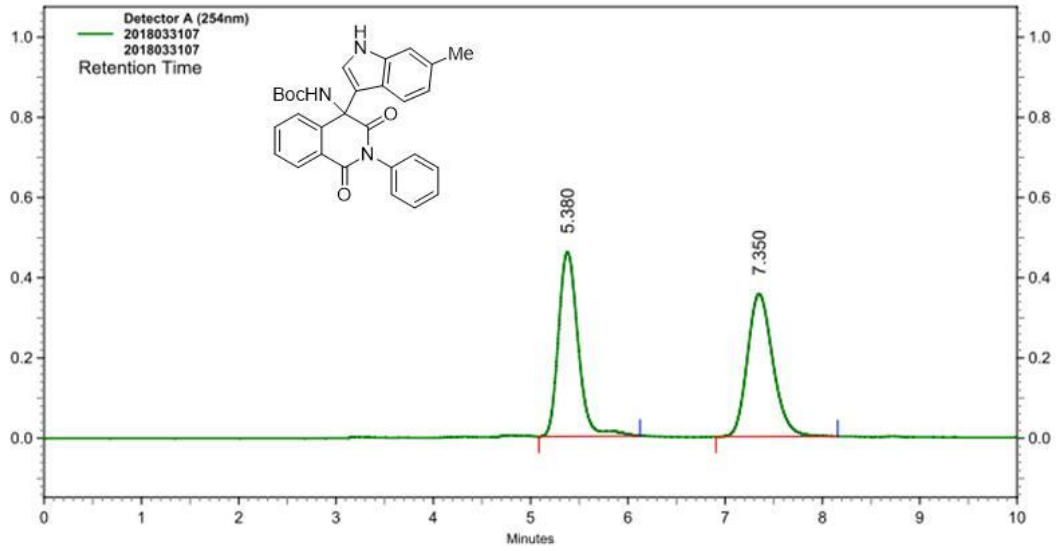
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	4.957	3596	0.23	38694	0.14
2	6.800	1555947	99.77	26769998	99.86
Totals		1559543	100.00	26808692	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 3ad

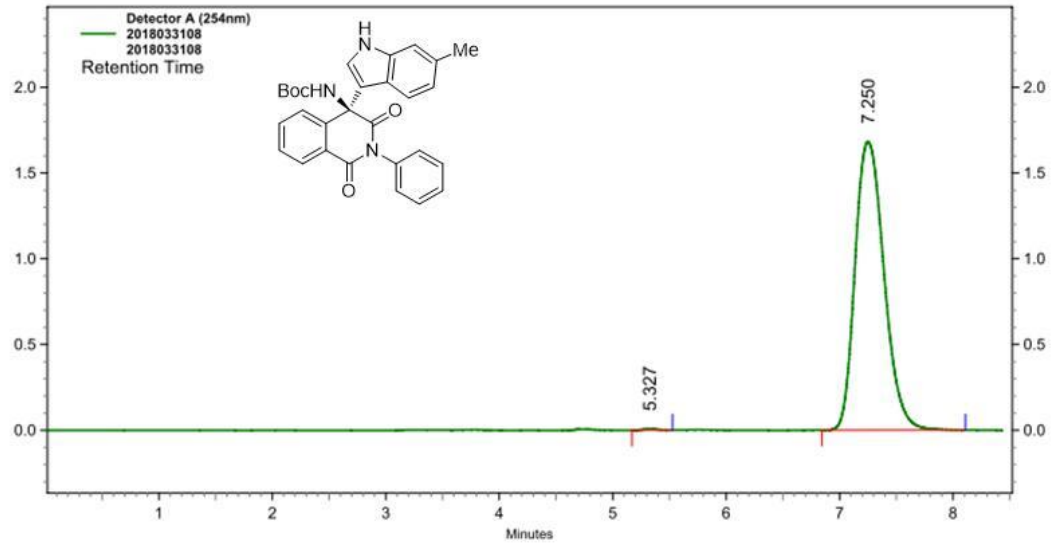






Detector A (254nm)

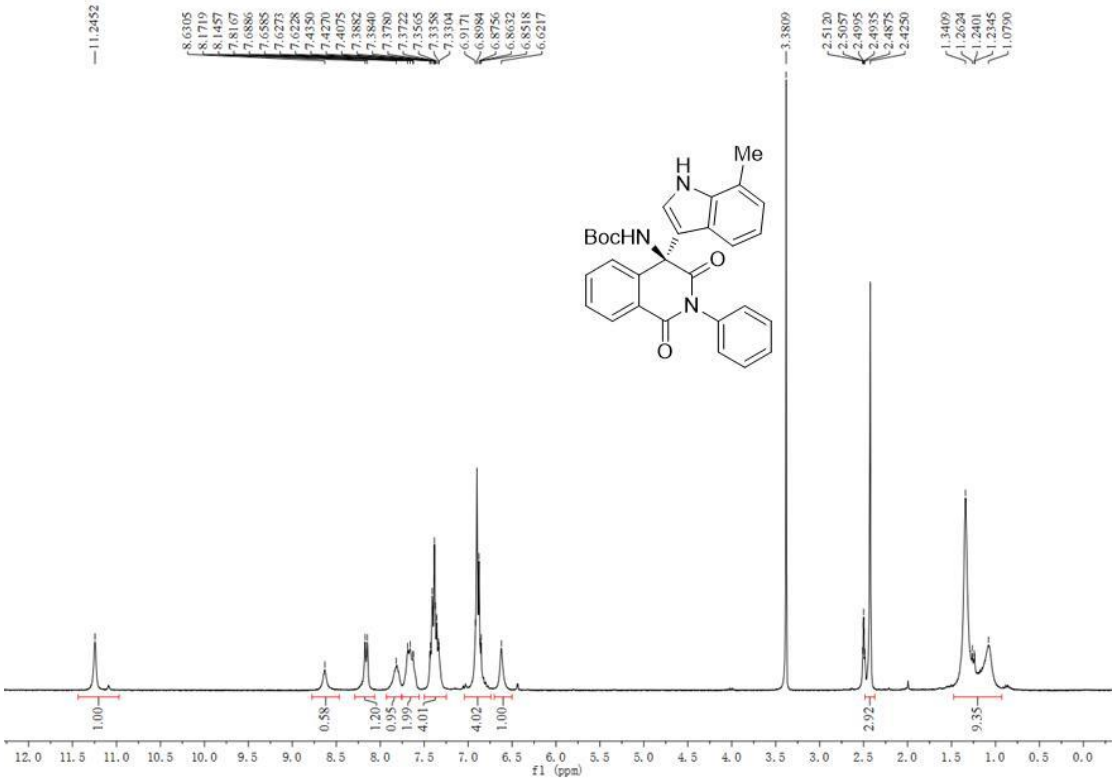
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	5.380	459479	56.35	6433884	49.84
2	7.350	355872	43.65	6475084	50.16
Totals		815351	100.00	12908968	100.00

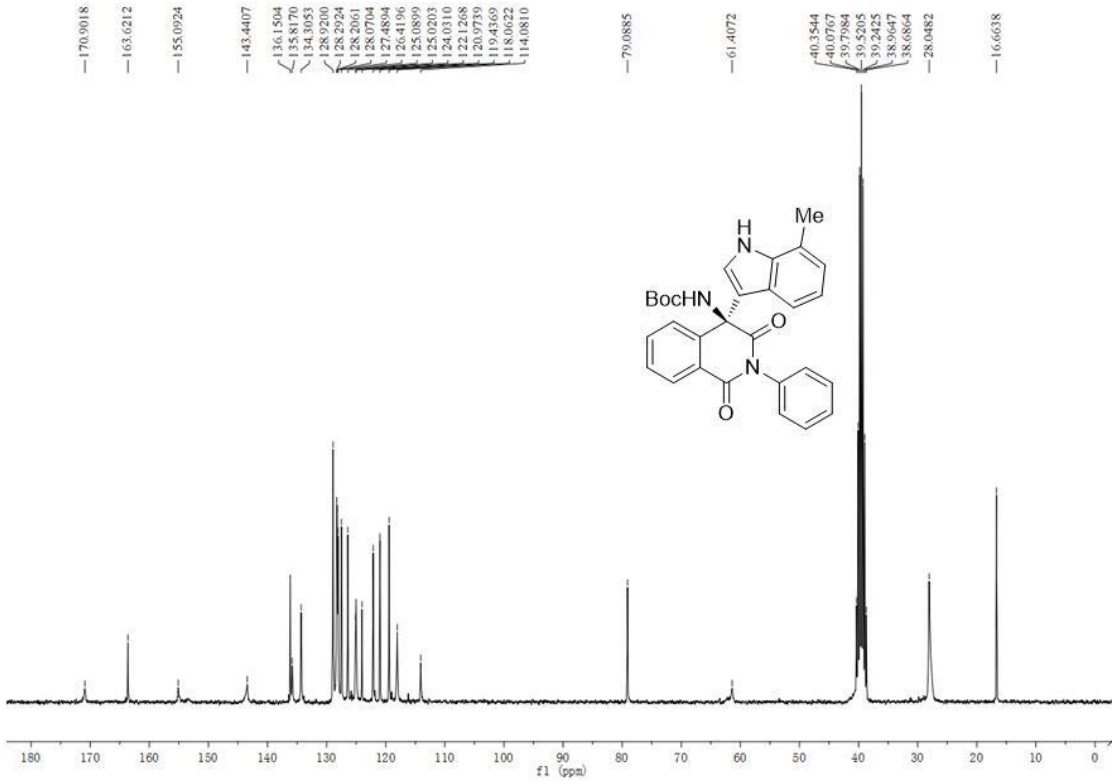


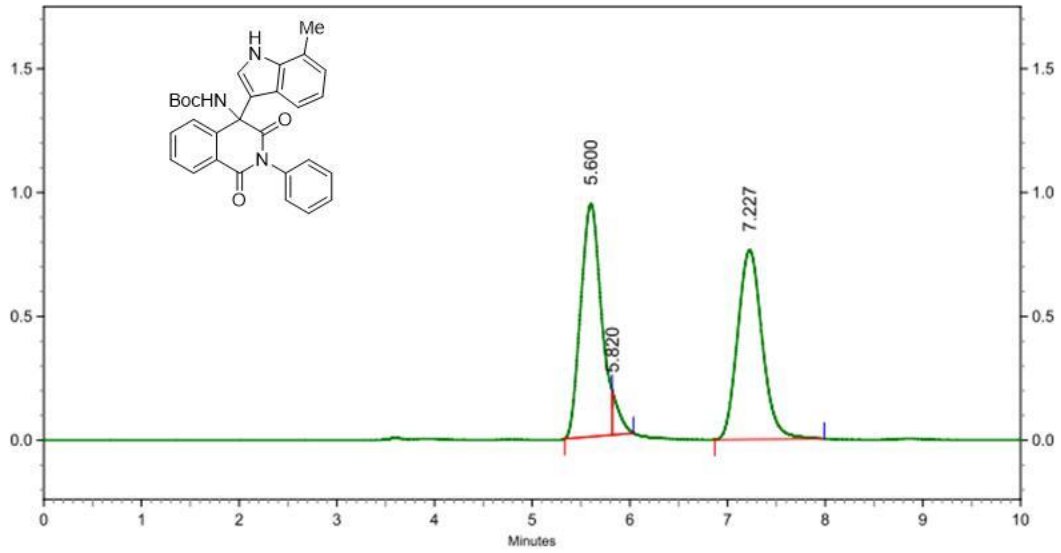
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	5.327	5431	0.32	54650	0.18
2	7.250	1680246	99.68	29873756	99.82
Totals		1685677	100.00	29928406	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 3ae

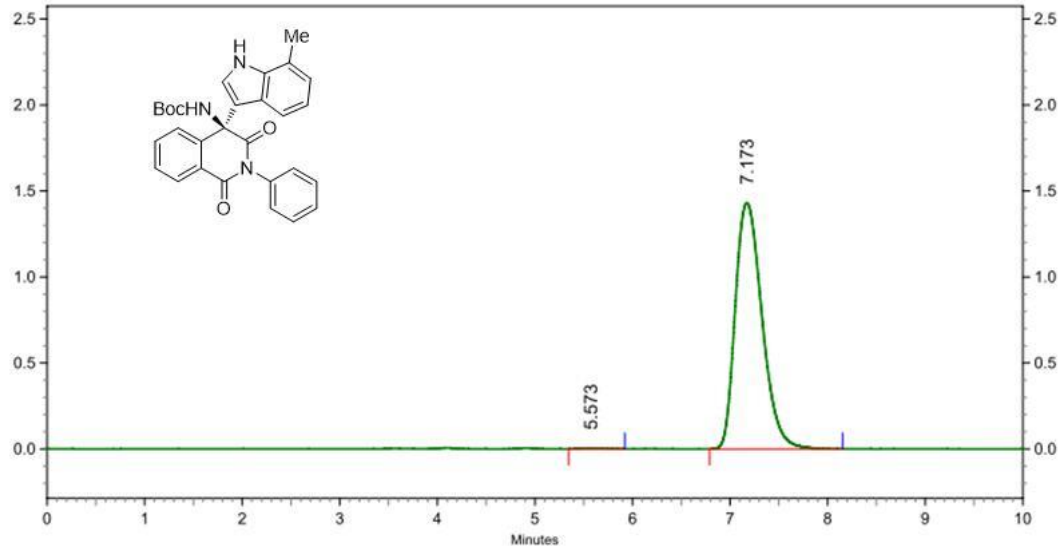






Detector A (254nm)

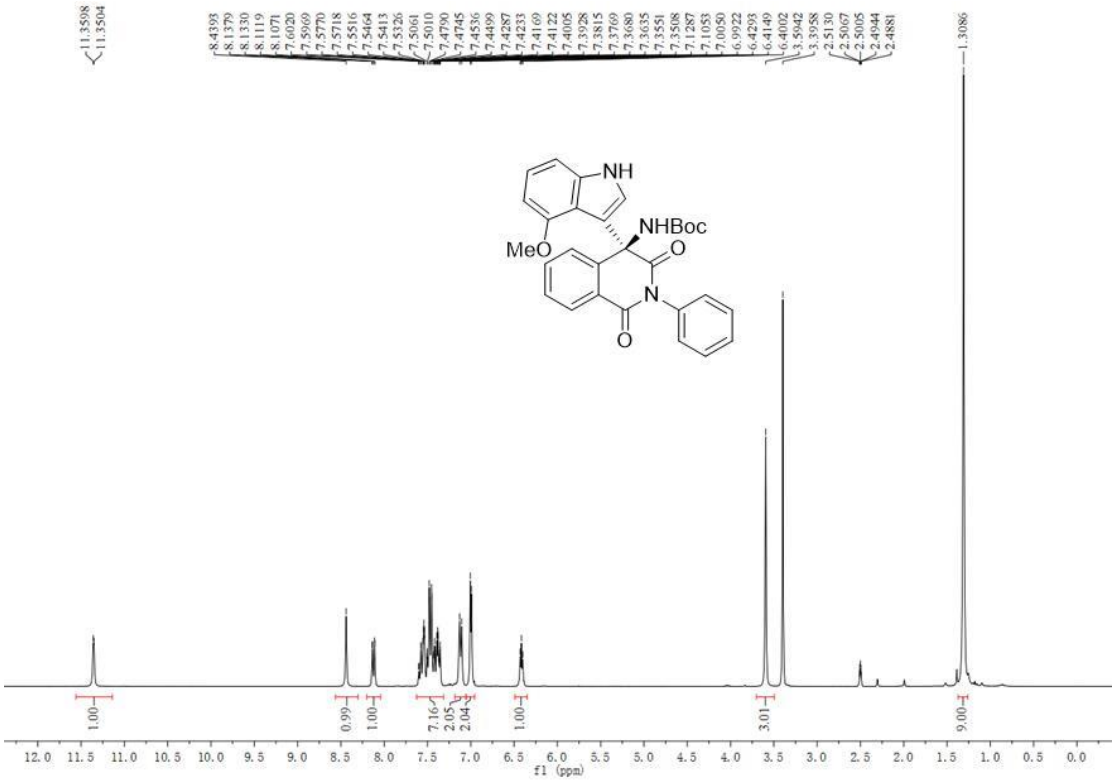
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	5.600	941044	49.99	13592203	48.83
2	5.820	177183	9.41	864294	3.10
3	7.227	764288	40.60	13381466	48.07
Totals		1882515	100.00	27837963	100.00

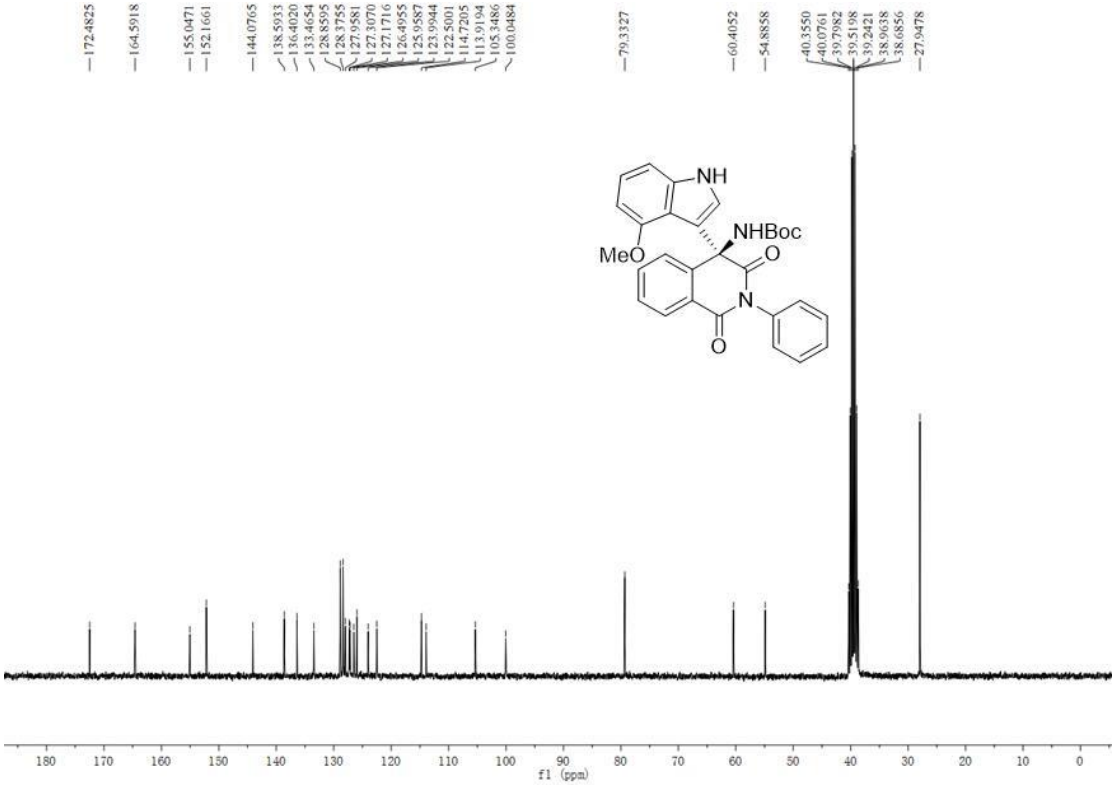


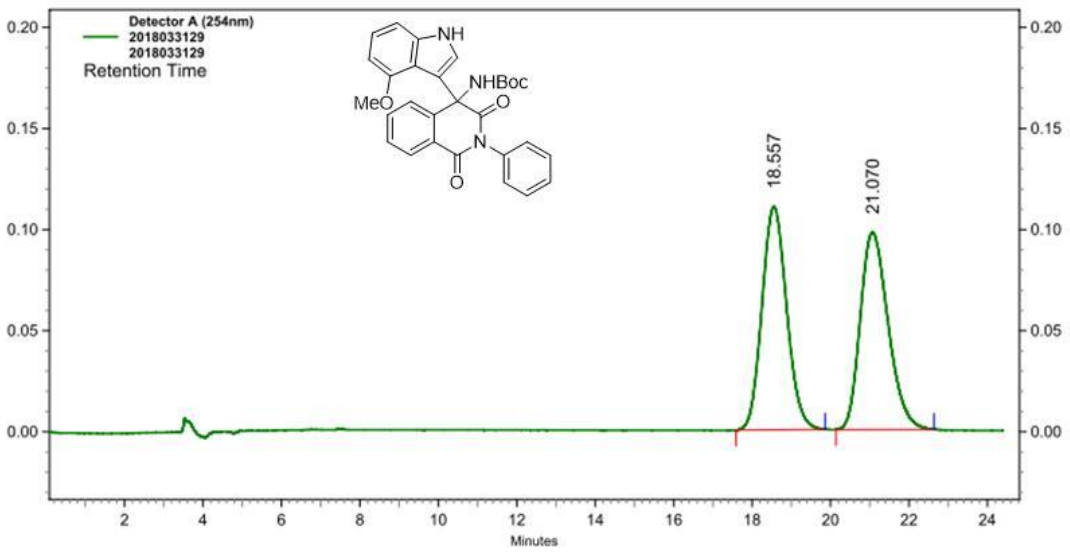
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	5.573	4825	0.34	87593	0.32
2	7.173	1430181	99.66	27273072	99.68
Totals		1435006	100.00	27360665	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 3af

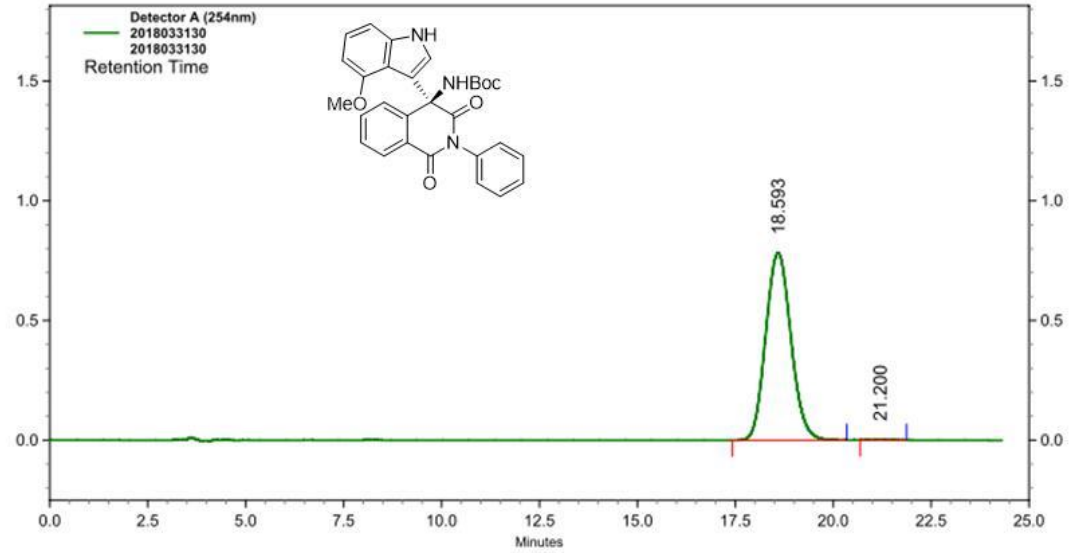






Detector A (254nm)

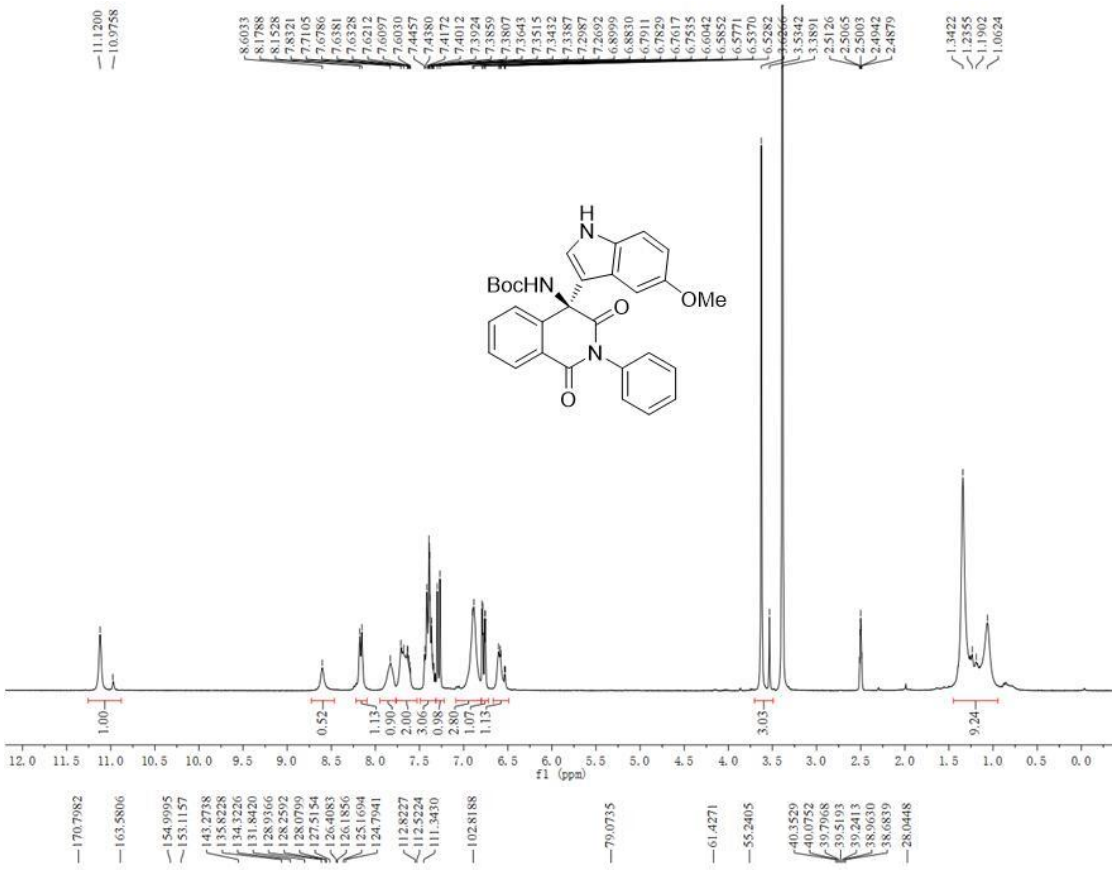
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	18.557	110267	53.06	4831844	50.06
2	21.070	97542	46.94	4821031	49.94
Totals		207809	100.00	9652875	100.00

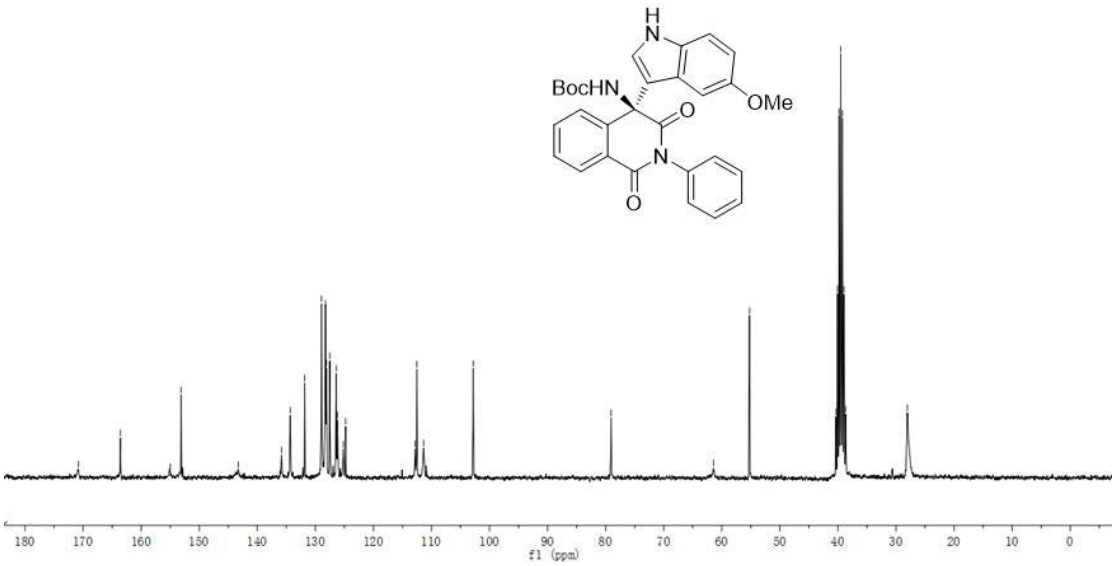


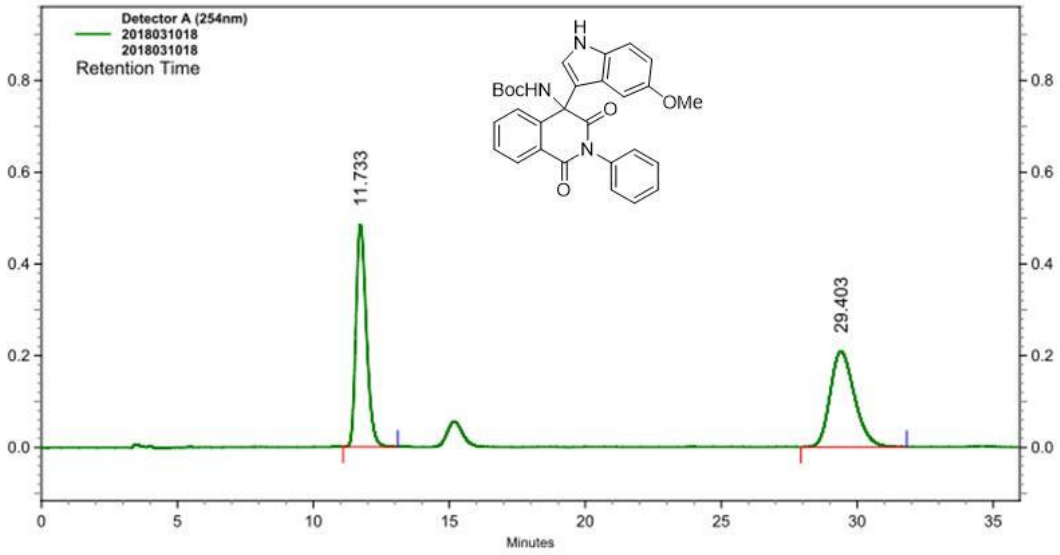
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	18.593	782259	99.68	35058033	99.71
2	21.200	2550	0.32	100438	0.29
Totals		784809	100.00	35158471	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 3ag

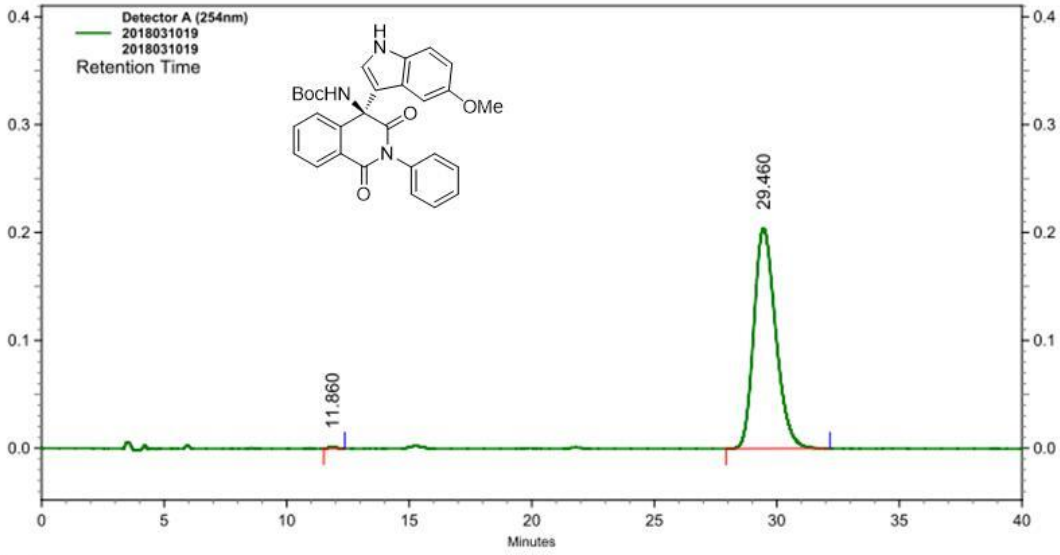






Detector A (254nm)

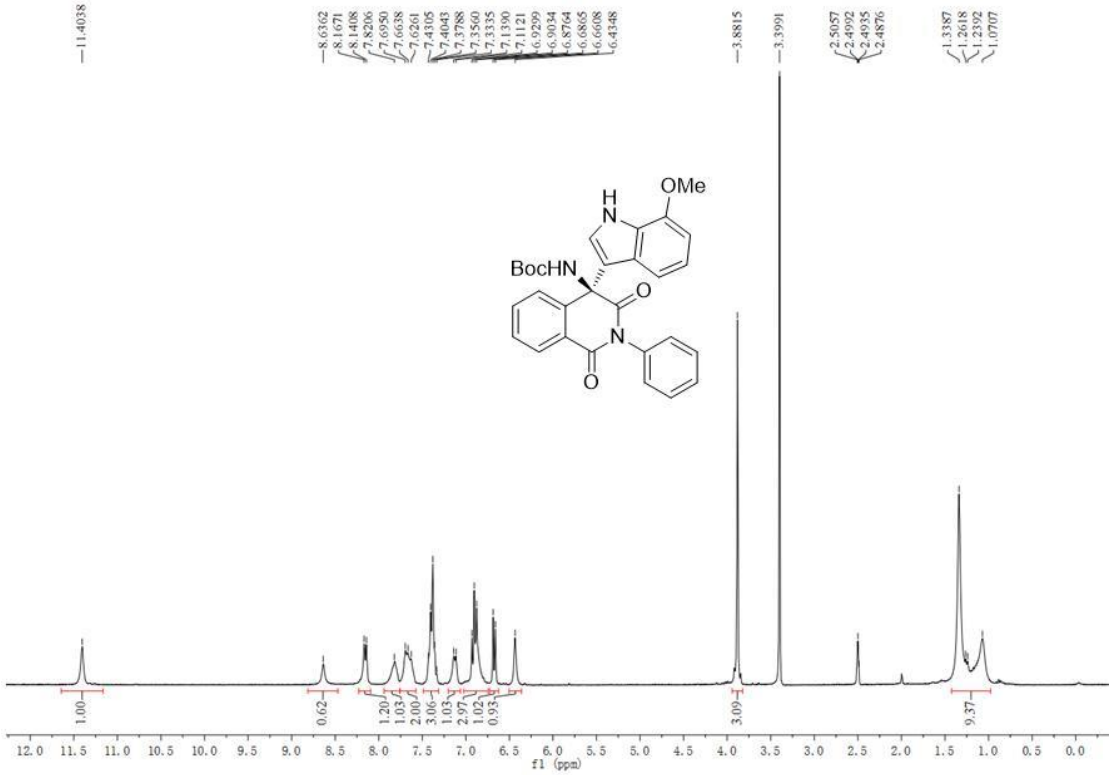
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	11.733	483139	69.89	12880068	49.88
2	29.403	208166	30.11	12941815	50.12
Totals		691305	100.00	25821883	100.00

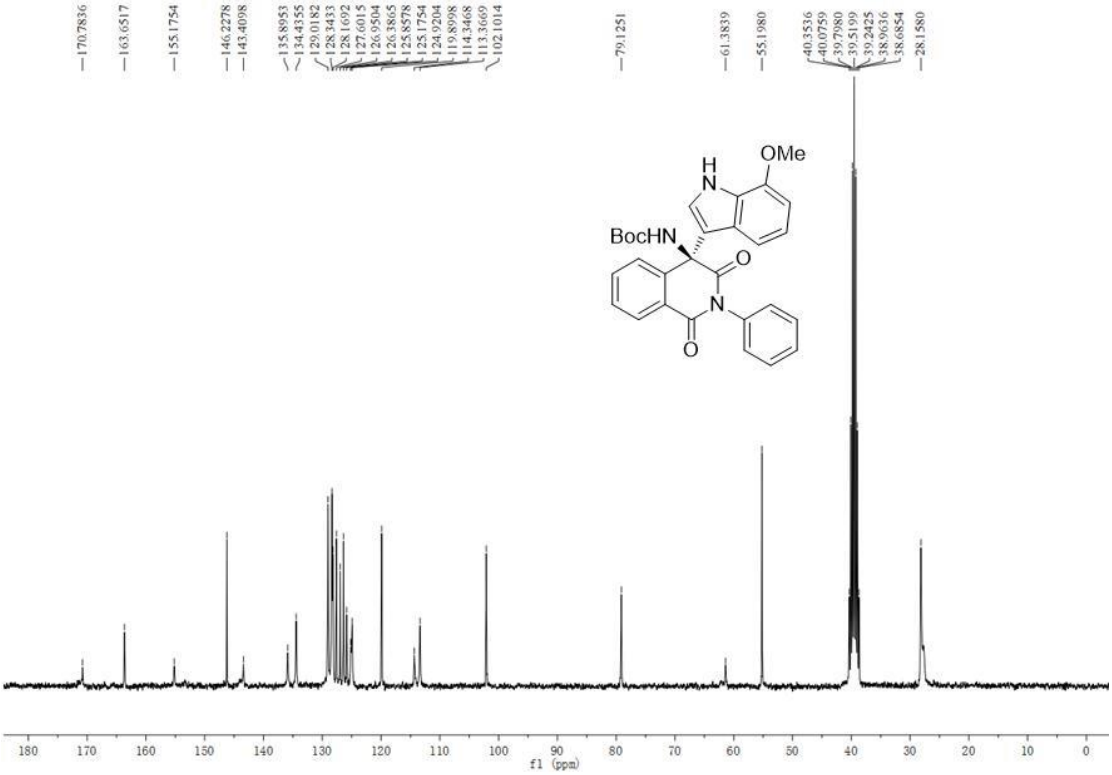


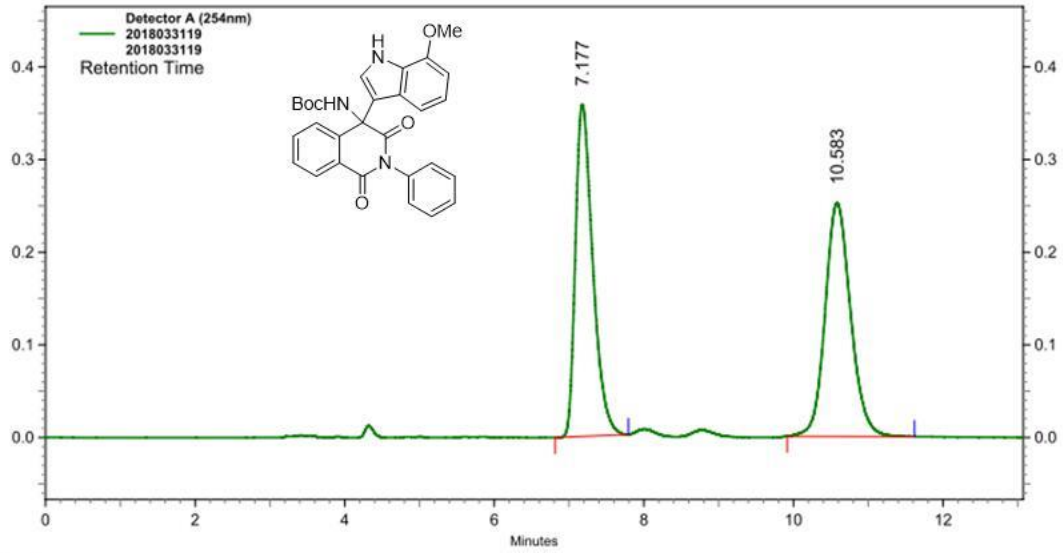
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	11.860	1303	0.63	30260	0.24
2	29.460	204380	99.37	12651549	99.76
Totals		205683	100.00	12681809	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 3ah

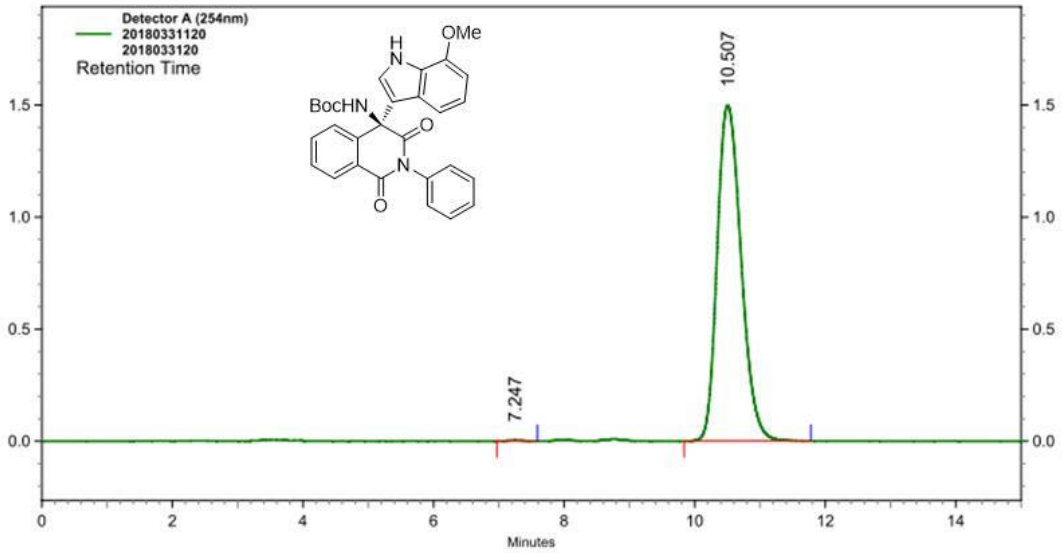






Detector A (254nm)

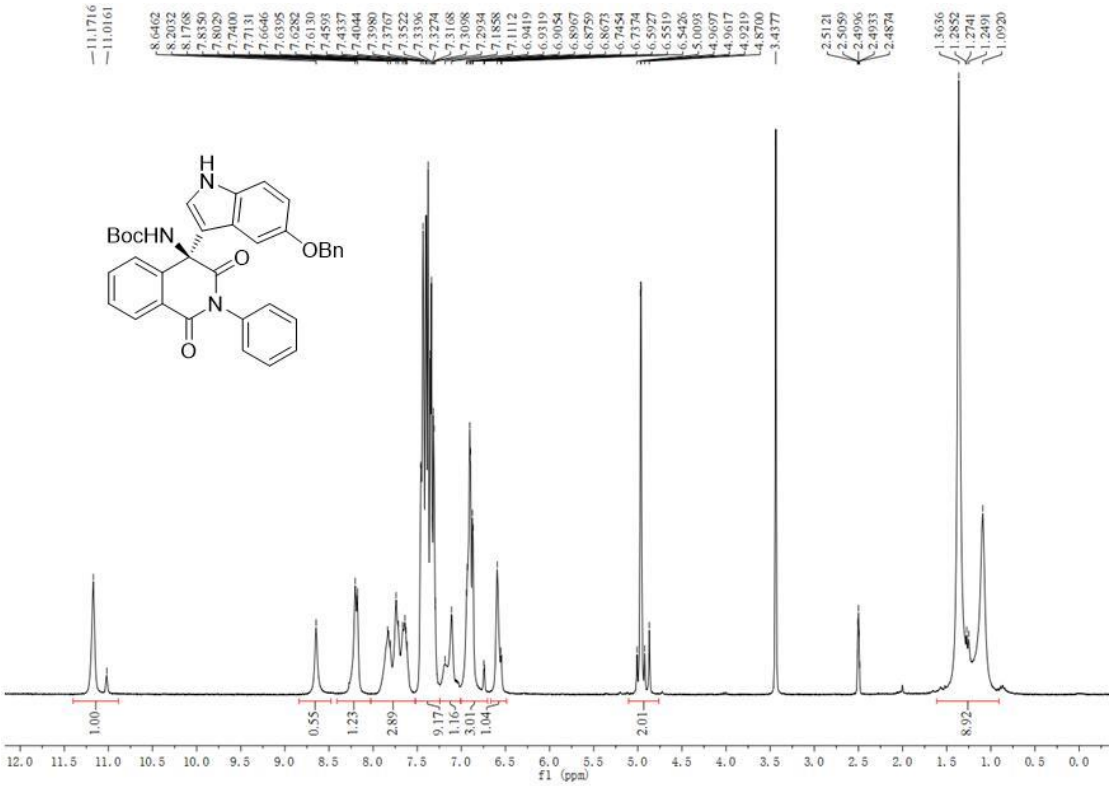
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	7.177	358230	58.69	5771035	49.18
2	10.583	252118	41.31	5964415	50.82
Totals		610348	100.00	11735450	100.00

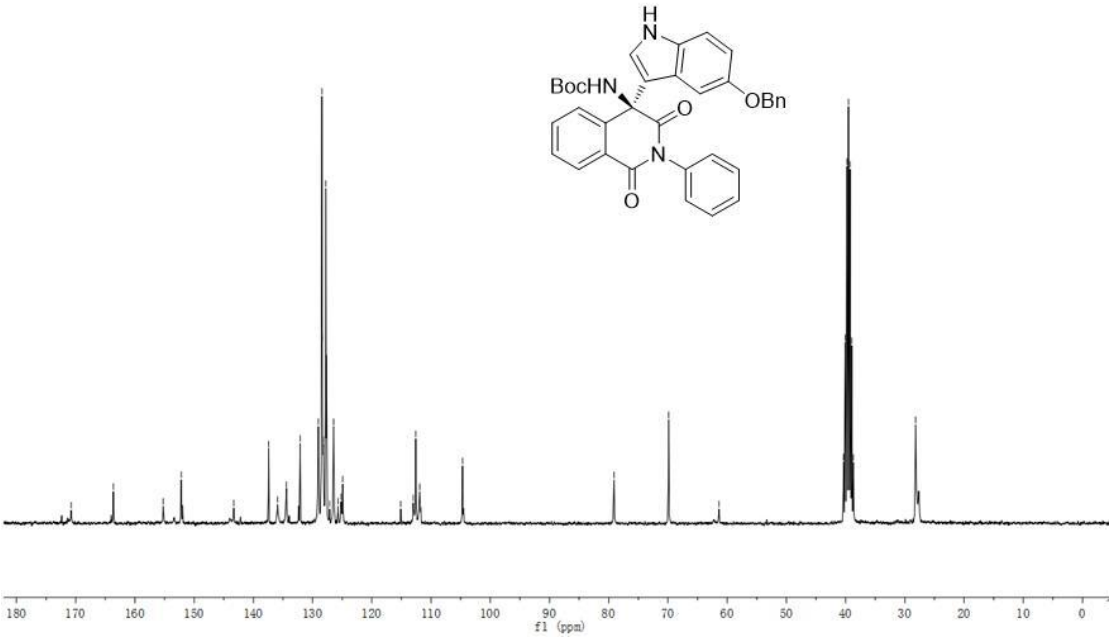


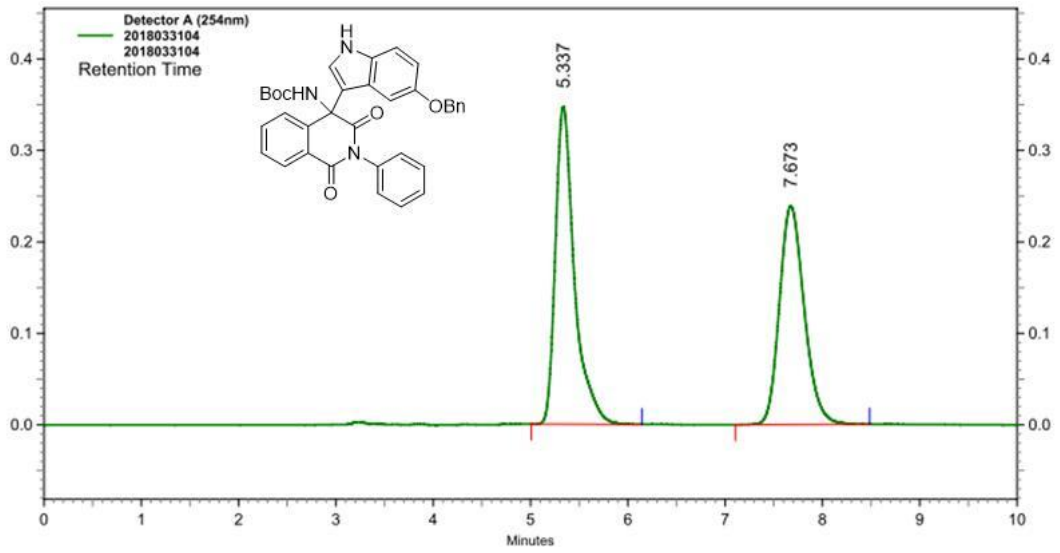
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	7.247	3121	0.21	53580	0.14
2	10.507	1497619	99.79	38187856	99.86
Totals		1500740	100.00	38241436	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 3ai

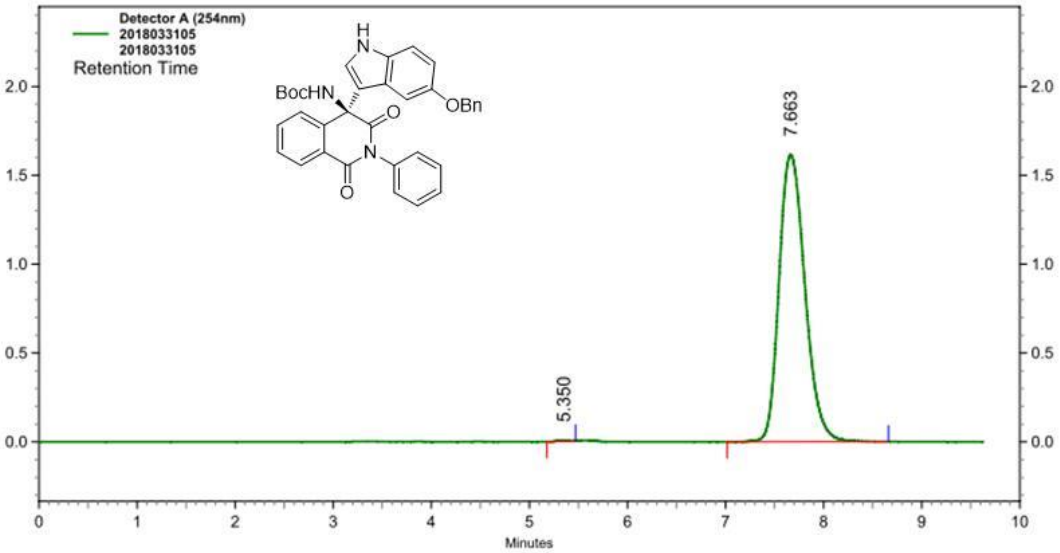






Detector A (254nm)

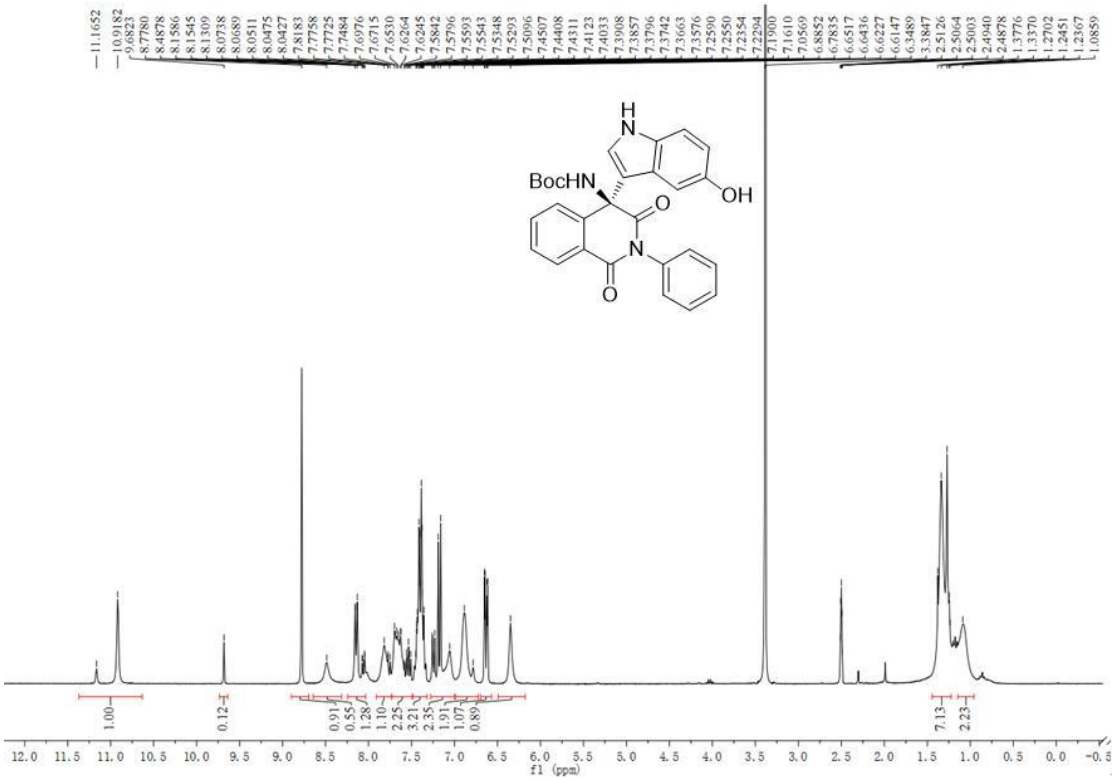
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	5.337	347120	59.25	4729397	52.78
2	7.673	238773	40.75	4231379	47.22
Totals		585893	100.00	8960776	100.00

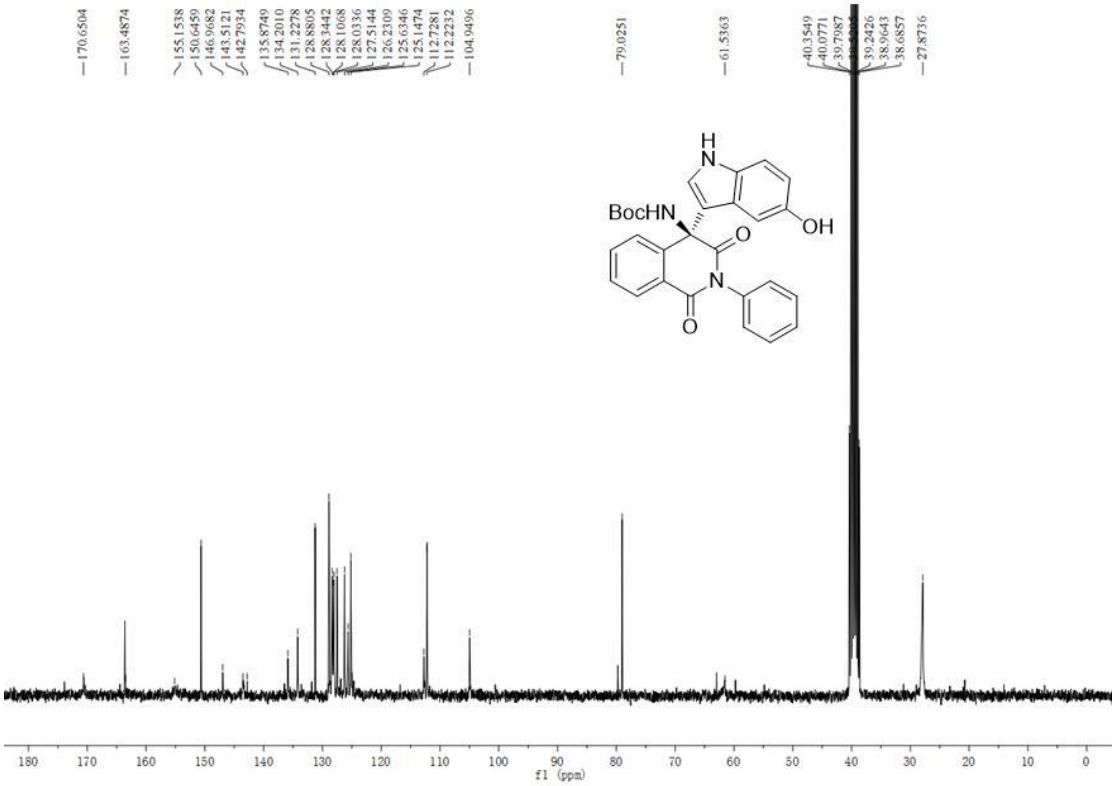


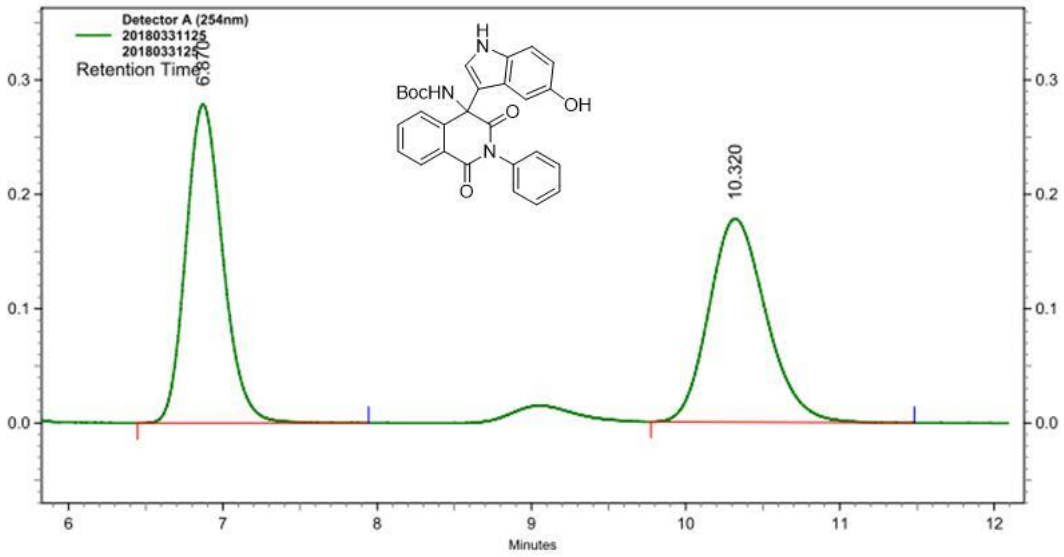
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	5.350	2971	0.18	22860	0.08
2	7.663	1613196	99.82	29587427	99.92
Totals		1616167	100.00	29610287	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 3aj

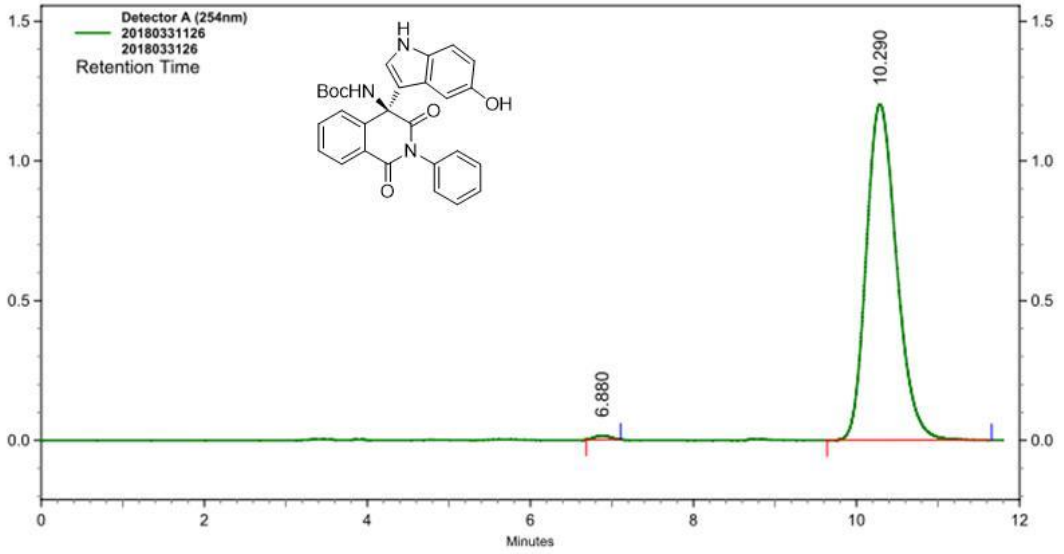






Detector A (254nm)

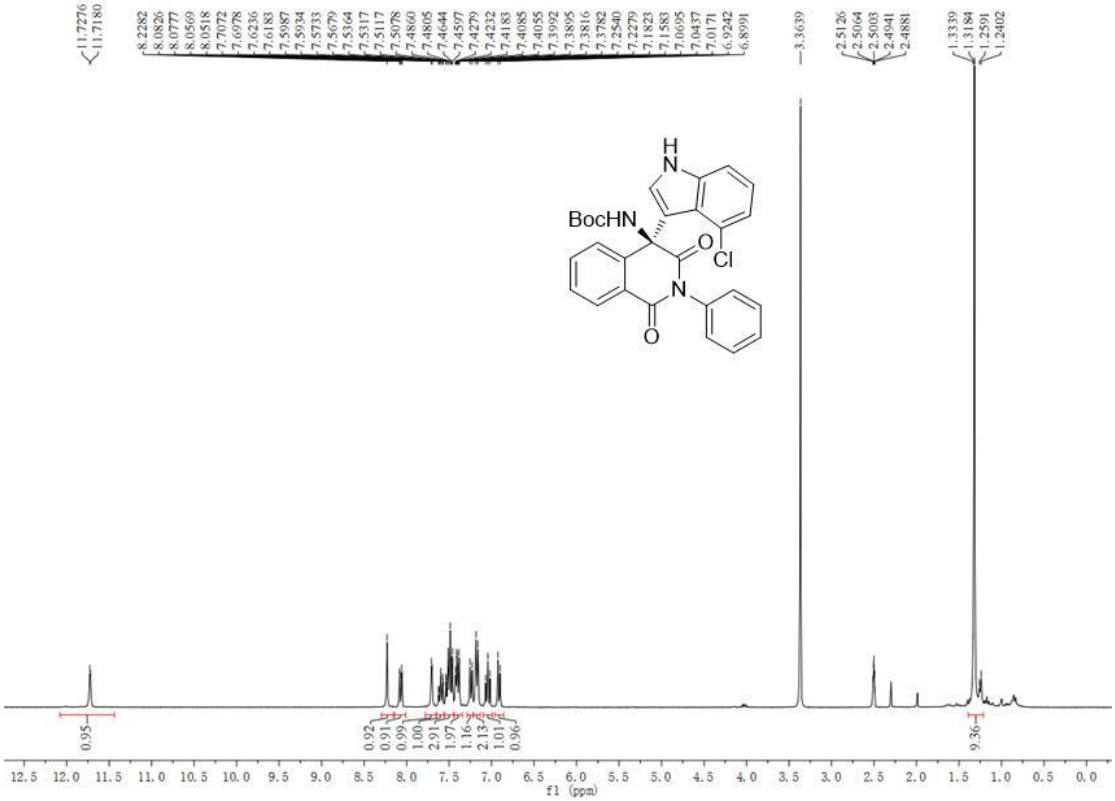
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	6.870	278560	61.03	4623562	50.23
2	10.320	177841	38.97	4581014	49.77
Totals		456401	100.00	9204576	100.00

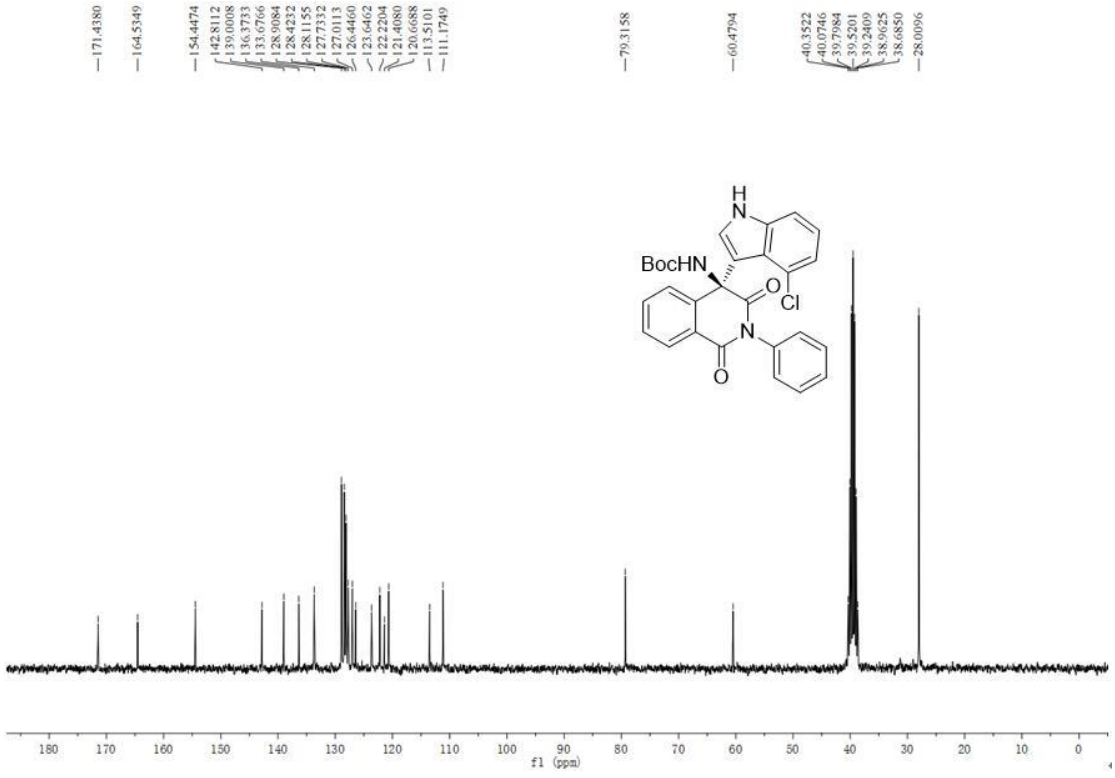


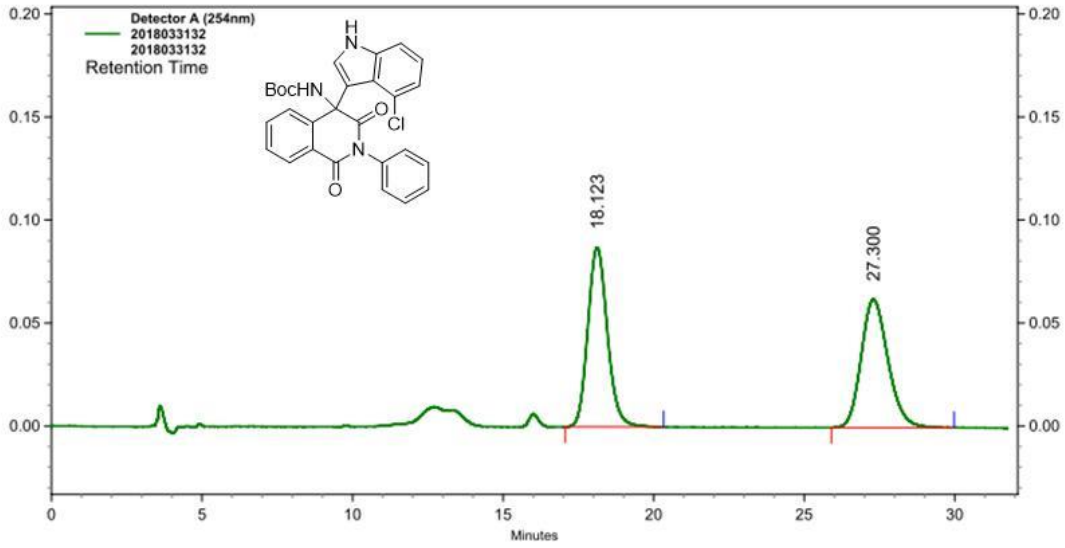
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	6.880	14230	1.17	189579	0.61
2	10.290	1201583	98.83	31009976	99.39
Totals		1215813	100.00	31199555	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 3ak

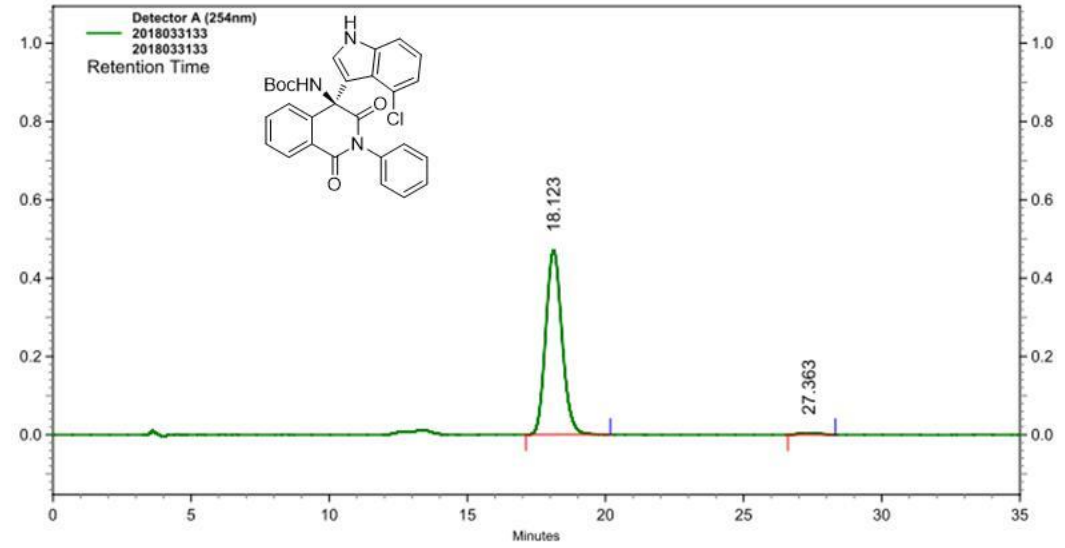






Detector A (254nm)

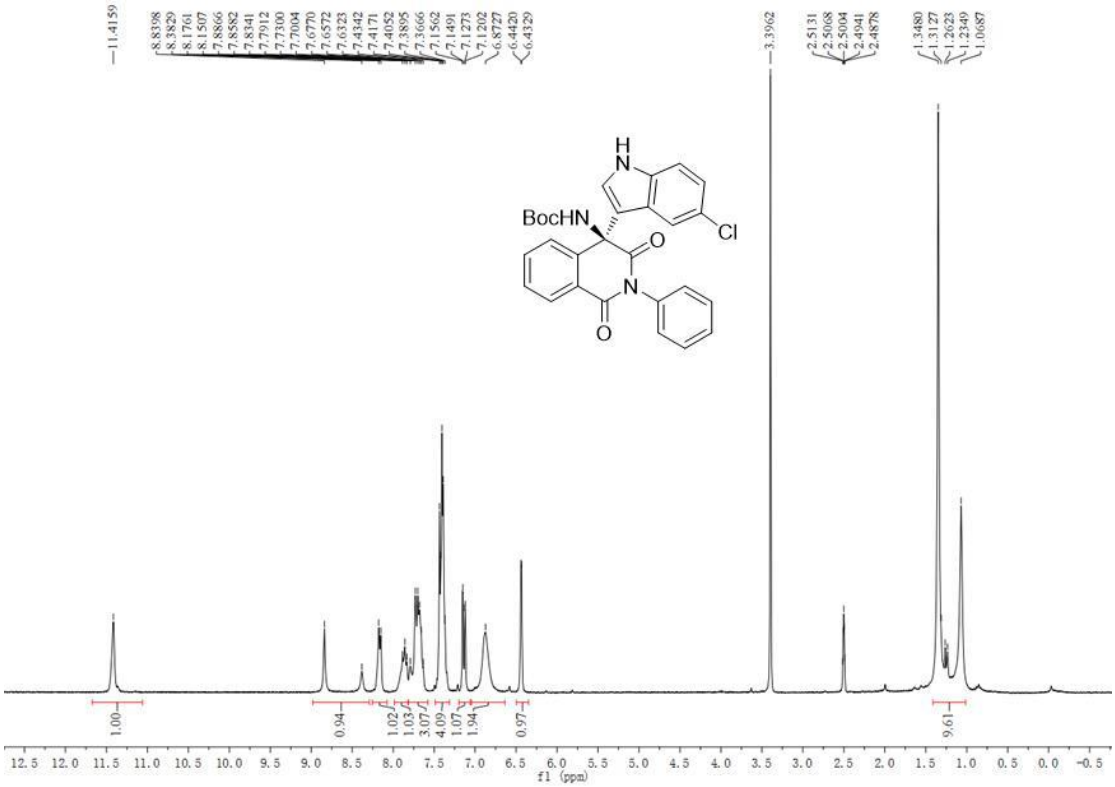
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	18.123	87096	58.31	3942225	50.55
2	27.300	62274	41.69	3856403	49.45
Totals		149370	100.00	7798628	100.00

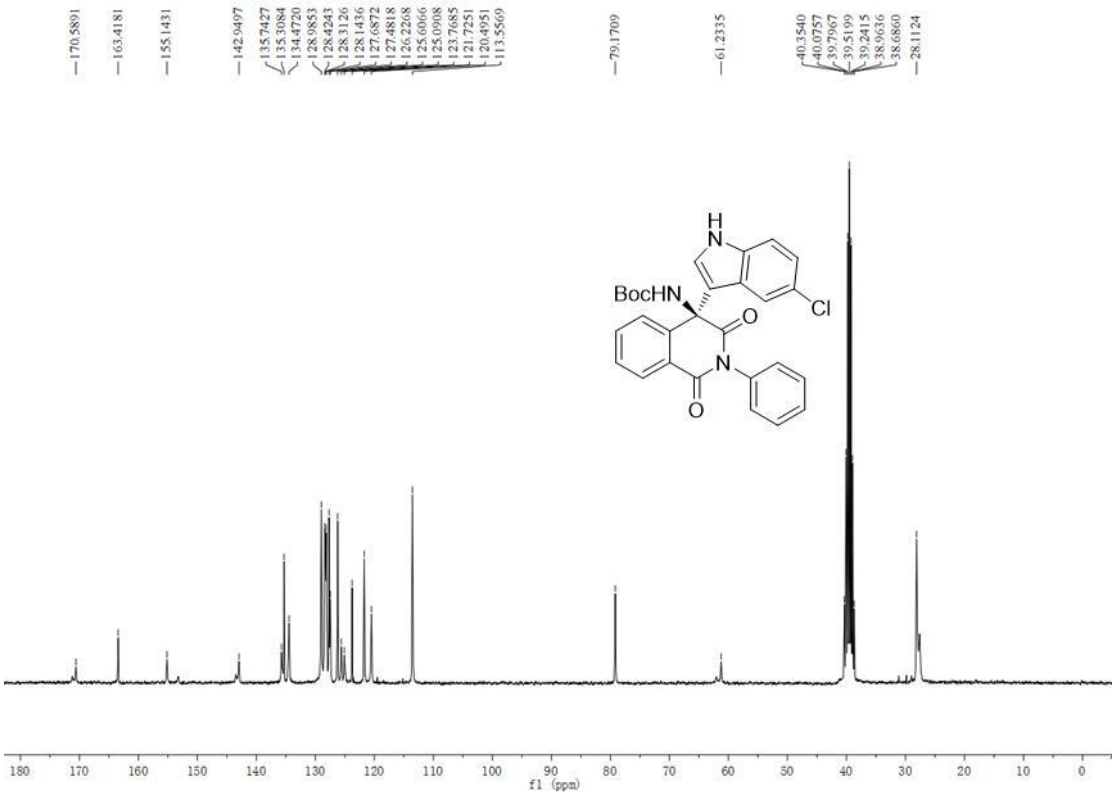


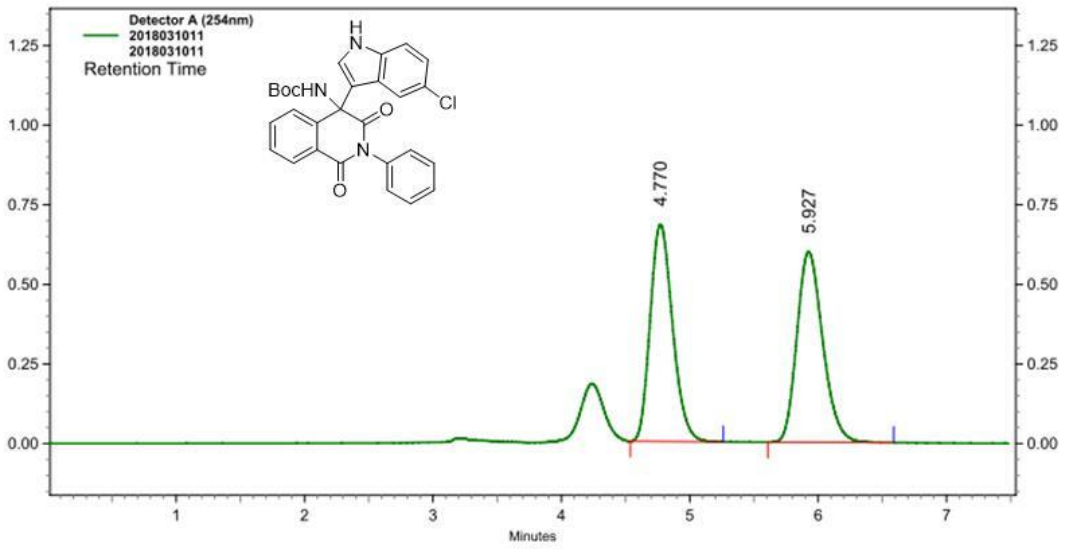
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	18.123	470069	99.16	19313250	98.93
2	27.363	3993	0.84	209839	1.07
Totals		474062	100.00	19523089	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 3al

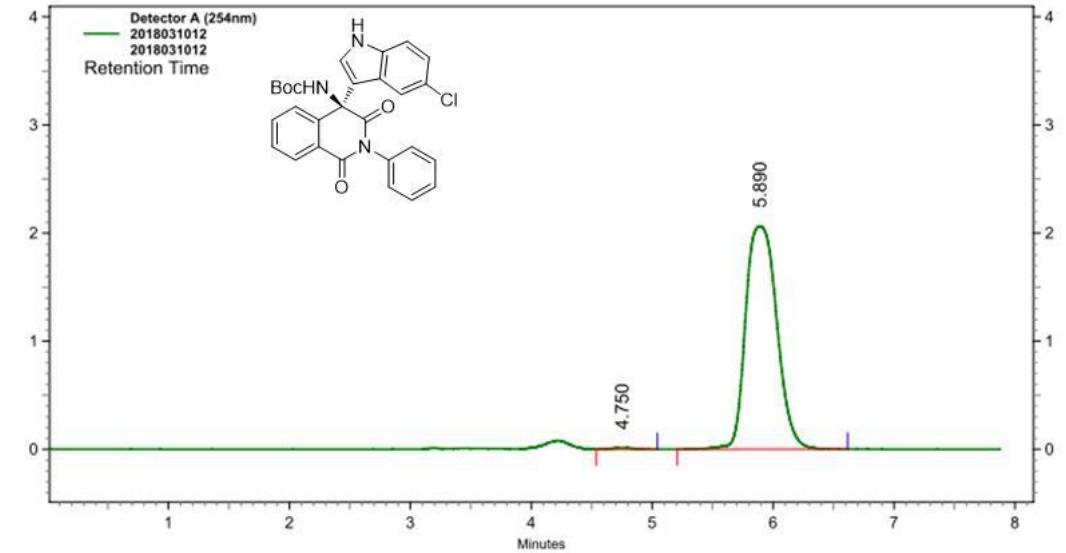






Detector A (254nm)

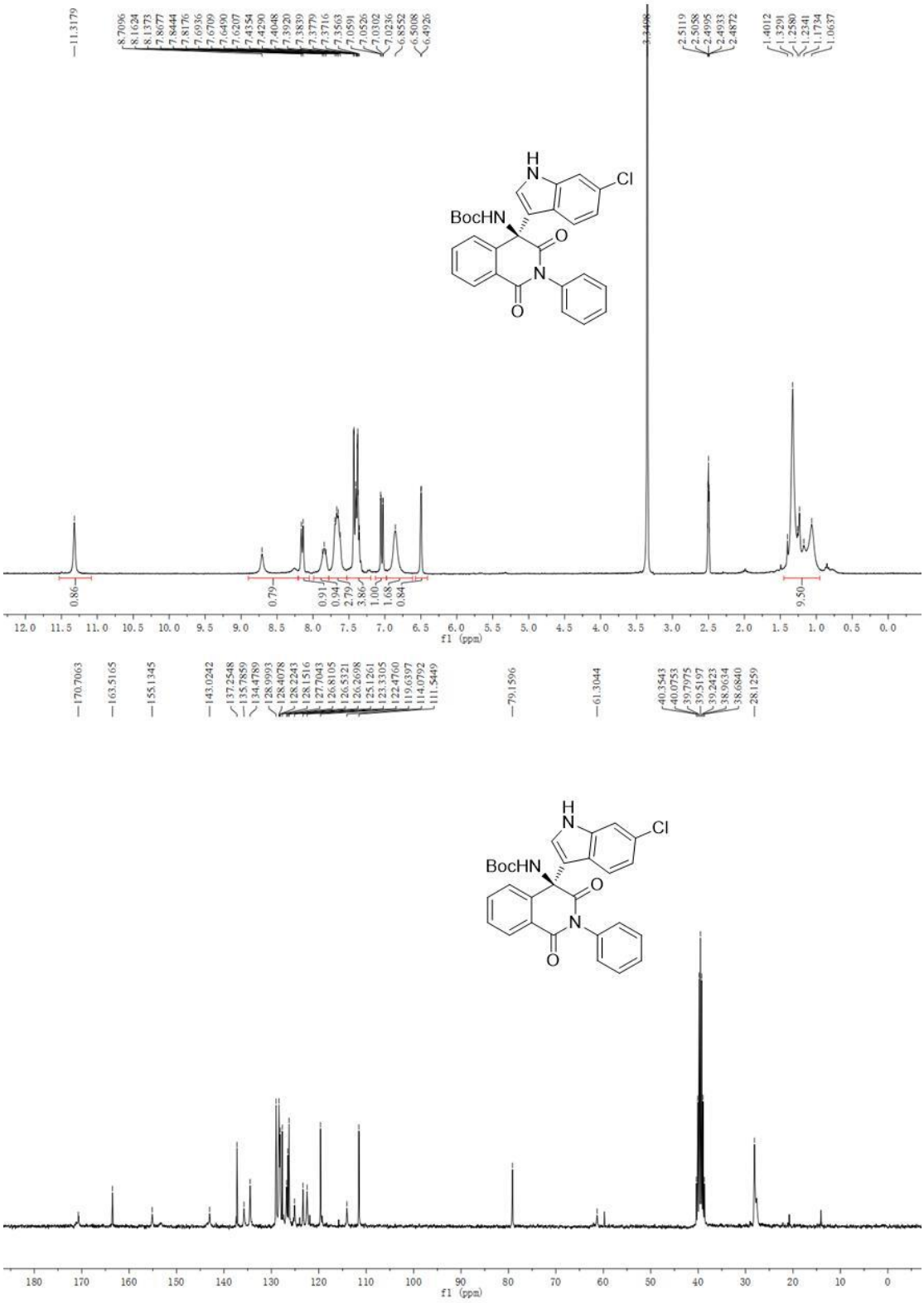
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	4.770	681893	53.27	8271049	49.68
2	5.927	598176	46.73	8377122	50.32
Totals		1280069	100.00	16648171	100.00

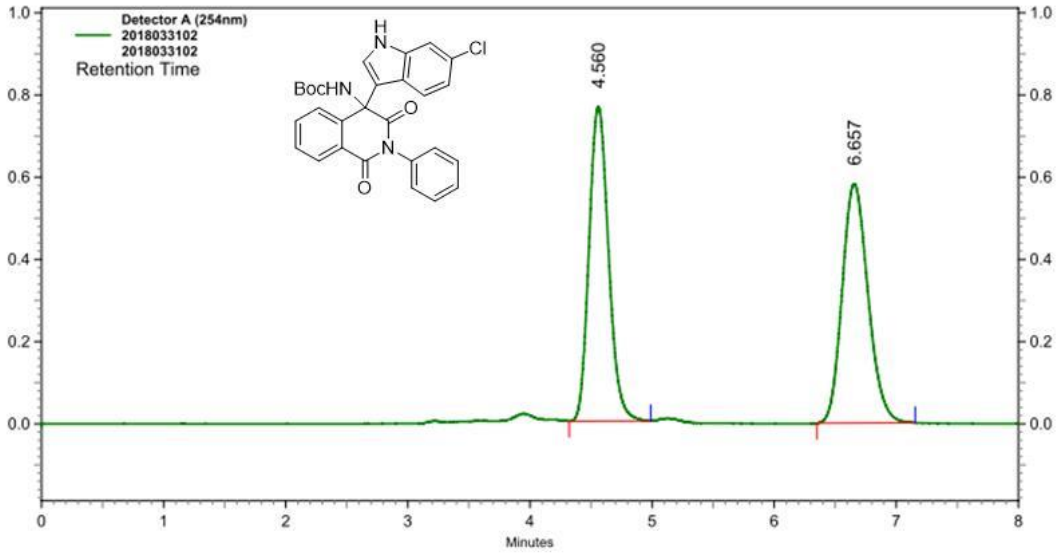


Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	4.750	13103	0.63	161928	0.44
2	5.890	2063176	99.37	36974310	99.56
Totals		2076279	100.00	37136238	100.00

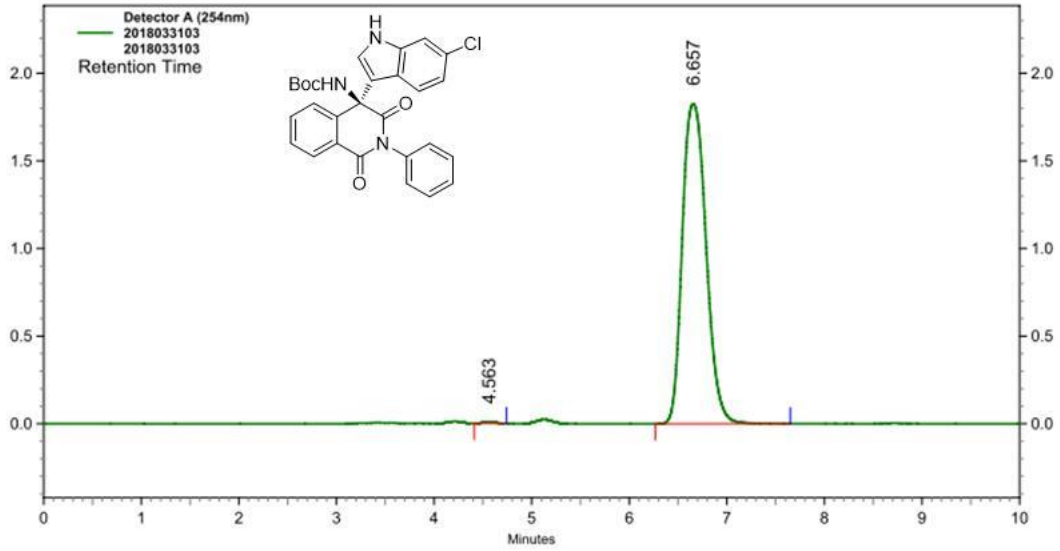
^{1}H NMR, ^{13}C NMR and HPLC spectra of 3am





Detector A (254nm)

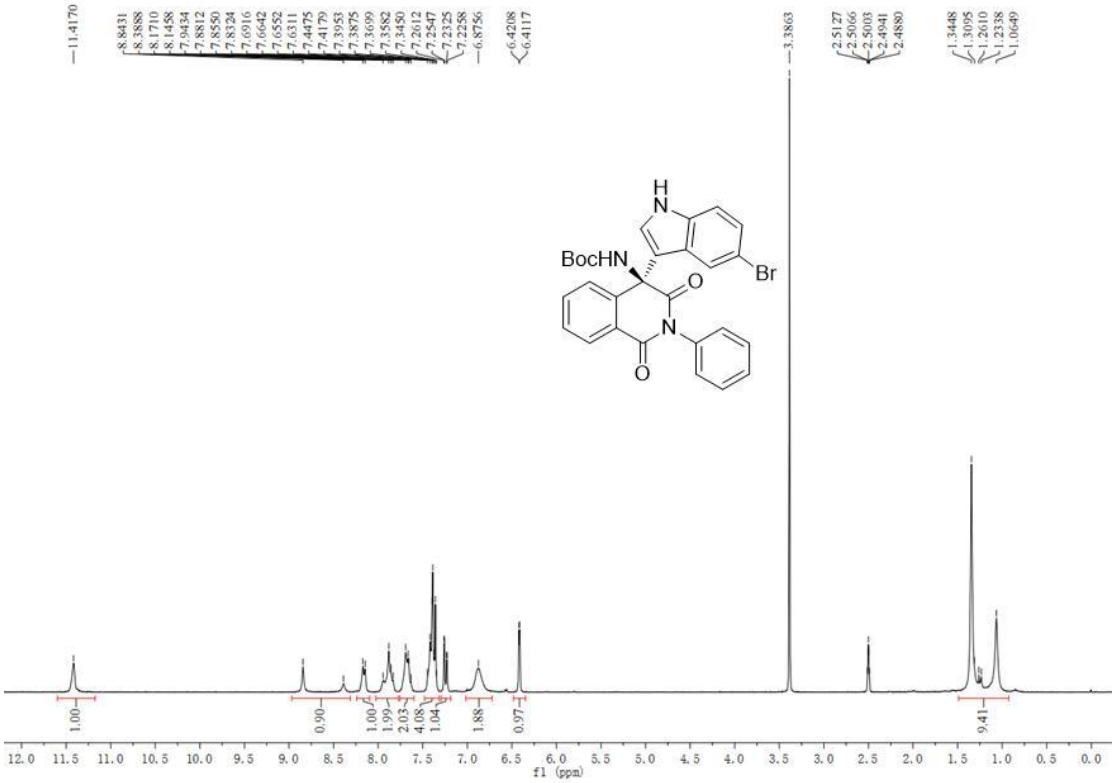
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	4.560	765318	56.80	8483701	49.73
2	6.657	582161	43.20	8575796	50.27
Totals		1347479	100.00	17059497	100.00

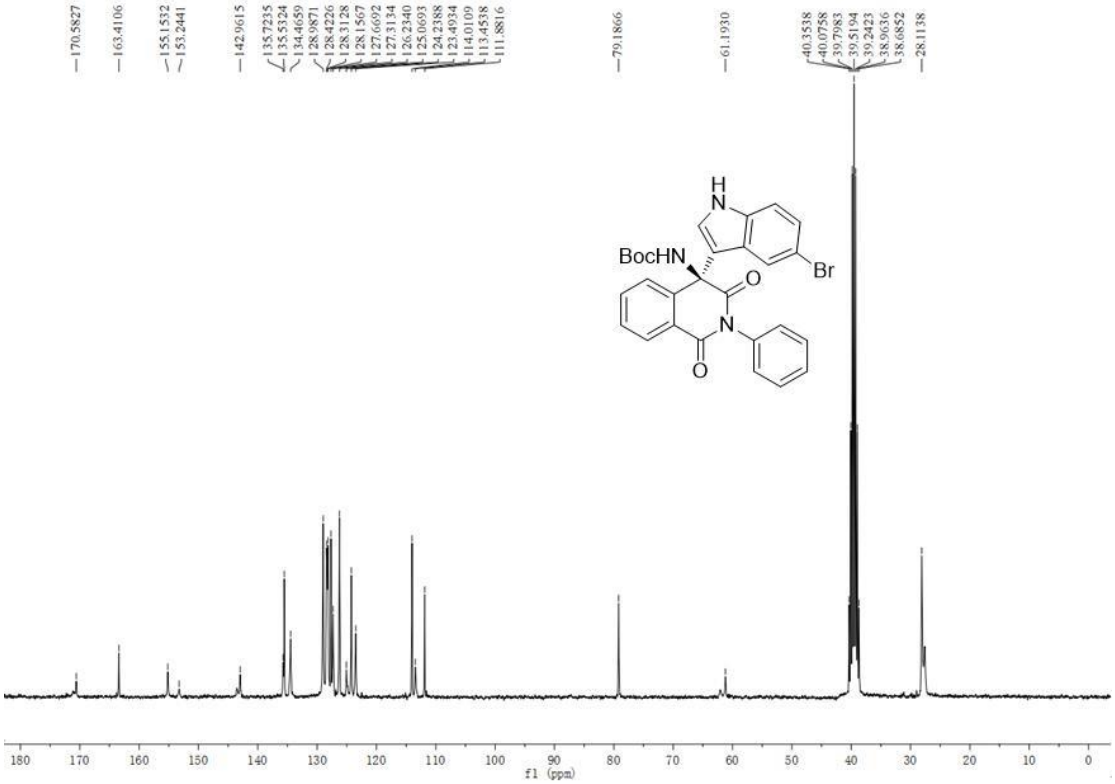


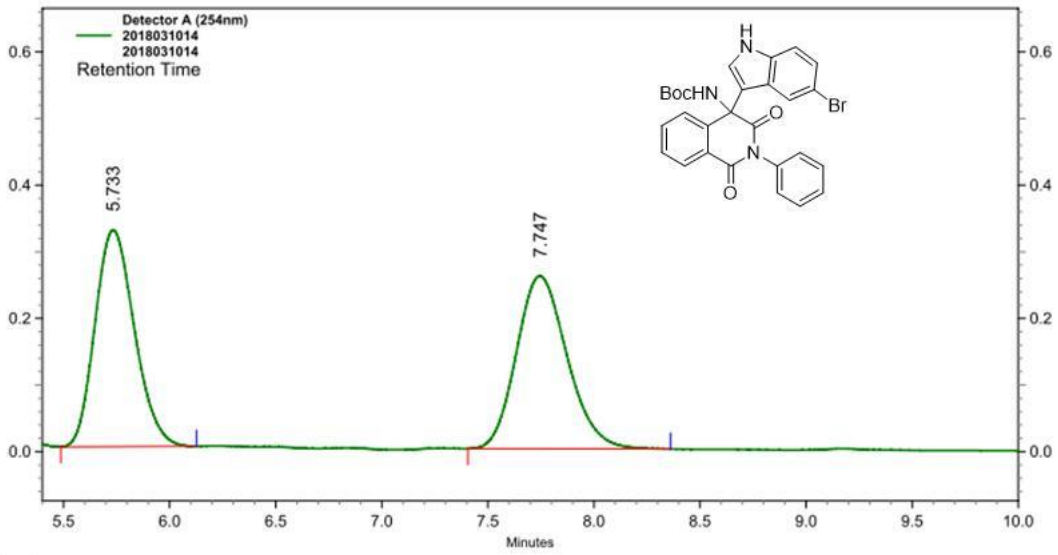
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	4.563	8271	0.45	78363	0.25
2	6.657	1824871	99.55	30881338	99.75
Totals		1833142	100.00	30959701	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 3an

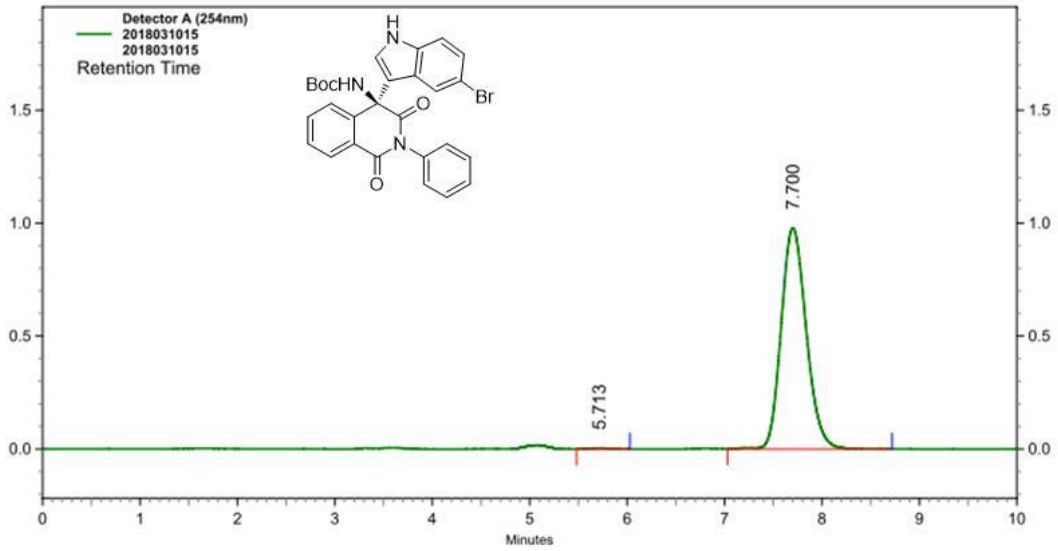






Detector A (254nm)

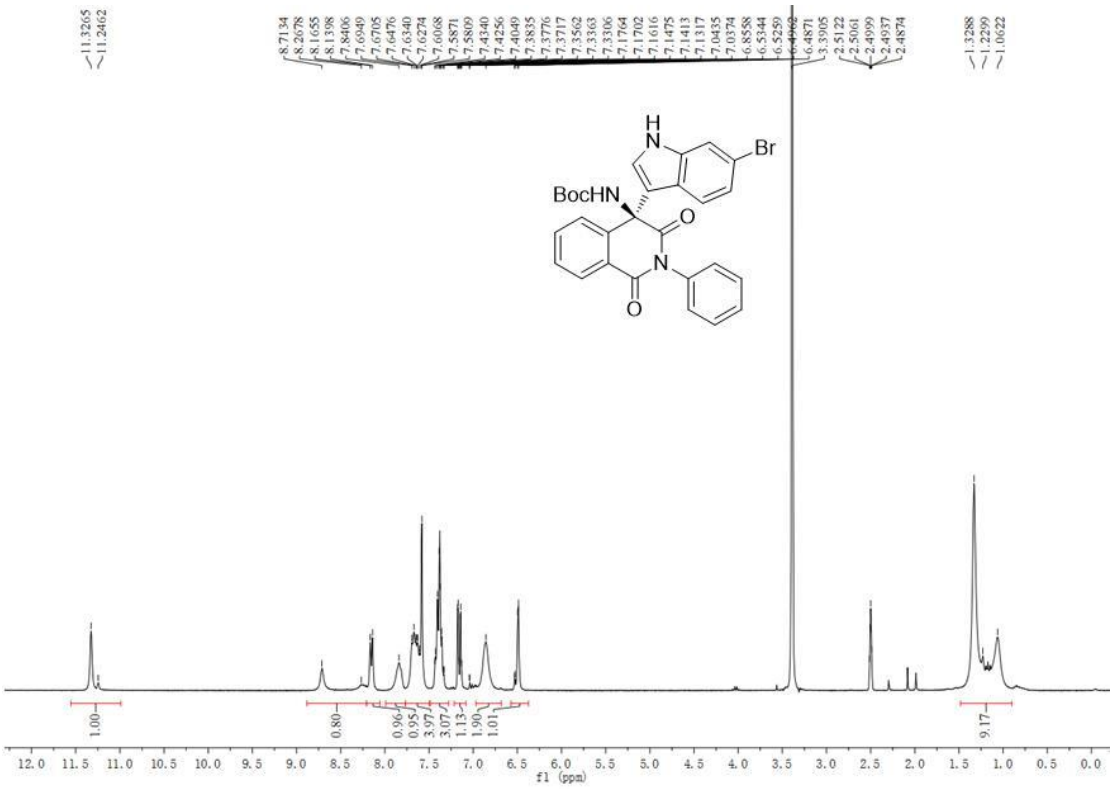
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	5.733	325341	55.64	4194086	49.36
2	7.747	259411	44.36	4303174	50.64
Totals		584752	100.00	8497260	100.00

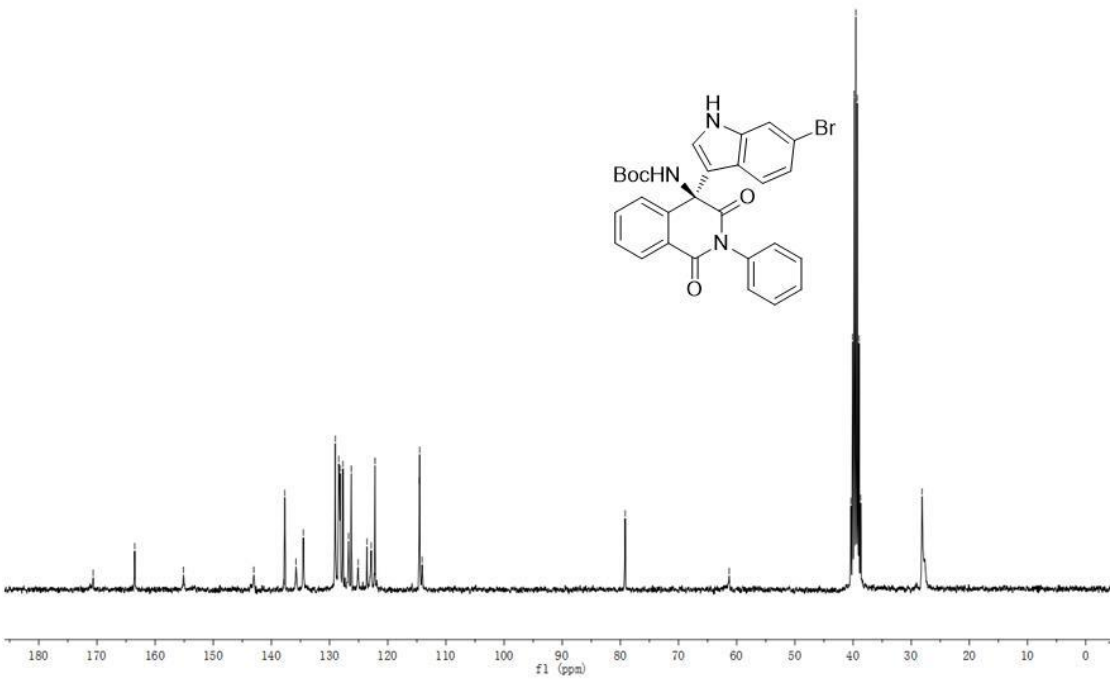


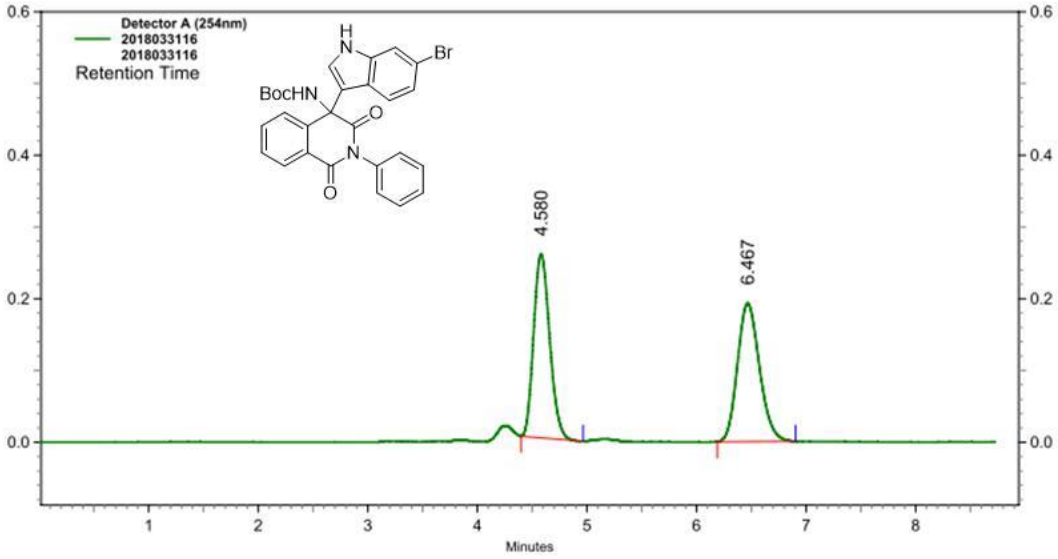
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	5.713	4285	0.44	60324	0.34
2	7.700	977972	99.56	17494467	99.66
Totals		982257	100.00	17554791	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 3ao

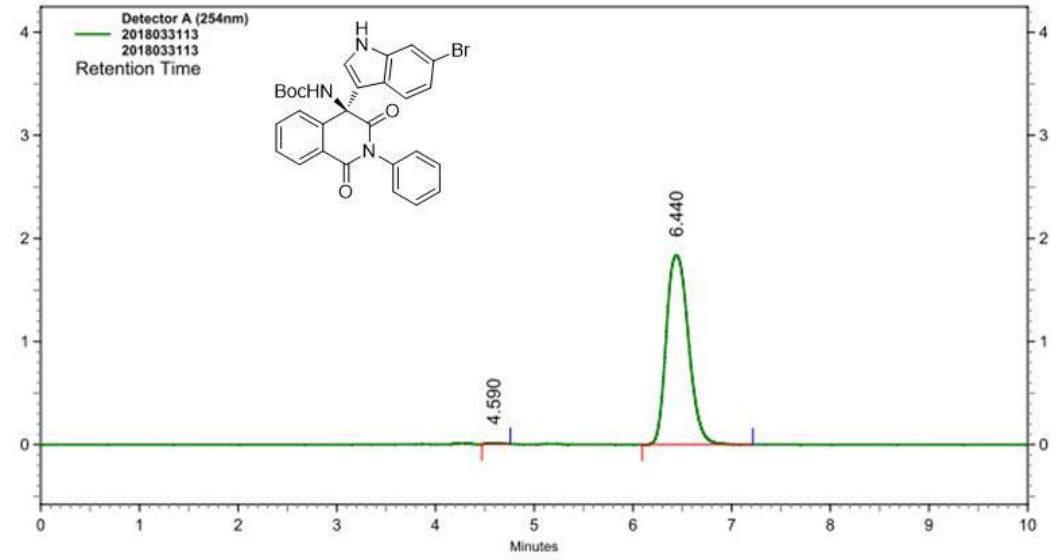






Detector A (254nm)

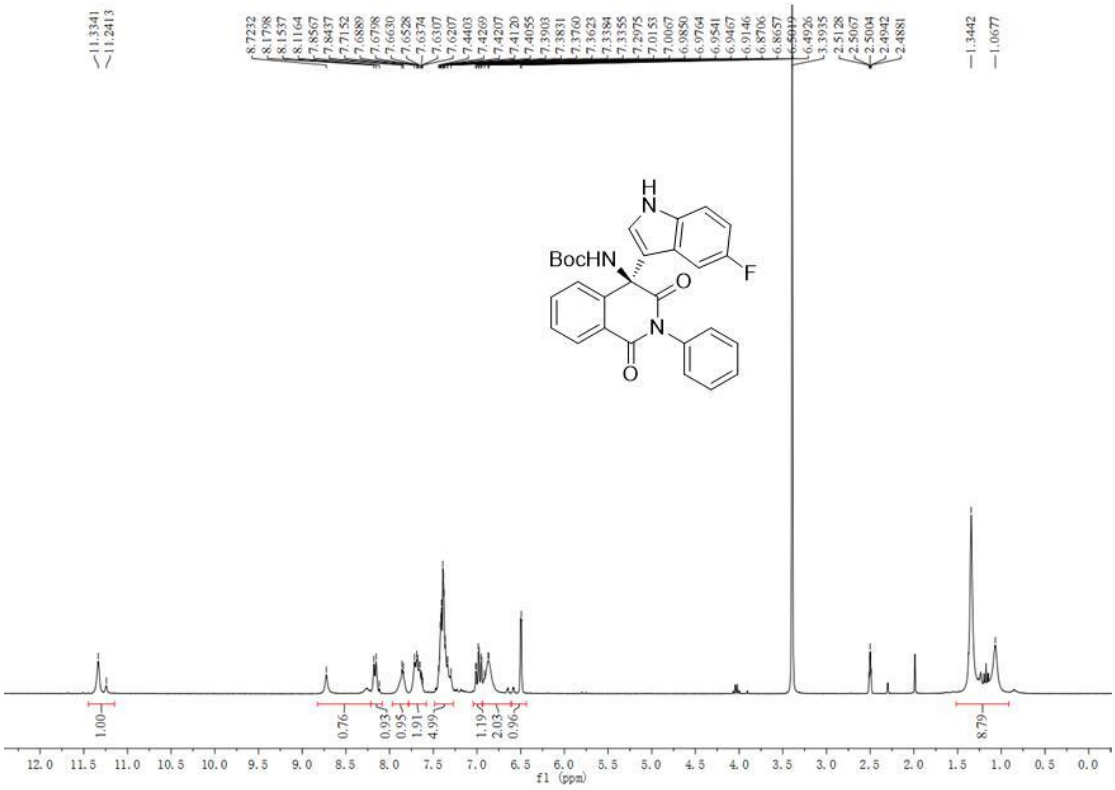
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	4.580	255838	57.04	2608304	49.20
2	6.467	192658	42.96	2693560	50.80
Totals		448496	100.00	5301864	100.00

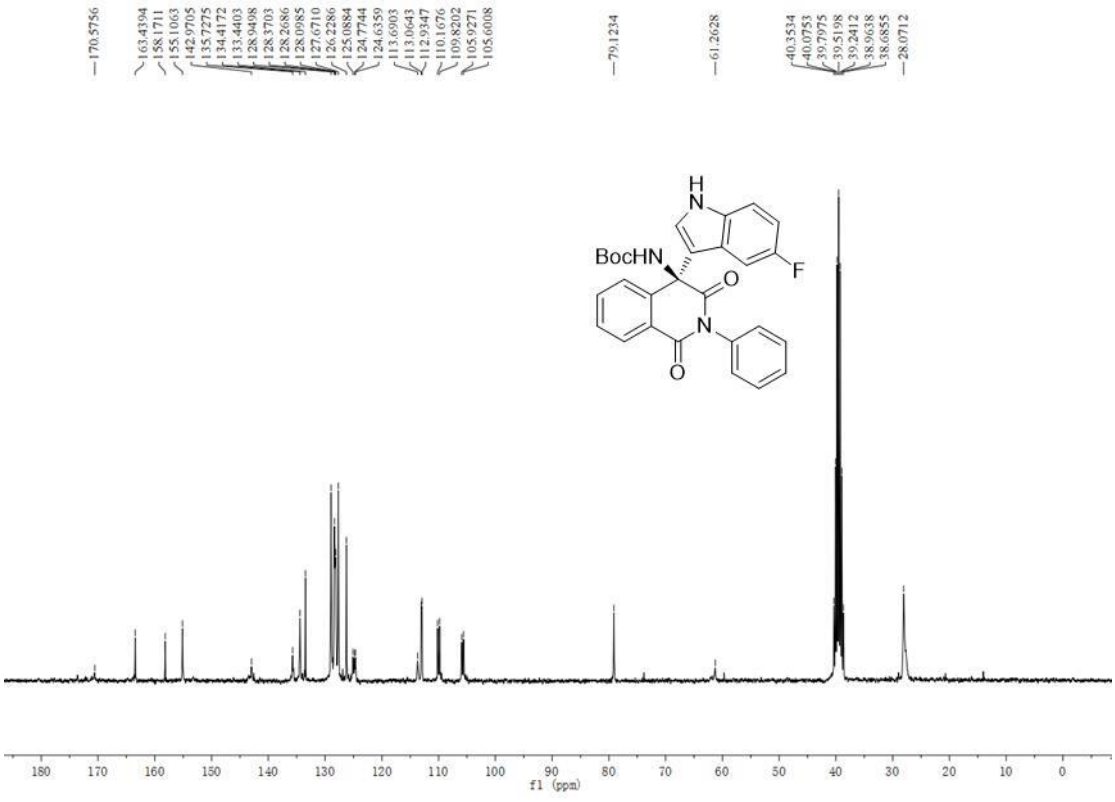


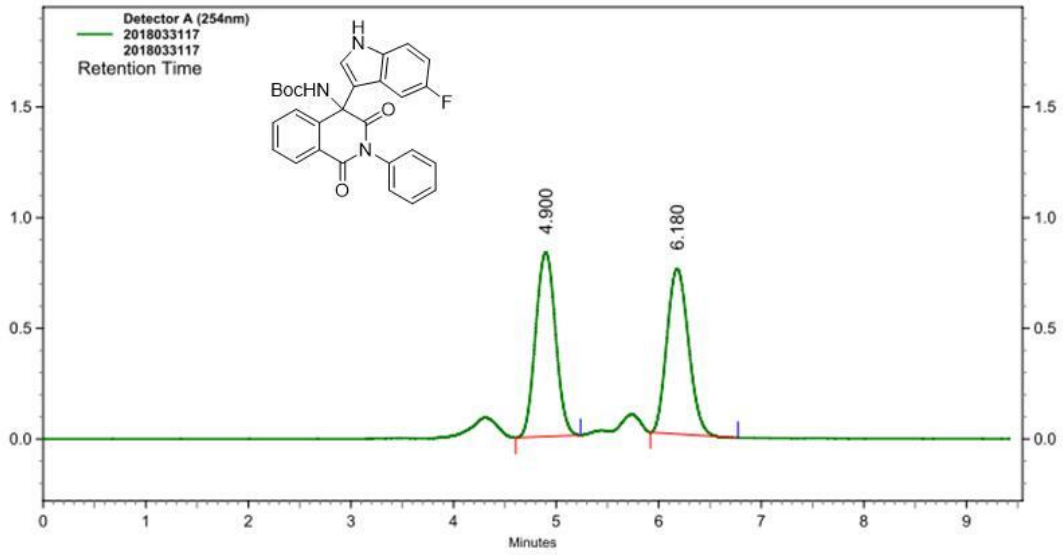
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	4.590	9649	0.52	83341	0.29
2	6.440	1833997	99.48	28732013	99.71
Totals		1843646	100.00	28815354	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 3ap

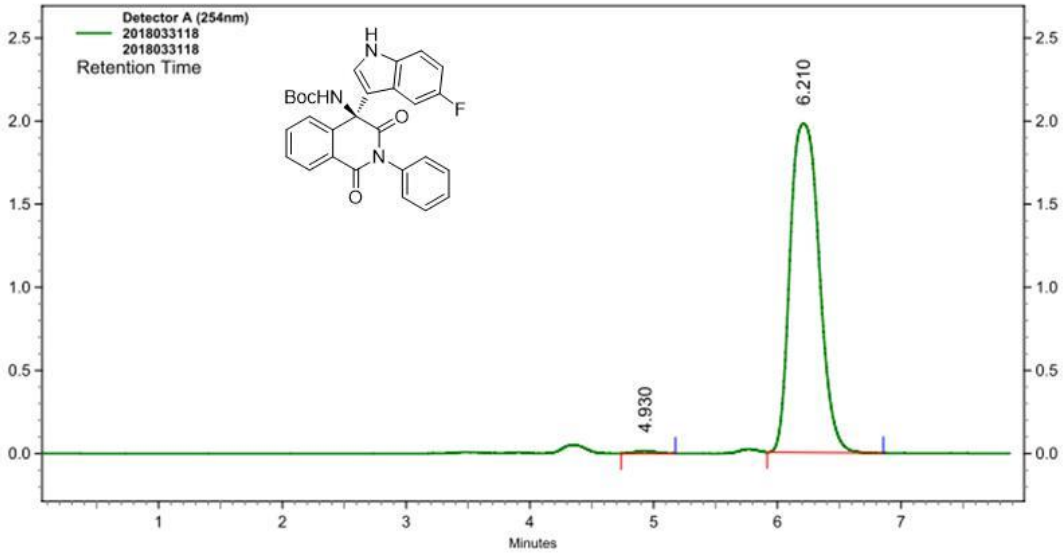






Detector A (254nm)

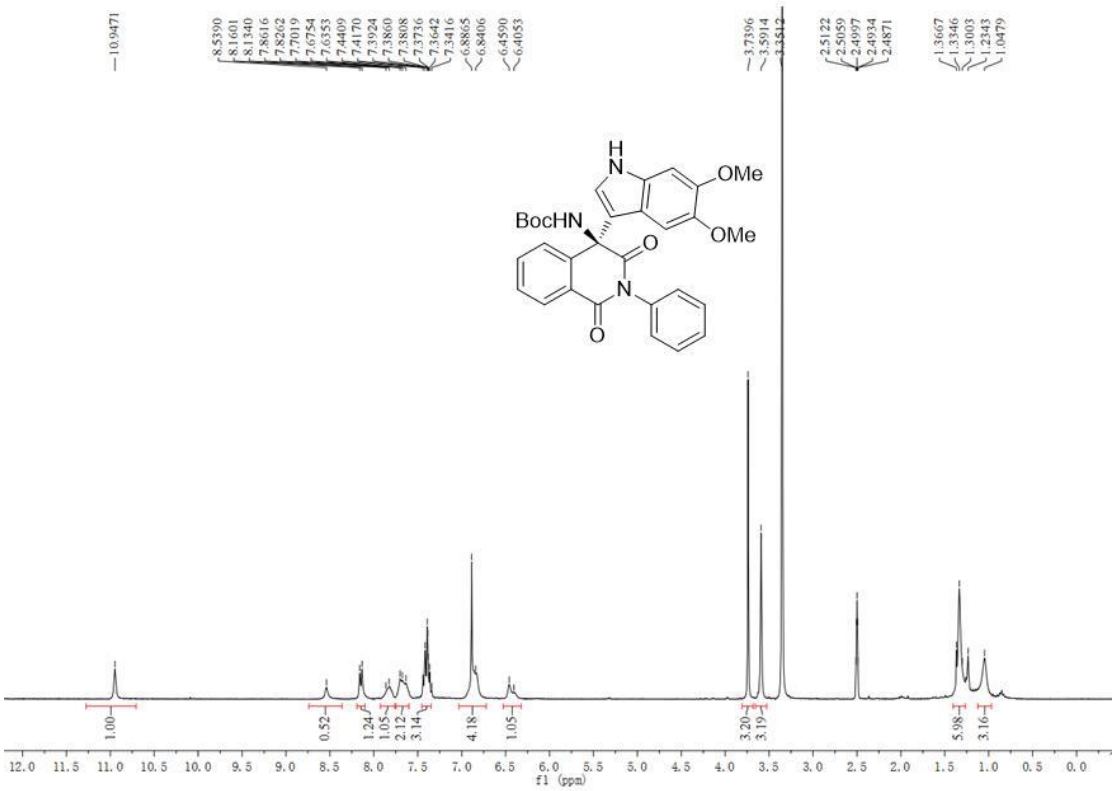
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	4.900	831848	52.70	11223639	50.65
2	6.180	746609	47.30	10936850	49.35
Totals		1578457	100.00	22160489	100.00

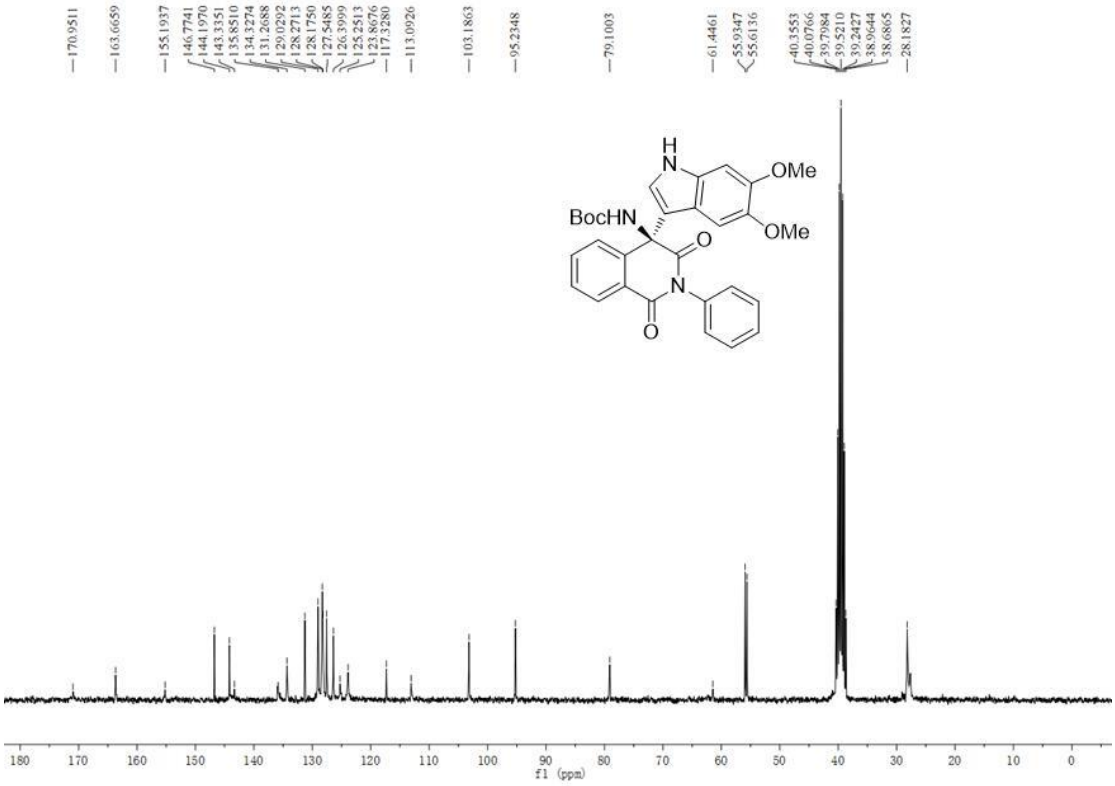


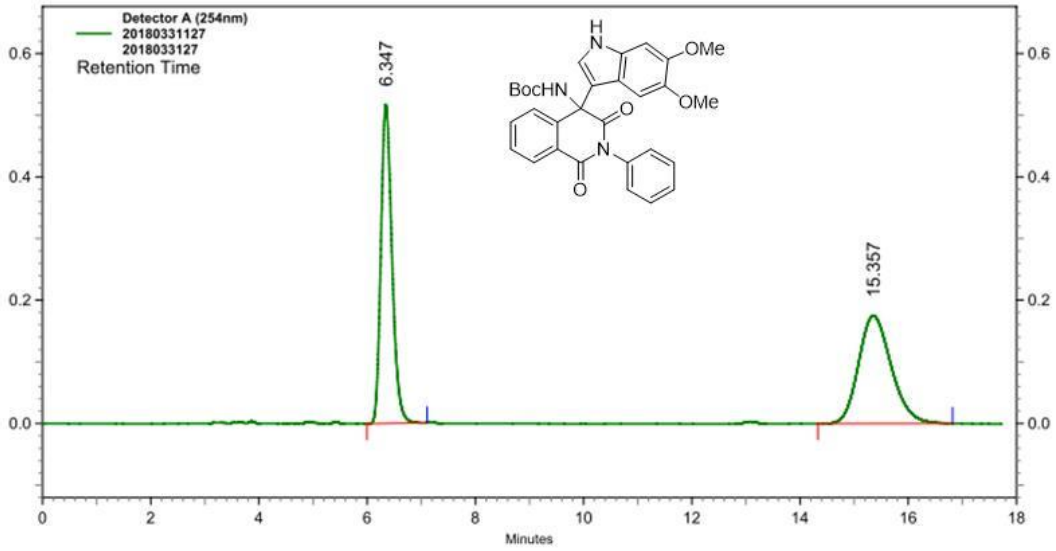
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	4.930	14663	0.74	166728	0.51
2	6.210	1977863	99.26	32364539	99.49
Totals		1992526	100.00	32531267	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 3aq

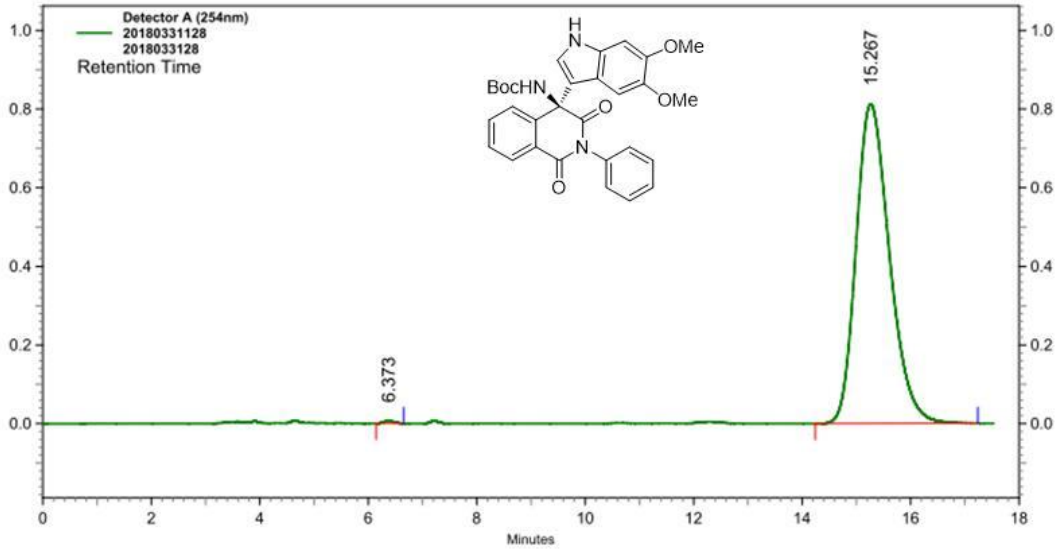






Detector A (254nm)

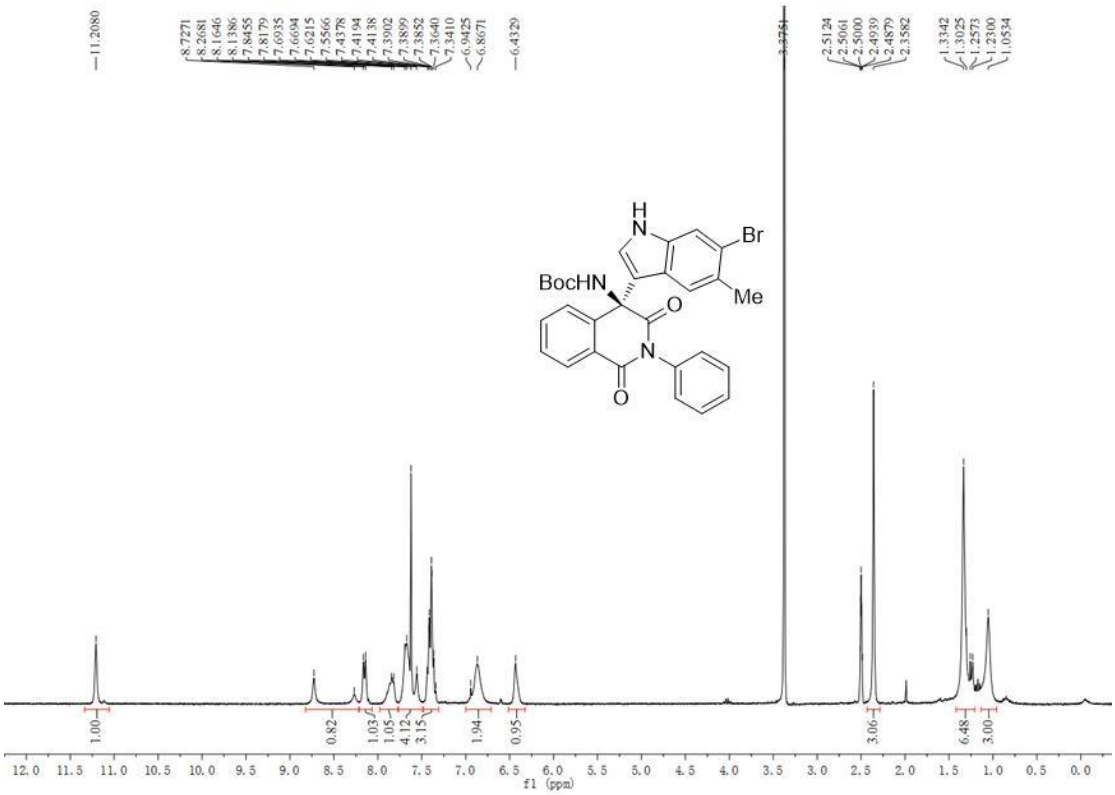
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	6.347	517052	74.74	7359130	50.10
2	15.357	174780	25.26	7329093	49.90
Totals		691832	100.00	14688223	100.00

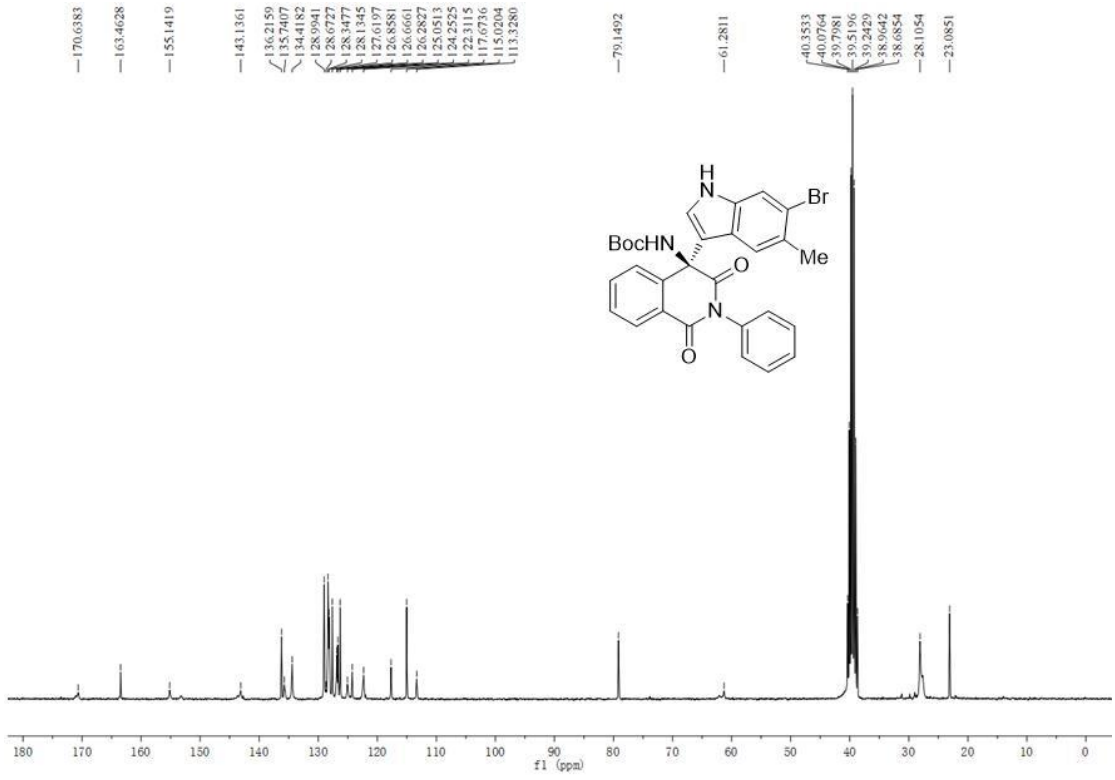


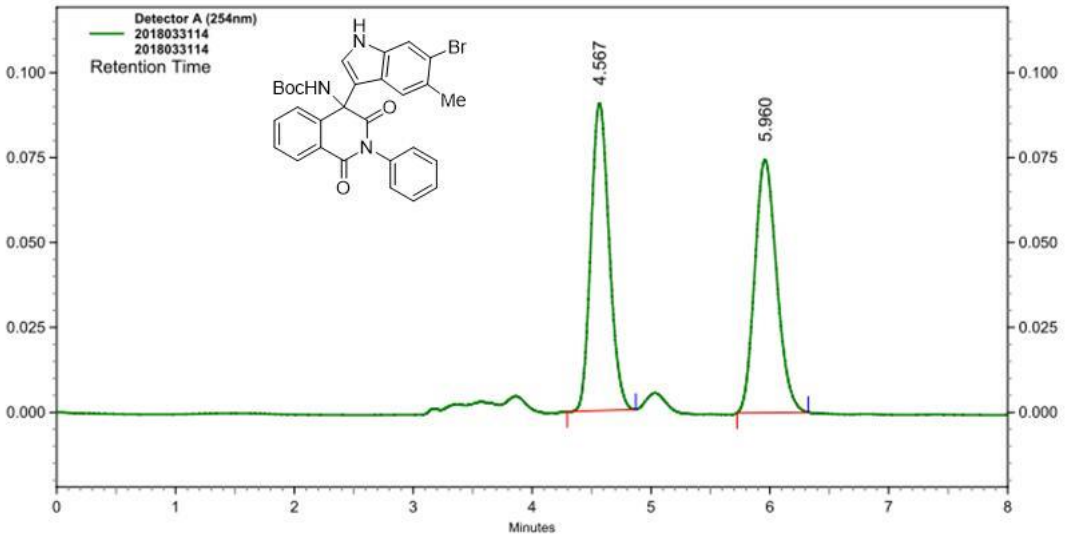
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	6.373	6384	0.78	84569	0.24
2	15.267	811958	99.22	34739710	99.76
Totals		818342	100.00	34824279	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 3ar

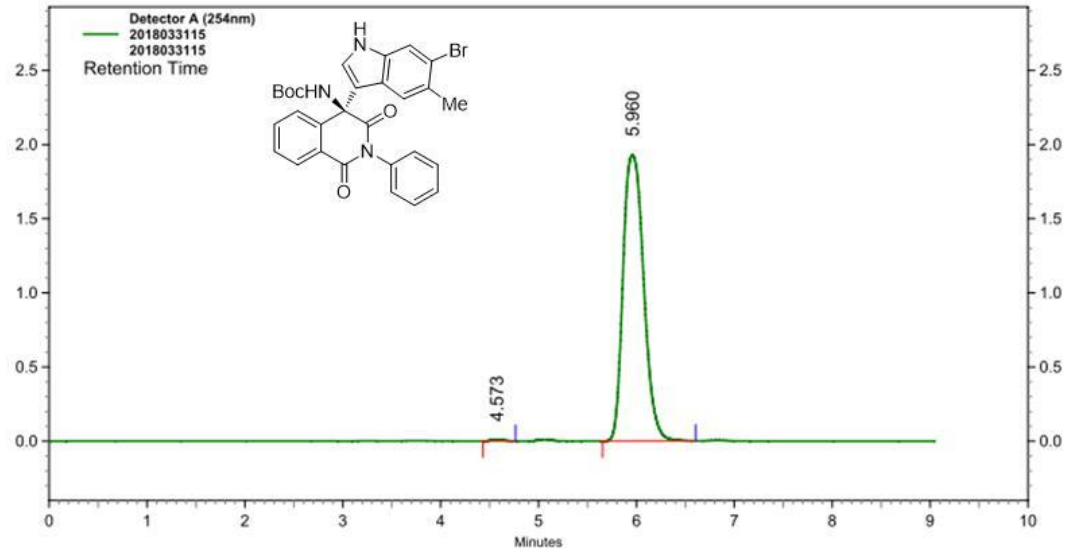






Detector A (254nm)

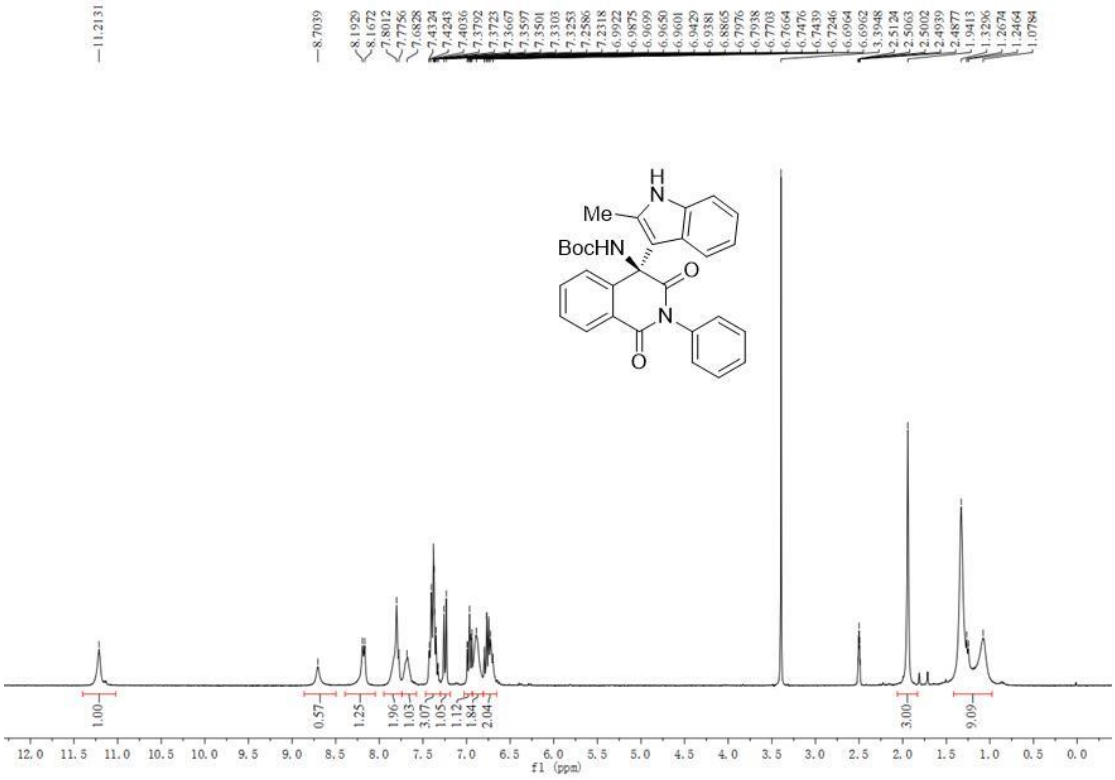
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	4.567	90551	54.86	966297	50.21
2	5.960	74496	45.14	958139	49.79
Totals		165047	100.00	1924436	100.00

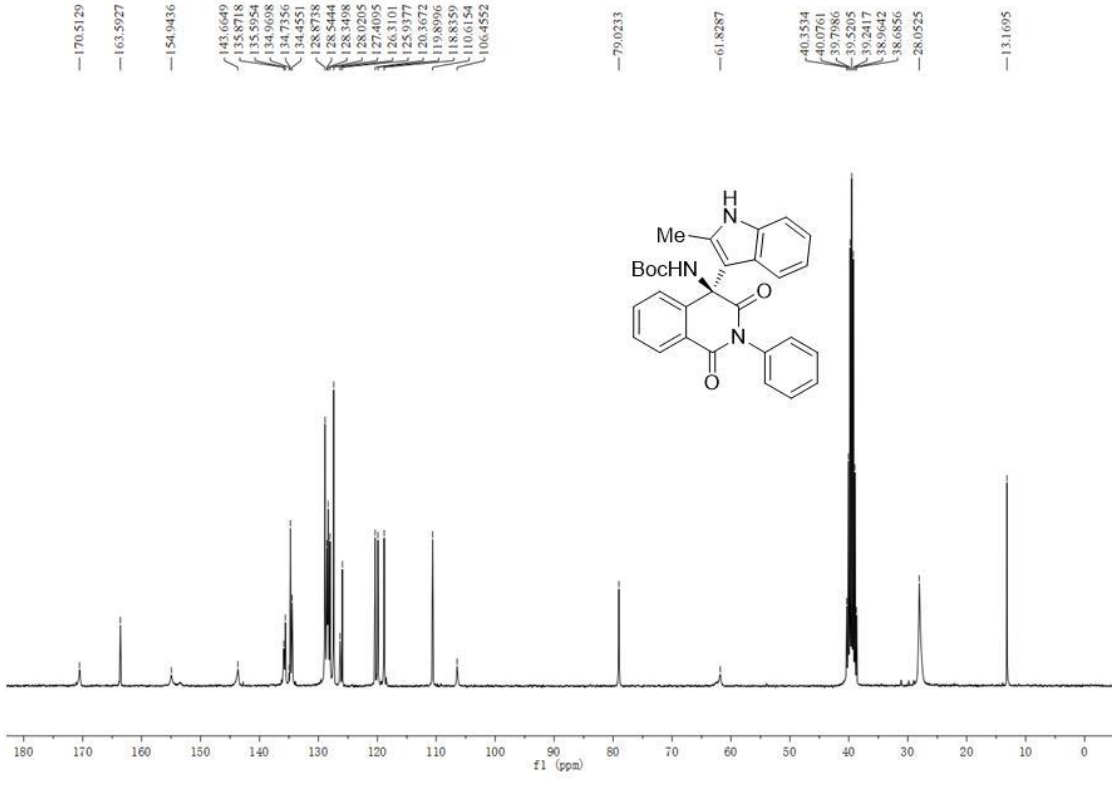


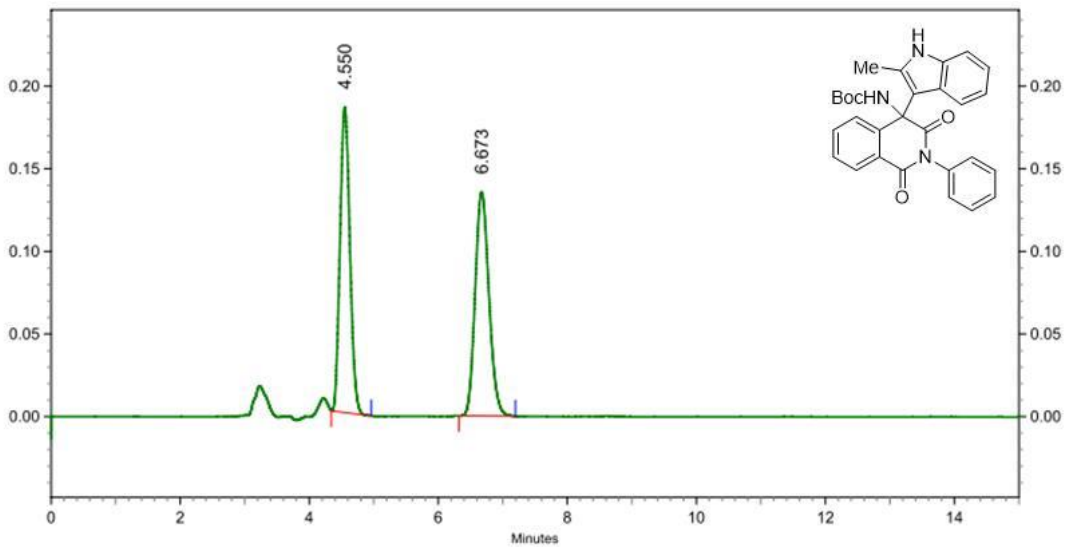
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	4.573	8878	0.46	83105	0.29
2	5.960	1928439	99.54	28234356	99.71
Totals		1937317	100.00	28317461	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 3as

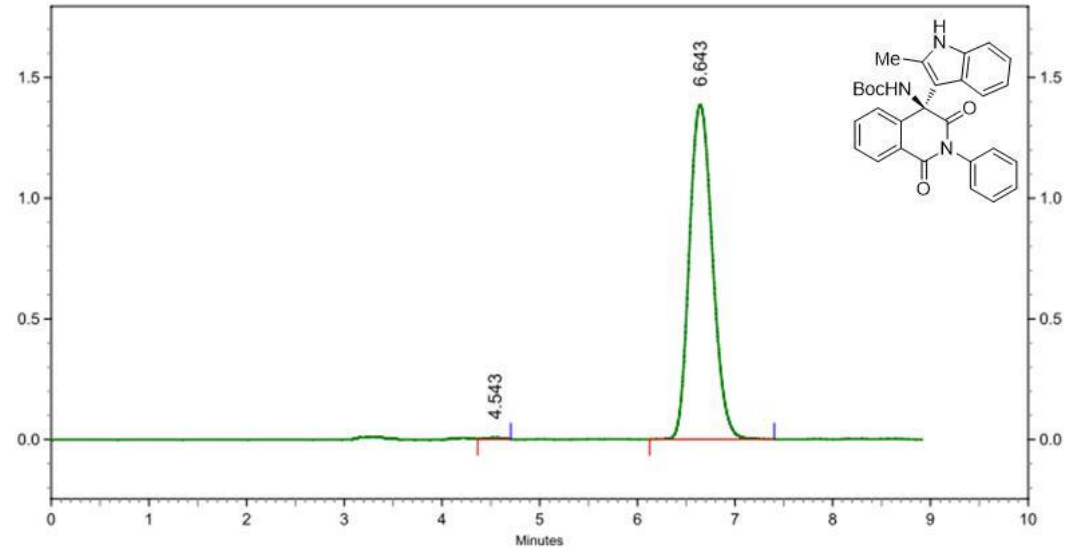






Detector A (254nm)

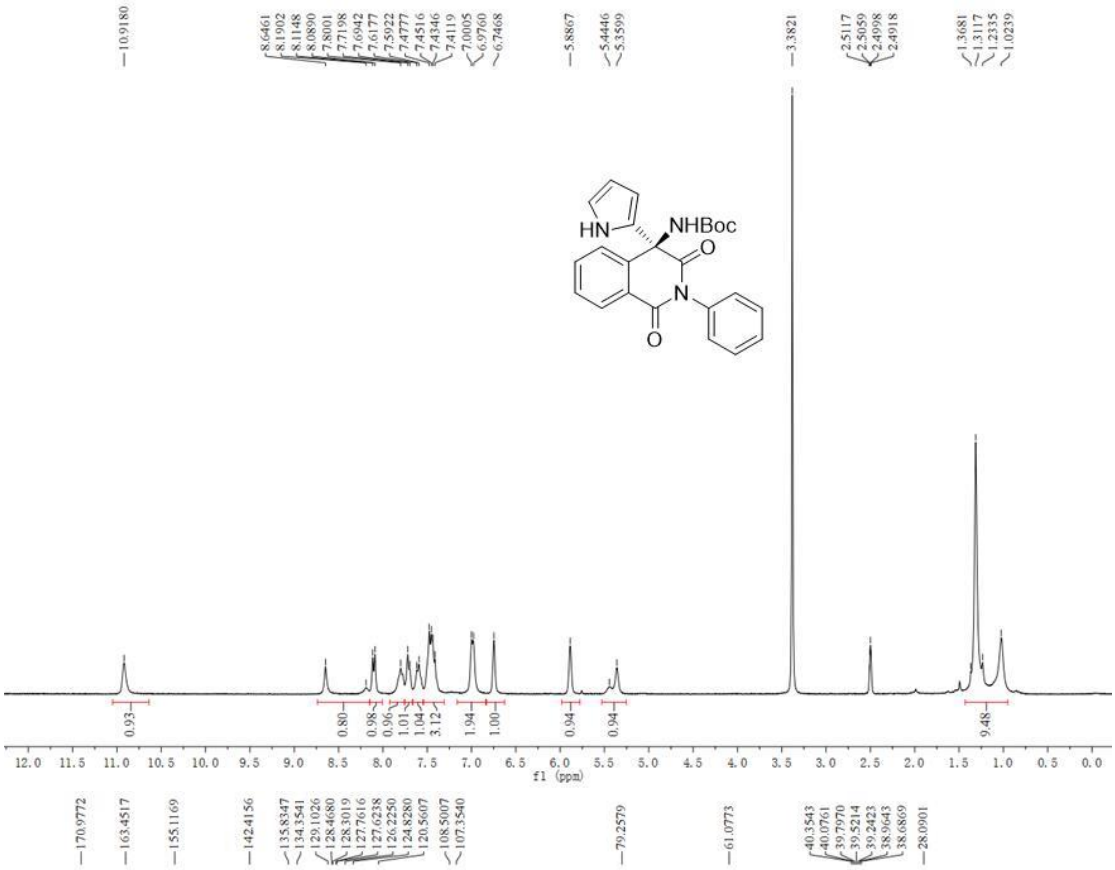
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	4.550	184719	57.71	1963093	49.37
2	6.673	135344	42.29	2013029	50.63
Totals		320063	100.00	3976122	100.00

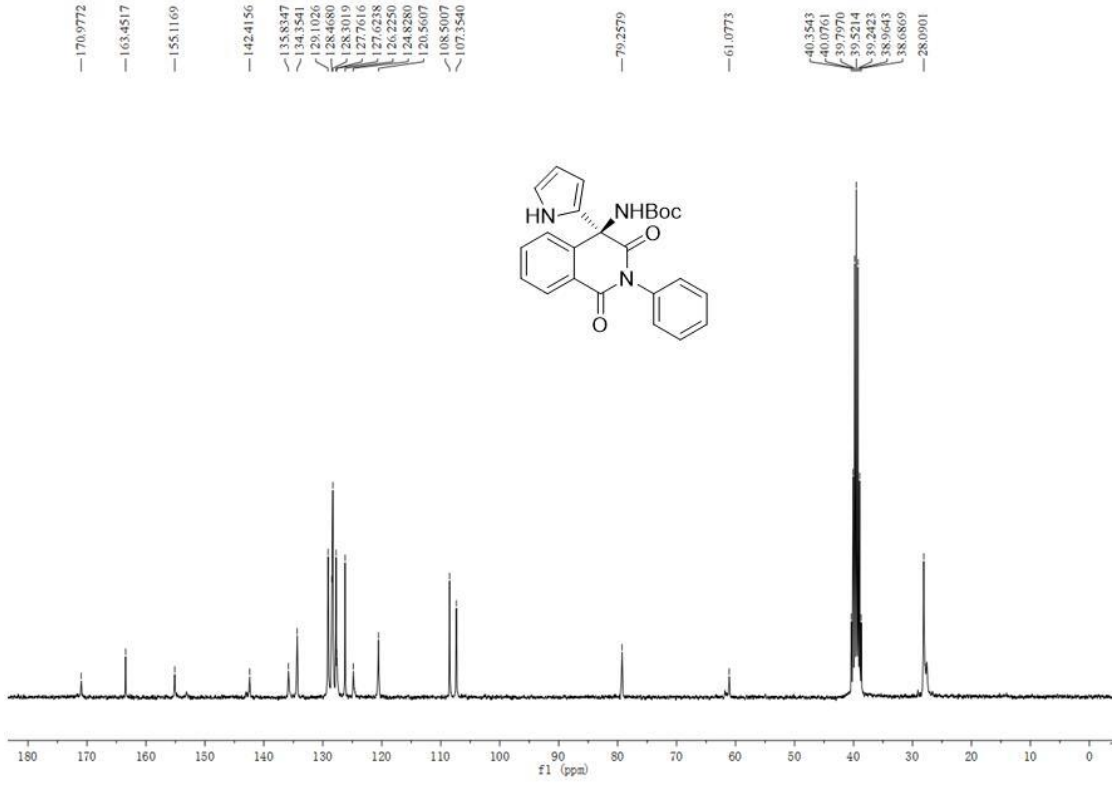


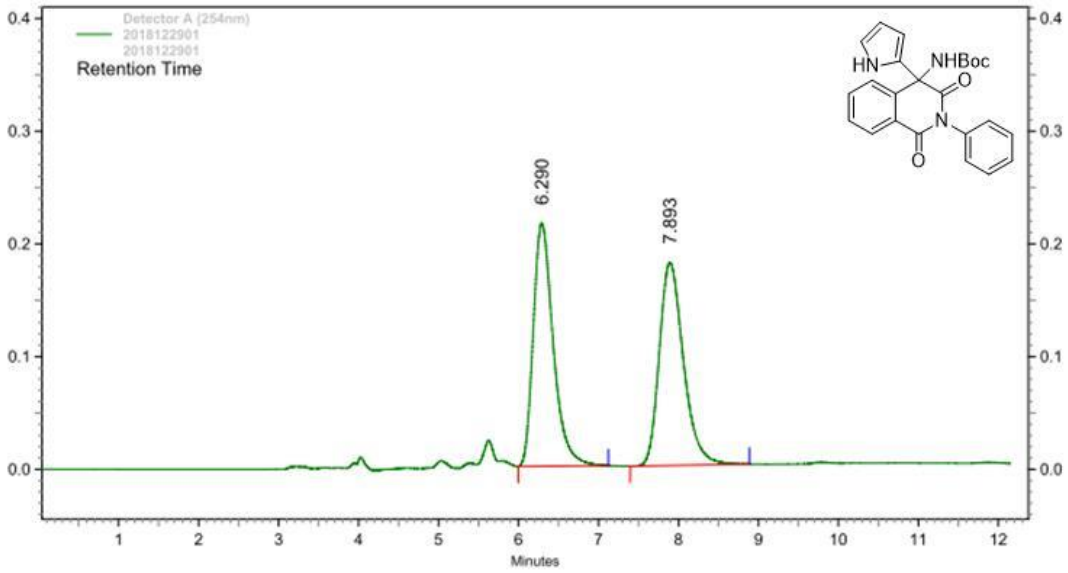
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	4.543	6669	0.48	65327	0.29
2	6.643	1385512	99.52	22775472	99.71
Totals		1392181	100.00	22840799	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 5a

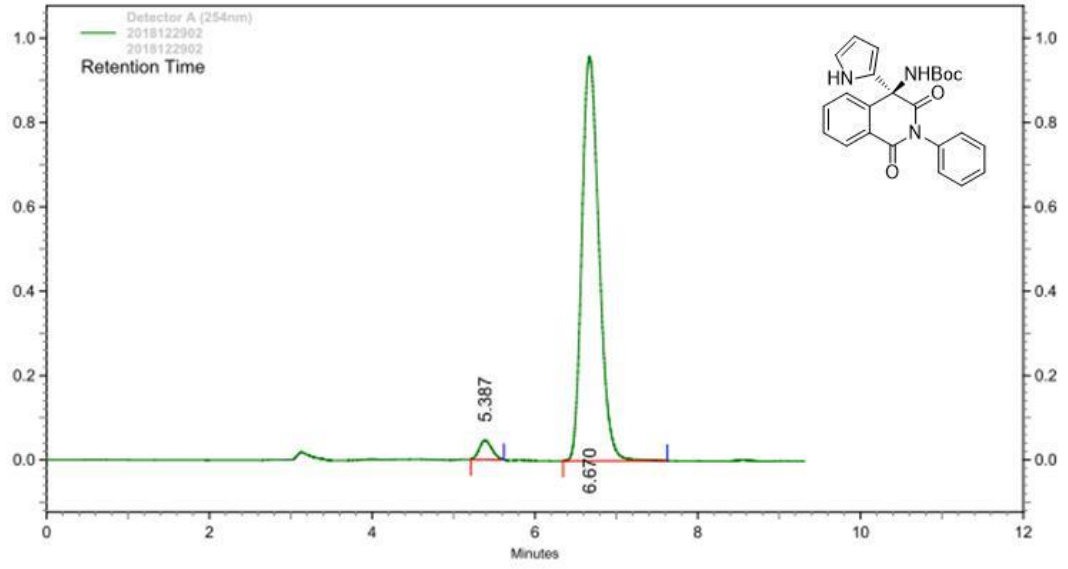






Detector A (254nm)

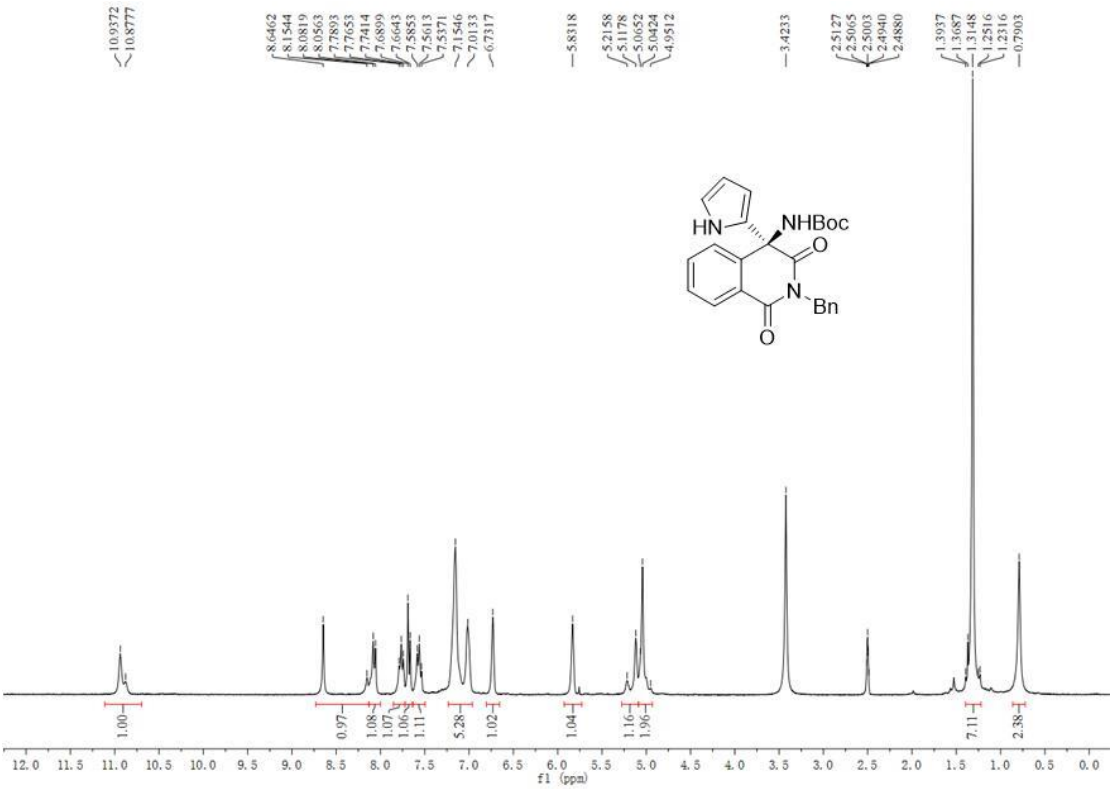
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	6.290	215298	54.47	3740305	49.73
2	7.893	179991	45.53	3780872	50.27
Totals		395289	100.00	7521177	100.00

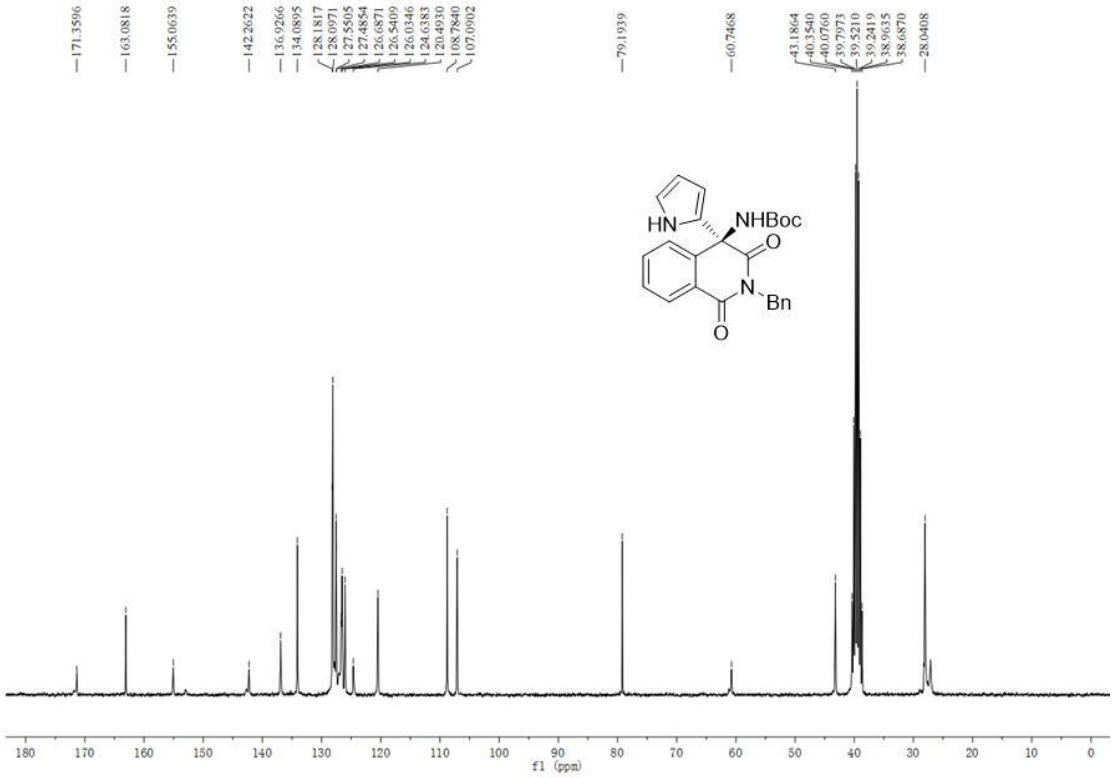


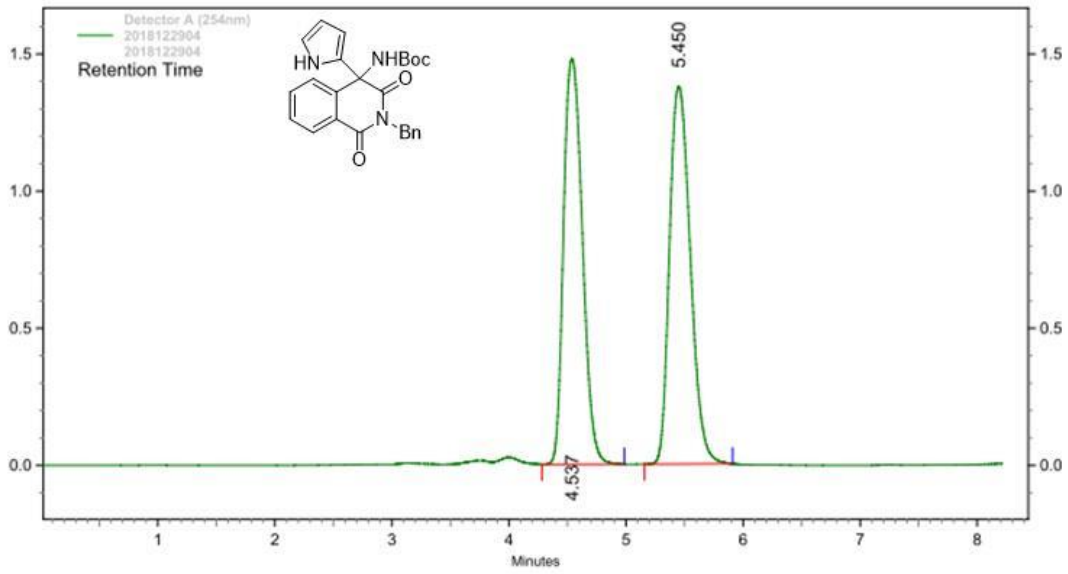
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	5.387	44882	4.47	487749	3.36
2	6.670	959404	95.53	14009476	96.64
Totals		1004286	100.00	14497225	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 5b

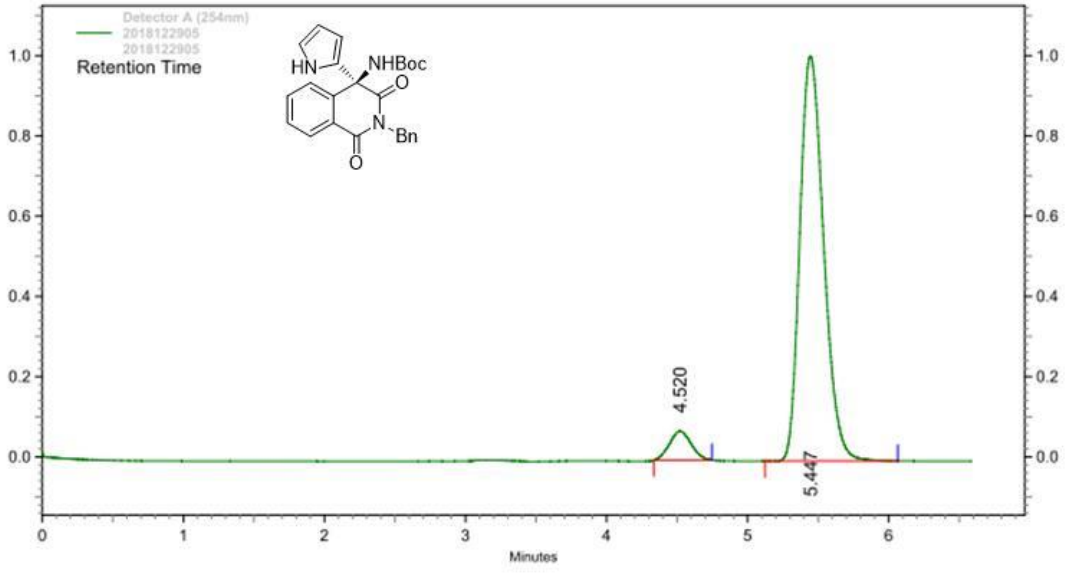






Detector A (254nm)

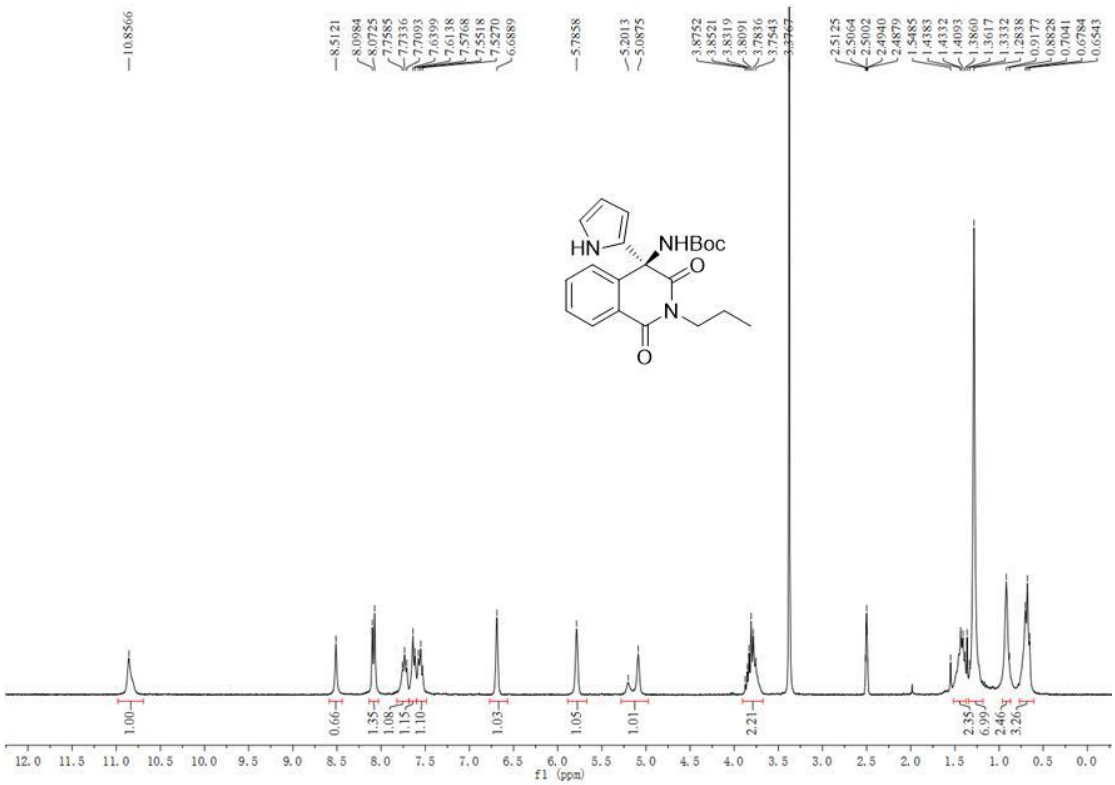
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	4.537	1478728	51.79	16524663	49.26
2	5.450	1376594	48.21	17018201	50.74
Totals		2855322	100.00	33542864	100.00

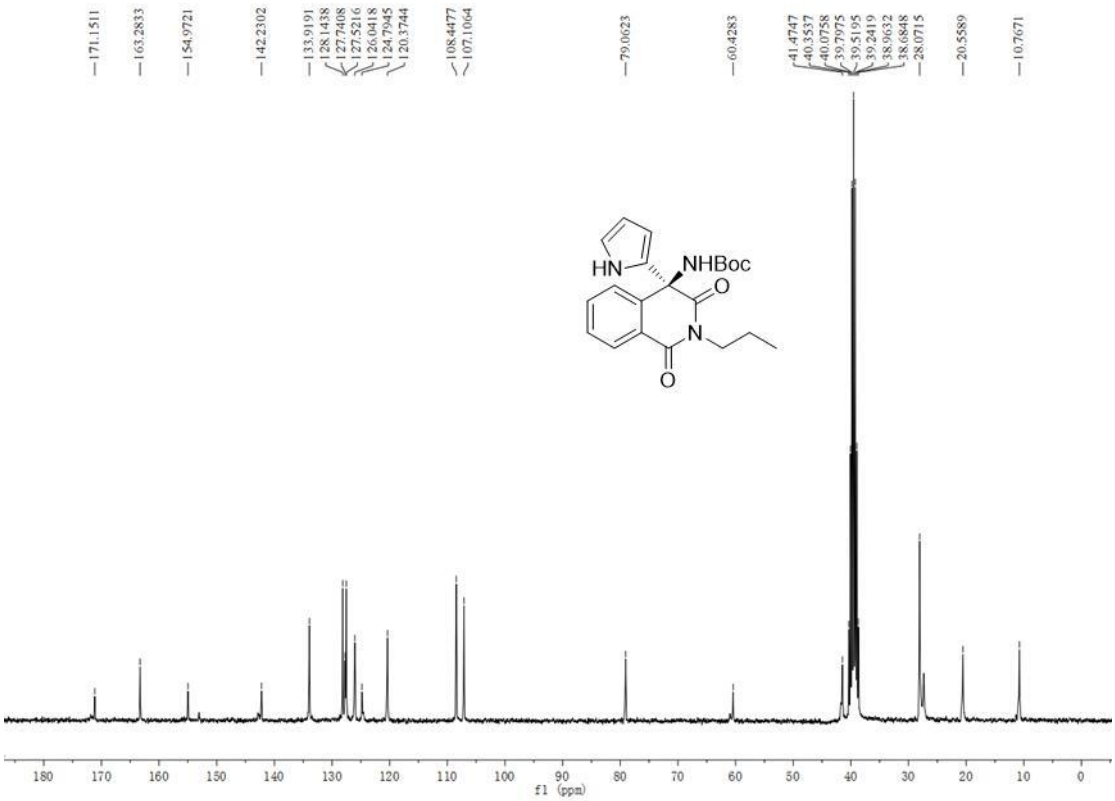


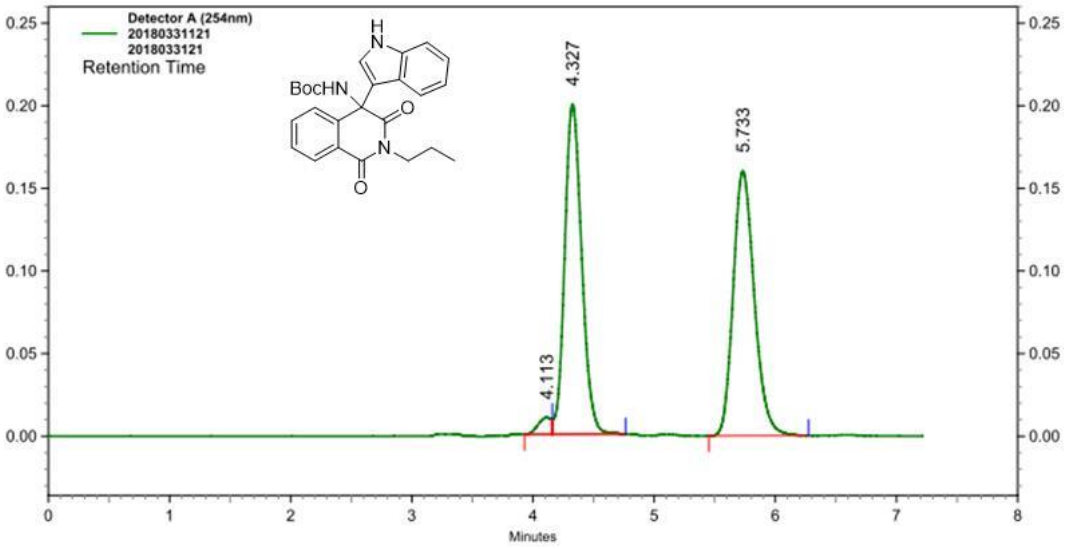
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	4.520	71881	6.65	773574	6.14
2	5.447	1008989	93.35	11833575	93.86
Totals		1080870	100.00	12607149	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 5c

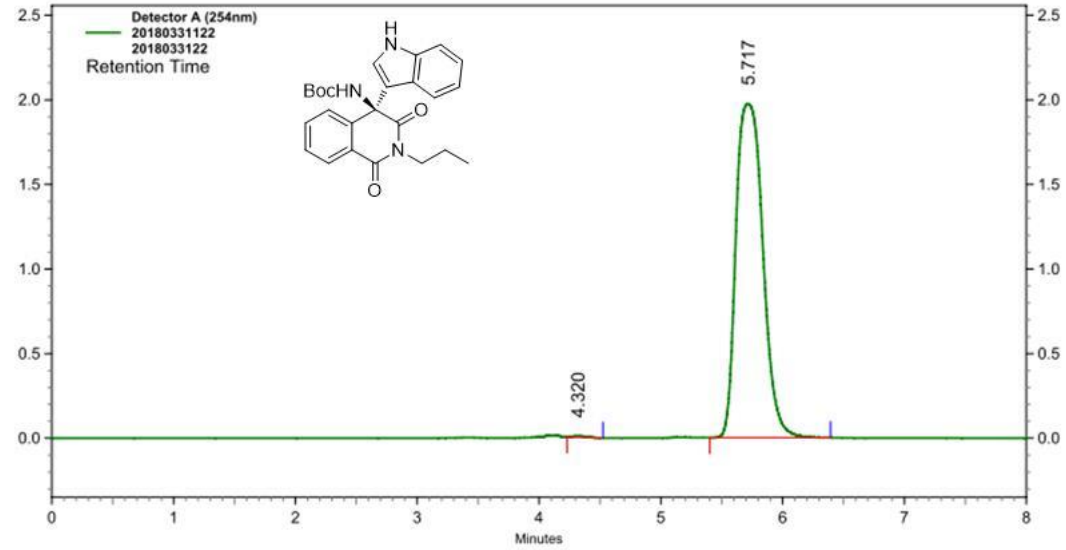






Detector A (254nm)

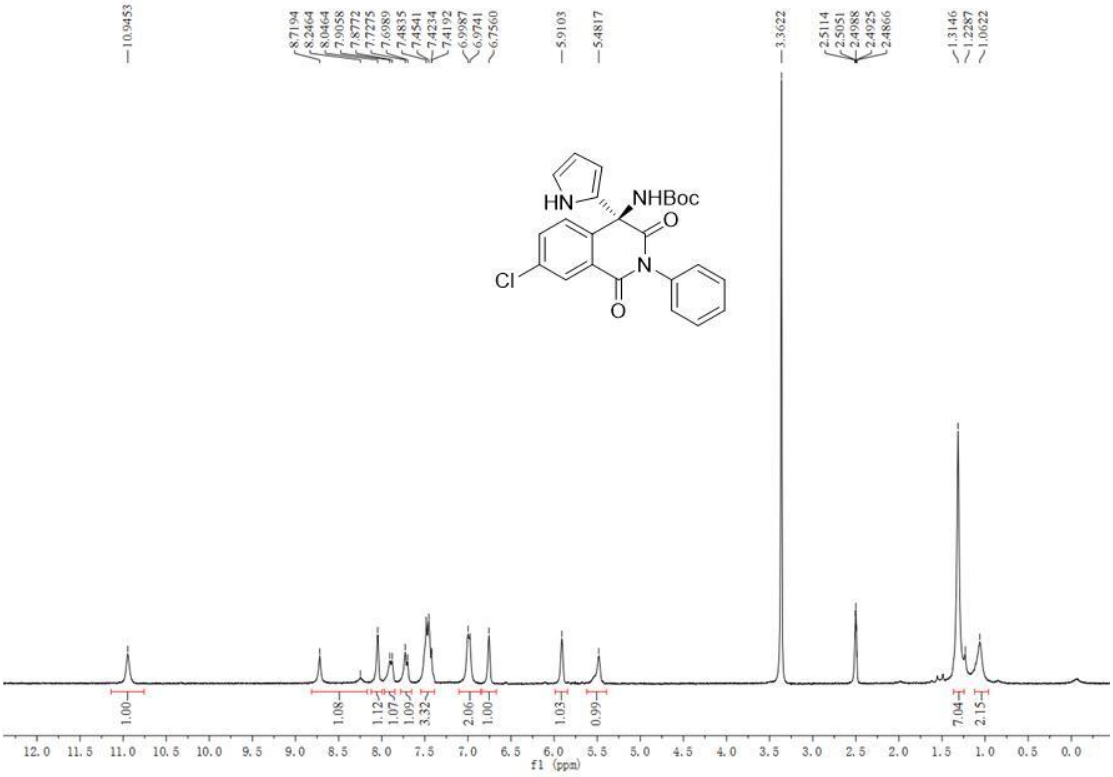
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	4.113	10070	2.72	75562	1.90
2	4.327	199673	53.97	1952156	49.18
3	5.733	160197	43.30	1941302	48.91
Totals		369940	100.00	3969020	100.00

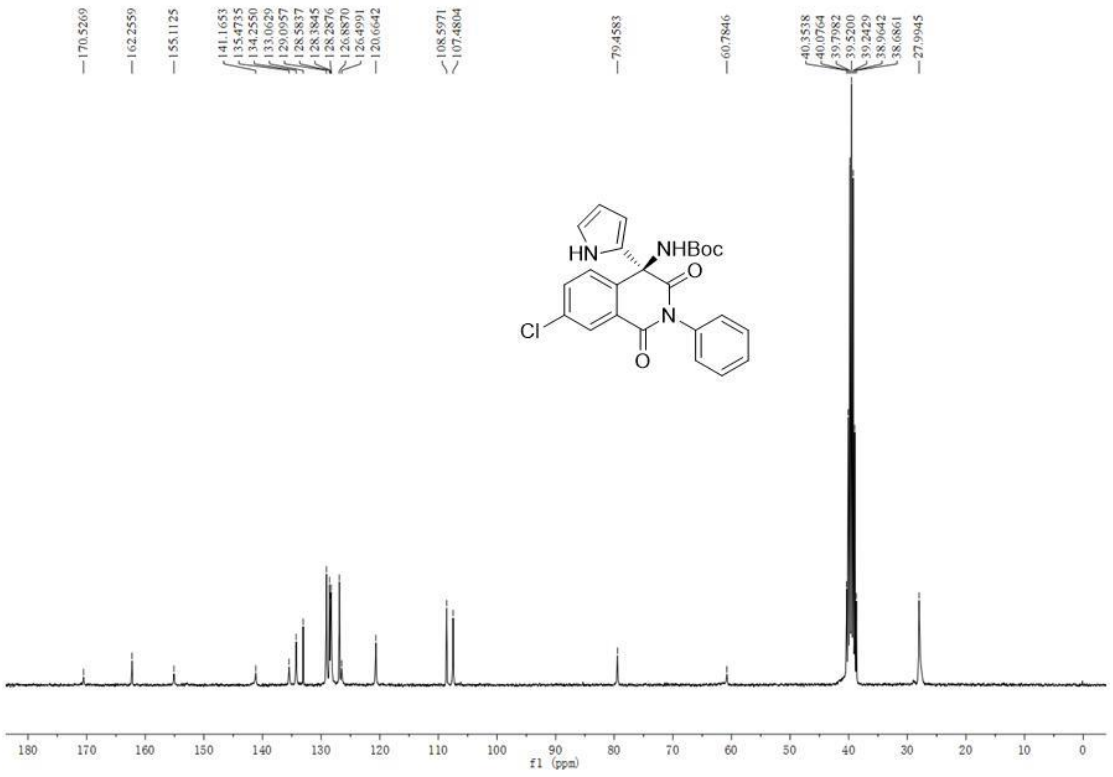


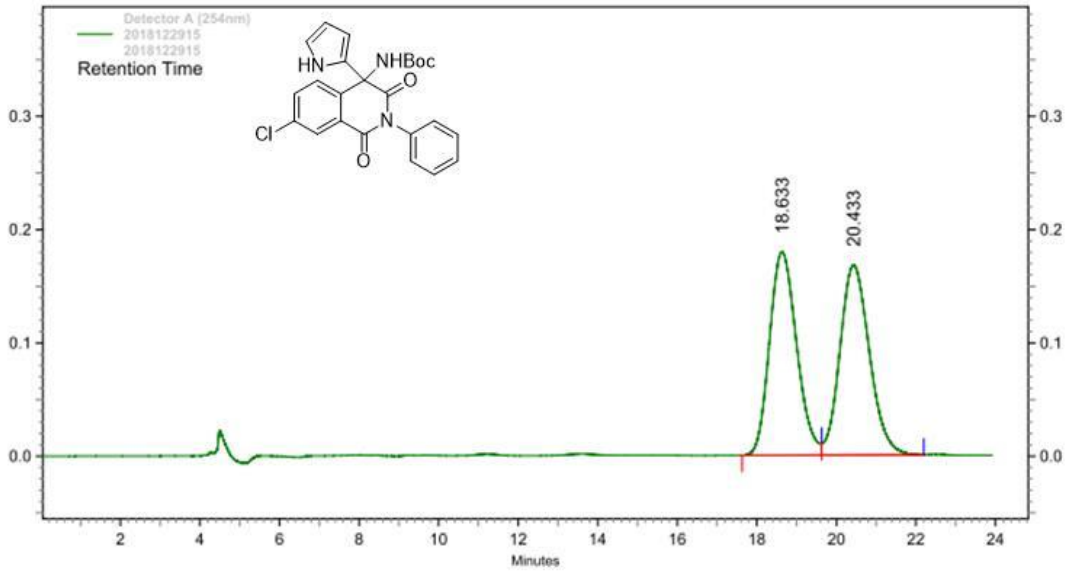
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	4.320	7084	0.36	52666	0.17
2	5.717	1973100	99.64	30244883	99.83
Totals		1980184	100.00	30297549	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 5d

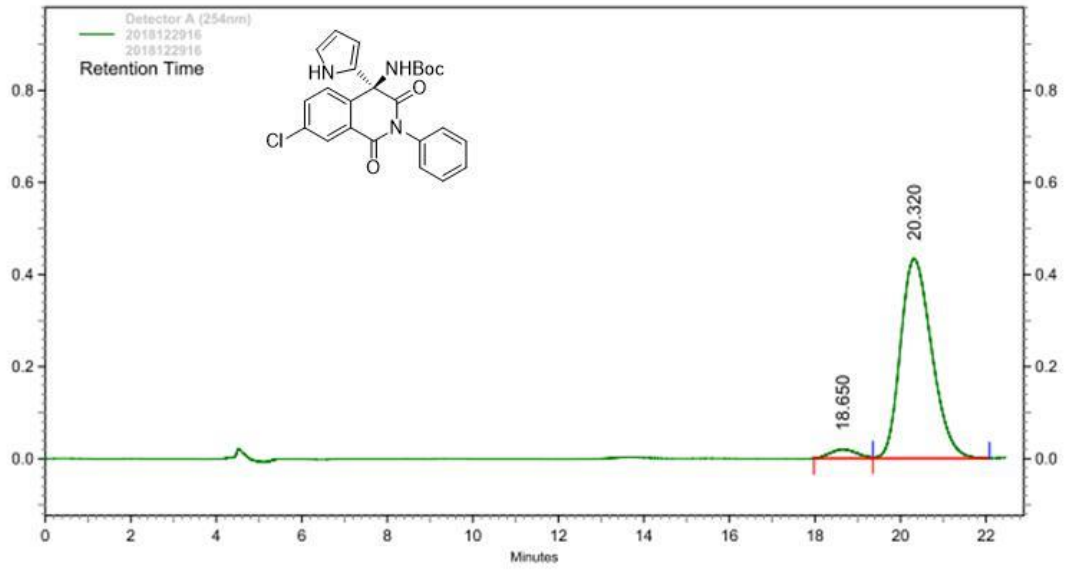






Detector A (254nm)

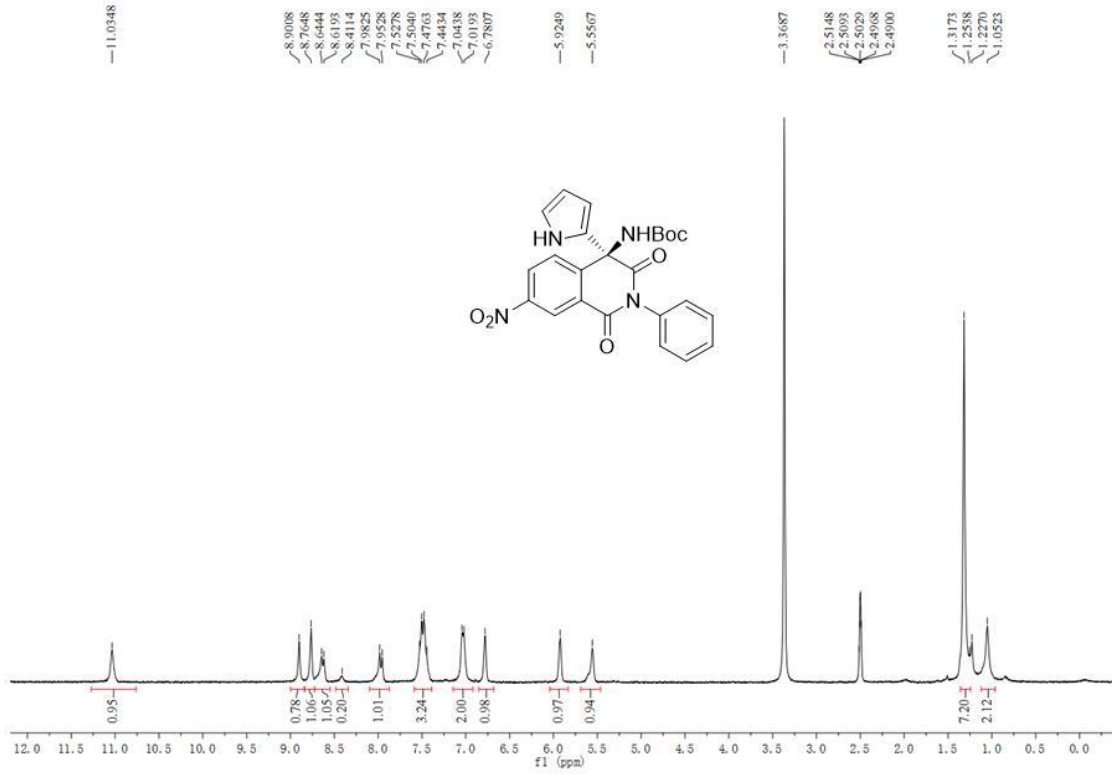
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	18.633	179177	51.68	8489077	49.57
2	20.433	167540	48.32	8634832	50.43
Totals		346717	100.00	17123909	100.00

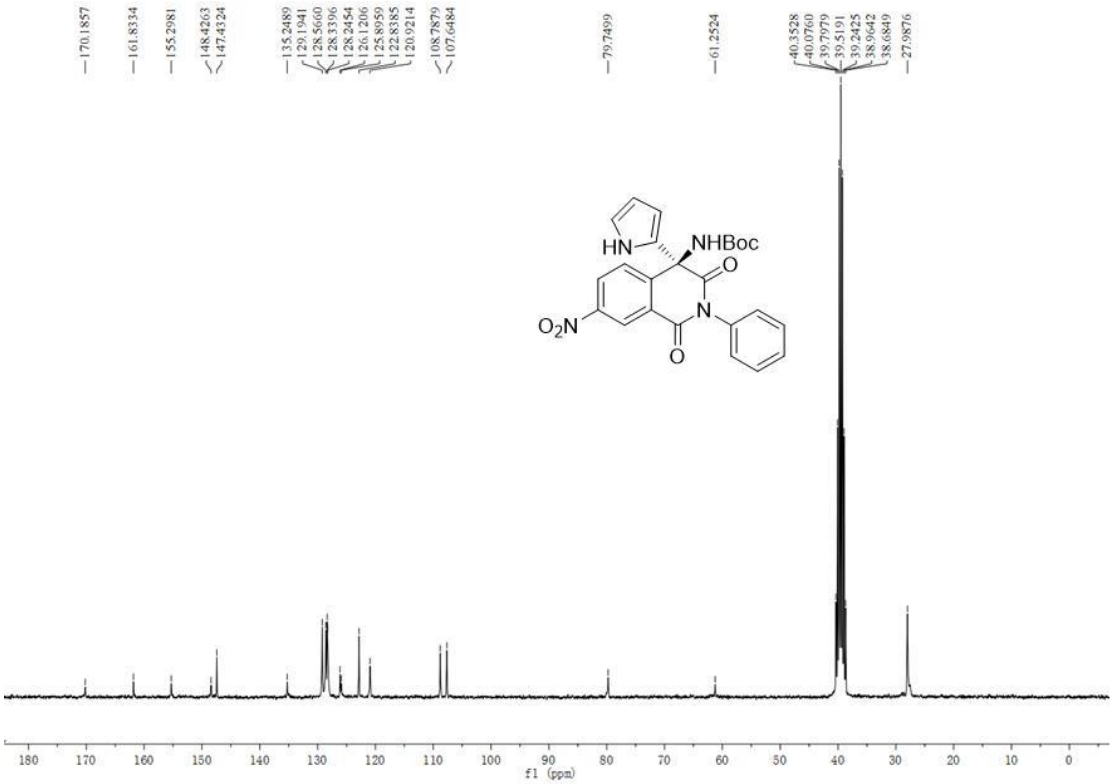


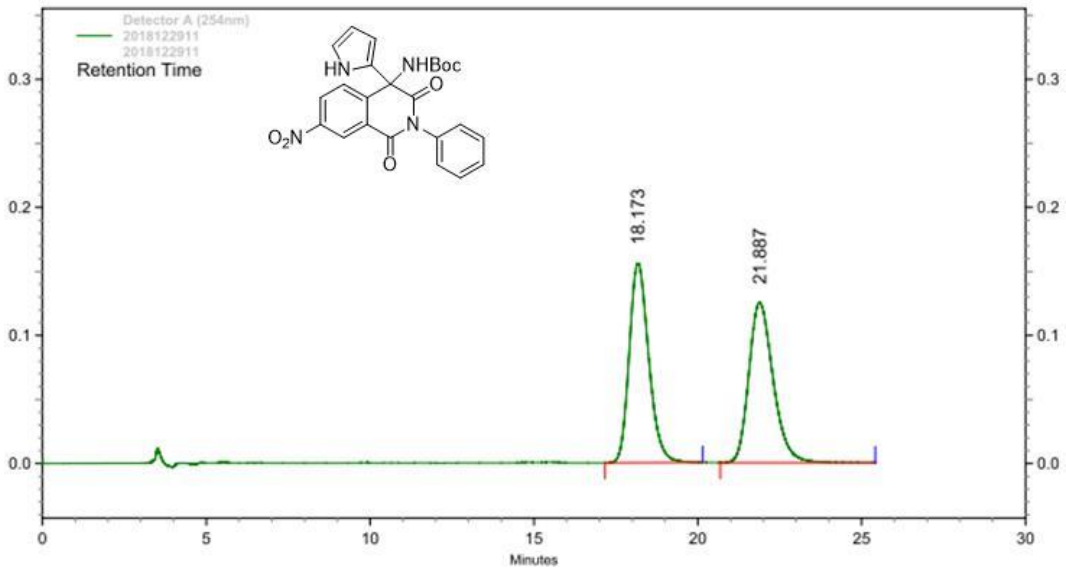
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	18.650	19357	4.28	846189	3.70
2	20.320	432989	95.72	21999230	96.30
Totals		452346	100.00	22845419	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 5e

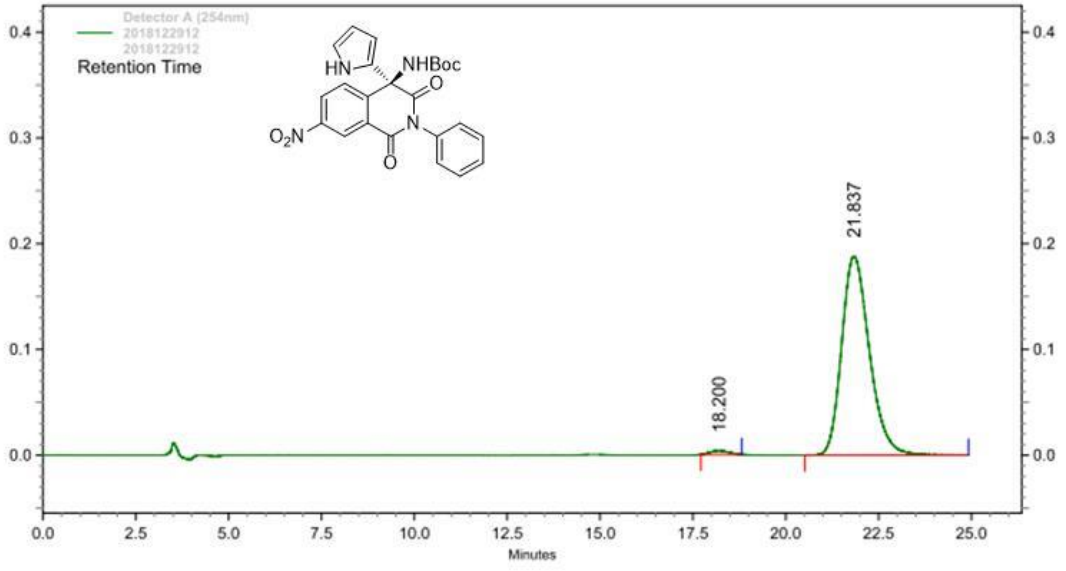






Detector A (254nm)

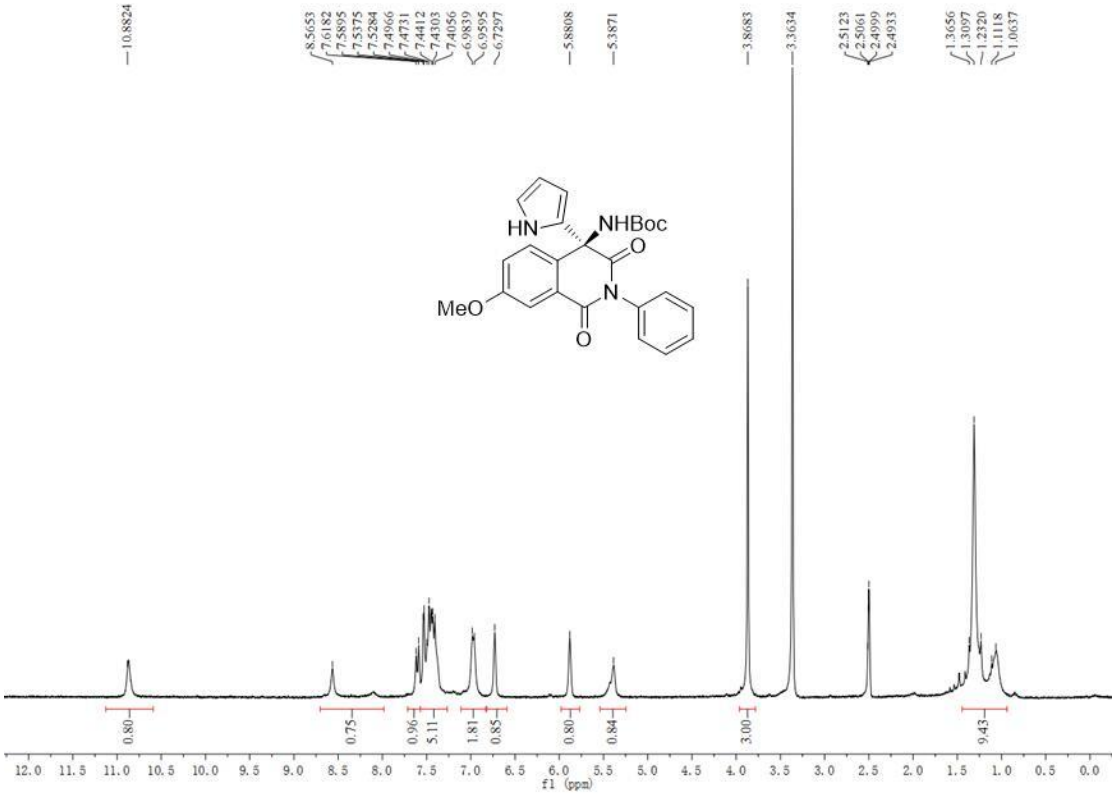
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	18.173	155733	55.49	6440961	49.95
2	21.887	124896	44.51	6454651	50.05
Totals		280629	100.00	12895612	100.00

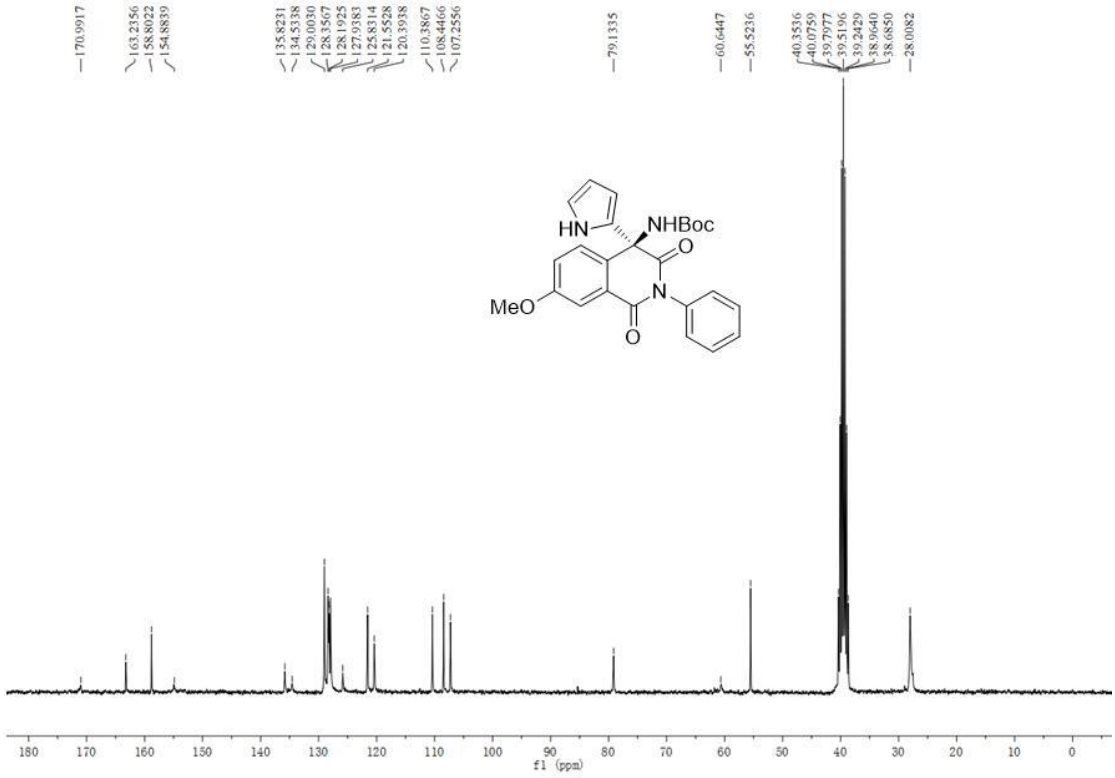


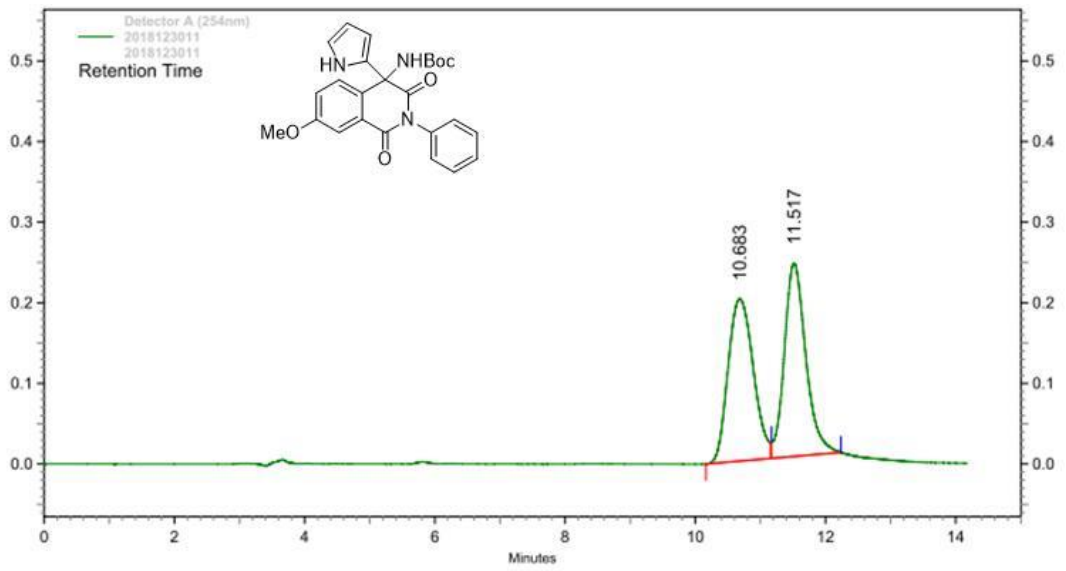
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	18.200	3487	1.82	122298	1.23
2	21.837	188175	98.18	9787878	98.77
Totals		191662	100.00	9910176	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 5f

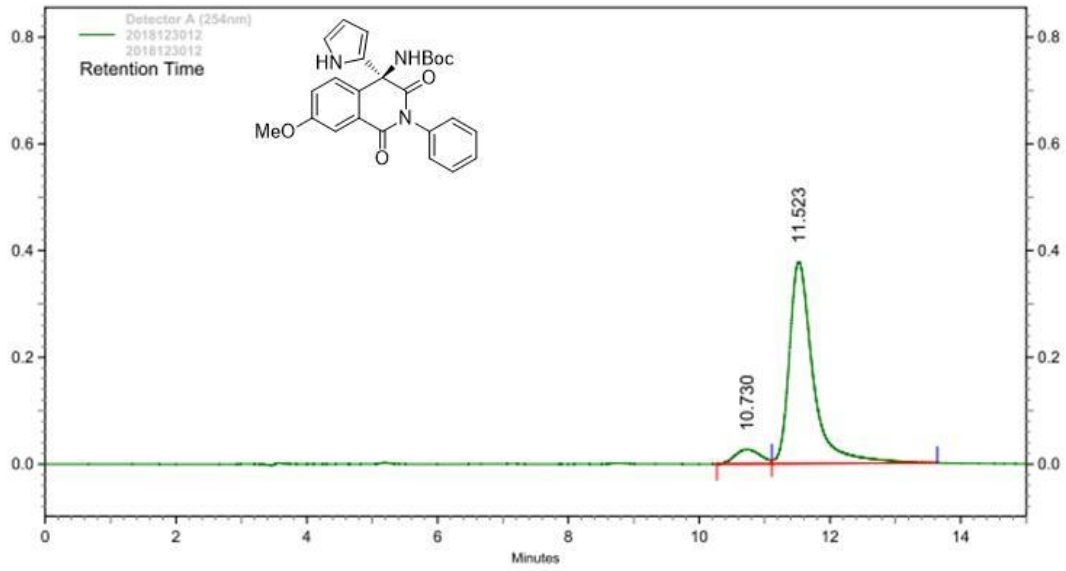






Detector A (254nm)

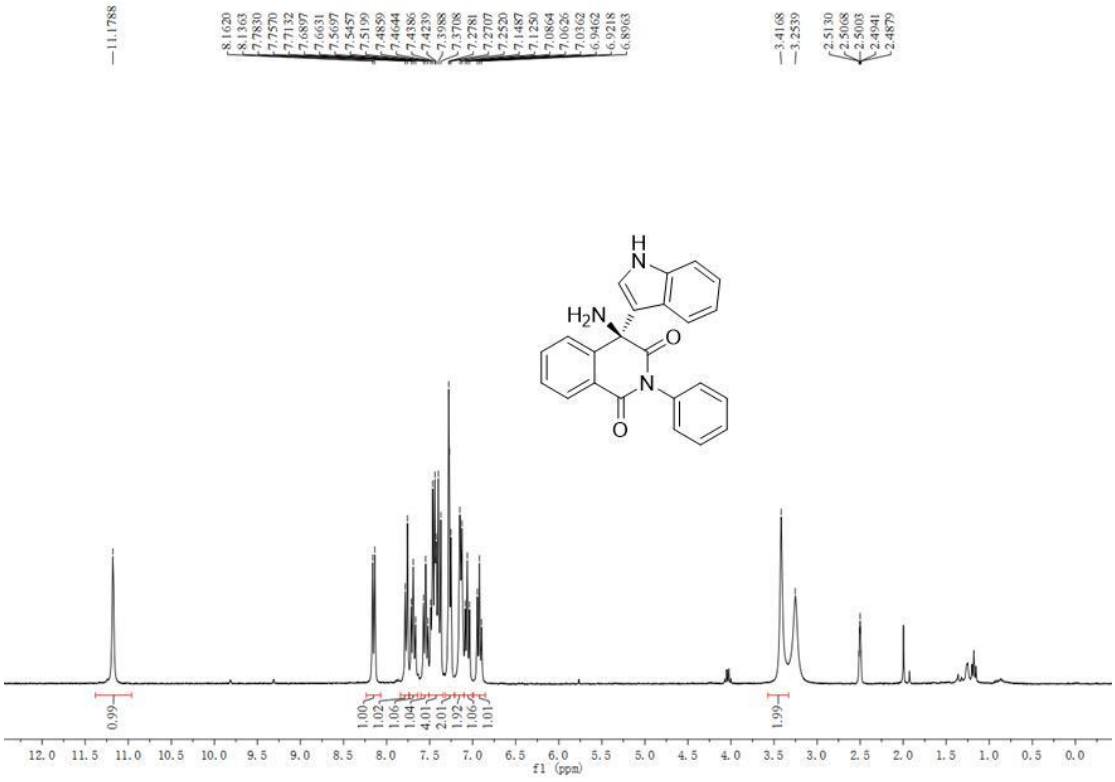
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	10.683	201094	45.60	5425391	49.62
2	11.517	239946	54.40	5509337	50.38
Totals		441040	100.00	10934728	100.00

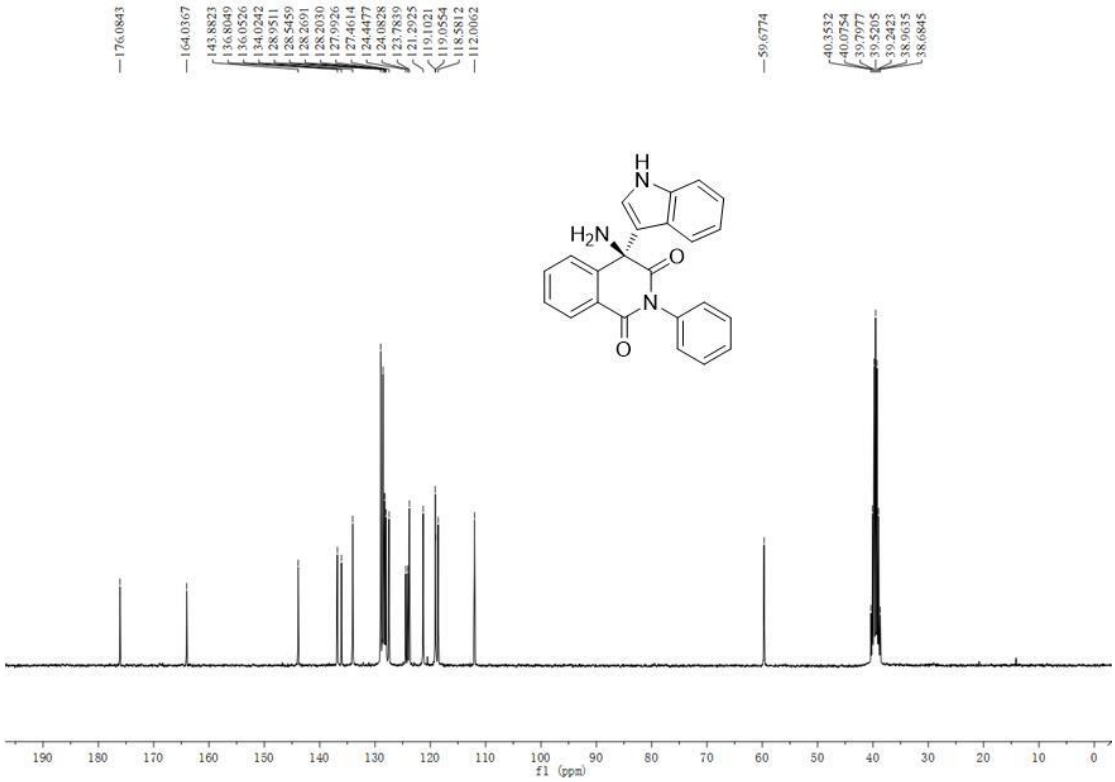


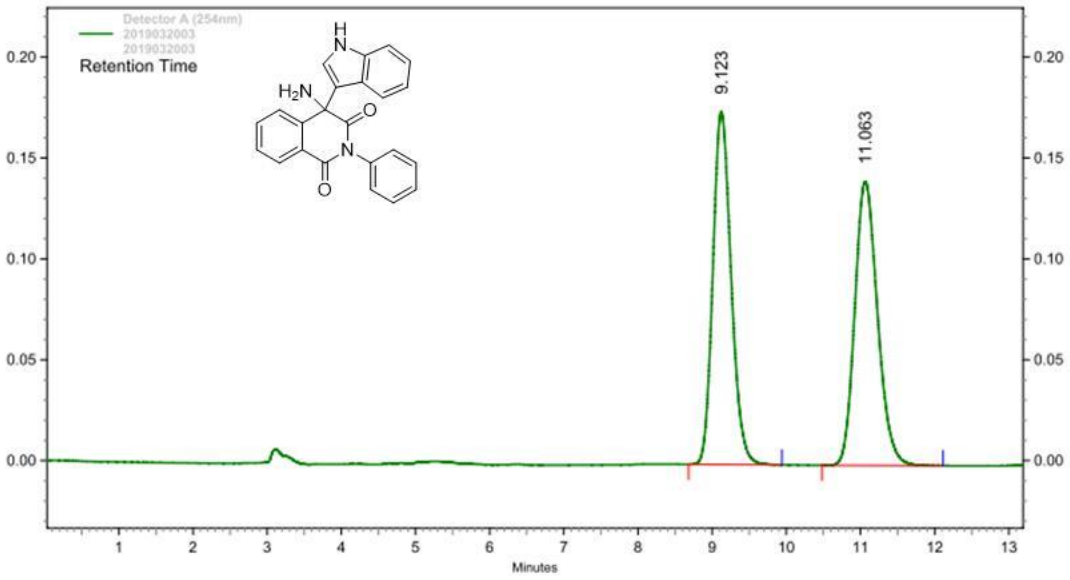
Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	10.730	26856	6.64	717277	6.99
2	11.523	377842	93.36	9538075	93.01
Totals		404698	100.00	10255352	100.00

^{1}H NMR, ^{13}C NMR and HPLC spectra of 6

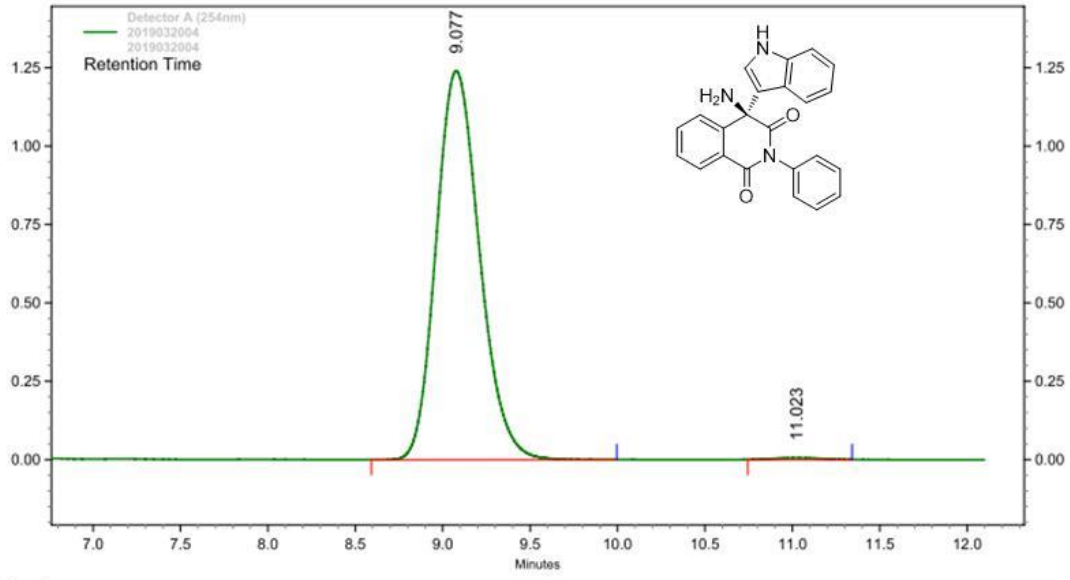






Detector A (254nm)

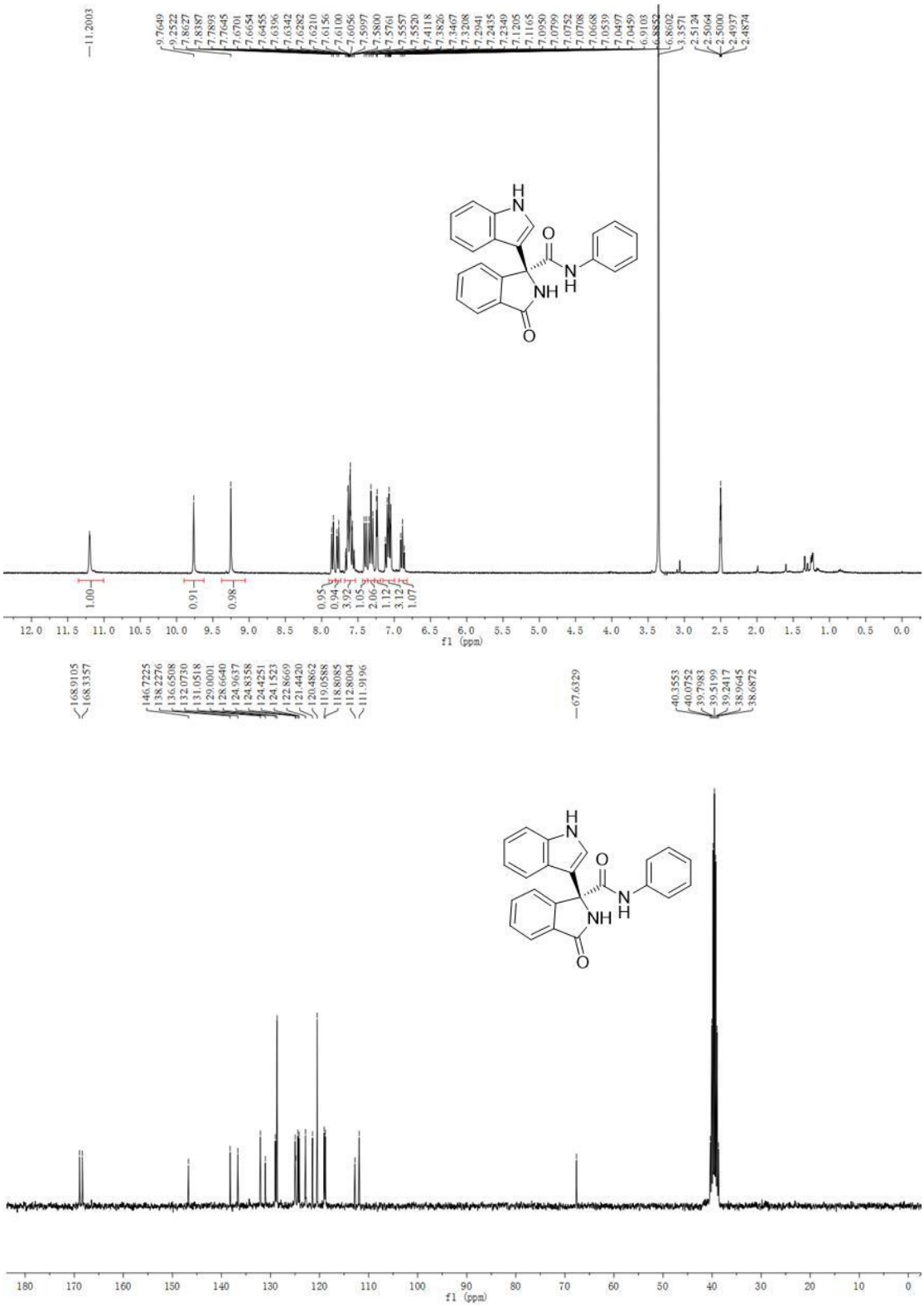
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	9.123	174818	55.40	2992463	49.96
2	11.063	140756	44.60	2997076	50.04
Totals		315574	100.00	5989539	100.00

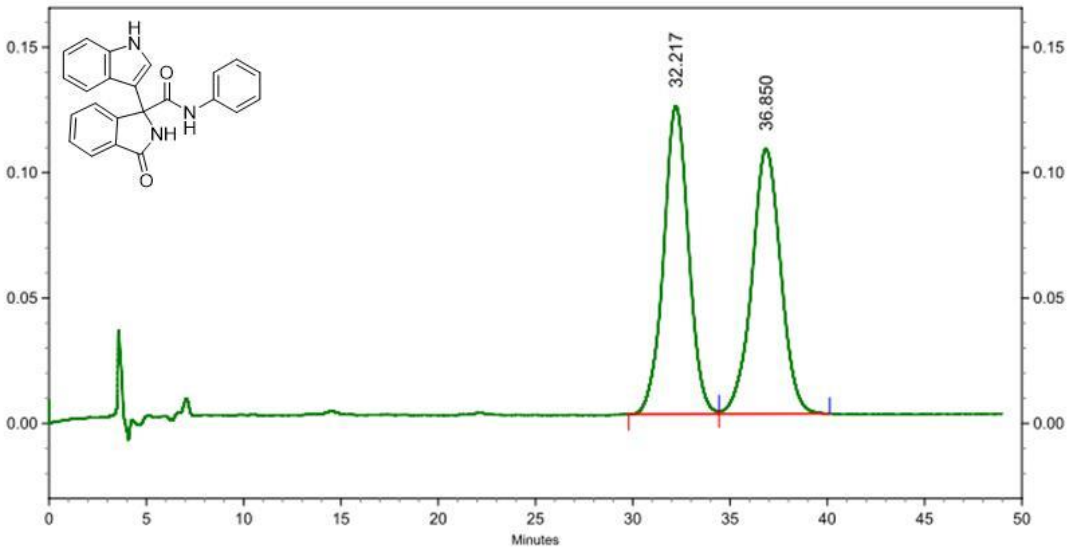


Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	9.077	1239681	99.55	21421048	99.52
2	11.023	5607	0.45	103064	0.48
Totals		1245288	100.00	21524112	100.00

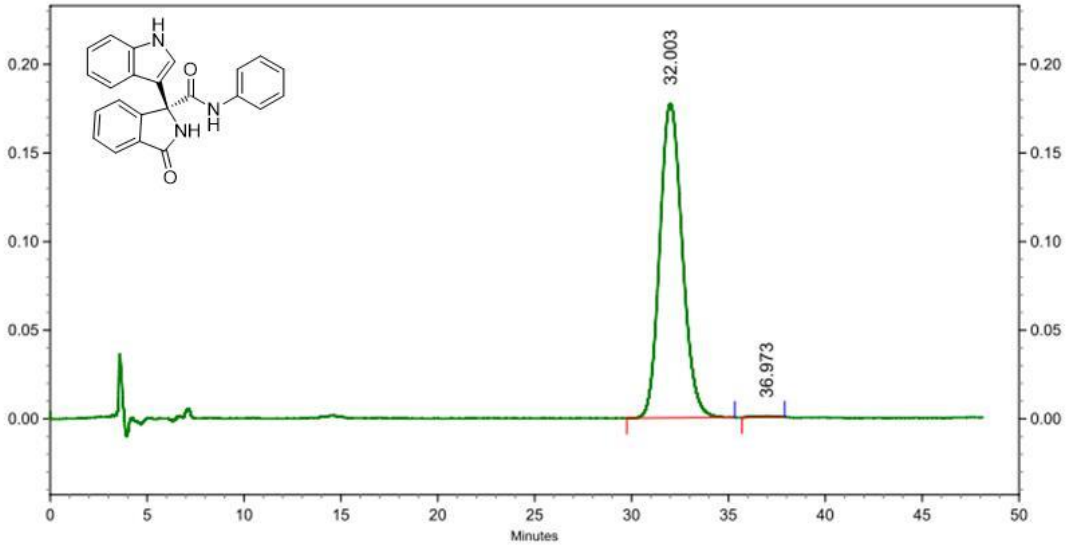
^{1}H NMR, ^{13}C NMR and HPLC spectra of 7





Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	32.217	122872	53.78	10996116	50.22
2	36.850	105603	46.22	10899379	49.78
Totals		228475	100.00	21895495	100.00



Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	32.003	177388	99.61	14315763	99.66
2	36.973	689	0.39	49288	0.34
Totals		178077	100.00	14365051	100.00