Supporting information

Direct Catalytic Asymmetric Synthesis of β-hydroxy Acids from Malonic acid

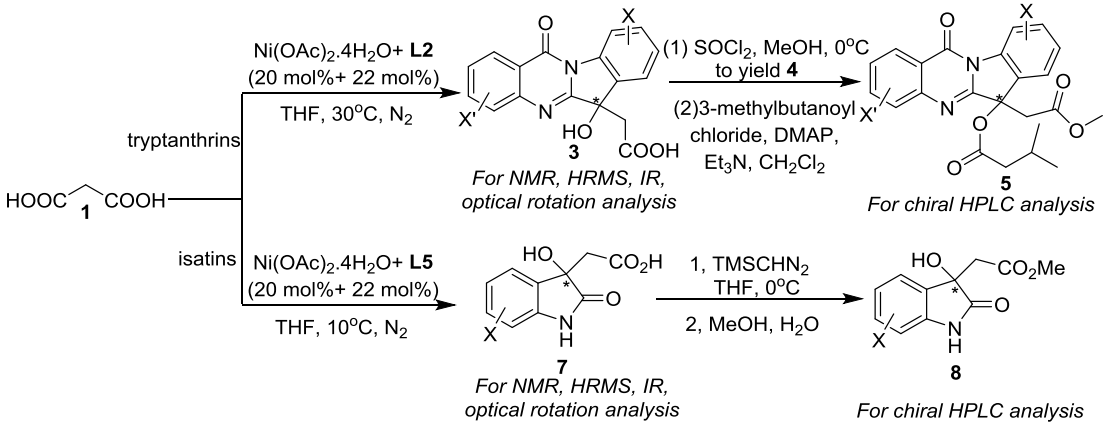
Hang Gao,‡ Zhenli Luo,‡ Pingjin Ge, Junqian He, Feng Zhou, Peipei Zheng and Jun Jiang*

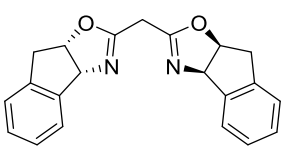
College of Chemistry and Materials Science, Wenzhou University, Wenzhou 325035, PR China.

E-mail: junjiang@wzu.edu.cn; ‡These authors contributed equally.

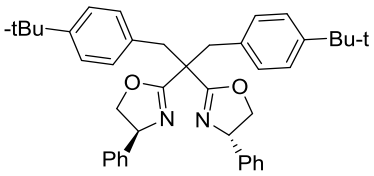
General: NMR spectra were recorded on Brucker-500MHz spectrometers. HRMS (Micromass GCT-MS) spectra were recorded on BRUKER micrOTOF-QII. Infrared spectra were recorded on a Nicolet MX-1E FT-IR spectromter. HPLC analysis was performed on Shimadzu LC-20A. Chiralpak AD-H, AS-H, IA were purchased from Daicel Chemical Industries, LTD. For HPLC analysis, **3a** was converted to **4a** via methyl esterification; **3b**-**3m** were converted to **5b**-**5m** by protection of the carboxyl and hydroxyl groups; **7** were converted to **8** via methyl esterification. Solvents for the column chromatography were distilled before use. Malonic acid was purchased from Amethyst Chemicals, Isatin and its derivatives were purchased from J&K, Tryptanthrin and its derivatives were synthesized according to literature.[1] THF, CH_2Cl_2 and CH_3OH were distilled before use.

Catalytic asymmetric synthesis of β-hydroxy acids with a quaternary stereocenter and corresponding derivatives





L2



L5

General procedure for the catalytic asymmetric synthesis of β-hydroxy acids 3 or 7 from malonic acid: $Ni(OAc)_2{\cdot}4H_2O$ (20% mmol), ligand (22 mol %) and 2.0 mL anhydrous THF were added to a Schlenk tube under nitrogen atmosphere. The mixture was stirred vigorously at room temperature for 1 hour, then malonic acid (0.4 mmol) and tryptanthrins or isatins (0.2 mmol) were added under nitrogen atmosphere, and the resulting mixture was stirred at the corresponding temperature for specific time until the reaction was completed. The reaction mixture was purified through flash column chromatography on a silica gel (eluent: dichloromethane: methanol = 50/1-20/1 or 20/1-15:1) to yield the targeting products.

General procedure for protection of the carboxyl group of 3:

$SOCl_2$ (1.2 mL) was added slowly to a solution of **3** in anhydrous CH_3OH (4.0 mL) at 0 °C, the resulting mixture was stirred at the same temperature for 4 hours followed by the addition of saturated aqueous $NaHCO_3$ solution (60 mL), and the reaction mixture was extracted with CH_2Cl_2 (4×10 mL). The combined organic phase was washed with brine (80 mL), and then dried over anhydrous Na_2SO_4, filtered and the solvent was removed in vacuo. The residue was purified through flash column chromatography on a silica gel (eluent: dichloromethane : ethyl acetate = 15/1-10/1) to yield **4**.

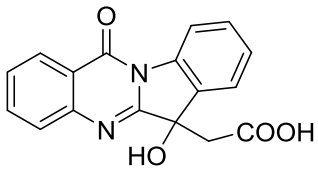
General procedure for the protection of the hydroxyl group of 4:

In a 100 mL round-bottom flask, DMAP (7.4 mg) and Et_3N (111.6 μL) were added to a solution of **4** in dichloromethane (10.0 mL) at 0 °C. The reaction mixture was stirred vigorously at the same temperature for 0.5 hour followed by a slow addition of isovaleryl chloride (0.4 mmol) in 5 minutes. The resulting mixture was stirred for another 10 min then saturated aqueous NH_4Cl solution (60 mL) was added. The reaction mixture was extracted with CH_2Cl_2 (4×10 mL), and the combined organic phase was washed with brine (80 mL), and then dried over anhydrous Na_2SO_4, filtered and the solvent was removed in vacuo. The residue was purified through flash

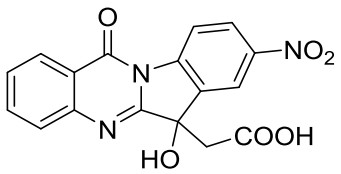
column chromatography on a silica gel (eluent: petroleum ether: ethyl acetate= 10/1-5/1) to yield products **5**.

General Procedure for protection of the carboxyl group of 7:

At 0 °C a solution of $TMSCH_2N_2$ in hexane (c= 2.0 M, 0.4 mL) was added slowly to a solution of **7** in anhydrous THF (2.0 mL). After stirring for 2 hours, CH_3OH (0.1 mL) was added and the reaction mixture was stirred for 30 minutes, then H_2O (0.5 mL) was added. The resulting mixture was extracted with CH_2Cl_2 (4×5 mL), and the combined organic phase was dried over anhydrous Na_2SO_4, filtered and the solvent was removed in vacuo. The residue was purified through flash column chromatography on a silica gel (eluent: petroleum ether: ethyl acetate = 1.5/1-1/1) to yield **8**.

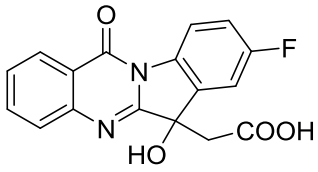


2-(6-hydroxy-11-oxo-10b,11-dihydro-6H-indeno[2,1-b]quinolin-6-yl)acetic acid (3a): 56.7mg, 92% yield; $[\alpha]_D^{30}$= -14.4 (c= 0.083 in acetone); enantiomeric excess: 90%, Daicel Chiralpak AS-H, hexane/iso-propanol= 90/10, flow rate 1.0 mL/min, 25^{o}C: t_R (minor) = 12.24 min, t_R (major) = 18.88 min. ^{1}H NMR (500 MHz, DMSO) δ(ppm) 3.36-3.43 (m, 2H), 6.58 (b, 1H), 7.38-7.41 (m, 1H), 7.51-7.54 (m, 1H), 7.62-7.65 (m, 1H), 7.70-7.71 (m, 1H), 7.81-7.82 (m, 1H), 7.89-7.92 (m, 1H), 8.31-8.32 (m, 1H), 8.41-8.43 (m, 1H), 12.29 (s, 1H); ^{13}C NMR (126 MHz, DMSO) δ(ppm) 43.69, 75.15, 116.44, 121.86, 124.45, 126.92, 127.06, 127.89, 128.02, 130.31, 134.12, 135.27, 139.79, 147.60, 159.34, 161.61, 170.77; IR (KBr) γ 3371, 2921, 1725, 1656, 1464, 774 cm^{-1}; HRMS (BRUKER micrOTOF-QII) exact mass calcd for $(C_{17}H_{13}N_2O_4)^+$ requires *m/z* 309.0875, found *m/z* 309.0877.

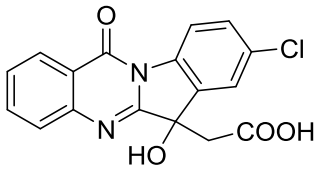


2-(6-hydroxy-8-nitro-12-oxo-6,12-dihydroindolo[2,1-b]quinazolin-6-yl)acetic acid (3b): 63.6mg, 90% yield; $[\alpha]_D^{30}$= -27.3 (c= 0.35 in DMSO); enantiomeric excess:

91%, Daicel Chiralpak IA, hexane/iso-propanol= 90/10, flow rate 1.0 mL/min, 25 °C: t_R (minor)= 14.45 min, t_R (major)= 19.04 min. ^{1}H NMR (500 MHz, acetone-d6) δ(ppm) 3.71 (dd, *J* =17, 55 Hz, 2H), 7.64-7.67 (m, 1H), 7.82 (m, 1H), 7.91-7.93 (m, 1H), 8.36-8.38 (m, 1H), 8.47-8.49 (m, 1H), 8.65 (m, 1H), 8.72 (m, 1H); ^{13}C NMR (126 MHz, acetone-d6) δ(ppm) 43.23, 75.67, 117.56, 120.56, 122.64, 127.28, 127.73, 128.69, 128.87, 136.06, 145.54, 147.12, 148.22, 160.16, 161.35, 170.94; IR (KBr) γ 3371, 2908, 1719, 1646, 1474, 776 cm^{-1}; HRMS (BRUKER micrOTOF-QII) exact mass calcd for $(C_{17}H_{12}N_3O_6)^+$ requires *m/z* 354.0726, found *m/z* 354.0726.

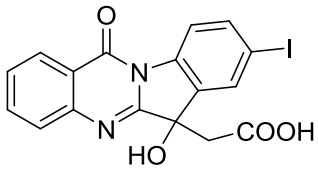


2-(8-fluoro-6-hydroxy-11-oxo-10b,11-dihydro-6H-indeno[2,1-b]quinolin-6-yl)acetic acid (3c): 56.7mg, 87% yield; $[\alpha]_D^{30}$= -11.2 (c= 0.52 in acetone); enantiomeric excess: 92%, Daicel Chiralpak AD-H, hexane/iso-propanol = 90/10, flow rate 1.0 mL/min, 25 °C: t_R (minor) = 12.73 min, t_R (major) = 17.91 min. ^{1}H NMR (500 MHz, acetone-d6) δ(ppm) 3.57 (dd, *J* = 17, 28.5 Hz, 2H), 7.28-7.31 (m, 1H), 7.58-7.63 (m, 2H), 7.78 (d, *J* = 8 Hz, 1H), 7.86-7.89 (m, 1H), 8.34 (d, *J* = 7 Hz, 1H), 8.50-8.52 (m, 1H); ^{13}C NMR (126 MHz, Acetone) δ(ppm) 43.35, 75.93, 112.52, 117.12, 118.77, 122.98, 127.44, 128.21, 128.68, 135.37, 137.12 148.46, 159.86, 161.11, 161.69, 163.05, 170.73; IR (KBr) γ 3483, 2914, 1725, 1672, 1470, 832, 766cm^{-1}; HRMS (BRUKER micrOTOF-QII)exact mass calcd for $(C_{17}H_{12}FN_2O_4)^+$ requires *m/z* 327.0781, found *m/z* 327.0783.

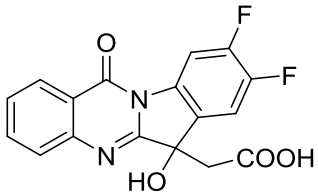


2-(8-chloro-6-hydroxy-12-oxo-6,12-dihydroindolo[2,1-b]quinazolin-6-yl)acetic acid (3d): 60.9mg, 89% yield; $[\alpha]_D^{30}$= -32.3 (c= 0.164 in acetone); enantiomeric excess: 90%, Daicel Chiralpak AD-H, hexane/iso-propanol= 90/10, flow rate 1.0 mL/min, 25 °C: t_R (minor) = 12.13 min, t_R (major) = 16.38 min. ^{1}H NMR (500 MHz, acetone-d6) δ(ppm) 3.59 (s, 2H), 7.56 (d, *J* = 8 Hz, 1H), 7.60-7.63 (m, 1H), 7.78-7.82 (m, 2H), 7.87-7.90 (m, 1H), 8.34(d, *J* = 7 Hz, 1H), 8.48 (d, *J* = 8 Hz, 1H); ^{13}C NMR

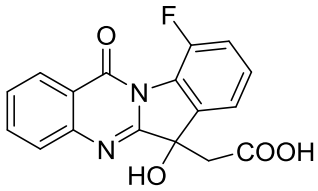
(126 MHz, Acetone) δ(ppm) 43.32, 75.93, 118.66, 122.90, 125.21, 127.51, 128.31, 128.73, 130.82, 132.27, 135.50, 136.48, 139.64, 148.48, 159.92, 161.39, 170.77; IR (KBr) γ 3483, 2921, 1725, 1653, 1460, 837, 766cm^{-1}; HRMS (BRUKER micrOTOF-QII) exact mass calcd for $(C_{17}H_{12}ClN_2O_4)^+$ requires *m/z* 343.0486, found *m/z* 343.0486.



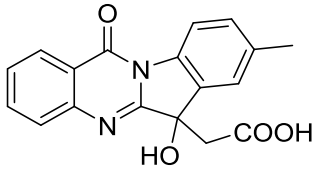
2-(6-hydroxy-8-iodo-12-oxo-6,12-dihydroindolo[2,1-b]quinazolin-6-yl)acetic acid (3e): 79.8mg, 92% yield; $[\alpha]_D^{30}$= -39.8 (c= 0.176 in acetone); enantiomeric excess: 91%, Daicel Chiralpak AD-H, hexane/iso-propanol= 90/10, flow rate 1.0 mL/min, 25 ^oC: t_R (minor) = 17.45 min, t_R (major) = 29.71 min; ^1H NMR (500 MHz, acetone-d6) δ(ppm) 3.58 (s, 2H), 7.60-7.63 (m, 1H), 7.78 (d, *J* = 8 Hz, 1H), 7.86-7.91 (m, 2H), 8.12 (s, 1H), 8.30 (m, 1H), 8.34 (m, 1H); ^{13}C NMR (126 MHz, acetone-d6) δ(ppm) 43.29, 75.71, 119.30, 122.90, 127.52, 128.31, 128.73, 133.90, 135.50, 136.78, 139.90, 140.71, 148.52, 159.96, 161.07, 170.78; IR (KBr) γ 3490, 2921, 1722, 1676, 1460, 762cm^{-1}; HRMS (BRUKER micrOTOF-QII) exact mass calcd for $(C_{17}H_{12}IN_2O_4)^+$ requires *m/z* 434.9842, found *m/z* 434.9846.



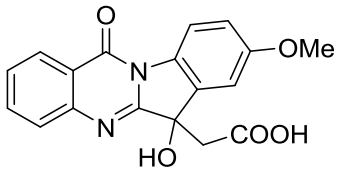
2-(8,9-difluoro-6-hydroxy-12-oxo-6,12-dihydroindolo[2,1-b]quinazolin-6-yl)acetic acid (3f): 62.6mg, 91% yield; $[\alpha]_D^{30}$= -23.4 (c= 0.316 in acetone); enantiomeric excess: 90%, Daicel Chiralpak IA, hexane/iso-propanol = 90/10, flow rate 1.0 mL/min, 25 ^oC: t_R (minor) = 10.98 min, t_R (major) = 15.27 min. ^1H NMR (500 MHz, acetone-d6) δ(ppm) 3.58 (m, 2H), 7.62-7.65 (m, 1H), 7.78-7.84 (m, 2H), 7.88-7.91 (m, 1H), 8.34 (d, *J* = 7 Hz, 1H), 8.39-8.43 (m, 1H); ^{13}C NMR (126 MHz, acetone-d6) δ(ppm) 43.28, 75.88, 107.12, 107.32, 114.30, 114.46, 122.73, 127.51, 128.46, 128.79, 135.67, 148.39, 159.84, 161.34, 170.73; IR (KBr) γ 3483, 2358, 1725, 1679, 1490, 764cm^{-1}; HRMS (BRUKER micrOTOF-QII) exact mass calcd for $(C_{17}H_{11}F_2N_2O_4)^+$ requires *m/z* 345.0687, found *m/z* 345.0681.



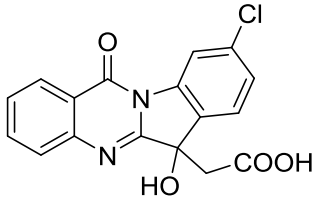
2-(10-fluoro-6-hydroxy-12-oxo-6,12-dihydroindolo[2,1-b]quinazolin-6-yl)acetic acid (3g): 59.9mg, 92% yield; $[\alpha]_D^{30}$= -22.6 (c= 0.553 in acetone); enantiomeric excess: 91%, Daicel Chiralpak AD-H, hexane/iso-propanol = 90/10, flow rate 1.0 mL/min, 25 ^oC: t_R (minor) = 22.00 min, t_R (major) = 23.69 min. ^1H NMR (500 MHz, acetone-d6) δ(ppm) 3.55 (dd, *J* = 16.5, 58 Hz, 2H), 7.30-7.34 (m, 1H), 7.42-7.46 (m, 1H), 7.57-7.61 (m, 2H), 7.75 (m, 1H), 7.84-7.87 (m, 1H), 8.31-8.33 (m, 1H); ^{13}C NMR (126 MHz, acetone-d6) δ(ppm) 43.88, 76.20, 119.88, 120.06, 120.74, 123.29, 127.93, 128.24, 129.37, 129.43, 135.39, 137.99, 148.14, 149.30, 151.34, 157.95, 161.68, 170.75; IR (KBr) γ 3381, 2352, 1696, 1444, 811, 759cm^{-1}; HRMS (BRUKER micrOTOF-QII) exact mass calcd for $(C_{17}H_{12}FN_2O_4)^+$ requires *m/z* 327.0781, found *m/z* 327.0776.



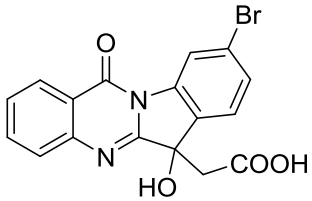
2-(6-hydroxy-8-methyl-12-oxo-6,12-dihydroindolo[2,1-b]quinazolin-6-yl)acetic acid (3h): 57.9mg, 90% yield; $[\alpha]_D^{30}$= -43.1 (c= 0.211 in acetone); enantiomeric excess: 87%, Daicel Chiralpak IA, hexane/iso-propanol = 90/10, flow rate 1.0 mL/min, 25 ^oC): t_R (minor) = 12.68 min, t_R (major) = 17.04 min. ^1H NMR (500 MHz, acetone-d6) δ(ppm) 2.42 (s, 3H), 3.52 (dd, *J* =16.5, 60 Hz, 2H), 7.32(d, *J* = 8 Hz, 1H), 7.55 (s, 1H), 7.58-7.61 (m, 1H), 7.76-7.78 (m, 1H), 7.84-7.86 (m, 1H), 8.33-8.36 (m, 2H); ^{13}C NMR (126 MHz, Acetone) δ(ppm) 21.30, 43.49, 75.98, 117.08, 123.08, 125.22, 127.40, 128.00, 128.59, 131.27, 134.15, 135.17, 137.29, 138.65, 148.54, 159.84, 162.05, 170.70; IR (KBr) γ 3291, 2914, 1749, 1646, 1470, 817, 767cm^{-1}; HRMS (BRUKER micrOTOF-QII) exact mass calcd for $(C_{18}H_{15}N_2O_4)^+$ requires *m/z* 323.1032, found *m/z* 323.1026.



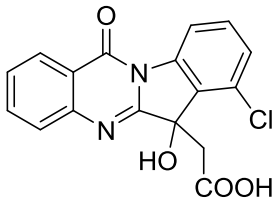
2-(6-hydroxy-8-methoxy-12-oxo-6,12-dihydroindolo[2,1-b]quinazolin-6-yl)acetic acid (3i): 60.1mg, 89% yield; $[\alpha]_D^{30}$= -22.0 (c= 0.486 in DMSO); enantiomeric excess: 87%, Daicel Chiralpak IA, hexane/iso-propanol= 90/10, flow rate 1.0 mL/min, 25 ^oC: t_R (major) = 20.16 min, t_R (minor) = 26.02 min. ^1H NMR (500 MHz, acetone-d6) δ(ppm) 3.53 (dd, *J* = 16.5, 42.6 Hz, 2H), 3.88 (s, 3H), 7.05 (d, *J* = 8 Hz, 1H), 7.34 (s, 1H), 7.57-7.60 (m, 1H), 7.75-7.77 (m, 1H), 7.83-7.86 (m, 1H), 8.32 (d, *J* =8 Hz, 1H), 8.39 (d, *J* = 9 Hz, 1H); ^{13}C NMR (126 MHz, acetone-d6) δ(ppm) 43.48, 56.14, 76.11, 110.81, 115.58, 118.27, 123.06, 127.33, 127.99, 128.55, 134.17, 135.07, 135.71, 148.47, 159.64, 162.07, 170.71; IR (KBr) γ 3344, 2921, 1722, 1649, 1487, 829, 779cm^{-1}; HRMS (BRUKER micrOTOF-QII) exact mass calcd for $(C_{18}H_{15}N_2O_5)^+$ requires *m/z* 339.0981, found *m/z* 339.0975.



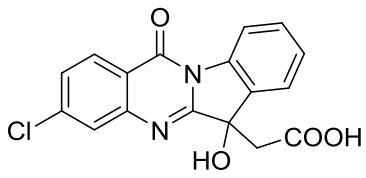
2-(9-chloro-6-hydroxy-12-oxo-6,12-dihydroindolo[2,1-b]quinazolin-6-yl)acetic acid (3j): 60.2mg, 88% yield; $[\alpha]_D^{30}$= -25.1 (c= 0.143 in DMSO); enantiomeric excess: 88%, Daicel Chiralpak IA, hexane/iso-propanol = 90/10, flow rate 1.0 mL/min, 25 ^oC: t_R (minor) = 17.08 min, t_R (major) = 18.30 min. ^1H NMR (500 MHz, acetone-d6) δ(ppm) 3.56 (dd, *J* = 17, 40 Hz, 2H), 7.43-7.45 (m, 1H), 7.61-7.64 (m, 1H), 7.77-7.80 (m, 2H), 7.87-7.90 (m, 1H), 8.34-8.36 (m, 1H), 8.52 (s, 1H); ^{13}C NMR (126 MHz, acetone-d6) δ(ppm) 43.39, 75.74, 117.41, 122.76, 126.18, 127.31, 127.55, 128.37, 128.72, 133.09, 135.62, 135.77, 141.82, 148.38, 160.05, 161.50, 170.74; IR (KBr) γ 3258, 2921, 1745, 1656, 1460, 772cm^{-1}; HRMS (BRUKER micrOTOF-QII) exact mass calcd for $(C_{17}H_{12}ClN_2O_4)^+$ requires *m/z* 343.0486, found *m/z* 343.0484.



2-(9-bromo-6-hydroxy-12-oxo-6,12-dihydroindolo[2,1-b]quinazolin-6-yl)acetic acid (3k): 67.9mg, 88% yield; $[\alpha]_D^{30}$= -11.7 (c= 0.754 in acetone); enantiomeric excess: 90%, Daicel Chiralpak AD-H, hexane/iso-propanol = 90/10, flow rate 1.0 mL/min, 25 °C: t_R (minor)= 16.35 min, t_R (major)= 18.59 min. ^{1}H NMR (500 MHz, acetone-d6) δ(ppm) 2.96 (s, 2H), 6.19 (b, 1H), 7.16-7.21 (m, 2H), 7.25 (m, 1H), 7.37-7.38 (m, 1H), 7.45-7.48 (m, 1H), 7.86 (d, *J* = 7 Hz, 1H), 8.12 (s, 1H); ^{13}C NMR (126 MHz, acetone-d6) δ(ppm) 43.91, 75.42, 119.53, 122.04, 123.04, 126.89, 127.48, 128.58, 128.64, 130.28, 134.12, 136.08, 141.34, 147.90, 159.81, 161.64, 171.31; IR (KBr) γ 3285, 2914, 1686, 1480, 776cm^{-1}; HRMS (BRUKER micrOTOF-QII) exact mass calcd for ($C_{17}H_{11}BrN_2O_4Na)^+$ requires *m/z* 408.9800, found *m/z* 408.9794.

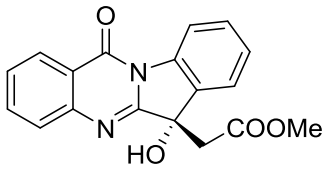


2-(7-chloro-6-hydroxy-12-oxo-6,12-dihydroindolo[2,1-b]quinazolin-6-yl)acetic acid (3l): 49.2mg, 72% yield; $[\alpha]_D^{30}$= -14.7 (c= 0.504 in acetone); enantiomeric excess: 67%, Daicel Chiralpak AD-H, hexane/iso-propanol = 95/5, flow rate 1.0 mL/min, 25 °C: t_R (minor)= 15.12 min, t_R (major)= 16.32 min. ^{1}H NMR (500 MHz, DMSO) δ(ppm) 3.59 (dd, *J* = 17, 145 Hz, 2H), 7.40 (d, *J* = 8 Hz, 1H), 7.54-7.57 (m, 1H), 7.63-7.66 (m, 1H), 7.82 (d, *J* = 8 Hz, 1H), 7.90-7.93 (m, 1H), 8.30 (d, *J* = 8 Hz, 1H), 8.45 (d, *J*= 8 Hz, 1H); ^{13}C NMR (126 MHz, DMSO) δ(ppm) 41.28, 75.67, 114.84, 121.21, 126.52, 127.61, 129.62, 130.17, 131.54, 135.04, 141.15, 148.95, 158.79, 160.42, 170.19; IR (KBr) γ 3275, 2919, 1730, 1683, 1439, 780cm^{-1}; HRMS (BRUKER micrOTOF-QII) exact mass calcd for $(C_{17}H_{12}ClN_2O_4)^+$ requires *m/z* 343.0486, found *m/z* 343.0495.

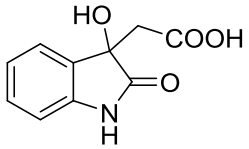


2-(3-chloro-6-hydroxy-12-oxo-6,12-dihydroindolo[2,1-b]quinazolin-6-yl)acetic acid (3m): 58.1mg, 85% yield; $[\alpha]_D^{30}$= -13.5 (c= 0.421 in acetone); enantiomeric excess: 83%, Daicel Chiralpak AD-H, hexane/iso-propanol = 95/5, flow rate 1.0

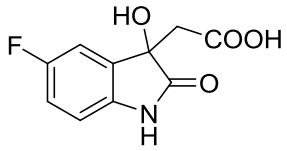
mL/min, 25 °C: t_R (major)= 18.47 min, t_R (minor)= 26.31 min. ^{1}H NMR (500 MHz, DMSO) δ(ppm) 3.37 (s, 2H), 7.38-7.41 (m, 1H), 7.51-7.54 (m, 1H), 7.66-7.71 (m, 2H), 7.90 (s, 1H), 8.30 (d, *J* = 8.5 Hz, 1H), 8.39 (d, *J* = 8 Hz, 1H); ^{13}C NMR (126 MHz, DMSO) δ(ppm) 43.23, 74.82, 115.96, 120.18, 123.98, 126.75, 127.66, 128.41, 129.85, 133.62, 139.06, 139.44, 148.24, 158.20, 162.75, 170.29; IR (KBr) γ 3255, 2920, 1726, 1666, 1465, 780cm^{-1}; HRMS (BRUKER micrOTOF-QII) exact mass calcd for $(C_{17}H_{12}ClN_2O_4)^+$ requires *m/z* 343.0486, found *m/z* 343.0492.



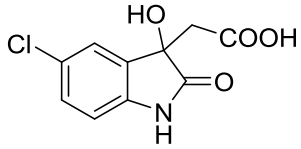
methyl (S)-2-(6-hydroxy-12-oxo-6,12-dihydroindolo[2,1-b]quinazolin-6-yl)acetate (*ent*-4a):[2] 59.9mg, 93% yield; $[\alpha]_D^{20}$= -23.7 (c= 0.23 in $CHCl_3$); enantiomeric excess: 91%, Daicel Chiralpak AS-H, hexane/iso-propanol= 90/10, flow rate 1.0 mL/min, 25°C: t_R (major)= 11.93 min, t_R (minor)= 21.22 min. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ(ppm) 3.36 (dd, J= 16.5, 61 Hz, 2H), 3.50 (s, 3H), 5.11 (s, 1H), 7.10-7.15 (m, 2H), 7.44-7.47 (m, 1H), 7.51 (d, J= 6 Hz, 1H), 7.72-7.73 (m, 2H), 8.15 (d, J= 8 Hz, 1H), 8.22-8.23 (m, 1H).



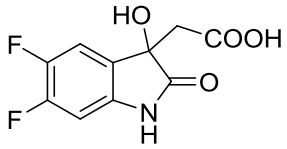
2-(3-hydroxy-2-oxoindolin-3-yl)acetic acid (7a): 31.4mg, 81% yield; $[\alpha]_D^{25}$= +12.4 (c= 0.113 in CH_3OH); enantiomeric excess: 76%, Daicel Chiralpak IA, hexane/iso-propanol = 90/10, flow rate 1.0 mL/min, 25 °C: t_R (major) = 20.28 min , t_R (minor) = 31.78 min. ^{1}H NMR (500 MHz, MeOD) δ(ppm) 3.05 (dd, *J* = 16, 28.5 Hz, 2H), 6.87 (d, *J* = 8 Hz, 1H), 7.01-7.04 (m, 1H), 7.23-7.26 (m, 1H), 7.36 (d, *J* = 7 Hz, 1H); ^{13}C NMR (126 MHz, MeOD) δ(ppm) 42.5, 74.70, 111.25, 123.49, 125.07, 130.82, 132.01, 143.70, 172.53, 181.04; IR (KBr) γ 3371, 2345, 1696, 1430, 893, 751cm^{-1}; HRMS (BRUKER micrOTOF-QII) exact mass calcd for $(C_{10}H_{10}NO_4)^+$ requires *m/z* 208.0610, found *m/z* 208.0604.



2-(5-fluoro-3-hydroxy-2-oxoindolin-3-yl)acetic acid (7b): yield: 37.3mg, 83%; $[\alpha]_D^{25}$= +12.0 (c= 0.133 in CH_3OH); enantiomeric excess: 78%, Daicel Chiralpak IA, hexane/iso-propanol= 85/15, flow rate 1.0 mL/min, 25 ^oC: t_R (minor)= 13.08 min , t_R (major) = 18.44 min. ^1H NMR (500 MHz, MeOD) δ(ppm) 3.07 (dd, J = 16, 20 Hz, 2H), 6.85-6.87 (m, 1H), 6.99-7.03 (m, 1H), 7.19-7.20 (m, 1H); ^{13}C NMR (126 MHz, MeOD) δ(ppm) 42.40, 74.94, 111.98, 113.07, 116.92, 133.88, 139.69, 161.46, 172.37, 180.98; IR (KBr) γ 3219, 2378, 1686, 1464, 890, 756cm^{-1}; HRMS (BRUKER micrOTOF-QII) exact mass calcd for $(C_{10}H_9FNO_4)^+$ requires *m/z* 226.0516, found *m/z* 226.0504.

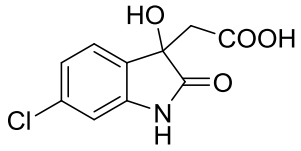


2-(5-chloro-3-hydroxy-2-oxoindolin-3-yl)acetic acid (7c): 35.2mg, 73% Yield; $[\alpha]_D^{25}$= +2.8 (c= 0.145 in CH_3OH); enantiomeric excess: 71%, Daicel Chiralpak IA, hexane/iso-propanol = 85/15, flow rate 1.0 mL/min, 25 ^oC: t_R (minor) = 13.23 min , t_R (major) = 19.59 min. ^1H NMR (500 MHz, MeOD) δ(ppm) 3.08 (dd, *J* = 17, 20 Hz, 2H), 6.87 (d, *J*= 8 Hz, 1H), 7.27 (d, *J*= 8 Hz, 1H), 7.40 (s, 1H); ^{13}C NMR (126 MHz, MeOD) δ(ppm) 42.35, 74.69, 112.39, 125.56, 128.65, 130.61, 134.08, 142.52, 172.34, 180.65; IR (KBr) γ 3364, 2358, 1692, 1474, 870, 772cm^{-1}; HRMS (BRUKER micrOTOF-QII) exact mass calcd for $(C_{10}H_8ClNO_4Na)^+$ requires *m/z* 264.0040, found *m/z* 264.0038.

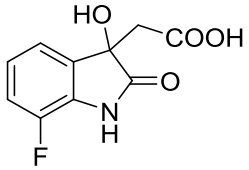


2-(5,6-difluoro-3-hydroxy-2-oxoindolin-3-yl)acetic acid (7d): 42.3mg, 87% yield; $[\alpha]_D^{25}$= +2.7 (c= 0.300 in CH_3OH); enantiomeric excess: 81%, Daicel Chiralpak IA, hexane/iso-propanol = 85/15, flow rate 1.0 mL/min, 25 ^oC: t_R (minor) = 13.02 min , t_R (major) = 18.91 min. ^1H NMR (500 MHz, MeOD) δ(ppm) 3.05 (s, 2H), 6.77-6.80 (m, 1H) 7.33-7.36 (m, 1H); ^{13}C NMR (126 MHz, MeOD) δ(ppm) 42.32, 74.55, 101.16,

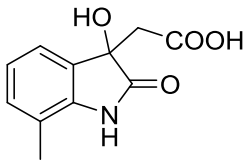
114.99, 128.02, 140.41, 146.8, 148.7, 151.40, 153.47, 172.33, 180.89; IR (KBr) γ 3305, 2365, 1699, 1467, 870, 776cm^{-1}; HRMS (BRUKER micrOTOF-QII) exact mass calcd for $(C_{10}H_7F_2NO_4Na)^+$ requires *m/z* 266.0241, found *m/z* 266.0248.



2-(6-chloro-3-hydroxy-2-oxoindolin-3-yl)acetic acid (7e): 41.5mg, 86% yield; $[\alpha]_D^{25}$= +18.7 (c= 0.257 in CH_3OH); enantiomeric excess: 80%, Daicel Chiralpak IA, hexane/iso-propanol = 85/15, flow rate 1.0 mL/min, 25 ^oC: t_R (minor) = 14.52 min , t_R (major) = 21.40 min. ^1H NMR (500 MHz, MeOD) δ(ppm) 3.09 (dd, *J* = 16, 27 Hz, 2H), 6.91(s, 1H), 7.03-7.04 (m, 1H), 7.35-7.36 (m, 1H); ^{13}C NMR (126 MHz, MeOD) δ(ppm) 42.38, 74.24, 111.64, 123.19, 126.30, 130.76, 136.33, 145.24, 172.39, 180.89; IR (KBr) γ 2974, 2557, 1709,1448, 870, 776cm^{-1}; HRMS (BRUKER micrOTOF-QII) exact mass calcd for $(C_{10}H_8ClNO_4Na)^+$ requires *m/z* 264.0040, found *m/z* 264.0035.

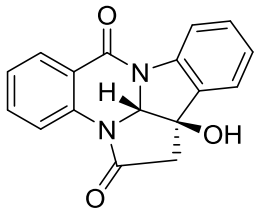


2-(7-fluoro-3-hydroxy-2-oxoindolin-3-yl)acetic acid (7f): 33.7mg, 75% yield; $[\alpha]_D^{25}$= +2.7 (c= 0.300 in CH_3OH); enantiomeric excess: 73%, Daicel Chiralpak IA, hexane/iso-propanol = 85/15, flow rate 1.0 mL/min, 25 ^oC): t_R (minor) = 18.88 min , t_R (major) = 21.12 min. ^1H NMR (500 MHz, MeOD) δ(ppm) 3.08 (dd, *J*= 16, 32 Hz, 2H), 6.99-7.03 (m, 1H), 7.04-7.08 (m, 1H), 7.1-7.20 (m, 1H); ^{13}C NMR (126 MHz, MeOD) δ(ppm) 42.62, 74.73, 117.65, 120.86, 124.25, 130.84, 135.13, 147.71, 149.64, 180.58; IR (KBr) γ 3309, 2358, 1695, 1467, 872, 775 cm^{-1}; HRMS (BRUKER micrOTOF-QII) exact mass calcd for $(C_{10}H_9FNO_4)^+$ requires *m/z* 226.0516, found *m/z* 226.0511.



2-(3-hydroxy-7-methyl-2-oxoindolin-3-yl)acetic acid (7g): 37.1mg, 84% yield; $[\alpha]_D^{28}$= +2.6 (c= 0.308 in CH_3OH); enantiomeric excess: 76%, Daicel Chiralpak IA, hexane/iso-propanol = 90/10, flow rate 1.0 mL/min, 25 °C): t_R (minor) = 19.72 min , t_R (major) = 23.2 min. ^{1}H NMR (500 MHz, MeOD) δ(ppm) 2.24 (s, 3H), 2.96-3.05 (m, 2H), 6.93(t, *J*= 7.5 Hz, 1H), 7.06 (d, *J*= 8 Hz, 1H), 7.19 (d, *J*= 7 Hz, 1H); ^{13}C NMR (126 MHz, MeOD) δ(ppm) 16.50, 74.95, 120.92, 122.39, 123.50, 131.74, 132.12, 142.00, 165.61, 173.13, 181.37; IR (KBr) γ 3301, 2338, 1690, 1466, 875, 776 cm^{-1}; HRMS (BRUKER micrOTOF-QII) exact mass calcd for $(C_{11}H_{12}NO_4)^+$ requires *m/z* 222.0761, found *m/z* 222.0765.

11b-hydroxy-2a1,11b-dihydro-7H-2a,7a-diazabenzo[b]cyclopenta[lm]fluorene-2,7(1H)-dione: 10



Followed the reported procedure:[3] to a stirred solution of **4a** (46.2 mg, 0.15 mmol) in MeOH: $CHCl_3$ (1: 1, 3 mL) was added $NaBH_4$ (11.2 mg, 0.3 mmol) in small portions at 25 °C. The reaction mixture was further stirred for 6h at 25 °C and quenched with 2N HCl. The organic phase was washed with brine and dried over Na_2SO_4, filtered and the solvent was removed in vacuo. The residue was purified through flash column chromatography on a silica gel (dichloromethane-ethyl acetate 20: 1) to provide the title product as white solid (27.5mg, yield: 63%). The spectral and optical rotation data of the final compound (-)-**10** were found to be in good agreement with the reported values.[4] $[\alpha]_D^{30}$= -213.0 (c= 0.114 in CH_3OH); enantiomeric excess: 89%, determined by HPLC (Daicel Chiralpak AD-H, hexane/iso-propanol= 90/10, flow rate 1.0 mL/min, 25 °C): t_R (minor) = 25.46 min, t_R (major) = 32.83 min. ^{1}H NMR (500 MHz, DMSO, 25 °C) δ(ppm) 3.05 (d, *J* = 18 Hz, 1H), 3.15 (d, *J* = 18 Hz, 1H), 5.80 (s, 1H), 6.70 (s, 1H), 7.23 (t, *J* = 8 Hz, 1H), 7.39-7.42 (m, 1H), 7.44-7.47 (m, 1H), 7.54 (d, *J* = 8 Hz, 1H), 7.71-7.76 (m, 2H), 7.93 (d, *J*= 8 Hz, 1H), 8.04 (d, *J* = 7 Hz, 1H).

Reference

[1] V. M. Sharma, P. Prasanna, K. V. Adi Seshu, B. Renuka, C. V. Laxman Rao, G.

Sunil Kumar, C. P. Narasimhulu, P. Aravind Babu, R. C. Puranik, D. Subramanyam,

A. Venkateswarlu, S. Rajagopal, K. B. S. Kumar, C. S. Rao, N. V. S. R. Mamidi, D. S.

Deevi, R. Ajaykumar, R. Rajagopalan, Bioorg. Med. Chem. Lett. 2002, 12, 2303-2307.

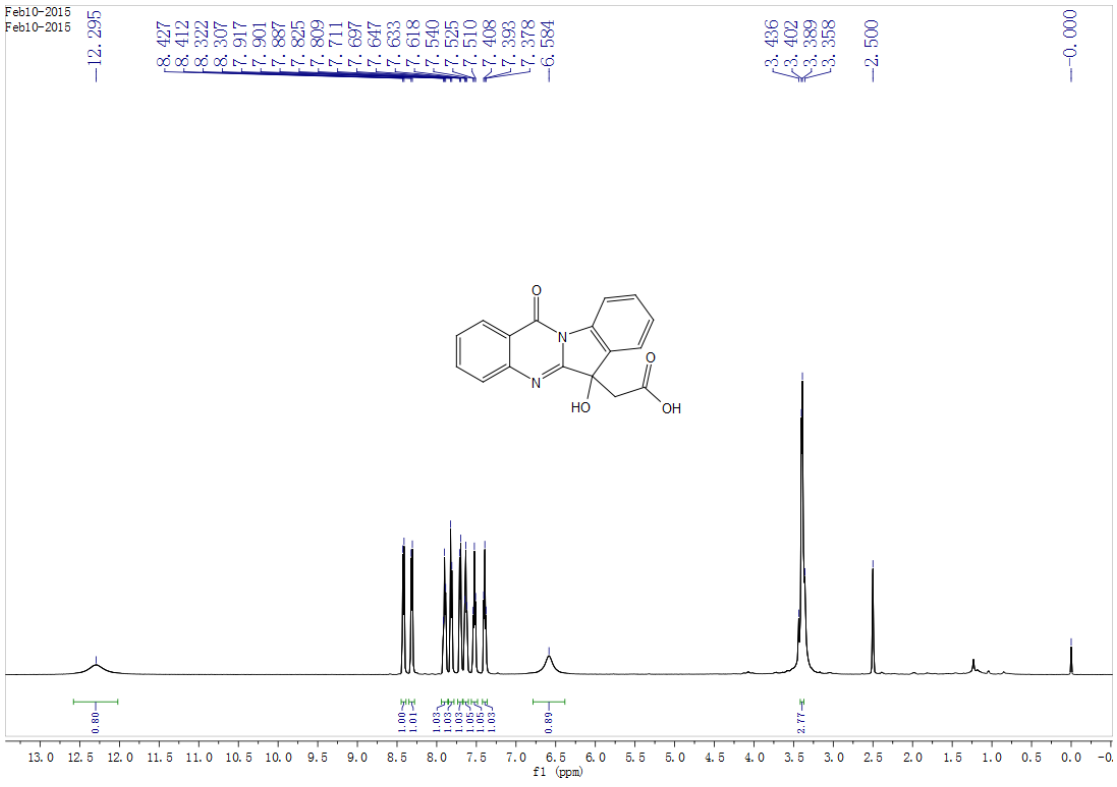
[2] C.-W. Jao, W.-C. Lin, Y.-T. Wu, P.-L. Wu, *J. Nat. Prod.* **2008**, *71*, 1275-1280.

[3] S. D. Vaidya, N. P. Argade, *Org. Lett.*, **2013**, *15*, 4006-4009.

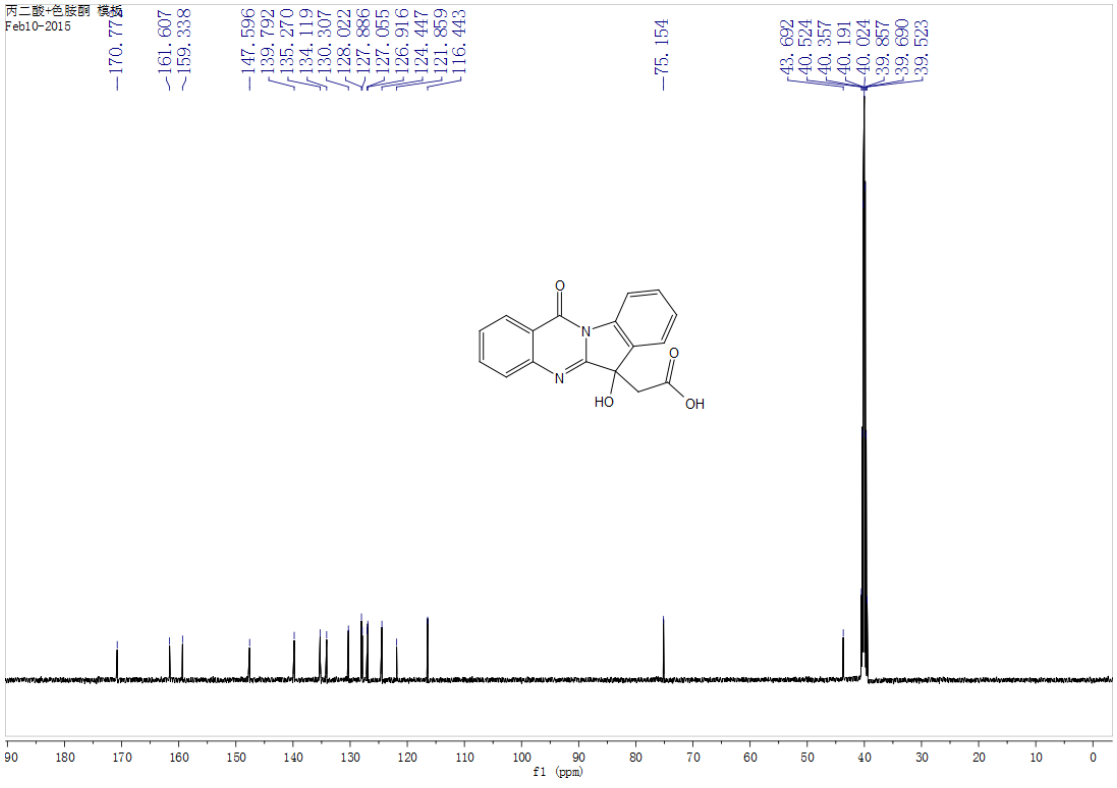
[4] M. Chen, L. Gan, S. Lin, X. Wang, L. Li, Y. Li, C. Zhu, Y. Wang, B. Jiang, J. Jiang, Y. Yang, J. Shi, *J. Nat. Prod.* **2012**, *75*, 1167-1176.

NMR data of products

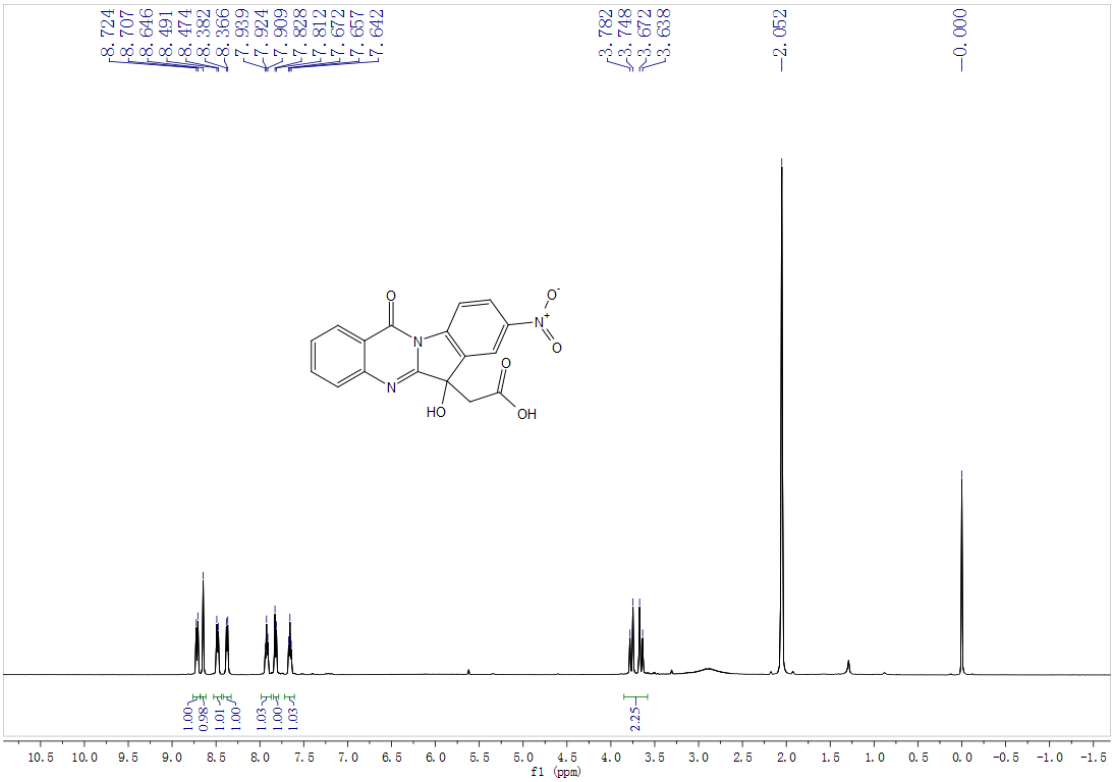
3a's ^{1}H NMR (500 MHz, DMSO)



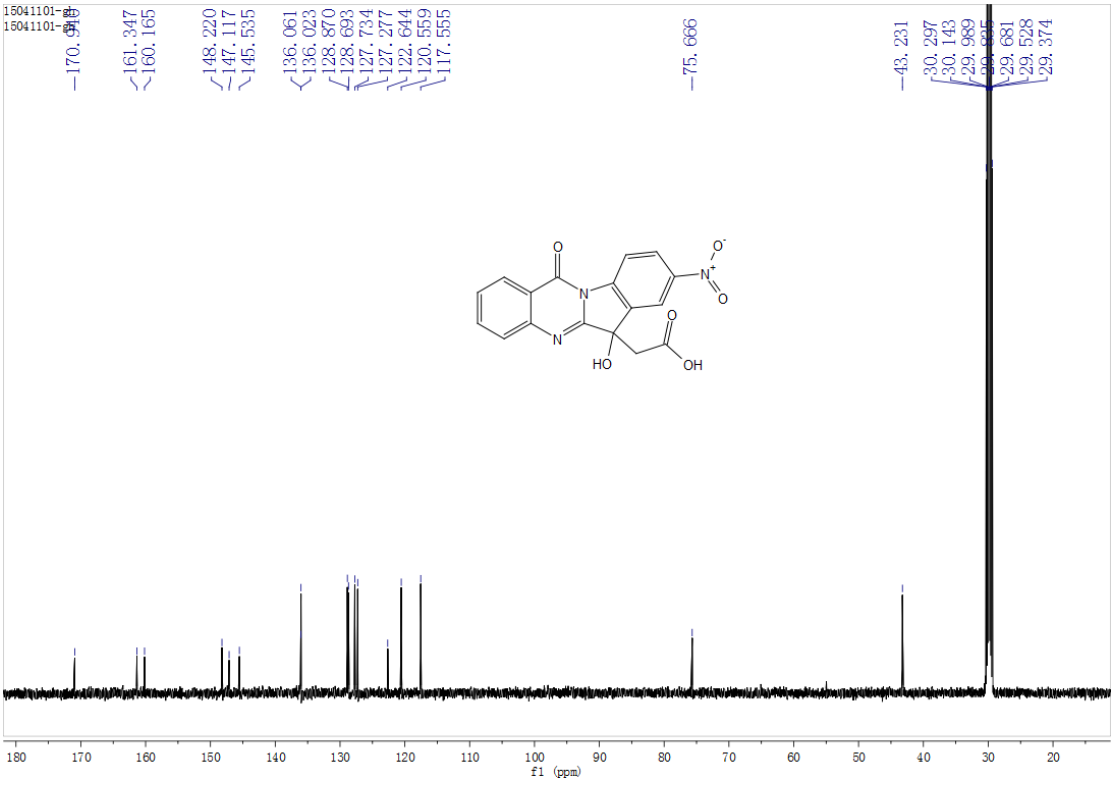
3a's ^{13}C NMR (126 MHz, DMSO)



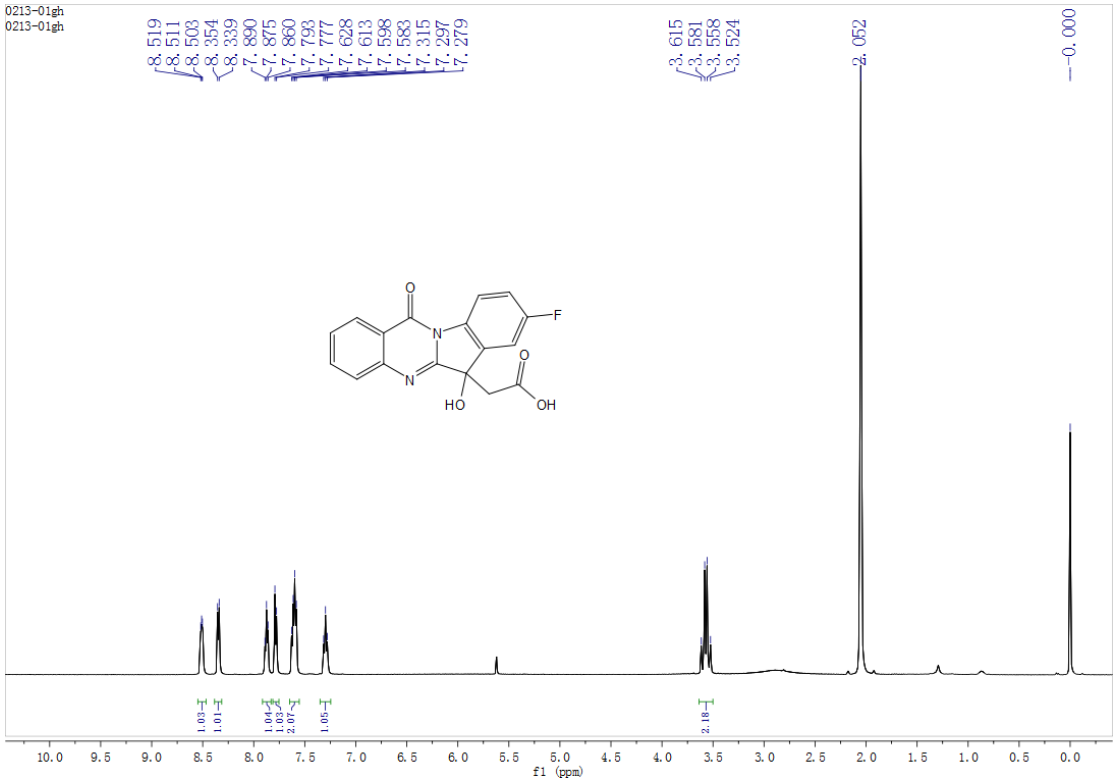
3b's ^{1}H NMR (500 MHz, Acetone-D6)



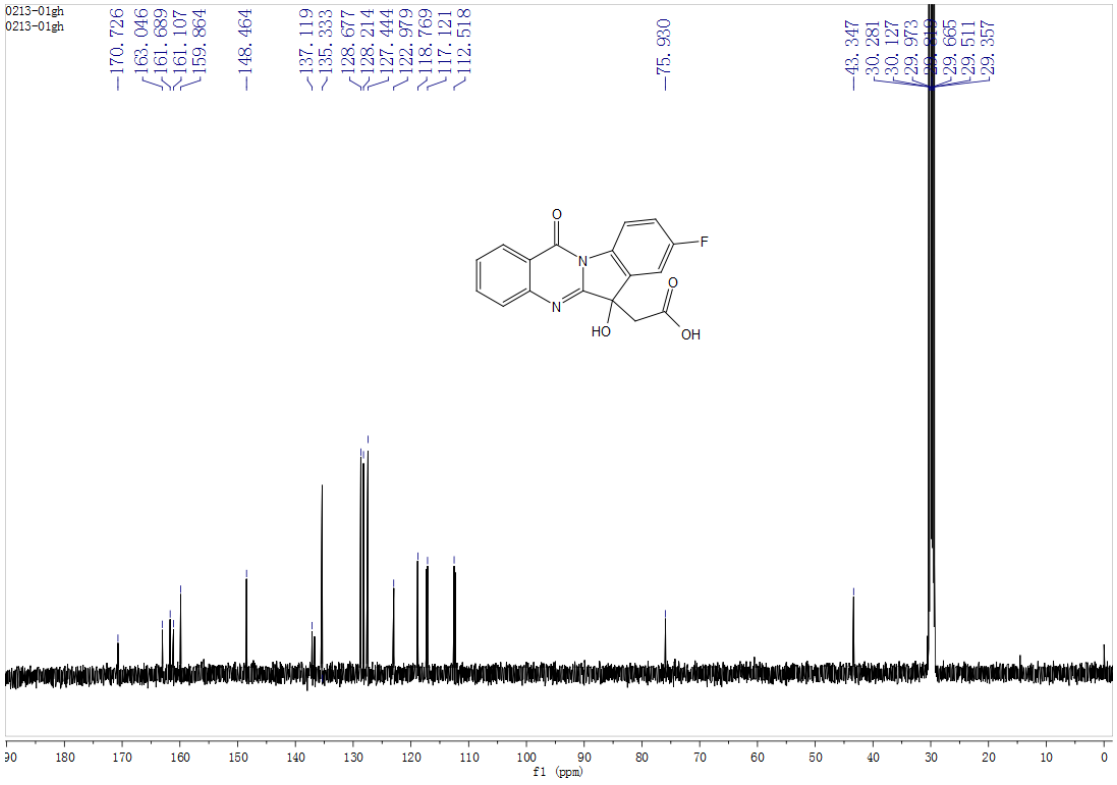
3b's ^{13}C NMR (126 MHz, Acetone-D6)



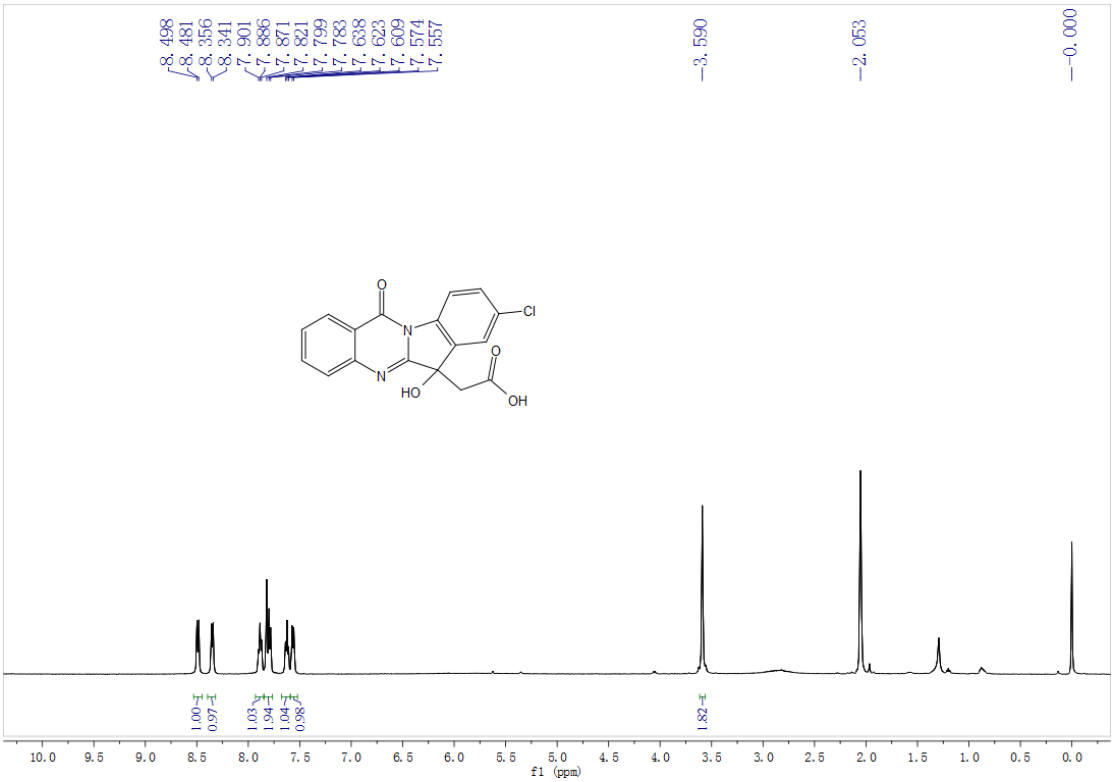
3c's ^{1}H NMR (500 MHz, Acetone-D6)



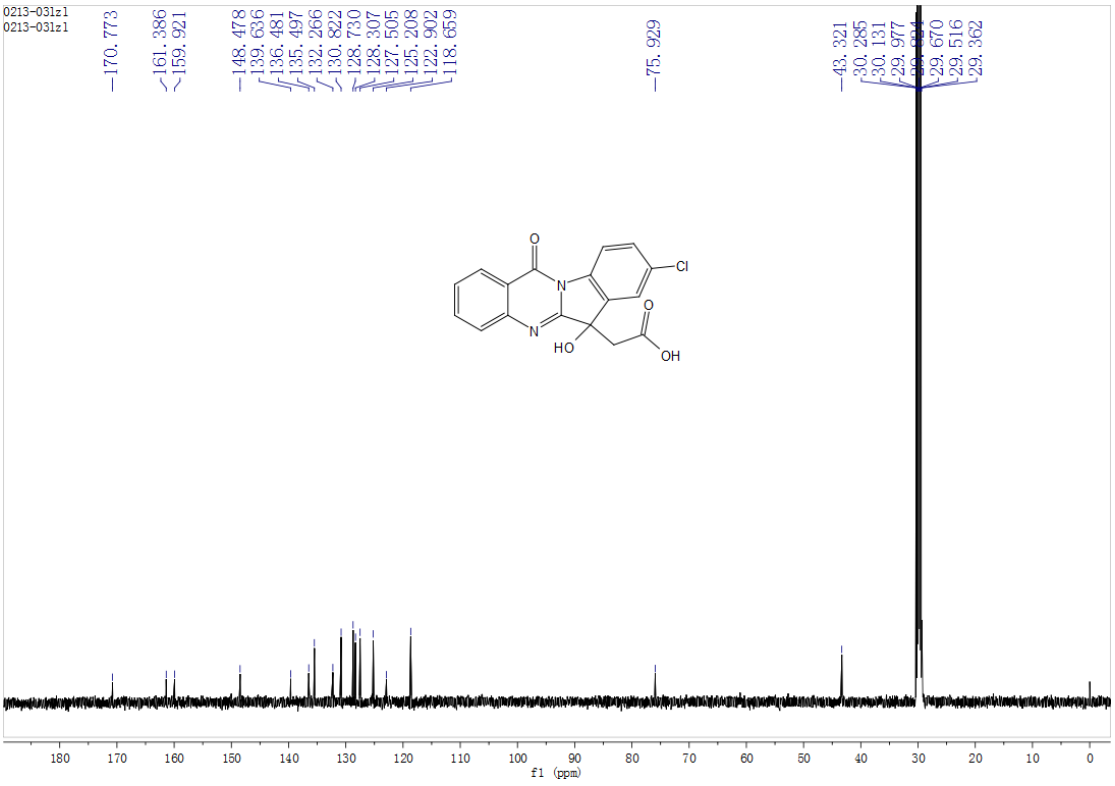
3c's ^{13}C NMR (126 MHz, Acetone-D6)



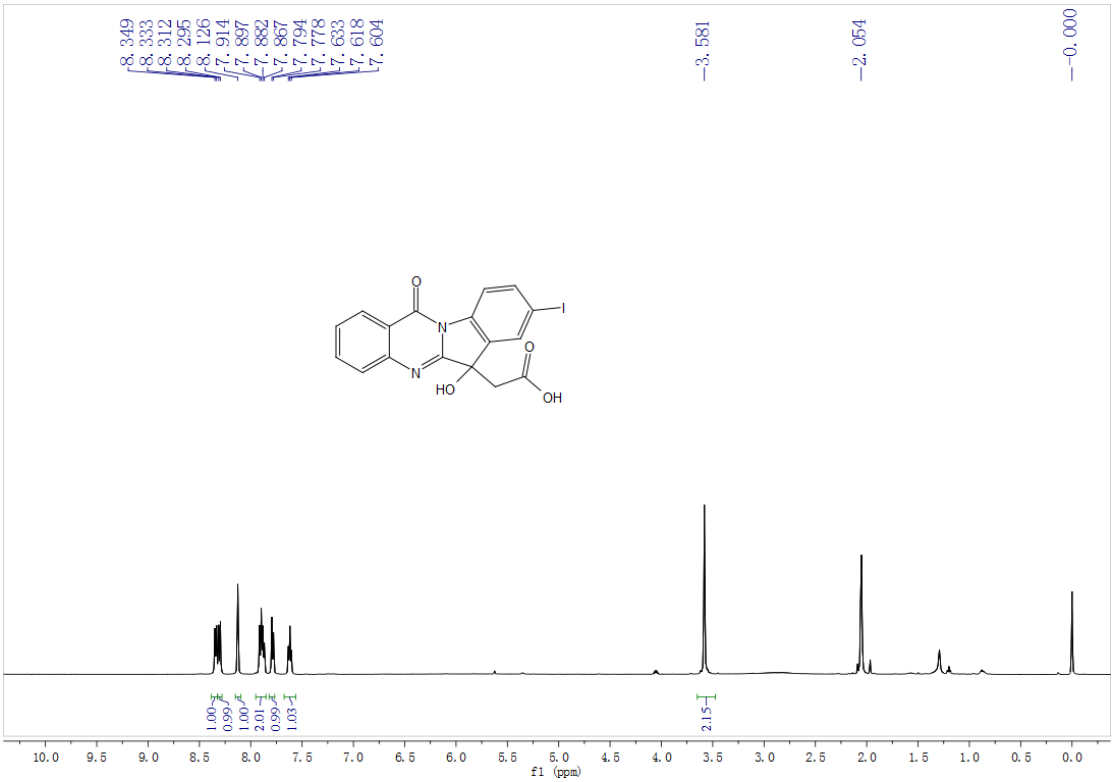
3d's ^{1}H NMR (500 MHz, Acetone-D6)



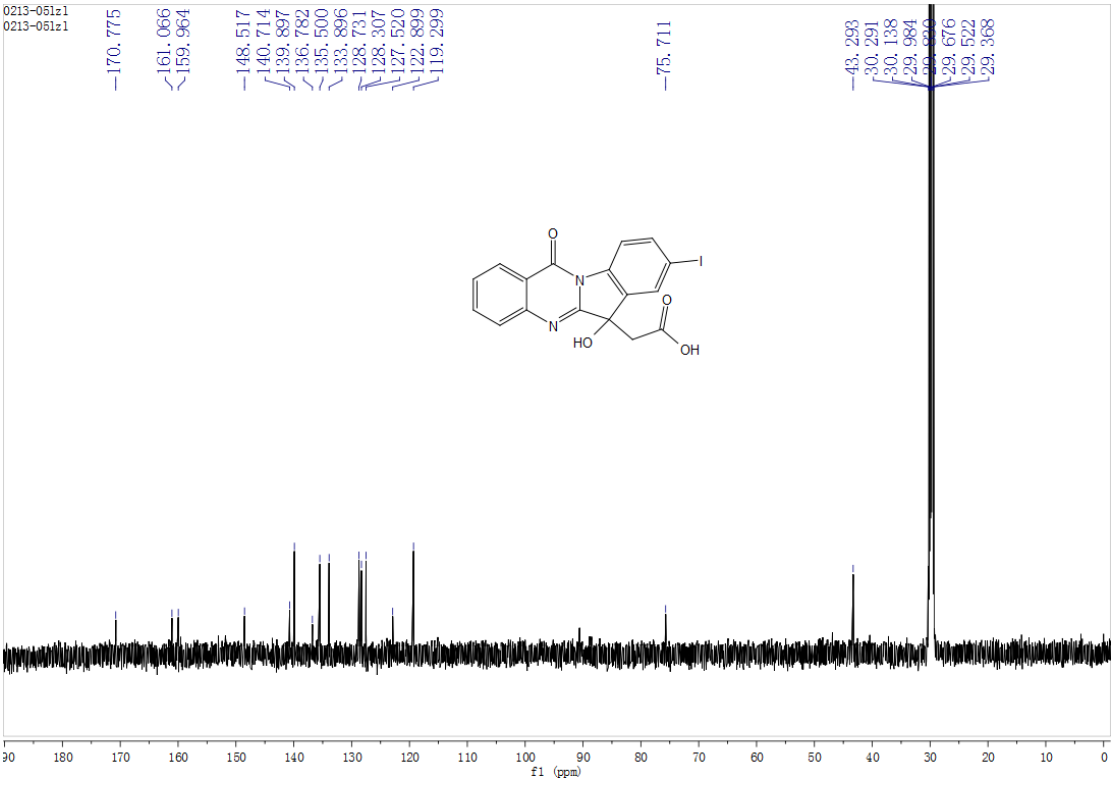
3d's ^{13}C NMR (126 MHz, Acetone-D6)



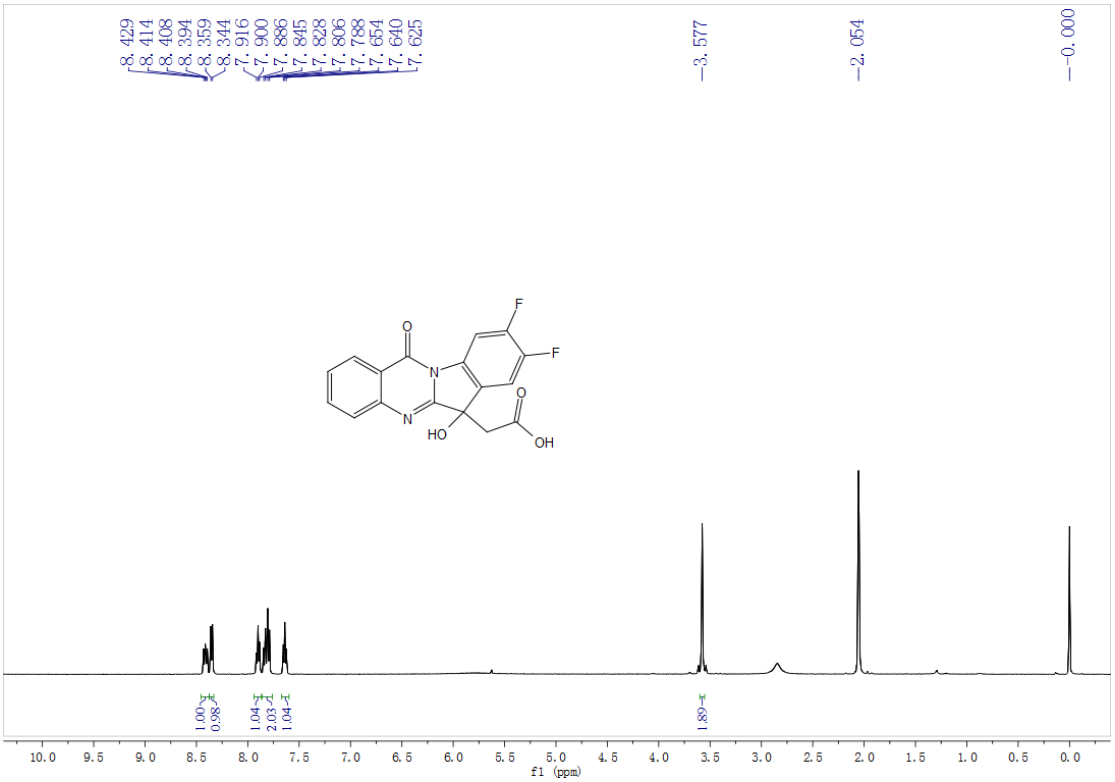
3e's ^{1}H NMR (500 MHz, Acetone-D6)



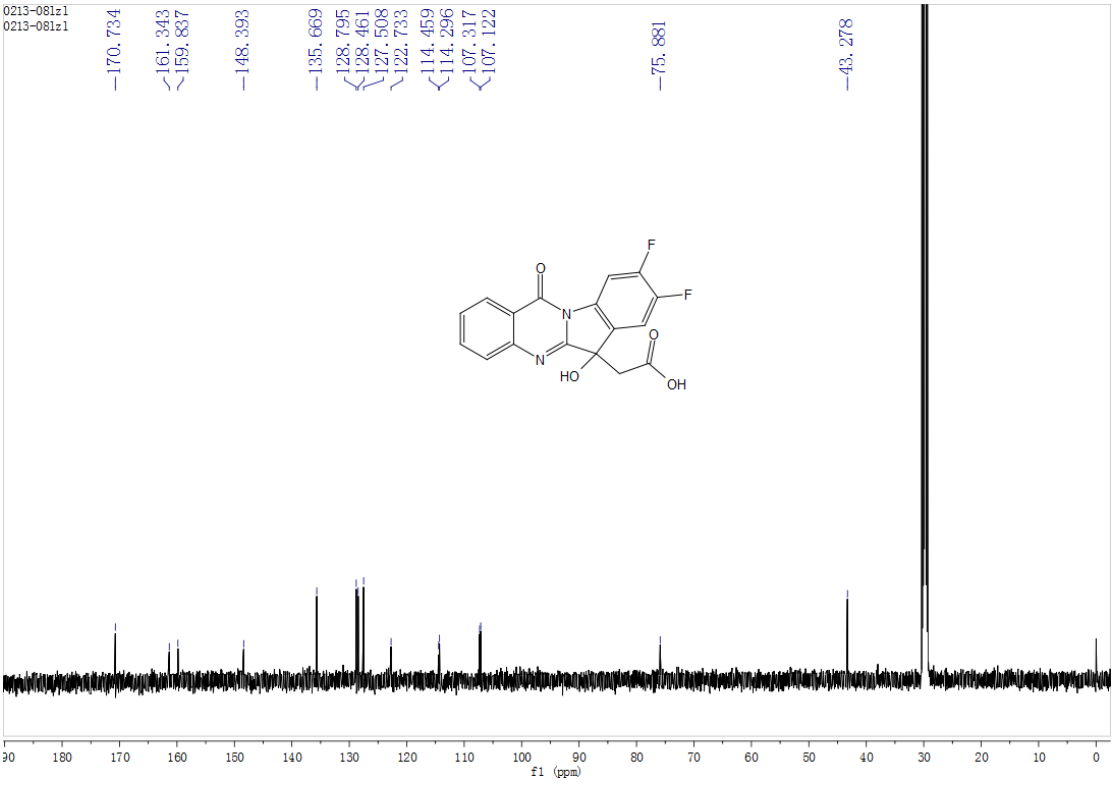
3e's ^{13}C NMR (126 MHz, Acetone-D6)



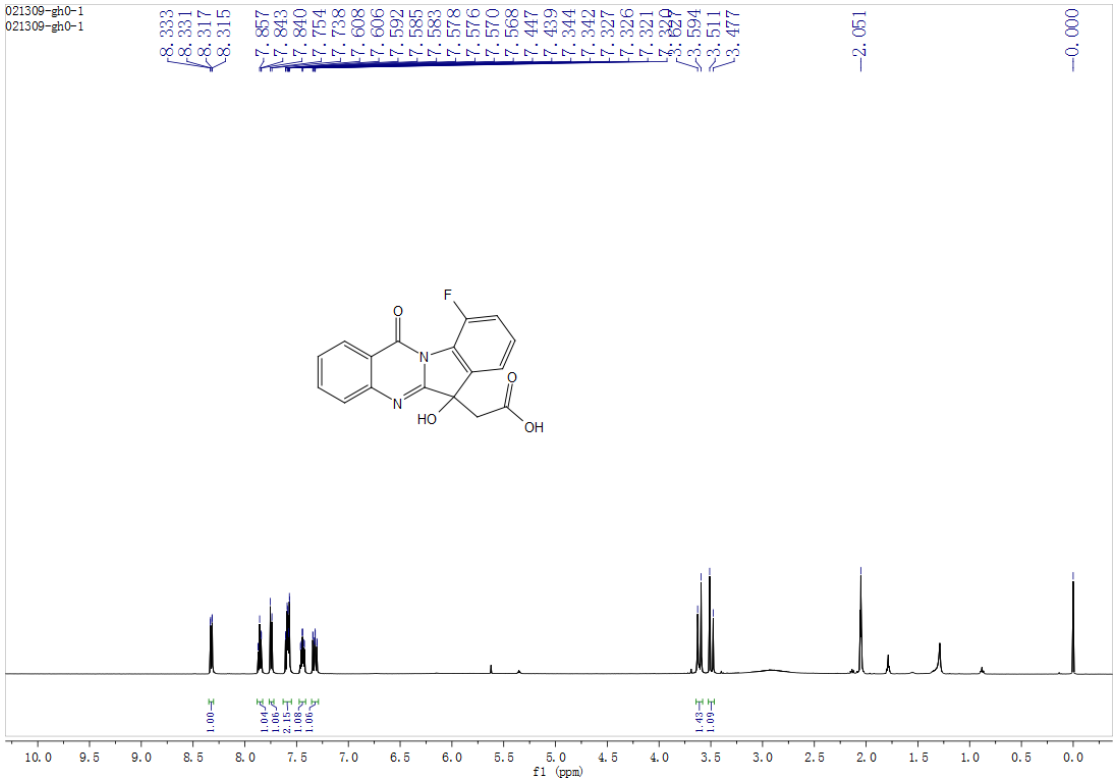
3f's ^{1}H NMR (500 MHz, Acetone-D6)



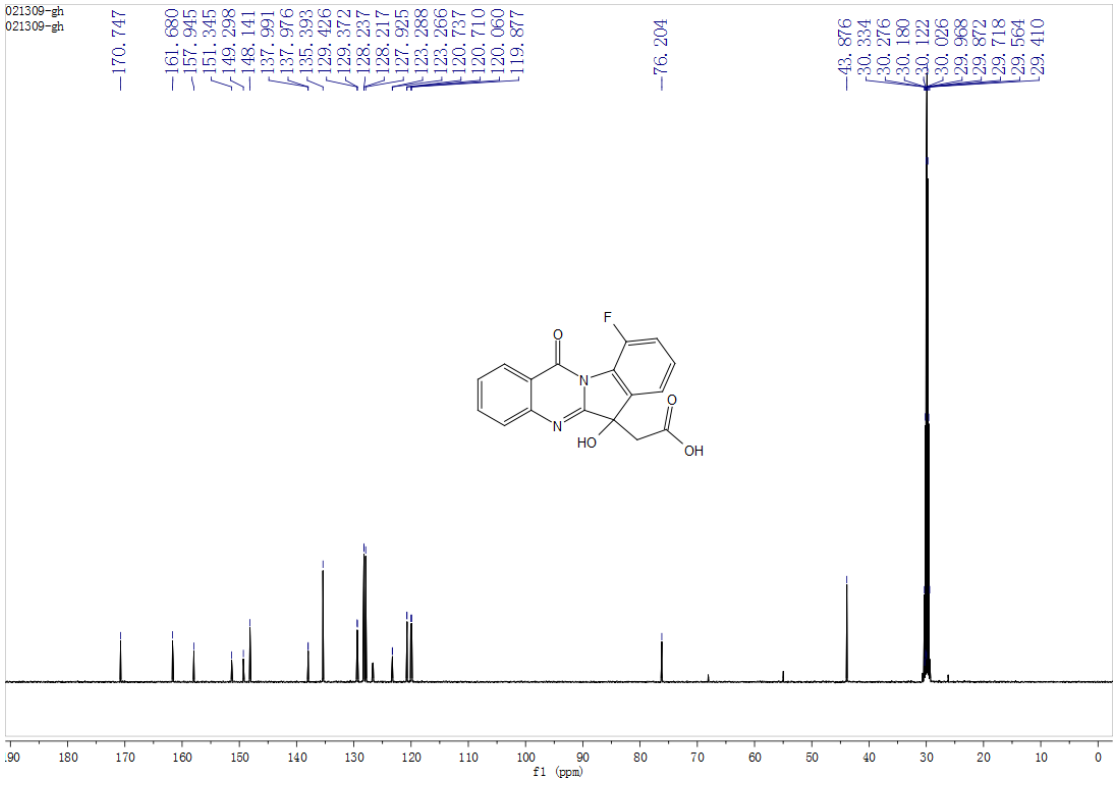
3f's ^{13}C NMR (126 MHz, Acetone-D6)



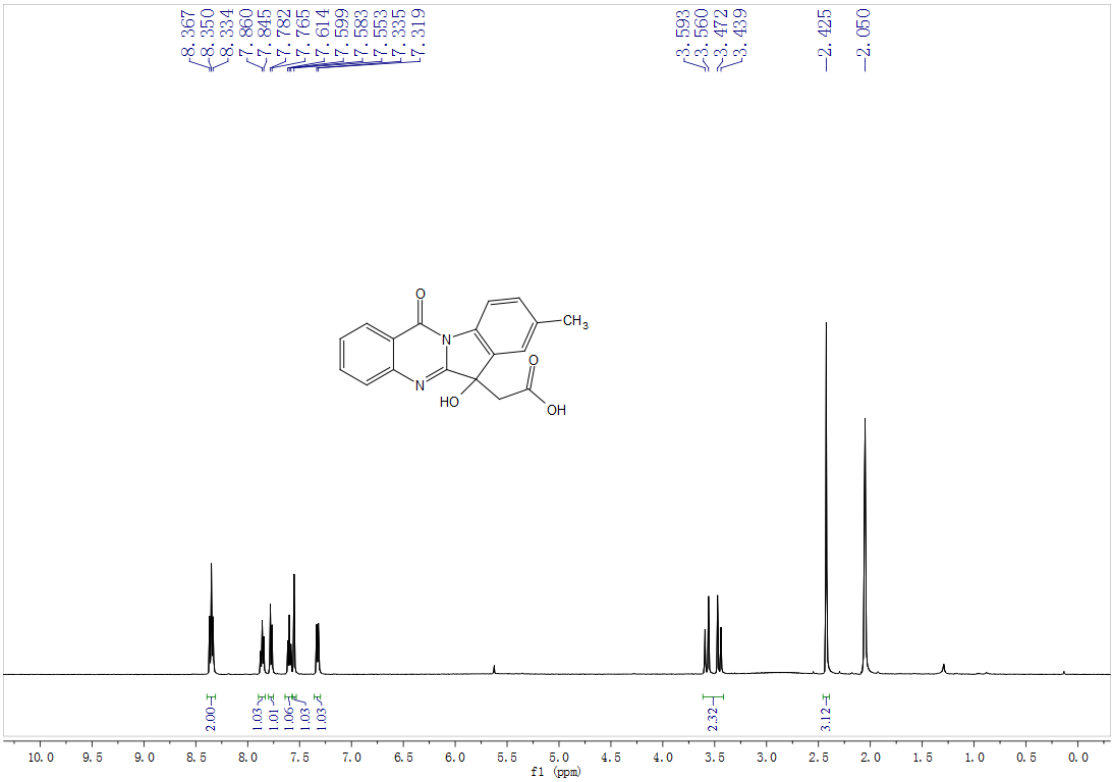
3g's ^{1}H NMR (500 MHz, Acetone-D6)



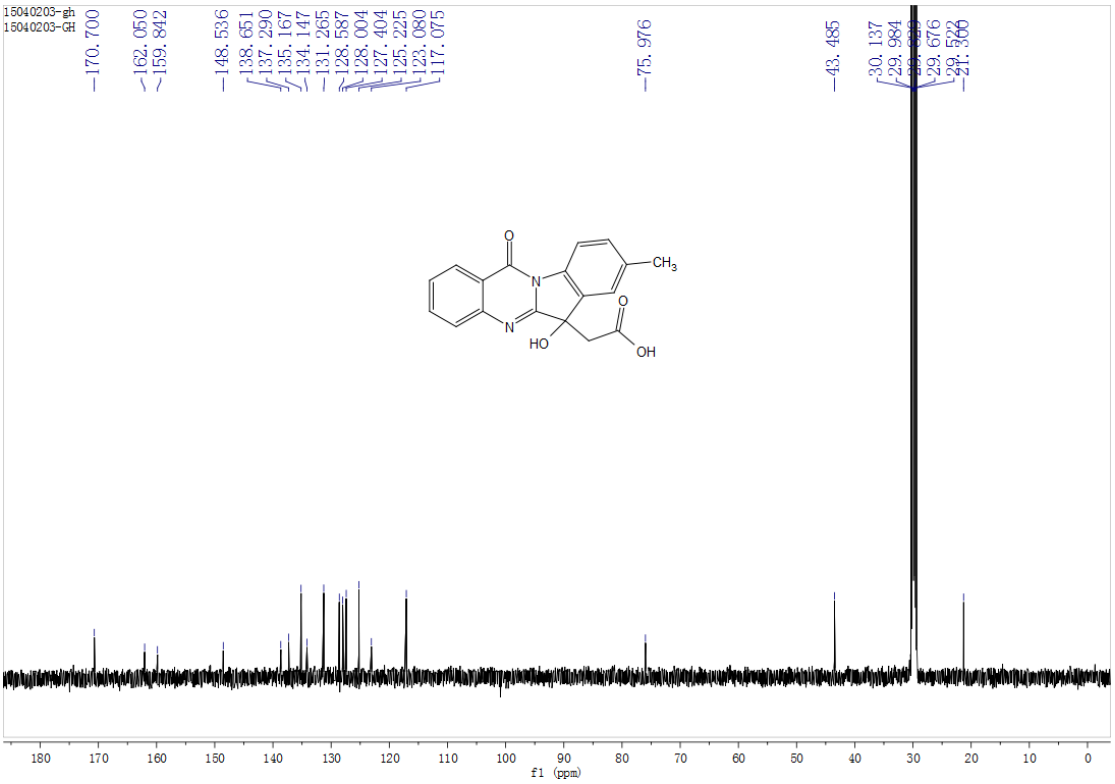
3g's ^{13}C NMR (126 MHz, Acetone-D6)



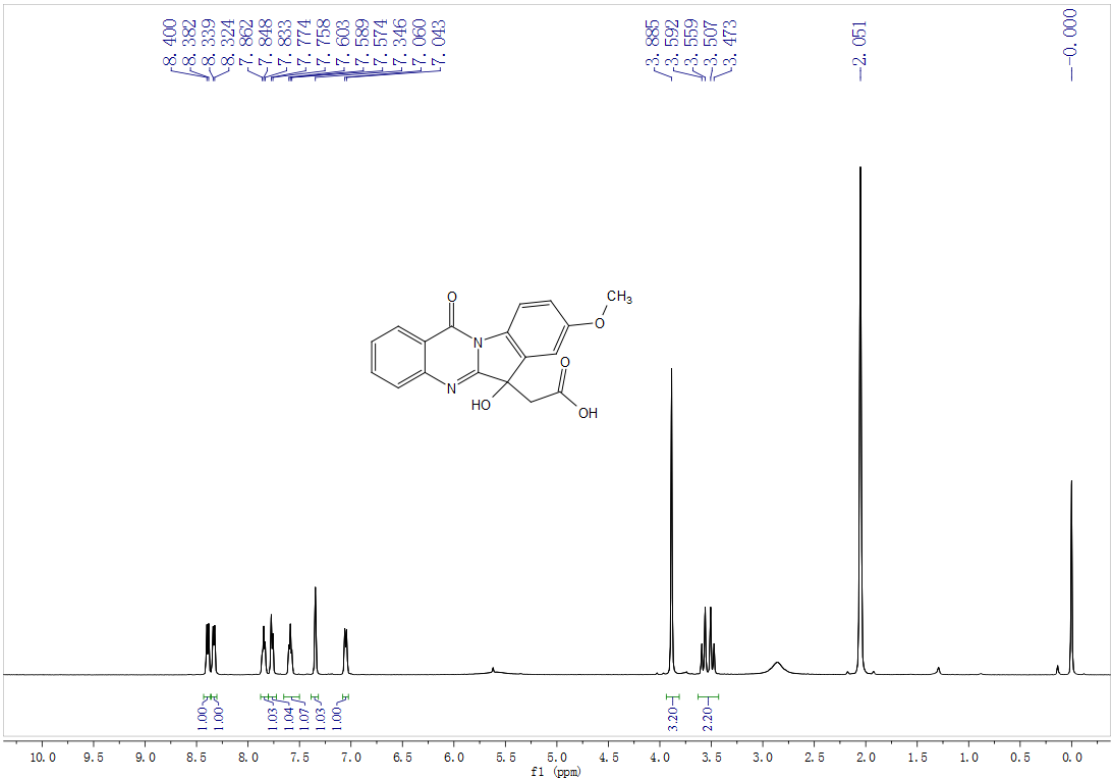
3h's ^{1}H NMR (500 MHz, Acetone-D6)



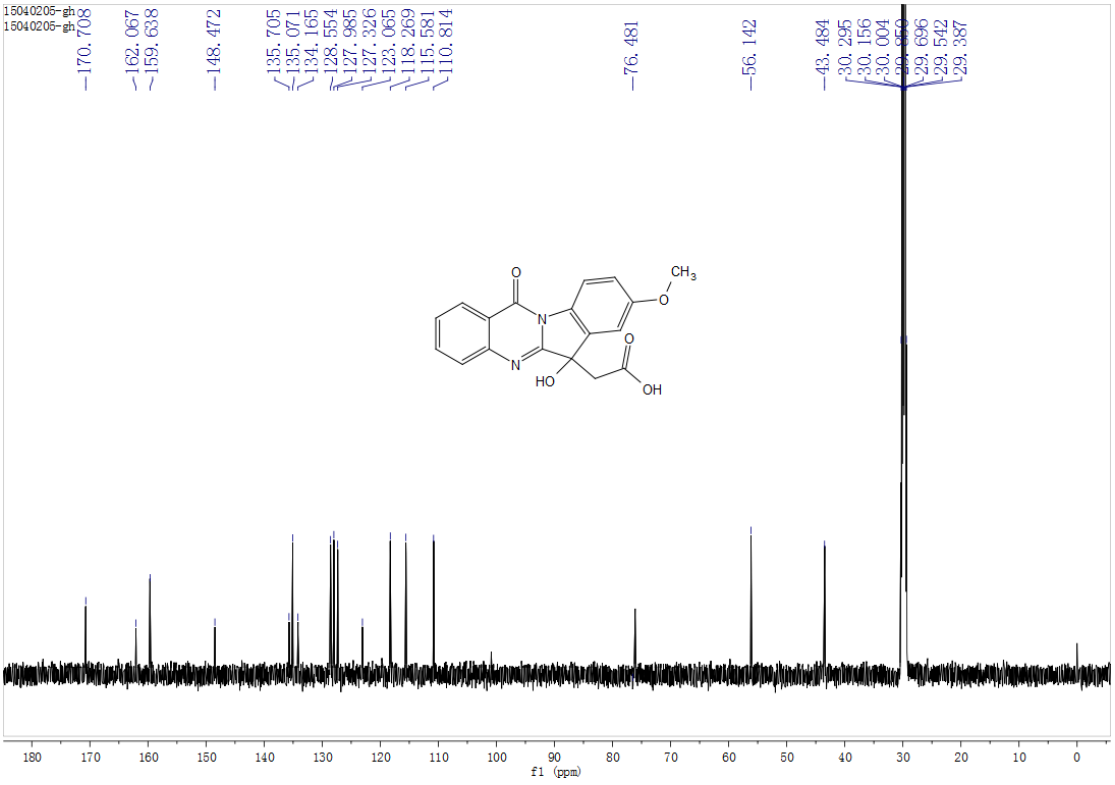
3h's ^{13}C NMR (126 MHz, Acetone-D6)



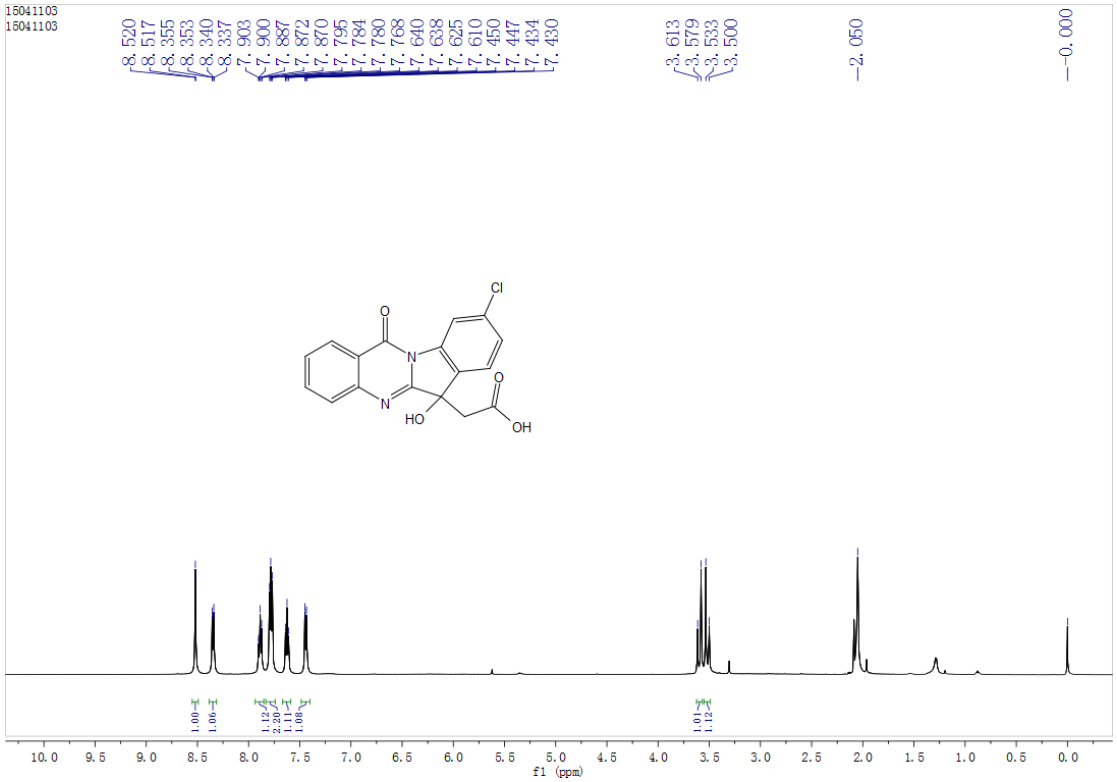
3i's ^{1}H NMR (500 MHz, Acetone-D6)



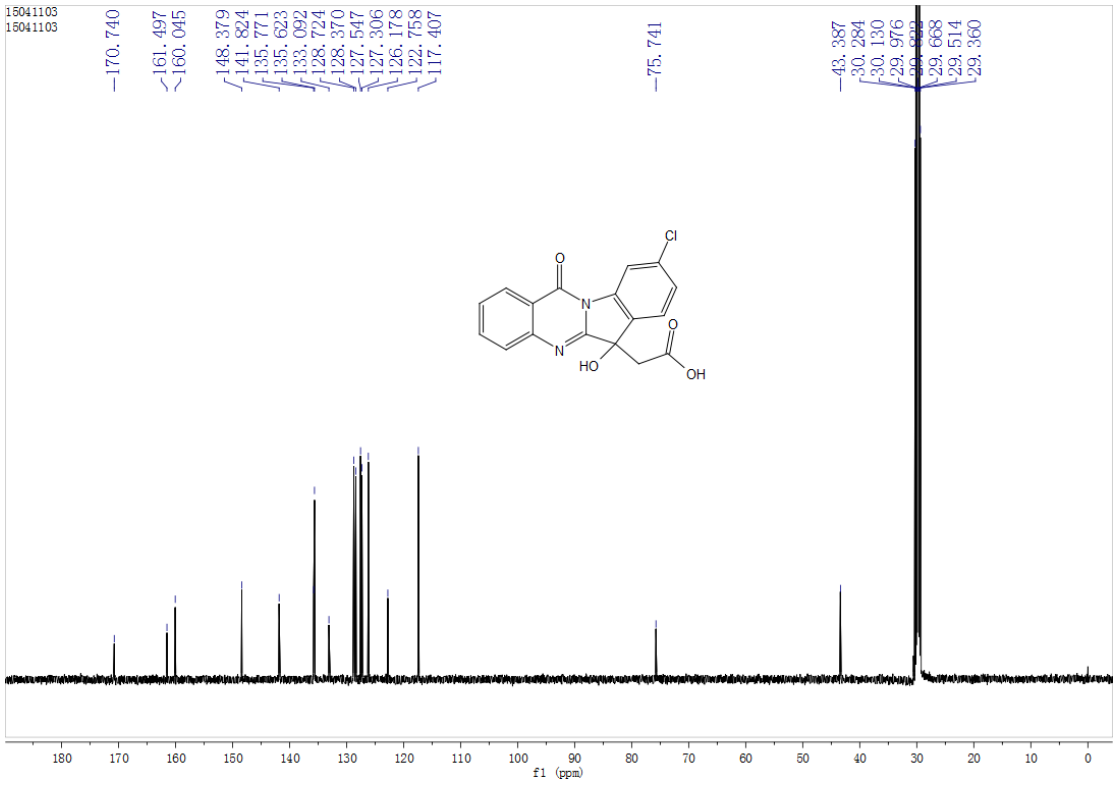
3i's 13C NMR (126 MHz, Acetone-D6)



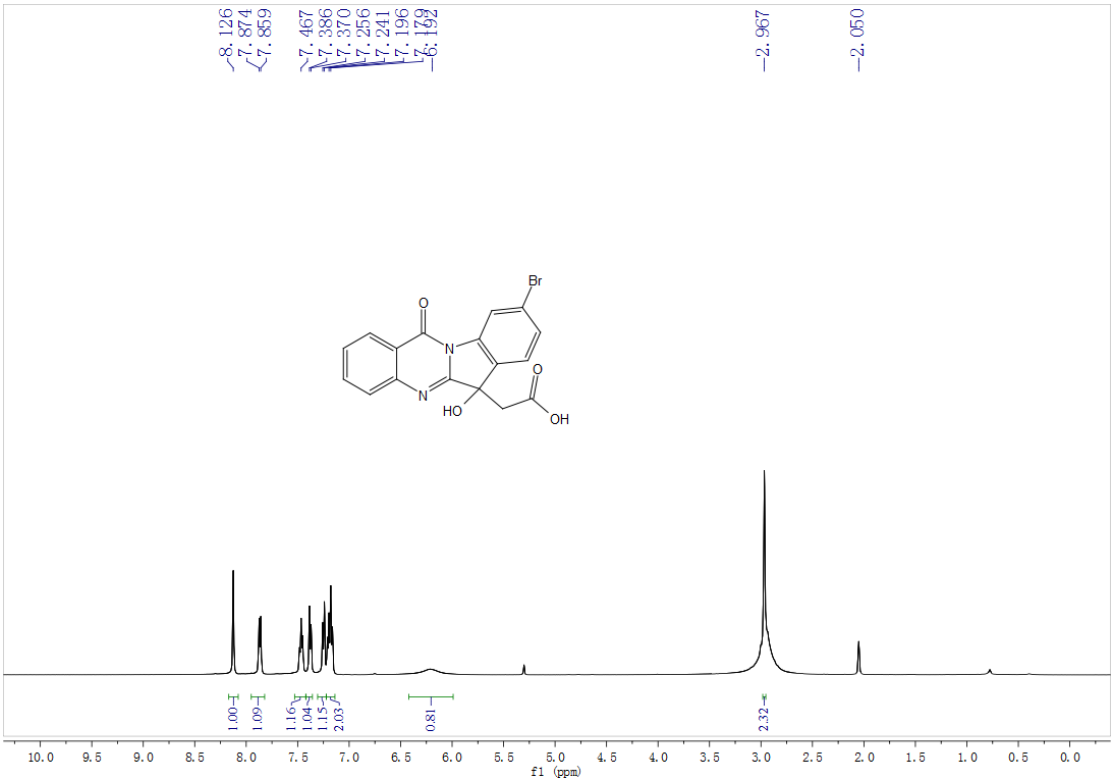
3j's ^{1}H NMR (500 MHz, Acetone-D6)



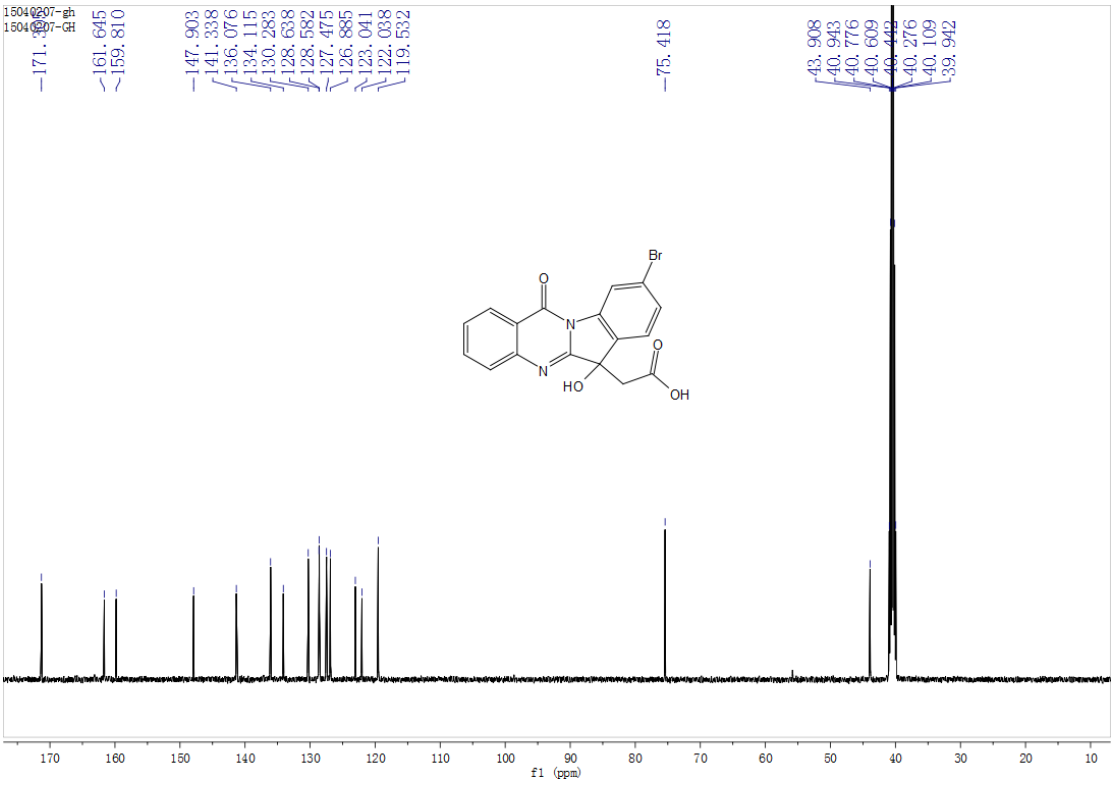
3j's ^{13}C NMR (126 MHz, Acetone-D6)



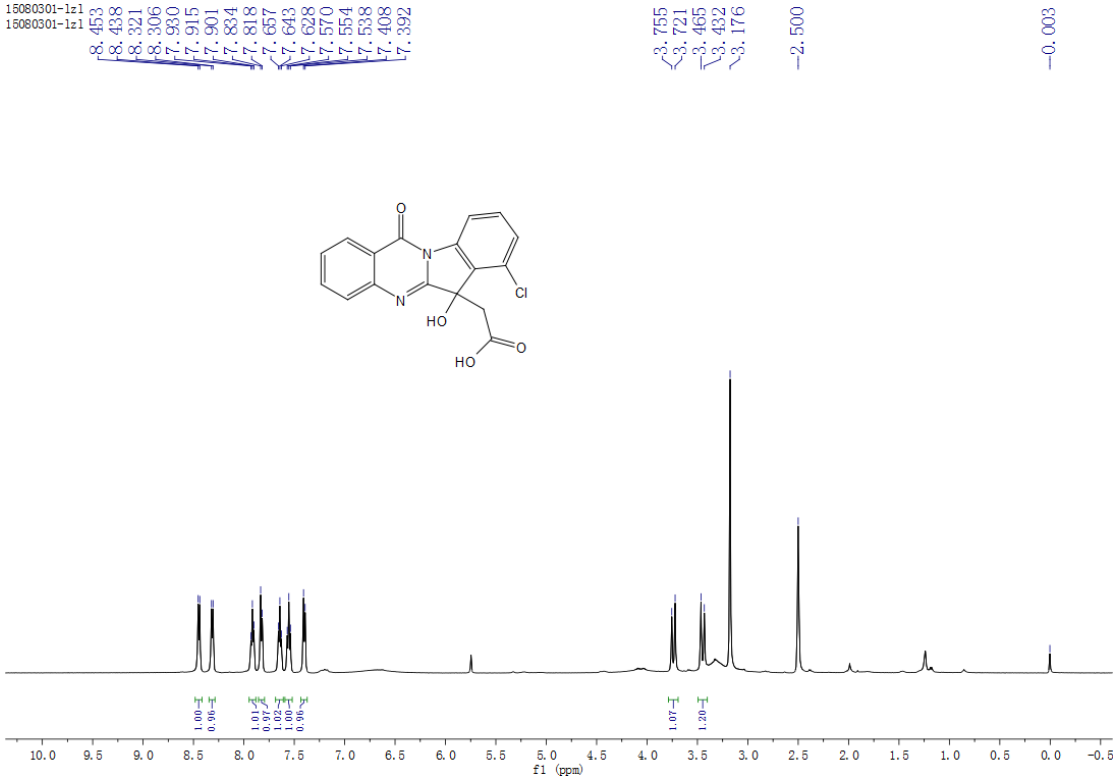
3k's ^{1}H NMR (500 MHz, Acetone-D6)



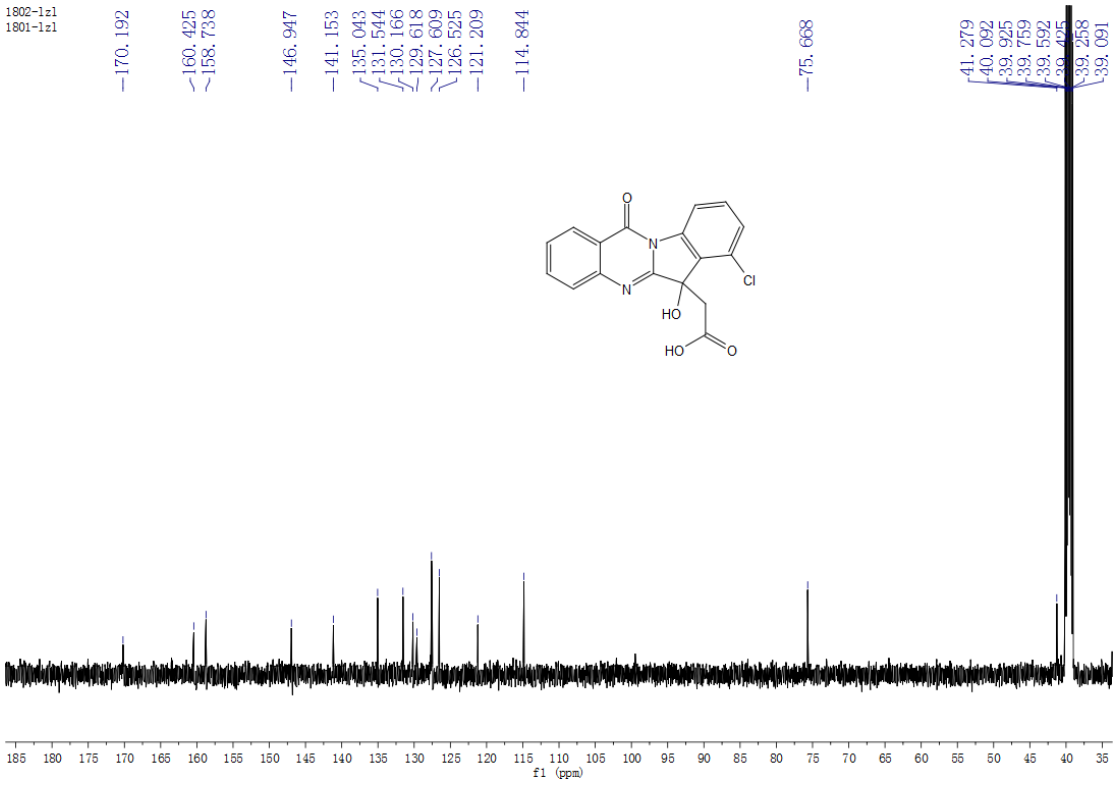
3k's ^{13}C NMR (126 MHz, Acetone-D6)



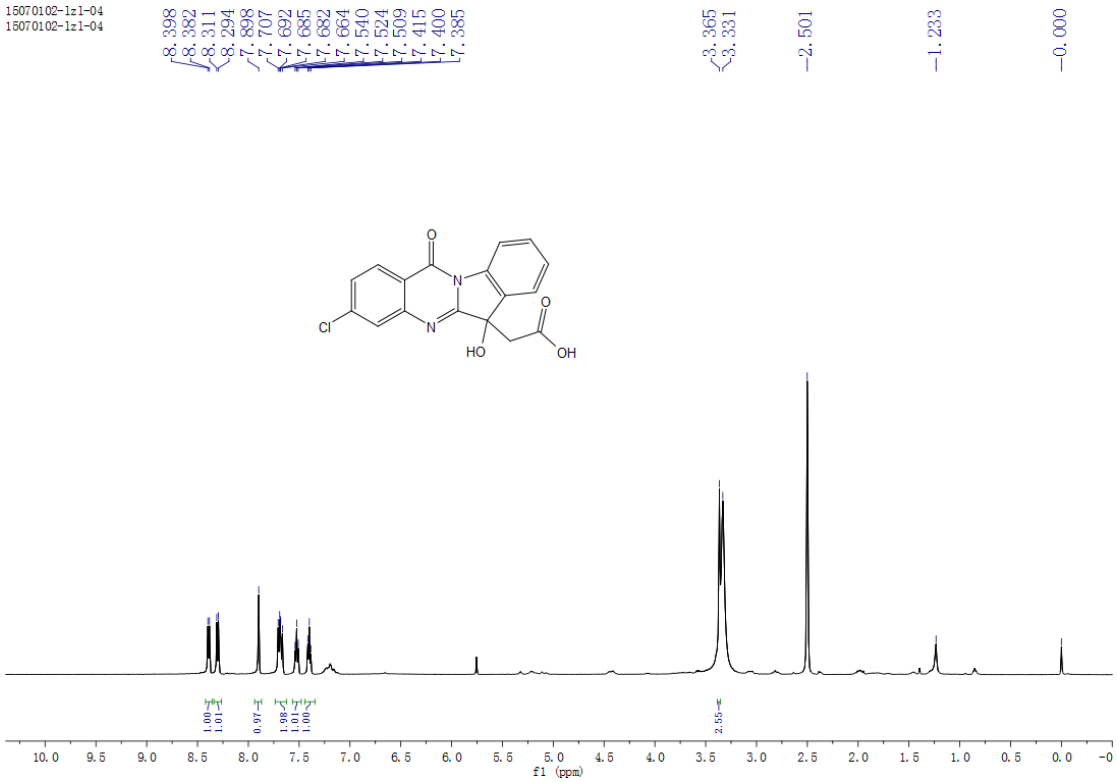
3l's ^{1}H NMR (500 MHz, DMSO)



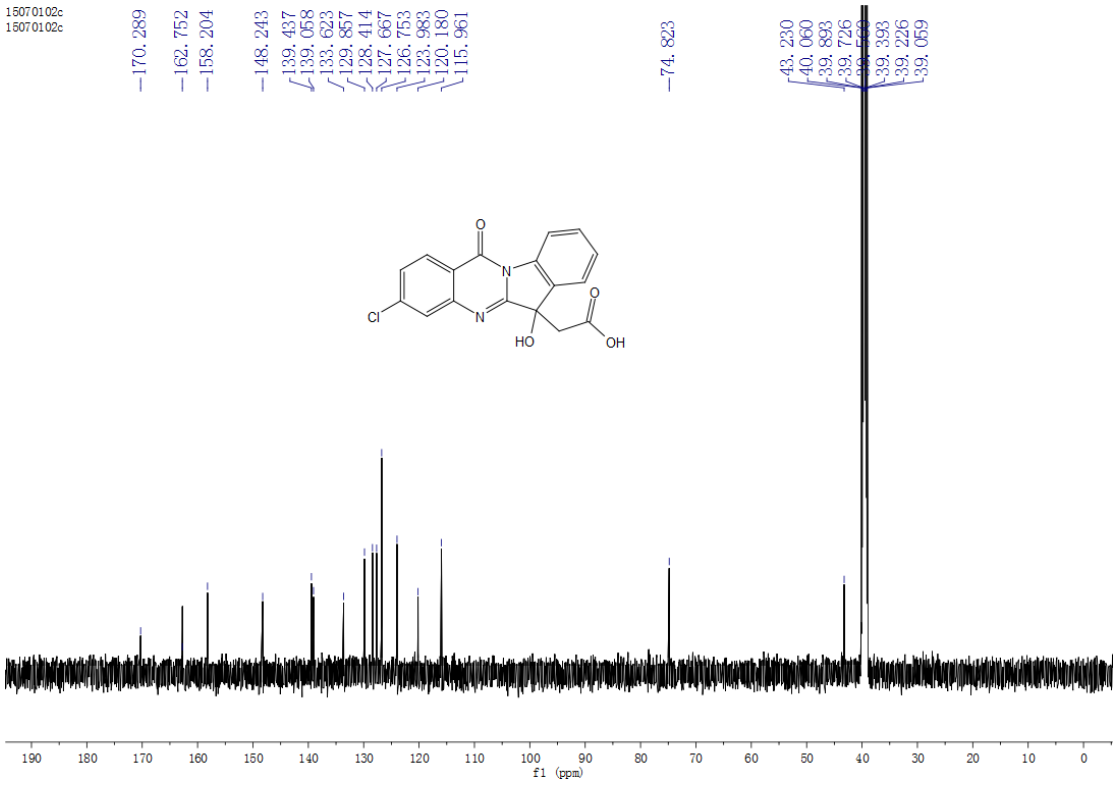
3l's ^{13}C NMR (126 MHz, DMSO)



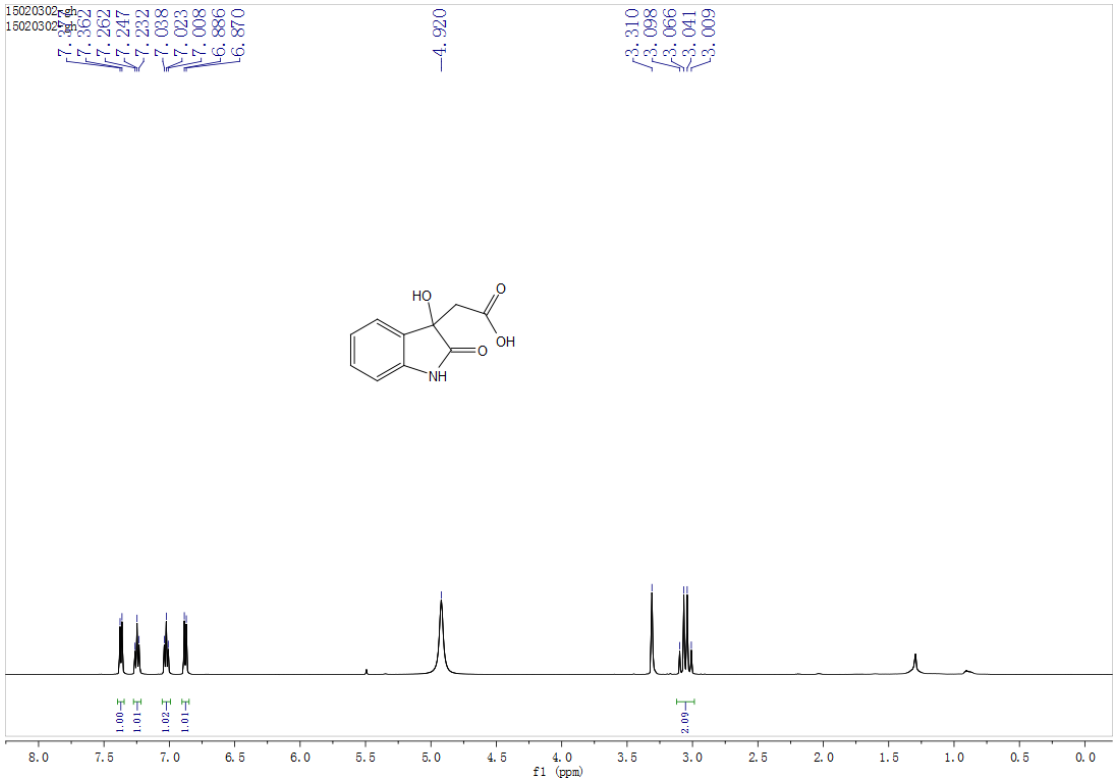
3m's ^{1}H NMR (500 MHz, DMSO)



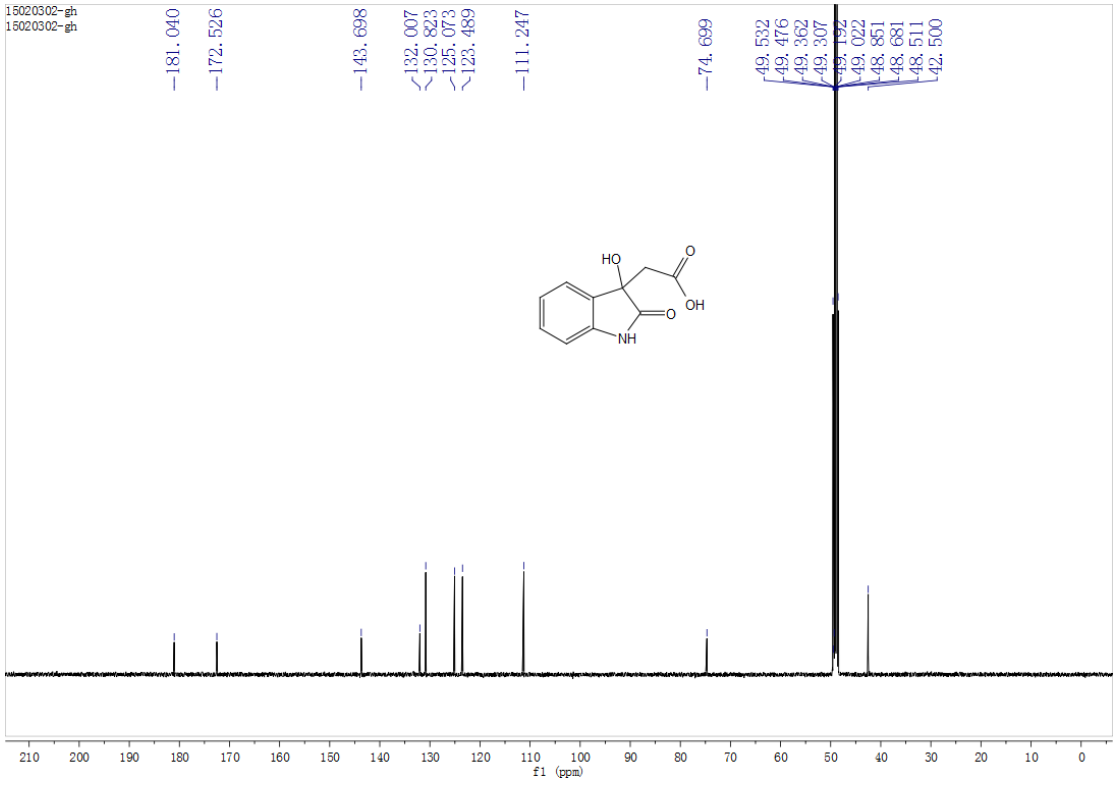
3m's ^{13}C NMR (126 MHz, DMSO)



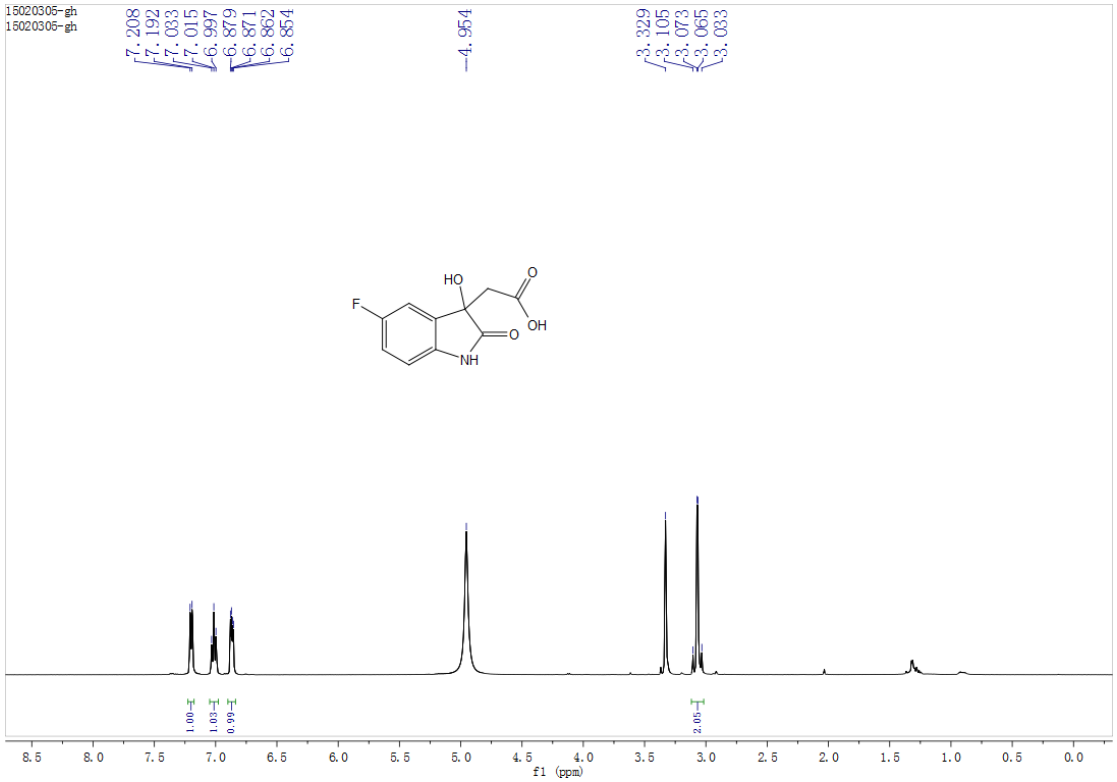
7a's ^{1}HNMR (500 MHz, MeOD)



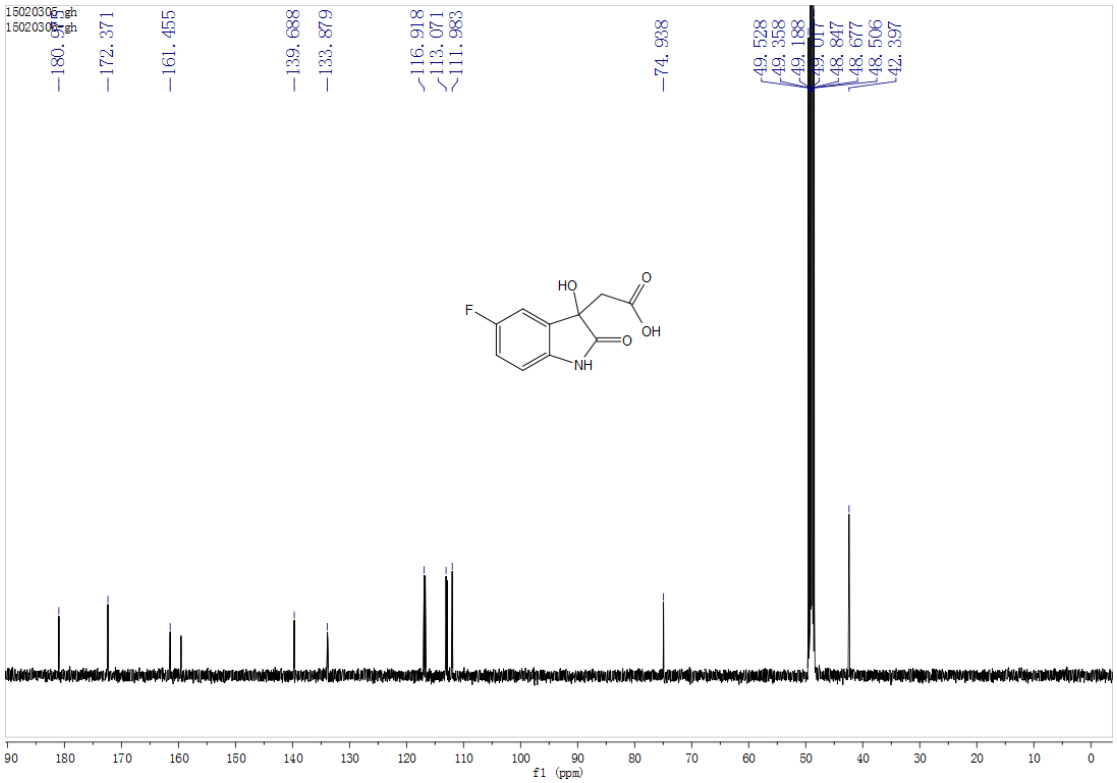
7a's ^{13}CNMR (126 MHz, MeOD)



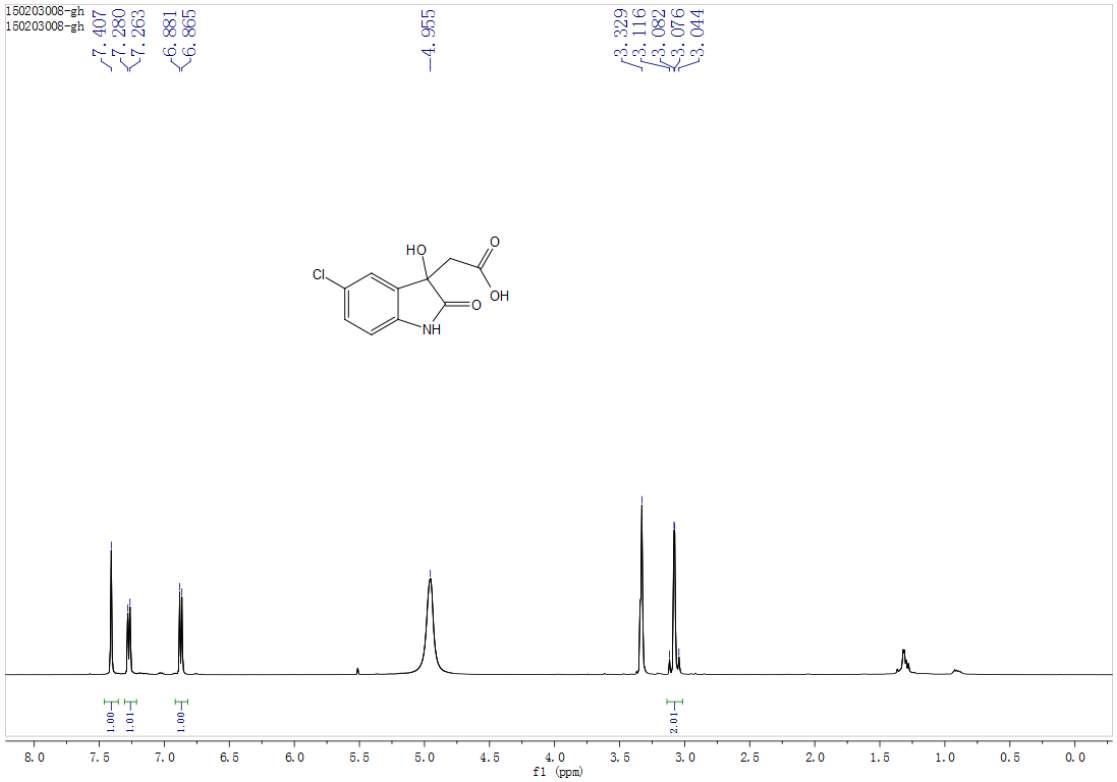
7b's ^{1}HNMR (500 MHz, MeOD)



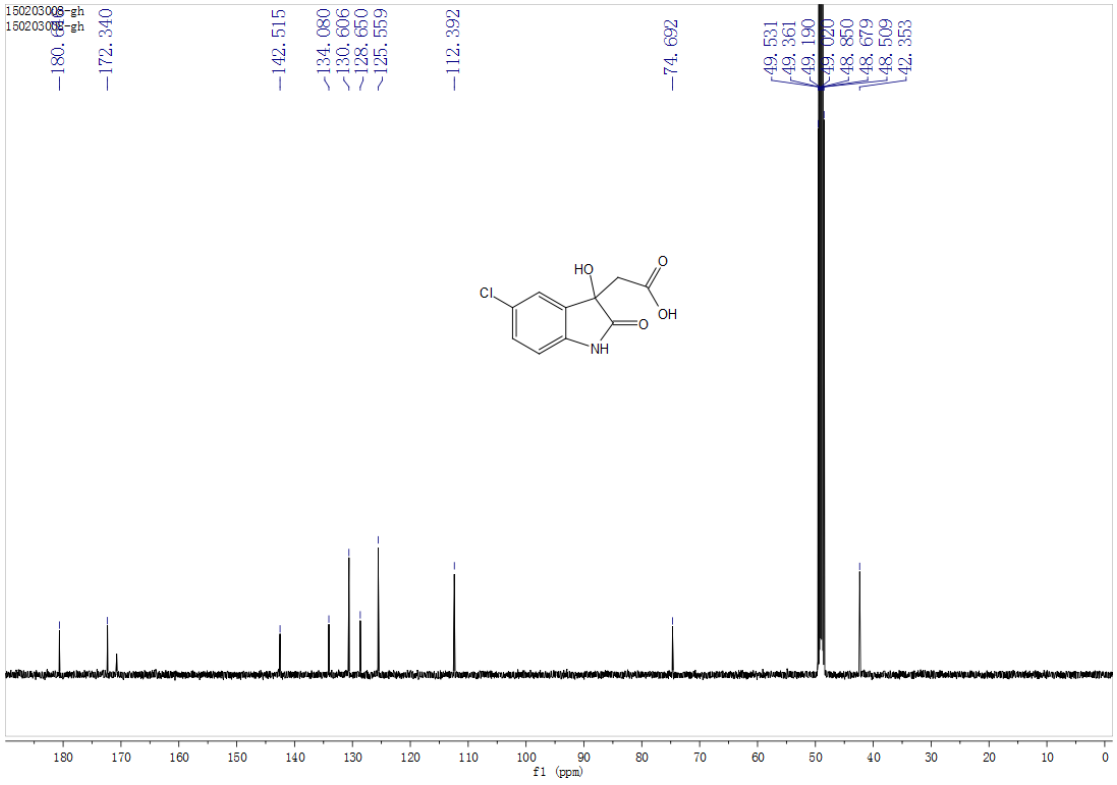
7b's ^{13}CNMR (126 MHz, MeOD)



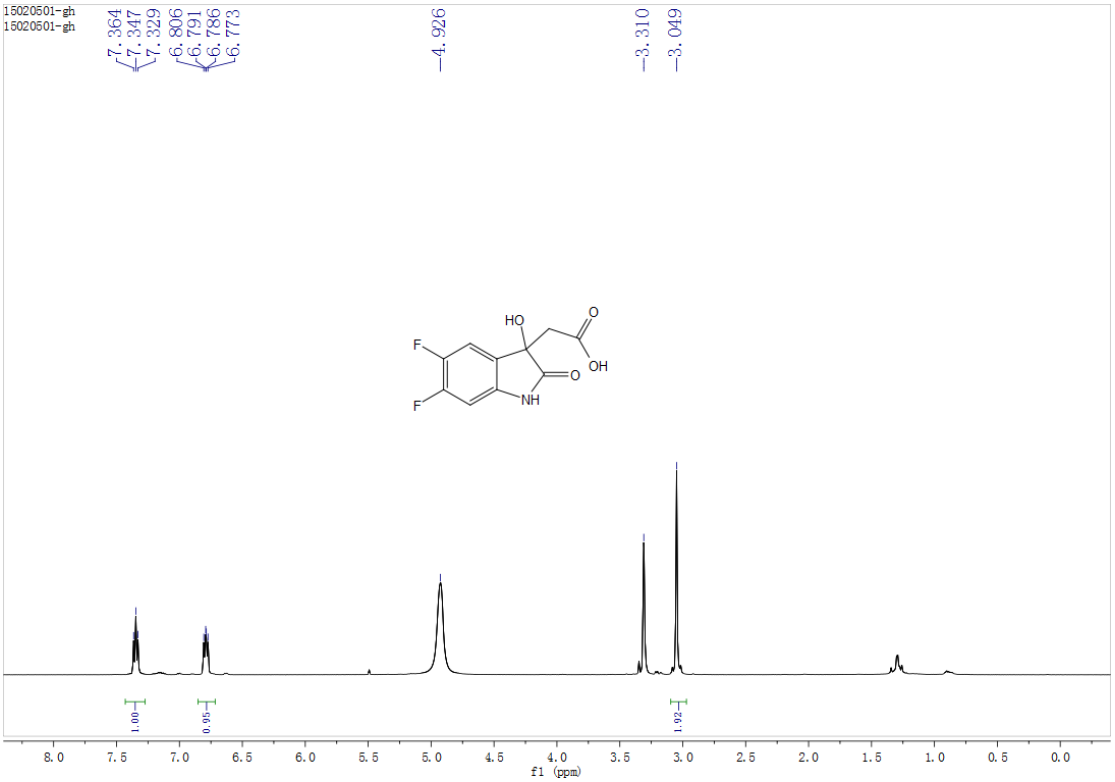
7c's ^{1}HNMR (500 MHz, MeOD)



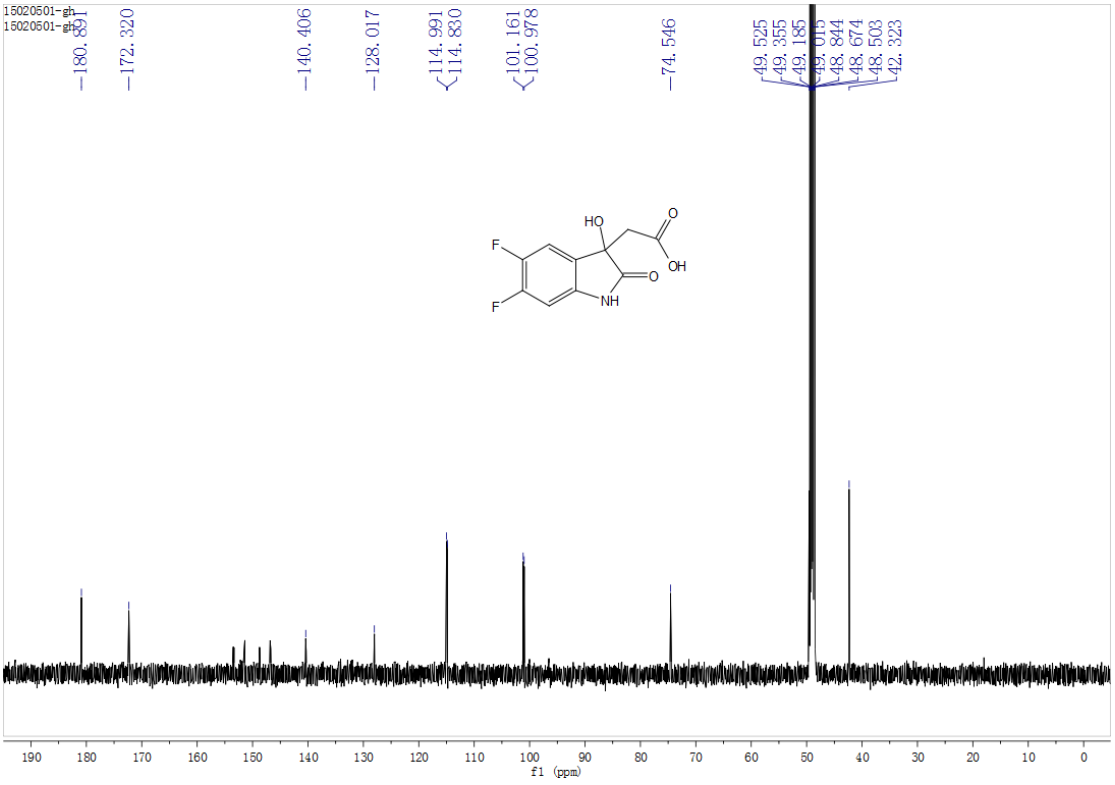
7c's ^{13}CNMR (126 MHz, MeOD)



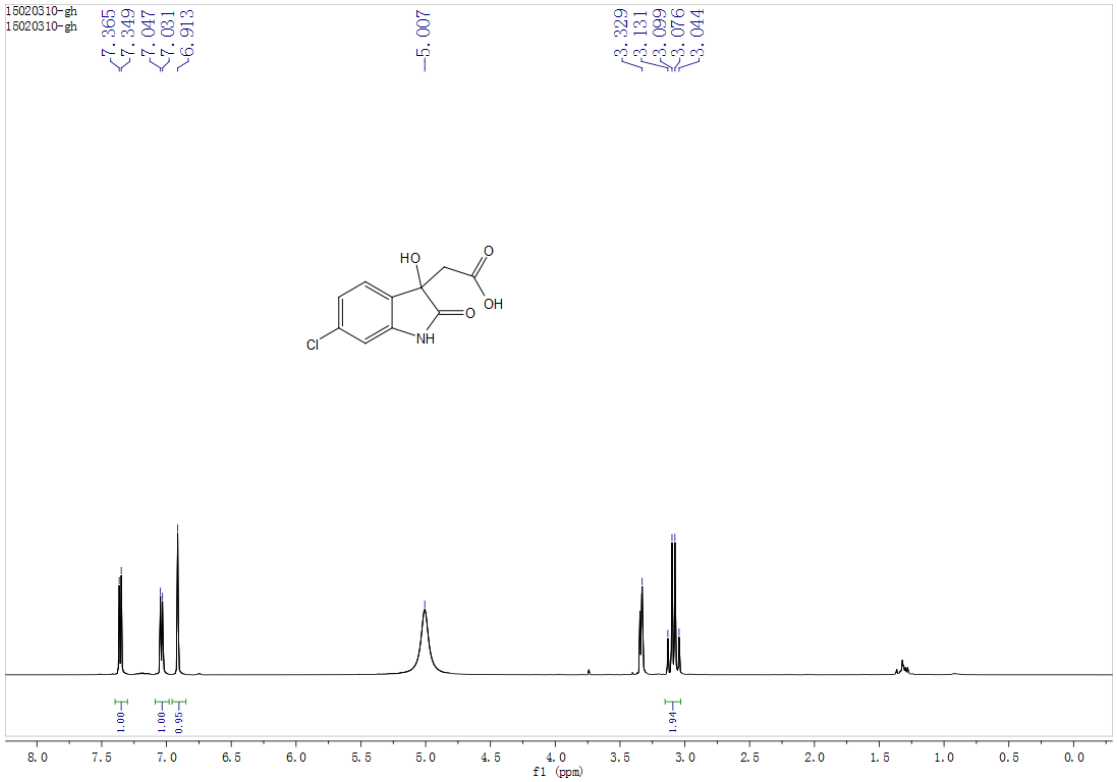
7d's ^{1}HNMR (500 MHz, MeOD)



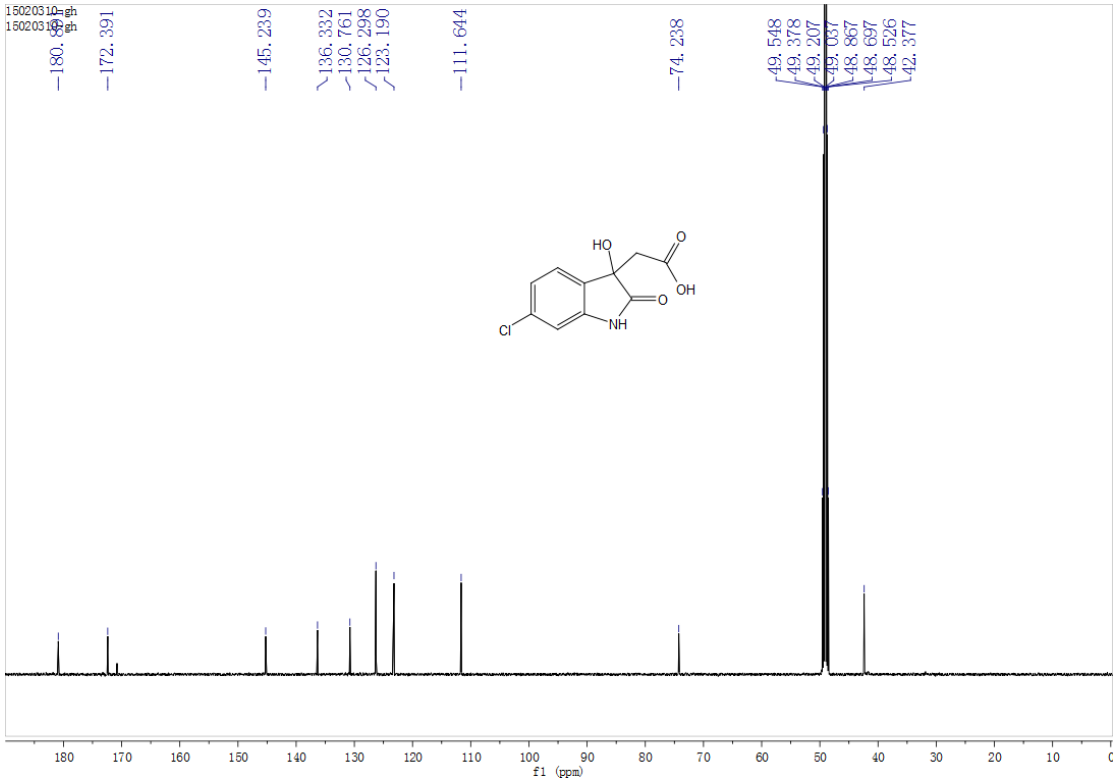
7d's ^{13}CNMR (126 MHz, MeOD)



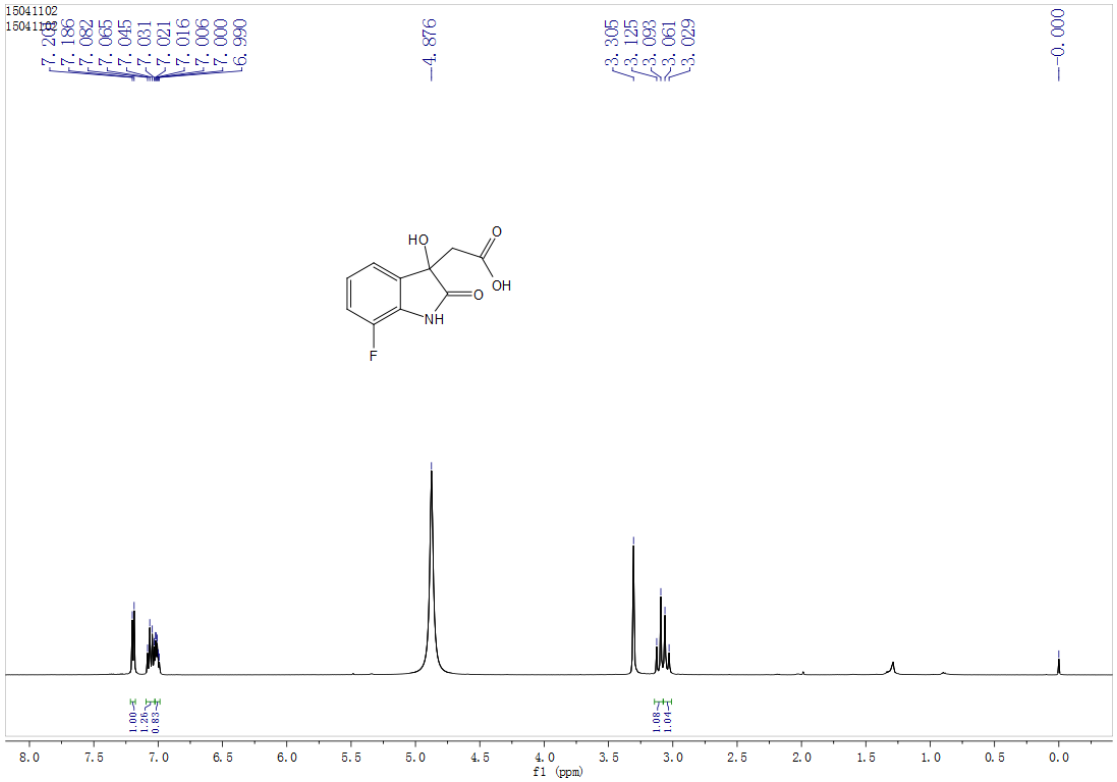
7e's ^{1}HNMR (500 MHz, MeOD)



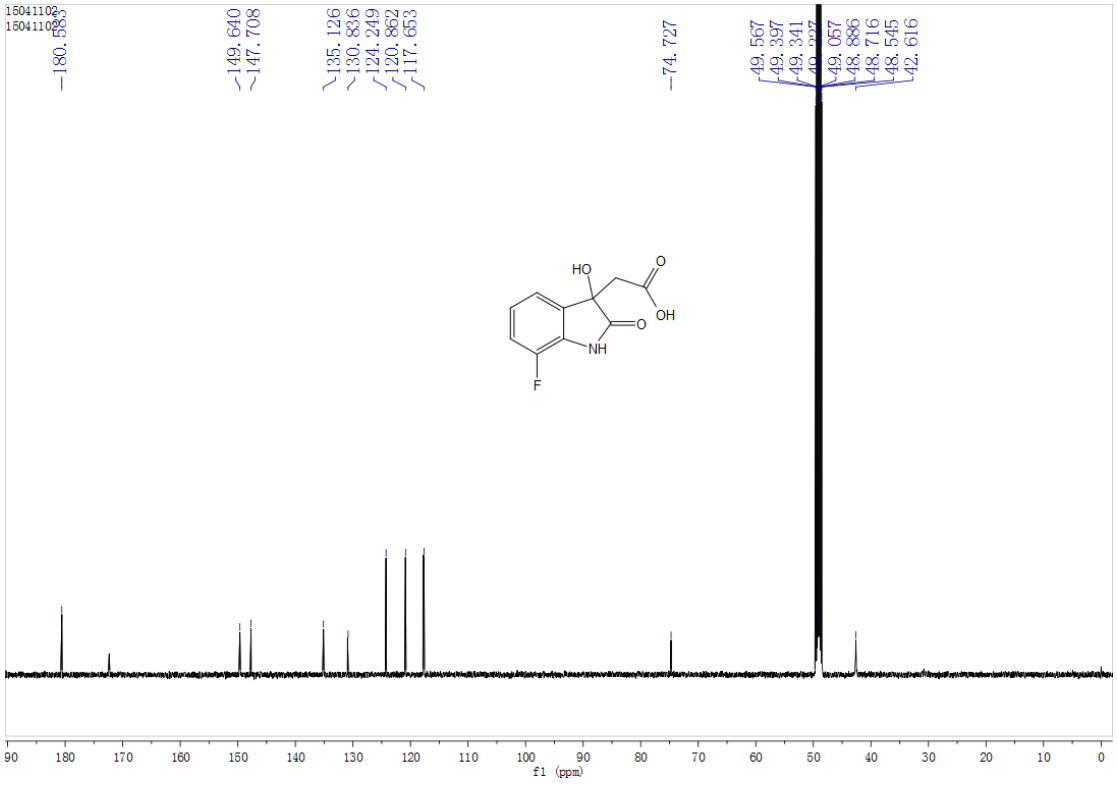
7e's ^{13}CNMR (126 MHz, MeOD)



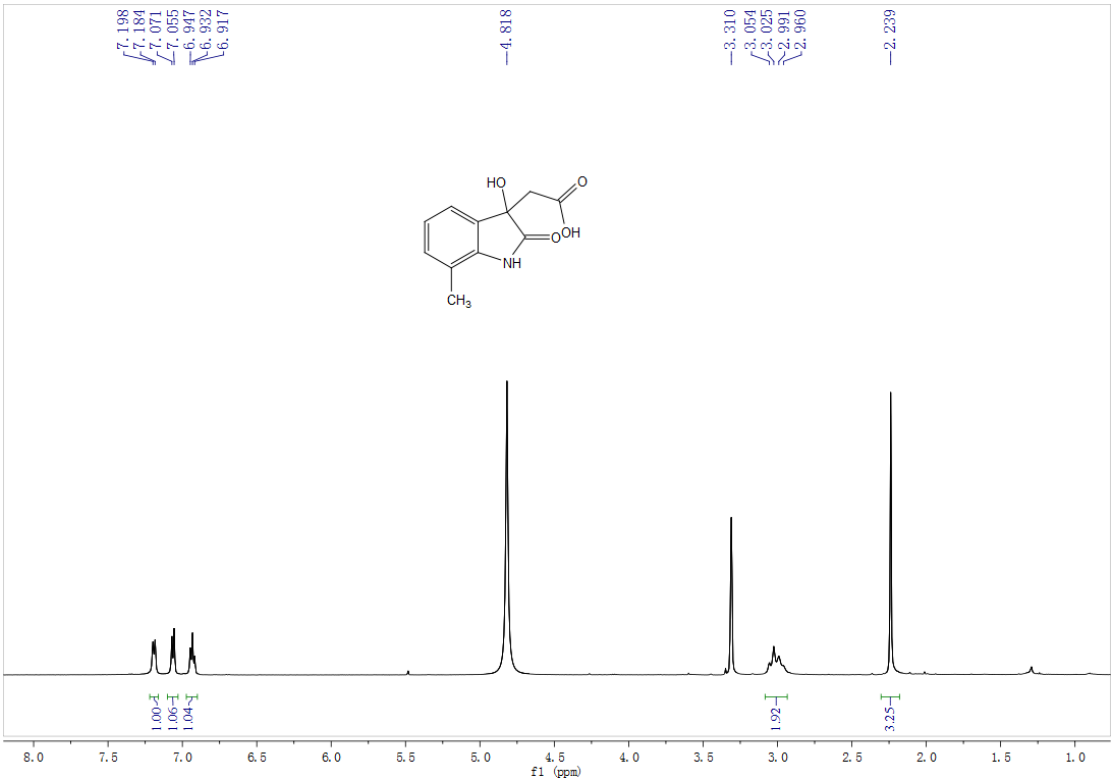
7f's ^{1}HNMR (500 MHz, MeOD)



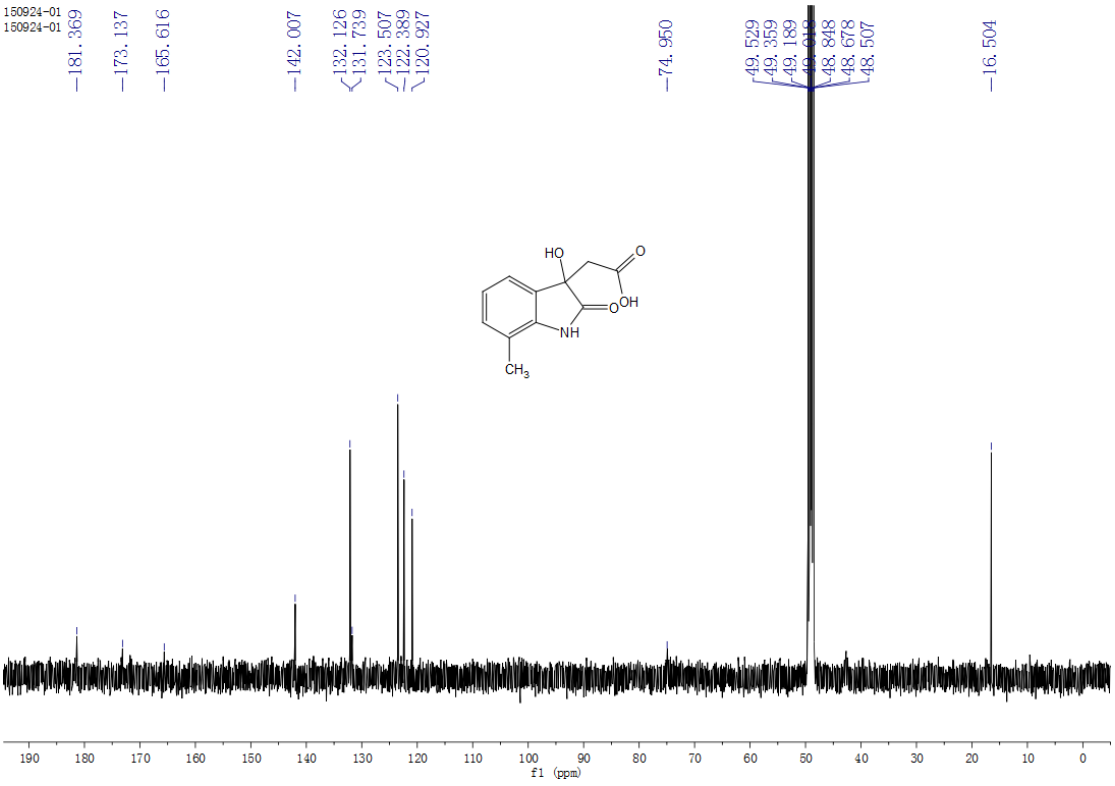
7f's ^{13}CNMR (126 MHz, MeOD)



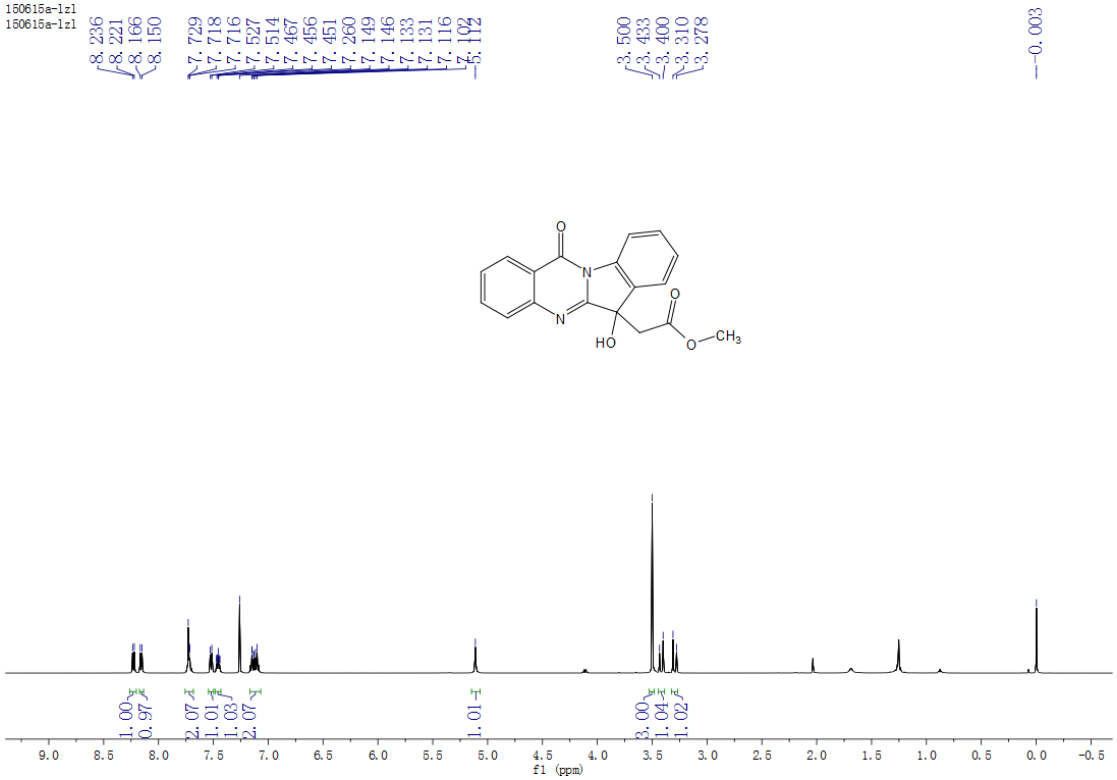
7g's ^{1}HNMR (500 MHz, MeOD)



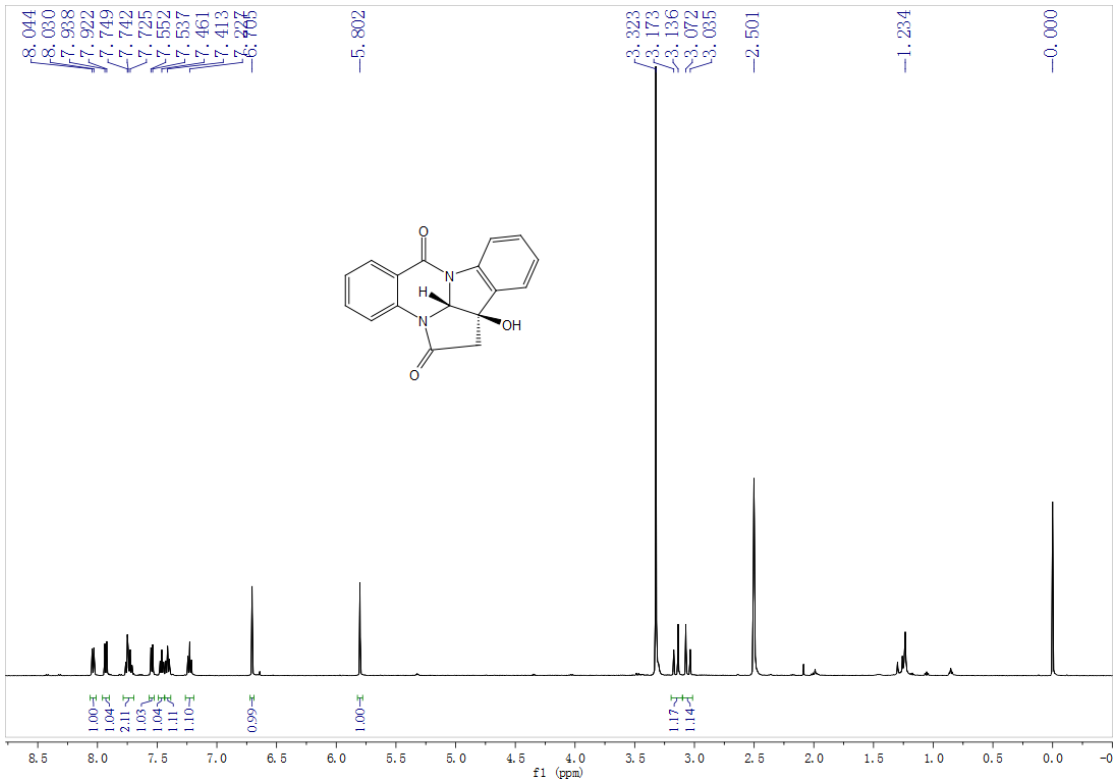
7g's ^{13}CNMR (126 MHz, MeOD)



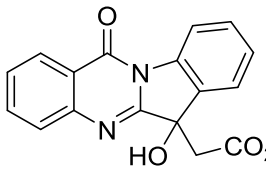
ent-**4a**'s ^{1}H NMR (500 MHz, $CDCl_3$)



10's ^{1}H NMR (500 MHz, DMSO)

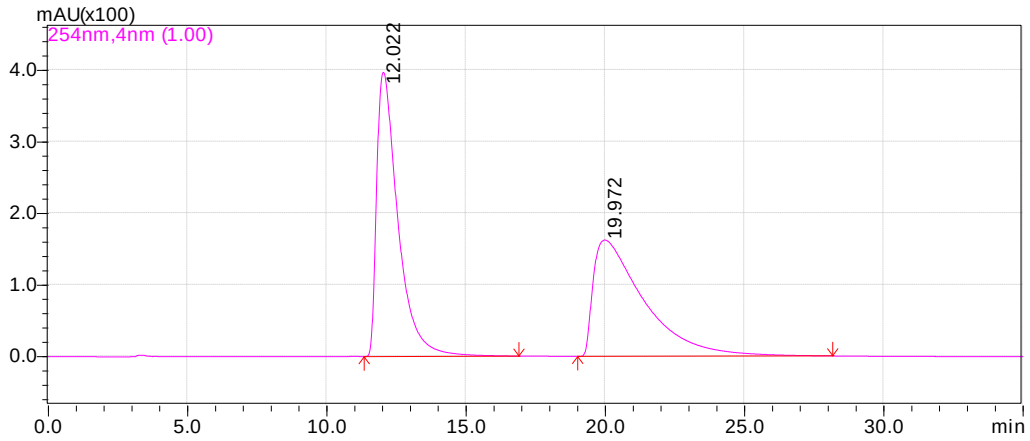


HPLC data of products

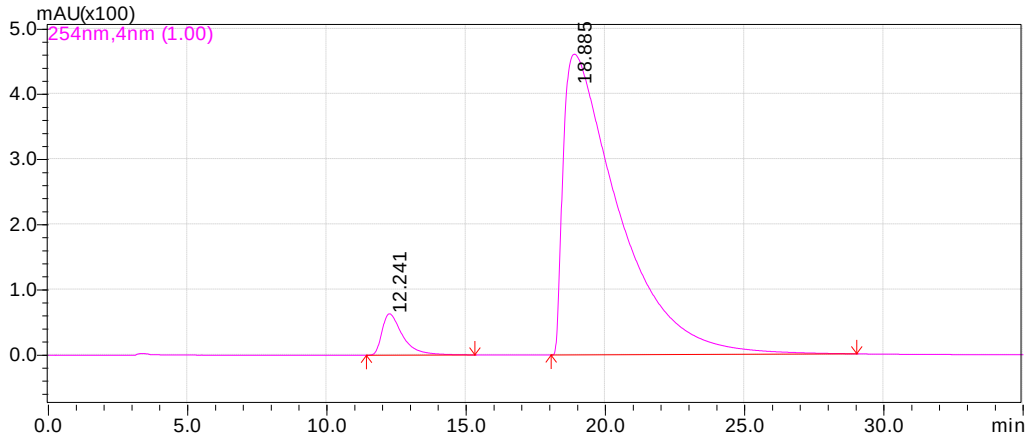


4a

Daicel Chiralpak AS-H, hexane/iso-propanol=90/10, flow rate 1.0mL/min, 25℃

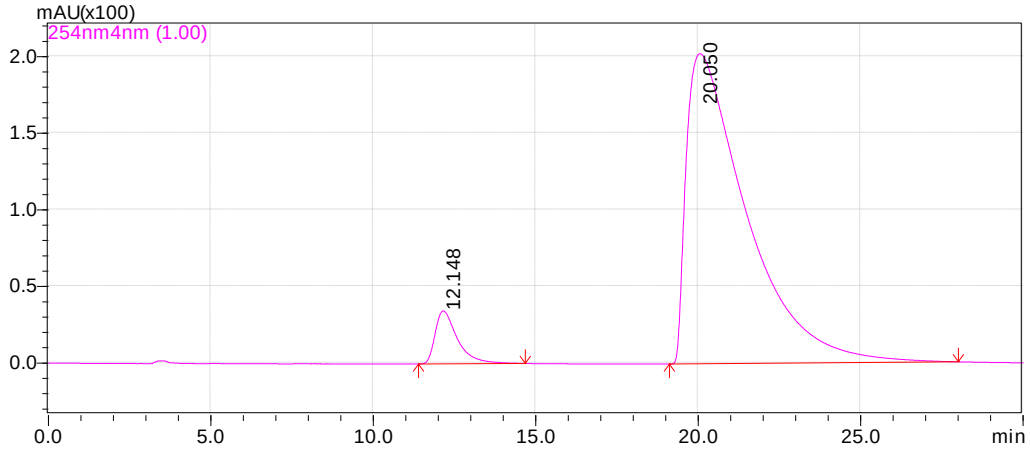


Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	12.022	21150970	396985	11.339	16.896	50.5396
2	19.972	20699340	162575	19.008	28.160	49.4604



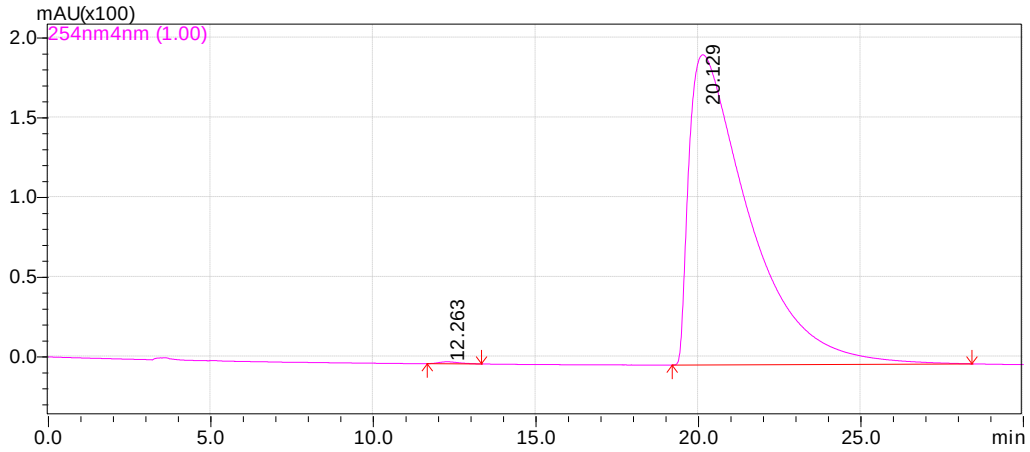
Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	12.241	3279777	63351	11.424	15.317	4.8595
2	18.885	64212841	461384	18.048	29.024	95.1405

4a in the gram scale reaction (Table 1, entry 18)

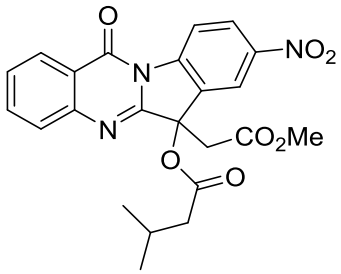


Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	12.148	1655279	34550	11.392	14.677	5.9400
2	20.050	26211434	202421	19.115	28.011	94.0600

4a after a single recrystallization (Table 1, entry 18)

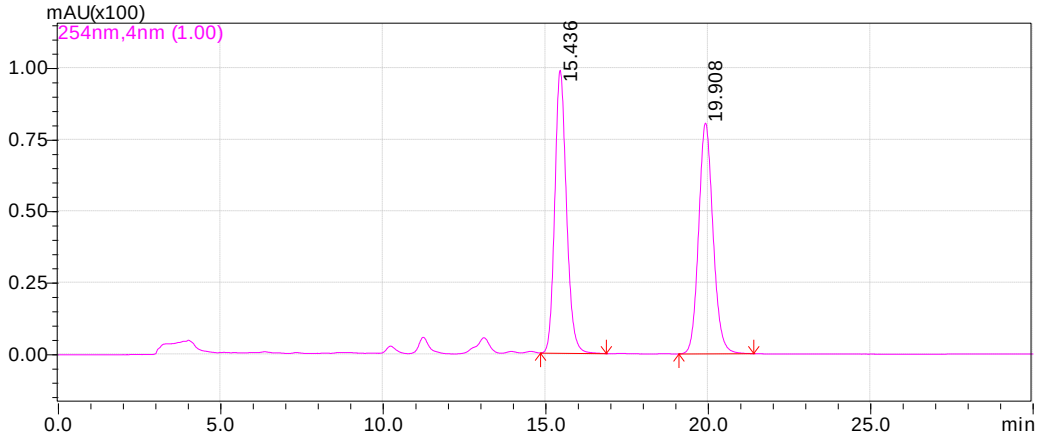


Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	12.263	56010	1291	11.659	13.323	0.2227
2	20.129	25093779	194572	19.189	28.416	99.7773

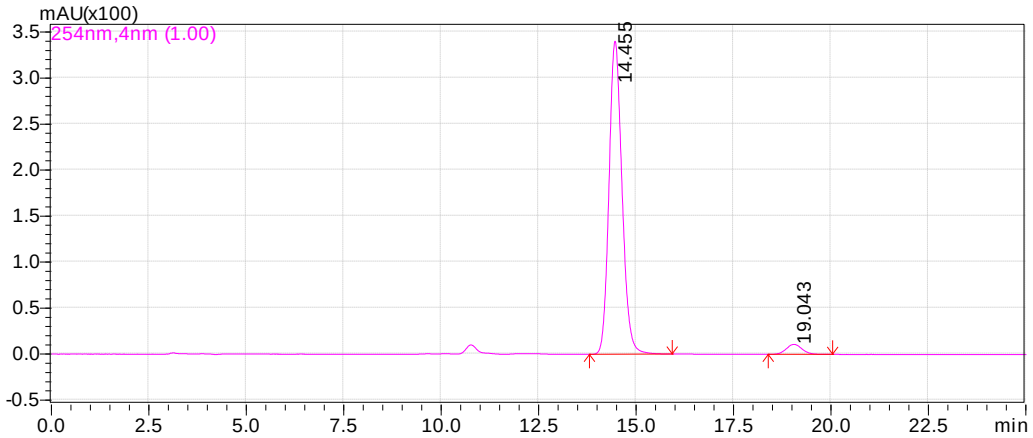


5b

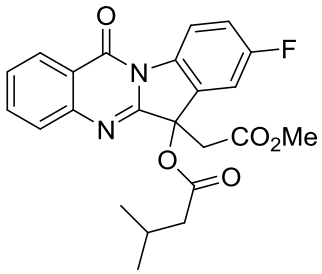
Daicel Chiralpak IA, hexane/iso-propanol=90/10, flow rate 1.0mL/min, 25℃



Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	15.436	2471829	98891	14.837	16.864	49.8790
2	19.908	2483825	80640	19.093	21.397	50.1210

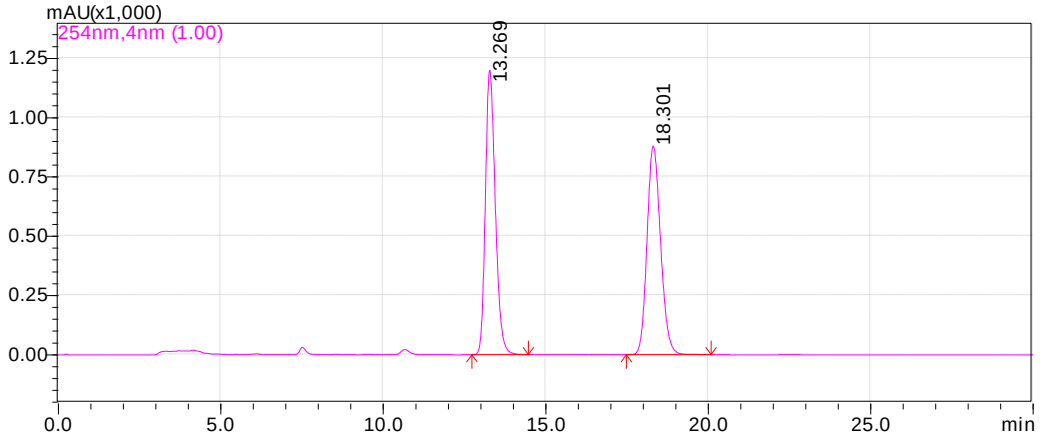


Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	14.455	7907663	340242	13.803	15.925	96.2368
2	19.043	309221	10931	18.389	20.043	3.7632

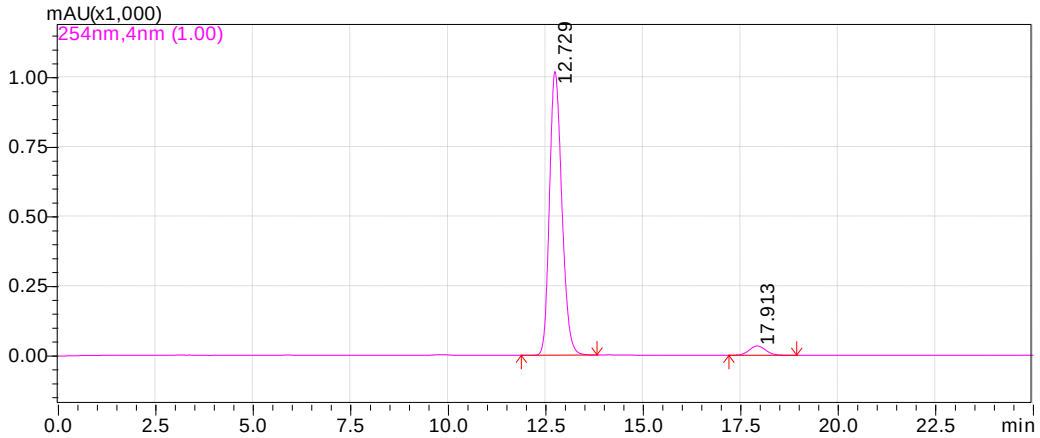


5c

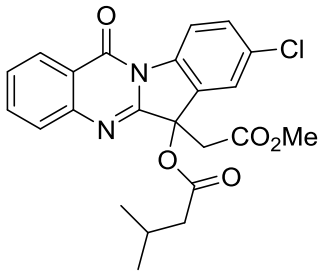
Daicel Chiralpak AD-H, hexane/iso-propanol=90/10, flow rate 1.0mL/min, 25℃



Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	13.269	25518708	1199060	12.725	14.464	49.9137
2	18.301	25606941	880771	17.483	20.085	50.0863

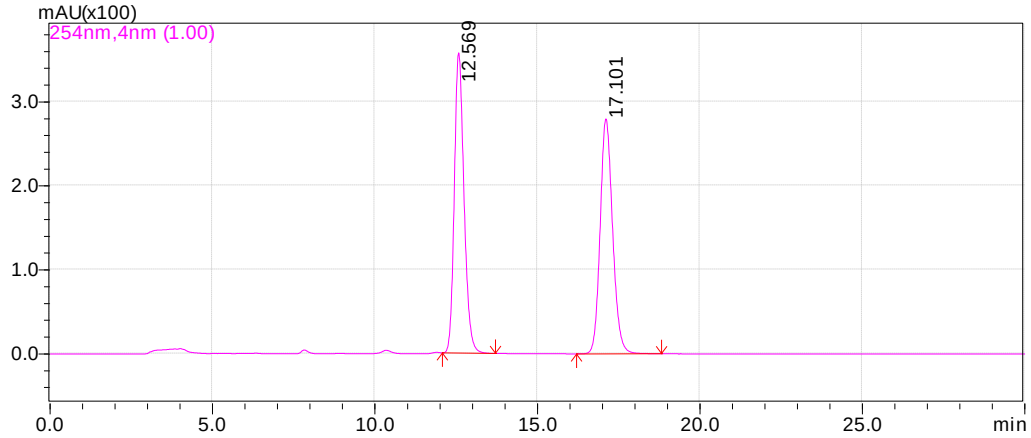


Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	12.729	22526260	1019260	11.872	13.813	95.8068
2	17.913	985918	33546	17.195	18.933	4.1932

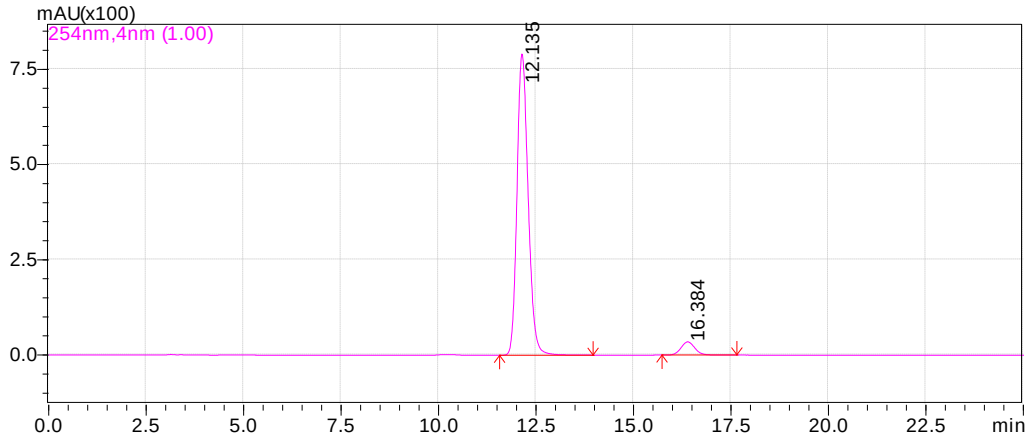


5d

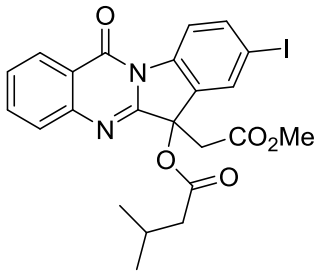
Daicel Chiralpak AD-H, hexane/iso-propanol=90/10, flow rate 1.0mL/min, 25℃



Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	12.569	7427837	357413	12.075	13.707	49.8584
2	17.101	7470026	279702	16.203	18.816	50.1416

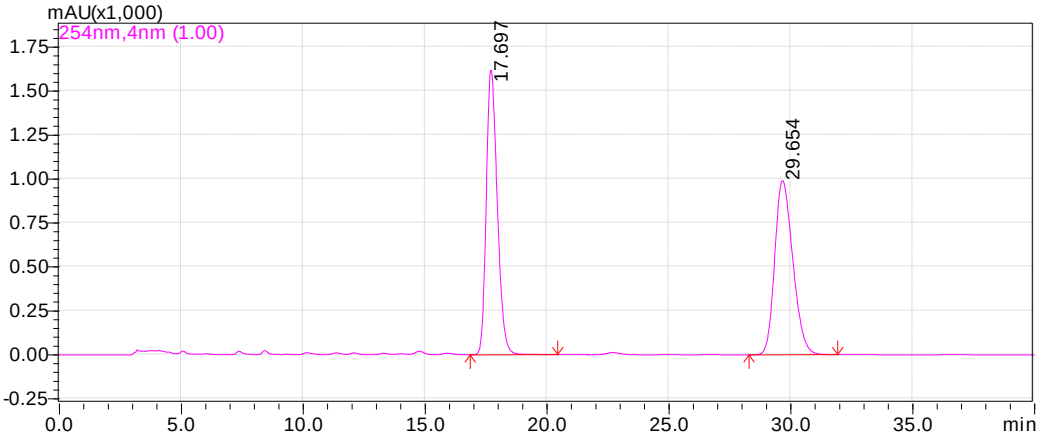


Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	12.135	15719010	790459	11.563	13.963	94.8138
2	16.384	859805	34678	15.733	17.653	5.1862

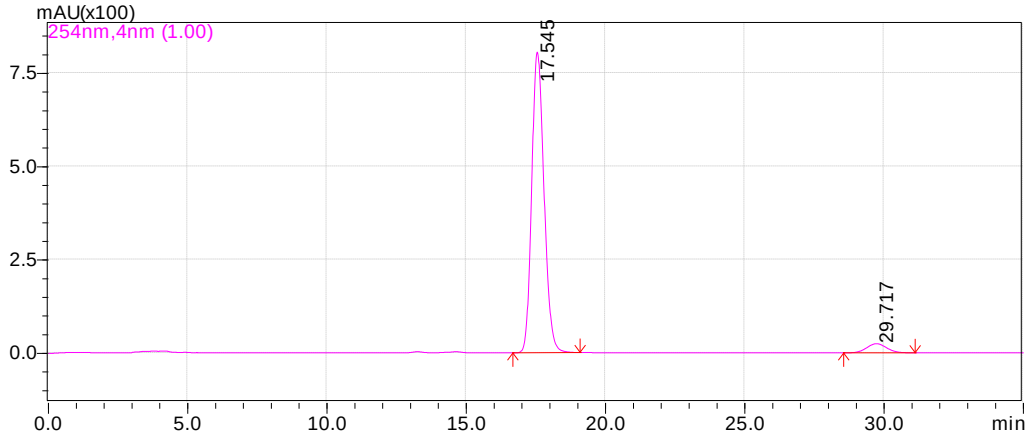


5e

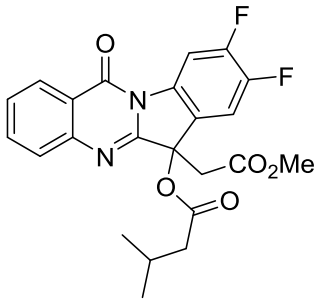
Daicel Chiralpak AD-H, hexane/iso-propanol=90/10, flow rate 1.0mL/min, 25℃



Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	17.697	51021363	1617915	16.853	20.437	49.9195
2	29.654	51185873	990009	28.288	31.925	50.0805

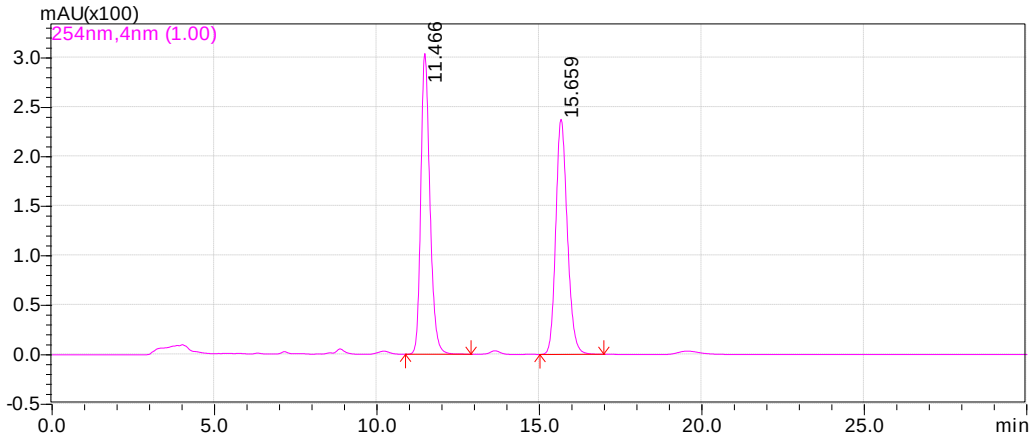


Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	17.545	24822983	805411	16.672	19.083	95.3343
2	29.717	1214835	24432	28.544	31.115	4.6657

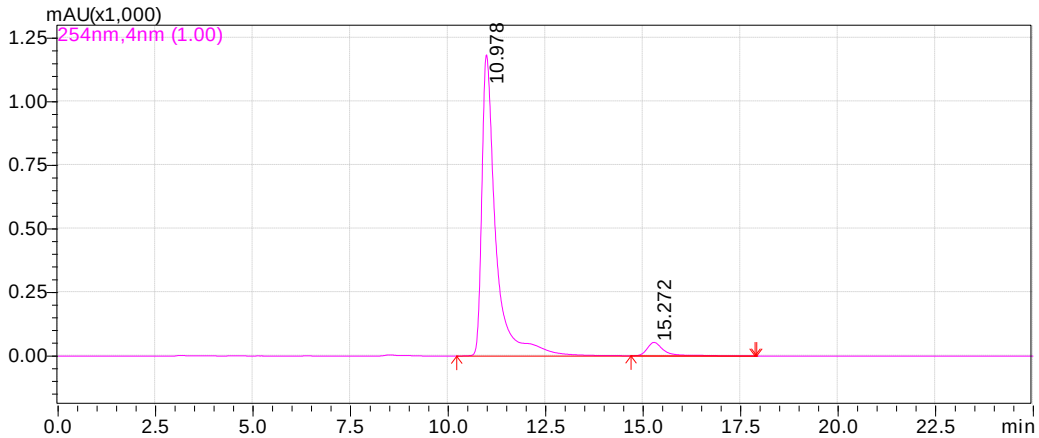


5f

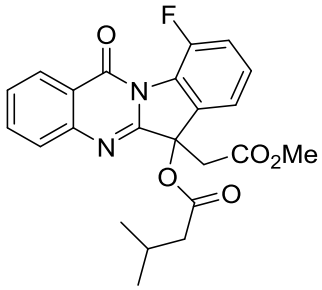
Daicel Chiralpak IA, hexane/iso-propanol=90/10, flow rate 1.0mL/min, 25℃



Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	11.466	5924739	303886	10.880	12.896	50.2530
2	15.659	5865090	237568	15.019	16.981	49.7470

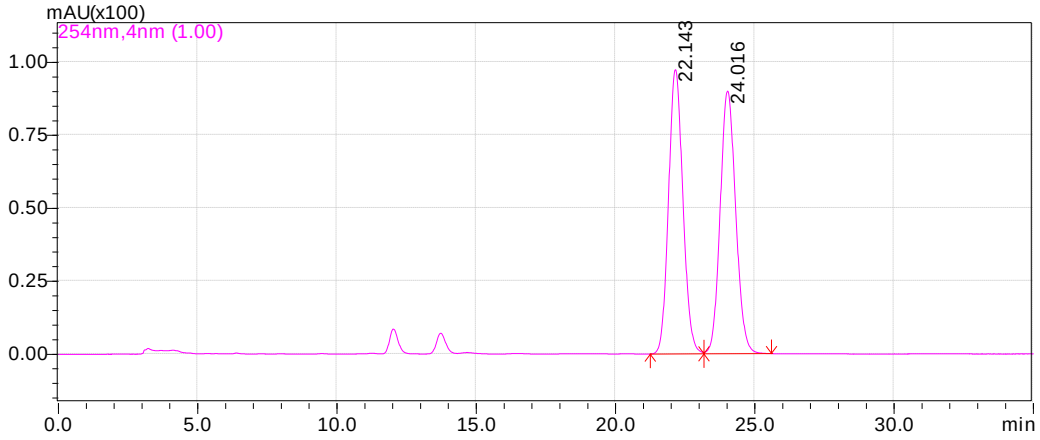


Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	10.978	29773681	1184497	10.219	17.909	94.9686
2	15.272	1577394	52521	14.688	17.867	5.0314

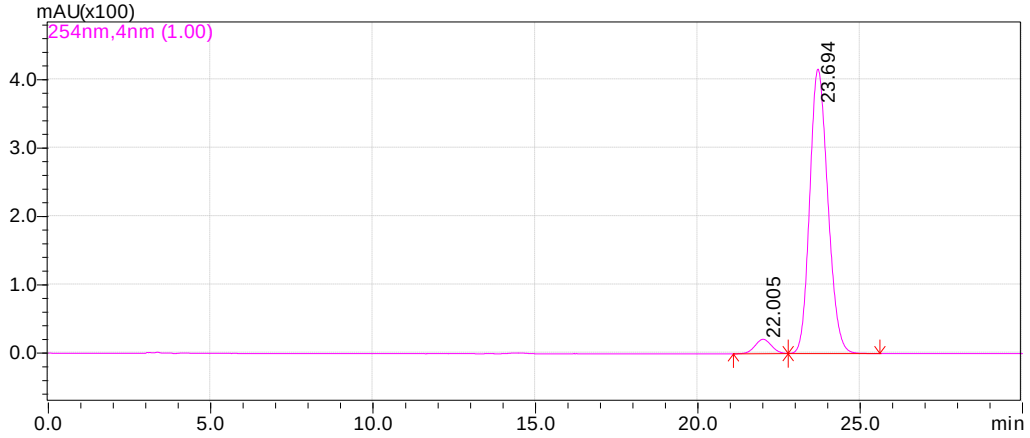


5g

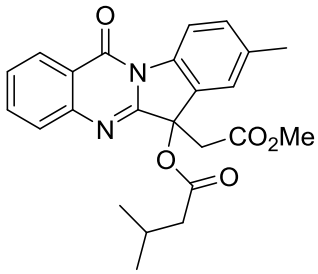
Daicel Chiralpak AD-H, hexane/iso-propanol=90/10, flow rate 1.0mL/min, 25℃



Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	22.143	3496104	97354	21.248	23.168	49.9738
2	24.016	3499770	90028	23.168	25.600	50.0262

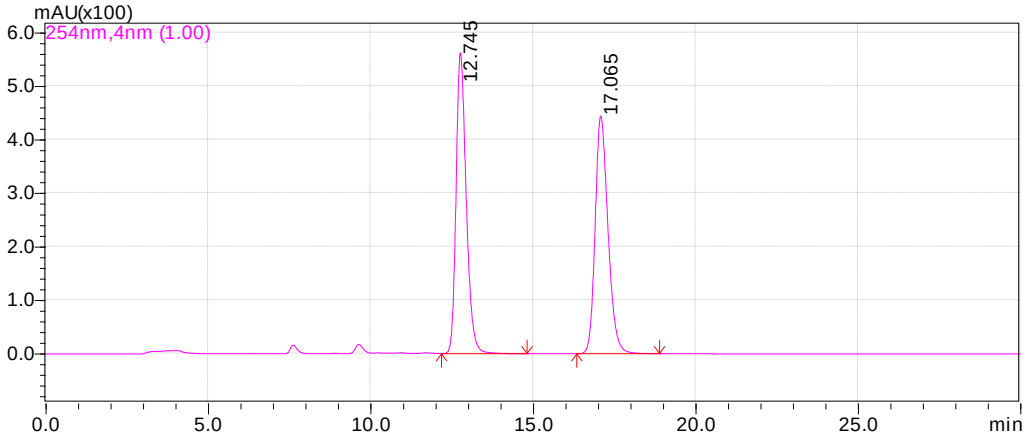


Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	22.005	762114	21198	21.099	22.784	4.5043
2	23.694	16157503	416251	22.784	25.611	95.4957

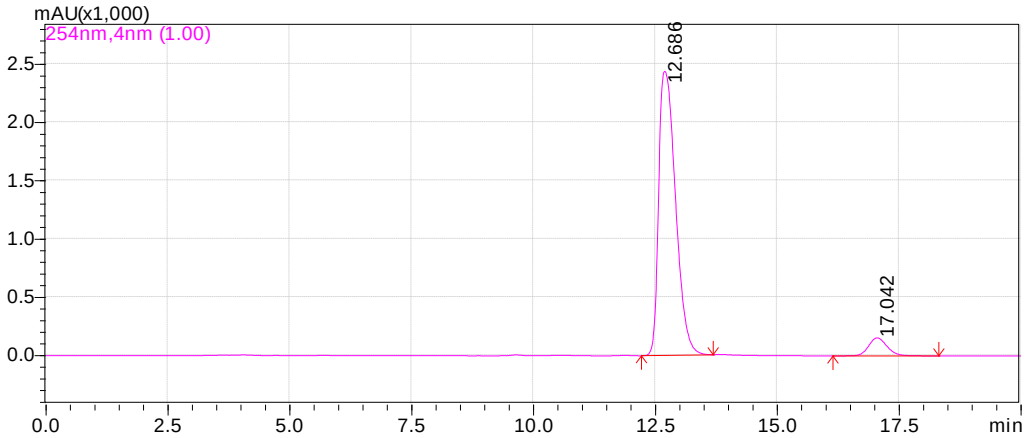


5h

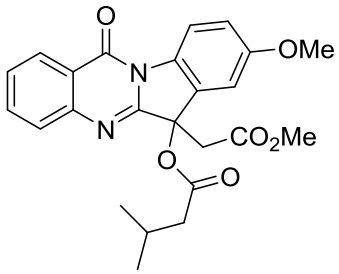
Daicel Chiralpak IA, hexane/iso-propanol=90/10, flow rate 1.0mL/min, 25℃



Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	12.745	12252065	562372	12.171	14.805	50.0443
2	17.065	12230389	444676	16.331	18.880	49.9557

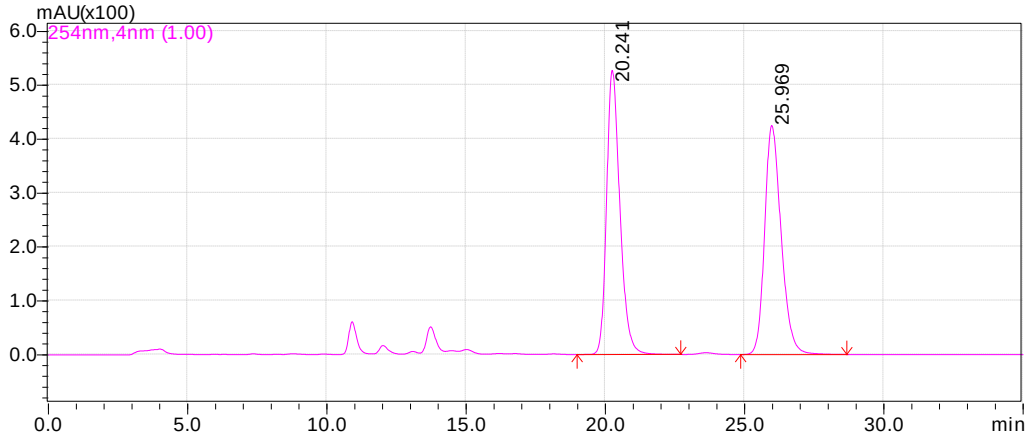


Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	12.686	58672215	2438048	12.213	13.685	93.5335
2	17.042	4056368	154470	16.139	18.315	6.4665

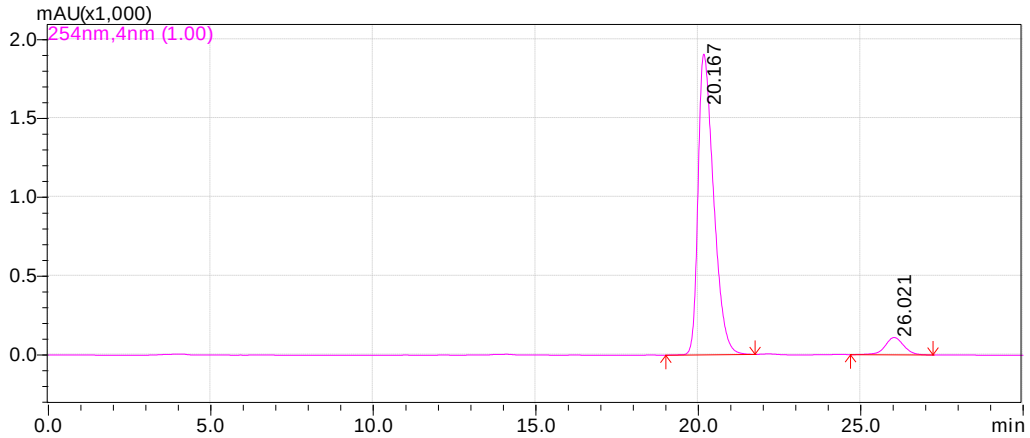


5i

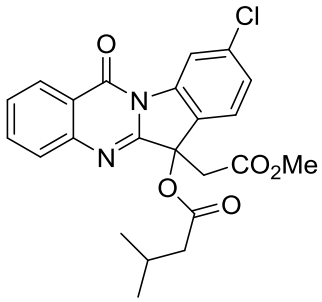
Daicel Chiralpak IA, hexane/iso-propanol=90/10, flow rate 1.0mL/min, 25℃



Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	20.241	17553807	527233	18.987	22.709	49.9957
2	25.969	17556815	424930	24.853	28.672	50.0043

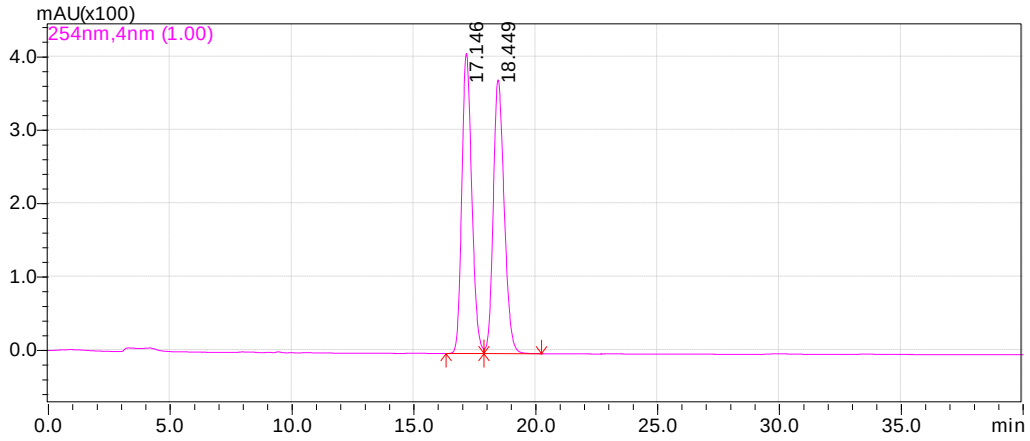


Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	20.167	63362379	1906316	18.997	21.749	93.5822
2	26.021	4345379	109415	24.683	27.221	6.4178

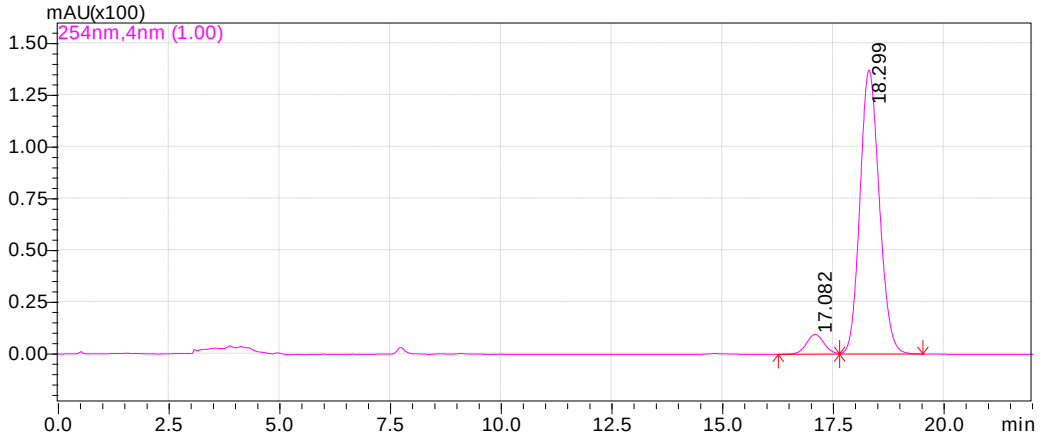


5j

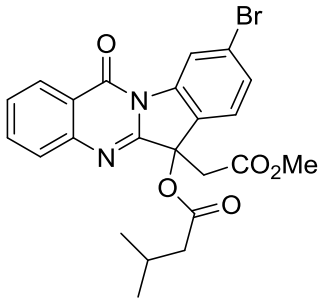
Daicel Chiralpak AD-H, hexane/iso-propanol=90/10, flow rate 1.0mL/min, 25℃



Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	17.146	11592856	408754	16.320	17.877	49.8516
2	18.449	11661896	373025	17.877	20.235	50.1484

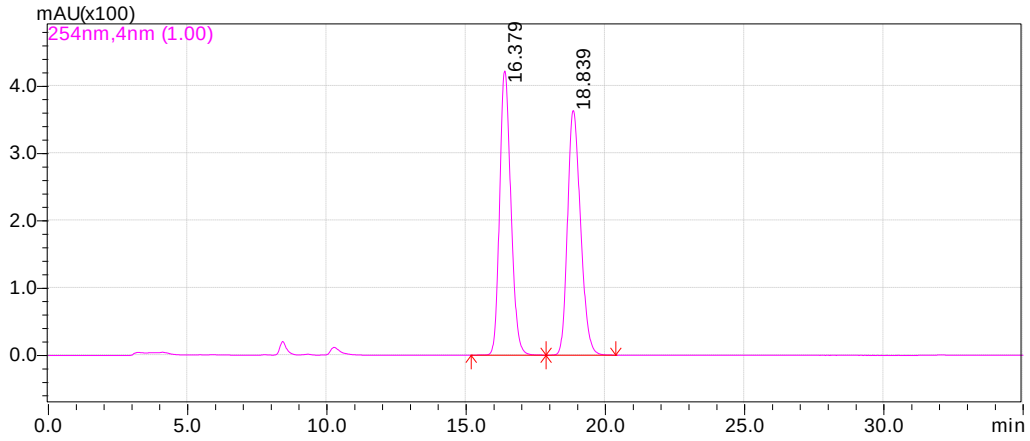


Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	17.082	272000	9570	16.256	17.643	6.1115
2	18.299	4178646	137304	17.643	19.520	93.8885

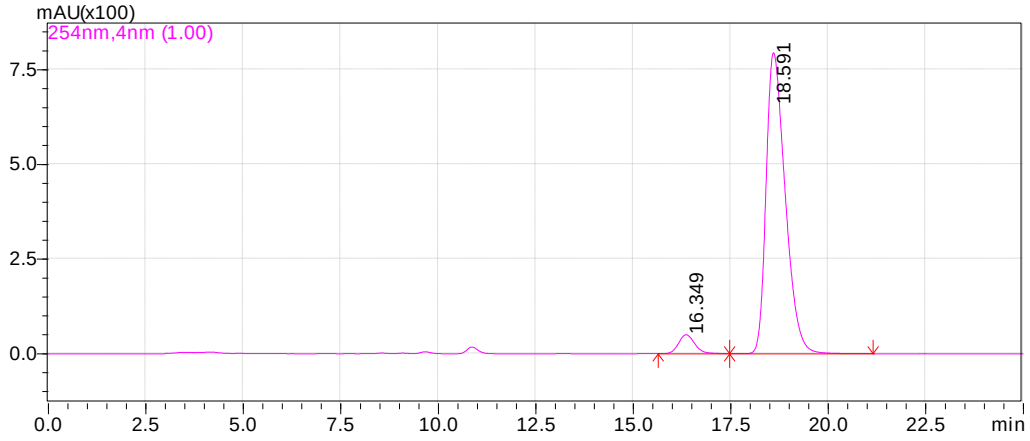


5k

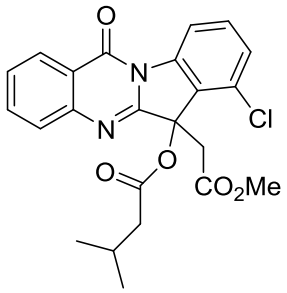
Daicel Chiralpak AD-H, hexane/iso-propanol=90/10, flow rate 1.0mL/min, 25℃



Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	16.379	11866073	422416	15.179	17.867	50.1009
2	18.839	11818270	363361	17.867	20.373	49.8991

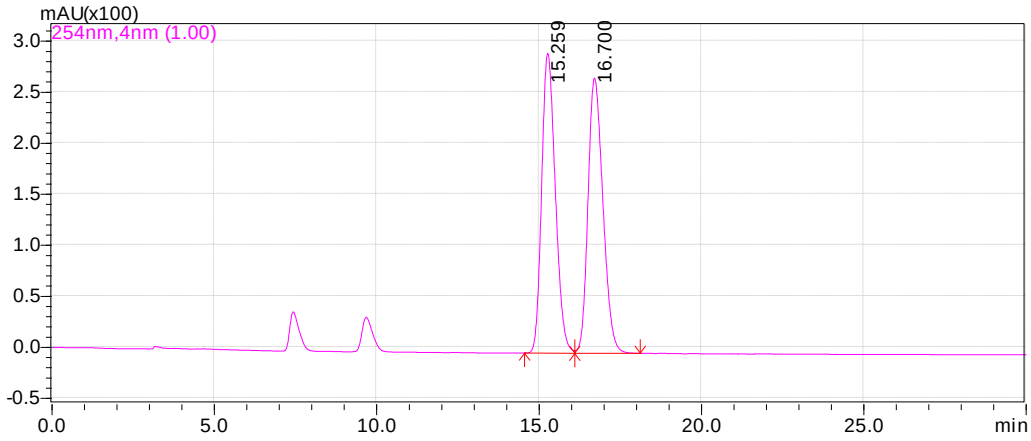


Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	16.349	1487101	50392	15.669	17.749	5.0936
2	18.591	27159985	794947	17.760	20.864	94.9064

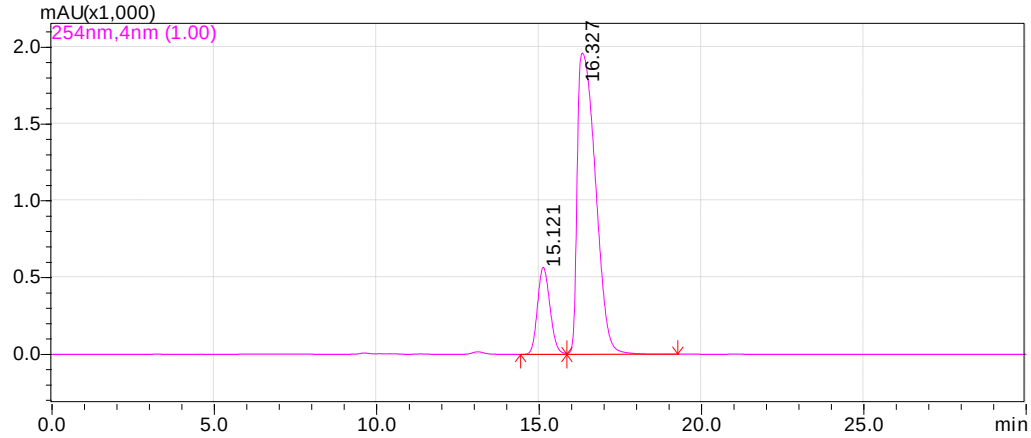


5l

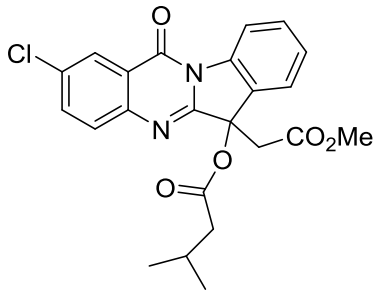
Daicel Chiralpak AD-H, hexane/iso-propanol=95/5, flow rate 1.0mL/min, 25℃



Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	15.259	8603266	293831	14.549	16.096	49.8952
2	16.700	8639392	269694	16.096	18.112	50.1048

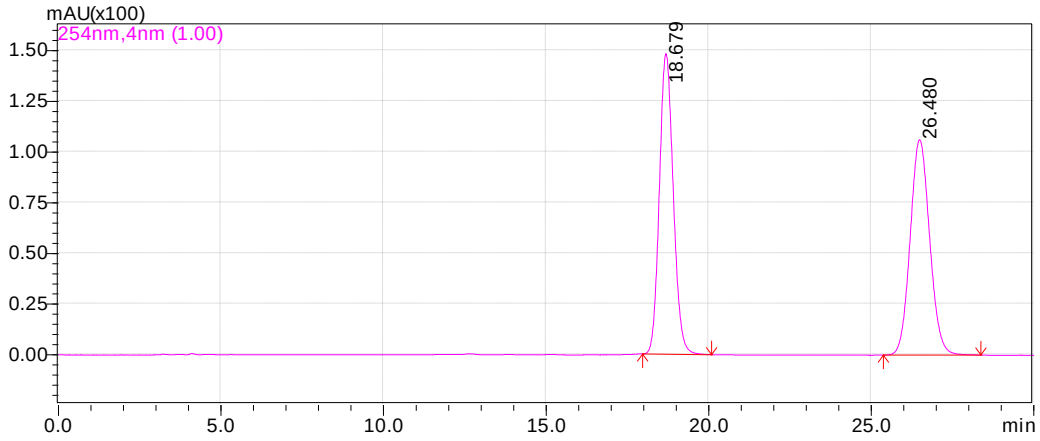


Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	15.121	15169436	566420	14.432	15.851	16.5207
2	16.327	76651399	1961922	15.851	19.275	83.4793

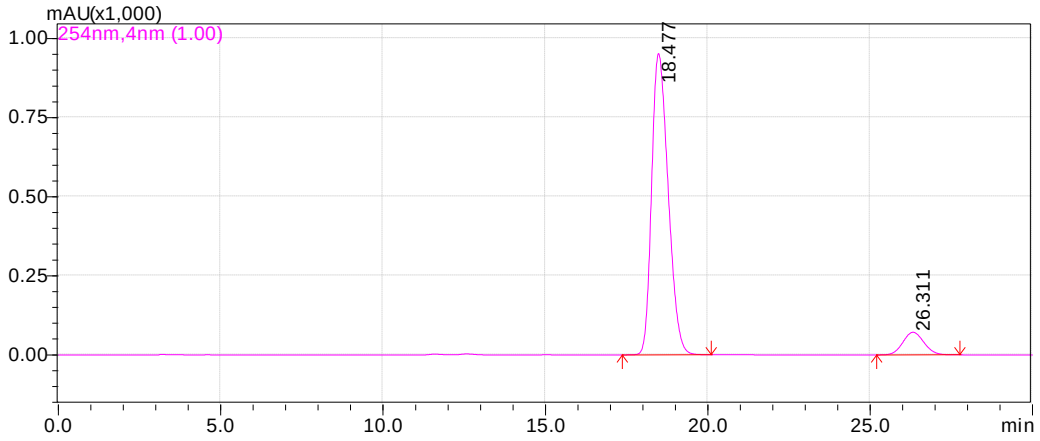


5m

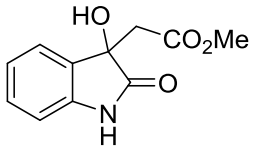
Daicel Chiralpak AD-H, hexane/iso-propanol=95/5, flow rate 1.0mL/min, 25℃



Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	18.679	4402574	148240	17.963	20.085	49.8865
2	26.480	4422610	106234	25.376	28.373	50.1135

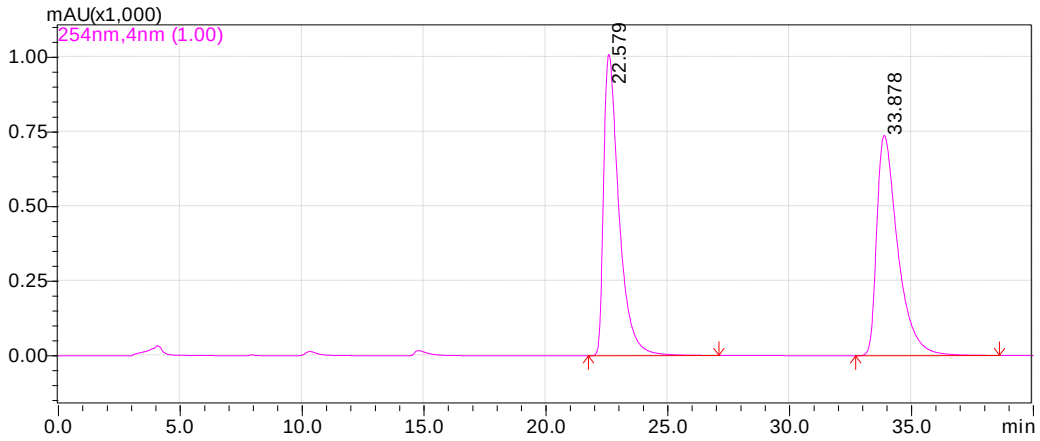


Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	18.477	33721168	952248	17.365	20.107	91.2623
2	26.311	3228544	71465	25.195	27.765	8.7377

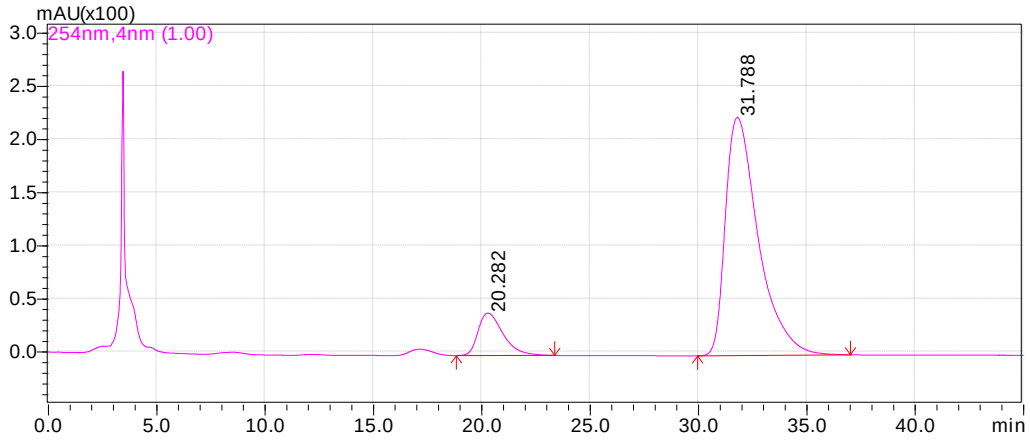


8a

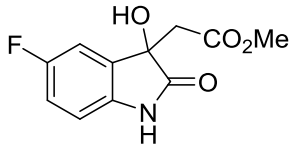
Daicel Chiralpak IA, hexane/iso-propanol=90/10, flow rate 1.0mL/min, 25℃



Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	22.579	44215740	1009644	21.739	27.104	49.8905
2	33.878	44409869	737956	32.704	38.603	50.1095

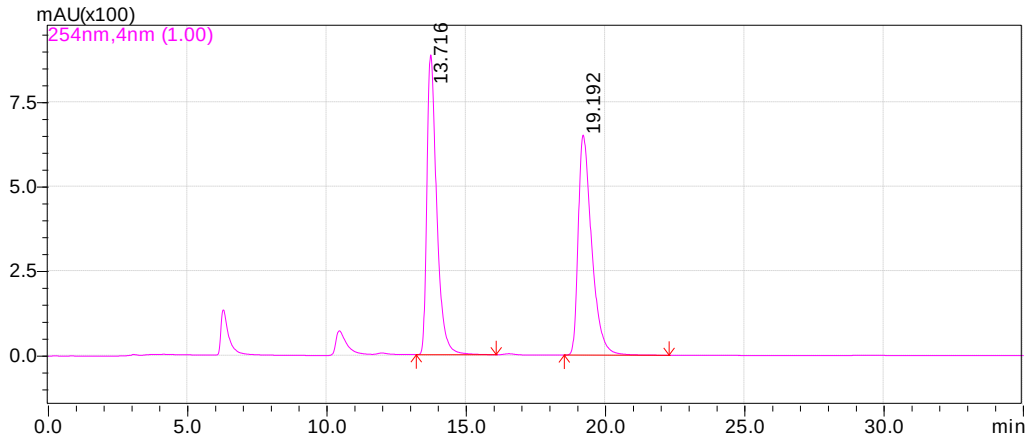


Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	20.282	3213107	39958	18.827	23.360	11.9352
2	31.788	23708193	224068	29.963	37.013	88.0648

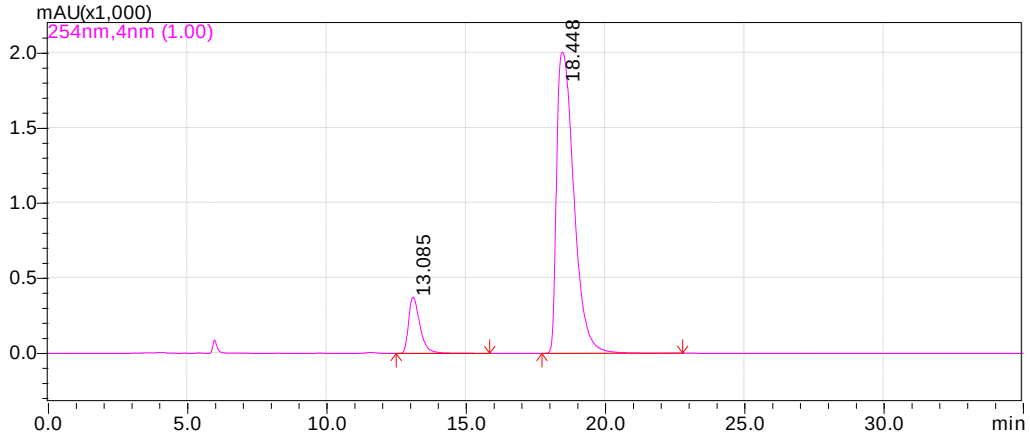


8b

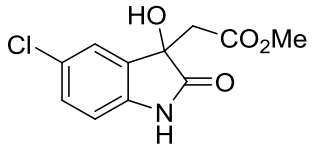
Daicel Chiralpak IA, hexane/iso-propanol=85/15, flow rate 1.0mL/min, 25℃



Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	13.716	21766505	886851	13.205	16.075	49.8702
2	19.192	21879773	651306	18.517	22.283	50.1298

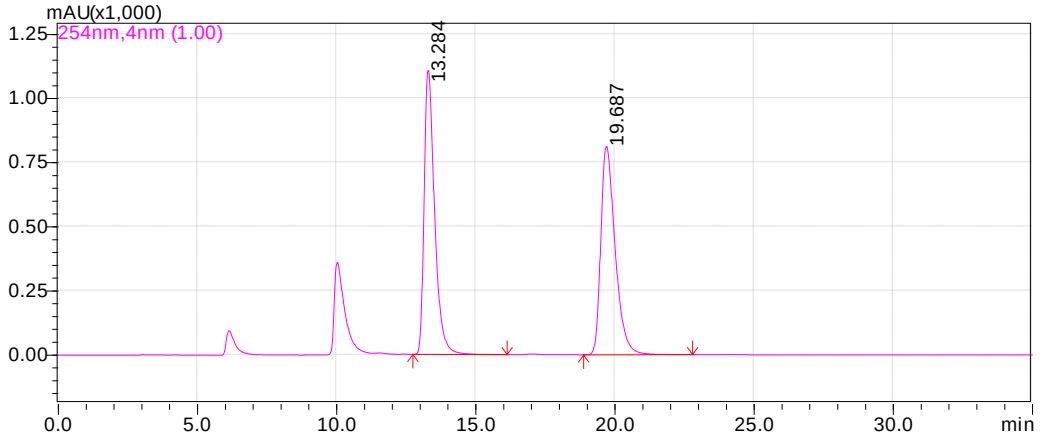


Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	13.085	10640019	374403	12.480	15.840	10.9556
2	18.448	86479029	2005720	17.717	22.763	89.0444

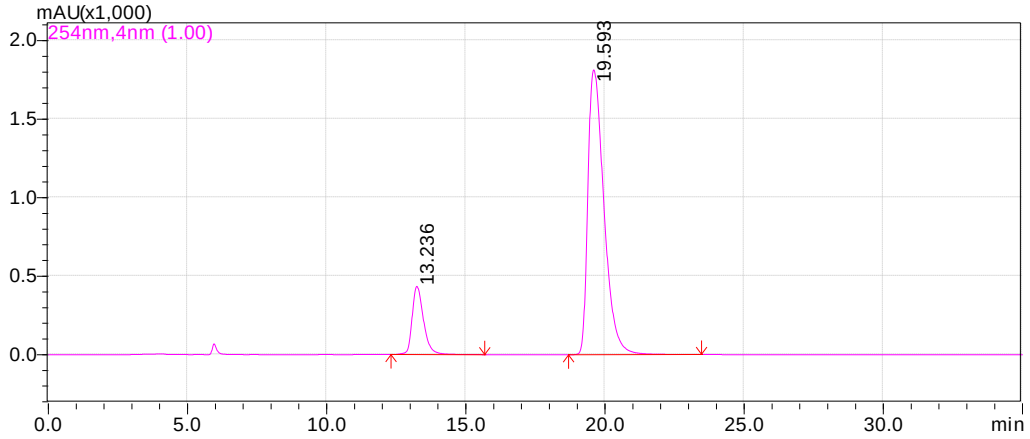


8c

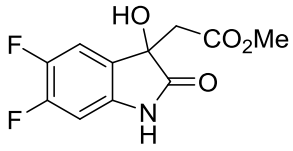
Daicel Chiralpak IA, hexane/iso-propanol=85/15, flow rate 1.0mL/min, 25℃



Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	13.284	28977114	1107313	12.736	16.128	49.8499
2	19.687	29151624	812422	18.869	22.784	50.1501

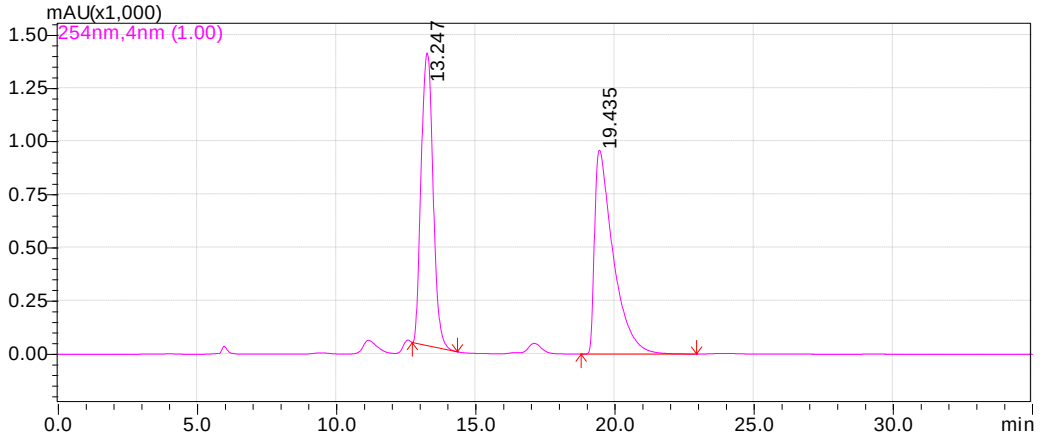


Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	13.236	12451925	434148	12.309	15.680	14.5956
2	19.593	72861227	1813190	18.688	23.467	85.4044

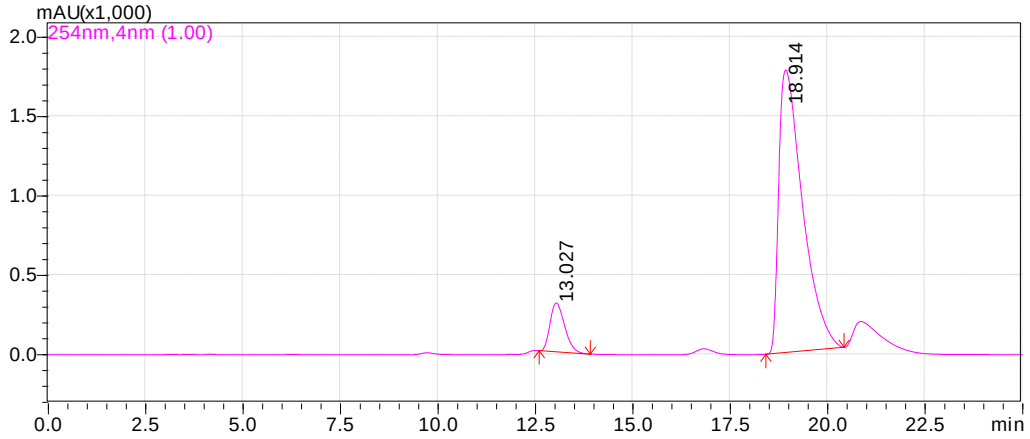


8d

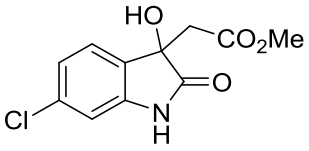
Daicel Chiralpak IA, hexane/iso-propanol=85/15, flow rate 1.0mL/min, 25℃



Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	13.247	41076434	1375456	12.715	14.336	47.8890
2	19.435	44697756	958689	18.784	22.933	52.1110

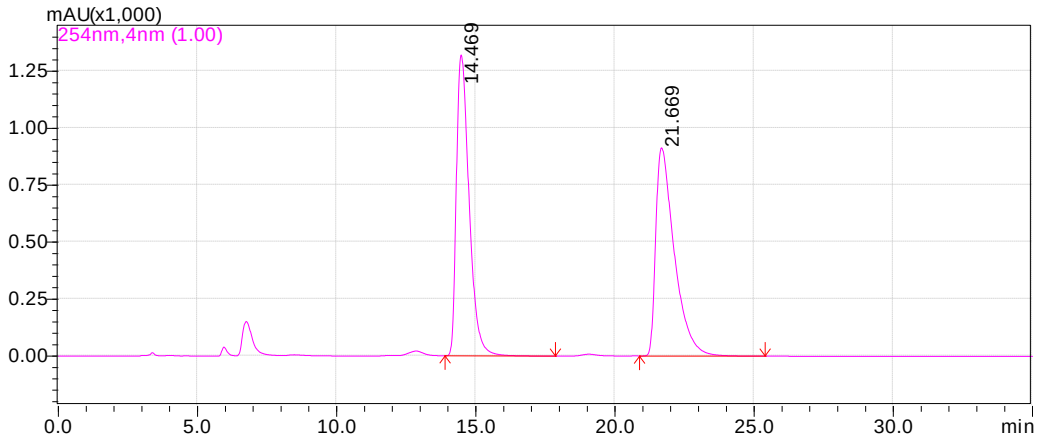


Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	13.027	8027034	308010	12.597	13.909	9.5534
2	18.914	75995673	1781087	18.411	20.416	90.4466

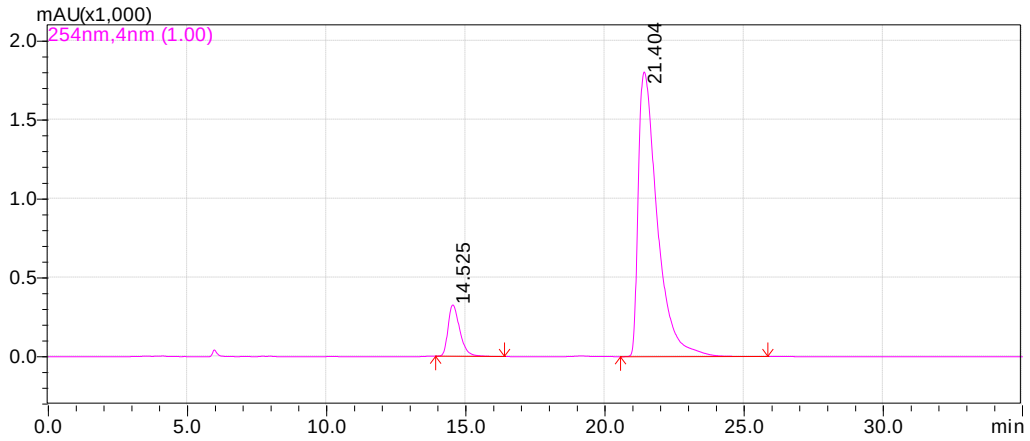


8e

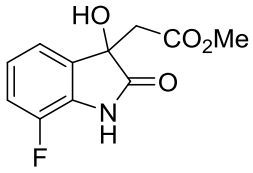
Daicel Chiralpak IA, hexane/iso-propanol=85/15, flow rate 1.0mL/min, 25℃



Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	14.469	42059813	1320743	13.899	17.856	49.7760
2	21.669	42438415	913974	20.885	25.397	50.2240

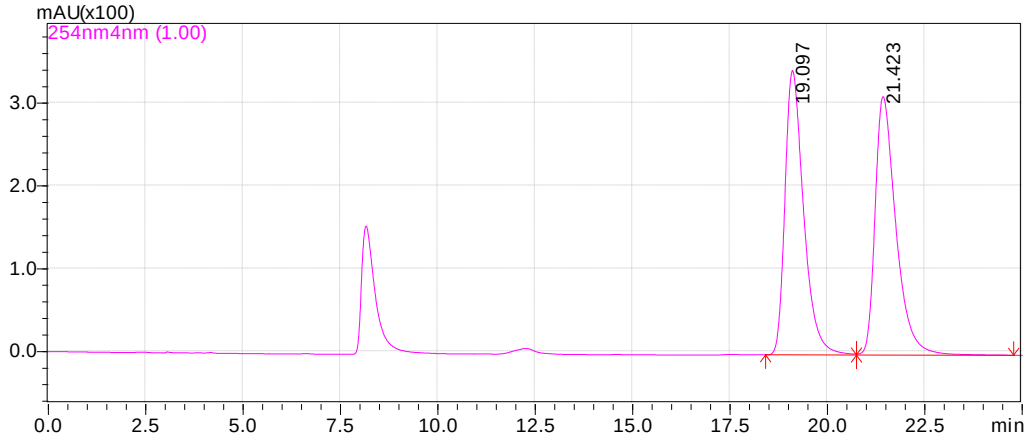


Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	14.525	9572505	324898	13.909	16.384	10.0316
2	21.404	85851008	1804846	20.555	25.845	89.9684

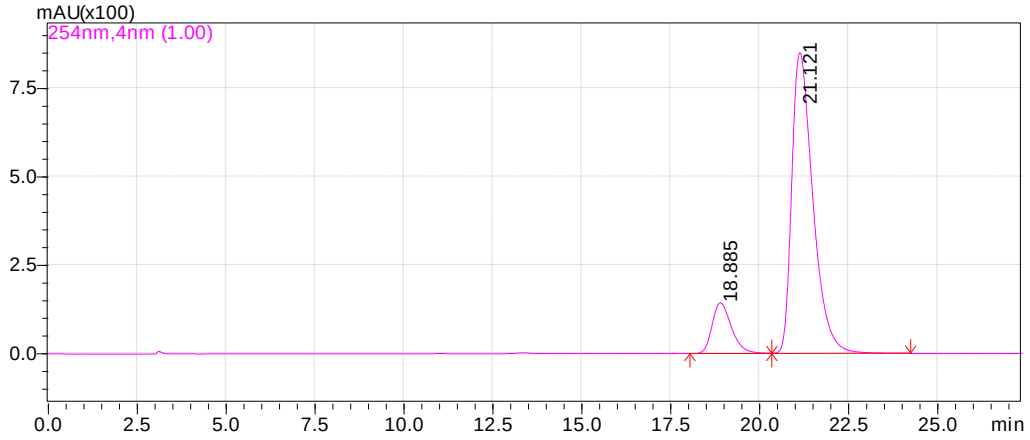


8f

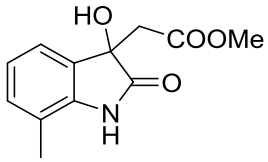
Daicel Chiralpak IA, hexane/iso-propanol=90/10, flow rate 1.0mL/min, 25℃



Peak#	Ret.Time	Area	Height	Peak Start	Peak End	Area%
1	19.097	11474426	343534	18.411	20.747	49.6746
2	21.423	11624778	312157	20.747	24.779	50.3254

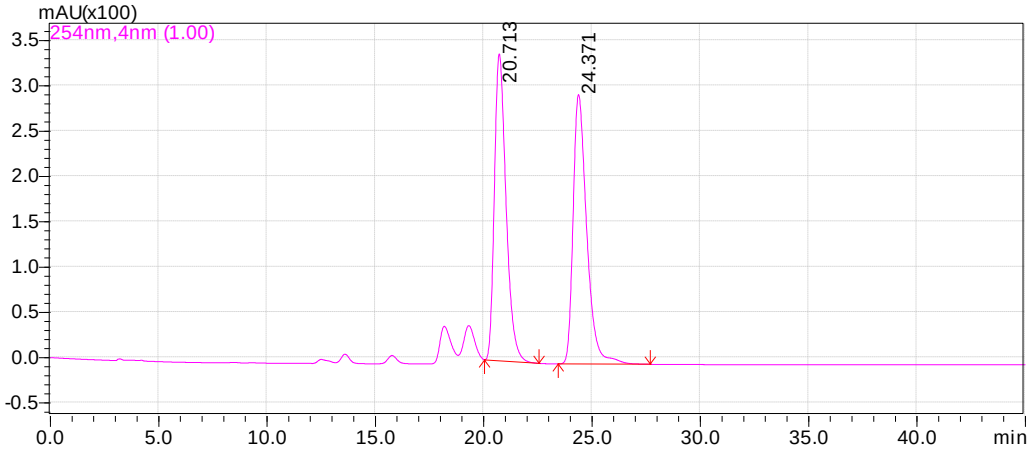


Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	18.885	5425697	143345	18.037	20.341	13.3655
2	21.121	35169079	850699	20.341	24.245	86.6345

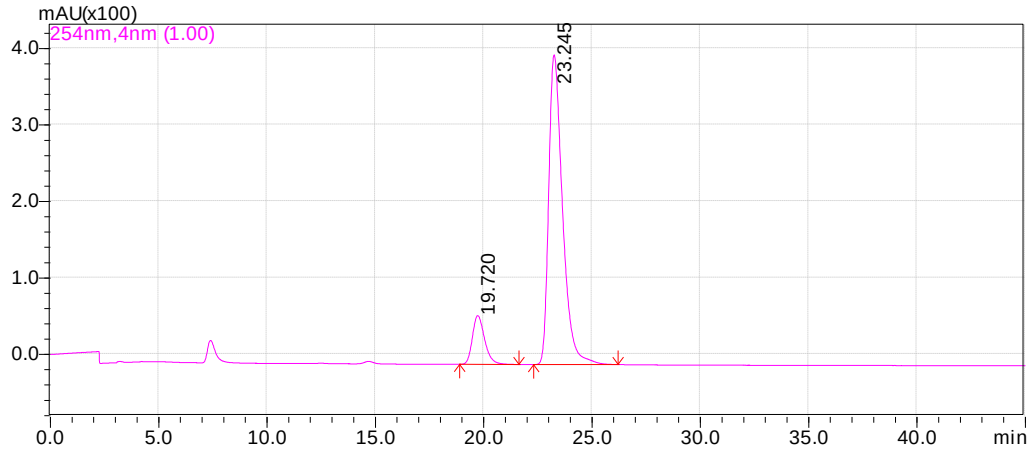


8g

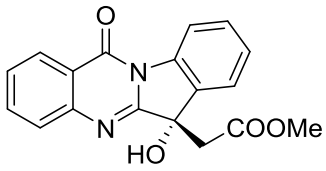
Daicel Chiralpak IA, hexane/iso-propanol=90/10, flow rate 1.0mL/min, 25℃



Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	20.713	12681700	338665	20.043	22.549	49.3312
2	24.371	13025548	297408	23.435	27.691	50.6688

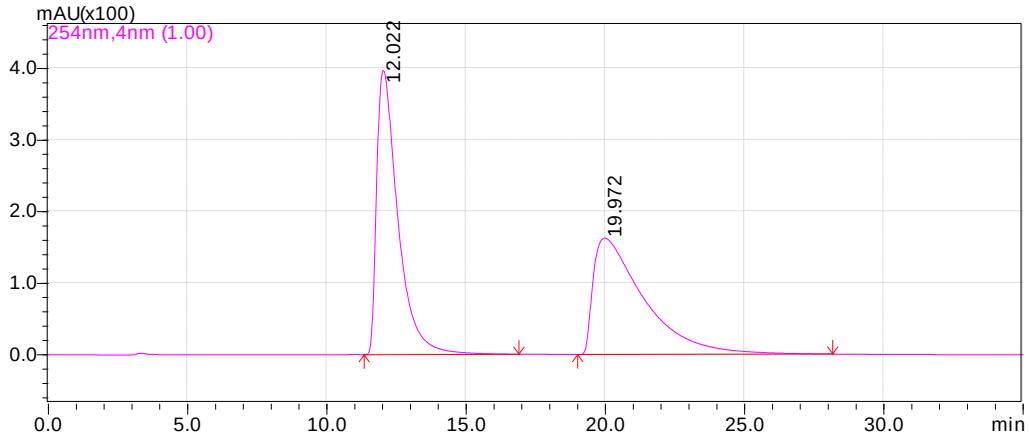


Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	19.720	2513640	63934	18.891	21.632	12.2491
2	23.245	18007430	405005	22.304	26.197	87.7509

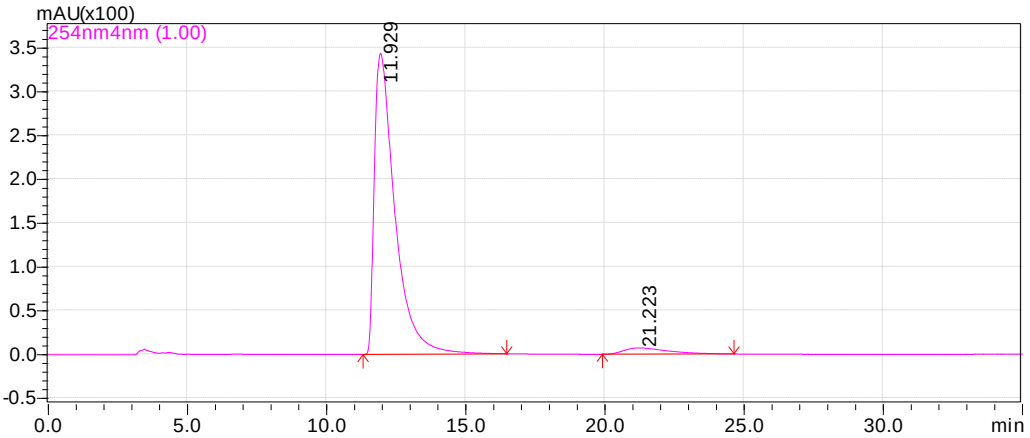


***ent*-4a**

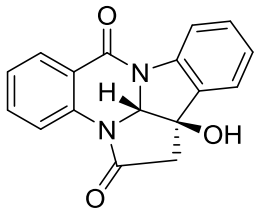
Daicel Chiralpak AS-H, hexane/iso-propanol= 90/10, flow rate 1.0 mL/min, 25°C



Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	12.022	21150970	396985	11.339	16.896	50.5396
2	19.972	20699340	162575	19.008	28.160	49.4604

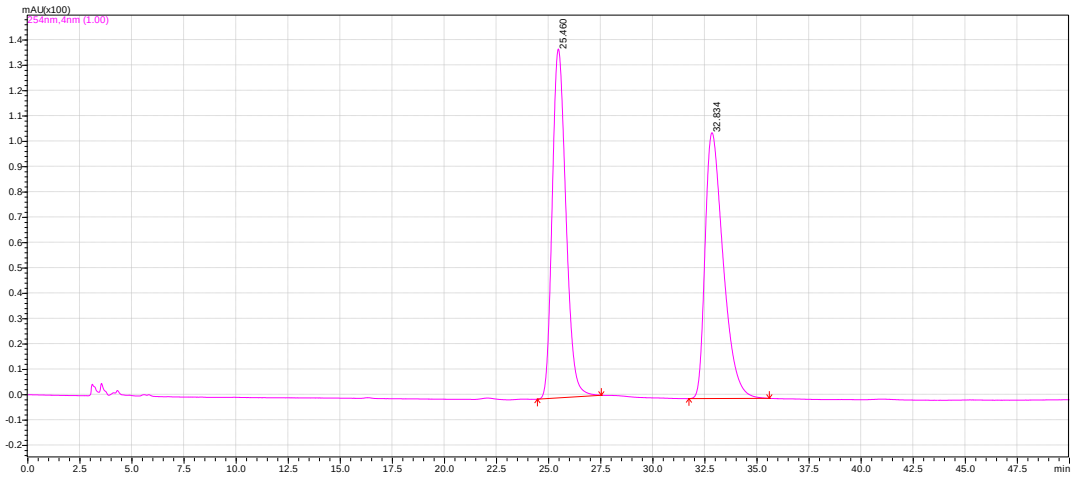


Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	11.929	17688090	343648	11.307	16.469	95.7056
2	21.223	793676	7180	19.904	24.629	4.2944

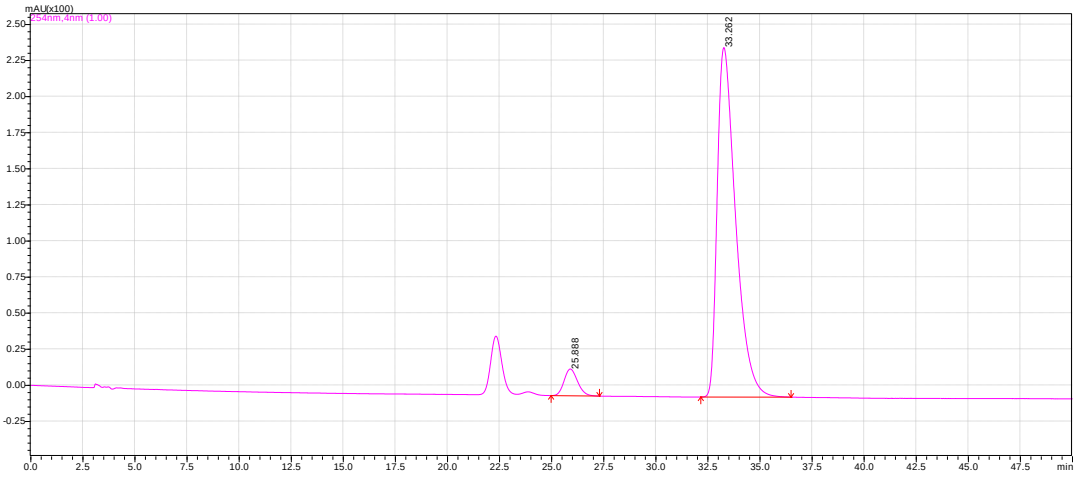


10

Daicel Chiralpak AD-H, hexane/iso-propanol= 90/10, flow rate 1.0 mL/min, 25°C



Peak#	Ret.Time	Area	Height	Peak Start	Peak End	Area%
1	25.460	6327130	137705	24.459	27.531	49.9233
2	32.834	6346568	104935	31.733	35.595	50.0767



Peak#	Ret.Time	Area	Height	Peak Start	Peak End	Area%
1	25.888	835152	29083	25.205	27.733	5.3177
2	33.262	23825164	372069	32.640	37.365	94.6823