Stereogenic cis-2-Substituted-N-Acetyl-3-hydroxy-indolines via Ruthenium(II)-Catalyzed Dynamic Kinetic Resolution-Asymmetric Transfer Hydrogenation

ZhonghuaLuo, [†]Guodong Sun, [‡,§]Zihong Zhou, [‡]Guozhu Liu, [‡]Baolei Luan, [‡]Yicao Lin, [‡] Lei Zhang, [*,†]Zhongqing Wang[*,‡,§]

[†]School of Biology and biological Engineering, South China University of Technology, Guangzhou 510640, P. R. China

[‡]HEC Research and Development Center, HEC Pharm Group, Dongguan 523871, P. R. China

[§]State Key Laboratory of Anti-Infective Drug Development, Sunshine Lake Pharma Co., Ltd, Dongguan 523871, P. R. China

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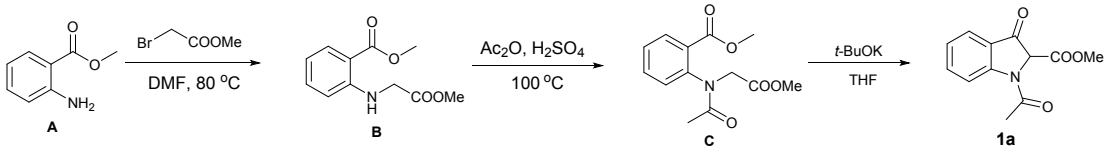
1. General Information.

If nospecially indicated, all reagents and solvents were used as commercially available without further purification.NMR spectra were measured on a BrukerAvance 400 spectrometer in the solventsindicated; chemical shifts are reported in units (ppm) by assigning TMS resonance in the ^{1}H spectrum as 0.00ppm, $CD_3OD$and d^6-DMSO resonances in the ^{13}C spectrum as 49.0 ppm and 39.5 ppm respectively. Coupling constants are reported in Hz withmultiplicities denoted as singlet (s), doublet (d), triplet (t), quartet (q), dd (doublet of doublets); m (multiplets),and etc. HRMS were performed on Fourier Transform Ion Cyclotron Resonance Mass Spectrometer.Analytical HPLC for liquid phase was carried out on an Agilent HPLC workstation, equipped with a DAICEL CHIRALPAK® OD-3 (4.6x 150mm, 3μm) column. Optical rotations weremeasured using a 1 mL cell with a 1 dm path length on a Jasco P-1030 polarimeter and are reported as follows: $[\alpha]_D^{20}$ (c in g per 100 mL solvent).

2. General procedure for the synthesis of2-substituted N-acetyl-3-hydroxy-indolines (1a~1p)

1) *Preparation of **1a~1n** according to the literature* [1]



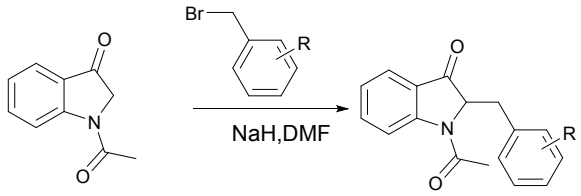
To a stirred solution of **A** (2.00 g, 13.2mmol) in (10 mL) DMF was added methyl bromoacetate(2.02 g, 13.2mmol) at room temperature, then the resulting solutionwas stirred for 12 h at 80 °C .Then the reaction mixture was allowed to rt and water was added (15 mL), the resulting solution was extracted with MTBE (20ml ×2). The combined extracts werewashed with water (20ml ×2) and concentrated under vacuum to afford **B** 2.75 gas a light yellowsolid, which was used for the next step directly.

To a solution of **B** (2.50 g, 11.2mmol) in acetic anhydride (5ml/g) was added catalytic amount of conc. H_2SO_4. Then the reaction mixture was stirred at 100 °C for 5h, evaporated Ac_2O under reduced pressure. Crudeproduct was dissolved in CH_2Cl_2 (30 mL) and washed twice with saturated aqueous $NaHCO_3$ (20ml ×2) and concentrated. The residue was purified by flash columnchromatography on silica gel using EA/n-hexane (2/1, v/v) mixture to affordthe pure product **C** (2.64 g, 89% yield) as a pale yellow oil.

To a stirred solution of**C** (2.6 g, 9.80mmol) in 20 mL dry THF at -10 °C under N_2 atmosphere wasadded t-BuOK (1.43 g, 12.74mmol, 1.3eq) in one protion.The mixture was allowed to stir at -10~0 °C for 1 h. Then HOAc (1.3eq) was added to adjust the pH to about 6, THF was removed under reduced pressure at 40 °C. Water (20 mL) was added to the residue and extracted with CH_2Cl_2(20ml ×2).The combined extracts were washed with water (20 mL) andconcentrated under vacuum.The residue was purified by flash column chromatography on silica gelusing ethyl acetate/n-hexane (3/7, v/v) mixture to afford the pure product **1a** (1.83 g, 80%yield) as a colorless solid.

1b~1n was synthesized according to the above procedure.

2) *Preparation of **1o** and **1p** according to the literature* [2]



1o,1p

1-acetylindolin-3-one (1.4 g, 8mmol) and DMF (20 mL) were added to a round-bottom flask. Then sodium hydride (60wt% in mineral oil,1.2 equiv.) was added potionwise at 0 °C. After the reaction mixture was stirred at 0 °C for 0.5~1.0h, benzyl bromide (8.8mmol, 1.1 equiv.) was addeddropwisevia a syringe. The solution was kept at room temperature for 20 h, then was quenched by saturated $NaHCO_3$solution and extracted with MTBE (20ml ×2), the organic phase was concentrated under vacuum and purified by flash column chromatography on silica gel to afford **1o**. **1p** was synthesized according to the above procedure.

^{1}H NMR (400 MHz, DMSO) δ 8.25 (s, 1H), 7.58 (t, J = 7.4 Hz, 2H), 7.14 (q, J = 7.1 Hz, 1H), 6.79 (d, J = 8.3 Hz, 1H), 6.36 (s, 1H), 6.26 (dd, J = 8.3, 2.2 Hz, 1H), 4.75 (dd, J = 6.8, 3.3 Hz, 1H), 3.62 (d, J = 9.6 Hz, 6H), 3.33 (dd, J = 13.9, 7.2 Hz, 1H), 3.08 (dd, J = 13.9, 3.4 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 198.43, 159.66, 158.50, 136.58, 131.65, 124.29, 123.52, 122.90, 114.83, 104.24, 97.83, 65.21, 55.01, 30.63, 23.55.

References

1)Yarlagadda, S.; Ramesh, B.; Reddy, C. R.; Srinivas, L.; Sridhar, B.; Reddy, B. V. S. *Org. Lett.***2017**, *19*, 170.

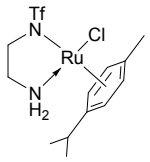
2)Guo, J.; Lin, Z.-H.; Chen, K.-B.; Xie, Y.; Chan, A.S.C.; Weng, J.; Lu, G.*Org. Chem. Front.***2017**,*4*, 1400.

3. Asymmetric Transfer Hydrogenation of 1a~1o Using Ru Catalysts.

Preparation of the Ru-catalysts:

Catalyst **R,R-C2** ((*R,R*)-Ts-DENEB) and **R,R-C3** ((R,R)-teth-TsDpen-RuCl) was purchased from Sinocompound Catalysts Co., Ltd. (China). Other metal catalysts (**R,R-C1, R,R-C4~C7**) were prepared by treatment of $[RuCl_2(p\text{-Cymene})]_2$ (1.0 eq)with (*R,R*)-diamine ligand (2.0 eq) and Et_3N (4.0 eq)in CH_2Cl_2 stirred for 5 hours at reflux, the catalysts were then obtained and used directly without further purification.

*Preparation of Rac-***2a**~**2o**:

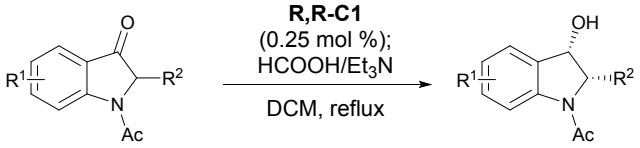


C8=

*Rac-***2a**~**2o**were synthesized by the same method: To a stirred solution of **1a~1o** (4.29 mmol), **C8** (0.20 mmol) and Et_3N (5.57 mmol) in 16 mL DCM was added HCOOH (13.7 mmol) dropwise, the

resulted mixture was stirred 24 hours at reflux. After that, the solvents was removed, the crude product was purified by flash column chromatography on silica gel using petroleum ether/ethyl acetate and afforded corresponding desired product.

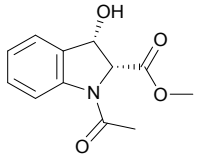
General procedure of the asymmetric hydrogen transfer reduction



1a~1p **2a~2p**

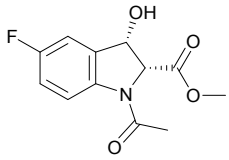
To a stirred solution of 2-substituted N-acetyl-3-hydroxy-indoline (4.29 mmol), **R,R-C1** (0.01 mmol) and Et_3N (5.57 mmol) in 16 mL DCM was added HCOOH (13.7 mmol) dropwise, the resulted mixture was stirred 15~18 hours* at reflux. After that, the solvents was removed, the crude product was purified by flash column chromatography on silica gel using petroleum ether/ethyl acetate (2:1, v/v) afforded desired product. The enantioselectivity of the productswas determined by HPLC analysis.Dr was determined by^{1}H NMRat 60^{o}C, >99:1 means thatonly a single diastereomer was visible in the ^{1}H NMR of the crude reaction mixture.

*The reaction time for **2m** and **2n** were 48h, and 24h for **2o** and **2p**.



(2R,3S)-N-acetyl-3-hydroxy-2-methoxycarbonyl-indoline (**2a**)

White solid, 0.997 g, 98% yield, ee: >99%, dr:>99:1; mp: 159.75 ^{o}C;$[\alpha]_D^{20}$=+92 (c = 2.0, DMSO). Enantiometric excess was determined by HPLC (DAICEL CHIRALPAK® OD-3(4.6x 150mm, 3μm), hexane/EtOH/TFA 70:30:0.1, flow rate 0.5 mL/min, t_{major} =7.77 min, t_{minor} =6.30 min, λ = 254 nm). Compound **2a** has two rotamers in MeOH at ambient temperature. ^{1}H NMR (400 MHz, MeOD) δ 8.15 (major, d, *J* = 7.6 Hz, 1H), 7.48-7.21 (both, m, 3.5H), 7.12 (both, t, *J* = 7.4 Hz, 1.5H), 5.71 (major, d, *J* = 8.7 Hz, 1H), 5.57 (minor, d, *J* = 7.2 Hz, 0.5H), 5.19 (major, d, *J* = 8.8 Hz, 1H), 5.07 (minor, d, *J* = 7.3 Hz, 0.5H), 3.78 (major, s, 3H), 3.72 (minor, s, 1.5H), 2.47 (minor, s, 1.5H), 2.10 (major, s, 3H).^{13}C NMR (101 MHz, MeOD) δ 171.43 (major), 170.97 (minor), 170.61 (major), 170 31 (minor), 143.65 (major), 142.14 (minor), 133.10 (major), 132.87 (minor), 130.86 (minor), 130.49 (major), 127.27 (minor), 126.00 (major), 125.50 (major), 124.96 (minor), 117.86 (major), 114.98 (minor), 72.58 (major), 70.21 (minor), 69.08 (major), 68.23 (minor), 52.80 (major), 52.37 (minor), 24.75(minor), 23.75 (major). HRMS [M + H]$^+$for $C_{12}H_{13}NO_4$, calculated: 236.0917; found 236.0921.

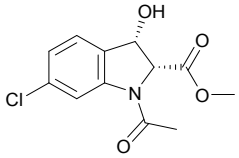


(2R,3S)-N-acetyl-5-fluoro-3-hydroxy-2-methoxycarbonyl-indoline (**2b**)

White solid, 1.01 g, 93% yield, ee: >97%, dr:>99:1; mp: 197.95 ^{o}C; $[\alpha]_D^{20}$+83 (c = 2.0, DMSO). Enantiometric excess was determined by HPLC (DAICEL CHIRALPAK® OD-3(4.6 x 150mm,

3μm), hexane/EtOH/TFA 70:30:0.1, flow rate 0.5 mL/min, tmajor =7.10 min, tminor =5.68 min, λ = 254 nm).

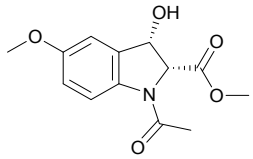
Compound **2b** has two rotamers in MeOH at ambient temperature. ^{1}H NMR (400 MHz, MeOD) δ 8.15-8.12 (major, dd, *J* = 8.4, 4.3 Hz, 1H), 7.32 (minor, s, 0.32 H), 7.12-7.00 (both, m, 2.67H), 5.72 (major, d, *J* = 8.9 Hz, 1H), 5.56 (minor, d, *J* = 7.9 Hz, 0.34H), 5.21 (major, d, *J* = 9.0 Hz, 1H), 5.11 (minor, d, *J* = 7.9 Hz, 0.34H), 3.78 (major, s, 3H), 3.72 (minor, s, 1H), 2.45 (minor, s, 1H), 2.09 (major, s, 3H). ^{13}C NMR (101 MHz, MeOD) δ 171.13 (major), 170.67 (minor), 170.47(major), 170.20 (minor), 161.95, 160.34, 139.84 (major), 138.42 (minor), 137.38 (minor), 135.53 (major), 119.02 (major), 118.97 (major), 117.19 (minor), 117.03 (minor), 116.79 (major), 116.64 (major), 116.19 (minor), 116.16 (minor), 114.12 (minor), 113.96 (minor), 112.86 (major), 112.69 (major), 72.18 (major), 69.95, (minor), 69.35 (major), 68.65 (minor), 52.85 (major), 52.43 (minor), 24.48 (minor), 23.48 (major).HRMS $[M + H]^+$for $C_{12}H_{12}FNO_4$, calculated: 254.0823; found 254.0817.



(2R,3S)-N-acetyl-6-chloro-3-hydroxy-2-methoxycarbonyl-indoline (**2c**)

White solid, 972 mg, 84% yield, ee: >98%, dr:>99:1; mp: 186.16°C; $[\alpha]_D^{20}$+83 (c = 2.0, DMSO).Enantiometric excess was determined by HPLC (DAICEL CHIRALPAK® OD-3(4.6x 150mm, 3μm), hexane/EtOH/TFA 70:30:0.1, flow rate 0.5 mL/min, t_{major} =6.94 min, t_{minor} =6.45 min, λ = 254 nm).

Compound **2c** has two rotamers in MeOH at ambient temperature.^{1}H NMR (400 MHz, MeOD) δ 8.17 (major, s, 1H), 7.30 (both, d, *J* = 7.5 Hz, 1.4H), 7.12 (both, d, *J* = 7.8 Hz, 1.2 H), 5.68 (major, d, *J* = 8.6 Hz, 1H), 5.53 (minor, s, 0.2H), 5.22 (major, d, *J* = 8.7 Hz, 1H), 5.10 (minor, s, 0.2H), 3.79 (both, s, 3.6H), 2.46 (minor, s, 0.6H), 2.10 (major, s, 3H).^{13}C NMR (101 MHz, MeOD) δ 171.60, 170.35, 144.74, 135.94, 131.97, 125.30, 117.87, 72.05, 69.43, 52.88, 23.66.HRMS $[M + H]^+$for $C_{12}H_{12}ClNO_4$, calculated: 270.0528; found 270.0535.

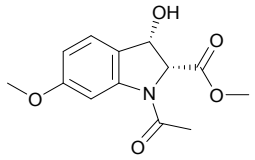


(2R,3S)-N-acetyl-3-hydroxy-5-methoxy-2-methoxycarbonyl-indoline (**2d**)

White solid, 897 mg, 79%yield,ee: >99%, dr:>99:1; mp:204.15°C; $[\alpha]_D^{20}$+87 (c = 2.0, DMSO).Enantiometric excess was determined by HPLC (DAICEL CHIRALPAK® OD-3(4.6x 150mm, 3μm), hexane/EtOH/TFA 70:30:0.1, flow rate 0.5 mL/min, t_{major} =9.33 min, t_{minor} =6.51 min, λ = 254 nm).

Compound **2d** has two rotamers in DMSO at ambient temperature.^{1}H NMR (400 MHz, DMSO-d^6) δ 7.98 (major, d, *J* = 8.6 Hz, 1H), 7.21 (minor, d, *J* = 8.6 Hz, 0.3H), 6.86 (both, dd, *J* = 24.1, 11.0 Hz, 2.6H), 6.37 (major, s, 1H), 6.20 (minor, s, 1H), 5.61 (major, d, *J* = 9.2 Hz, 1H), 5.48 (minor, d, *J* = 9.0 Hz, 0.3H), 5.22 (major, d, *J* = 9.2 Hz, 1H), 4.97 (minor, d, *J* = 9.2 Hz, 0.3H), 3.73 (both, s, 4H), 3.68 (major, s, 3H), 3.59 (minor, s, 1H), 2.34 (minor, s, 1H).1.98 (major, s, 3H).^{13}C NMR (101 MHz, DMSO-d^6) δ 169.12, 167.61, 155.92, 135.87, 133.85, 116.55, 114.17, 110.04, 70.66, 67.18, 55.37, 51.90,

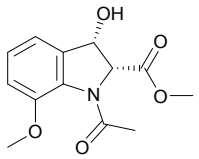
23.18.HRMS [M + H]+for $C_{13}H_{15}NO_5$, calculated: 266.1023; found 266.1033.



(2R,3S)-N-acetyl-3-hydroxy-6-methoxy-2-methoxycarbonyl-indoline (**2e**)

White solid, 921 mg, 81%yield,ee: >98%, dr:>99:1; mp:166.50°C; $[\alpha]_D^{20}$+84 (c = 2.0, DMSO).Enantiometric excess was determined by HPLC (DAICEL CHIRALPAK® OD-3(4.6x 150mm, 3μm), hexane/EtOH/TFA 70:30:0.1, flow rate 0.5 mL/min, t_{major} =8.37 min, t_{minor} =7.41 min, λ = 254 nm).

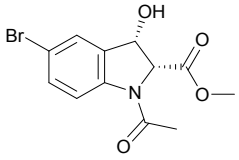
Compound **2e** has two rotamers in MeOH at ambient temperature.^{1}H NMR (400 MHz, MeOD) δ 7.80 (major, s, 1H), 7.29 (minor, s, 0.4H), 7.23 (major, d, *J* = 8.0 Hz, 1H), 6.85 (minor, s, 0.4H), 6.69 (both, d, *J* = 7.8 Hz, 1.4H), 5.63 (major, d, *J* = 8.5 Hz, 1H), 5.49 (minor, s, 0.4H), 5.19 (major, d, *J* = 8.6 Hz, 1H), 5.06 (minor, s, 0.4H), 3.76 (both, d, *J* = 25.2 Hz, 8.4H), 2.47 (minor, s, 1.2H), 2.09 (major, s, 3H).^{13}C NMR (101 MHz, MeOD) δ 171.55, 170.64, 162.53, 145.00, 126.50, 111.38, 103.92, 72.10, 69.90, 56.01, 52.78, 23.81, 9.61.HRMS [M + H]+for $C_{13}H_{15}NO_5$, calculated: 266.1023; found 266.1035.



(2R,3S)-N-acetyl-3-hydroxy-7-methoxy-2-methoxycarbonyl-indoline (**2f**)

White solid, 966 mg, 85%yield, ee: >94%, dr:>99:1; mp:132.79°C; $[\alpha]_D^{20}$+165 (c = 2.0, DMSO).Enantiometric excess was determined by HPLC (DAICEL CHIRALPAK® OD-3(4.6x 150mm, 3μm), hexane/EtOH/TFA 70:30:0.1, flow rate 0.5 mL/min, t_{major} =9.55 min, t_{minor} =5.35 min, λ = 254 nm).

^{1}H NMR (400 MHz, MeOD) δ 7.18 (t, *J* = 7.8 Hz, 1H), 7.03 (d, *J* = 8.2 Hz, 1H), 6.99 (d, *J* = 7.4 Hz, 1H), 5.72 (d, *J* = 8.5 Hz, 1H), 5.25 (d, *J* = 8.6 Hz, 1H), 3.89 (s, 3H), 3.67 (s, 3H), 2.21 (s, 3H).^{13}C NMR (101 MHz, MeOD) δ 173.36, 170.66, 149.62, 138.78, 131.34, 127.82, 118.14, 114.65, 72.70, 71.19, 56.34, 52.36, 23.67.HRMS [M + H]+for $C_{13}H_{15}NO_5$, calculated: 266.1023; found 266.1030.

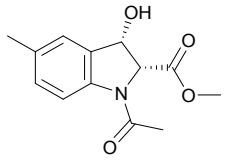


(2R,3S)-N-acetyl-5-bromo-3-hydroxy-2-methoxycarbonyl-indoline (**2g**)

White solid, 1.16 g, 85%yield, ee: 96%, dr:>99:1; mp:190.42°C; $[\alpha]_D^{20}$+50 (c = 2.0, DMSO). Enantiometric excess was determined by HPLC (DAICEL CHIRALPAK® OD-3(4.6x 150mm, 3μm), hexane/EtOH/TFA 70:30:0.1, flow rate 0.5 mL/min, t_{major} =7.80 min, t_{minor} =6.62 min, λ = 254 nm).

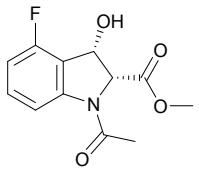
Compound **2g** has two rotamers in DMSO at ambient temperature.^{1}H NMR (400 MHz, DMSO-d^6) δ 8.00 (major, d, *J* = 8.4 Hz, 1H), 7.58-7.36 (both, m, 2.6H), 7.28 (minor, s, 0.2H), 6.49 (major, s, 1H), 6.31 (minor, s, 0.2H), 5.64 (major, d, *J* = 8.5 Hz, 1H), 5.52 (minor, s, 0.2H), 5.27 (major, d, *J* = 9.2 Hz, 1H), 4.99 (minor, s, 0.2H), 3.69 (major, s, 3H), 3.60 (minor, s, 0.6H), 2.38 (minor, s, 0.6H), 2.02 (major,

s, 3H).^{13}C NMR (101 MHz, DMSO-d^6) δ 168.79, 168.61, 141.55, 135.18, 131.63, 127.56, 117.54, 114.95, 70.22, 67.02, 52.03, 45.69, 23.34.HRMS [M + H]$^+$for $C_{13}H_{12}BrNO_4$, calculated: 314.0022; found 314.0031.



(2R,3S)-N-acetyl-3-hydroxy-5-methyl-2-methoxycarbonyl-indoline (**2h**)

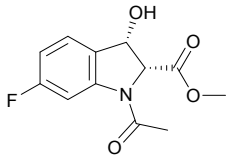
White solid, 975mg, 91% yield, ee: >99%, dr:>99:1; mp:201.96^{o}C; $[\alpha]_D^{20}$+81 (c = 2.0, DMSO). Enantiometric excess was determined by HPLC (DAICEL CHIRALPAK® OD-3(4.6x 150mm, 3μm), hexane/EtOH/TFA 70:30:0.1, flow rate 0.5 mL/min, t_{major} =8.46 min, t_{minor} =5.91 min, λ = 254 nm). Compound **2h** has two rotamers in DMSO at ambient temperature.^{1}H NMR (400 MHz, DMSO-d^6) δ 7.94 (major, d, J = 8.1 Hz, 1H), 7.28-6.94 (both, m, 3H), 6.32 (major, s, 1H), 6.17 (minor, s, 0.3H), 5.60 (major, d, J = 9.1 Hz, 1H), 5.47 (minor, d, J = 8.2 Hz,0.3H), 5.21 (major, d, J = 9.2 Hz, 1H), 4.95 (minor, d, J = 8.8 Hz, 0.3H), 3.68 (major, s, 3H), 3.58 (minor, s, 1H), 2.36 (minor, s, 0.3H), 2.28 (both, s, 4H), 1.99 (major, s, 3H).^{13}C NMR (101 MHz, DMSO-d^6) δ 169.12, 168.05, 140.07, 132.65, 132.44, 129.27, 125.19, 115.53, 70.65, 67.16, 51.89, 45.64, 23.35, 20.48.HRMS [M + H]$^+$for $C_{13}H_{15}NO_4$, calculated: 250.1074; found 250.1080.



(2R,3S)-N-acetyl-4-fluoro-3-hydroxy-2-methoxycarbonyl-indoline (**2i**)

White solid, 952 mg, 88% yield, ee: >98%, dr:>99:1; mp:191.00^{o}C; $[\alpha]_D^{20}$+103 (c = 2.0, DMSO). Enantiometric excess was determined by HPLC (DAICEL CHIRALPAK® OD-3(4.6 x 150mm, 3μm), hexane/EtOH/TFA 70:30:0.1, flow rate 0.5 mL/min, tmajor =7.88 min, tminor =7.09 min, λ = 254 nm).

Compound **2i** has two rotamers in MeOH at ambient temperature.^{1}H NMR (400 MHz, MeOD) δ 7.98 (major, s, 1H), 7.33 (both, s, 1.5H), 7.18 (minor, s, 0.5H), 6.83 (both, t, J = 8.3 Hz, 1.5H), 5.86 (major, s, 1H), 5.73 (minor, s, 0.5H), 5.24 (major, s, 1H), 5.08 (minor, s, 0.5H), 3.80 (both, s, 4.5H), 2.47 (minor, s, 1.5H), 2.09 (major, s, 3H).^{13}C NMR (101 MHz, DMSO-d^6) δ 168.71, 160.47, 158.02, 144.82, 131.59, 131.51, 118.48, 112.01, 110.38, 68.33, 67.66, 52.04, 45.67, 23.60.HRMS [M + H]$^+$for $C_{12}H_{12}FNO_4$, calculated: 254.0823; found 254.0834.

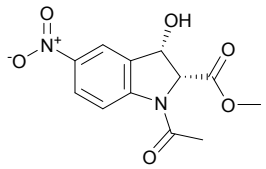


(2R,3S)-N-acetyl-6-fluoro-3-hydroxy-2-methoxycarbonyl-indoline (**2j**)

White solid, 992 mg, 91%yield,ee: >98%, dr:>99:1; mp:152.69^{o}C; $[\alpha]_D^{20}$+76 (c = 2.0, DMSO).Enantiometric excess was determined by HPLC (DAICEL CHIRALPAK® OD-3(4.6 x

150mm, 3μm), hexane/EtOH/TFA 70:30:0.1, flow rate 0.5 mL/min, tmajor =6.71min, tminor =6.15 min, λ = 254 nm).

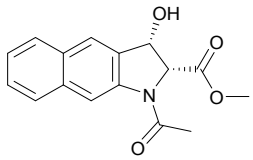
Compound **2j** has two rotamers in MeOH at ambient temperature.^{1}H NMR (400 MHz, MeOD) δ 7.88 (major, d, *J* = 10.2 Hz, 1H), 7.35 (both, d, *J* = 21.5 Hz, 1.3H), 7.11 (minor, s, 0.3H), 6.85 (both, t, *J* = 5.3 Hz, 1.3H), 5.68 (major, d, *J* = 5.7 Hz, 1H), 5.53 (minor, s, 0.3H), 5.24 (major, d, *J* = 5.7 Hz, 1H), 5.10 (minor, s, 0.3H), 3.79 (major, s, 3H), 3.73 (minor, s, 0.9H), 2.46 (minor, s, 0.9H), 2.09 (major, s, 3H).^{13}C NMR (101 MHz, MeOD) δ171.62, 170.41, 166.10, 163.69, 145.01, 128.90, 127.03, 111.96, 111.72, 105.67, 105.36, 71.98, 69.75, 52.85, 23.64.HRMS [M + H]$^{+}$for $C_{12}H_{12}FNO_4$, calculated: 254.0823; found 254.0823.



(2R,3S)-N-acetyl-3-hydroxy-5-nitro-2-methoxycarbonyl-indoline (**2k**)

White solid,601 mg, 50%yield,ee: 97%, dr:>99:1; mp:135.15^{o}C; $[\alpha]_D^{20}$+71 (c = 2.0, DMSO).Enantiometric excess was determined by HPLC (DAICEL CHIRALPAK® OD-3(4.6x 150mm, 3μm), hexane/EtOH/TFA 70:30:0.1, flow rate 0.5 mL/min, t_{major} =9.78 min, t_{minor} =7.85 min, λ = 322 nm).

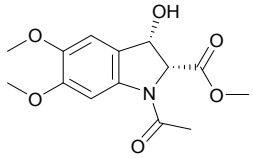
Compound **2k** has two rotamers in MeOH at ambient temperature.^{1}H NMR (400 MHz, MeOD) δ 8.51 - 8.07 (both, m, 3.5H), 7.50 (minor, s, 0.3H), 5.76 (both, s, 1.3H), 5.30 (both, s, 1.3H), 3.79 (both, s, 3.9H), 2.52 (minor, s, 0.9H), 2.15 (major, s, 3H).^{13}C NMR (101 MHz, DMSO-*d*^{6}) δ169.48, 168.49, 147.46, 143.10, 134.30, 125.91, 120.55, 115.49, 69.75, 67.45, 52.16, 23.56.HRMS [M + H]$^{+}$for $C_{12}H_{12}N_2O_6$, calculated: 281.0768; found 281.0782.



(2R, 3S)-N-acetyl-3-hydroxy-2-methoxycarbonyl-2,3-dihydro-1H-benzo[f]indole (**2l**)

White solid,1.12 g, 92%yield,ee: 97%, dr:>99:1; mp:215.64^{o}C; $[\alpha]_D^{20}$+16 (c = 2.0, DMSO).Enantiometric excess was determined by HPLC (DAICEL CHIRALPAK® OD-3(4.6 x 150mm, 3μm), hexane/EtOH/TFA 70:30:0.1, flow rate 0.5 mL/min, tmajor =9.74 min, tminor =8.61 min, λ = 254 nm).

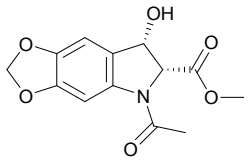
Compound **2l** has two rotamers in DMSO at ambient temperature.^{1}H NMR (400 MHz, DMSO-*d*^{6}) δ 8.50 (major, s, 1H), 8.04 -7.73 (both, m, 4.3H), 7.55-7.32 (both, m, 2.3H), 6.57 (major, d, *J* = 4.1 Hz, 1H), 6.41 (minor, s, 0.3H), 5.80 (major, s, 1H), 5.67 (minor, s, 0.3H), 5.33 (major, d, *J* = 8.7 Hz, 1H), 5.09 (minor, s, 0.3H), 3.66 (both, d, *J* = 34.5 Hz, 4H), 2.56 (minor, s, 1H), 2.12 (major, s, 3H).^{13}C NMR (101 MHz, DMSO-*d*^{6}) δ169.76, 169.37, 140.63, 134.48, 134.40, 130.86, 128.11, 126.78, 125.09, 124.15, 112.36, 70.84, 67.74, 52.53, 24.12.HRMS [M + H]$^{+}$for $C_{16}H_{15}NO_4$, calculated: 286.1074; found 286.1081.



(2R,3S)-N-acetyl-3-hydroxy-5,6-dimethoxy-2-methoxycarbonyl-indoline (2m)

White solid, 1.02 g, 81%yield,ee: >99%, dr:>99:1; mp: 160.05 °C; $[\alpha]_D^{20}$+82 (c = 2.0, DMSO).Enantiometric excess was determined by HPLC (DAICEL CHIRALPAK® OD-3 (4.6x 150mm, 3μm), hexane/EtOH/TFA 70:30:0.1, flow rate 0.5 mL/min, t_{major} = 7.77 min, t_{minor} = 6.30 min, λ = 254 nm).

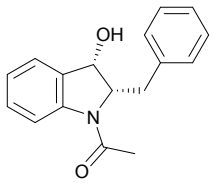
Compound **2m** has two rotamers in DMSO at ambient temperature.^{1}H NMR (400 MHz, DMSO-*d*^{6}) δ 7.83 (major, s, 1H), 7.14 (minor, s, 0.3H), 6.90 (both, d, *J* = 12.5 Hz, 1.4H), 6.23 (major, d, *J* = 4.0 Hz, 1H), 6.05 (minor, s, 0.3H), 5.60 (major, dd, *J* = 11.3, 5.6 Hz, 1H), 5.45 (minor, s, 0.3H), 5.23 (major, d, *J* = 6.0 Hz, 1H), 4.95 (minor, d, *J* = 5.8 Hz, 0.3H), 3.93 (minor, s, 0.8H), 3.81 (minor, s, 0.9H), 3.74 (major, d, *J* = 2.7 Hz, 6H), 3.69 (major, s, 3H), 3.59 (minor, s, 0.8H), 2.13 (minor, s, 0.8H), 1.99 (major, s, 3H).^{13}C NMR (101 MHz, DMSO-*d*^{6}) δ 169.08, 167.72, 149.04, 145.52, 136.08, 123.36, 108.41, 101.04, 70.64, 67.43, 55.87, 55.66, 51.88, 23.31.HRMS [M + H]$^+$for $C_{14}H_{17}NO_6$, calculated: 296.1129; found 296.1133.



(6R,7S)-N-acetyl-7-hydroxy-6-methoxycarbonyl-6,7-dihydro-5H-[1,3]dioxolo[4,5-f]indole (2n)

Colorless oil,0.99g, 83%yield,ee: >99%, dr:>99:1; $[\alpha]_D^{20}$+73 (c = 2.0, DMSO).Enantiometric excess was determined by HPLC (DAICEL CHIRALPAK® OD-3(4.6x 150mm, 3μm), hexane/EtOH/TFA 70:30:0.1, flow rate 0.5 mL/min, t_{major} =10.13 min, t_{minor} =7.82 min, λ = 254 nm).

Compound **2n** has two rotamers in DMSO at ambient temperature.^{1}H NMR (400 MHz, DMSO-*d*^{6}) δ 7.68 (major, s, 1H), 6.99 (minor, s, 0.2H), 6.80 (both, s, 1.2H), 6.25 (major, d, *J* = 4.8 Hz, 1H), 6.01 (both, s, 2.6H), 5.53 (major, s, 1H), 5.40 (minor, s, 0.2H), 5.23 (major, d, *J* = 9.1 Hz, 1H), 4.96 (minor, s, 0.2H), 3.69 (major, s, 3H), 3.59 (minor, s, 0.6H), 2.35 (minor, s, 0.6H), 1.97 (major, s, 3H).^{13}C NMR (101 MHz, DMSO-*d*^{6}) δ 169.06, 167.91, 147.51, 143.56, 136.81, 124.95, 104.94, 101.45, 98.15, 70.36, 67.65, 52.00, 23.33.HRMS [M + H]$^+$for $C_{13}H_{13}NO_6$, calculated: 280.0816; found 280.0825.

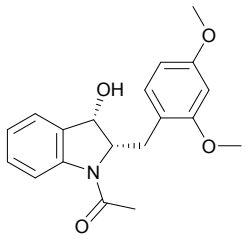


1-((2S,3S)-2-benzyl-3-hydroxyindolin-1-yl)ethanone (2o)

Yellow solid, 1.10g, 96%yield,ee: -96%, dr:>99:1; mp: 106.79°C; $[\alpha]_D^{20}$-89 (c = 2.0, DMSO).Enantiometric excess was determined by HPLC (DAICEL CHIRALPAK® OD-3(4.6x 150mm, 3μm), hexane/EtOH/TFA 70:30:0.1, flow rate 0.5 mL/min, t_{major} =4.89 min, t_{minor} =5.65 min, λ = 254 nm).

^{1}H NMR (400 MHz, MeOD) δ 8.01 (d, *J* = 45.4 Hz, 1H), 7.38 (d, *J* = 7.3 Hz, 1H), 7.33-7.02 (m, 7H),

5.56 (d, *J* = 6.2 Hz, 1H), 4.57 (s, 1H), 3.15 (d, *J* = 13.6 Hz, 1H), 2.57 (s, 1H), 1.35 (s, 3H). ^{13}C NMR (101 MHz, CD_3OD) δ 171.55, 164.36, 141.49, 139.69, 136.13, 131.03, 129.41, 127.59, 125.81, 124.96, 119.59, 73.89, 68.85, 35.04, 22.68.HRMS [M + H]$^+$for $C_{17}H_{17}NO_2$, calculated: 268.1332; found 268.1340.



1-((2S,3S)-2-(2,4-dimethoxybenzyl)-3-hydroxyindolin-1-yl)ethanone (2p)

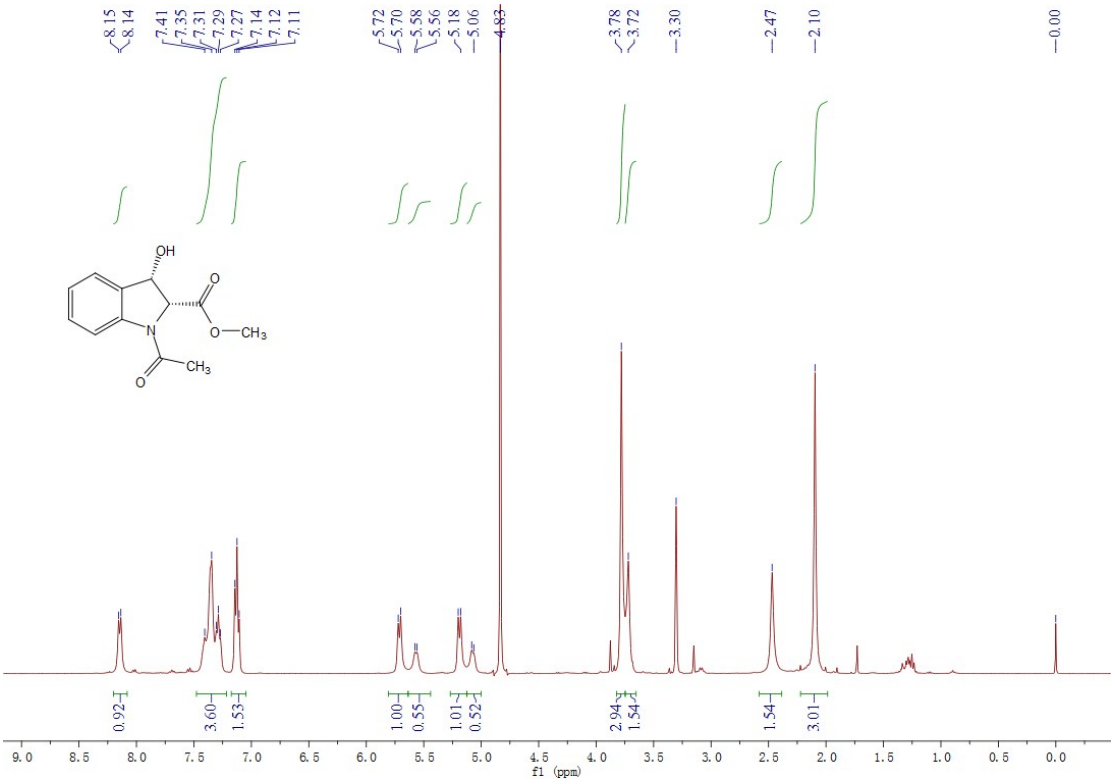
Yellow solid, 1.3g, 94%yield,ee: -99%, dr:>99:1; mp: 141.44°C; $[\alpha]_D^{20}$-145 (c = 2.0, DMSO).Enantiometric excess was determined by HPLC (DAICEL CHIRALPAK® OD-3(4.6x 150mm, 3μm), hexane/EtOH/TFA 70:30:0.1, flow rate 0.5 mL/min, t_{major} =5.07 min, t_{minor} =6.21 min, λ = 254 nm).

^{1}H NMR (400 MHz, MeOD) δ 8.00 (d, *J* = 55.4 Hz, 1H), 7.37 (d, *J* = 7.3 Hz, 1H), 7.24 (t, *J* = 7.7 Hz, 1H), 7.13 (t, *J* = 7.4 Hz, 1H), 6.80 (d, *J* = 8.2 Hz, 1H), 6.47 (s, 1H), 6.39 (d, *J* = 8.2 Hz, 1H), 5.53 (d, *J* = 7.0 Hz, 1H), 4.61 (s, 1H), 3.75 (d, *J* = 8.3 Hz, 6H), 3.16 (dd, *J* = 13.9, 3.3 Hz, 1H), 2.44 (dd, *J* = 13.8, 10.6 Hz, 1H), 1.46 (s, 3H).^{13}C NMR (101 MHz, CD_3OD) δ171.50, 161.75, 160.20, 141.78, 136.15, 133.17, 129.25, 124.78, 119.62, 119.45, 105.48, 99.14, 73.99, 67.30, 55.78, 55.77, 29.07, 22.36.HRMS [M + H]$^+$for $C_{19}H_{21}NO_4$, calculated: 328.1543; found 327.1553.

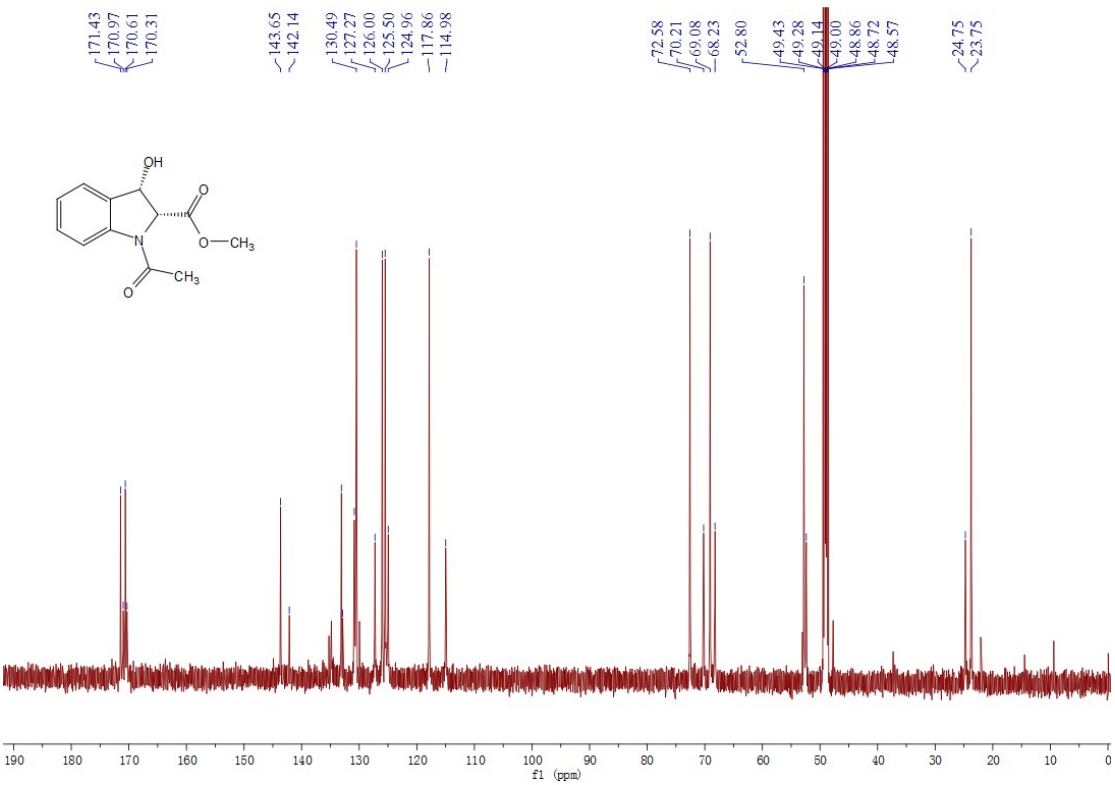
4. NMR Spectra for 2a~2p.

(2R,3S)-methyl 1-acetyl-3-hydroxyindoline-2-carboxylate, 2a

^{1}H NMR (400 MHz, MeOD)

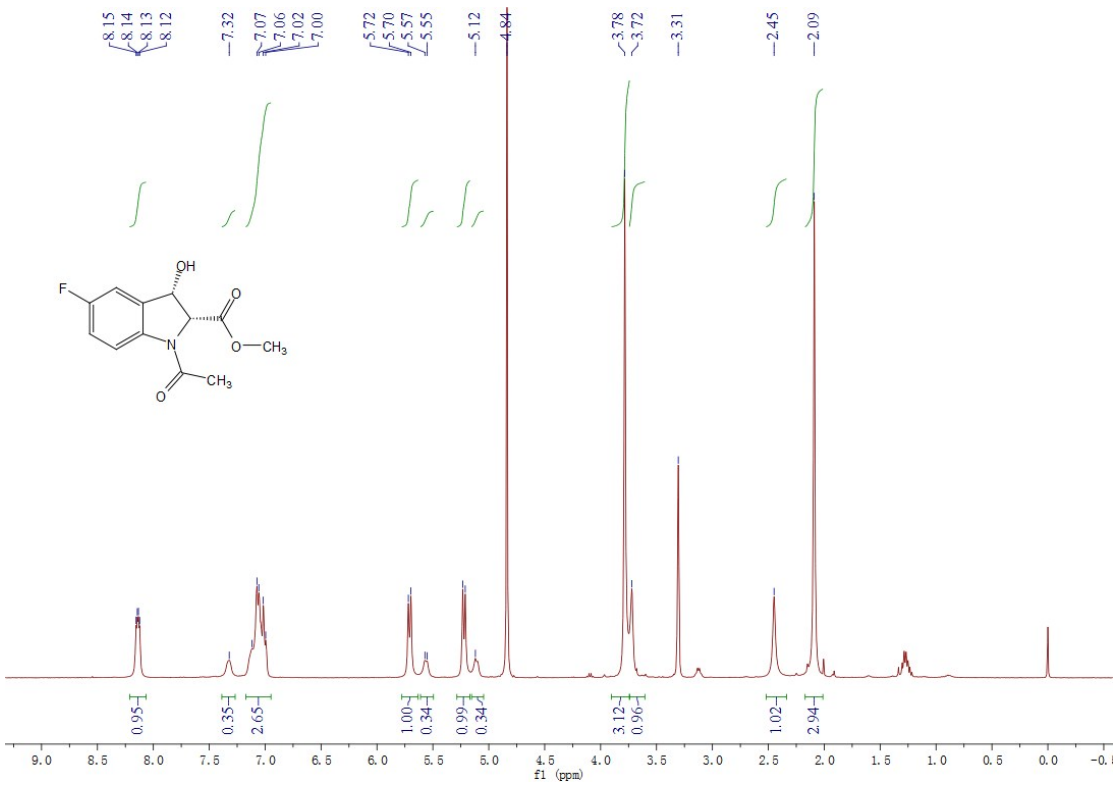


^{13}C NMR (101 MHz, MeOD)

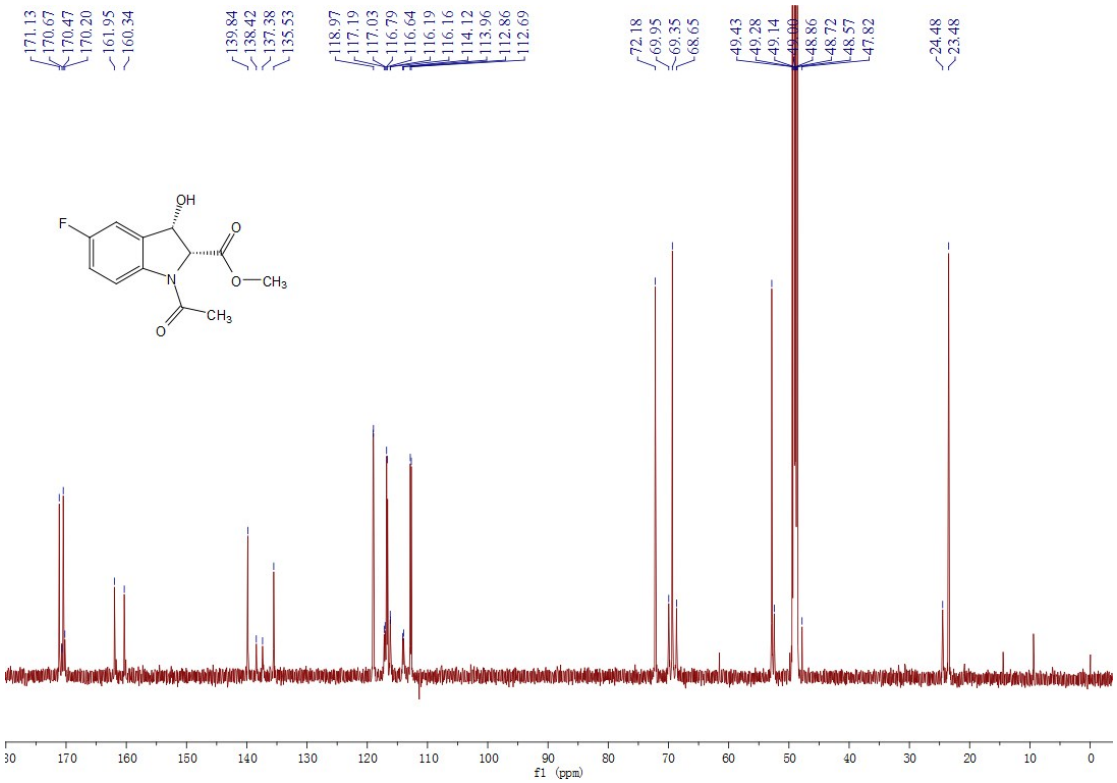


(2R,3S)-methyl 1-acetyl-5-fluoro-3-hydroxyindoline-2-carboxylate, 2b

^{1}H NMR (400 MHz, MeOD)

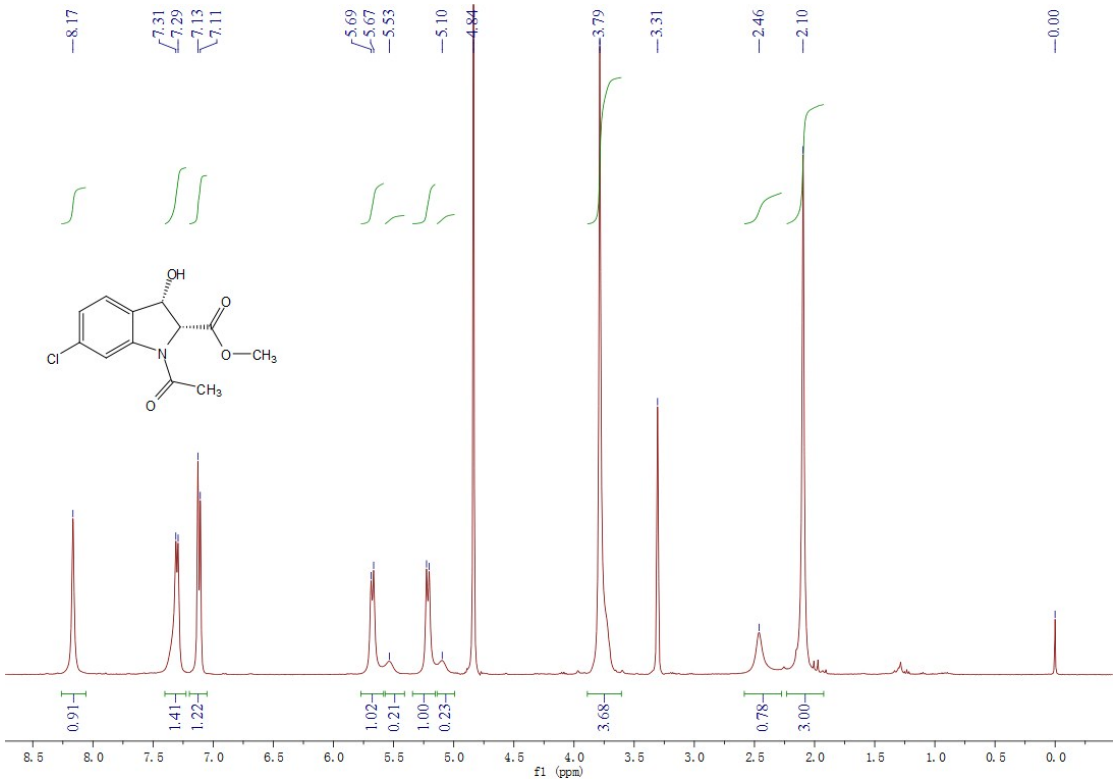


^{13}C NMR (101 MHz, MeOD)

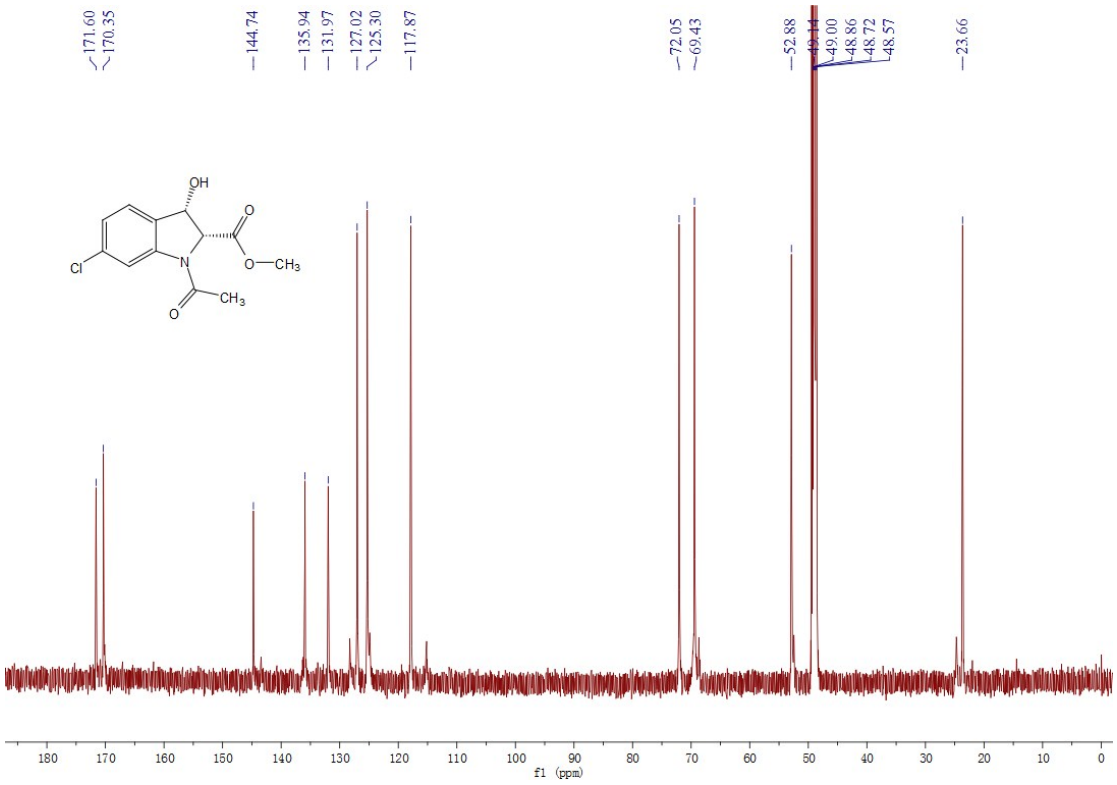


(2R,3S)-methyl 1-acetyl-6-chloro-3-hydroxyindoline-2-carboxylate, 2c

^{1}H NMR (400 MHz, MeOD)

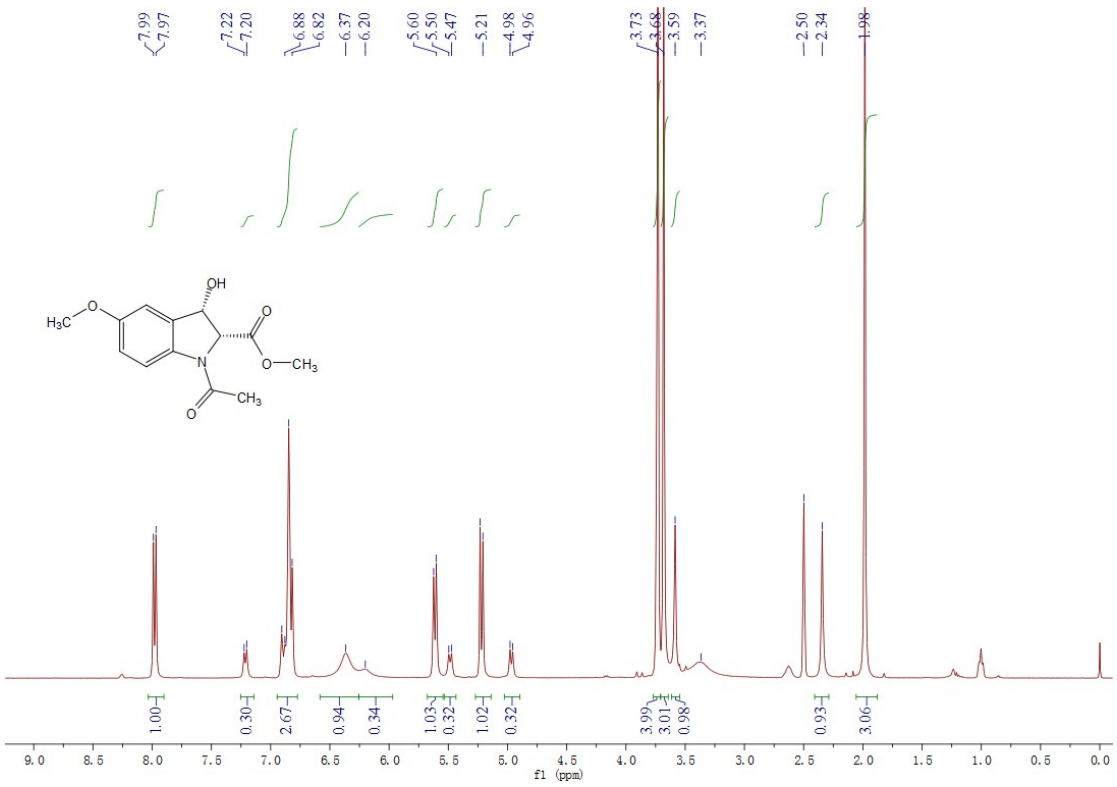


^{13}C NMR (101 MHz, MeOD)

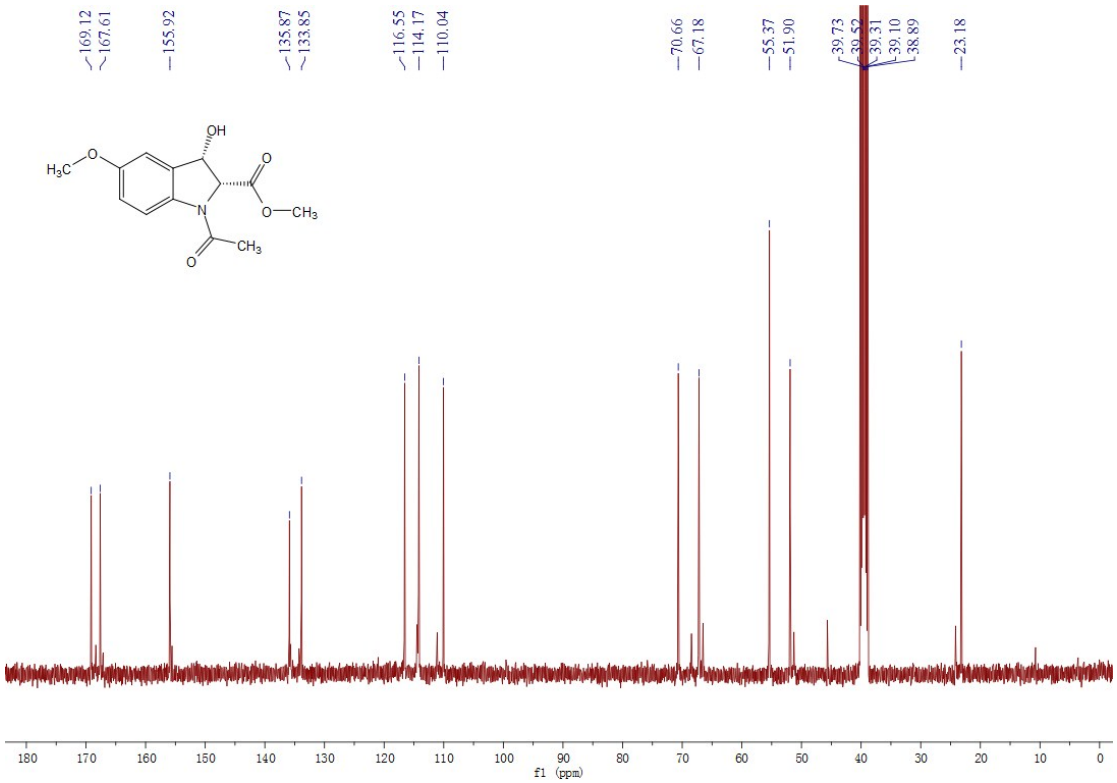


(2R,3S)-methyl 1-acetyl-3-hydroxy-5-methoxyindoline-2-carboxylate, 2d

^{1}H NMR (400 MHz, DMSO-*d*^{6})

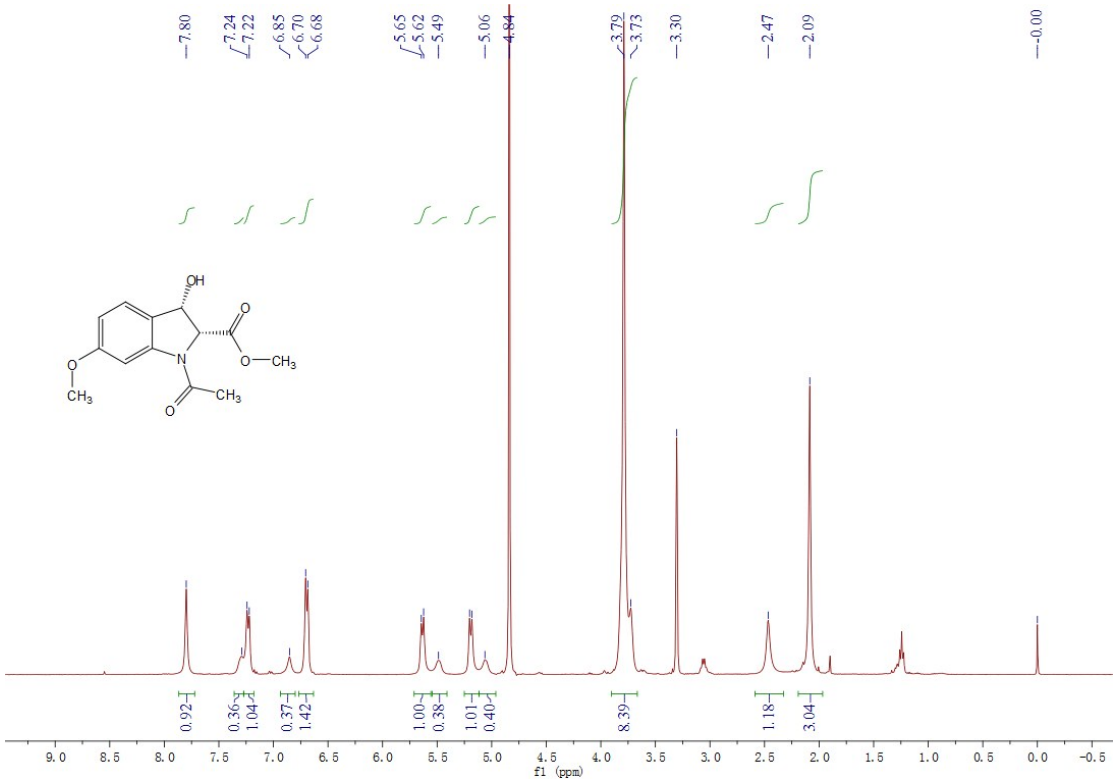


^{13}C NMR (101 MHz, DMSO-*d*^{6})

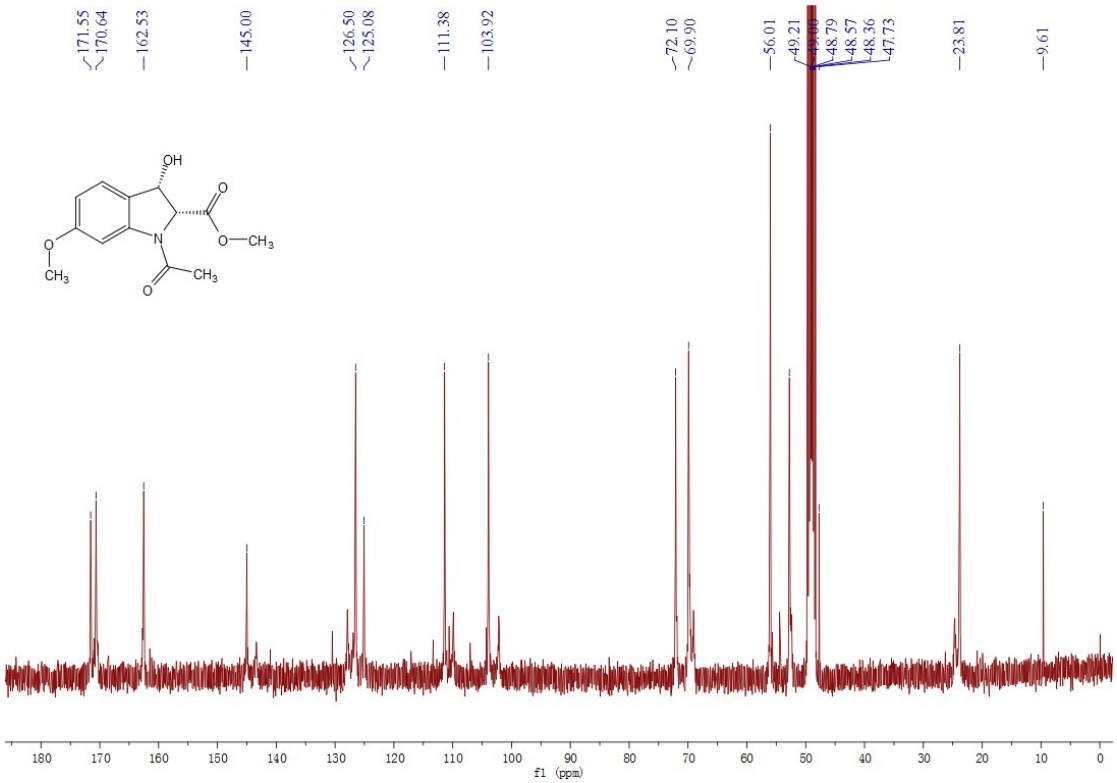


(2R,3S)-methyl 1-acetyl-3-hydroxy-6-methoxyindoline-2-carboxylate, 2e

^{1}H NMR (400 MHz, MeOD)

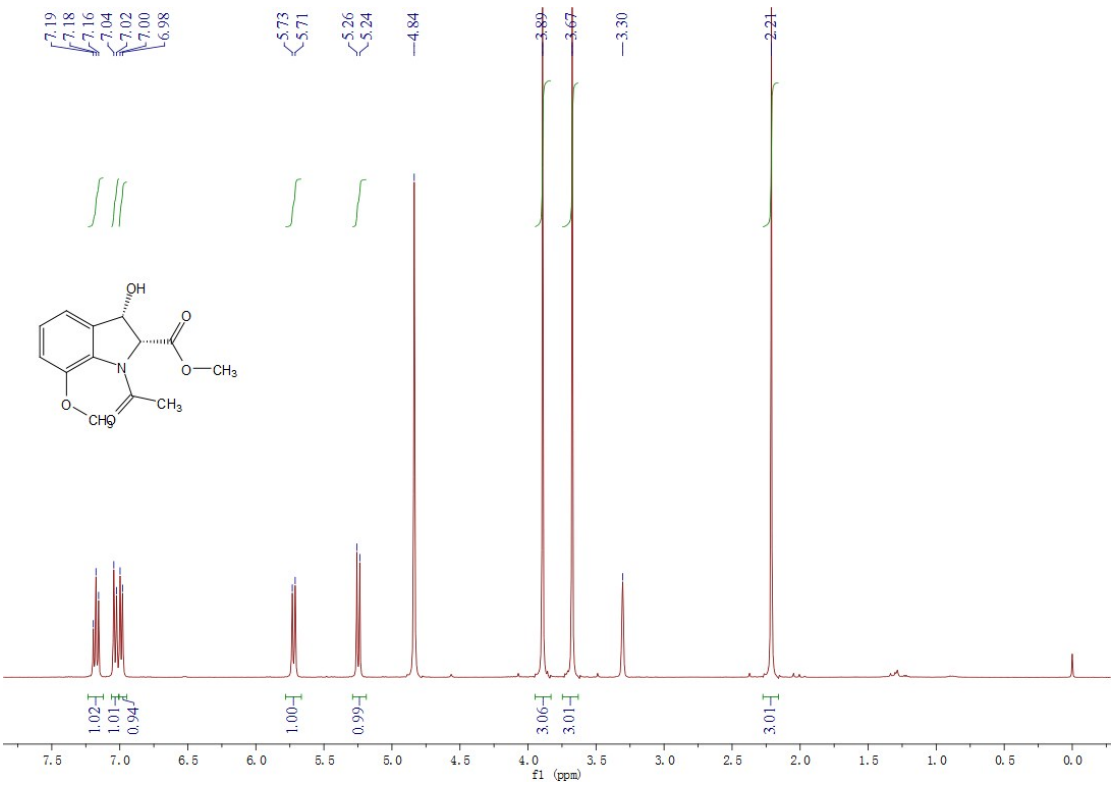


^{13}C NMR (101 MHz, MeOD)

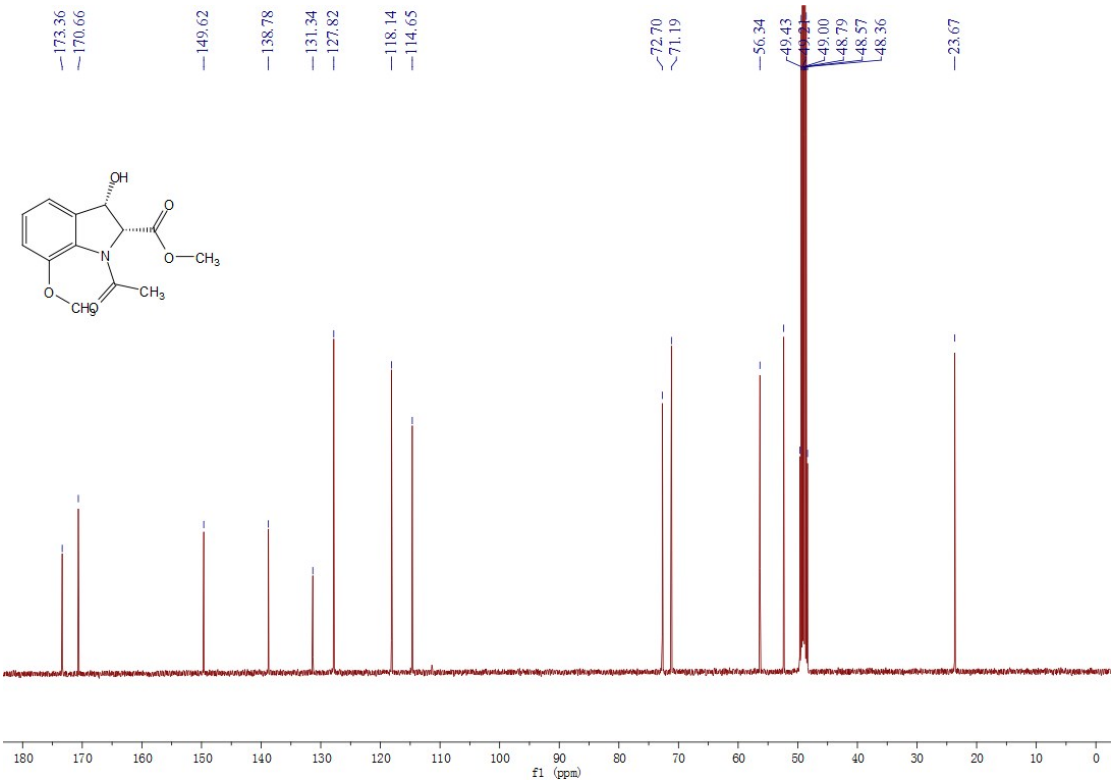


(2R,3S)-methyl 1-acetyl-3-hydroxy-7-methoxyindoline-2-carboxylate, 2f

^{1}H NMR (400 MHz, MeOD)

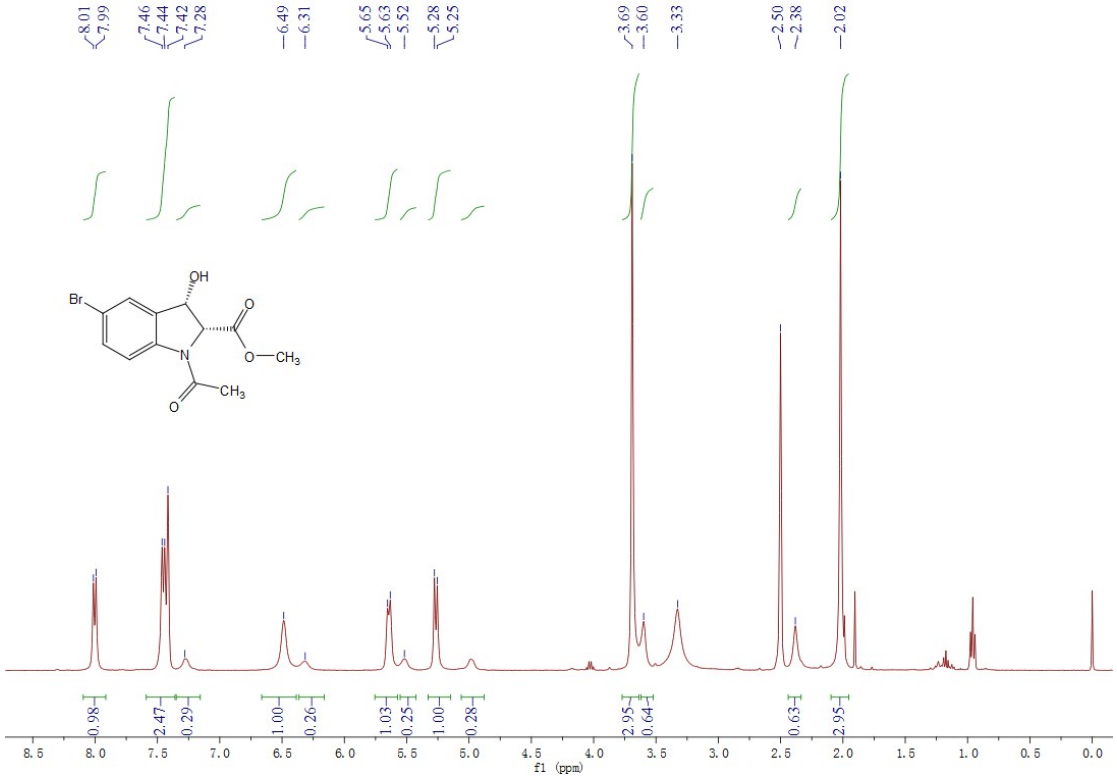


^{13}C NMR (101 MHz, MeOD)

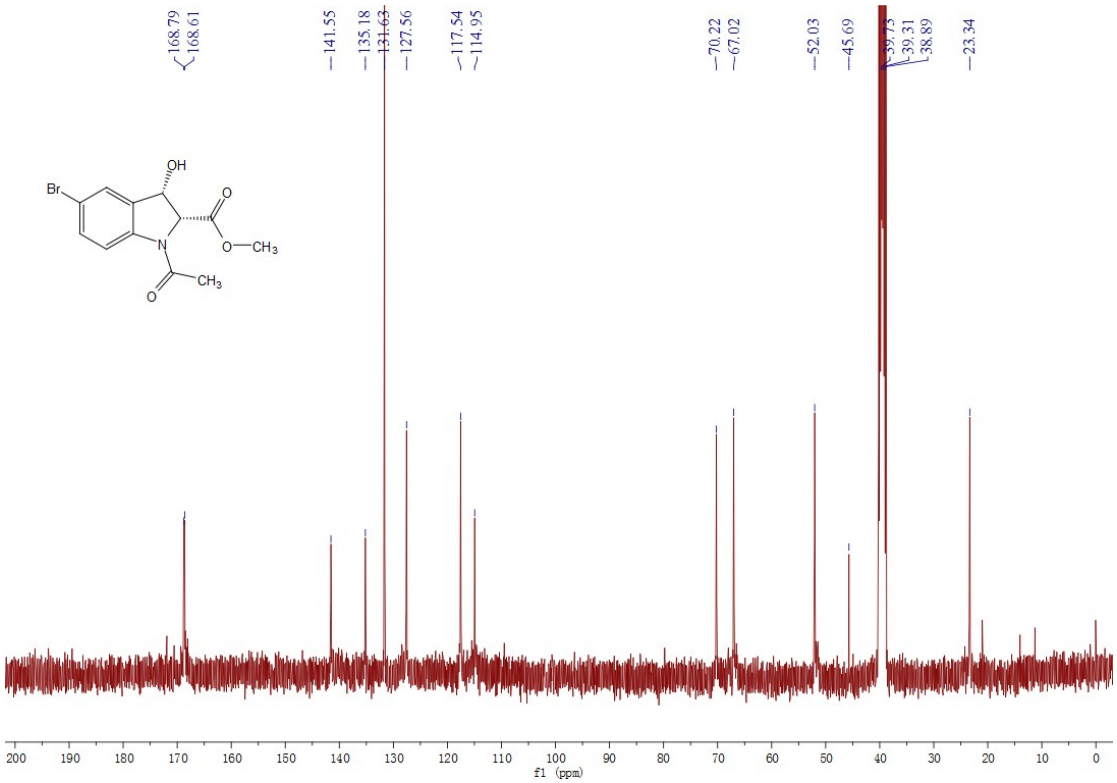


(2R,3S)-methyl 1-acetyl-5-bromo-3-hydroxyindoline-2-carboxylate, 2g

^{1}H NMR (400 MHz, DMSO-d^{6})

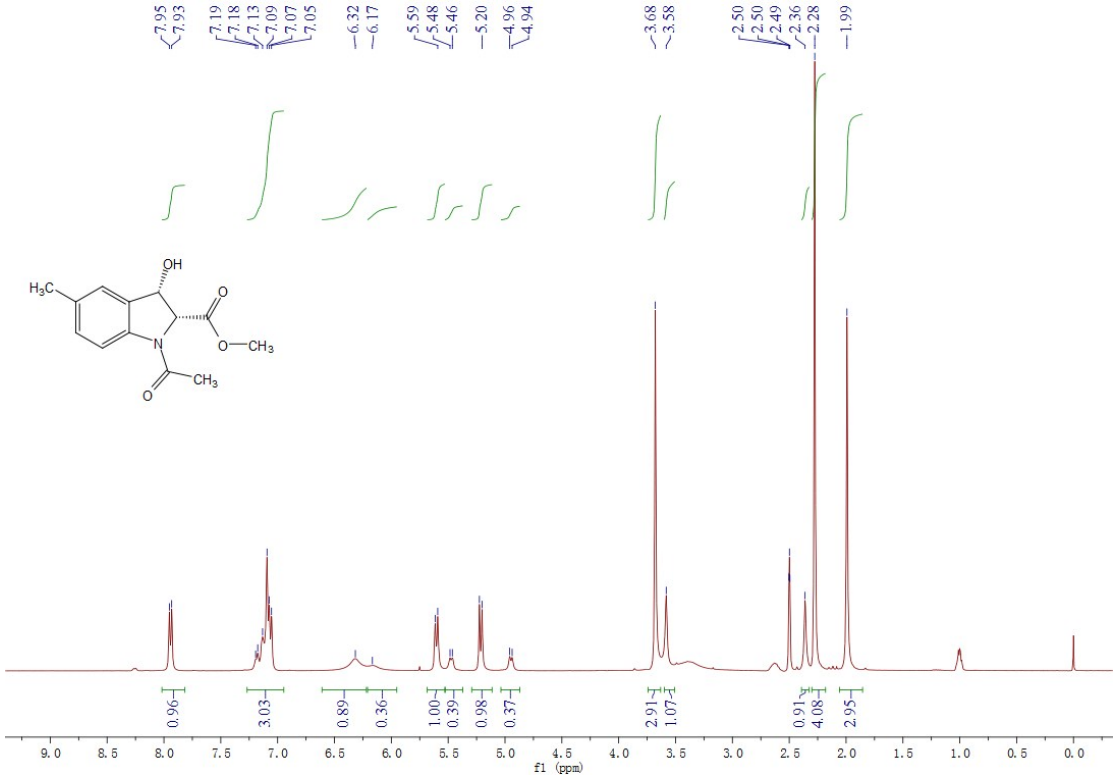


^{13}C NMR (101 MHz, DMSO-d^{6})

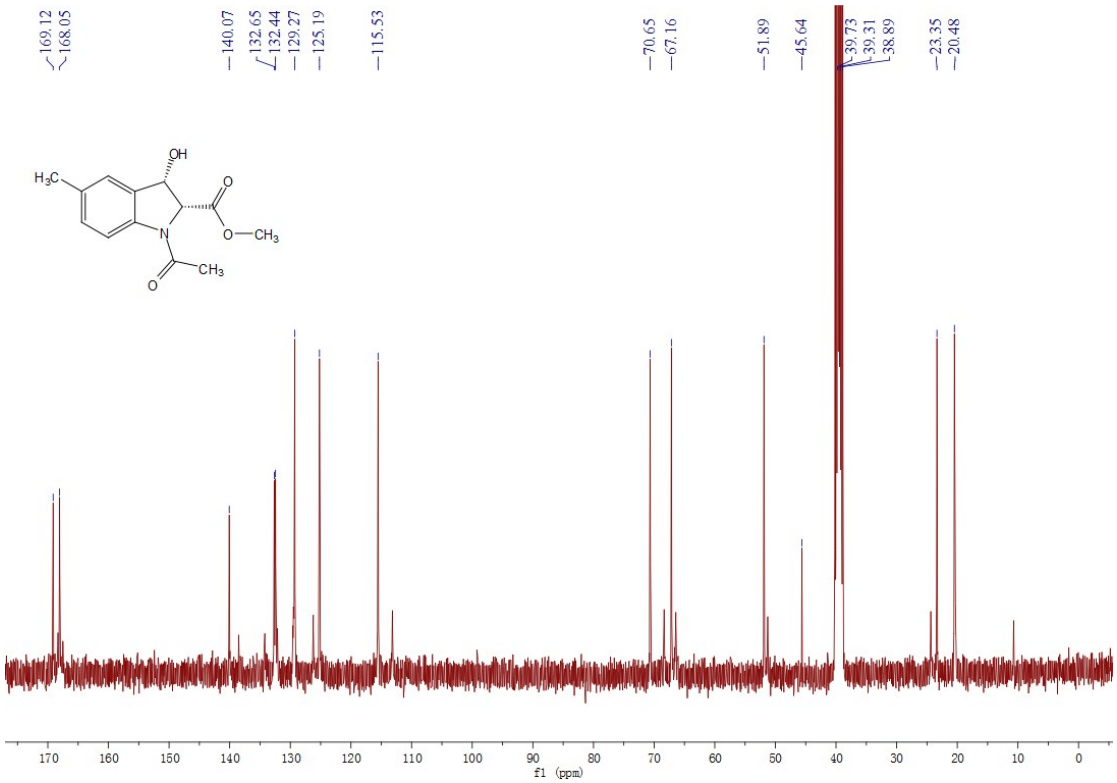


(2R,3S)-methyl 1-acetyl-3-hydroxy-5-methylindoline-2-carboxylate, 2h

^{1}H NMR (400 MHz, DMSO-d^{6})

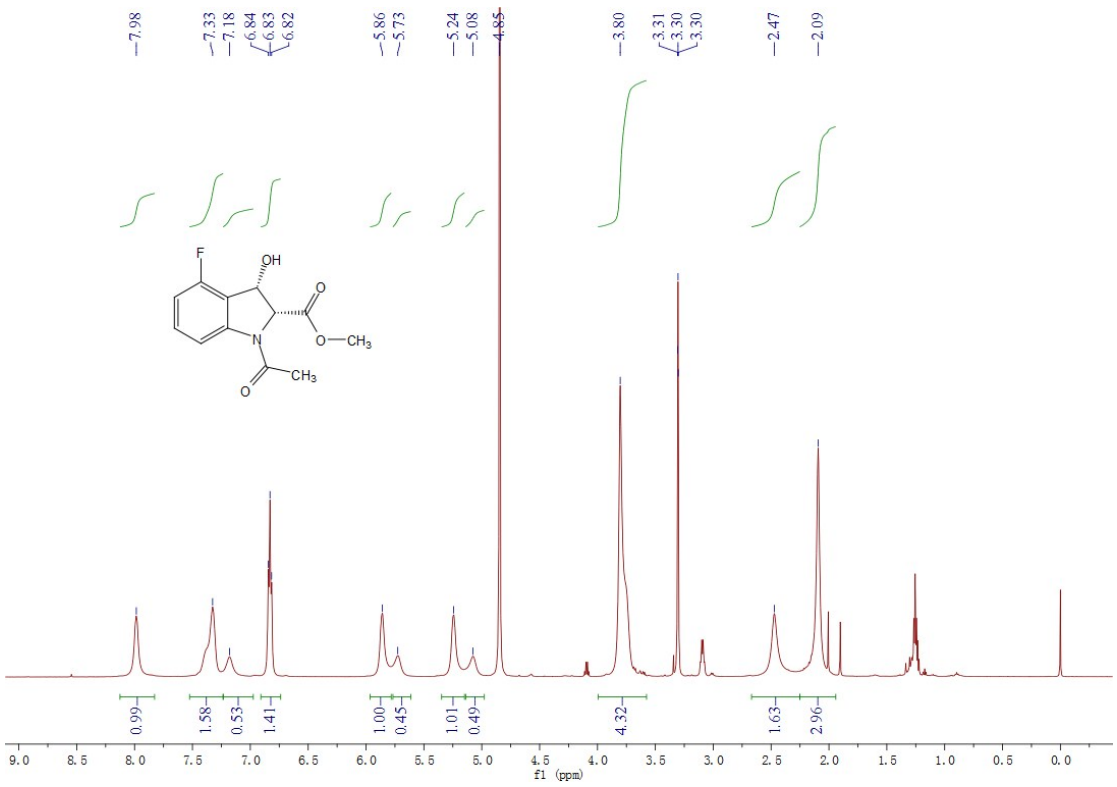


^{13}C NMR (101 MHz, DMSO-d^{6})

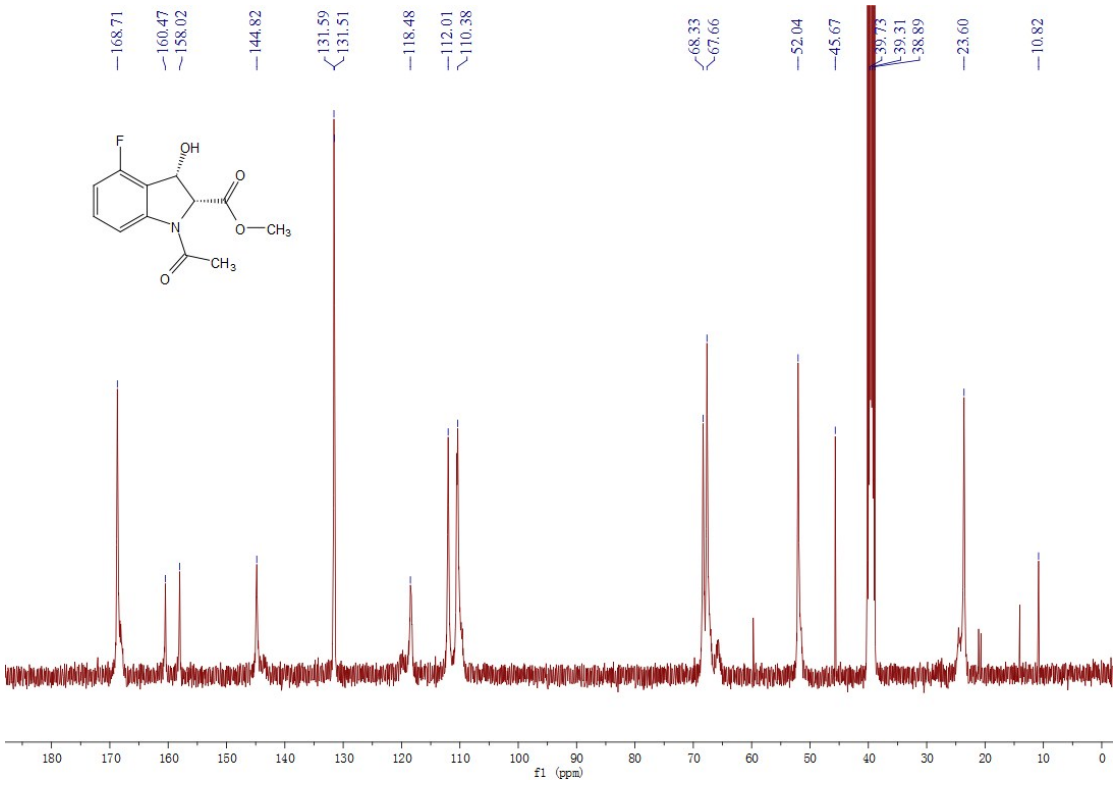


(2R,3S)-methyl 1-acetyl-4-fluoro-3-hydroxyindoline-2-carboxylate, 2i

^{1}H NMR (400 MHz, MeOD)

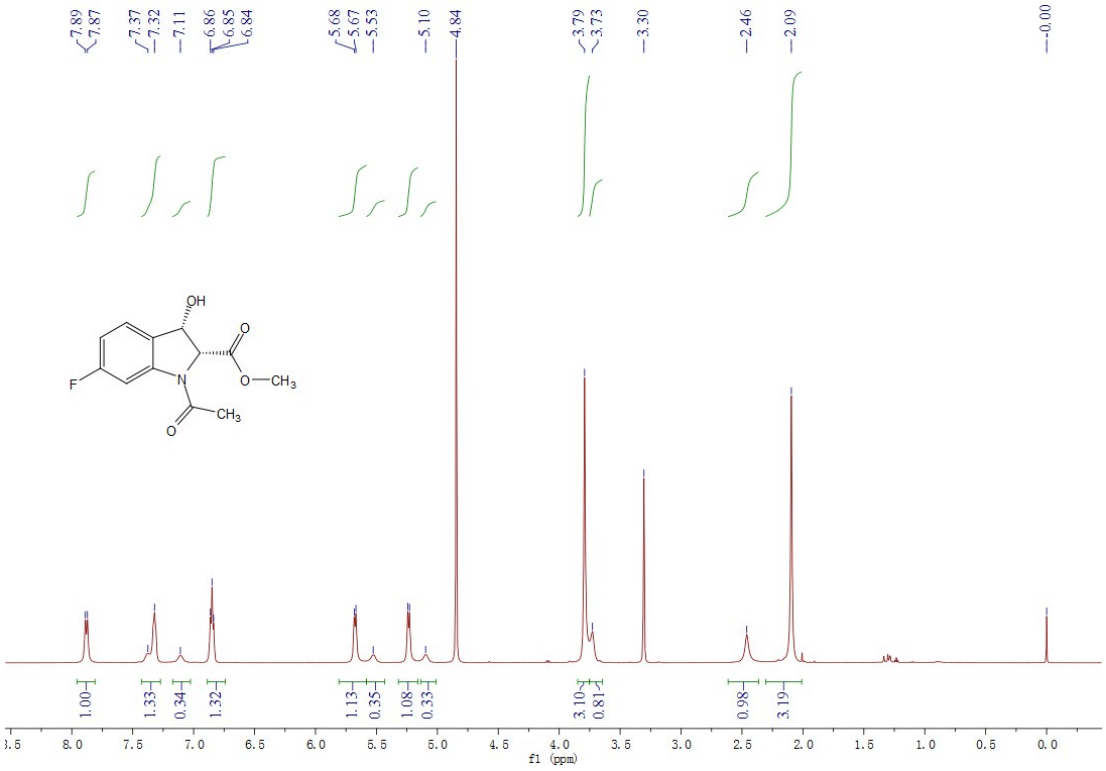


^{13}C NMR (101 MHz, DMSO-*d*^{6})

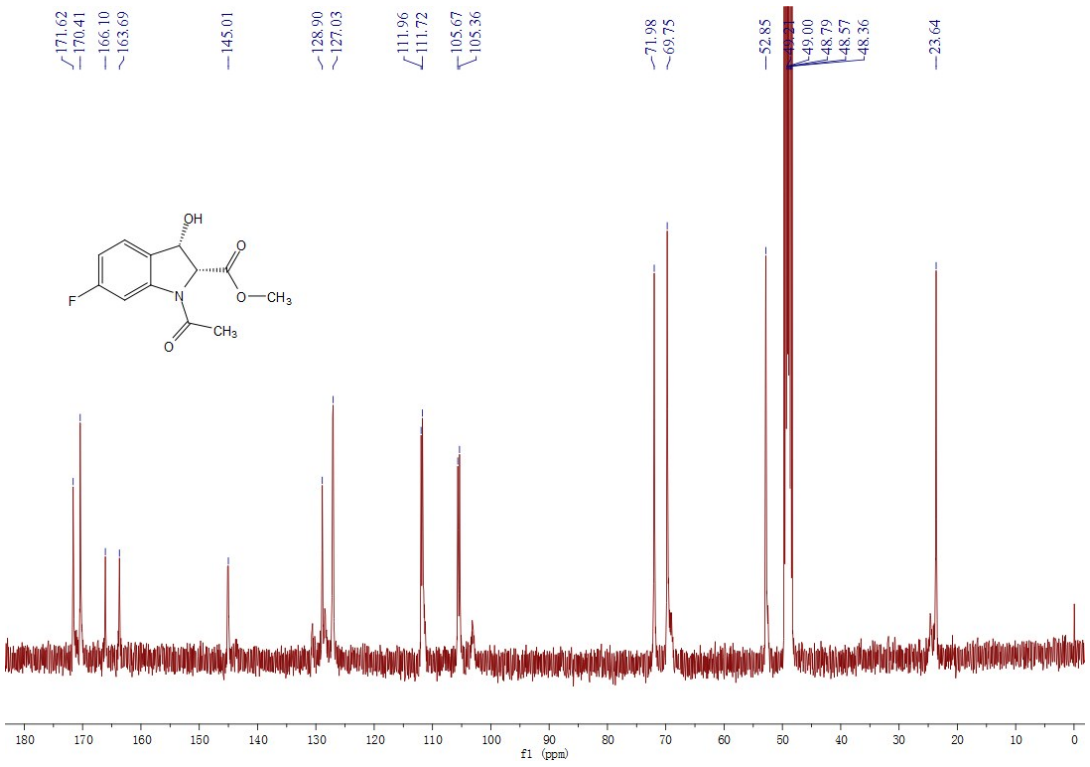


(2R,3S)-methyl 1-acetyl-6-fluoro-3-hydroxyindoline-2-carboxylate, 2j

^{1}H NMR (400 MHz, MeOD)

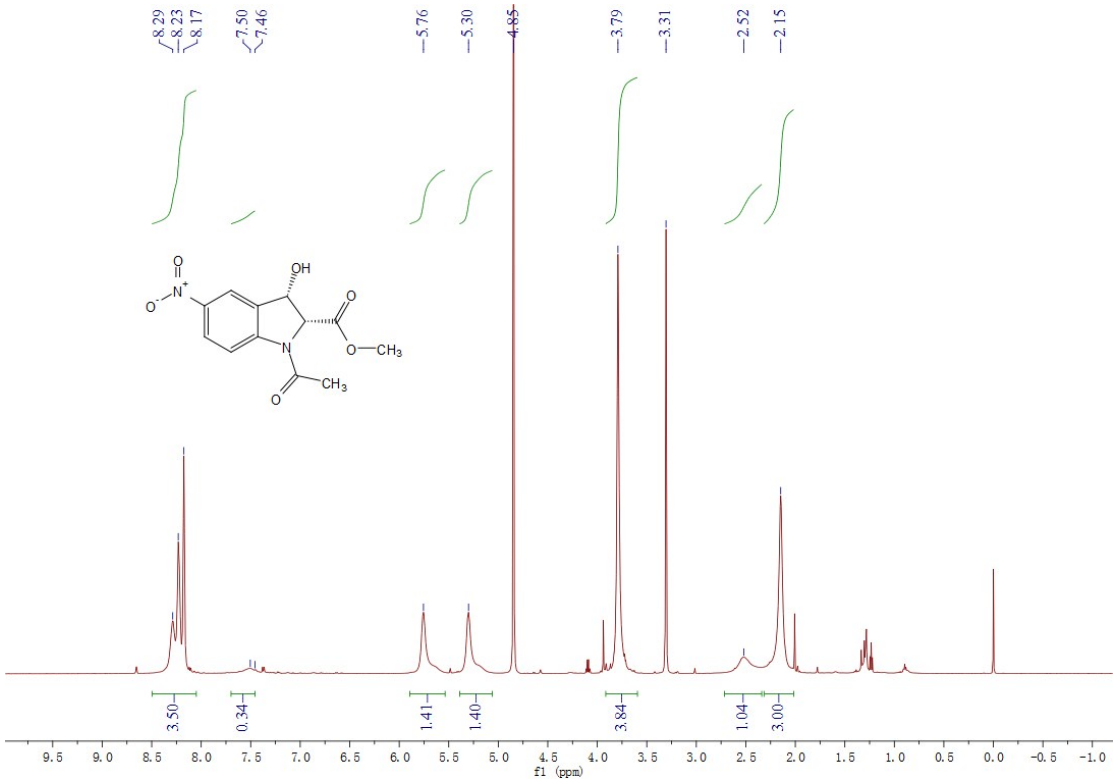


^{13}C NMR (101 MHz, MeOD)

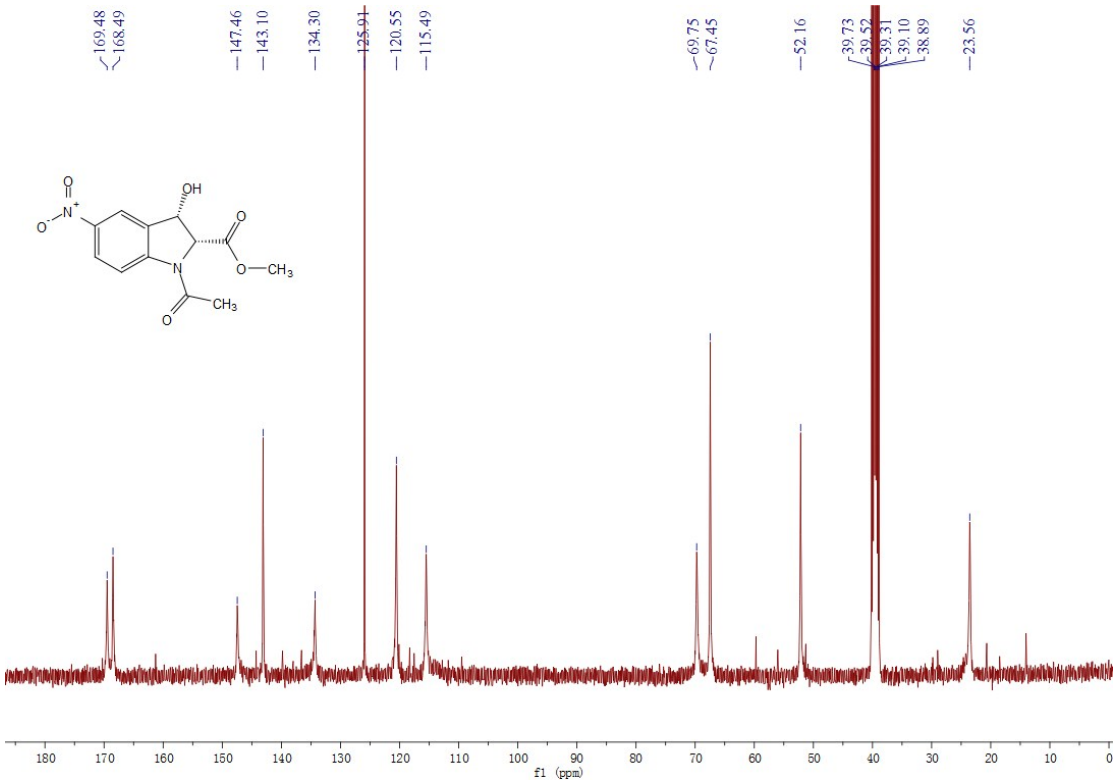


(2R,3S)-methyl 1-acetyl-3-hydroxy-5-nitroindoline-2-carboxylate, 2k

^{1}H NMR (400 MHz, MeOD)

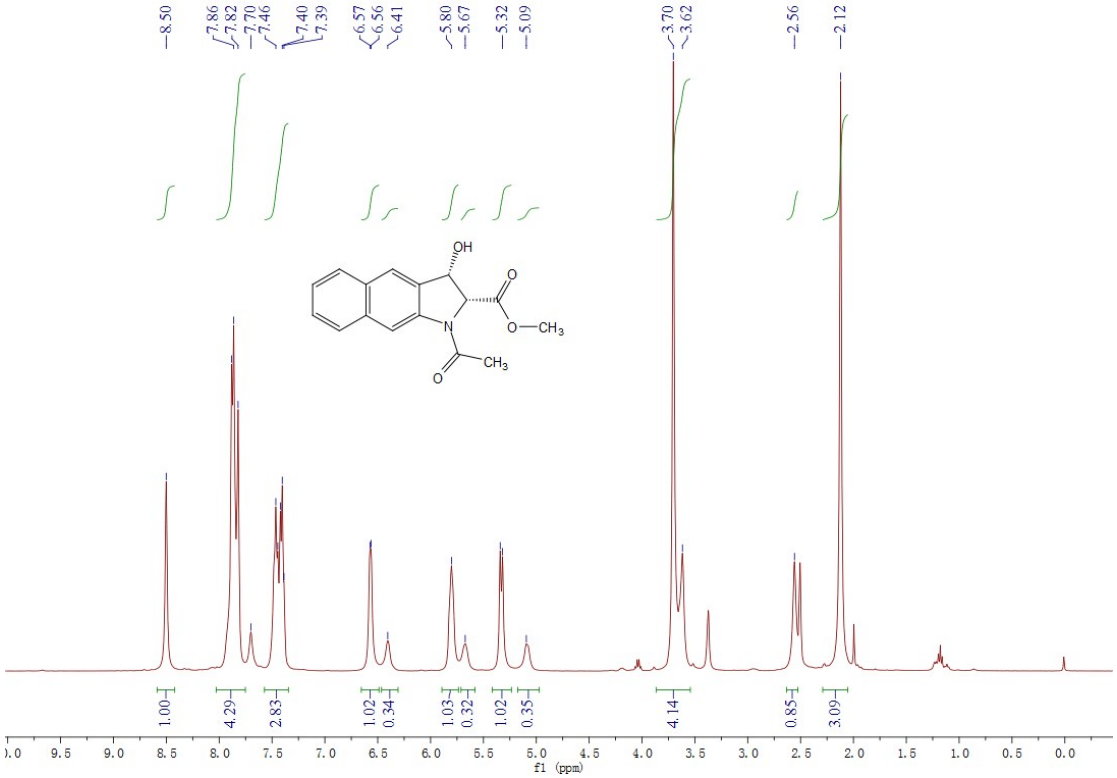


^{13}C NMR (101 MHz, DMSO-*d*^{6})

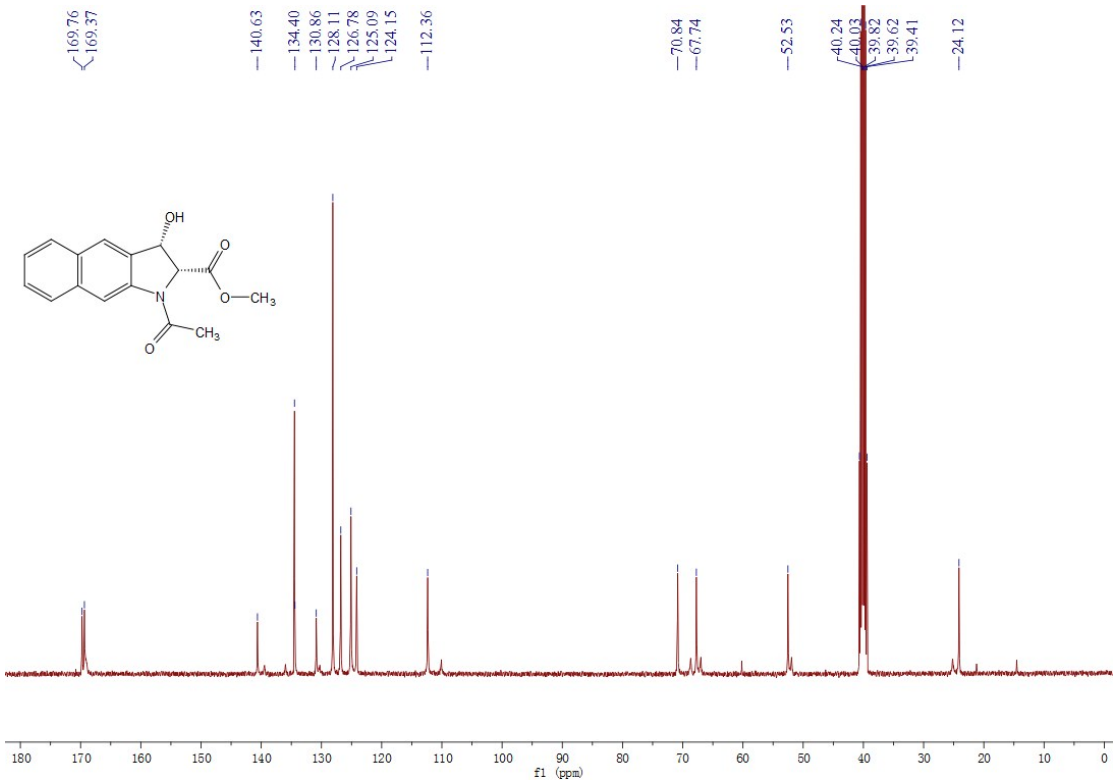


(2R,3S)-methyl 1-acetyl-3-hydroxy-2,3-dihydro-1H-benzo[f]indole-2-carboxylate, 2l

^{1}H NMR (400 MHz, DMSO-*d*^{6})

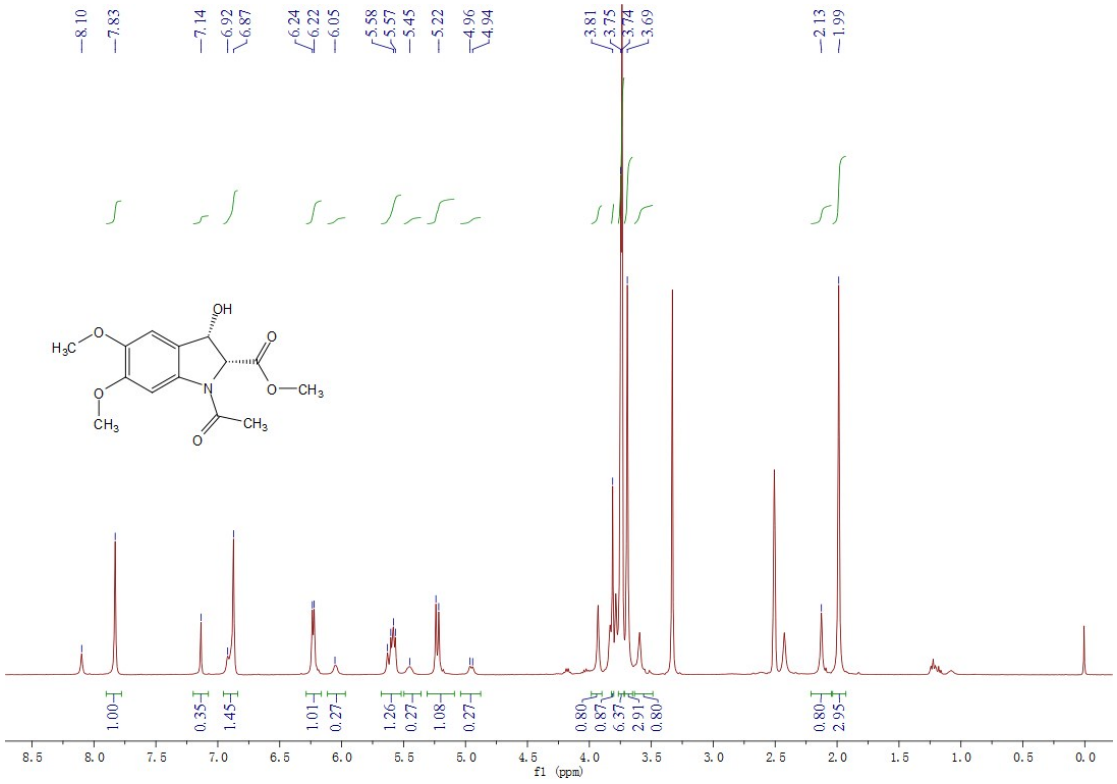


^{13}C NMR (101 MHz, DMSO-*d*^{6})

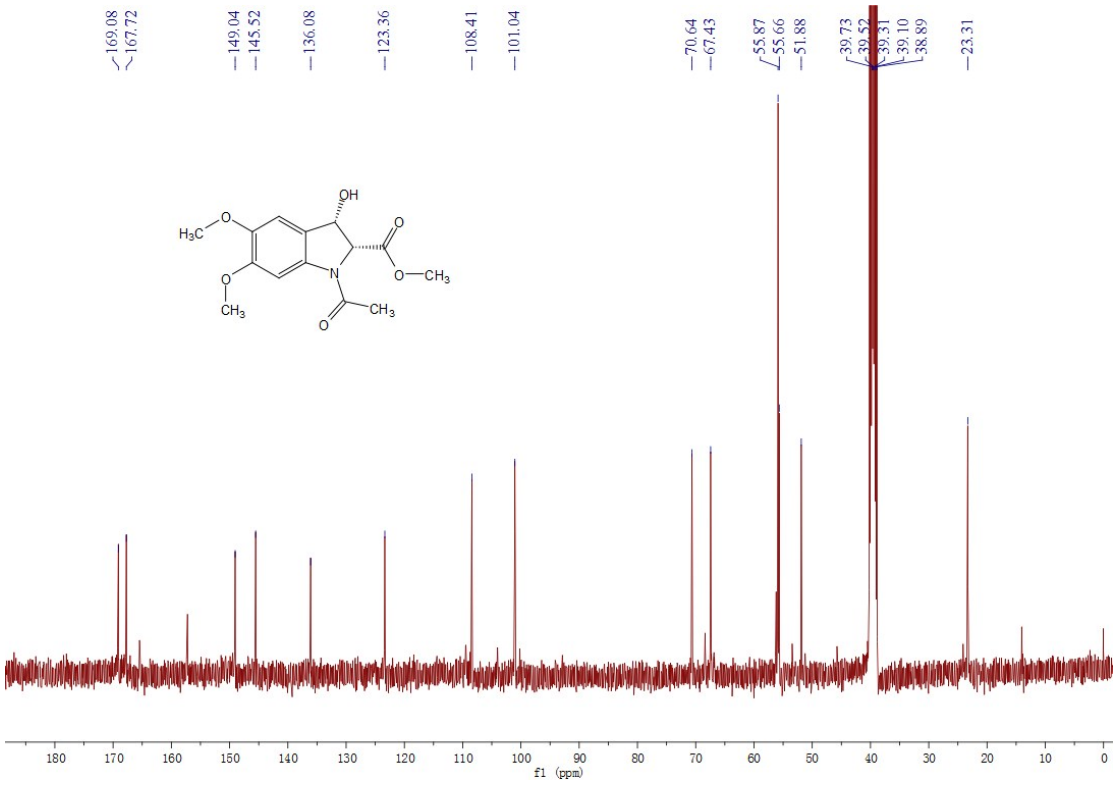


(2R,3S)-methyl 1-acetyl-3-hydroxy-5,6-dimethoxyindoline-2-carboxylate, 2m

^{1}H NMR (400 MHz, DMSO-d^{6})

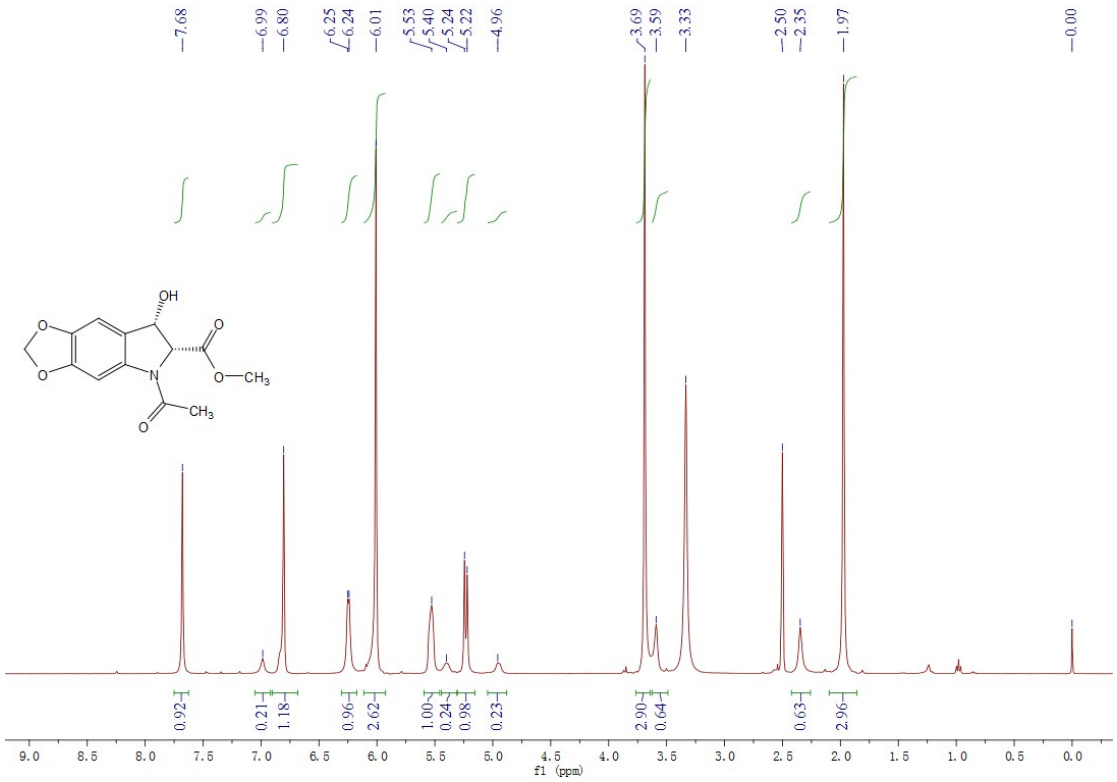


^{13}C NMR (101 MHz, DMSO-d^{6})

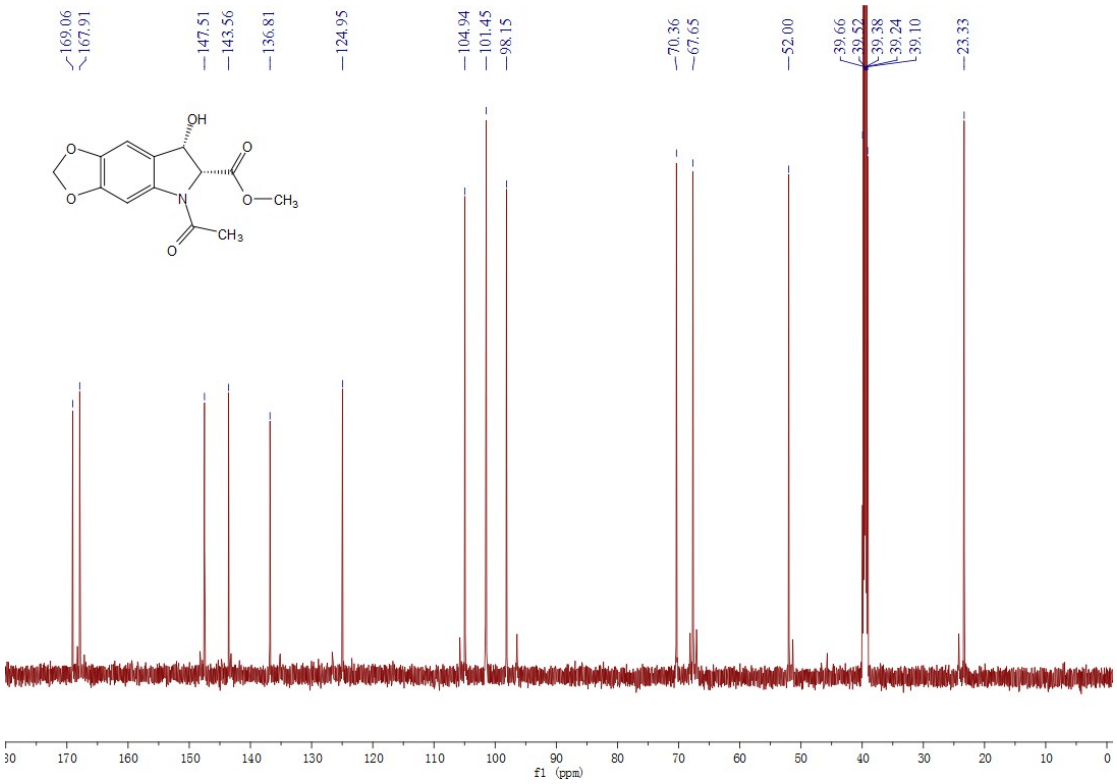


(6R,7S)-methyl 5-acetyl-7-hydroxy-6,7-dihydro-5H-[1,3]dioxolo[4,5-f]indole-6-carboxylate, 2n

^{1}H NMR (400 MHz, DMSO-d^{6})

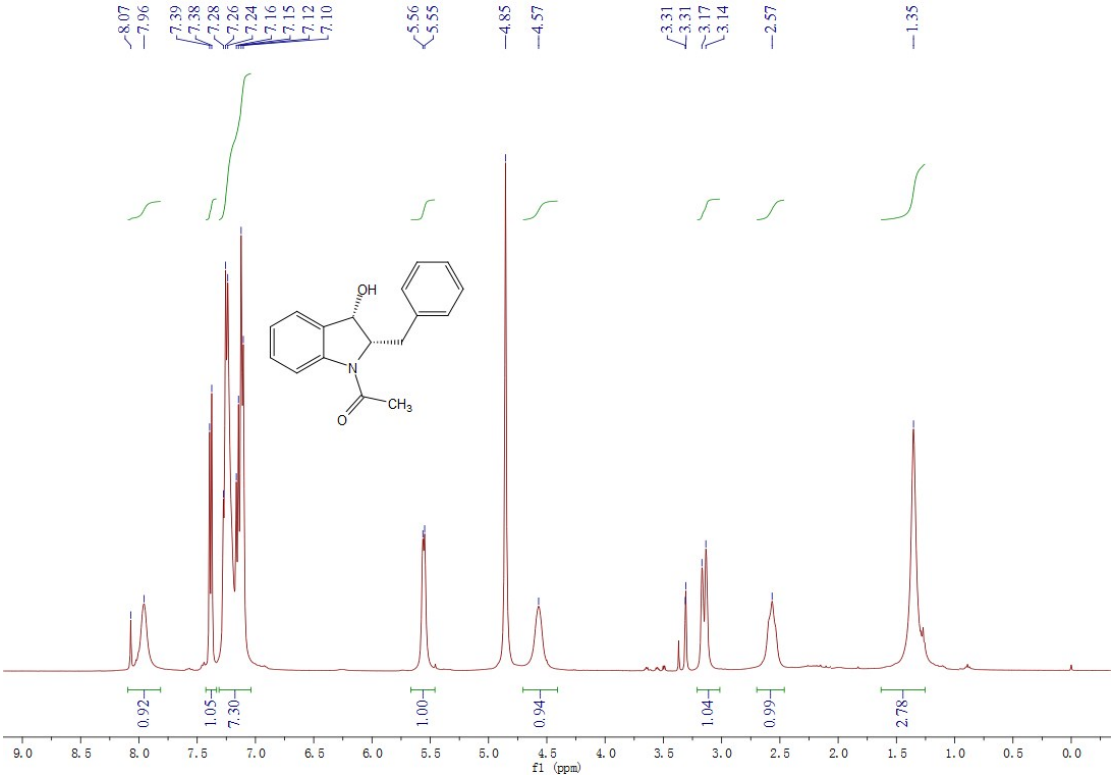


^{13}C NMR (101 MHz, DMSO-d^{6})

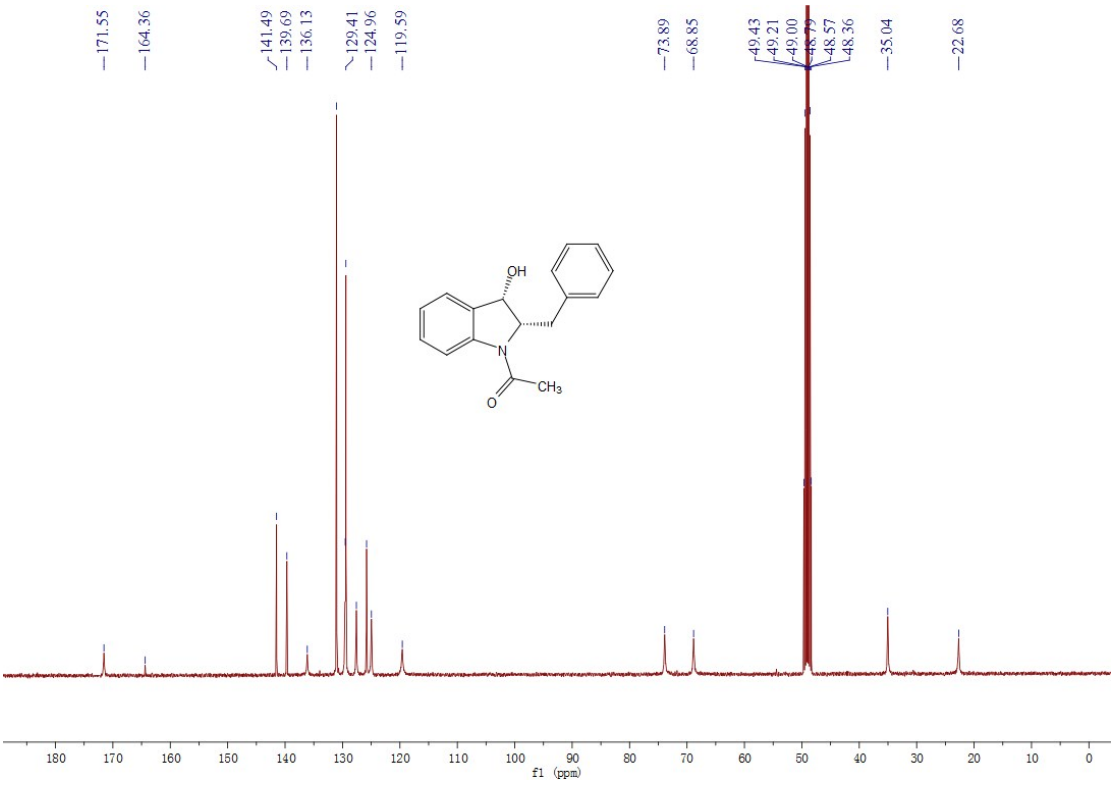


1-((2S,3S)-2-benzyl-3-hydroxyindolin-1-yl)ethanone, 2o

^{1}H NMR (400 MHz, MeOD)

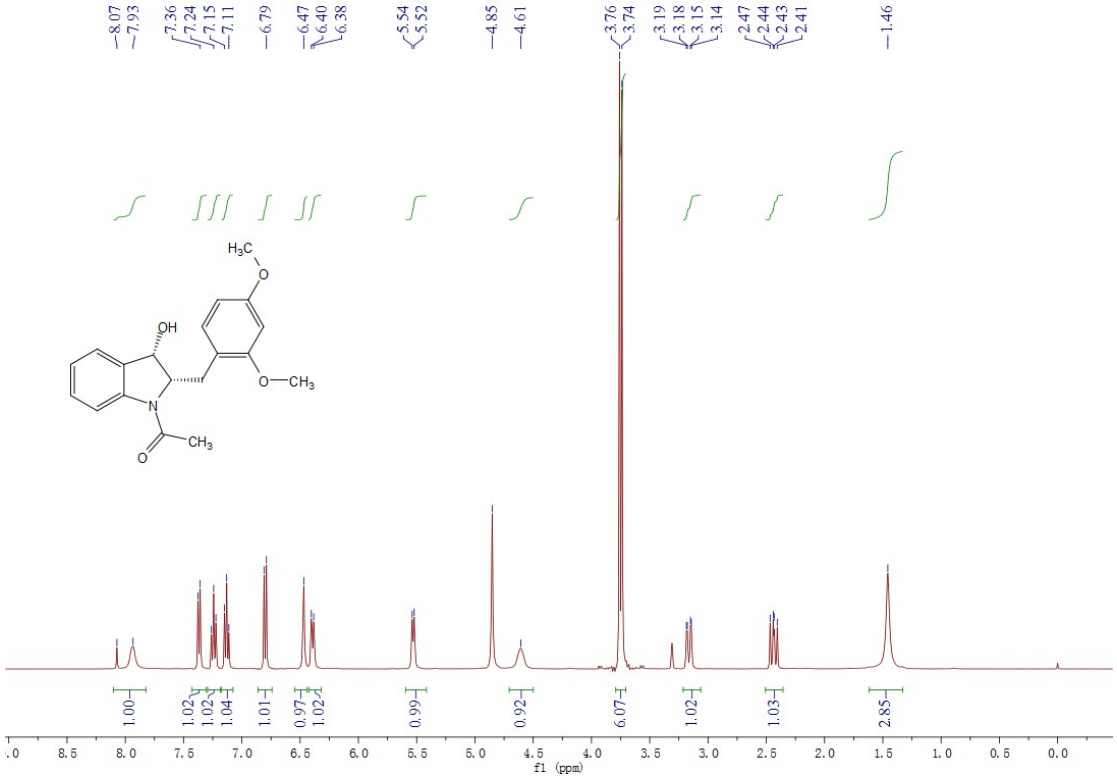


^{13}C NMR (101 MHz, CD_3OD)

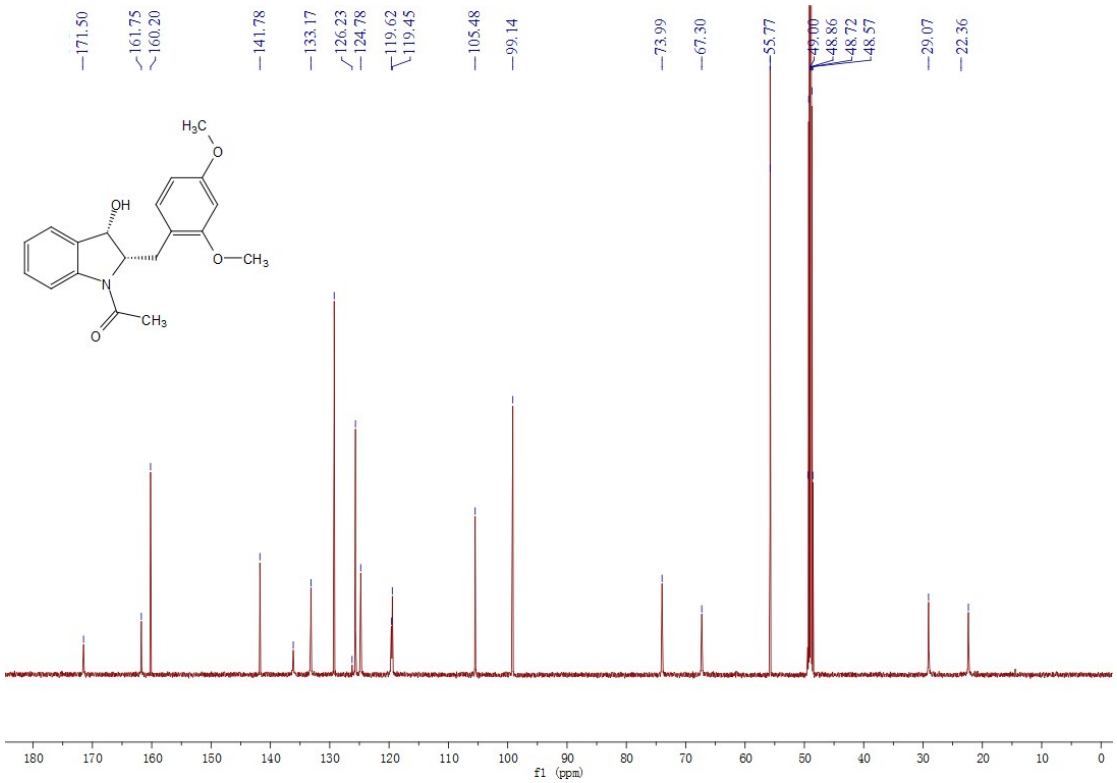


1-((2S,3S)-2-(2,4-dimethoxybenzyl)-3-hydroxyindolin-1-yl)ethanone, 2p

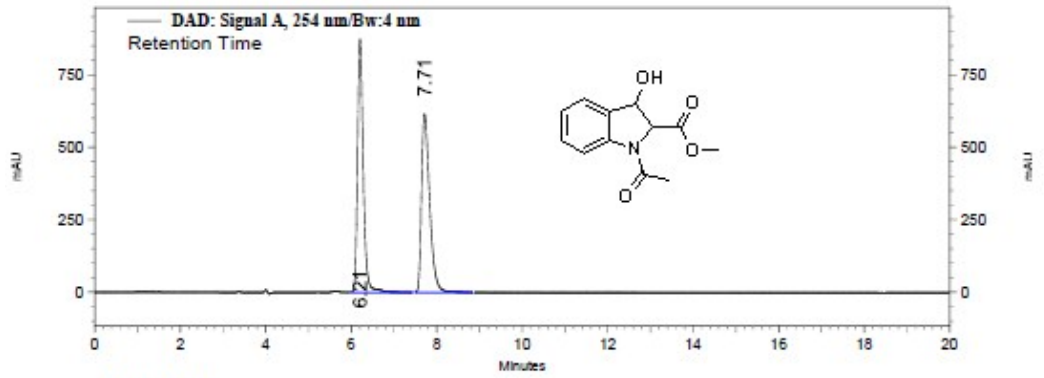
^{1}H NMR (400 MHz, MeOD)



^{13}C NMR (101 MHz, CD_3OD)

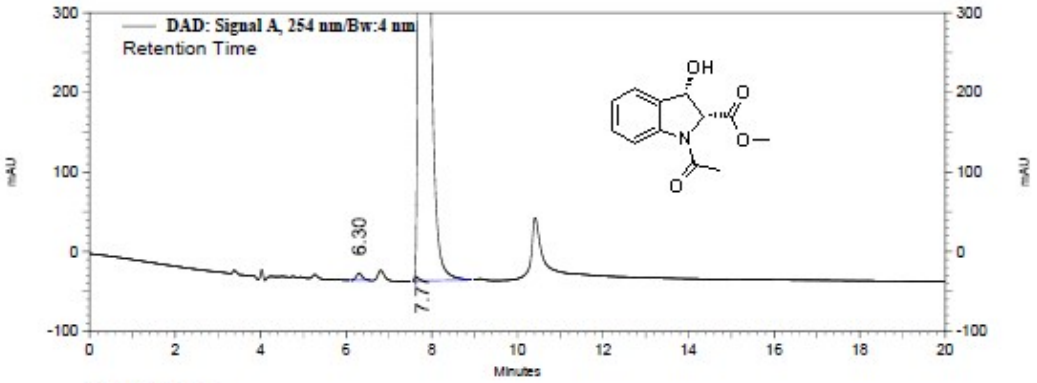


5. HPLC Chromatograms for 2a~2p.



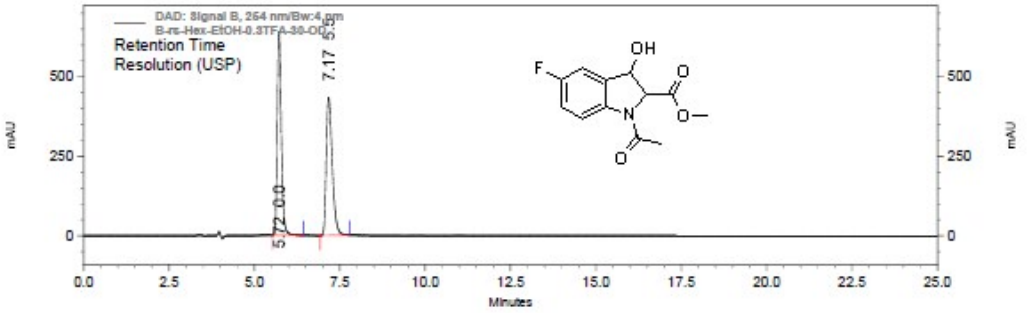
DAD: Signal A, 254 nm/Bw:4 nm Results

Pk #	R T	Area	Area Percent	Height	Theoretical plates (USP)	Resolution (USP)
1	6.21	17267499	50.047	1830290	10923	0.00
2	7.71	17234736	49.953	1290174	7874	5.15
Totals		34502235	100.000	3120464		



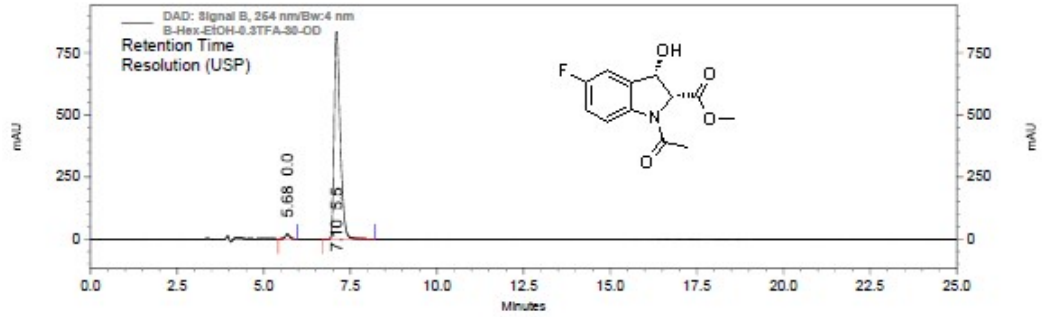
DAD: Signal A, 254 nm/Bw:4 nm Results

Pk #	R T	Area	Area Percent	Height	Theoretical plates (USP)	Resolution (USP)
1	6.30	185874	0.457	18767	9611	0.00
2	7.77	40518296	99.543	2822475	6960	4.68
Totals		40704170	100.000	2841242		



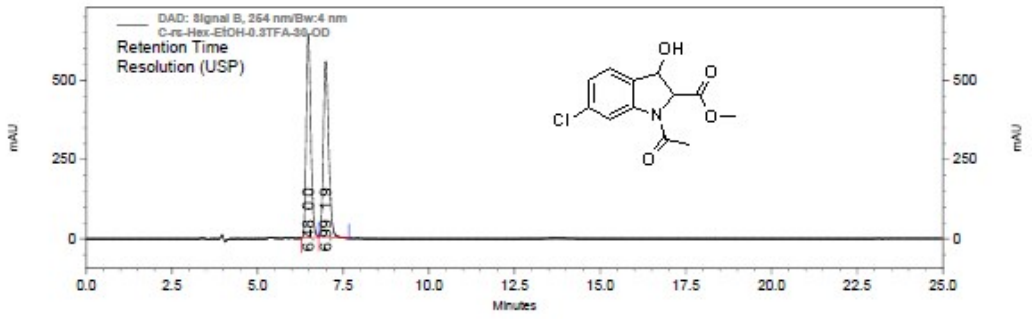
DAD: Signal B, 254 nm/Bw:4 nm Results

Pk #	Retention Time	Area	Area Percent	Theoretical plates	Resolution	Asymmetry	Peak purity
1	5.72	11119524	50.03	11550	0.0	1.3	1.000
2	7.17	11105410	49.97	8054	5.5	1.5	1.000
Totals		22224934	100.00				



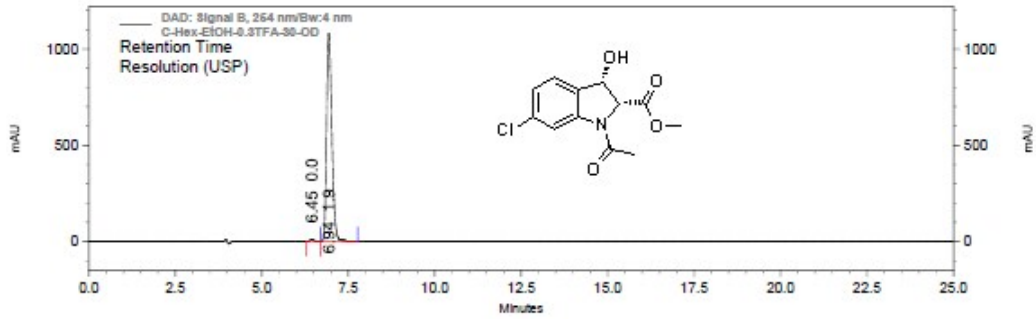
DAD: Signal B, 254 nm/Bw:4 nm Results

Pk #	Retention Time	Area	Area Percent	Theoretical plates	Resolution	Asymmetry	Peak purity
1	5.68	315543	1.49	12504	0.0	1.1	0.847
2	7.10	20917570	98.51	8212	5.5	1.5	1.000
Totals		21233113	100.00				



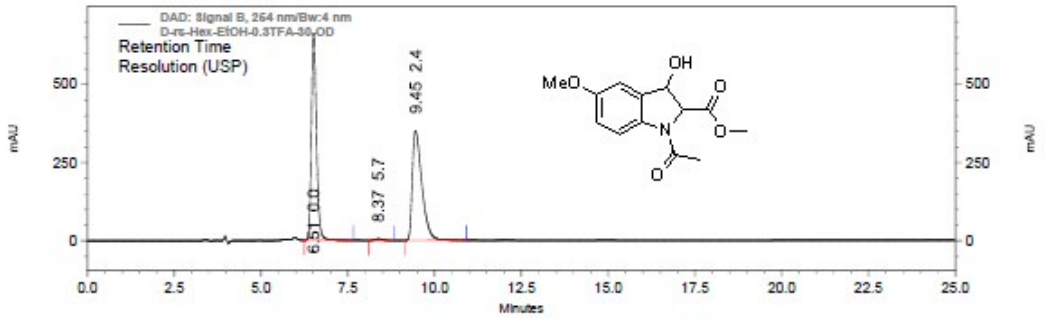
DAD: Signal B, 254 nm/Bw:4 nm Results

Pk #	Retention Time	Area	Area Percent	Theoretical plates	Resolution	Asymmetry	Peak purity
1	6.48	12401028	49.90	11447	0.0	1.2	1.000
2	6.99	12448661	50.10	9755	1.9	1.3	1.000
Totals		24849689	100.00				



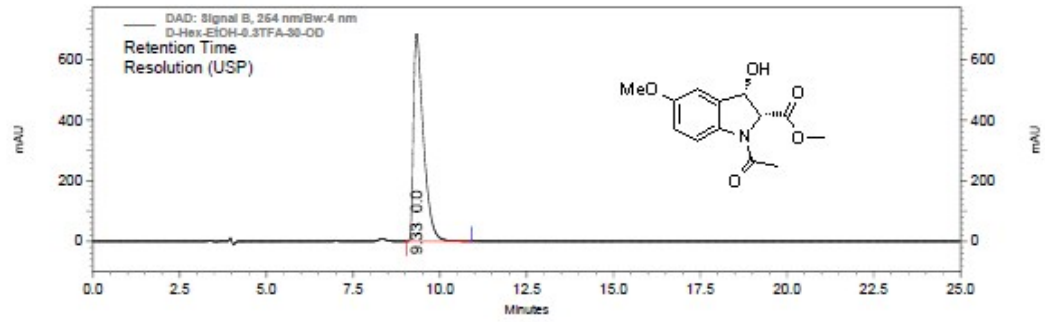
DAD: Signal B, 254 nm/Bw:4 nm Results

Pk #	Retention Time	Area	Area Percent	Theoretical plates	Resolution	Asymmetry	Peak purity
1	6.45	169323	0.70	12138	0.0	1.2	0.767
2	6.94	23991233	99.30	9877	1.9	1.3	1.000
Totals		24160556	100.00				



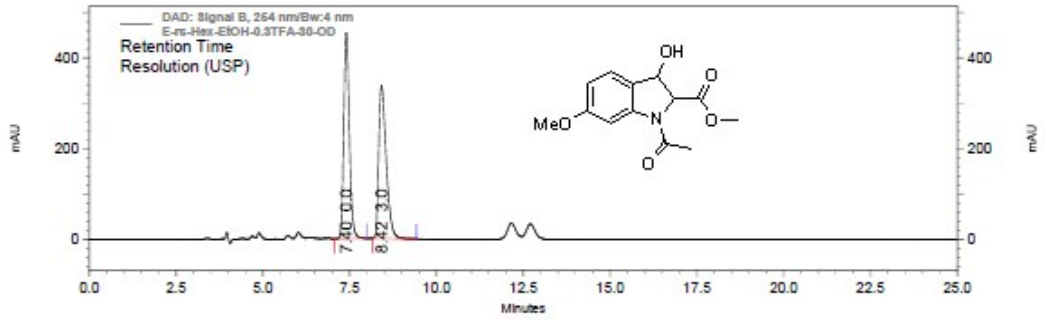
DAD: Signal B, 254 nm/Bw:4 nm Results

Pk #	Retention Time	Area	Area Percent	Theoretical plates	Resolution	Asymmetry	Peak purity
1	6.51	14136512	49.71	9970	0.0	1.3	1.000
2	8.37	163042	0.57	7120	5.7	1.2	0.625
3	9.45	14141089	49.72	5632	2.4	1.8	1.000
Totals		28440643	100.00				



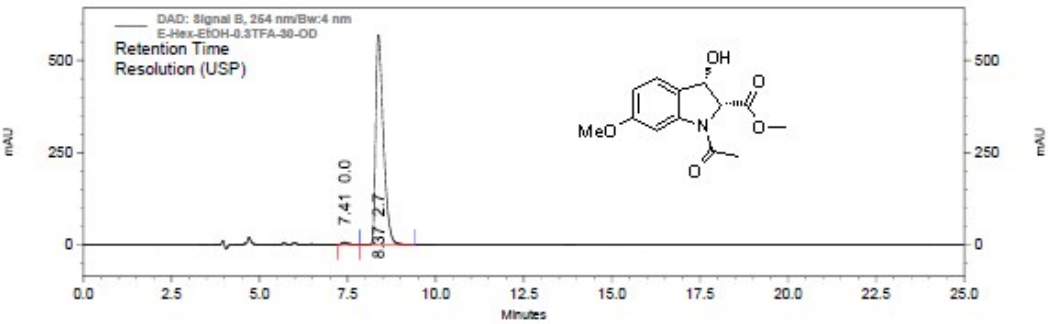
DAD: Signal B, 254 nm/Bw:4 nm Results

Pk #	Retention Time	Area	Area Percent	Theoretical plates	Resolution	Asymmetry	Peak purity
1	9.33	28564408	100.00	5162	0.0	2.1	1.000
Totals		28564408	100.00				



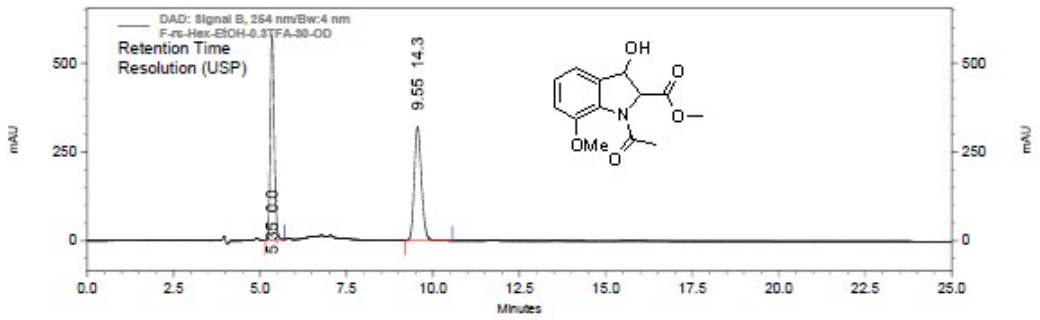
DAD: Signal B, 254 nm/Bw:4 nm Results

Pk #	Retention Time	Area	Area Percent	Theoretical plates	Resolution	Asymmetry	Peak purity
1	7.40	10649455	50.12	10219	0.0	1.2	1.000
2	8.42	10598055	49.88	7317	3.0	1.5	1.000
Totals		21247510	100.00				



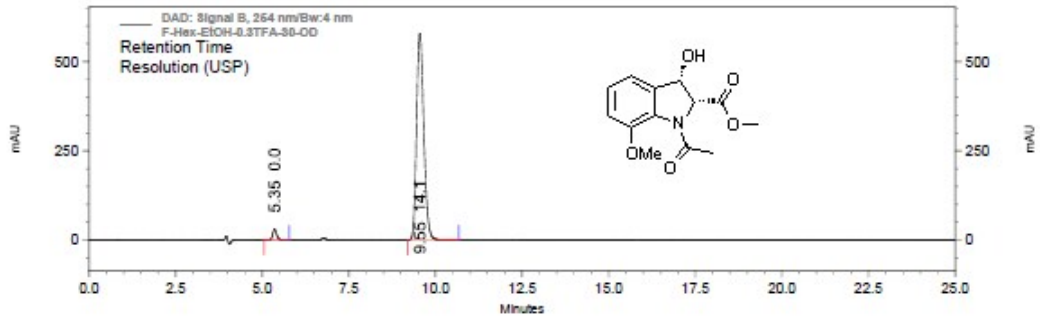
DAD: Signal B, 254 nm/Bw:4 nm Results

Pk #	Retention Time	Area	Area Percent	Theoretical plates	Resolution	Asymmetry	Peak purity
1	7.41	163967	0.89	8834	0.0	1.5	0.669
2	8.37	18179909	99.11	6841	2.7	1.7	1.000
Totals		18343876	100.00				



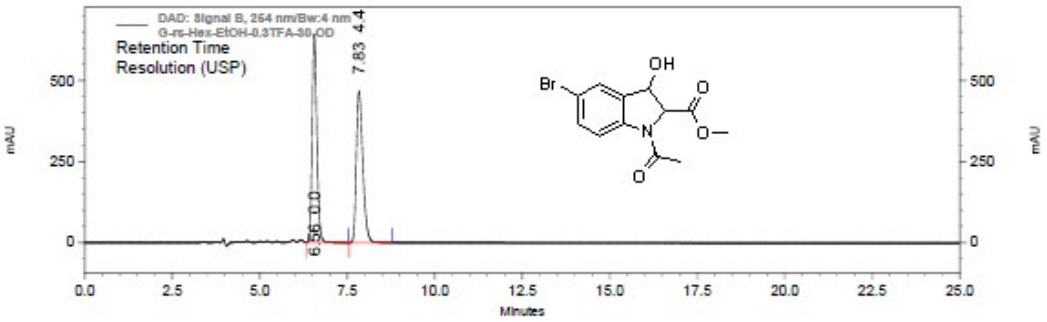
DAD: Signal B, 254 nm/Bw:4 nm
Results

Pk #	Retention Time	Area	Area Percent	Theoretical plates	Resolution	Asymmetry	Peak purity
1	5.35	9585146	49.83	10613	0.0	1.2	1.000
2	9.55	9651554	50.17	10106	14.3	1.2	1.000
Totals		19236700	100.00				



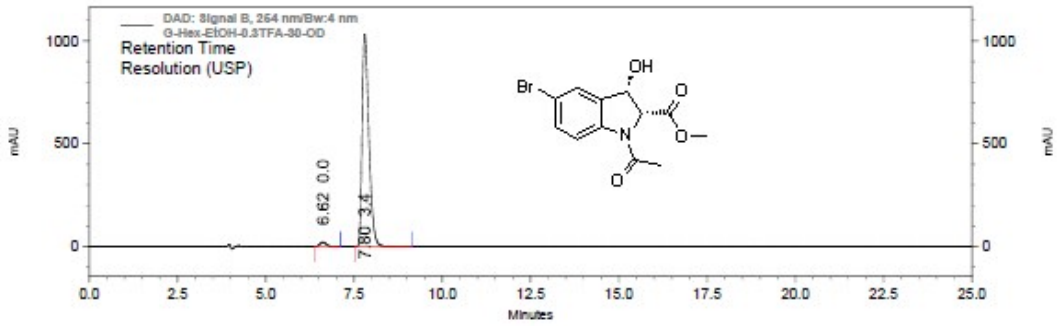
DAD: Signal B, 254 nm/Bw:4 nm
Results

Pk #	Retention Time	Area	Area Percent	Theoretical plates	Resolution	Asymmetry	Peak purity
1	5.35	508277	2.80	10414	0.0	1.2	0.968
2	9.55	17662349	97.20	9849	14.1	1.2	1.000
Totals		18170626	100.00				



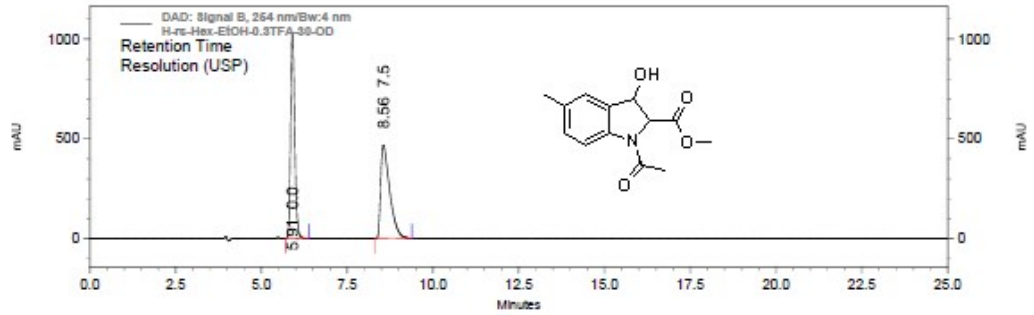
DAD: Signal B, 254 nm/Bw:4 nm Results

Pk #	Retention Time	Area	Area Percent	Theoretical plates	Resolution	Asymmetry	Peak purity
1	6.56	12608207	50.00	11531	0.0	1.2	1.000
2	7.83	12606726	50.00	8509	4.4	1.4	1.000
Totals		25214933	100.00				



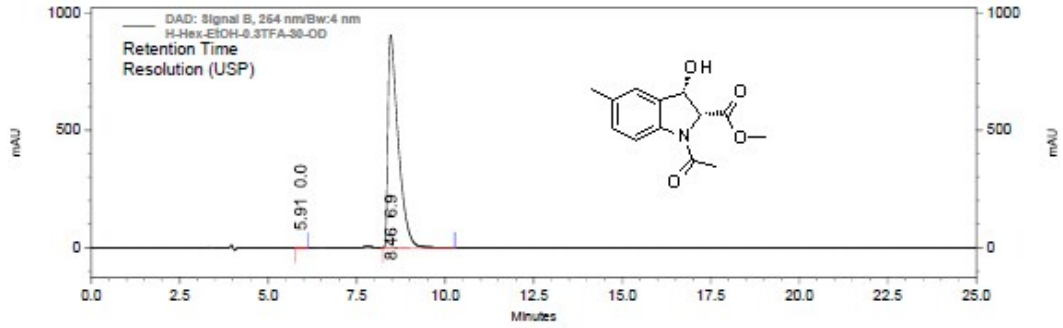
DAD: Signal B, 254 nm/Bw:4 nm Results

Pk #	Retention Time	Area	Area Percent	Theoretical plates	Resolution	Asymmetry	Peak purity
1	6.62	567081	1.93	6037	0.0	1.1	0.986
2	7.80	28798933	98.07	7867	3.4	1.5	1.000
Totals		29366014	100.00				



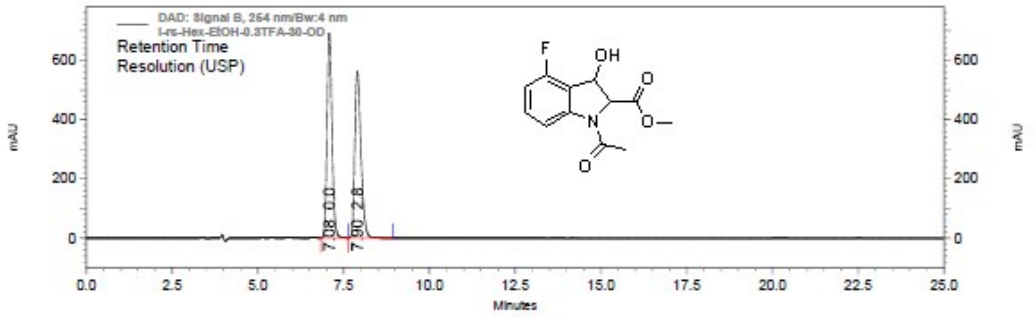
DAD: Signal B, 254 nm/Bw:4 nm
Results

Pk #	Retention Time	Area	Area Percent	Theoretical plates	Resolution	Asymmetry	Peak purity
1	5.91	18061743	50.05	11639	0.0	1.2	1.000
2	8.56	18027056	49.95	4979	7.5	2.0	1.000
Totals		36088799	100.00				



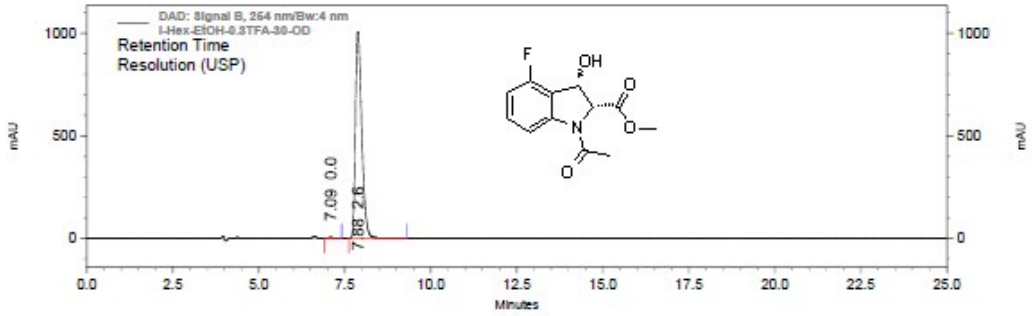
DAD: Signal B, 254 nm/Bw:4 nm
Results

Pk #	Retention Time	Area	Area Percent	Theoretical plates	Resolution	Asymmetry	Peak purity
1	5.91	6038	0.02	12330	0.0	1.2	0.464
2	8.46	38213363	99.98	4126	6.9	2.5	1.000
Totals		38219401	100.00				



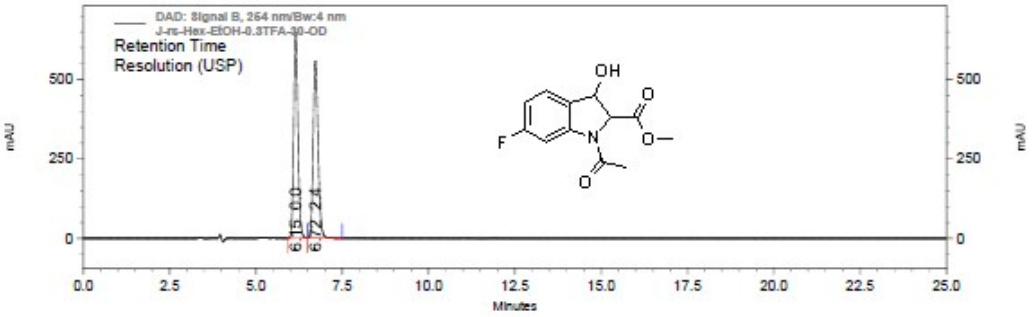
DAD: Signal B, 254 nm/Bw:4 nm Results

Pk #	Retention Time	Area	Area Percent	Theoretical plates	Resolution	Asymmetry	Peak purity
1	7.08	14559341	49.81	11497	0.0	1.2	1.000
2	7.90	14672668	50.19	9271	2.8	1.4	1.000
Totals		29232009	100.00				



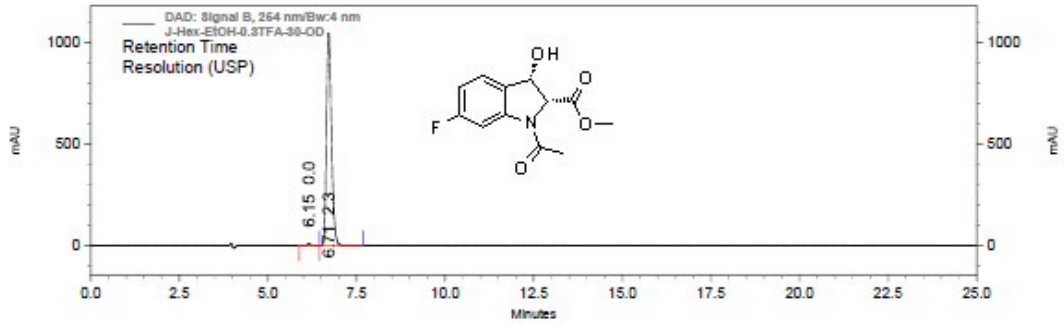
DAD: Signal B, 254 nm/Bw:4 nm Results

Pk #	Retention Time	Area	Area Percent	Theoretical plates	Resolution	Asymmetry	Peak purity
1	7.09	99161	0.37	11503	0.0	1.2	0.695
2	7.88	27011734	99.63	8638	2.6	1.5	1.000
Totals		27110895	100.00				



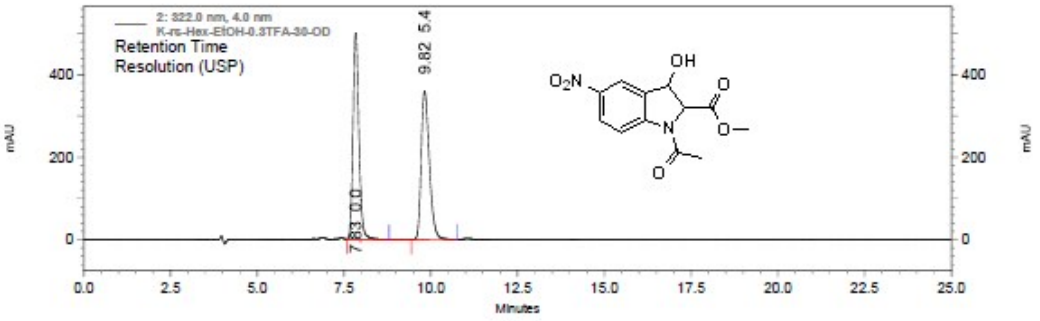
DAD: Signal B, 254 nm/Bw:4 nm Results

Pk #	Retention Time	Area	Area Percent	Theoretical plates	Resolution	Asymmetry	Peak purity
1	6.15	11504527	49.97	12157	0.0	1.2	1.000
2	6.72	11518353	50.03	10754	2.4	1.2	1.000
Totals		23022880	100.00				



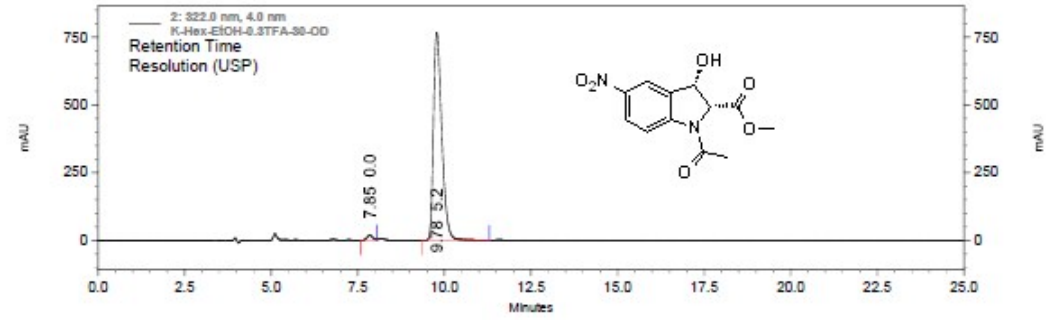
DAD: Signal B, 254 nm/Bw:4 nm Results

Pk #	Retention Time	Area	Area Percent	Theoretical plates	Resolution	Asymmetry	Peak purity
1	6.15	136881	0.62	12293	0.0	1.2	0.797
2	6.71	21948271	99.38	10524	2.3	1.3	1.000
Totals		22085152	100.00				



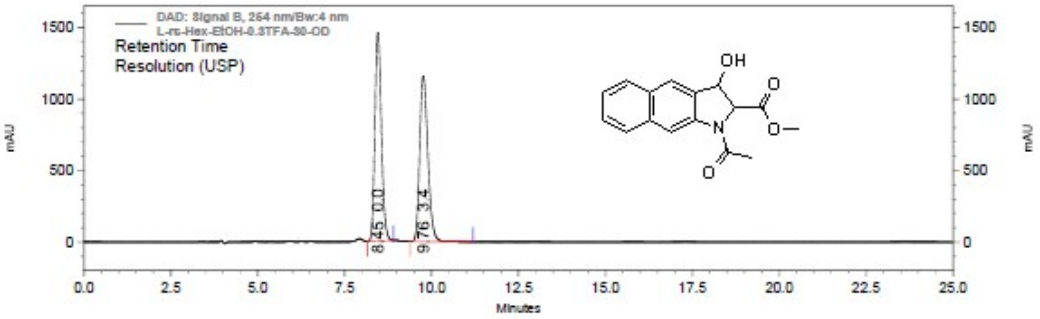
2: 322.0 nm, 4.0 nm
Results

Pk #	Retention Time	Area	Area Percent	Theoretical plates	Resolution	Asymmetry	Peak purity
1	7.83	12401380	50.21	10493	0.0	1.2	1.000
2	9.82	12299360	49.79	8419	5.4	1.4	1.000
Totals		24700740	100.00				



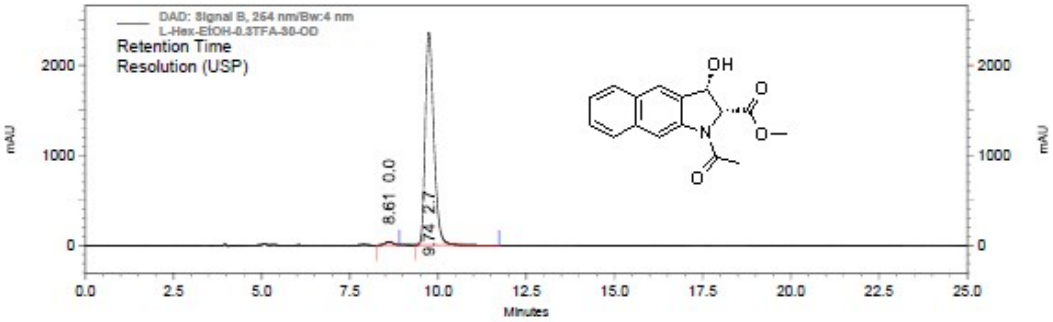
2: 322.0 nm, 4.0 nm
Results

Pk #	Retention Time	Area	Area Percent	Theoretical plates	Resolution	Asymmetry	Peak purity
1	7.85	430499	1.59	10316	0.0	0.0	0.903
2	9.78	26713768	98.41	8009	5.2	1.5	1.000
Totals		27144267	100.00				



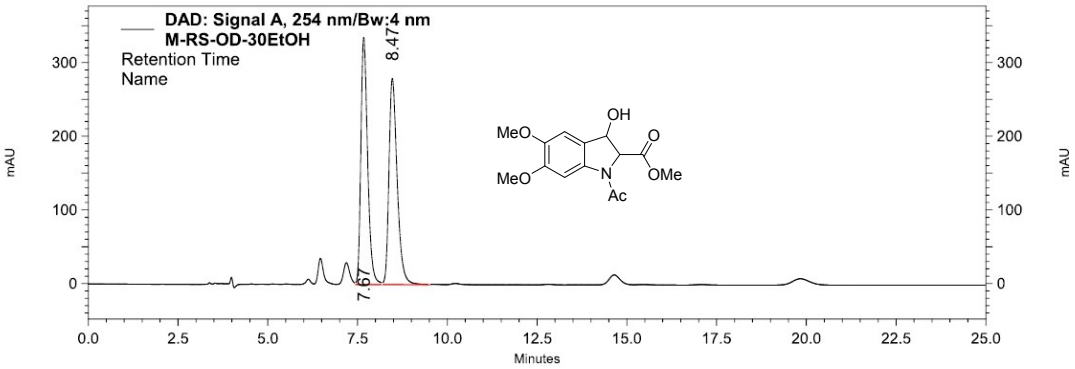
DAD: Signal B, 254 nm/Bw:4 nm Results

Pk #	Retention Time	Area	Area Percent	Theoretical plates	Resolution	Asymmetry	Peak purity
1	8.45	39745174	49.83	9642	0.0	1.2	1.000
2	9.76	40020107	50.17	8061	3.4	1.3	1.000
Totals		79765281	100.00				



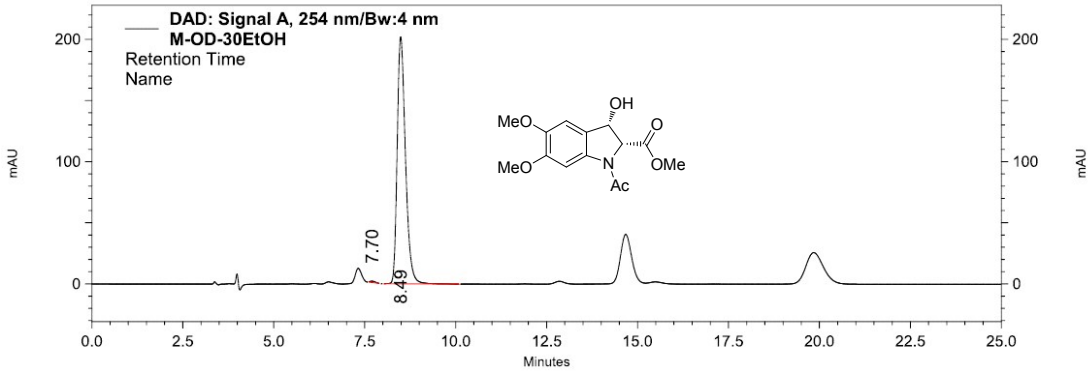
DAD: Signal B, 254 nm/Bw:4 nm Results

Pk #	Retention Time	Area	Area Percent	Theoretical plates	Resolution	Asymmetry	Peak purity
1	8.61	1173656	1.38	7816	0.0	1.0	0.972
2	9.74	84004224	98.62	7737	2.7	1.3	1.000
Totals		85177880	100.00				



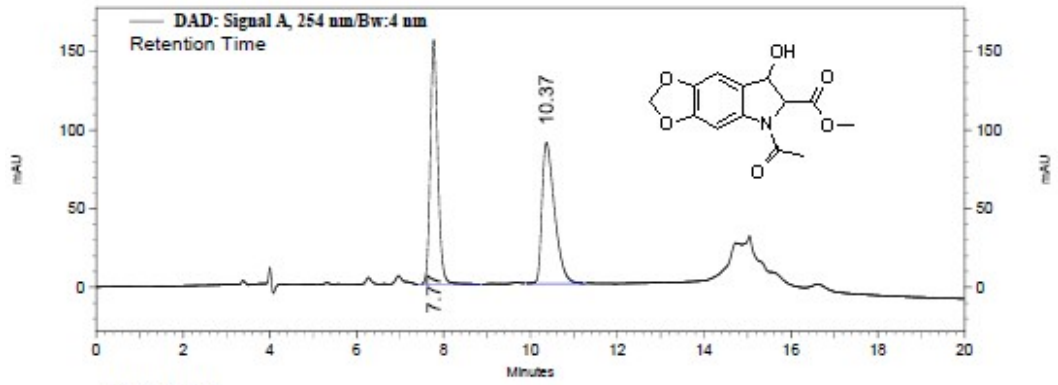
DAD: Signal A, 254 nm/Bw:4 nm Results

Pk #	R T	Height	Area	Area %	Resolution (USP)	Asymmetry	Theoretical plates (USP)	Peak purity
1	7.67	703686	9206942	49.53	0.0	1.3	8144	0.960
2	8.47	586991	9380570	50.47	2.1	1.4	6731	0.905
Totals		1290677	18587512	100.00				



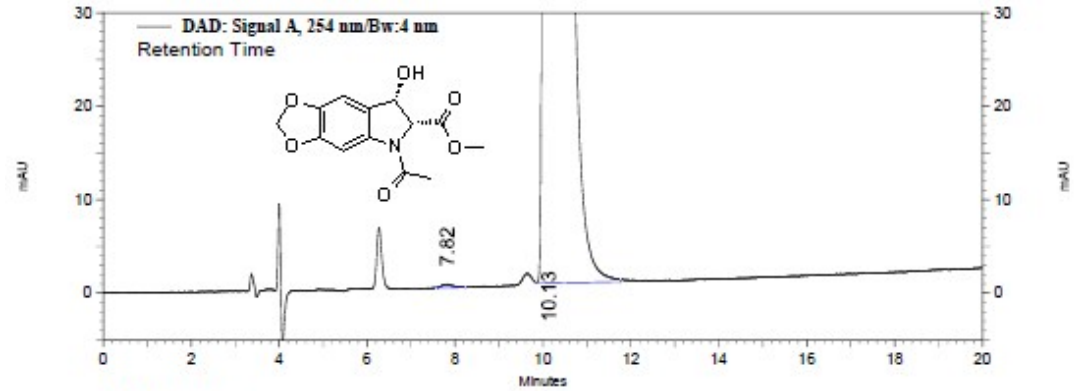
DAD: Signal A, 254 nm/Bw:4 nm Results

Pk #	R T	Height	Area	Area %	Resolution (USP)	Asymmetry	Theoretical plates (USP)	Peak purity
1	7.70	2327	23442	0.35	0.0	1.4	13150	0.533
2	8.49	423528	6680544	99.65	2.3	1.4	6847	1.000
Totals		425855	6703986	100.00				



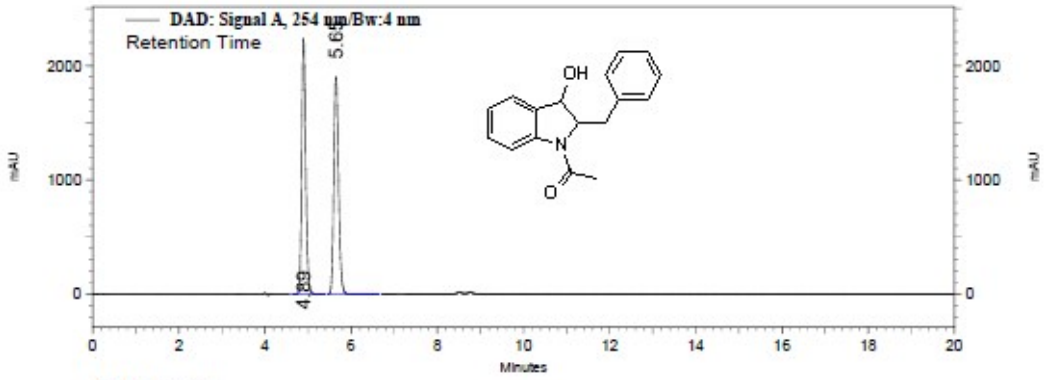
DAD: Signal A, 254 nm/Bw:4 nm Results

Pk #	R T	Area	Area Percent	Height	Theoretical plates (USP)	Resolution (USP)
1	7.77	3907479	50.662	325755	9925	0.00
2	10.37	3805287	49.338	188055	6038	6.13
Totals		7712766	100.000	513810		



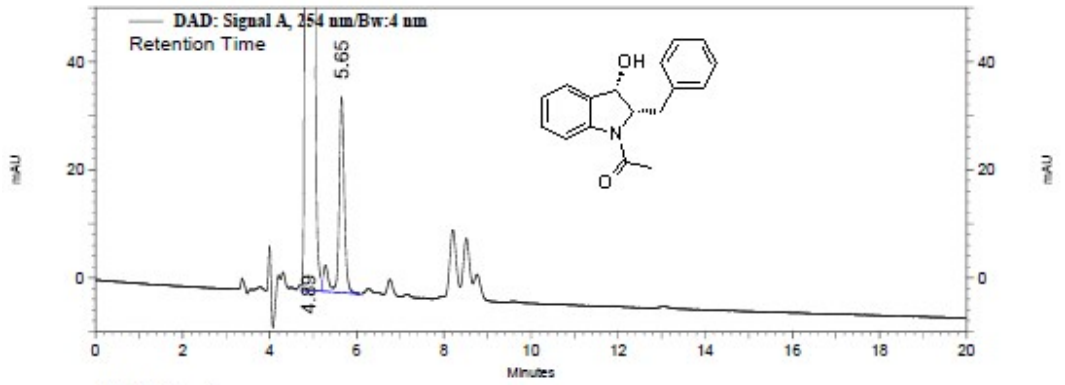
DAD: Signal A, 254 nm/Bw:4 nm Results

Pk #	R T	Area	Area Percent	Height	Theoretical plates (USP)	Resolution (USP)
1	7.82	11748	0.061	722	5969	0.00
2	10.13	19267707	99.939	787931	3930	4.40
Totals		19279455	100.000	788653		



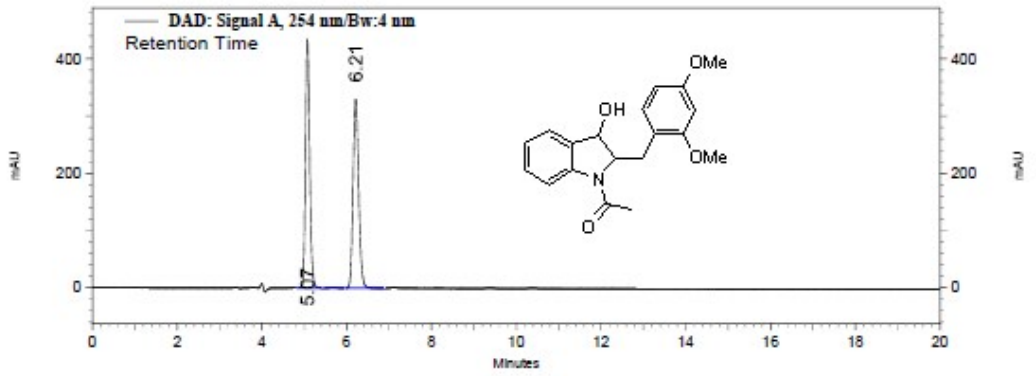
DAD: Signal A, 254 nm/Bw:4 nm Results

Pk #	R T	Area	Area Percent	Height	Theoretical plates (USP)	Resolution (USP)
1	4.89	30163488	49.855	4691104	13590	0.00
2	5.65	30338460	50.145	3994211	12730	4.09
Totals		60501948	100.000	8685315		



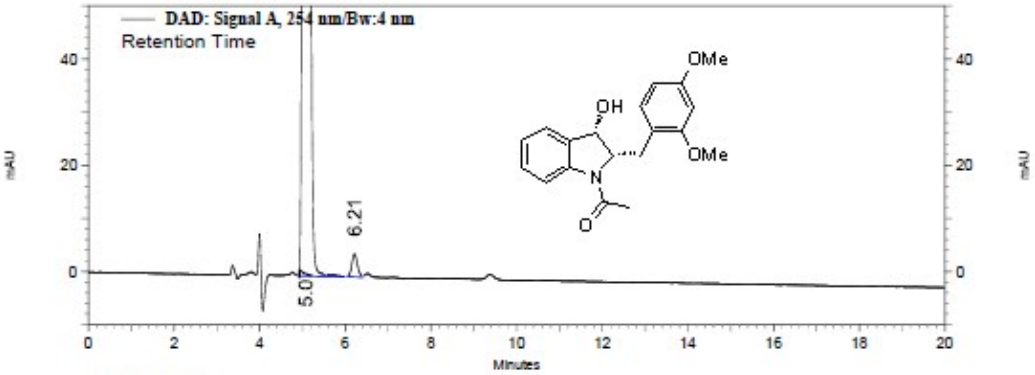
DAD: Signal A, 254 nm/Bw:4 nm Results

Pk #	R T	Area	Area Percent	Height	Theoretical plates (USP)	Resolution (USP)
1	4.89	33093896	98.205	5087060	13320	0.00
2	5.65	604845	1.795	75990	12499	4.09
Totals		33698741	100.000	5163050		



DAD: Signal A, 254 nm/Bw:4 nm Results

Pk #	R T	Area	Area Percent	Height	Theoretical plates (USP)	Resolution (USP)
1	5.07	6320893	49.885	910550	12498	0.00
2	6.21	6350145	50.115	690876	10565	5.39
Totals		12671038	100.000	1601426		



DAD: Signal A, 254 nm/Bw:4 nm Results

Pk #	R T	Area	Area Percent	Height	Theoretical plates (USP)	Resolution (USP)
1	5.07	14390508	99.416	2074980	12554	0.00
2	6.21	84571	0.584	9034	10271	5.35
Totals		14475079	100.000	2084014		