[*Supporting Information*]

Organocatalytic asymmetric Henry reaction of isatins: Highly enantioselective synthesis of 3-hydroxy-2-oxindoles

Yong Zhang, Zhi-Jun Li, Hai-Sen Xu, Yuan Zhang, and Wei Wang*

State Key Laboratory of Applied Organic Chemistry, College of Chemistry and Chemical Engineering, Lanzhou University, Lanzhou, Gansu 730000, P. R. China

Fax: + 86 931 891 5557; E-mail: wang_wei@lzu.edu.cn

Note: *This work was presented as a poster at the 5th ChemComm International Symposium (May 18, 2011, Lanzhou). When we were about to submit the manuscript, independent but very silimar work from the group of Prof. Wei Wang (University of New Mexico) appeared in advance: Chem. – Eur. J.,* 2011, **17**, 7791 *(published online on May 30, 2011; sumbitted on April 4, 2011). To avoid possible confusion, please note that the corresponding author of this manuscript, Prof. Wei Wang at Lanzhou University, is distinct from Prof. Wei Wang at University of New Mexico. Their native names are also of different characters.*

Contents

1. General information

General methods

All the reactions were carried out with dried glasswares. NMR spectra were recorded on a liquid NMR spectrometer (400 MHz for ^{1}H and 100 MHz for ^{13}C) using Me_2C=O-d_6 as the solvent. The residual proton in Me_2C=O-d_6 (δ = 2.05) served as an internal standard for ^{1}H NMR, and the ^{13}C-atom of Me_2C=O-d_6 was used as an internal standard (δ = 29.9) for ^{13}C NMR. Chemical shifts are reported in ppm and the coupling constants *J* are given in Hz. The following abbreviations were used to explain the multiplicities: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). Infrared spectra were recorded on an FT-IR spectrometer, and only major peaks were reported in cm^{-1}. HRMS and ESI data were obtained by the ESI ionization sources. Optical rotations were determined with 0.1 dm tube using 589 nm at 23 °C. Enantiomeric excess (*ee*) values were determined by HPLC with chiral AD-H or OJ-H column and the detection was done by UV detector at 254 nm. Purification of the products was performed by column chromatography on silica gel (200–300 mesh).

Materials

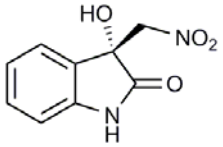
Catalysts QD was purchased from Aldrich company and used without further purification. C6'-OH cinchona alkaloid catalysts (Q-**1a** to Q-**1d** and QD-**1a** to QD-**1d**) were prepared according to the literature procedures.[1] Catalysts Q-**1e**[2] and QD-**2**[3] were also prepared according to the literature procedures, respectively. Isatins were commercially available. The *N*-methyl or *N*-benzyl protected isatins were prepared according to the literature method.[4] All solvents were purified according to the standard procedures.

1. (a) H. Li, Y. Wang, L. Tang and L. Deng, *J. Am. Chem. Soc*., 2004, **126**, 9906; (b) H. Li, Y. Wang, L. Tang, F. Wu, X. Liu, C. Guo, B. M. Foxman and L. Deng, *Angew. Chem., Int. Ed*., 2005, **44**, 105.
2. M. Bandini, R. Sinisi and A. Umani-Ronchi, *Chem. Commun*., 2008, 4360.
3. B. Vakulya, S. Varga, A. Csámpai and T. Soós, *Org. Lett.*, 2005, **7**, 1967
4. L. E. Overman and E. A. Peterson, *Tetrahedron*, 2003, **59**, 6905.

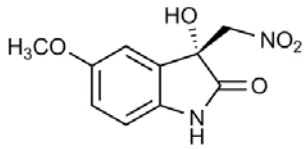
2. Experimental section

2.1 Genaral procedure for catalytic asymmetric Henry reaction of isatins

To a flame-dried test tube was added isatin **1** (0.1 mmol) and catalyst Q-**1e** (10 mol%), followed by anhydrous THF (1 mL). The reaction mixture was stirred at 5 °C under argon for 10 minutes. Nitromethane **2** (1.0 mmol, 10.0 equiv., 54 μL) was then added through a syringe in one portion. The resulting mixture was stirred at 5 °C for the indicated time. After the reaction was completed, the reaction mixture was directly subjected to silica gel flash chromatography using PE/acetone (v/v = 4/1 to 2/1) as eluent to afford the desired product **3** with the yield and enantiomeric excess showed in the main text. (**Cautions**: The product **3** could be racemized under heat or in protic solvent. When the product **3** was concentrated, the temperature should not exceed 30 °C).

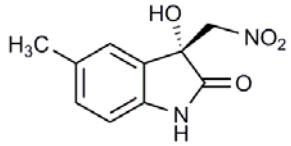


(*R*)-3-hydroxy-3-(nitromethyl)indolin-2-one (3a): 96% yield; $[\alpha]_D^{23}$ = -64 (*c* 0.9, THF); 92% ee, determined by HPLC analysis using Daicel chiral AD-H column, Hexane/*i*-PrOH = 85:15. Flow rate: 1.0 mL/min, detection at 254 nm, t (major) = 10.85 min, t (minor) = 15.14 min; **IR**: ν 3315 1725 1621 1554 1473 1379 1190 1121 755 664 cm^{-1}; **^{1}H NMR** (400 MHz, Me_2C=O-d_6) δ (ppm) 9.58 (s, 1H, NH), 7.49 (d, *J* = 7.6 Hz, 1H), 7.31 (td, *J* = 7.6 Hz, 1.2 Hz, 1H), 7.04 (td, *J* = 7.6 Hz, 1.2 Hz, 1H), 6.95 (d, *J* = 7.6 Hz, 1H), 5.71 (s, 1H, OH), 5.09 (d, *J* = 12.8 Hz, 1H), 5.05 (d, *J* = 12.8 Hz, 1H); **^{13}C NMR** (100 MHz, Me_2C=O-d_6) δ (ppm) 176.5, 143.7, 131.5, 128.6, 125.7, 123.1, 111.2, 79.3, 74.1.

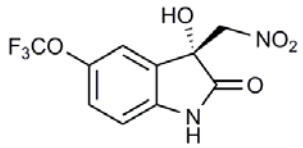


(*R*)-3-hydroxy-5-methoxy-3-(nitromethyl)indolin-2-one (3b): 96% yield; $[\alpha]_D^{23}$ = -35 (*c* 1.0, THF); 92% ee, determined by HPLC analysis using Daicel chiral AD-H column, Hexane/*i*-PrOH = 85:15. Flow rate: 1.0 mL/min, detection at 254 nm, t (major) = 15.25 min, t (minor) = 22.73 min; **IR**: ν 3398 3261 1734 1620 1553 1480 1425 1378 1228 1185 1090 887 829 739 665 cm^{-1}; **^{1}H NMR** (400 MHz, Me_2C=O-d_6)

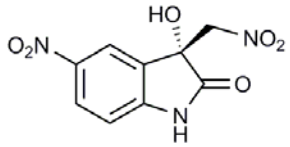
δ (ppm) 9.43 (s, 1H), 7.16 (t, J = 1.2 Hz, 1H), 6.87 (d, J = 1.5 Hz, 2H), 5.71 (s, 1H), 5.07 (s, 2H), 3.76 (s, 3H). **^{13}C NMR** (100 MHz, Me_2C=O-d_6) δ (ppm) 176.5, 156.8, 136.7, 129.7, 116.1, 112.6, 111.7, 79.2, 74.4, 56.1. **ESI-HRMS**: calcd. for [$C_{10}H_{10}N_2O_5$ + NH_4] 256.0928, found 256.0931.



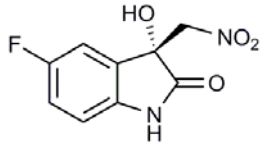
(*R*)-3-hydroxy-5-methyl-3-(nitromethyl)indolin-2-one (3c): 95% yield; $[\alpha]_D^{23}$ = -28 (*c* 1.0, THF); 92% ee, determined by HPLC analysis using Daicel chiral AD-H column, Hexane/*i*-PrOH = 85:15. Flow rate: 1.0 mL/min, detection at 254 nm, t (major) = 10.64 min, t (minor) = 15.49 min; **IR**: ν 3324 3267 1752 1731 1626 1556 1495 1424 1380 1307 1202 1162 1072 1044 831 799 666 593 cm^{-1}; **^{1}H NMR** (400 MHz, Me_2C=O-d_6) δ (ppm) 9.48 (s, 1H), 7.31 (s, 1H), 7.12 (dd, J = 7.9, 0.9 Hz, 1H), 6.84 (d, J = 7.9 Hz, 1H), 5.65 (s, 1H), 5.07 (d, J = 12.9 Hz, 1H), 5.02 (d, J = 12.9 Hz, 1H), 2.29 (s, 3H). **^{13}C NMR** (100 MHz, Me_2C=O-d_6) δ (ppm) 176.5, 141.2, 132.5, 131.7, 128.6, 126.3, 110.9, 79.2, 74.1, 21.1. **ESI-HRMS**: calcd. for [$C_{10}H_{10}N_2O_4$ + NH_4] 240.0979, found 240.0980.



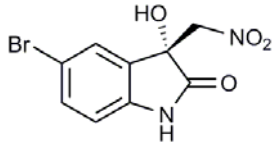
(*R*)-3-hydroxy-5-(trifluoromethoxy)-3-(nitromethyl) indolin-2-one (3d): 97% yield; $[\alpha]_D^{23}$ = -29 (*c* 1.0, THF); 87% ee, determined by HPLC analysis using Daicel chiral AD-H column, Hexane/*i*-PrOH = 85:15. Flow rate: 1.0 mL/min, detection at 254 nm, t (major) = 6.79 min, t (minor) = 10.70 min; **IR**: ν 3305 1739 1631 1559 1488 1422 1379 1266 1220 1190 1168 888 833 741 667 cm^{-1}; **^{1}H NMR** (400 MHz, Me_2C=O-d_6) δ (ppm) 9.80 (s, 1H), 7.55 (d, J = 1.4 Hz, 1H), 7.31 (dd, J = 8.5, 1.6 Hz, 1H), 7.07 (d, J = 8.5 Hz, 1H), 5.99 (s, 1H), 5.18 (d, J = 13.3 Hz, 1H), 5.13 (d, J = 13.3 Hz, 1H). **^{13}C NMR** (100 MHz, Me_2C=O-d_6) δ (ppm) 176.4, 145.0, 142.9 130.3, 124.8 121.6 (q, $^1J_{CF}$ = 254 Hz), 119.9, 112.1, 78.8, 74.1. **ESI-HRMS**: calcd. for [$C_{10}H_{10}N_2O_4$ + NH_4] 310.0645, found 310.0642.



(*R*)-3-hydroxy-5-nitro-3-(nitromethyl)indolin-2-one (3e): 97% yield; $[\alpha]_D^{23}$ = -41 (*c* 1.0, THF); 84% ee, determined by HPLC analysis using Daicel chiral AD-H column, Hexane/*i*-PrOH = 85:15. Flow rate: 1.0 mL/min, detection at 254 nm, t (major) = 12.36 min, t (minor) = 16.84 min; **IR**: ν 3314 1746 1690 1626 1558 1527 1481 1380 1342 1259 1189 1113 1086 912 842 748 662 cm^{-1}; **^{1}H NMR** (400 MHz, Me_2C=O-d_6) δ (ppm) 10.26 (s, 1H), 8.47 (d, J = 2.2 Hz, 1H), 8.31 (dd, J = 8.7, 2.2 Hz, 1H), 7.21 (d, J = 8.7 Hz, 1H), 6.16 (s, 1H), 5.37 (d, J = 13.8 Hz, 1H), 5.22 (d, J = 13.8 Hz, 1H). **^{13}C NMR** (100 MHz, Me_2C=O-d_6) δ (ppm) 176.6, 149.9, 144.1, 129.8, 128.4, 121.7, 111.4, 78.3, 73.5. **ESI-HRMS**: calcd. for [$C_9H_7N_3O_6$ + NH_4] 271.0673, found 271.0668.

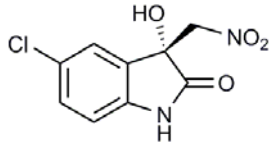


(*R*)-5-fluoro-3-hydroxy-3-(nitromethyl)indolin-2-one (3f): 97% yield; $[\alpha]_D^{23}$ = -52 (*c* 1.0, THF); 91% ee, determined by HPLC analysis using Daicel chiral AD-H column, Hexane/*i*-PrOH = 85:15. Flow rate: 1.0 mL/min, detection at 254 nm, t (major) = 10.19 min, t (minor) = 13.24 min; **IR**: ν 3290 1729 1631 1556 1488 1421 1379 1271 1190 1068 824 cm^{-1}; **^{1}H NMR** (400 MHz, Me_2C=O-d_6) δ (ppm) 9.63 (s, 1H), 7.36 (dd, J = 8.1, 2.6 Hz, 1H), 7.10 (td, J = 9.1, 2.6 Hz, 1H), 6.97 (dd, J = 8.5, 4.3 Hz, 1H), 5.89 (s, 1H), 5.11 (s, 2H). **^{13}C NMR** (100 MHz, Me_2C=O-d_6) δ (ppm) 176.4, 159.7(d, $^1J_{CF}$ = 237 Hz), 139.9, 130.3 (d, $^3J_{CF}$ = 8 Hz), 117.7 (d, $^2J_{CF}$ = 24 Hz), 113.6 (d, $^2J_{CF}$ = 24 Hz), 112.1 (d, $^3J_{CF}$ = 8 Hz), 79.0, 74.2. **ESI-HRMS**: calcd. for [$C_9H_7FN_2O_4$ + NH_4] 244.0728, found 244.0731.

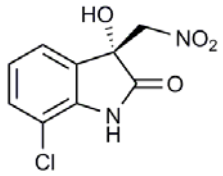


(*R*)-5-bromo-3-hydroxy-3-(nitromethyl)indolin-2-one (3g): 96% yield; $[\alpha]_D^{23}$ = -44 (*c* 1.0, THF); 86% ee, determined by HPLC analysis using Daicel chiral AD-H column, Hexane/*i*-PrOH = 85:15. Flow rate: 1.0 mL/min, detection at 254 nm, t (major) = 9.76 min, t (minor) = 14.25 min; **IR**: ν 3287 1734 1616 1554 1473 1441 1378 1308 1187 1066 822 cm^{-1}; **^{1}H NMR** (400 MHz, Me_2C=O-d_6) δ (ppm) 9.74 (s,

1H), 7.70 (d, *J* = 1.8 Hz, 1H), 7.49 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.94 (d, *J* = 8.3 Hz, 1H), 5.90 (s, 1H), 5.16 (d, *J* = 13.4 Hz, 1H), 5.11 (d, *J* = 13.4 Hz, 1H). **^{13}C NMR** (100 MHz, Me_2C=O-d_6) δ (ppm) 176.0, 143.1, 134.2, 131.1, 128.9, 115.0, 113.1, 78.7, 73.9. **ESI-HRMS**: calcd. for [$C_9H_7BrN_2O_4$ + NH_4] 303.9927, found 303.9934 and 305.9903.

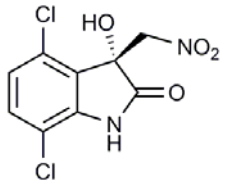


(*R*)-5-chloro-3-hydroxy-3-(nitromethyl)indolin-2-one (3h): 96% yield; $[\alpha]_D^{23}$ = -26 (*c* 1.0, THF); 90% ee, determined by HPLC analysis using Daicel chiral AD-H column, Hexane/*i*-PrOH = 85:15. Flow rate: 1.0 mL/min, detection at 254 nm, t (major) = 9.58 min, t (minor) = 14.13 min; **IR**: ν 3311 3231 1724 1689 1613 1556 1496 1474 1434 1380 1317 1201 1170 1086 1023 832 773 666 cm^{-1}; **^{1}H NMR** (400 MHz, Me_2C=O-d_6) δ (ppm) 9.72 (s, 1H), 7.57 (d, *J* = 2.1 Hz, 1H), 7.35 (dd, *J* = 8.3, 2.2 Hz, 1H), 6.99 (d, *J* = 8.3 Hz, 1H), 5.90 (s, 1H), 5.16 (d, *J* = 13.3 Hz, 1H), 5.11 (d, *J* = 13.3 Hz, 1H). **^{13}C NMR** (100 MHz, Me_2C=O-d_6) δ (ppm) 176.1, 142.6, 131.3, 130.7, 127.8, 126.1, 112.6, 78.8, 74.0. **ESI-HRMS**: calcd. for [$C_9H_7ClN_2O_4$ + NH_4] 260.0433, found 260.0428.

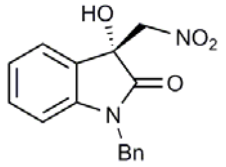


(*R*)-7-chloro-3-hydroxy-3-(nitromethyl)indolin-2-one (3i): 96% yield; $[\alpha]_D^{23}$ = -28 (*c* 0.9, THF); 90% ee, determined by HPLC analysis using Daicel chiral AD-H column, Hexane/*i*-PrOH = 85:15. Flow rate: 1.0 mL/min, detection at 254 nm, t (major) = 12.60 min, t (minor) = 16.80 min; **IR**: ν 3277 1735 1623 1556 1476 1420 1379 1322 1221 1179 1144 1071 794 737 cm^{-1}; **^{1}H NMR** (400 MHz, Me_2C=O-d_6) δ (ppm) 9.96 (s, 1H), 7.48 (d, *J* = 7.4 Hz, 1H), 7.37 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.09 (m, 1H), 5.91 (s, 1H), 5.15 (d, *J* = 13.3 Hz, 1H), 5.11 (d, *J* = 13.3 Hz, 1H). **^{13}C NMR** (100 MHz, Me_2C=O-d_6) δ (ppm) 176.1, 141.5, 131.4, 130.5, 124.4, 124.3, 115.8, 78.9, 74.6. **ESI-HRMS**: calcd. for [$C_9H_7ClN_2O_4$ + NH_4] 260.0433, found 260.0439.

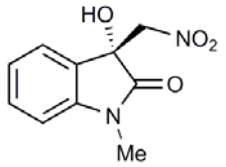
.



(*R*)-4,7-dichloro-3-hydroxy-3-(nitromethyl)indolin-2-one (3j): 97% yield; $[\alpha]_D^{23}$ = -18 (*c* 0.9, THF); 71% ee, determined by HPLC analysis using Daicel chiral AD-H column, Hexane/*i*-PrOH = 85:15. Flow rate: 1.0 mL/min, detection at 254 nm, t (major) = 10.53 min, t (minor) = 17.0 min; **IR**: ν 3276 1741 1618 1556 1471 1423 1380 1306 1168 1073 953 796 665 cm^{-1}; **^{1}H NMR** (400 MHz, Me_2C=O-d_6) δ (ppm) 10.18 (s, 1H), 7.41 (d, J = 8.8 Hz, 1H), 7.07 (d, J = 8.8 Hz, 1H), 6.11 (s, 1H), 5.46 (d, J = 13.6 Hz, 1H), 5.25 (d, J = 13.6 Hz, 1H). **^{13}C NMR** (100 MHz, Me_2C=O-d_6) δ (ppm) 175.4, 143.5, 133.0, 131.0, 126.3, 125.1, 114.9, 77.0, 75.4. **ESI-HRMS**: calcd. for [$C_9H_6Cl_2N_2O_4$ + NH_4] 294.0043, found 294.0050.



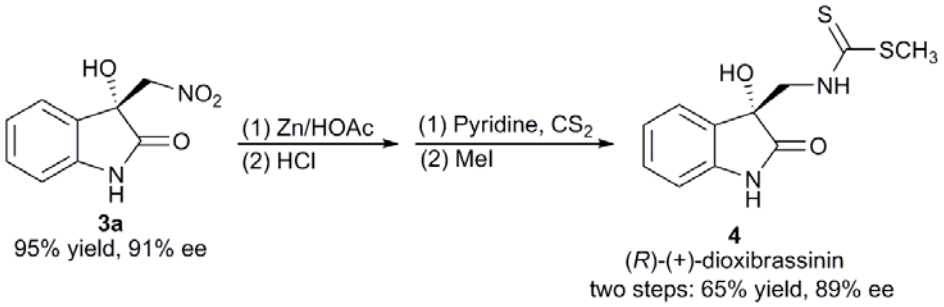
(*R*)-1-benzyl-3-hydroxy-3-(nitromethyl)indolin-2-one (3k): 95% yield; $[\alpha]_D^{23}$ = -31 (*c* 1.0, THF); 76% ee, determined by HPLC analysis using Daicel chiral OJ-H column, Hexane/*i*-PrOH = 85:15. Flow rate: 1.0 mL/min, detection at 254 nm, t (minor) = 31.59 min, t (major) = 33.52 min; **IR**: ν 3358 1711 1614 1554 1491 1468 1426 1377 1179 1076 753 700 cm^{-1}; **^{1}H NMR** (400 MHz, Me_2C=O-d_6) δ (ppm) 7.54 (dd, J = 7.4, 1.2 Hz, 1H), 7.43 (m, 2H), 7.34 (m, 2H), 7.28 (m, 2H), 7.07 (td, J = 7.6, 0.9 Hz, 1H), 6.87 (d, J = 7.9 Hz, 1H), 5.88 (s, 1H), 5.20 (d, J = 13.0 Hz, 1H), 5.15 (d, J = 13.0 Hz, 1H), 5.00 (d, J = 15.9 Hz, 1H), 4.94 (d, J = 15.9 Hz, 1H). **^{13}C NMR** (100 MHz, Me_2C=O-d_6) δ (ppm) 175.4, 144.7, 137.1, 131.5, 129.6, 128.4, 128.3, 128.1, 125.4, 123.7, 110.7, 79.1, 73.9, 44.3. **ESI-MS**: m/z: 299.2 $[M + H]^+$.



(*R*)-1-methyl-3-hydroxy-3-(nitromethyl)indolin-2-one (3l): 95% yield; $[\alpha]_D^{23}$ = -70 (*c* 0.6, THF); 91% ee, determined by HPLC analysis using Daicel chiral AD-H column, Hexane/*i*-PrOH = 90:10. Flow rate: 1.0 mL/min, detection at 254 nm, t (minor) = 14.90 min, t (major) = 13.77 min; **IR**: ν 3346 1716 1615 1554 1495 1472 1425 1380 1352 1247 1113 1097 756 cm^{-1}; **^{1}H NMR** (400 MHz, Me_2C=O-d_6) δ (ppm)

7.51 (dd, J = 7.4, 0.7 Hz, 1H), 7.40 (td, J = 7.8, 1.2 Hz, 1H), 7.10 (td, J = 7.6, 0.8 Hz, 1H), 7.02 (d, J = 7.9 Hz, 1H), 5.71 (s, 1H), 5.09 (d, J = 13.0 Hz, 1H), 5.05 (d, J = 13.0 Hz, 1H), 3.20 (s, 3H); **^{13}C NMR** (100 MHz, Me_2C=O-d_6) δ (ppm) 175.01, 145.58, 131.59, 128.06, 125.26, 123.55, 109.74, 79.34, 73.84, 26.58. **ESI-MS**: m/z: 223.2 $[M + H]^+$.

2.2 Synthesis of (*R*)-(+)-dioxibrassinin (4)



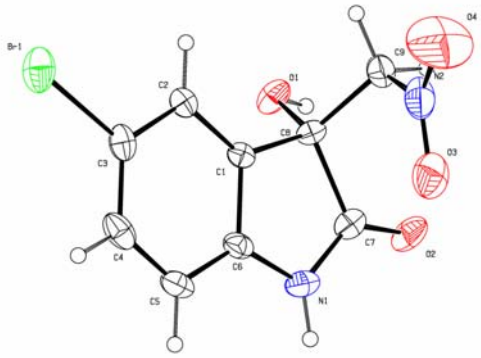
3a
95% yield, 91% ee

4
(*R*)-(+)-dioxibrassinin
two steps: 65% yield, 89% ee

To the solution of **3a** (96 mg, 0.46 mmol, 1.0 equiv., 91% ee) in acetic acid (6.0 mL), zinc dust (1.19 g, 1.84 mmol, 40.0 equiv.) was added slowly. After 15 h at r.t., the mixture was filtered over Celite, washed with methanol, and then acidified with concentrated HCl (0.5 mL). After removal of solvent and acid, pyridine (1.0 mL) and Et_3N (0.2 mL) were added and the mixture was cooled to 0 ^oC. Thereafter, CS_2 (44 μL) was added. After 2 h at 0 ^oC, MeI (46 μL) was added and the mixture was stirred at r.t. for 5 h, followed by the treatment with concentrated HCl (1.5 mL) and extraction with EtOAc. The combined organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography (CH_2Cl_2/CH_3OH = 90:1-70:1) to give a white foam of **(*R*)-(+)-dioxibrassinin (4)[5]:** 65% yield (over two steps); $[\alpha]_D^{23}$ = +10 (*c* 0.6, CH_3OH); 89% ee, determined by HPLC analysis using Daicel chiral AD-H column, Hexane/*i*-PrOH = 85:15. Flow rate: 1.0 mL/min, detection at 254 nm, t (minor) = 12.68 min, t (major) = 17.56 min; **IR**: ν 3269 1719 1622 1509 1472 1379 1331 1254 1222 1189 1096 943 754 cm^{-1}; **^{1}H NMR** (400 MHz, Me_2C=O-d_6) δ (ppm) 9.51 (s, 1H), 8.85 (s, 1H), 7.44 (d, J = 7.4 Hz, 1H), 7.28 (td, J = 7.7, 1.1 Hz, 1H), 7.03 (td, J = 7.6, 0.7 Hz, 1H), 6.96 (t, J = 11.0 Hz, 1H), 5.46 (s, 1H), 4.41 (dd, J = 14.0, 6.1 Hz, 1H), 3.88 (dd, J = 14.0, 3.9 Hz, 1H) 2.58 (s, 3H). **^{13}C NMR** (100 MHz, Me_2C=O-d_6) δ (ppm) 200.4, 178.5, 142.5, 130.8, 130.7, 125.4, 123.3, 111.1, 75.0, 53.5, 18.05. **ESI-MS**: m/z: 269.1 $[M + H]^+$.

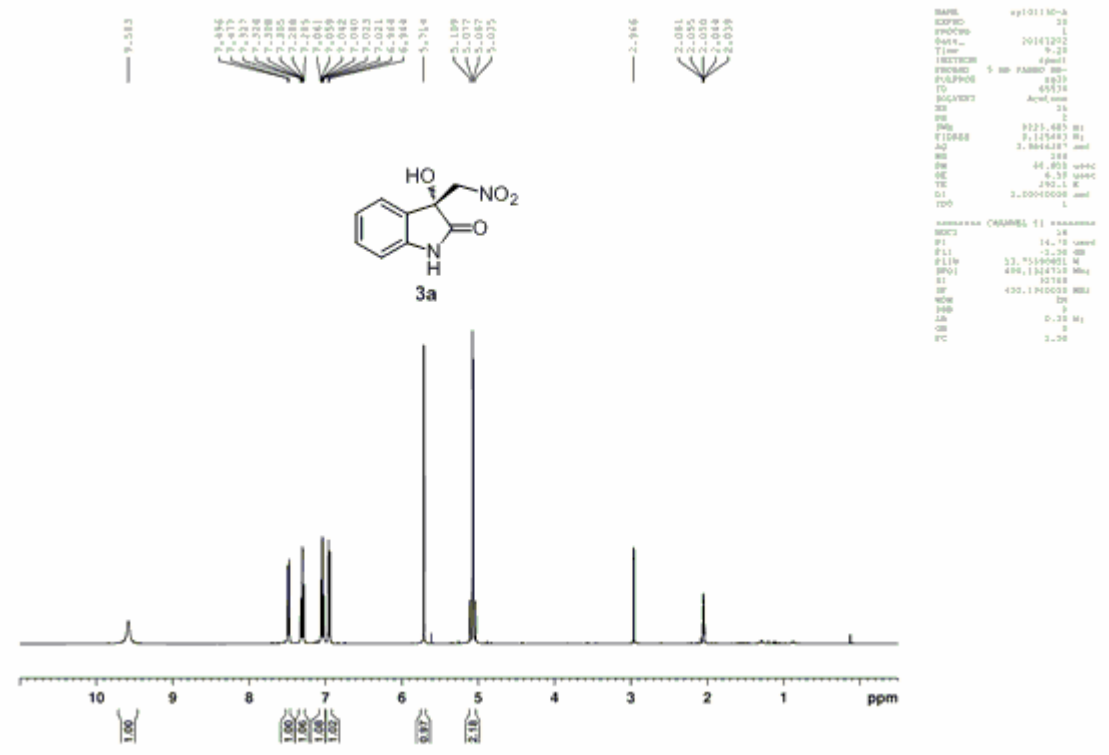
5. K. Monde, K. Sasaki, A. Shirata and M. Takasugi, *Phytochemistry*, 1991, **30**, 2915.

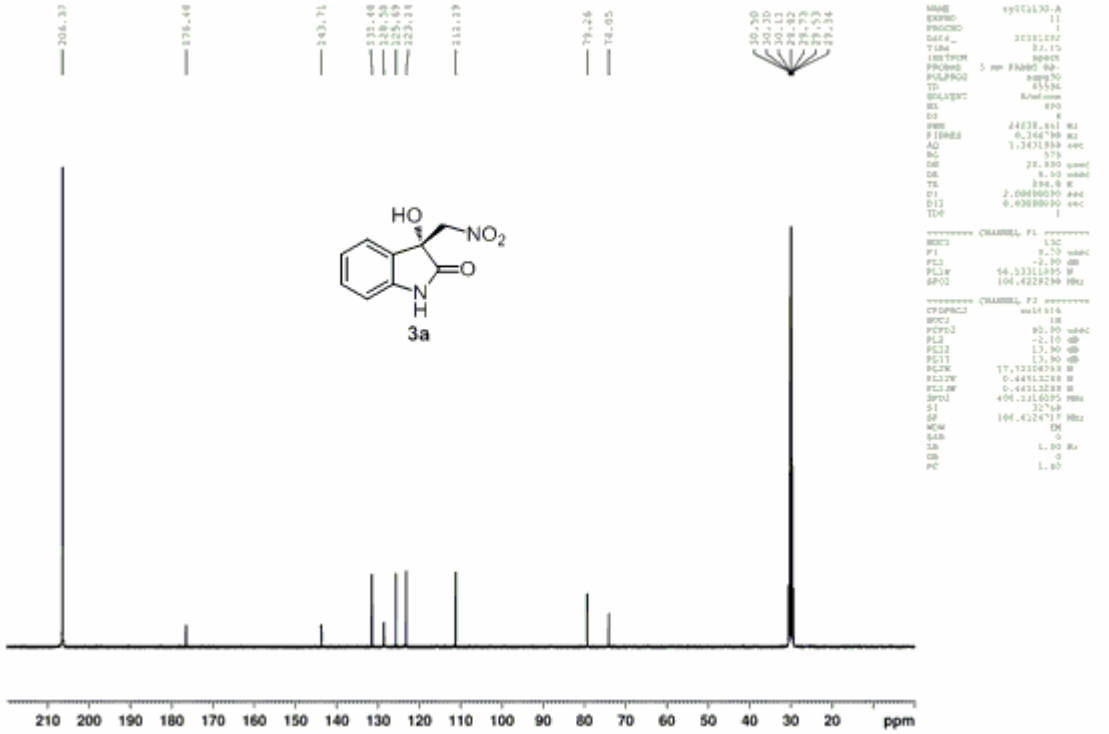
3. Crystal data and structure refinement for enantiopure product 3g



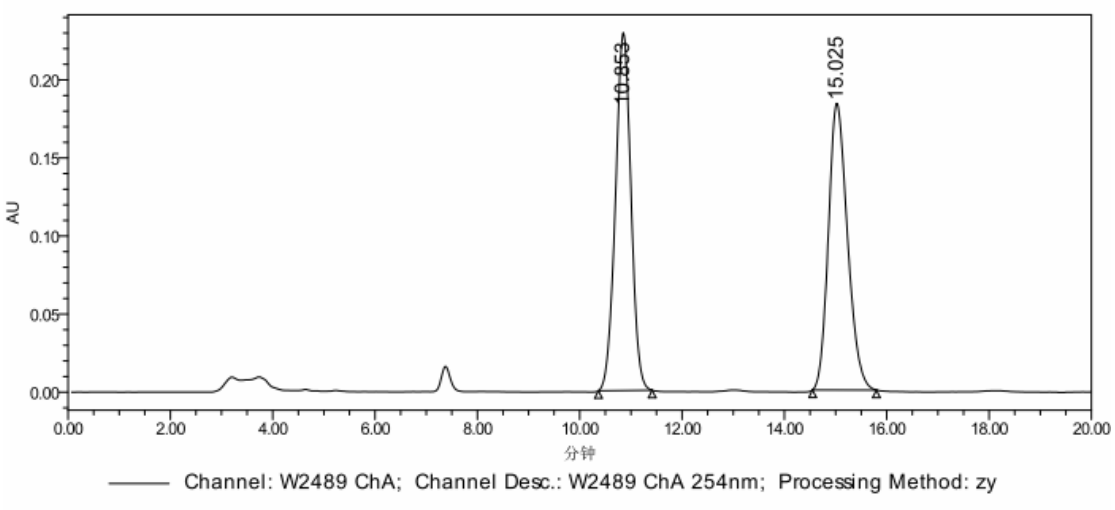
Compound reference	p21
Chemical formula	$C_9H_7BrN_2O_4$
Formula Mass	287.08
Crystal system	Monoclinic
a/Å	7.437(15)
b/Å	6.480(13)
c/Å	10.87(2)
α/°	90.00
β/°	90.185(17)
γ/°	90.00
Unit cell volume/Å^3	523.6(18)
Temperature/K	296(2)
Space group	*P2(1)*
No. of formula units per unit cell, *Z*	2
No. of reflections measured	3567
No. of independent reflections	1895
R_{int}	0.0669
Final R_1 values ($I > 2\sigma(I)$)	0.0488
Final $wR(F^2)$ values ($I > 2\sigma(I)$)	0.1074
Final R_1 values (all data)	0.0776
Final $wR(F^2)$ values (all data)	0.1191
Goodness of fit on F^2	0.981
Flack parameter	0.024(19)
CCDC number	828228

4. NMR spectra and HPLC chromatograms

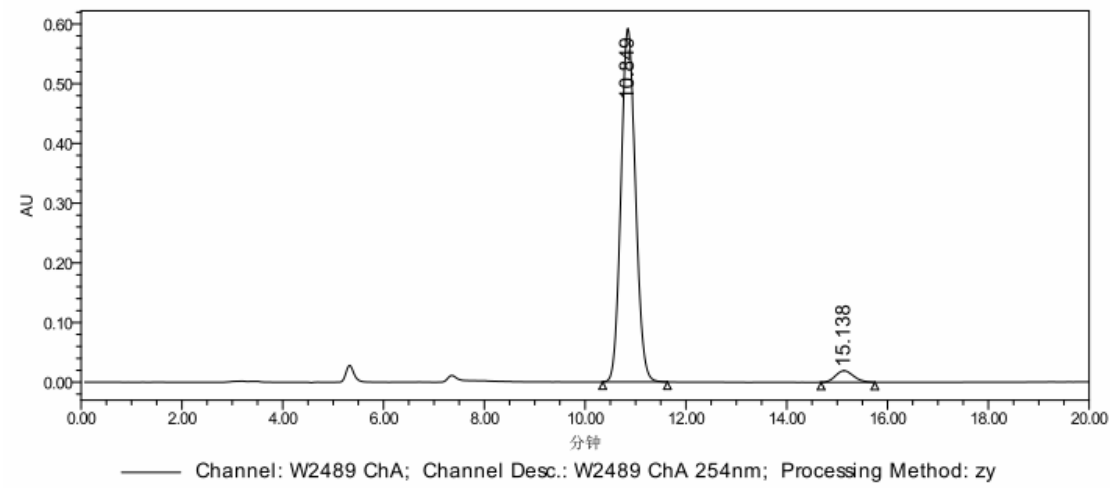




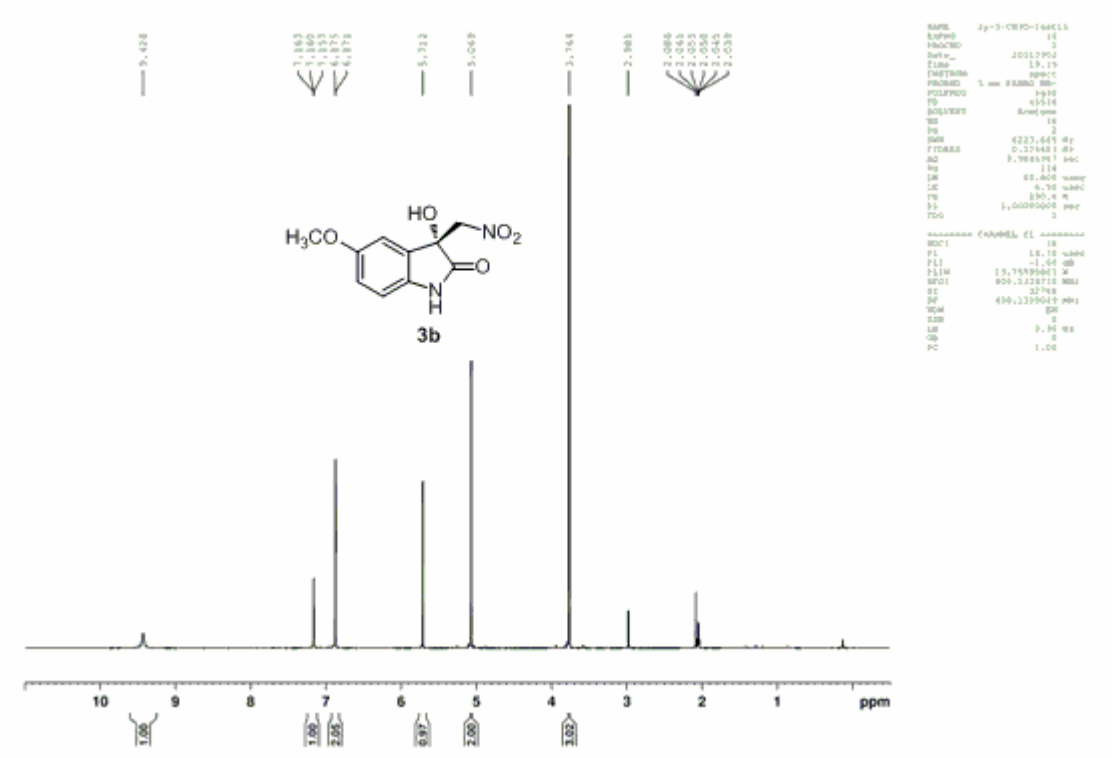
3a racemic



3a chiral

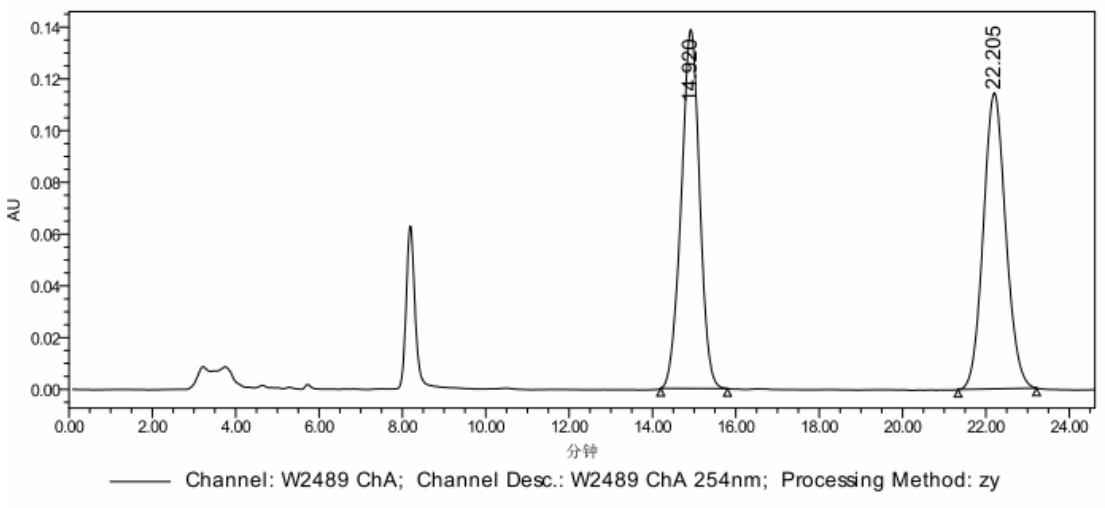


	Retention Time	Area	% Area	Height
1	10.849	11791646	96.10	591896
2	15.138	479160	3.90	19217

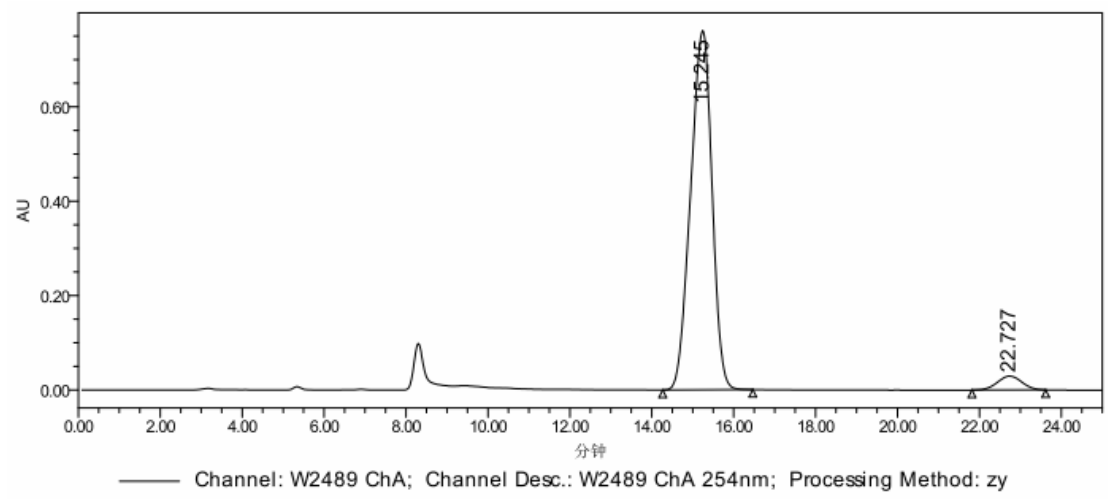

HO
NO2
H3CO
O
N
H
3b
ppm


HO
NO2
H3CO
O
N
H
3b
ppm

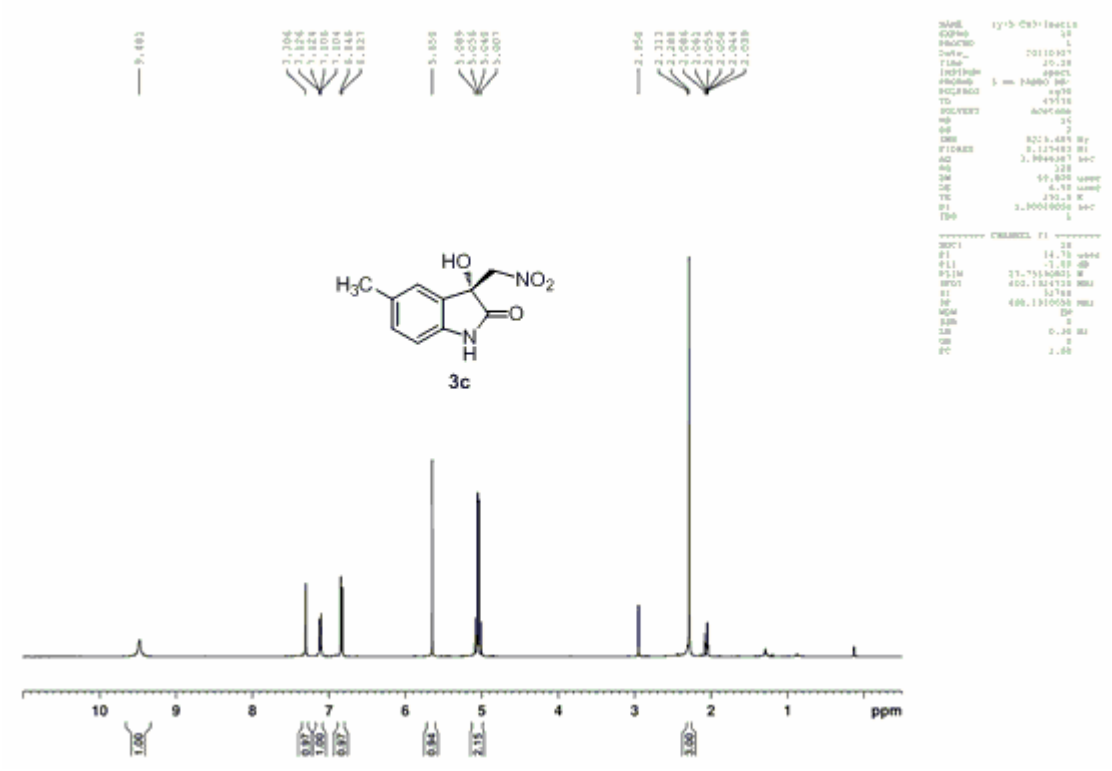
3b racemic

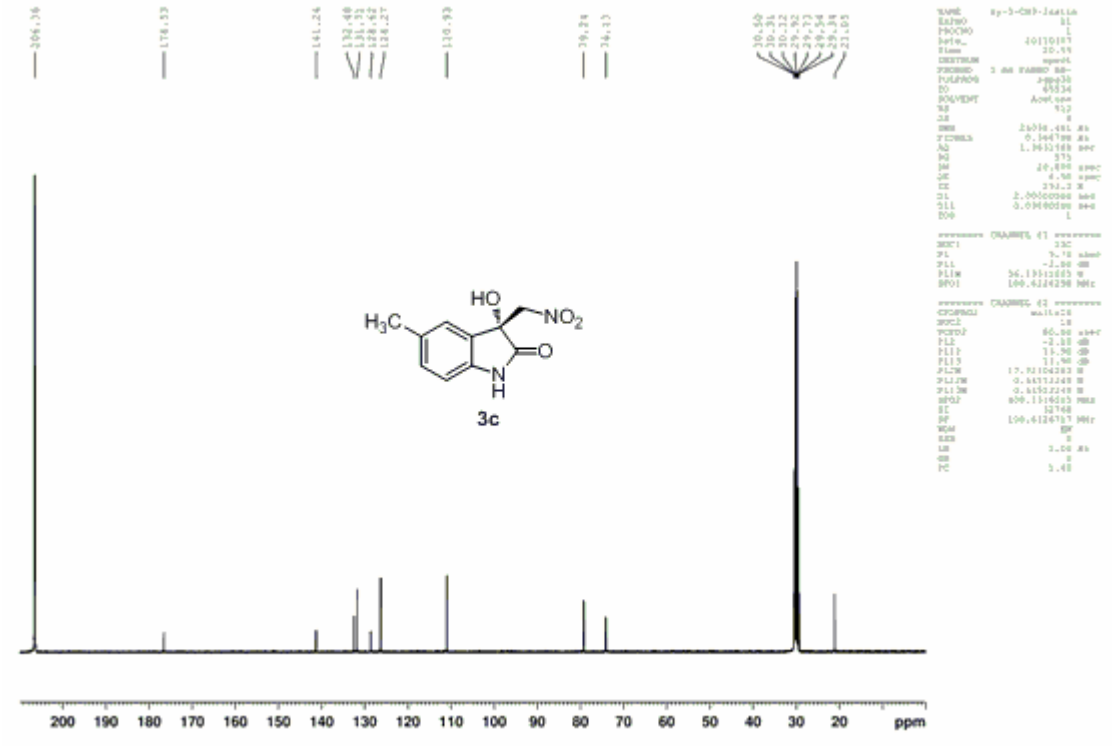


3b chiral

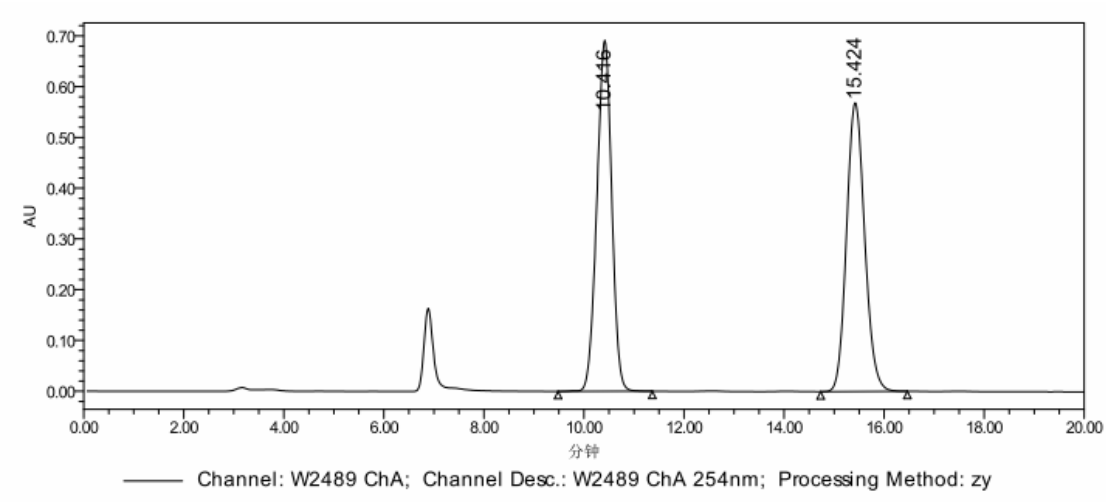


	Retention Time	Area	% Area	Height
1	15.245	27630868	95.78	760897
2	22.727	1218318	4.22	29417

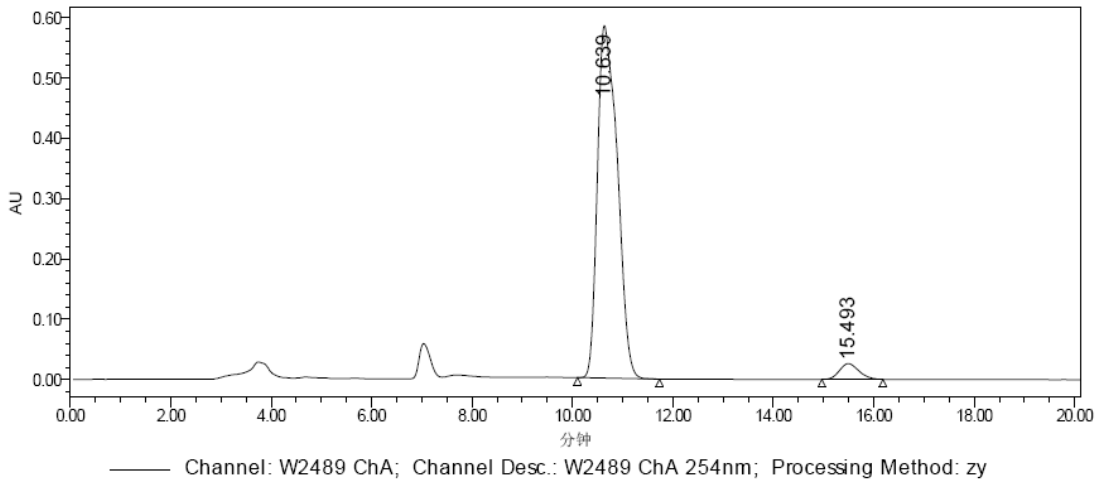

HO
NO2
H3C
O
N
H
3c
10
9
8
7
6
5
4
3
2
1
ppm


HO
NO2
H3C
O
N
H
3c
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

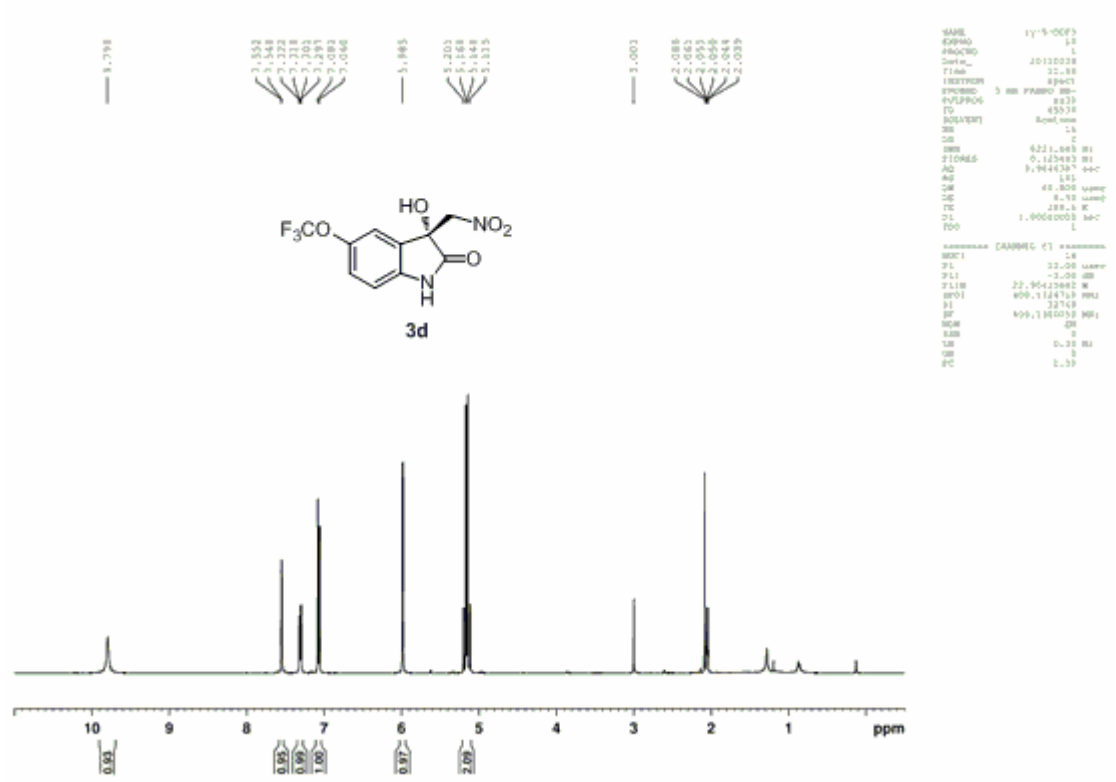
3c racemic

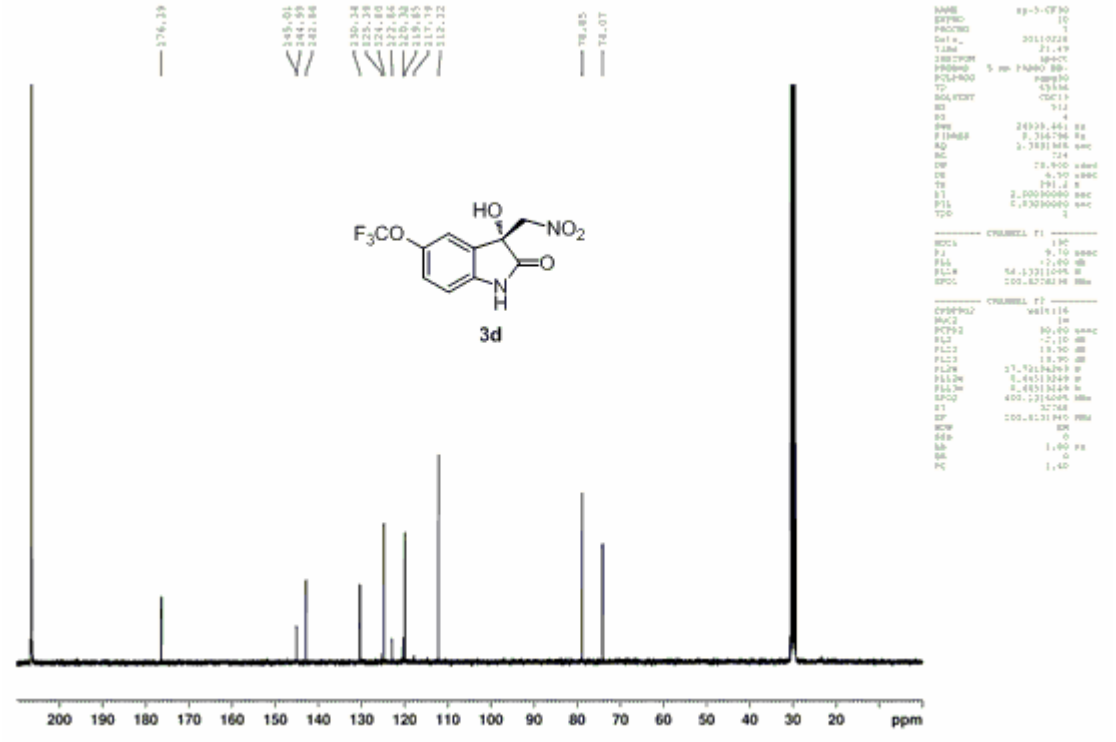


3c chiral

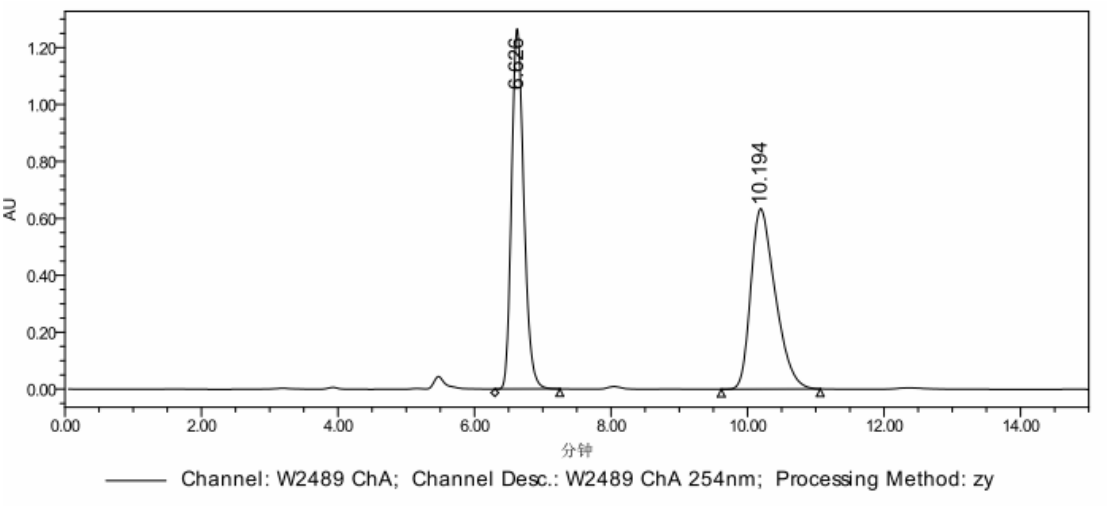


	Retention Time	Area	% Area	Height
1	10.639	16028350	95.78	583686
2	15.493	707042	4.22	26261

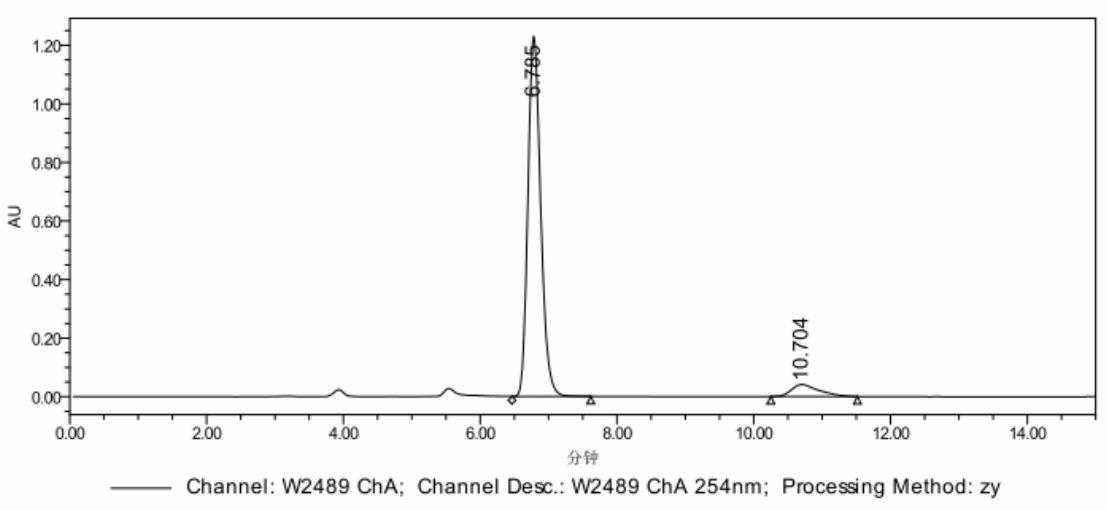

HO
F3CO
NO2
O
N
H
3d
ppm


HO
F3CO
NO2
O
N
H
3d
ppm

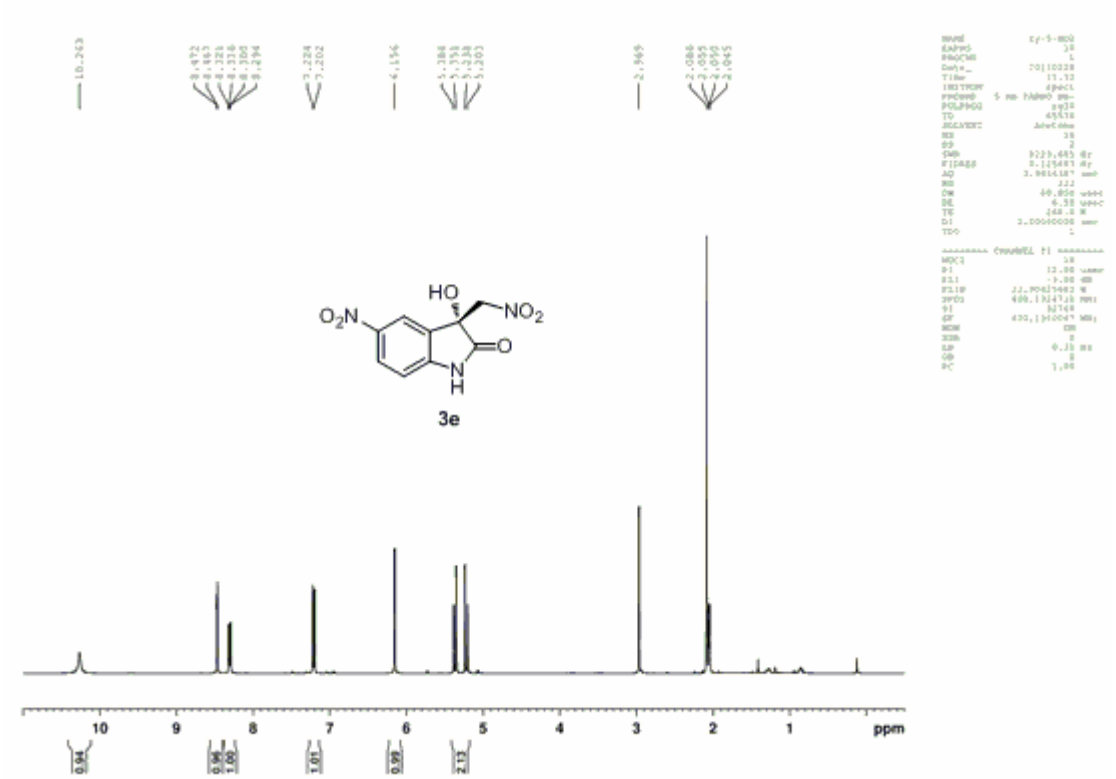
3d racemic

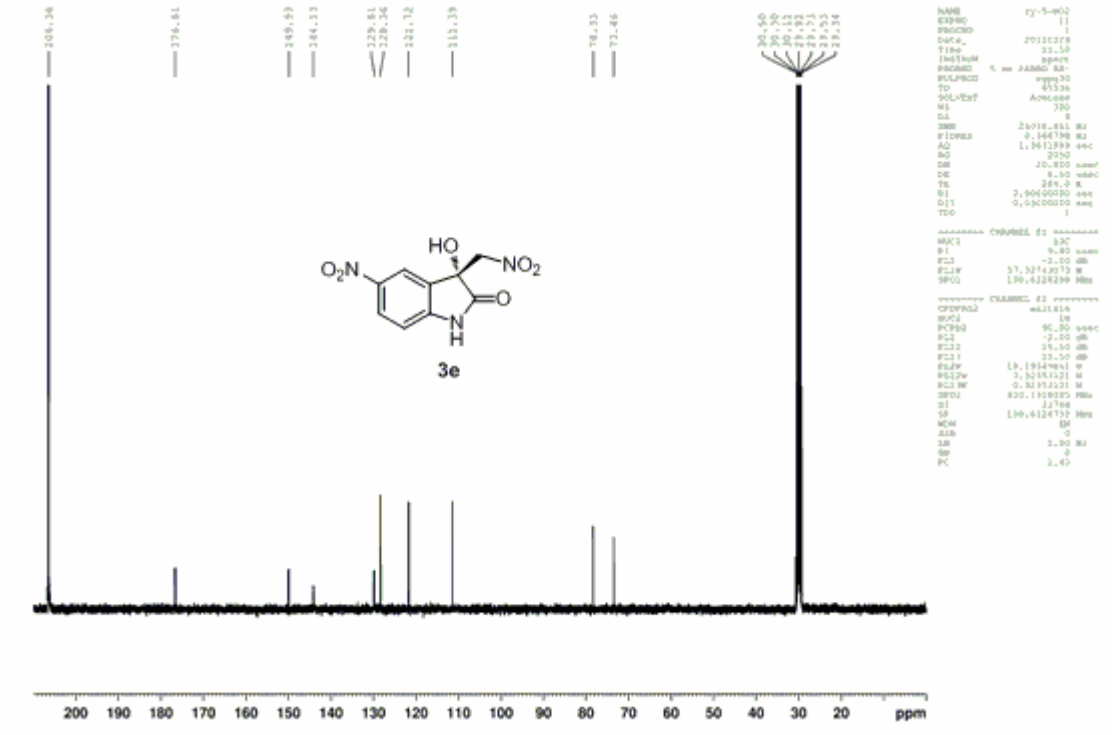


3d chiral

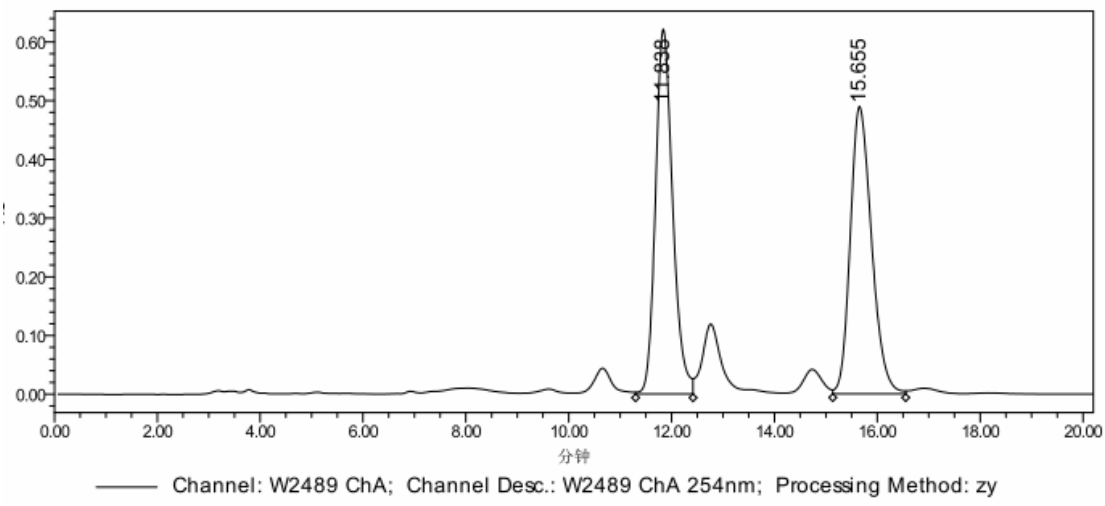


	Retention Time	Area	% Area	Height
1	6.785	15973513	93.25	1229268
2	10.704	1155652	6.75	41297

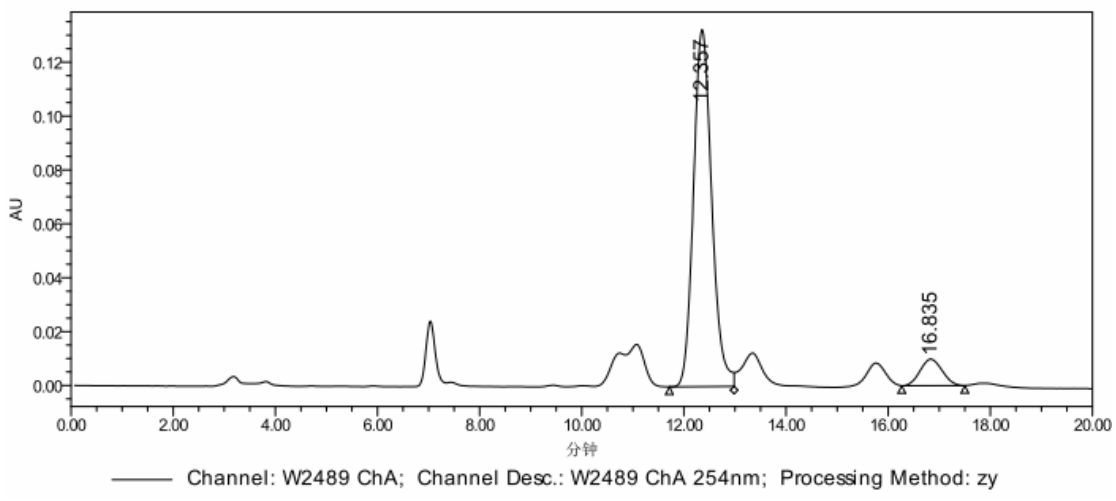

HO
O_2N
NO_2
O
N
H
3e
ppm


HO
O_2N
NO_2
O
N
H
3e
ppm

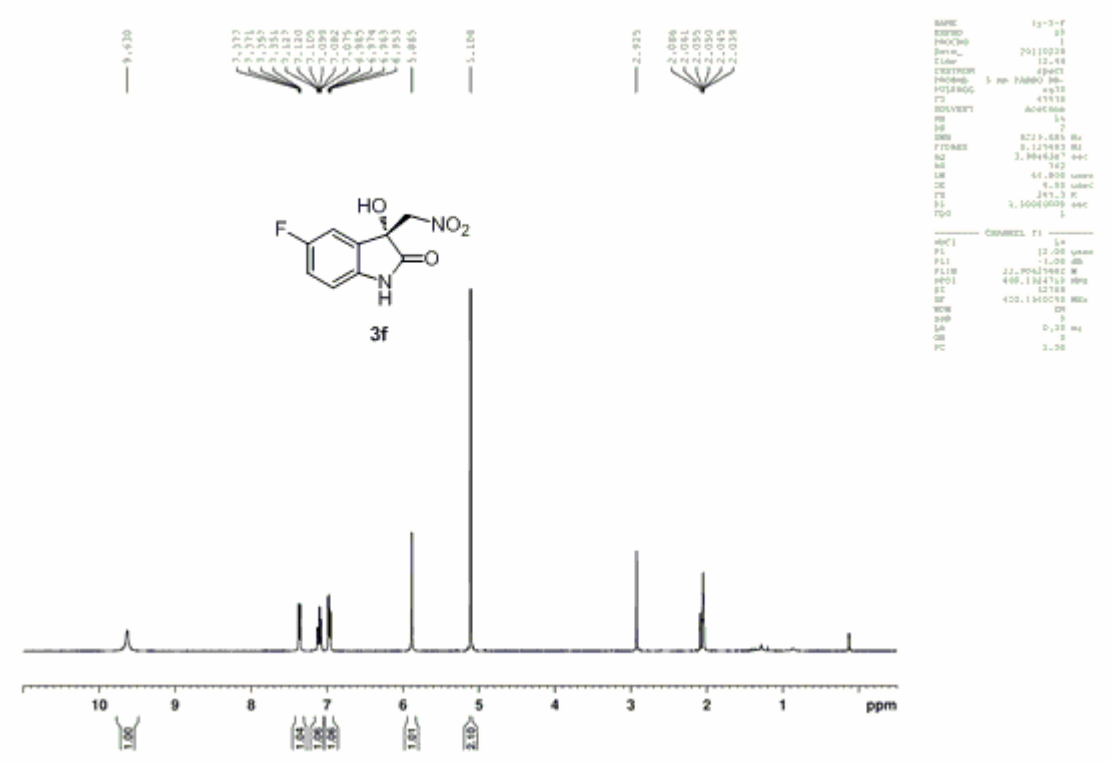
3e racemic

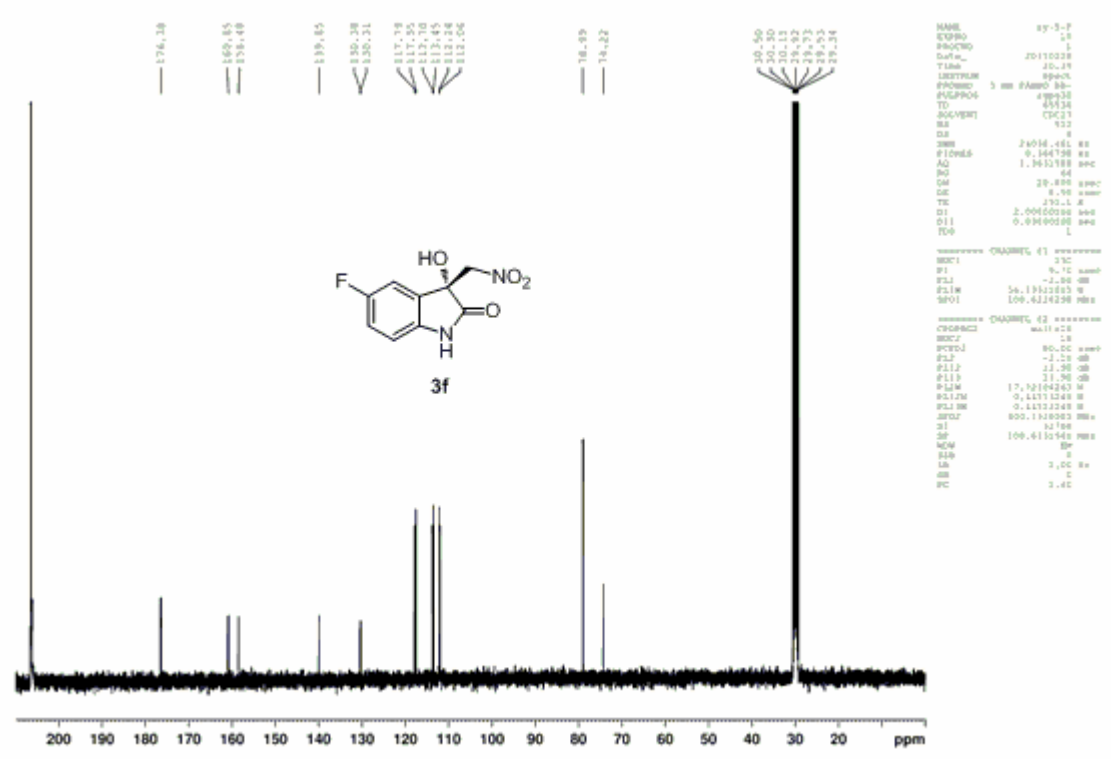


3e chiral

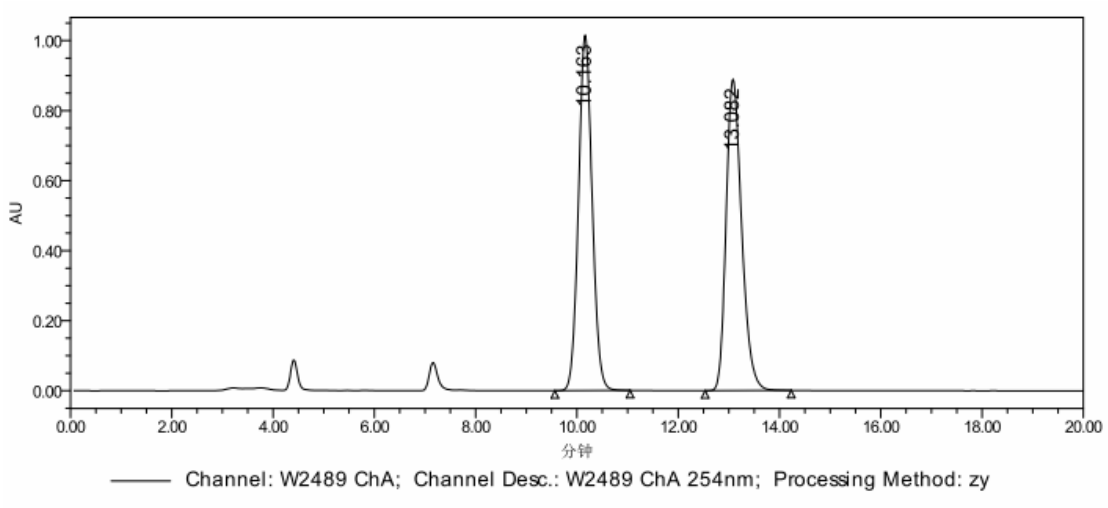


	Retention Time	Area	% Area	Height
1	12.357	3291733	91.84	132451
2	16.835	292589	8.16	9837

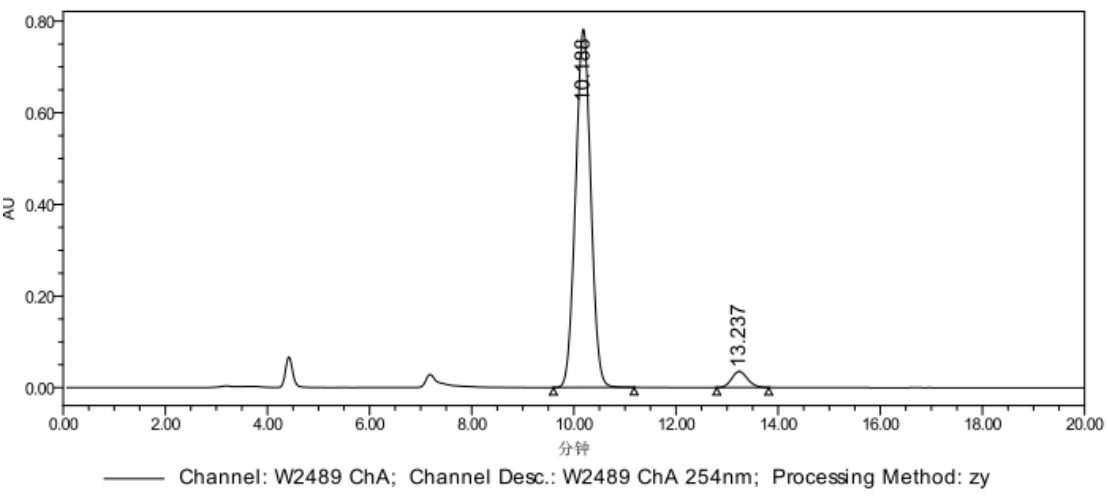

HO
F
NO2
O
N
H
3f
10
9
8
7
6
5
4
3
2
1
ppm


HO
F
NO2
O
N
H
3f
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

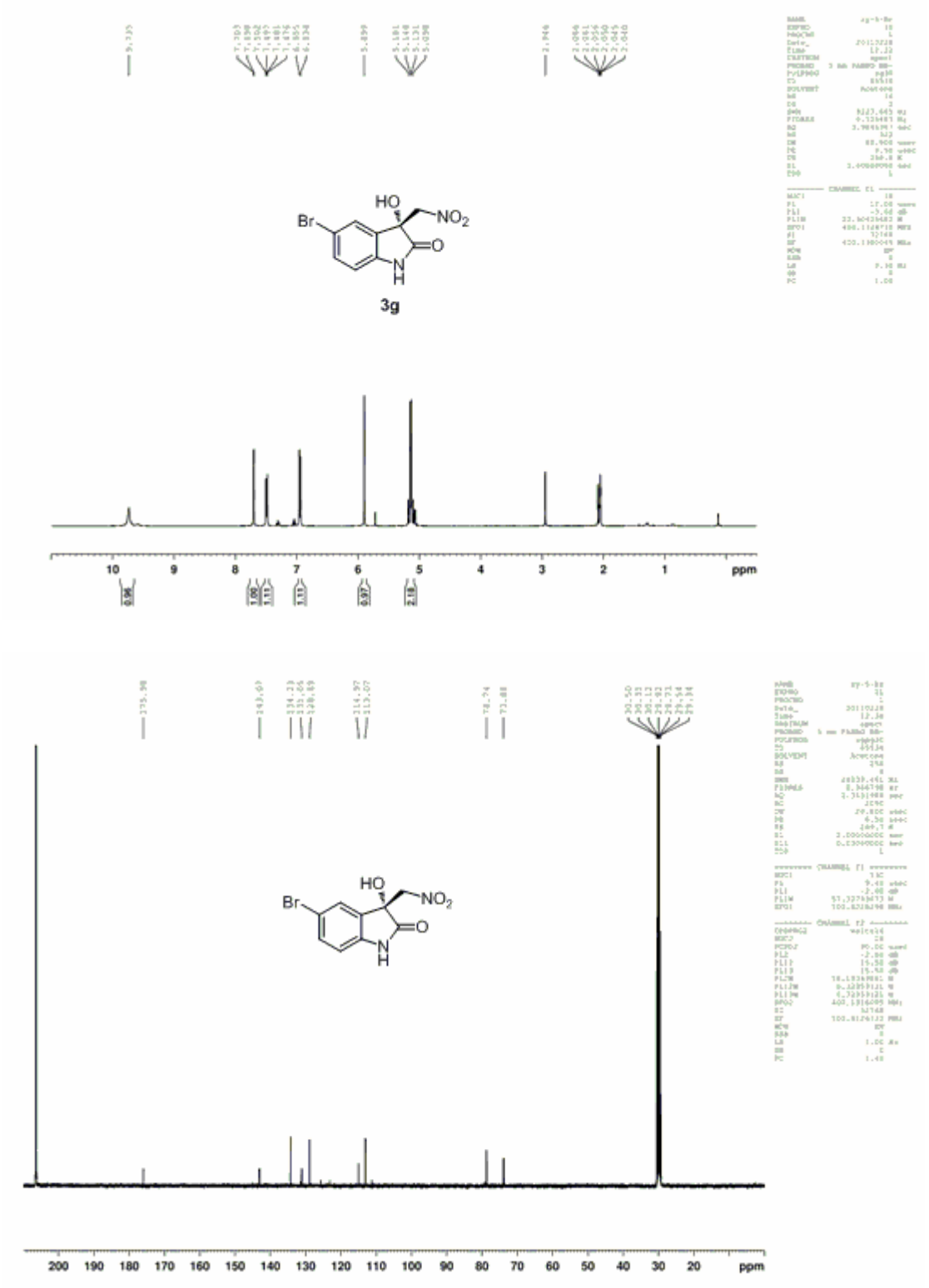
3f racemic



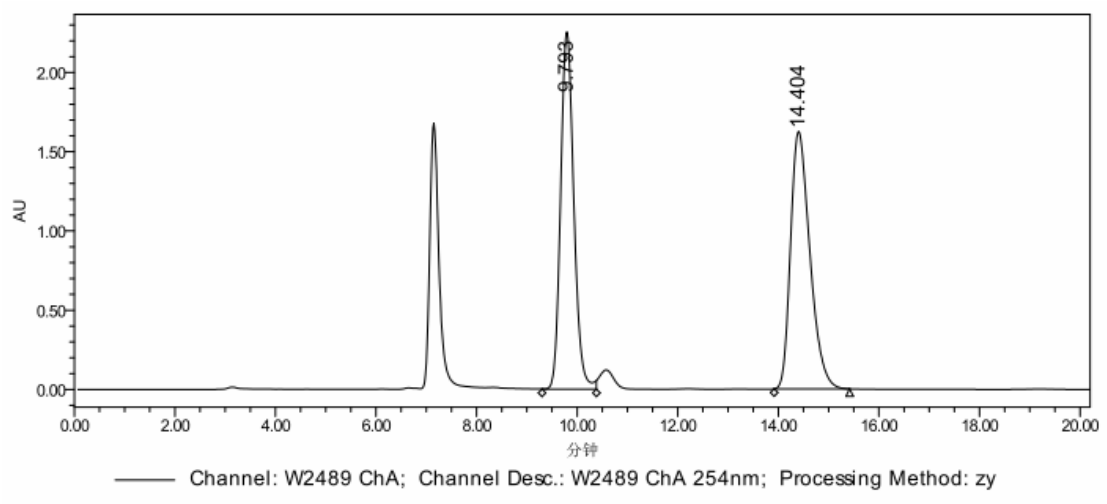
3f chiral



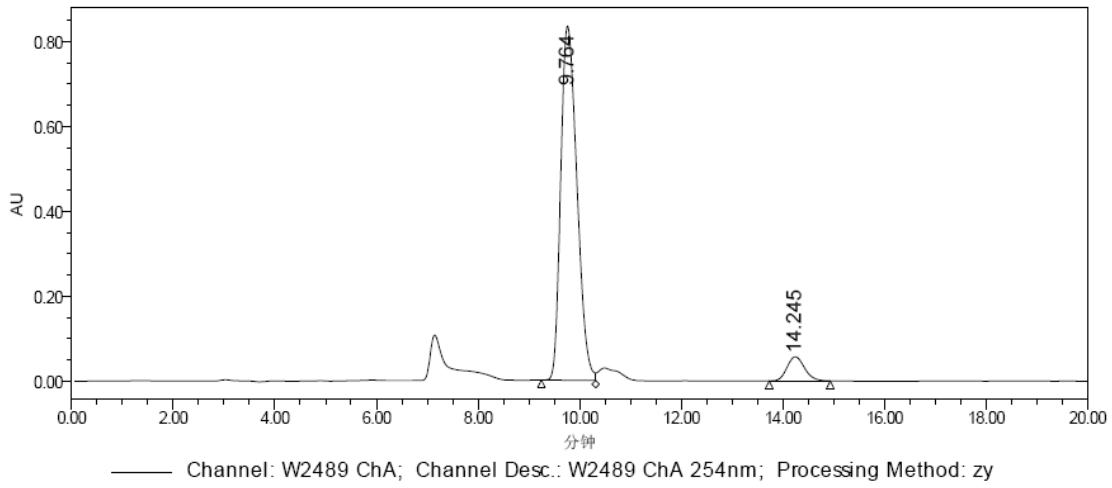
	Retention Time	Area	% Area	Height
1	10.188	16192217	95.51	781798
2	13.237	760789	4.49	35349


HO
Br
NO2
O
N
H
3g
10
9
8
7
6
5
4
3
2
1
ppm
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

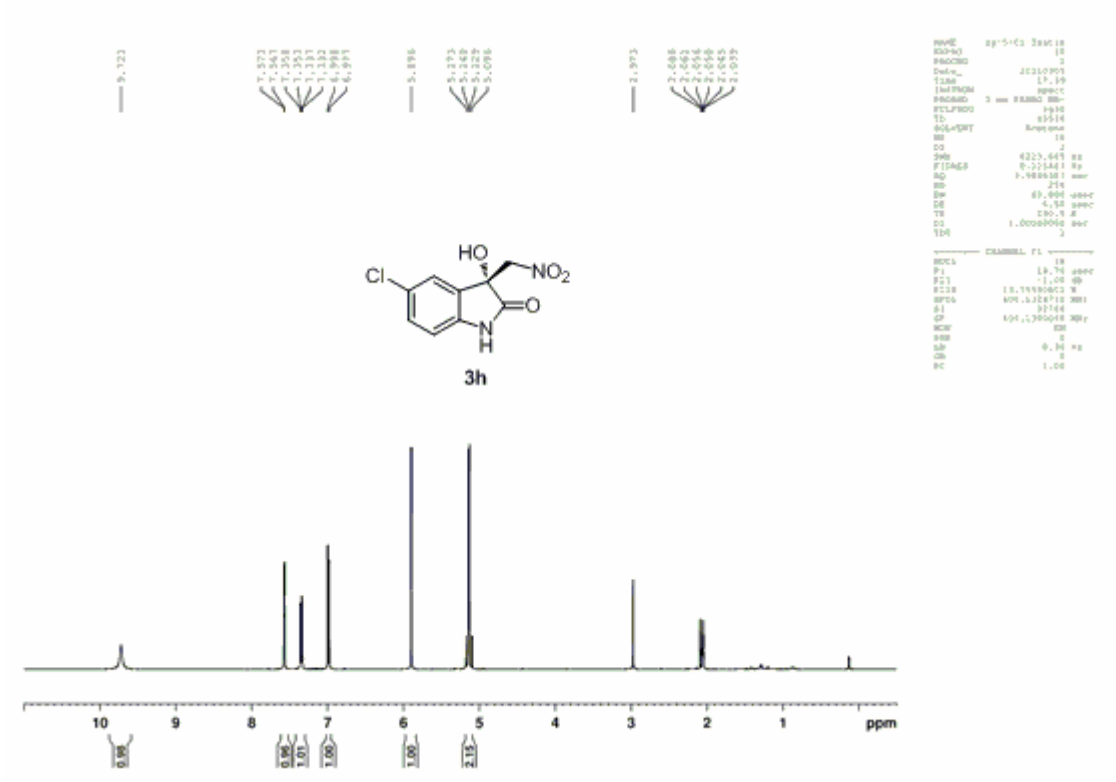
3g racemic

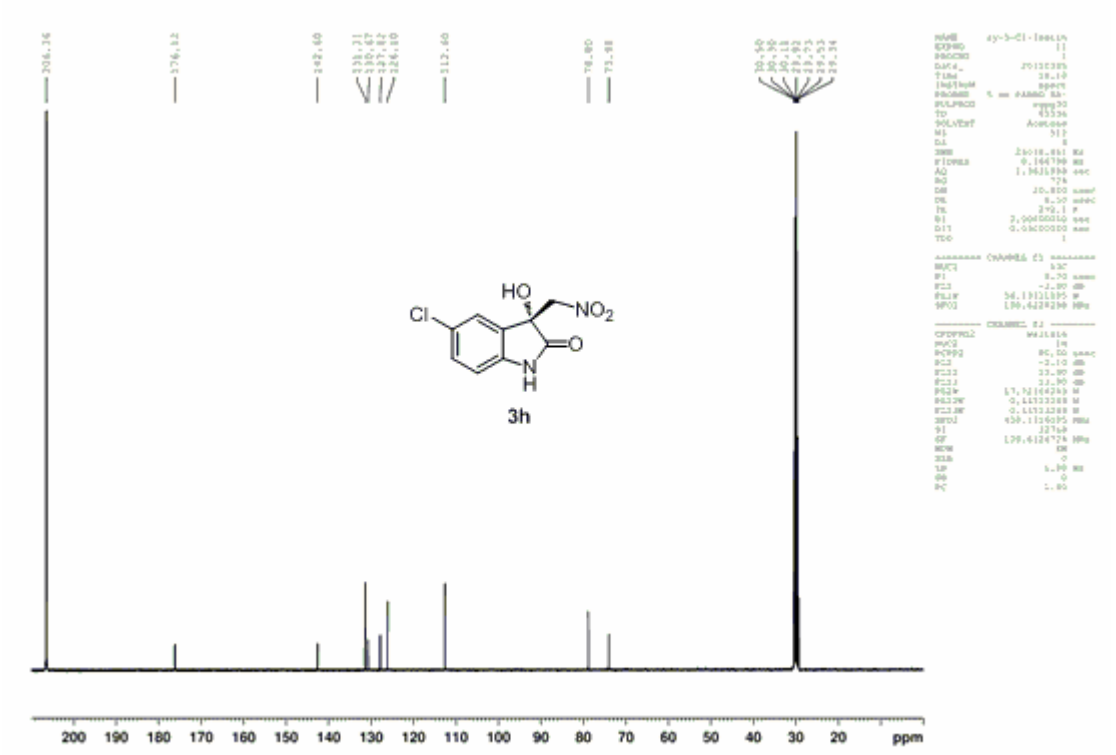


3g chiral

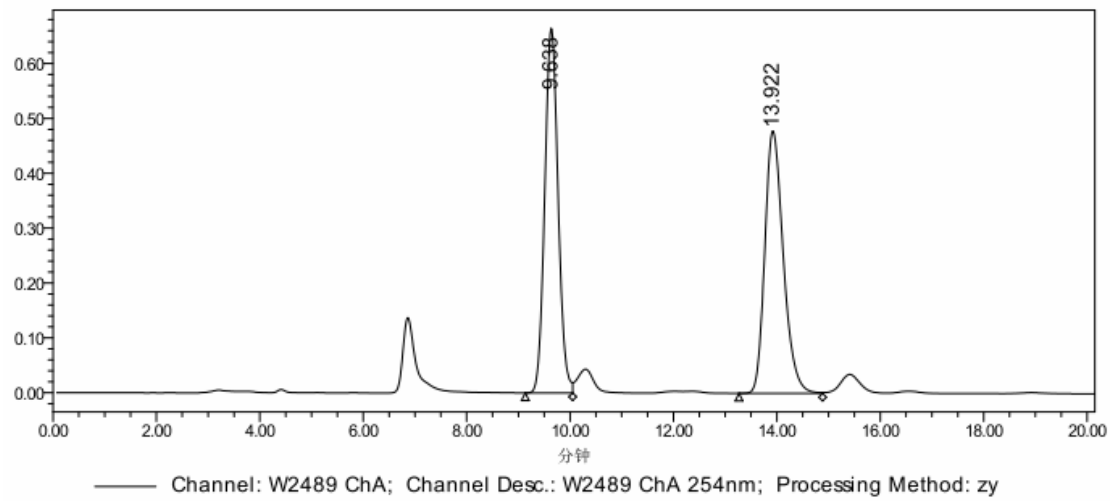


	Retention Time	Area	% Area	Height
1	9.764	18487819	93.12	835079
2	14.245	1364906	6.88	57049

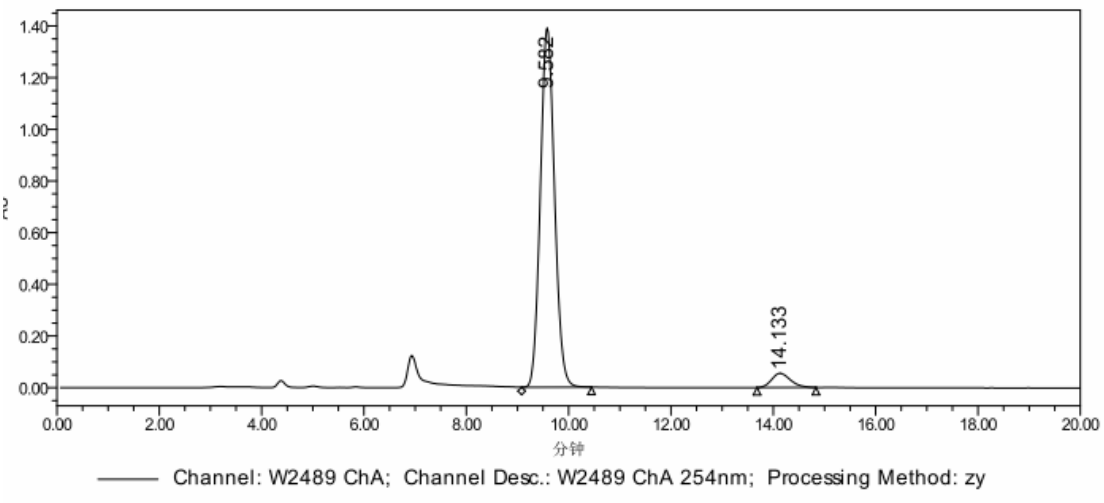




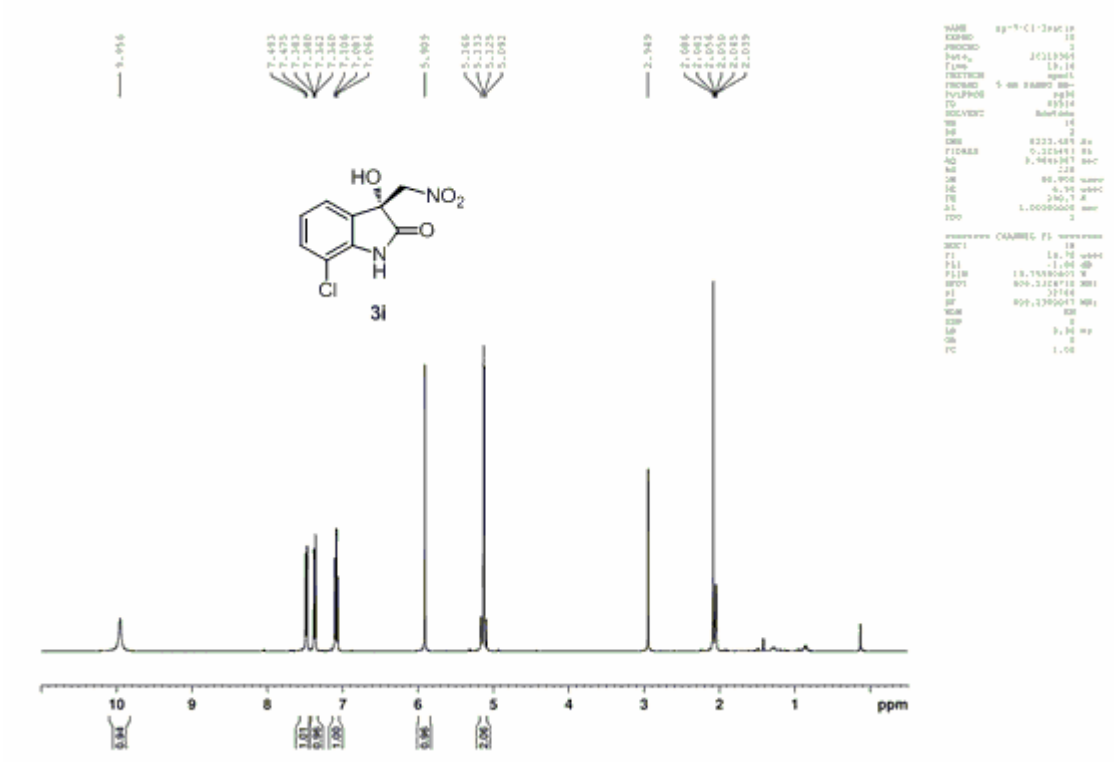
3h racemic

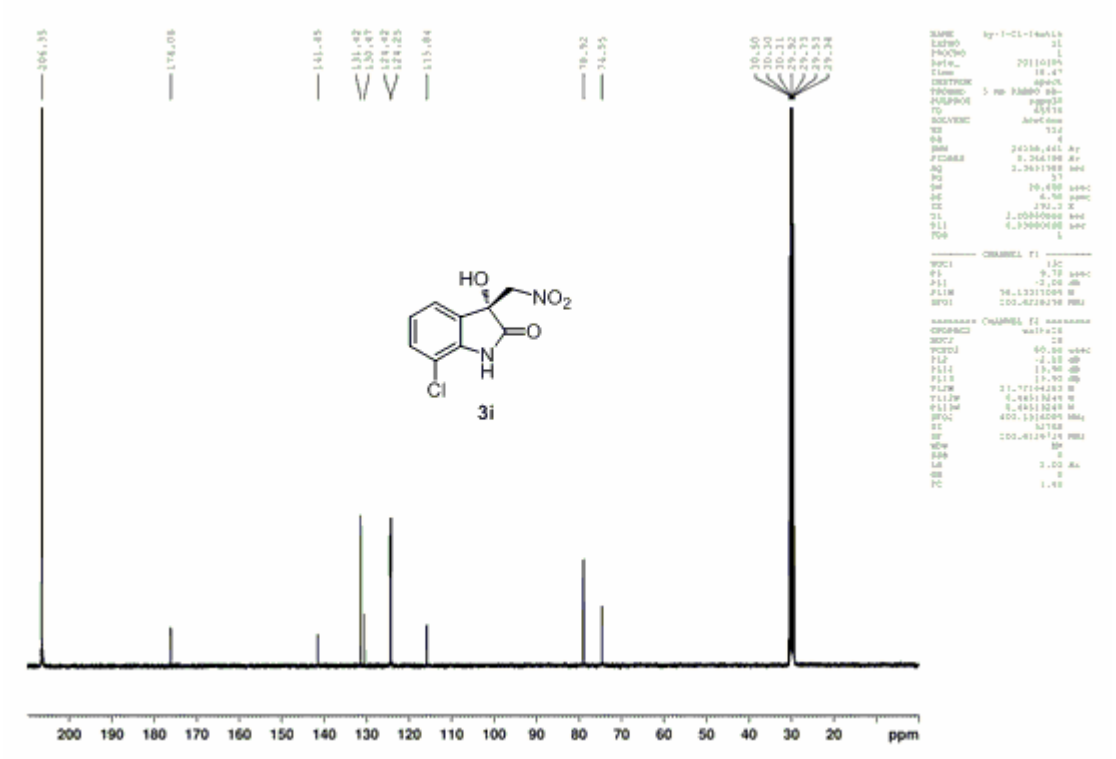


3h chiral

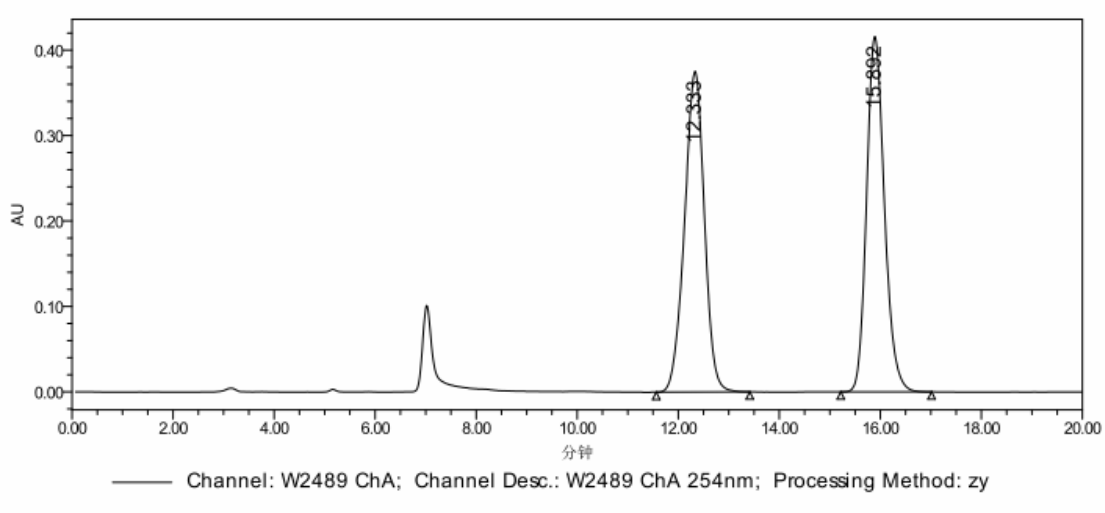


	Retention Time	Area	% Area	Height
1	9.582	26710512	95.03	1389681
2	14.133	1397104	4.97	54946

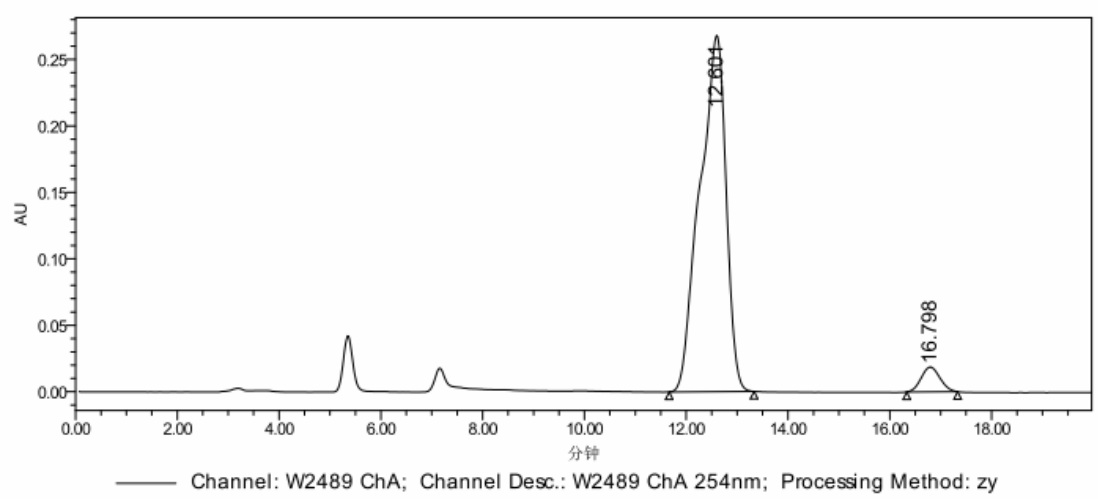

HO
NO2
O
N
H
Cl
3i
10
9
8
7
6
5
4
3
2
1
ppm


HO
NO2
O
N
H
Cl
3i
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

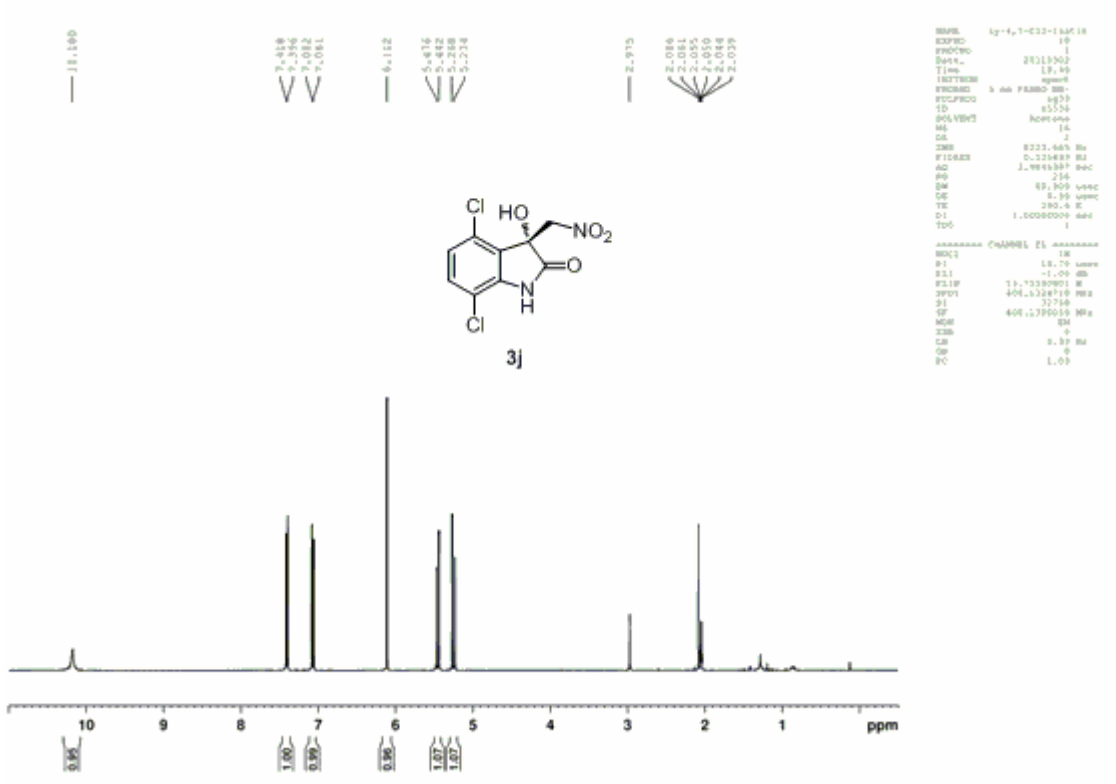
3i racemic

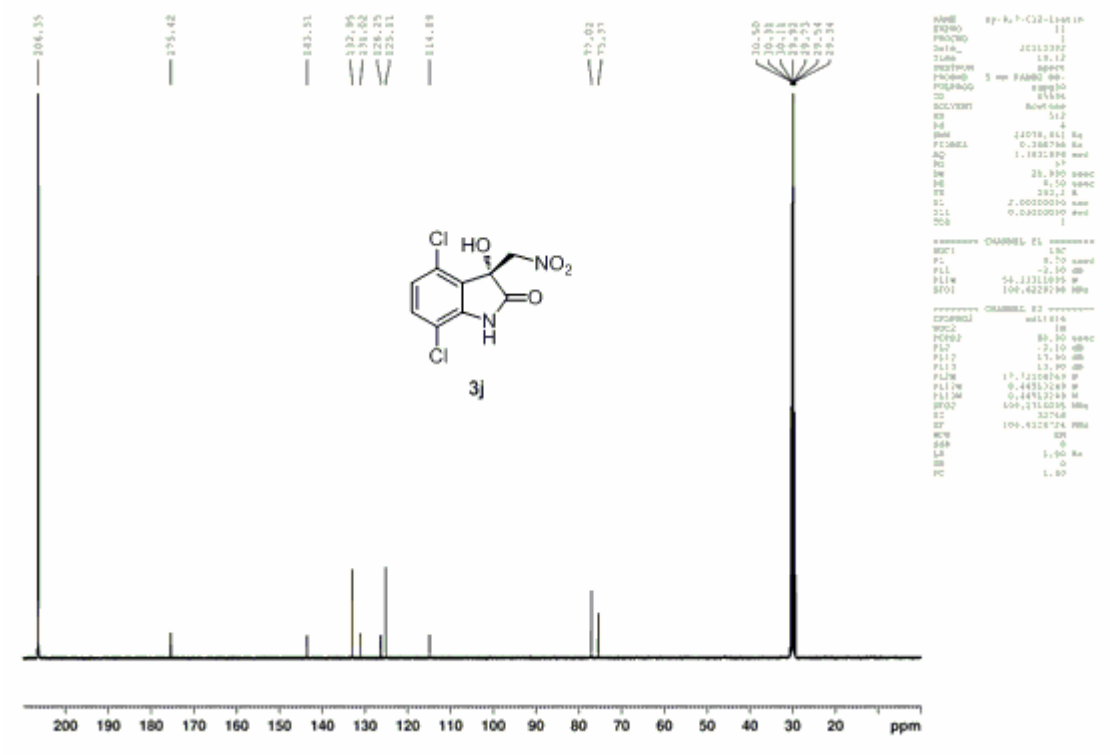


3i chiral

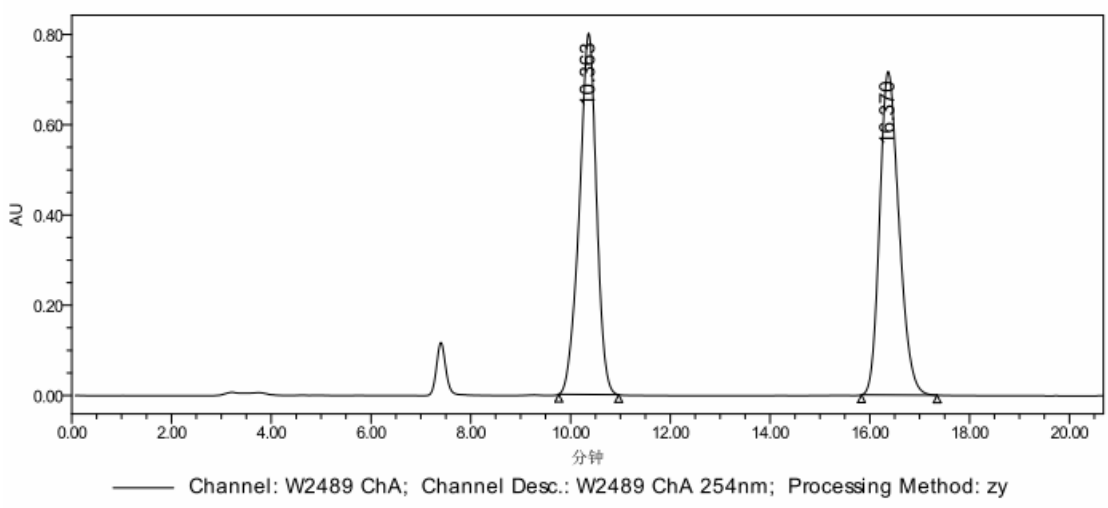


	Retention Time	Area	% Area	Height
1	12.601	9569166	95.26	267902
2	16.798	476576	4.74	18558

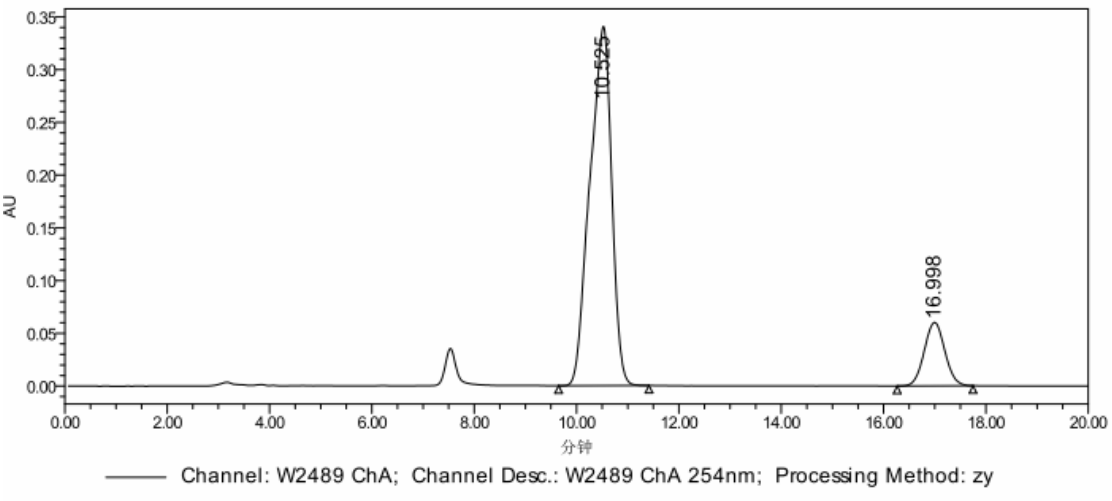

Cl
HO
NO2
O
N
H
Cl
3j
10
9
8
7
6
5
4
3
2
1
ppm


Cl
HO
NO2
O
N
H
Cl
3j
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

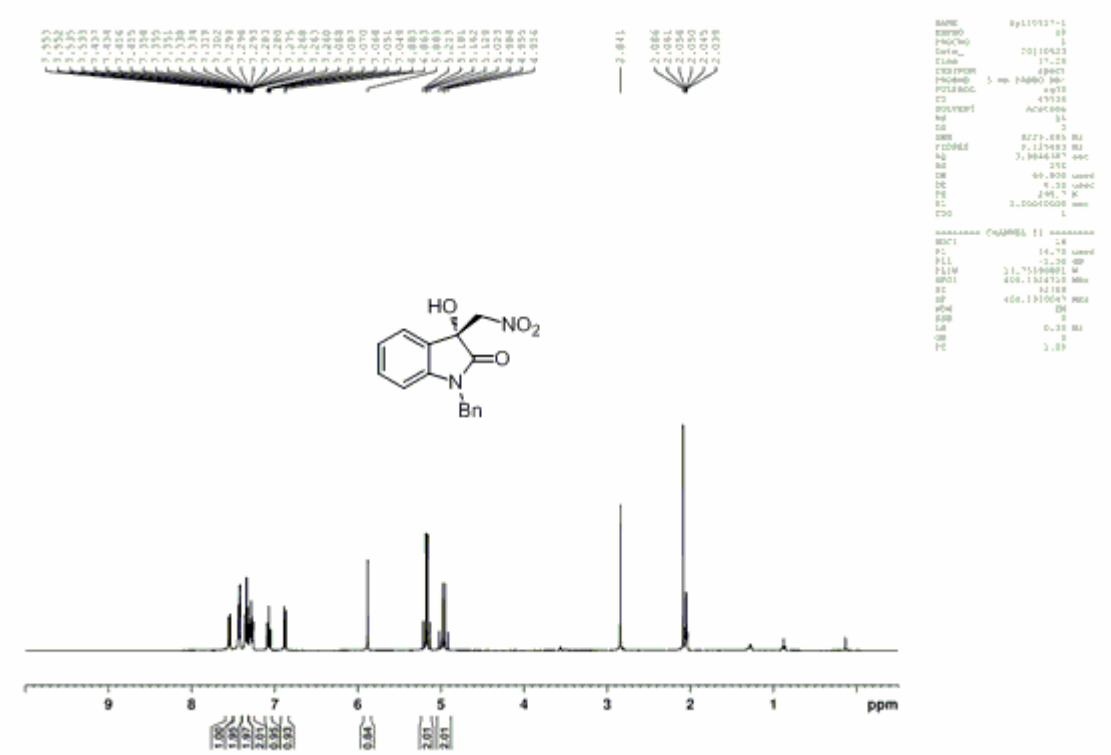
3j racemic

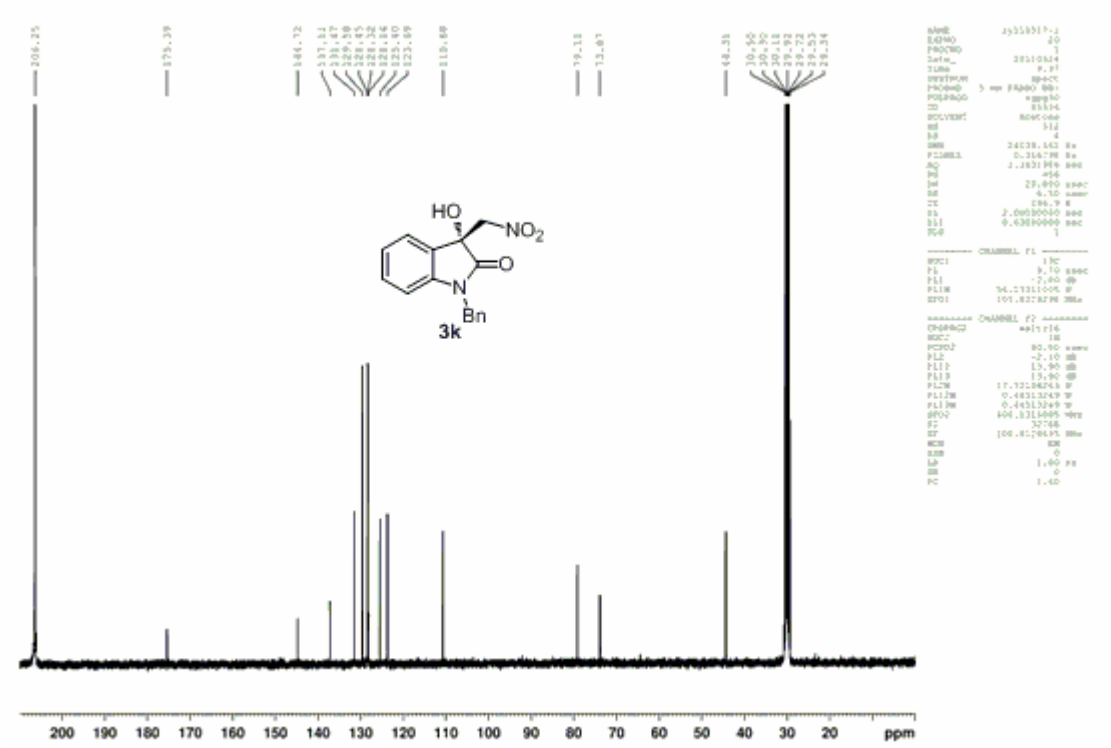


3j chiral

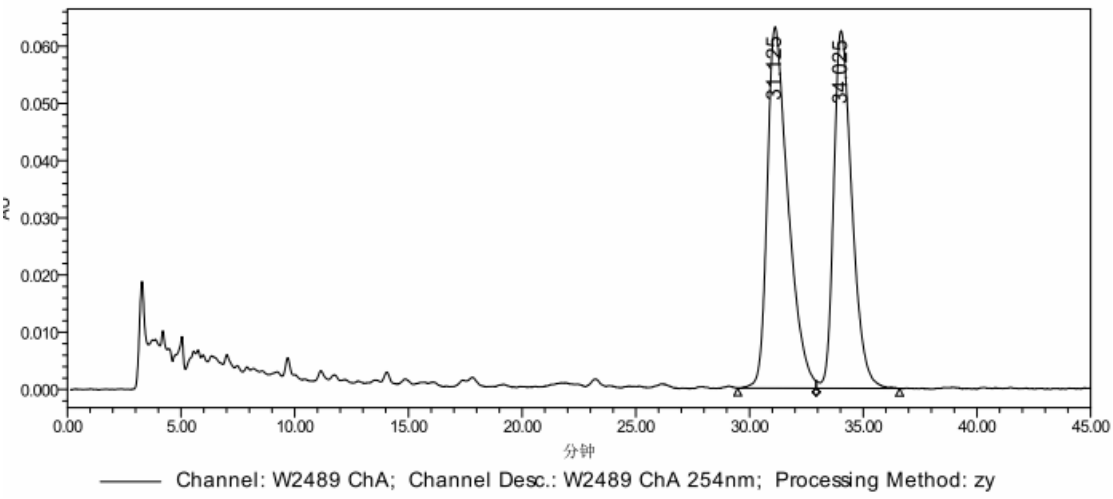


	Retention Time	Area	% Area	Height
1	10.525	10063760	85.67	340546
2	16.998	1682918	14.33	60050

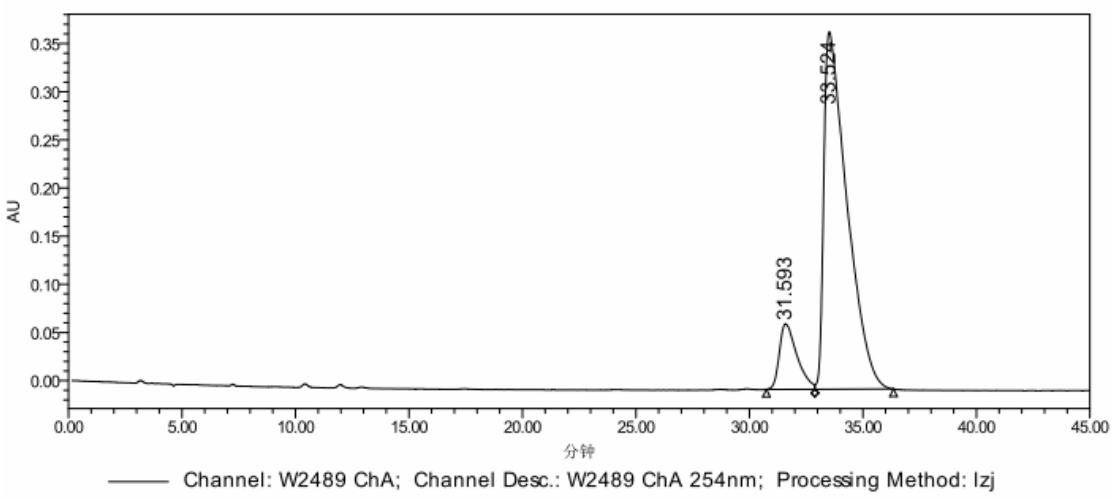

HO
NO2
O
N
Bn
9
8
7
6
5
4
3
2
1
ppm


HO
NO2
O
N
Bn
3k
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

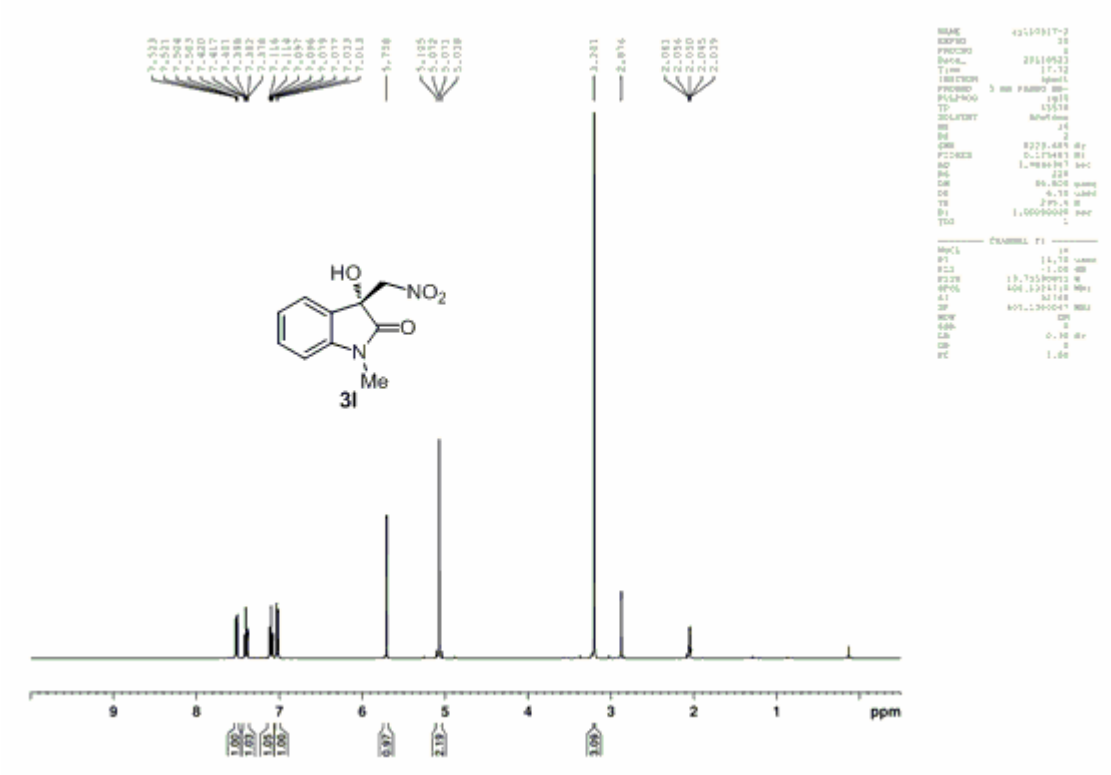
3k racemic

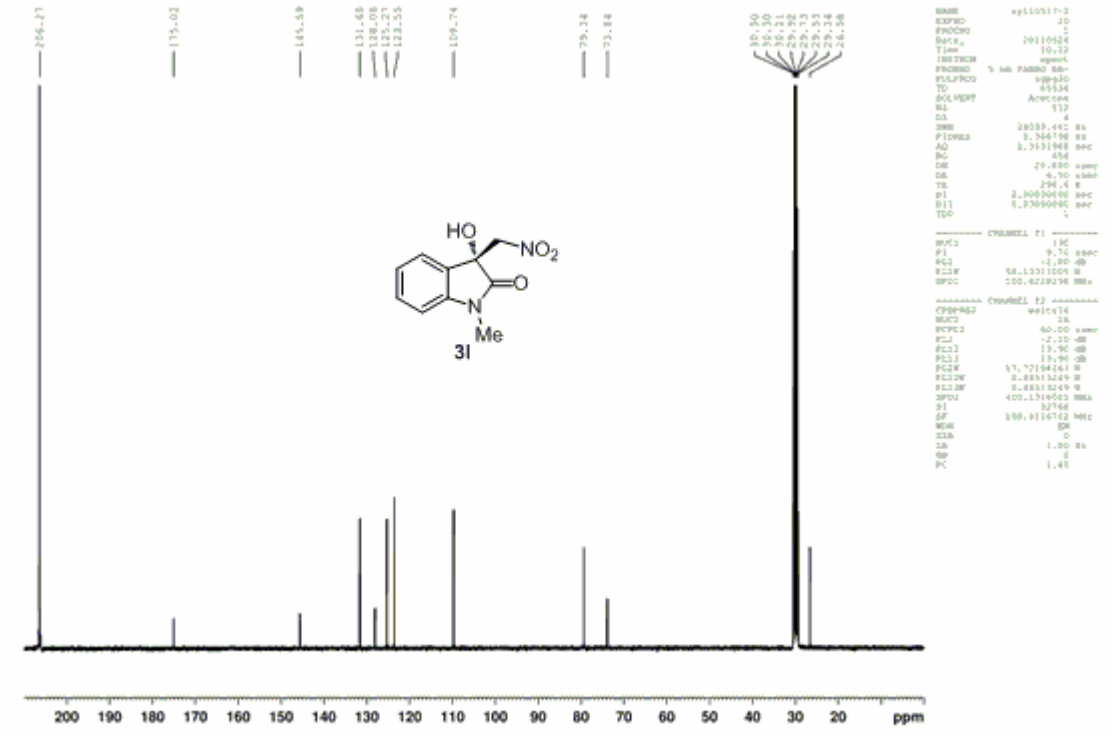


3k chiral

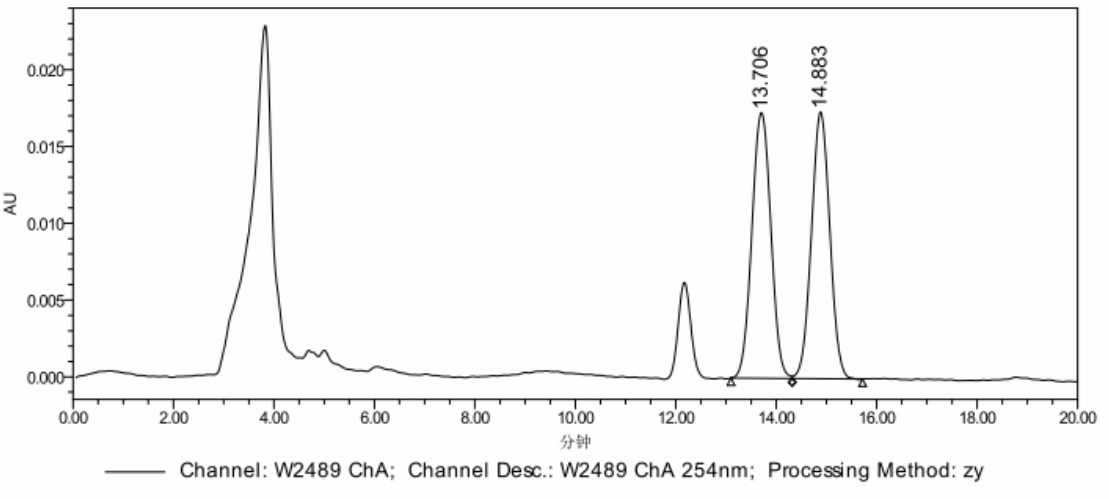


	Retention Time	Area	% Area	Height
1	31.593	3645669	12.17	67851
2	33.524	26305201	87.83	370864

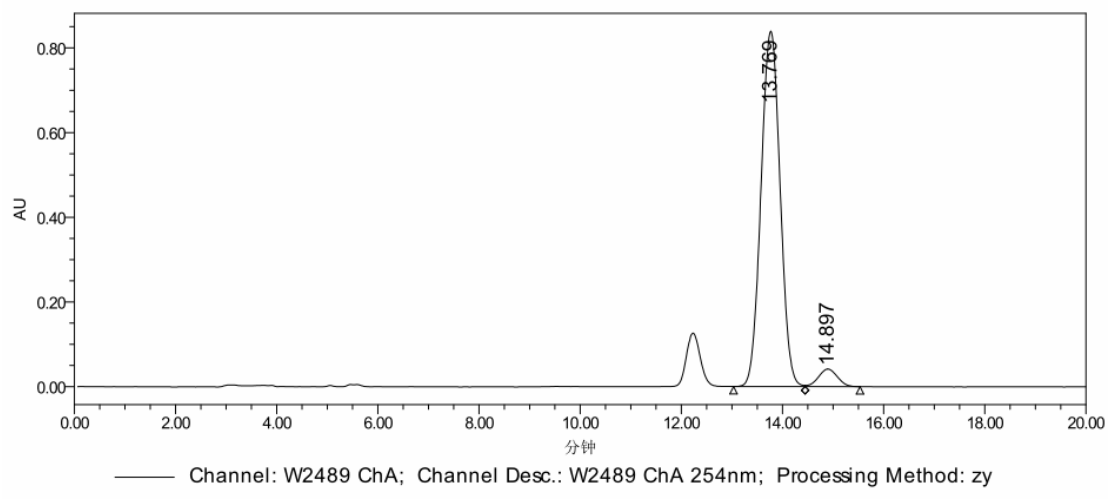

HO
NO2
O
N
Me
3l
ppm


HO
NO2
O
N
Me
3l
ppm

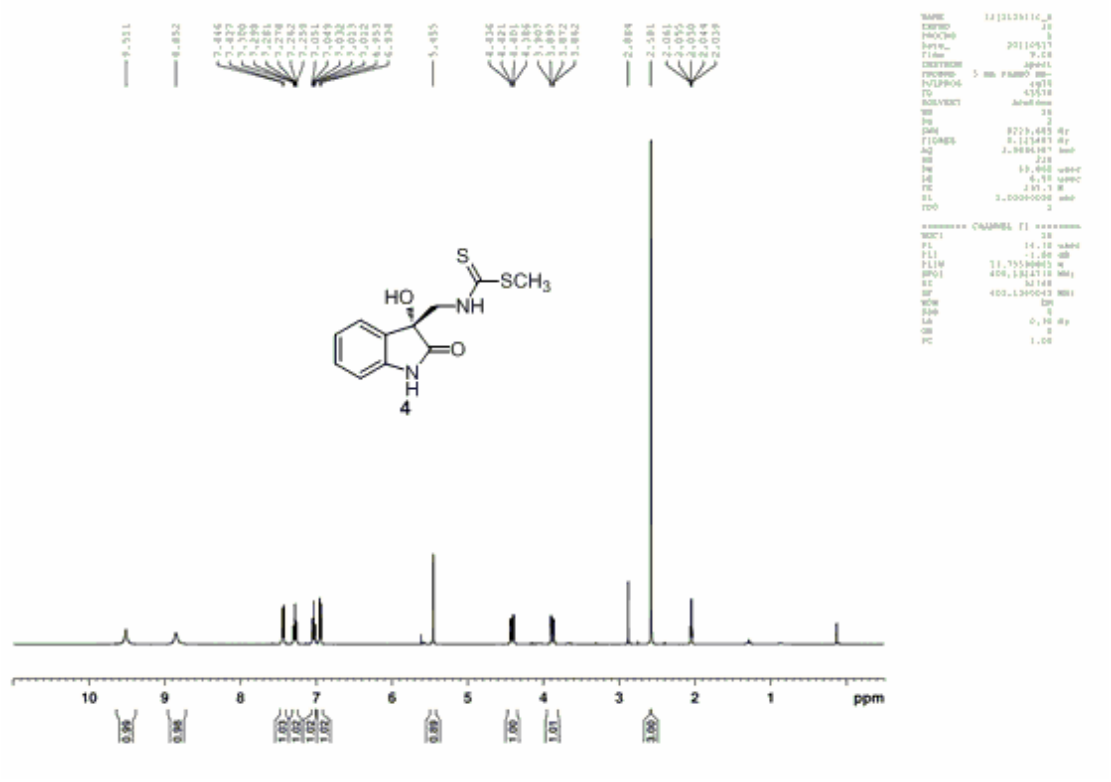
3l racemic

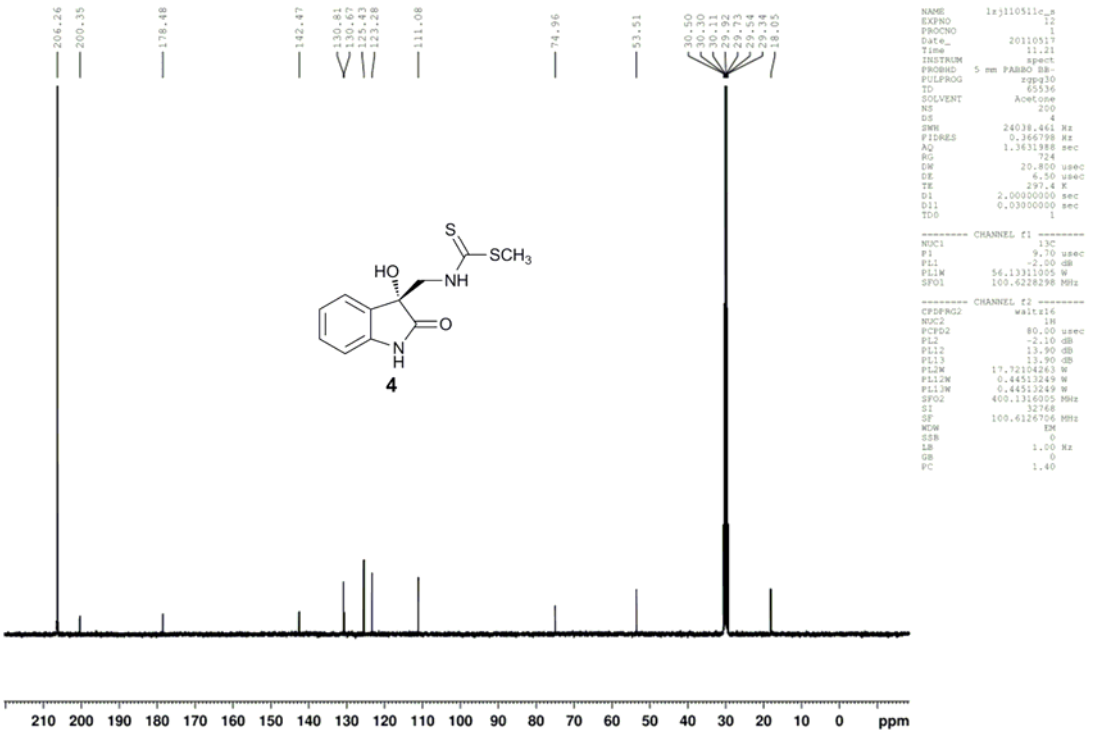


3l chiral

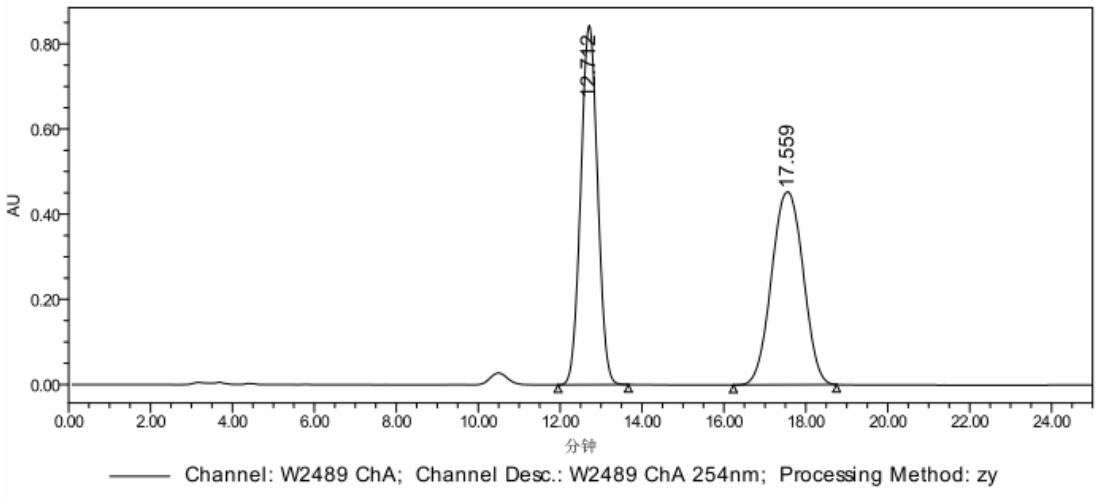


	Retention Time	Area	% Area	Height
1	13.769	22013753	95.35	839325
2	14.897	1072535	4.65	41580

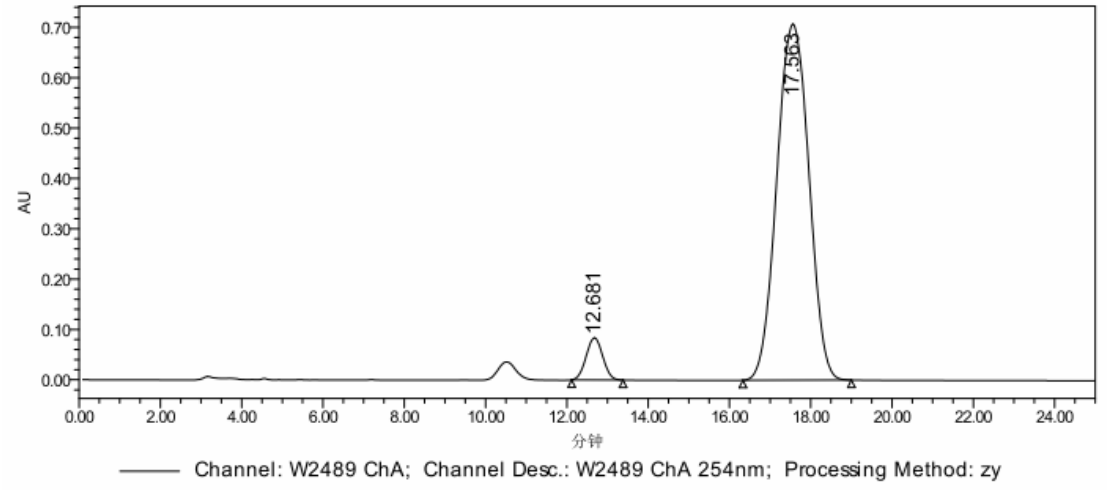

HO
NH
S
SCH3
O
N
H
4
ppm


HO
NH
S
SCH3
O
N
H
4
ppm

4 racemic



4 chiral



	Retention Time	Area	% Area	Height
1	12.681	2369338	5.75	83517
2	17.563	38814497	94.25	707543