A Solid-Supported Organocatalyst for Asymmetric Mannich Reaction to Construct C2-quaternary Indolin-3-ones

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Supporting Information

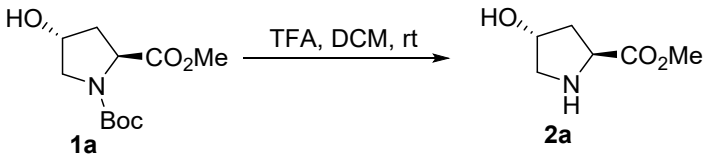
Contents:

1. General methods:

Unless otherwise stated, all commercial reagents were used as received. All experiments were monitored by analytical thin-layer chromatography (TLC). TLC was performed on silica gel plates with F-254 indicator and compounds were visualized by irradiation with UV light and/or by treatment with a solution of phosphomolybdic acid in ethanol followed by heating. Flash chromatography was carried out utilizing silica gel (200-300 mesh). ^{1}H NMR, ^{13}C NMR spectra were recorded on 400 MHz or 100 MHz spectrometers, The spectra were recorded in $CDCl_3$ or DMSO-d_6 as solvents at room temperature, ^{1}H NMR, ^{13}C NMR spectra were recorded on a JNM-ECS400 (400 M) spectrometer (400 MHz ^{1}H, 100 MHz ^{13}C). ^{1}H and ^{13}C NMR chemical shifts are reported in ppm relative to either the residual solvent peak or TMS as an internal standard: $CDCl_3$ (^{1}H NMR: δ 7.26, singlet; ^{13}C NMR: δ 77.0, triplet), DMSO-d_6 (^{1}H NMR: δ 2.50, singlet, ^{13}C NMR: δ 39.5, multiplet). Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, dd = doublet), integration, coupling constant (Hz) and assignment. Data for ^{13}C NMR are reported as chemical shift. High resolution mass spectrometry (HRMS) was performed on a Thermofisher (Vanquish (UPLC)-Q-Exactive Plus) mass instrument (ESI) and methanol was used to dissolve the sample. Enantiomeric excess values were determined by HPLC using a Chiralcel IC-H and Chiralcel OD-H column on Essential LC-16 series and eluting with i-PrOH and n-hexane. Optical rotation was measured on the Rudolph Autopol 1 polarimeter with $[\alpha]_D$ values reported in degrees; concentration (c) is in g/100 mL. Elemental analyses (C, H, O, N) were performed by vario Micro cube, Elementar, Germany. 2-Aryl-3*H*-indol-3-ones **9** could be conveniently prepared according to the literature procedure.[1,2,3]

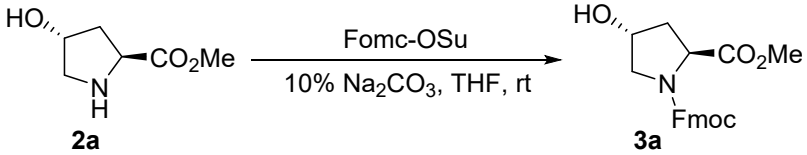
2. Synthesis of 2-chlorotrityl chloride resin-supported catalyst 6a, 6b, 8a and 8b

Synthesis of methyl (2*S*,4*R*)-4-hydroxypyrrolidine-2-carboxylate (2a)



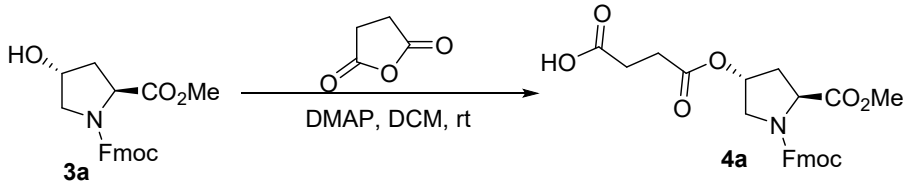
Compound **1a** (10g, 40.77 mmol) was dissolved in solution of DCM (50 mL) and then added the TFA (30 mL), After this addition, the mixture was stirred for about 4 h at room temperature. The solvent and TFA were removed under reduced pressure to give compound **2a** as a colorless oil in 95 % yield (5.62 g, 38.72 mmol).

Synthesis of 1-((9*H*-fluoren-9-yl)methyl) 2-methyl(2*S*,4*R*)-4-hydroxypyrrolidine-1,2-dicarboxylate (3a)



Compound **2a** (5.62 g, 38.72 mmol) was dissolved in solution of 10% Na_2CO_3 (30 mL) and then added the mixture of N-(9-Fluorenylmethoxycarbonyloxy)succinimide (19.59 g, 58.08 mmol) and THF (60 mL). After this addition, the mixture was stirred for about 4 h at room temperature. The solvent was removed under reduced pressure. The mixture was extracted with DCM(2 × 100 mL) and then washed with brine. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo after filtration to give crude product. The crude product was purified by column chromatography (PE:EA = 3:1) to give compound **3a** as a colorless oil in 79% yield (11.23 g, 30.59 mmol).

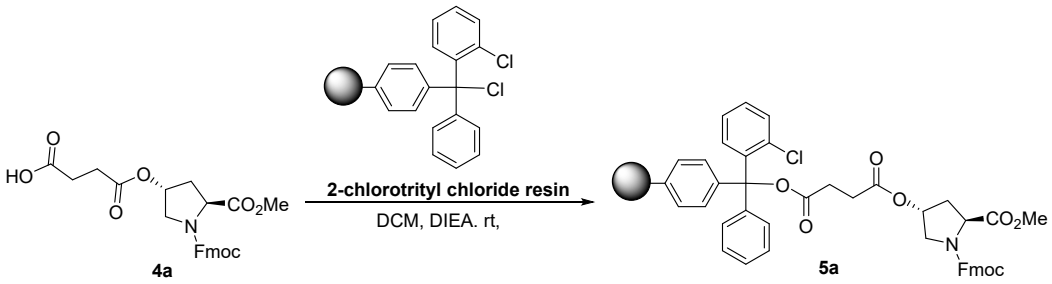
Synthesis of 4-(((3*R*,5*S*)-1-(((9H-fluoren-9-yl)methoxy)carbonyl)-5-(methoxycarbonyl)pyrrolidin-3-yl)oxy)-4-oxobutanoic acid (4a)



To a stirred solution of compound **3a** (11.23 g, 30.59 mmol) and succinic anhydride (6.12 g, 60.18 mmol) in anhydrous DCM (50 mL) was added DMAP (1.87 g, 15.30 mmol) at room temperature. After stirring for 12 h, the mixture was adjusted to PH 3-4 with citric acid. The reaction mixture was extracted with DCM(2 × 200 mL) and then washed with brine. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo after filtration to give crude product. The crude product was purified by column chromatography (CH_2Cl_2:MeOH = 30:1) to give

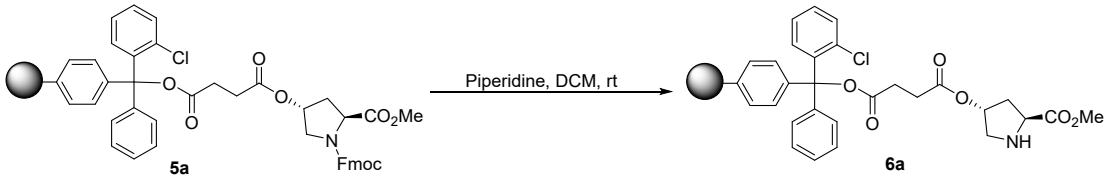
compound **4a** as a colorless oil in 85% yield (12.15 g, 26.00 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.35 (s, 1H), 7.75-7.68 (m, 2H), 7.60 – 7.50 (m, 2H), 7.39 – 7.34 (m, 2H), 7.33 – 7.26 (m, 2H), 5.29 (d, *J* = 13.9 Hz, 1H), 4.60 – 4.30 (m, 3H), 4.19 (dt, *J* = 12.9, 6.7 Hz, 1H), 3.72 (s, 3H), 3.59 (s, 2H), 2.60 (d, *J* = 7.1 Hz, 4H), 2.47 – 2.32 (m, 1H), 2.29 – 2.04 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ176.7, 172.6, 171.8, 154.9, 143.9, 143.8, 141.3, 141.3, 127.8, 127.2, 125.2, 125.0, 124.9, 120.1, 120.1, 73.1, 72.1, 67.9, 57.9, 52.6, 47.0, 36.6, 35.5, 29.0, 28.8; HRMS (ESI): calculated $[M-H]^+$ for $C_{25}H_{24}NO_6$: 466.1435, found $[M-H]^+$: 466.1415

Synthesis of resin 5a



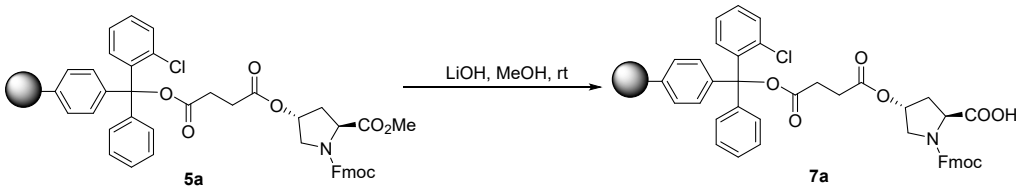
Measure out 3 g of 2-chlorotrityl chloride resin (100-200 mesh, 1% DVB, 1.179 mmol/g) and place it in a clean vessel. Add DCM (10 mL) to the vessel and incubate at room temperature with shaking for 3 h. Then wash vessel and resin with DCM (5mL) three times. A solution of compound **4a** (8.3 g, 17.68 mmol) dissolved in anhydrous DCM (20 mL). The resulting DCM solution was poured into the resin in vessel. And then add DIPEA (2.92 mL, 17.68 mmol), after shaking for 15 mins, DIPEA (2.92 mL, 17.68 mmol) was added for shaking overnight. Then MeOH (HPLC) (0.5 mL) was added into the mixture for shaking 15 mins. Finally, the resin was washed with DCM (10 mL) six times and dried to obtain resin **5a** (2.96 g).

Synthesis of the 2-chlorotrityl chloride resin-supported catalysts 6a



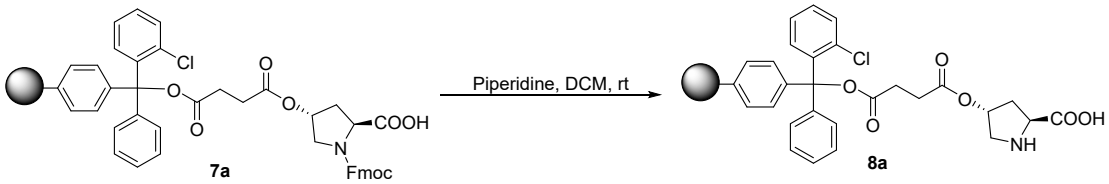
Place resin **5a** (1.36 g) in a clean container, add DCM (10 ml) to the vessel and incubate at room temperature with shaking. After shaking for 15 mins, Piperidine (29.36 μL, 20 mol%) was added to the mixture for shaking 1 h. Then the resin was washed with DCM (5 mL) six times and dried to obtain resin **6a** (1.32 g). The loading rate of supported catalyst **6a** was determined by elemental analysis. Elemental analysis (%) = C, 71.280, H, 4.557, O, 6.252, N, 0.270. *f* (N) = 0.193 mmol/g.

Synthesis of resin 7a



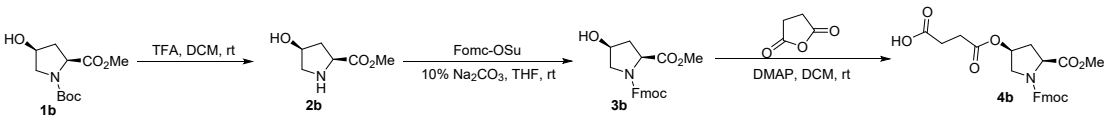
Place resin **5a** (1.6 g) in a clean container, LiOH (226.39 mg, 9.43 mmol) dissolved in anhydrous MeOH (5 mL) was added into the vessel and incubate at room temperature with shaking overnight. The resin was washed with MeOH (5 mL) and 5 ml DCM (5 mL) three times and dried to obtain resin **7a** (1.58 g).

Synthesis of the 2-chlorotrityl chloride resin-supported catalysts 8a



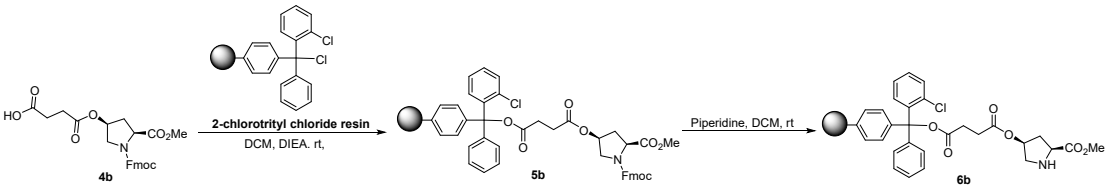
Place resin **7a** (1.58 g) in a clean container, add DCM (10 ml) to the vessel and incubate at room temperature with shaking. After shaking for 15 mins, piperidine (34.11 μL, 20 mol%) was added to the mixture for shaking 1 h. Then the resin was washed with DCM (5 mL) six times and dried to obtain resin **8a** (1.55 g) The loading rate of supported catalyst **8a** was determined by elemental analysis. Elemental analysis (%) = C, 81.190, H, 4.852, O, 8.588, N, 0.670. *f* (N) = 0.479 mmol/g.

Synthesis of 4-(((3*S*,5*S*)-1-(((9H-fluoren-9-yl)methoxy)carbonyl)-5-(methoxycarbonyl)pyrrolidin-3-yl)oxy)-4-oxobutanoic acid (4b)



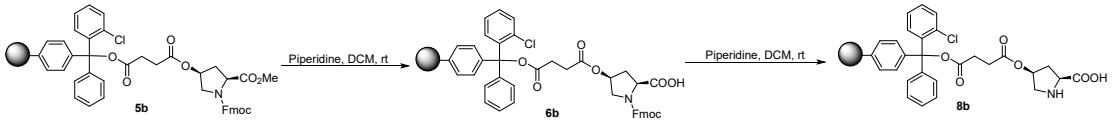
Compound **4b** (23.7 g, 88% yield) was prepared from *cis*-N-Boc-4-hydroxy-L-proline methyl ester **1b** (20.0 g, 81.63 mmol) as starting material, by using a similar procedure to that described for the preparation of **4a**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.60 (s, 1H), 7.89 – 7.68 (m, 2H), 7.67 – 7.49 (m, 2H), 7.42 – 7.35 (m, 2H), 7.34 – 7.26 (m, 2H), 5.28 (d, *J* = 22.5 Hz, 1H), 4.72 – 4.05 (m, 4H), 3.75 (s, 3H), 3.71 – 3.61 (m, 2H), 2.63-2.48 (m, 4H), 2.46 – 2.24 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.0, 171.9, 171.6, 154.8, 154.6, 144.0, 143.7, 141.3, 127.8, 127.1, 125.2, 125.1, 124.9, 120.1, 120.1, 73.2, 72.2, 67.9, 58.0, 52.6, 47.2, 36.5, 35.5, 29.0, 28.6; HRMS (ESI): calculated $[M-H]^+$ for $C_{25}H_{24}NO_6$: 466.1435, found $[M-H]^+$: 466.1425.

Synthesis of the 2-chlorotrityl chloride resin-supported catalysts 6b



The resin **5b** (5.85 g) and supported catalyst **6b** (1.1 g) were prepared from **4b** and 2-chlorotrityl chloride resin (7 g, 1.179 mmol/g) as starting material, by using a similar procedure to that described for the preparation of resin **6a**. The loading rate of supported catalyst **6a** was determined by elemental analysis. Elemental analysis (%) = C, 81.380, H, 4.990, O, 9.388, N, 0.410. *f* (N) = 0.293 mmol/g.

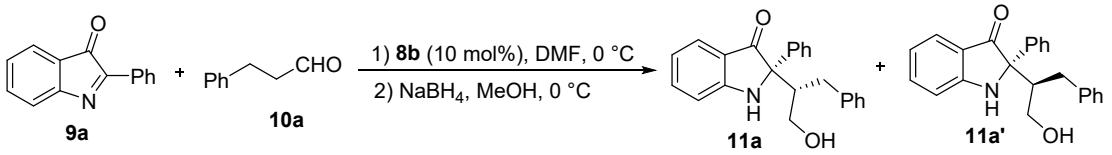
Synthesis of the 2-chlorotrityl chloride resin-supported catalysts 8b



The supported catalyst **8b** (5.76 g) was prepared from resin **5b** (5.85 g) as starting material, by using a similar procedure to that described for the preparation of resin **8a**. The loading rate of supported catalyst **8b** was determined by elemental analysis. Elemental analysis (%) = C, 80.540, H, 4.825, O, 7.092, N, 0.330. *f* (N) = 0.236 mmol/g.

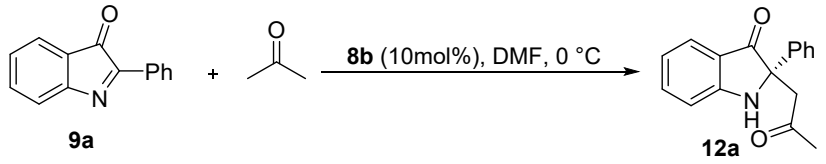
3. General Procedure for the Synthesis of 11a, 11a' and 12a

The Synthesis of aldehydes 11a and11a' as an example of General Procedure



To a solution of 2-aryl-3*H*-indol-3-one **9a** (0.10 mmol), **10a** (0.20 mmol) and solid-supported catalyst **8b** (10 mol%) in DMF (1.0 mL) was stirred at 0 °C. The mixture was further stirred for the required period of time (as judged by TLC analysis). Then, the mixture was extracted with EtOAc. The organic extracts were washed with H_2O and brine, dried over anhydrous Na_2SO_4, and then concentrated. The crude product was then poured into the suspension of excess $NaBH_4$ (0.2 mmol) in methanol (1 mL) at 0 °C. After stirring for 10 min, the solution was treated with saturated aqueous $NaHCO_3$. The mixture was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo after filtration to give crude product. The crude product was purified by flash column chromatography (eluted with petroleum ether/EtOAc = 15/1 to 8/1) to afford the desired product **11a** and **11a'**.

The Synthesis of aldehydes 12a as an example of General Procedure

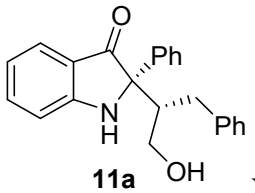


To a solution of 2-aryl-3*H*-indol-3-one **9a** (0.10 mmol), acetone (0.20 mmol) and solid-supported catalyst **8b** (10 mol%) in DMF (1.0 mL) was stirred at 0 °C. The mixture was further stirred for the required period of time (as judged by TLC analysis). Then, the mixture was extracted with EtOAc. The organic extracts were

washed with H_2O and brine, dried over anhydrous Na_2SO_4, and then concentrated. The crude product was purified by flash column chromatography (eluted with petroleum ether/EtOAc = 10/1 to 8/1) to afford the desired product **12a**.

4. Analytical Data of 11a (11a')-11o and 12a-12d[4]

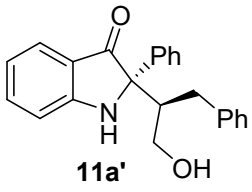
(*S*)-2((*S*)-1-Hydroxy-3-phenylpropan-2yl)-2-phenyindolin-3-one (11a)



11a

Yellow solid; Reaction times: 60 h; dr: 6.3:1; Yield: 79%; m. p.: 57-59 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 – 7.61 (m, 2H), 7.60 – 7.54 (m, 1H), 7.51 – 7.42 (m, 1H), 7.41 – 7.34 (m, 2H), 7.33 – 7.28 (m, 1H), 7.28 – 7.20 (m, 2H), 7.20 – 7.15 (m, 1H), 7.15 – 7.07 (m, 2H), 6.97 (dd, *J* = 8.2, 0.6 Hz, 1H), 6.84 (dd, *J* = 7.6, 7.2 Hz, 1H), 5.38 (s, 1H), 3.55 (dd, *J* = 11.8, 2.8 Hz, 1H), 3.45 (dd, *J* = 11.8, 5.2 Hz, 1H), 2.90 – 2.80 (m, 1H), 2.74 – 2.56 (m, 2H), 2.35 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.2, 160.7, 139.8, 138.5, 137.6, 129.2, 129.1, 128.6, 128.0, 126.4, 125.8, 125.4, 120.7, 120.0, 112.7, 75.4, 61.0, 49.9, 31.9; The Enantiomeric excess (ee) was determined by HPLC with an IC-H column (n-hexane/i-PrOH = 90:10, flow rate 1.0 mL/min, λ = 365 nm), t_R = 15.24 min (major), t_R = 22.03 min (minor), 96% ee; [α]25 D = +170.8 (*c* 0.96, CH_2Cl_2); HRMS (ESI): calculated $[M+H]^+$ for $C_{23}H_{22}NO_2$: 344.1645, found $[M+H]^+$: 344.1648.

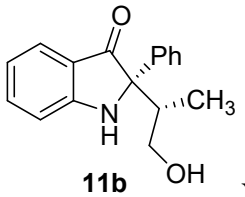
(*S*)-2-((*R*)-1-hydroxy-3-phenylpropan-2-yl)-2-phenylindolin-3-one (11a')



11a'

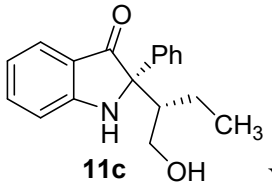
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 – 7.60 (m, 2H), 7.56 – 7.49 (m, 1H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.31 – 7.20 (m, 3H), 7.20 – 7.08 (m, 3H), 6.94 (d, *J* = 8.2 Hz, 1H), 6.81 (t, *J* = 7.4 Hz, 1H), 3.55 (dd, *J* = 11.8, 2.8 Hz, 1H), 3.45 (dd, *J* = 11.8, 5.4 Hz, 1H), 2.91 – 2.80 (m, 1H), 2.74 – 2.55 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.2, 160.7, 139.8, 138.5, 137.6, 129.1, 129.0, 128.5, 127.9, 126.3, 125.8, 125.3, 120.6, 119.7, 112.7, 75.4, 60.9, 49.9, 31.9; HRMS (ESI): calculated $[M+H]^+$ for $C_{23}H_{22}NO_2$: 344.1645, found $[M+H]^+$: 344.1647.

(*S*)-2-((*S*)-1-Hydroxypropan-2-yl)-2-phenylindolin-3-one (11b)



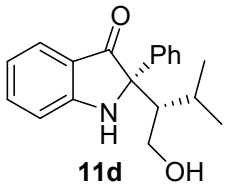
11b Yellow solid; Reaction times: 48 h; dr: 9:1; Yield: 82%; m. p.: 196-198 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.96 (s, 1H), 7.53 (d, J = 7.2 Hz, 2H), 7.44 (t, J = 7.2 Hz, 1H), 7.33 (q, J = 7.6 Hz, 3H), 7.25 (q, J = 6.4 Hz, 1H), 6.99 (d, J = 8.4 Hz, 1H), 6.64 (t, J = 7.6 Hz, 1H), 4.47 (t, J = 5.2 Hz, 1H), 3.30 – 3.21 (m, 1H), 3.17 – 3.07 (m, 1H), 2.67 – 2.54 (m, 1H), 0.77 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 201.7, 161.6, 139.2, 137.8, 128.9, 127.7, 126.1, 124.6, 119.1, 117.6, 112.0, 74.2, 62.6, 44.3, 12.8; The Enantiomeric excess (ee) was determined by HPLC with an IC-H column (n-hexane/i-PrOH = 90:10, flow rate 1.0 mL/min, λ = 365 nm), t_R = 12.36 min (major), t_R = 16.64 min (minor), 97% ee; [α]25 D = +337.6 (*c* 1.09, MeOH); HRMS (ESI): calculated $[M+H]^+$ for $C_{17}H_{18}NO_2$: 268.1332, found $[M+H]^+$: 268.1337.

(*S*)-2-((*S*)-1-Hydroxybutan-2-yl)-2-phenylindolin-3-one (11c)



11c Yellow solid; Reaction times: 48 h; dr: 11:1; Yield: 80%; m. p.: 141-143 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 – 7.55 (m, 1H), 7.55 – 7.53 (m, 1H), 7.53 – 7.51 (m, 1H), 7.50 – 7.44 (m, 1H), 7.38 – 7.30 (m, 2H), 7.29 – 7.24 (m, 1H), 6.99 (d, J = 7.6 Hz, 1H), 6.84 (t, J = 7.6 Hz, 1H), 5.28 (s, 1H), 3.72 – 3.58 (m, 2H), 2.51 – 2.43 (m, 1H), 2.38 (s, 1H), 1.47 – 1.29 (m, 2H), 0.92 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.6, 160.6, 138.6, 137.6, 128.9, 127.8, 125.7, 125.4, 120.8, 119.9, 112.6, 75.9, 61.4, 49.3, 18.9, 12.4; The Enantiomeric excess (ee) was determined by HPLC with an IC-H column (n-hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, λ = 365 nm), t_R = 7.18 min (major), t_R = 9.19 min (minor), 97% ee; [α]25 D = +252.6 (*c* 0.95, CH_2Cl_2); HRMS (ESI): calculated $[M+H]^+$ for $C_{18}H_{20}NO_2$: 282.1488, found $[M+H]^+$: 282.1493.

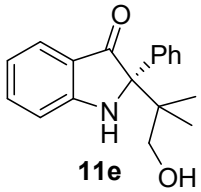
(*S*)-2((*S*)-1-Hydroxy-3-methylbutan-2-yl)-2-phenylindolin-3-one (11d)



11d Yellow solid; Reaction times: 60 h; dr: 10:1; Yield: 76%; m. p.: 137-140 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 – 7.57 (m, 2H), 7.52 (d, J = 7.6 Hz, 1H), 7.49 – 7.41 (m, 1H), 7.36 – 7.29 (m, 2H), 7.28 – 7.21 (m, 1H), 7.00 (d, J = 8.0 Hz, 1H), 6.79 (t, J = 7.6 Hz, 1H), 5.40 (s, 1H), 3.80 – 3.68 (m, 2H), 2.84 – 2.76 (m, 1H), 1.94 – 1.78 (m, 2H), 0.99 (d, J = 7.6 Hz, 3H), 0.85 (d, J = 7.2 Hz, 3H); ^{13}C NMR

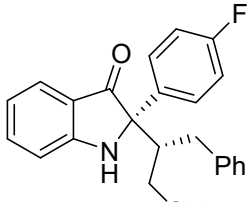
(100 MHz, $CDCl_3$): δ 202.4, 160.2, 138.7, 137.2, 128.8, 127.7, 125.7, 125.4, 120.2, 119.5, 112.1, 75.4, 60.4, 52.6, 26.8, 23.1, 18.5; The Enantiomeric excess (ee) was determined by HPLC with an IC-H column (n-hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, λ = 365 nm), t_R = 7.91 min (major), t_R = 12.30 min (minor), 92% ee; [α]25 D = +372.4 (*c* 0.87, CH_2Cl_2); HRMS (ESI): calculated $[M+H]^+$ for $C_{19}H_{22}NO_2$: 296.1645, found $[M+H]^+$: 296.1648.

(*R*)-2-(1-Hydroxy-2-methylpropan-2-yl)-2-phenylindolin-3-one (11e)



11e Yellow solid; Reaction times: 72 h; Yield: 48%; m. p.: 155-156 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.86 – 7.81 (m, 2H), 7.55 (dd, *J* = 8.0, 0.4 Hz, 1H), 7.40 (td, *J* = 7.6, 1.2 Hz, 1H), 7.36 – 7.30 (m, 1H), 7.29 – 7.27 (m, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 6.72 (td, *J* = 7.2, 0.8 Hz, 1H), 6.70 (s, 1H), 3.42 (dd, *J* = 11.2, 5.6 Hz, 1H), 3.26 (d, *J* = 11.2 Hz, 1H), 2.71 (s, 1H), 1.06 (s, 3H), 1.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.1, 160.6, 137.5, 136.5, 128.1, 127.7, 127.7, 124.7, 121.3, 118.3, 111.9, 75.6, 70.3, 42.2, 20.6, 19.3; The Enantiomeric excess (ee) was determined by HPLC with an IC-H column (n-hexane/i-PrOH = 90:10, flow rate 1.0 mL/min, λ = 254 nm), t_R = 7.62 min (major), t_R = 13.58 min (minor), 77% ee; [α]25 D = +124.6 (*c* 0.61, CH_2Cl_2); HRMS (ESI): calculated $[M+H]^+$ for $C_{18}H_{20}NO_2$: 282.1488, found $[M+H]^+$: 282.1489.

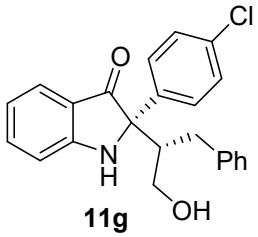
(*S*)-2-(4-Fluorophenyl)-2-((*S*)-2-hydroxy-1-phenylethyl)indolin-3-one (11f)



11f Yellow solid; Reaction times: 48 h; dr: 6.1:1; Yield: 83%; m. p.: 52-54 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.68 – 7.62 (m, 2H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.49 (td, *J* = 8.4, 1.2 Hz, 1H), 7.29 – 7.23 (m, 2H), 7.22 – 7.16 (m, 1H), 7.13 – 7.03 (m, 4H), 6.98 (d, *J* = 8.4 Hz, 1H), 6.86 (t, *J* = 7.2 Hz, 1H), 5.33 (s, 1H), 3.58 – 3.39 (m, 2H), 2.85 – 2.74 (m, 1H), 2.70 (dd, *J* = 13.2, 3.2 Hz, 1H), 2.59 (dd, *J* = 13.2, 11.2 Hz, 1H), 2.05 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.2, 162.3 (d, *J* = 246.0 Hz), 160.6, 139.6, 137.7, 134.3 (d, *J* = 3.0 Hz), 129.1, 128.6, 127.8 (d, *J* = 8.0 Hz), 126.5, 125.4, 120.6, 120.0, 116.0 (d, *J* = 21.0 Hz), 112.8, 74.7, 60.9, 50.0, 31.9; ^{19}F NMR ($CDCl_3$, 376 MHz): δ = -114.54 ppm; The Enantiomeric excess (ee) was determined by HPLC with an IC-H column (n-hexane/i-PrOH = 90:10, flow rate 1.0 mL/min, λ = 365 nm), t_R = 10.64 min (minor), t_R = 11.40 min (major), 72% ee; [α]25

D = +104.1 (*c* 1.46, CH_2Cl_2); HRMS (ESI): calculated $[M+H]^+$ for $C_{23}H_{21}FNO_2$: 362.1550, found $[M+H]^+$: 362.1539.

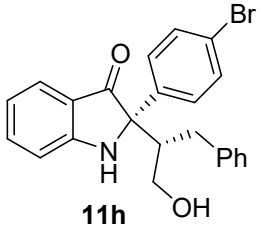
(*S*)-2-(4-Chlorophenyl)-2-((*S*)-1-hydroxy-3-phenylpropan-2-yl)indolin-3-one (11g)



11g

Yellow solid; Reaction times: 48 h; dr: 5:1; Yield: 81%; m. p.: 68-70 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ^{1}H NMR (400 MHz,) δ 7.62 (d, *J* = 8.5 Hz, 2H), 7.55 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.50 – 7.43 (m, 1H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.29 – 7.16 (m, 3H), 7.09 (d, *J* = 7.6 Hz, 2H), 6.95 (d, *J* = 8.0 Hz, 1H), 6.83 (t, *J* = 7.2 Hz, 1H), 5.63 (s, 1H), 3.59 – 3.38 (m, 2H), 2.87 – 2.78 (m, 1H), 2.72 – 2.50 (m, 2H), 2.33 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.2, 160.8, 139.5, 137.9, 137.2, 134.0, 129.1, 129.1, 128.7, 127.5, 126.5, 125.4, 120.3, 119.9, 112.8, 74.8, 60.9, 49.9, 32.0; The Enantiomeric excess (ee) was determined by HPLC with an IC-H column (n-hexane/i-PrOH = 90:10, flow rate 1.0 mL/min, λ = 365 nm), t_R = 9.65 min (minor), t_R = 11.25 min (major), 84% ee; [α]25 D = +46.0 (*c* 1.74, CH_2Cl_2); HRMS (ESI): calculated $[M+H]^+$ for $C_{23}H_{21}ClNO_2$: 378.1255, found $[M+H]^+$: 378.1246.

(*S*)-2-(4-Bromophenyl)-2-((*S*)-1-hydroxy-3-phenylpropan-2-yl)indolin-3-one (11h)

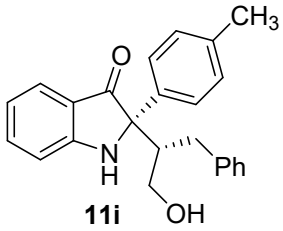


11h

Yellow solid; Reaction times: 48 h; dr: 7.3:1; Yield: 78%; m. p.: 114-116 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, *J* = 8.4 Hz, 3H), 7.52 – 7.44 (m, 3H), 7.28 – 7.24 (m, 2H), 7.23 – 7.17 (m, 1H), 7.10 (d, *J* = 7.2 Hz, 2H), 6.97 (dd, *J* = 8.0, 0.4 Hz, 1H), 6.85 (t, *J* = 7.6 Hz, 1H), 5.49 (s, 1H), 3.54 (dd, *J* = 11.6, 7.2 Hz, 1H), 3.44 (dd, *J* = 11.6, 5.6 Hz, 1H), 2.86 – 2.77 (m, 1H), 2.73 – 2.53 (m, 2H), 2.20 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.0, 160.7, 139.5, 137.8, 137.8, 132.1, 129.1, 128.7, 127.8, 126.5, 125.4, 122.2, 120.4, 120.0, 112.8, 74.8, 60.9, 49.8, 32.0; The Enantiomeric excess (ee) was determined by HPLC with an IC-H column (n-hexane/i-PrOH = 90:10, flow rate 1.0 mL/min, λ = 365 nm), t_R = 9.73 min (minor), t_R = 11.68

min (major), 86% ee; [α]25 D = +99.3 (*c* 1.41, CH_2Cl_2); HRMS (ESI): calculated $[M+H]^+$ for $C_{23}H_{21}BrNO_2$: 422.0750, found $[M+H]^+$: 422.0734.

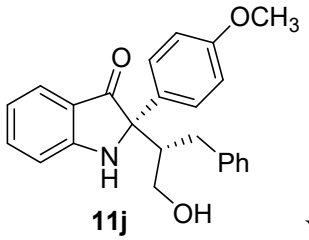
(*S*)-2-((*S*)-2-Hydroxy-1-phenylethyl)-2-(*p*-tolyl)indolin-3-one (11i)



11i

Yellow solid; Reaction times: 48 h; dr: 4.2:1; Yield: 76%; m. p.: 52-54 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, *J* = 7.6 Hz, 1H), 7.54 – 7.45 (m, 3H), 7.31-7.27 (m, 1H), 7.25 – 7.23 (m, 1H), 7.22 – 7.12 (m, 5H), 6.97 (d, *J* = 8.2 Hz, 1H), 6.85 (t, *J* = 7.6 Hz, 1H), 5.40 (s, 1H), 3.55 (dd, *J* = 12.0, 5.6 Hz, 1H), 3.45 (dd, *J* = 12.0, 5.2 Hz, 1H), 2.87 – 2.77 (m, 1H), 2.75 – 2.56 (m, 2H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.4, 160.6, 140.0, 137.8, 137.6, 135.4, 129.8, 129.2, 128.5, 126.3, 125.6, 125.4, 120.8, 119.9, 112.7, 75.4, 60.9, 49.7, 31.9, 21.1; The Enantiomeric excess (ee) was determined by HPLC with an IC-H column (n-hexane/i-PrOH = 90:10, flow rate 1.0 mL/min, λ = 365 nm), t_R = 16.87 min (minor), t_R = 18.90 min (major), 51% ee; [α]25 D = +120.0 (*c* 0.70, CH_2Cl_2); HRMS (ESI): calculated $[M+H]^+$ for $C_{24}H_{24}NO_2$: 358.1801, found $[M+H]^+$: 358.1803.

(*S*)-2-((*S*)-1-hydroxy-3-phenylpropan-2-yl)-2-(4-methoxyphenyl)indolin-3-one (11j)

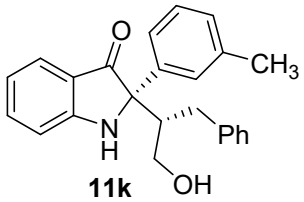


11j

Yellow solid; Reaction times: 48 h; dr: 5:1; Yield: 73%; m. p.: 73-75 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 – 7.51 (m, 3H), 7.50 – 7.43 (m, 1H), 7.29 – 7.11 (m, 5H), 7.00 – 6.80 (m, 4H), 5.48 (s, 1H), 3.77 (s, 3H), 3.57 – 3.35 (m, 2H), 2.85 – 2.75 (m, 1H), 2.75 – 2.50 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.7, 160.7, 159.3, 140.0, 137.7, 130.3, 129.2, 128.6, 127.0, 126.3, 125.4, 120.6, 119.8, 114.4, 112.8, 75.1, 60.9, 55.4, 49.8, 31.9; The Enantiomeric excess (ee) was determined by HPLC with an IC-H column (n-hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, λ = 365 nm), t_R = 9.21 min (minor), t_R = 11.01 min (major), 90% ee; [α]25 D

= +97.4 (*c* 0.78, CH_2Cl_2); HRMS (ESI): calculated $[M+H]^+$ for $C_{24}H_{24}NO_3$: 374.1750, found $[M+H]^+$: 374.1745.

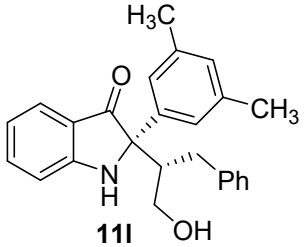
(*S*)-2-((*S*)-1-Hydroxy-3-phenylpropan-2-yl)-2-(m-tolyl)indolin-3-one (11k)



11k

Yellow solid; Reaction times: 60 h; dr: 3.4:1; Yield: 67%; m. p.: 54-56 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, *J* = 7.2 Hz, 1H), 7.52 – 7.46 (m, 1H), 7.44 – 7.38 (m, 2H), 7.31 – 7.27 (m, 3H), 7.23 – 7.09 (m, 4H), 6.98 (d, *J* = 8.0 Hz, 1H), 6.86 (t, *J* = 7.2 Hz, 1H), 5.33 (s, 1H), 3.55 (dd, *J* = 12.0, 2.4 Hz, 1H), 3.50 – 3.40 (m, 1H), 2.86 – 2.76 (m, 1H), 2.73 – 2.59 (m, 2H), 2.48 (s, 1H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.3, 160.7, 140.0, 138.8, 138.4, 137.7, 129.2, 129.0, 128.8, 128.5, 126.4, 126.3, 125.4, 122.8, 120.8, 120.0, 112.9, 75.6, 60.9 49.9, 31.9, 21.8; The Enantiomeric excess (ee) was determined by HPLC with an IC-H column (n-hexane/i-PrOH = 90:10, flow rate 1.0 mL/min, λ = 365 nm), t_R = 14.98 min (major), t_R = 20.20 min (minor), 80% ee; [α]25 D = +180.5 (*c* 0.82, CH_2Cl_2); HRMS (ESI): calculated $[M+H]^+$ for $C_{24}H_{24}NO_2$: 358.1801, found $[M+H]^+$: 358.1807.

(*S*)-2-(3,5-Dimethylphenyl)-2-((*S*)-1-hydroxy-3-phenylpropan-2-yl)indolin-3-one (11l)

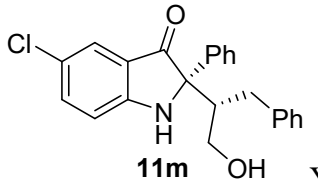


11l

Yellow solid; Reaction times: 60 h; dr: 3:1; Yield: 61%; m. p.: 67-69 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, *J* = 8.0 Hz, 1H), 7.48 (td, *J* = 7.2, 1.2 Hz, 1H), 7.30 – 7.23 (m, 2H), 7.21 – 7.13 (m, 5H), 6.98 (d, *J* = 8.0 Hz, 1H), 6.93 (s, 1H), 6.86 (t, *J* = 7.6 Hz, 1H), 5.30 (s, 1H), 3.54 (dd, *J* = 12.0, 2.4 Hz, 1H), 3.44 (dd, *J* = 12.0, 4.8 Hz, 1H), 2.83 – 2.74 (m, 1H), 2.70 – 2.61 (m, 2H), 2.31 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.4, 160.7, 140.1, 138.7, 138.3, 137.7, 129.8, 129.2, 128.5, 126.3, 125.4, 123.4, 121.0, 120.0, 112.8, 75.7, 61.0, 50.0, 31.8, 21.7; The Enantiomeric excess (ee) was determined by HPLC with an IC-H column (n-hexane/i-

PrOH = 90:10, flow rate 1.0 mL/min, λ = 365 nm), t_R = 11.74 min (minor), t_R = 13.98 min (major), 79% ee; [α]25 D = +130.1 (*c* 1.23, CH_2Cl_2); HRMS (ESI): calculated $[M+H]^+$ for $C_{25}H_{26}NO_2$: 372.1958, found $[M+H]^+$: 372.1953.

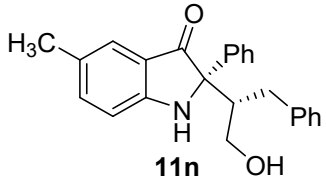
(*S*)-5-chloro-2-((*S*)-1-hydroxy-3-phenylpropan-2-yl)-2-phenylindolin-3-one (11m)



11m

Yellow solid; Reaction times: 72 h; dr: 2:1; Yield: 38%; m. p.: 58-60 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 – 7.55 (m, 3H), 7.52 – 7.46 (m, 1H), 7.36 – 7.23 (m, 4H), 7.22 – 7.16 (m, 1H), 7.11 (d, *J* = 5.6 Hz, 2H), 6.98 (d, *J* = 8.0 Hz, 1H), 6.86 (t, *J* = 7.6 Hz, 1H), 5.41 (s, 1H), 3.58 – 3.40 (m, 2H), 2.87 – 2.77 (m, 1H), 2.72 – 2.53 (m, 2H), 2.08 – 2.02 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.2, 158.9, 139.6, 138.1, 137.4, 129.1, 129.1, 128.6, 128.2, 126.5, 125.8, 125.0, 124.6, 121.7, 113.9, 76.0, 61.1, 50.0, 32.1; The Enantiomeric excess (ee) was determined by HPLC with an IC-H column (n-hexane/i-PrOH = 90:10, flow rate 1.0 mL/min, λ = 365 nm), t_R = 10.62 min (major), t_R = 11.46 min (minor), 89% ee; [α]25 D = +135.1 (*c* 0.77, CH_2Cl_2); HRMS (ESI): calculated $[M+H]^+$ for $C_{23}H_{21}ClNO_2$: 378.1255, found $[M+H]^+$: 378.1253.

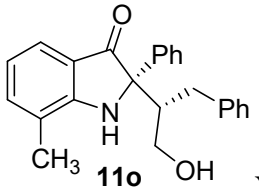
(*S*)-2-((*S*)-1-hydroxy-3-phenylpropan-2-yl)-5-methyl-2-phenylindolin-3-one (11n)



11n

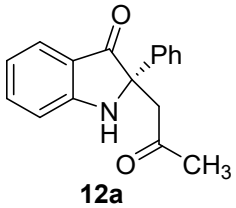
Yellow solid; Reaction times: 60 h; dr: 2.3:1; Yield: 56%; m. p.: 53-54 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (dd, *J* = 8.0, 0.8 Hz, 2H), 7.38 (t, *J* = 8.0 Hz, 3H), 7.33 – 7.22 (m, 4H), 7.22 – 7.12 (m, 3H), 6.91 (d, *J* = 8.4 Hz, 1H), 5.38 (s, 1H), 3.56 (dd, *J* = 11.6, 2.4 Hz, 1H), 3.45 (dd, *J* = 12.0, 4.8 Hz, 1H), 2.89 – 2.60 (m, 2H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.4, 159.2, 140.0, 139.2, 138.6, 129.6, 1292, 129.1, 128.6, 128.0, 126.3, 125.8, 124.7, 120.8, 112.8, 76.0, 60.9, 49.8, 31.9, 20.7; The Enantiomeric excess (ee) was determined by HPLC with an IC-H column (n-hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, λ = 365 nm), t_R = 7.93 min (major), t_R = 13.01 min (minor), 82% ee; [α]25 D = +163.9 (*c* 0.61, CH_2Cl_2); HRMS (ESI): calculated $[M+H]^+$ for $C_{24}H_{24}NO_2$: 358.1801, found $[M+H]^+$: 358.1809.

(*S*)-2-((*S*)-1-Hydroxy-3-phenylpropan-2-yl)-methyl-2-phenylindolin-3-one (11o).



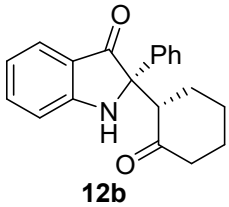
11o Yellow solid; Reaction times: 60 h; dr: 5:1; Yield: 63%; m.p.: 129-132 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 – 7.61 (m, 2H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.42 – 7.36 (m, 2H), 7.34 – 7.24 (m, 4H), 7.23 – 7.12 (m, 3H), 6.80 (t, *J* = 7.6 Hz, 1H), 5.07 (s, 1H), 3.55 (dd, *J* = 11.6, 2.8 Hz, 1H), 3.46 (dd, *J* = 12.0, 5.2 Hz, 1H), 2.93 – 2.82 (m, 1H), 2.78 – 2.64 (m, 2H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.7, 159.9, 139.9, 138.5, 137.6, 129.3, 129.1, 128.6, 128.0, 126.4, 125.8, 122.7, 121.9, 120.2, 120.1, 75.6, 60.8, 49.7, 31.8, 15.9; The Enantiomeric excess (ee) was determined by HPLC with an IC-H column (n-hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, λ = 365 nm), t_R = 9.34 min (major), t_R = 12.58 min (minor), 84% ee; [α]25 D = +77.8 (*c* 0.72, CH_2Cl_2); HRMS (ESI): calculated $[M+H]^+$ for $C_{24}H_{24}NO_2$: 358.1801, found $[M+H]^+$: 358.1806.

(*S*)-2-(2-Oxopropyl)-2-phenylindolin-3-one (12a)



12a Yellow solid; Reaction times: 72 h; Yield: 46%; m. p.: 104-106 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 – 7.52 (m, 3H), 7.48 (qd, *J* = 7.2, 0.8 Hz, 1H), 7.34 – 7.28 (m, 2H), 7.28 – 7.22 (m, 1H), 6.95 (d, *J* = 8.0 Hz, 1H), 6.80 (dq, *J* = 12.0, 0.8 Hz, 1H), 6.14 (s, 1H), 3.74 (d, *J* = 17.2 Hz, 1H), 2.72 (d, *J* = 13.2 Hz, 1H), 2.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.0, 200.4, 160.2, 137.9, 137.8, 128.8, 127.8, 125.7, 125.5, 119.1, 118.3, 112.0, 69.1, 49.5, 31.6; The Enantiomeric excess (ee) was determined by HPLC with an IC-H column (n-hexane/i-PrOH = 90:10, flow rate 1.0 mL/min, λ = 365 nm), t_R = 13.68 min (minor), t_R = 14.07 min (major), 69% ee; [α]25 D = +227.6 (*c* 0.58, CH_2Cl_2); HRMS (ESI): calculated $[M+Na]^+$ for $C_{17}H_{15}NNaO_2$: 288.0995, found $[M+Na]^+$: 288.0973.

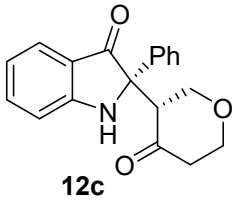
(*S*)-2-((*S*)-2-Oxocyclohexyl)-2-phenylindolin-3-one (12b)



12b Yellow solid; Reaction times: 60 h; dr: >20:1; Yield: 64%; m. p.: 154-156 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 – 7.52 (m, 3H), 7.44 (t, *J* = 7.2 Hz, 1H), 7.35 – 7.22 (m, 3H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.84 (t, *J* = 7.6 Hz, 1H), 5.21 (s,

1H), 3.52 (dd, *J* = 13.2, 5.2 Hz, 1H), 2.42 – 2.26 (m, 2H), 2.10 – 1.82 (m, 3H), 1.75 – 1.43 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.3, 200.9, 159.6, 137.5, 136.4, 128.9, 128.9, 127.9, 125.6, 125.0, 125.0, 121.4, 119.4, 111.9, 71.5, 58.7, 42.1, 28.5, 26.8, 25.2; The Enantiomeric excess (ee) was determined by HPLC with an OD-H column (n-hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, λ = 365 nm), t_R = 12.27 min (minor), t_R = 14.63 min (major), 98% ee; [α]25 D = +309.4 (*c* 1.06, CH_2Cl_2); HRMS (ESI): calculated $[M+Na]^+$ for $C_{19}H_{20}NNaO_2$: 328.1308, found $[M+Na]^+$: 328.1315.

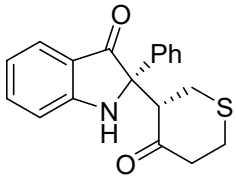
(*S*)-2-((*R*)-4-Oxotetrahydro-2*H*-pyran-3-yl)-2-phenylindolin-3-one (12c)



12c

Yellow solid; Reaction times: 60 h; dr: >20:1; Yield: 58%; m. p.: 100-102 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, *J* = 8.0 Hz, 1H), 7.56 – 7.52 (m, 2H), 7.47 (qd, *J* = 7.2, 1.6 Hz, 1H), 7.37 – 7.31 (m, 2H), 7.29 – 7.26 (m, 1H), 6.98 (d, *J* = 8.4 Hz,1H), 6.87 (qd, *J* = 7.6, 0.8 Hz, 1H), 5.26 (s, 1H), 4.21 – 4.12 (m, 1H), 4.07 (qd, *J* = 6.0, 1.6 Hz, 1H), 3.78 – 3.68 (m, 2H), 3.61 (dd, *J* = 10.8, 10.0 Hz, 1H), 2.68 – 2.58 (m, 1H), 2.37 (td, *J* = 15.2, 3.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.8, 199.4, 159.5, 136.8, 136.1, 129.2, 129.2, 128.3, 125.4, 125.4,120.6, 119.9, 111.9, 70.0, 68.9, 67.8, 57.8, 42.4; The Enantiomeric excess (ee) was determined by HPLC with an OD-H column (n-hexane/i-PrOH = 80:20, flow rate 1.0 mL/min, λ = 365 nm), t_R = 13.23 min (minor), t_R = 18.11 min (major), 96% ee; [α]25 D = +308.6 (*c* 0.70, CH_2Cl_2); HRMS (ESI): calculated $[M+Na]^+$ for $C_{29}H_{17}NNaO_3$: 330.1101, found $[M+Na]^+$: 330.1127.

(*S*)-2-((*S*)-4-Oxotetrahydro-2*H*-thiopyran-3-yl)-2-phenylindolin-3-one (12d)



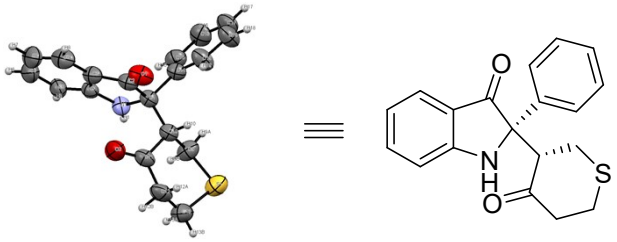
12d

Yellow solid; Reaction times: 60 h; dr: >20:1; Yield: 55%; m. p.: 116-119 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.53 (m, 3H), 7.46 (qd, *J* = 7.2, 1.2 Hz, 1H), 7.38 – 7.27 (m, 3H), 6.98 (d, *J* = 8.0 Hz, 1H), 6.86 (t, *J* = 7.2 Hz, 1H), 5.27 (s, 1H), 3.85 (dd, *J* = 10.4, 6.0 Hz, 1H), 2.99 – 2.76 (m,4H), 2.76-2.68 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.4, 199.7, 159.4, 136.7, 136.5, 129.2, 128.3, 125.6, 125.3, 121.0, 119.9, 112.0, 71.6, 60.4, 44.4, 30.7, 29.5; The Enantiomeric excess (ee) was determined by HPLC with an OD-H column (n-hexane/i-PrOH = 80:20, flow rate

1.0 mL/min, λ = 365 nm), t_R = 11.18 min (minor), t_R = 19.87 min (major), 99% ee; [α]25 D = +280.0 (*c* 1.40, CH_2Cl_2); HRMS (ESI): calculated $[M+Na]^+$ for $C_{19}H_{17}NNaO_3S$: 346.0873, found $[M+Na]^+$: 346.0873.

5. X-ray Crystallographic Data of 12d (CCDC: 2105997)[4]

The single crystals of compound **12d** for X-ray analysis was grown from the mixed solution of hexane and isopropanol (V/V = 10/1). Compounds **12d** was collected at 100 K on a Rigaku Oxford Diffraction Supernova Dual Source, Cu at Zero equipped with an AtlasS2 CCD using Cu Kα radiation. Data reduction was carried out with the diffractometer's software.[5] The structures were solved by direct methods using Olex2 software,[6] and the non-hydrogen atoms were located from the trial structure and then refined anisotropically with SHELXL-2018[7] using a full-matrix least squares procedure based on F2. The weighted *R* factor, *wR* and goodness-of-fit *S* values were obtained based on F2. The hydrogen atom positions were fixed geometrically at the calculated distances and allowed to ride on their parent atoms. Crystallographic data for the structure reported in this paper have been deposited at the Cambridge Crystallographic Data Center and allocated with the deposition numbers: **CCDC 2105997** for compound **12d**.[4] The molecule of **12d** showing the atom-numbering. Displacement ellipsoids drawn at 30% probability level and H-atoms are shown as small arbitrary radii.



CCDC 2105997 **12d**

X-ray Crystallographic Data of **12d**

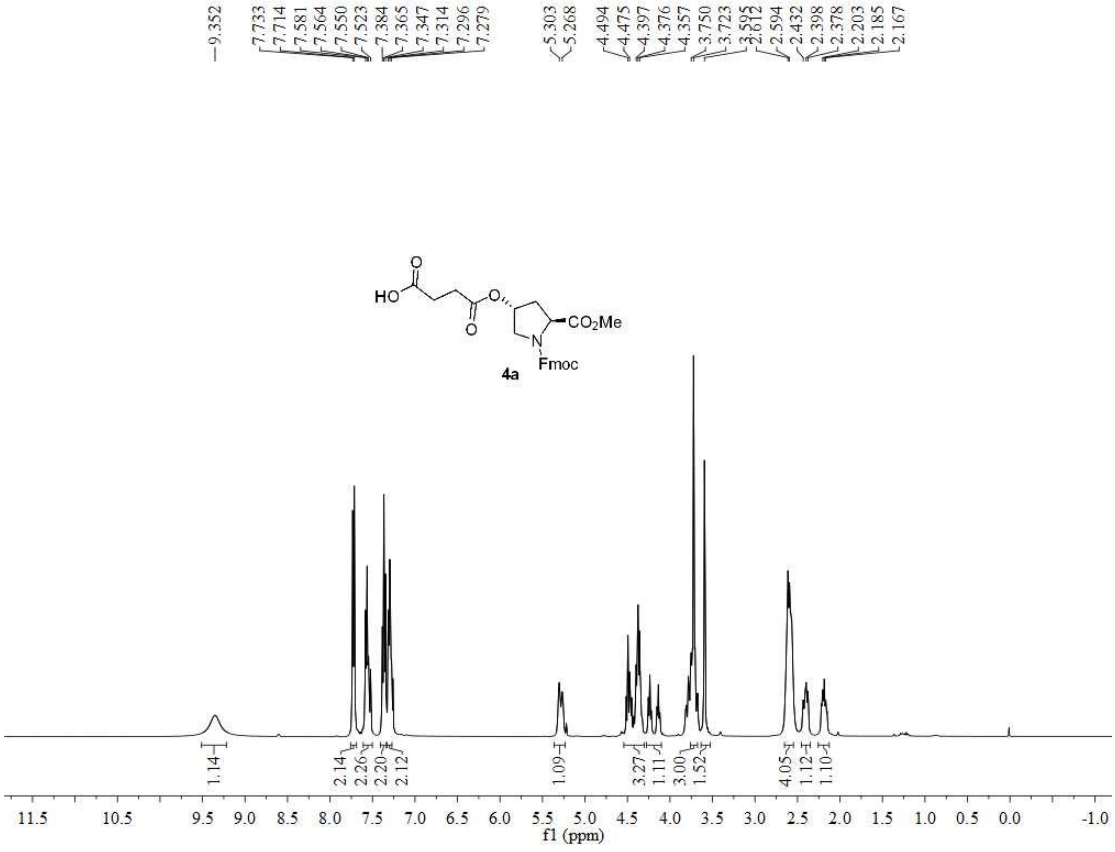
Empirical formula	$C_{19}H_{17}NO_2S$
Formula weight	323.40
Temperature/K	273.15
Crystal system	monoclinic
Space group	$P2_1$
a/Å	9.0741(3)
b/Å	22.5343(8)

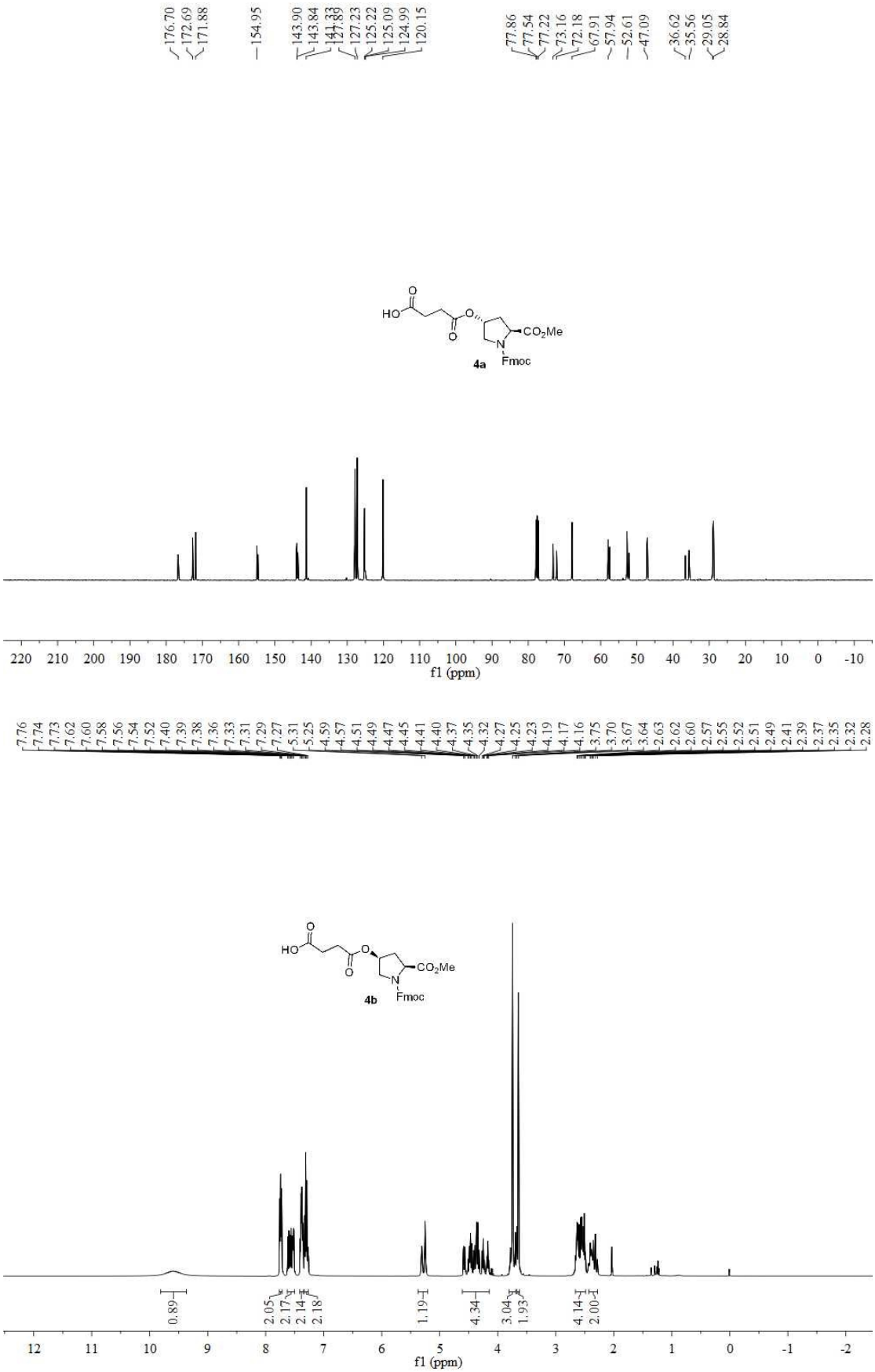
c/Å	9.5317(3)
α/°	90.00
β/°	108.193(2)
γ/°	90.00
Volume/Å^3	1851.60(11)
Z	4
ρ_{calc}mg/mm^3	1.160
m/mm^{-1}	1.614
F(000)	680.0
Crystal size/mm^3	? × ? × ?
2Θ range for data collection	10.52 to 144.58°
Index ranges	$-11 \leq h \leq 11$, $-27 \leq k \leq 27$, $-11 \leq l \leq 11$
Reflections collected	33663
Independent reflections	6921[R(int) = 0.0488]
Data/restraints/parameters	6921/1/416
Goodness-of-fit on F^2	1.130
Final R indexes [I>=2σ (I)]	R_1 = 0.0729, wR_2 = 0.1988
Final R indexes [all data]	R_1 = 0.0793, wR_2 = 0.2133
Largest diff. peak/hole / e Å^{-3}	0.53/-0.67
Flack parameter	0.07(2)

6. References

1. A. C. Lindsay, I. K. H. Leung, J. Sperry, *Org. Lett*. 2016, **18**, 5404.
2. K.-Q. Ling, *Synth. Commun*. 1995, **23**, 3831.
3. M. Yamashita, Y. Nishizono, S. Himekawa, A. Iida, *Tetrahedron*. 2016, **72**, 4123.
4. Y.-L. Zhao, J.-X. An, F.-F. Yang, X. Guan, X.-Z. Fu, Z.-Q. Li, D.-P. Wang, M. Zhou, Y.-Y. Yang, B. He. *Adv. Synth. Catal.* 2022, DOI: 10.1002/adsc.202101498.
5. Agilent Technologies, CrysAlisPRO, Version 1.171.36.28, 2013.
6. O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, *J. Appl. Cryst*. 2009, **42**, 339-341.
7. D. Kratzert, J. J. Holstein, I. Krossing, *J. Appl. Cryst*. 2015, **48**, 933-938.

7. NMR spectra[4]

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127.23
125.22
125.09
124.99
120.15
77.86
77.54
77.22
73.16
72.18
67.91
57.94
52.61
47.09
36.62
35.56
29.05
28.84
HO
O
O
O
O
N
CO2Me
Fmoc
4a
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)
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7.74
7.73
7.62
7.60
7.58
7.56
7.54
7.52
7.40
7.39
7.38
7.36
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7.31
7.29
7.27
5.31
5.25
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4.51
4.49
4.47
4.45
4.41
4.40
4.37
4.35
4.32
4.27
4.25
4.23
4.19
4.17
4.16
3.75
3.70
3.67
3.64
2.63
2.62
2.60
2.57
2.55
2.52
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2.41
2.39
2.37
2.35
2.32
2.28
HO
O
O
O
O
N
CO2Me
Fmoc
4b
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2.05
2.17
2.14
2.18
1.19
4.34
3.04
1.93
4.14
2.00
12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
f1 (ppm)


177.02
171.93
171.66
154.88
154.60
144.09
143.72
141.38
127.89
127.17
125.28
125.16
124.97
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120.10
77.72
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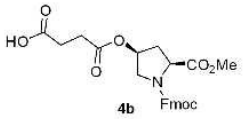
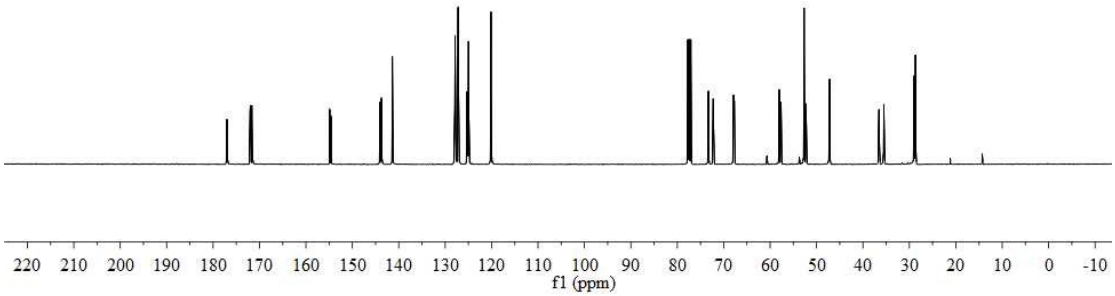
28.68


HO
O
O
O
CO2Me
N
Fmoc

4b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7.593
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7.574
7.499
7.497
7.479
7.461
7.459
7.405
7.387
7.366
7.322
7.321
7.284
7.275
7.260
7.239
7.204
7.186
7.144
7.127
6.991
6.970
6.867
6.849
3.580
3.573
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3.544
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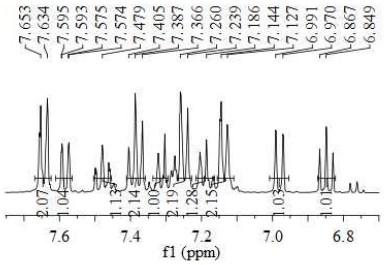
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7.405
7.387
7.366
7.260
7.239
7.186
7.144
7.127
6.991
6.970
6.867
6.849
2.07
1.04
1.13
2.14
1.00
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2.15
1.03
1.01
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7.2
7.0
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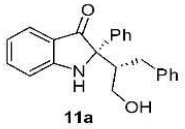
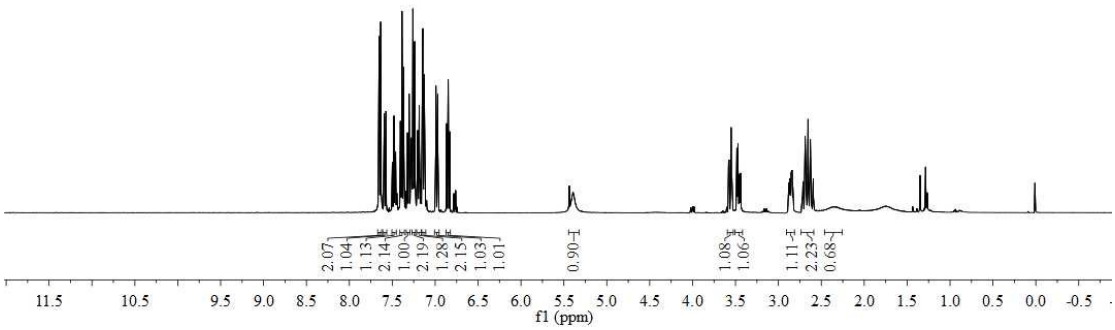
f1 (ppm)


O
Ph
N
H
Ph
OH

11a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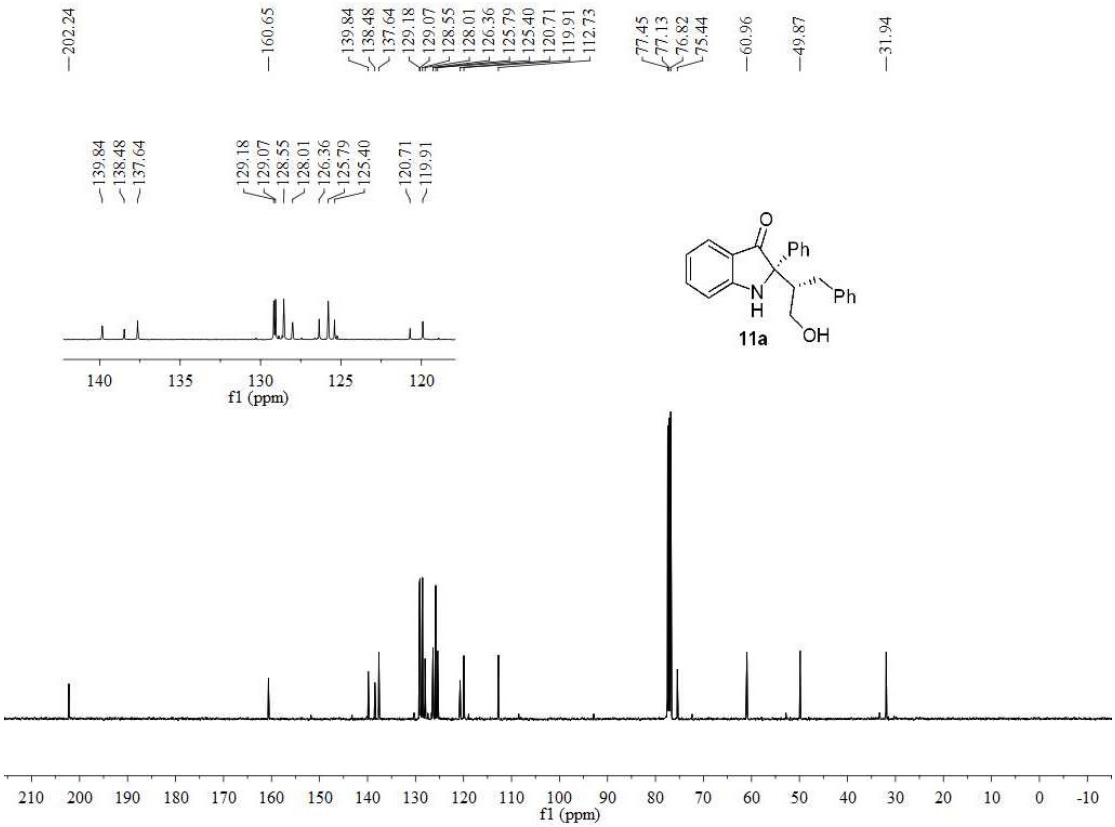
2.15
1.03
1.01
0.90
1.08
1.06
1.11
2.23
0.68
11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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N
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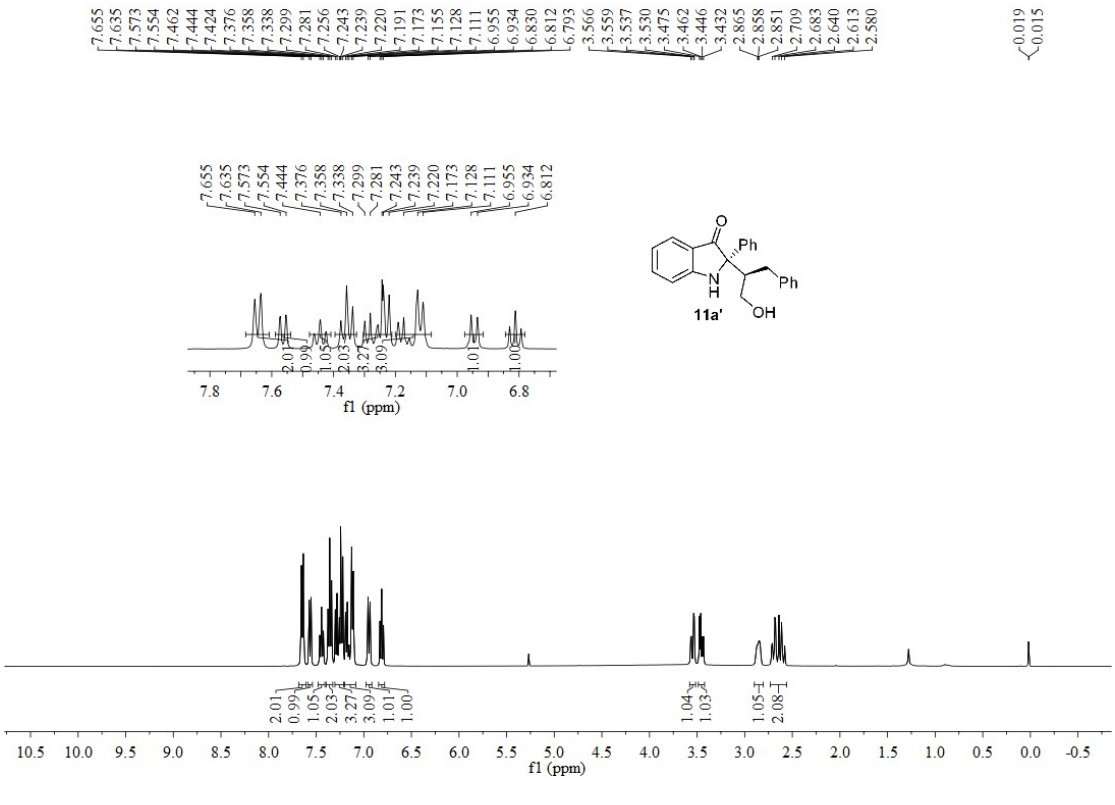
Ph
OH
11a
f1 (ppm)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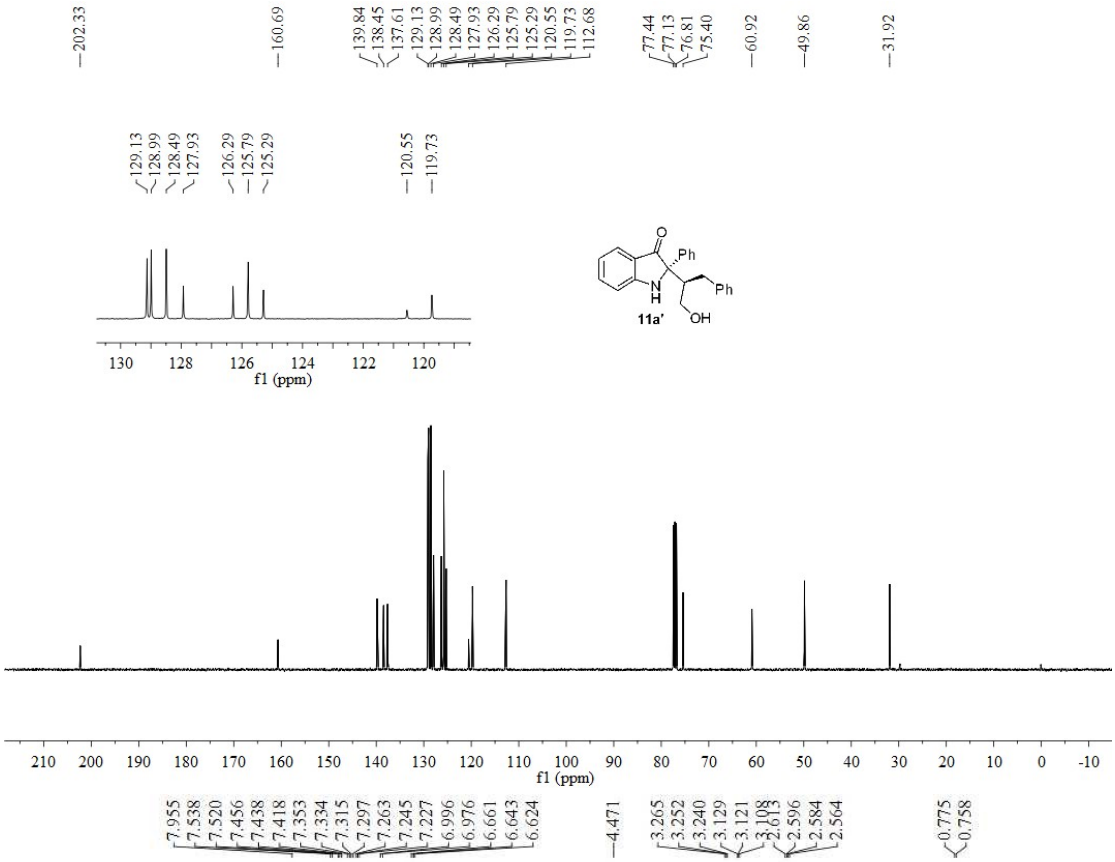
f1 (ppm)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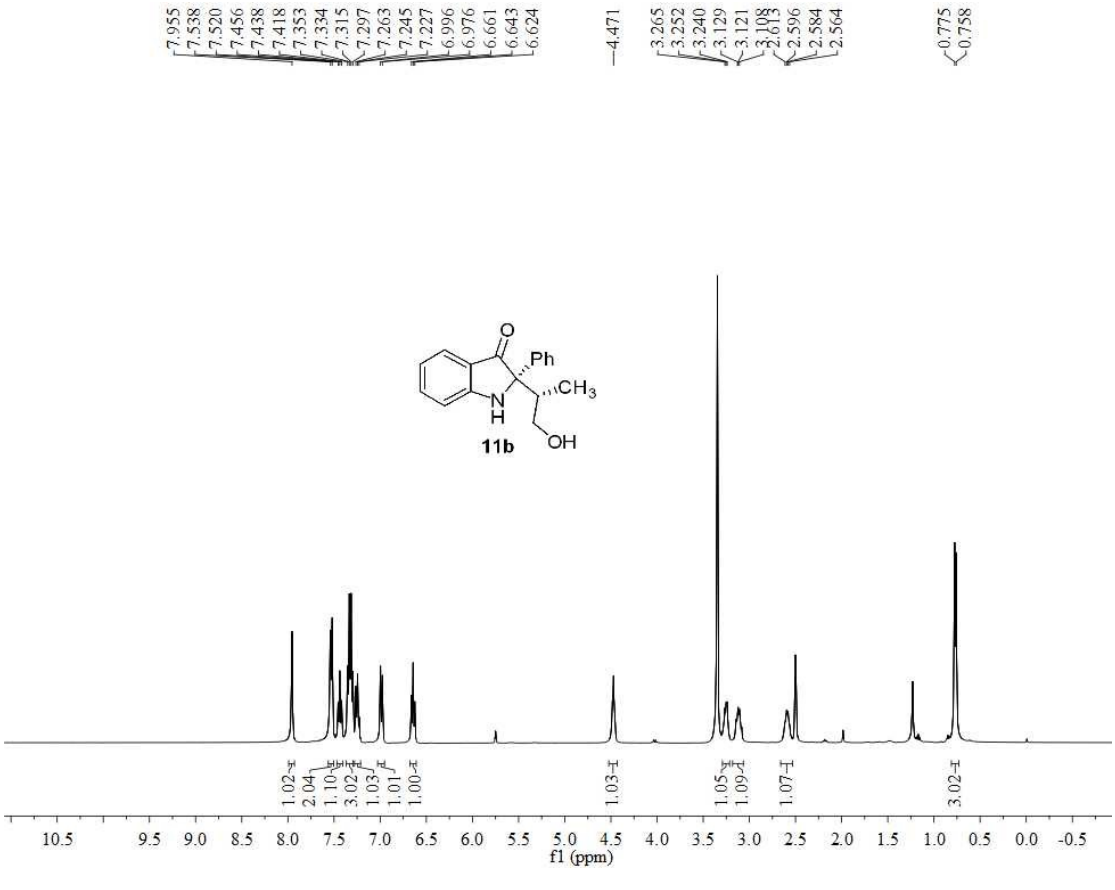
f1 (ppm)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2.613
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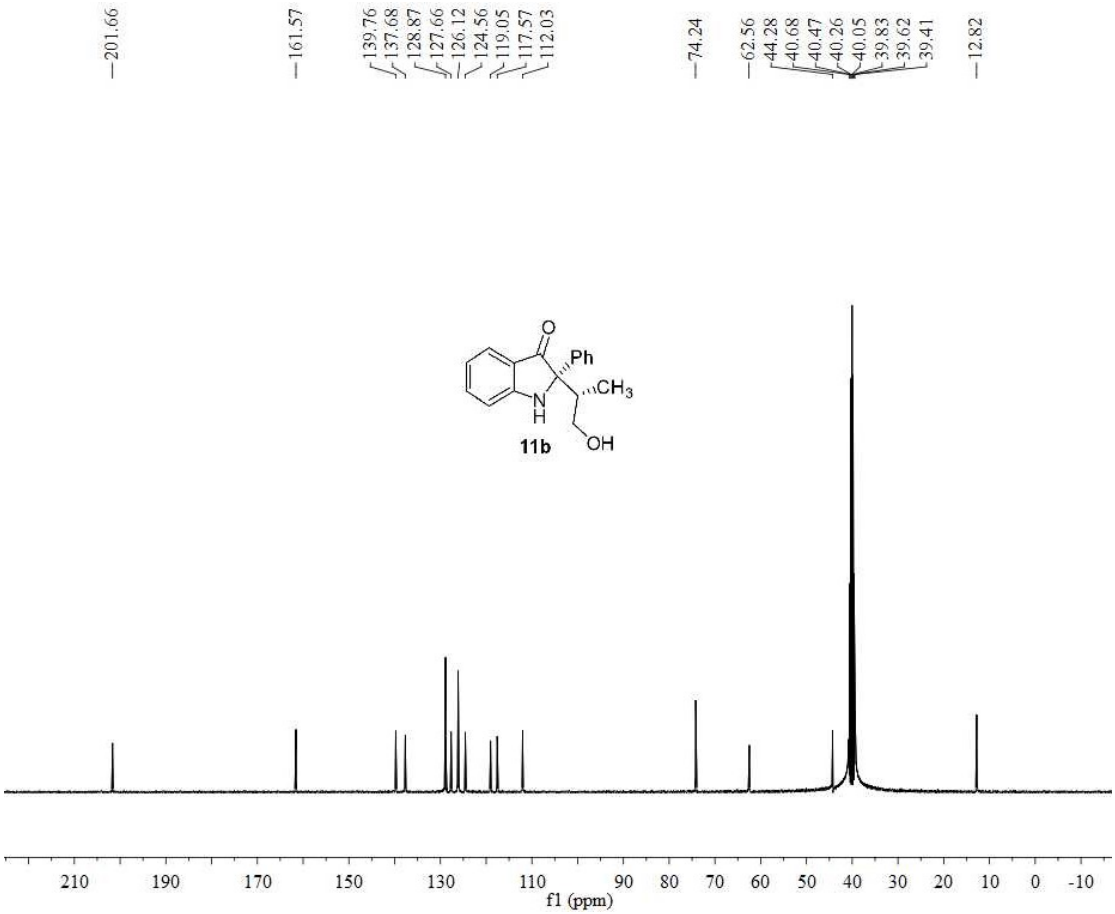
f1 (ppm)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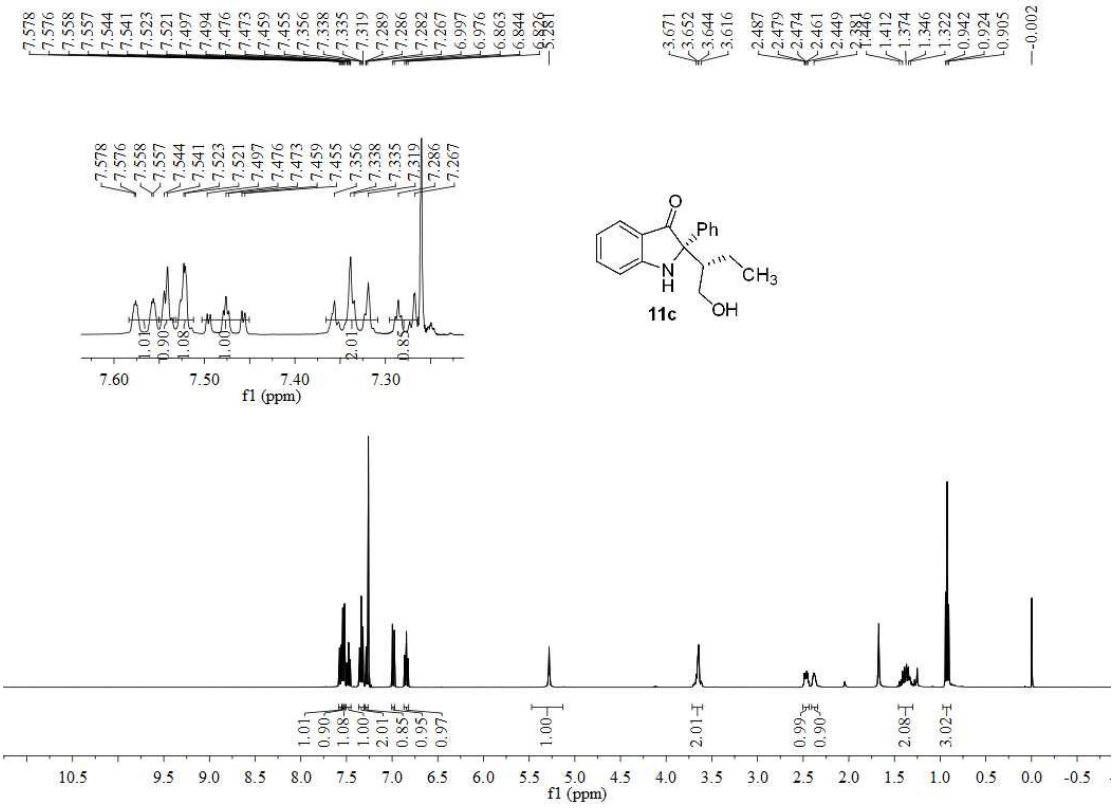
f1 (ppm)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OH
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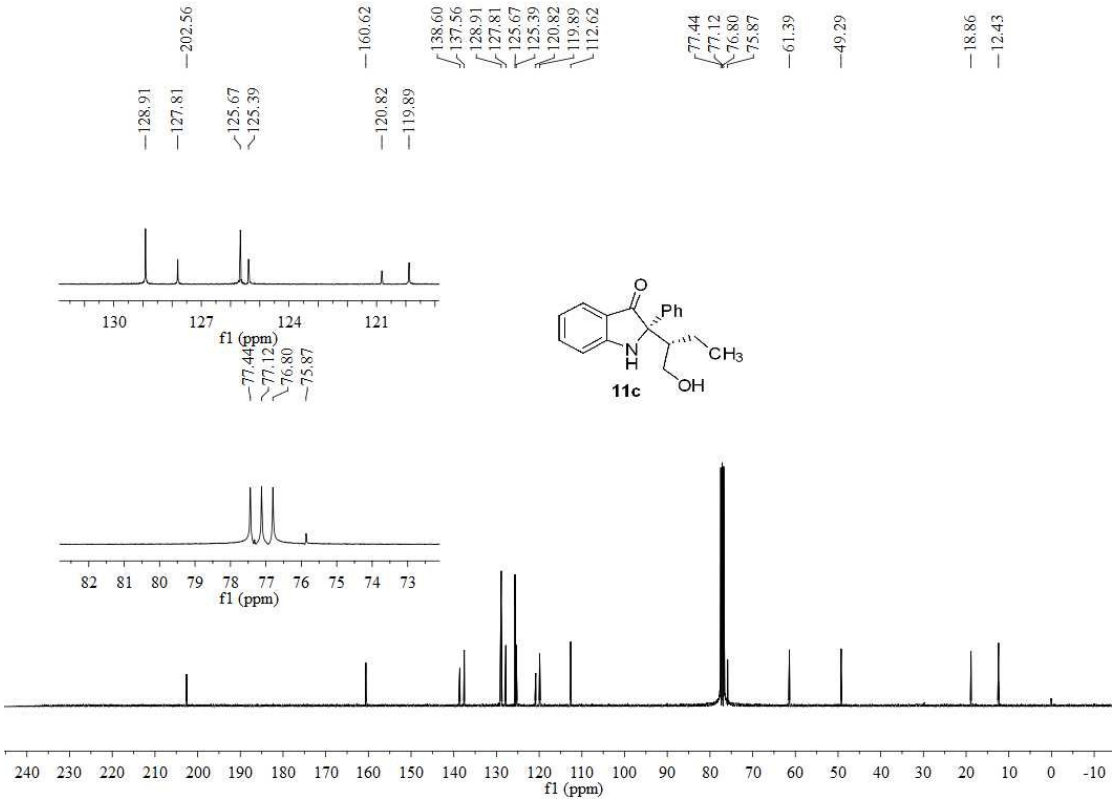
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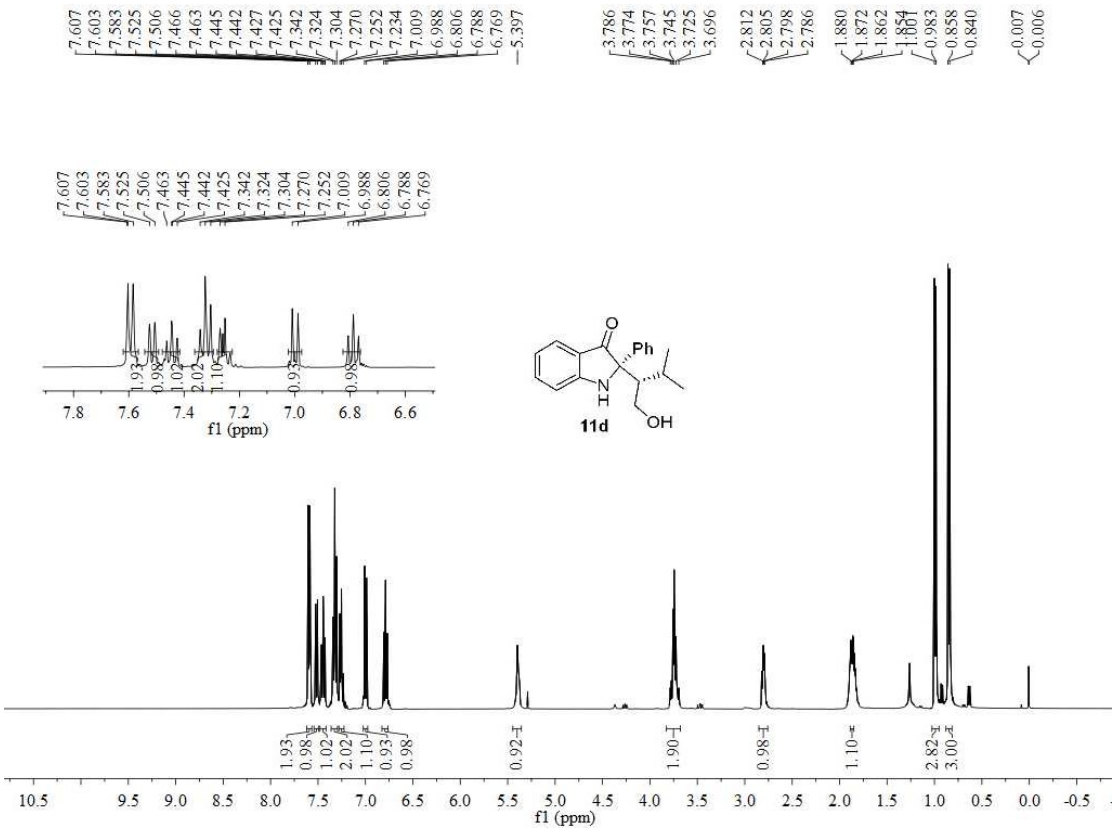
112.62
77.44
77.12
76.80
75.87
61.39
49.29
18.86
12.43
128.91
127.81
125.67
125.39
120.82
119.89
f1 (ppm)
Ph
CH3
OH
11c
f1 (ppm)
f1 (ppm)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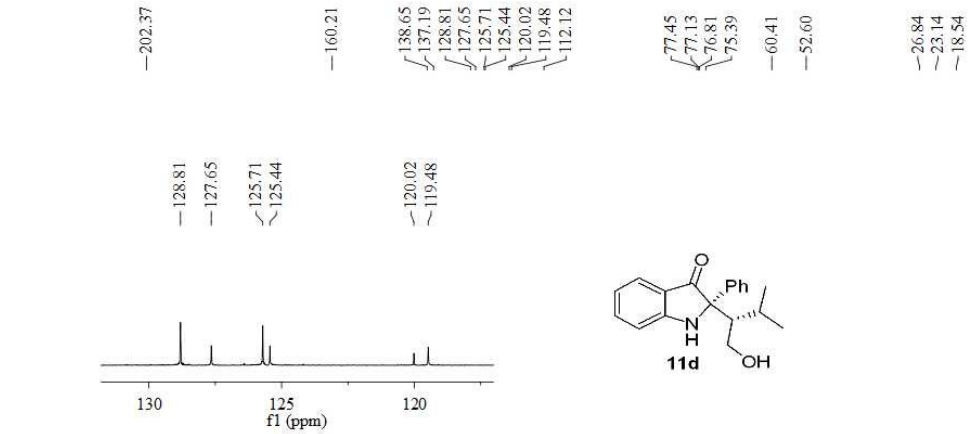
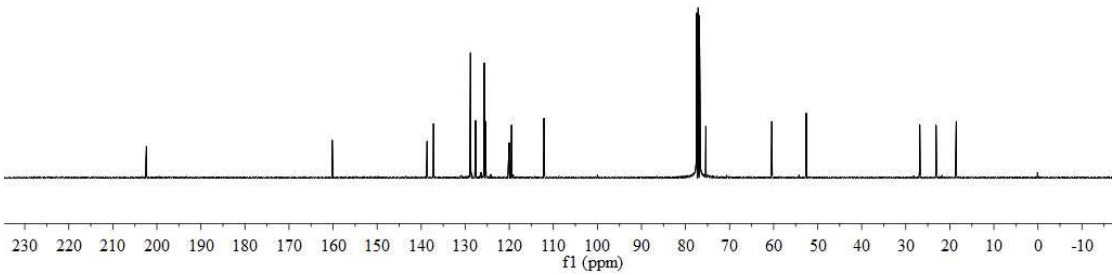
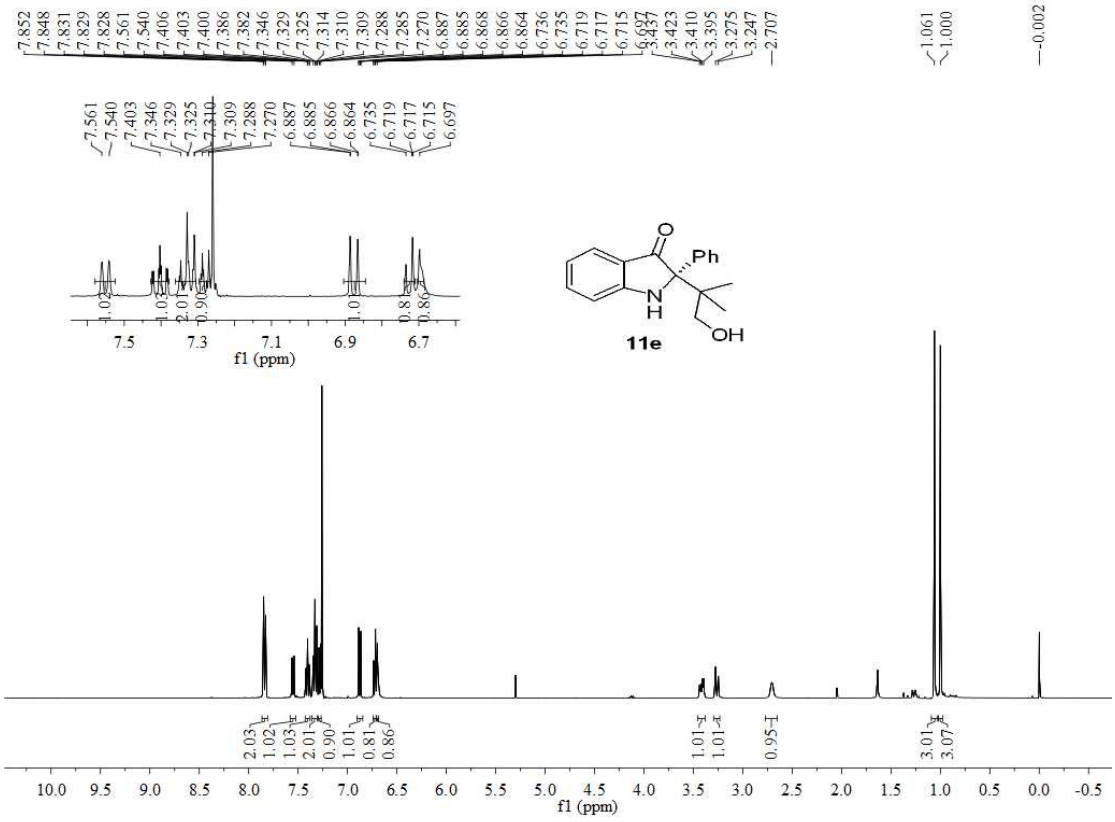
7.603
7.583
7.525
7.506
7.466
7.463
7.445
7.442
7.427
7.425
7.342
7.324
7.304
7.270
7.252
7.234
7.009
6.988
6.806
6.788
6.769
5.397
3.786
3.774
3.757
3.745
3.725
3.696
2.812
2.805
2.798
2.786
1.880
1.872
1.862
1.854
1.001
0.983
0.858
0.840
0.007
0.006
1.93
0.98
1.02
2.02
1.10
0.93
0.98
0.92
1.90
0.98
1.10
2.82
3.00
f1 (ppm)
Ph
OH
11d
f1 (ppm)


202.37
160.21
138.65
137.19
128.81
127.65
125.71
125.44
120.02
119.48
112.12
77.45
77.13
76.81
75.39
60.41
52.60
26.84
23.14
18.54
128.81
127.65
125.71
125.44
120.02
119.48
130
125
120
f1 (ppm)
O
Ph
N
H
OH
11d


230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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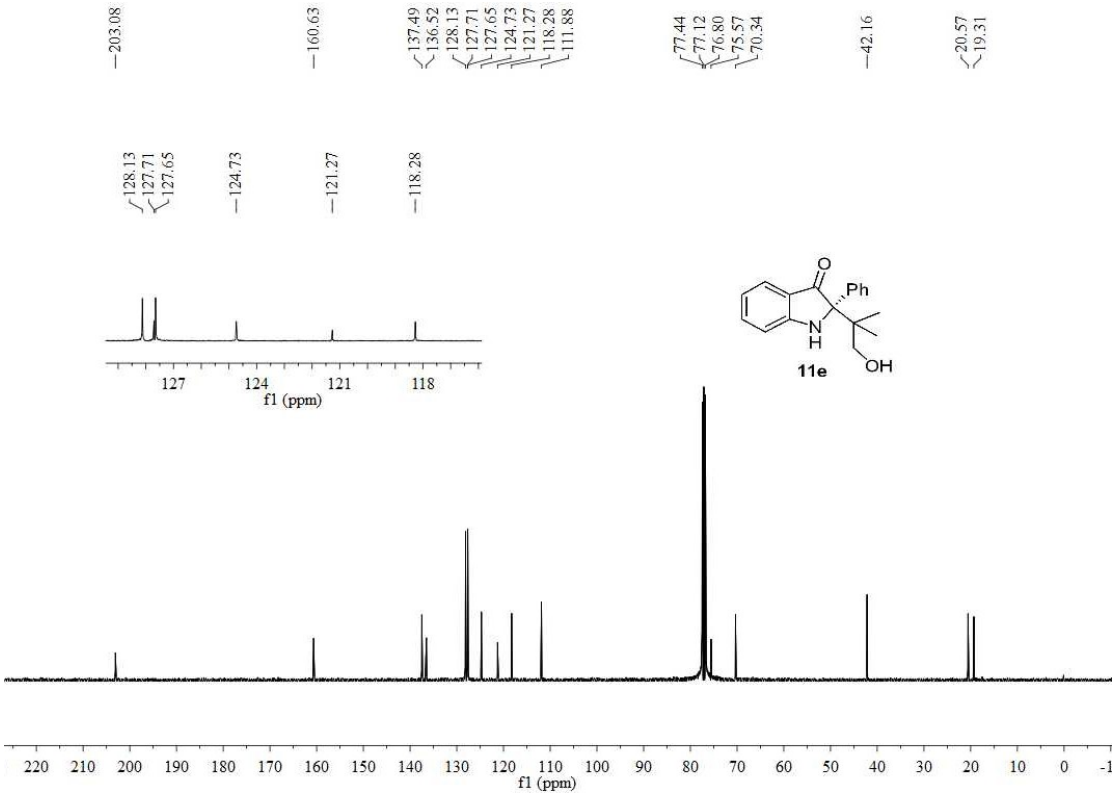
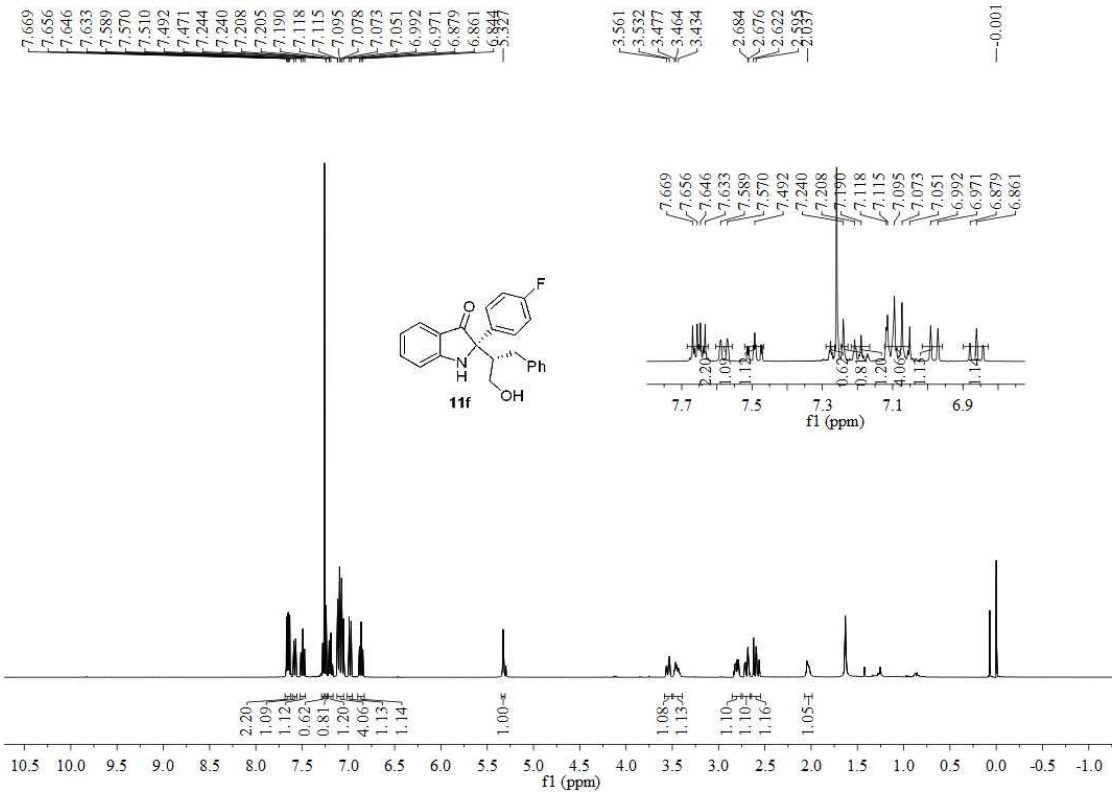
7.831
7.829
7.828
7.561
7.540
7.406
7.403
7.400
7.386
7.382
7.346
7.329
7.325
7.314
7.310
7.309
7.288
7.285
7.270
6.887
6.885
6.868
6.866
6.864
6.736
6.735
6.719
6.717
6.715
6.697
3.437
3.423
3.410
3.395
3.275
3.247
2.707
1.061
1.000
-0.002
1.02
1.03
2.01
0.90
1.0
0.81
0.86
7.5
7.3
7.1
6.9
6.7
f1 (ppm)
O
Ph
N
H
OH
11e
2.03
1.02
1.03
2.01
0.90
1.01
0.81
0.86
1.01
1.01
0.95
3.01
3.07
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


203.08
160.63
137.49
136.52
128.13
127.71
127.65
124.73
121.27
118.28
111.88
77.44
77.12
76.80
75.57
70.34
42.16
20.57
19.31
Ph
OH
11e
f1 (ppm)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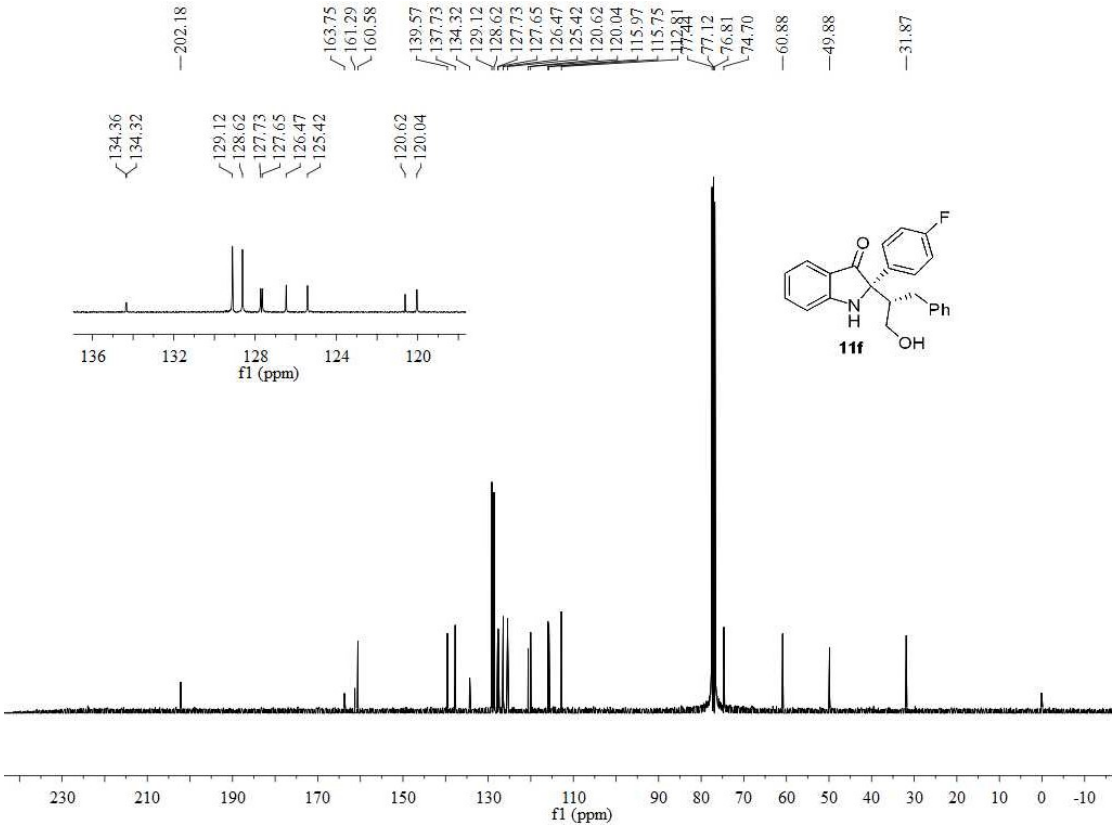
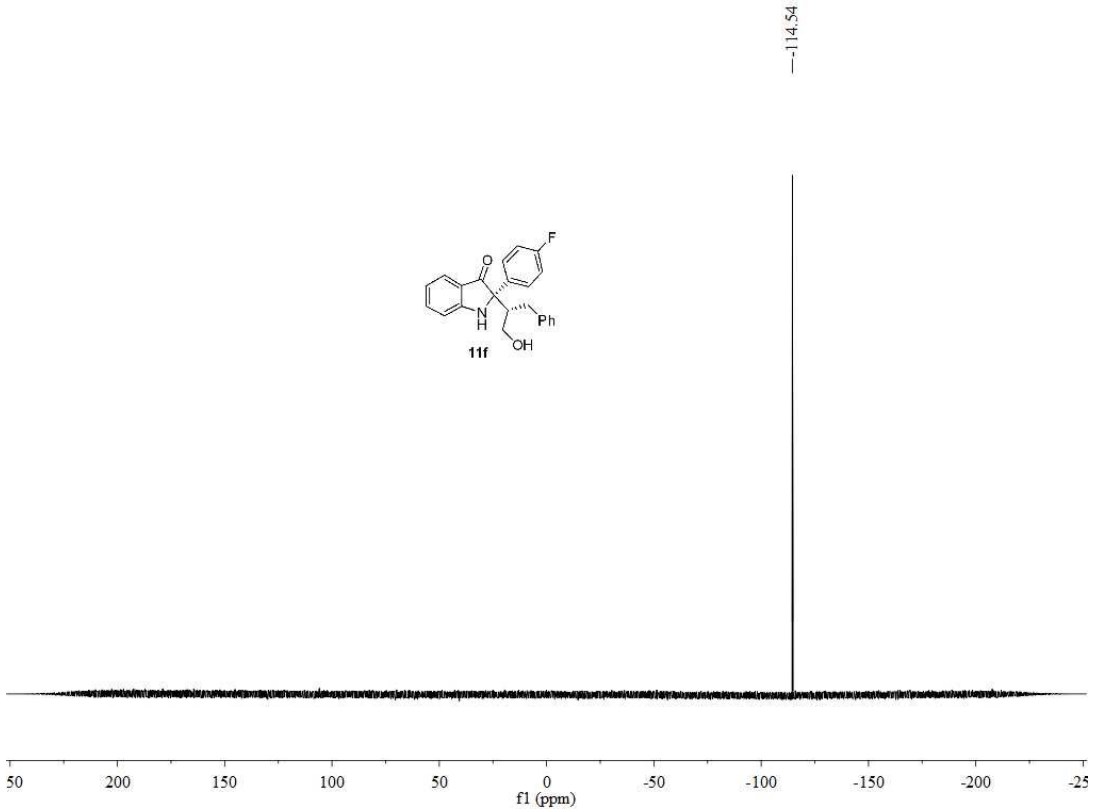
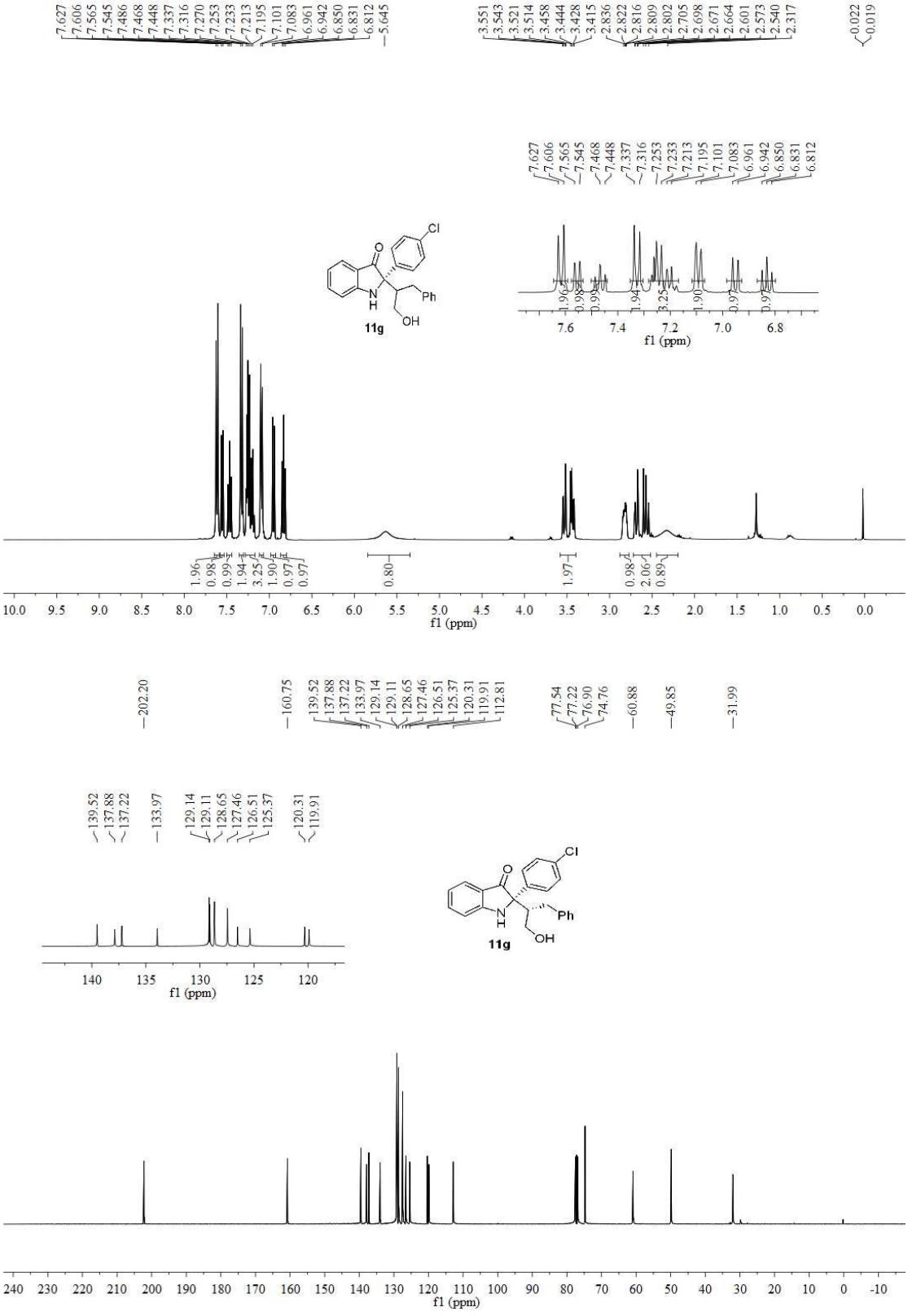
7.656
7.646
7.633
7.589
7.570
7.510
7.492
7.471
7.244
7.240
7.208
7.205
7.190
7.118
7.115
7.095
7.078
7.073
7.051
6.992
6.971
6.879
6.861
3.561
3.532
3.477
3.464
3.434
2.684
2.676
2.622
2.595
2.037
0.001
F
Ph
OH
11f
f1 (ppm)


202.18
163.75
161.29
160.58
139.57
137.73
134.32
129.12
128.62
127.73
127.65
126.47
125.42
120.62
120.04
115.97
115.75
77.44
77.12
76.81
74.70
60.88
49.88
31.87
134.36
134.32
129.12
128.62
127.73
127.65
126.47
125.42
120.62
120.04
136
132
128
124
120
f1 (ppm)
F
O
N
H
Ph
OH
11f
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


-114.54
F
O
N
H
Ph
OH
11f
50
200
150
100
50
0
-50
-100
-150
-200
-25
f1 (ppm)


11g
f1 (ppm)


7.574
7.553
7.509
7.504
7.482
7.465
7.278
7.266
7.241
7.216
7.198
7.180
7.107
7.090
6.978
6.958
6.868
6.850
6.831
5.485
3.550
3.528
3.448
3.419
2.837
2.823
2.810
2.796
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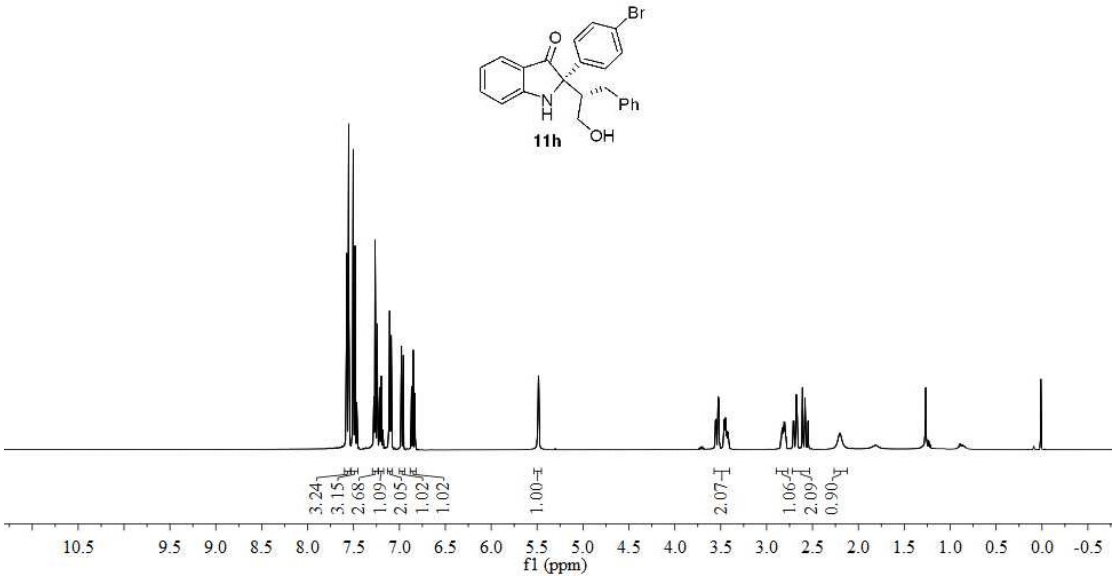
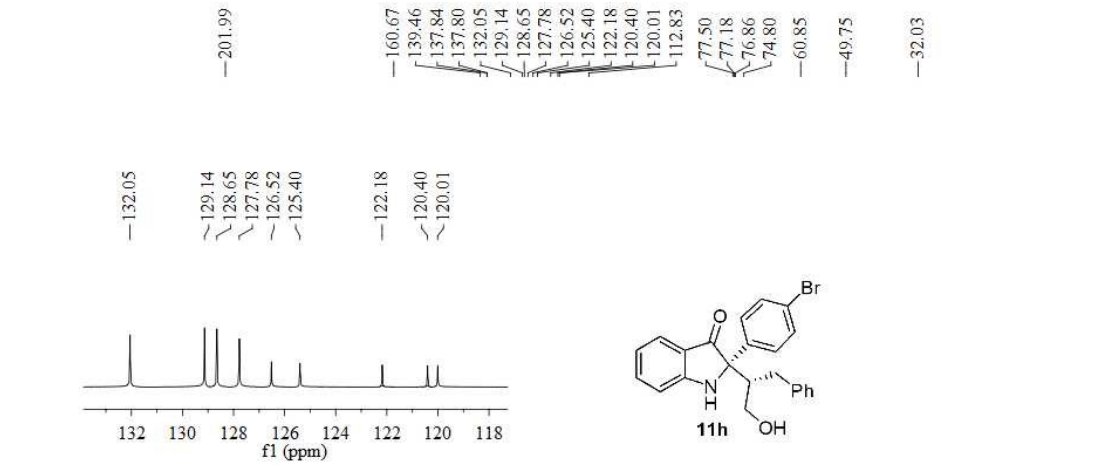
2.702
2.676
2.669
2.609
2.581
2.548
2.201
0.013
0.011


Br
O
N
H
Ph
OH
11h
3.24
3.15
2.68
1.09
2.05
1.02
1.02
1.00
2.07
1.06
2.09
0.90
10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


201.99
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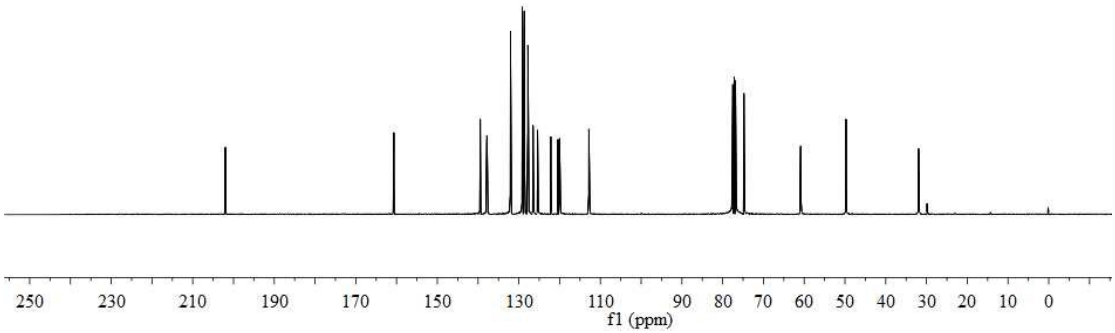
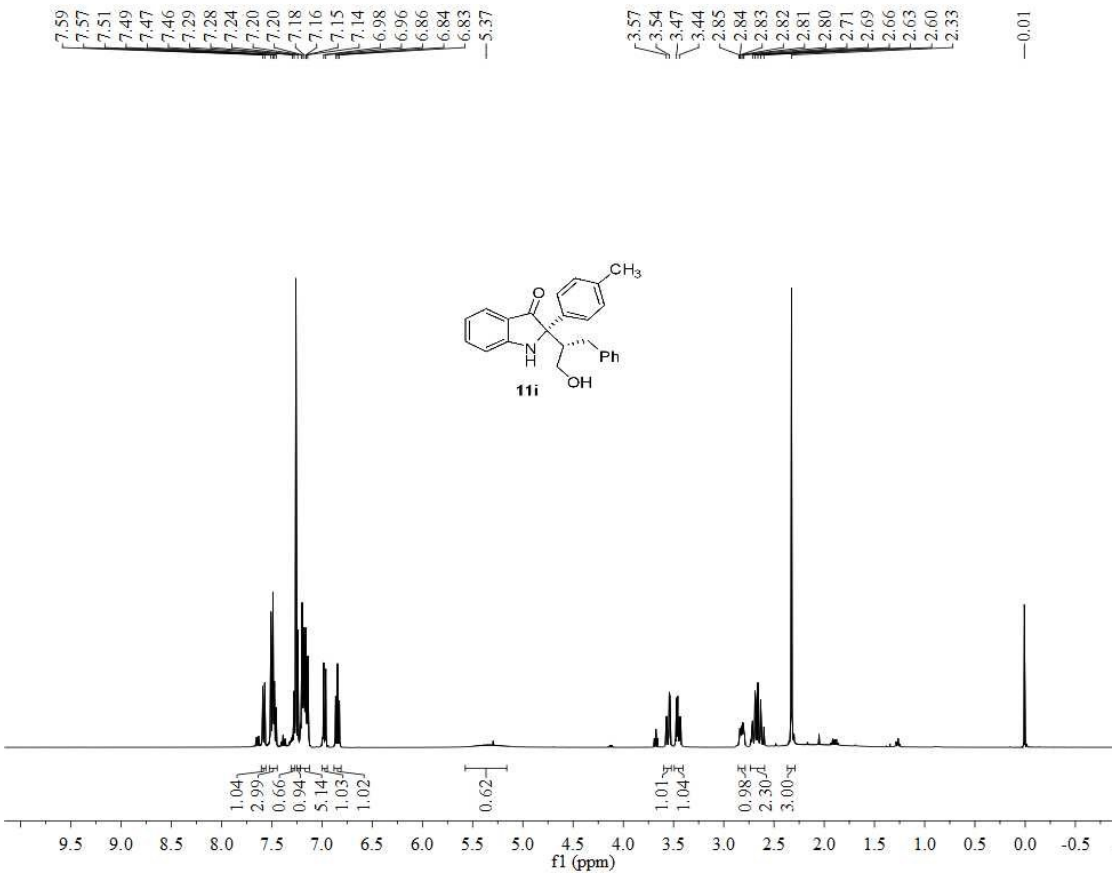
137.80
132.05
129.14
128.65
127.78
126.52
125.40
122.18
120.40
120.01
112.83
77.50
77.18
76.86
74.80
60.85
49.75
32.03

132.05
129.14
128.65
127.78
126.52
125.40
122.18
120.40
120.01
132 130 128 126 124 122 120 118
f1 (ppm)

Br
O
N
H
Ph
OH
11h


250 230 210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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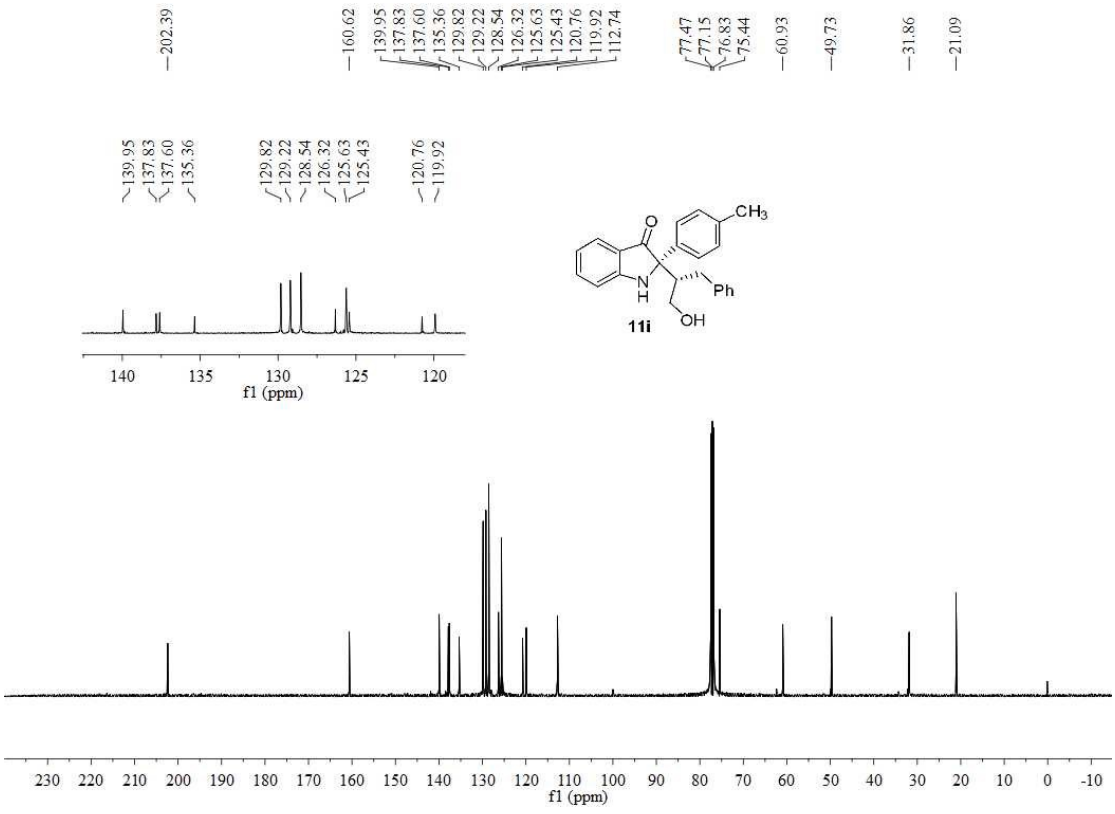
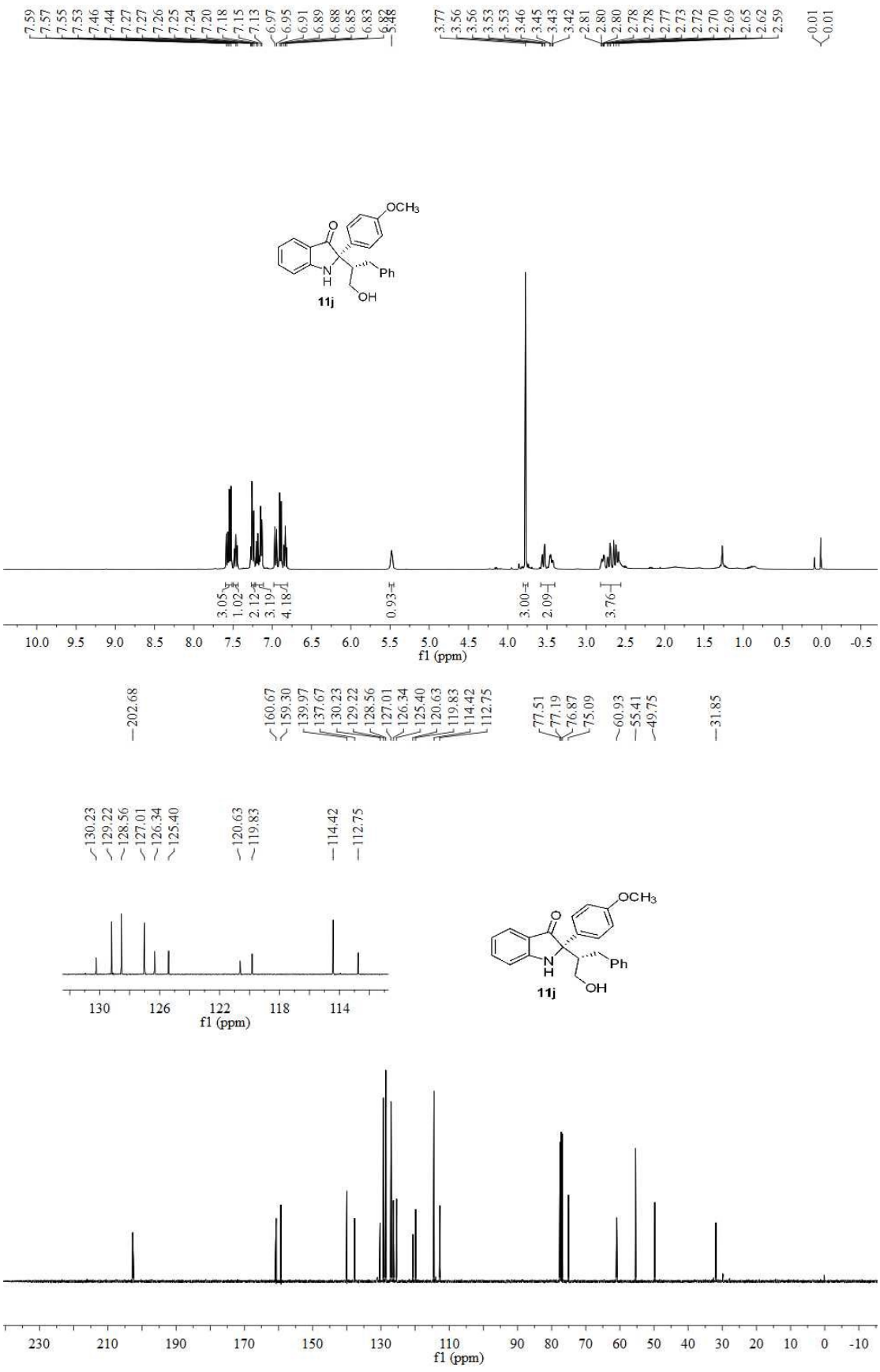
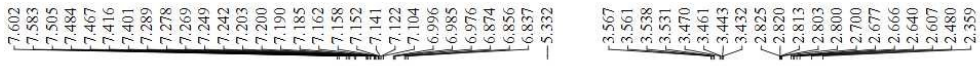
7.57
7.51
7.49
7.47
7.46
7.29
7.28
7.24
7.20
7.20
7.18
7.16
7.15
7.14
6.98
6.96
6.86
6.84
6.83
5.37
3.57
3.54
3.47
3.44
2.85
2.84
2.83
2.82
2.81
2.80
2.71
2.69
2.66
2.63
2.60
2.33
0.01
CH3
O
N
H
Ph
OH
11i
1.04
2.99
0.66
0.94
5.14
1.03
1.02
0.62
1.01
1.04
0.98
2.30
3.00
f1 (ppm)


202.39
160.62
139.95
137.83
137.60
135.36
129.82
129.22
128.54
126.32
125.63
125.43
120.76
119.92
112.74
77.47
77.15
76.83
75.44
60.93
49.73
31.86
21.09
CH3
O
N
H
Ph
OH
11i
f1 (ppm)


7.59 7.57 7.55 7.53 7.46 7.44 7.27 7.27 7.26 7.25 7.24 7.20 7.18 7.15 7.13 6.97 6.95 6.91 6.89 6.88 6.85 6.83 6.82 5.48
3.77 3.56 3.56 3.53 3.53 3.46 3.45 3.43 3.42 2.81 2.80 2.80 2.78 2.78 2.77 2.73 2.72 2.70 2.69 2.65 2.62 2.59
0.01 0.01
OCH3
O
N
H
Ph
OH
11j
3.05 1.02 2.12 3.19 4.18 0.93 3.00 2.09 3.76
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
202.68
160.67 159.30 139.97 137.67 130.23 129.22 128.56 127.01 126.34 125.40 120.63 119.83 114.42 112.75
77.51 77.19 76.87 75.09
60.93 55.41 49.75
31.85
130.23 129.22 128.56 127.01 126.34 125.40 120.63 119.83 114.42 112.75
130 126 122 118 114
f1 (ppm)
OCH3
O
N
H
Ph
OH
11j
230 210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.269
7.249
7.242
7.203
7.200
7.190
7.185
7.162
7.158
7.152
7.141
7.122
7.104
6.996
6.985
6.976
6.874
6.856
6.837
5.332
3.567
3.561
3.538
3.531
3.470
3.461
3.443
3.432
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2.803
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2.666
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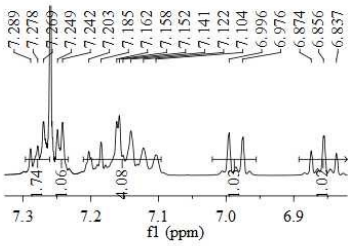
2.359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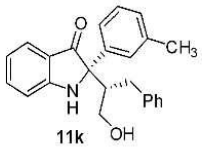
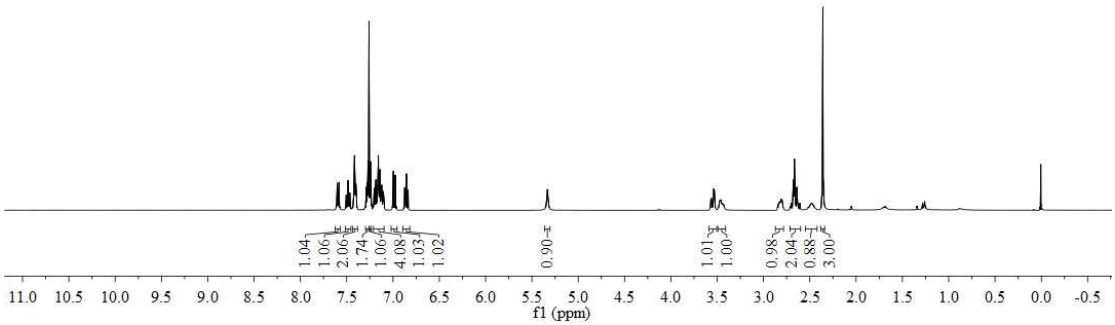
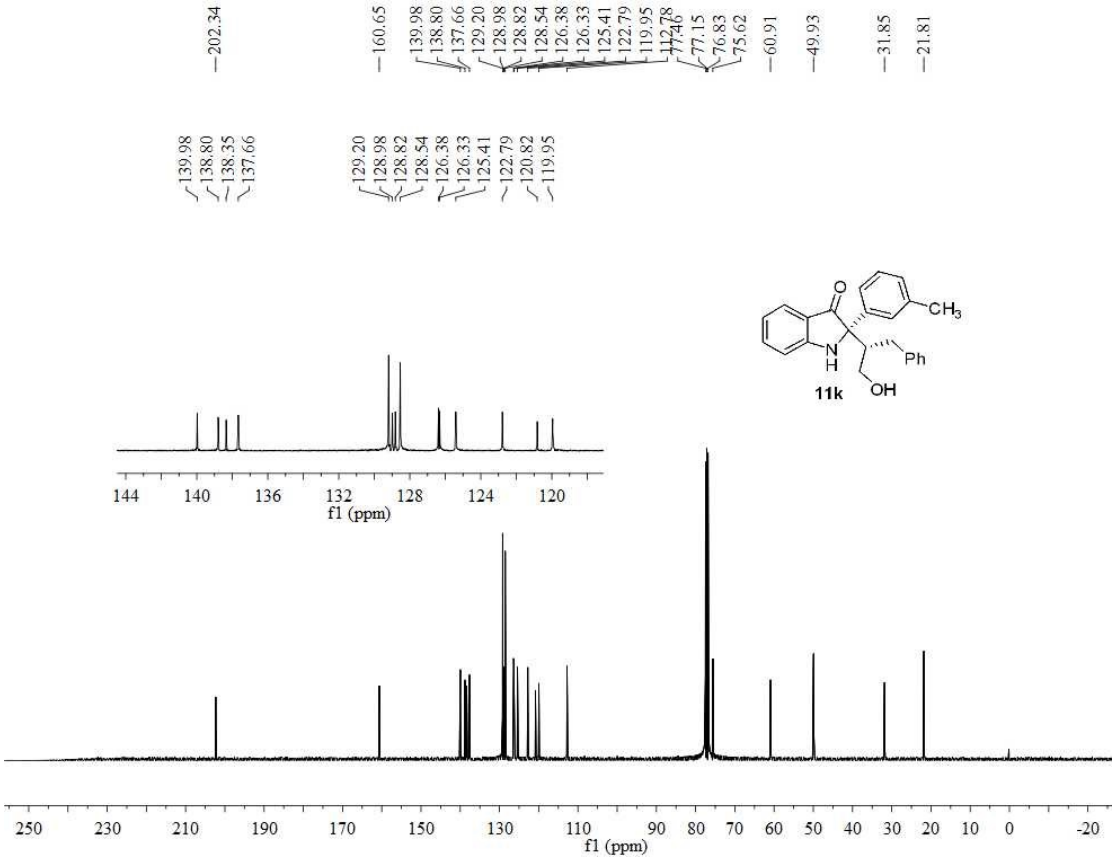
7.278
7.269
7.249
7.242
7.203
7.185
7.162
7.158
7.152
7.141
7.122
7.104
6.996
6.976
6.874
6.856
6.837
1.74
1.06
4.08
1.03
1.02
7.3
7.2
7.1
7.0
6.9
f1 (ppm)


O
CH3
N
H
Ph
OH
11k


1.04
1.06
2.06
1.74
1.06
4.08
1.03
1.02
0.90
1.01
1.00
0.98
2.04
0.88
3.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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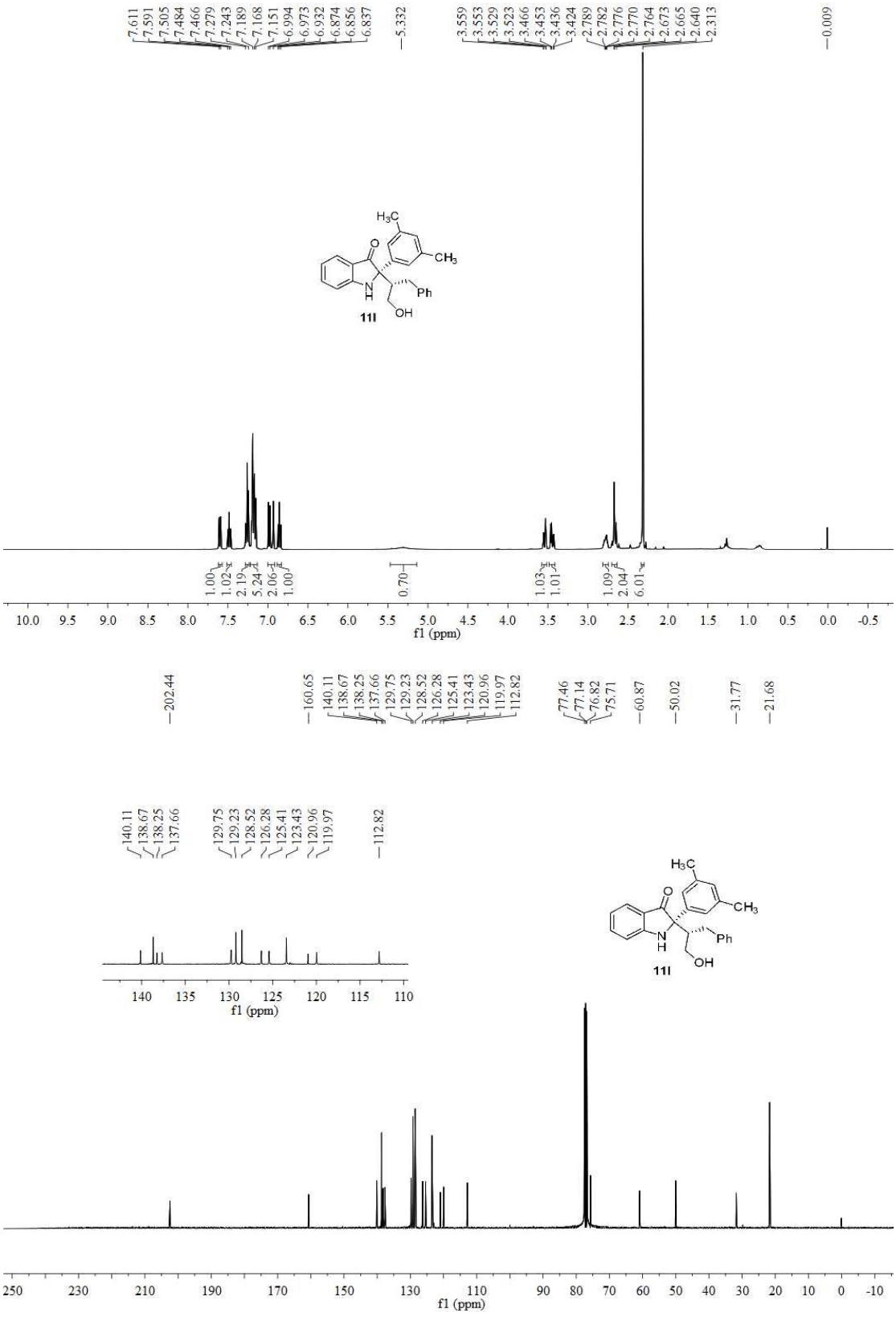
138.80
137.66
129.20
128.98
128.82
128.54
126.38
126.33
125.41
122.79
119.95
77.46
77.15
76.83
75.62
60.91
49.93
31.85
21.81
139.98
138.80
138.35
137.66
129.20
128.98
128.82
128.54
126.38
126.33
125.41
122.79
120.82
119.95
144 140 136 132 128 124 120
f1 (ppm)
O
CH3
N
H
Ph
OH
11k
250 230 210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0 -20
f1 (ppm)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7.466
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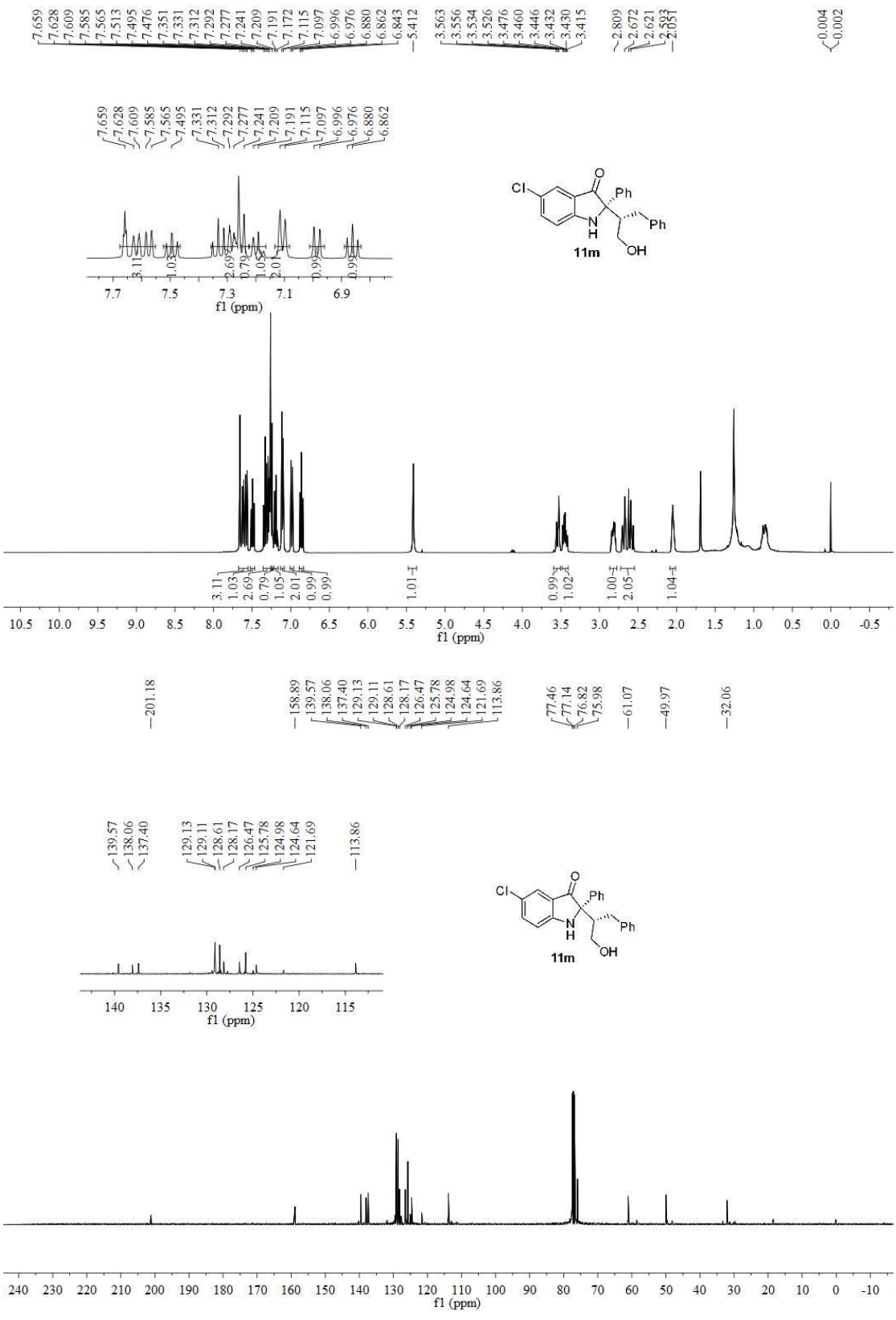
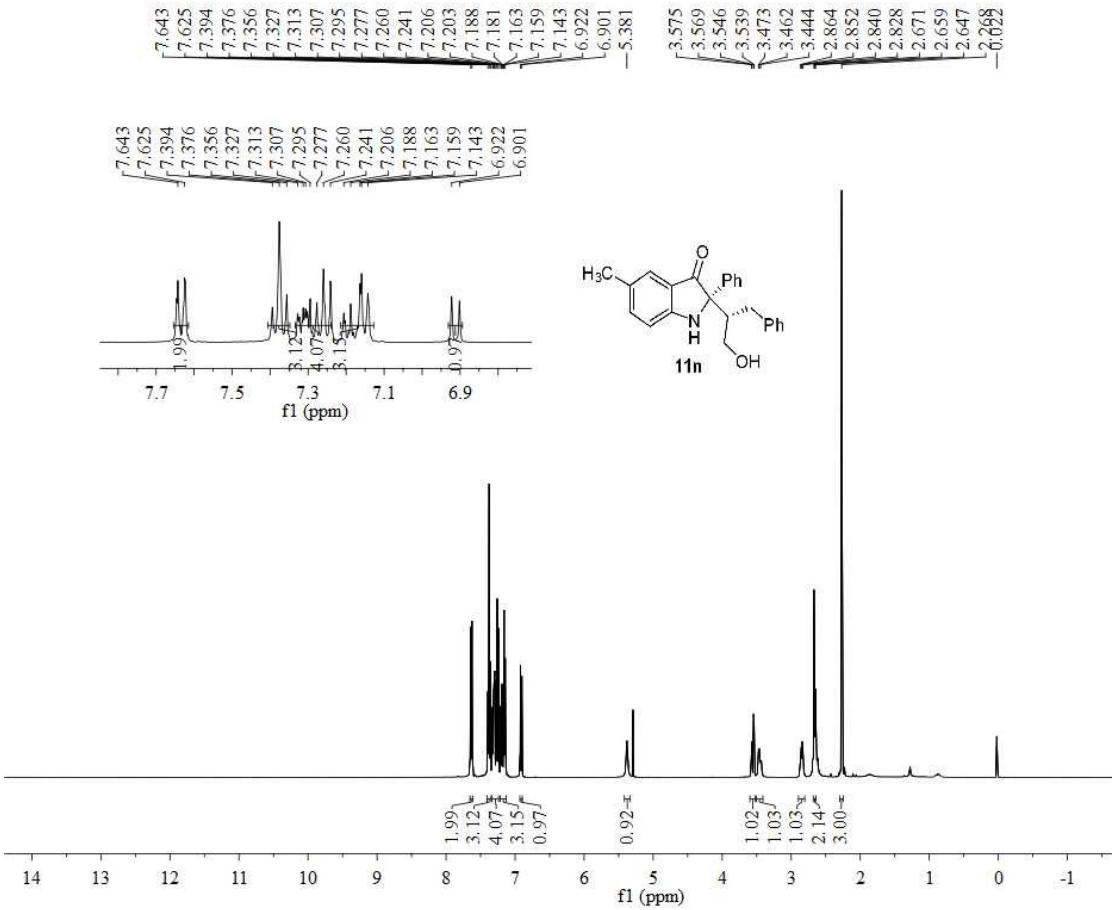
7.243
7.189
7.168
7.151
6.994
6.973
6.932
6.874
6.856
6.837
5.332
3.559
3.553
3.529
3.523
3.466
3.453
3.436
3.424
2.789
2.782
2.776
2.770
2.764
2.673
2.665
2.640
2.313
0.009
H3C
CH3
O
N
H
Ph
OH
11l
1.00
1.02
2.19
5.24
2.06
1.00
0.70
1.03
1.01
1.09
2.04
6.01
f1 (ppm)
202.44
160.65
140.11
138.67
138.25
137.66
129.75
129.23
128.52
126.28
125.41
123.43
120.96
119.97
112.82
77.46
77.14
76.82
75.71
60.87
50.02
31.77
21.68
f1 (ppm)
f1 (ppm)


11m
f1 (ppm)
11m
f1 (ppm)
f1 (ppm)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7.327
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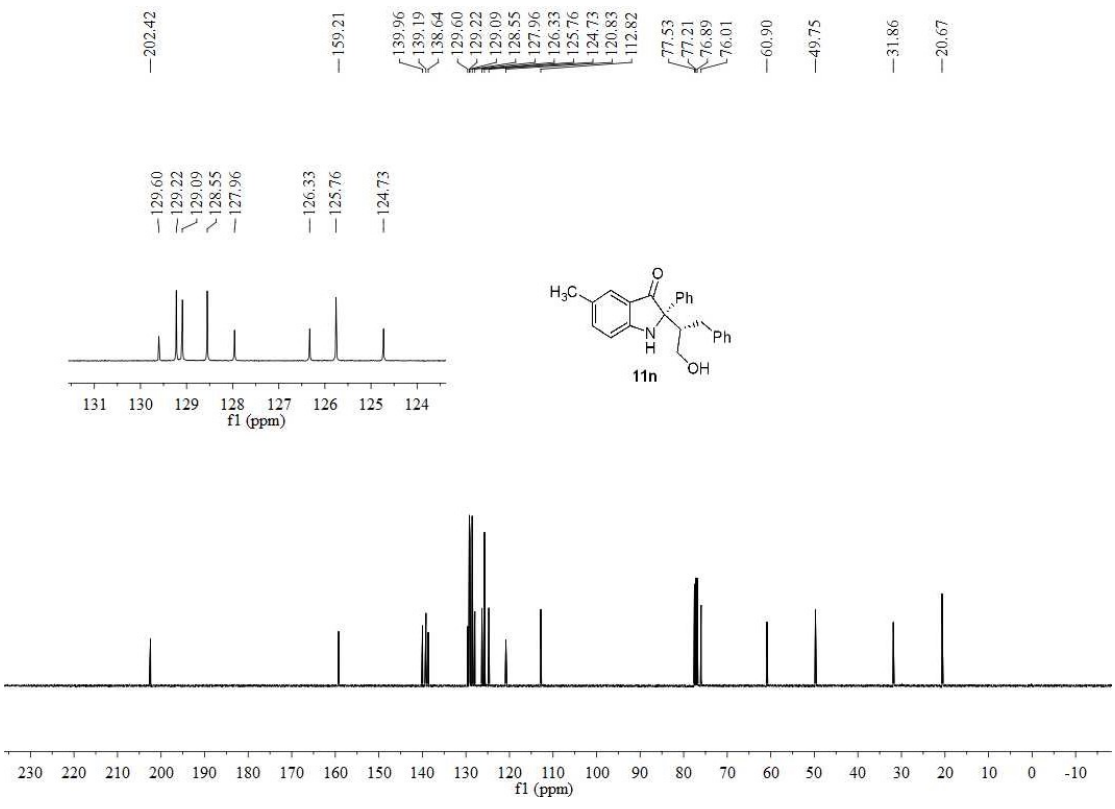
7.307
7.295
7.277
7.260
7.241
7.206
7.203
7.188
7.181
7.163
7.159
7.143
6.922
6.901
5.381
3.575
3.569
3.546
3.539
3.473
3.462
3.444
2.864
2.852
2.840
2.828
2.671
2.659
2.647
0.022
1.99
3.12
4.07
3.15
0.97
0.92
1.02
1.03
1.03
2.14
3.00
f1 (ppm)
11n


202.42
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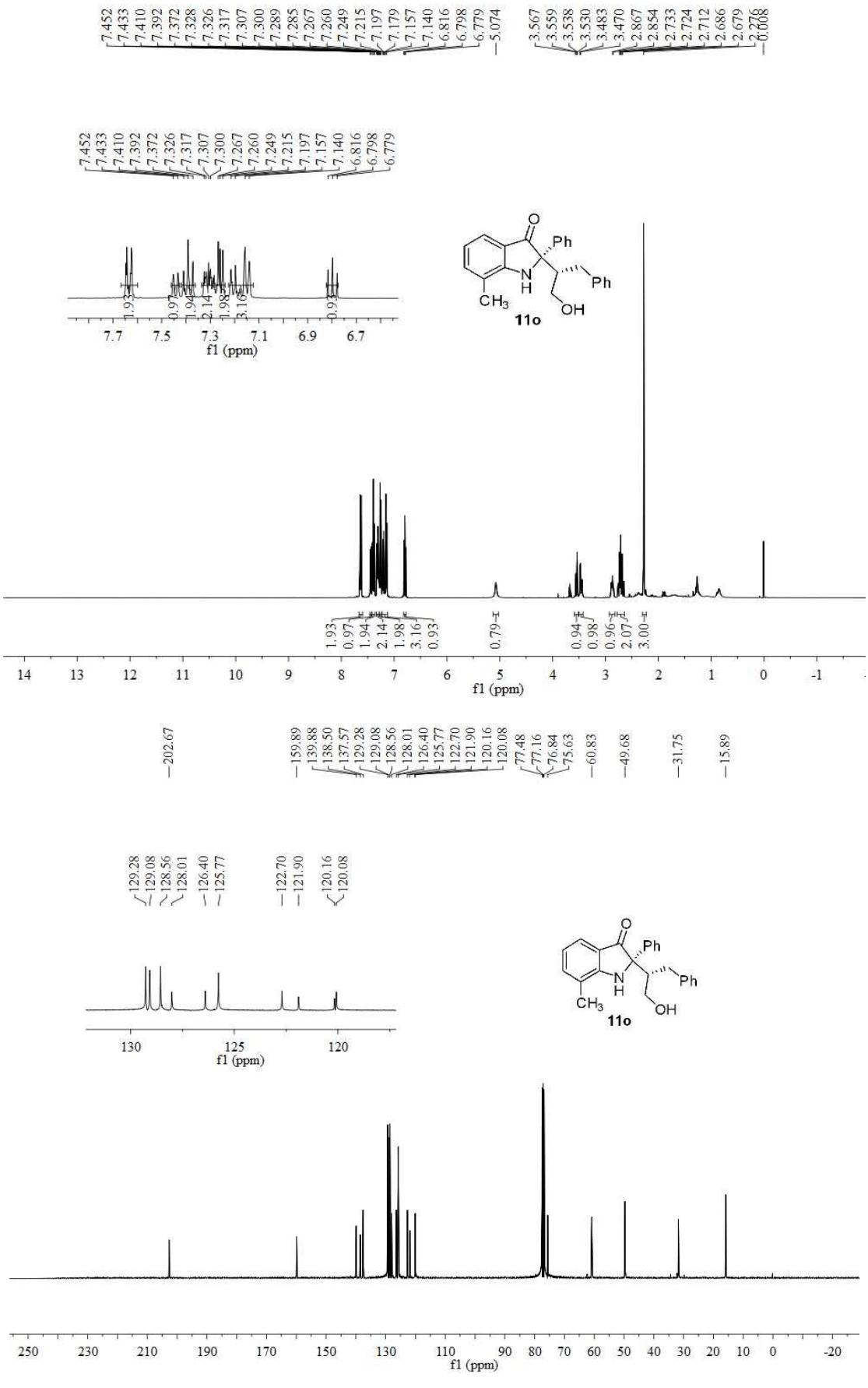
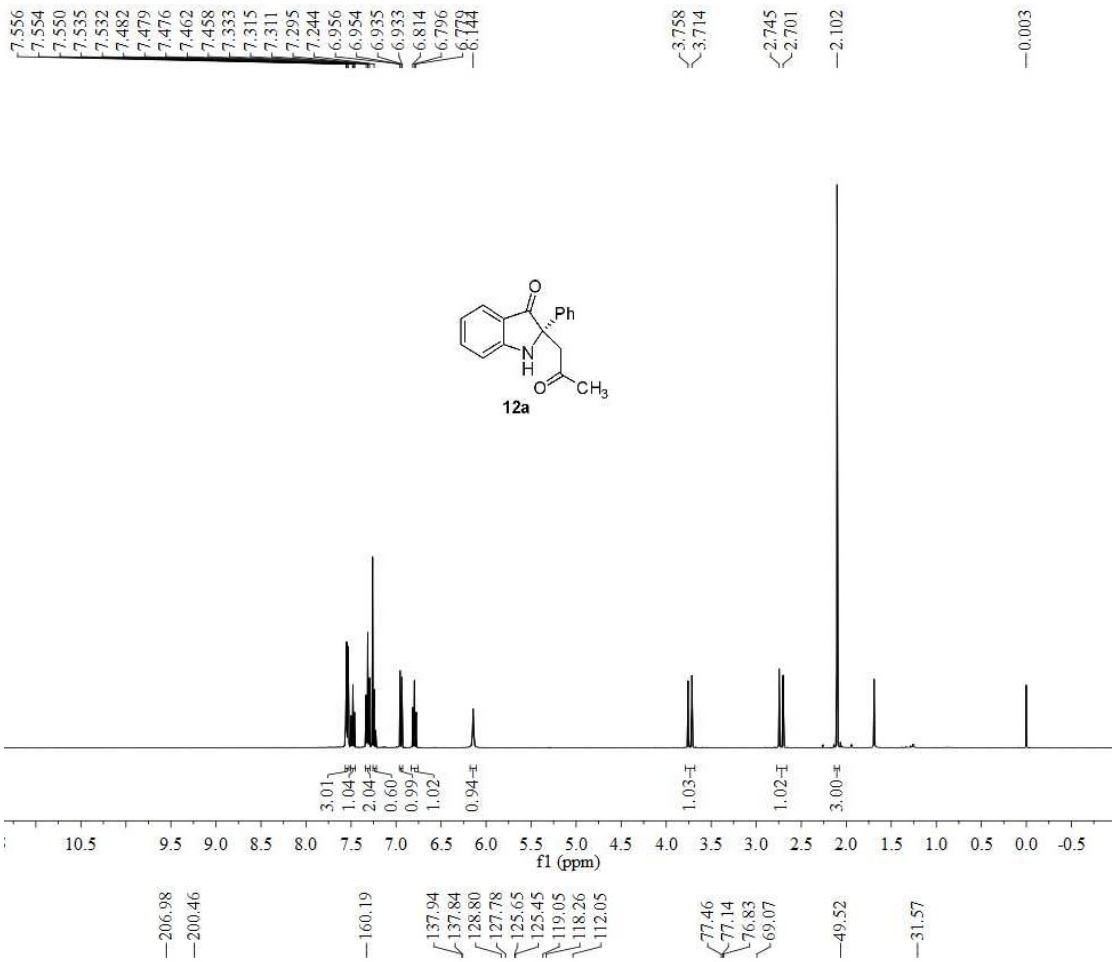
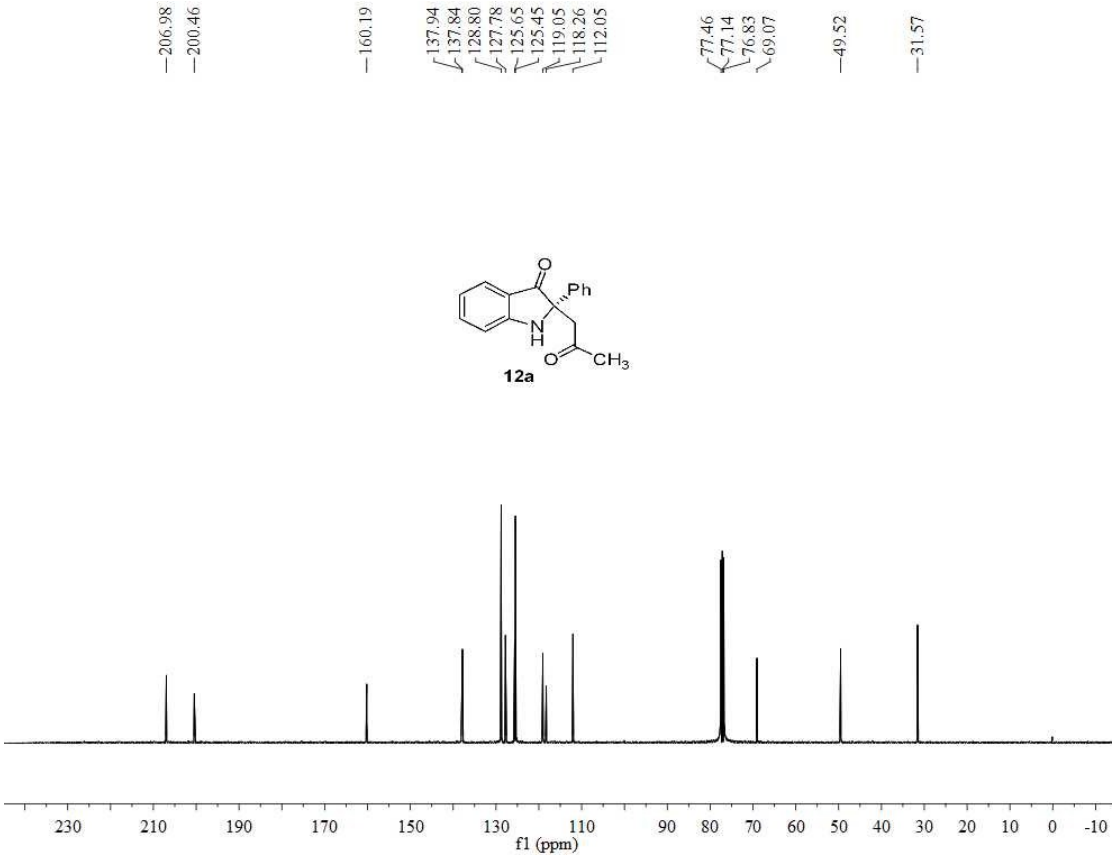
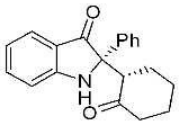
139.96
139.19
138.64
129.60
129.22
129.09
128.55
127.96
126.33
125.76
124.73
77.53
77.21
76.89
76.01
60.90
49.75
31.86
20.67
f1 (ppm)
11n


11o
f1 (ppm)
11o
f1 (ppm)
f1 (ppm)

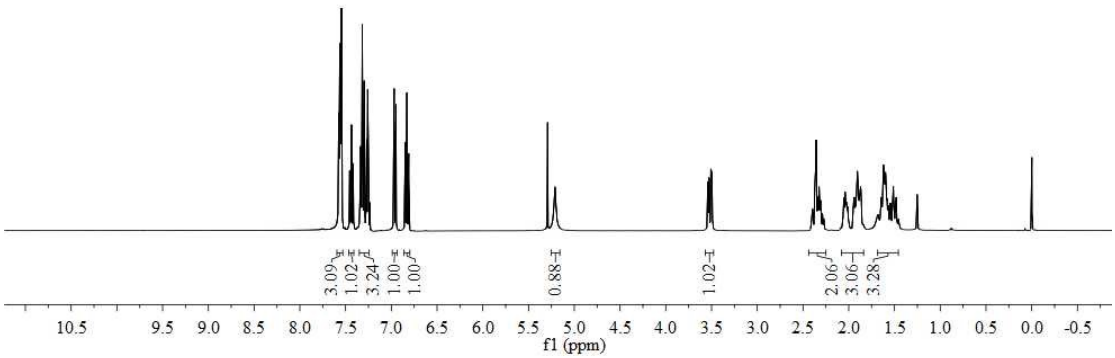

7.556
7.554
7.550
7.535
7.532
7.482
7.479
7.476
7.462
7.458
7.333
7.315
7.311
7.295
7.244
6.956
6.954
6.935
6.933
6.814
6.796
6.779
6.144
3.758
3.714
2.745
2.701
2.102
0.003
Ph
N
H
O
CH3
12a
3.01
1.04
2.04
0.60
0.99
1.02
0.94
1.03
1.02
3.00
f1 (ppm)

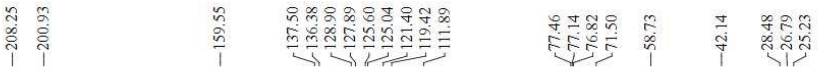

206.98
200.46
160.19
137.94
137.84
128.80
127.78
125.65
125.45
119.05
118.26
112.05
77.46
77.14
76.83
69.07
49.52
31.57
Ph
N
H
O
CH3
12a
f1 (ppm)

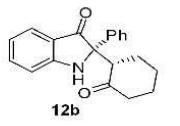

7.575
7.563
7.558
7.545
7.455
7.437
7.417
7.335
7.317
7.297
7.272
7.260
7.258
7.253
7.236
6.970
6.951
6.848
6.829
6.811
5.211
3.541
3.527
3.508
3.495
2.355
2.324
2.053
2.040
1.944
1.930
1.905
1.871
1.621
1.598
1.512
1.481
0.000
-0.001


O
Ph
N
H
O

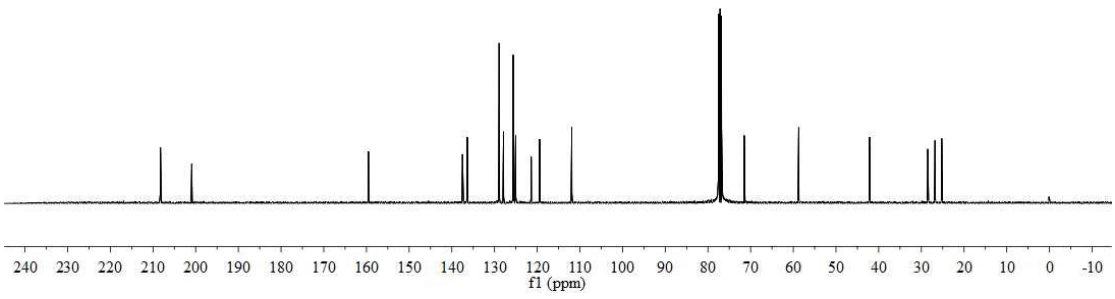
12b

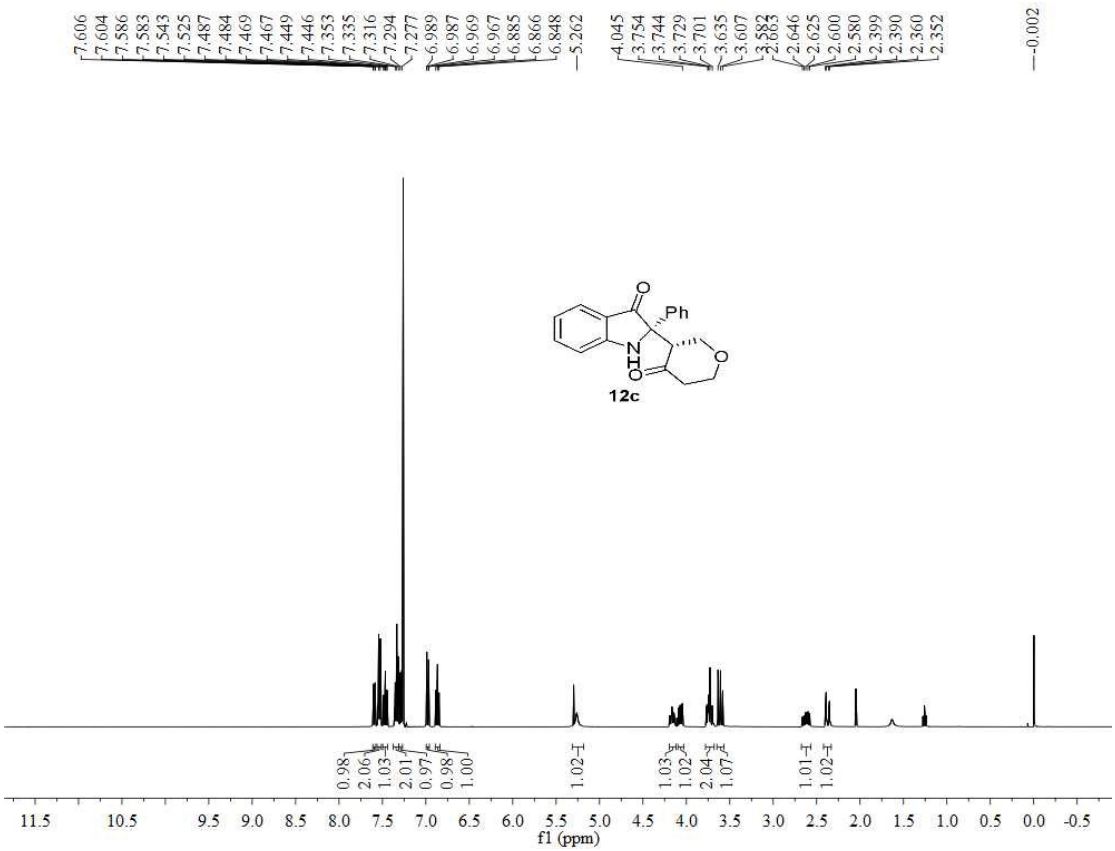

3.09
1.02
3.24
1.00
1.00
0.88
1.02
2.06
3.06
3.28
10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

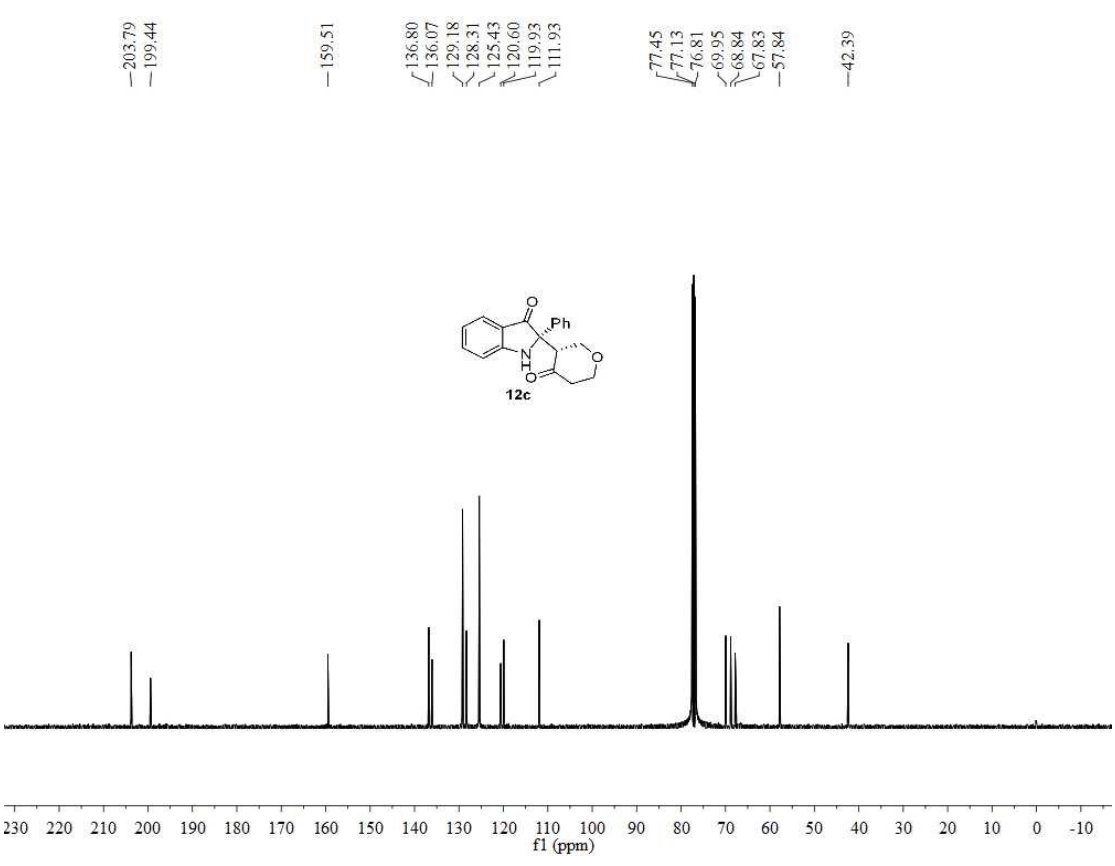

208.25
200.93
159.55
137.50
136.38
128.90
127.89
125.60
125.04
121.40
119.42
111.89
77.46
77.14
76.82
71.50
58.73
42.14
28.48
26.79
25.23

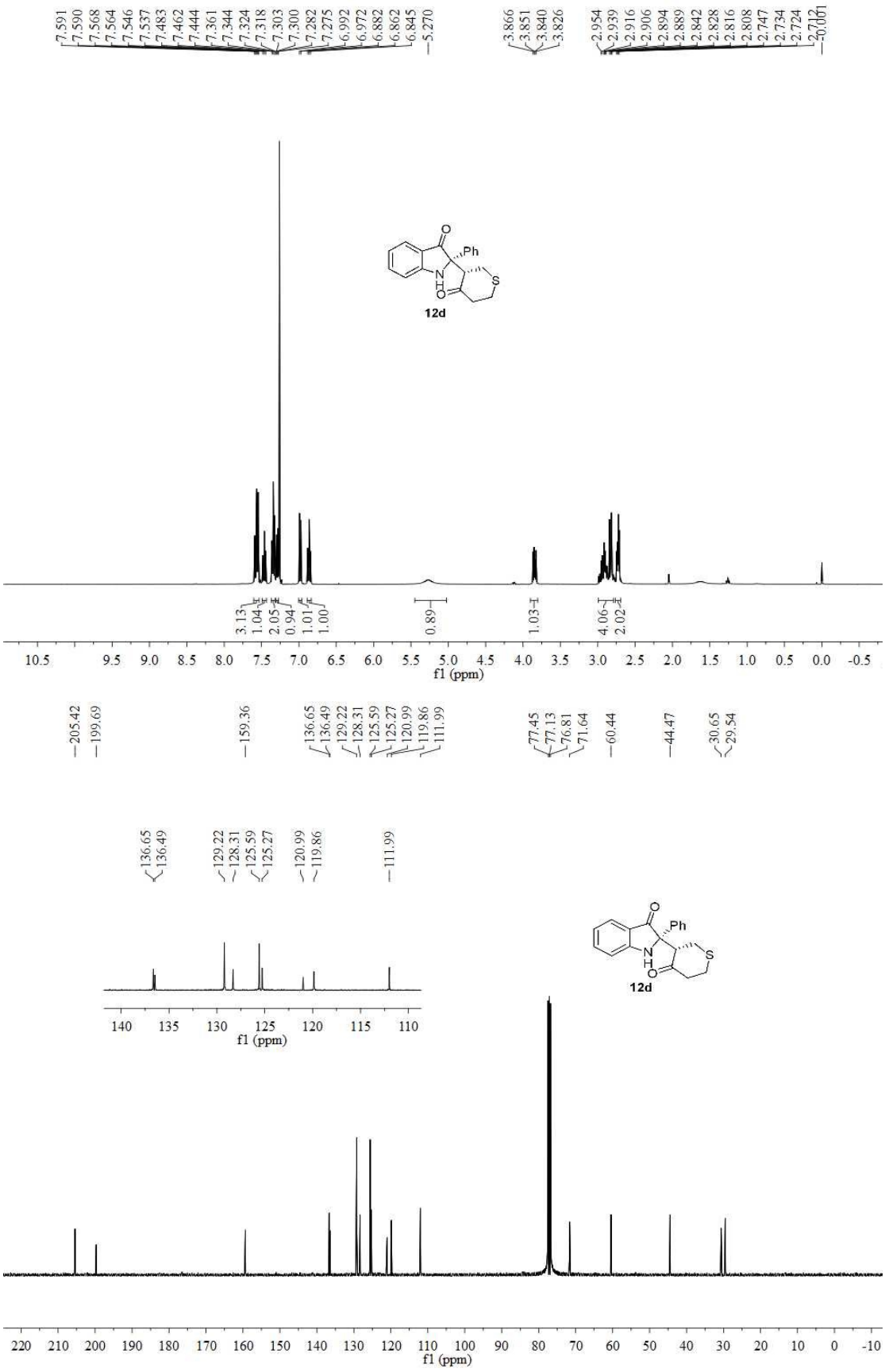

O
Ph
N
H
O

12b

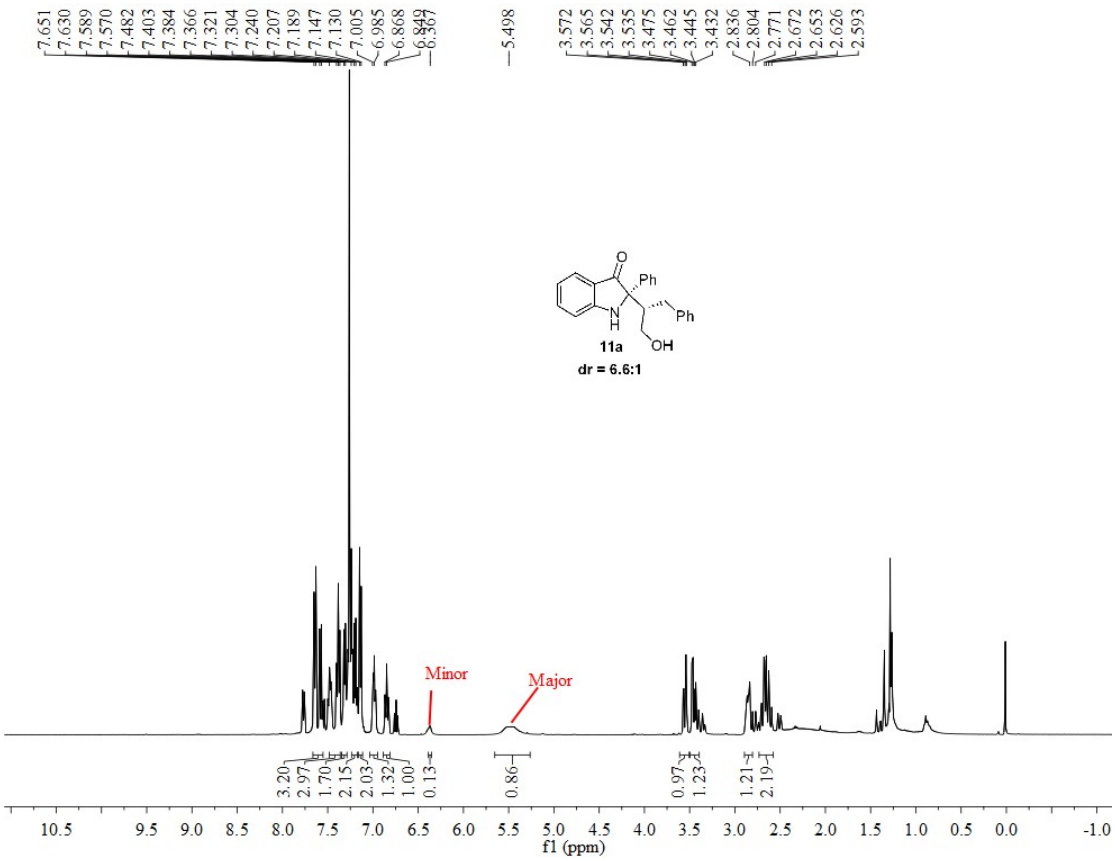

240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

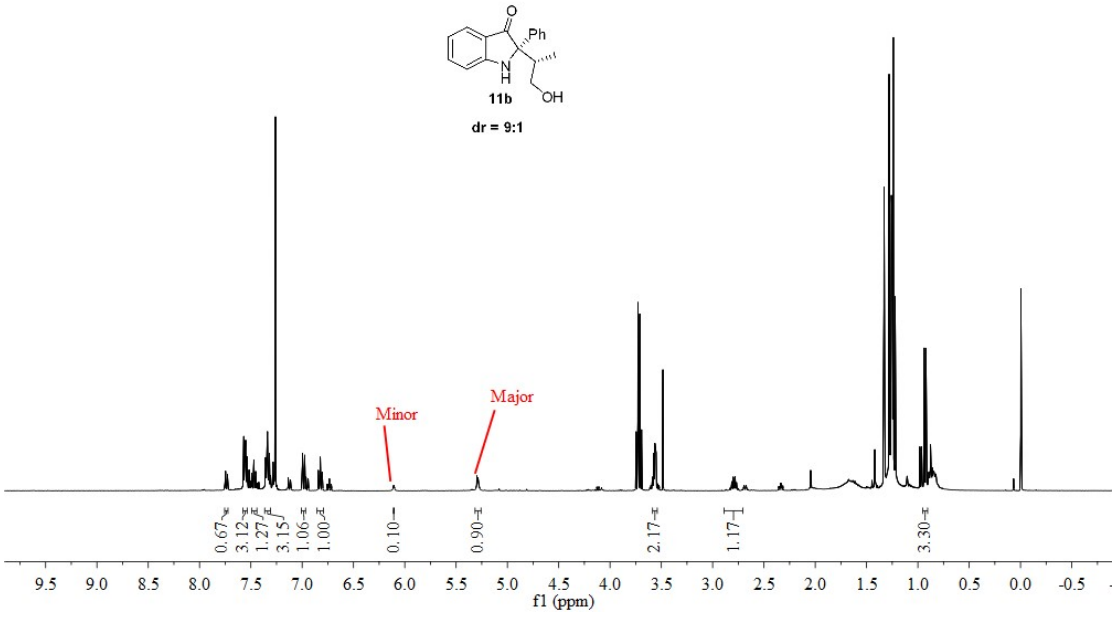

7.606
7.604
7.586
7.583
7.543
7.525
7.487
7.484
7.469
7.467
7.449
7.446
7.353
7.335
7.316
7.294
7.277
6.989
6.987
6.969
6.967
6.885
6.866
6.848
5.262
4.045
3.754
3.744
3.729
3.701
3.635
3.607
3.582
3.583
2.646
2.625
2.600
2.580
2.399
2.390
2.360
2.352
-0.002
Ph
O
N
H
O
O
12c
0.98
2.06
1.03
2.01
0.97
0.98
1.00
1.02
1.03
1.02
2.04
1.07
1.01
1.02
11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

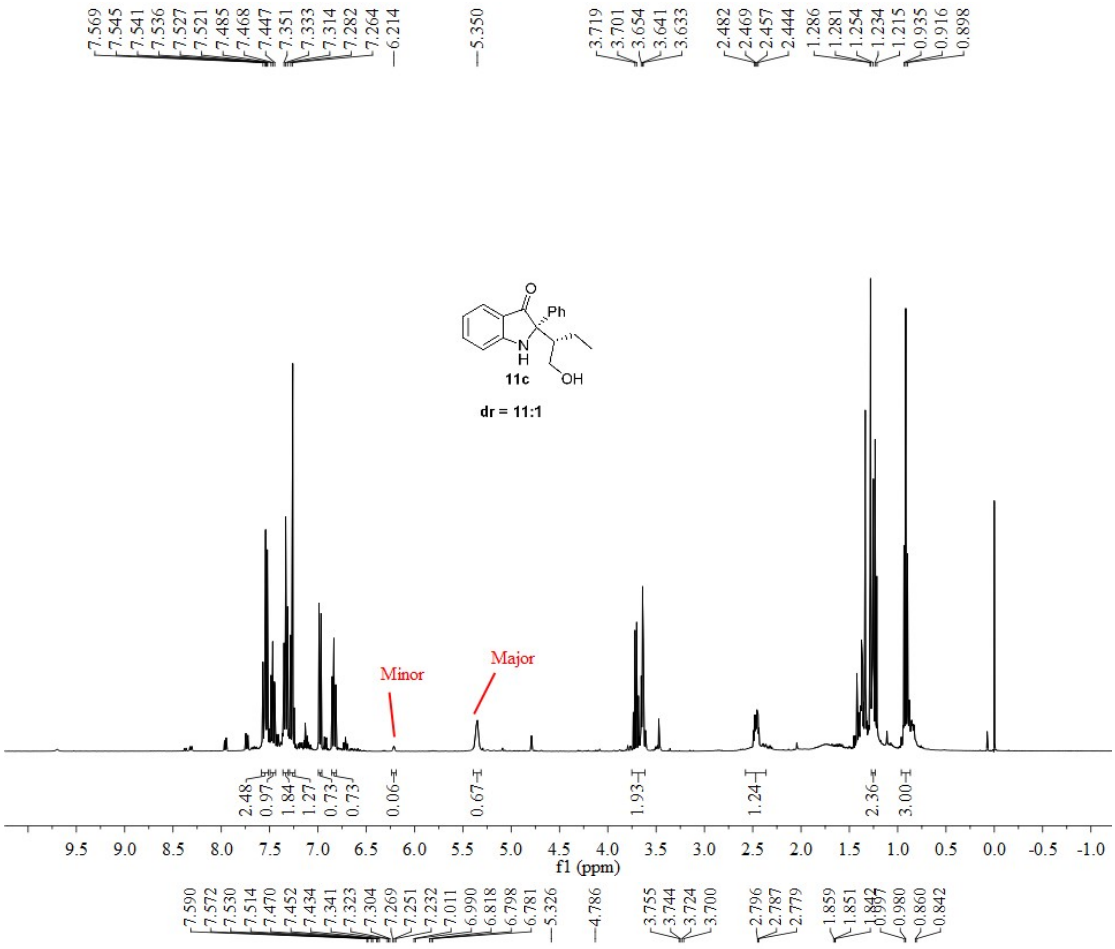

203.79
199.44
159.51
136.80
136.07
129.18
128.31
125.43
120.60
119.93
111.93
77.45
77.13
76.81
69.95
68.84
67.83
57.84
42.39
Ph
O
N
H
O
O
12c
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

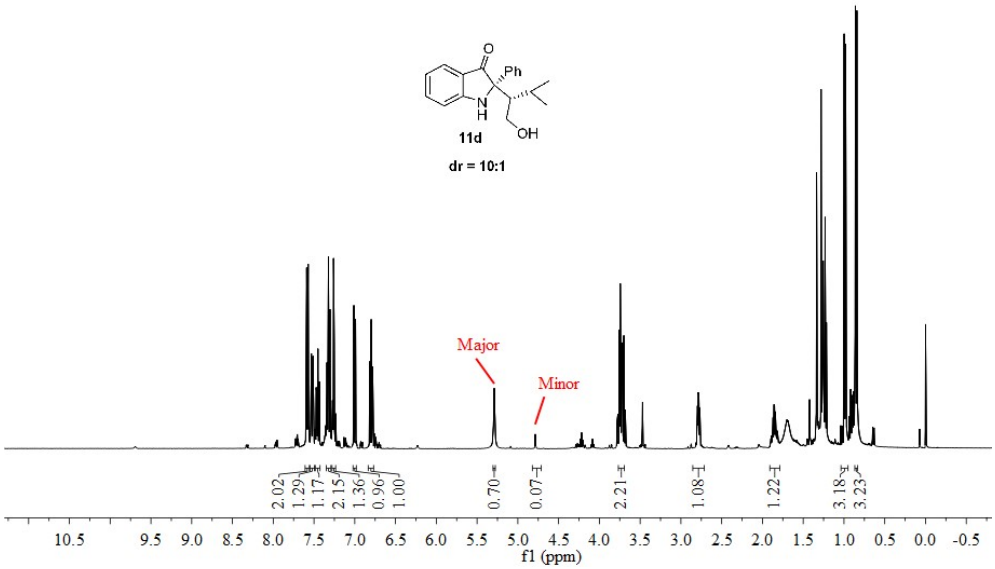

7.591
7.590
7.568
7.564
7.546
7.537
7.483
7.462
7.444
7.361
7.344
7.324
7.318
7.303
7.300
7.282
7.275
6.992
6.972
6.882
6.862
6.845
5.270
3.866
3.851
3.840
3.826
2.954
2.939
2.916
2.906
2.894
2.889
2.842
2.828
2.816
2.808
2.747
2.734
2.724
2.712
0.001
Ph
N
H
O
S
12d
3.13
1.04
2.05
0.94
1.01
1.00
0.89
1.03
4.06
2.02
f1 (ppm)
205.42
199.69
159.36
136.65
136.49
129.22
128.31
125.59
125.27
120.99
119.86
111.99
77.45
77.13
76.81
71.64
60.44
44.47
30.65
29.54
f1 (ppm)
f1 (ppm)

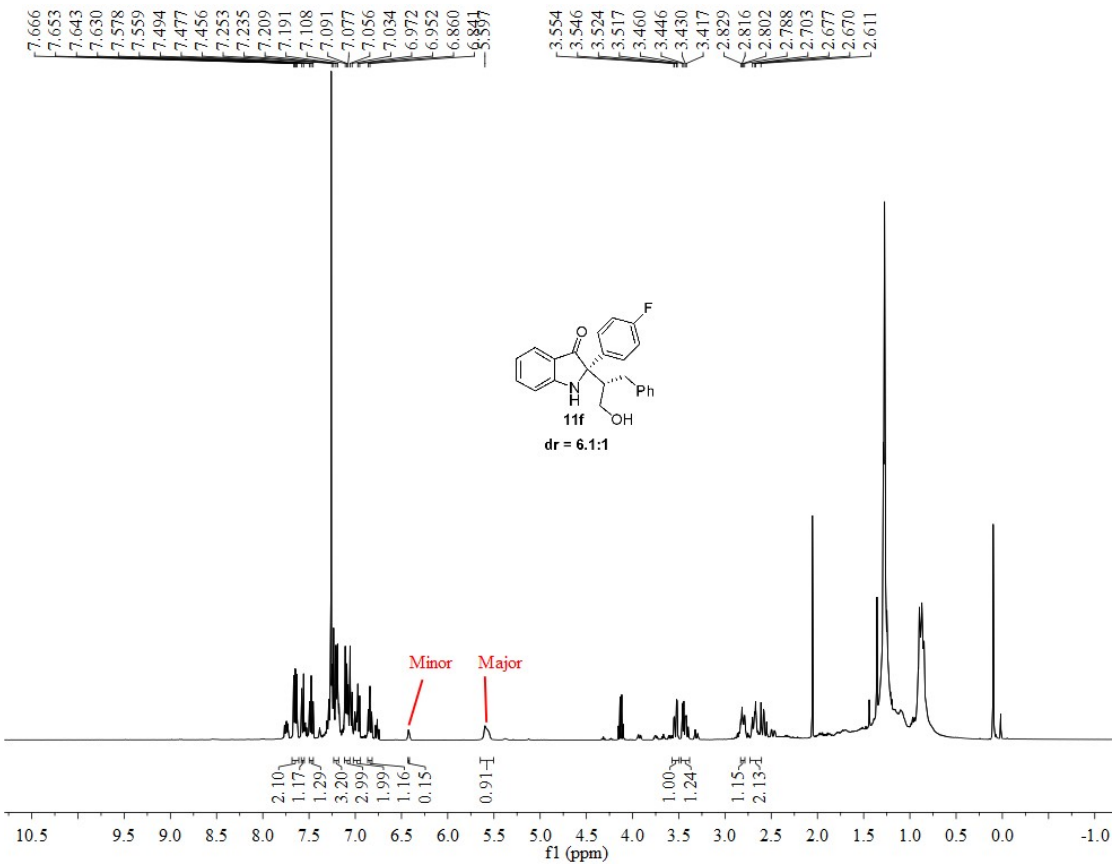
8. ^{1}H NMR spectra of crude products to determine diastereomeric ratio

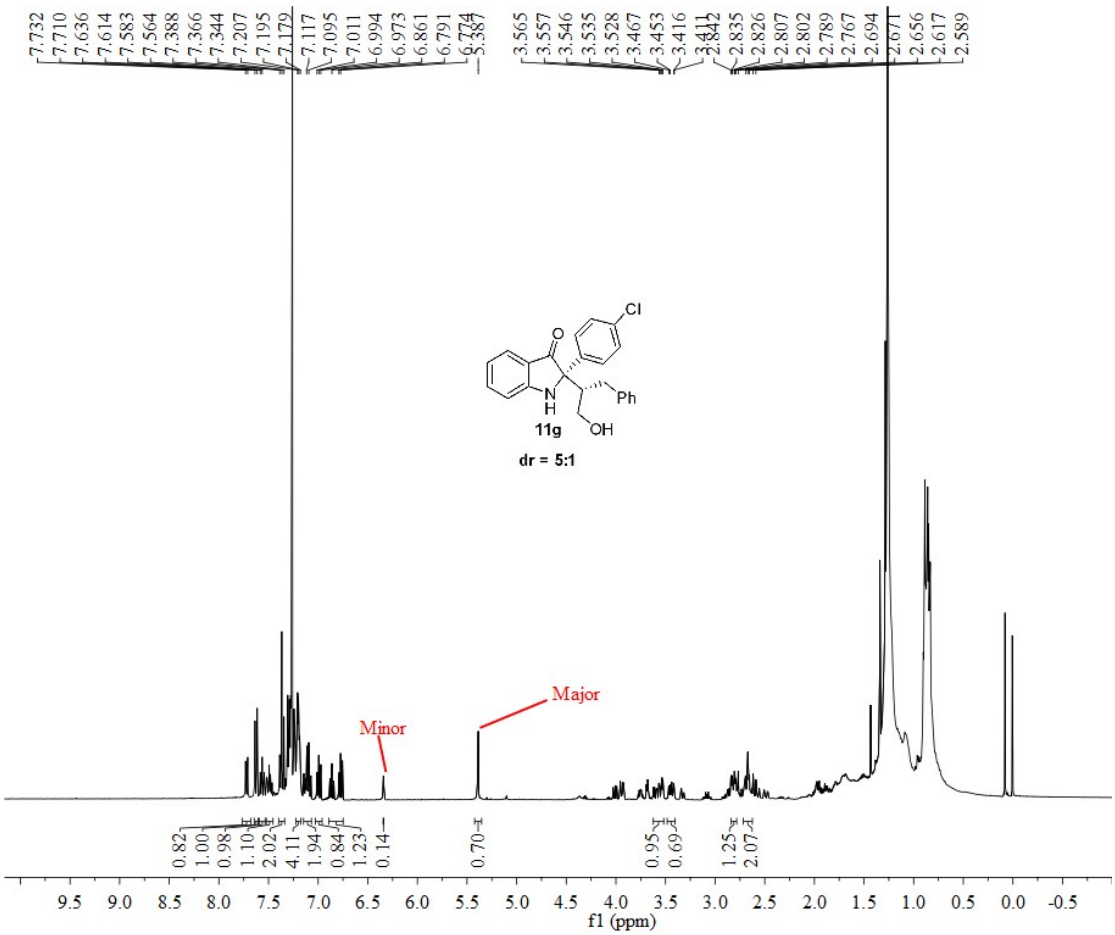


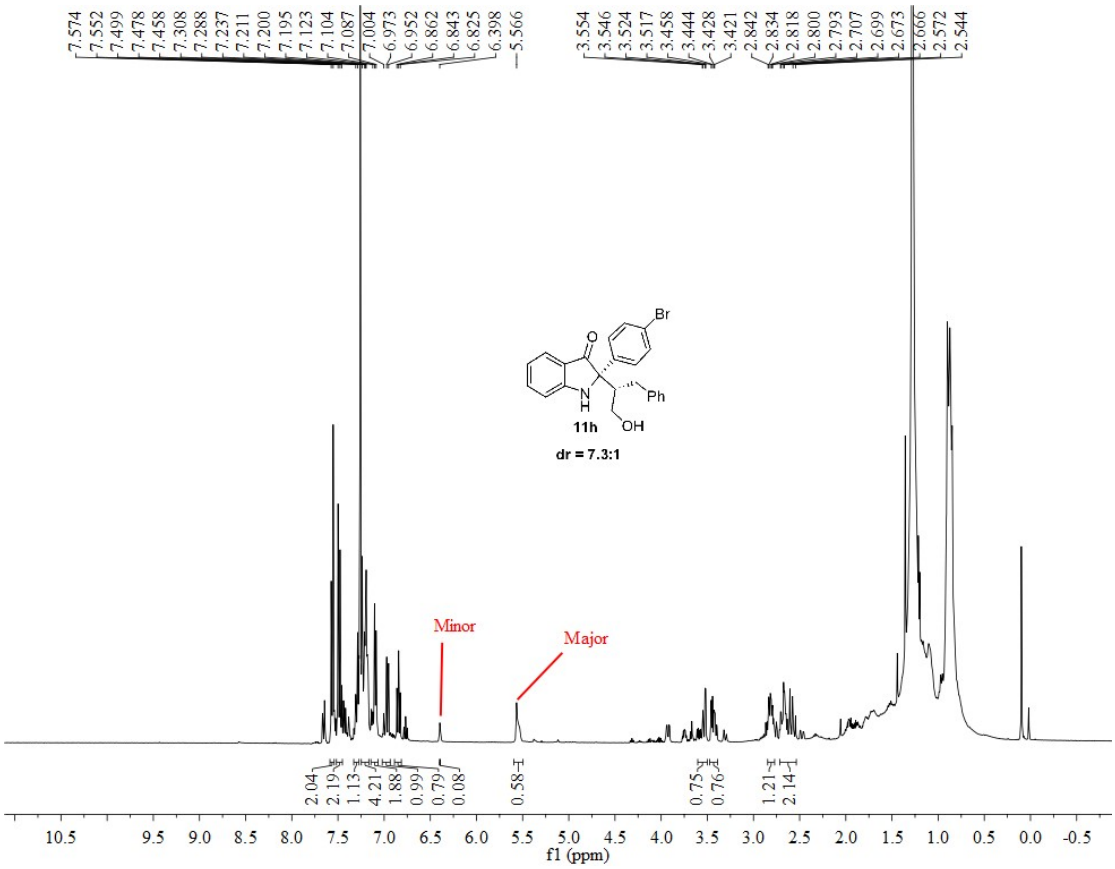


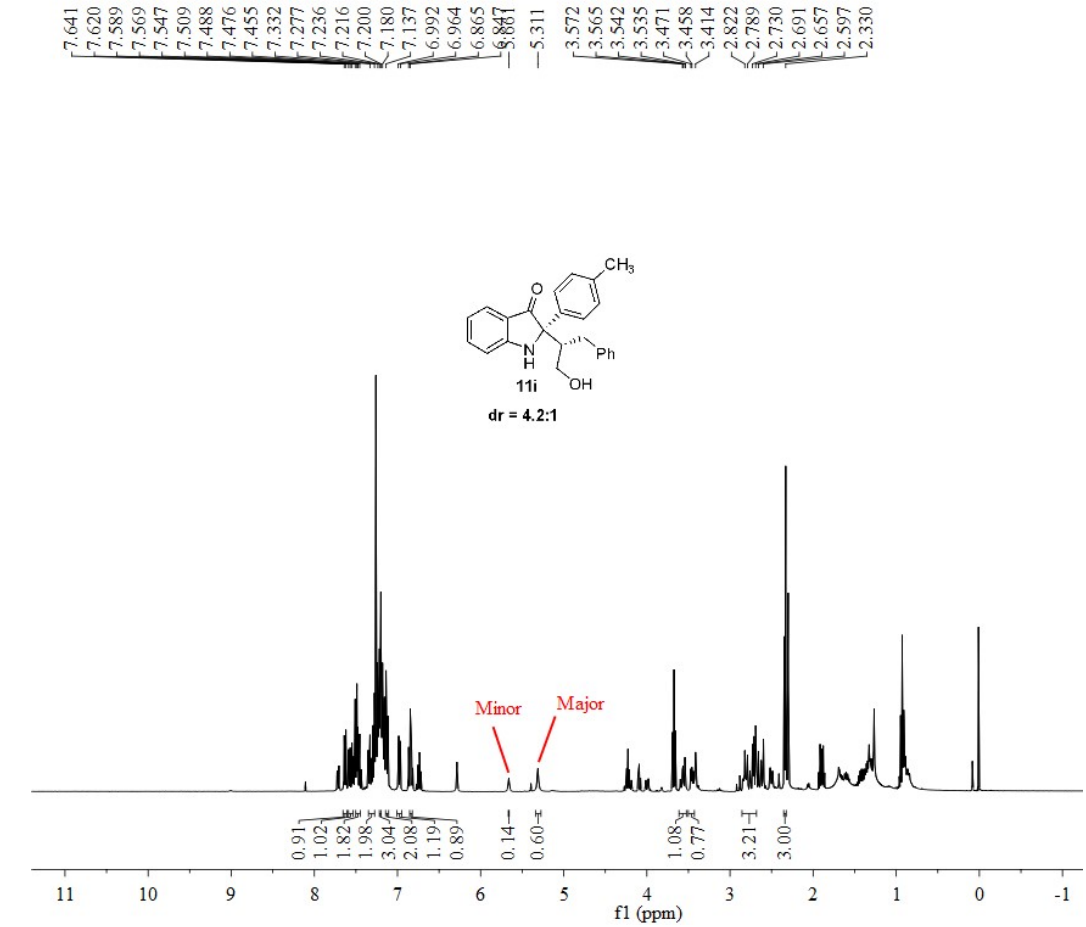

11c
dr = 11:1
Minor
Major
f1 (ppm)

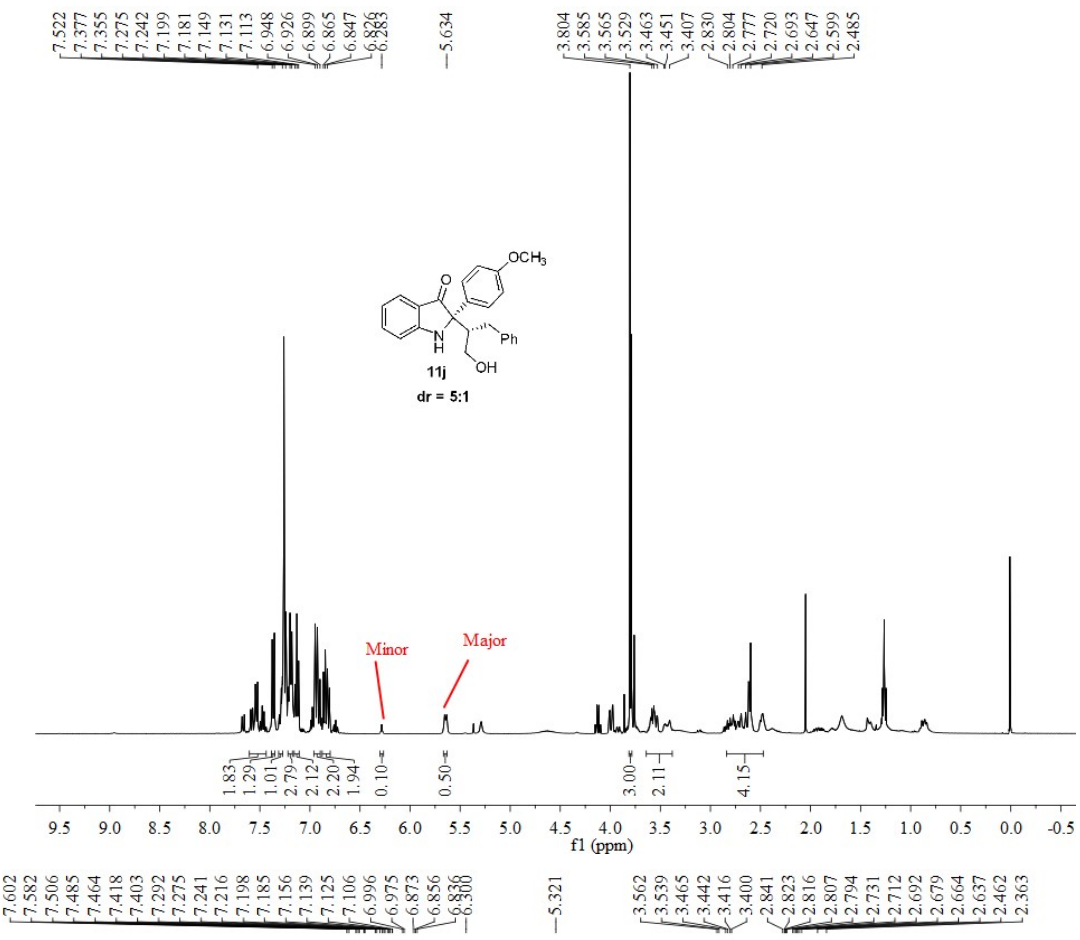

11d
dr = 10:1
Major
Minor
f1 (ppm)

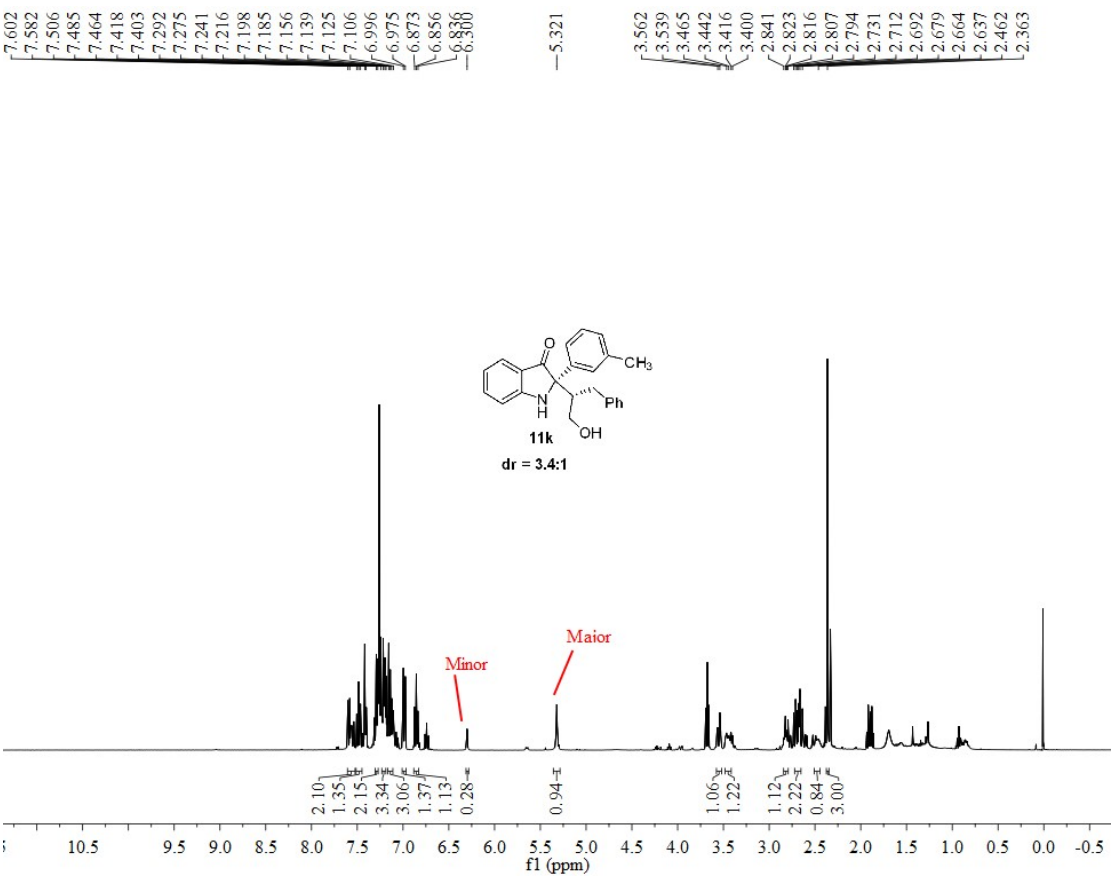

11f
dr = 6.1:1
Minor
Major
f1 (ppm)

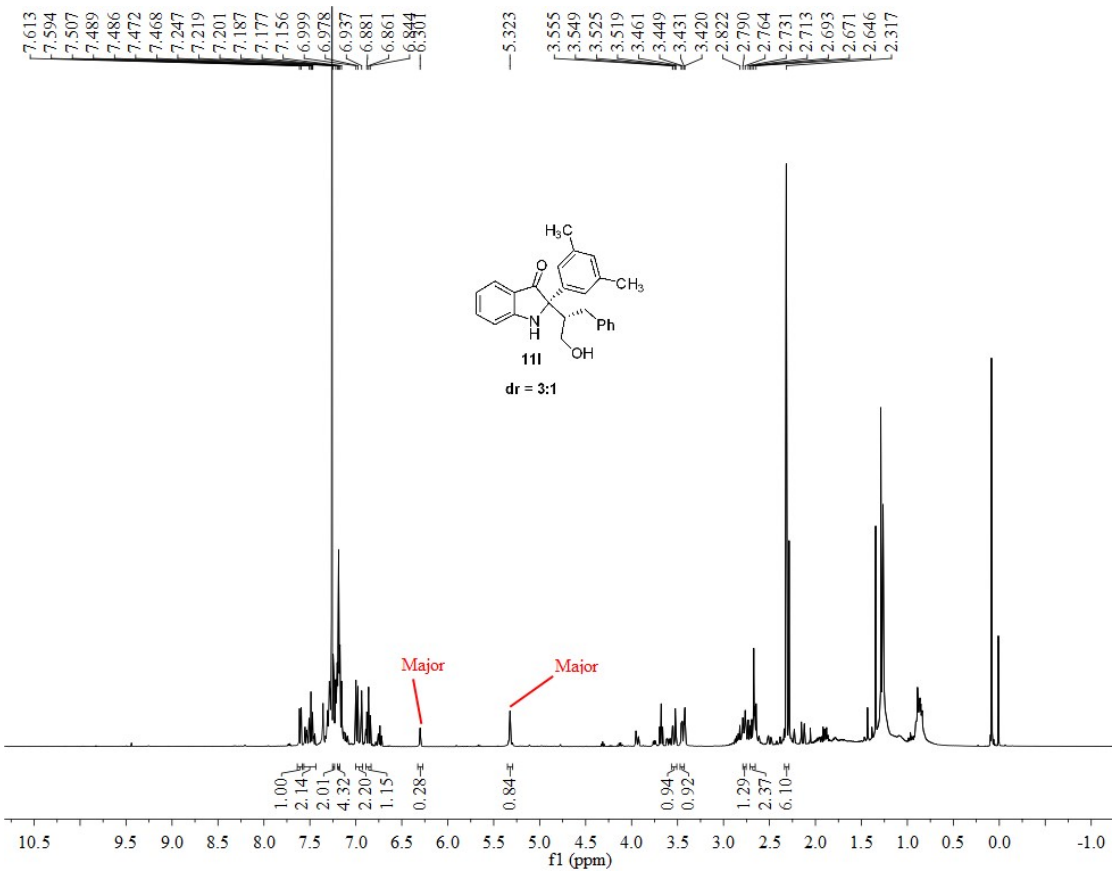

11g
dr = 5:1
Minor
Major
f1 (ppm)

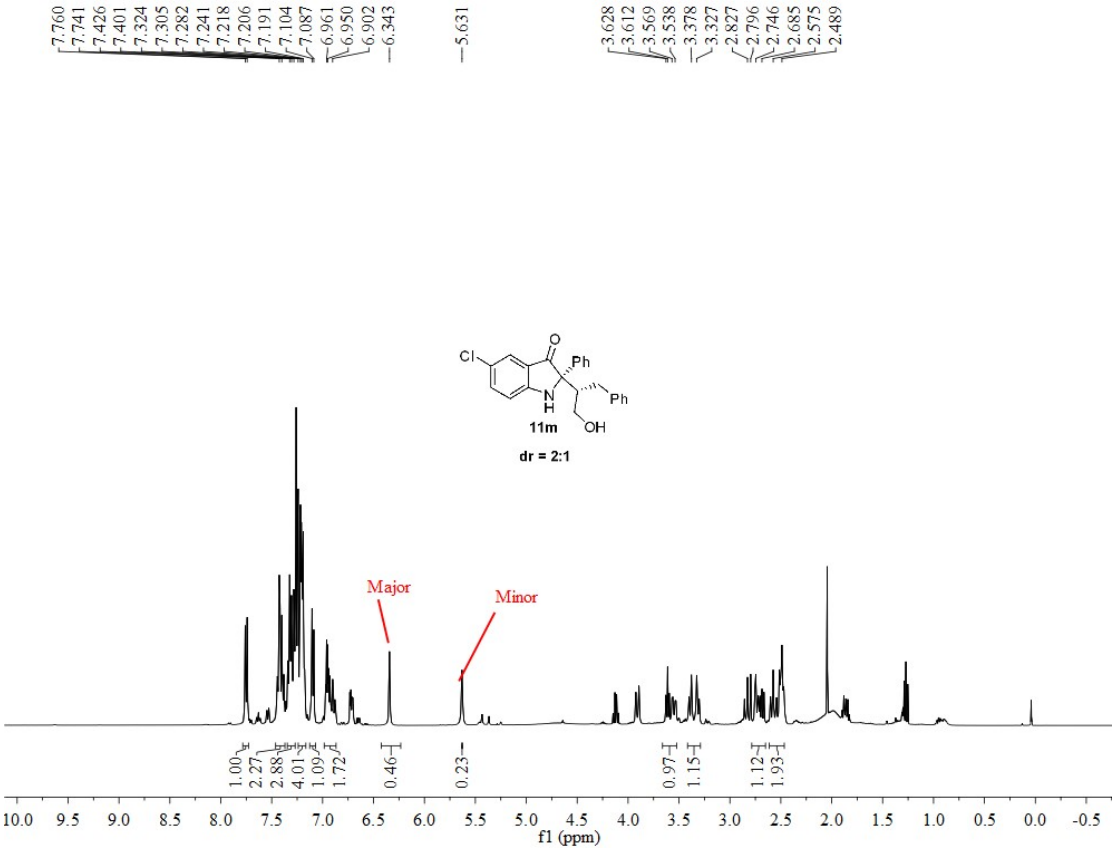

7.574
7.552
7.499
7.478
7.458
7.308
7.288
7.237
7.211
7.200
7.195
7.123
7.104
7.087
7.004
6.973
6.952
6.862
6.843
6.825
6.398
5.566
3.554
3.546
3.524
3.517
3.458
3.444
3.428
3.421
2.842
2.834
2.818
2.800
2.793
2.707
2.699
2.673
2.666
2.572
2.544
Br
O
N
H
Ph
OH
11h
dr = 7.3:1
Minor
Major
2.04
2.19
1.13
4.21
1.88
0.99
0.79
0.08
0.58
0.75
0.76
1.21
2.14
f1 (ppm)

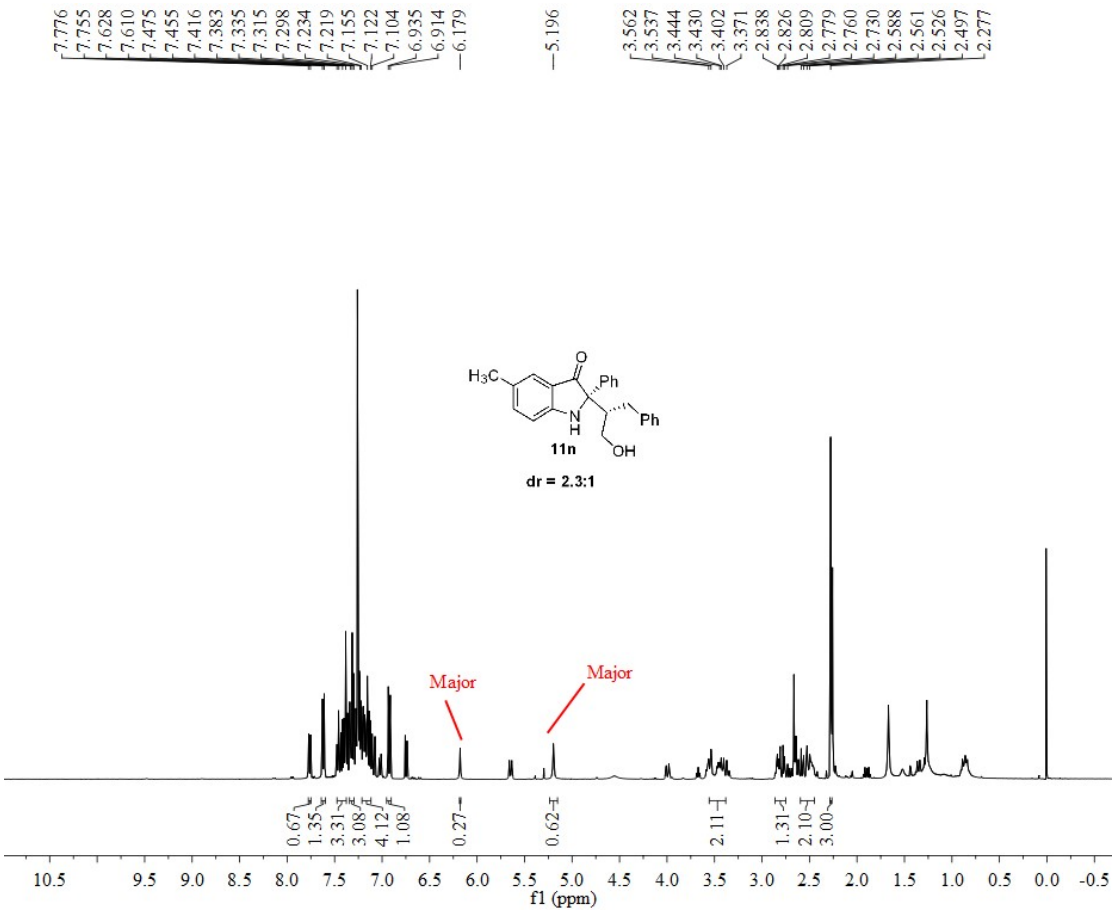

7.641
7.620
7.589
7.569
7.547
7.509
7.488
7.476
7.455
7.332
7.277
7.236
7.216
7.200
7.180
7.137
6.992
6.964
6.865
6.847
6.841
5.881
5.311
3.572
3.565
3.542
3.535
3.471
3.458
3.414
2.822
2.789
2.730
2.691
2.657
2.597
2.330
CH3
O
N
H
Ph
OH
11i
dr = 4.2:1
Minor
Major
0.91
1.02
1.82
1.98
3.04
2.08
1.19
0.89
0.14
0.60
1.08
0.77
3.21
3.00
f1 (ppm)


7.522
7.377
7.355
7.275
7.242
7.199
7.181
7.149
7.131
7.113
6.948
6.926
6.899
6.865
6.847
6.826
6.283
5.634
3.804
3.585
3.565
3.529
3.463
3.451
3.407
2.830
2.804
2.777
2.720
2.693
2.647
2.599
2.485
OCH3
O
N
H
Ph
OH
11j
dr = 5:1
Minor
Major
1.83
1.29
1.01
2.79
2.12
2.20
1.94
0.10
0.50
3.00
2.11
4.15
f1 (ppm)


7.602
7.582
7.506
7.485
7.464
7.418
7.403
7.292
7.275
7.241
7.216
7.198
7.185
7.156
7.139
7.125
7.106
6.996
6.975
6.873
6.856
6.836
6.300
5.321
3.562
3.539
3.465
3.442
3.416
3.400
2.841
2.823
2.816
2.807
2.794
2.731
2.712
2.692
2.679
2.664
2.637
2.462
2.363
CH3
O
N
H
Ph
OH
11k
dr = 3.4:1
Minor
Maior
2.10
1.35
2.15
3.34
3.06
1.37
1.13
0.28
0.94
1.06
1.22
1.12
2.22
0.84
3.00
f1 (ppm)


7.613
7.594
7.507
7.489
7.486
7.472
7.468
7.247
7.219
7.201
7.187
7.177
7.156
6.999
6.978
6.937
6.881
6.861
6.844
6.301
5.323
3.555
3.549
3.525
3.519
3.461
3.449
3.431
3.420
2.822
2.790
2.764
2.731
2.713
2.693
2.671
2.646
2.317
H3C
CH3
O
N
H
Ph
OH
11l
dr = 3:1
Major
Major
1.00
2.14
2.01
4.32
2.20
1.15
0.28
0.84
0.94
0.92
1.29
2.37
6.10
f1 (ppm)


7.760
7.741
7.426
7.401
7.324
7.305
7.282
7.241
7.218
7.206
7.191
7.104
7.087
6.961
6.950
6.902
6.343
5.631
3.628
3.612
3.569
3.538
3.378
3.327
2.827
2.796
2.746
2.685
2.575
2.489
Cl
O
Ph
N
H
Ph
OH
11m
dr = 2:1
Major
Minor
1.00
2.27
2.88
4.01
1.09
1.72
0.46
0.23
0.97
1.15
1.12
1.93
f1 (ppm)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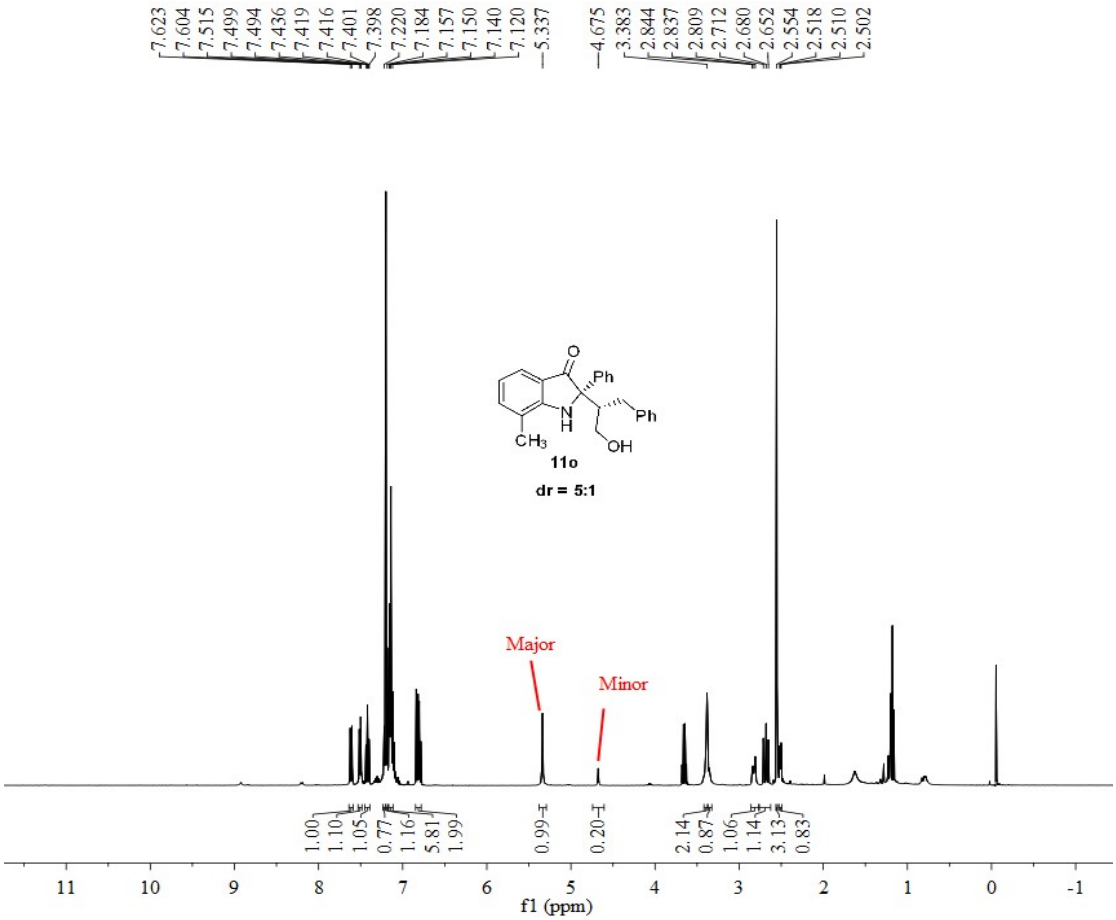
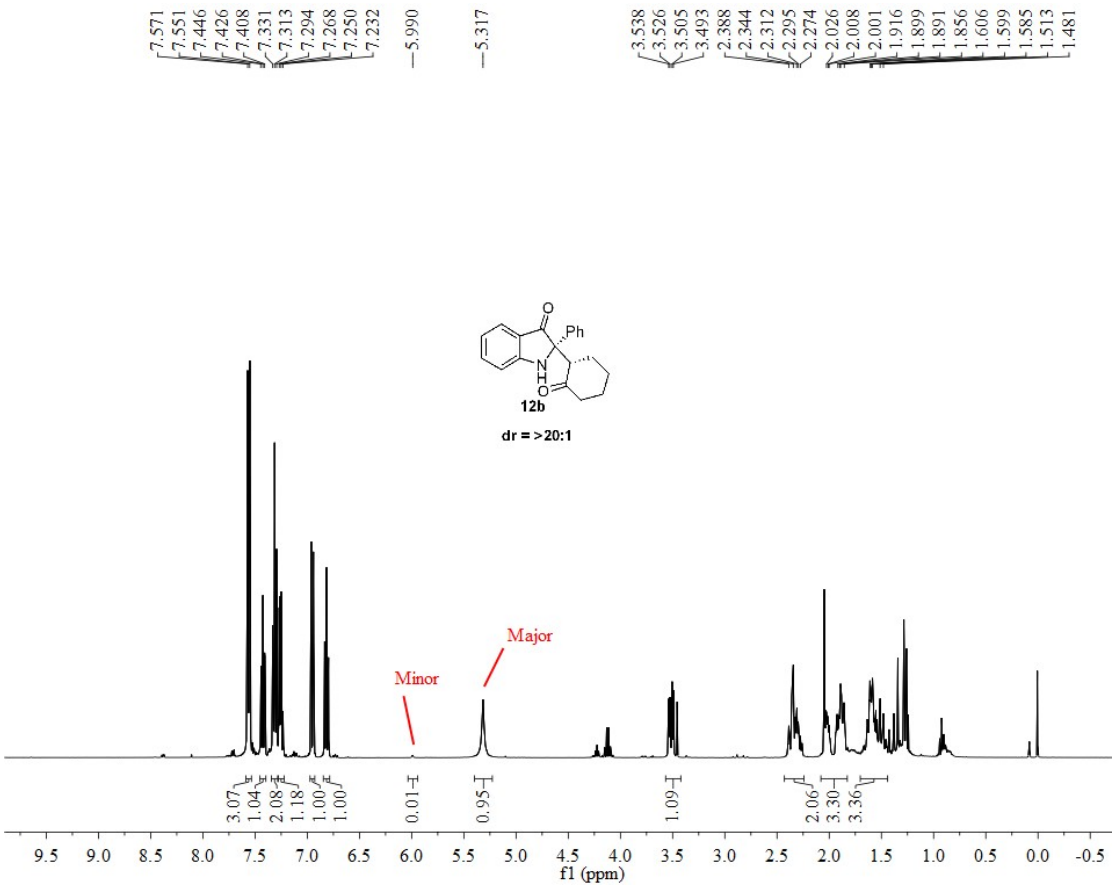
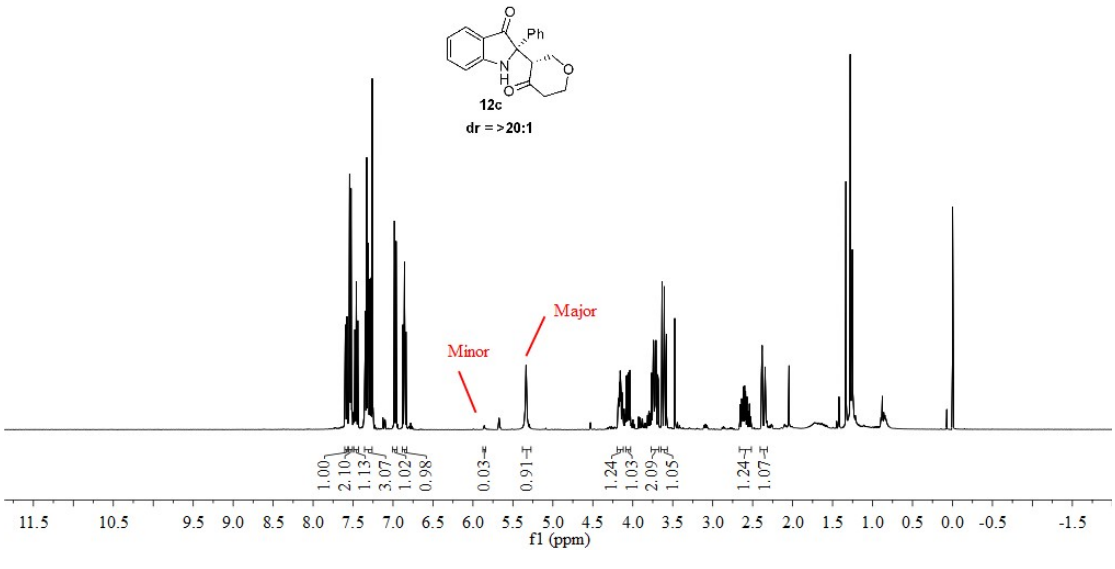
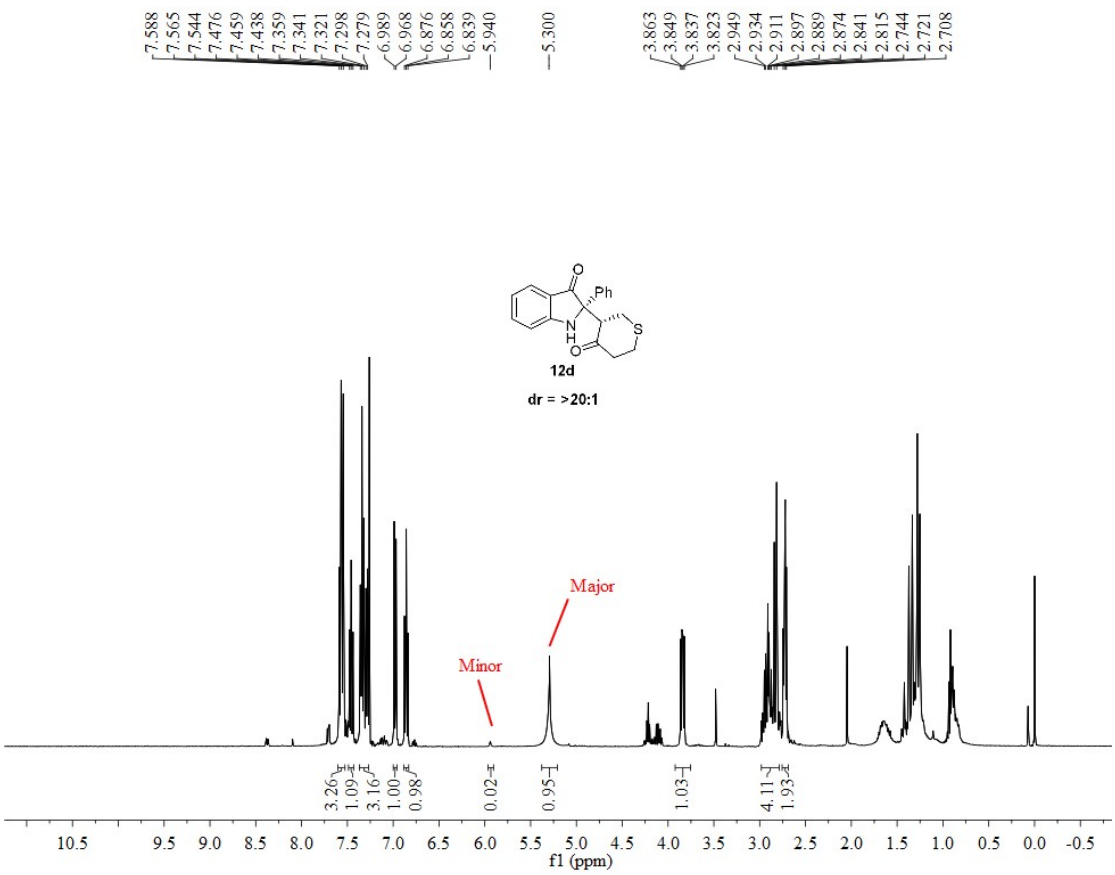
7.755
7.628
7.610
7.475
7.455
7.416
7.383
7.335
7.315
7.298
7.234
7.219
7.155
7.122
7.104
6.935
6.914
6.179
5.196
3.562
3.537
3.444
3.430
3.402
3.371
2.838
2.826
2.809
2.779
2.760
2.730
2.588
2.561
2.526
2.497
2.277
H3C
O
Ph
N
H
Ph
OH
11n
dr = 2.3:1
Major
Major
0.67
1.35
3.31
3.08
4.12
1.08
0.27
0.62
2.11
1.31
2.10
3.00
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


7.623
7.604
7.515
7.499
7.494
7.436
7.419
7.416
7.401
7.398
7.220
7.184
7.157
7.150
7.140
7.120
5.337
4.675
3.383
2.844
2.837
2.809
2.712
2.680
2.652
2.554
2.518
2.510
2.502
O
Ph
N
H
Ph
CH3
OH
11o
dr = 5:1
Major
Minor
1.00
1.10
1.05
0.77
1.16
5.81
1.99
0.99
0.20
2.14
0.87
1.06
1.14
3.13
0.83
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

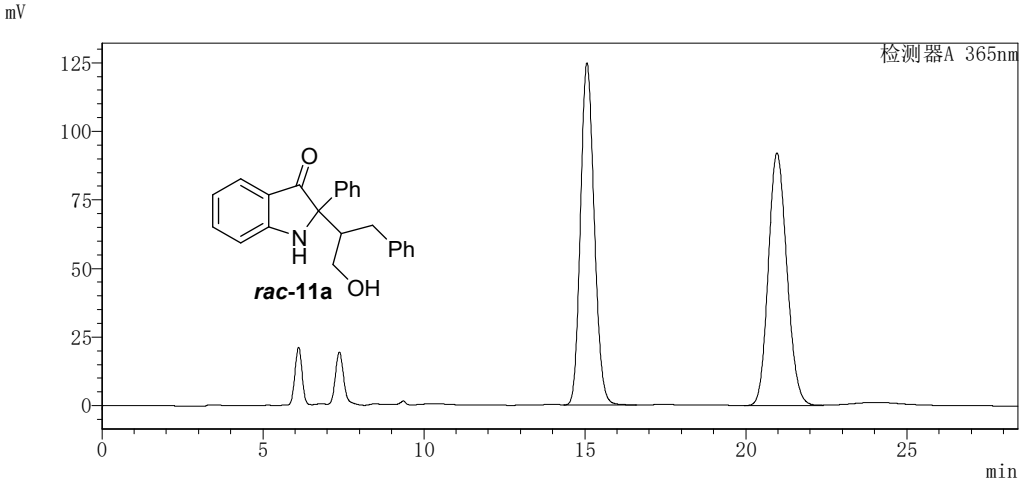

12b
dr = >20:1
Major
Minor
f1 (ppm)


12c
dr = >20:1
Major
Minor
f1 (ppm)

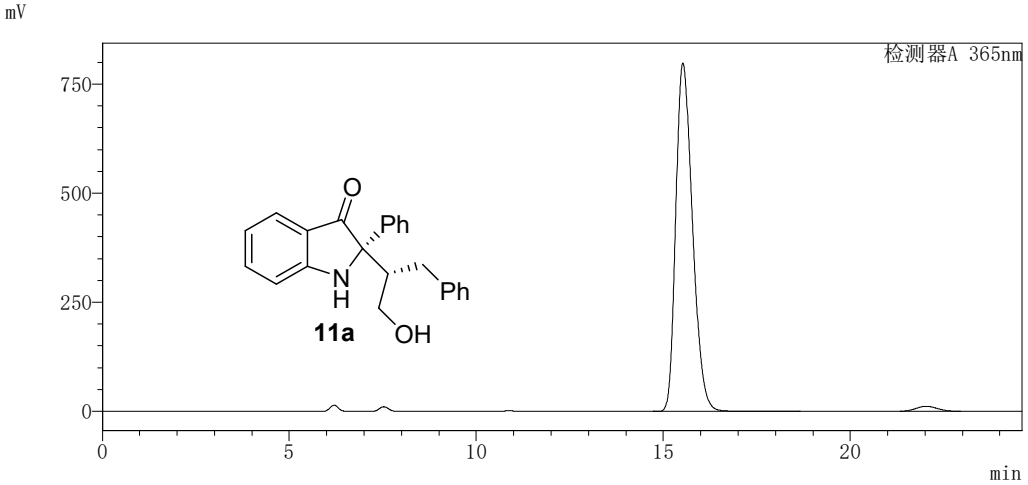

7.588
7.565
7.544
7.476
7.459
7.438
7.359
7.341
7.321
7.298
7.279
6.989
6.968
6.876
6.858
6.839
5.940
5.300
3.863
3.849
3.837
3.823
2.949
2.934
2.911
2.897
2.889
2.874
2.841
2.815
2.744
2.721
2.708
Ph
O
N
H
S
O
12d
dr = >20:1
Major
Minor
3.26
1.09
3.16
1.00
0.98
0.02
0.95
1.03
4.11
1.93
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

9. HPLC spectra

HPLC using an IC-H column (hexane:*i*-PrOH=90:10, 1 mL/min)

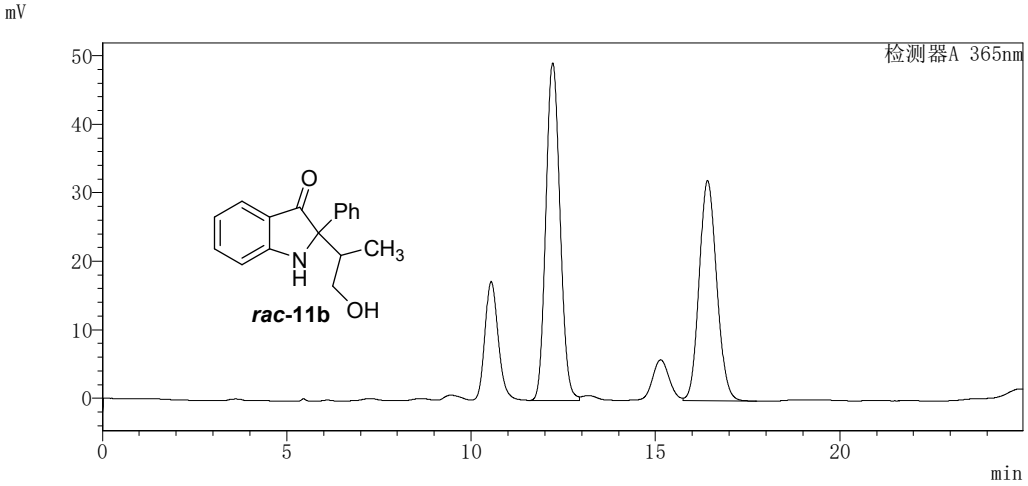


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	15.065	3697380	124802	50.052
2	PDA 365 nm	20.967	3689647	92012	49.948

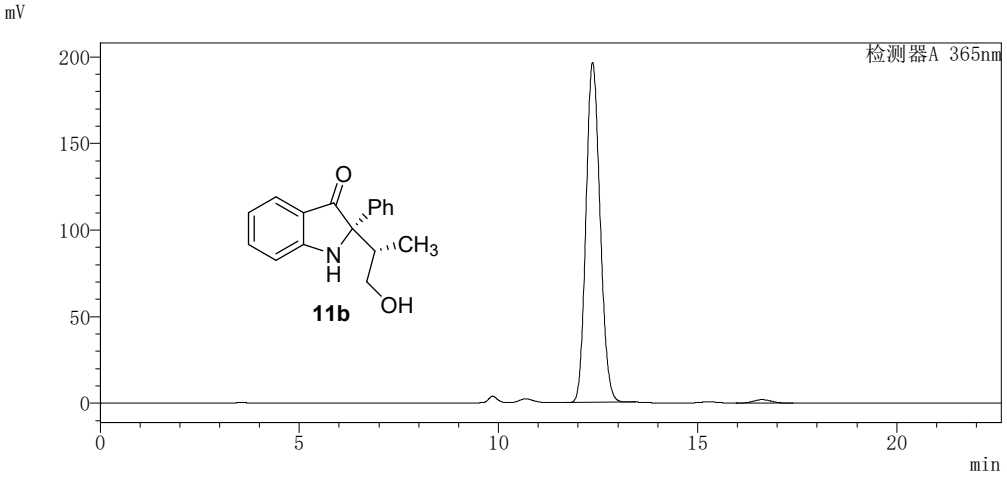


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	15.524	24865290	799369	98.167
2	PDA 365 nm	22.030	464203	11519	1.833

HPLC using an IC-H column (hexane:*i*-PrOH=90:10, 1 mL/min)

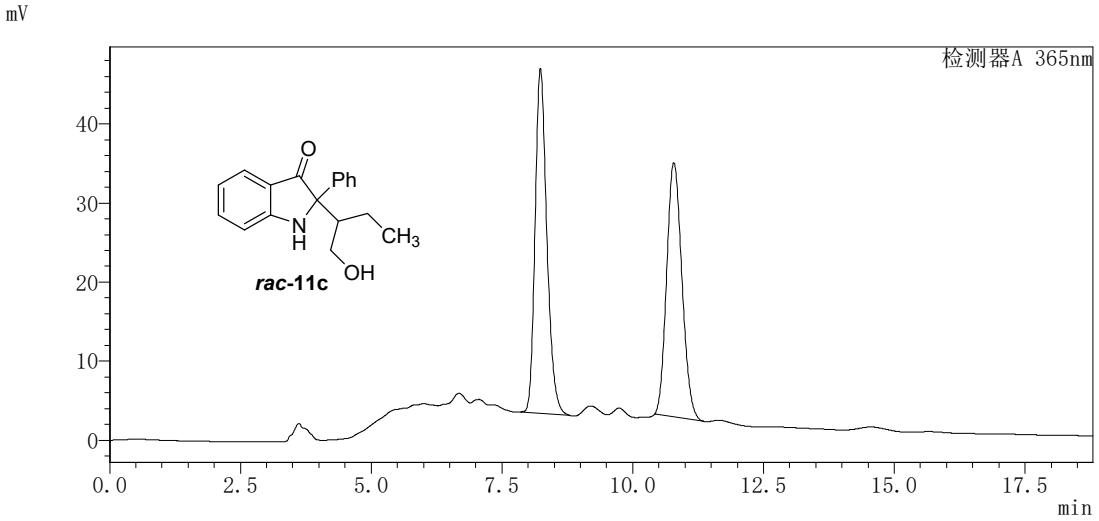


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	12.212	1315223	49318	55.235
2	PDA 365 nm	16.411	1065908	32165	44.765

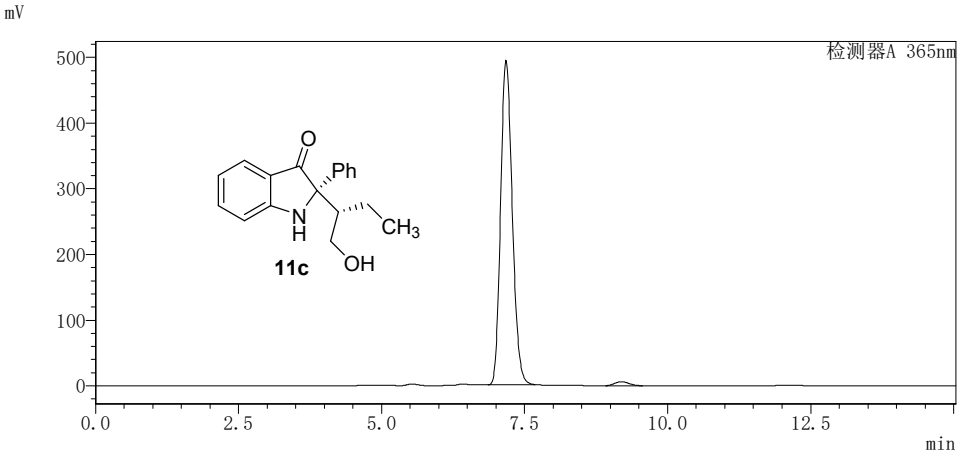


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	12.363	4833403	196408	98.711
2	PDA 365 nm	16.614	63105	2007	1.289

HPLC using an IC-H column (hexane:*i*-PrOH=80:20, 1 mL/min)

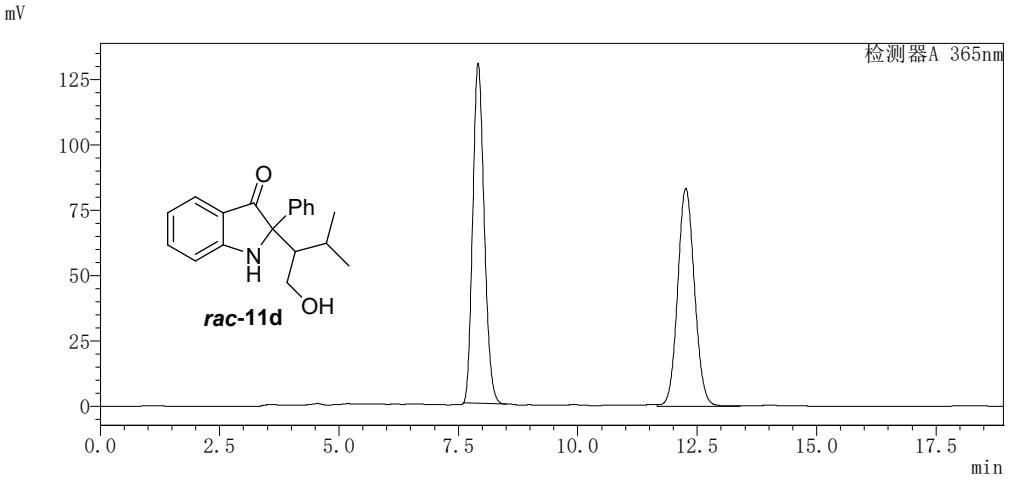


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	8.235	882520	43464	51.204
2	PDA 365 nm	10.786	650411	32107	48.796

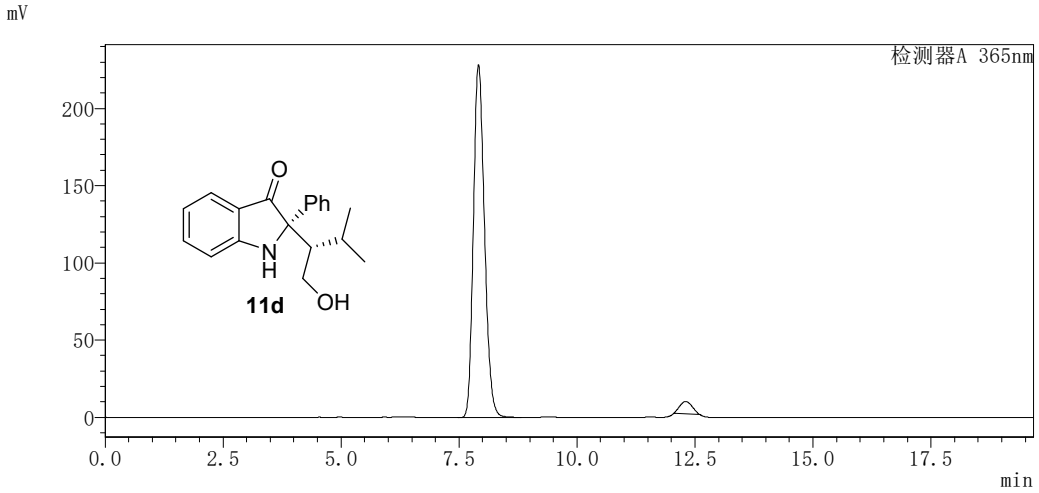


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	7.175	6999260	494573	98.583
2	PDA 365 nm	9.193	100600	5974	1.417

HPLC using an IC-H column (hexane:*i*-PrOH=80:20, 1 mL/min)

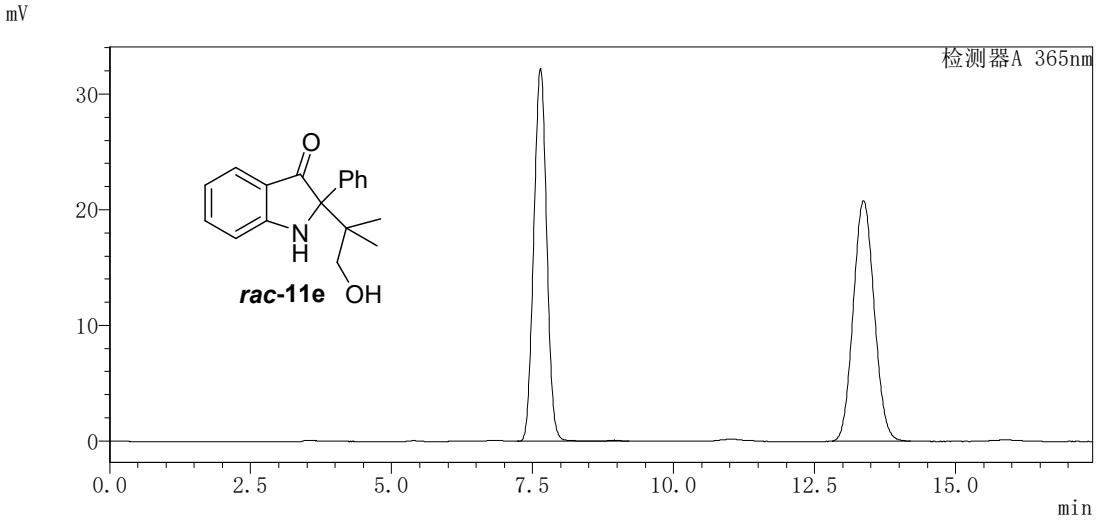


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	7.910	2163138	130181	51.626
2	PDA 365 nm	12.260	2026840	83312	48.374

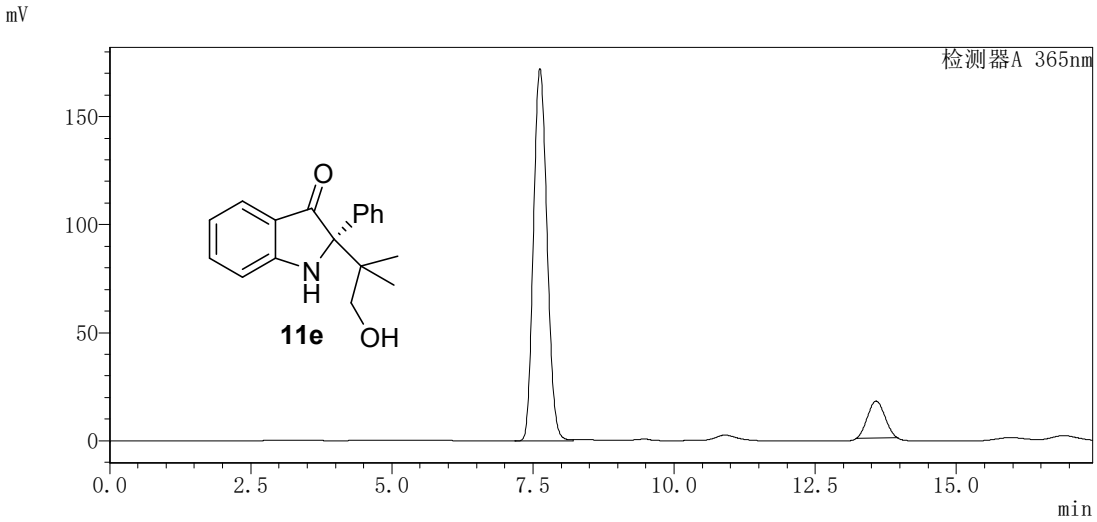


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	7.912	3739356	228475	96.324
2	PDA 365 nm	12.303	142709	7837	3.676

HPLC using an IC-H column (hexane:*i*-PrOH=90:10, 1 mL/min)

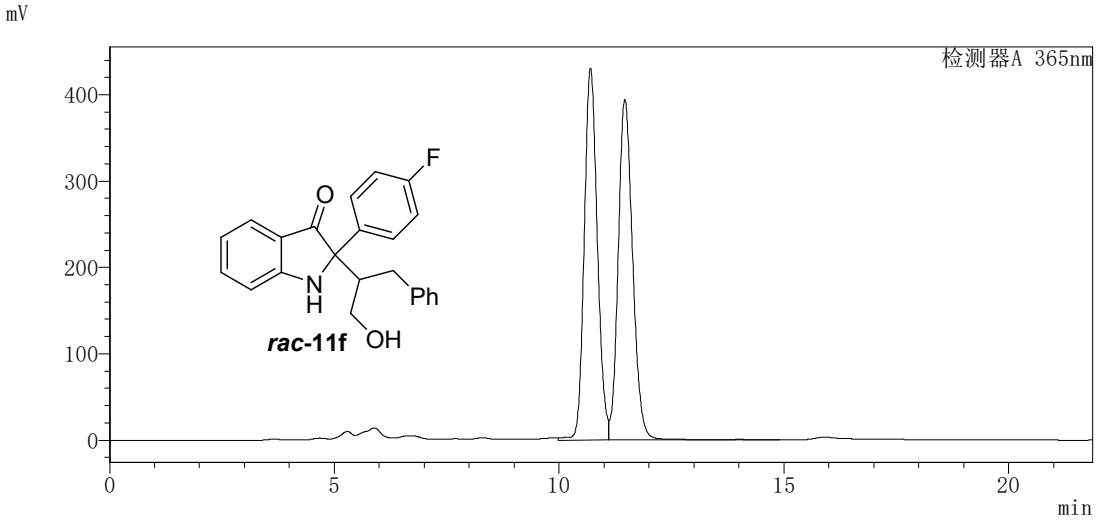


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	7.641	515006	32284	48.943
2	PDA 365 nm	13.367	537256	20802	51.057

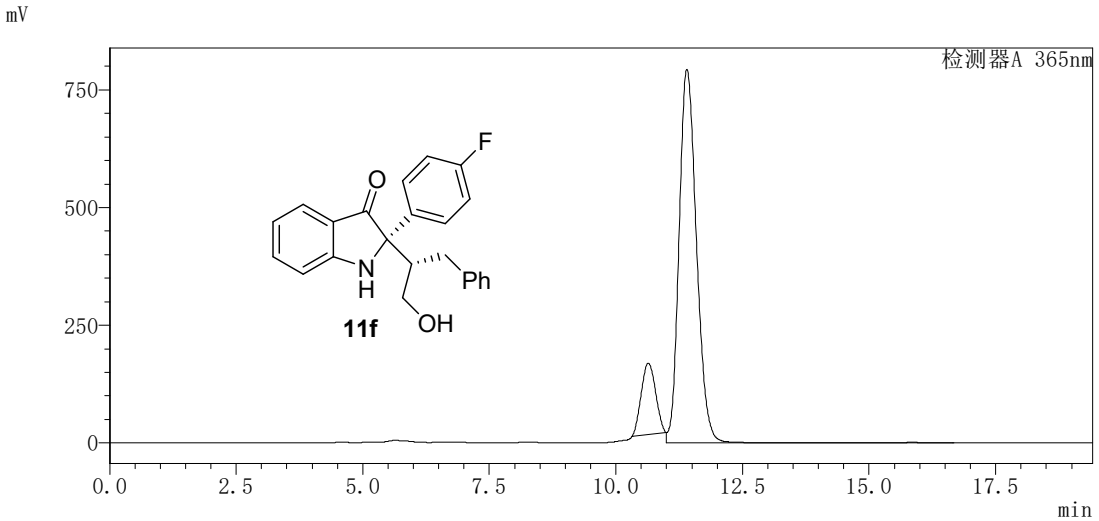


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	7.623	2885803	172338	88.779
2	PDA 365 nm	13.578	364760	17090	11.221

HPLC using an IC-H column (hexane:*i*-PrOH=90:10, 1 mL/min)

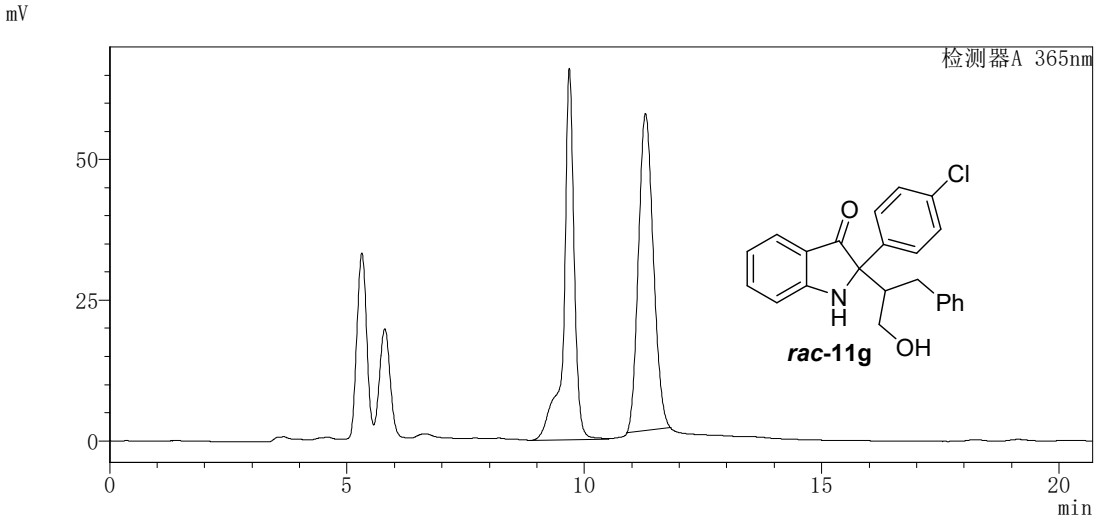


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	10.695	8742636	430938	49.655
2	PDA 365 nm	11.459	8864110	394652	50.345

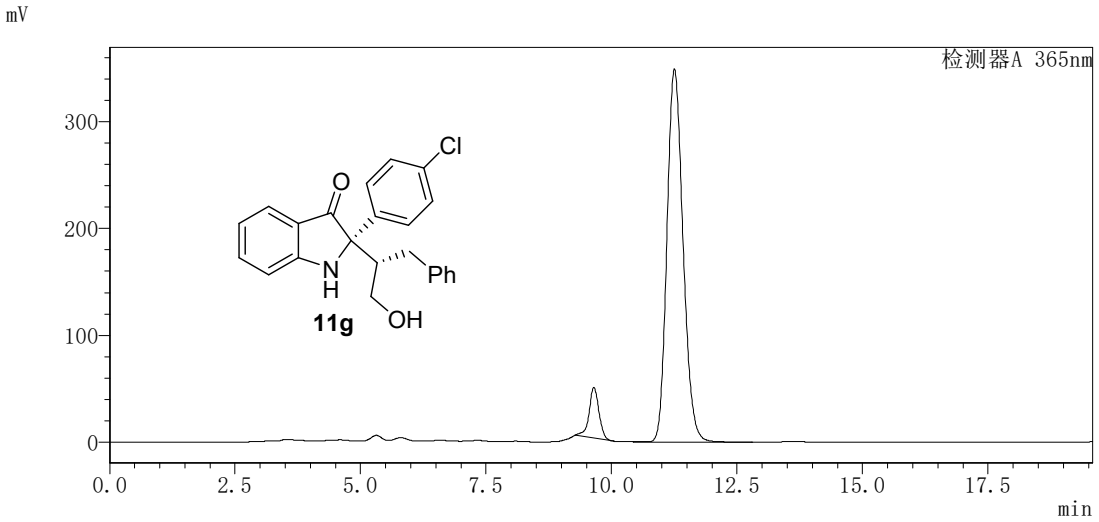


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	10.639	3011208	152160	13.659
2	PDA 365 nm	11.401	19035093	794046	86.341

HPLC using an IC-H column (hexane:*i*-PrOH=90:10, 1 mL/min)

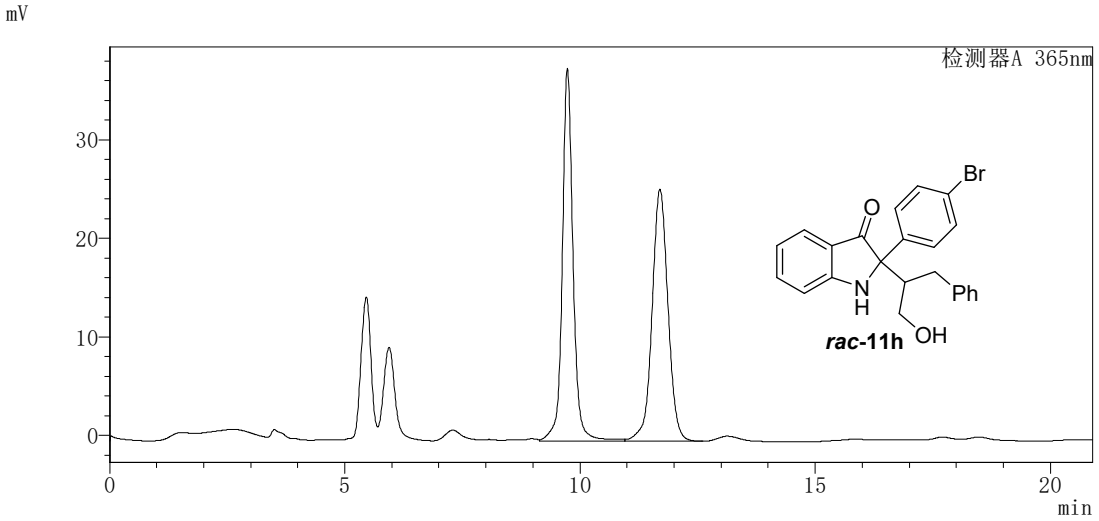


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	9.683	998719	66047	44.859
2	PDA 365 nm	11.288	1227648	56310	55.141

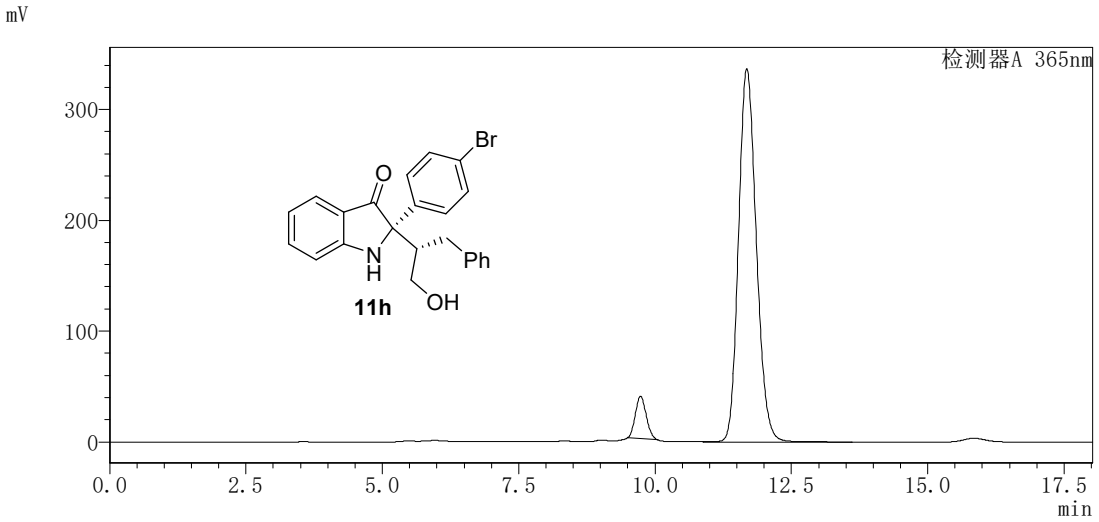


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	9.654	654394	47437	7.748
2	PDA 365 nm	11.250	7791587	349494	92.152

HPLC using an IC-H column (hexane:*i*-PrOH=90:10, 1 mL/min)

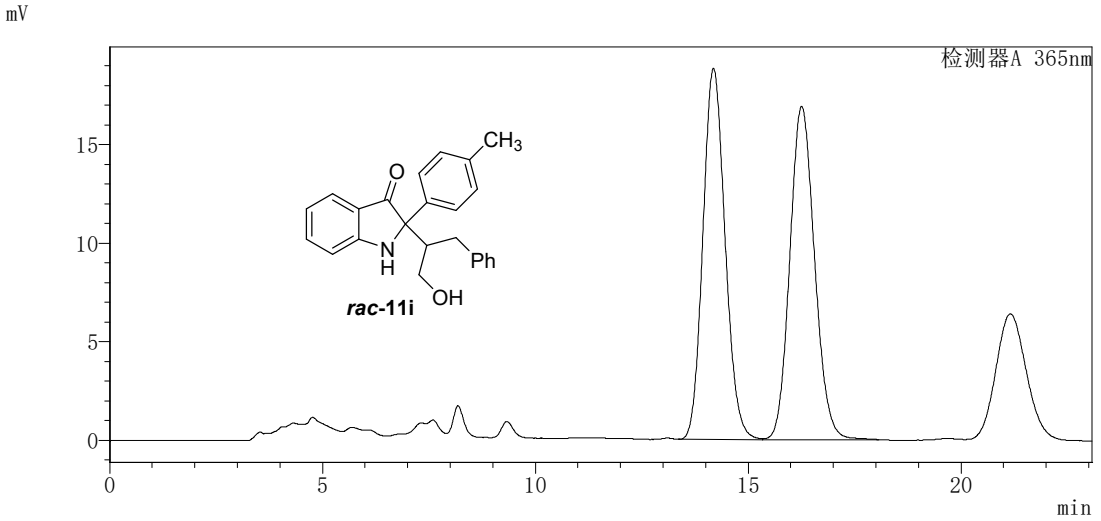


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	9.731	604756	37869	50.130
2	PDA 365 nm	11.699	601631	25578	49.870

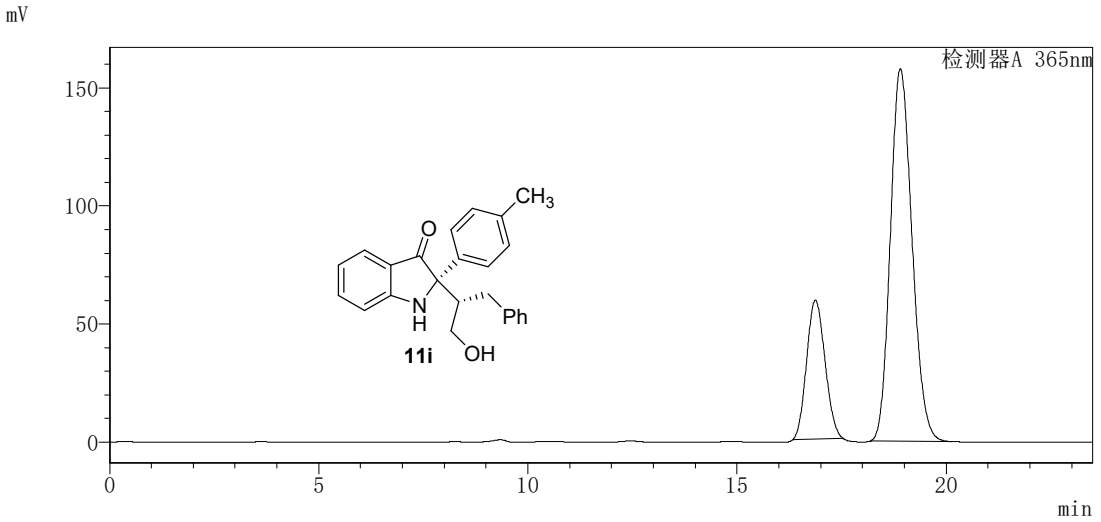


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	9.732	537003	38403	6.554
2	PDA 365 nm	11.682	7656664	337168	93.446

HPLC using an IC-H column (hexane:*i*-PrOH=90:10, 1 mL/min)

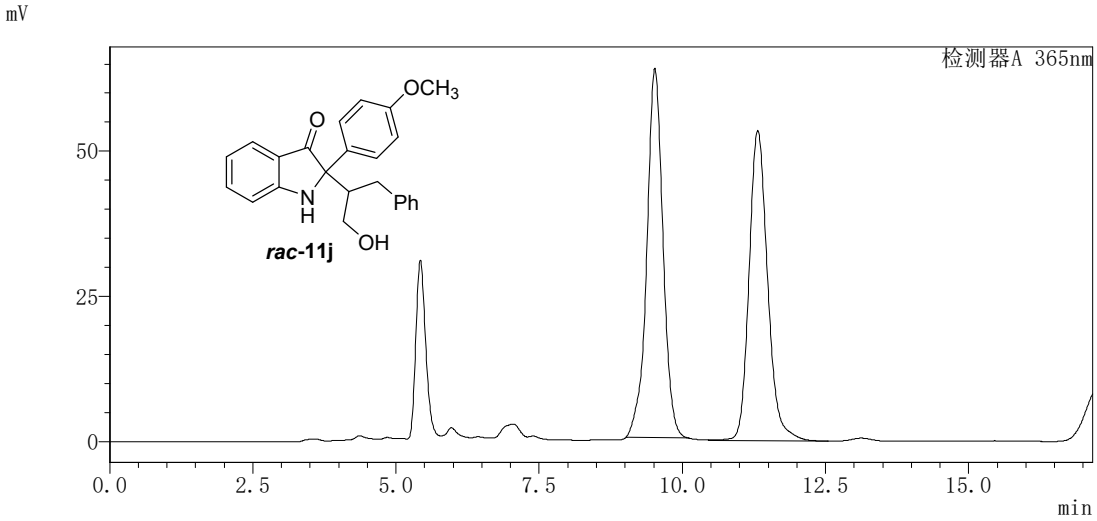


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	14.184	681883	18847	49.949
2	PDA 365 nm	16.254	683272	16918	50.051

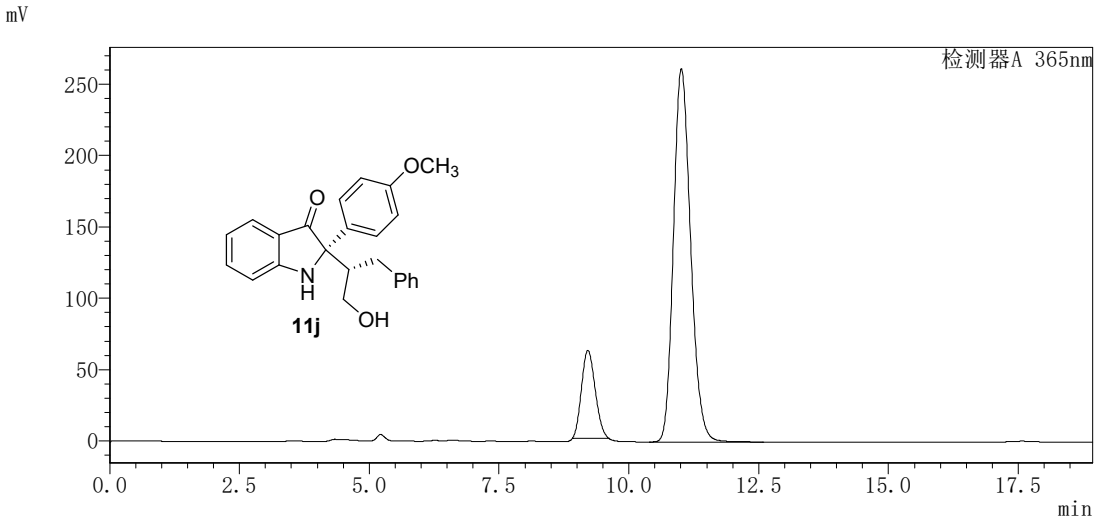


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	16.870	1796956	58863	24.037
2	PDA 365 nm	18.903	5678929	157878	75.963

HPLC using an IC-H column (hexane:*i*-PrOH=80:20, 1 mL/min)

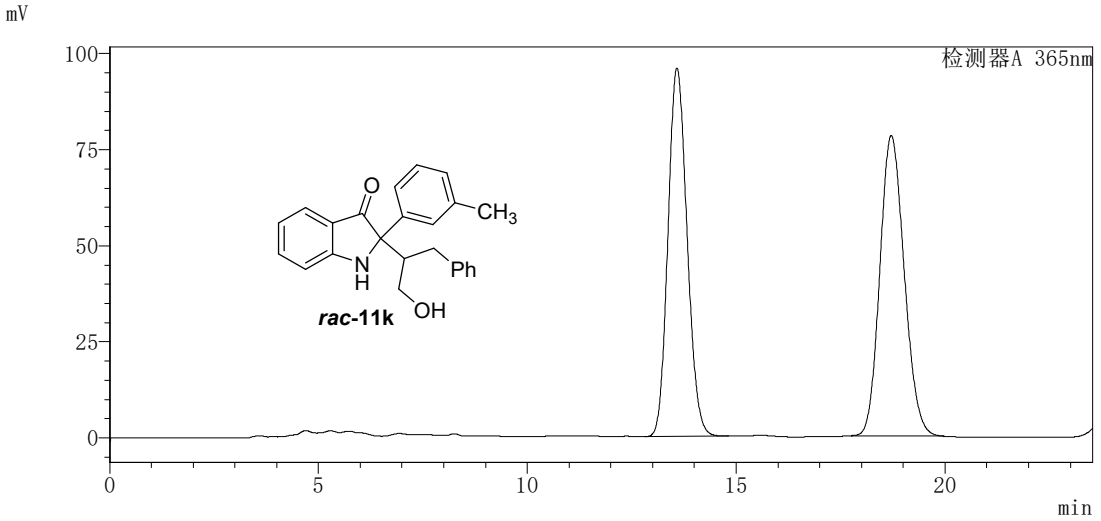


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	9.519	1252300	63646	50.895
2	PDA 365 nm	11.316	120280	53443	49.105

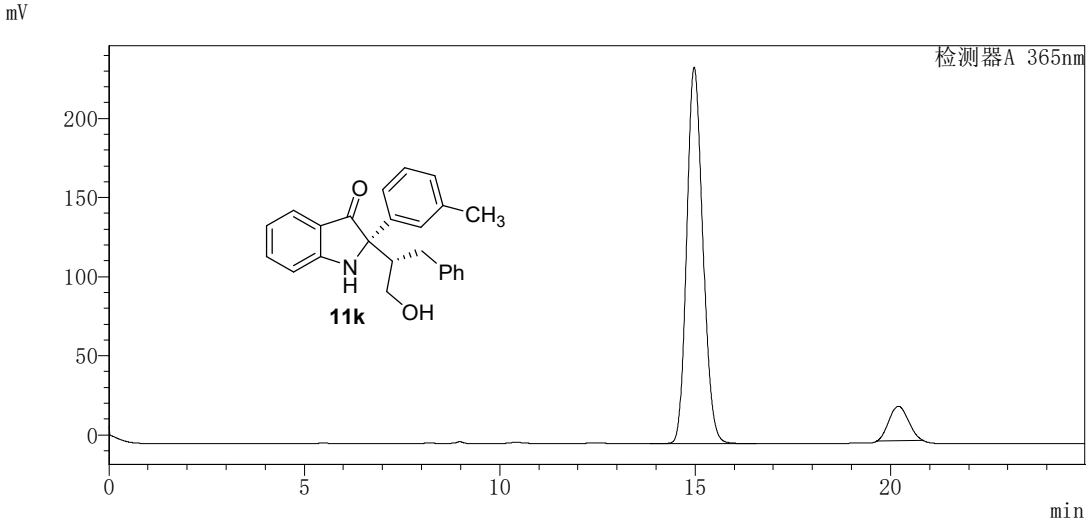


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	9.210	1137068	61758	15.864
2	PDA 365 nm	11.011	6030419	261735	84.136

HPLC using an IC-H column (hexane:*i*-PrOH=90:10, 1 mL/min)

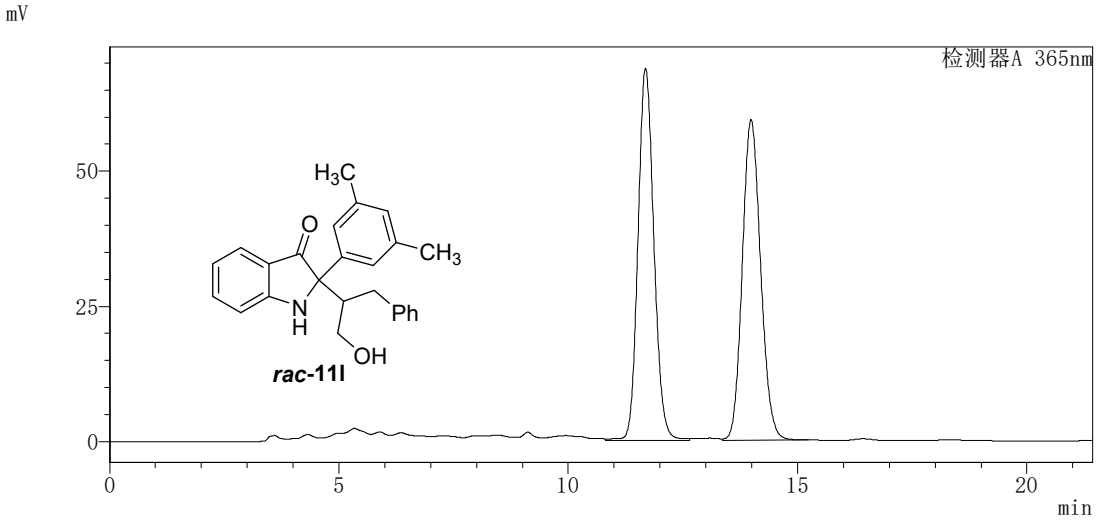


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	13.582	3050703	95860	49.019
2	PDA 365 nm	18.711	3172842	78140	50.981

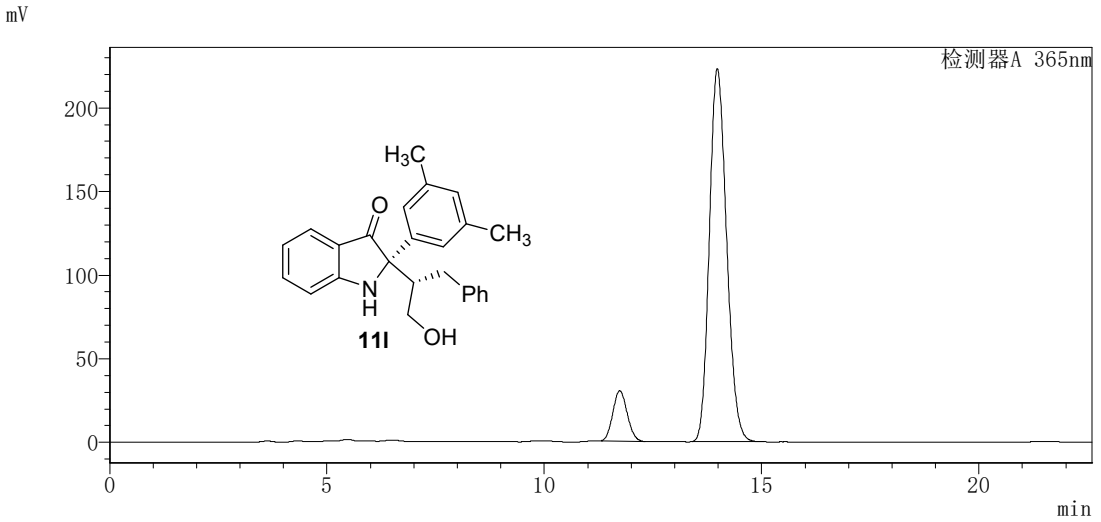


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	14.975	686211	238037	90.068
2	PDA 365 nm	20.196	756677	21913	9.932

HPLC using an IC-H column (hexane:*i*-PrOH=90:10, 1 mL/min)

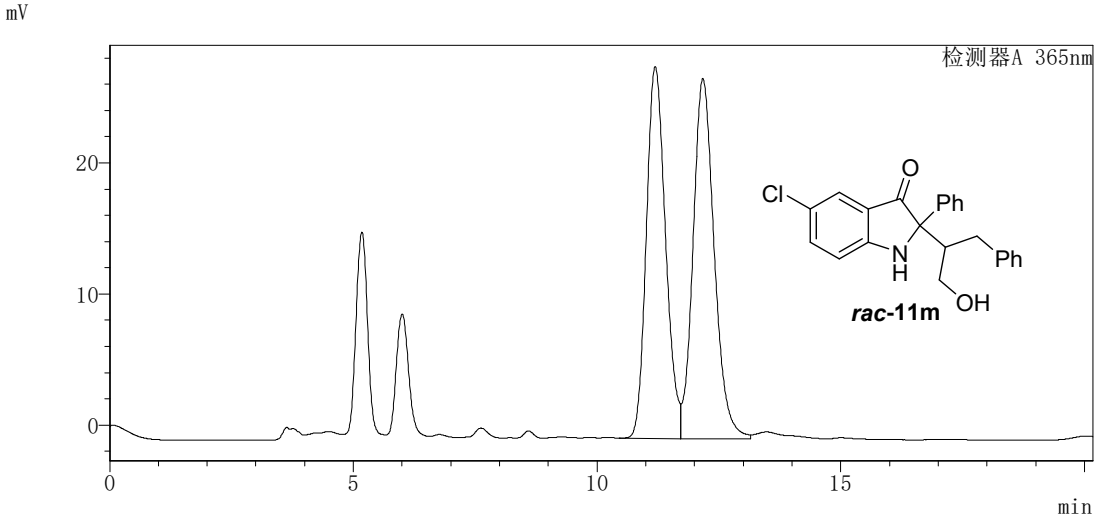


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	11.684	1661979	68852	50.212
2	PDA 365 nm	13.984	1647963	59285	49.788

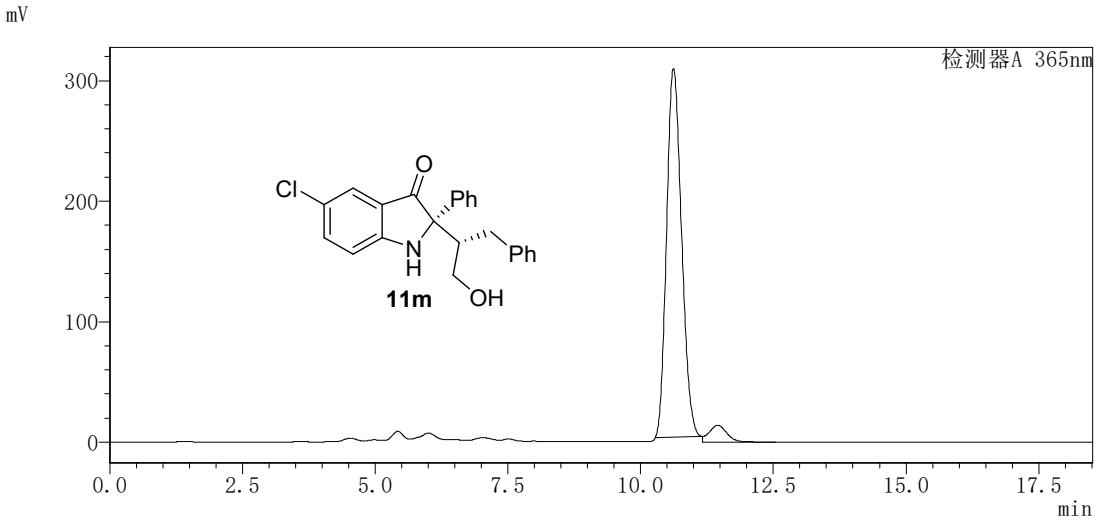


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	11.735	688900	30080	10.072
2	PDA 365 nm	13.980	6151066	223150	89.928

HPLC using an IC-H column (hexane:*i*-PrOH=90:10, 1 mL/min)

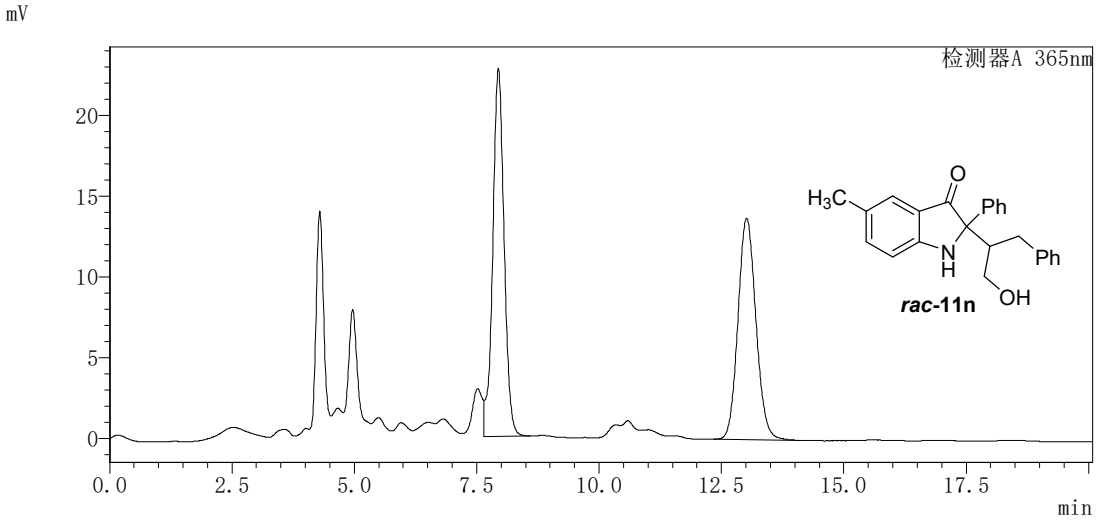


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	11.192	778341	28382	48.407
2	PDA 365 nm	12.170	829565	27460	51.593

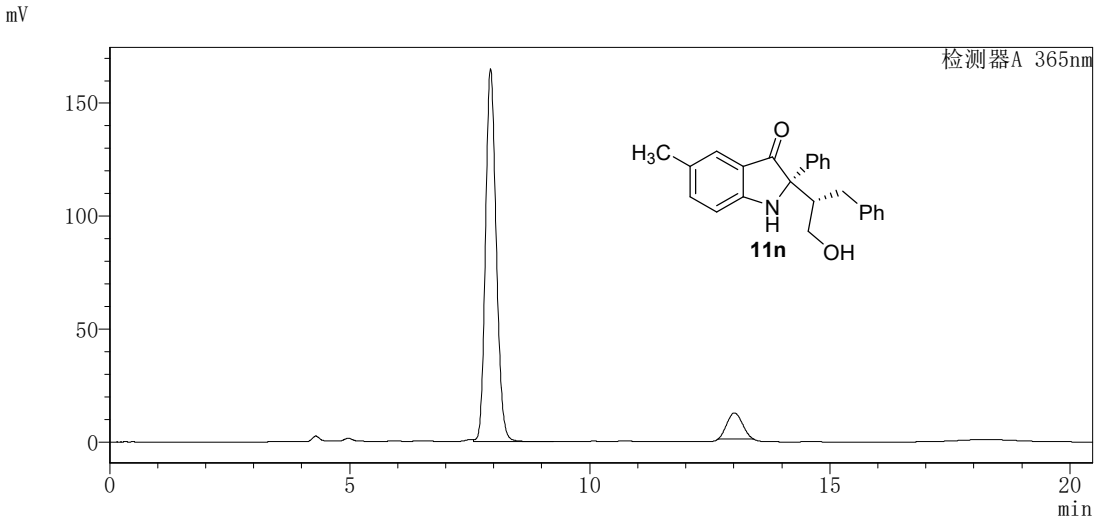


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	10.619	6001518	305997	94.909
2	PDA 365 nm	11.455	321939	13872	5.091

HPLC using an IC-H column (hexane:*i*-PrOH=80:20, 1 mL/min)

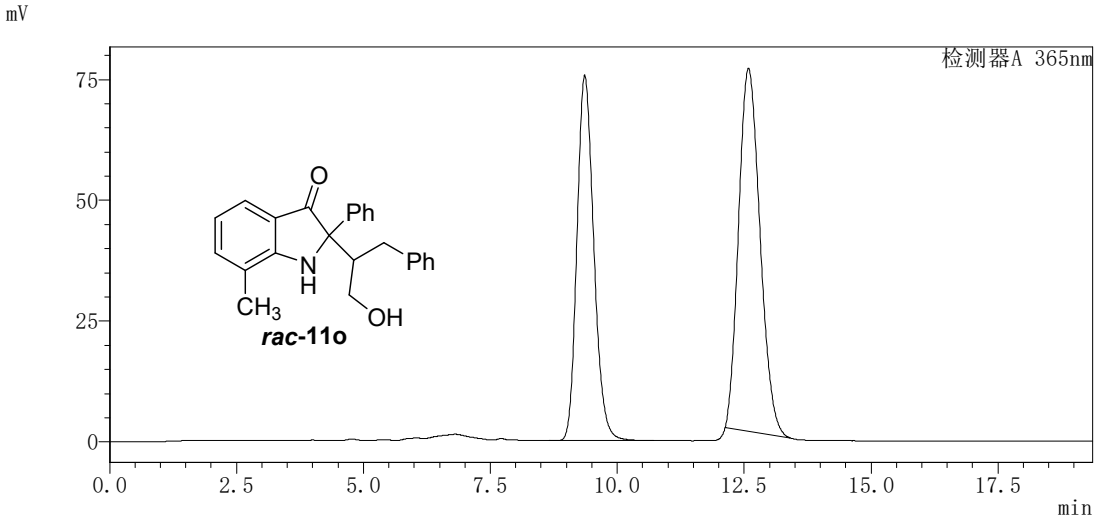


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	7.940	365539	22808	51.089
2	PDA 365 nm	13.012	349952	13723	48.911

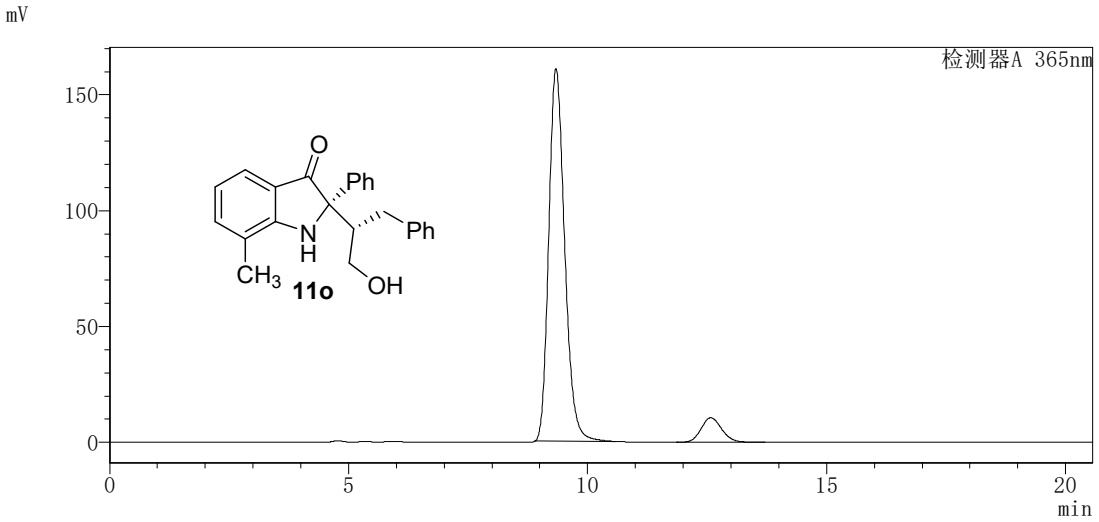


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	7.932	2568243	165357	91.969
2	PDA 365 nm	13.012	254971	11482	9.031

HPLC using an IC-H column (hexane:*i*-PrOH=80:20, 1 mL/min)

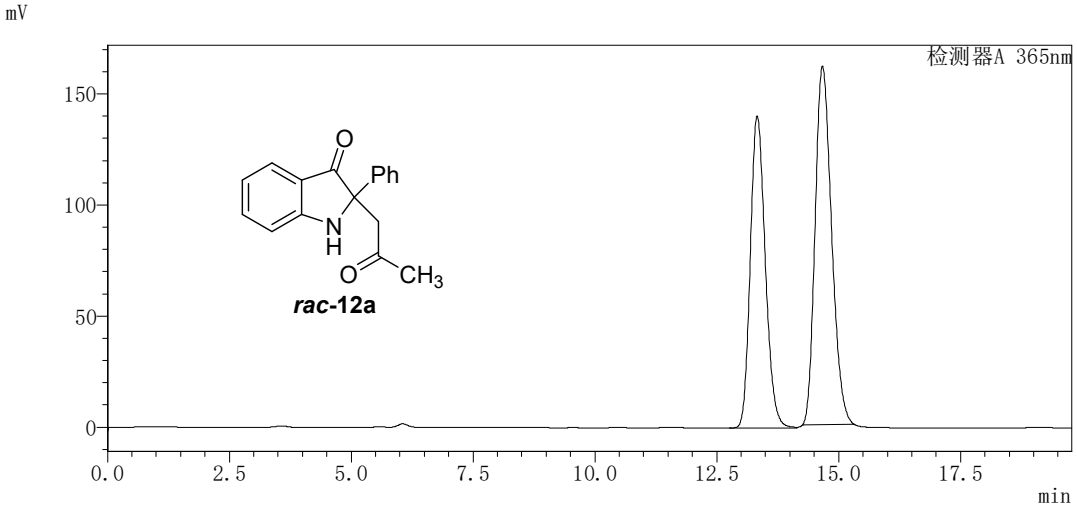


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	9.359	1748390	75720	44.305
2	PDA 365 nm	12.585	2197852	75153	55.695

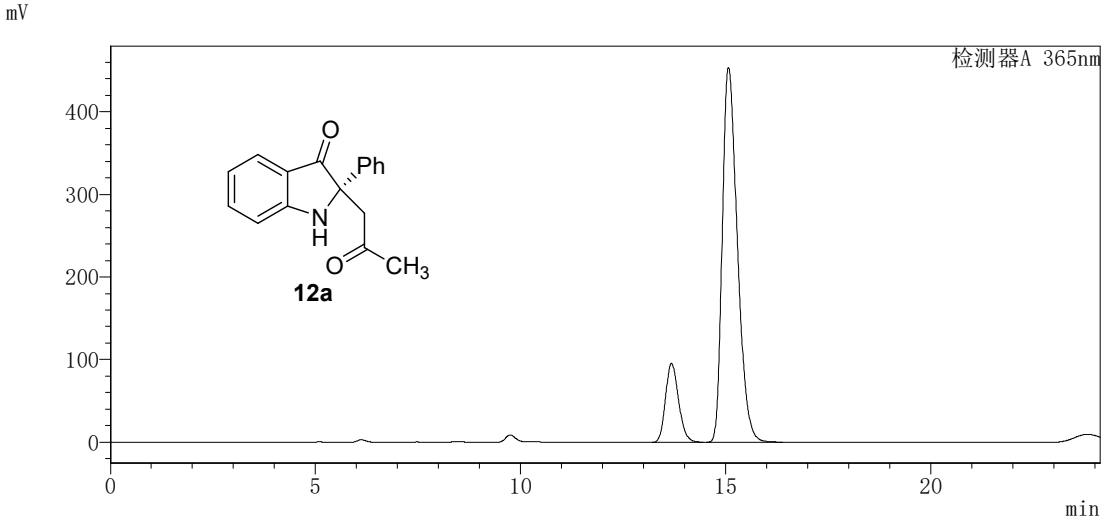


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	9.338	3717695	160857	92.116
2	PDA 365 nm	12.577	318206	10576	7.884

HPLC using an IC-H column (hexane:*i*-PrOH=90:10, 1 mL/min)

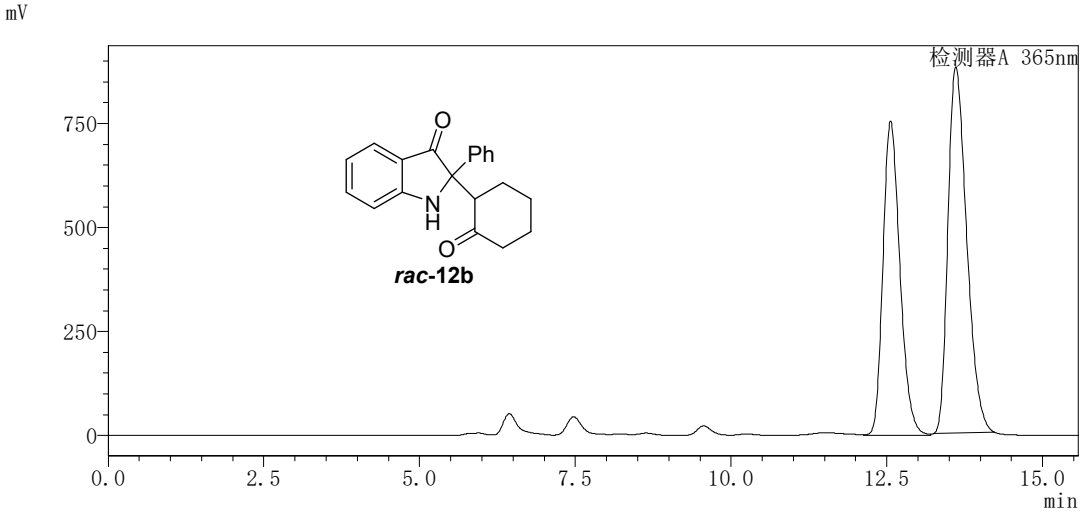


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	13.328	3009153	140520	44.261
2	PDA 365 nm	14.667	3789475	161504	55.739

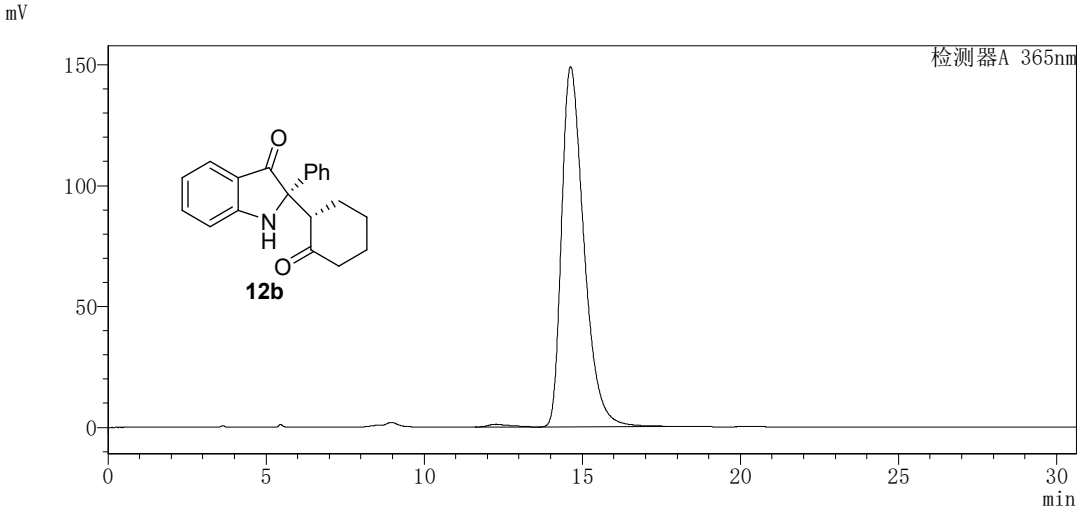


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	13.676	2116911	95570	15.439
2	PDA 365 nm	14.065	11594318	453830	84.561

HPLC using an OD-H column (hexane:*i*-PrOH=80:20, 1 mL/min)

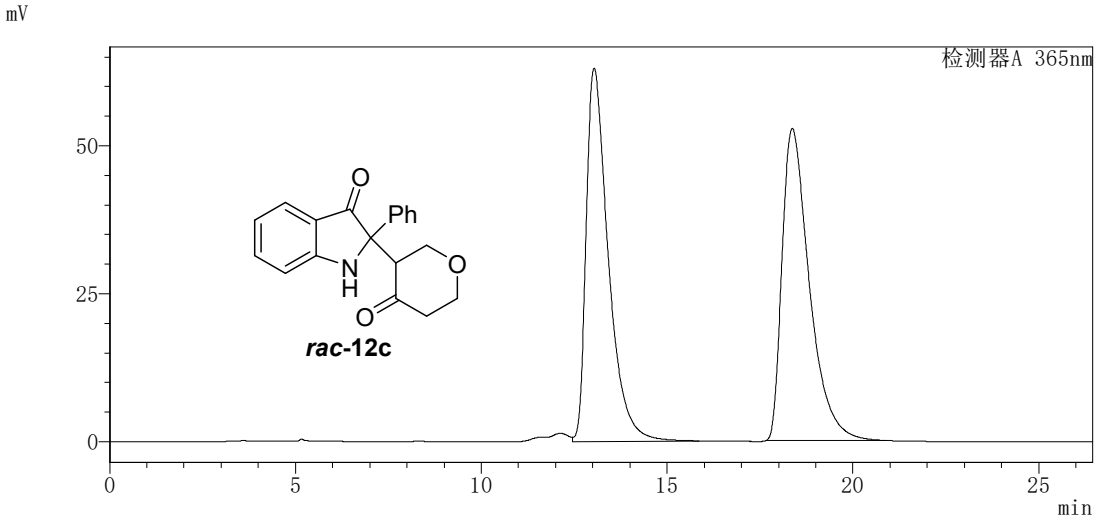


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	12.559	14327362	758617	43.794
2	PDA 365 nm	13.605	18387789	880691	56.206

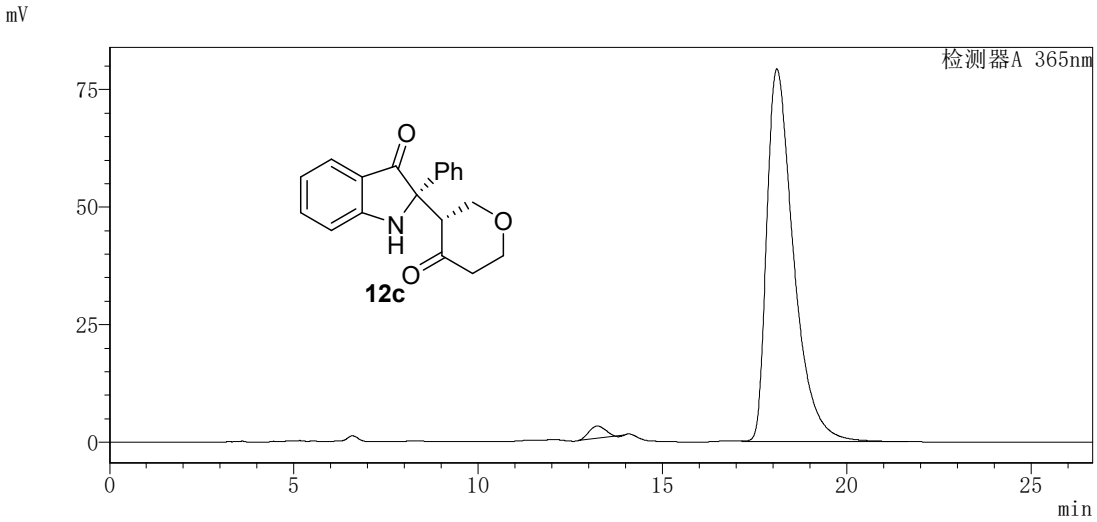


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	12.272	52838	1123	0.719
2	PDA 365 nm	14.631	7297431	149045	99.281

HPLC using an OD-H column (hexane:*i*-PrOH=80:20, 1 ml/min)

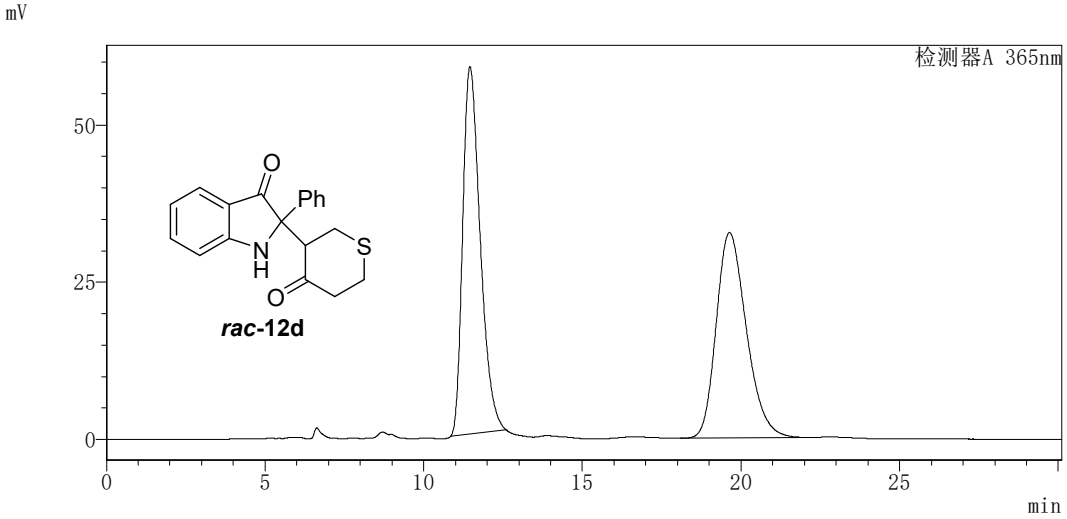


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	13.036	2605355	63060	49.102
2	PDA 365 nm	18.369	2700637	52731	50.898

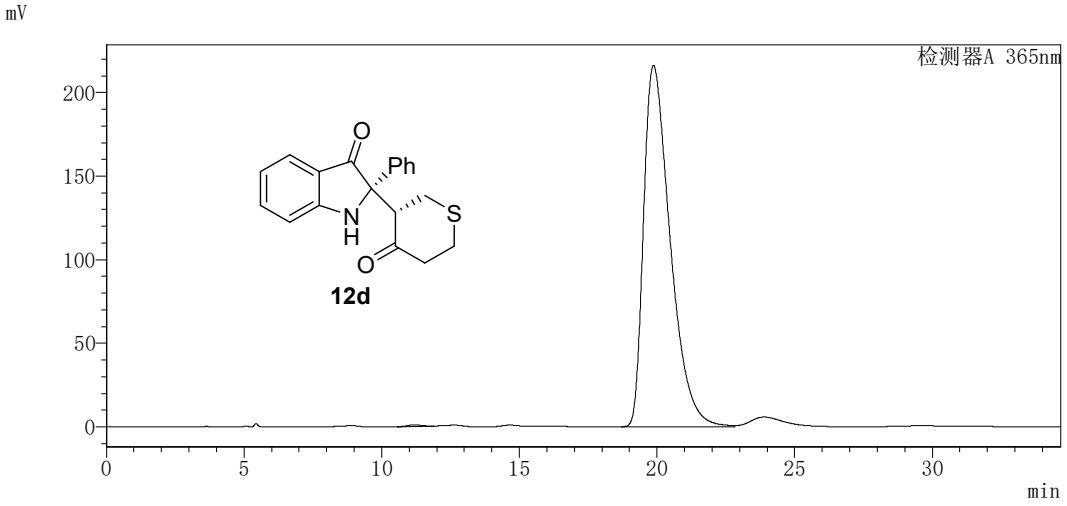


Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	13.229	79590	2585	1.935
2	PDA 365 nm	18.106	4034322	79418	98.065

HPLC using an OD-H column (hexane:*i*-PrOH=80:20, 1 mL/min)



Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	11.458	2239238	58420	50.928
2	PDA 365 nm	19.636	2157630	32658	49.072



Peak	Processed Channel	Retention Time (min)	Peak Area (mAU*s)	Peak Hight (mAU)	Peak Area (%)
1	PDA 365 nm	11.183	34551	917	0.238
2	PDA 365 nm	19.871	14512252	216170	99.762