Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

UV Light-Driven Asymmetric Vinylogous Aldol Reaction of Isatins with 2-Alkylbenzophenones and Enantioselective Synthesis of 3-Hydroxyoxindoles

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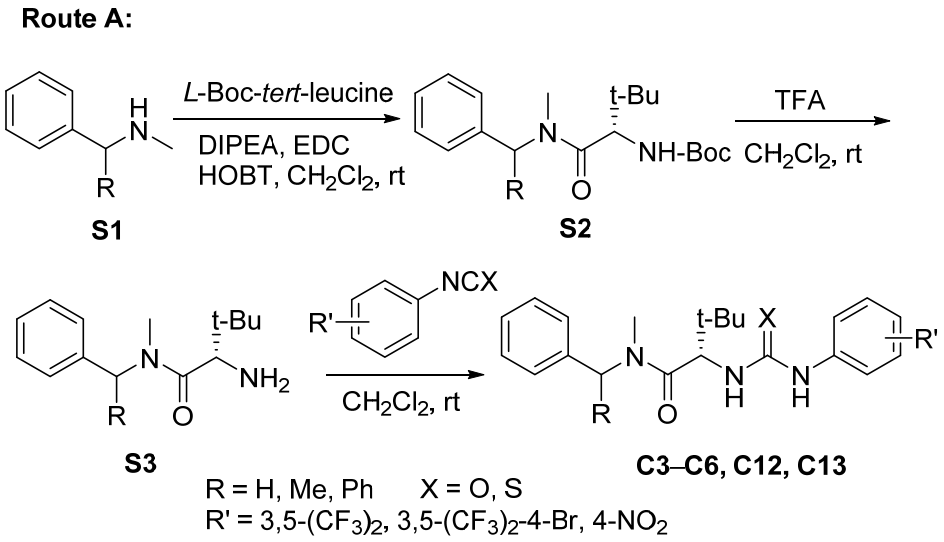
1. General information

All reactions were carried out under nitrogen atmosphere and anhydrous conditions. Commercially available chemicals were used directly without further purification. Anhydrous solvents were distilled by conventional procedures prior to use. Flash column chromatography was performed on silica gel (200–300 mesh) using a mixture of petroleum ether (PE)/ethyl acetate (EA) or methanol/ethyl acetate as the eluent. ^{1}H, ^{13}C, ^{19}F NMR spectra were recorded in $CDCl_3$ (or DMSO-*d*6) on Bruker 400 MHz. For ^{1}H, ^{13}C NMR spectra, TMS was chosen as an internal standard. For ^{19}F NMR spectra, $CFCl_3$ was set as the external standard. HRMS spectra were obtained on Varian 7.0T FTMS. Specific optical rotations were measured using IP-digi 300 (LED 589 nm) at 25 ºC in a 10 cm cell and concentrations were given in g/100 mL. HPLC was recorded on SSI HPLC 1500 equipped with chiral stationary columns from DACIEL (AD-H, OD, AS, IA, IC). UV lamp is a commercially available 3W/365 nm LED. Isatins[1] , benzophenones[2], catalysts **C1**[3] and **C2**[4] were prepared according to the previous reported procedures. Commercially available benzophenones **2a**, **2y** were purchased.

2. Experimental procedures

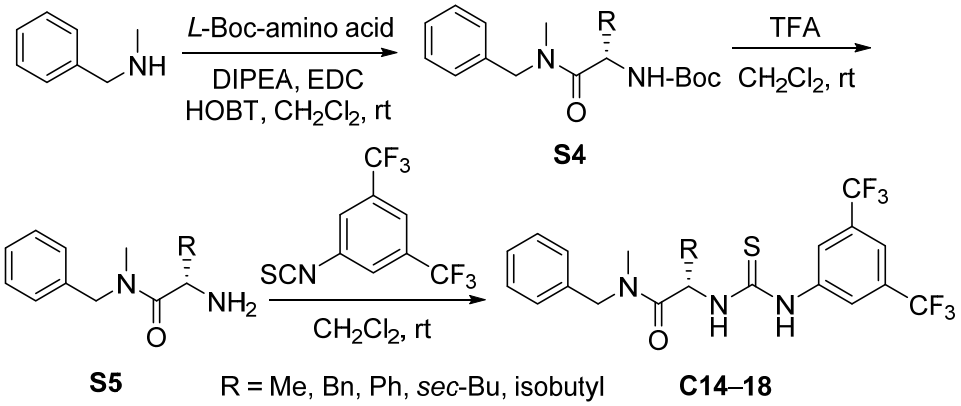
Synthesis of chiral catalysts [5]



Route A: To a stirred solution of amine **S1** (0.7 mL, 5.5 mmol) in CH_2Cl_2 (30 mL) were added DIPEA (1.3 mL, 7.5 mmol), 1-hydroxybenzotriazole (HOBT) (0.76 g, 5.5 mmol), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC) (1.05 g, 5.5 mmol) and *N*-Boc-*L*-*tert*-leucine (1.15 g, 5 mmol) in sequence. The resulting mixture was stirred at room temperature for 24 h. It was then diluted with Et_2O (30 mL) and washed with 1*N* HCl (50 mL), saturated $NaHCO_3$ aqueous solution (50 mL), and brine (50 mL) respectively. The organic layer was collected and dried over anhydrous Na_2SO_4. After filtration and removal of solvent and volatile components under reduced pressure, intermediate **S2** was obtained as colorless oil (1.6 g). To a solution of **S2** (0.80 g) in CH_2Cl_2 (15 mL) was added trifluoroacetic acid (3 mL). After the

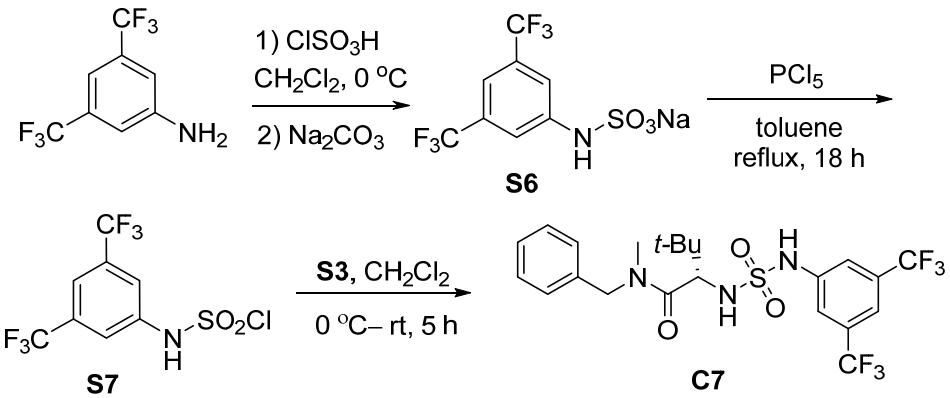
resulting mixture was stirred at rt for 2 h, it was quenched with saturated Na_2CO_3 aqueous solution (10 mL) and extracted with CH_2Cl_2 (12 mL × 3). The organic layers were combined and dried over Na_2SO_4. After filtration and removal of solvent and volatile components under reduced pressure, intermediate **S3** was obtained as pale-yellow oil. Without further purification, **S3** was then mixed with CH_2Cl_2 (5 mL), triethylamine (0.75 mL, 5 mmol) and isothiocyanate or isocyanate (1 mL, excessive). The resulting mixture was stirred at rt overnight. After removal of solvent and volatile components under reduced pressure, the crude product was subjected to column chromatography isolation (PE: EA = 3:1–1:1) to give the catalysts **C3**–**C6**, **C12** and **C13**. Catalysts **C8**–**C11** were also prepared from the corresponding secondary amines by similar procedures.

Route B:



Route B: To a stirred solution of *N*-methyl benzylamine (0.7 mL, 5.5 mmol) in CH_2Cl_2 (30 mL) were added DIPEA (1.3 mL, 7.5 mmol), HOBT (0.76 g, 5.5 mmol), EDC (1.05g, 5.5 mmol), and *N*-Boc-*L*-amino acid (5 mmol) in sequence. The resulting mixture was stirred at rt for 24 h. It was then diluted with Et_2O (30 mL) and washed with 1*N* HCl (50 mL), saturated $NaHCO_3$ aqueous solution (50 mL) and brine (50 mL), respectively. The organic layer was dried over Na_2SO_4. After filtration and concentration under reduced pressure, intermediate **S4** as colorless oil or white solid was obtained. To a solution of **S4** (0.8 g) in CH_2Cl_2 (15 mL) was added trifluoroacetic acid (3 mL). The resulting mixture was stirred at rt for 2 h. It was then quenched with saturated Na_2CO_3 aqueous solution (10 mL) and extracted with CH_2Cl_2 (12 mL × 3). The organic layers were combined and dried over Na_2SO_4. After filtration and removal of solvent and volatile components under reduced pressure, intermediate **S5** was collected. Without further purification, **S5** was then mixed with CH_2Cl_2 (5 mL), triethylamine (0.75 mL) and 3,5-bis(trifluoromethyl)phenyl isothiocyanate (0.9 mL, 5 mmol). The resulting mixture was then stirred at rt overnight. After removal of solvent and volatile components under reduced pressure, the crude product was purified by column chromatography (PE: EA= 3:1–1:1) to give catalysts **C14–C18**.

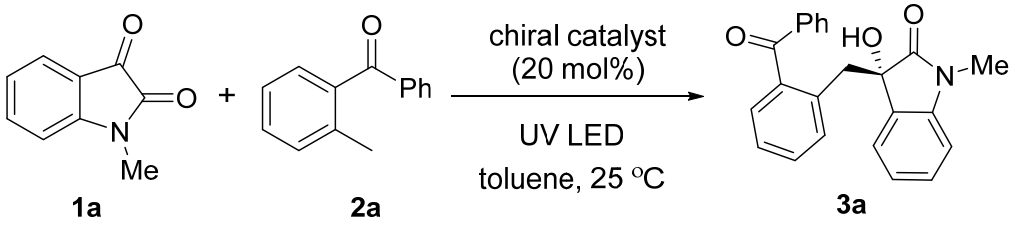
Route C:



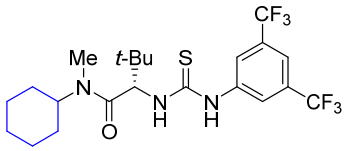
Route C: To a solution of 3,5-bis(trifluoromethyl)aniline (1.1 mL, 7.2 mmol) in CH_2Cl_2 (5 mL), chlorosulfonic acid (0.16 mL, 2.4 mmol) was dropwise added at 0 °C in 20 min by the means of microsyringe, and the resulting reaction mixture was stirred at 0 ºC for 2 h. A solution of Na_2CO_3 (0.381 g, 3.6 mmol) in water (5 mL) was then added to quench the reaction. The aqueous phase was collected and extracted with CH_2Cl_2 (10 mL × 3). Organic layers were discarded. Evaporation of the aqueous phase under reduced pressure brought about a white solid intermediate **S6**, which was used in the next step without further purification.

To a suspension of **S6** (0.92 g, 2.4 mmol) in toluene (5 mL) was added PCl_5 (0.53 g, 2.4 mmol) and the resulting mixture was heated under reflux with stirring for 18 h. The reaction mixture was then cooled to rt, and was then filtered through a celite pad. The filtrate was concentrated under reduced pressure to dryness to give intermediate **S7** (0.476 g) as a brown solid. Intermediate **S7** (0.50 g, 1.7 mmol) was dissolved in CH_2Cl_2 (15 ml) and intermediate **S3** (0.281g, 1.2 mmol) was added into it at 0 ºC. The resulting mixture was stirred for 5 h while being naturally warmed to rt. After removal of solvent and volatile components under reduced pressure, the crude product was subjected to column chromatography isolation (PE:EA = 10:1) to give solid catalyst **C7**.

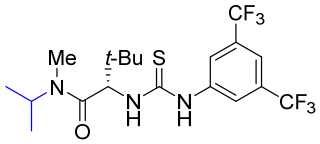
Screening of catalysts



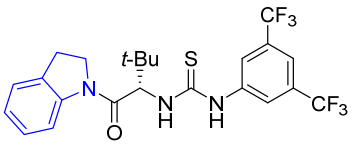
A mixture of **1a** (16 mg, 0.1 mmol) and **2a** (60 mg, 0.3 mmol) and the catalyst (0.02 mmol) in toluene (2.0 mL) was stirred for 2 to 8 h under the irradiation of UV light (365 nm, 3 W) at 25 °C until **1a** was completely consumed (monitored by TLC). After removal of solvent and volatile components under reduced pressure, the crude product was subjected to flash column chromatography isolation on silica gel (eluent: PE:EA = 4:1) to give **3a**. The catalyst efficiency was evaluated with regard to yield and enantioselectivity.



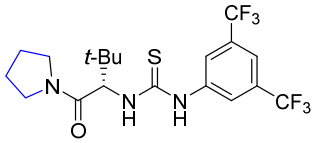
C8 yield 77%, *er* 89.5:10.5



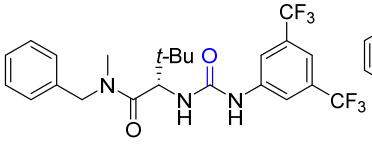
C9 yield 82%, *er* 87.5:12.5



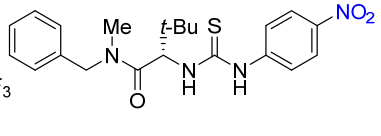
C10 yield 67%, *er* 85:15



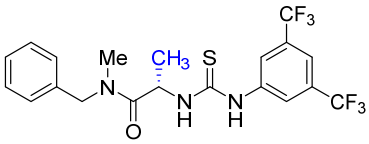
C11 yield 73%, *er* 89.5:10.5



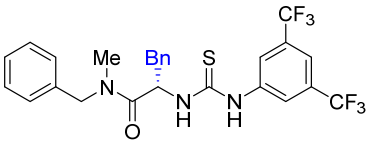
C12 yield 90%, *er* 77.5:22.5



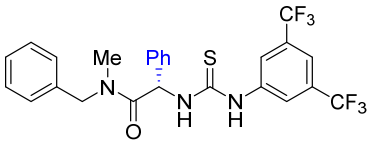
C13 yield 80%, *er* 69:31



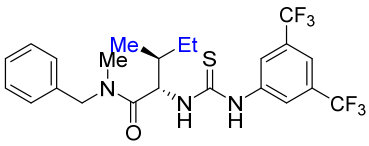
C14 yield 92%, *ee* 87.5:12.5



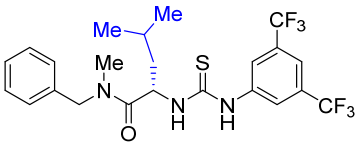
C15 yield 84%, *er* 84:16



C16 yield 76%, *er* 78.5:21.5

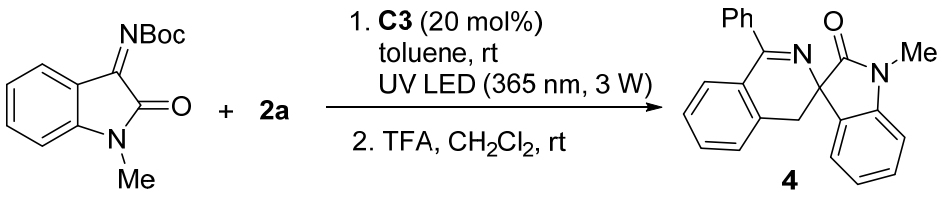


C17 yield 87%, *er* 87.5:12.5



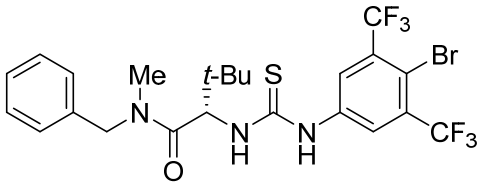
C18 yield 90%, *er* 80:20

The aza-aldol reaction of 3-imino oxindole and 2-methylbenzophenone 2a and synthesis of spirocyclic compound 4.



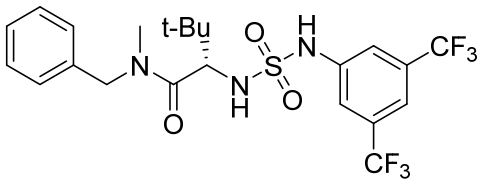
A mixture of 3-imino oxindole (26 mg, 0.1 mmol), **2a** (60 mg, 0.3 mmol), and catalyst **C3** (0.02 mmol) in toluene (2.0 mL) was stirred at rt (25 °C) for 6 h under the irradiation of UV LED light (365 nm, 3 W). Then 1 mL of CH_2Cl_2 was added into the reaction, followed by the addition of TFA (1 mL). The resulting mixture was stirred at rt for 2 h, and was then quenched by saturated Na_2CO_3 aqueous solution (2.0 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 mL). The organic layers were combined and dried over Na_2SO_4. After filtration and removal of solvent and volatile components under reduced pressure, the residue was subjected to flash column chromatography isolation on silica gel (PE:EA = 5:1). Compound **4** was obtained as a white solid (17 mg, 56% yield).

3. Analytical data for catalysts and compounds 3 and 4.



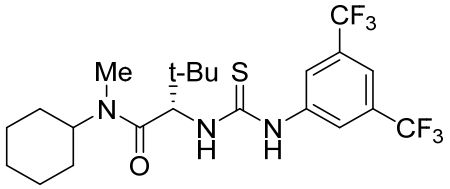
(*S*)-*N*-Benzyl-2-(3-(4-bromo-3,5-bis(trifluoromethyl)phenyl)thioureido)-*N*,3,3-trimethyl butanamide (C4)

White solid; 1.45 g, overall 50% yield (PE: EA = 10:1); m.p. 147.4–149.0 °C; 5:1 rotamers; **major rotamer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (br s, 1H), 8.04 – 7.88 (m, 1H), 7.87 (s, 2H), 7.29 (s, 1H), 7.27 – 7.07 (m, 4H), 5.66 (d, *J* = 9.0 Hz, 1H), 4.94 (d, *J* = 14.4 Hz, 1H), 4.25 (d, *J* = 14.3 Hz, 1H), 3.28 (s, 3H), 1.15 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.6, 173.9, 138.3, 135.4, 132.5 (q, *J* = 31.3 Hz), 128.7, 128.0, 127.9, 126.4 – 125.6 (m), 122.3 (q, *J* = 274.5 Hz), 113.2, 61.2, 52.0, 36.67, 36.2, 27.2. $[\alpha]_D^{25}$ = -11.0 (c = 0.3 in $CHCl_3$). HRMS-ESI: calcd. for $C_{23}H_{24}BrF_6N_3OS$ $[M+H]^+$ 582.0649, found 582.0652.



(*S*)-*N*-Benzyl-2-((*N*-(3,5-bis(trifluoromethyl)phenyl)sulfamoyl)amino)-*N*,3,3-trimethyl butanamide (C7)

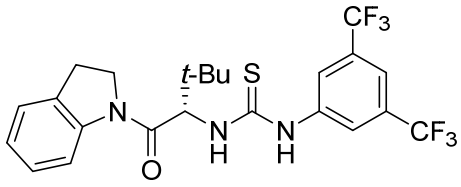
White amorphous solid; 75 mg, 21% yield (PE: EA = 10:1); 4:1 rotamers; **major rotamer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 – 8.40 (m, 1H), 7.69 (s, 2H), 7.55 (d, *J* = 4.1 Hz, 1H), 7.32 – 7.03 (m, 5H), 6.50 – 6.42 (m, 1H), 4.82 (d, *J* = 14.6 Hz, 1H), 4.21 (d, *J* = 10.2 Hz, 1H), 4.09 (d, *J* = 14.6 Hz, 1H), 2.88 (s, 3H), 0.98 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.7, 138.7, 134.8, 131.5 (q, *J* = 33.5 Hz), 127.7, 126.9, 126.7, 122.0 (q, *J* = 271.8 Hz), 118.0 (d, *J* = 4.1 Hz), 116.3 – 115.8 (m), 58.9, 50.5, 35.0, 34.7, 25.5. $[\alpha]_D^{25}$ = +5.67 (c = 0.6 in $CHCl_3$). HRMS-ESI: calcd. $C_{22}H_{25}F_6N_3O_3S$ for $[M-H]^-$ 524.1443, found 524.1446.



(*S*)-2-(3-(3,5-Bis(trifluoromethyl)phenyl)thioureido)-*N*-cyclohexyl-*N*,3,3-trimethyl butanamide (C8)

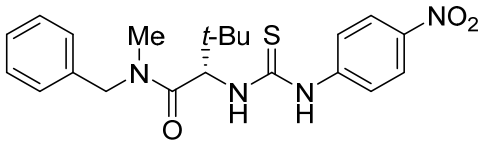
White solid; 1.31 g, overall 53% yield (PE:EA = 10:1); m.p. 201.5–202.3 °C; 1.1:1 rotamers; **major rotamer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.18 (br s, 1H), 8.08 – 7.82 (m, 3H), 7.60 (s, 1H), 5.61 (dd, *J* = 9.1, 2.6 Hz, 1H), 4.32 (tt, *J* = 11.3, 3.8 Hz, 1H), 3.15 (s, 3H), 2.01 – 1.69 (m, 4H), 1.66 – 1.54 (m, 2H), 1.50 – 1.23 (m, 4H), 1.12 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.7, 172.4, 140.0, 131.8 (q, *J* = 33.8 Hz), 124.5, 121.7, 118.8 – 117.7 (m), 61.5, 54.0, 36.2, 31.1, 29.2,

27.2, 25.5, 25.2. $[\alpha]_D^{25}$ = -11.8 (c = 0.6 in $CHCl_3$). HRMS-ESI: calcd. for $C_{22}H_{29}F_6N_3OS$ $[M-H]^-$ 496.1857, found 496.1860.



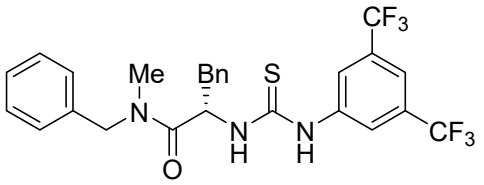
(*S*)-1-(3,5-Bis(trifluoromethyl)phenyl)-3-(1-(indolin-1-yl)-3,3-dimethyl-1-oxobutan-2-yl) thiourea (C10)

White solid; 1.53 g, overall 61% yield (PE: EA = 6:1); m.p. 72.1–74.0 °C; 4:1 rotamers; **major rotamer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (br s, 1H), 8.20 – 8.09 (m, 2H), 7.48 (s, 2H), 7.40 (s, 1H), 7.25 – 7.17 (m, 1H), 7.15 – 6.97 (m, 2H), 5.46 (d, *J* = 9.0 Hz, 1H), 5.18 – 4.83 (m, 1H), 4.34 – 4.11 (m, 1H), 3.29 – 3.06 (m, 2H), 1.25 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.0, 172.4, 141.3, 139.6, 132.9, 131.1 (q, *J* = 33.6 Hz), 127.3, 125.6 (d, *J* = 5.1 Hz), 123.8 – 123.5 (m), 122.9 (q, *J* = 273.4 Hz), 118.3 – 117.8 (m), 117.2, 64.0, 49.9, 35.9, 28.0, 27.2. $[\alpha]_D^{25}$ = -42.0 (c = 0.1 in $CHCl_3$). HRMS-ESI: calcd. for $C_{23}H_{23}F_6N_3OS$ $[M-H]^-$ 502.1388, found 502.1391.



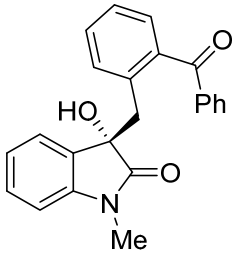
(*S*)-*N*-Benzyl-*N*,3,3-trimethyl-2-(3-(4-nitrophenyl)thioureido)butanamide (C13)

Light yellow solid; 1.46 g, overall 71% yield (PE: EA = 10:1); m.p. 81.8–82.3 °C; 3:1 rotamers; **major rotamer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.65 (br s, 1H), 9.08 (br s,1H), 8.12 (d, *J* = 9.1 Hz, 2H), 7.75 (d, *J* = 7.7 Hz, 1H), 7.59 (d, *J* = 9.0 Hz, 2H), 7.37 – 7.30 (m, 1H), 7.30 – 7.15 (m, 3H), 5.60 (d, *J* = 9.1 Hz, 1H), 4.80 (d, *J* = 14.6 Hz, 1H), 4.36 (d, *J* = 14.6 Hz, 1H), 3.22 (s, 3H), 1.09 (s, 9H).^{13}C NMR (101 MHz, $CDCl_3$) δ 180.9, 173.0, 144.3, 143.9, 135.8, 128.8, 128.7, 127.9, 124.6, 122.6, 60.9, 51.8, 36.6, 36.2, 27.2. $[\alpha]_D^{25}$ = +57.3 (c = 0.6 in $CHCl_3$). HRMS-ESI: calcd. for $C_{21}H_{26}N_4O_3S$ $[M-H]^-$ 413.1647, found 413.1650.



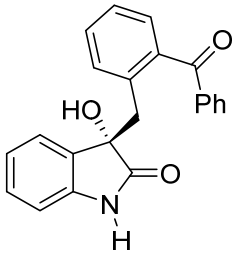
(*S*)-*N*-Benzyl-2-(3-(3,5-bis(trifluoromethyl)phenyl)thioureido) *N*-methyl 3-phenyl propanamide (C15)

White solid. 1.32g, overall 49% yield (PE:EA = 8:1); m.p. 66.5–67.8 °C; 4:1 rotamers; **major rotamer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.23 (br s, 1H), 8.87 (br s, 1H), 7.97 (d, *J* = 3.8 Hz, 2H), 7.43 (s, 1H), 7.38–7.28 (m, 5H), 7.28–7.26 (m, 1H), 7.19–7.08 (m, 4H), 5.59 – 5.47 (m, 1H), 4.93 – 4.82 (m, 1H), 4.36 – 4.24 (m, 1H), 3.34 – 3.16 (m, 2H), 2.92 (d, *J* = 4.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.6, 174.9, 140.0, 135.4 (d, *J* = 7.6 Hz), 130.9 (q, *J* = 33.4 Hz), 129.3, 128.9, 128.7, 127.6, 127.5, 124.2, 123.1 (q, *J* = 272.6 Hz), 117.8 (dd, *J* = 7.0, 3.4 Hz), 56.6, 52.3, 38.7, 35.2. $[\alpha]_D^{25}$ = +7.33 (c = 0.3 in $CHCl_3$). HRMS-ESI: calcd. for $C_{26}H_{23}F_6N_3OS$ $[M-H]^-$ 538.1388, found 538.1391.



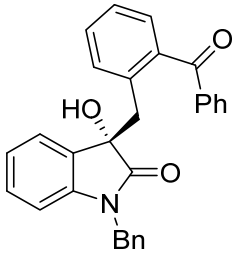
(*S*)-3-(2-Benzoylbenzyl)-3-hydroxy-1-methylindolin-2-one (3a)

White solid; 29 mg, 82% yield (PE:EA = 3.5:1); m.p. 104.0–105.5 °C; 93:7 *er* (HPLC analysis on a Daicel Chiralpak AD-H column: hexane/*i*-PrOH = 80:20, flow rate 1.00 mL/min, λ = 254 nm; τ_{major} = 11.605 min, τ_{minor} = 15.107 min); $[\alpha]_D^{25}$ = +50.3 (c = 0.3 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.71 (m, 2H), 7.59 (t, 1H), 7.51 – 7.38 (m, 4H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.31 – 7.19 (m, 2H), 6.98 – 6.86 (m, 2H), 6.79 (d, *J* = 7.8 Hz, 1H), 5.88 (br s, 1H), 3.63 (d, *J* = 13.9 Hz, 1H), 3.16 (s, 3H), 2.97 (d, *J* = 13.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.0, 178.4, 143.2, 138.6, 137.6, 134.9, 133.6, 133.4, 131.0, 130.9, 130.6, 130.2, 130.1, 129.3, 128.4, 128.2, 126.2, 125.3, 122.4, 108.2, 76.3, 40.7, 26.2. HRMS-ESI: calcd. for $C_{23}H_{19}NO_3$ $[M+H]^+$ 358.1443, found 358.1441.



(*S*)-3-(2-Benzoylbenzyl)-3-hydroxyindolin-2-one (3b)

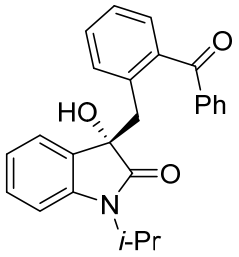
White solid; 33 mg, 95% yield (PE:EA = 1:1); m.p. 174.5–175.3 °C; 61:39 *er* (HPLC analysis on a Daicel Chiralpak AD-H column: hexane/*i*-PrOH = 80:20, flow rate 1.00 mL/min, λ = 254 nm; τ_{major} = 11.553 min, τ_{minor} = 13.772 min). $[\alpha]_D^{25}$ = +25.3 (c = 0.3 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (br s, 1H), 7.82 – 7.71 (m, 2H), 7.60 (t, *J* = 6.9 Hz, 1H), 7.53 – 7.40 (m, 4H), 7.36 (td, *J* = 7.6, 1.0 Hz, 1H), 7.23 – 7.17 (m, 2H), 6.99 – 6.88 (m, 2H), 6.86 (d, *J* = 7.8 Hz, 1H), 6.12 (br s, 1H), 3.62 (d, *J* = 13.9 Hz, 1H), 3.01 (d, *J* = 13.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.2, 180.7, 140.2, 138.6, 137.7, 134.7, 133.7, 133.4, 131.0, 130.9, 130.75, 130.65, 129.3, 128.3, 126.3, 125.7, 122.3, 110.2, 76.7, 40.8. HRMS-ESI: calcd. for $C_{22}H_{17}NO_3$ $[M+H]^+$ 344.1287, found 344.1289.



(*S*)-3-(2-Benzoylbenzyl)-1-benzyl-3-hydroxyindolin-2-one (3c)

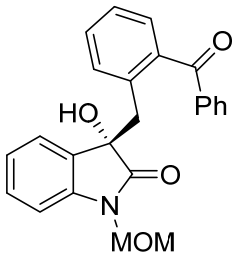
White solid; 41 mg, 95% yield (PE:EA = 4:1); m.p. 189.5–190.5 °C; 86:14 *er* (HPLC analysis on a Daicel Chiralpak AD-H column: hexane/*i*-PrOH = 80:20, flow rate 1.00 mL/min, λ = 254 nm;

τ_{major} = 13.943 min, τ_{minor} = 16.548 min). $[\alpha]_D^{25}$ = +8.0 (c = 0.3 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.63 (m, 2H), 7.60 – 7.54 (m, 1H), 7.45 (dd, *J* = 7.3, 1.7 Hz, 1H), 7.41 – 7.33 (m, 4H), 7.32 – 7.23 (m, 4H), 7.16 – 7.10 (m, 2H), 7.09 – 6.99 (m, 2H), 6.88 – 6.74 (m, 1H), 6.61 (d, *J* = 7.8 Hz, 1H), 5.43 (br s, 1H), 5.05 (d, *J* = 15.8 Hz, 1H), 4.64 (d, *J* = 15.7 Hz, 1H), 3.82 (d, *J* = 13.7 Hz, 1H), 3.09 (d, *J* = 13.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.8, 178.3, 142.3, 138.7, 137.5, 133.8, 133.3, 130.9, 130.8, 130.7, 129.9, 129.3, 128.7, 128.2, 127.5, 127.2, 126.3, 125.4, 122.5, 109.2, 76.5, 43.7, 40.8. HRMS-ESI: calcd. for $C_{29}H_{23}NO_3$ $[M+H]^+$ 434.1756, found 434.1748.



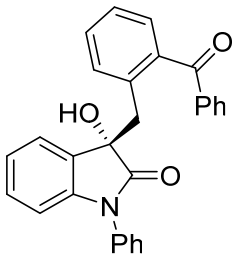
(*S*)-3-(2-Benzoylbenzyl)-3-hydroxy-1-isopropylindolin-2-one (3d)

White solid; 35 mg, 91% yield (PE:EA = 4:1); m.p. 135.7–136.5 °C; 89:11 *er* (HPLC analysis on a Daicel Chiralpak AD-H column: hexane/*i*-PrOH = 80:20, flow rate 1.00 mL/min, λ = 254 nm; τ_{major} = 10.095 min, τ_{minor} = 17.540 min). $[\alpha]_D^{25}$ = +17.7 (c = 0.3 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.8 Hz, 2H), 7.59 (t, *J* = 7.2 Hz, 1H), 7.48–7.29 (m, 6H), 7.18 (t, *J* = 7.7 Hz, 1H), 7.00 (d, *J* = 7.3 Hz, 1H), 6.91 (d, *J* = 7.3 Hz, 1H), 6.84 (t, *J* = 7.4 Hz, 1H), 5.30 (br s, 1H), 4.50 (m, 1H), 3.70 (d, *J* = 13.7 Hz, 1H), 2.97 (d, *J* = 13.7 Hz, 1H), 1.42 (d, *J* = 7.0 Hz, 3H), 1.39 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.8, 178.0, 141.8, 138.7, 137.6, 134.8, 133.5, 133.3, 131.0, 130.8, 130.5, 130.4, 129.2, 128.2, 126.2, 125.5, 122.0, 109.8, 76.1, 43.9, 40.9, 19.4, 19.1. HRMS-ESI: calcd. for $C_{25}H_{23}NO_3$ $[M+H]^+$ 386.1756, found 386.1749.



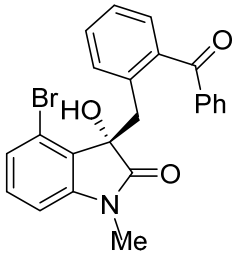
(*S*)-3-(2-Benzoylbenzyl)-3-hydroxy-1-(methoxymethyl)indolin-2-one (3e)

White solid; 29 mg, 76% yield (PE:EA = 3.5:1); m.p. 161.8–161.5 °C; 93:7 *er* (HPLC analysis on a Daicel Chiralpak AD-H column: hexane/*i*-PrOH = 80:20, flow rate 1.00 mL/min, λ = 254 nm; τ_{major} = 11.723 min, τ_{minor} = 16.780 min). $[\alpha]_D^{25}$ = +33.0 (c = 0.3 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.71 (m, 2H), 7.65 – 7.55 (m, 1H), 7.52 – 7.40 (m, 4H), 7.38 – 7.30 (m, 1H), 7.29 – 7.19 (m, 3H), 7.05 – 6.97 (m, 2H), 6.94 (t, *J* = 7.5 Hz, 1H), 5.90 (br s, 1H), 5.15 (d, *J* = 10.9 Hz, 1H), 5.03 (d, *J* = 10.9 Hz, 1H), 3.69 (d, *J* = 13.8 Hz, 1H), 3.26 (s, 3H), 3.01 (d, *J* = 13.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.0, 178.9, 141.4, 138.7, 137.6, 134.6, 133.7, 133.4, 131.0, 130.9, 130.7, 129.8, 129.5, 128.3, 126.4, 125.5, 123.0, 109.7, 76.6, 71.6, 56.2, 41.0. HRMS-ESI: calcd. for $C_{24}H_{21}NO_4$ $[M+H]^+$ 388.1547, found 388.1549.



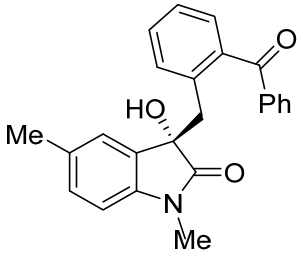
(*S*)-3-(2-Benzoylbenzyl)-3-hydroxy-1-phenylindolin-2-one (3f)

White solid; 36 mg, 87% yield (PE:EA = 4:1); m.p. 64.5–66.8 °C; 83:17 *ee* (HPLC analysis on a Daicel Chiralpak IA column: hexane/*i*-PrOH = 80:20, flow rate 1.00 mL/min, λ = 254 nm; τ_{major} = 13.205 min, τ_{minor} = 15.107 min). $[\alpha]_D^{25}$ = -16.3 (c = 0.3 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 – 7.68 (m, 2H), 7.64 – 7.54 (m, 1H), 7.53 – 7.45 (m, 3H), 7.45 – 7.38 (m, 4H), 7.37 – 7.28 (m, 4H), 7.19 – 7.12 (m, 1H), 7.08 (d, *J* = 7.3 Hz, 1H), 6.92 (t, *J* = 7.5 Hz, 1H), 6.76 (d, *J* = 7.9 Hz, 1H), 5.47 (br s, 1H), 3.79 (d, *J* = 13.7 Hz, 1H), 3.17 (d, *J* = 13.7 Hz, 1H).^{13}C NMR (101 MHz, $CDCl_3$) δ 198.8, 177.5, 143.0, 138.6, 137.6, 134.7, 134.1, 133.6, 133.3, 130.97, 130.96, 130.7, 129.8, 129.5, 129.3, 128.2, 128.0, 126.4, 126.3, 125.5, 123.0, 109.4, 76.6, 41.1. HRMS-ESI: calcd. for $C_{28}H_{21}NO_3$ $[M+H]^+$ 420.1600, found 420.1598.



(*S*)-3-(2-Benzoylbenzyl)-4-bromo-3-hydroxy-1-methylindolin-2-one (3g)

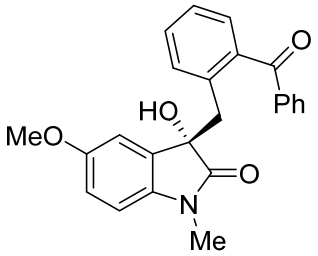
White solid; 33 mg, 77% yield (PE:EA = 2:1); m.p. 174.2–175.4 °C; 81:19 *er* (HPLC analysis on a Daicel Chiralpak AD-H column: hexane/*i*-PrOH = 80:20, flow rate 1.00 mL/min, λ = 254 nm; τ_{major} = 23.012 min, τ_{minor} = 27.133 min). $[\alpha]_D^{25}$ = -22.3 (c = 0.3 in $CHCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 8.2, 1.1 Hz, 2H), 7.63 – 7.53 (m, 1H), 7.47 – 7.37 (m, 3H), 7.35 – 7.22 (m, 3H), 7.09 – 6.96 (m, 2H), 6.66 (dd, *J* = 7.5, 0.9 Hz, 1H), 4.92 (br s, 1H), 3.73 (d, *J* = 13.8 Hz, 1H), 3.53 (d, *J* = 13.8 Hz, 1H), 3.05 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.9, 175.3, 143.8, 137.6, 136.5, 132.8, 132.3, 132.1, 129.8, 129.7, 129.4, 127.6, 127.2, 126.1, 125.3, 118.5, 106.1, 77.4, 38.0, 25.2. HRMS-ESI: calcd. for $C_{23}H_{18}BrNO_3$ $[M+H]^+$ 436.0548, found 436.0544.



(*S*)-3-(2-Benzoylbenzyl)-3-hydroxy-1,5-dimethylindolin-2-one (3h)

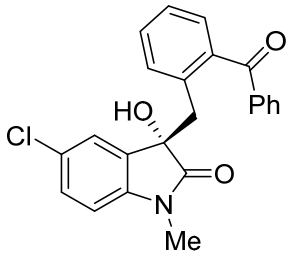
White solid; 32 mg, 86% yield (PE:EA = 4:1); m.p. 196.8–198.3 °C; 95:5 *er* (HPLC analysis on a Daicel Chiralpak IA column: hexane/*i*-PrOH = 80:20, flow rate 1.00 mL/min, λ = 254 nm; τ_{major} =

10.193 min, τ_{minor} = 12.300 min). $[\alpha]_D^{25}$ = +31.7 (c = 0.3 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.65 (m, 2H), 7.66 – 7.57 (m, 1H), 7.51 – 7.29 (m, 6H), 7.03 (d, *J* = 7.8 Hz, 1H), 6.82 (s, 1H), 6.67 (d, *J* = 7.9 Hz, 1H), 5.20 (br s, 1H), 3.75 (d, *J* = 13.7 Hz, 1H), 3.14 (s, 3H), 3.05 (d, *J* = 13.7 Hz, 1H), 2.12 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.9, 178.2, 140.8, 138.6, 137.7, 134.9, 133.6, 133.3, 132.2, 130.9, 130.8, 130.4, 130.0, 129.5, 128.2, 126.2, 126.1, 107.9, 76.6, 40.6, 26.2, 20.8. HRMS-ESI: calcd. for $C_{24}H_{21}NO_3$ $[M+H]^+$ 372.1600, found 372.1599.



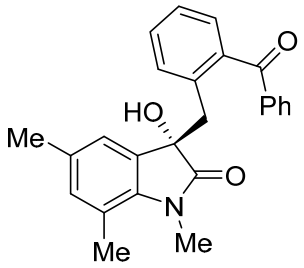
(*S*)-3-(2-Benzoylbenzyl)-3-hydroxy-5-methoxy-1-methylindolin-2-one (3i)

White solid; 33 mg, 85% yield (PE:EA = 2:1); m.p. 163.3–164.2 °C; 93:7 *er* (HPLC analysis on a Daicel Chiralpak AD-H column: hexane/*i*-PrOH = 80:20, flow rate 1.00 mL/min, λ = 254 nm; τ_{major} = 12.127 min, τ_{minor} = 15.922 min). $[\alpha]_D^{25}$ = +64.0 (c = 0.2 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.8 Hz, 2H), 7.62 – 7.55 (m, 1H), 7.50 – 7.26 (m, 6H), 6.79 – 6.70 (m, 1H), 6.67 (d, *J* = 8.4 Hz, 1H), 6.59 – 6.47 (m, 1H), 5.63 (br s, 1H), 3.72 (d, *J* = 13.8 Hz, 1H), 3.59 (s, 3H), 3.12 (s, 3H), 2.99 (d, *J* = 13.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.8, 178.1, 155.7, 138.7, 137.7, 136.5, 134.8, 133.6, 133.3, 131.1, 130.9, 130.8, 130.4, 128.2, 126.2, 114.5, 112.0, 108.7, 76.9, 55.6, 40.6, 26.3. HRMS-ESI: calcd. for $C_{24}H_{21}NO_4$ $[M+H]^+$ 388.1549, found 388.1543.



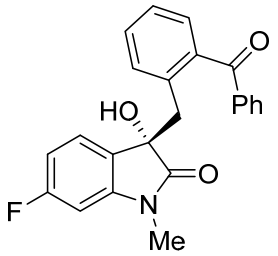
(*S*)-3-(2-Benzoylbenzyl)-5-chloro-3-hydroxy-1-methylindolin-2-one (3j)

White solid; 28 mg, 72% yield (PE:EA = 4:1); m.p. 57.8–59.7 °C; 84:16 *er* (HPLC analysis on a Daicel Chiralpak AD-H column: hexane/*i*-PrOH = 90:10, flow rate 1.00 mL/min, λ = 254 nm; τ_{major} = 9.95 min, τ_{minor} = 11.657 min). $[\alpha]_D^{25}$ = +36.0 (c = 0.3 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.2 Hz, 2H), 7.62 (t, *J* = 7.3 Hz, 1H), 7.53 – 7.40 (m, 4H), 7.39 – 7.32 (m,1H), 7.20 (d, *J* = 7.7 Hz, 1H), 6.85 (s, 2H), 6.79 (s, 1H), 5.97 (br s, 1H), 3.66 (d, *J* = 13.8 Hz, 1H), 3.14 (s, 3H), 2.93 (d, *J* = 13.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.0, 178.4, 144.5, 138.5, 137.5, 135.2, 134.6, 133.55, 133.51, 131.0, 130.7, 128.9, 128.5, 128.3, 126.4, 126.3, 122.2, 108.9, 76.1, 40.6, 26.3. HRMS-ESI: calcd. for $C_{23}H_{18}ClNO_3$ $[M+H]^+$ 392.1053, found 392.1048.



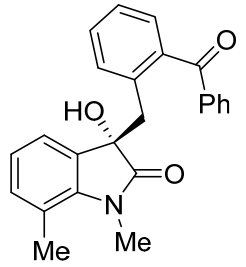
(S)-3-(2-Benzoylbenzyl)-3-hydroxy-1,5,7-trimethylindolin-2-one (3k)

White solid; 30 mg, 77% yield (PE:EA = 4:1); m.p. 190.0–191.2 °C; 96:4 *er* (HPLC analysis on a Daicel Chiralpak AD-H column: hexane/*i*-PrOH = 80:20, flow rate 1.00 mL/min, λ = 254 nm; τ_{major} = 9.715 min, τ_{minor} = 11.300 min). $[\alpha]_D^{25}$ = +20.3 (c = 0.3 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.64 (m, 2H), 7.62 – 7.56 (m, 1H), 7.43 (q, *J* = 7.5, 6.5 Hz, 3H), 7.37 – 7.27 (m, 2H), 7.27 – 7.22 (m, 1H), 6.72 (s, 1H), 6.64 (s, 1H), 5.17 (br s, 1H), 3.67 (d, *J* = 13.7 Hz, 1H), 3.37 (s, 3H), 3.03 (d, *J* = 13.7 Hz, 1H), 2.46 (s, 3H), 2.04 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.8, 178.8, 138.6, 138.2, 137.7, 134.9, 133.7, 133.5, 133.2, 132.0, 130.9, 130.8, 130.7, 130.3, 128.1, 126.1, 123.8, 119.3, 75.9, 40.9, 29.5, 20.5, 18.8. HRMS-ESI: calcd. for $C_{25}H_{23}NO_3$ $[M+H]^+$ 386.1755, found 386.1756.



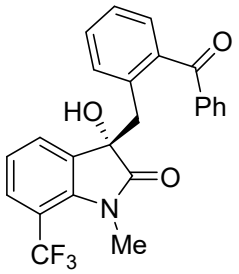
(*S*)-3-(2-Benzoylbenzyl)-6-fluoro-3-hydroxy-1-methylindolin-2-one (3l)

White solid; 26 mg, 69% yield (PE:EA = 3:1); m.p. 55.7–56.4 °C; 88:12 *er* (HPLC analysis on a Daicel Chiralpak AD-H column: hexane/*i*-PrOH = 90:10, flow rate 1.00 mL/min, λ = 254 nm; τ_{major} = 10.085 min, τ_{minor} = 12.517 min). $[\alpha]_D^{25}$ = +46.7 (c = 0.3 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 8.2, 1.0 Hz, 2H), 7.66 – 7.58 (m, 1H), 7.51 – 7.42 (m, 4H), 7.36 (td, *J* = 7.6, 1.1 Hz, 1H), 7.24 – 7.19 (m, 1H), 6.89 (dd, *J* = 8.1, 5.5 Hz, 1H), 6.70 – 6.47 (m, 2H), 5.97 (br s, 1H), 3.64 (d, *J* = 13.8 Hz, 1H), 3.15 (s, 3H), 2.92 (d, *J* = 13.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.0, 178.6, 163.8 (d, *J* = 246.5 Hz), 144.9 (d, *J* = 11.7 Hz), 138.6, 137.6, 134.7, 133.5 (d, *J* = 6.3 Hz), 131.1, 131.0, 130.6, 128.9, 128.4, 126.6 (d, *J* = 9.9 Hz), 126.4, 125.6 (d, *J* = 2.6 Hz), 108.3 (d, *J* = 22.1 Hz), 97.1 (d, *J* = 27.5 Hz), 75.9, 40.7, 26.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.3. HRMS-ESI: calcd. for $C_{23}H_{18}FNO_3$ $[M+H]^+$ 376.1349, found 376.1350.



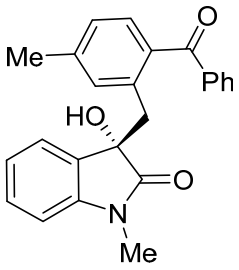
(S)-3-(2-Benzoylbenzyl)-3-hydroxy-1,7-dimethylindolin-2-one (3m)

White solid; 29 mg, 78% yield (PE:EA = 3:1); m.p. 137.5–138.1 °C; 93:7 *er* (HPLC analysis on a Daicel Chiralpak AD-H column: hexane/*i*-PrOH = 80:20, flow rate 1.00 mL/min, λ = 254 nm; τ_{major} = 12.103min, τ_{minor} = 15.695 min). $[\alpha]_D^{25}$ = +19.3 (c = 0.3 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.70 (m, 2H), 7.65 – 7.55 (m, 1H), 7.50 – 7.37 (m, 4H), 7.36 – 7.29 (m, 1H), 7.21 (d, *J* = 7.7 Hz, 1H), 6.96 (d, *J* = 6.9 Hz, 1H), 6.86 – 6.68 (m, 2H), 5.58 (br s, 1H), 3.58 (d, *J* = 13.8 Hz, 1H), 3.42 (s, 3H), 2.97 (d, *J* = 13.8 Hz, 1H), 2.53 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 198.9, 179.0, 140.7, 138.7, 137.7, 134.9, 133.7, 133.3, 133.1, 131.0, 130.9, 130.7, 130.4, 128.2, 126.2, 123.1, 122.3, 119.7, 75.6, 41.1, 29.6, 19.0. HRMS-ESI: calcd. for $C_{24}H_{21}NO_3$ $[M+H]^+$ 372.1600, found 372.1598.



(*S*)-3-(2-Benzoylbenzyl)-3-hydroxy-1-methyl-7-(trifluoromethyl)indolin-2-one (3n)

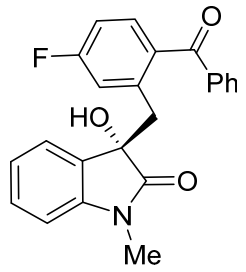
White solid; 32 mg, 70% yield (PE:EA = 3:1); m.p. 135.3–136.8 °C; 75:25 *er* (HPLC analysis on a Daicel Chiralpak AD-H column: hexane/*i*-PrOH = 80:20, flow rate 1.00 mL/min, λ = 254 nm; τ_{major} = 6.460 min, τ_{minor} = 8.167 min). $[\alpha]_D^{25}$ = +12.0 (c = 0.3 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.70 (m, 2H), 7.67 – 7.58 (m, 1H), 7.55 – 7.42 (m, 5H), 7.40 – 7.33 (m, 1H), 7.15 (t, *J* = 6.4 Hz, 2H), 6.98 (t, *J* = 7.7 Hz, 1H), 6.22 (br s, 1H), 3.60 (d, *J* = 13.9 Hz, 1H), 3.39 – 3.36 (m, 3H), 2.97 (d, *J* = 13.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.2, 179.2, 141.1, 138.4, 137.5, 134.3, 133.71, 133.68, 133.0, 131.2, 131.1, 130.8, 128.7, 128.4, 127.2 (q, *J* = 5.9 Hz), 123.5 (q, *J* = 271.4 Hz), 121.7, 112.6 (q, *J* = 32.9 Hz), 74.4, 41.2, 28.9 (q, *J* = 6.4 Hz).^{19}F NMR (376 MHz, $CDCl_3$) δ -53.0. HRMS-ESI: calcd. for $C_{24}H_{18}F_3NO_3$ $[M+H]^+$ 426.1317, found 426.1311.



(*S*)-3-(2-Benzoyl-5-methylbenzyl)-3-hydroxy-1-methylindolin-2-one (3o)

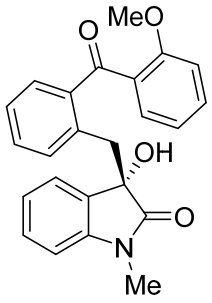
White solid; 20 mg, 52% yield (PE:EA = 3:1); m.p. 163.0–164.5 °C; 96:4 *er* (HPLC analysis on a Daicel Chiralpak AD-H column: hexane/*i*-PrOH = 80:20, flow rate 1.00 mL/min, λ = 254 nm; τ_{major} = 10.397 min, τ_{minor} = 14.698 min). $[\alpha]_D^{25}$ = +73.0 (c = 0.2 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.72 (m, 2H), 7.64 – 7.56 (m, 1H), 7.48 – 7.41 (m, 2H), 7.34 (d, *J* = 7.9 Hz, 1H), 7.31 – 7.27 (m, 1H), 7.18 – 7.11 (m, 1H), 7.01 – 6.98 (m, 1H), 6.97 – 6.90 (m, 2H), 6.83 – 6.75 (m, 1H), 6.18 (br s, 1H), 3.62 (d, *J* = 13.8 Hz, 1H), 3.19 (s, 3H), 2.89 (d, *J* = 13.8 Hz, 1H), 2.39 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.1, 178.6, 143.2, 141.2, 138.0, 135.8, 135.1, 134.6, 133.2,

131.6, 131.0, 130.4, 129.3, 128.2, 126.9, 125.4, 122.2, 108.2, 76.3, 40.7, 26.3, 21.5. HRMS-ESI: calcd. for $C_{24}H_{21}NO_3$ $[M+Na]^+$ 394.1419, found 394.1417.



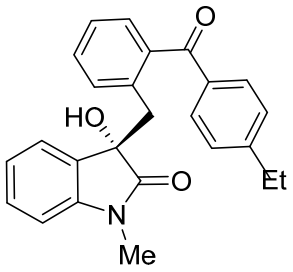
(*S*)-3-(2-Benzoyl-5-fluorobenzyl)-3-hydroxy-1-methylindolin-2-one (3p)

White solid; 29 mg, 78% yield (PE:EA = 3:1); m.p. 67.3–68.7 °C; 88:12 *er* (HPLC analysis on a Daicel Chiralpak AD-H column: hexane/*i*-PrOH = 80:20, flow rate 1.00 mL/min, λ = 254 nm; τ_{major} = 10.593 min, τ_{minor} = 13.227 min). $[\alpha]_D^{25}$ = +24.3 (c = 0.3 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.66 (m, 2H), 7.62 – 7.55 (m, 1H), 7.48 – 7.39 (m, 3H), 7.29 – 7.25 (m, 1H), 7.08 – 6.88 (m, 4H), 6.79 (d, *J* = 7.8 Hz, 1H), 5.61 (br s, 1H), 3.62 (d, *J* = 13.8 Hz, 1H), 3.15 (s, 3H), 2.95 (d, *J* = 13.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.9, 178.1, 163.4 (d, *J* = 253.5 Hz), 143.2, 138.7 (d, *J* = 8.5 Hz), 137.7, 134.9 (d, *J* = 3.0 Hz), 133.5, 133.3 (d, *J* = 9.0 Hz), 130.9, 130.0, 129.6, 128.3, 125.0, 122.6, 120.5 (d, *J* = 21.9 Hz), 113.4 (d, *J* = 21.5 Hz), 108.4, 76.1, 40.6, 26.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.31 – -113.03 (m). HRMS-ESI: calcd. for $C_{23}H_{18}FNO_3$ $[M+H]^+$ 376.1349, found 376.1348.



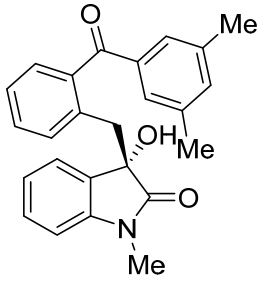
(*S*)-3-Hydroxy-3-(2-(2-methoxybenzoyl)benzyl)-1-methylindolin-2-one (3q)

White solid; 32 mg, 82% yield (PE:EA = 2:1); m.p. 65.7–66.3 °C; 94:6 *er* (HPLC analysis on a Daicel Chiralpak AD-H column: hexane/*i*-PrOH = 80:20, flow rate 1.00 mL/min, λ = 254 nm; τ_{major} = 18.635 min, τ_{minor} = 26.337 min). $[\alpha]_D^{25}$ = +58.0 (c = 0.1 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.36 (m, 4H), 7.34 – 7.24 (m, 2H), 7.13 (d, *J* = 7.7 Hz, 1H), 7.07 – 6.91 (m, 4H), 6.84 (d, *J* = 7.8 Hz, 1H), 5.94 (br s, 1H), 3.64 (s, 3H), 3.61 (d, *J* = 14.0 Hz, 1H), 3.21 (s, 3H), 3.12 (d, *J* = 13.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.5, 178.3, 158.3, 143.2, 140.7, 134.3, 133.8, 133.5, 131.3, 130.9, 130.7, 130.6, 129.3, 129.1, 126.6, 125.2, 122.3, 120.6, 111.9, 108.1, 76.4, 55.7, 40.9, 26.2. HRMS-ESI: calcd. for $C_{24}H_{21}NO_4$ $[M+H]^+$ 388.1549, found 388.1544.



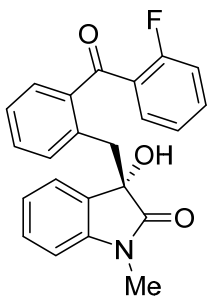
(*S*)-3-(2-(4-Ethylbenzoyl)benzyl)-3-hydroxy-1-methylindolin-2-one (3r)

White solid; 31 mg, 80% yield (PE:EA = 3:1); m.p. 103.1–104.6 °C; 90:10 *er* (HPLC analysis on a Daicel Chiralpak AD-H column: hexane/*i*-PrOH = 80:20, flow rate 1.00 mL/min, λ = 254 nm; τ_{major} = 12.845 min, τ_{minor} = 19.637 min). $[\alpha]_D^{25}$ = +37.7 (c = 0.3 in $CHCl_3$). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.42 (d, *J* = 8.0 Hz, 2H), 7.39 – 7.18 (m, 5H), 7.16 – 7.05 (m, 2H), 6.80 (d, *J* = 7.8 Hz, 1H), 6.74 – 6.65 (m, 2H), 6.08 (br s, 1H), 3.53 (d, *J* = 13.4 Hz, 1H), 3.10 (d, *J* = 13.4 Hz, 1H), 2.93 (s, 3H), 2.68 (q, *J* = 7.2 Hz, 2H), 1.22 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 196.6, 177.2, 149.4, 142.9, 139.5, 135.1, 134.5, 132.3, 130.4, 130.3, 129.6, 129.1, 128.9, 127.8, 126.1, 124.3, 122.1, 108.3, 76.2, 39.1, 28.4, 25.9, 15.4. HRMS-ESI: calcd. for $C_{25}H_{23}NO_3$ $[M+H]^+$ 386.1756, found 386.1755.



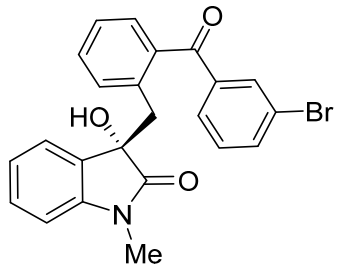
(*S*)-3-(2-(3,5-Dimethylbenzoyl)benzyl)-3-hydroxy-1-methylindolin-2-one (3s)

White solid; 34 mg, 83% yield (PE:EA = 3:1); m.p. 188.0–189.0 °C; 93:7 *er* (HPLC analysis on a Daicel Chiralpak OD column: hexane/*i*-PrOH = 97:3, flow rate 1.00 mL/min, λ = 254 nm; τ_{major} = 63.833 min, τ_{minor} = 34.058 min), $[\alpha]_D^{25}$ = +54.0 (c = 0.3 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (td, *J* = 7.5, 1.5 Hz, 1H), 7.39 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.35 – 7.28 (m, 3H), 7.28 – 7.17 (m, 3H), 6.96 (dd, *J* = 7.3, 1.0 Hz, 1H), 6.90 (td, *J* = 7.5, 0.8 Hz, 1H), 6.78 (d, *J* = 7.8 Hz, 1H), 5.99 (br s, 1H), 3.57 (d, *J* = 13.9 Hz, 1H), 3.16 (s, 3H), 2.94 (d, *J* = 13.9 Hz, 1H), 2.33 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.6, 178.4, 143.2, 138.9, 137.9, 137.8, 135.2, 134.8, 133.6, 130.9, 130.5, 130.4, 129.3, 128.8, 126.2, 125.3, 122.4, 108.1, 76.2, 40.8, 26.3, 21.2. HRMS-ESI: calcd. for $C_{25}H_{23}NO_3$ $[M+H]^+$ 408.1574, found 408.1576.



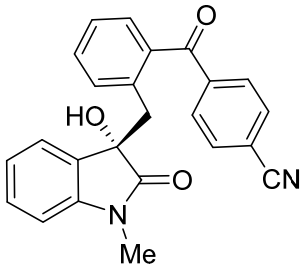
(*S*)-3-(2-(2-Fluorobenzoyl)benzyl)-3-hydroxy-1-methylindolin-2-one (3t)

White solid; 34 mg, 91% yield (PE:EA = 3.5:1); m.p. 120.1–122.5 °C; 90:10 *er* (HPLC analysis on a Daicel Chiralpak AD-H column: hexane/*i*-PrOH = 80:20, flow rate 1.00 mL/min, λ = 254 nm; τ_{major} = 11.803 min, τ_{minor} = 17.203 min). $[\alpha]_D^{25}$ = +36.7 (c = 0.3 in $CHCl_3$). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.69 – 7.60 (m, 1H), 7.40 – 7.32 (m, 2H), 7.32 – 7.24 (m, 3H), 7.21 (d, *J* = 7.9 Hz, 2H), 7.18 – 7.12 (m, 1H), 6.86 (d, *J* = 7.7 Hz, 1H), 6.80 (t, *J* = 7.4 Hz, 1H), 6.73 (d, *J* = 7.3 Hz, 1H), 6.11 (s, 1H), 3.68 (d, *J* = 13.2 Hz, 1H), 3.17 (d, *J* = 13.2 Hz, 1H), 2.98 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 194.0 , 177.5 , 160.9 (d, *J* = 255.0 Hz), 143.4 , 140.0 , 135.1 , 134.9 (d, *J* = 8.9 Hz), 133.2 , 132.3 – 132.1 (m), 130.8 , 130.7 , 129.8 (d, *J* = 1.4 Hz), 129.5 , 127.0 (d, *J* = 11.2 Hz), 126.9 , 124.7 , 124.6 (d, *J* = 3.4 Hz), 122.3 , 117.0 (d, *J* = 21.9 Hz), 108.7 , 76.6 , 39.0 , 26.2. ^{19}F NMR (376 MHz, DMSO) δ -111.8. HRMS-ESI: calcd. for $C_{23}H_{18}FNO_3$ $[M+H]^+$ 376.1349, found 376.1351.



(*S*)-3-(2-(3-Bromobenzoyl)benzyl)-3-hydroxy-1-methylindolin-2-one (3u)

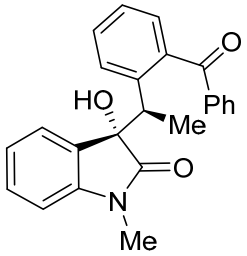
White solid; 38 mg, 87% yield (PE:EA = 4:1); m.p. 143.3–144.8 °C; 92:8 *er* (HPLC analysis on a Daicel Chiralpak AD-H column: hexane/*i*-PrOH = 85:15, flow rate 1.00 mL/min, λ = 254 nm; τ_{major} = 17.393min, τ_{minor} = 29.277 min). $[\alpha]_D^{25}$ = +85.7 (c = 0.3 in $CHCl_3$). ^{1}H NMR (400 MHz, DMSO) δ 7.84 (d, *J* = 7.6 Hz, 1H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.49 – 7.43 (m, 2H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.24 – 7.10 (m, 3H), 6.82 (d, *J* = 7.8 Hz, 1H), 6.78 – 6.64 (m, 1H), 6.13 (s, 1H), 3.63 (d, *J* = 13.2 Hz, 1H), 3.15 (d, *J* = 13.3 Hz, 1H), 2.94 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 196.5, 178.1, 144.0, 140.5, 139.4, 136.6, 135.8, 133.8, 133.6, 131.6, 131.2, 130.21, 130.17, 130.0, 127.2, 125.2, 123.1, 122.6, 109.3, 77.4, 39.9, 26.9. HRMS-ESI: calcd. for $C_{23}H_{18}BrNO_3$ $[M+H]^+$ 436.0548, found 436.0543.



(*S*)-4-(2-((3-Hydroxy-1-methyl-2-oxoindolin-3-yl)methyl)benzoyl)benzonitrile (3v)

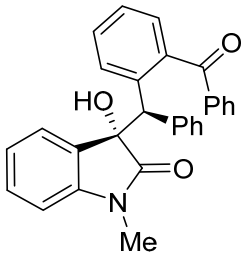
White solid; 37 mg, 93% yield (PE:EA = 3:1); m.p. 166.4–167.2 °C; 91:9 *er* (HPLC analysis on a Daicel Chiralpak AS column: hexane/ *i*-PrOH = 80:20, flow rate 1.00 mL/min, λ = 254 nm; τ_{major} = 34.058 min, τ_{minor} = 60.155 min). $[\alpha]_D^{25}$ = +43.7 (c = 0.3 in $CHCl_3$). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.96 (d, *J* = 8.2 Hz, 2H), 7.63 (d, *J* = 8.2 Hz, 2H), 7.40 (t, *J* = 7.5 Hz, 1H), 7.34 – 7.27 (m, 1H), 7.21 – 7.11 (m, 3H), 6.83 (d, *J* = 7.8 Hz, 1H), 6.74 – 6.66 (m, 2H), 6.08 (s, 1H), 3.62 (d, *J* = 13.2 Hz, 1H), 3.11 (d, *J* = 13.2 Hz, 1H), 2.93 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 195.6, 176.9, 142.8, 140.7, 138.1, 134.7, 132.8, 132.2, 131.9, 130.5, 130.2, 130.1, 129.1, 129.0,

126.1, 124.1, 121.9, 114.6, 108.2, 76.0, 38.7, 25.7. HRMS-ESI: calcd. for $C_{24}H_{18}N_2O_3$ $[M+Na]^+$ 405.1215, found 405.1215.



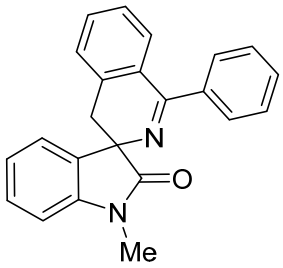
(*S*)-3-((*R*)-1-(2-Benzoylphenyl)ethyl)-3-hydroxy-1-methylindolin-2-one (3w)

White solid; 21 mg, 54% yield (PE:EA = 3:1); m.p. 142.6–143.4 °C; 8:1 *dr*, 82:18 *er* (**major**) (HPLC analysis on a Daicel Chiralpak IC column: hexane/*i*-PrOH = 70:30, flow rate 1.00 mL/min, λ = 254 nm; τ_{major} = 23.328 min, τ_{minor} = 18.425 min). $[\alpha]_D^{25}$ = + 40.3 (c = 0.3 in $CHCl_3$). **major**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 – 7.74 (m, 1H), 7.69 – 7.10 (m, 8H), 7.04 (t, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 3.9 Hz, 1H), 6.83 (d, *J* = 7.8 Hz, 1H), 6.48 (s, 1H), 4.84 (br s, 1H), 3.68 (q, *J* = 7.1 Hz, 1H), 3.19 (s, 3H), 1.00 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.8, 179.0, 144.6, 140.5, 138.9, 137.72, 133.71, 131.2, 130.5, 129.6, 129.5, 128.3, 127.9, 126.9, 126.1, 123.6, 122.1, 108.0, 79.2, 41.0, 26.1, 15.7. HRMS-ESI: calcd. for $C_{24}H_{21}NO_3$ $[M+Na]^+$ 394.1419, found 394.1417.



(*S*)-3-((*R*)-(2-Benzoylphenyl)(phenyl)methyl)-3-hydroxy-1-methylindolin-2-one (3x)

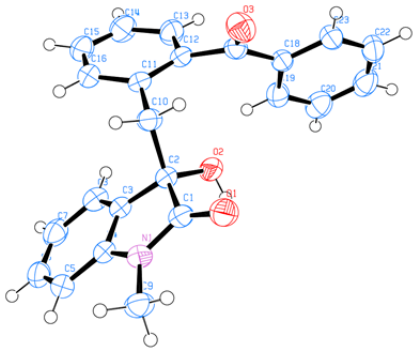
White solid; 25 mg, 55% yield (PE:EA = 3:1); m.p. 99.0–100.5 °C; 14:1 *dr*, 95:5 *er* (**major**) (HPLC analysis on a Daicel Chiralpak IC column: hexane/*i*-PrOH = 70:30, flow rate 1.00 mL/min, λ = 254 nm; τ_{major} = 9.255 min, τ_{minor} = 7.457 min). $[\alpha]_D^{25}$ = +100.0 (c = 0.2 in $CHCl_3$). **major**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 – 7.87 (m, 1H), 7.72 – 6.69 (m, 16H), 6.09 (d, *J* = 7.4 Hz, 1H), 5.73 – 5.31 (br s, 1H), 4.47 (s, 1H), 3.13 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.7, 178.7, 146.3, 143.9, 142.7, 139.3, 138.4, 134.5, 133.6, 133.4, 131.0, 129.5, 129.1, 128.4, 128.2, 127.9, 127.7, 127.1, 126.5, 125.9, 122.7, 108.1, 78.4, 49.3, 26.4. HRMS-ESI: calcd. for $C_{29}H_{23}NO_3$ $[M+Na]^+$ 456.1576, found 456.1573.

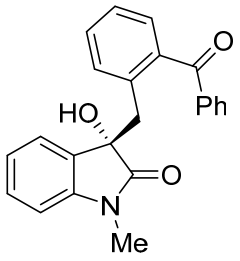


1-Methyl-1'-phenyl-4'H-spiro[indoline-3,3'-isoquinolin]-2-one (4)

White solid; 17 mg, 56% yield (PE:EA = 5:1); m.p. 59.4–61.3 °C; 52:48 *er* (HPLC analysis on a Daicel Chiralpak AD-H column: hexane/*i*-PrOH = 80:20, flow rate 1.00 mL/min, λ = 254 nm; τ_{major} = 5.557 min, τ_{minor} = 6.447 min). $[\alpha]_D^{25}$ = + 16.0 (c = 0.1 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.51 (m, 2H), 7.46 – 7.30 (m, 6H), 7.29 – 7.19 (m, 2H), 6.84 (d, *J* = 7.8 Hz, 1H), 6.75 (td, *J* = 7.6, 0.8 Hz, 1H), 6.41 (d, *J* = 7.4 Hz, 1H), 3.63 (d, *J* = 15.7 Hz, 1H), 3.27 (s, 3H), 2.90 (d, *J* = 15.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.9, 168.8, 143.1, 138.3, 135.2, 131.5, 130.2, 129.6, 129.3, 129.2, 129.0, 128.8, 128.3, 128.1, 127.4, 123.4, 122.6, 108.4, 66.0, 33.4, 26.6. HRMS-ESI: calcd. for $C_{23}H_{18}N_2O$ $[M+H]^+$ 339.1497, found 339.1494.

4. ORTEP drawings of 3a, 3w and 4

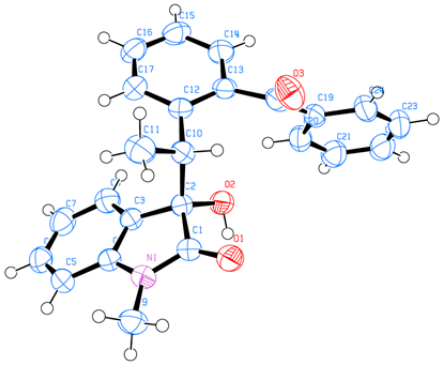


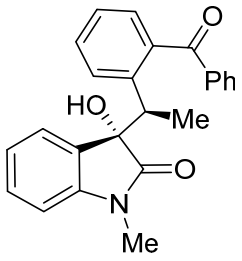


3a

Table 1. Crystal data and structure refinement for 3a (CCDC 1996461)

Identification code	**3a**
Empirical formula	$C_{23}H_{19}NO_3$
Formula weight	357.39
Temperature/K	295.15
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	6.04785(4)
b/Å	13.36306(6)
c/Å	21.94319(11)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	1773.400(17)
Z	4
ρ_{calc}g/cm^3	1.339
μ/mm^{-1}	0.714
F(000)	752.0
Crystal size/mm^3	0.36 × 0.18 × 0.14
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	7.746 to 158.372
Index ranges	$-7 \le h \le 5$, $-16 \le k \le 16$, $-27 \le l \le 27$
Reflections collected	21423
Independent reflections	3749 [R_{int} = 0.0242, R_{sigma} = 0.0174]
Data/restraints/parameters	3749/0/247
Goodness-of-fit on F^2	1.065
Final R indexes [I>=2σ (I)]	R_1 = 0.0265, wR_2 = 0.0716
Final R indexes [all data]	R_1 = 0.0271, wR_2 = 0.0720
Largest diff. peak/hole / e Å^{-3}	0.15/-0.12
Flack parameter	-0.01(4)

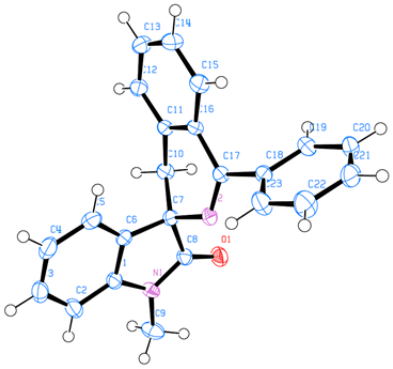


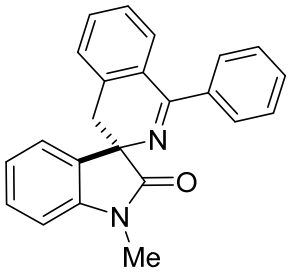


3w

Table 2. Crystal data and structure refinement for 3w (CCDC 1996462)

Identification code	**3w**
Empirical formula	$C_{24}H_{21}NO_3$
Formula weight	371.42
Temperature/K	294.15 K
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	6.53150(10)
b/Å	13.40120(10)
c/Å	21.6517(2)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	1895.17(4)
Z	4
ρ_{calc}g/cm^3	1.302
μ/mm^{-1}	0.687
F(000)	784.0
Crystal size/mm^3	0.36 x 0.16 x 0.14
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	7.758 to 159.352 deg.
Index ranges	$-7 \le h \le 5$, $-16 \le k \le 17$, $-27 \le l \le 27$
Reflections collected	14063
Independent reflections	3823[R_{int} = 0.0356, R_{sigma} = 0.0297]
Data/restraints/parameters	3823/0/260
Goodness-of-fit on F^2	1.066
Final R indexes [I>=2σ (I)]	R_1 = 0.0322, wR_2 = 0.0863
Final R indexes [all data]	R_1 = 0.0335, wR_2 = 0.0875
Largest diff. peak/hole / e Å^{-3}	0.14/-0.13
Flack parameter	-0.07(11)



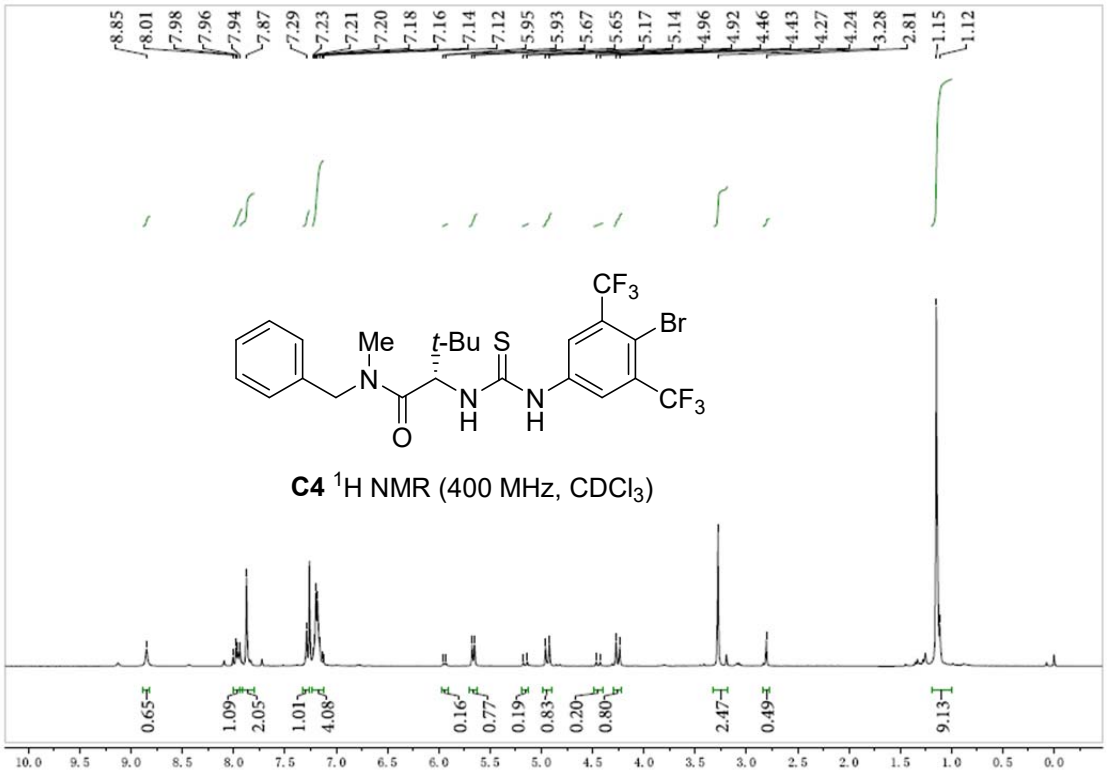


4

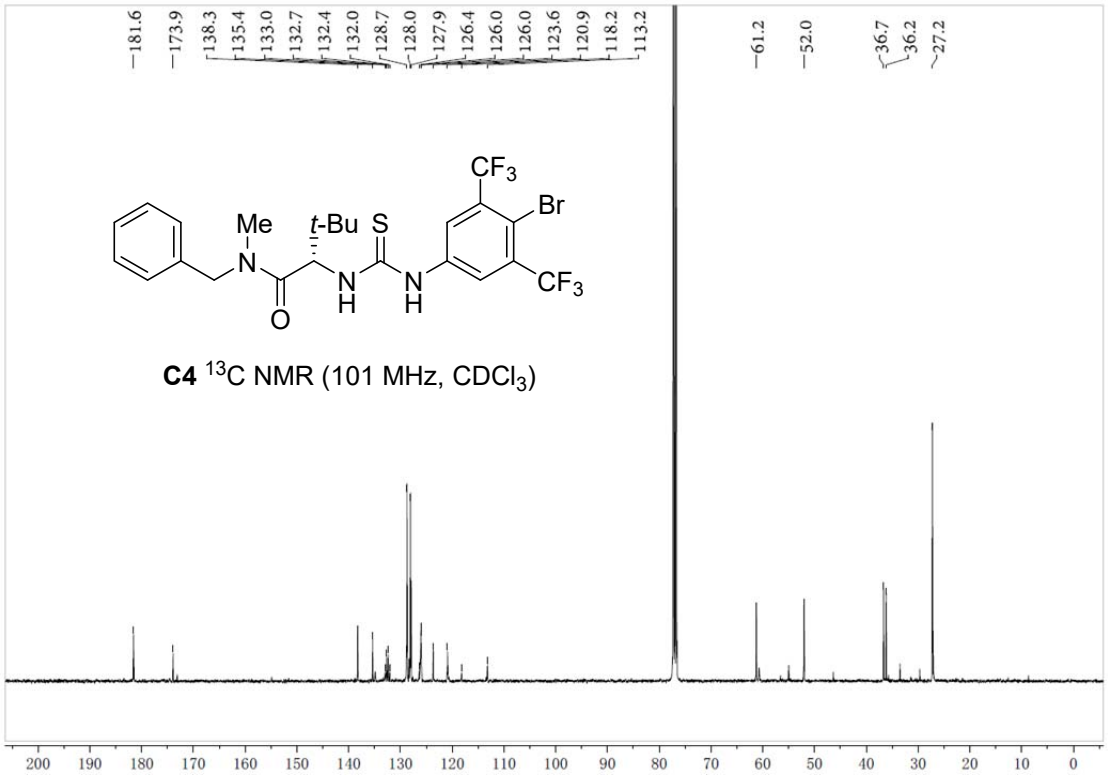
Table 3. Crystal data and structure refinement for 4 (CCDC 1996463)

Identification code	**4**
Empirical formula	$C_{23}H_{18}N_2O$
Formula weight	338.39
Temperature/K	113.15 K
Wavelength	0.71073 A
Crystal system	Triclinic
Space group	P-1
Unit cell dimensions	a = 8.4653(17) A alpha = 82.97(3) deg. b = 10.802(2) A beta = 67.84(3) deg. c = 11.181(2) A gamma = 69.97(3) deg.
Volume/Å^3	889.6(4)
Z	2
ρ_{calc}g/cm^3	1.263
Absorption coefficient /mm^{-1}	0.078
F(000)	356
Crystal size/mm^3	0.200 x 0.180 x 0.120
Radiation	MoKα (λ = 0.71073)
2 Θ range for data collection/°	3.934 to 55.54 deg.
Index ranges	$-10 \leq h \leq 11$, $-14 \leq k \leq 14$, $-14 \leq l \leq 14$
Reflections collected	10578
Independent reflections	4134 [R_{int} = 0.0494, R_{sigma} = 0.0988]
Absorption correction	Semi-empirical from equivalents
Data/restraints/parameters	4134/0/236
Goodness-of-fit on F^2	1.064
Final R indexes [I>=2σ (I)]	R_1 = 0.0390, wR_2 = 0.0760
Final R indexes [all data]	R_1 = 0.0813, wR_2 = 0.0862
Largest diff. peak/hole / e Å^{-3}	0.28/-0.22

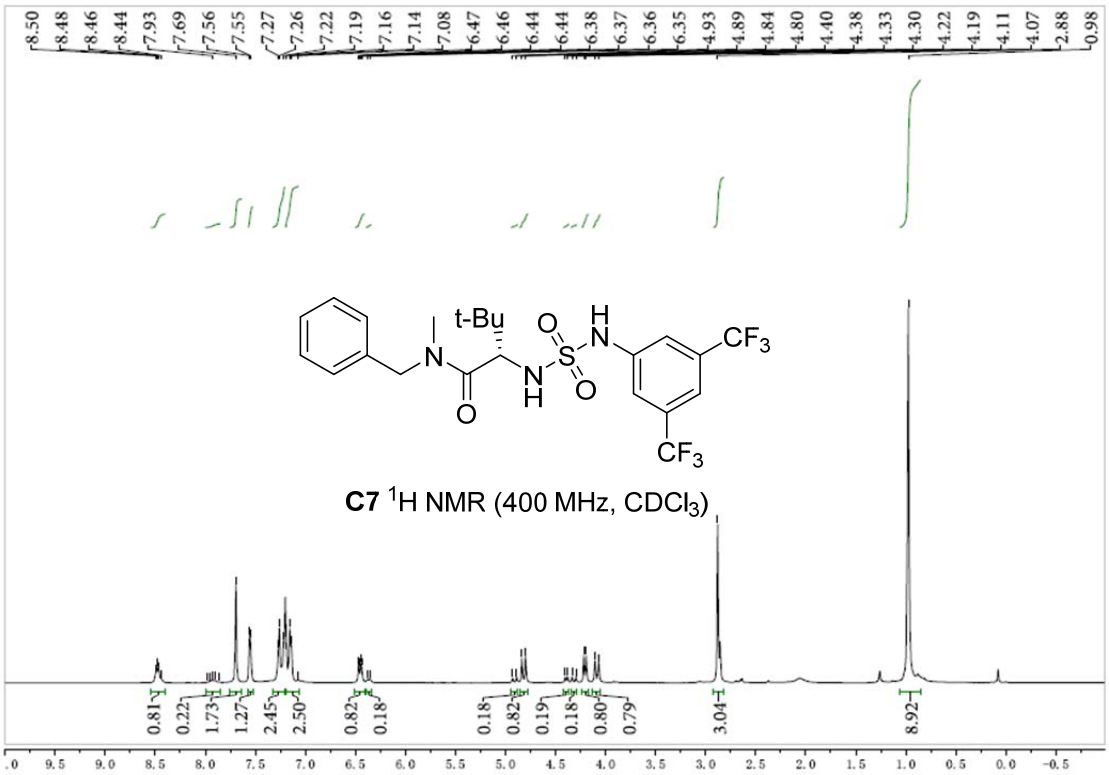
5. NMR spectra



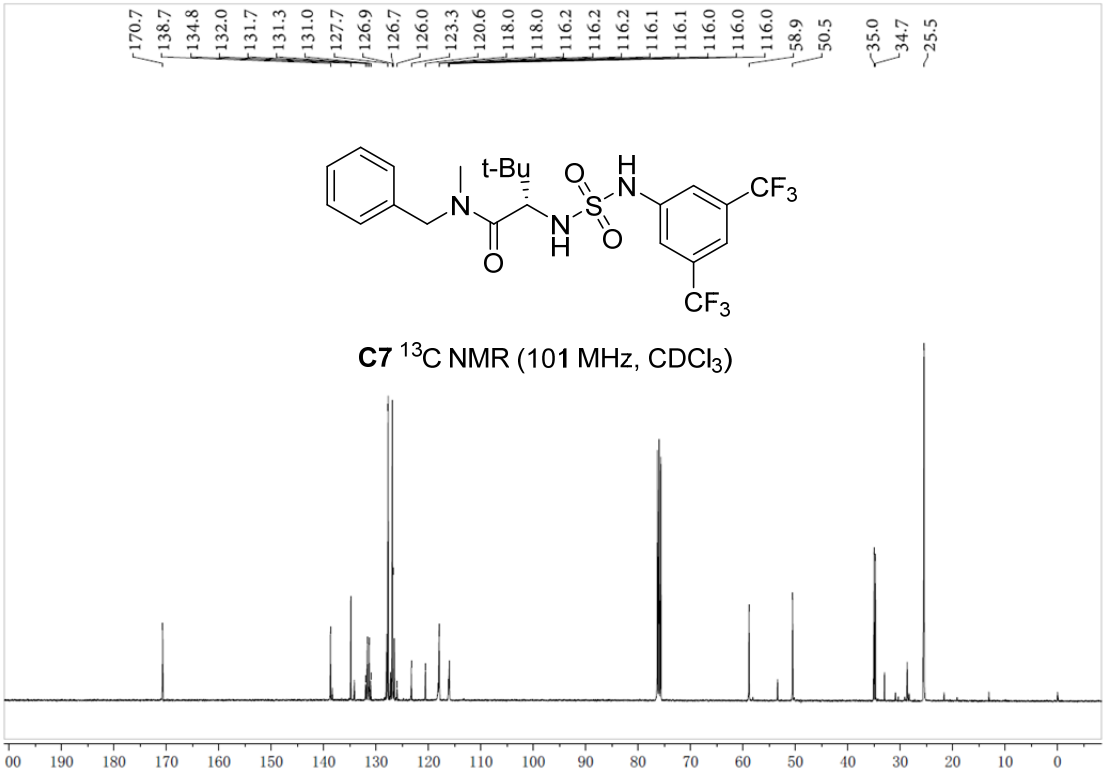
C4 ^{1}H NMR (400 MHz, $CDCl_3$)



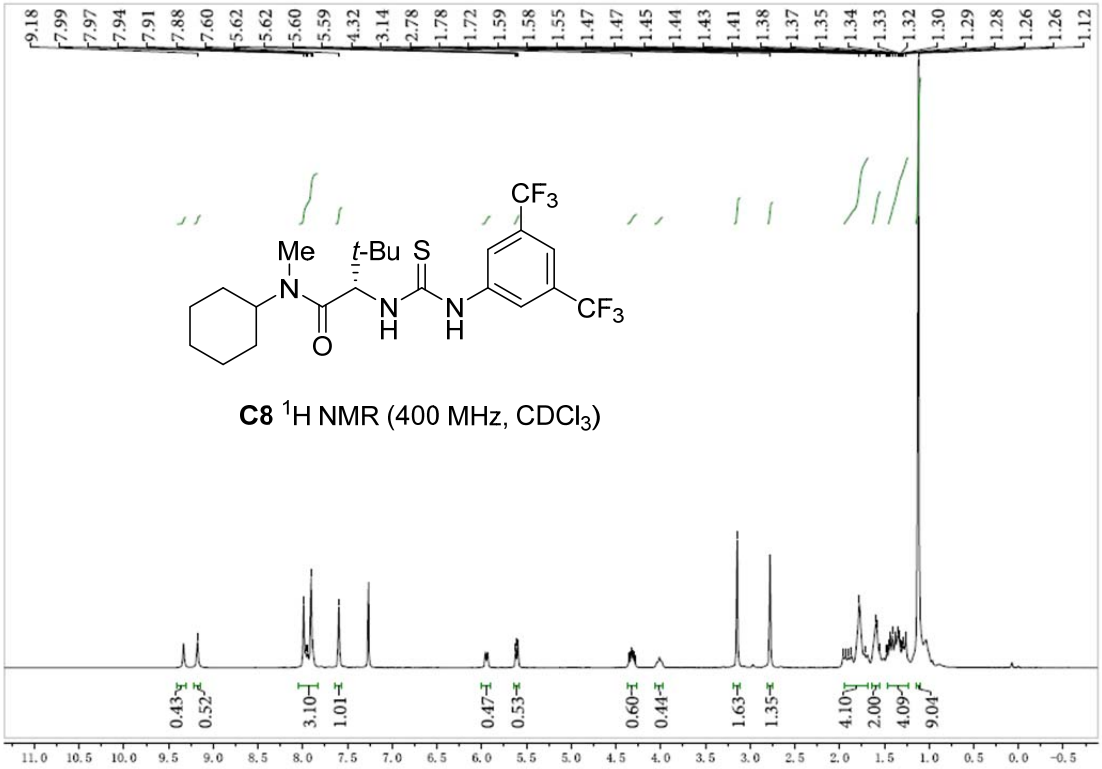
C4 ^{13}C NMR (101 MHz, $CDCl_3$)



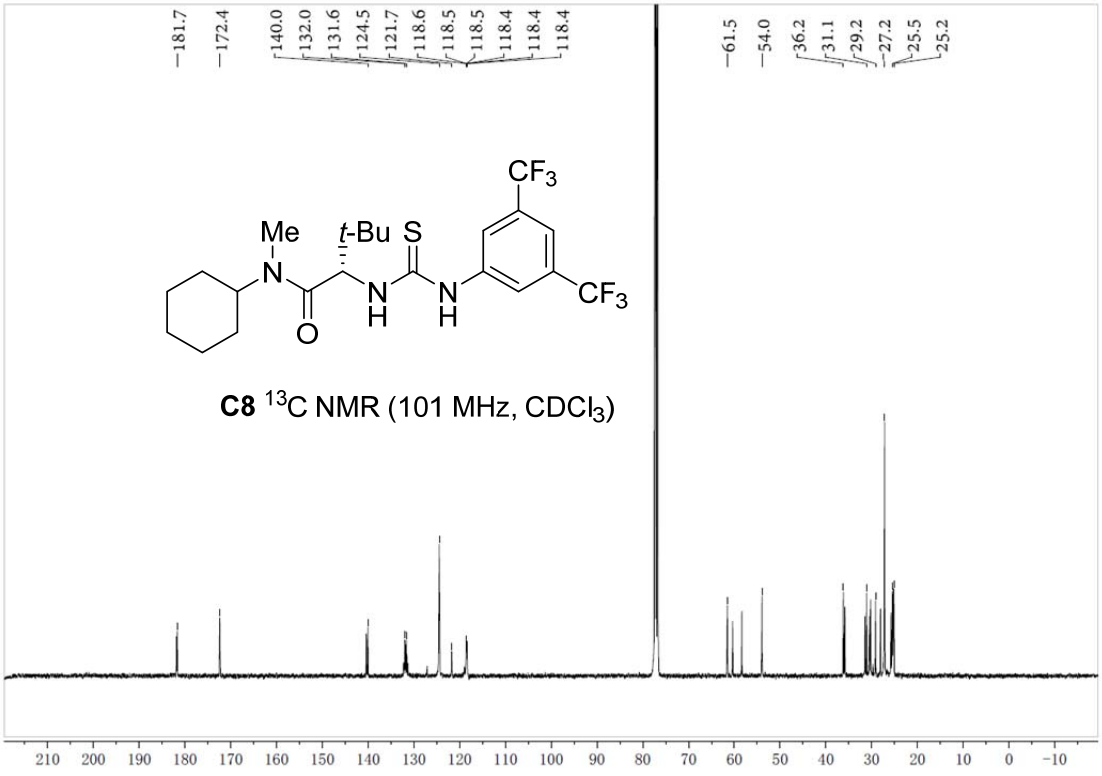
C7 ^{1}H NMR (400 MHz, $CDCl_3$)



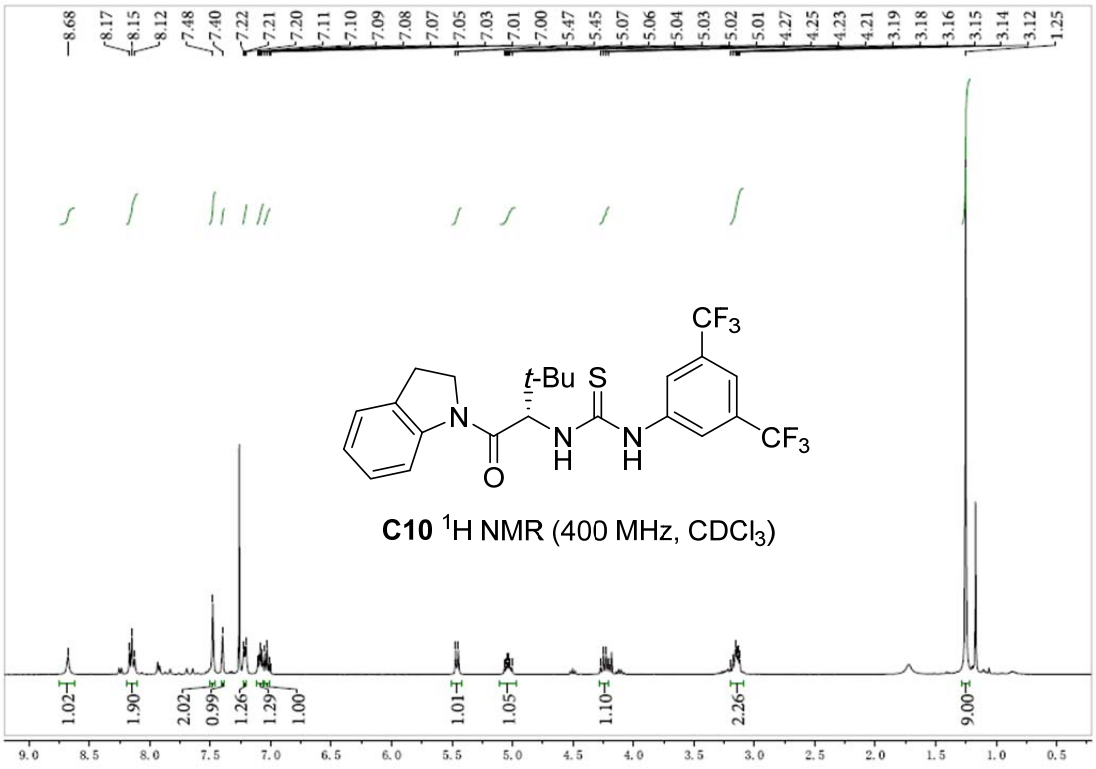
C7 ^{13}C NMR (101 MHz, $CDCl_3$)



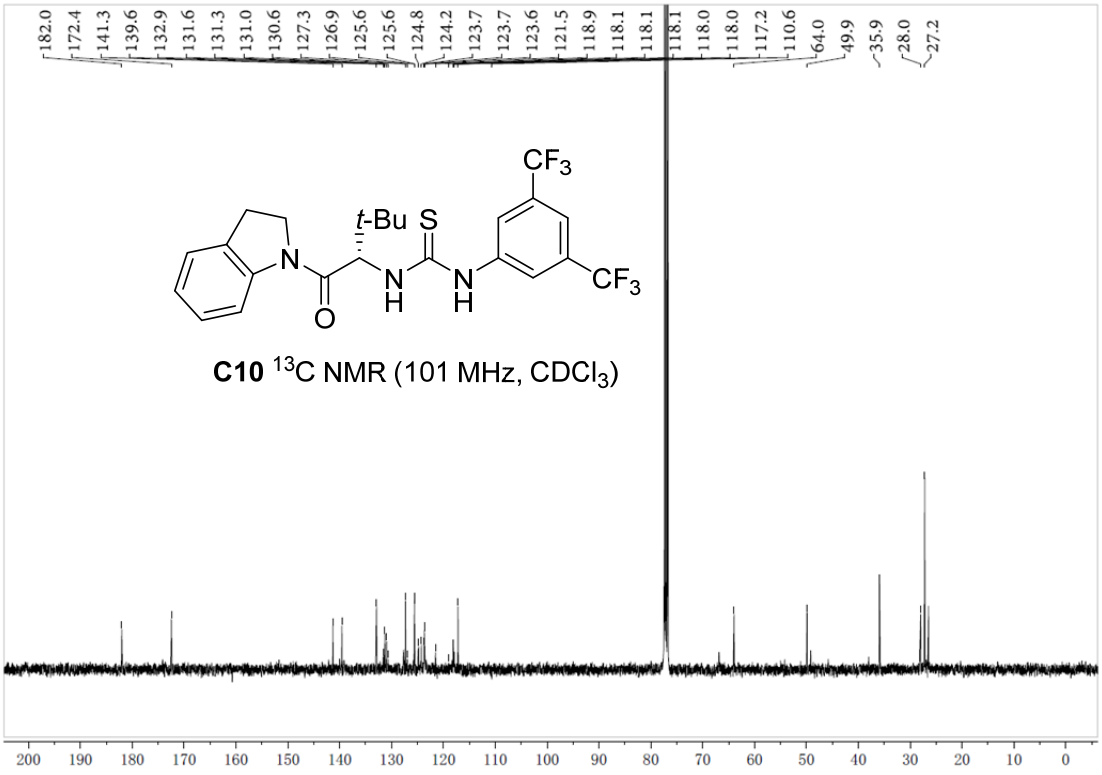
C8 ^{1}H NMR (400 MHz, $CDCl_3$)



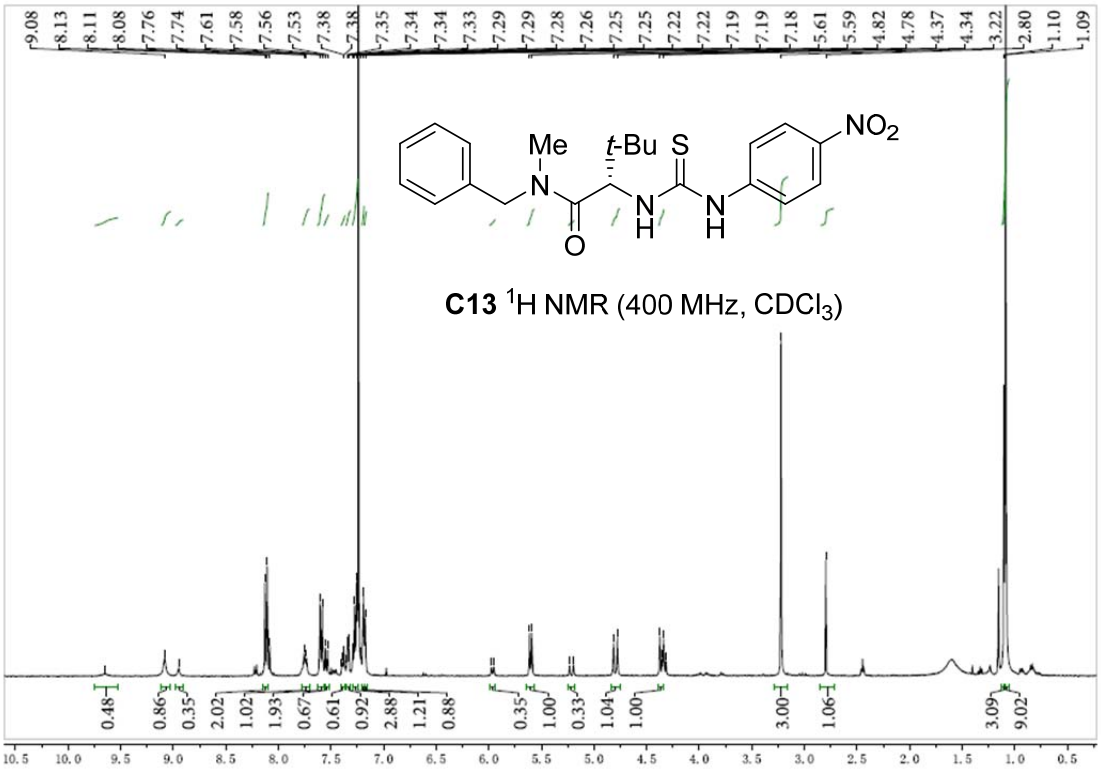
C8 ^{13}C NMR (101 MHz, $CDCl_3$)



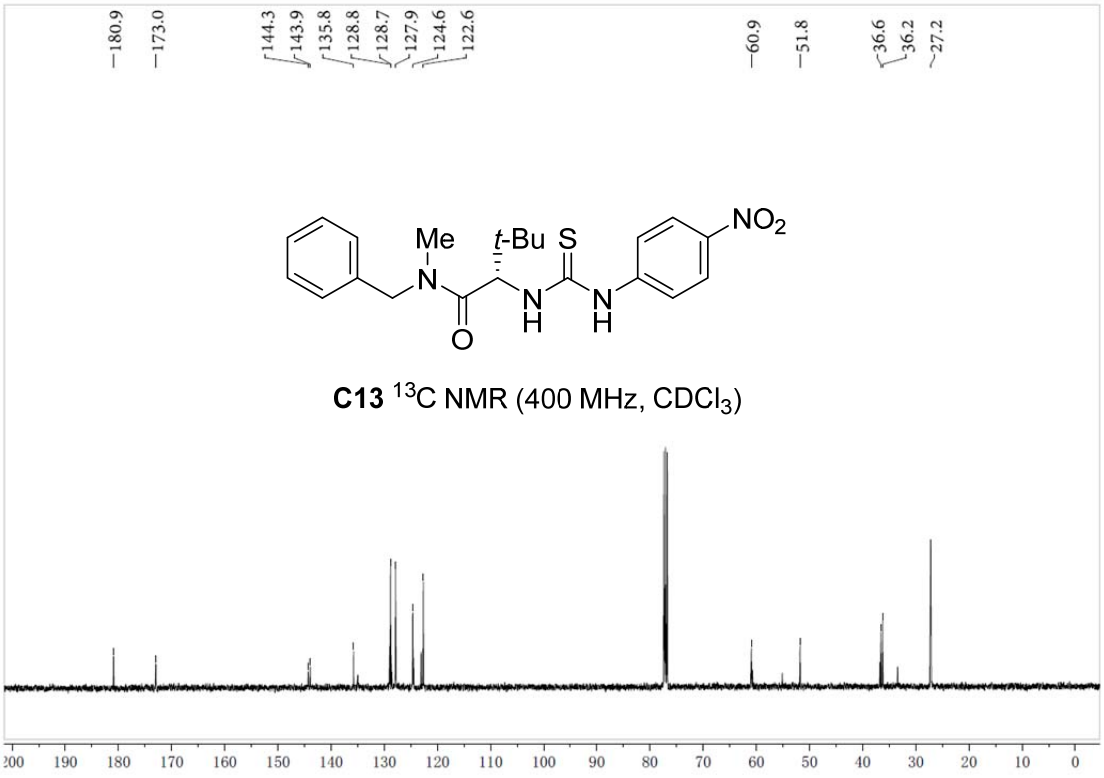
C10 ^{1}H NMR (400 MHz, $CDCl_3$)



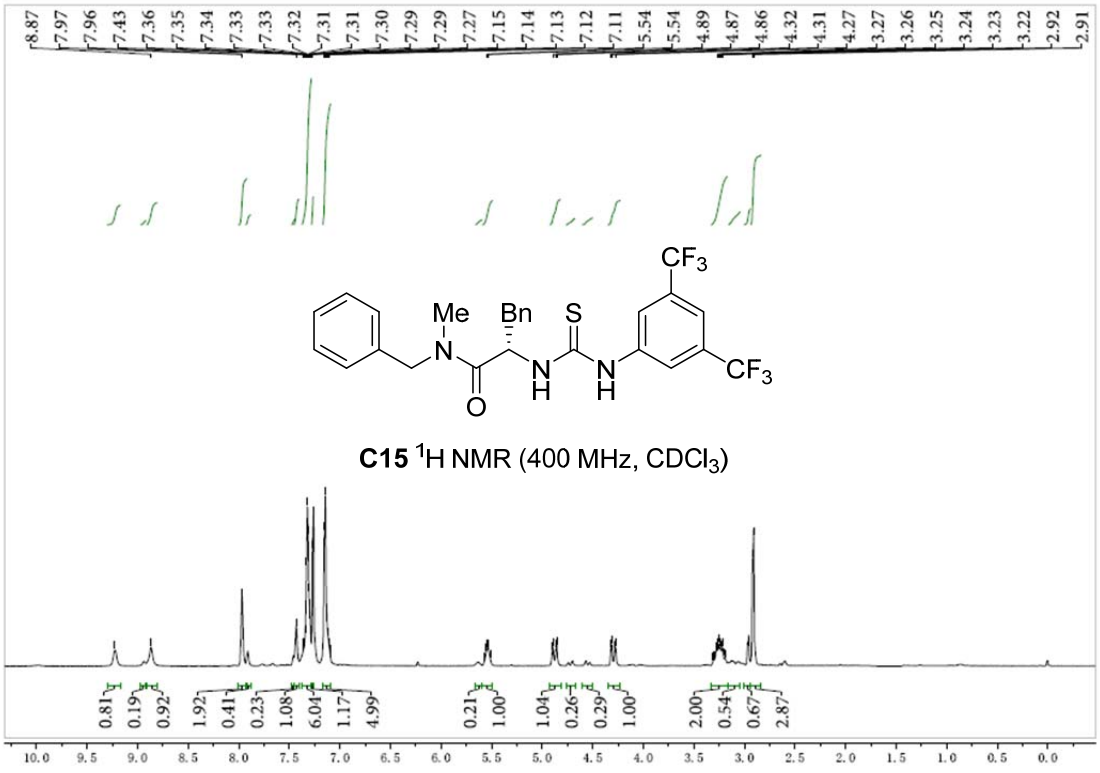
C10 ^{13}C NMR (101 MHz, $CDCl_3$)



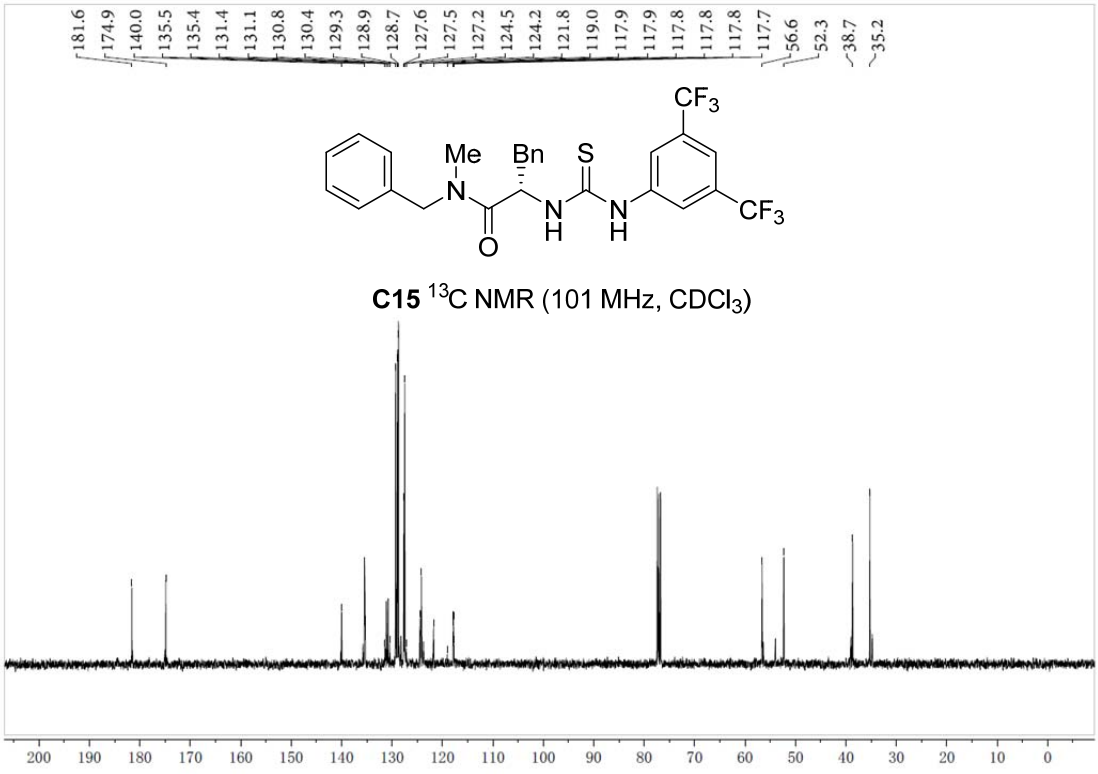
C13 ^{1}H NMR (400 MHz, $CDCl_3$)



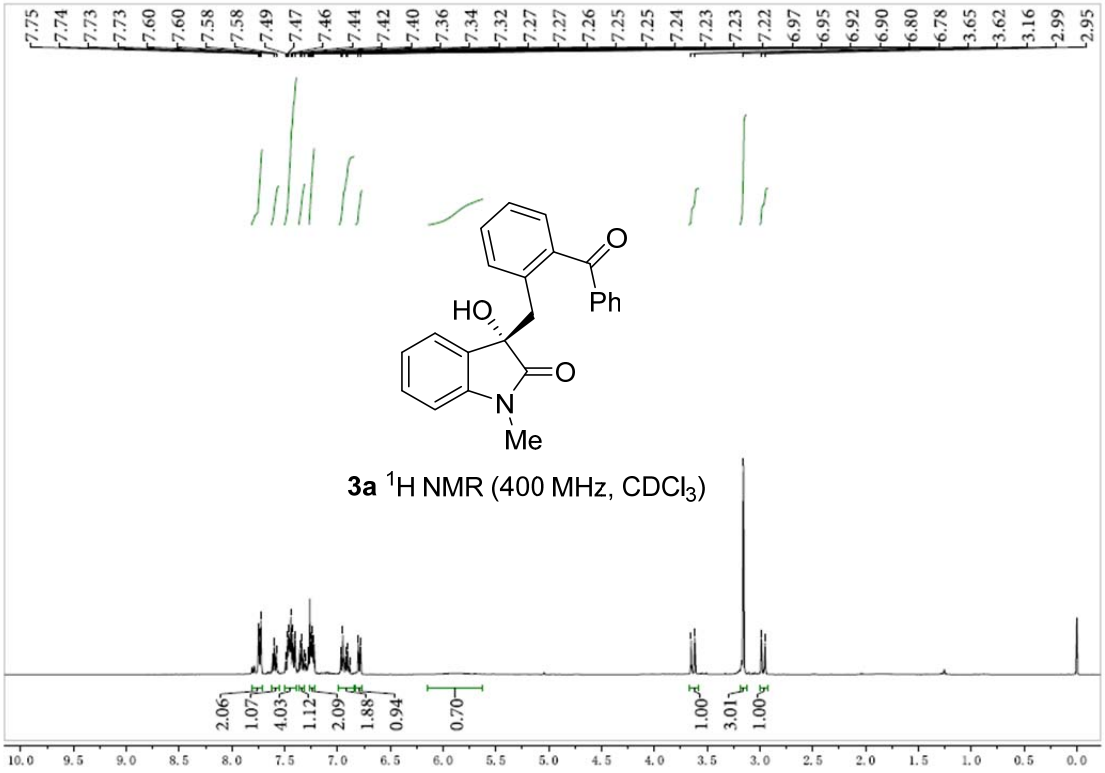
C13 ^{13}C NMR (400 MHz, $CDCl_3$)



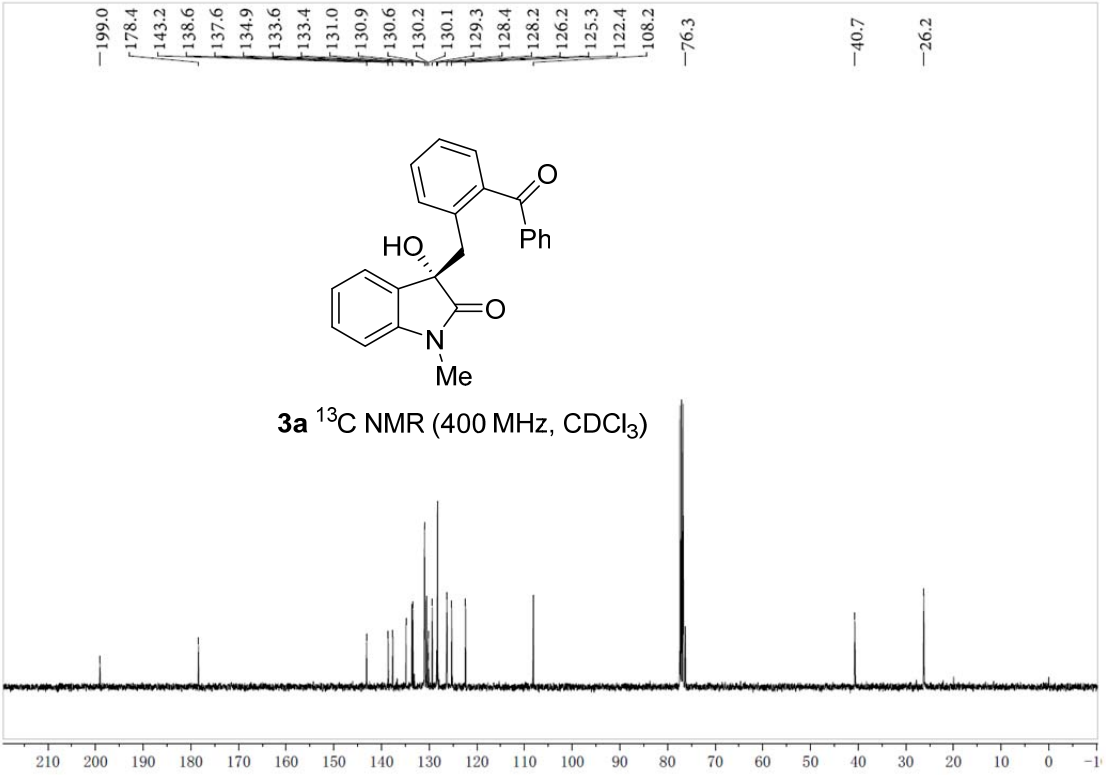
C15 ^{1}H NMR (400 MHz, $CDCl_3$)



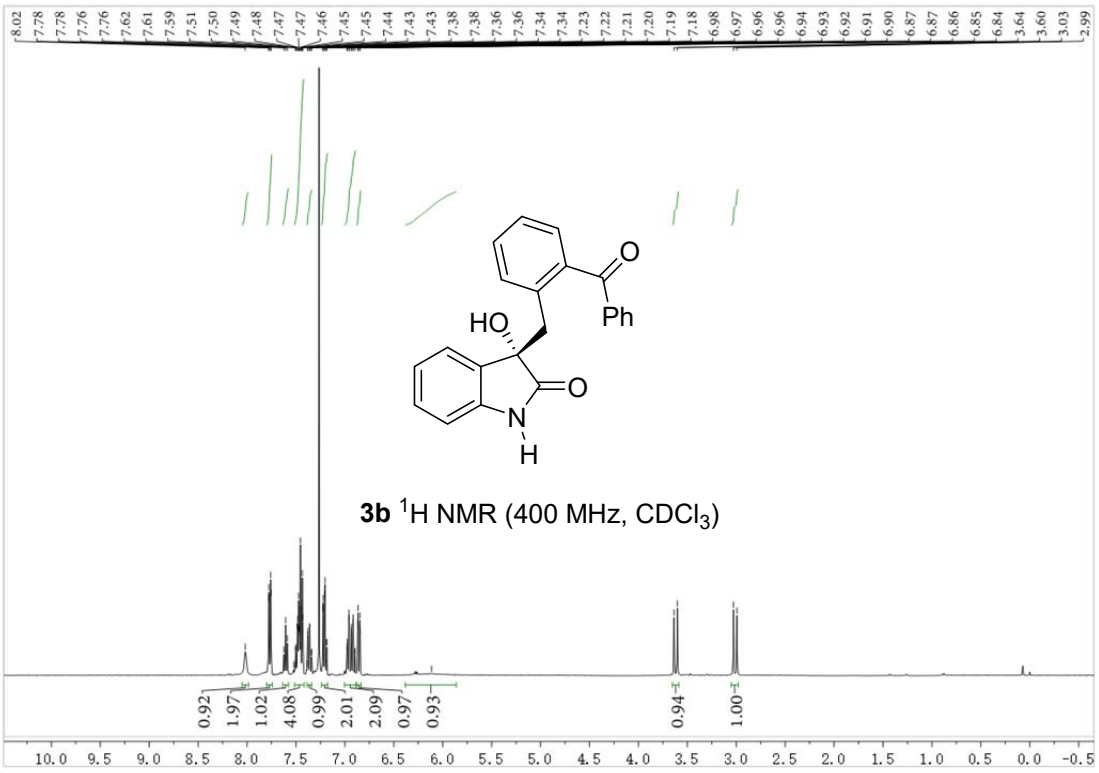
C15 ^{13}C NMR (101 MHz, $CDCl_3$)



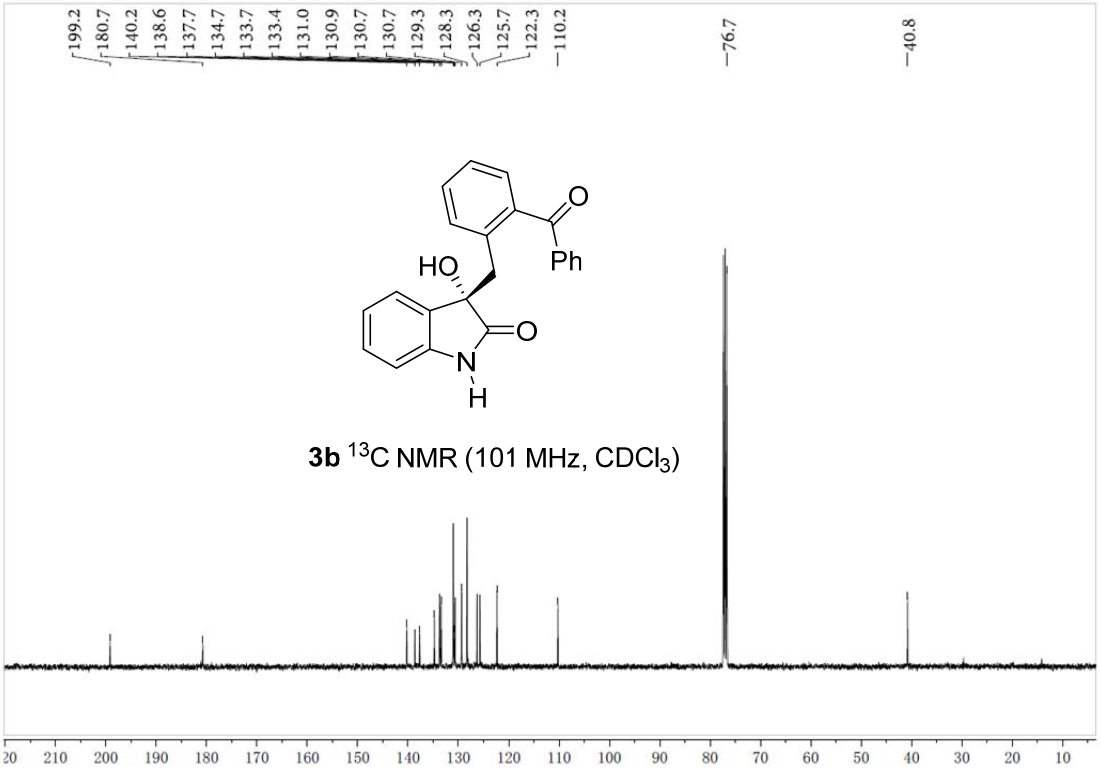
3a ^{1}H NMR (400 MHz, $CDCl_3$)



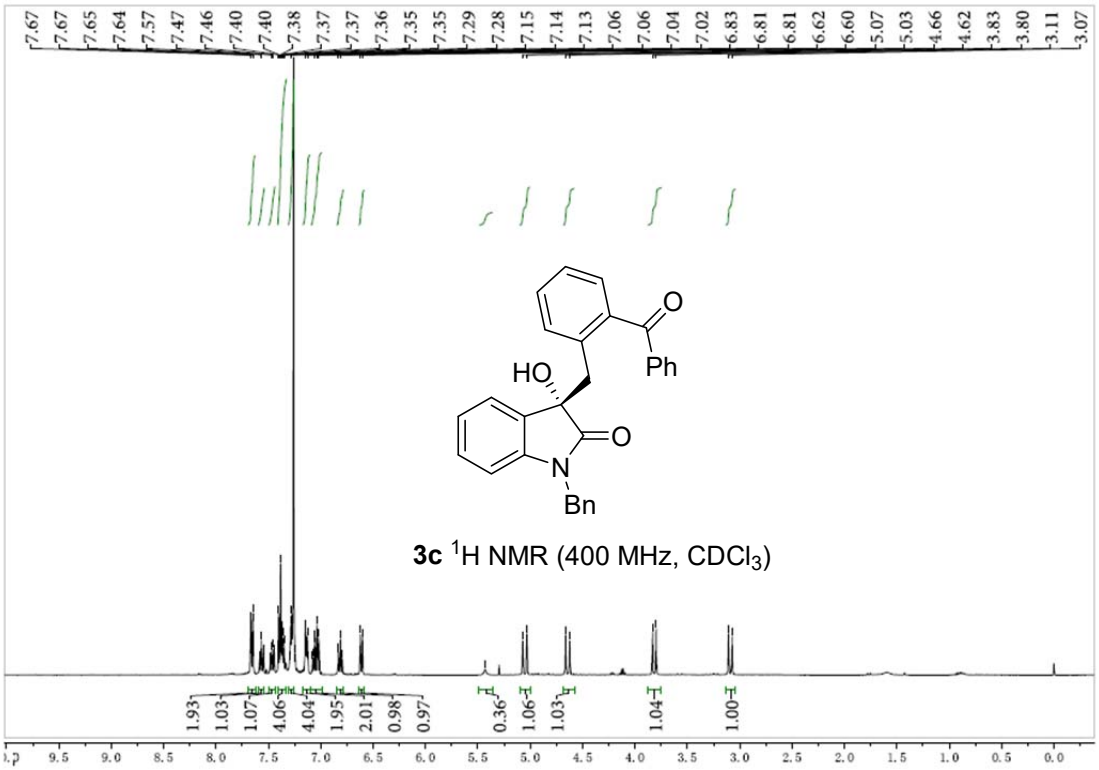
3a ^{13}C NMR (400 MHz, $CDCl_3$)



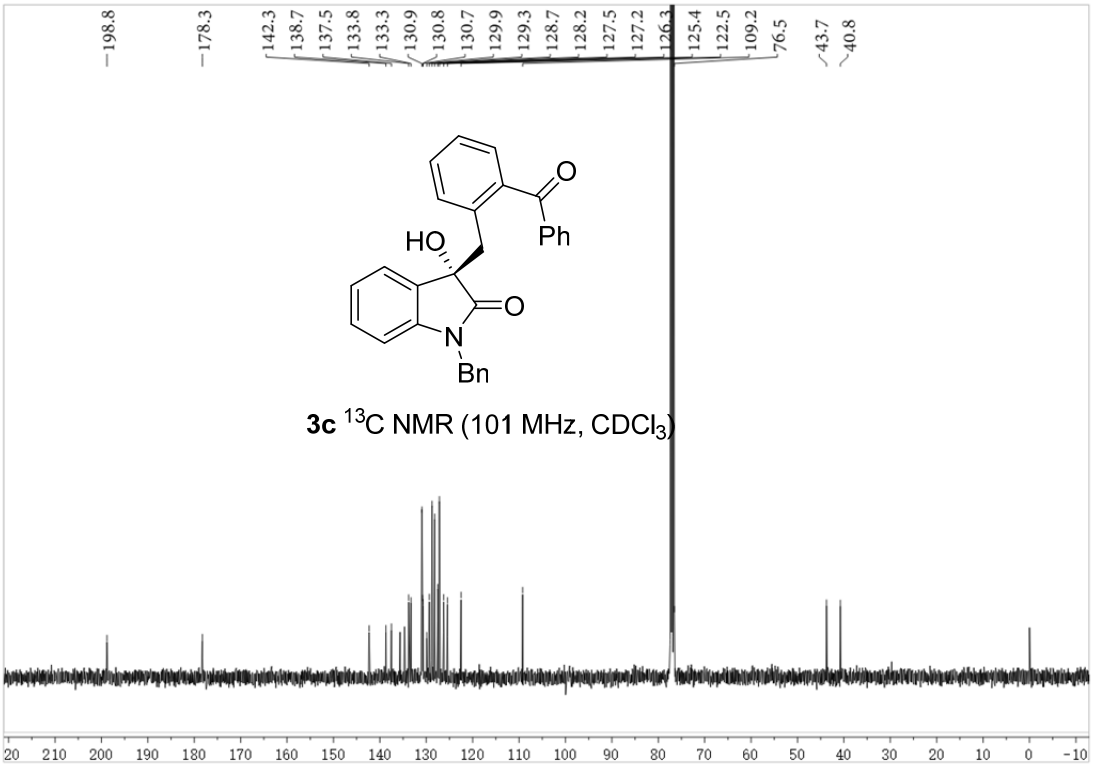
3b ^{1}H NMR (400 MHz, $CDCl_3$)



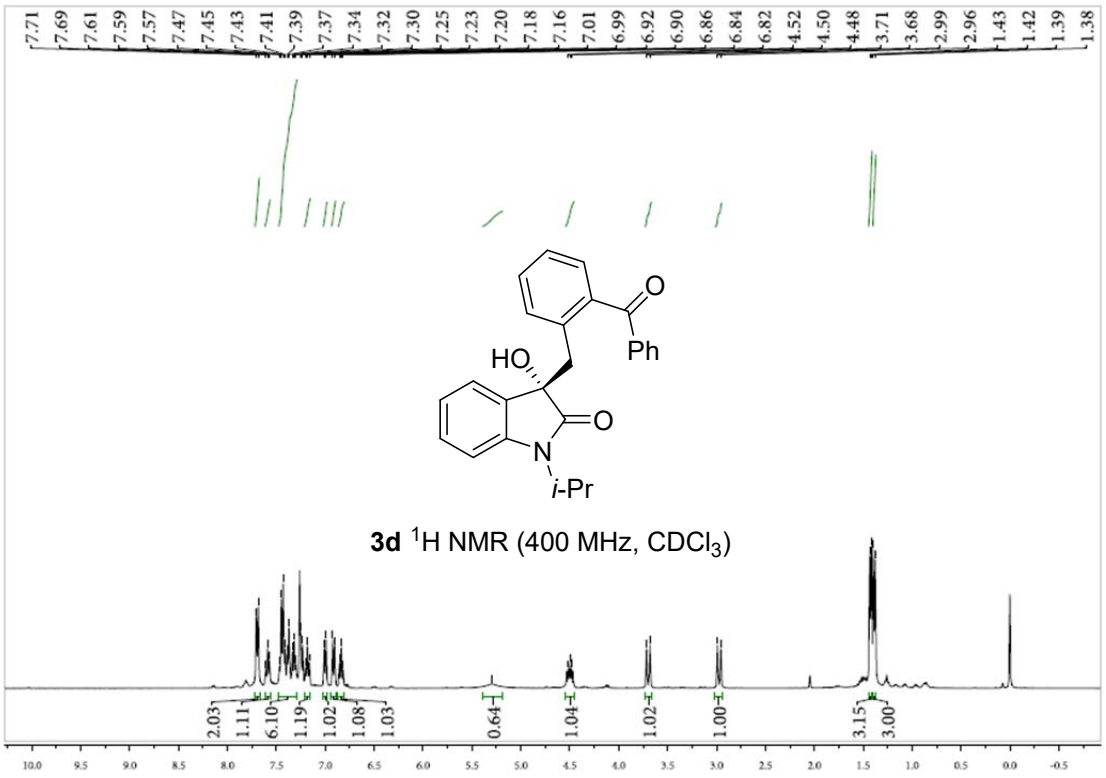
3b ^{13}C NMR (101 MHz, $CDCl_3$)



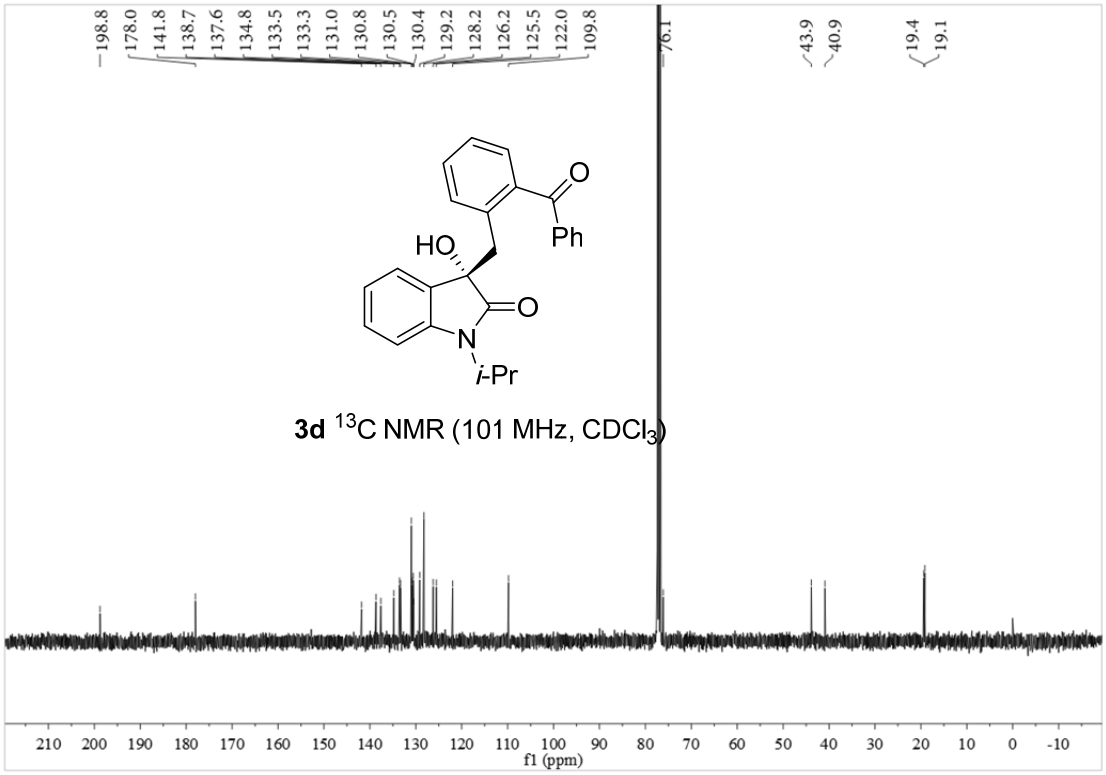
3c ^{1}H NMR (400 MHz, $CDCl_3$)



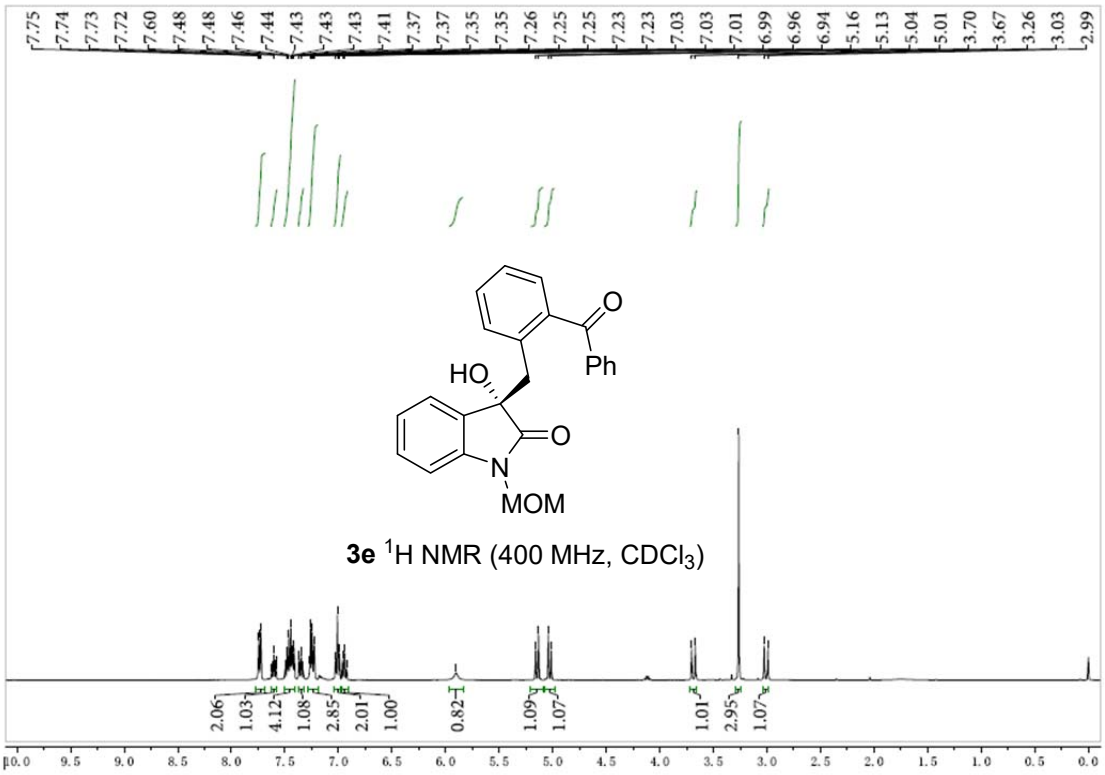
3c ^{13}C NMR (101 MHz, $CDCl_3$)



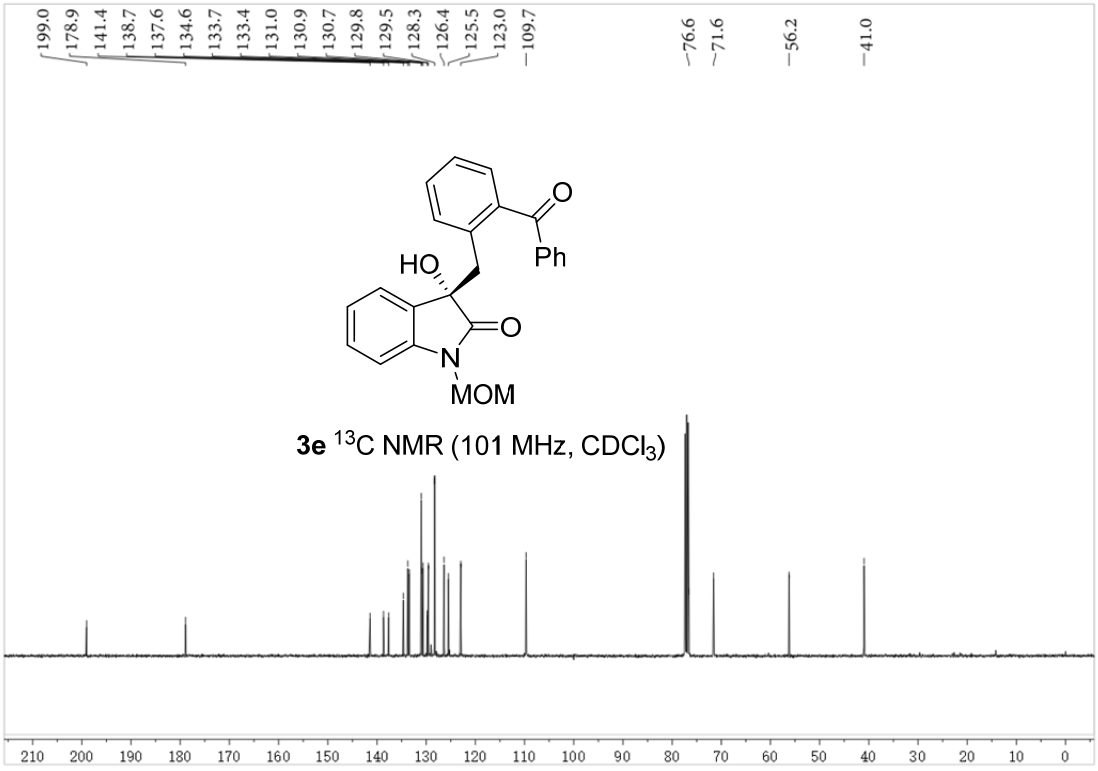
3d ^{1}H NMR (400 MHz, $CDCl_3$)



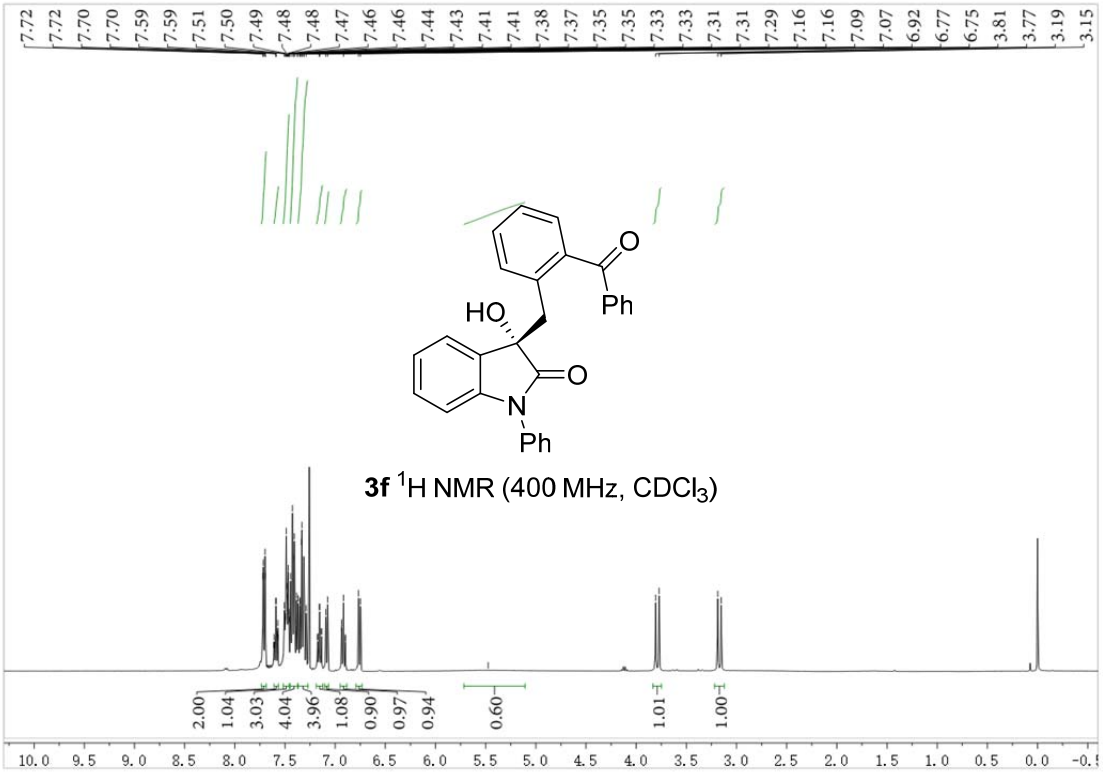
3d ^{13}C NMR (101 MHz, $CDCl_3$)



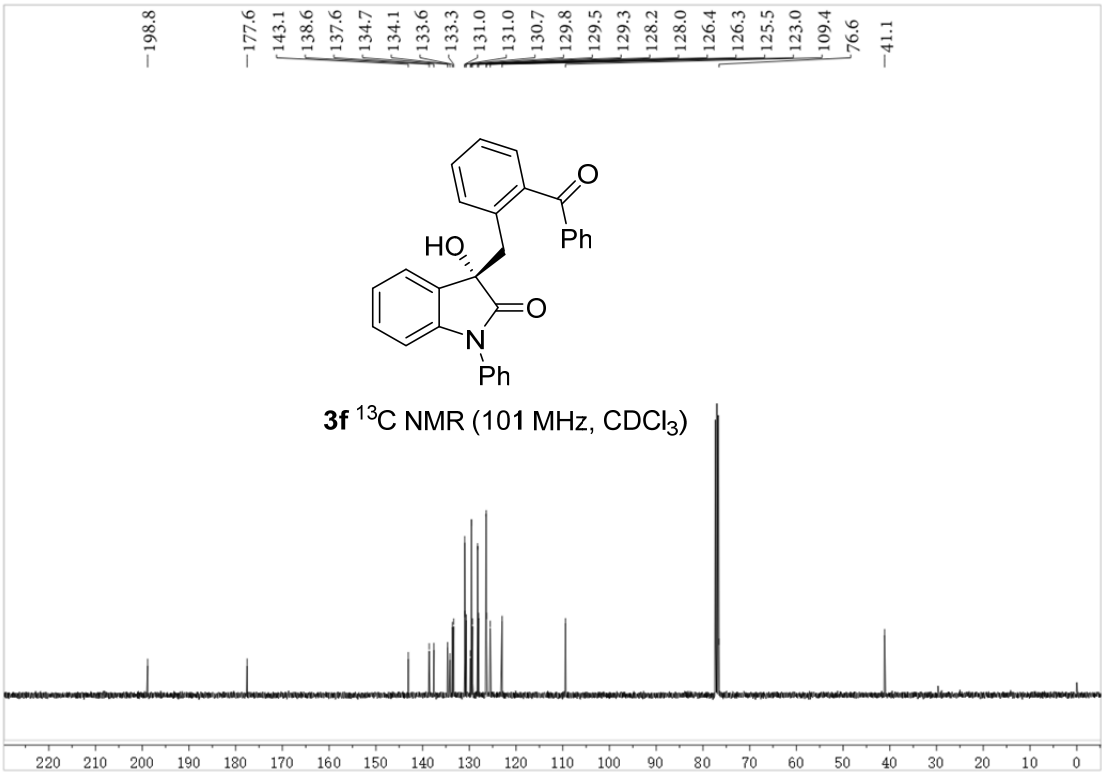
3e ^{1}H NMR (400 MHz, $CDCl_3$)



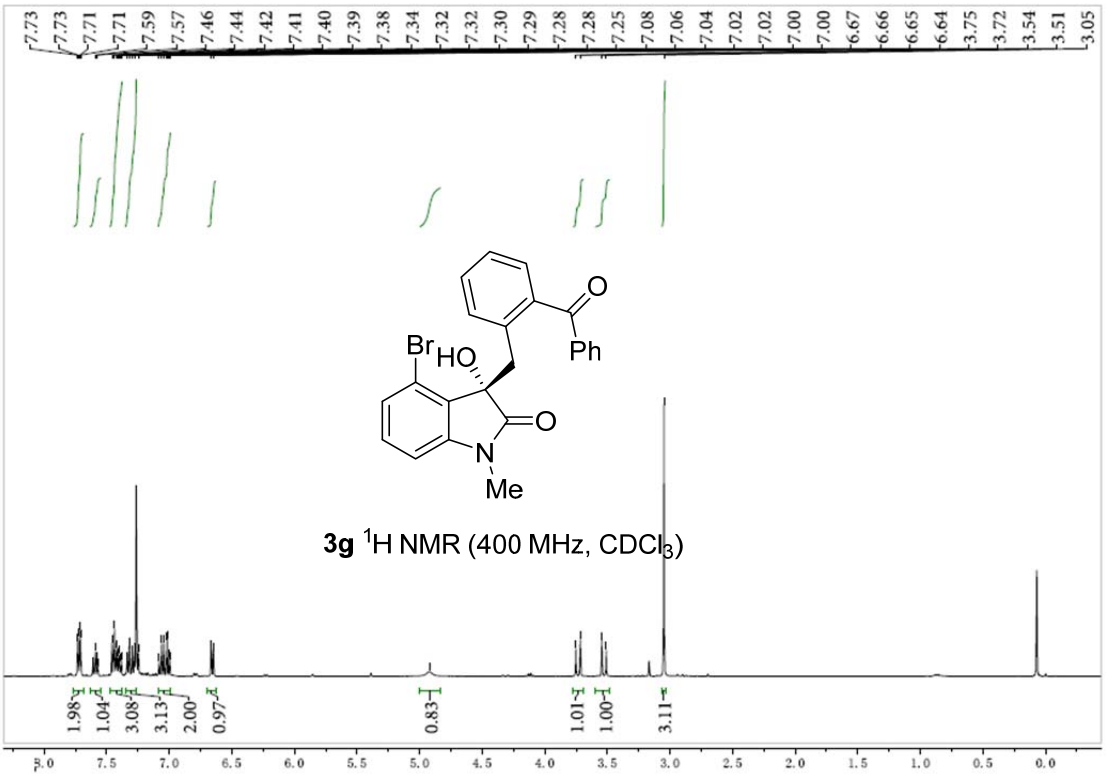
3e ^{13}C NMR (101 MHz, $CDCl_3$)



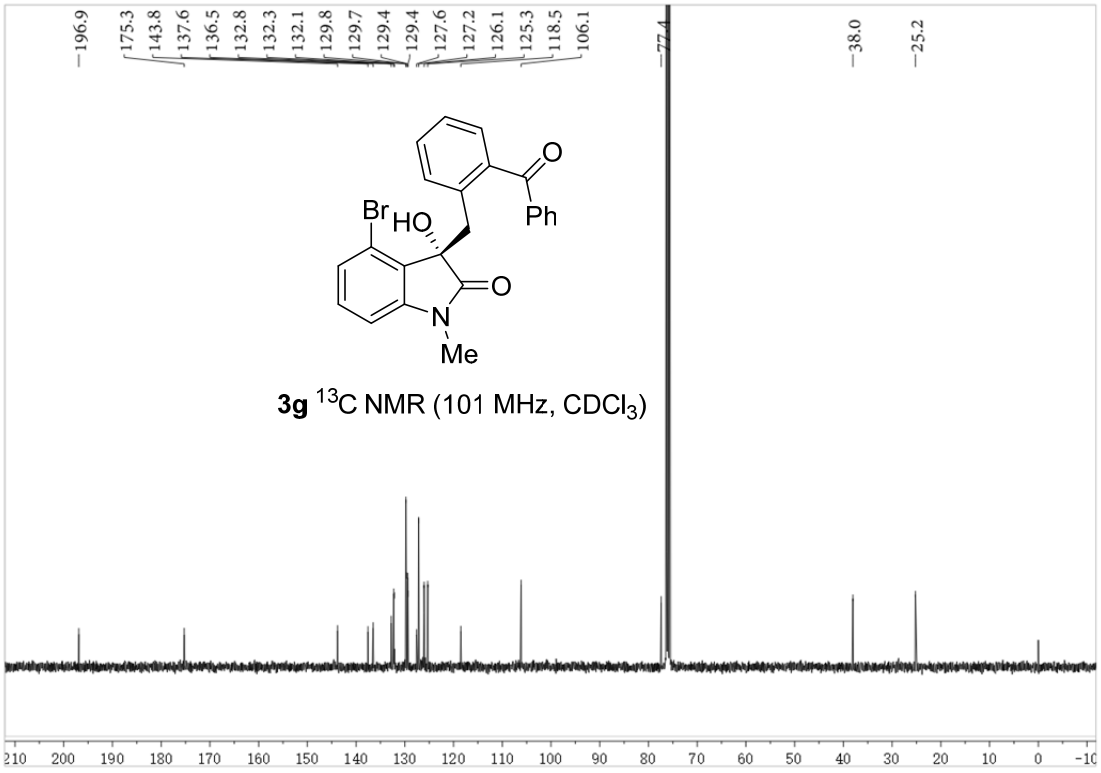
3f ^{1}H NMR (400 MHz, $CDCl_3$)



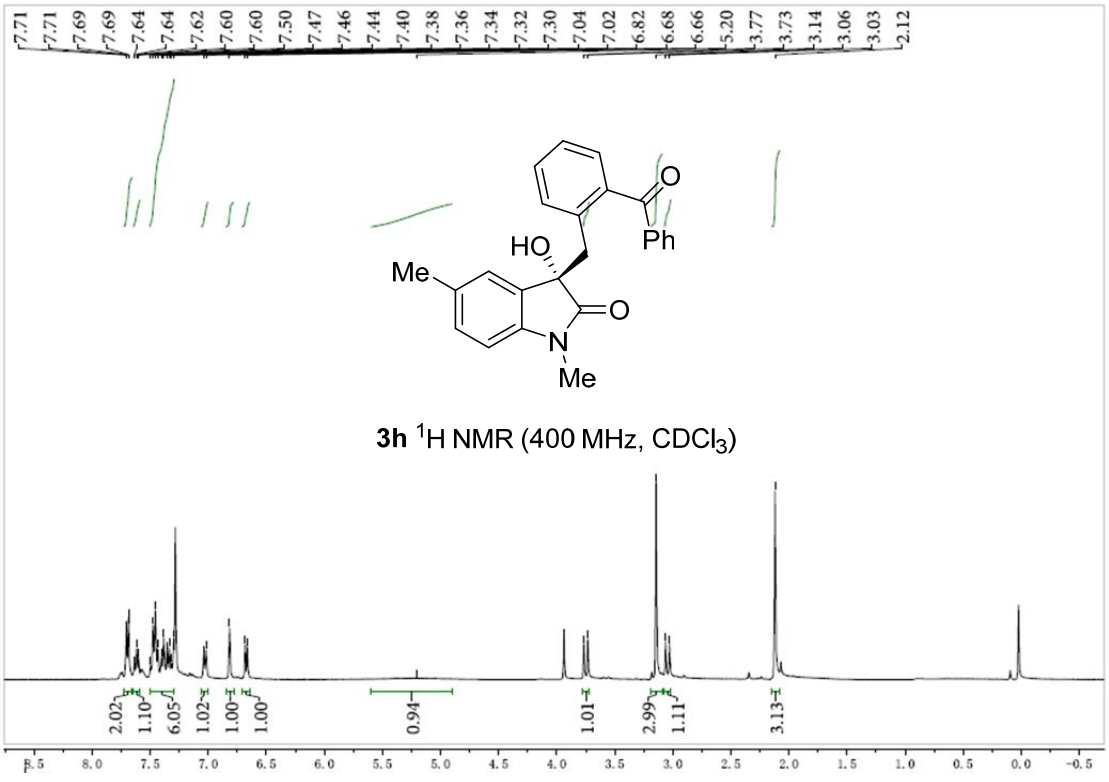
3f ^{13}C NMR (101 MHz, $CDCl_3$)



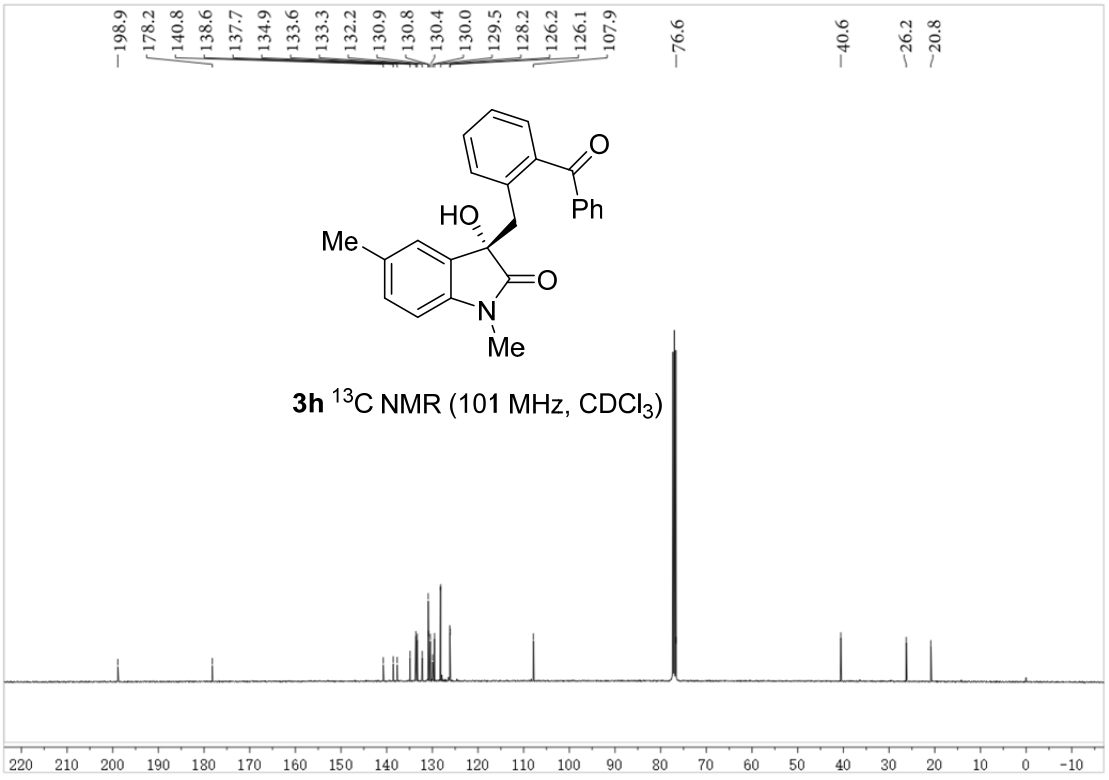
3g ^{1}H NMR (400 MHz, $CDCl_3$)



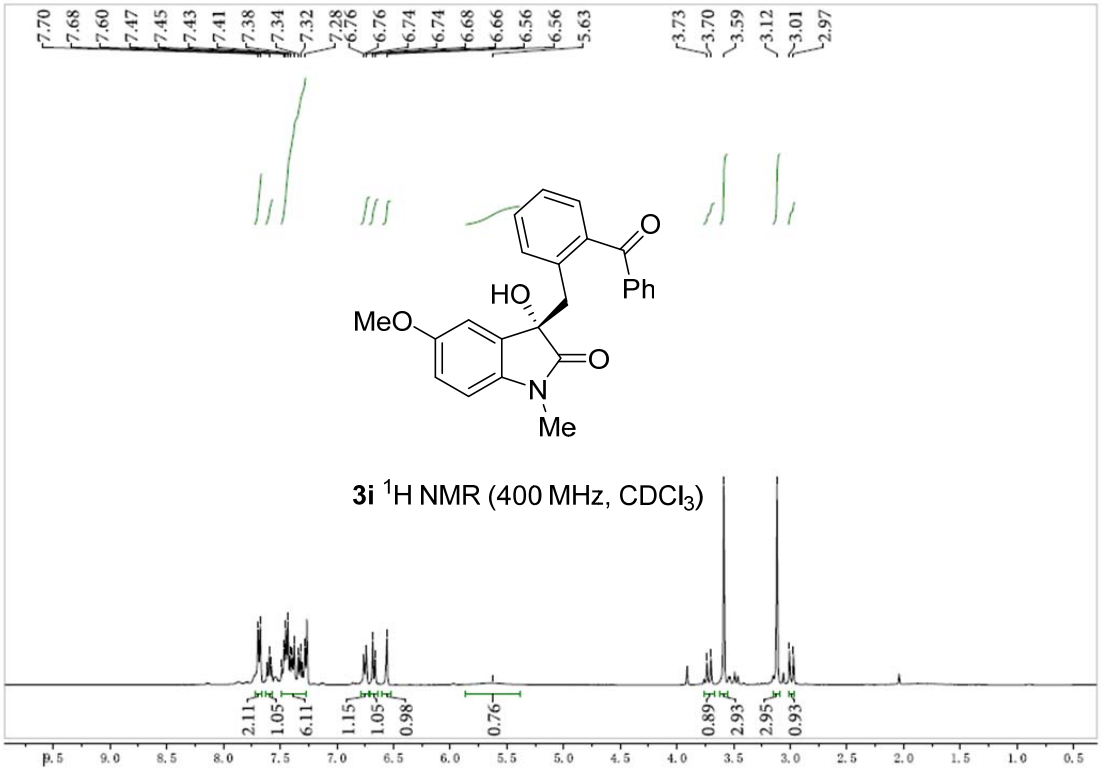
3g ^{13}C NMR (101 MHz, $CDCl_3$)



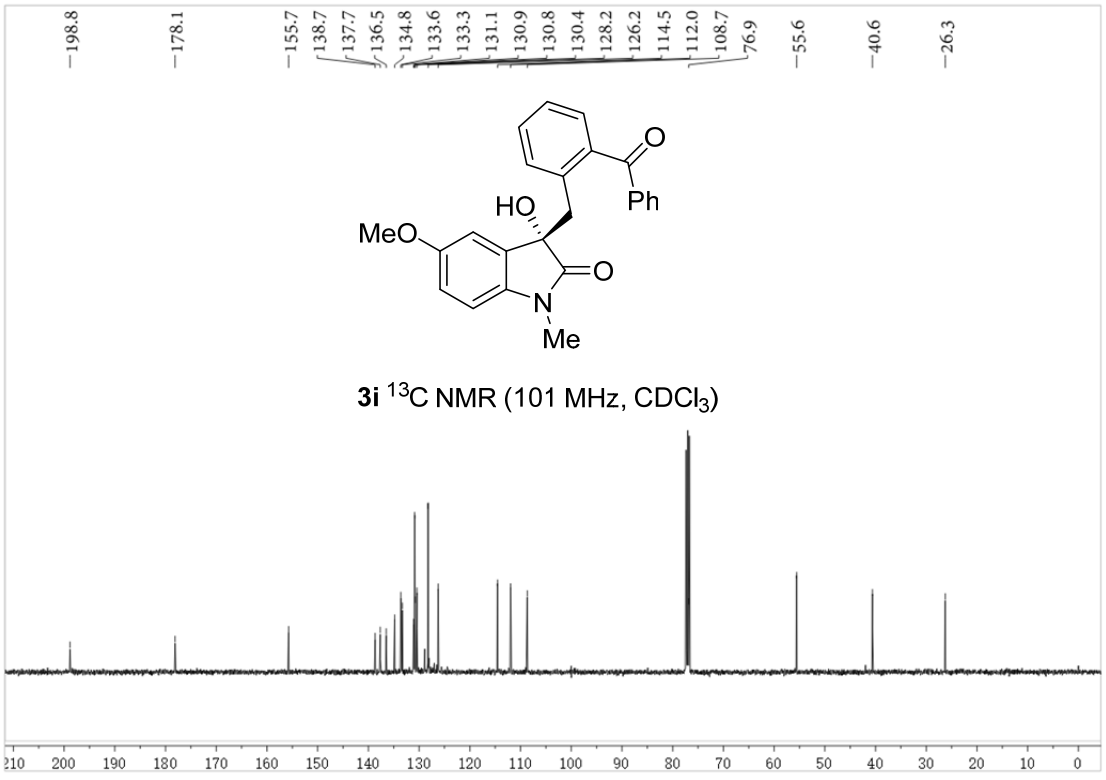
3h ^{1}H NMR (400 MHz, $CDCl_3$)



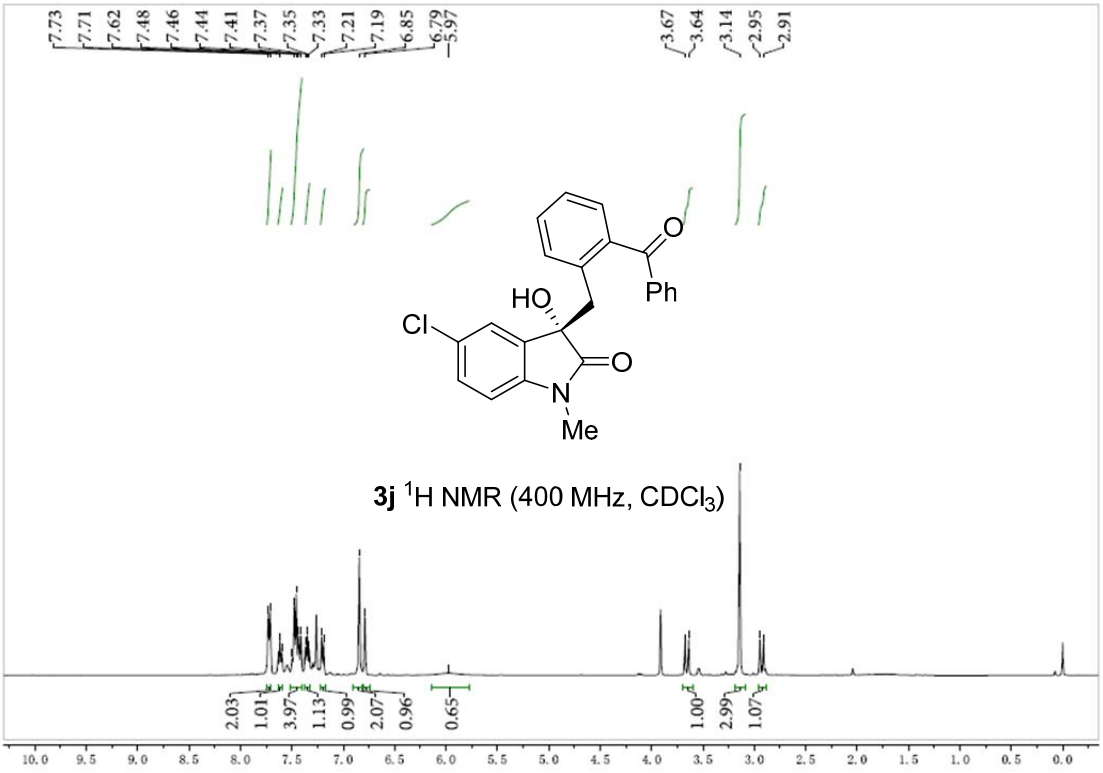
3h ^{13}C NMR (101 MHz, $CDCl_3$)



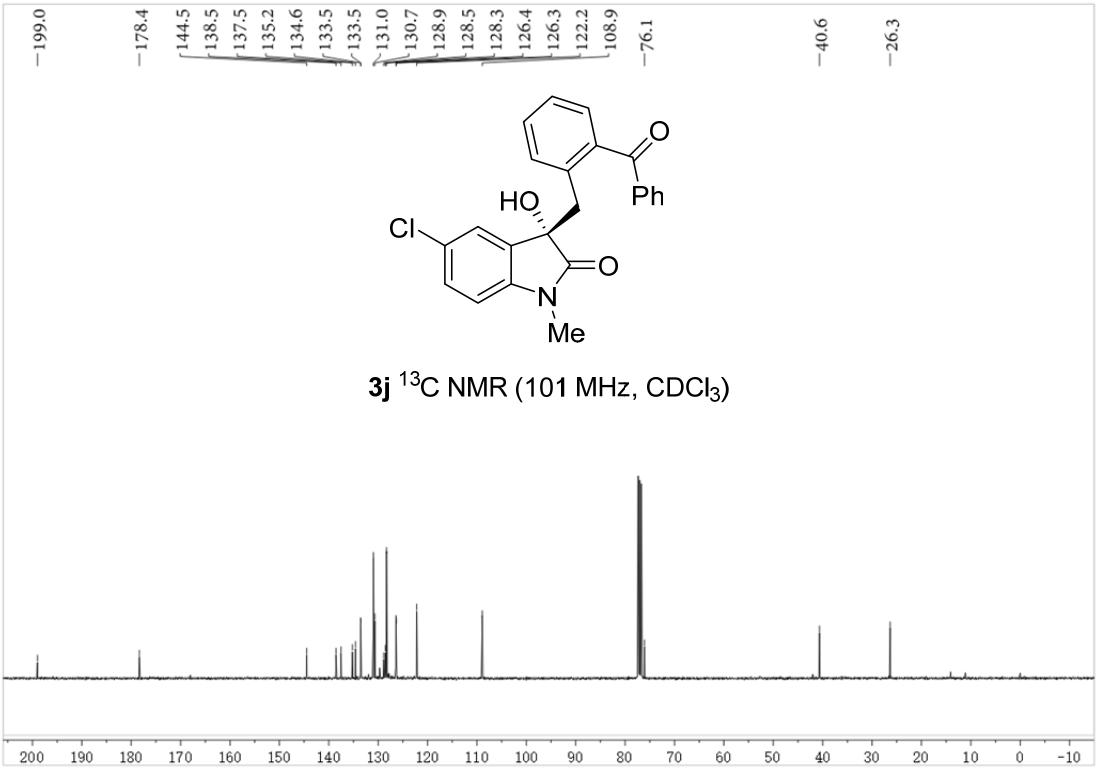
3i ^{1}H NMR (400 MHz, $CDCl_3$)



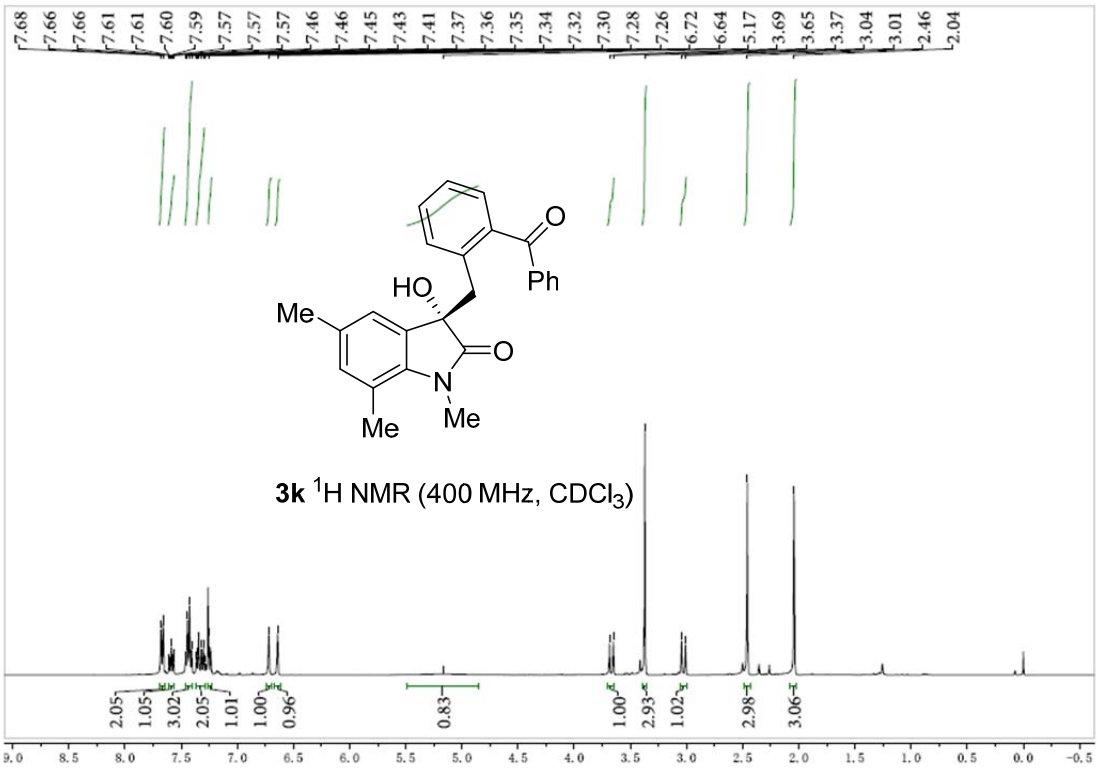
3i ^{13}C NMR (101 MHz, $CDCl_3$)



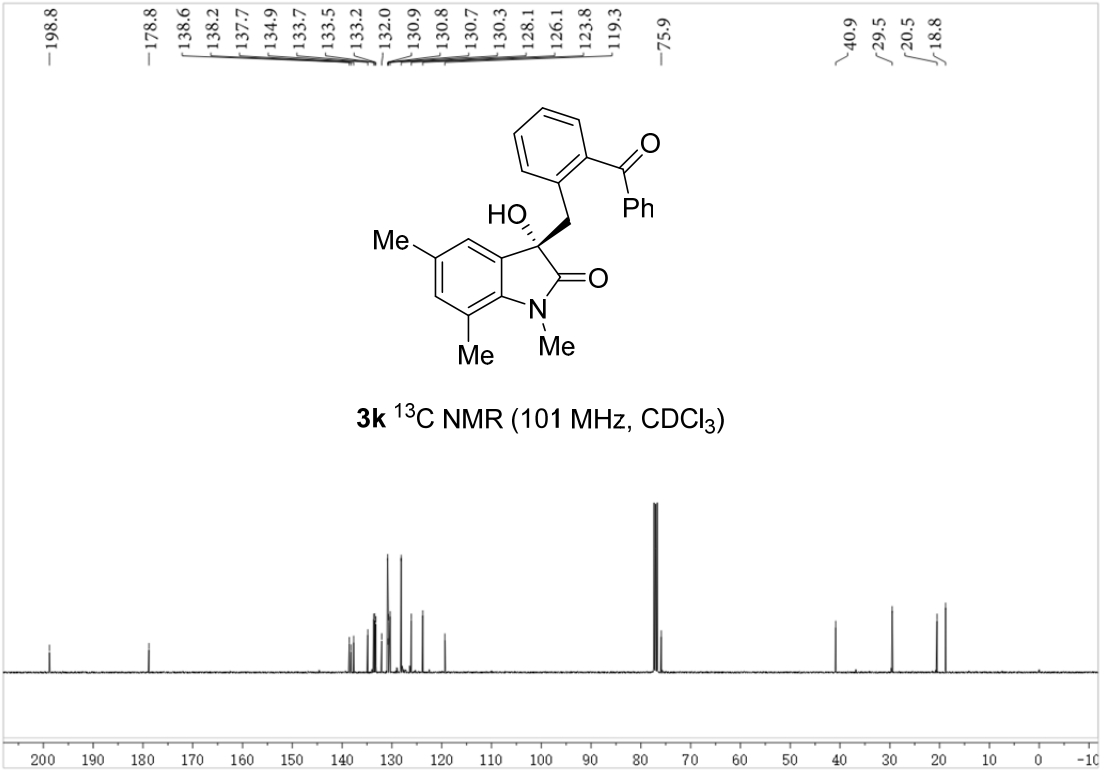
3j ^{1}H NMR (400 MHz, $CDCl_3$)



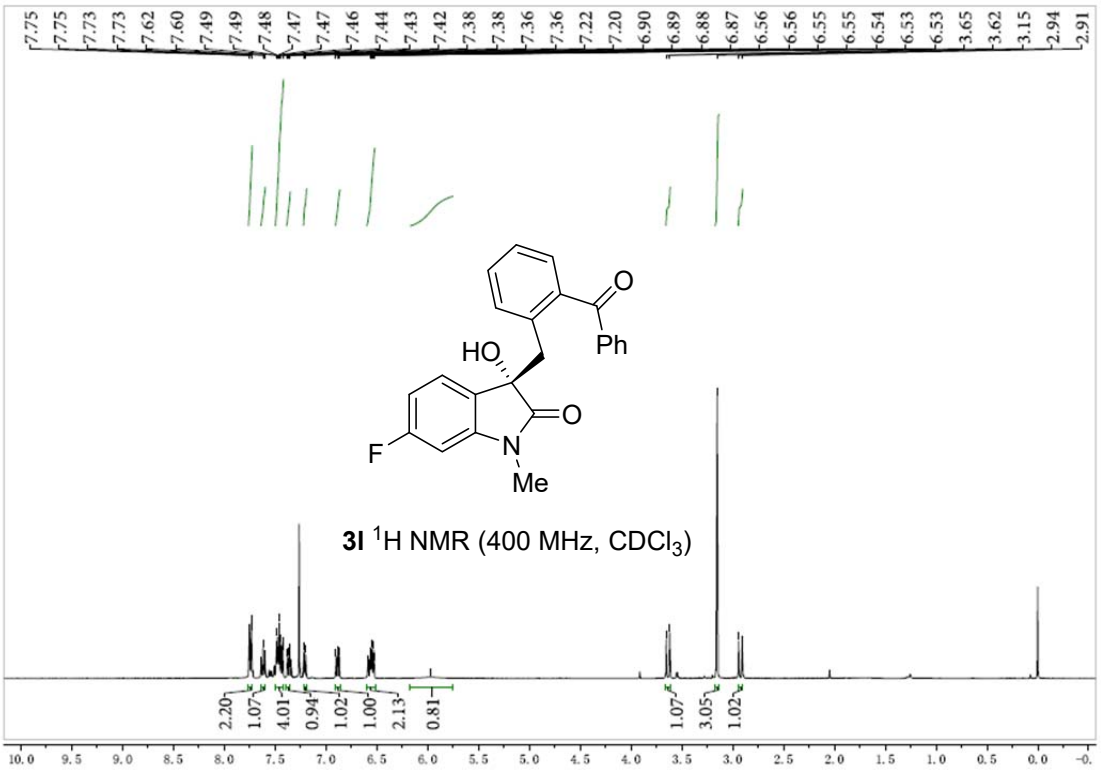
3j ^{13}C NMR (101 MHz, $CDCl_3$)



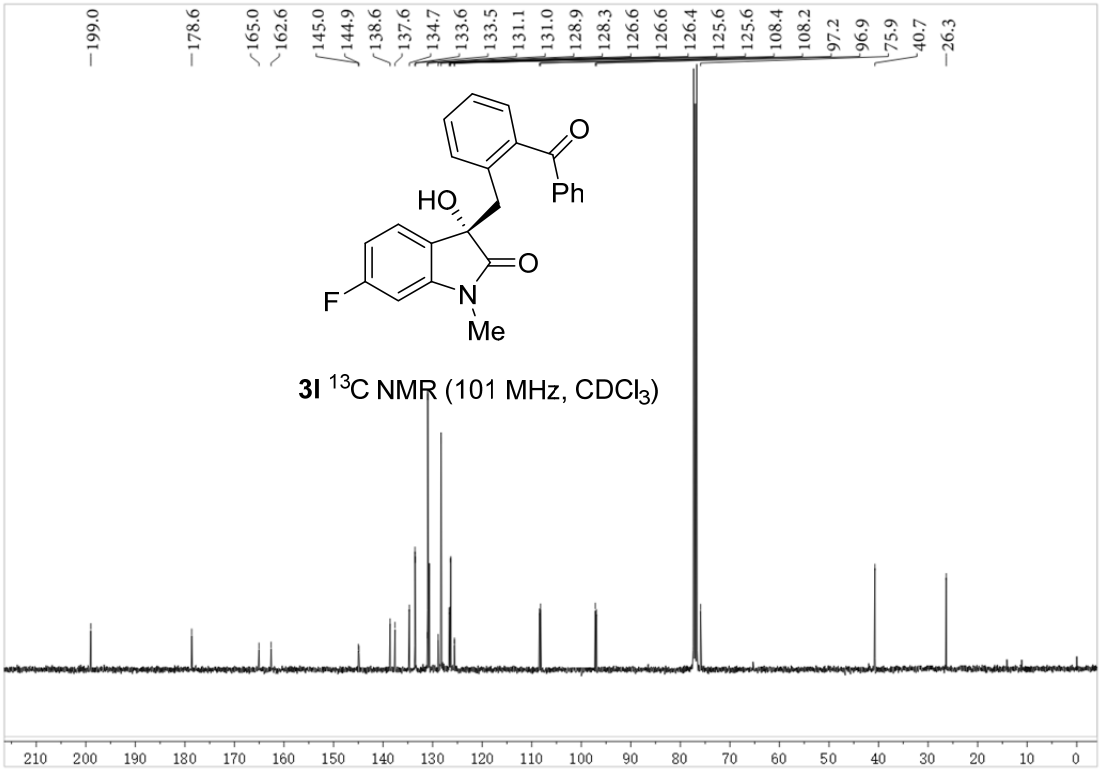
3k ^{1}H NMR (400 MHz, $CDCl_3$)



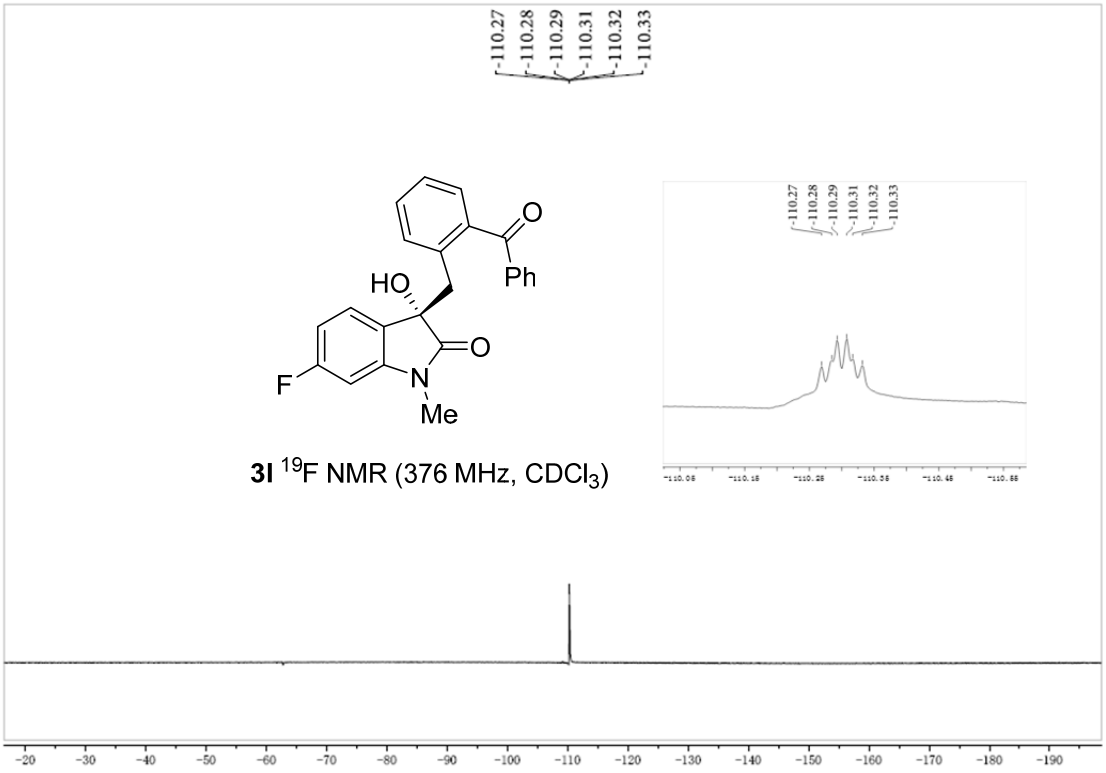
3k ^{13}C NMR (101 MHz, $CDCl_3$)



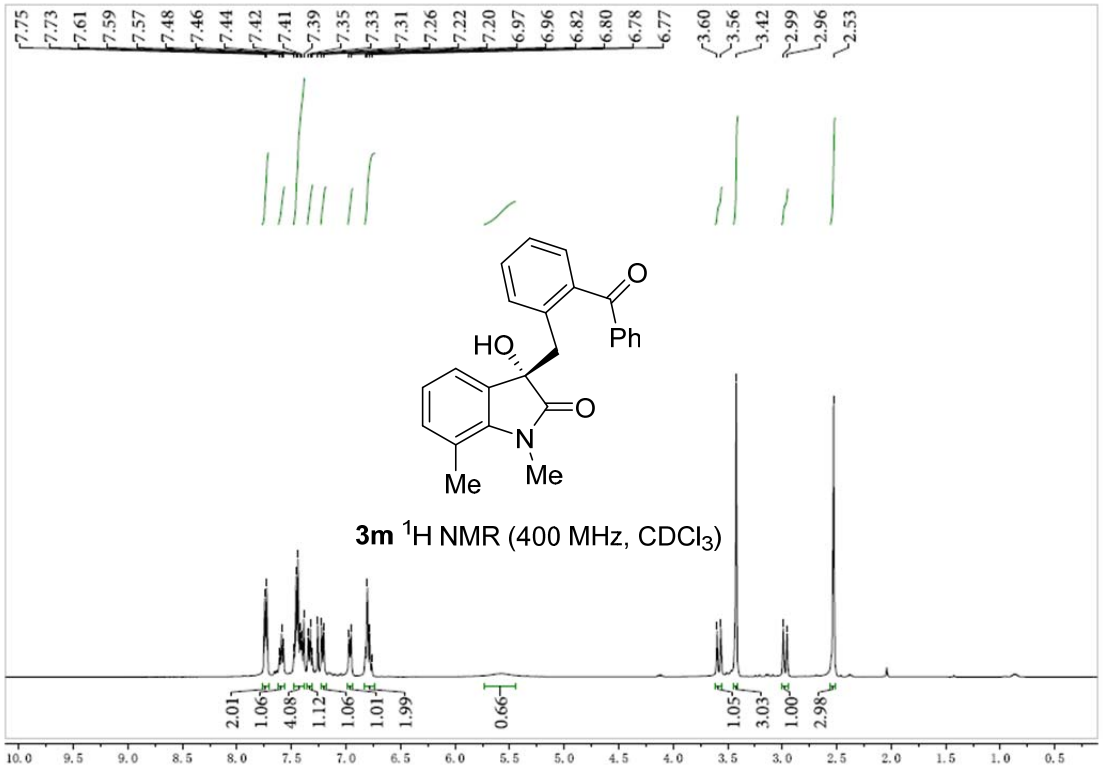
3l ^{1}H NMR (400 MHz, $CDCl_3$)



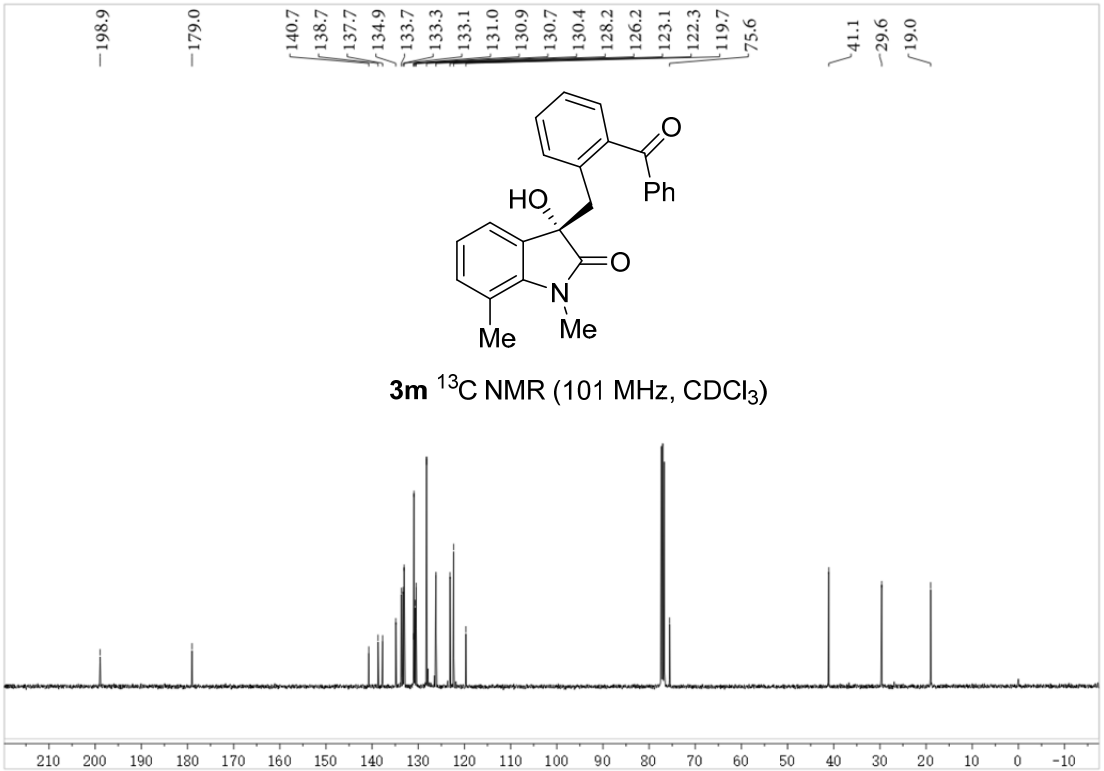
3l ^{13}C NMR (101 MHz, $CDCl_3$)



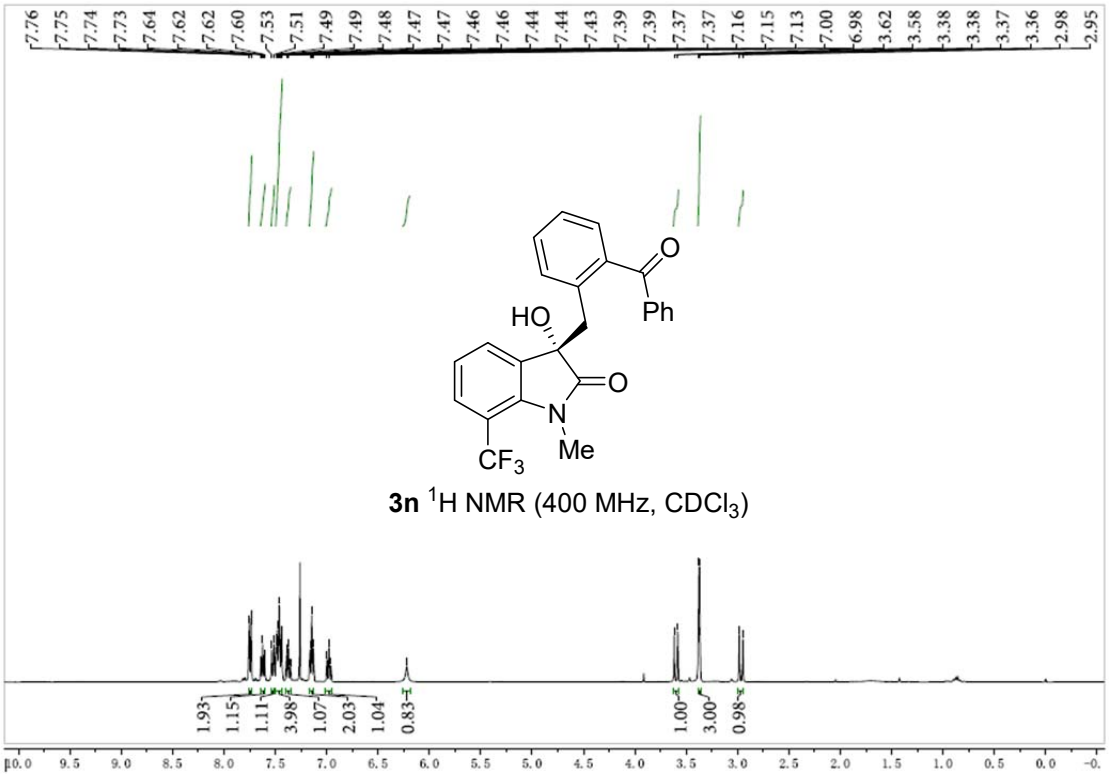
3l ^{19}F NMR (376 MHz, $CDCl_3$)



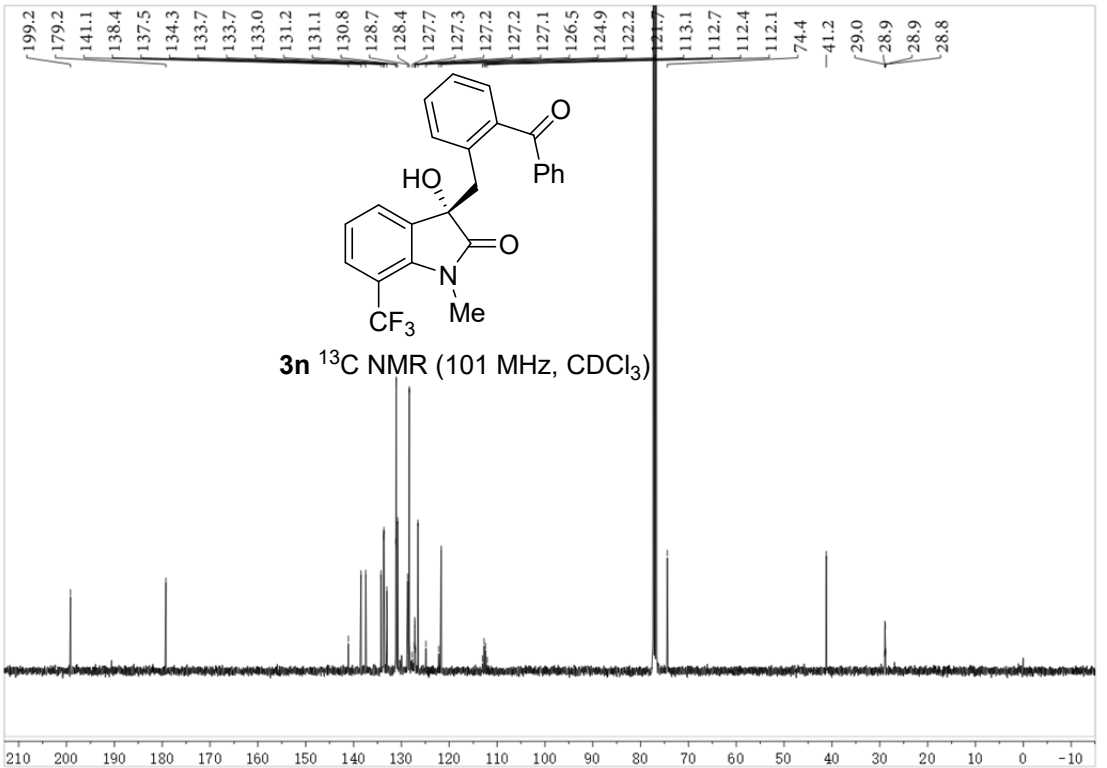
3m ^{1}H NMR (400 MHz, $CDCl_3$)



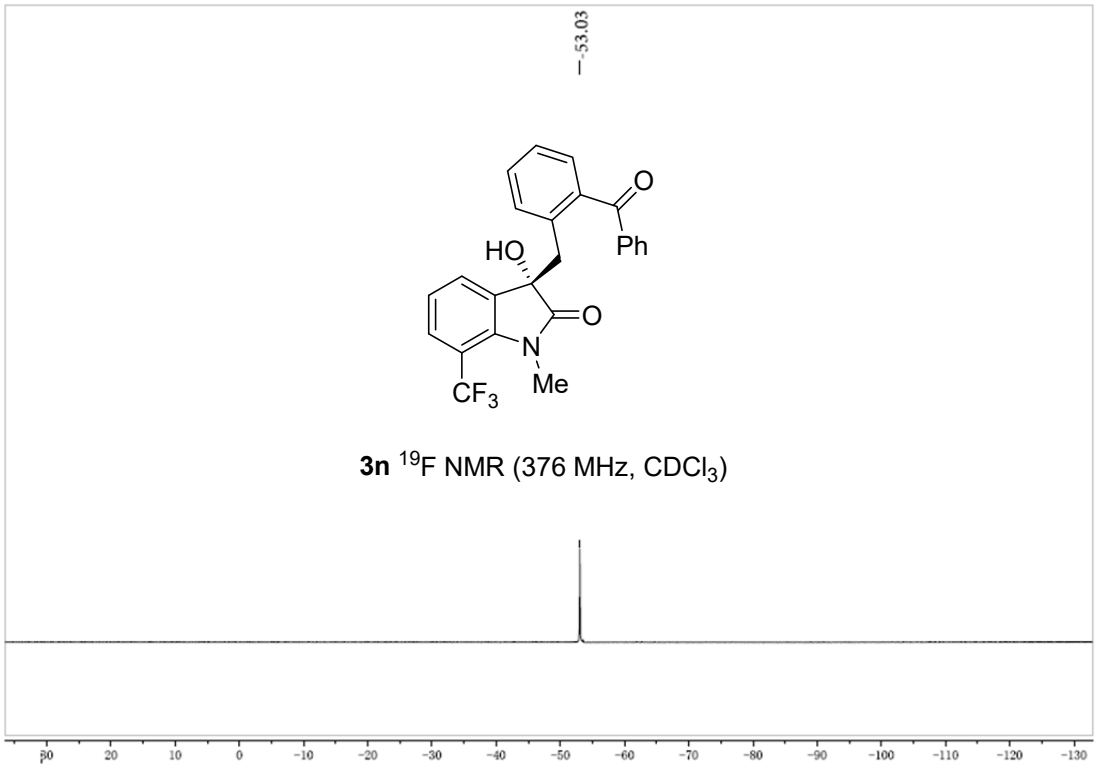
3m ^{13}C NMR (101 MHz, $CDCl_3$)



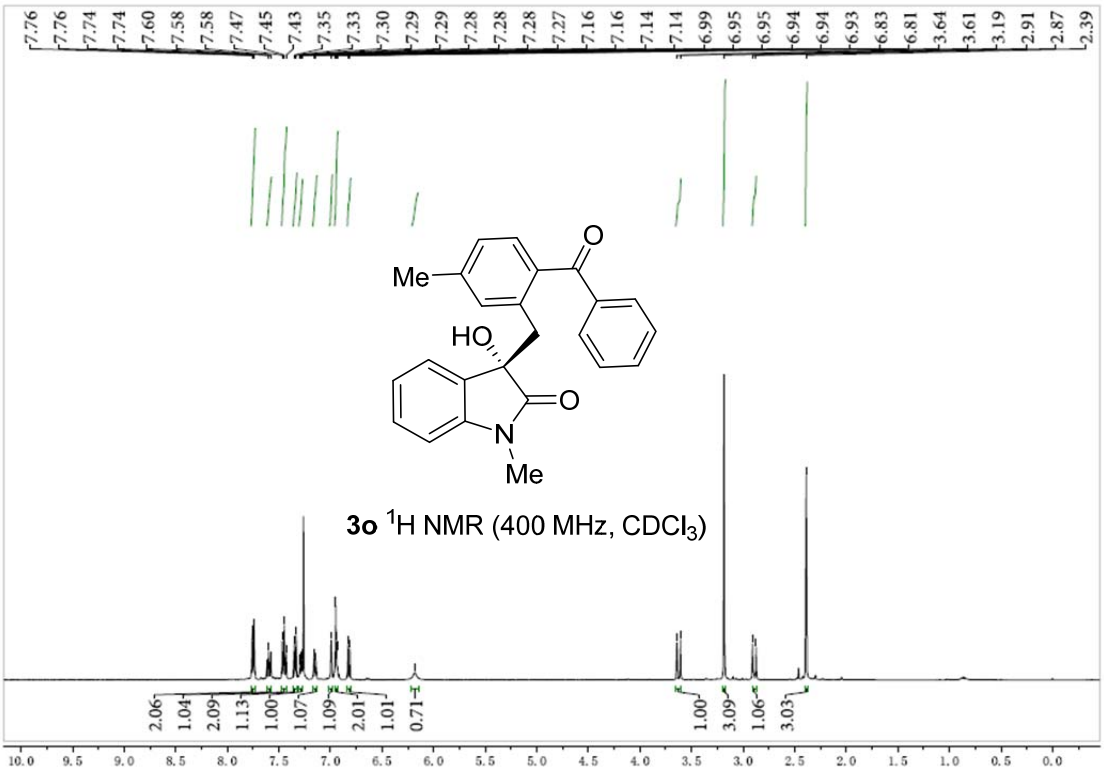
3n ^{1}H NMR (400 MHz, $CDCl_3$)



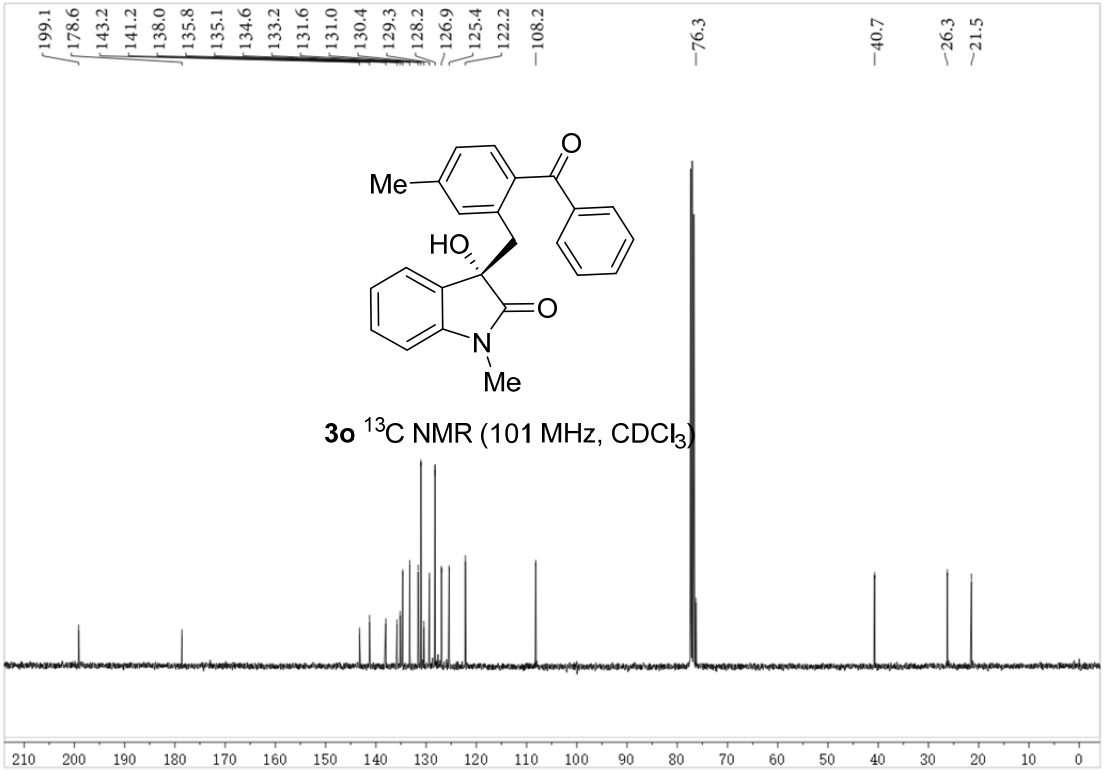
3n ^{13}C NMR (101 MHz, $CDCl_3$)



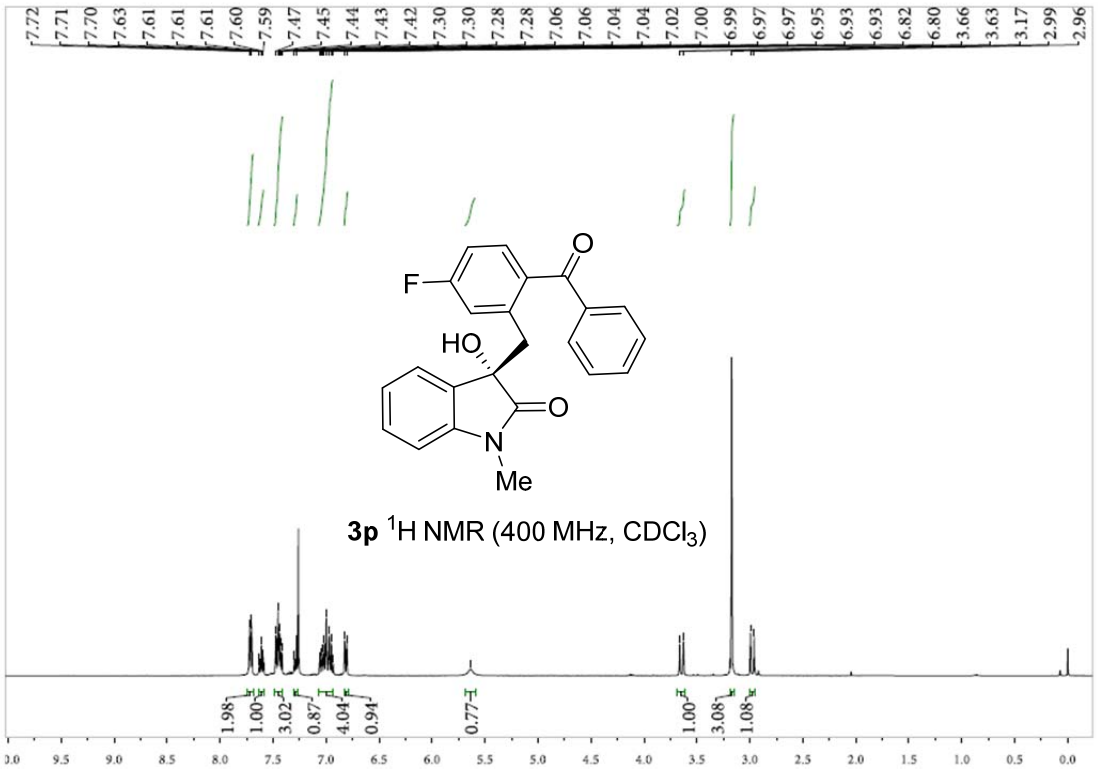
3n ^{19}F NMR (376 MHz, $CDCl_3$)

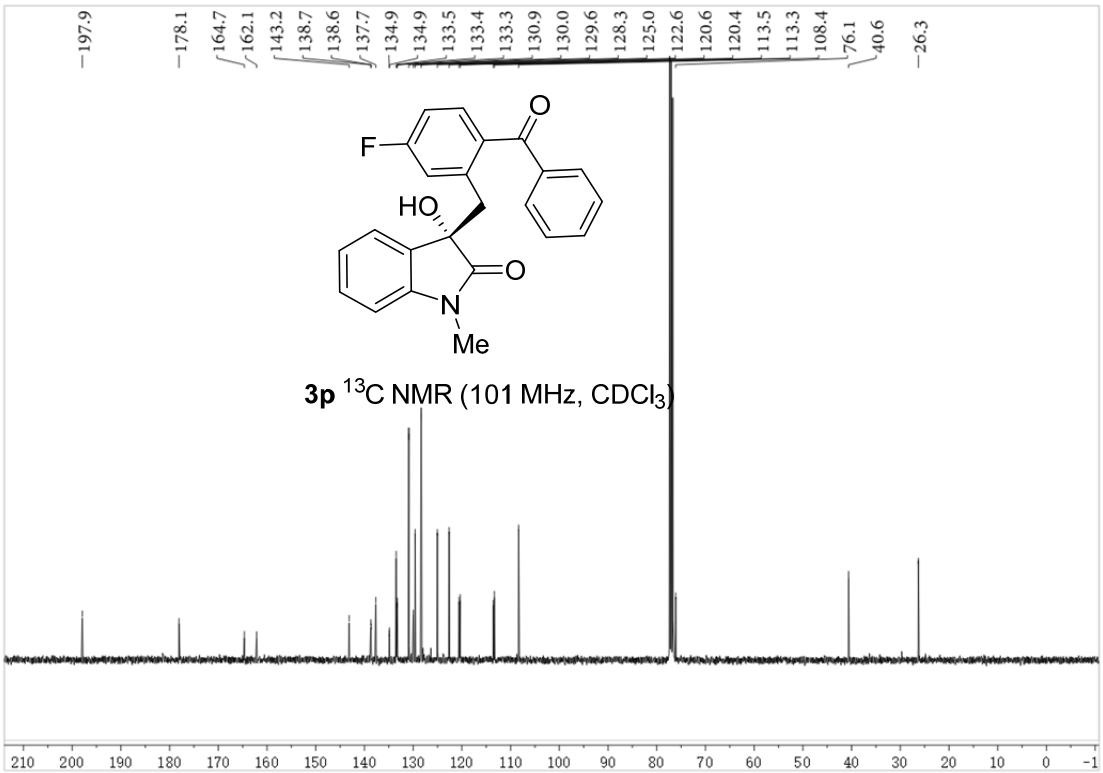


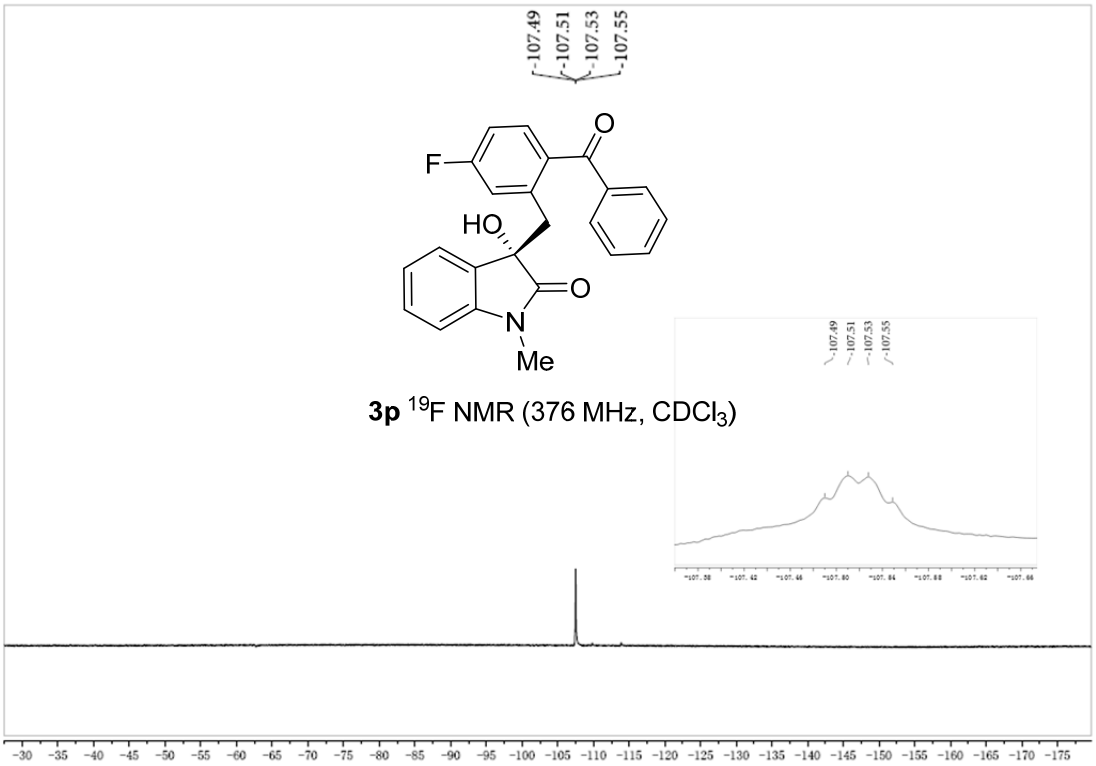
3o ^{1}H NMR (400 MHz, $CDCl_3$)



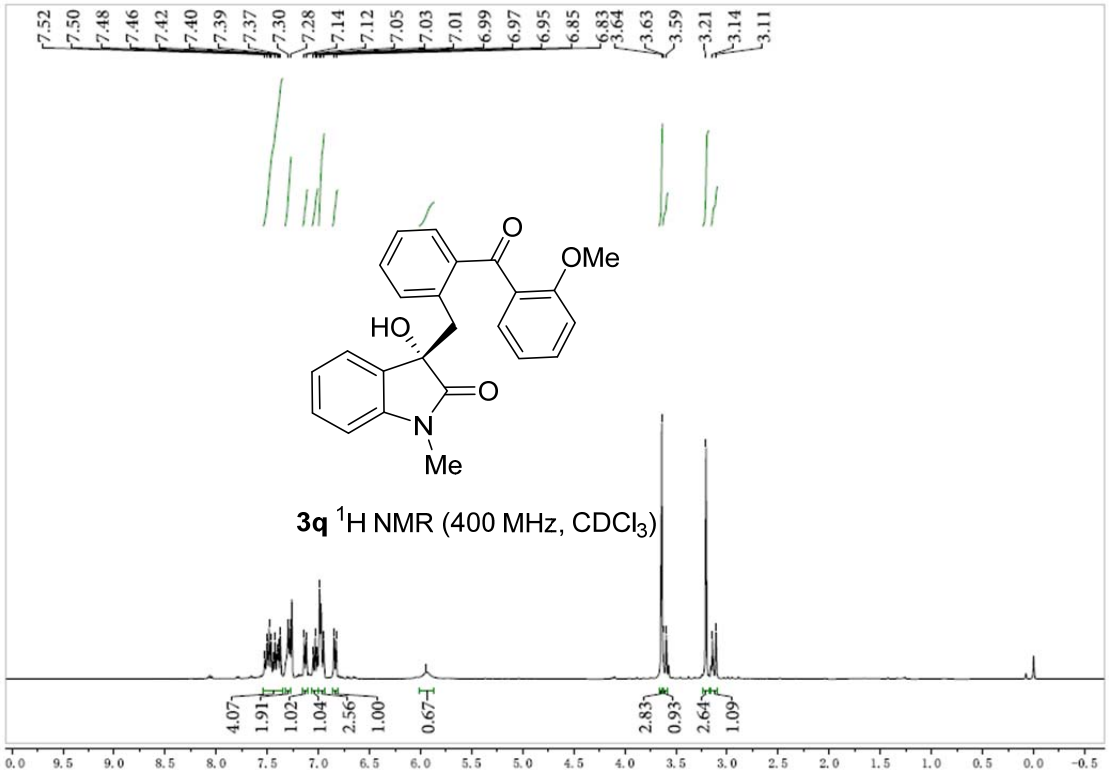
3o ^{13}C NMR (101 MHz, $CDCl_3$)

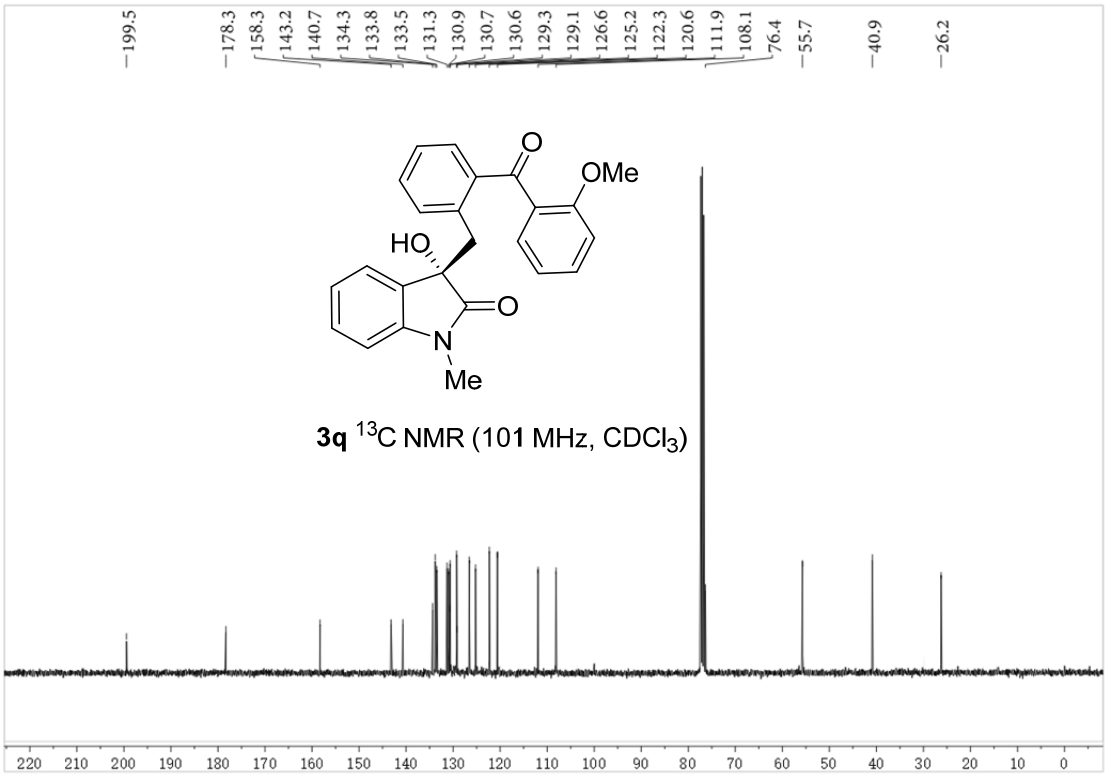

F
O
HO
O
N
Me
3p ^{1}H NMR (400 MHz, $CDCl_3$)

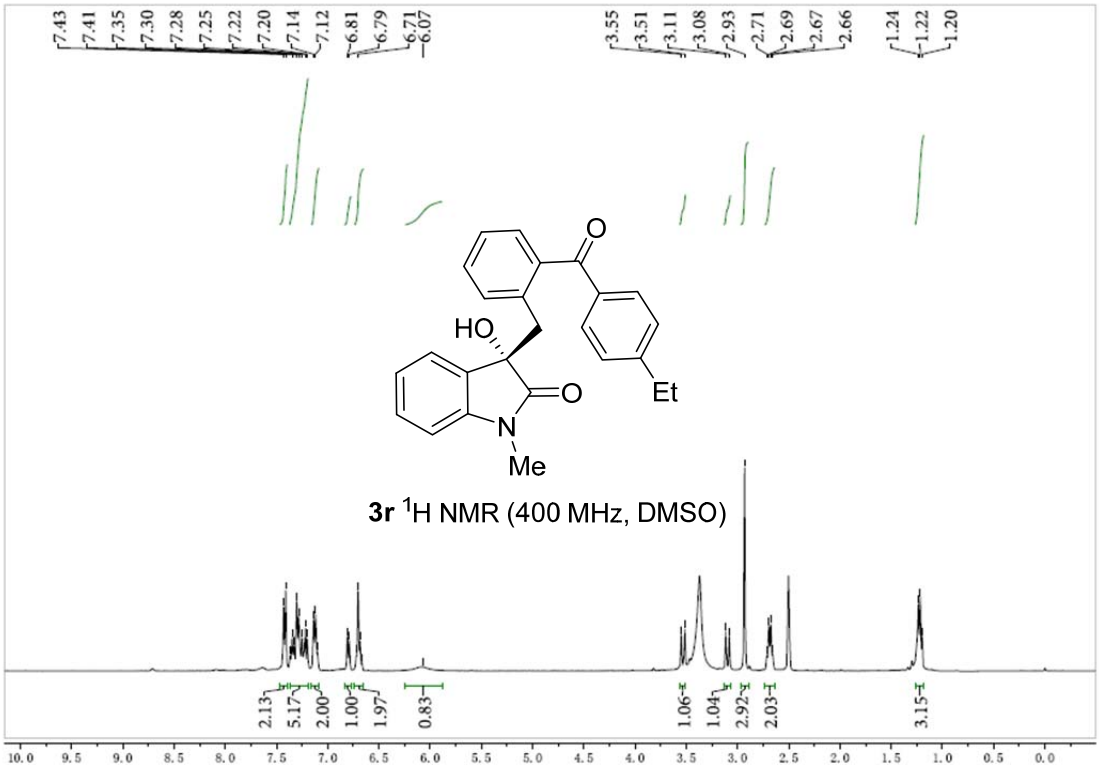

F
O
HO
O
N
Me
3p ^{13}C NMR (101 MHz, $CDCl_3$)



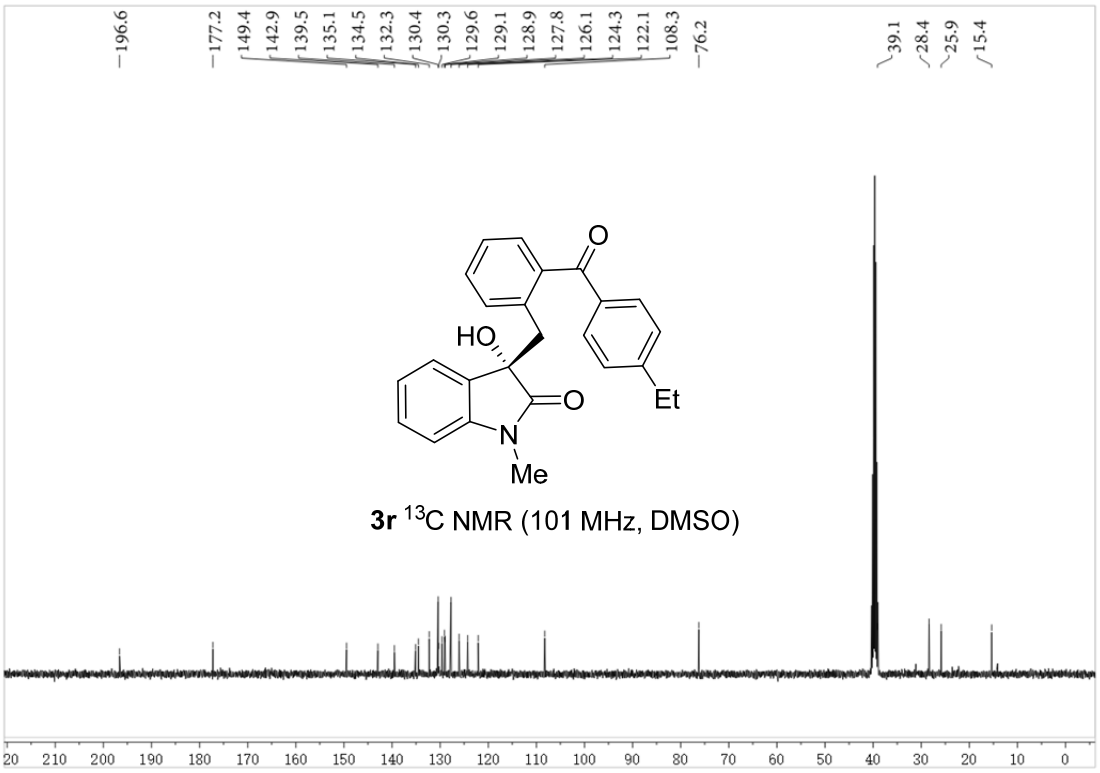
3p ^{19}F NMR (376 MHz, $CDCl_3$)


7.52
7.50
7.48
7.46
7.42
7.40
7.39
7.37
7.30
7.28
7.14
7.12
7.05
7.03
7.01
6.99
6.97
6.95
6.85
6.83
3.64
3.63
3.59
3.21
3.14
3.11
O
OMe
HO
O
N
Me
3q 1H NMR (400 MHz, CDCl3)
4.07
1.91
1.02
1.04
2.56
1.00
0.67
2.83
0.93
2.64
1.09

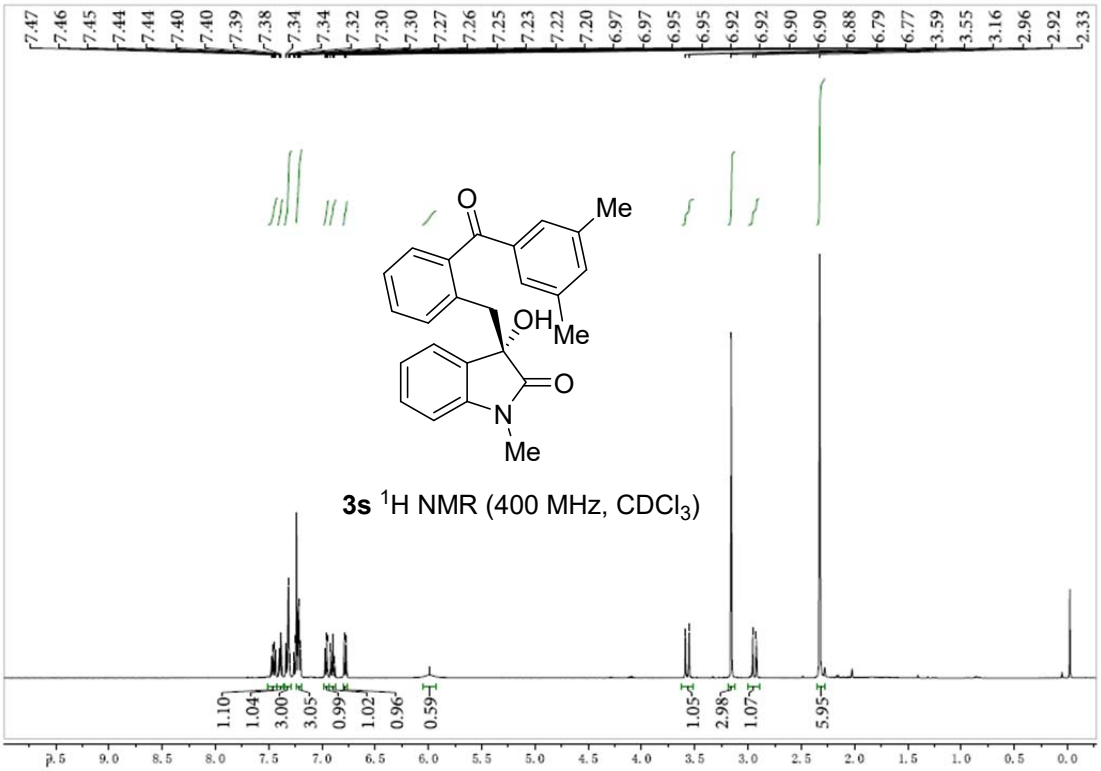

199.5
178.3
158.3
143.2
140.7
134.3
133.8
133.5
131.3
130.9
130.7
130.6
129.3
129.1
126.6
125.2
122.3
120.6
111.9
108.1
76.4
55.7
40.9
26.2
O
OMe
HO
O
N
Me
3q 13C NMR (101 MHz, CDCl3)



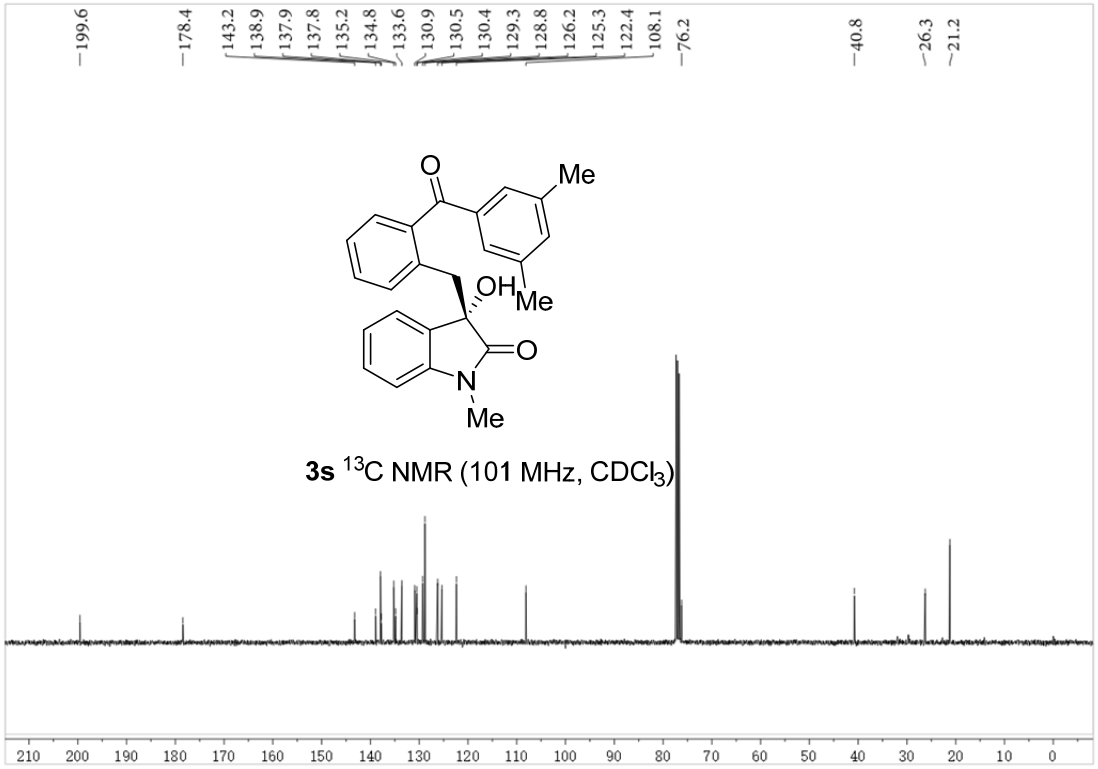
3r ^{1}H NMR (400 MHz, DMSO)



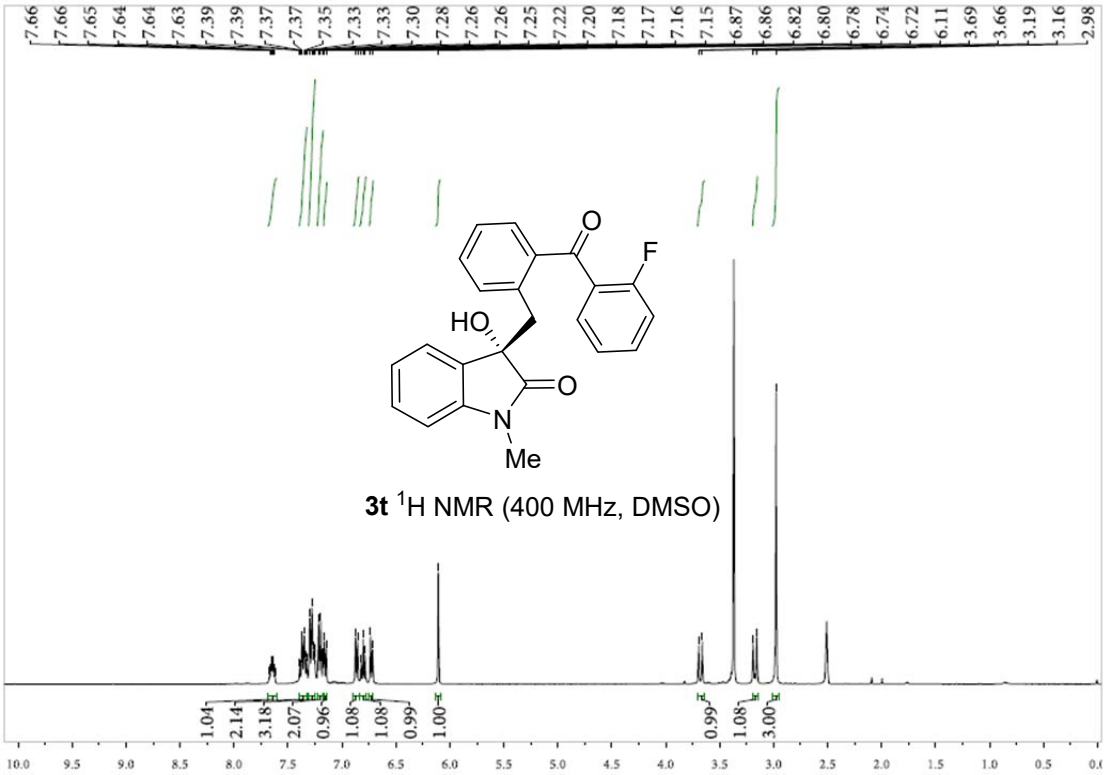
3r ^{13}C NMR (101 MHz, DMSO)



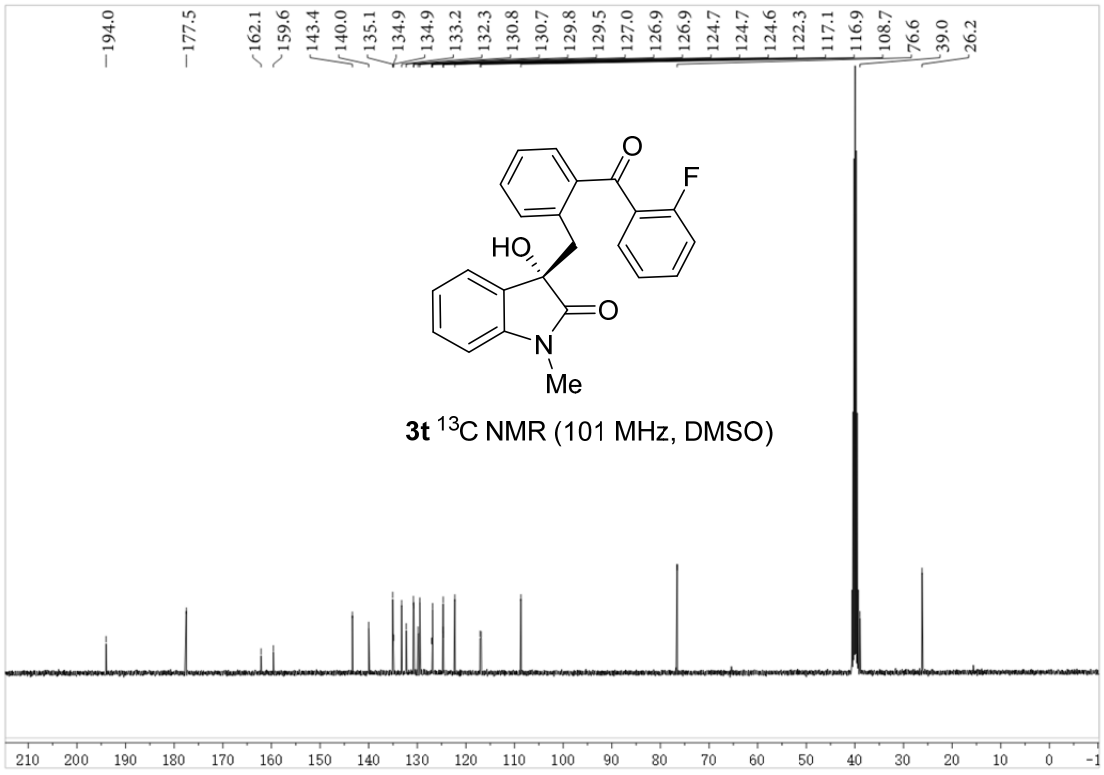
3s ^{1}H NMR (400 MHz, $CDCl_3$)



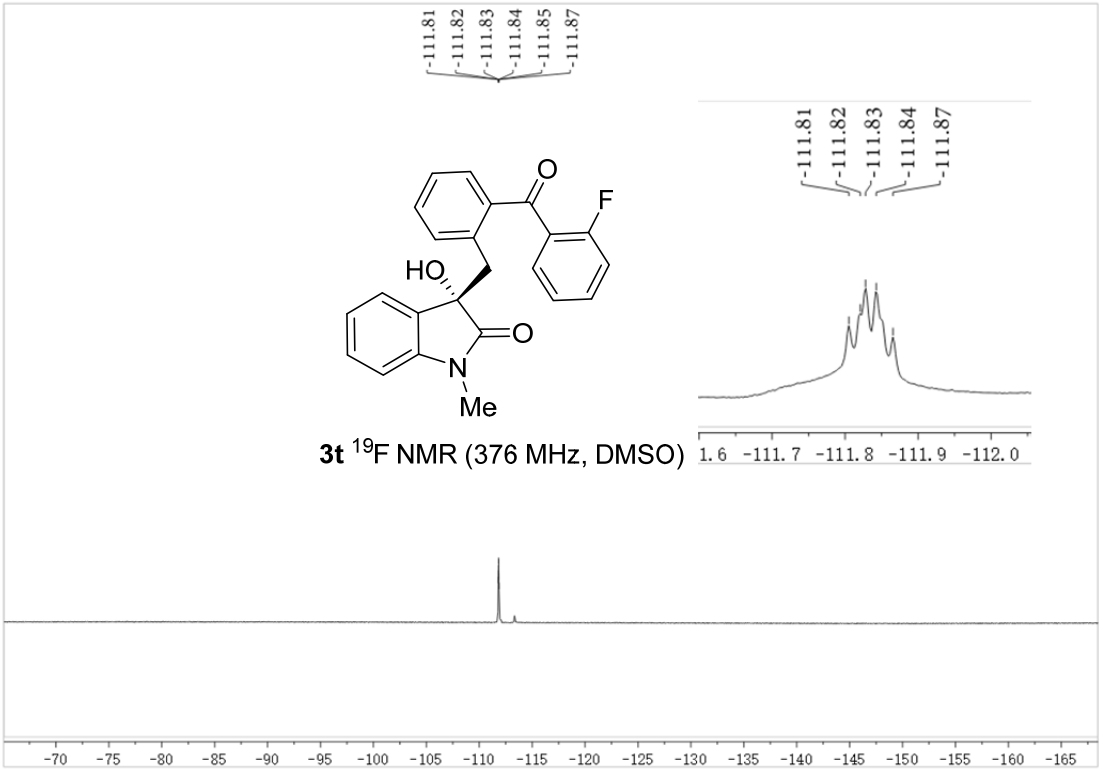
3s ^{13}C NMR (101 MHz, $CDCl_3$)



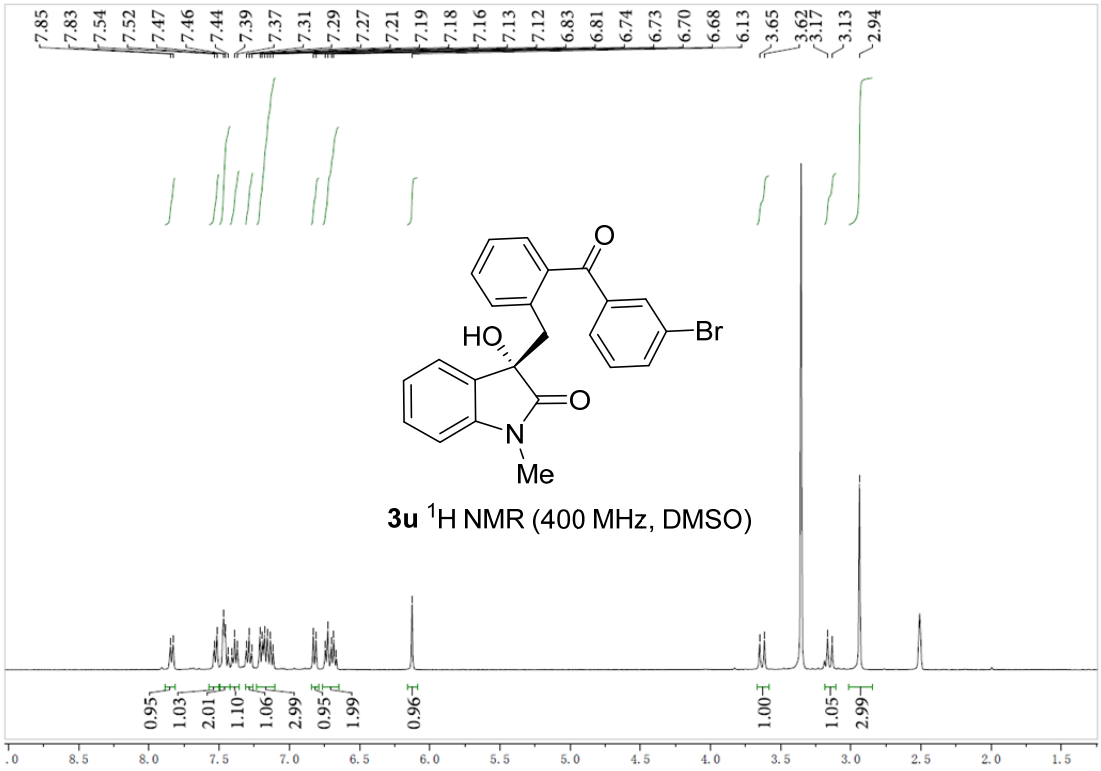
3t ^{1}H NMR (400 MHz, DMSO)



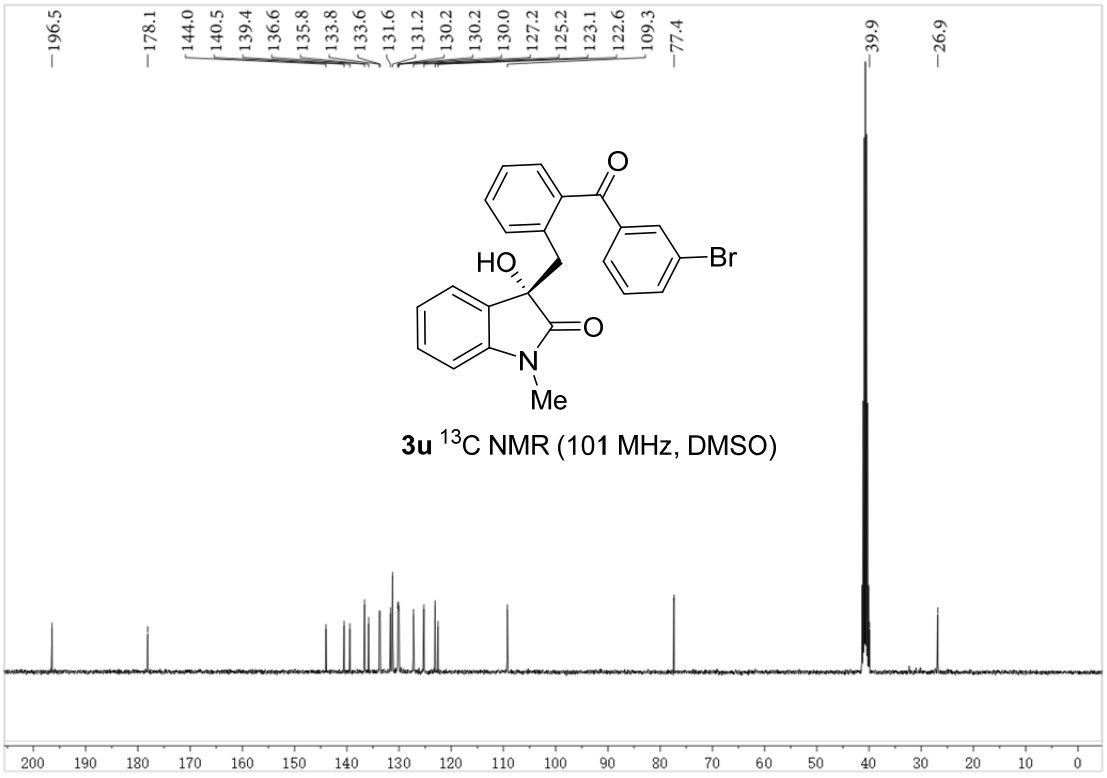
3t ^{13}C NMR (101 MHz, DMSO)



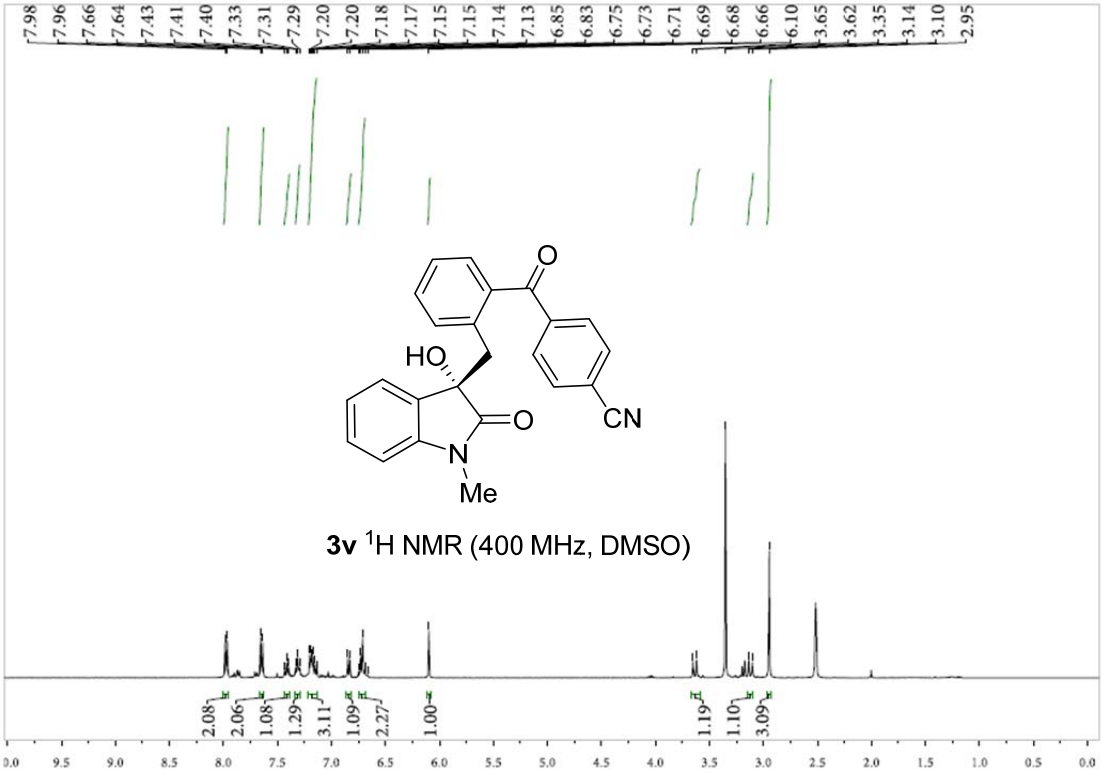
3t ^{19}F NMR (376 MHz, DMSO)



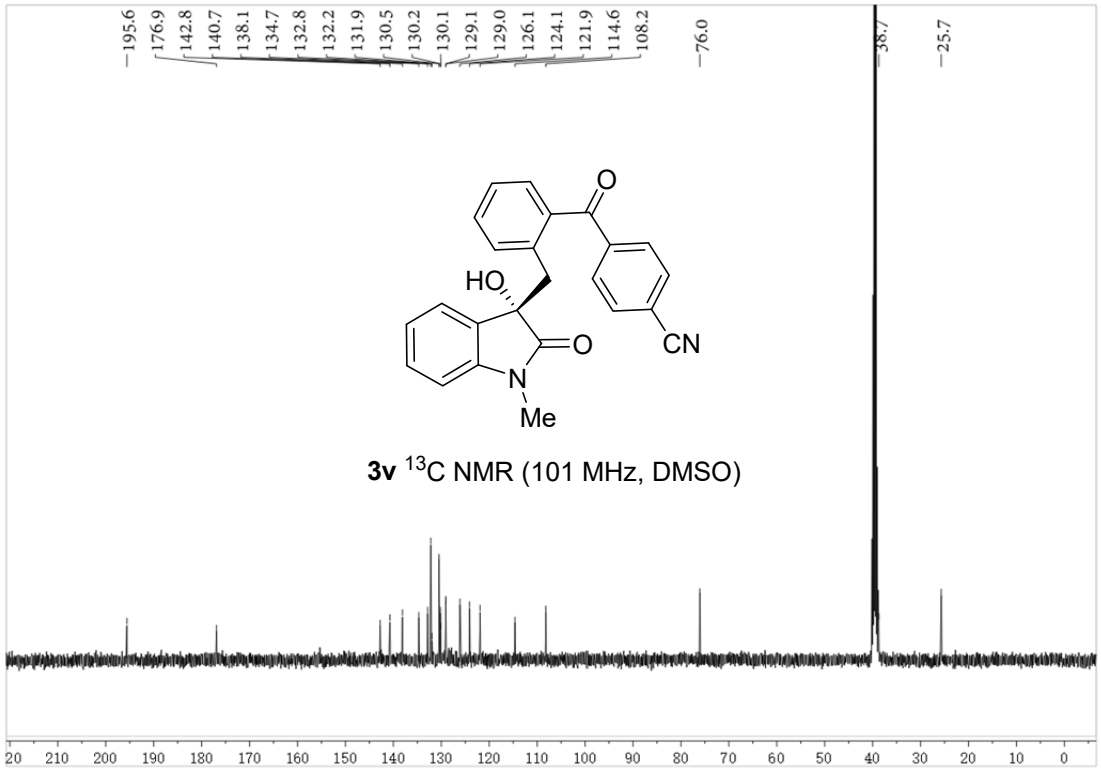
3u ^{1}H NMR (400 MHz, DMSO)



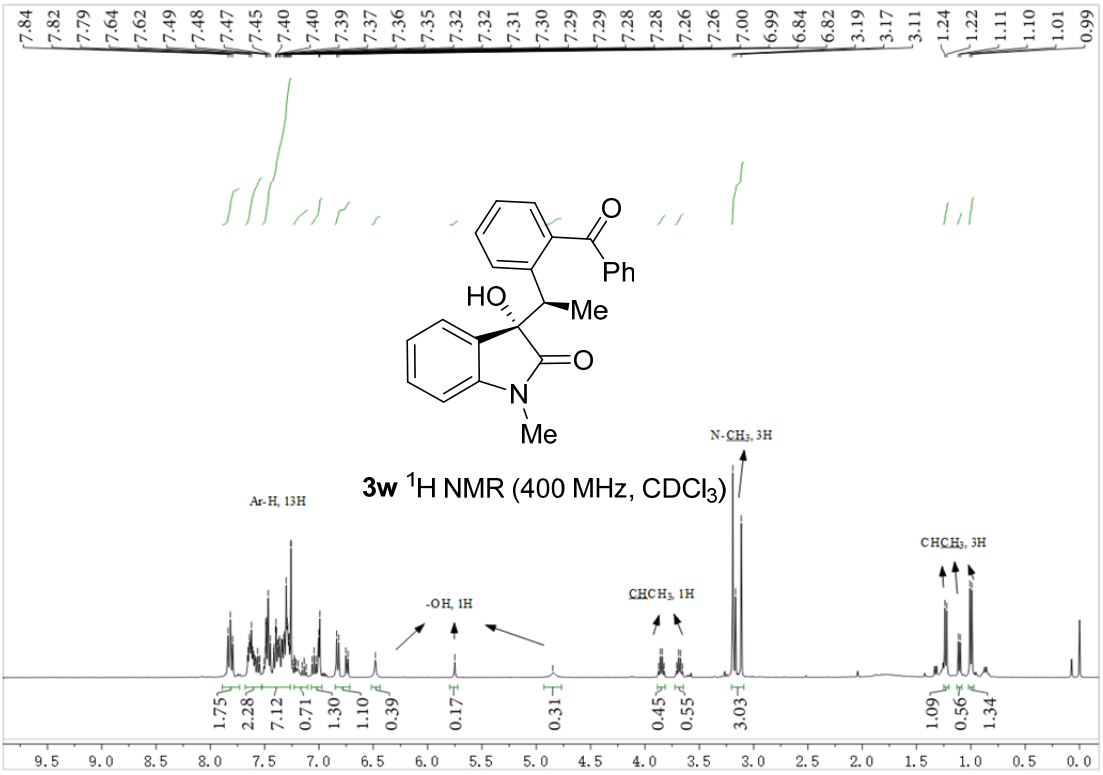
3u ^{13}C NMR (101 MHz, DMSO)



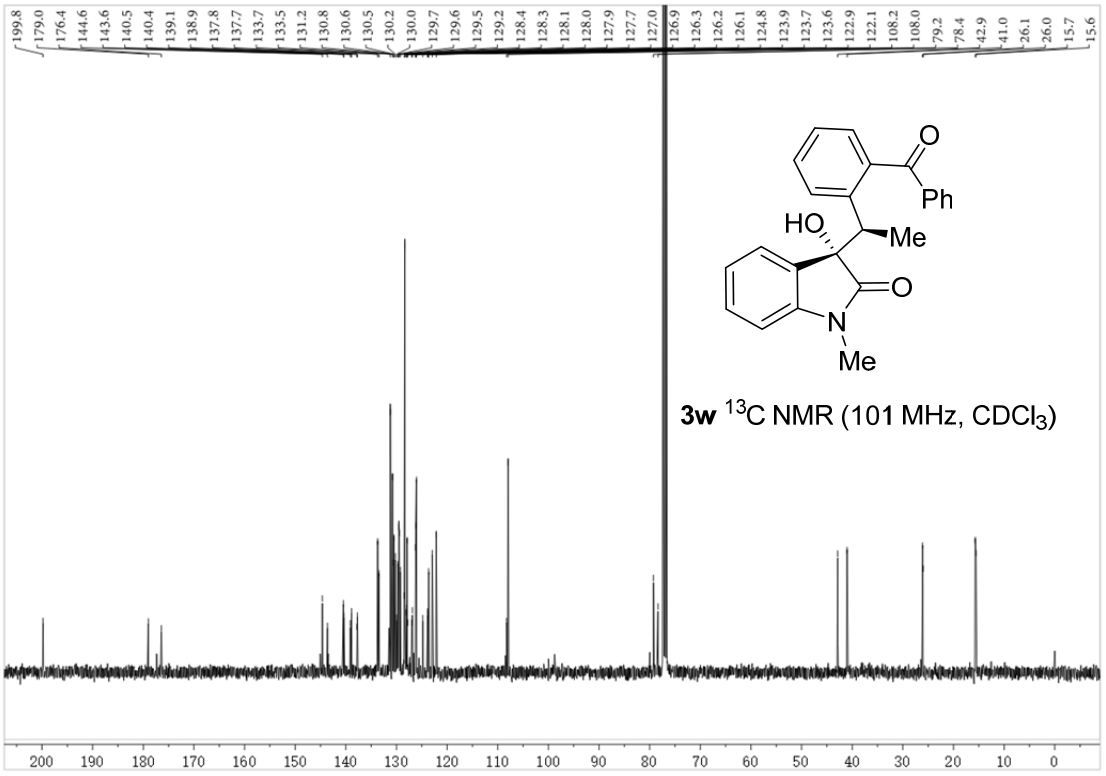
3v ^{1}H NMR (400 MHz, DMSO)



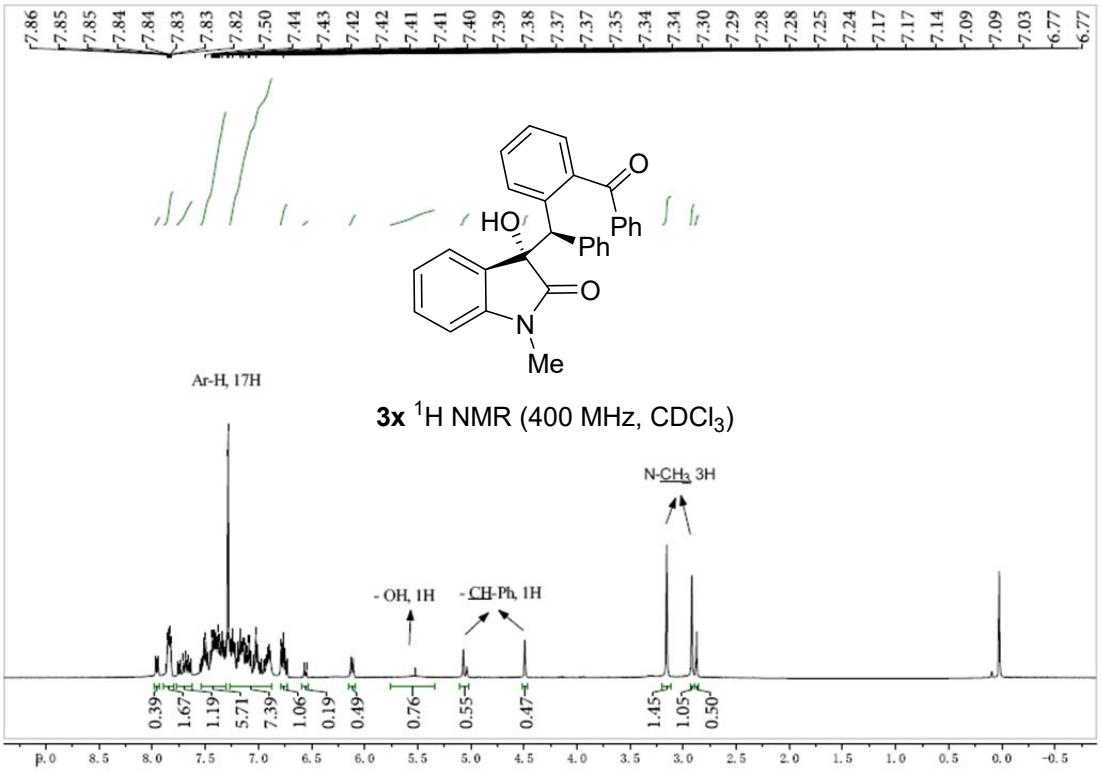
3v ^{13}C NMR (101 MHz, DMSO)



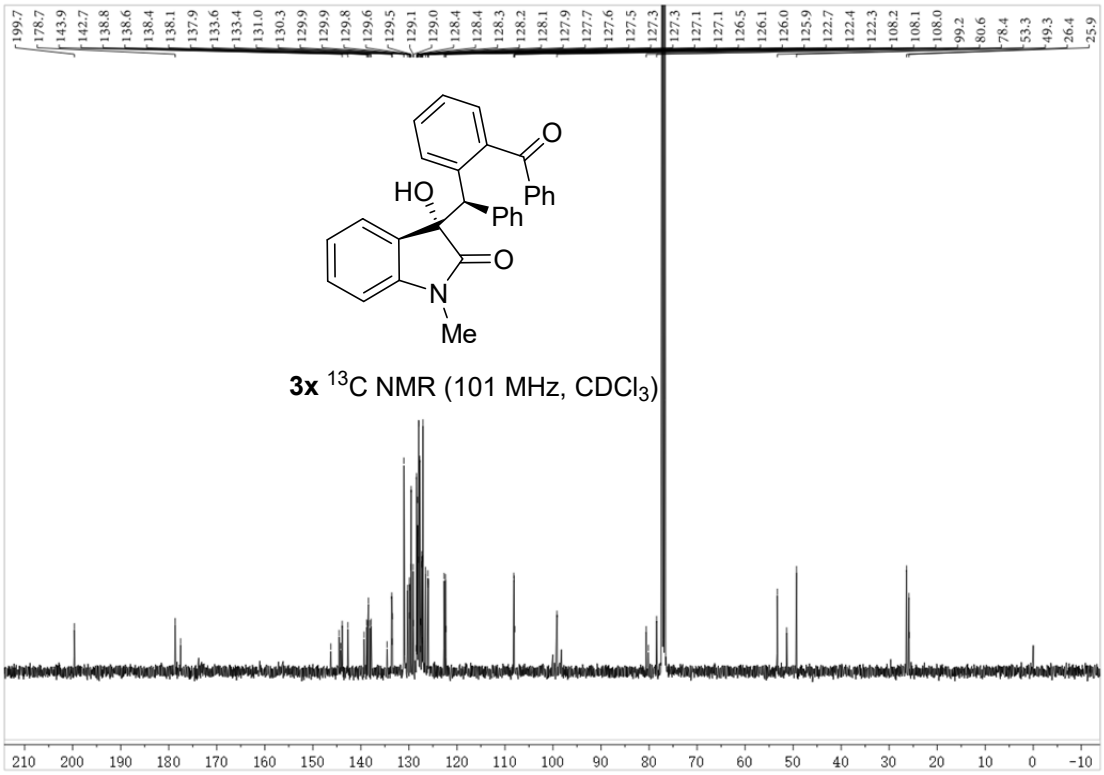
3w ^{1}H NMR (400 MHz, $CDCl_3$)



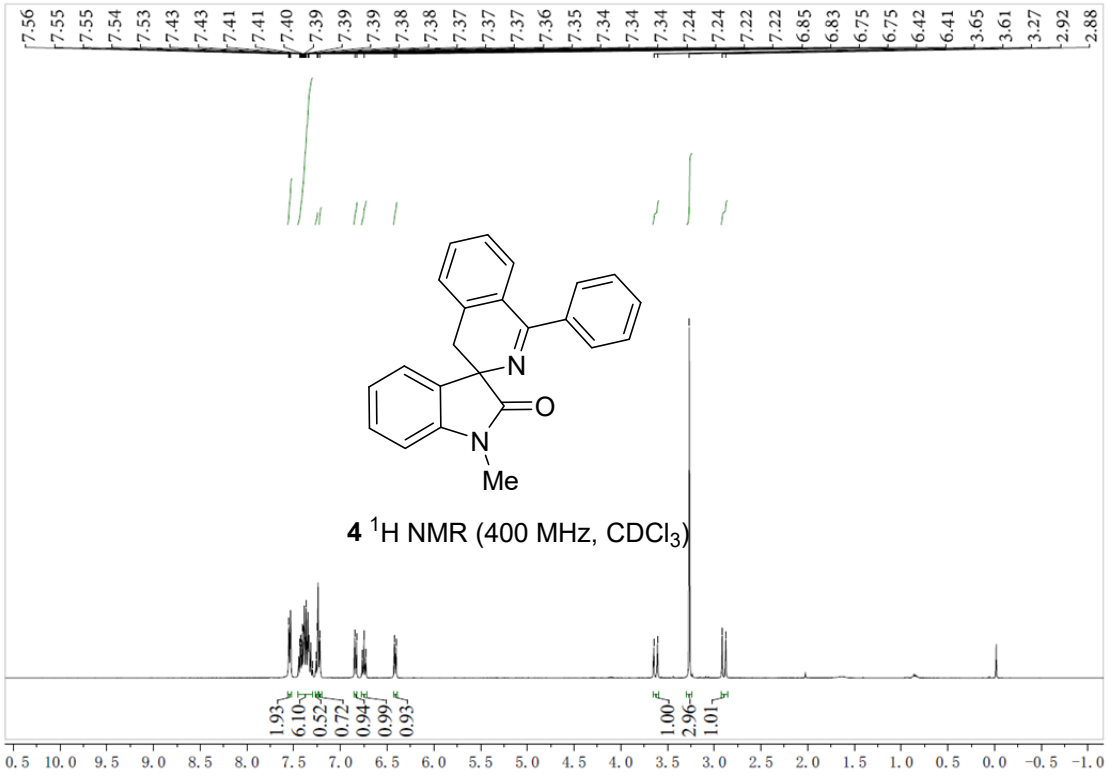
3w ^{13}C NMR (101 MHz, $CDCl_3$)



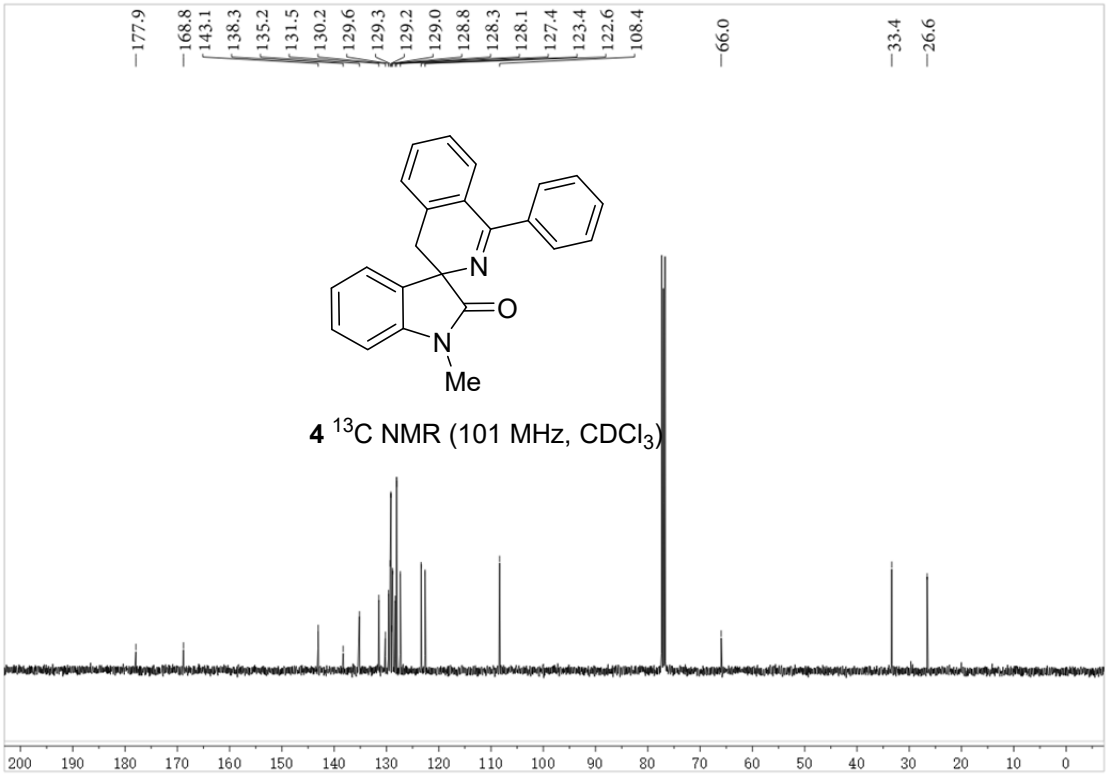
3x ^{1}H NMR (400 MHz, $CDCl_3$)



3x ^{13}C NMR (101 MHz, $CDCl_3$)



4 ^{1}H NMR (400 MHz, $CDCl_3$)

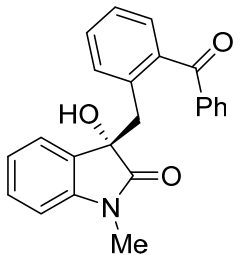


4 ^{13}C NMR (101 MHz, $CDCl_3$)

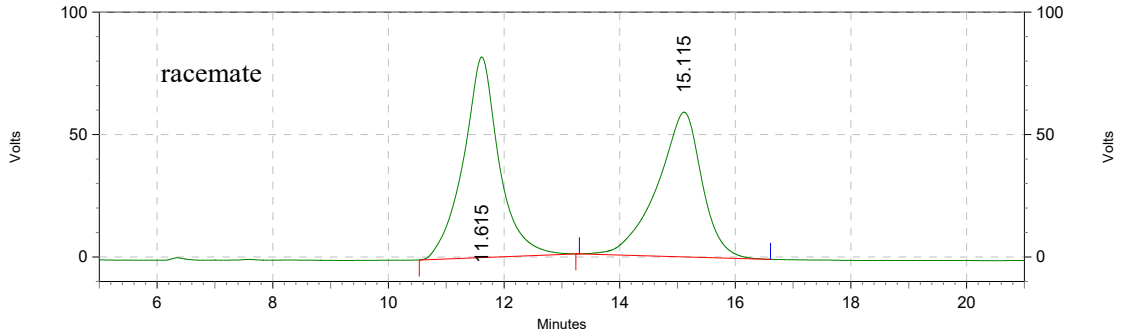
6. Chiral HPLC data

HPLC parameters

Compound	Column	Eluents	Flow rate
3a	Chiral AD-H column	Hexane/*i*-PrOH(80/20)	1mL/min
3b	Chiral AD-H column	Hexane/*i*-PrOH(80/20)	1mL/min
3c	Chiral AD-H column	Hexane/*i*-PrOH(80/20)	1mL/min
3d	Chiral AD-H column	Hexane/*i*-PrOH(80/20)	1mL/min
3e	Chiral AD-H column	Hexane/*i*-PrOH(80/20)	1mL/min
3f	Chiral IA column	Hexane/*i*-PrOH(80/20)	1mL/min
3g	Chiral AD-H column	Hexane/*i*-PrOH(80/20)	1mL/min
3h	Chiral IA column	Hexane/*i*-PrOH(80/20)	1mL/min
3i	Chiral AD-H column	Hexane/*i*-PrOH(80/20)	1mL/min
3j	Chiral AD-H column	Hexane/*i*-PrOH(80/20)	1mL/min
3k	Chiral AD-H column	Hexane/*i*-PrOH(90/10)	1mL/min
3l	Chiral AD-H column	Hexane/*i*-PrOH(90/10)	1mL/min
3m	Chiral AD-H column	Hexane/*i*-PrOH(80/20)	1mL/min
3n	Chiral AD-H column	Hexane/*i*-PrOH(80/20)	1mL/min
3o	Chiral AD-H column	Hexane/*i*-PrOH(80/20)	1mL/min
3p	Chiral AD-H column	Hexane/*i*-PrOH(80/20)	1mL/min
3q	Chiral AD-H column	Hexane/*i*-PrOH(80/20)	1mL/min
3r	Chiral AD-H column	Hexane/*i*-PrOH(80/20)	1mL/min
3s	Chiral OD column	Hexane/*i*-PrOH(97/3)	1mL/min
3t	Chiral AD-H column	Hexane/*i*-PrOH(80/20)	1mL/min
3u	Chiral AD-H column	Hexane/*i*-PrOH(85/15)	1mL/min
3v	Chiral AS column	Hexane/*i*-PrOH(80/20)	1mL/min
3w	Chiral IC column	Hexane/*i*-PrOH(70/30)	1mL/min
3x	Chiral IC column	Hexane/*i*-PrOH(70/30)	1mL/min
4	Chiral AD-H column	Hexane/*i*-PrOH(80/20)	1mL/min



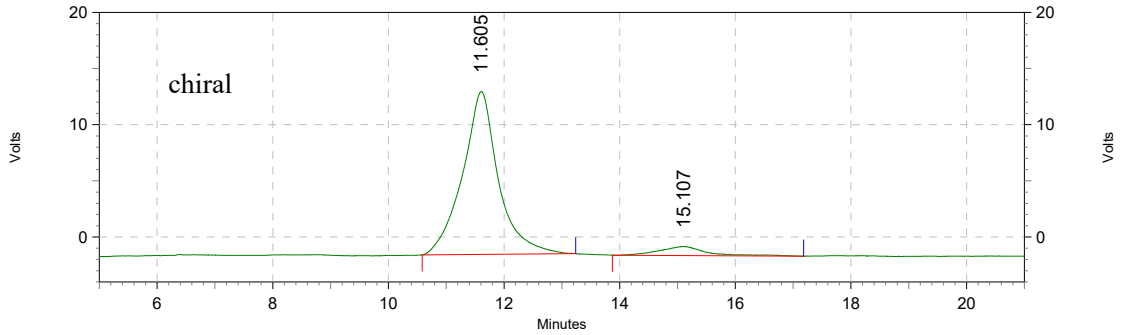
3a



UV1000-254nm

Results

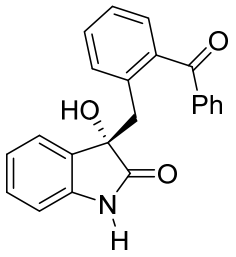
Retention time	Area	Area%	Height	Height%
11.615	3511714	51.619	81917	58.094
15.115	3162135	48.381	59091	41.906
Totals	6673849	100.000	141008	100.000



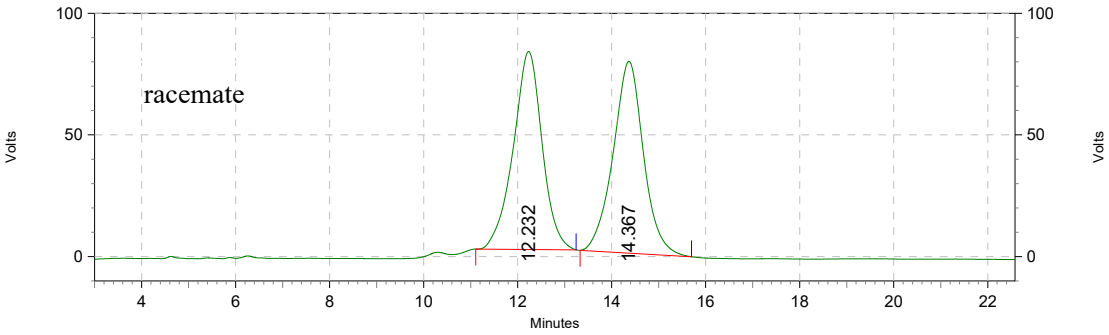
UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
11.605	624930	93.164	14498	94.740
15.107	45854	6.836	805	5.260
Totals	670784	100.000	15303	100.000



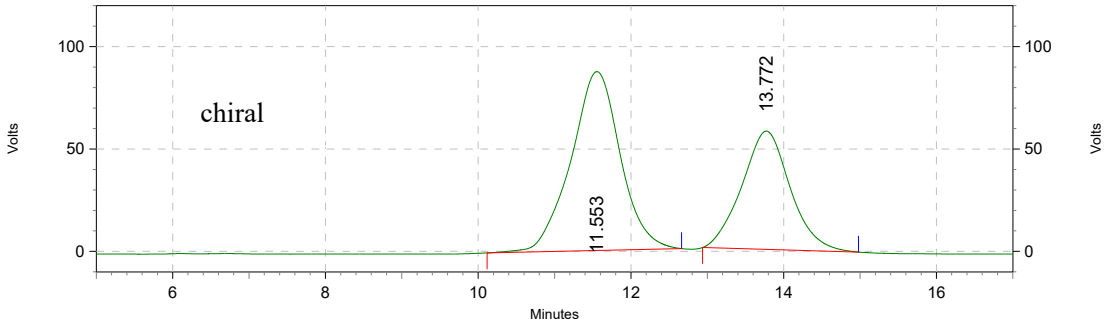
3b



UV1000-254nm

Results

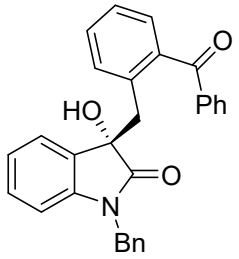
Retention time	Area	Area%	Height	Height%
12.232	3478882	49.563	81338	50.779
14.367	3540268	50.437	78841	49.221
Totals	7019150	100.000	160179	100.000



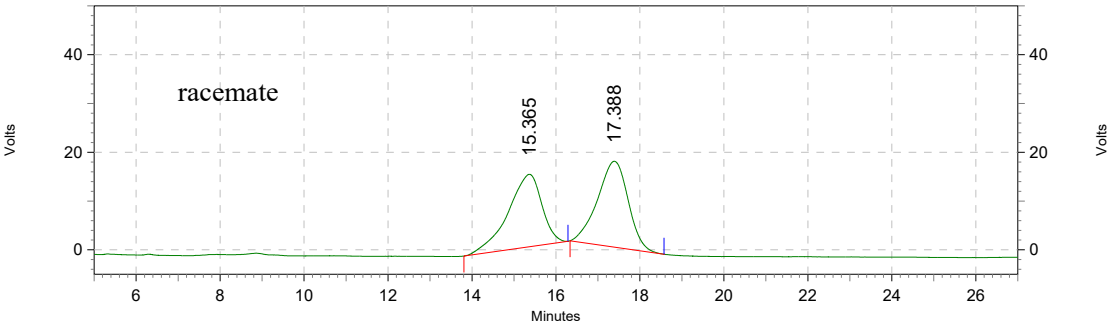
UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
11.553	3913892	60.655	87332	60.187
13.772	2538857	39.345	57770	39.813
Totals	6452749	100.000	145102	100.000



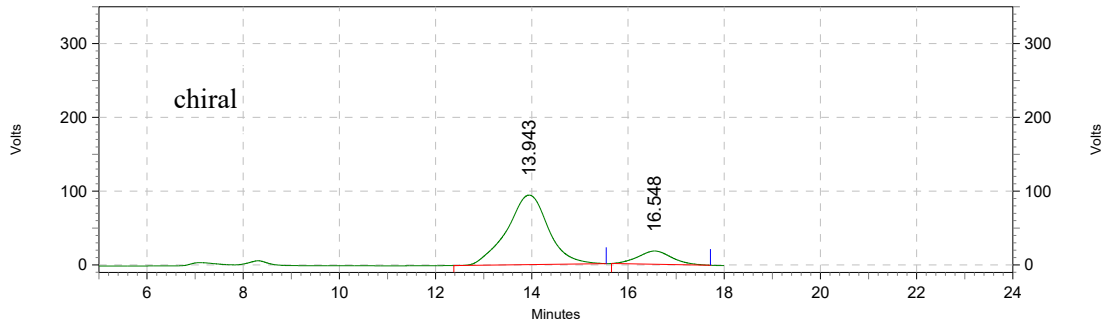
3c



UV1000-254nm

Results

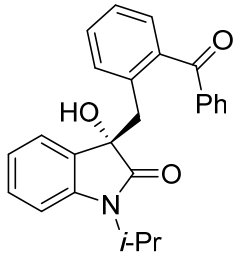
Retention time	Area	Area%	Height	Height%
15.365	835001	48.351	14847	45.783
17.388	891960	51.649	17582	54.217
Totals	1726961	100.000	32429	100.000



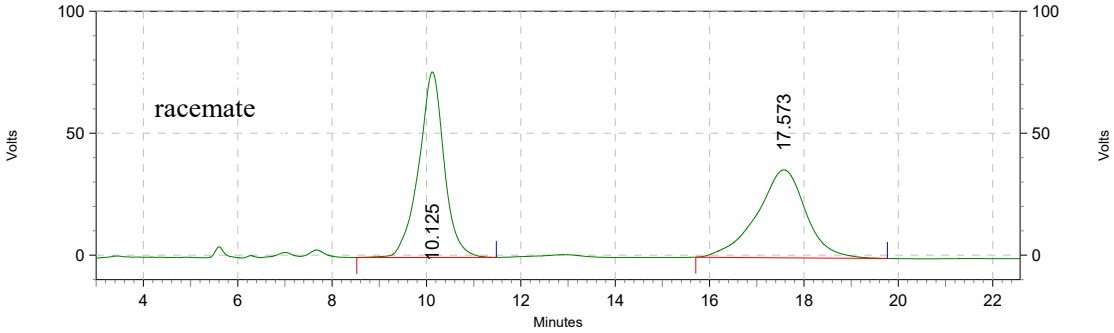
UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
13.943	5624287	86.516	94138	84.000
16.548	876577	13.484	17931	16.000
Totals	6500864	100.000	112069	100.000



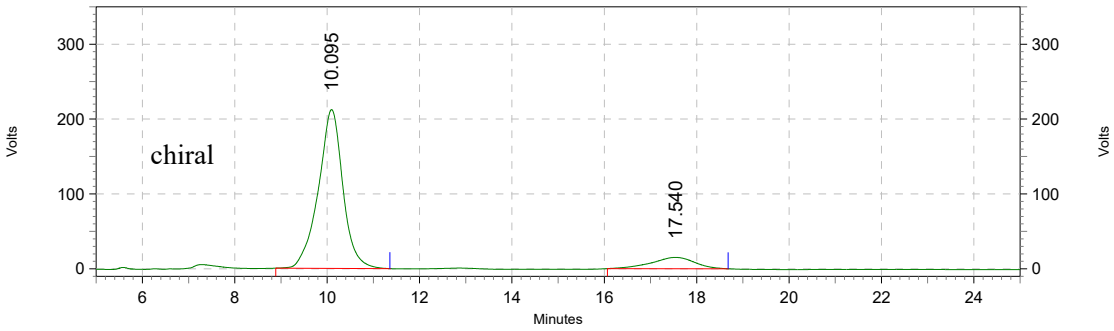
3d



UV1000-254nm

Results

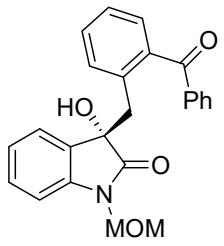
Retention time	Area	Area%	Height	Height%
10.125	2846357	52.301	76010	67.855
17.573	2595944	47.699	36008	32.145
Totals	5442301	100.000	112018	100.000



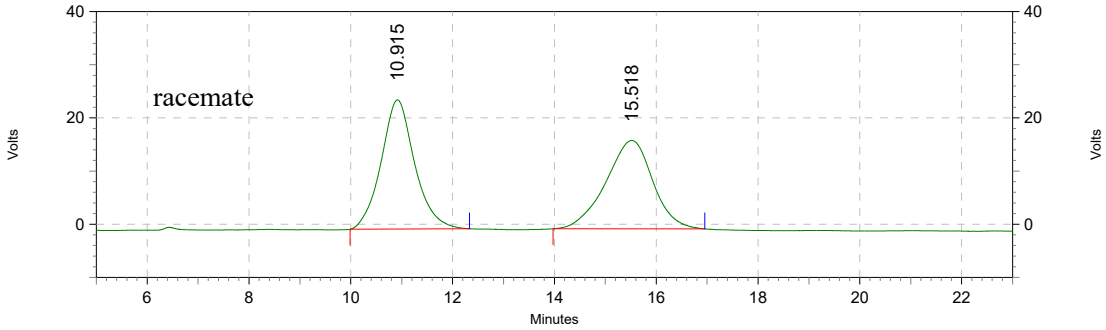
UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
10.095	7824474	88.836	212101	93.345
17.540	983311	11.164	15121	6.655
Totals	8807785	100.000	227222	100.000



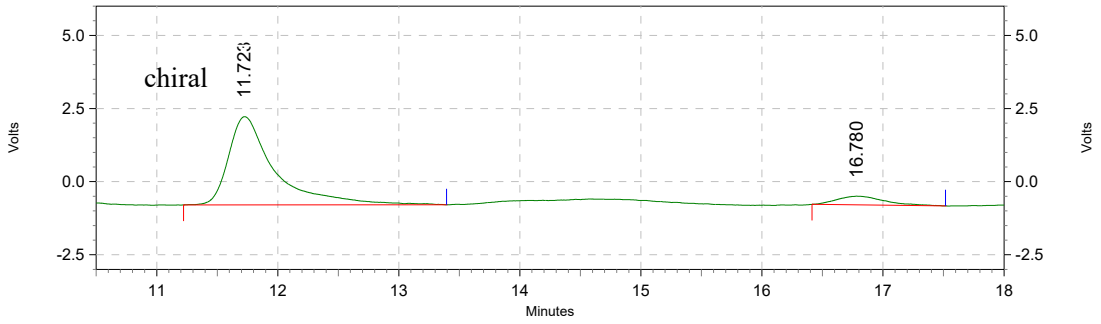
3e



UV1000-254nm

Results

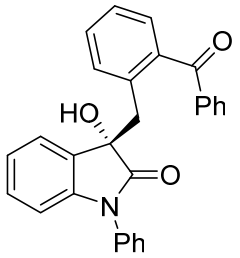
Retention time	Area	Area%	Height	Height%
10.915	1109496	50.985	24302	59.385
15.518	1066629	49.015	16621	40.615
Totals	2176125	100.000	40923	100.000



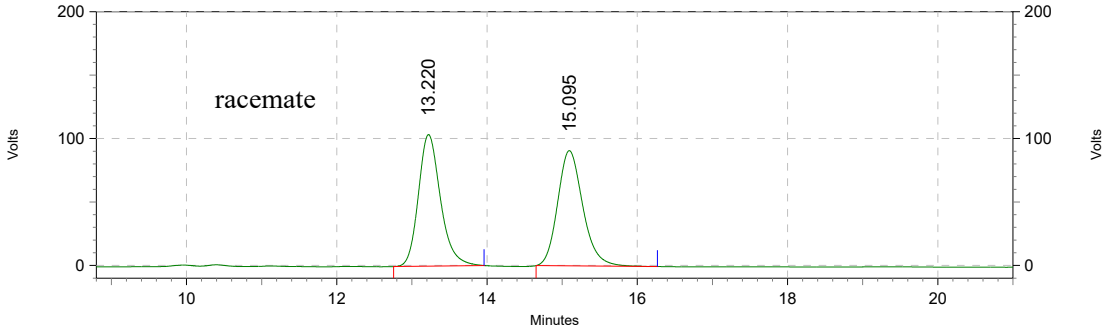
UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
11.723	80063	92.892	3014	91.030
16.780	8023	7.108	297	8.970
Totals	88086	100.000	3311	100.000



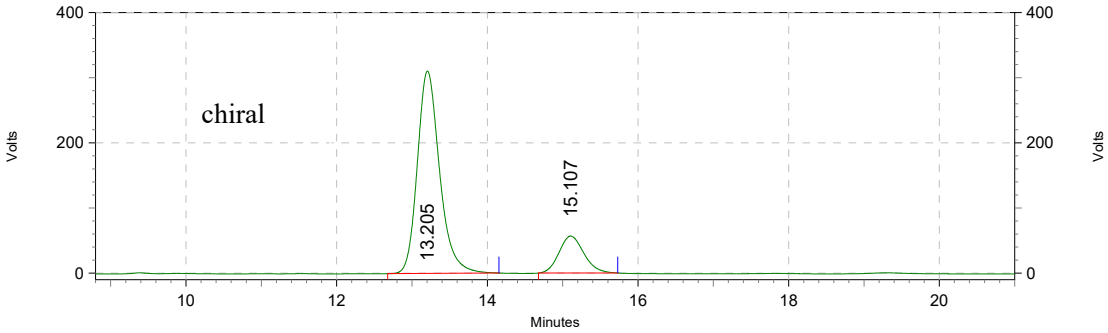
3f



UV1000-254nm

Results

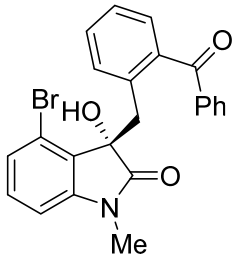
Retention time	Area	Area%	Height	Height%
13.220	2116708	50.054	103732	53.319
15.095	2112153	49.946	90819	46.681
Totals	4228861	100.000	194551	100.000



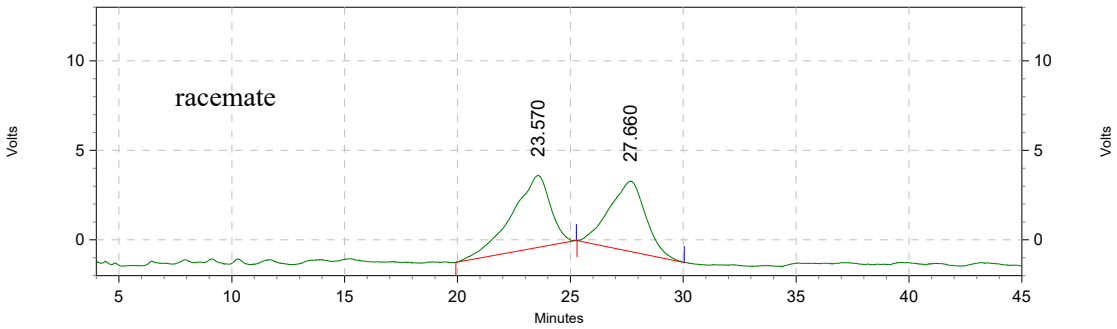
UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
13.205	6371168	83.052	310710	84.560
15.107	1300123	16.948	56735	15.440
Totals	7671291	100.000	367445	100.000



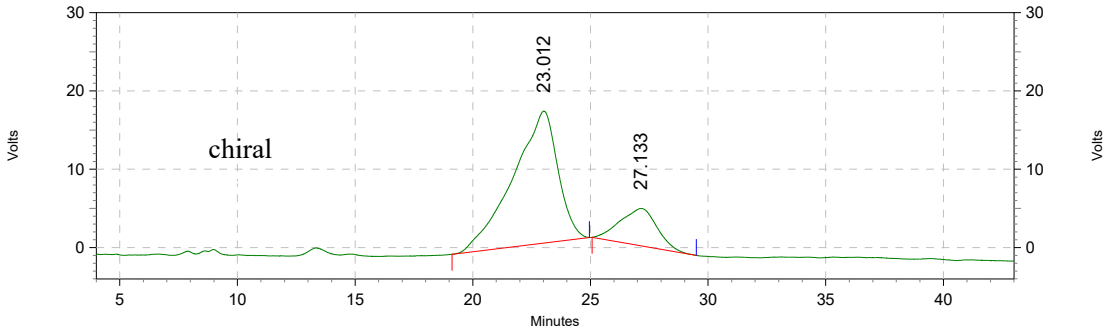
3g



UV1000-254nm

Results

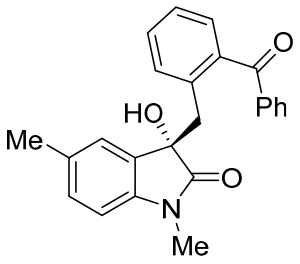
Retention time	Area	Area%	Height	Height%
23.570	481398	50.198	4017	50.541
27.660	440848	49.802	3931	49.459
Totals	922246	100.000	7948	100.000



UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
23.012	2240764	81.162	16854	77.948
27.133	520089	18.838	4768	22.052
Totals	2760853	100.000	21622	100.000



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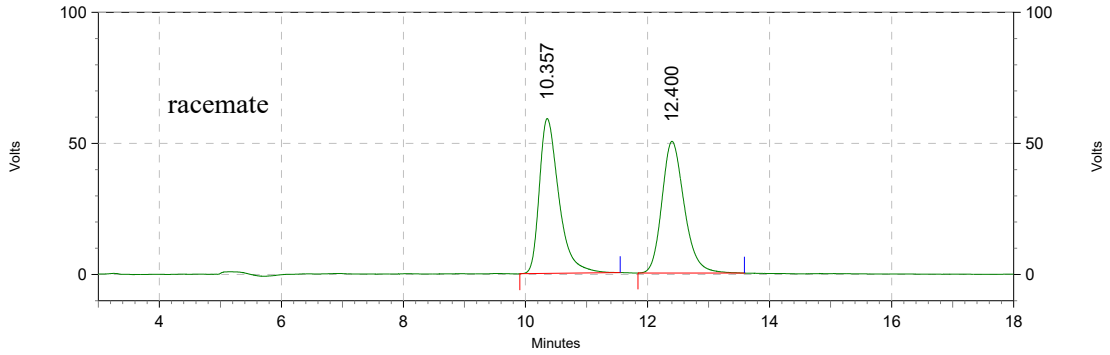
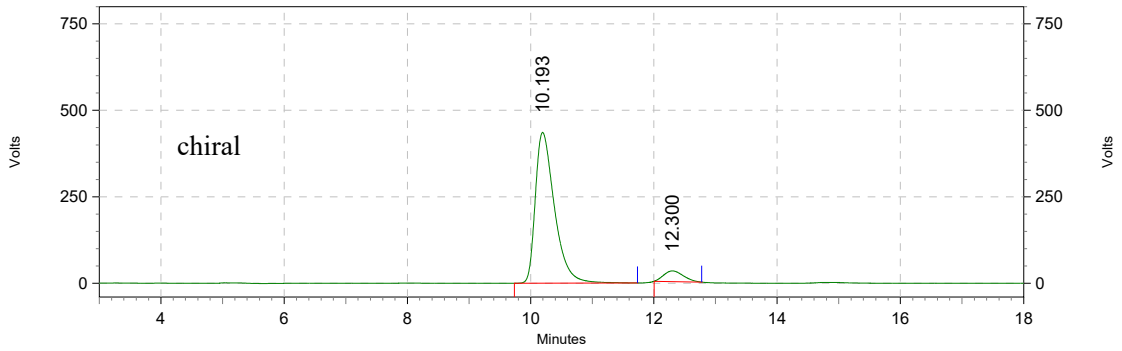


UV1000-254nm

Results

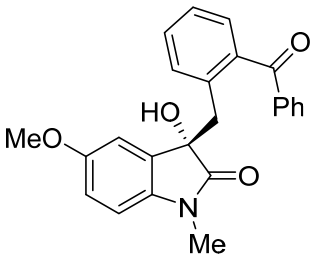
Retention time	Area	Area%	Height	Height%
10.357	1311490	50.706	59075	54.033
12.400	1274969	49.294	50257	45.967
Totals	2586459	100.000	109332	100.000



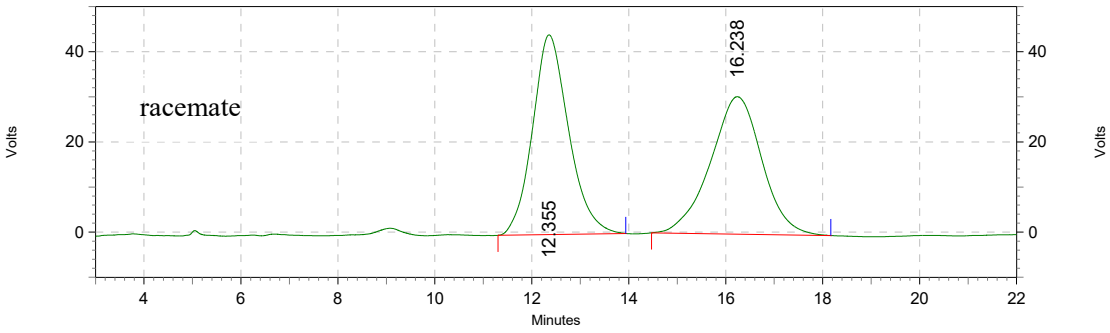
UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
10.193	12508331	94.800	436148	93.385
12.300	686111	5.200	30894	6.615
Totals	13194442	100.000	467042	100.000



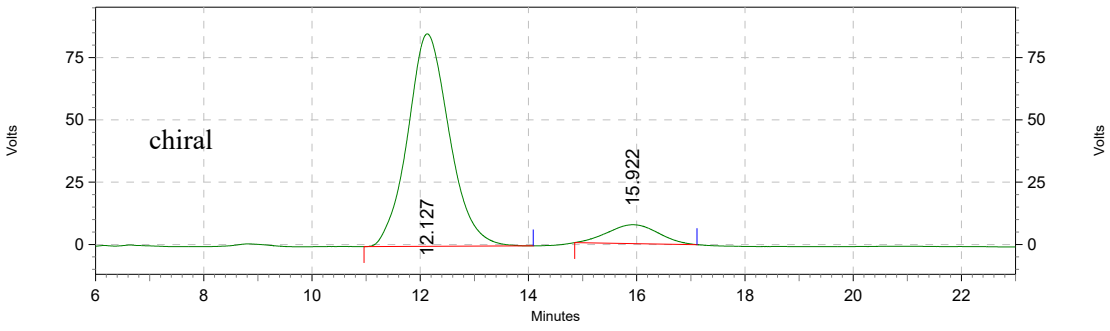
3i



UV1000-254nm

Results

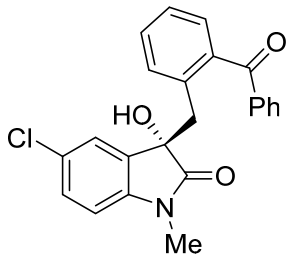
Retention time	Area	Area%	Height	Height%
12.355	2289632	50.472	44256	59.232
16.238	2246833	49.528	30460	40.768
Totals	4536465	100.000	74716	100.000



UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
12.127	4554744	92.743	85272	91.858
15.922	492464	7.257	7558	8.142
Totals	5047208	100.000	92830	100.000



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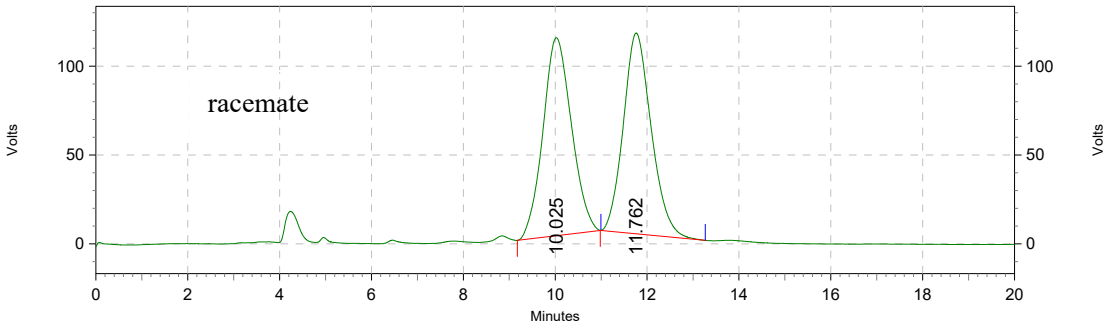
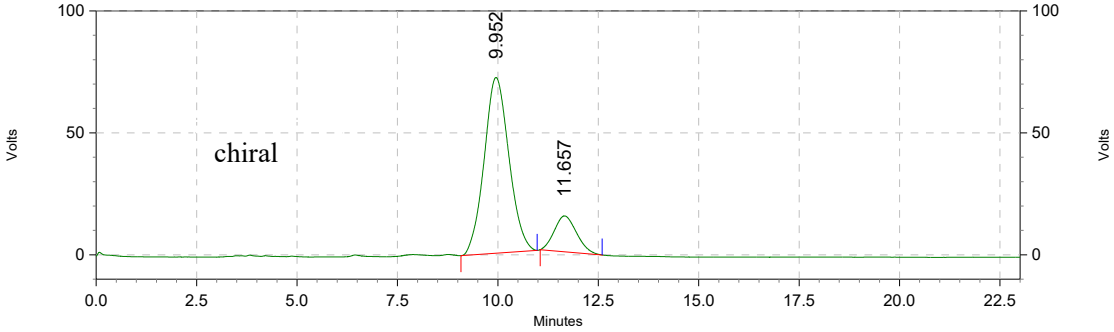


UV1000-254nm

Results

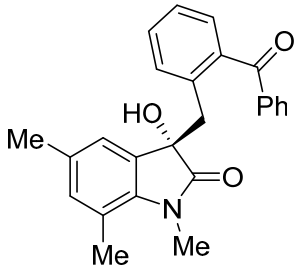
Retention time	Area	Area%	Height	Height%
10.025	4802543	50.212	111395	49.663
11.762	4761983	49.788	112909	50.337
Totals	9564526	100.000	224304	100.000



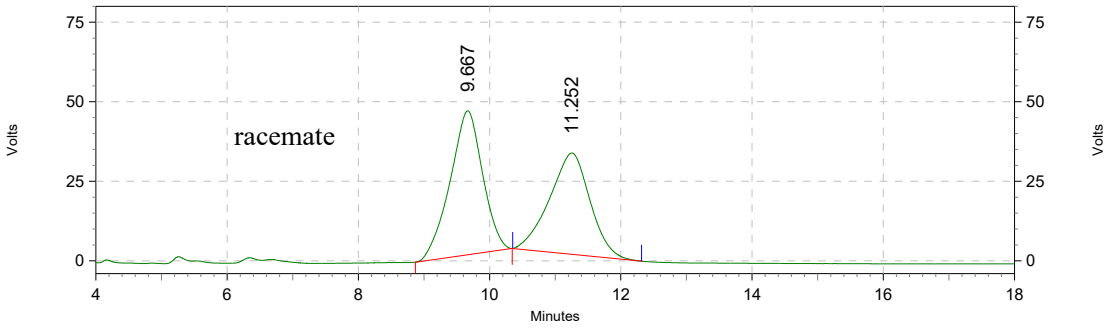
UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
9.952	3093973	84.494	72078	83.061
11.657	567811	15.506	14699	16.939
Totals	3661784	100.000	86777	100.000



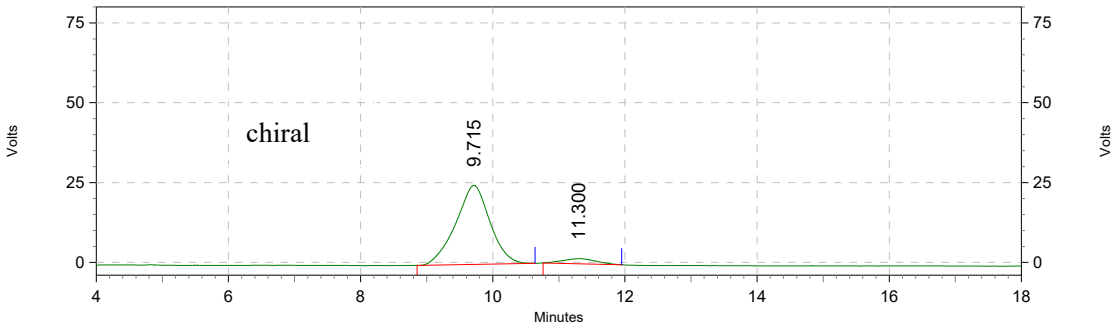
3k



UV1000-254nm

Results

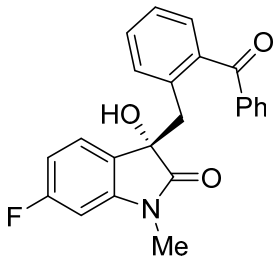
Retention time	Area	Area%	Height	Height%
9.667	1557386	50.361	45257	58.701
11.252	1535058	49.639	31840	41.299
Totals	3092444	100.000	77097	100.000



UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
9.715	889670	96.153	24760	93.973
11.300	35595	3.847	1588	6.027
Totals	925265	100.000	26348	100.000



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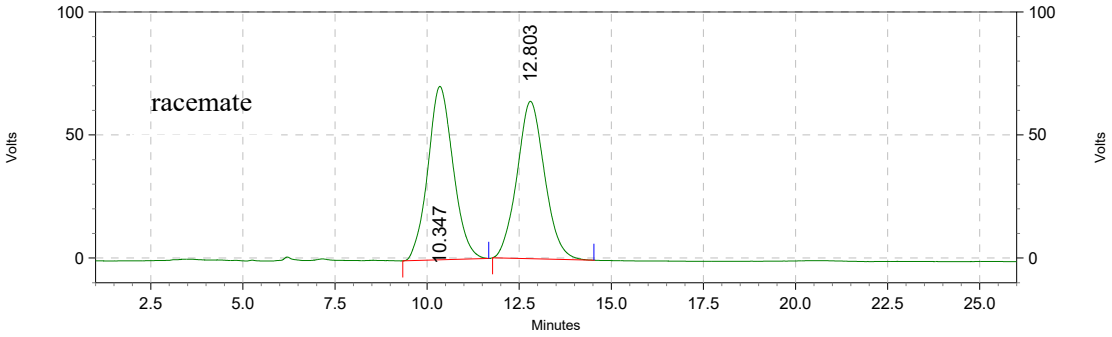
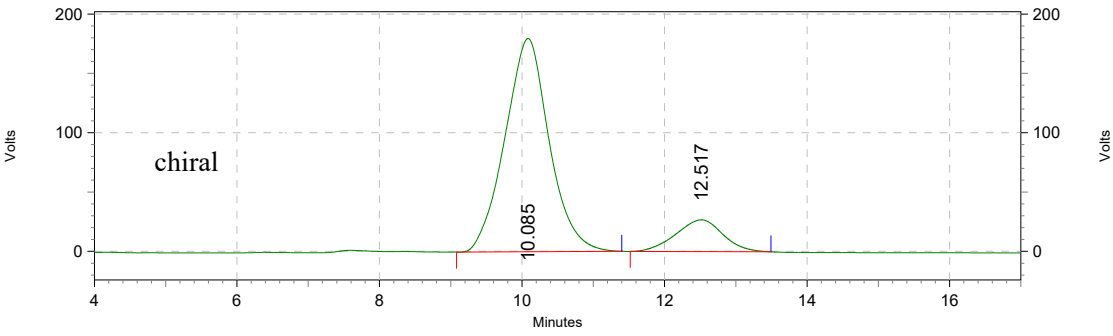


UV1000-254nm

Results

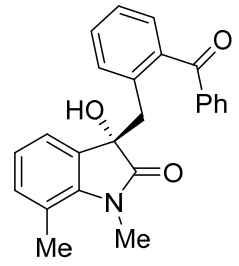
Retention time	Area	Area%	Height	Height%
10.347	3363518	50.287	70440	52.422
12.803	3325166	49.713	63932	47.578
Totals	6688684	100.000	134372	100.000



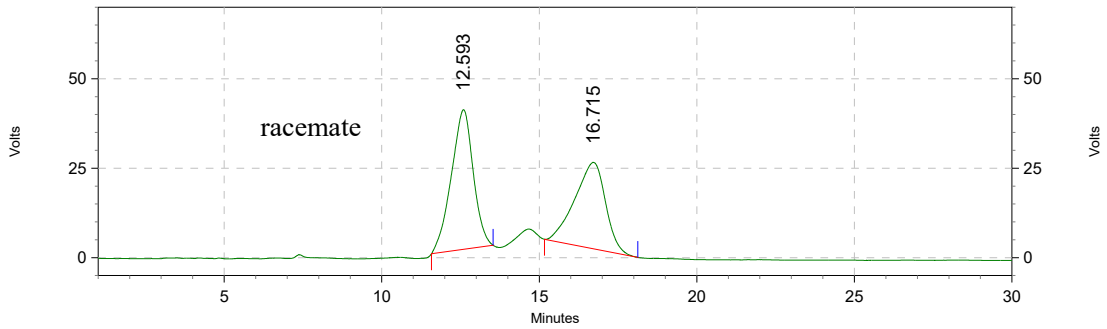
UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
10.085	7743223	87.302	179735	87.037
12.517	1229051	12.698	26770	12.963
Totals	8972274	100.000	206505	100.000



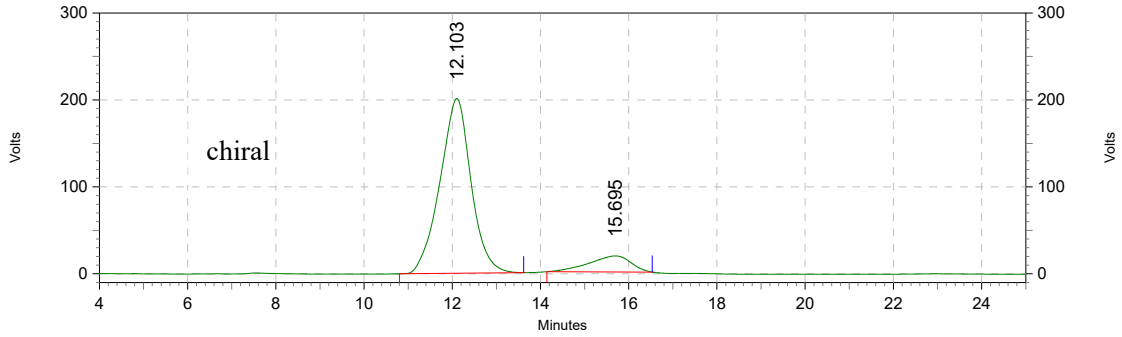
3m



UV1000-254nm

Results

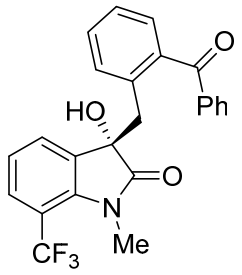
Retention time	Area	Area%	Height	Height%
12.593	1891611	53.651	39036	61.777
16.715	1634150	46.349	24153	38.223
Totals	3525761	100.000	63189	100.000



UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
12.103	15010420	92.910	200990	91.596
15.695	1215307	7.090	18442	8.404
Totals	16225727	100.000	219432	100.000



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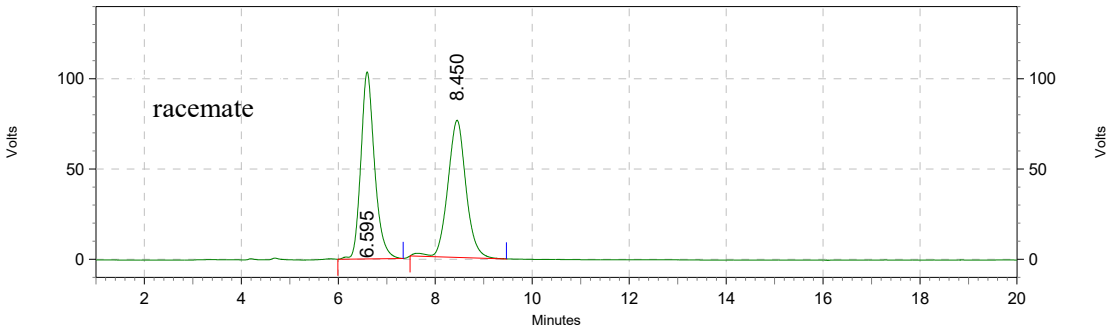
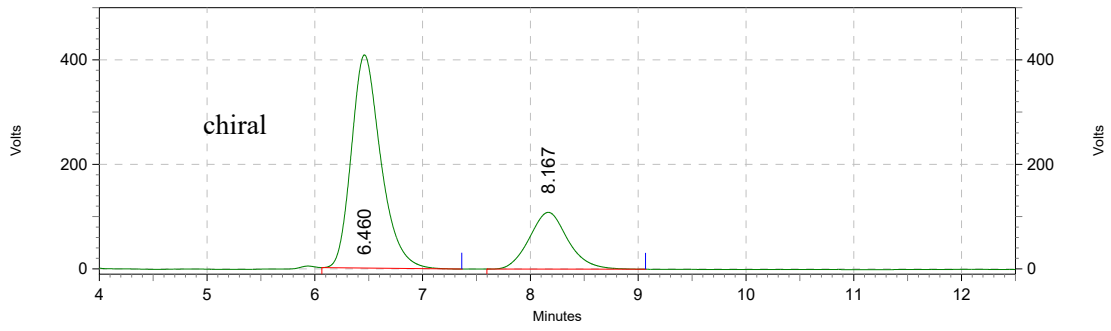


UV1000-254nm

Results

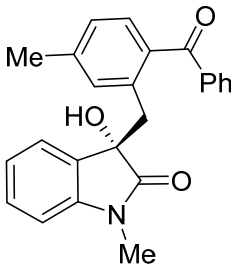
Retention time	Area	Area%	Height	Height%
6.595	2030295	50.656	103559	57.697
8.450	1977749	49.344	75929	42.303
Totals	4008044	100.000	179488	100.000



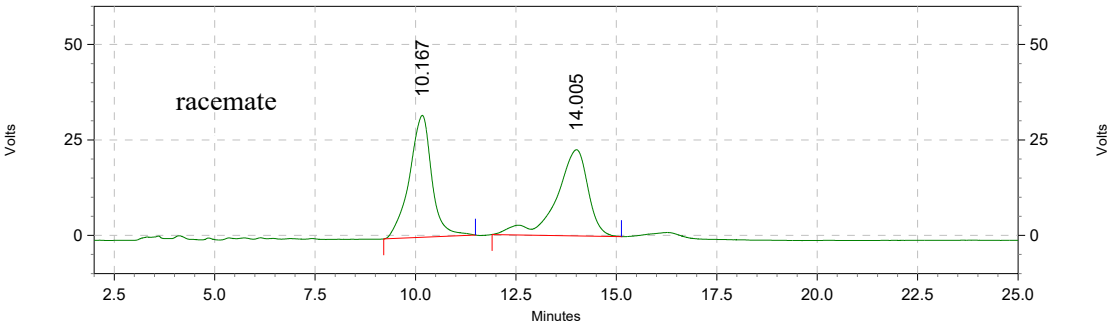
UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
6.460	7750194	75.132	407969	78.958
8.167	2704346	24.868	108723	21.042
Totals	10454540	100.000	516692	100.000



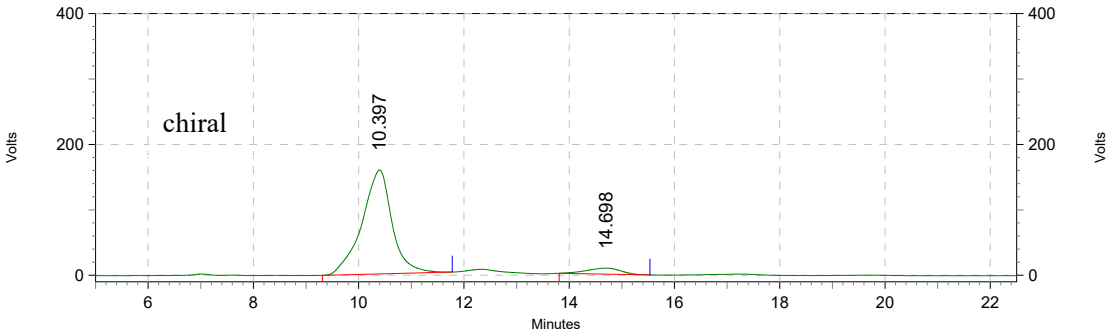
3o



UV1000-254nm

Results

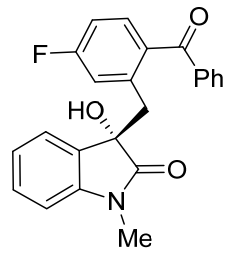
Retention time	Area	Area%	Height	Height%
10.167	1236643	50.048	31933	58.602
14.005	1234248	49.952	22558	41.398
Totals	2470891	100.000	54491	100.000



UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
10.397	6885792	95.355	160258	94.572
14.698	411981	4.645	9198	5.428
Totals	7297773	100.000	169456	100.000



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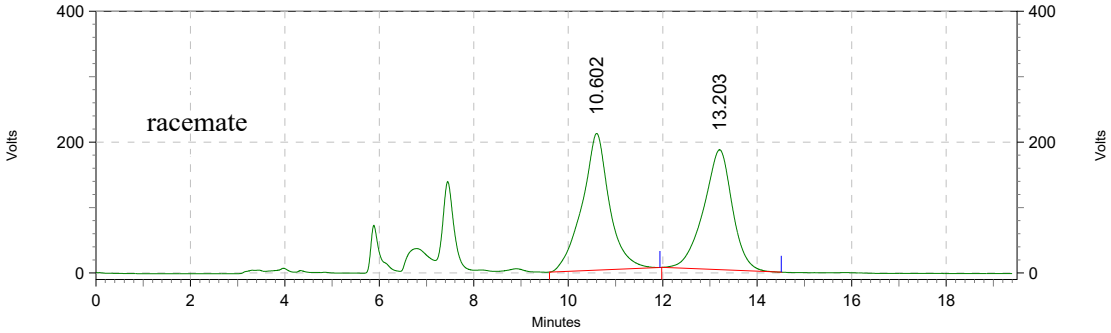
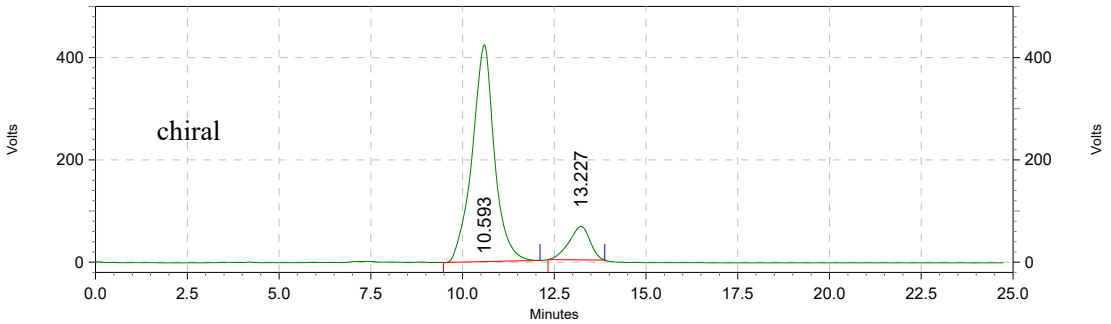


UV1000-254nm

Results

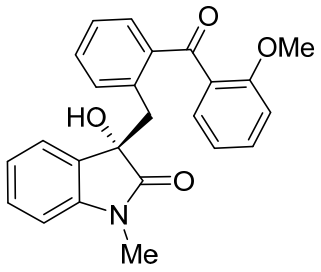
Retention time	Area	Area%	Height	Height%
10.602	8337152	51.863	208848	53.246
13.203	7738133	48.137	183382	46.754
Totals	16075285	100.000	392230	100.000



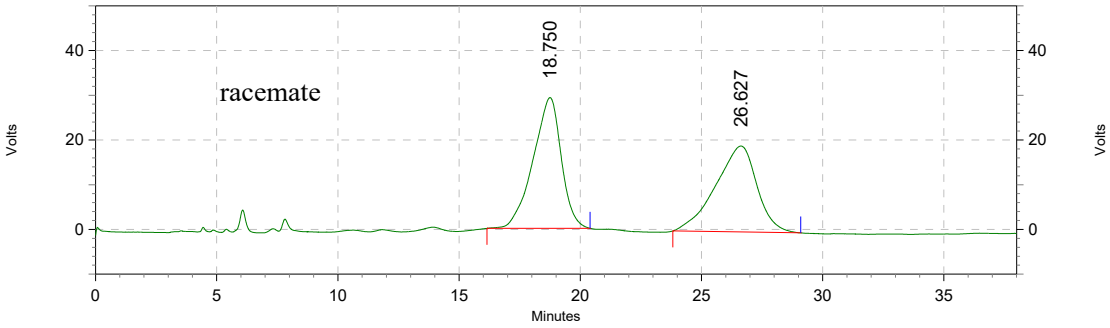
UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
10.593	17866467	87.427	423847	86.630
13.227	2616308	12.573	65414	13.370
Totals	20482775	100.000	489261	100.000



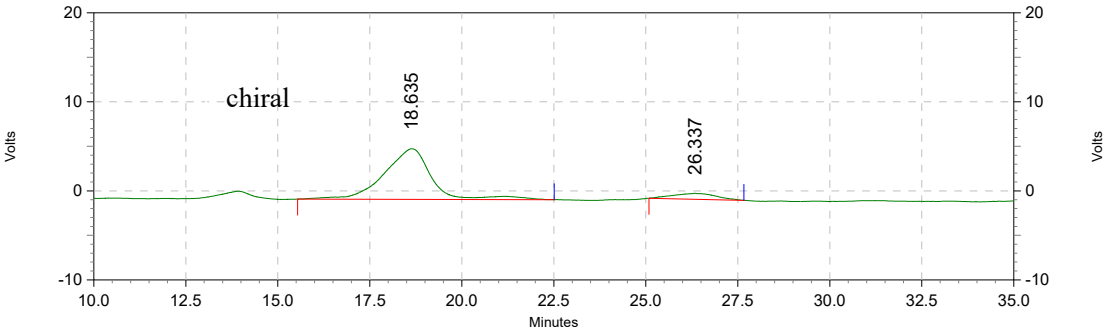
3q



UV1000-254nm

Results

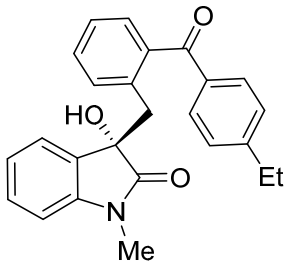
Retention time	Area	Area%	Height	Height%
18.750	2366396	50.853	29257	60.349
26.627	2286969	49.147	19223	39.651
Totals	4653365	100.000	48480	100.000



UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
18.635	758989	93.423	5685	89.485
26.337	53433	6.577	668	10.515
Totals	563823	100.000	6353	100.000



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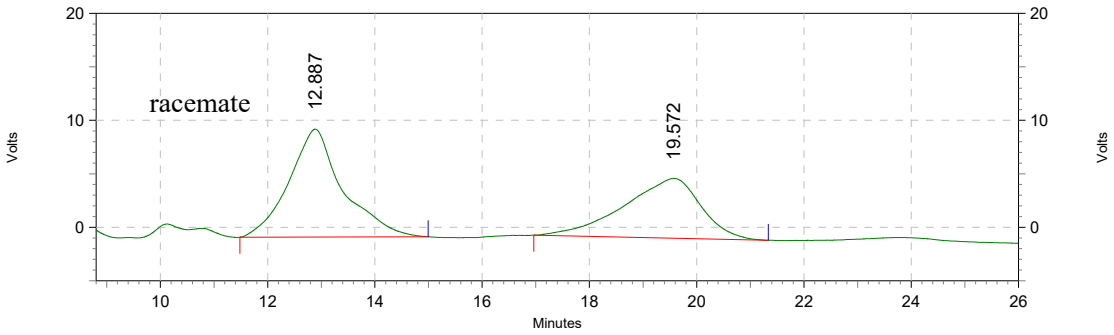
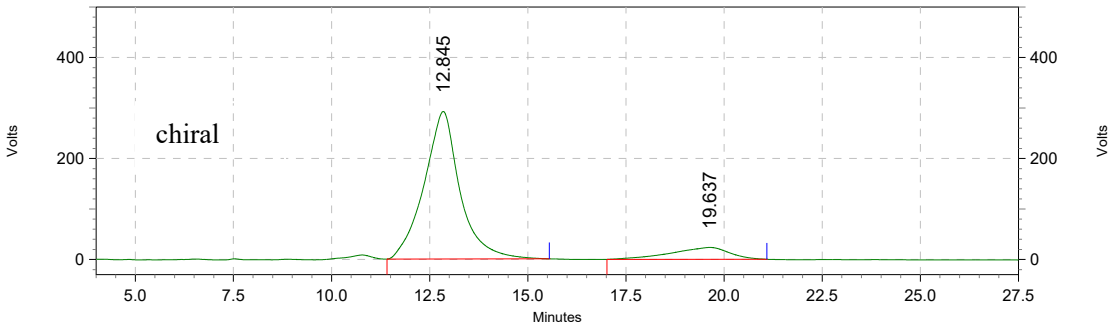


UV1000-254nm

Results

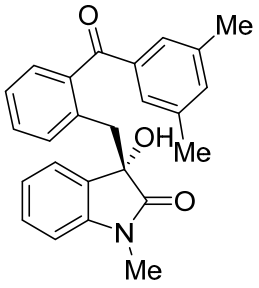
Retention time	Area	Area%	Height	Height%
12.887	702389	51.824	10088	64.288
19.572	652946	48.176	5604	35.712
Totals	1355335	100.000	15692	100.000



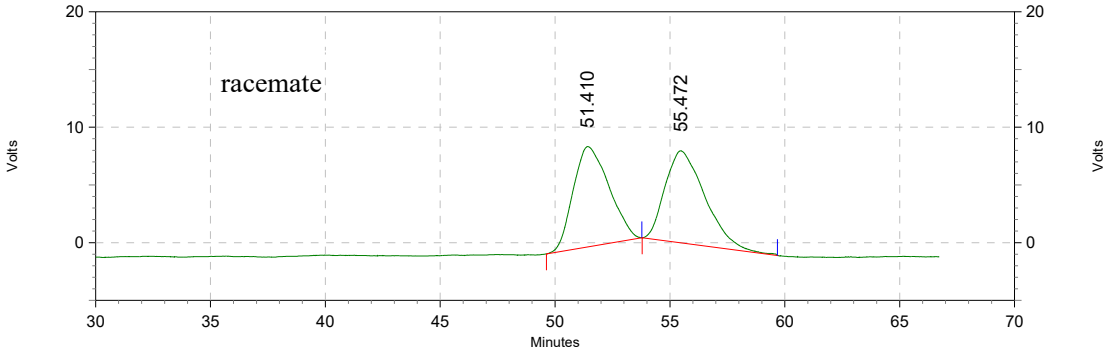
UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
12.845	18548420	89.760	292276	92.580
19.637	2138312	10.240	23426	7.420
Totals	20686732	100.000	315702	100.000



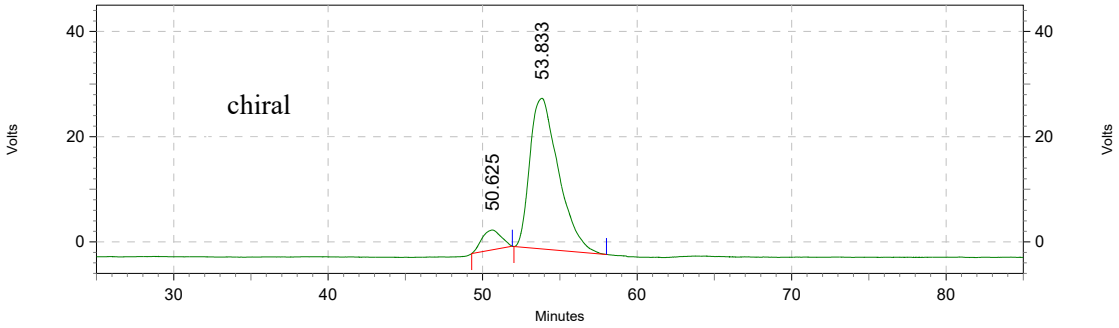
3s



UV1000-254nm

Results

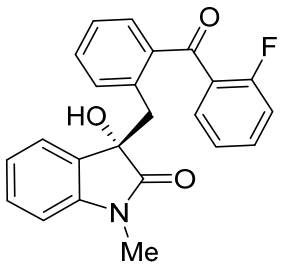
Retention time	Area	Area%	Height	Height%
51.410	940146	49.265	8696	52.153
55.472	968215	50.735	7978	47.847
Totals	1908361	100.000	16674	100.000



UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
50.625	330517	7.203	3772	11.641
53.833	3698573	92.797	28630	88.359
Totals	4029090	100.000	32402	100.000



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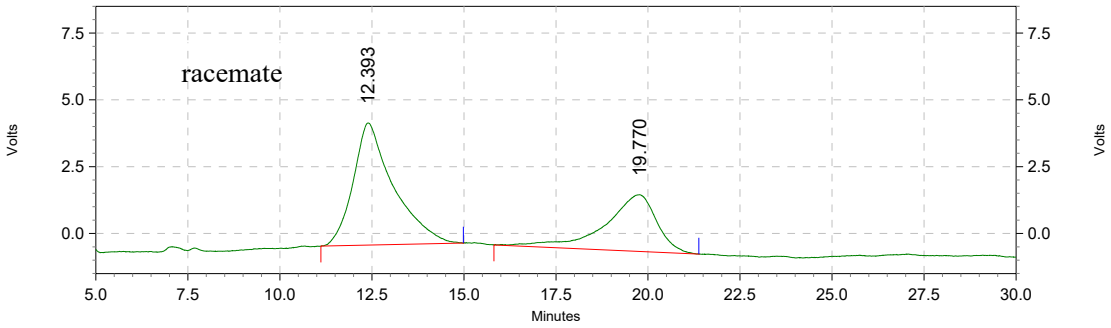
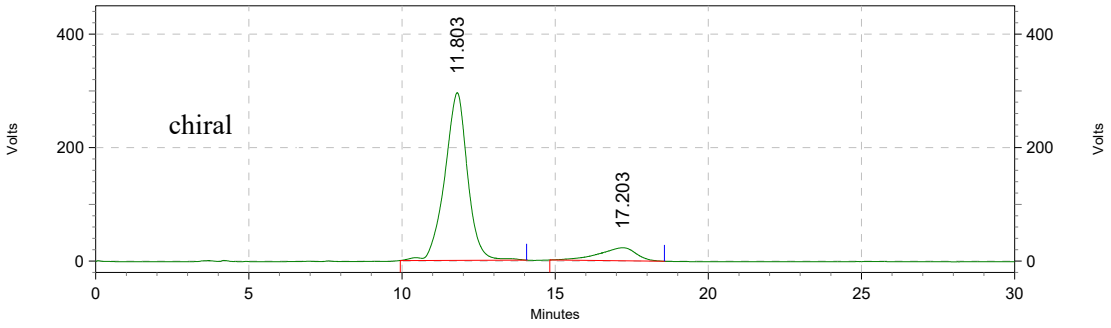


UV1000-254nm

Results

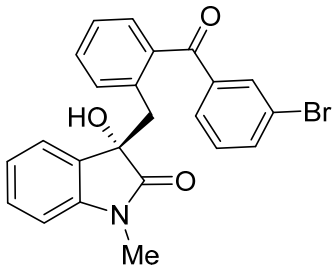
Retention time	Area	Area%	Height	Height%
12.393	347220	52.715	4570	68.280
19.770	311454	47.285	2123	31.720
Totals	658674	100.000	6693	100.000



UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
11.803	15247819	89.637	295304	92.781
17.203	1954738	10.363	22977	7.219
Totals	17202557	100.000	318281	100.000



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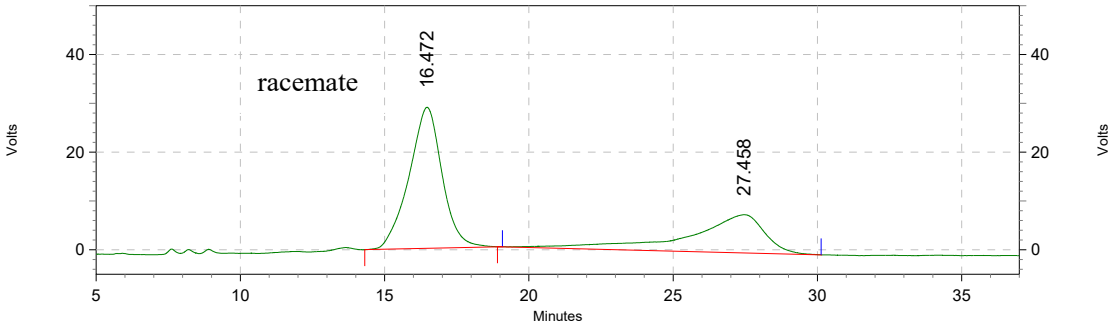
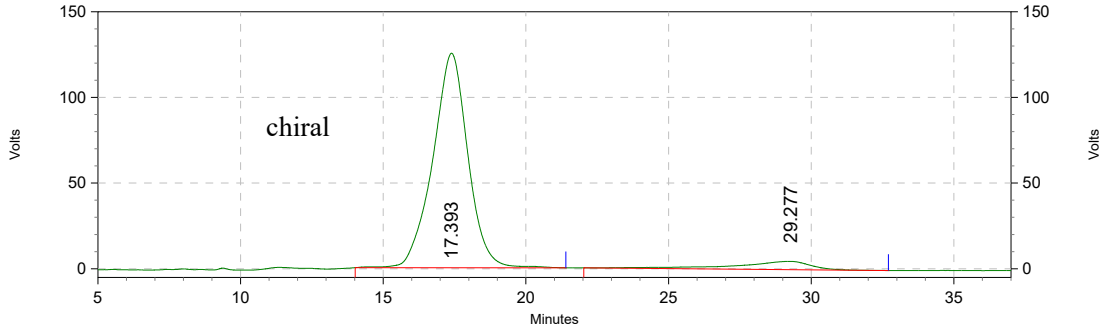


UV1000-254nm

Results

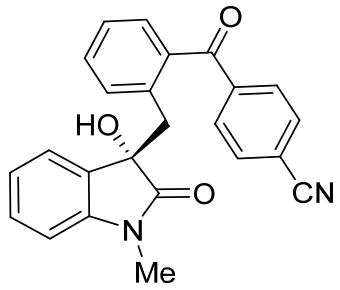
Retention time	Area	Area%	Height	Height%
16.472	2300410	51.529	28901	78.700
27.458	2163891	48.471	7822	21.300
Totals	4464301	100.000	36723	100.000



UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
17.393	10703041	92.332	125140	96.263
29.277	888810	7.668	4858	3.737
Totals	11591851	100.000	129998	100.000



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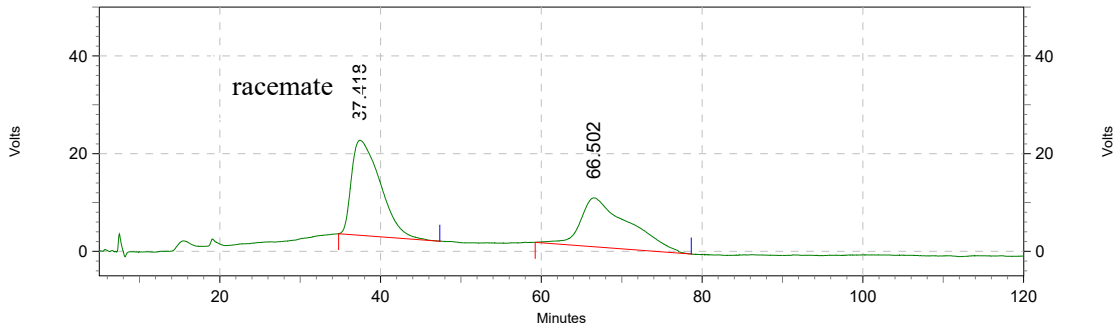
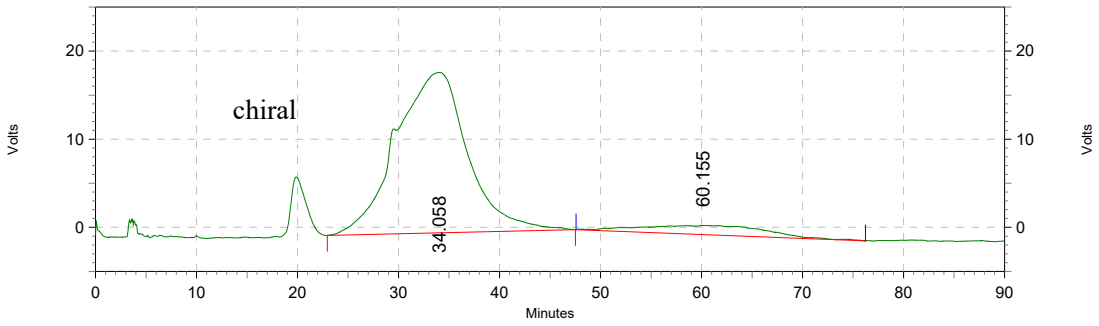


UV1000-254nm

Results

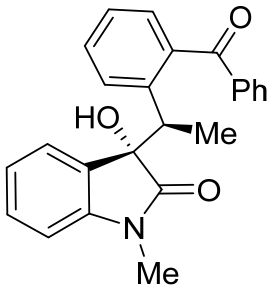
Retention time	Area	Area%	Height	Height%
37.418	4852518	51.837	19434	66.014
66.502	4508590	48.163	10005	33.986
Totals	9361108	100.000	29439	100.000



UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
34.058	9013161	90.889	18201	94.610
60.155	903555	9.111	1037	5.390
Totals	9916716	100.000	19238	100.000



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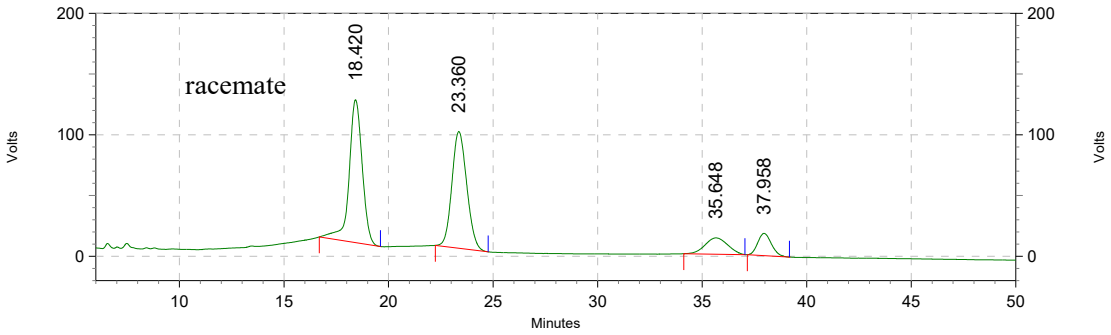
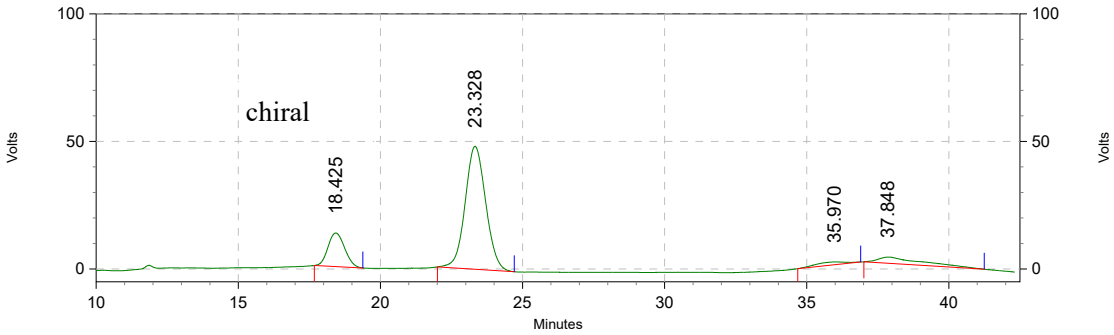


UV1000-254nm

Results

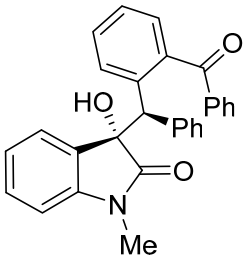
Retention time	Area	Area%	Height	Height%
18.420	5143432	43.810	117607	47.912
23.360	4752716	40.482	96101	39.151
35.648	1011563	8.116	13405	5.461
37.958	832644	7.592	18350	7.476
Totals	11740355	100.000	245463	100.000



UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
18.425	538224	16.127	13166	20.293
23.328	2429304	72.791	48191	74.276
35.970	84790	2.541	1099	1.694
37.848	285069	8.541	2425	3.738
Totals	3337387	100.000	64881	100.000



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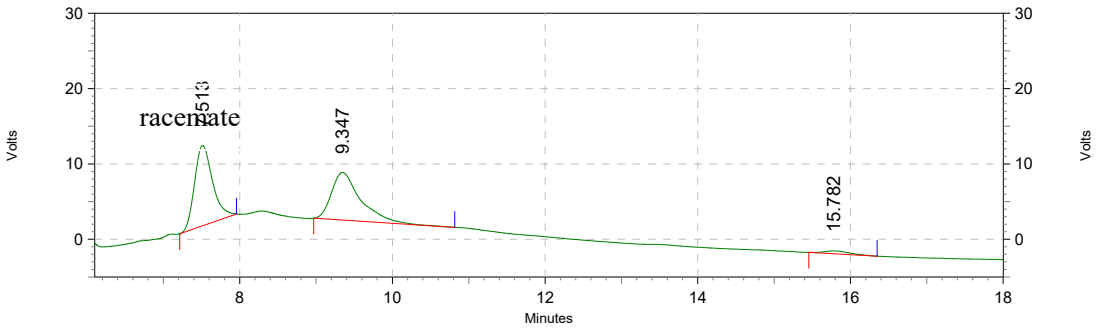
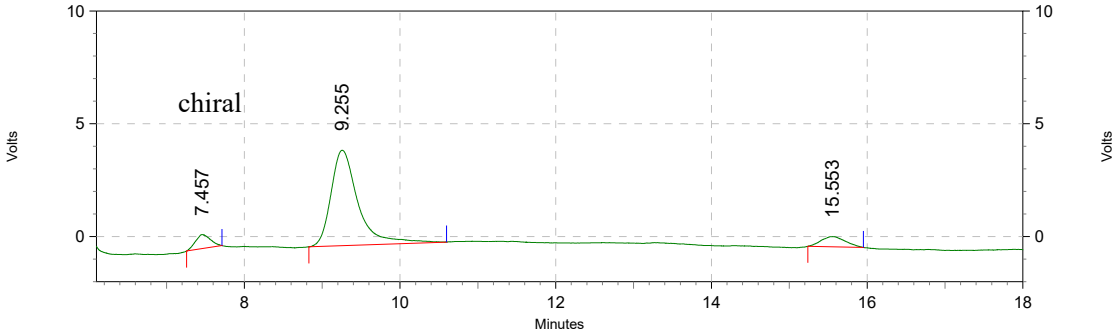


UV1000-254nm

Results

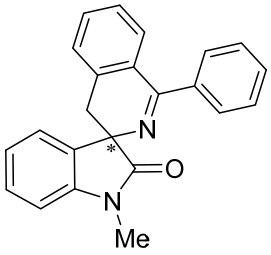
Retention time	Area	Area%	Height	Height%
7.483	829196	49.748	49955	61.700
9.312	807964	48.474	29625	36.590
15.742	29646	1.778	1385	1.711
Totals	1666806	100.000	80965	100.000



UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
7.457	6766	4.670	621	11.584
9.255	128368	88.602	4288	79.985
15.553	9748	6.728	452	8.431
Totals	144882	100.000	5361	100.000



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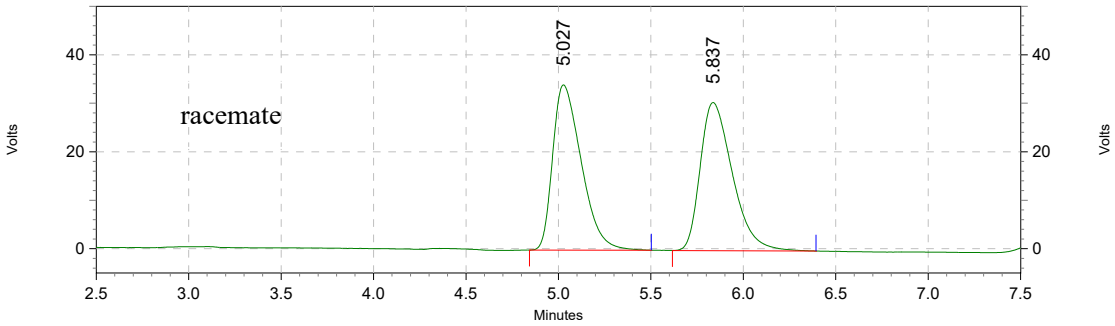
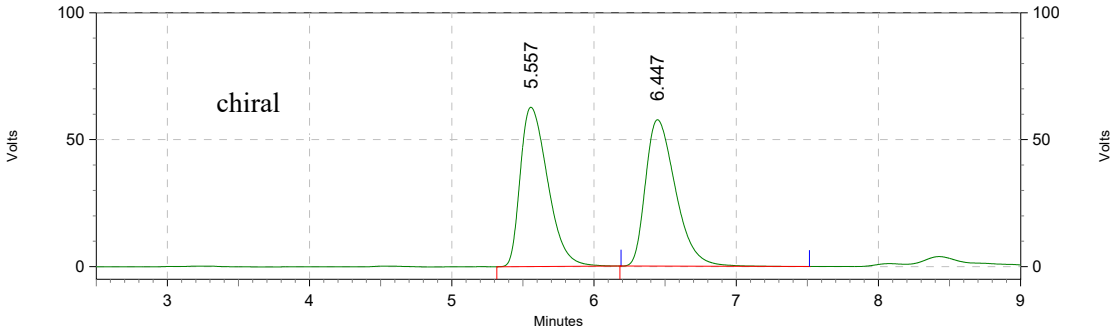


UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
5.027	366326	49.778	34067	52.726
5.837	369597	50.222	30544	47.274
Totals	735923	100.000	64611	100.000



UV1000-254nm

Results

Retention time	Area	Area%	Height	Height%
5.557	911009	51.838	62730	52.100
6.447	846407	48.162	57673	47.900
Totals	1687362	100.000	120403	100.000

7. References

1 For the preparation of isatins, please see: (a) S. E. Denmark and L. R. Cullen, Development of a phase-transfer-catalyzed, [2,3]-wittig rearrangement, *J. Org. Chem.*, 2015, **80**, 11818-11848; (b) D. J. Vyas, R. Fröhlich and M. Oestreich, Stereochemical surprises in the Lewis acid-mediated allylation of isatins, *J. Org. Chem.*, 2010, **75**, 6720-6723; (c) T. Itoh, H. Ishikawa and Y. Hayashi, Asymmetric aldol reaction of acetaldehyde and isatin derivatives for the total syntheses of ent-convolutamydine E and CPC-1 and a half fragment of madindoline A and B, *Org. Lett.*, 2009, **11**, 3854-3857.

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