Supporting Information

Catalytic Asymmetric Aldol Addition Reactions of 3-Fluoro-Indolinone Derived Enolates

Lijun Zhang, Wenzhong Zhang, Haibo Mei, Jianlin Han,* Vadim A. Soloshonok* and Yi Pan

1. General information 2
2. General synthetic procedures and experimental methods 2
2.1. General procedures for the preparation of **racemic-9** for HPLC analysis 2
2.2. General procedures for asymmetric detrifluoroacetylative aldol reaction 3
2.3. General procedures for the SDE tests 3
2.3.1. Sublimation SDE tests 3
2.3.2. Achiral gravity-driven column chromatography SDE tests 3
3. Characterization data of compounds **13** 4
4. X-ray crystallography 14
4.1. X-ray crystallography for **13q** (CCDC number: 1507543) 14
6. NMR spectra 15
6.1. NMR spectra of α-fluorinated gem-diols **13** 15
6. HPLC spectra 58
6.1. HPLC spectra of products **13** 58
6.2. HPLC spectra of achiral gravity-driven column chromatography SDE tests 79

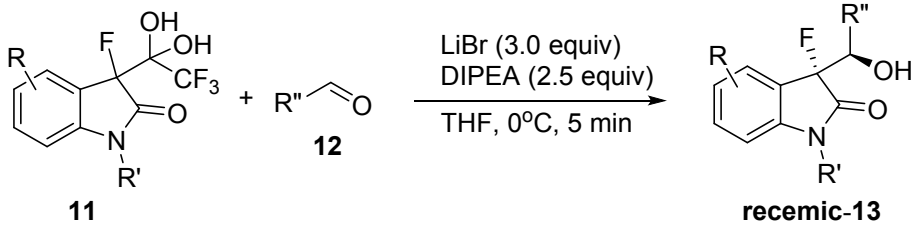
1. General information

All commercial reagents were used without additional purification unless otherwise specified. Solvents were purified and dried according to standard methods prior to use. All reactions were carried out under an argon atmosphere with dry, freshly distilled solvents under anhydrous conditions, unless otherwise noted. All experiments were monitored by thin layer chromatography (TLC) using UV light as visualizing agent. TLC was performed on pre-coated silica gel plated. Column chromatography was performed using silica gel 60 (300-400 mesh).

^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz) and ^{19}F NMR (376 MHz) were measured on a Bruker AVANCE III-400 spectrometer. Chemical shifts are reported in ppm (δ) relative to internal tetramethylsilane (TMS, δ 0.0 ppm) or with the solvent reference relative to TMS employed as the internal standard. Data are reported as follows: chemical shift (multiplicity [singlet (s), doublet (d), triplet (t), quartet (q), broad (br) and multiplet (m)], coupling constants [Hz], integration). Melting points are uncorrected. Values of optical rotation were measured on Rudolph Automatic Polarimeter A21101 at the wavelength of the sodium D-line (589 nm). Infrared spectra were obtained on Bruker Vector 22 in KBr pellets. HRMS were recorded on a LTQ-Orbitrap XL (Thermofisher, U. S. A.). HPLC analysis was performed on Shimadzu SPD-20A using Daicel Chiralpak AD, OJ, IC Column.

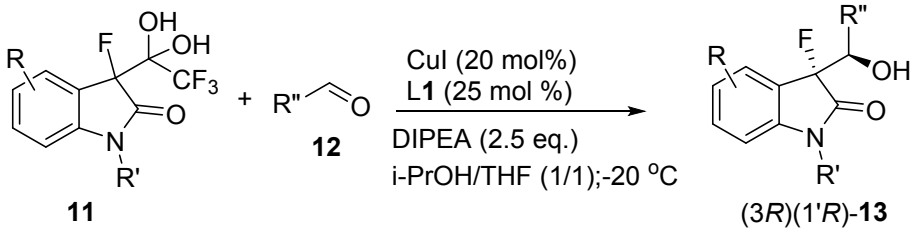
2. General synthetic procedures and experimental methods

2.1. General procedures for the preparation of **racemic-9** for HPLC analysis



To a solution of *α*-fluorinated gem-diols **11** (0.5 mmol), aldehyde **12** (0.6 mmol, 1.2 equiv), and LiBr (1.5 mmol, 3.0 equiv) in THF (10 mL), was added DIPEA (1.25 mmol, 2.5 equiv) dropwise. After 5 min, the reaction was quenched with saturated aqueous NH_4Cl (5 mL) followed by H_2O (20 mL). The organic layer was taken and the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic layers were washed with H_2O (2 × 50 mL) and brine solution (1 × 50 mL) and dried with anhydrous Na_2SO_4, filtered and the solvent was removed to give the crude product, which was purified by column chromatography to afford the corresponding products **racemic-13**.

2.2. General procedures for asymmetric detrifluoroacetylative aldol reaction



The bisoxazoline ligand **L1** (11.45 mg, 0.025 mmol) and CuI (3.8 mg, 0.020 mmol) were dissolved in 0.1 mL of anhydrous THF under argon at room temperature and stirred for 1h. Then,at -20°C the *α*-fluorinated gem-diols **11** (0.1 mmol) and aldehyde **12** (0.12 mmol) dossolved in 0.4 mL of THF was added, and added 0.5mL iPrOH, at last was added DIPEA (0.25 mmol) dropwise. The mixture was stirred until the *α*-fluorinated *gem*-diols **11** disappeared (monitored by TLC). The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography to afford products **13**.

2.3. General procedures for the SDE tests

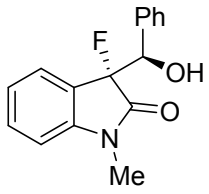
2.3.1. Sublimation SDE tests

Compound **13a** (white solid, 78% ee) was cautiously introduced in the sublimation apparatus which was connected to a vacuum pump and the gas phase was evacuated. But no sublimation phenomenon was observed after 24h at 20 °C under 10 mmHg, and no obvious changes of the weight and ee value were detected.

2.3.2. Achiral gravity-driven column chromatography SDE tests

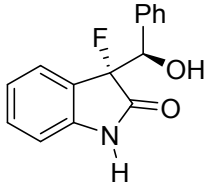
compound **13a** (white solid, 78% ee) was used as the starting sample for the gravity-driven column chromatography SDE tests over achiral silica gel (45g, 300-400 mesh) with the mixed solvent system ether acetate-petroleum ether in the ratio 1:20 as the eluent. Column flow rates were targeted to 40 mL/h amounting to total elution times of several hours. Finally 6 × 10 mL aliquots were collected, chiral HPLC analysis of the collected fractions showed that the early eluting fractions were enantiomerically enriched in comparison to the starting sample while the later eluting fractions were enantiomerically depleted. The ee values of the first and last fractions were 80% and 76%.

3. Characterization data of compounds 13



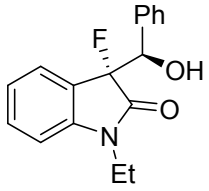
(R)-3-fluoro-3-((R)-hydroxy(phenyl)methyl)-1-methylindolin-2-one (13a)

White solid, yield 74%, dr 81:19, ee 90%, m.p. 115 - 116 °C, $[\alpha]_D^{25}$ = +5.0 (c = 0.24 , CH_2Cl_2). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.28 (m, 6H), 6.95 (t, *J* = 7.5 Hz, 1H), 6.74 (d, *J* = 7.9 Hz, 1H), 6.67 (d, *J* = 7.5 Hz, 1H), 5.45 (dd, *J* = 8.1, 5.9 Hz, 1H), 3.13 (s, 3H), 2.94 (d, *J* = 5.9 Hz, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -162.93 (s, 1F).^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.69 (d, *J* = 20.6 Hz), 144.97 (d, *J* = 5.6 Hz), 136.86, 131.41 (d, *J* = 3.0 Hz), 128.41, 127.83, 127.30 (d, *J* = 2.0 Hz), 126.18 , 122.89, 122.71 (d, *J* = 2.2 Hz), 108.58, 93.09 (d, *J* = 192.9 Hz), 74.28 (d, *J* = 31.1 Hz), 26.18. IR (cm^{-1}): 3355.6, 1691, 1617, 1471, 1380, 1100, 1056, 1012, 706. HRMS (TOF MS ESI): calcd for $C_{16}H_{14}FNO_2Na^+$ $[M+Na]^+$ 294.0901, found 294.0903. The dr value was determined by ^{19}F NMR, and ee value was determined by chiral stationary phase HPLC analysis using a Daicel Chiralpak AD column (90:10 hexanes/*i*-PrOH at 1.0 mL/min, λ = 254 nm).



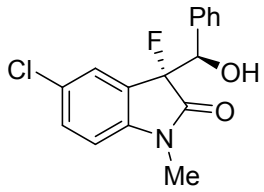
(R)-3-fluoro-3-((R)-hydroxy(phenyl)methyl)indolin-2-one (13b)

Light red solid, yield 77%, dr 72:28, ee 79%, m.p. 128 - 129 °C, $[\alpha]_D^{25}$ = +127.4 (c = 0.12 , CH_2Cl_2). ^1H NMR (400 MHz, Methanol-d_4) δ 7.29 – 7.22 (m, 5H), 7.19 - 7.14 (m, 1H), 6.77 – 6.68 (m, 2H), 6.21 (d, *J* = 7.6 Hz, 1H), 5.18 (d, *J* = 8.1 Hz, 1H). ^{19}F NMR (376 MHz, Methanol-d_4) δ -162.64 (s, 1F). ^{13}C NMR (101 MHz, Methanol-d_4) δ 175.29 (d, *J* = 19.9 Hz), 143.65 (d, *J* = 6.1 Hz), 138.32, 130.87 (d, *J* = 3.1 Hz), 127.76, 127.34 (d, *J* = 2.4 Hz), 127.22, 126.31, 123.47 (d, *J* = 18.4 Hz), 121.43 (d, *J* = 2.9 Hz), 109.94, 93.63 (d, *J* = 190.2 Hz), 72.90 (d, *J* = 31.7 Hz). IR (cm^{-1}): 3216, 2918, 2520, 2393, 1718, 1617, 1467, 1336, 1048, 749, 585. HRMS (TOF MS ESI): calcd for $C_{15}H_{12}FNO_2Na^+$ $[M+Na]^+$ 280.0744, found 280.0746. The dr value was determined by F NMR, and ee value was determined by chiral stationary phase HPLC analysis using a Daicel Chiralpak IC column (90:10 hexanes/*i*-PrOH at 1.0 mL/min, λ = 254 nm).



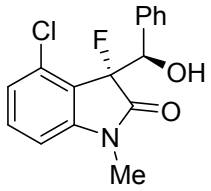
(R)-1-ethyl-3-fluoro-3-((R)-hydroxy(phenyl)methyl)indolin-2-one (13c)

Yellow solid, yield 48%, dr 69:31, ee 18%, m.p. 150 - 151 °C, [α] = +4.5 (c = 0.18, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 – 7.21 (m, 6H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.79 – 6.70 (m, 2H), 5.44 (dd, *J* = 7.9, 5.7 Hz, 1H), 3.73 (dq, *J* = 14.5, 7.3 Hz, 1H), 3.55 (dq, *J* = 14.4, 7.2 Hz, 1H), 3.34 (t, *J* = 7.0 Hz, 1H), 1.10 (t, *J* = 7.3 Hz, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -163.88 (s, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.08 (d, *J* = 20.6 Hz), 143.95 (d, *J* = 5.5 Hz), 136.67, 131.38 (d, *J* = 2.9 Hz), 128.34, 127.82, 127.31 (d, *J* = 1.7 Hz), 126.14, 123.17 (d, *J* = 18.5 Hz), 122.58 (d, *J* = 2.7 Hz), 108.72, 93.04 (d, *J* = 193.4 Hz), 74.69 (d, *J* = 30.7 Hz), 34.72, 12.21. IR (cm^{-1}): 3379, 1709, 1614, 1390, 1379, 1210, 1058, 705. HRMS (TOF MS ESI): calcd for $C_{17}H_{16}FNO_2Na$ $^+$[M+Na]$^+$ 308.1057, found 308.1060. The dr value was determined by F NMR, and ee value was determined by chiral stationary phase HPLC analysis using a Daicel Chiralpak AD column (90:10 hexanes/*i*-PrOH at 1.0 mL/min, λ = 254 nm).



(R)-5-chloro-3-fluoro-3-((R)-hydroxy(phenyl)methyl)-1-methylindolin-2-one (13d)

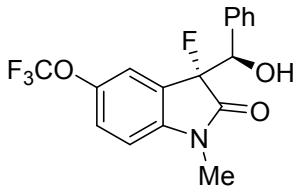
Yellow solid, yield 84%, dr 61:39, ee 68%, m.p. 155 - 156 °C, [α] = +23.2 (c = 0.37 , CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.29 (m, 1H), 6.69 (dd, *J* = 8.3, 1.3 Hz, 1H), 6.51 (t, *J* = 2.0 Hz, 1H), 5.43 (dd, *J* = 8.2, 3.5 Hz, 1H), 3.13 (s, 3H), 2.96 (d, *J* = 5.5 Hz, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -163.10 (s, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.21 (d, *J* = 20.6 Hz), 143.55 (d, *J* = 5.4 Hz), 136.37, 131.18 (d, *J* = 2.8 Hz), 128.78, 128.10 (d, *J* = 3.1 Hz), 127.99, 127.24 (d, *J* = 2.0 Hz), 126.75, 109.49, 92.69 (d, *J* = 194.2 Hz), 74.13 (d, *J* = 31.1 Hz), 26.33. IR (cm^{-1}): 3331, 2159, 1706, 1611, 1489, 1375, 1104, 832, 740, 696, 636. HRMS (TOF MS ESI): calcd for $C_{16}H_{13}ClFNO_2Na^+$ [M+Na]$^+$ 328.0511, found 328.0513. The dr value was determined by F NMR, and ee value was determined by chiral stationary phase HPLC analysis using a Daicel Chiralpak AD column (90:10 hexanes/*i*-PrOH at 1.0 mL/min, λ = 254 nm).



(R)-4-chloro-3-fluoro-3-((R)-hydroxy(phenyl)methyl)-1-methylindolin-2-one (13e)

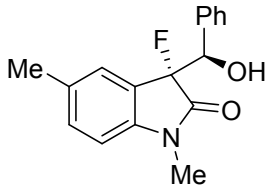
Light red solid, yield 89%, dr 58:42, ee 56%, m.p. 136 - 137 °C, [α] = +7.0 (c = 0.28, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.29 (m, 5H), 6.90 (ddd, *J* = 7.9, 1.8, 0.9 Hz, 1H), 6.77 (t, *J* = 1.5 Hz, 1H), 6.44 (dd, *J* = 8.0, 2.0 Hz, 1H), 5.44 (dd, *J* = 8.0, 4.4 Hz, 1H), 3.15 (s, 3H), 2.81 (d, *J* = 5.6 Hz, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -162.11 (s, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.63 (d, *J* = 20.5 Hz), 146.35 (d, *J* = 5.6 Hz), 137.47 (d, *J* = 3.5 Hz), 136.61, 128.67, 127.99, 127.23 (d, *J* = 2.2 Hz), 122.53 (d, *J* = 2.6 Hz), 121.00 (d, *J* = 18.9 Hz), 109.44, 92.51 (d, *J* = 193.2 Hz), 73.98 (d, *J* = 31.8 Hz), 26.34. IR (cm^{-1}): 3497, 2920, 2849, 1733, 1615, 1377, 1196, 1061, 749, 649. HRMS (TOF MS ESI): calcd for $C_{16}H_{13}ClFNO_2Na^+$

[M+Na]$^+$ 328.0511, found 328.0514. The dr value was determined by F NMR, and ee value was determined by chiral stationary phase HPLC analysis using a Daicel Chiralpak IC column (90:10 hexanes/*i*-PrOH at 1.0 mL/min, λ = 254 nm).



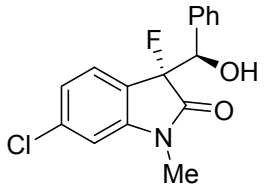
(R)-3-fluoro-3-((R)-hydroxy(phenyl)methyl)-1-methyl-5-(trifluoromethoxy)indolin-2-one (13f)

Yellow solid, yield 92%, dr 43:57, ee 30%, m.p. 134 - 135 °C, [α] = +1.5 (c = 0.28 , CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 – 7.28 (m, 5H), 7.21 (d, *J* = 8.5 Hz, 1H), 6.77 (dd, *J* = 8.5, 1.3 Hz, 1H), 6.36 (t, *J* = 2.0 Hz, 1H), 5.46 (d, *J* = 8.3 Hz, 1H), 3.18 (s, 3H), 2.93 (s, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -58.49 (s, 3F), -163.22 (s, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.56 (d, *J* = 20.5 Hz), 144.33 (d, *J* = 2.4 Hz), 143.74 (d, *J* = 5.5 Hz), 136.32, 128.84, 128.05, 127.22 (d, *J* = 2.0 Hz), 124.58 (d, *J* = 2.2 Hz), 123.97 (d, *J* = 18.3 Hz), 120.91(q, J = 258.6Hz), 120.52, 109.05, 92.58 (d, *J* = 193.9 Hz), 74.00 (d, *J* = 31.6 Hz), 26.41. IR (cm^{-1}): 3406, 2159, 2030, 1700, 1621, 1491, 1377, 1165, 1030, 695. HRMS (TOF MS ESI): calcd for $C_{17}H_{13}F_4NO_3Na^+$ [M+Na]$^+$ 378.0724, found 378.0727.The dr value was determined by F NMR, and ee value was determined by chiral stationary phase HPLC analysis using a Daicel Chiralpak AD column (90:10 hexanes/*i*-PrOH at 1.0 mL/min, λ = 254 nm).



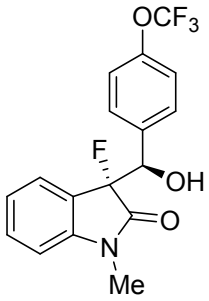
(R)-3-fluoro-3-((R)-hydroxy(phenyl)methyl)-1,5-dimethylindolin-2-one (13g)

Yellow solid, yield 72%, dr 81:19, ee 87% , m.p. 131 - 132 °C, [α] = +40.5 (c = 0.32, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 – 7.20 (m, 5H), 7.11 (d, *J* = 7.9 Hz, 1H), 6.64 – 6.60 (m, 1H), 6.46 (s, 1H), 5.43 (dd, *J* = 8.1, 6.0 Hz, 1H), 3.12 (d, *J* = 6.1 Hz, 1H), 3.09 (s, 3H), 2.21 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -162.80 (s, 1F) .^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.50 (d, *J* = 20.8 Hz), 142.50 (d, *J* = 5.5 Hz), 136.85, 132.34 (d, *J* = 2.8 Hz), 131.55 (d, *J* = 3.0 Hz), 128.39, 127.74, 127.31 (d, *J* = 1.9 Hz), 126.93, 122.77 (d, *J* = 18.3 Hz), 108.30, 93.20 (d, *J* = 193.0 Hz), 74.45 (d, *J* = 31.0 Hz), 26.17, 20.94 .IR (cm^{-1}): 3335, 1701, 1493, 1374, 1123, 1056, 1016, 828, 699. HRMS (TOF MS ESI): calcd for $C_{17}H_{16}FNO_2Na^+$[M+Na]$^+$ 308.1057, found 308.1059. The dr value was determined by F NMR, and ee value was determined by chiral stationary phase HPLC analysis using a Daicel Chiralpak IC column (90:10 hexanes/*i*-PrOH at 1.0 mL/min, λ = 254 nm).



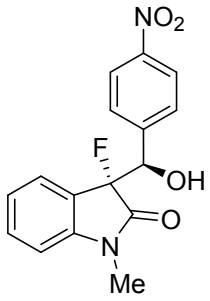
(R)-6-chloro-3-fluoro-3-((R)-hydroxy(phenyl)methyl)-1-methylindolin-2-one (13h)

Yellow solid, yield 83%, dr 59:41, ee 59%, m.p. 112 -113 °C, [α] = +15.0 (c = 0.24, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.27 (m, 1H), 6.91 - 6.88 (m, 1H), 6.77 (t, *J* = 1.5 Hz, 1H), 6.43 (dd, *J* = 8.0, 2.0 Hz, 1H), 5.44 (dd, *J* = 8.1, 5.6 Hz, 1H), 3.14 (s, 3H), 2.89 (d, *J* = 5.6 Hz, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -162.09 (s, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.65 (d, *J* = 20.5 Hz), 146.35 (d, *J* = 5.5 Hz), 137.46 (d, *J* = 3.4 Hz), 136.62, 128.66, 127.98, 127.25, 127.23, 122.52 (d, *J* = 2.7 Hz), 121.00 (d, *J* = 18.7 Hz), 109.44 (d, *J* = 0.6 Hz), 92.51 (d, *J* = 193.2 Hz), 73.95 (d, *J* = 31.8 Hz), 26.34. IR (cm^{-1}): 3497, 1733, 1616, 1497, 1455, 1378, 1295, 1196, 1061, 1011, 850, 720, 705. HRMS (TOF MS ESI): calcd for $C_{16}H_{13}ClFNO_2Na^+$ $[M+Na]^+$ 328.0511, found 328.0508.The dr value was determined by F NMR, and ee value was determined by chiral stationary phase HPLC analysis using a Daicel Chiralpak IC column (90:10 hexanes/*i*-PrOH at 1.0 mL/min, λ = 254 nm).



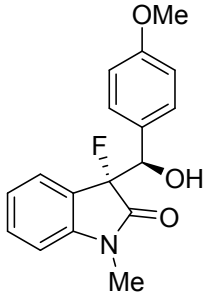
(R)-3-fluoro-3-((R)-hydroxy(4-(trifluoromethoxy)phenyl)methyl)-1-methylindolin-2-one (13i)

Yellow solid, yield 66%, dr 80:20, ee 86%, m.p. 157 - 158 °C, [α] = -7.7 (c = 0.37, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 – 7.31 (m, 3H), 7.16 (dd, *J* = 8.9, 1.1 Hz, 2H), 7.01 – 6.92 (m, 1H), 6.77 (d, *J* = 8.0 Hz, 1H), 6.64 (d, *J* = 7.5 Hz, 1H), 5.47 (d, *J* = 7.8 Hz, 1H), 3.13 (s, 3H), 3.05 (s, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -57.85 (s, 3F), -163.00 (s, 1F).^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.46 (d, *J* = 20.5 Hz), 149.26 (d, *J* = 2.1 Hz), 144.95 (d, *J* = 5.6 Hz), 135.61, 131.86, 131.64 (d, *J* = 2.7 Hz), 128.82 (d, *J* = 2.2 Hz), 125.98, 122.89 (d, *J* = 2.7 Hz), 122.54 (d, *J* = 18.2 Hz), 120.44 (q, *J* = 257.2 Hz), 120.21, 120.11, 108.74, 93.05 (d, *J* = 193.6 Hz), 73.56 (d, *J* = 31.4 Hz), 26.20. IR (cm^{-1}): 3257, 1701, 1616, 1471, 1333, 1060, 1012, 703. HRMS (TOF MS ESI): calcd for $C_{17}H_{13}F_4NO_3Na^+$ $[M+Na]^+$ 378.0724, found 378.0728.The dr value was determined by F NMR, and ee value was determined by chiral stationary phase HPLC analysis using a Daicel Chiralpak OJ column (90:10 hexanes/*i*-PrOH at 1.0 mL/min, λ = 254 nm).



(R)-3-fluoro-3-((R)-hydroxy(4-nitrophenyl)methyl)-1-methylindolin-2-one (13j)

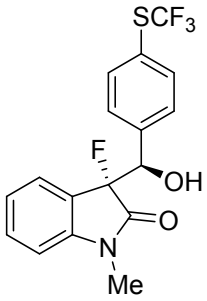
Yellow solid, yield 90%, dr 57:43, ee 70%, m.p. 96 - 97 °C , [α] =18.919 (c = 0.07, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.19 (d, *J* = 8.8 Hz, 2H), 7.53 (d, *J* = 8.3 Hz, 2H), 7.41 – 7.34 (m, 1H), 6.97 (tt, *J* = 7.6, 0.9 Hz, 1H), 6.80 (d, *J* = 7.9 Hz, 1H), 6.57 (dt, *J* = 7.4, 1.7 Hz, 1H), 5.56 (d, *J* = 7.6 Hz, 1H), 3.16 (s,3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -162.19 (s, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.21 (d, *J* = 20.6 Hz), 147.87, 143.90 (d, *J* = 5.7 Hz), 142.21 (d, *J* = 5.6 Hz), 131.81 (d, *J* = 2.8 Hz), 128.62 – 128.57 (m), 126.78, 123.34 (d, *J* = 2.4 Hz), 122.88, 121.85 (d, *J* = 19.1 Hz), 108.72, 93.95 (d, *J* = 195.5 Hz), 75.23 (d, *J* = 26.9 Hz), 26.09 .IR (cm^{-1}): 3376, 1718, 1617, 1518, 1348, 1050, 1012, 820. HRMS (TOF MS ESI): calcd for $C_{16}H_{13}FN_2O_4Na^+$ $[M+Na]^+$ 339.0752, found 339.0746. The dr value was determined by F NMR, and ee value was determined by chiral stationary phase HPLC analysis using a Daicel Chiralpak AD column (90:10 hexanes/*i*-PrOH at 1.0 mL/min, λ = 254 nm).



(R)-3-fluoro-3-((R)-hydroxy(4-methoxyphenyl)methyl)-1-methylindolin-2-one (13k)

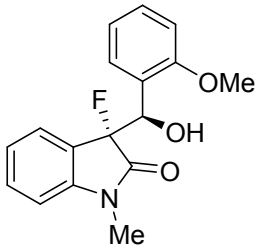
Yellow solid, yield 64%, dr 75:25, ee 79%, m.p. 105 - 106 °C, [α] = -17.9 (c = 0.27 , CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 (tt, *J* = 7.7, 1.6 Hz, 1H), 7.20 (d, *J* = 8.8 Hz, 2H), 6.97 (t, *J* = 7.6 Hz, 1H), 6.86 – 6.80 (m, 2H), 6.77 – 6.70 (m, 2H), 5.40 (dd, *J* = 8.2, 5.5 Hz, 1H), 3.81 (s, 3H), 3.14 (s, 3H), 2.86 (d, *J* = 5.8 Hz, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -162.75(s, 1F).^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.71 (d, *J* = 20.8 Hz), 159.64, 144.96 (d, *J* = 5.5 Hz), 131.34 (d, *J* = 3.0 Hz), 128.87, 128.49 (d, *J* = 1.8 Hz), 126.15, 122.93 (d, *J* = 18.3 Hz), 122.67 (d, *J* = 2.7 Hz), 113.24, 108.56, 93.12 (d, *J* = 192.3 Hz), 74.09 (d, *J* = 31.3 Hz), 55.25, 26.17. IR (cm^{-1}): 3366, 2164, 1691, 1617, 1514, 1473, 1380, 1305, 1258, 1104, 747, 683.

HRMS (TOF MS ESI): calcd for $C_{17}H_{16}FNO_3Na^+$ $[M+Na]^+$ 324.1006, found 324.1012.The dr value was determined by F NMR, and ee value was determined by chiral stationary phase HPLC analysis using a Daicel Chiralpak AD column (90:10 hexanes/*i*-PrOH at 1.0 mL/min, λ = 254 nm).



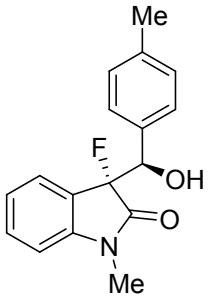
(R)-3-fluoro-3-((R)-hydroxy(4-((trifluoromethyl)thio)phenyl)methyl)-1-methylindolin-2-one (13l)

Yellow solid, yield 85%, dr 76:24, ee 75%, m.p. 140 -141 °C , $[\alpha]_D^{25}$ = -8.37 (c = 0.53, CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.76 (d, *J* = 8.2 Hz, 2H), 7.51 (dd, *J* = 8.2, 1.7 Hz, 2H), 7.43 – 7.35 (m, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 6.88 (t, *J* = 7.6 Hz, 1H), 6.38 (dd, *J* = 5.4, 1.4 Hz, 1H), 6.16 (dt, *J* = 7.6, 1.7 Hz, 1H), 5.27 (dd, *J* = 7.9, 5.3 Hz, 1H), 3.16 (s, 3H).^{19}F NMR (376 MHz, DMSO-d_6) δ -42.22 (s, 3F), -160.41 (s, 1F). ^{13}C NMR (101 MHz, DMSO-d_6) δ 172.24 (d, *J* = 20.1 Hz), 145.91 (d, *J* = 5.8 Hz), 142.98 (d, *J* = 1.2 Hz), 135.93, 131.95 (d, *J* = 3.0 Hz),130.13 (q, *J* = 309.06 Hz) 129.52 (d, *J* = 2.5 Hz), 125.86, 123.04 (d, *J* = 2.3 Hz), 122.82 , 122.63 , 122.47 (d, *J* = 2.9 Hz), 109.69, 94.22, 92.33, 71.91 (d, *J* = 31.6 Hz), 26.59. IR (cm^{-1}): 3289, 2032, 1700, 1614, 1474, 1383, 1106, 1010, 759. HRMS (TOF MS ESI): calcd for $C_{17}H_{13}F_4NO_2SNa^+$[M+Na]$^+$ 394.0495, found 394.0499. The dr value was determined by F NMR, and ee value was determined by chiral stationary phase HPLC analysis using a Daicel Chiralpak OJ column (90:10 hexanes/*i*-PrOH at 1.0 mL/min, λ = 254 nm).



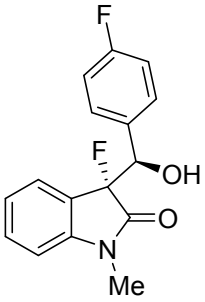
(R)-3-fluoro-3-((R)-hydroxy(2-methoxyphenyl)methyl)-1-methylindolin-2-one (13m)

Colorless solid, yield 45%, dr 91:9, ee 73%, m.p. 108 - 109 °C, $[\alpha]_D^{25}$ = -14.7 (c = 0.26, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.14 (m, 3H), 7.07 – 7.00 (m, 1H), 6.99 – 6.87 (m, 2H), 6.71 (dd, *J* = 15.7, 8.1 Hz, 2H), 5.72 (t, *J* = 8.5 Hz, 1H), 4.14 (d, *J* = 8.3 Hz, 1H), 3.58 (s, 3H), 3.12 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -163.78 (s, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.71 (d, *J* = 21.0 Hz), 156.96, 144.67 (d, *J* = 5.4 Hz), 131.13 (d, *J* = 2.9 Hz), 129.62, 129.01 (d, *J* = 1.7 Hz), 126.15, 124.44 (d, *J* = 2.8 Hz), 123.26 (d, *J* = 18.6 Hz), 122.15 (d, *J* = 2.6 Hz), 120.50, 110.51, 108.21, 93.37 (d, *J* = 195.1 Hz), 72.12 (d, *J* = 31.1 Hz), 54.91, 26.10. IR (cm^{-1}): 3434, 2164, 2034, 1716, 1614, 1243, 1047, 752. HRMS (TOF MS ESI): calcd for $C_{17}H_{17}FNO_2^+$ [M+H]$^+$286.1238, found 286.1237.The dr value was determined by F NMR, and ee value was determined by chiral stationary phase HPLC analysis using a Daicel Chiralpak AD column (90:10 hexanes/*i*-PrOH at 1.0 mL/min, λ = 254 nm).



(R)-3-fluoro-3-((R)-hydroxy(p-tolyl)methyl)-1-methylindolin-2-one (13n)

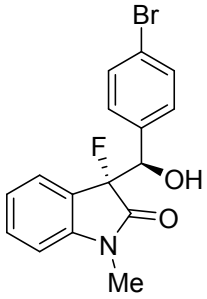
Yellow solid, yield 64%, dr 79:21 ee 87%, m.p. 132 - 133 °C, $[\alpha]_D^{25}$ = -27.2 (c = 0.27, CH_2Cl_2), ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 - 7.31 (m, 1H), 7.17 (d, *J* = 7.9 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 6.96 (t, *J* = 7.6 Hz, 1H), 6.73 (dd, *J* = 16.7, 7.7 Hz, 2H), 5.42 (dd, *J* = 8.1, 5.7 Hz, 1H), 3.14 (s, 3H), 2.84 (d, *J* = 5.9 Hz, 1H), 2.34 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -162.75 (s, 1F). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.91 (d, *J* = 20.8 Hz), 145.00 (d, *J* = 5.5 Hz), 138.07, 134.00, 131.31 (d, *J* = 2.9 Hz), 128.51, 127.25 (d, *J* = 1.9 Hz), 126.27, 122.91 (d, *J* = 18.3 Hz), 122.64 (d, *J* = 2.7 Hz), 108.57, 93.10 (d, *J* = 192.2 Hz), 74.00 (d, *J* = 31.3 Hz), 26.18 , 21.21. IR (cm^{-1}): 3370, 1697, 1616, 1470, 1381, 1199, 1081, 1012, 751. HRMS (TOF MS ESI): calcd for $C_{17}H_{16}FNO_2Na^+$[M+Na]$^+$ 308.1057, found 308.1059.The dr value was determined by F NMR, and ee value was determined by chiral stationary phase HPLC analysis using a Daicel Chiralpak IC column (90:10 hexanes/*i*-PrOH at 1.0 mL/min, λ = 254 nm).



(R)-3-fluoro-3-((R)-(4-fluorophenyl)(hydroxy)methyl)-1-methylindolin-2-one (13o)

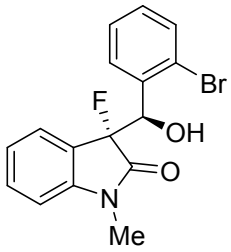
Yellow solid, yield 29%, dr 80:20, ee 92%, m.p. 132 - 133 °C, $[\alpha]_D^{25}$ = -5.06 (c = 0.16, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 - 7.32 (m, 1H), 7.29 - 7.25 (m, 2H), 7.03 – 6.93 (m, 3H), 6.76 (d, *J* = 7.9 Hz, 1H), 6.67 (dt, *J* = 7.4, 1.8 Hz, 1H), 5.43 (dd, *J* = 8.0, 5.8 Hz, 1H), 3.13 (s, 3H), 3.08 (d, *J* = 5.9 Hz, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -113.56 (s, 1F), -162.91 (s, 1F) .^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.39 (d, *J* = 20.6 Hz), 163.99, 161.54, 144.93 (d, *J* = 5.5 Hz), 132.66 – 132.32 (m), 131.55 (d, *J* = 2.8 Hz), 129.01 (dd, *J* = 8.3, 2.0 Hz), 125.97, 122.80 (d, *J* = 2.8 Hz), 122.64 (d, *J* = 18.6 Hz), 114.81 (d, *J* = 21.6 Hz), 108.68, 93.94, 92.02, 73.90 (d, *J* = 31.3 Hz), 26.19. IR (cm^{-1}): 3338, 1689, 1605, 1472, 1420, 1381, 1314, 1222, 1060, 836, 744, 683. HRMS (TOF MS ESI): calcd for $C_{16}H_{13}F_2NO_2Na^+$ [M+Na]$^+$ 312.0807, found 312.0810.The dr value was determined by F NMR, and ee value was determined by chiral

stationary phase HPLC analysis using a Daicel Chiralpak AD column (90:10 hexanes/*i*-PrOH at 1.0 mL/min, λ = 254 nm).



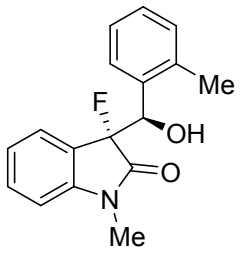
(R)-3-((R)-(4-bromophenyl)(hydroxy)methyl)-3-fluoro-1-methylindolin-2-one (13p)

Light red solid, yield 80%, dr 72:28, ee 66%, m.p. 145 - 146 °C,[α] = +2.1 (c = 0.39 , CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 – 7.42 (m, 2H), 7.40 – 7.30 (m, 1H), 7.18 (d, *J* = 8.3 Hz, 2H), 6.98 (tt, *J* = 7.5, 0.9 Hz,1H), 6.77 (d, *J* = 7.9 Hz, 1H), 6.68 (dt, *J* = 7.4, 1.7 Hz, 1H), 5.41 (dd, *J* = 7.9, 5.4 Hz, 1H), 3.14 (s, 3H), 3.05 (d, *J* = 5.8 Hz, 1H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -162.62 (s, 1F) .^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.42 (d, *J* = 20.6 Hz), 144.96 (d, *J* = 5.5 Hz), 135.97, 131.61 (d, *J* = 3.0 Hz), 131.01, 129.03 (d, *J* = 2.1 Hz), 126.04, 122.86 (d, *J* = 2.7 Hz), 122.56, 122.51 (d, *J* = 18.3 Hz), 108.76, 92.82 (d, *J* = 193.2 Hz), 73.70 (d, *J* = 31.4 Hz), 26.24. IR (cm^{-1}): 3368, 1691, 1617, 1471, 1382, 1199, 1100, 1073, 1012, 755. HRMS (TOF MS ESI): calcd for $C_{16}H_{13}BrFNO_2Na^+$ $[M+Na]^+$ 372.0006, found 372.0009.The dr value was determined by F NMR, and ee value was determined by chiral stationary phase HPLC analysis using a Daicel Chiralpak AD column (90:10 hexanes/*i*-PrOH at 1.0 mL/min, λ = 254 nm).



(R)-3-((R)-(2-bromophenyl)(hydroxy)methyl)-3-fluoro-1-methylindolin-2-one (13q)

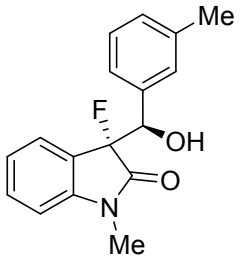
Light red solid, yield 93%, dr 58:42, ee 62%, m.p. 170 - 172 °C, [α] = +22.0 (c = 0.43 , CH_2Cl_2)**.** ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.48 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.40 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.36 – 7.27 (m, 2H), 7.20 (dt, *J* = 7.4, 1.6 Hz, 1H), 7.18 – 7.11 (m, 1H), 7.05 – 6.98 (m, 1H), 6.74 (d, *J* = 7.8 Hz, 1H), 5.95 (dd, *J* = 9.3, 5.6 Hz, 1H), 3.40 (d, *J* = 6.2 Hz, 1H), 3.16 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -164.72 (s, 1F) .^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.38, 144.42 (d, *J* = 5.4 Hz), 136.30 (d, *J* = 2.5 Hz), 132.97, 131.52 (d, *J* = 2.8 Hz), 130.09 , 129.28 , 126.96 , 126.75 , 124.07 , 122.63 (d, *J* = 18.2 Hz), 122.62 (d, *J* = 2.7 Hz), 108.47 , 93.52 (d, *J* = 195.3 Hz), 73.52 (d, *J* = 31.0 Hz), 26.24 .IR (cm^{-1}): 3351, 2161, 1708, 1615, 1467, 1379, 1198, 1101, 1019, 819, 583, 605. HRMS (TOF MS ESI): calcd for $C_{16}H_{13}BrFNO_2Na^+$ $[M+Na]^+$372.0006, found 372.0010.The dr value was determined by F NMR, and ee value was determined by chiral stationary phase HPLC analysis using a Daicel Chiralpak AD column (90:10 hexanes/*i*-PrOH at 1.0 mL/min, λ = 254 nm).



(R)-3-fluoro-3-((R)-hydroxy(o-tolyl)methyl)-1-methylindolin-2-one (13r)

Yellow solid, yield 63%, dr 83:17, ee 93%, m.p. 145 - 147 °C, [α] = -7.8 (c = 0.28 , CH_2Cl_2)

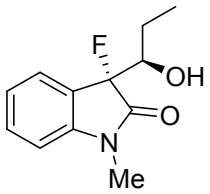
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.14 (m, 5H), 6.94 (t, *J* = 7.5 Hz, 1H), 6.79 (d, *J* = 7.8 Hz, 1H), 6.73 – 6.67 (m, 1H), 5.74 (t, *J* = 5.6 Hz, 1H), 3.16 (s, 3H), 2.90 (d, *J* = 5.1 Hz, 1H), 2.42 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -163.15 (s, 1F) .^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.22 (d, *J* = 20.4 Hz), 145.19 (d, *J* = 5.7 Hz), 137.12, 135.50, 131.37 (d, *J* = 3.0 Hz), 130.55 , 128.38 , 127.83 , 126.94 , 125.17 , 122.70 (d, *J* = 18.3 Hz), 122.36 (d, *J* = 2.7 Hz), 108.51 , 94.23 (d, *J* = 191.6 Hz), 70.39 (d, *J* = 33.5 Hz), 26.28 , 19.81 (d, *J* = 6.0 Hz). IR (cm^{-1}): 3371, 1710, 1616, 1498, 1471, 1379, 1214, 1099, 1050, 751, 733. HRMS (TOF MS ESI): calcd for $C_{17}H_{16}FNO_3Na^+$ $[M+Na]^+$ 324.1006, found 324.1010.The dr value was determined by F NMR, and ee value was determined by chiral stationary phase HPLC analysis using a Daicel Chiralpak IC column (90:10 hexanes/*i*-PrOH at 1.0 mL/min, λ = 254 nm).



(R)-3-fluoro-3-((R)-hydroxy(m-tolyl)methyl)-1-methylindolin-2-one (13s)

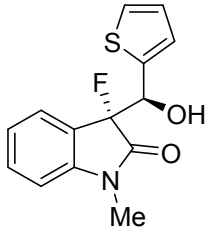
Yellow solid, yield 67%, dr 78:22, ee 85%, m.p. 249 - 250 °C, [α] = -5.6 (c = 0.29 , CH_2Cl_2)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.29 (m, 1H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.14 – 7.04 (m, 3H), 6.95 (t, *J* = 7.6 Hz, 1H), 6.75 (d, *J* = 7.8 Hz, 1H), 6.71 – 6.64 (m, 1H), 5.42 (dd, *J* = 8.1, 5.5 Hz, 1H), 3.14 (s, 3H), 2.88 (d, *J* = 5.9 Hz, 1H), 2.31 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -162.96 (s, 1F).^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.57 (d, *J* = 20.7 Hz), 144.97 (d, *J* = 5.4 Hz), 137.48, 136.64 (d, *J* = 0.8Hz), 131.39 (d, *J* = 2.9 Hz), 129.15, 127.94 (d, *J* = 1.9 Hz), 127.72 , 126.21, 124.30 (d, *J* = 1.6 Hz), 122.80 (d, *J* = 18.4 Hz), 122.62 (d, *J* = 2.7 Hz), 108.52, 96.01 (d, *J* = 798.2 Hz), 74.50 (d, *J* = 31.1 Hz), 26.15 , 21.39 .IR (cm^{-1}): 3296, 1701, 1615, 1473, 1380, 1105, 1060, 1012, 757. HRMS (TOF MS ESI): calcd for $C_{17}H_{17}FNO_2^+$ $[M+H]^+$, 286.1238, found 286.1236.The dr value was determined by F NMR, and ee value was determined by chiral stationary phase HPLC analysis using a Daicel Chiralpak IC column (90:10 hexanes/*i*-PrOH at 1.0 mL/min, λ = 254 nm).



(R)-3-fluoro-3-((R)-1-hydroxypropyl)-1-methylindolin-2-one (13t)

Yellow solid, yield 70%, dr 77:23, ee 92%, m.p. 115 - 116 °C , [α] = - 10.7 (c = 0.24 , CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 – 7.36 (m, 2H), 7.12 (tt, *J* = 7.5, 0.9 Hz, 1H), 6.89 – 6.82 (m, 1H), 4.20 – 4.03 (m, 1H), 3.20 (s, 3H), 2.61 (d, *J* = 7.7 Hz, 1H), 1.67-1.57 (m, 1H), 1.48 - 1.37(m, 1H), 1.01 (t, *J* = 7.4 Hz, 3H). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -166.41 (s, 1F) .^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.62 (d, *J* = 21.2 Hz), 144.84 (d, *J* = 5.3 Hz), 131.45 (d, *J* = 3.0 Hz), 125.33, 123.92 (d, *J* = 18.4 Hz), 123.26 (d, *J* = 2.9 Hz), 108.88, 93.29 (d, *J* = 191.2 Hz), 74.96 (d, *J* = 28.2 Hz), 26.21, 24.10 (d, *J* = 2.4 Hz), 10.33 .IR (cm^{-1}): 3450, 1715, 1613, 1462, 1381, 1240, 1089, 1024, 787. HRMS (TOF MS ESI): calcd for $C_{12}H_{14}FNO_2Na^+$[M+Na]$^+$ 246.0901, found 246.0896.The dr value was determined by F NMR, and ee value was determined by chiral stationary phase HPLC analysis using a Daicel Chiralpak AD column (90:10 hexanes/*i*-PrOH at 1.0 mL/min, λ = 254 nm).

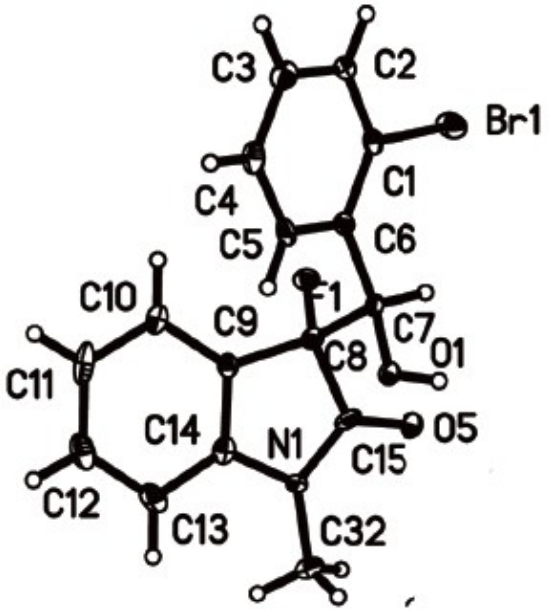


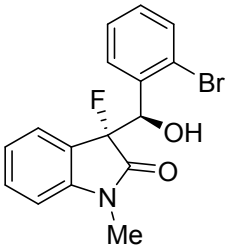
(R)-3-fluoro-3-((S)-hydroxy(thiophen-2-yl)methyl)-1-methylindolin-2-one (13u)

Yellow solid, yield 77%, dr 79:21, ee 52%, m.p. 113 - 114 °C, [α] = -11.6 (c = 0.29 , CH_2Cl_2)**.** ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.33 (m, 1H), 7.29 – 7.23 (m, 1H), 7.03 – 6.93 (m, 3H), 6.86 – 6.63 (m, 2H), 5.71 – 5.64 (m, 1H), 3.64 (d, *J* = 6.9 Hz, 1H), 3.14 (s, 3H).^{19}F NMR (376 MHz, Chloroform-*d*) δ -162.17 (s, 1F).^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.29 (d, *J* = 20.8 Hz), 145.15 (d, *J* = 5.4 Hz), 140.78, 131.71 (d, *J* = 3.0 Hz), 126.85 , 126.01 , 125.49 (d, *J* = 2.3 Hz), 125.42, 123.06 (d, *J* = 2.7 Hz), 122.52 (d, *J* = 18.3 Hz), 108.74, 92.49 (d, *J* = 192.7 Hz), 71.56 (d, *J* = 33.3 Hz), 26.25 .IR (cm^{-1}): 3352, 1706, 1612, 1493, 1467, 1381, 1059, 1009, 838. HRMS (TOF MS ESI): calcd for $C_{14}H_{12}FNO_2SNa^+$ [M+Na]$^+$ 300.0465, found 300.0466.The dr value was determined by F NMR, and ee value was determined by chiral stationary phase HPLC analysis using a Daicel Chiralpak IC column (90:10 hexanes/*i*-PrOH at 1.0 mL/min, λ = 254 nm).

4. X-ray crystallography

4.1. X-ray crystallography for **13q** (CCDC number: 1507543)

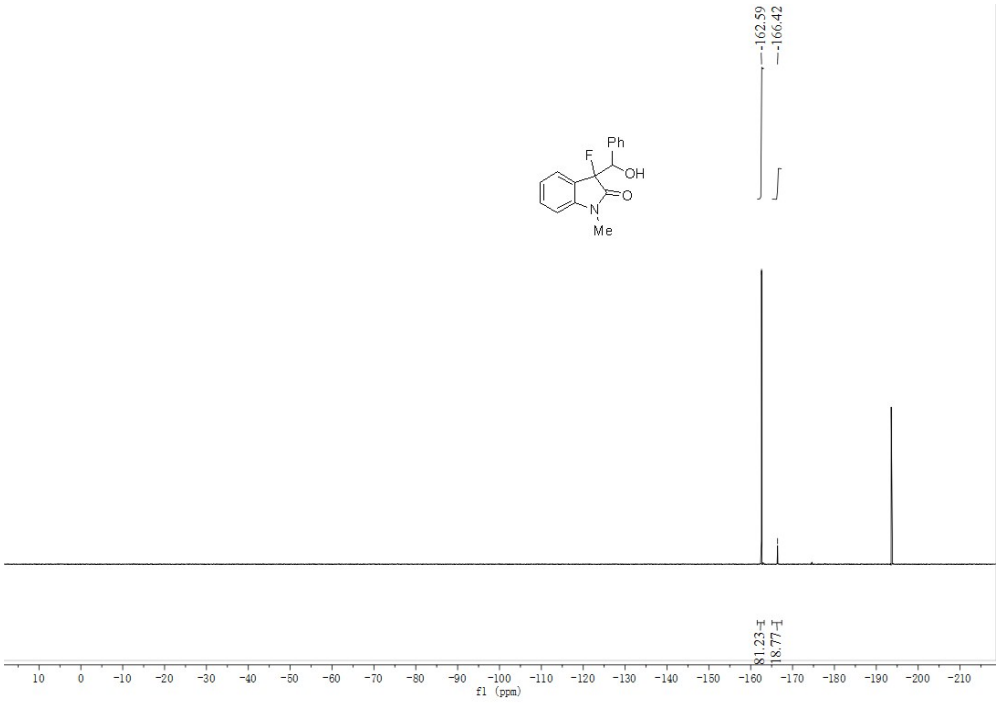




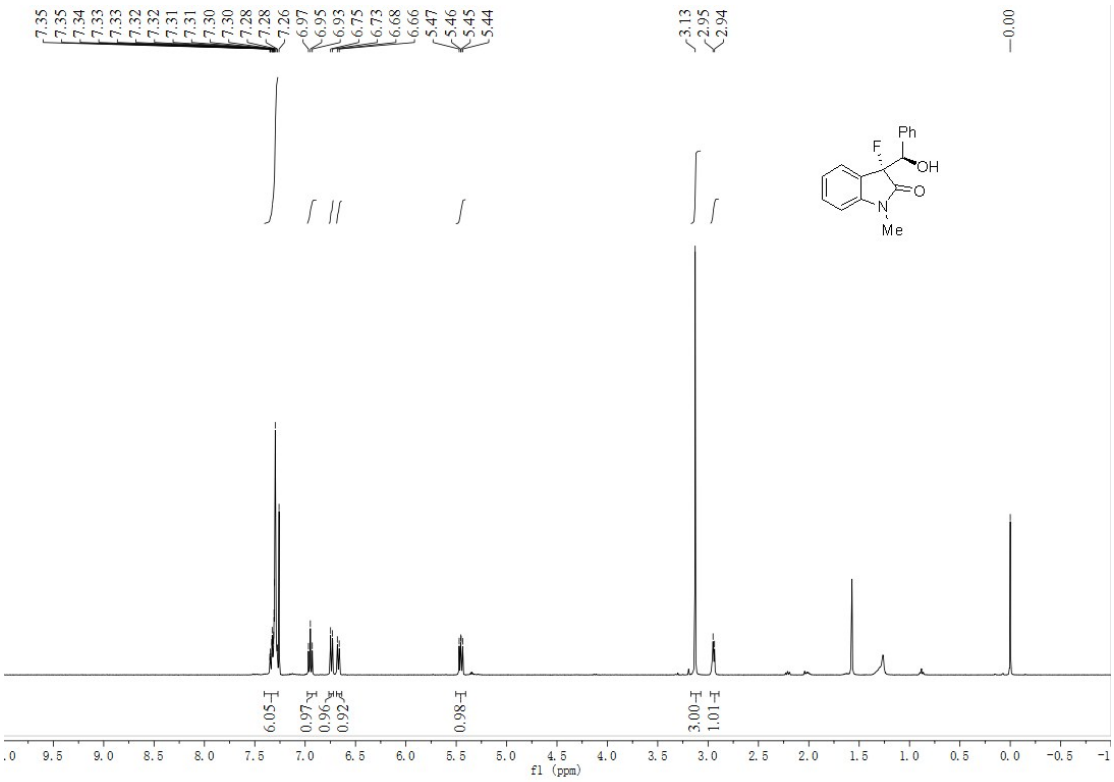
6. NMR spectra

6.1. NMR spectra of *α*-fluorinated gem-diols 13

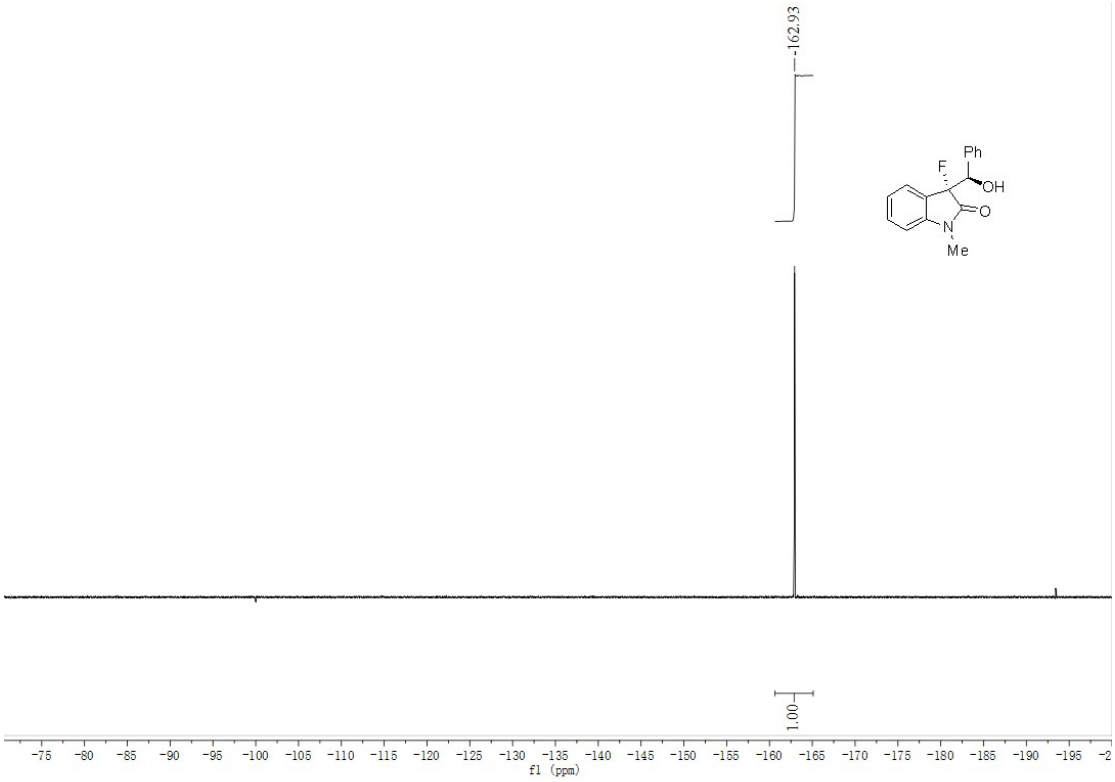
Crude ^{19}FNMR (376 MHz, $CDCl_3$) spectra of **13a**



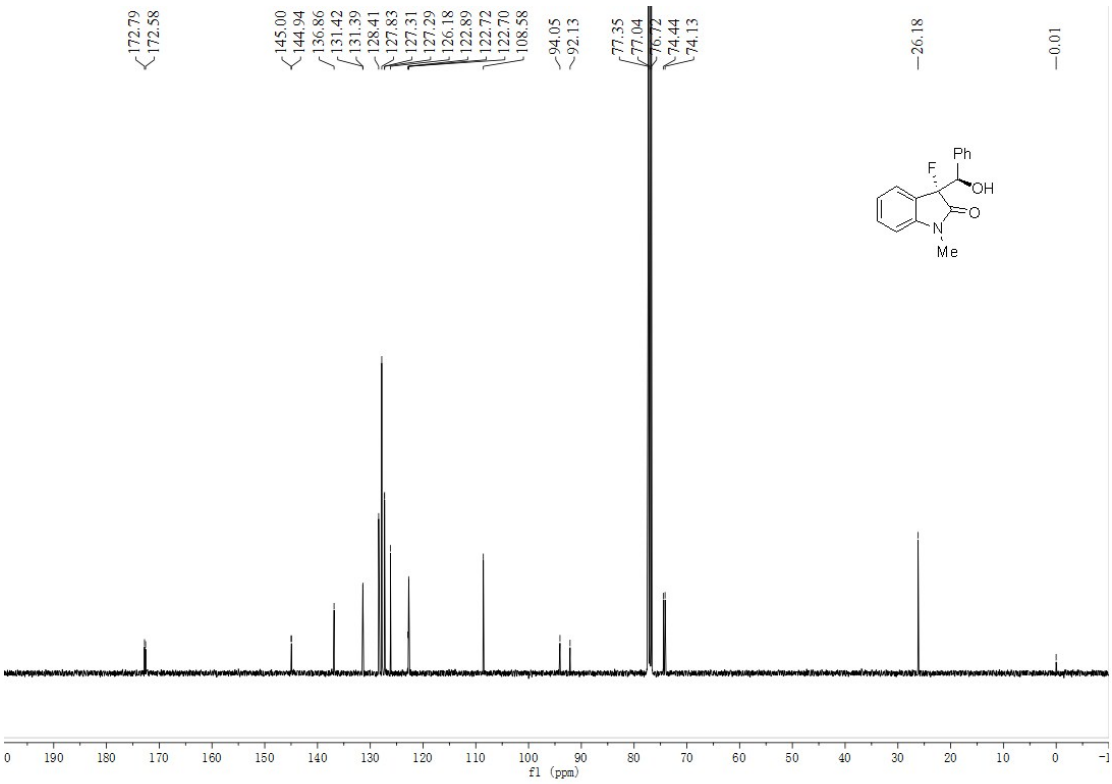
^{1}H NMR (400 MHz, $CDCl_3$) spectra of **13a**



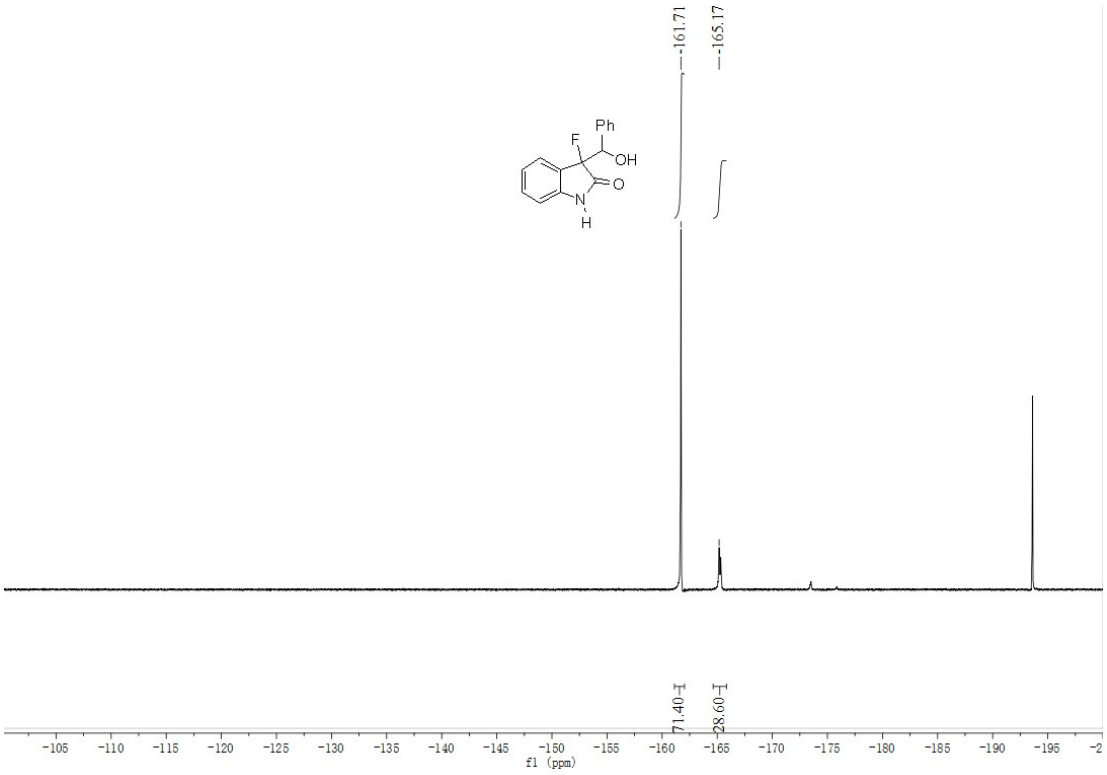
^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13a**



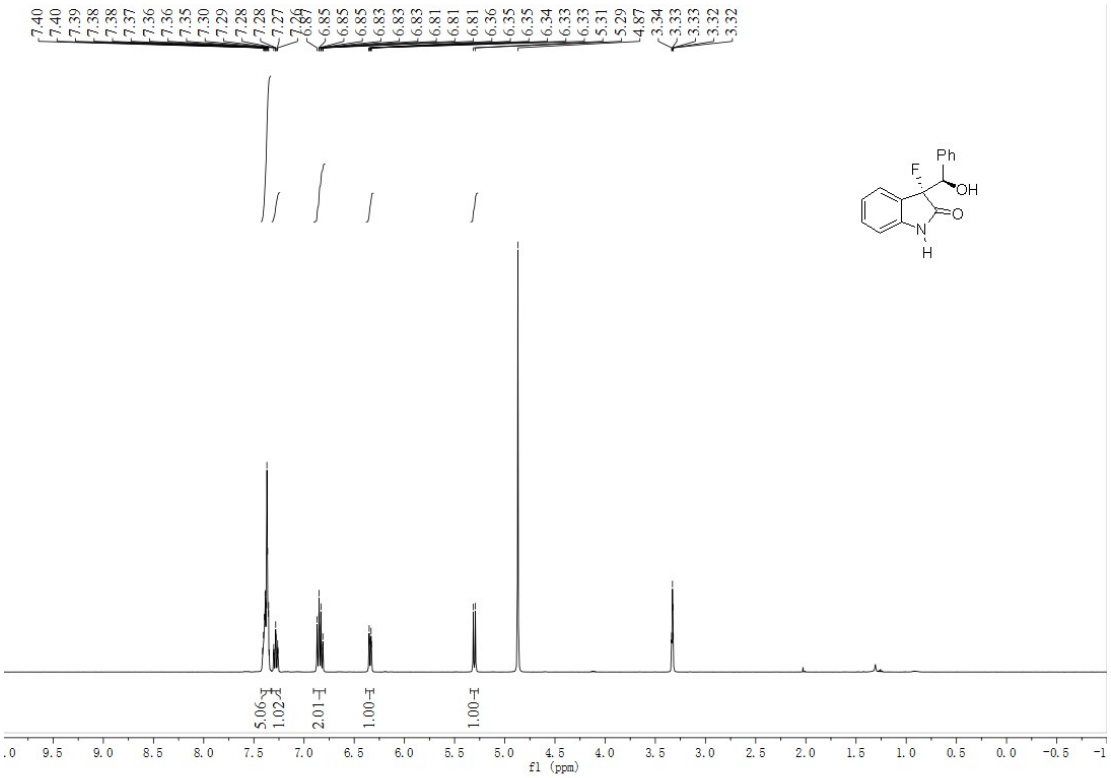
^{13}C NMR (101 MHz, $CDCl_3$) spectra of **13a**



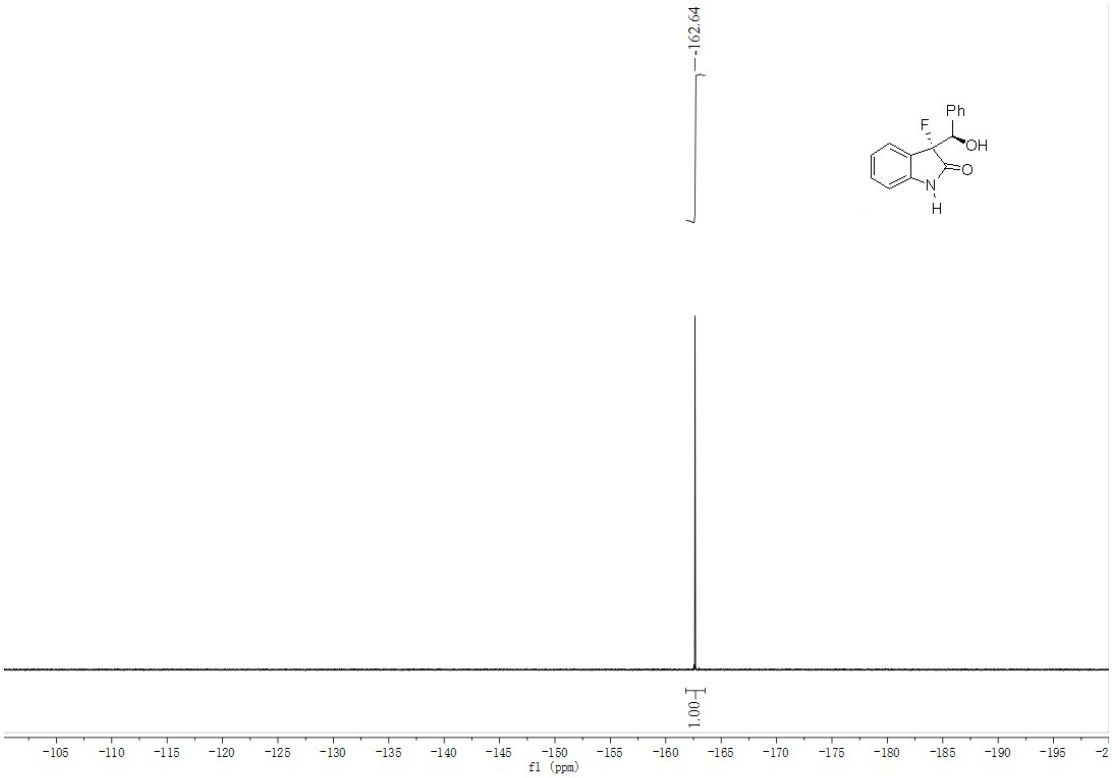
Crude ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13b**



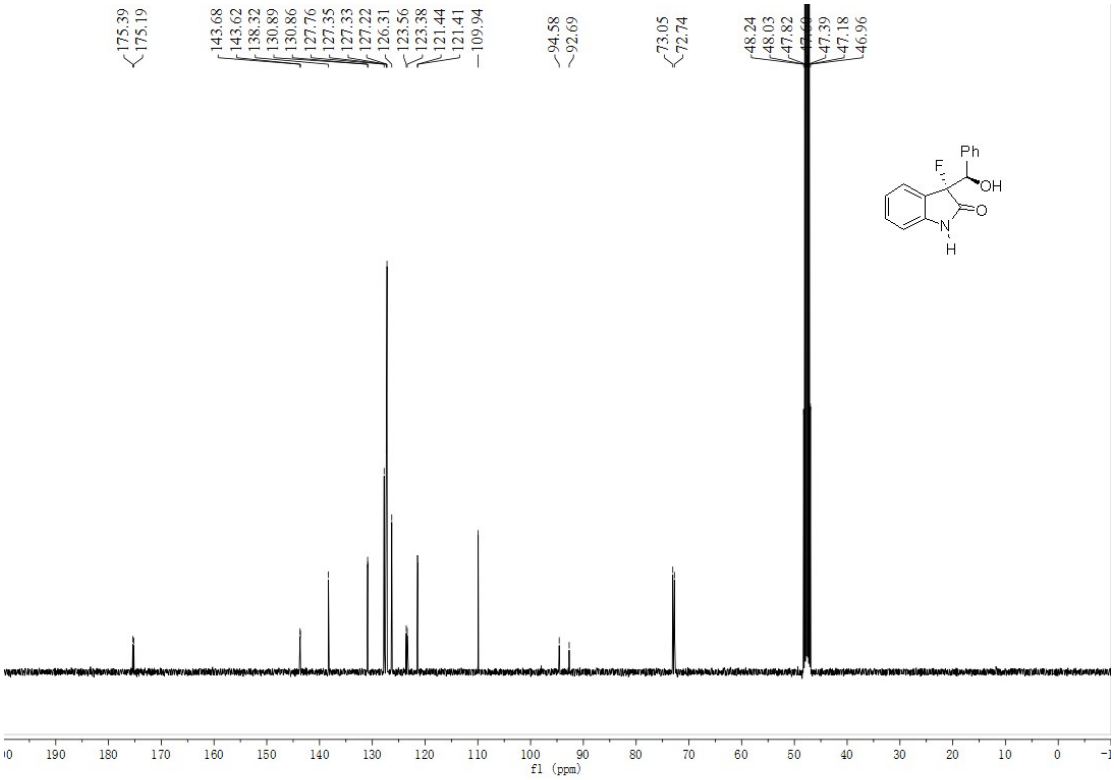
^{1}H NMR (400 MHz, $CDCl_3$) spectra of **13b**



^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13b**

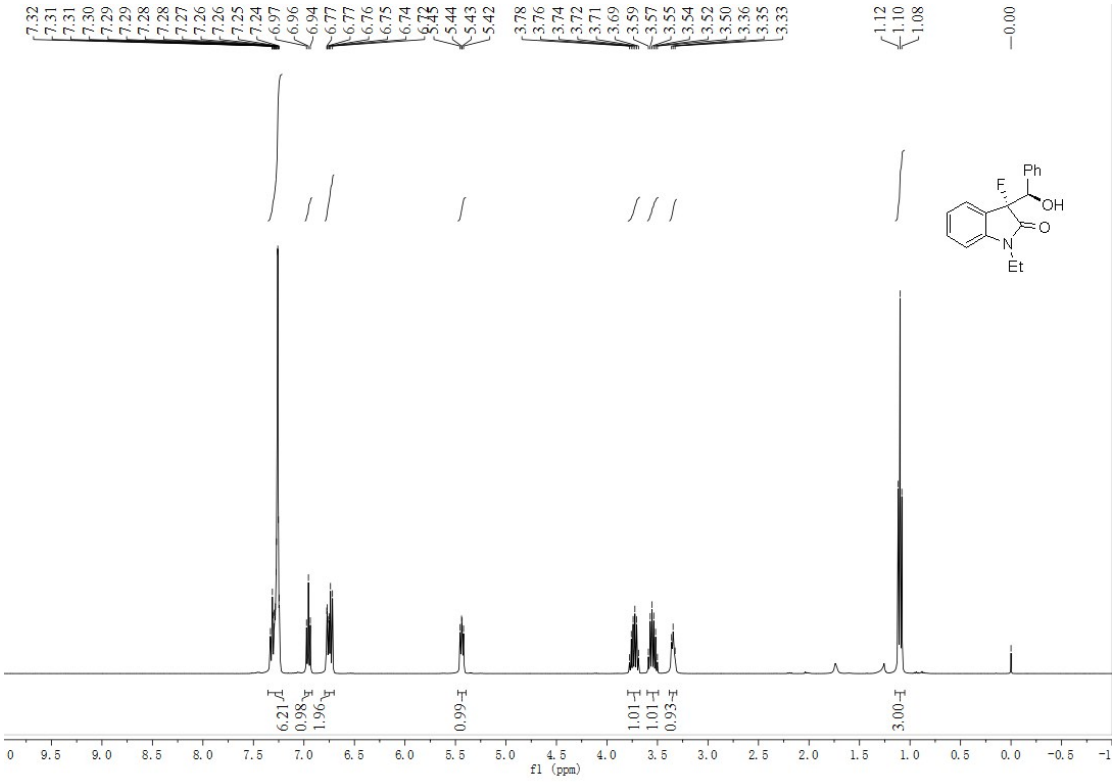


^{13}C NMR (101 MHz, $CDCl_3$) spectra of **13b**



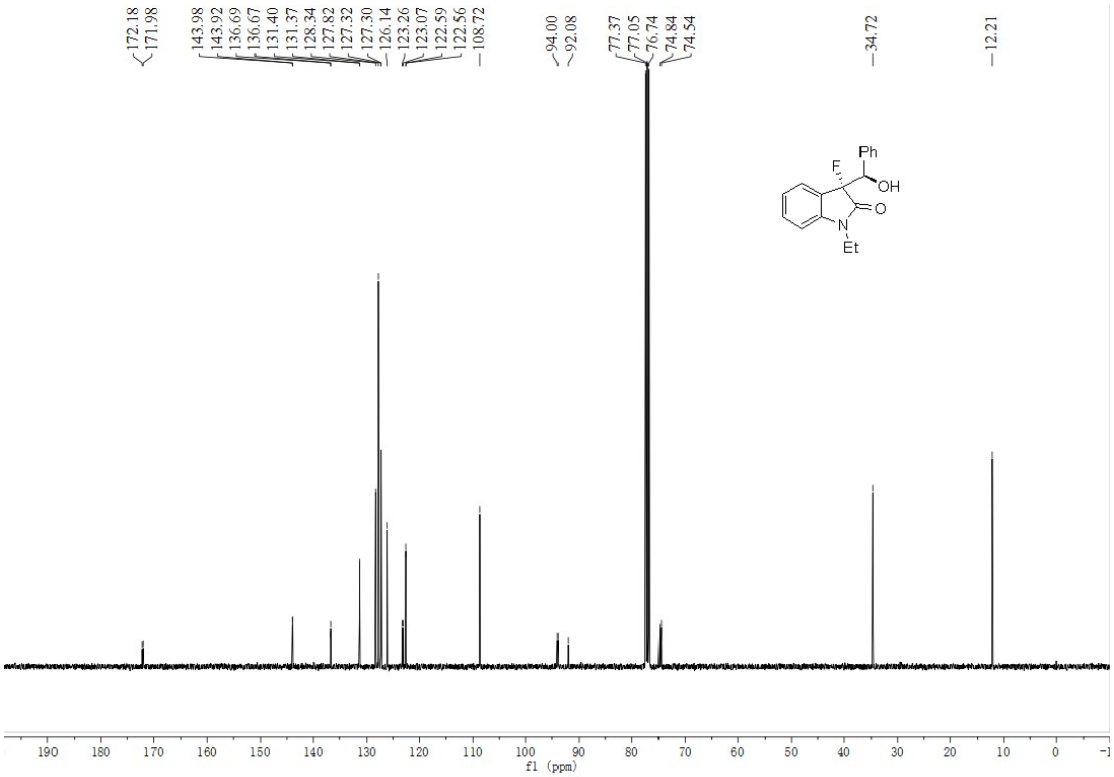
Crude ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13c**

^{1}H NMR (400 MHz, $CDCl_3$) spectra of **13c**

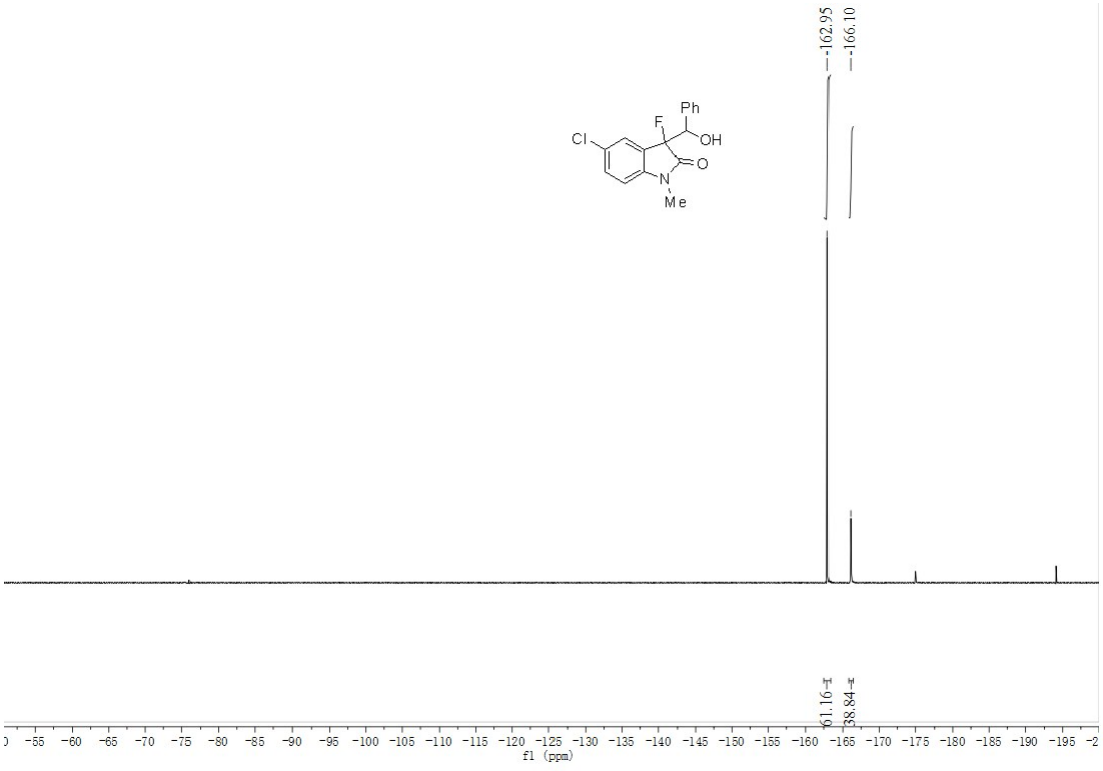


^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13c**

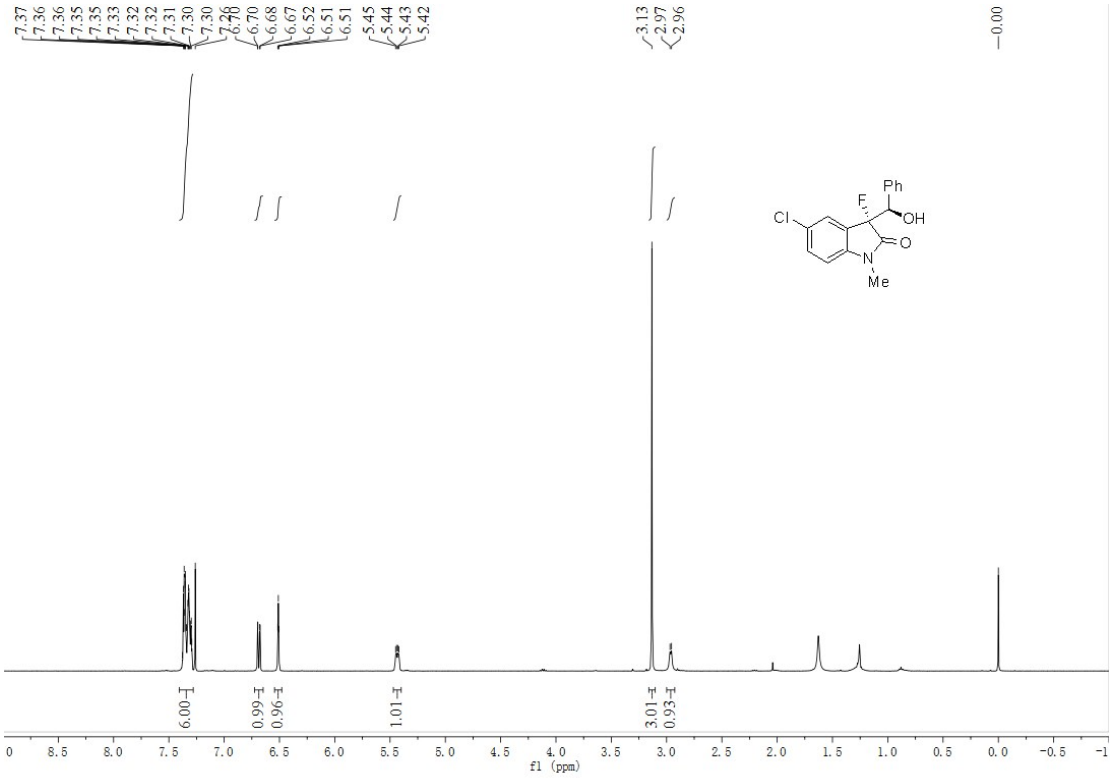
^{13}CNMR (101 MHz, $CDCl_3$) spectra of **13c**



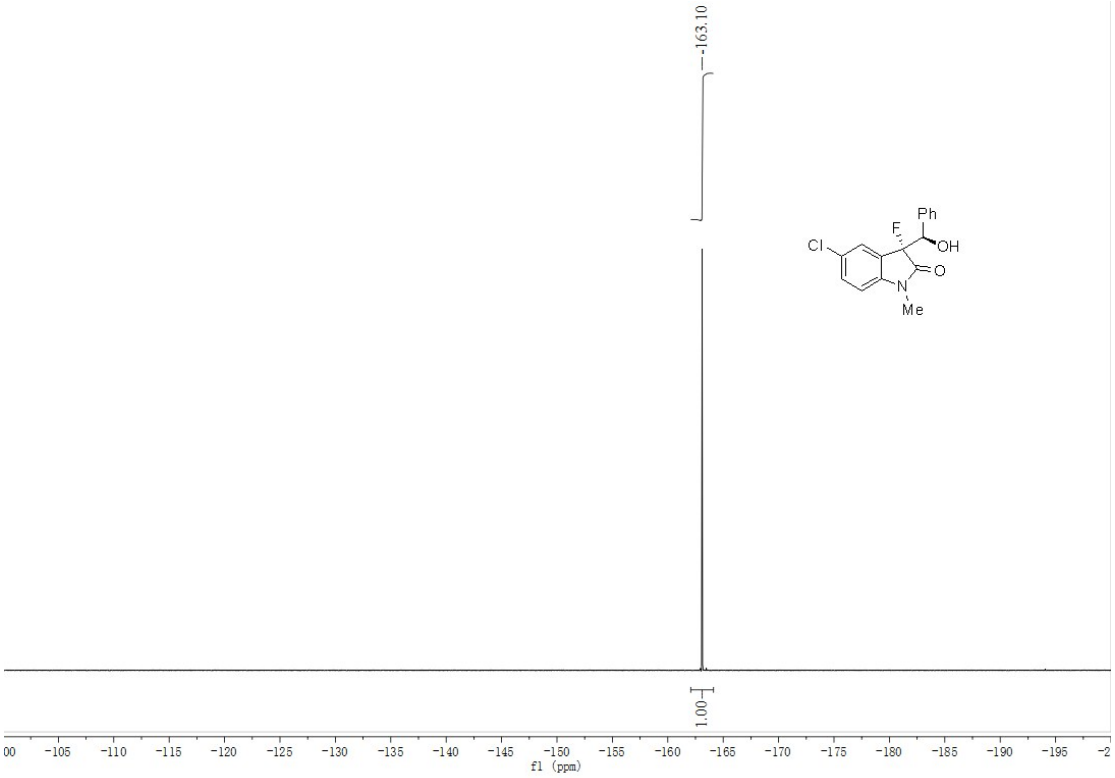
Crude ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13d**



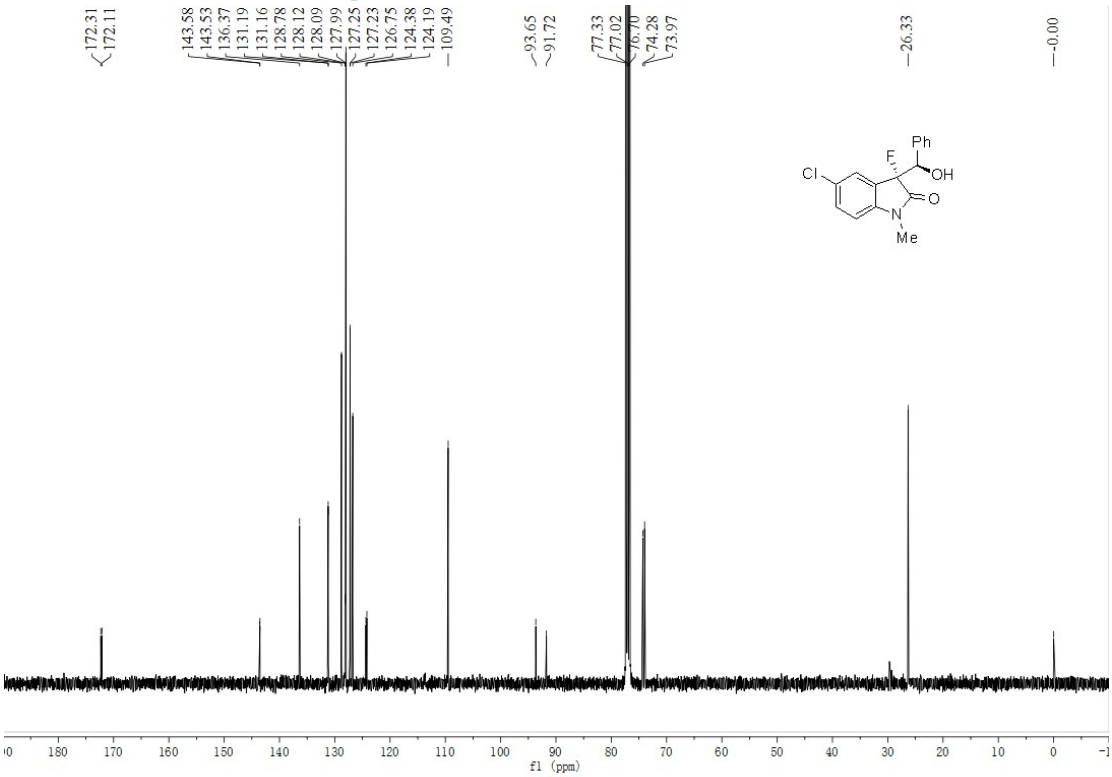
^{1}H NMR (400 MHz, $CDCl_3$) spectra of **13d**



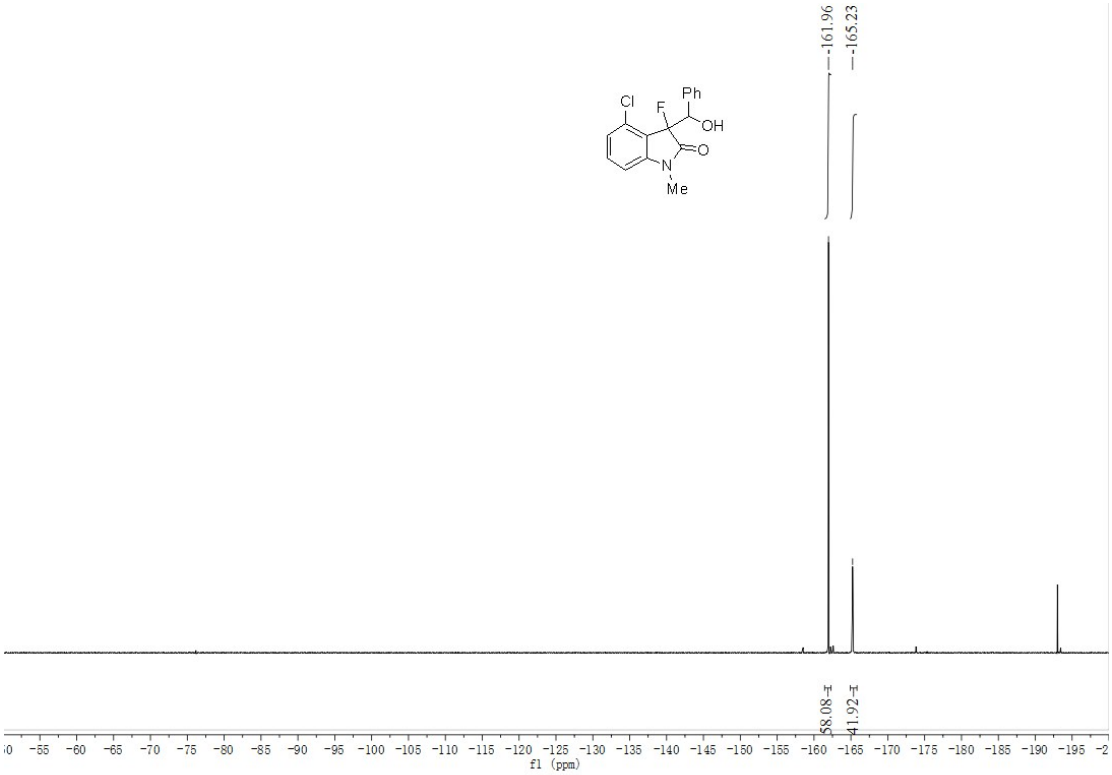
^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13d**



^{13}C NMR (101 MHz, $CDCl_3$) spectra of **13d**

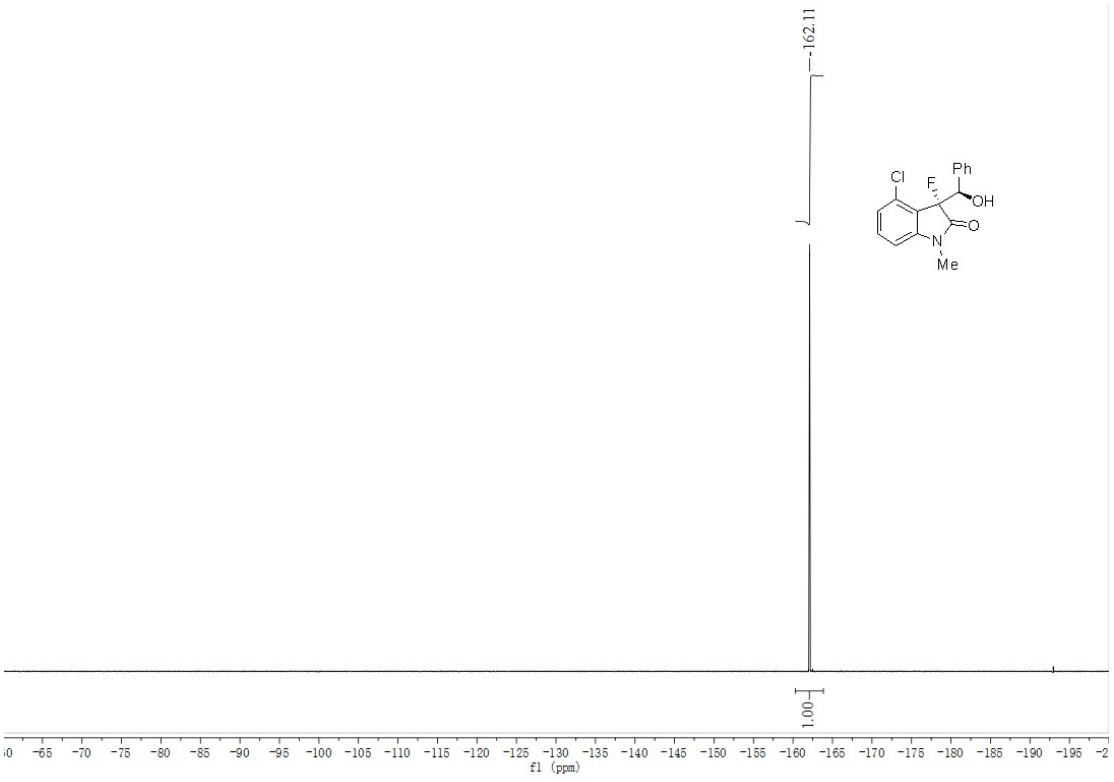


Crude ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13e**

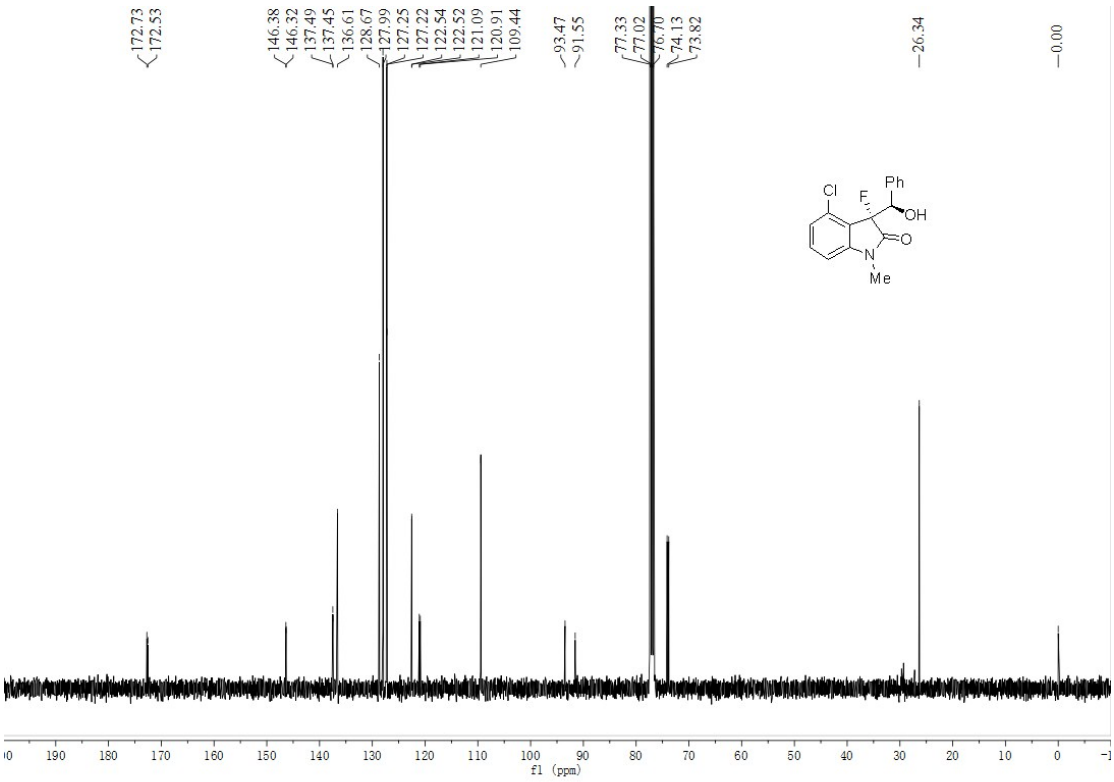


^{1}H NMR (400 MHz, $CDCl_3$) spectra of **13e**

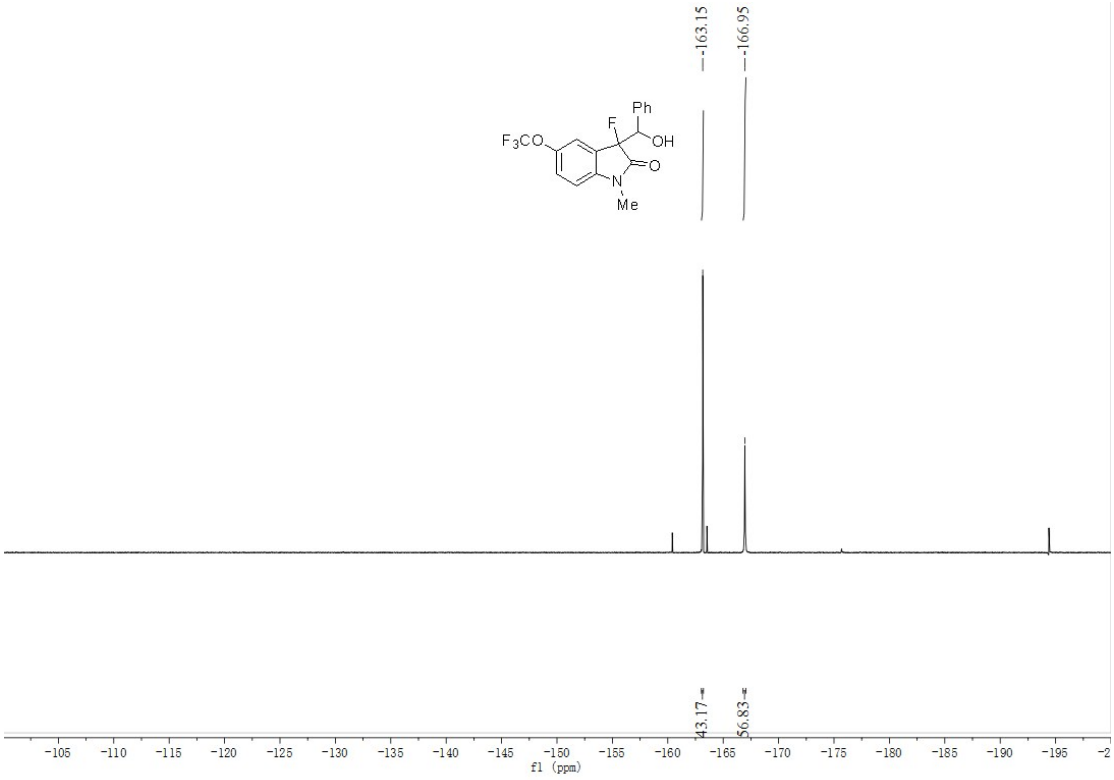
^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13e**



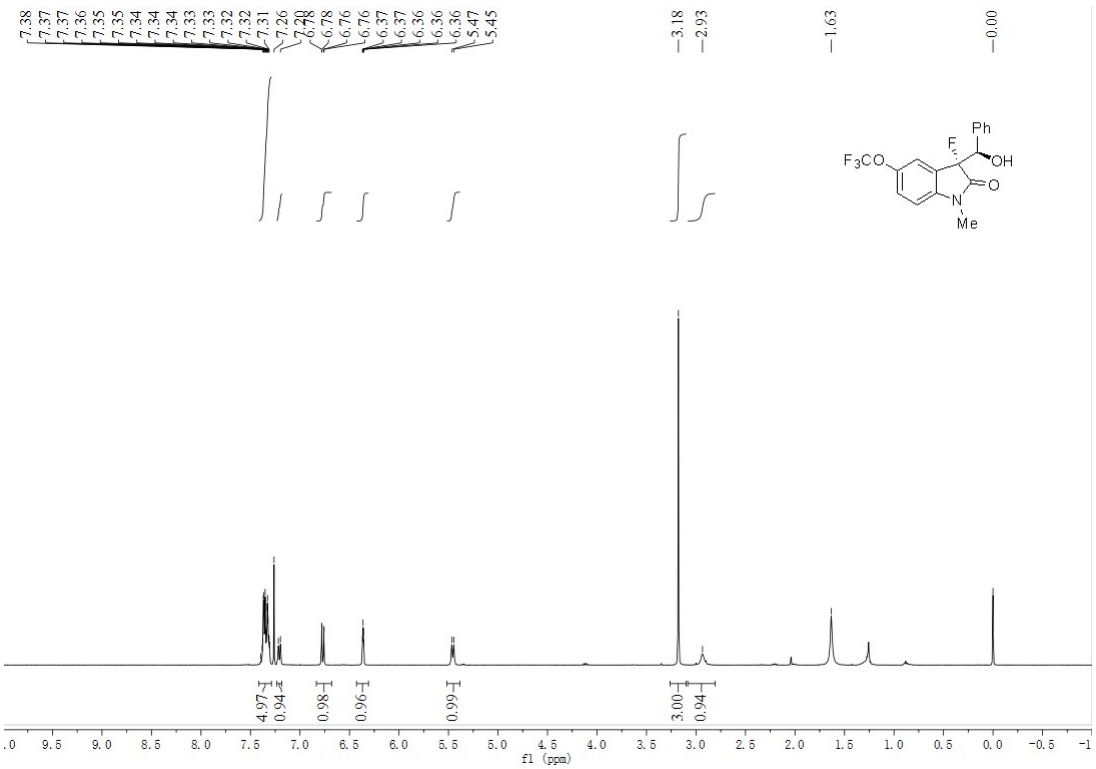
^{13}C NMR (101 MHz, $CDCl_3$) spectra of **13e**



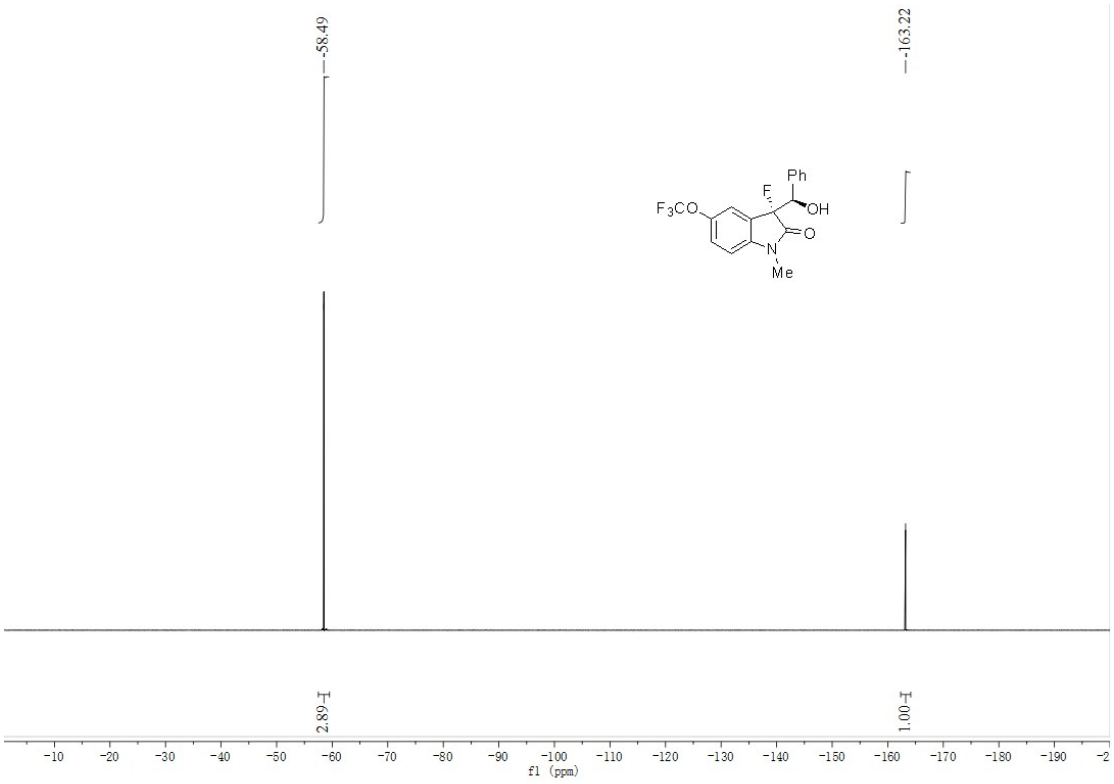
Crude ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13f**



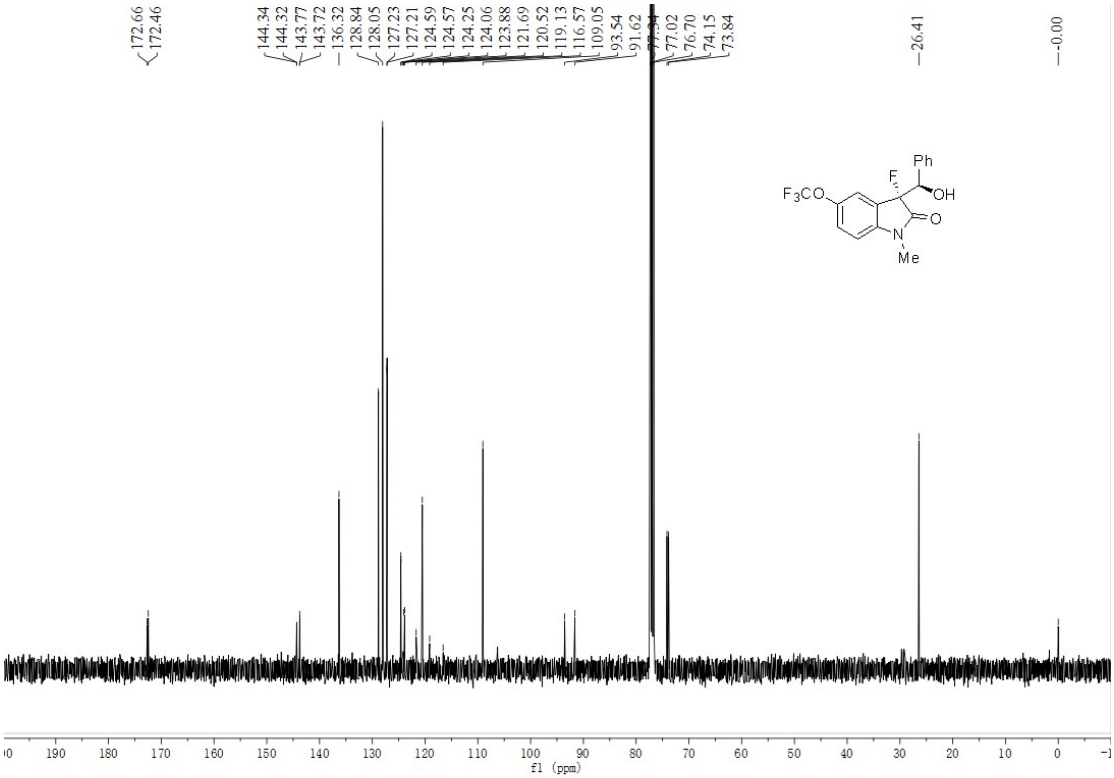
^{1}H NMR (400 MHz, $CDCl_3$) spectra of **13f**



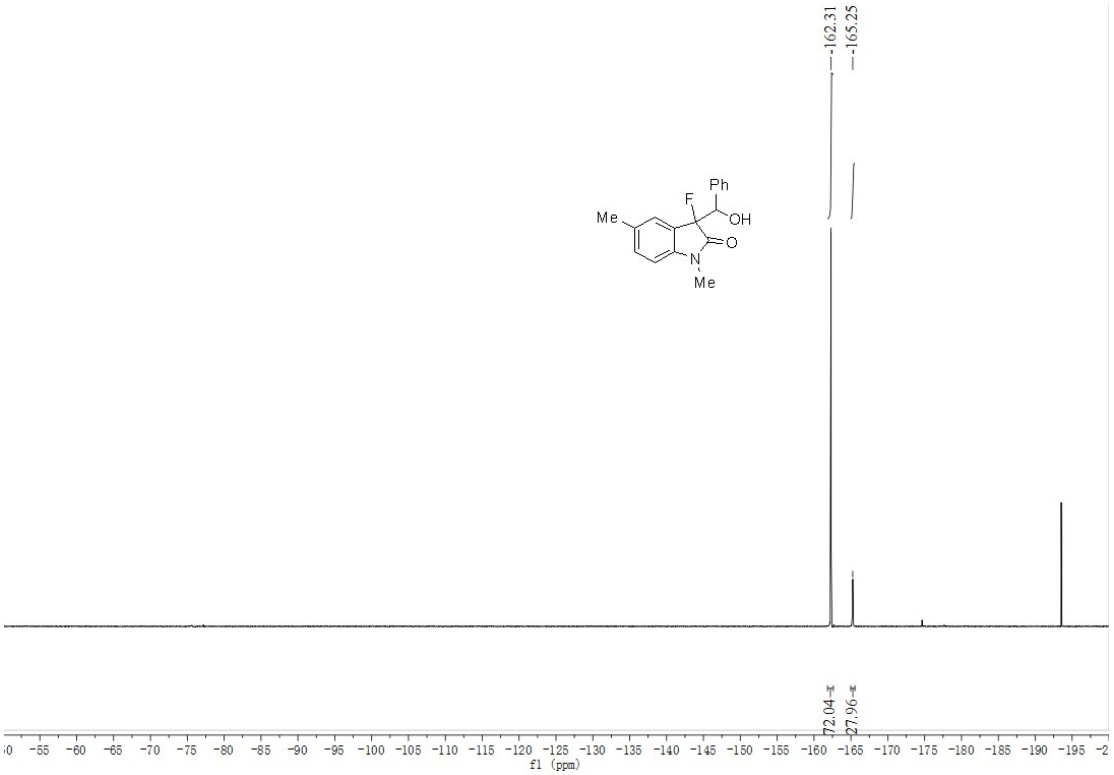
^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13f**



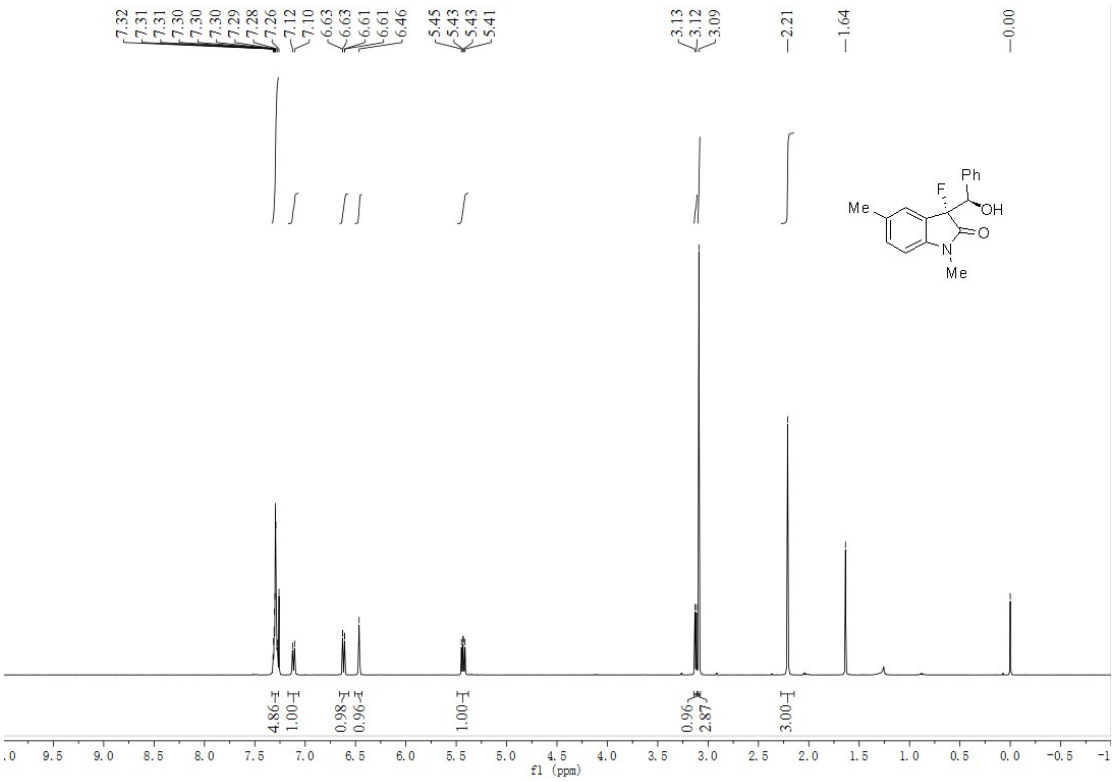
^{13}C NMR (101 MHz, $CDCl_3$) spectra of **13f**



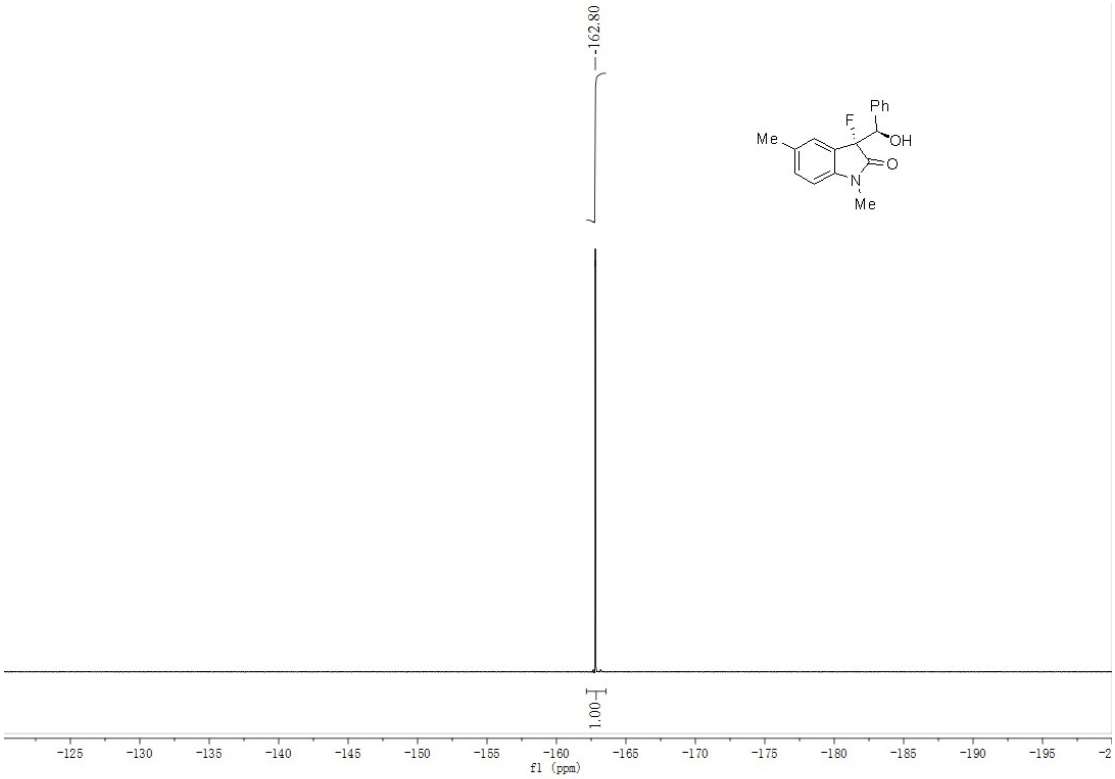
Crude ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13g**



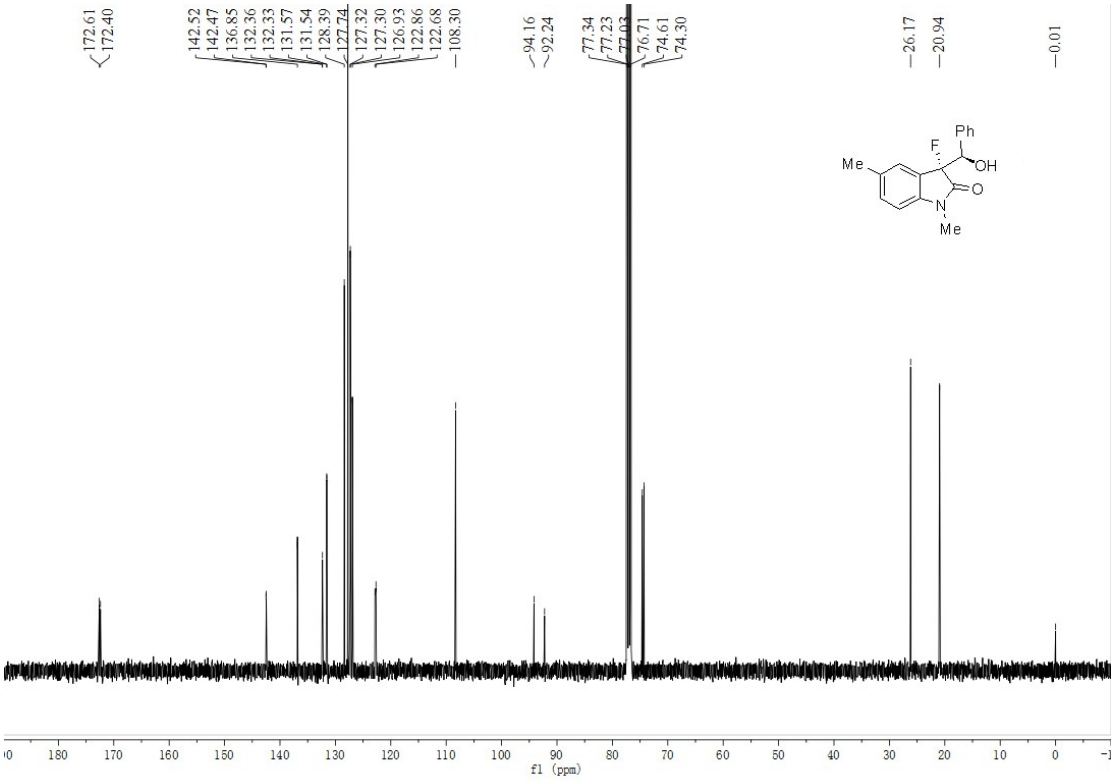
^{1}H NMR (400 MHz, $CDCl_3$) spectra of **13g**



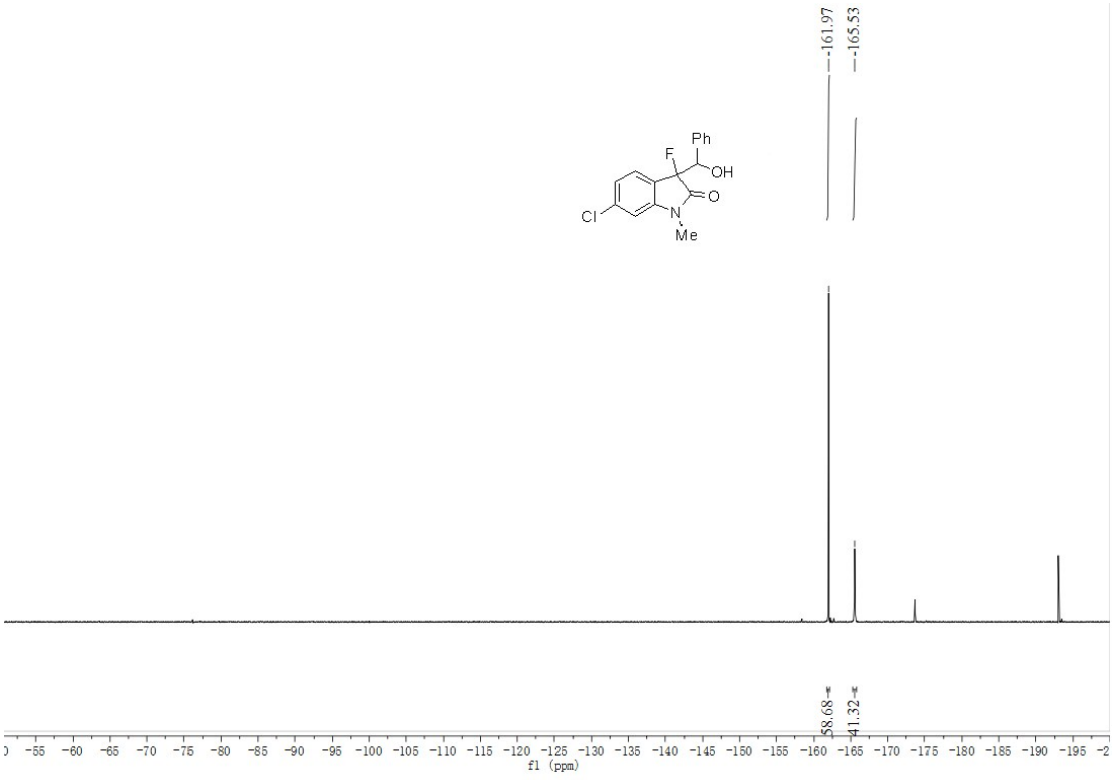
^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13g**



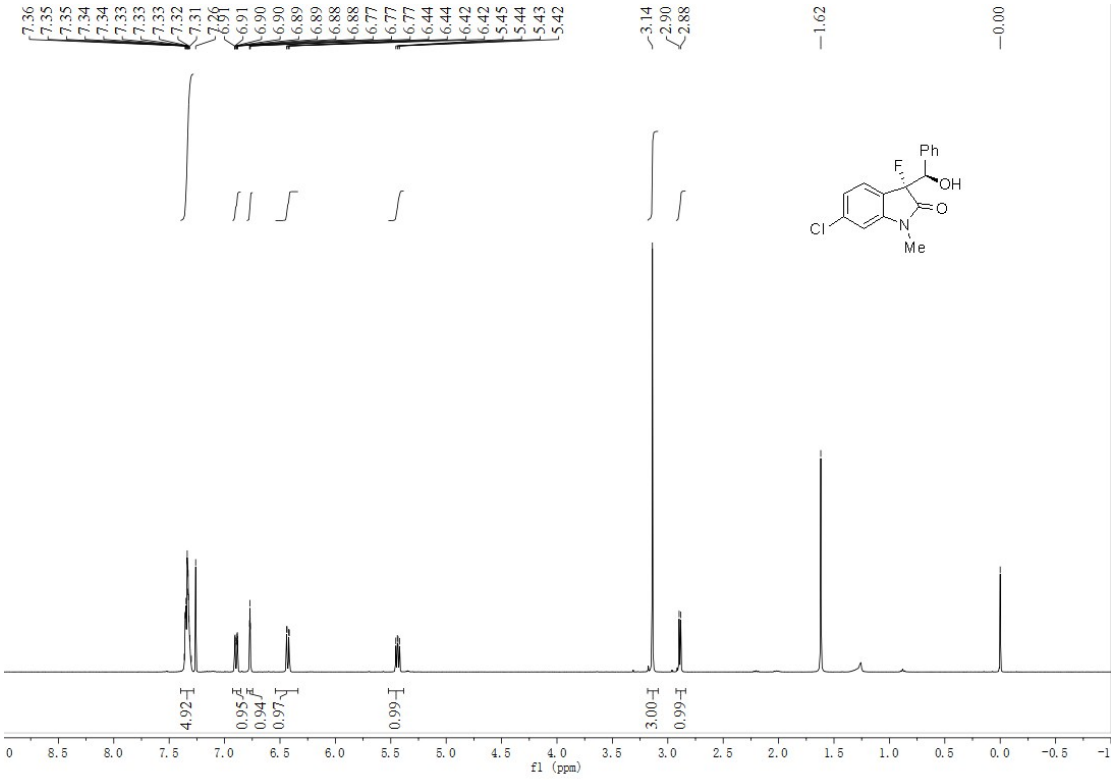
^{13}C NMR (101 MHz, $CDCl_3$) spectra of **13g**



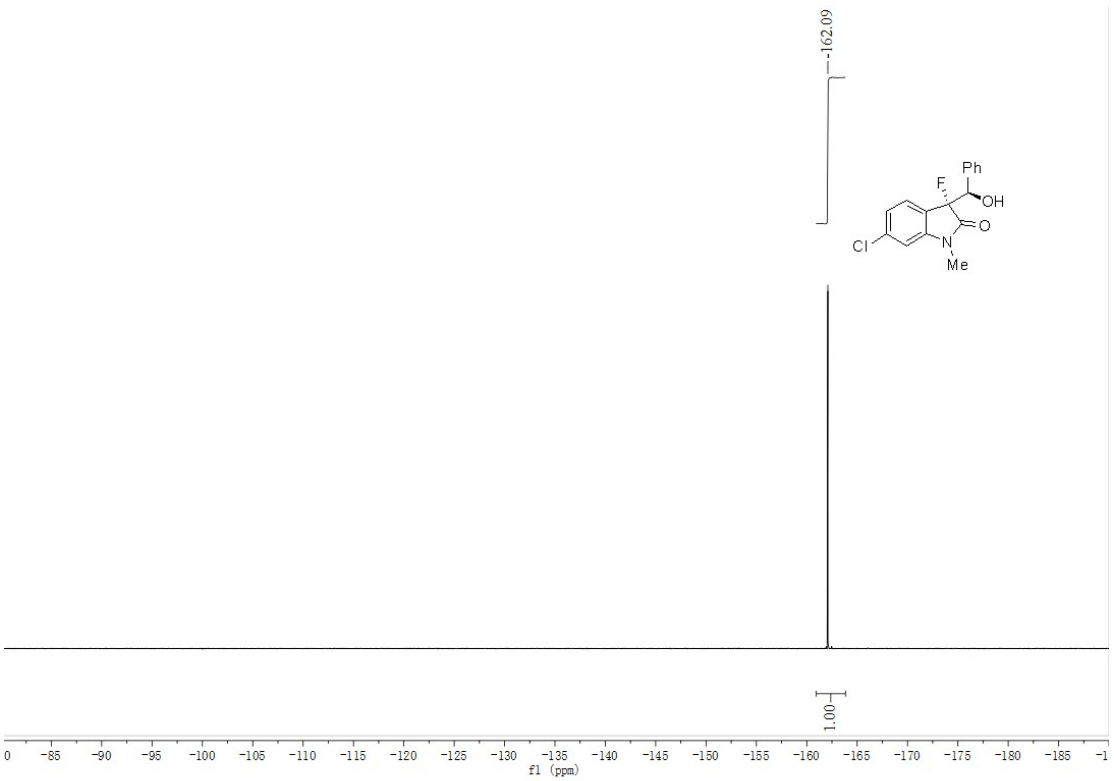
Crude ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13h**



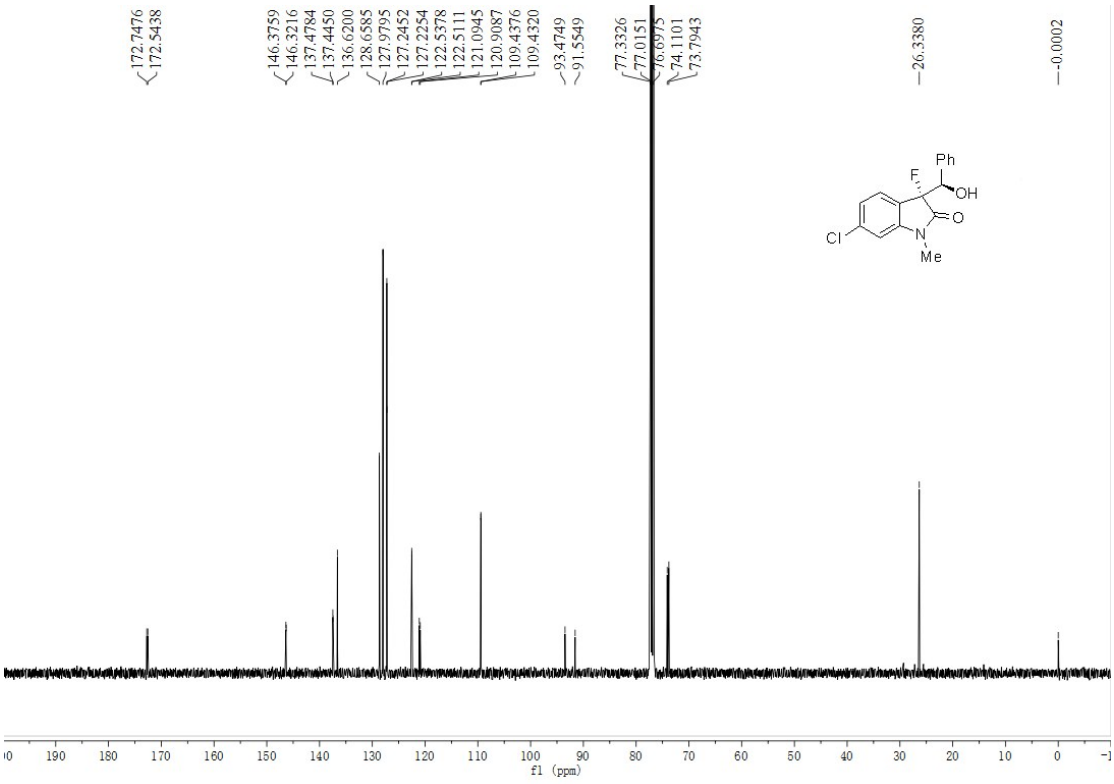
^{1}H NMR (400 MHz, $CDCl_3$) spectra of **13h**



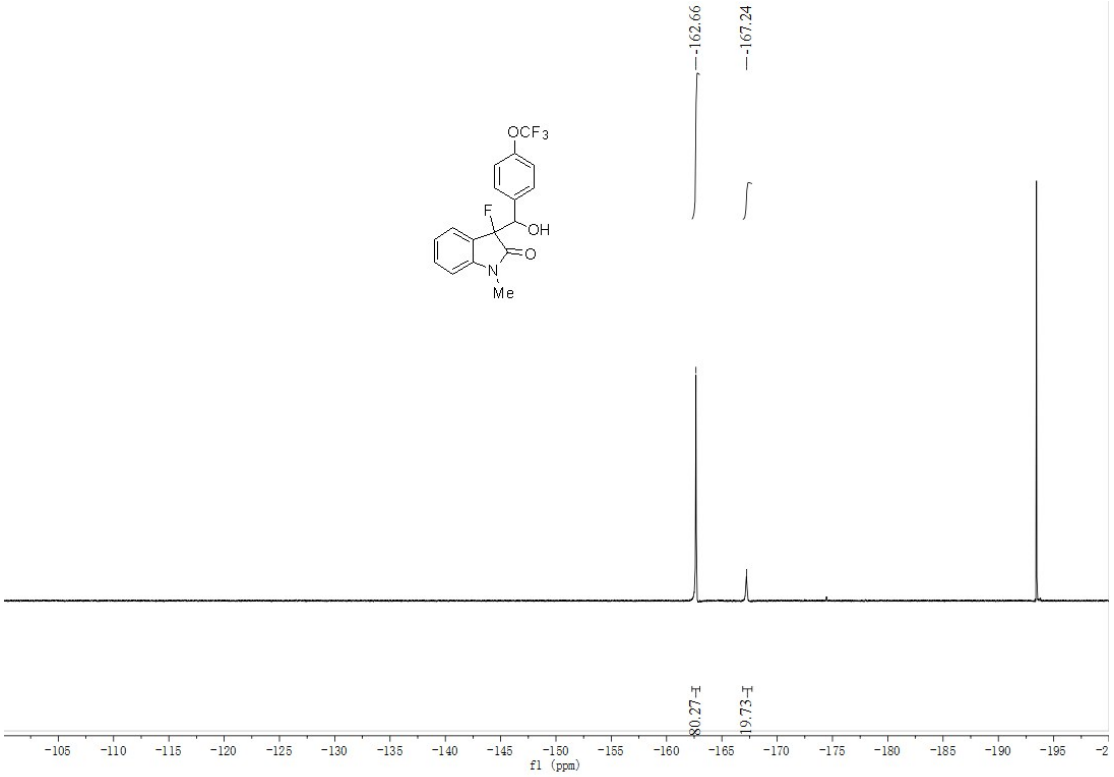
^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13h**



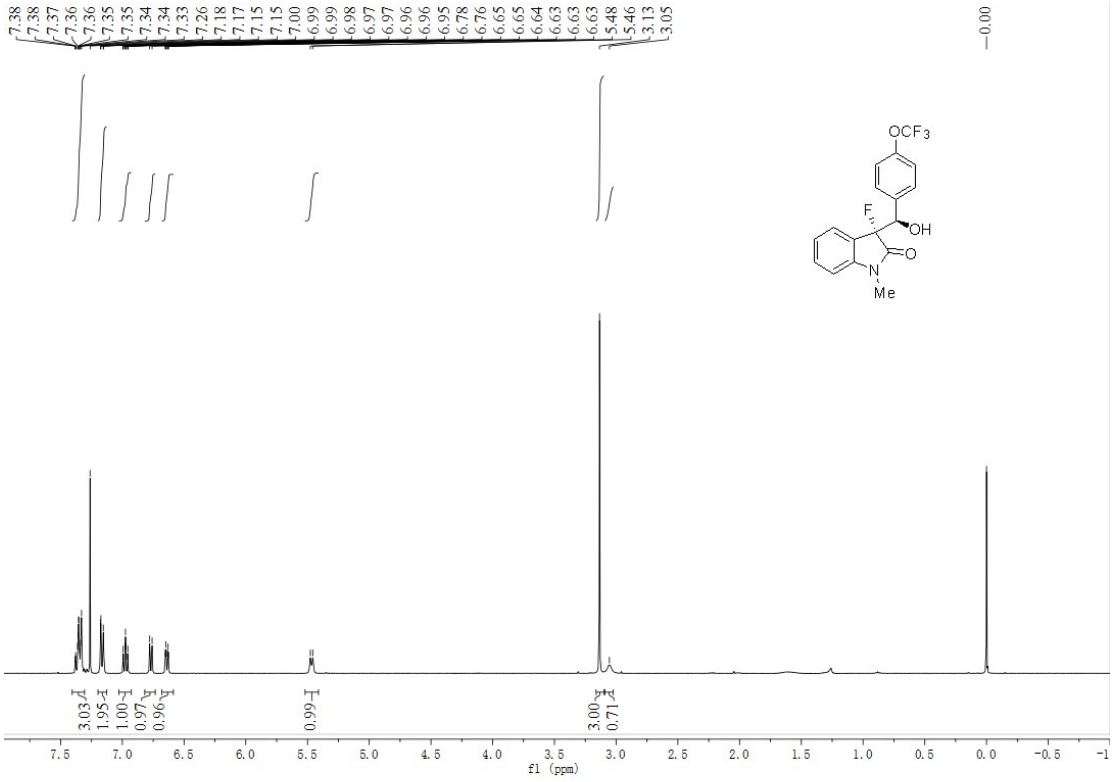
^{13}C NMR (101 MHz, $CDCl_3$) spectra of **13h**



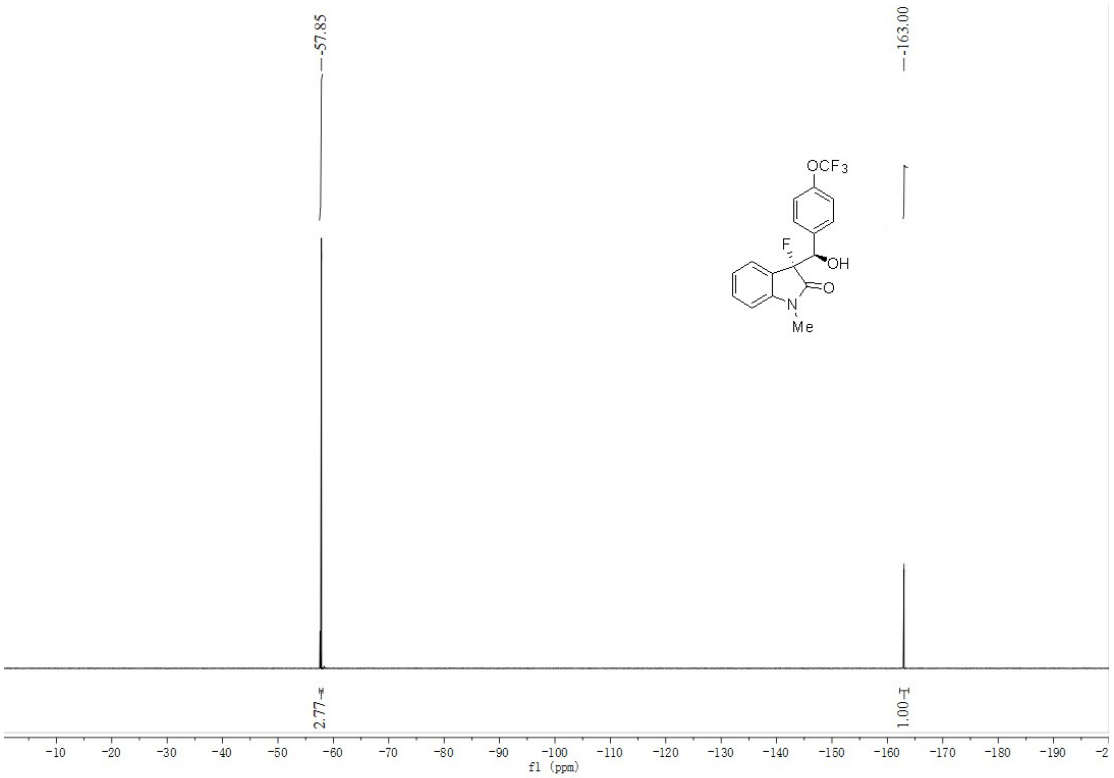
Crude ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13i**



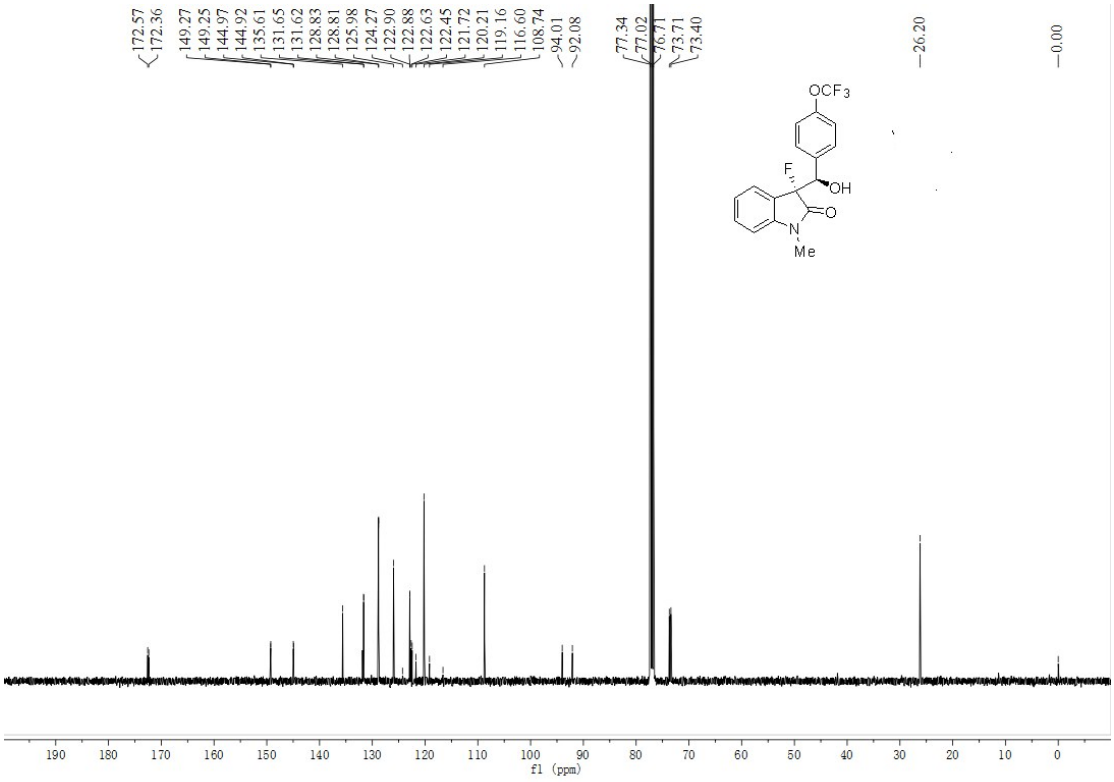
^{1}H NMR (400 MHz, $CDCl_3$) spectra of **13i**



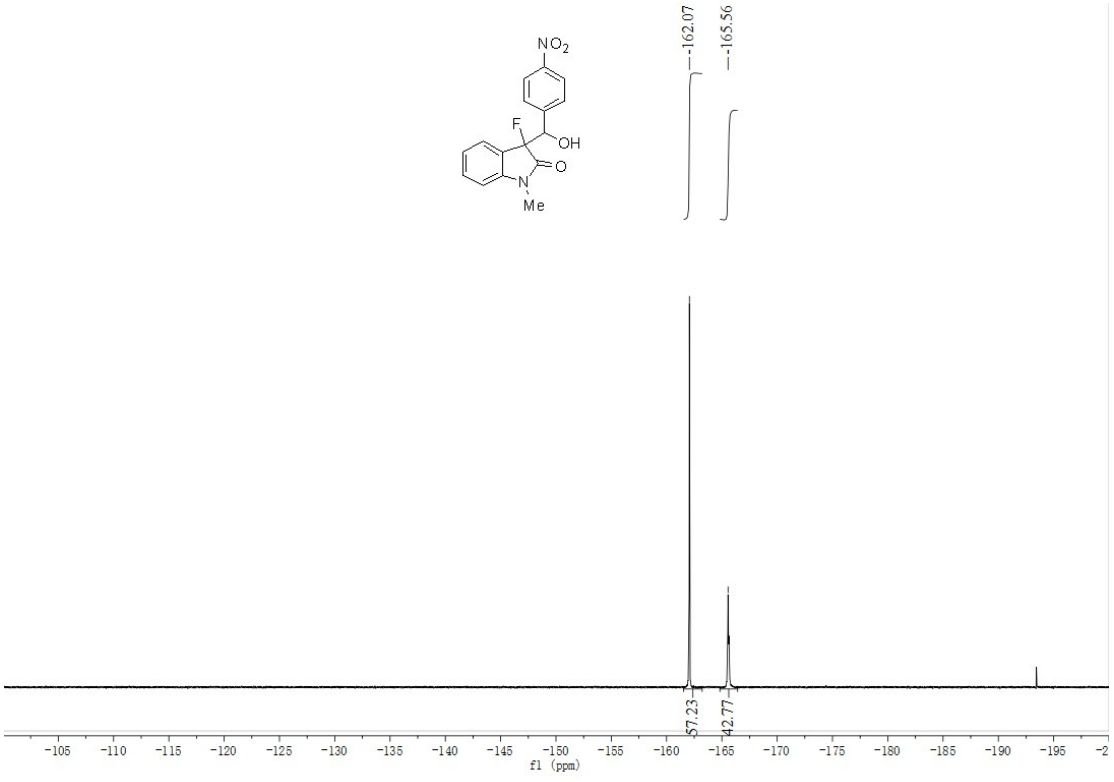
^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13i**



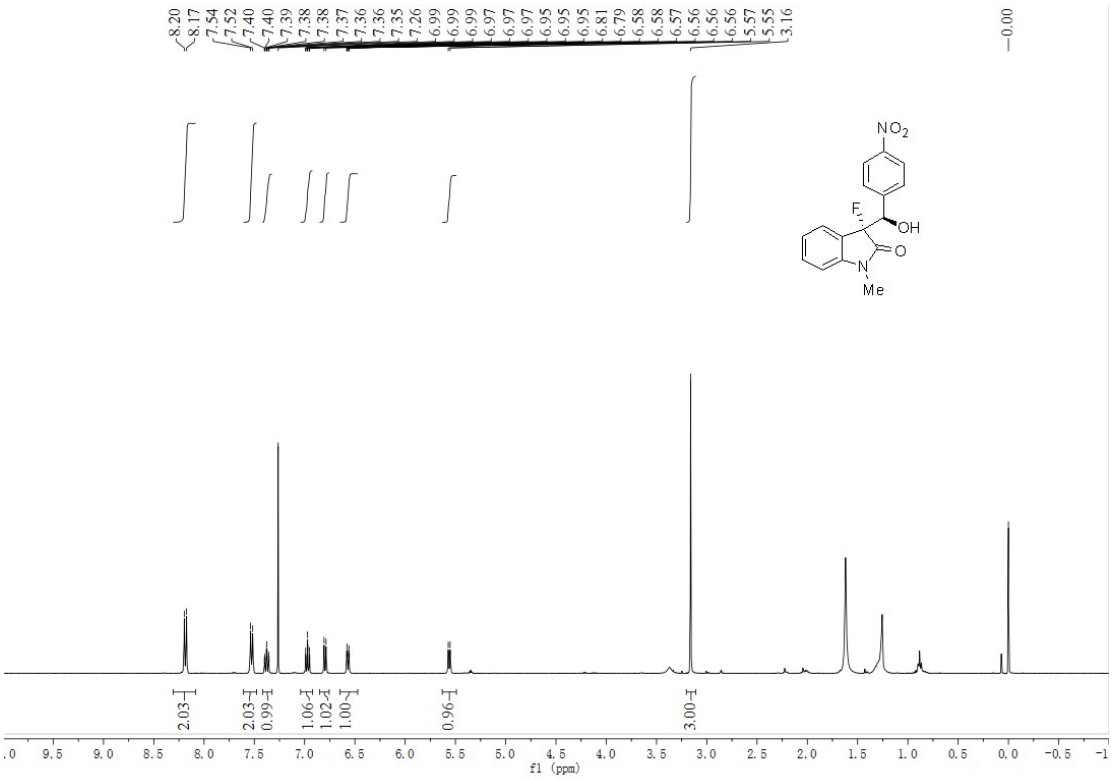
^{13}C NMR (101 MHz, $CDCl_3$) spectra of **13i**



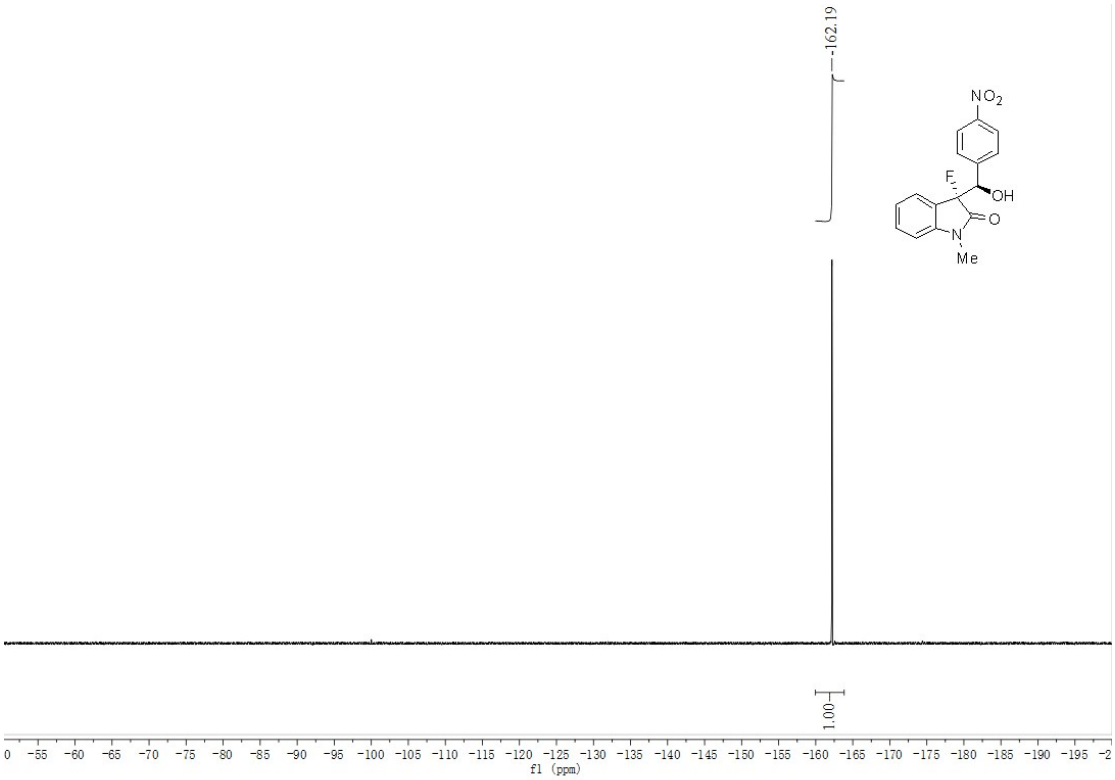
Crude ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13j**



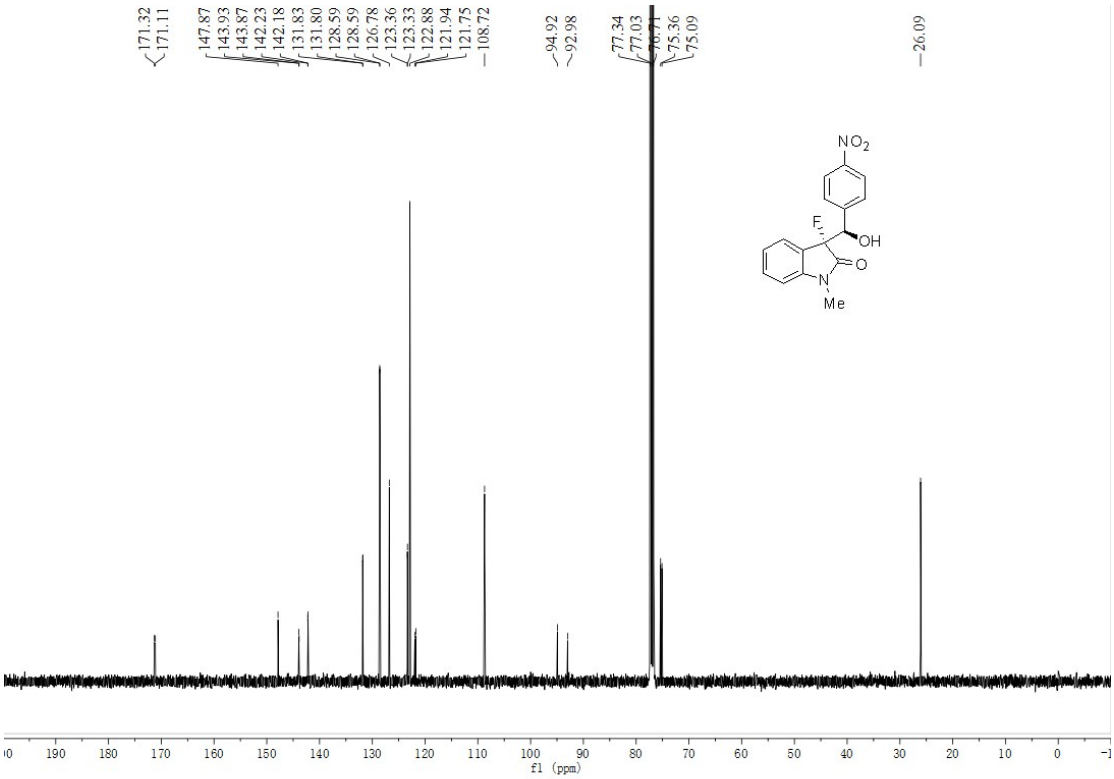
[1]HNMR (400 MHz, $CDCl_3$) spectra of **13j**



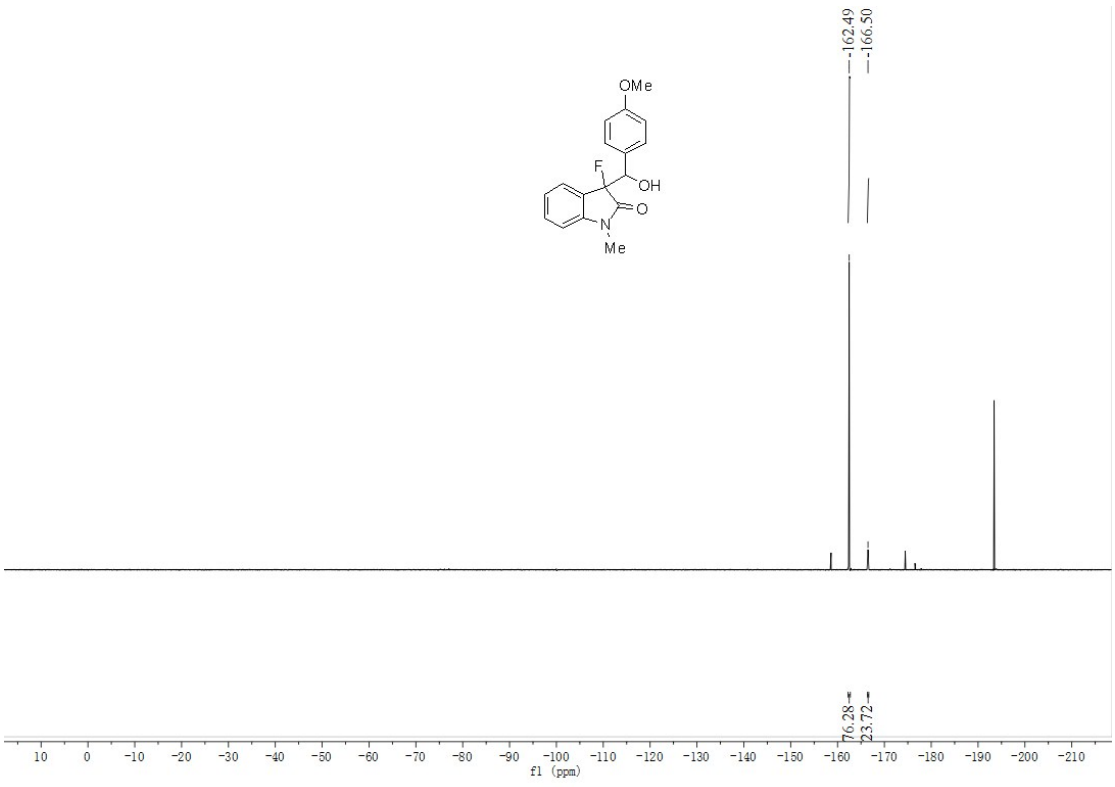
[19]F NMR (376 MHz, $CDCl_3$) spectra of **13j**



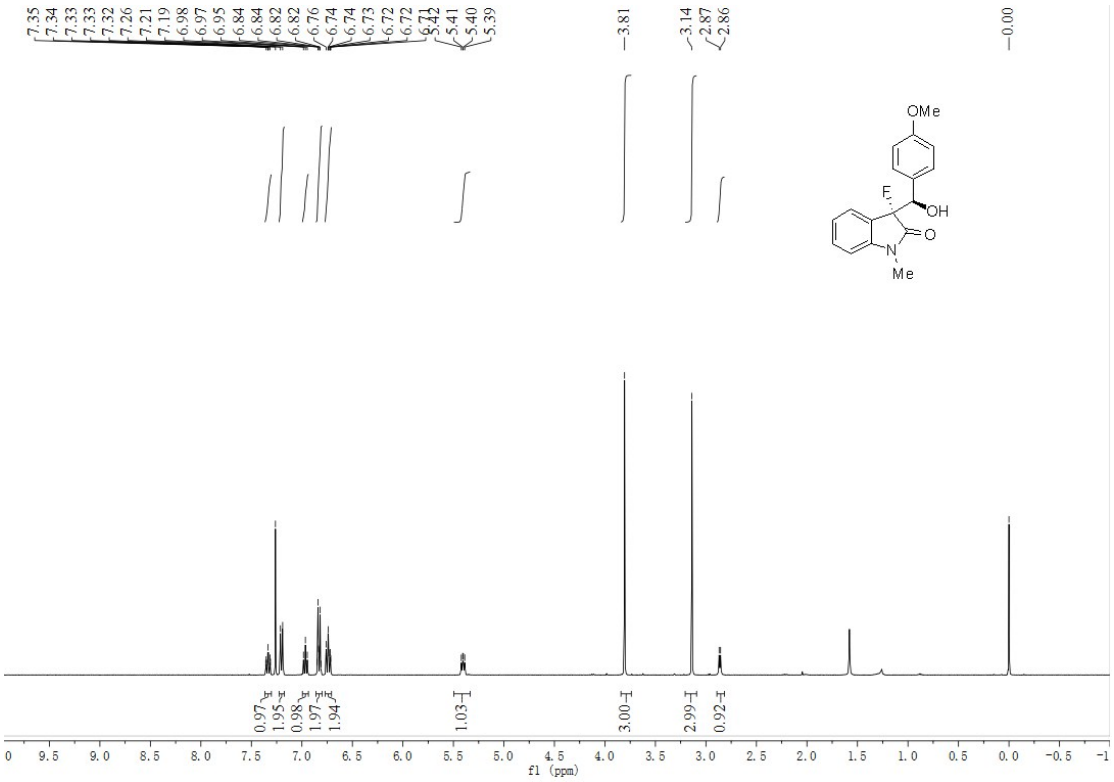
^{13}C NMR (101 MHz, $CDCl_3$) spectra of **13j**



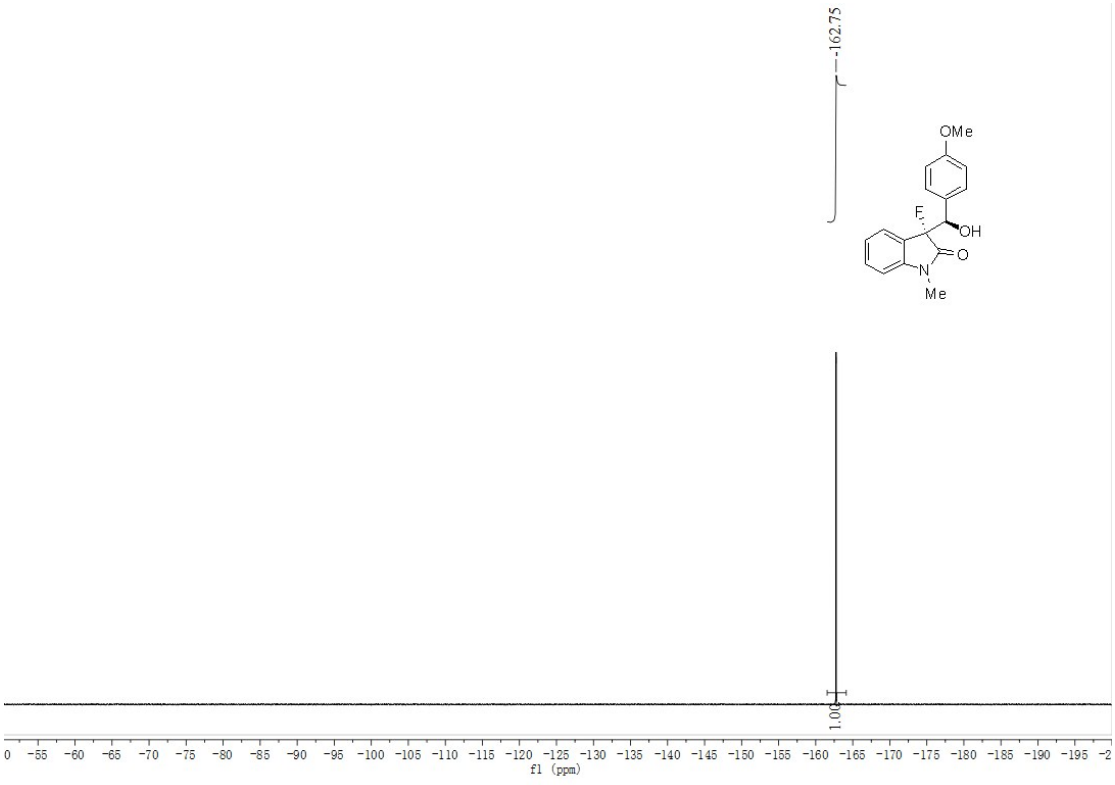
Crude ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13k**



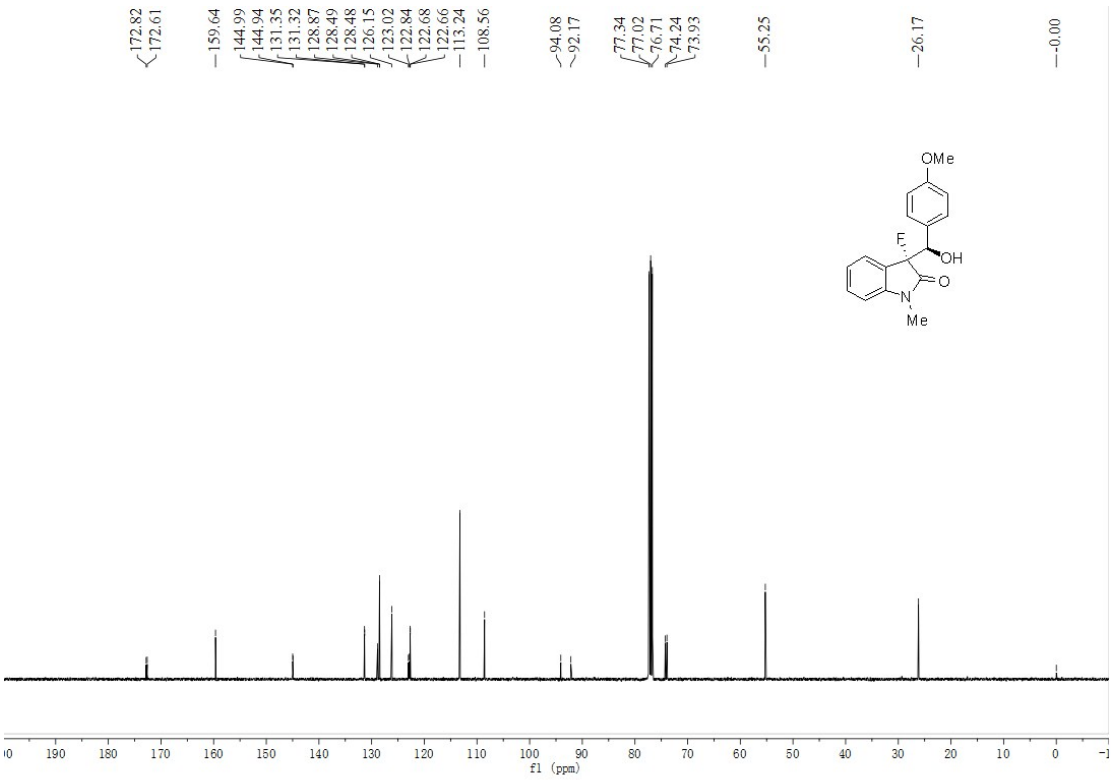
^{1}H NMR (400 MHz, $CDCl_3$) spectra of **13k**



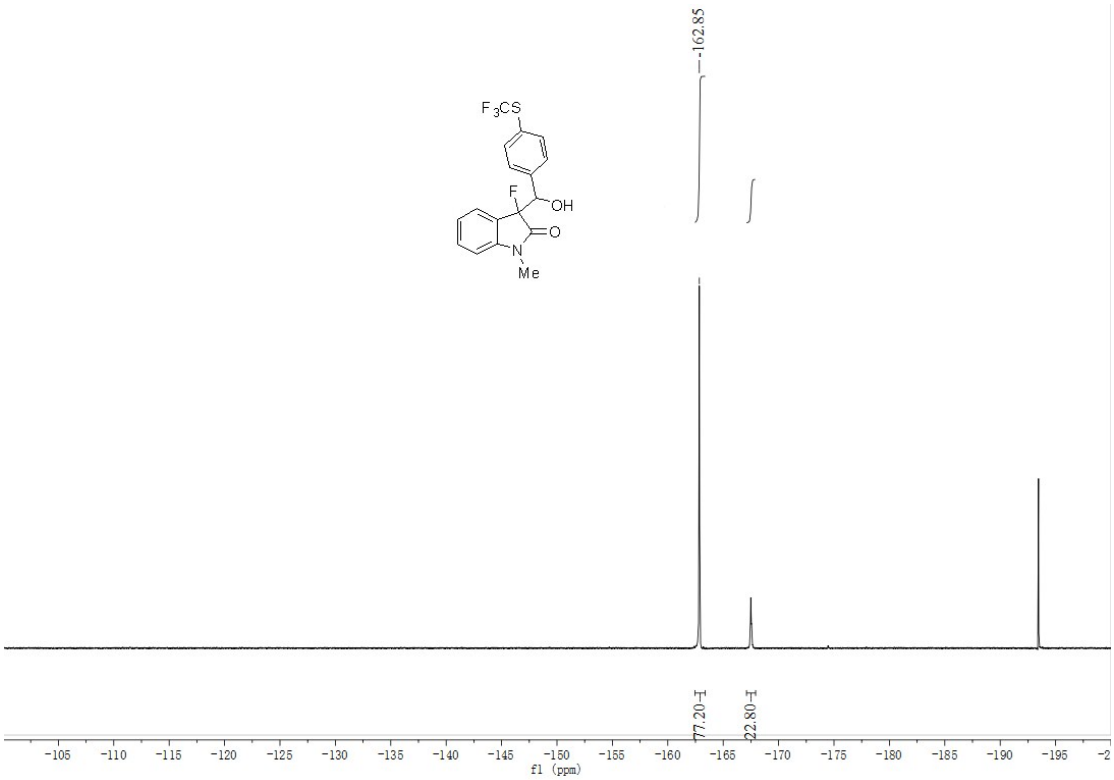
^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13k**



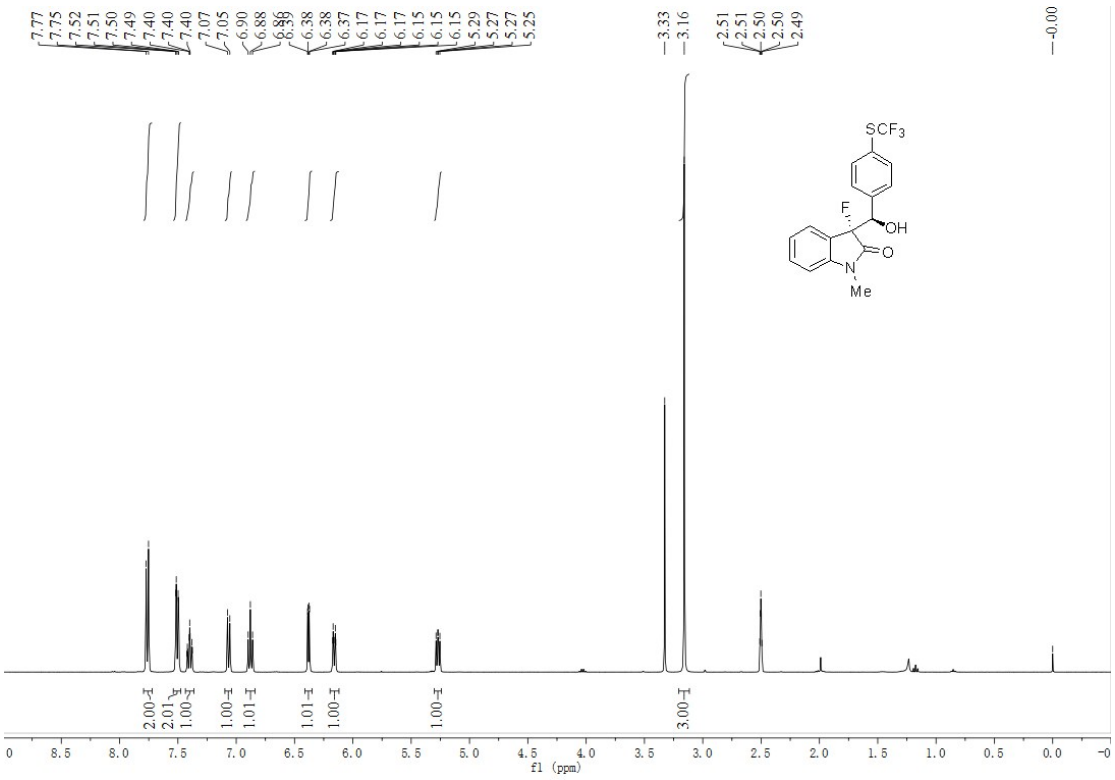
^{13}C NMR (101 MHz, $CDCl_3$) spectra of **13k**



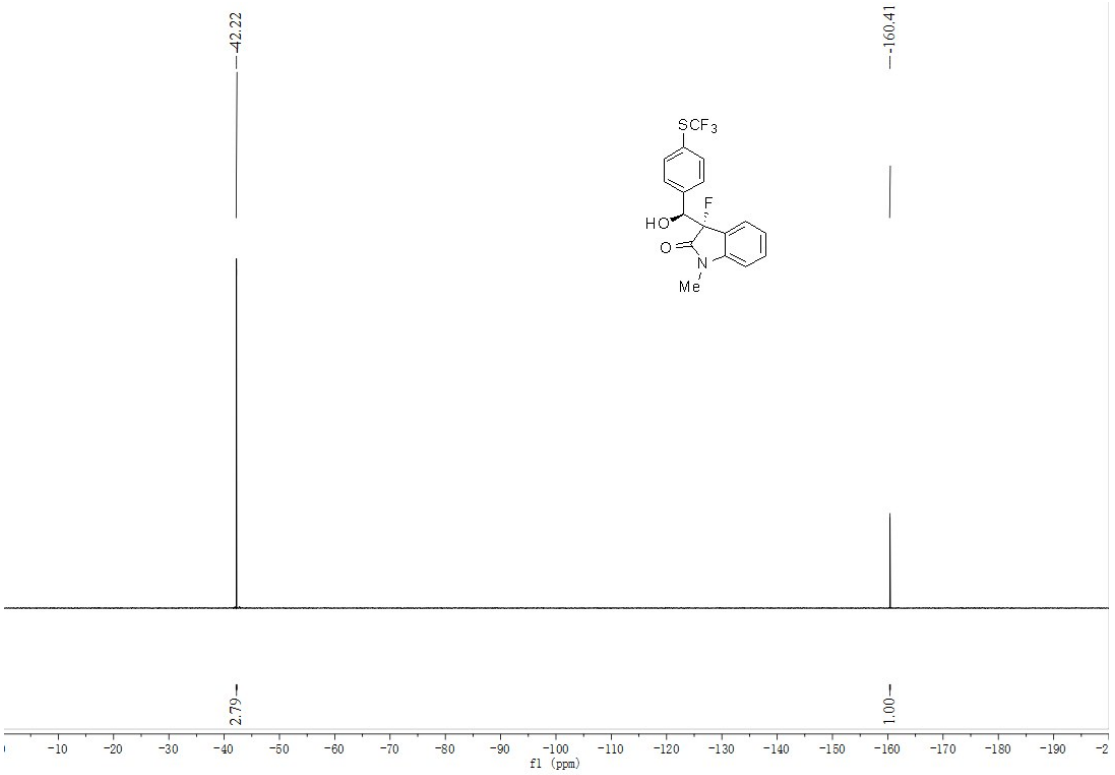
Crude ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13l**



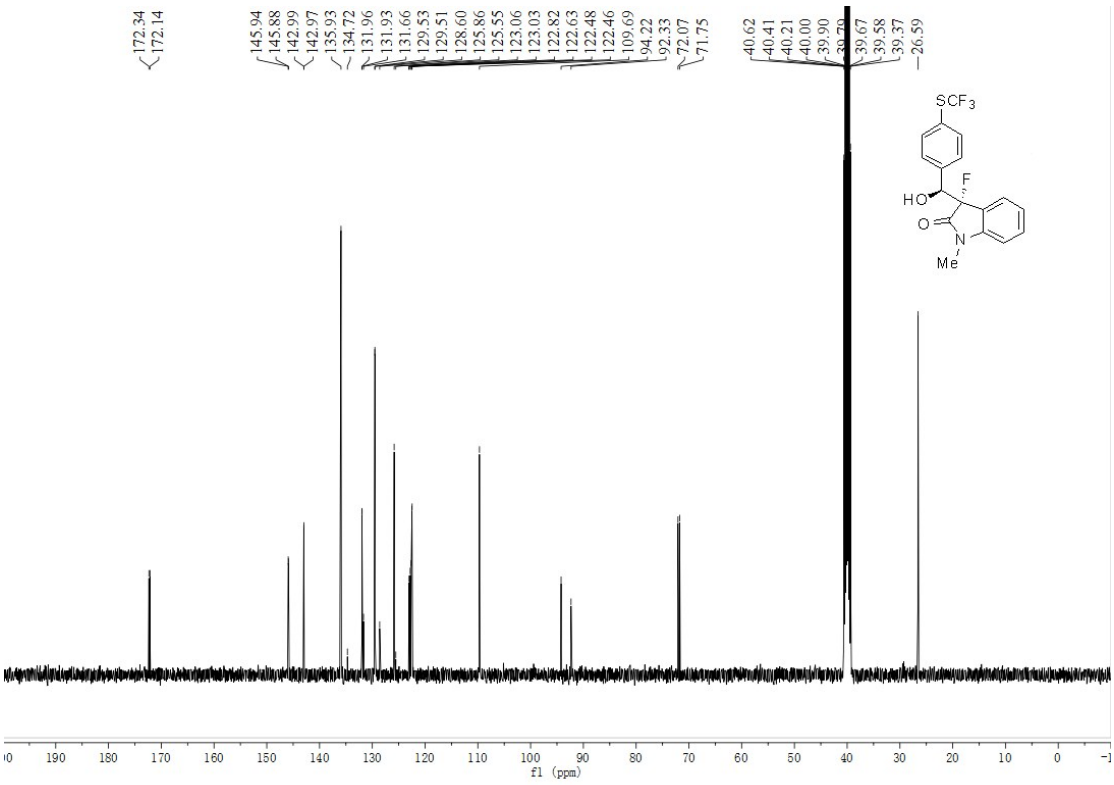
^{1}H NMR (400 MHz, $CDCl_3$) spectra of **13l**



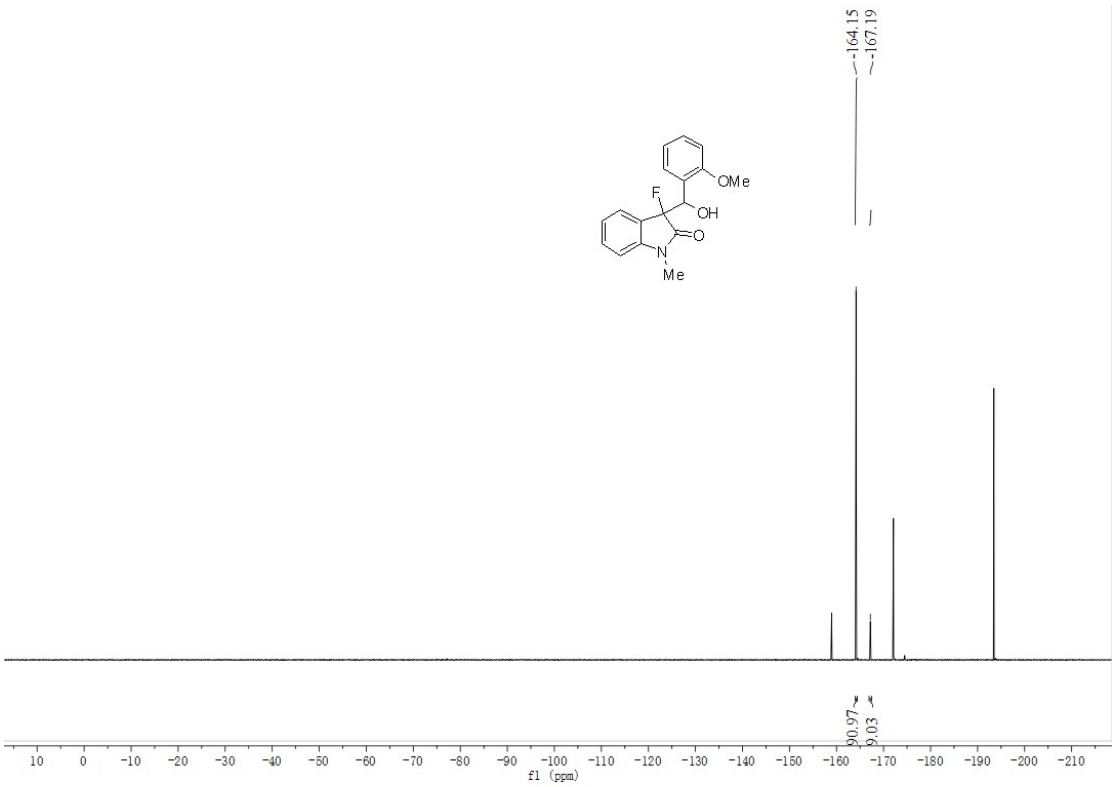
^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13l**



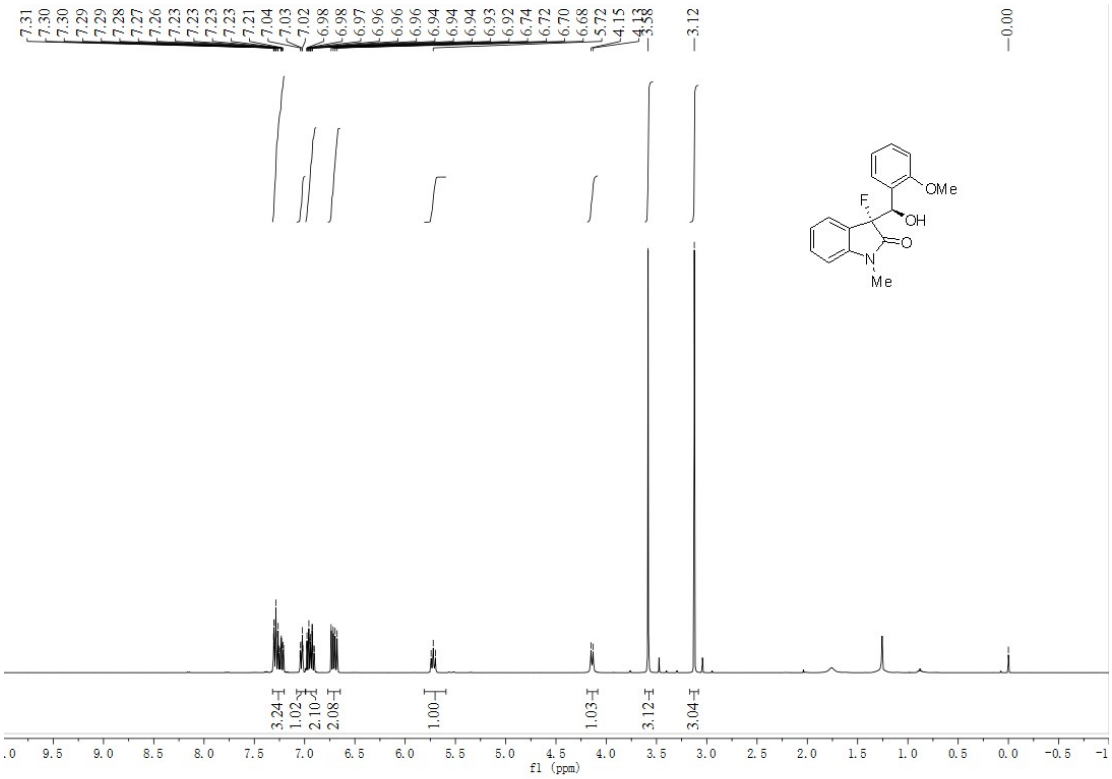
^{13}C NMR (101 MHz, $CDCl_3$) spectra of **13l**



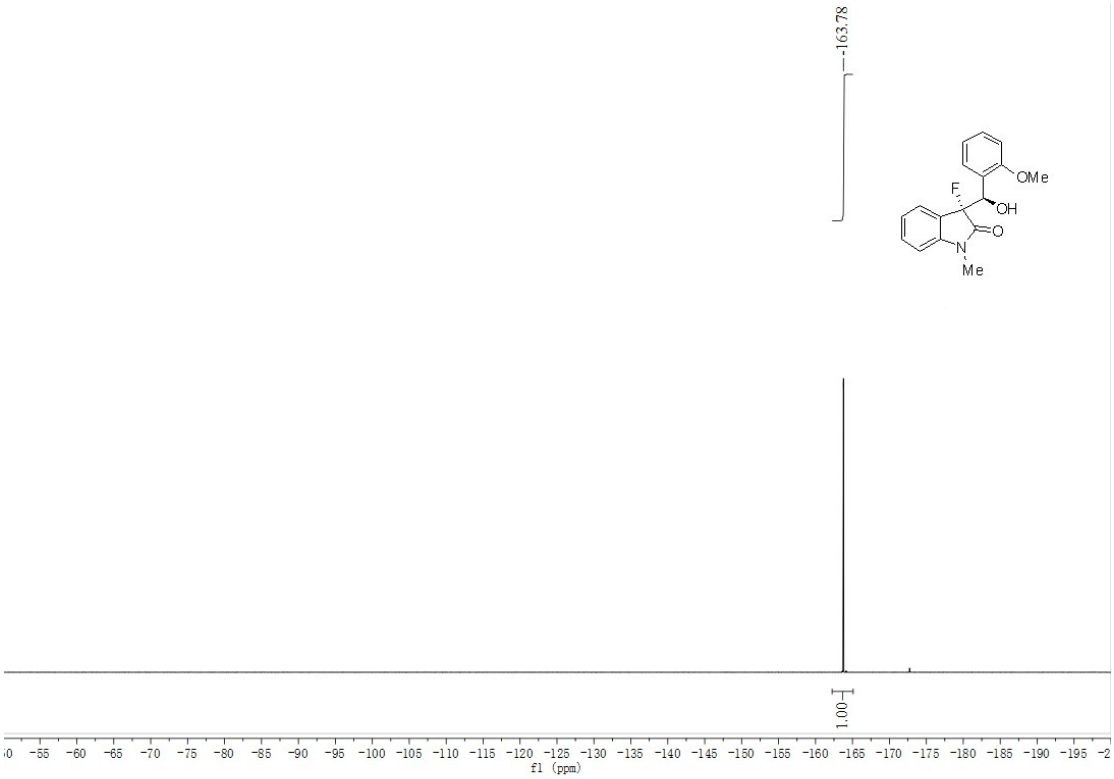
Crude ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13m**



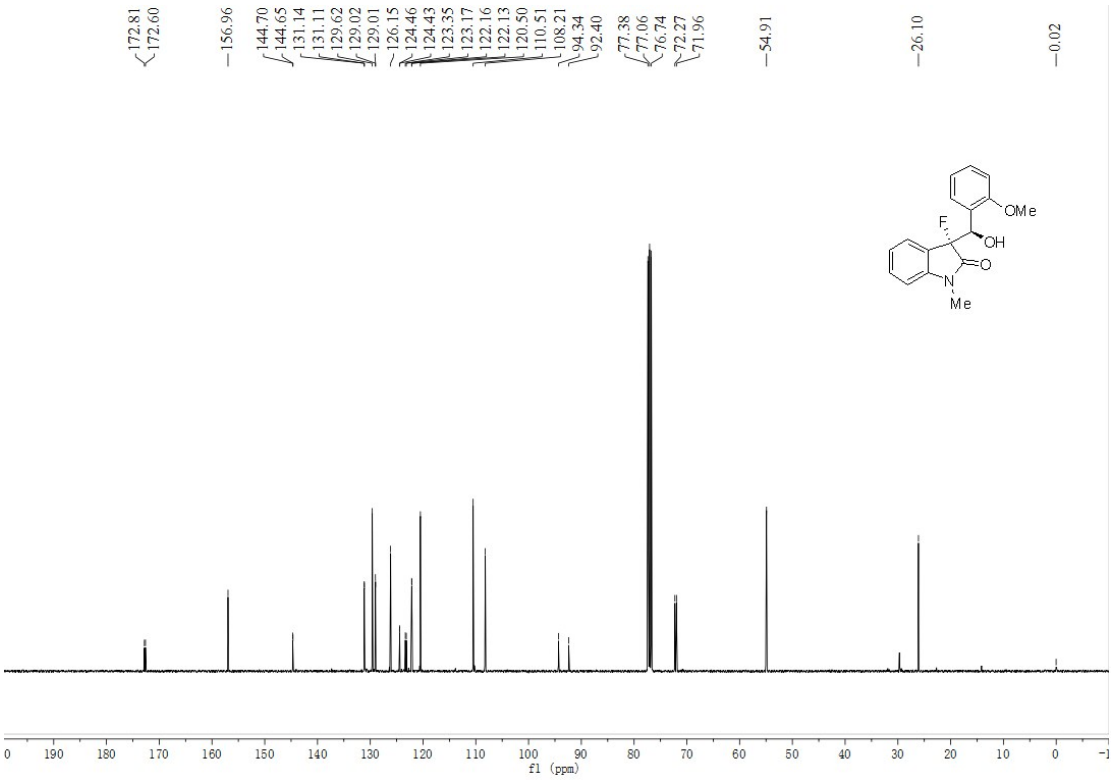
^{1}H NMR (400 MHz, $CDCl_3$) spectra of **13m**



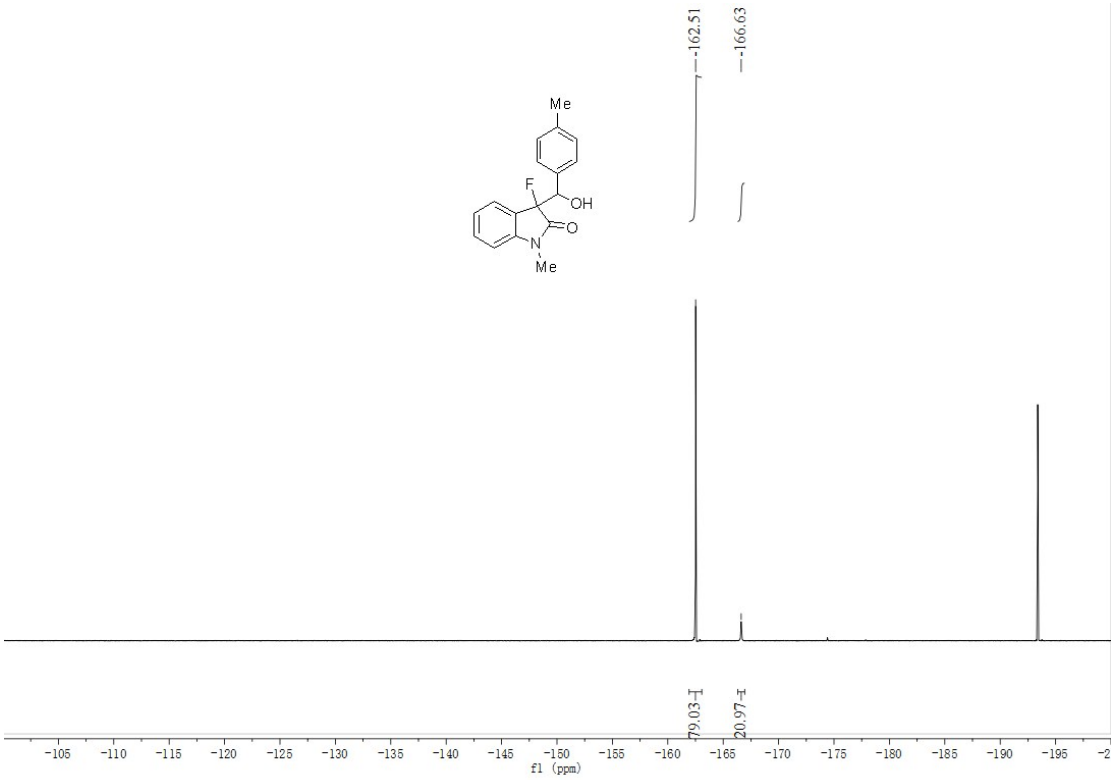
^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13m**



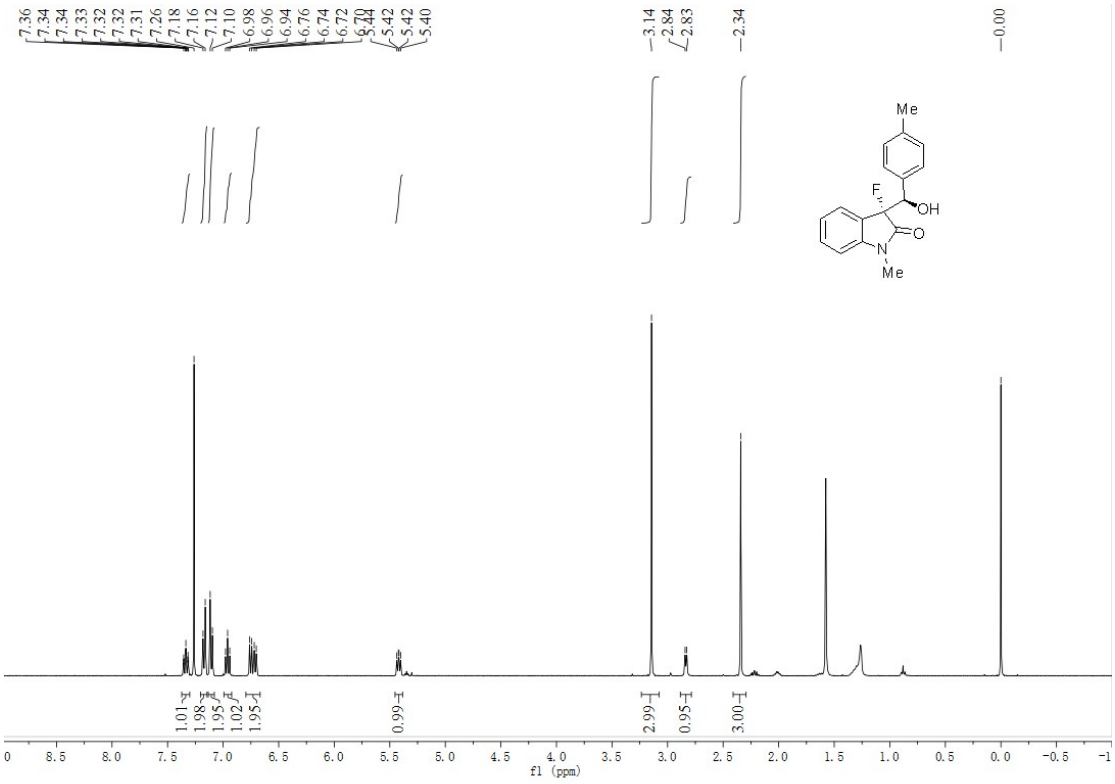
^{13}C NMR (101 MHz, $CDCl_3$) spectra of **13m**



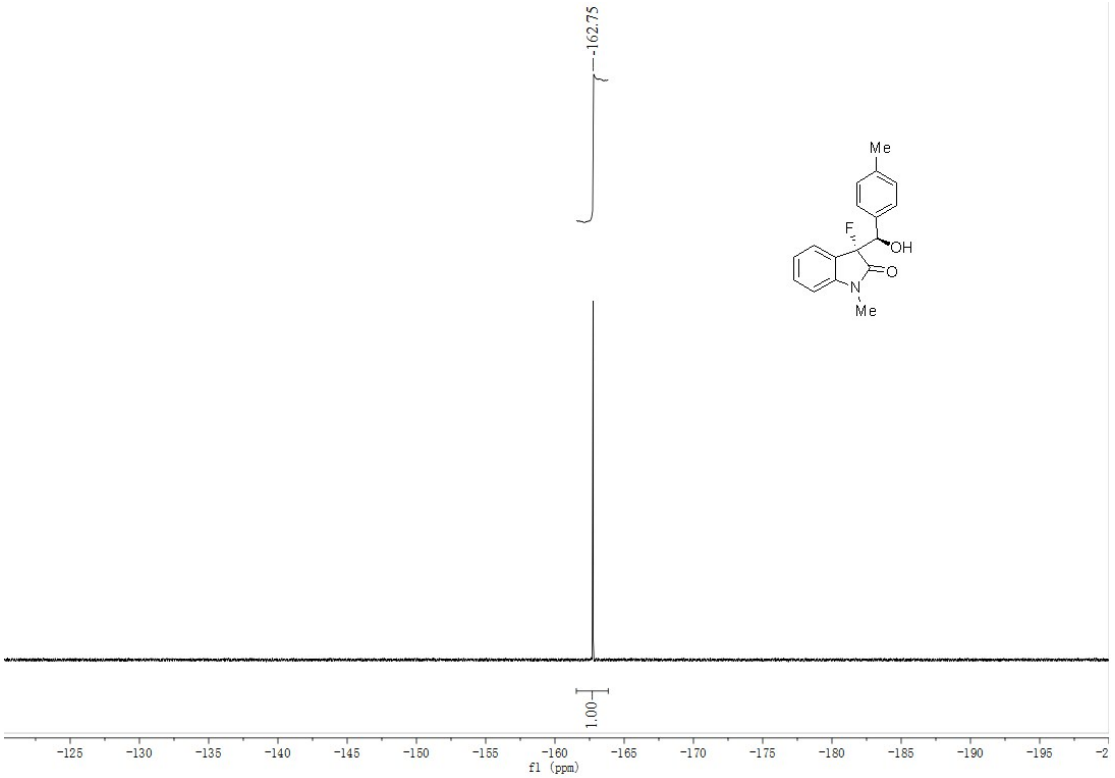
Crude ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13n**



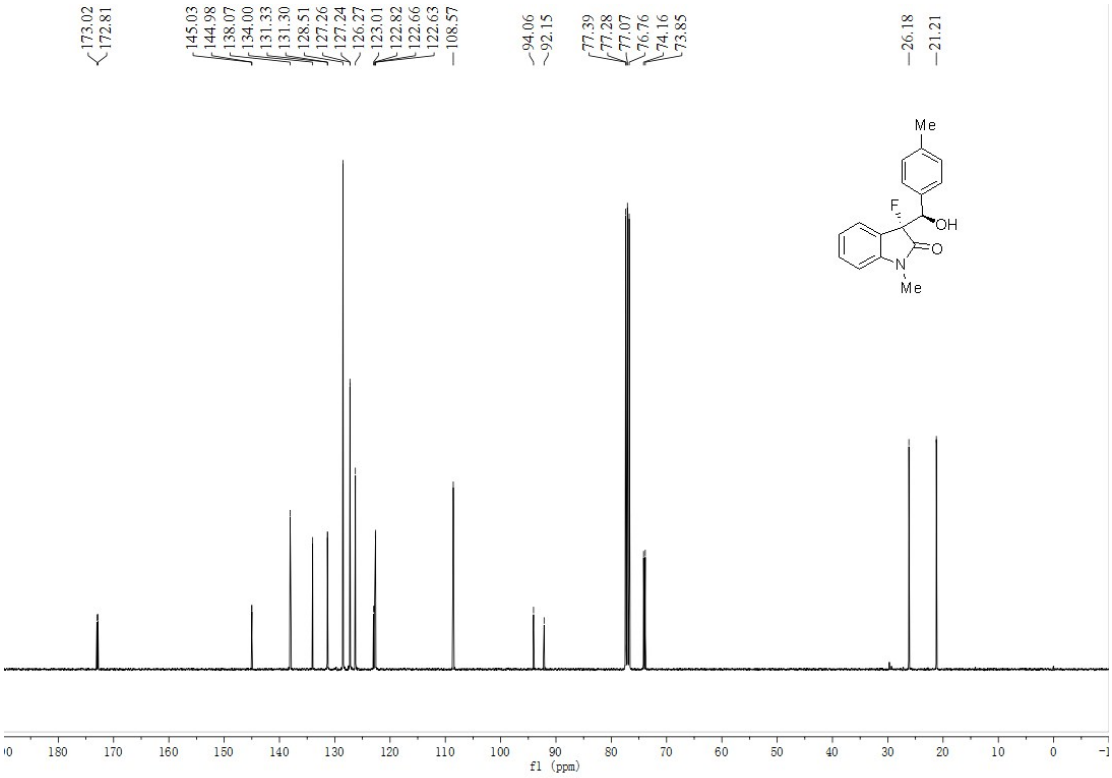
^{1}H NMR (400 MHz, $CDCl_3$) spectra of **13n**



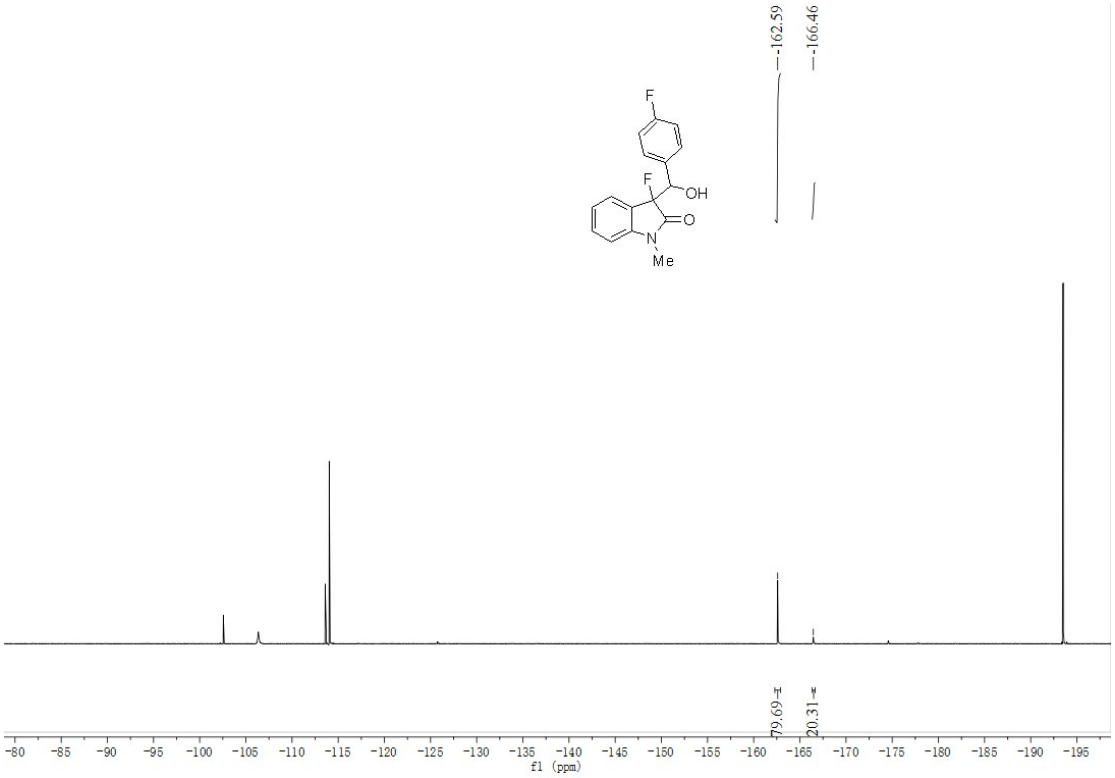
^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13n**



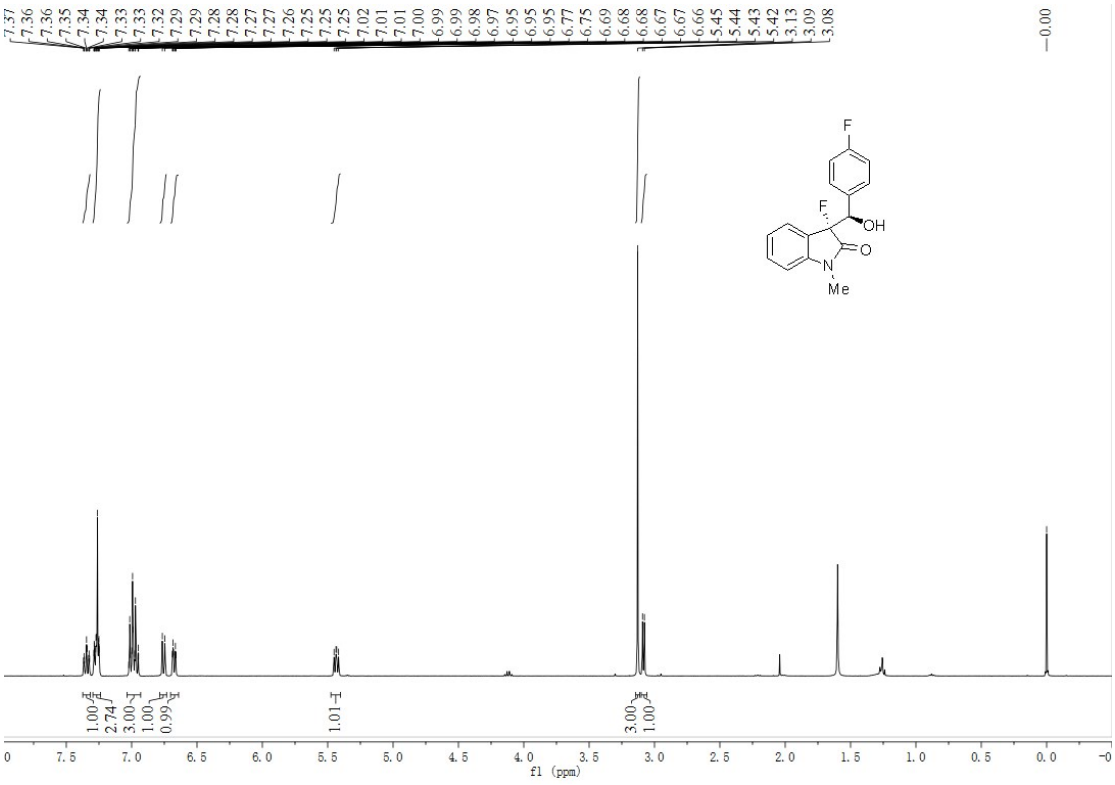
^{13}C NMR (101 MHz, $CDCl_3$) spectra of **13n**



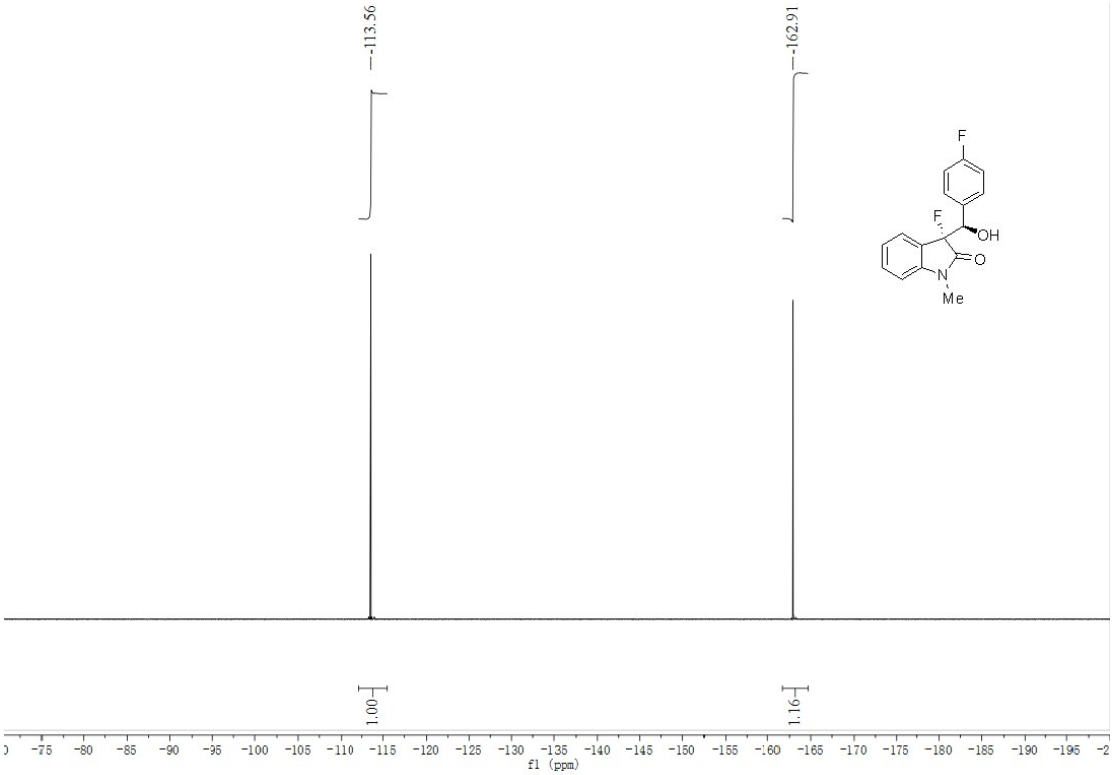
Crude ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13o**



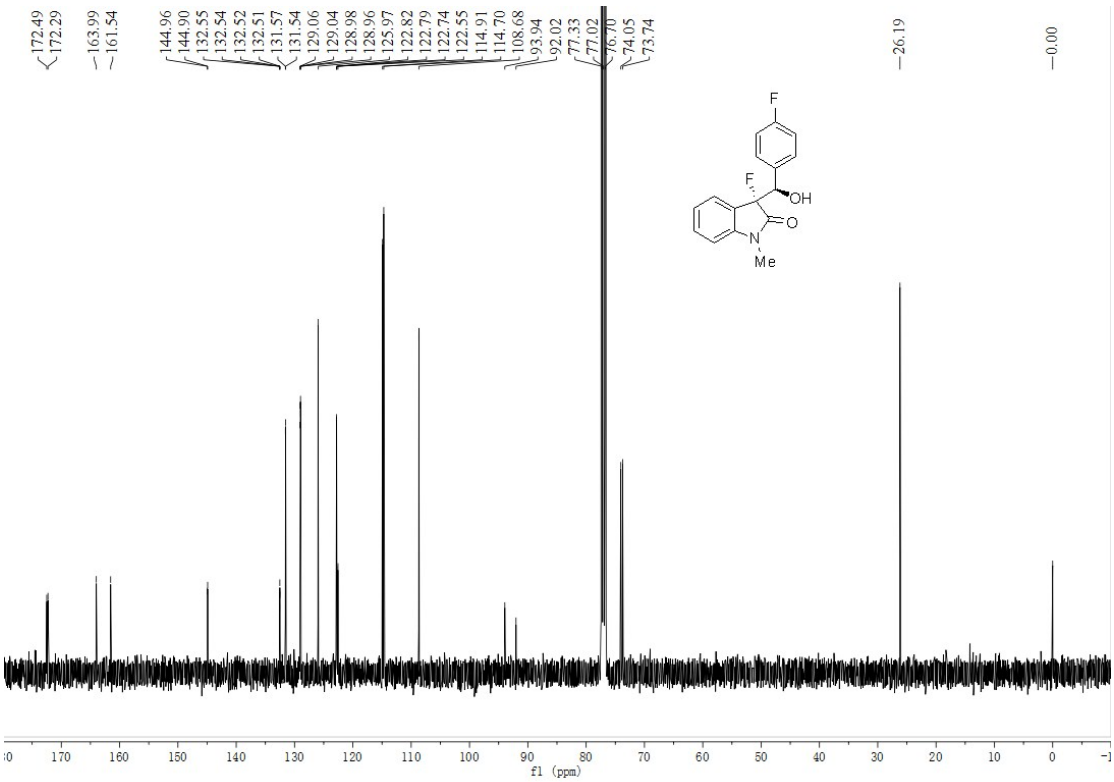
^{1}H NMR (400 MHz, $CDCl_3$) spectra of **13o**



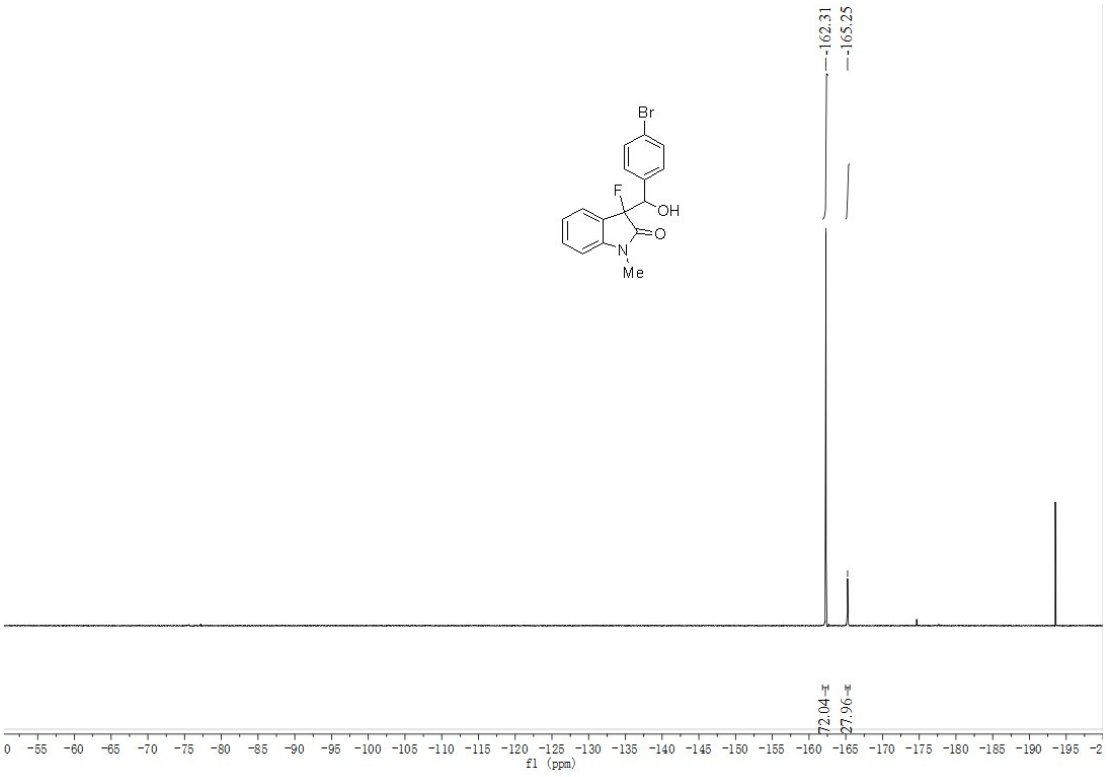
^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13o**



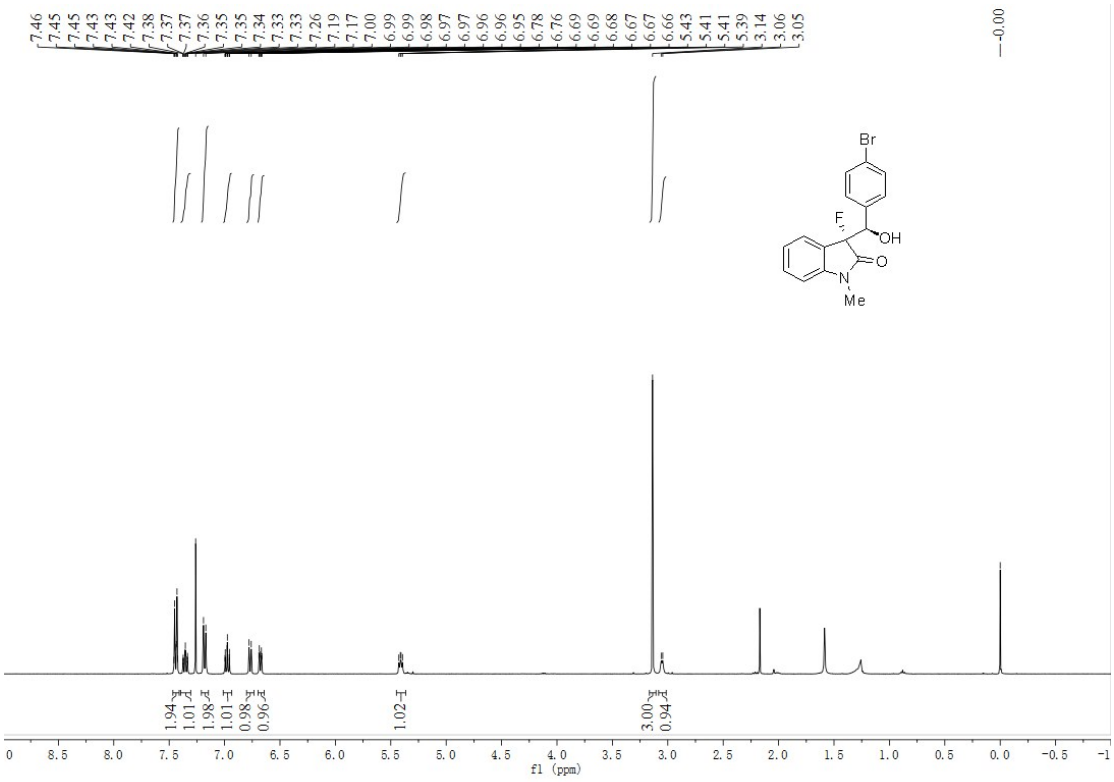
^{13}C NMR (101 MHz, $CDCl_3$) spectra of **13o**



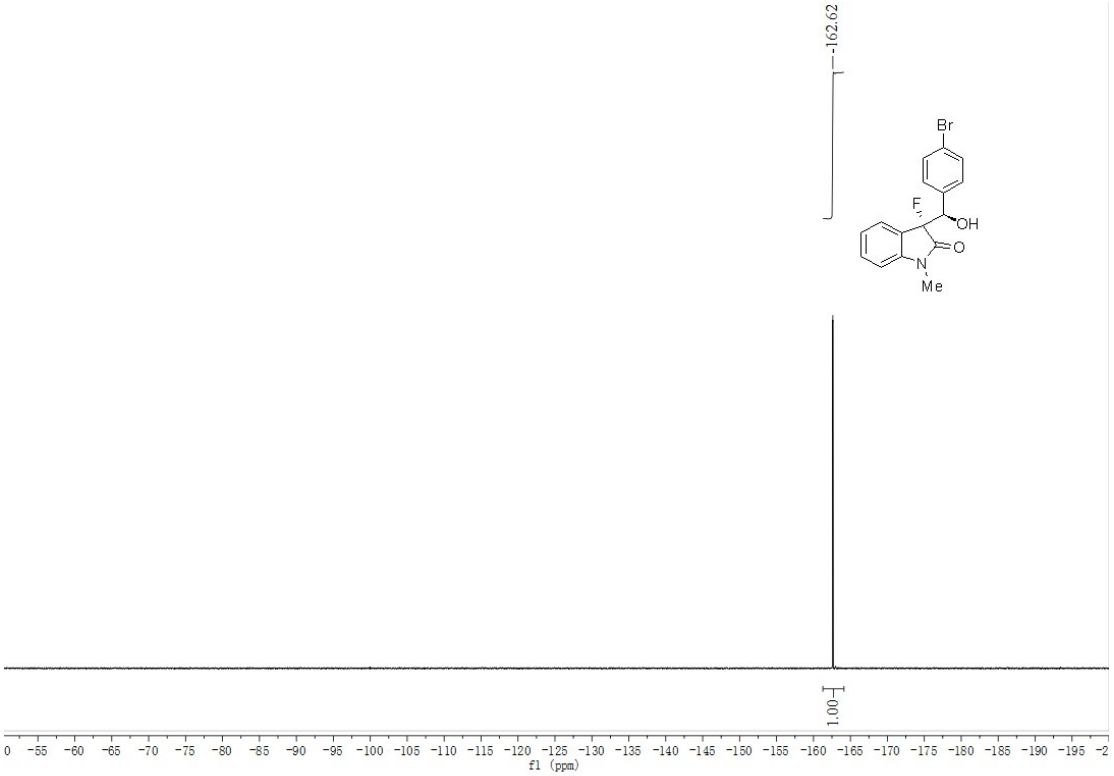
Crude ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13p**



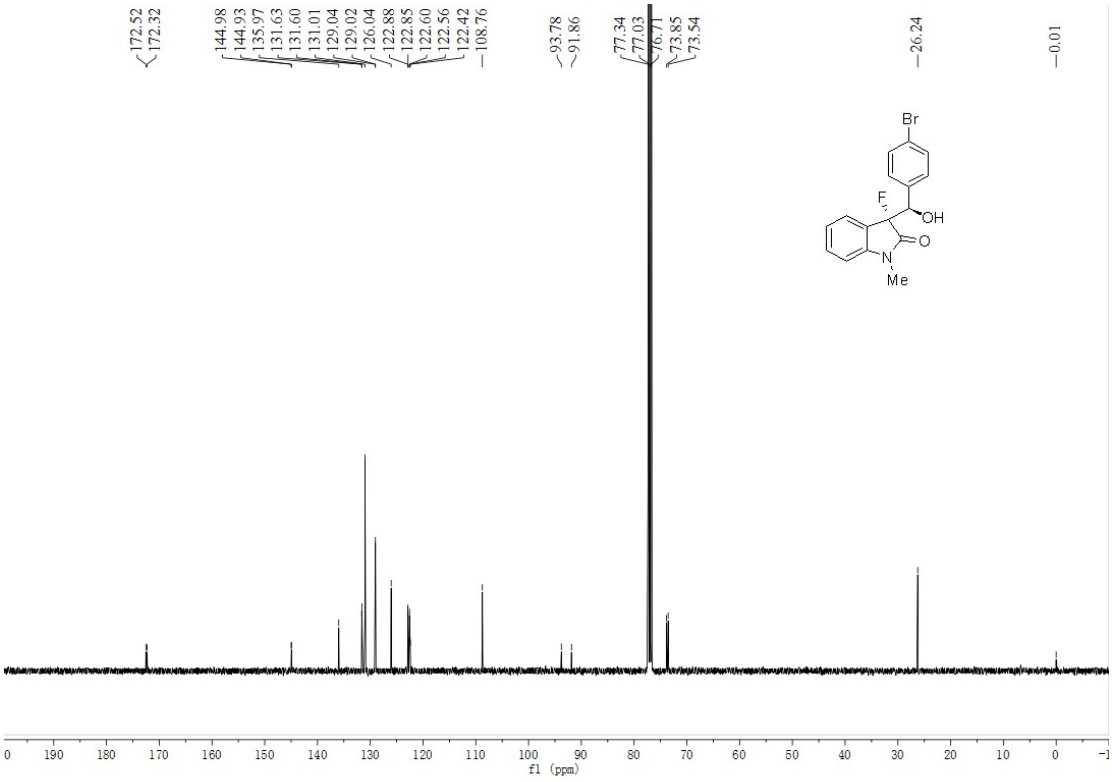
^{1}HNMR (400 MHz, $CDCl_3$) spectra of **13P**



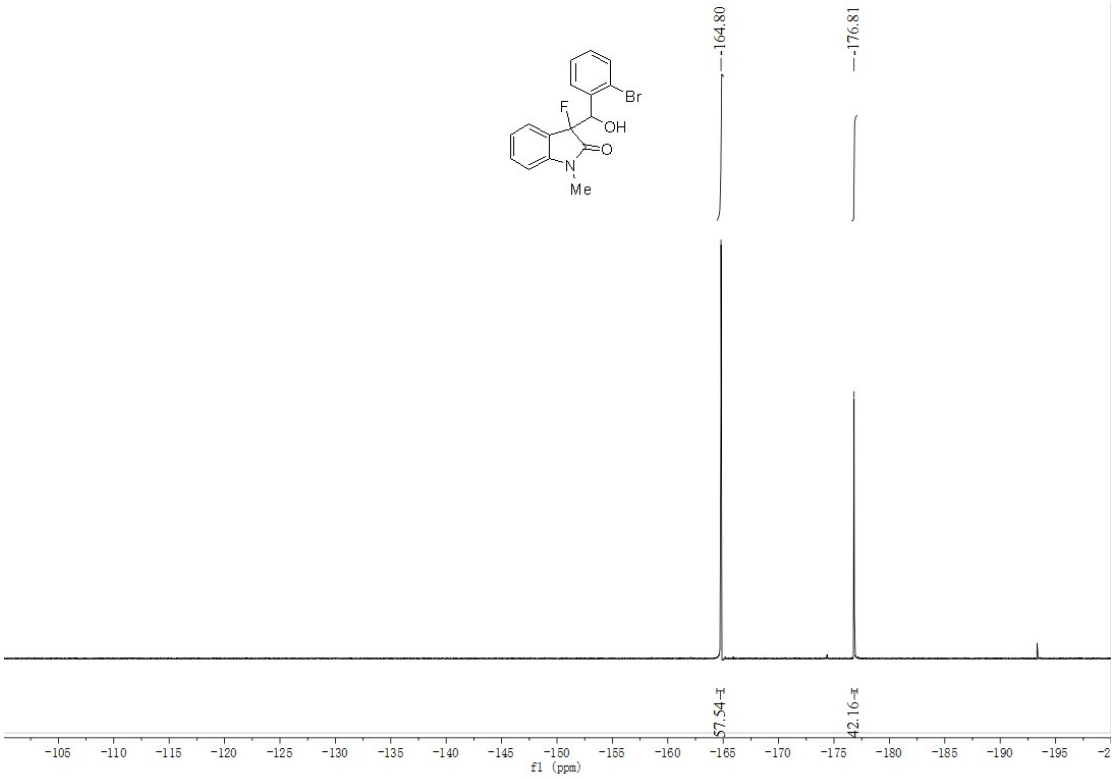
^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13p**



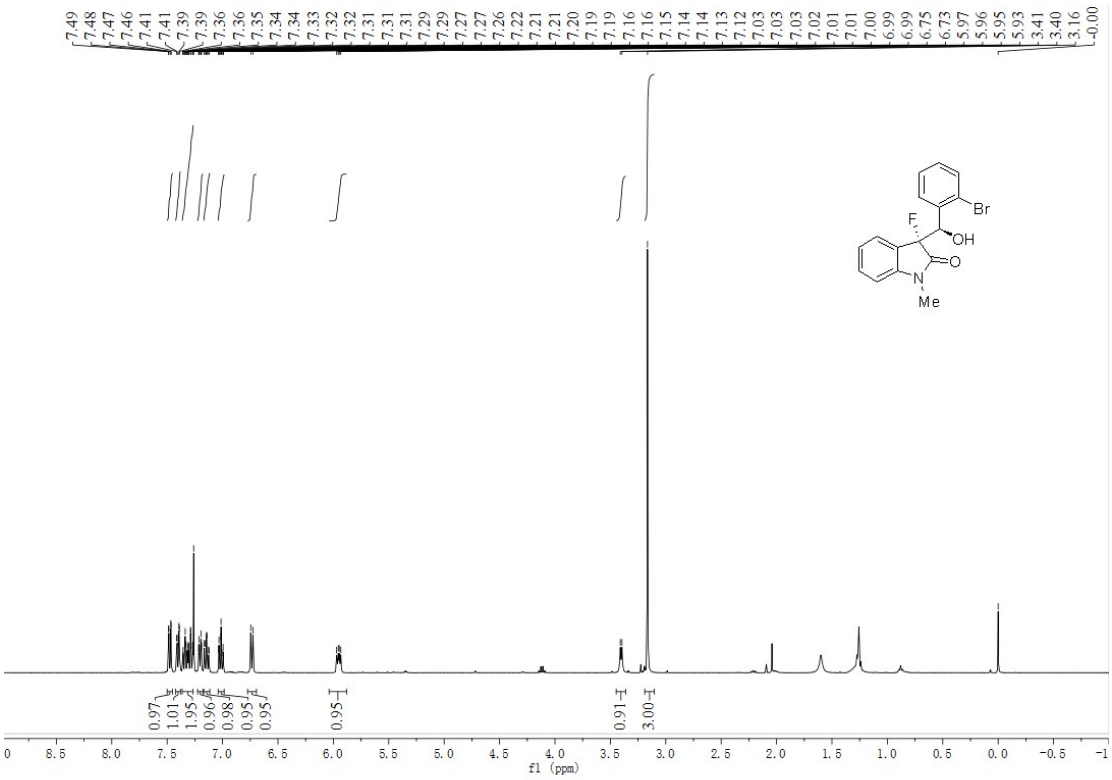
^{13}C NMR (101 MHz, $CDCl_3$) spectra of **13p**



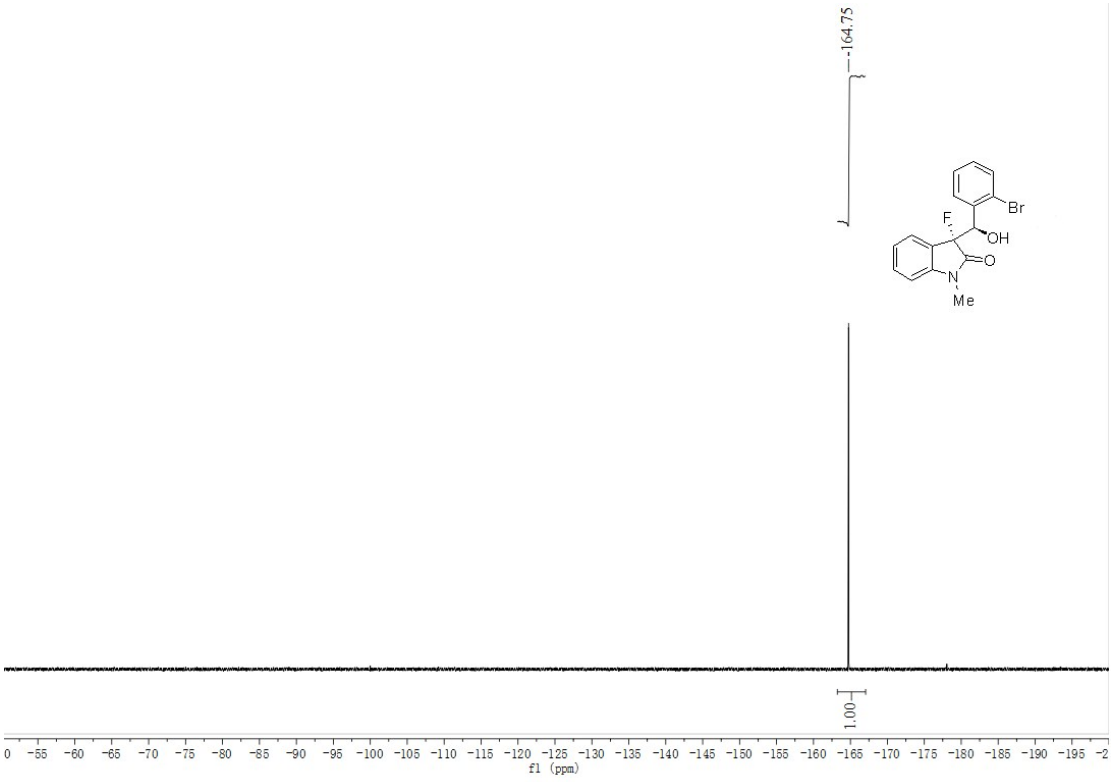
Crude ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13q**



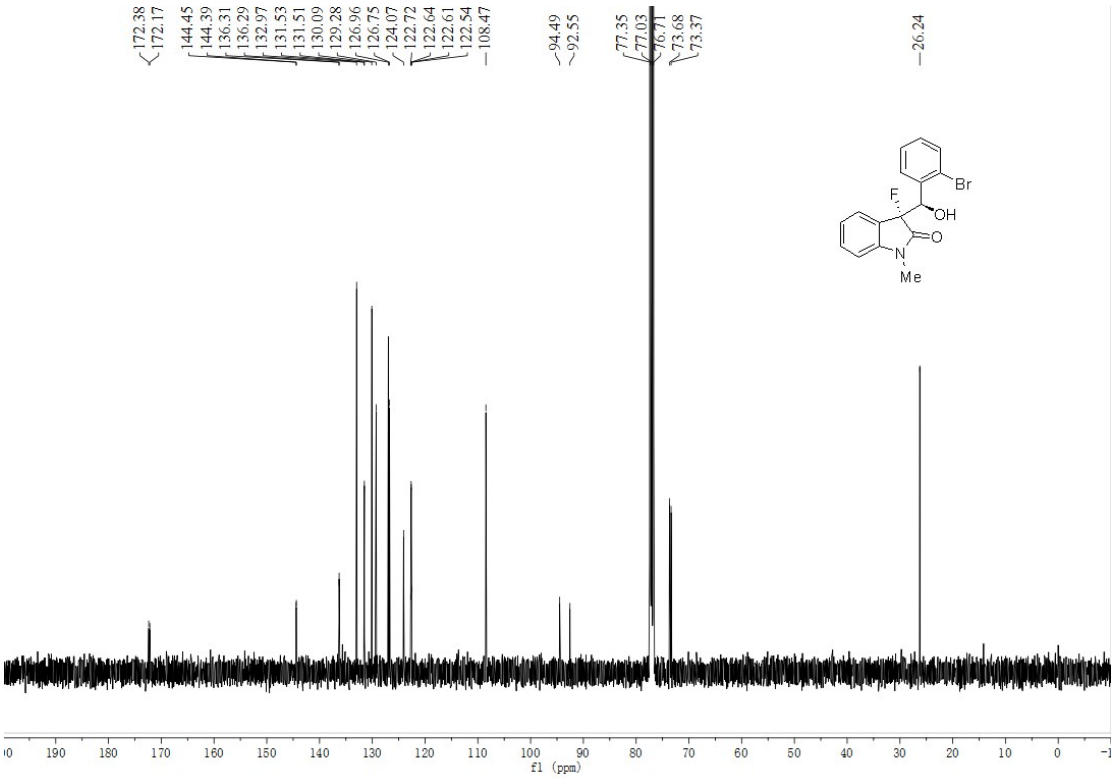
^{1}H NMR (400 MHz, $CDCl_3$) spectra of **13q**



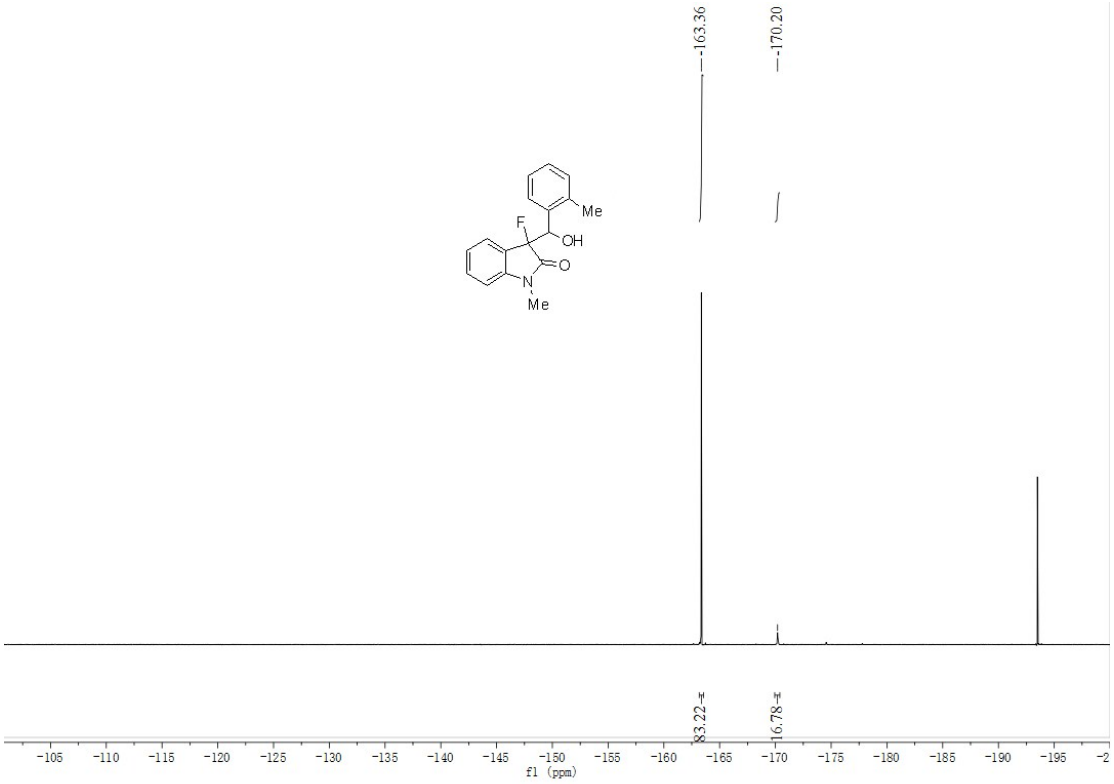
^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13q**



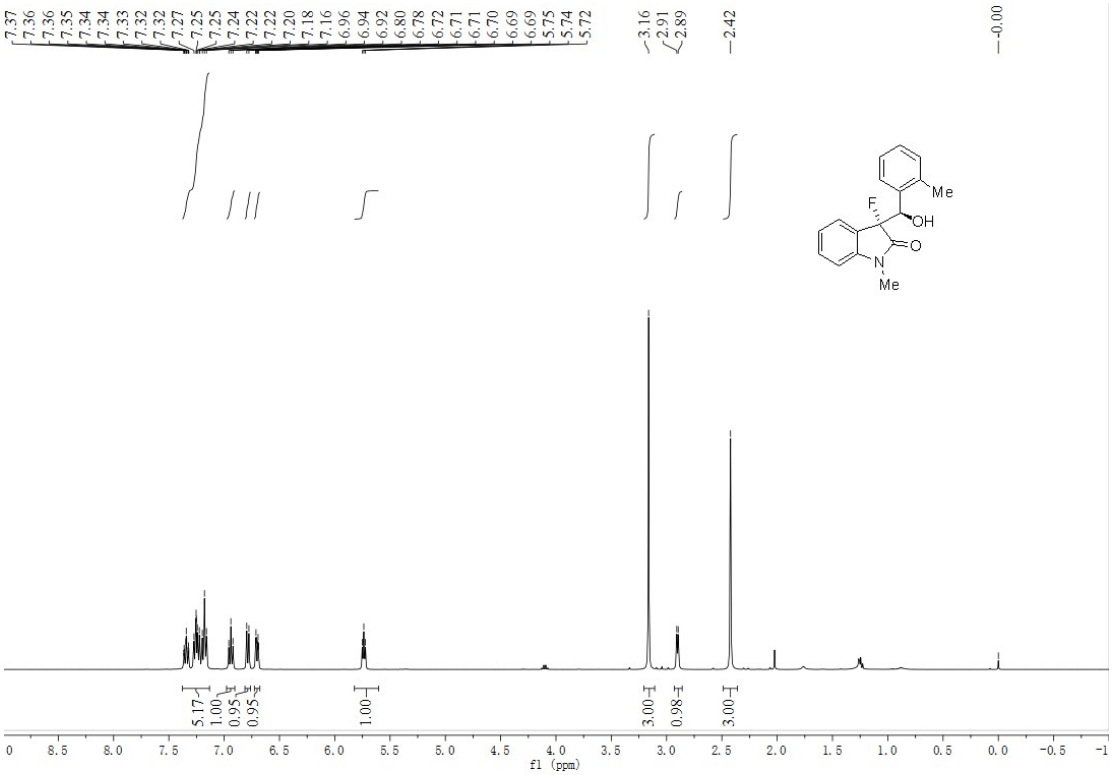
^{13}C NMR (101 MHz, $CDCl_3$) spectra of **13q**



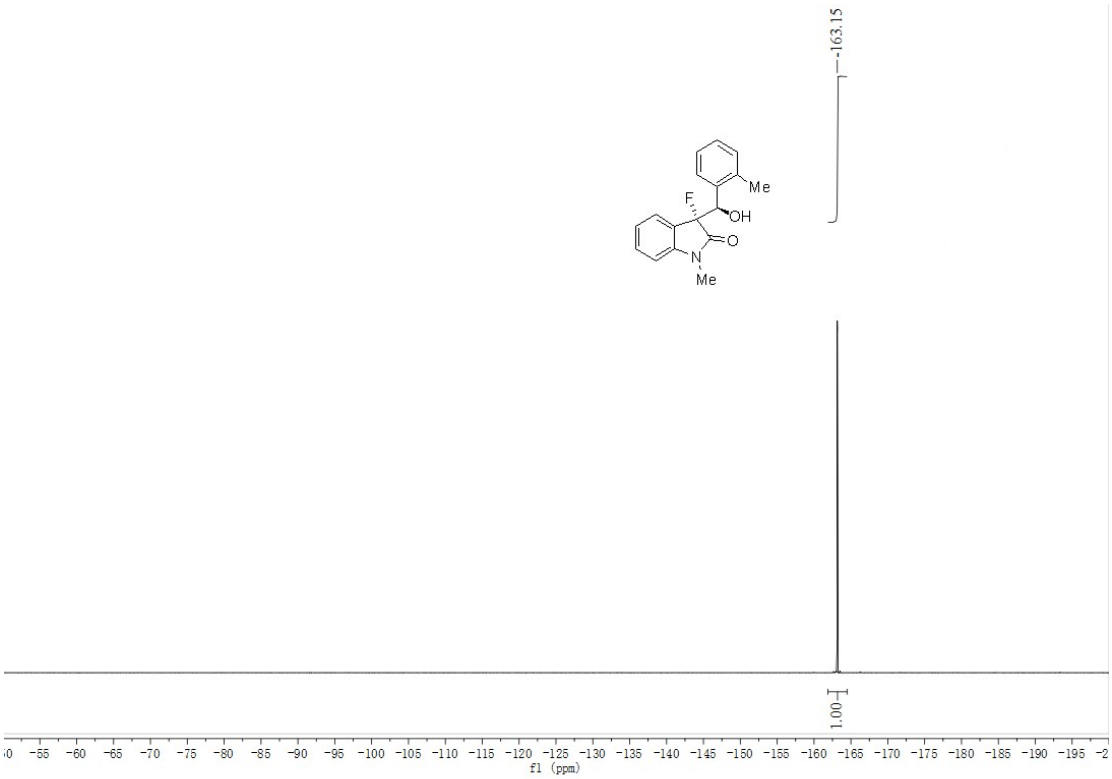
Crude ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13r**



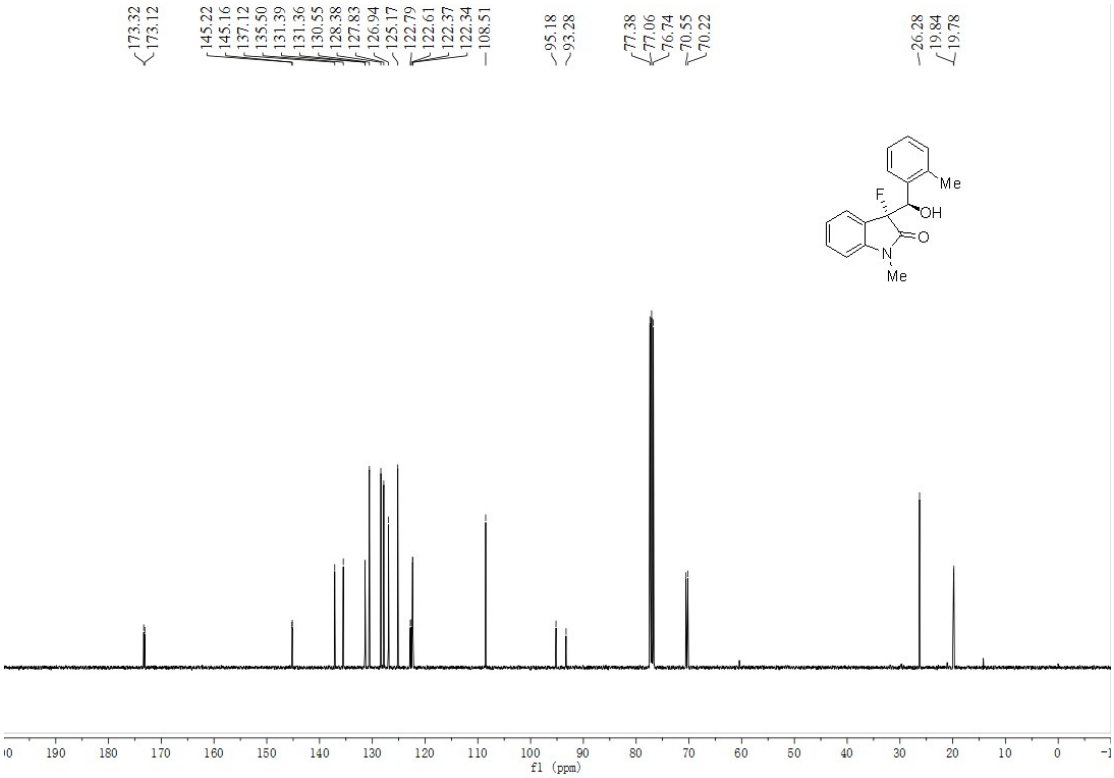
^{1}H NMR (400 MHz, $CDCl_3$) spectra of **13r**



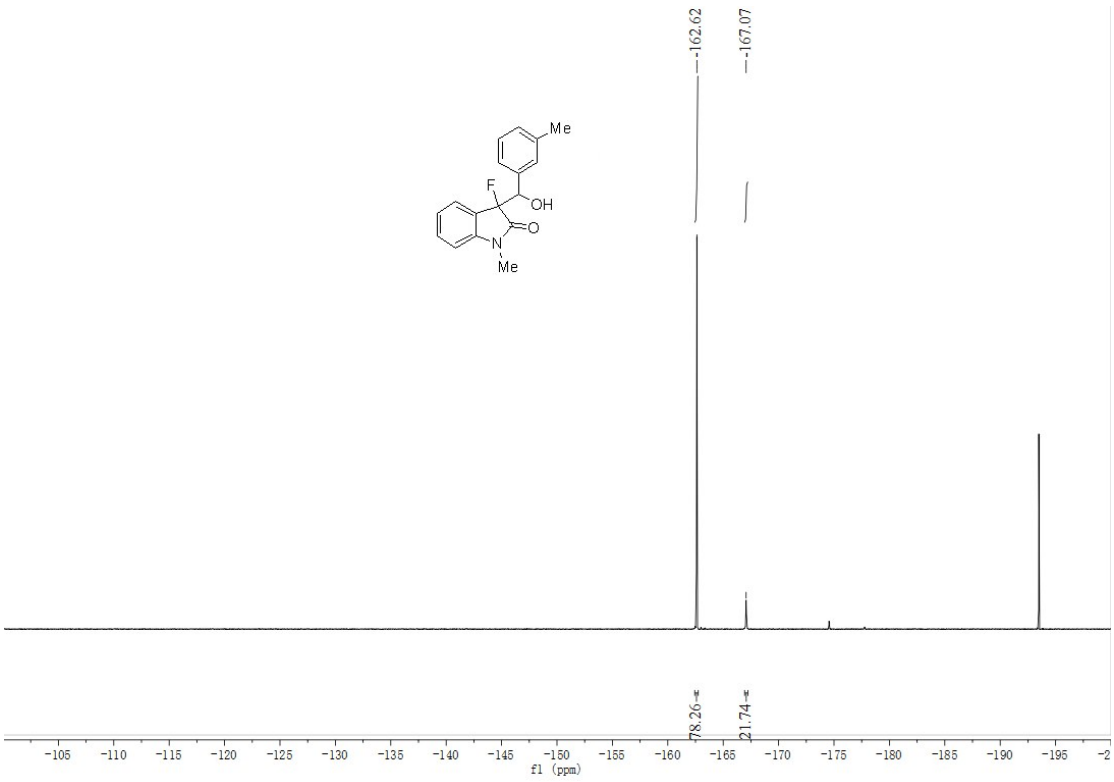
^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13r**



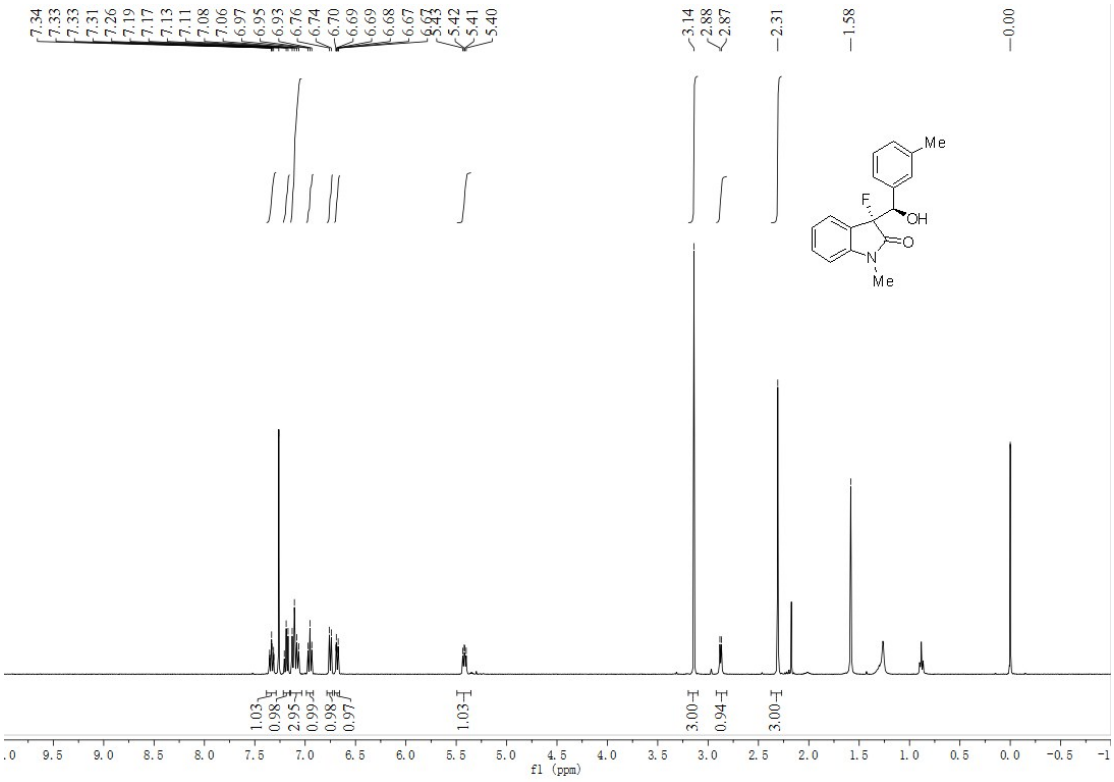
^{13}C NMR (101 MHz, $CDCl_3$) spectra of **13r**



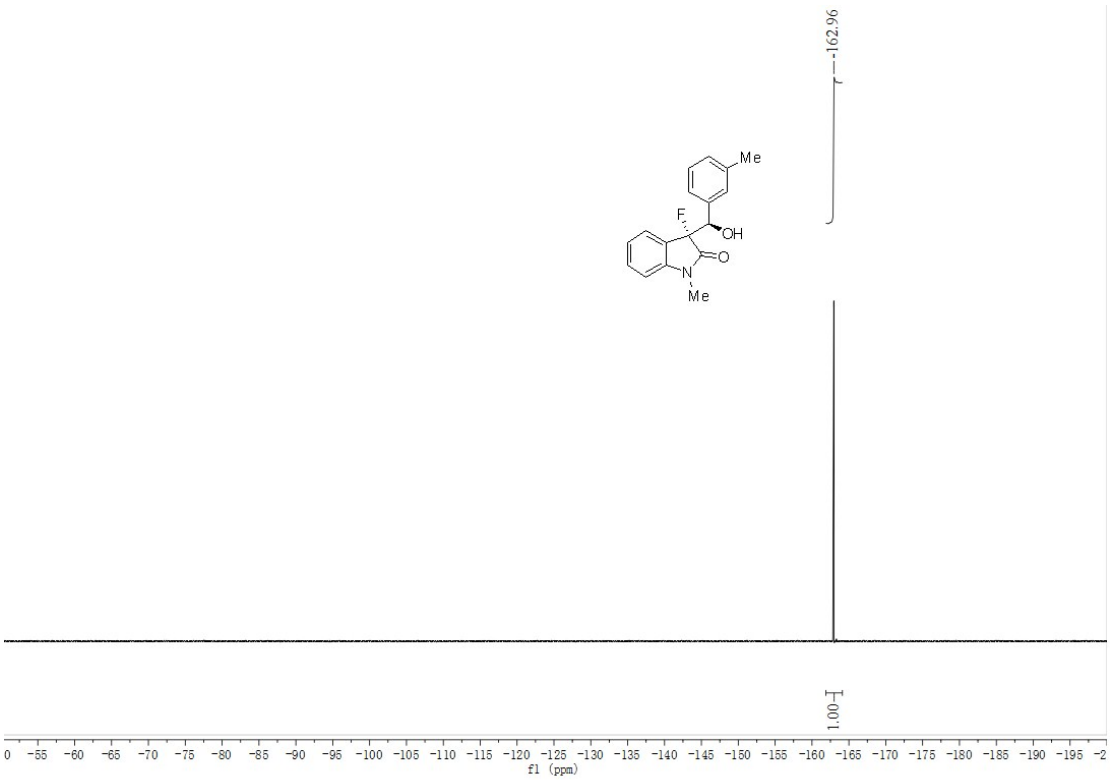
Crude ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13u**



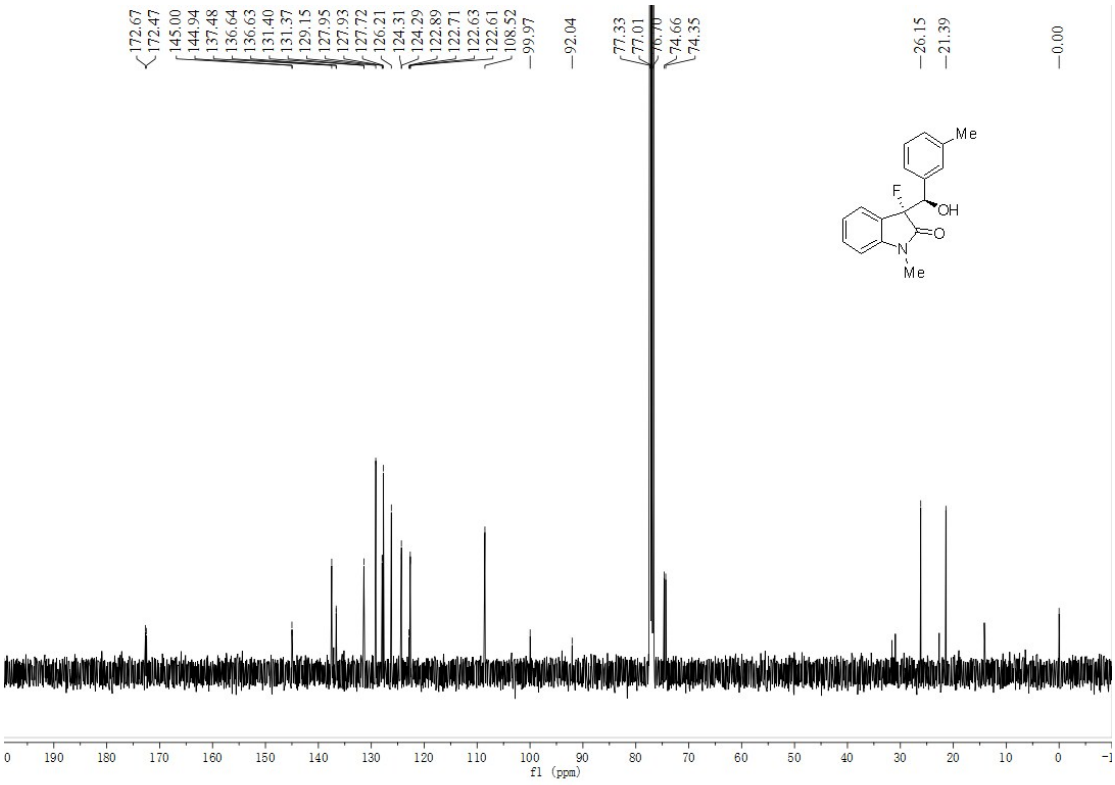
^{1}H NMR (400 MHz, $CDCl_3$) spectra of **13s**



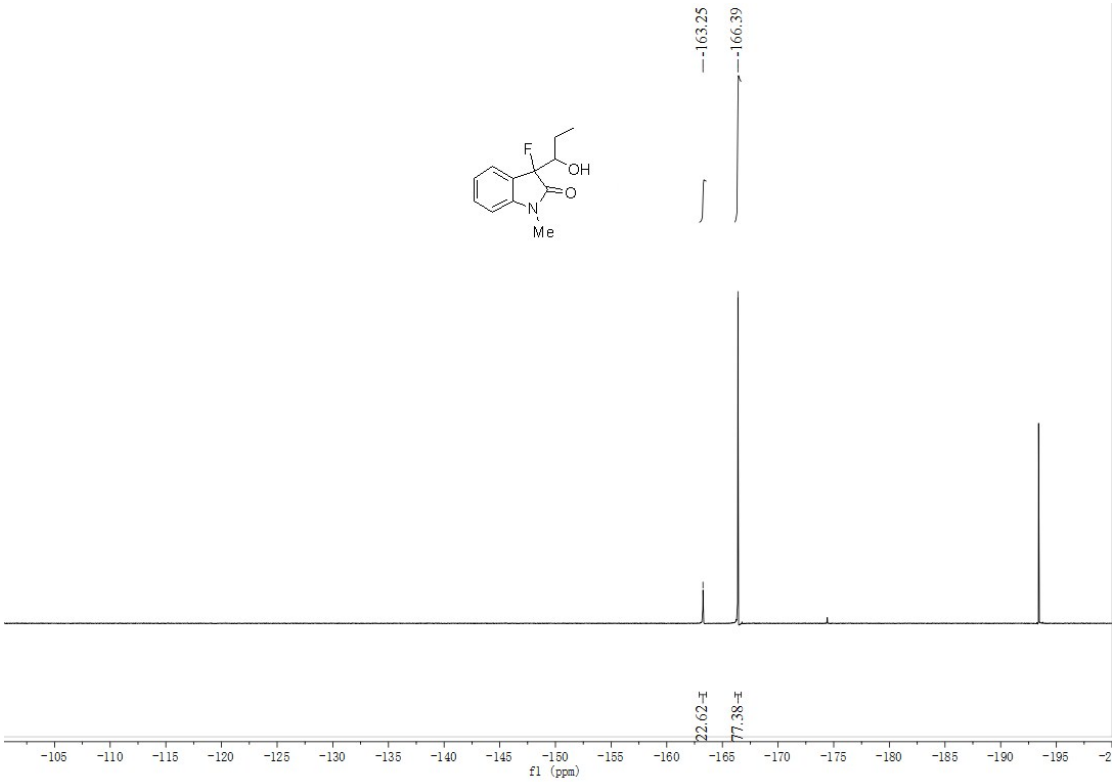
^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13s**



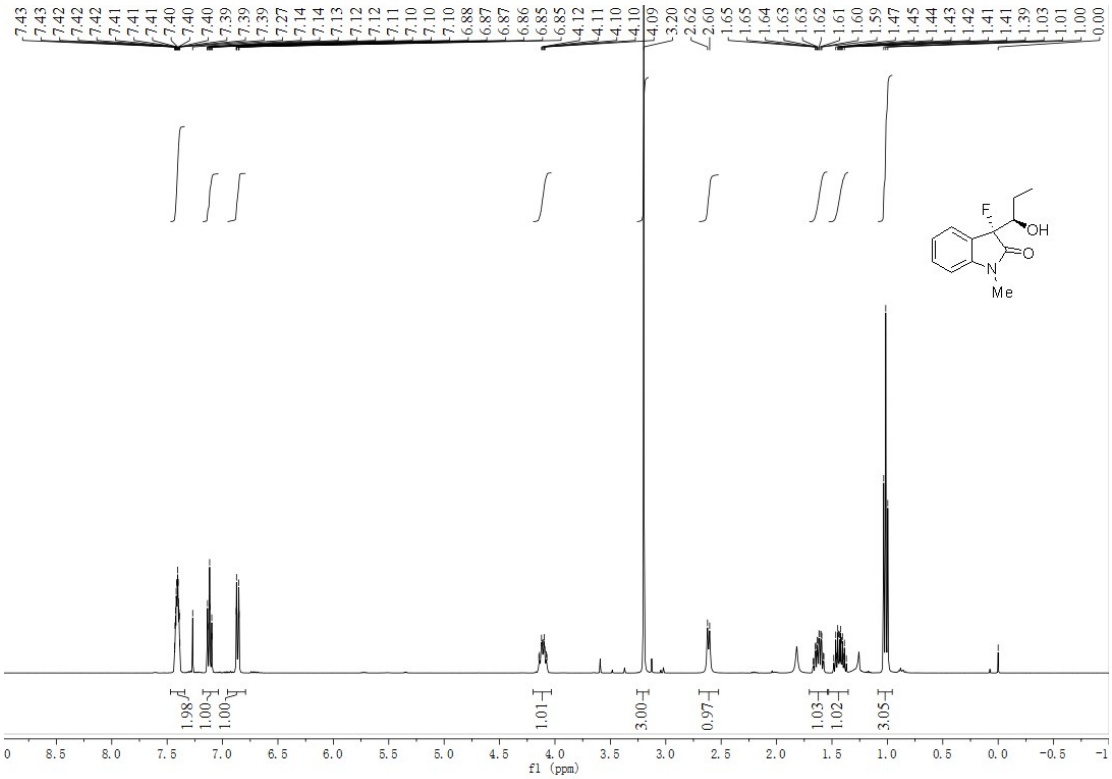
^{13}C NMR (101 MHz, $CDCl_3$) spectra of **13s**



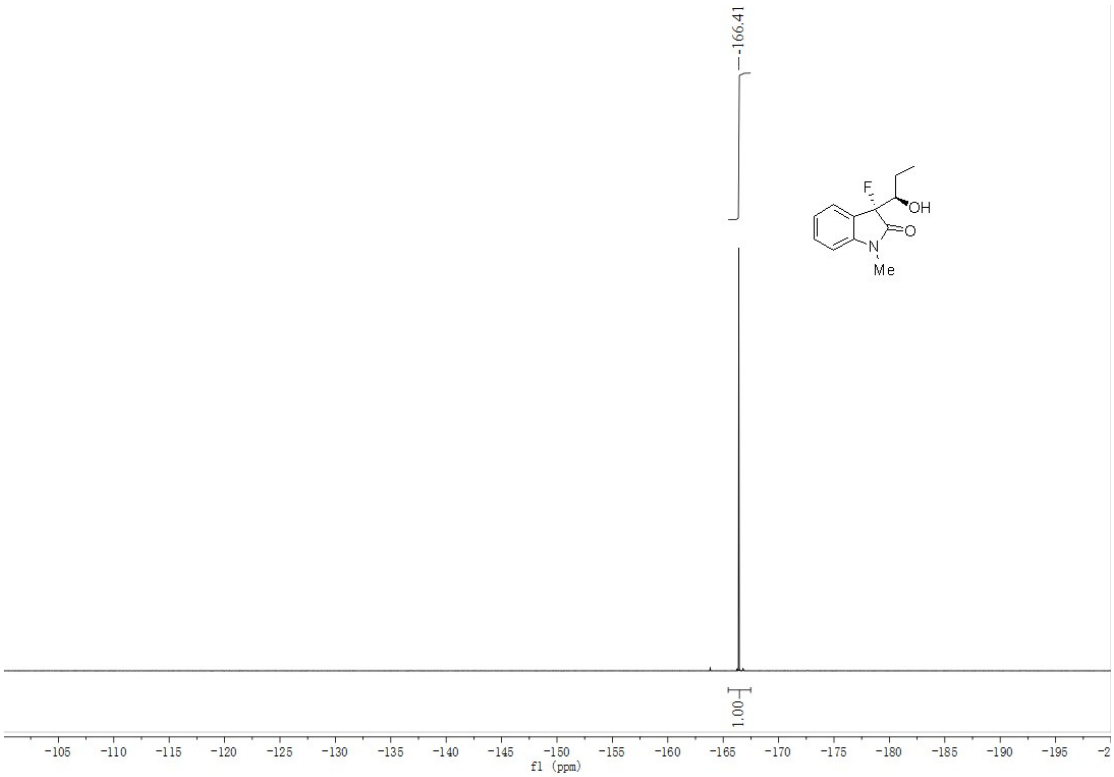
Ceude ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13t**



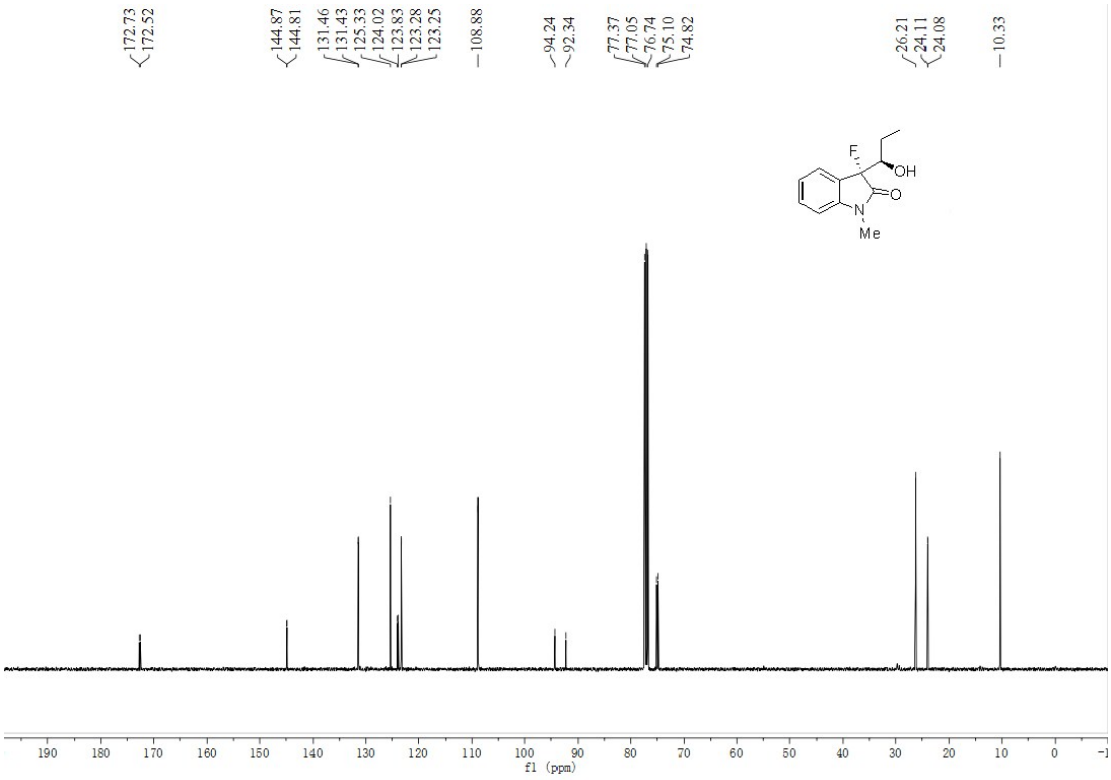
^{1}H NMR (400 MHz, $CDCl_3$) spectra of **13t**



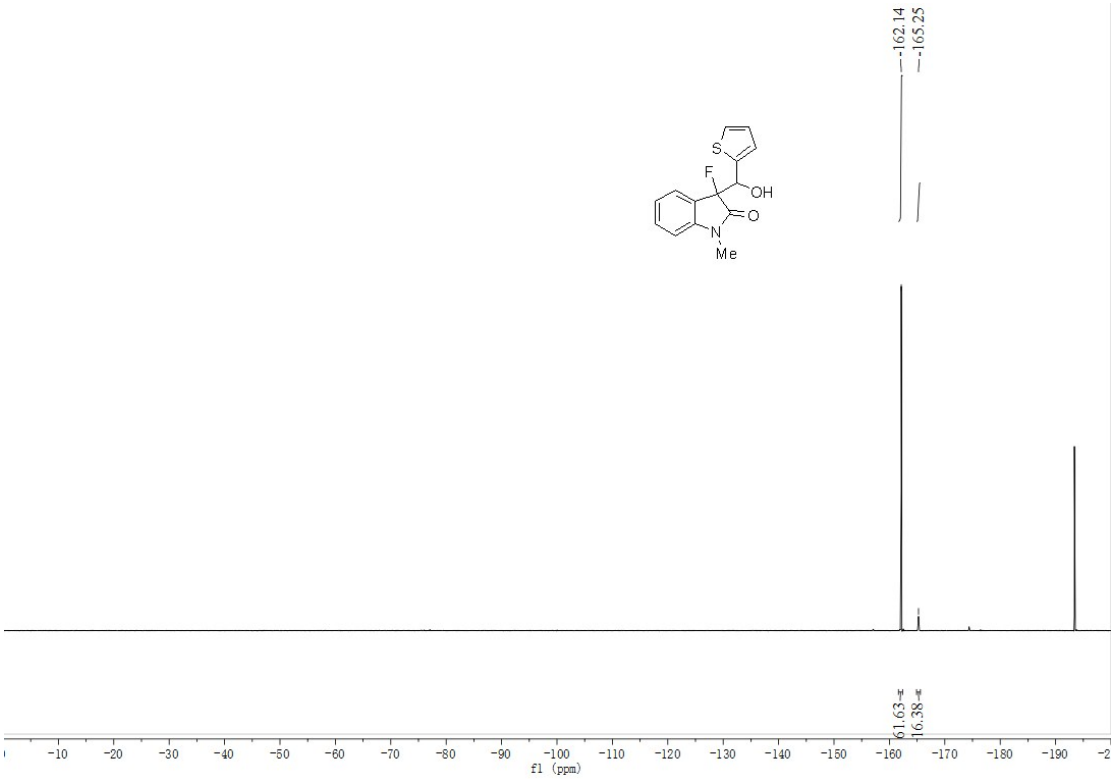
^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13t**



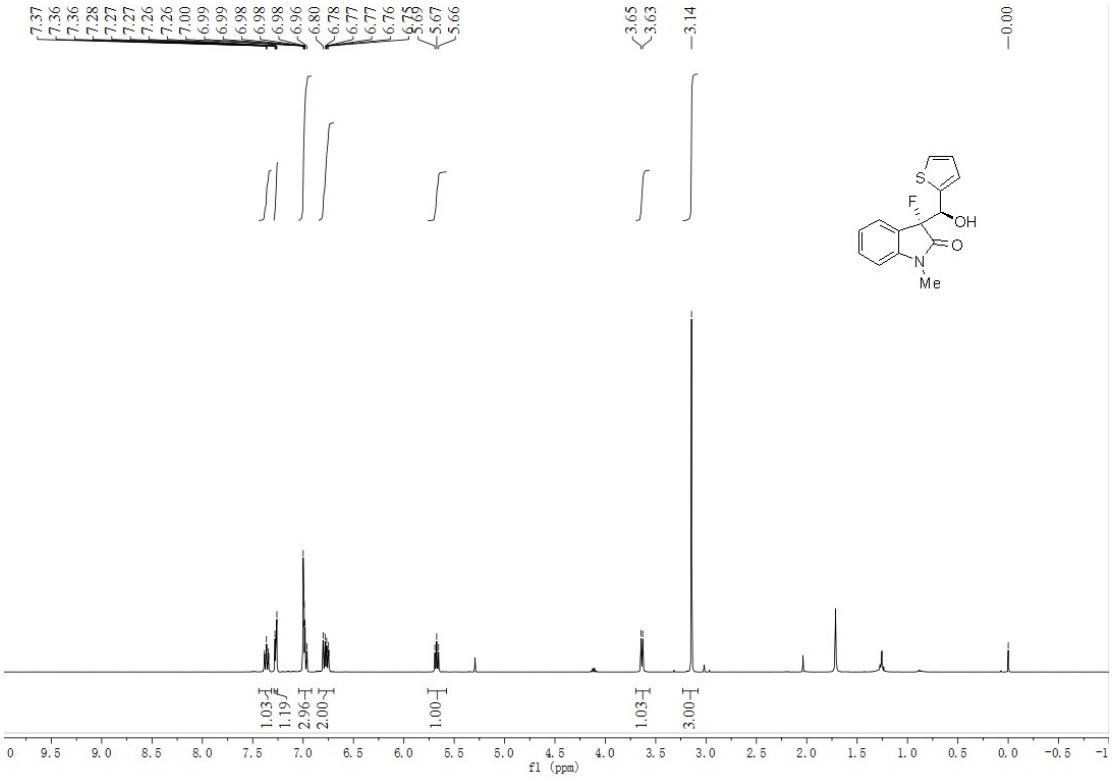
^{13}C NMR (101 MHz, $CDCl_3$) spectra of **13t**



Crude ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13u**

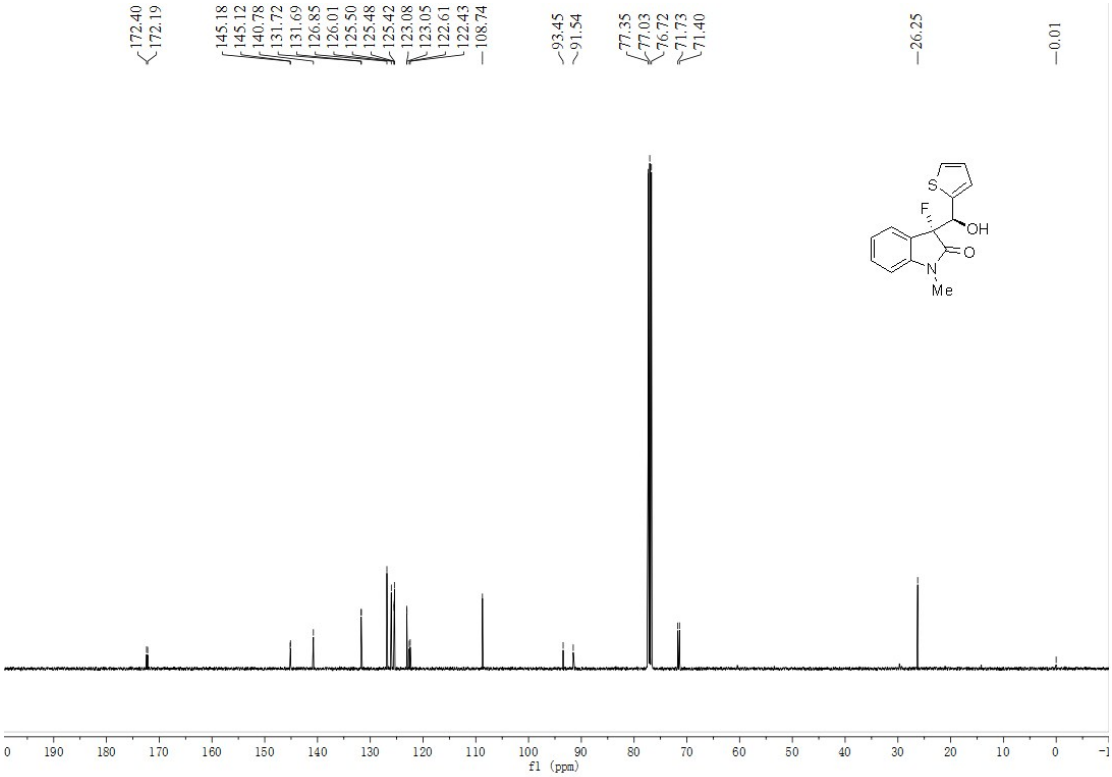


^{1}H NMR (400 MHz, $CDCl_3$) spectra of **13u**



^{19}F NMR (376 MHz, $CDCl_3$) spectra of **13u**

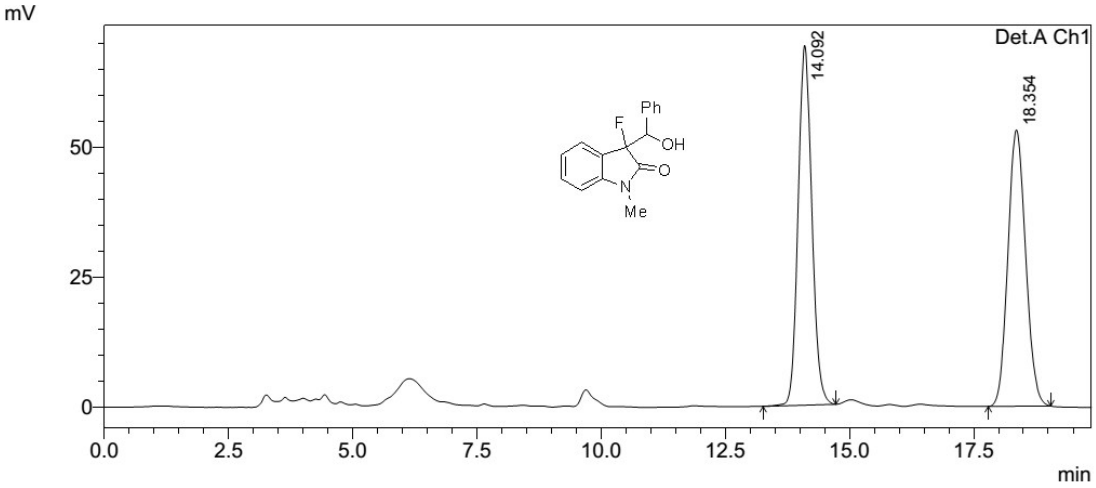
^{13}C NMR (101 MHz, $CDCl_3$) spectra of **13u**



6. HPLC spectra

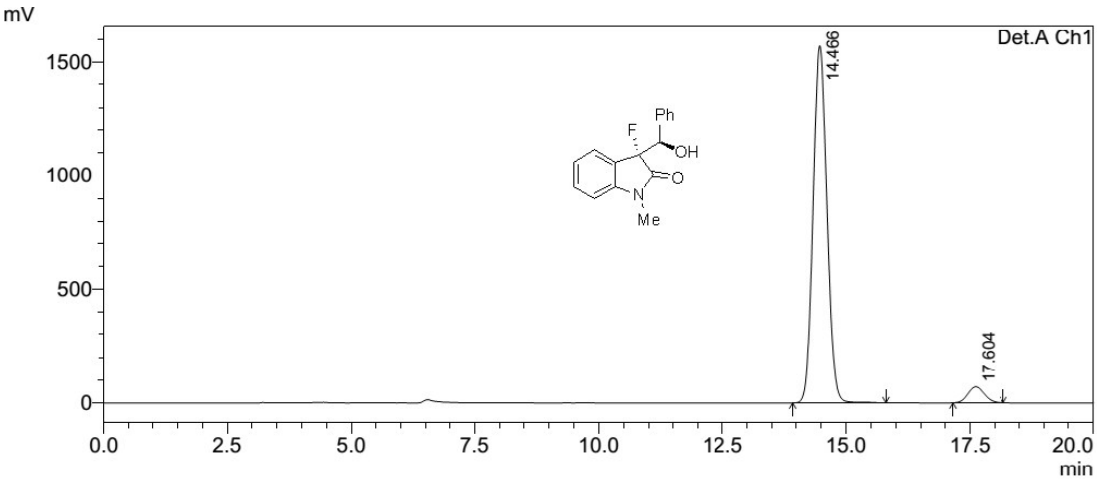
6.1. HPLC spectra of products 13

HPLC spectra of **racemic - 13a**



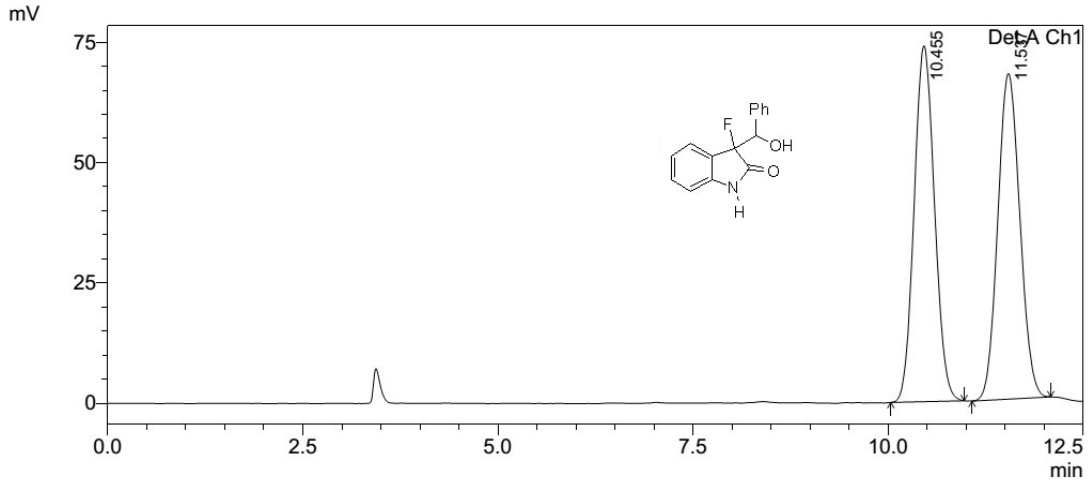
Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.092	1338412	69289	50.302	56.544
2	18.354	1322365	53251	49.698	43.456
Total		2660777	122540	100.000	100.000

HPLC spectra of product **13a**



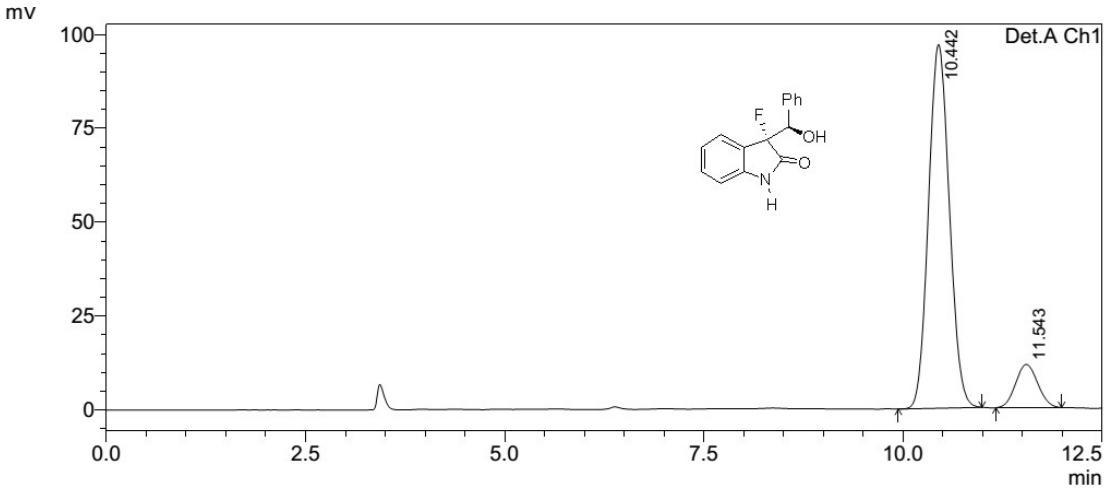
Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.466	30417609	1570423	94.972	95.745
2	17.604	1610525	69798	5.028	4.255
Total		32028134	1640221	100.000	100.000

HPLC spectra of **racemic – 13b**



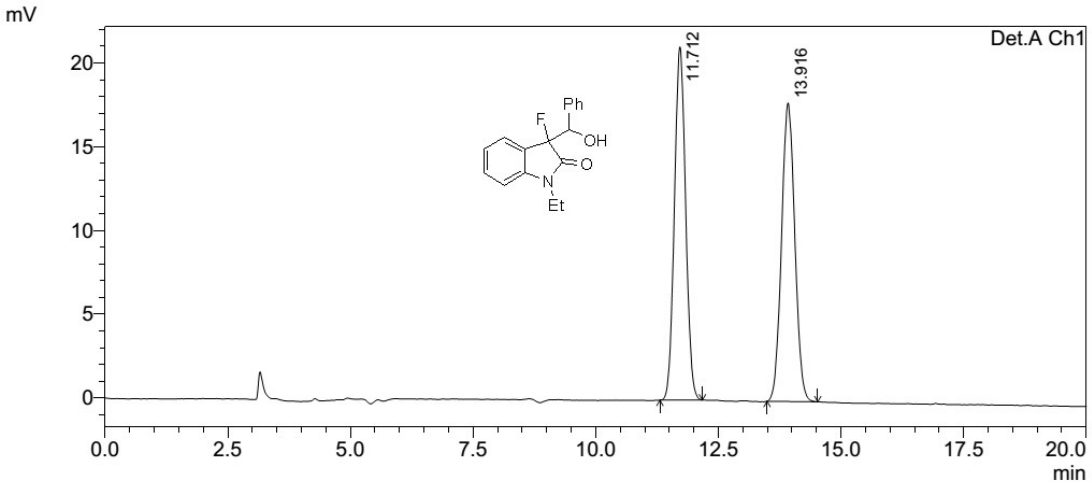
Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.455	1341890	73970	50.247	52.213
2	11.537	1328699	67700	49.753	47.787
Total		2670589	141669	100.000	100.000

HPLC spectra of product **13b**



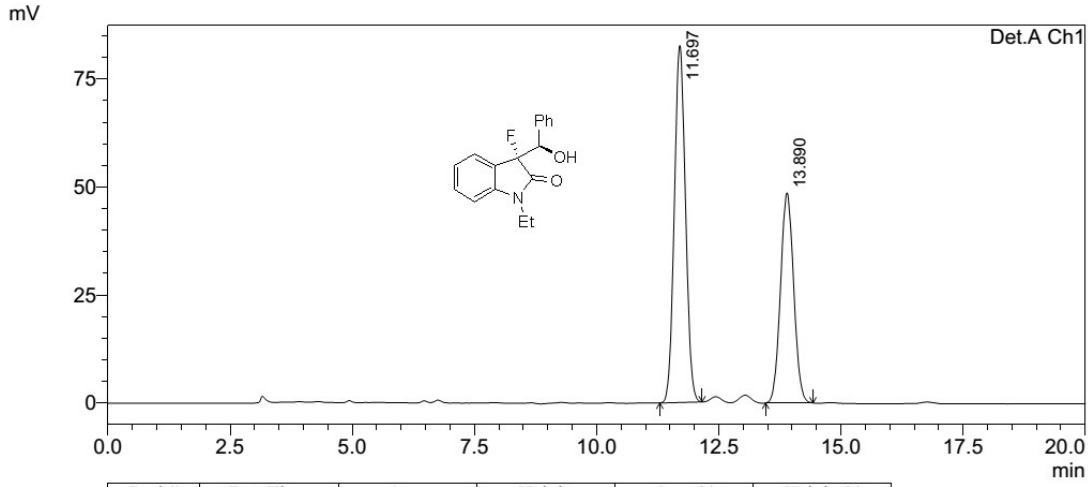
Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.442	1766111	96867	88.834	89.362
2	11.543	221999	11531	11.166	10.638
Total		1988110	108398	100.000	100.000

HPLC spectra of **racemic – 13c**



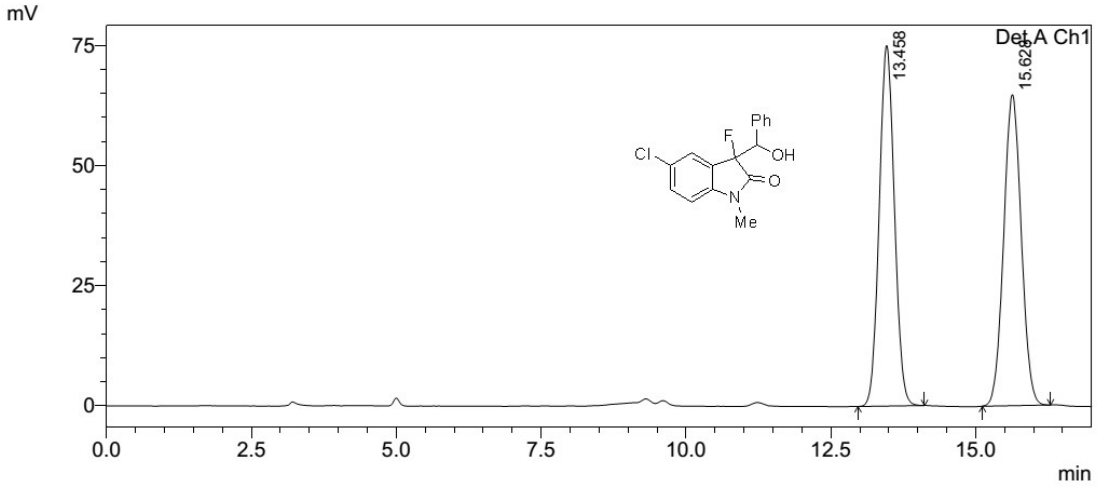
Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.712	335845	21095	49.988	54.209
2	13.916	336005	17819	50.012	45.791
Total		671850	38914	100.000	100.000

HPLC spectra of product **13c**



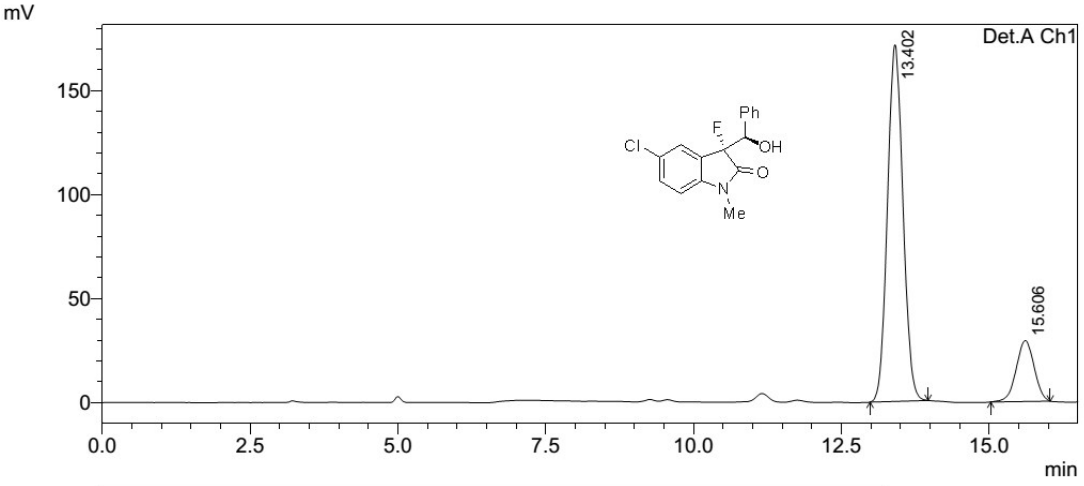
Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.697	1315126	82663	59.009	62.953
2	13.890	913578	48647	40.991	37.047
Total		2228704	131309	100.000	100.000

HPLC spectra of **racemic – 13d**



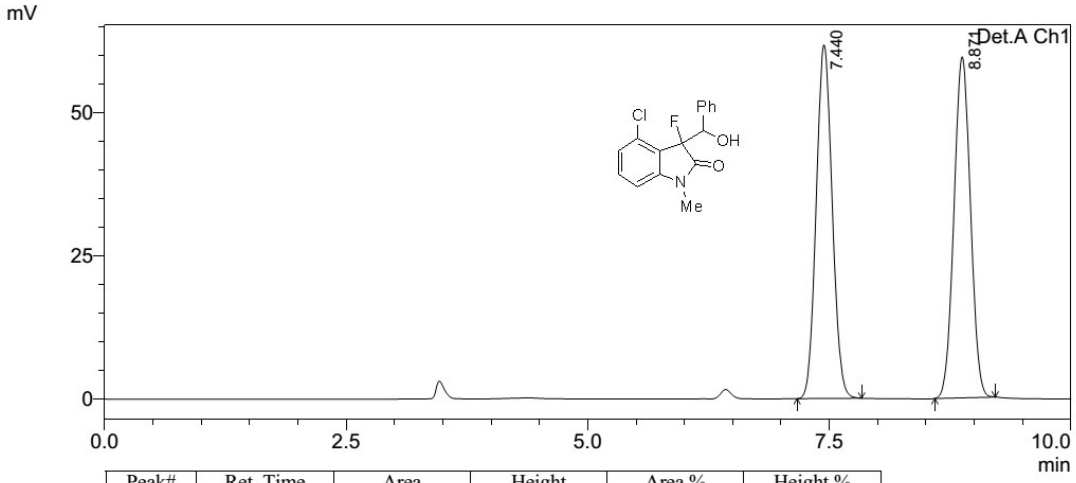
Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.458	1369686	74975	50.062	53.675
2	15.628	1366280	64709	49.938	46.325
Total		2735967	139685	100.000	100.000

HPLC spectra of product **13d**



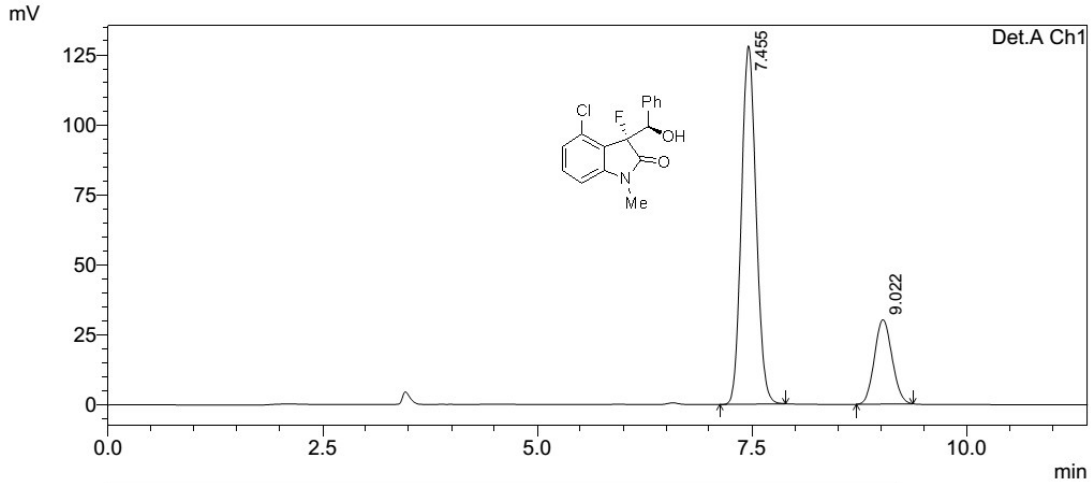
Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.402	3138588	171599	83.524	85.408
2	15.606	619137	29318	16.476	14.592
Total		3757725	200917	100.000	100.000

HPLC spectra of **racemic – 13e**



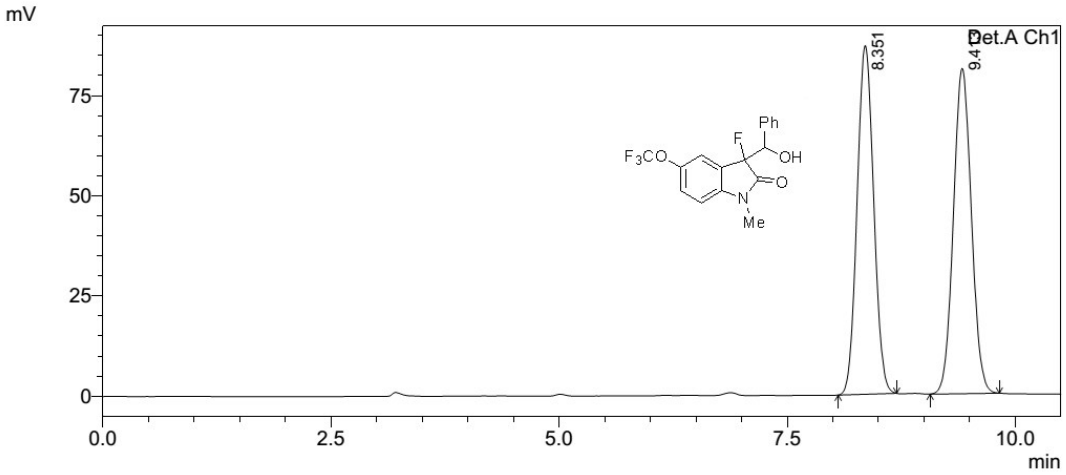
Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.440	711874	61767	50.131	50.896
2	8.871	708159	59594	49.869	49.104
Total		1420033	121361	100.000	100.000

HPLC spectra of product **13e**



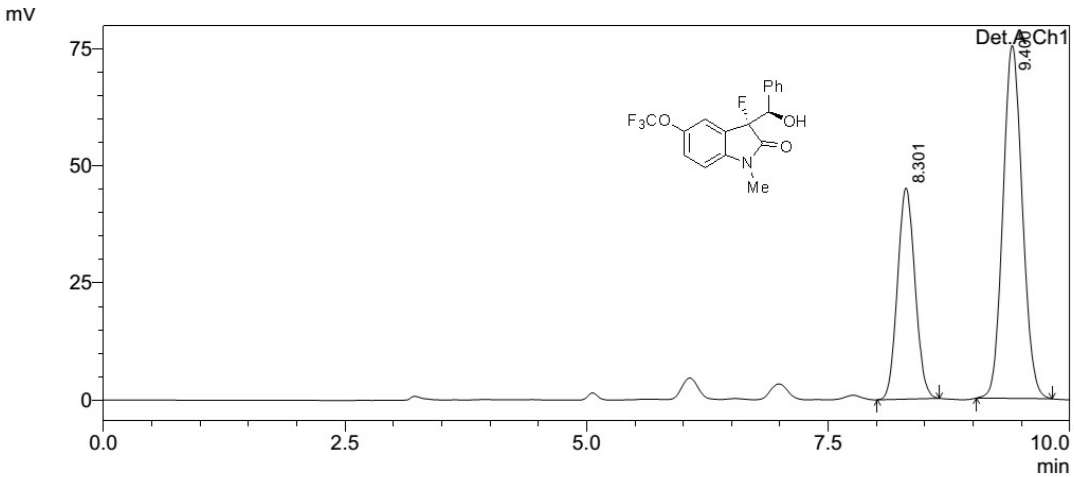
Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.455	1527149	128127	77.979	80.926
2	9.022	431257	30200	22.021	19.074
Total		1958406	158327	100.000	100.000

HPLC spectra of **racemic – 13f**



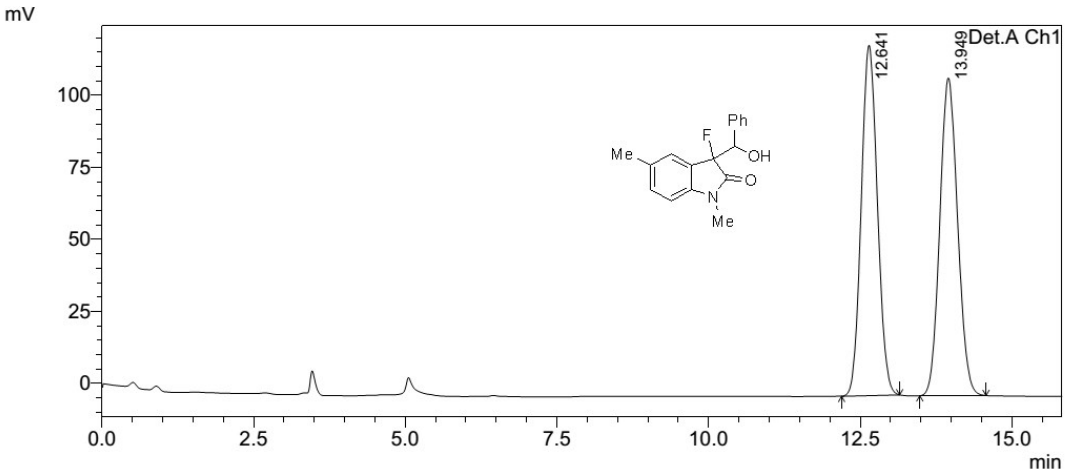
Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.351	1099234	86989	49.690	51.718
2	9.413	1112935	81208	50.310	48.282
Total		2212169	168196	100.000	100.000

HPLC spectra of product **13f**



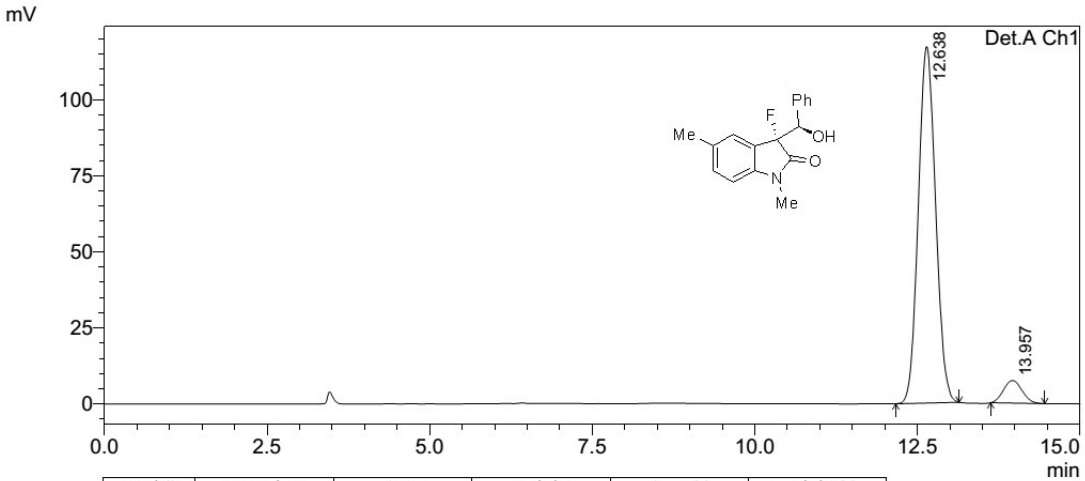
Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.301	569872	45108	35.062	37.442
2	9.400	1055467	75367	64.938	62.558
Total		1625338	120475	100.000	100.000

HPLC spectra of **racemic – 13g**



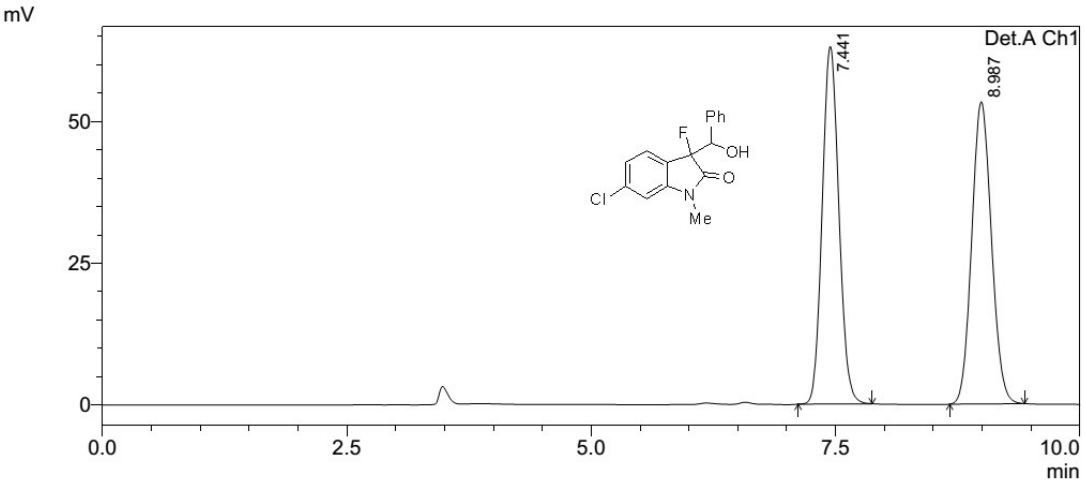
Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.641	2249308	121578	49.977	52.450
2	13.949	2251417	110218	50.023	47.550
Total		4500726	231797	100.000	100.000

HPLC spectra of product **13g**



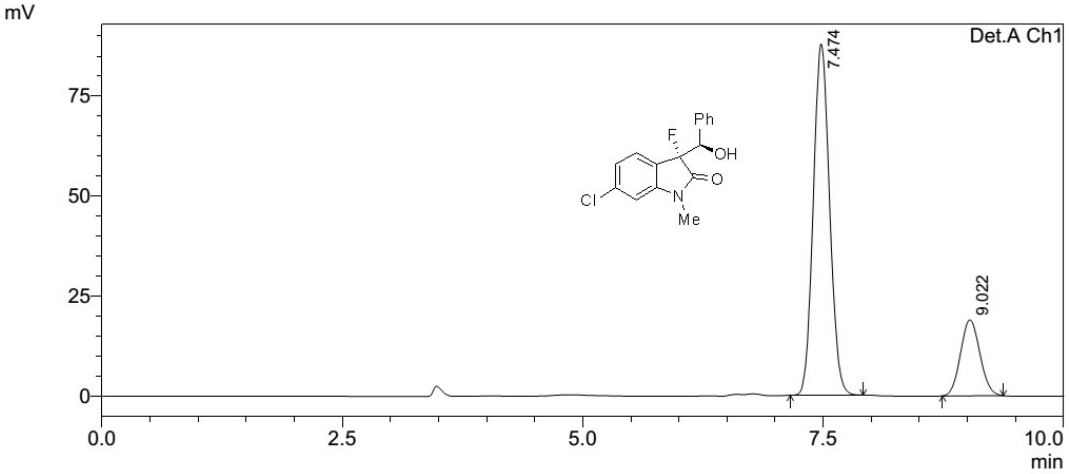
Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.638	2167110	117187	93.650	94.035
2	13.957	146933	7433	6.350	5.965
Total		2314043	124621	100.000	100.000

HPLC spectra of **racemic** – **13**h



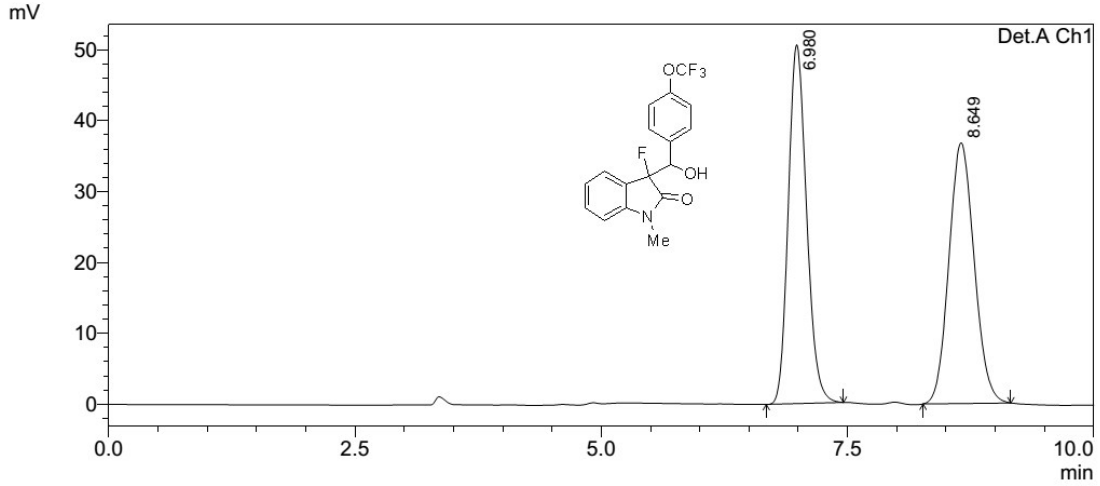
Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.441	747451	63015	49.972	54.164
2	8.987	748288	53326	50.028	45.836
Total		1495739	116342	100.000	100.000

HPLC spectra of product **13h**



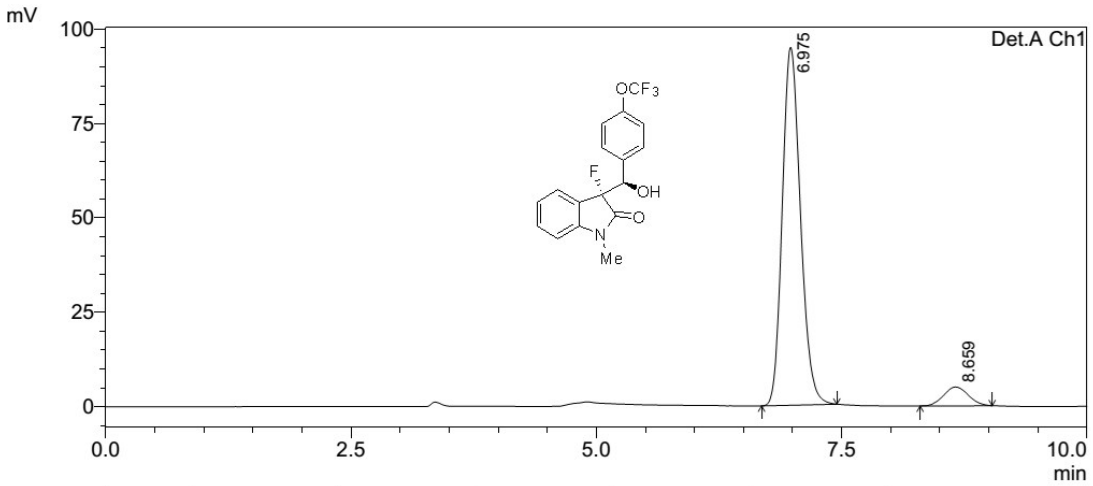
Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.474	1037288	87847	79.572	82.206
2	9.022	266304	19015	20.428	17.794
Total		1303592	106862	100.000	100.000

HPLC spectra of **racemic – 13i**



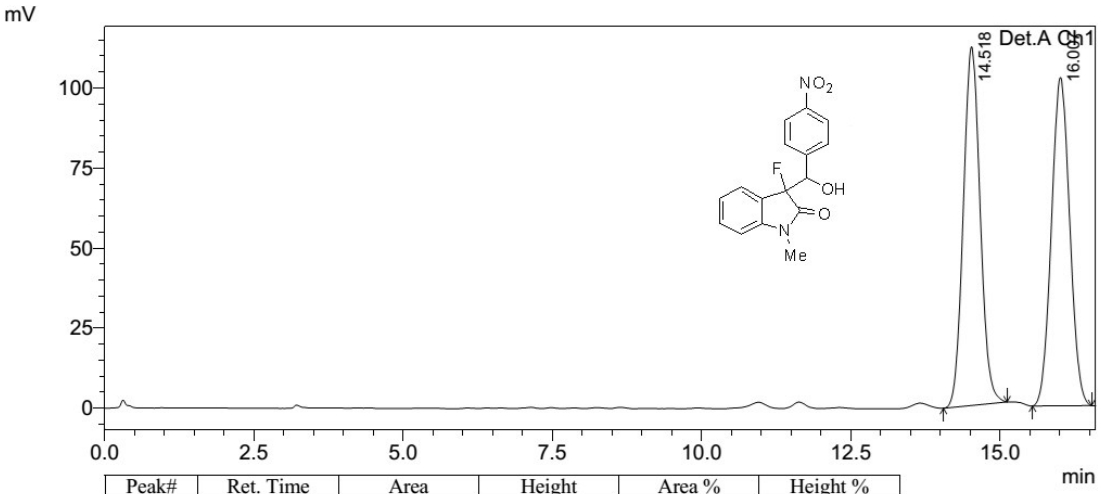
Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.980	653875	50644	49.868	57.926
2	8.649	657335	36784	50.132	42.074
Total		1311210	87427	100.000	100.000

HPLC spectra of product **13i**



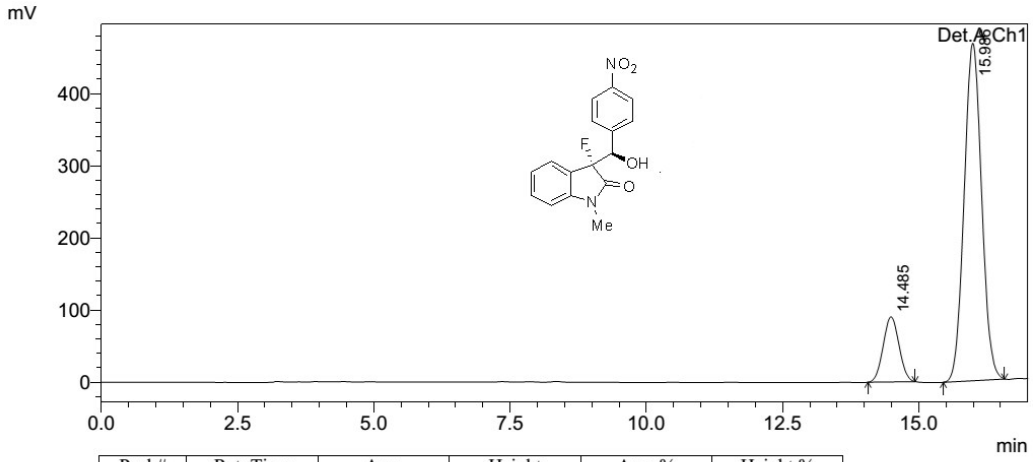
Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.975	1220546	94767	93.278	94.970
2	8.659	87953	5019	6.722	5.030
Total		1308499	99786	100.000	100.000

HPLC spectra of **racemic – 13j**



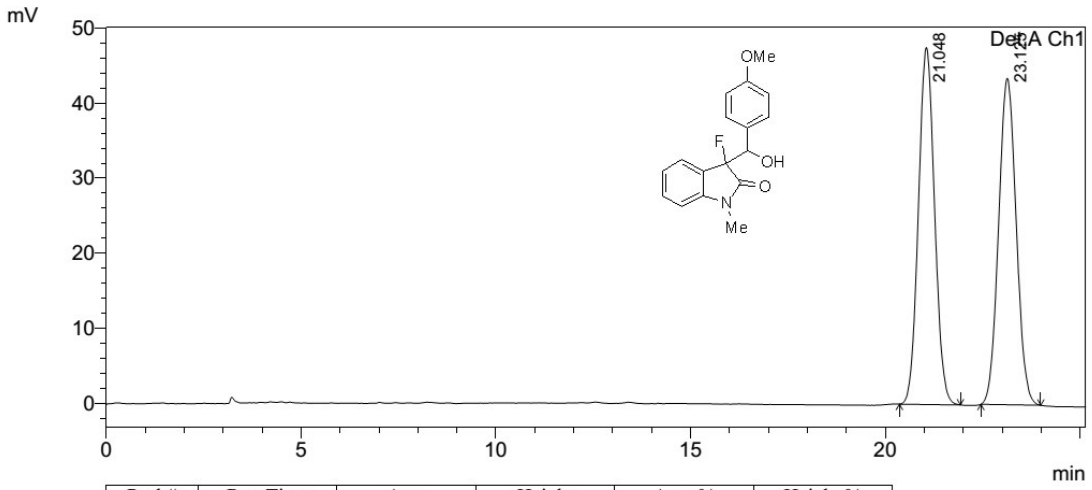
Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.518	2198998	112063	50.156	52.206
2	16.007	2185282	102594	49.844	47.794
Total		4384281	214657	100.000	100.000

HPLC spectra of product **13j**



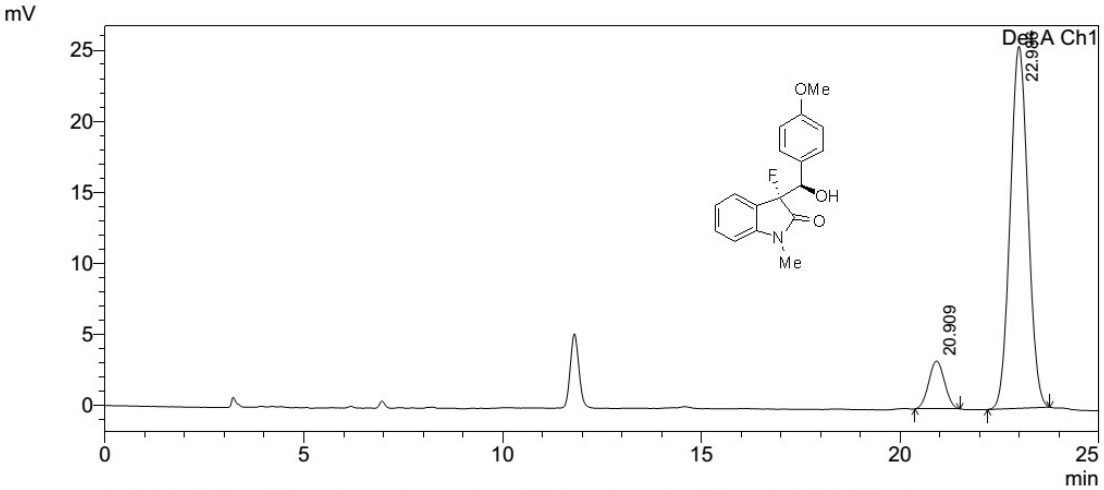
Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.485	1824850	90312	14.878	16.180
2	15.986	10440741	467872	85.122	83.820
Total		12265591	558184	100.000	100.000

HPLC spectra of **racemic – 13k**



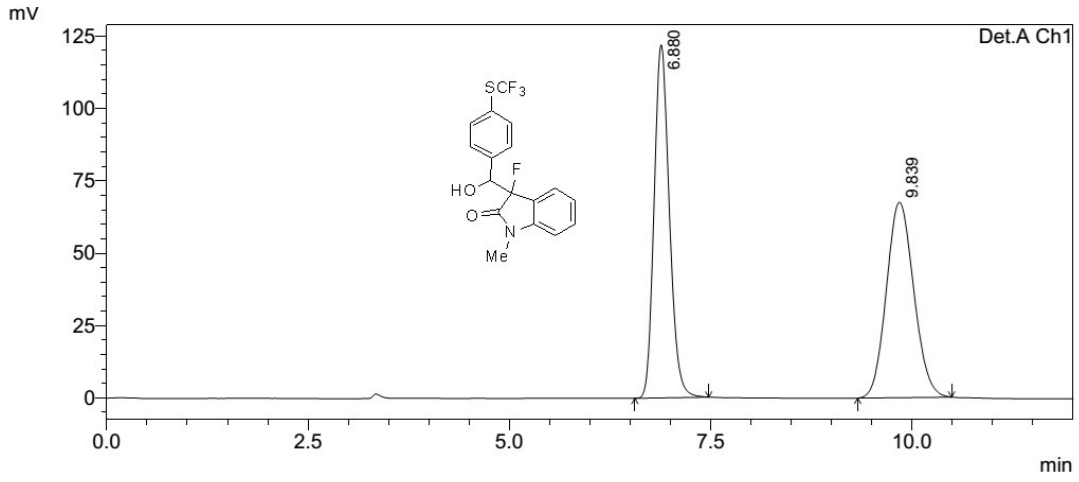
Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.048	1371215	47508	50.119	52.243
2	23.125	1364701	43428	49.881	47.757
Total		2735916	90936	100.000	100.000

HPLC spectra of product **13k**



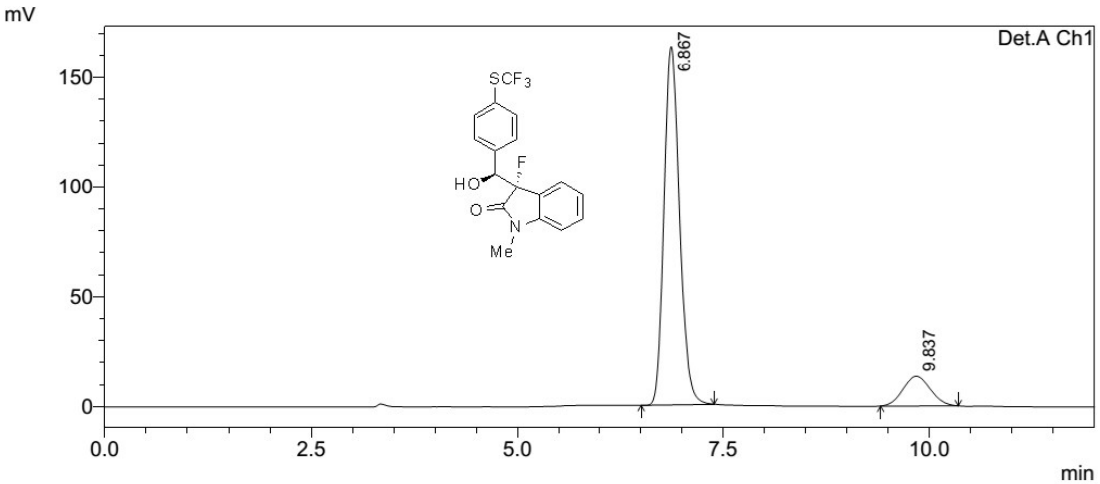
Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.909	93486	3371	10.545	11.690
2	22.986	793088	25464	89.455	88.310
Total		886574	28834	100.000	100.000

HPLC spectra of **racemic – 13l**



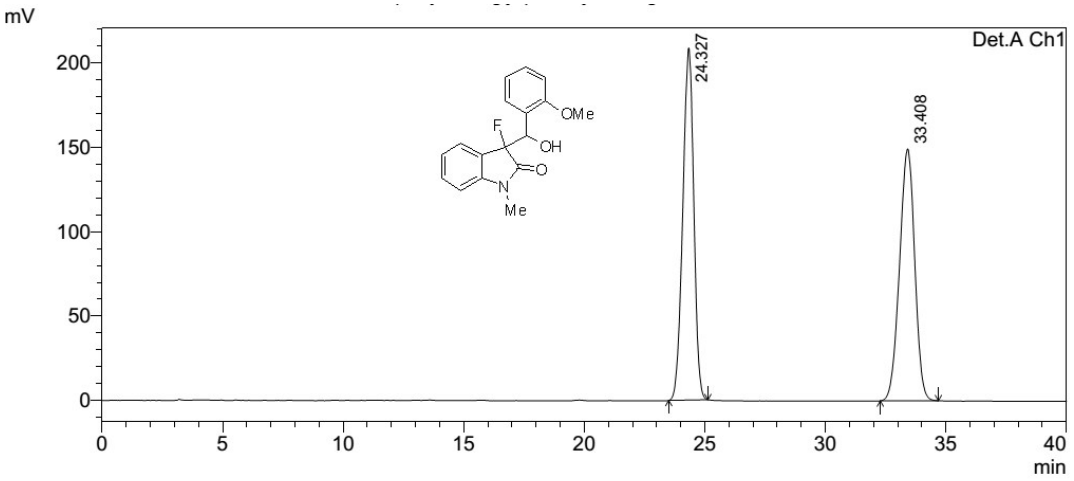
Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.880	1607732	121990	50.180	64.366
2	9.839	1596179	67535	49.820	35.634
Total		3203911	189525	100.000	100.000

HPLC spectra of product **13l**



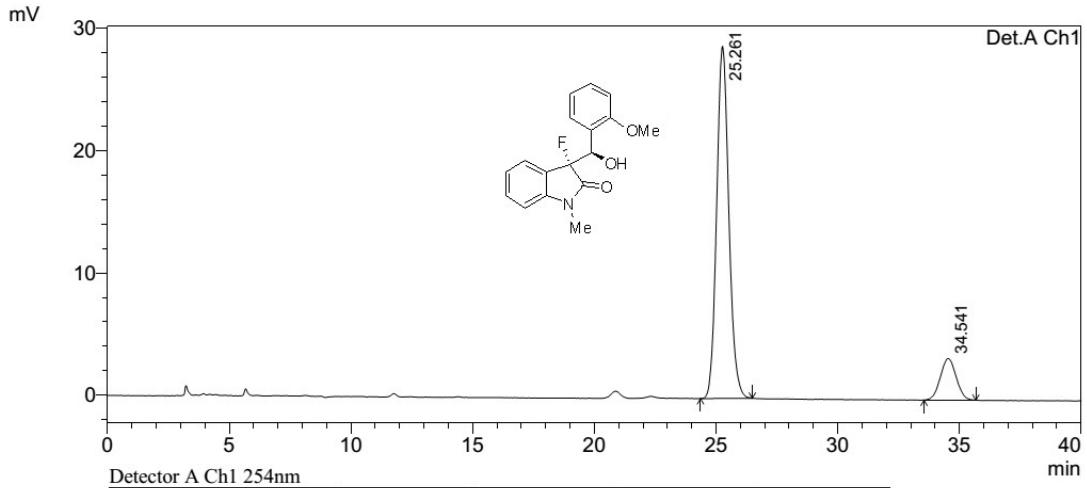
Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.867	2140571	163252	87.361	92.389
2	9.837	309701	13449	12.639	7.611
Total		2450272	176701	100.000	100.000

HPLC spectra of **racemic – 13m**



Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.327	6622738	208801	50.354	58.295
2	33.408	6529626	149377	49.646	41.705
Total		13152364	358178	100.000	100.000

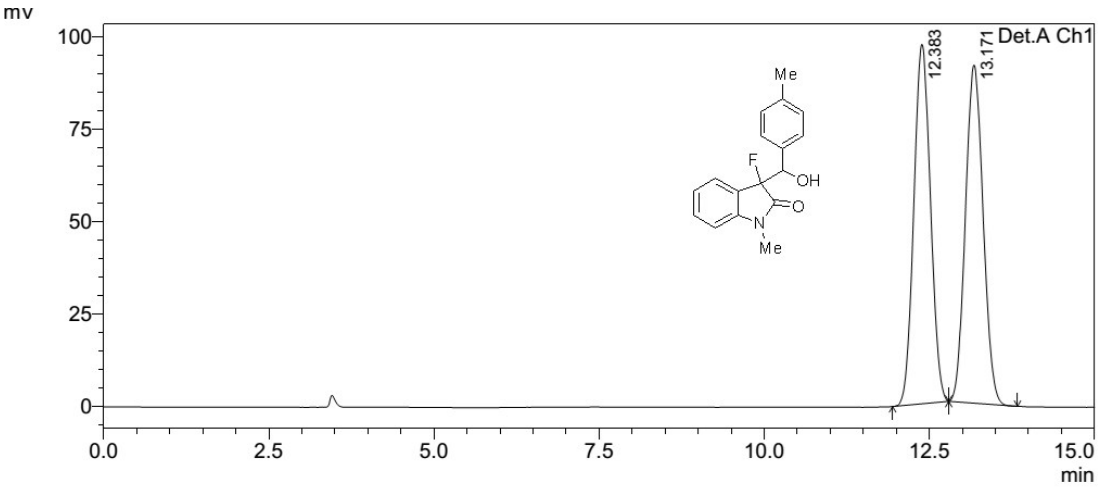
HPLC spectra of product **13m**



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.261	998762	28803	86.671	89.460
2	34.541	153602	3393	13.329	10.540
Total		1152365	32196	100.000	100.000

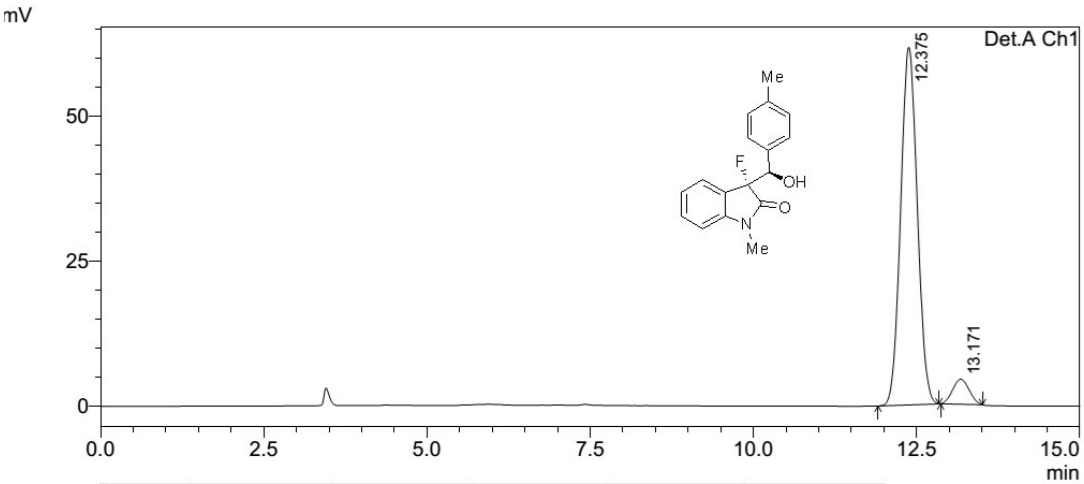
HPLC spectra of **racemic – 13n**



Detector A Ch1 254nm

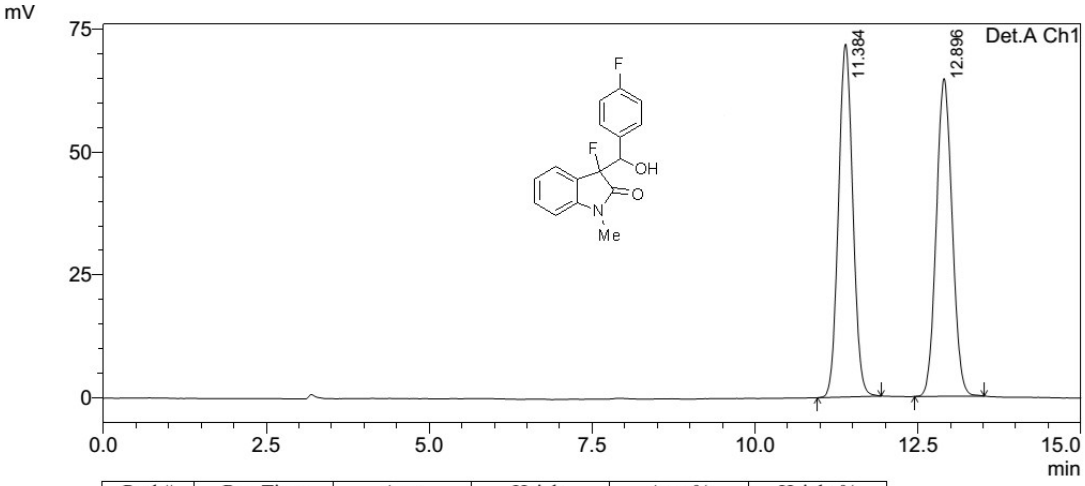
Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.383	1703614	97178	49.972	51.520
2	13.171	1705553	91443	50.028	48.480
Total		3409167	188621	100.000	100.000

HPLC spectra of product **13n**



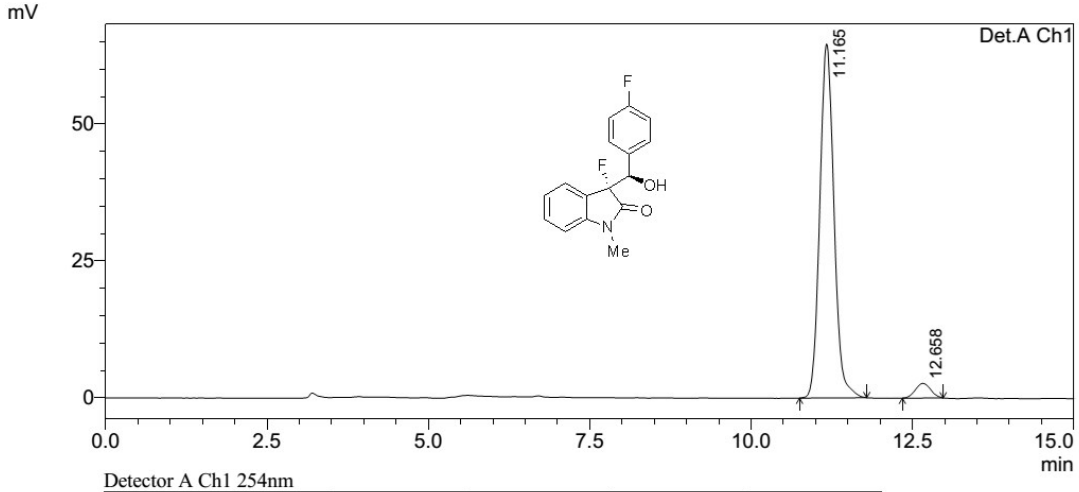
Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.375	1094026	61675	93.500	93.457
2	13.171	76056	4318	6.500	6.543
Total		1170082	65993	100.000	100.000

HPLC spectra of **racemic – 13o**



Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.384	1100210	71750	50.045	52.600
2	12.896	1098250	64658	49.955	47.400
Total		2198461	136408	100.000	100.000

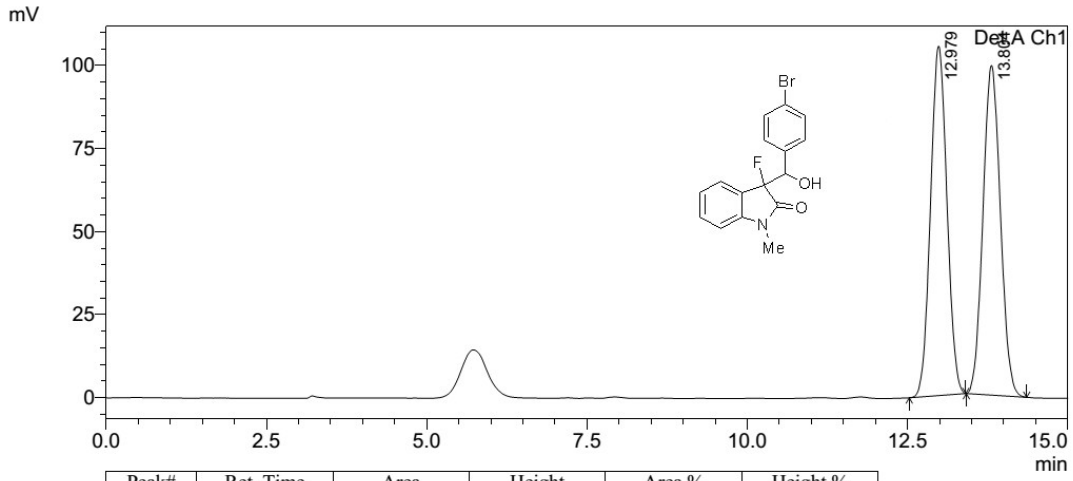
HPLC spectra of product **13o**



Detector A Ch1 254nm

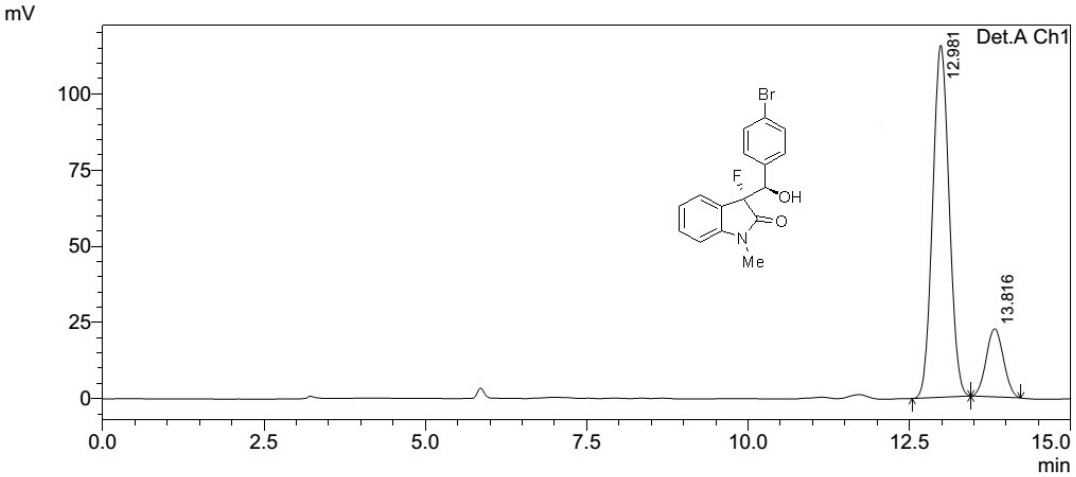
Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.165	989570	64625	95.746	95.993
2	12.658	43971	2698	4.254	4.007
Total		1033541	67322	100.000	100.000

HPLC spectra of **racemic – 13p**



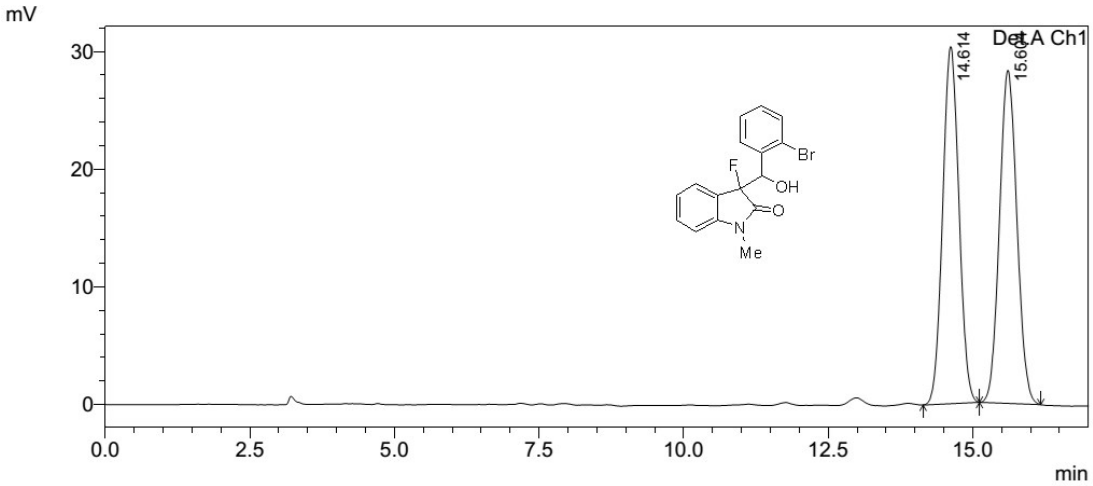
Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.979	1867760	105192	49.943	51.462
2	13.804	1871999	99217	50.057	48.538
Total		3739758	204409	100.000	100.000

HPLC spectra of product **13p**



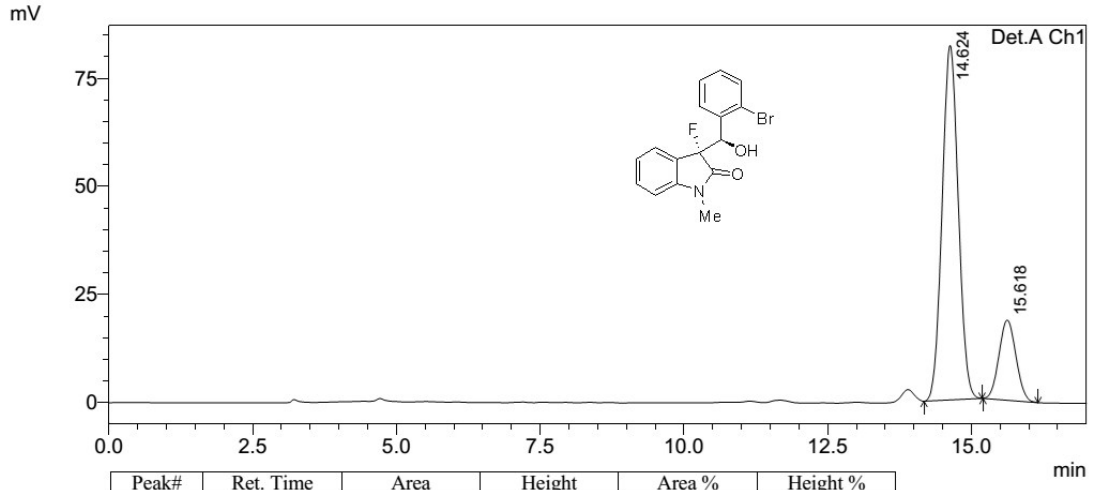
Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.981	2055201	115470	83.201	83.805
2	13.816	414948	22314	16.799	16.195
Total		2470149	137784	100.000	100.000

HPLC spectra of **racemic – 13q**



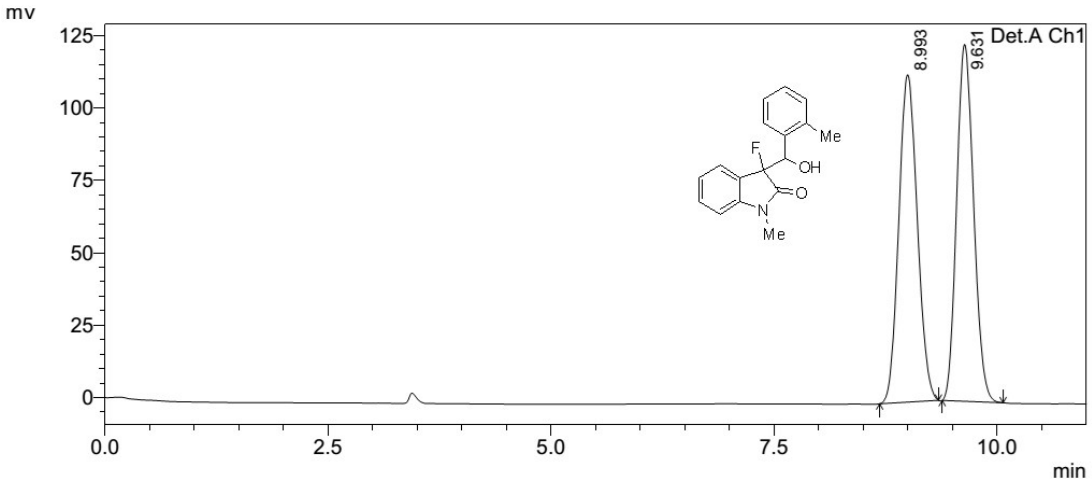
Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.614	593021	30351	49.981	51.736
2	15.604	593476	28314	50.019	48.264
Total		1186497	58665	100.000	100.000

HPLC spectra of product **13q**



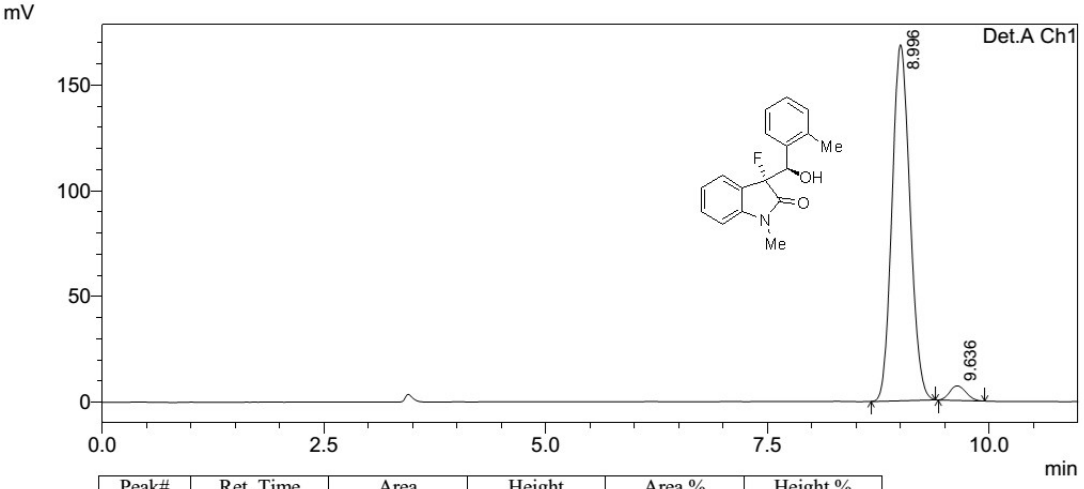
Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.624	1601112	81984	80.807	81.551
2	15.618	380284	18547	19.193	18.449
Total		1981397	100530	100.000	100.000

HPLC spectra of **racemic – 13r**



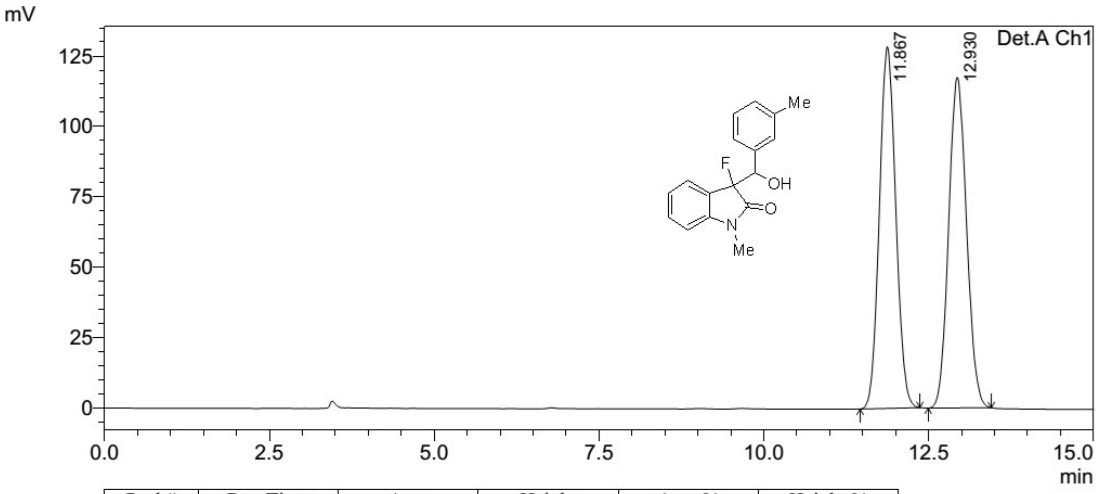
Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.993	1637407	113051	49.995	47.838
2	9.631	1637732	123268	50.005	52.162
Total		3275138	236319	100.000	100.000

HPLC spectra of product **13r**



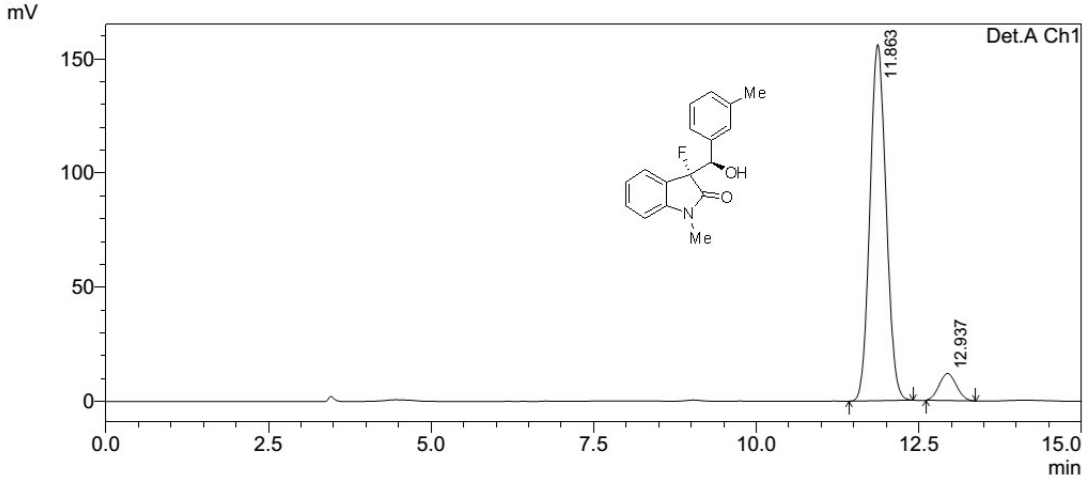
Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.996	2376211	168445	96.390	96.048
2	9.636	89004	6932	3.610	3.952
Total		2465215	175376	100.000	100.000

HPLC spectra of **racemic – 13s**



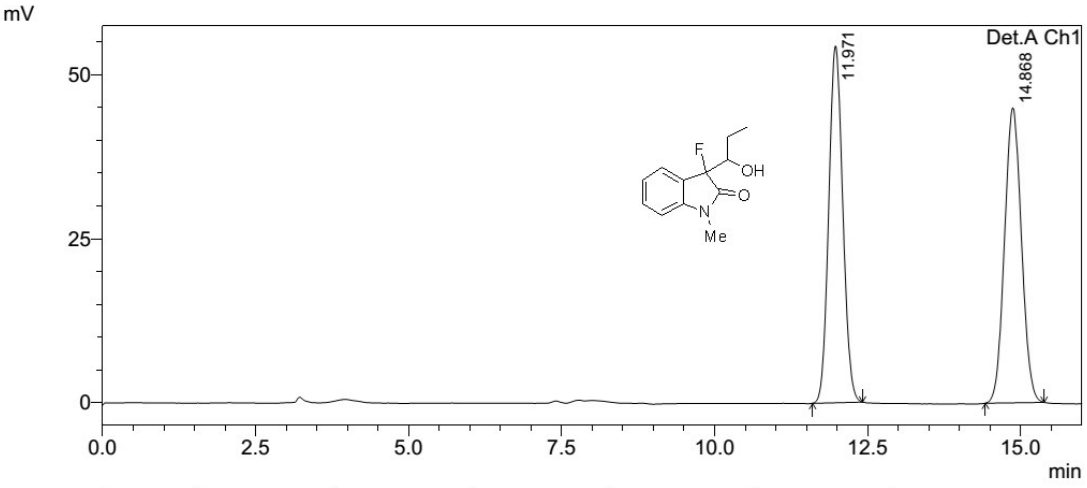
Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.867	2225188	128391	50.033	52.235
2	12.930	2222252	117404	49.967	47.765
Total		4447439	245796	100.000	100.000

HPLC spectra of product **13s**



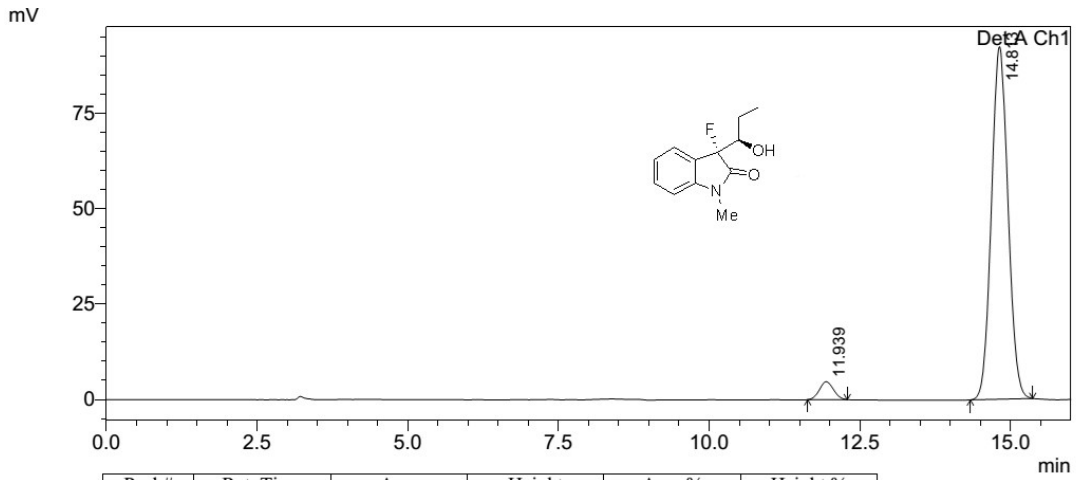
Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.863	2705533	156118	92.531	92.945
2	12.937	218385	11849	7.469	7.055
Total		2923918	167967	100.000	100.000

HPLC spectra of **racemic – 13t**



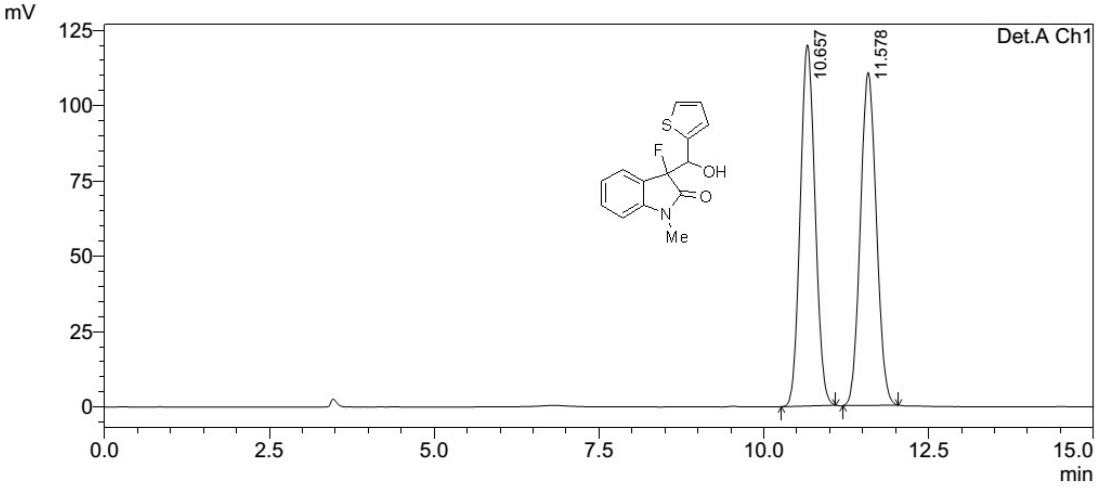
Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.971	867720	54361	50.064	54.747
2	14.868	865501	44934	49.936	45.253
Total		1733221	99296	100.000	100.000

HPLC spectra of product **13t**



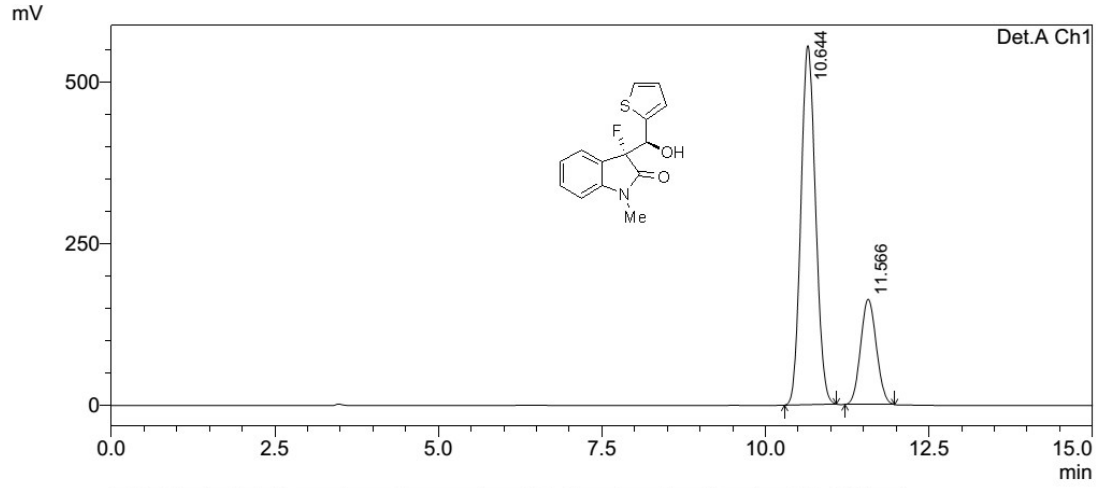
Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.939	76366	4706	4.129	4.847
2	14.813	1773258	92372	95.871	95.153
Total		1849624	97078	100.000	100.000

HPLC spectra of **racemic – 13u**



Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.657	1879069	119861	50.102	52.024
2	11.578	1871396	110535	49.898	47.976
Total		3750465	230395	100.000	100.000

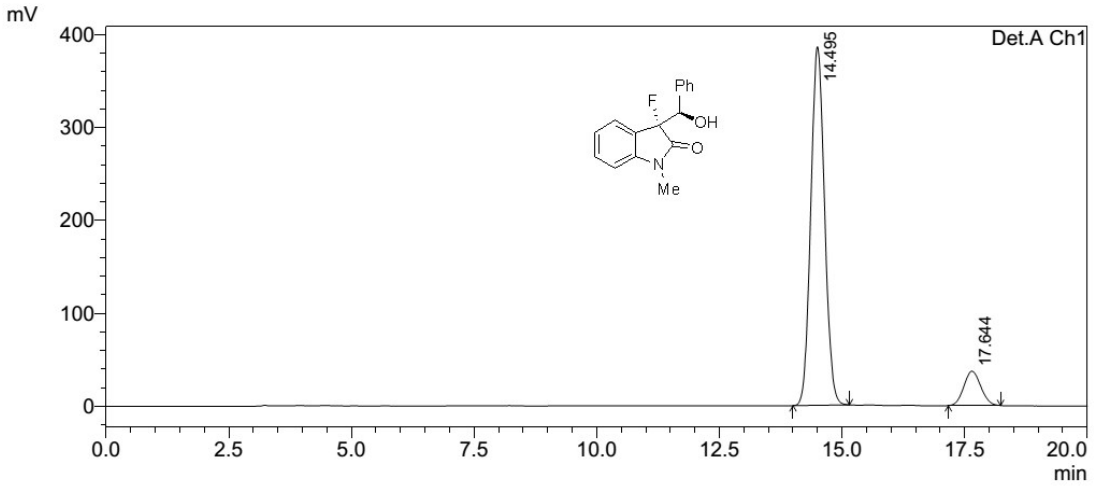
HPLC spectra of product of **13u**



Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.644	8685682	555856	76.039	77.307
2	11.566	2736978	163167	23.961	22.693
Total		11422660	719023	100.000	100.000

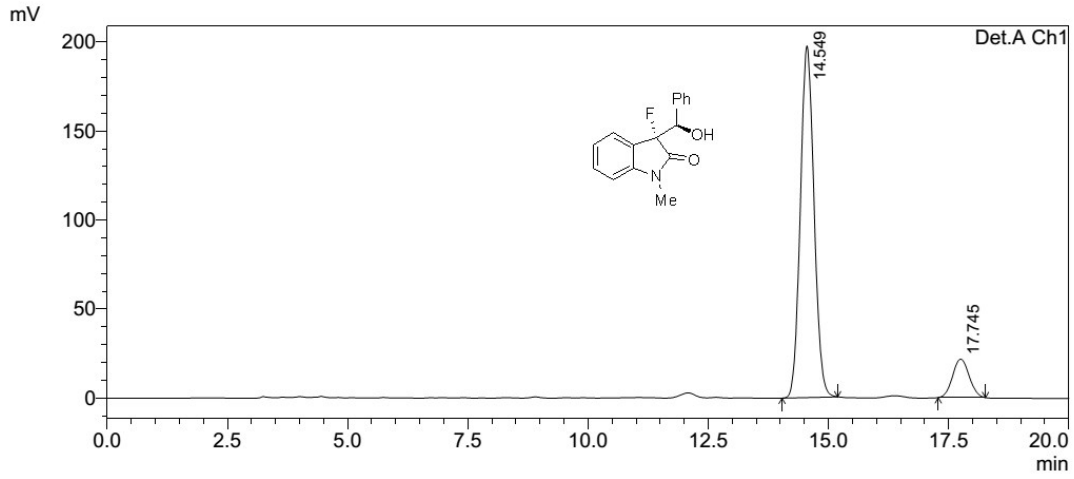
6.2. HPLC spectra of achiral gravity-driven column chromatography SDE tests

HPLC spectra of the first fraction:



Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.495	7549698	385994	89.457	91.252
2	17.644	889769	37006	10.543	8.748
Total		8439467	423000	100.000	100.000

HPLC spectra of the last fraction:



Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.549	3912209	197563	88.308	90.108
2	17.745	517990	21689	11.692	9.892
Total		4430199	219252	100.000	100.000