Electronic Supplementary Information

Palladium-Catalyzed Enantioselective Umpolung Allylation of Amido-Tethered Allylic Carbonates with Isatin-Derived Ketimines

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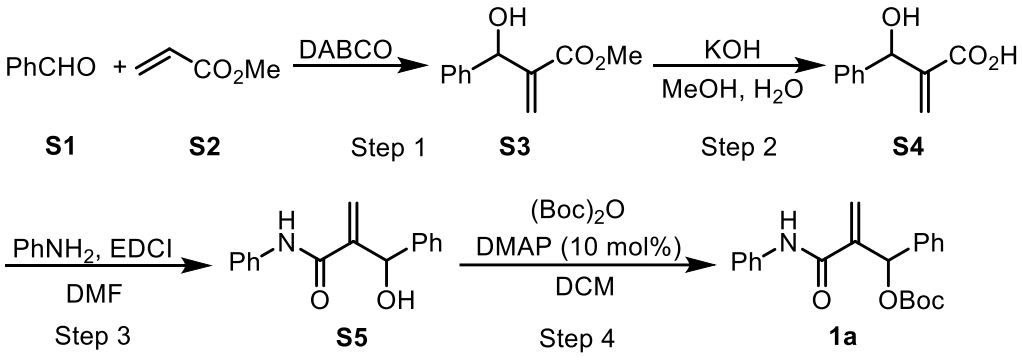
General Information

All reactions were performed under N_2 atmospheres in glassware with magnetic stirring. Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. All solvents were purified and dried according to standard methods prior to use. Organic solutions were concentrated under reduced pressure on a rotary evaporator or an oil pump. Reactions were monitored through thin layer chromatography (TLC) on silica gel–precoated glass plates. Chromatograms were visualized by fluorescence quenching with UV light at 254 nm. Flash column chromatography was performed using Qingdao Haiyang flash silica gel (200-300 mesh). ^{1}H, ^{13}C NMR spectra were recorded in $CDCl_3$ using a 300MHz or 500MHz NMR instrument (referenced internally to Me_4Si). Chemical shifts (δ, ppm) are relative to tetramethylsilane (TMS) with the resonance of the non-deuterated solvent or TMS as the internal standard. ^{1}H NMR data are reported as follows: chemical shift, multiplicity (s = singlet; d = doublet; t = triplet; m = multiplet), coupling constant (Hz), and integral. Data for ^{13}C NMR is reported in terms of chemical shift. Optical rotation was obtained on an Autopol V Plus polarimeter. Accurate mass measurements were performed with an Agilent instrument equipped with the ESI-MS technique.

Preparation of Starting Materials

Representative Procedure for the Preparation of *tert*-Butyl (1-phenyl-2-(phenylcarbamoyl)allyl) carbonate[1]



(1) The DABCO (100 mmol, 11.2 g) was dissolved into the mixture of benzaldehyde **S1** (100 mmol, 10.2 mL) and methyl acrylate **S2** (150 mmol, 13.4 mL) and the mixture was stirred at room temperature for 3 days or until complete consumption of the starting material as determined by

[1] H.-L. Cui, L. Jiang, H. Tan, S. Liu. *Adv. Synth. Catal.* **2019**, *361*, 4772.

TLC. Then, the product was extracted with EtOAc (50 mL × 3) and the organic layers were combined, washed with saturated brine and dried with Na_2SO_4. The solvent was removed under vacuum and the crude product was purified by column chromatography (Petroleum ether: EtOAc = 5: 1) to give the product methyl 2-(hydroxy(phenyl)methyl)acrylate **S3** as colorless oily liquid (18.94 g, 98.6% yield).

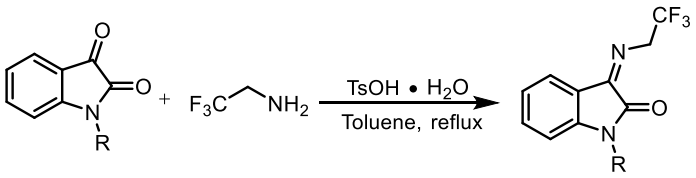
(2) The product methyl 2-(hydroxy(phenyl)methyl)acrylate **S3** (18.94 g, 98.6 mmol) was dissolved into 60 mL of MeOH, then KOH (aqueous) (6.7 g of KOH dissolved into 120 mL of H_2O) was added via dropper. The mixture was stirred at room temperature for 15 hours. After the reaction was complete, the pH of solution was adjusted to **1** with HCl (aqueous). Then, the solution was extracted with EtOAc (50 mL × 3) and the organic layers were combined, washed with saturated brine, dried with Na_2SO_4. The solvent was removed under vacuum to give the product **S4** as colorless oily liquid (17.2 g, 98% yield) without further purification.

(3) The EDCI (35.7 mmol, 6.8 g) was dissolved into the mixture of **S4** (29.8 mmol, 5.3 g) and aniline (35.7 mmol, 3.2 mL) in 60 mL of DMF. The resulting mixture was stirred at room temperature overnight, and then 50 mL of water was added into the mixture. The resulting mixture was extracted with EtOAc. The organic layer was washed with water for three times and dried with Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by flash column (Petroleum ether : EtOAc = 2: 1) to give the product **S5** as yellow solid (5.3 g, 71% yield).

(4) The product **S5** (21 mmol, 5.3 g) was dissolved into 30 mL of CH_2Cl_2, then the mixture of $(Boc)_2O$ (23.1 mmol, 5.5 mL) and DMAP (2.1 mmol, 258 mg) in 15 mL of CH_2Cl_2 was added into the former solution via dropper. The resulting mixture was stirred at 0 ℃ for 20 min and then was monitored through TLC. Once the reaction was complete, the reaction was quenched with 1N HCl and the reaction mixture was washed with $NaHCO_3$ (aqueous) and the organic layer was dried with Na_2SO_4. After the solvent was removed under vacuum, the crude product was purified by column chromatography (Petroleum ether : EtOAc = 8: 1) to give the final product **1a** as yellow solid (5.0 g, 66% yield).

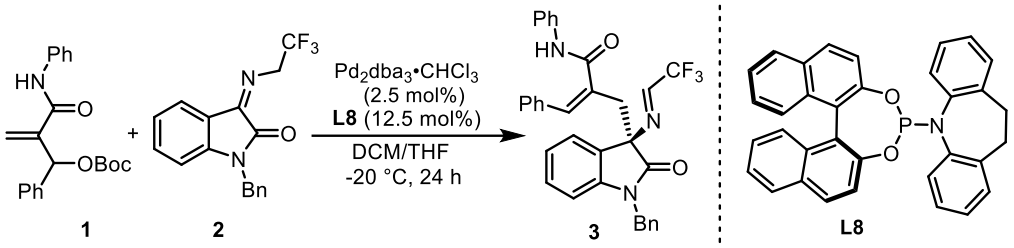
Representative Procedure for the Preparation of *N*-(2,2,2-trifluoroethyl) isatin-derived imines 2[2]

N-(2,2,2-Trifluoroethyl) isatin-derived imines were synthesized according to literature procedure.



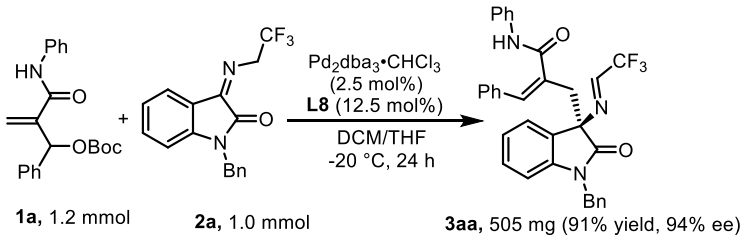
Isatin (1.0 equiv) was dissolved in toluene (30 mL), followed by the addition of 2,2,2-trifluoroethylamine (1.5 equiv) and *p*-toluenesulfonic acid (0.1 equiv). The mixture was then refluxed until complete disappearance of the starting materials (monitored by TLC). The solution was cooled to room temperature. After evaporation of the solvent, the crude residue was purified by re-crystallization from methanol, affording the resulting ketimine.

General Procedure for Allylation Reaction



Under a nitrogen atmosphere, an oven-dried 10 mL of Schlenk tube was charged with *tert*-butyl (1-phenyl-2-(phenylcarbamoyl)allyl)carbonate **1** (0.12 mmol), imines **2** (0.1 mmol), $Pd_2(dba)_3{\cdot}CHCl_3$ (2.5 mol%, 2.6 mg), **L8** (12.5 mol%, 6.4 mg) and 0.5 mL of CH_2Cl_2 and 0.5 mL of THF. The reaction solution was then vigorously stirred at -20 °C. Once the starting material was completely consumed (monitored by TLC), the mixture was concentrated to dryness. The residue was purified by flash column to afford the product **3**.

The Scale-up Allylation Reaction

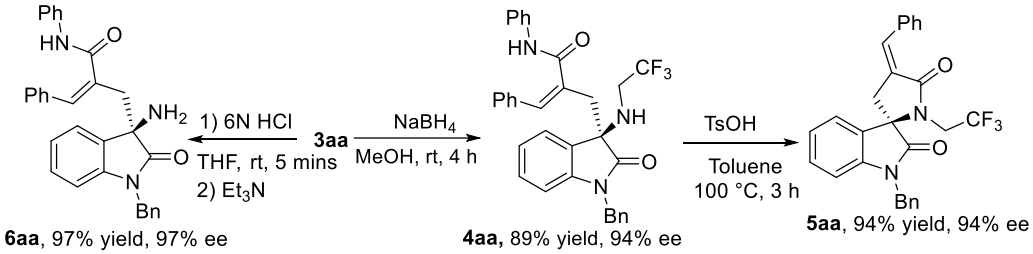


Under a nitrogen atmosphere, an oven-dried 50 mL of Schlenk tube was charged with *tert*-butyl (1-phenyl-2-(phenylcarbamoyl)allyl)carbonate **1a** (424 mg), imines **2a** (318 mg), $Pd_2(dba)_3{\cdot}CHCl_3$ (2.5 mol%), **L8** (12.5 mol%) and 5 mL of CH_2Cl_2 and 5 mL of THF. The reaction solution was then

[2] X. -Y. Gao, R.-J. Yan, B.-X. Xiao, W. Du, Ł. Albrecht, Y. -Ch. Chen. *Org. Lett.* **2019**, *21*, 9628.

vigorously stirred at -20 °C. Once the starting material was completely consumed (monitored by TLC), the mixture was concentrated to dryness. The residue was purified by flash column to afford the product **3aa** (505 mg, 91% yield, 94% ee).

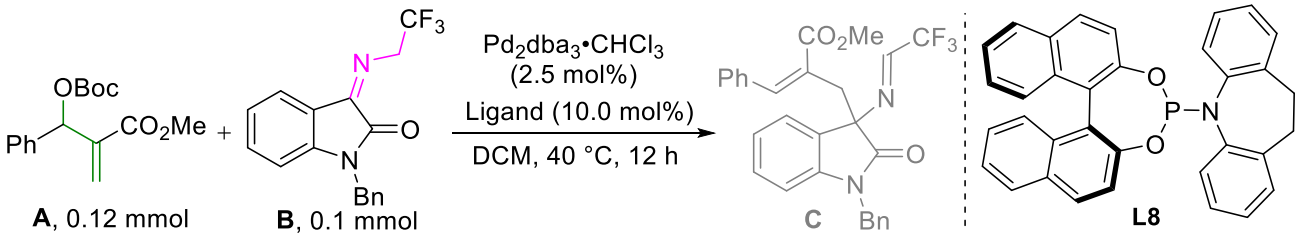
The Further Transformation



The $NaBH_4$ (10.0 equiv.) was slowly added to the solution of **3aa** (55.3 mg, 0.1 mmol) in 1mL of MeOH in an oven-dried 10 mL of Schlenk tube, and the mixture was stirred at rt for 4 h. Once the starting material was completely consumed (monitored by TLC), the mixture was concentrated to dryness. The residue was purified by flash column to afford the product **4aa** (49.3 mg, 89% yield, 94% ee). Then, in a 10 mL round-bottom flask, **4aa** (0.1 mmol) and TsOH (0.02 mmol) were dissolved in 2 mL of toluene. The resulting reaction mixture was stirred at 100 ℃ for 3 hours. The solvent was removed by rotary evaporation, **5aa** were obtained by flash column (PE/EA= 6/1) as yellow semi-solid.

The 6N HCl solution was slowly added to the solution of **3aa** (55.3 mg, 0.1 mmol) in 1mL of THF in 10 mL of Schlenk tube, and the mixture was stirred at rt for 5 mins. Then, adding 0.2 mL of Et_3N to the mixture, and the resulting mixture was concentrated to dryness. The residue was purified by flash column to afford the product **6aa** (97% yield, 97% ee).

The Investigation on Reaction of Classical MBH Carbonate

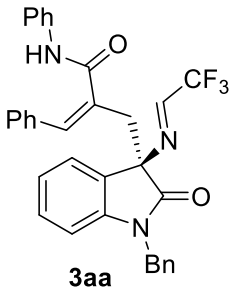


entry	ligand	yield (%)	ee (%)
1	PPh_3	messy	/
2	dppbz	messy	/
3	dppf	messy	/
4	Xantphos	messy	/
5	1,10-phen	messy	/
6[a]	**L8**	NR	/

[a] In mixed solvent of DCM (0.5 mL) and THF (0.5 mL) at –20 °C for 24 h

Characterization Data of All Products

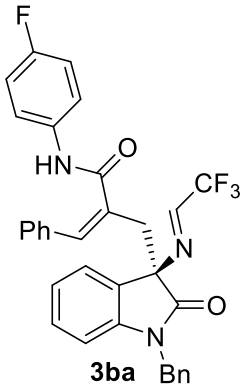
(*Z*)-2-(((*R*)-1-benzyl-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-*N*,3-diphenylacrylamide (3aa)



3aa

The title compound **3aa** was prepared according to the general procedure as described above in 99% yield (54.6 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford yellow solid. mp = 112 – 114 °C. $[\alpha]^{25}_{D}$ = – 48 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (q, *J* = 3.2 Hz, 1H), 7.58 (s, 1H), 7.35 (d, *J* = 7.9 Hz, 2H), 7.32 – 7.26 (m, 5H), 7.28 – 7.20 (m, 5H), 7.09 (q, *J* = 7.8 Hz, 2H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.69 (d, *J* = 7.8 Hz, 1H), 4.98 (d, *J* = 15.5 Hz, 1H), 4.64 (d, *J* = 15.5 Hz, 1H), 3.52 (q, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.7, 167.8, 150.6 (q, *J* = 39.4, 39.0 Hz), 141.7, 138.0, 137.3, 135.5, 134.9, 133.2, 129.9, 129.0, 128.88, 128.85, 128.8, 128.7, 128.6, 128.3, 128.1, 127.5, 125.9, 124.3, 123.5, 118.9 (q, *J* = 275.7 Hz), 115.6, 109.7, 71.6, 44.0, 35.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.16. IR (film) ν_{max} 3751, 3649, 1734, 1698, 1653, 1559, 1489, 1362, 1275, 1175, 764, 421 cm^{-1}; HRMS (ESI): m/z for $C_{33}H_{26}F_3N_3NaO_2^+$ $[M+Na]^+$ calcd.: 576.1869, found: 576.1863. HPLC analysis: **3aa**, 95% ee (IA, hexane : isopropanol =85 : 15, 1 mL/min, UV: 254 nm), t_R =17.1 min (major), 24.8 min (minor).

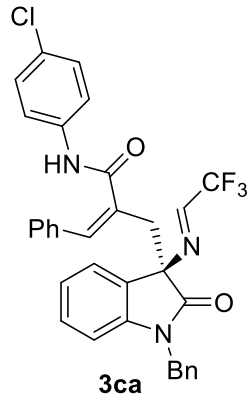
(*Z*)-2-(((*R*)-1-benzyl-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-*N*-(4-fluorophenyl)-3-phenylacrylamide (3ba)



3ba

The title compound 3ba was prepared according to the general procedure as described above in 94% yield (53.6 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford yellow solid. mp = 124 – 126 °C. $[\alpha]^{25}_{D}$ = – 32 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (q, *J* = 3.2 Hz, 1H), 7.69 (s, 1H), 7.33 (d, *J* = 5.0 Hz, 2H), 7.30 (d, *J* = 5.0 Hz, 3H), 7.29 – 7.27 (m, 3H), 7.24 (d, *J* = 5.4 Hz, 2H), 7.20 (dd, *J* = 9.0, 5.2 Hz, 3H), 7.12 (t, *J* = 7.9 Hz, 1H), 6.99 – 6.93 (m, 4H), 6.71 (d, *J* = 7.9 Hz, 1H), 5.02 (d, *J* = 15.4 Hz, 1H), 4.62 (d, *J* = 15.5 Hz, 1H), 3.56 – 3.48 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.5, 167.3, 160.2 (d, *J* = 248.6 Hz), 150.6 (q, *J* = 38.6 Hz), 141.8, 137.7, 135.50, 135.47, 130.33, 130.26, 130.10, 130.07, 129.8, 129.73, 129.70, 129.0, 128.7, 128.1, 127.5, 127.2, 125.8, 124.3, 124.20, 124.17, 123.5, 122.7 (d, *J* = 14.6 Hz), 120.1, 118.9 (q, *J* = 275.9 Hz), 115.7 (d, *J* = 21.5 Hz), 109.6, 71.5, 44.0, 35.7. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.15, –113.03. IR (film) ν_{max} 3649, 3054, 1717, 1684, 1653, 1541, 1457, 1339, 1264, 896, 731, 425 cm^{-1}; HRMS (ESI): m/z for $C_{33}H_{25}F_4N_3NaO_2^+$ $[M+Na]^+$ calcd.: 594.1775, found: 594.1772. HPLC analysis: 3ba, 92% ee (IA, hexane : isopropanol =85 : 15, 1 mL/min, UV: 254 nm), t_R =24.9 min (major), 36.4 min (minor).

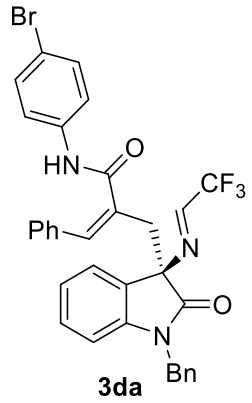
(*Z*)-2-(((*R*)-1-benzyl-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-*N*-(4-chlorophenyl)-3-phenylacrylamide (3ca)



3ca

The title compound **3ca** was prepared according to the general procedure as described above in 95% yield (55.7 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford yellow solid. mp = 82 – 84 °C. $[\alpha]^{25}_{D}$ = – 160 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (q, *J* = 3.2 Hz, 1H), 7.66 (s, 1H), 7.33 – 7.28 (m, 8H), 7.28 – 7.19 (m, 8H), 7.11 (t, *J* = 7.2 Hz, 1H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.70 (d, *J* = 7.8 Hz, 1H), 5.02 (d, *J* = 15.5 Hz, 1H), 4.62 (d, *J* = 15.5 Hz, 1H), 3.51 (q, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.7, 167.8, 150.6 (q, *J* = 38.6 Hz), 141.7, 137.8, 136.6, 135.4, 134.8, 132.8, 129.9, 129.2, 129.1, 128.8, 128.7, 128.6, 128.4, 128.1, 127.5, 127.4, 125.83, 123.5, 121.3, 118.8 (q, *J* = 275.7 Hz), 109.7, 71.6, 44.0, 35.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.14. IR (film) ν_{max} 3055, 1716, 1614, 1492, 1398, 1264, 1175, 1092, 896, 731, 509, 457 cm^{-1}; HRMS (ESI): m/z for $C_{33}H_{25}ClF_3N_3NaO_2^+$ $[M+Na]^+$ calcd.: 610.1479, found: 610.1473. HPLC analysis: **3ca**, 92% ee (IA, hexane : isopropanol =85 : 15, 1 mL/min, UV: 254 nm), t_R =29.2 min (major), 42.6 min (minor).

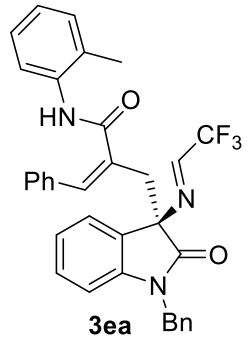
(*Z*)-2-(((*R*)-1-benzyl-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-*N*-(4-bromophenyl)-3-phenylacrylamide (3da)



3da

The title compound **3da** was prepared according to the general procedure as described above in 93% yield (58.6 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford yellow solid. mp = 100 – 102 °C. $[\alpha]^{25}_{D}$ = – 32 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (q, *J* = 3.2 Hz, 1H), 7.66 (s, 1H), 7.30 (dt, *J* = 8.1, 3.5 Hz, 9H), 7.25 – 7.20 (m, 7H), 7.11 (t, *J* = 7.2 Hz, 1H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.70 (d, *J* = 7.8 Hz, 1H), 5.02 (d, *J* = 15.5 Hz, 1H), 4.62 (d, *J* = 15.5 Hz, 1H), 3.56 – 3.47 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.7, 167.7, 150.6 (q, *J* = 39.0 Hz), 141.7, 137.8, 136.6, 135.4, 134.8, 132.8, 129.9, 129.2, 129.1, 129.0, 128.8, 128.7, 128.6, 128.5, 128.4, 128.1, 127.5, 127.4, 125.9, 123.5,121.6, 121.3, 118.9 (q, *J* = 270.1 Hz), 109.6, 71.6, 44.0, 35.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.13. IR (film) ν_{max} 3853, 3649, 1717, 1653, 1559, 1522, 1489, 1263, 749, 457 cm^{-1}; HRMS (ESI): m/z for $C_{33}H_{25}BrF_3N_3NaO_2^+$ $[M+Na]^+$ calcd.: 654.0974, found: 654.0971. HPLC analysis: **3da**, 95% ee (IA, hexane : isopropanol =85 : 15, 1 mL/min, UV: 254 nm), t_R =31.6 min (major), 44.9 min (minor).

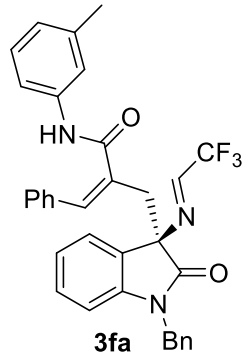
(*Z*)-2-(((*R*)-1-benzyl-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-3-phenyl-*N*-(o-tolyl)acrylamide (3ea)



3ea

The title compound **3ea** was prepared according to the general procedure as described above in 74% yield (42.0 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford yellow solid. mp = 83 – 85 °C. $[\alpha]_D^{25}$ = – 56 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (q, *J* = 3.2 Hz, 1H), 7.68 (d, *J* = 8.1 Hz, 1H), 7.44 (s, 1H), 7.24 – 7.20 (m, 4H), 7.18 (dd, *J* = 5.1, 3.3 Hz, 4H), 7.15 (dd, *J* = 11.0, 3.6 Hz, 4H), 7.11 – 7.07 (m, 3H), 6.99 (t, *J* = 7.4 Hz, 1H), 6.93 (t, *J* = 7.6 Hz, 1H), 6.64 (d, *J* = 7.9 Hz, 1H), 4.89 (d, *J* = 15.6 Hz, 1H), 4.62 (d, *J* = 15.6 Hz, 1H), 3.55 – 3.36 (m, 2H), 2.15 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.9, 168.0, 150.8 (q, *J* = 39.0 Hz), 141.9, 138.6, 138.1, 137.5, 135.7, 132.5, 132.0, 129.9, 129.4, 129.11, 129.07, 128.8, 128.2, 127.72, 127.66, 126.1, 124.3, 123.5, 120.1, 119.0 (q, *J* = 276.4 Hz), 109.7, 71.7, 44.1, 36.1, 21.4. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.36. IR (film) ν_{max} 3853, 3649, 1717, 1684, 1559, 1541, 1489, 1362, 1263, 1174, 749, 457 cm^{-1}; HRMS (ESI): m/z for $C_{34}H_{28}F_3N_3NaO_2^+$ $[M+Na]^+$ calcd.: 590.2025, found: 590.2020. HPLC analysis: **3ea**, 88% ee (IC, hexane : isopropanol =85 : 15, 1 mL/min, UV: 254 nm), t_R =12.7 min (major), 15.1 min (minor).

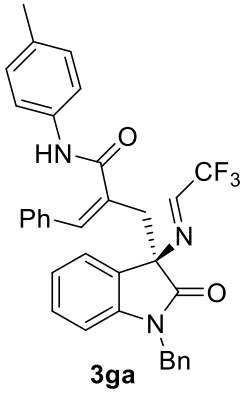
(*Z*)-2-(((*R*)-1-benzyl-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-3-phenyl-*N*-(m-tolyl)acrylamide (3fa)



3fa

The title compound **3fa** was prepared according to the general procedure as described above in 90% yield (51.0 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford yellow solid. mp = 120 – 122 °C. $[\alpha]_D^{25}$ = – 40 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 – 7.77 (m, 1H), 7.53 (d, *J* = 5.2 Hz, 1H), 7.29 (d, *J* = 5.1 Hz, 7H), 7.25 (d, *J* = 4.8 Hz, 3H), 7.22 (d, *J* = 3.5 Hz, 2H), 7.16 (d, *J* = 3.8 Hz, 3H), 7.10 (t, *J* = 7.7 Hz, 1H), 6.95 (t, *J* = 7.5 Hz, 1H), 6.90 (t, *J* = 3.4 Hz, 1H), 6.69 (d, *J* = 7.9 Hz, 1H), 4.98 (d, *J* = 15.5 Hz, 1H), 4.64 (d, *J* = 15.5 Hz, 1H), 3.53 (s, 2H), 2.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 166.6, 149.5 (q, *J* = 39.0, 38.5 Hz), 140.6, 136.2, 134.4, 134.3, 133.8, 132.8, 132.1, 128.8, 128.2, 127.9, 127.8, 127.5, 127.2, 127.0, 126.4, 124.8, 122.4, 119.1, 117.8 (q, *J* = 275.9 Hz), 108.5, 70.5, 42.9, 34.7, 19.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.36. IR (film) ν_{max} 3853, 3751, 3054, 1717, 1507, 1420, 1264, 896, 731, 703, 457 cm^{-1}; HRMS (ESI): m/z for $C_{34}H_{28}F_3N_3NaO_2^+$ $[M+Na]^+$ calcd.: 590.2025, found: 590.2020. HPLC analysis: **3fa**, 95% ee (IA, hexane : isopropanol =75 : 25, 1 mL/min, UV: 254 nm), t_R =9.0 min (major), 12.7 min (minor).

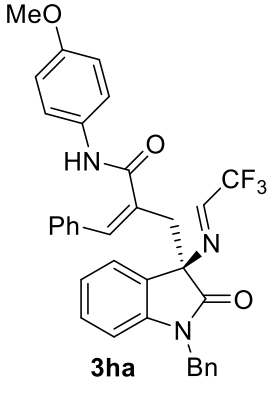
(*Z*)-2-(((*R*)-1-benzyl-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-3-phenyl-*N*-(p-tolyl)acrylamide (3ga)



3ga

The title compound **3ga** was prepared according to the general procedure as described above in 91% yield (51.6 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford yellow solid. mp = 121 – 123 °C. [α] $^{25}_{D}$ = – 80 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (q, *J* = 3.2 Hz, 1H), 7.50 (s, 1H), 7.24 – 7.17 (m, 6H), 7.14 (ddt, *J* = 15.0, 6.1, 3.5 Hz, 8H), 7.05 – 6.97 (m, 3H), 6.87 (t, *J* = 7.5 Hz, 1H), 6.61 (d, *J* = 7.9 Hz, 1H), 4.87 (d, *J* = 15.5 Hz, 1H), 4.56 (d, *J* = 15.5 Hz, 1H), 3.44 (s, 2H), 2.22 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.8, 167.7, 150.6 (q, *J* = 39.0, 38.5 Hz), 141.7, 137.3, 135.5, 135.4, 134.9, 133.9, 133.2, 129.8, 129.3, 129.0, 128.9, 128.6, 128.3, 128.1, 127.5, 125.9, 123.5, 118.9 (q, *J* = 275.3 Hz), 109.6, 71.6, 44.0, 35.8, 20.9. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.14. IR (film) ν_{max} 3751, 3649, 2925, 1717, 1654, 1521, 1489, 1362, 1265, 1174, 740, 454 cm^{-1}; HRMS (ESI): m/z for $C_{34}H_{28}F_3N_3NaO_2^+$ $[M+Na]^+$ calcd.: 590.2025, found: 590.2020. HPLC analysis: **3ga**, 90% ee (IA, hexane : isopropanol =85 : 15, 1 mL/min, UV: 254 nm), t_R =9.3 min (minor), 10.5 min (major).

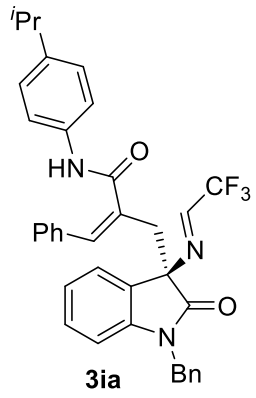
(*Z*)-2-(((*R*)-1-benzyl-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-*N*-(4-methoxyphenyl)-3-phenylacrylamide (3ha)



3ha

The title compound **3ha** was prepared according to the general procedure as described above in 95% yield (55.4 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc=5:1) to afford yellow solid. mp = 88 – 90 °C. [α] $^{25}_{D}$ = – 32 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (q, *J* = 3.1 Hz, 1H), 7.43 (s, 1H), 7.25 – 7.18 (m, 6H), 7.20 – 7.15 (m, 5H), 7.13 (dd, *J* = 6.7, 3.0 Hz, 2H), 7.05 (t, *J* = 7.1 Hz, 1H), 6.89 (t, *J* = 7.5 Hz, 1H), 6.75 (d, *J* = 9.0 Hz, 2H), 6.63 (d, *J* = 7.8 Hz, 1H), 4.91 (d, *J* = 15.5 Hz, 1H), 4.57 (d, *J* = 15.5 Hz, 1H), 3.72 (s, 3H), 3.45 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 166.5, 155.4, 149.6 (q, *J* = 39.4, 38.9 Hz), 140.7, 136.4, 134.4, 133.9, 132.0, 130.0, 128.8, 128.0, 127.8, 127.5, 127.2, 127.0, 126.5, 124.9, 122.4, 120.8, 117.9 (q, *J* = 282.2 Hz), 112.9, 108.5, 70.5, 54.4, 43.0, 34.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.13. IR (film) ν_{max} 3853, 3735, 3649, 1717, 1653, 1559, 1508, 1457, 1264, 896, 748, 431 cm^{-1}; HRMS (ESI): m/z for $C_{34}H_{28}F_3N_3NaO_3^+$ $[M+Na]^+$calcd.: 606.1974, found: 606.1971. HPLC analysis: **3ha**, 93% ee (IA, hexane : isopropanol =80 : 20, 1 mL/min, UV: 254 nm), t_R =29.2 min (major), 35.0 min (minor).

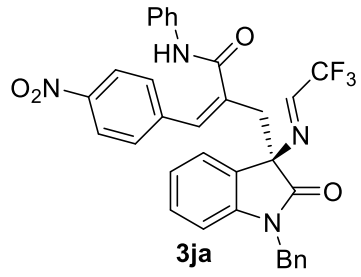
(*Z*)-2-(((*R*)-1-benzyl-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-*N*-(4-isopropylphenyl)-3-phenylacrylamide (3ia)



3ia

The title compound **3ia** was prepared according to the general procedure as described above in 68% yield (40.4 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford yellow solid. mp = 85 – 87 °C. $[\alpha]^{25}_{D}$ = – 48 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (q, *J* = 3.2 Hz, 1H), 7.46 (s, 1H), 7.21 (d, *J* = 6.6 Hz, 7H), 7.19 – 7.17 (m, 3H), 7.17 – 7.14 (m, 3H), 7.07 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 7.7 Hz, 1H), 6.89 (t, *J* = 7.5 Hz, 1H), 6.62 (d, *J* = 7.8 Hz, 1H), 4.88 (d, *J* = 15.5 Hz, 1H), 4.58 (d, *J* = 15.5 Hz, 1H), 3.45 (s, 2H), 2.80 (p, *J* = 6.9 Hz, 1H), 1.16 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.7, 167.6, 150.6 (q, *J* = 38.6 Hz), 145.0, 141.7, 137.4, 135.6, 135.5, 134.9, 133.2, 129.8, 129.0, 128.94, 128.86, 128.6, 128.3, 128.1, 127.6, 127.5, 127.4, 126.8, 126.6, 126.0, 123.4, 120.2, 118.8 (q, *J* = 282.2 Hz), 109.6, 71.5, 44.0, 35.8, 33.6, 24.0. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.13. IR (film) ν_{max} 3853, 3649, 2926, 1717, 1654, 1517, 1489, 1363, 1265, 739, 515, 451 cm^{-1}; HRMS (ESI): m/z for $C_{36}H_{32}F_3N_3NaO_2^+$ $[M+Na]^+$ calcd.: 618.2338, found: 618.2332. HPLC analysis: **3ia**, 95% ee (IA, hexane : isopropanol =90 : 10, 1 mL/min, UV: 254 nm), t_R =28.3 min (major), 34.2 min (minor).

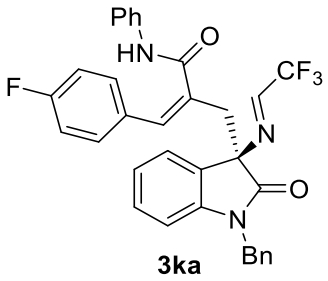
(*Z*)-2-(((*R*)-1-benzyl-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-3-(4-nitrophenyl)-*N*-phenylacrylamide (3ja)



3ja

The title compound **3ja** was prepared according to the general procedure as described above in 72% yield (43.1 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 6:1) to afford yellow solid. mp = 118 – 120 °C. $[\alpha]^{25}_{D}$ = – 24 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.4 Hz, 2H), 7.69 (s, 1H), 7.62 (q, *J* = 3.2 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.7 Hz, 7H), 7.18 (q, *J* = 5.8, 4.8 Hz, 3H), 7.09 (t, *J* = 7.8 Hz, 1H), 7.04 (t, *J* = 7.3 Hz, 1H), 6.92 (t, *J* = 7.6 Hz, 1H), 6.70 (d, *J* = 7.8 Hz, 1H), 4.97 (d, *J* = 15.4 Hz, 1H), 4.54 (d, *J* = 15.4 Hz, 1H), 3.36 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.4, 167.1, 150.9 (q, *J* = 38.6 Hz), 147.2, 141.62, 141.57, 137.6, 136.3, 135.3, 134.9, 130.2, 129.6, 129.3, 129.2, 129.11, 129.08, 129.0, 128.8, 128.6, 128.3, 127.6, 127.51, 127.48, 127.2, 125.7, 124.6, 123.9, 123.73, 123.66, 120.2, 119.4, 118.7 (q, *J* = 275.8 Hz), 109.9, 71.6, 44.0, 36.0. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.11. IR (film) ν_{max} 3853, 3649, 3055, 1717, 1540, 1457, 1347, 1264, 1176, 896, 731, 458 cm^{-1}; HRMS (ESI): m/z for $C_{33}H_{25}F_3N_4NaO_4^+$ $[M+Na]^+$ calcd.: 621.1720, found: 621.1718. HPLC analysis: **3ja**, 82% ee (IA, hexane : isopropanol =75 : 25, 1 mL/min, UV: 254 nm), t_R =19.5 min (minor), 26.0 min (major).

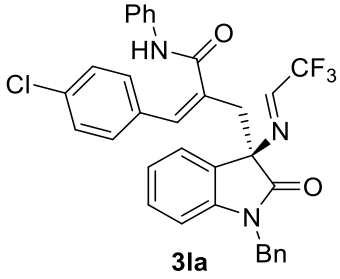
(*Z*)-2-(((*R*)-1-benzyl-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-3-(4-fluorophenyl)-*N*-phenylacrylamide (3ka)



3ka

The title compound **3ka** was prepared according to the general procedure as described above in 91% yield (52.0 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford yellow solid. mp = 120 – 122 °C. [α] $^{25}_{D}$ = – 32 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (q, *J* = 3.1 Hz, 1H), 7.36 (s, 1H), 7.23 (dd, *J* = 7.4, 2.4 Hz, 5H), 7.21 – 7.13 (m, 8H), 7.05 – 6.98 (m, 3H), 6.98 (d, *J* = 10.2 Hz, 1H), 6.86 (t, *J* = 7.5 Hz, 1H), 6.60 (d, *J* = 7.8 Hz, 1H), 4.95 – 4.81 (m, 1H), 4.58 (d, *J* = 15.5 Hz, 1H), 3.44 (d, *J* = 2.2 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.6, 167.4, 160.3 (d, *J* = 248.6 Hz), 150.7 (q, *J* = 38.6 Hz), 141.9, 137.8, 135.61, 135.57, 130.44, 130.37, 130.21, 130.18, 129.9, 129.84, 129.81, 129.2, 128.8, 128.2, 127.6, 127.3, 125.9, 124.4, 124.3, 124.3, 123.6, 122.8 (d, *J* = 14.6 Hz), 120.2, 119.0 (d, *J* = 276.4 Hz), 115.8 (d, *J* = 21.5 Hz), 109.7, 71.6, 44.1, 35.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.24, –113.03. IR (film) ν_{max} 3853, 3649, 3055, 1717, 1522, 1457, 1264, 1176, 896, 731, 450 cm^{-1}; HRMS (ESI): m/z for $C_{33}H_{25}F_4N_3NaO_2^+$ $[M+Na]^+$ calcd.: 594.1775, found: 594.1771. HPLC analysis: **3ka**, 92% ee (IA, hexane : isopropanol =90 : 10, 1 mL/min, UV: 254 nm), t_R =27.5 min (major), 41.3 min (minor).

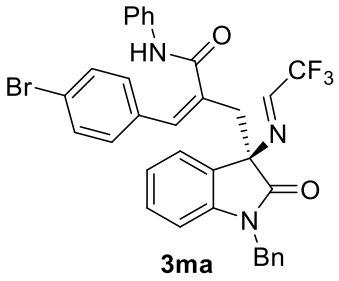
(*Z*)-2-(((*R*)-1-benzyl-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-3-(4-chlorophenyl)-*N*-phenylacrylamide (3la)



3la

The title compound **3la** was prepared according to the general procedure as described above in 89% yield (52.2 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford yellow solid. mp = 140 – 142 °C. [α] $^{25}_{D}$ = – 16 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (q, *J* = 3.1 Hz, 1H), 7.63 (s, 1H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.31 (dd, *J* = 5.0, 1.9 Hz, 3H), 7.30 – 7.27 (m, 2H), 7.25 (d, *J* = 3.2 Hz, 2H), 7.24 – 7.21 (m, 4H), 7.17 – 7.06 (m, 4H), 6.97 (t, *J* = 7.6 Hz, 1H), 6.72 (d, *J* = 7.8 Hz, 1H), 5.03 (d, *J* = 15.5 Hz, 1H), 4.61 (d, *J* = 15.5 Hz, 1H), 3.47 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.6, 167.6, 150.7 (q, *J* = 38.9 Hz), 141.7, 137.8, 136.1, 135.4, 134.3, 133.8, 133.3, 130.2, 120.0, 129.1, 128.81, 128.77, 128.2, 127.5, 127.4, 125.8, 124.4, 123.5, 120.1, 118.8 (q, *J* = 275.8 Hz), 109.7, 71.6, 44.0, 35.9. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.11. IR (film) ν_{max} 3853, 3751, 3649, 2988, 1717, 1541, 1457, 1264, 896, 731, 457 cm^{-1}. HRMS (ESI): m/z for $C_{33}H_{25}ClF_3N_3NaO_2^+$ $[M+Na]^+$ calcd.: 610.1479, found: 610.1473. HPLC analysis: **3la**, 90% ee (IA, hexane : isopropanol =90 : 10, 1 mL/min, UV: 254 nm), t_R =28.3 min (major), 33.9 min (minor).

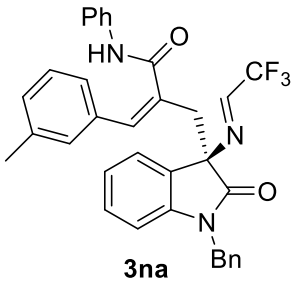
(Z)-2-(((R)-1-benzyl-2-oxo-3-(((E)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-3-(4-bromophenyl)-N-phenylacrylamide (3ma)



3ma

The title compound **3ma** was prepared according to the general procedure as described above in 78% yield (49.2 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford yellow solid. mp = 178 – 180 °C. $[\alpha]^{25}_{D}$ = – 40 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) 7.75 (q, *J* = 3.1 Hz, 1H), 7.64 (s, 1H), 7.37 (dd, *J* = 12.0, 7.9 Hz, 4H), 7.34 – 7.29 (m, 3H), 7.31 – 7.24 (m, 3H), 7.24 – 7.20 (m, 3H), 7.12 (dd, *J* = 16.7, 7.6 Hz, 2H), 7.07 (d, *J* = 8.3 Hz, 2H), 6.97 (t, *J* = 7.5 Hz, 1H), 6.73 (d, *J* = 7.9 Hz, 1H), 5.03 (d, *J* = 15.5 Hz, 1H), 4.61 (d, *J* = 15.5 Hz, 1H), 3.46 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.6, 167.6, 150.7 (q, *J* = 38.6 Hz). 141.7, 137.8, 136.1, 135.4, 133.9, 133.7, 131.8, 130.4, 130.1, 130.0, 129.08, 129.07, 129.0, 128.9, 128.8, 128.2, 127.5, 127.4, 125.8, 124.4, 123.5, 122.6, 120.1, 118.8 (q, *J* = 275.8, 275.4 Hz). 109.7, 71.6, 44.0, 35.9. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.12. IR (film) ν_{max} 3853, 3649, 3054, 2987, 2306, 1717, 1541, 1421, 1264, 896, 703, 457 cm^{-1}. HRMS (ESI): m/z for $C_{33}H_{25}BrF_3N_3NaO_2^+$ $[M+Na]^+$ calcd.: 654.0974, found: 654.0970. HPLC analysis: **3ma**, 90% ee (IA, hexane : isopropanol =90 : 10, 1 mL/min, UV: 254 nm), t_R =30.5 min (major), 36.1 min (minor).

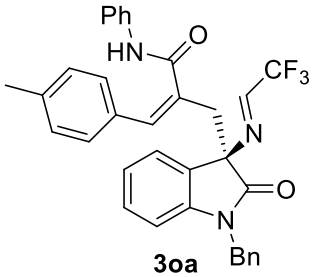
(*Z*)-2-(((*R*)-1-benzyl-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-*N*-phenyl-3-(*m*-tolyl)acrylamide (3na)



3na

The title compound **3na** was prepared according to the general procedure as described above in 87% yield (49.3 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford yellow solid. mp = 120 – 122 °C. $[\alpha]^{25}_{D}$ = – 80 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (q, *J* = 3.2 Hz, 1H), 7.61 (s, 1H), 7.38 (d, *J* = 7.2 Hz, 2H), 7.29 (td, *J* = 7.8, 7.1, 3.0 Hz, 6H), 7.26 – 7.20 (m, 3H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.10 (q, *J* = 8.2, 7.3 Hz, 2H), 7.03 (d, *J* = 7.7 Hz, 1H), 7.00 – 6.93 (m, 2H), 6.70 (d, *J* = 7.8 Hz, 1H), 4.96 (d, *J* = 15.6 Hz, 1H), 4.67 (d, *J* = 15.5 Hz, 1H), 3.52 (d, *J* = 2.8 Hz, 2H), 2.26 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.8, 167.8, 150.8 (q, *J* = 39.1 Hz), 141.7, 138.2, 138.0, 137.7, 135.4, 134.8, 132.9, 129.8, 129.5, 129.1, 129.0, 128.93, 128.89, 128.7, 128.5, 128.1, 127.7, 127.5, 127.3, 125.9, 124.2, 123.4, 120.1, 118.9 (q, *J* = 276.4 Hz), 109.6, 71.5, 44.0, 36.0, 21.4. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.12. IR (film) ν_{max} 3853, 3751, 3649, 3055, 1717, 1541, 1420, 1264, 896, 731, 425 cm^{-1}; HRMS (ESI): m/z for $C_{34}H_{28}F_3N_3NaO_2^+$ $[M+Na]^+$ calcd.: 590.2025, found: 590.2023. HPLC analysis: **3na**, 98% ee (IA, hexane : isopropanol =90 : 10, 1 mL/min, UV: 254 nm), t_R =25.4 min (major), 33.4 min (minor).

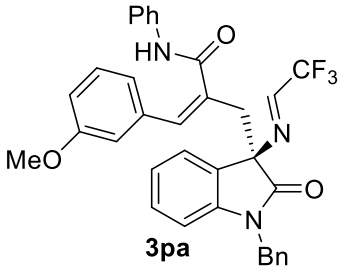
(*Z*)-2-(((*R*)-1-benzyl-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-*N*-phenyl-3-(*p*-tolyl)acrylamide (3oa)



3oa

The title compound **3oa** was prepared according to the general procedure as described above in 92% yield (52.2 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford yellow solid. mp = 128 – 130 °C. $[\alpha]_D^{25}$ = – 16 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (q, *J* = 3.2 Hz, 1H), 7.47 (s, 1H), 7.33 – 7.28 (m, 6H), 7.27 (d, *J* = 2.7 Hz, 3H), 7.25 (d, *J* = 4.3 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.13 – 7.06 (m, 4H), 6.95 (t, *J* = 7.4 Hz, 1H), 6.70 (d, *J* = 7.8 Hz, 1H), 5.00 (d, *J* = 15.5 Hz, 1H), 4.63 (d, *J* = 15.5 Hz, 1H), 3.55 (s, 2H), 2.35 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.8, 167.9, 150.6 (q, *J* = 39.0 Hz), 141.7, 138.4, 137.9, 137.4, 135.5, 132.3, 131.8, 129.8, 129.3, 128.99, 128.95, 128.7, 128.1, 127.60, 127.55, 126.0, 124.2, 123.4, 120.0, 118.9 (d, *J* = 274.26 Hz), 109.5, 71.6, 44.0, 35.9, 21.3. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.13. IR (film) ν_{max} 3853, 3751, 3649, 1717, 1541, 1507, 1457, 1263, 749, 448 cm^{-1}. HRMS (ESI): m/z for $C_{34}H_{28}F_3N_3NaO_2^+$ $[M+Na]^+$ calcd.: 590.2025, found: 590.2023. HPLC analysis: **3oa**, 98% ee (IA, hexane : isopropanol =75 : 25, 1 mL/min, UV: 254 nm), t_R =10.4 min (major), 15.3 min (minor).

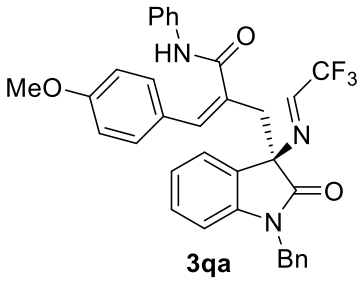
(*Z*)-2-(((*R*)-1-benzyl-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-3-(3-methoxyphenyl)-*N*-phenylacrylamide (3pa)



3pa

The title compound **3pa** was prepared according to the general procedure as described above in 93% yield (54.2 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 6:1) to afford yellow solid. mp = 124 – 126 °C. $[\alpha]_D^{25}$ = – 64 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (q, *J* = 3.1 Hz, 1H), 7.52 (s, 1H), 7.31 – 7.27 (m, 7H), 7.26 – 7.22 (m, 5H), 7.20 (dd, *J* = 6.7, 3.1 Hz, 2H), 7.12 (td, *J* = 7.8, 1.3 Hz, 1H), 6.96 (td, *J* = 7.6, 1.0 Hz, 1H), 6.82 (d, *J* = 9.1 Hz, 2H), 6.70 (d, *J* = 7.8 Hz, 1H), 4.98 (d, *J* = 15.5 Hz, 1H), 4.65 (d, *J* = 15.5 Hz, 1H), 3.79 (s, 3H), 3.52 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.7, 167.8, 159.7, 150.6 (q, *J* = 39.3 Hz), 141.7, 137.9, 137.2, 136.2, 135.5, 133.4, 129.8, 129.6, 129.0, 128.7, 128.1, 127.54, 127.51, 125.9, 124.2, 123.5, 121.3, 120.0, 118.9 (q, *J* = 275.94 Hz), 114.4, 114.1, 109.6, 71.6, 55.3, 44.0, 36.0. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.17. IR (film) ν_{max} 3853, 3751, 3649, 1717, 1653, 1541, 1507, 1489, 1457, 1263, 749, 457 cm^{-1}; HRMS (ESI): m/z for $C_{34}H_{28}F_3N_3NaO_3^+$ $[M+Na]^+$ calcd.: 606.1974, found: 606.1970. HPLC analysis: **3pa**, 97% ee (IA, hexane : isopropanol =85 : 15, 1 mL/min, UV: 254 nm), t_R =17.2 min (major), 26.6 min (minor).

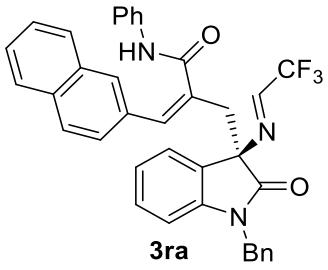
(*Z*)-2-(((*R*)-1-benzyl-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-3-(4-methoxyphenyl)-*N*-phenylacrylamide (3qa)



3qa

The title compound **3qa** was prepared according to the general procedure as described above in 72% yield (41.9 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 6:1) to afford yellow solid. mp = 118 – 120 °C. [α] $^{25}_{D}$ = – 80 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (q, *J* = 3.2 Hz, 1H), 7.35 (s, 1H), 7.23 (d, *J* = 7.1 Hz, 5H), 7.21 – 7.17 (m, 7H), 7.14 (s, 1H), 7.05 – 6.96 (m, 2H), 6.87 (t, *J* = 7.6 Hz, 1H), 6.75 (d, *J* = 8.7 Hz, 2H), 6.63 (d, *J* = 7.7 Hz, 1H), 4.96 (d, *J* = 15.5 Hz, 1H), 4.54 (d, *J* = 15.5 Hz, 1H), 3.74 (s, 3H), 3.49 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.8, 168.2, 159.8, 150.6 (q, *J* = 38.9 Hz), 141.7, 138.0, 137.1, 135.6, 131.1, 130.7, 129.8, 129.0, 128.7, 128.1, 127.7, 127.5, 127.2, 126.0, 124.1, 123.4, 120.5, 119.3, 118.7 (q, *J* = 261.96 Hz), 109.6, 71.6, 55.3, 44.0, 36.0. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.14. IR (film) ν_{max} 3853, 3751, 3649, 1717, 1653, 1541, 1489, 1457, 1263, 749, 703, 425 cm^{-1}; HRMS (ESI): m/z for $C_{34}H_{28}F_3N_3NaO_3^+$ $[M+Na]^+$ calcd.: 606.1974, found: 606.1970. HPLC analysis: **3qa**, 97% ee (IA, hexane : isopropanol =85 : 15, 1 mL/min, UV: 254 nm), t_R =19.6 min (major), 29.7 min (minor).

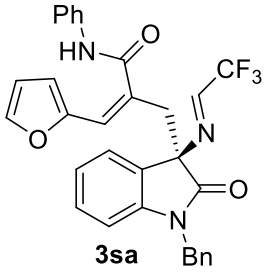
(*Z*)-2-(((*R*)-1-benzyl-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-3-(naphthalen-2-yl)-*N*-phenylacrylamide (3ra)



3ra

The title compound **3ra** was prepared according to the general procedure as described above in 97% yield (58.4 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford yellow solid. mp = 140 – 142 °C. [α] $^{25}_{D}$ = – 72 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 – 7.78 (m, 2H), 7.74 (d, *J* = 8.5 Hz, 1H), 7.70 – 7.63 (m, 3H), 7.53 – 7.44 (m, 3H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.31 (q, *J* = 6.7, 5.3 Hz, 4H), 7.20 (d, *J* = 5.6 Hz, 5H), 7.11 (q, *J* = 7.4 Hz, 2H), 6.94 (t, *J* = 7.5 Hz, 1H), 6.72 (d, *J* = 7.9 Hz, 1H), 4.97 (d, *J* = 15.5 Hz, 1H), 4.64 (d, *J* = 15.5 Hz, 1H), 3.60 (q, *J* = 3.0 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.8, 167.9, 150.8 (q, *J* = 39.3 Hz), 141.7, 138.0, 137.5, 135.4, 133.3, 133.1, 132.9, 132.3, 129.9, 129.0, 128.8, 128.4, 128.3, 128.2, 128.0, 127.7, 127.4, 126.7, 126.49, 126.47, 125.9, 124.3, 123.5, 120.1, 118.9 (q, *J* = 276.3 Hz), 109.7, 71.6, 44.0, 36.2. ^{19}F NMR (471 MHz, $CDCl_3$) δ –70.96. IR (film) ν_{max} 3853, 3751, 3676, 1717, 1653, 1559, 1541, 1507, 1457, 1275, 749, 452 cm^{-1}; HRMS (ESI): m/z for $C_{37}H_{28}F_3N_3NaO_2^+$ $[M+Na]^+$ calcd.: 626.2025, found: 626.2020. HPLC analysis: **3ra**, 94% ee (IA, hexane : isopropanol =85 : 15, 1 mL/min, UV: 254 nm), t_R =19.4 min (major), 26.2 min (minor).

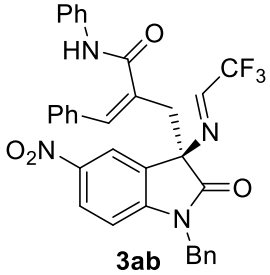
(*Z*)-2-(((*R*)-1-benzyl-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-3-(furan-2-yl)-*N*-phenylacrylamide (3sa)



3sa

The title compound **3sa** was prepared according to the general procedure as described above in 80% yield (43.4 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 5:1) to afford yellow solid. mp = 96 – 98 °C. $[\alpha]^{25}_{D}$ = – 64 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.76 (q, *J* = 3.2 Hz, 1H), 7.52 (d, *J* = 7.3 Hz, 2H), 7.37 – 7.32 (m, 4H), 7.31 (d, *J* = 6.0 Hz, 2H), 7.22 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.14 – 7.05 (m, 2H), 6.87 – 6.81 (m, 2H), 6.75 (d, *J* = 7.9 Hz, 1H), 6.47 (d, *J* = 3.5 Hz, 1H), 6.25 (dd, *J* = 3.5, 1.8 Hz, 1H), 5.11 (d, *J* = 15.4 Hz, 1H), 4.65 (d, *J* = 15.4 Hz, 1H), 3.85 (d, *J* = 14.5 Hz, 1H), 3.72 (d, *J* = 14.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.0, 167.0, 151.4 (q, *J* = 38.8 Hz), 151.1, 144.2, 141.8, 138.2, 135.6, 129.8, 129.03, 128.98, 128.8, 128.1, 127.7, 127.5, 126.4, 126.3, 125.5, 124.3, 123.0, 120.4, 120.2, 116.2, 111.6, 109.4, 72.0, 44.0, 36.4. ^{19}F NMR (471 MHz, $CDCl_3$) δ –70.97. IR (film) ν_{max} 3853, 3751, 3649, 1717, 1653, 1541, 1457, 1275, 896, 764, 703, 416 cm^{-1}; HRMS (ESI): m/z for $C_{31}H_{24}F_3N_3NaO_3^+$ $[M+Na]^+$ calcd.: 566.1661, found: 566.1660. HPLC analysis: **3sa**, 94% ee (OD-H, hexane : isopropanol =75 : 25, 1 mL/min, UV: 254 nm), t_R =15.0 min (major), 21.1 min (minor).

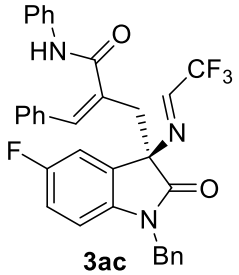
(*Z*)-2-(((*R*)-1-benzyl-5-nitro-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-*N*,3-diphenylacrylamide (3ab)



3ab

The title compound **3ab** was prepared according to the general procedure as described above in 70% yield (41.8 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 6:1) to afford yellow solid. mp = 94 – 96 °C. $[\alpha]^{25}_{D}$ = – 40 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 2.3 Hz, 1H), 7.93 – 7.84 (m, 2H), 7.48 – 7.42 (m, 1H), 7.28 – 7.19 (m, 7H), 7.19 (d, *J* = 1.5 Hz, 2H), 7.16 (td, *J* = 4.2, 2.0 Hz, 5H), 7.00 (t, *J* = 7.4 Hz, 1H), 6.62 (d, *J* = 8.7 Hz, 1H), 4.88 (d, *J* = 15.7 Hz, 1H), 4.65 (d, *J* = 15.7 Hz, 1H), 3.63 – 3.38 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.5, 167.2, 151.0 (q, *J* = 38.6 Hz), 147.3, 141.71, 141.66, 137.7, 136.4, 135.4, 134.9, 130.3, 129.7, 129.4, 129.3, 129.2, 129.1, 129.0, 128.9, 128.7, 128.4, 127.60, 127.57, 127.3, 125.8, 124.7, 124.0, 123.8, 123.7, 122.1, 118.4 (q, *J* = 275.8 Hz), 110.0, 71.7, 44.1, 36.0. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.12. IR (film) ν_{max} 3649, 3054, 1717, 1684, 1653, 1541, 1457, 1339, 1264, 896, 731, 425 cm^{-1}; HRMS (ESI): m/z for $C_{33}H_{25}F_3N_4NaO_4^+$ $[M+Na]^+$ calcd.: 621.1720, found: 621.1721. HPLC analysis: **3ab**, 95% ee (IA, hexane : isopropanol =80 : 20, 1 mL/min, UV: 254 nm), t_R =22.8 min (minor), 24.8 min (major).

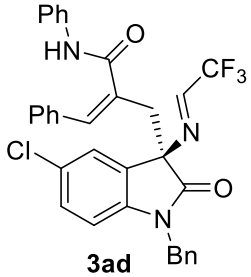
(*Z*)-2-(((*R*)-1-benzyl-5-fluoro-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-*N*,3-diphenylacrylamide (3ac)



3ac

The title compound **3ac** was prepared according to the general procedure as described above in 85% yield (48.5 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford yellow solid. mp = 100 – 102 °C. [α] $^{25}_{D}$ = – 40 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (q, *J* = 3.1 Hz, 1H), 7.54 (s, 1H), 7.41 (d, *J* = 7.9 Hz, 2H), 7.38 – 7.31 (m, 4H), 7.34 – 7.27 (m, 6H), 7.20 (ddd, *J* = 10.5, 7.9, 2.8 Hz, 3H), 7.13 – 7.08 (m, 1H), 6.52 (d, *J* = 8.3 Hz, 1H), 4.90 (d, *J* = 15.6 Hz, 1H), 4.65 (d, *J* = 15.6 Hz, 1H), 3.54 (q, *J* = 2.9 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.6, 167.5, 159.3 (d, *J* = 243.1 Hz), 151.1 (q, *J* = 39.1 Hz), 137.8, 137.5, 135.1, 134.7, 132.8, 129.2, 128.8, 128.7, 128.5, 128.2, 127.5, 124.4, 119.9, 116.2 (d, *J* = 23.7 Hz), 114.0 (d, *J* = 25.0 Hz), 112.4 (d, *J* = 42.9 Hz), 110.2 (d, *J* = 7.9 Hz), 71.4, 44.2, 35.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.32, –118.50. IR (film) ν_{max} 3735, 3649, 2924, 1717, 1507, 1489, 1265, 1175, 749, 502, 425 cm^{-1}; HRMS (ESI): m/z for $C_{33}H_{25}F_4N_3NaO_2^+$ $[M+Na]^+$ calcd.: 594.1775, found: 594.1773. HPLC analysis: **3ac**, 94% ee (AS-H, hexane : isopropanol =80 : 20, 1 mL/min, UV: 254 nm), t_R =10.2 min (major), 14.7 min (minor).

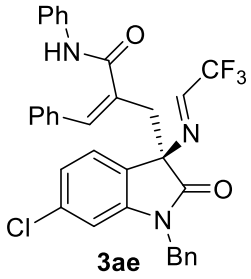
(*Z*)-2-(((*R*)-1-benzyl-5-chloro-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-*N*,3-diphenylacrylamide (3ad)



3ad

The title compound **3ad** was prepared according to the general procedure as described above in 83% yield (48.7 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford yellow solid. mp = 108 – 110 °C. [α] $^{25}_{D}$ = – 48 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.46 (s, 1H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.27 – 7.16 (m, 11H), 7.11 (d, *J* = 7.1 Hz, 3H), 7.01 (t, *J* = 7.5 Hz, 1H), 6.93 (d, *J* = 8.7 Hz, 1H), 6.47 (d, *J* = 8.3 Hz, 1H), 4.82 (d, *J* = 15.6 Hz, 1H), 4.55 (d, *J* = 15.6 Hz, 1H), 3.46 (q, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.3, 166.4, 150.0 (q, *J* = 39.1 Hz), 139.1, 136.8, 136.4, 134.0, 133.6, 131.7, 128.7, 128.3, 128.0, 127.9, 127.84, 127.76, 127.7, 127.5, 127.4, 127.2, 126.4, 125.2, 123.3, 118.9, 117.74 (q, *J* = 275.8 Hz), 109.5, 70.2, 43.1, 34.7. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.23. IR (film) ν_{max} 3735, 3649, 1717, 1653, 1559, 1541, 1457, 1263, 749, 421 cm^{-1}; HRMS (ESI): m/z for $C_{33}H_{25}ClF_3N_3NaO_2^+$ $[M+Na]^+$ calcd.: 610.1479, found: 610.1474. HPLC analysis: **3ad**, 97% ee (OX-H, hexane : isopropanol =95 : 5, 1 mL/min, UV: 254 nm), t_R =31.5 min (major), 37.6 min (minor).

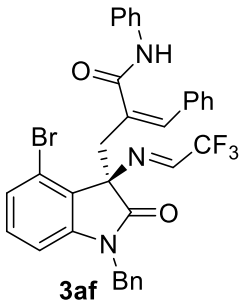
(*Z*)-2-(((*R*)-1-benzyl-6-chloro-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-*N*,3-diphenylacrylamide (3ae)



3ae

The title compound **3ae** was prepared according to the general procedure as described above in 84% yield (49.3 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford yellow solid. mp = 90 – 92 °C. $[\alpha]_D^{25}$ = – 168 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (q, *J* = 3.1 Hz, 1H), 7.40 (s, 1H), 7.35 – 7.29 (m, 5H), 7.29 – 7.26 (m, 6H), 7.24 (dd, *J* = 7.1, 3.3 Hz, 4H), 7.16 (d, *J* = 8.0 Hz, 1H), 7.08 (tt, *J* = 5.3, 3.5 Hz, 1H), 6.89 (dd, *J* = 8.0, 1.8 Hz, 1H), 6.65 (d, *J* = 1.8 Hz, 1H), 4.94 (d, *J* = 15.6 Hz, 1H), 4.58 (d, *J* = 15.5 Hz, 1H), 3.53 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.8, 167.8, 150.8 (q, *J* = 39.0 Hz), 142.9, 137.7, 137.2, 135.9, 135.0, 134.6, 132.9, 129.2, 128.88, 128.85, 128.7, 128.5, 128.4, 127.6, 127.0, 125.9, 124.4, 123.4, 118.8 (q, *J* = 275.8 Hz), 115.5, 110.1, 71.0, 44.1, 35.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.21. IR (film) ν_{max} 3649, 3055, 1717, 1670, 1522, 1489, 1264, 1175, 1076, 735, 702, 425 cm^{-1}; HRMS (ESI): m/z for $C_{33}H_{25}ClF_3N_3NaO_2^+$ $[M+Na]^+$ calcd.: 610.1479, found: 610.1474. HPLC analysis: **3ae**, 93% ee (IA, hexane : isopropanol =80 : 20, 1 mL/min, UV: 254 nm), t_R =6.2 min (major), 8.4 min (minor).

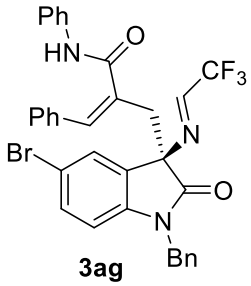
(*Z*)-2-(((*R*)-1-benzyl-4-bromo-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-*N*,3-diphenylacrylamide (3af)



3af

The title compound **3af** was prepared according to the general procedure as described above in 75% yield (47.3 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford yellow solid. mp = 127 – 129 °C. $[\alpha]_D^{25}$ = – 32 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (q, *J* = 3.1 Hz, 1H), 7.50 (s, 1H), 7.42 – 7.38 (m, 2H), 7.35 (t, *J* = 5.8 Hz, 2H), 7.33 (d, *J* = 1.8 Hz, 1H), 7.34 – 7.27 (m, 9H), 7.19 (ddd, *J* = 12.4, 7.9, 2.9 Hz, 3H), 7.11 (t, *J* = 7.4 Hz, 1H), 6.52 (d, *J* = 8.4 Hz, 1H), 4.91 (d, *J* = 15.5 Hz, 1H), 4.64 (d, *J* = 15.6 Hz, 1H), 3.61 – 3.47 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.8, 167.9, 150.7 (q, *J* = 38.6 Hz), 141.8, 137.9, 136.7, 135.5, 134.9, 132.9, 130.0, 129.2, 129.1, 128.9, 128.8, 128.7, 128.5, 128.2, 127.6, 127.5, 125.9, 123.6, 121.4, 118.9 (q, *J* = 275.7 Hz), 109.8, 71.7, 44.1, 35.9. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.32. IR (film) ν_{max} 3839, 3750, 3676, 1717, 1653, 1559, 1522, 1507, 1457, 1263, 749, 425 cm^{-1}. HRMS (ESI): m/z for $C_{33}H_{25}BrF_3N_3NaO_2^+$ $[M+Na]^+$ calcd.: 654.0974, found: 654.0968. HPLC analysis: **3af**, 96% ee (IA, hexane : isopropanol =80 : 20, 1 mL/min, UV: 254 nm), t_R =10.0 min (major), 14.1 min (minor).

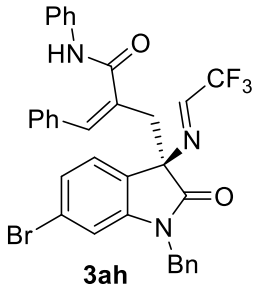
(*Z*)-2-(((*R*)-1-benzyl-5-bromo-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-*N*,3-diphenylacrylamide (3ag)



3ag

The title compound **3ag** was prepared according to the general procedure as described above in 82% yield (51.7 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford yellow solid. mp = 166 – 168 °C. $[\alpha]_D^{25}$ = – 48 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) 7.87 (q, *J* = 3.1 Hz, 1H), 7.50 (s, 1H), 7.40 (d, *J* = 7.5 Hz, 2H), 7.37 – 7.32 (m, 4H), 7.33 – 7.27 (m, 8H), 7.19 (ddd, *J* = 11.9, 7.9, 2.8 Hz, 3H), 7.11 (t, *J* = 7.4 Hz, 1H), 6.52 (d, *J* = 8.4 Hz, 1H), 4.91 (d, *J* = 15.6 Hz, 1H), 4.64 (d, *J* = 15.6 Hz, 1H), 3.58 – 3.49 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.3, 167.5, 151.1 (q, *J* = 38.9 Hz), 140.6, 137.8, 137.5, 134.9, 134.6, 132.7, 132.6, 129.9, 129.6, 129.1, 129.0, 128.93, 128.90, 128.8, 128.7, 128.6, 128.5, 128.3, 128.2, 127.5, 127.3, 124.4, 120.6, 120.0, 118.8 (q, *J* = 275.9 Hz), 116.3, 111.0, 71.2, 44.1, 35.7. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.21. IR (film) ν_{max} 3853, 3750, 3676, 1717, 1653, 1541, 1457, 1263, 749, 425 cm^{-1}. HRMS (ESI): m/z for $C_{33}H_{25}BrF_3N_3NaO_2^+$ $[M+Na]^+$ calcd.: 654.0974, found: 654.0968. HPLC analysis: **3ag**, 96% ee (IA, hexane : isopropanol =80 : 20, 1 mL/min, UV: 254 nm), t_R =13.0 min (minor), 13.9 min (major).

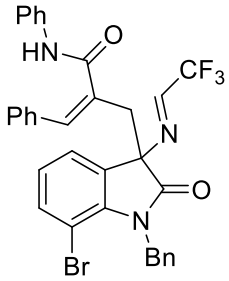
(*Z*)-2-(((*R*)-1-benzyl-6-bromo-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-*N*,3-diphenylacrylamide (3ah)



3ah

The title compound **3ah** was prepared according to the general procedure as described above in 76% yield (48.0 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford yellow solid. mp = 140 – 142 °C. $[\alpha]_D^{25}$ = – 24 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (q, *J* = 3.2 Hz, 1H), 7.36 – 7.31 (m, 7H), 7.31 – 7.28 (m, 4H), 7.26 (d, *J* = 6.6 Hz, 3H), 7.24 (d, *J* = 1.7 Hz, 1H), 7.22 (s, 1H), 7.13 – 7.09 (m, 2H), 7.06 (dd, *J* = 7.9, 1.7 Hz, 1H), 4.94 (d, *J* = 15.5 Hz, 1H), 4.58 (d, *J* = 15.5 Hz, 1H), 3.53 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.6, 167.7, 150.8 (q, *J* = 38.6 Hz), 143.0, 137.6, 137.1, 135.0, 134.6, 132.9, 129.2, 128.9, 128.7, 128.5, 128.4, 127.6, 127.3, 126.4, 126.3, 124.4, 123.8, 120.0, 118.8 (q, *J* = 275.8 Hz), 112.8, 71.1, 44.1, 35.7. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.21. IR (film) ν_{max} 3853, 3649, 2925, 1717, 1654, 1605, 1540, 1489, 1264, 1174, 735, 457 cm^{-1}. HRMS (ESI): m/z for $C_{33}H_{25}BrF_3N_3NaO_2^+$ $[M+Na]^+$ calcd.: 654.0974, found: 654.0968. HPLC analysis: **3ah**, 92% ee (IA, hexane : isopropanol =85 : 15, 1 mL/min, UV: 254 nm), t_R =15.2 min (major), 22.5 min (minor).

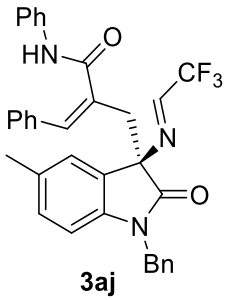
(*Z*)-2-(((*R*)-1-benzyl-7-bromo-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-*N*,3-diphenylacrylamide (3ai)



3ai

The title compound **3ai** was prepared according to the general procedure as described above in 77% yield (48.5 mg). It was purified by flash column chromatography (Petroleum ether: EtOAc = 7:1) to afford yellow solid. mp = 124 – 126 °C. $[\alpha]_D^{25}$ = – 16 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (q, *J* = 3.1 Hz, 1H), 7.53 (s, 1H), 7.33 – 7.28 (m, 2H), 7.28 – 7.23 (m, 2H), 7.23 – 7.21 (m, 2H), 7.22 – 7.17 (m, 5H), 7.18 (s, 2H), 7.15 (dd, *J* = 7.5, 2.1 Hz, 2H), 7.10 (dd, *J* = 7.8, 1.9 Hz, 2H), 7.06 – 6.99 (m, 1H), 6.80 – 6.75 (m, 1H), 5.30 – 5.14 (m, 2H), 3.44 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.6, 166.6, 150.0 (q, *J* = 39.1 Hz), 138.3, 136.7, 136.3, 136.0, 134.6, 133.6, 131.9, 130.0, 127.8, 127.74, 127.68, 127.6, 127.4, 126.5, 125.6, 124.0, 123.7, 123.4, 119.0, 117.7 (q, *J* = 276.4 Hz), 101.8, 69.5, 43.6, 35.1. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.21. IR (film) ν_{max} 3055, 2927, 1716, 1654, 1497, 1339, 1264, 1161, 896, 732, 508, 457 cm^{-1}. HRMS (ESI): m/z for $C_{33}H_{25}BrF_3N_3NaO_2^+$ $[M+Na]^+$ calcd.: 654.0974, found: 654.0968. HPLC analysis: **3ai**, 93% ee (IA, hexane : isopropanol =80 : 20, 1 mL/min, UV: 254 nm), t_R =10.8 min (major), 15.3 min (minor).

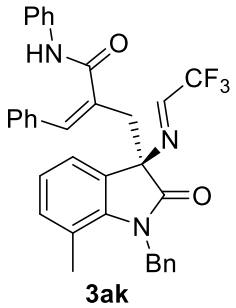
(*Z*)-2-(((*R*)-1-benzyl-5-methyl-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-*N*,3-diphenylacrylamide (3aj)



3aj

The title compound **3aj** was prepared according to the general procedure as described above in 96% yield (54.4 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford orange-yellow solid. mp = 108 – 110 °C. $[\alpha]_D^{25}$ = – 56 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (q, *J* = 3.2 Hz, 1H), 7.51 (s, 1H), 7.30 (d, *J* = 7.3 Hz, 2H), 7.25 – 7.18 (m, 8H), 7.18 (d, *J* = 2.1 Hz, 2H), 7.17 (s, 1H), 7.14 (dd, *J* = 7.3, 2.3 Hz, 2H), 7.00 (t, *J* = 7.4 Hz, 1H), 6.91 (s, 1H), 6.77 (d, *J* = 8.0 Hz, 1H), 6.48 (d, *J* = 8.0 Hz, 1H), 4.85 (d, *J* = 15.5 Hz, 1H), 4.54 (d, *J* = 15.5 Hz, 1H), 3.46 (d, *J* = 2.2 Hz, 2H), 2.05 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.6, 166.8, 150.0, 149.5 (q, *J* = 38.5 Hz), 149.1, 138.2, 137.0, 136.3, 134.5, 133.9, 132.1, 132.0, 129.1, 127.9, 127.8, 127.7, 127.5, 127.2, 127.0, 126.5, 126.3, 125.6, 123.1, 118.8, 117.8 (q, *J* = 275.8 Hz), 108.3, 70.7, 43.0, 34.6, 19.9. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.31. IR (film) ν_{max} 3853, 3676, 2925, 1717, 1653, 1541, 1497, 1339, 1264, 1180, 749, 457 cm^{-1}. HRMS (ESI): m/z for $C_{34}H_{28}F_3N_3NaO_2^+$ $[M+Na]^+$ calcd.: 590.2025, found: 590.2021. HPLC analysis: **3aj**, 93% ee (IC, hexane : isopropanol =95 : 5, 1 mL/min, UV: 254 nm), t_R =19.9 min (minor), 23.8 min (major).

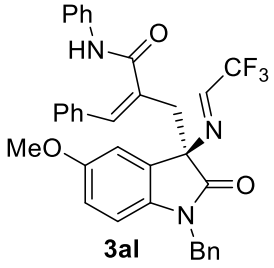
(*Z*)-2-(((*R*)1-benzyl-7-methyl-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-*N*,3-diphenylacrylamide (3ak)



3ak

The title compound **3ak** was prepared according to the general procedure as described above in 99% yield (56.1 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford yellow solid. mp = 92 – 94 °C. $[\alpha]^{25}_{D}$ = – 16 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, *J* = 3.9 Hz, 1H), 7.76 (dd, *J* = 3.2, 1.2 Hz, 1H), 7.46 (d, *J* = 8.3 Hz, 2H), 7.36 (s, 1H), 7.32 – 7.24 (m, 8H), 7.21 (dd, *J* = 7.3, 2.2 Hz, 2H), 7.13 – 7.08 (m, 2H), 7.08 – 7.04 (m, 2H), 6.95 – 6.90 (m, 2H), 5.04 (q, 2H), 3.50 (q, 2H), 2.16 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.8, 167.7, 150.6 (q, *J* = 38.5 Hz), 139.9, 138.1, 137.3, 137.1, 135.0, 133.8, 133.4, 129.0, 128.84, 128.81, 128.59, 128.55, 128.2, 127.5, 125.7, 124.2, 123.6, 123.5, 120.6, 120.0, 118.9 (q, *J* = 275.6 Hz), 70.8, 45.2, 36.2, 18.7. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.34. IR (film) ν_{max} 3853, 3751, 3649, 1717, 1541, 1507, 1457, 1264, 736, 457 cm^{-1}. HRMS (ESI): m/z for $C_{34}H_{28}F_3N_3NaO_2^+$ $[M+Na]^+$ calcd.: 590.2025, found: 590.2021. HPLC analysis: **3ak**, 93% ee (IA, hexane : isopropanol =90 : 10, 1 mL/min, UV: 254 nm), t_R =20.3 min (major), 29.3 min (minor).

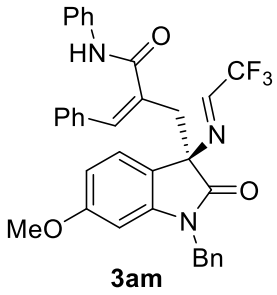
(*Z*)-2-(((*R*)-1-benzyl-5-methoxy-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-*N*,3-diphenylacrylamide (3al)



3al

The title compound **3al** was prepared according to the general procedure as described above in 93% yield (54.2 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford red solid. mp = 152 – 154 °C. $[\alpha]^{25}_{D}$ = – 64 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (q, *J* = 3.2 Hz, 1H), 7.54 (s, 1H), 7.35 (d, *J* = 7.3 Hz, 2H), 7.30 (dd, *J* = 4.9, 2.4 Hz, 4H), 7.29 – 7.23 (m, 5H), 7.22 (dd, *J* = 7.2, 2.3 Hz, 2H), 7.11 – 7.04 (m, 1H), 6.86 (d, *J* = 1.5 Hz, 1H), 6.57 (d, *J* = 1.5 Hz, 2H), 4.95 (d, *J* = 15.5 Hz, 1H), 4.60 (d, *J* = 15.5 Hz, 1H), 3.60 (s, 3H), 3.54 (d, *J* = 7.4 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.4, 168.0, 167.9, 150.8 (q, *J* = 38.7 Hz), 150.3, 138.0, 137.1, 135.6, 134.8, 133.2, 129.0, 128.9, 128.8, 128.73, 128.69, 128.6, 128.5, 128.3, 128.1, 127.5, 127.4, 124.5, 119.9, 118.9 (q, *J* = 275.9 Hz), 114.0, 112.9, 110.1, 71.9, 55.7, 44.1, 35.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.17. IR (film) ν_{max} 3853, 3649, 2926, 1717, 1653, 1541, 1497, 1264, 1178, 896, 732, 457 cm^{-1}. HRMS (ESI): m/z for $C_{34}H_{28}F_3N_3NaO_3^+$ $[M+Na]^+$ calcd.: 606.1974, found: 606.1970. HPLC analysis: **3al**, 92% ee (IA, hexane : isopropanol =80 : 20, 1 mL/min, UV: 254 nm), t_R =14.7 min (minor), 17.0 min (major).

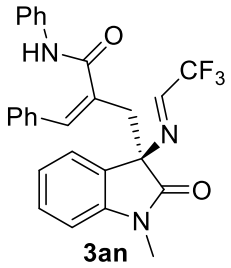
(*Z*)-2-(((*R*)-1-benzyl-6-methoxy-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-*N*,3-diphenylacrylamide (3am)



3am

The title compound **3am** was prepared according to the general procedure as described above in 94% yield (54.8 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford yellow solid. mp = 118 – 120 °C. $[\alpha]^{25}_{D}$ = – 64 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (q, *J* = 3.1 Hz, 1H), 7.50 (s, 1H), 7.32 – 7.23 (m, 12H), 7.22 – 7.17 (m, 2H), 7.12 (t, *J* = 7.1 Hz, 1H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.82 (d, *J* = 9.0 Hz, 2H), 6.70 (d, *J* = 7.8 Hz, 1H), 4.98 (d, *J* = 15.5 Hz, 1H), 4.65 (d, *J* = 15.5 Hz, 1H), 3.80 (s, 3H), 3.52 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.2, 168.0, 161.2, 150.2 (q, *J* = 39.1 Hz), 143.2, 137.9, 137.0, 135.7, 134.8, 133.3, 129.1, 129.0, 128.78, 128.76, 128.7, 128.6, 128.4, 128.2, 127.7, 127.6, 127.5, 127.3, 124.1, 119.8, 118.9 (q, *J* = 276.4 Hz), 118.7, 106.8, 97.8, 71.4, 55.4, 44.0, 35.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.09. IR (film) ν_{max} 3853, 3751, 3649, 1717, 1653, 1541, 1507, 1457, 1263, 749, 703, 420 cm^{-1}. HRMS (ESI): m/z for $C_{34}H_{28}F_3N_3NaO_3^+$ $[M+Na]^+$ calcd.: 606.1974, found: 606.1970. HPLC analysis: **3am**, 87% ee (IA, hexane : isopropanol =80 : 20, 1 mL/min, UV: 254 nm), t_R =15.2 min (major), 25.7 min (minor).

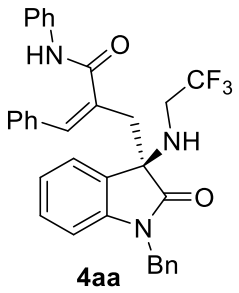
(*Z*)-2-(((*R*)-1-methyl-2-oxo-3-(((*E*)-2,2,2-trifluoroethylidene)amino)indolin-3-yl)methyl)-*N*,3-diphenylacrylamide (3an)



3an

The title compound **3an** was prepared according to the general procedure as described above in 91% yield (43.4 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 7:1) to afford yellow solid. mp = 120 – 122 °C. $[\alpha]^{25}_{D}$ = – 56 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$)δ 7.84 (s, 1H), 7.77 (q, J = 3.2 Hz, 1H), 7.55 – 7.49 (m, 2H), 7.36 – 7.30 (m, 2H), 7.32 – 7.25 (m, 3H), 7.20 – 7.13 (m, 3H), 7.14 – 7.10 (m, 1H), 7.00 (td, J = 7.6, 1.0 Hz, 1H), 6.79 (d, J = 7.9 Hz, 1H), 3.44 (q, J = 14.4 Hz, 2H), 3.08 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.6, 167.6, 150.7 (q, J = 38.5 Hz), 142.6, 138.0, 137.4, 135.0, 133.3, 129.9, 128.9, 128.8, 128.5, 128.2, 127.9, 125.4, 124.3, 123.4, 120.6, 120.2, 119.9, 118.9 (q, *J* = 276.4 Hz), 108.7, 71.7, 35.8, 26.3. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.34. IR (film) ν_{max} 3853, 3649, 3050, 1711, 1603, 1541, 1507, 1467, 1273, 749, 703, 422 cm^{-1}. HRMS (ESI): m/z for $C_{27}H_{22}F_3N_3O_2Na^+$ $[M+Na]^+$ calcd.: 500.1556, found: 500.1555. HPLC analysis: **3an**, 92% ee (IA, hexane : isopropanol =85 : 15, 1 mL/min, UV: 254 nm), t_R =17.2 min (major), 30.6 min (minor).

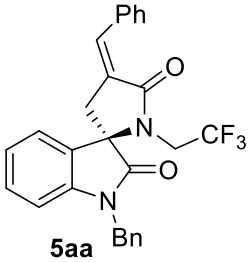
(*R*,*Z*)-2-((1-benzyl-2-oxo-3-((2,2,2-trifluoroethyl)amino)indolin-3-yl)methyl)-*N*,3-diphenylacrylamide (4aa)



4aa

The title compound **4aa** was prepared according to the general procedure as described above in 89% yield (49.3 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 10:1) to afford yellowish solid. mp = 170 – 172 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.45 – 7.41 (m, 2H), 7.35 – 7.26 (m, 6H), 7.28 – 7.18 (m, 4H), 7.20 – 7.08 (m, 4H), 7.01 – 6.93 (m, 3H), 6.70 (d, *J* = 7.7 Hz, 1H), 4.96 (d, *J* = 15.5 Hz, 1H), 4.67 (d, *J* = 15.5 Hz, 1H), 3.29 (d, *J* = 14.3 Hz, 1H), 3.14 (d, *J* = 14.3 Hz, 1H), 2.98 (p, *J* = 9.0 Hz, 1H), 2.65 (s, 1H), 2.51 (q, *J* = 12.9, 11.1 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.9, 168.3, 142.8, 137.9, 137.4, 135.7, 134.8, 133.8, 129.9, 129.0, 128.8, 128.5, 128.4, 128.2, 128.0, 127.5, 126.7, 125.7, 124.4, 123.3, 120.5, 109.5, 66.0, 45.6 (q, *J* = 32.7 Hz), 44.0, 35.9. ^{19}F NMR (471 MHz, $CDCl_3$) δ –71.35. IR (film) ν_{max} 3741, 3649, 1734, 1698, 1653, 1559, 1489, 1362, 1275, 1175, 764, 420 cm^{-1}. HRMS (ESI): m/z for $C_{33}H_{29}F_3N_3O_2^+$ $[M+H]^+$ calcd.: 556.2214, found: 556.2216. HPLC analysis: **4aa**, 94% ee (OX-H, hexane : isopropanol =80 : 20, 1 mL/min, UV: 254 nm), t_R =10.5 min (minor), 16.2 min (major).

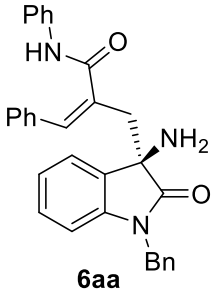
(*R*,*Z*)-1-benzyl-4'-benzylidene-1'-(2,2,2-trifluoroethyl)spiro[indoline-3,2'-pyrrolidine]-2,5'-dione (5aa)



5aa

The title compound **5aa** was prepared according to the general procedure as described above in 94% yield (43.4 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 6:1) to afford yellowish oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (t, J = 2.8 Hz, 1H), 7.47 – 7.44 (m, 2H), 7.42 – 7.25 (m, 9H), 7.21 (d, J = 6.2 Hz, 1H), 7.09 (t, J = 7.3 Hz, 1H), 6.83 (d, J = 7.9 Hz, 1H), 4.99 (d, J = 15.6 Hz, 1H), 4.84 (d, J = 15.5 Hz, 1H), 3.84 (dq, J = 15.5, 9.3 Hz, 1H), 3.70 (dq, J = 15.4, 9.1 Hz, 1H), 3.57 (dd, J = 17.2, 2.7 Hz, 1H), 3.28 (dd, J = 17.2, 2.9 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ174.9, 170.9, 142.9, 135.2, 134.9, 133.7, 130.7, 120.0, 129.3, 129.0, 128.9, 128.1, 127.5, 127.0, 125.9, 124.1, 123.8, 110.1, 66.2, 44.5, 43.0 (q, J = 35.9 Hz), 38.0. IR (film) ν_{max} 3755, 3629, 1744, 1698, 1653, 1573, 1494, 1362, 1253, 1055, 784, 423 cm^{-1}. HRMS (ESI): m/z for $C_{27}H_{21}F_3N_2O_2Na^+$ $[M+Na]^+$ calcd.: 485.1447.1713, found: 485.1446. HPLC analysis: **5aa**, 94% ee (OD-H, hexane : isopropanol =70 : 30, 1 mL/min, UV: 254 nm), t_R =9.4 min (minor), 10.1 min (major).

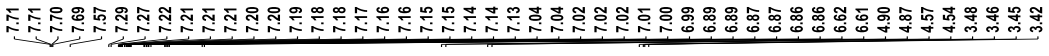
(*R*,*Z*)-2-((3-amino-1-benzyl-2-oxoindolin-3-yl)methyl)-N,3-diphenylacrylamide (6aa)

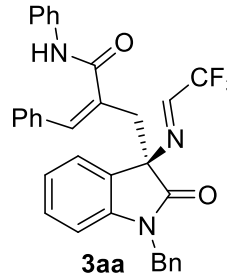


6aa

The title compound **6aa** was prepared according to the general procedure as described above in 97% yield (45.7 mg). It was purified by flash column chromatography (Petroleum ether : EtOAc = 1:1) to afford white semi-solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ11.66 (s, 1H), 7.82 (s, 1H), 7.75 – 7.63 (m, 2H), 7.39 – 7.29 (m, 7H), 7.23 – 7.04 (m, 5H), 6.96 (dt, J = 21.3, 7.6 Hz, 3H), 6.74 (d, J = 7.9 Hz, 1H), 6.55 (d, J = 7.7 Hz, 2H), 5.06 (d, J = 15.5 Hz, 1H), 4.59 (d, J = 15.5 Hz, 1H), 3.14 – 2.91 (m, 2H), 2.35 (s, 1H). ^{13}C NMR (126 MHz, CDCl3) δ 176.5, 171.7, 142.3, 135.3, 135.1, 132.5, 130.2, 129.9, 129.8, 129.3, 129.1, 129.0, 128.8, 128.0, 127.5, 127.3, 123.8, 118.6, 115.1, 109.8, 61.3, 44.3, 38.8. IR (film) ν_{max} 3729, 1954, 1798, 1653, 1573, 1494, 1362, 1253, 1155, 784, 478 cm^{-1}. HRMS (ESI): m/z for $C_{31}H_{27}N_3O_2Na^+$ $[M+Na]^+$ calcd.: 496.1995, found: 496.1996. HPLC analysis: **6aa**, 97% ee (IA, hexane : isopropanol =60 : 40, 1 mL/min, UV: 254 nm), t_R =14.3 min (minor), 17.0 min (major).

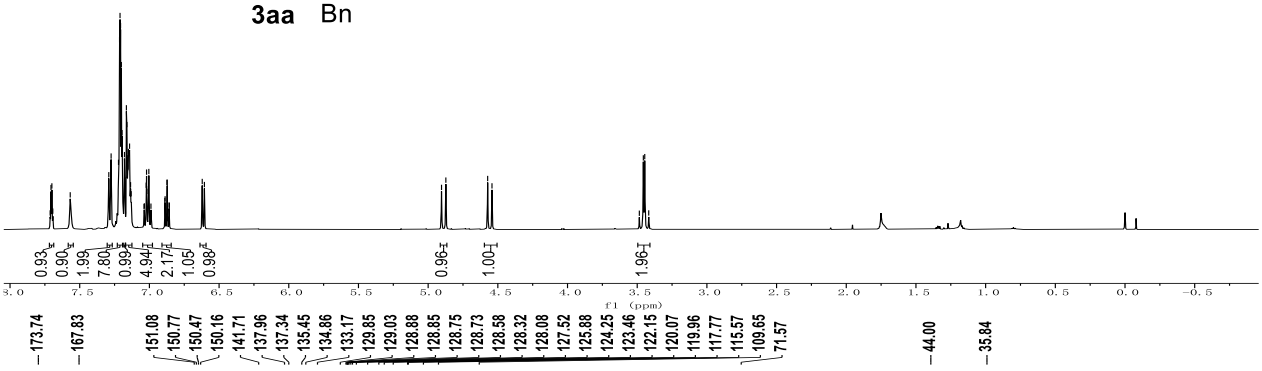
^{1}H, ^{13}C and ^{19}F NMR Spectra of All Products

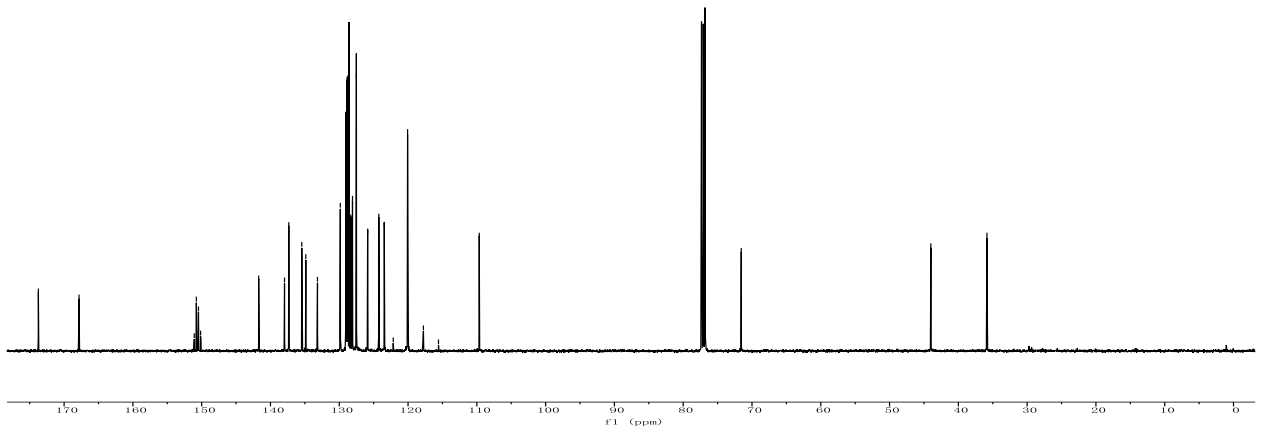


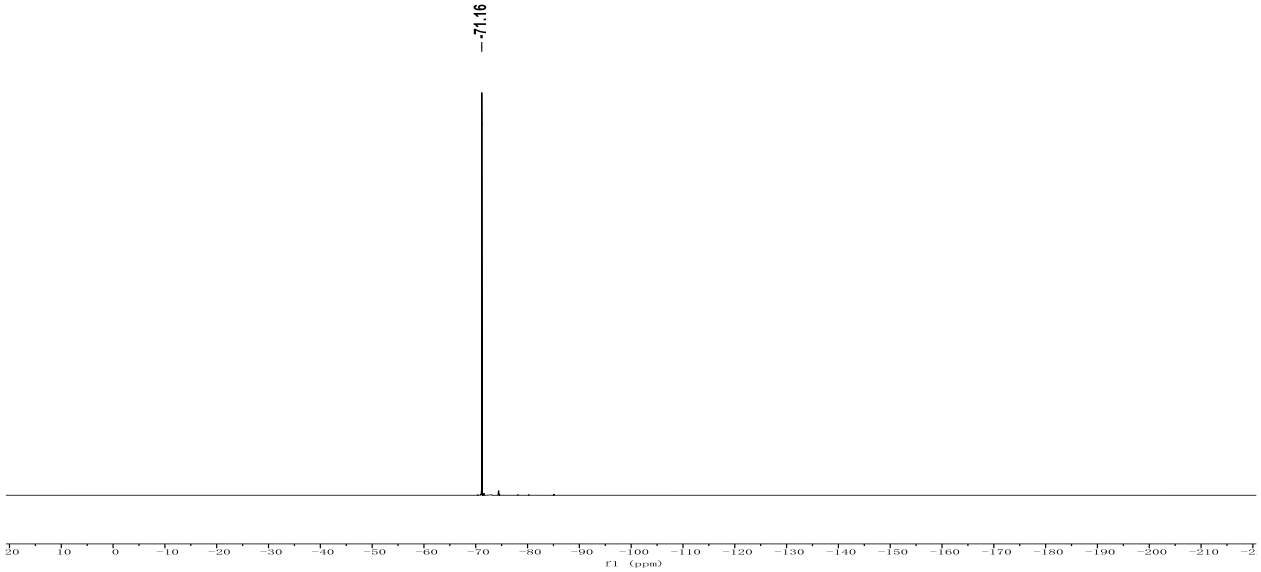


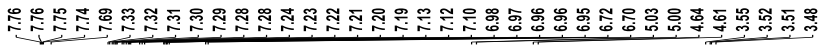
3aa

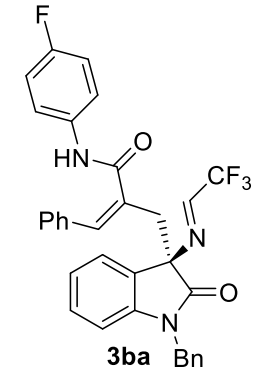
^{1}H NMR (500 MHz, $CDCl_3$)
^{13}C NMR (126 MHz, $CDCl_3$)
^{19}F NMR (471 MHz, $CDCl_3$)





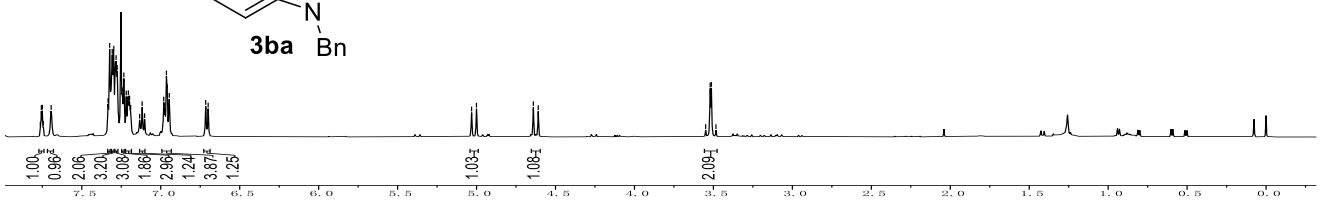


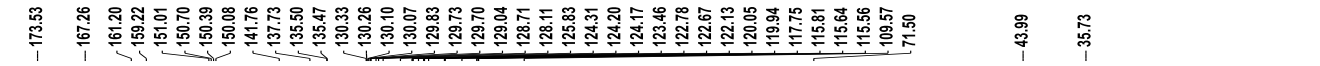


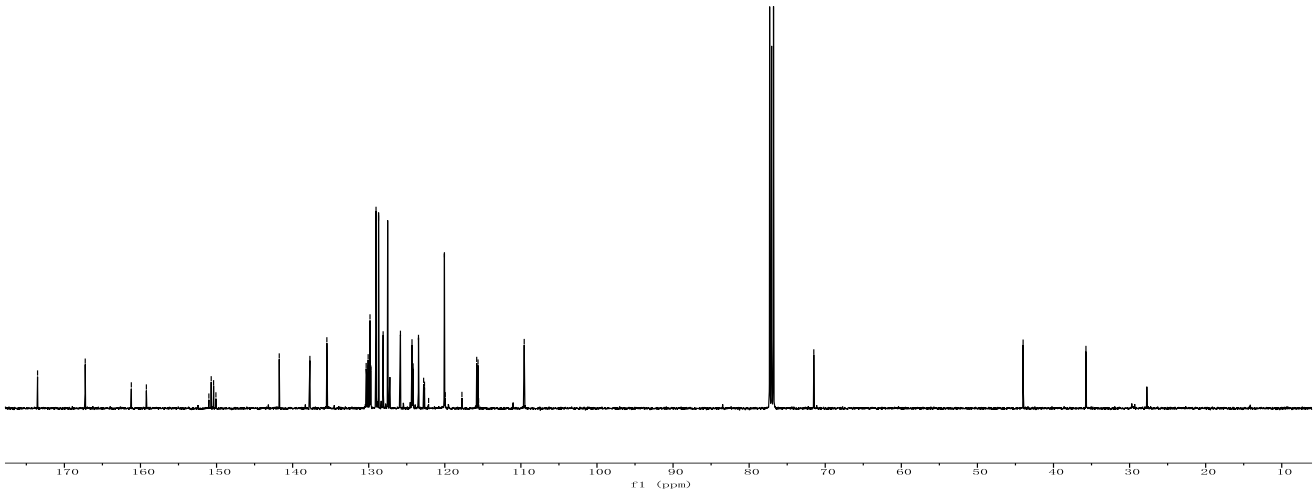


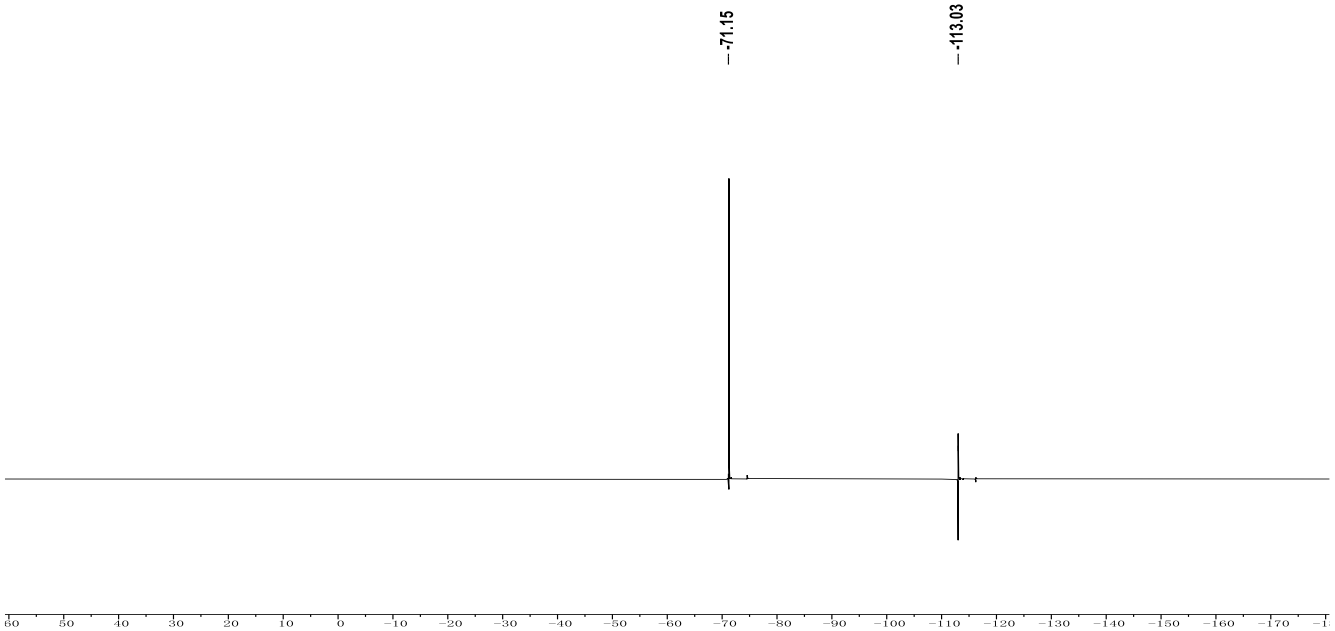
3ba

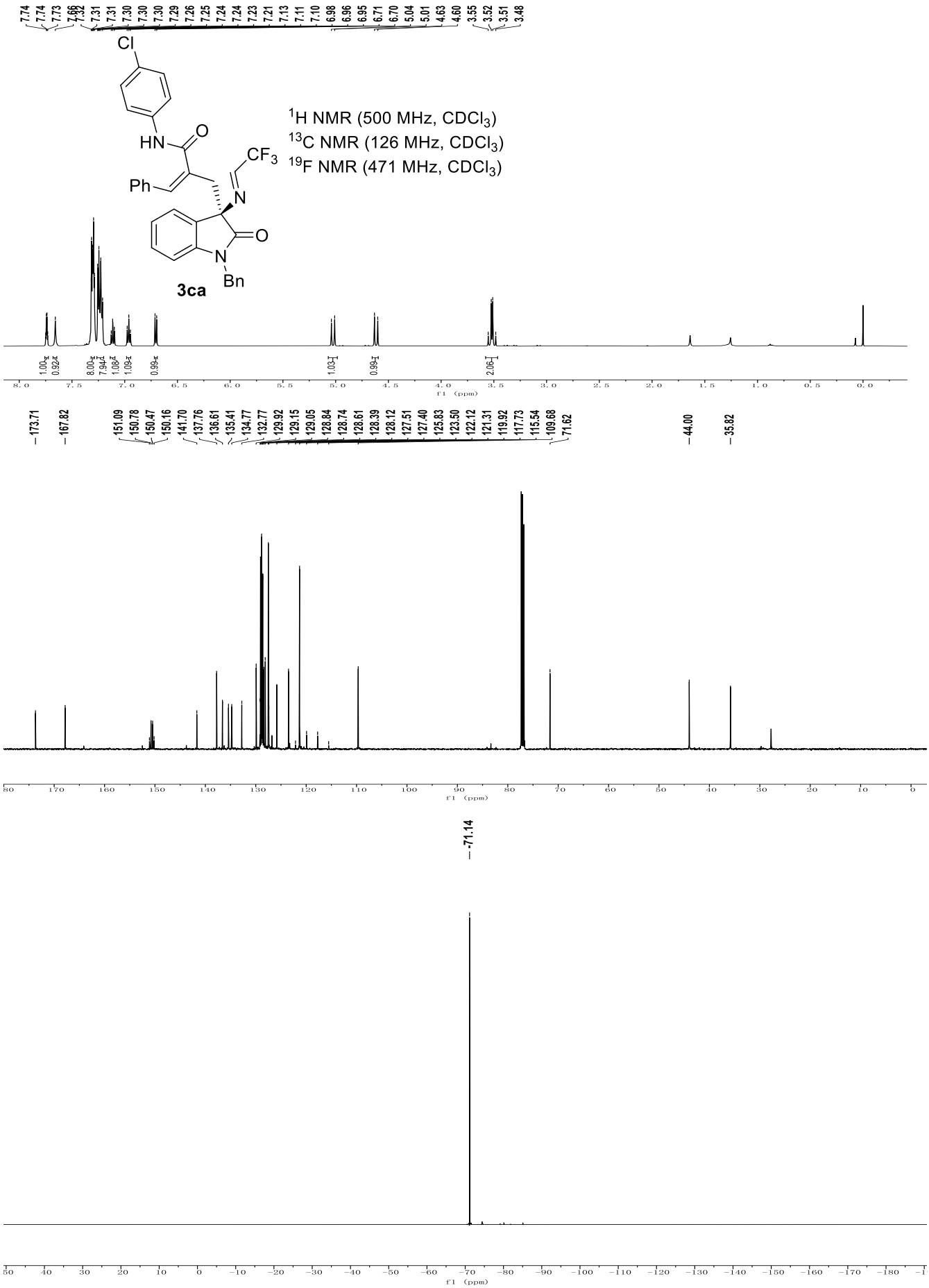
^{1}H NMR (500 MHz, $CDCl_3$)
^{13}C NMR (126 MHz, $CDCl_3$)
^{19}F NMR (471 MHz, $CDCl_3$)

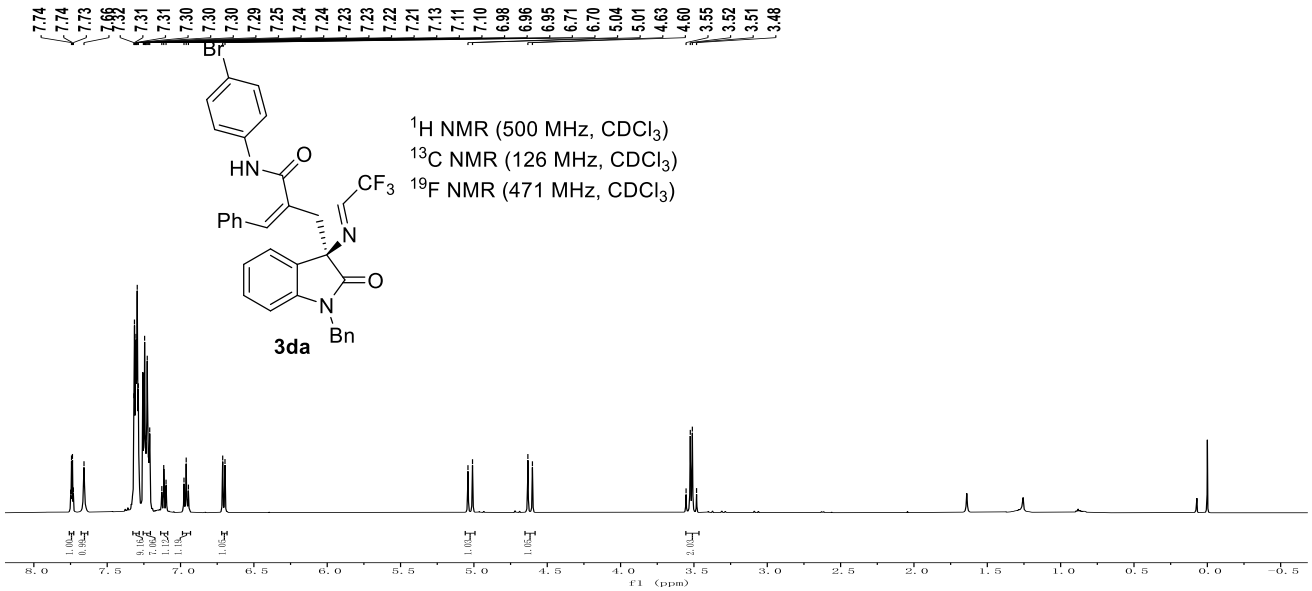









7.74 7.74 7.73 7.66 7.32 7.31 7.31 7.30 7.30 7.30 7.29 7.26 7.25 7.24 7.24 7.23 7.21 7.13 7.11 7.10 6.98 6.96 6.95 6.71 6.70 5.04 5.01 4.63 4.60 3.55 3.52 3.51 3.48
Cl
HN
O
CF3
Ph
N
O
N
Bn
3ca
1H NMR (500 MHz, CDCl3)
13C NMR (126 MHz, CDCl3)
19F NMR (471 MHz, CDCl3)
1.00 0.92 8.00 7.94 1.08 1.09 0.99 1.03 0.99 2.06
f1 (ppm)
173.71 167.82 151.09 150.78 150.47 150.16 141.70 137.76 136.61 135.41 134.77 132.77 129.92 129.15 129.05 128.84 128.74 128.61 128.39 128.12 127.51 127.40 125.83 123.50 122.12 121.31 119.92 117.73 115.54 109.68 71.62 44.00 35.82
f1 (ppm)
-71.14
f1 (ppm)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7.74
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7.21
7.13
7.11
7.10
6.98
6.96
6.95
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5.04
5.01
4.63
4.60
3.55
3.52
3.51
3.48
Br
HN
O
CF3
Ph
N
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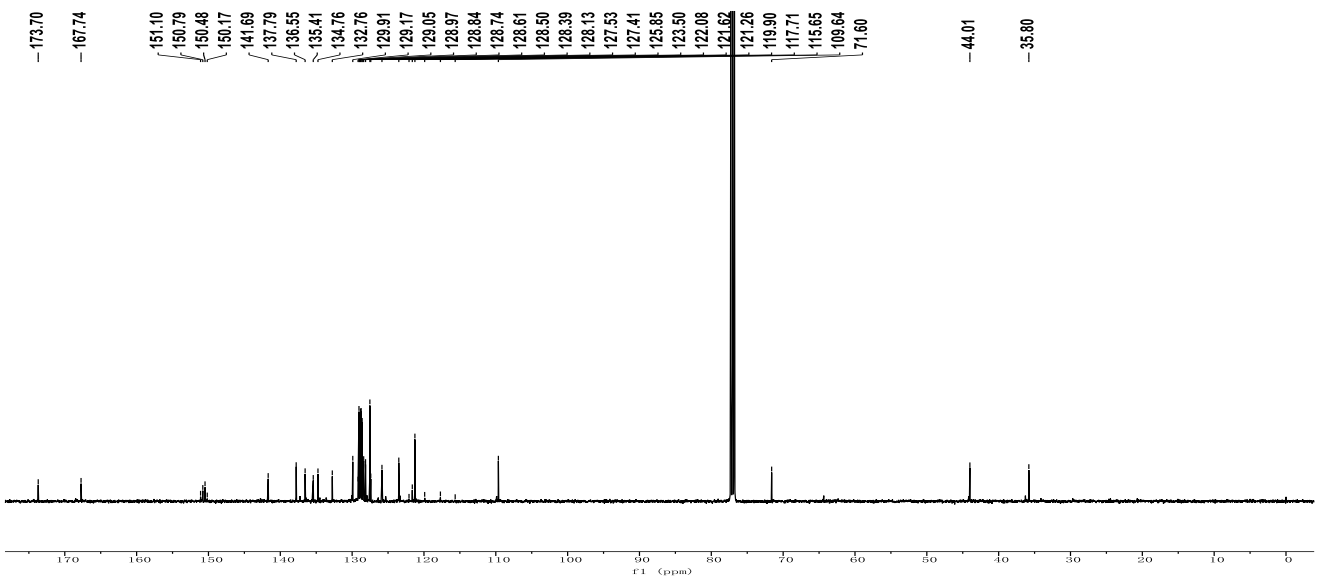
N
Bn
3da
1H NMR (500 MHz, CDCl3)
13C NMR (126 MHz, CDCl3)
19F NMR (471 MHz, CDCl3)
f1 (ppm)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167.74
151.10
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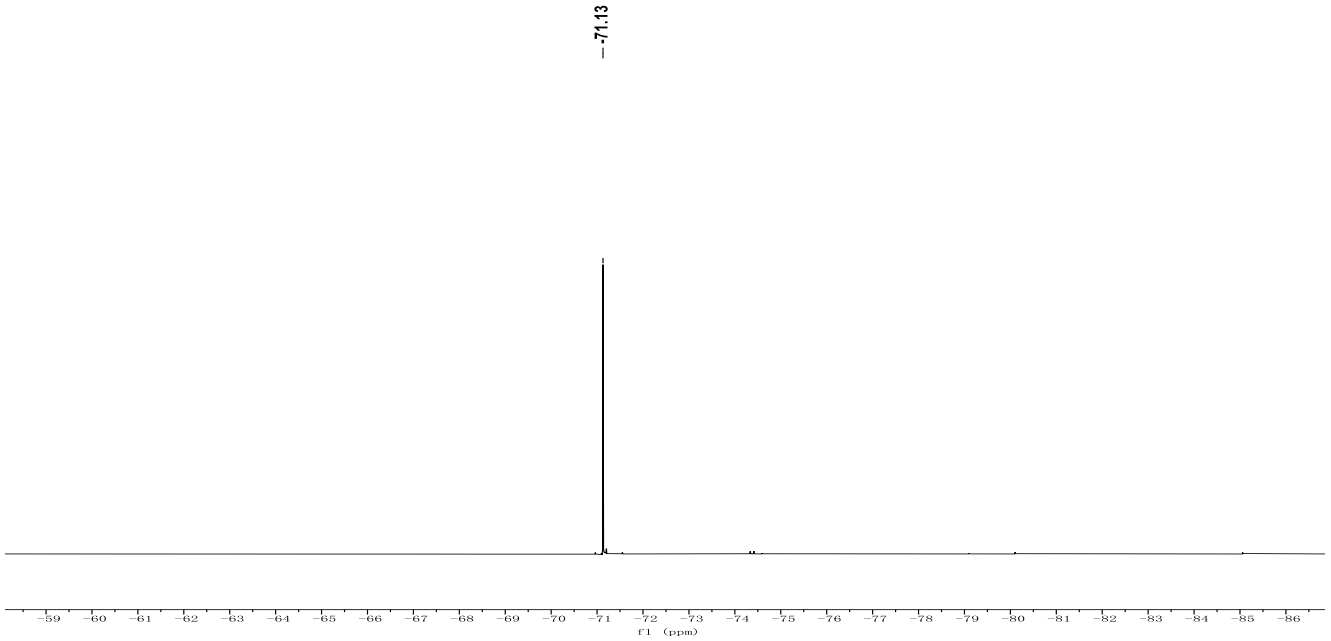
150.48
150.17
141.69
137.79
136.55
135.41
134.76
132.76
129.91
129.17
129.05
128.97
128.84
128.74
128.61
128.50
128.39
128.13
127.53
127.41
125.85
123.50
122.08
121.62
121.26
119.90
117.71
115.65
109.64
71.60
44.01
35.80
f1 (ppm)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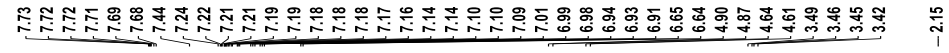
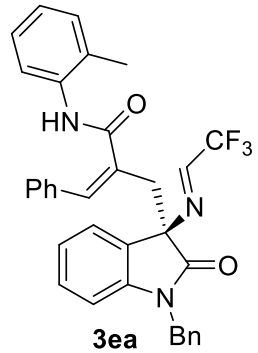
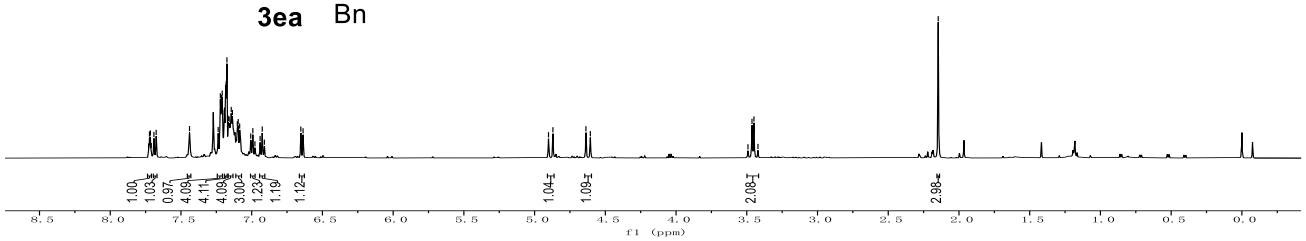
f1 (ppm)

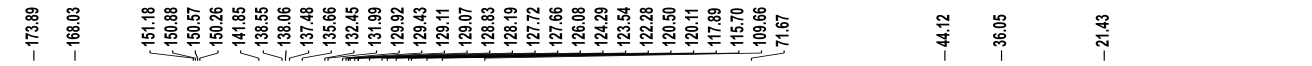


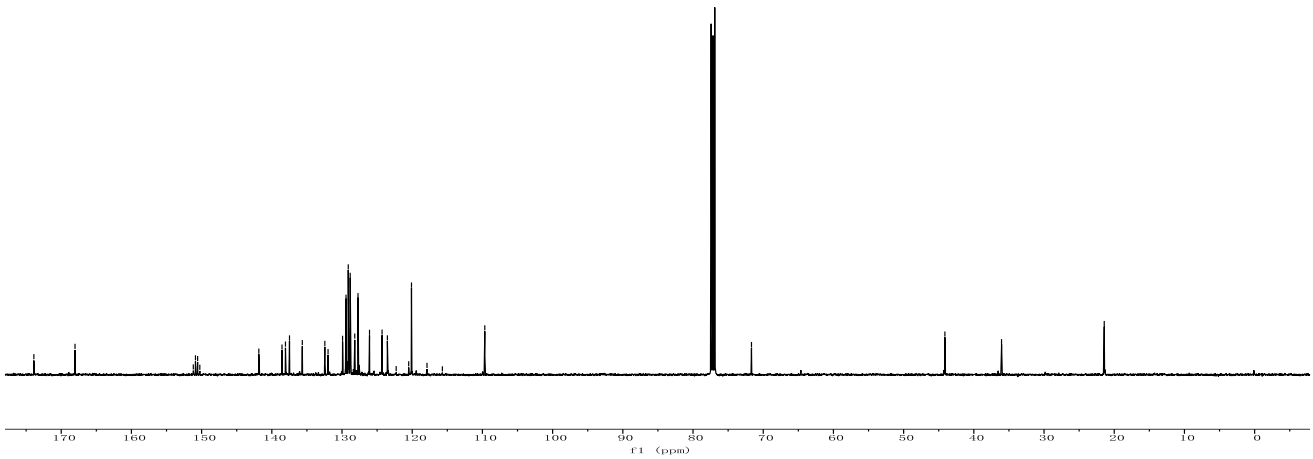


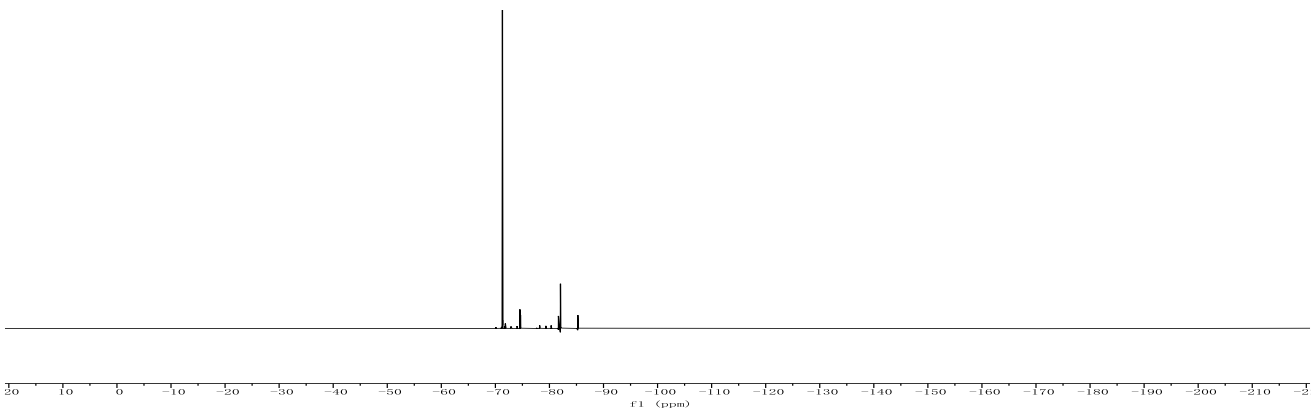
3ea

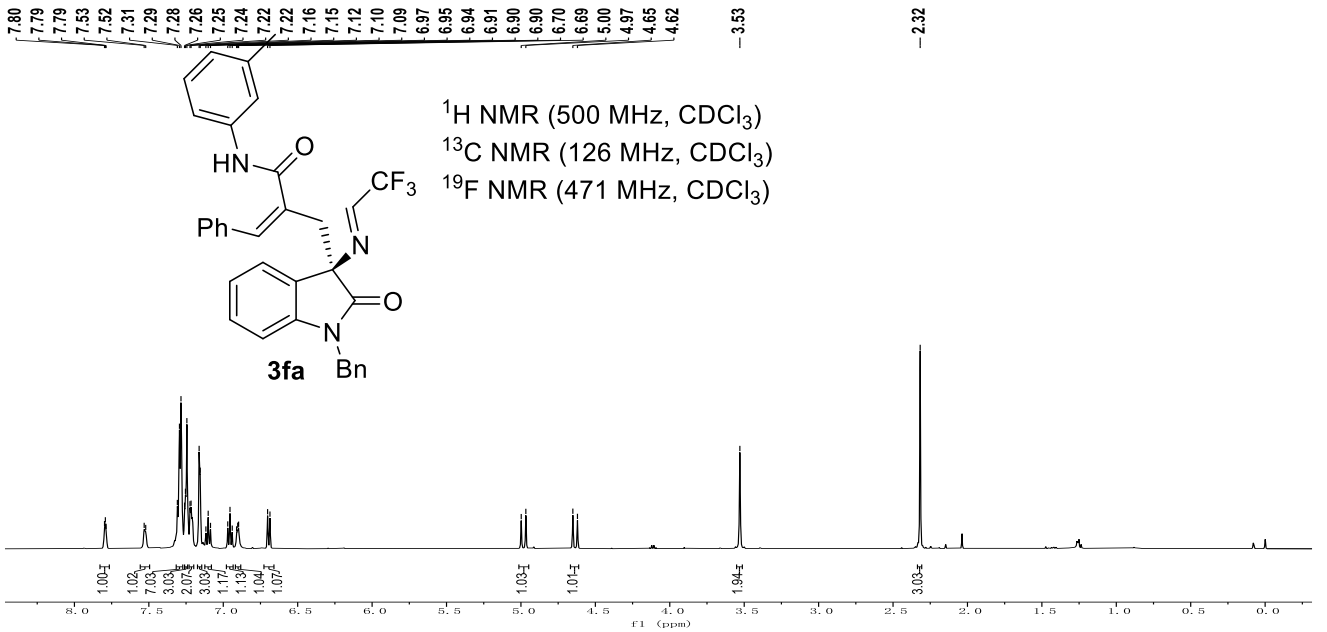
^{1}H NMR (500 MHz, $CDCl_3$)
^{13}C NMR (126 MHz, $CDCl_3$)
^{19}F NMR (471 MHz, $CDCl_3$)







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7.79
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7.12
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7.09
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6.95
6.94
6.91
6.90
6.90
6.70
6.69
5.00
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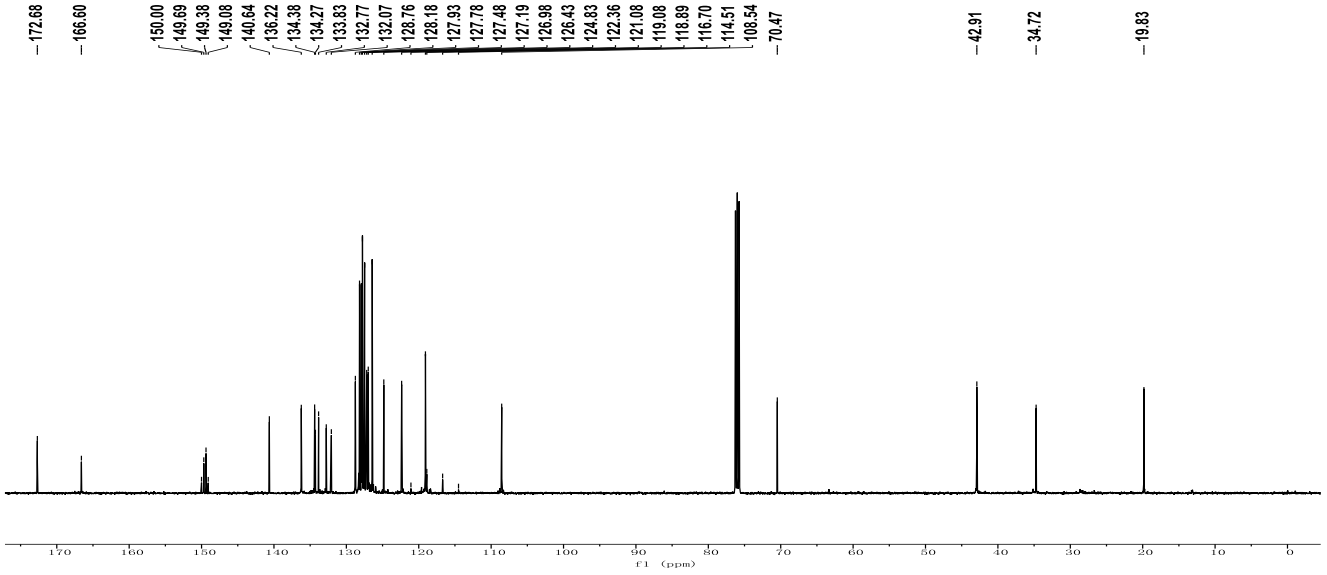
4.65
4.62
3.53
2.32
HN
O
CF3
Ph
N
O
N
Bn
3fa
1H NMR (500 MHz, CDCl3)
13C NMR (126 MHz, CDCl3)
19F NMR (471 MHz, CDCl3)
1.00
1.02
7.03
3.03
2.07
3.03
1.17
1.13
1.04
1.07
1.03
1.01
1.94
3.03
f1 (ppm)


172.68
166.60
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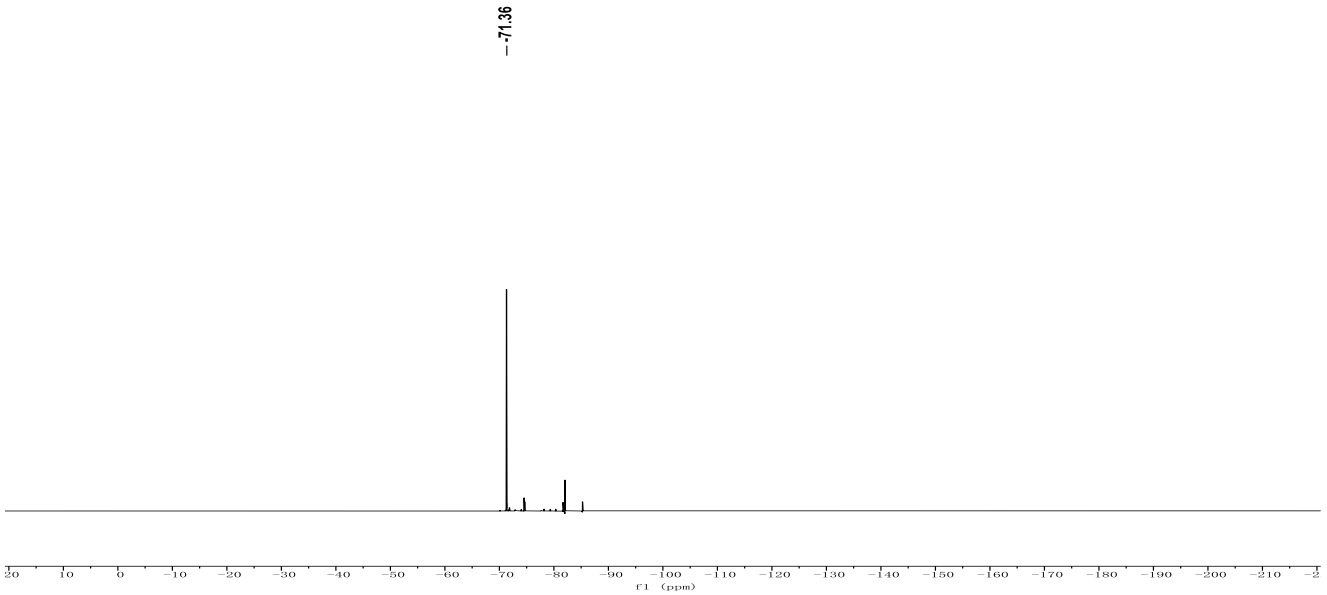
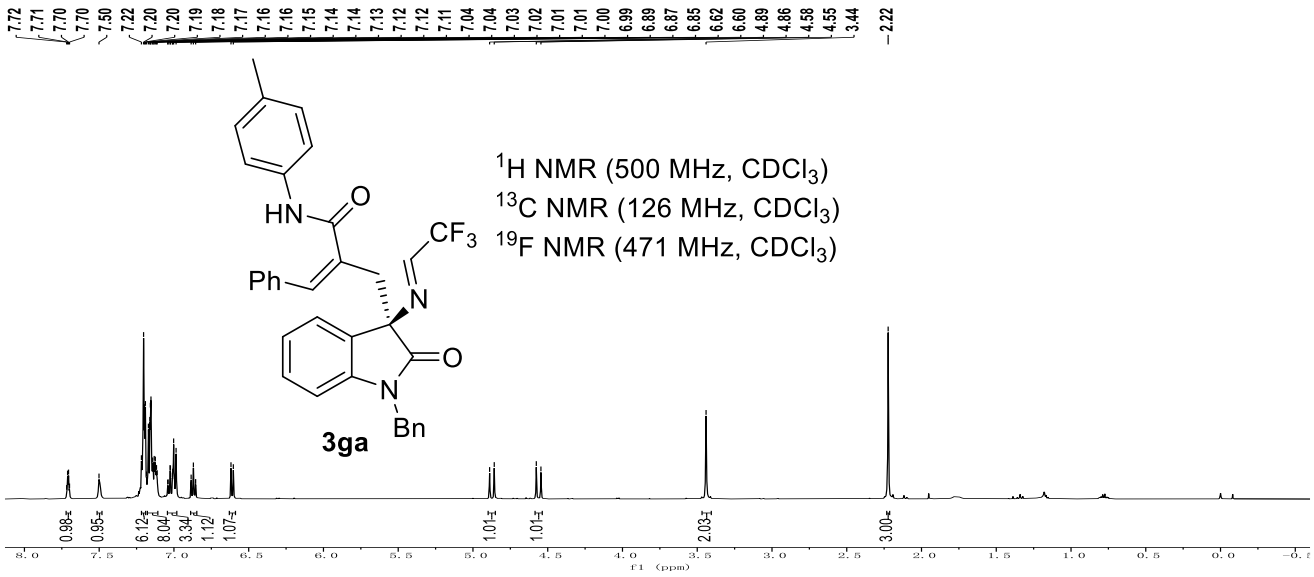
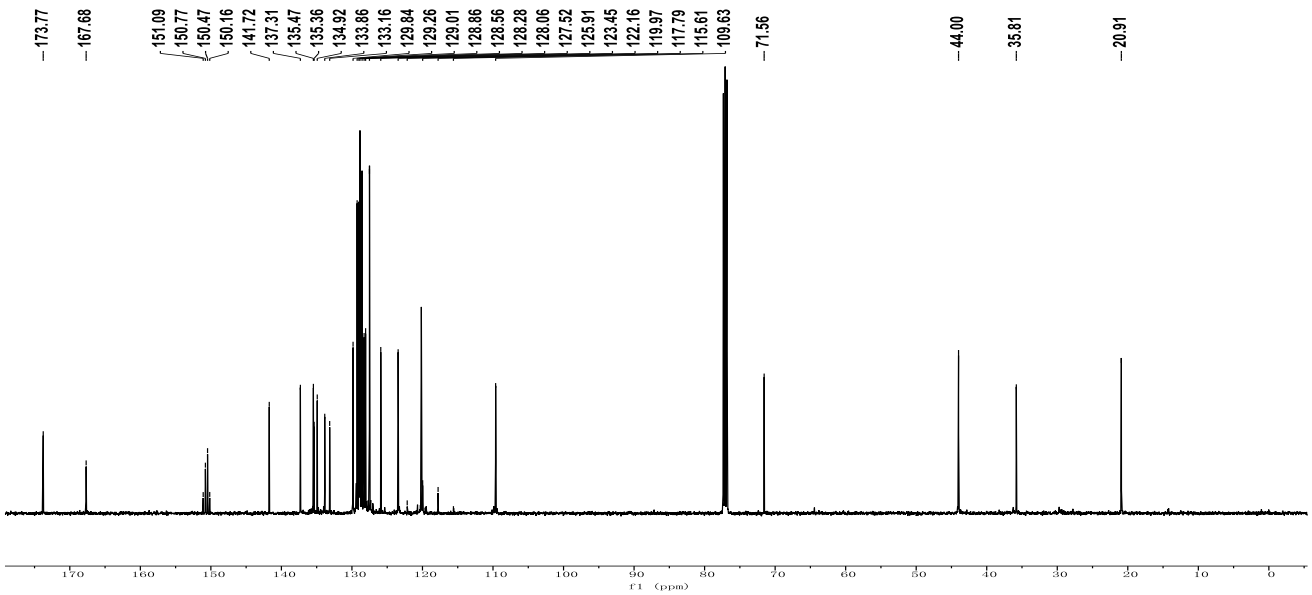
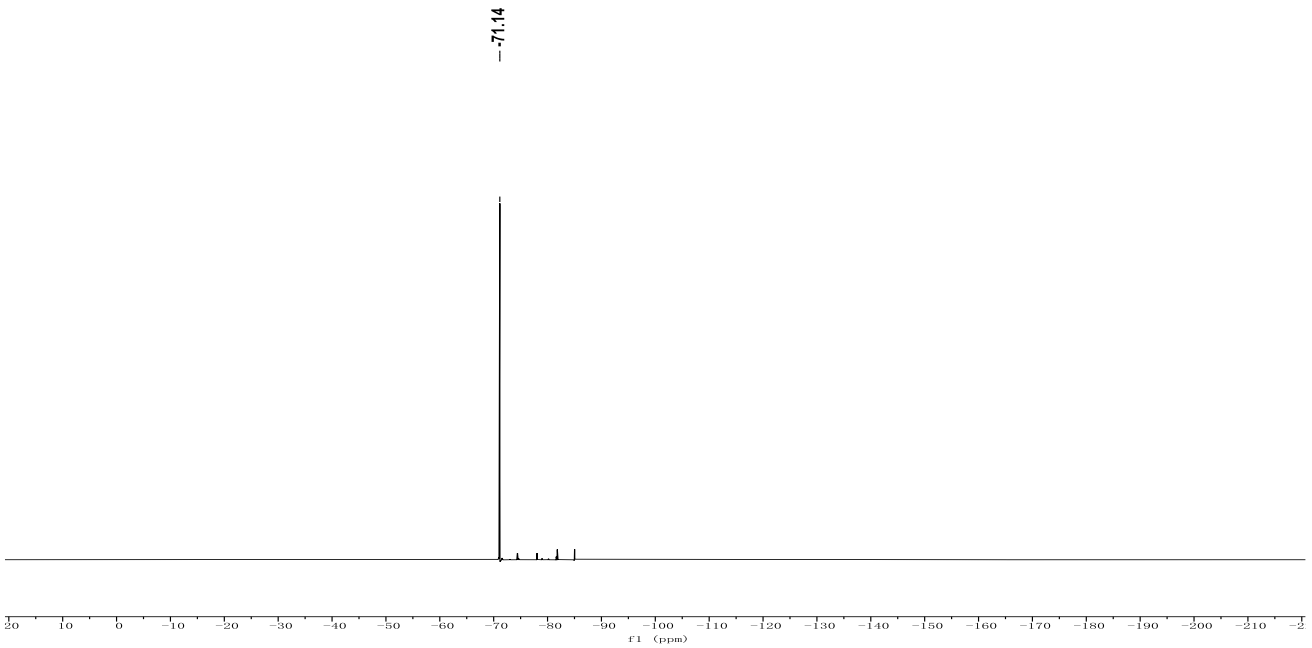
149.08
140.64
136.22
134.38
134.27
133.83
132.77
132.07
128.76
128.18
127.93
127.78
127.48
127.19
126.98
126.43
124.83
122.36
121.08
119.08
118.89
116.70
114.51
108.54
70.47
42.91
34.72
19.83
f1 (ppm)


-71.36
f1 (ppm)


7.72 7.71 7.70 7.70 7.50 7.22 7.20 7.20 7.19 7.18 7.17 7.16 7.16 7.15 7.14 7.14 7.13 7.12 7.12 7.11 7.04 7.04 7.03 7.02 7.01 7.01 7.00 6.99 6.89 6.87 6.85 6.62 6.60 4.89 4.86 4.58 4.55 3.44 2.22
HN
O
CF3
Ph
N
O
N
Bn
3ga
1H NMR (500 MHz, CDCl3)
13C NMR (126 MHz, CDCl3)
19F NMR (471 MHz, CDCl3)
0.98 0.95 6.12 8.04 3.34 1.12 1.07 1.01 1.01 2.03 3.00
f1 (ppm)


173.77 167.68 151.09 150.77 150.47 150.16 141.72 137.31 135.47 135.36 134.92 133.86 133.16 129.84 129.26 129.01 128.86 128.56 128.28 128.06 127.52 125.91 123.45 122.16 119.97 117.79 115.61 109.63 71.56 44.00 35.81 20.91
f1 (ppm)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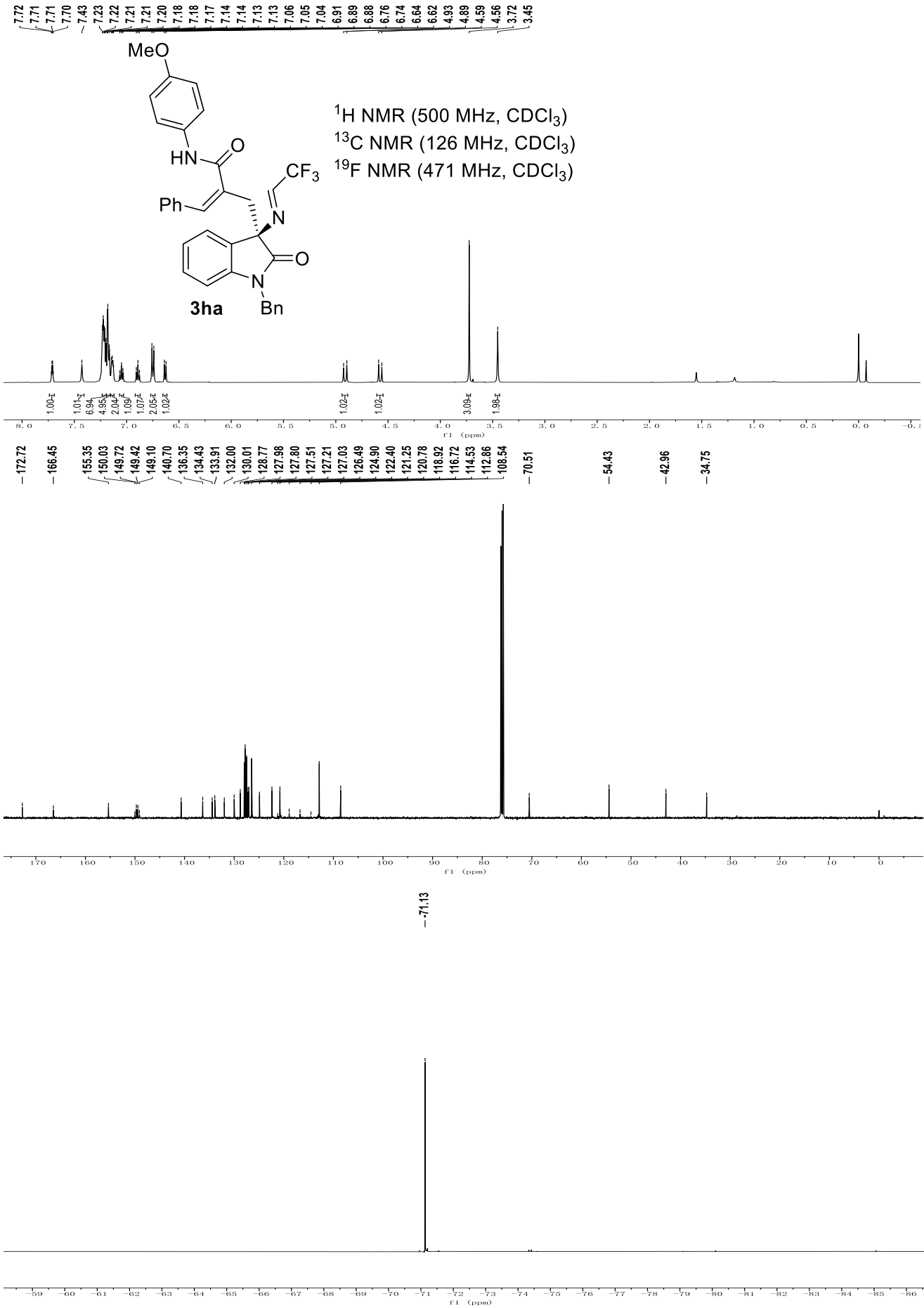
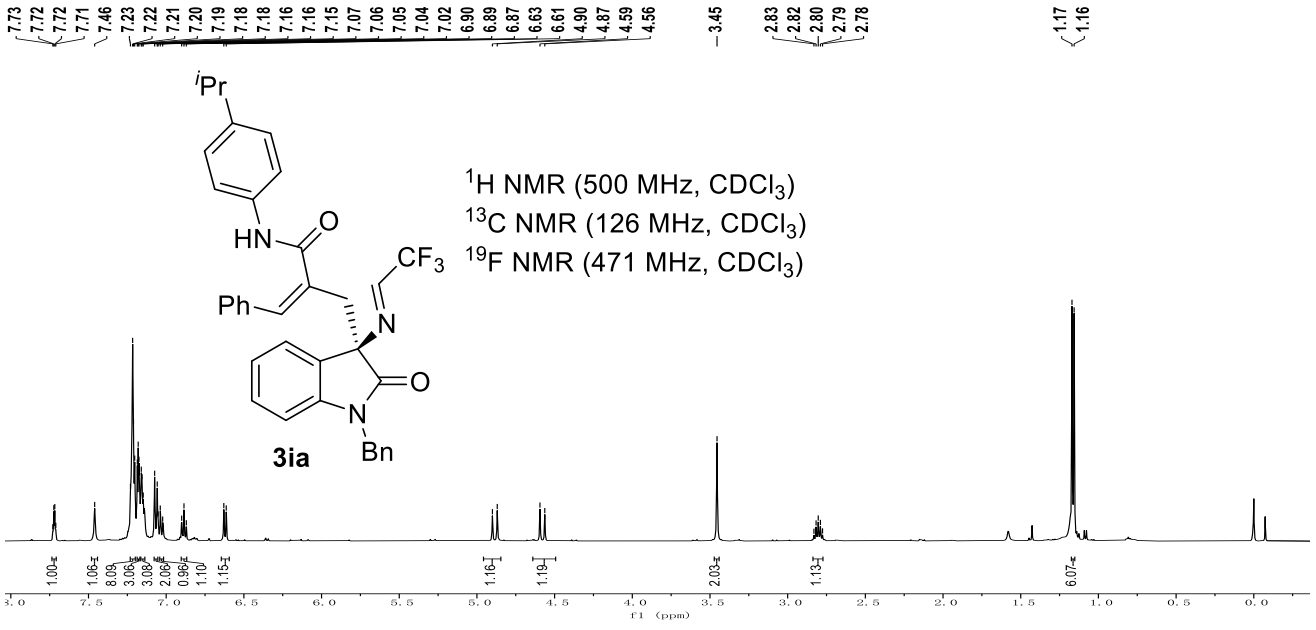

7.72 7.71 7.71 7.70 7.43 7.23 7.22 7.21 7.21 7.20 7.18 7.18 7.17 7.14 7.14 7.13 7.13 7.06 7.05 7.04 6.91 6.89 6.88 6.76 6.74 6.64 6.62 4.93 4.89 4.59 4.56 3.72 3.45
MeO
HN
O
CF3
Ph
N
O
N
Bn
3ha
1H NMR (500 MHz, CDCl3)
13C NMR (126 MHz, CDCl3)
19F NMR (471 MHz, CDCl3)
1.00 1.01 6.94 4.95 2.04 1.09 1.07 2.05 1.02 1.02 1.02 3.09 1.98
f1 (ppm)
172.72 166.45 155.35 150.03 149.72 149.42 149.10 140.70 136.35 134.43 133.91 132.00 130.01 128.77 127.98 127.80 127.51 127.21 127.03 126.49 124.90 122.40 121.25 120.78 118.92 116.72 114.53 112.86 108.54 70.51 54.43 42.96 34.75
f1 (ppm)
-71.13
f1 (ppm)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7.19
7.18
7.18
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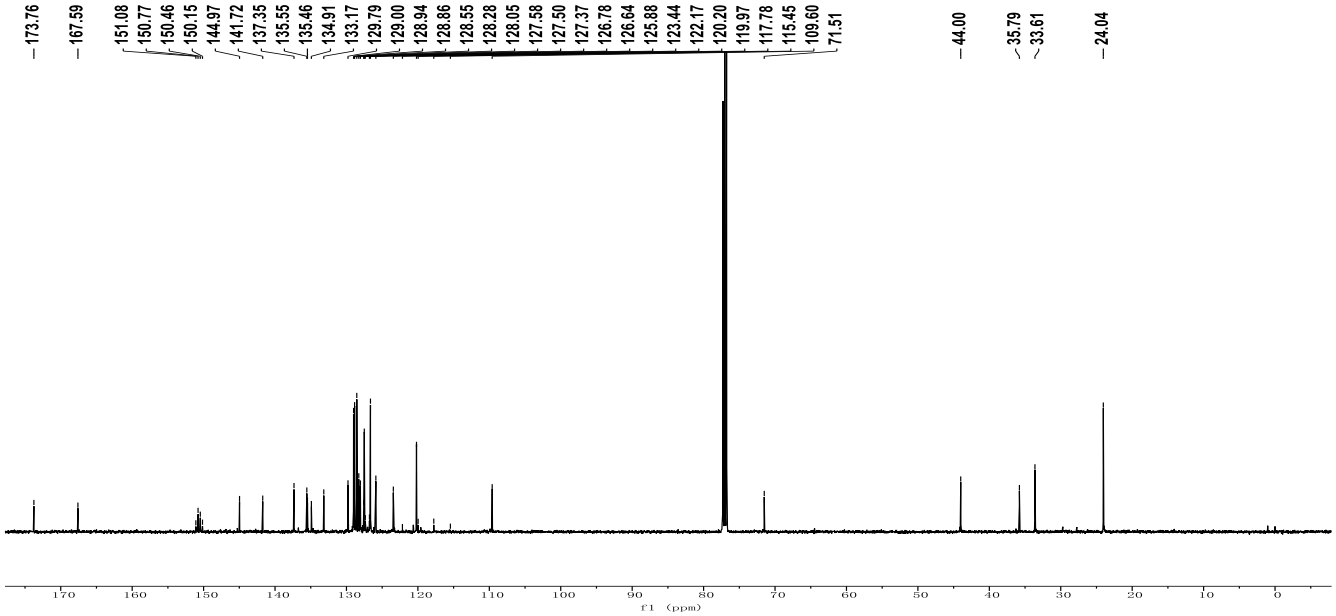
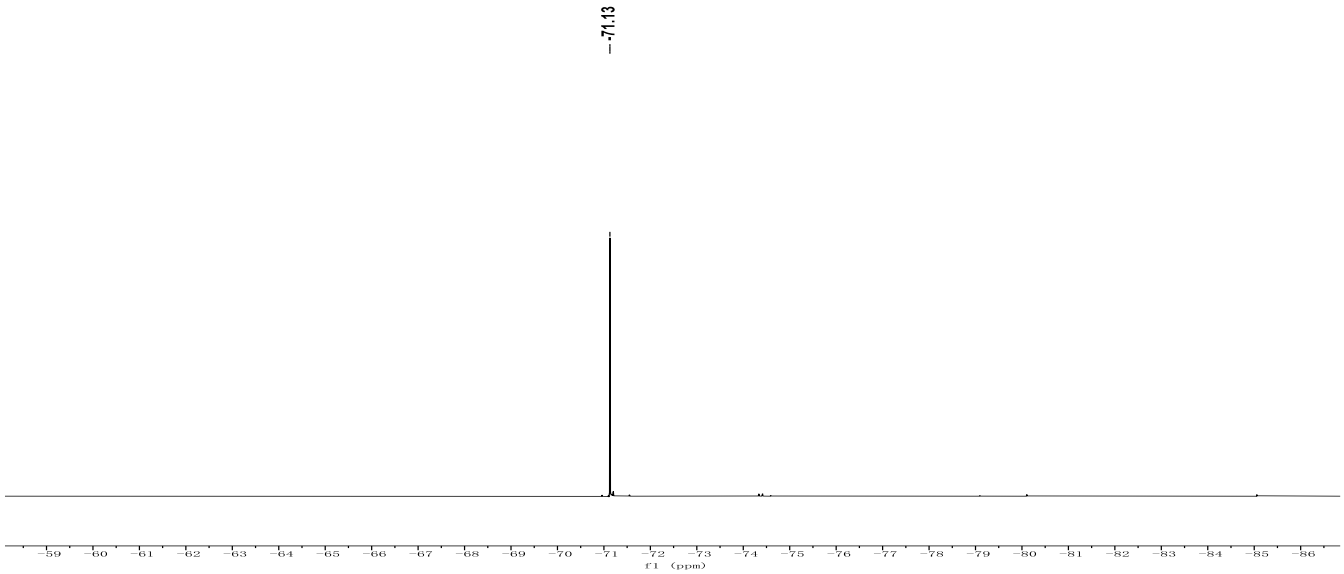
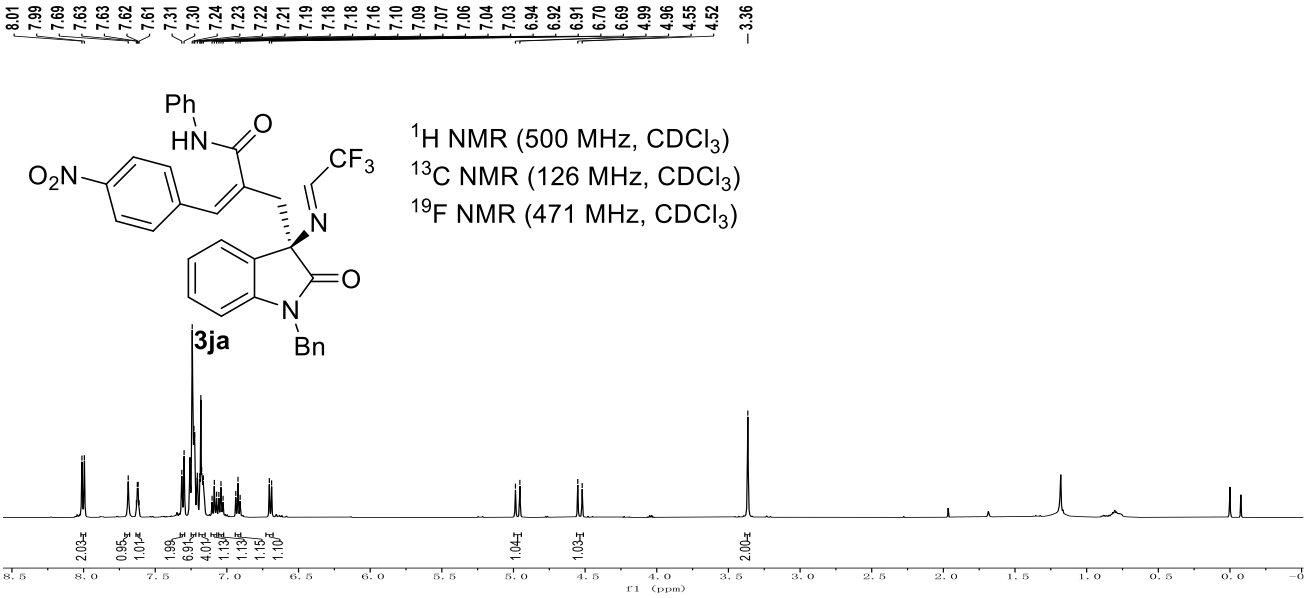
7.16
7.15
7.07
7.06
7.05
7.04
7.02
6.90
6.89
6.87
6.63
6.61
4.90
4.87
4.59
4.56
3.45
2.83
2.82
2.80
2.79
2.78
1.17
1.16
iPr
HN
O
CF3
Ph
N
O
N
Bn
3ia
1H NMR (500 MHz, CDCl3)
13C NMR (126 MHz, CDCl3)
19F NMR (471 MHz, CDCl3)
1.00
1.06
8.09
3.06
3.08
2.06
0.96
1.10
1.15
1.16
1.19
2.03
1.13
6.07
f1 (ppm)

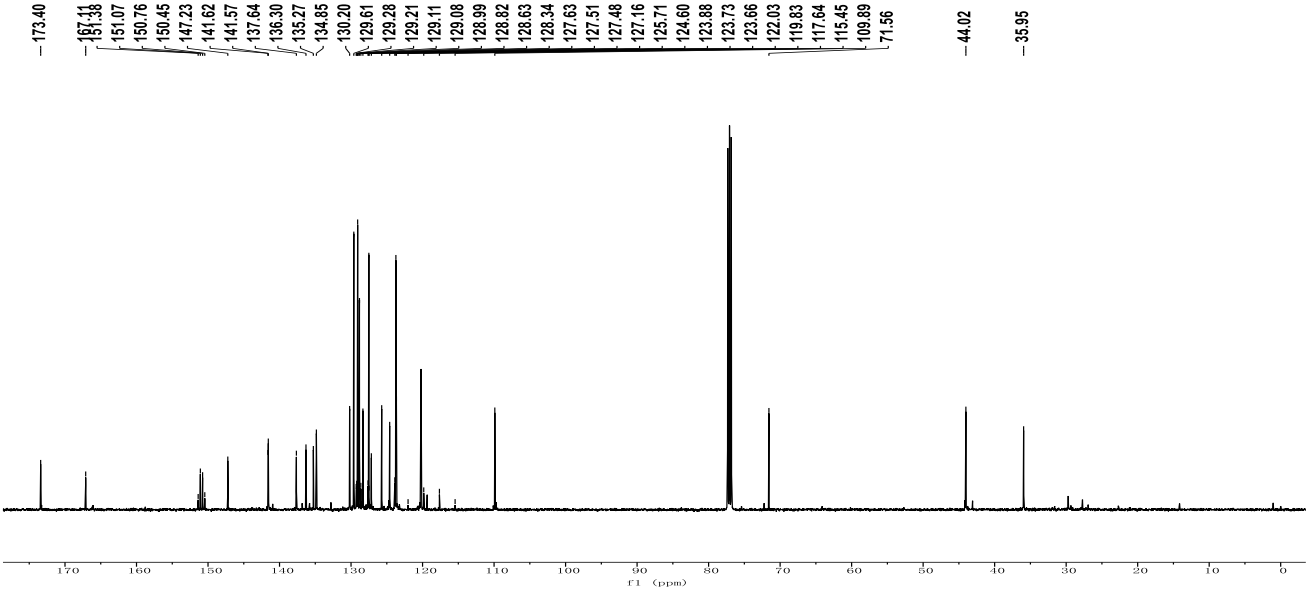

173.76
167.59
151.08
150.77
150.46
150.15
144.97
141.72
137.35
135.55
135.46
134.91
133.17
129.79
129.00
128.94
128.86
128.55
128.28
128.05
127.58
127.50
127.37
126.78
126.64
125.88
123.44
122.17
120.20
119.97
117.78
115.45
109.60
71.51
44.00
35.79
33.61
24.04
f1 (ppm)

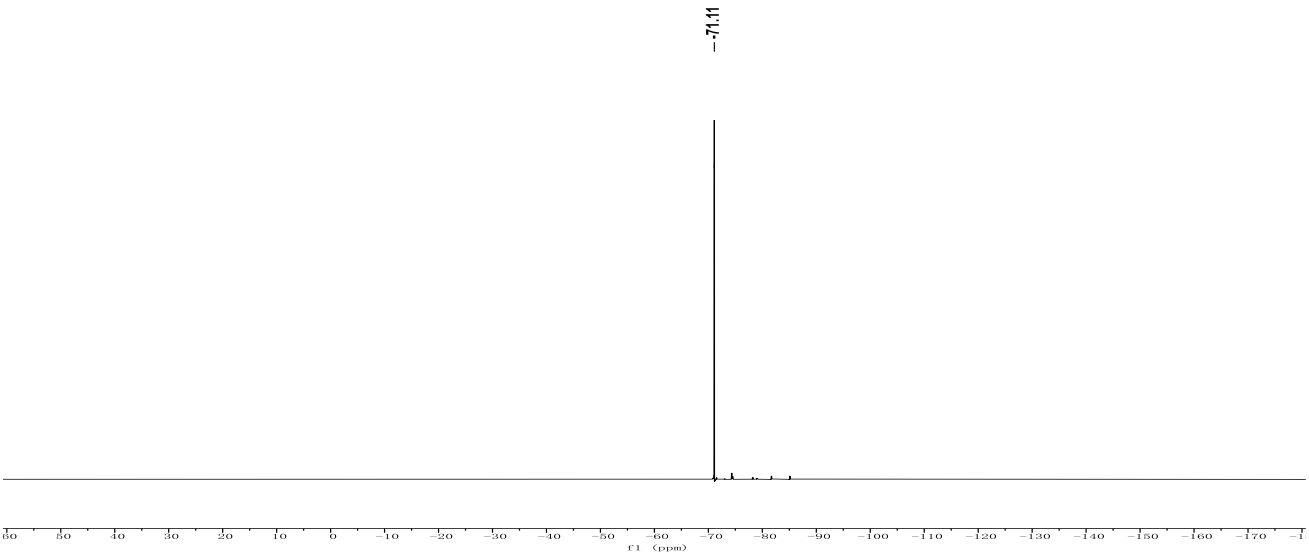

-71.13
f1 (ppm)

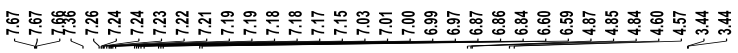
3ja

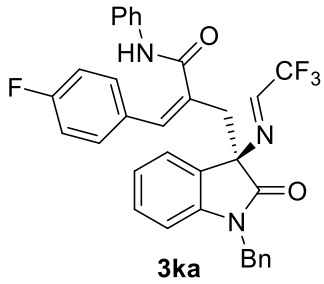
^{1}H NMR (500 MHz, $CDCl_3$)
^{13}C NMR (126 MHz, $CDCl_3$)
^{19}F NMR (471 MHz, $CDCl_3$)





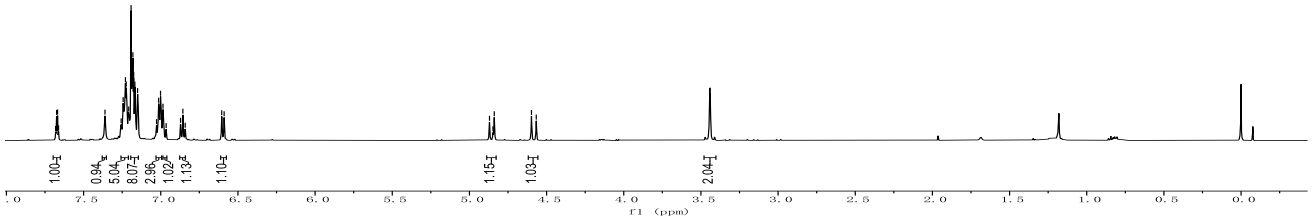


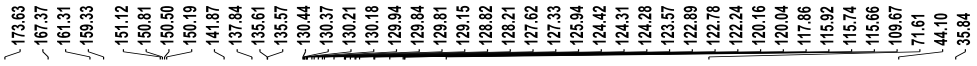


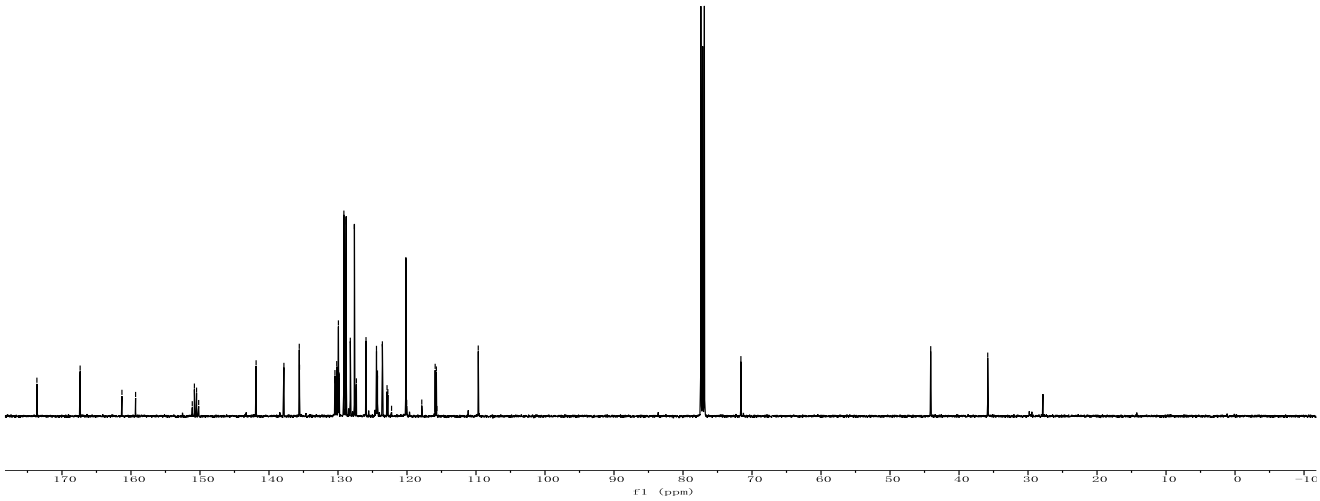


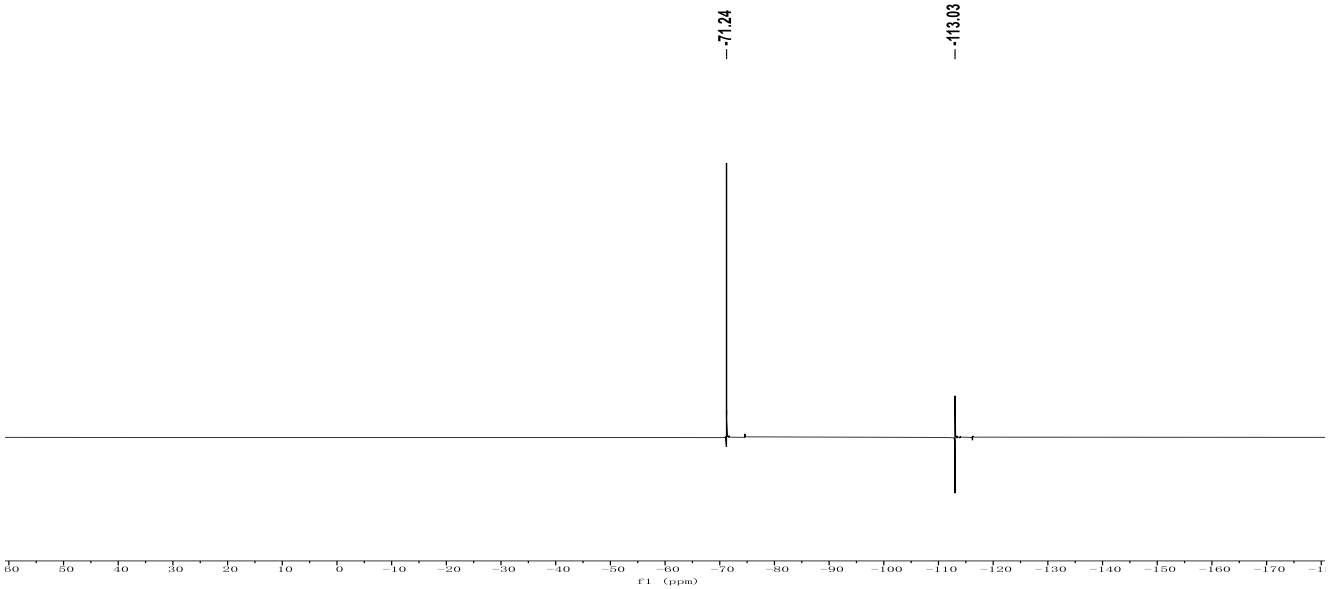
3ka

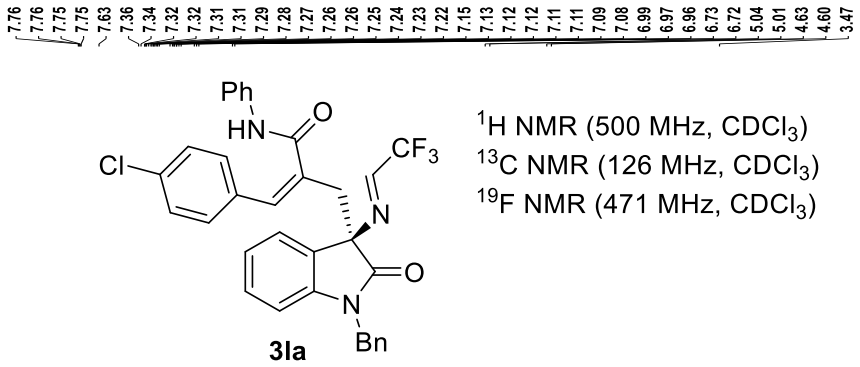
^{1}H NMR (500 MHz, $CDCl_3$)
^{13}C NMR (126 MHz, $CDCl_3$)
^{19}F NMR (471 MHz, $CDCl_3$)





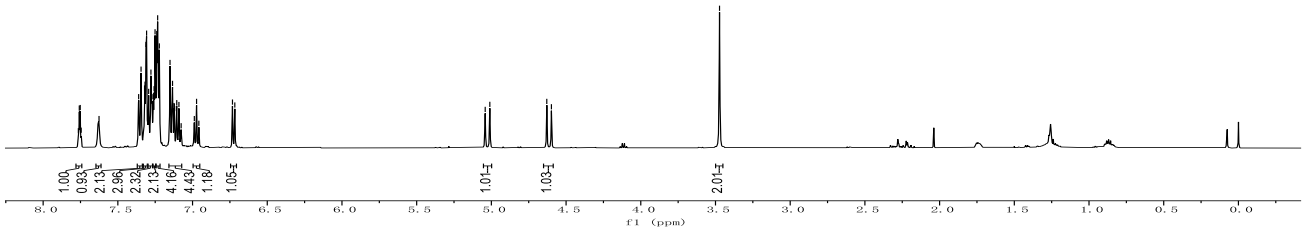


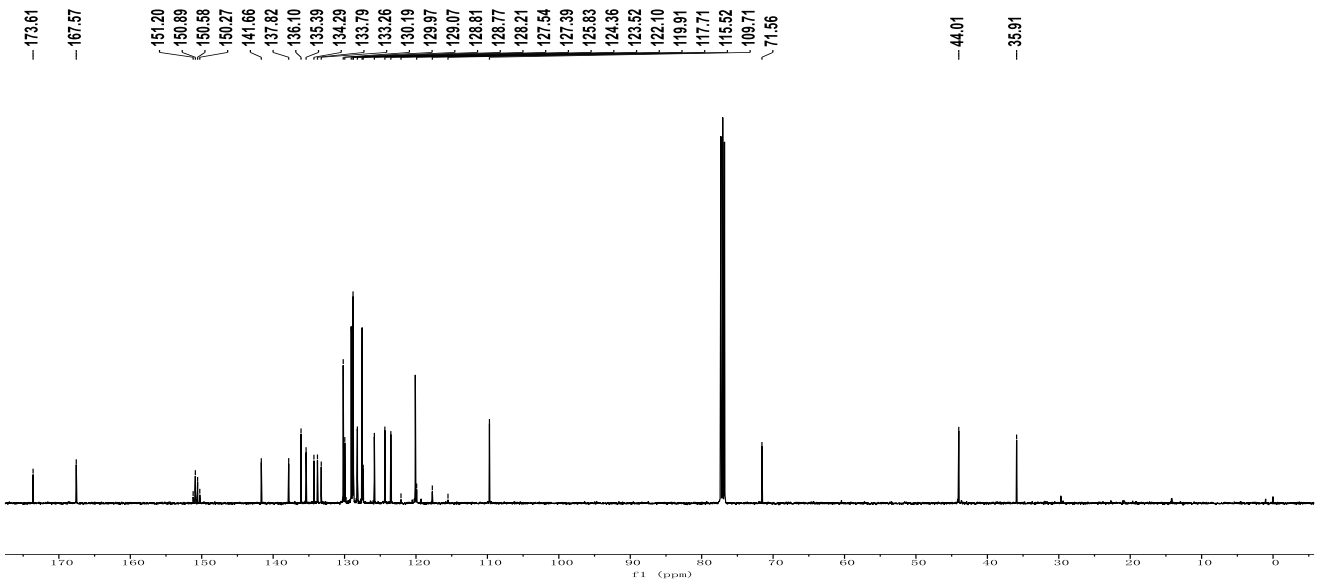


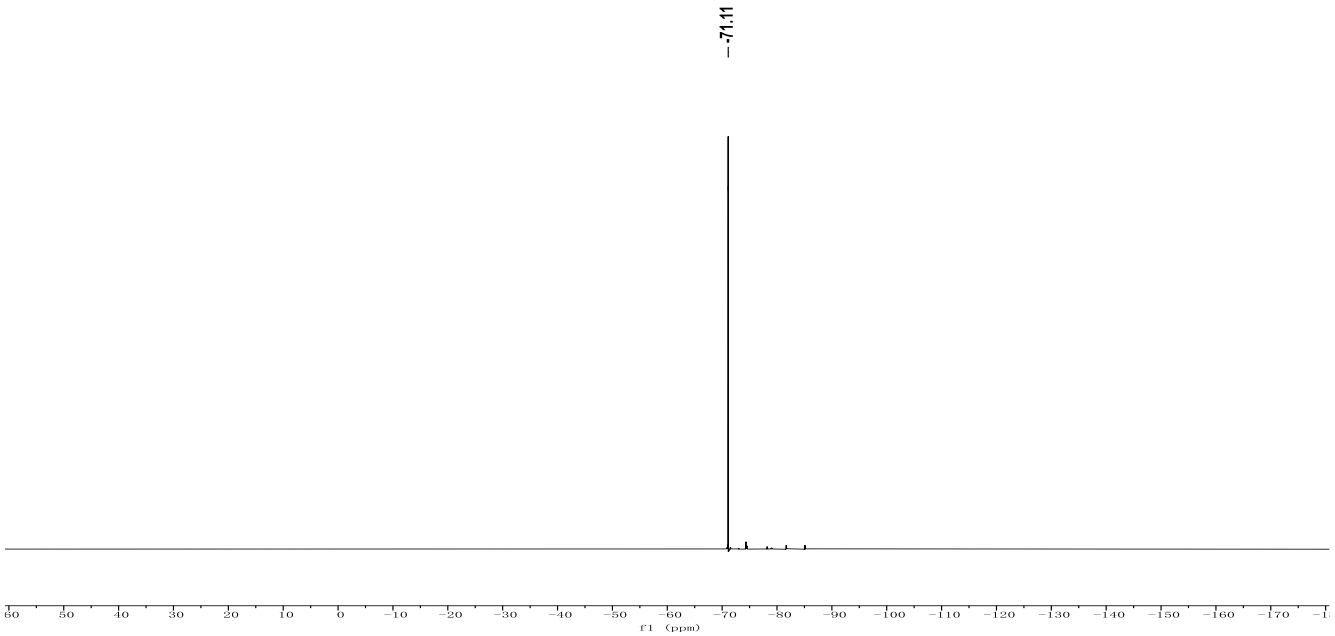


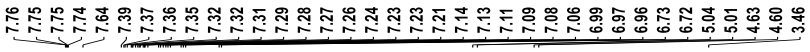
3la

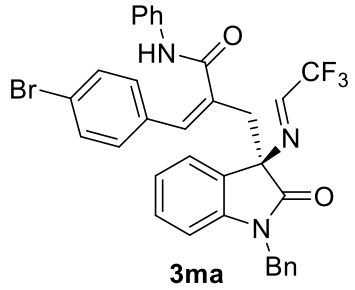
^{1}H NMR (500 MHz, $CDCl_3$)
^{13}C NMR (126 MHz, $CDCl_3$)
^{19}F NMR (471 MHz, $CDCl_3$)





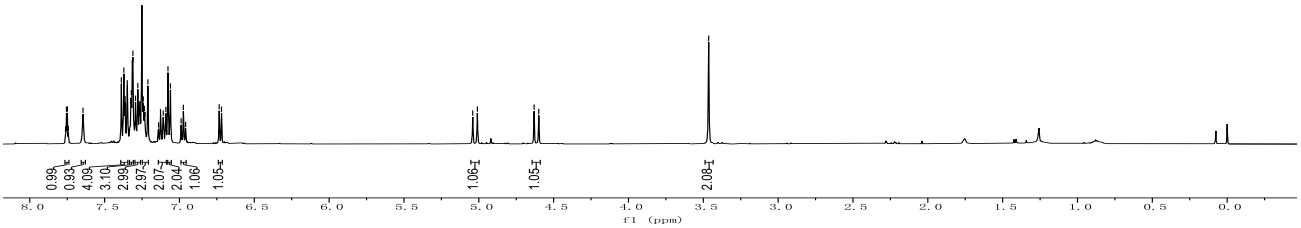


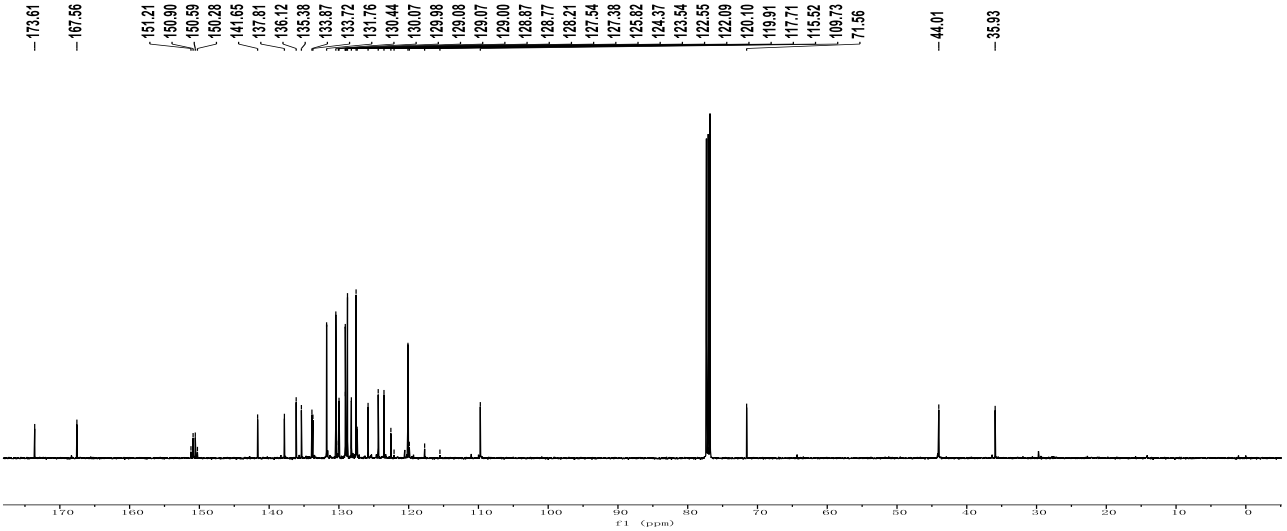


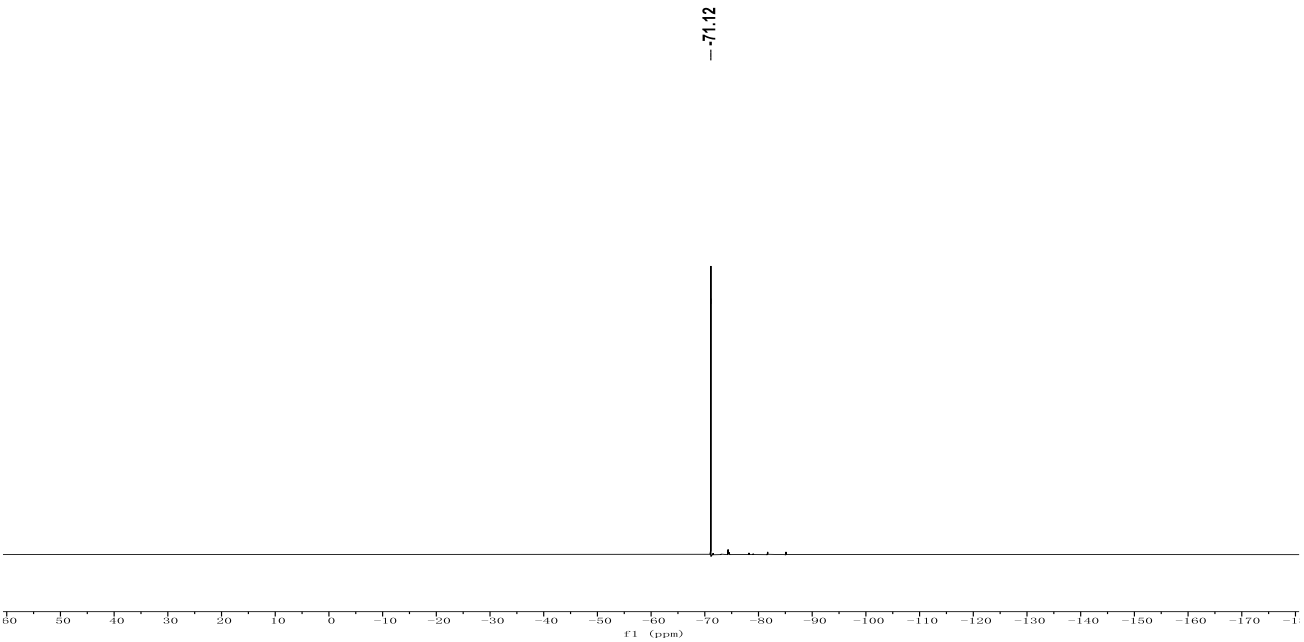


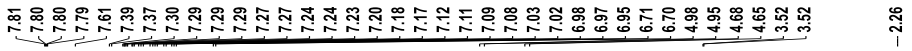
3ma

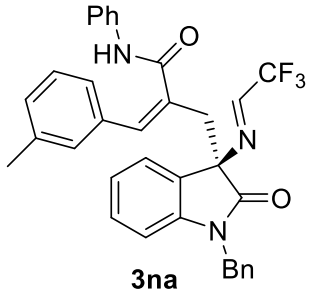
^{1}H NMR (500 MHz, $CDCl_3$)
^{13}C NMR (126 MHz, $CDCl_3$)
^{19}F NMR (471 MHz, $CDCl_3$)





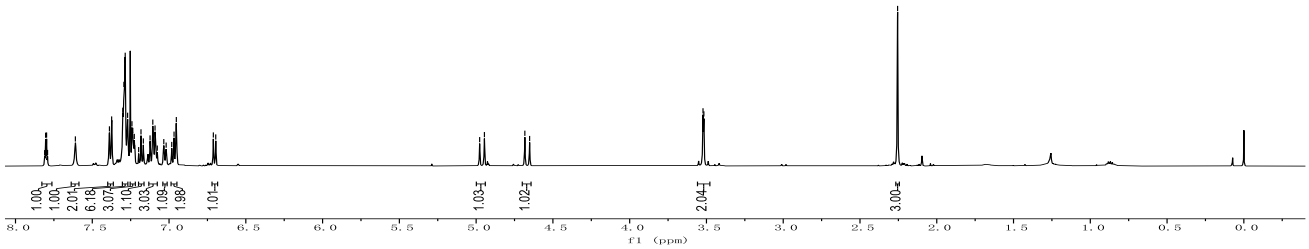


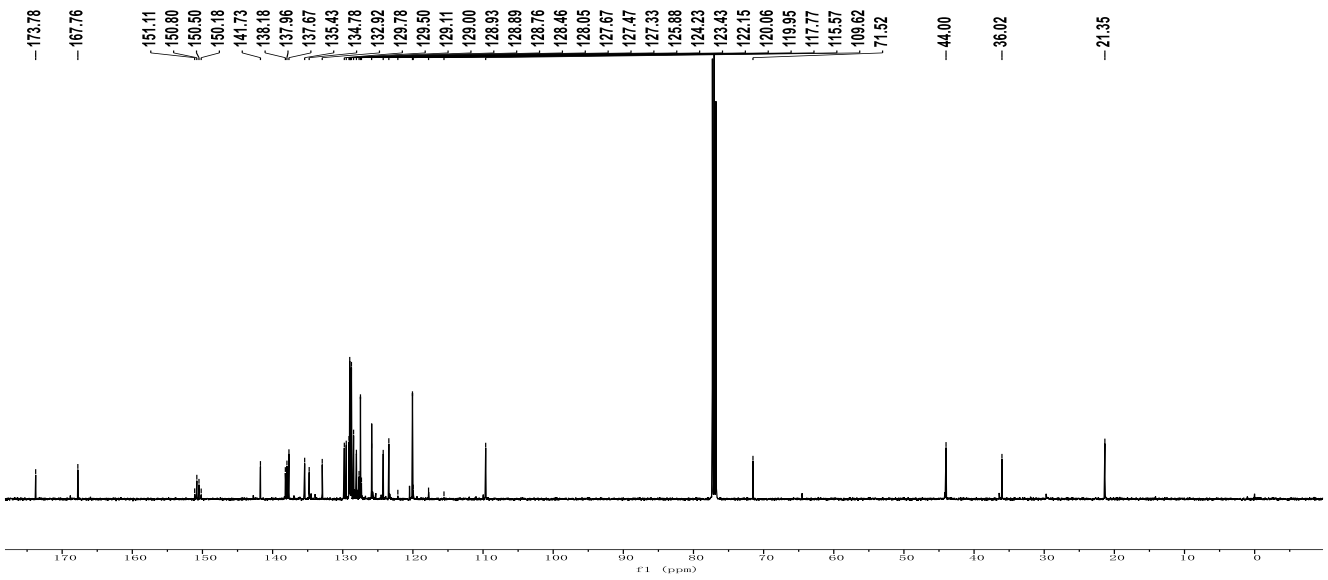


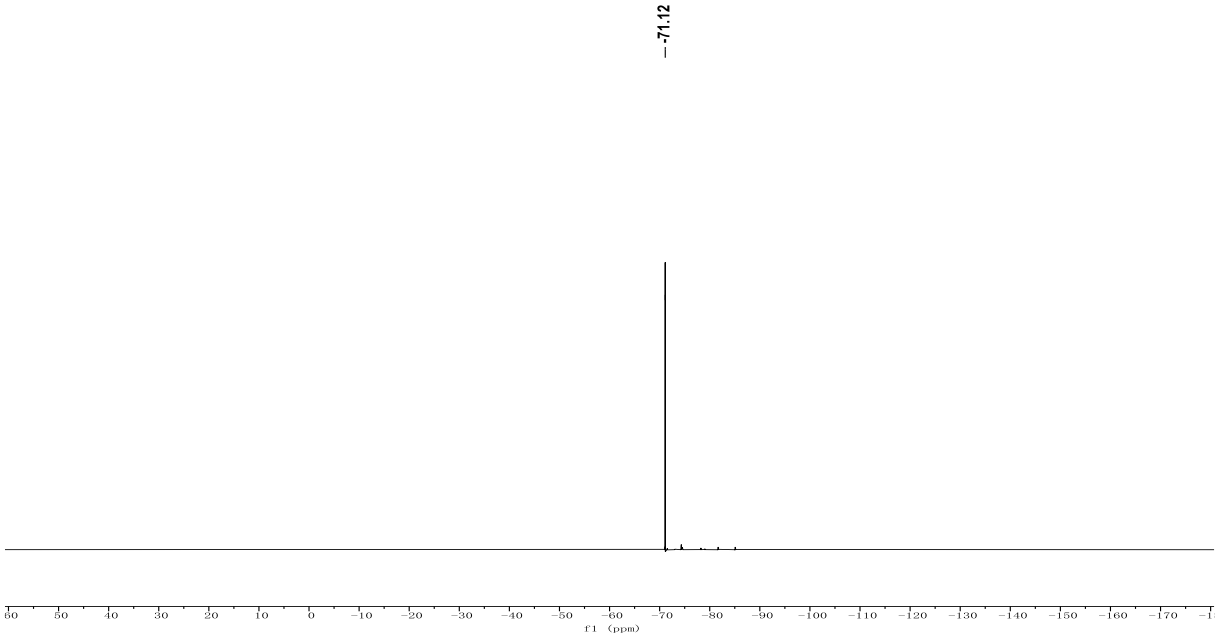


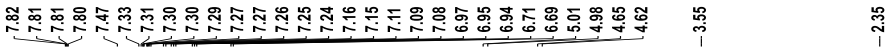
3na

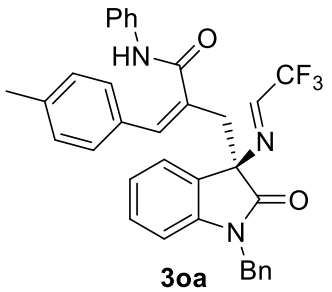
^{1}H NMR (500 MHz, $CDCl_3$)
^{13}C NMR (126 MHz, $CDCl_3$)
^{19}F NMR (471 MHz, $CDCl_3$)





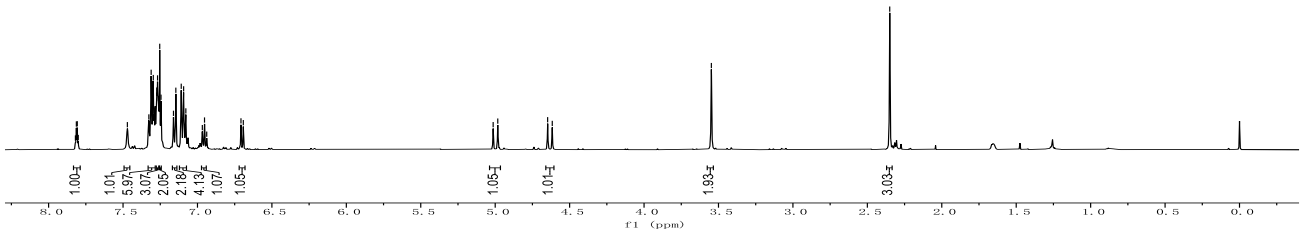


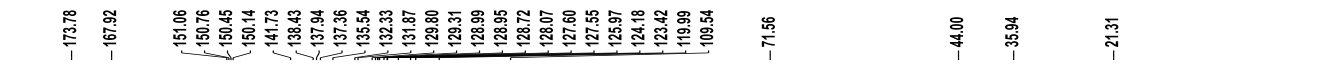


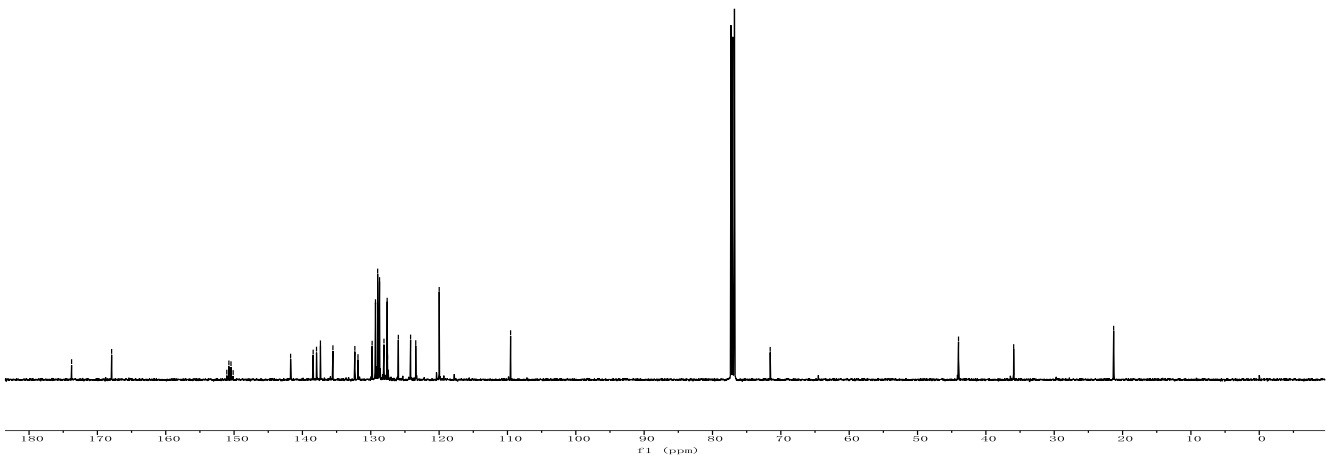


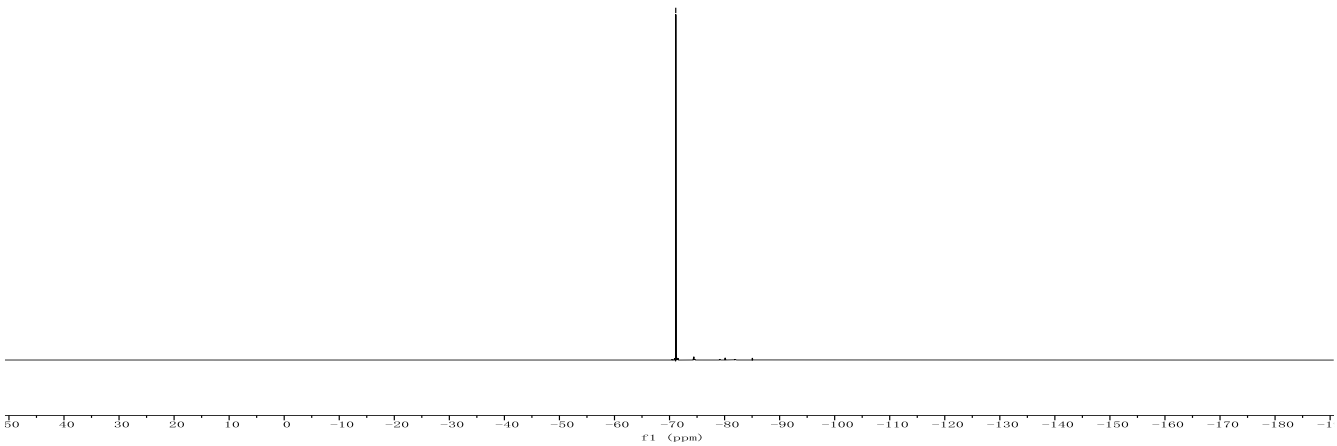
3oa

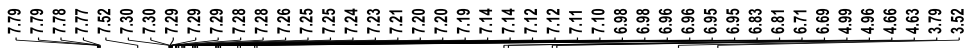
^{1}H NMR (500 MHz, $CDCl_3$)
^{13}C NMR (126 MHz, $CDCl_3$)
^{19}F NMR (471 MHz, $CDCl_3$)

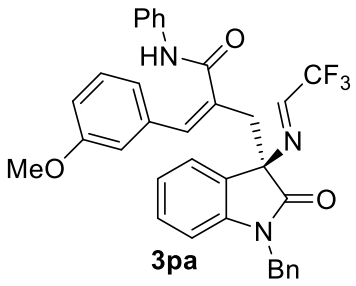






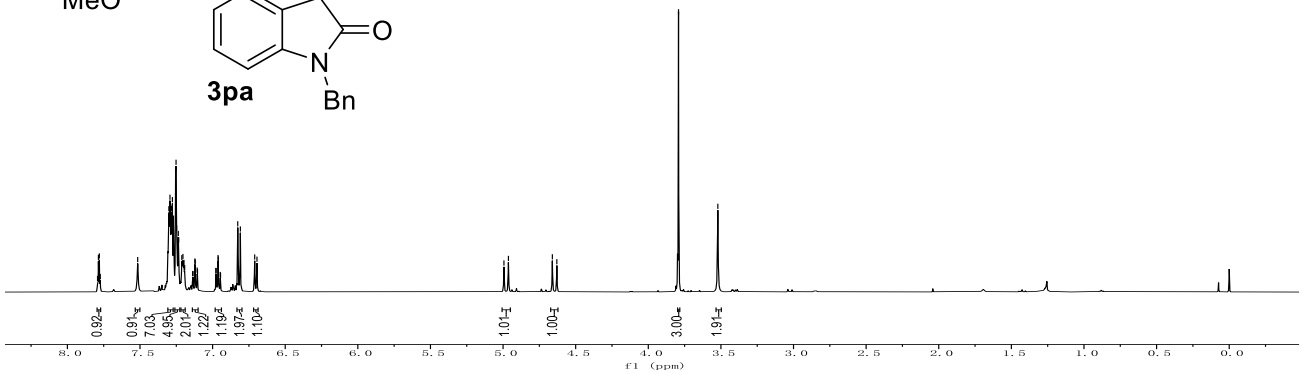


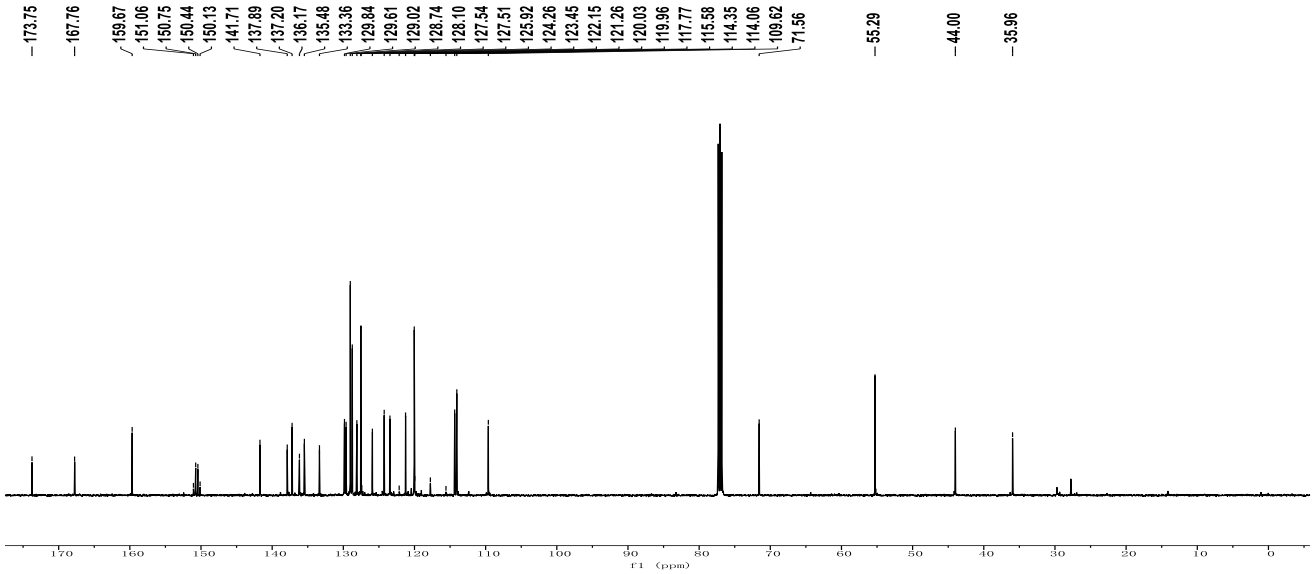


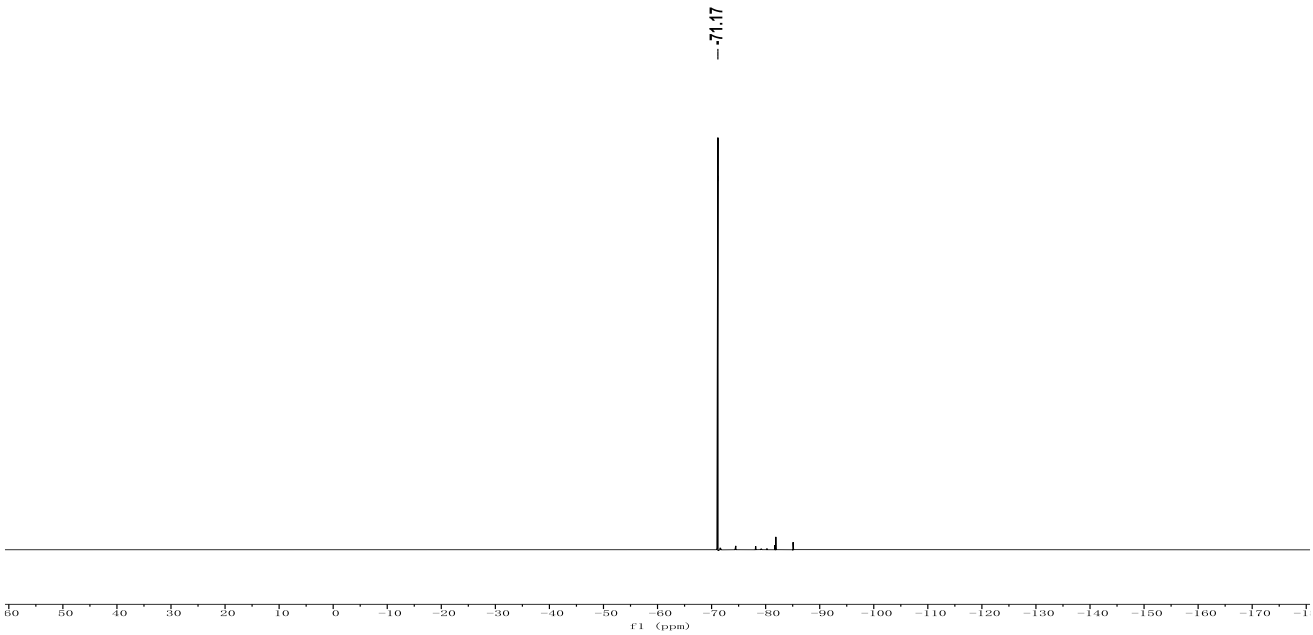


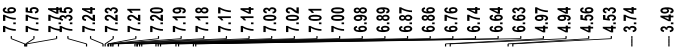
3pa

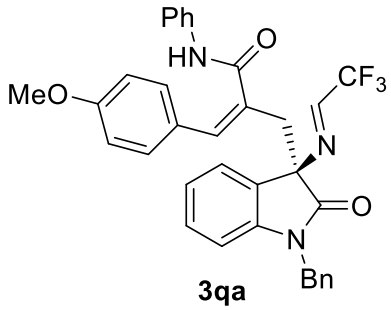
^{1}H NMR (500 MHz, $CDCl_3$)
^{13}C NMR (126 MHz, $CDCl_3$)
^{19}F NMR (471 MHz, $CDCl_3$)





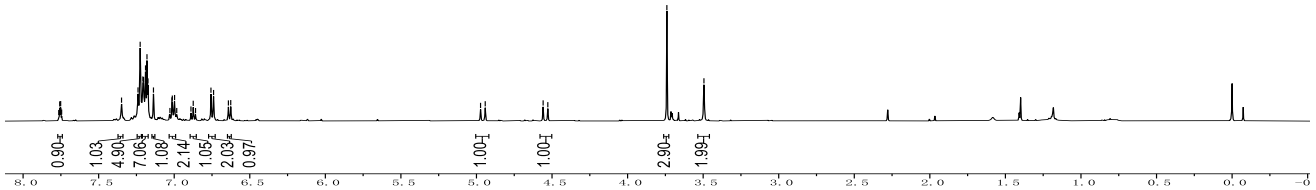


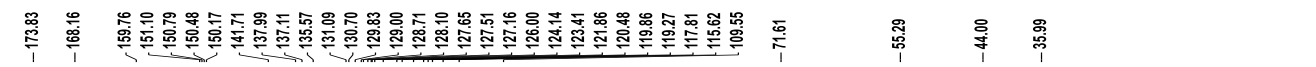


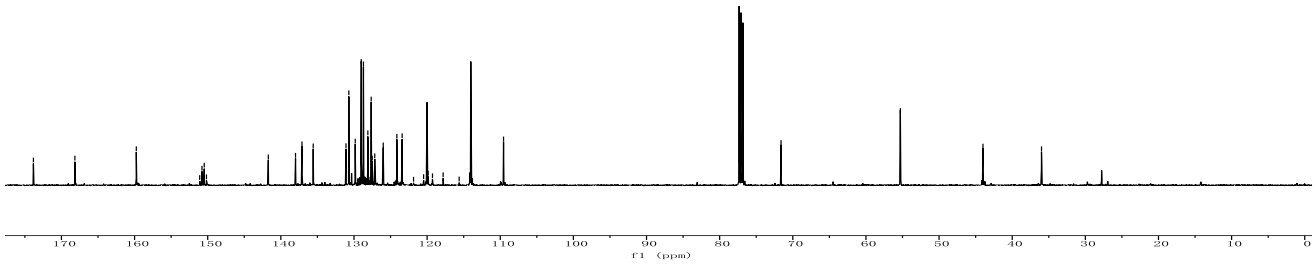


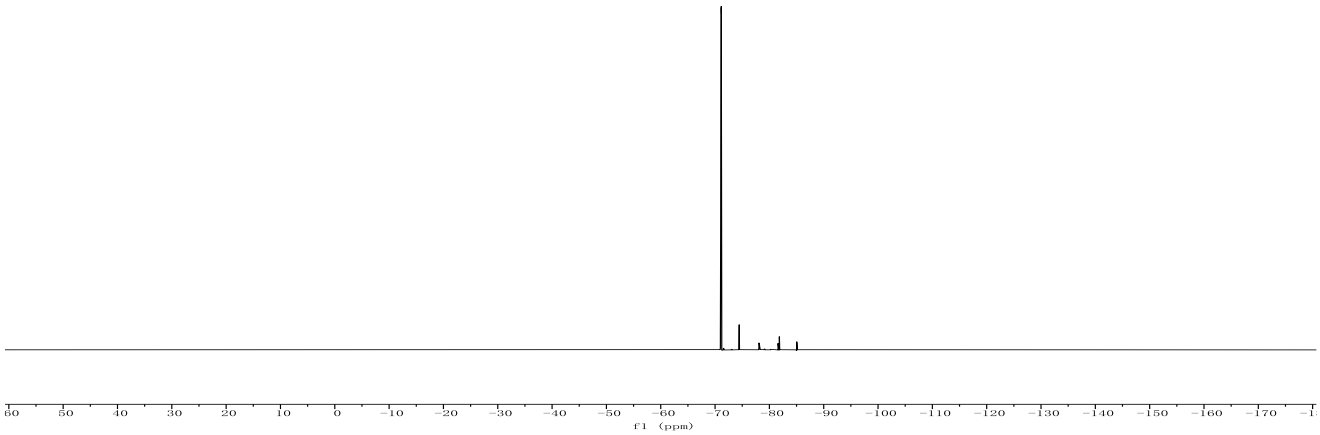
3qa

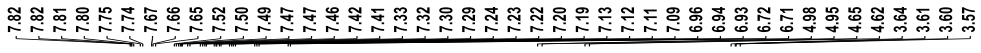
^{1}H NMR (500 MHz, $CDCl_3$)
^{13}C NMR (126 MHz, $CDCl_3$)
^{19}F NMR (471 MHz, $CDCl_3$)

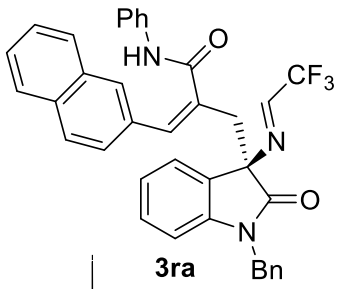






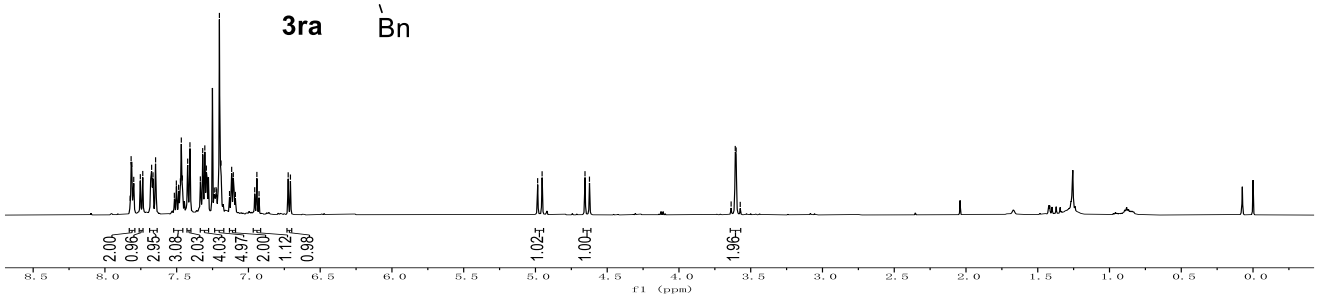


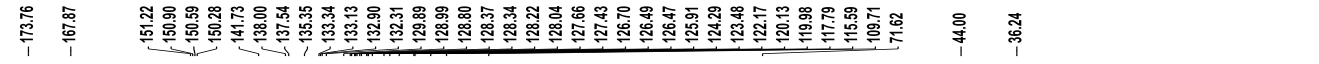


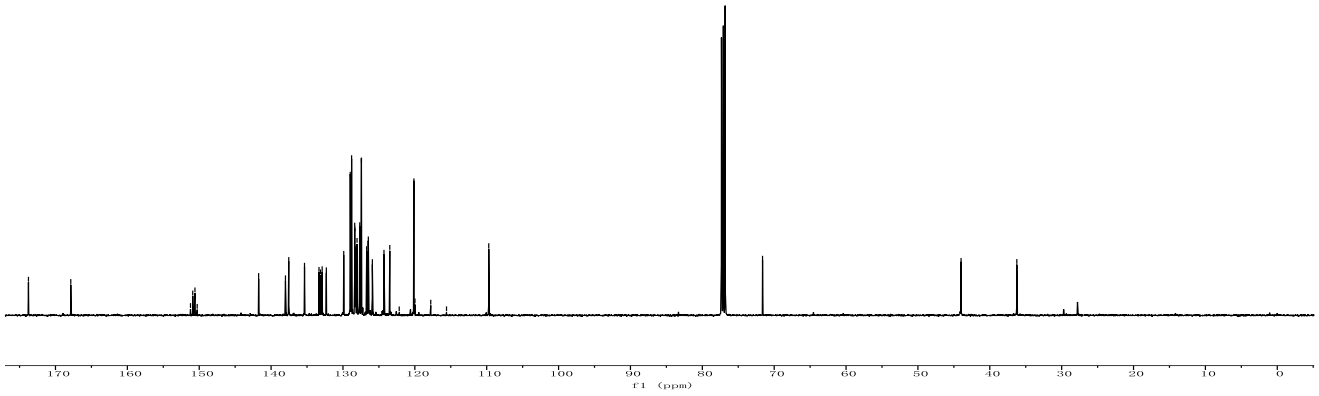


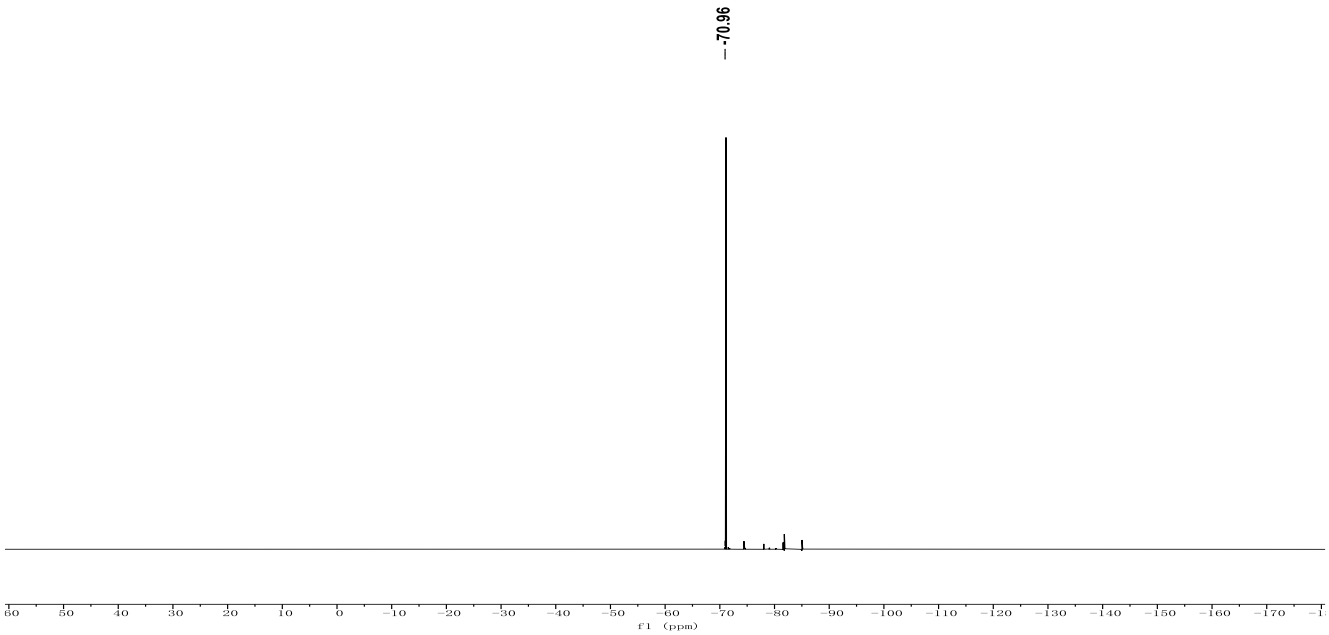
3ra

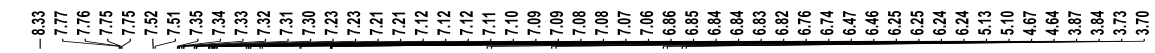
^{1}H NMR (500 MHz, $CDCl_3$)
^{13}C NMR (126 MHz, $CDCl_3$)
^{19}F NMR (471 MHz, $CDCl_3$)

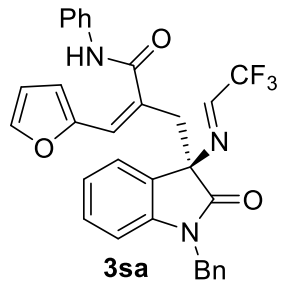






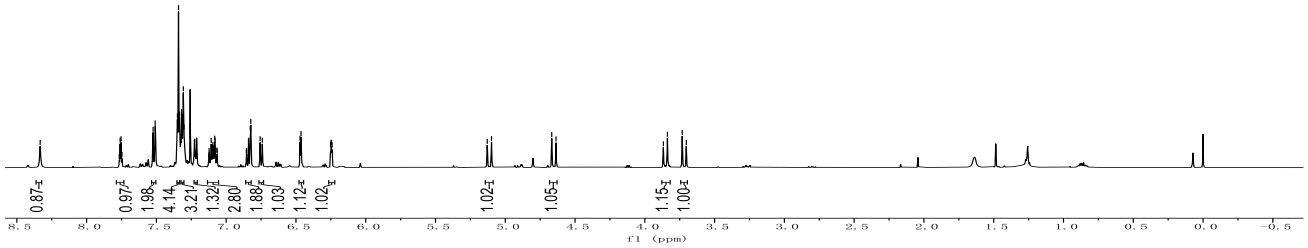


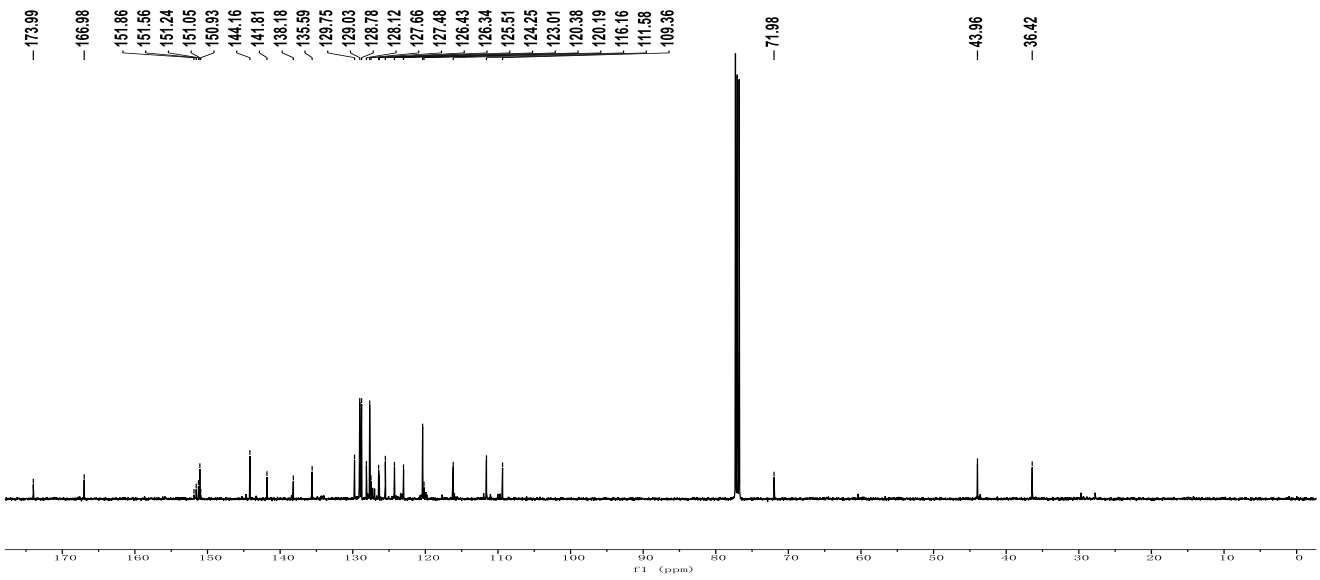


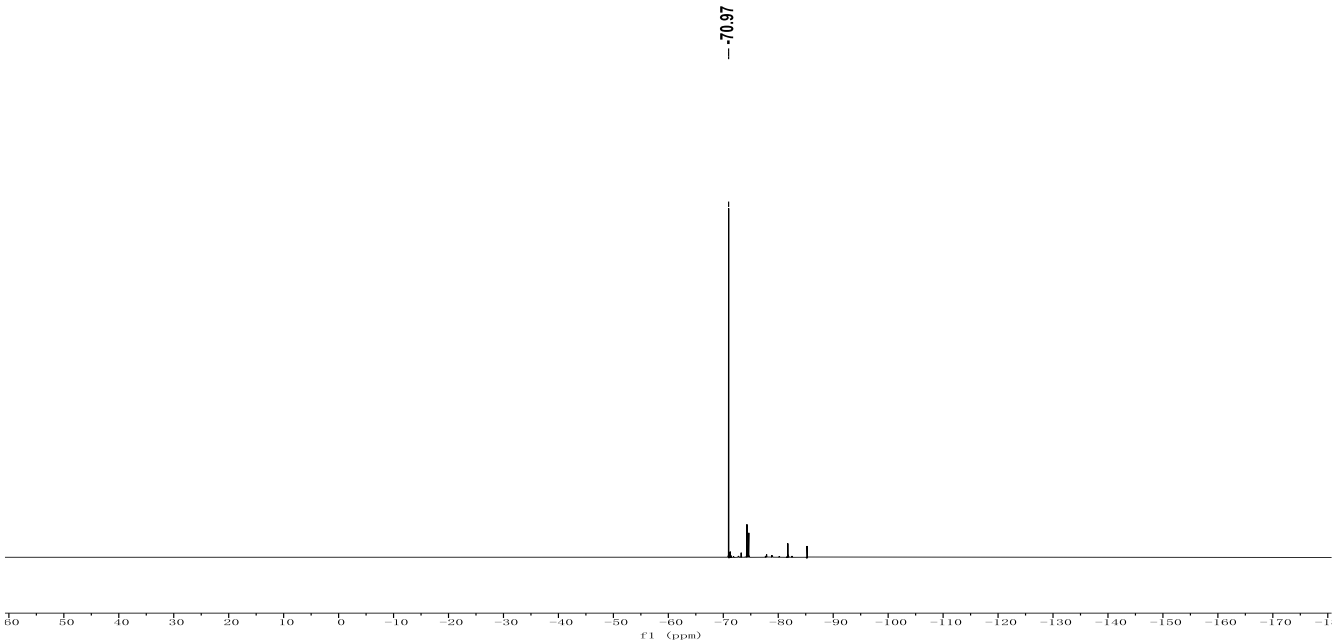


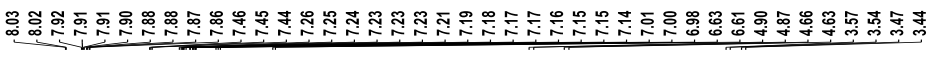
3sa

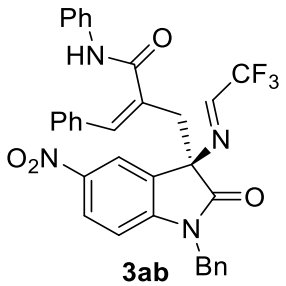
^{1}H NMR (500 MHz, $CDCl_3$)
^{13}C NMR (126 MHz, $CDCl_3$)
^{19}F NMR (471 MHz, $CDCl_3$)





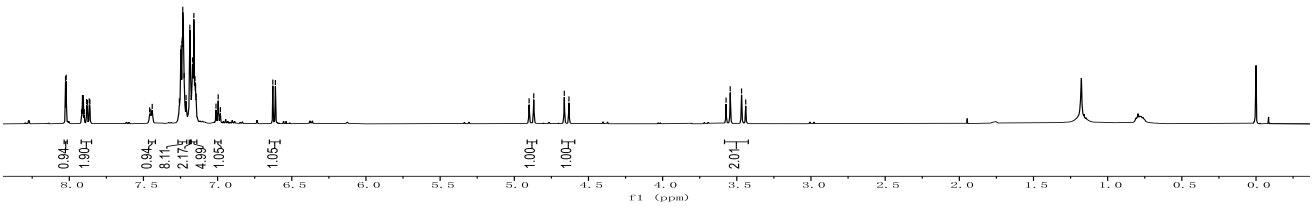


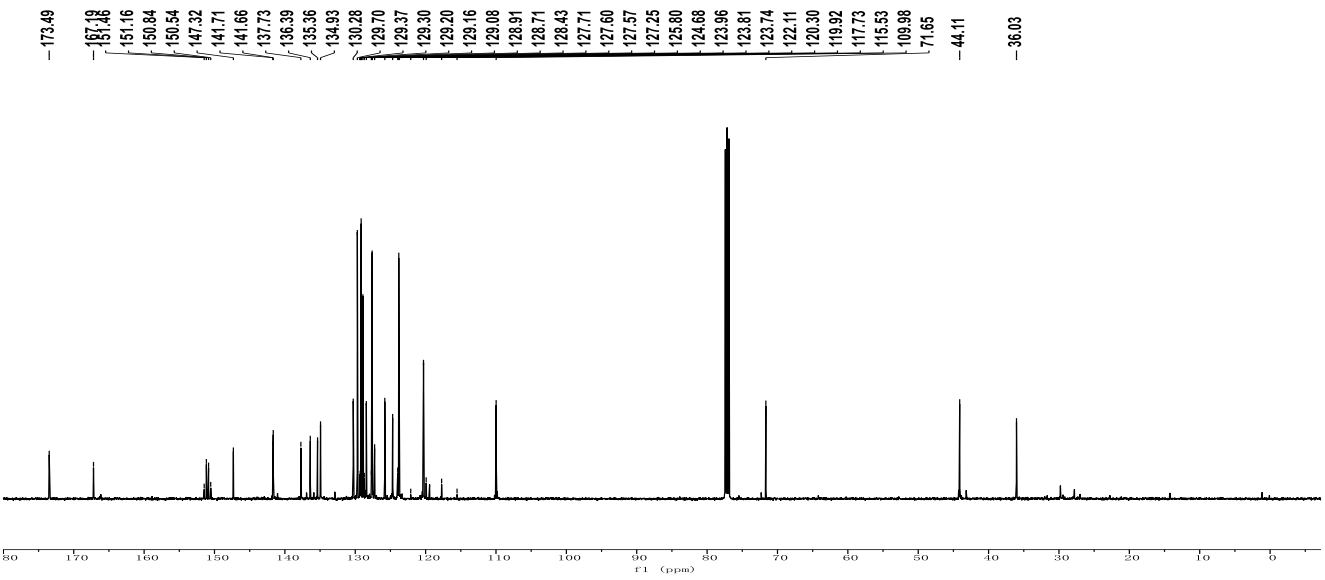


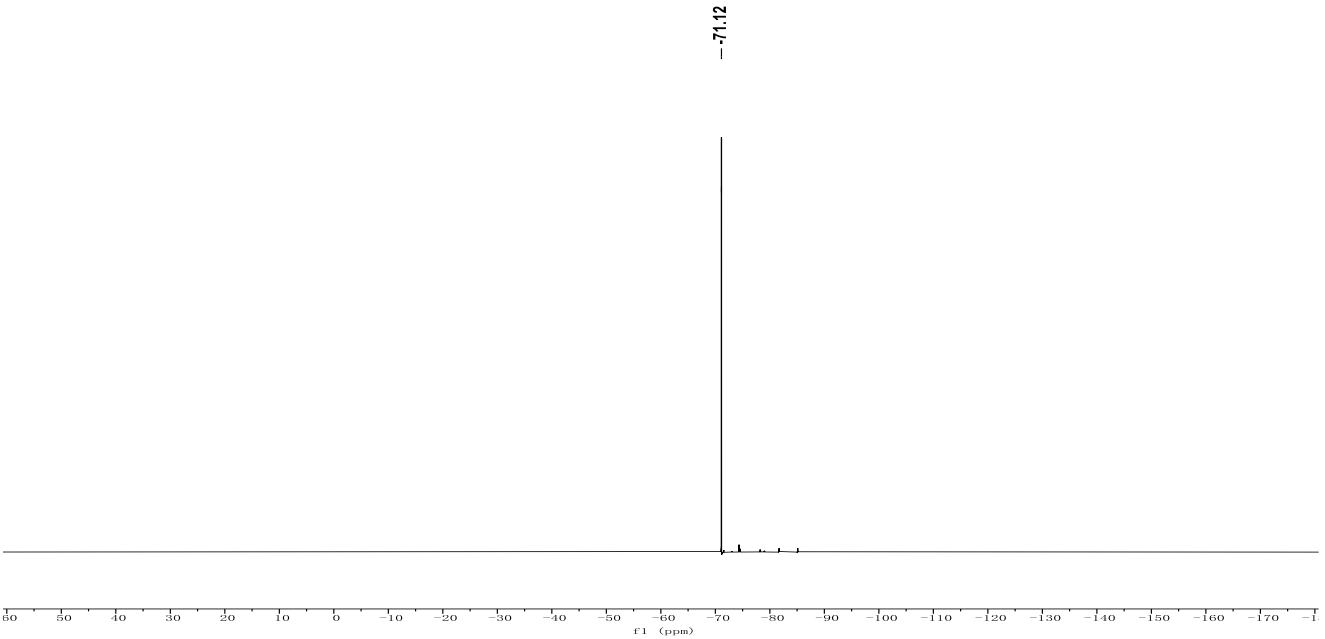


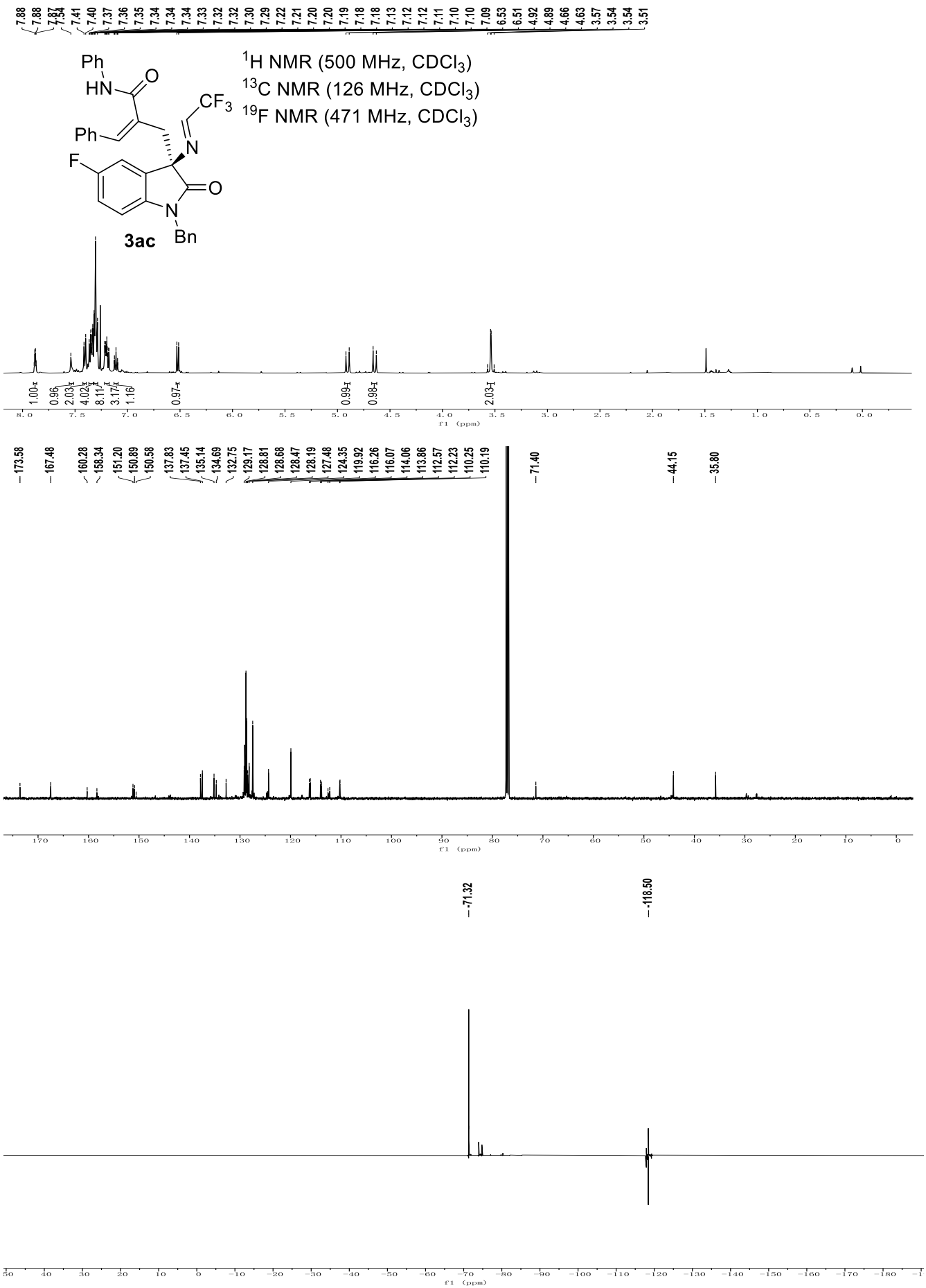
3ab

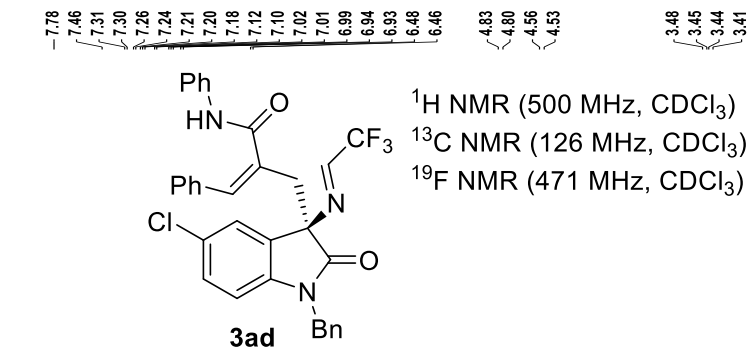
^{1}H NMR (500 MHz, $CDCl_3$)
^{13}C NMR (126 MHz, $CDCl_3$)
^{19}F NMR (471 MHz, $CDCl_3$)





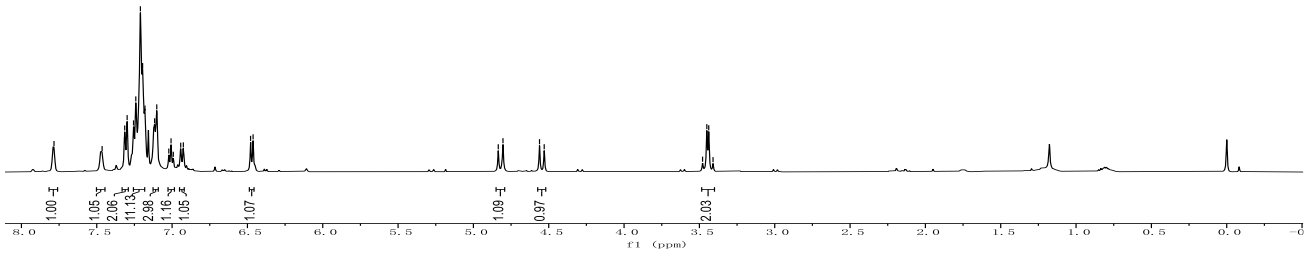


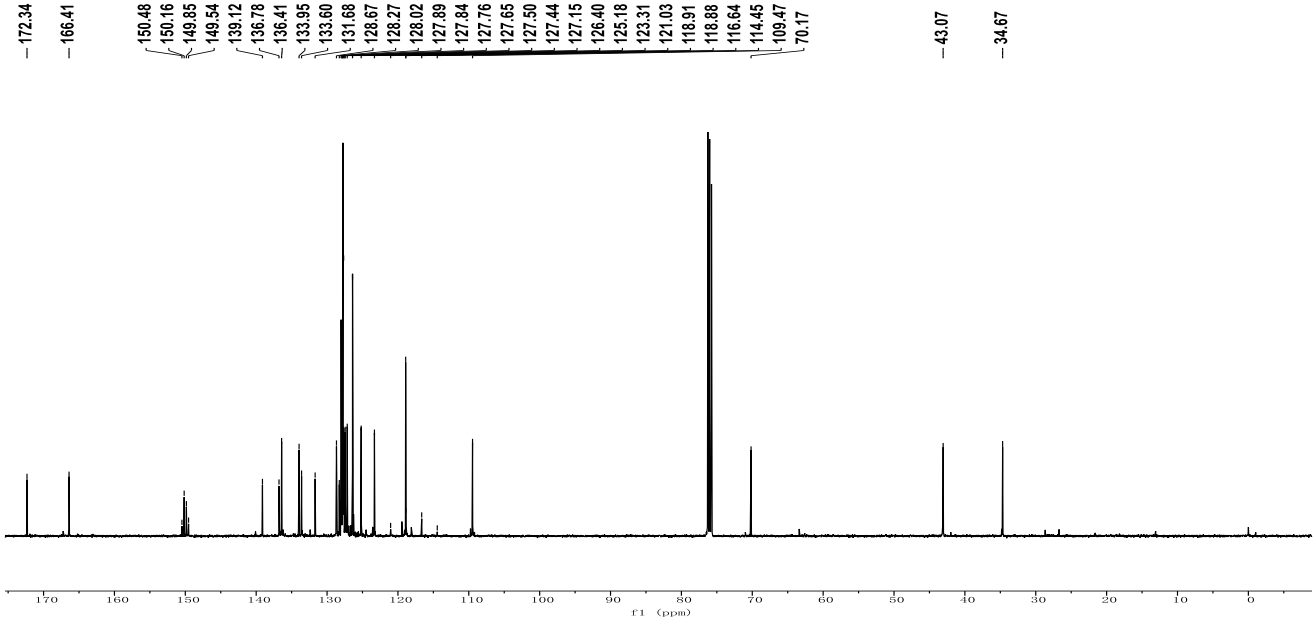

7.88 7.88 7.87 7.84 7.41 7.40 7.37 7.36 7.35 7.34 7.34 7.34 7.33 7.32 7.32 7.30 7.29 7.22 7.21 7.20 7.20 7.19 7.18 7.18 7.13 7.12 7.12 7.11 7.10 7.10 7.09 6.53 6.51 4.92 4.89 4.66 4.63 3.57 3.54 3.54 3.51
Ph
HN
O
CF3
Ph
N
F
O
N
Bn
3ac
1H NMR (500 MHz, CDCl3)
13C NMR (126 MHz, CDCl3)
19F NMR (471 MHz, CDCl3)
1.00 0.96 2.03 4.02 8.11 3.17 1.16 0.97 0.99 0.98 2.03
f1 (ppm)
173.58 167.48 160.28 158.34 151.20 150.89 150.58 137.83 137.45 135.14 134.69 132.75 129.17 128.81 128.68 128.47 128.19 127.48 124.35 119.92 116.26 116.07 114.06 113.86 112.57 112.23 110.25 110.19 71.40 44.15 35.80
f1 (ppm)
-71.32 -118.50
f1 (ppm)

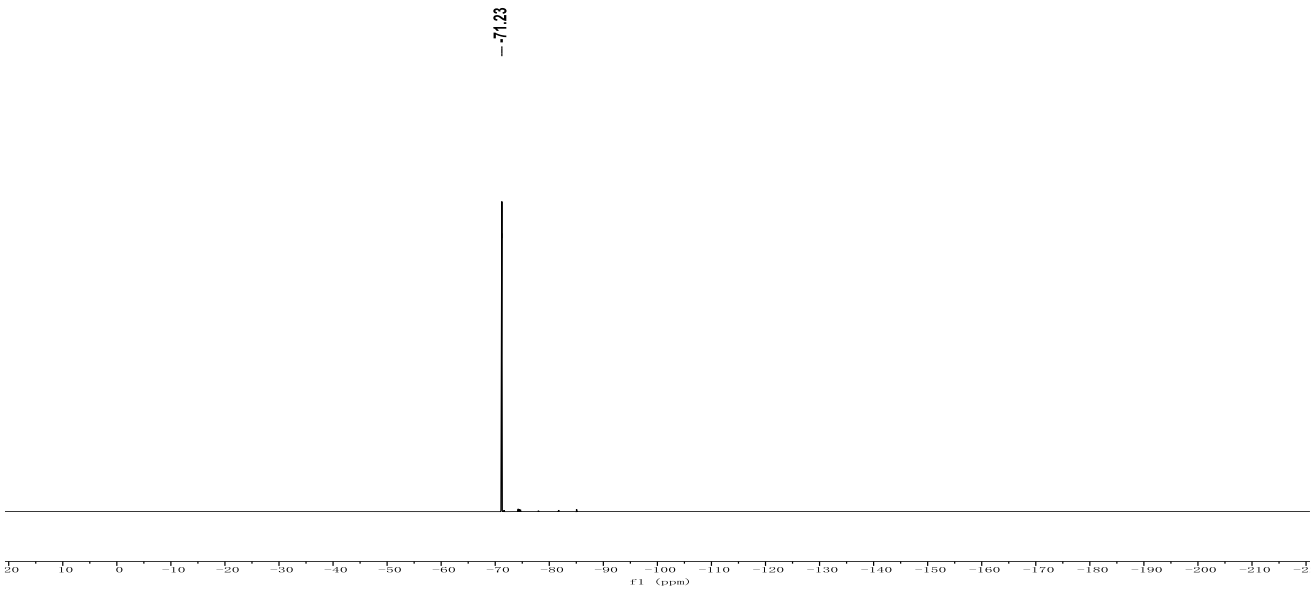


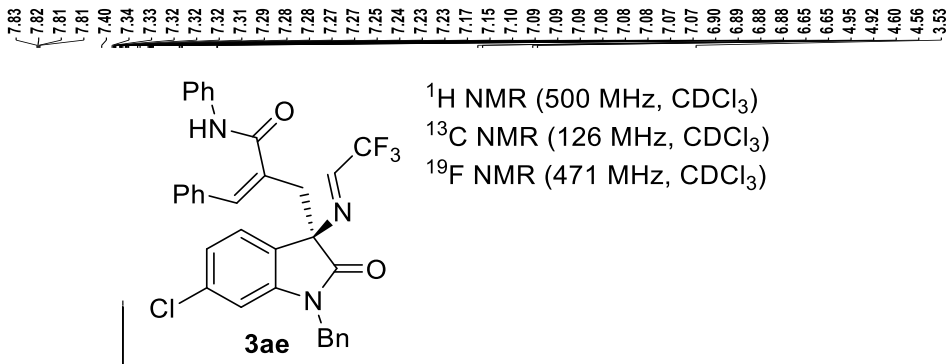
3ad

^{1}H NMR (500 MHz, $CDCl_3$)
^{13}C NMR (126 MHz, $CDCl_3$)
^{19}F NMR (471 MHz, $CDCl_3$)

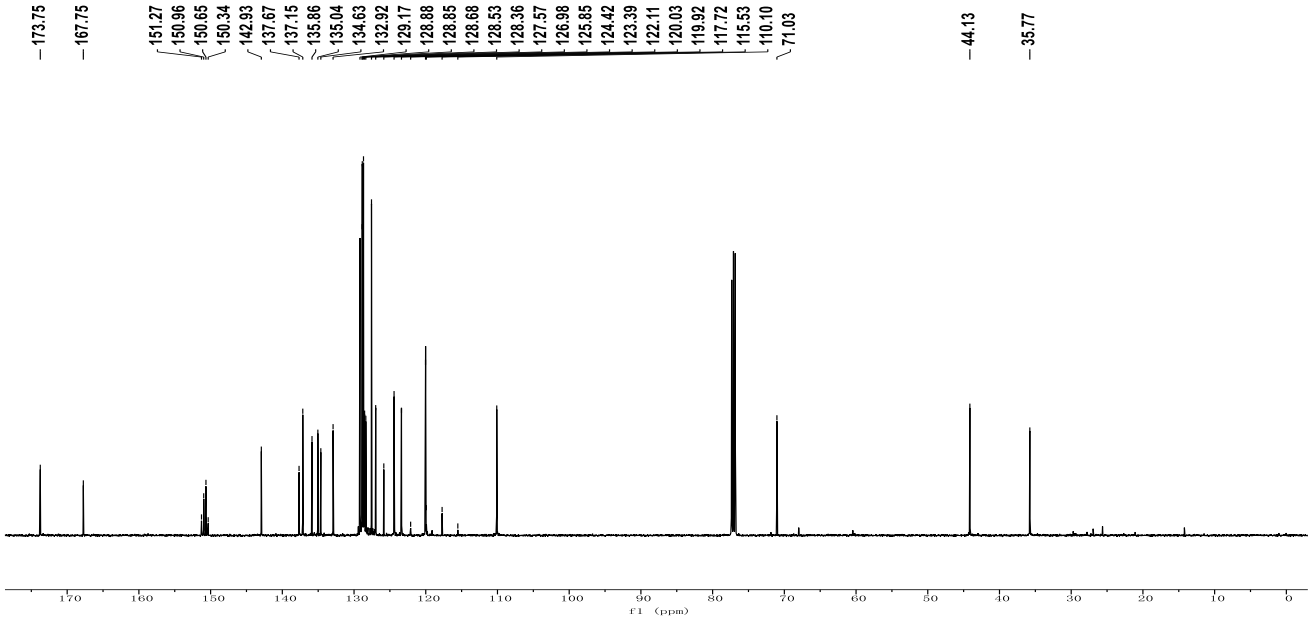


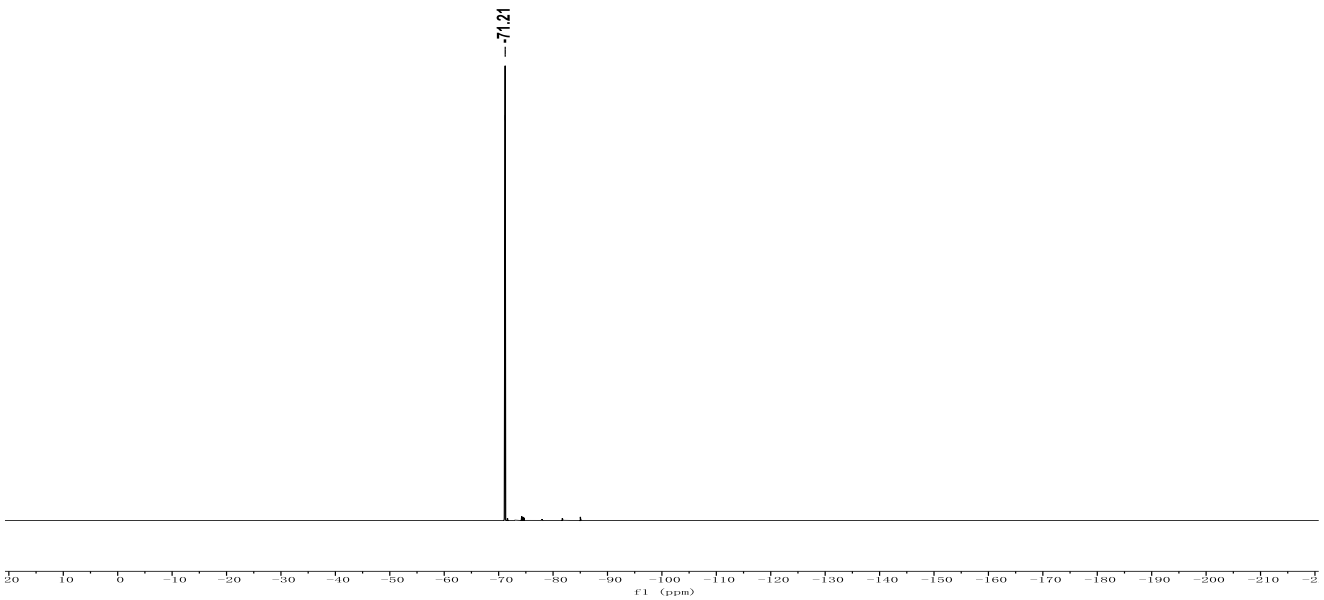




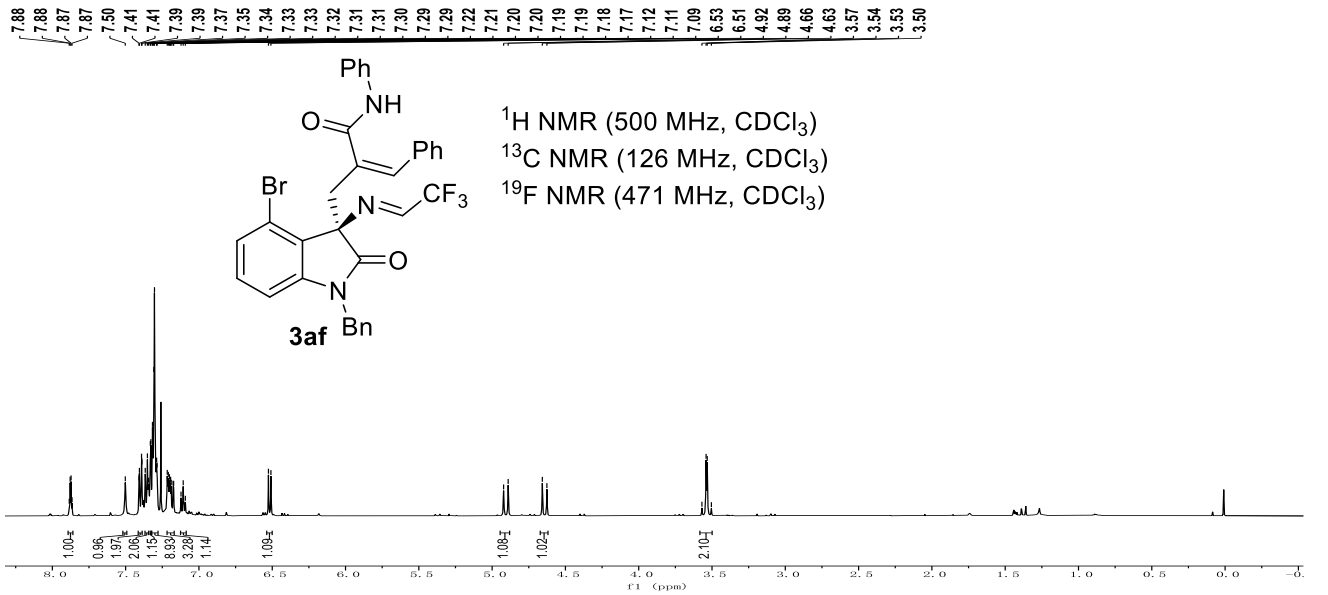


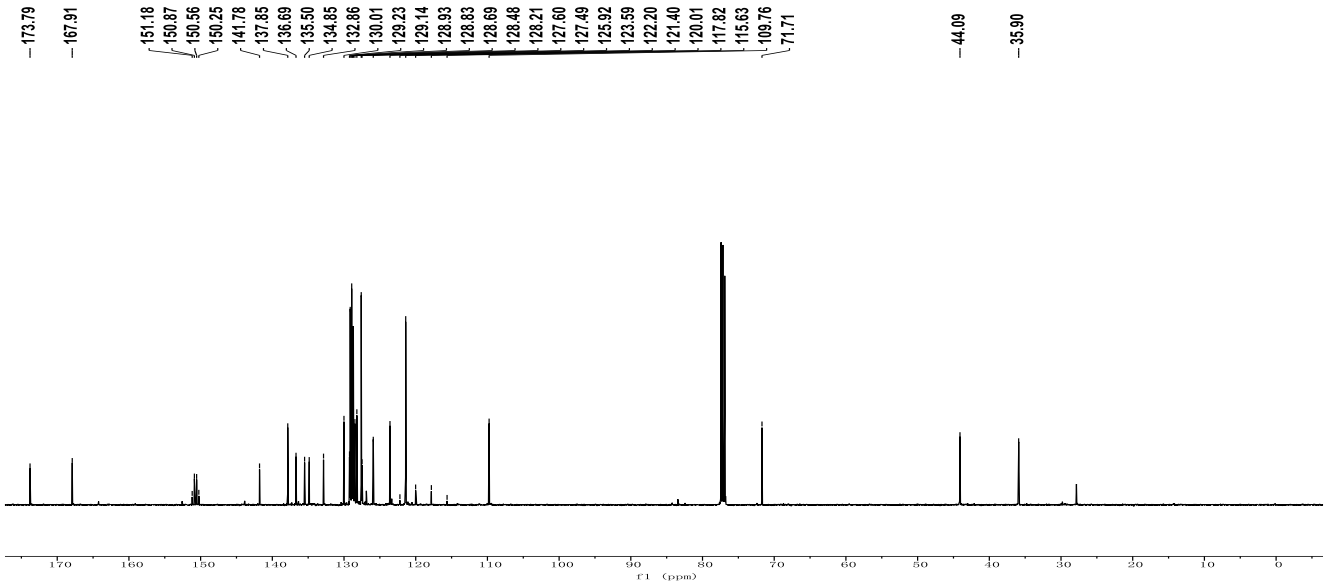
^{1}H NMR (500 MHz, $CDCl_3$)
^{13}C NMR (126 MHz, $CDCl_3$)
^{19}F NMR (471 MHz, $CDCl_3$)

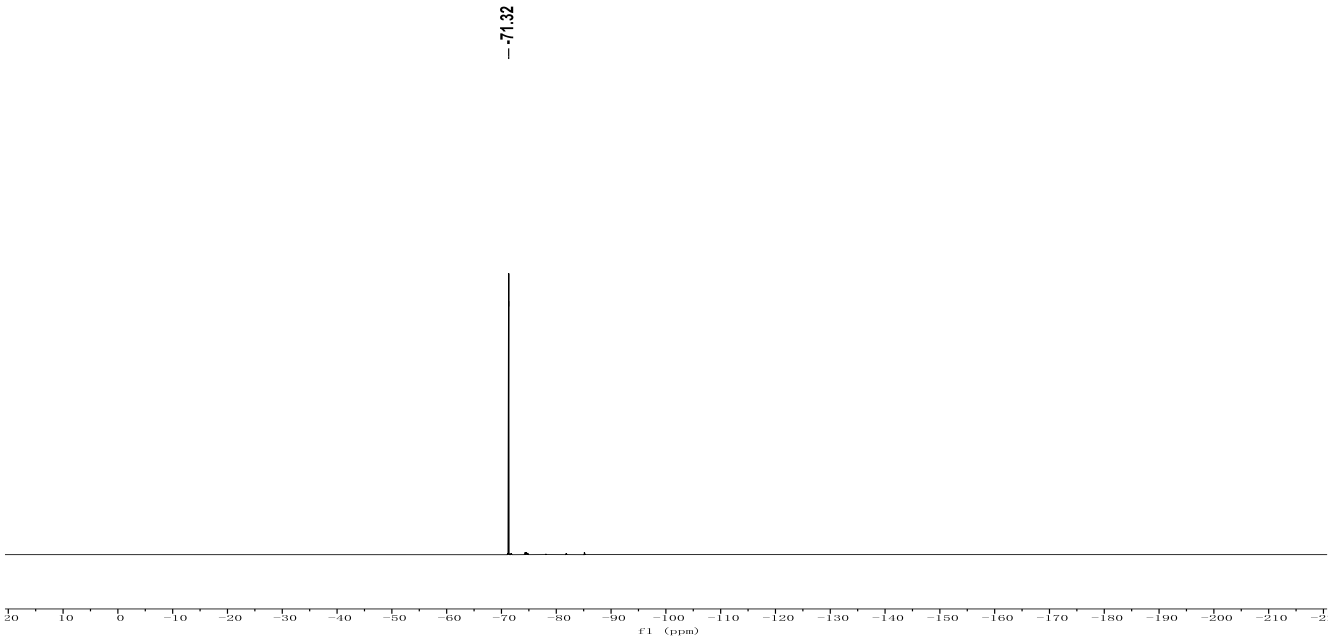


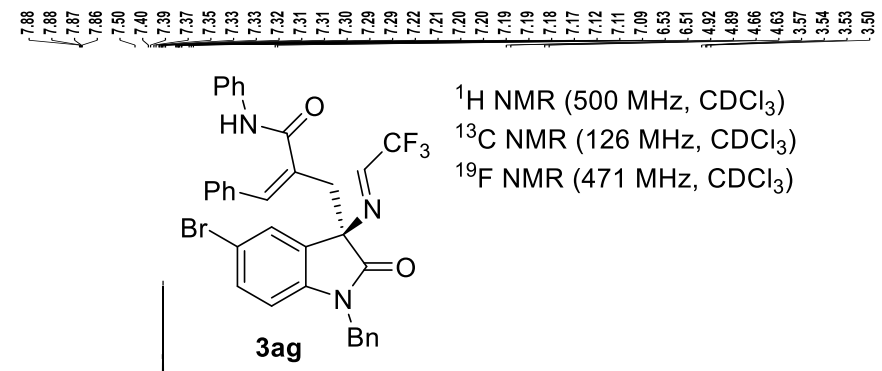


^{1}H NMR (500 MHz, $CDCl_3$)
^{13}C NMR (126 MHz, $CDCl_3$)
^{19}F NMR (471 MHz, $CDCl_3$)

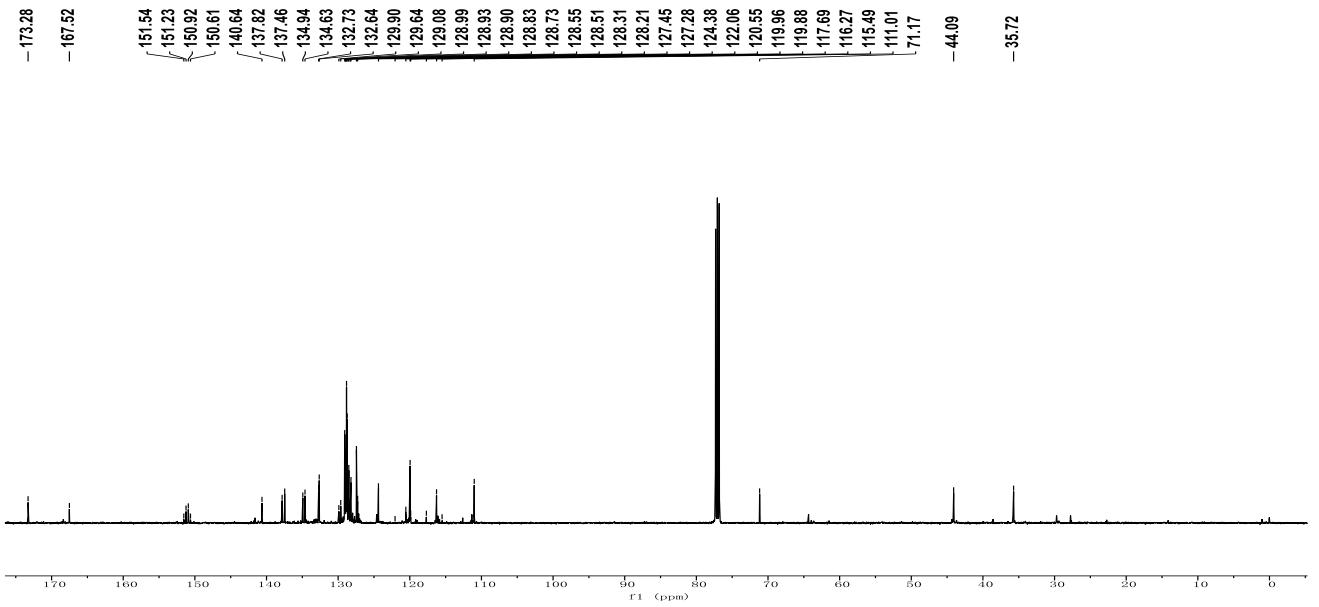


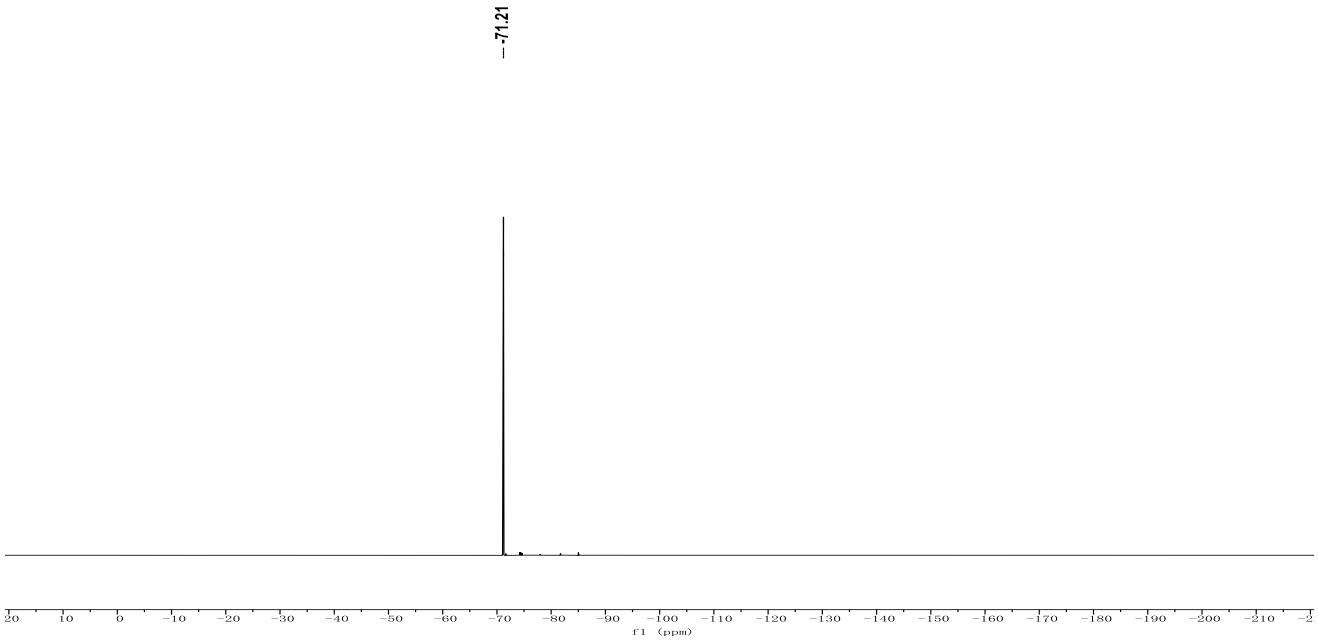






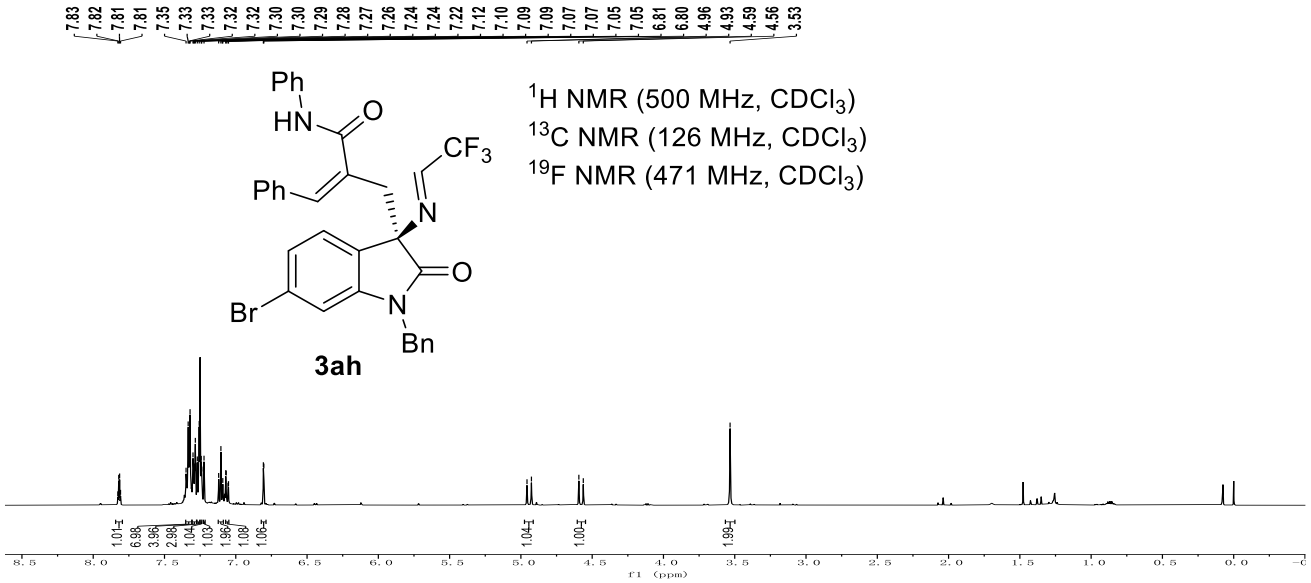
^{1}H NMR (500 MHz, $CDCl_3$)
^{13}C NMR (126 MHz, $CDCl_3$)
^{19}F NMR (471 MHz, $CDCl_3$)

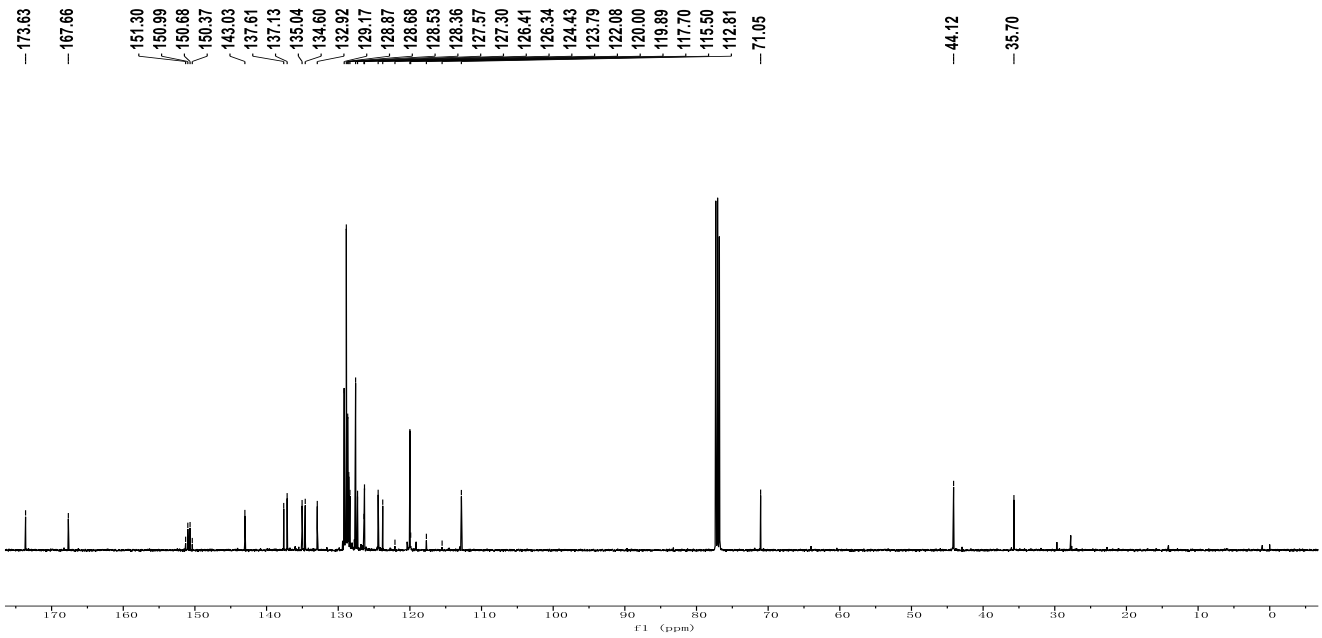


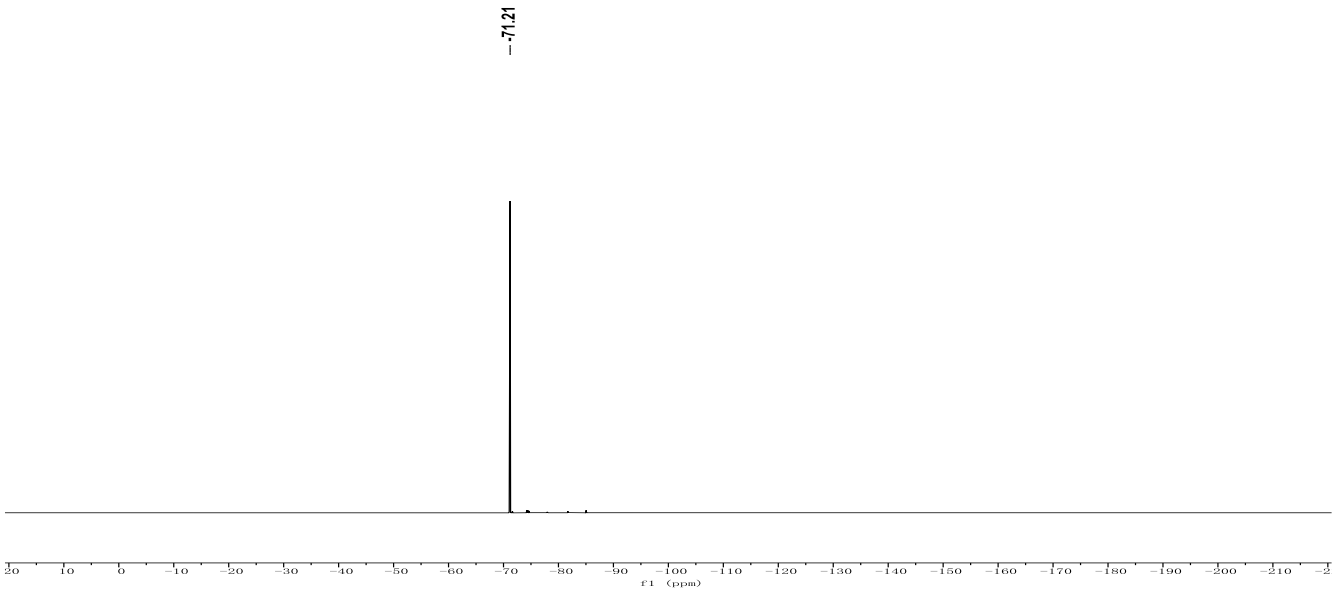


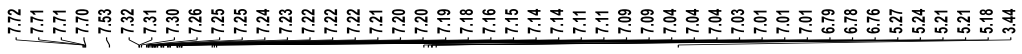
3ah

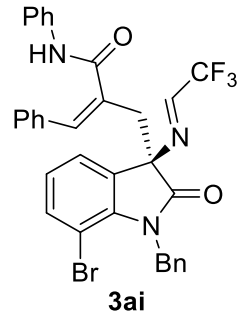
^{1}H NMR (500 MHz, $CDCl_3$)
^{13}C NMR (126 MHz, $CDCl_3$)
^{19}F NMR (471 MHz, $CDCl_3$)





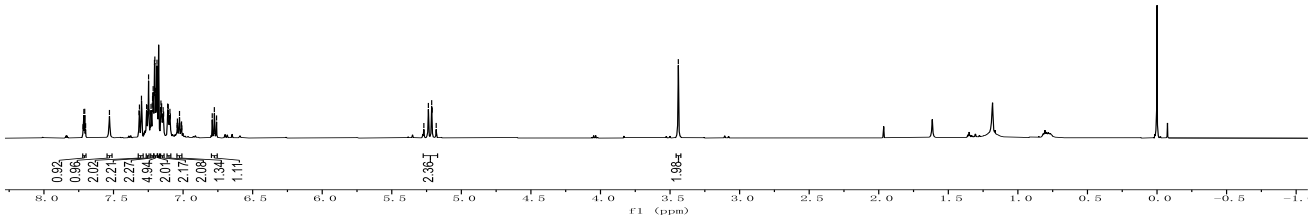


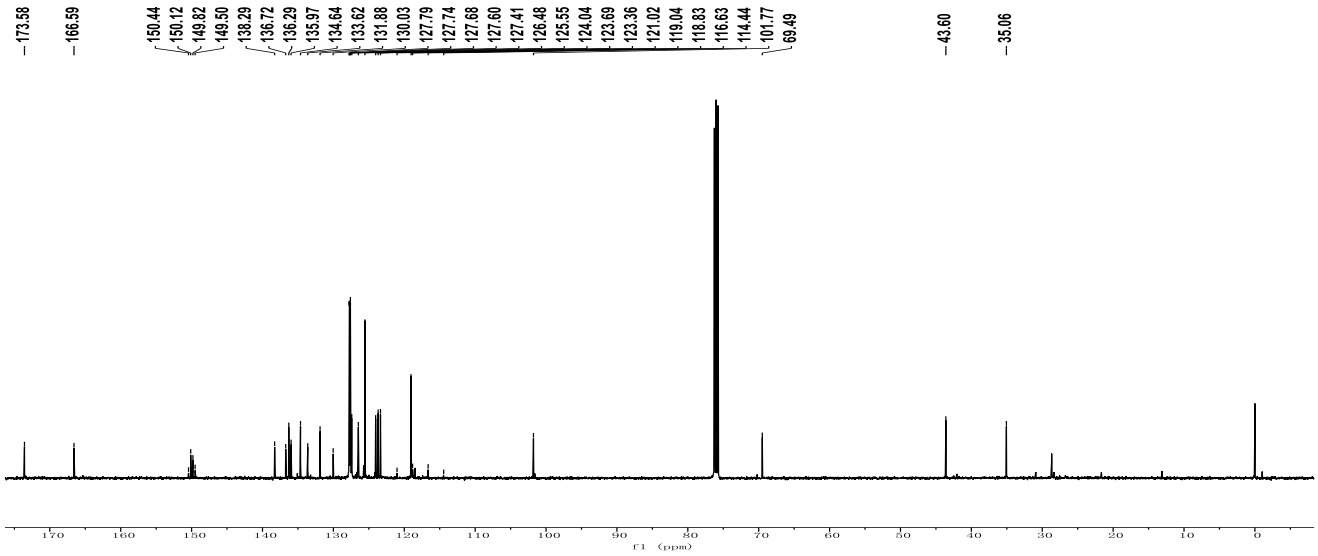


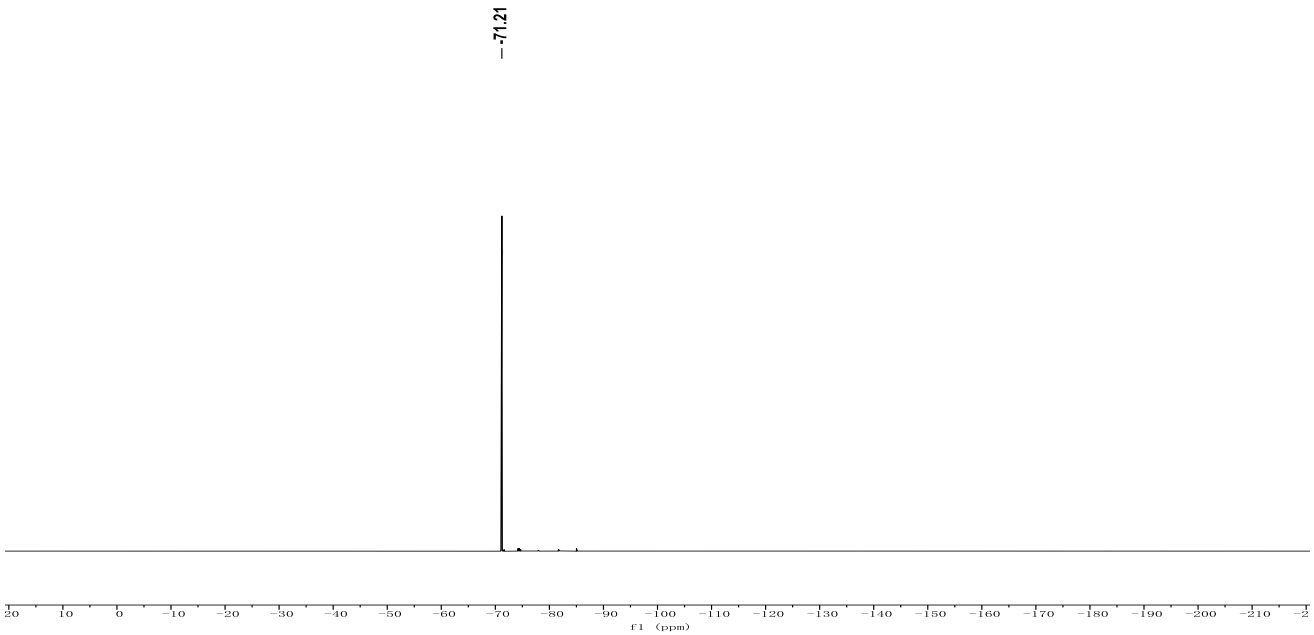


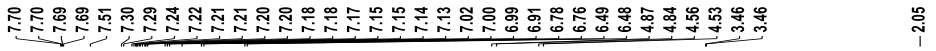
3ai

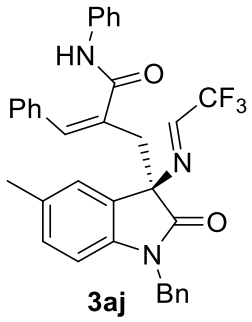
^{1}H NMR (500 MHz, $CDCl_3$)
^{13}C NMR (126 MHz, $CDCl_3$)
^{19}F NMR (471 MHz, $CDCl_3$)





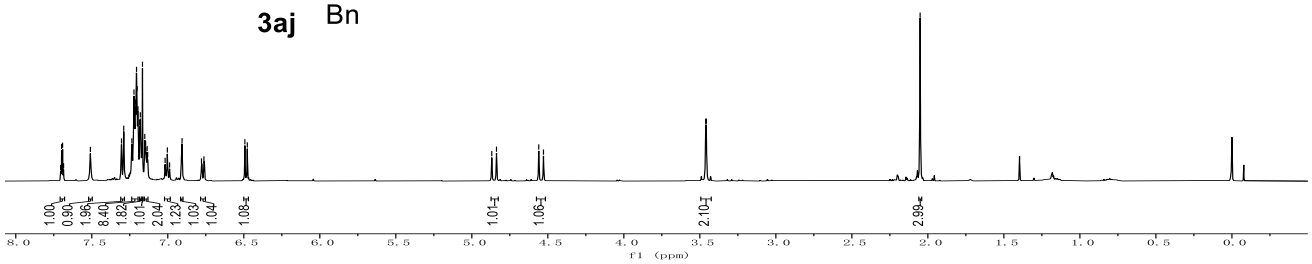


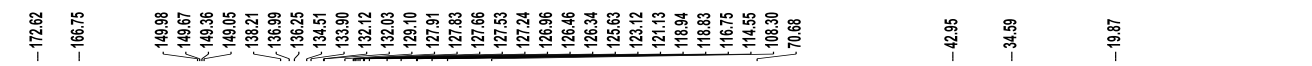


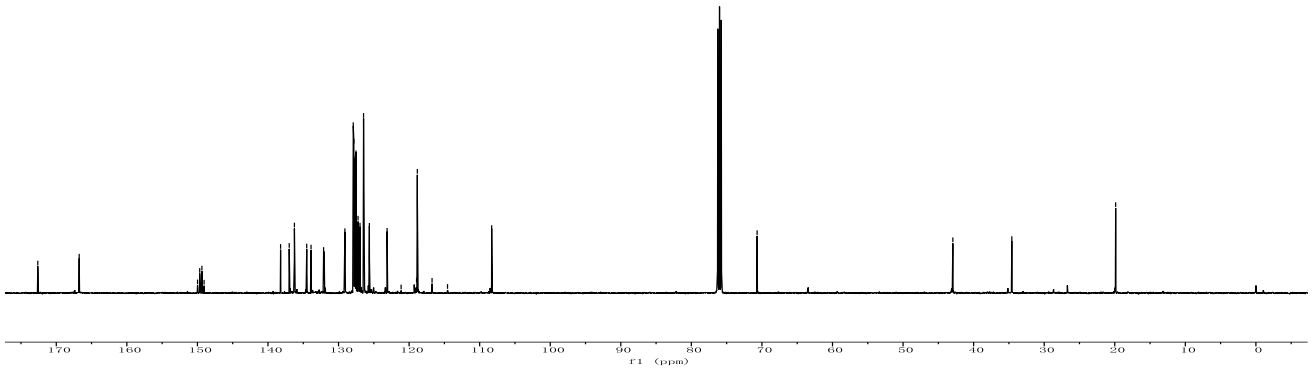


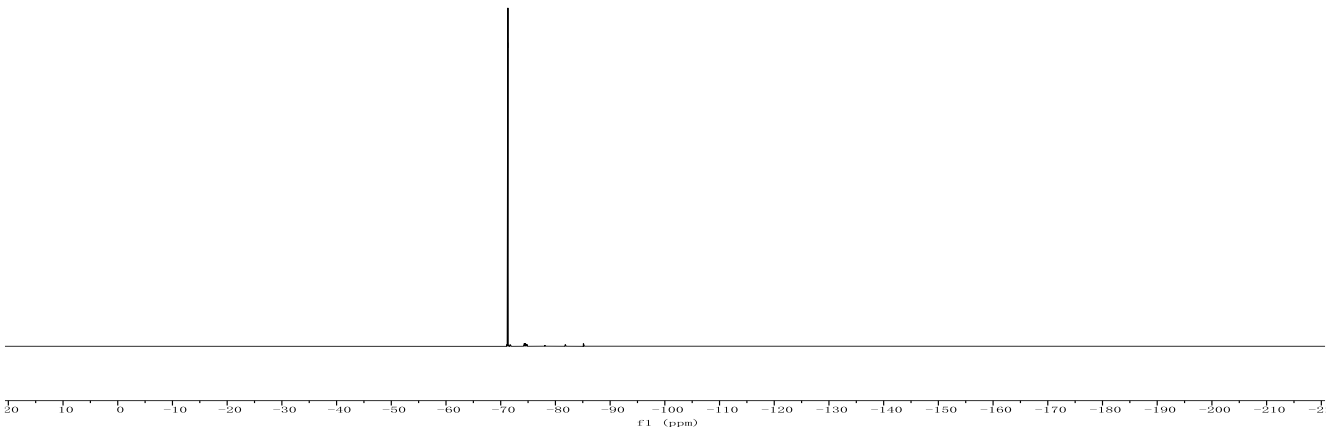
3aj

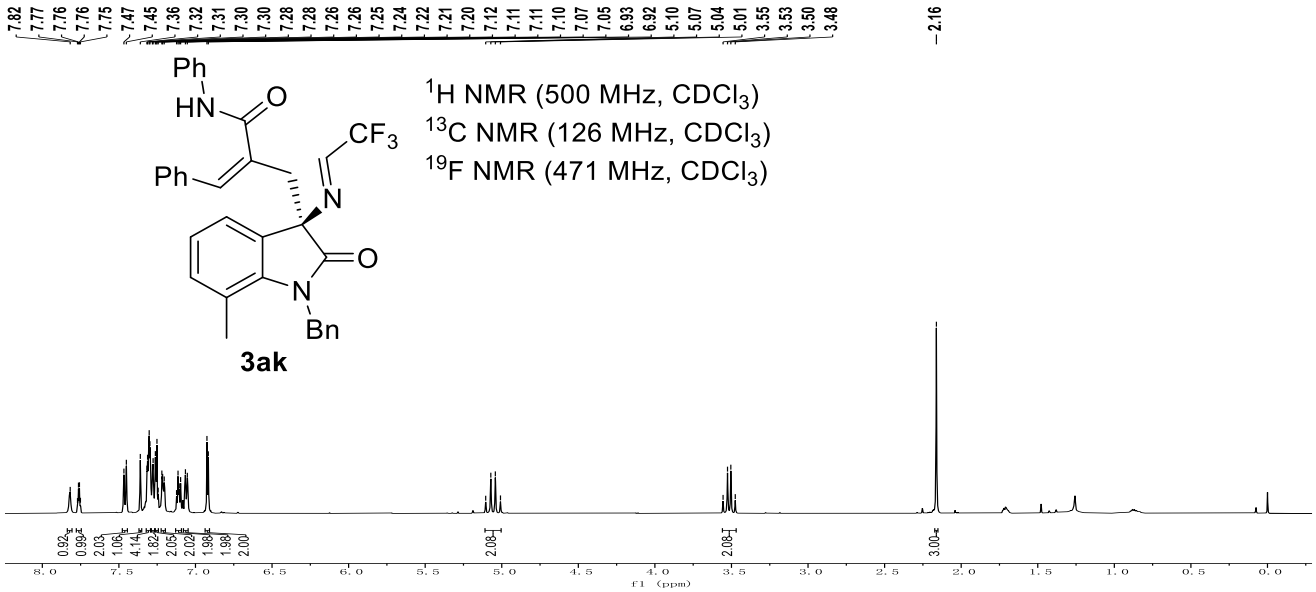
^{1}H NMR (500 MHz, $CDCl_3$)
^{13}C NMR (126 MHz, $CDCl_3$)
^{19}F NMR (471 MHz, $CDCl_3$)

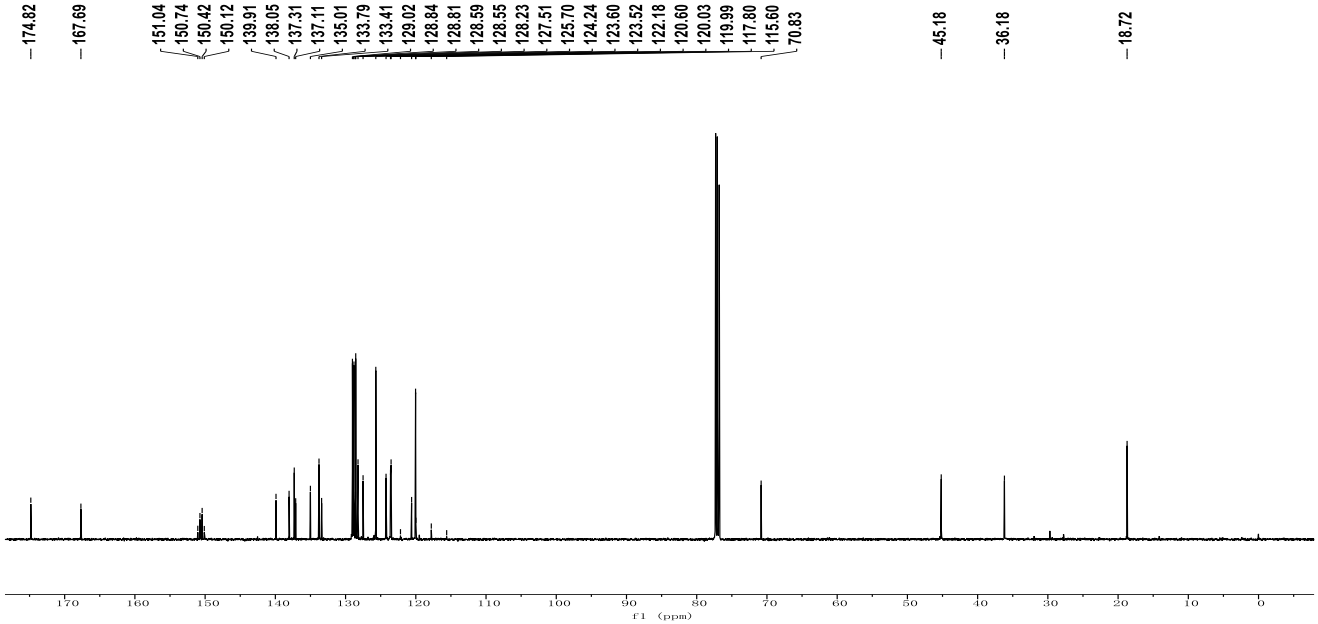


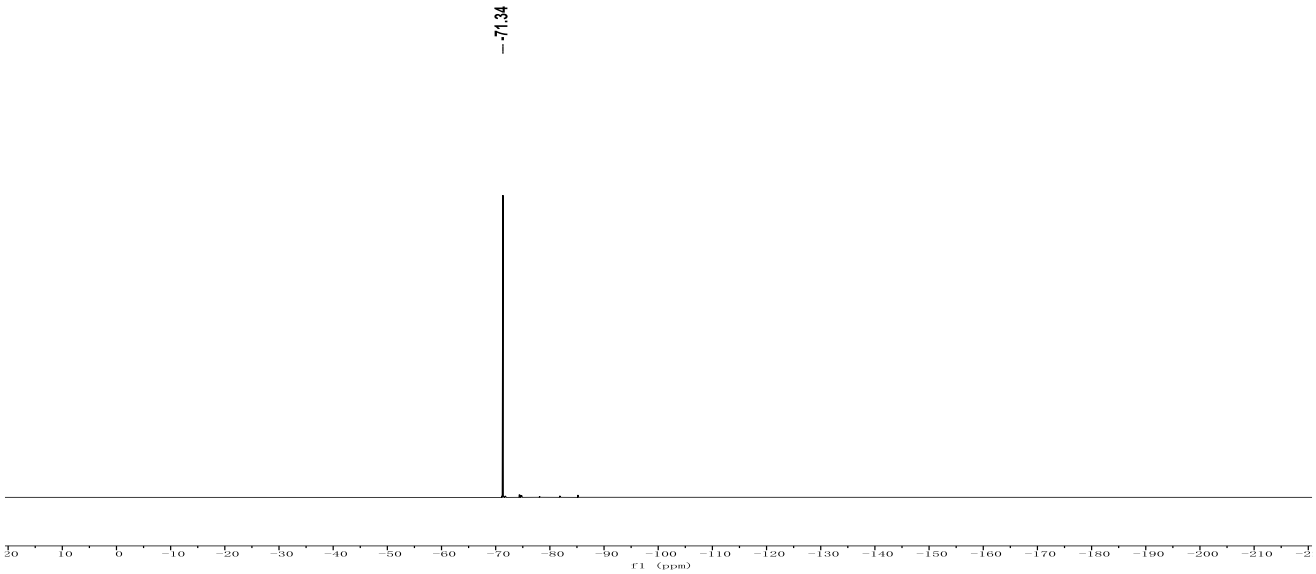


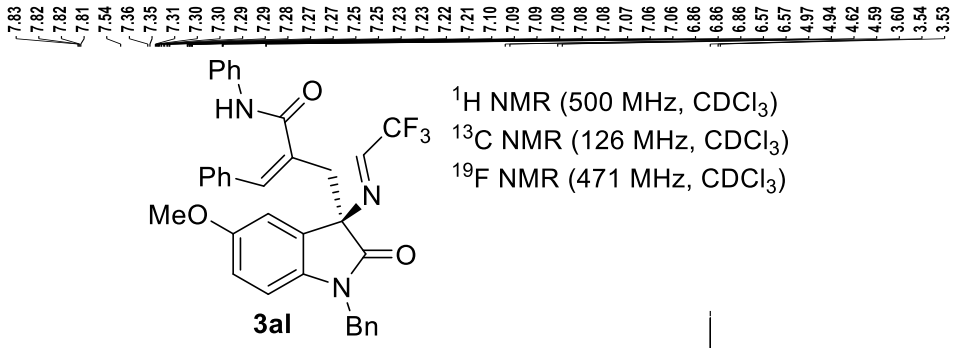




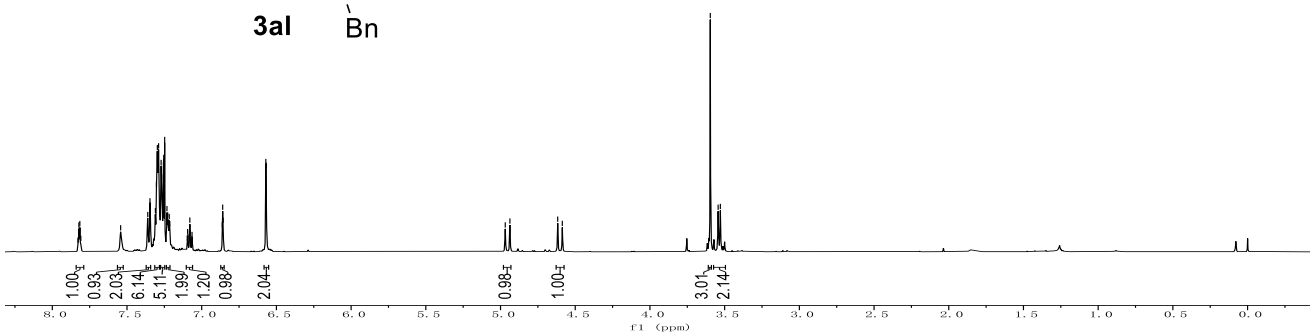

7.82 7.77 7.76 7.76 7.75 7.47 7.45 7.36 7.32 7.31 7.30 7.30 7.28 7.26 7.26 7.25 7.24 7.22 7.21 7.20 7.12 7.11 7.11 7.10 7.07 7.05 6.93 6.92 5.10 5.07 5.04 5.01 3.55 3.53 3.50 3.48 2.16
Ph
HN
O
CF3
Ph
N
O
N
Bn
3ak
1H NMR (500 MHz, CDCl3)
13C NMR (126 MHz, CDCl3)
19F NMR (471 MHz, CDCl3)
0.92 0.99 2.03 1.06 4.14 1.82 2.05 2.02 1.98 1.98 2.00 2.08 2.08 3.00
f1 (ppm)

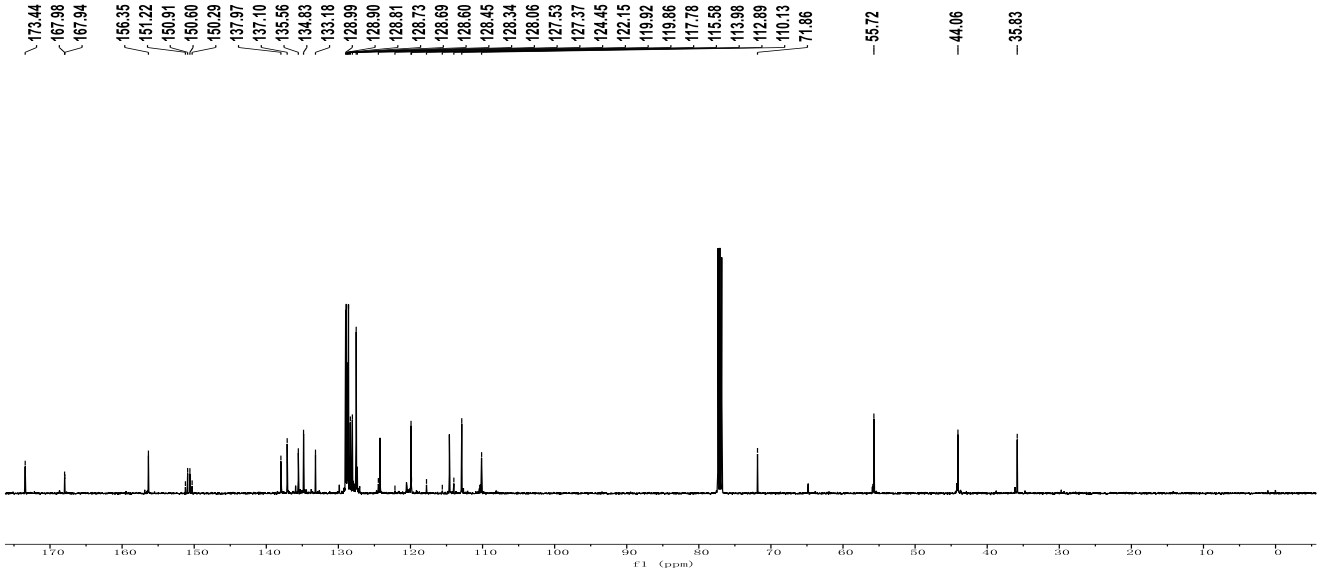

174.82 167.69 151.04 150.74 150.42 150.12 139.91 138.05 137.31 137.11 135.01 133.79 133.41 129.02 128.84 128.81 128.59 128.55 128.23 127.51 125.70 124.24 123.60 123.52 122.18 120.60 120.03 119.99 117.80 115.60 70.83 45.18 36.18 18.72
f1 (ppm)

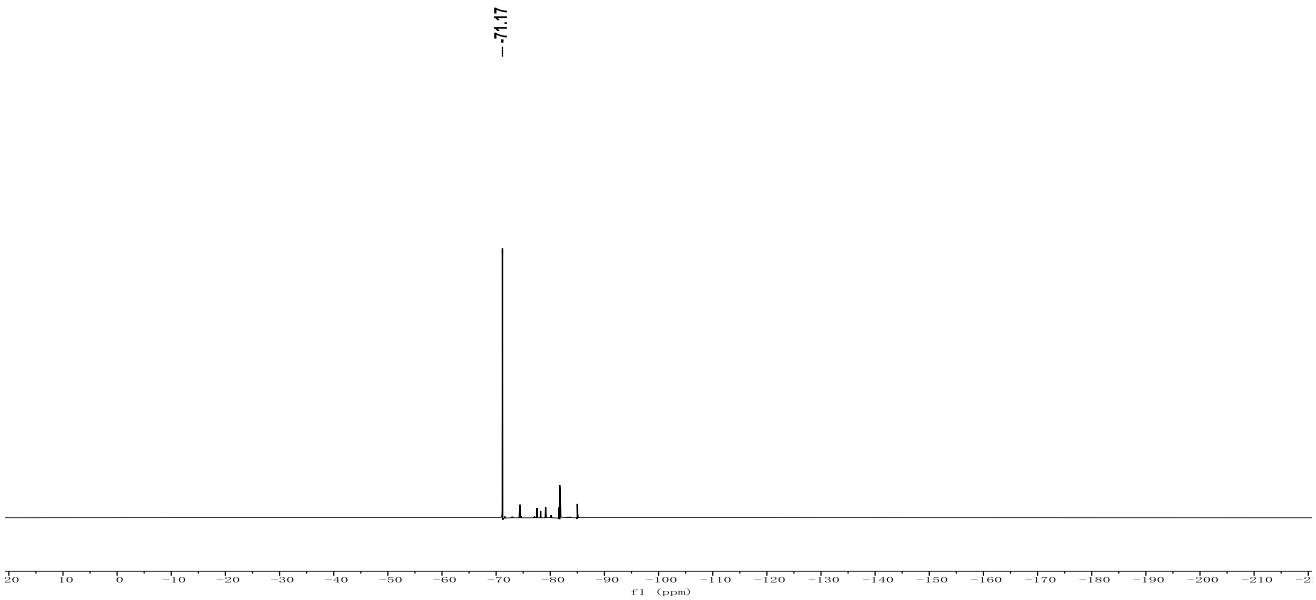

71.34
f1 (ppm)

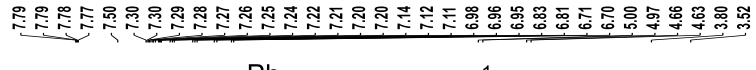


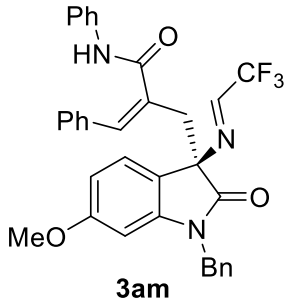
^{1}H NMR (500 MHz, $CDCl_3$)
^{13}C NMR (126 MHz, $CDCl_3$)
^{19}F NMR (471 MHz, $CDCl_3$)





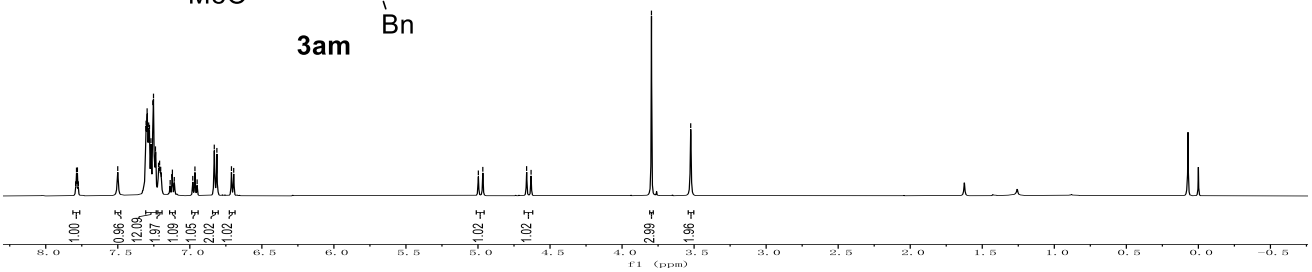


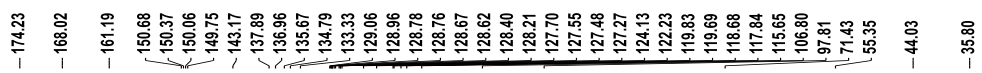


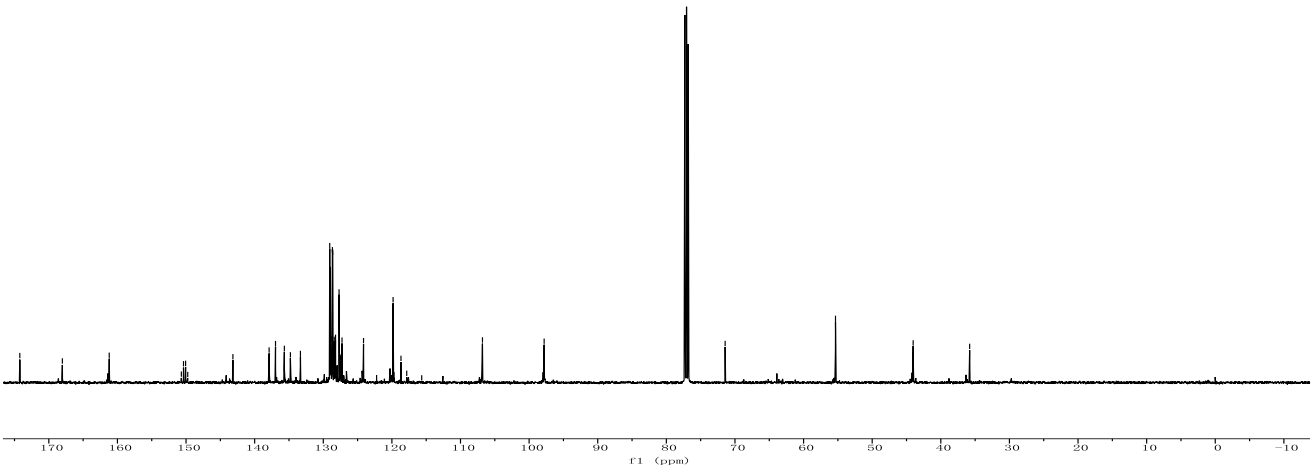


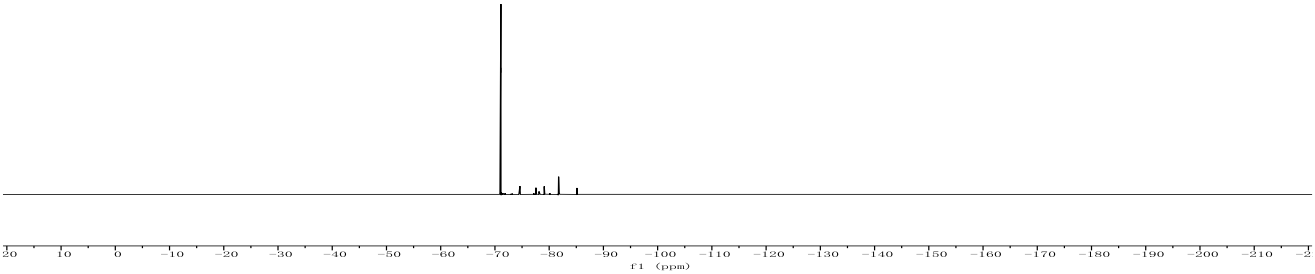
3am

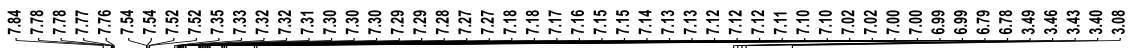
^{1}H NMR (500 MHz, $CDCl_3$)
^{13}C NMR (126 MHz, $CDCl_3$)
^{19}F NMR (471 MHz, $CDCl_3$)

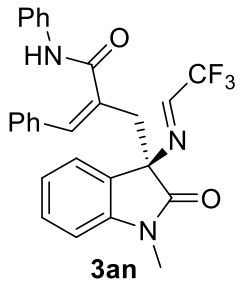






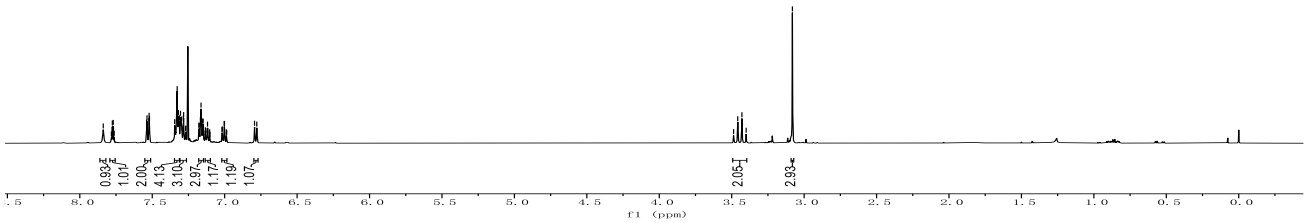


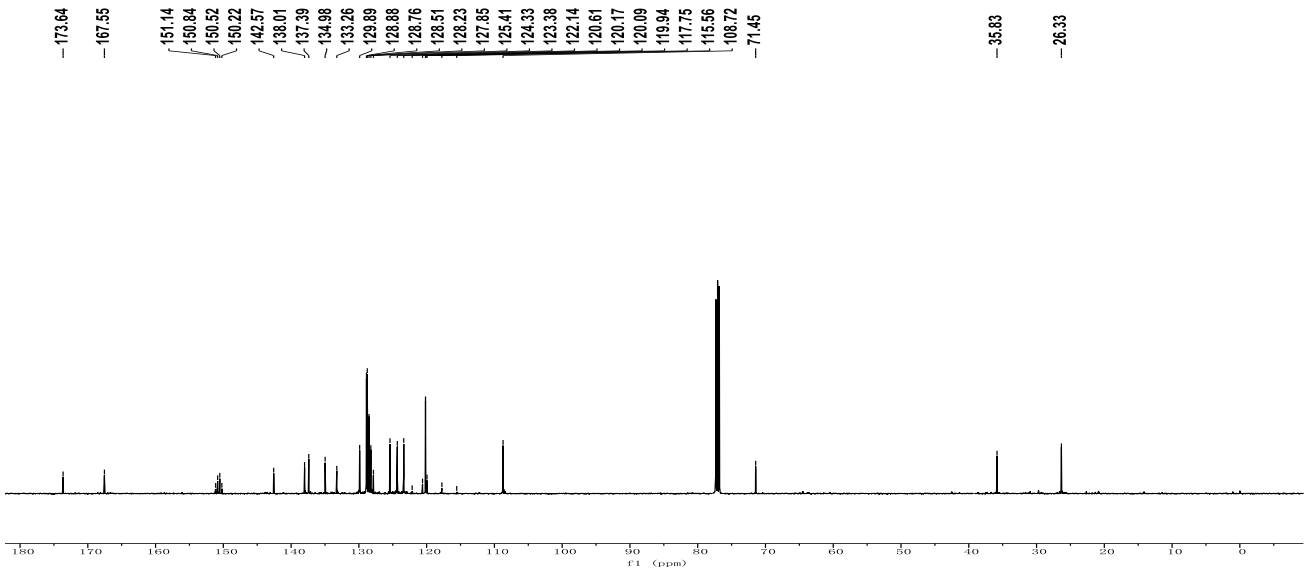


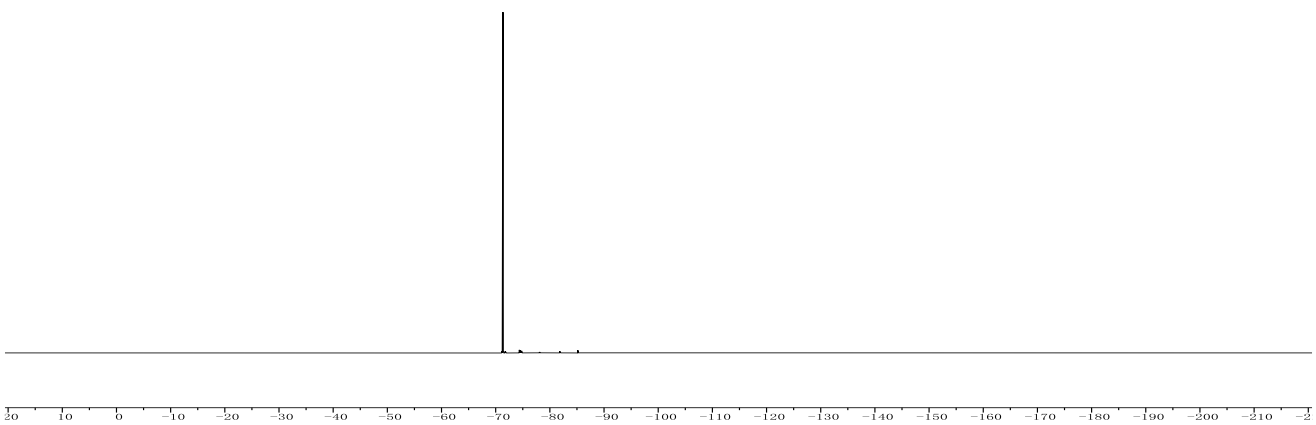


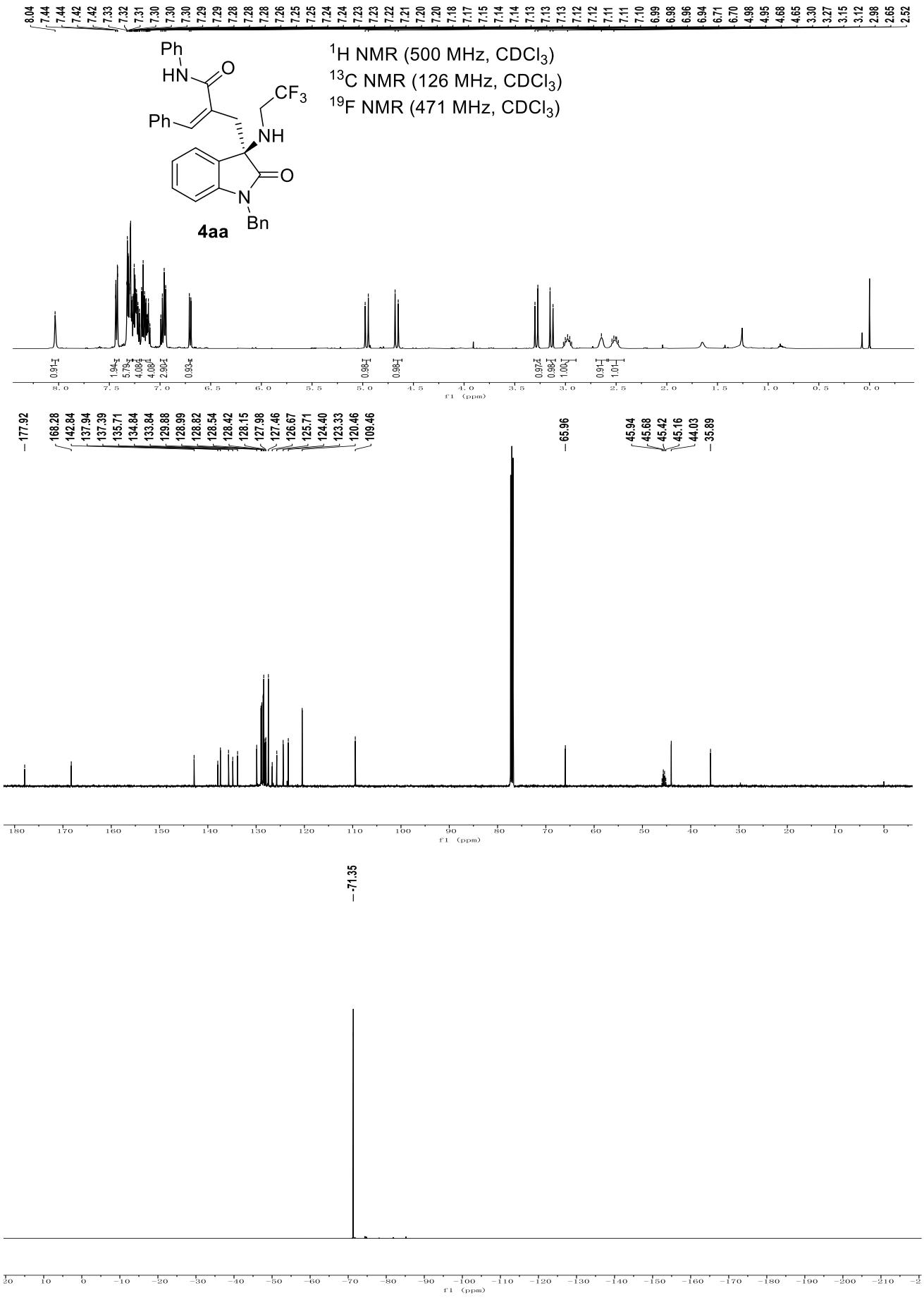
3an

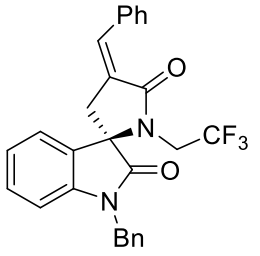
^{1}H NMR (500 MHz, $CDCl_3$)
^{13}C NMR (126 MHz, $CDCl_3$)
^{19}F NMR (471 MHz, $CDCl_3$)







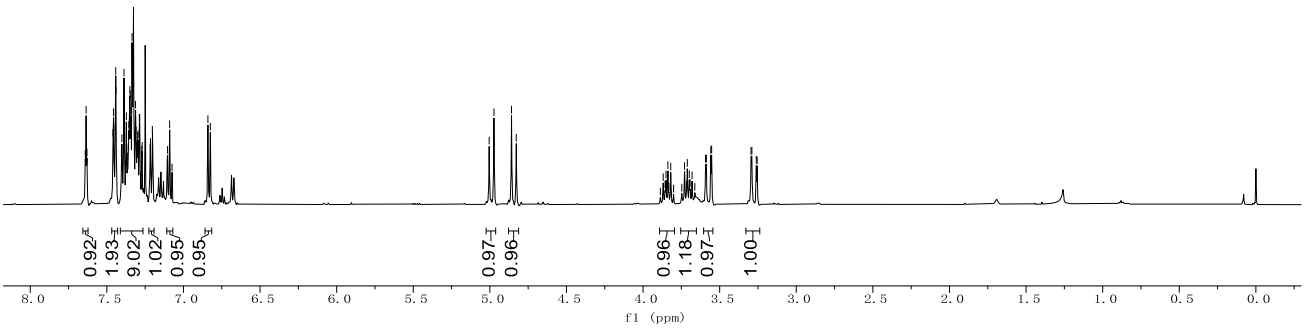

8.04 7.44 7.44 7.42 7.42 7.33 7.32 7.31 7.30 7.30 7.30 7.29 7.29 7.28 7.28 7.28 7.26 7.25 7.25 7.24 7.24 7.23 7.23 7.22 7.21 7.20 7.20 7.18 7.17 7.15 7.14 7.14 7.13 7.13 7.13 7.12 7.12 7.11 7.11 7.10 6.99 6.98 6.96 6.94 6.71 6.70 4.98 4.95 4.68 4.65 3.30 3.27 3.15 3.12 2.98 2.65 2.52
Ph
HN
O
CF3
Ph
NH
O
N
Bn
4aa
1H NMR (500 MHz, CDCl3)
13C NMR (126 MHz, CDCl3)
19F NMR (471 MHz, CDCl3)
0.91 1.94 5.79 4.08 4.08 2.90 0.93 0.98 0.99 0.97 0.98 1.00 0.91 1.01
f1 (ppm)
177.92 168.28 142.84 137.94 137.39 135.71 134.84 133.84 129.88 128.99 128.82 128.54 128.42 128.15 127.98 127.46 126.67 125.71 124.40 123.33 120.46 109.46 65.96 45.94 45.68 45.42 45.16 44.03 35.89
f1 (ppm)
-71.35
f1 (ppm)

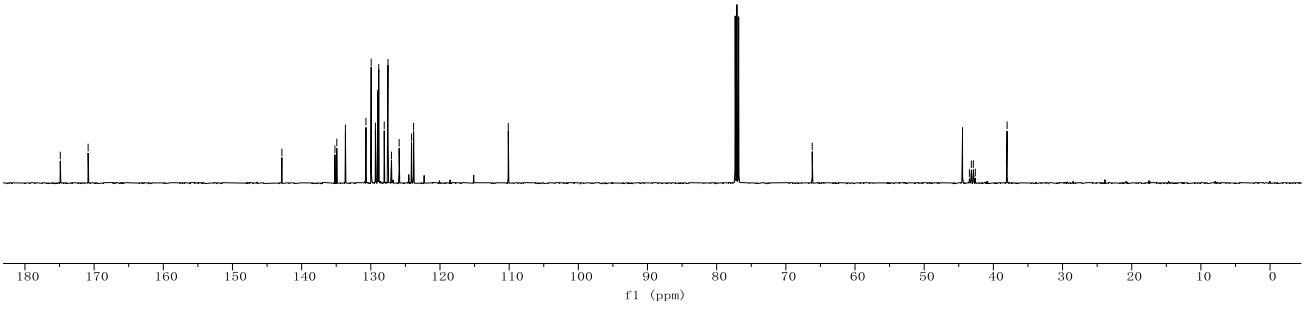


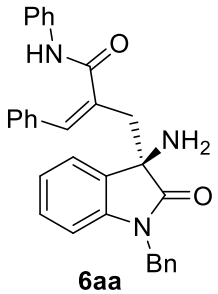
5aa

^{1}H NMR (500 MHz, $CDCl_3$)

^{13}C NMR (126 MHz, $CDCl_3$)



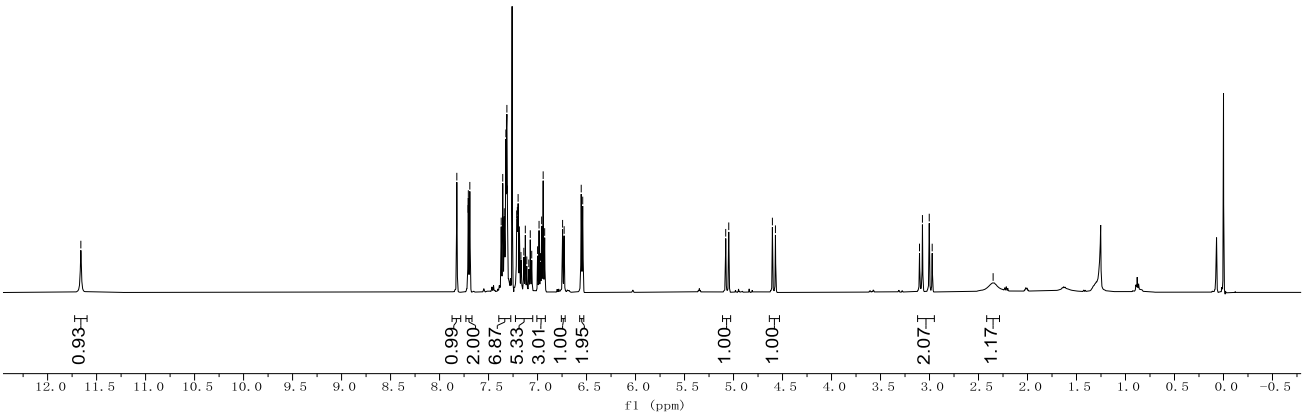


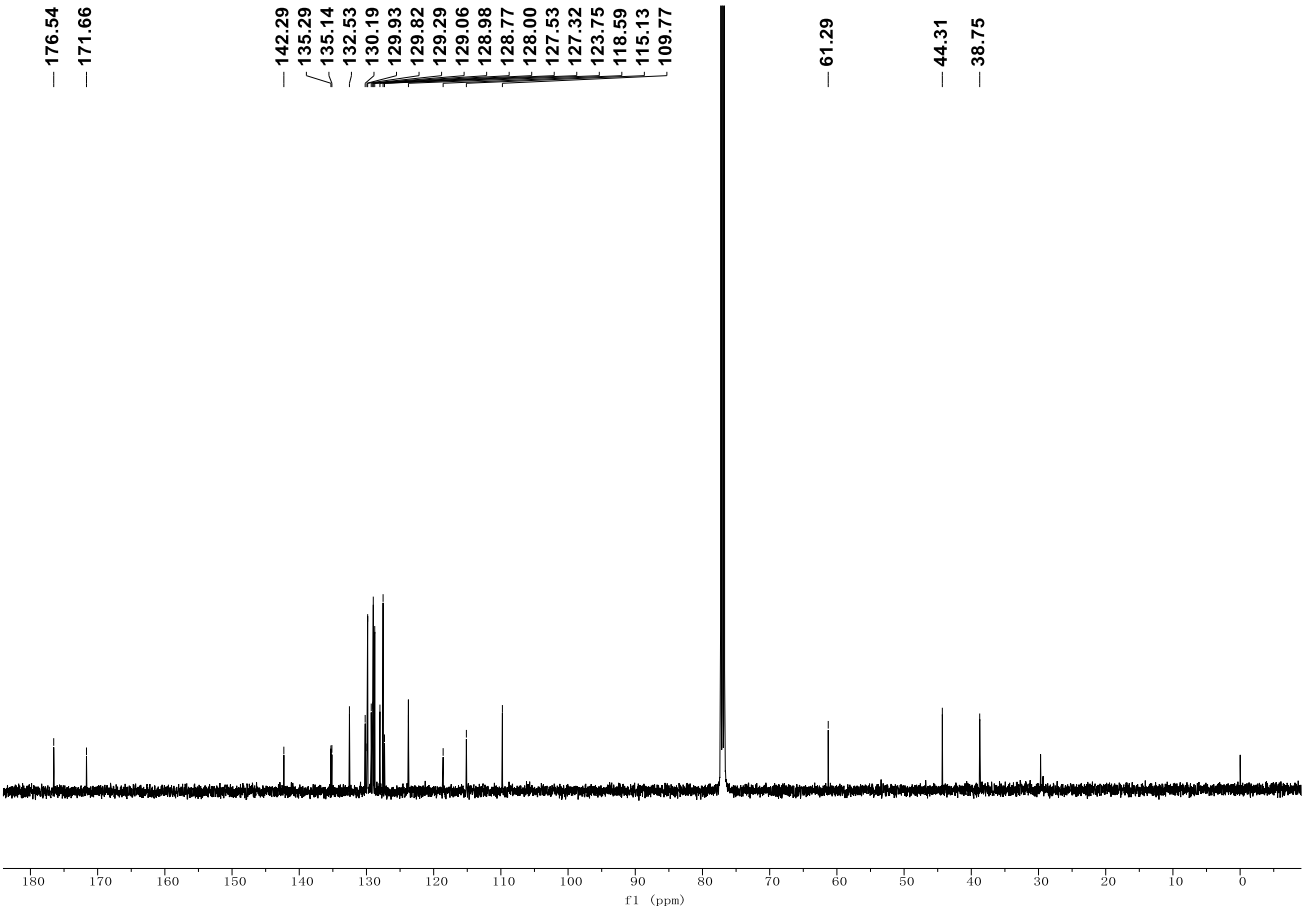


6aa

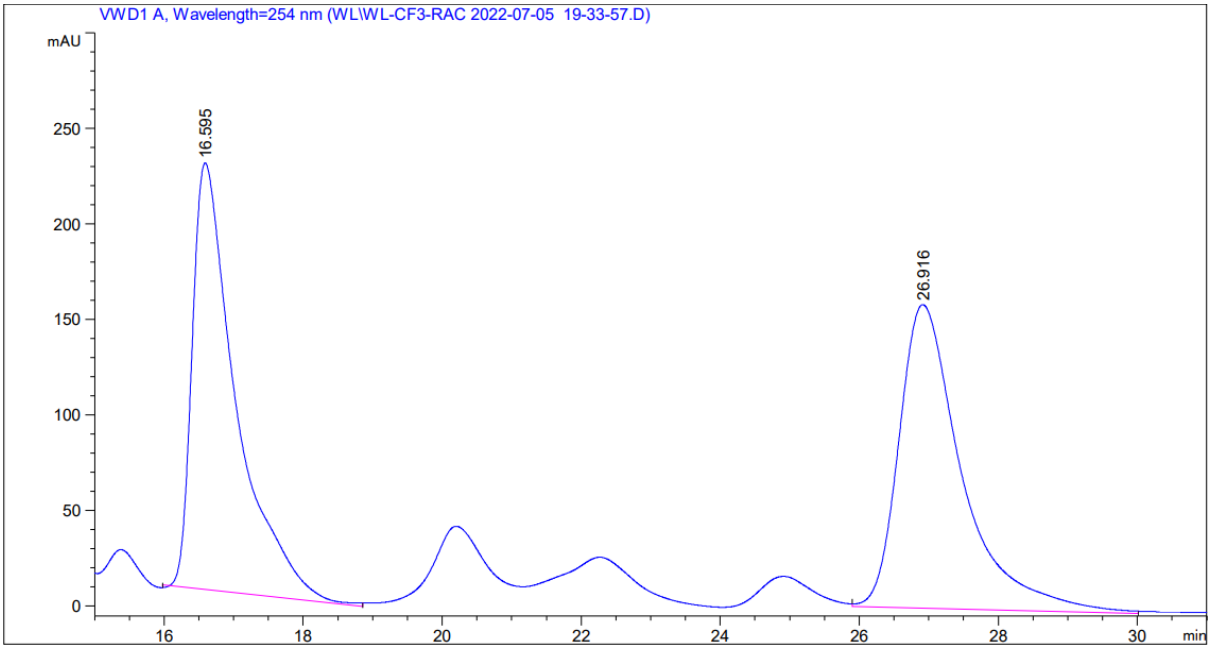
^{1}H NMR (500 MHz, $CDCl_3$)

^{13}C NMR (126 MHz, $CDCl_3$)



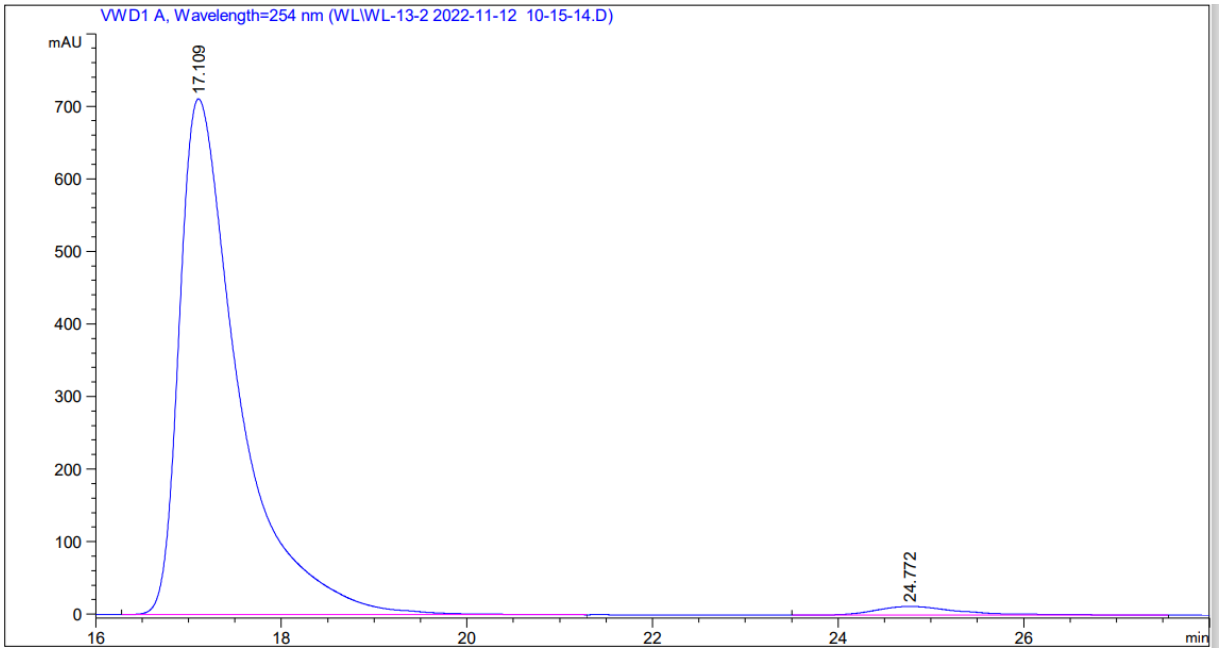


HPLC chromatogram of racemic compound 3aa



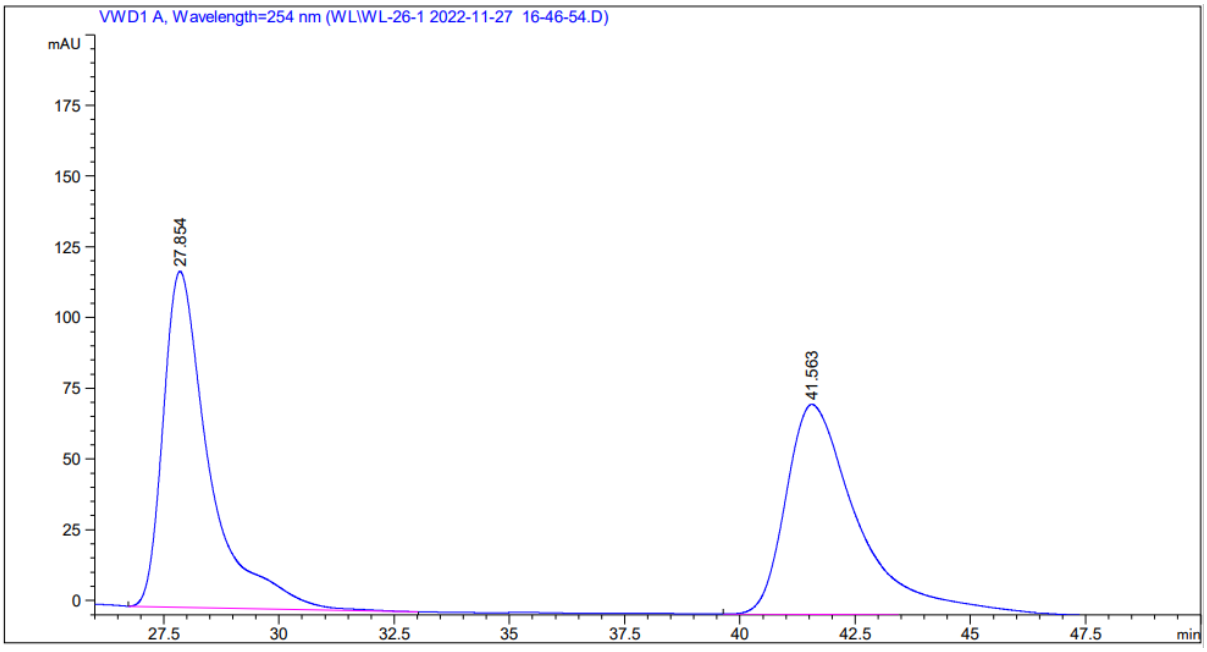
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.595	MM R	0.7271	9734.13477	223.11272	49.4458
2	26.916	MM R	1.0450	9952.34277	158.72899	50.5542

HPLC chromatogram of chiral compound 3aa



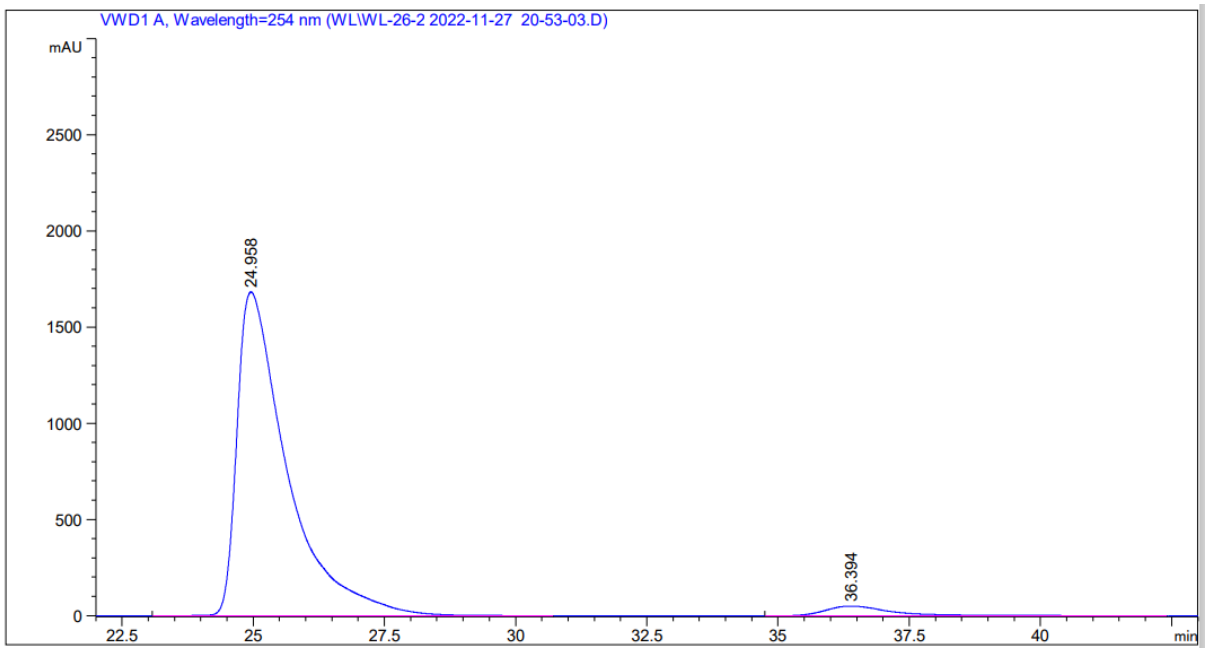
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.109	BB	0.6499	3.14929e4	710.83368	97.6397
2	24.772	BB	0.9433	761.28558	11.96446	2.3603

HPLC chromatogram of racemic compound 3ba



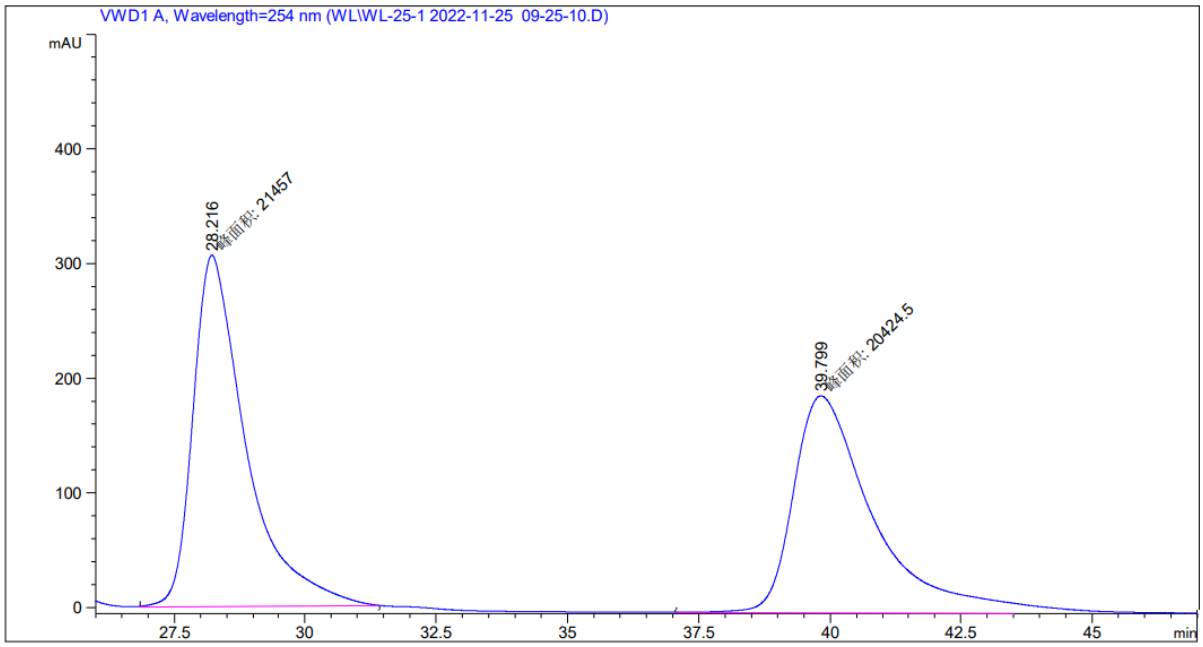
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.854	BB	1.0219	8240.65430	118.70357	50.2860
2	41.563	BB	1.6102	8146.90723	74.30226	49.7140

HPLC chromatogram of chiral compound 3ba



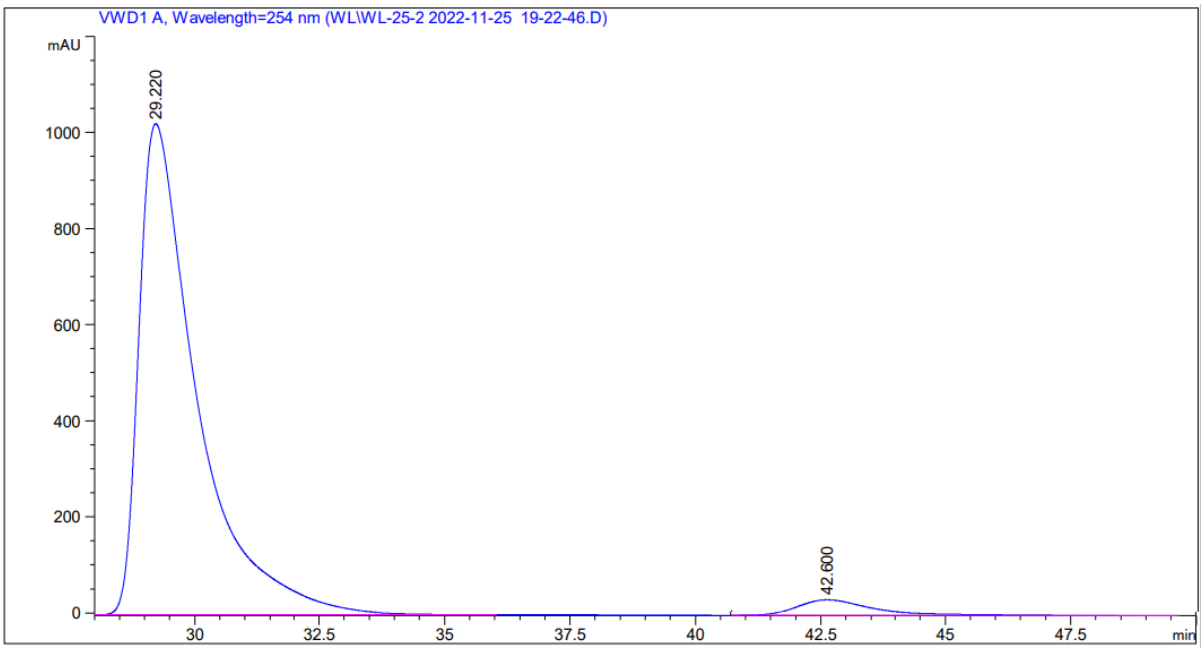
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.958	BB	0.9601	1.11655e5	1682.83582	96.0849
2	36.394	BB	1.2847	4549.58447	50.08916	3.9151

HPLC chromatogram of racemic compound 3ca



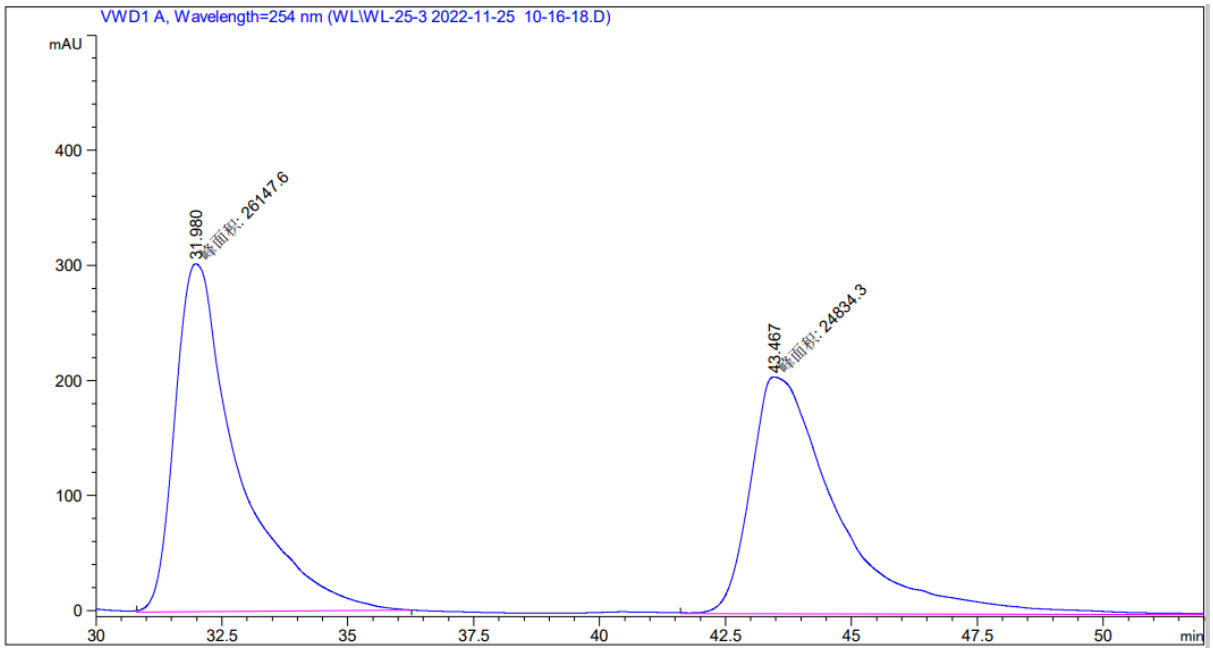
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.216	MM	1.1668	2.14570e4	306.49557	51.2327
2	39.799	MM	1.7975	2.04245e4	189.37833	48.7673

HPLC chromatogram of chiral compound 3ca



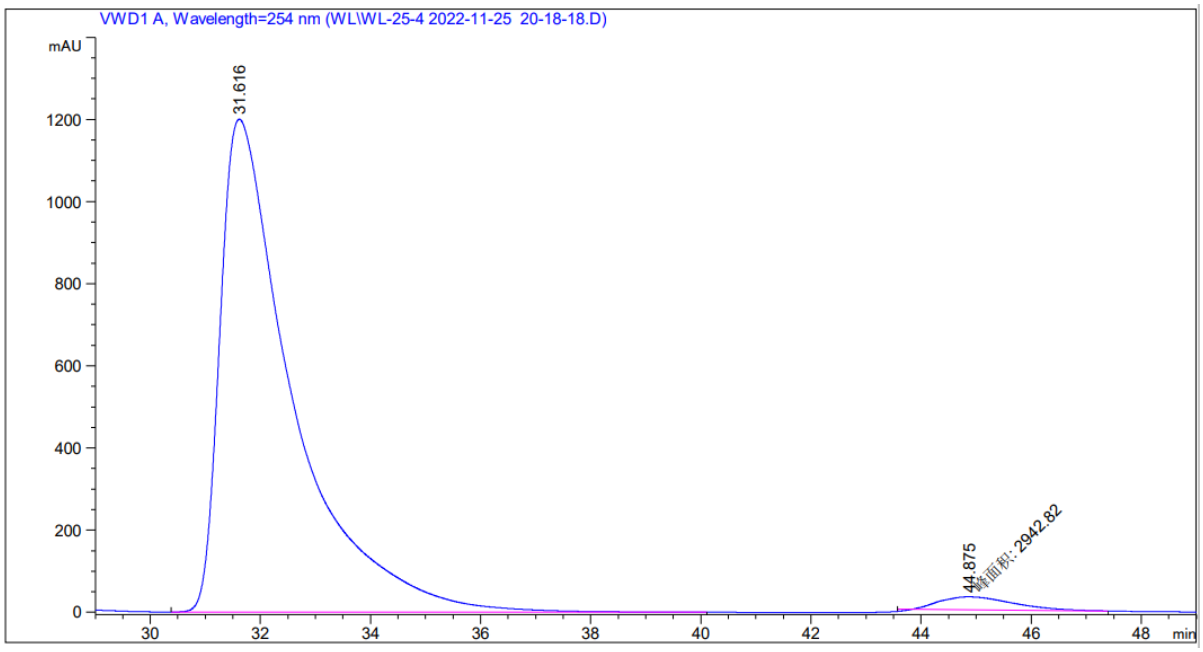
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.220	BB	1.1615	8.19214e4	1021.60590	95.8592
2	42.600	BB	1.5881	3538.74976	32.47910	4.1408

HPLC chromatogram of racemic compound 3da



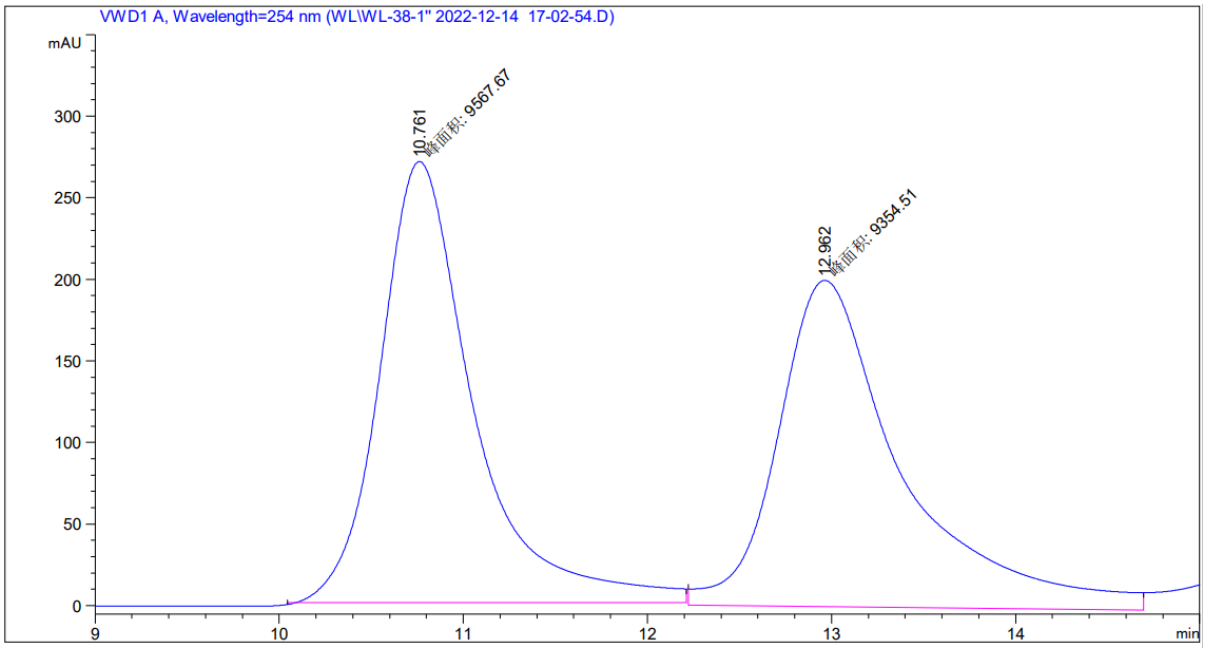
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.980	MM	1.4410	2.61476e4	302.43356	51.2880
2	43.467	MM	2.0114	2.48343e4	205.77625	48.7120

HPLC chromatogram of chiral compound 3da



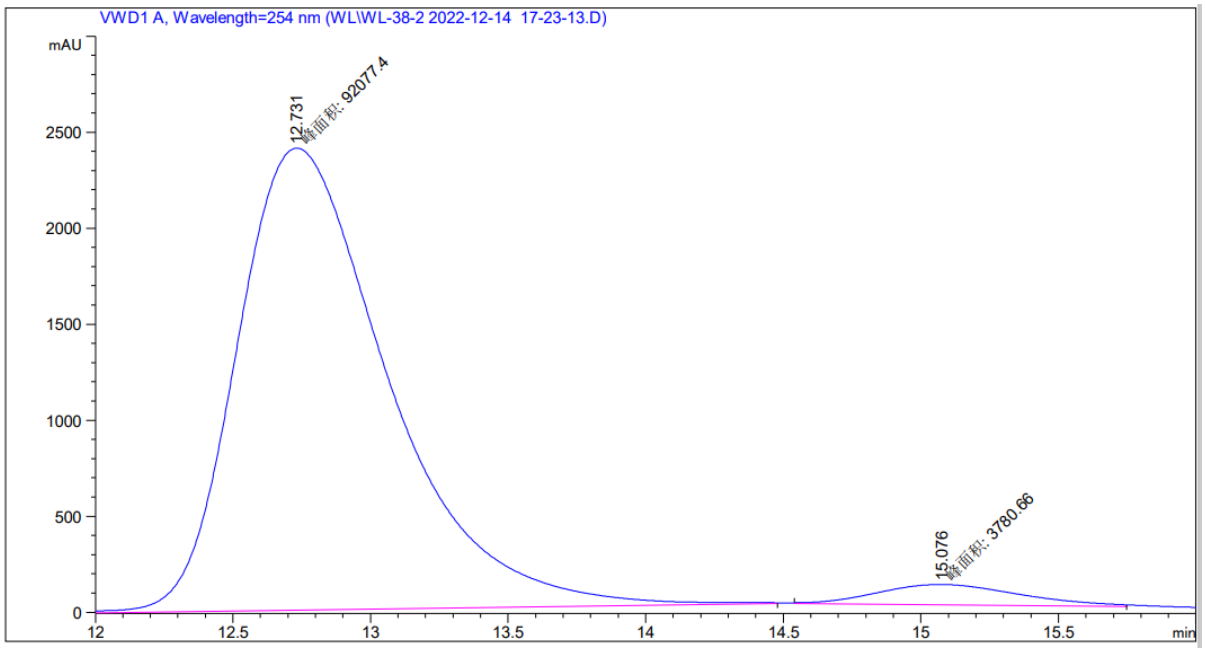
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.616	BB	1.2942	1.09738e5	1199.61084	97.3884
2	44.875	MM	1.5509	2942.82275	31.62551	2.6116

HPLC chromatogram of racemic compound 3ea



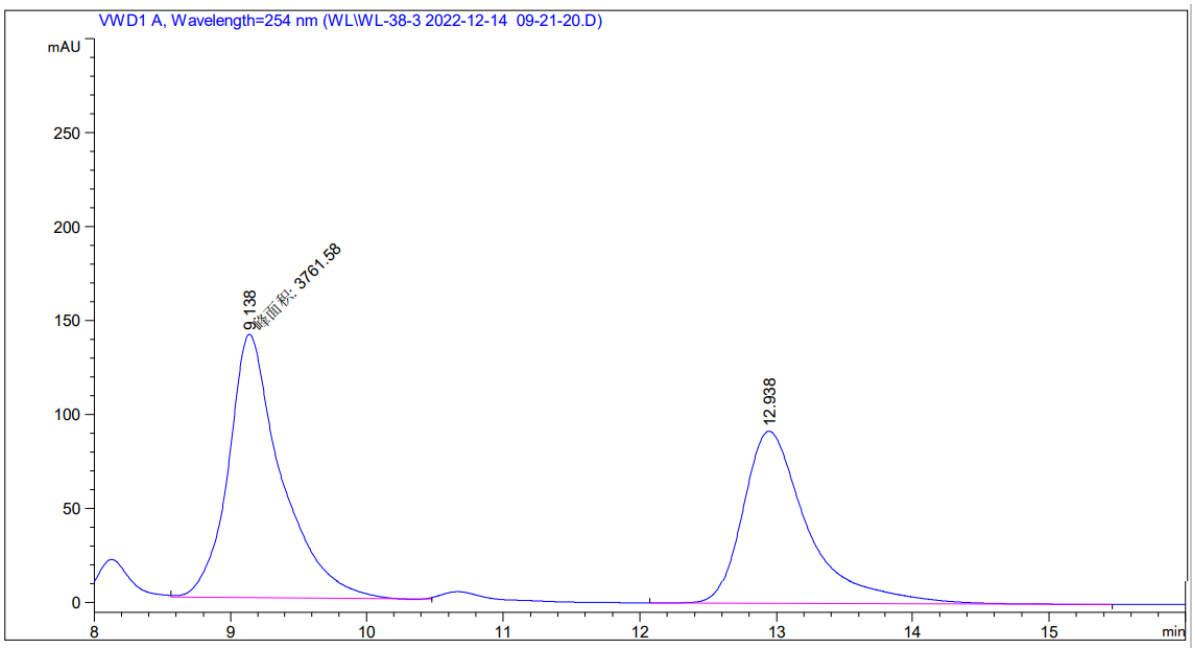
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.761	MM	0.5897	9567.66504	270.40744	50.5632
2	12.962	MM	0.7801	9354.50879	199.86559	49.4368

HPLC chromatogram of chiral compound 3ea



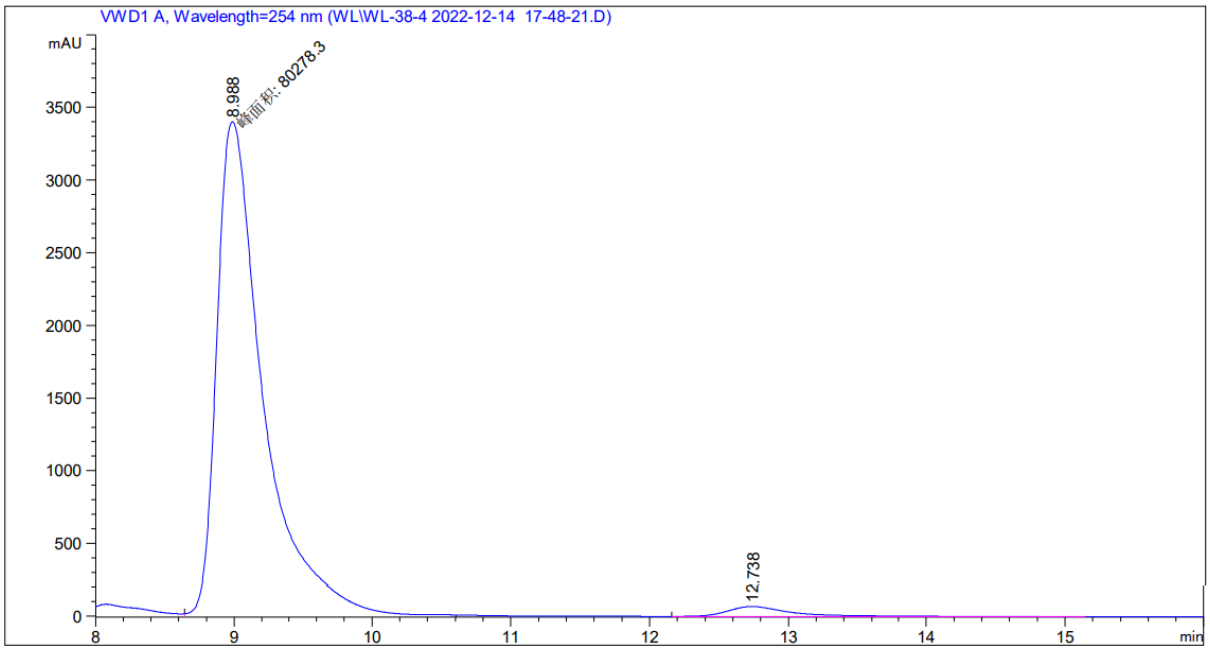
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.731	MM	0.6376	9.20774e4	2406.83862	96.0560
2	15.076	MM	0.5969	3780.66089	105.55573	3.9440

HPLC chromatogram of racemic compound 3fa



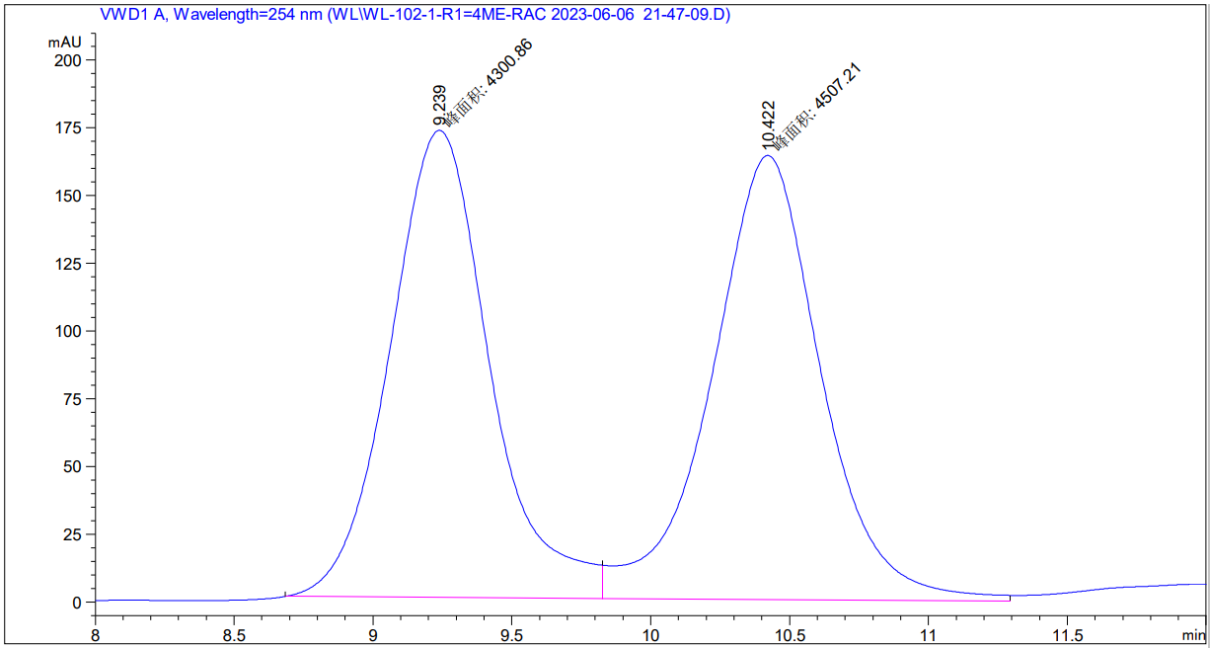
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.138	MM	0.4478	3761.58130	140.01384	55.4583
2	12.938	BB	0.4903	3021.14282	91.48936	44.5417

HPLC chromatogram of chiral compound 3fa



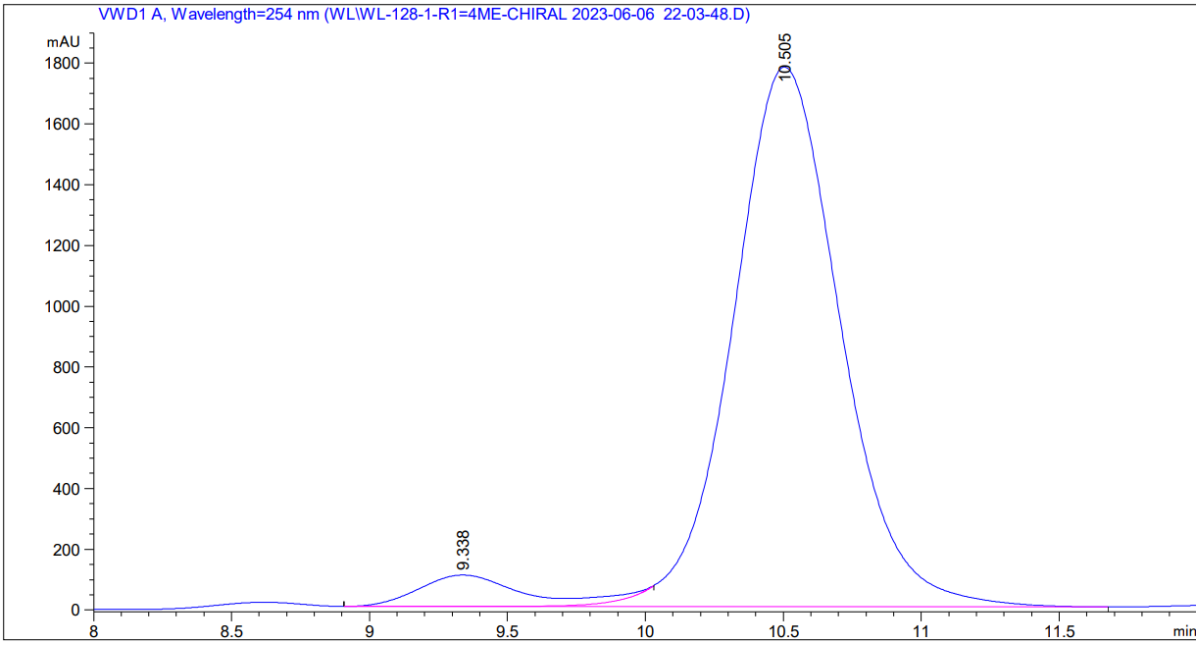
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.988	MM	0.3922	8.02783e4	3411.83716	97.4272
2	12.738	BB	0.4564	2119.95459	68.06794	2.5728

HPLC chromatogram of racemic compound 3ga



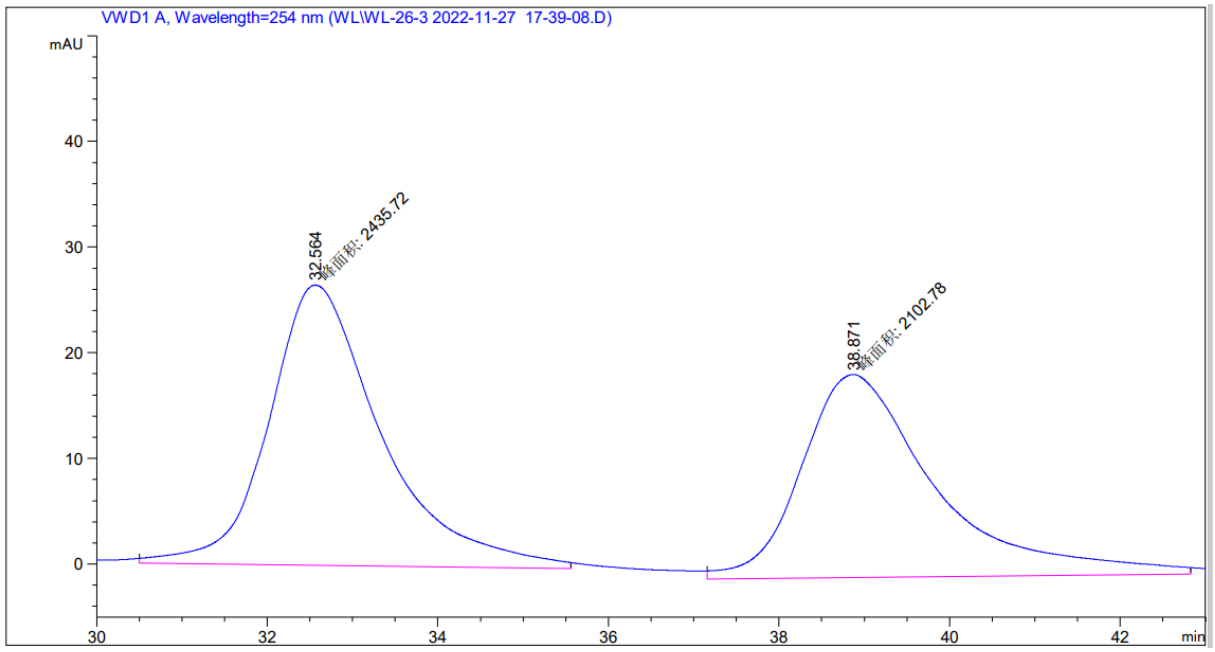
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.239	MM	0.4159	4300.86133	172.34732	48.8286
2	10.422	MM	0.4583	4507.21143	163.92238	51.1714

HPLC chromatogram of chiral compound 3ga



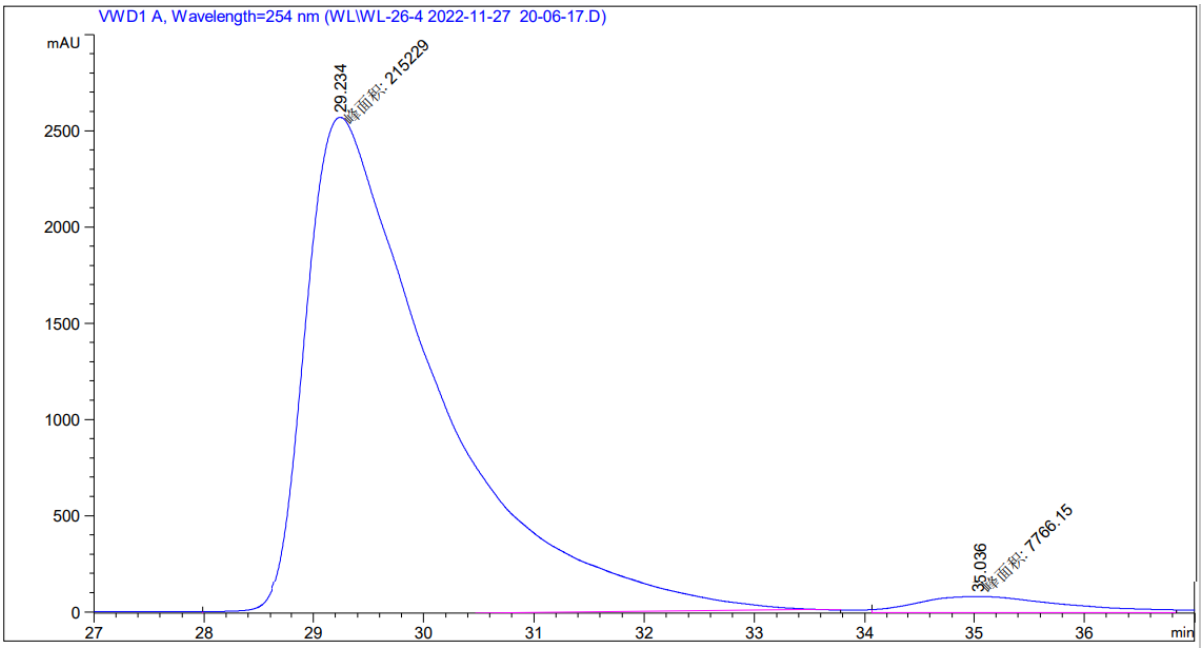
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.338	BV E	0.3964	2746.70874	103.56533	5.3890
2	10.505	VB R	0.4157	4.82218e4	1776.39014	94.6110

HPLC chromatogram of racemic compound 3ha



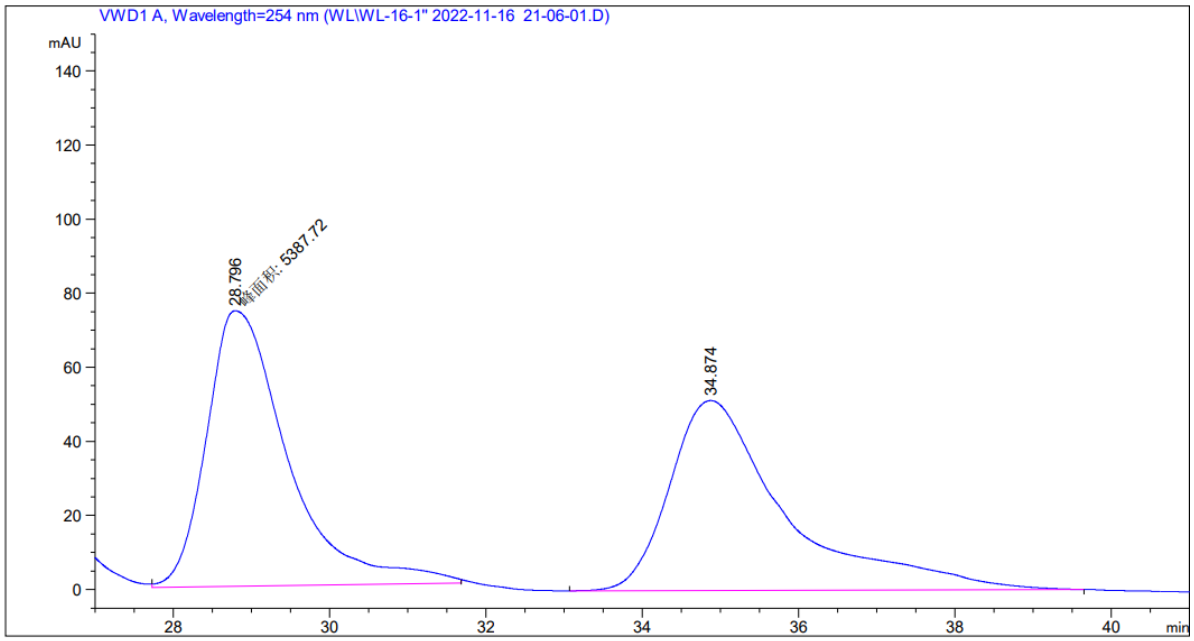
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	32.564	MM	1.5314	2435.72437	26.50941	53.6679
2	38.871	MM	1.8233	2102.78394	19.22138	46.3321

HPLC chromatogram of chiral compound 3ha



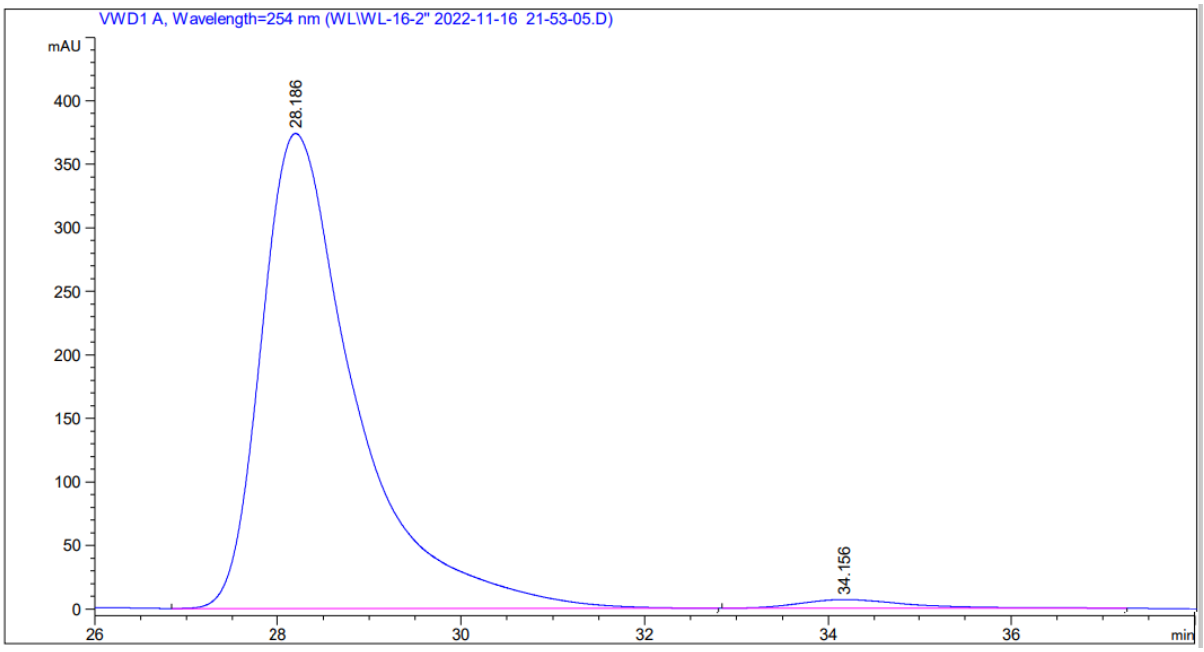
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.234	MM	1.3887	2.15229e5	2583.06885	96.5173
2	35.036	MM	1.5436	7766.15479	83.85501	3.4827

HPLC chromatogram of racemic compound 3ia



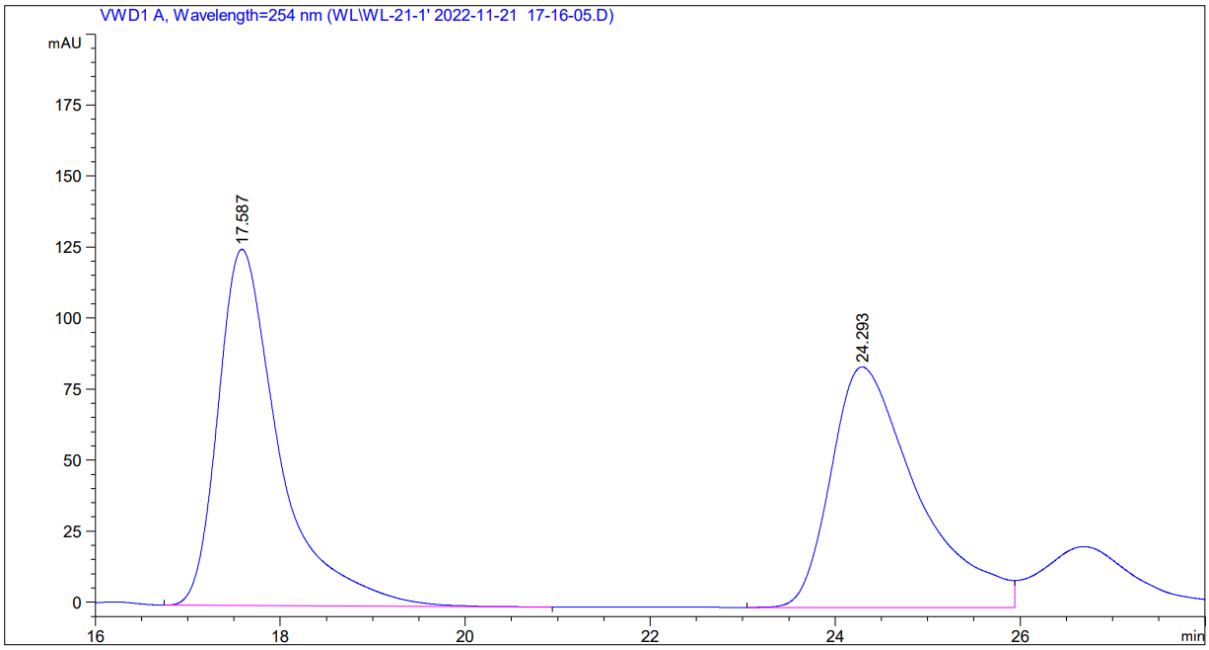
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.796	MM	1.2072	5387.71582	74.38067	50.4885
2	34.874	BB	1.4856	5283.46387	51.25689	49.5115

HPLC chromatogram of chiral compound 3ia



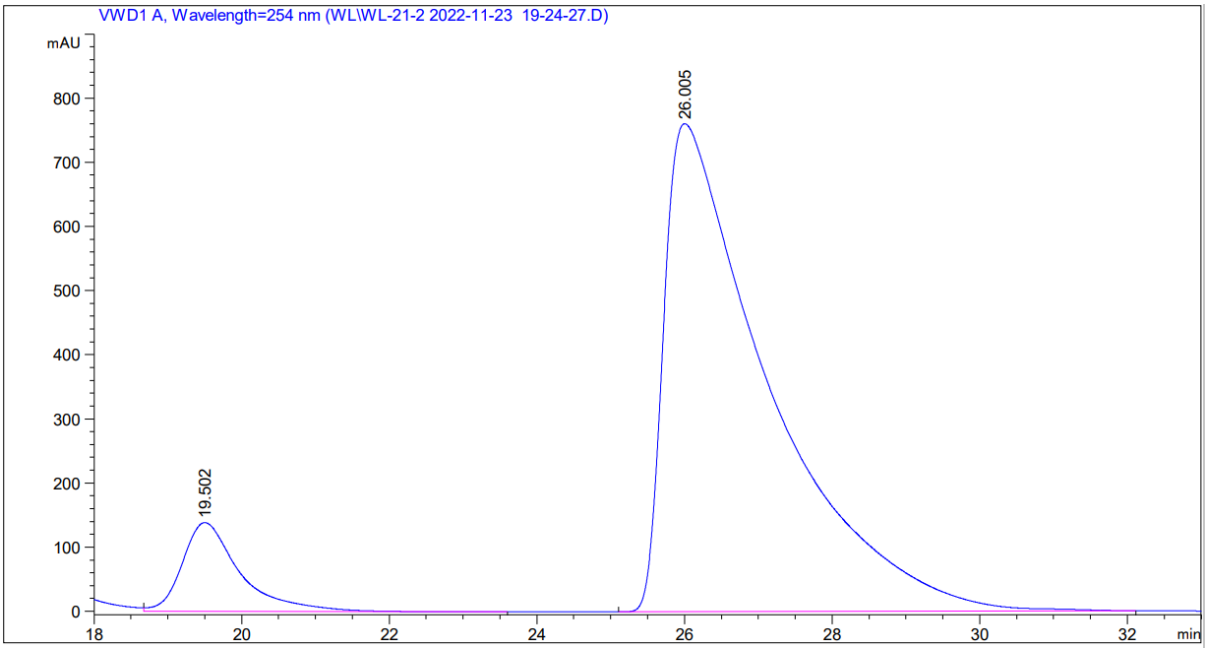
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.186	BB	1.0410	2.66613e4	373.86484	97.9036
2	34.156	BB	1.1253	570.90363	6.80154	2.0964

HPLC chromatogram of racemic compound 3ja



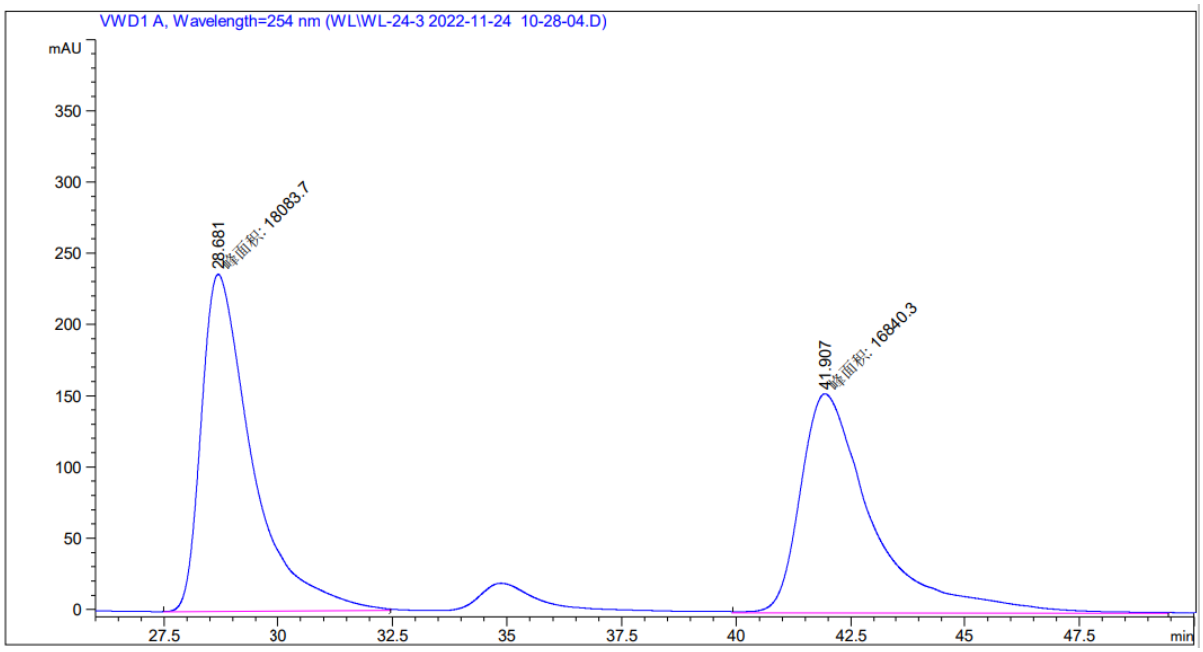
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.587	BB	0.6764	5755.62500	125.42605	51.1096
2	24.293	BV	0.9527	5505.71777	84.66127	48.8904

HPLC chromatogram of chiral compound 3ja



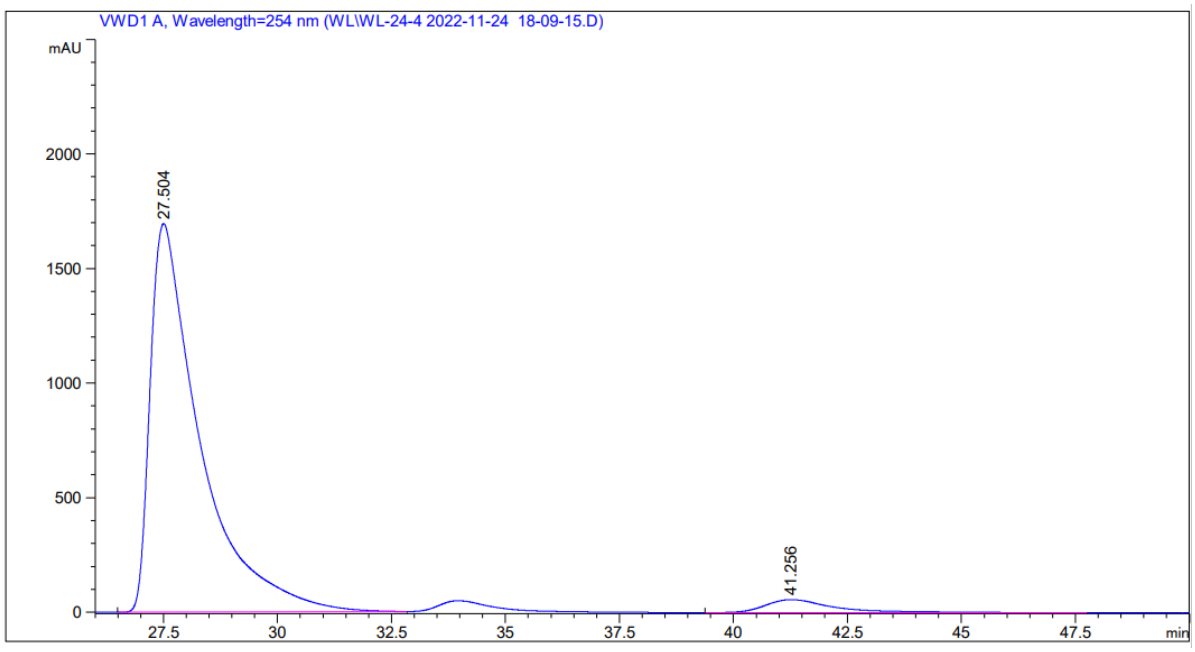
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.502	VB	0.8023	7535.58301	138.39215	9.1842
2	26.005	BB	1.3746	7.45139e4	760.82520	90.8158

HPLC chromatogram of racemic compound 3ka



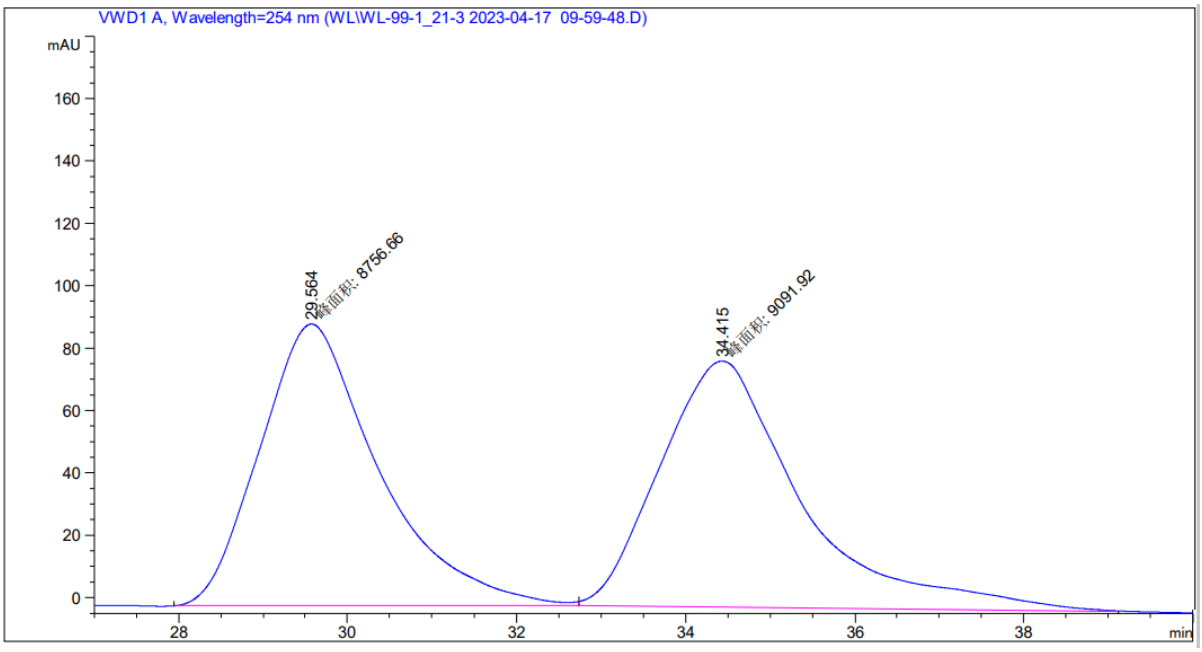
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.681	MM	1.2741	1.80837e4	236.55052	51.7801
2	41.907	MM	1.8256	1.68403e4	153.73897	48.2199

HPLC chromatogram of chiral compound 3ka



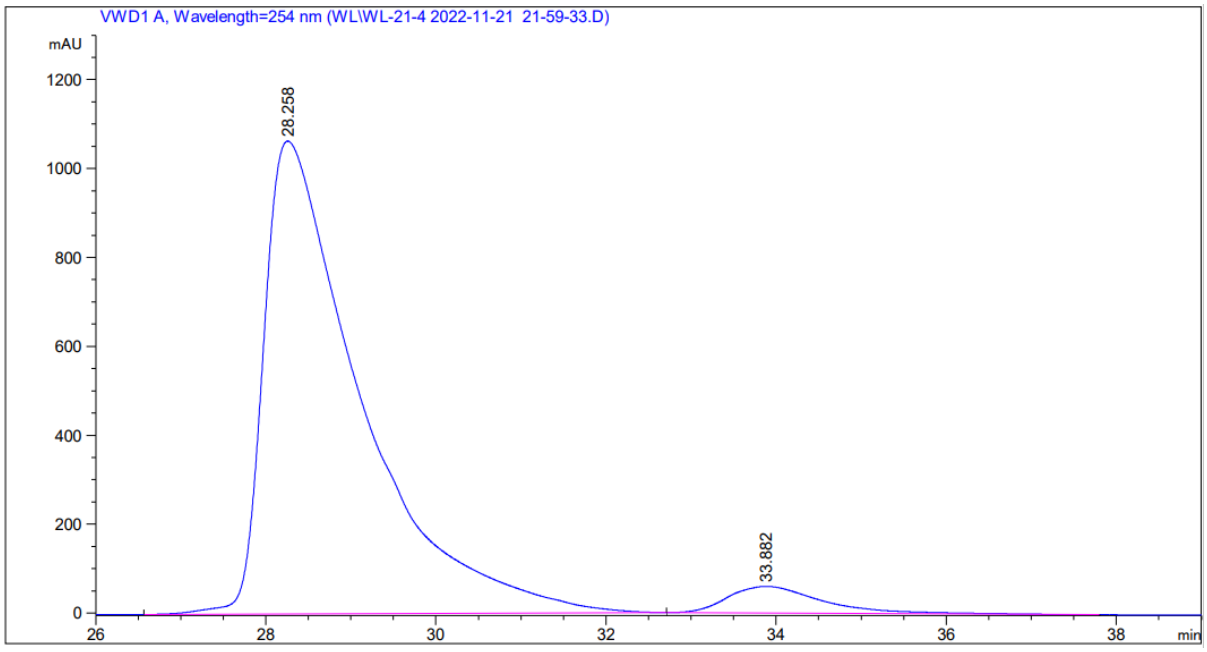
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.504	BB	1.0589	1.28476e5	1695.77661	95.6321
2	41.256	BB	1.5123	5868.06641	56.42514	4.3679

HPLC chromatogram of racemic compound 3la



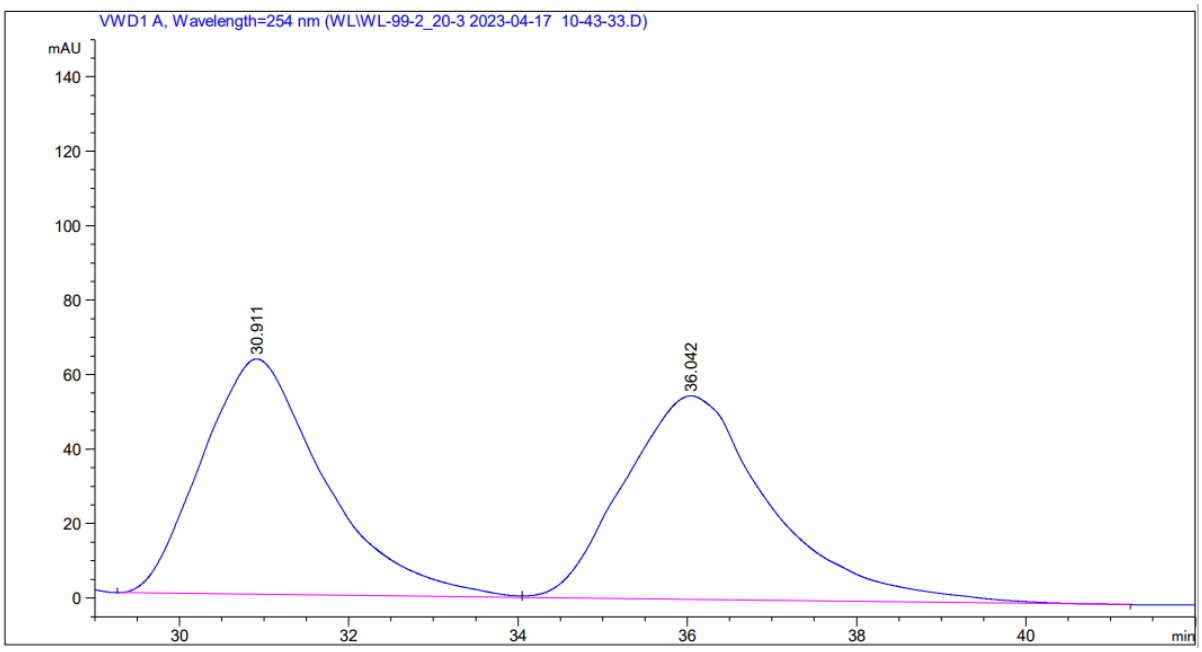
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.564	MM	1.6179	8756.66211	90.20351	49.0608
2	34.415	MM	1.9223	9091.92285	78.82776	50.9392

HPLC chromatogram of chiral compound 3la



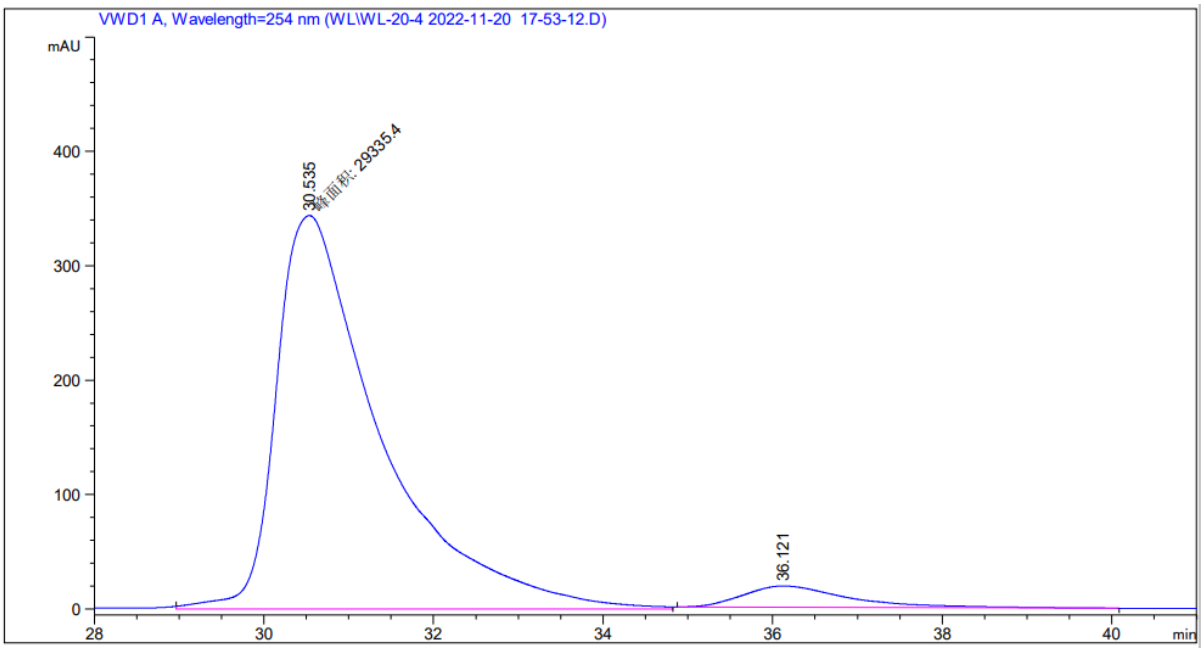
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.258	BB	1.1213	8.41767e4	1063.64722	94.7566
2	33.882	BB	1.1752	4657.92529	60.03628	5.2434

HPLC chromatogram of racemic compound 3ma



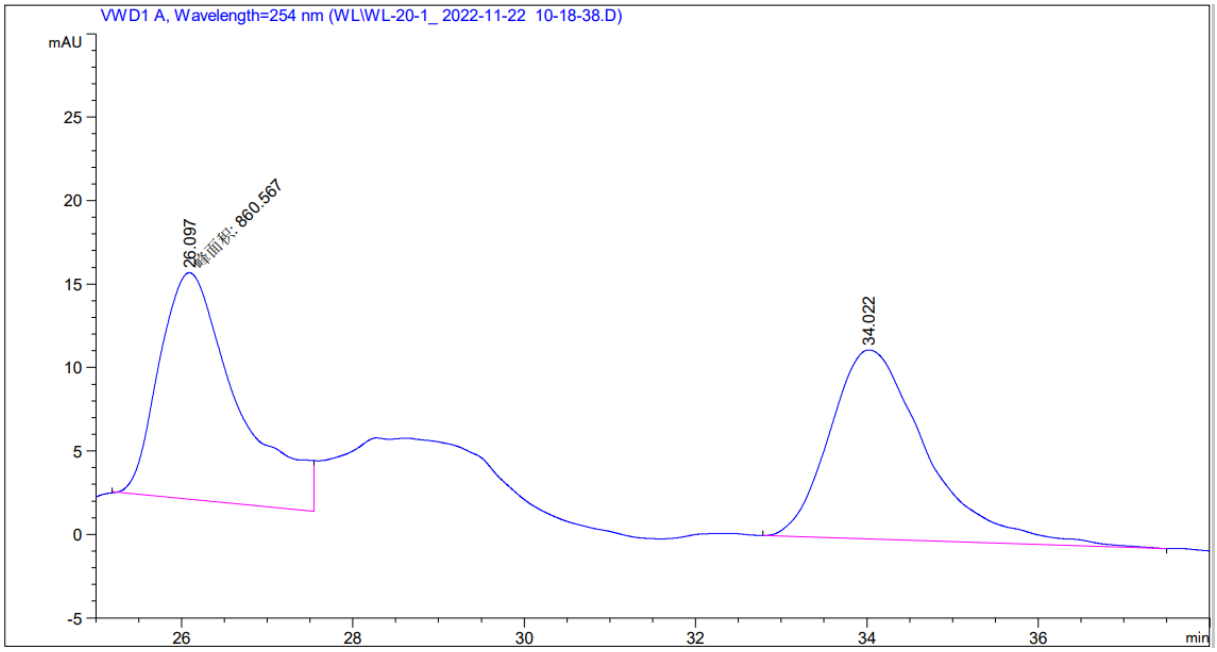
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.911	BV	1.4837	6348.95703	63.21774	49.2133
2	36.042	VB	1.7459	6551.94580	54.68330	50.7867

HPLC chromatogram of chiral compound 3ma



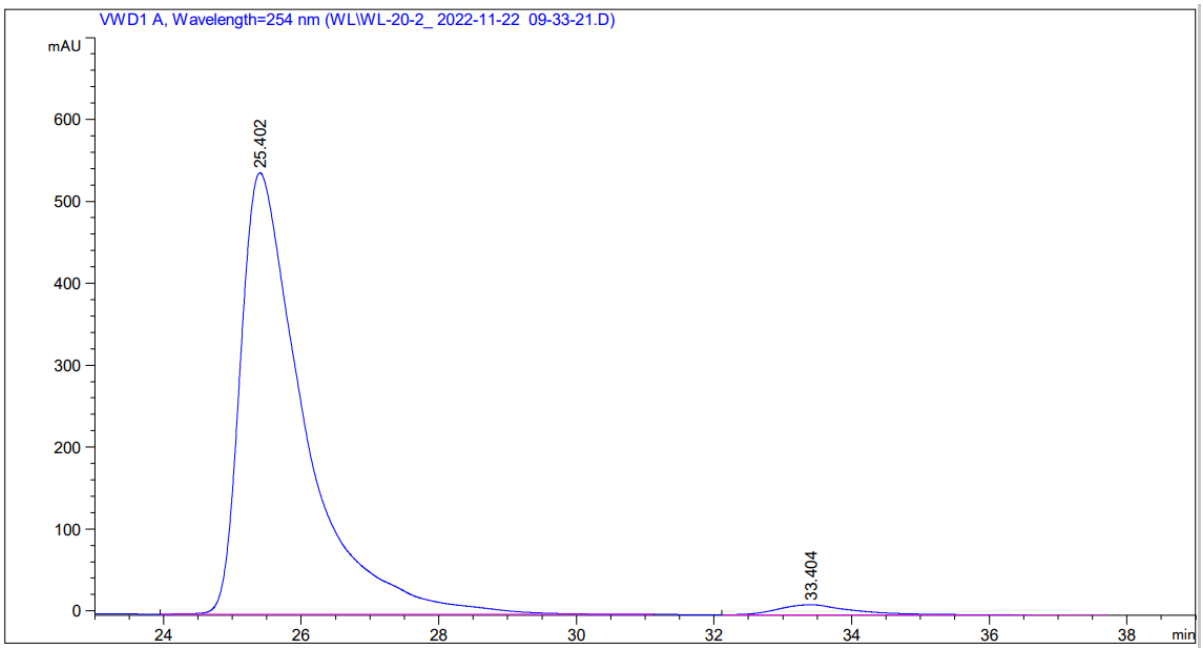
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.535	MM	1.4225	2.93354e4	343.71689	94.8048
2	36.121	BB	1.2478	1607.54736	18.57317	5.1952

HPLC chromatogram of racemic compound 3na



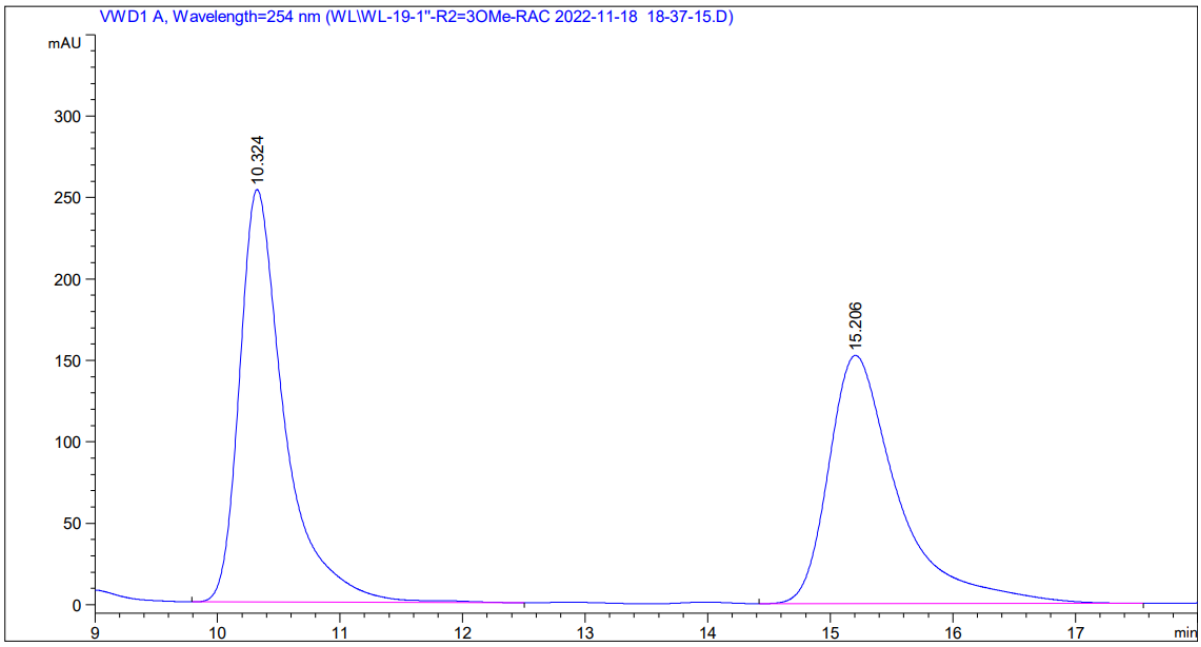
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.097	MM	1.0576	860.56720	13.56189	49.2367
2	34.022	BB	1.1174	887.24908	11.31984	50.7633

HPLC chromatogram of chiral compound 3na



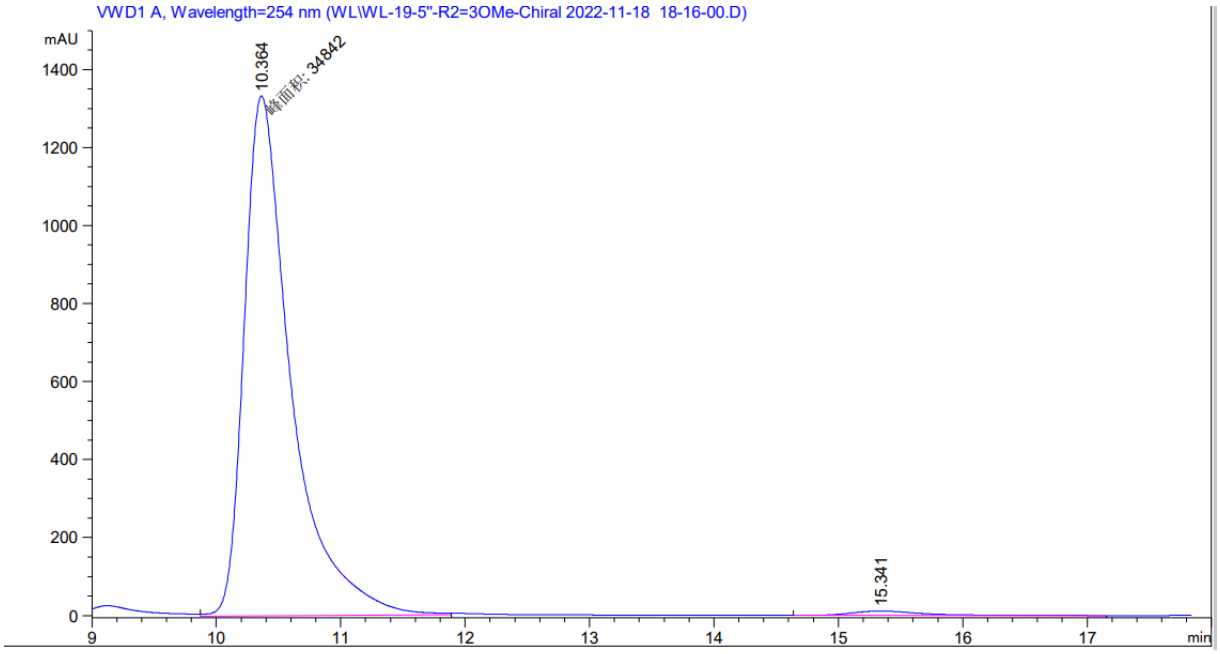
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.402	BB	0.9244	3.46165e4	538.93243	97.2959
2	33.404	BB	1.1201	962.06354	12.37305	2.7041

HPLC chromatogram of racemic compound 3oa



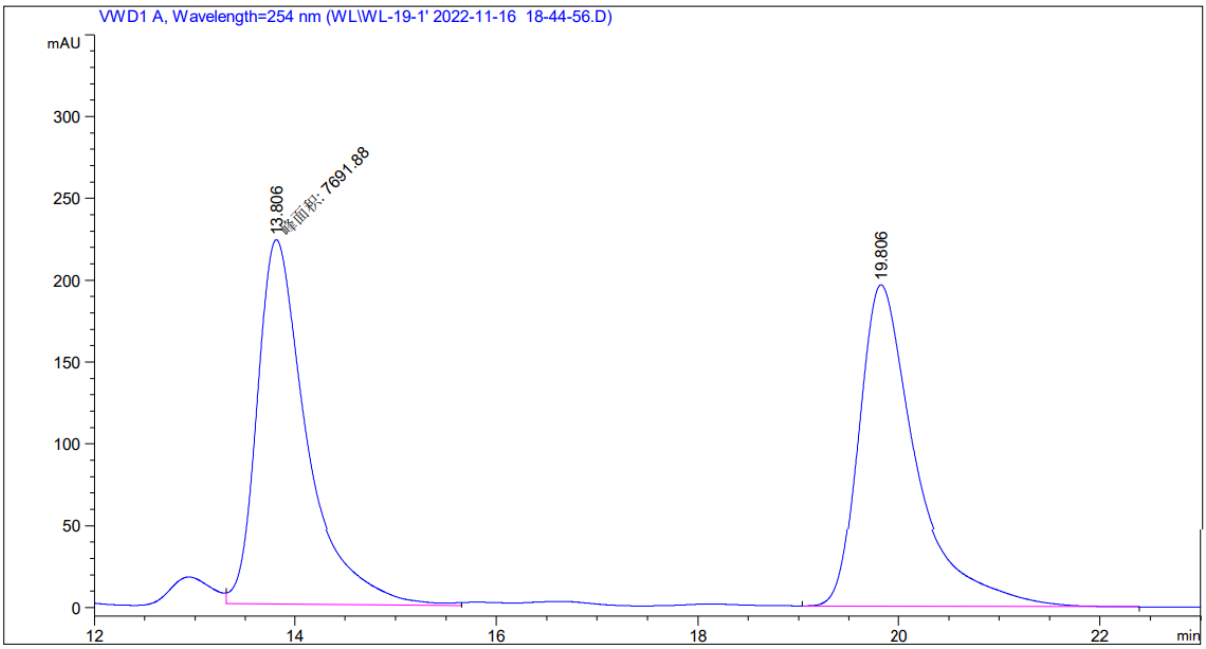
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.324	BB	0.3757	6440.18701	253.20317	51.9270
2	15.206	BB	0.5765	5962.19189	152.35883	48.0730

HPLC chromatogram of chiral compound 3oa



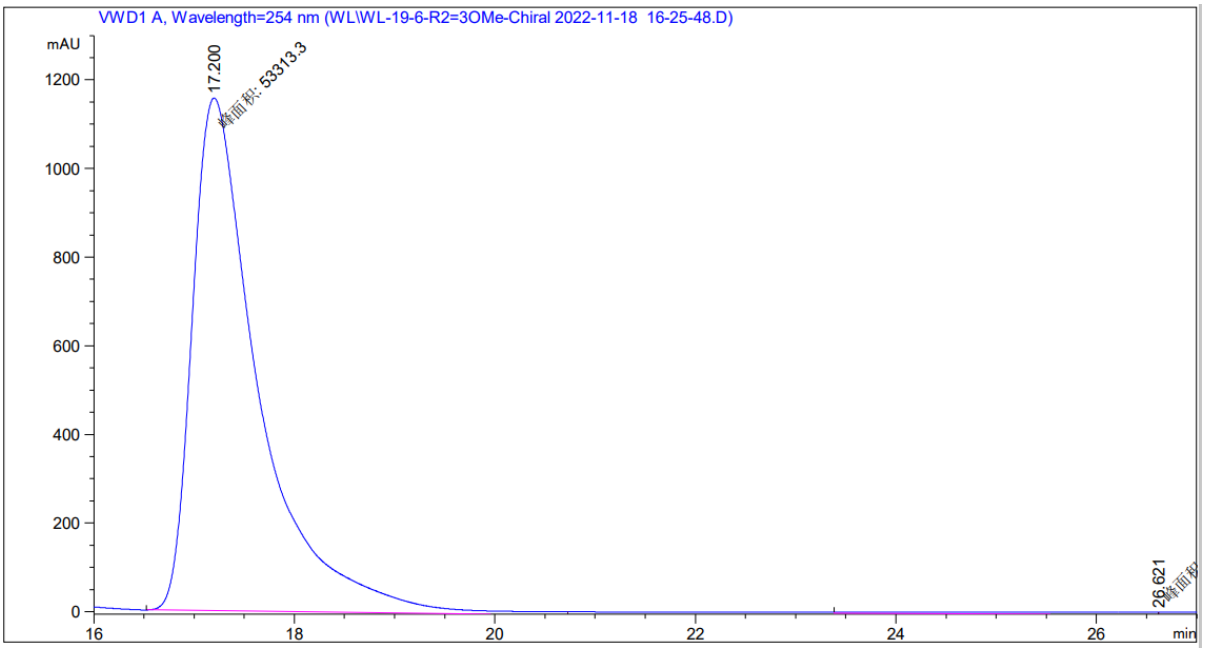
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.364	MM	0.4360	3.48420e4	1331.99011	98.7527
2	15.341	BB	0.5904	440.07642	11.17481	1.2473

HPLC chromatogram of racemic compound 3pa



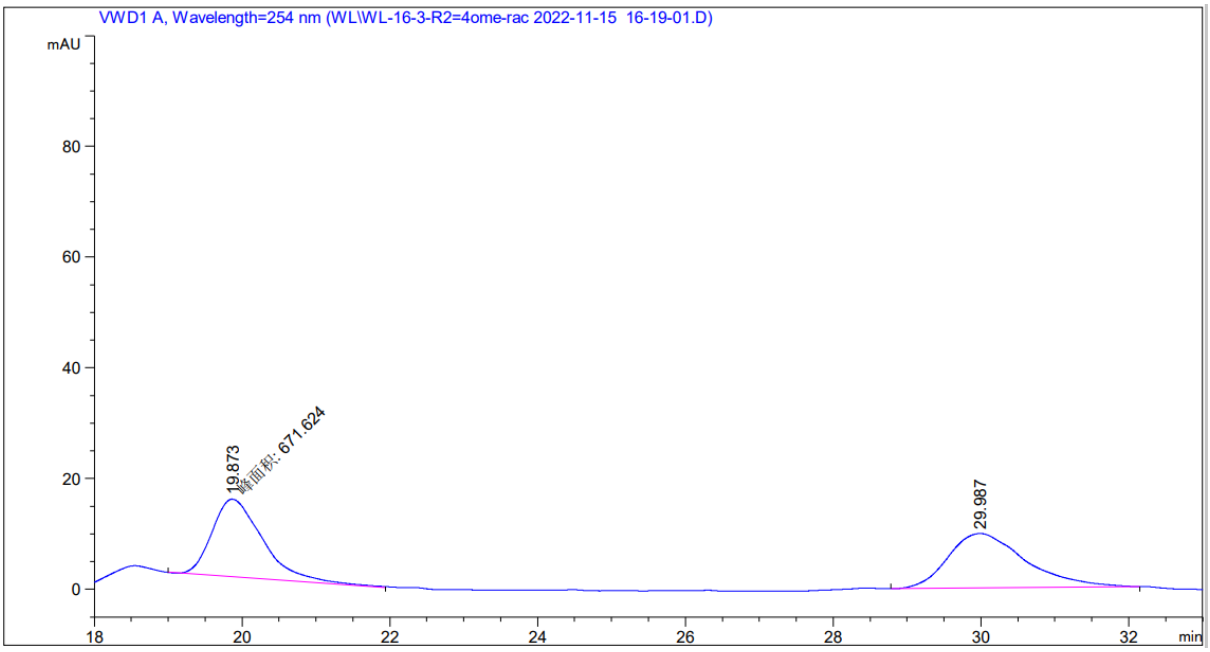
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.806	MM	0.5760	7691.88477	222.56355	49.8901
2	19.806	BB	0.5822	7725.76611	196.27890	50.1099

HPLC chromatogram of chiral compound 3pa



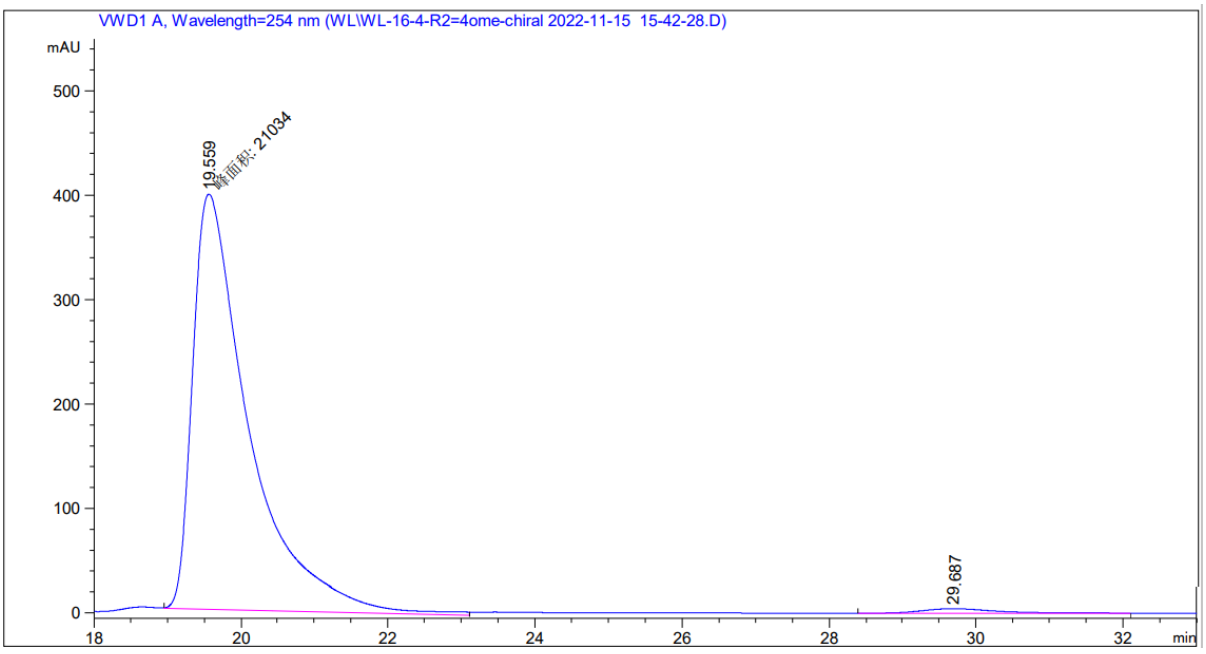
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.200	MM	0.7687	5.33133e4	1155.95874	98.6088
2	26.621	MM	2.0732	752.17511	6.04681	1.3912

HPLC chromatogram of racemic compound 3qa



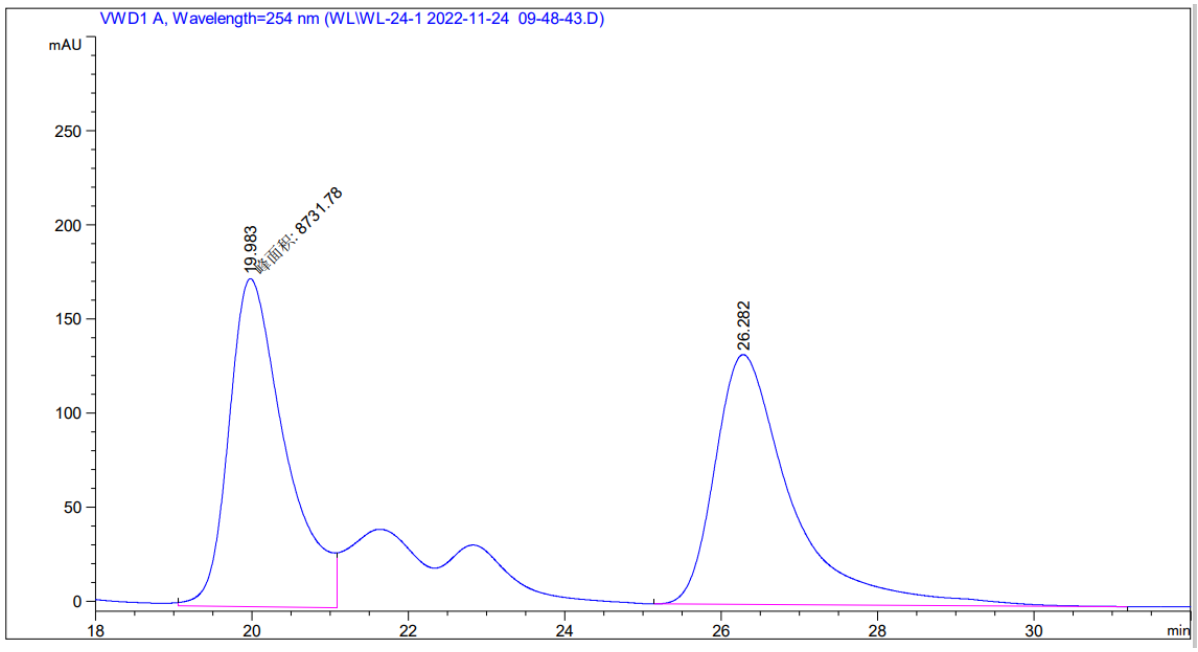
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.873	MM	0.7978	671.62360	14.03162	48.3559
2	29.987	BB	1.0335	717.29266	9.85132	51.6441

HPLC chromatogram of chiral compound 3qa



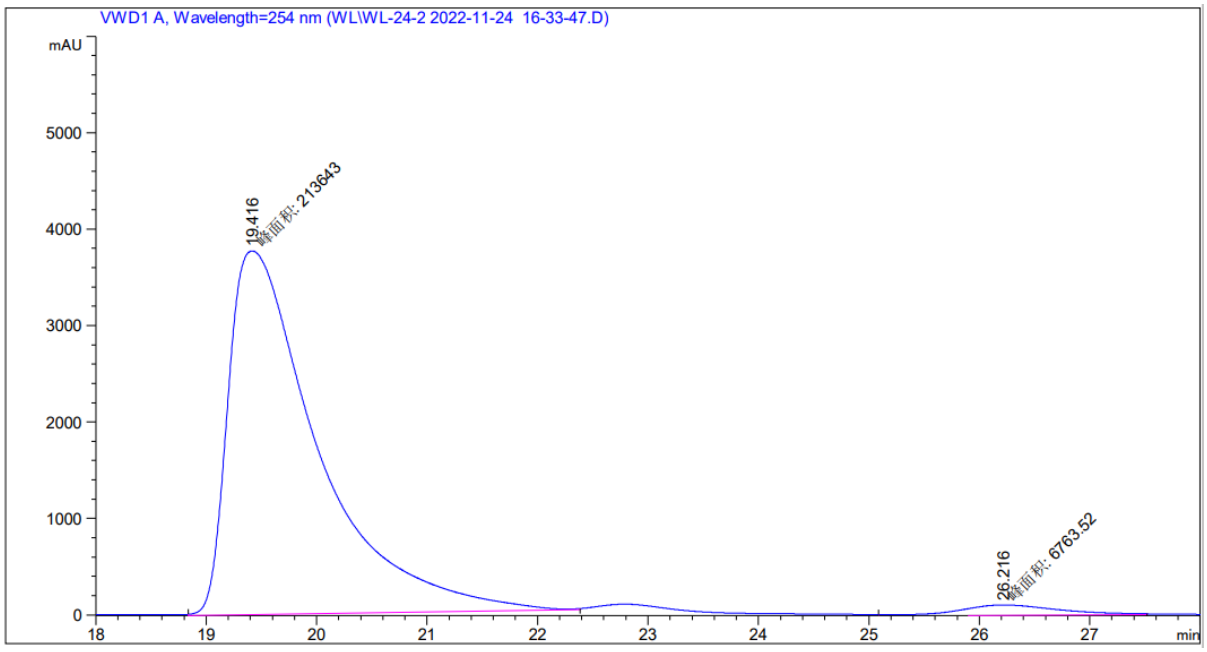
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.559	MM	0.8812	2.10340e4	397.82950	98.5934
2	29.687	BB	0.9603	300.08990	4.29404	1.4066

HPLC chromatogram of racemic compound 3ra



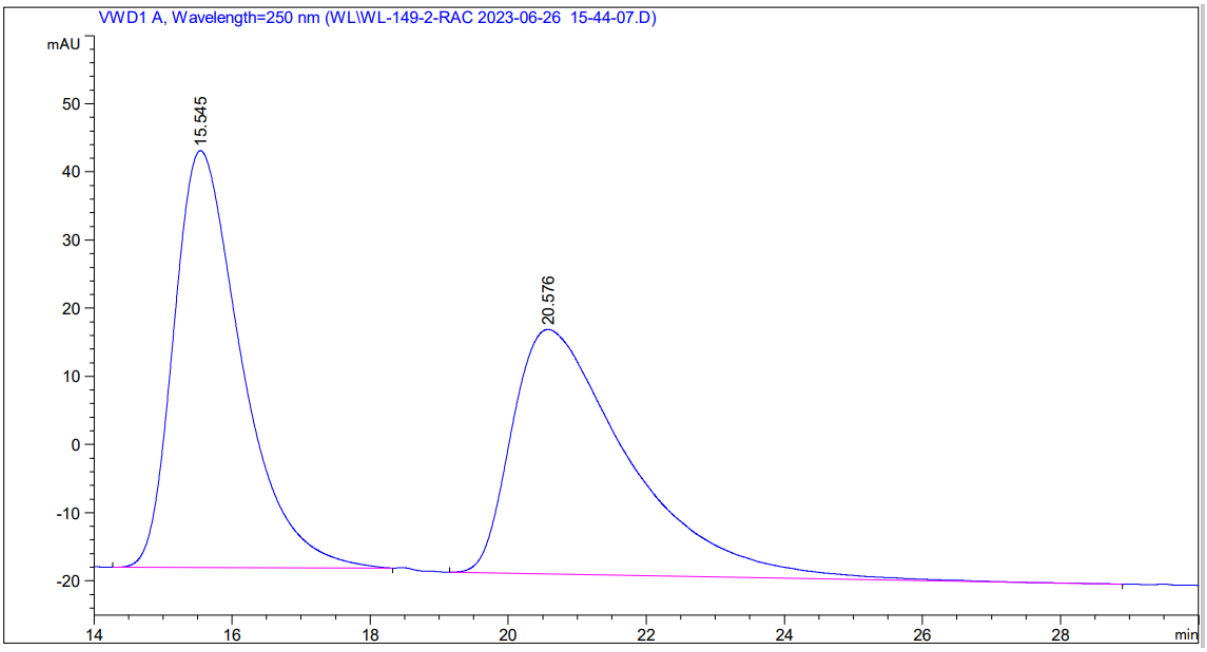
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.983	MM	0.8357	8731.78320	174.14961	49.4631
2	26.282	BB	0.9960	8921.34961	132.58292	50.5369

HPLC chromatogram of chiral compound 3ra



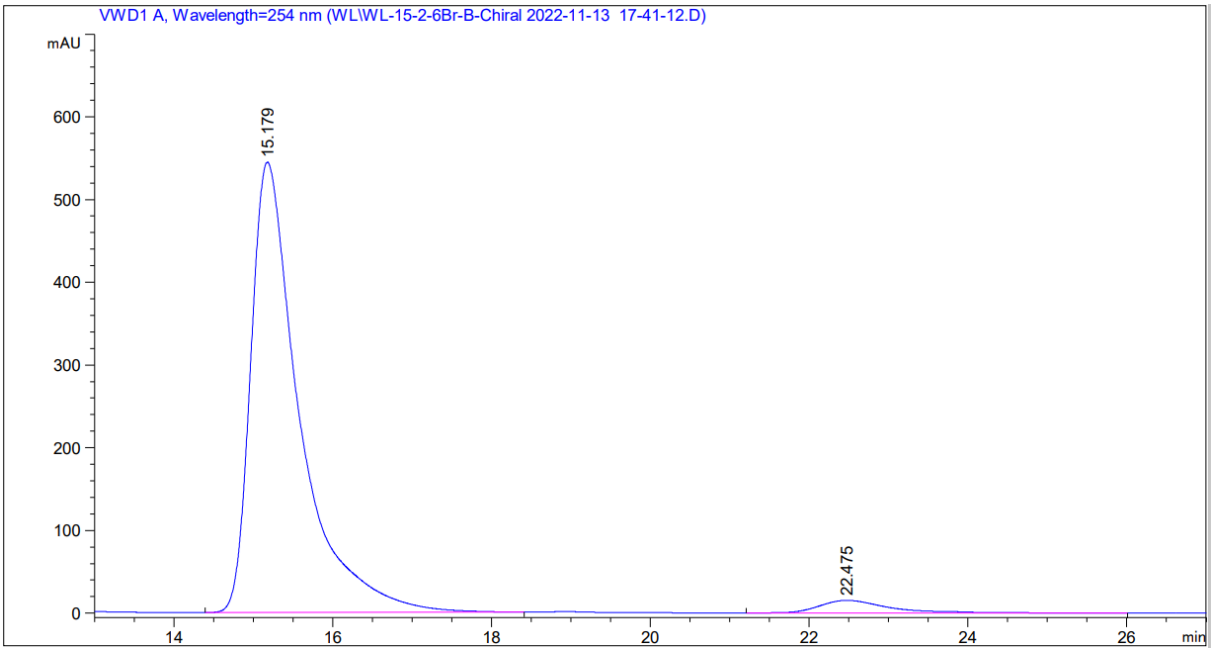
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.416	MM	0.9441	2.13643e5	3771.60767	96.9314
2	26.216	MM	1.0606	6763.51514	106.28451	3.0686

HPLC chromatogram of racemic compound 3sa



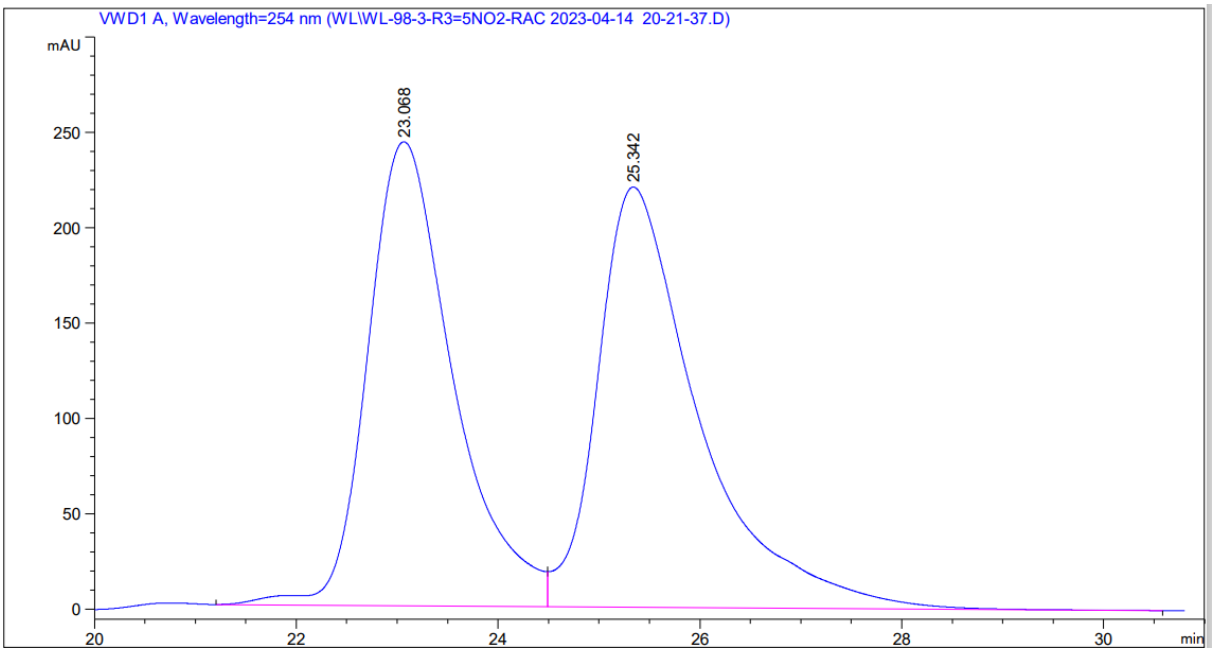
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.545	BB	1.0247	4166.75342	61.17151	49.7447
2	20.576	BB	1.6774	4209.51807	35.89039	50.2553

HPLC chromatogram of chiral compound 3sa



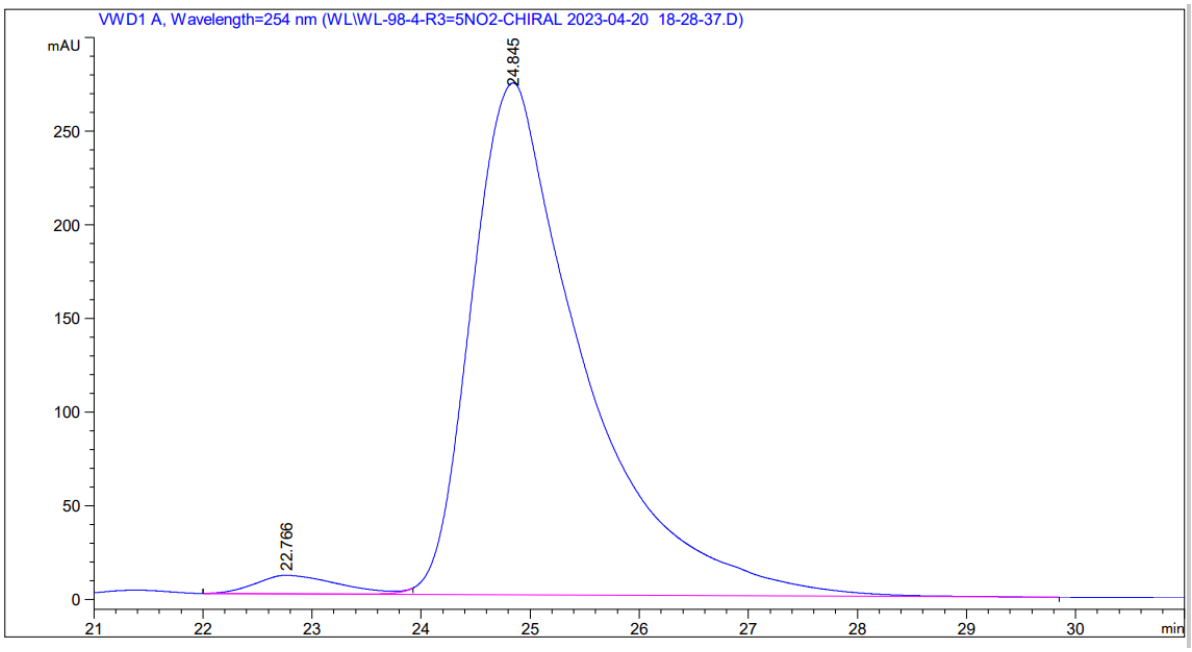
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.978	BB	0.9822	2.98778e4	453.74811	97.1572
2	21.139	BB	1.6552	874.21472	6.78963	2.8428

HPLC chromatogram of racemic compound 3ab



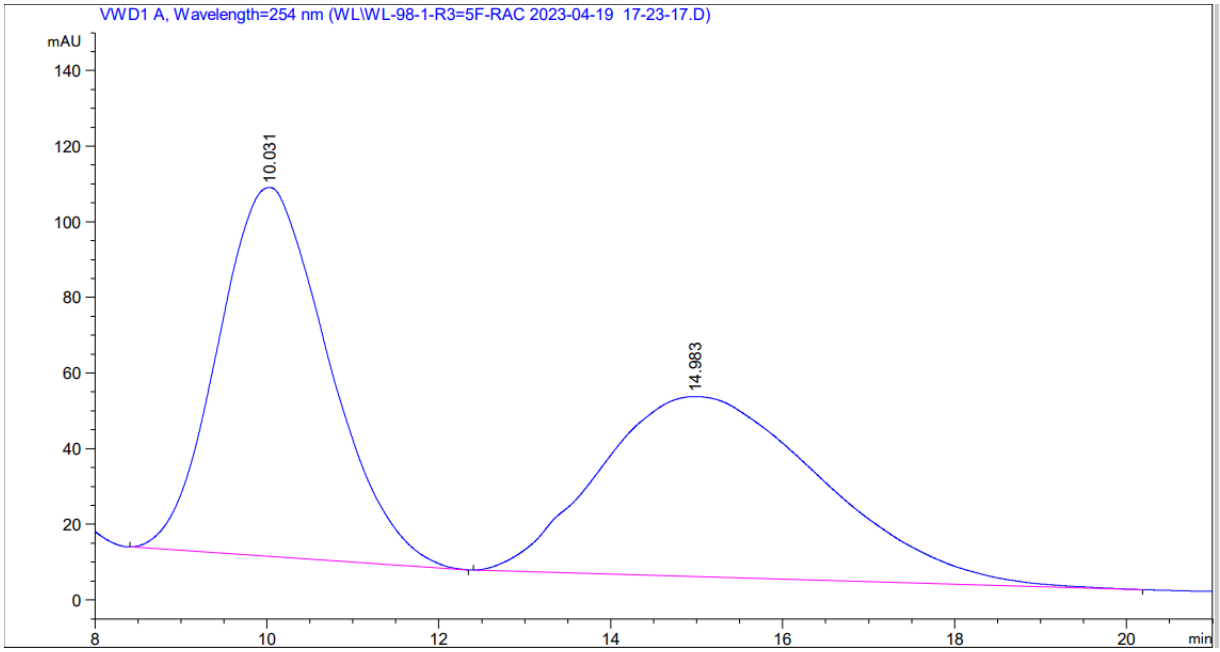
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.068	VV R	0.8796	1.43085e4	243.05489	48.2292
2	25.342	VB A	1.0291	1.53592e4	220.10809	51.7708

HPLC chromatogram of chiral compound 3ab



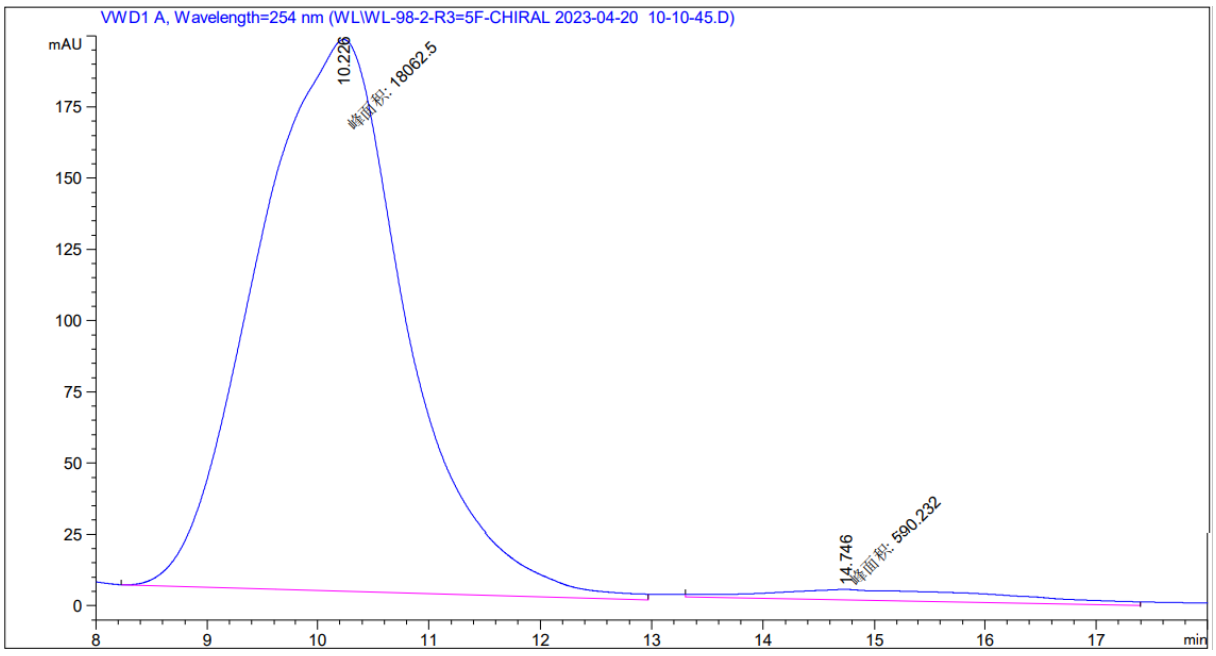
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.766	BV E	0.7892	514.73071	9.87444	2.5744
2	24.845	VB R	1.0174	1.94797e4	273.02283	97.4256

HPLC chromatogram of racemic compound 3ac



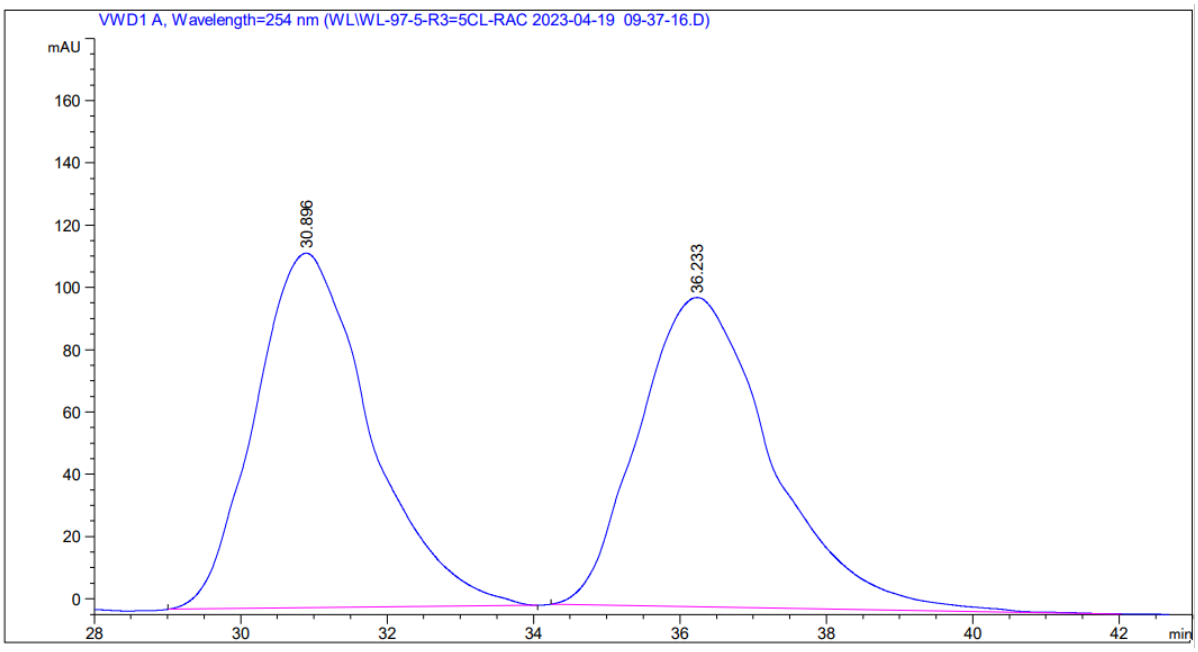
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.031	BB	1.3802	8710.21777	97.59608	50.3836
2	14.983	BB	2.4206	8577.58594	47.61674	49.6164

HPLC chromatogram of chiral compound 3ac



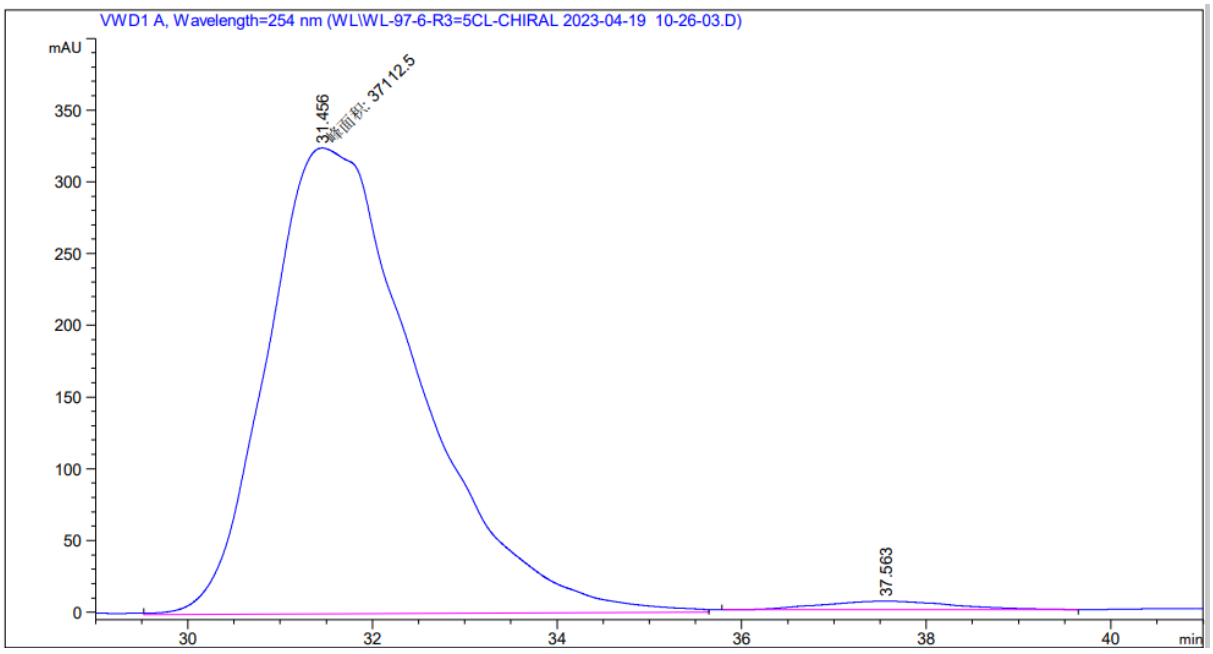
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.226	MM	1.5555	1.80625e4	193.52879	96.8357
2	14.746	MM	2.6894	590.23193	3.65771	3.1643

HPLC chromatogram of racemic compound 3ad



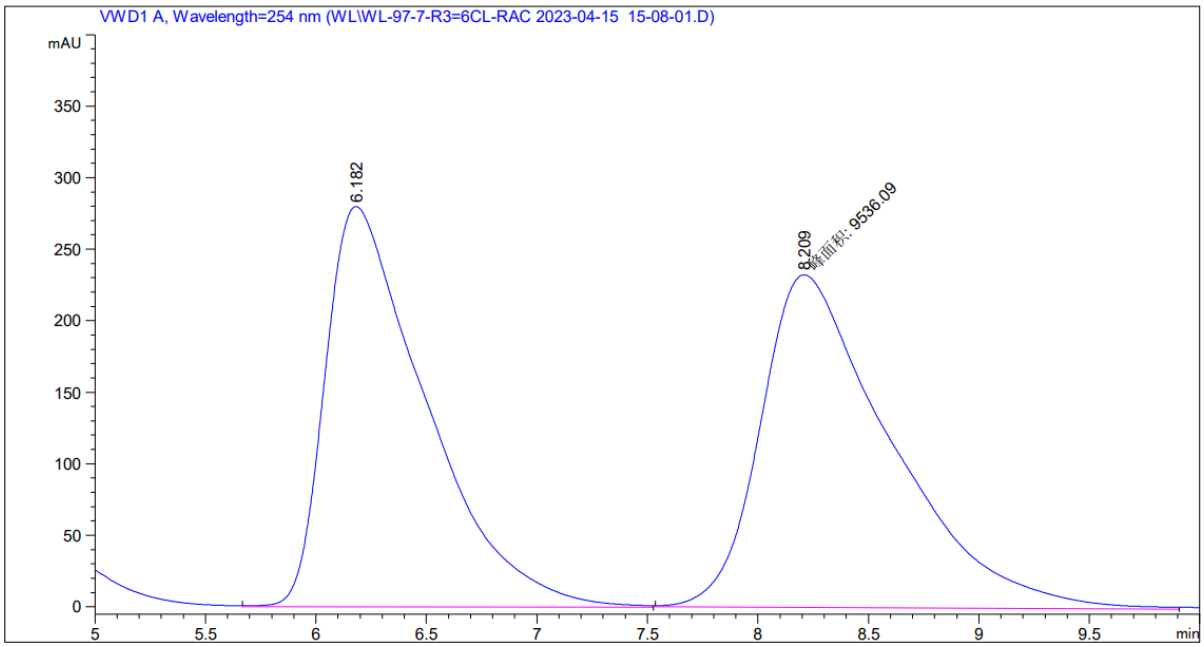
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.896	BB	1.4979	1.24017e4	113.84195	49.8362
2	36.233	BB	1.7106	1.24832e4	99.30011	50.1638

HPLC chromatogram of chiral compound 3ad



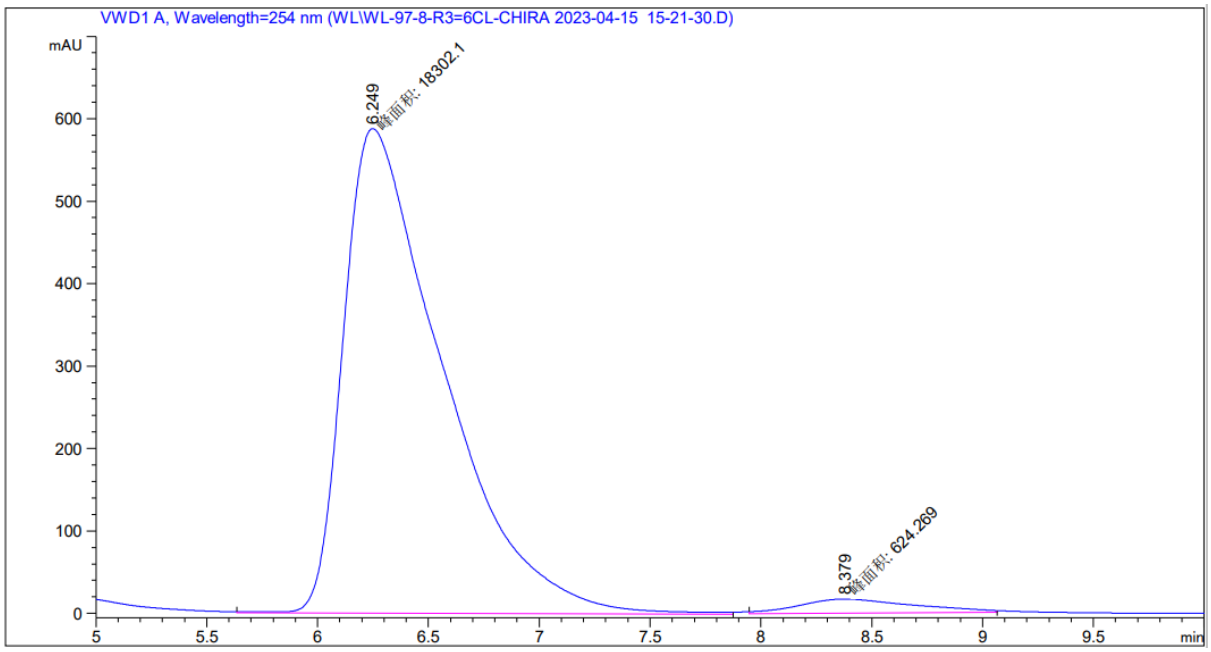
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.456	MM	1.9049	3.71125e4	324.71173	98.4245
2	37.563	BB	1.2271	594.06952	6.04195	1.5755

HPLC chromatogram of racemic compound 3ae



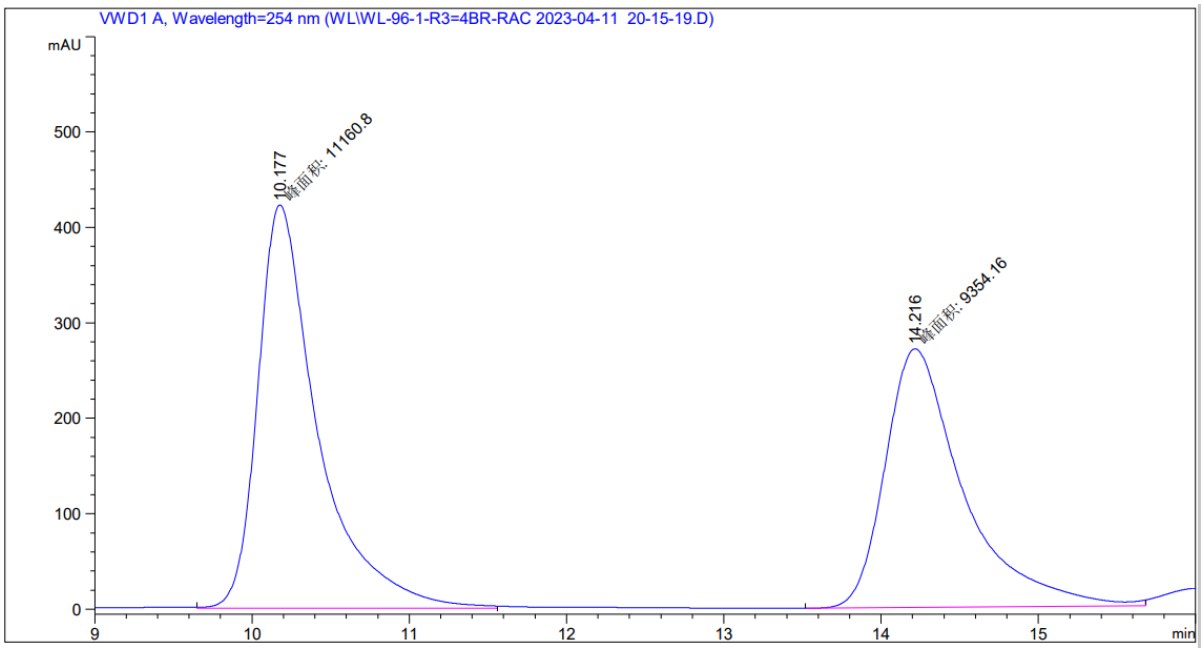
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.182	VV	0.4588	8891.47168	279.71945	48.2509
2	8.209	MM	0.6835	9536.09180	232.52554	51.7491

HPLC chromatogram of chiral compound 3ae



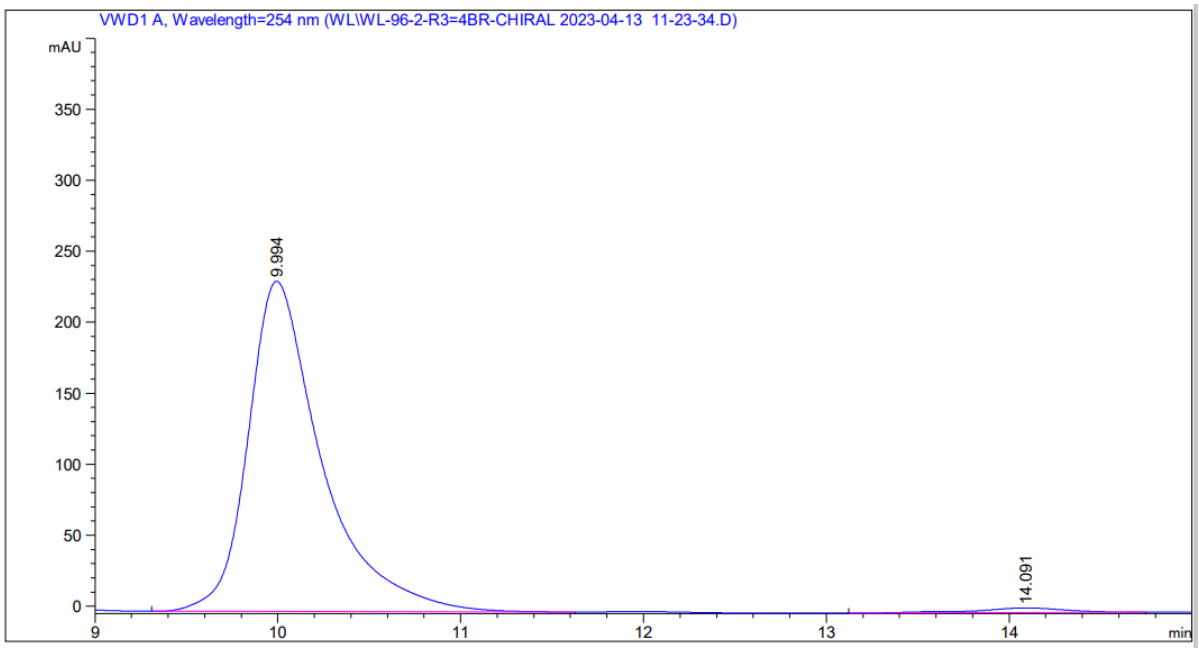
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.249	MM	0.5187	1.83021e4	588.09729	96.7016
2	8.379	MM	0.6084	624.26874	17.10121	3.2984

HPLC chromatogram of racemic compound 3af



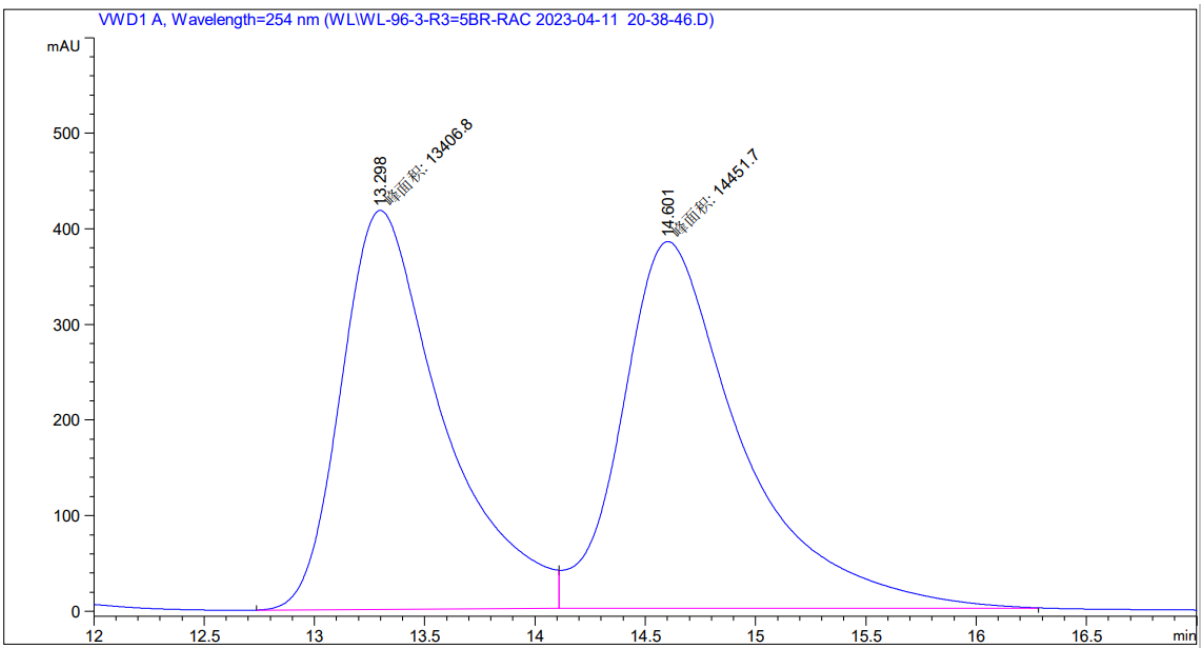
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.177	MM	0.4406	1.11608e4	422.21512	54.4033
2	14.216	MM	0.5757	9354.15723	270.82816	45.5967

HPLC chromatogram of chiral compound 3af



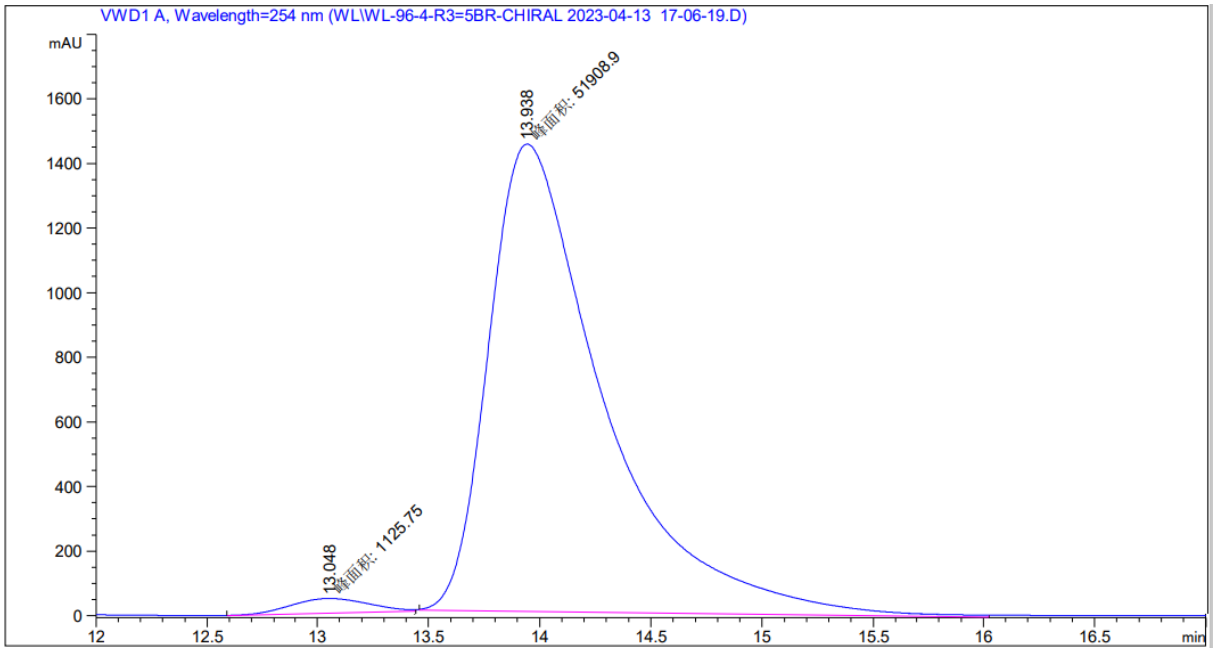
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.994	BB	0.4073	6505.18994	232.59254	98.2835
2	14.091	BB	0.4975	113.60966	3.27656	1.7165

HPLC chromatogram of racemic compound 3ag



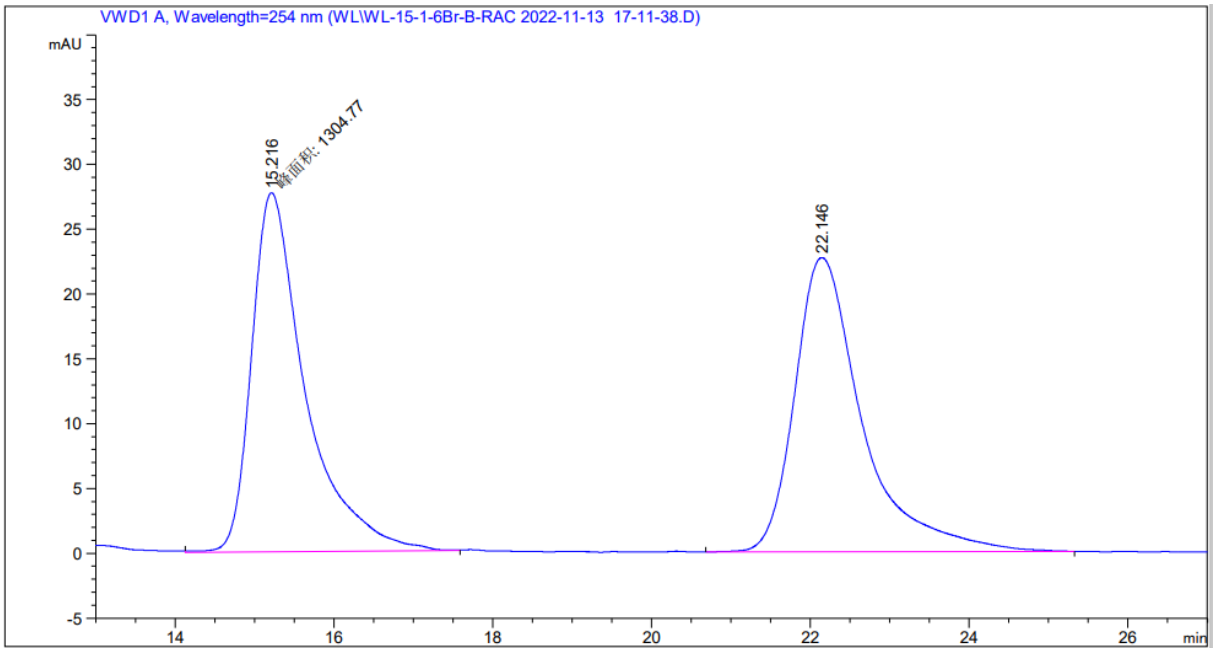
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.298	MM	0.5354	1.34068e4	417.31442	48.1246
2	14.601	MM	0.6283	1.44517e4	383.36484	51.8754

HPLC chromatogram of chiral compound 3ag



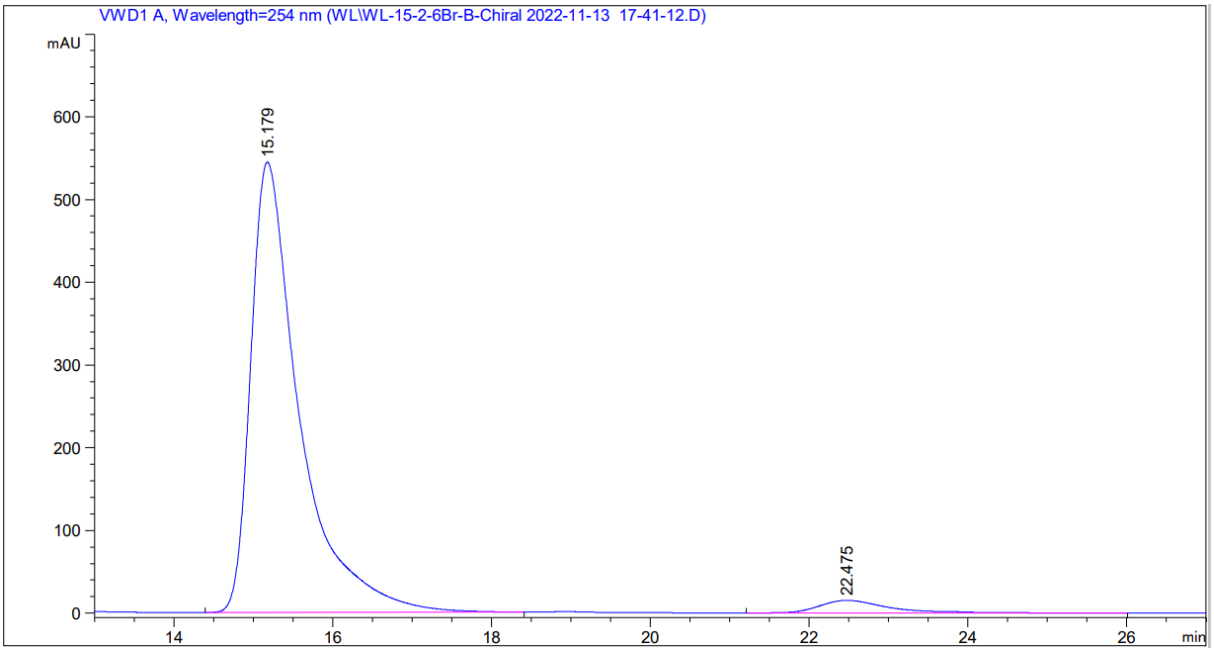
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.048	MM	0.4110	1125.74744	45.65448	2.1227
2	13.938	MM	0.5985	5.19089e4	1445.60266	97.8773

HPLC chromatogram of racemic compound 3ah



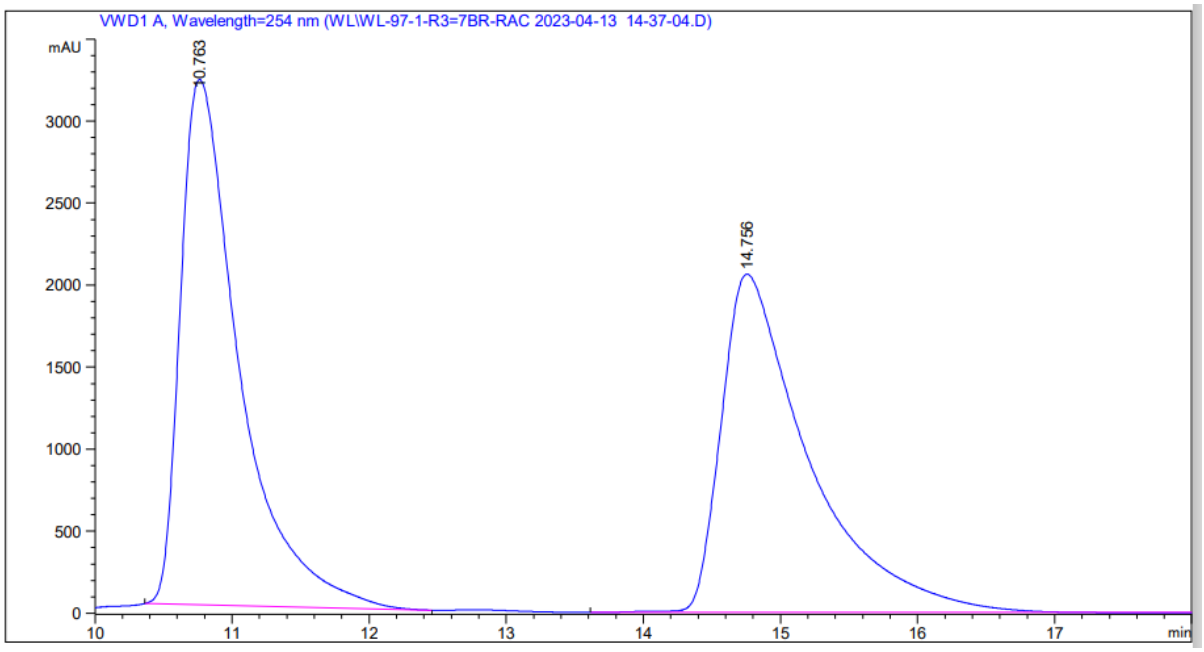
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.216	MM	0.7846	1304.77332	27.71628	49.3337
2	22.146	BB	0.8737	1340.01904	22.69889	50.6663

HPLC chromatogram of chiral compound 3ah



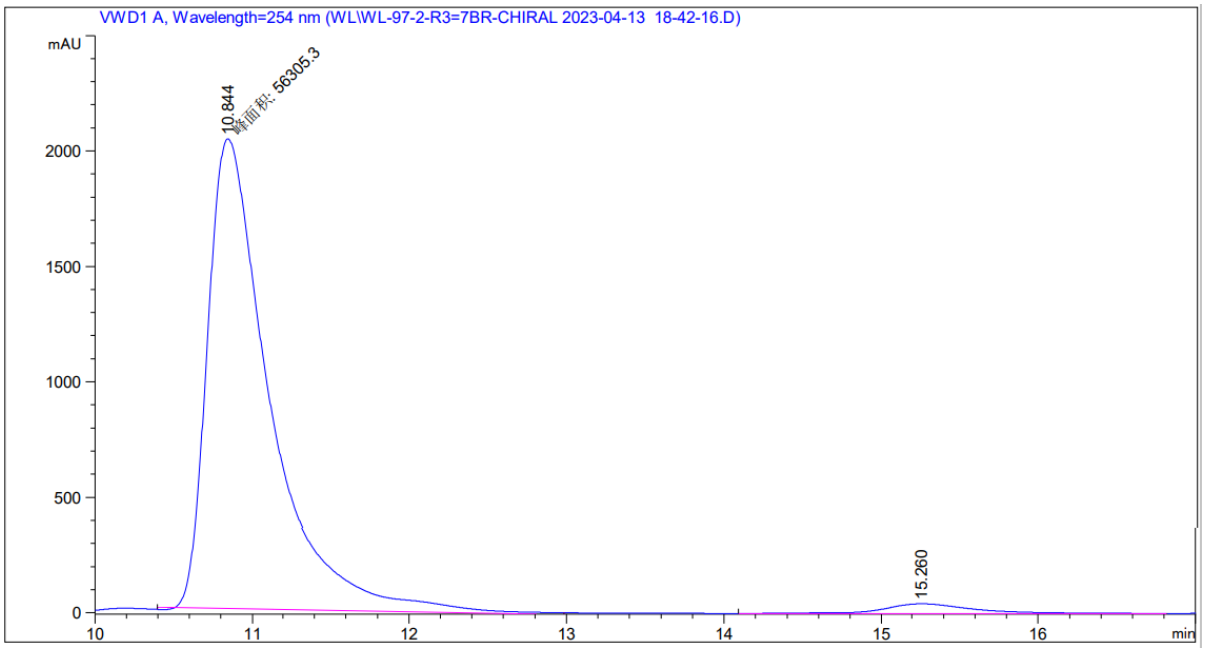
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.179	BB	0.6274	2.31589e4	544.30719	96.1389
2	22.475	BB	0.9082	930.09729	15.23523	3.8611

HPLC chromatogram of racemic compound 3ai



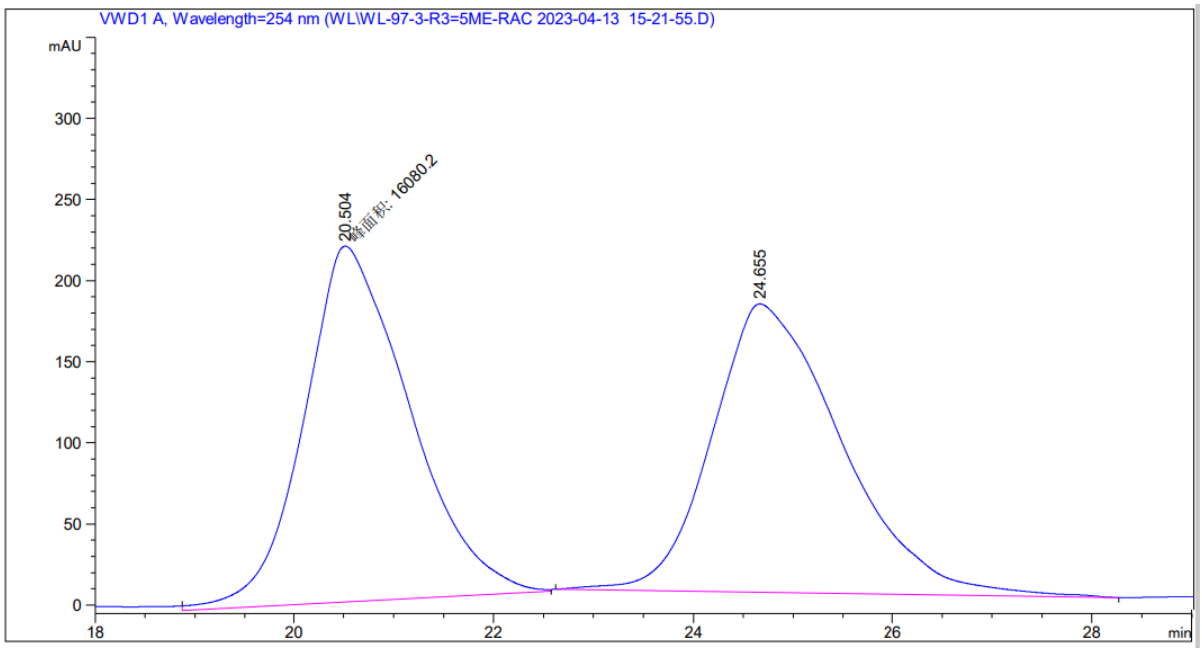
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.763	BB	0.4231	9.55428e4	3202.20142	51.0923
2	14.756	BB	0.6251	9.14575e4	2063.39673	48.9077

HPLC chromatogram of chiral compound 3ai



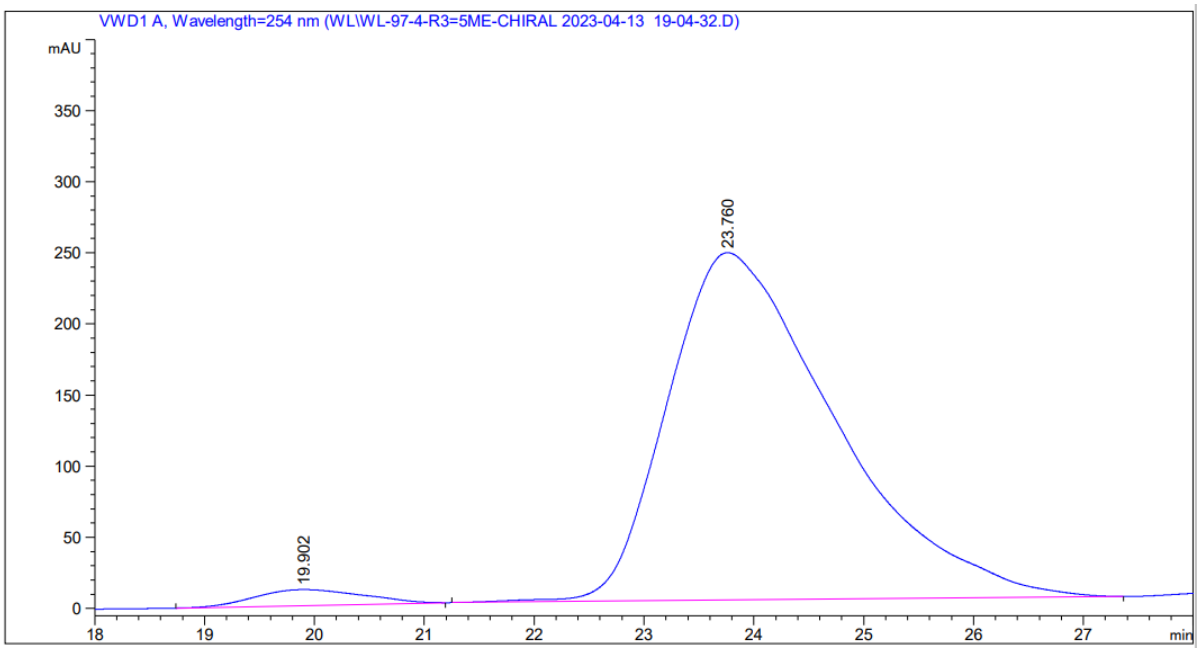
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.844	MM	0.4612	5.63053e4	2034.52771	97.1772
2	15.260	BB	0.5772	1635.56628	41.91501	2.8228

HPLC chromatogram of racemic compound 3aj



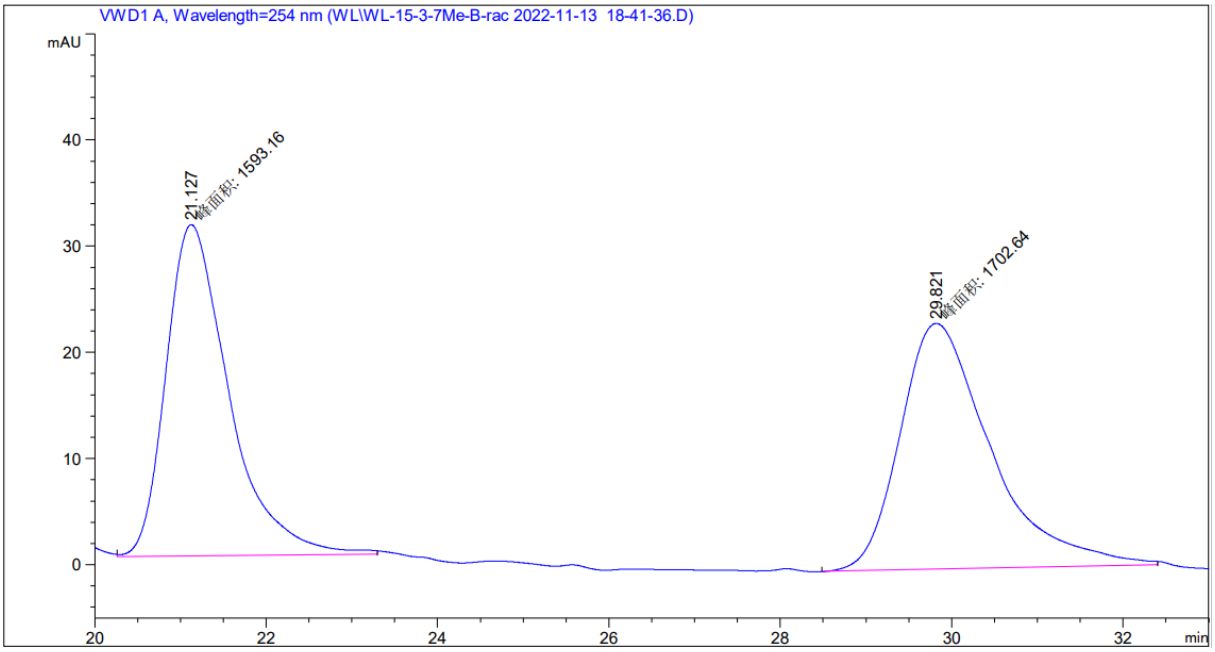
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.504	MM	1.2218	1.60802e4	219.34219	50.0643
2	24.655	BB	1.3868	1.60389e4	177.73795	49.9357

HPLC chromatogram of chiral compound 3aj



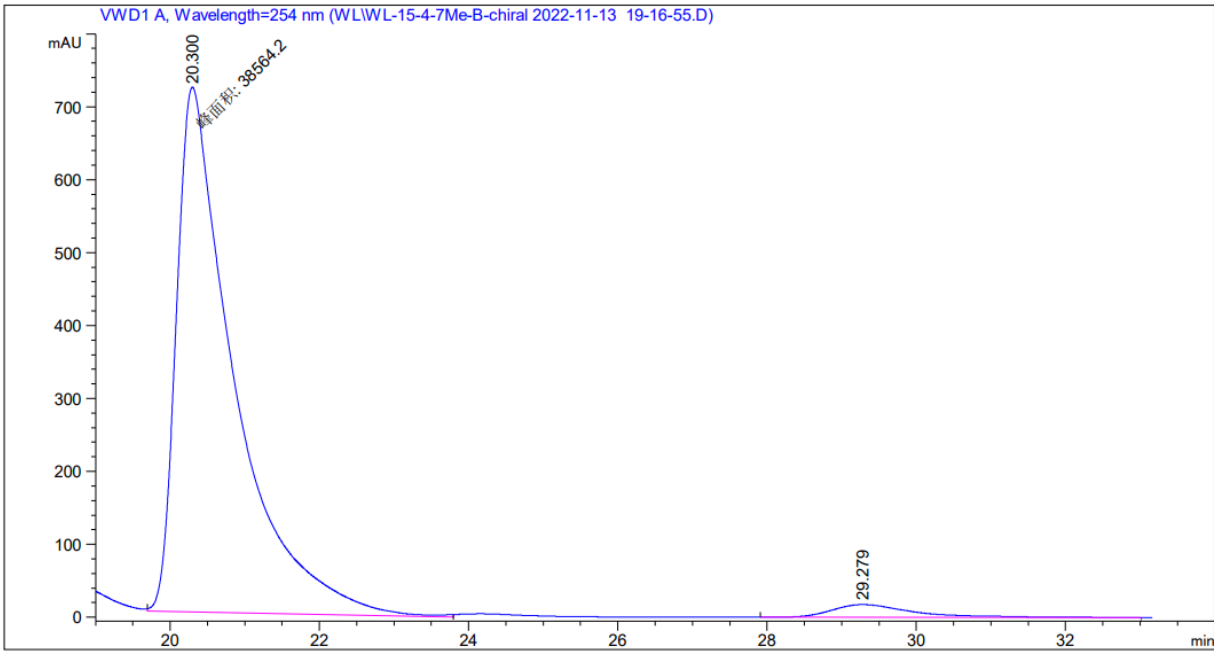
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.902	BB	1.0067	757.17200	11.18623	2.8451
2	23.760	BB	1.5679	2.58563e4	244.28194	97.1549

HPLC chromatogram of racemic compound 3ak



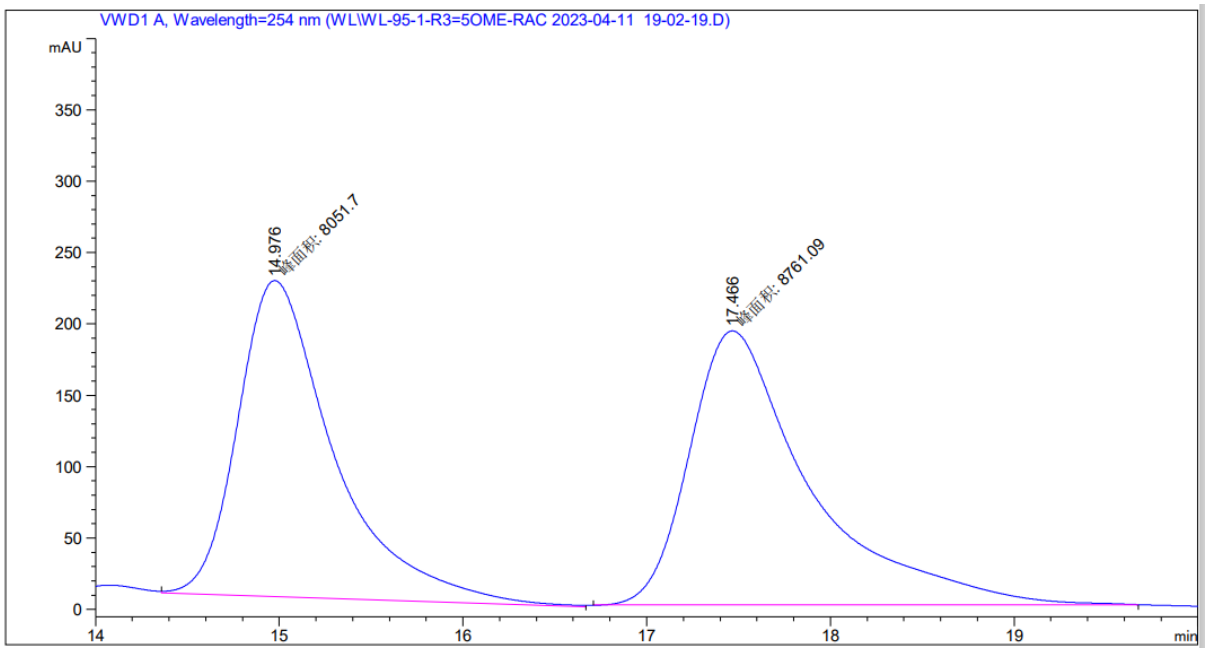
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.127	MM	0.8516	1593.16479	31.18139	48.3391
2	29.821	MM	1.2270	1702.64233	23.12717	51.6609

HPLC chromatogram of chiral compound 3ak



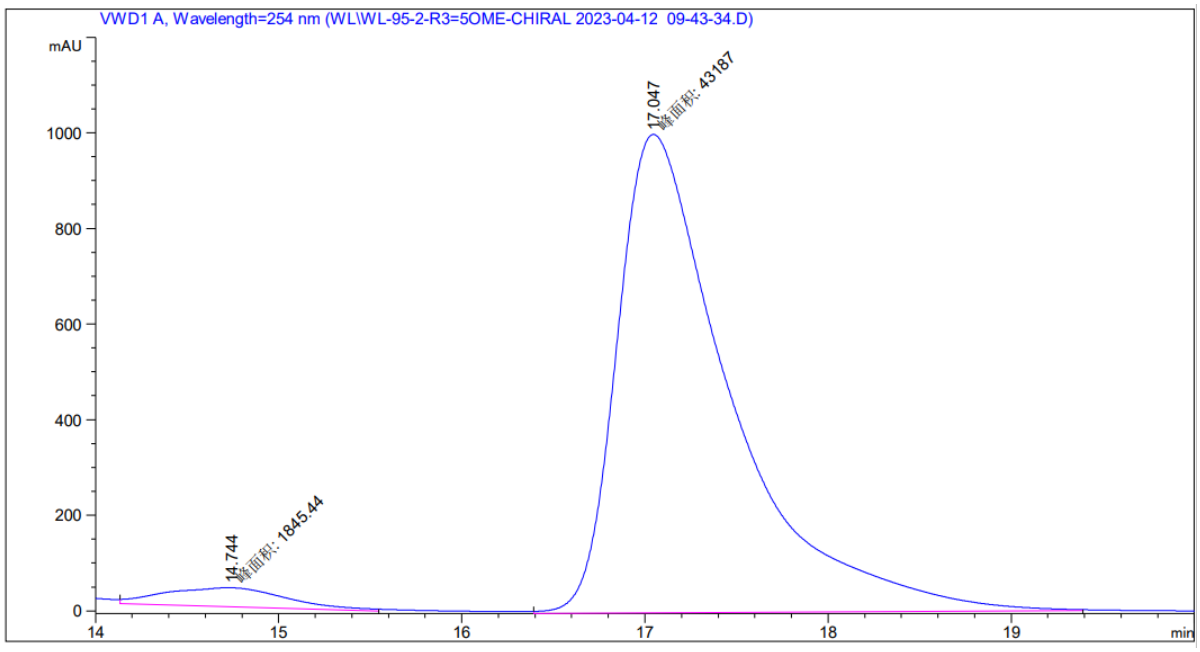
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.300	MM	0.8931	3.85642e4	719.63861	96.6771
2	29.279	BB	1.0911	1325.51294	17.55102	3.3229

HPLC chromatogram of racemic compound 3al



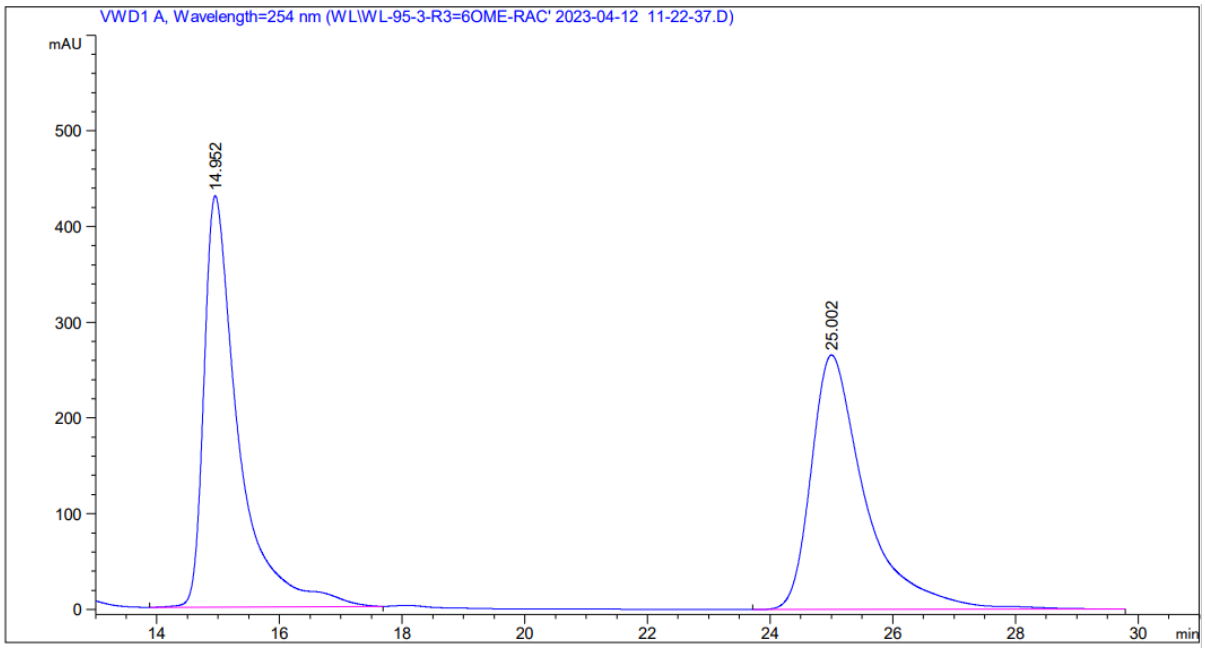
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.976	MM	0.6062	8051.70313	221.38652	47.8903
2	17.466	MM	0.7603	8761.09277	192.05644	52.1097

HPLC chromatogram of chiral compound 3al



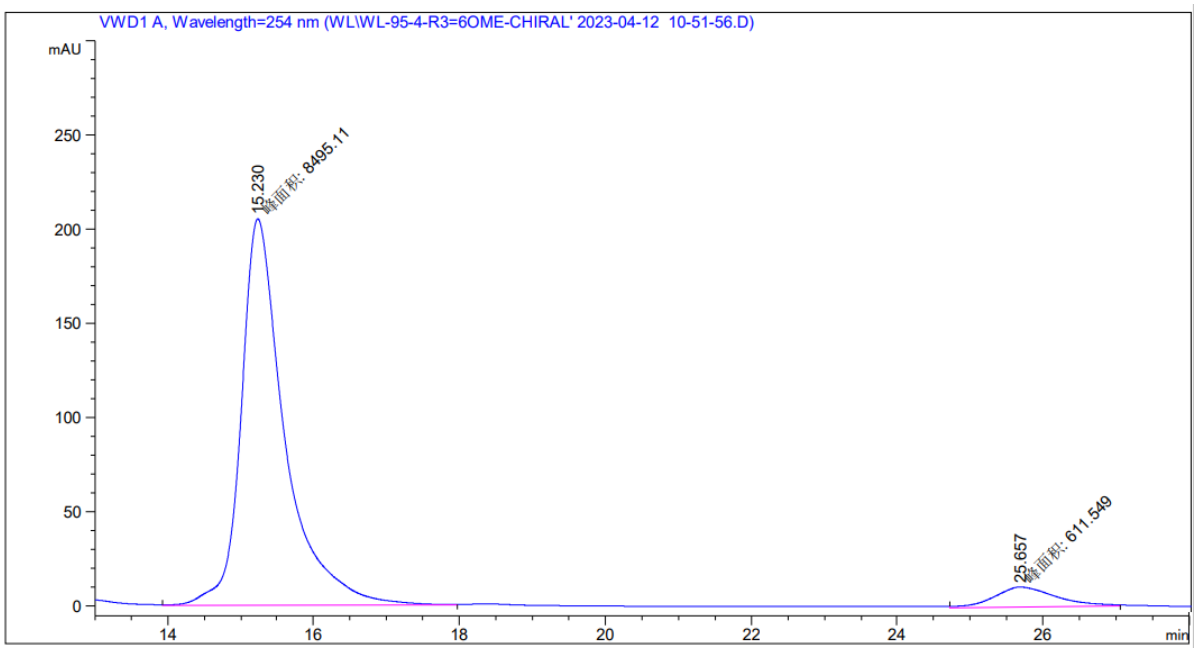
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.744	MM	0.7720	1845.43567	39.84261	4.0980
2	17.047	MM	0.7195	4.31870e4	1000.38239	95.9020

HPLC chromatogram of racemic compound 3am



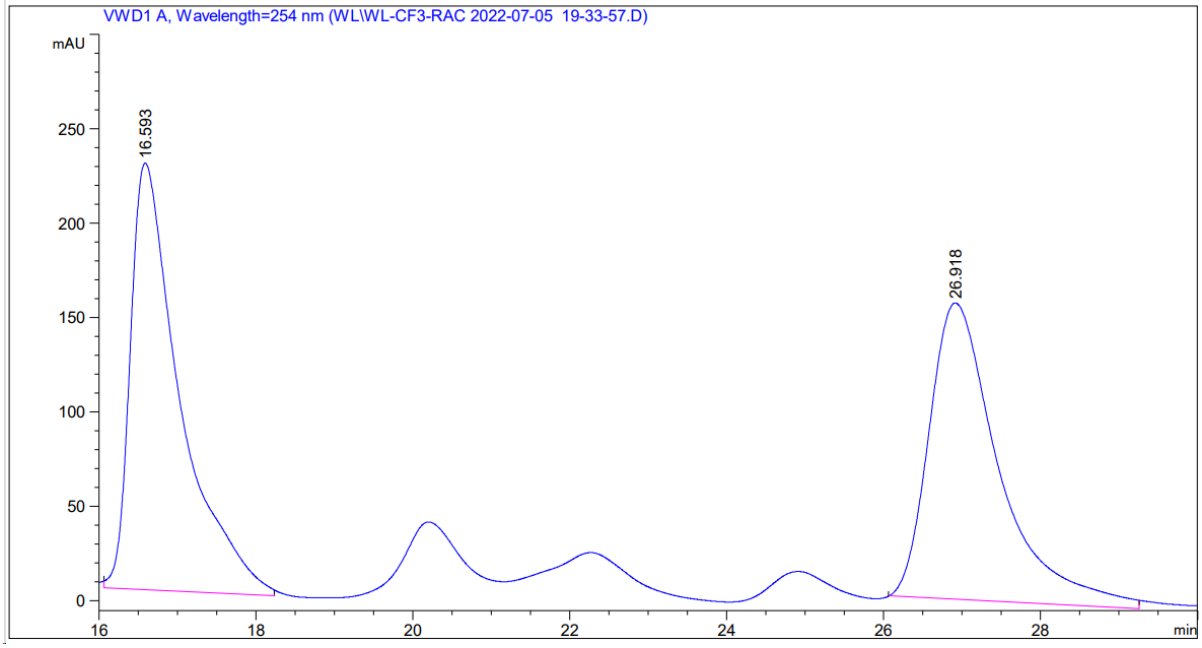
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.952	BB	0.5635	1.67018e4	429.68689	50.7157
2	25.002	BBA	0.8961	1.62304e4	265.90964	49.2843

HPLC chromatogram of chiral compound 3am



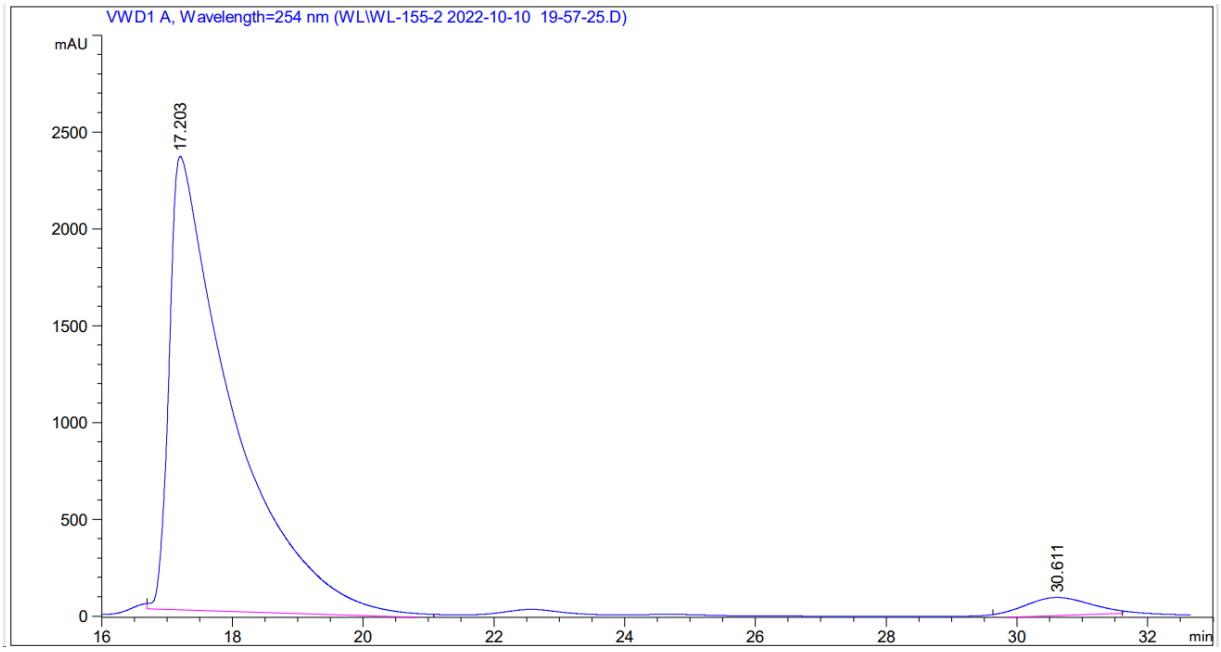
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.230	MM	0.6904	8495.10938	205.06395	93.2846
2	25.657	MM	0.9661	611.54858	10.55004	6.7154

HPLC chromatogram of racemic compound 3an



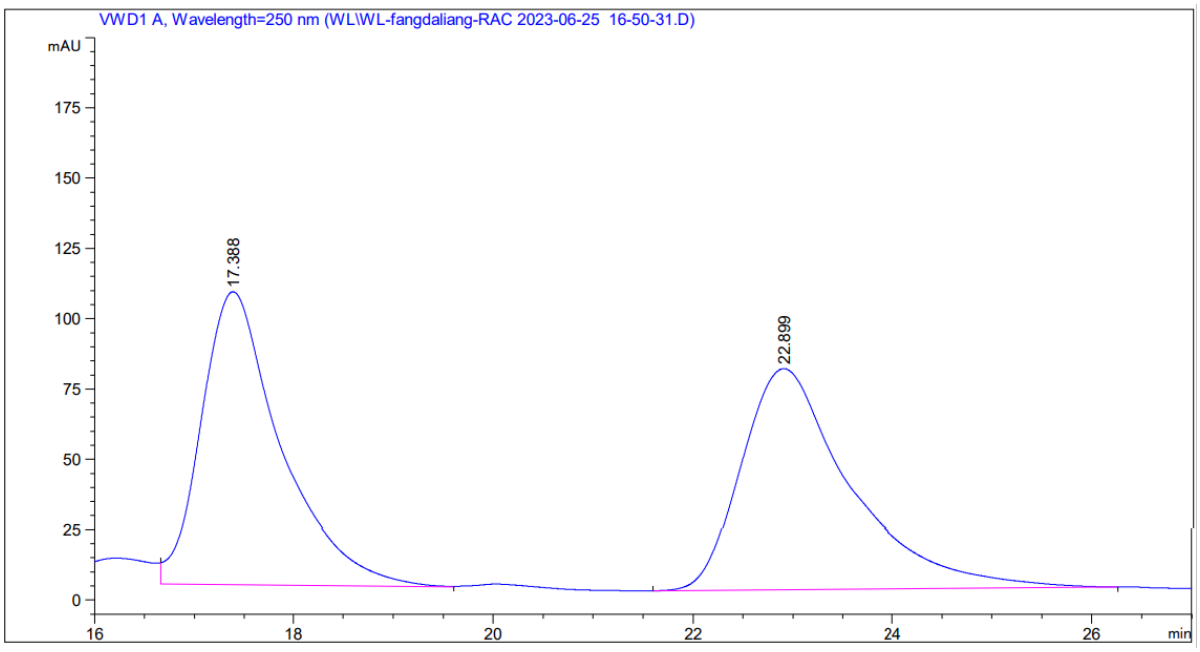
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.593	MM R	0.7301	9891.26172	225.80803	50.6318
2	26.918	MM R	1.0250	9644.42578	156.81590	49.3682

HPLC chromatogram of chiral compound 3an



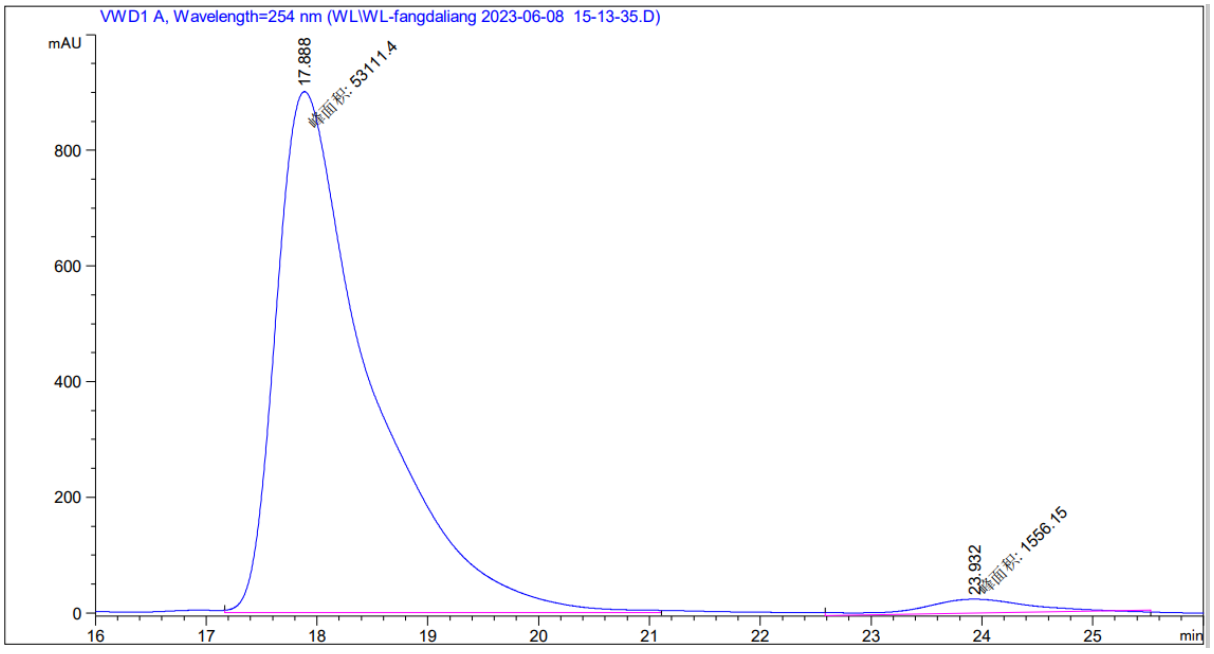
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.203	MM R	1.1025	1.54922e5	2341.87280	95.9212
2	30.611	MM R	1.1785	6587.65234	93.16697	4.0788

HPLC chromatogram of racemic compound 3aa



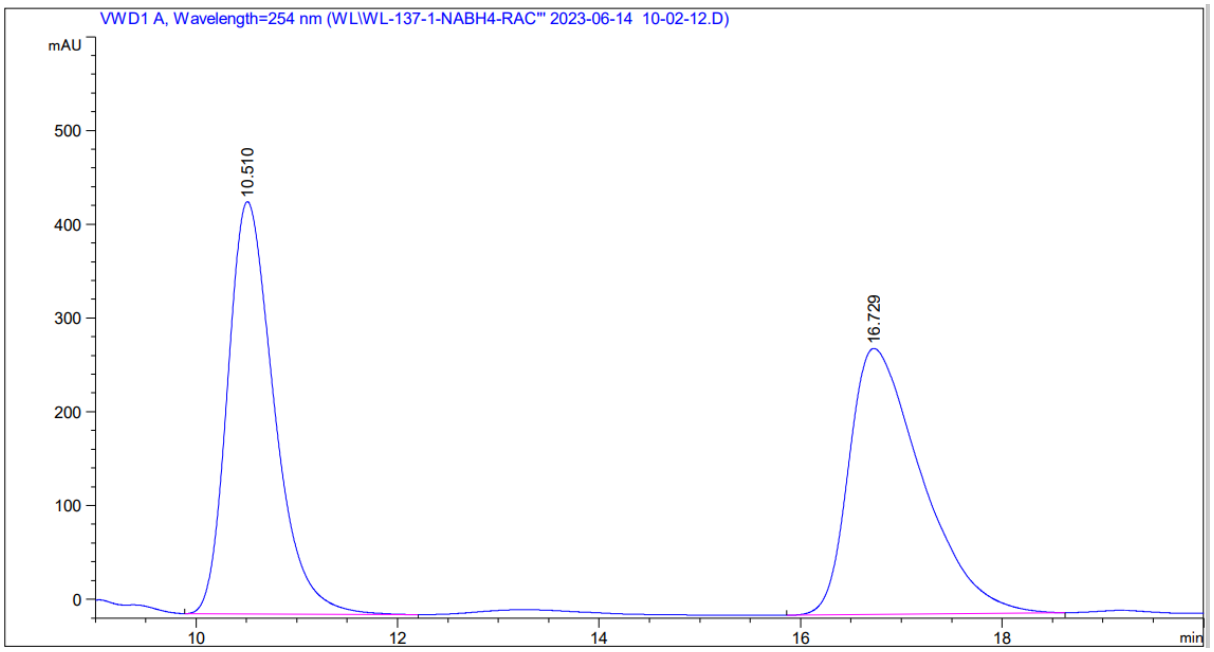
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.388	MM R	0.9035	5778.84619	104.08220	49.1280
2	22.899	BB	1.1169	5983.99902	78.62432	50.8720

HPLC chromatogram of chiral product 3aa from scale-up reaction



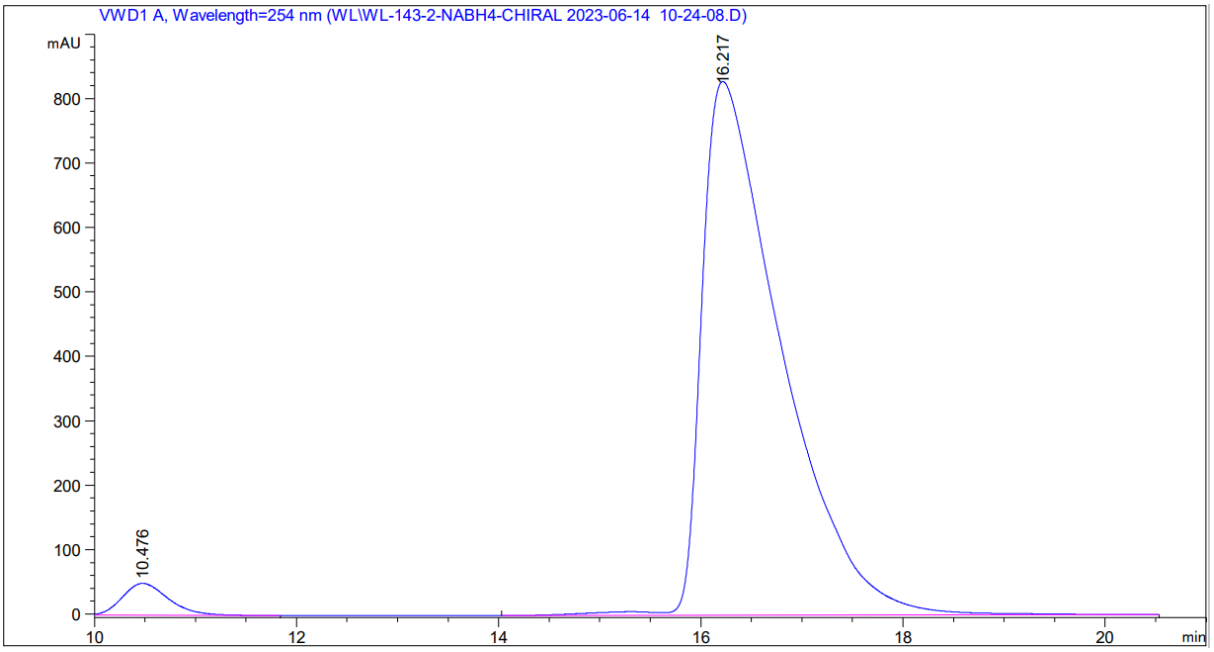
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.888	MM	0.9826	5.31114e4	900.82404	97.1534
2	23.932	MM	1.0933	1556.14905	23.72223	2.8466

HPLC chromatogram of racemic compound 4aa



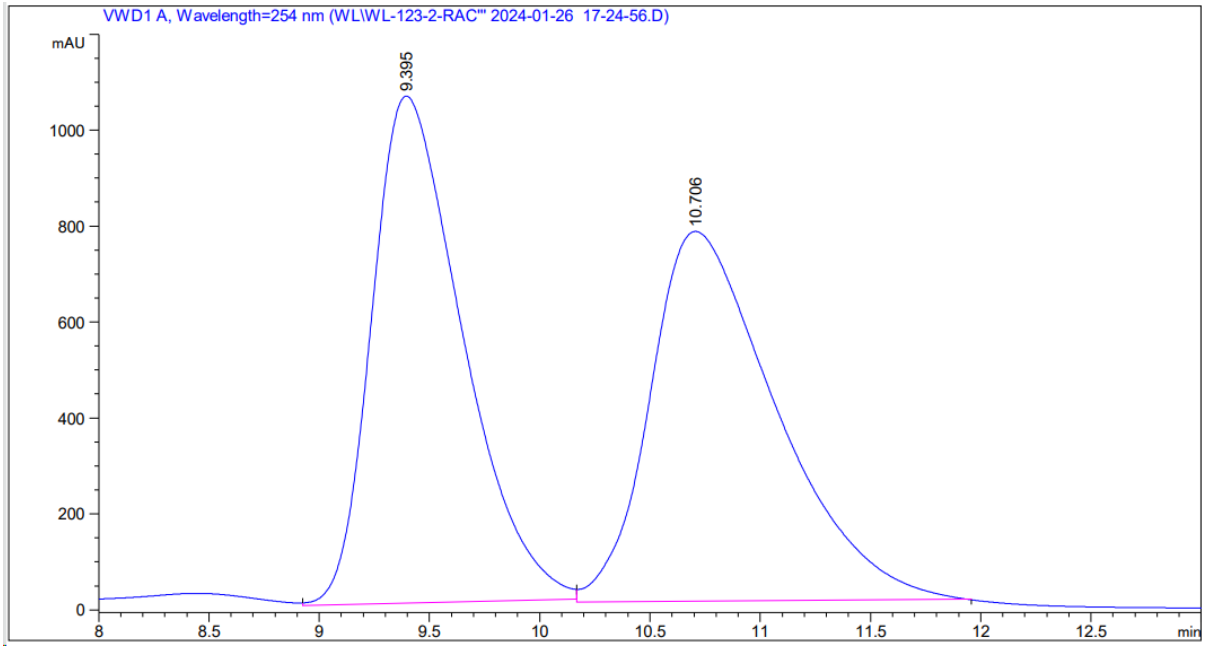
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.510	BB	0.4910	1.40615e4	439.80283	49.7127
2	16.729	BB	0.7527	1.42240e4	283.80222	50.2873

HPLC chromatogram of chiral compound 4aa



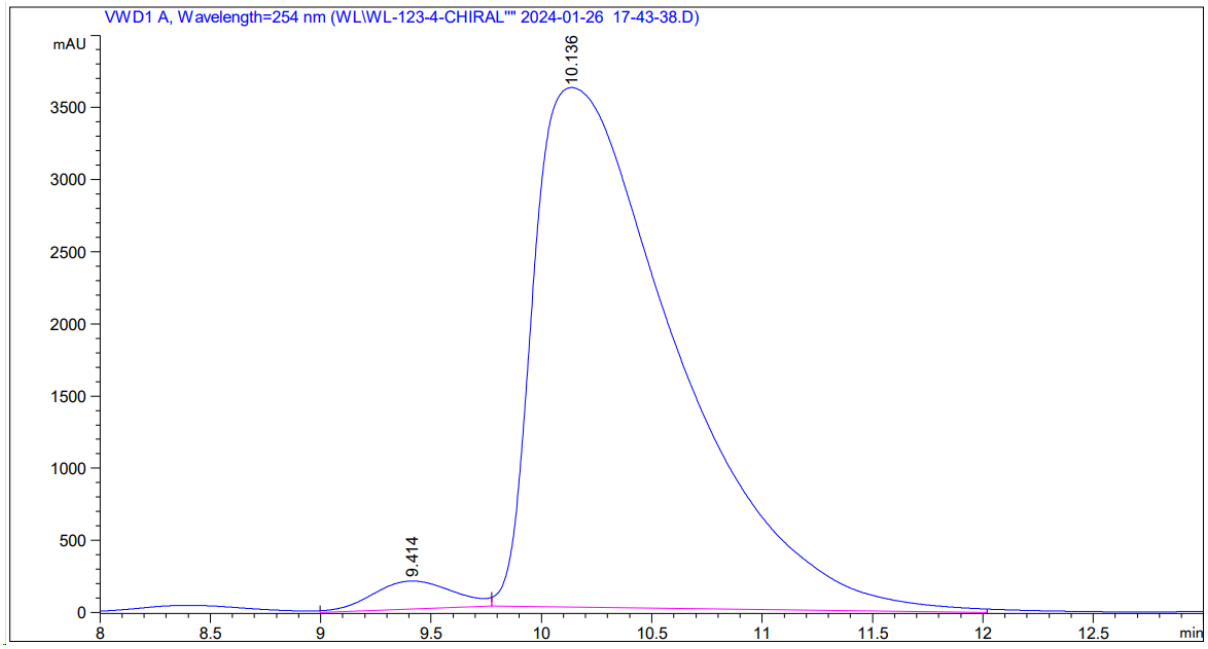
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.479	MM R	0.5041	1454.31274	48.08153	3.1171
2	16.217	VBAR	0.8054	4.52021e4	828.37299	96.8829

HPLC chromatogram of racemic compound 5aa



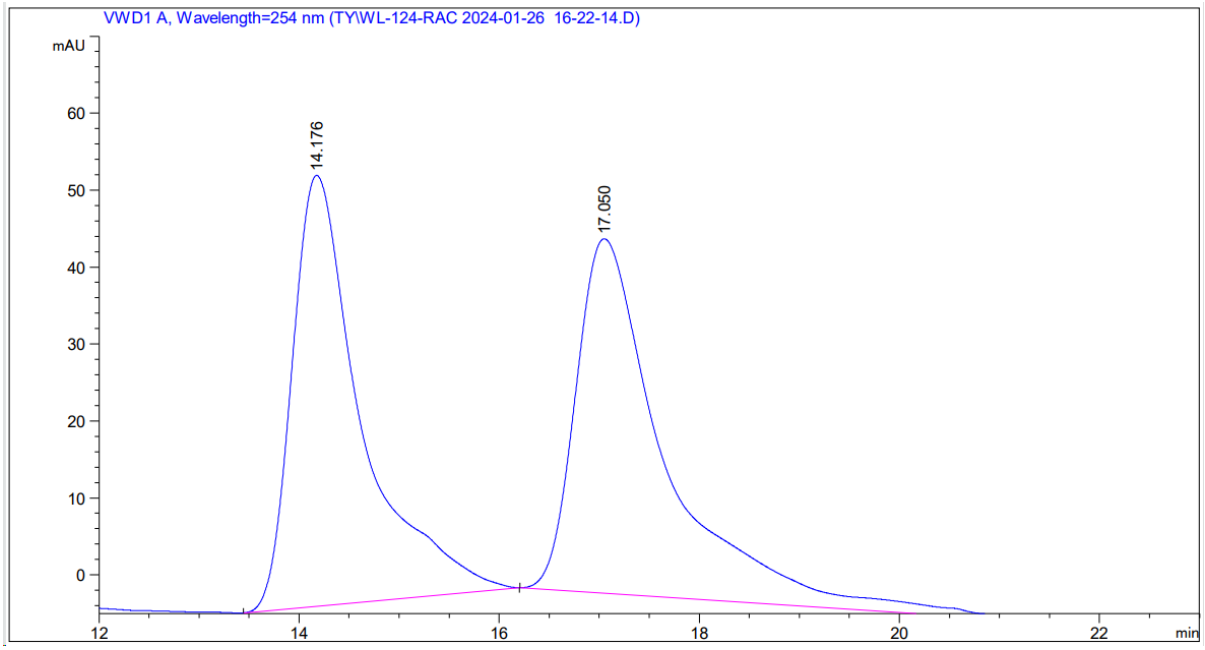
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.395	MMR	0.4496	3.01640e4	1056.59668	49.5717
2	10.706	MMR	0.6550	3.06852e4	770.80634	50.4283

HPLC chromatogram of chiral compound 5aa



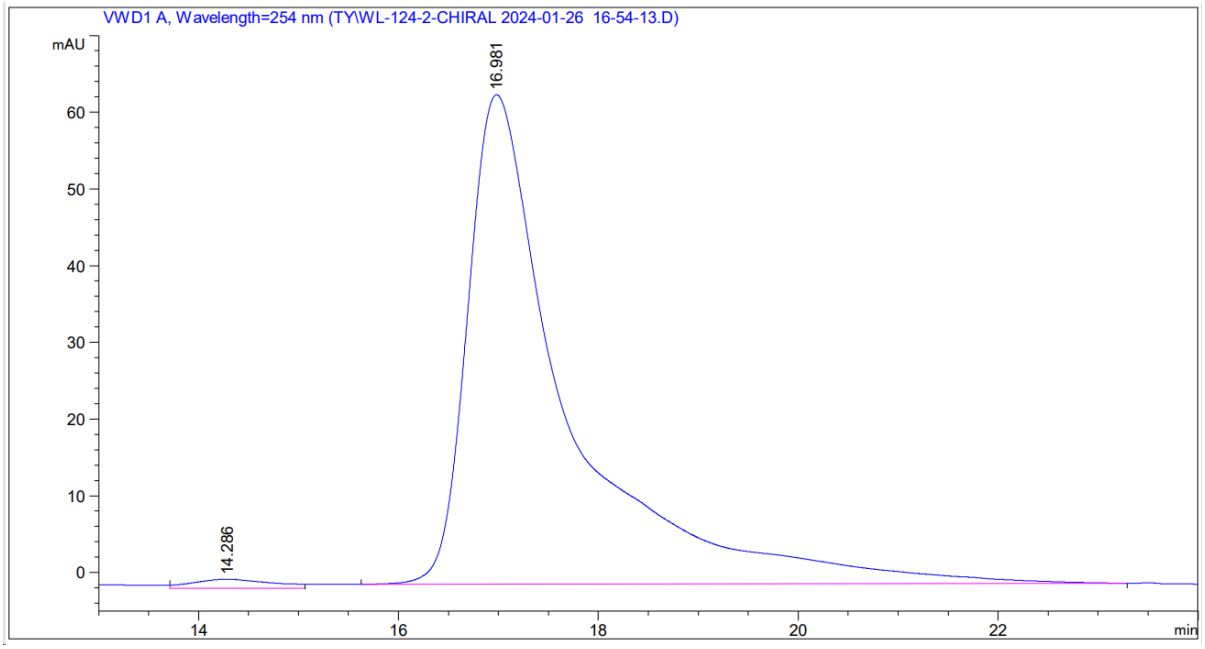
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.414	MM R	0.4289	4988.87305	193.84207	2.9999
2	10.136	MM R	0.5964	1.61312e5	3599.57275	97.0001

HPLC chromatogram of racemic compound 6aa



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.176	BB	0.7013	2688.88330	55.98430	48.2020
2	17.050	BB	0.9048	2889.48535	46.06744	51.7980

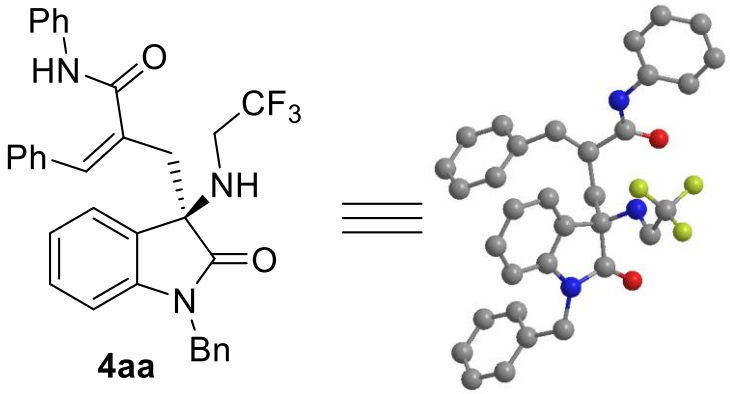
HPLC chromatogram of chiral compound 6aa



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.286	MM R	0.9215	63.56802	1.14968	1.4051
2	16.981	BB	0.9849	4460.48975	63.78477	98.5949

X-ray Crystallographic Data of Product 4aa

Crystallographic data for **4aa** has been deposited with the Cambridge Crystallographic Data Centre as deposition number CCDC 2279302. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223336033.



4aa

Table S1. Crystal data and structure refinement for 4aa

Identification code	**4aa**
Empirical formula	$C_{33}H_{28}F_3N_3O_2$
Formula weight	555.2134
Temperature/K	293(2)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	8.24050(10)
b/Å	13.6044(3)
c/Å	25.8384(5)
α/°	90
β/°	90
γ/°	90

Volume/Å^3	2896.67(9)
Z	54
ρ_{calc}g/cm^3	1.920
μ/mm^{-1}	1.986
F(000)	1674.0
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	6.842 to 153.696
Index ranges	-10 ≤ h ≤ 9, -17 ≤ k ≤ 15, -32 ≤ l ≤ 32
Reflections collected	25069
Independent reflections	5874 [R_{int} = 0.0403, R_{sigma} = 0.0285]
Data/restraints/parameters	5874/0/370
Goodness-of-fit on F^2	0.990
Final R indexes [I>=2σ (I)]	R_1 = 0.0725, wR_2 = 0.2142
Final R indexes [all data]	R_1 = 0.0796, wR_2 = 0.2293
Largest diff. peak/hole / e Å^{-3}	0.37/-0.29
Flack parameter	-0.09(9)