Bicyclic Guanidinium-Catalyzed Enantioselective Phase-Transfer Alkylation: Direct Access to Pyrroloindolines and Furoindolines

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Supporting Information

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1. General Information

General Procedures and Methods

Experiments involving moisture and/or air sensitive components were performed under a positive pressure of nitrogen in oven-dried glassware equipped with a rubber septum inlet. Dried solvents and liquid reagents were transferred by oven-dried syringes or hypodermic syringe cooled to ambient temperature in a desiccator. Reactions mixtures were stirred in 4 mL sample vial with Teflon-coated magnetic stirring bars unless otherwise stated. Moisture in non-volatile reagents/compounds was removed in high *vacuo* by means of an oil pump and subsequent purging with nitrogen. Solvents were removed in vacuo under ~30 mmHg and heated with a water bath at 30–35 °C using rotary evaporator with aspirator.

All experiments were monitored by analytical thin layer chromatography (TLC). TLC was performed on pre-coated plates, 60 F_{254}. After elution, plate was visualized under UV illumination at 254 nm for UV active material. Further visualization was achieved by staining $KMnO_4$, ceric molybdate, or anisaldehyde solution. For those using the aqueous stains, the TLC plates were heated on a hot plate.

Columns for flash chromatography (FC) contained silica gel 200–300 mesh. Columns were packed as slurry of silica gel in petroleum ether and equilibrated solution using the appropriate solvent system. The elution was assisted by applying pressure of about 2 atm with an air pump.

Instrumentations

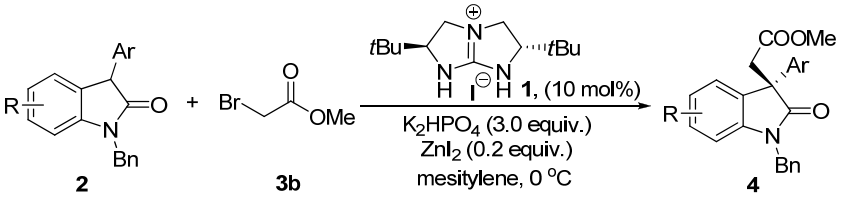
Proton nuclear magnetic resonance (^{1}H NMR) and carbon NMR (^{13}C NMR) spectra were recorded in $CDCl_3$ otherwise stated. ^{1}H (400 MHz) and ^{13}C (100 MHz) were performed on a 400MHz spectrometer. Chemical shifts are reported in parts per million (ppm), using the residual solvent signal as an internal standard: $CDCl_3$ (^{1}H NMR: δ 7.26, singlet; ^{13}C NMR: δ 77.0, triplet). Multiplicities were given as: *s* (singlet), *d* (doublet), *t* (triplet), *q* (quartet), *quintet*, *m* (multiplets), *dd* (doublet of doublets), *dt* (doublet of triplets), and *br* (broad). Coupling constants (*J*) were recorded in Hertz (Hz). The number of proton atoms (*n*) for a given resonance was indicated by *n*H. The number of carbon atoms (*n*) for a given resonance was indicated by *n*C. HRMS was reported in units of mass of charge ratio (m/z). Mass samples were dissolved in CH_3CN (HPLC Grade) unless otherwise stated. Optical rotations were recorded on a polarimeter with a sodium lamp of wavelength 589 nm and reported as follows; $[\alpha]_{\lambda}^{T^{\circ}C}$ (c = g/100 mL, solvent). Melting points were determined on a melting point apparatus.

Enantiomeric excesses were determined by chiral High Performance Liquid Chromatography (HPLC) analysis. UV detection was monitored at 254 nm, 230 nm and 210 nm at the same time. HPLC samples were dissolved in HPLC grade isopropanol (IPA) unless otherwise stated.

Materials

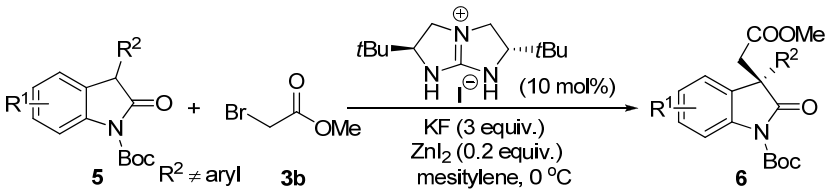
All commercial reagents were purchased with the highest purity grade. They were used without further purification unless specified. All solvents used, mainly petroleum ether (PE) and ethyl acetate (EtOAc), were distilled. Anhydrous CH_2Cl_2 was freshly distilled from CaH_2 and stored under N_2 atmosphere. Toluene, mesitylene, *m*-xylene and THF were freshly distilled from sodium/benzophenone before use. All compounds synthesized were stored in a −40 °C freezer and light-sensitive compounds were protected with aluminium foil.

2. General Experimental Procedure for Bicyclic Guanidinium-Catalyzed Alkylation of *N*-Bn-3-Aryl-2-Oxindoles 2 to Methyl Bromoacetate 3b



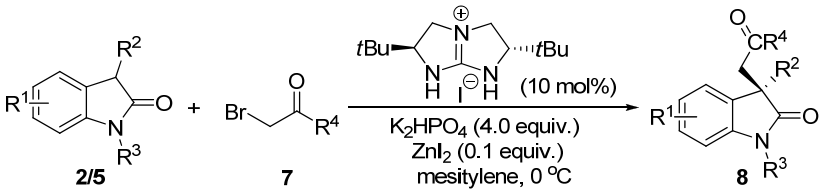
N-Bn-3-aryl-2-oxindoles **2** (0.1 mmol, 1.0 equiv), **1** (4.6 mg, 0.01 mmol, 0.1 equiv), K_2HPO_4 (55 mg, 0.3mmol, 3 equiv), and ZnI_2 (6 mg, 0.2 mmol, 0.2 equiv) were dissolved in mesitylene (1.0 mL), and stirred at 0 ^oC for 5 minutes. Then methyl bromoacetate **3b** (15 uL, 0.15 mmol, 1.5 equiv) was added. The reaction mixture was stirred at 0^oC and monitored by TLC. Upon complete consumption of **2**, the reaction mixture was directly loaded onto a short silica gel column, followed by gradient elution with PE/EA mixture (15/1−5/1 ratio). Removing the solvent in vacuo, afforded products **4a-v**.

3. General Experimental Procedure for Bicyclic Guanidinium-Catalyzed Alkylation of *N*-Boc-3-Benzyl/Propargyl/Allyl/Alkyl-2-Oxindoles 5 to 3b



N-Boc-3-benzyl/propargyl/allyl/alkyl-2-oxindoles **5** (0.1 mmol, 1.0 equiv), **1** (4.6 mg, 0.01 mmol, 0.1 equiv), KF (20mg, 0.3mmol, 3 equiv), and ZnI_2 (6 mg, 0.2 mmol, 0.2 equiv) were dissolved in mesitylene (1.0 mL). And stirred at 0°C for 5 minutes, then methyl bromoacetate **3b** (15 uL, 0.15 mmol, 1.5 equiv) was added. The reaction mixture was stirred at 0 °C and monitored by TLC. Upon complete consumption of **5**, the reaction mixture was directly loaded onto a short silica gel column, followed by gradient elution with PE/EA mixture (15/1–5/1 ratio). Removing the solvent in vacuo, afforded products **6a-j**.

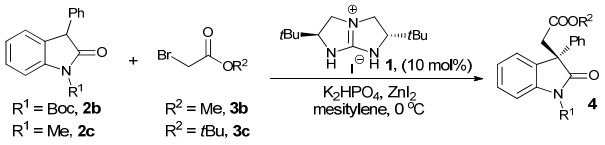
4. General Experimental Procedure for Bicyclic Guanidinium-Catalyzed Alkylation of 3-Substituted-2-Oxindoles 2/5 to Activated Bromomethane 7



3-Substituted-2-oxindoles **2/5** (0.1 mmol, 1.0 equiv), **1** (4.6 mg, 0.01 mmol, 0.1 equiv), K_2HPO_4 (70 mg, 0.3 mmol, 4 equiv), and ZnI_2 (3.2 mg, 0.1 mmol, 0.2 equiv) were dissolved in mesitylene (1.0 ml). And stirred at 0 ^oC for 5 minutes, then activated bromomethane **7** (0.2 mmol, 2 equiv) was added. The reaction mixture was stirred at 0 ^oC and monitored by TLC. Upon complete consumption of **2/5**, the reaction mixture was directly loaded onto a short silica gel column, followed by gradient elution with PE/EA mixture (15/1–2/1 ratio). Removing the solvent in vacuo, afforded products **8a-i**.

5. Condition Investigations of Alkylation of 3-phenyl-2-oxindoles 2 to bromoacetates 3

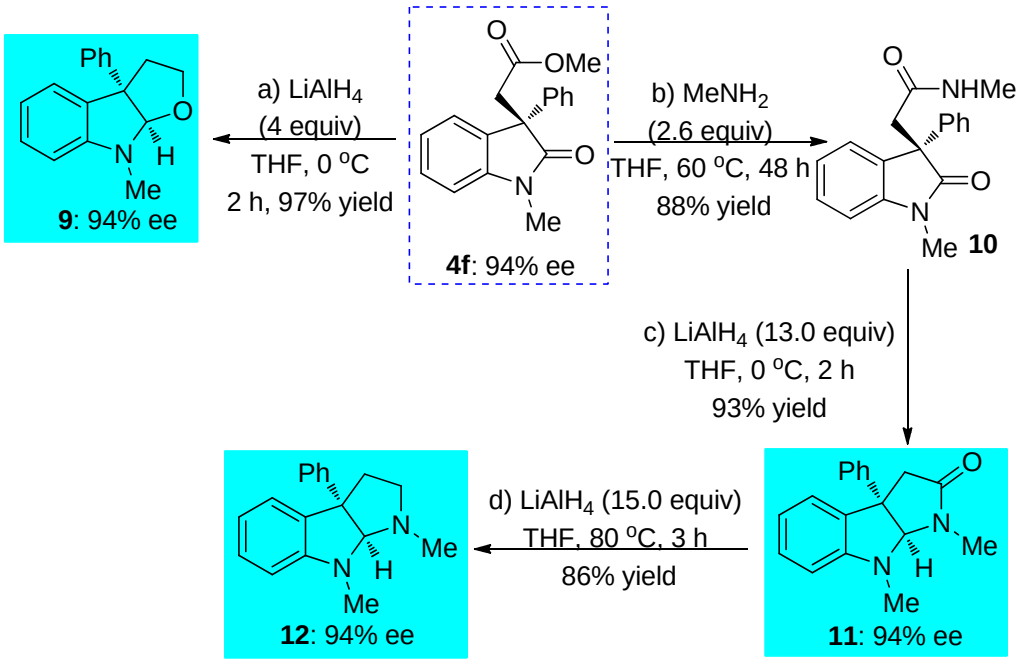
We moved on to evaluate bromoacetate **3** by varying the R^2 substituent (entries 1–2). The results shown that methyl group (**3b**) could improve the reactivity and enantioselectivity (entry 1). *tert*-Butyl bromoacetate **3c** resulted in a sluggish reaction (entry 2). In the process, we also found that R^1, the *N*-substituent group of **2**, could lead to different reaction results (entries 3–5). When R^1 was Boc (**2b**), the reactivity could be increased but enantioselectivity was decreased (entries 3–4). After a prolonged reaction time (96 h), adduct **4f** derived from *N*-methyl-3-phenyl-2-oxindole (R^1 = Me, **2c**) could be obtained in 93% yield with 94% *ee* (entry 5). Accordingly, **2a** and **3b** were selected as the model substrates to investigate the effects of K_2HPO_4 and ZnI_2 (entries 6–9). When the amount of K_2HPO_4 was reduced to 1.0 equivalent, the reaction became very slowly (entry 6). The combination of 3.0 equivalents of K_2HPO_4 and 0.2 equivalents of ZnI_2 reveals the best results, affording the adduct **4b** in 97% yield and 95% *ee* within 60 hours (entry 8).



entry	**2**	**3**	K_2HPO_4 (equiv.)	ZnI_2 (equiv.)	*t* (h)	**4**	yield (%)[b]	*ee* %[c]
1	**2a**	**3b**	3.0	0.5	72	**4b**	95	95
2	**2a**	**3c**	3.0	0.5	72	**4c**	trace	n.d.
3	**2b**	**3c**	3.0	0.5	78	**4d**	87	89
4	**2b**	**3b**	3.0	0.5	45	**4e**	99	91
5	**2c**	**3b**	3.0	0.5	96	**4f**	93	94
6	**2a**	**3b**	1.0	0.5	72	**4b**	trace	n.d.
7	**2a**	**3b**	5.0	0.5	60	**4b**	99	93
8	**2a**	**3b**	3.0	0.2	60	**4b**	97	95
9	**2a**	**3b**	3.0	0.1	60	**4b**	92	93

[a] Conditions: **2** (0.05 mmol), **3** (0.075 mmol), mesitylene (0.5 mL). [b] Isoated yields based on **2**. [c] Determined by chiral-phase HPLC analysis.

6. Synthesis and Characterization of 9-12



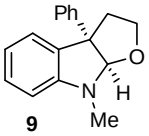
a) To a cold (0 °C) solution of **4f** (131 mg, 0.49 mmol) in THF (30 mL) was added $LiAlH_4$ (76 mg, 2.0 mmol. 4.0 equiv) in small portions under nitrogen atmosphere. The reaction mixture was stirred for 2 hours at 0 °C and then treated with several drops of saturated brine until the evolution of H_2 ceased. Then the reaction mixture was washed with ethyl acetate (3 x 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (PE/EA = 20/1), affording product **9** (119 mg) as a colorless oil in 97% yield and with 94% ee.[1]

b) To a solution of **4f** (117 mg, 0.4 mmol) in MeOH (8.0 mL) was added 33% NH_2Me solution (4.0 mL) at 0 °C. The resulting mixture was stirred for 48 hours at 60 °C. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel (PE/EA = 1/1) to afford compound **10** (103.6 mg) as a colorless oil in 88% yield and 94% ee.[2]

c) To methyl amide **10** (170 mg, 0.58 mmol) in THF (40 mL) at 0 °C, $LiAlH_4$ (290 mg, 7.5 mmol, 13.0 equiv) was added under nitrogen atmosphere. The resulting mixture was stirred for 2 hours at 0 °C, and then quenched with several drops of saturated brine. The reaction mixture was subsequently washed with ethyl acetate (3 x 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (PE/EA = 2/1), affording product **11** (150.1 mg) as a white solid in 93% yield with 94% ee.[3]

d) To compound **11** (120 mg, 0.4 mmol) in THF (30 mL) at room temperature, $LiAlH_4$ (230 mg, 6.0 mmol, 15.0 equiv) was added under nitrogen atmosphere. The resulting mixture was stirred at 85 °C. Upon completion of the reaction (around 2.5 hrs), the mixture was cooled to room temperature and quenched with several drops of saturated brine. Then the reaction mixture was washed with ethyl acetate (3 x 10

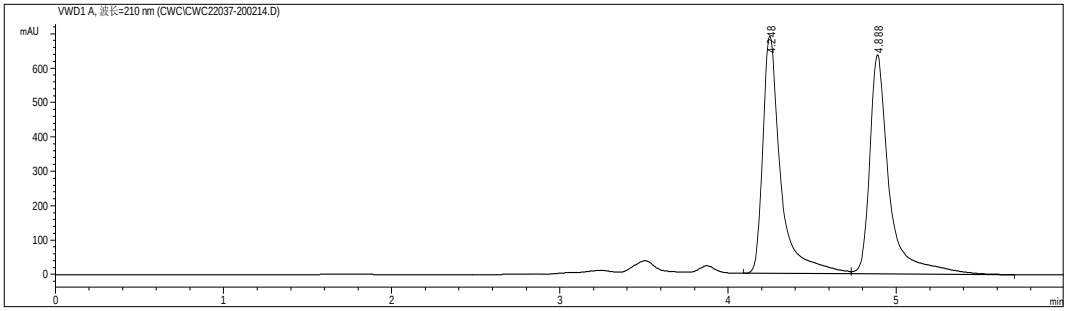
mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (PE/EA = 2/1), affording product **12** (90.9 mg) as a colorless oil in 86% yield and 95% ee.[1]

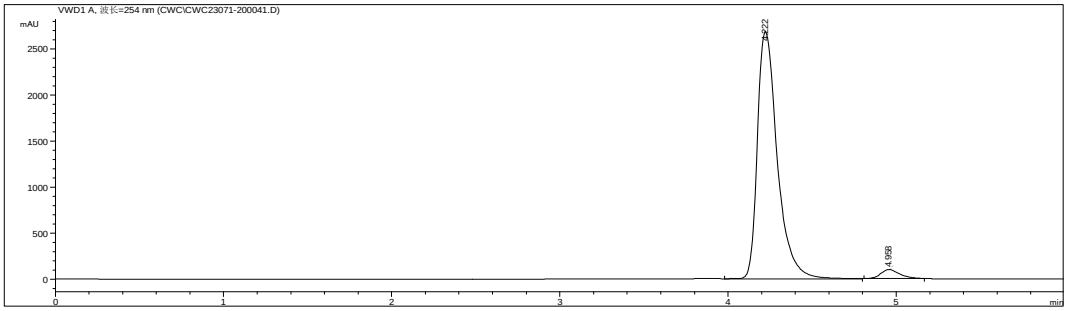


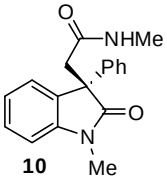
9

Colorless oil, 97% yield; 94% ee; $[\alpha]_D^{26}$ +245.7(*c* 0.51, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.35–7.28 (m, 4H), 7.24–7.20 (m, 1H), 7.14 (td, *J* = 7.7, 1.2 Hz, 1H), 7.00 (dd, *J* = 7.3, 0.8 Hz, 1H), 6.69 (td, *J* = 7.4, 0.9 Hz, 1H), 6.46 (d, *J* = 7.8 Hz, 1H), 5.44 (s, 1H), 4.16–4.12 (m, 1H), 3.56 (ddd, *J* = 11.7, 8.5, 4.5 Hz, 1H), 2.98 (s, 3H), 2.74 (td, *J* = 11.7, 7.2 Hz, 1H), 2.49 (dd, *J* = 11.7, 4.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.0, 144.0, 133.1, 128.6, 128.5, 126.7, 126.2, 124.2, 117.7, 105.5, 105.4, 68.2, 60.8, 40.8, 30.8. HRMS (ESI) m/z 252.1383 ($M+H^+$), calc. for $C_{17}H_{18}NO$ 252.1388.

The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 4.2 min (major) and 5.0 min (minor).



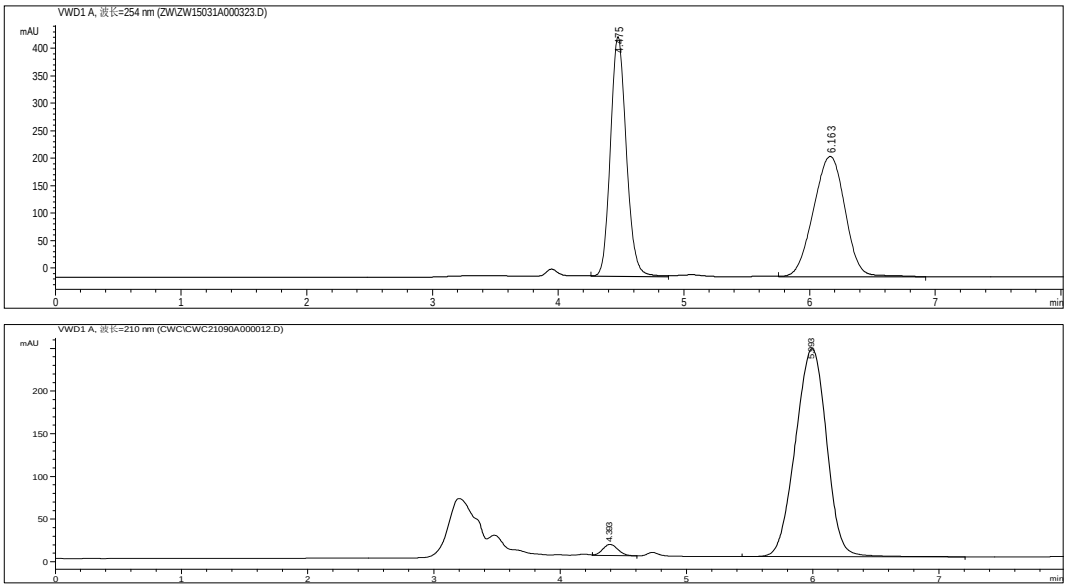


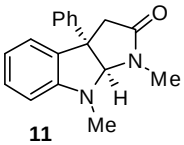


10

White solid, Mp 153.2–153.4 °C; 88% yield; 94% ee; $[\alpha]_D^{26}$ +99.8 (*c* 0.64, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.33–7.19 (m, 7H), 7.07 (td, *J* = 7.5, 0.7 Hz, 1H), 6.87 (d, *J* = 7.8 Hz, 1H), 6.21 (s, 1H), 3.36 (d, *J* = 15.2 Hz, 1H), 3.24 (s, 3H), 3.00 (d, *J* = 15.2 Hz, 1H), 2.55 (d, *J* = 4.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.9, 169.3, 143.5, 139.3, 131.8, 128.8, 128.6, 127.6, 126.5, 124.5, 122.8, 108.6, 54.2, 43.9, 26.7, 26.2. HRMS (ESI) m/z 295.1456 ($M+H^+$), calc. for $C_{18}H_{19}O_2N_2$ 295.1447.

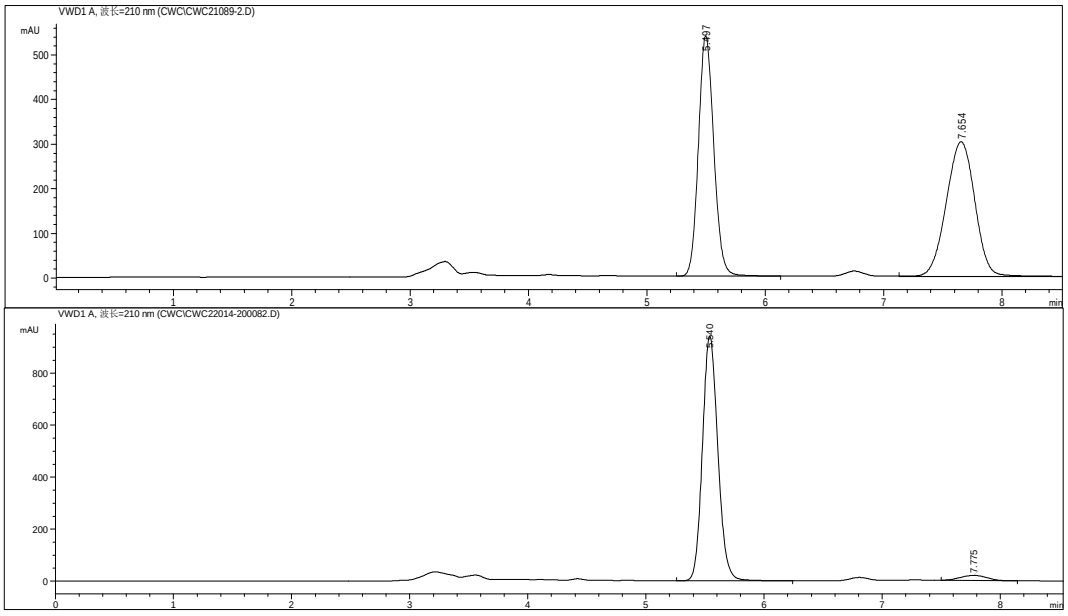
The ee was determined by HPLC analysis. CHIRALCEL ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 60/40; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 4.4 min (minor) and 6.6 min (major).

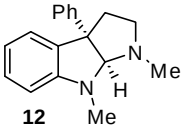




11 White solid, Mp 165.9–166.5 °C; 93% yield; 94% ee; $[\alpha]_D^{26}$ +72.0 (*c* 0.24, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 (t, *J* = 7.4 Hz, 2H), 7.24–7.18 (m, 4H), 7.05 (d, *J* = 7.3 Hz, 1H), 6.80 (t, *J* = 7.1 Hz, 1H), 6.55 (d, *J* = 7.8 Hz, 1H), 4.97 (s, 1H), 3.26 (d, *J* = 17.2 Hz, 1H), 3.13–3.09 (m, 4H), 2.98 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 149.5, 144.4, 133.8, 129.1, 128.9, 127.1, 126.0, 124.8, 119.1, 108.0, 93.1, 53.8, 44.3, 35.3, 28.6. HRMS (ESI) m/z 279.1494 ($M+H^+$), calc. for $C_{18}H_{19}N_2O$ 279.1497.

The ee was determined by HPLC analysis. CHIRALCEL ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 5.5 min (major) and 7.8 min (minor).

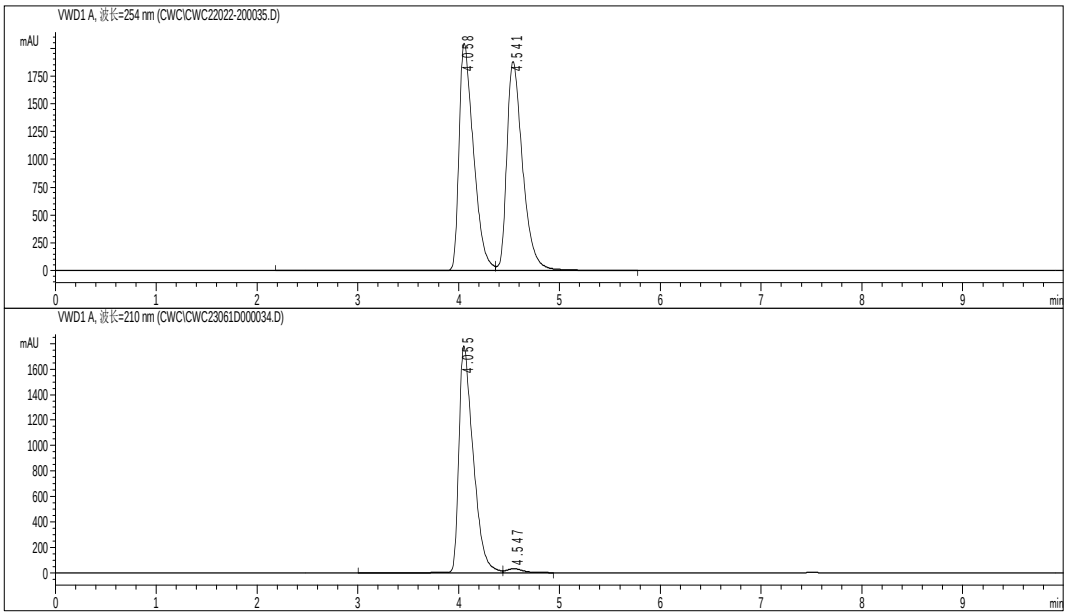




12 Colorless oil, 86% yield; 94% ee; $[\alpha]_D^{26}$ +178.4 (*c* 0.40, $CHCl_3$);^1H NMR (400 MHz, $CDCl_3$) δ 7.31–7.27 (m, 4H), 7.23–7.16 (m, 1H), 7.11 (td, *J* = 7.8, 1.2 Hz, 1H), 6.91 (dd,

J = 7.3, 0.8 Hz, 1H), 6.66 (td, *J* = 7.4, 0.8 Hz, 1H), 6.48 (d, *J* = 7.8 Hz, 1H), 4.51 (s, 1H), 3.00 (s, 3H), 2.91–2.87 (m, 1H), 2.78–2.69 (m, 2H), 2.54 (s, 3H), 2.30–2.24 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.2, 146.8, 135.1, 128.4, 128.0, 126.5, 126.2, 124.5, 117.6, 106.6, 98.2, 61.4, 53.4, 39.8, 38.5, 35.9. HRMS (ESI) m/z 265.1704 ($M+H^+$), calc. for $C_{18}H_{21}N_2$ 265.1705.

The ee was determined by HPLC analysis. LUX Amylose-2 (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/0; flow rate 1.0 mL/min; 25 ^{o}C; 210 nm; retention time: 4.0min (major) and 4.5 min (minor)



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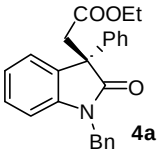
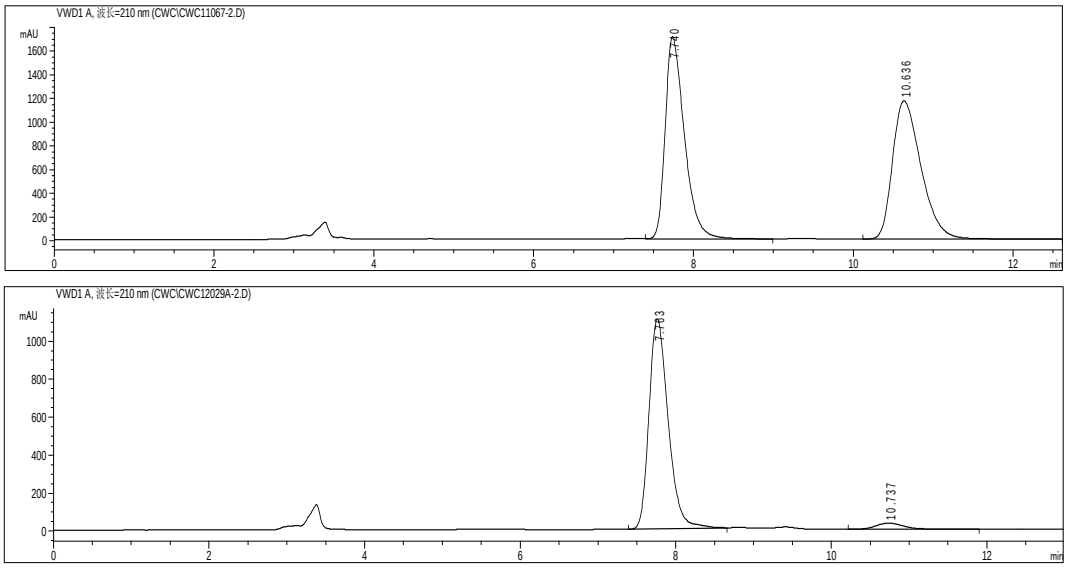
7. Characterization of Adducts

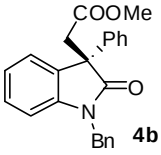


4a

Colorless oil, 95% yield; 93% ee; $[\alpha]_D^{26}$ –62.5 (*c* 0.29, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.19 (m, 12H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.77 (d, *J* = 7.6 Hz, 1H), 5.05 (d, *J* = 15.8 Hz, 1H), 4.82 (d, *J* = 15.8 Hz, 1H), 3.97–3.89 (m, 1H), 3.85–3.77 (m, 1H), 3.65 (d, *J* = 15.6 Hz, 1H), 3.29 (d, *J* = 15.6 Hz, 1H), 0.91 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.1, 169.6, 143.7, 139.4, 136.0, 131.2, 128.8, 128.7, 128.5, 127.7, 127.5, 127.4, 126.6, 124.6, 122.6, 109.4, 60.6, 53.4, 44.2, 41.9, 13.8. HRMS (ESI) m/z 386.1767 ($M+H^+$), calc. for $C_{25}H_{23}O_3N$ 386.1756.

The ee was determined by HPLC analysis. CHIRALCEL ODH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 7.8 min (major) and 10.7 min (minor).

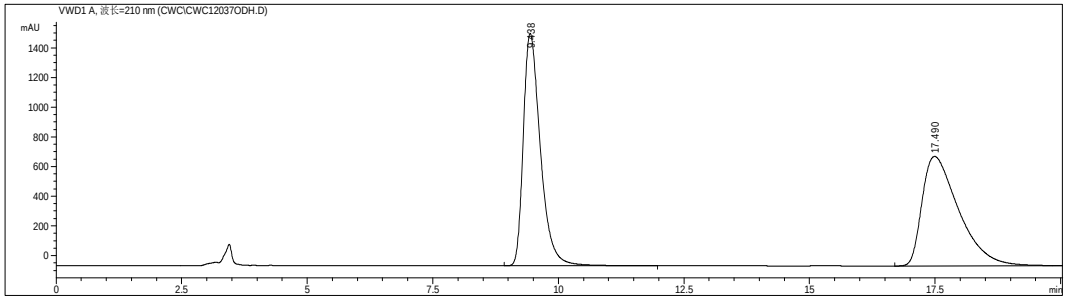


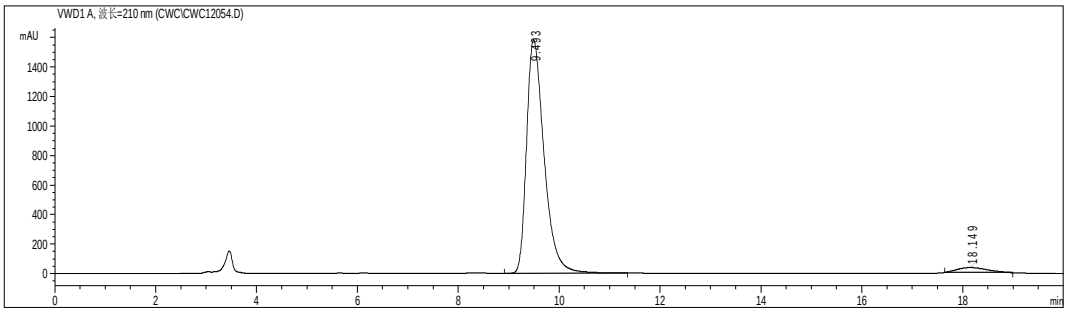


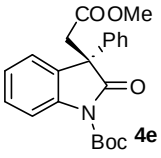
4b

Colorless oil, 97% yield; 95% ee; $[\alpha]_D^{26}$ –31.5 (*c* 0.47, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.27 (m, 10H), 7.25–7.19 (m, 2H), 7.07 (td, *J* = 7.6, 0.9 Hz, 1H), 6.78 (d, *J* = 7.8 Hz, 1H), 4.94 (dd, *J* = 45.6, 15.8 Hz, 2H), 3.64 (d, *J* = 16.2 Hz, 1H), 3.40 (s, 3H), 3.31 (d, *J* = 16.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.0, 170.0, 143.6, 139.3, 135.9, 131.1, 128.7, 128.6, 128.5, 127.6, 127.5, 127.4, 126.5, 124.4, 122.5, 109.4, 53.3, 51.6, 44.2, 41.6; HRMS (ESI) m/z 372.1609 ($M+H^+$), calc. for $C_{24}H_{22}O_3N$ 372.1600.

The ee was determined by HPLC analysis. CHIRALCEL ODH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 9.5 min (major) and 18.1 min (minor).



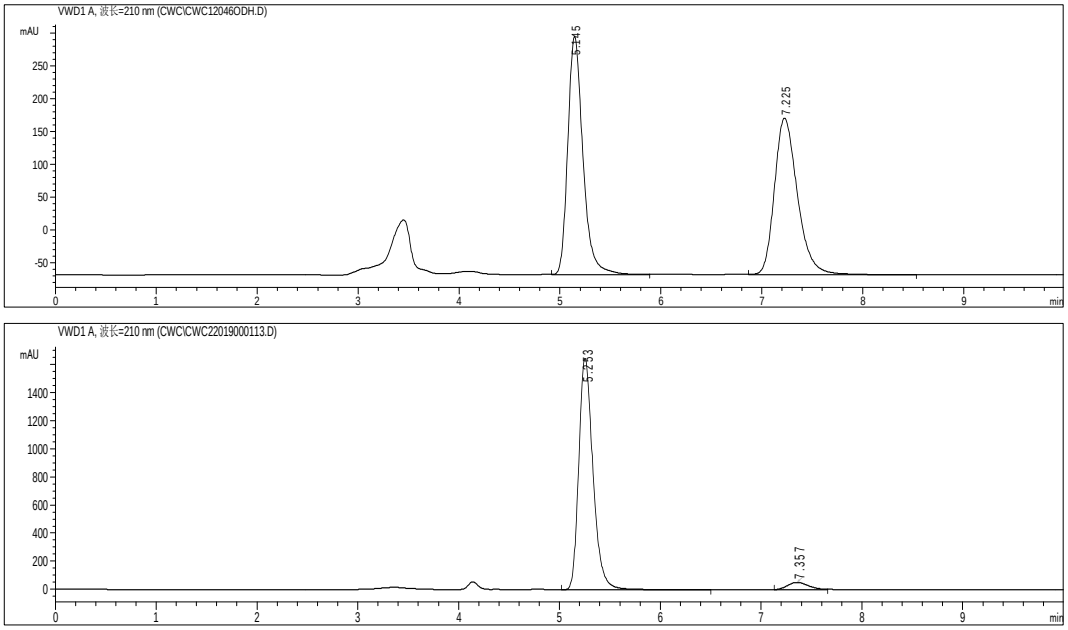


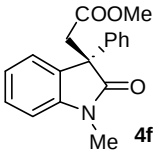


4e

Colorless oil, 99% yield; 91% ee; $[\alpha]_D^{26}$ –57.7 (*c* 0.38, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.2 Hz, 1H), 7.40–7.36 (m, 1H), 7.32–7.27 (m, 4H), 7.22 (qd, *J* = 7.8, 1.4 Hz, 3H), 3.71 (d, *J* = 16.5 Hz, 1H), 3.47 (s, 3H), 3.24 (d, *J* = 16.5 Hz, 1H), 1.62 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.2, 170.0, 149.4, 140.6, 138.7, 129.8, 128.9, 128.8, 128.0, 126.8, 124.5, 124.1, 115.5, 84.3, 53.6, 51.9, 42.4, 28.1. HRMS (ESI) m/z 382.1651 ($M+H^+$), calc. for $C_{22}H_{24}O_5N$ 382.1654

The ee was determined by HPLC analysis. CHIRALCEL ODH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 5.2 min (major) and 7.4 min (minor).

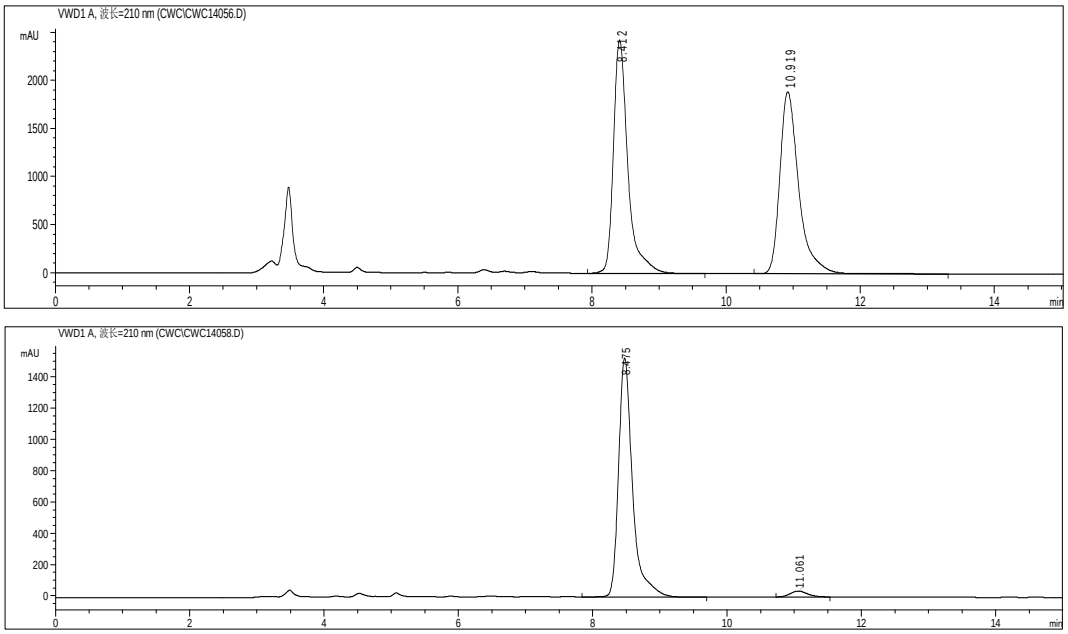


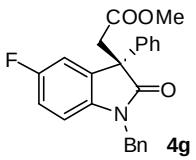


4f

Colorless oil, 93% yield; 94% ee; $[\alpha]_D^{26}$ –92.4 (*c* 0.28, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.22 (m, 7H), 7.10 (dd, *J* = 11.0, 4.0 Hz, 1H), 6.92 (d, *J* = 7.8 Hz, 1H), 3.56 (d, *J* = 16.3 Hz, 1H), 3.45 (s, 3H), 3.30 – 3.25 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.0, 170.1, 144.6, 139.1, 131.1, 128.7, 127.6, 126.6, 124.5, 122.5, 108.4, 53.2, 51.7, 41.8, 26.7. HRMS (ESI) m/z 296.1282 ($M+H^+$), calc. for $C_{18}H_{18}O_3N$ 296.1287

The ee was determined by HPLC analysis. CHIRALCEL ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 8.5 min (major) and 11.1 min (minor).

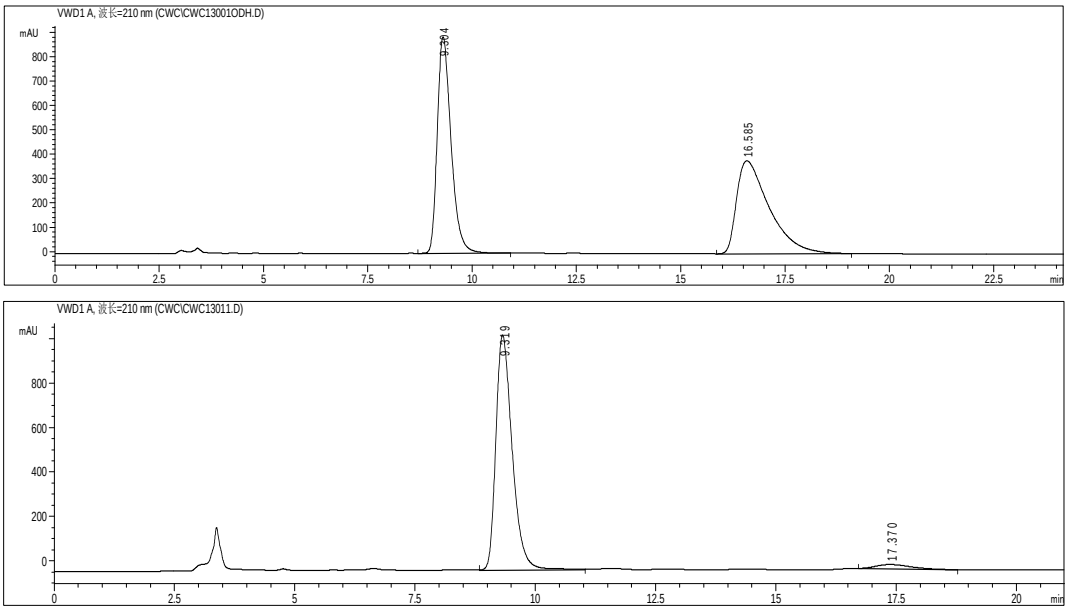


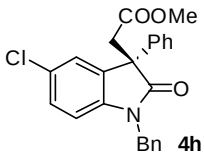


4g

Colorless oil, 98% yield; 94% ee; $[\alpha]_D^{26}$ –29.8 (*c* 0.28, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.32–7.27 (m, 9H), 7.05 (dd, *J* = 7.9, 2.6 Hz, 1H), 6.91 (td, *J* = 8.9, 2.6 Hz, 1H), 6.67 (dd, *J* = 8.6, 4.2 Hz, 1H), 4.99 (d, *J* = 15.8 Hz, 1H), 4.87 (d, *J* = 15.8 Hz, 1H), 3.63 (d, *J* = 16.6 Hz, 1H), 3.47 (s, 3H), 3.31 (d, *J* = 16.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.8, 169.9, 160.3, 157.9, 139.6, 138.7, 135.6, 132.9 (two peaks), 128.8 (two peaks), 127.9, 127.6, 127.3, 126.4, 114.8 (two peaks), 112.6 (two peaks), 110.0 (two peaks), 53.7, 51.8, 44.39, 41.30. HRMS (ESI) m/z 390.1499 ($M+H^+$), calc. for $C_{24}H_{21}FNO_3$ 390.1505.

The ee was determined by HPLC analysis. CHIRALCEL ODH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 ^oC; 210 nm; retention time: 9.3min (major) and 17.4 min (minor).



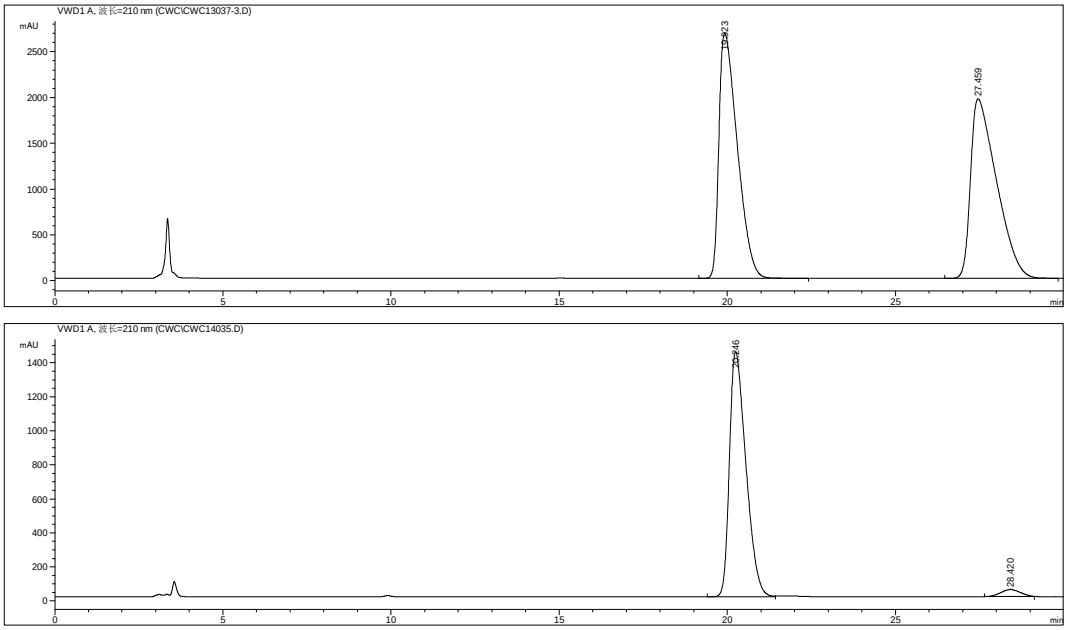


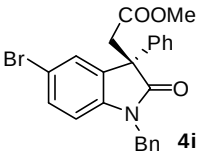
4h

Colorless oil, 99% yield; 94% ee; $[\alpha]_D^{26}$ –92.6 (*c* 0.36, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.35–7.27 (m, 10H), 7.18 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.68 (d, *J* = 8.3 Hz, 1H),

4.93 (dd, J = 44.7, 15.8 Hz, 2H), 3.64 (d, J = 16.7 Hz, 1H), 3.48 (s, 3H), 3.31 (d, J = 16.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.6, 177.6, 169.8, 142.2, 138.6, 135.4, 133.1, 128.9, 128.8, 128.5, 127.9, 127.6, 127.3, 126.4, 124.7, 110.4, 77.3, 77.2, 77.0, 76.7, 61.8, 53.4, 51.8, 44.4, 41.2. HRMS (ESI) m/z 406.1209 ($M+H^+$), calc. for $C_{24}H_{21}ClNO_3$ 406.1210.

The ee was determined by HPLC analysis. CHIRALCEL ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 ^{o}C; 210 nm; retention time: 20.2min (major) and 28.4 min (minor).

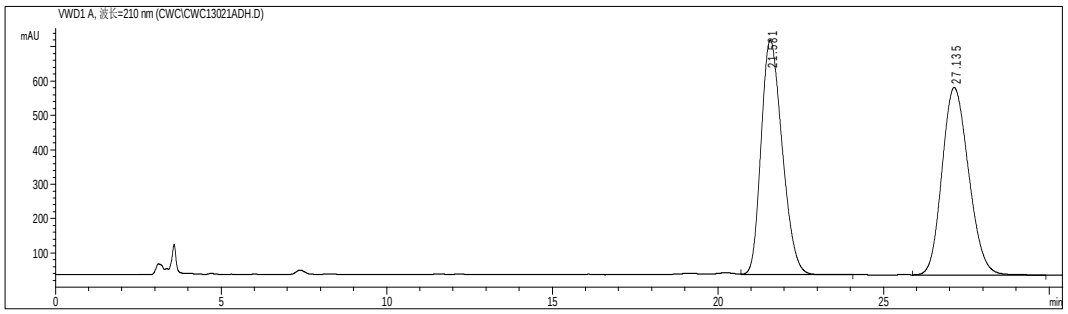


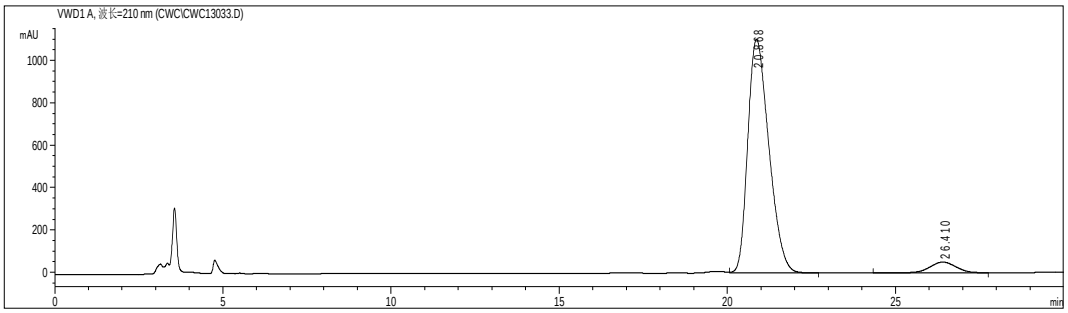


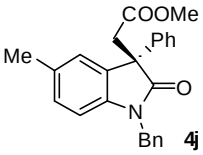
4i

Colorless oil, 99% yield; 93% ee; $[\alpha]_D^{26}$ –82.6 (*c* 0.64, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (s, 1H), 7.34–7.28 (m, 10H), 6.64 (d, J = 8.3 Hz, 1H), 4.93 (dd, J = 44.5, 15.8 Hz, 2H), 3.64 (d, J = 16.7 Hz, 1H), 3.48 (s, 3H), 3.31 (d, J = 16.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.5, 169.9, 142.8, 138.6, 135.4, 133.5, 131.4, 128.9, 128.8, 128.0, 127.7, 127.4, 127.3, 126.4, 115.2, 110.9, 53.4, 51.8, 44.3, 41.2. HRMS (ESI) m/z 450.0709 ($M+H^+$), calc. for $C_{24}H_{21}BrNO_3$ 450.0705.

The ee was determined by HPLC analysis. CHIRALCEL ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 ^{o}C; 210 nm; retention time: 20.9 min (major) and 26.4 min (minor).



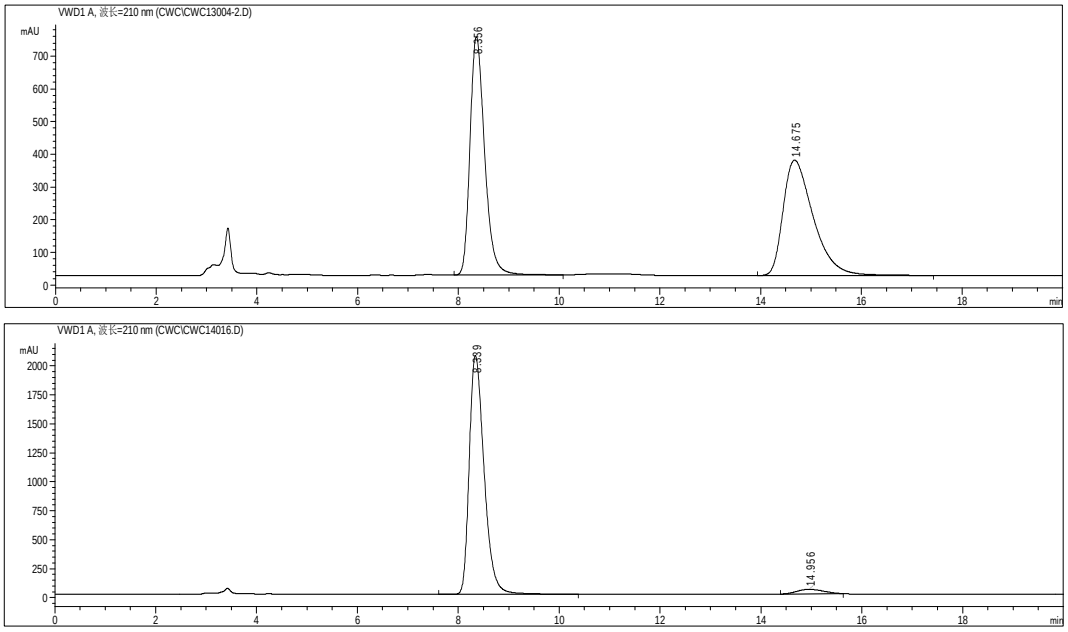


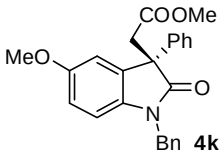


4j

Colorless oil, 96% yield; 93% ee; $[\alpha]_D^{26}$ –68.6 (*c* 0.54, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.27 (m, 9H), 7.05 (dd, *J* = 7.9, 2.6 Hz, 1H), 6.91 (td, *J* = 8.9, 2.6 Hz, 1H), 6.67 (dd, *J* = 8.6, 4.2 Hz, 1H), 4.99 (d, *J* = 15.8 Hz, 1H), 4.87 (d, *J* = 15.8 Hz, 1H), 3.63 (d, *J* = 16.6 Hz, 1H), 3.47 (s, 3H), 3.31 (d, *J* = 16.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.0, 170.1, 141.2, 139.5, 136.0, 132.0, 131.2, 128.8, 128.7, 128.6, 127.6, 127.4, 127.4, 126.6, 125.2, 109.2, 53.4, 51.6, 44.3, 41.4, 21.2. HRMS (ESI) m/z 386.1760 ($M+H^+$), calc. for $C_{25}H_{24}NO_3$ 386.1756.

The ee was determined by HPLC analysis. CHIRALCEL ODH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 8.3 min (major) and 14.9 min (minor).

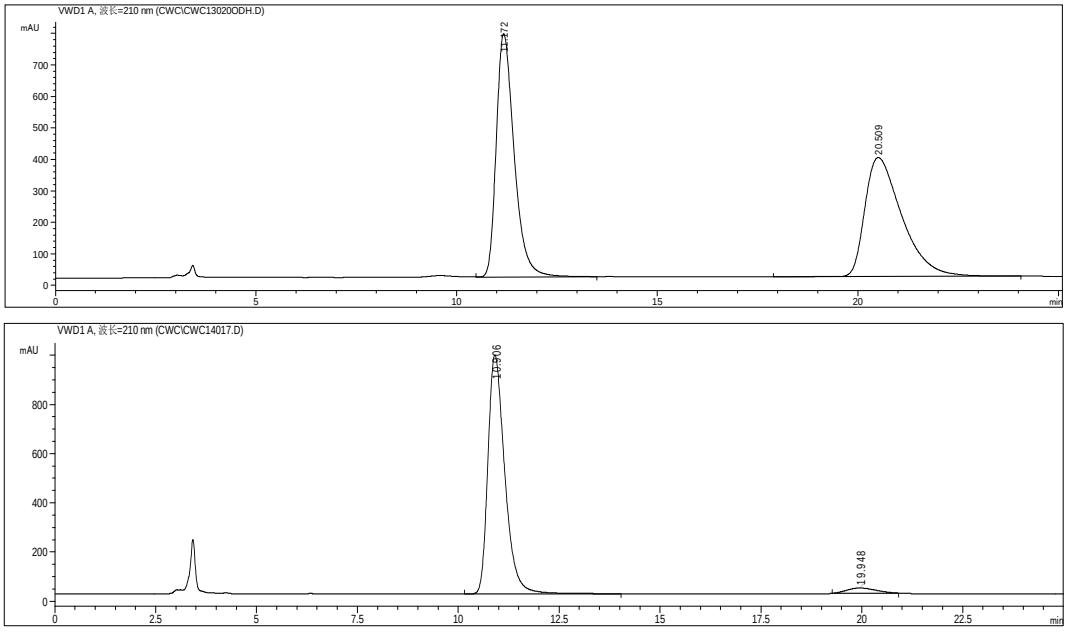


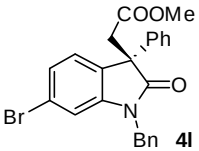


4k

Colorless oil, 90% yield; 93% ee; $[\alpha]_D^{26}$ -49.8 (*c* 0.36, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.29 (m, 9H), 6.90 (d, *J* = 2.3 Hz, 1H), 6.74 (dd, *J* = 8.5, 2.4 Hz, 1H), 6.66 (d, *J* = 8.5 Hz, 1H), 4.92 (dd, *J* = 42.9, 15.7 Hz, 2H), 3.75 (s, 3H), 3.64 (d, *J* = 16.4 Hz, 1H), 3.44 (s, 3H), 3.30 (d, *J* = 16.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.8, 170.0, 155.8, 139.3, 137.1, 136.0, 132.6, 128.8, 128.6, 127.7, 127.5, 127.4, 126.5, 112.6, 112.0, 109.7, 55.7, 53.7, 51.7, 44.3, 41.4. HRMS (ESI) m/z 402.1701 ($M+H^+$), calc. for $C_{25}H_{24}NO_4$ 402.1705.

The ee was determined by HPLC analysis. CHIRALCEL ODH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 ^{o}C; 254 nm; retention time: 10.9 min (major) and 19.9 min (minor).

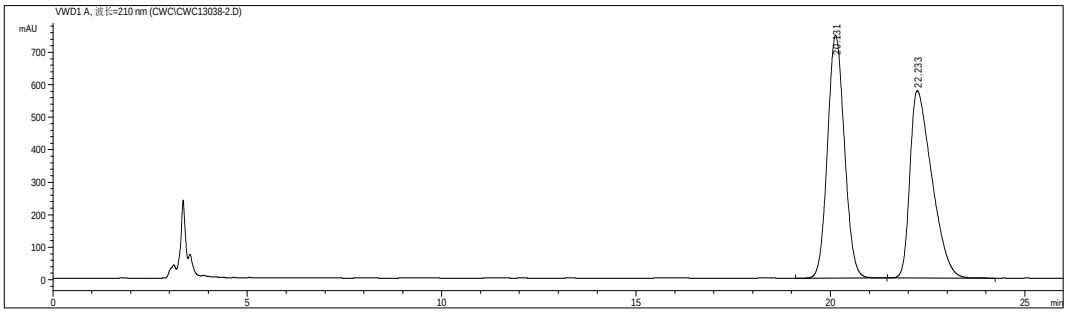


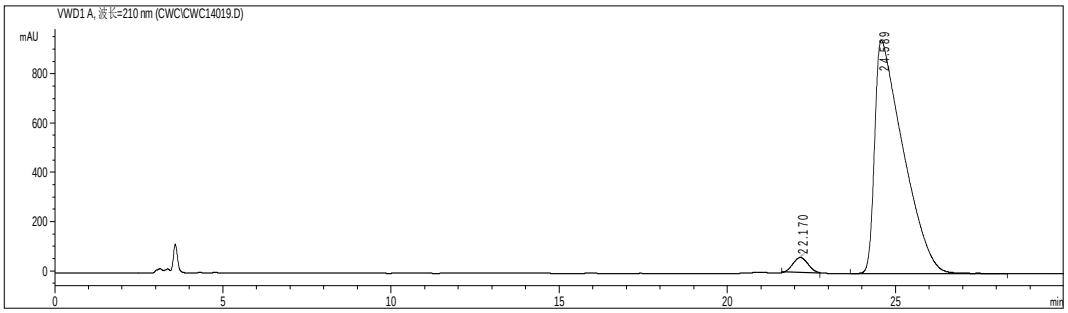


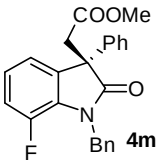
4l

Colorless oil, 95% yield; 94% ee; $[\alpha]_D^{26}$ –54.3 (*c* 0.26, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.29 (m, 10H), 7.18 (dd, *J* = 27.3, 7.9 Hz, 2H), 6.92 (s, 1H), 4.98 (d, *J* = 15.8 Hz, 1H), 4.84 (d, *J* = 15.8 Hz, 1H), 3.64 (d, *J* = 16.4 Hz, 1H), 3.45 (s, 3H), 3.30 (d, *J* = 16.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.9, 169.9, 145.0, 138.6, 135.3, 130.2, 128.9, 128.8, 127.9, 127.7, 127.3, 126.4, 125.6, 125.4, 122.2, 112.8, 53.0, 51.8, 44.3, 41.3. HRMS (ESI) m/z 450.0710 ($M+H^+$), calc. for $C_{24}H_{21}NO_3Br$ 450.0705.

The ee was determined by HPLC analysis. CHIRALCEL ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 ^{o}C; 210 nm; retention time: 22.2 min (minor) and 24.6 min (major).



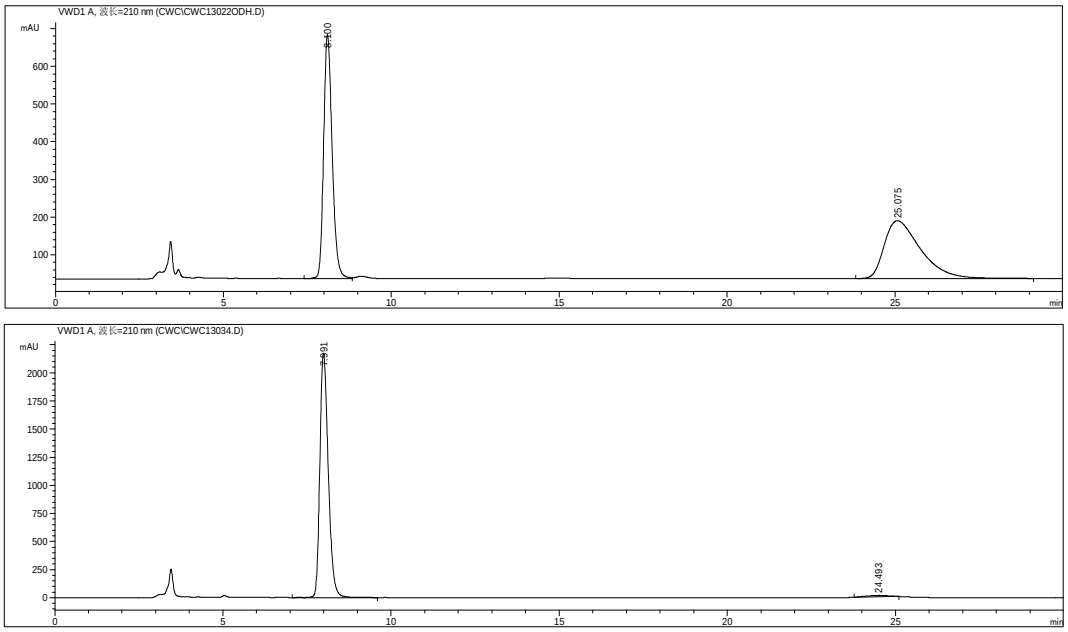


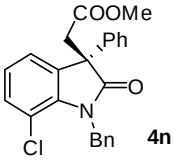


4m

Colorless oil, 93% yield; 97% ee; $[\alpha]_D^{26}$ –62.3 (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.19 (m, 13H), 7.04 (t, *J* = 7.8 Hz, 1H), 5.37 (dd, *J* = 16.2, 9.5 Hz, 2H), 3.70 (d, *J* = 16.5 Hz, 1H), 3.49 (s, 3H), 3.32 (d, *J* = 16.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.6, 169.9, 139.9, 138.9, 137.8, 134.2, 131.2, 128.8, 128.4, 127.9, 127.0, 126.6, 126.5, 123.4, 122.9, 115.7, 53.0, 51.8, 45.3, 41.5. HRMS (ESI) m/z 390.1512 ($M+H^+$), calc. for $C_{24}H_{21}NO_3F$ 390.1505.

The ee was determined by HPLC analysis. CHIRALCEL ODH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 8.0 min (major) and 24.5 min (minor).

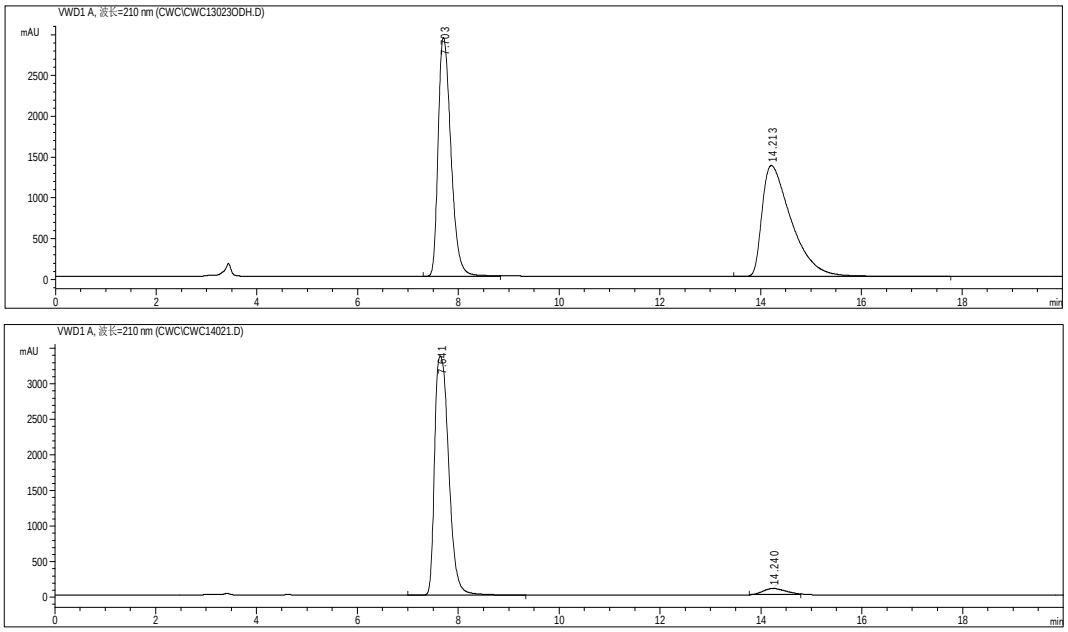


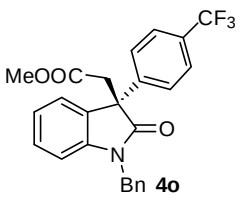


4n

Colorless oil, 96% yield; 93% ee; $[\alpha]_D^{26}$ –78.5 (*c* 0.54, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.21 (m, 10H), 7.07–7.00 (m, *J* = 12.2, 6.4, 3.2 Hz, 3H), 5.07 (dd, *J* = 15.4, 15.1 Hz, 2H), 3.65 (d, *J* = 16.3 Hz, 1H), 3.38 (s, 3H), 3.29 (d, *J* = 16.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.7, 169.8, 148.8, 146.3, 138.8, 137.1, 134.2 (two peaks), 128.8, 128.4, 127.9, 127.6, 127.4, 126.4, 123.2 (two peaks), 120.3 (two peaks), 116.8 (two peaks), 53.5, 51.7, 45.7 (two peaks), 41.6. HRMS (ESI) m/z 406.1211 ($M+H^+$), calc. for $C_{24}H_{21}NO_3Cl$ 406.1210.

The ee was determined by HPLC analysis. CHIRALCEL ODH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 7.6 min (major) and 14.2 min (minor).

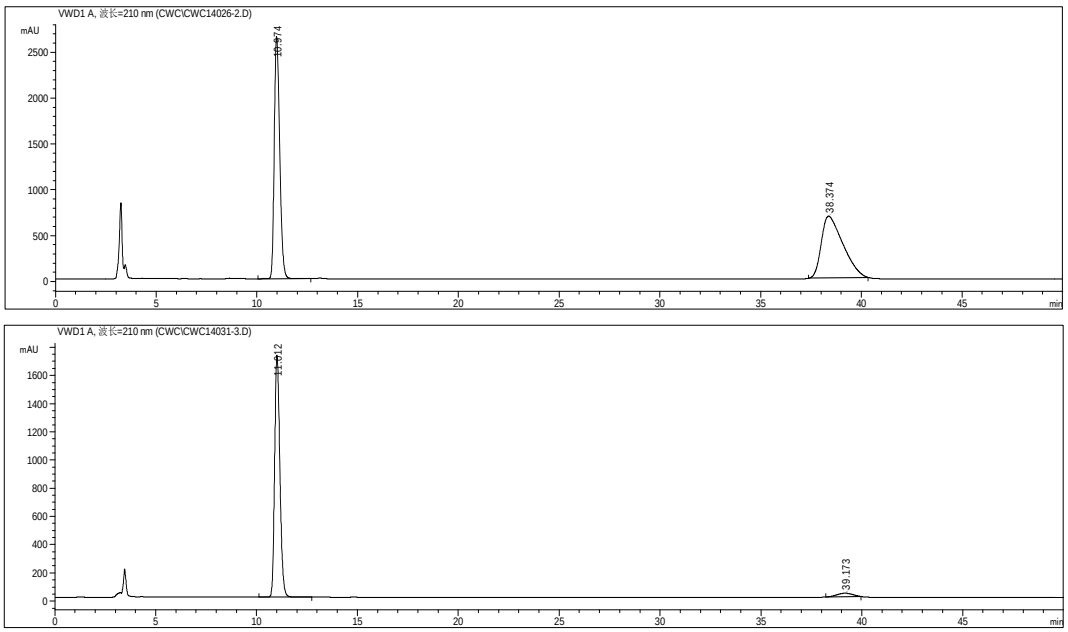


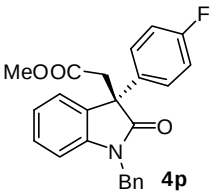


4o

Colorless oil, 96% yield; 92% ee; $[\alpha]_D^{26}$ –69.3 (*c* 0.25, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.32–7.24 (m, 6H), 7.10 (t, *J* = 7.5 Hz, 1H), 6.82 (d, *J* = 7.8 Hz, 1H), 4.94 (dd, *J* = 42.2, 15.7 Hz, 2H), 3.58 (d, *J* = 16.3 Hz, 1H), 3.43 (s, 3H), 3.34 (d, *J* = 16.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.3, 169.7, 143.6, 143.2, 143.2, 135.7, 130.3, 129.0, 128.8, 127.6, 127.4, 127.1, 125.7, 125.6, 124.6, 122.8, 109.7, 53.3, 51.8, 44.4, 41.5. HRMS (ESI) m/z 440.1476 ($M+H^+$), calc. for $C_{25}H_{21}NO_3F_3$ 440.1474.

The ee was determined by HPLC analysis. CHIRALCEL ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 ^{o}C; 210 nm; retention time: 11.0 min (major) and 29.2 min (minor).



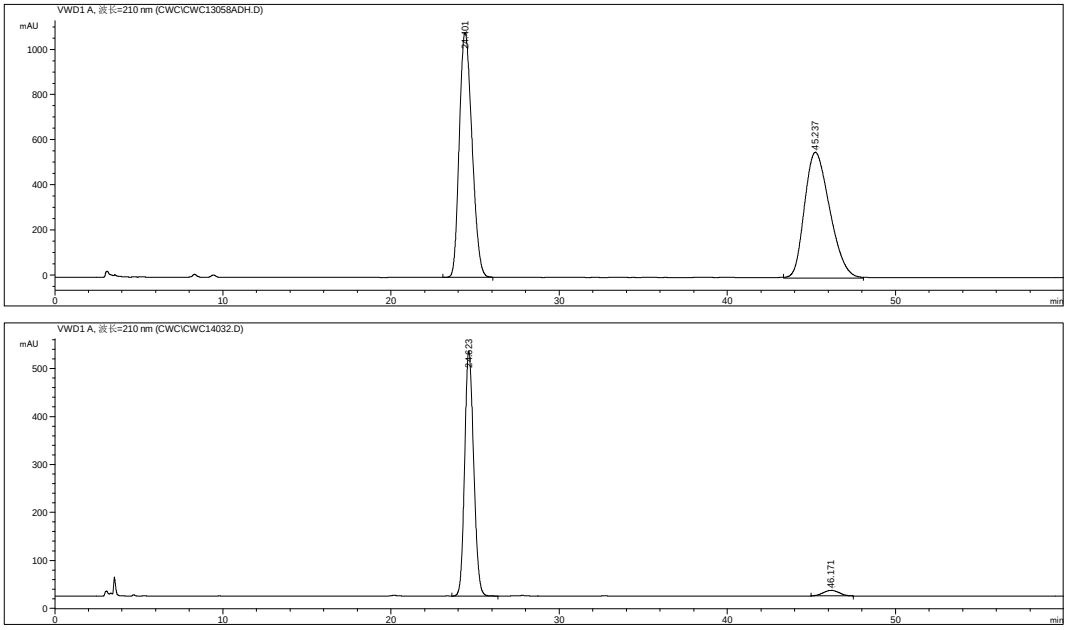


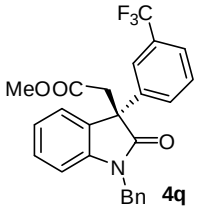
4p

Colorless oil, 93% yield; 93% ee; $[\alpha]_D^{26}$ –45.0 (*c* 0.49, $CHCl_3$); ^{1}H NMR (400 MHz,

$CDCl_3$) δ 7.33–7.24 (m, 8H), 7.11 (t, *J* = 7.5 Hz, 1H), 7.04–6.99 (m, 2H), 6.82 (d, *J* = 7.8 Hz, 1H), 4.96 (dd, *J* = 47.3, 15.7 Hz, 2H), 3.60 (d, *J* = 16.2 Hz, 1H), 3.43 (s, 3H), 3.31 (d, *J* = 16.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.9, 169.8, 163.5, 161.0, 143.5, 135.8, 134.9, 130.8, 128.7, 128.4, 127.6, 127.3, 124.5, 122.6, 115.5, 109.6, 52.8, 51.7, 44.2, 41.8. HRMS (ESI) m/z 390.1508 ($M+H^+$), calc. for $C_{24}H_{21}NO_3F$ 390.1505.

The ee was determined by HPLC analysis. CHIRALCEL ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 24.6min (major) and 46.2 min (minor).

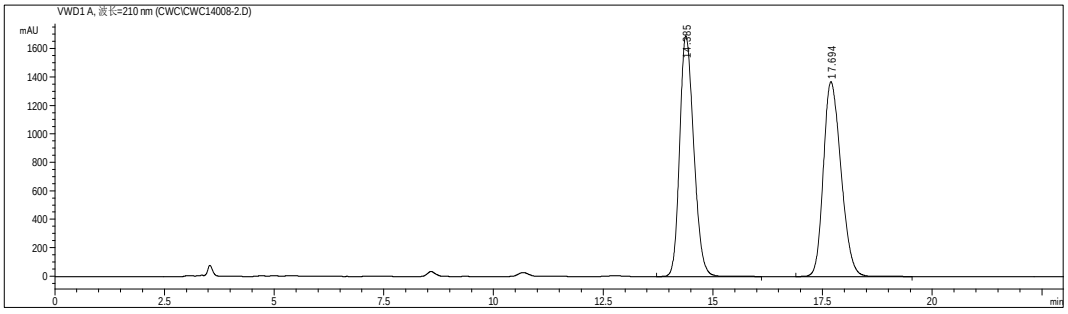


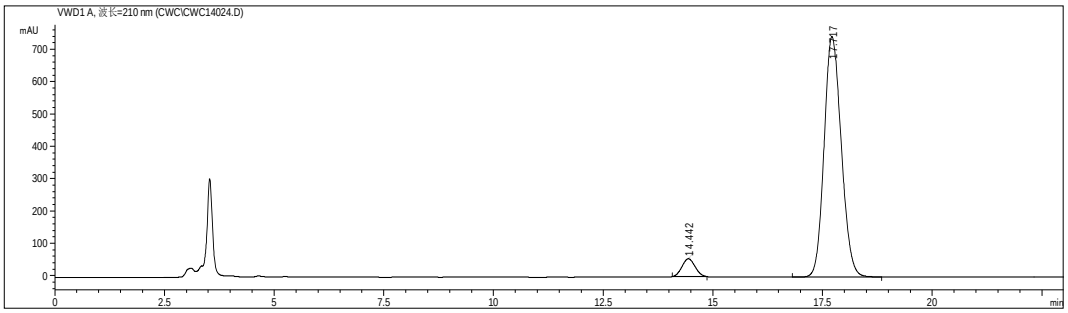


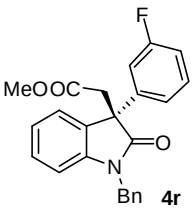
4q

Colorless oil, 99% yield; 90% ee; $[\alpha]_D^{26}$ –74.5 (*c* 0.59, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57–7.53 (m, 3H), 7.44 (t, *J* = 8.1 Hz, 1H), 7.30–7.24 (m, 3H) 7.10 (t, *J* = 7.5 Hz, 1H), 6.82 (d, *J* = 7.8 Hz, 1H), 4.95 (dd, *J* = 54.0, 15.7 Hz, 2H), 3.60 (d, *J* = 16.2 Hz, 1H), 3.42 (s, 3H), 3.34 (d, *J* = 16.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.3, 169.6, 143.5, 140.4, 135.7, 130.3, 130.2, 129.2, 129.0, 128.7, 127.6, 127.4, 124.6 (two peaks), 124.5, 123.5, 123.4, 122.9, 109.7, 53.1, 51.8, 44.3, 41.5. HRMS (ESI) m/z 440.1473 ($M+H^+$), calc. for $C_{25}H_{21}NO_3F_3$ 440.1474.

The ee was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 14.4 min (major) and 17.7 min (minor).



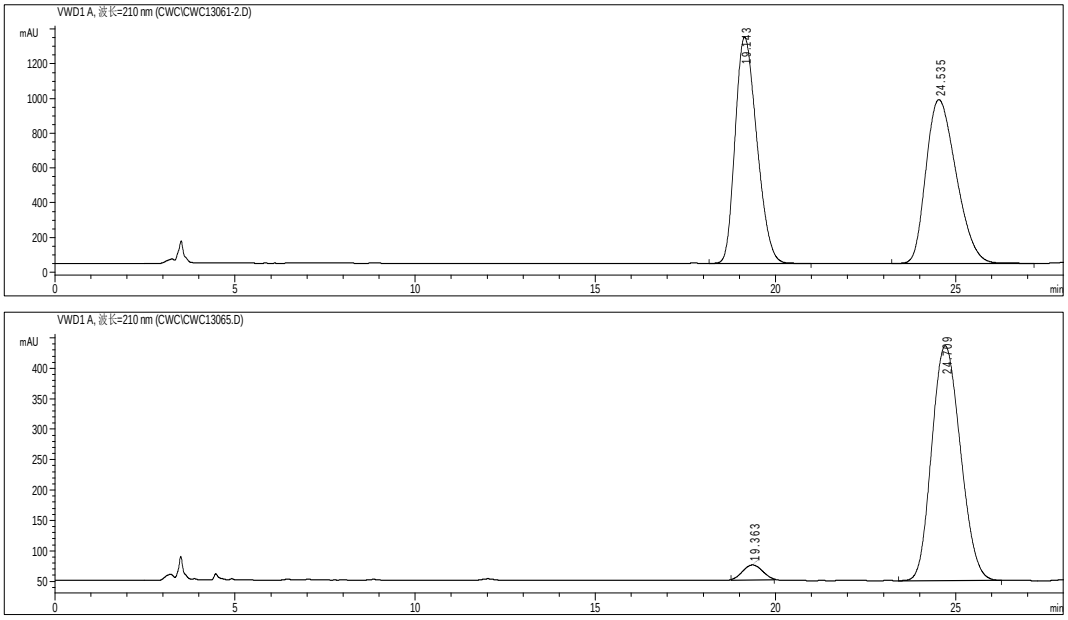


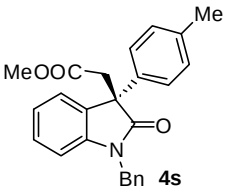


4r

Colorless oil, 93% yield; 92% ee; $[\alpha]_D^{26}$ –53.4 (*c* 0.33, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.24 (m, 9H), 7.11 (t, *J* = 7.5 Hz, 1H), 7.04–6.99 (m, 2H), 6.82 (d, *J* = 7.8 Hz, 1H), 4.96 (dd, *J* = 47.3, 15.7 Hz, 2H), 3.60 (d, *J* = 16.2 Hz, 1H), 3.43 (s, 3H), 3.31 (d, *J* = 16.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.5, 169.8, 164.1, 161.6, 143.6, 141.7, 135.8, 130.5, 130.2, 128.8, 128.7, 127.6, 127.4, 124.5, 122.7, 122.3, 114.4, 109.6, 53.1, 51.7, 44.3, 41.6. HRMS (ESI) m/z 390.1508 ($M+H^+$), calc. for $C_{24}H_{21}NO_3F$ 390.1505.

The ee was determined by HPLC analysis. CHIRALCEL ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 19.4 min (major) and 24.7 min (minor).

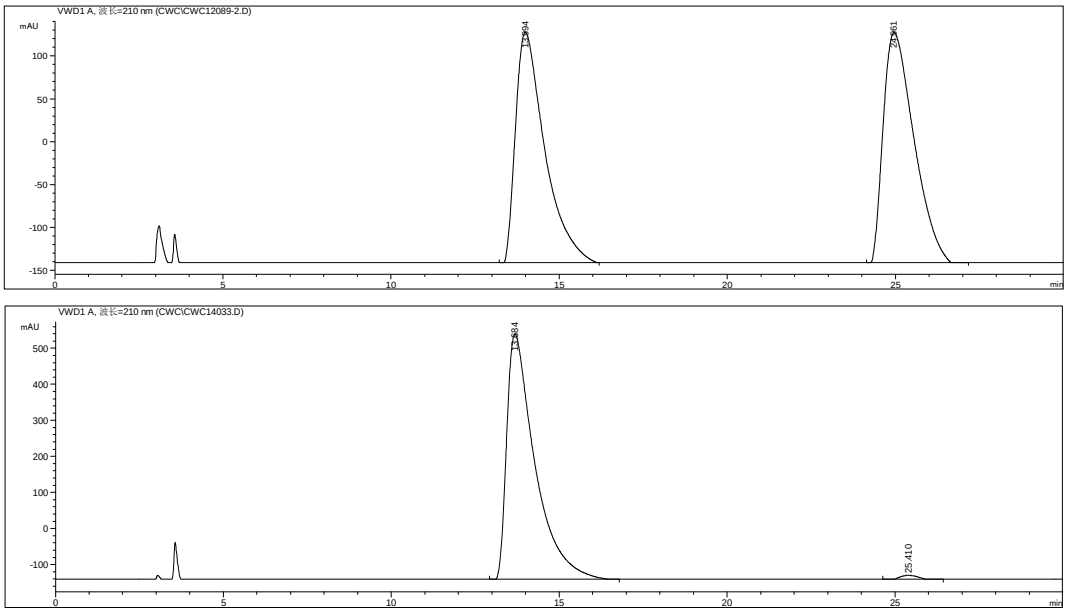


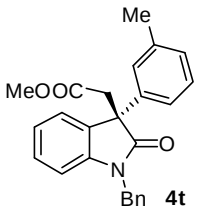


4s

Colorless oil, 99% yield; 98% ee; $[\alpha]_D^{26}$ –90.4 (*c* 0.31, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.19 (m, 9H), 7.12–7.04 (m, 3H), 6.77 (d, *J* = 7.8 Hz, 1H), 4.93 (dd, *J* = 42.9, 15.8 Hz, 2H), 3.63 (d, *J* = 16.2 Hz, 1H), 3.39 (s, 3H), 3.29 (d, *J* = 16.2 Hz, 1H), 2.31 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.2, 170.1, 143.6, 137.4, 136.4, 136.0, 131.3, 129.4, 128.7, 128.4, 127.5, 127.4, 126.4, 124.4, 122.5, 109.4, 53.0, 51.6, 44.2, 41.6, 20.9. HRMS (ESI) m/z 386.1761 ($M+H^+$), calc. for $C_{25}H_{24}NO_3$ 386.1756.

The ee was determined by HPLC analysis. CHIRALCEL ODH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 90/10; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 13.7 min (major) and 25.4 min (minor).

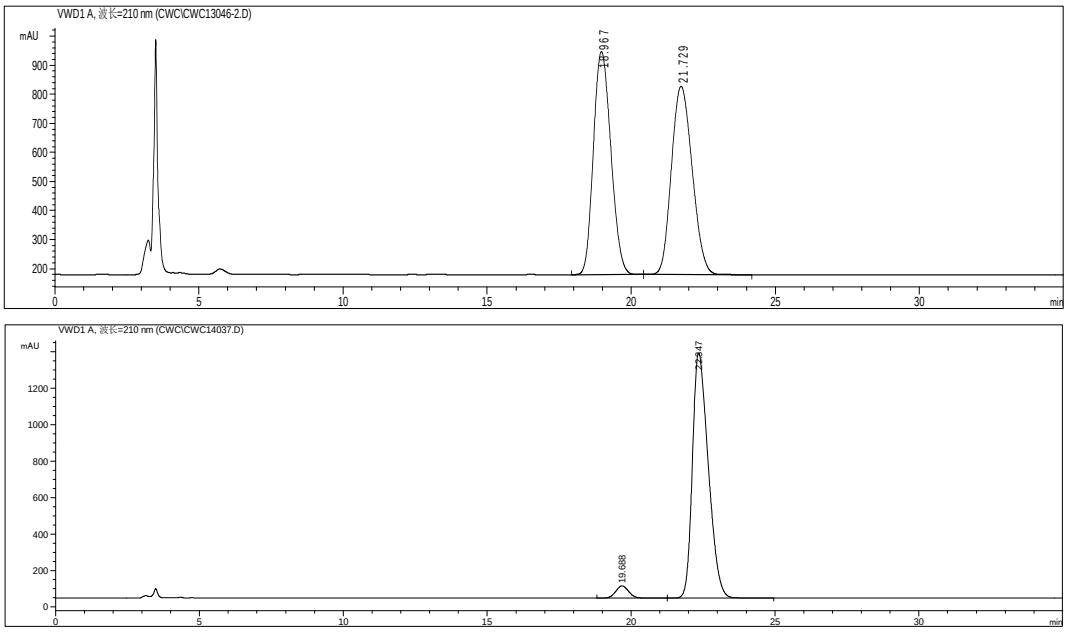


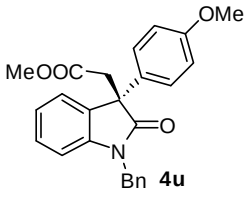


4t

Colorless oil,93% yield; 93% ee; $[\alpha]_D^{26}$ –65.7 (*c* 0.41, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.27 (m, 9H), 7.05 (dd, *J* = 7.9, 2.6 Hz, 1H), 6.91 (td, *J* = 8.9, 2.6 Hz, 1H), 6.67 (dd, *J* = 8.6, 4.2 Hz, 1H), 4.99 (d, *J* = 15.8 Hz, 1H), 4.87 (d, *J* = 15.8 Hz, 1H), 3.63 (d, *J* = 16.6 Hz, 1H), 3.47 (s, 3H), 3.31 (d, *J* = 16.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.1, 170.1, 143.6, 139.3, 138.4, 136.0, 131.4, 128.6, 128.6, 128.4, 127.5, 127.4, 127.2, 124.4, 123.5, 122.5, 109.4, 53.2, 51.6, 44.2, 41.5, 35.8, 21.6. HRMS (ESI) m/z 386.1760 ($M+H^+$), calc. for $C_{25}H_{24}NO_3$ 386.1756.

The ee was determined by HPLC analysis. CHIRALCEL ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 ^{o}C; 210 nm; retention time: 19.7 min (minor) and 22.3 min (major).



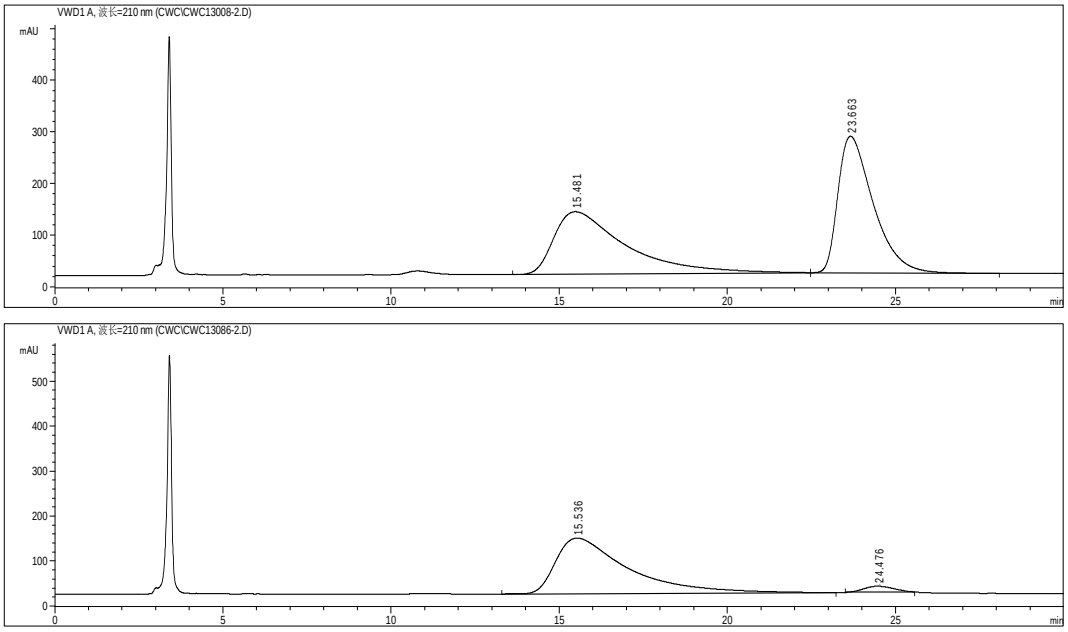


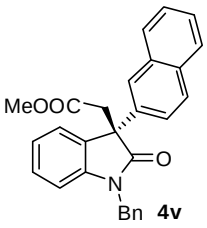
4u

Colorless oil, 92% yield; 91% ee; $[\alpha]_D^{26}$ –95.7 (*c* 0.34, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.19 (m, 9H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.83 (d, *J* = 8.8 Hz, 2H),

6.77 (d, J = 7.8 Hz, 1H), 4.93 (dd, J = 43.6, 15.8 Hz, 2H), 3.77 (s, 3H), 3.61 (d, J = 16.2 Hz, 1H), 3.39 (s, 3H), 3.27 (d, J = 16.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.3, 170.1, 159.0, 143.6, 136.0, 131.2, 128.7, 128.5, 127.7, 127.5, 127.4, 124.4, 122.5, 114.1, 109.4, 55.2, 52.6, 51.6, 44.2, 41.7. HRMS (ESI) m/z 402.1711 ($M+H^+$), calc. for $C_{25}H_{24}NO_4$ 402.1705.

The ee was determined by HPLC analysis. CHIRALCEL ODH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 15.5 min (major) and 24.5 min (minor).

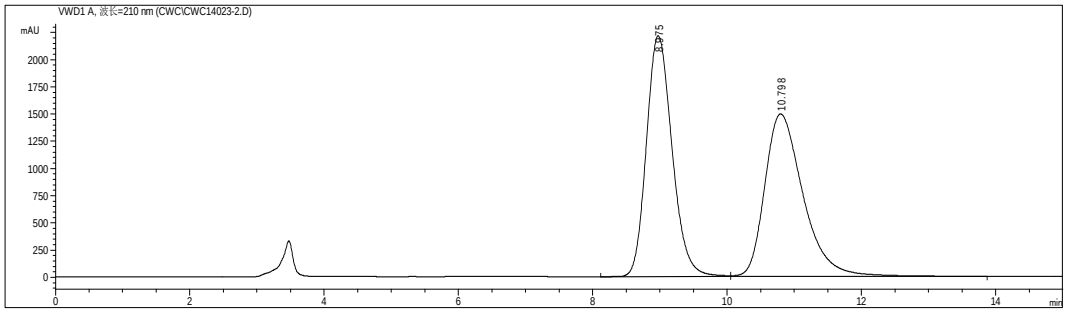


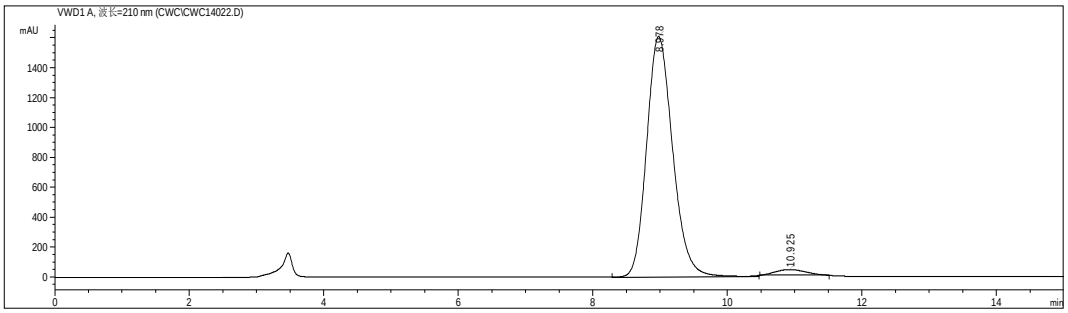


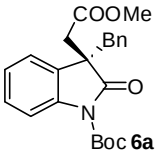
4v

Colorless oil, 90% yield; 95% ee; $[\alpha]_D^{26}$ –44.7 (c 0.22, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81–7.71 (m, 4H), 7.53–7.45 (m, 4H), 7.35–7.24 (m, 6H), 7.11 (t, J = 7.5 Hz, 1H), 6.83 (d, J = 7.8 Hz, 1H), 4.98 (dd, J = 56.9, 15.7 Hz, 2H), 3.77 (d, J = 16.2 Hz, 1H), 3.55–3.35 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.0, 170.0, 143.7, 136.6, 136.0, 133.2, 132.6, 131.2, 128.7, 128.6, 128.6, 128.2, 127.5, 127.4, 126.3, 126.2, 125.5, 124.5, 124.4, 122.6, 109.5, 53.4, 51.7, 44.3, 41.5. HRMS (ESI) m/z 422.1755 ($M+H^+$), calc. for $C_{28}H_{24}NO_3$ 422.1756.

The ee was determined by HPLC analysis. CHIRALCEL ASH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 9.0 min (major) and 10.9 min (minor).

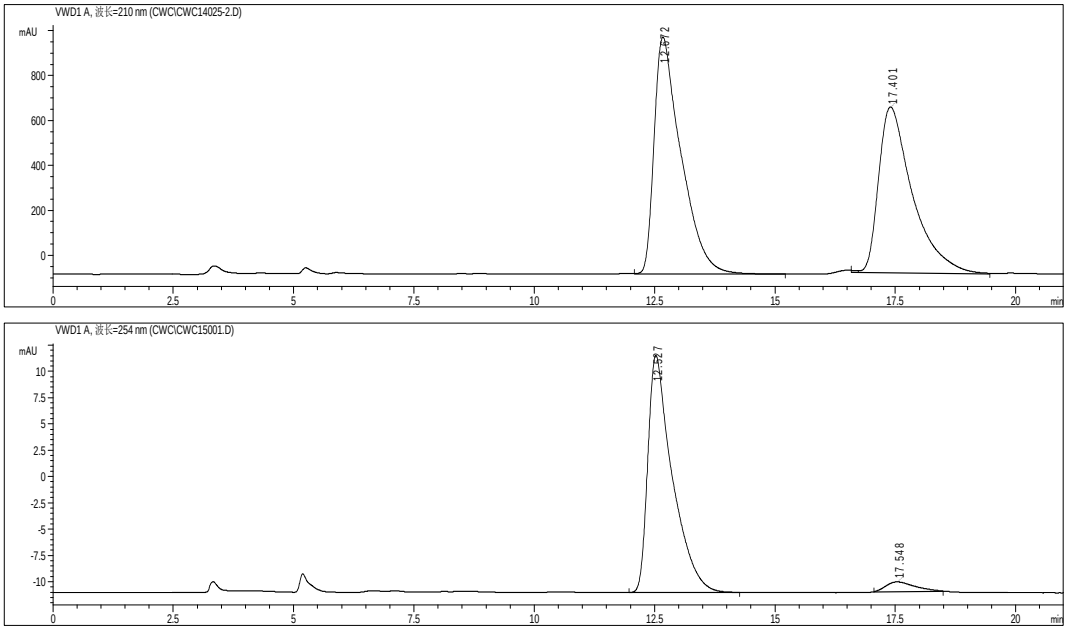


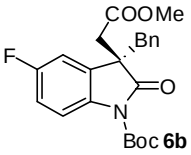




Colorless oil, 90% yield; 91% ee; $[\alpha]_D^{26}$ –87.7 (*c* 0.29, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.1 Hz, 1H), 7.24–7.18 (m, 1H), 7.13–7.03 (m, 5H), 6.78 (d, *J* = 7.2 Hz, 2H), 3.45 (s, 3H), 3.26 (d, *J* = 16.7 Hz, 1H), 3.08–2.96 (m, 3H), 1.57 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.5, 169.9, 148.8, 140.2, 134.0, 130.0, 129.1, 128.4, 127.7, 127.0, 123.8, 122.6, 114.9, 83.8, 51.8, 51.5, 45.2, 40.7, 28.0. HRMS (ESI) m/z 418.1631 ($M+Na^+$), calc. for $C_{23}H_{25}NO_5Na$ 418.1630.

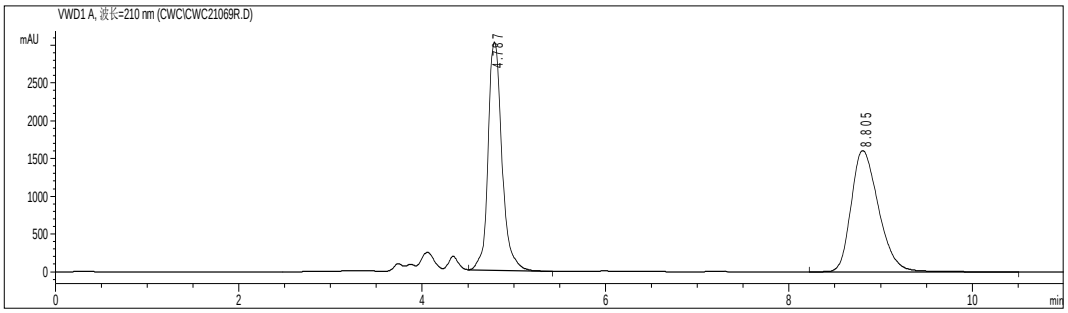
The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 90/10; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 12.5 min (major) and 17.5 min (minor).

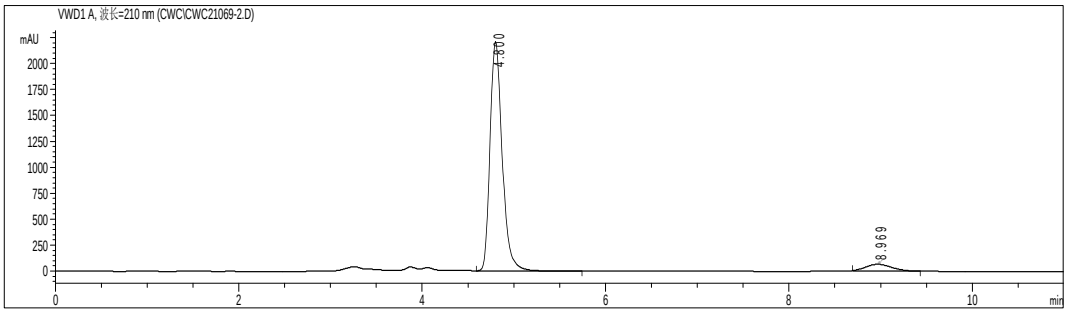


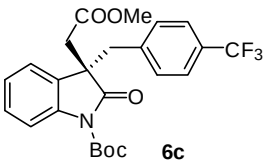


Colorless oil, 90% yield; 91% ee; $[\alpha]_D^{26}$ –60.0 (*c* 0.22, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 8.9, 4.6 Hz, 1H), 7.16–7.07 (m, 3H), 6.91 (td, *J* = 9.0, 2.6 Hz, 1H), 6.78 (dd, *J* = 14.0, 5.1 Hz, 3H), 3.49 (s, 3H), 3.26 (d, *J* = 17.0 Hz, 1H), 3.07 (d, *J* = 12.9 Hz, 1H), 3.00–2.93 (m, 2H), 1.56 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1, 169.8, 160.7, 158.3, 148.7, 136.2, 136.1, 133.6, 131.1, 130.0, 127.8, 127.2, 116.2, 114.8, 110.2, 84.0, 51.9, 51.8, 45.1, 40.5, 28.0. HRMS (ESI) m/z 414.1707 ($M+H^+$), calc. for $C_{23}H_{25}NO_5F$ 414.1717.

The ee was determined by HPLC analysis. CHIRALCEL ODH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 60/40; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 4.8 min (major) and 9.0 min (minor).



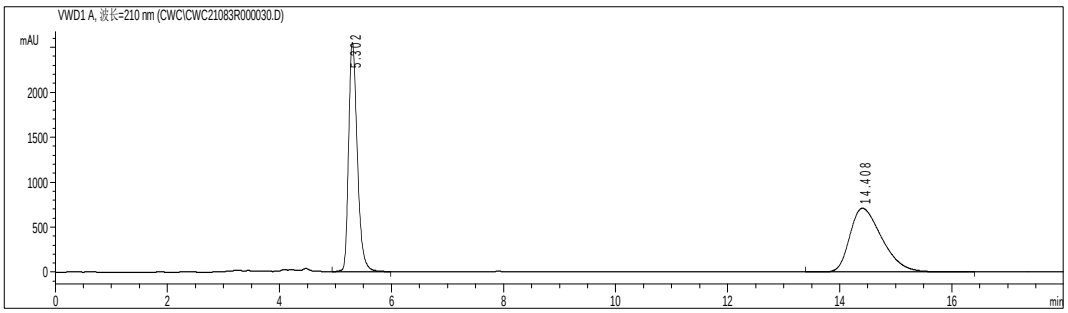


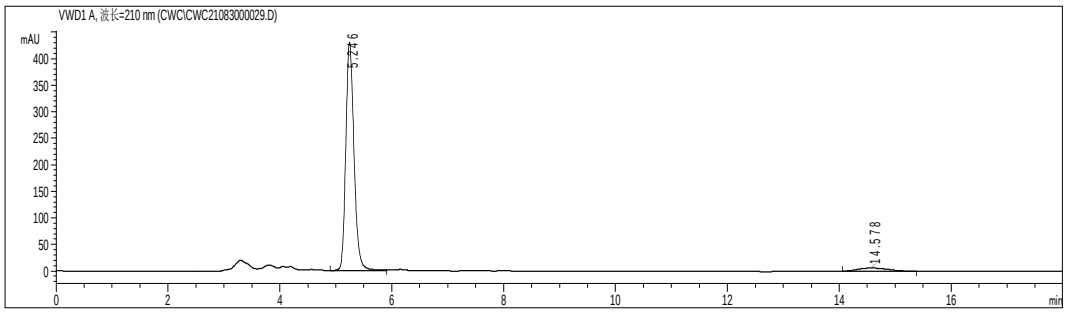


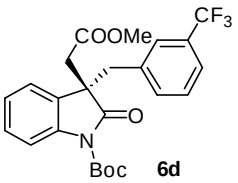
6c

Colorless oil, 93% yield; 92% ee; $[\alpha]_D^{26}$ –121.2 (*c* 0.29, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.1 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.25–7.22 (m, 1H), 7.17–7.13 (m, 2H), 6.87 (d, *J* = 8.1 Hz, 2H), 3.47 (s, 3H), 3.26 (d, *J* = 16.7 Hz, 1H), 3.15 (d, *J* = 12.7 Hz, 1H), 3.06 (d, *J* = 12.7 Hz, 1H), 2.99 (d, *J* = 16.7 Hz, 1H), 1.54 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.0, 169.7, 148.4, 140.2, 138.2, 130.3, 128.8, 128.6, 124.6, 124.6, 124.5, 124.1, 122.5, 115.1, 84.1, 51.9, 51.5, 44.8, 40.8, 28.0. HRMS (ESI) m/z 486.1503 ($M+Na^+$), calc. for $C_{24}H_{24}NO_5NaF_3$ 486.1504.

The ee was determined by HPLC analysis. CHIRALCEL ODH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 5.2 min (major) and 14.6 min (minor).



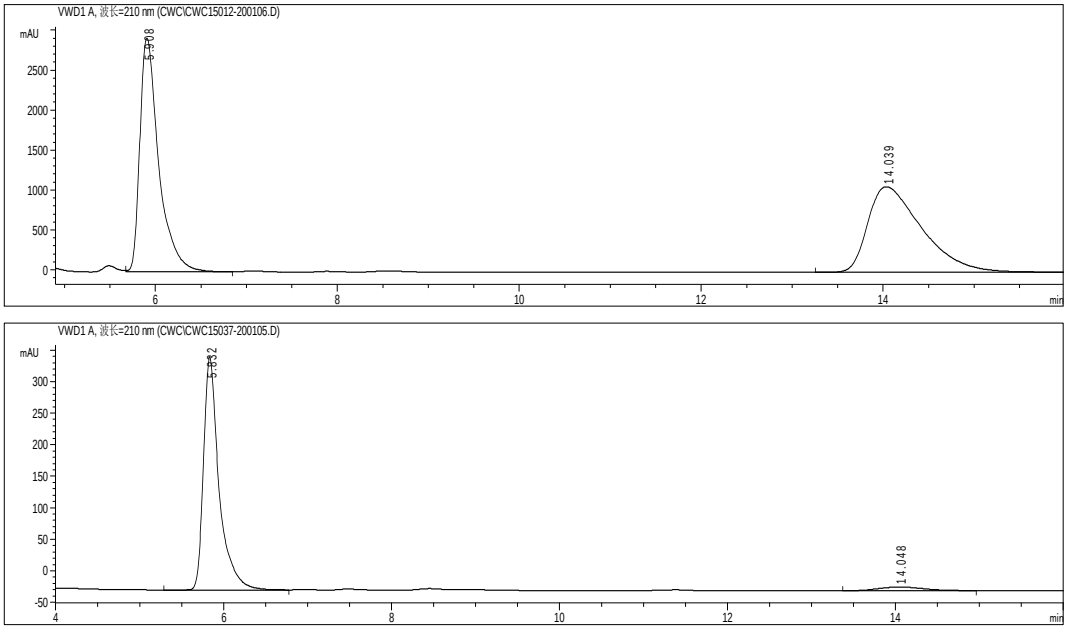


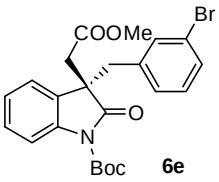


6d

Colorless oil, 87% yield; 94% ee; $[\alpha]_D^{26}$ –74.2 (*c* 0.31, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.2 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 1H), 7.26–7.13 (m, 4H), 6.98 (d, *J* = 7.9 Hz, 1H), 6.94 (s, 1H), 3.47 (s, 3H), 3.47 (s, 3H), 3.26 (d, *J* = 16.7 Hz, 1H), 3.11 (dd, *J* = 47.6, 12.8 Hz, 2H), 2.99 (d, *J* = 16.7 Hz, 1H), 1.54 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9, 169.8, 148.6, 140.1, 135.0, 133.3, 130.2, 129.9, 128.8, 128.5, 128.2, 126.6, 124.1, 123.9, 122.5, 115.1, 84.0, 51.9, 51.6, 44.8, 40.8, 27.9. HRMS (ESI) m/z 486.1514 ($M+Na^+$), calc. for $C_{24}H_{24}NO_5F_3Na$ 486.1504.

The ee was determined by HPLC analysis. CHIRALCEL ODH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 5.8 min (major) and 14.0 min (minor).

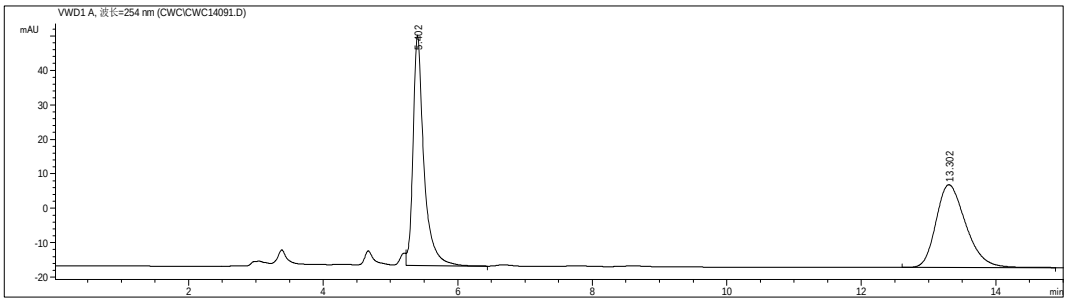


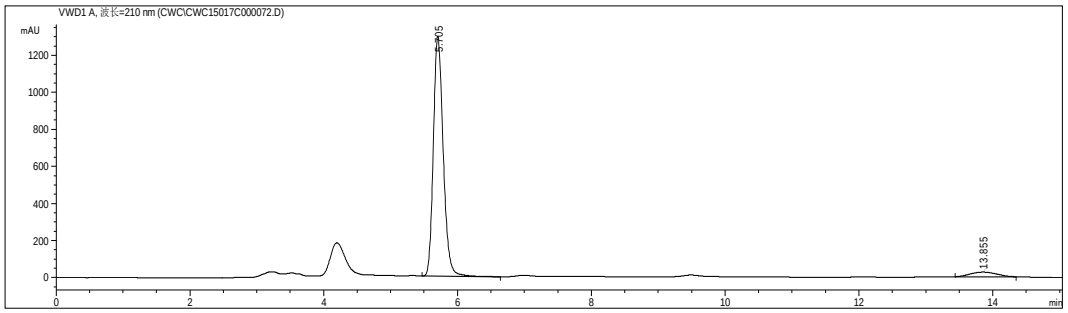


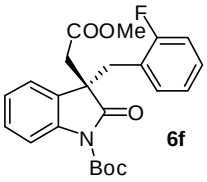
6e

Colorless oil, 90% yield; 92% ee; $[\alpha]_D^{26}$ –54.3 (*c* 0.26, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.1 Hz, 1H), 7.24–7.20 (m, 1H), 7.12–7.03 (m, 5H), 6.78 (d, *J* = 6.8 Hz, 2H), 3.45 (s, 3H), 3.26 (d, *J* = 16.7 Hz, 1H), 3.09–2.96 (m, 3H), 1.57 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.6, 170.0, 148.8, 140.2, 134.0, 130.1, 129.1, 128.4, 127.7, 127.0, 123.9, 122.7, 115.0, 83.8, 77.4, 51.8, 51.6, 45.2, 40.7, 28.1. HRMS (ESI) m/z 474.0926 ($M+H^+$), calc. for $C_{23}H_{25}NO_5Br$ 474.0916.

The ee was determined by HPLC analysis. CHIRALCEL ODH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 5.7 min (major) and 13.8 min (minor).

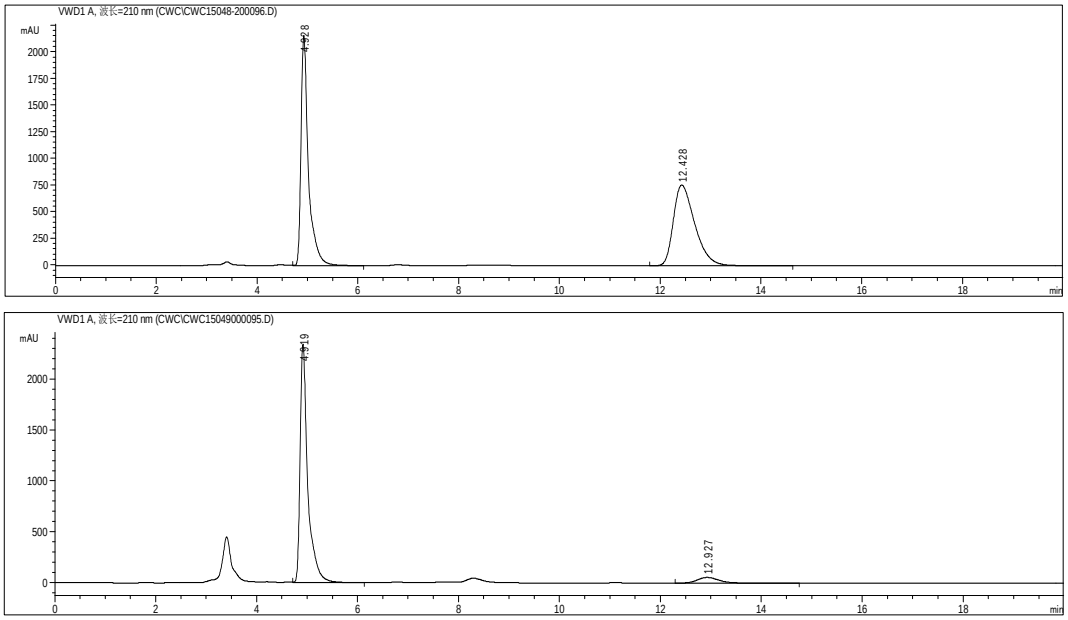


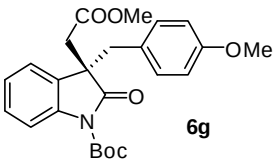




Colorless oil, 85% yield; 91% ee; $[\alpha]_D^{26}$ –84.83 (*c* 0.20, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.2 Hz, 1H), 7.24–7.20 (m, 1H), 7.14–7.10 (m, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.98–6.92 (m, 3H), 6.86–6.82 (m, 1H), 3.44 (s, 3H), 3.28 (d, *J* = 16.8 Hz, 2H), 3.23 (d, *J* = 13.4 Hz, 2H) 2.97 (m, 2H), 1.61 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.6, 170.0, 149.0, 139.9, 132.2, 132.2, 129.2, 129.1, 128.8, 128.5, 123.8, 123.5, 123.5, 123.0, 115.3, 115.0, 114.8, 84.0, 51.8, 50.9, 40.4, 37.2, 28.1. HRMS (ESI) m/z 414.1718 ($M+H^+$), calc. for $C_{23}H_{25}NO_5F$ 414.1717.

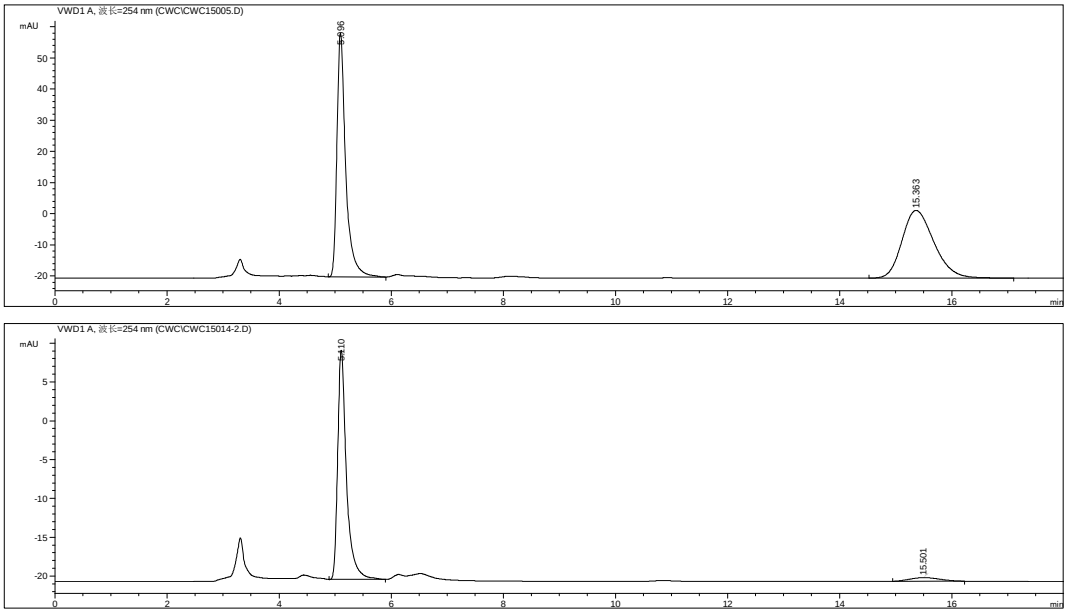
The ee was determined by HPLC analysis. CHIRALCEL ODH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 ^{o}C; 210 nm; retention time: 4.9 min (major) and 12.9 min (minor).

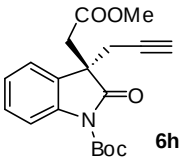




Colorless oil, 76% yield; 92% ee; $[\alpha]_D^{26}$ –96.8 (*c* 0.20, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.1 Hz, 1H), 7.25–7.20 (m, 1H), 7.11 (t, *J* = 7.4 Hz, 1H), 7.03 (d, *J* = 6.7 Hz, 1H), 6.70 (d, *J* = 8.6 Hz, 2H), 6.61 (d, *J* = 8.6 Hz, 2H), 3.70 (s, 3H), 3.44 (s, 3H), 3.23 (d, *J* = 16.7 Hz, 1H), 3.03–2.93 (m, 3H), 1.57 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.6, 170.0, 158.6, 148.8, 140.2, 131.1, 129.3, 128.4, 126.1, 123.8, 122.7, 115.1, 113.2, 83.8, 55.1, 51.8, 51.7, 44.4, 40.6, 28.1. HRMS (ESI) m/z 426.1923 ($M+H^+$), calc. for $C_{24}H_{28}NO_6$ 426.1917.

The ee was determined by HPLC analysis. CHIRALCEL ODH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 ^{o}C; 210 nm; retention time: 5.11 min (major) and 15.5 min (minor).

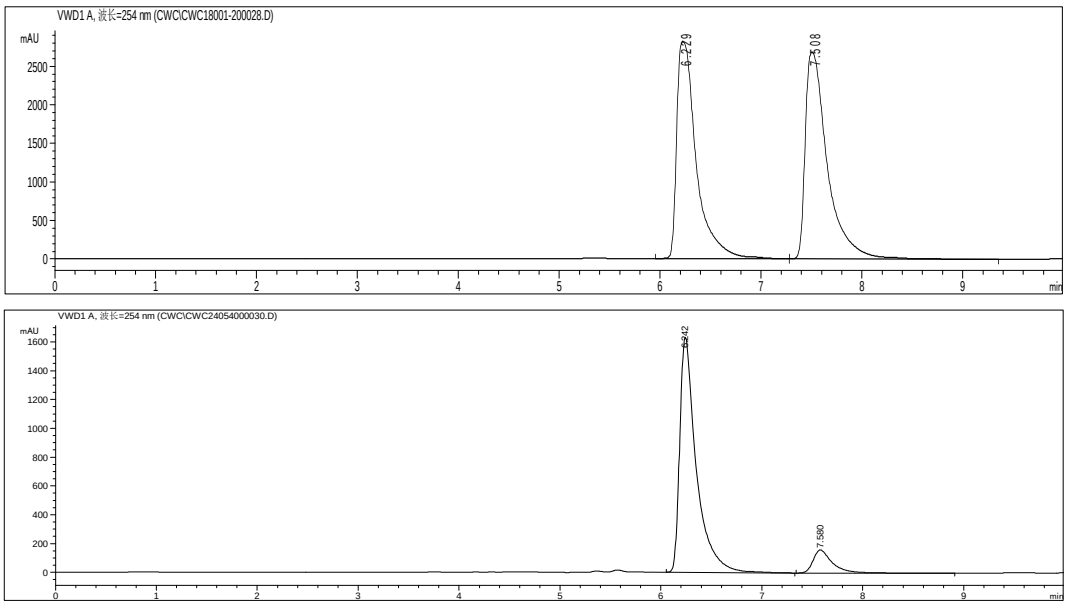


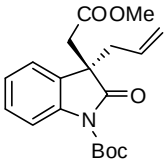


6h

Colorless oil, 56% yield; 87% ee; $[\alpha]_D^{26}$ –194.8 (*c* 0.21, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.2 Hz, 1H), 7.40 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.34 (td, *J* = 8.0, 1.4 Hz, 1H), 7.16 (td, *J* = 7.6, 0.9 Hz, 1H), 3.47 (s, 3H), 3.16 (dd, *J* = 36.9, 16.8 Hz, 2H), 2.72 (dd, *J* = 16.6, 2.6 Hz, 1H), 2.51 (dd, *J* = 16.6, 2.6 Hz, 1H), 2.08 (t, *J* = 2.6 Hz, 1H), 1.65 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 169.8, 149.2, 140.0, 129.0, 128.9, 124.3, 122.8, 115.2, 84.4, 78.1, 72.4, 51.9, 48.2, 40.0, 28.6, 28.1. HRMS (ESI) m/z 344.1502 ($M+H^+$), calc. for $C_{19}H_{22}NO_5$ 344.1498.

The ee was determined by HPLC analysis. CHIRALPAK IB (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 90/10; flow rate 1.0 mL/min; 25 ^{o}C; 210 nm; retention time: 6.2 min (major) and 7.6 min (minor).

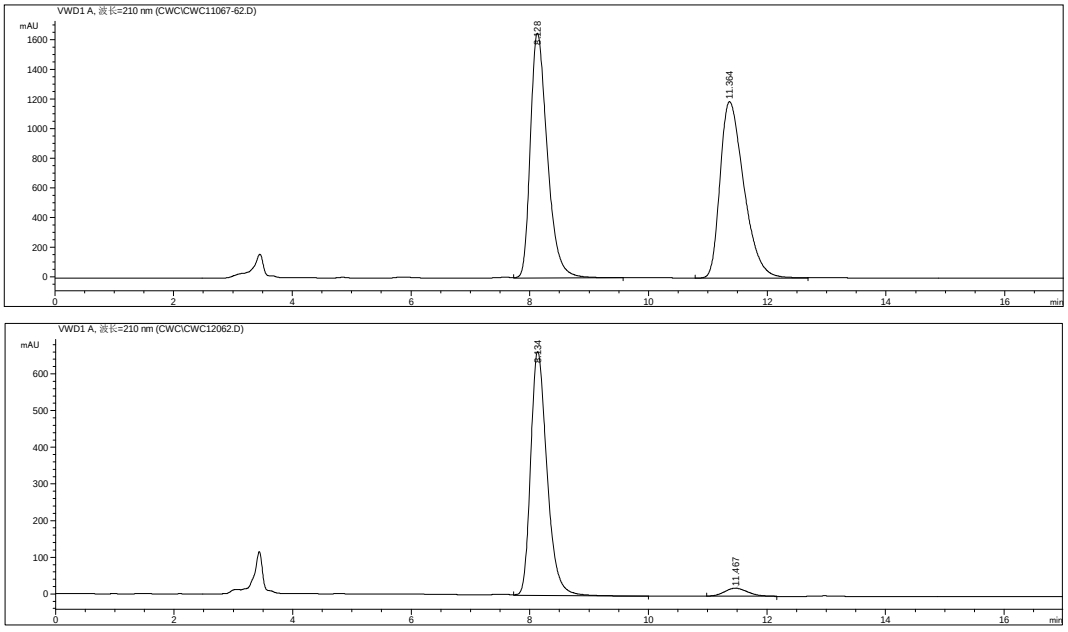


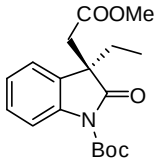


6i

Colorless oil, 83% yield; 87% ee; $[\alpha]_D^{26}$ –116.8 (*c* 0.20, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.2 Hz, 1H), 7.32–7.27 (m, 1H), 7.16–7.11 (m, 2H), 5.53–5.42(m, 1H), 5.04 (d, *J* = 5.1 Hz, 1H), 5.01 (s, 1H), 3.44 (s, 3H), 3.10 (d, *J* = 16.7 Hz, 1H), 2.89 (d, *J* = 16.7 Hz, 1H), 2.49 (d, *J* = 7.4 Hz, 2H), 1.64 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.5, 170.0, 149.2, 140.1, 130.7, 129.7, 128.5, 124.2, 122.4, 120.2, 115.2, 84.2, 51.8, 50.0, 43.0, 40.8, 28.1. HRMS (ESI) m/z 346.1649 ($M+H^+$), calc. for $C_{19}H_{24}NO_5$ 346.1654.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 85/15; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 8.4 min (major) and 11.5 min (minor).

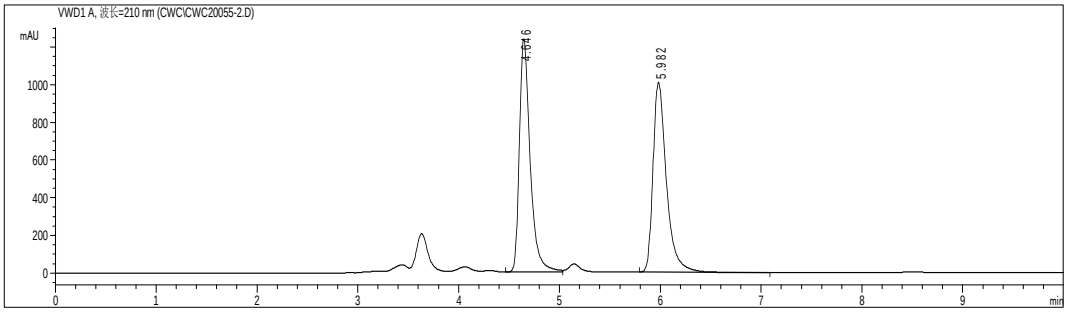


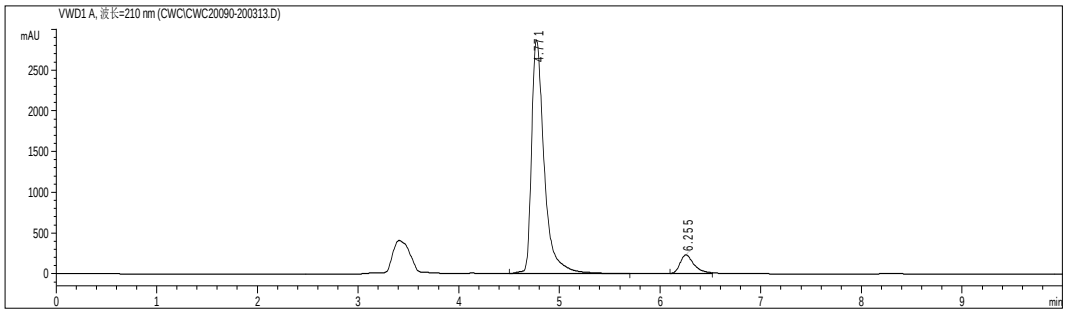


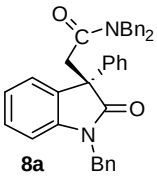
6j

Colorless oil, 72% yield; 85% ee; $[\alpha]_D^{26}$ –145.8 (*c* 0.20, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.1 Hz, 1H), 7.32–7.28 (m, 1H), 7.17–7.11 (m, 2H), 3.44 (s, 3H), 3.10 (d, *J* = 16.6 Hz, 1H), 2.87 (d, *J* = 16.6 Hz, 1H), 1.96–1.87 (m, 1H), 1.81–1.72 (m, 1H), 1.65 (s, 9H), 0.65 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.2, 170.1, 149.3, 140.5, 129.8, 128.4, 124.3, 122.1, 115.1, 84.1, 51.8, 50.6, 41.6, 32.4, 28.2, 8.1. HRMS (ESI) m/z 334.1656 ($M+H^+$), calc. for $C_{18}H_{24}NO_5$ 334.1654.

The ee was determined by HPLC analysis. CHIRALPAK IB (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 4.8 min (major) and 6.2 min (minor).



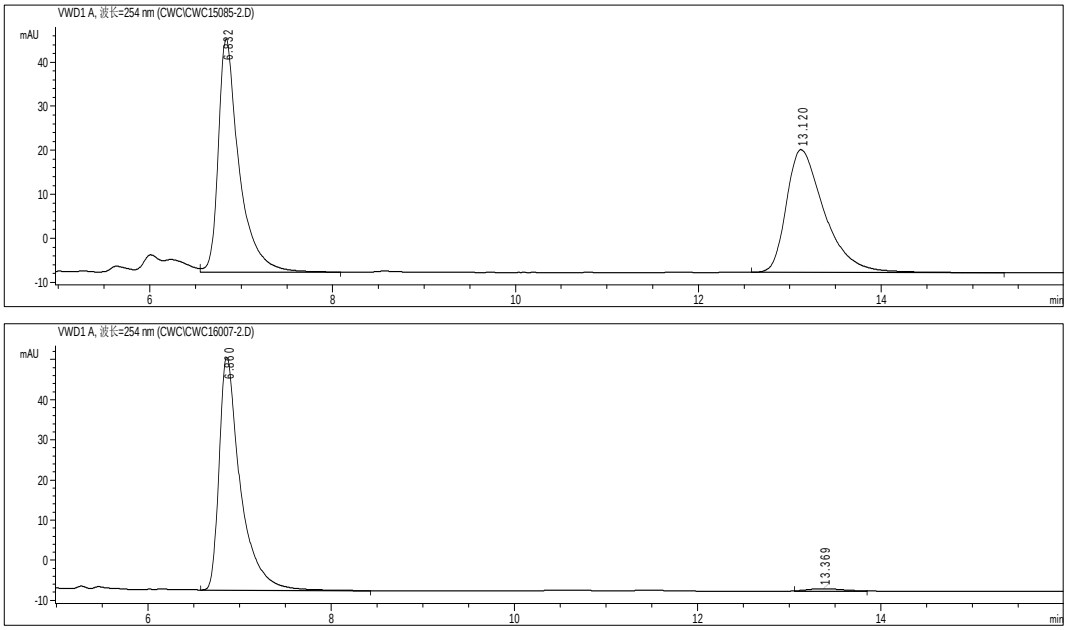


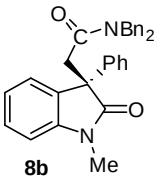


8a

White solid, Mp 164.3–164.6 °C; 62% yield; 95% ee; $[\alpha]_D^{26}$ +35.8 (*c* 0.39, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.40–7.20 (m, 18H), 7.14 (d, *J* = 7.2 Hz, 2H), 7.09 (t, *J* = 7.4 Hz, 1H), 6.95 (dd, *J* = 6.2, 3.0 Hz, 2H), 6.77 (d, *J* = 7.8 Hz, 1H), 5.17 (d, *J* = 16.0 Hz, 1H), 4.87 (d, *J* = 16.0 Hz, 1H), 4.53–4.40 (m, 4H), 3.72 (d, *J* = 16.1 Hz, 1H), 3.51 (d, *J* = 16.1 Hz, 1H).^{13}C NMR (100 MHz, $CDCl_3$) δ 178.8, 169.4, 144.2, 139.8, 136.9, 136.2, 136.2, 131.8, 129.0, 128.6, 128.6, 128.5, 128.2, 128.1, 127.7, 127.5, 127.2, 127.2, 127.1, 126.8, 126.2, 123.9, 122.0, 109.6, 53.9, 49.8, 48.1, 44.2, 41.0. HRMS (ESI) m/z 537.2537 ($M+H^+$), calc. for $C_{37}H_{33}N_2O_2$ 537.2542

The ee was determined by HPLC analysis. CHIRALCEL ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 6.9 min (major) and 13.4 min (minor).



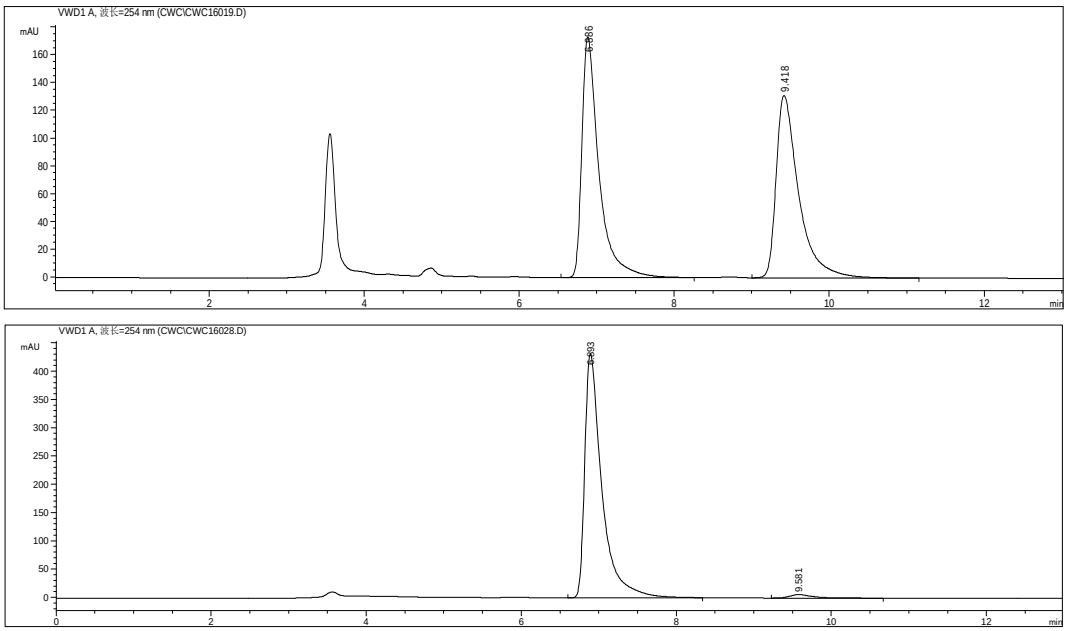


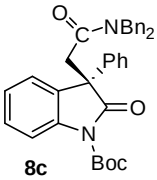
8b

White solid, Mp 239.7–240.3 °C; 88% yield; 94% ee; $[\alpha]_D^{26}$ +36.5 (*c* 0.32, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.42–7.30 (m, 6H), 7.27–7.19 (m, 7H), 7.16–7.10 (m, 3H), 6.95 (d, *J* = 7.7 Hz, 1H), 6.90 (dd, *J* = 6.3, 3.0 Hz, 2H), 4.42 (dt, *J* = 17.5, 13.1 Hz, 4H), 3.63 (d, *J* = 16.1 Hz, 1H), 3.46 (d, *J* = 16.1 Hz, 1H), 3.28 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.8, 169.5, 145.2, 139.6, 136.9, 136.2, 131.7, 129.0, 128.6, 128.5, 128.5, 128.1, 127.7, 127.5, 127.3, 126.9, 126.3, 124.1, 122.0, 108.6, 53.8, 49.9, 48.2, 41.3, 26.9, 26.8. HRMS (ESI) m/z 461.2230 ($M+H^+$), calc. for $C_{31}H_{29}N_2O_2$ 461.2229.

The ee was determined by HPLC analysis. CHIRALCEL ADH (4.6 mm i.d. x 250 mm);

Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 6.9 min (major) and 9.6 min (minor).

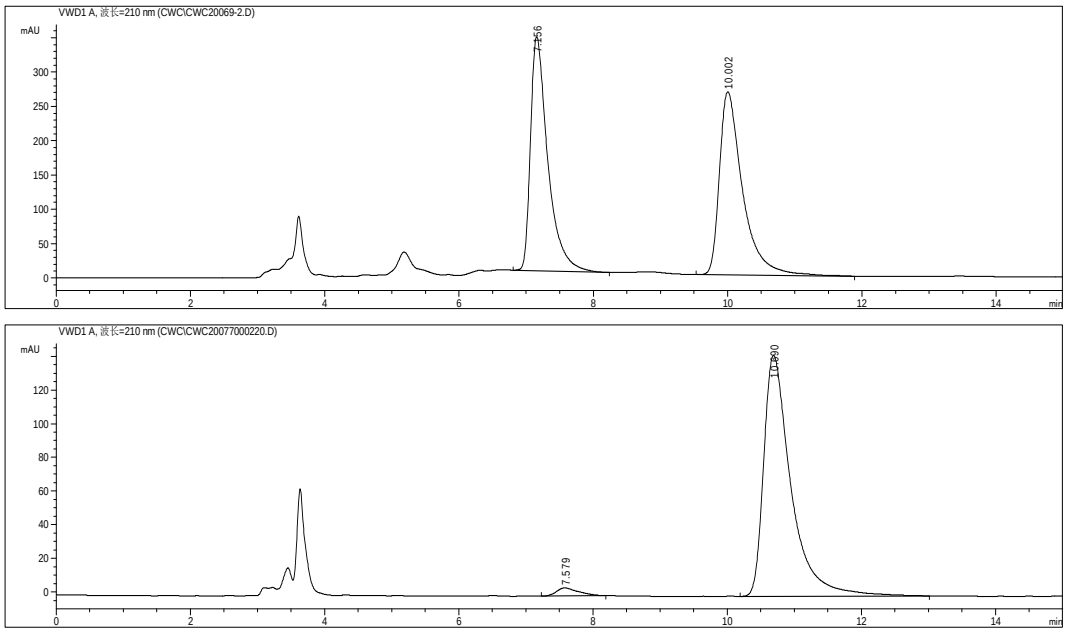




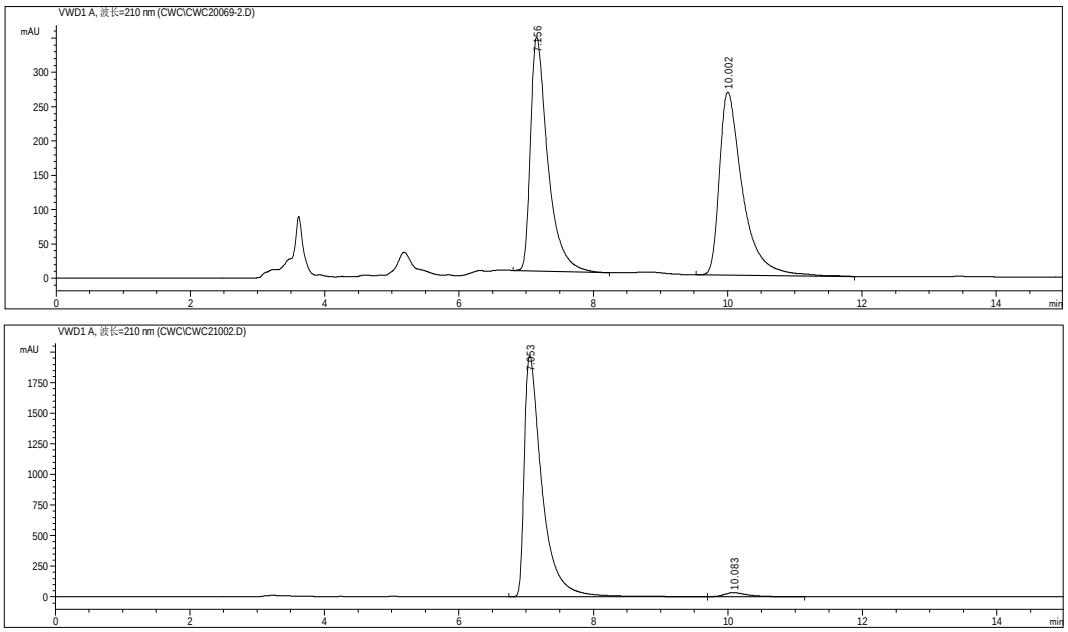
8c

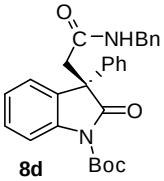
White solid, Mp 149.6–150.1 °C; 96% yield; 96% ee; $[\alpha]_D^{26}$ +28.7 (*c* 0.87, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.1 Hz, 1H), 7.45–7.32 (m, 4H), 7.30–7.26 (m, 3H), 7.26–7.22(m, 6H), 7.12 (dd, *J* = 8.6, 3.9 Hz, 3H), 6.91 (dd, *J* = 6.0, 3.4 Hz, 2H), 4.48–4.34 (m, 4H), 3.77 (d, *J* = 16.3 Hz, 1H), 3.42 (d, *J* = 16.3 Hz, 1H), 1.63 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 169.3, 149.6, 141.2, 139.1, 136.8, 136.0, 130.6, 129.1, 128.7, 128.6, 128.5, 128.1, 127.8, 127.4, 127.1, 126.3, 123.9, 123.6, 115.8, 84.0, 54.2, 49.8, 48.2, 42.3, 28.2. HRMS (ESI) m/z 547.2609 ($M+H^+$), calc. for $C_{35}H_{35}N_2O_4$ 547.2597.

The ee was determined by HPLC analysis. CHIRALCEL ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 7.6 min (minor) and 10.1 min (major).



***Ent*-8c**: 95% ee, CHIRALCEL ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 7.6 min (major) and 10.1 min (minor).

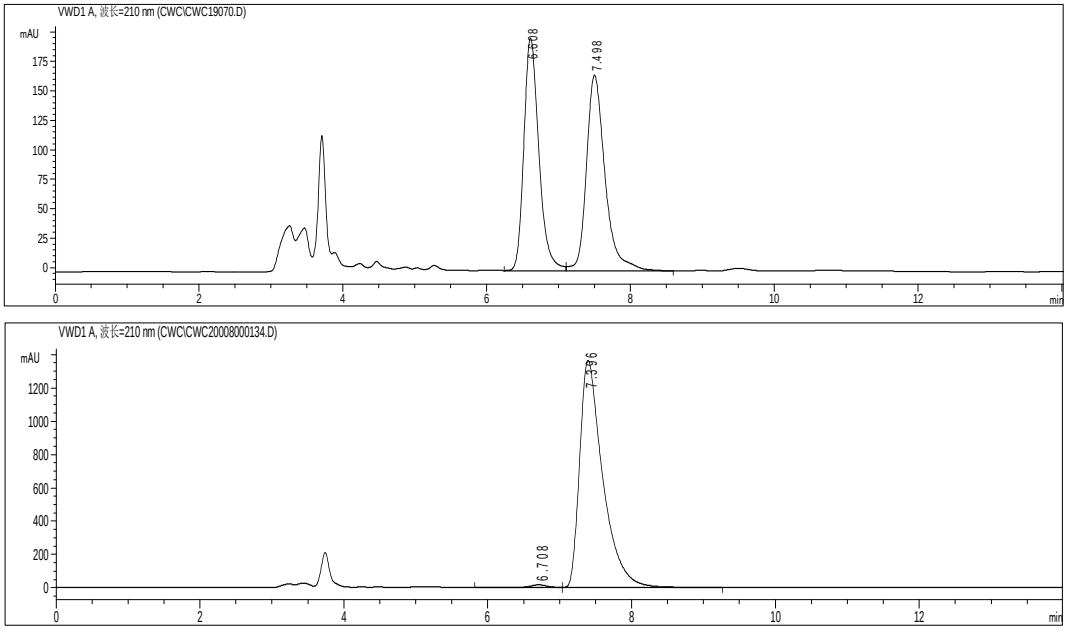




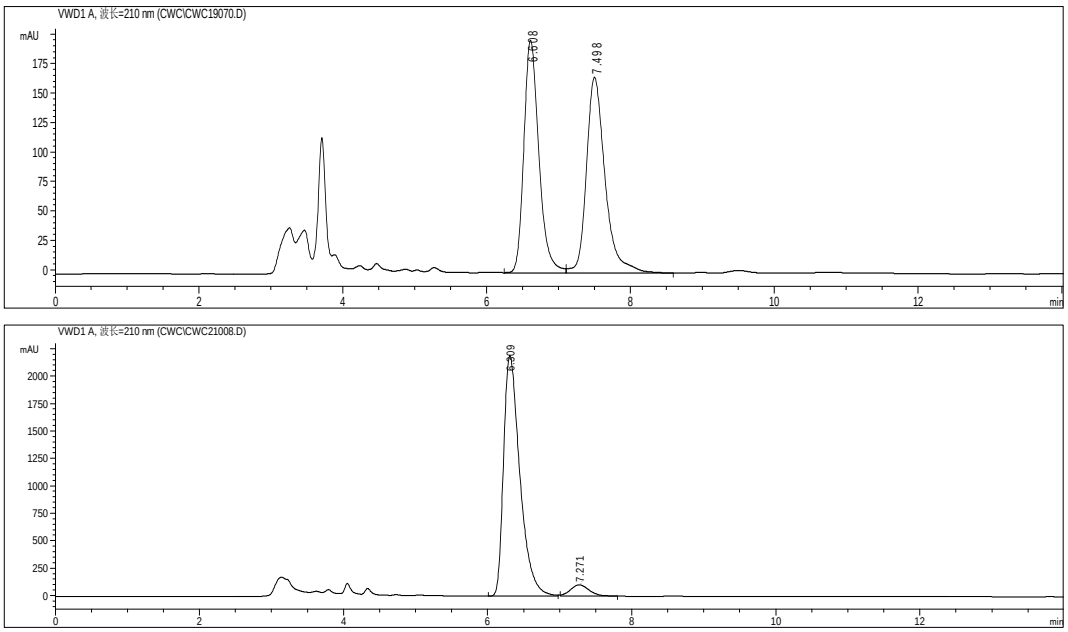
8d

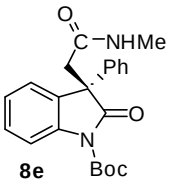
Colorless oil, 66% yield; 92% ee; $[\alpha]_D^{26}$ +97.3 (*c* 0.69, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.1 Hz, 1H), 7.41–7.37 (m, 1H), 7.30–7.28 (m, 4H), 7.20–7.20 (m, 4H), 6.92 (dd, *J* = 6.5, 2.9 Hz, 2H), 5.93 (s, 1H), 4.29 (d, *J* = 6.2 Hz, 1H), 4.18 (d, *J* = 5.4 Hz, 1H), 3.64 (d, *J* = 15.0 Hz, 1H), 3.04 (d, *J* = 15.0 Hz, 1H), 1.60 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 168.2, 149.3, 140.3, 139.1, 137.9, 129.8, 128.9, 128.6, 127.9, 127.6, 127.4, 126.8, 124.4, 124.4, 115.6, 84.4, 54.4, 44.8, 43.4, 28.1. HRMS (ESI) m/z 457.2123 ($M+H^+$), calc. for $C_{28}H_{29}N_2O_4$ 457.2127.

The ee was determined by HPLC analysis. CHIRALCEL ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 6.7 min (minor) and 7.4 min (major).



***Ent*-8d**: 98% ee, CHIRALCEL ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 6.3 min (major) and 7.3 min (minor).

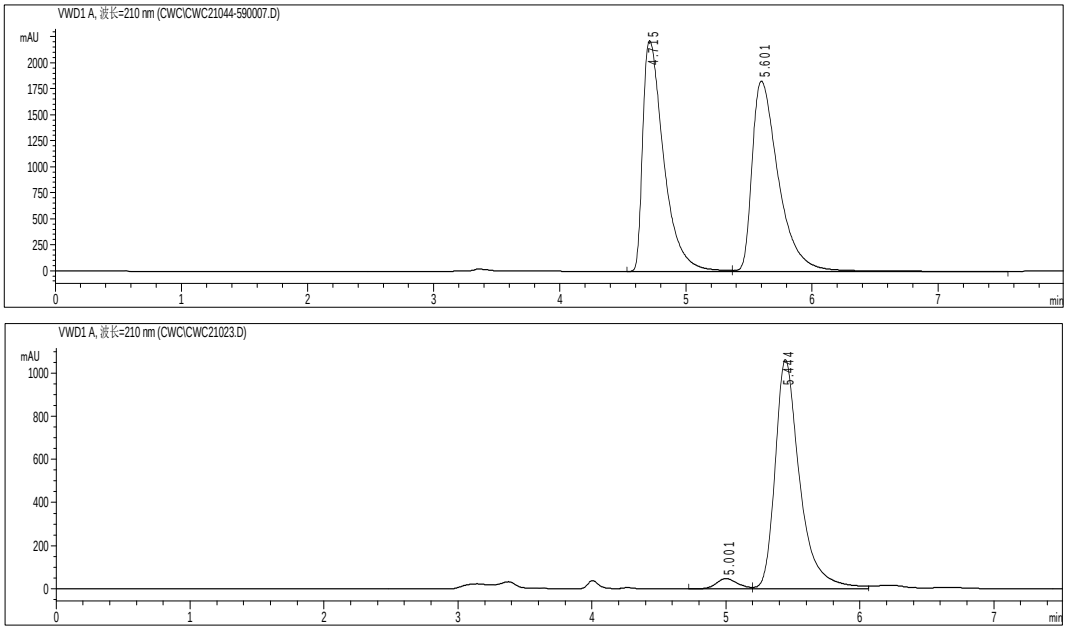




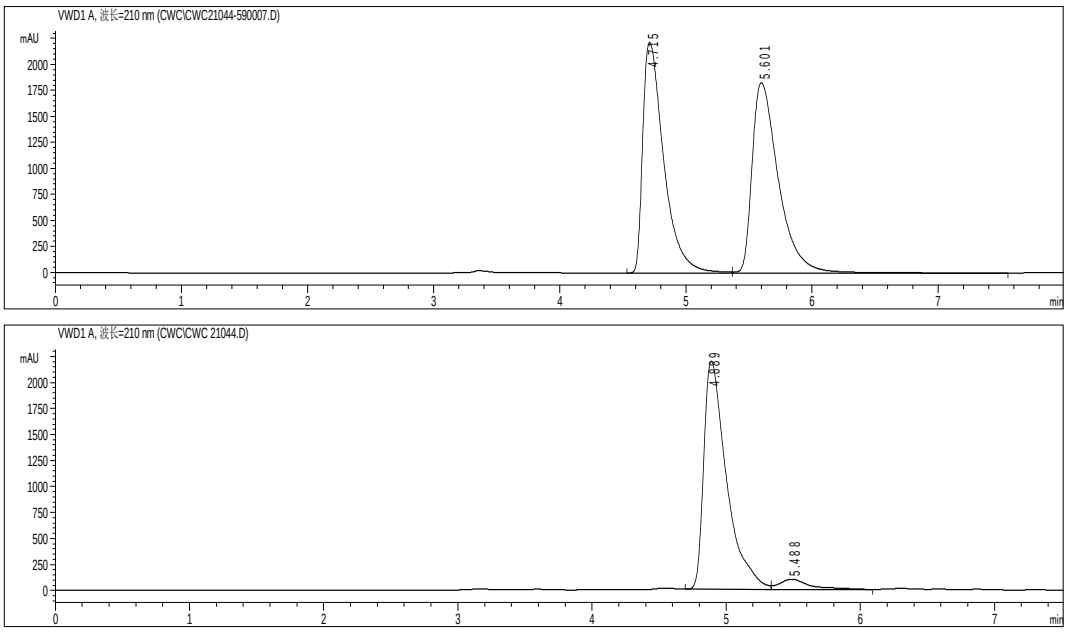
8e

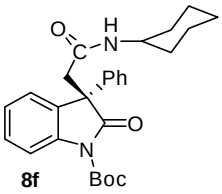
White solid, Mp 115.1–115.9 °C; 93% yield; 93% ee; $[\alpha]_D^{26}$ +78.4 (*c* 0.75, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.2 Hz, 1H), 7.35–7.31 (m, 1H), 7.27–7.21 (m, 4H), 7.17 (td, *J* = 7.4, 0.8 Hz, 1H), 5.61 (s, 1H), 3.54 (d, *J* = 15.2 Hz, 1H), 3.02 (d, *J* = 15.2 Hz, 1H), 2.58 (d, *J* = 4.8 Hz, 3H), 1.59 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9, 168.9, 149.3, 140.3, 139.1, 130.1, 128.8, 128.7, 127.8, 126.8, 124.2, 124.1, 115.6, 84.3, 54.2, 44.5, 28.1, 26.3. HRMS (ESI) m/z 381.1823 ($M+H^+$), calc. for $C_{22}H_{25}N_2O_4$ 381.1814.

The ee was determined by HPLC analysis. CHIRALCEL ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 5.0 min (minor) and 5.4 min (major).



***Ent*-8e**: 90% ee, CHIRALCEL ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 4.9 min (major) and 5.5 min (minor).

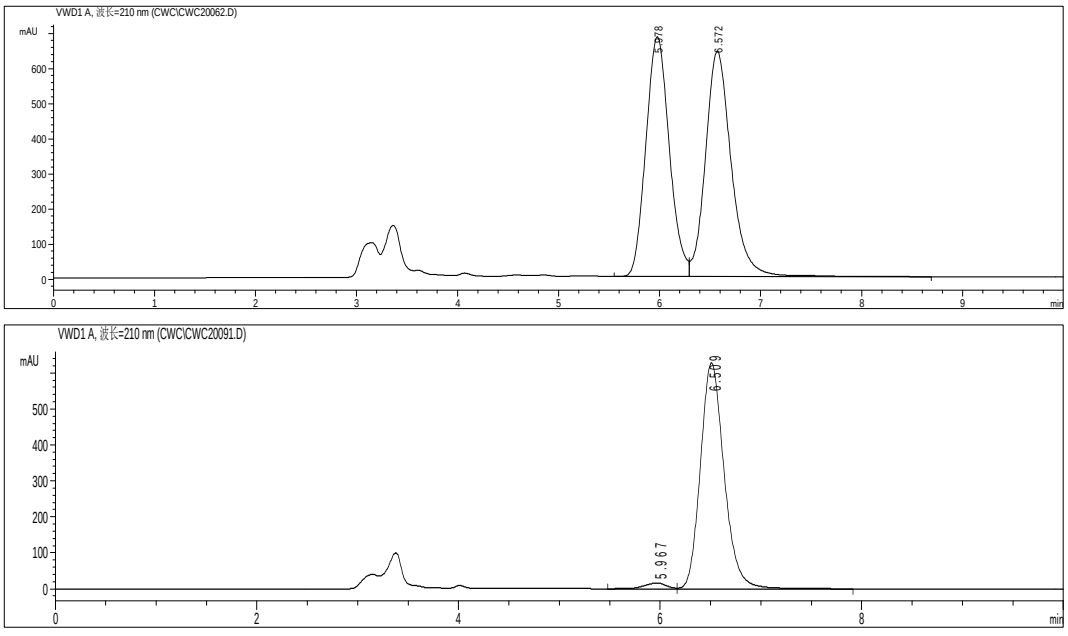




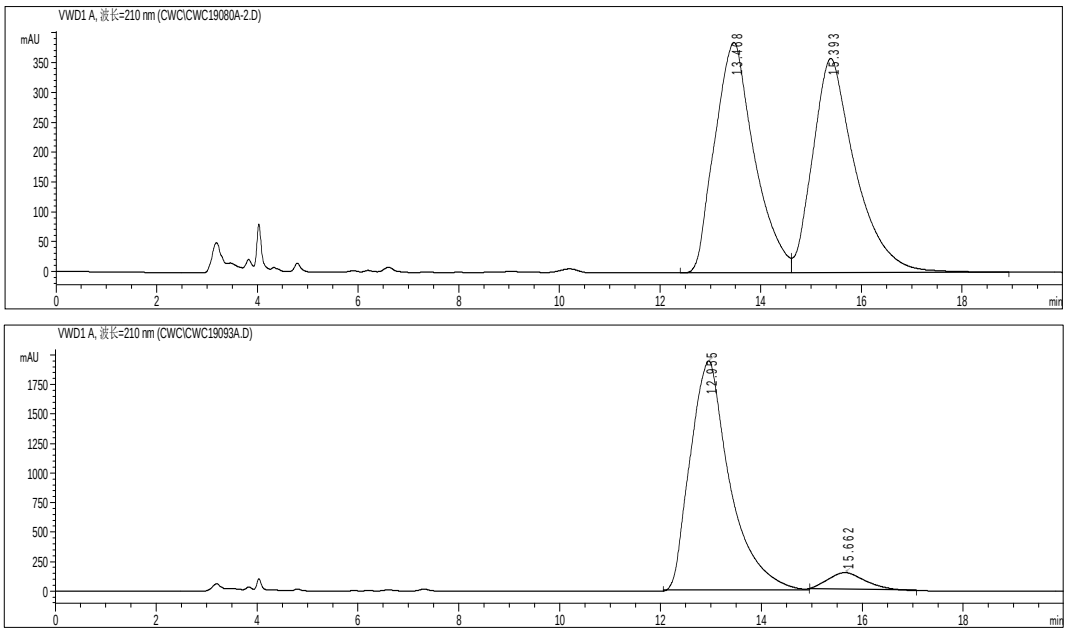
8f

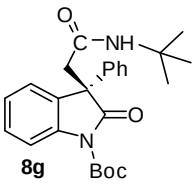
White solid, Mp 164.1–164.4 °C; 91% yield; 95% ee; $[\alpha]_D^{26}$ +103.6 (*c* 0.59, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.1 Hz, 1H), 7.32 (dd, *J* = 11.4, 4.1 Hz, 1H), 7.27–7.22 (m, 5H), 7.18 (t, *J* = 7.5 Hz, 1H), 5.43 (d, *J* = 8.9 Hz, 1H), 3.48 (d, *J* = 14.4 Hz, 1H), 2.94 (d, *J* = 14.4 Hz, 1H), 1.68–1.49 (m, 4H) , 1.60 (s, 9H), 1.25–0.78 (m, 7H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 167.1, 149.2, 140.1, 139.2, 129.8, 128.8, 127.8, 126.8, 124.6, 124.4, 115.4, 84.3, 54.6, 47.9, 45.0, 32.8, 32.8, 28.1, 25.4, 24.6. HRMS (ESI) m/z 449.2437 ($M+H^+$), calc. for $C_{27}H_{33}N_2O_4$ 449.2440.

The ee was determined by HPLC analysis. CHIRALCEL ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 6.0 min (minor) and 6.5 min (major).



***ent*-8f**: 91% ee, CHIRALCEL ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 90/10; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 13.0 min (major) and 15.7 min (minor).

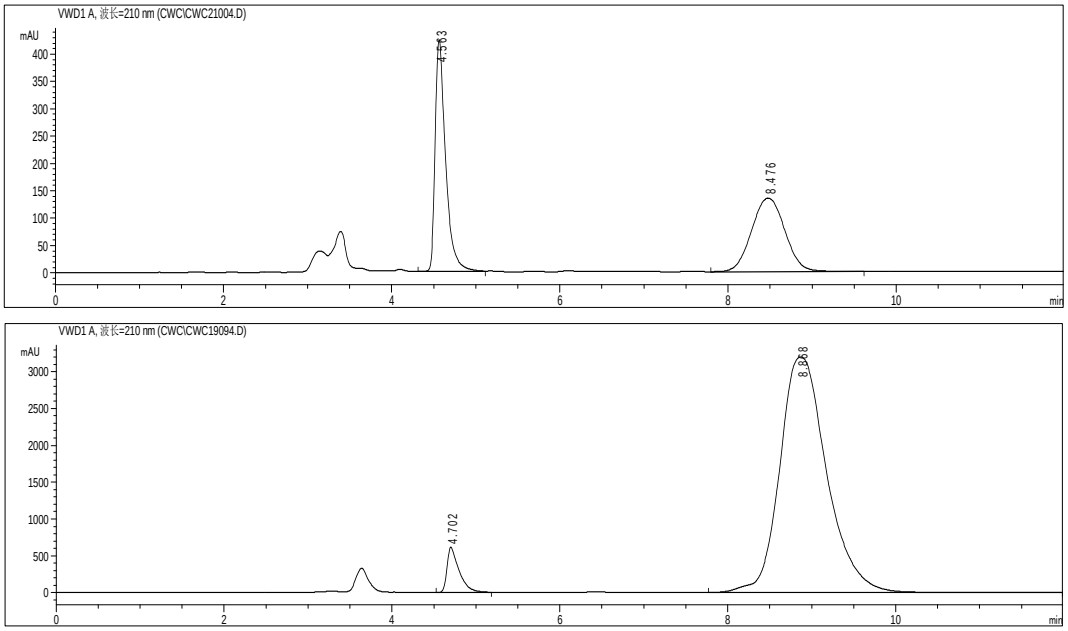




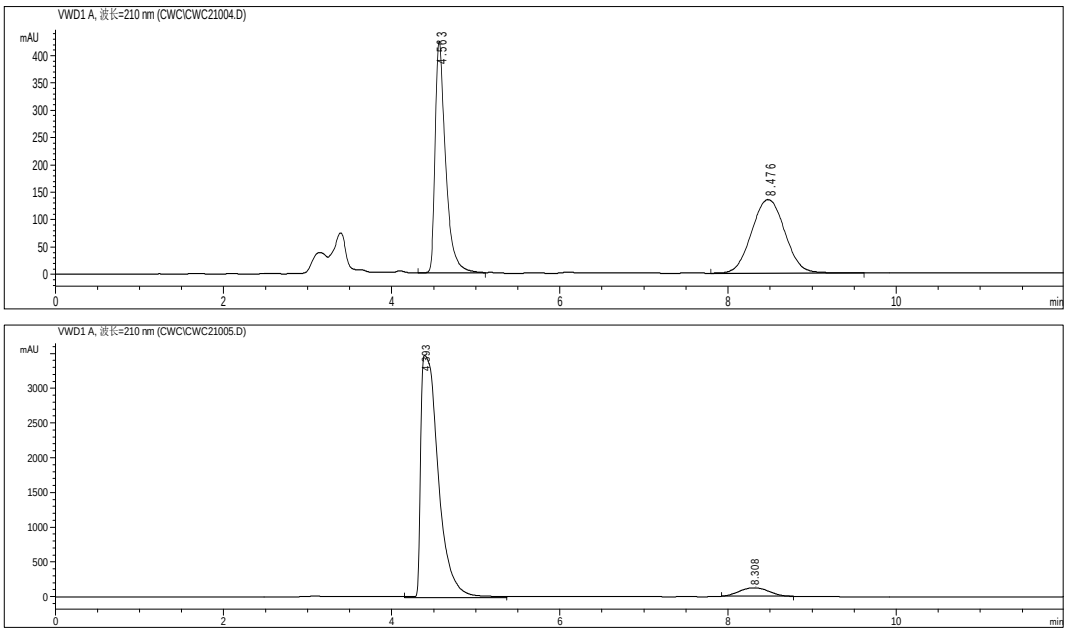
8g

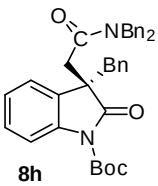
Colorless oil, 86% yield; 90% ee; $[\alpha]_D^{26}$ +167.4 (*c* 0.56, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.2 Hz, 1H), 7.38–7.33 (m, 1H), 7.30–7.27 (m, 5H), 7.24–7.20 (m, 1H),5.39 (s, 1H), 3.42 (d, *J* = 14.1 Hz, 1H), 2.90 (d, *J* = 14.1 Hz, 1H), 1.62 (s, 9H), 1.06 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 167.3, 149.2, 140.0, 139.1, 129.7, 128.7, 127.8, 126.8, 124.8, 124.4, 115.3, 84.4, 54.8, 51.0, 46.1, 28.3, 28.1. HRMS (ESI) m/z 423.2287 ($M+H^+$), calc. for $C_{25}H_{31}N_2O_4$ 423.2284.

The ee was determined by HPLC analysis. CHIRALCEL ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 4.7 min (major) and 8.9 min (minor).



***Ent*-8g**: 91% ee, CHIRALCEL ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 4.5 min (major) and 8.3 min (minor).

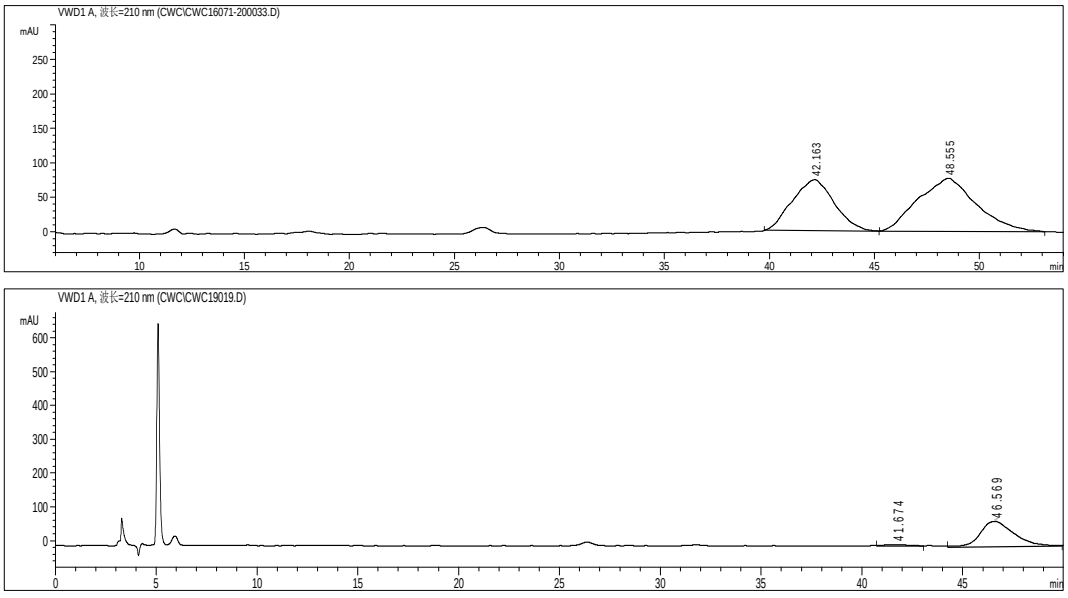


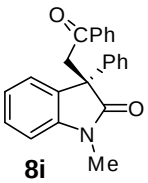


8h

Colorless oil, 90% yield; 93% ee; $[\alpha]_D^{26}$ +99.2 (*c* 0.38, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.0 Hz, 1H), 7.42–7.32 (m, 3H), 7.24–7.20 (m, 4H), 7.13–7.02 (m, 6H), 6.93–6.91 (m, 2H), 6.84 (d, *J* = 7.4 Hz, 1H), 6.72 (d, *J* = 7.2 Hz, 2H), 4.48–4.37 (m, 4H), 3.33 (d, *J* = 16.3 Hz, 1H), 3.16 (d, *J* = 16.3 Hz, 1H), 3.03 (d, *J* = 12.6 Hz, 1H), 2.92 (d, *J* = 12.6 Hz, 1H), 1.56 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.1, 169.3, 148.9, 140.7, 136.8, 136.3, 134.3, 130.2, 130.1, 129.1, 128.5, 128.1, 128.1, 127.8, 127.6, 127.3, 126.9, 126.4, 123.4, 122.0, 115.3, 83.4, 52.4, 50.0, 48.4, 45.5, 40.3, 28.1. HRMS (ESI) m/z 561.2748 ($M+H^+$), calc. for $C_{36}H_{37}N_2O_4$ 561.2753.

The ee was determined by HPLC analysis. CHIRALCEL ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 97/03; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 41.7 min (minor) and 46.6 min (major).

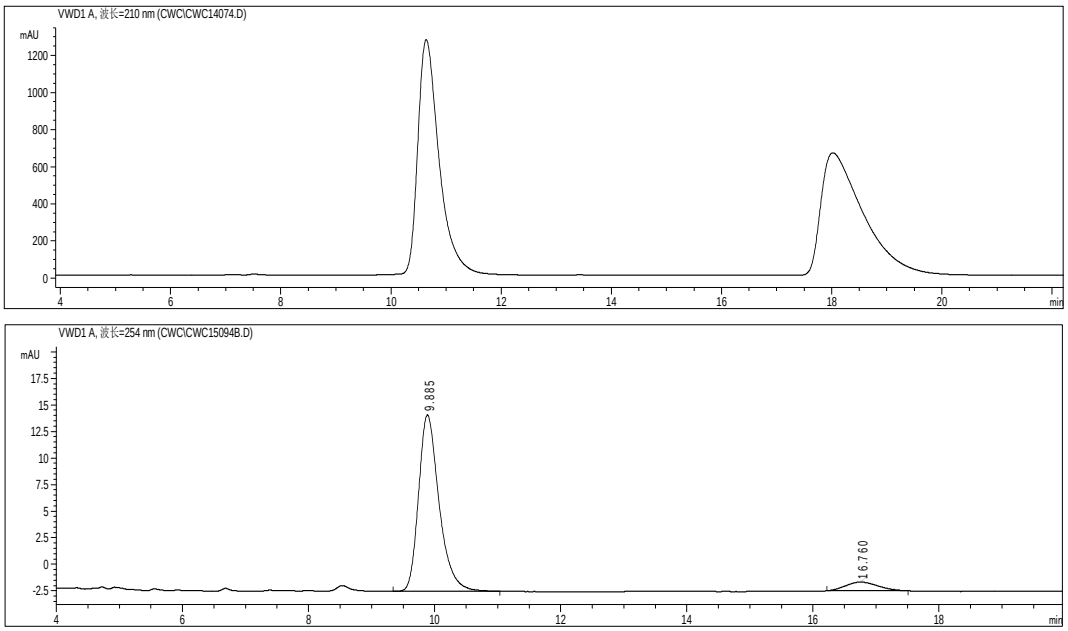




8i

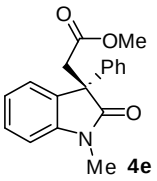
White solid, Mp 181.0–181.6 °C; 75% yield; 87% ee; $[\alpha]_D^{26}$ –229.8 (*c* 0.36, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.55–7.50 (m, 1H), 7.46–7.38 (m, 4H), 7.35–7.25(m, 5H), 7.05 (td, *J* = 7.6, 1.0 Hz, 1H), 6.95 (d, *J* = 7.7 Hz, 1H), 4.13 (q, *J* = 18.0 Hz, 2H), 3.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.8, 178.6, 144.8, 139.6, 136.4, 133.3, 131.6, 128.7, 128.6, 128.4, 128.0, 127.6, 126.8, 124.1, 122.2, 108.5, 53.1, 47.0, 26.8. HRMS (ESI) m/z 342.1486 ($M+H^+$), calc. for $C_{23}H_{20}NO_2$ 342.1494.

The ee was determined by HPLC analysis. CHIRALCEL ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 9.9 min (major) and 16.8 min (minor).



8. Determination of the Absolution Configuration of Alkylation Adducts

Absolute configurations of **4a-v**, **6a-j**, **8a-i**, **9-13** are determined by the comparation of the optical rotations of **4e** with the reported result.[1]



4e

Reported: 76% ee, $[\alpha]_D^{26}$ – 81.8 (*c* 0.64, $CHCl_3$), *R* configuration

4e: 94% ee, $[\alpha]_D^{26}$ –92.4 (*c* 0.28, $CHCl_3$). In this context, the absolute configuration of the above-mentioned compounds is designated as *R*.

Reference:

1. Ma, S.; Han, X.; Krishnan, S.; Virgil, S. C.; Stoltz B. M. *Angew. Chem. Int. Ed.* **2009**, *48*, 8037.

9. Mechanism Investigations

First, we treated guanidinium **1** using solid K_2HPO_4, solid K_2CO_3 and NaOH (2.0 *N*, aqueous) individually, to produce the corresponding products as **1'**, **1''** and **1'''**.[1] The ^{1}H NMR spectra shown that the chemical shifts of H^a (**1**) and H^b (1') are identical (around 8.1 ppm), but both of H^c (**1''**) and H^d (**1'''**) have obvious shifts to high-fields (Figure 1). We have previously shown that bicyclic guanidiniums can be basified using solid K_2CO_3 to generate the corresponding guanidines.[1-2] In this context, we suggested that guanidinium **1** can be basified by the strong bases such as solid K_2CO_3 and NaOH (2.0 *N*, aq.); however, solid K_2HPO_4 as the mild base is not able to do that, and **1'** should precisely be guanidinium **1**.

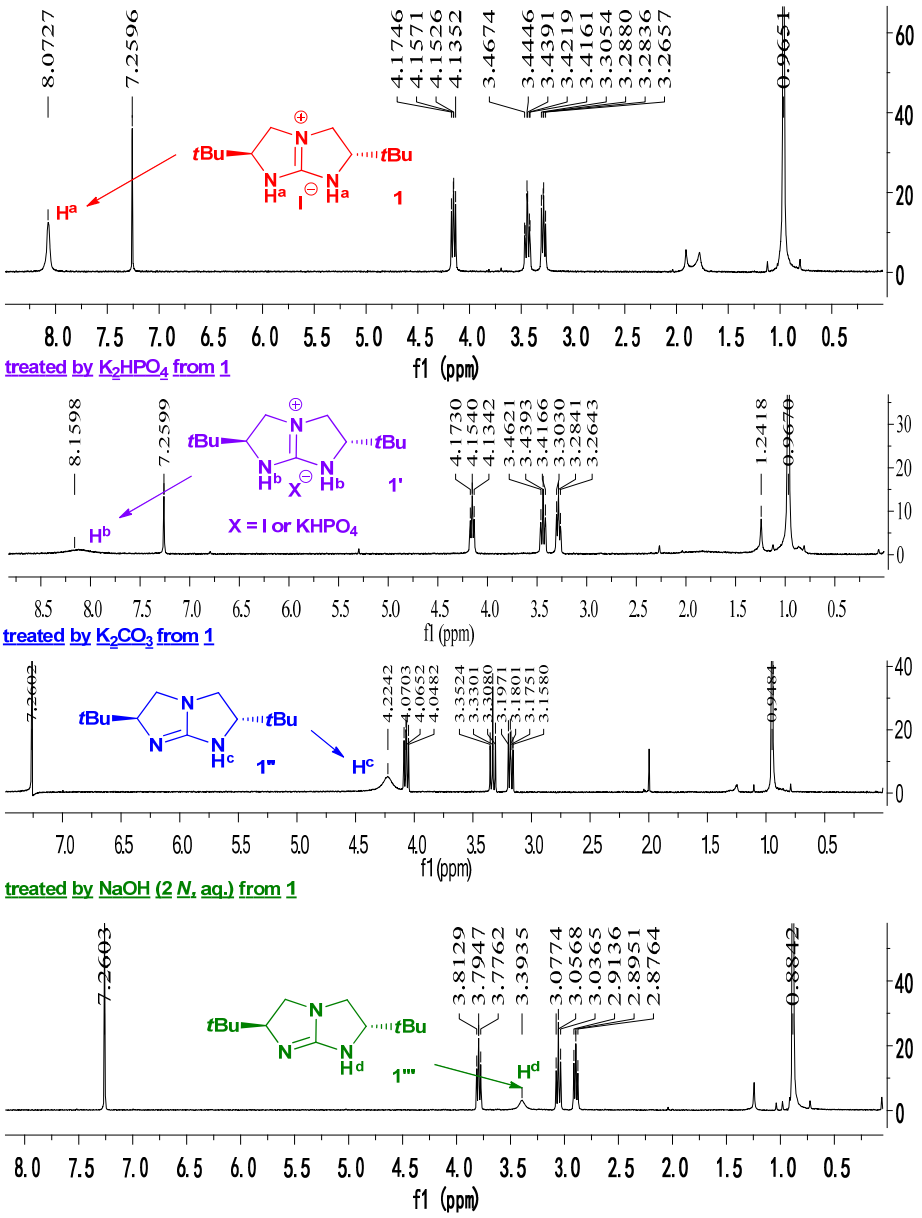


Figure 1. ^{1}H NMR Spectra of **1**, **1'**, **1''** and **1'''**

Next, we investigated the alkylation of *N*-benzyl-3-phenyl-2-oxindole **2a** to methyl bromoacetate **3b** without the catalyst **1** (Figure 2, eqn. 1); no reaction occurred under the conditions, indicating that K_2HPO_4 cannot make the reaction work when without **1**. The alkylation also did not proceed by using **1** or **1'** as the

promoter in the absence of K_2HPO_4 (Figure 2, eqn. 2–3). Guanidine **1”** could make the reaction work smoothly, affording the adduct **4b** in 83% yield and with 87% *ee* after 72 hours (Figure 2, eqn. 4). Meanwhile, guanidine **1”’** gave adduct at a slower reaction with slight decreased in enantioselectivity (eqn. 5). Guanidine **1”** and **1”’** have slightly different chemical shifts of ^{1}H NMR spectra and catalytic activities; this might be caused by their different interactions with H_2O, which could be demonstrated by the ORTEP diagram of guanidinium **1** from X-ray analysis (Figure 3).[3] Therefore, we rationalized that in the presence of a weak base, guanidinium **1** acts as a PTC (eqn. 6). On the other hand, when strong bases were utilized, guanidinium should play a role of guanidine as a base generated *in situ* (eqn. 7).

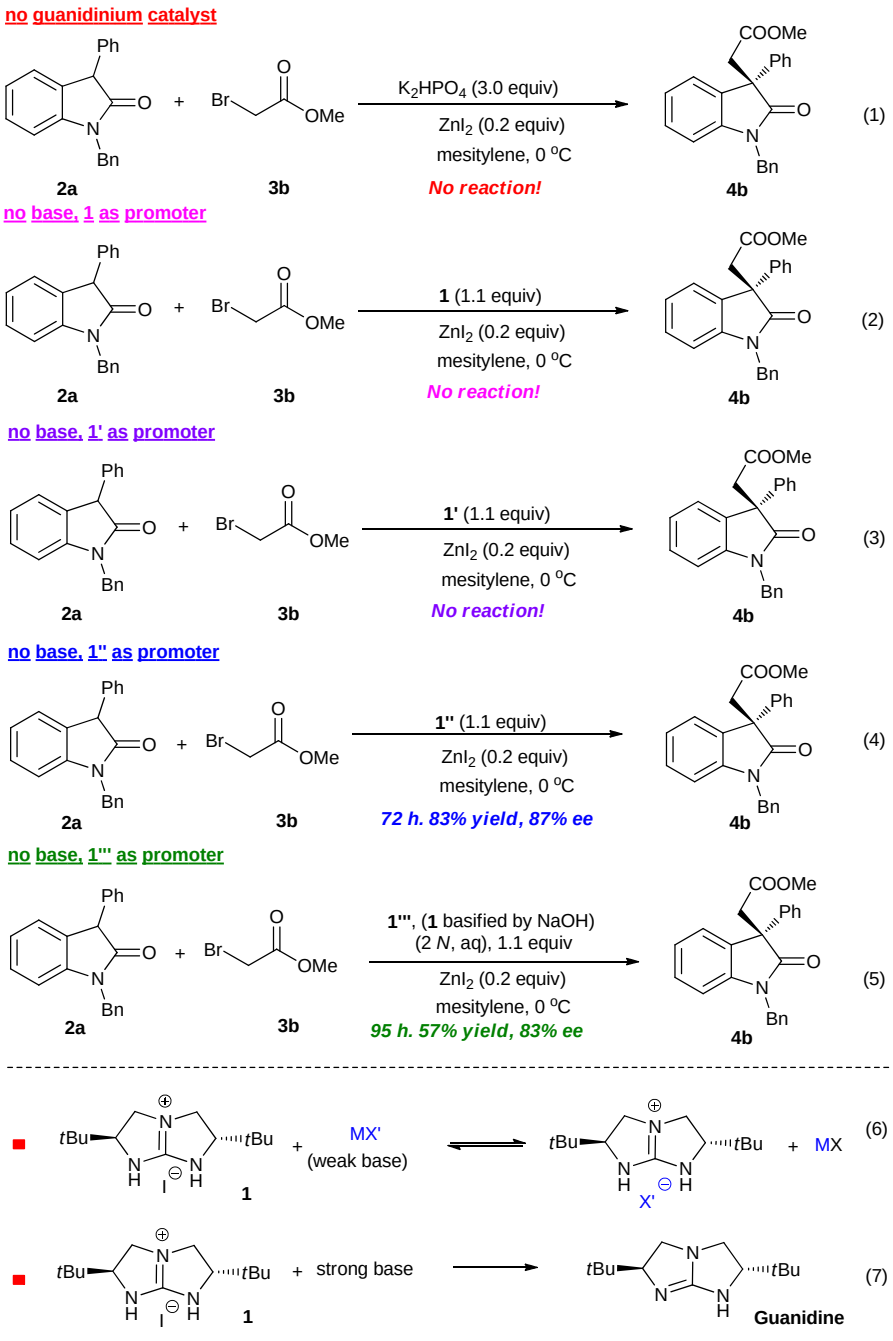


Figure 2. An investigation of the reaction mechanism.

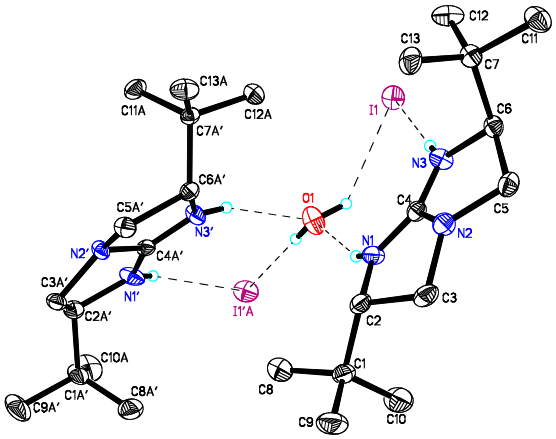
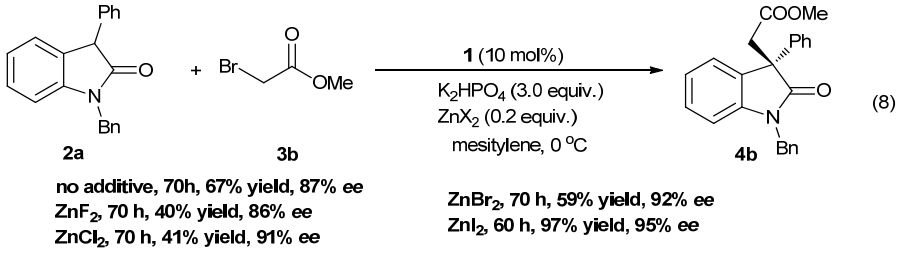


Figure 3. ORTEP diagram of guanidinium 1 from the X-ray analysis (CCDC-937953).



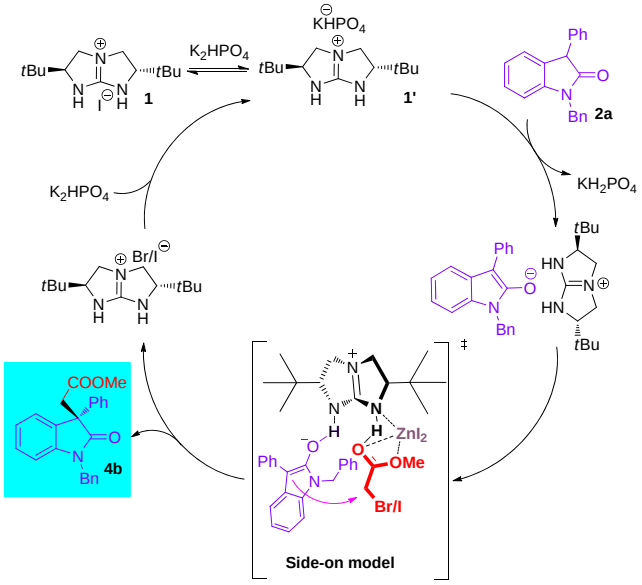
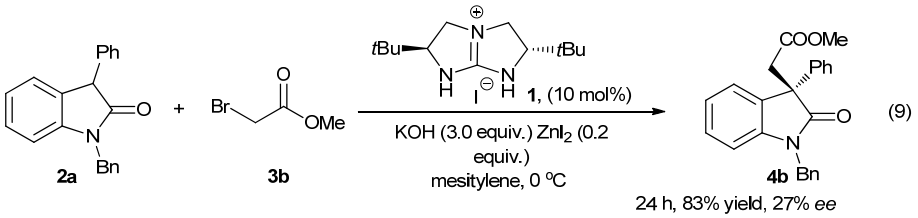


Figure 4. Plausible reaction mechanism and side-on transition state.

Subsequently, the effects of various zinc halides as additives was examined (eqn. 8) and the results showed that ZnF_2 and $ZnCl_2$ decreased reaction rates. It might be due to their stronger acidity that diminishes the deprotonation rate of the reaction. The best results were still obtained by using ZnI_2 as additive. We suggested that a halide-exchange between ZnI_2 and methyl bromoacetate could enhance the reaction rate, and a cooperative catalysis between guanidinium and ZnI_2 occurred which enhanced the enantioselectivity. Collectively, a phase-transfer mechanism and a plausible side-on transition state (TS)[2c,4]

are thus proposed for this reaction (Figure 4).



The reaction of **2a** and **3b** by utilizing 3.0 equivalent of KOH as inorganic strong base was also performed under the established conditions (eqn. 9). The results indicated that the background reaction was existing promoted by KOH, leading to the poor enantioselectivity.

References:

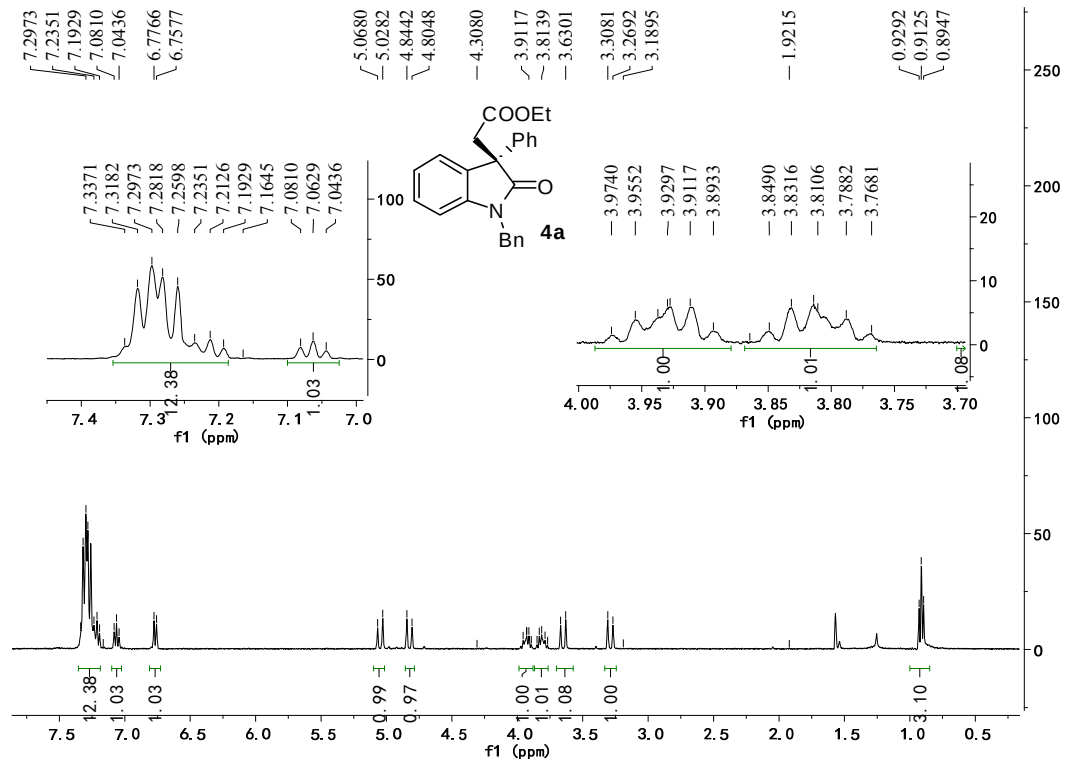
1. The procedure is according to the reference: W. Ye, J. Xu, C.-T. Tan, C.-H. Tan, *Tetrahedron Lett.* **2005**, *46*, 6875.

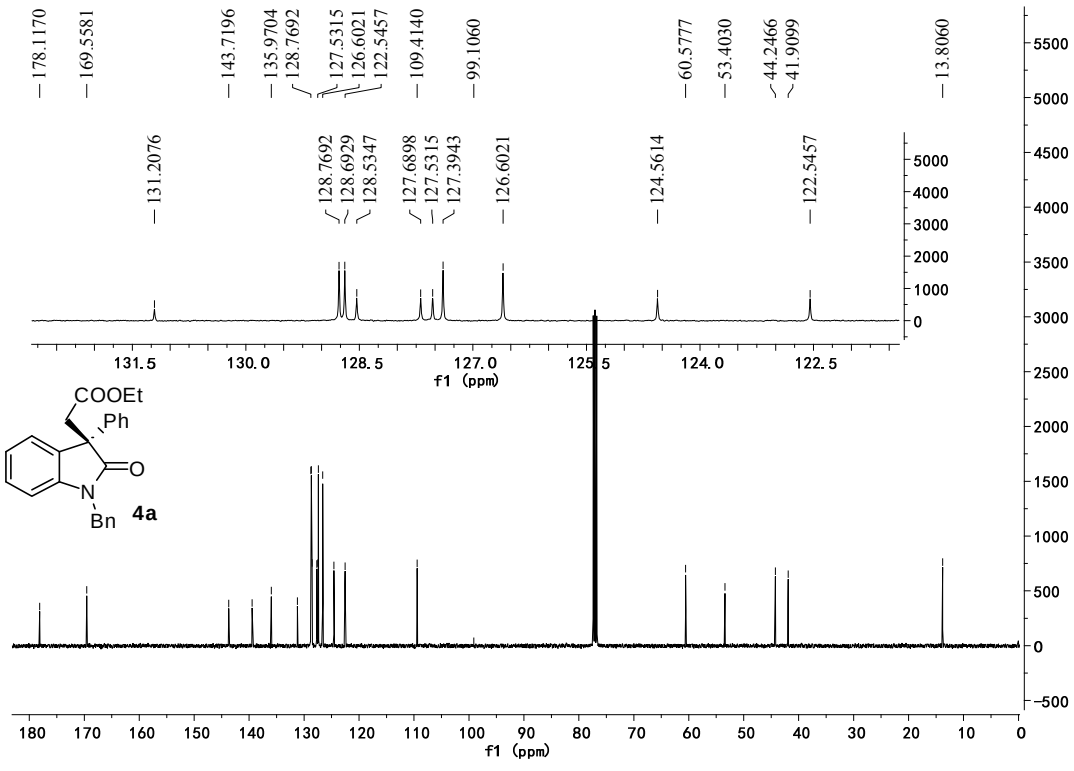
2. For selected our contributions on the development of chiral bicylic guanidine **1**, see: (*a*) J. Shen, T. T. Nguyen, Y.-P. Goh, W. P. Ye, X. Fu, J. Y. Xu, C.-H. Tan, *J. Am. Chem. Soc.* 2006, **128**, 13692; (*b*) D. S. Leow, S. S. Lin, S. K. Chittimalla, X. Fu, C.-H. Tan, *Angew. Chem. Int. Ed.* 2008, **47**, 5641; (*c*) Z. Jiang, Y. Pan, Y. Zhao, T. Ma, R. Lee, Y. Yang, K.-W. Huang, M. W. Wong, C.-H. Tan, *Angew. Chem. Int. Ed.* 2009, **48**, 3627; (*d*) H. Liu, D. Leow, K.-W. Huang, C.-H. Tan, *J. Am. Chem. Soc.* 2009, **131**, 7212; (*e*) J. Wang, J. Chen, C. W. Kee, C.-H. Tan, *Angew. Chem. Int. Ed.* 2012, **51**, 2382. (*f*) L. Li, W. Chen, W. Yang, Y. Pan, H. Liu, C.-H. Tan, Z. Jiang, *Chem. Commun.* 2012, **48**, 5124.

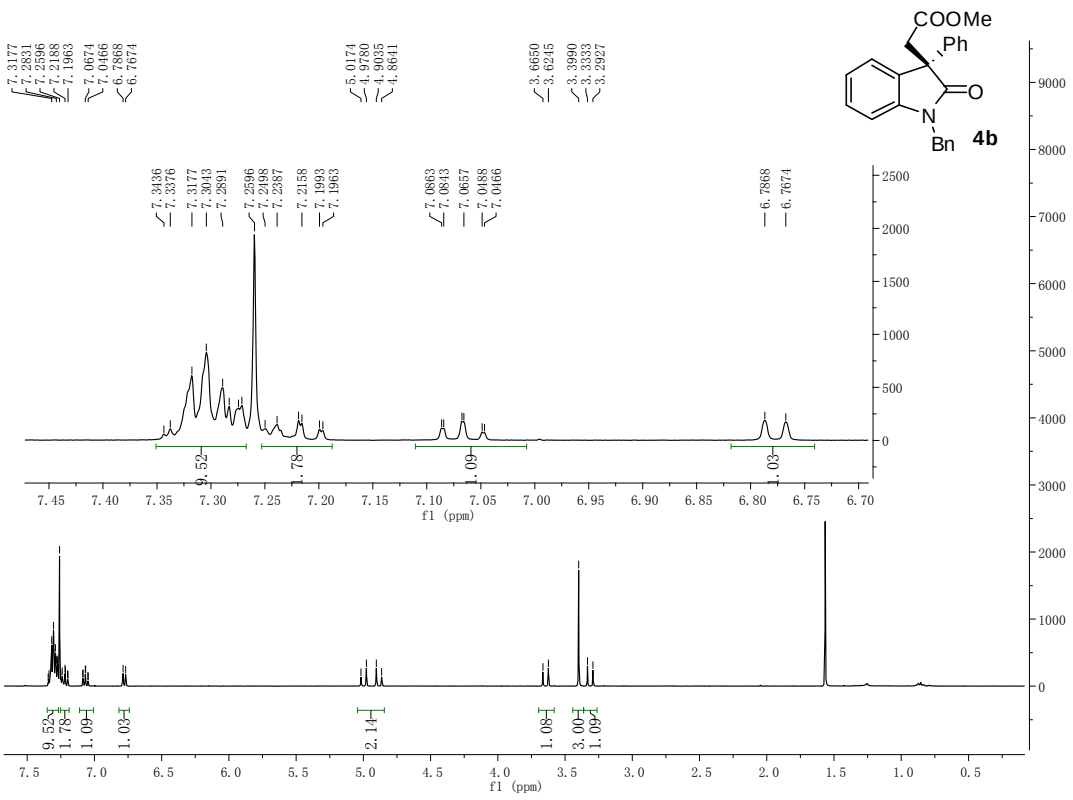
3. CCDC-937953 (**1**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

4. R. Lee, X. Lim, T. Chen, G. K. Tan, C.-H. Tan, K.-W. Huang, *Tetrahedron Lett.* 2009, **50**, 1560.

10. Copies of NMR spectra






COOMe
Ph
O
N
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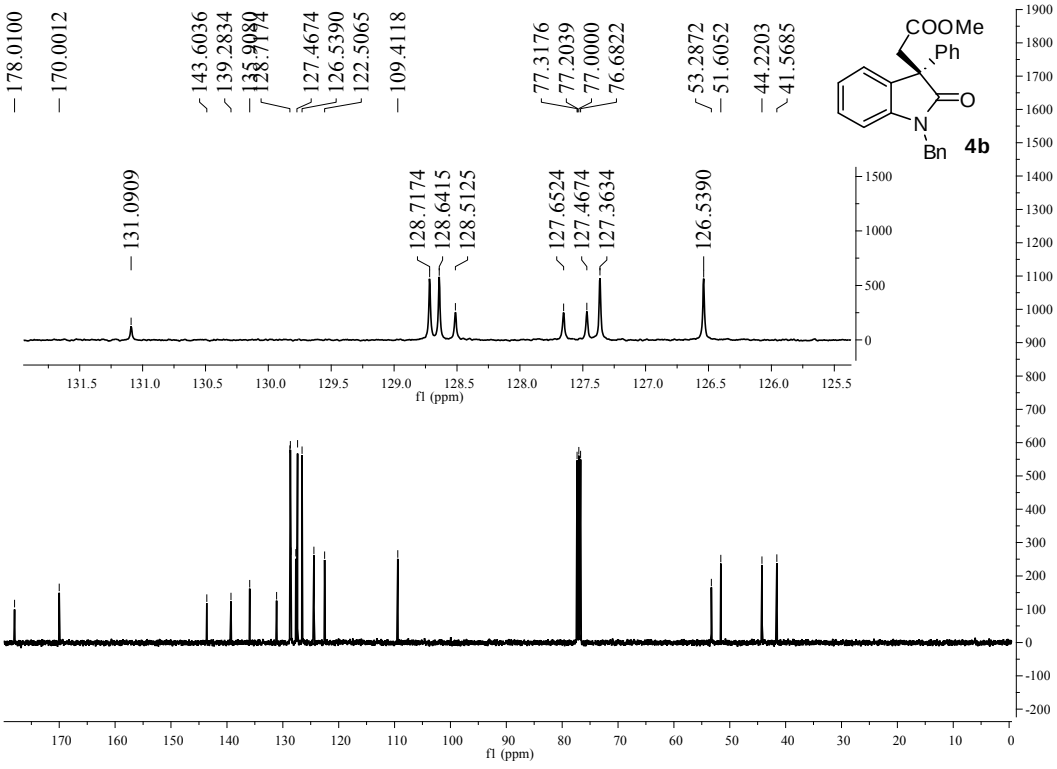
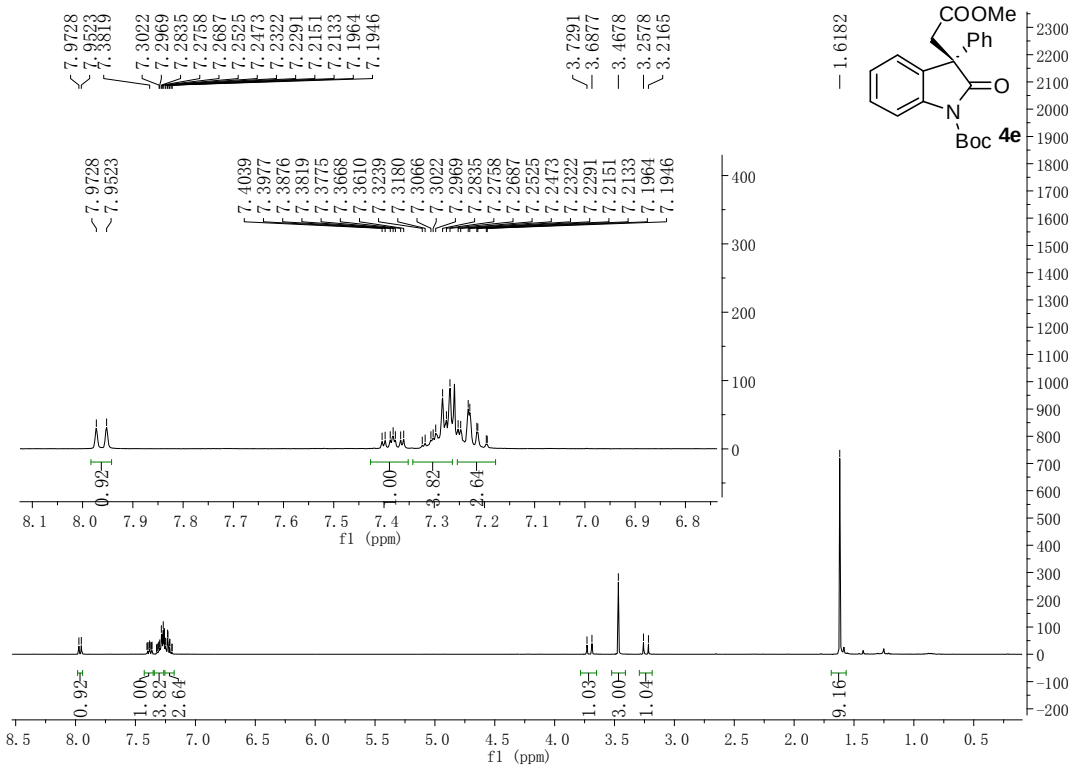
4b
f1 (ppm)


COOMe
Ph
O
N
Bn
4b
f1 (ppm)


7.9728
7.9523
7.3819
7.3022
7.2969
7.2835
7.2758
7.2687
7.2525
7.2473
7.2322
7.2291
7.2151
7.2133
7.1964
7.1946
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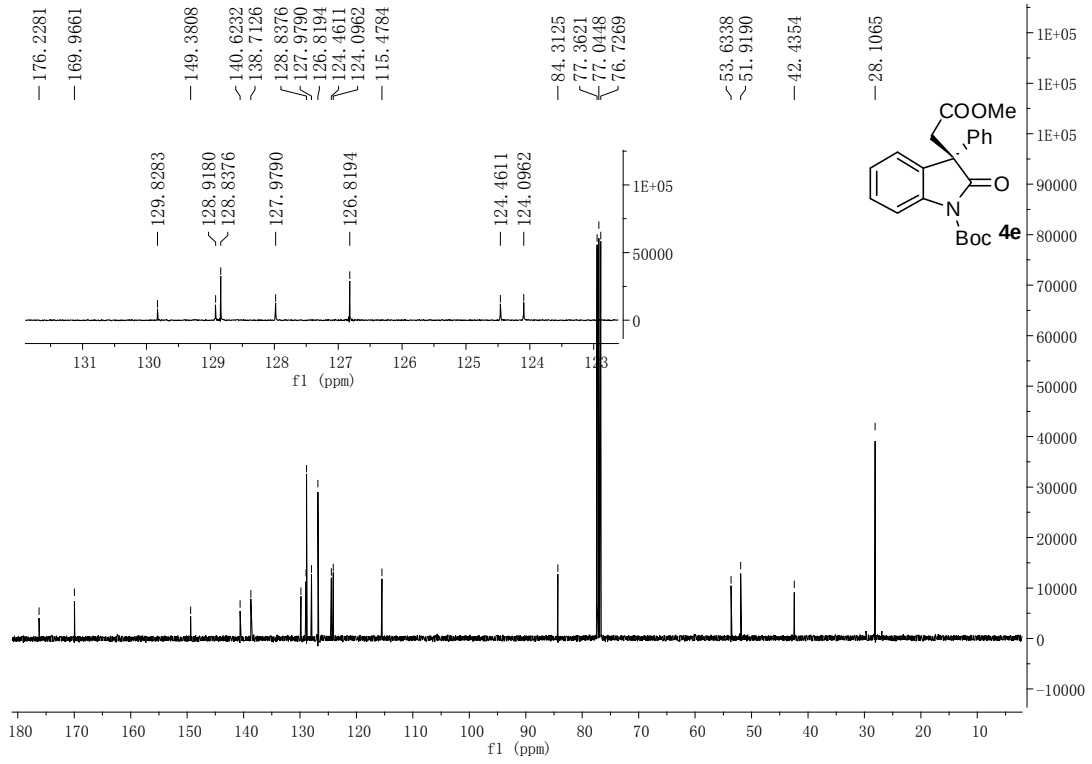
Ph
O
N
Boc
4e
f1 (ppm)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128.9180
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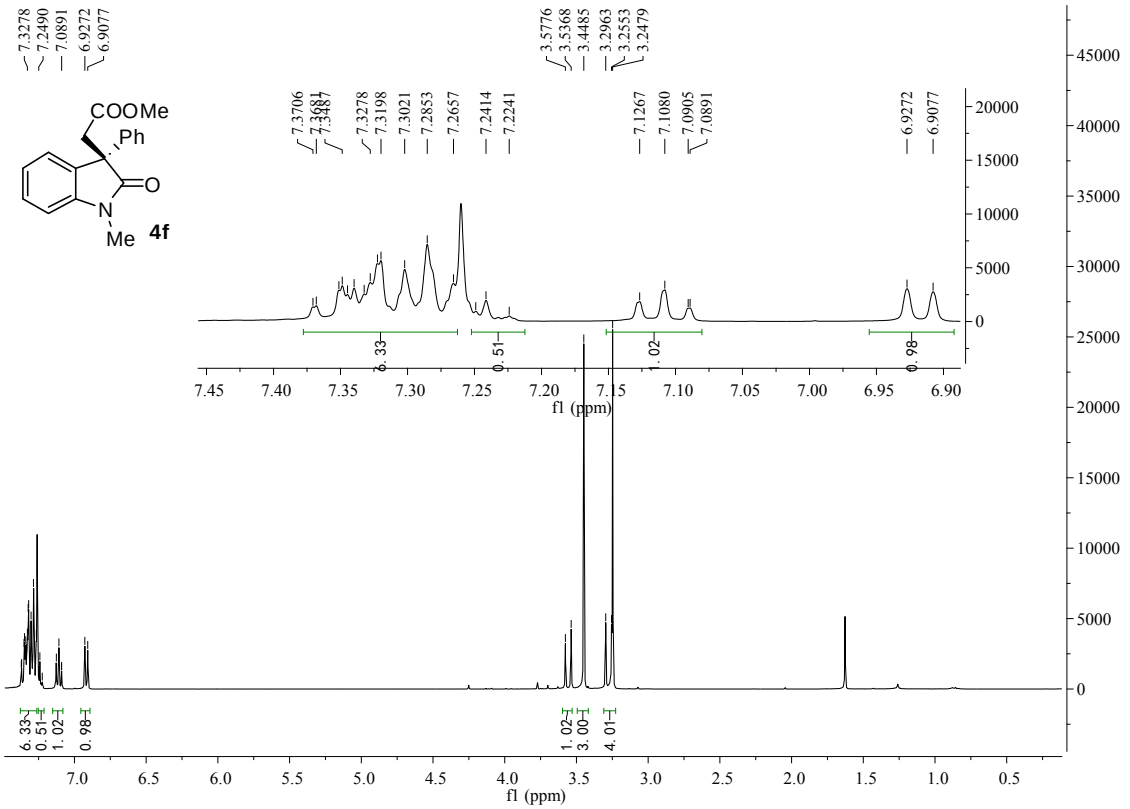
124.0962
COOMe
Ph
O
N
Boc
4e
f1 (ppm)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3.2479
COOMe
Ph
O
N
Me
4f
7.3706
7.3681
7.3487
7.3278
7.3198
7.3021
7.2853
7.2657
7.2414
7.2241
7.1267
7.1080
7.0905
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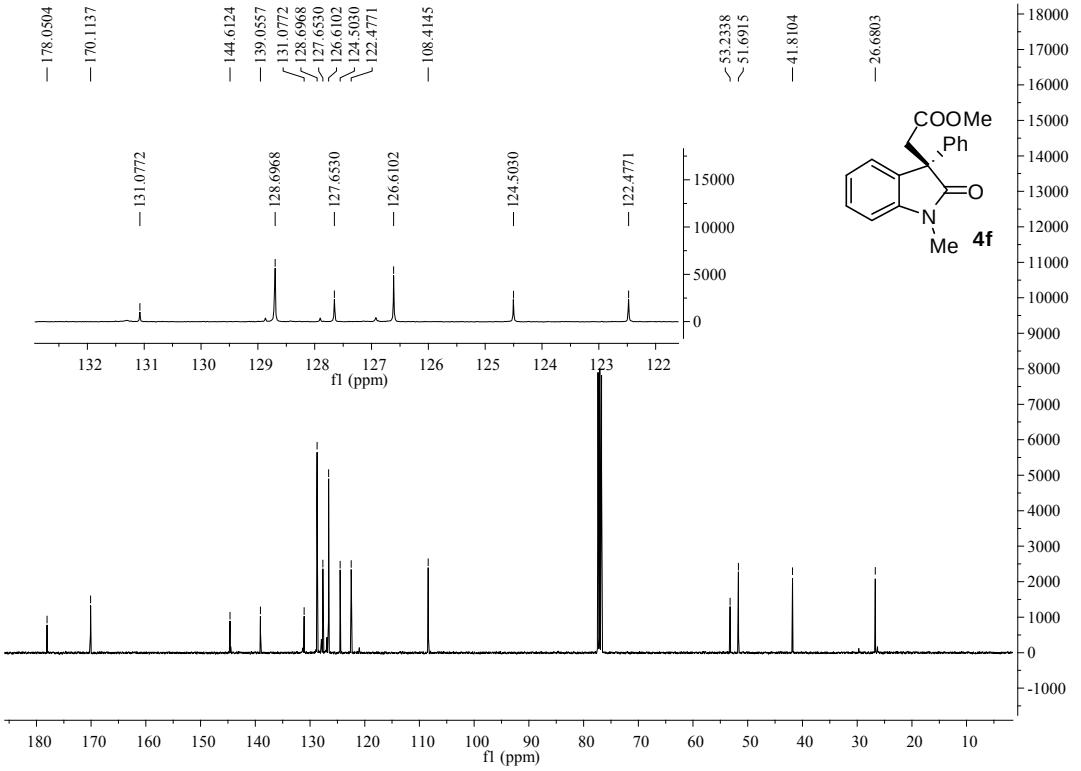
6.9077
6.33
0.51
1.02
0.98
f1 (ppm)
1.02
3.00
4.01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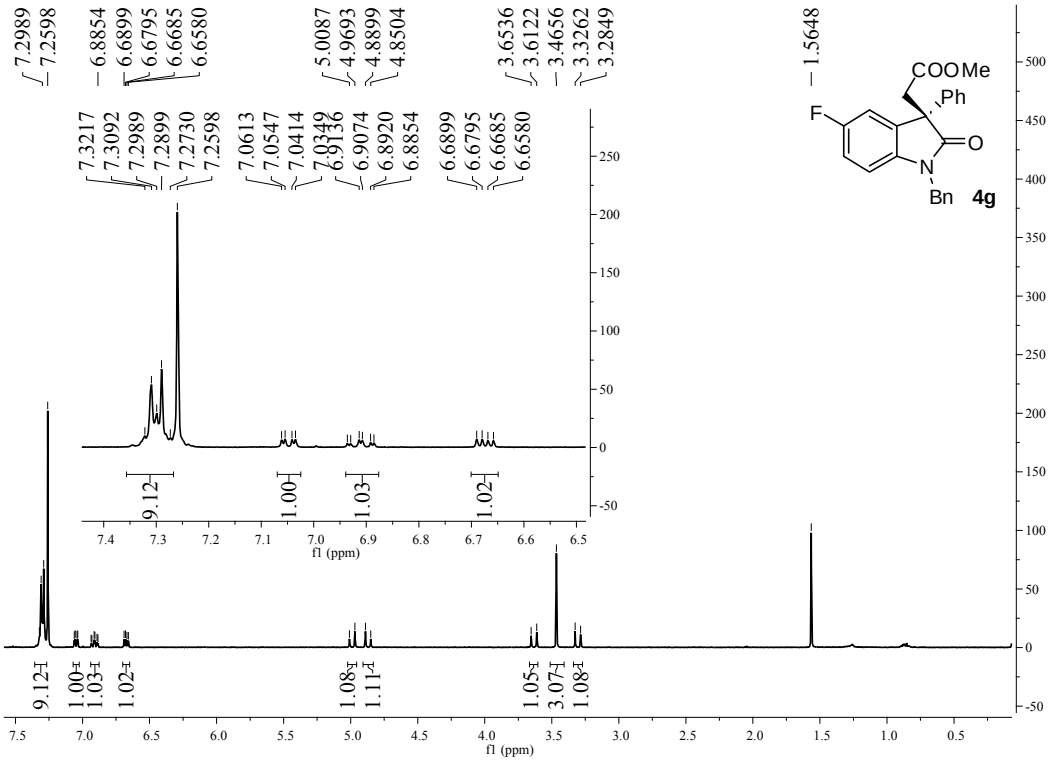
COOMe
Ph
O
N
Me
4f
f1 (ppm)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3.6536
3.6122
3.4656
3.3262
3.2849
1.5648
COOMe
Ph
F
O
N
Bn
4g
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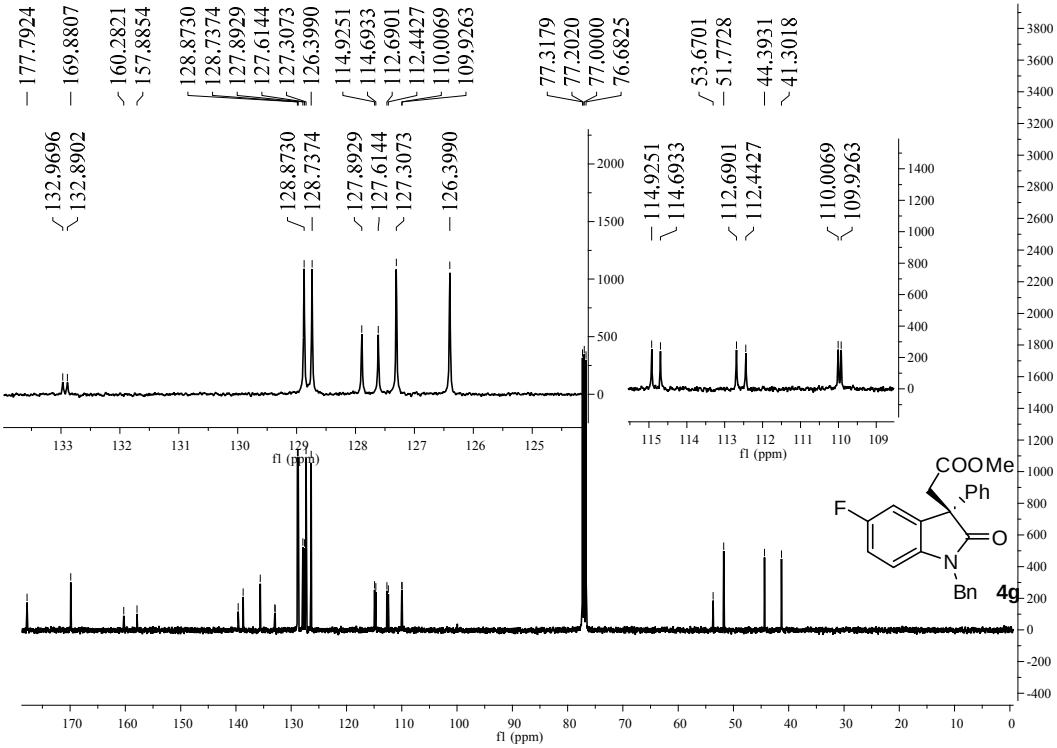
1.00
1.03
1.02
1.08
1.11
1.05
3.07
1.08
f1 (ppm)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112.4427
110.0069
109.9263
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77.2020
77.0000
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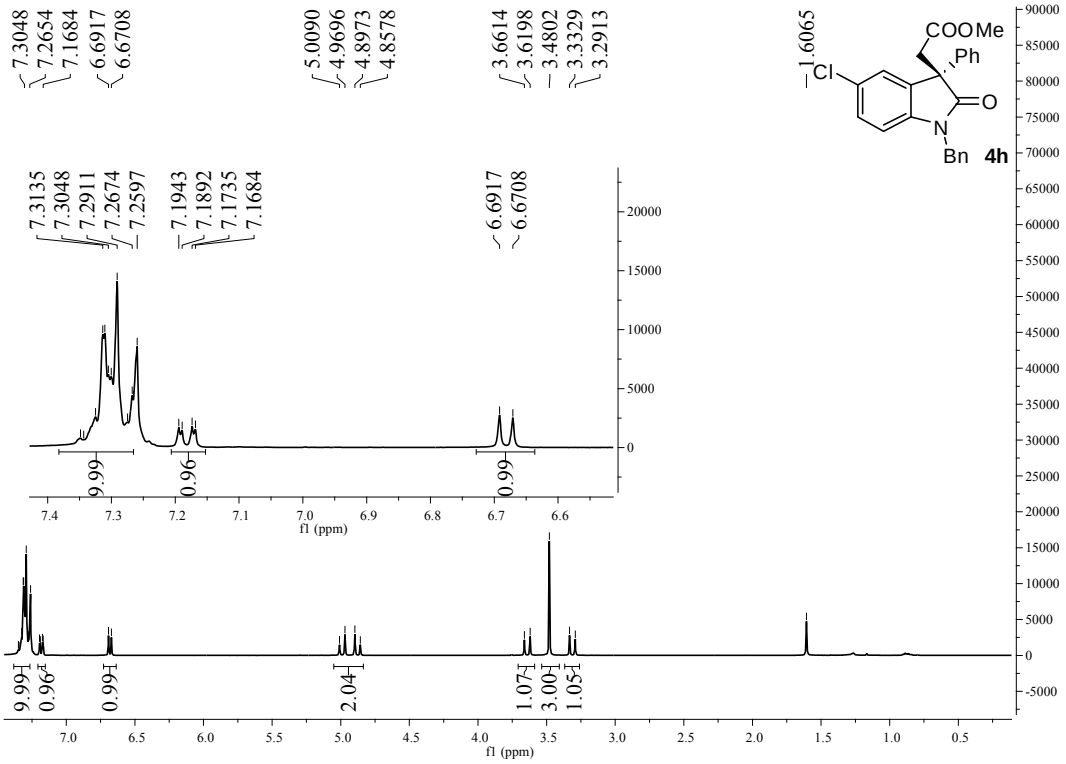
51.7728
44.3931
41.3018
COOMe
Ph
F
O
N
Bn
4g
f1 (ppm)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3.4802
3.3329
3.2913
1.6065
COOMe
Ph
Cl
O
N
Bn
4h
7.3135
7.3048
7.2911
7.2674
7.2597
7.1943
7.1892
7.1735
7.1684
6.6917
6.6708
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f1 (ppm)
9.99
0.96
0.99
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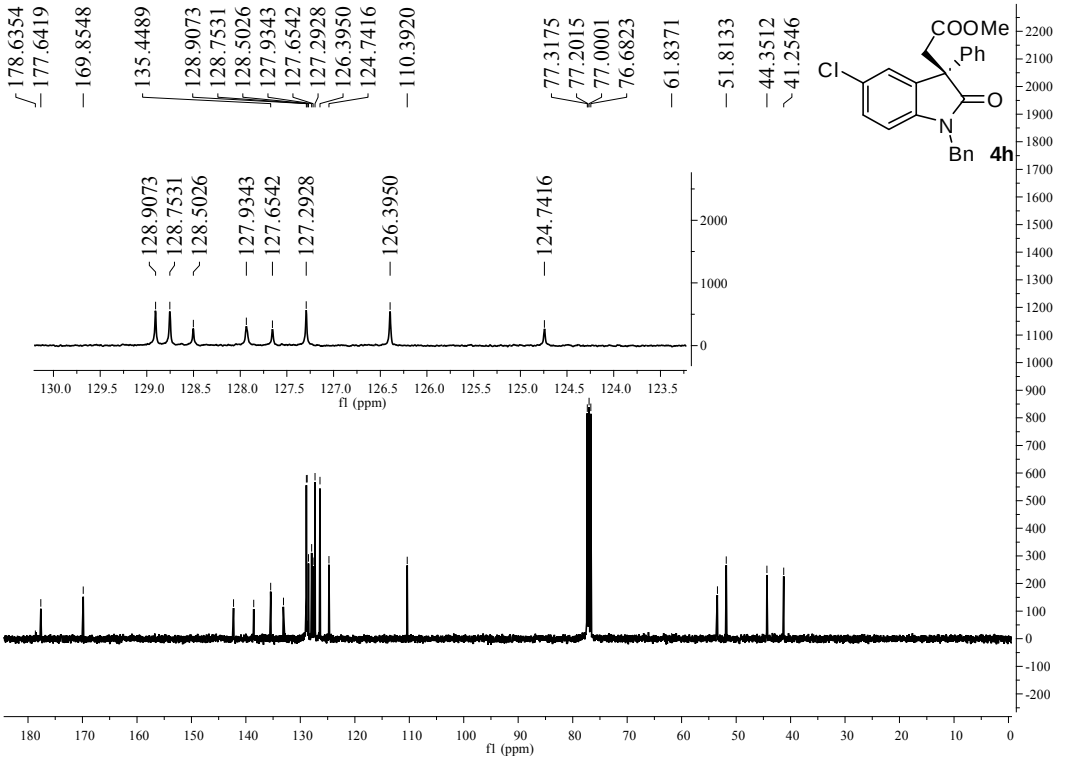
1.07
3.00
1.05
f1 (ppm)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126.3950
124.7416
110.3920
77.3175
77.2015
77.0001
76.6823
61.8371
51.8133
44.3512
41.2546
COOMe
Ph
Cl
O
N
Bn
4h
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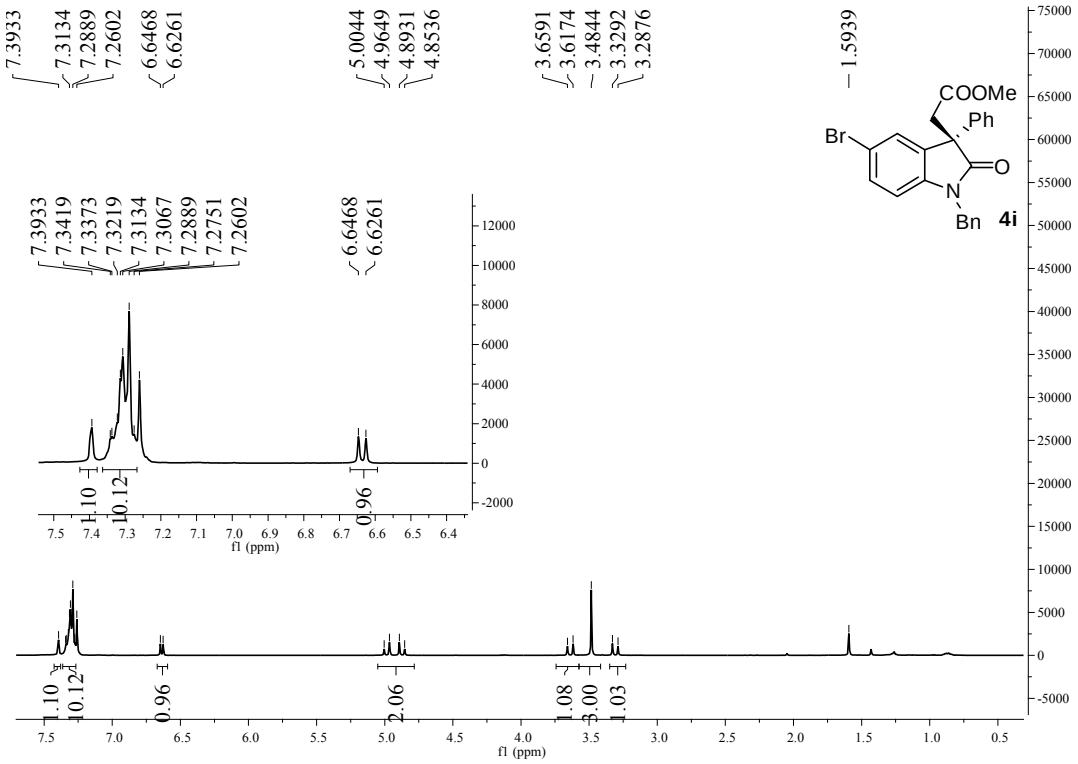
127.9343
127.6542
127.2928
126.3950
124.7416
f1 (ppm)
f1 (ppm)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6.6261
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3.6591
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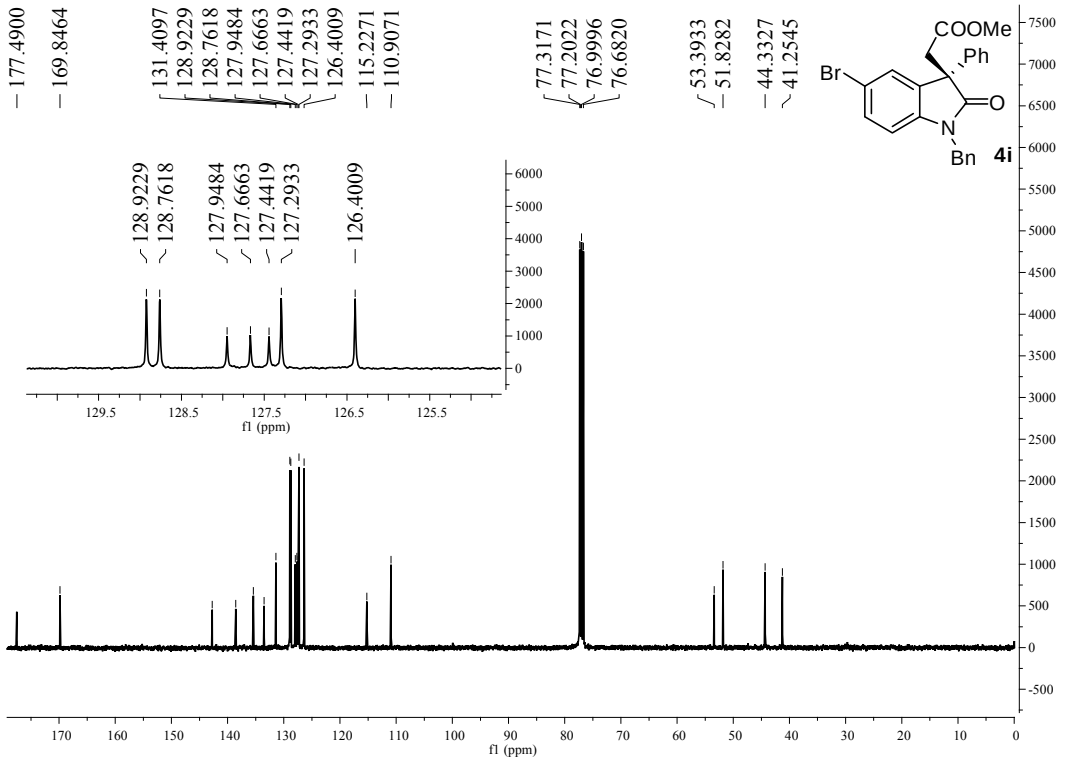
3.2876
1.5939
COOMe
Ph
Br
O
N
Bn
4i
f1 (ppm)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77.2022
76.9996
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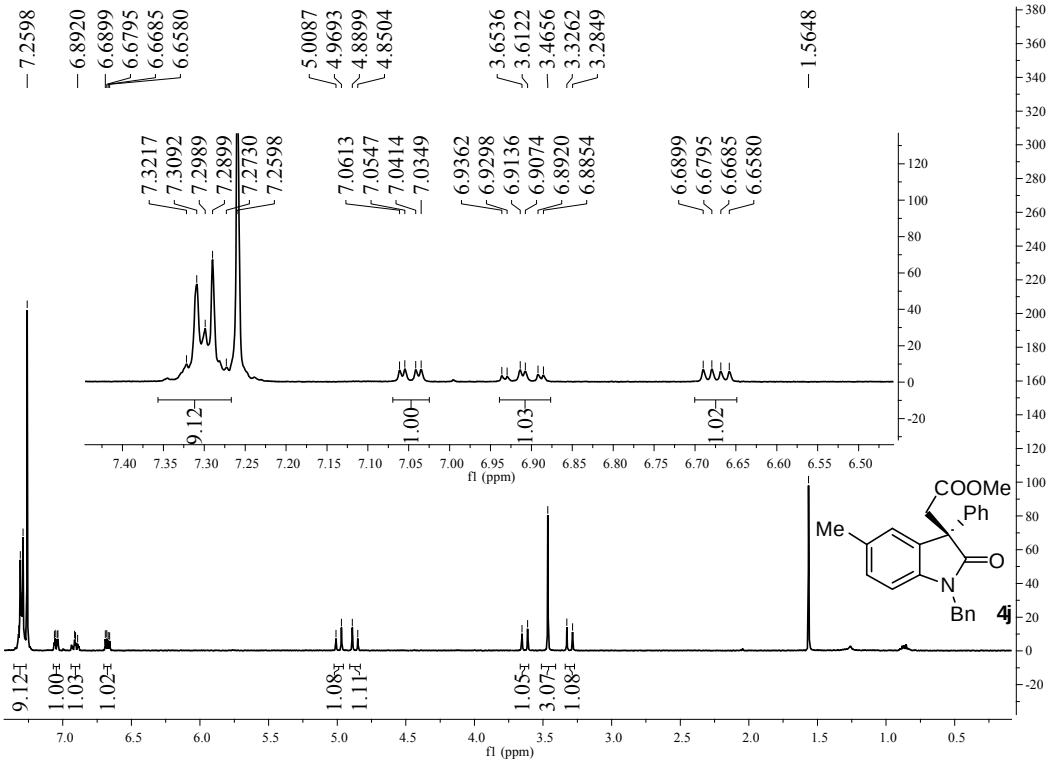
41.2545
COOMe
Ph
Br
O
N
Bn
4i
f1 (ppm)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3.4656
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7.0613
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7.0414
7.0349
6.9362
6.9298
6.9136
6.9074
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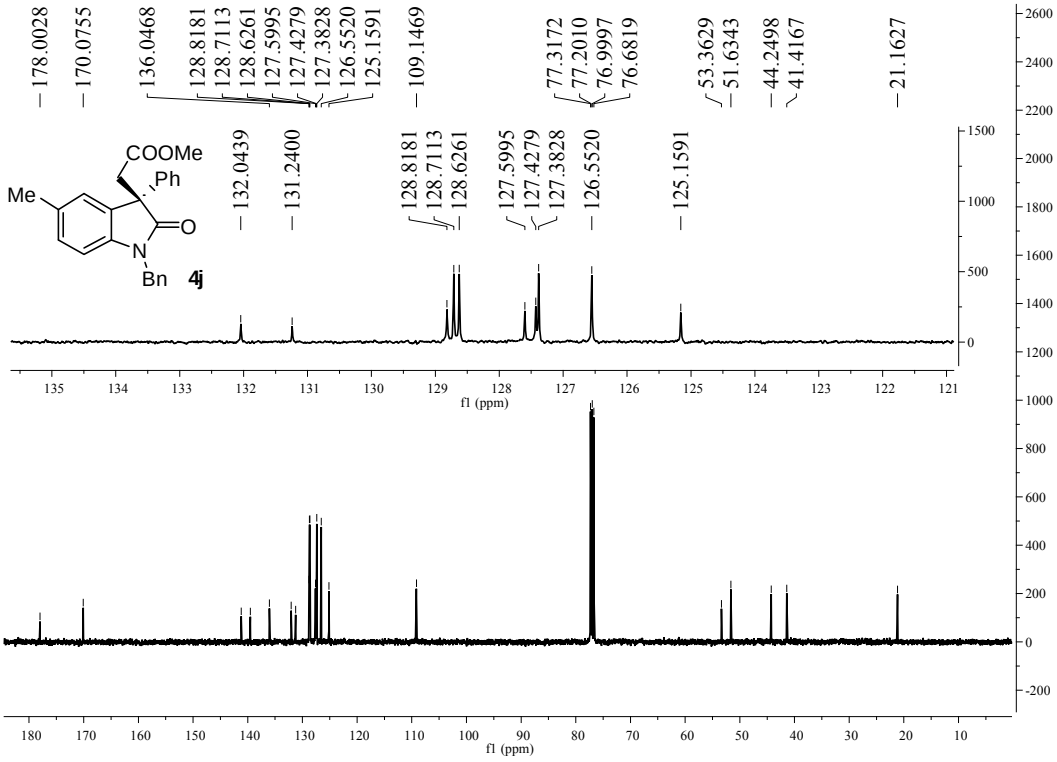
6.8854
6.6899
6.6795
6.6685
6.6580
9.12
1.00
1.03
1.02
1.08
1.11
1.05
3.07
1.08
f1 (ppm)
COOMe
Ph
Me
O
N
Bn
4j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128.7113
128.6261
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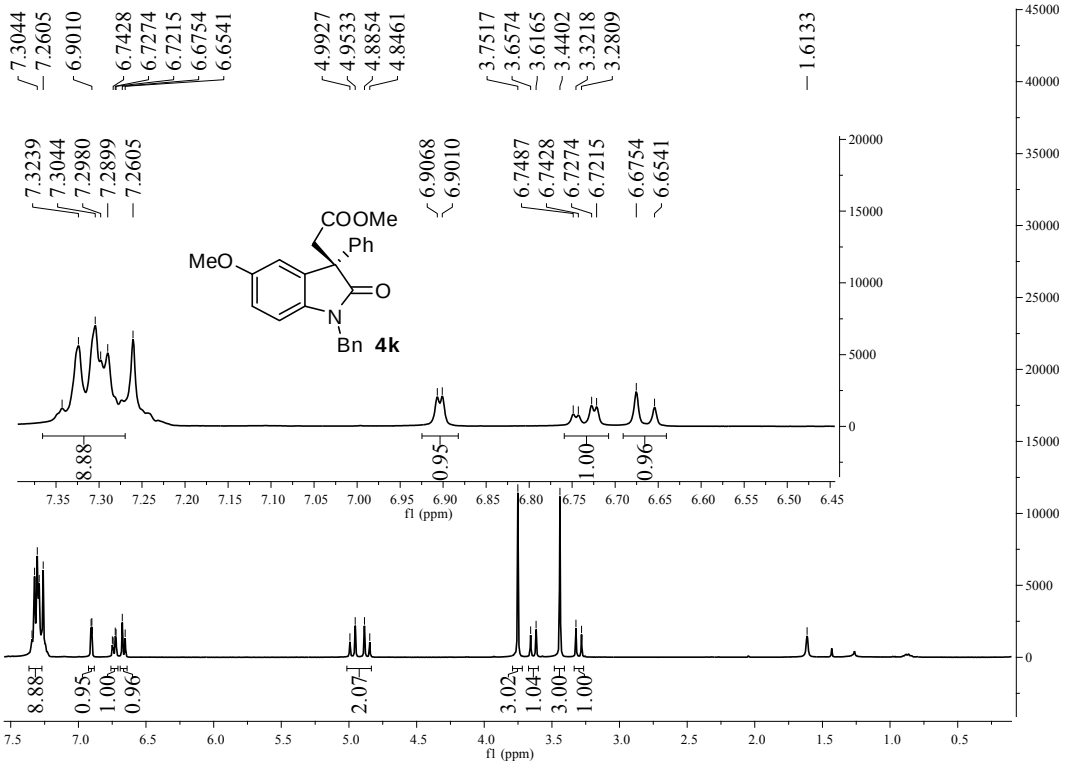
f1 (ppm)
COOMe
Ph
Me
O
N
Bn
4j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4.8461
3.7517
3.6574
3.6165
3.4402
3.3218
3.2809
1.6133
COOMe
Ph
MeO
O
N
Bn 4k
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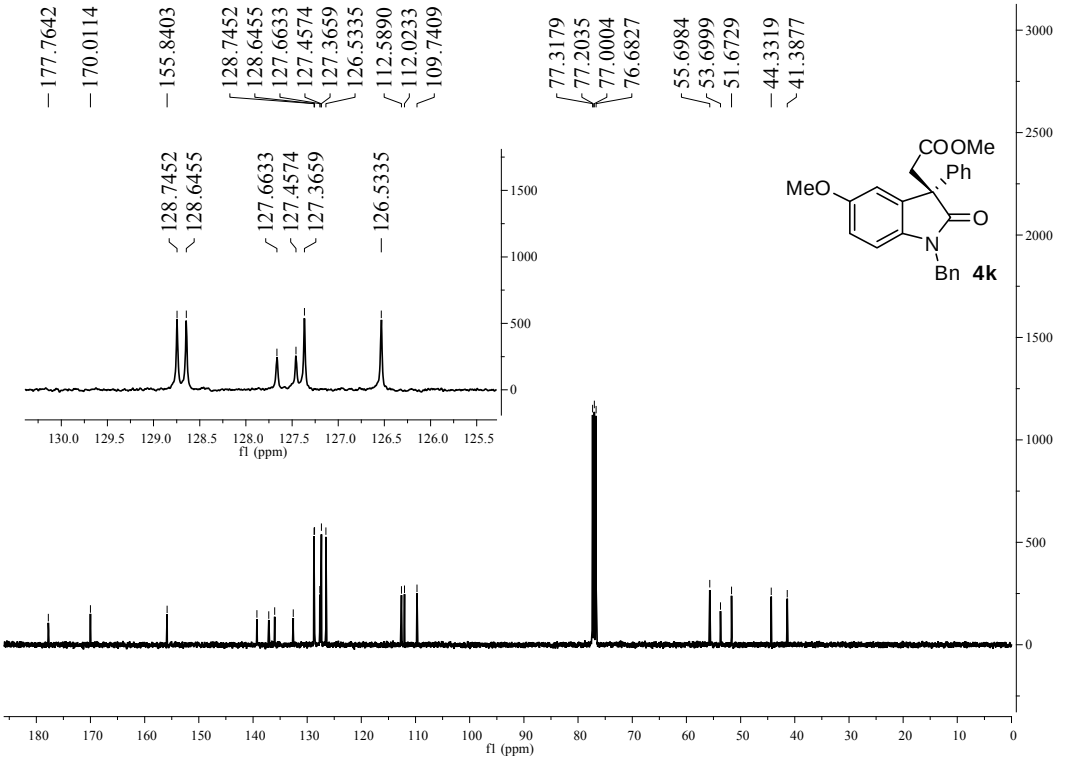
1.00
0.96
2.07
3.02
1.04
3.00
1.00
f1 (ppm)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77.2035
77.0004
76.6827
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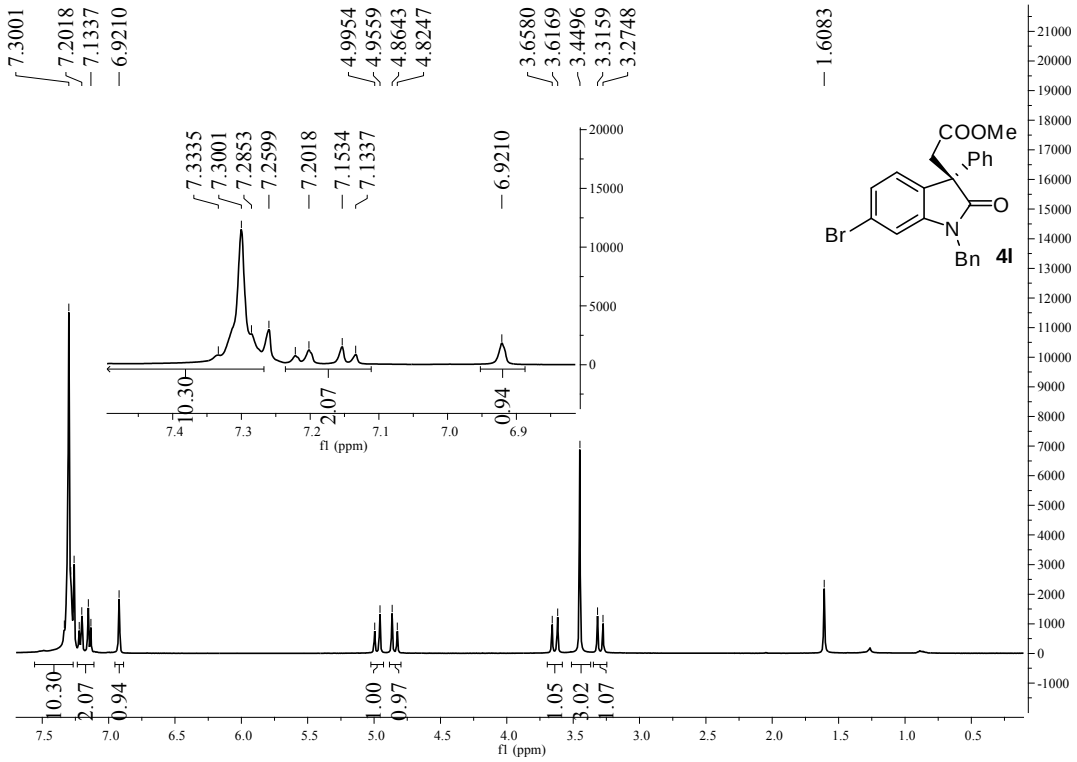
41.3877
COOMe
Ph
MeO
O
N
Bn 4k
f1 (ppm)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3.3159
3.2748
1.6083
7.3335
7.3001
7.2853
7.2599
7.2018
7.1534
7.1337
6.9210
10.30
2.07
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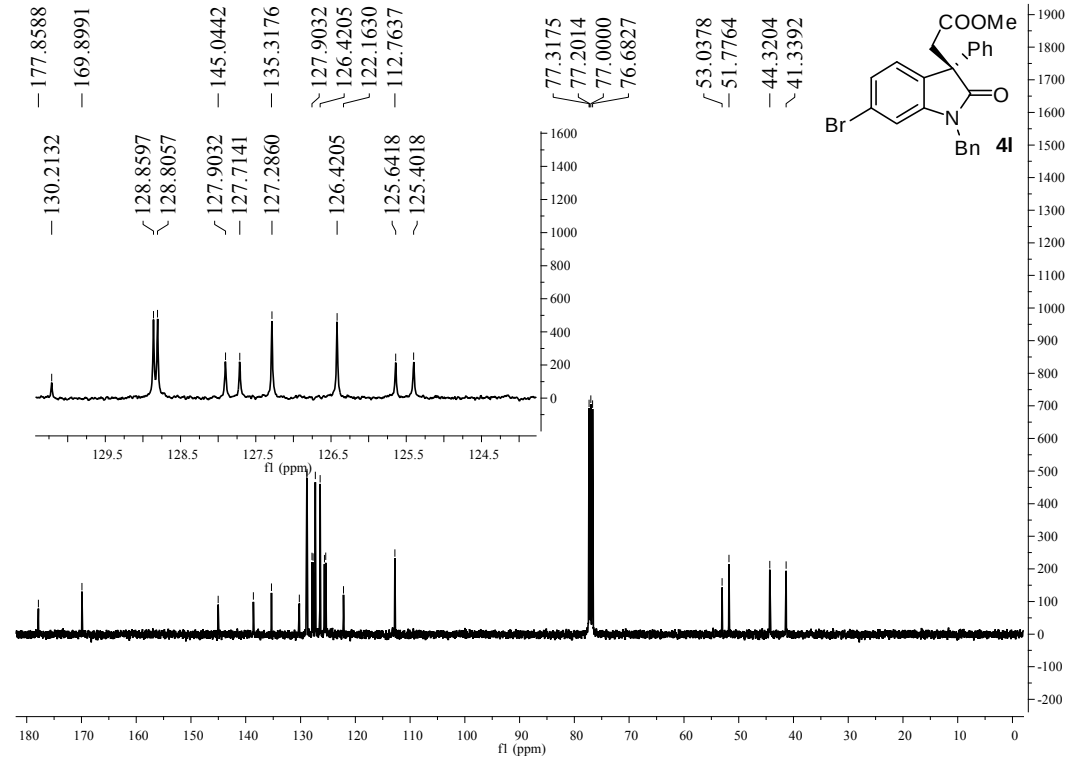
1.05
3.02
1.07
f1 (ppm)
COOMe
Ph
O
N
Br
Bn
4l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41.3392
130.2132
128.8597
128.8057
127.9032
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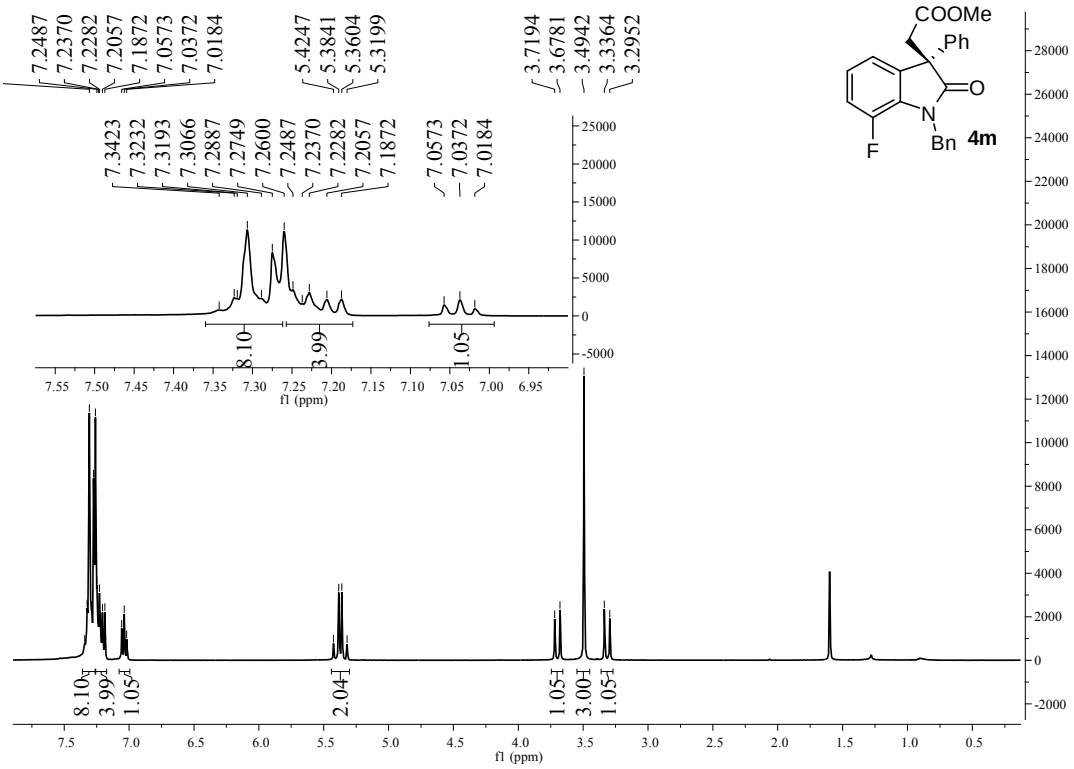
126.4205
125.6418
125.4018
f1 (ppm)
COOMe
Ph
O
N
Br
Bn
4l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7.2749
7.2600
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7.2370
7.2282
7.2057
7.1872
7.0573
7.0372
7.0184
8.10
3.99
1.05
f1 (ppm)
8.10
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1.05
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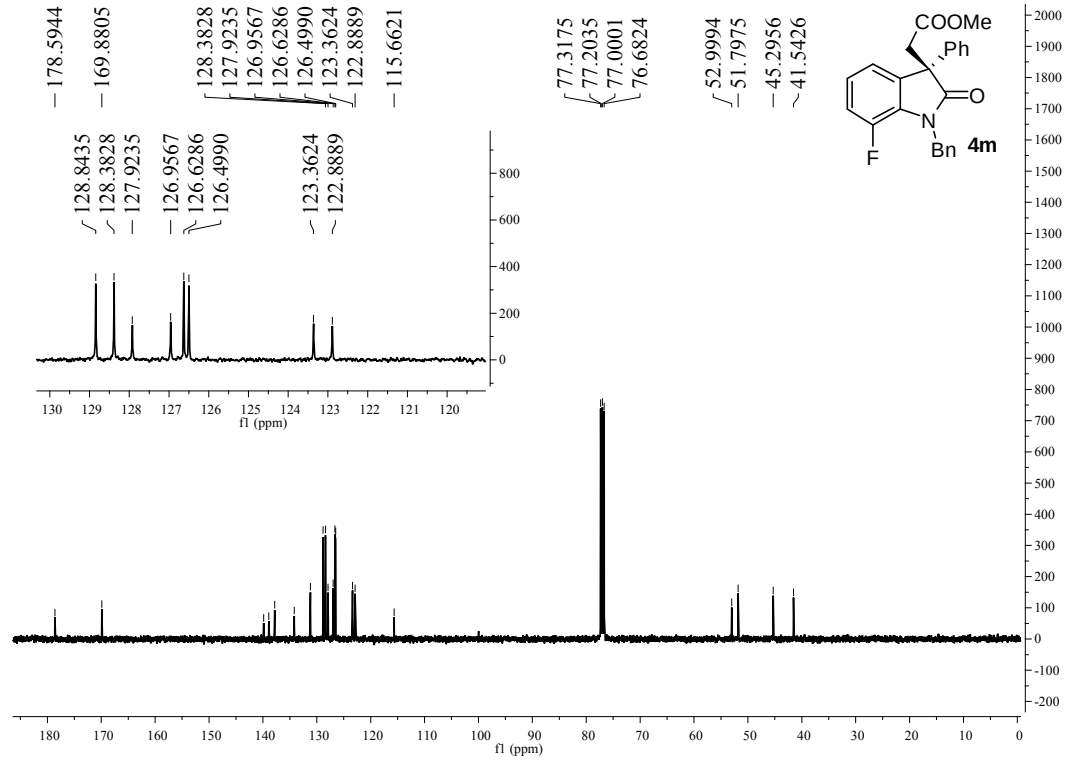
1.05
3.00
1.05
f1 (ppm)
COOMe
Ph
O
N
Bn
F
4m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128.8435
128.3828
127.9235
126.9567
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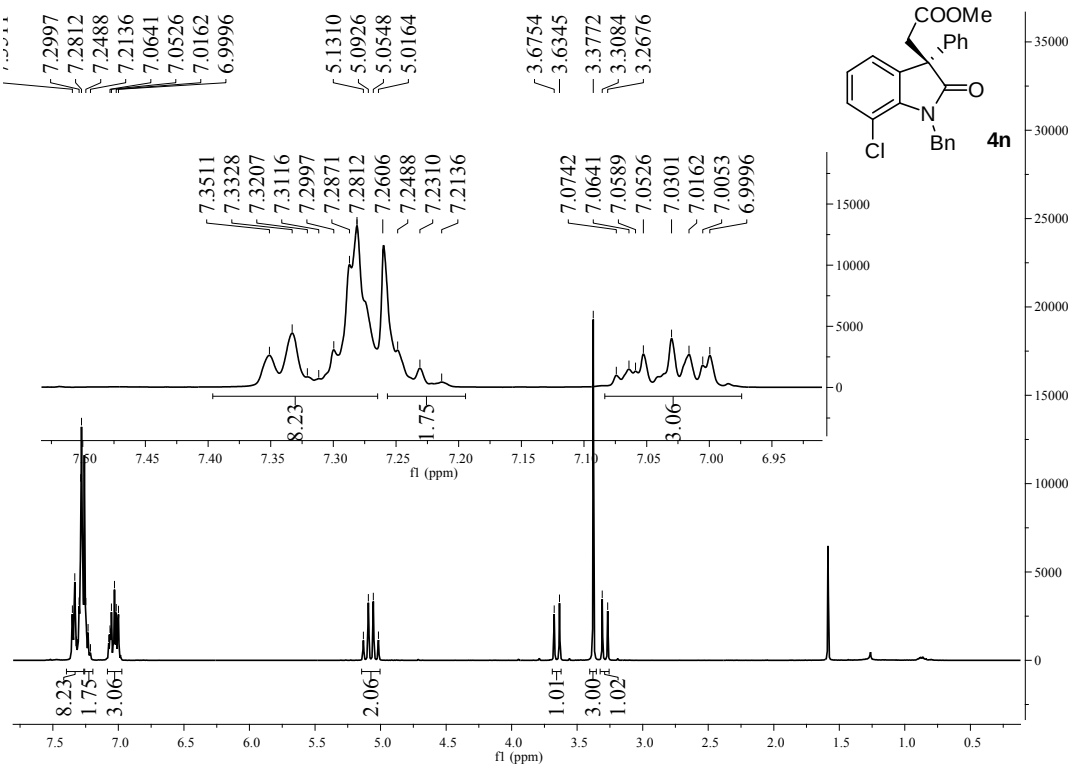
122.8889
f1 (ppm)
f1 (ppm)
COOMe
Ph
O
N
Bn
F
4m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8.23
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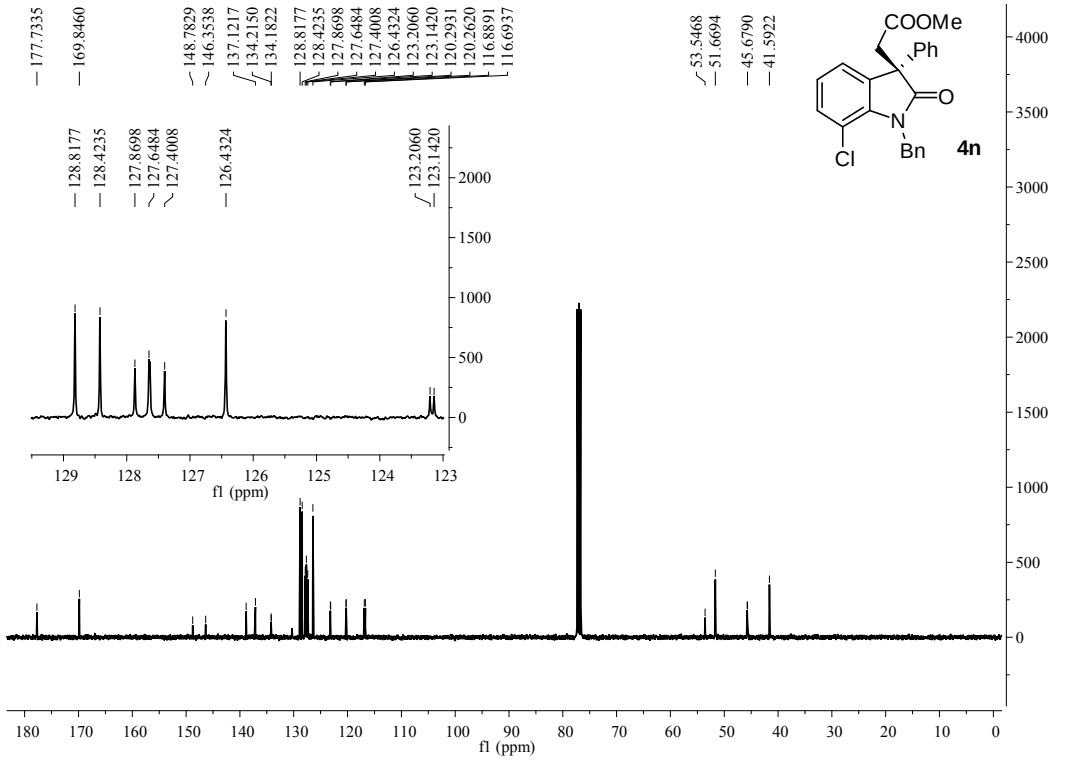
1.02
f1 (ppm)
COOMe
Ph
O
N
Bn
Cl
4n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123.1420
120.2931
120.2620
116.8891
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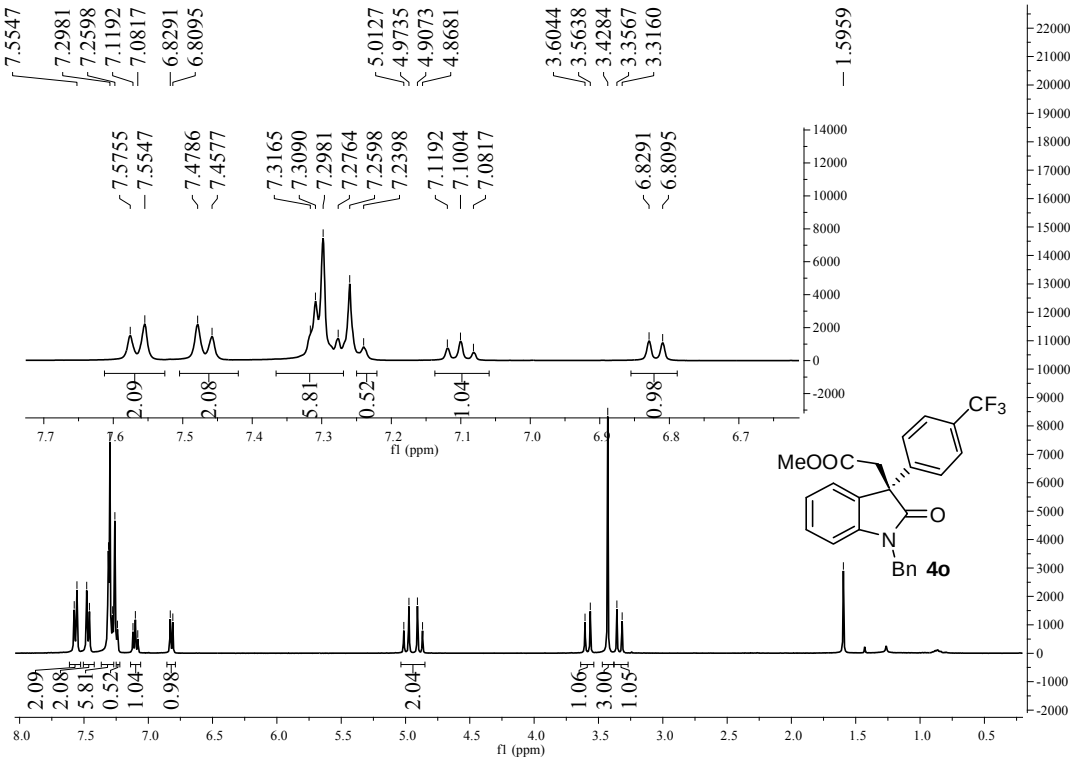
41.5922
f1 (ppm)
COOMe
Ph
O
N
Bn
Cl
4n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4.8681
3.6044
3.5638
3.4284
3.3567
3.3160
1.5959
2.09
2.08
5.81
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2.04
1.06
3.00
1.05
f1 (ppm)
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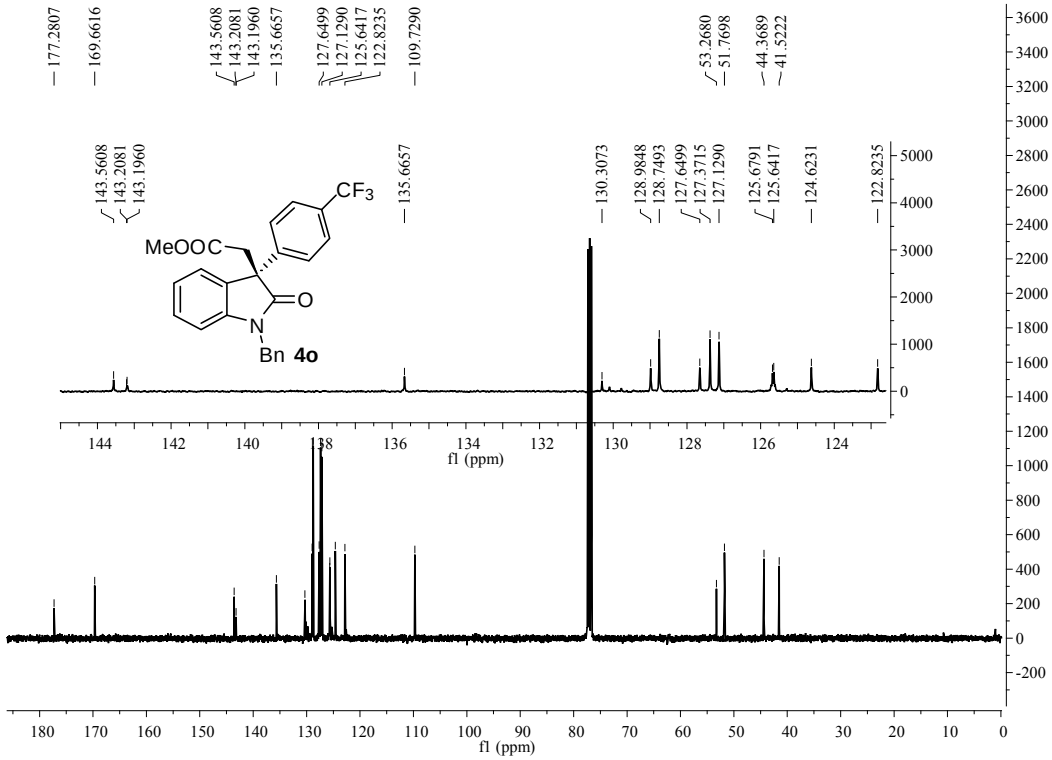
CF3
O
N
Bn 4o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130.3073
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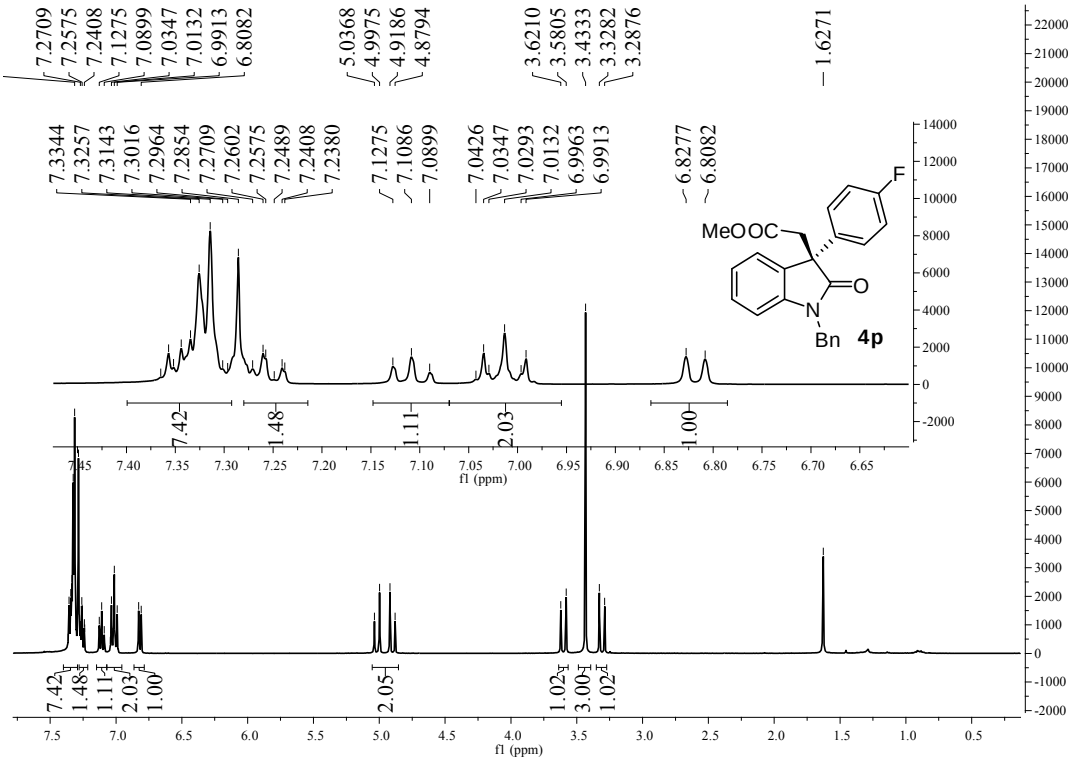
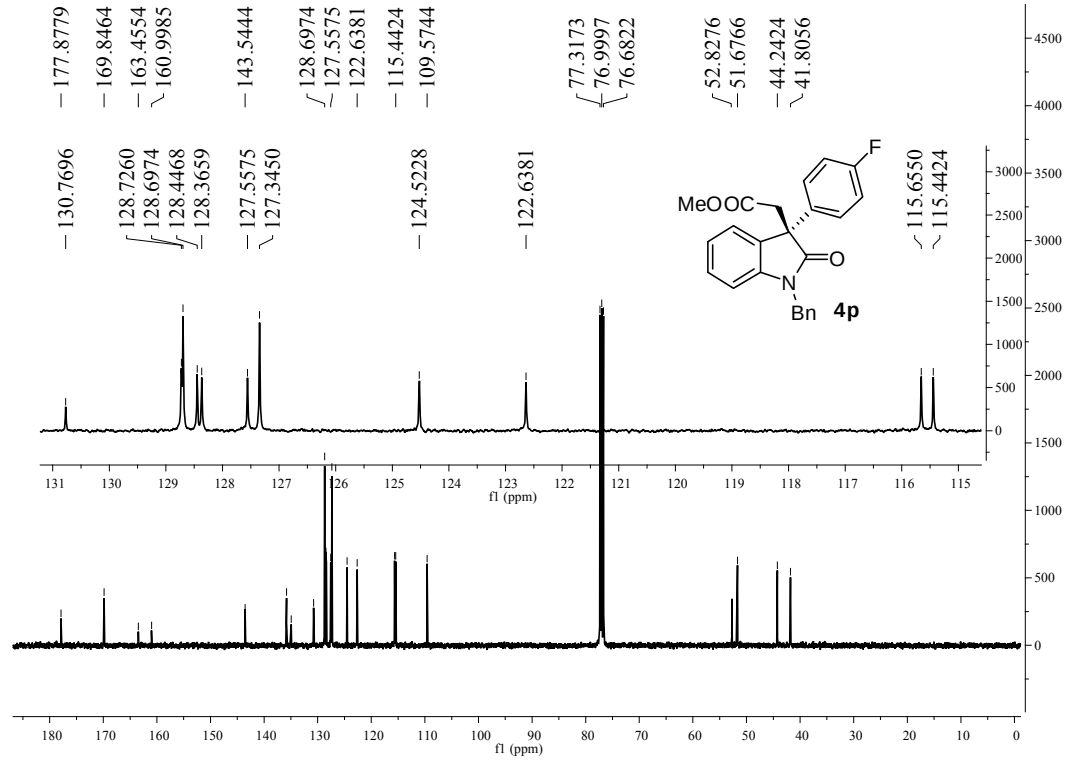
f1 (ppm)
MeOOC
CF3
O
N
Bn 4o


MeOOC
F
O
N
Bn
4p
f1 (ppm)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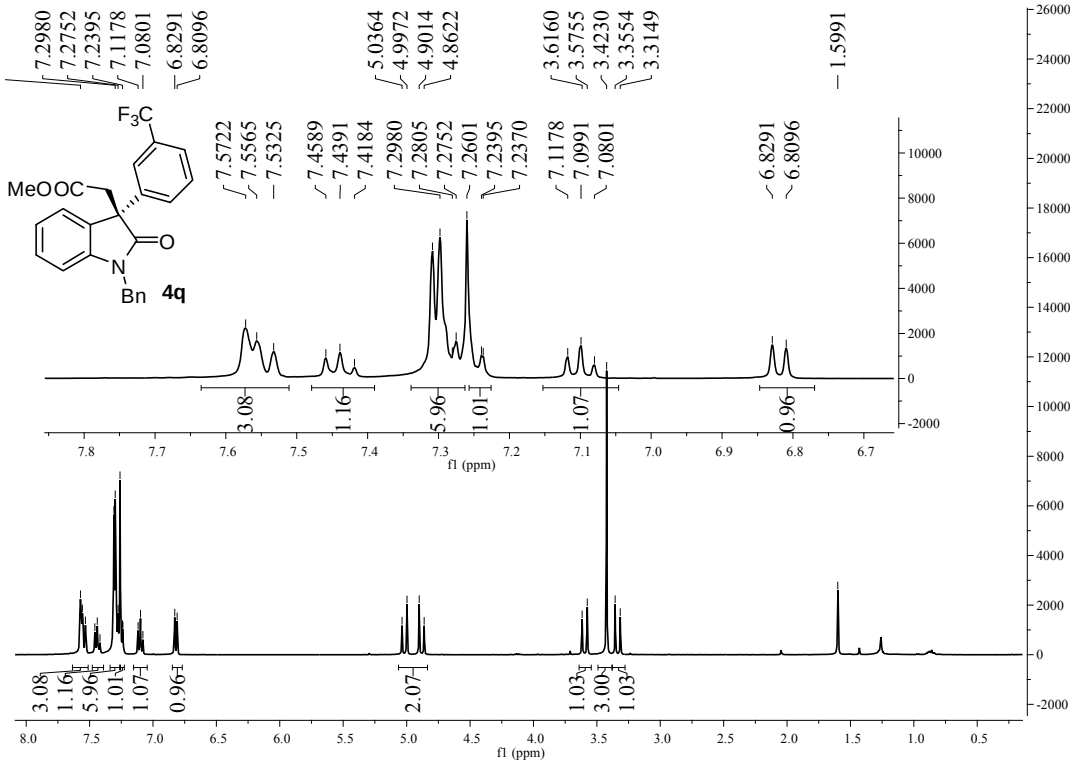
F
O
N
Bn
4p
f1 (ppm)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F3C
MeOOC
O
N
Bn
4q
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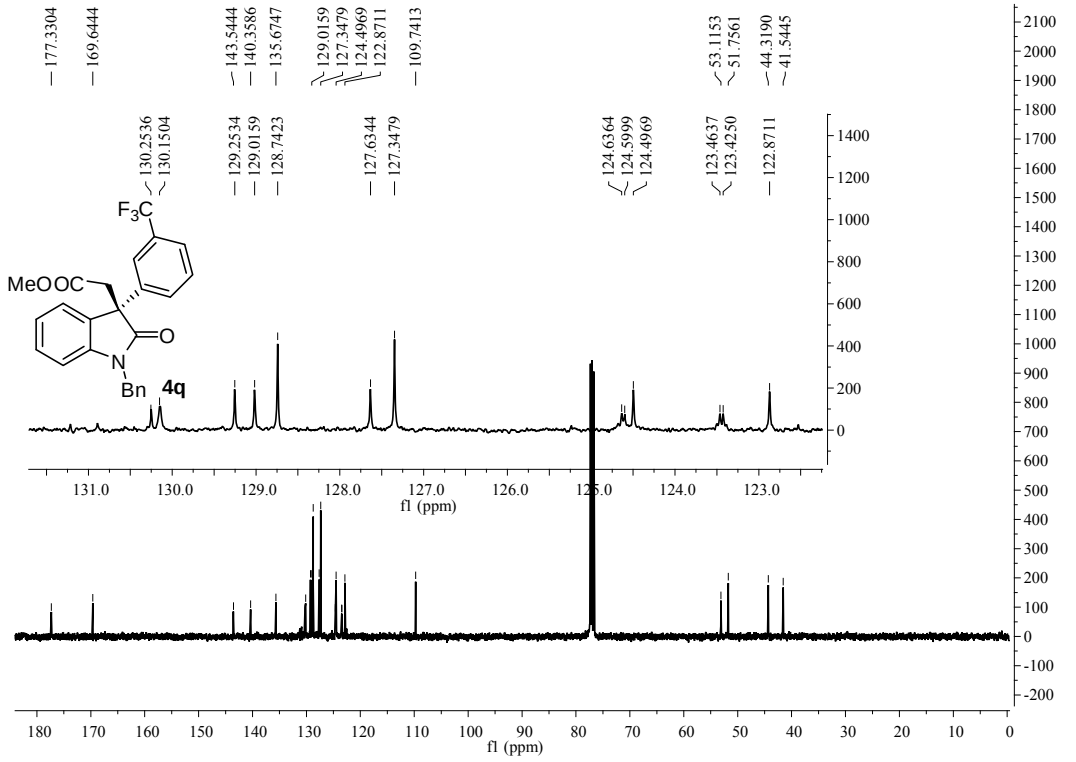
f1 (ppm)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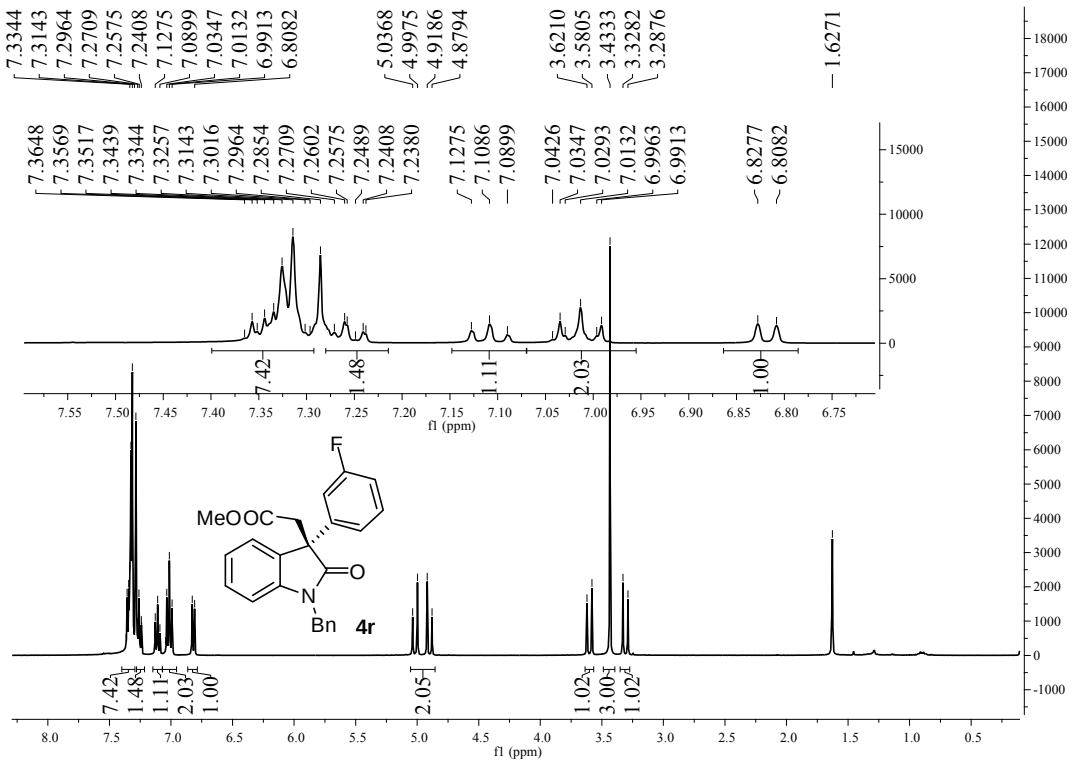
127.6344
127.3479
124.6364
124.5999
124.4969
123.4637
123.4250
122.8711
F3C
MeOOC
O
N
Bn
4q
f1 (ppm)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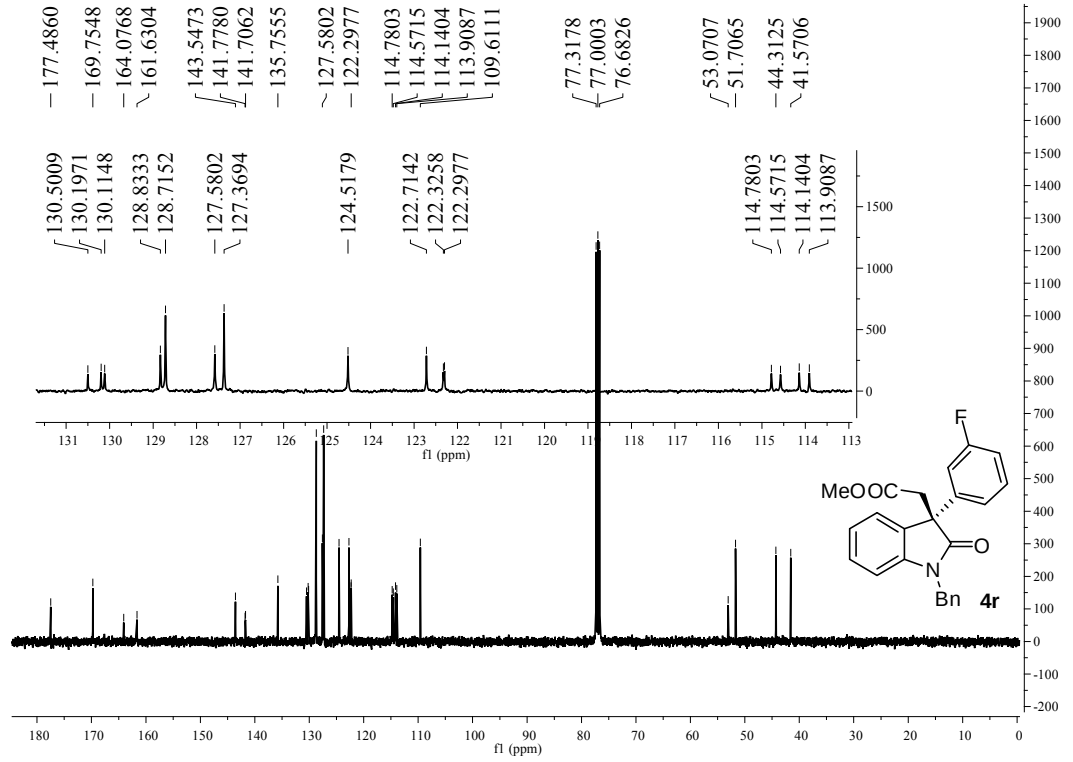
7.2408
7.1275
7.0899
7.0347
7.0132
6.9913
6.8082
5.0368
4.9975
4.9186
4.8794
3.6210
3.5805
3.4333
3.3282
3.2876
1.6271
7.42
1.48
1.11
2.03
1.00
2.05
1.02
3.00
1.02
f1 (ppm)
F
MeOOC
O
N
Bn
4r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141.7062
135.7555
127.5802
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114.7803
114.5715
114.1404
113.9087
109.6111
77.3178
77.0003
76.6826
53.0707
51.7065
44.3125
41.5706
130.5009
130.1971
130.1148
128.8333
128.7152
127.5802
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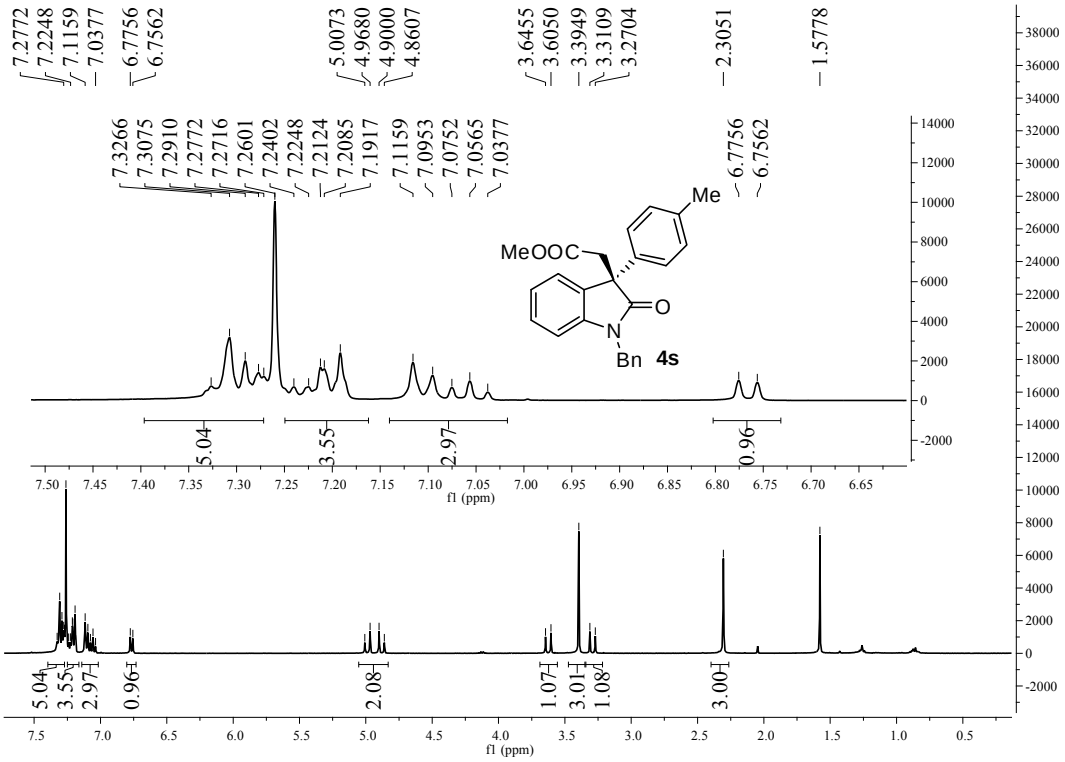
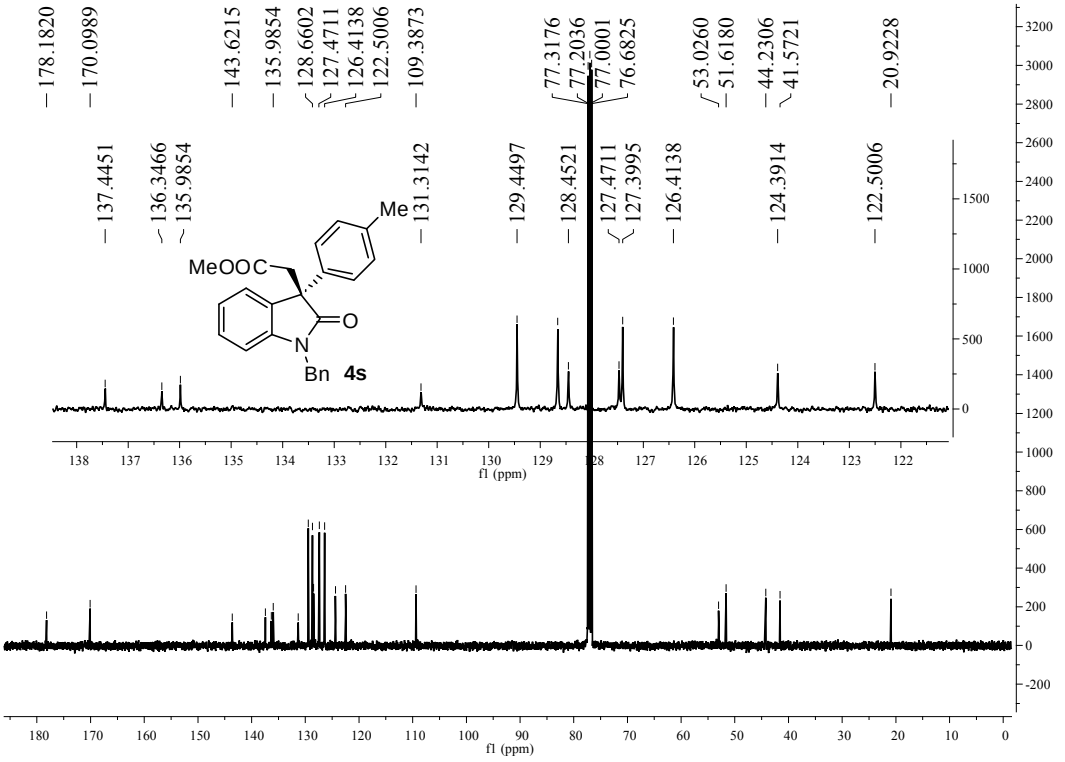
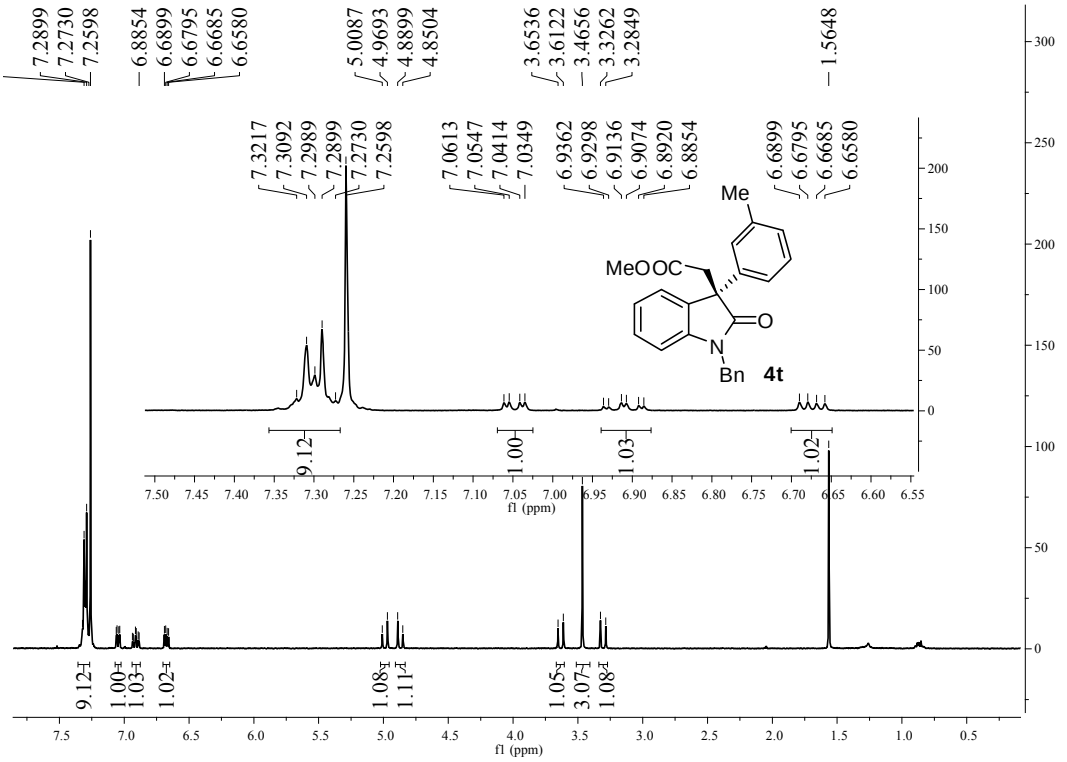
122.7142
122.3258
122.2977
f1 (ppm)
F
MeOOC
O
N
Bn
4r



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5.0087
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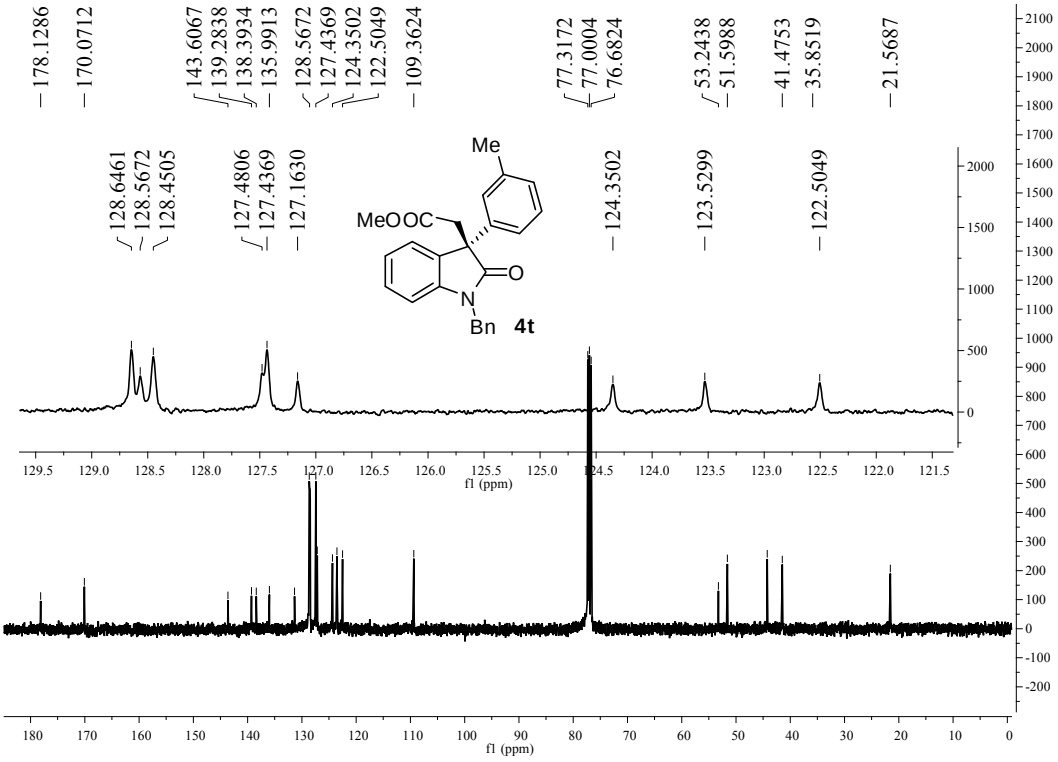
4.8899
4.8504
3.6536
3.6122
3.4656
3.3262
3.2849
1.5648
Me
MeOOC
O
N
Bn
4t
9.12
1.00
1.03
1.02
1.08
1.11
1.05
3.07
1.08
f1 (ppm)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128.5672
127.4369
124.3502
122.5049
109.3624
77.3172
77.0004
76.6824
53.2438
51.5988
41.4753
35.8519
21.5687
128.6461
128.5672
128.4505
127.4806
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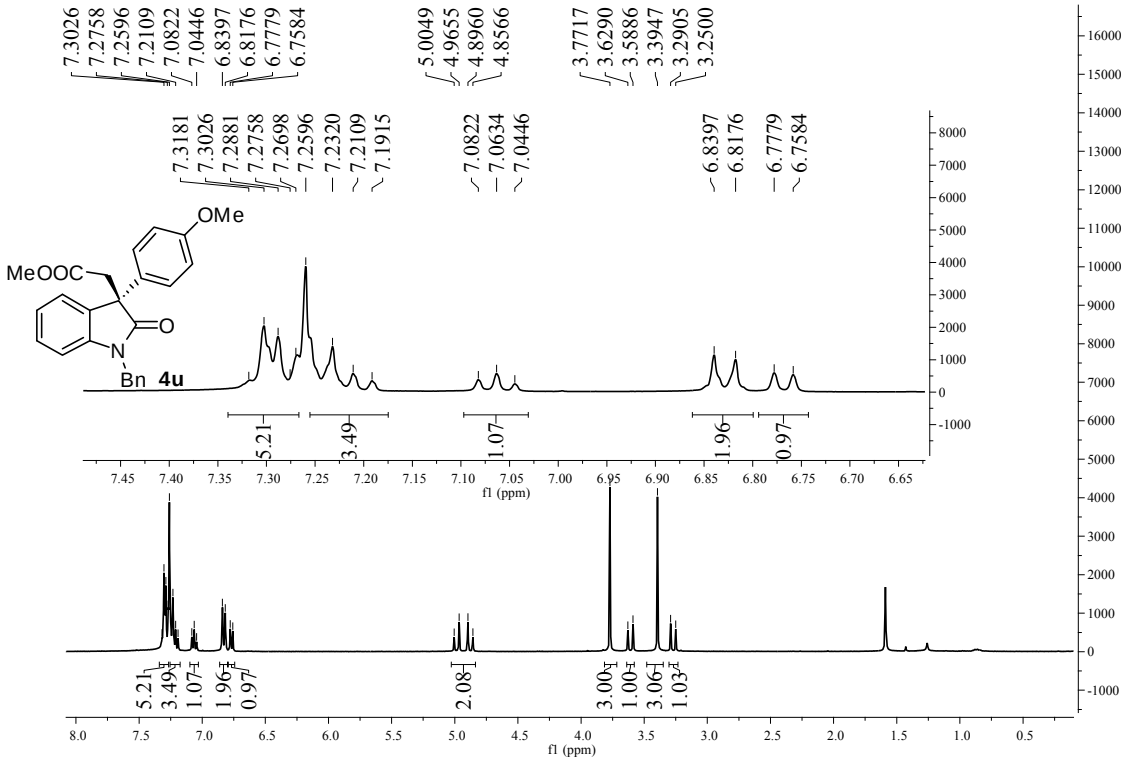
124.3502
123.5299
122.5049
Me
MeOOC
O
N
Bn
4t
f1 (ppm)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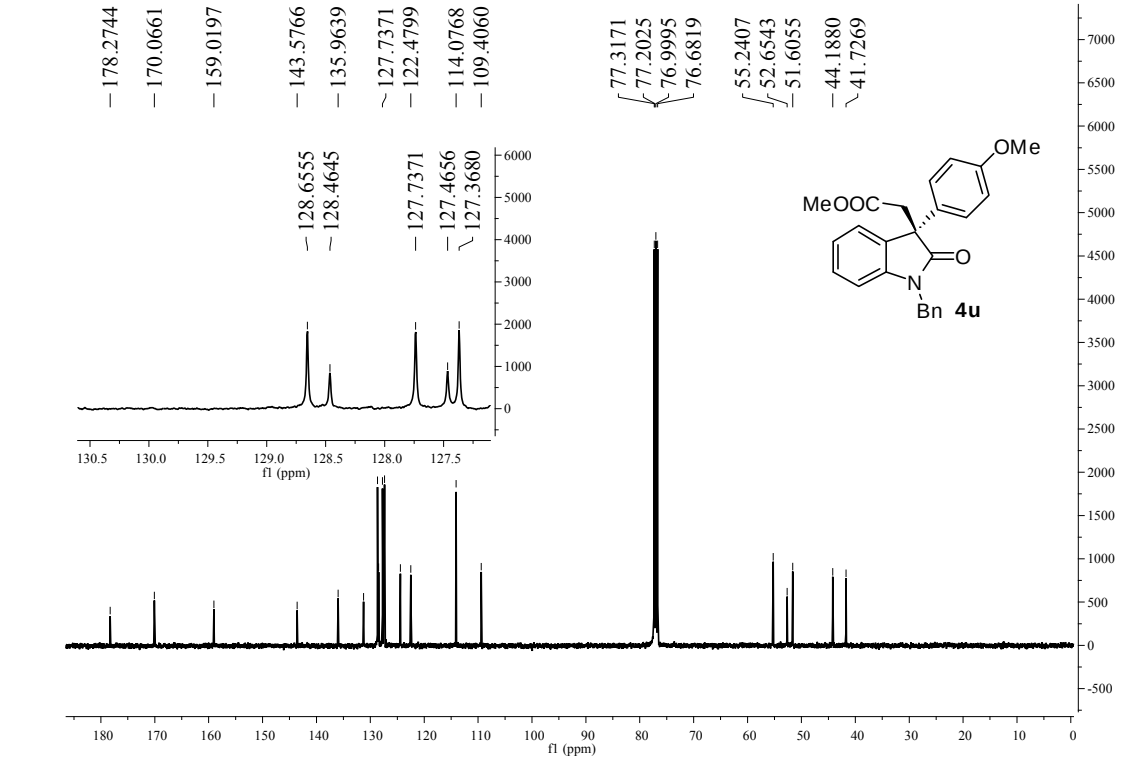
7.0822
7.0446
6.8397
6.8176
6.7779
6.7584
5.0049
4.9655
4.8960
4.8566
3.7717
3.6290
3.5886
3.3947
3.2905
3.2500
OMe
MeOOC
O
N
Bn 4u
5.21
3.49
1.07
1.96
0.97
2.08
3.00
1.00
3.06
1.03
f1 (ppm)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122.4799
114.0768
109.4060
77.3171
77.2025
76.9995
76.6819
55.2407
52.6543
51.6055
44.1880
41.7269
128.6555
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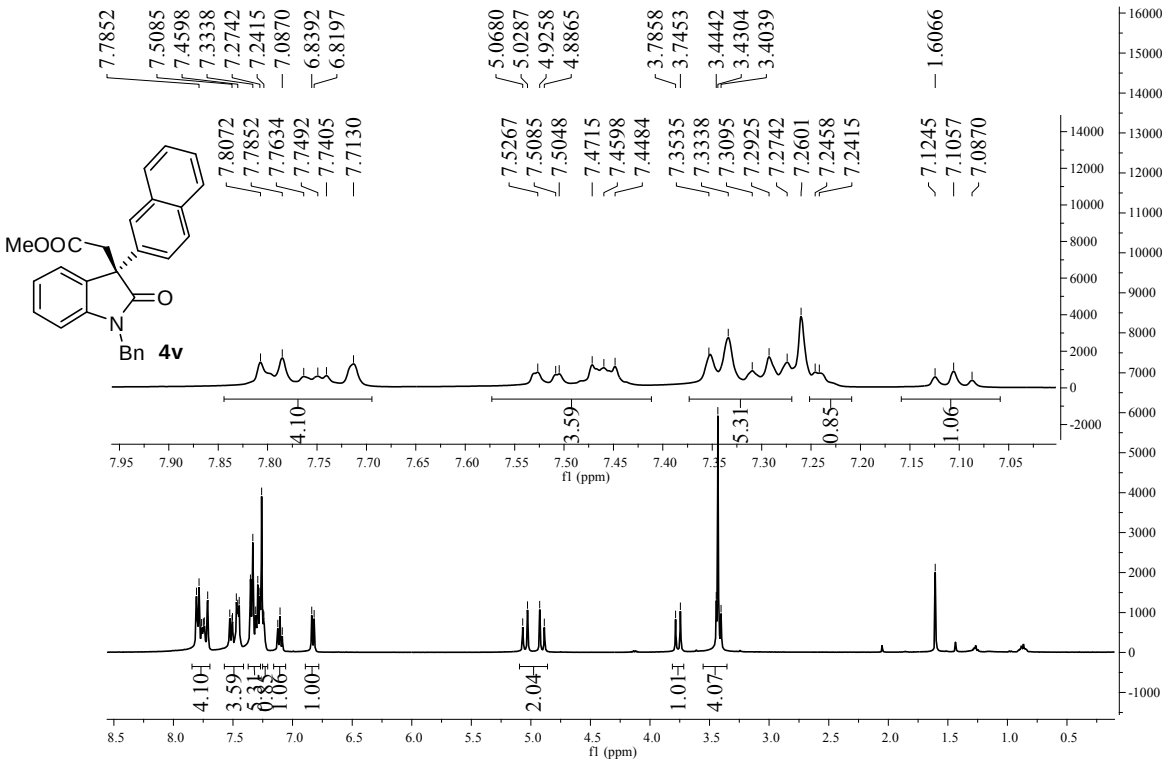
127.7371
127.4656
127.3680
OMe
MeOOC
O
N
Bn 4u
f1 (ppm)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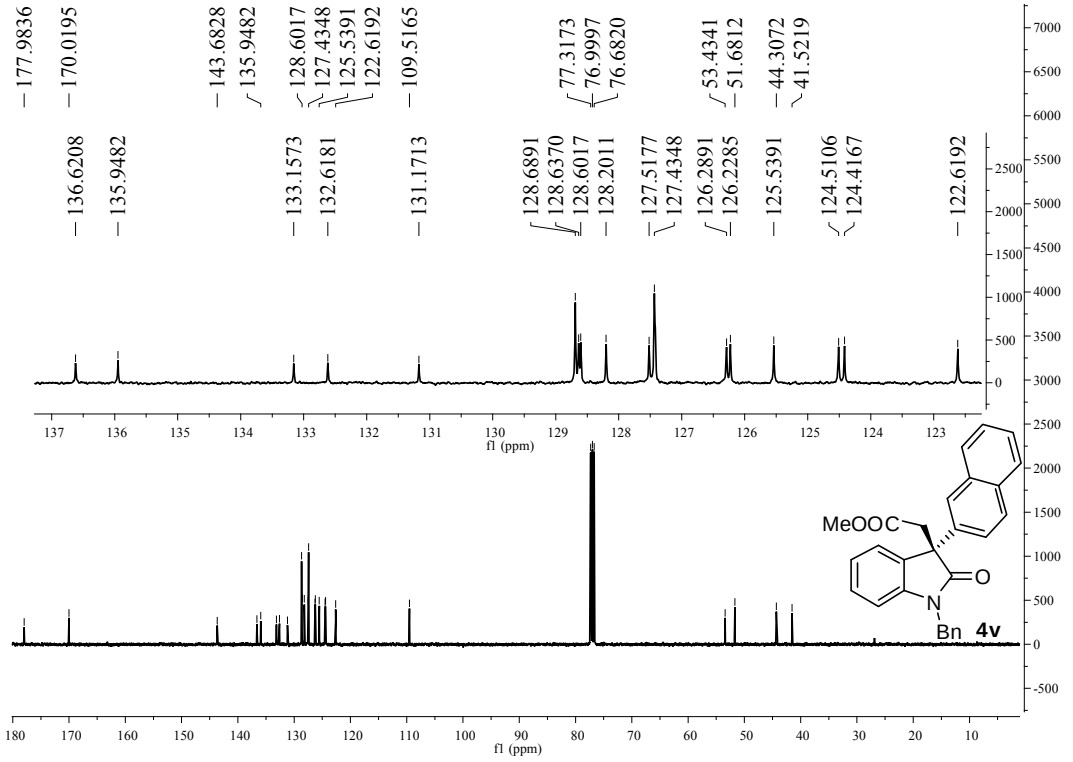
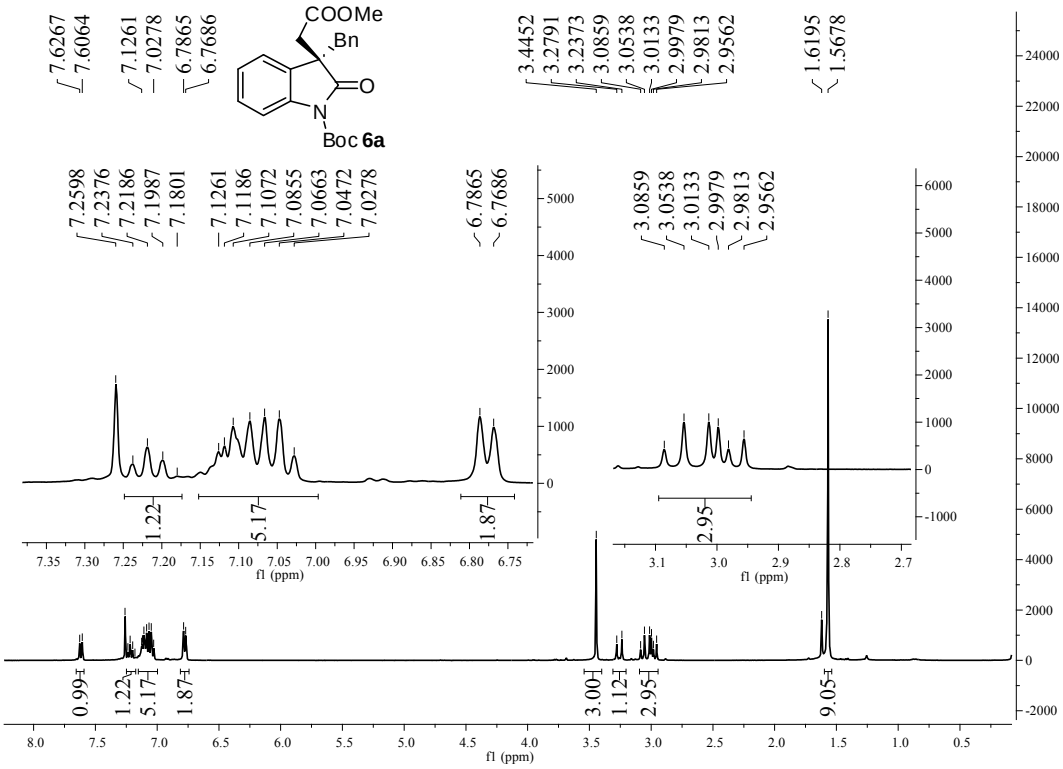
O
N
Bn 4v
f1 (ppm)


MeOOC
O
N
Bn 4v
f1 (ppm)


COOMe
Bn
O
N
Boc 6a
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7.0278
6.7865
6.7686
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3.2791
3.2373
3.0859
3.0538
3.0133
2.9979
2.9813
2.9562
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0.99
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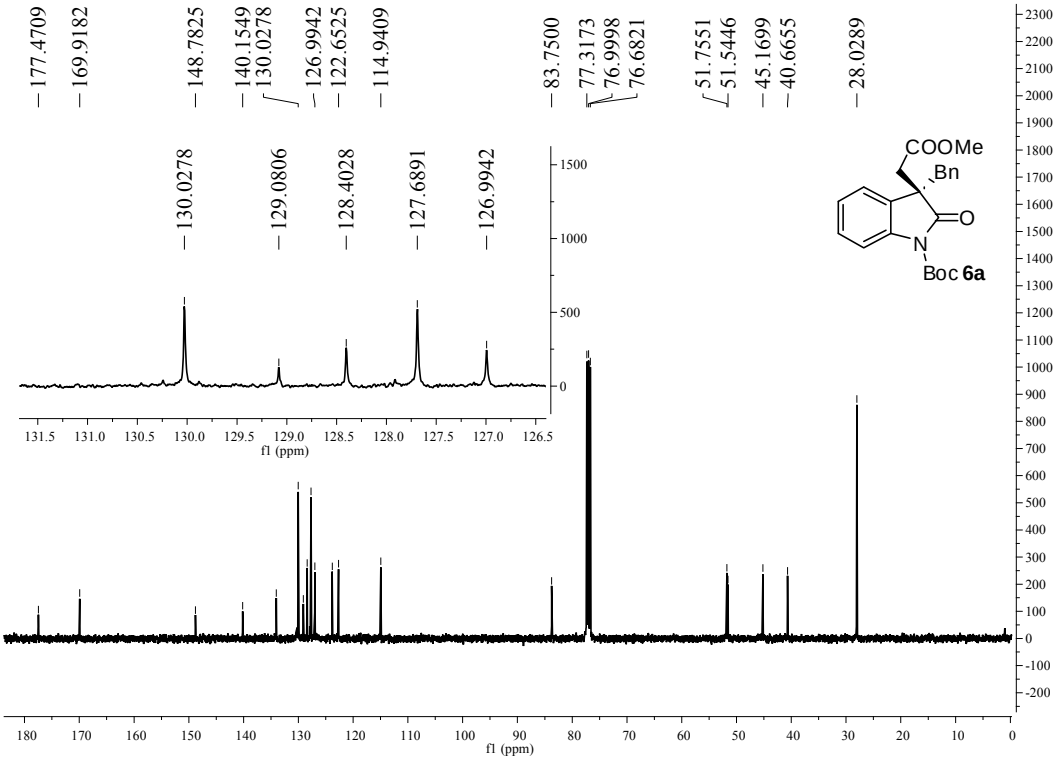
5.17
1.87
3.00
1.12
2.95
9.05
f1 (ppm)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45.1699
40.6655
28.0289
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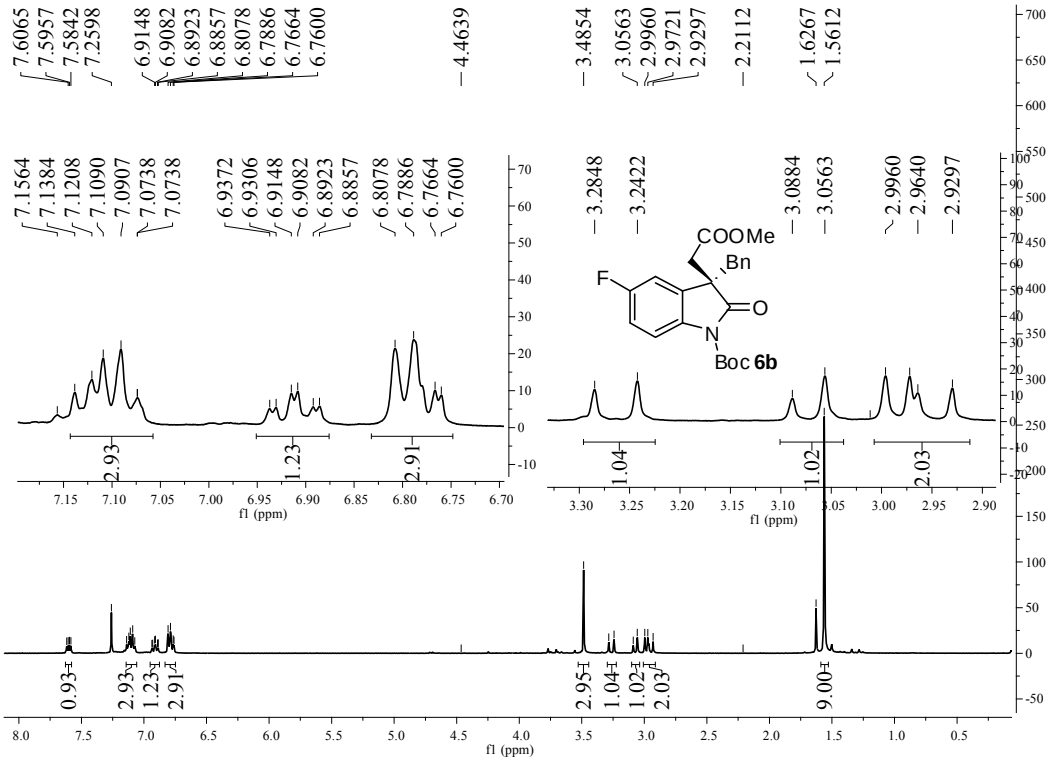
128.4028
127.6891
126.9942
COOMe
Bn
O
N
Boc 6a
f1 (ppm)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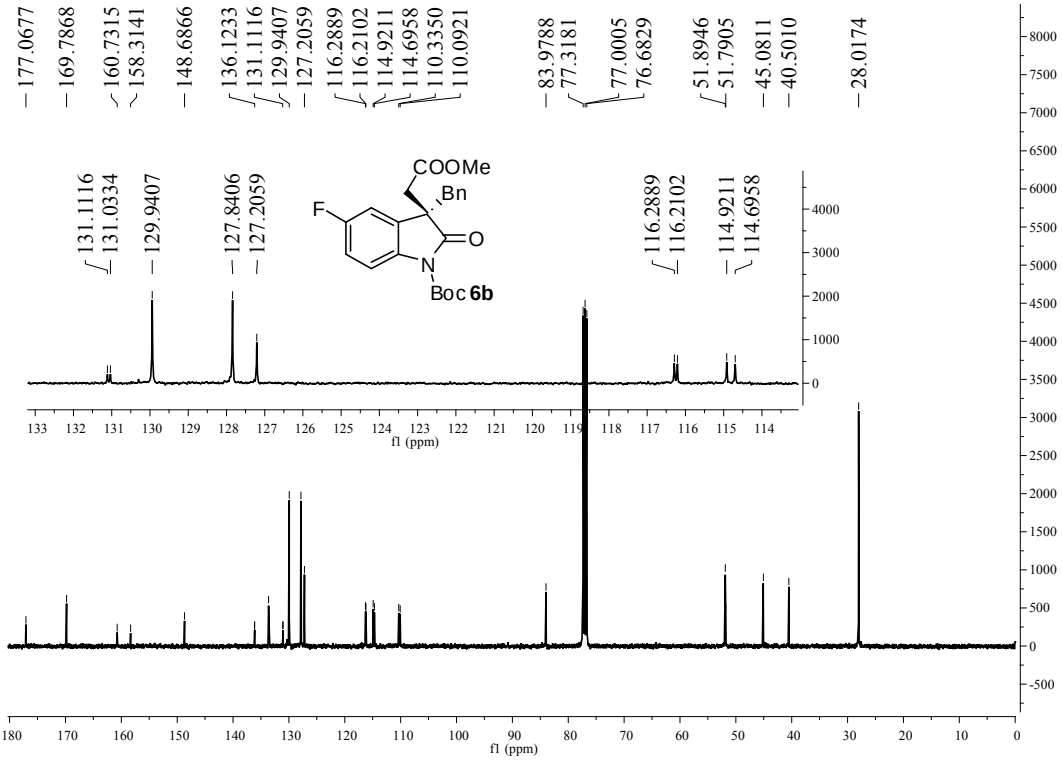
2.9960
2.9721
2.9297
2.2112
1.6267
1.5612
COOMe
Bn
F
O
N
Boc 6b
2.93
1.23
2.91
1.04
1.02
2.03
0.93
2.93
1.23
2.91
2.95
1.04
1.02
2.03
9.00
f1 (ppm)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136.1233
131.1116
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127.2059
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116.2102
114.9211
114.6958
110.3350
110.0921
83.9788
77.3181
77.0005
76.6829
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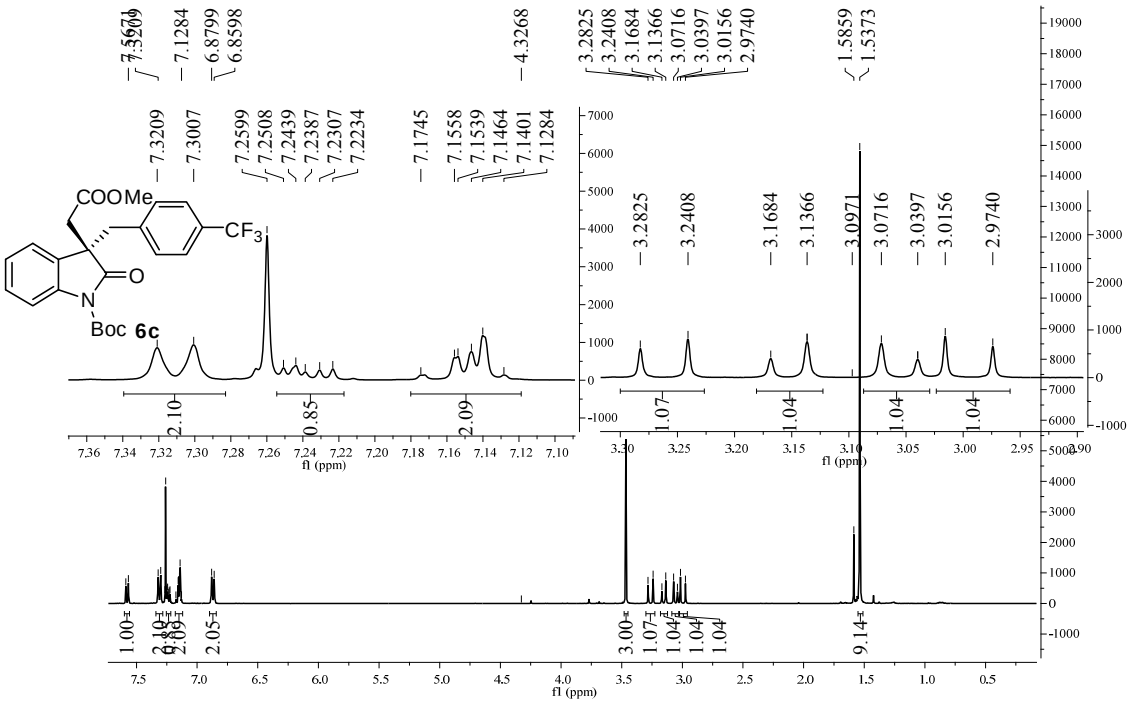
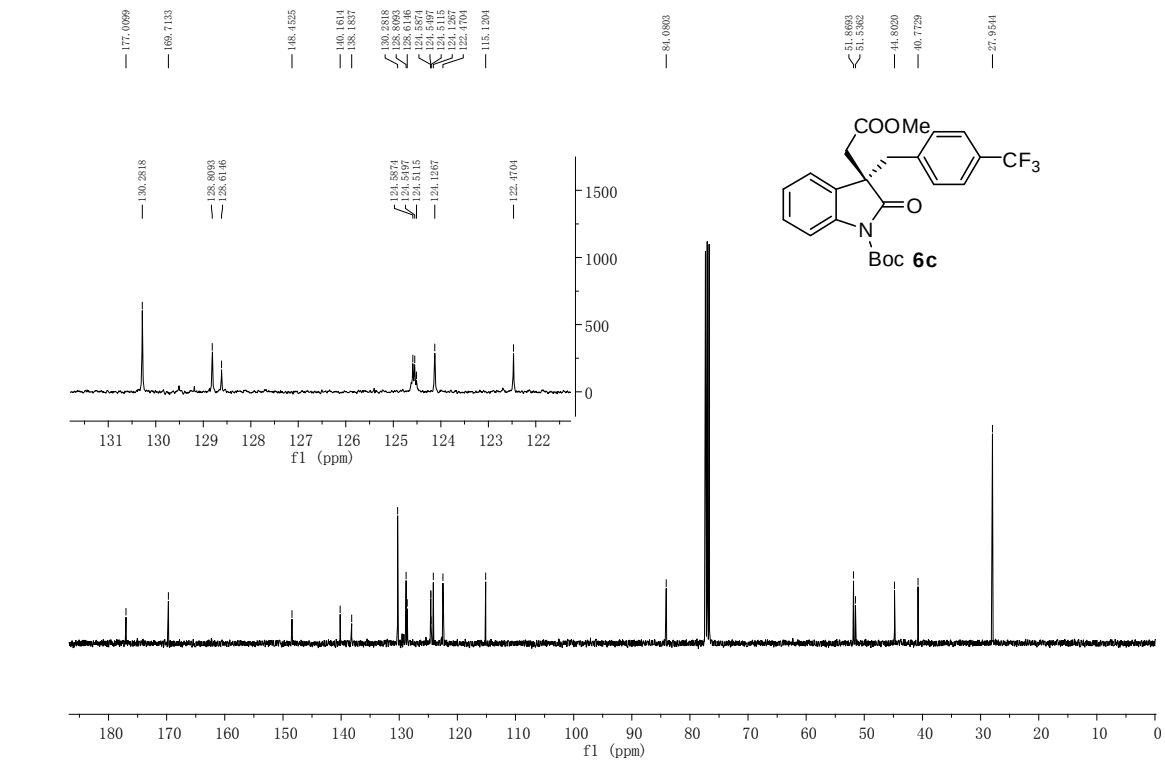
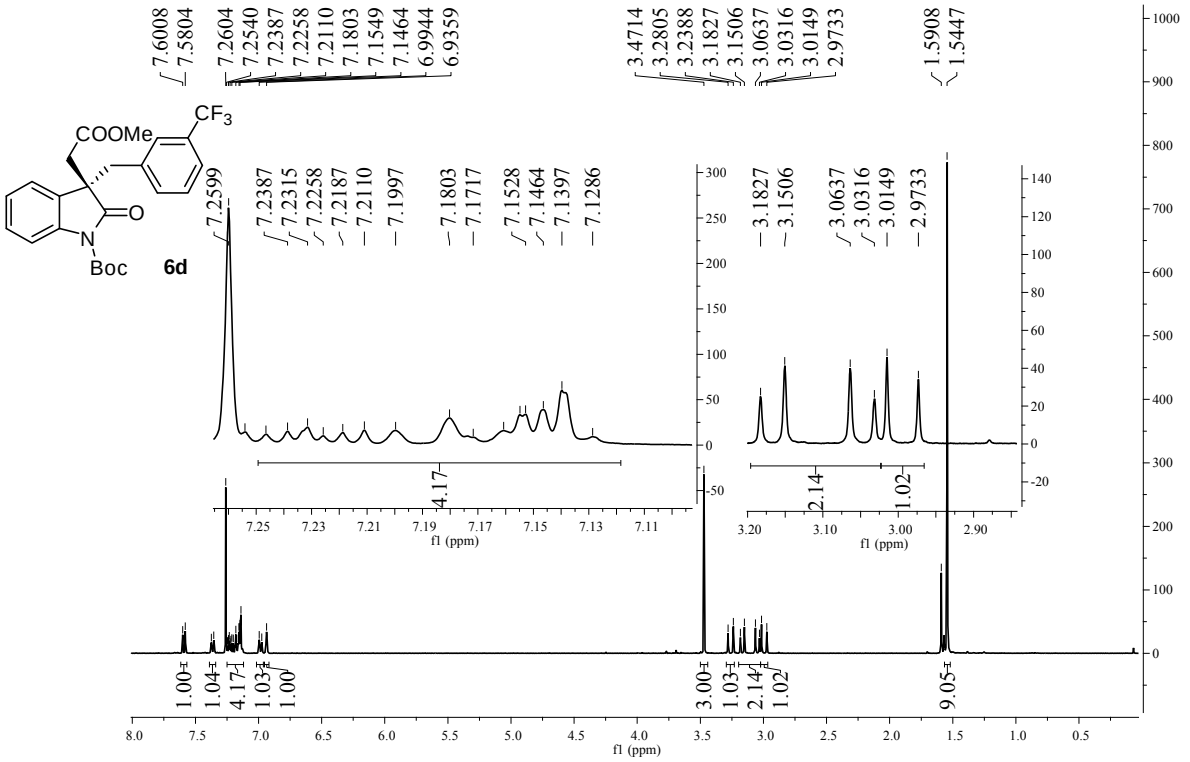
51.7905
45.0811
40.5010
28.0174
COOMe
Bn
F
O
N
Boc 6b
f1 (ppm)



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6.9359
3.4714
3.2805
3.2388
3.1827
3.1506
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2.9733
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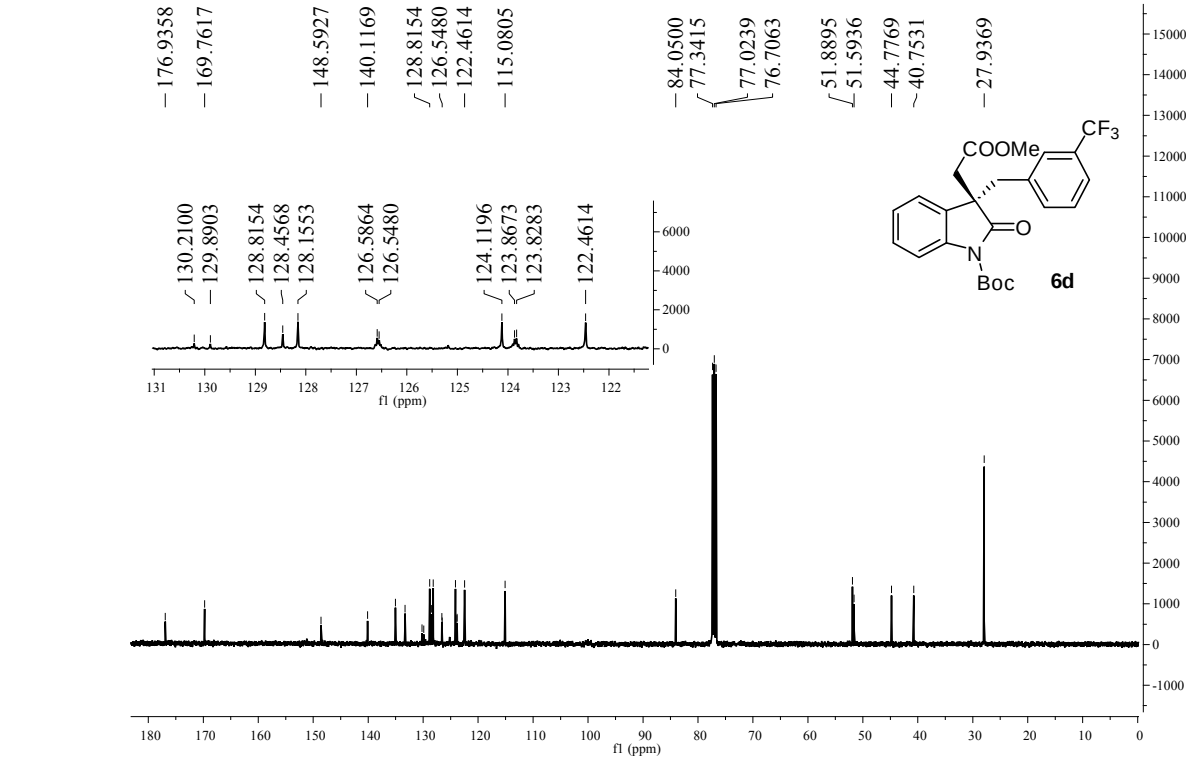
1.5447
COOMe
CF3
N
Boc
6d
f1 (ppm)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76.7063
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51.5936
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27.9369
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129.8903
128.8154
128.4568
128.1553
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123.8673
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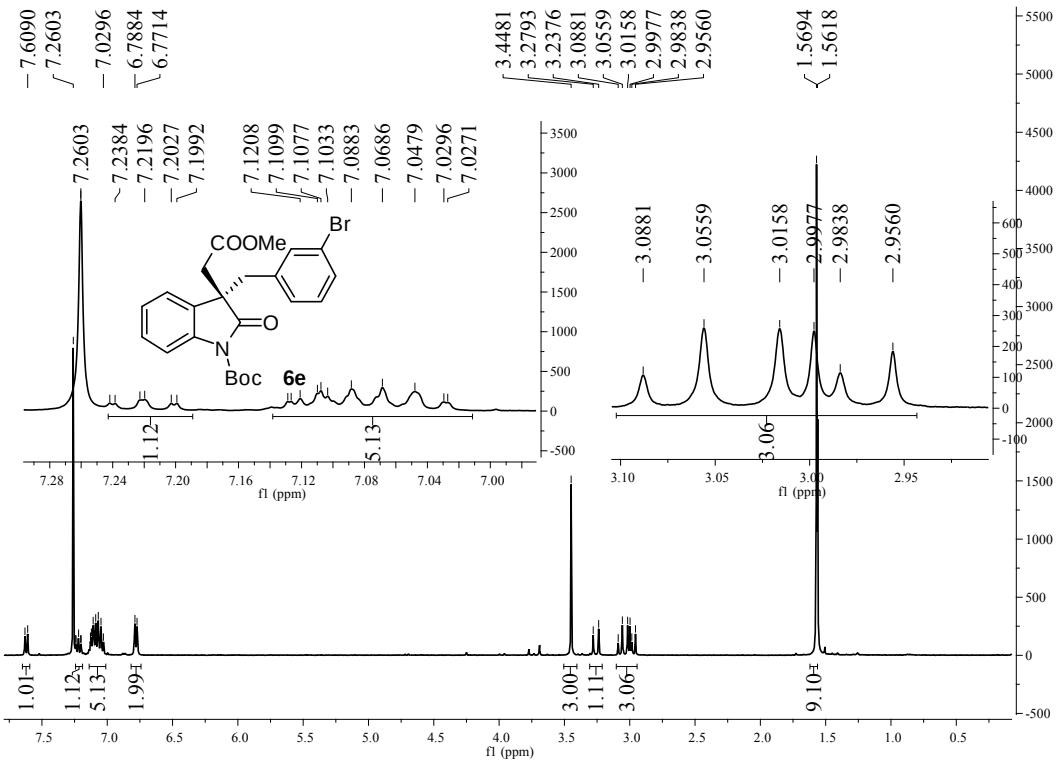
COOMe
CF3
N
Boc
6d
f1 (ppm)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3.0158
2.9977
2.9838
2.9560
1.5694
1.5618
COOMe
Br
O
N
Boc
6e
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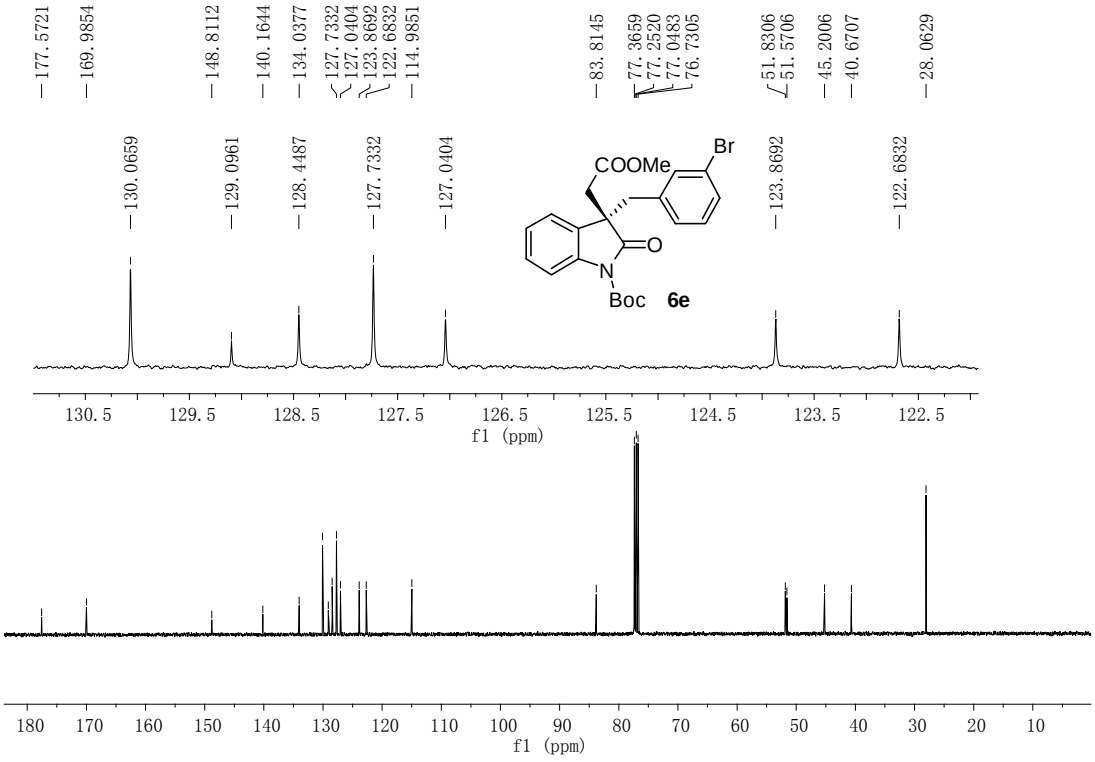
1.12
5.13
1.99
3.00
1.11
3.06
9.10
f1 (ppm)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77.2520
77.0483
76.7305
51.8306
51.5706
45.2006
40.6707
28.0629
130.0659
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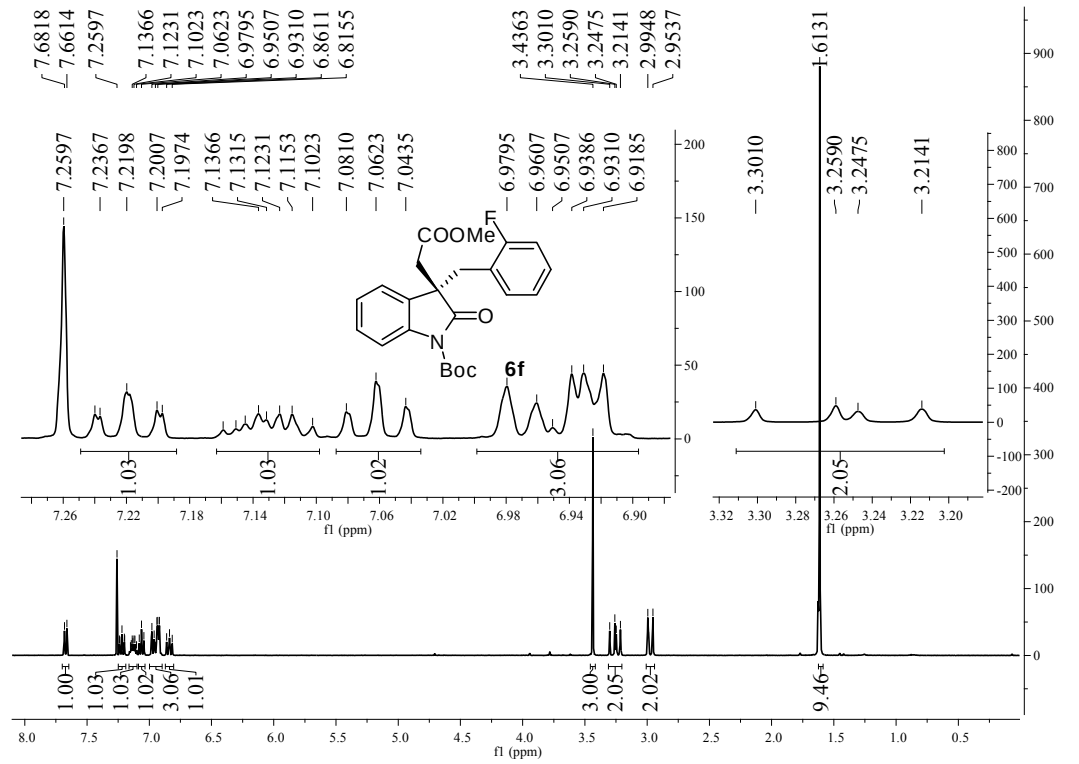
COOMe
Br
O
N
Boc
6e
f1 (ppm)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6.9310
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6.8155
3.4363
3.3010
3.2590
3.2475
3.2141
2.9948
2.9537
1.6131
COOMe
F
O
N
Boc
6f
1.03
1.03
1.02
3.06
2.05
1.00
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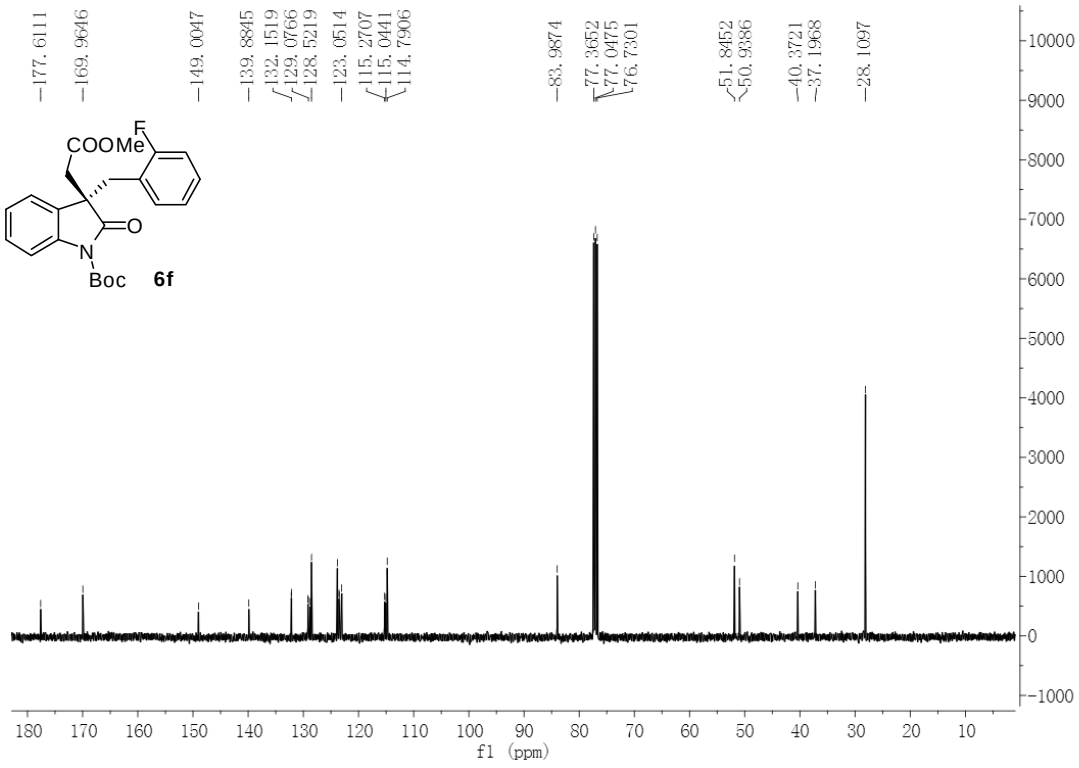
1.03
1.02
3.06
1.01
3.00
2.05
2.02
9.46
f1 (ppm)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77.0475
76.7301
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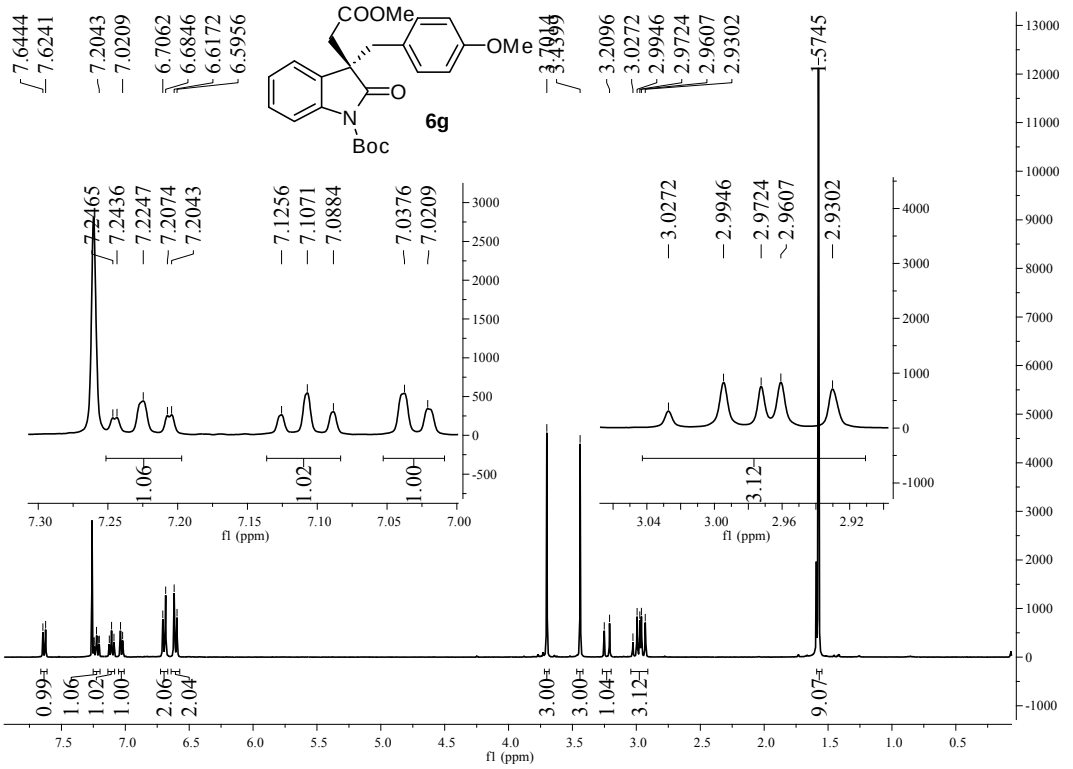
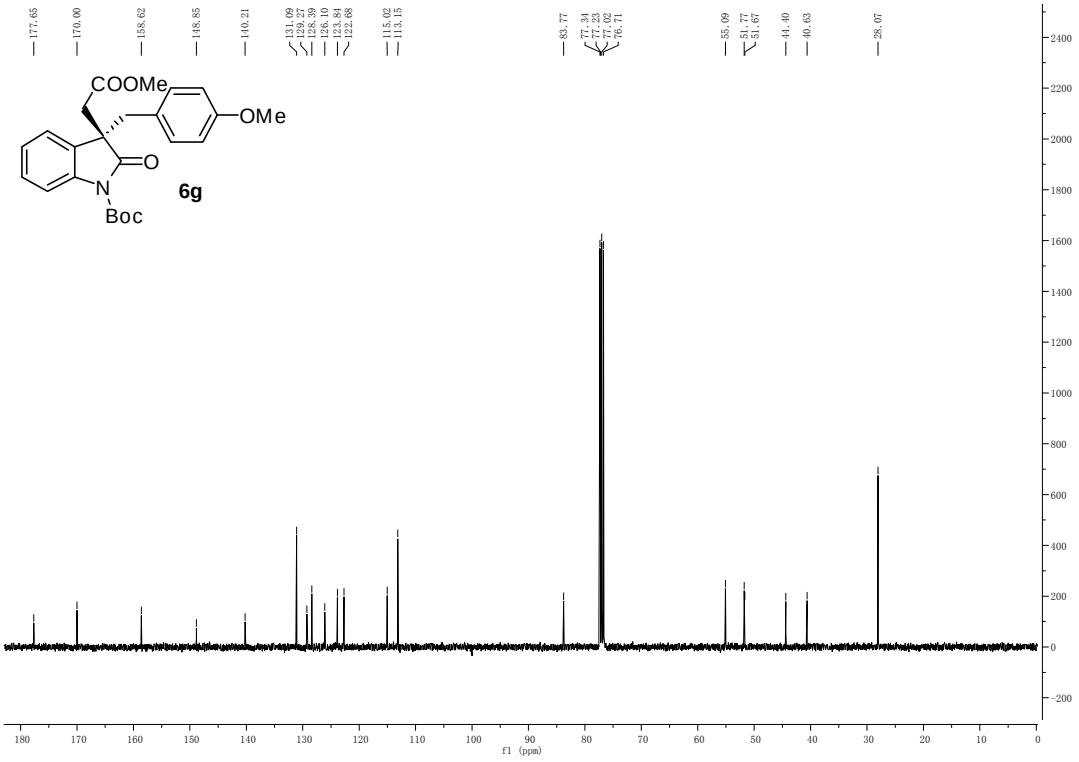
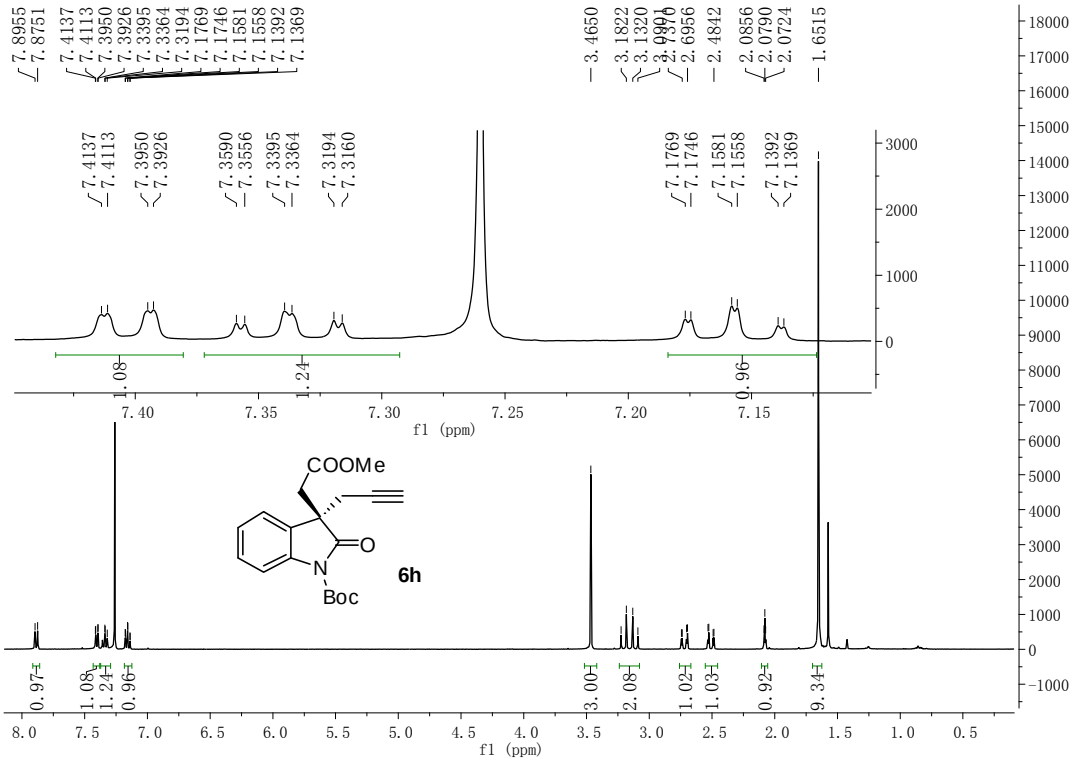
COOMe
F
O
N
Boc
6f
f1 (ppm)



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7.1581
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7.1392
7.1369
3.4650
3.1822
3.1320
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2.0856
2.0790
2.0724
1.6515
1.08
1.24
0.96
f1 (ppm)
COOMe
O
N
Boc
6h
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3.00
2.08
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1.03
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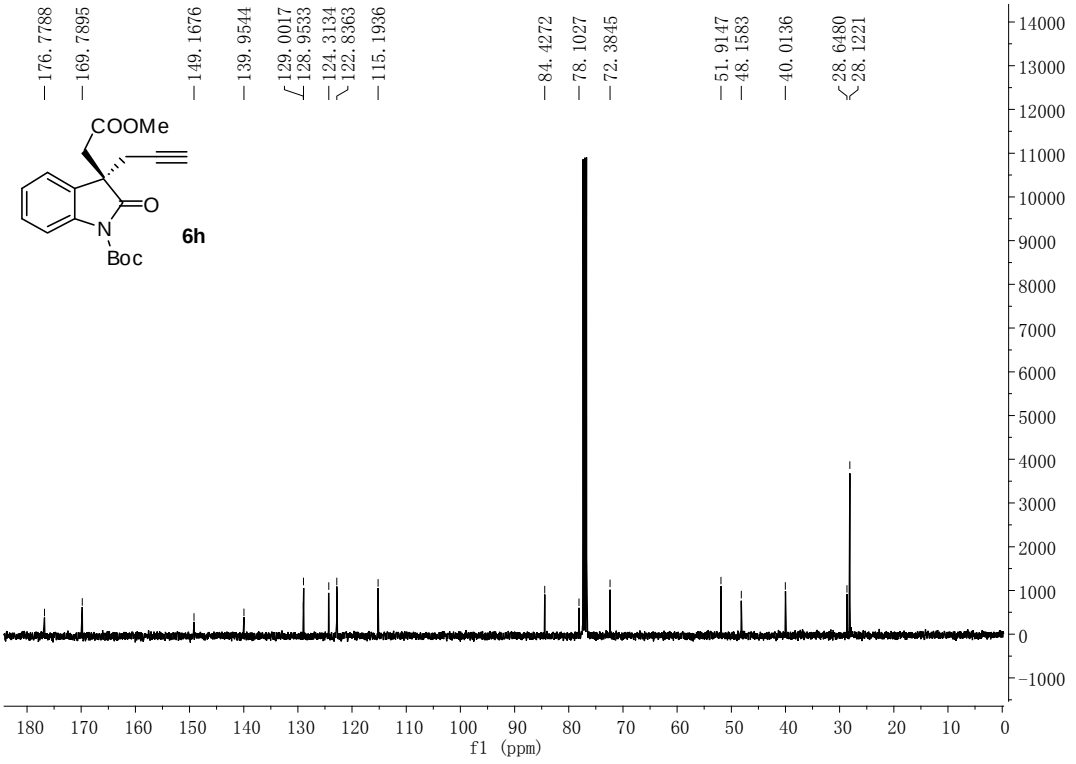
f1 (ppm)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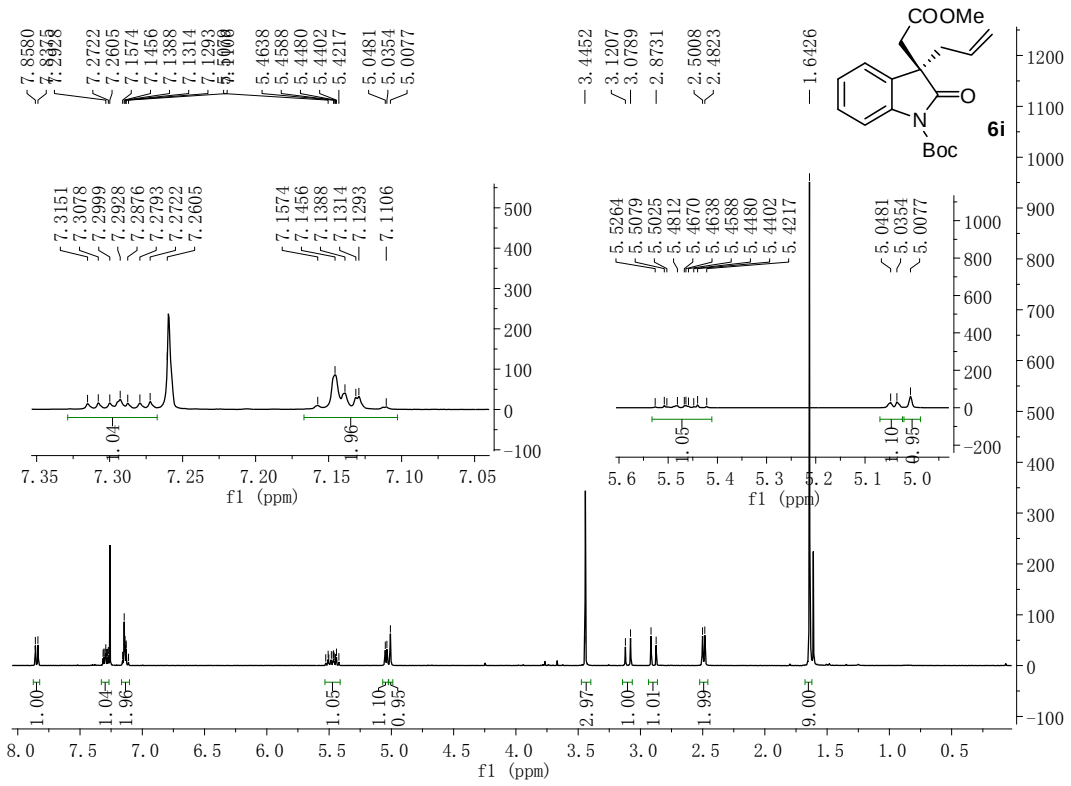
COOMe
O
N
Boc
6h
f1 (ppm)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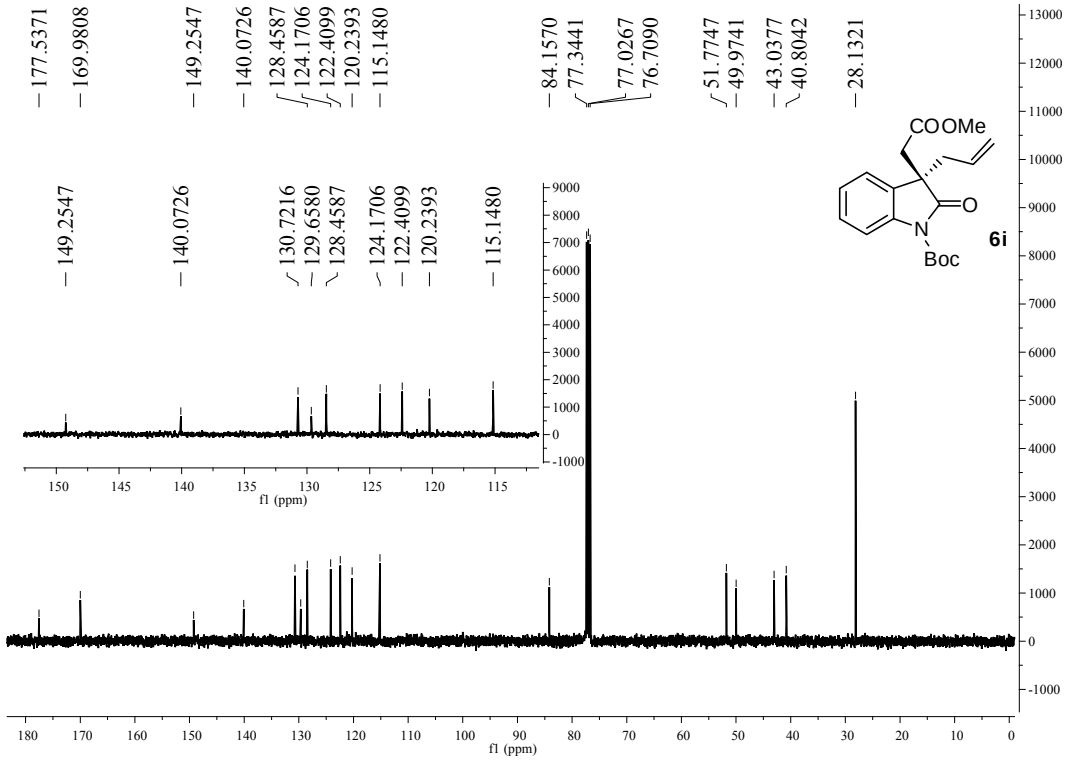
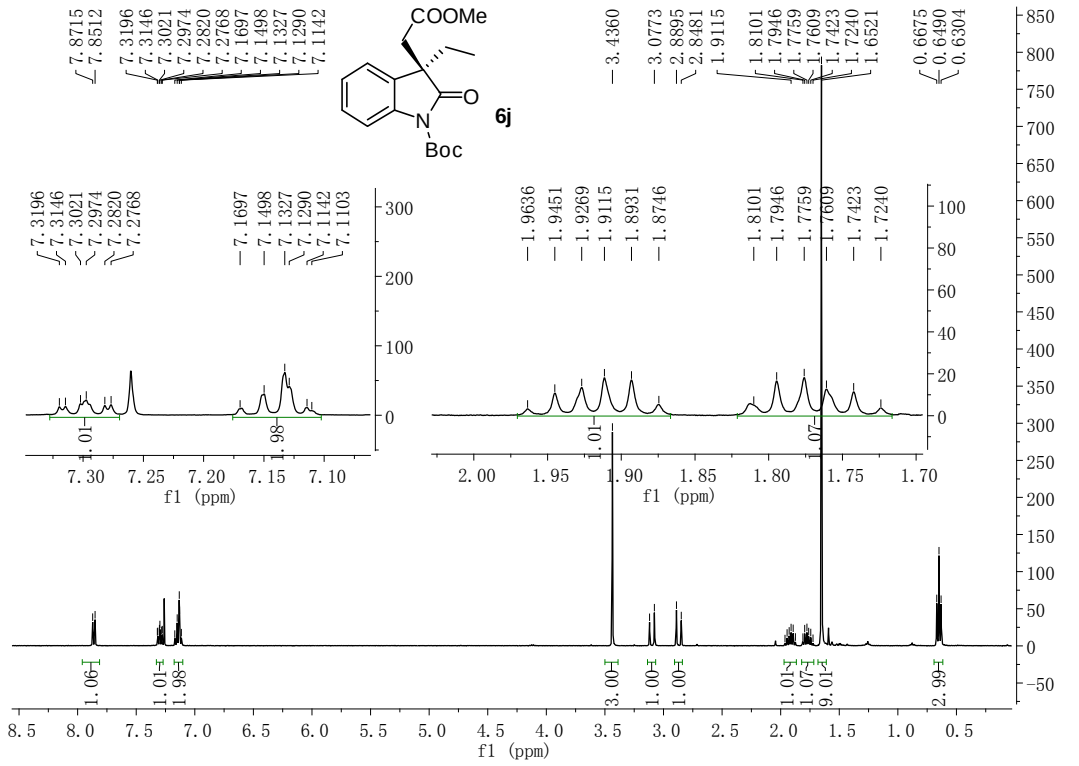
Boc
6i
f1 (ppm)


COOMe
N
Boc
6i
f1 (ppm)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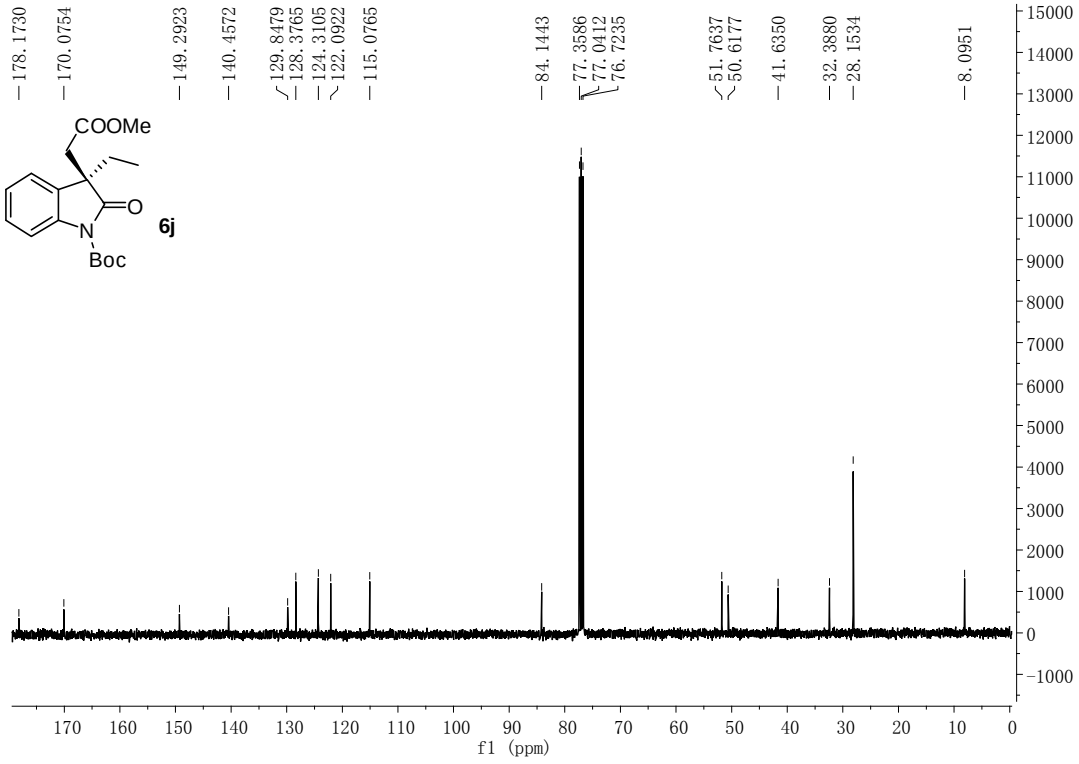
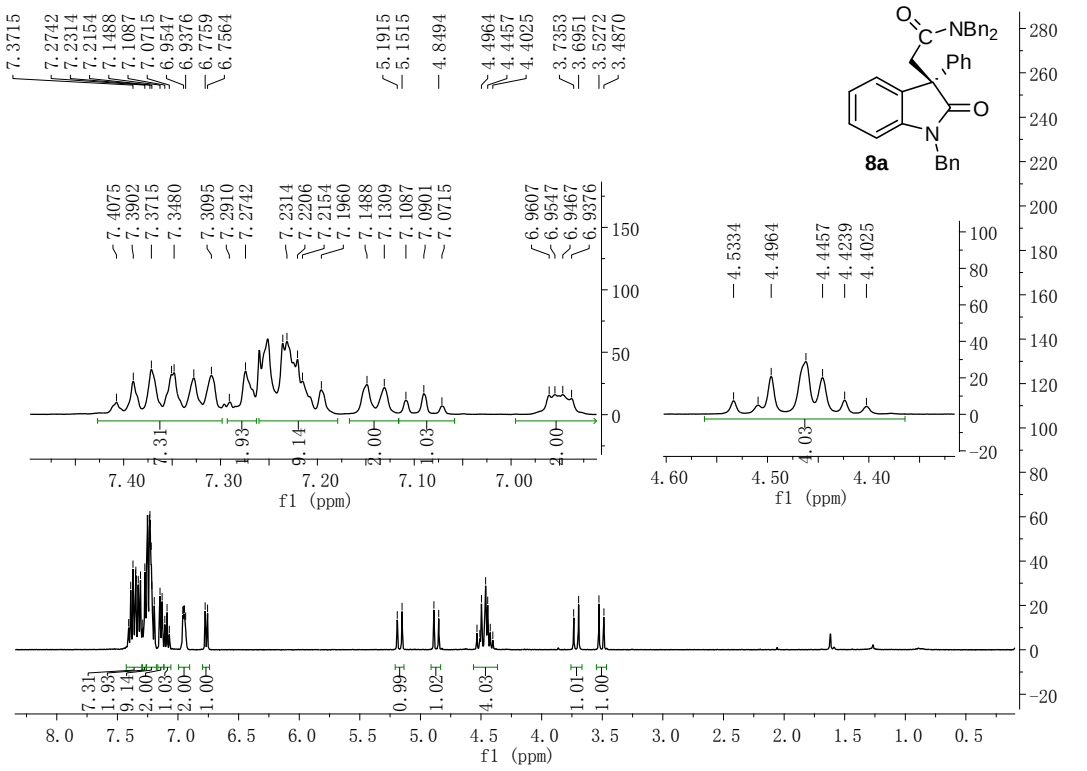
O
N
Boc
6j
f1 (ppm)


COOMe
O
N
Boc
6j
f1 (ppm)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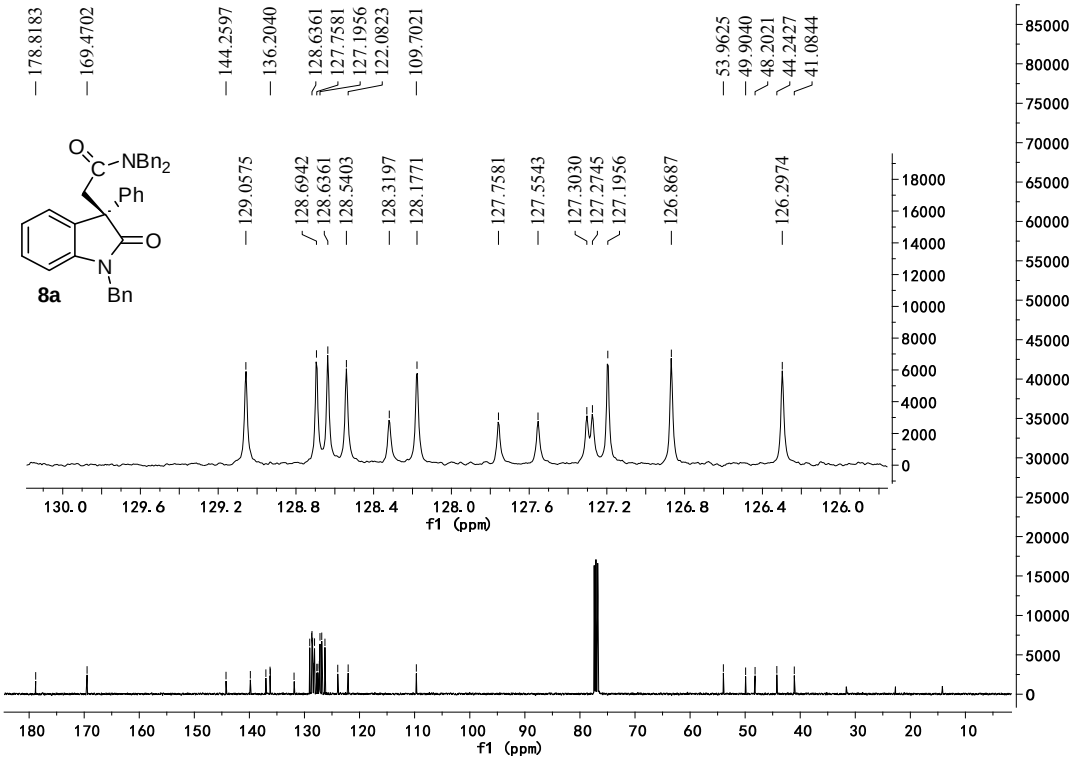
f1 (ppm)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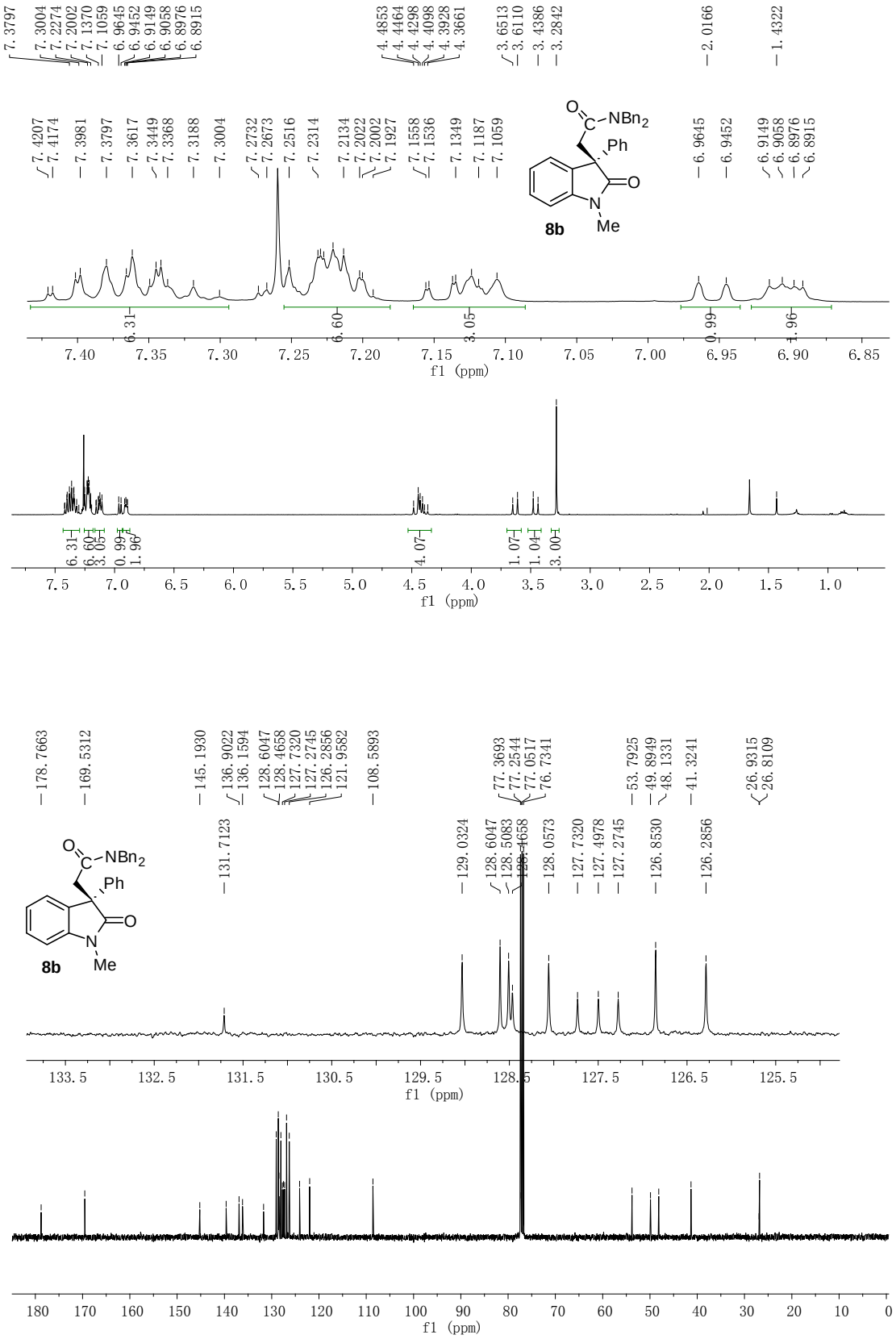
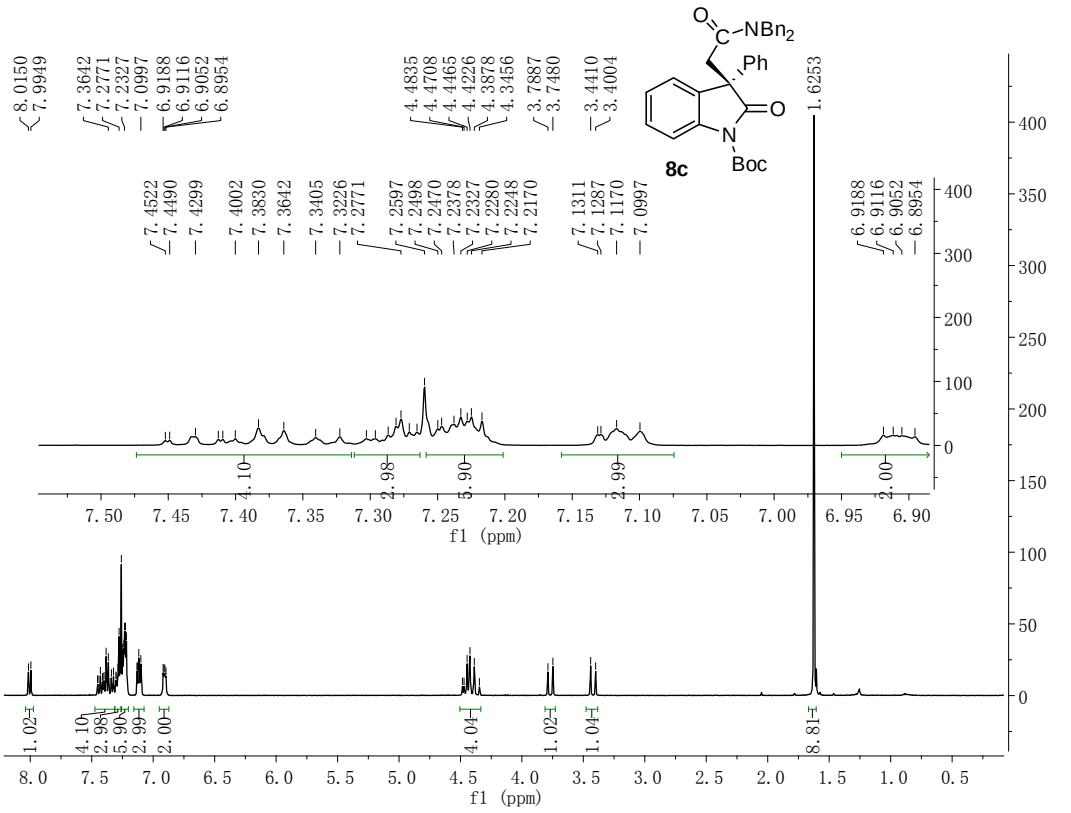
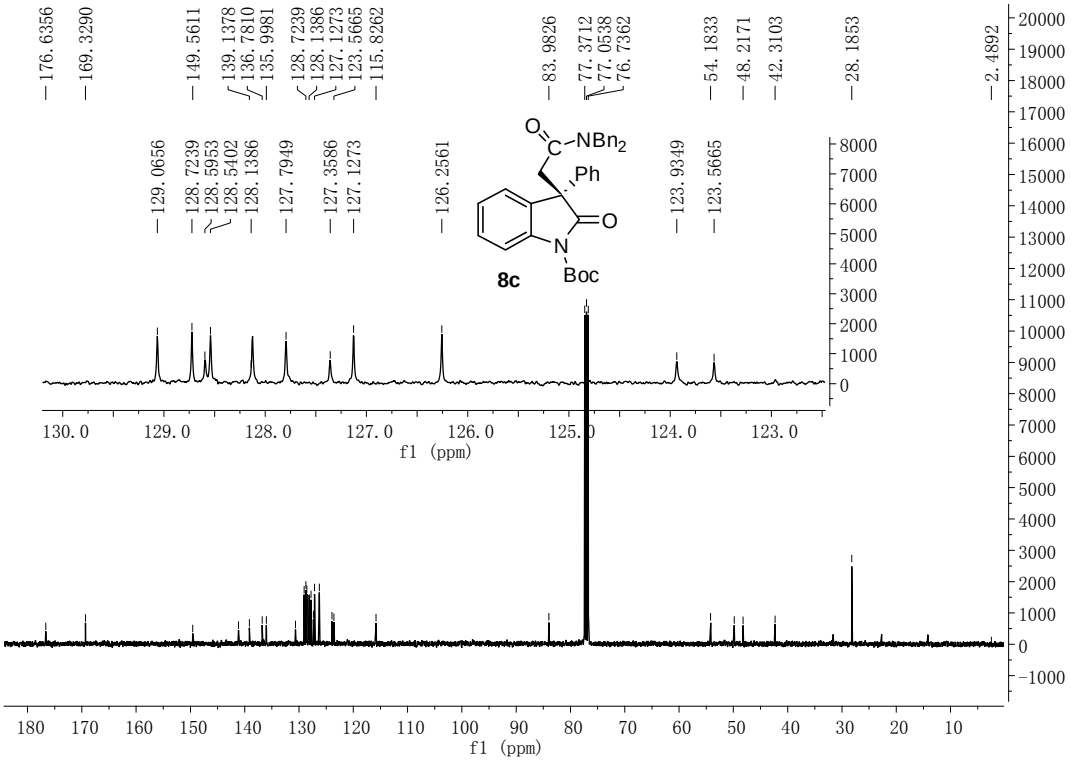
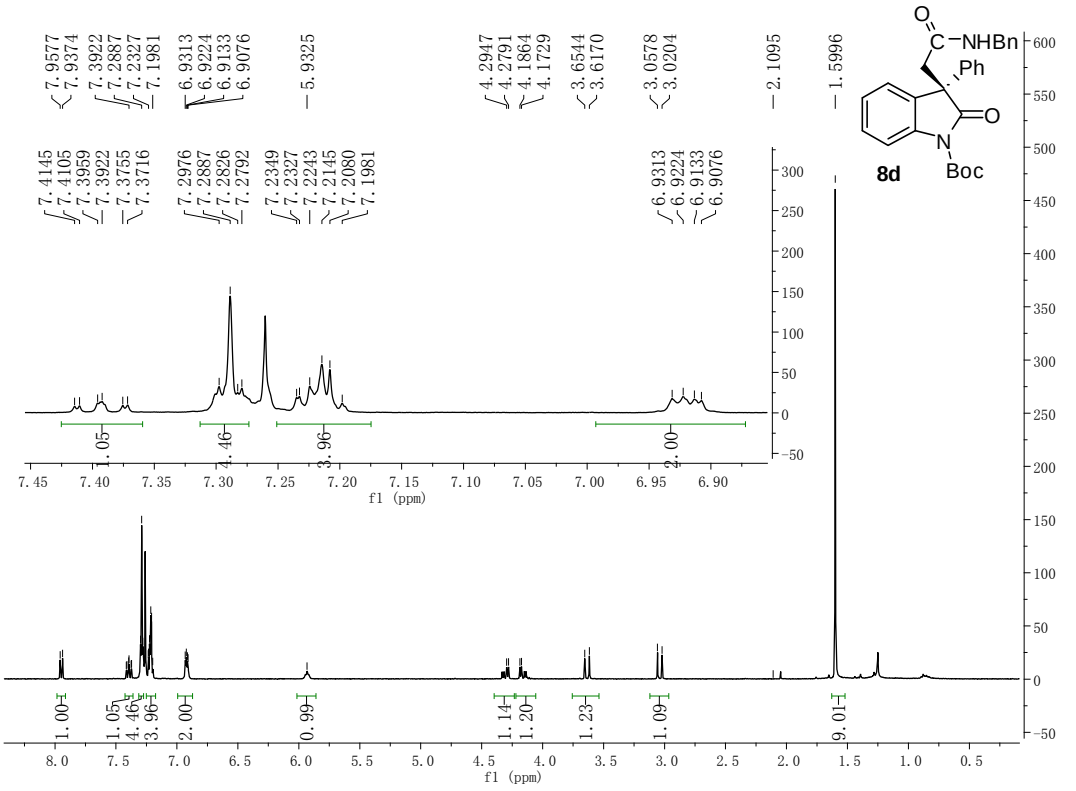

8b
f1 (ppm)
8b
f1 (ppm)


8c
f1 (ppm)


8c
f1 (ppm)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6.9313
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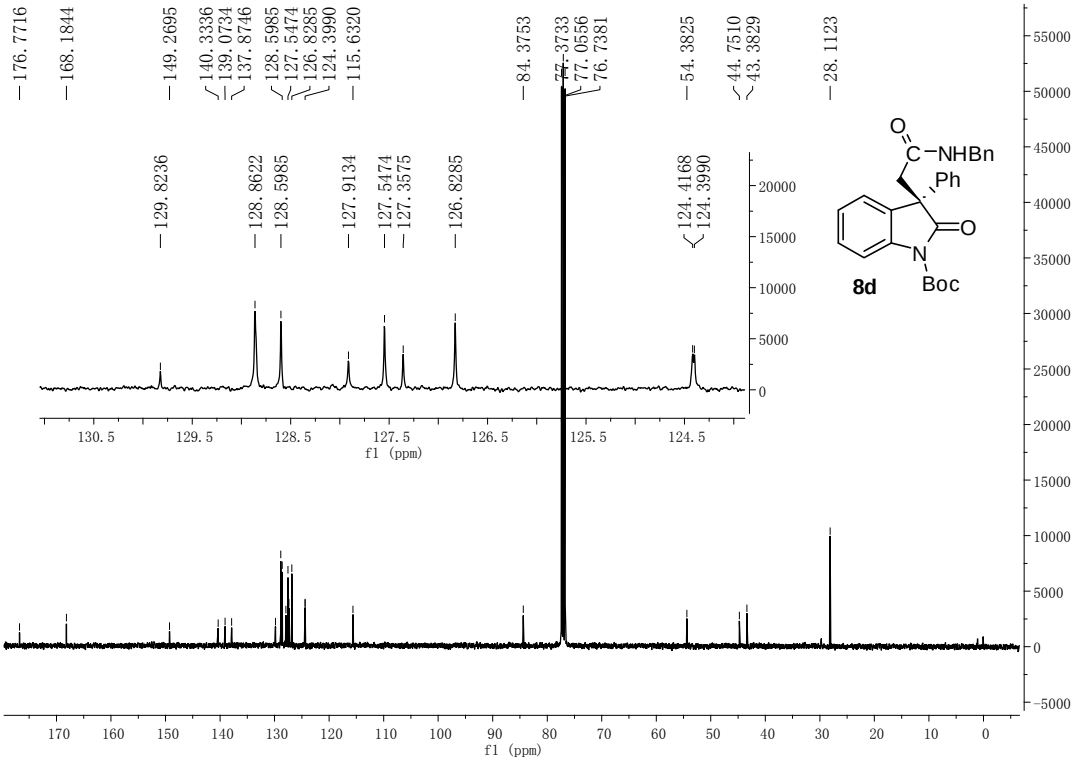
6.9133
6.9076
5.9325
4.2947
4.2791
4.1864
4.1729
3.6544
3.6170
3.0578
3.0204
2.1095
1.5996
7.4145
7.4105
7.3959
7.3922
7.3755
7.3716
7.2976
7.2887
7.2826
7.2792
7.2349
7.2327
7.2243
7.2145
7.2080
7.1981
6.9313
6.9224
6.9133
6.9076
1.05
4.46
3.96
2.00
f1 (ppm)
1.00
1.05
4.46
3.96
2.00
0.99
1.14
1.20
1.23
1.09
9.01
f1 (ppm)
O
C
NHBn
Ph
O
N
Boc
8d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149.2695
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128.5985
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126.8285
124.3990
115.6320
84.3753
77.3733
77.0556
76.7381
54.3825
44.7510
43.3829
28.1123
129.8236
128.8622
128.5985
127.9134
127.5474
127.3575
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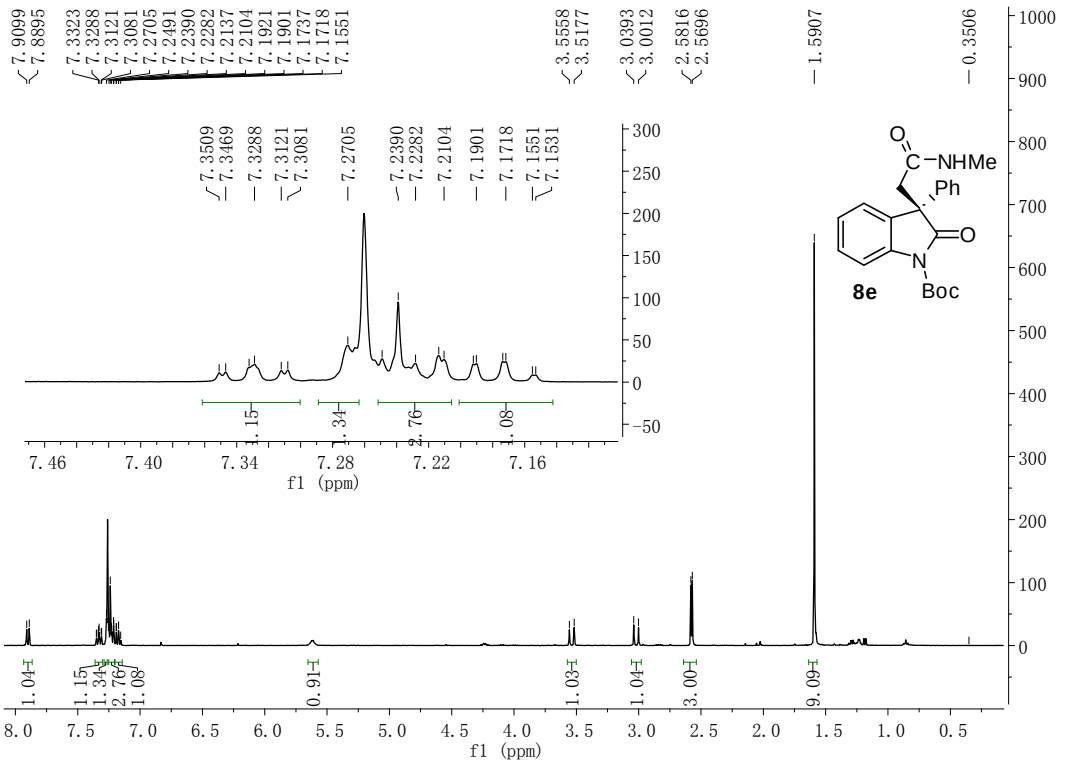
124.4168
124.3990
f1 (ppm)
O
C
NHBn
Ph
O
N
Boc
8d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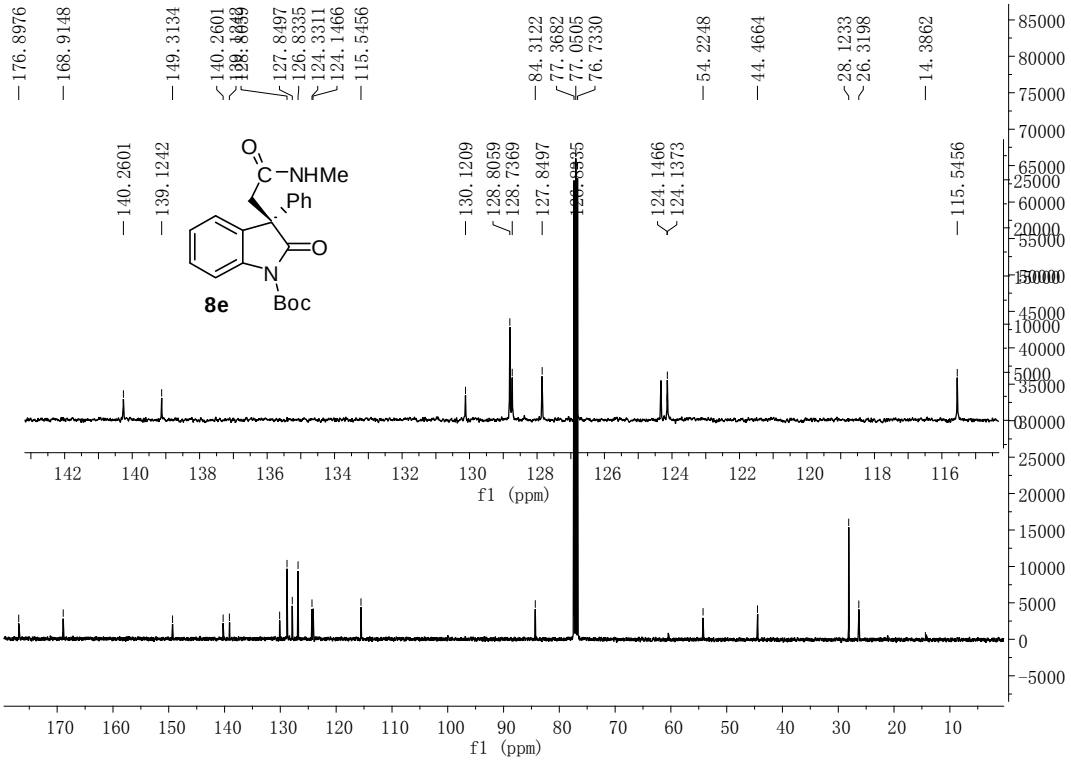
7.3121
7.3081
7.2705
7.2491
7.2390
7.2282
7.2137
7.2104
7.1921
7.1901
7.1737
7.1718
7.1551
3.5558
3.5177
3.0393
3.0012
2.5816
2.5696
1.5907
0.3506
7.3509
7.3469
7.3288
7.3121
7.3081
7.2705
7.2390
7.2282
7.2104
7.1901
7.1718
7.1551
7.1531
1.15
1.34
2.76
1.08
7.46
7.40
7.34
7.28
7.22
7.16
f1 (ppm)
1.04
1.15
1.34
2.76
1.08
0.91
1.03
1.04
3.00
9.09
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
O
C
NHMe
Ph
O
N
Boc
8e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128.8059
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127.8497
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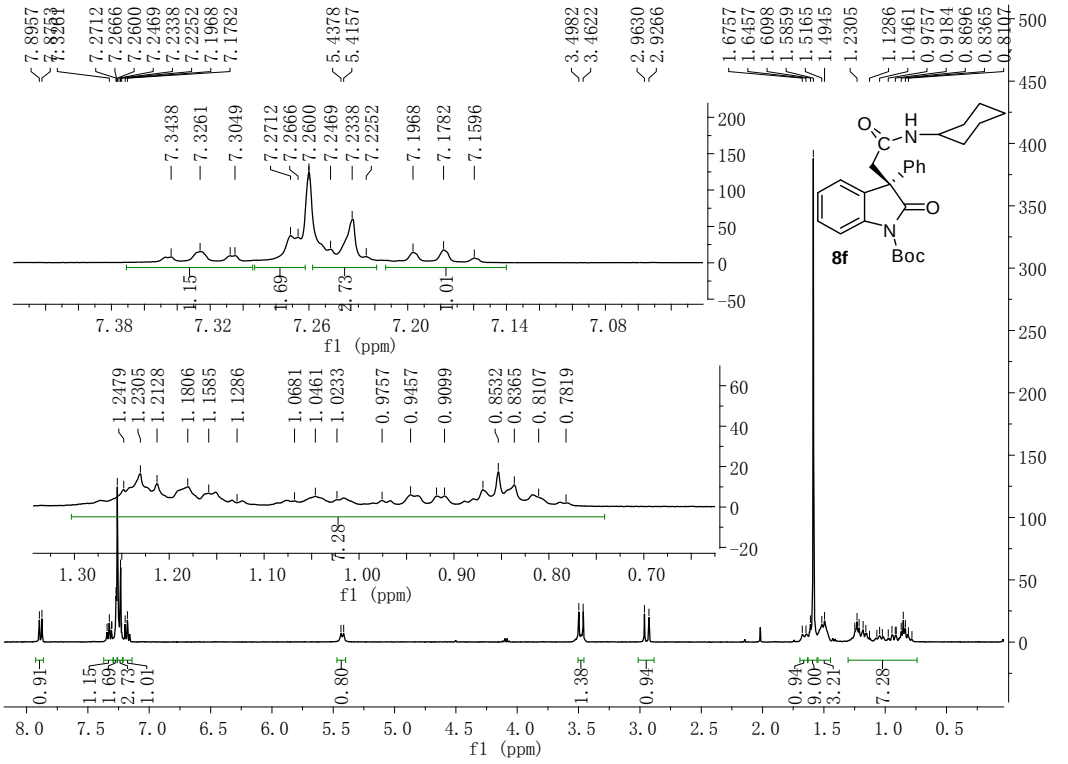
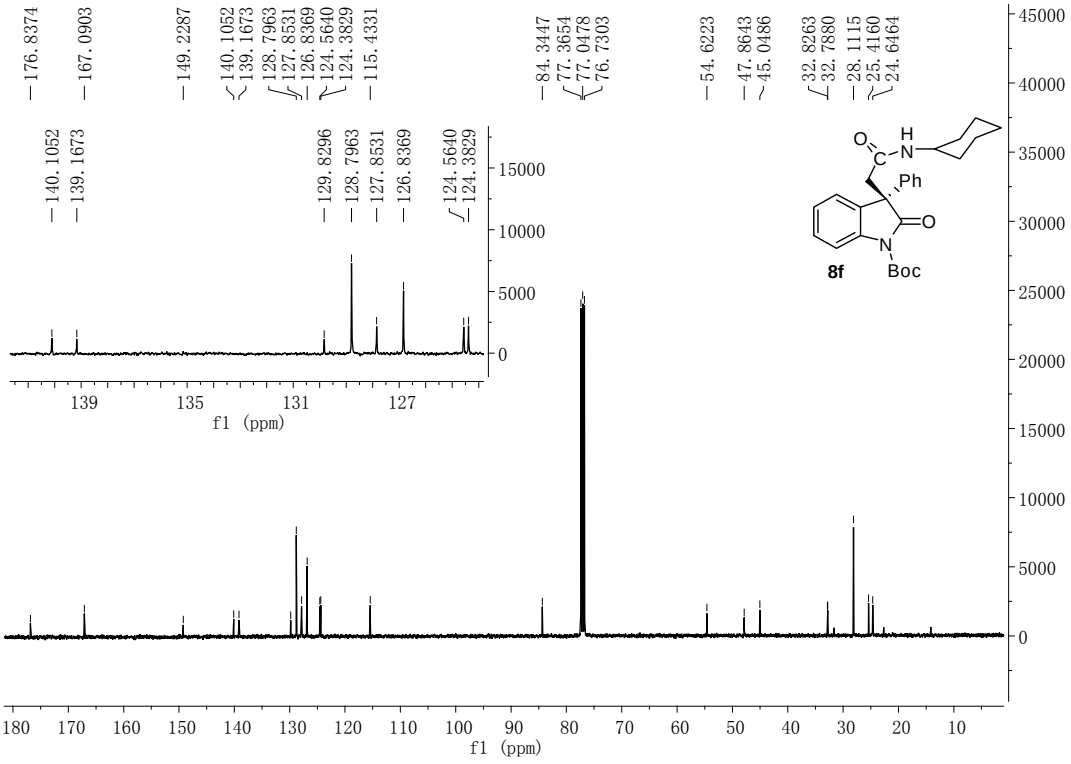
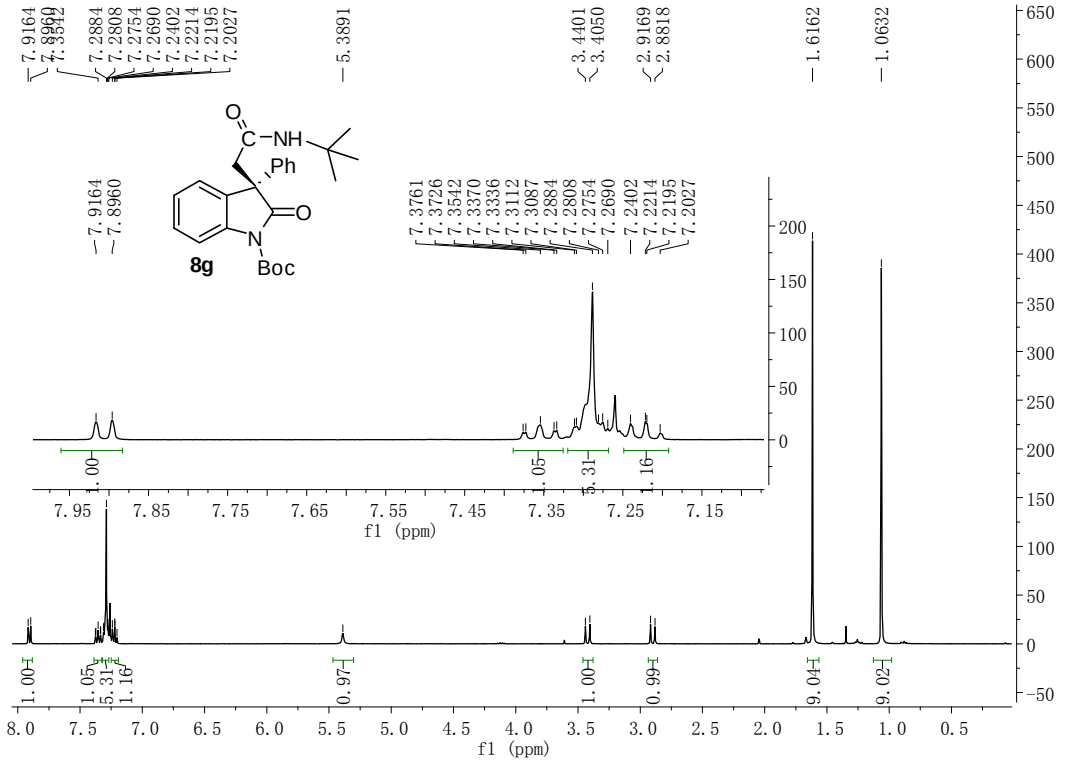
124.3311
124.1466
124.1373
115.5456
84.3122
77.3682
77.0505
76.7330
54.2248
44.4664
28.1233
26.3198
14.3862
O
C
NHMe
Ph
O
N
Boc
8e
142
140
138
136
134
132
130
128
126
124
122
120
118
116
f1 (ppm)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


8f
Boc
Ph
f1 (ppm)


8f
Boc
Ph
f1 (ppm)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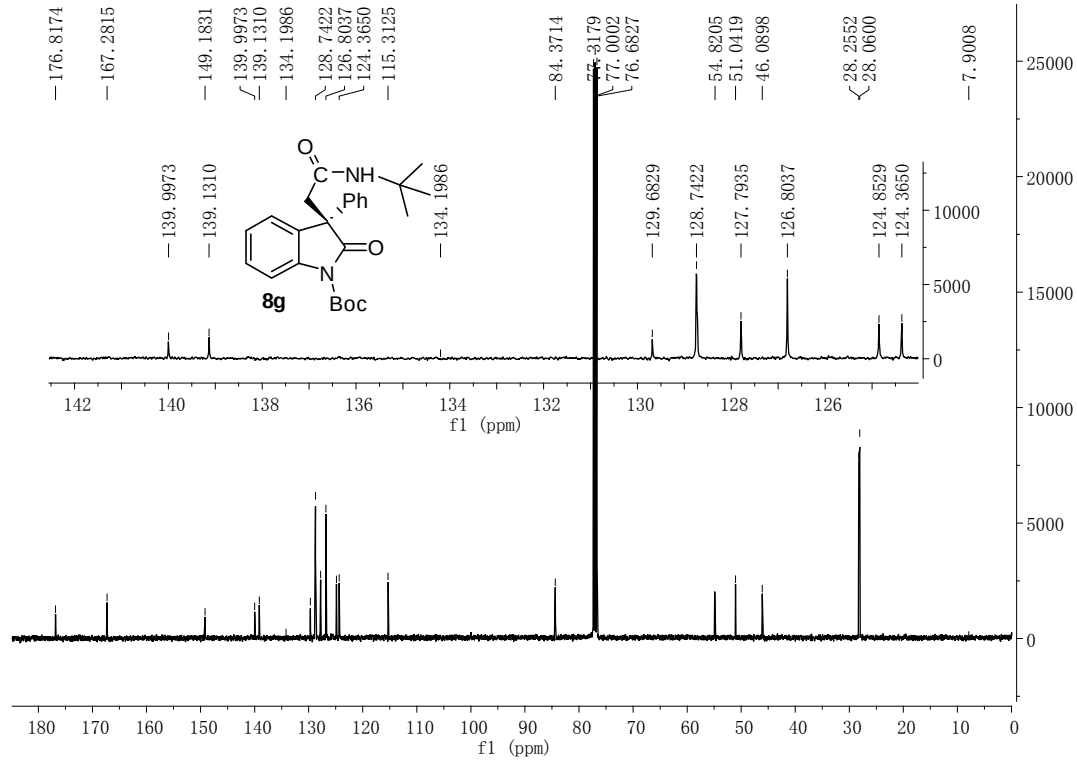
7.3542
7.2884
7.2808
7.2754
7.2690
7.2402
7.2214
7.2195
7.2027
5.3891
3.4401
3.4050
2.9169
2.8818
1.6162
1.0632
O
C–NH
Ph
O
N
Boc
8g
f1 (ppm)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139.1310
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128.7422
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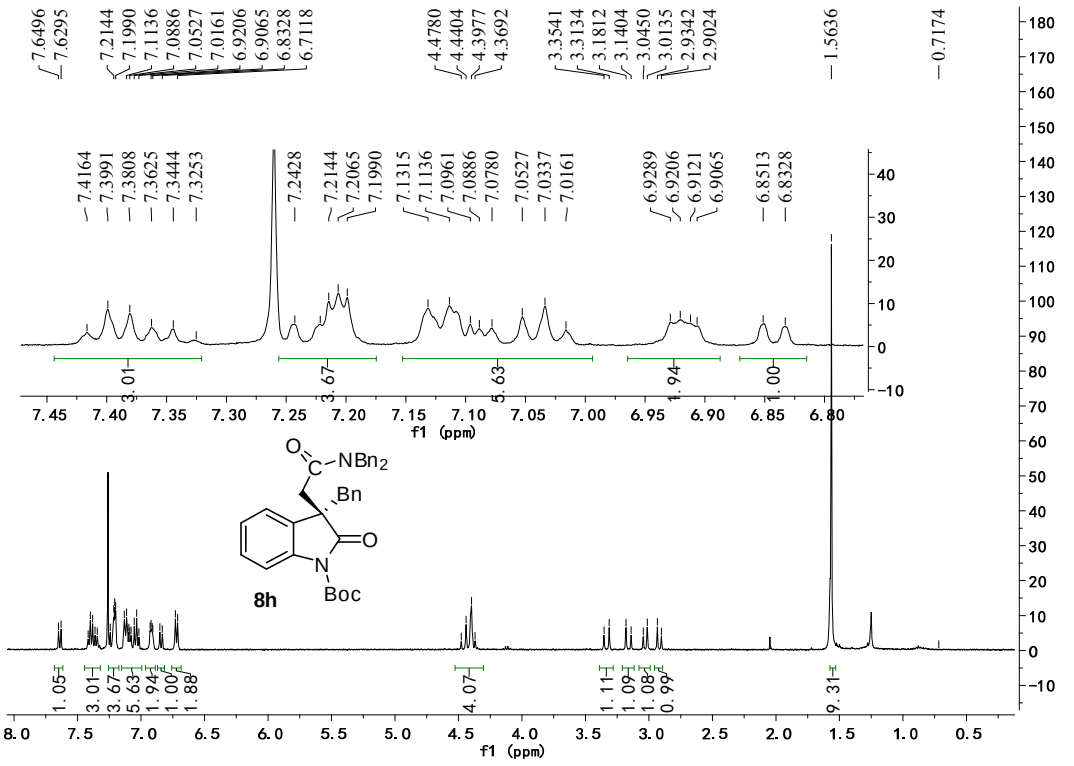
124.3650
115.3125
84.3714
77.3179
77.0002
76.6827
54.8205
51.0419
46.0898
28.2552
28.0600
7.9008
129.6829
128.7422
127.7935
126.8037
124.8529
124.3650
O
C–NH
Ph
O
N
Boc
8g
f1 (ppm)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7.0527
7.0161
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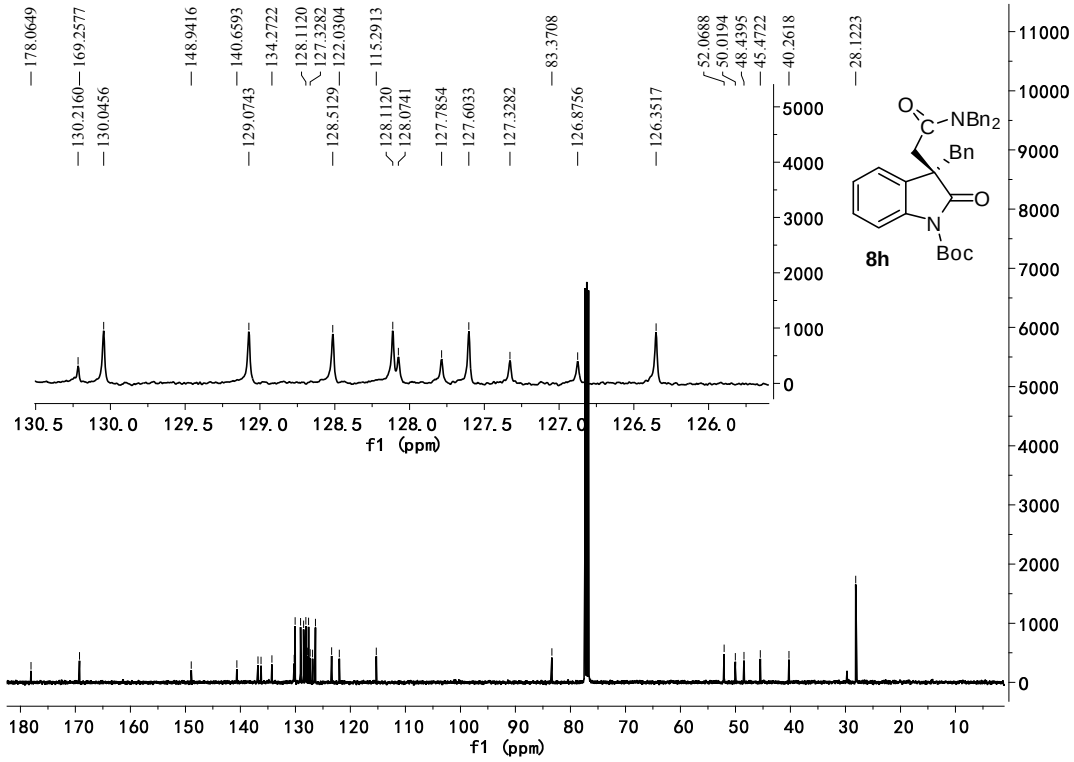
6.9065
6.8328
6.7118
4.4780
4.4404
4.3977
4.3692
3.3541
3.3134
3.1812
3.1404
3.0450
3.0135
2.9342
2.9024
1.5636
0.7174
7.4164
7.3991
7.3808
7.3625
7.3444
7.3253
7.2428
7.2144
7.2065
7.1990
7.1315
7.1136
7.0961
7.0886
7.0780
7.0527
7.0337
7.0161
6.9289
6.9206
6.9121
6.9065
6.8513
6.8328
3.01
3.67
5.63
1.94
1.00
f1 (ppm)
NBn2
Bn
Boc
8h
1.05
3.01
3.67
5.63
1.94
1.00
1.88
4.07
1.11
1.09
1.08
0.99
9.31
f1 (ppm)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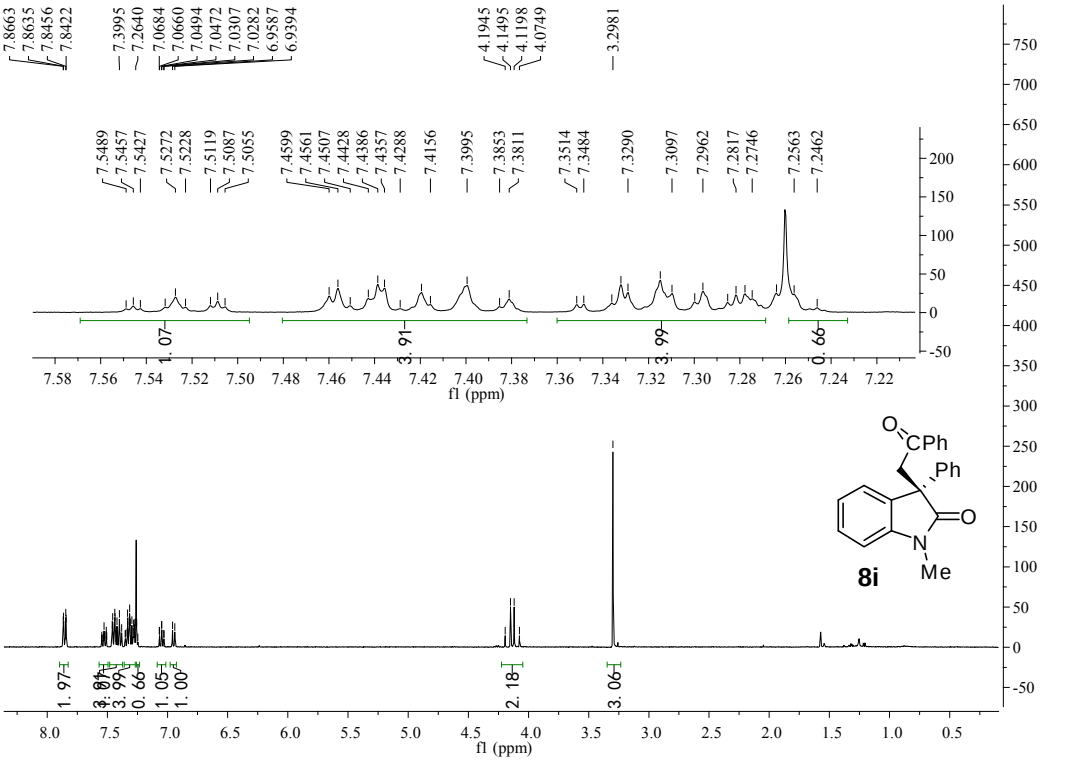
128.1120
128.0741
127.7854
127.6033
127.3282
83.3708
126.8756
126.3517
52.0688
50.0194
48.4395
45.4722
40.2618
28.1223
f1 (ppm)
NBn2
Bn
Boc
8h
f1 (ppm)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7.0494
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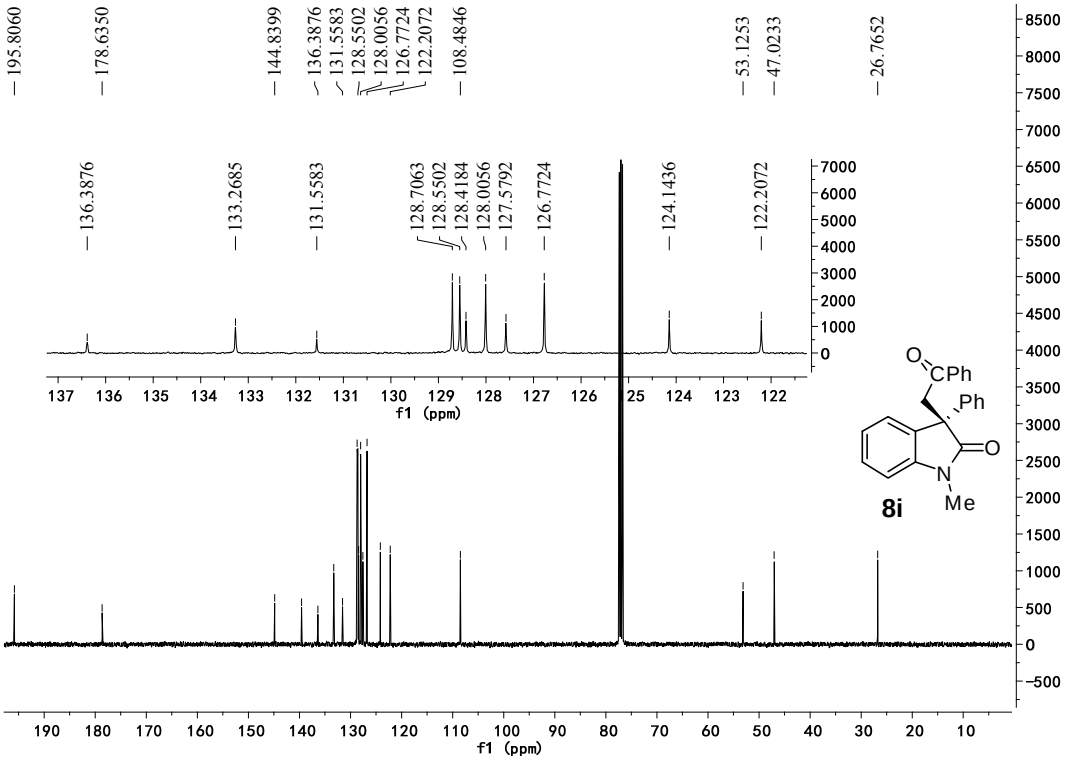
7.0282
6.9587
6.9394
4.1945
4.1495
4.1198
4.0749
3.2981
7.5489
7.5457
7.5427
7.5272
7.5228
7.5119
7.5087
7.5055
7.4599
7.4561
7.4507
7.4428
7.4386
7.4357
7.4288
7.4156
7.3995
7.3853
7.3811
7.3514
7.3484
7.3290
7.3097
7.2962
7.2817
7.2746
7.2563
7.2462
1.07
3.91
3.99
0.66
f1 (ppm)
O
CPh
Ph
O
N
Me
8i
1.97
3.01
3.99
0.66
1.05
1.00
2.18
3.06
f1 (ppm)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131.5583
128.5502
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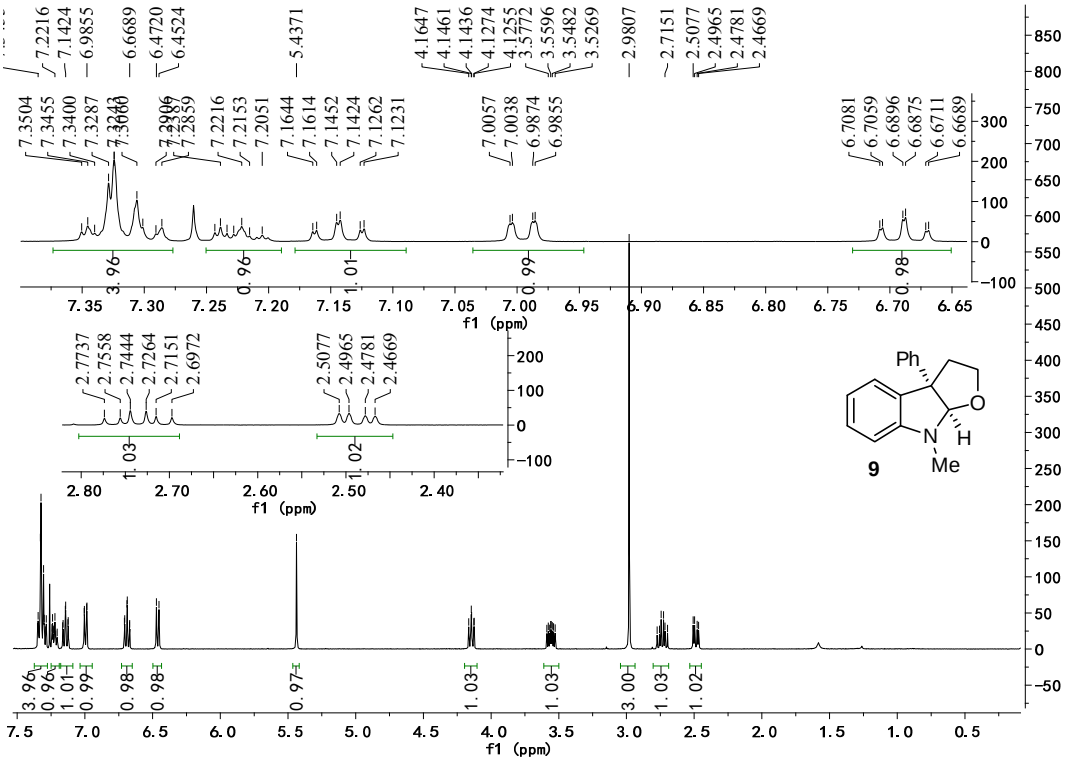
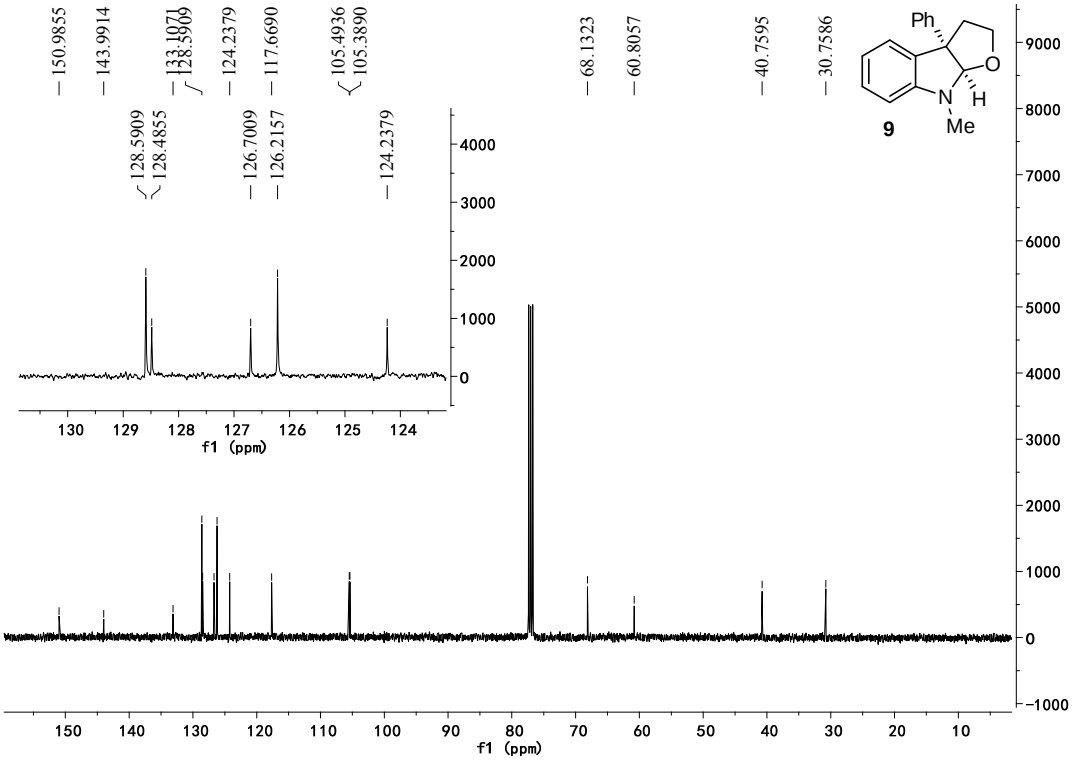
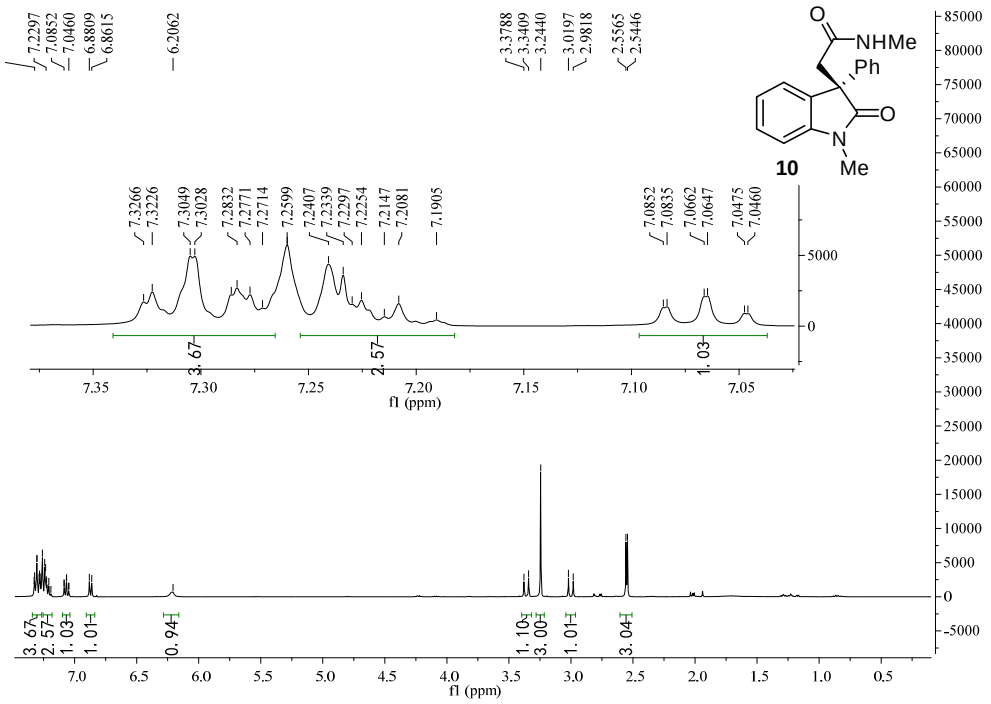
126.7724
122.2072
108.4846
53.1253
47.0233
26.7652
136.3876
133.2685
131.5583
128.7063
128.5502
128.4184
128.0056
127.5792
126.7724
124.1436
122.2072
f1 (ppm)
O
CPh
Ph
O
N
Me
8i
f1 (ppm)


Ph
O
N
H
Me
9
f1 (ppm)


Ph
O
N
H
Me
9
f1 (ppm)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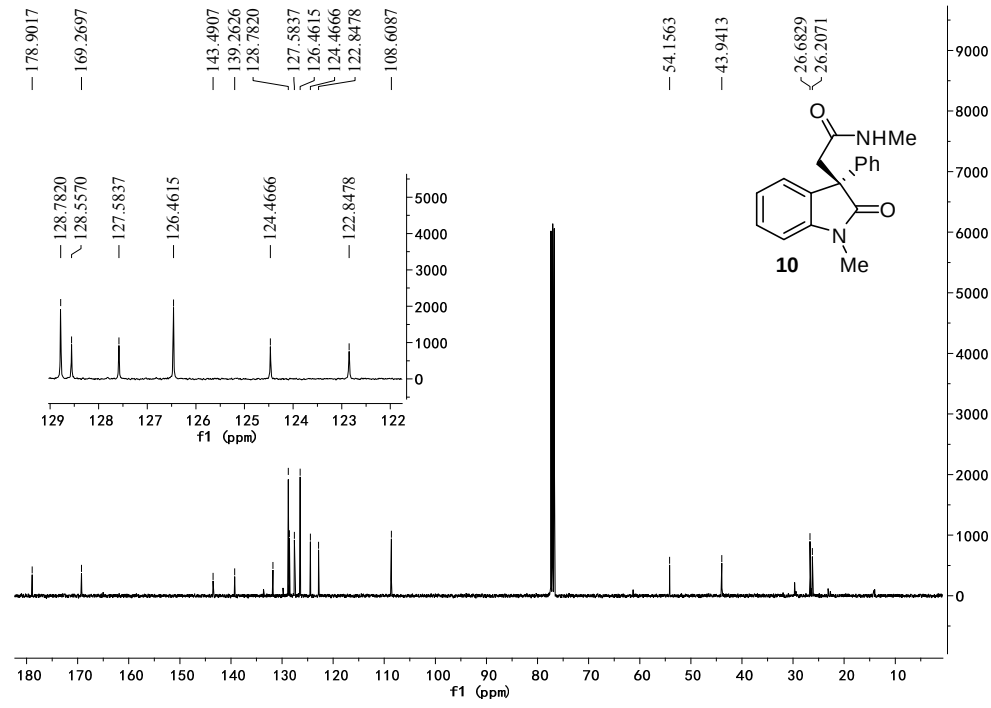
6.8615
6.2062
3.3788
3.3409
3.2440
3.0197
2.9818
2.5565
2.5446
NHMe
Ph
O
N
Me
10
7.3266
7.3226
7.3049
7.3028
7.2832
7.2771
7.2714
7.2599
7.2407
7.2339
7.2297
7.2254
7.2147
7.2081
7.1905
7.0852
7.0835
7.0662
7.0647
7.0475
7.0460
3.67
2.57
1.03
f1 (ppm)
1.10
3.00
1.01
3.04
0.94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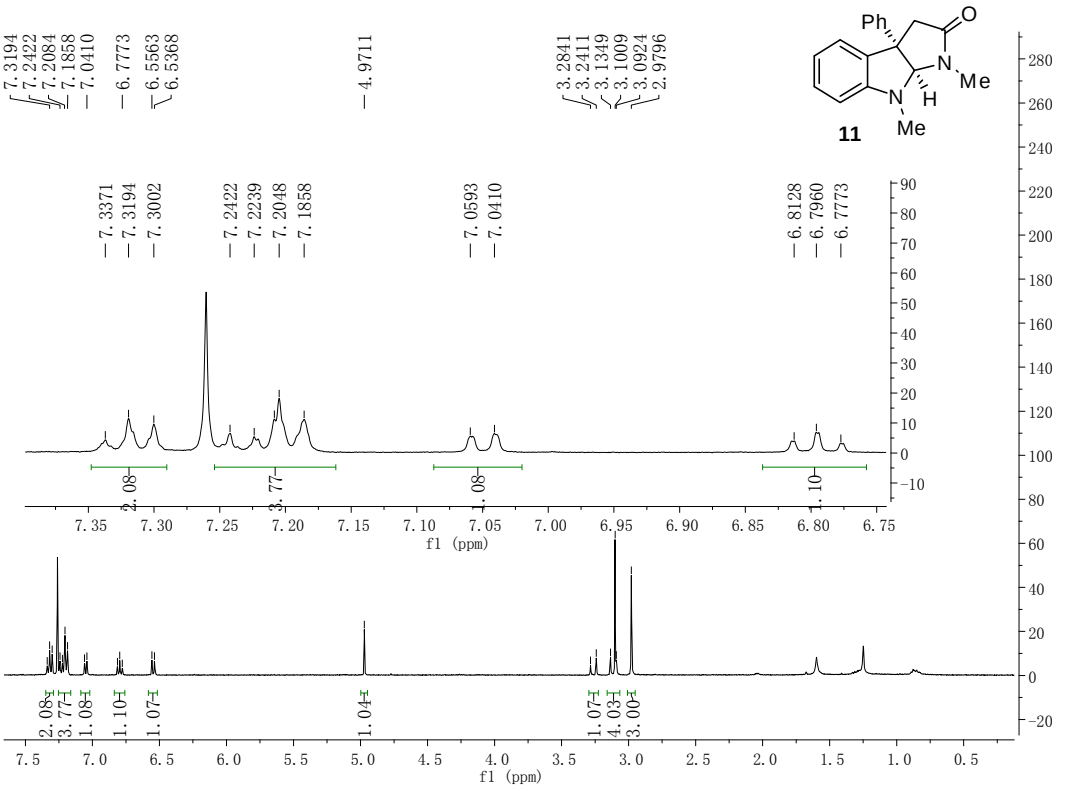
43.9413
26.6829
26.2071
NHMe
Ph
O
N
Me
10
f1 (ppm)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7.0410
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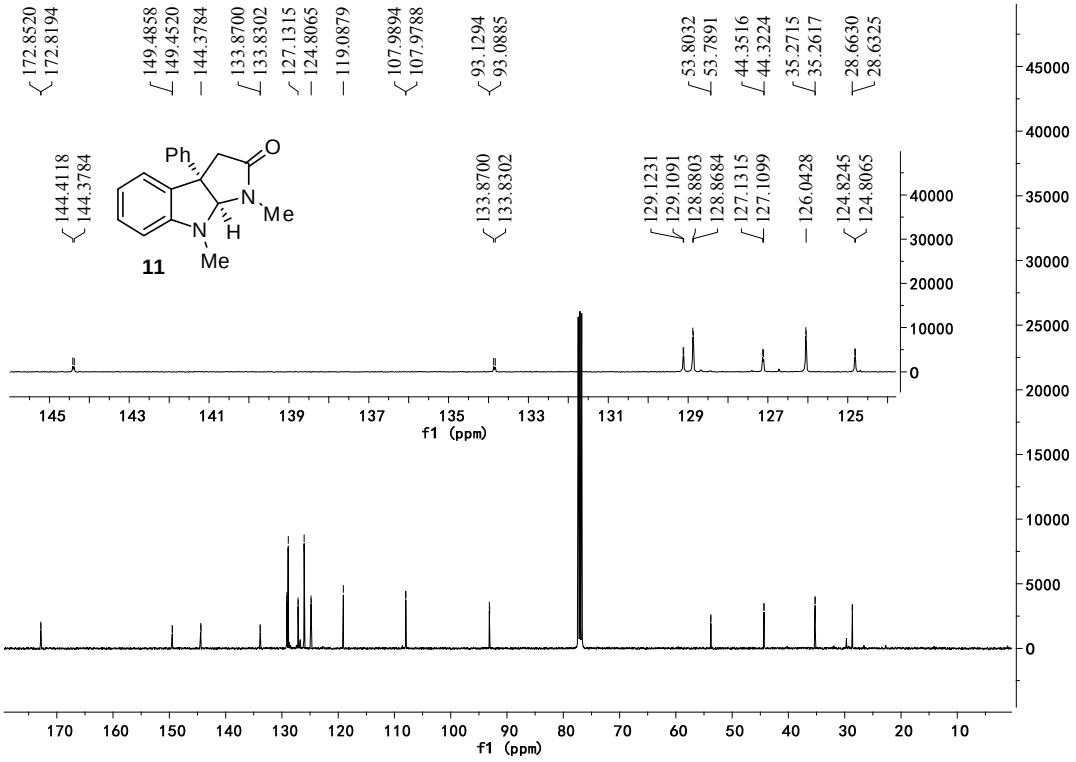
6.5563
6.5368
4.9711
3.2841
3.2411
3.1349
3.1009
3.0924
2.9796
Ph
O
N
Me
N
H
Me
11
7.3371
7.3194
7.3002
7.2422
7.2239
7.2048
7.1858
7.0593
7.0410
6.8128
6.7960
6.7773
2.08
3.77
1.08
1.10
f1 (ppm)
2.08
3.77
1.08
1.10
1.07
1.04
1.07
4.03
3.00
f1 (ppm)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149.4520
144.3784
133.8700
133.8302
127.1315
124.8065
119.0879
107.9894
107.9788
93.1294
93.0885
53.8032
53.7891
44.3516
44.3224
35.2715
35.2617
28.6630
28.6325
144.4118
144.3784
Ph
O
N
Me
N
H
Me
11
133.8700
133.8302
129.1231
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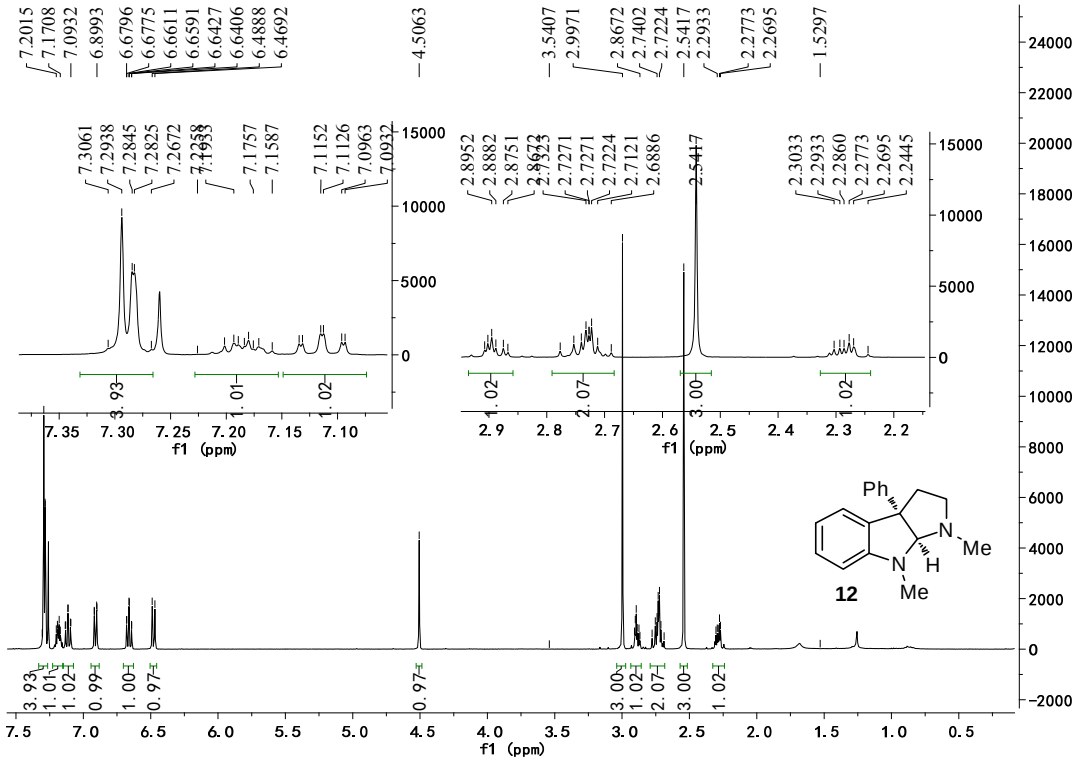
127.1315
127.1099
126.0428
124.8245
124.8065
f1 (ppm)
f1 (ppm)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6.4888
6.4692
4.5063
3.5407
2.9971
2.8672
2.7402
2.7224
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2.2773
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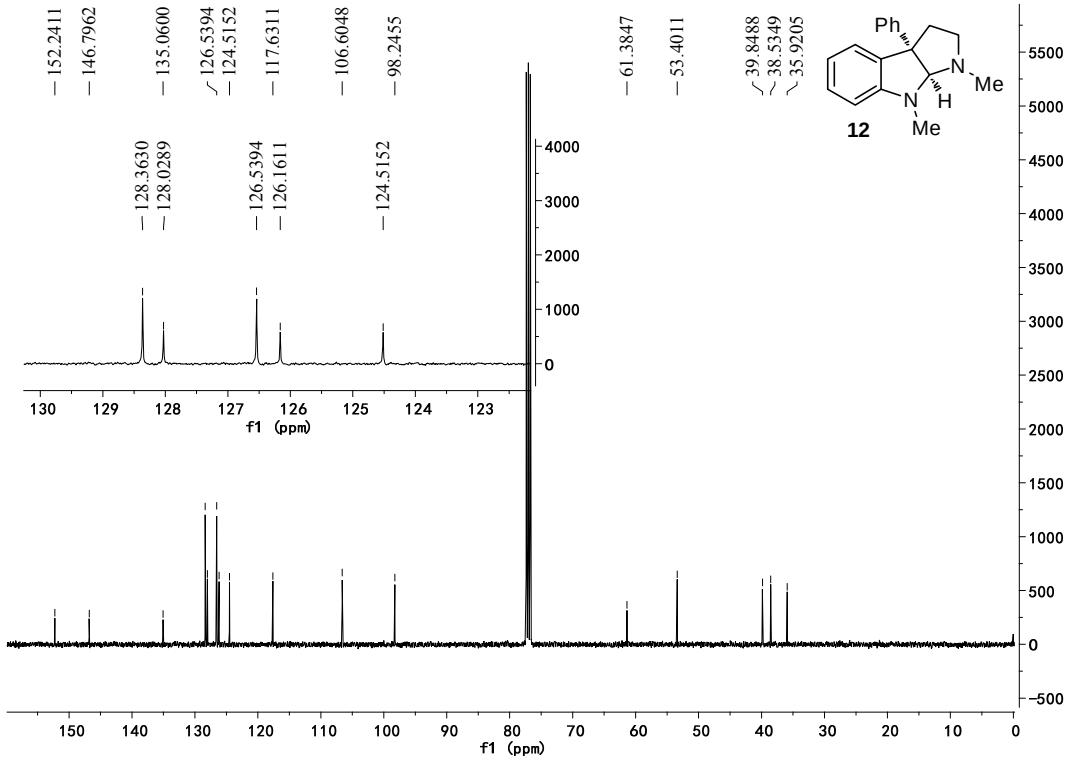
Ph
N
Me
N
H
Me
12
f1 (ppm)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35.9205
128.3630
128.0289
126.5394
126.1611
124.5152
Ph
N
Me
N
H
Me
12
f1 (ppm)