

Supporting Information

Iridium-catalyzed Enantioselective Reductive Amination of Aromatic Ketones

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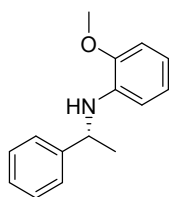
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1. General remarks

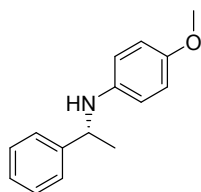
Unless otherwise specified, all experiments dealing with air- or moisture-sensitive compounds were performed using standard Schlenk techniques. All other commercial chemicals were purchased from J&K or Energy Chemical (Shanghai, China) in the highest purity and used without purification. THF, *t*-butyl methyl ether (TBME) and toluene were distilled from sodium benzophenone ketyl. CH₂Cl₂, CHCl₃ and ethyl acetate were distilled from CaH₂ under an atmosphere of argon. NMR spectra were recorded on a Bruker 400 MHz NMR spectrometer. Optical rotations were measured on a PERKIN ELMER polarimeter 343 instrument. HRMS were recorded on ZAB-HS spectrometer with ES ionization (ESI). Enantiomeric excesses were determined by Daicel chiral column on an Agilent 1260 Series HPLC instrument.

2. General procedure for DARA of aromatic ketones¹

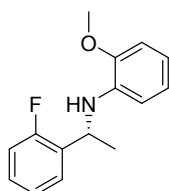
In a glass tube equipped with a stir bar, the catalyst (1 mol %) was prepared *in situ* from [Ir(COD)Cl]₂ (0.0025 mmol, 1.6 mg) and (*R*)-Cy-ax-Josiphos (0.0055 mmol, 4.0 mg) in anhydrous toluene (1 mL) over 30 min, then aromatic ketone (0.5 mmol), *o*-anisidine (0.6 mmol), Ti(O^{*i*}Pr)₄ (0.5 mmol, 142 mg), I₂ (0.05 mmol, 12.7 mg) and toluene (1 mL) was added subsequently. The glass tube was then placed into an autoclave, followed by replacing air with H₂ three times. The autoclave was charged with hydrogen to 50 atm, and then the reaction mixture was stirred at 50 °C for 20 h. After releasing the hydrogen, the solution was neutralized with saturated NaHCO₃, extracted with EtOAc and concentrated to afford the crude product. After flash chromatography with a column of silica gel, the desired amine products (yield: 80 – 97 %) were obtained.



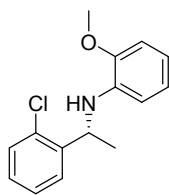
(*R*)-2-methoxy-*N*-(1-phenylethyl)aniline (**3a**)²: white solid; 107.9 mg, 95 % yield, 89 % *ee*; ¹H NMR (400 MHz, CDCl₃) δ 7.41-7.34 (m, 2H), 7.34-7.26 (m, 2H), 7.21 (m, 1H), 6.76 (m, 1H), 6.69 (m, 1H), 6.60 (td, *J* = 7.7, 1.6 Hz, 1H), 6.33 (m, 1H), 4.63 (s, 1H), 4.47 (m, 1H), 3.88 (s, 3H), 1.55 (d, *J* = 6.7 Hz, 3H); Enantiomeric excess was determined by HPLC on a Chiralpak OD-H column, Hex/IPA = 90: 10, 1 mL/min, 254 nm, *t*_S = 4.95 min (minor), *t*_R = 6.11 min (major).



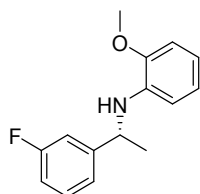
(*R*)-4-methoxy-*N*-(1-phenylethyl)aniline (**3a'**)³: white solid; 90.8 mg, 80 % yield, 77 % *ee*; ¹H NMR (400 MHz, CDCl₃) δ 7.34 (m, 4H), 7.26-7.13 (m, 1H), 6.77-6.63 (m, 2H), 6.55-6.38 (m, 2H), 4.49-4.33 (m, 1H), 3.88-3.72 (m, 1H), 3.69 (d, *J* = 2.8 Hz, 3H), 1.50 (dd, *J* = 6.8, 2.9 Hz, 3H). Enantiomeric excess was determined by HPLC on a Chiralpak OD-H column, Hex/IPA = 97: 3, 1 mL/min, 254 nm, *t*_S = 11.11 min (major), *t*_R = 12.65 min (minor).



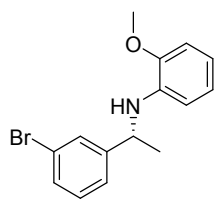
(*R*)-*N*-(1-(2-fluorophenyl)ethyl)-2-methoxyaniline (**3b**)¹: white solid; 104.2 mg, 85 % yield, 91 % *ee*; ¹H NMR (400 MHz, CDCl₃) δ 7.37-7.30 (m, 1H), 7.17 (ddd, *J* = 13.5, 6.3, 1.7 Hz, 1H), 7.06-6.96 (m, 2H), 6.76 (dd, *J* = 7.8, 1.2 Hz, 1H), 6.70 (td, *J* = 7.7, 1.4 Hz, 1H), 6.61 (td, *J* = 7.7, 1.5 Hz, 1H), 6.33 (dd, *J* = 7.8, 1.4 Hz, 1H), 4.86-4.78 (m, 1H), 4.62 (s, 1H), 3.88 (s, 3H), 1.56 (d, *J* = 6.7 Hz, 3H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak OD-H column, Hex/IPA = 99: 1, 1 mL/min, 254 nm, *t*_S = 10.59 min (minor), *t*_R = 13.15 min (major).



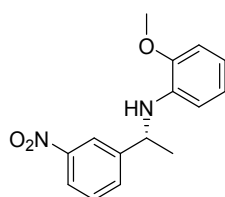
(*R*)-*N*-(1-(2-chlorophenyl)ethyl)-2-methoxyaniline (**3c**): white solid; 104.4 mg, 80 % yield, 70 % *ee*; **¹H NMR** (400 MHz, CDCl₃) δ 7.42 (dd, *J* = 7.2, 2.2 Hz, 1H), 7.39-7.27 (m, 1H), 7.21-7.03 (m, 2H), 6.75 (dd, *J* = 7.8, 1.4 Hz, 1H), 6.68 (td, *J* = 7.6, 1.5 Hz, 1H), 6.60 (td, *J* = 7.7, 1.6 Hz, 1H), 6.19 (dd, *J* = 7.8, 1.6 Hz, 1H), 4.89 (q, *J* = 6.7 Hz, 1H), 4.68 (s, 1H), 3.89 (s, 3H), 1.53 (d, *J* = 6.6 Hz, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 146.54, 142.26, 136.67, 132.50, 129.59, 127.91, 127.35, 126.69, 121.26, 116.55, 110.92, 109.28, 55.45, 50.03, 23.01; **HRMS (ESI)** calcd for C₁₅H₁₇ClNO [M+H]⁺: 262.0999, Found: 262.0992. Enantiomeric excess was determined by chiral HPLC on a Chiralpak OD-H column, Hex/IPA = 95: 5, 1mL/min, 254 nm, *t*_S = 4.96 min (minor), *t*_R = 6.20 min (major).



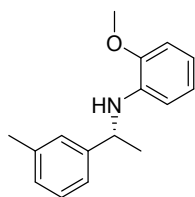
(*R*)-*N*-(1-(3-fluorophenyl)ethyl)-2-methoxyaniline (**3e**): white solid; 116.4 mg, 95 % yield; 92 % *ee*; [α]_D²⁵ -66.0 (*c* = 0.41, CHCl₃); **¹H NMR** (400 MHz, CDCl₃) δ 7.29-7.21 (m, 1H), 7.14 (d, *J* = 7.7 Hz, 1H), 7.11-7.02 (m, 1H), 6.94-6.83 (m, 1H), 6.78-6.75 (m, 1H), 6.69 (m, 1H), 6.66-6.56 (m, 1H), 6.29 (m, 1H), 4.61 (s, 1H), 4.44 (q, *J* = 6.8 Hz, 1H), 3.88 (s, 3H), 1.53 (d, *J* = 6.7 Hz, 3H); **¹³C NMR** (101 MHz, CDCl₃) δ 163.26 (d, *J* = 245.7 Hz), 148.53 (d, *J* = 6.5 Hz), 146.56, 136.91, 130.06 (d, *J* = 8.1 Hz), 121.46 (d, *J* = 2.7 Hz), 121.12, 116.61, 113.64 (d, *J* = 21.1 Hz), 112.65 (d, *J* = 21.8 Hz), 110.97, 109.32, 55.40, 53.05, 25.09; **HRMS (ESI)** calcd for : C₁₅H₁₆FNO [M+H]⁺: 246.1294, Found: 246.1294 . Enantiomeric excess was determined by chiral HPLC on a Chiralpak OD-H column, Hex/IPA = 99: 1, 1 mL/min, 254 nm, *t*_S = 6.22 min (minor), *t*_R = 10.06 min (major).



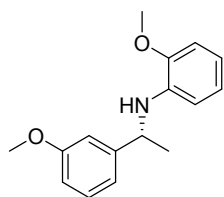
(*R*)-*N*-(1-(3-bromophenyl)ethyl)-2-methoxyaniline (**3f**): colorless oil; 147.9 mg, 97 % yield; 93 % *ee*; $[\alpha]_D^{25}$ -44.8 ($c = 0.5$, CHCl_3); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.56 (t, $J = 1.9$ Hz, 1H), 7.38 (m, 1H), 7.33 (m, 1H), 7.21 (t, $J = 7.8$ Hz, 1H), 6.81 (dd, $J = 7.8$, 1.5 Hz, 1H), 6.75 (td, $J = 7.3$, 1.2 Hz, 1H), 6.67 (td, $J = 7.7$, 1.6 Hz, 1H), 6.32 (dd, $J = 7.7$, 1.6 Hz, 1H), 4.65 (s, 1H), 4.44 (m, 1H), 3.93 (s, 3H), 1.57 (d, $J = 6.8$ Hz, 3H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 147.95, 146.34, 136.65, 130.03, 129.73, 128.73, 124.27, 122.59, 120.93, 116.46, 110.77, 109.11, 55.20, 52.88, 24.97; **HRMS (ESI)** calcd for $\text{C}_{15}\text{H}_{16}\text{BrNO}$ $[\text{M}+\text{H}]^+$: 306.0494, Found: 306.0486. Enantiomeric excess was determined by chiral HPLC on a Chiralpak OD-H column, Hex/IPA = 99: 1, 1 mL/min, 215 nm, $t_S = 9.47$ min (minor), $t_R = 16.78$ min (major).



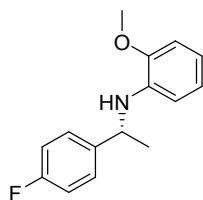
(*R*)-2-methoxy-*N*-(1-(3-nitrophenyl)ethyl)aniline (**3g**)⁴: white solid; 129.3 mg, 95 % yield; 91 % *ee*; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.28-8.19 (m, 1H), 8.08 (d, $J = 8.1$ Hz, 1H), 7.71 (d, $J = 7.6$ Hz, 1H), 7.47 (t, $J = 7.9$ Hz, 1H), 6.78 (m, 1H), 6.72-6.54 (m, 2H), 6.21 (m, 1H), 4.69 (s, 1H), 4.55 (p, $J = 6.5$ Hz, 1H), 3.90 (s, 3H), 1.58 (d, $J = 6.7$ Hz, 3H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak OD-H column, Hex/IPA = 90: 10, 1 mL/min, 254 nm, $t_S = 11.11$ min (minor), $t_R = 19.28$ min (major).



(*R*)-2-methoxy-*N*-(1-(*m*-tolyl)ethyl)aniline (**3h**)⁴: white solid; 108.5 mg, 90 % yield; 94 % *ee*; ¹H NMR (400 MHz, CDCl₃) δ 7.22-7.11 (m, 3H), 7.06-6.97 (m, 1H), 6.75 (dd, *J* = 7.9, 1.4 Hz, 1H), 6.70 (td, *J* = 7.7, 1.4 Hz, 1H), 6.60 (td, *J* = 7.7, 1.6 Hz, 1H), 6.35 (dd, *J* = 7.8, 1.5 Hz, 1H), 4.60 (s, 1H), 4.41 (q, *J* = 6.7 Hz, 1H), 3.87 (s, 3H), 2.32 (s, 3H), 1.53 (d, *J* = 6.7 Hz, 3H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak OD-H column, Hex/IPA = 99: 1, 1 mL/min, 215 nm, *t*_S = 10.58 min (minor), *t*_R = 13.60 min (major).

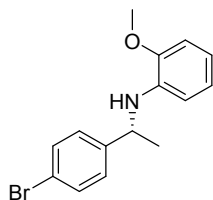


(*R*)-2-methoxy-*N*-(1-(3-methoxyphenyl)ethyl)aniline (**3i**): white solid; 123.4 mg, 96 % yield; 95 % *ee*; [α]_D²⁵ -62.4 (*c* = 0.62, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.36-7.25 (m, 2H), 6.94-6.81 (m, 2H), 6.75 (m, 1H), 6.70 (m, 1H), 6.60 (m, 1H), 6.36 (dd, *J* = 7.8, 1.6 Hz, 1H), 4.58 (s, 1H), 4.43 (q, *J* = 6.8 Hz, 1H), 3.87 (s, 3H), 3.77 (s, 3H), 1.52 (d, *J* = 6.7 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 159.78, 147.25, 146.42, 137.09, 129.43, 121.01, 118.05, 116.19, 111.75, 111.49, 110.90, 109.13, 55.22, 54.93, 53.22, 24.92; HRMS (ESI) calcd for C₁₆H₁₉NO₂ [M+H]⁺: 258.1494, Found: 258.1490. Enantiomeric excess was determined by chiral HPLC on a Chiralpak OD-H column, Hex/IPA = 90: 10, 1 mL/min, 254 nm, *t*_S = 6.66 min (minor), *t*_R = 8.74 min (major).

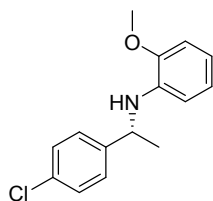


(*R*)-*N*-(1-(4-fluorophenyl)ethyl)-2-methoxyaniline (**3j**)²: white solid; 118.9 mg, 97 % yield; 95 % *ee*; ¹H NMR (400 MHz, CDCl₃) δ 7.32 (m, 2H), 7.09-6.88 (m, 2H), 6.83-6.74 (m, 1H), 6.74-6.66 (m, 1H), 6.62 (m, 1H), 6.29 (m, 1H), 4.71-4.53 (m, 1H), 4.51-4.34 (m, 1H), 3.88 (s, 3H), 1.52 (d, *J* = 6.7 Hz, 3H). Enantiomeric excess was

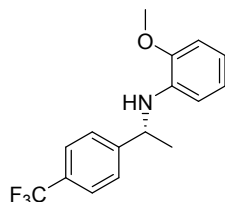
determined by chiral HPLC on a Chiralpak OD-H column, Hex/IPA = 99: 1, 1 mL/min, 254 nm, t_S = 8.60 min (minor), t_R = 13.69 min (major).



(*R*)-*N*-(1-(4-bromophenyl)ethyl)-2-methoxyaniline (**3k**)⁵: yellow oil; 144.9 mg, 95 % yield; 99 % *ee*; ¹H NMR (400 MHz, CDCl₃) δ 7.42 (d, J = 8.2 Hz, 2H), 7.24 (d, J = 8.3 Hz, 2H), 6.77 (m, 1H), 6.69 (m, 1H), 6.62 (m, 1H), 6.27 (d, J = 7.8, 1H), 4.60 (s, 1H), 4.42 (p, J = 6.5 Hz, 1H), 3.89 (s, 3H), 1.52 (d, J = 6.7 Hz, 3H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak OD-H column, Hex/IPA = 99: 1, 1 mL/min, 254 nm, t_S = 6.75 min (minor), t_R = 10.39 min (major).

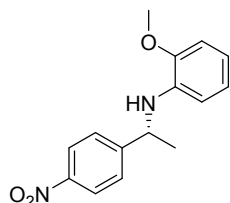


(*R*)-*N*-(1-(4-chlorophenyl)ethyl)-2-methoxyaniline (**3l**)²: yellow oil; 125.3 mg, 96 % yield; 93 % *ee*; ¹H NMR (400 MHz, CDCl₃) δ 7.34-7.20 (m, 4H), 6.76 (d, J = 7.8 Hz, 1H), 6.69 (m, 1H), 6.62 (m, 1H), 6.26 (m, 1H), 4.60 (s, 1H), 4.43 (m, 1H), 3.88 (s, 3H), 1.52 (d, J = 6.7 Hz, 3H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak OD-H column, Hex/IPA = 99: 1, 1 mL/min, 254 nm, t_S = 6.39 min (minor), t_R = 9.69 min (major).

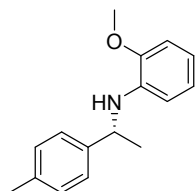


(*R*)-2-methoxy-*N*-(1-(4-(trifluoromethyl)phenyl)ethyl)aniline (**3m**)²: white solid; 141.7 mg, 96 % yield; 96 % *ee*; ¹H NMR (400 MHz, CDCl₃) δ 7.56 (d, J = 8.0 Hz,

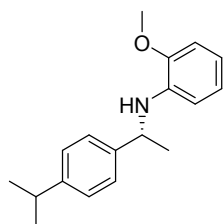
2H), 7.48 (d, $J = 8.0$ Hz, 2H), 6.78 (m, 1H), 6.66 (m, 2H), 6.23 (m, 1H), 4.65 (d, $J = 4.8$ Hz, 1H), 4.51 (p, $J = 6.5$ Hz, 1H), 3.90 (s, 3H), 1.55 (s, 3H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak OD-H column, Hex/IPA = 95: 5, 1 mL/min, 254 nm, $t_S = 6.61$ min (minor), $t_R = 11.26$ min (major).



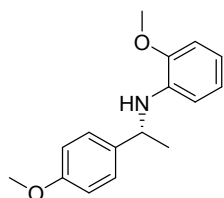
(*R*)-2-methoxy-*N*-(1-(4-nitrophenyl)ethyl)aniline (**3n**)⁵: yellow oil; 129.3 mg, 95 % yield; 96 % *ee*; **¹H NMR** (400 MHz, CDCl₃) δ 8.24-8.07 (m, 2H), 7.60-7.44 (m, 2H), 6.78 (m, 1H), 6.73-6.57 (m, 2H), 6.16 (dd, $J = 7.2, 2.0$ Hz, 1H), 4.68 (s, 1H), 4.61-4.46 (m, 1H), 3.90 (s, 3H), 1.57 (d, $J = 6.8$ Hz, 3H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak OD-H column, Hex/IPA = 90: 10, 1 mL/min, 254 nm, $t_S = 8.58$ min (minor), $t_R = 9.69$ min (major).



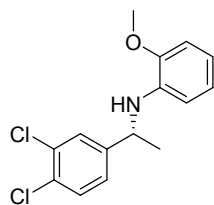
(*R*)-2-methoxy-*N*-(1-(*p*-tolyl)ethyl)aniline (**3o**)²: white solid; 117.0 mg, 97 % yield; 96 % *ee*; **¹H NMR** (400 MHz, CDCl₃) δ 7.37-7.19 (m, 2H), 7.11 (d, $J = 8.0$ Hz, 2H), 6.75 (m, 1H), 6.70 (m, 1H), 6.59 (m, 1H), 6.35 (m, 1H), 4.60 (s, 1H), 4.44 (p, $J = 6.3$ Hz, 1H), 3.87 (s, 3H), 2.31 (s, 3H), 1.53 (d, $J = 6.8$, 3H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak OD-H column, Hex/IPA = 99: 1, 1 mL/min, 254 nm, $t_S = 5.24$ min (minor), $t_R = 6.46$ min (major).



(*R*)-*N*-(1-(4-isopropylphenyl)ethyl)-2-methoxyaniline (**3p**): white solid; 129.2 mg, 96 % yield; 95 % *ee*; $[\alpha]_D^{25}$ -32.4 (*c* = 0.6, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.28 (d, *J* = 7.9 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 6.88-6.65 (m, 2H), 6.60 (m, 1H), 6.38 (m, 1H), 4.59 (s, 1H), 4.45 (q, *J* = 6.8 Hz, 1H), 3.87 (s, 3H), 2.87 (hept, *J* = 6.9 Hz, 1H), 1.53 (d, *J* = 6.7 Hz, 3H), 1.22 (d, *J* = 6.9 Hz, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 147.22, 146.56, 142.67, 137.34, 126.58, 125.77, 121.17, 116.16, 110.96, 109.27, 55.41, 52.93, 33.68, 24.94, 24.01, 23.97; HRMS (ESI) calcd for C₁₈H₂₃NO [M+H]⁺: 270.1858, Found: 270.1851. Enantiomeric excess was determined by chiral HPLC on a Chiralpak OD-H column, Hex/IPA = 95: 5, 1 mL/min, 254 nm, *t*_S = 4.63 min (minor), *t*_R = 5.73 min (major).

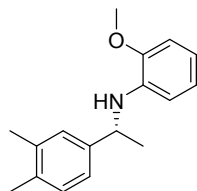


(*R*)-2-methoxy-*N*-(1-(4-methoxyphenyl)ethyl)aniline (**3q**)²: white solid; 123.4 mg, 96 % yield; 90 % *ee*; ¹H NMR (400 MHz, CDCl₃) δ 7.36-7.25 (m, 2H), 6.94-6.81 (m, 2H), 6.75 (m, 1H), 6.70 (m, 1H), 6.60 (m, 1H), 6.36 (dd, *J* = 7.8, 1.6 Hz, 1H), 4.58 (s, 1H), 4.43 (q, *J* = 6.8 Hz, 1H), 3.87 (s, 3H), 3.77 (s, 3H), 1.52 (d, *J* = 6.7 Hz, 3H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak OD-H column, Hex/IPA = 95: 5, 1 mL/min, 254 nm, *t*_S = 7.18 min (minor), *t*_R = 8.90 min (major).

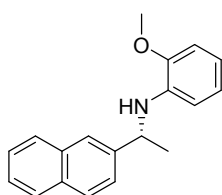


(*R*)-*N*-(1-(3,4-dichlorophenyl)ethyl)-2-methoxyaniline (**3r**): yellow oil; 141.6 mg, 96 % yield; 94 % *ee*; $[\alpha]_D^{25}$ -12.8 (*c* = 0.6, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.46 (m, 1H), 7.36 (m, 1H), 7.20 (m, 1H), 6.78 (m, 1H), 6.70 (m, 1H), 6.64 (m, 1H), 6.24 (m, 1H), 4.60 (s, 1H), 4.39 (m, 1H), 3.89 (s, 3H), 1.52 (d, *J* = 6.7, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 146.52, 146.11, 136.61, 132.60, 130.59, 130.48, 127.85, 125.26,

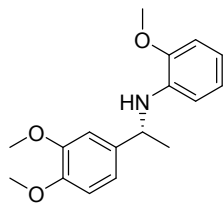
121.08, 116.87, 110.92, 109.30, 55.38, 52.68, 25.10; **HRMS (ESI)** calcd for $C_{15}H_{15}Cl_2NO$ $[M+H]^+$: 296.0603, Found: 296.0604. Enantiomeric excess was determined by chiral HPLC on a Chiralpak OD-H column, Hex/IPA = 95: 5, 1 mL/min, 254 nm, t_S = 7.51 min (minor), t_R = 12.50 min (major).



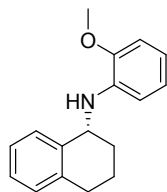
(*R*)-*N*-(1-(3,4-dimethylphenyl)ethyl)-2-methoxyaniline (**3s**): white solid; 121.2 mg, 95 % yield; 92 % *ee*; $[\alpha]_D^{25}$ -57.9 (c = 1.0, $CHCl_3$); **1H NMR** (400 MHz, $CDCl_3$) δ 7.10 (m, 3H), 6.74 (m, 2H), 6.61 (m, 1H), 6.47-6.28 (m, 1H), 4.59 (s, 1H), 4.50-4.31 (m, 1H), 3.89 (m, 3H), 2.24 (m, 6H), 1.53 (m, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 146.70, 143.11, 137.56, 136.75, 135.03, 129.95, 127.27, 123.32, 121.33, 116.28, 111.14, 109.37, 55.50, 53.20, 25.30, 20.01, 19.50; **HRMS (ESI)** calcd for $C_{17}H_{21}NO$ $[M+H]^+$: 256.1701, Found: 256.1716. Enantiomeric excess was determined by chiral HPLC on a Chiralpak OD-H column, Hex/IPA = 95: 5, 1 mL/min, 254 nm, t_S = 5.15 min (minor), t_R = 6.35 min (major).



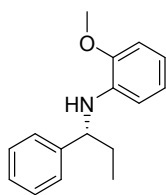
(*R*)-2-methoxy-*N*-(1-(naphthalen-2-yl)ethyl)aniline (**3t**)²: white solid; 124.7 mg, 90 % yield; 89 % *ee*; **1H NMR** (400 MHz, $CDCl_3$) δ 8.10-7.65 (m, 4H), 7.51 (dt, J = 8.5, 1.9 Hz, 1H), 7.48-7.31 (m, 2H), 6.77 (dt, J = 7.7, 1.7 Hz, 1H), 6.74-6.51 (m, 2H), 6.37 (m, 1H), 4.72 (s, 1H), 4.63 (m, 1H), 3.91 (d, J = 1.4 Hz, 3H), 1.62 (dd, J = 6.8, 1.9 Hz, 3H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak OD-H column, Hex/IPA = 95: 5, 1 mL/min, 254 nm, t_S = 6.92 min (minor), t_R = 9.22 min (major).



(*R*)-*N*-(1-(3,4-dimethoxyphenyl)ethyl)-2-methoxyaniline (**3u**): white solid; 139.3 mg, 97 % yield; 88 % *ee*; $[\alpha]_D^{25}$ -65.2 ($c = 1.0$, CHCl₃); **¹H NMR** (400 MHz, CDCl₃) δ 6.91 (m, 2H), 6.85-6.77 (m, 1H), 6.76 (m, 1H), 6.71 (td, $J = 7.6, 1.4$ Hz, 1H), 6.61 (m, 1H), 6.38 (m, 1H), 4.57 (s, 1H), 4.40 (q, $J = 6.7$ Hz, 1H), 3.88 (s, 3H), 3.85 (d, $J = 2.2$ Hz, 3H), 1.53 (d, $J = 6.7$ Hz, 3H); **¹³C NMR** (101 MHz, CDCl₃) δ 149.21, 147.85, 146.63, 138.26, 137.42, 121.20, 117.78, 116.41, 111.28, 109.26, 55.91, 55.44, 53.29, 25.17; **HRMS (ESI)** calcd for C₁₇H₂₁NO₃ [M+Na]⁺: 310.1419, Found: 310.1389. Enantiomeric excess was determined by chiral HPLC on a Chiralpak OD-H column, Hex/IPA = 90: 10, 1 mL/min, 254 nm, $t_S = 13.29$ min (minor), $t_R = 15.47$ min (major).



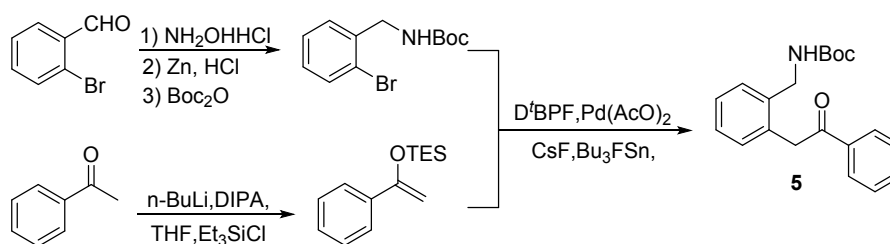
(*R*)-*N*-(2-methoxyphenyl)-1,2,3,4-tetrahydronaphthalen-1-amine (**3v**): white solid; 113.9 mg, 90 % yield; 96 % *ee*; $[\alpha]_D^{25}$ -12.6 ($c = 1.0$, CHCl₃); **¹H NMR** (400 MHz, CDCl₃) δ 7.58-7.29 (m, 1H), 7.30-7.02 (m, 3H), 6.98-6.83 (m, 1H), 6.83-6.73 (m, 2H), 6.73-6.57 (m, 1H), 4.62 (m, 1H), 4.51 (m, 1H), 3.79 (s, 3H), 2.81 (m, 2H), 2.08-1.67 (m, 4H); **¹³C NMR** (101 MHz, CDCl₃) δ 146.67, 138.37, 137.68, 137.46, 129.38, 128.95, 127.00, 126.07, 121.25, 115.95, 109.67, 109.62, 55.36, 50.64, 29.39, 28.63, 19.45; **HRMS (ESI)** calcd for C₁₇H₁₉NO [M+H]⁺: 254.1545, Found: 254.1543. Enantiomeric excess was determined by chiral HPLC on a Chiralpak OD-H column, Hex/IPA = 95: 5, 1 mL/min, 254 nm, $t_S = 6.20$ min (minor), $t_R = 13.38$ min (major).



(*R*)-2-methoxy-*N*-(1-phenylpropyl)aniline (**3w**)²: white solid; 73.5 mg, 61 % yield; 87 % *ee*; ¹H NMR (400 MHz, CDCl₃) δ 7.32 (m, 4H), 7.21 (t, *J* = 6.4 Hz, 1H), 6.75 (d, *J* = 7.8 Hz, 1H), 6.68 (t, *J* = 7.6 Hz, 1H), 6.59 (t, *J* = 7.7 Hz, 1H), 6.34 (d, *J* = 7.8 Hz, 1H), 4.69 (s, 1H), 4.21 (t, *J* = 6.1 Hz, 1H), 3.88 (s, 3H), 1.86 (tq, *J* = 13.7, 6.8 Hz, 2H), 0.97 (t, *J* = 7.4 Hz, 3H).

3. Intramolecular asymmetric reductive amination reaction

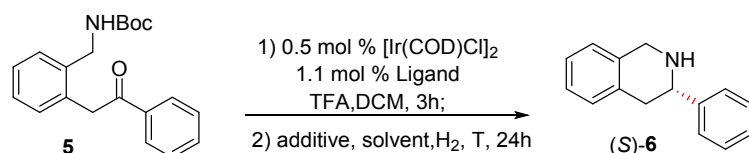
3.1 Synthesis of *tert*-butyl (2-(2-oxo-2-phenylethyl) benzyl) carbamate **5**⁶



The substrate (**5**) of intramolecular asymmetric reductive amination reaction was prepared according to the literature procedure without modification.

3.2 Condition optimization of intramolecular asymmetric reductive amination

Table S1: Optimization of intramolecular asymmetric reductive amination^a

						
Entry	Ligand	Additive	Solvent	T (°C)/ P (atm)	Yield ^b (%)	<i>Ee</i> ^c (%)
1	(<i>R</i>)- ⁱ Bu- ax-Josiphos	10 % I ₂ , Ti(O ⁱ Pr) ₄ (1.0 equiv)	toluene	50/50	55	29

2	(<i>R</i>)-Cy- ax-Josiphos	10 % I ₂ , Ti(O ^{<i>i</i>} Pr) ₄ (1.0 equiv)	toluene	50/50	52	19
3	(<i>R</i>)-Ph- ax-Josiphos	10 % I ₂ , Ti(O ^{<i>i</i>} Pr) ₄ (1.0 equiv)	toluene	50/50	53	65
4	(<i>R</i>)-Xyl- ax-Josiphos	10 % I ₂ , Ti(O ^{<i>i</i>} Pr) ₄ (1.0 equiv)	toluene	50/50	58	58
5	(<i>R</i>)-Ph- ax-Josiphos	10 % I ₂ , 5 % (m/v) 4Å MS Ti(O ^{<i>i</i>} Pr) ₄ (1.0 equiv)	toluene	50/50	42	83
6	(<i>R</i>)-Ph- ax-Josiphos	5 % (m/v) 4Å MS Ti(O ^{<i>i</i>} Pr) ₄ (1.0 equiv)	toluene	50/50	49	82
7	(<i>R</i>)-Ph- ax-Josiphos	10 % I ₂ , 5 % (m/v) 4Å MS	toluene	50/50	68	84
8	(<i>R</i>)-Ph- ax-Josiphos	5 % (m/v) 4Å MS	toluene	50/50	70	84
9	(<i>R</i>)-Ph- ax-Josiphos	5 % (m/v) 4Å MS	DCM	50/50	52	64
10	(<i>R</i>)-Ph- ax-Josiphos	5 % (m/v) 4Å MS	THF	50/50	50	75
11	(<i>R</i>)-Ph- ax-Josiphos	5 % (m/v) 4Å MS	TBME	50/50	62	74
12	(<i>R</i>)-Ph- ax-Josiphos	5 % (m/v) 4Å MS	1,4- Dioxane	50/50	55	75
13	(<i>R</i>)-Ph- ax-Josiphos	5 % (m/v) 4Å MS	EtOAc	50/50	42	81
14	(<i>R</i>)-Ph- ax-Josiphos	5 % (m/v) 4Å MS	CHCl ₃	50/50	50	62
15	(<i>R</i>)-Ph- ax-Josiphos	5 % (m/v) 4Å MS	toluene	30/50	69	83
16	(<i>R</i>)-Ph- ax-Josiphos	5 % (m/v) 4Å MS	toluene	30/20	30	84

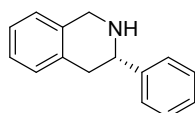
^aReaction conditions: Ir/ligand/substrate = 1:2.2:200, (substrate) = 0.25 M.

^bIsolated yields after column chromatography ^cEantiomeric excesses were determined by chiral HPLC after the products were converted into the corresponding acetamides. The absolute configuration is assigned by comparison of the rotation sign with literature.⁷

3.3 Procedure for one-pot *N*-Boc deprotection and intramolecular asymmetric reductive amination.

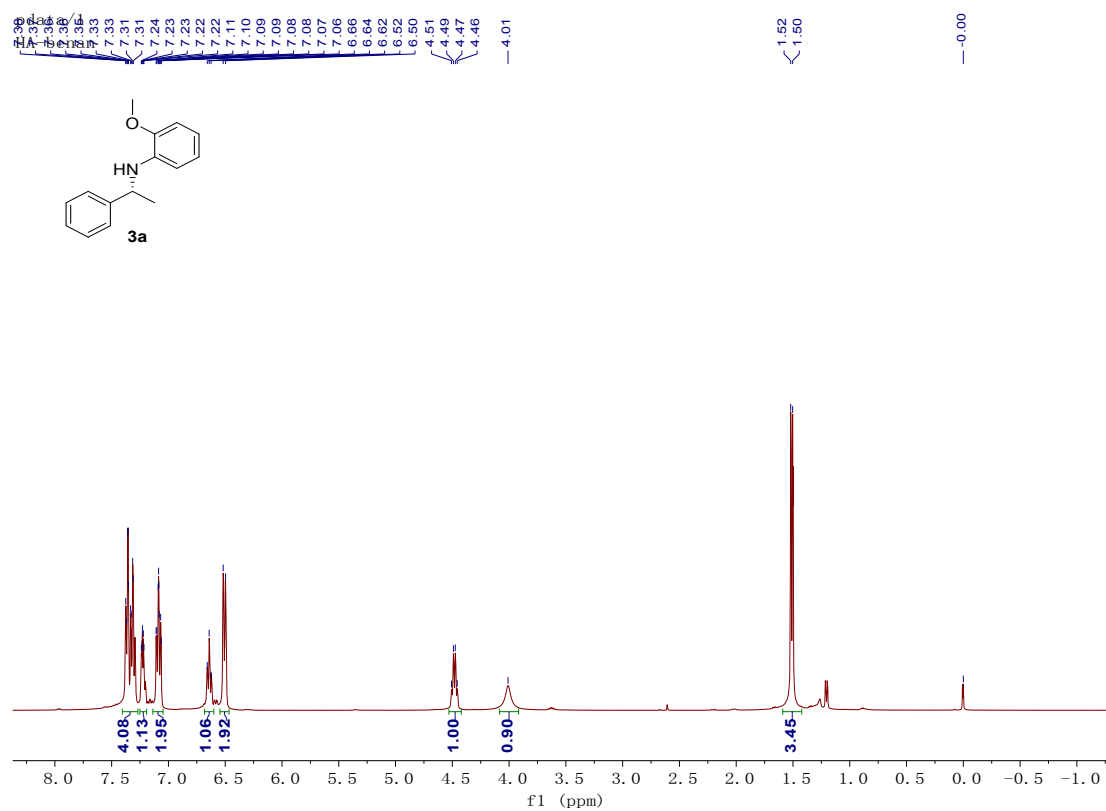
Substrate **5** (0.5 mmol) and TFA (3 mmol) were stirred in CH₂Cl₂ under argon for 3 h,

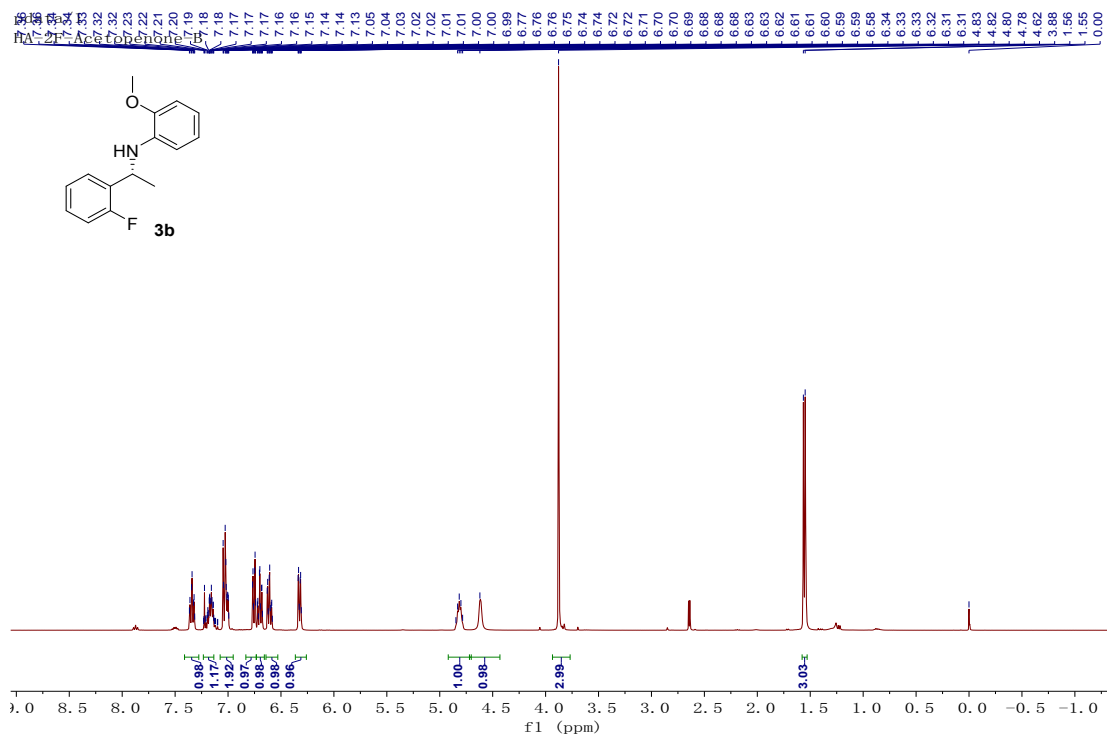
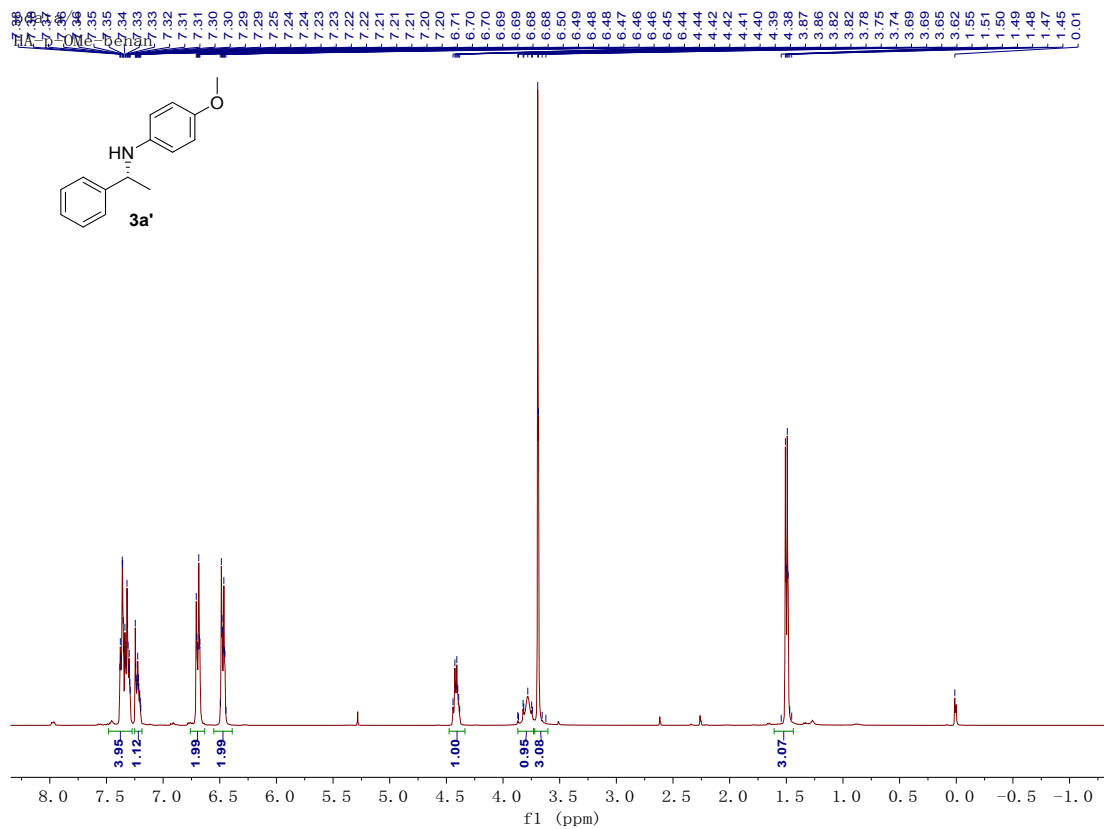
and then all volatiles were removed. In a glass tube equipped with a stir bar, the catalyst (1 mol %) was prepared *in situ* from [Ir(COD)Cl]₂ and (*R*)-Cy-ax-Josiphos in anhydrous toluene (1 mL) over 30min. The obtained *N*-Boc deprotected substance was dissolved in toluene (1 mL) and then transferred to the above catalyst solution followed by the addition of 4Å molecular sieves (5 % m/v, 100 mg). The glass tube was then placed into an autoclave, followed by replacing air with H₂ three times. The autoclave was charged with hydrogen to 50 atm, and then the reaction mixture was stirred at room temperature for 24 h. The resulted solution was neutralized with aqueous sodium bicarbonate solution. The organic phase was concentrated and passed through a short column of silica gel to remove the metal complex to give the chiral tetrahydroisoquinoline product, which was then converted to the corresponding acetamide and analyzed by chiral HPLC to determine the enantiomeric excess.

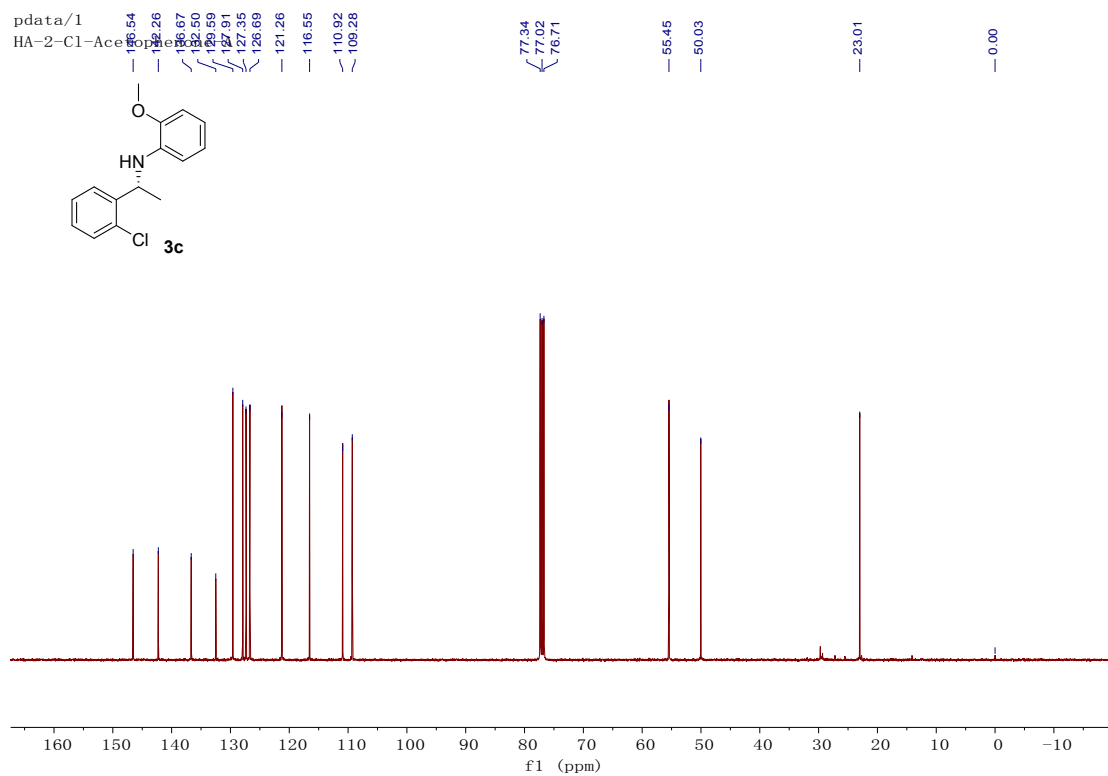
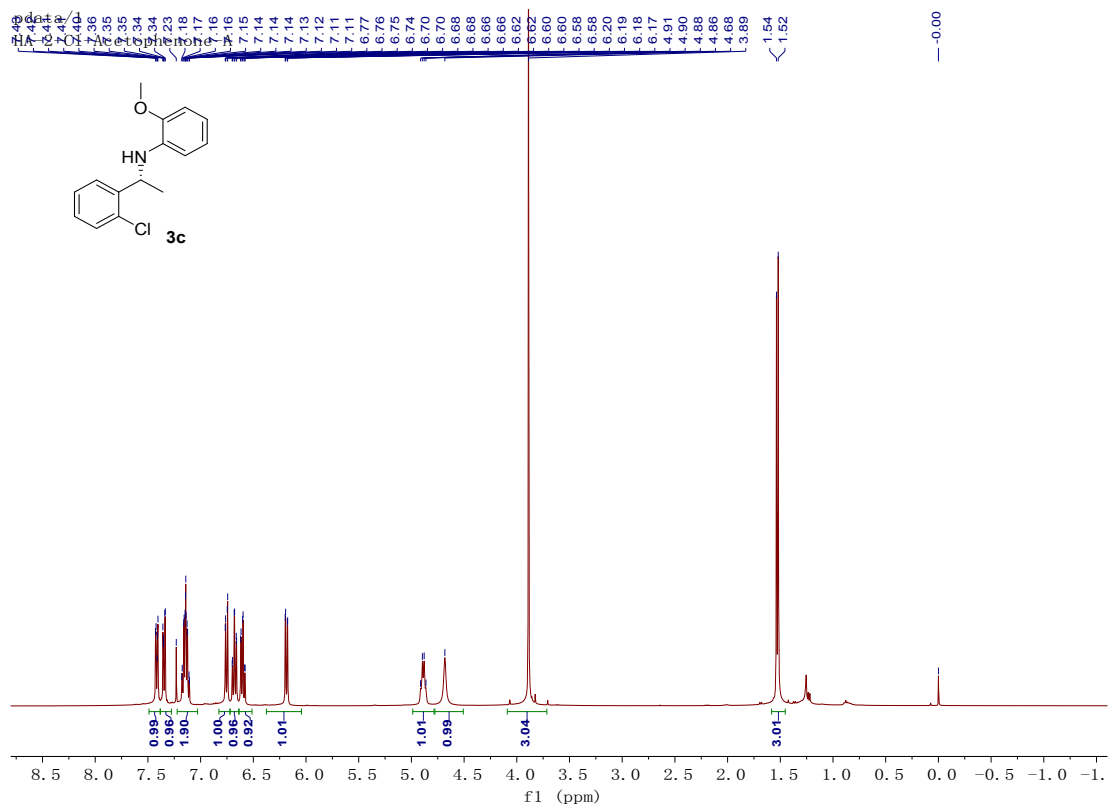


(*S*)-3-phenyl-1,2,3,4-tetrahydroisoquinoline (**6**)⁷: white solid; 73 mg, 70 % yield; 84 % *ee*; ¹H NMR (400 MHz, CDCl₃) δ 7.44 (d, *J* = 7.9 Hz, 2H), 7.37 (t, *J* = 7.4 Hz, 2H), 7.33-7.27 (m, 1H), 7.13 (m, 4H), 4.28 (d, *J* = 15.6 Hz, 1H), 4.17 (d, *J* = 15.6 Hz, 1H), 4.02 (t, *J* = 7.4 Hz, 1H), 2.99 (d, *J* = 7.3 Hz, 2H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 75: 25, 1 mL/min, 215 nm, *t_R* = 19.06 min (minor), *t_S* = 26.88 min (major).

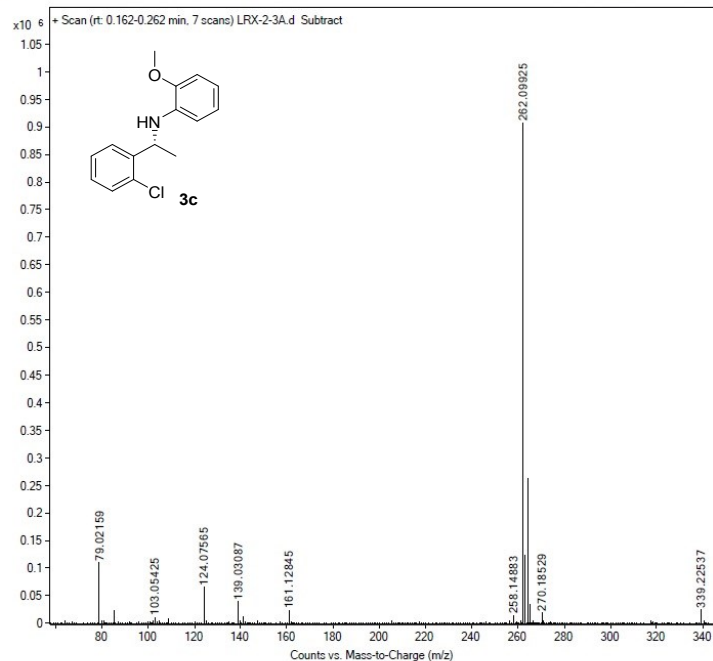
4. NMR spectra and HRMS



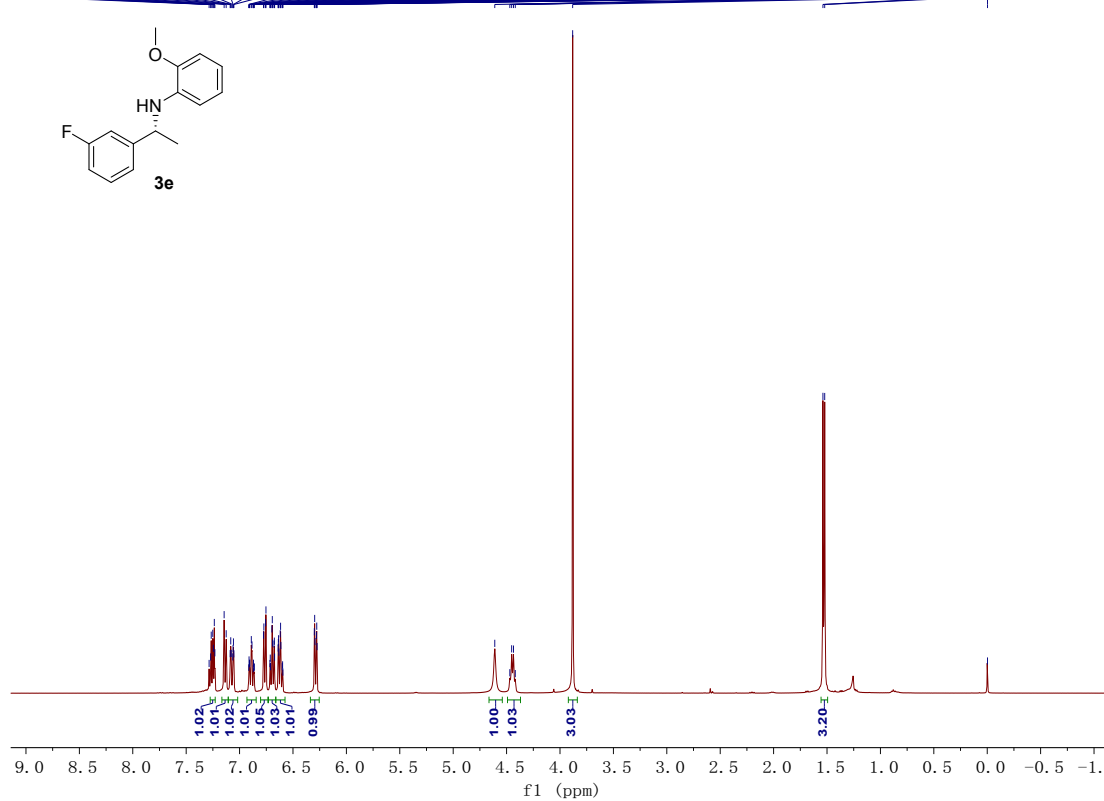


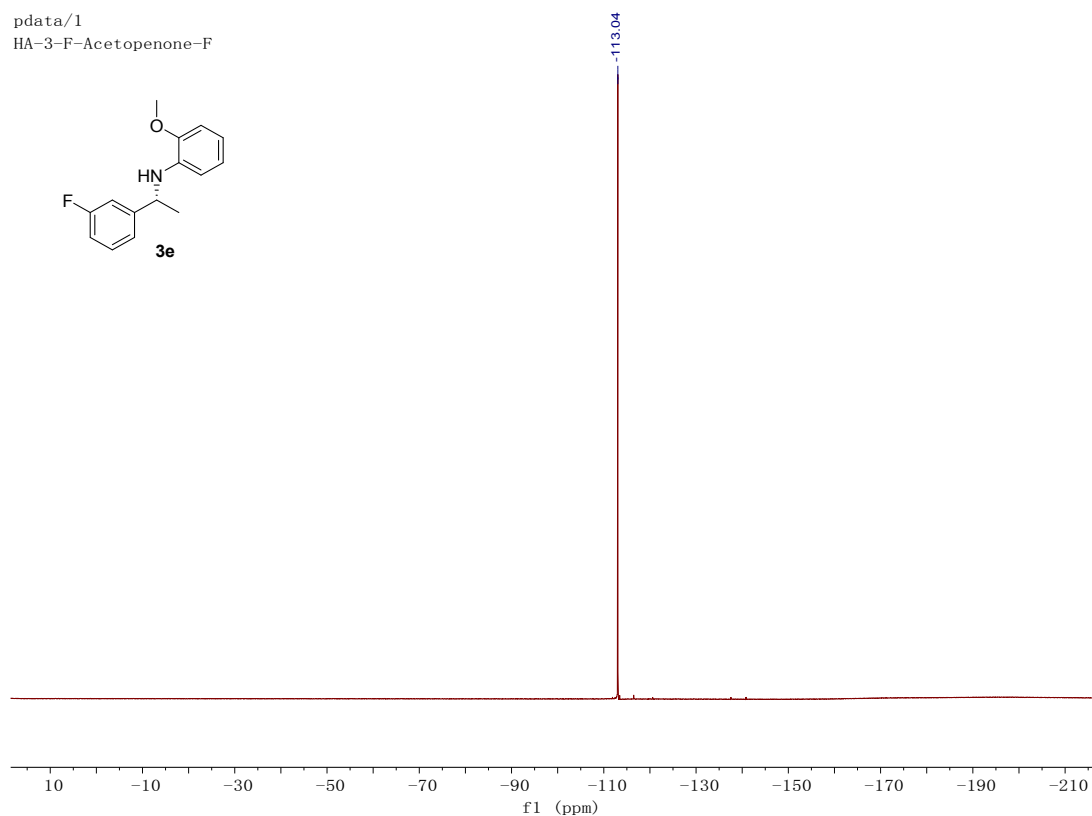
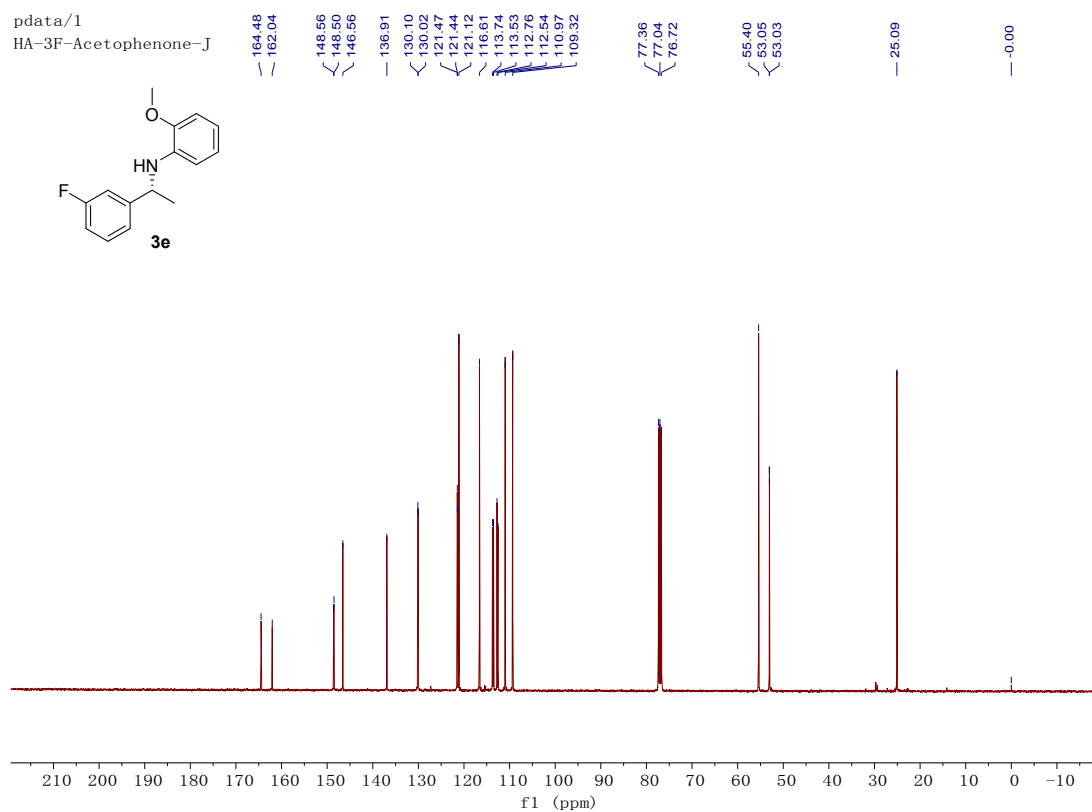


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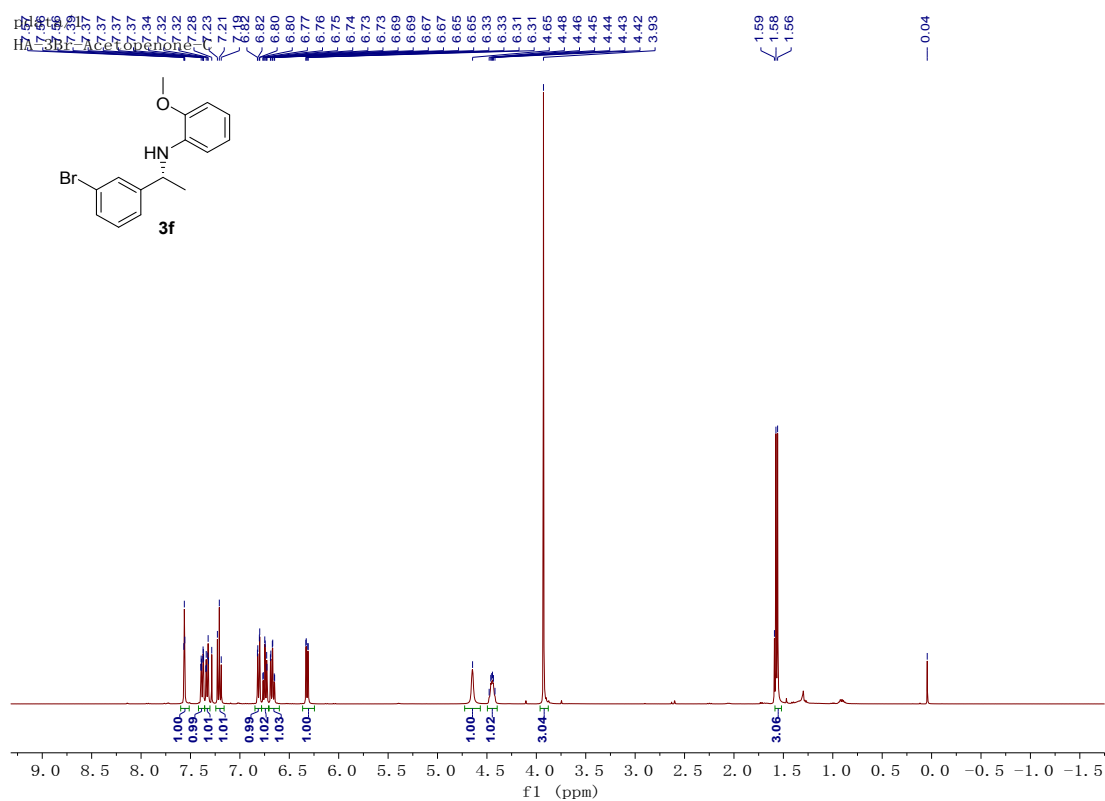
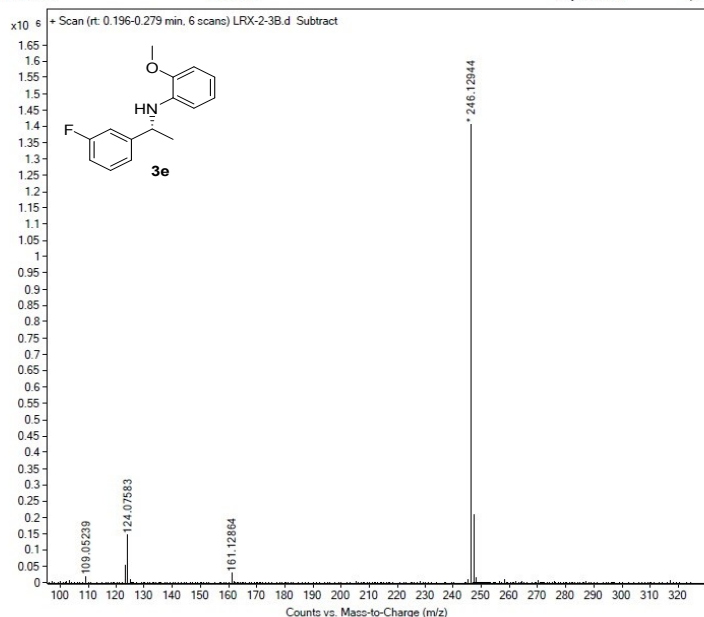


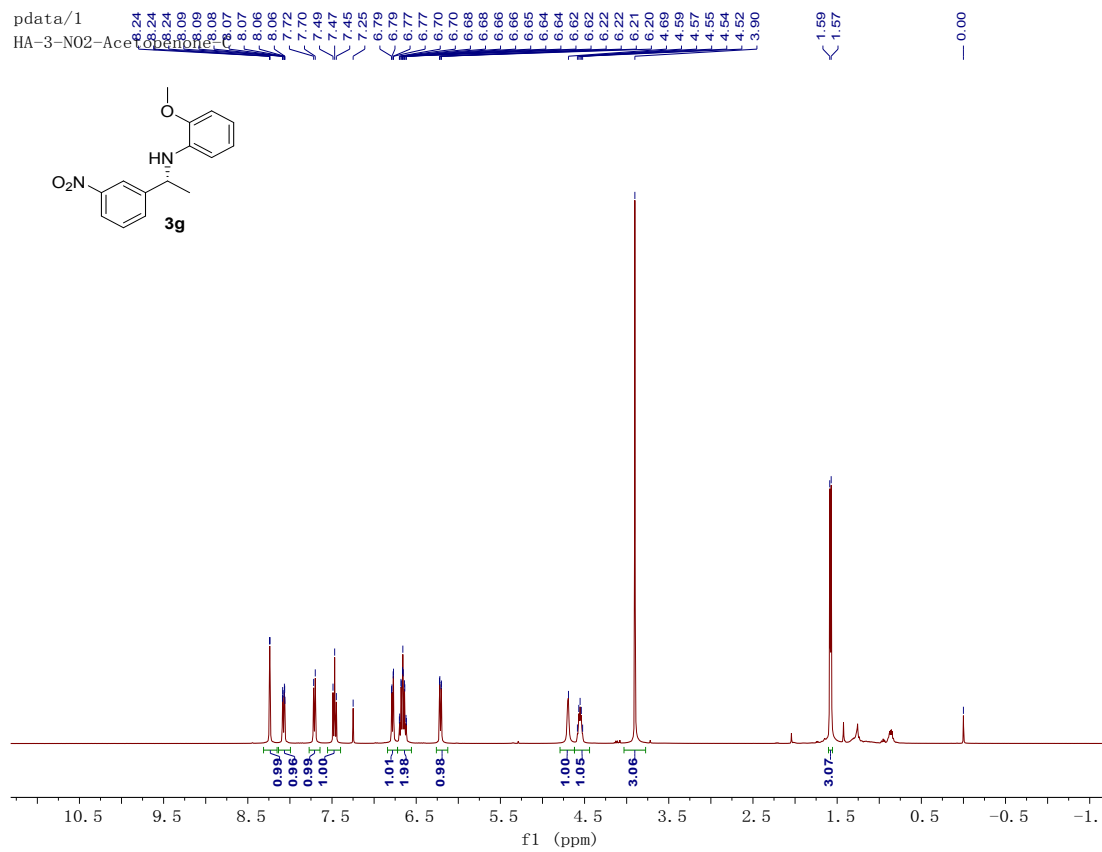
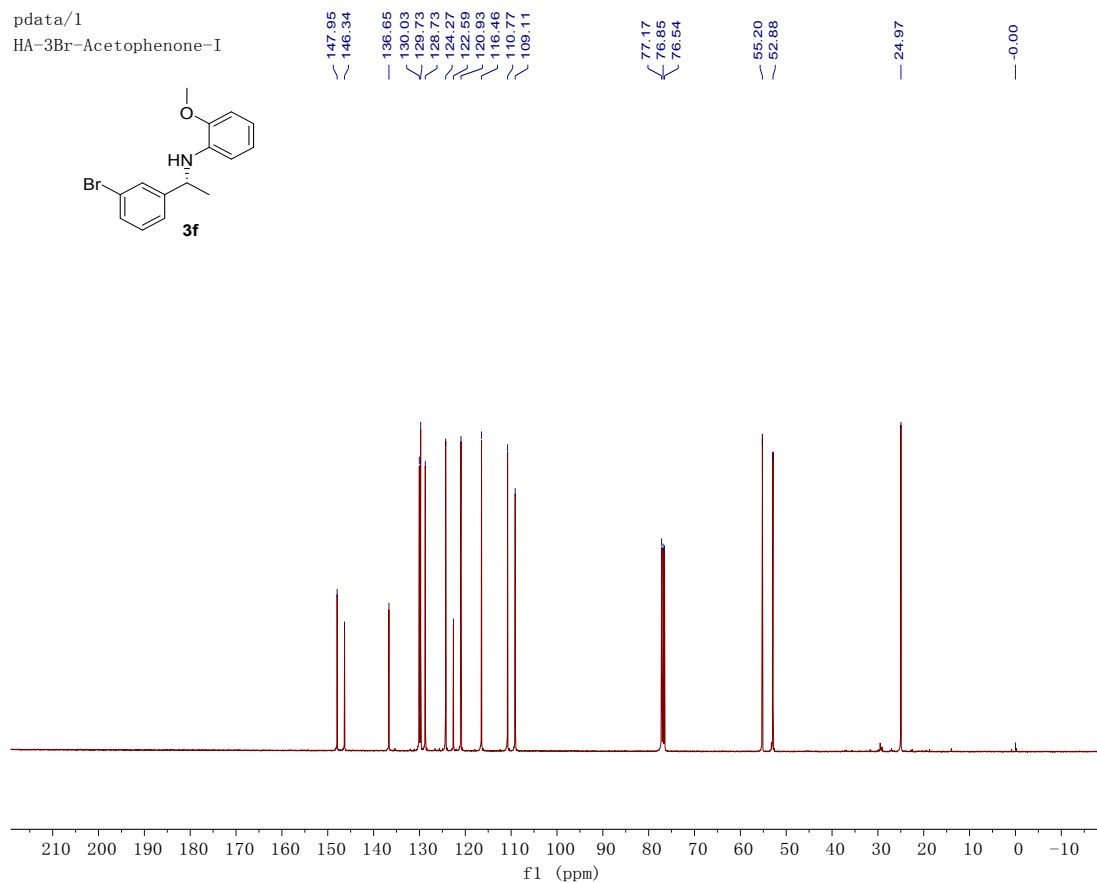
data 1
HA 3-11 Acetophenone

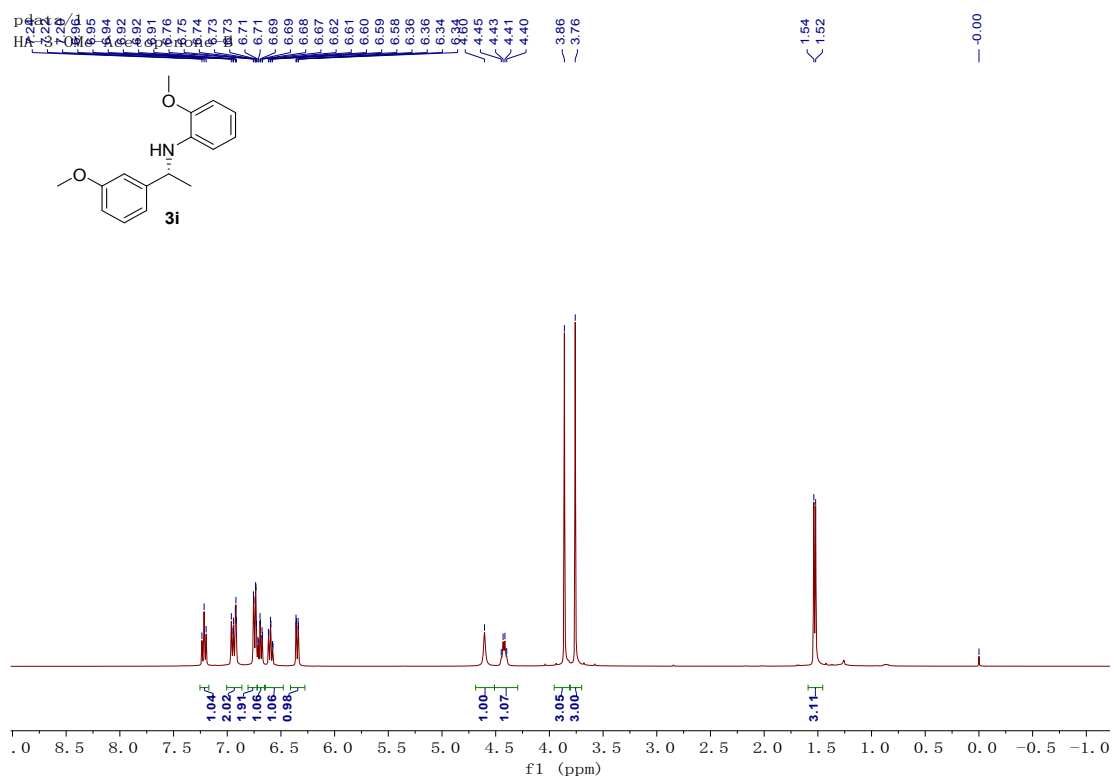
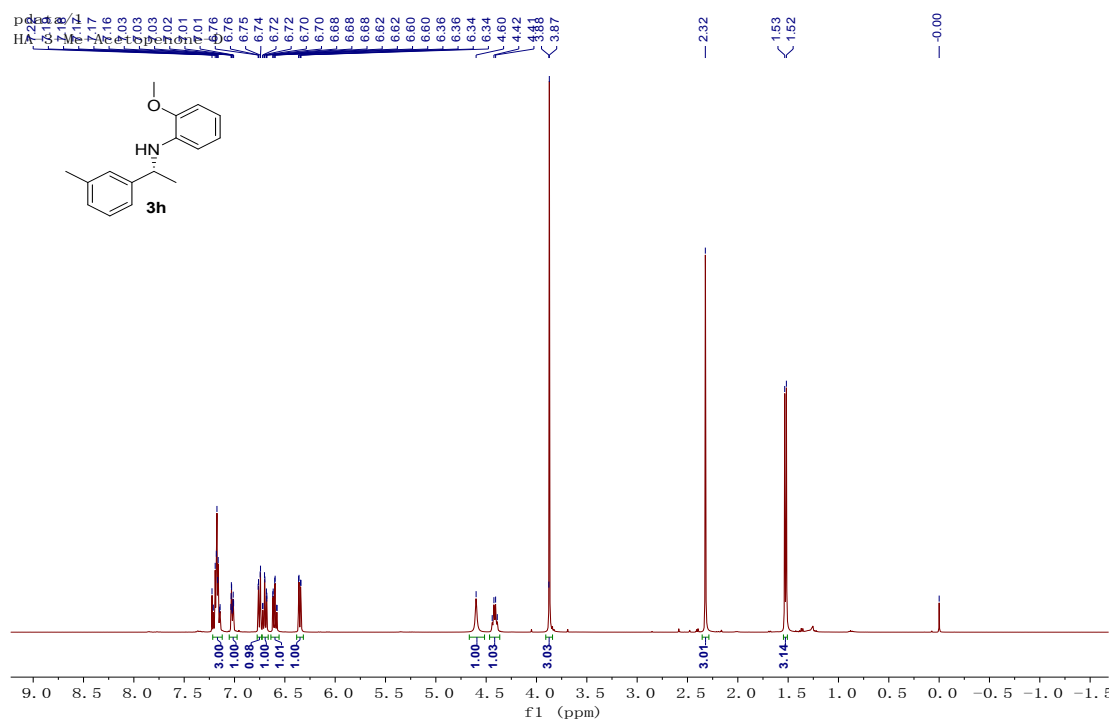


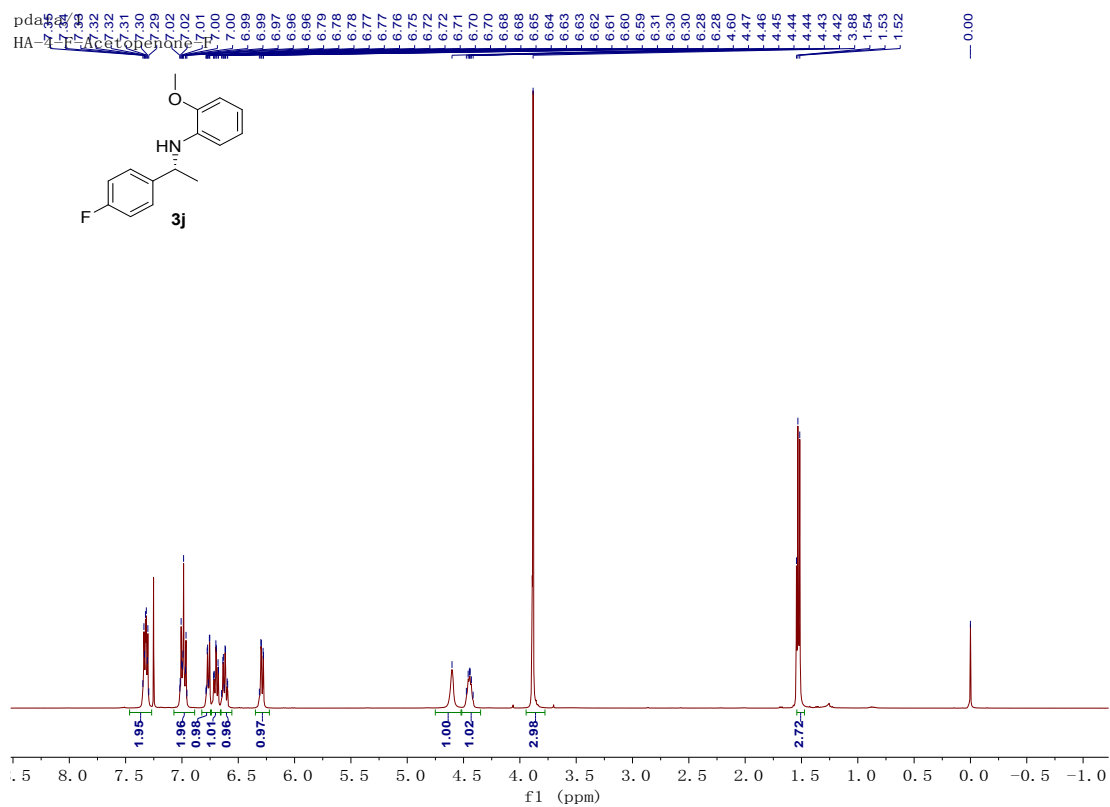
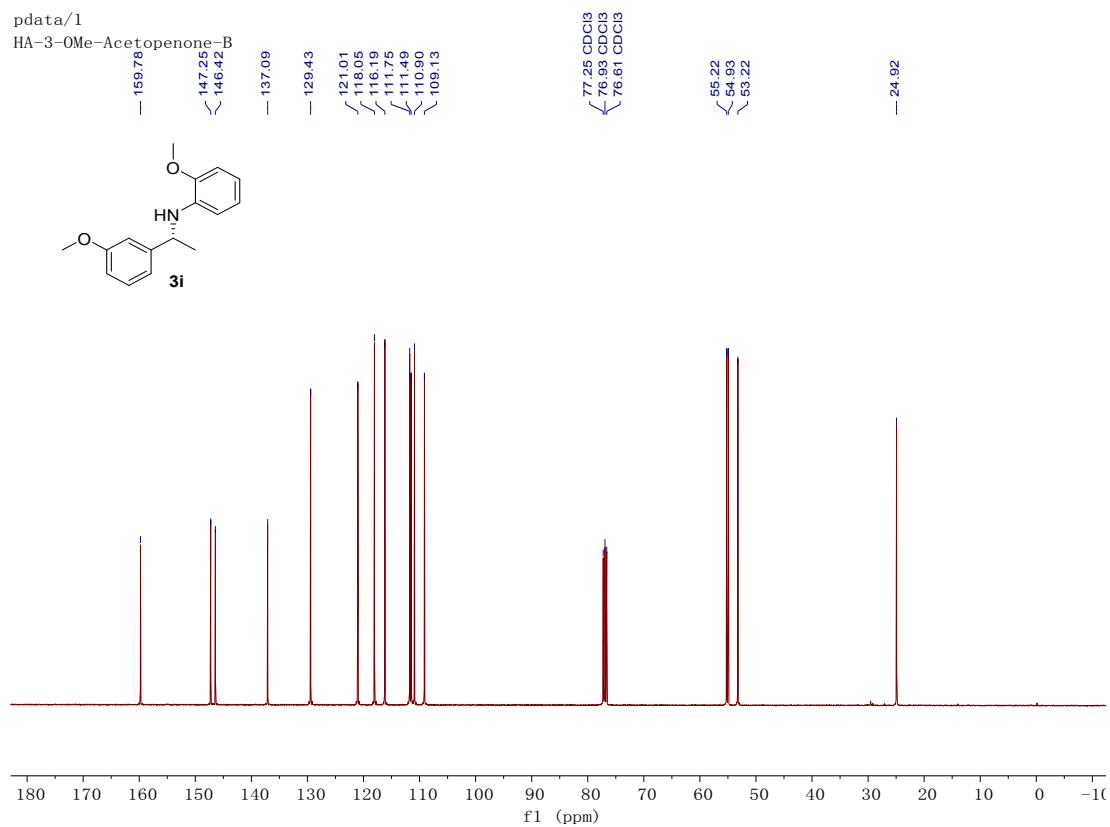


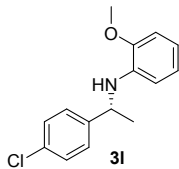
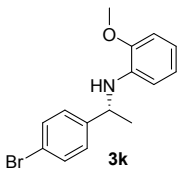
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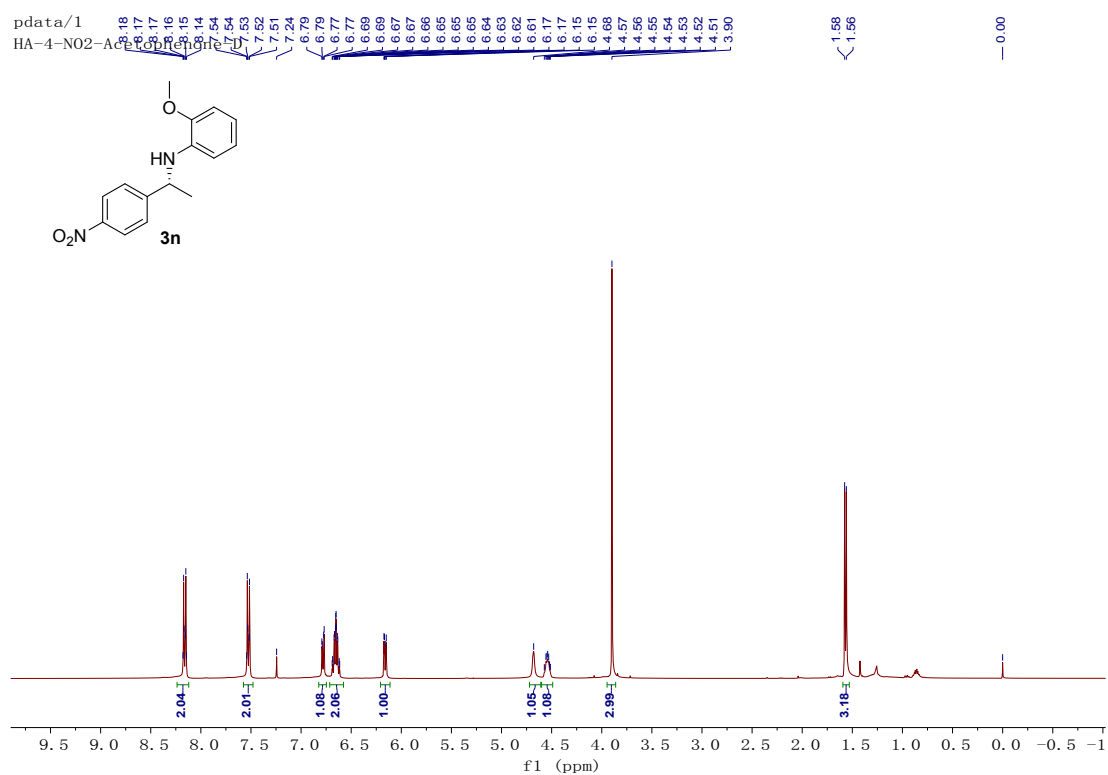
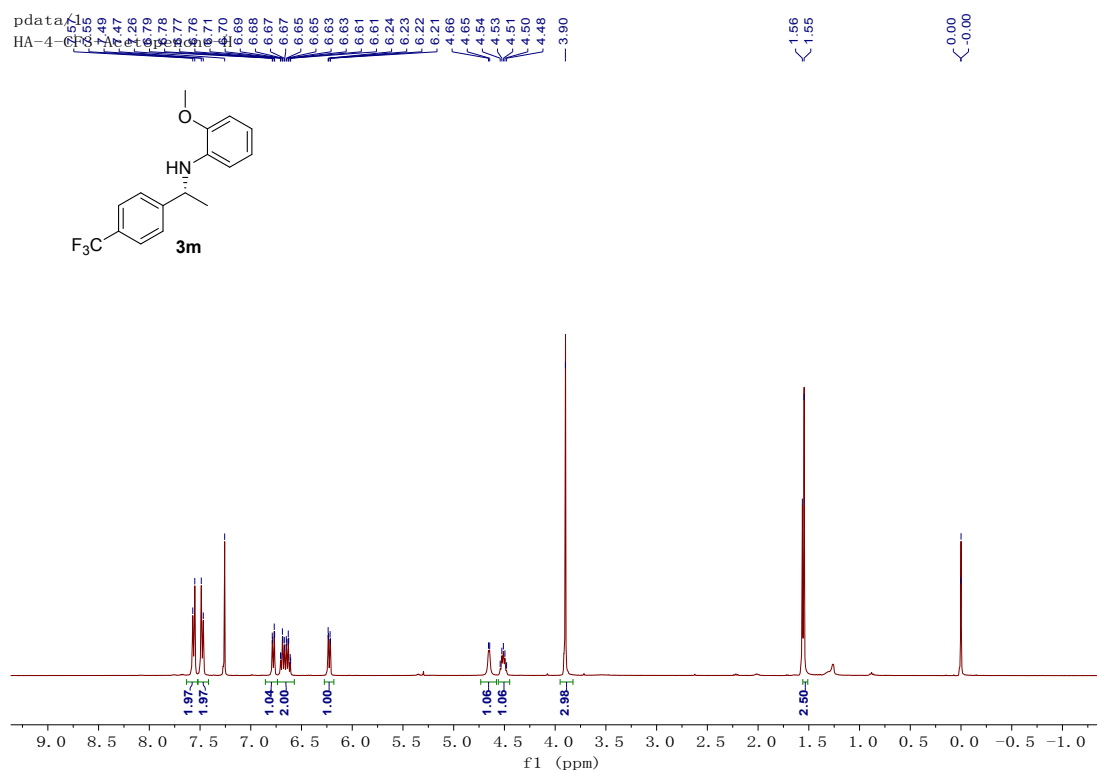


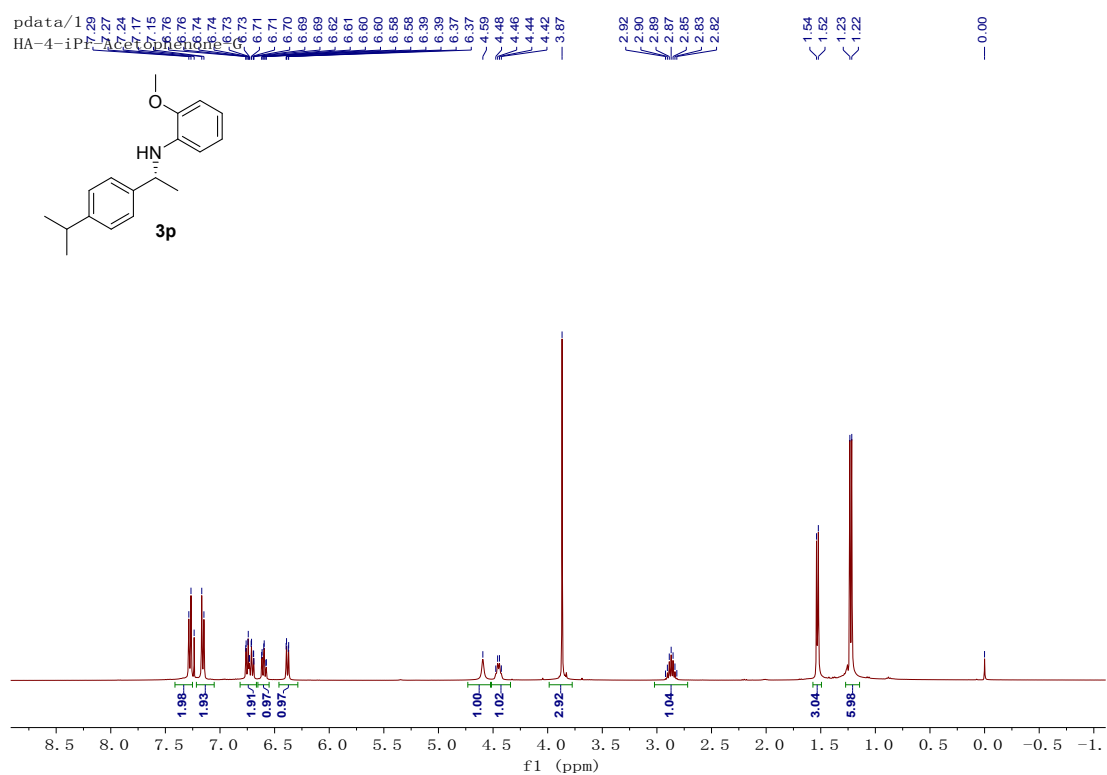
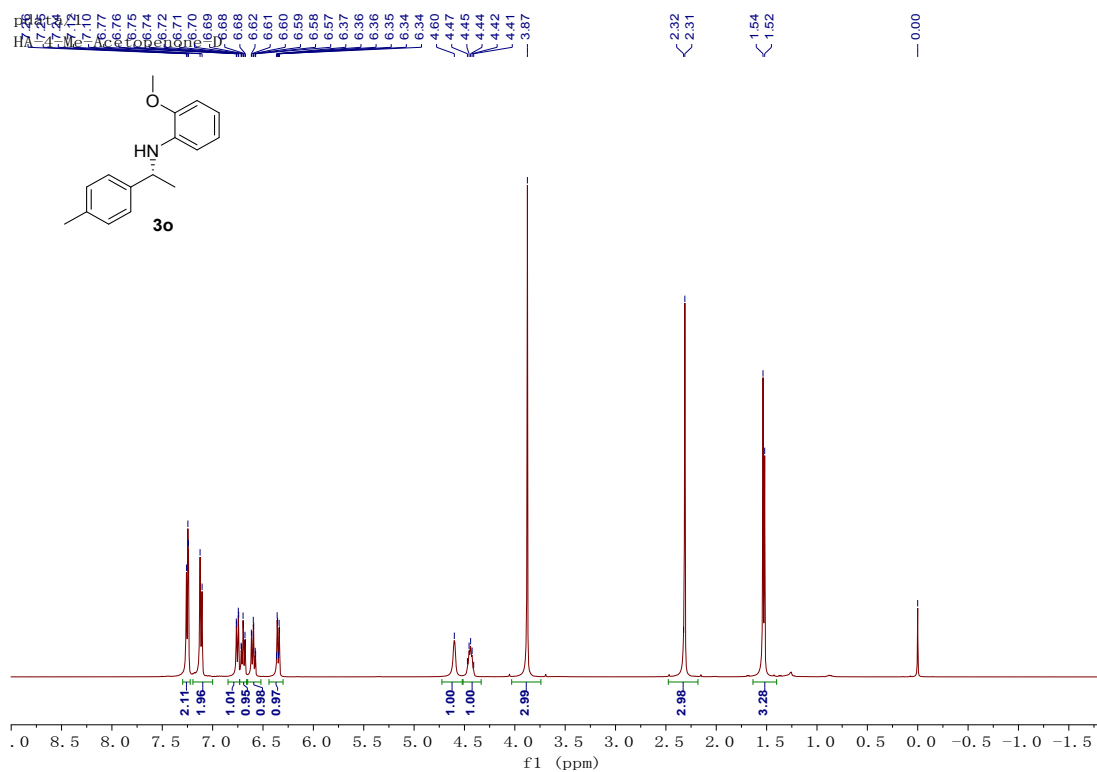


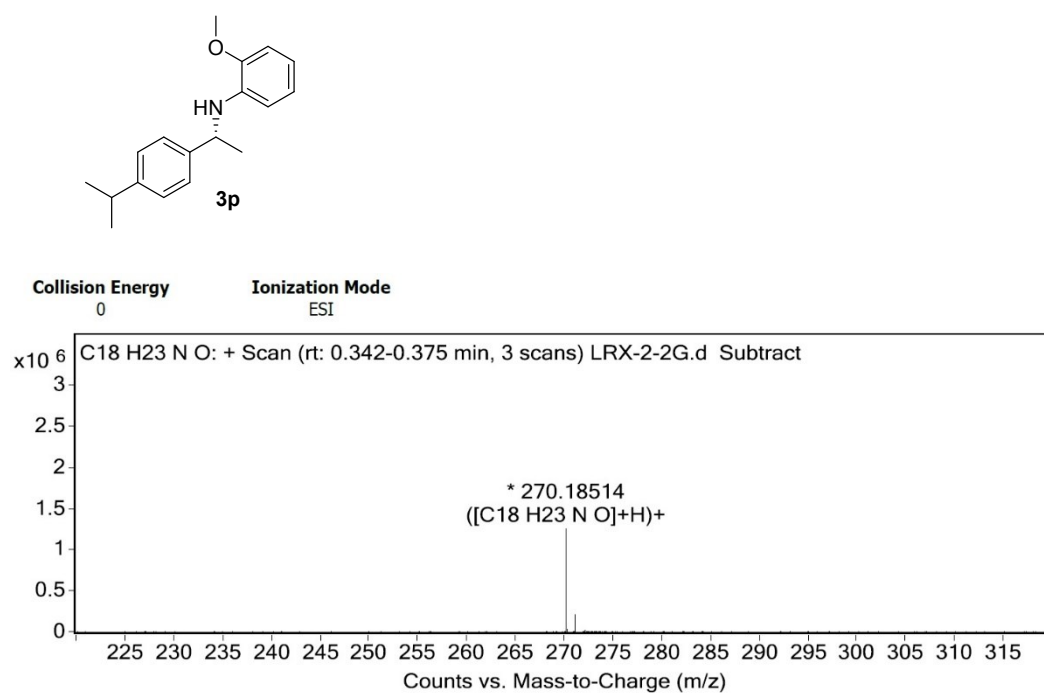
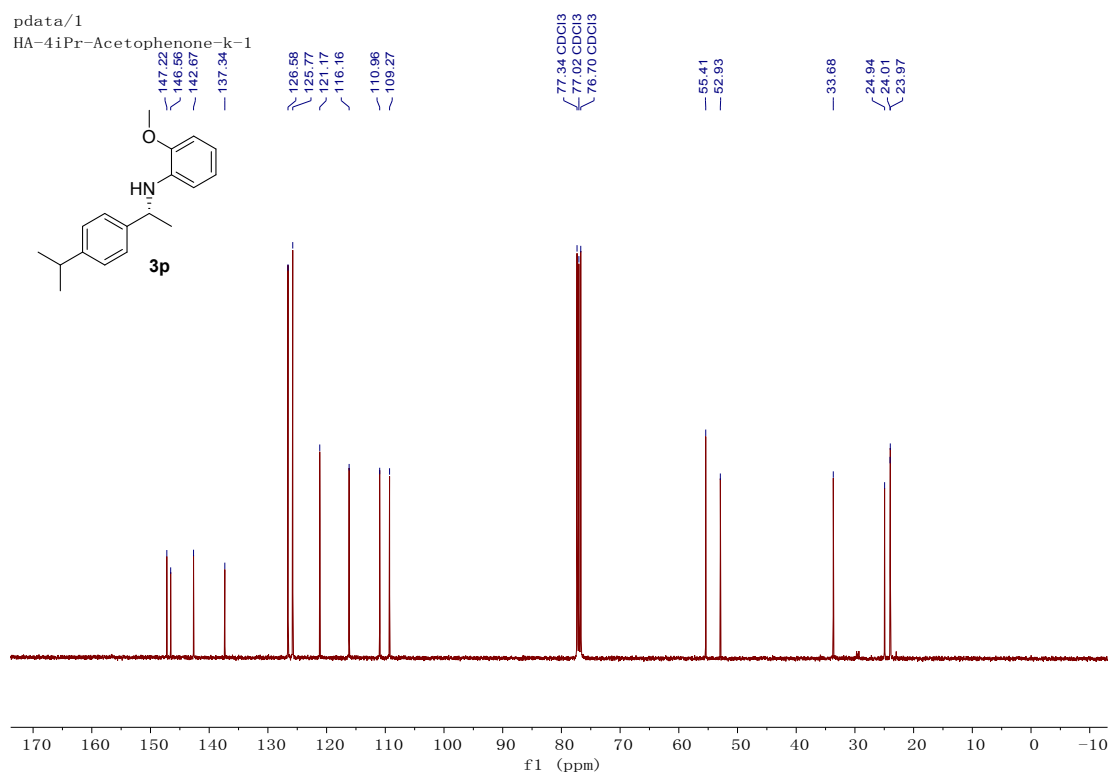


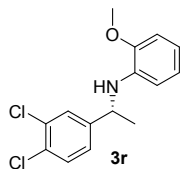
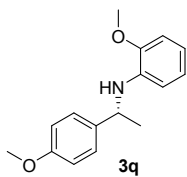


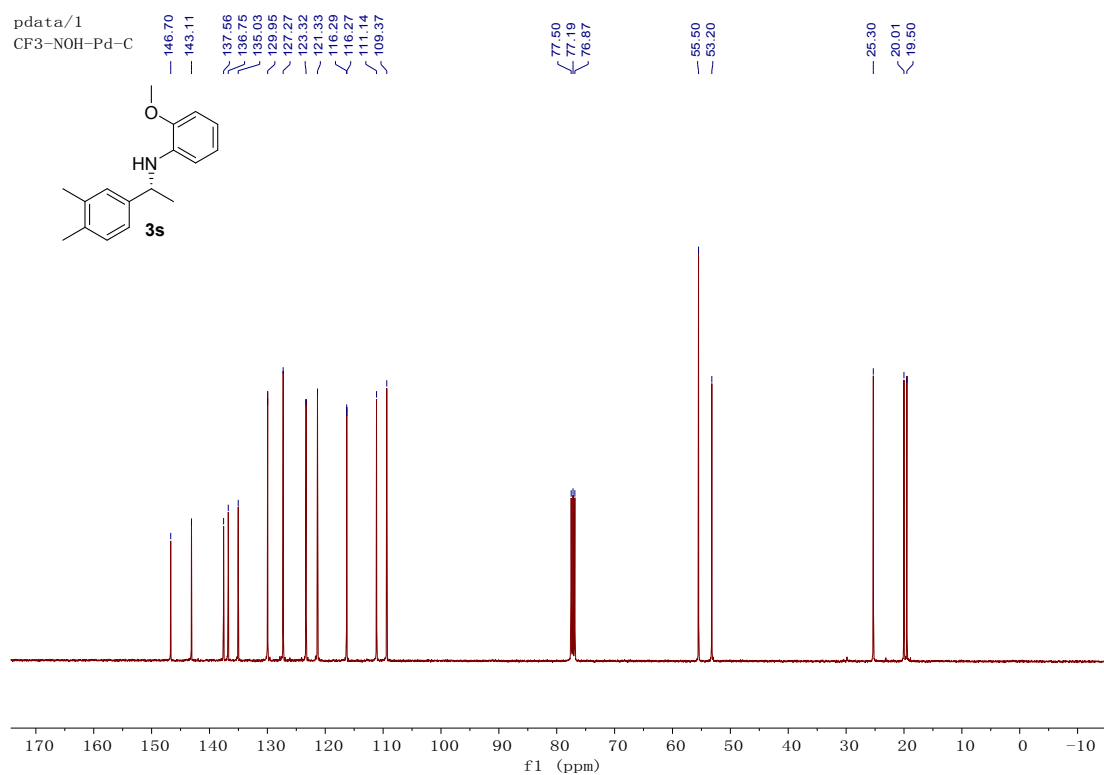
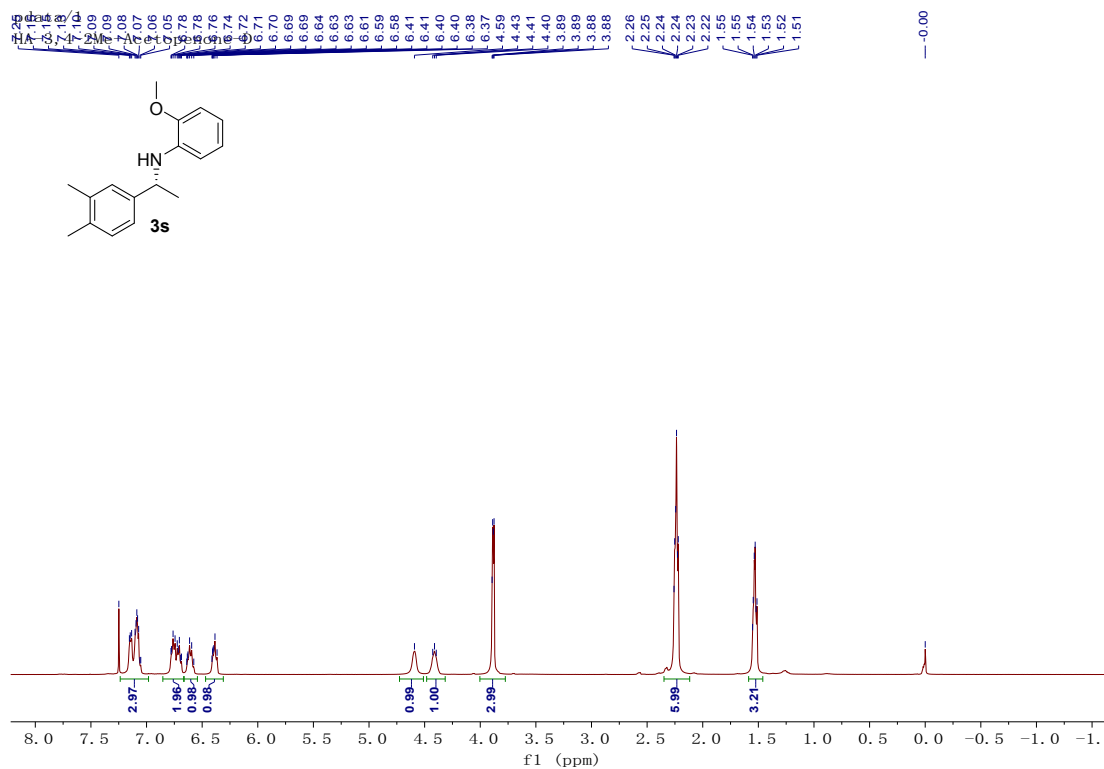




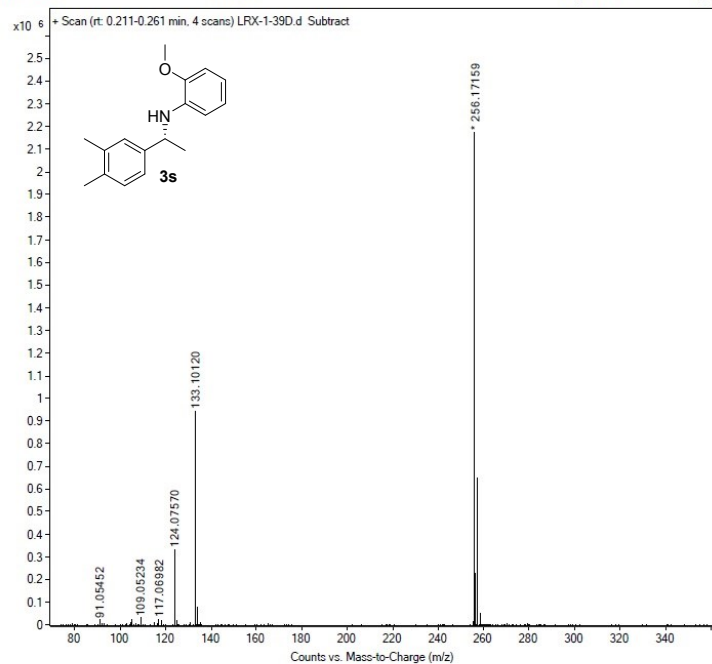






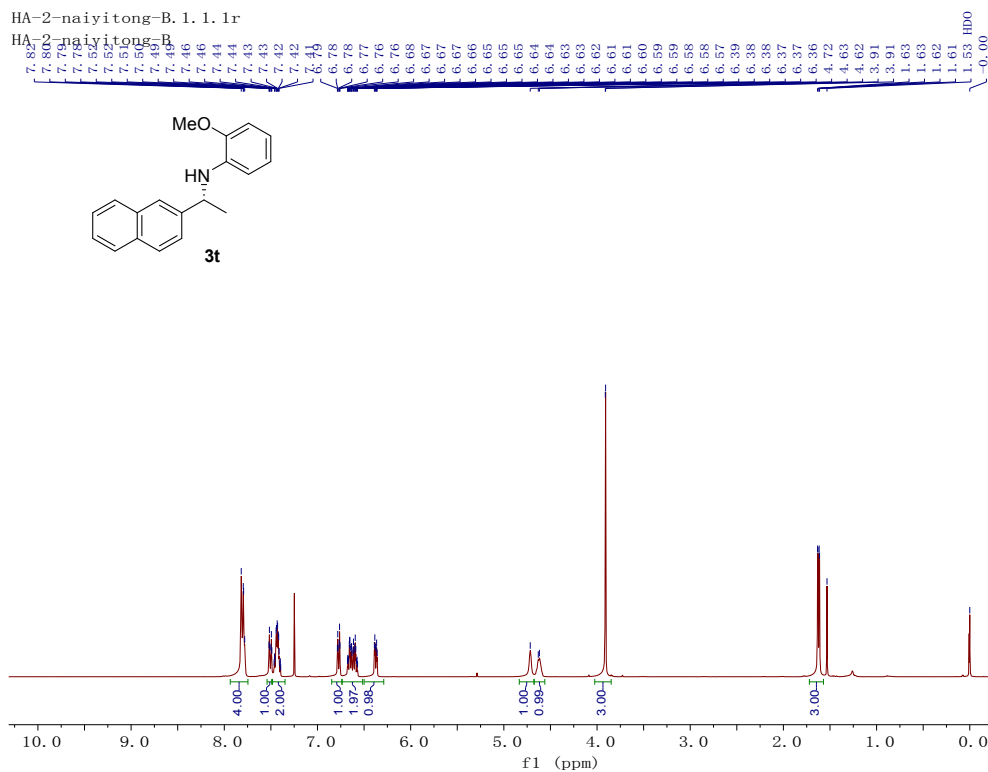


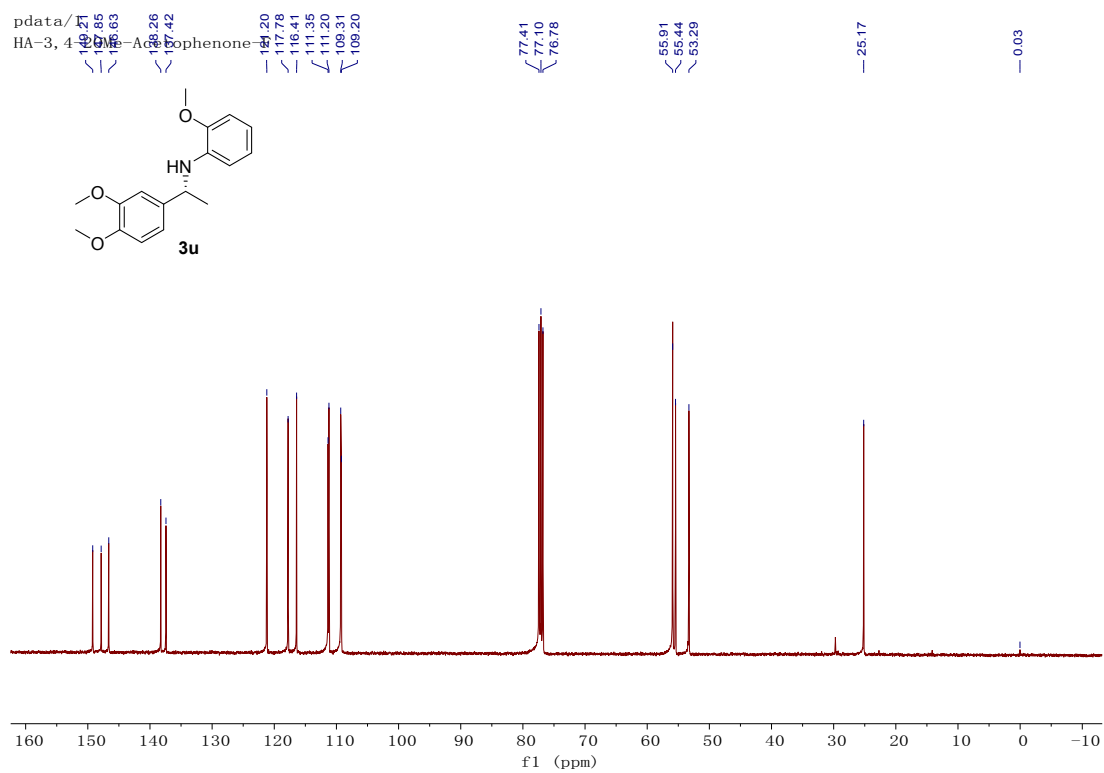
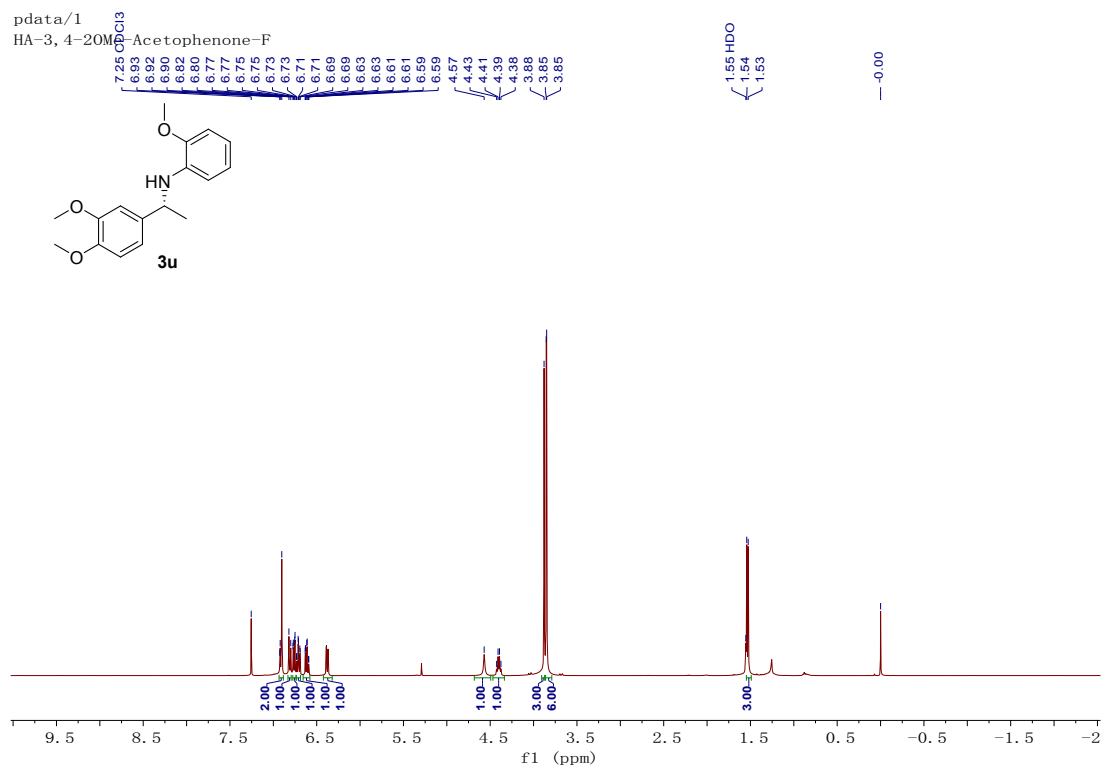
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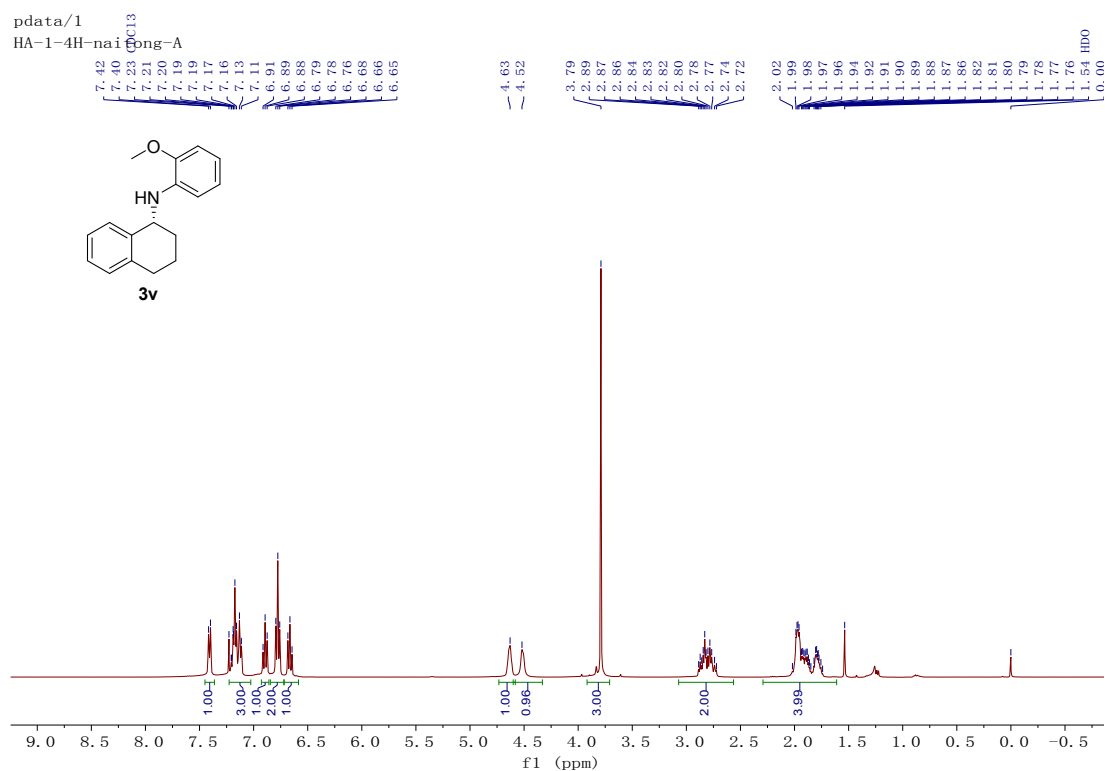
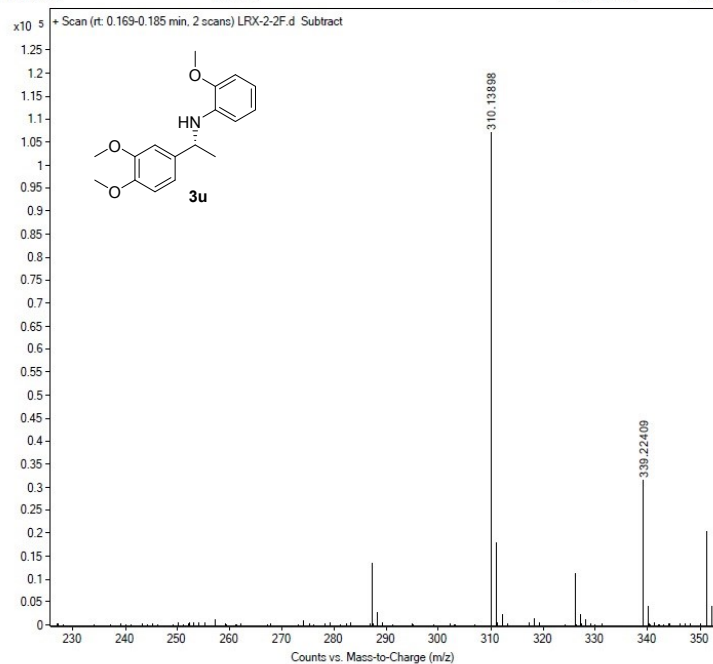
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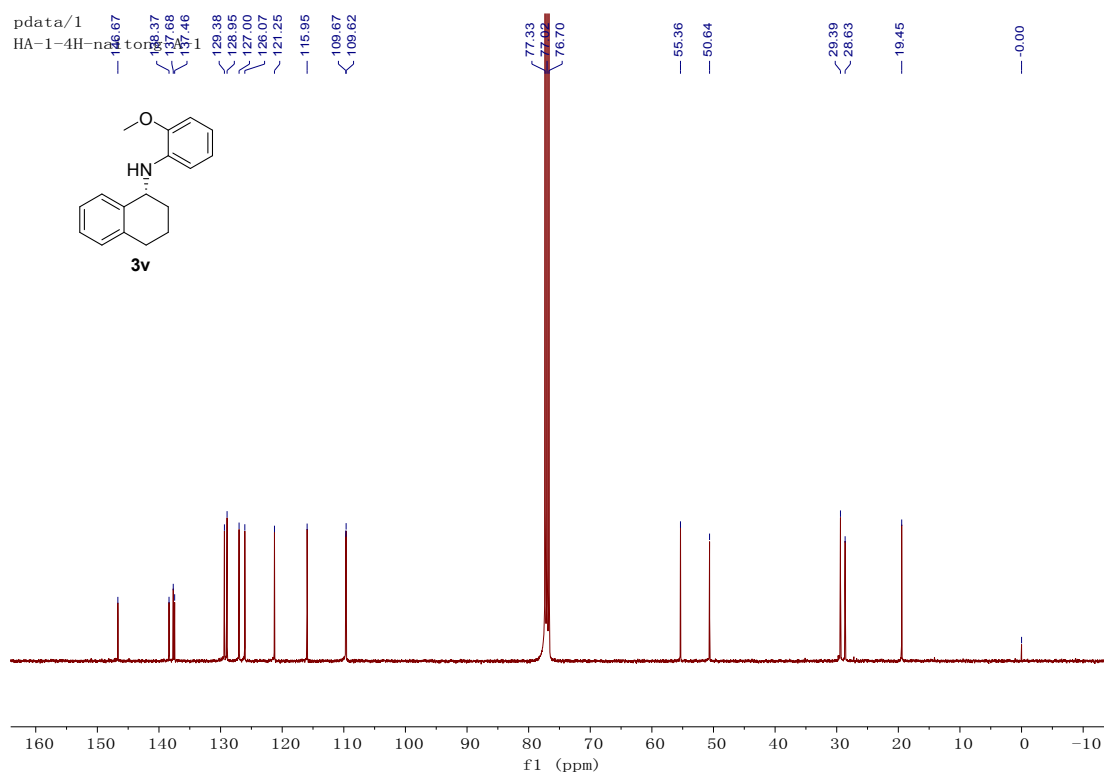
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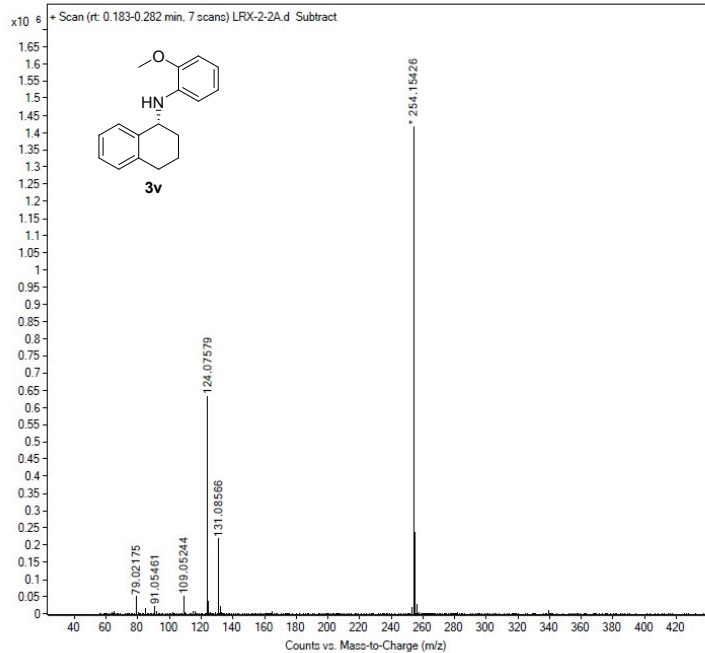


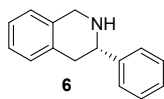
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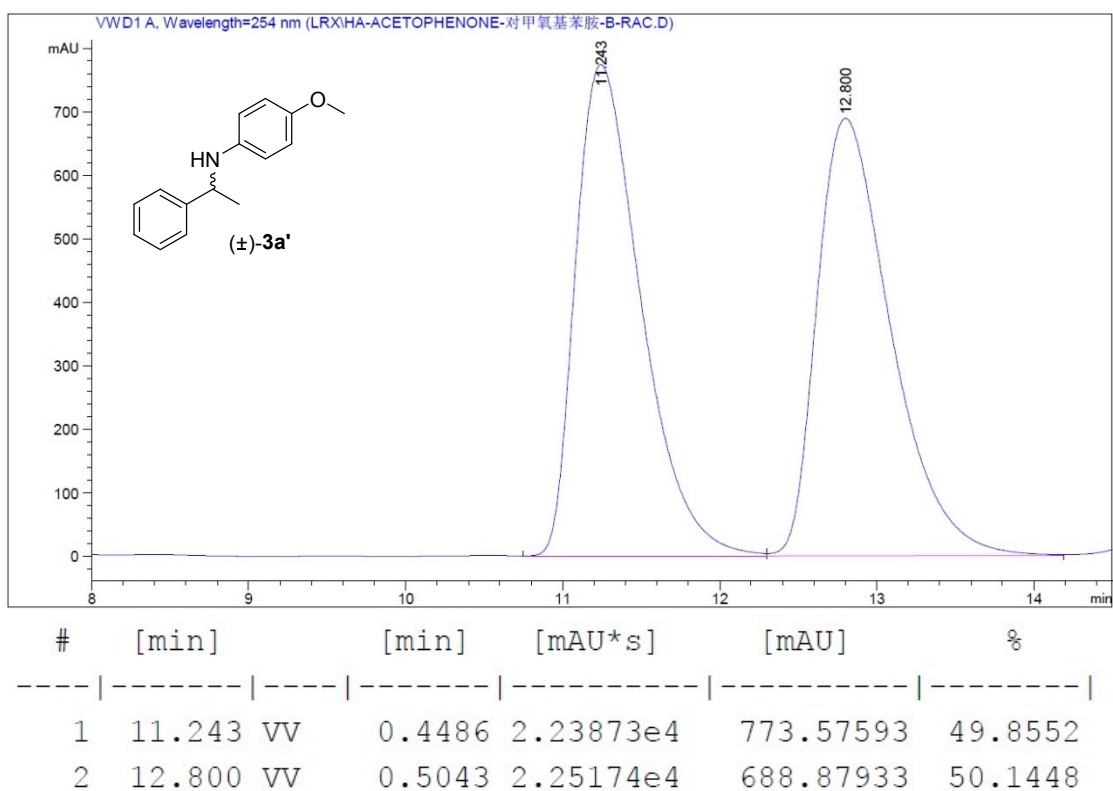
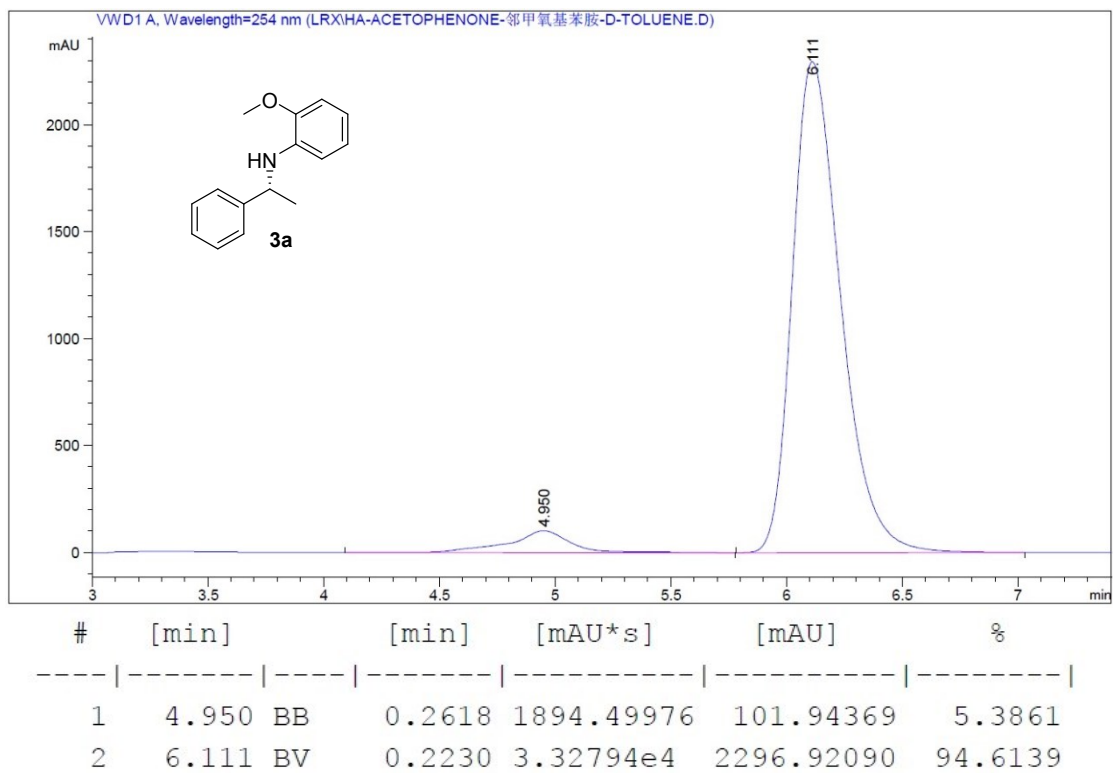


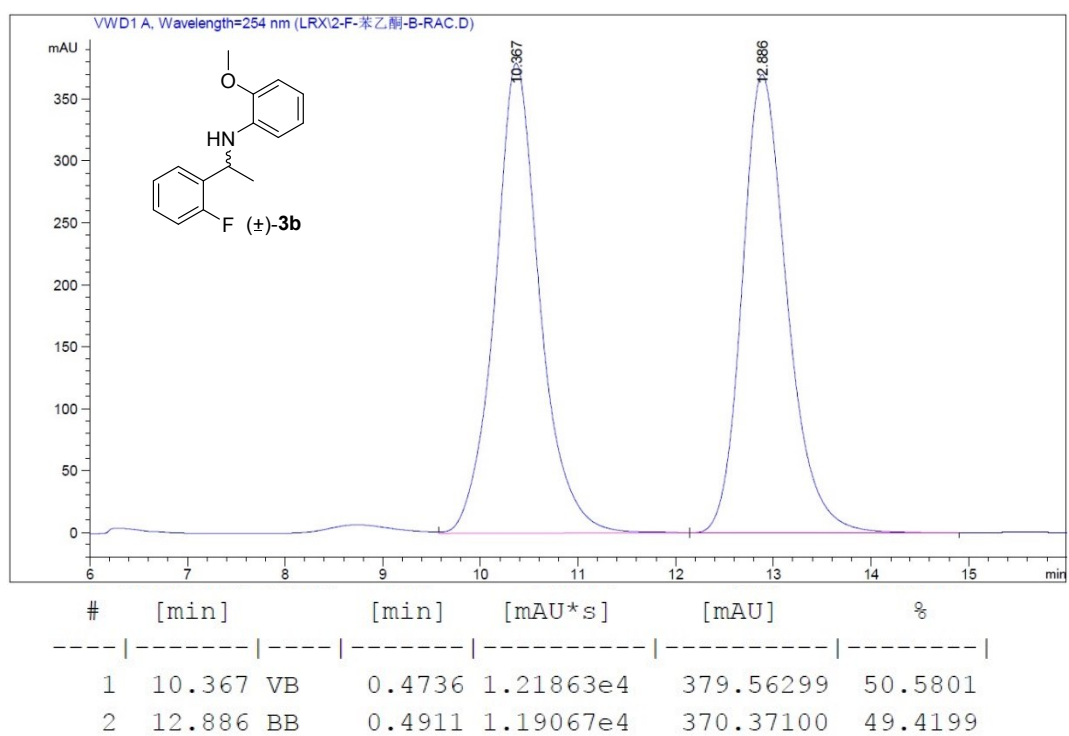
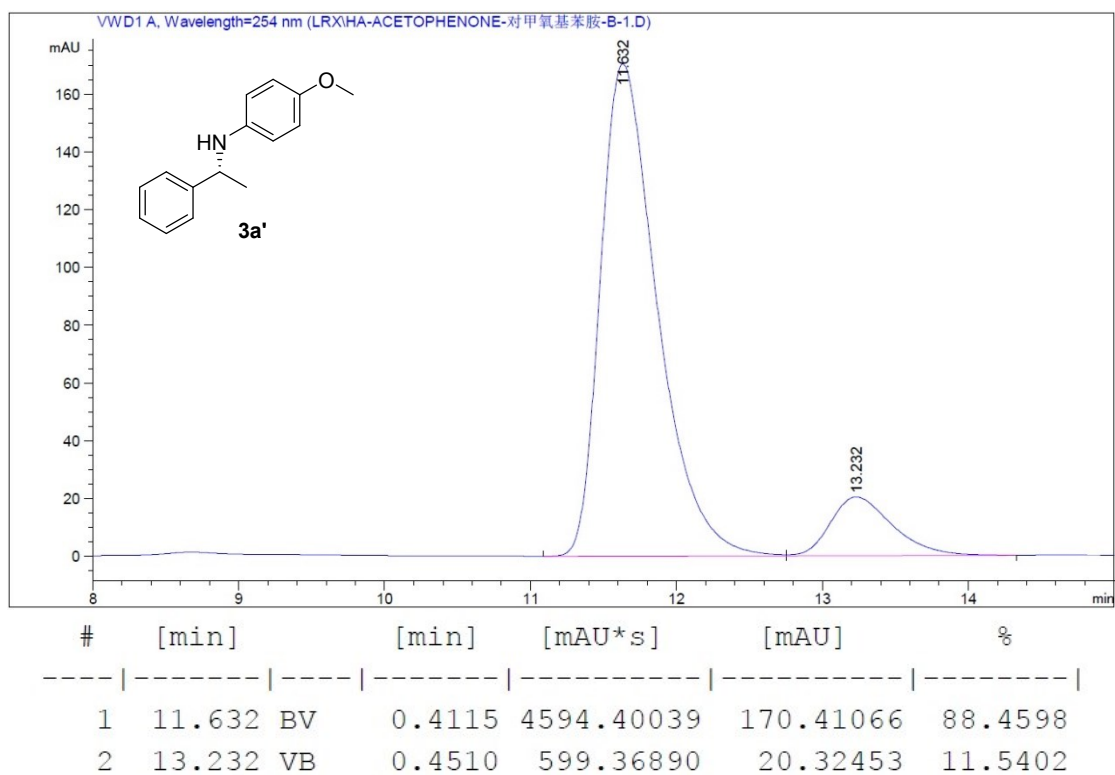


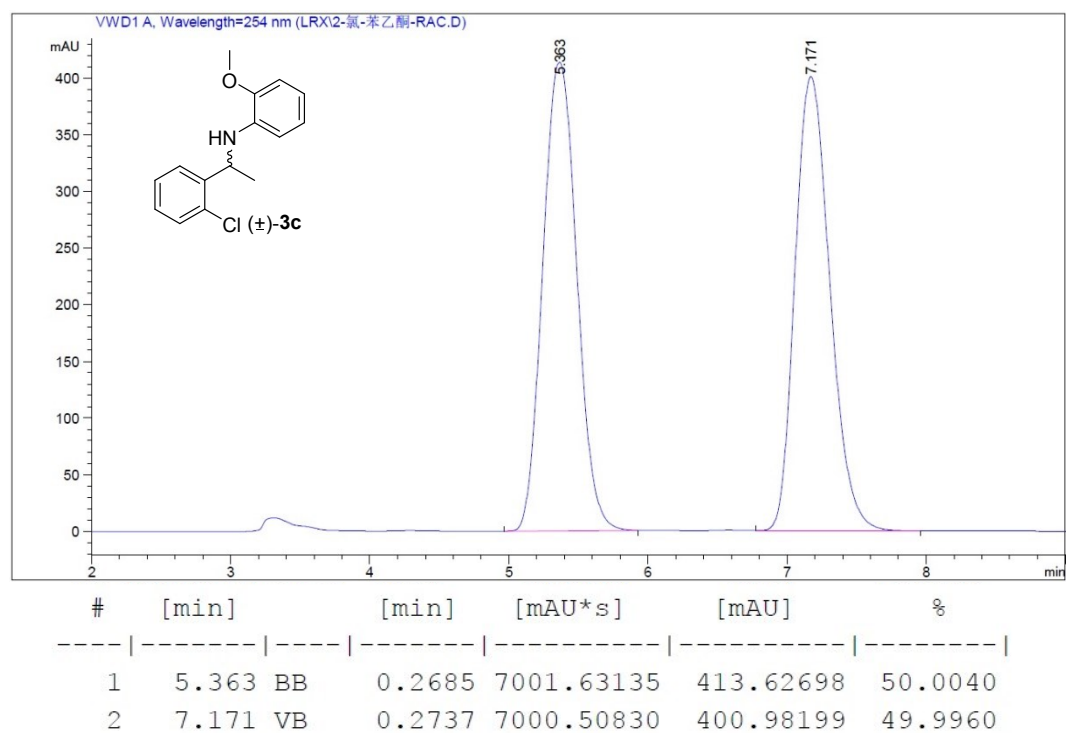
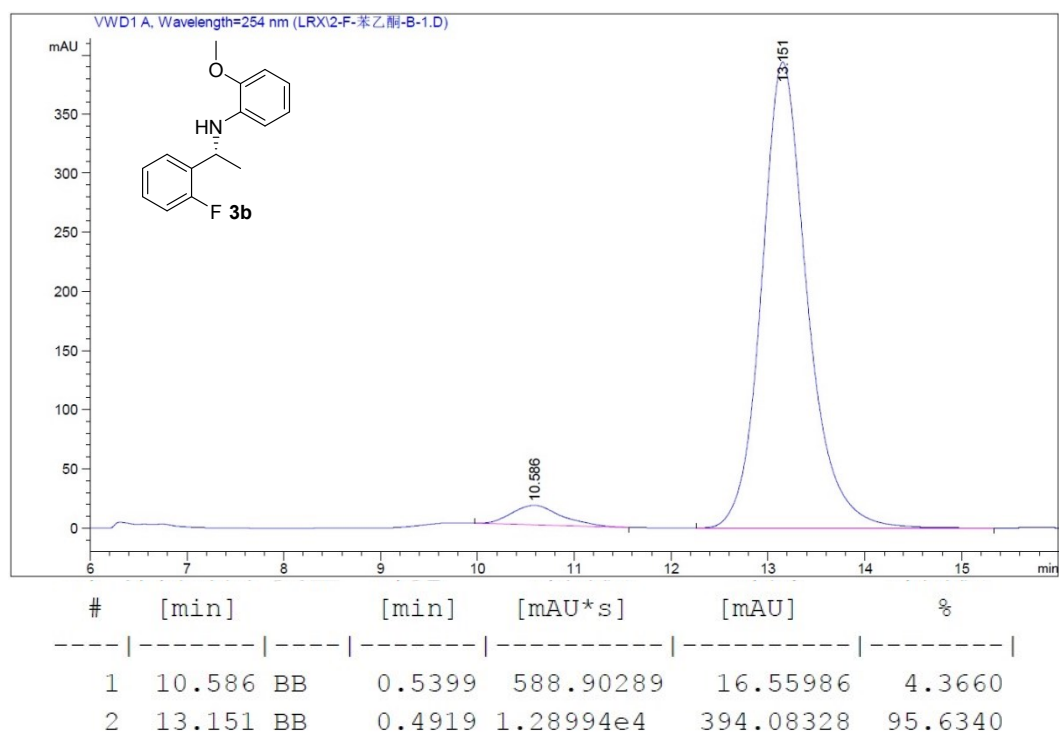
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User Name		Inj Vol	1	InjPosition	
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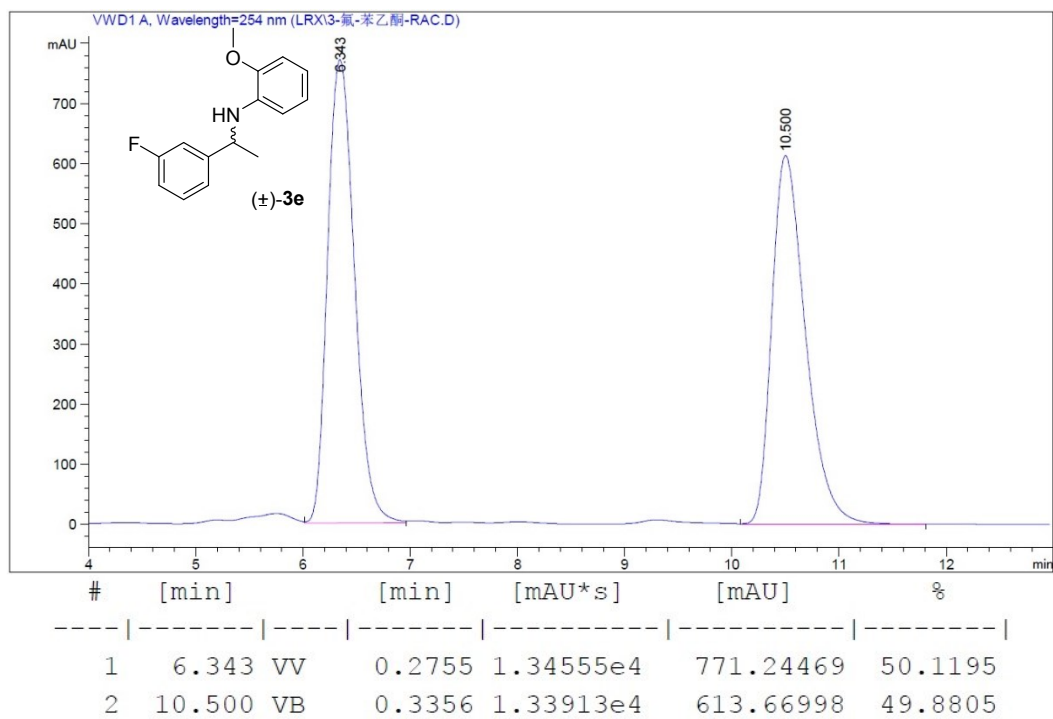
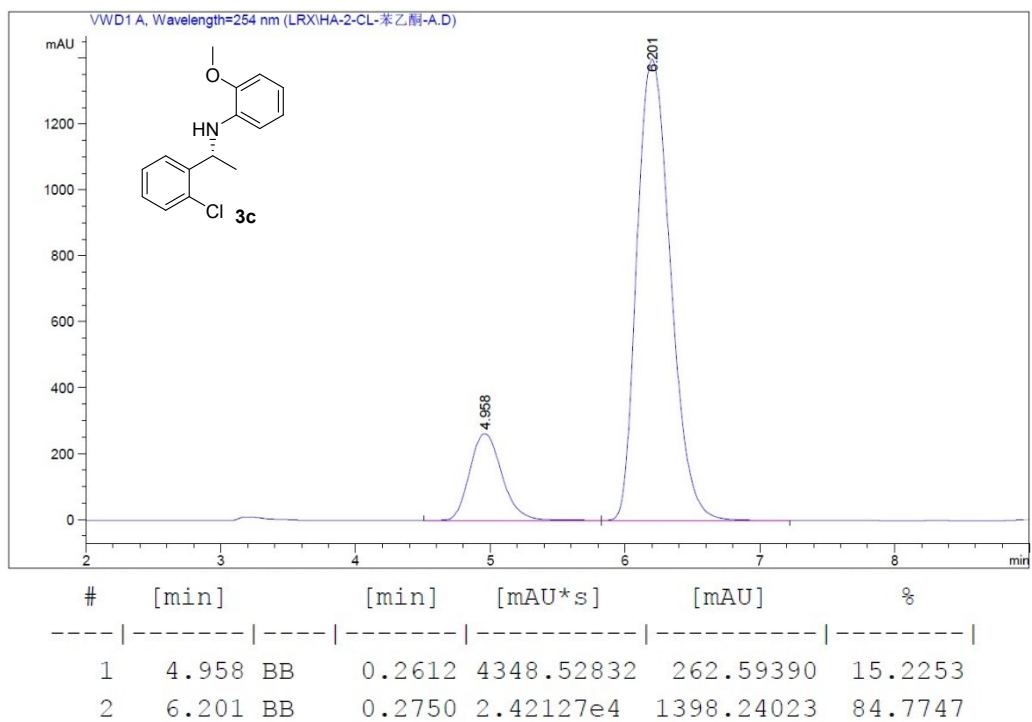


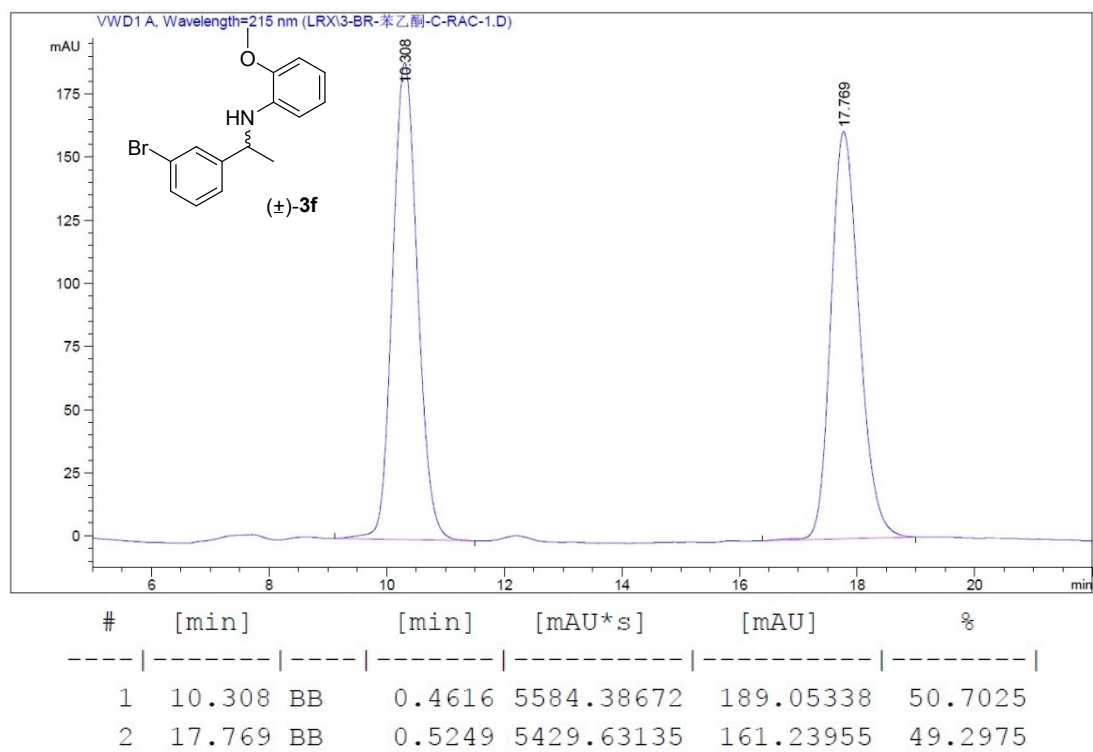
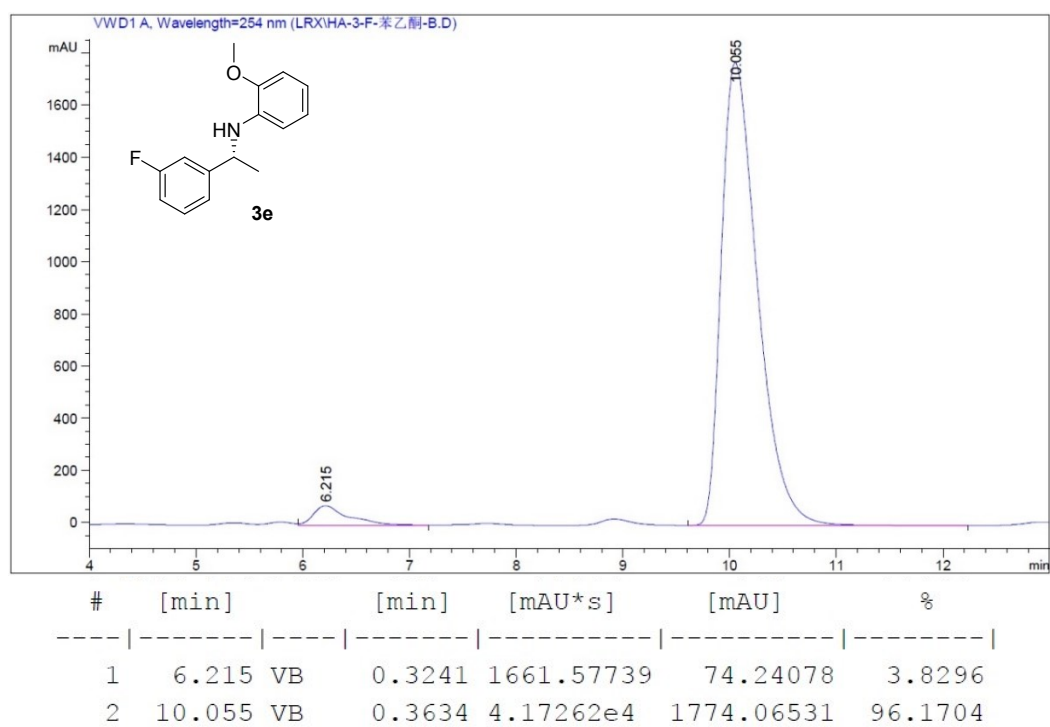


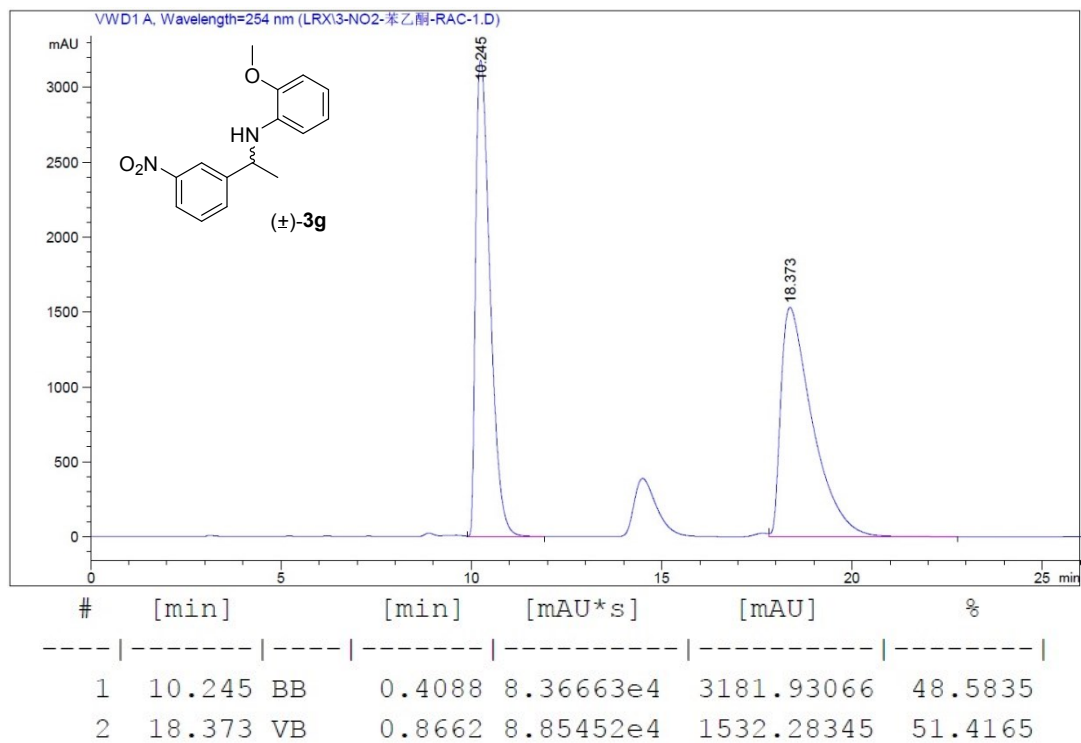
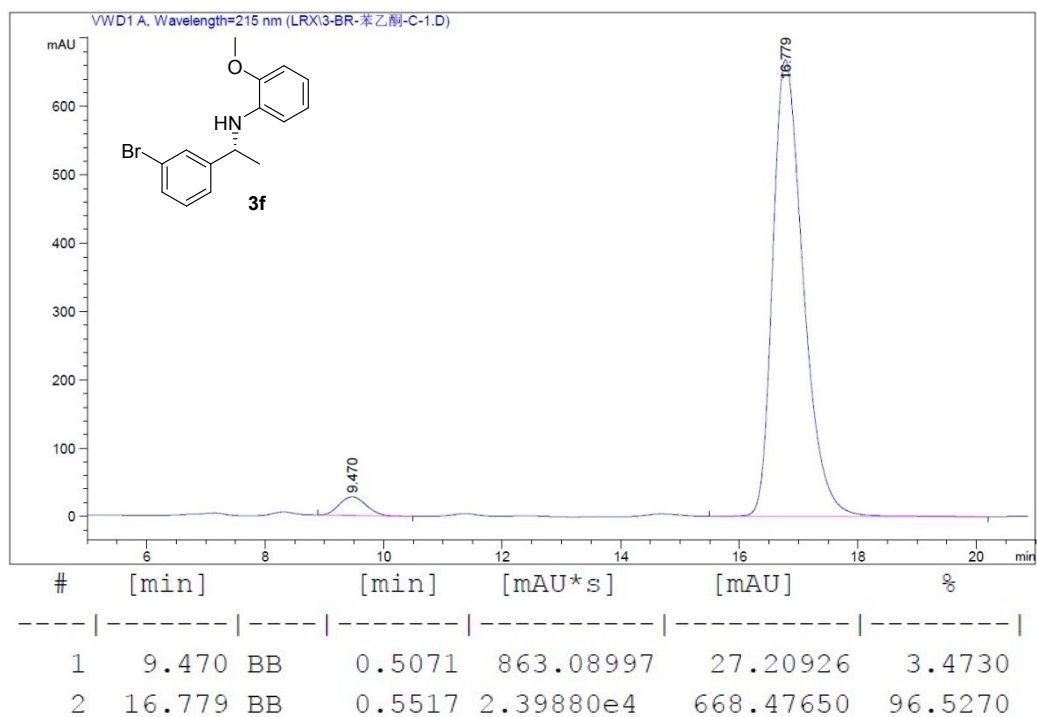


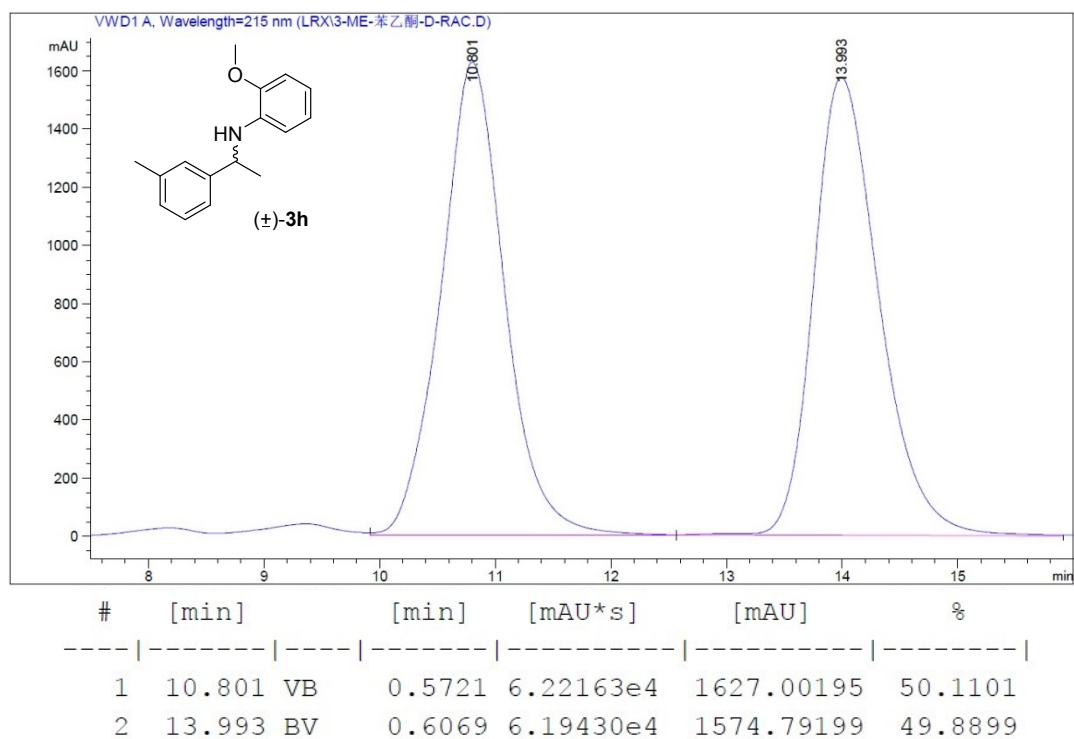
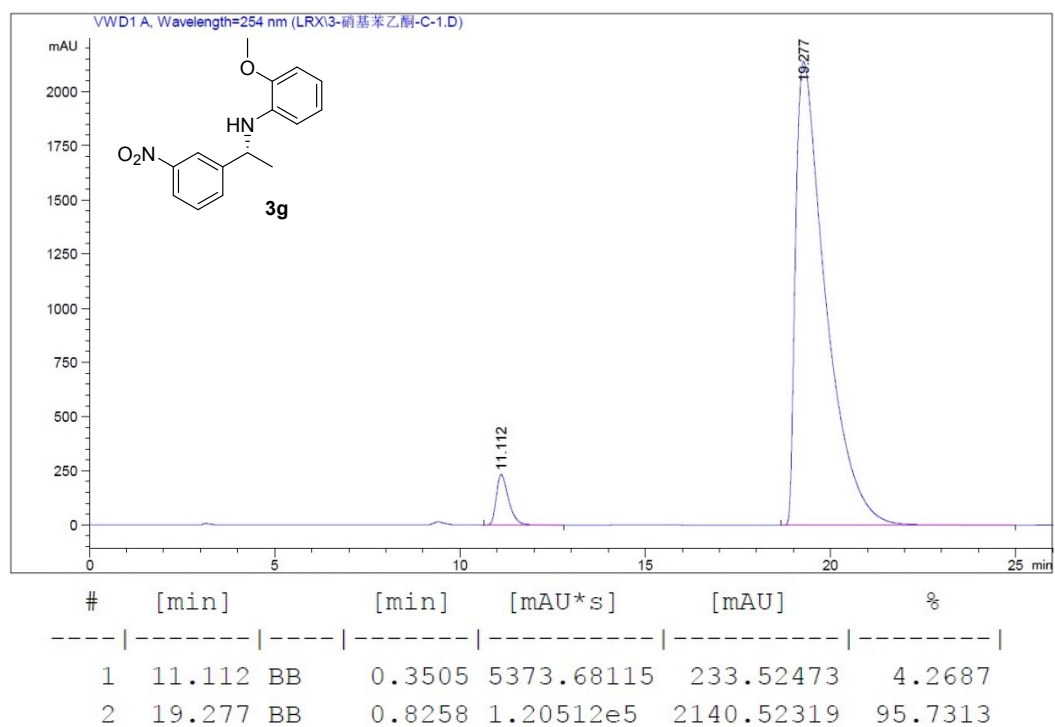


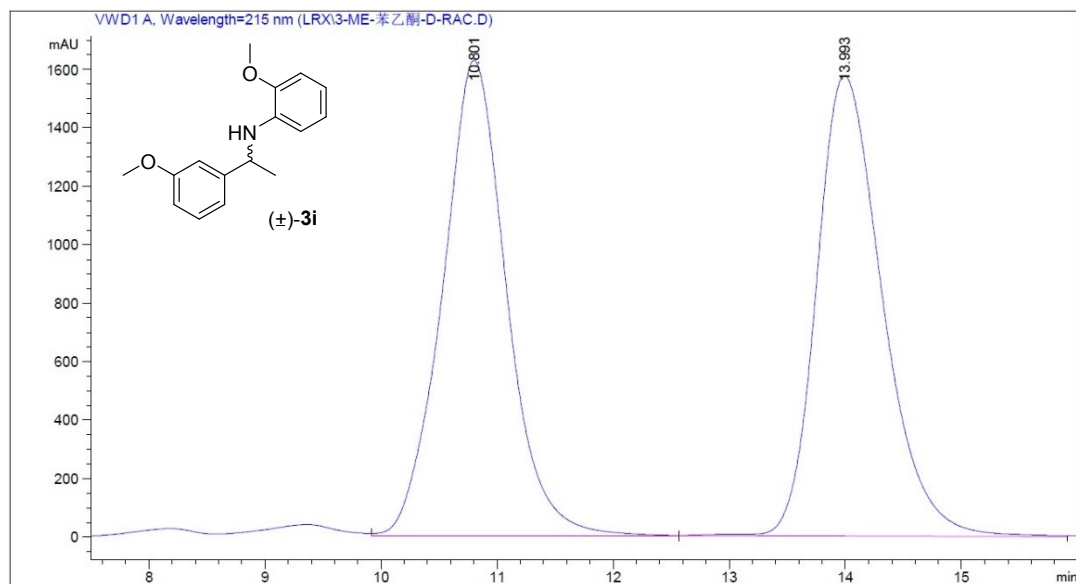
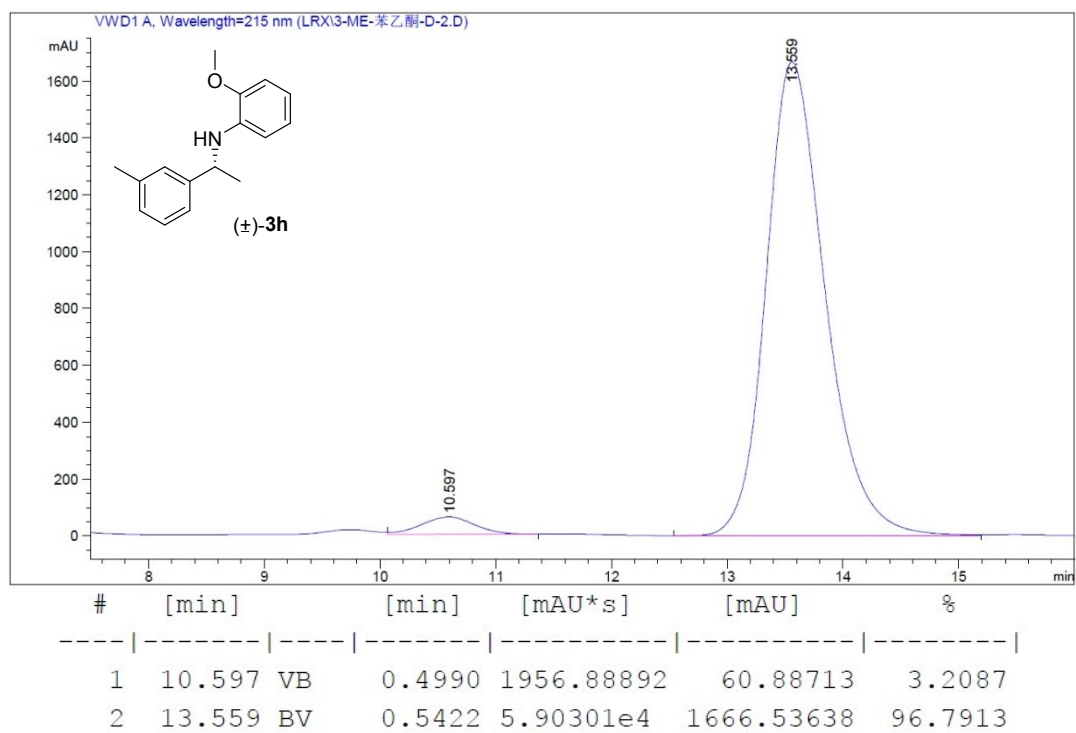


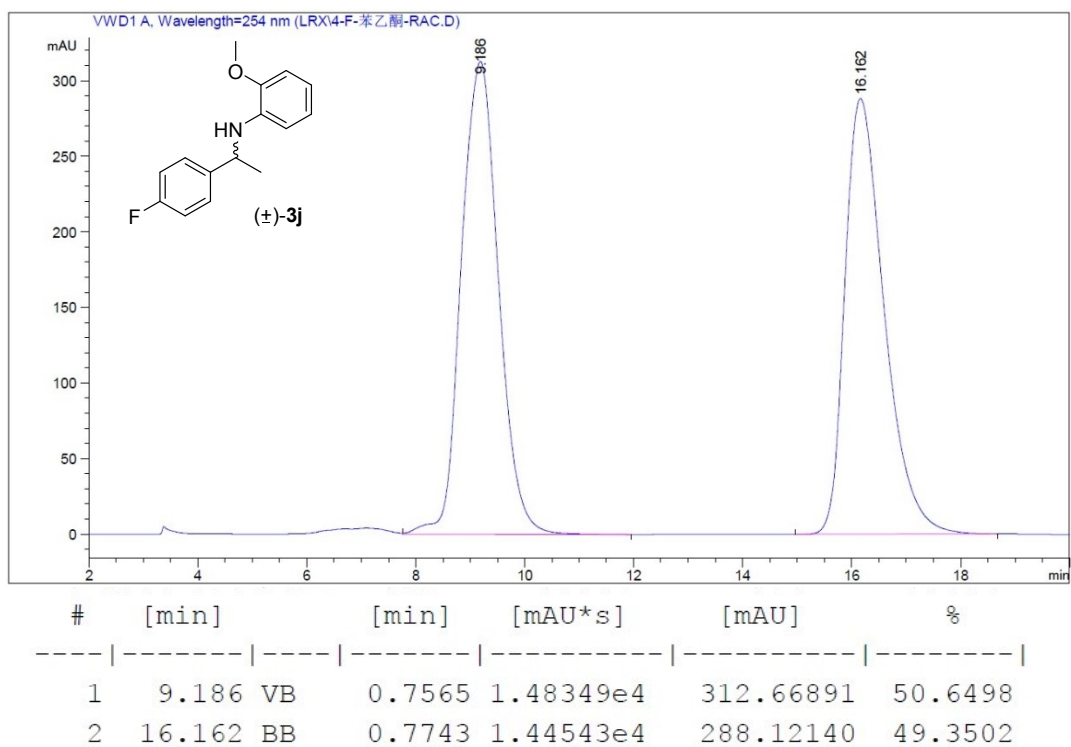
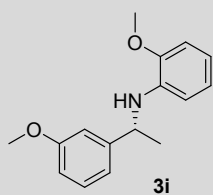


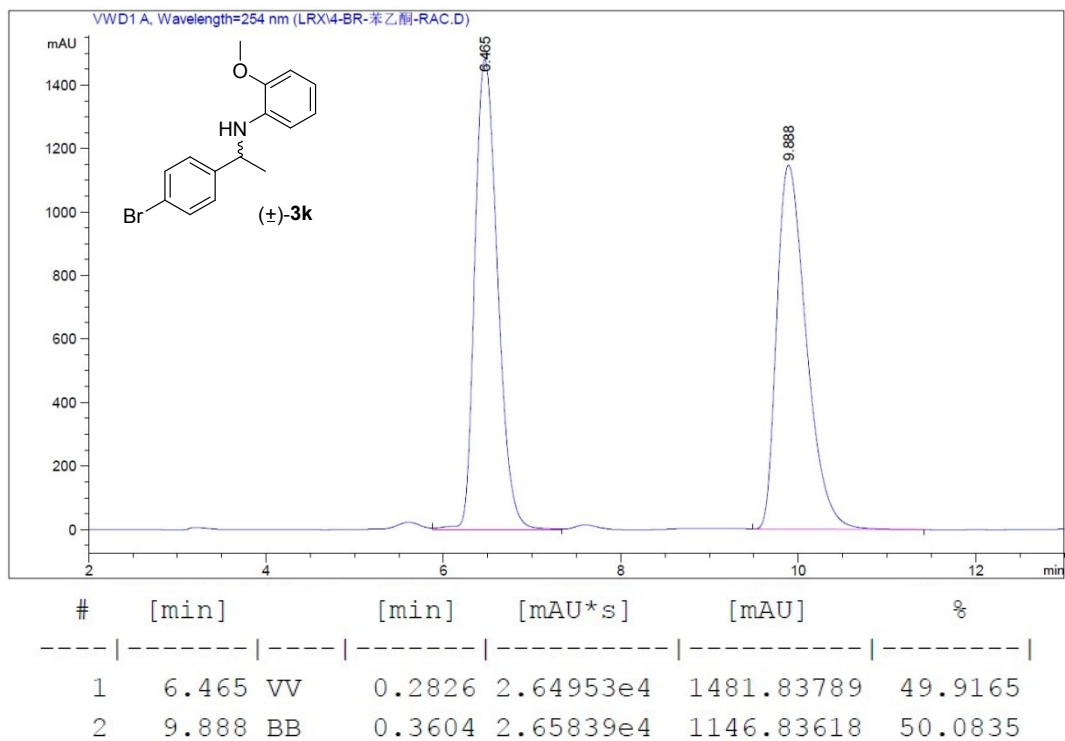
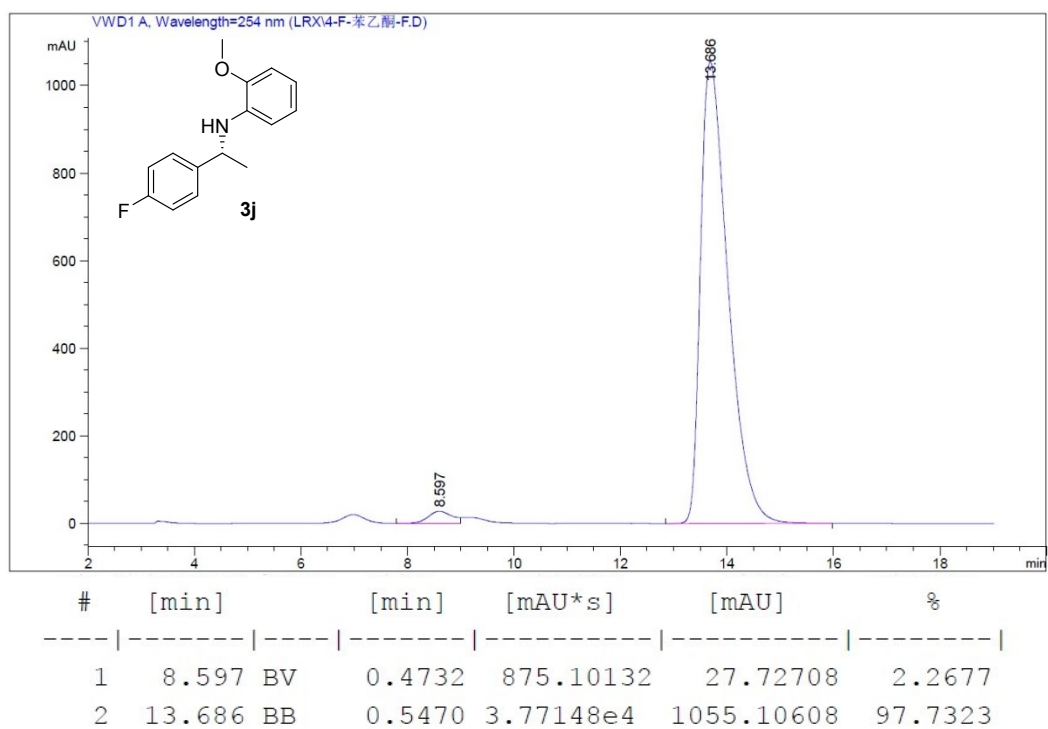


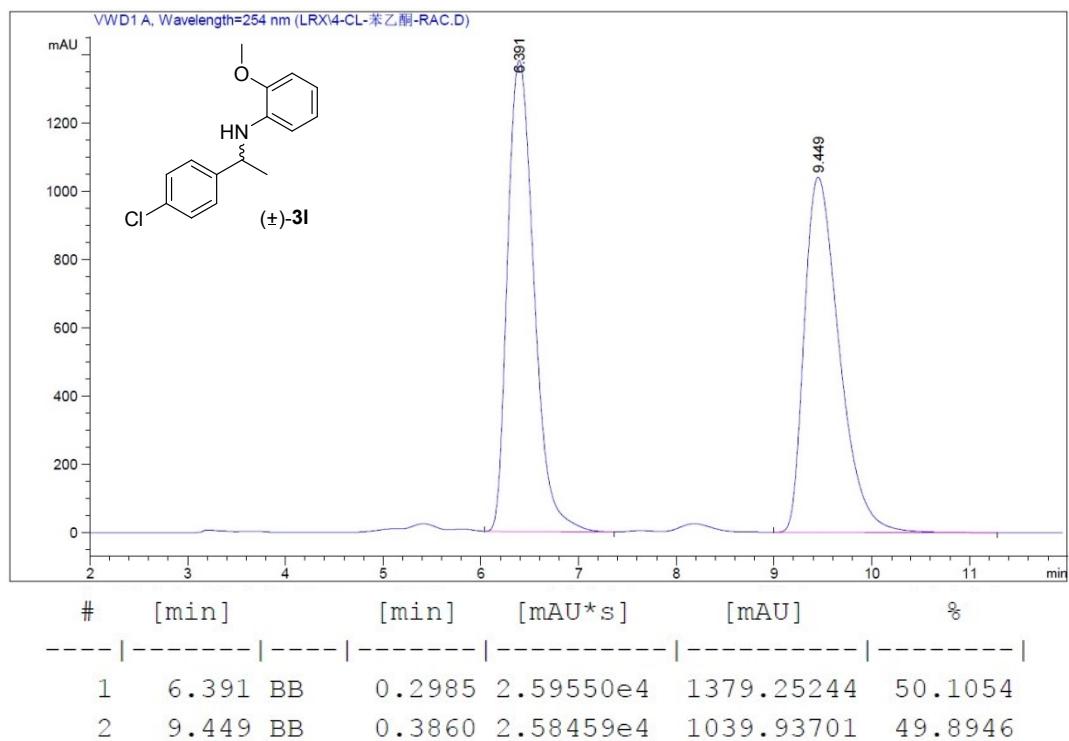
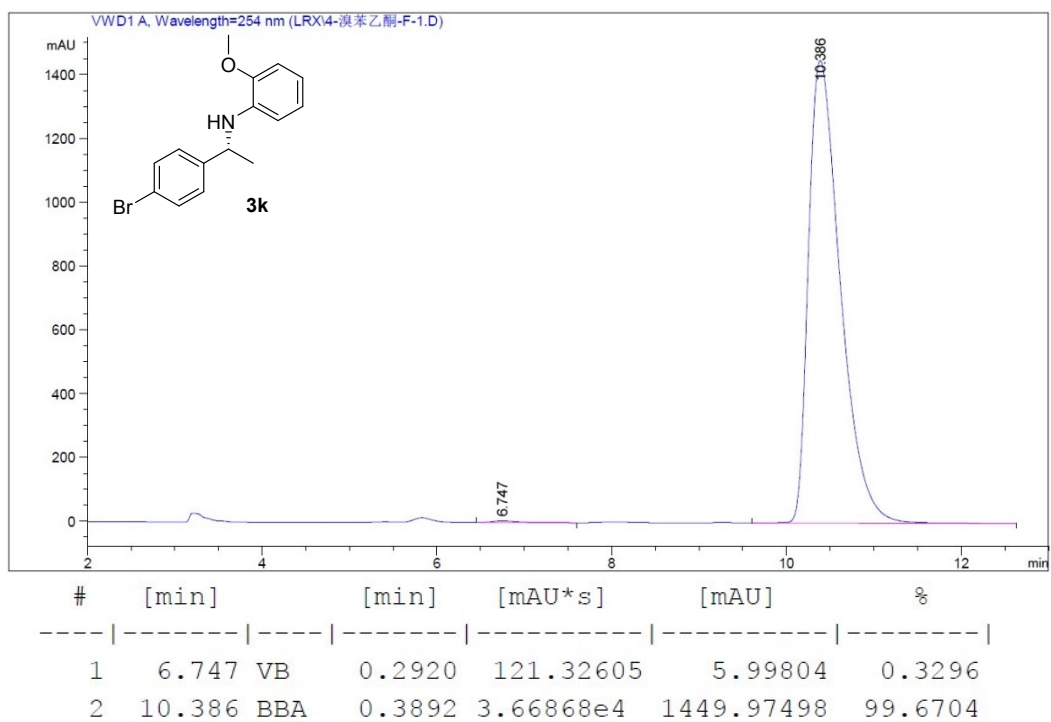


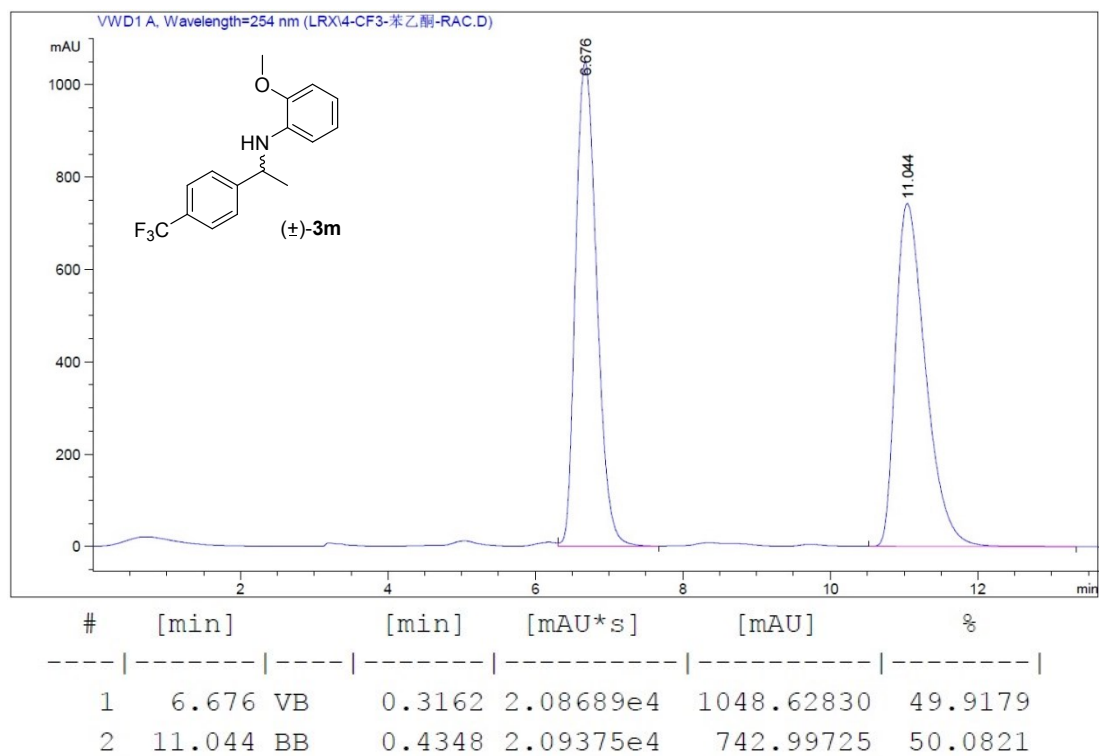
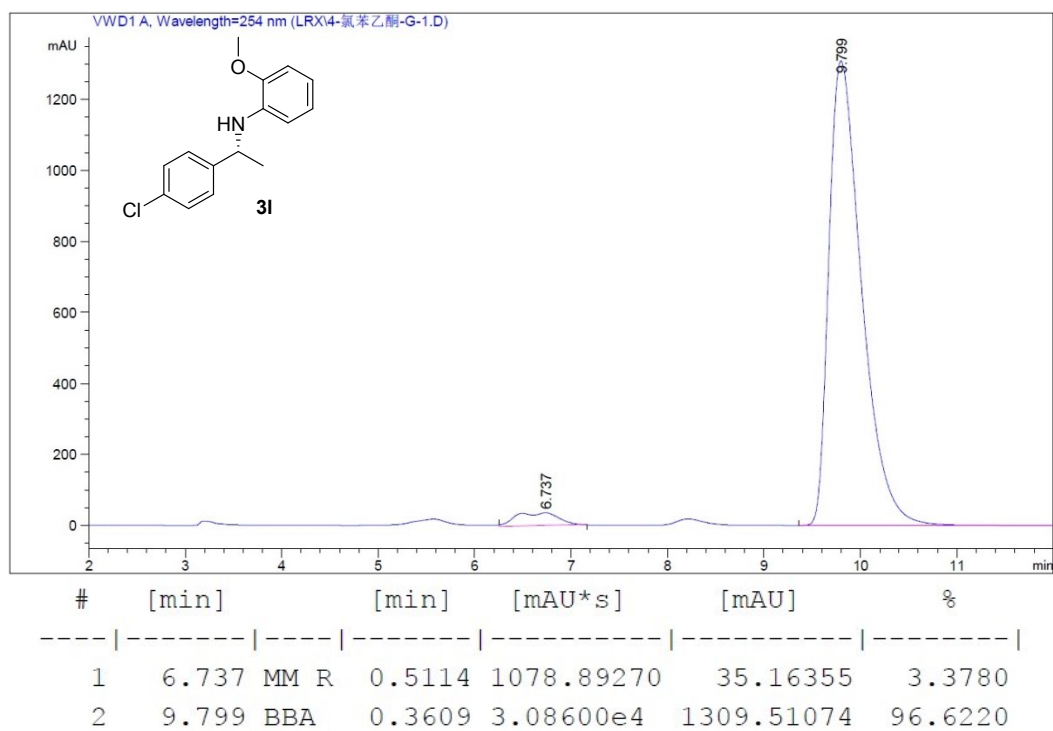


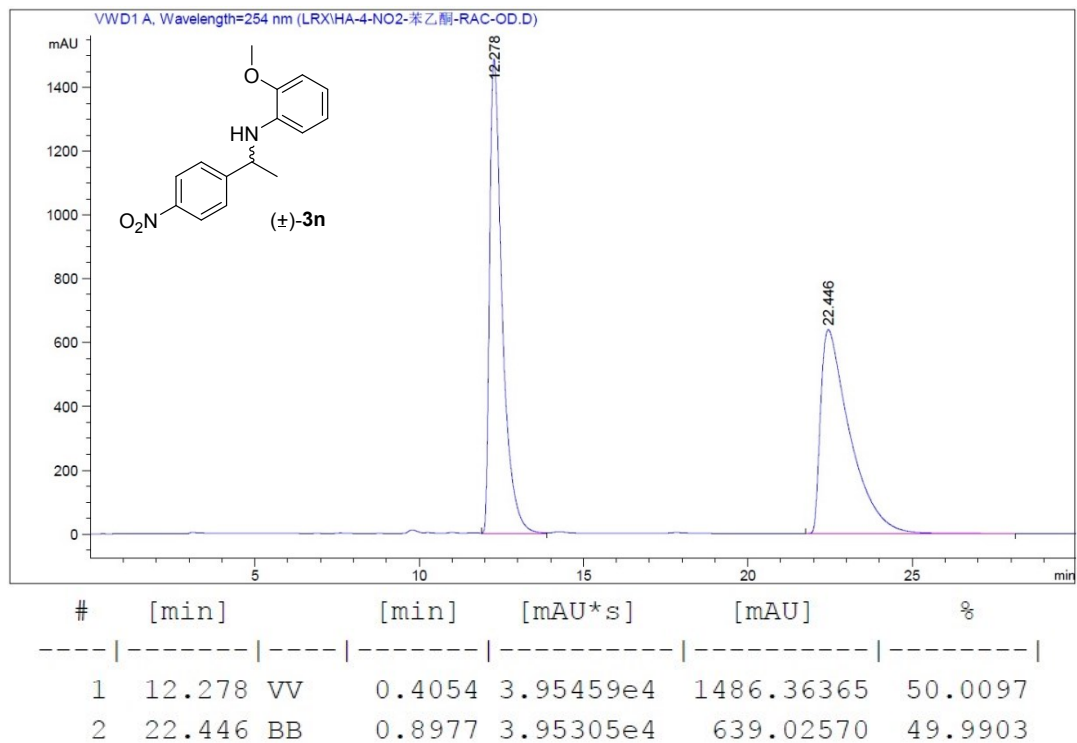
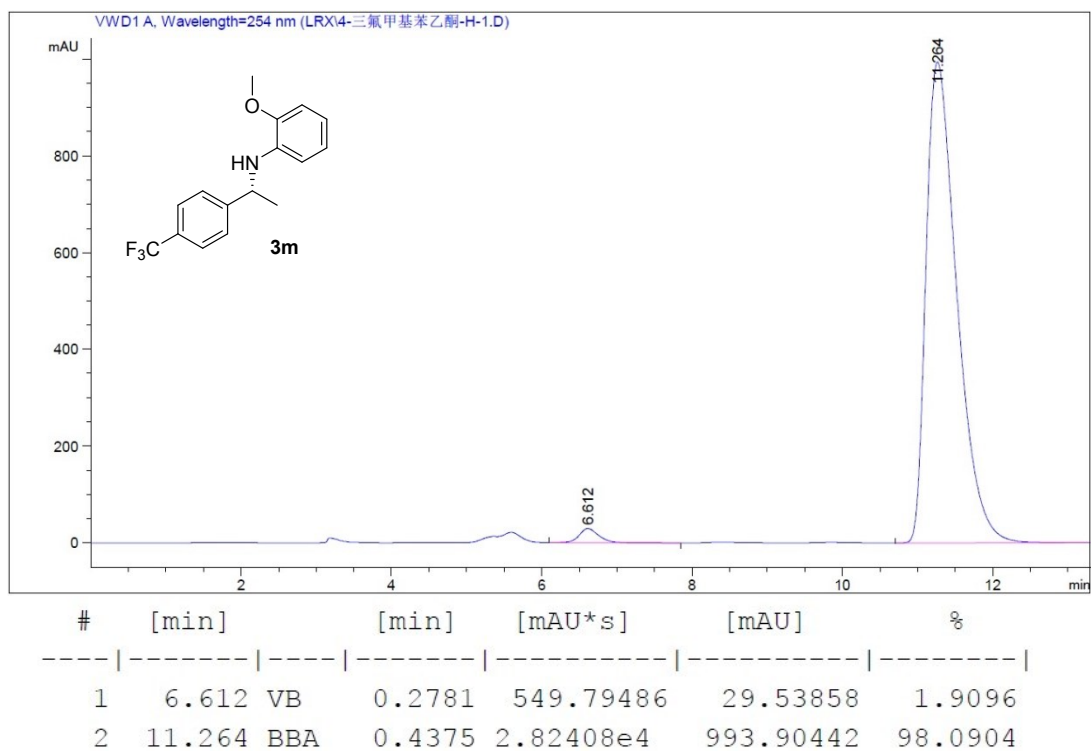


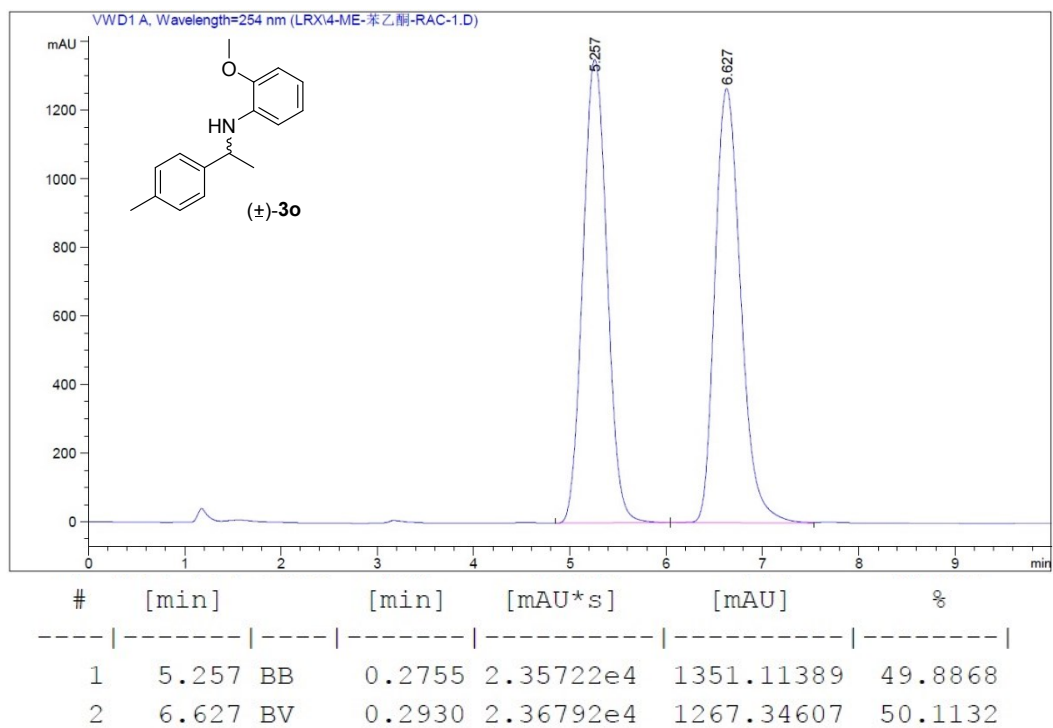
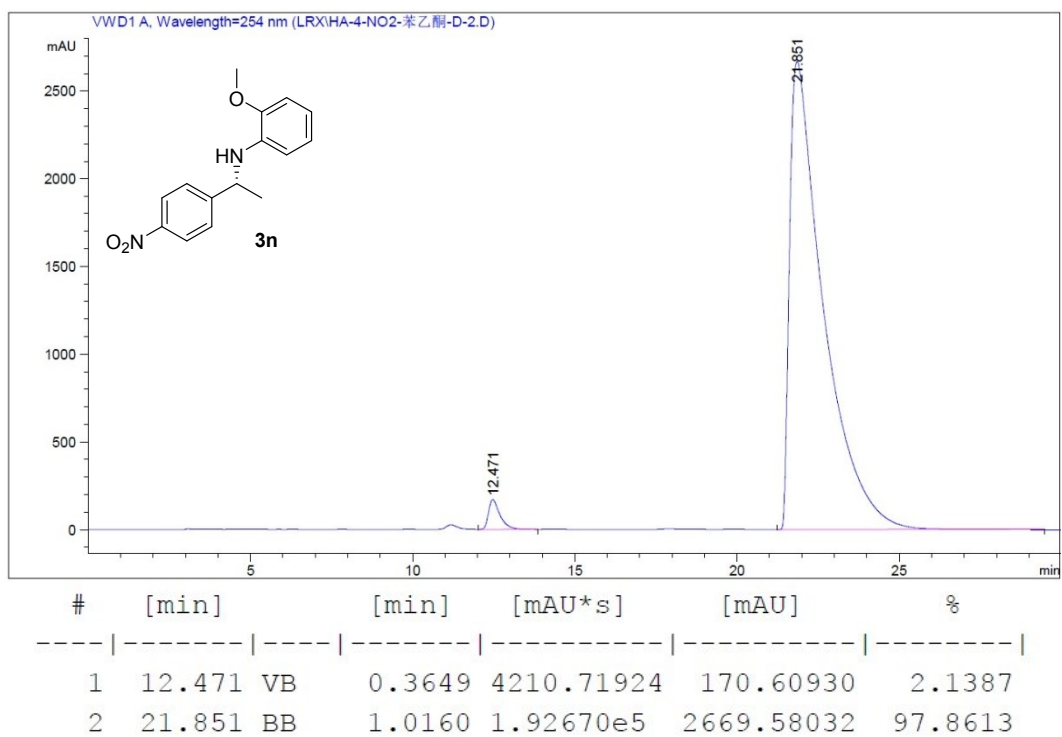


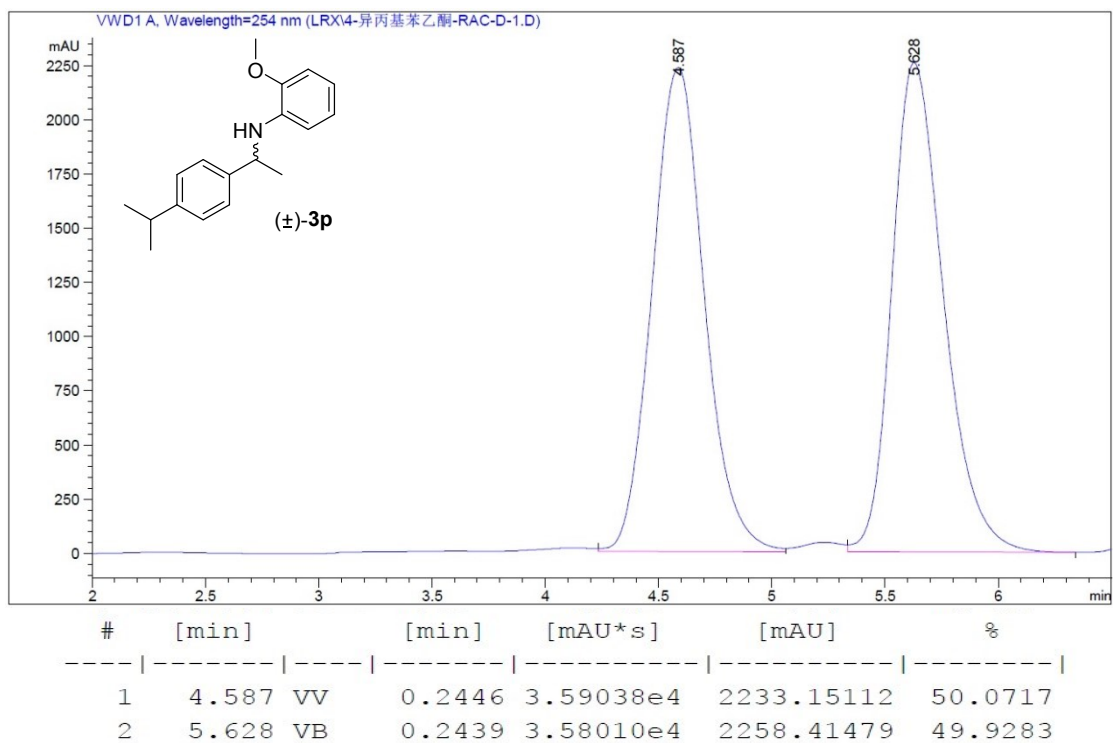
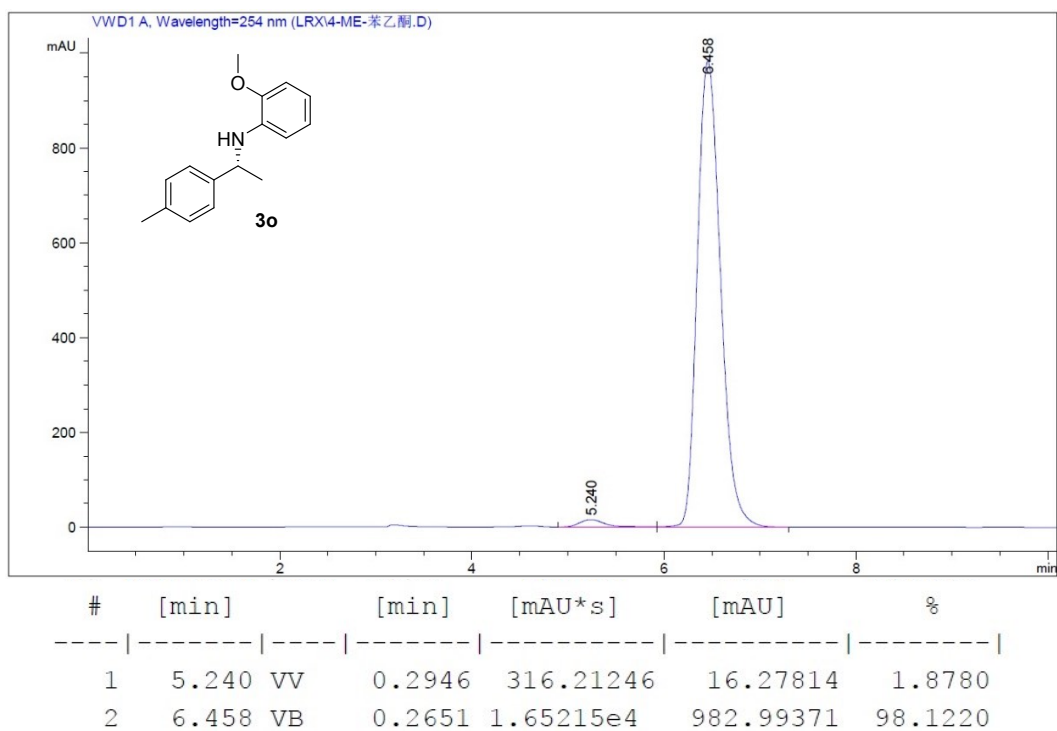


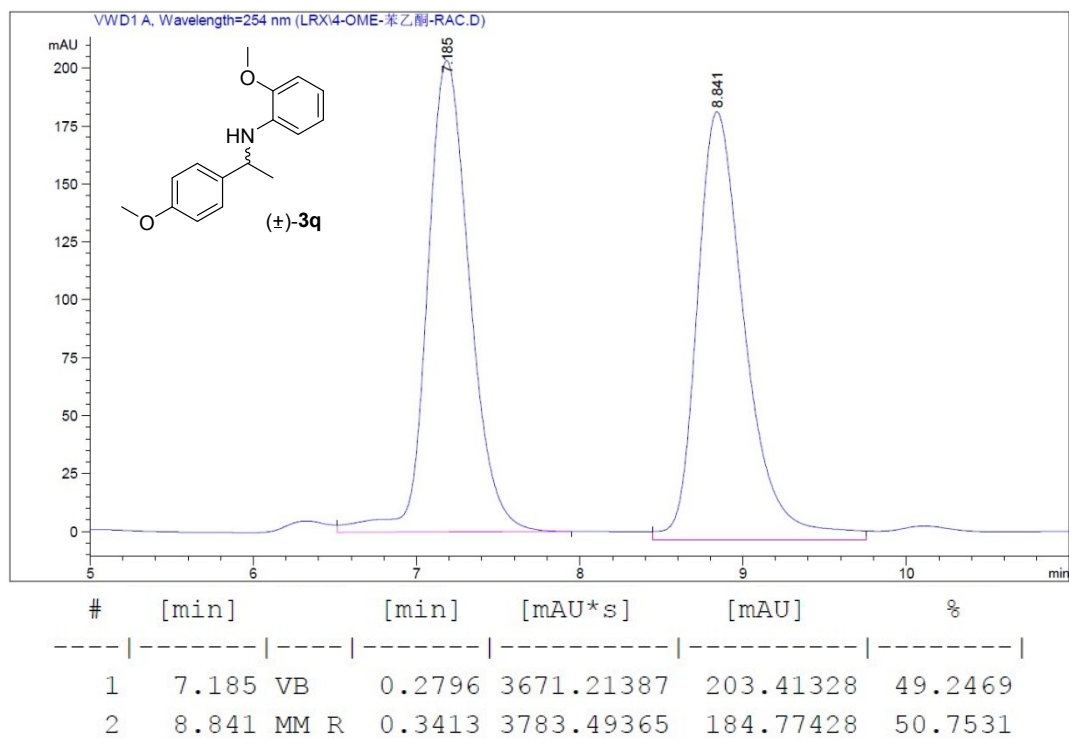
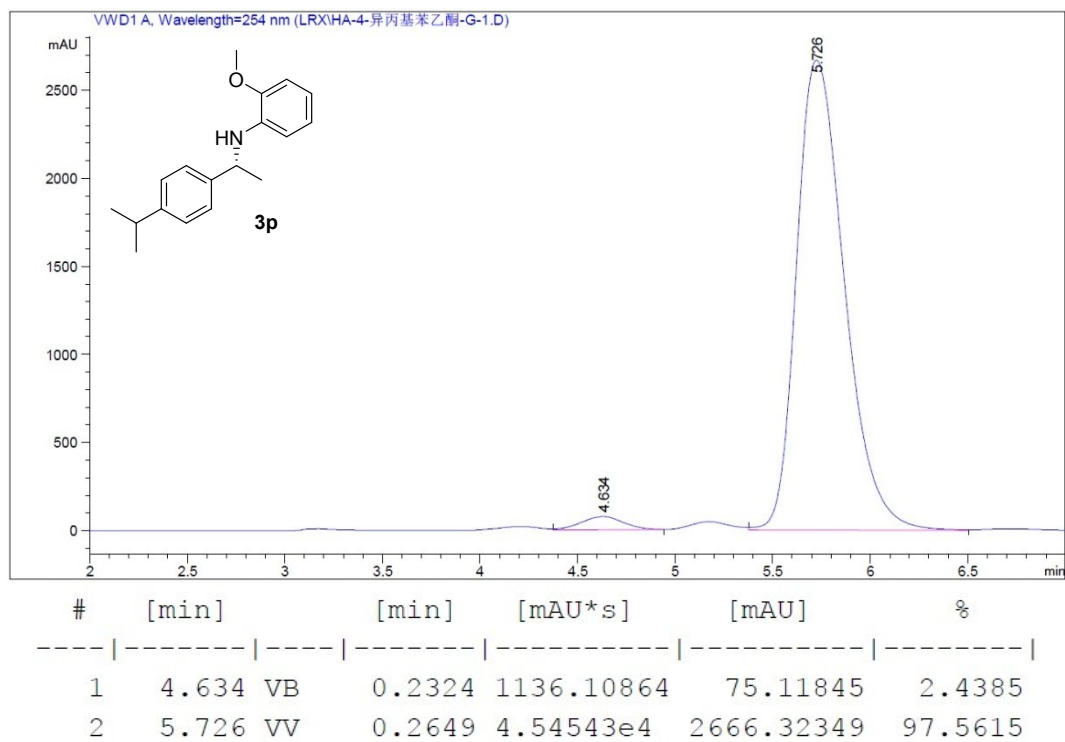


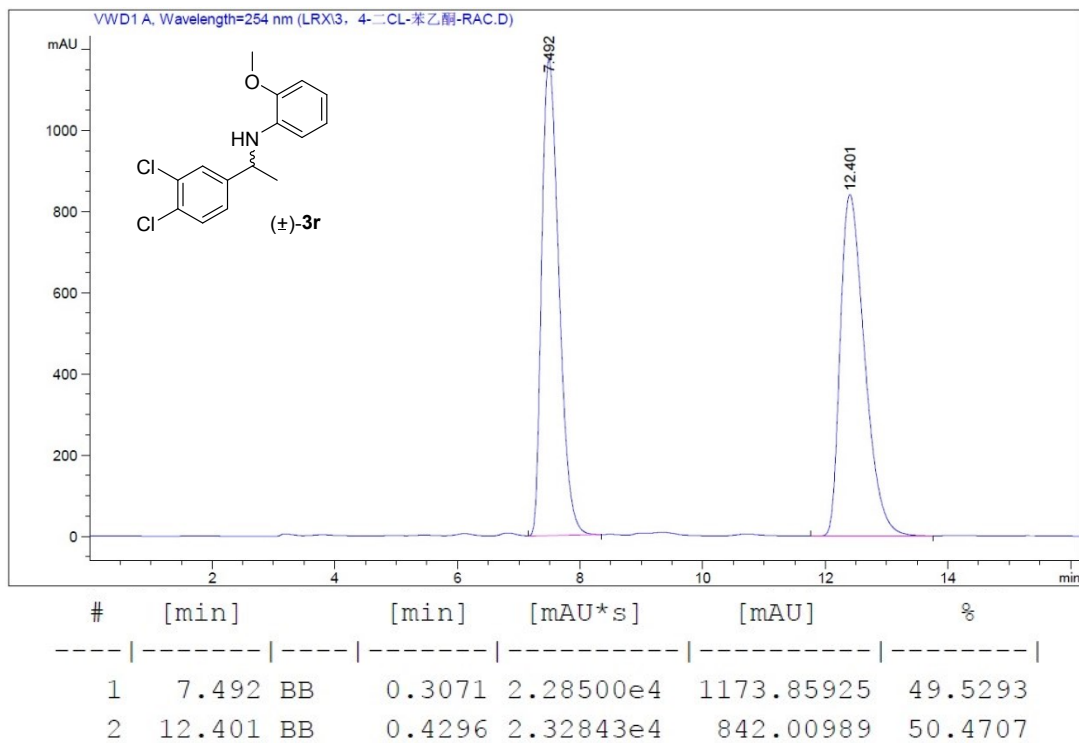
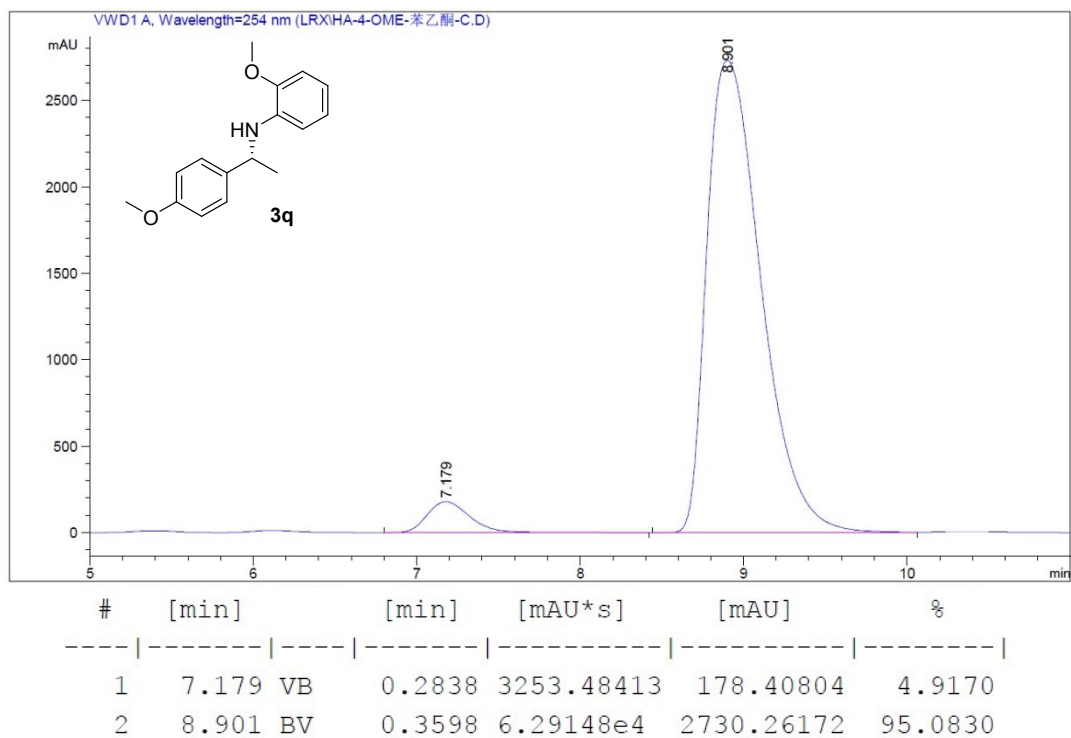


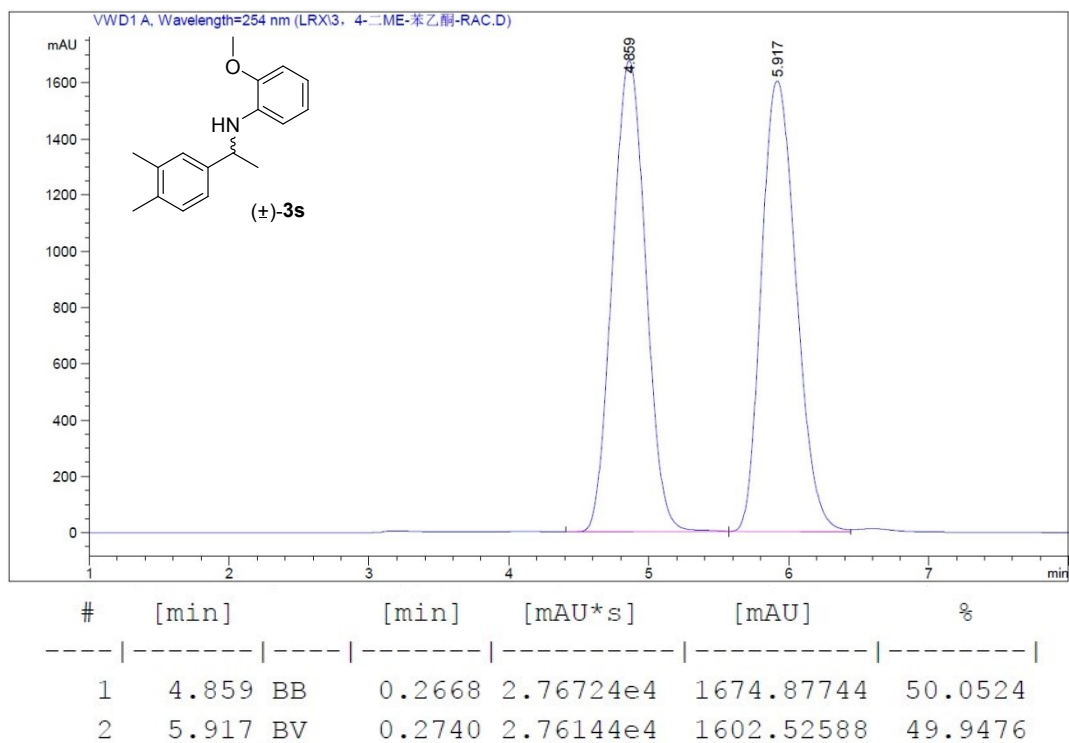
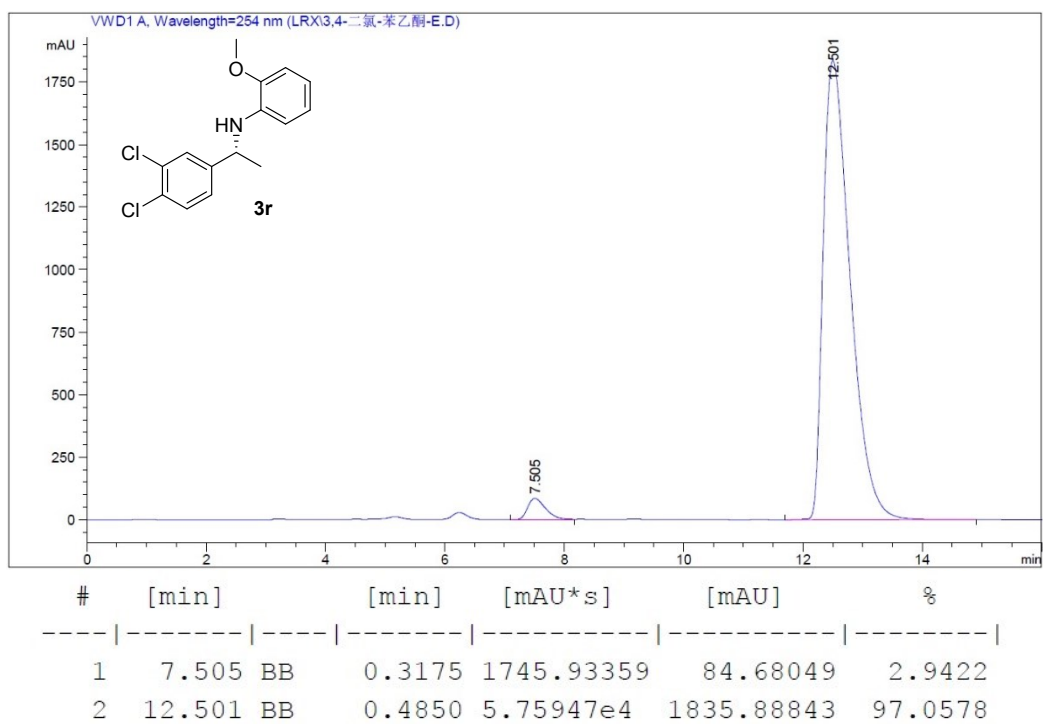


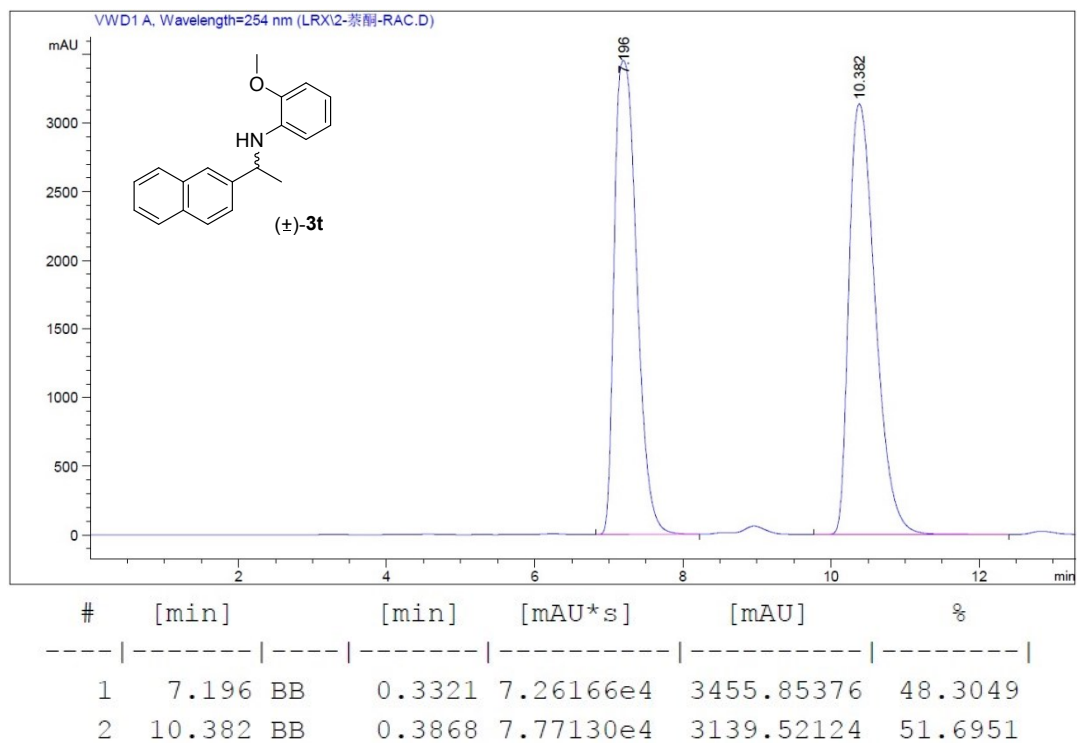
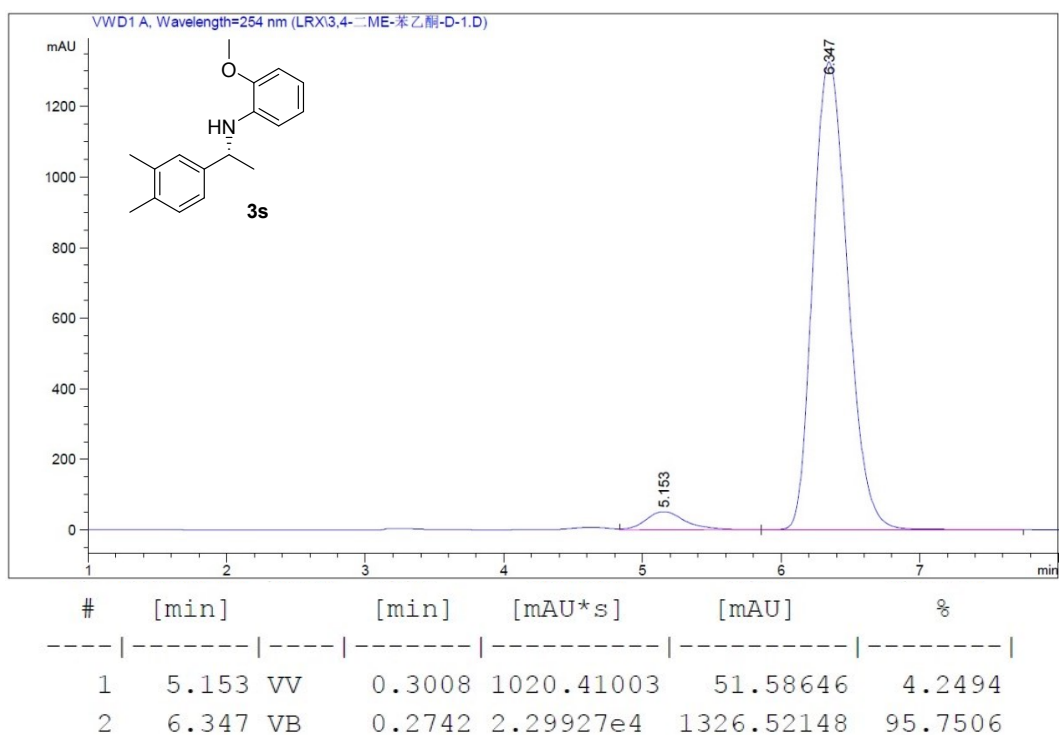


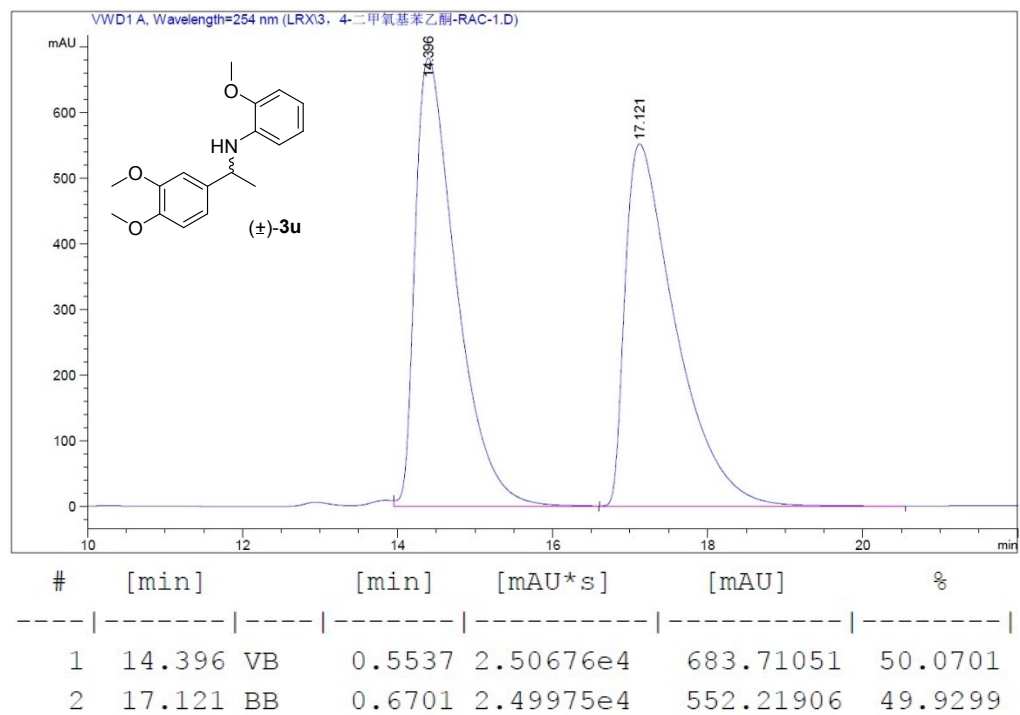
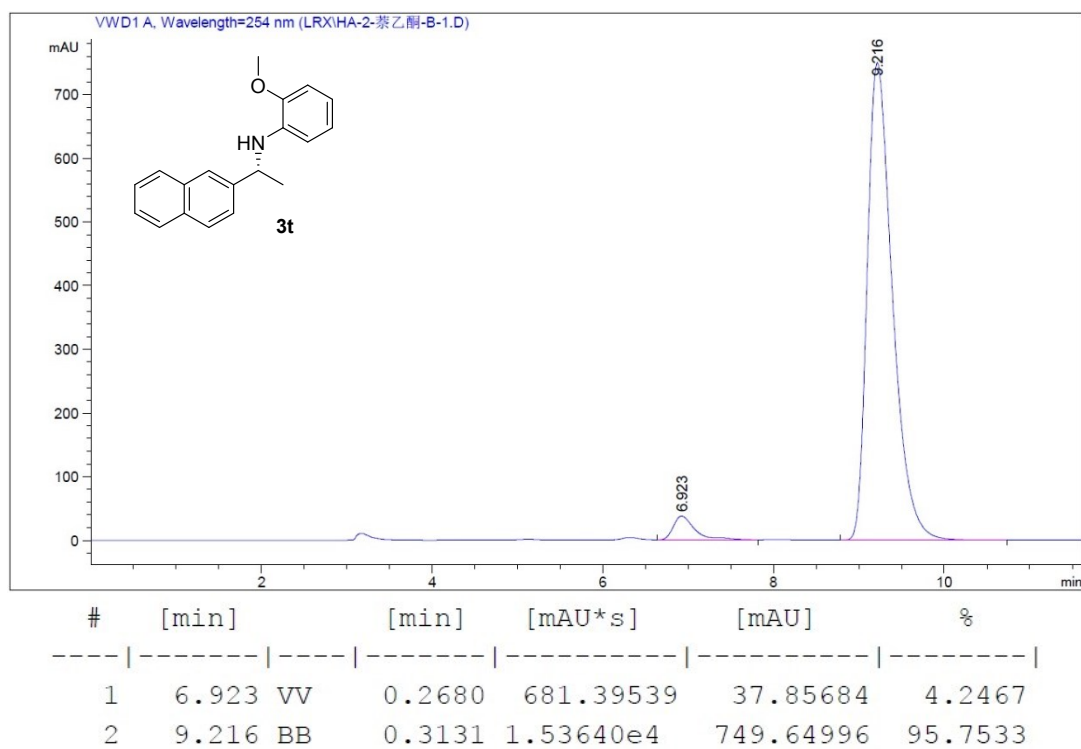


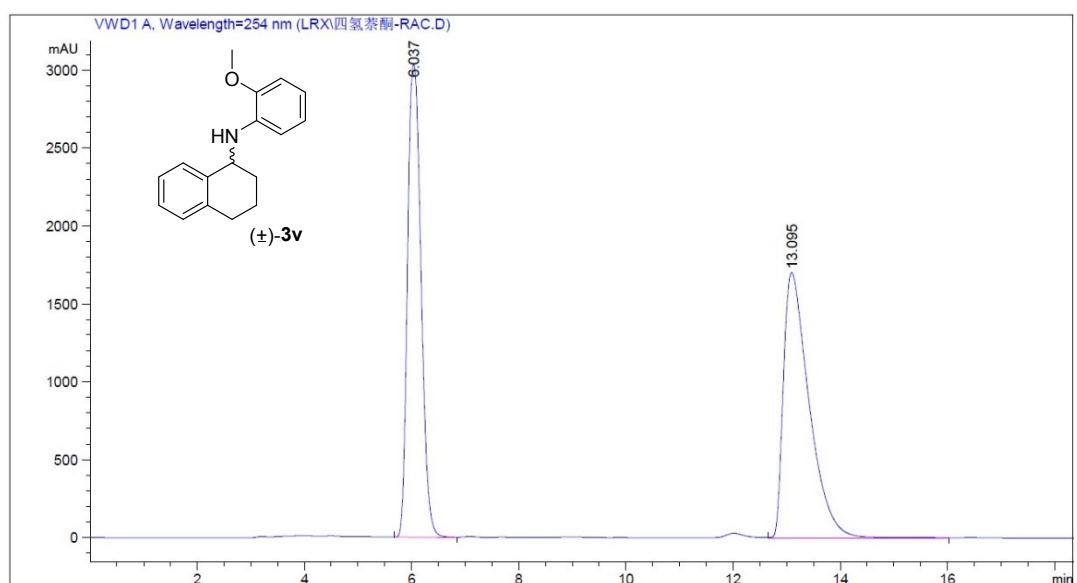
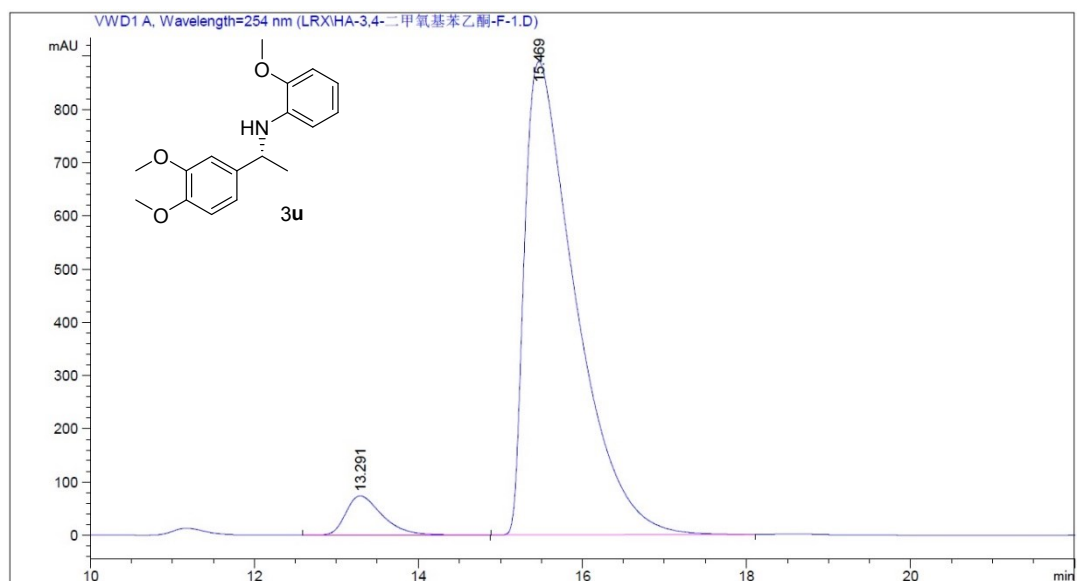


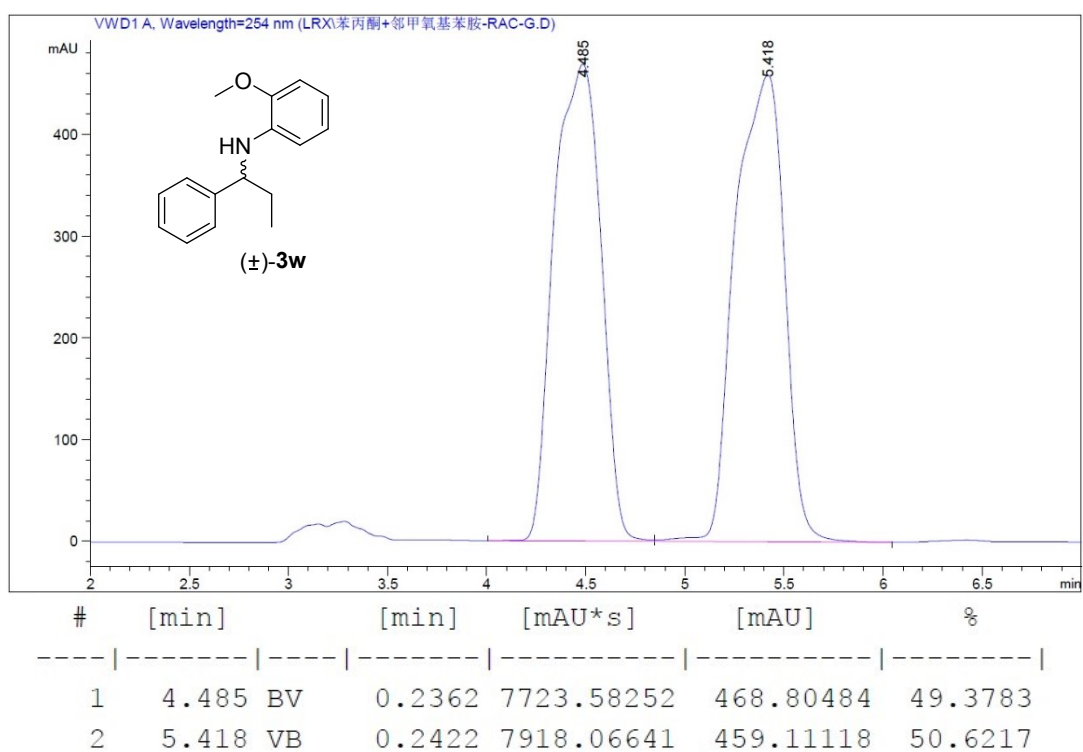
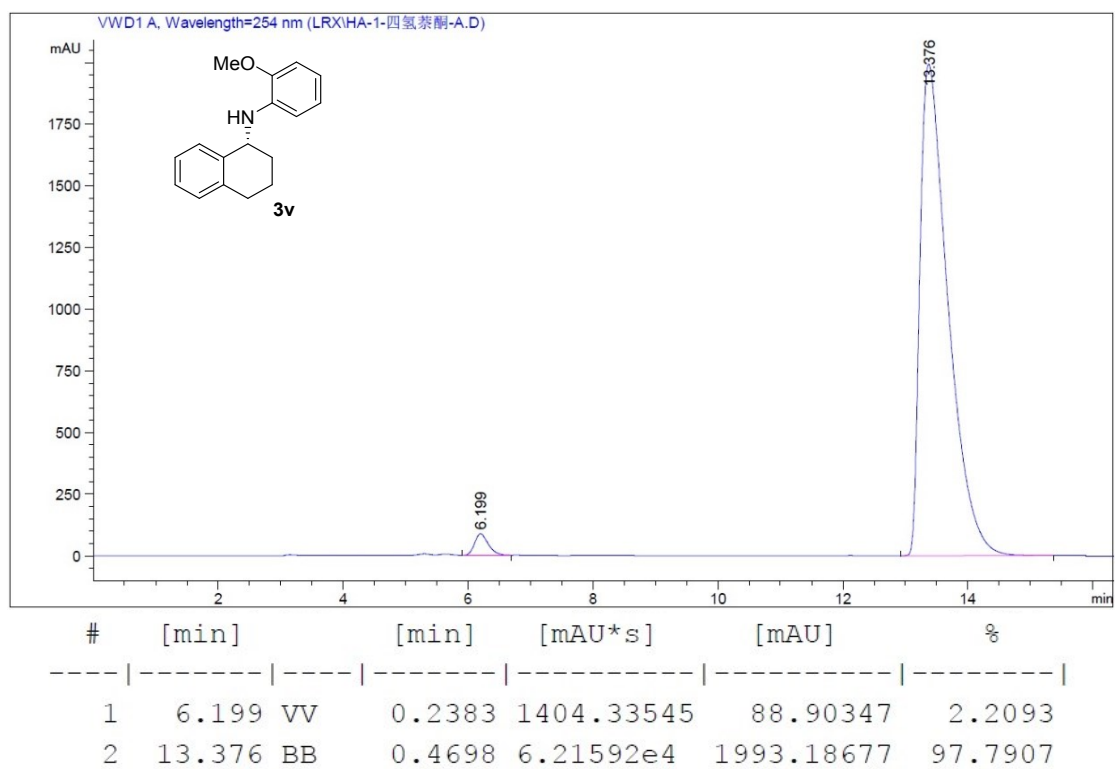


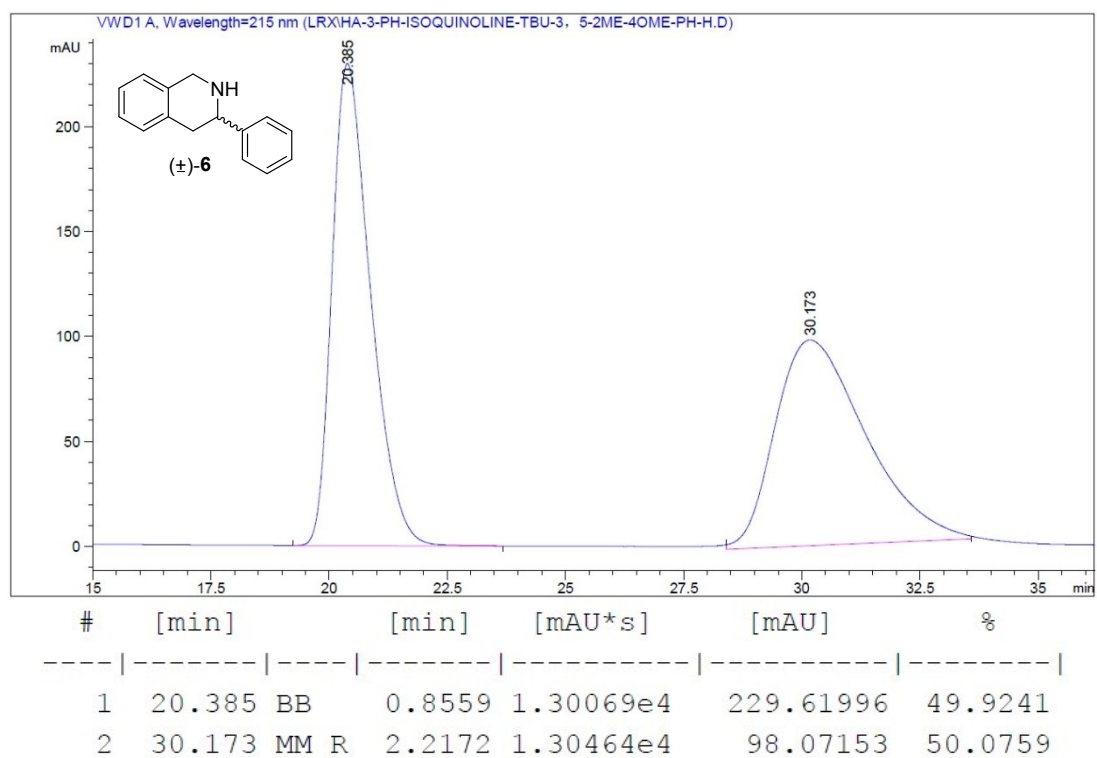
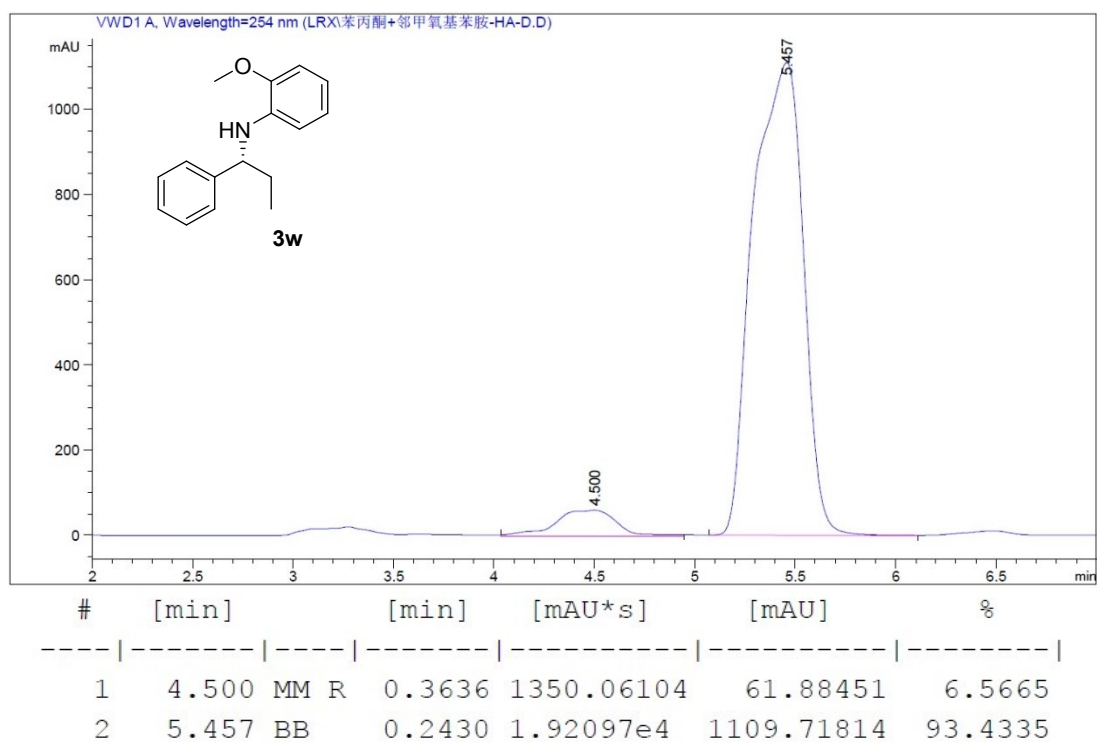


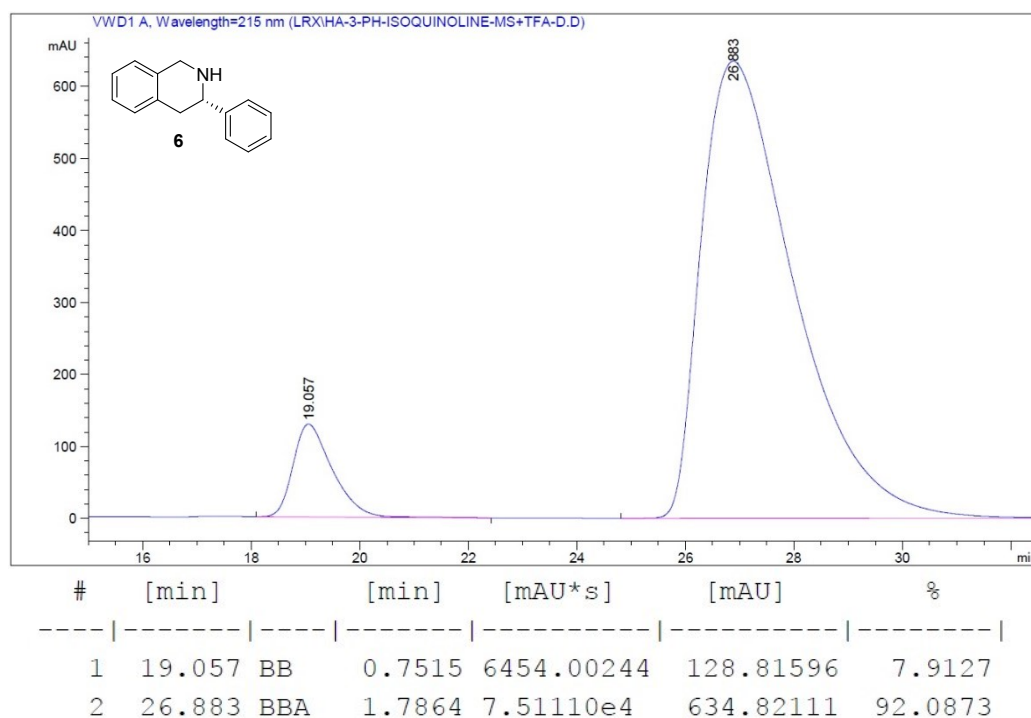












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