

Supporting Information

Josiphos-type Binaphane Ligands for Iridium-Catalyzed Enantioselective Hydrogenation of 1-Aryl-Substituted Dihydroisoquinolines

Huifang Nie,[†] Yupu Zhu,[†] Xiaomu Hu,[†] Zhao Wei,[†] Lin Yao,[†] Gang Zhou,[†]

Pingan Wang,^{*,†} Ru Jiang,^{*,†} and Shengyong Zhang^{*,†}

* Corresponding authors

School of Pharmacy, Fourth Military Medical University, Xi'an, 710032, China

E-mail: syzhang@fmmu.edu.cn

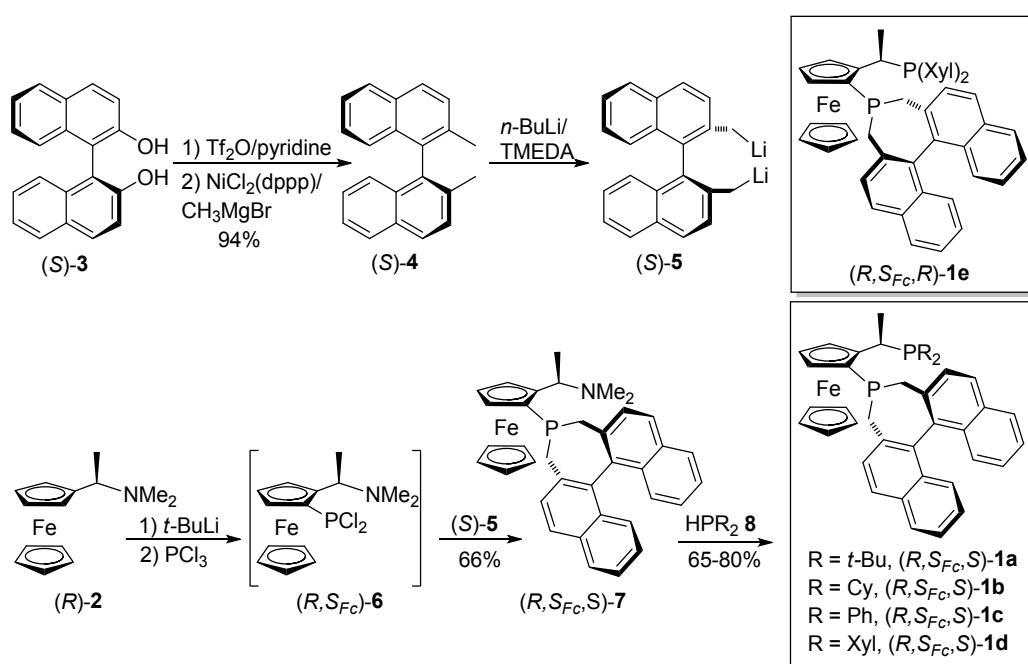
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1. General remarks

(*R*)-Ugi's amine (**2**) was purchased from XylMED Biomedical (Xi'an, China). All other commercial chemicals were purchased from J&K or Energy Chemical (Shanghai, China) in the highest purity and used without purification. All reactions and manipulations were performed using standard Schlenk techniques. 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 analyses were performed on a Perkin-Elmer Model 343 Polarimeter. HRMS were recorded on ZAB-HS spectrometer with ES ionization (ESI). HPLC analysis was performed on an Agilent 1260 Infinity instrument with a chiral stationary phase using a Daicel Chiralcel OD-H column or a Daicel Chiralcel AD-H column (*n*-hexane/*iso*-propanol mixtures as solvent).

2. General procedure for synthesis of ligands¹⁻³



(*S*)-**4**. To a solution of (*S*)-**3** (10 g, 36 mmol) in CH₂Cl₂ (50 mL) at 0 °C were added pyridine (8.5 g, 108 mmol, 3.0 equiv) and subsequently trifluoromethanesulfonic anhydride (22 g, 78 mmol, 2.2 equiv). The reaction was allowed to warm to room temperature and stirred for 5 h. The reaction was quenched by the addition of water (100 mL), and the organic phases were separated. The aqueous layer was further extracted with CH₂Cl₂ (2×50 mL). The combined organic phases were washed with brine (100 mL), dried over Na₂SO₄, and concentrated under reduced pressure. The crude product was used in the next step without further purification.

1,3-Bis-(diphenylphosphino)propane nickel (II) chloride (976 mg, 1.8 mmol, 5 mol %) was placed in a flame-dried Schlenk flask, the above prepared product (36 mmol) in TBME (150 mL) was added. The suspension was cooled to 0 °C, and methylmagnesium bromide (3.0 M in Et₂O, 36 mL, 108 mmol, 3.0 equiv) was added dropwise. The cooling bath was removed and the reaction was stirred at room temperature overnight. The mixture was cooled to 0 °C and was carefully quenched by the addition of hydrochloric acid (2 M, 35 mL). The phases were separated, and the aqueous phase was extracted with TBME (2 × 100 mL). The combined organic extracts were washed with brine, dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel using PE as eluent, affording (*S*)-**4** (9.54 g, 33.8 mmol) as a white solid (yield: 94 %). Characterization of (*S*)-**4**: ¹H NMR (400 MHz, CDCl₃) δ 7.88 (t, *J* = 7.1 Hz, 4H), 7.50 (d, *J* = 8.3 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 2H), 7.19 (t, *J* = 7.6 Hz, 2H), 7.04 (d, *J* = 8.4 Hz, 2H), 2.03 (s, 6H).

(*R*_C,*S*_{Fc},*S*_{ax})-**7**. A solution of *n*-BuLi (1.6 M in *n*-hexane, 32 mL, 51.2 mmol, 2.5 equiv) was concentrated under vacuum and the resulting oil was dissolved in TBME (15 mL). A solution of (*S*)-**4** (5.64 g, 20 mmol) in TBME (40 mL) was added over a dropping funnel during 20 min to give a red solution. Afterwards, TMEDA (7.8 mL, 52 mmol, distilled over CaH₂) was added slowly, and the resulting solution was stirred for 24 h at room temperature. The supernatant solution was decanted via a tube. The crystals were washed twice with dry *n*-hexane (10 mL, removed by a tube)

and dried under vacuum to give dilithium salt **5** (3.53 g, 12 mmol) as deep red crystals (yield: 60 %).

To a solution of (*R*)-Ugi's amine (**2**) (2.57 g, 10 mmol) in TBME (20 mL) was added *t*-BuLi (1.3 M in *n*-pentane, 8.5 mL, 11 mmol, 1.1 equiv) at 0 °C. After addition was completed, the mixture was warmed to room temperature, and stirred for 1.5 h at room temperature. The mixture was then cooled to -78 °C and a solution of PCl₃ (1 mL, 11.46 mmol) in TBME (5 mL) was added slowly, and the mixture was warmed to room temperature overnight to afford the dichlorophosphine (*R*_C,*S*_{Fe})-**6**. After the mixture was cooled to -20 °C, a suspension of dilithium salt **5** (2.94 g, 10 mmol) in TBME was added via a cannula. The mixture was stirred overnight from -20 °C to room temperature and quenched by the addition of saturated NH₄Cl solution (40 mL). The organic layer was separated and dried over Na₂SO₄ and the solvent was removed under reduced pressure. The residue was purified by chromatography to afford (*R*_C,*S*_{Fe},*S*_{ax})-**7** (3.74 g, 6.6 mmol) as a yellow foam (yield: 66 %). Characterization of (*R*_C,*S*_{Fe},*S*_{ax})-**7**: [α]_D²⁵ -465.7 (*c* = 0.25, CHCl₃); ¹H NMR (400 Hz, CDCl₃) δ 8.05-8.00 (m, 1H), 7.99-7.89 (m, 3H), 7.80-7.74 (m, 1H), 7.60-7.52 (m, 1H), 7.46-7.36 (m, 2H), 7.26-7.18 (m, 3H), 7.16-7.10 (m, 1H), 4.37 (s, 1H), 4.27 (s, 1H), 4.23 (s, 5H), 4.20-4.12 (m, 2H), 3.29-2.98 (m, 3H), 2.69-2.59 (m, 1H), 2.18 (s, 6H), 1.27 (d, *J* = 6.7 Hz, 3H); ¹³C NMR (101 Hz, CDCl₃) δ 135.96, 134.98, 133.75, 132.76, 132.52, 132.45, 132.28, 132.14, 128.83, 128.37, 128.28, 128.00, 127.88, 127.09, 126.94, 126.72, 125.89, 125.71, 124.87, 124.62, 97.93, 77.82, 69.66, 69.43, 68.26, 67.99, 56.92, 39.11, 35.36, 30.30, 8.02; ³¹P NMR (162 Hz, CDCl₃) δ -6.09; HRMS (ESI) calcd for C₃₆H₃₅FeNP[M+H]⁺: 568.1857, Found: 568.1844.

(*R*_C,*S*_{Fe},*R*_{ax})-**7'** was synthesized from (*R*)-**5** (2.94 g, 10 mmol) and (*R*)-**2** (2.57 g, 10 mmol) according to the same procedure of (*R*_C,*S*_{Fe},*S*_{ax})-**7**. Characterization of (*R*_C,*S*_{Fe},*R*_{ax})-**7'**: yellow foam; 3.69 g, 65%; [α]_D²⁵ -247.6 (*c* = 0.25, CHCl₃); ¹H NMR (400Hz, CDCl₃) δ 7.98-7.89 (m, 3H), 7.72 (t, *J* = 8.4 Hz, 2H), 7.44 (t, *J* = 7.2 Hz, 2H), 7.56-7.51 (m, 1H), 7.29-7.20 (m, 3H), 6.78 (d, *J* = 8.3 Hz, 1H), 4.34 (s, 1H), 4.18-4.11 (m, 1H), 4.09 (s, 1H), 4.06 (s, 5H), 3.39 (s, 1H), 2.91-2.74 (m, 3H),

2.62-2.53 (m, 1H), 2.18 (s, 6H), 1.29 (d, $J = 6.7$ Hz, 3H); ^{13}C NMR (101 Hz, CDCl_3) δ 135.48, 135.16, 133.81, 132.71, 132.33, 132.21, 132.07, 131.83, 128.93, 128.20, 128.12, 127.56, 126.96, 126.72, 126.54, 125.79, 125.63, 124.84, 124.46, 96.83, 73.53, 70.30, 69.49, 69.26, 67.48, 56.80, 39.17, 32.80, 29.56, 7.89; ^{31}P NMR (162 Hz, CDCl_3) δ -6.58; HRMS (ESI) calcd for $\text{C}_{36}\text{H}_{35}\text{FeNP}[\text{M}+\text{H}]^+$: 568.1857, Found: 568.1839.

(R_C, S_{Fc}, S_{ax}) -**1**. (R_C, S_{Fc}, S_{ax}) -**7** (567 mg, 1 mmol) was suspended in anhydrous and degassed acetic acid (5 mL), under an argon atmosphere. After the addition of R_2PH [$(t\text{-Bu})_2\text{PH}$, 160 mg, 11 mmol (a); Cy_2PH , 218 mg, 11 mmol (b); Ph_2PH , 205 mg, 11 mmol (c); $(\text{Xyl})_2\text{PH}$, 242 mg, 11 mmol (d)], the mixture was stirred at 95 °C for 1~4 h [1 h (a), 1.5 h (b), 3 h (c), 4 h (d)]. The solvent was then evaporated in vacuo and the residue was dissolved in CH_2Cl_2 (20 mL). The organic layer was successively washed with water, saturated NaHCO_3 solution and brine, and dried over Na_2SO_4 . After solvent was evaporated under vacuum, the crude product was purified with chromatography (EtOAc/PE) to afford the desired diphosphine ligands **1** (yield: 65-80 %).

Characterization of (R_C, S_{Fc}, S_{ax}) -**1a**: orange power; 434 mg, 65%; $[\alpha]_{\text{D}}^{25}$ -200.2 ($c = 0.25$, CHCl_3); ^1H NMR (400 Hz, CDCl_3) δ 8.06-8.01 (m, 1H), 7.98-7.89 (m, 3H), 7.86-7.76 (m, 1H), 7.66-7.56 (m, 1H), 7.46-7.37 (m, 2H), 7.26-7.16 (m, 3H), 7.16-7.10 (m, 1H), 4.36-4.25 (m, 7H), 4.15 (s, 1H), 3.96-3.84 (m, 1H), 3.60-3.50 (m, 1H), 3.35-3.23 (m, 1H), 3.15-3.00 (m, 1H), 2.63 (dd, $J = 11.3, 4.5$ Hz, 1H), 1.83 (dd, $J = 6.9, 3.1$ Hz, 3H), 1.45 (d, $J = 10.4$ Hz, 9H), 1.03 (d, $J = 10.6$ Hz, 9H); ^{13}C NMR (101 Hz, CDCl_3) δ 136.48, 135.45, 133.77, 132.51, 132.45, 132.28, 132.18, 128.92, 128.37, 128.25, 128.02, 127.84, 127.05, 127.00, 126.77, 125.89, 125.67, 124.88, 124.58, 102.47, 70.14, 69.43, 68.72, 67.89, 36.54, 34.04, 31.70, 30.75, 16.60; ^{31}P NMR (162 Hz, CDCl_3) δ 52.92 (d, $J = 44.2$ Hz), -10.07 (d, $J = 44.4$ Hz); HRMS (ESI) calcd for $\text{C}_{42}\text{H}_{47}\text{FeP}_2 [\text{M}+\text{H}]^+$: 669.2502, Found: 669.2493.

Characterization of (R_C, S_{Fc}, S_{ax}) -**1b**: orange foam; 490 mg, 68%; $[\alpha]_{\text{D}}^{25}$ -598.4 ($c = 0.25$,

CHCl₃); **¹H NMR** (400 Hz, CDCl₃) δ 8.06-8.00 (m, 1H), 7.97-7.88 (m, 3H), 7.83-7.74 (m, 1H), 7.65-7.58 (m, 1H), 7.48-7.35 (m, 2H), 7.26-7.16 (m, 3H), 7.15-7.07 (m, 1H), 4.31-4.10 (m, 8H), 3.77-3.62 m, 1H), 3.40-3.20 (m, 2H), 3.15-3.00 (m, 1H), 2.67-2.57 (m, 1H), 1.96-1.63 (m, 10H), 1.59-1.40 (m, 10H), 1.32-1.00 (m, 5H); **¹³C NMR** (101 Hz, CDCl₃) δ 136.29, 135.07, 133.78, 132.50, 132.40, 132.21, 128.83, 128.35, 128.23, 127.99, 127.84, 127.06, 126.99, 126.72, 125.87, 125.64, 124.89, 124.57, 101.01, 69.85, 69.30, 68.16, 67.78, 32.92, 31.86, 31.26, 30.05, 27.66, 27.50, 27.07, 26.70, 26.46, 15.09; **³¹P NMR** (162 MHz, CDCl₃) δ 17.22 (d, J = 35.4 Hz), -10.25 (d, J = 35.2 Hz); **HRMS (ESI)** calcd for C₄₆H₅₁FeP₂ [M+H]⁺: 721.2815, Found: 721.2808.

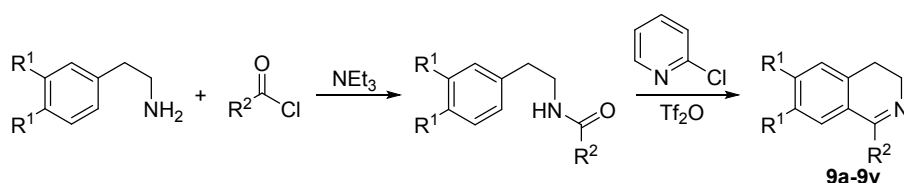
Characterization of (*R*_C,*S*_{FC},*S*_{ax})-**1c**: orange solid; 567 mg, 80%; [α]_D²⁵ -698.9 (c = 0.25, CHCl₃); **¹H NMR** (400 Hz, CDCl₃) δ 8.09-8.03 (m, 1H), 8.02-7.95 (m, 1H), 7.93-7.83 (m, 2H), 7.82-7.75 (m, 1H), 7.51-7.17 (m, 16H), 7.16-7.10 (m, 1H), 4.31 (s, 5H), 4.15 (s, 2H), 3.96-3.88 (m, 1H), 3.83 (s, 1H), 3.32-3.23 (m, 1H), 3.07 (t, J = 14.3 Hz, 1H), 2.92 (t, J = 12.5 Hz, 1H), 2.54 (dd, J = 11.7, 4.2 Hz, 1H), 1.42 (t, J = 7.4 Hz, 3H); **¹³C NMR** (101 Hz, CDCl₃) δ 137.97, 137.78, 135.85, 135.32, 135.12, 134.66, 134.46, 134.26, 133.79, 132.60, 132.51, 132.35, 132.25, 132.20, 132.03, 131.88, 129.10, 128.71, 128.29, 128.03, 127.87, 127.80, 127.55, 127.14, 127.06, 126.69, 125.91, 125.67, 124.98, 124.65, 98.71, 69.80, 69.27, 68.74, 68.09, 35.80, 30.65, 16.41; **³¹P NMR** (162 Hz, CDCl₃) δ 10.98 (d, J = 23.5 Hz), -10.82 (d, J = 23.5 Hz); **HRMS (ESI)** calcd for C₄₆H₃₉FeP₂ [M+H]⁺: 709.1876, Found: 709.1874.

Characterization of (*R*_C,*S*_{FC},*S*_{ax})-**1d**: orange solid; 535 mg, 70%; [α]_D²⁵ -564.5 (c = 0.25, CHCl₃); **¹H NMR** (400 Hz, CDCl₃) δ 8.09-8.03 (m, 1H), 8.02-7.96 (m, 1H), 7.93-7.83 (m, 2H), 7.82-7.76 (m, 1H), 7.54-7.44 (m, 2H), 7.43-7.36 (m, 1H), 7.28-7.18 (m, 3H), 7.16-7.10 (m, 1H), 7.03-6.93 (m, 3H), 6.91-6.82 (m, 3H), 4.30 (s, 5H), 4.17 (s, 1H), 4.14 (s, 1H), 3.89-3.80 (m, 1H), 3.78 (s, 1H), 3.33-3.23 (m, 1H), 3.14-3.00 (m, 2H), 2.55 (dd, J = 11.7, 4.3 Hz, 1H), 2.29 (s, 6H), 2.24 (s, 6H), 1.40 (t, J = 7.1 Hz, 3H); **¹³C NMR** (101 Hz, CDCl₃) δ 137.78, 137.61, 137.03, 136.95, 135.95, 134.74, 134.05, 133.82, 133.03, 132.83, 132.53, 132.39, 132.25, 130.73,

129.63, 129.49, 129.27, 128.78, 128.26, 128.05, 127.90, 127.24, 127.08, 126.72, 125.92, 125.68, 124.99, 124.66, 99.00, 69.66, 69.25, 68.48, 68.33, 35.95, 30.84, 21.47, 21.29, 16.23; ^{31}P NMR (162 Hz, CDCl_3) δ 10.12 (d, $J = 17.5$ Hz), -10.96 (d, $J = 17.2$ Hz); **HRMS (ESI)** calcd for $\text{C}_{50}\text{H}_{47}\text{FeP}_2$ $[\text{M}+\text{H}]^+$: 765.2502, Found: 765.2492.

(R_C, S_{Fc}, R_{ax}) -**1e** was prepared from (R_C, S_{Fc}, R_{ax}) -**7'** (567 mg, 1 mmol) and $(\text{Xyl})_2\text{PH}$ (242 mg, 11 mmol) according to the same synthesis procedure of (R_C, S_{Fc}, S_{ax}) -**1d**. Characterization of (R_C, S_{Fc}, R_{ax}) -**1e**: orange solid; 550 mg, 72%; $[\alpha]_D^{25}$ -122.7 ($c = 0.25$, CHCl_3); ^1H NMR (400 Hz, CDCl_3) δ 8.02-7.90 (m, 3H), 7.84-7.78 (m, 1H), 7.76-7.70 (m, 1H), 7.50-7.40 (m, 2H), 7.37-7.32 (m, 1H), 7.29-7.20 (m, 3H), 7.05-6.85 (m, 7H), 4.10 (s, 6H), 3.92 (s, 1H), 3.89-3.80 (m, 1H), 3.30 (s, 1H), 3.05-2.80 (m, 2H), 2.55-2.40 (m, 2H), 2.34 (s, 6H), 2.27 (s, 6H), 1.47-1.39 (m, 3H); ^{13}C NMR (101 Hz, CDCl_3) δ 137.57, 137.30, 137.07, 135.04, 134.56, 134.37, 133.72, 132.87, 132.67, 132.48, 132.15, 131.86, 130.74, 130.07, 129.91, 129.55, 129.29, 128.18, 127.45, 126.85, 126.65, 125.80, 125.65, 124.91, 124.61, 98.47, 71.98, 69.66, 69.41, 68.99, 67.99, 32.59, 29.94, 21.40, 21.34, 17.19; ^{31}P NMR (162 Hz, CDCl_3) δ 11.69 (d, $J = 23.5$ Hz), -10.34 (d, $J = 23.5$ Hz); **HRMS (ESI)** calcd for $\text{C}_{50}\text{H}_{47}\text{FeP}_2$ $[\text{M}+\text{H}]^+$: 765.2502, Found: 765.2505.

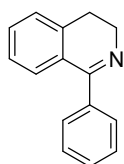
2. General procedure for synthesis of 1-aryl-3,4-DHIQs^{4,5}



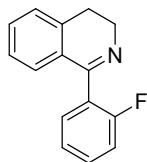
1-aryl-3,4-DHIQs (**9a-9v**) were synthesized from corresponding 2-arylethyl amine and arylcarbonyl chloride according to reported literature methods. The preparation was performed in air atmosphere. Carbonyl chloride (10.0 mmol) was slowly added to a solution of 2-arylethylamine (10.0 mmol) and triethylamine (15 mmol) in CH_2Cl_2 (60 mL) at 0 °C. After stirring at room temperature for 12 h, the mixture was concentrated and the residue was dissolved in EtOAc (40 mL). The solution was

transferred into a separation funnel and washed with saturated NH_4Cl solution (40 mL). The aqueous layer was further extracted with EtOAc (2×40 mL). The combined organic layers were washed with brine (80 mL) and dried over Na_2SO_4 . Solvent was evaporated to give the *N*-acyl-2-arylethylamine, which was used in the next step without further purification.

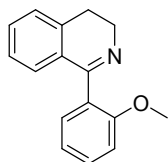
To a solution of the resulting *N*-acyl-2-arylethylamine (10.0 mmol) and 2-chloropyridine (12.0 mmol, 1.2 equiv) in CH_2Cl_2 (60 mL) was slowly added trifluoromethanesulfonic anhydride (11.0 mmol, 1.1 equiv) via syringe dropwise at -78 °C. Then the mixture was stirred at -78 °C for 10 min and slowly warm to room temperature overnight. The reaction was quenched with saturated NaHCO_3 solution and extracted with CH_2Cl_2 (3×50 mL). The combined organic extracts were washed with brine and dried over Na_2SO_4 . After solvent was evaporated under vacuum, the crude product was purified with chromatography (EtOAc/PE) to yield desired product (yield: 65-95 %).



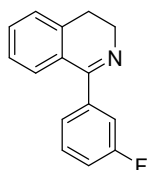
1-phenyl-3,4-dihydroisoquinoline (**9a**):⁵ light yellow liquid; 1.86 g, 90% yield; ^1H NMR (400 MHz, CDCl_3) δ 7.68-7.59 (m, 2H), 7.51-7.38 (m, 4H), 7.34-7.24 (m, 3H), 3.94-3.81 (m, 2H), 2.90-2.75 (m, 2H).



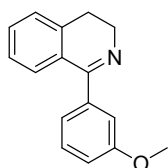
1-(2-fluorophenyl)-3,4-dihydroisoquinoline (**9b**):⁶ yellow solid; 1.82 g, 81% yield; ^1H NMR (400 MHz, DMSO) δ 7.68-7.59 (m, 2H), 7.44-7.38 (m, 1H), 7.34-7.21 (m, 4H), 6.92 (d, $J = 7.7$ Hz, 1H), 3.82-3.72 (m, 2H), 2.81-2.73 (m, 2H).



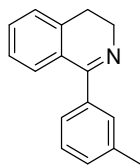
1-(2-methoxyphenyl)-3,4-dihydroisoquinoline (**9c**):⁵ yellow solid; 1.78 g; 75% yield; **¹H NMR** (400 MHz, CDCl₃) δ 7.42-7.30 (m, 3H), 7.22 (d, J = 7.4 Hz, 1H), 7.16 (t, J = 7.2 Hz, 1H), 7.07-7.01 (m, 1H), 6.99-6.93 (m, 2H), 4.05-3.75 (m, 2H), 3.68 (s, 3H), 2.94-2.78 (m, 2H).



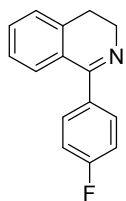
1-(3-fluorophenyl)-3,4-dihydroisoquinoline (**9d**):⁷ yellow oil; 1.91 g, 85% yield; **¹H NMR** (400 MHz, CDCl₃) δ 7.47-7.39 (m, 3H), 7.38-7.35 (m, 1H), 7.32-7.25 (m, 3H), 7.20-7.12 (m, 1H), 3.92-3.82 (m, 2H), 2.87-2.77 (m, 2H).



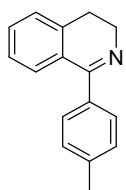
1-(3-methoxyphenyl)-3,4-dihydroisoquinoline (**9e**):⁸ yellow solid; 1.94 g, 82% yield; **¹H NMR** (400 MHz, CDCl₃) δ 7.45-7.39 (m, 1H), 7.38-7.25 (m, 4H), 7.21-7.15 (m, 2H), 7.05-7.00 (m, 1H), 3.91-3.85 (m, 2H), 3.87 (s, 3H), 2.87-2.80 (m, 2H).



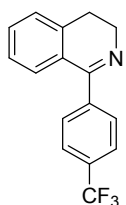
1-(3-methylphenyl)-3,4-dihydroisoquinoline (**9f**):⁵ yellow oil; 2.03 g, 92% yield; **¹H NMR** (400 MHz, CDCl₃) δ 7.50-7.45 (m, 1H), 7.45-7.37 (m, 2H), 7.36-7.24 (m, 5H), 3.93-3.83 (m, 2H), 2.88-2.79 (m, 2H), 2.42 (s, 3H).



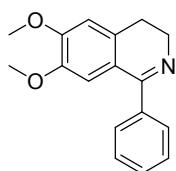
1-(4-fluorophenyl)-3,4-dihydroisoquinoline (**9g**):⁷ yellow solid; 1.98 g, 88% yield; **¹H NMR** (400 MHz, CDCl₃) δ 7.67-7.58 (m, 2H), 7.46-7.38 (m, 1H), 7.32-7.24 (m, 3H), 7.17-7.09 (m, 2H), 3.90-3.80 (m, 2H), 2.87-2.77 (m, 2H).



1-(4-methylphenyl)-3,4-dihydroisoquinoline (**9h**):⁵ white solid; 2.1 g, 95% yield; **¹H NMR** (400 MHz, CDCl₃) δ 7.56-7.44 (m, 2H), 7.42-7.34 (m, 1H), 7.29-7.16 (m, 5H), 3.88-3.78 (m, 2H), 2.85-2.72 (m, 2H), 2.41 (s, 3H).

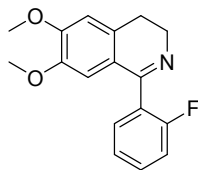


1-(4-(trifluoromethyl)phenyl)-3,4-dihydroisoquinoline (**9i**):⁵ white solid; 2.53 g, 92% yield; **¹H NMR** (400 MHz, CDCl₃) δ 7.82-7.61 (m, 4H), 7.46-7.36 (m, 1H), 7.33-7.23 (m, 2H), 7.22-7.15 (m, 1H), 3.98-3.79 (m, 2H), 2.82 (t, J = 7.4 Hz, 2H).

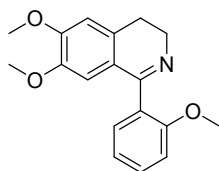


6,7-dimethoxy-1-phenyl-3,4-dihydroisoquinoline (**9j**):⁵ white solid; 2.40 g, 90% yield; **¹H NMR** (400 MHz, CDCl₃) δ 7.67-7.58 (m, 2H), 7.50-7.40 (m, 3H), 6.81 (d, J = 4.8 Hz, 2H), 3.97 (s, 3H), 3.84 (t, J = 7.5 Hz, 2H), 3.75 (s, 3H), 2.76 (t, J = 7.4 Hz,

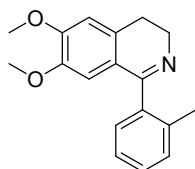
2H).



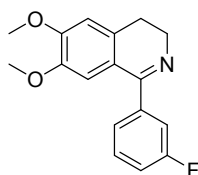
1-(2-fluorophenyl)-6,7-dimethoxy-3,4-dihydroisoquinoline (**9k**):⁹ yellow oil; 2.28 g, 80% yield; ¹H NMR (400 MHz, DMSO) δ 7.57-7.42 (m, 2H), 7.36-7.25 (m, 2H), 6.98 (s, 1H), 6.45 (s, 1H), 3.83 (s, 3H), 3.73 (t, J = 7.7 Hz, 2H), 3.54 (s, 3H), 2.71 (t, J = 7.7 Hz, 2H).



6,7-dimethoxy-1-(2-methoxyphenyl)-3,4-dihydroisoquinoline (**9l**):⁹ yellow solid; 1.96 g, 66% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.45 -7.35 (m, 2H), 7.09 -7.03 (m, 1H), 6.97 (d, J = 8.2 Hz, 1H), 6.76 (s, 1H), 6.54 (s, 1H), 4.18 -3.80 (m, 2H), 3.95 (s, 3H), 3.72 (s, 3H), 3.67 (s, 3H), 2.81 (s, 2H).

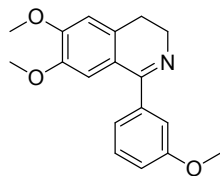


6,7-dimethoxy-1-(2-methylphenyl)-3,4-dihydroisoquinoline (**9m**):⁹ light yellow oil; 1.97 g, 70% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.35-7.22 (m, 4H), 6.78 (s, 1H), 6.45 (s, 1H), 3.95 (s, 3H), 3.98-3.76 (m, 2H), 3.65 (s, 3H), 2.81 (t, J = 7.6 Hz, 2H), 2.16 (s, 3H).

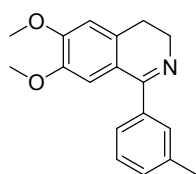


1-(3-fluorophenyl)-6,7-dimethoxy-3,4-dihydroisoquinoline (**9n**):¹⁰ white solid; 2.51 g,

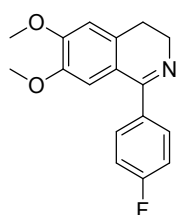
88% yield; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.46-7.33 (m, 3H), 7.21-7.12 (m, 1H), 6.80 (d, $J = 9.7$ Hz, 2H), 3.97 (s, 3H), 3.84 (t, $J = 7.6$ Hz, 2H), 3.76 (s, 3H), 2.80-2.72 (m, 2H).



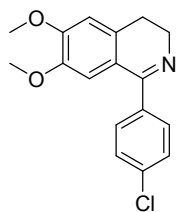
6,7-dimethoxy-1-(3-methoxyphenyl)-3,4-dihydroisoquinoline (**9o**):⁹ white solid; 2.23 g, 75% yield; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.35 (t, $J = 7.9$ Hz, 1H), 7.22-7.16 (m, 2H), 7.04-6.99 (m, 1H), 6.85 (s, 1H), 6.80 (s, 1H), 3.97 (s, 3H), 3.87 (s, 3H), 3.86-3.81 (m, 2H), 3.76 (s, 3H), 2.80-2.72 (m, 2H).



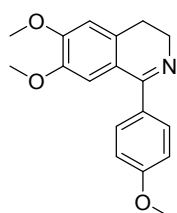
6,7-dimethoxy-1-(3-methylphenyl)-3,4-dihydroisoquinoline (**9p**):⁹ yellow oil; 2.53 g, 90% yield; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.50 (s, 1H), 7.42-7.37 (m, 1H), 7.33 (t, $J = 7.4$ Hz, 1H), 7.30-7.26 (m, 1H), 6.84 (s, 1H), 6.81 (s, 1H), 3.98 (s, 3H), 3.87-3.80 (m, 2H), 3.75 (s, 3H), 2.80-2.72 (m, 2H), 2.42 (s, 3H).



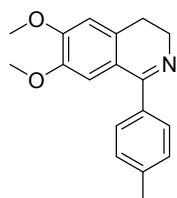
1-(4-fluorophenyl)-6,7-dimethoxy-3,4-dihydroisoquinoline (**9q**):⁹ white solid; 2.65 g, 93% yield; $^1\text{H NMR}$ (400 MHz, DMSO) δ 7.67-7.55 (m, 2H), 7.28 (t, $J = 8.5$ Hz, 2H), 7.01 (s, 1H), 6.69 (s, 1H), 3.85 (s, 3H), 3.66 (t, $J = 7.4$ Hz, 2H), 3.62 (s, 3H), 2.66 (t, $J = 7.4$ Hz, 2H).



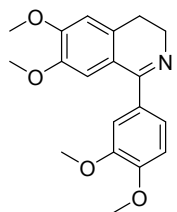
1-(4-chlorophenyl)-6,7-dimethoxy-3,4-dihydroisoquinoline (**9r**):⁷ white solid; 2.71 g, 90% yield; ¹H NMR (400 MHz, DMSO) δ 7.56 (d, J = 8.4 Hz, 2H), 7.41 (d, J = 8.4 Hz, 2H), 6.79 (s, 1H), 6.74 (s, 1H), 3.95 (s, 3H), 3.86-3.77 (m, 2H), 3.74 (s, 3H), 2.80-2.66 (m, 2H).



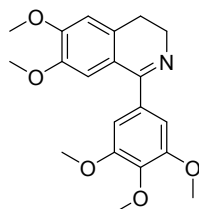
6,7-dimethoxy-1-(4-methoxyphenyl)-3,4-dihydroisoquinoline (**9s**):⁹ white solid; 2.38 g, 90% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.63-7.56 (m, 2H), 7.00-6.93 (m, 2H), 6.86 (s, 1H), 6.80 (s, 1H), 3.97 (s, 3H), 3.88 (s, 3H), 3.82-3.77 (m, 2H), 3.77 (s, 3H), 2.79-2.69 (m, 2H).



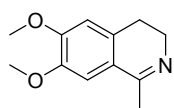
6,7-dimethoxy-1-(4-methylphenyl)-3,4-dihydroisoquinoline (**9t**):⁸ yellow solid; 1.83 g, 65% yield; ¹H NMR (400 MHz, DMSO) δ 7.50-7.42 (m, 2H), 7.29-7.21 (m, 2H), 6.99 (s, 1H), 6.72 (s, 1H), 3.84 (s, 3H), 3.67-3.62 (m, 2H), 3.60 (s, 3H), 2.68-2.60 (m, 2H), 2.37 (s, 3H).



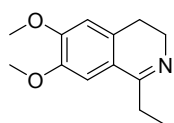
1-(3,4-dimethoxyphenyl)-6,7-dimethoxy-3,4-dihydroisoquinoline (**9u**):⁵ white solid; 3.04 g, 93% yield; ¹H NMR (400 MHz, DMSO) δ 7.24 (s, 1H), 7.16 (d, J = 8.4 Hz, 1H), 6.96-6.85 (m, 2H), 6.79 (d, J = 2.1 Hz, 1H), 3.95 (s, 3H), 3.94 (s, 3H), 3.92 (s, 3H), 3.82-3.77 (m, 2H), 3.76 (s, 3H), 2.72 (t, J = 7.6 Hz, 1H).



6,7-dimethoxy-1-(3,4,5-trimethoxyphenyl)-3,4-dihydroisoquinoline (**9v**):⁵ white solid; 3.28 g, 92% yield; ¹H NMR (400 MHz, DMSO) δ 6.88 (s, 1H), 6.86 (s, 2H), 6.80 (s, 1H), 3.96 (s, 3H), 3.90 (s, 3H), 3.87 (s, 6H), 3.84-3.78 (m, 2H), 3.77 (s, 3H), 2.73 (t, J = 7.4 Hz, 2H).



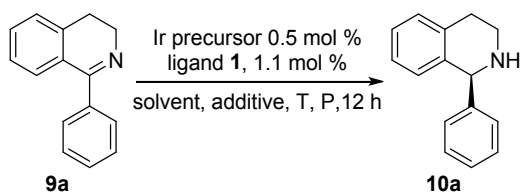
6,7-dimethoxy-1-methyl-3,4-dihydroisoquinoline (**9w**):¹¹ yellow oil; 1.44 g, 70% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.00 (s, 1H), 6.70 (s, 1H), 3.93 (d, J = 3.5 Hz, 6H), 3.69-3.60 (m, 2H), 2.70-2.60 (m, 2H), 2.38 (s, 3H).



6,7-dimethoxy-1-ethyl-3,4-dihydroisoquinoline (**9x**):¹¹ yellow oil; 1.71 g, 78% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.00 (s, 1H), 6.69 (s, 1H), 3.90 (d, J = 4.6 Hz, 6H), 3.73-3.37 (m, 2H), 2.79-2.67 (m, 2H), 2.68-2.53 (m, 2H), 1.22 (t, J = 7.4 Hz, 3H).

4. Optimization of AH reaction conditions

Table S1: Optimization of reaction conditions for the AH of **9a**^a



Entry	Ir precursor	Ligand	Solvent	Additive	T (°C)/ P (atm)	Conv. ^b %	ee ^c %
1	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	toluene	I ₂ , TFA	30/50	> 99	81
2	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1b	toluene	I ₂ , TFA	30/50	> 99	60
3	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1c	toluene	I ₂ , TFA	30/50	> 99	22
4	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1d	toluene	I ₂ , TFA	30/50	> 99	65
5	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>R</i> _{ax})- 1e	toluene	I ₂ , TFA	30/50	> 99	15
6 ^d	[Ir(COD) ₂] ₂ BF ₄	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	toluene	I ₂ , TFA	30/50	> 99	79

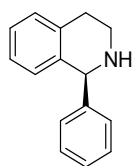
7	[Ir(COD) ₂]BArF	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	toluene	I ₂ , TFA	30/50	> 99	80
8	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	CHCl ₃	I ₂ , TFA	30/50	98	68
9	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	CH ₂ Cl ₂	I ₂ , TFA	30/50	96	56
10	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	1,4-dioxane	I ₂ , TFA	30/50	> 99	32
11	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	THF	I ₂ , TFA	30/50	> 99	84
12	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	TBME	I ₂ , TFA	30/50	55	33
13	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	EtOAc	I ₂ , TFA	30/50	> 99	55
14	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	THF	none	30/50	> 99	74
15	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	THF	I ₂	30/50	> 99	75
16	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	THF	TFA	30/50	> 99	85
17	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	THF	CH ₃ COOH	30/50	> 99	80
18	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	THF	HCOOH	30/50	> 99	85
19	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	THF	TsOH	30/50	> 99	82
20	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	THF	PhCOOH	30/50	> 99	83
21	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	THF	98 % H ₂ SO ₄	30/50	> 99	86
22	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	THF	36 % HCl	30/50	> 99	97
23	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	THF	40 % HBr	30/50	> 99	> 99
24	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	THF	57 % HI	30/50	> 99	58
25 ^e	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	THF	40 % HBr	30/50	> 99	93
26	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	THF	40 % HBr	30/30	75	99
27 ^f	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	THF	40 % HBr	30/30	85	98
28 ^g	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	THF	40 % HBr	30/50	89	99
29 ^{g,f}	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	THF	40 % HBr	30/50	90	99
30 ^g	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	THF	40 % HBr	50/50	98	99
31 ^h	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	THF	40 % HBr	50/50	65	98
32 ^{h,f}	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	THF	40 % HBr	50/50	85	98

^aReaction conditions : Ir/ligand/additive/substrate = 1:2.2:20:200, (substrate) = 0.25 M, 50 atm H₂, 12 h. ^bConversions were determined by ¹H NMR. ^cEantiomeric excesses were determined by chiral HPLC after the products were converted into the corresponding

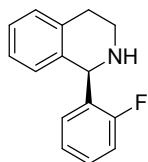
acetamides. ^dIr precursor amount is 1 mol %. ^eAdditive amount is 1 mol %. ^fReaction time is 24 h. ^gCatalyst loading is 0.1 mol %. ^hCatalyst loading is 0.02 mol %.

5. General procedure for AH and scaled-up catalytic hydrogenation

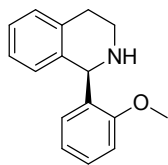
To a hydrogenation vessel was added the catalyst precursor [Ir(COD)Cl]₂ (1.6 mg, 2.4 μmol), ligand (*R*_C,*S*_{FC},*S*_{ax})-**1a** (3.6 mg, 5.4 μmol) and THF (1 mL) under nitrogen atmosphere. The mixture was stirred for 20 min at room temperature to give a homogeneous solution. Then imine substrates **9** (0.5 mmol) and 40 % HBr (7 μL, 0.05 mmol, 10 mol %) were added and the total solution was made to 2.0 mL. The resulting vessel was transferred to an autoclave, which was replaced with 50 atm of H₂ for 3 times, and the reaction mixtures were stirred at room temperature for 12 h. The hydrogen gas was released slowly and the solution was concentrated. The residue was dissolved in EtOAc (20 mL), washed with saturated NaHCO₃ solution, brine and dried over Na₂SO₄. The solvent was evaporated to afford the crude product, which was analyzed by ¹H NMR to determine the conversions. The resulting product reacted with acetic anhydride to yield the corresponding acetamide, which was analyzed by HPLC on a chiral stationary phase to determine the enantiomeric excesses.



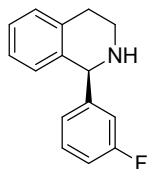
(*S*)-1-phenyl-1,2,3,4-tetrahydroisoquinoline (**10a**):⁵ white solid; 103.5 mg, 99% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.35-7.24 (m, 5H), 7.17-7.12 (m, 2H), 7.07-7.00 (m, 1H), 6.75 (d, *J* = 7.7 Hz, 1H), 5.11 (s, 1H), 3.33-3.22 (m, 1H), 3.15-2.99 (m, 2H), 2.88-2.77 (m, 1H), 1.99 (s, 1H); Enantiomeric excess was determined by HPLC for the corresponding acetamide, Chiralpak OD-H + OD-H column, Hex/IPA = 96.5:3.5, 1 mL/min.



(*R*)-1-(2-fluorophenyl)-1,2,3,4-tetrahydroisoquinoline (**10b**): white solid; 112.2 mg, 98% yield; ^1H NMR (400 MHz, CDCl_3) δ 7.30-7.20 (m, 1H), 7.18-7.12 (m, 2H), 7.11-7.00 (m, 4H), 6.82-6.74 (m, 1H), 5.51 (s, 1H), 3.27-3.17 (m, 1H), 3.14-3.05 (m, 1H), 3.04-2.93 (m, 1H), 2.90-2.82 (m, 1H), 2.02 (s, 1H); ^{13}C NMR (101 MHz, CDCl_3) δ 162.34, 159.89, 137.07, 135.70, 131.74, 131.60, 130.83, 129.15, 128.90, 127.72, 126.43, 125.78, 123.97, 115.58, 115.35, 54.70, 41.77, 29.64; HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{15}\text{FN}$ $[\text{M}+\text{H}]^+$: 228.1189, Found: 228.1184; Enantiomeric excess was determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 95:5, 1 mL/min.

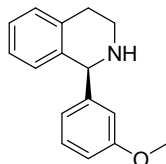


(*R*)-1-(2-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (**10c**):⁵ yellow oil; 115.9 mg, 97% yield; ^1H NMR (400 MHz, CDCl_3) δ 7.24-7.20 (m, 1H), 7.17-7.12 (m, 2H), 7.08-7.02 (m, 1H), 6.94-6.92 (m, 1H), 6.86-6.76 (m, 3H), 5.55 (s, 1H), 3.86 (s, 3H), 3.16-3.08 (m, 1H), 3.06-2.98 (m, 1H), 2.94-2.86 (m, 2H), 2.31 (s, 1H); Enantiomeric excess was determined by HPLC for the corresponding acetamide, Chiralpak OD-H column, Hex/IPA = 95:5, 1 mL/min.

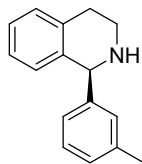


(*S*)-1-(3-fluorophenyl)-1,2,3,4-tetrahydroisoquinoline (**10d**):⁷ white solid; 112.2 mg, 98% yield; ^1H NMR (400 MHz, CDCl_3) δ 7.32-7.26 (m, 1H), 7.32-7.26 (m, 2H), 7.19-7.12 (m, 2H), 7.01-6.91 (m, 2H), 6.78-6.72 (m, 1H), 5.10 (s, 1H), 3.30-3.20 (m, 1H), 3.14-2.97 (m, 2H), 2.88-2.75 (m, 1H), 1.94 (s, 1H); Enantiomeric excess was

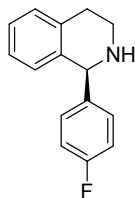
determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 95:5, 1 mL/min.



(*S*)-1-(3-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (**10e**):⁸ yellow oil; 117.1 mg, 98% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.28-7.20 (m, 1H), 7.18-7.10 (m, 2H), 7.08-7.00 (m, 1H), 6.90-6.76 (m, 4H), 5.08 (s, 1H), 3.77 (s, 3H), 3.33-3.22 (m, 1H), 3.14-2.97 (m, 2H), 2.87-2.77 (m, 1H), 2.04 (s, 1H); Enantiomeric excess was determined by HPLC for the corresponding acetamide, Chiralpak OD-H column, Hex/IPA = 90:10, 1 mL/min.

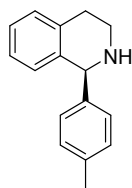


(*S*)-1-(3-methylphenyl)-1,2,3,4-tetrahydroisoquinoline (**10f**):⁵ white solid; 109.3 mg, 98% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.24-7.18 (m, 1H), 7.17-7.12 (m, 2H), 7.11-7.07 (m, 2H), 7.07-6.99 (m, 2H), 6.76 (d, *J* = 7.7 Hz, 1H), 5.06 (s, 1H), 3.24-3.22 (m, 1H), 3.14-3.00 (m, 2H), 2.88-2.78 (m, 1H), 2.32 (s, 3H), 2.06 (s, 1H); Enantiomeric excess was determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 90:10, 1 mL/min.

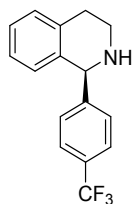


(*S*)-1-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinoline (**10g**):⁷ white solid; 112.4 mg, 99% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.27-7.19 (m, 2H), 7.18-7.12 (m, 2H), 7.07-6.95 (m, 3H), 6.72 (d, *J* = 7.7 Hz, 1H), 5.08 (s, 1H), 3.31-3.19 (m, 1H), 3.14-2.96 (m, 2H), 2.87-2.77 (m, 1H), 1.94 (s, 1H); Enantiomeric excess was

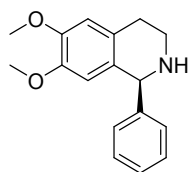
determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 95:5, 1 mL/min.



(*S*)-1-(4-methylphenyl)-1,2,3,4-tetrahydroisoquinoline (**10h**):⁵ white solid; 110.4 mg, 99% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.22-7.14 (m, 6H), 7.12-7.04 (m, 1H), 6.81 (d, *J* = 7.7 Hz, 1H), 5.14 (s, 1H), 3.37-.25 (m, 1H), 3.18-3.01 (m, 2H), 2.93-2.81 (m, 1H), 2.48-4-2.41 (m, 1H), 2.39 (s, 3H); Enantiomeric excess was determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 95:5, 1 mL/min.

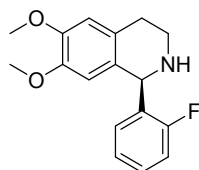


(*S*)-1-(4-(trifluoromethyl)phenyl)-1,2,3,4-tetrahydroisoquinoline (**10i**):⁵ white solid; 137.1 mg, 99% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.58 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 4.4 Hz, 2H), 7.10-7.00 (m, 1H), 6.70 (d, *J* = 7.8 Hz, 1H), 5.17 (s, 1H), 3.29-3.18 (m, 1H), 3.14-2.97 (m, 2H), 2.89-2.77 (m, 1H), 2.05 (s, 1H); Enantiomeric excess was determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 95:5, 1 mL/min.

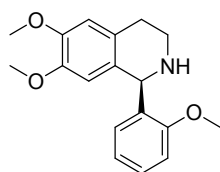


(*S*)-6,7-dimethoxy-1-phenyl-1,2,3,4-tetrahydroisoquinoline (**10j**):⁵ white solid; 131.8 mg, 98% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.39-7.30 (m, 3H), 7.28-7.25 (m, 1H), 6.66 (s, 1H), 6.27 (s, 1H), 5.08 (s, 1H), 3.90 (s, 3H), 3.66 (s, 3H), 3.30-3.20 (m, 1H), 3.12-3.03 (m, 1H), 3.01-2.89 (m, 1H), 2.83-2.72 (m, 1H), 2.14 (s, 1H); Enantiomeric

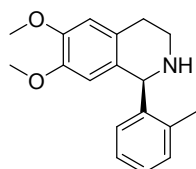
excess was determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 90:10, 1 mL/min.



(*R*)-1-(2-fluorophenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (**10k**):⁹ brown oil; 139.2 mg, 97% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.30-7.20 (m, 1H), 7.14-6.94 (m, 3H), 6.64 (s, 1H), 6.28 (s, 1H), 5.45 (s, 1H), 3.88 (s, 3H), 3.67 (s, 3H), 3.19-3.10 (m, 1H), 3.08-3.00 (m, 1H), 2.93-2.74 (m, 2H), 1.97 (s, 1H); Enantiomeric excess was determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 92:8, 1 mL/min.

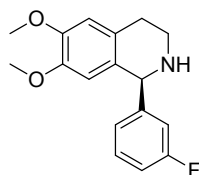


(*R*)-6,7-dimethoxy-1-(2-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (**10l**):⁹ brown oil; 140.5 mg, 94% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.25-7.20 (m, 1H), 6.93 (d, *J* = 7.8 Hz, 1H), 6.85-6.76 (m, 2H), 6.64 (s, 1H), 6.32 (s, 1H), 5.49 (s, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.68 (s, 3H), 3.09-2.93 (m, 2H), 2.89-2.72 (m, 2H), 2.09 (s, 1H); Enantiomeric excess was determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 90:10, 1 mL/min.

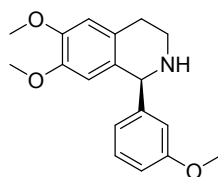


(*S*)-6,7-dimethoxy-1-(2-methylphenyl)-1,2,3,4-tetrahydroisoquinoline (**10m**):⁹ brown oil; 133.0 mg, 94% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.22-7.14 (m, 2H), 7.12-7.07 (m, 1H), 6.98 (d, *J* = 7.4 Hz, 1H), 6.63 (s, 1H), 6.19 (s, 1H), 5.28 (s, 1H), 3.88 (s, 3H), 3.63 (s, 3H), 3.26-3.18 (m, 1H), 3.09-2.99 (m, 1H), 2.97-2.85 (m, 1H),

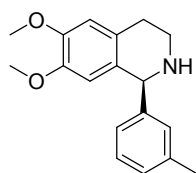
2.80-2.70 (m, 1H), 2.43 (s, 3H), 1.94 (s, 1H); Enantiomeric excess was determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 92:8, 1 mL/min.



(*S*)-1-(3-fluorophenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (**10n**):¹² white solid; 140.6 mg, 98% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.34-7.28 (m, 1H), 7.09 (d, *J* = 7.6 Hz, 1H), 7.03-6.94 (m, 2H), 6.66 (s, 1H), 6.26 (s, 1H), 5.08 (s, 1H), 3.90 (s, 3H), 3.68 (s, 3H), 3.26-3.17 (m, 1H), 3.11-3.01 (m, 1H), 2.99-2.88 (m, 1H), 2.84-2.74 (m, 1H), 2.18 (s, 1H); Enantiomeric excess was determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 90:10, 1 mL/min.

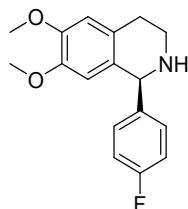


(*S*)-6,7-dimethoxy-1-(3-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (**10o**):⁸ yellow solid; 145.0 mg, 97% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.29-7.18 (m, 1H), 6.88-6.74 (m, 3H), 6.63 (s, 1H), 6.27 (s, 1H), 5.02 (s, 1H), 3.87 (s, 3H), 3.78 (s, 3H), 3.65 (s, 3H), 3.26-3.16 (m, 1H), 3.08-2.98 (m, 1H), 2.97-2.86 (m, 1H), 2.80-2.69 (m, 1H), 1.93 (s, 1H); Enantiomeric excess was determined by HPLC for the corresponding acetamide, Chiralpak OD-H column, Hex/IPA = 90:10, 1 mL/min.

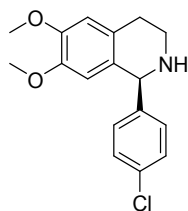


(*S*)-6,7-dimethoxy-1-(3-methylphenyl)-1,2,3,4-tetrahydroisoquinoline (**10p**):⁹ yellow solid; 138.7 mg, 98% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.26-7.20 (m, 1H), 7.14-7.08 (m, 2H), 7.07-7.02 (m, 1H), 6.66 (s, 1H), 6.28 (s, 1H), 5.05 (s, 1H), 3.90 (s,

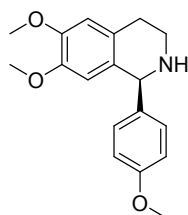
3H), 3.67 (s, 3H), 3.28-3.19 (m, 1H), 3.11-2.90 (m, 2H), 2.85-2.73 (m, 1H), 2.35 (s, 3H), 2.19 (s, 1H); Enantiomeric excess was determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 90:10, 1 mL/min.



(*S*)-1-(4-fluorophenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (**10q**):⁹ yellow solid; 142.1 mg, 99% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.27-7.22 (m, 2H), 7.03 (t, J = 8.7 Hz, 2H), 6.65 (s, 1H), 6.22 (s, 1H), 5.07 (s, 1H), 3.90 (s, 3H), 3.67 (s, 3H), 3.28-3.16 (m, 1H), 3.12-3.02 (m, 1H), 3.01-2.89 (m, 1H), 2.82-2.72 (m, 1H), 2.15 (s, 1H); Enantiomeric excess was determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 85:15, 1 mL/min.

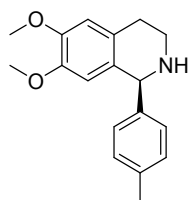


(*S*)-1-(4-chlorophenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (**10r**):⁷ colorless oil; 149.9 mg, 99% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.28 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 8.5 Hz, 2H), 6.63 (s, 1H), 6.20 (s, 1H), 5.02 (s, 1H), 3.86 (s, 3H), 3.64 (s, 3H), 3.23-3.13 (m, 1H), 3.08-2.98 (m, 1H), 2.96-2.85 (m, 1H), 2.79-2.66 (m, 1H), 2.05 (s, 1H); Enantiomeric excess was determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 80:20, 1 mL/min.

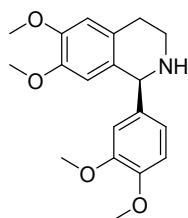


(*S*)-6,7-dimethoxy-1-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (**10s**):⁹ yellow

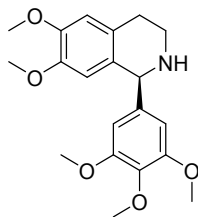
solid; 146.5 mg, 98% yield; **¹H NMR** (400 MHz, CDCl₃) δ 7.22-7.14 (m, 2H), 6.90-6.80 (m, 2H), 6.62 (s, 1H), 6.25 (s, 1H), 5.00 (s, 1H), 3.87 (s, 3H), 3.80 (s, 3H), 3.65 (s, 3H), 3.26-3.16 (m, 1H), 3.10-2.98 (m, 1H), 2.97-2.86 (m, 1H), 2.79-2.69 (m, 1H), 1.91 (s, 1H); Enantiomeric excess was determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 85:15, 1 mL/min.



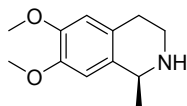
(*S*)-6,7-dimethoxy-1-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (**10t**):⁸ yellow solid; 138.7 mg, 98% yield; **¹H NMR** (400 MHz, CDCl₃) δ 7.22-7.10 (m, 4H), 6.65 (s, 1H), 6.28 (s, 1H), 5.05 (s, 1H), 3.90 (s, 3H), 3.67 (s, 3H), 3.26-3.17 (m, 1H), 3.10-3.01 (m, 1H), 2.99-2.89 (m, 1H), 2.82-2.72 (m, 1H), 2.36 (s, 3H), 2.13 (s, 1H); Enantiomeric excess was determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 90:10, 1 mL/min.



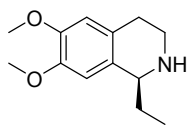
(*S*)-1-(3,4-dimethoxyphenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (**10u**):⁵ white solid; 162.9 mg, 99% yield; **¹H NMR** (400 MHz, CDCl₃) δ 6.87-6.74 (m, 3H), 6.63 (s, 1H), 6.27 (s, 1H), 4.98 (s, 1H), 3.86 (s, 6H), 3.82 (s, 3H), 3.64 (s, 3H), 3.30-3.15 (m, 1H), 3.10-3.00 (m, 1H), 2.99-2.88 (m, 1H), 2.78-2.65 (m, 1H), 2.18 (s, 1H); Enantiomeric excess was determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 80:20, 1 mL/min.



(*S*)-6,7-dimethoxy-1-(3,4,5-trimethoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (**10v**):⁵ white solid; 177.7 mg, 99% yield; ¹H NMR (400 MHz, CDCl₃) δ 6.63 (s, 1H), 6.50 (s, 2H), 6.31 (s, 1H), 4.98 (s, 1H), 3.88 (s, 3H), 3.85 (s, 3H), 3.81 (s, 6H), 3.68 (s, 3H), 3.30-3.16 (m, 1H), 3.10-3.00 (m, 1H), 3.00-2.85 (m, 1H), 2.80-2.65 (m, 1H), 2.12 (s, 1H); Enantiomeric excess was determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 80:20, 1 mL/min.



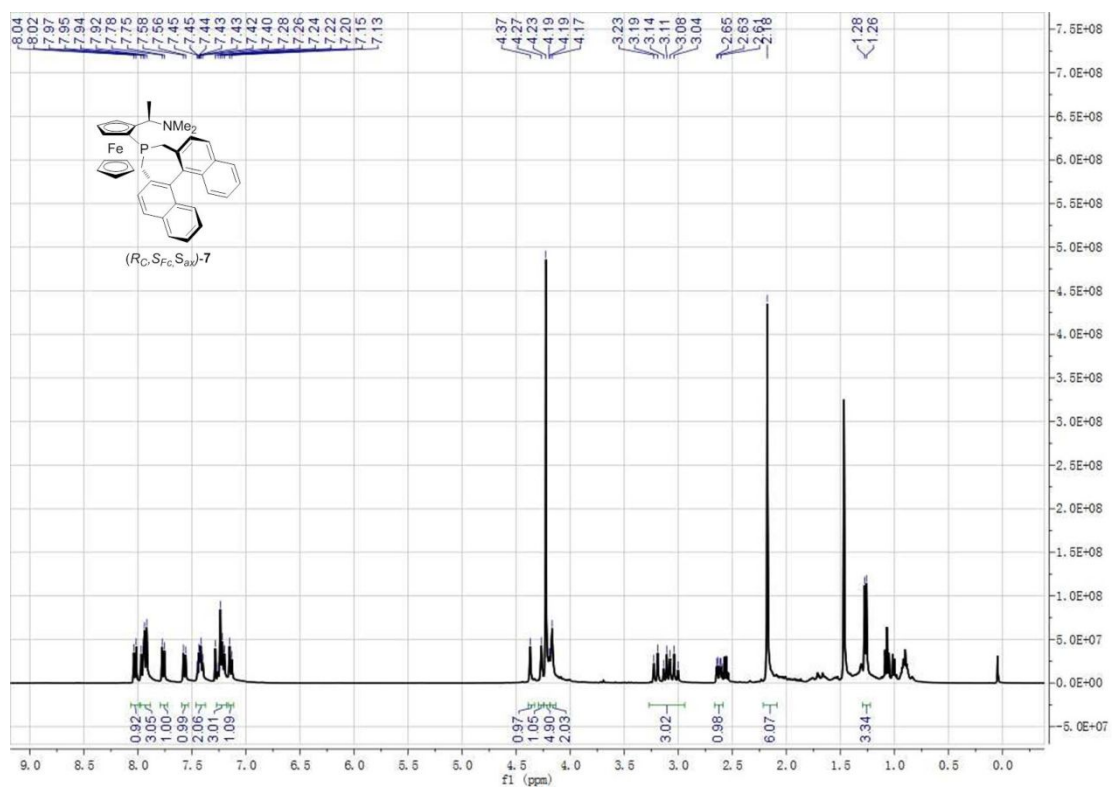
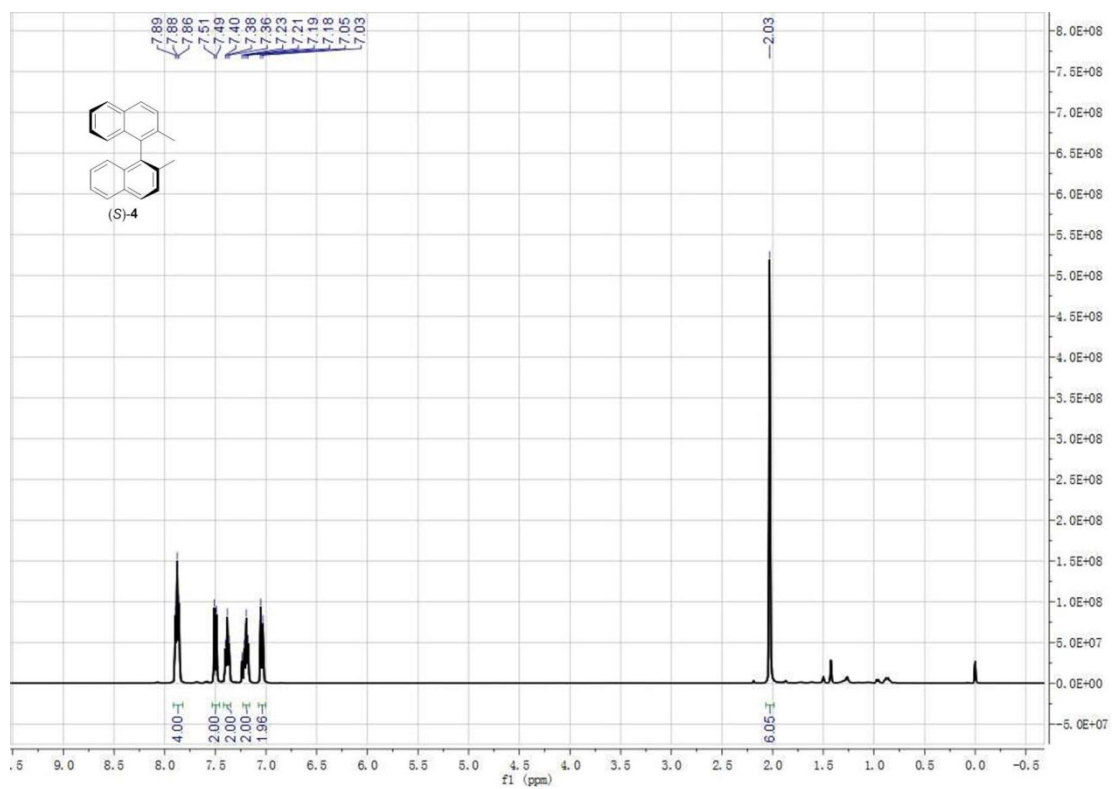
(*S*)-6,7-dimethoxy-1-methyl-1,2,3,4-tetrahydroisoquinoline (**10w**):¹¹ yellow oil; 101.4 mg, 98% yield; ¹H NMR (400 MHz, CDCl₃) δ 6.63 (s, 1H), 6.57 (s, 1H), 4.10-4.00 (m, 1H), 3.86 (s, 6H), 3.41-3.15 (m, 1H), 3.06-2.94 (m, 1H), 2.85-2.72 (m, 1H), 2.70-2.60 (m, 1H), 1.74 (s, 1H), 1.44 (d, *J* = 6.7 Hz, 3H); Enantiomeric excess was determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 90:10, 1 mL/min.

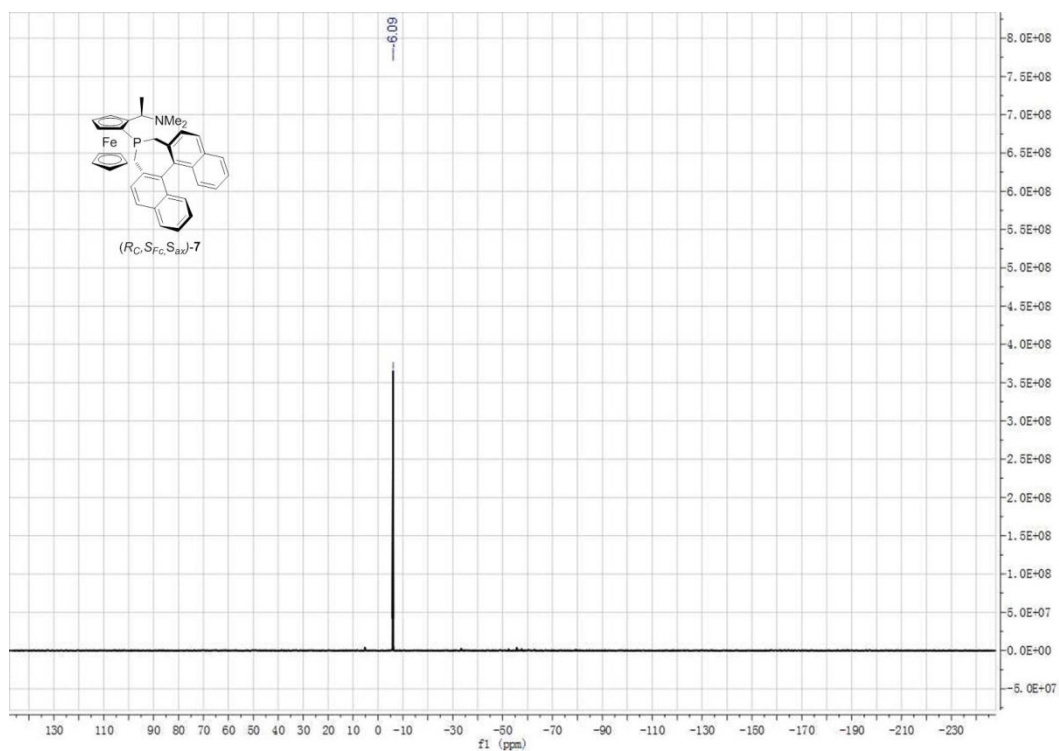
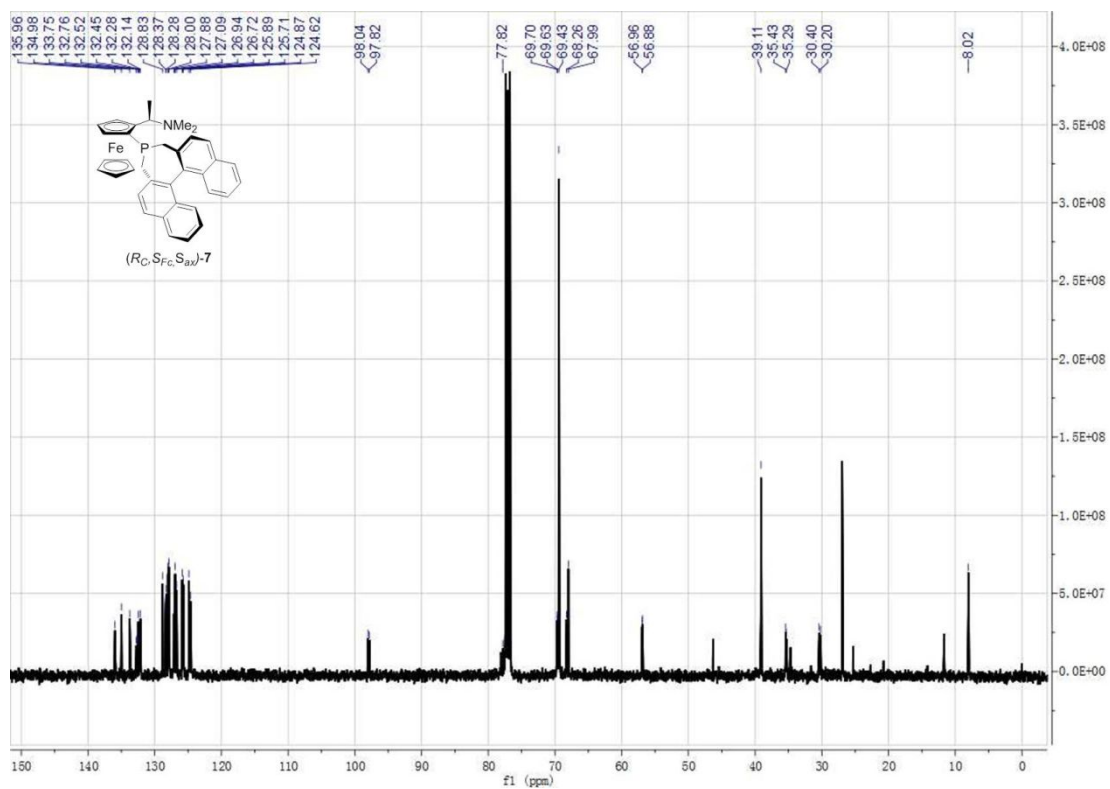


(*S*)-6,7-dimethoxy-1-ethyl-1,2,3,4-tetrahydroisoquinoline (**10x**):¹¹ yellow oil; 108.3 mg, 98% yield; ¹H NMR (400 MHz, CDCl₃) δ 6.62 (s, 1H), 6.57 (s, 1H), 3.85 (s, 6H), 3.87-3.81 (m, 1H), 3.31-3.14 (m, 1H), 3.01-2.91 (m, 1H), 2.80-2.70 (m, 1H), 2.70-2.59 (m, 1H), 1.97-1.82 (m, 1H), 1.77-1.57 (m, 2H), 1.02 (t, *J* = 7.4 Hz, 3H); Enantiomeric excess was determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 92:8, 1 mL/min.

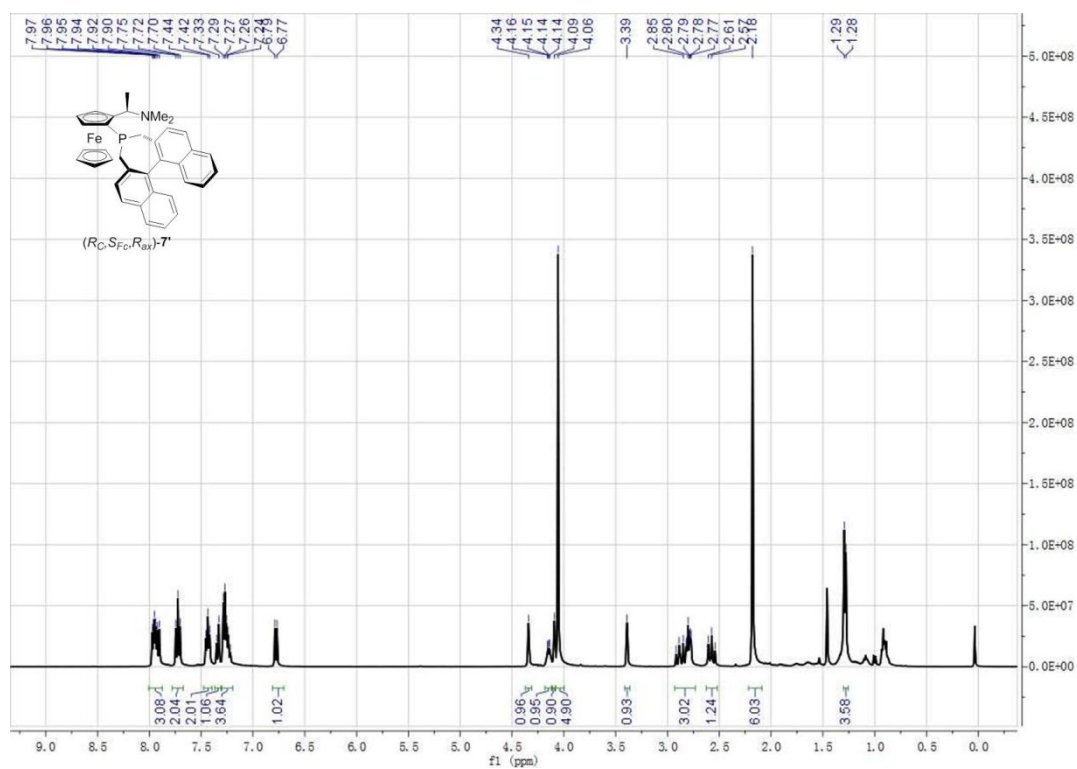
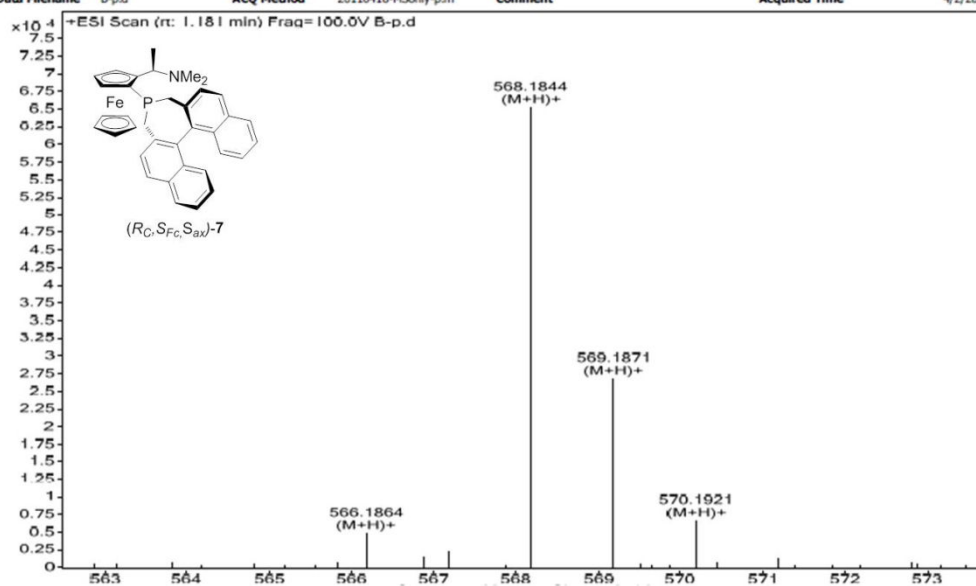
Gram-scale catalytic hydrogenation: According to the above procedure, the catalyst solution was prepared with $[\text{Ir}(\text{COD})\text{Cl}]_2$ (1.6 mg, 2.4 μmol), ligand (R_C, S_{Fc}, S_{ax}) -**1a** (3.6 mg, 5.4 μmol) and THF (1 mL) under nitrogen atmosphere. To a hydrogenation vessel was added a solution of imine substrates **9a** (3 g, 14.5 mmol) in THF (60 mL) and 40 % HBr (0.22 mL, 1.45 mmol, 10 mol %). The resulting vessel was transferred to an autoclave, which was replaced with 50 atm of H_2 for 3 times, and the reaction mixtures were stirred at 50 °C for 24 h. After the reaction cooled to room temperature, the hydrogen gas was released slowly and the solution was concentrated. The residue was dissolved in EtOAc (100 mL), washed with saturated NaHCO_3 solution, brine and dried over Na_2SO_4 . The solvent was evaporated to afford the crude product, which was purified with chromatography (EtOAc/PE) to yield chiral 1-phenyl THIQ (2.85 g, 94 %, 98 % *ee*).

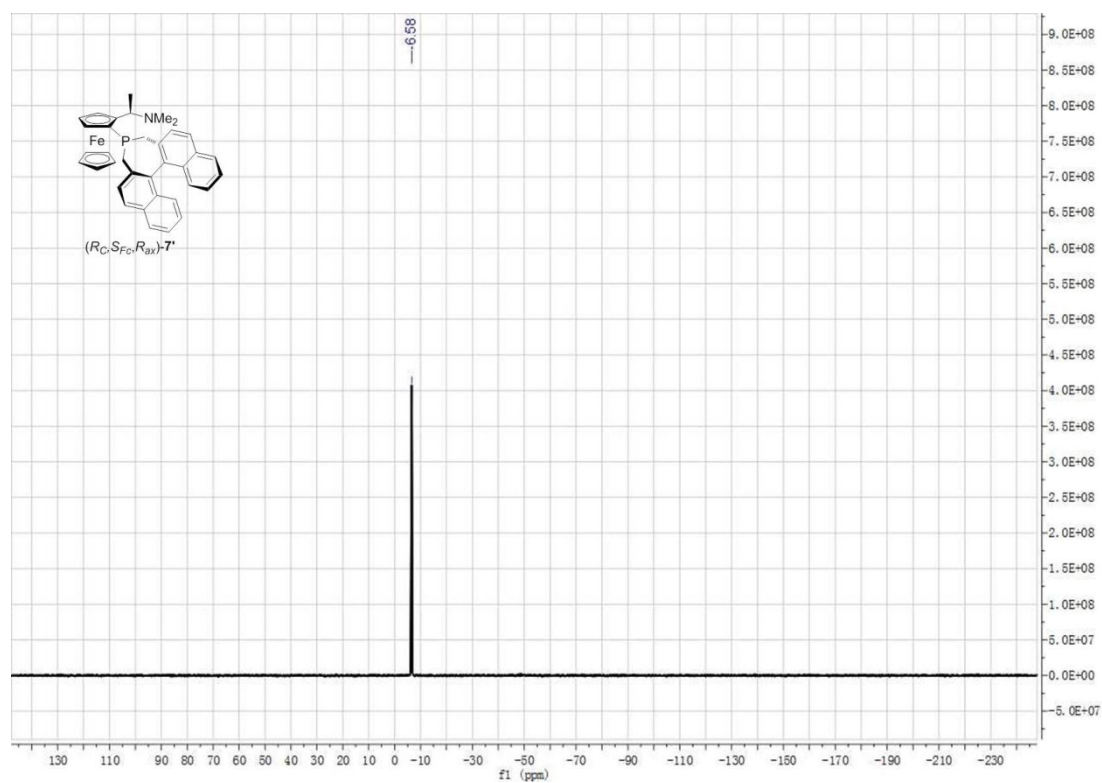
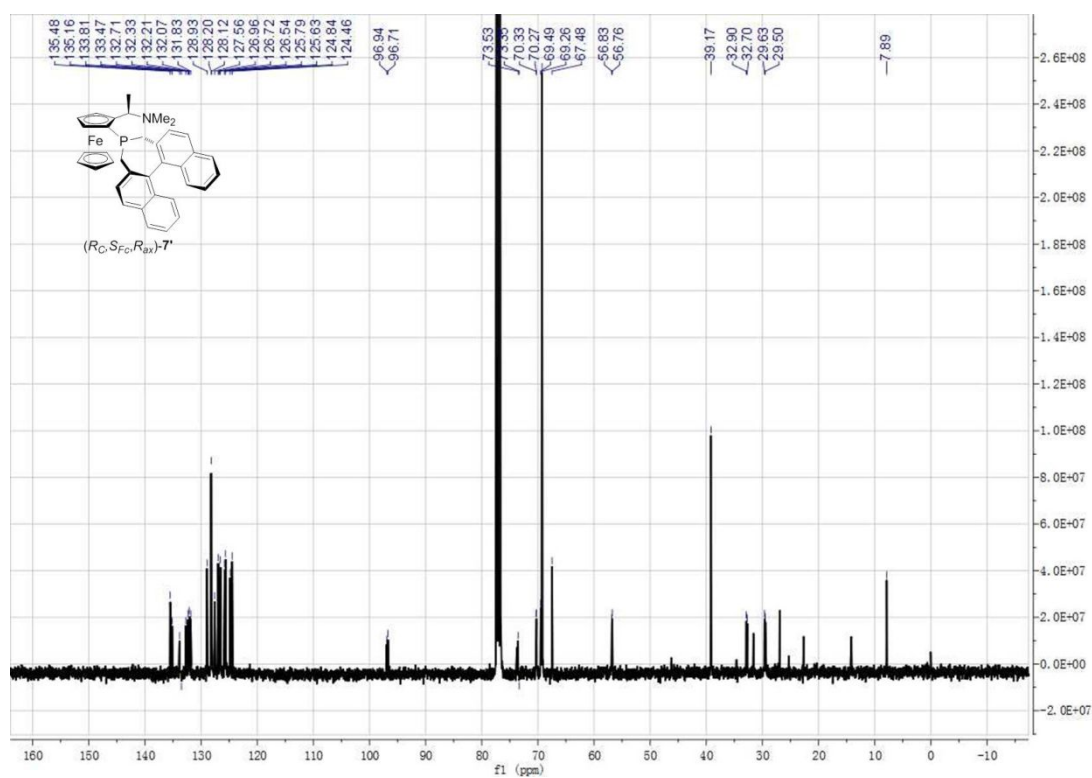
6. NMR spectra and HRMS



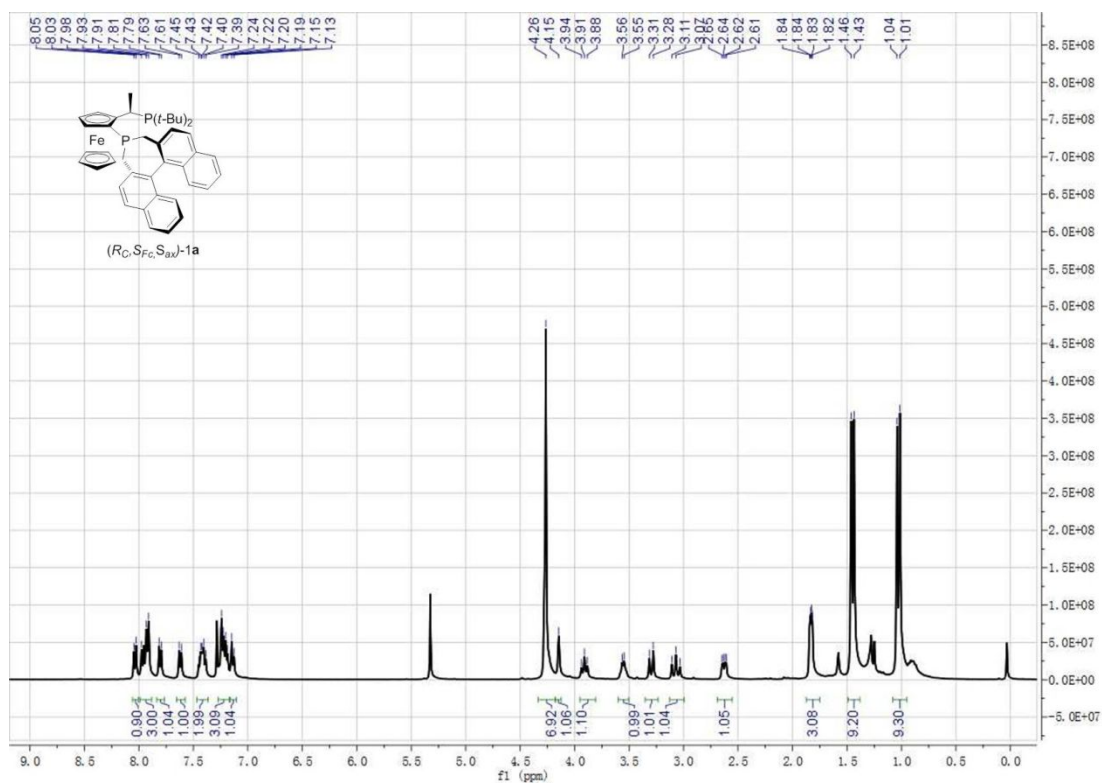
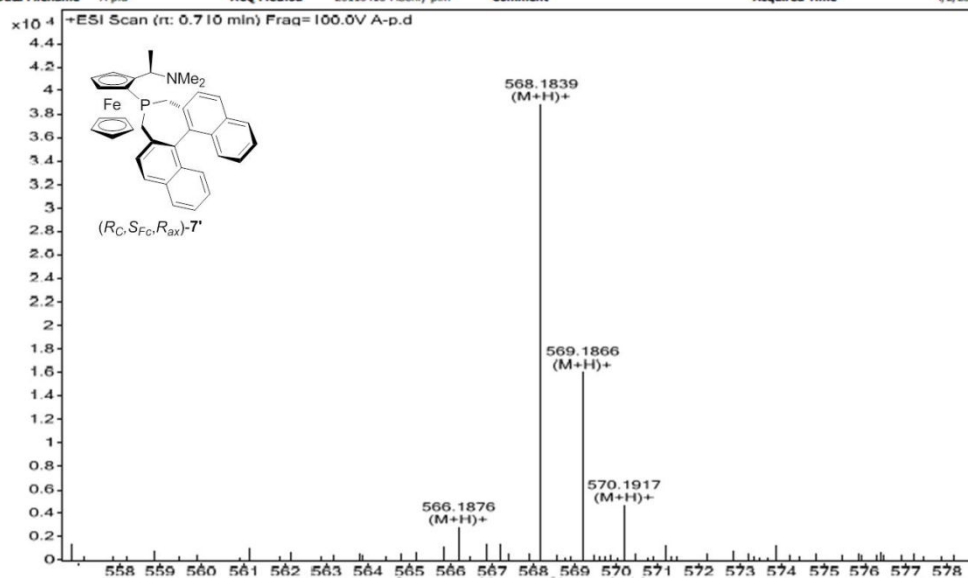


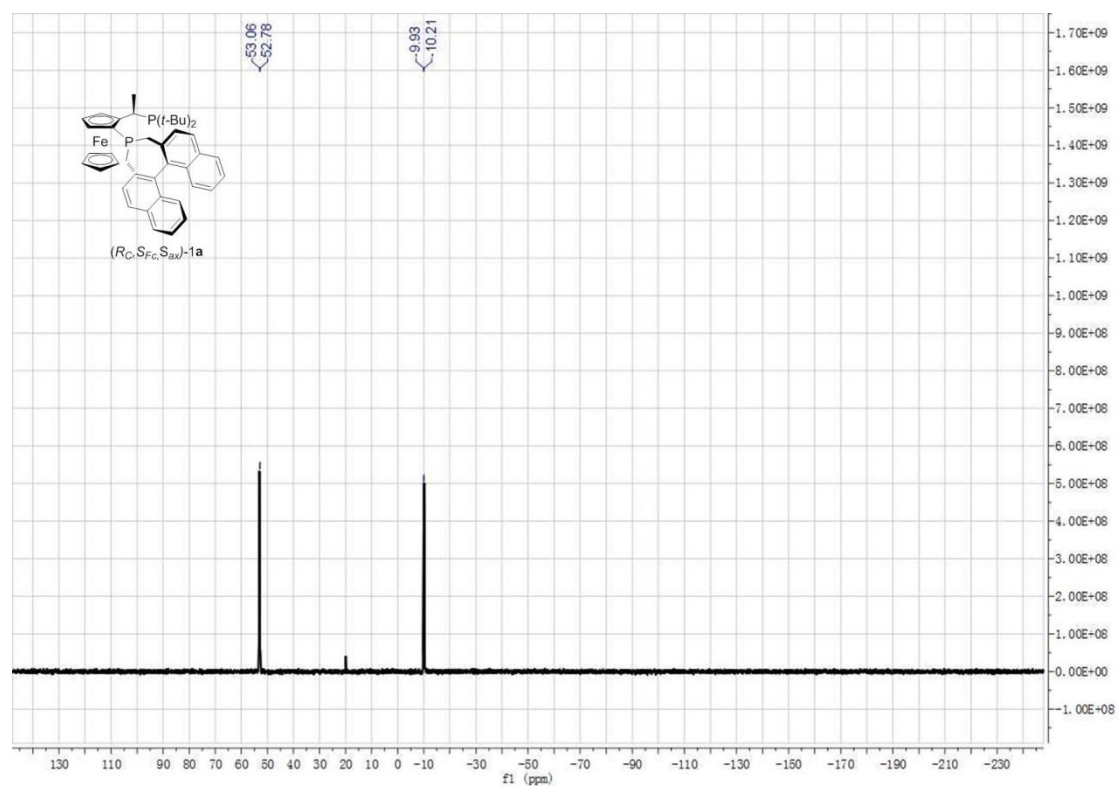
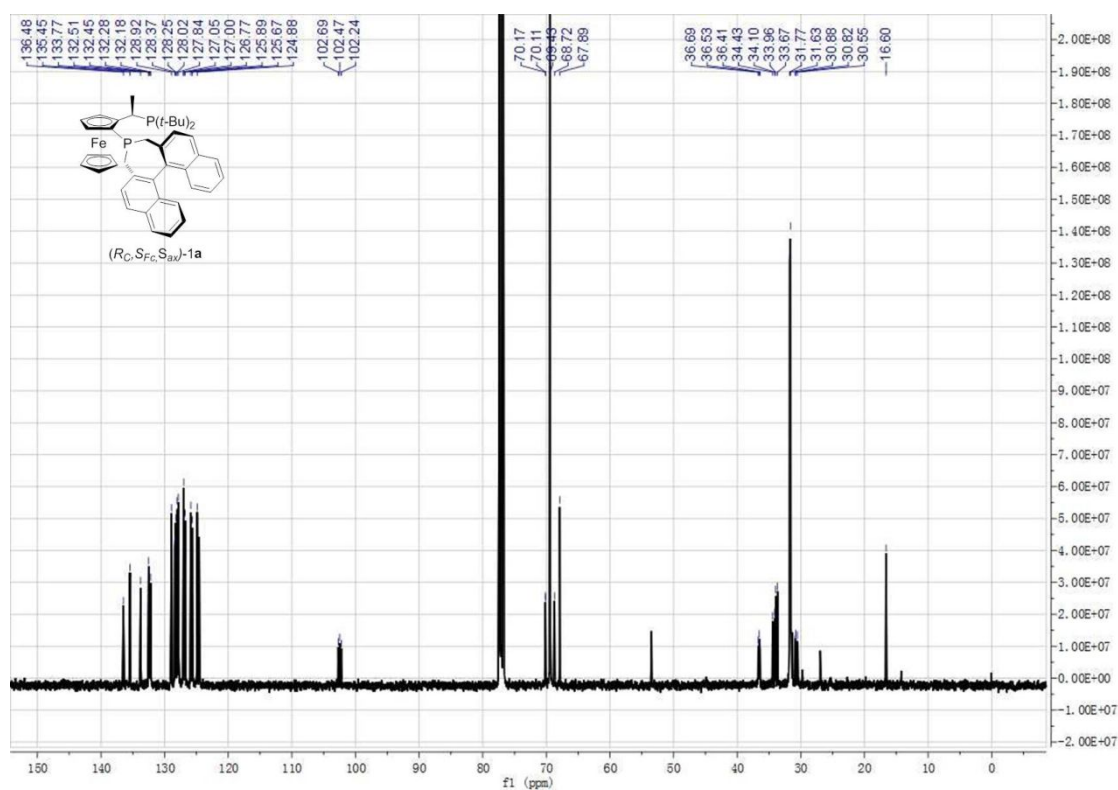
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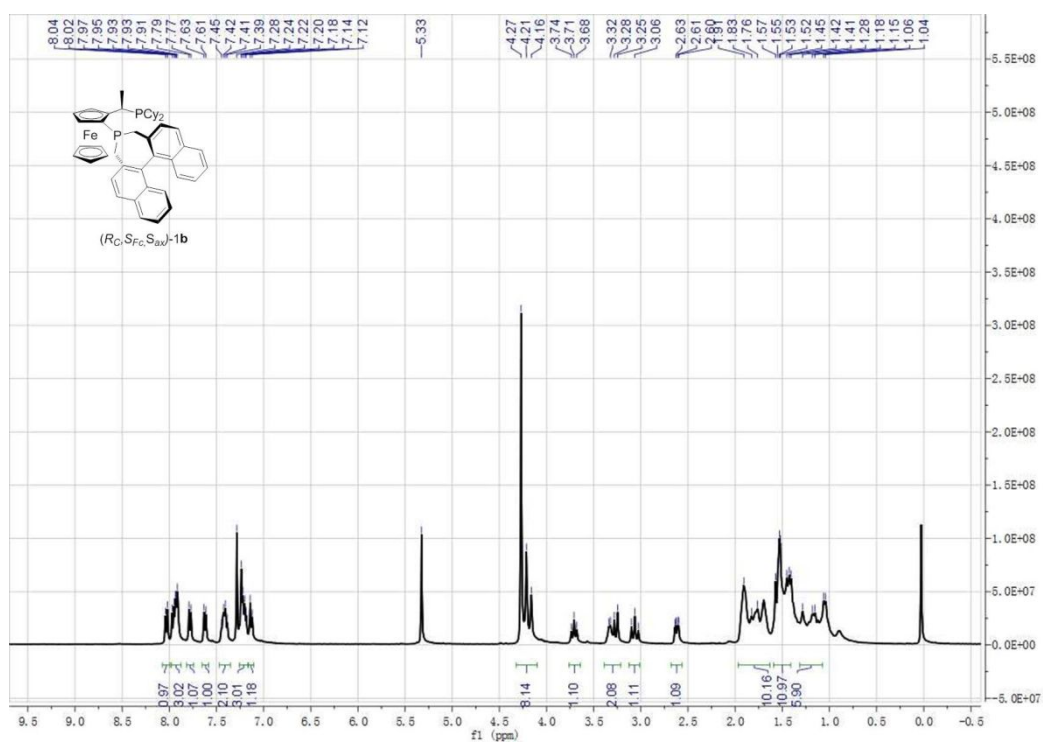
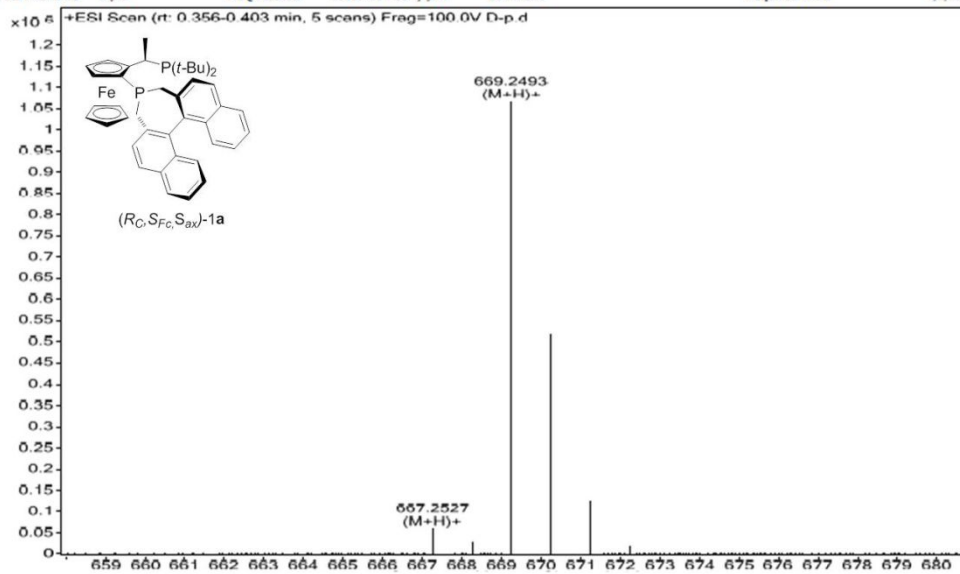


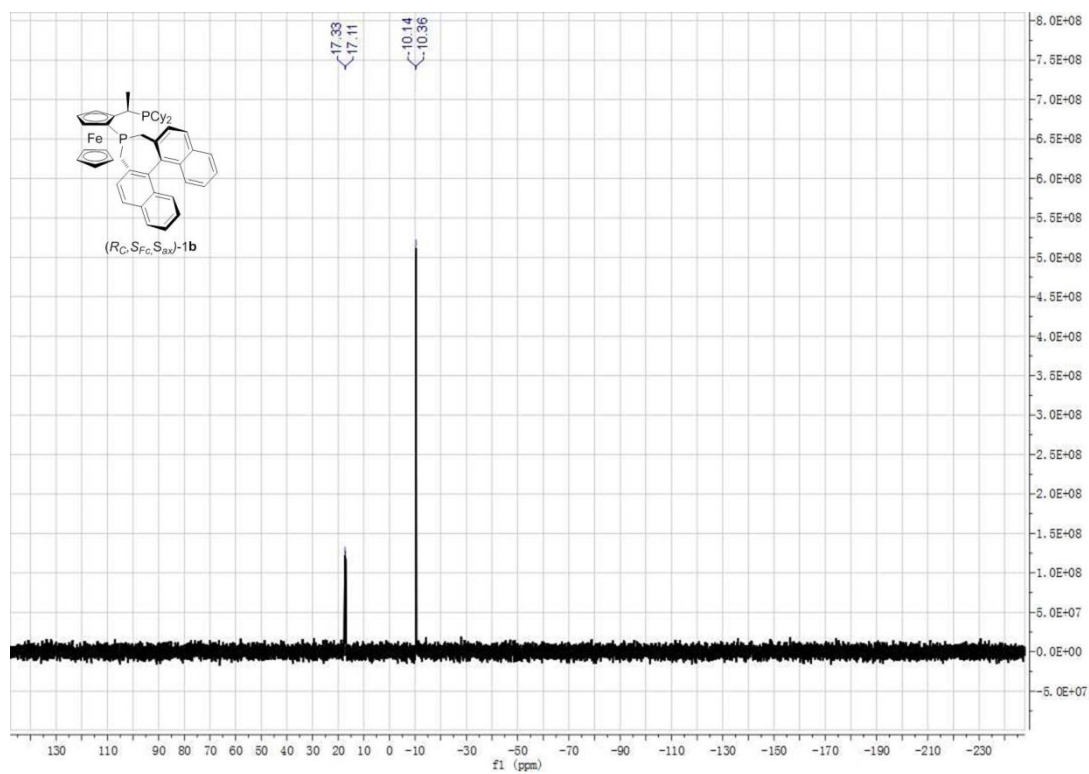
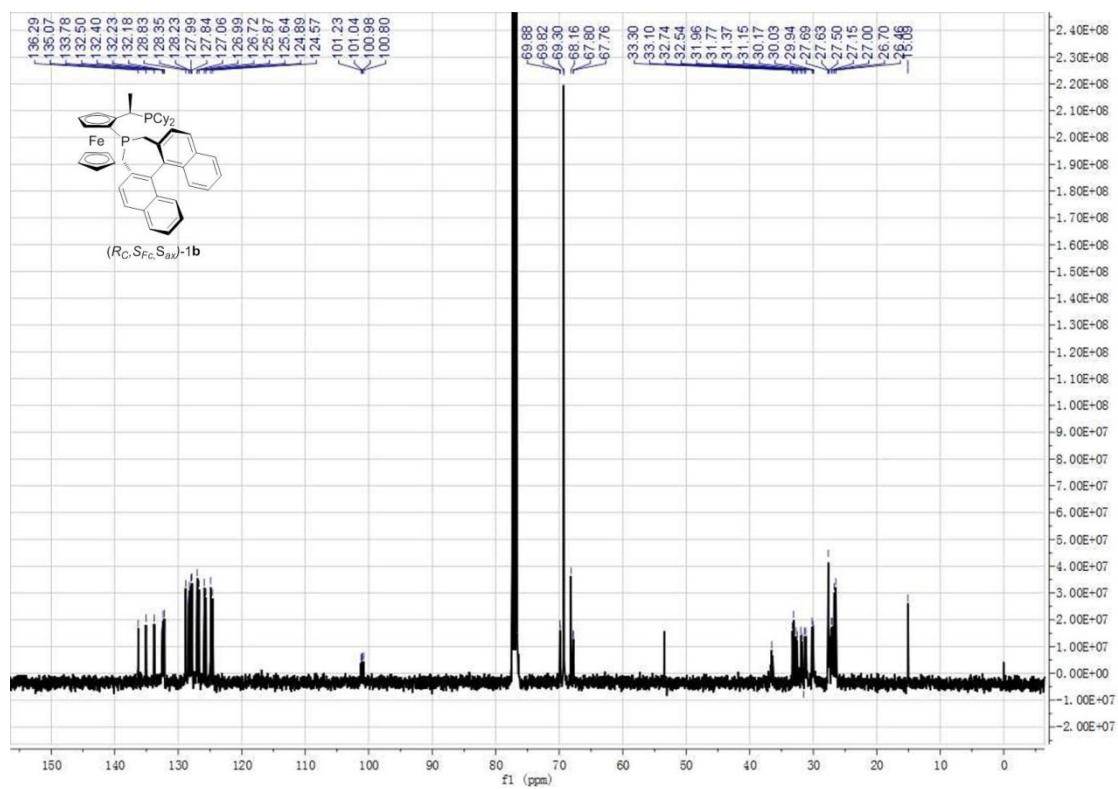
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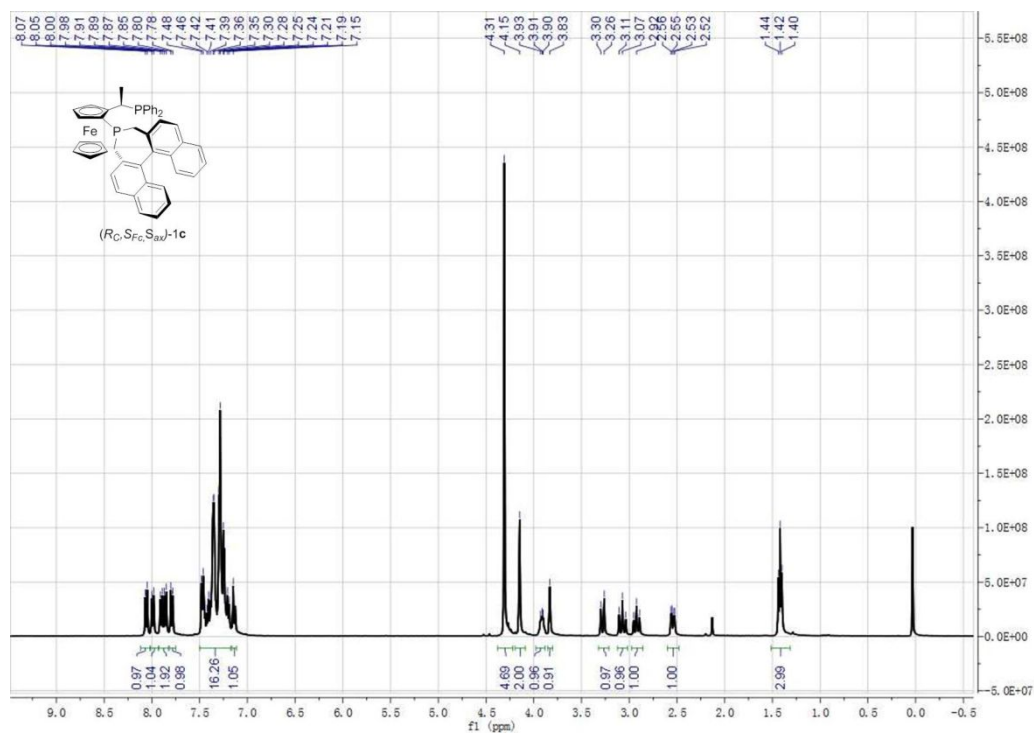
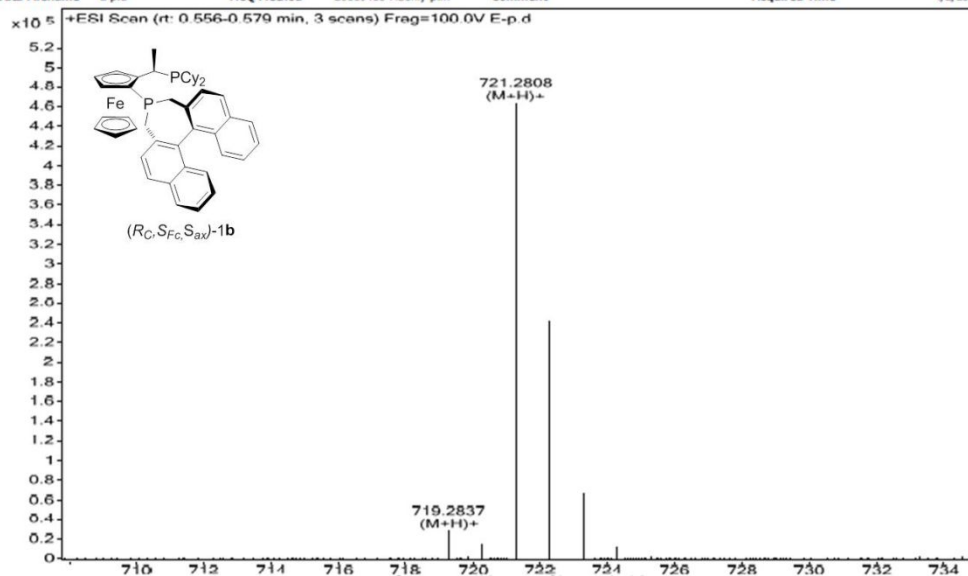


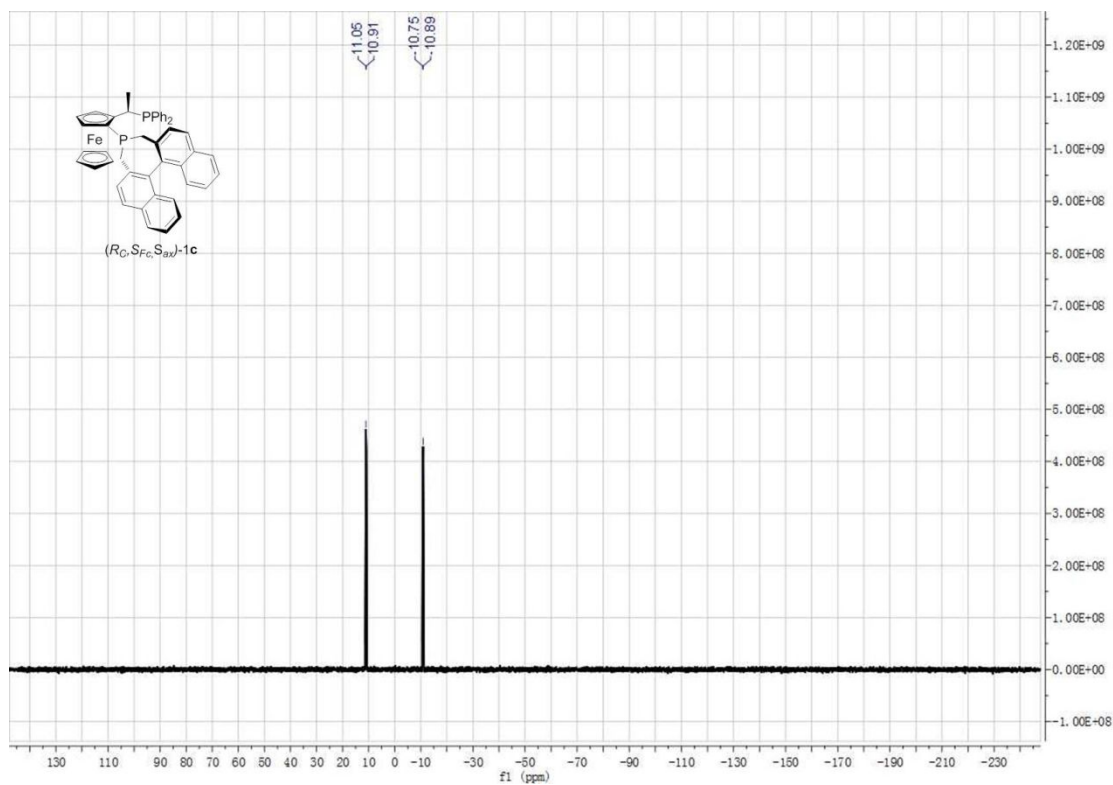
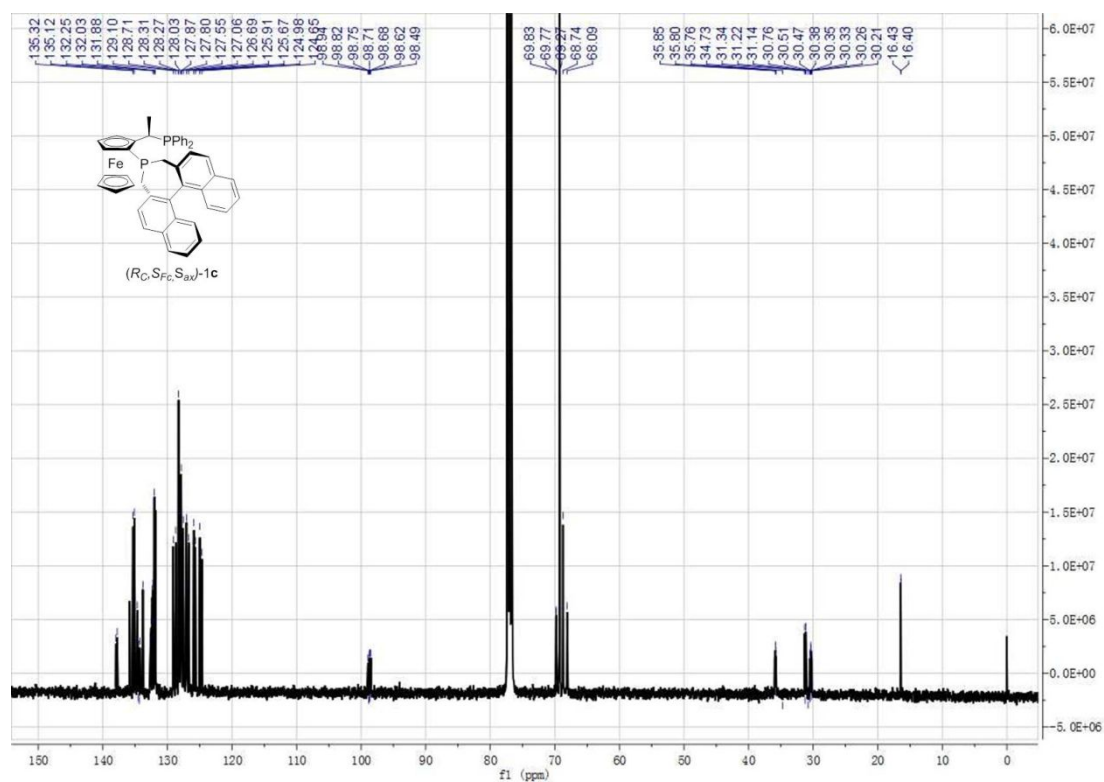
Sample Name	Position	P2e5	Instrument Name	Instrument 1	User Name	QTOF-PC/QTOF
Inj Vol	0.1	InjPosition	SampleType	Sample	IRM Calibration Status	Success
Data Filename	D-p.d	ACQ Method	Comment		Acquired Time	4/2/2018 4:31:43 PM



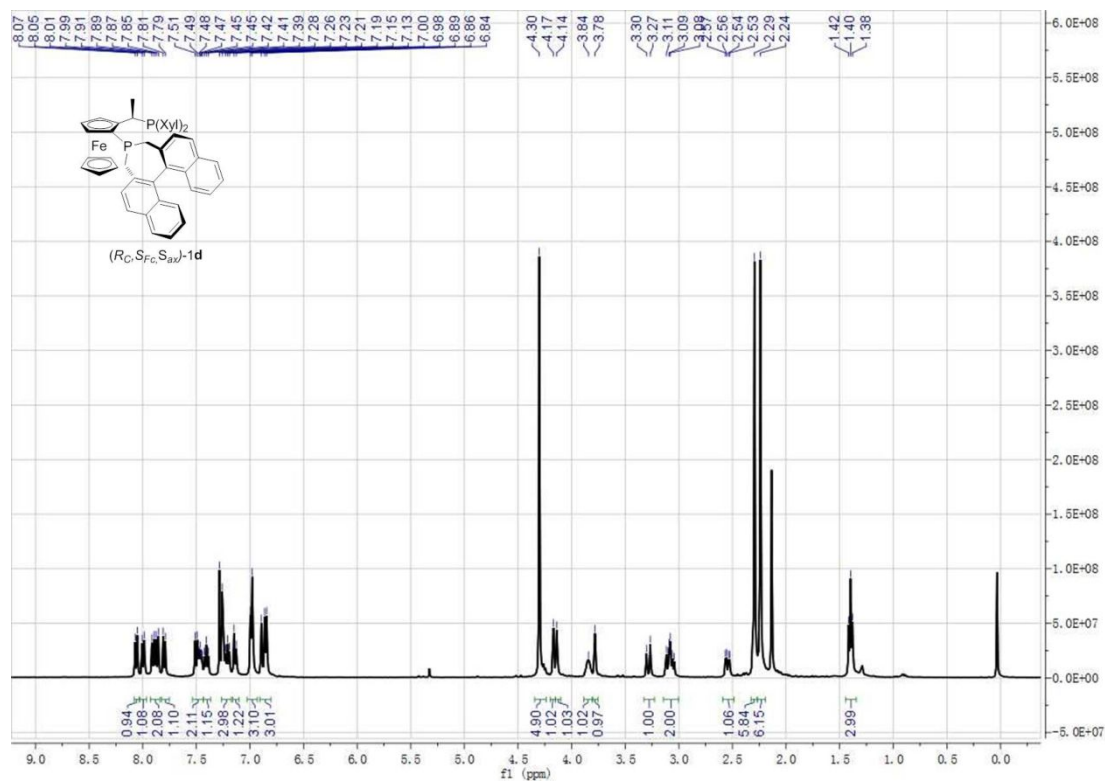
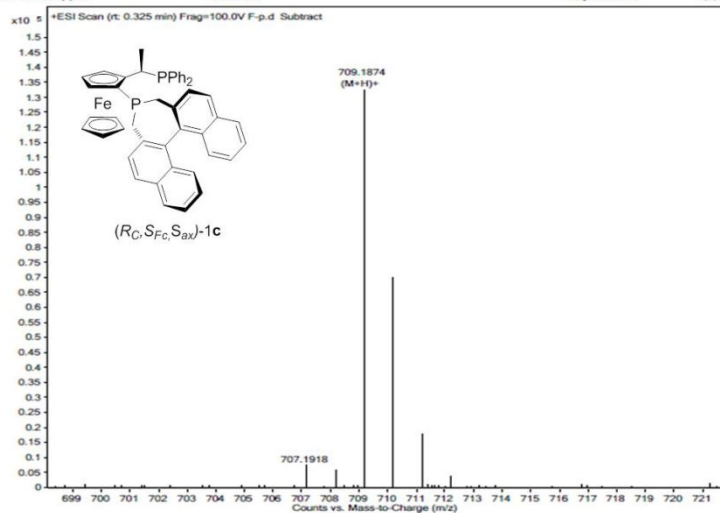


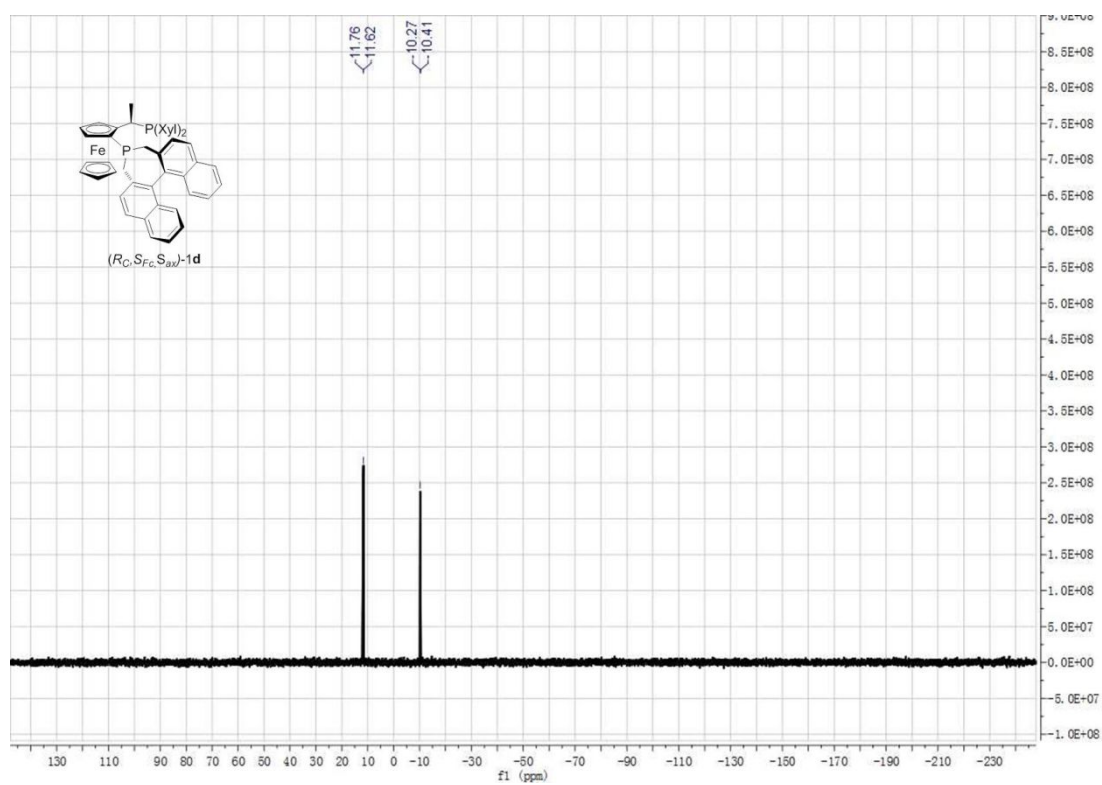
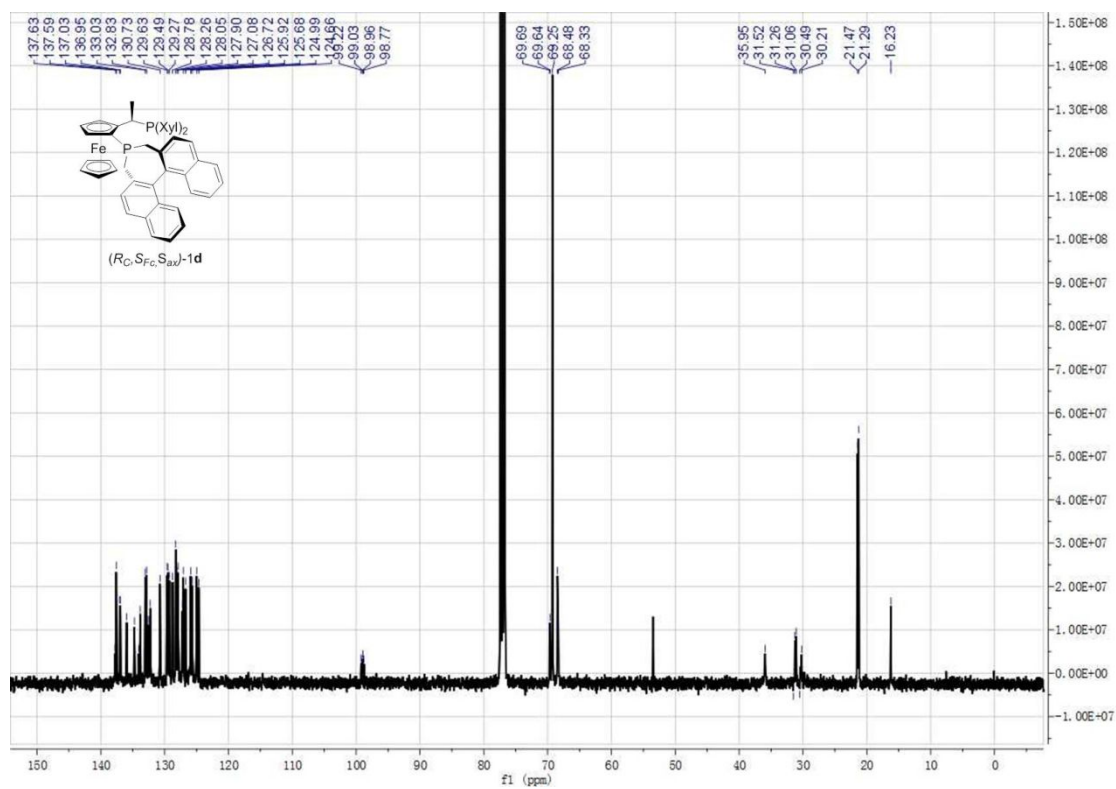
Sample Name	Position	P2e6	Instrument Name	Instrument 1	User Name	QTOF-PC/QTOF
Inj Vol	0.1	InjPosition	SampleType	Sample	IRM Calibration Status	Success
Data Filename	E-p.d	ACQ Method	Comment		Acquired Time	4/2/2018 4:34:44 PM



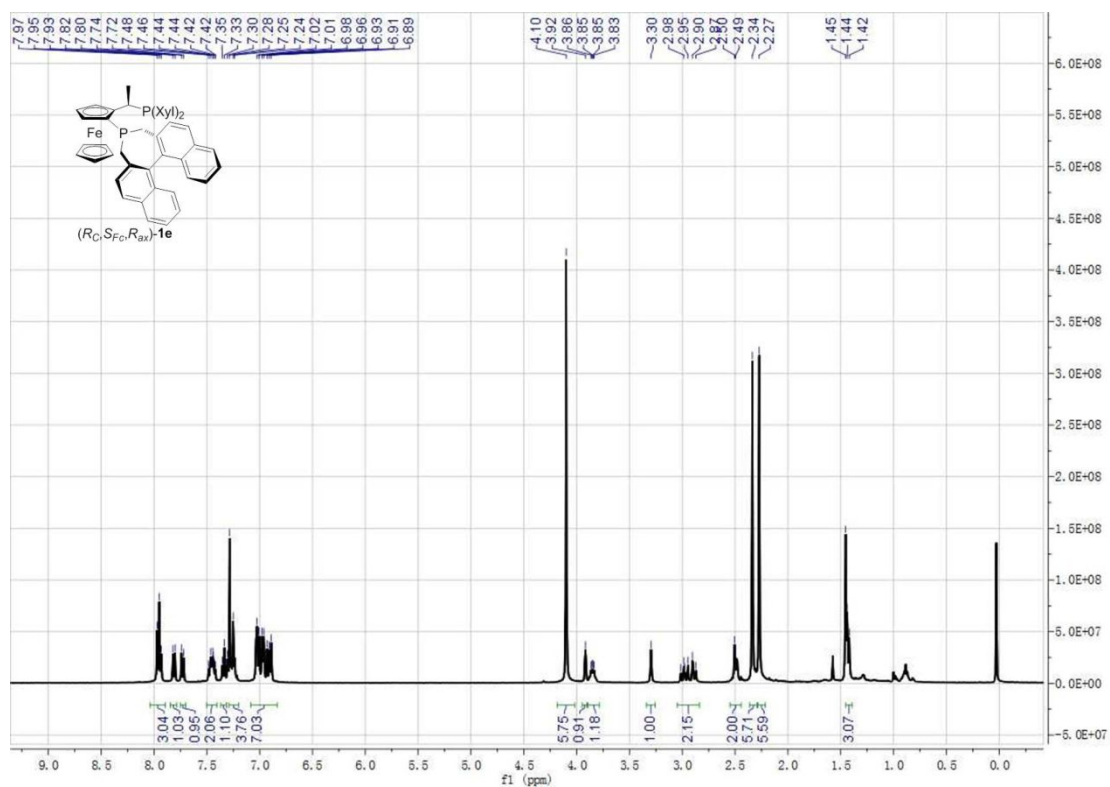
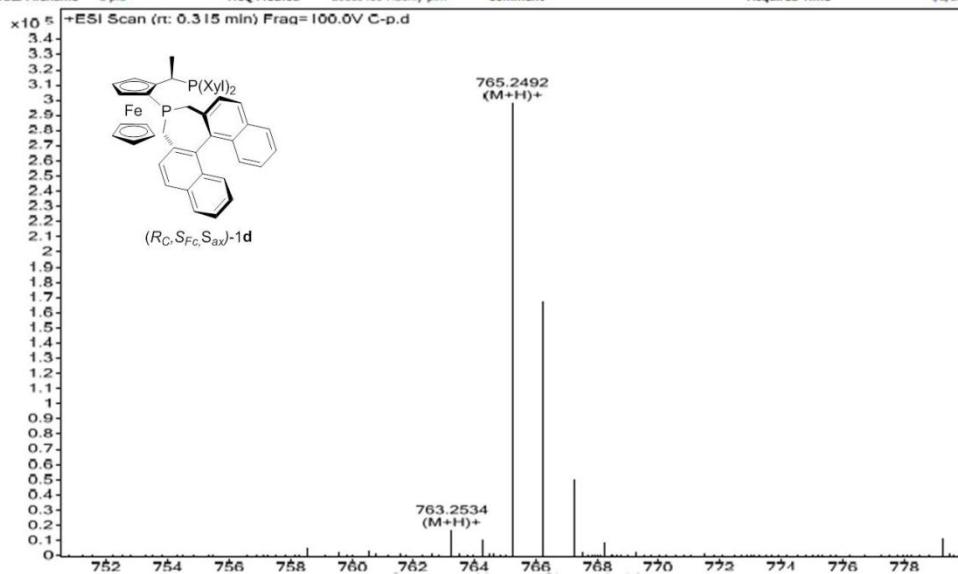


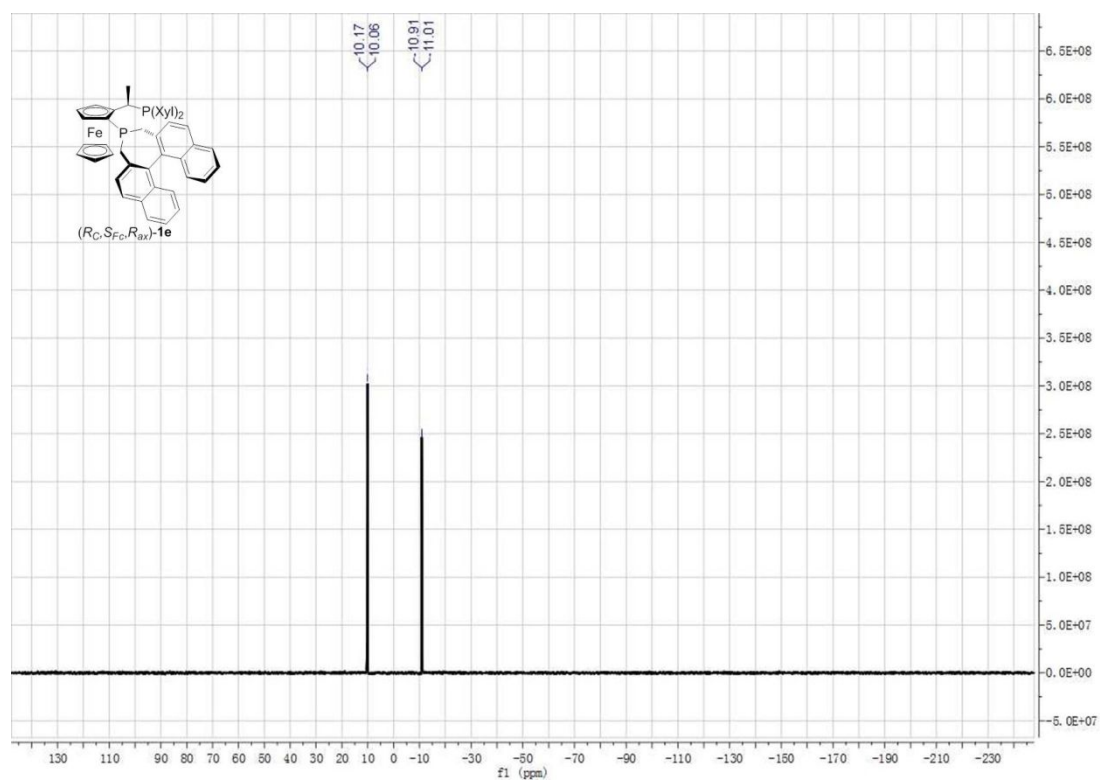
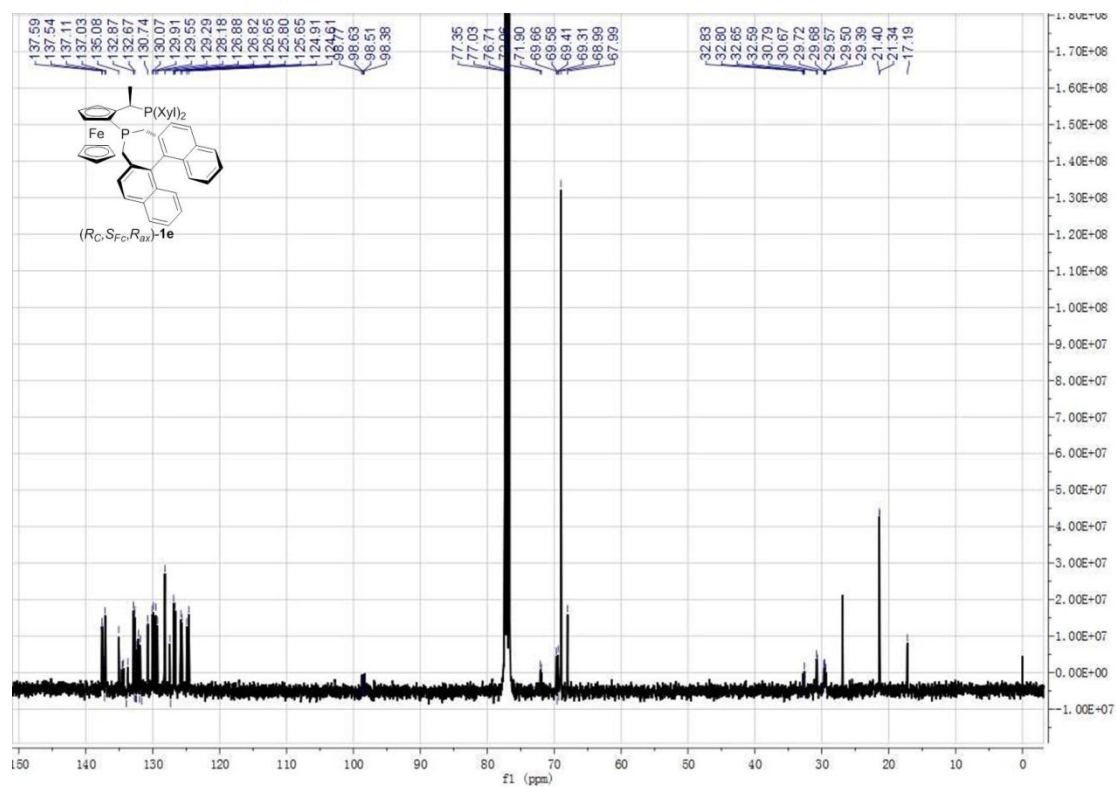
Sample Name	QTOF-PC/QTOF	Position	p2E7	Instrument Name	Instrument 1
User Name		Inj Vol	0.1	InjPosition	
Sample Type	Sample	IRM Calibration Status	Success	Data Filename	F-p.d
ACQ Method	20110418-M50nlyp-p.m	Comment		Acquired Time	4/3/2018 9:55:28 AM



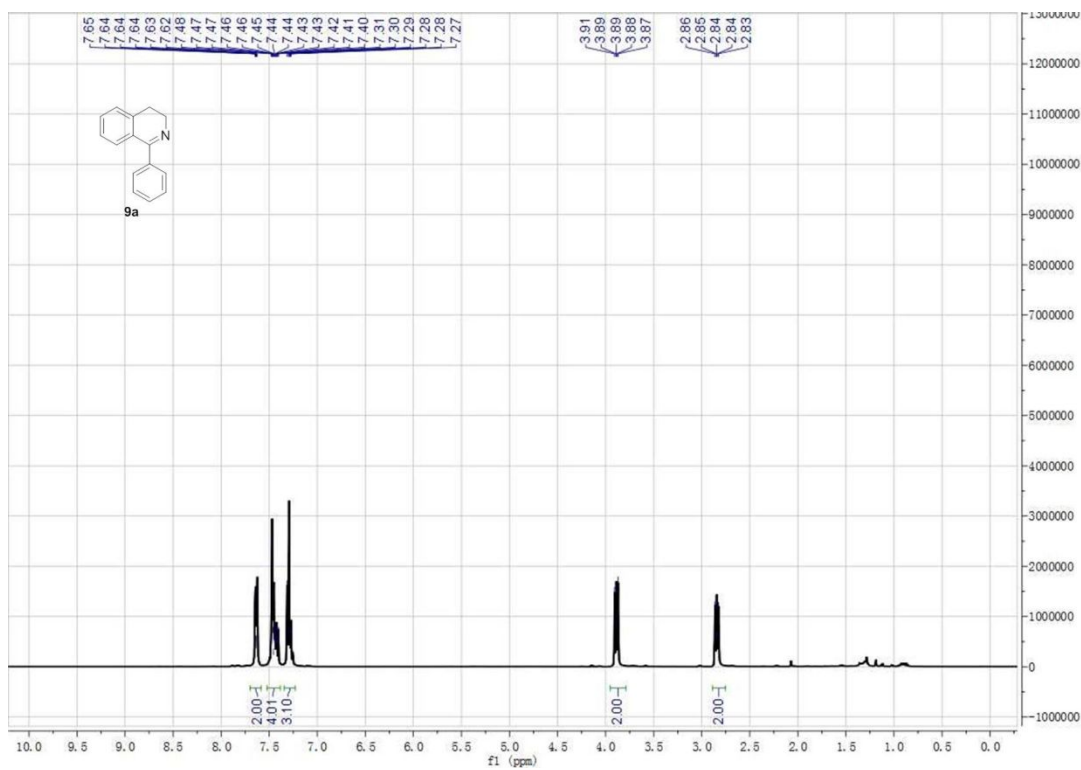
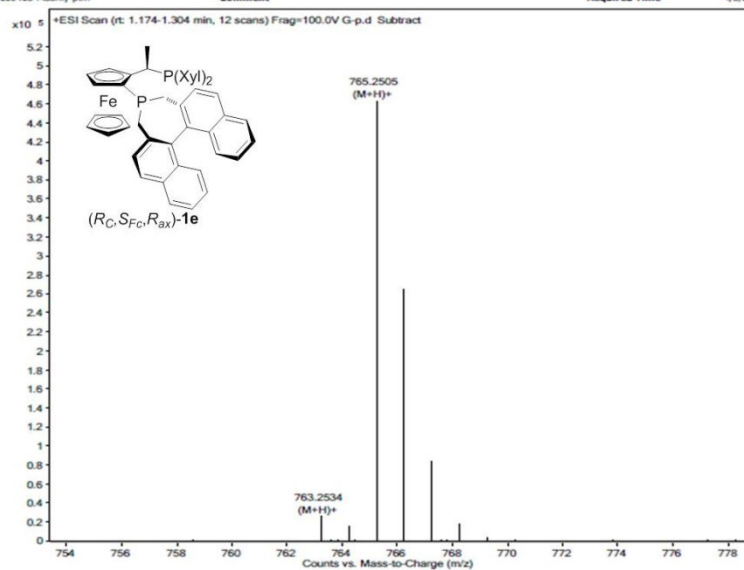


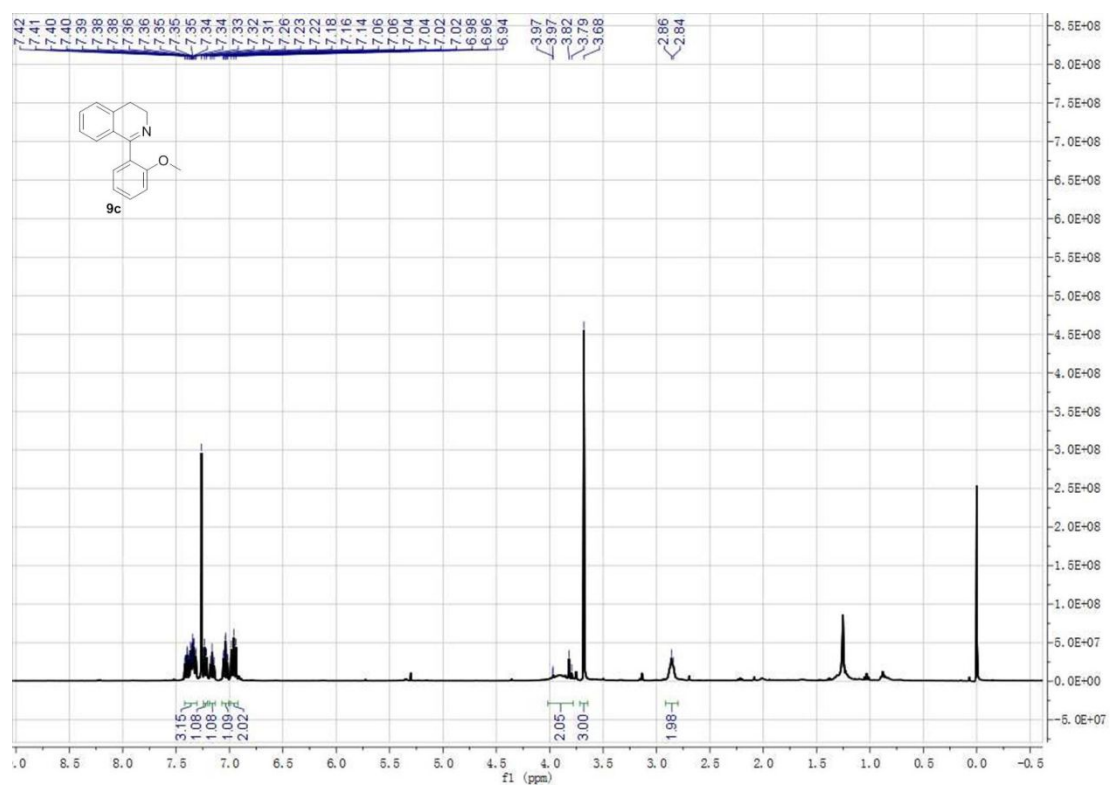
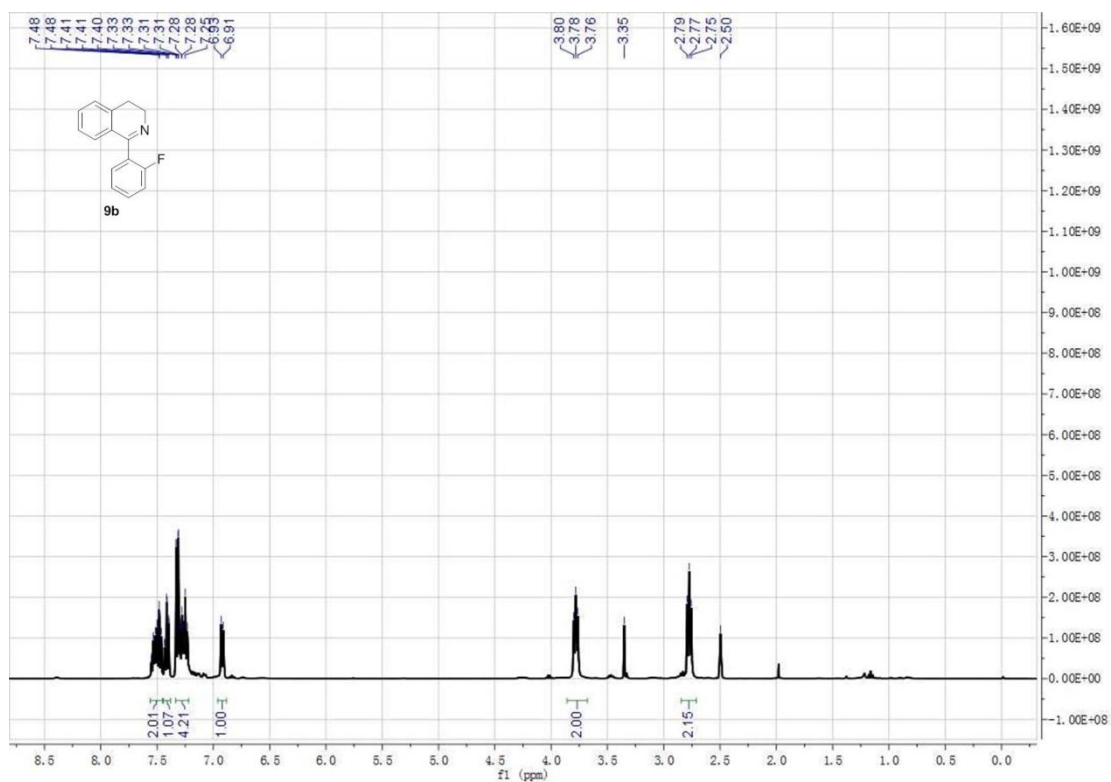
Sample Name	Position	Instrument Name	User Name	QTOF-PC/QTOF
Inj Vol 0.1	P2e4	Instrument 1	IRM Calibration Status	Success
Data Filename C-p.d	ACQ Method 20110418-MSonly-p.m	Sample	Acquired Time	4/2/2018 4:28:37 PM

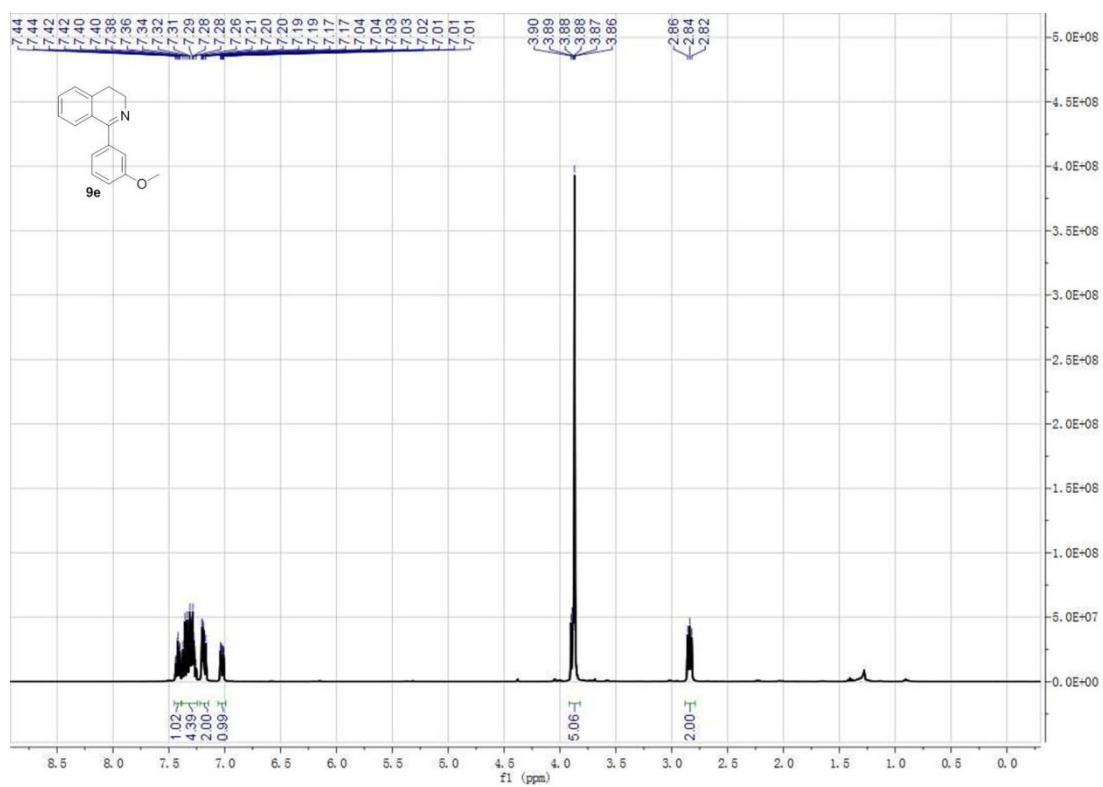
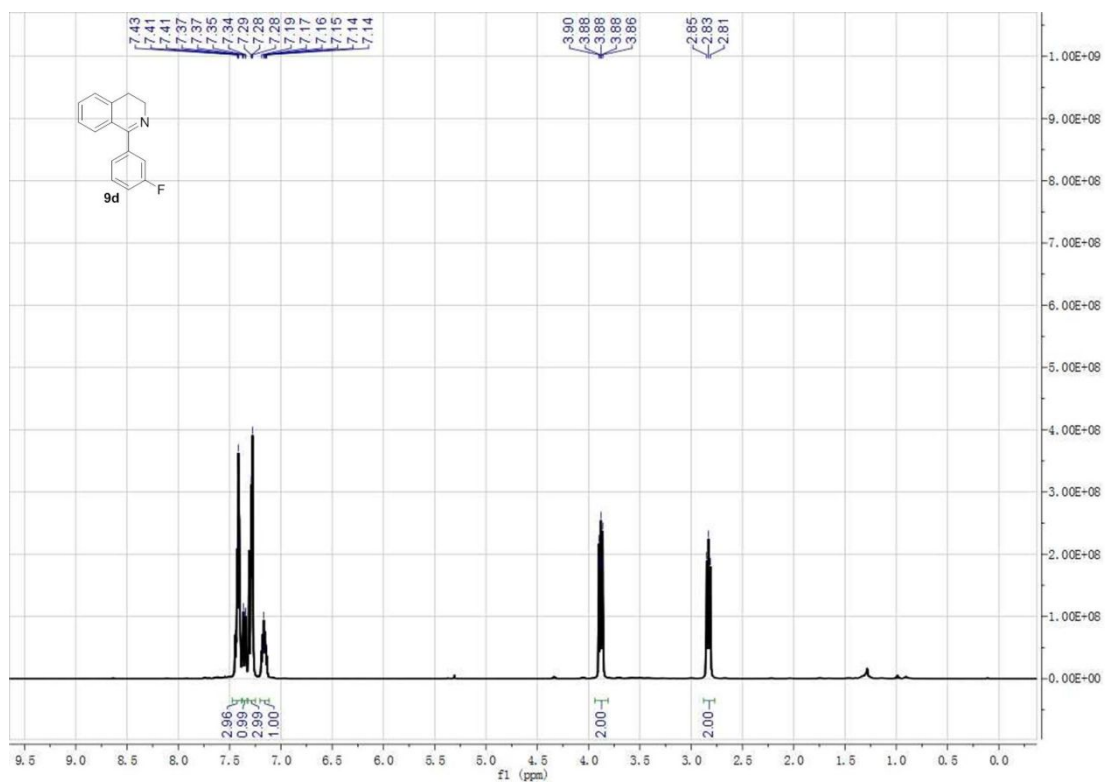


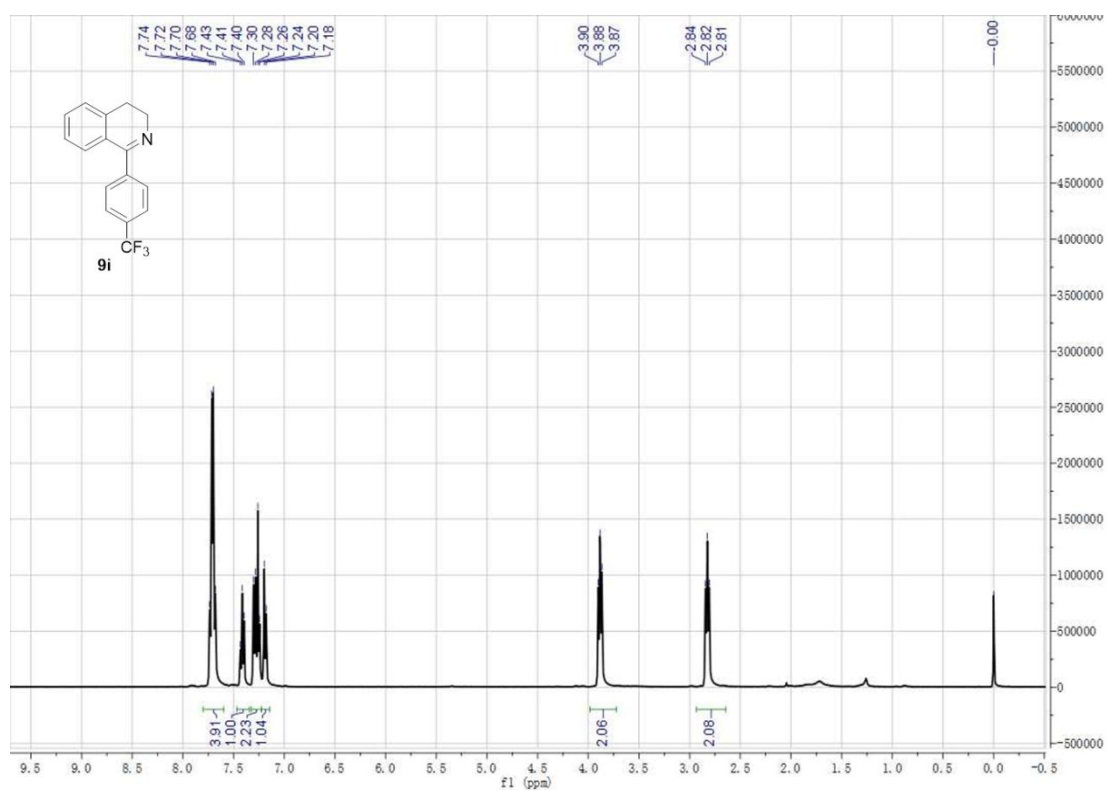
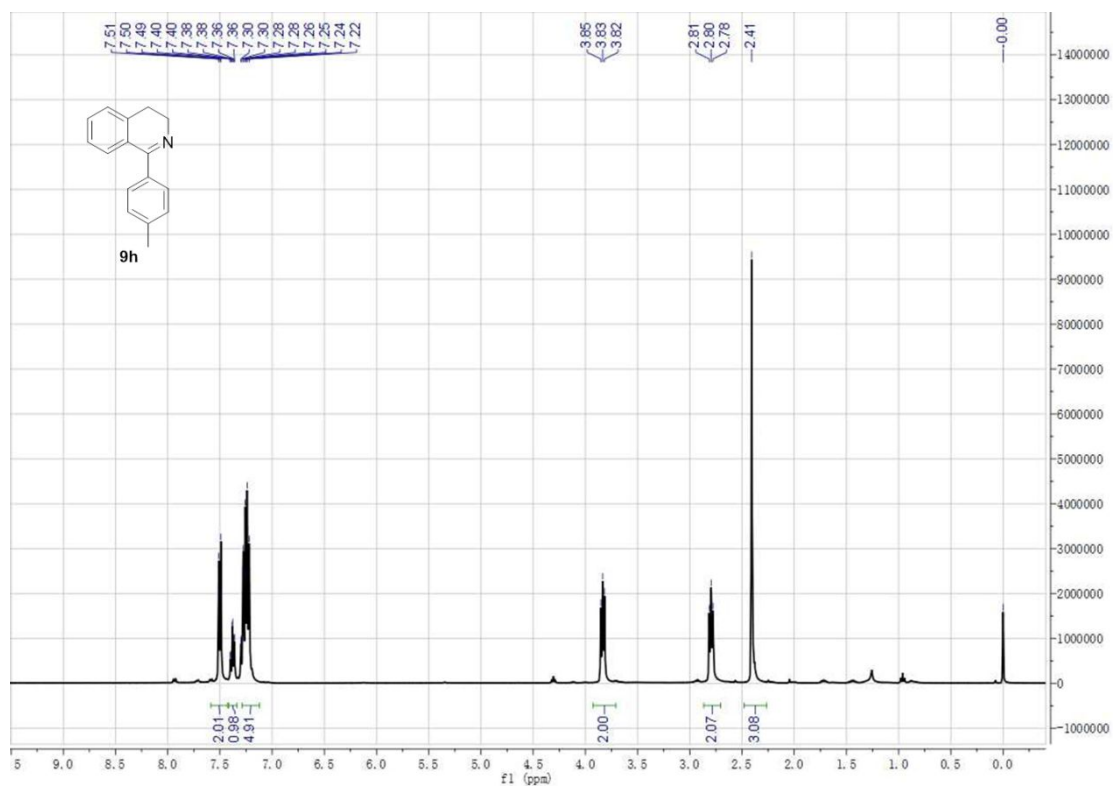


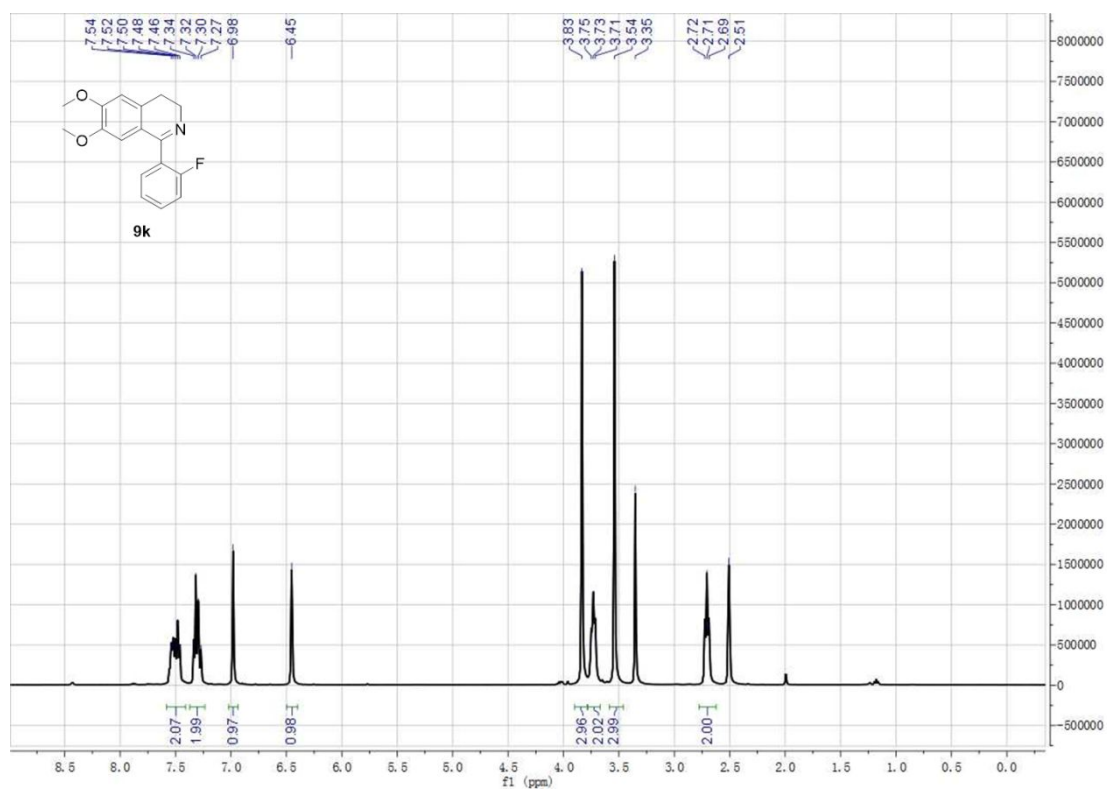
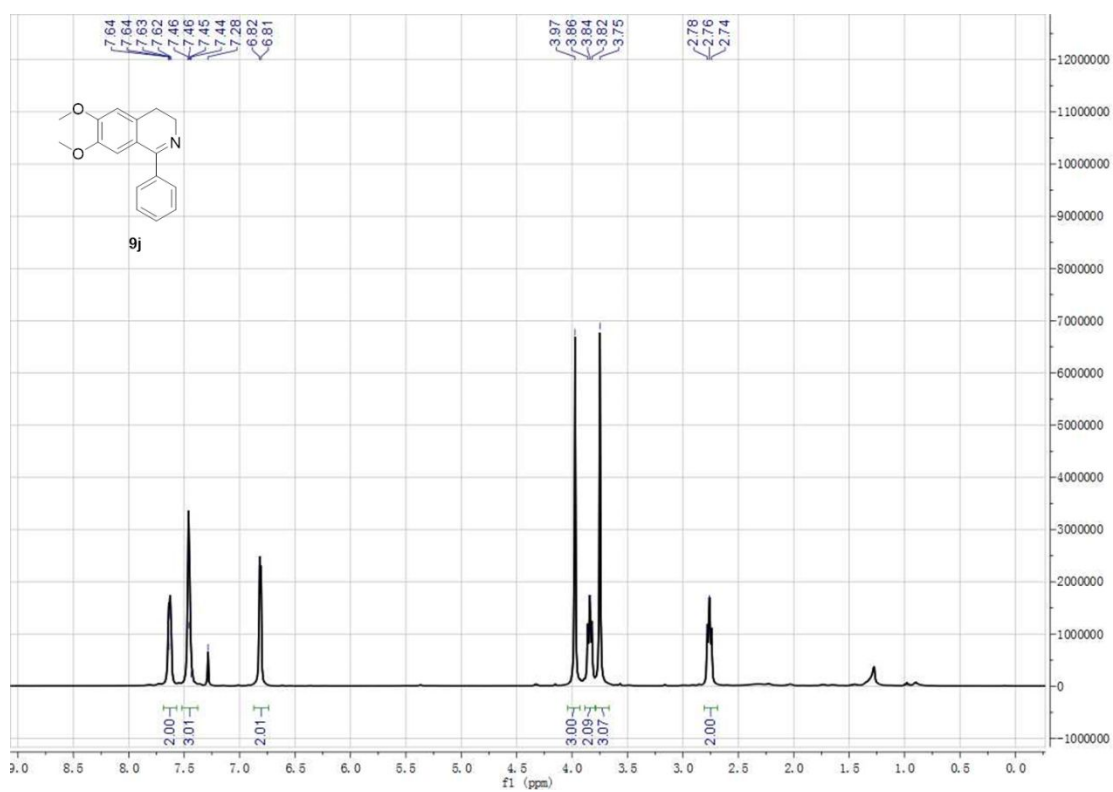
Sample Name	QTOF-PC/QTOF	Position	p2E8	Instrument Name	Instrument 1
User Name	Sample	Inj Vol	0.1	InjPosition	
Sample Type	20110418-MSonly-p.m	IRM Calibration Status	Success	Data Filename	G.p.d
ACQ Method		Comment		Acquired Time	4/3/2018 9:58:09 AM

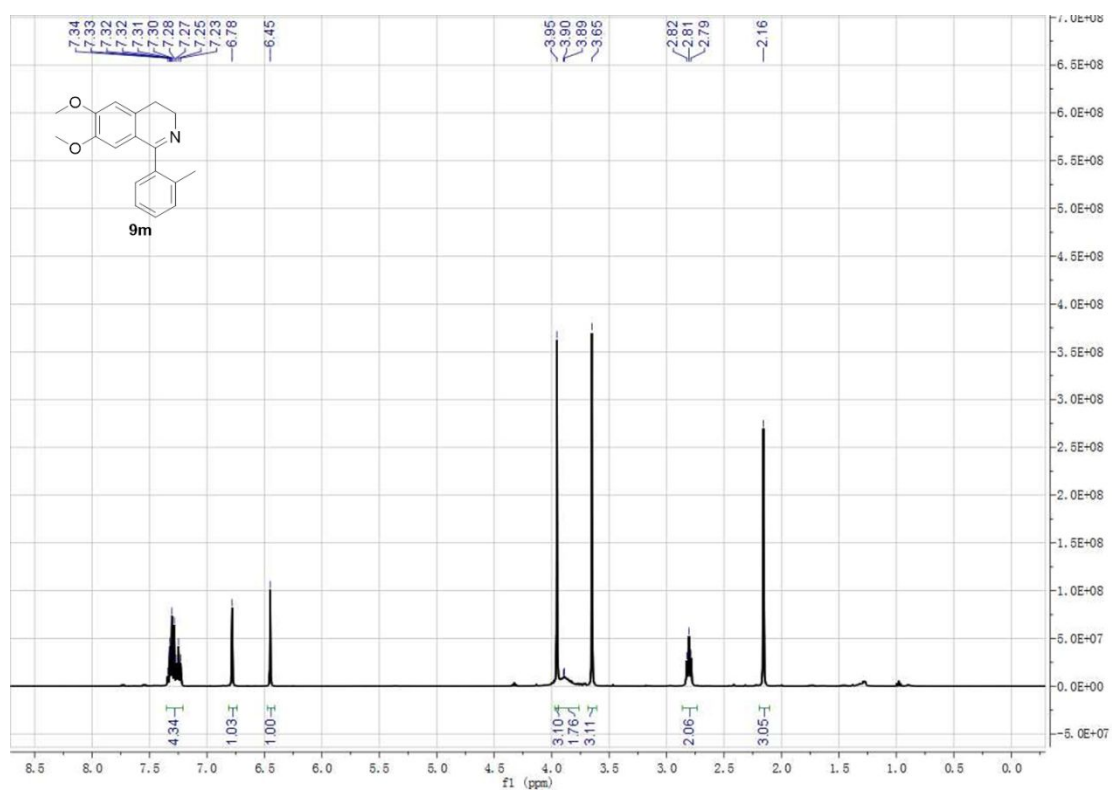
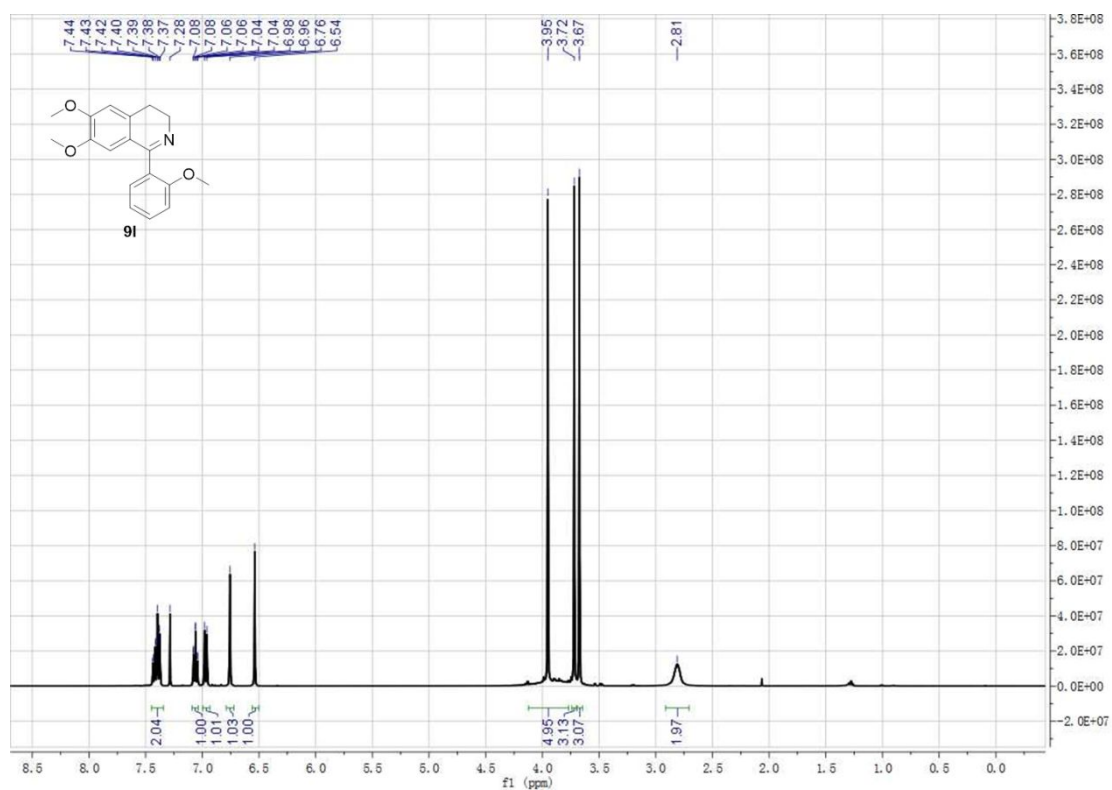


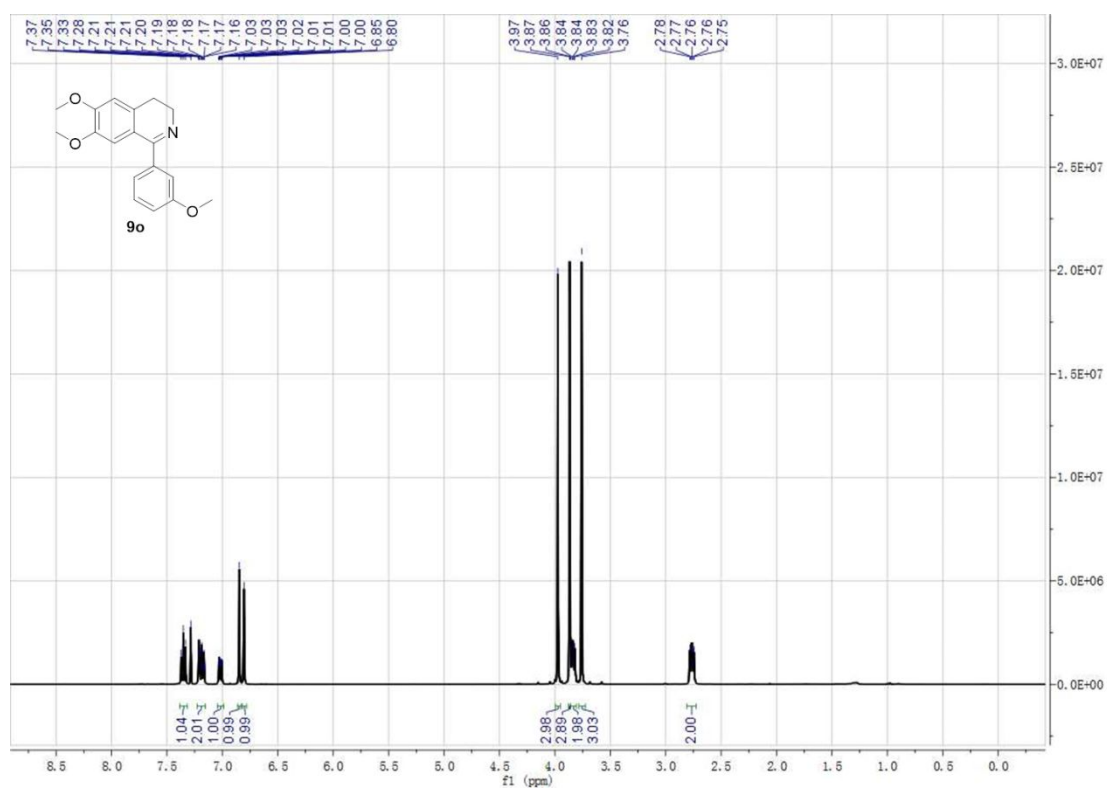
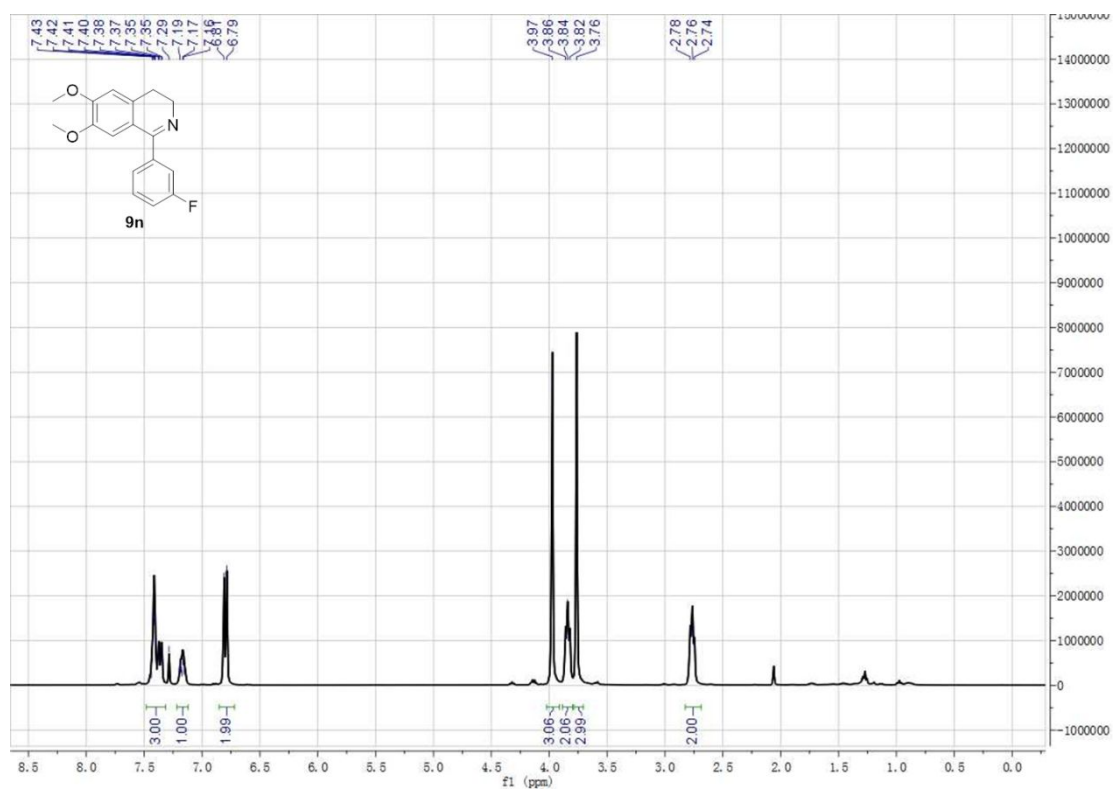


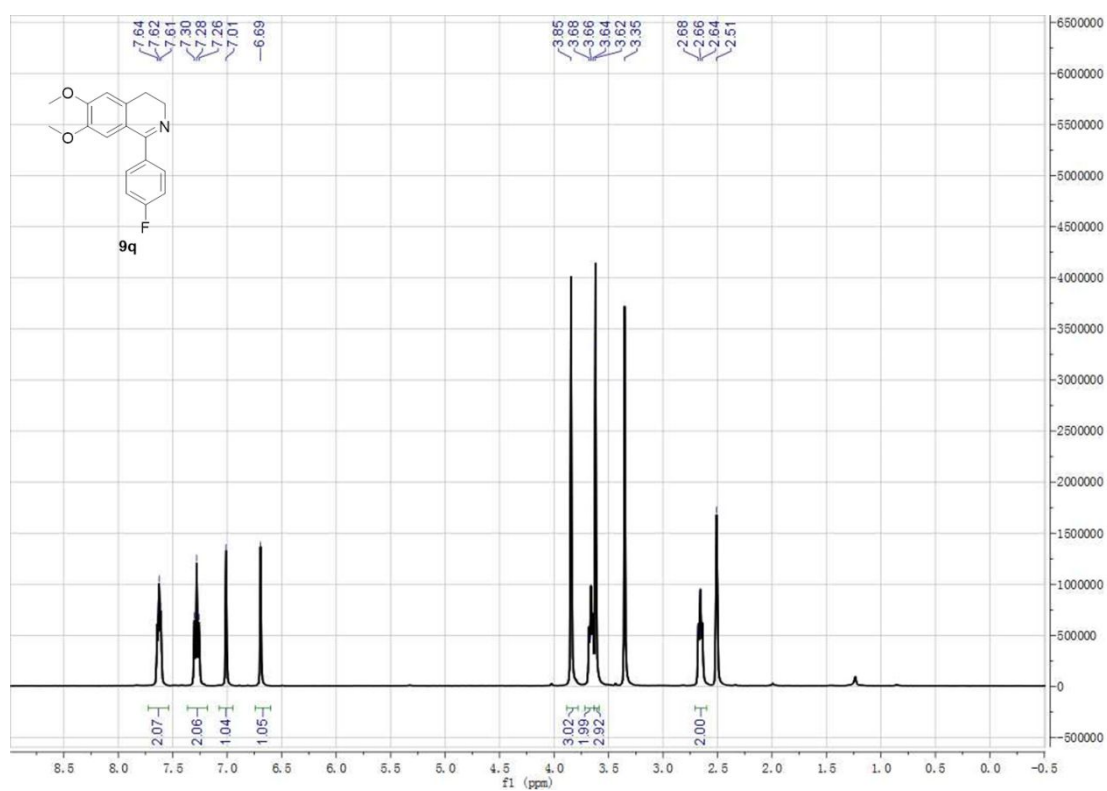
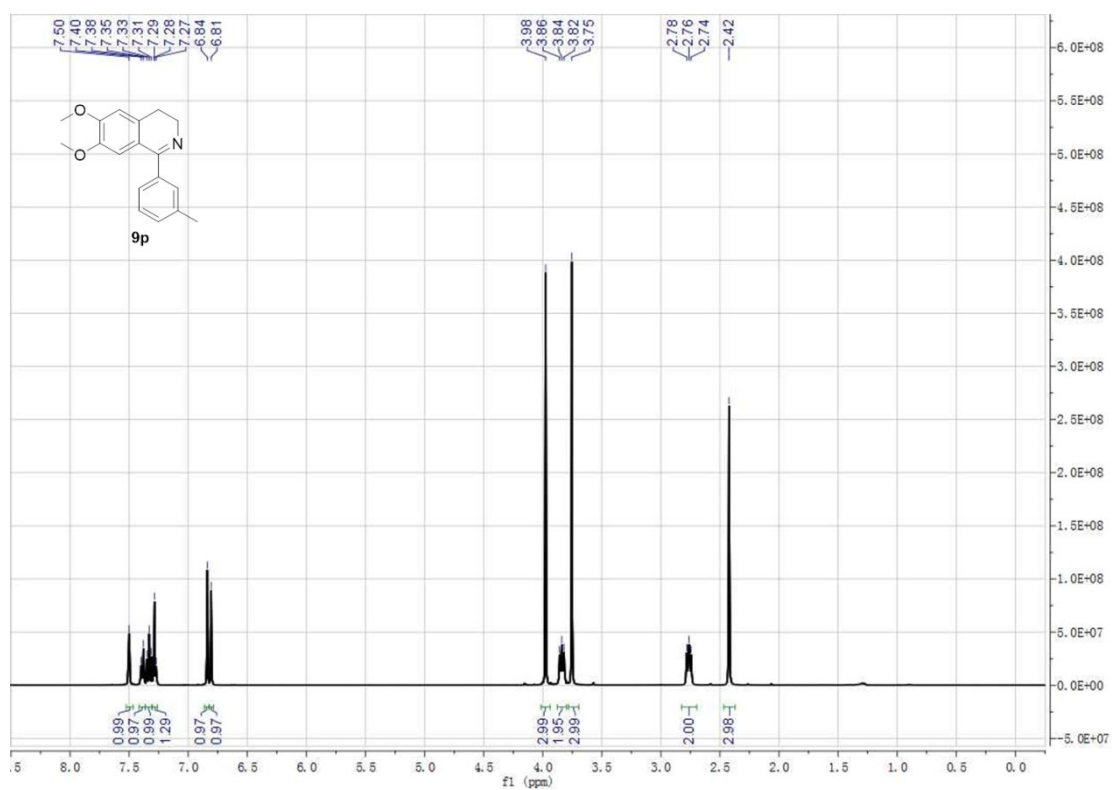


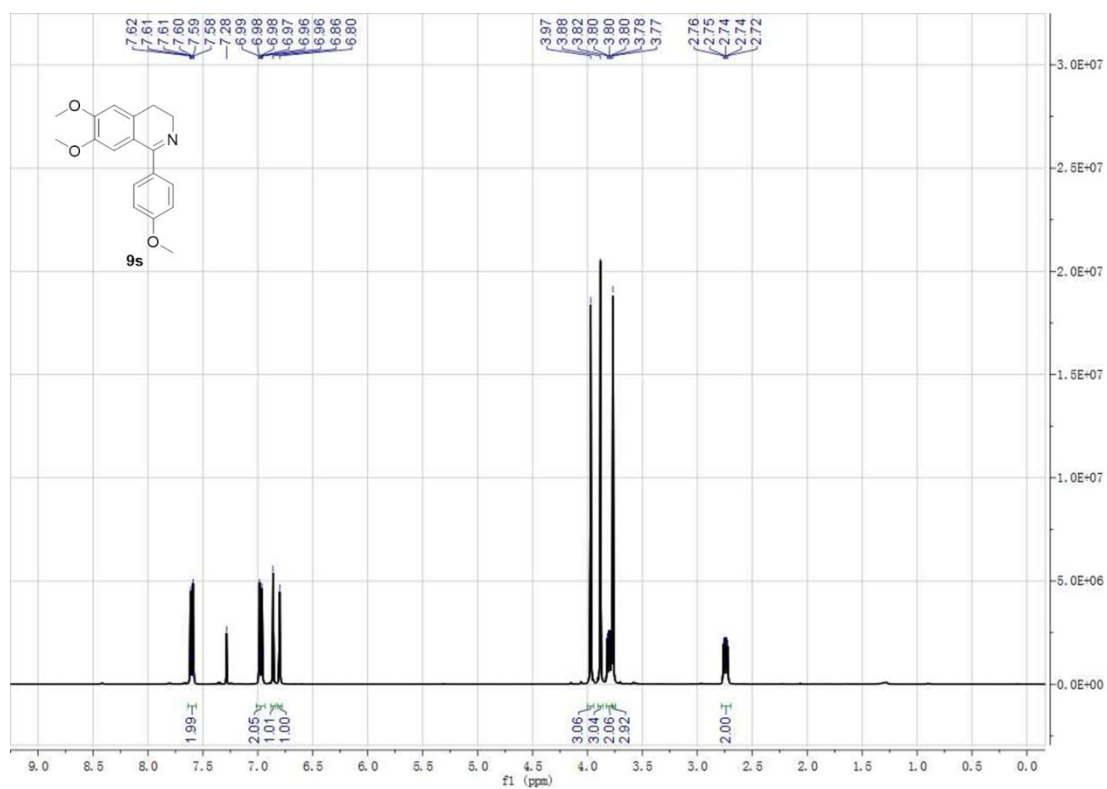
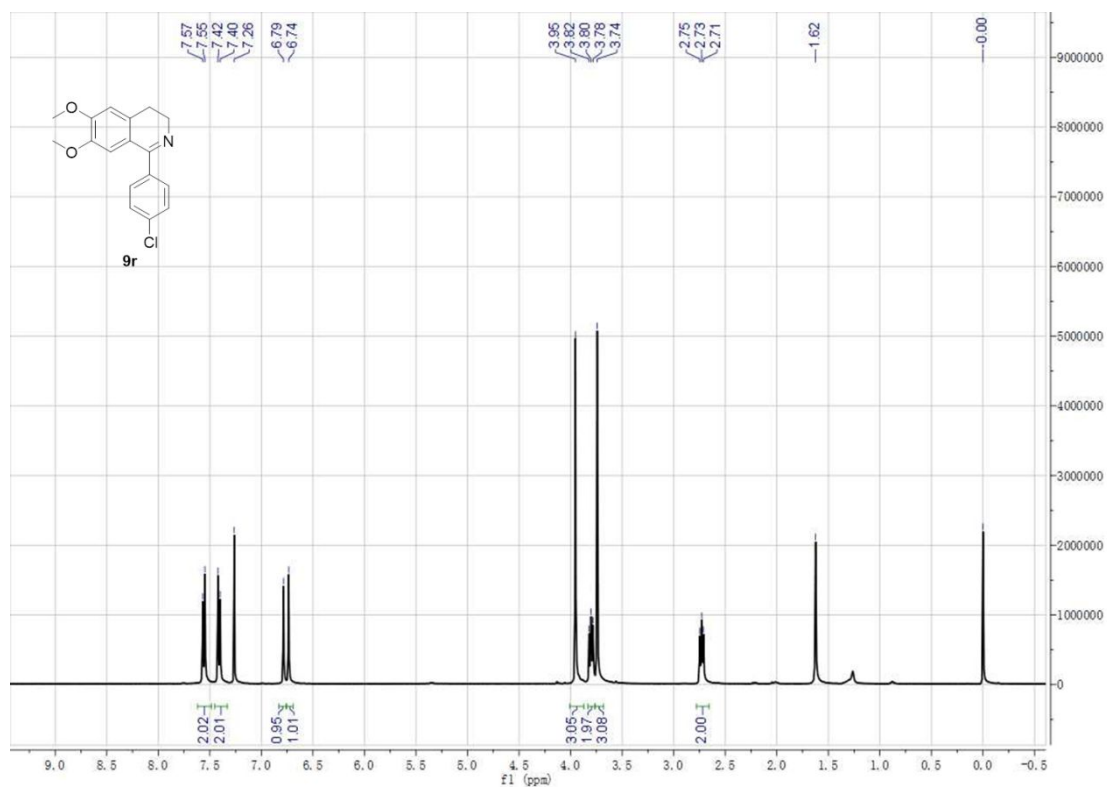


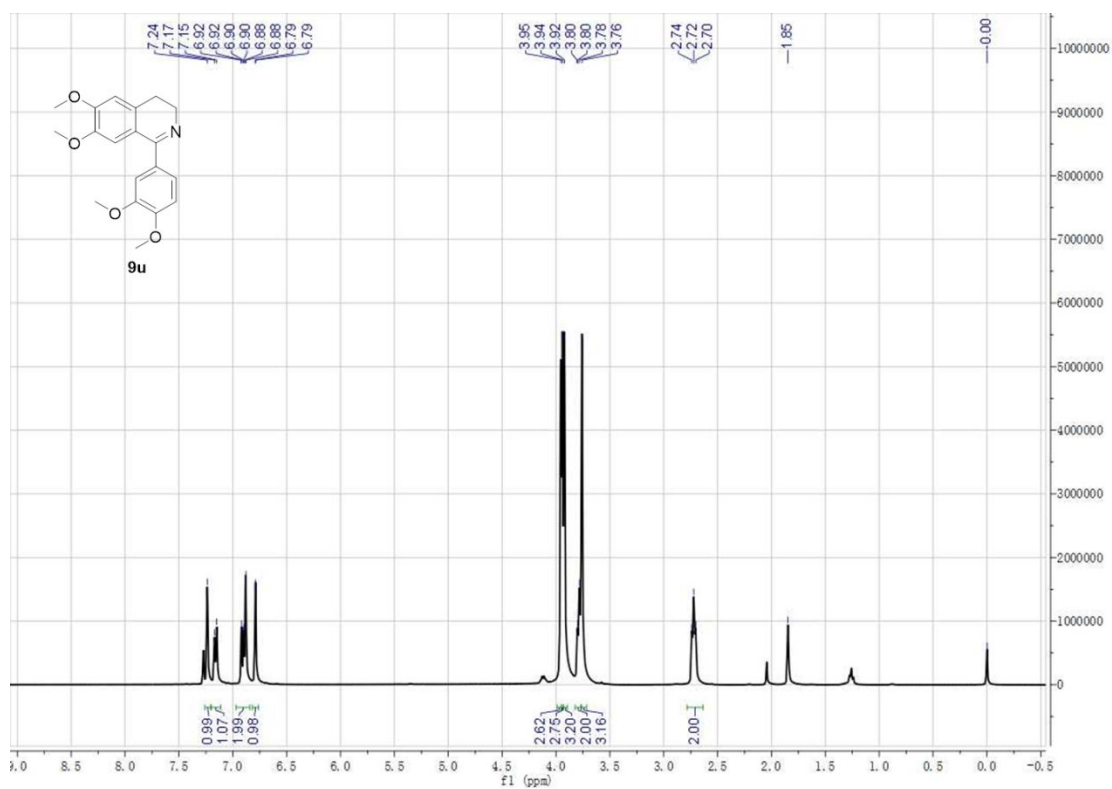
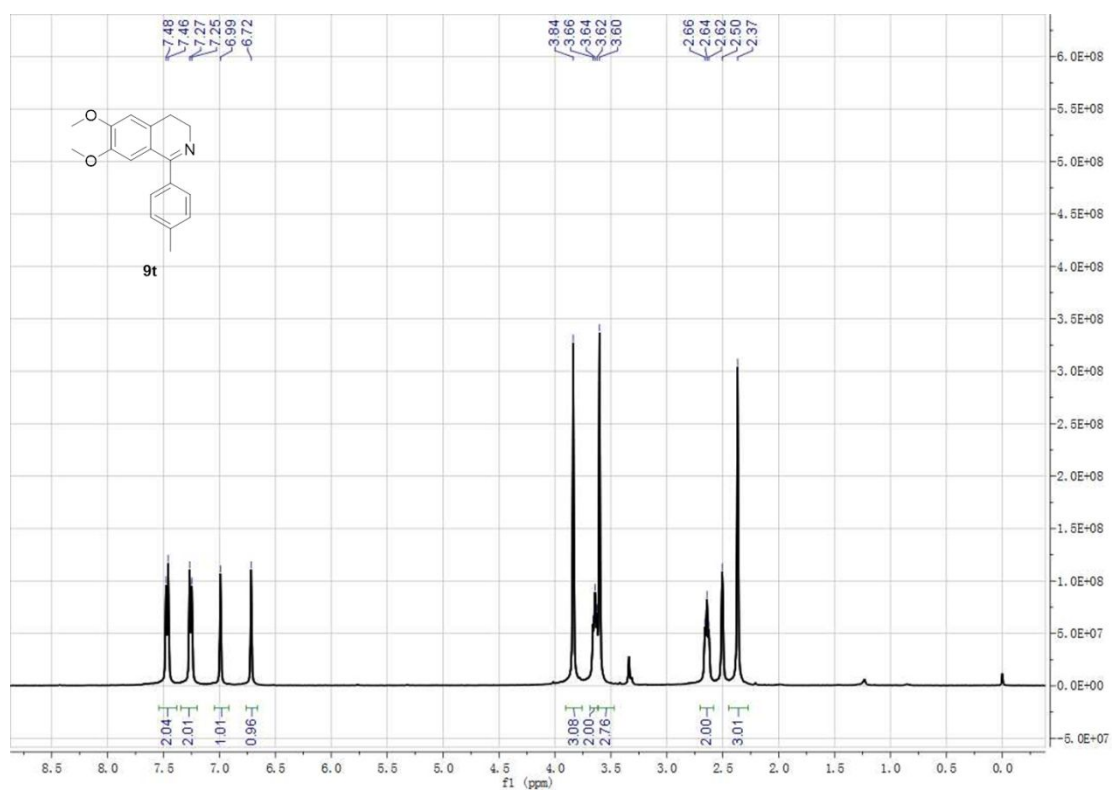


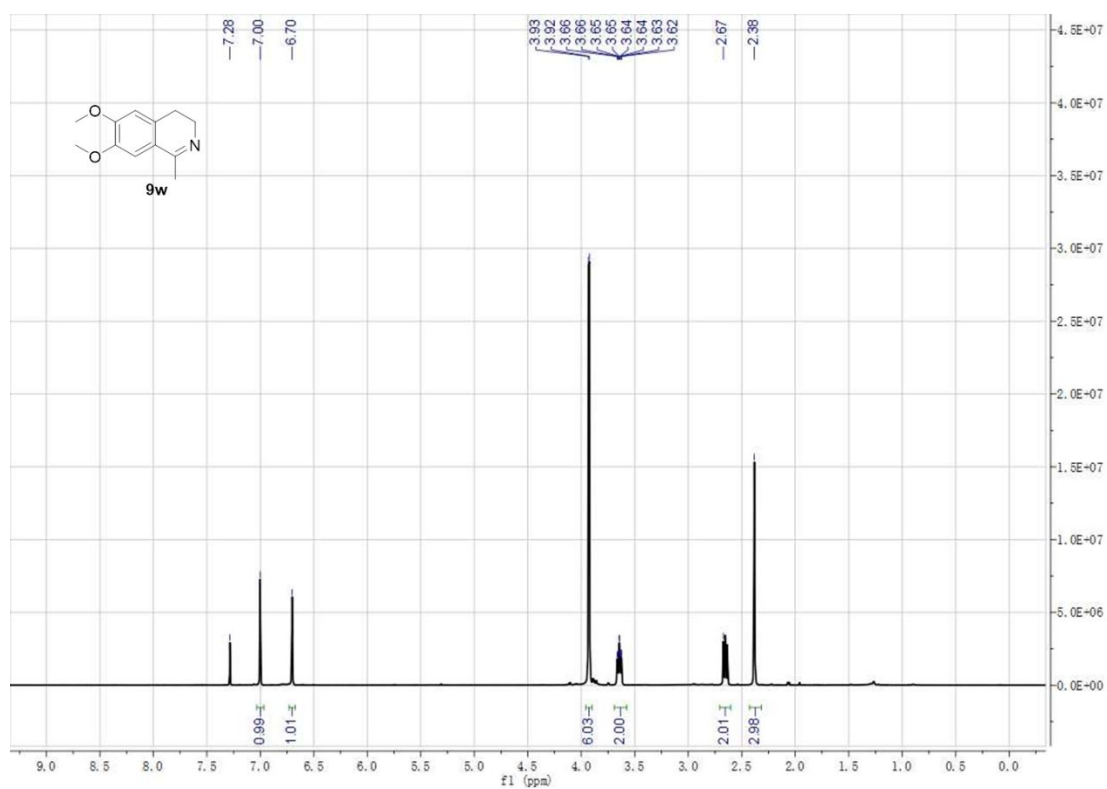
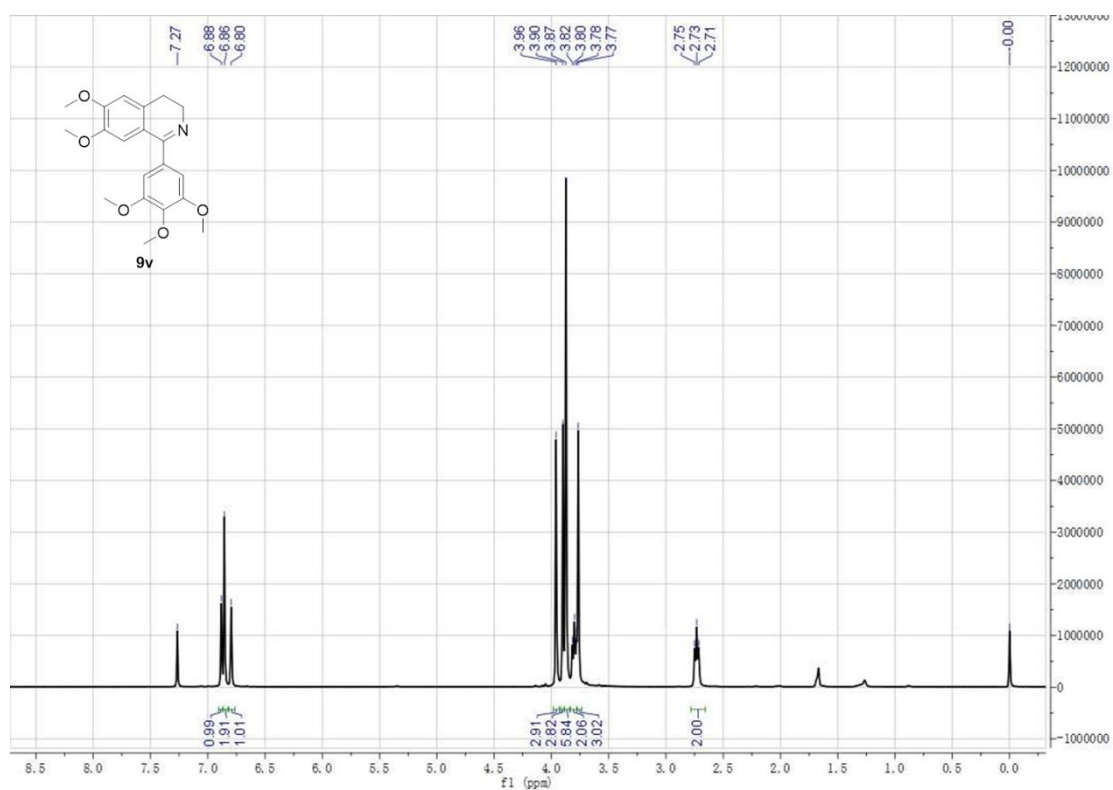


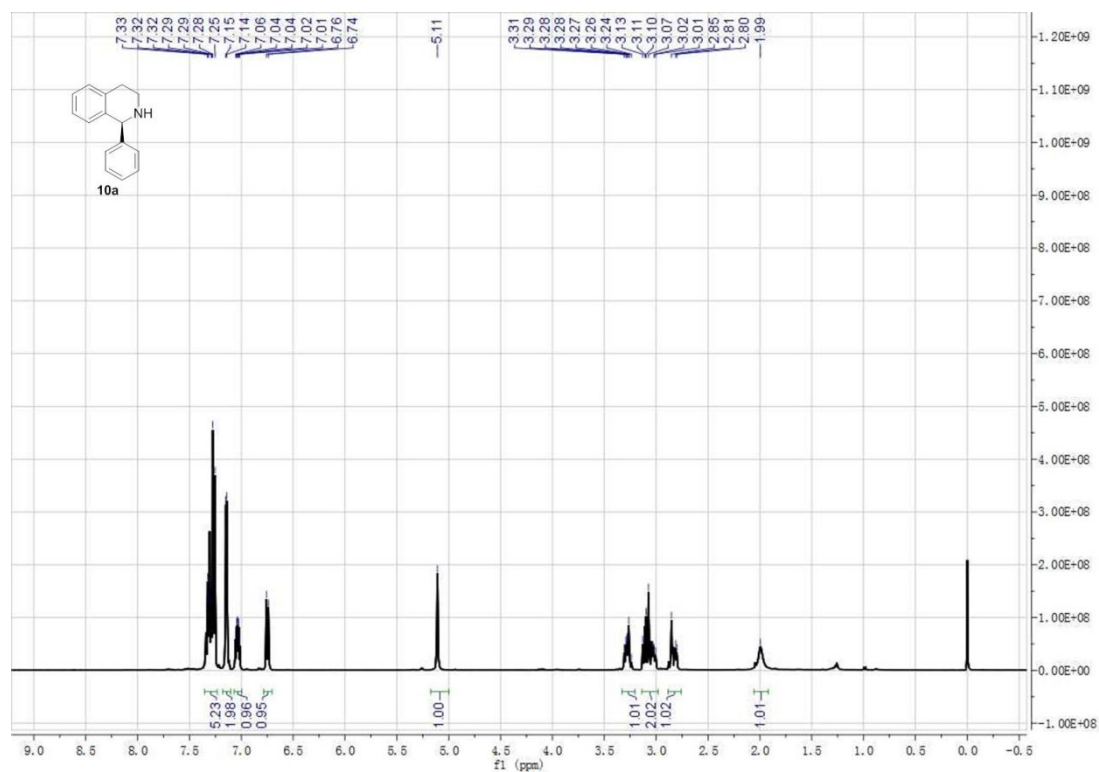
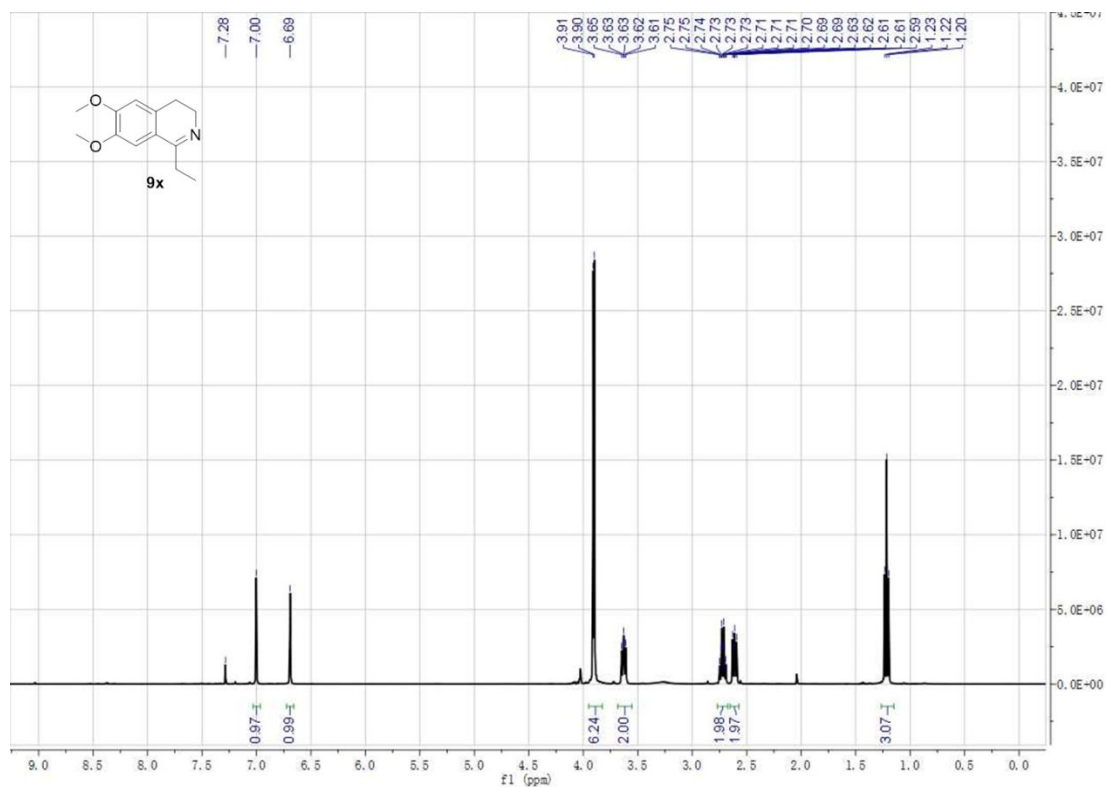


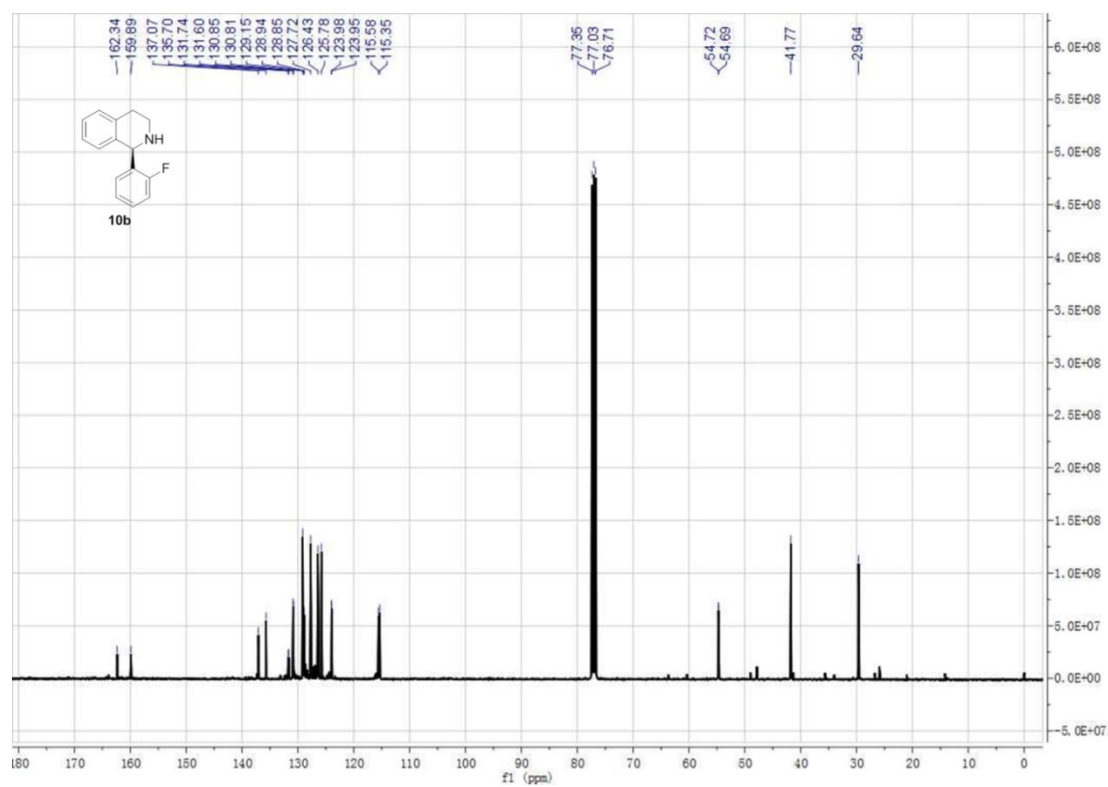
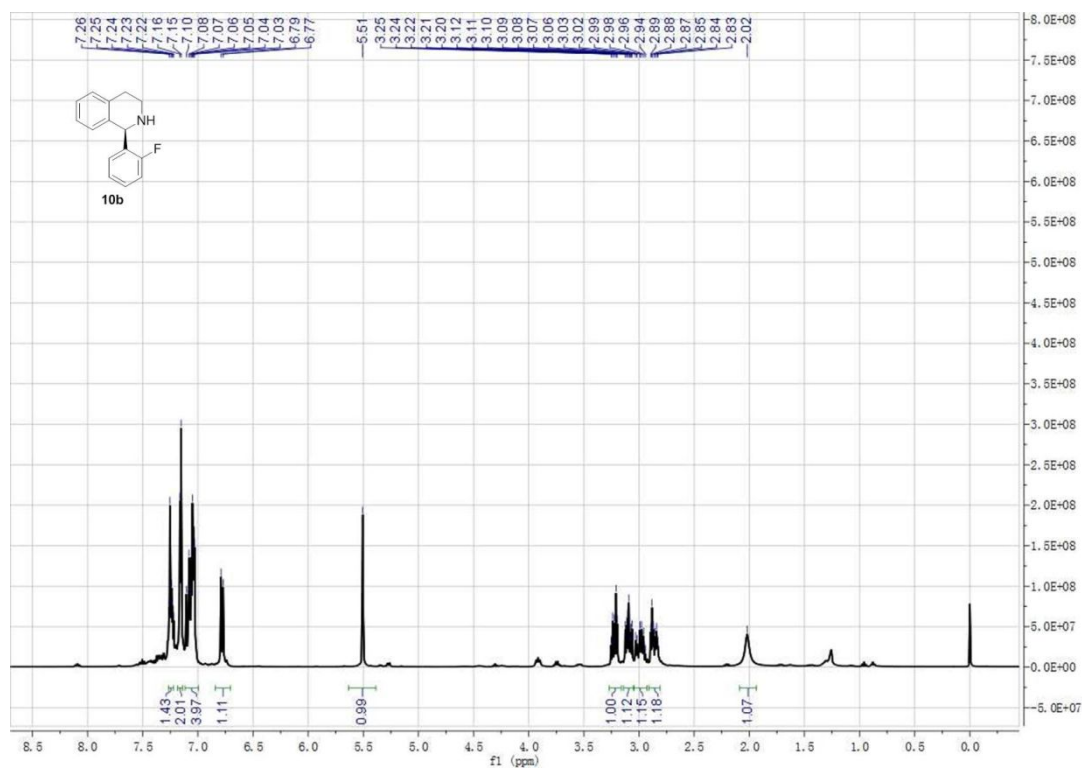




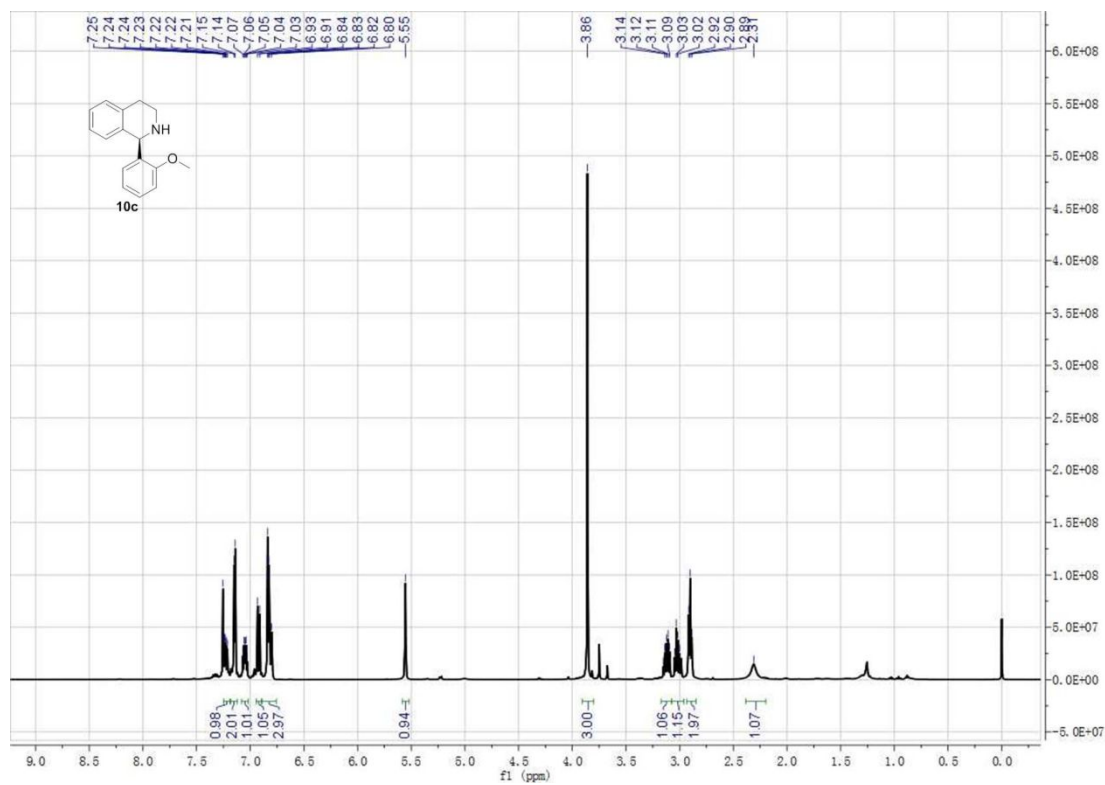
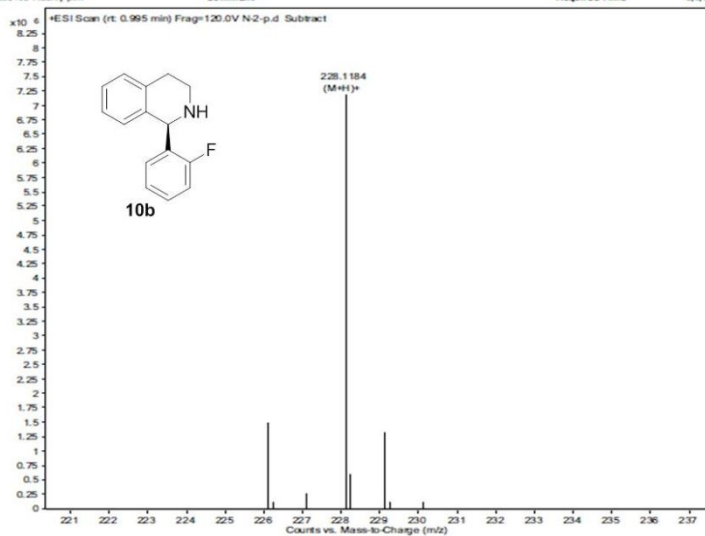


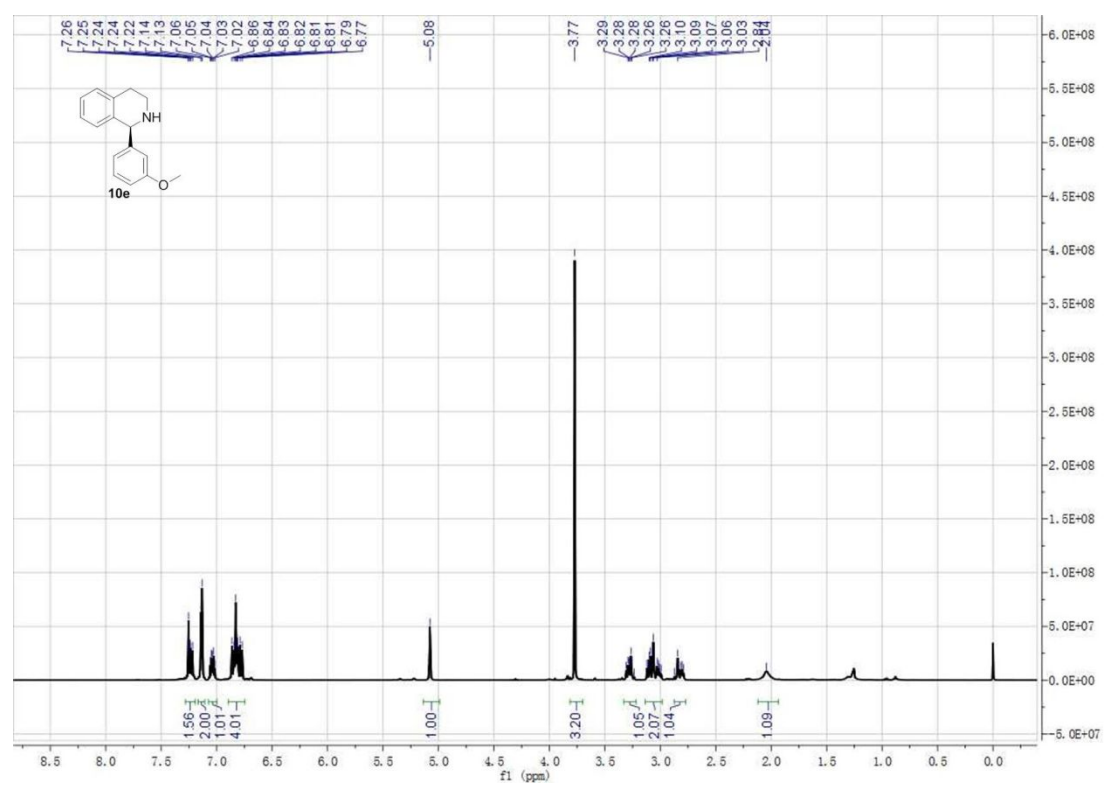
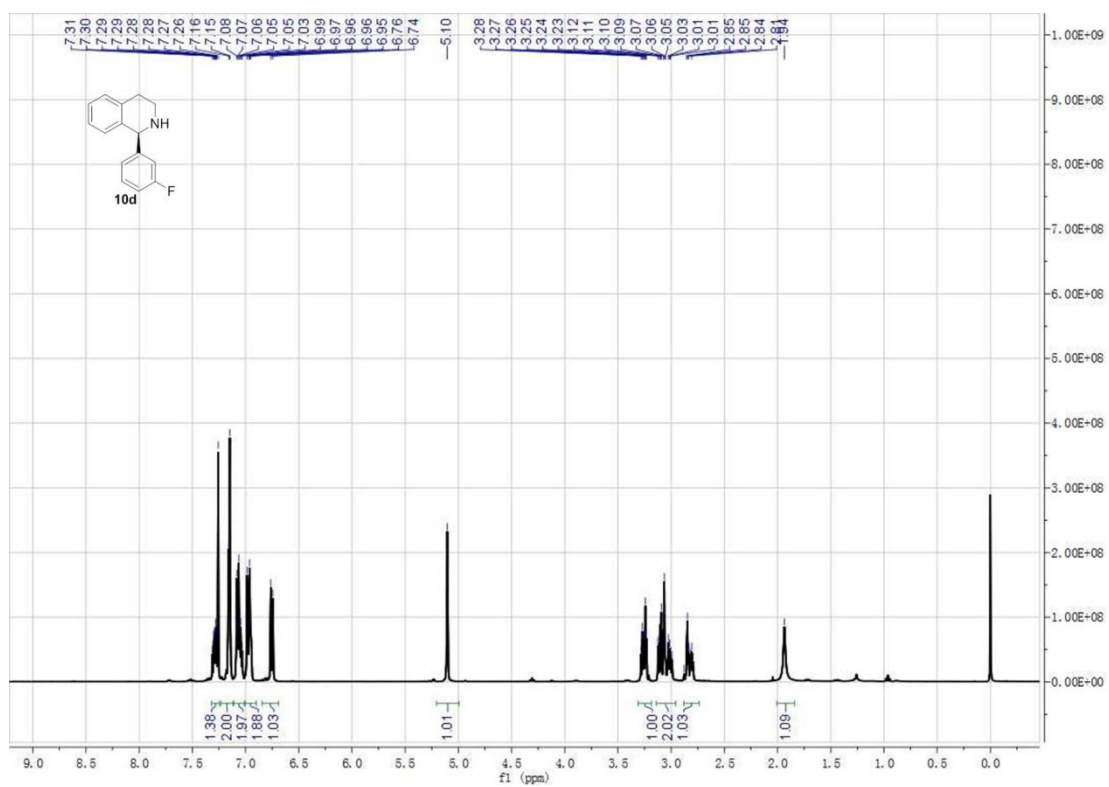


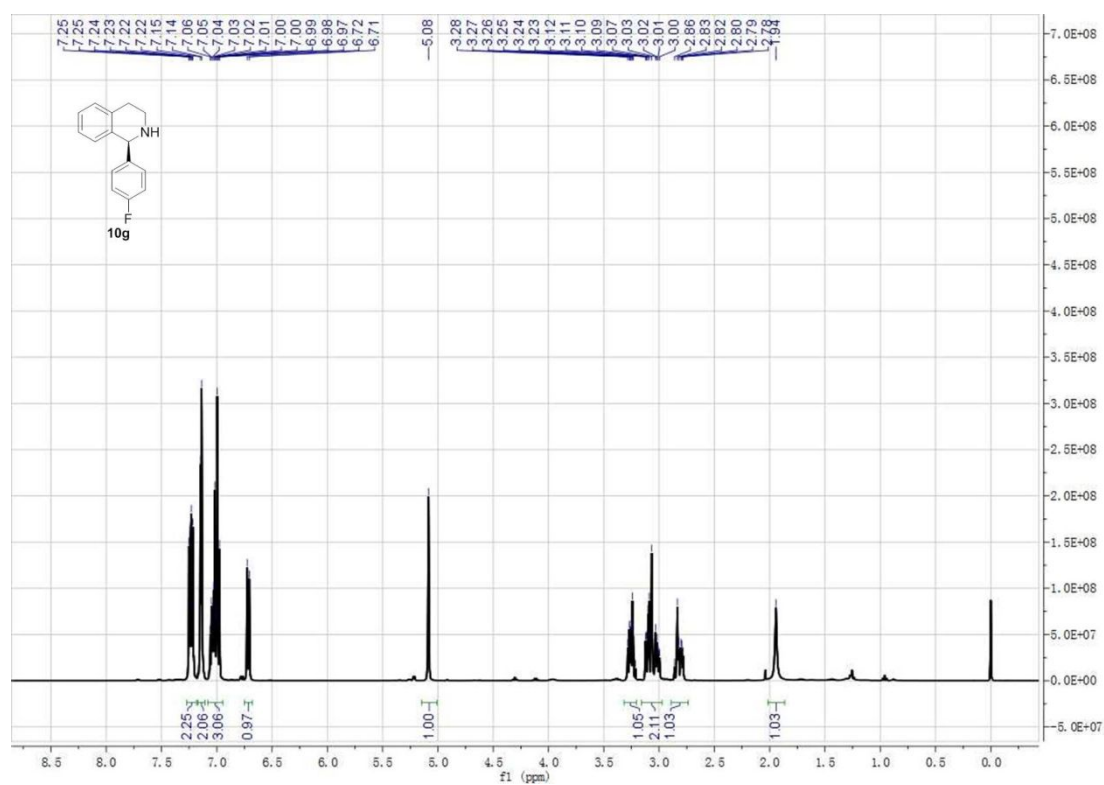
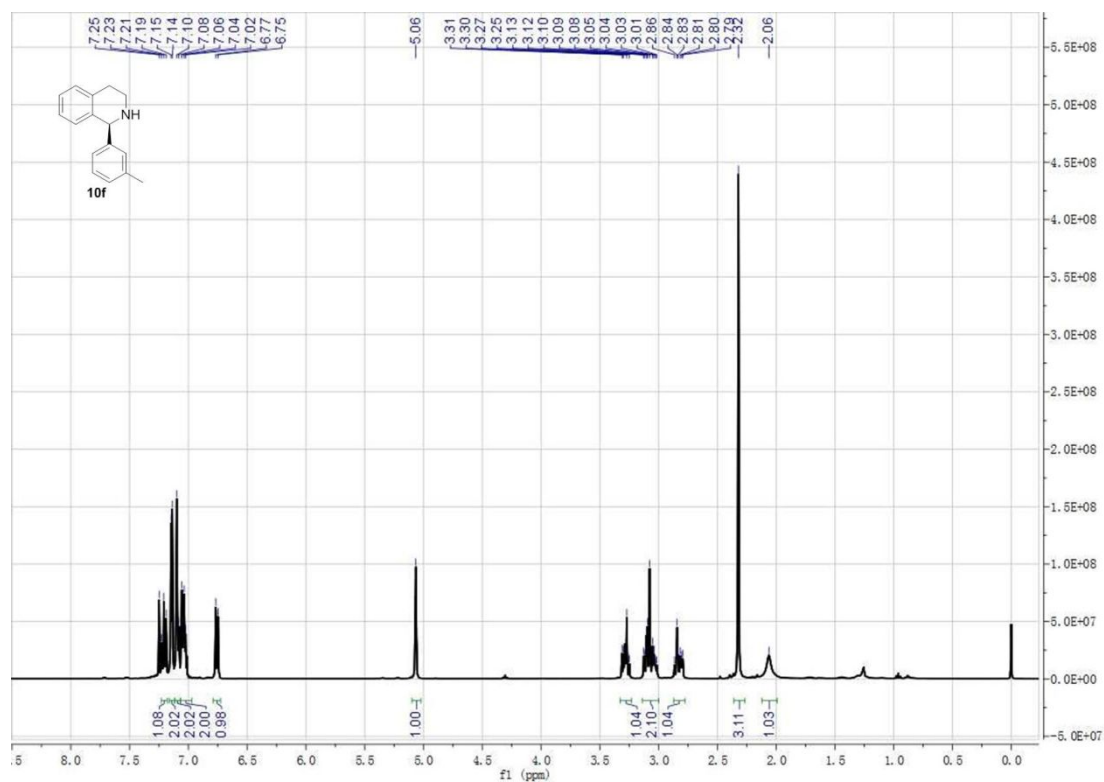


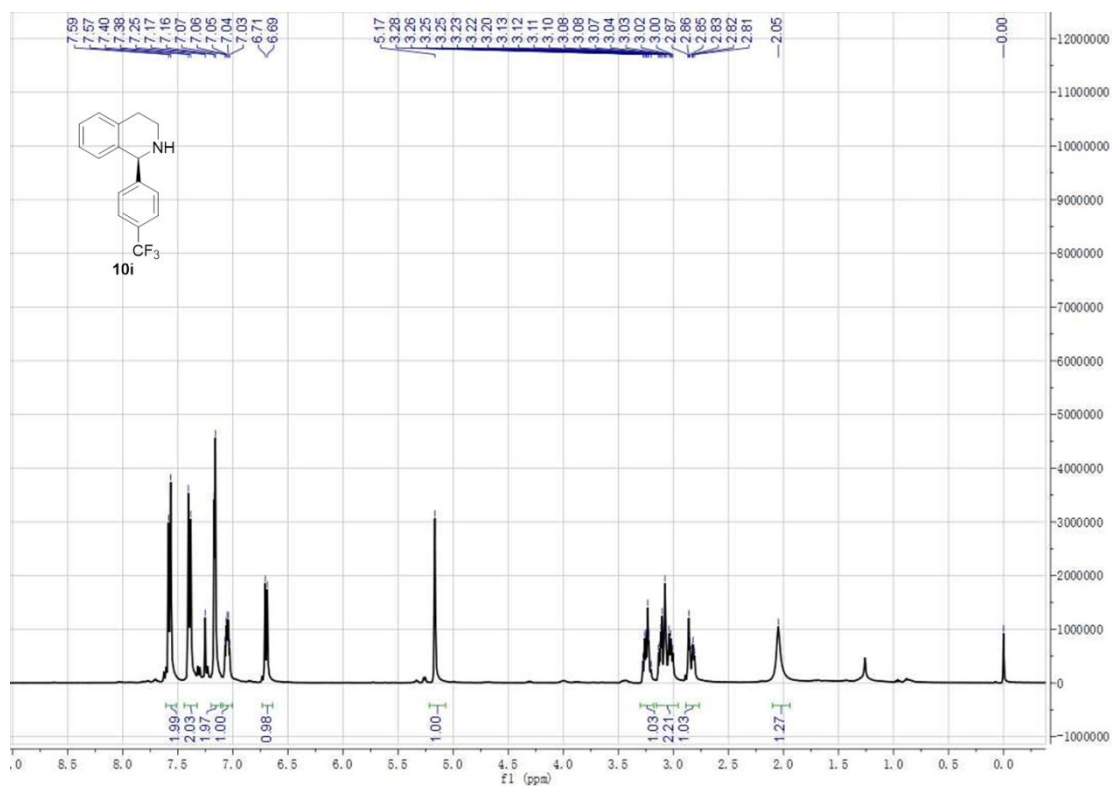
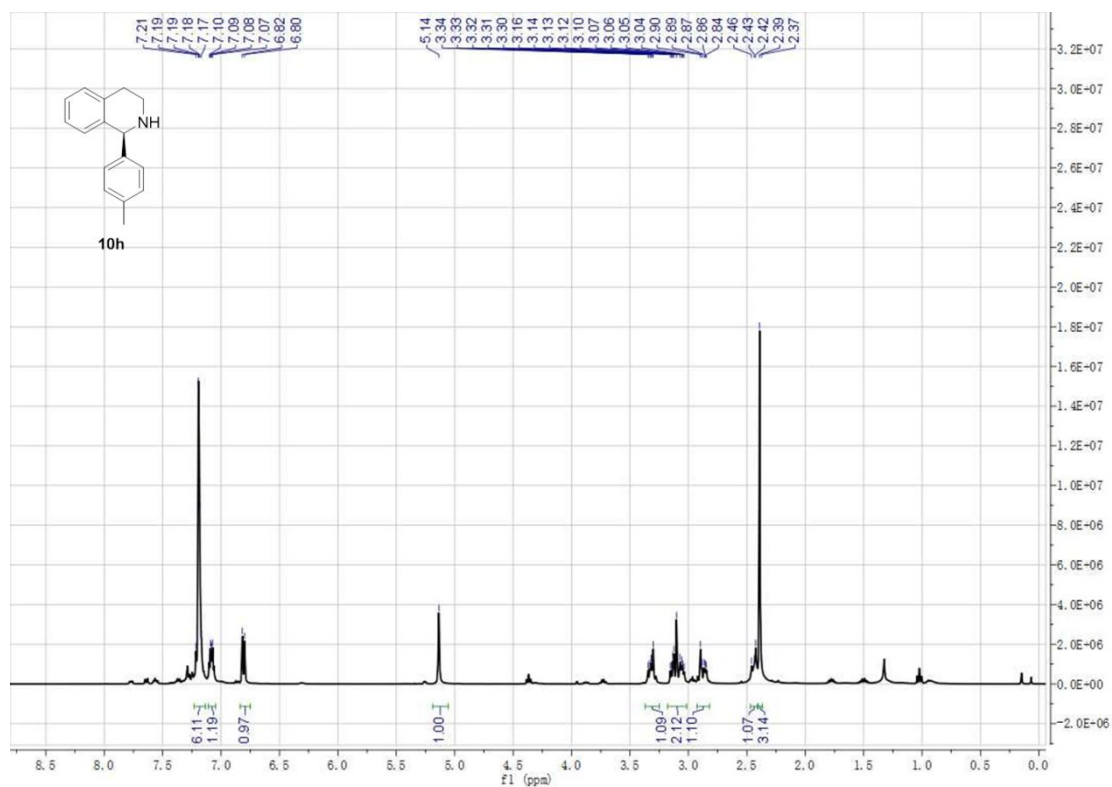


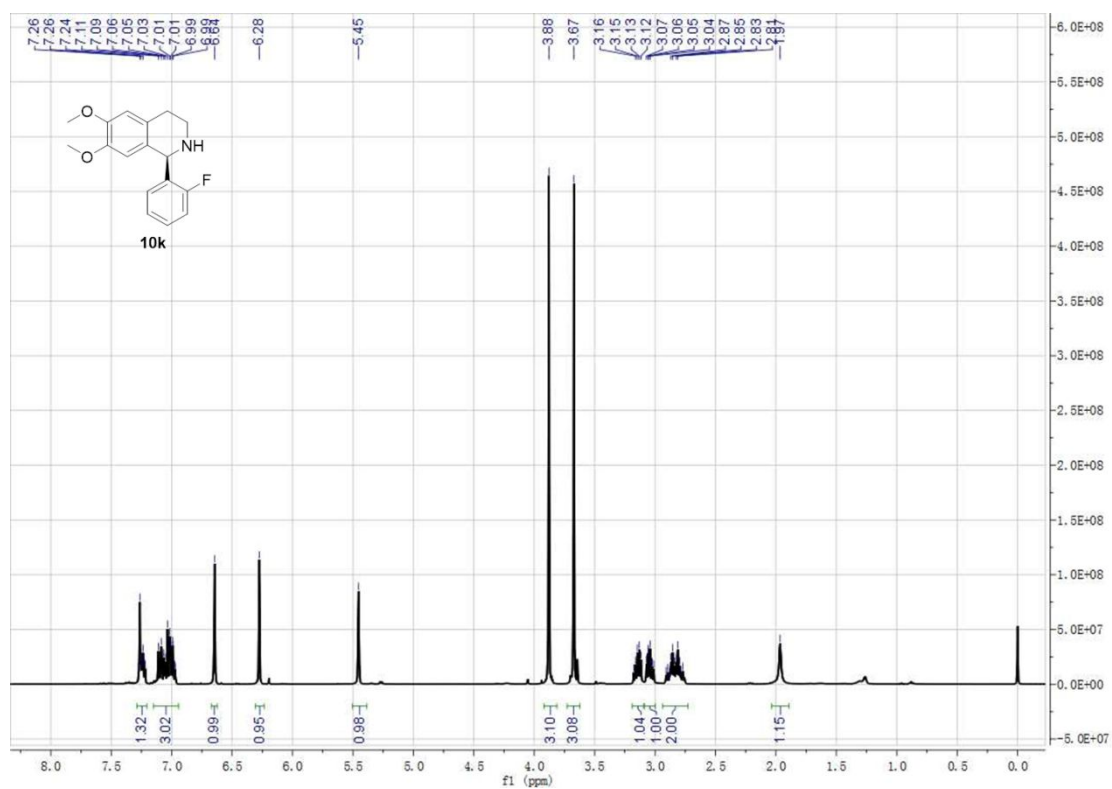
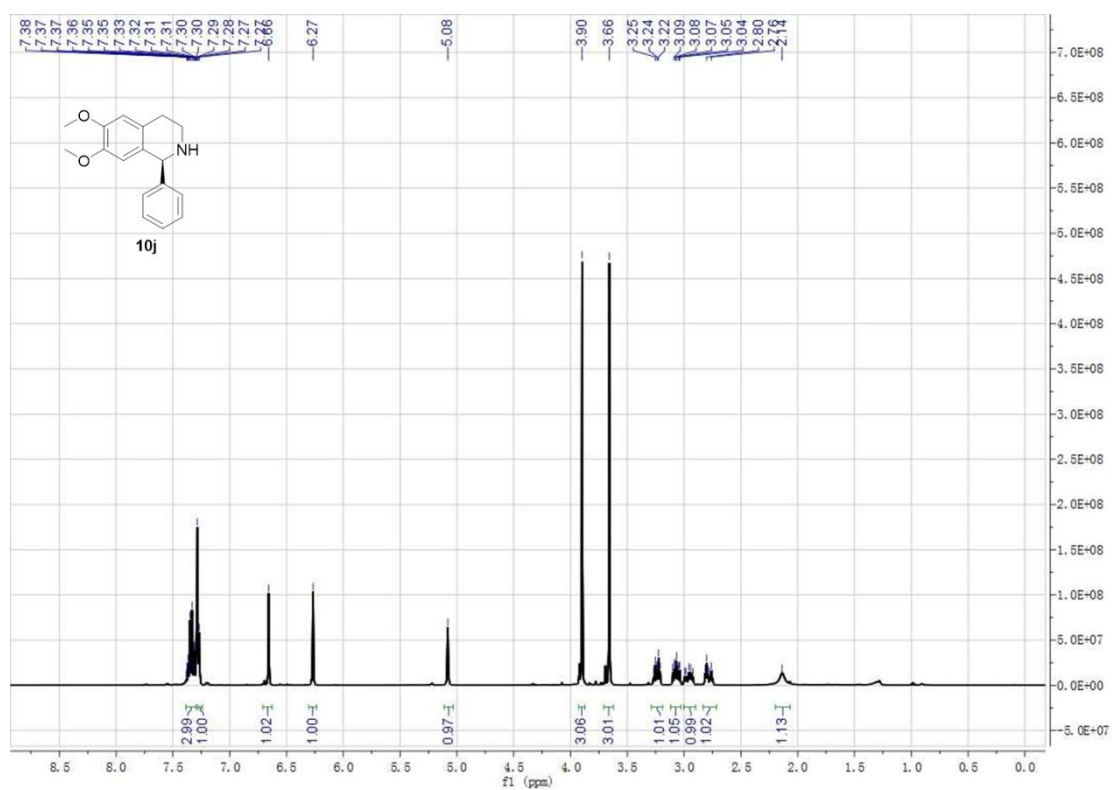
Sample Name	QT01-PC1/QT01	Position	p206	Instrument Name	Instrument 1
User Name		Inj Vol	1	Inj Position	
Sample Type	20110418-N2-p.d	IRH Calibration Status	Success	Data Filename	N2-p.d
ACQ Method	20110418-N2-p.d	Comment		Acquired Time	3/1/2019 1:13:41 PM

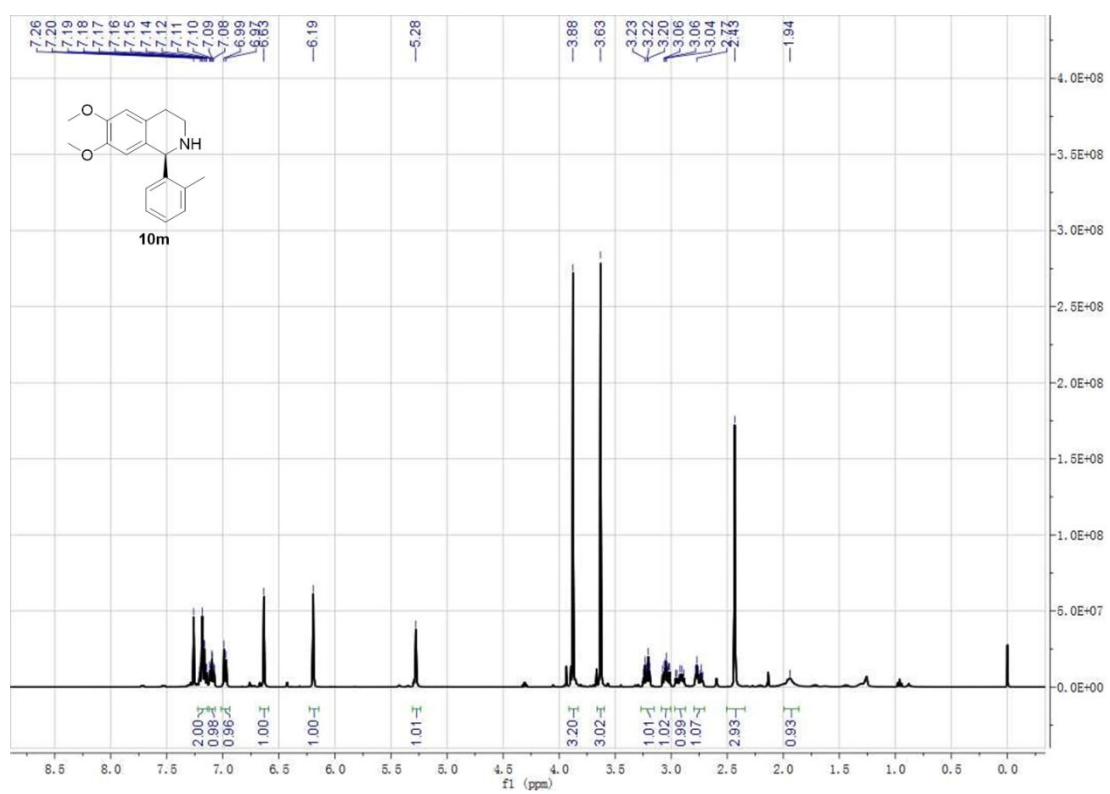
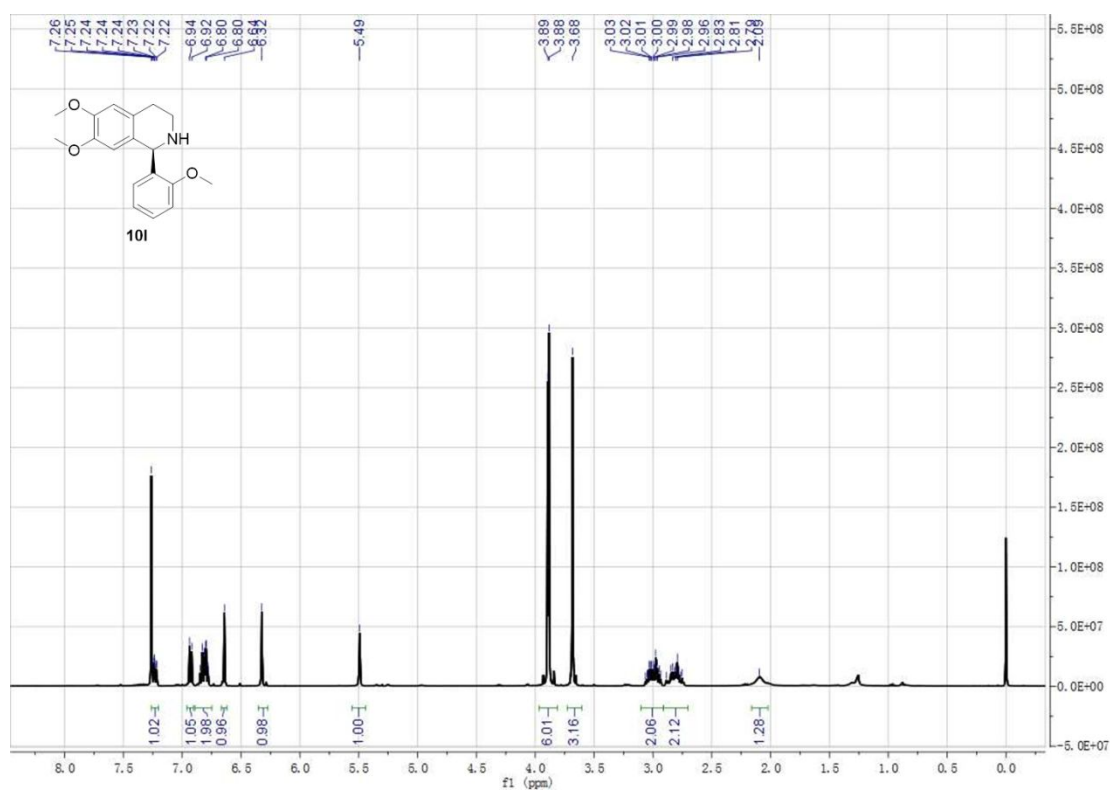


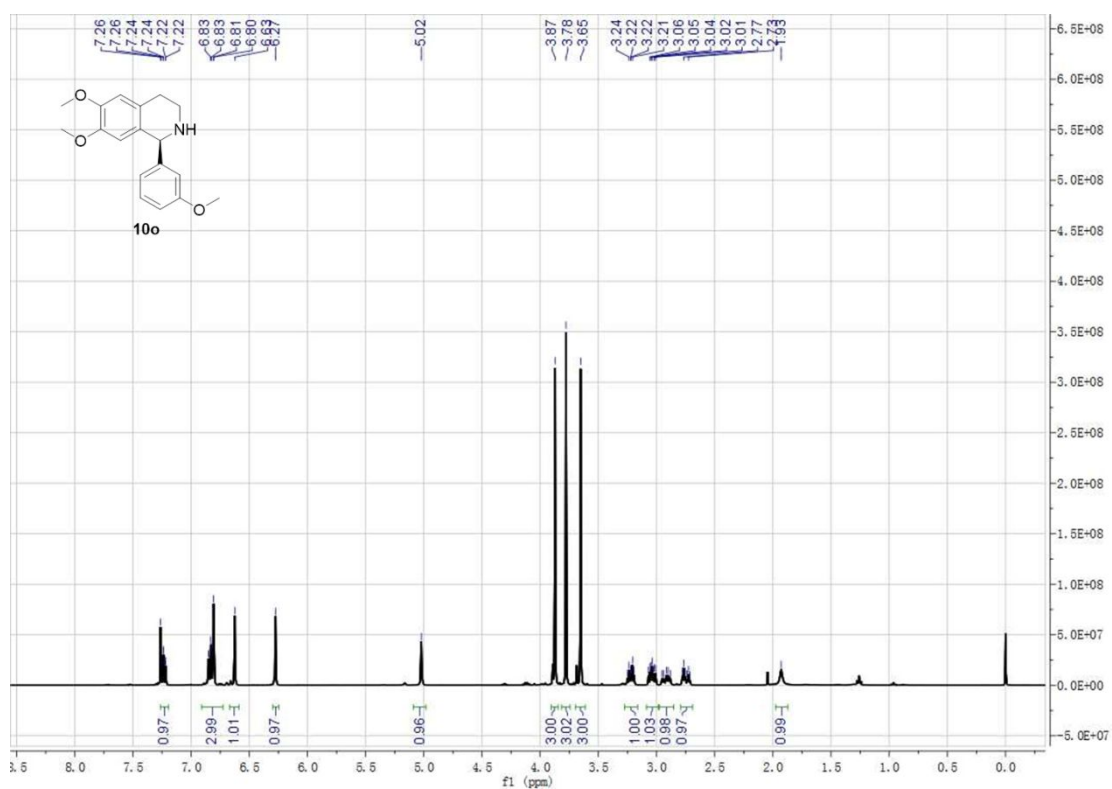
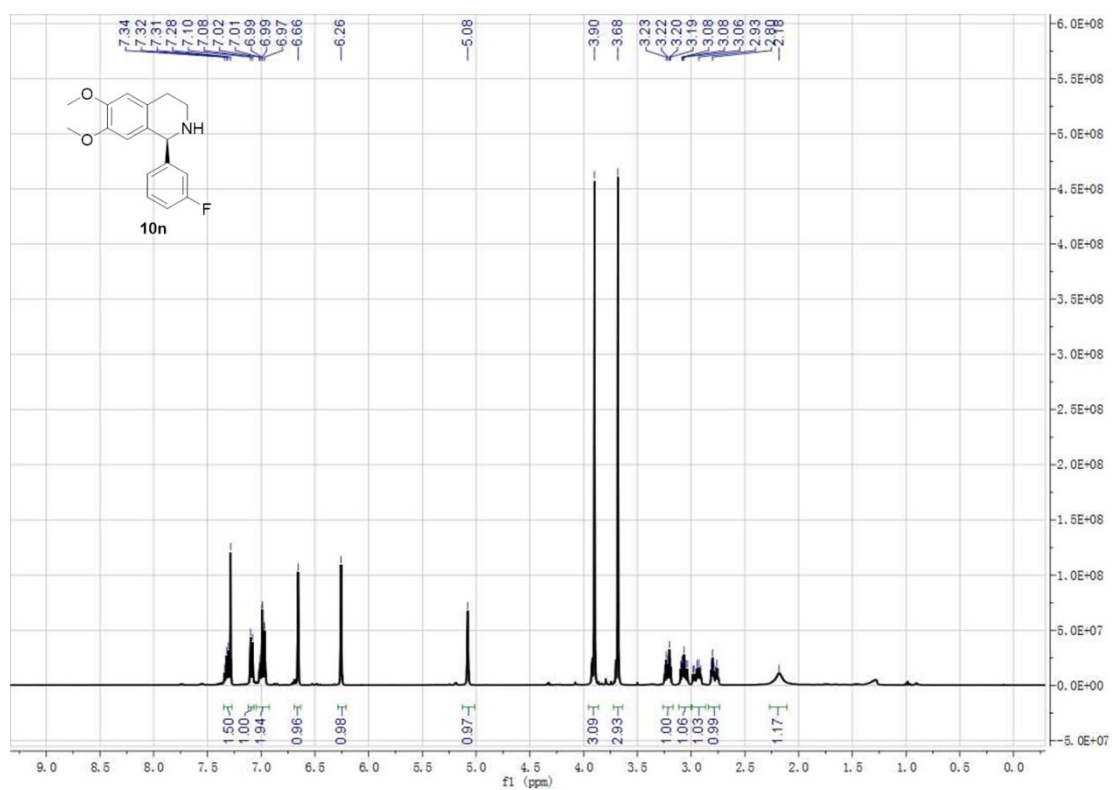


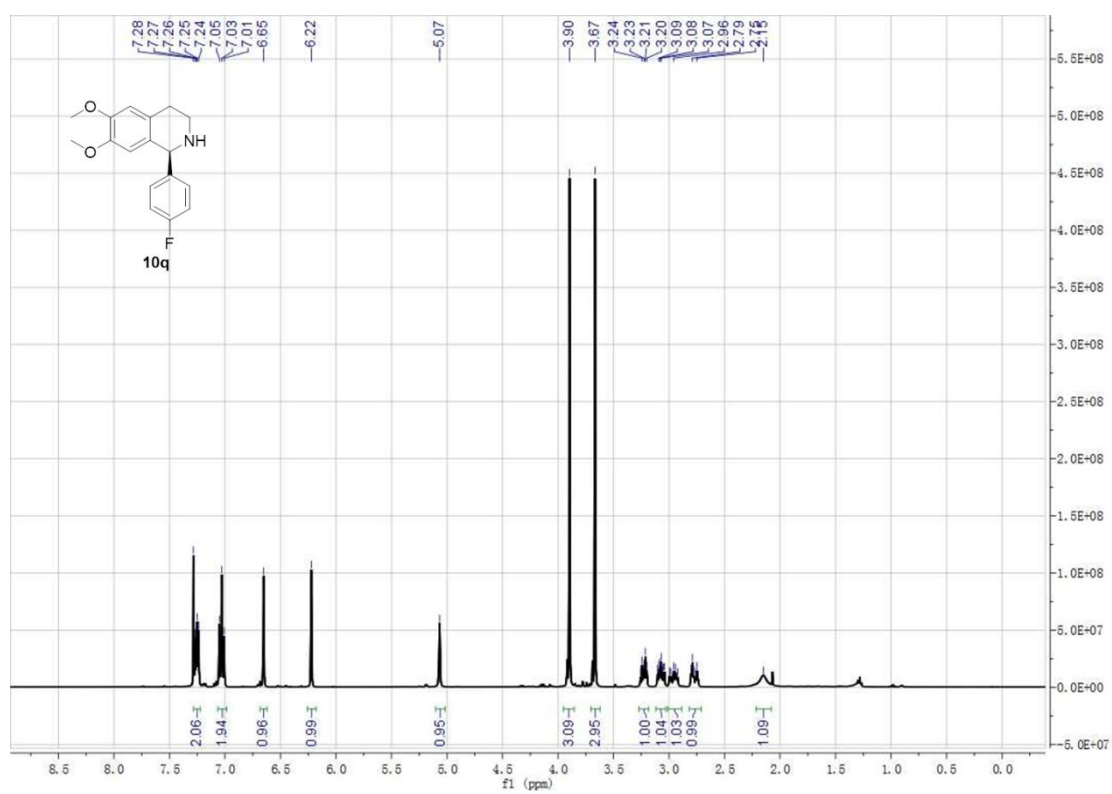
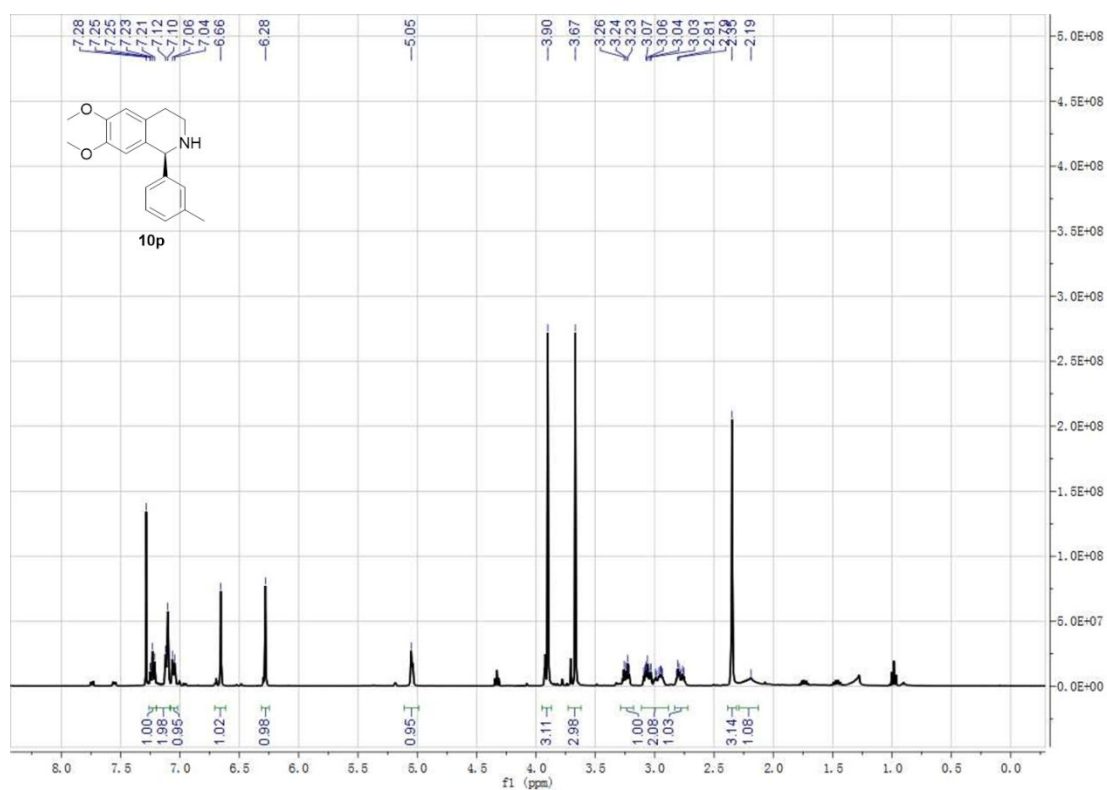


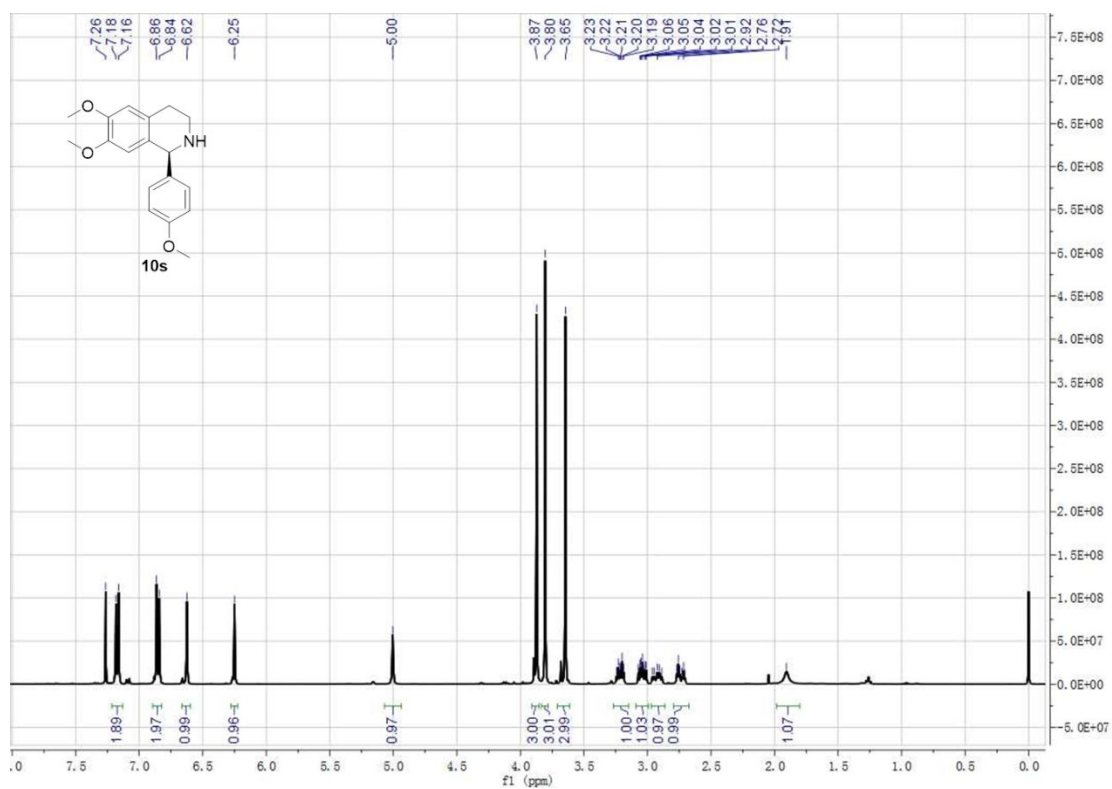
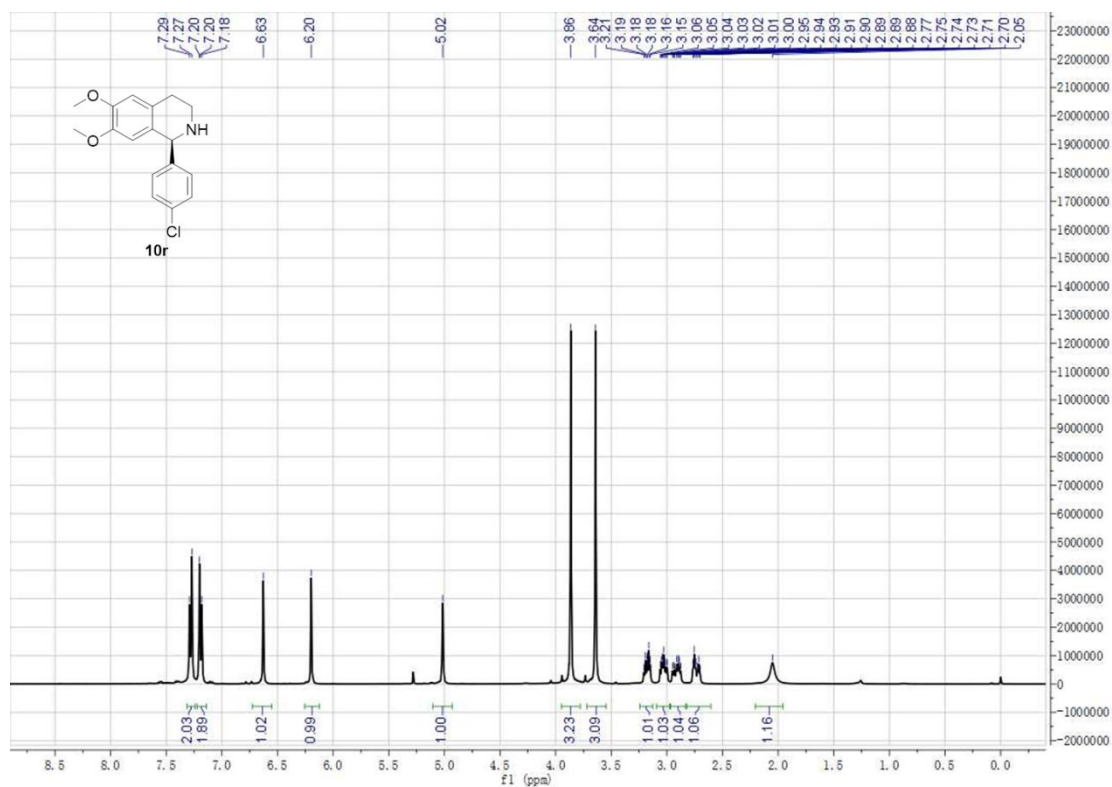


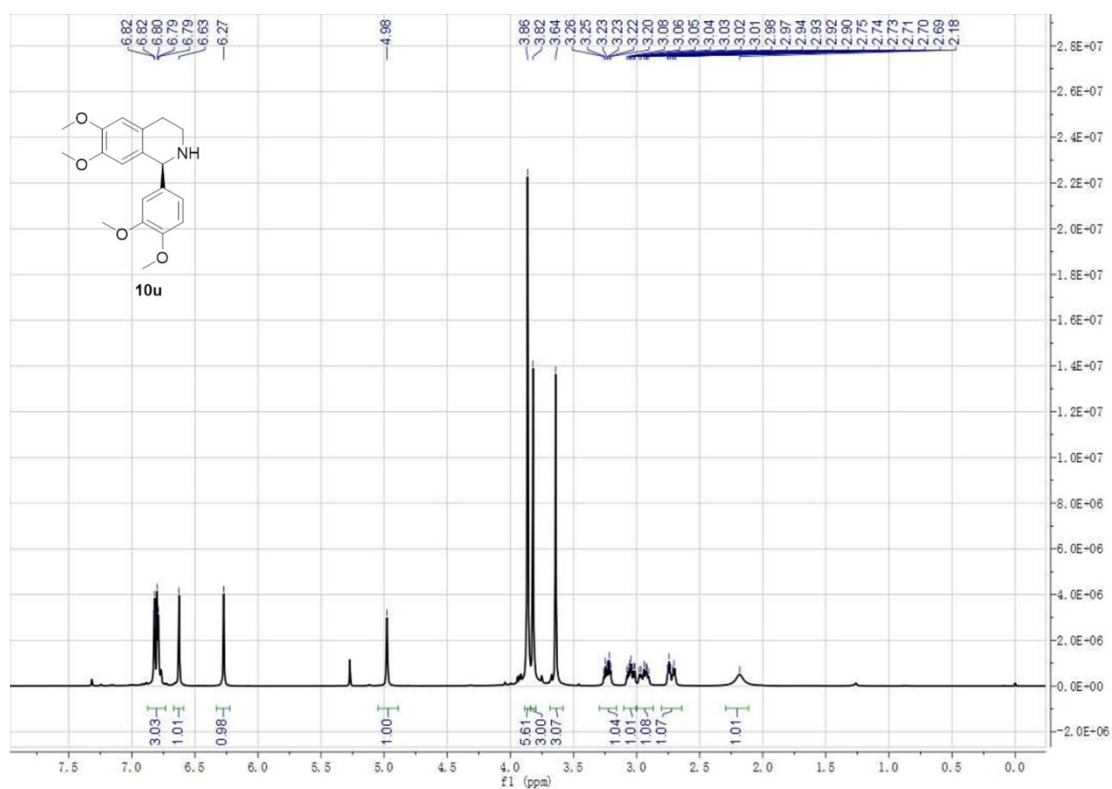
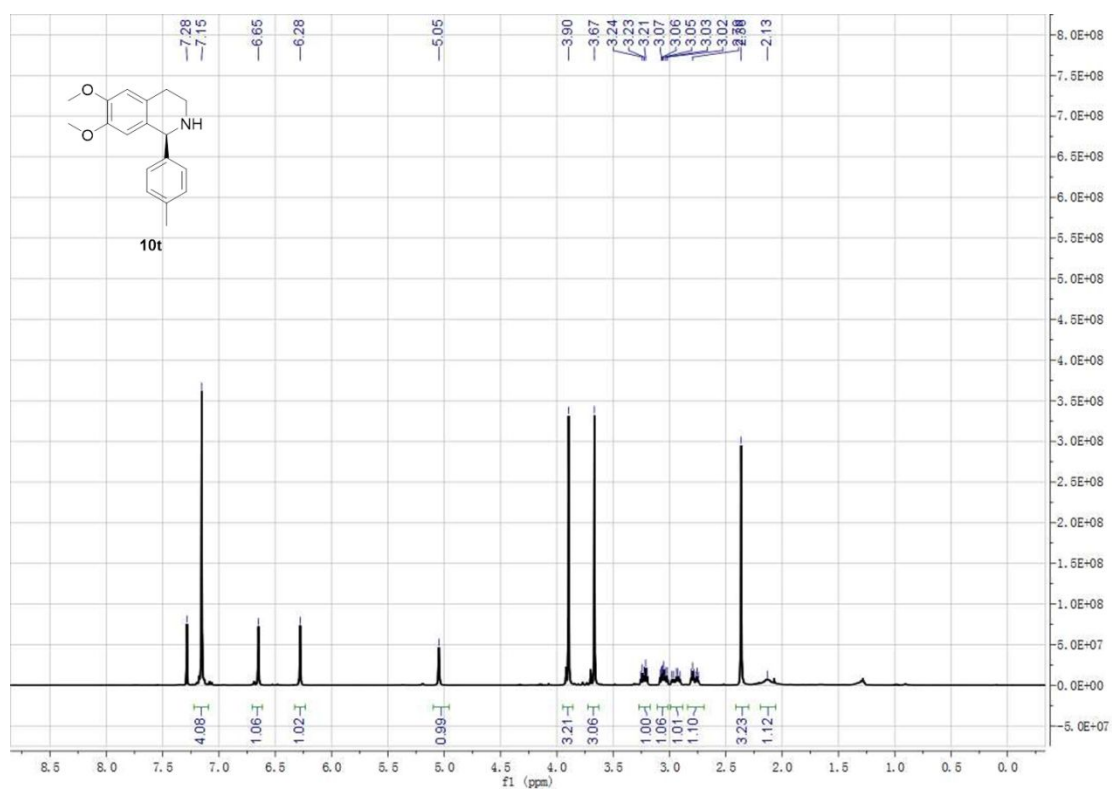


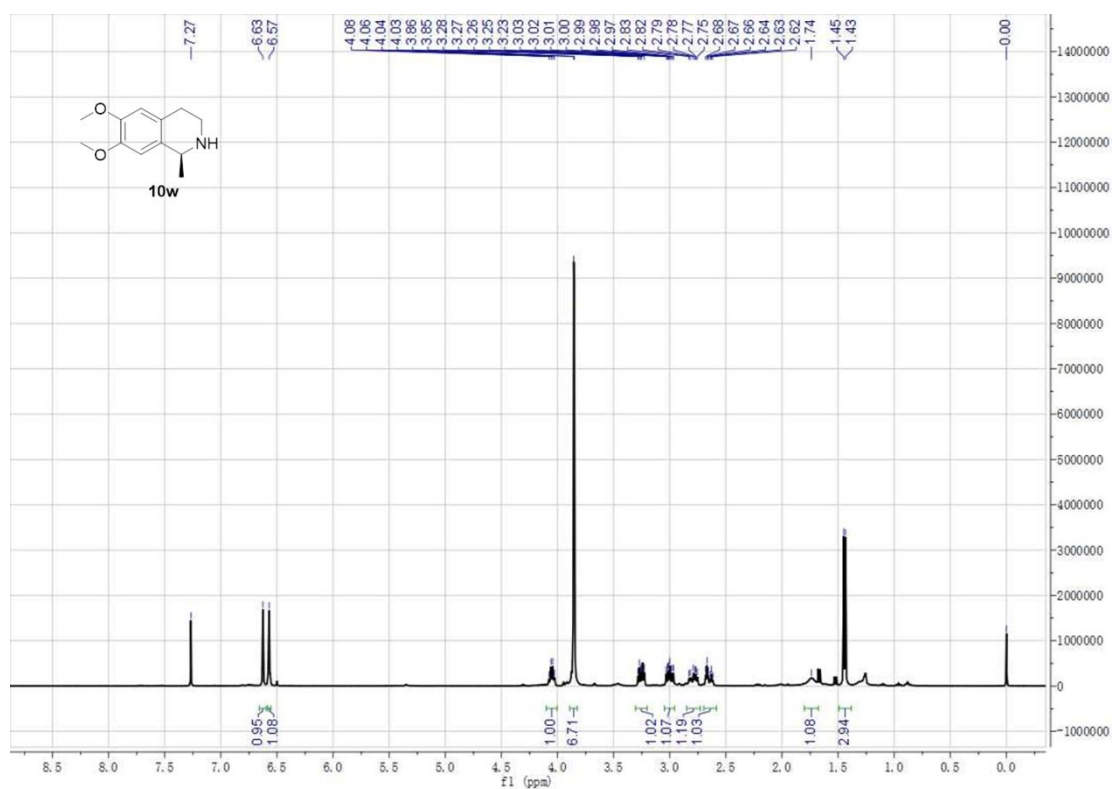
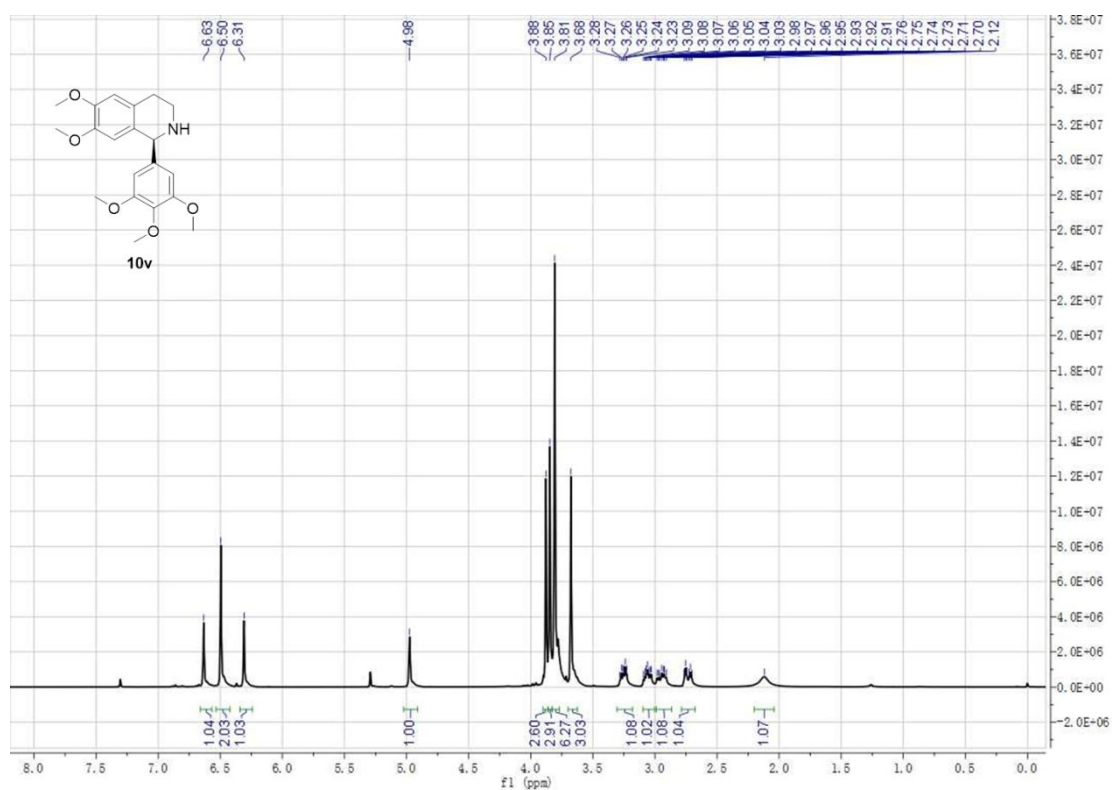


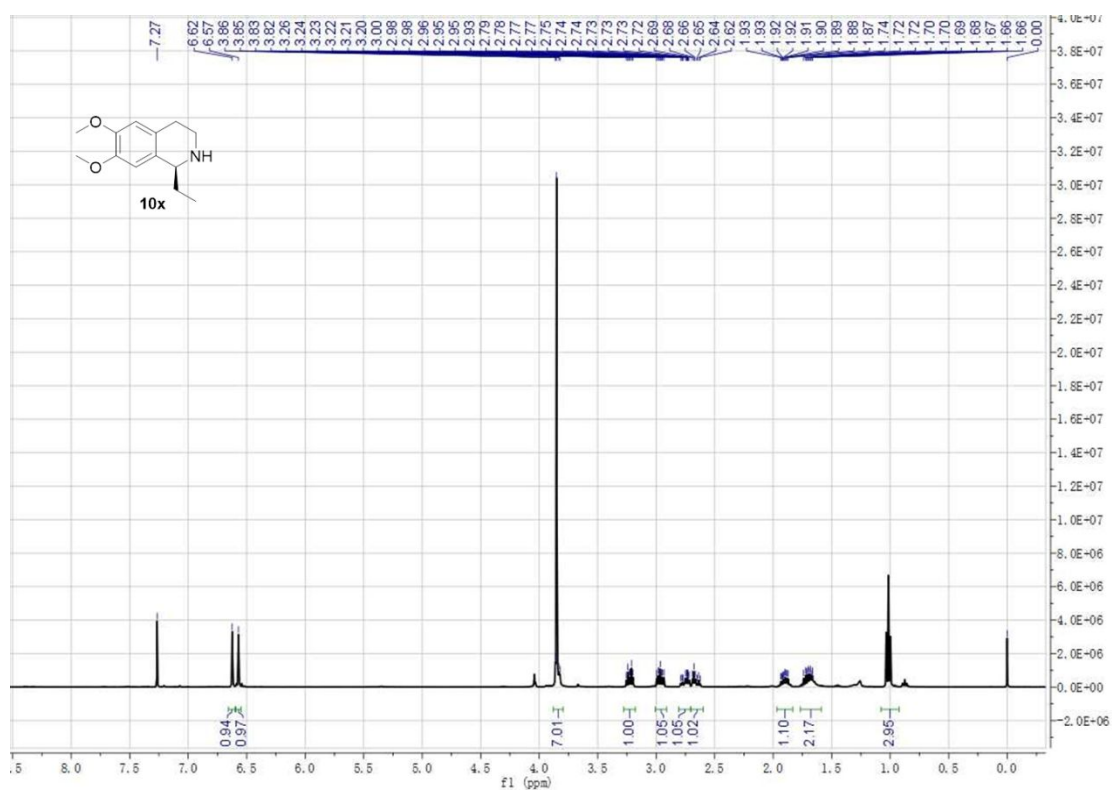




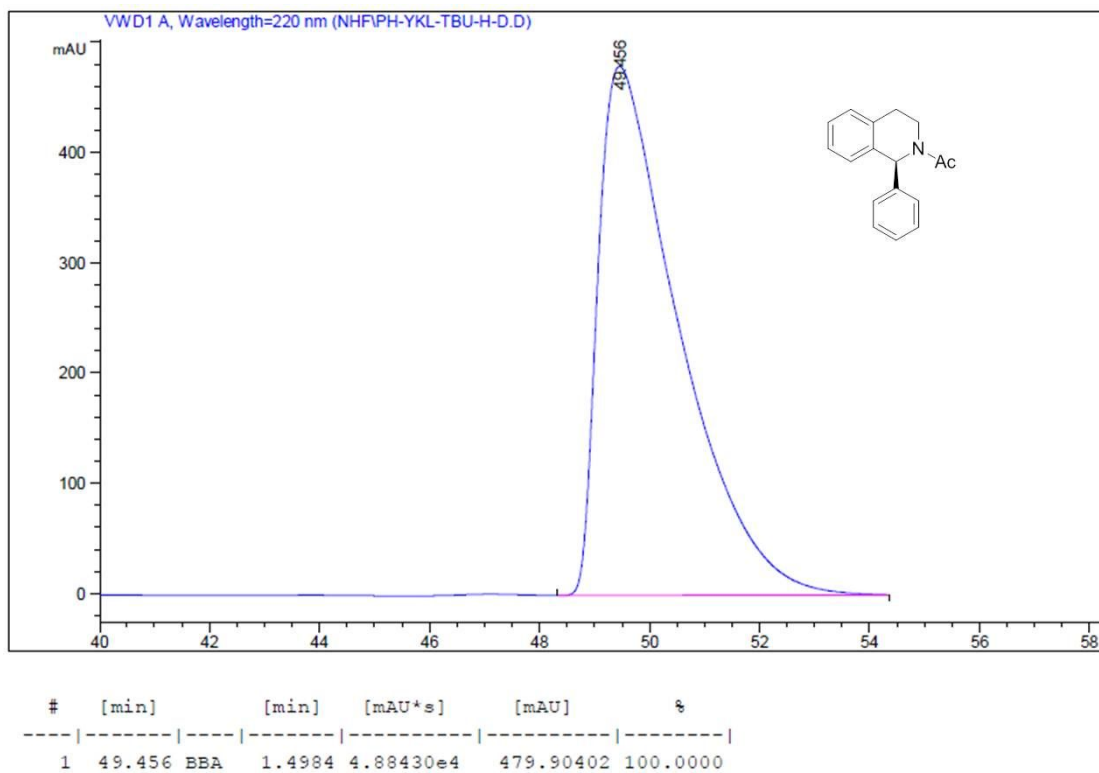
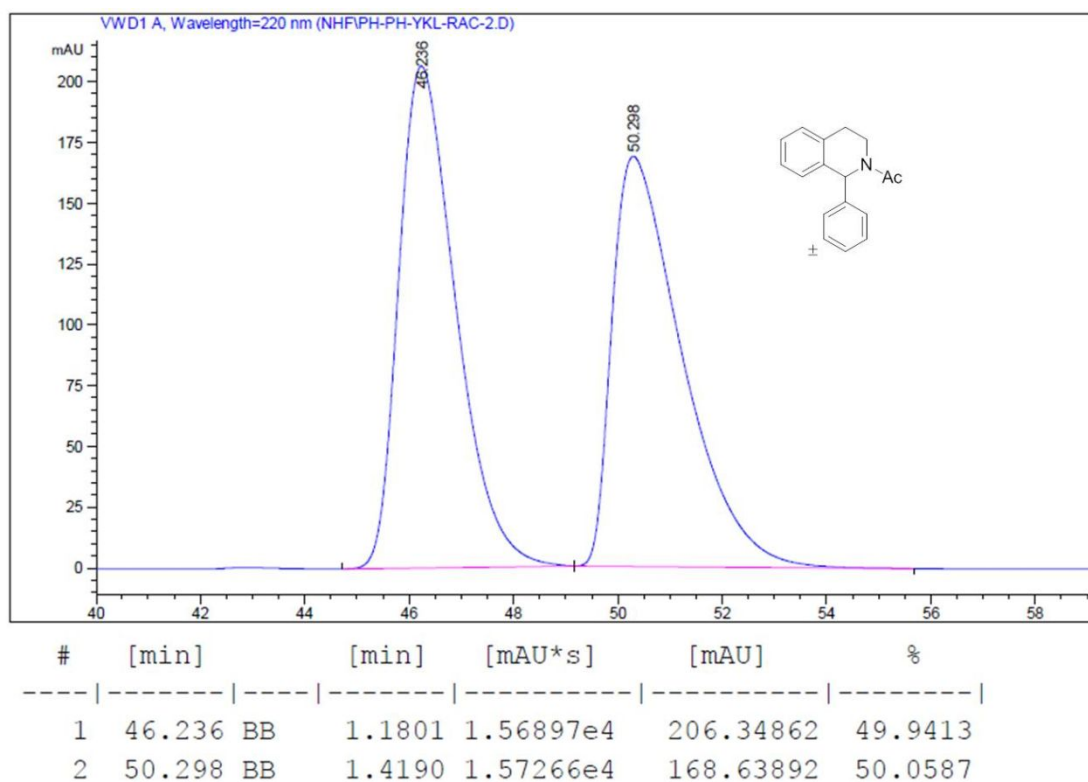


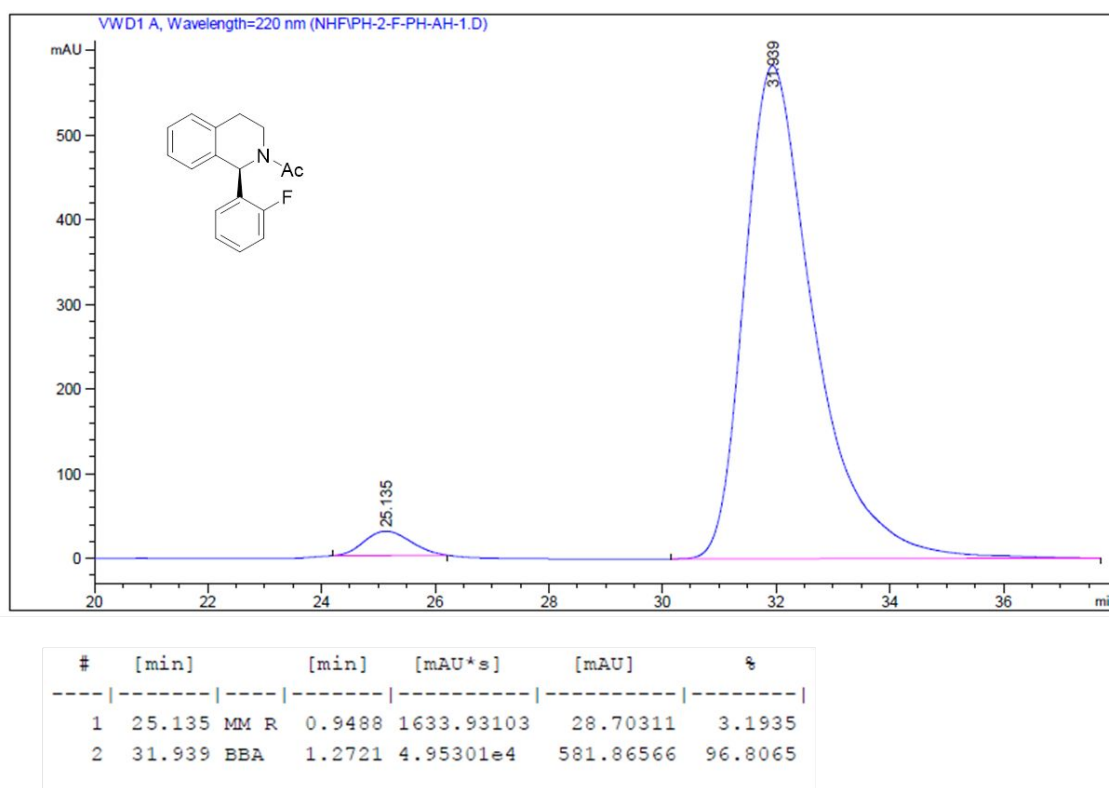
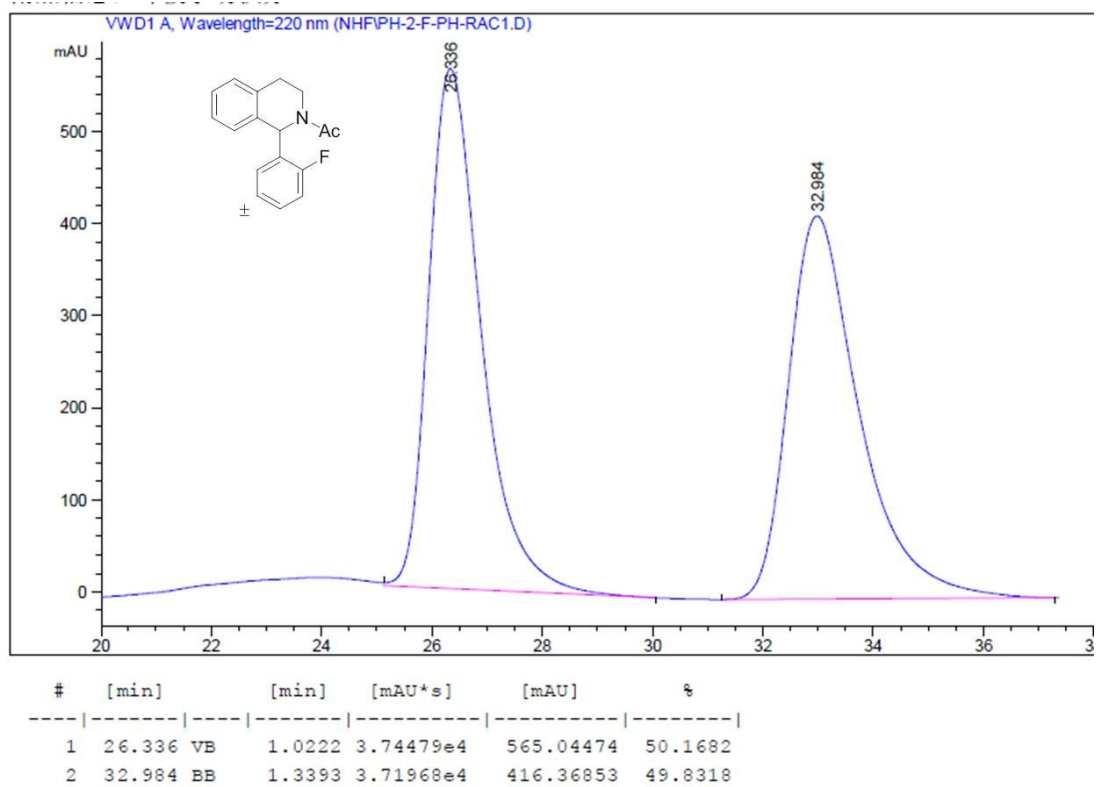


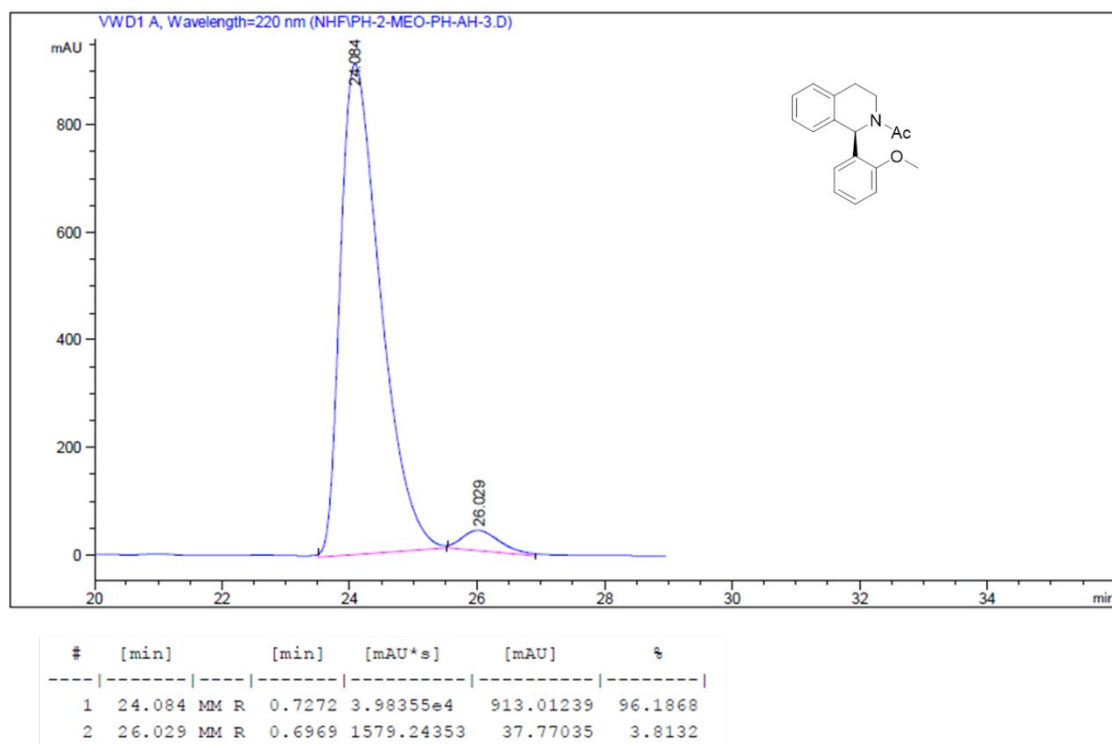
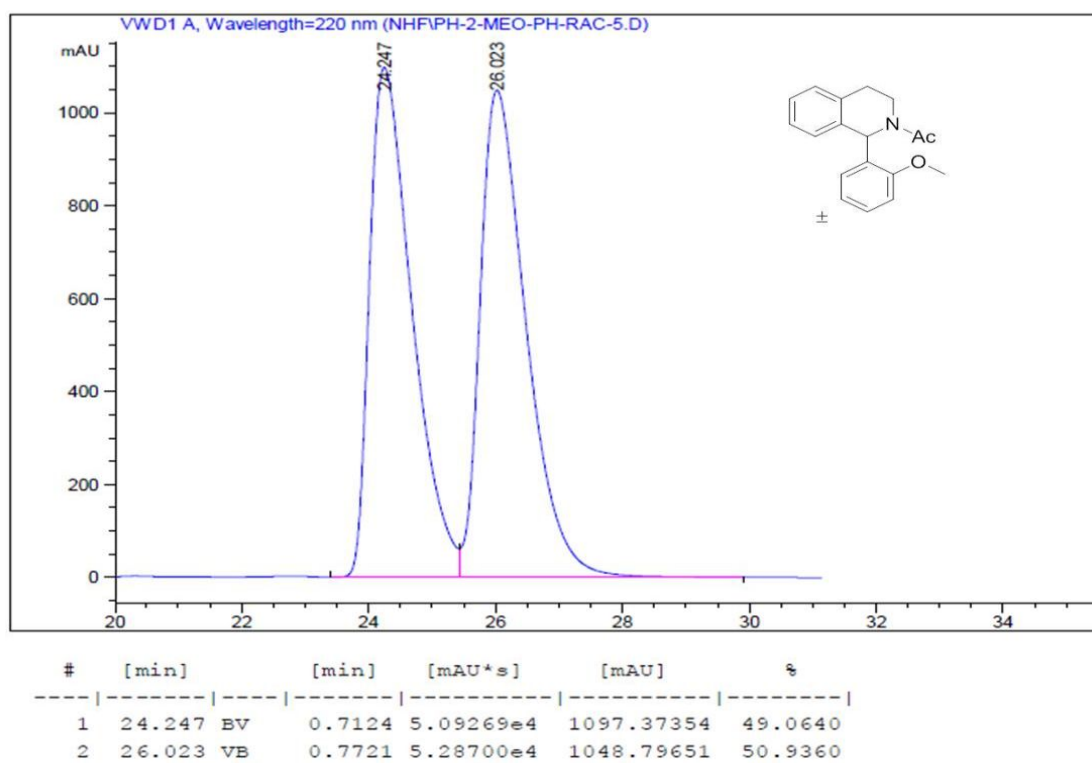


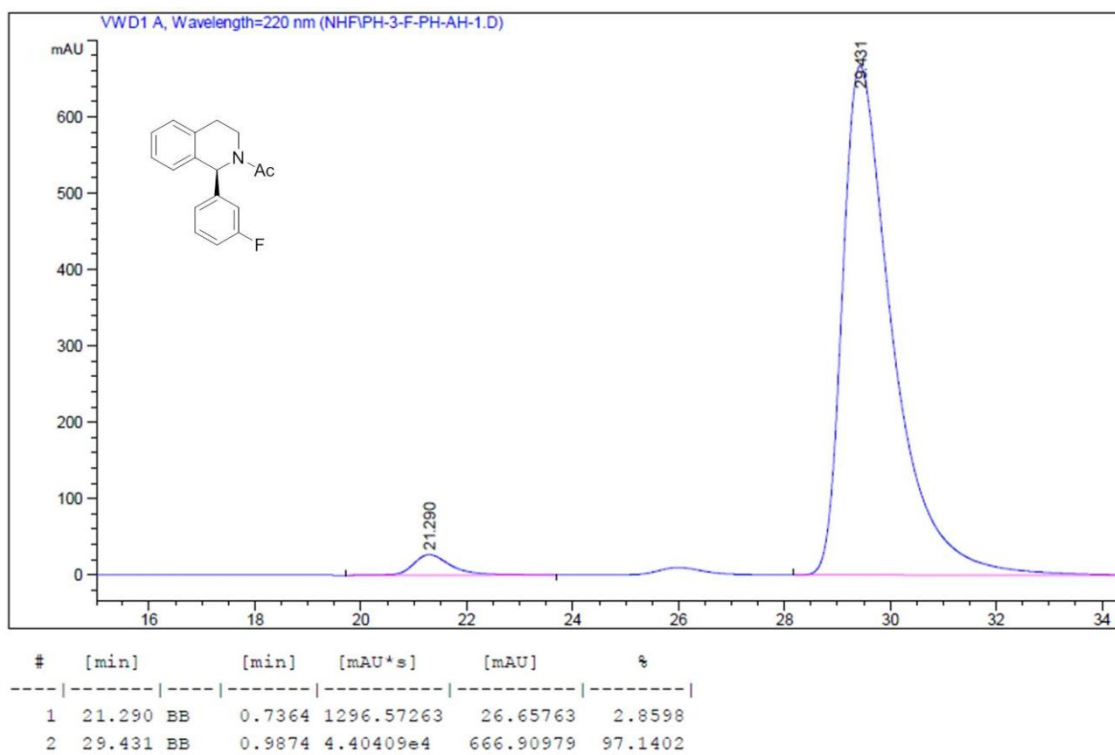
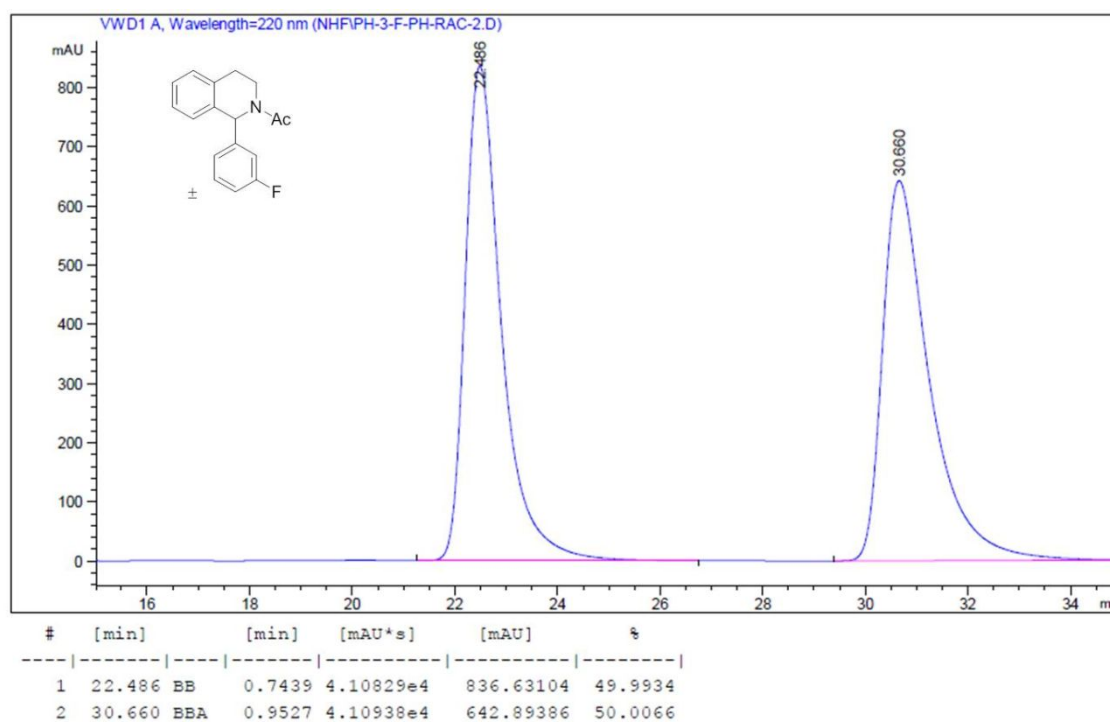


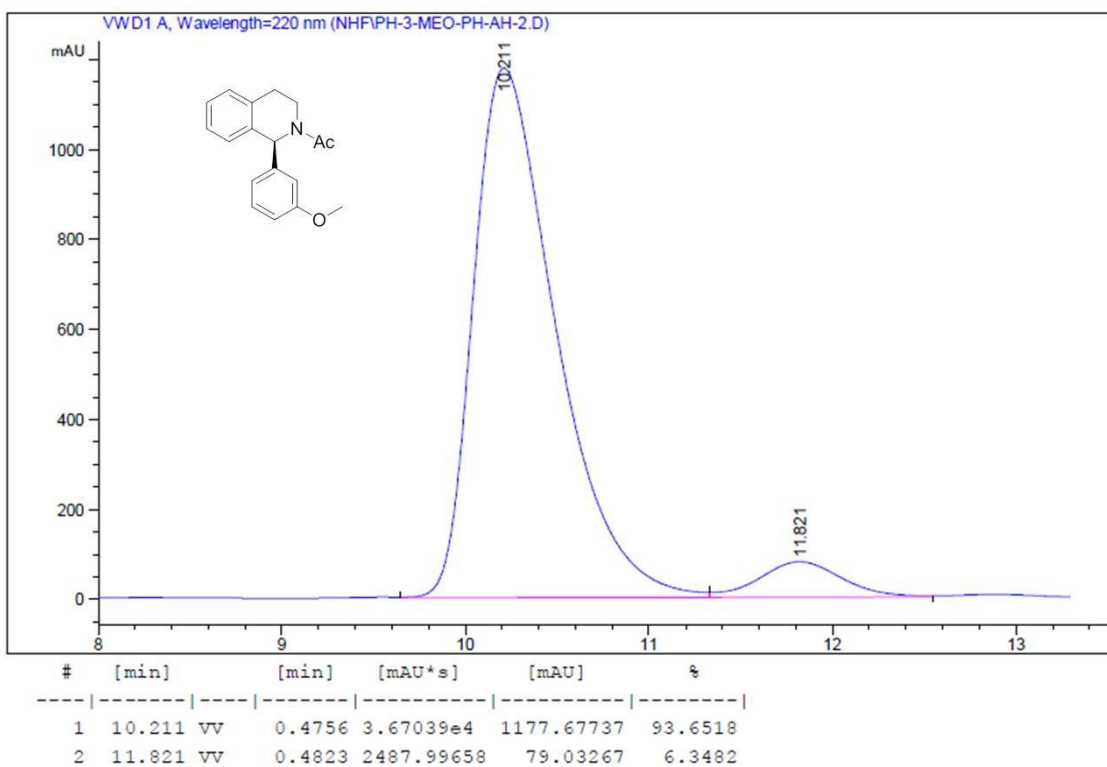
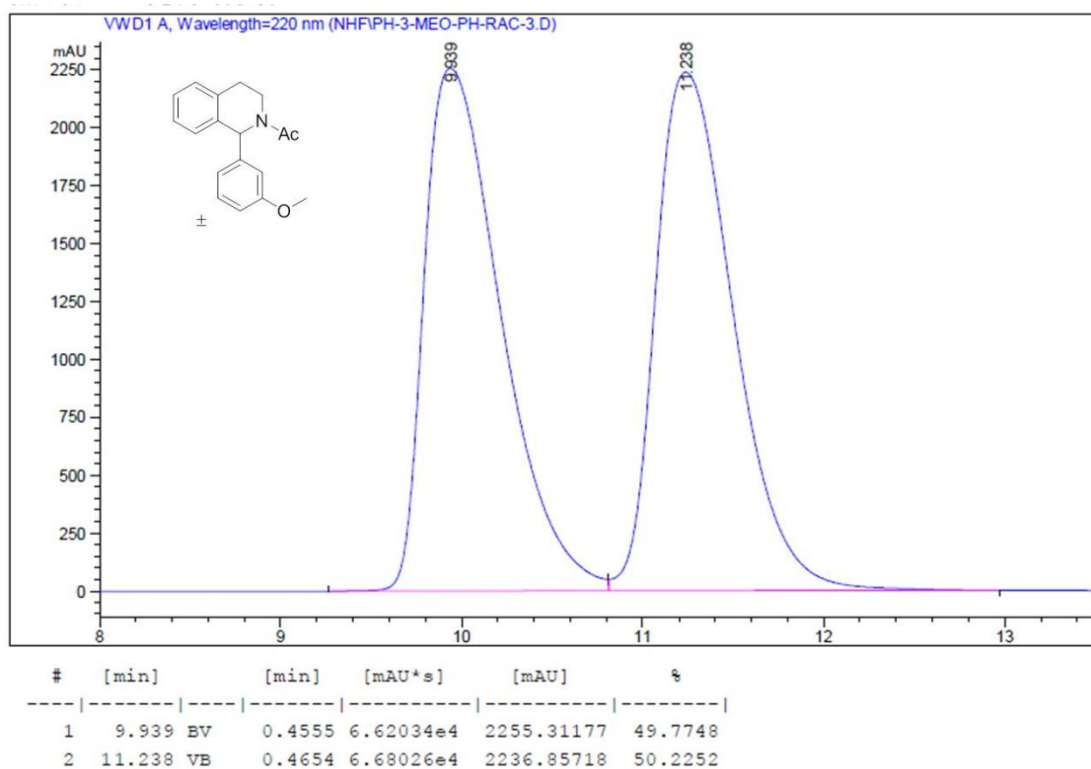
7. HPLC spectra

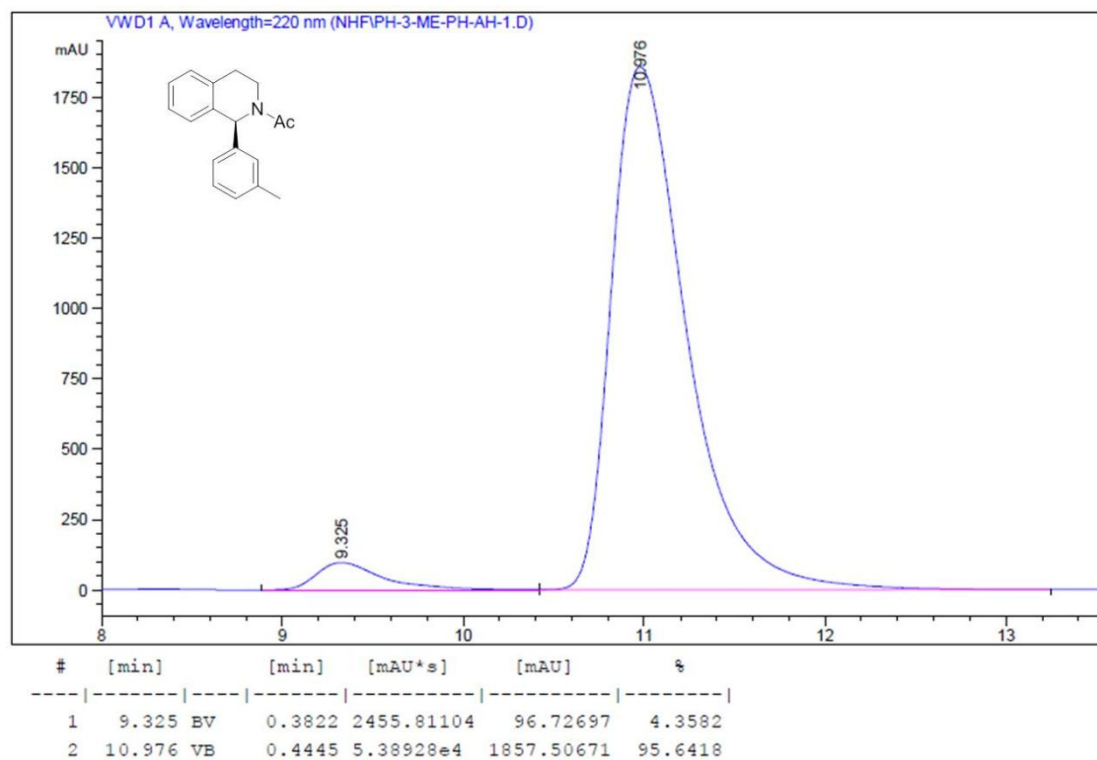
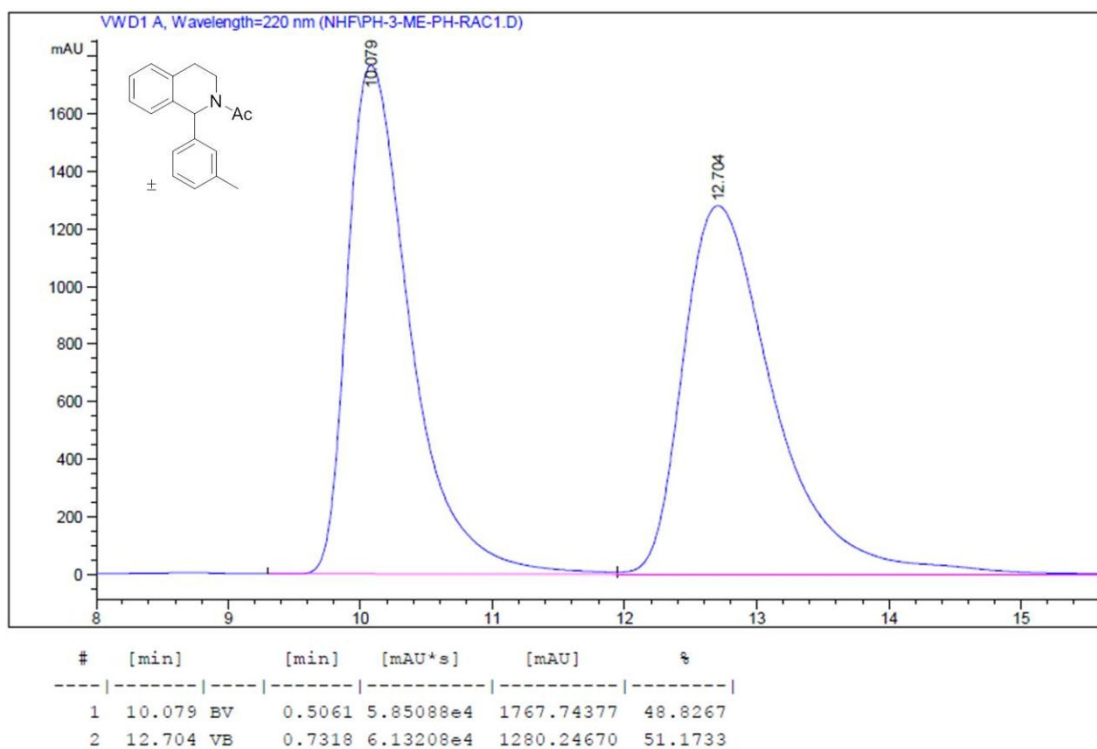


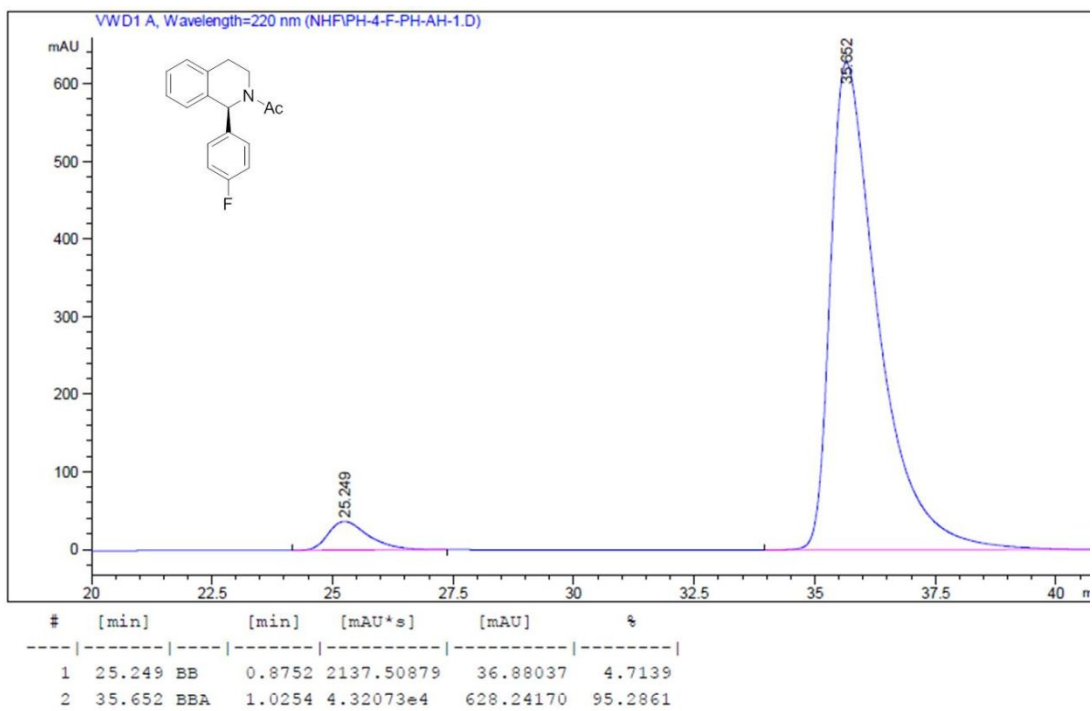
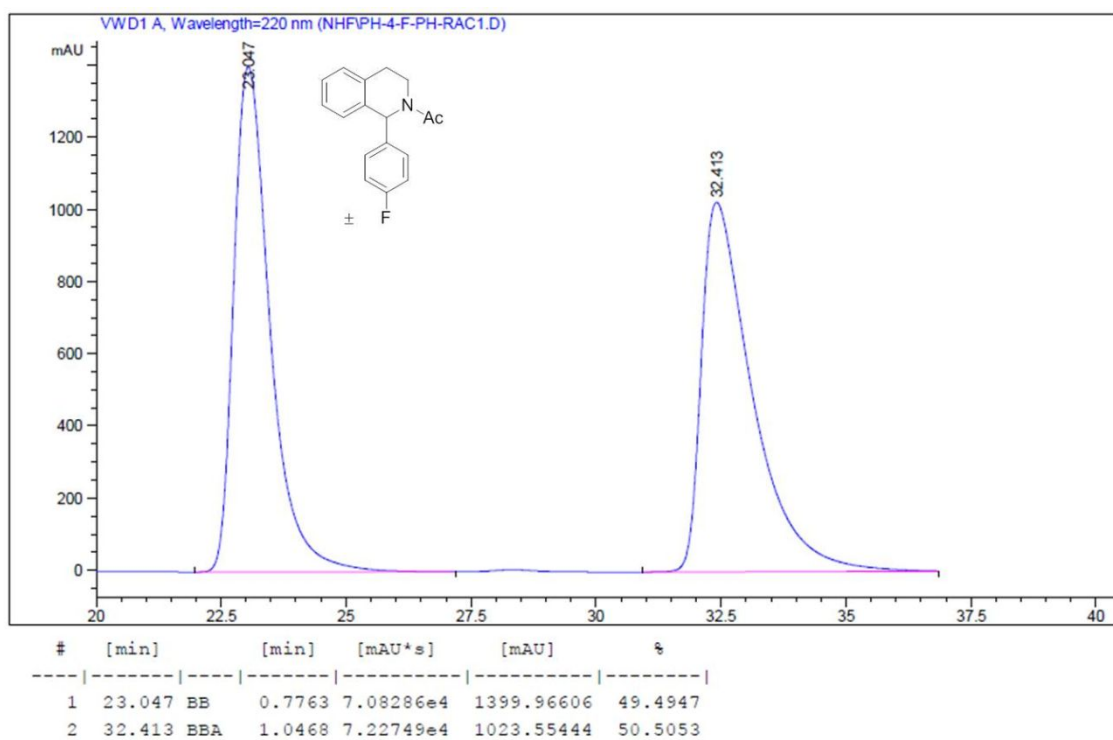


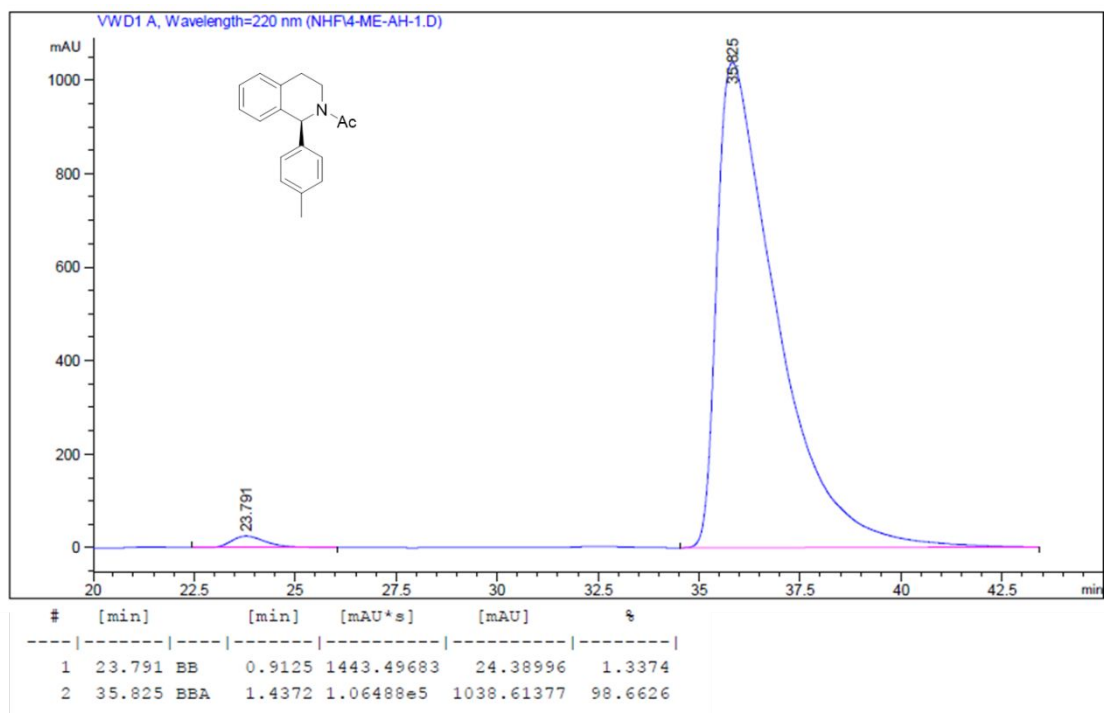
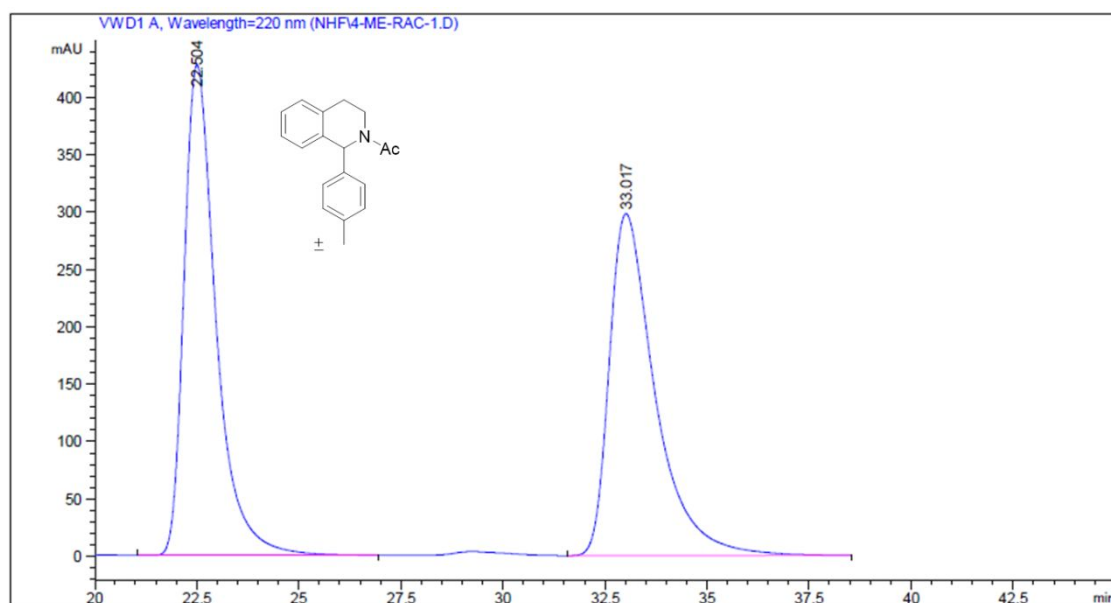


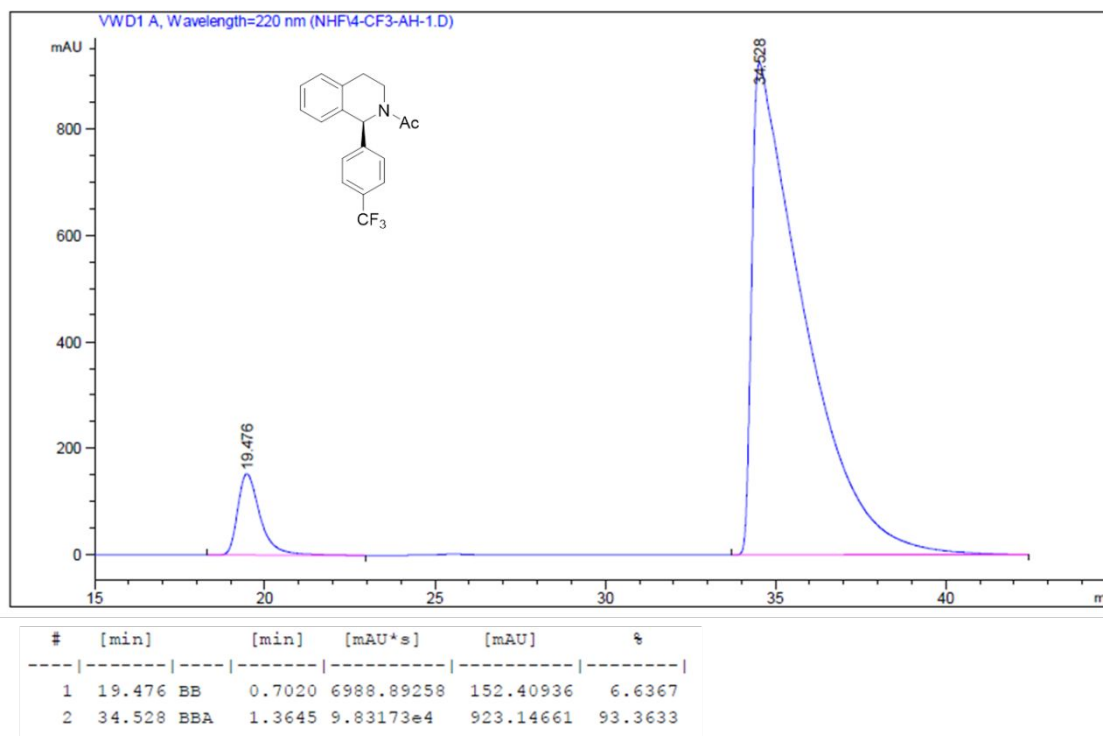
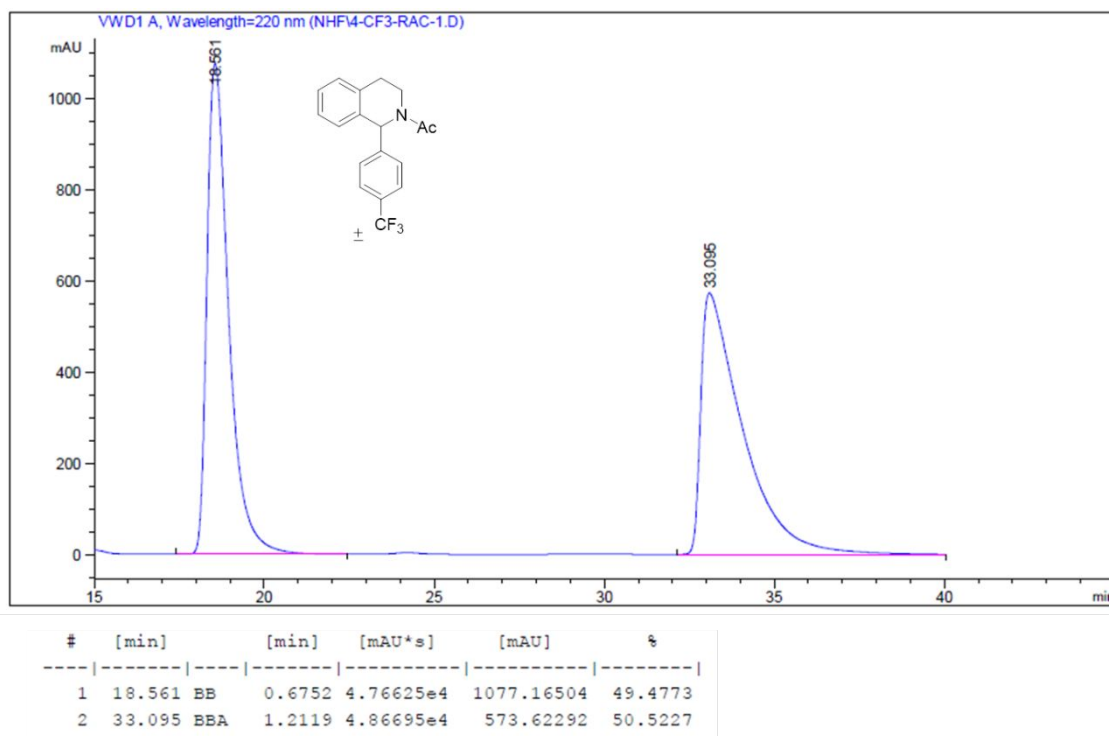


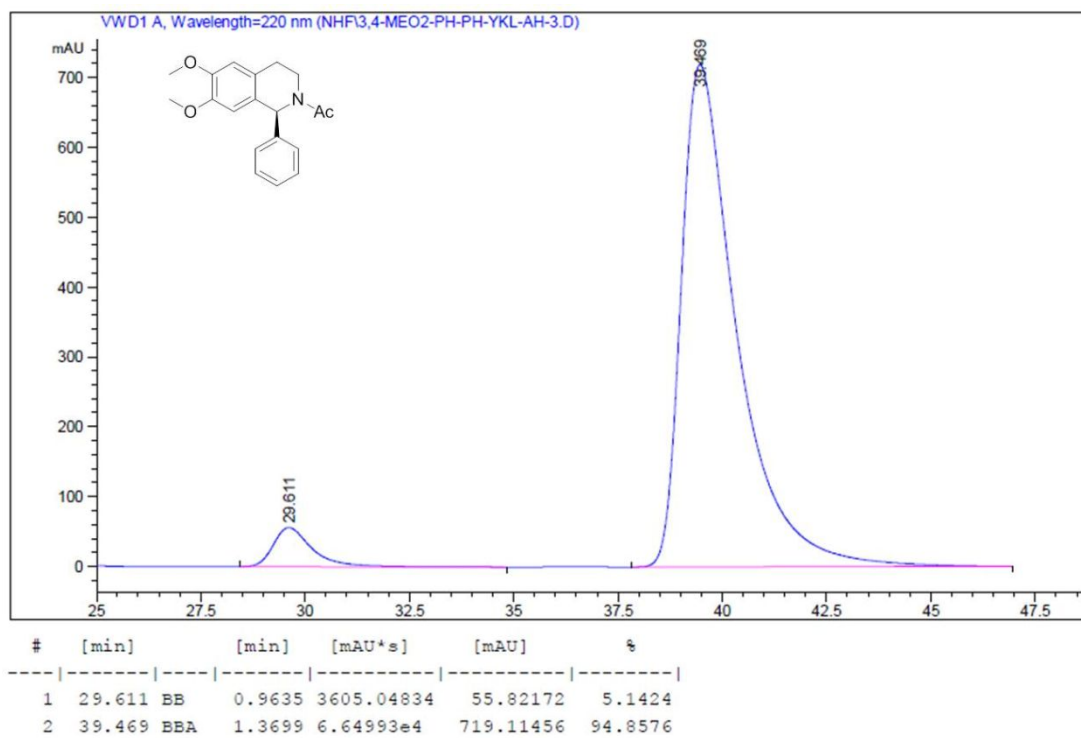
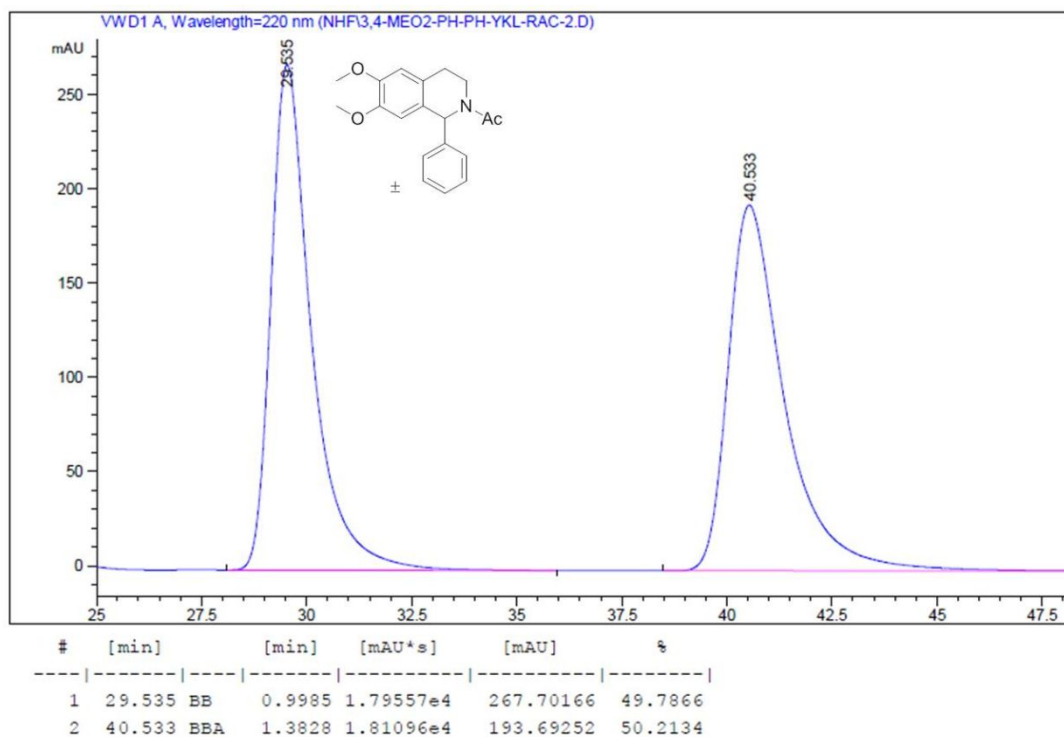


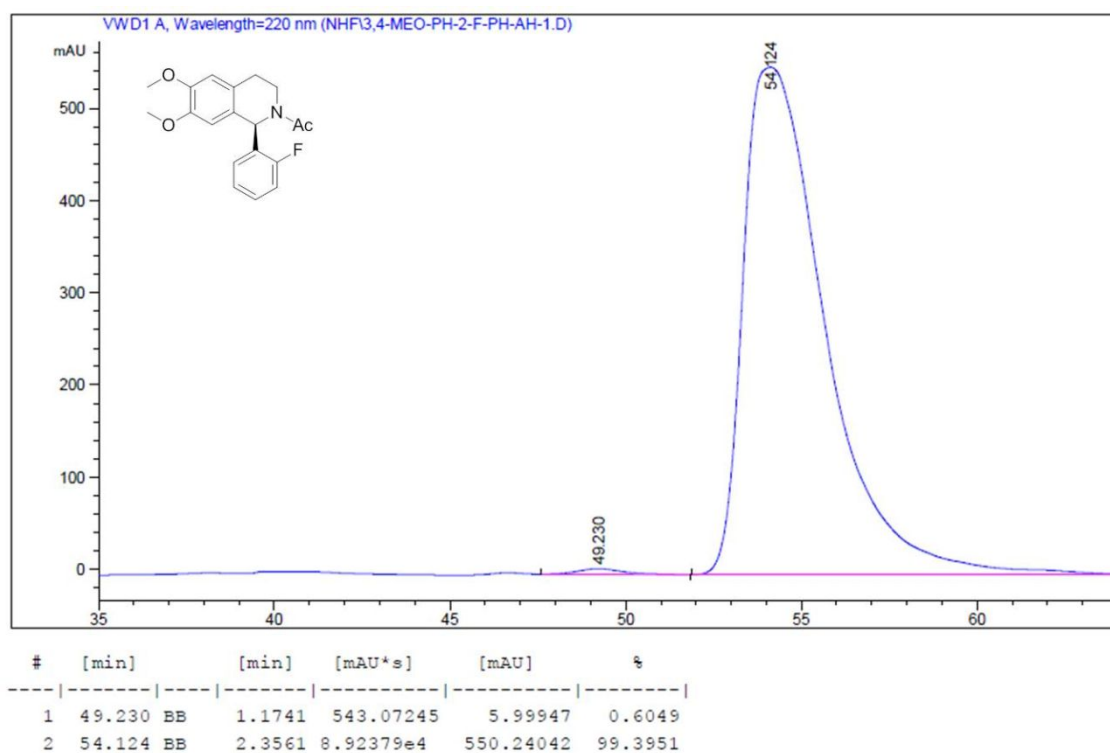
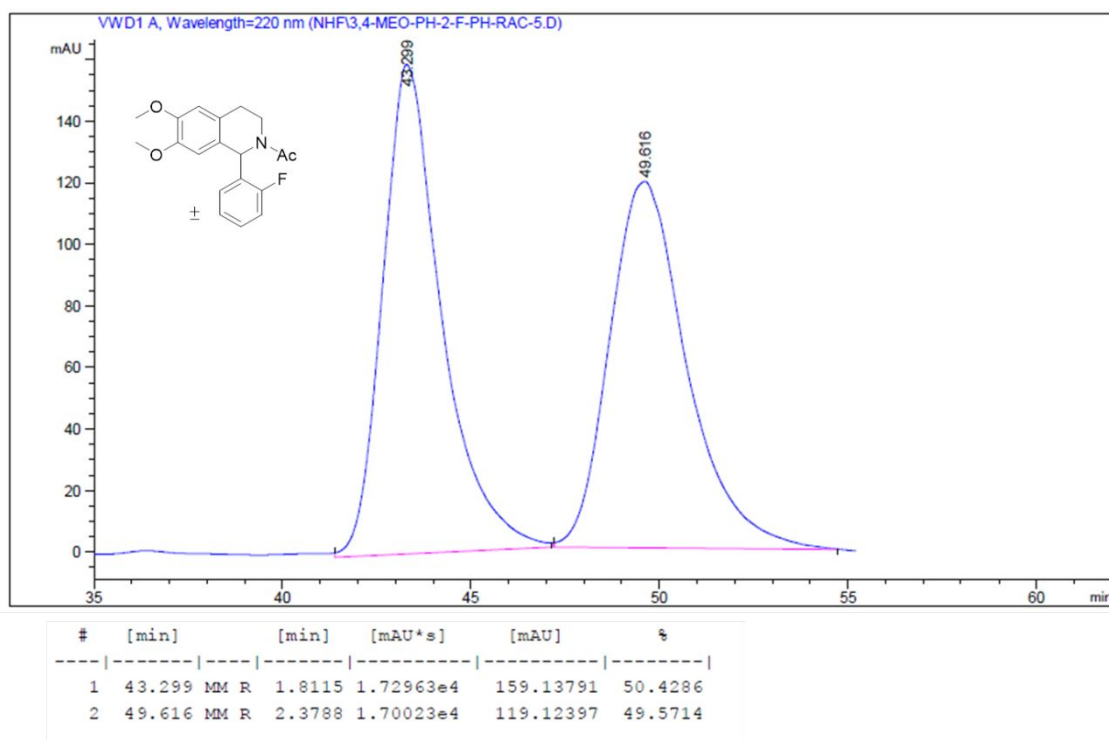


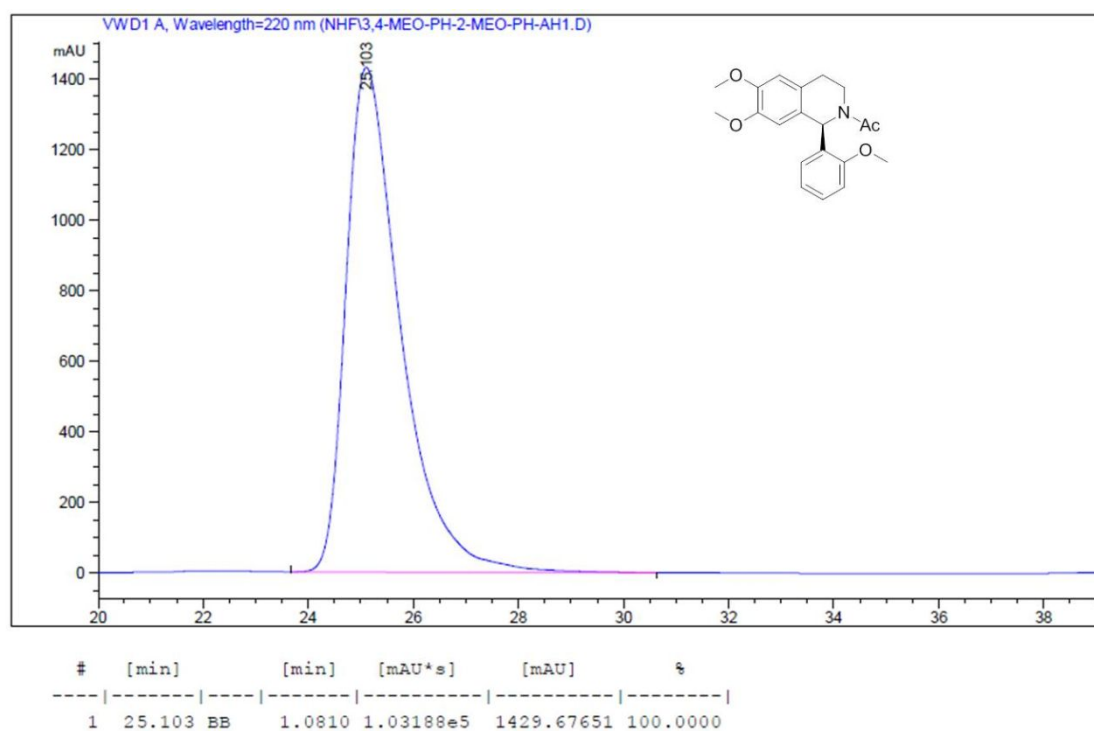
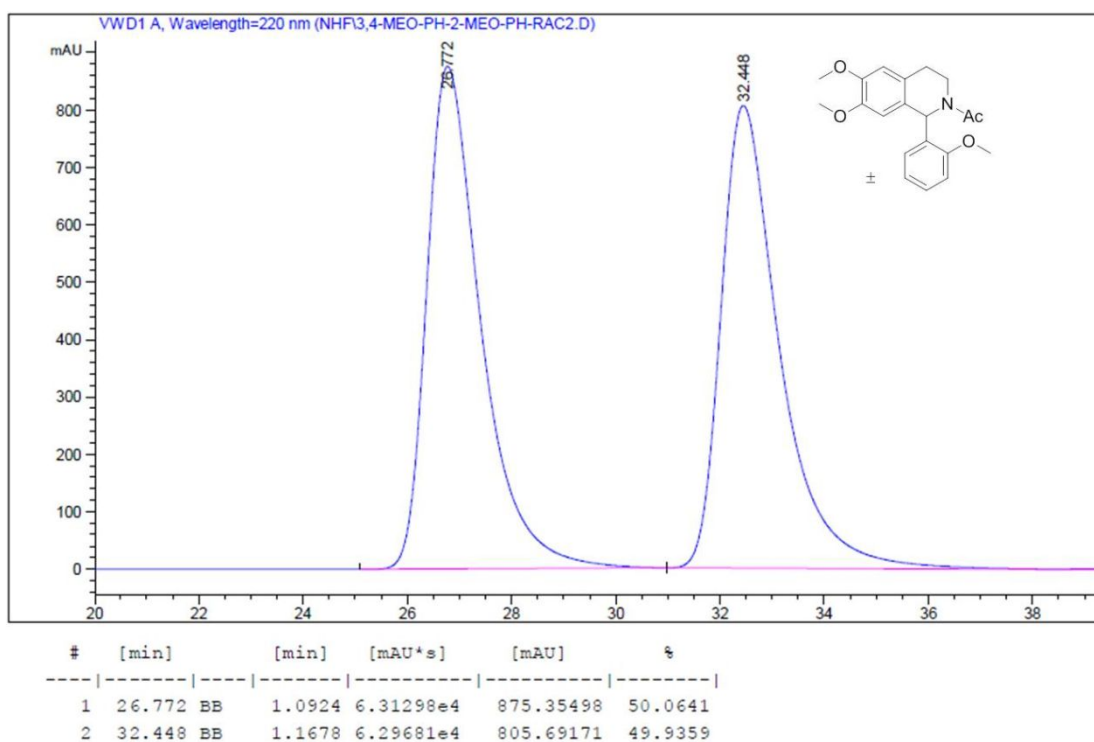


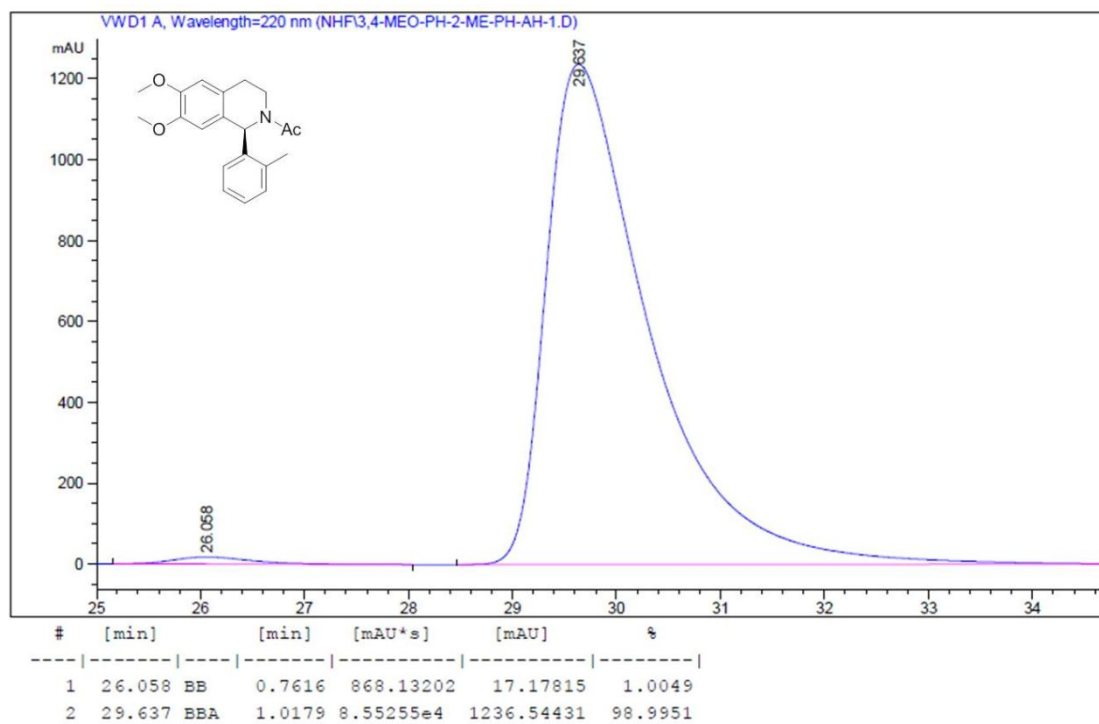
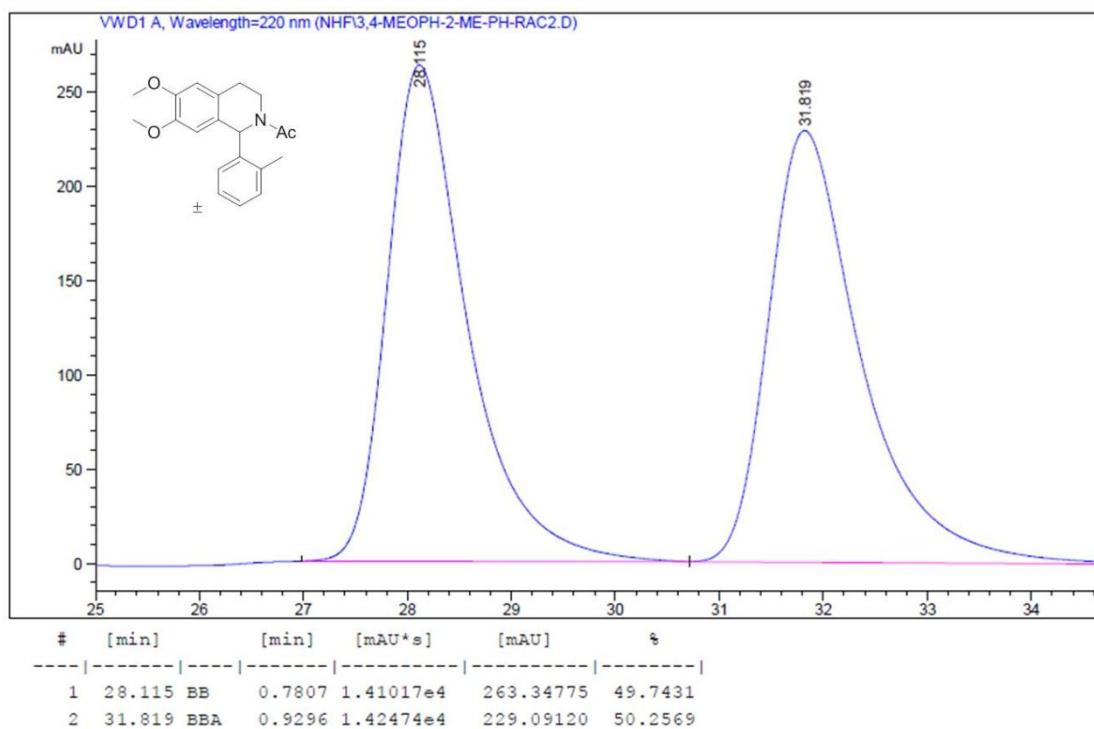


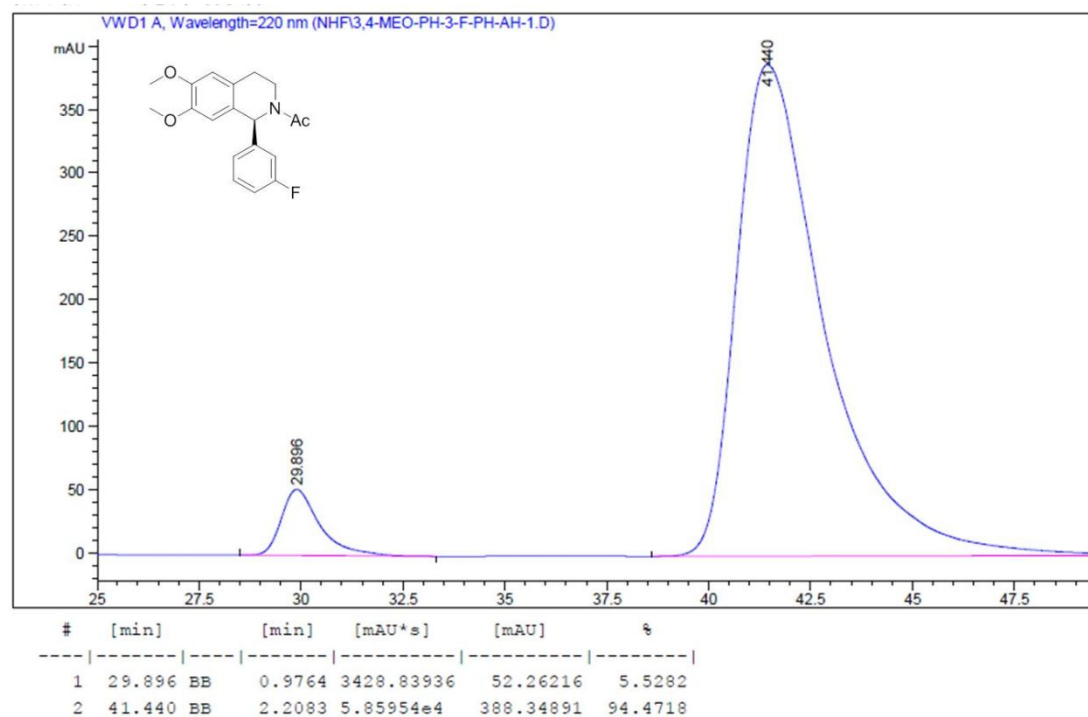
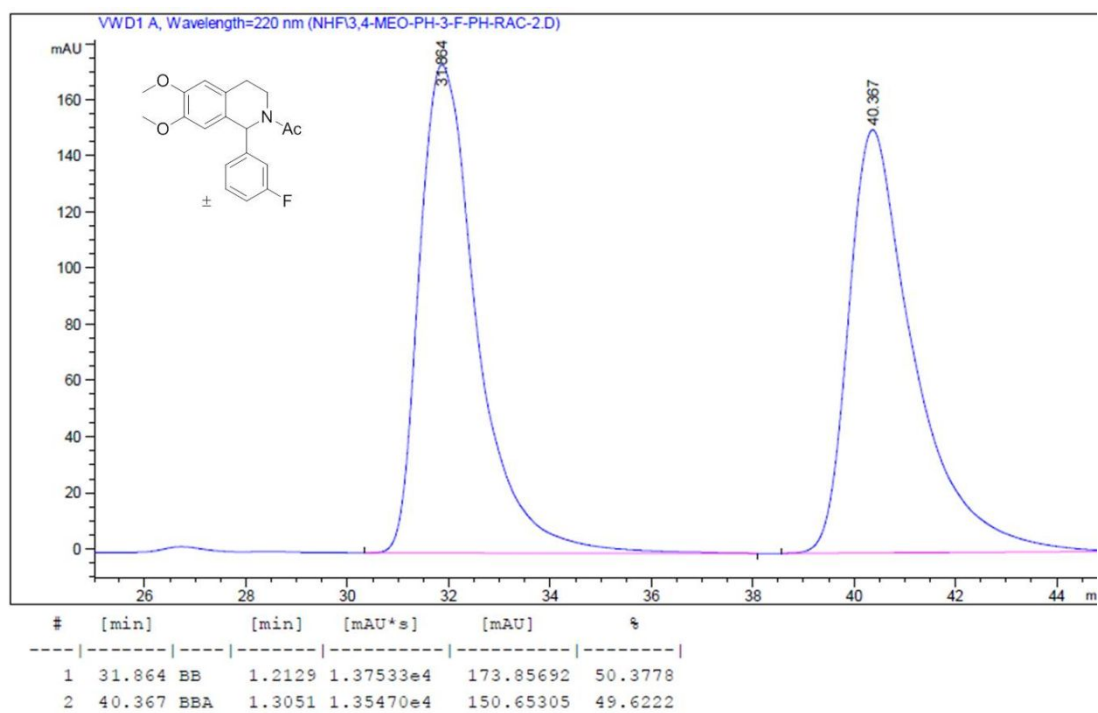


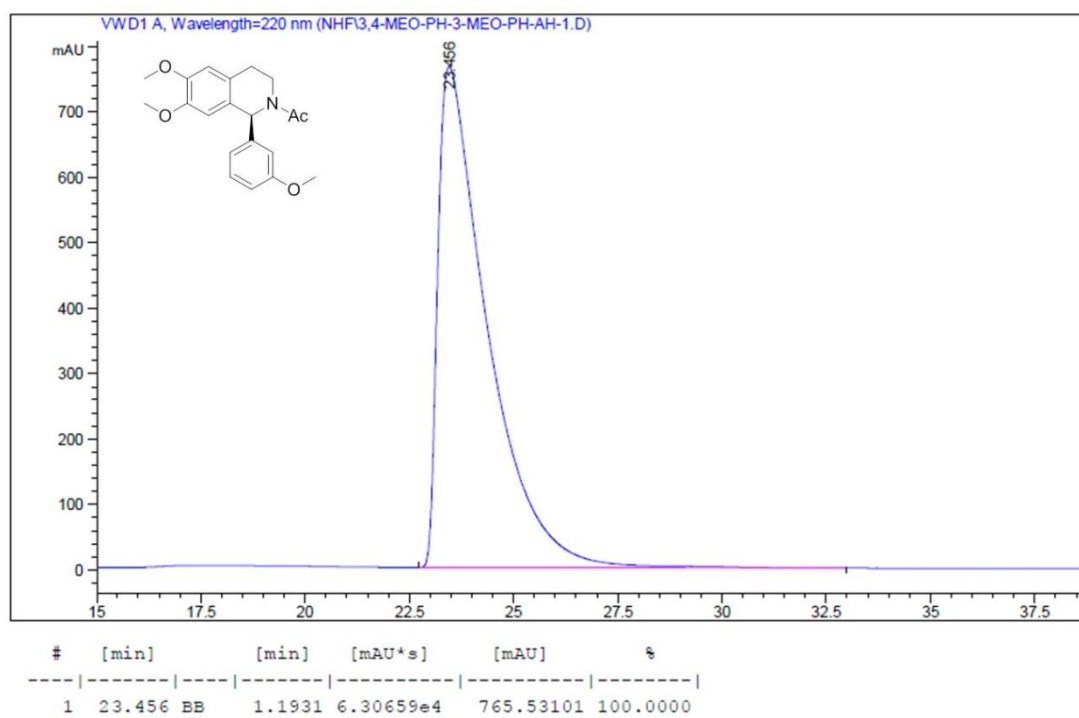
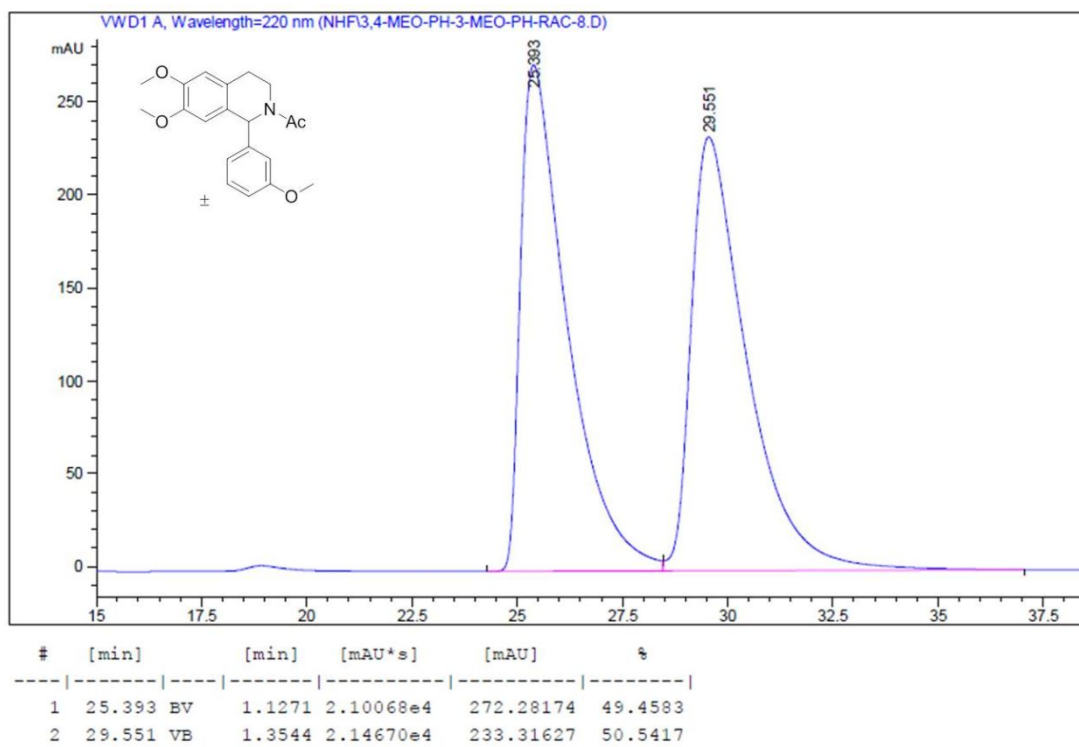


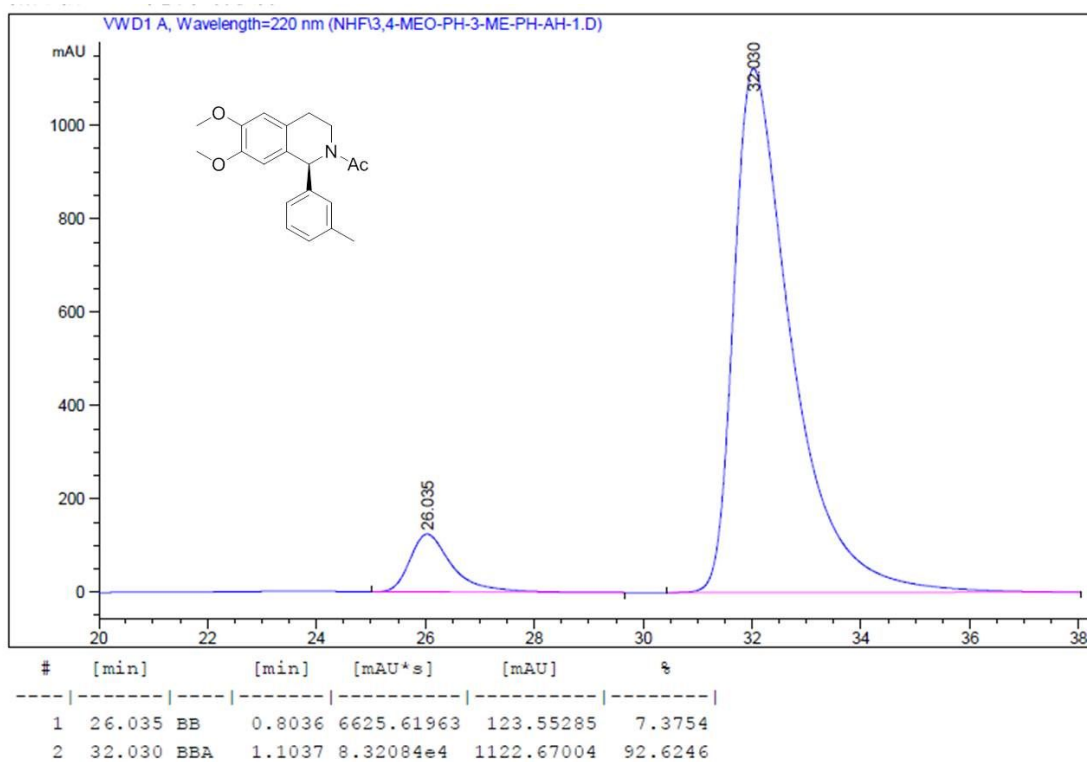
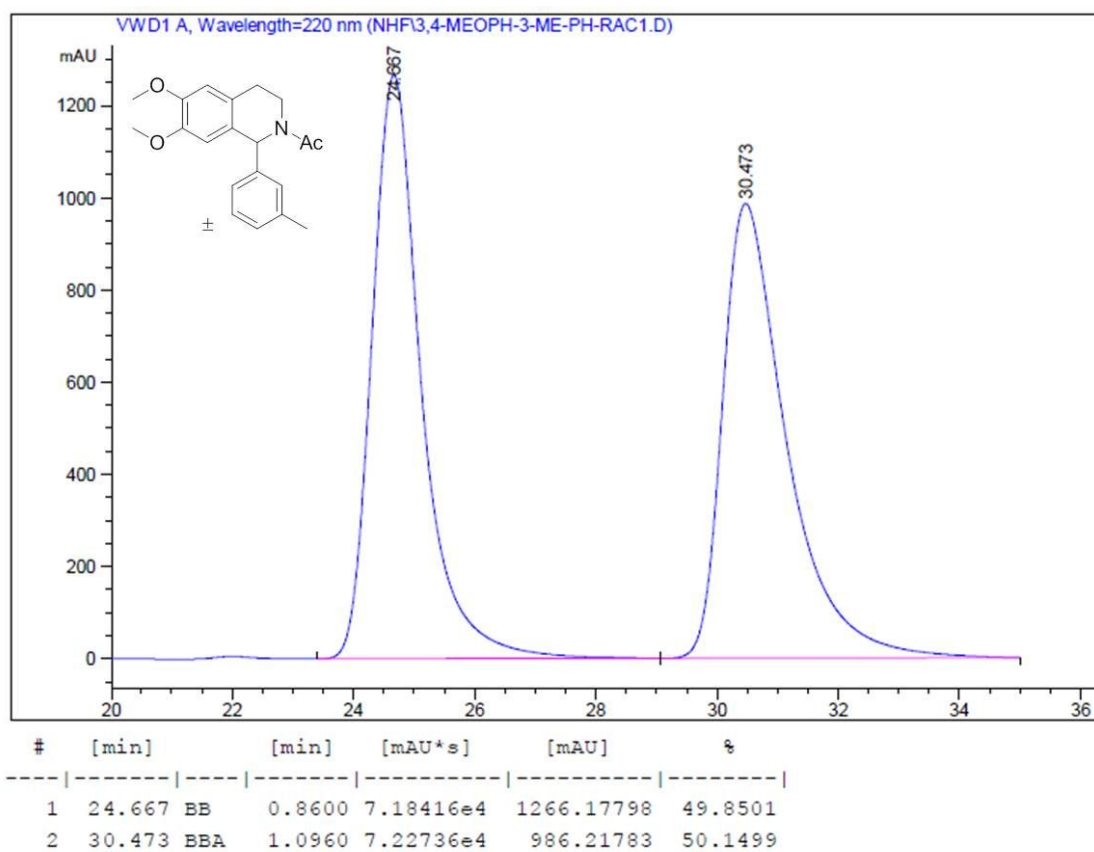


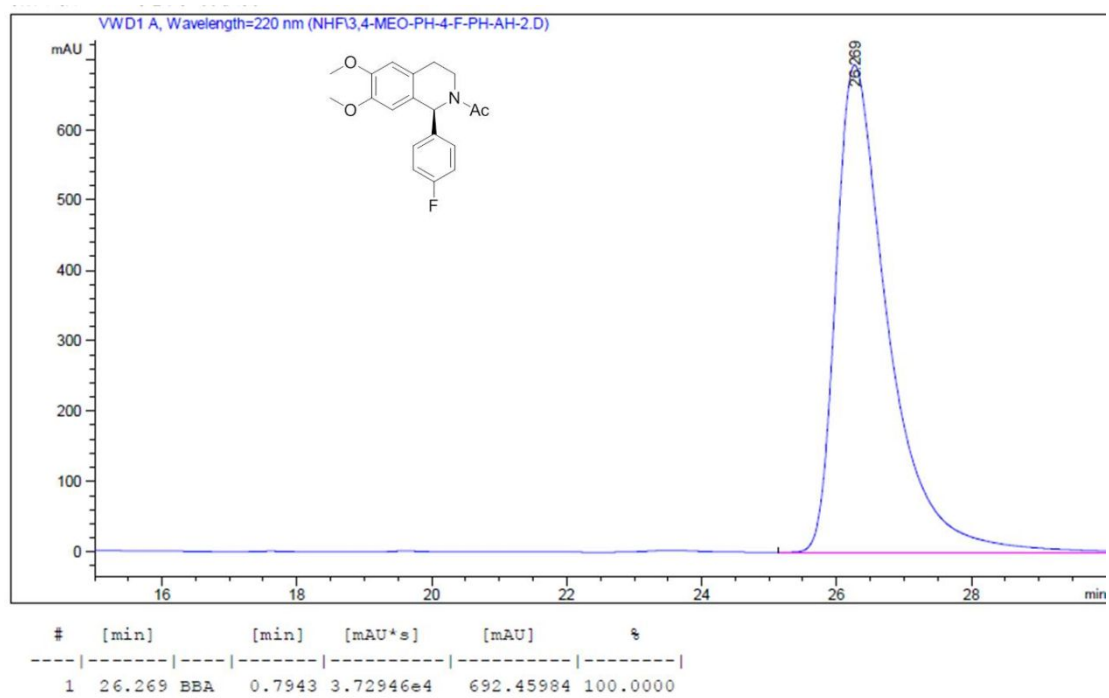
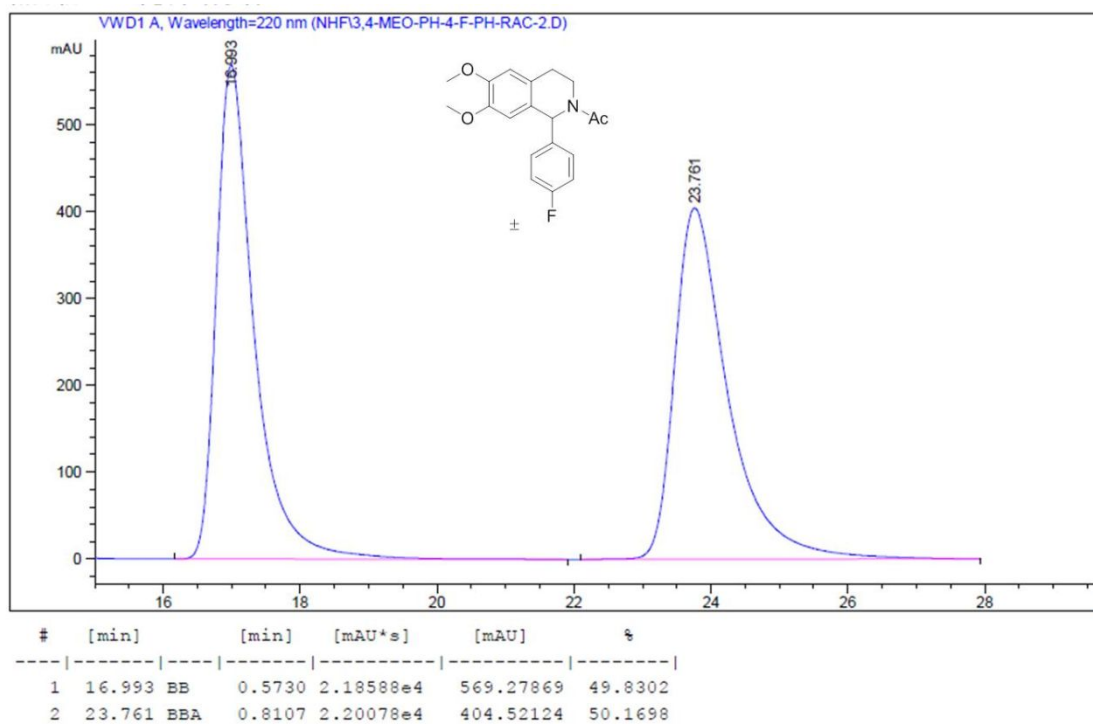


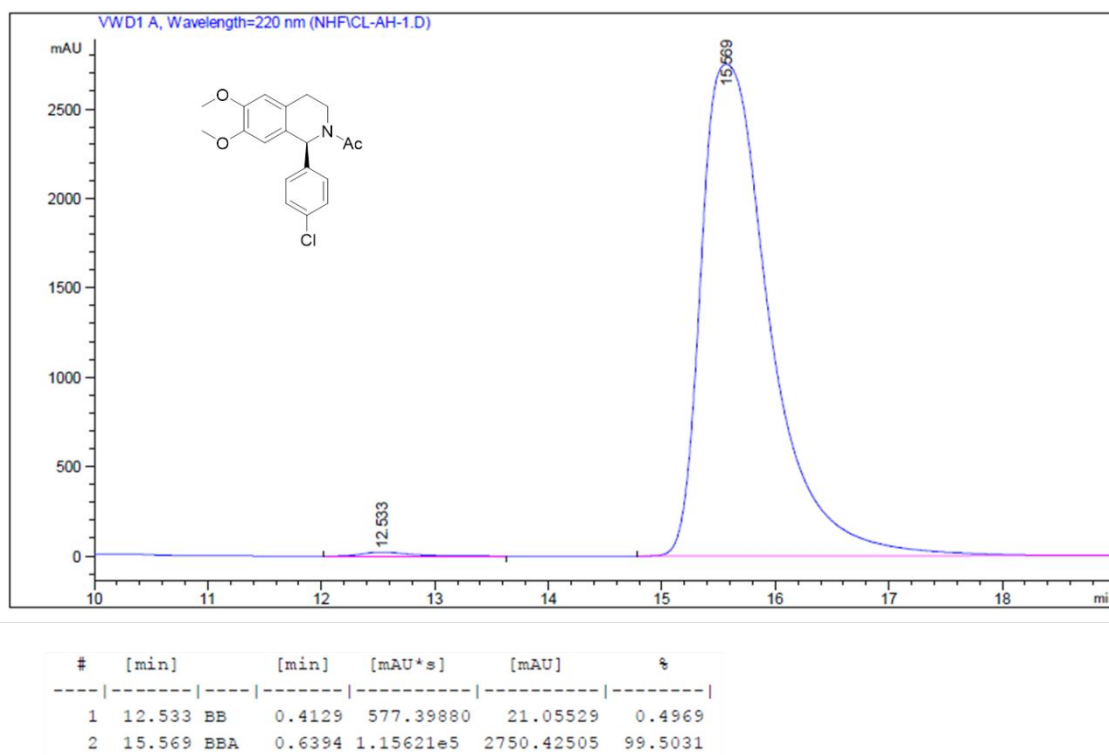
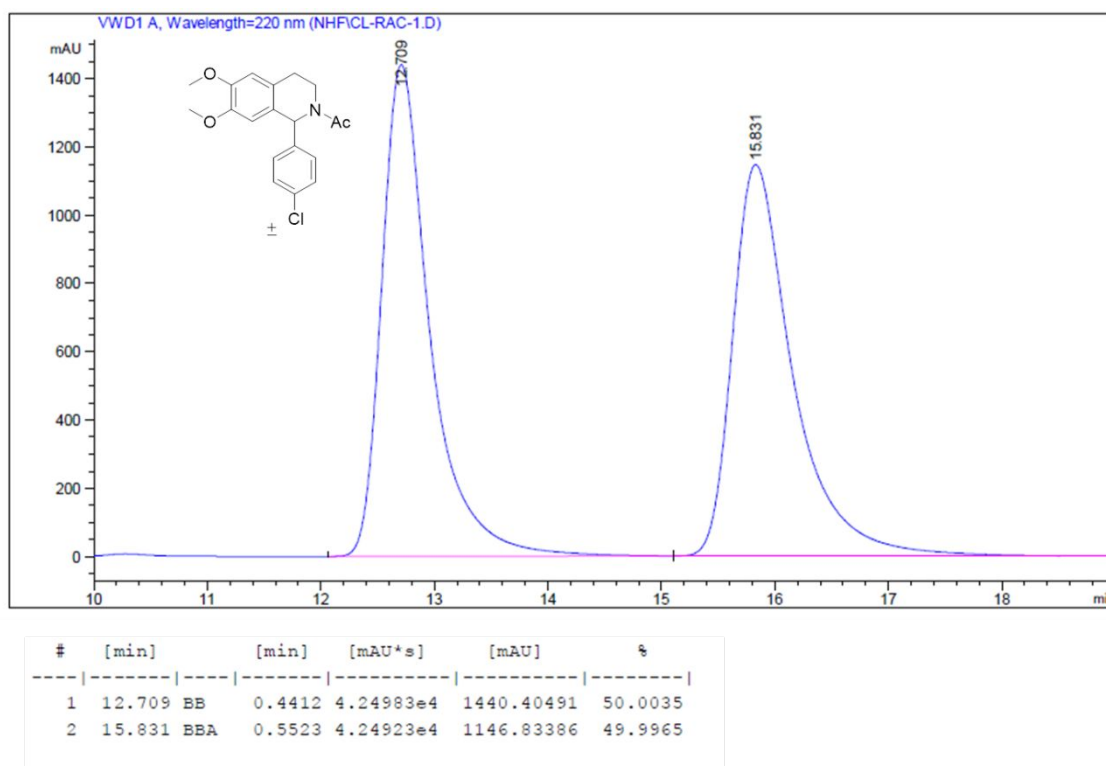


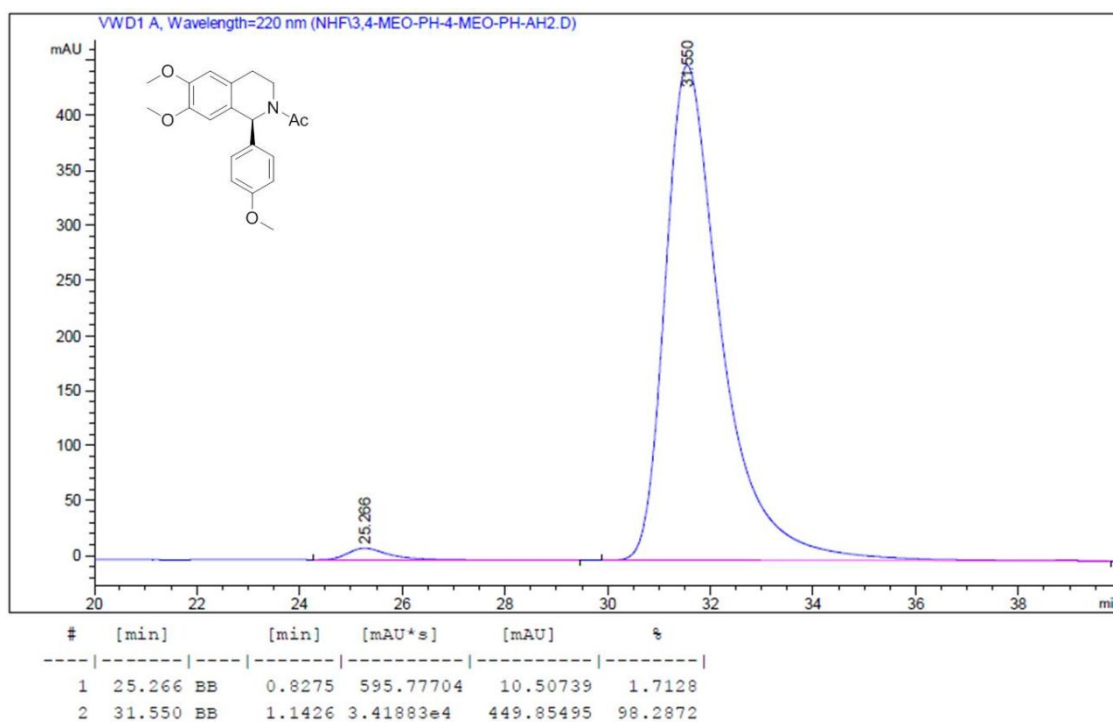
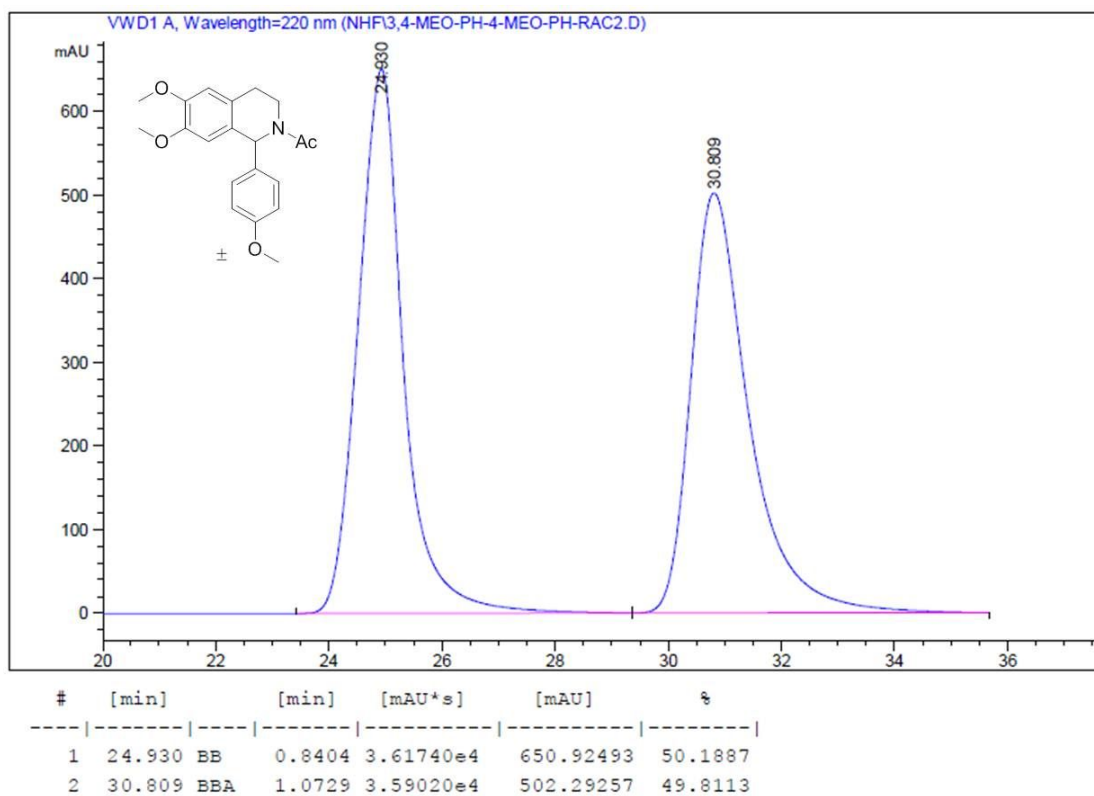


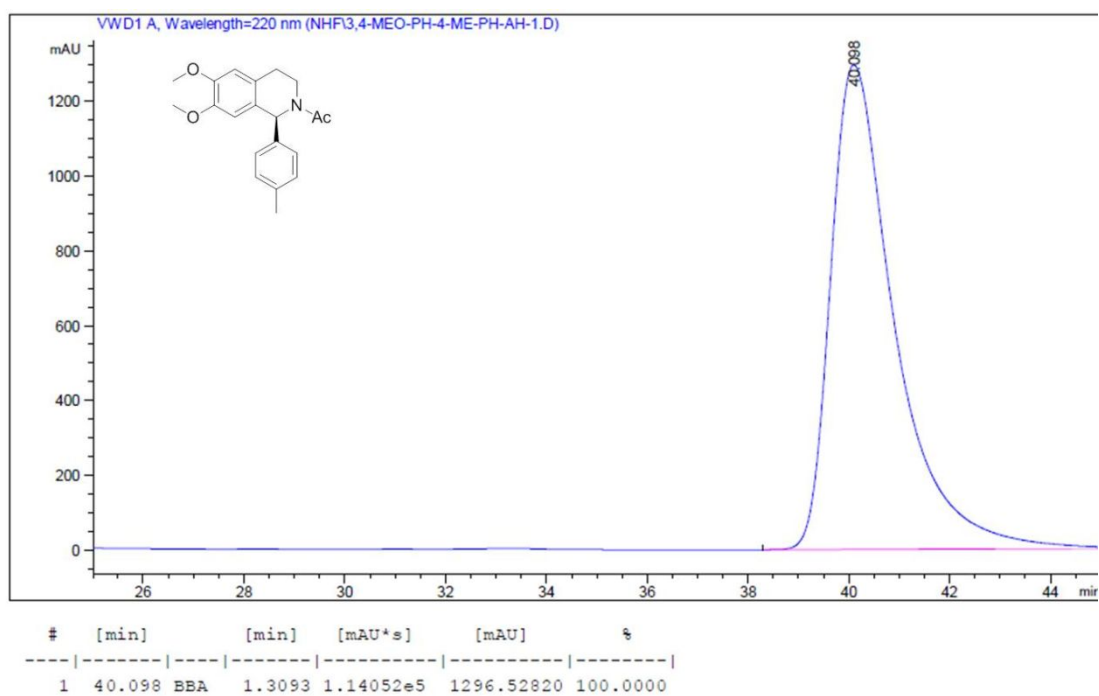
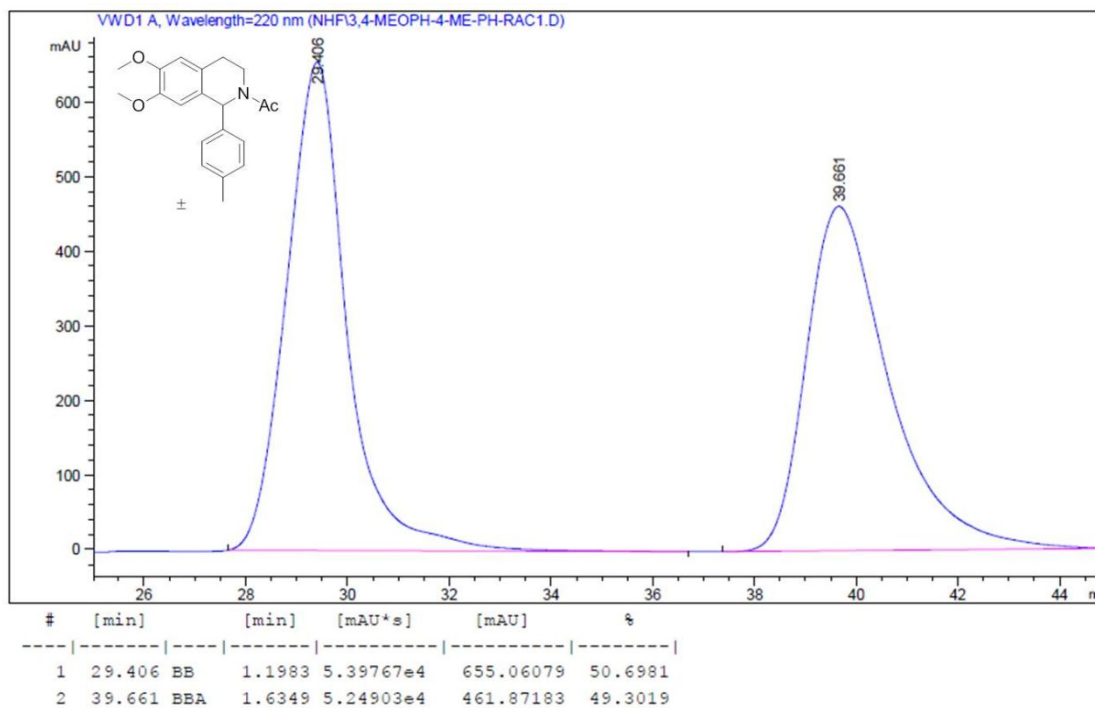


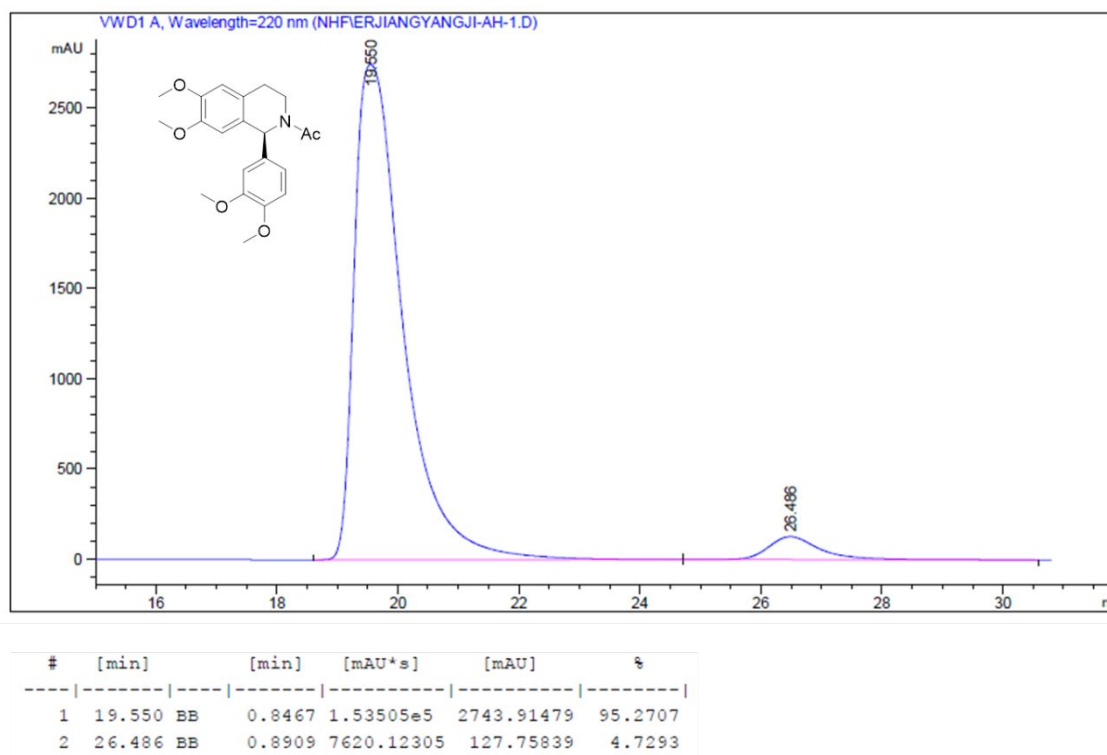
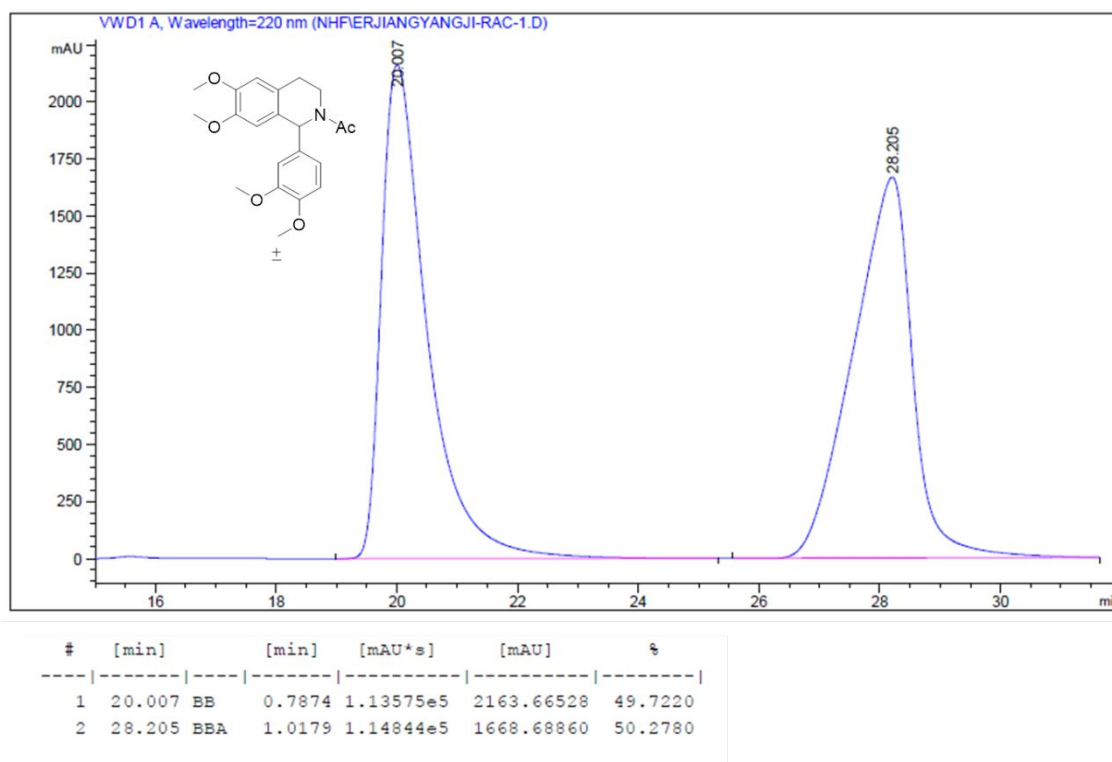


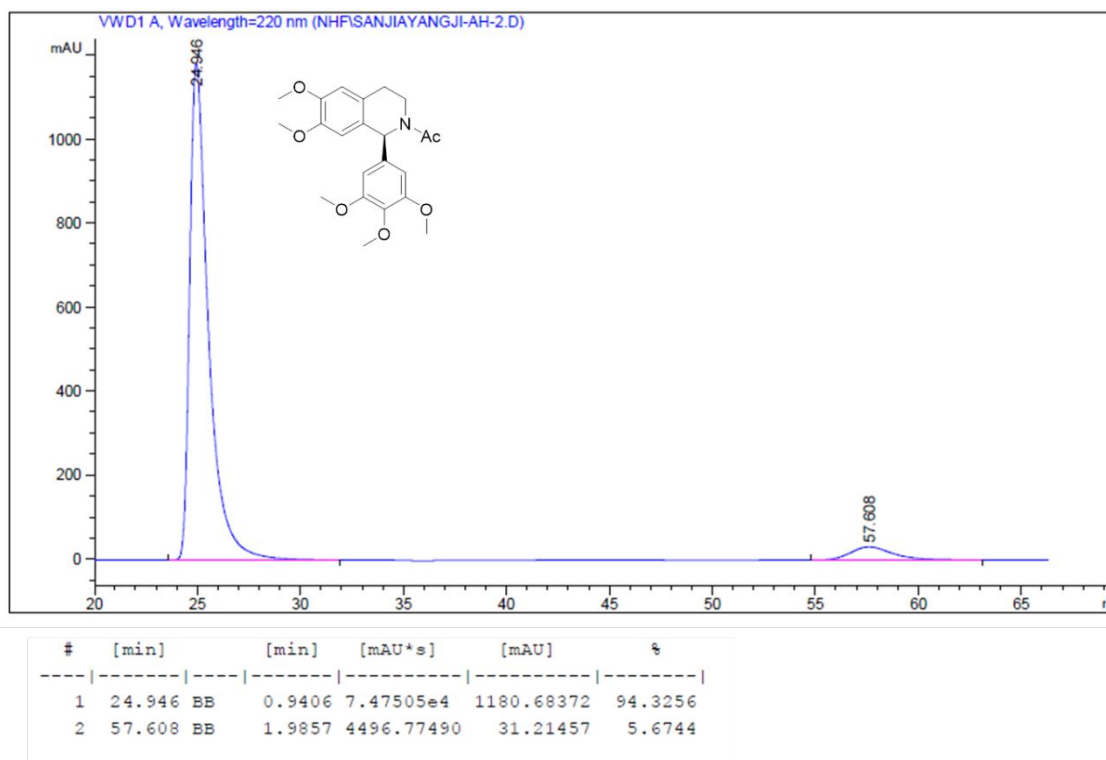
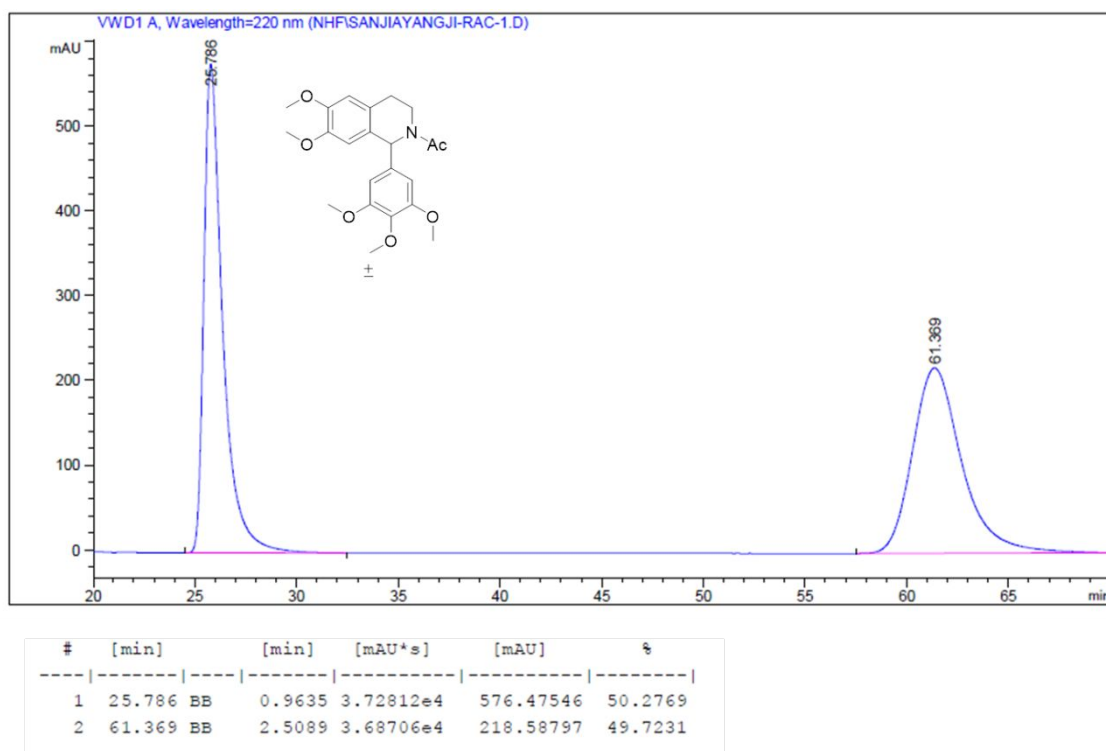


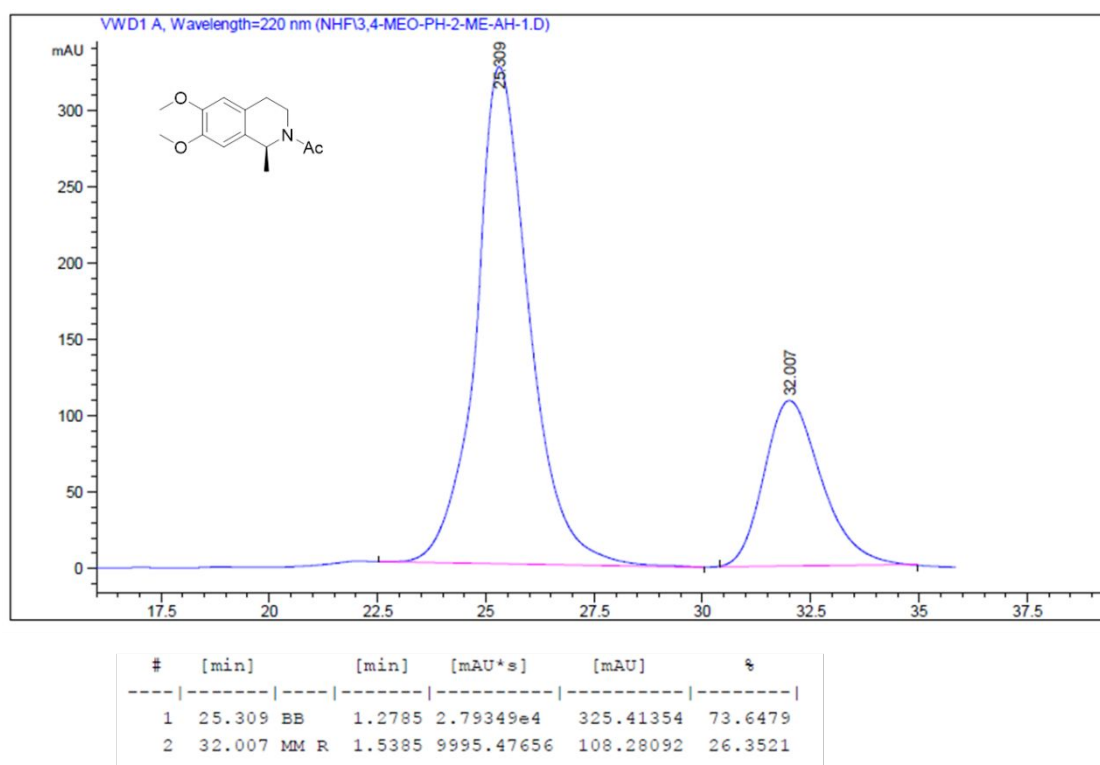
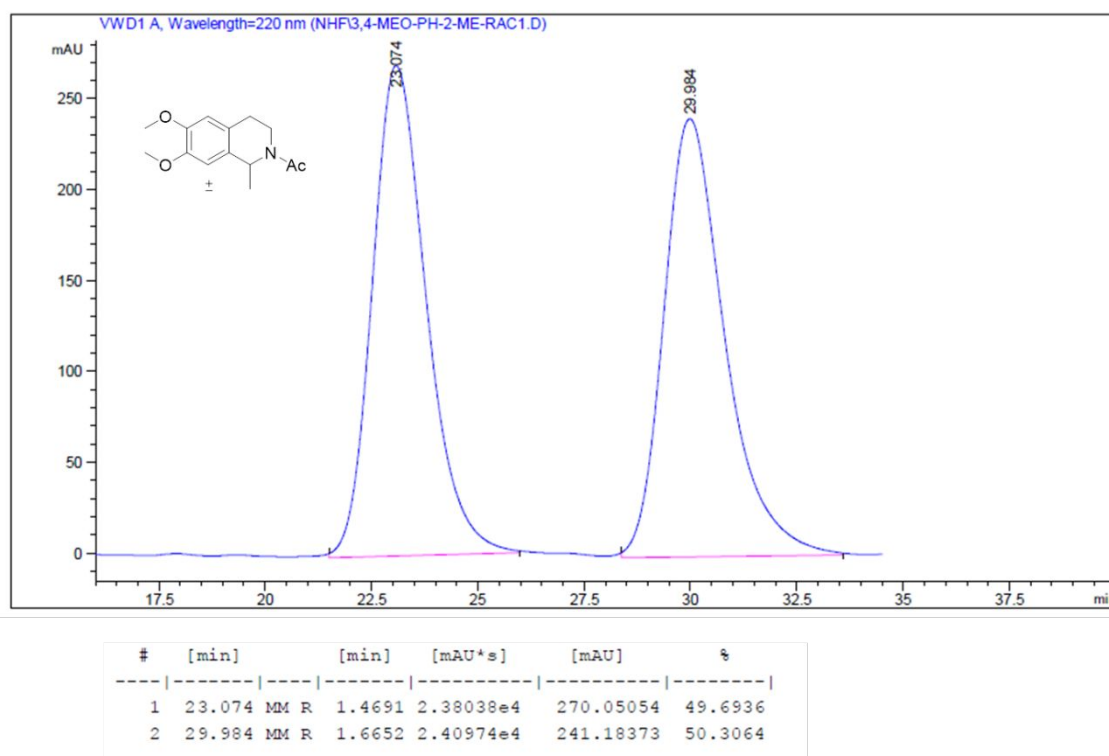


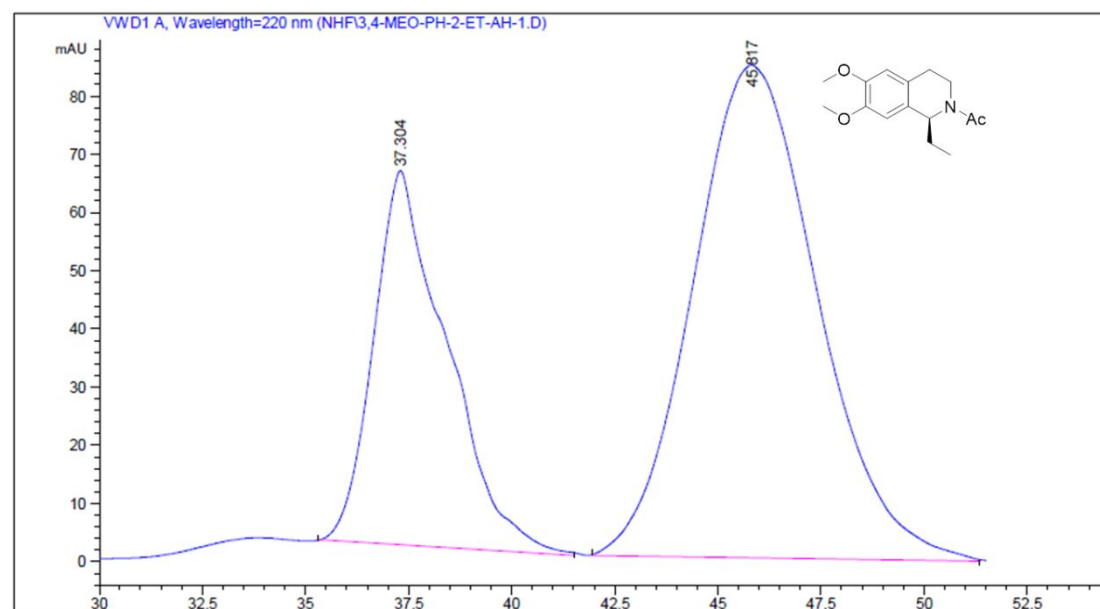
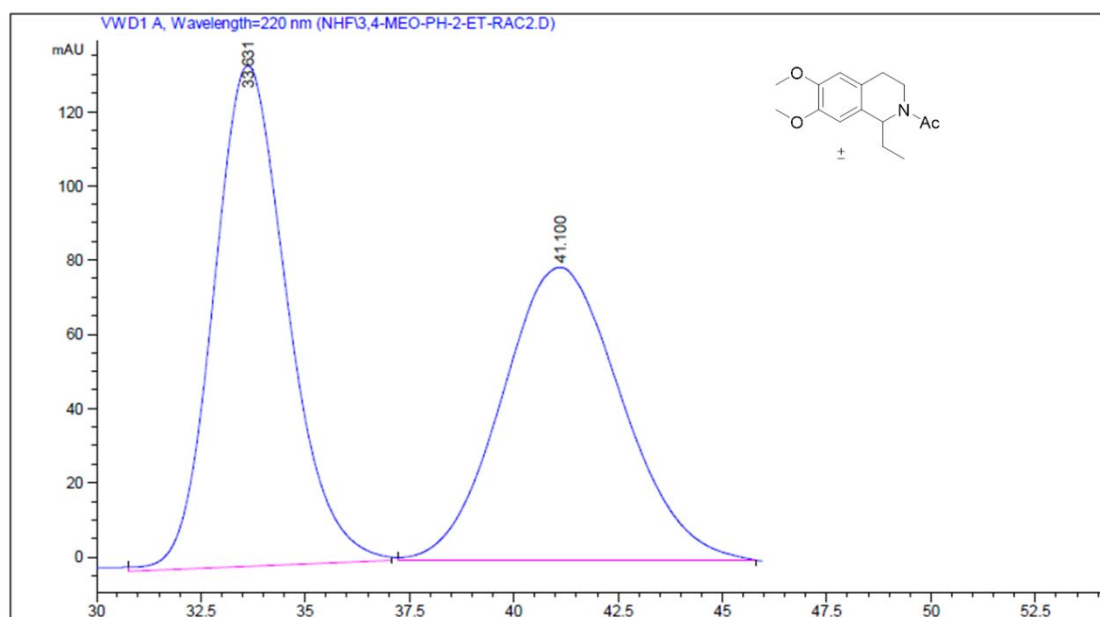












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