

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

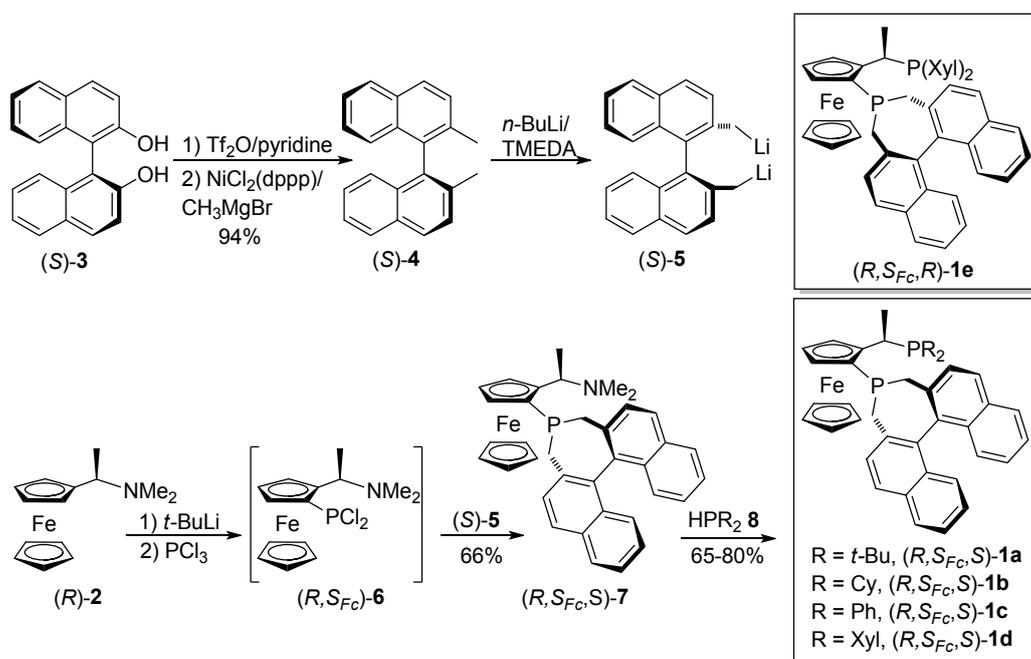
Contents

1. General remarks	S2
2. General procedure for synthesis of ligands	S2
3. General procedure for synthesis of 1-aryl-3,4-DHIQs	S7
4. Optimization of AH reaction conditions	S15
5. General procedure for AH and scaled-up catalytic hydrogenation	S16
6. NMR spectra and HRMS	S26
7. HPLC spectra	S66

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*_{Fc})-**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*_{Fc},*S*_{ax})-**7** (3.74 g, 6.6 mmol) as a yellow foam (yield: 66 %). Characterization of (*R*_C,*S*_{Fc},*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*_{Fc},*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*_{Fc},*S*_{ax})-**7**. Characterization of (*R*_C,*S*_{Fc},*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.

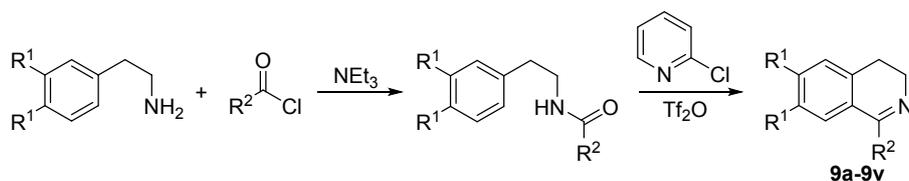
Characterization of (*R*_C,*S*_{FC},*S*_{ax})-**1c**: orange solid; 567 mg, 80%; [α]_D²⁵ -698.9 (*c* = 0.25, CHCl₃); **¹H NMR** (400 Hz, CDCl₃) δ 8.09-8.03 (m, 1H), 8.02-7.95 (m, 1H), 7.93-7.83 (m, 2H), 7.82-7.75 (m, 1H), 7.51-7.17 (m, 16H), 7.16-7.10 (m, 1H), 4.31 (s, 5H), 4.15 (s, 2H), 3.96-3.88 (m, 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.

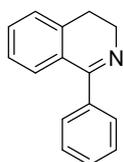
2. General procedure for synthesis of 1-aryl-3,4-DHIQs^{4,5}



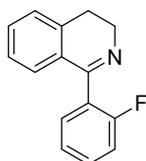
1-aryl-3,4-DHIQs (**9a-9v**) were synthesized from corresponding 2-arylethyl amine and arylcarbonyl chloride according to reported literature methods. The preparation was performed in air atmosphere. Carbonyl chloride (10.0 mmol) was slowly added to a solution of 2-arylethylamine (10.0 mmol) and triethylamine (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.

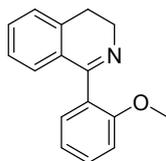
To a solution of the resulting *N*-acyl-2-arylethylamine (10.0 mmol) and 2-chloropyridine (12.0 mmol, 1.2 equiv) in CH_2Cl_2 (60 mL) was slowly added trifluoromethanesulfonic anhydride (11.0 mmol, 1.1 equiv) via syringe dropwise at -78 °C. Then the mixture was stirred at -78 °C for 10 min and slowly 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 %).



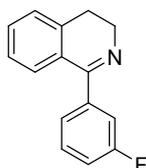
1-phenyl-3,4-dihydroisoquinoline (**9a**):⁵ light yellow liquid; 1.86 g, 90% yield; ^1H NMR (400 MHz, CDCl_3) δ 7.68-7.59 (m, 2H), 7.51-7.38 (m, 4H), 7.34-7.24 (m, 3H), 3.94-3.81 (m, 2H), 2.90-2.75 (m, 2H).



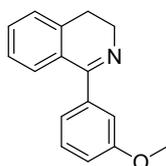
1-(2-fluorophenyl)-3,4-dihydroisoquinoline (**9b**):⁶ yellow solid; 1.82 g, 81% yield; ^1H NMR (400 MHz, DMSO) δ 7.68-7.59 (m, 2H), 7.44-7.38 (m, 1H), 7.34-7.21 (m, 4H), 6.92 (d, $J = 7.7$ Hz, 1H), 3.82-3.72 (m, 2H), 2.81-2.73 (m, 2H).



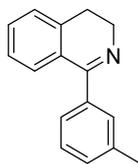
1-(2-methoxyphenyl)-3,4-dihydroisoquinoline (**9c**):⁵ yellow solid; 1.78 g; 75% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.42-7.30 (m, 3H), 7.22 (d, $J = 7.4$ Hz, 1H), 7.16 (t, $J = 7.2$ Hz, 1H), 7.07-7.01 (m, 1H), 6.99-6.93 (m, 2H), 4.05-3.75 (m, 2H), 3.68 (s, 3H), 2.94-2.78 (m, 2H).



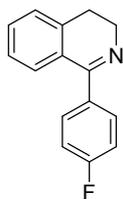
1-(3-fluorophenyl)-3,4-dihydroisoquinoline (**9d**):⁷ yellow oil; 1.91 g, 85% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.47-7.39 (m, 3H), 7.38-7.35 (m, 1H), 7.32-7.25 (m, 3H), 7.20-7.12 (m, 1H), 3.92-3.82 (m, 2H), 2.87-2.77 (m, 2H).



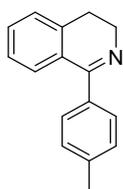
1-(3-methoxyphenyl)-3,4-dihydroisoquinoline (**9e**):⁸ yellow solid; 1.94 g, 82% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.45-7.39 (m, 1H), 7.38-7.25 (m, 4H), 7.21-7.15 (m, 2H), 7.05-7.00 (m, 1H), 3.91-3.85 (m, 2H), 3.87 (s, 3H), 2.87-2.80 (m, 2H).



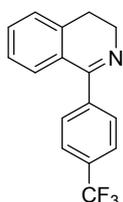
1-(3-methylphenyl)-3,4-dihydroisoquinoline (**9f**):⁵ yellow oil; 2.03 g, 92% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.50-7.45 (m, 1H), 7.45-7.37 (m, 2H), 7.36-7.24 (m, 5H), 3.93-3.83 (m, 2H), 2.88-2.79 (m, 2H), 2.42 (s, 3H).



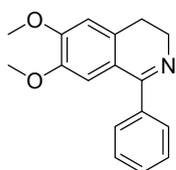
1-(4-fluorophenyl)-3,4-dihydroisoquinoline (**9g**):⁷ yellow solid; 1.98 g, 88% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.67-7.58 (m, 2H), 7.46-7.38 (m, 1H), 7.32-7.24 (m, 3H), 7.17-7.09 (m, 2H), 3.90-3.80 (m, 2H), 2.87-2.77 (m, 2H).



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).

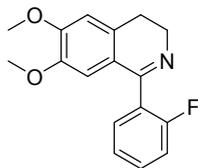


1-(4-(trifluoromethyl)phenyl)-3,4-dihydroisoquinoline (**9i**):⁵ white solid; 2.53 g, 92% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.82-7.61 (m, 4H), 7.46-7.36 (m, 1H), 7.33-7.23 (m, 2H), 7.22-7.15 (m, 1H), 3.98-3.79 (m, 2H), 2.82 (t, *J* = 7.4 Hz, 2H).

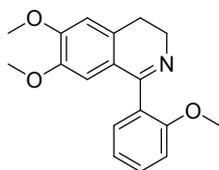


6,7-dimethoxy-1-phenyl-3,4-dihydroisoquinoline (**9j**):⁵ white solid; 2.40 g, 90% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.67-7.58 (m, 2H), 7.50-7.40 (m, 3H), 6.81 (d, *J* = 4.8 Hz, 2H), 3.97 (s, 3H), 3.84 (t, *J* = 7.5 Hz, 2H), 3.75 (s, 3H), 2.76 (t, *J* = 7.4 Hz,

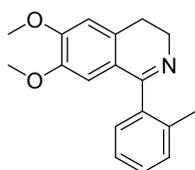
2H).



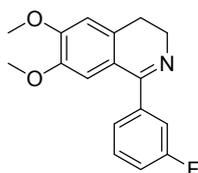
1-(2-fluorophenyl)-6,7-dimethoxy-3,4-dihydroisoquinoline (**9k**):⁹ yellow oil; 2.28 g, 80% yield; ¹H NMR (400 MHz, DMSO) δ 7.57-7.42 (m, 2H), 7.36-7.25 (m, 2H), 6.98 (s, 1H), 6.45 (s, 1H), 3.83 (s, 3H), 3.73 (t, $J = 7.7$ Hz, 2H), 3.54 (s, 3H), 2.71 (t, $J = 7.7$ Hz, 2H).



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).

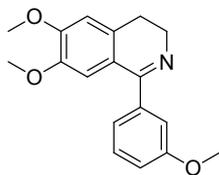


6,7-dimethoxy-1-(2-methylphenyl)-3,4-dihydroisoquinoline (**9m**):⁹ light yellow oil; 1.97 g, 70% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.35-7.22 (m, 4H), 6.78 (s, 1H), 6.45 (s, 1H), 3.95 (s, 3H), 3.98-3.76 (m, 2H), 3.65 (s, 3H), 2.81 (t, $J = 7.6$ Hz, 2H), 2.16 (s, 3H).

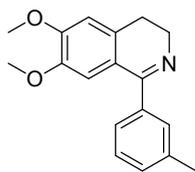


1-(3-fluorophenyl)-6,7-dimethoxy-3,4-dihydroisoquinoline (**9n**):¹⁰ white solid; 2.51 g,

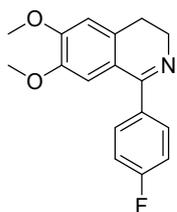
88% yield; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.46-7.33 (m, 3H), 7.21-7.12 (m, 1H), 6.80 (d, $J = 9.7$ Hz, 2H), 3.97 (s, 3H), 3.84 (t, $J = 7.6$ Hz, 2H), 3.76 (s, 3H), 2.80-2.72 (m, 2H).



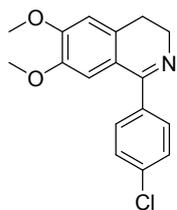
6,7-dimethoxy-1-(3-methoxyphenyl)-3,4-dihydroisoquinoline (**9o**):⁹ white solid; 2.23 g, 75% yield; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.35 (t, $J = 7.9$ Hz, 1H), 7.22-7.16 (m, 2H), 7.04-6.99 (m, 1H), 6.85 (s, 1H), 6.80 (s, 1H), 3.97 (s, 3H), 3.87 (s, 3H), 3.86-3.81 (m, 2H), 3.76 (s, 3H), 2.80-2.72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



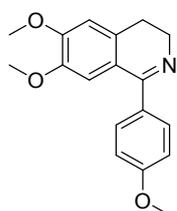
6,7-dimethoxy-1-(3-methylphenyl)-3,4-dihydroisoquinoline (**9p**):⁹ yellow oil; 2.53 g, 90% yield; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.50 (s, 1H), 7.42-7.37 (m, 1H), 7.33 (t, $J = 7.4$ Hz, 1H), 7.30-7.26 (m, 1H), 6.84 (s, 1H), 6.81 (s, 1H), 3.98 (s, 3H), 3.87-3.80 (m, 2H), 3.75 (s, 3H), 2.80-2.72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



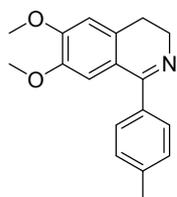
1-(4-fluorophenyl)-6,7-dimethoxy-3,4-dihydroisoquinoline (**9q**):⁹ white solid; 2.65 g, 93% yield; $^1\text{H NMR}$ (400 MHz, DMSO) δ 7.67-7.55 (m, 2H), 7.28 (t, $J = 8.5$ Hz, 2H), 7.01 (s, 1H), 6.69 (s, 1H), 3.85 (s, 3H), 3.66 (t, $J = 7.4$ Hz, 2H), 3.62 (s, 3H), 2.66 (t, $J = 7.4$ Hz, 2H).



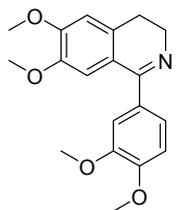
1-(4-chlorophenyl)-6,7-dimethoxy-3,4-dihydroisoquinoline (**9r**):⁷ white solid; 2.71 g, 90% yield; ¹H NMR (400 MHz, DMSO) δ 7.56 (d, J = 8.4 Hz, 2H), 7.41 (d, J = 8.4 Hz, 2H), 6.79 (s, 1H), 6.74 (s, 1H), 3.95 (s, 3H), 3.86-3.77 (m, 2H), 3.74 (s, 3H), 2.80-2.66 (m, 2H).



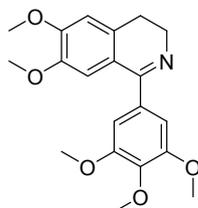
6,7-dimethoxy-1-(4-methoxyphenyl)-3,4-dihydroisoquinoline (**9s**):⁹ white solid; 2.38 g, 90% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.63-7.56 (m, 2H), 7.00-6.93 (m, 2H), 6.86 (s, 1H), 6.80 (s, 1H), 3.97 (s, 3H), 3.88 (s, 3H), 3.82-3.77 (m, 2H), 3.77 (s, 3H), 2.79-2.69 (m, 2H).



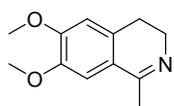
6,7-dimethoxy-1-(4-methylphenyl)-3,4-dihydroisoquinoline (**9t**):⁸ yellow solid; 1.83 g, 65% yield; ¹H NMR (400 MHz, DMSO) δ 7.50-7.42 (m, 2H), 7.29-7.21 (m, 2H), 6.99 (s, 1H), 6.72 (s, 1H), 3.84 (s, 3H), 3.67-3.62 (m, 2H), 3.60 (s, 3H), 2.68-2.60 (m, 2H), 2.37 (s, 3H).



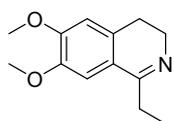
1-(3,4-dimethoxyphenyl)-6,7-dimethoxy-3,4-dihydroisoquinoline (**9u**):⁵ white solid; 3.04 g, 93% yield; ¹H NMR (400 MHz, DMSO) δ 7.24 (s, 1H), 7.16 (d, $J = 8.4$ Hz, 1H), 6.96-6.85 (m, 2H), 6.79 (d, $J = 2.1$ Hz, 1H), 3.95 (s, 3H), 3.94 (s, 3H), 3.92 (s, 3H), 3.82-3.77 (m, 2H), 3.76 (s, 3H), 2.72 (t,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



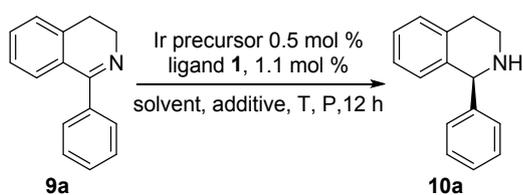
6,7-dimethoxy-1-methyl-3,4-dihydroisoquinoline (**9w**):¹¹ yellow oil; 1.44 g, 70% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.00 (s, 1H), 6.70 (s, 1H), 3.93 (d, $J = 3.5$ Hz, 6H), 3.69-3.60 (m, 2H), 2.70-2.60 (m, 2H), 2.38 (s, 3H).



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 %	<i>ee</i> ^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]BF ₄	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	toluene	I ₂ , TFA	30/50	> 99	79

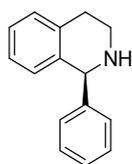
7	[Ir(COD) ₂]BArF	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	toluene	I ₂ , TFA	30/50	> 99	80
8	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	CHCl ₃	I ₂ , TFA	30/50	98	68
9	[Ir(COD)Cl] ₂	(<i>R</i> _C , <i>S</i> _{Fc} , <i>S</i> _{ax})- 1a	CH ₂ Cl ₂	I ₂ , TFA	30/50	96	56
10	[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

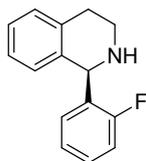
acetamides. ^dIr precursor amount is 1 mol %. ^eAdditive amount is 1 mol %. ^fReaction time is 24 h. ^gCatalyst loading is 0.1 mol %. ^hCatalyst loading is 0.02 mol %.

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

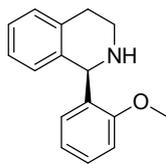
To a hydrogenation vessel was added the catalyst precursor [Ir(COD)Cl]₂ (1.6 mg, 2.4 μmol), ligand (*R_C,S_{Fc},S_{ax}*)-**1a** (3.6 mg, 5.4 μmol) and THF (1 mL) under nitrogen atmosphere. The mixture was stirred for 20 min at room temperature to give a homogeneous solution. Then imine substrates **9** (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.



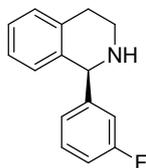
(*S*)-1-phenyl-1,2,3,4-tetrahydroisoquinoline (**10a**):⁵ white solid; 103.5 mg, 99% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.35-7.24 (m, 5H), 7.17-7.12 (m, 2H), 7.07-7.00 (m, 1H), 6.75 (d, *J* = 7.7 Hz, 1H), 5.11 (s, 1H), 3.33-3.22 (m, 1H), 3.15-2.99 (m, 2H), 2.88-2.77 (m, 1H), 1.99 (s, 1H); Enantiomeric 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; $^1\text{H NMR}$ (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); $^{13}\text{C NMR}$ (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.

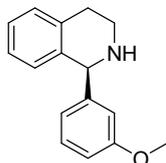


(*R*)-1-(2-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (**10c**):⁵ yellow oil; 115.9 mg, 97% yield; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.24-7.20 (m, 1H), 7.17-7.12 (m, 2H), 7.08-7.02 (m, 1H), 6.94-6.92 (m, 1H), 6.86-6.76 (m, 3H), 5.55 (s, 1H), 3.86 (s, 3H), 3.16-3.08 (m, 1H), 3.06-2.98 (m, 1H), 2.94-2.86 (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.

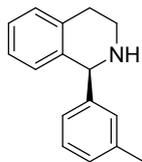


(*S*)-1-(3-fluorophenyl)-1,2,3,4-tetrahydroisoquinoline (**10d**):⁷ white solid; 112.2 mg, 98% yield; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.32-7.26 (m, 1H), 7.32-7.26 (m, 2H), 7.19-7.12 (m, 2H), 7.01-6.91 (m, 2H), 6.78-6.72 (m, 1H), 5.10 (s, 1H), 3.30-3.20 (m, 1H), 3.14-2.97 (m, 2H), 2.88-2.75 (m, 1H),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

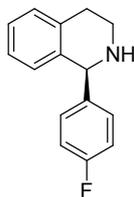
determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 95:5, 1 mL/min.



(*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.

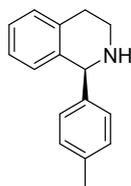


(*S*)-1-(3-methylphenyl)-1,2,3,4-tetrahydroisoquinoline (**10f**):⁵ white solid; 109.3 mg, 98% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.24-7.18 (m, 1H), 7.17-7.12 (m, 2H), 7.11-7.07 (m, 2H), 7.07-6.99 (m, 2H), 6.76 (d, *J* = 7.7 Hz, 1H), 5.06 (s, 1H), 3.24-3.22 (m, 1H), 3.14-3.00 (m, 2H), 2.88-2.78 (m, 1H), 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.

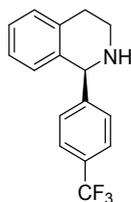


(*S*)-1-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinoline (**10g**):⁷ white solid; 112.4 mg, 99% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.27-7.19 (m, 2H), 7.18-7.12 (m, 2H), 7.07-6.95 (m, 3H), 6.72 (d, *J* = 7.7 Hz, 1H), 5.08 (s, 1H), 3.31-3.19 (m, 1H), 3.14-2.96 (m, 2H), 2.87-2.77 (m, 1H), 1.94 (s, 1H); Enantiomeric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

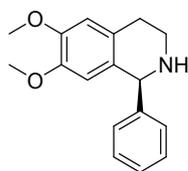
determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 95:5, 1 mL/min.



(*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.

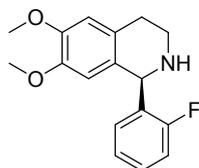


(*S*)-1-(4-(trifluoromethyl)phenyl)-1,2,3,4-tetrahydroisoquinoline (**10i**):⁵ white solid; 137.1 mg, 99% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.58 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 4.4 Hz, 2H), 7.10-7.00 (m, 1H), 6.70 (d, *J* = 7.8 Hz, 1H), 5.17 (s, 1H), 3.29-3.18 (m, 1H), 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.

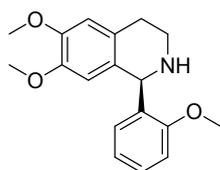


(*S*)-6,7-dimethoxy-1-phenyl-1,2,3,4-tetrahydroisoquinoline (**10j**):⁵ white solid; 131.8 mg, 98% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.39-7.30 (m, 3H), 7.28-7.25 (m, 1H), 6.66 (s, 1H), 6.27 (s, 1H), 5.08 (s, 1H), 3.90 (s, 3H), 3.66 (s, 3H), 3.30-3.20 (m, 1H), 3.12-3.03 (m, 1H), 3.01-2.89 (m, 1H), 2.83-2.72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

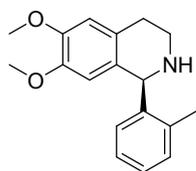
excess was determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 90:10, 1 mL/min.



(*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.

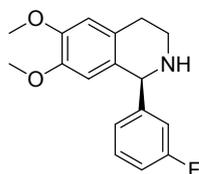


(*R*)-6,7-dimethoxy-1-(2-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (**10l**):⁹ brown oil; 140.5 mg, 94% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.25-7.20 (m, 1H), 6.93 (d, *J* = 7.8 Hz, 1H), 6.85-6.76 (m, 2H), 6.64 (s, 1H), 6.32 (s, 1H), 5.49 (s, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.68 (s, 3H), 3.09-2.93 (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.

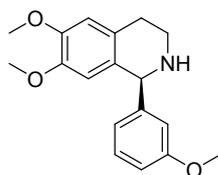


(*S*)-6,7-dimethoxy-1-(2-methylphenyl)-1,2,3,4-tetrahydroisoquinoline (**10m**):⁹ brown oil; 133.0 mg, 94% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.22-7.14 (m, 2H), 7.12-7.07 (m, 1H), 6.98 (d, *J* = 7.4 Hz, 1H), 6.63 (s, 1H), 6.19 (s, 1H), 5.28 (s, 1H), 3.88 (s, 3H), 3.63 (s, 3H), 3.26-3.18 (m, 1H), 3.09-2.99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

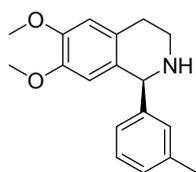
2.80-2.70 (m, 1H), 2.43 (s, 3H), 1.94 (s, 1H); Enantiomeric excess was determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 92:8, 1 mL/min.



(*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.

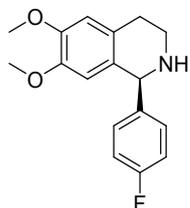


(*S*)-6,7-dimethoxy-1-(3-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (**10o**):⁸ yellow solid; 145.0 mg, 97% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.29-7.18 (m, 1H), 6.88-6.74 (m, 3H), 6.63 (s, 1H), 6.27 (s, 1H), 5.02 (s, 1H), 3.87 (s, 3H), 3.78 (s, 3H), 3.65 (s, 3H), 3.26-3.16 (m, 1H), 3.08-2.98 (m, 1H), 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.

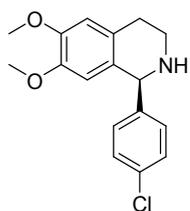


(*S*)-6,7-dimethoxy-1-(3-methylphenyl)-1,2,3,4-tetrahydroisoquinoline (**10p**):⁹ yellow solid; 138.7 mg, 98% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.26-7.20 (m, 1H), 7.14-7.08 (m, 2H), 7.07-7.02 (m, 1H), 6.66 (s, 1H), 6.28 (s, 1H), 5.05 (s, 1H), 3.90 (s,

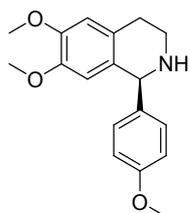
3H), 3.67 (s, 3H), 3.28-3.19 (m, 1H), 3.11-2.90 (m, 2H), 2.85-2.73 (m, 1H), 2.35 (s, 3H), 2.19 (s, 1H); Enantiomeric excess was determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 90:10, 1 mL/min.



(*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.

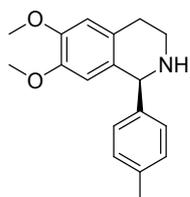


(*S*)-1-(4-chlorophenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (**10r**):⁷ colorless oil; 149.9 mg, 99% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.28 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 8.5 Hz, 2H), 6.63 (s, 1H), 6.20 (s, 1H), 5.02 (s, 1H), 3.86 (s, 3H), 3.64 (s, 3H), 3.23-3.13 (m, 1H), 3.08-2.98 (m, 1H), 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.

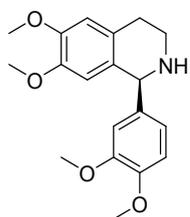


(*S*)-6,7-dimethoxy-1-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (**10s**):⁹ yellow

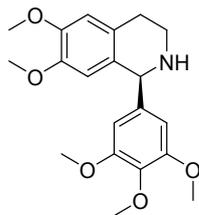
solid; 146.5 mg, 98% yield; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.22-7.14 (m, 2H), 6.90-6.80 (m, 2H), 6.62 (s, 1H), 6.25 (s, 1H), 5.00 (s, 1H), 3.87 (s, 3H), 3.80 (s, 3H), 3.65 (s, 3H), 3.26-3.16 (m, 1H), 3.10-2.98 (m, 1H), 2.97-2.86 (m, 1H), 2.79-2.69 (m, 1H), 1.91 (s, 1H); Enantiomeric excess was determined by HPLC for the corresponding acetamide, Chiralpak AD-H column, Hex/IPA = 85:15, 1 mL/min.



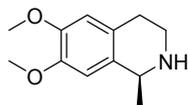
(*S*)-6,7-dimethoxy-1-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (**10t**):⁸ yellow solid; 138.7 mg, 98% yield; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.22-7.10 (m, 4H), 6.65 (s, 1H), 6.28 (s, 1H), 5.05 (s, 1H), 3.90 (s, 3H), 3.67 (s, 3H), 3.26-3.17 (m, 1H), 3.10-3.01 (m, 1H), 2.99-2.89 (m, 1H), 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.



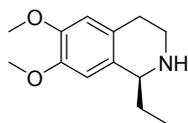
(*S*)-1-(3,4-dimethoxyphenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (**10u**):⁵ white solid; 162.9 mg, 99% yield; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 6.87-6.74 (m, 3H), 6.63 (s, 1H), 6.27 (s, 1H), 4.98 (s, 1H), 3.86 (s, 6H), 3.82 (s, 3H), 3.64 (s, 3H), 3.30-3.15 (m, 1H), 3.10-3.00 (m, 1H), 2.99-2.88 (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.



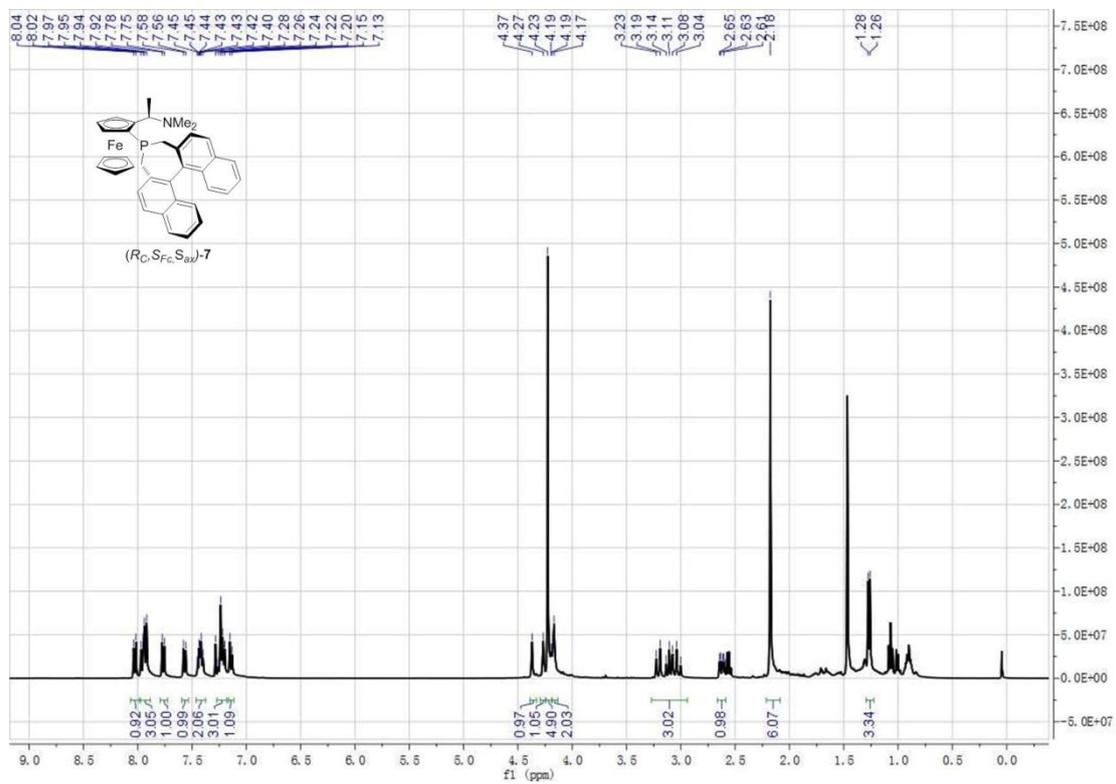
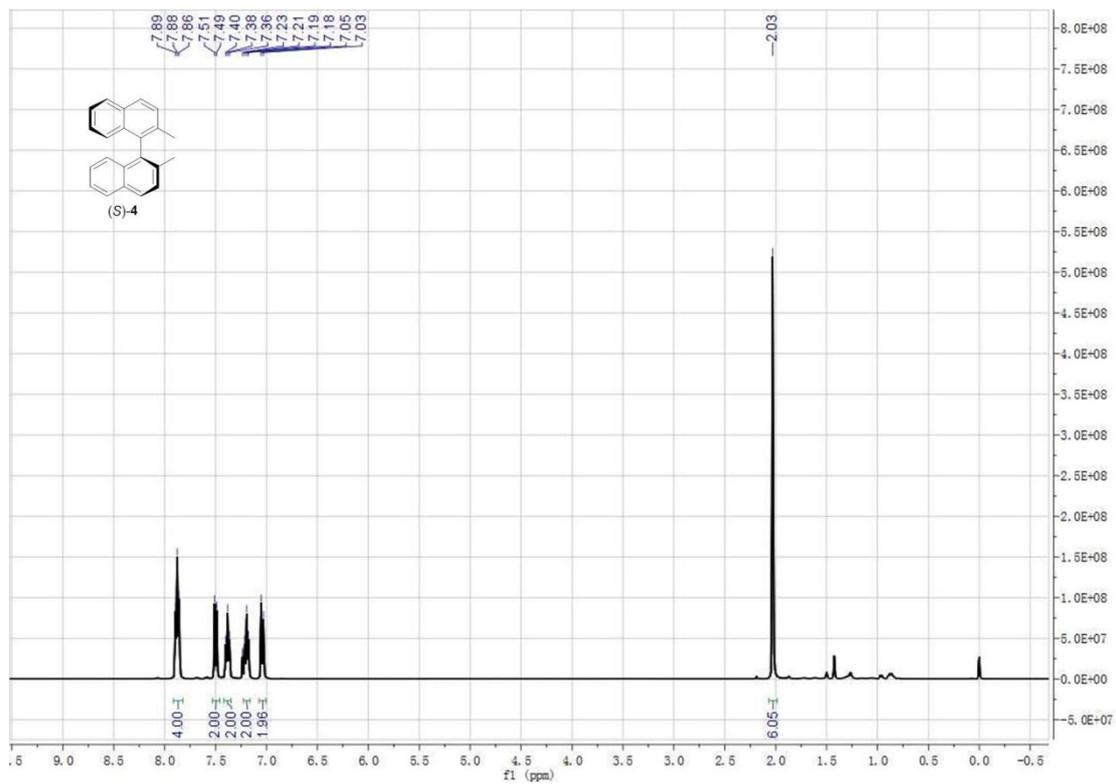
(*S*)-6,7-dimethoxy-1-methyl-1,2,3,4-tetrahydroisoquinoline (**10w**):¹¹ yellow oil; 101.4 mg, 98% yield; ¹H NMR (400 MHz, CDCl₃) δ 6.63 (s, 1H), 6.57 (s, 1H), 4.10-4.00 (m, 1H), 3.86 (s, 6H), 3.41-3.15 (m, 1H), 3.06-2.94 (m, 1H), 2.85-2.72 (m, 1H), 2.70-2.60 (m, 1H), 1.74 (s, 1H), 1.44 (d, *J* = 6.7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

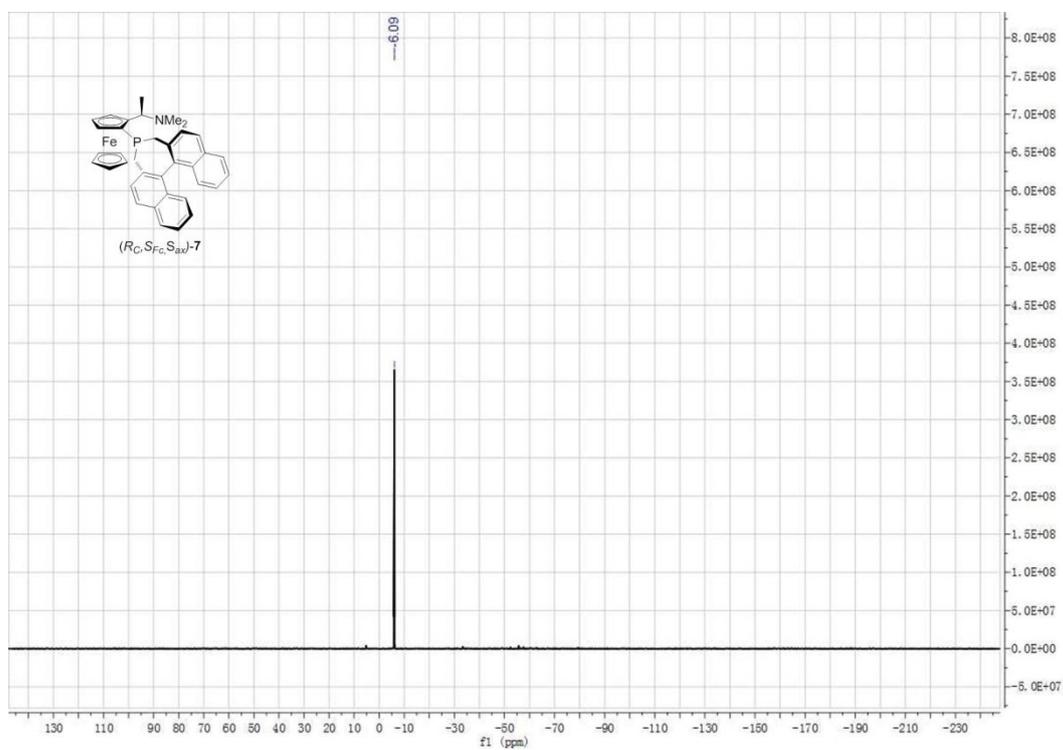
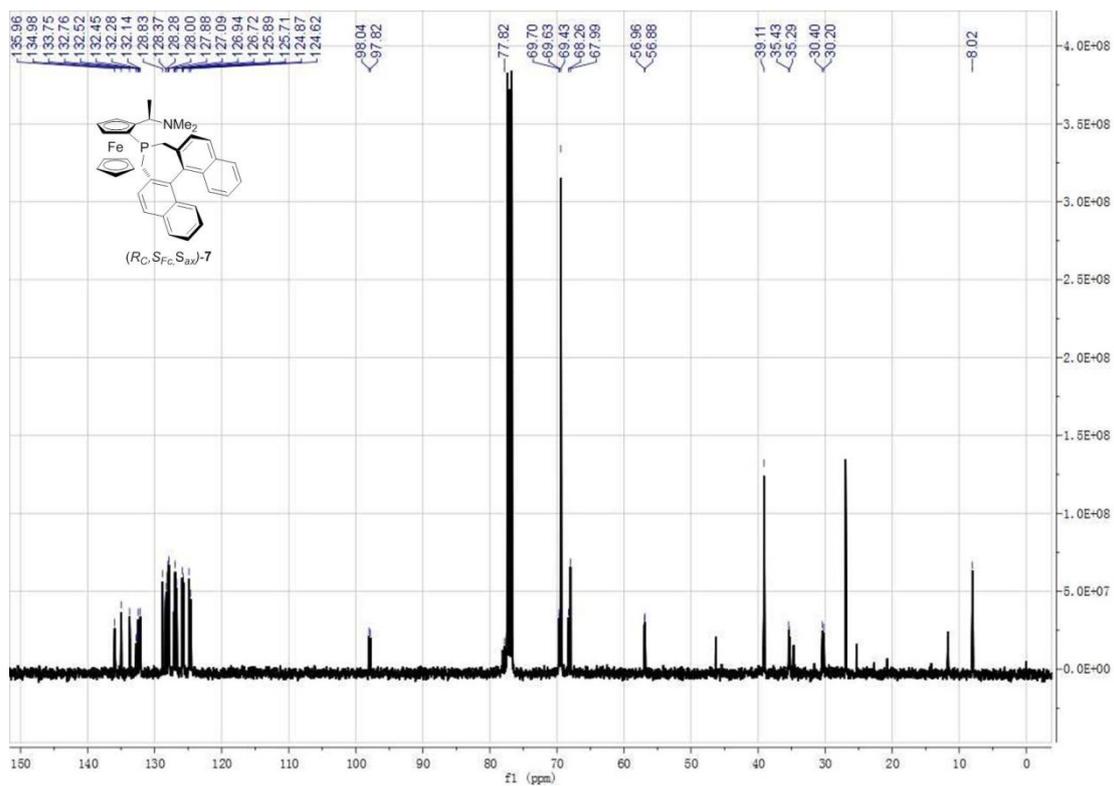


(*S*)-6,7-dimethoxy-1-ethyl-1,2,3,4-tetrahydroisoquinoline (**10x**):¹¹ yellow oil; 108.3 mg, 98% yield; ¹H NMR (400 MHz, CDCl₃) δ 6.62 (s, 1H), 6.57 (s, 1H), 3.85 (s, 6H), 3.87-3.81 (m, 1H), 3.31-3.14 (m, 1H), 3.01-2.91 (m, 1H), 2.80-2.70 (m, 1H), 2.70-2.59 (m, 1H), 1.97-1.82 (m, 1H), 1.77-1.57 (m, 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.

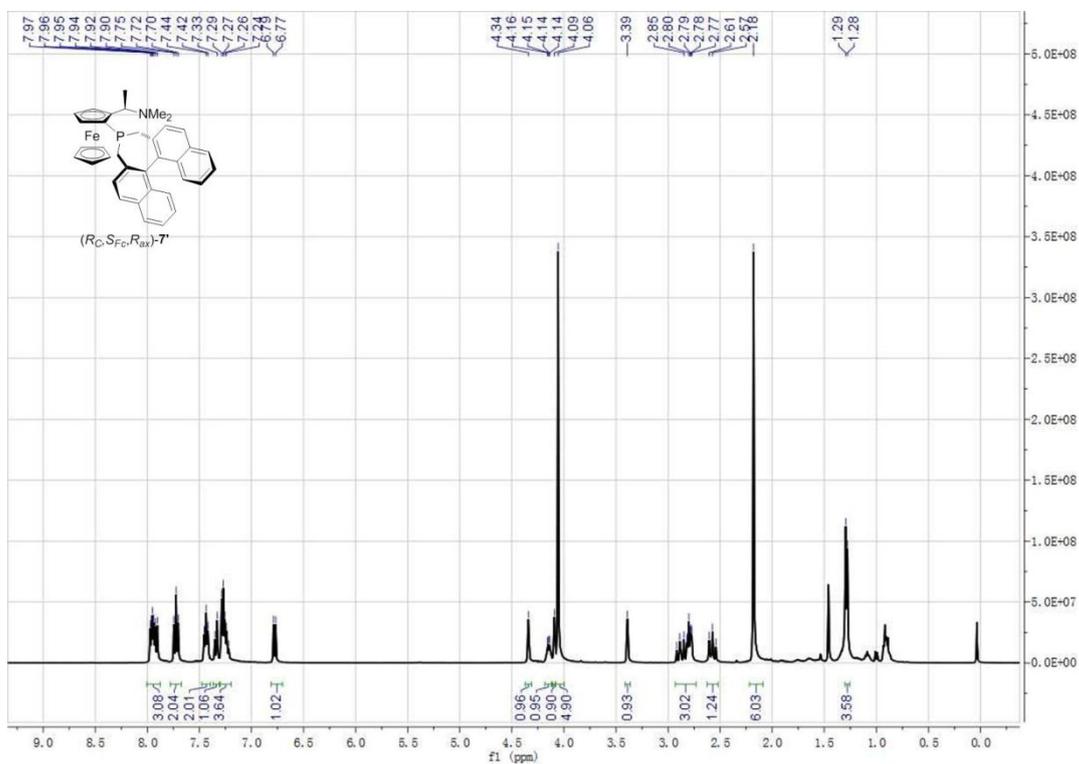
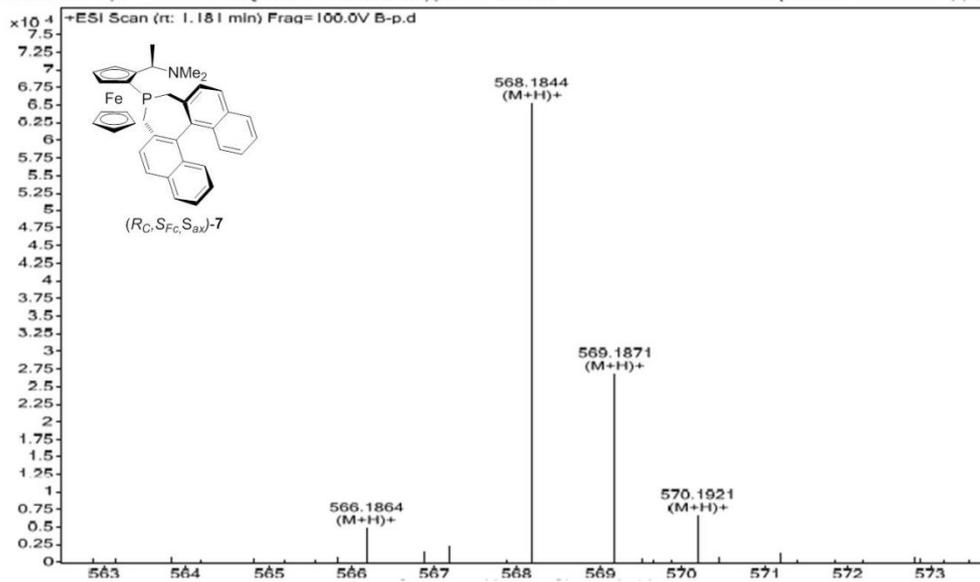
Gram-scale catalytic hydrogenation: According to the above procedure, the catalyst solution was prepared with $[\text{Ir}(\text{COD})\text{Cl}]_2$ (1.6 mg, 2.4 μmol), ligand (R_C, S_{Fc}, S_{ax})-**1a** (3.6 mg, 5.4 μmol) and THF (1 mL) under nitrogen atmosphere. To a hydrogenation vessel was added a 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*).

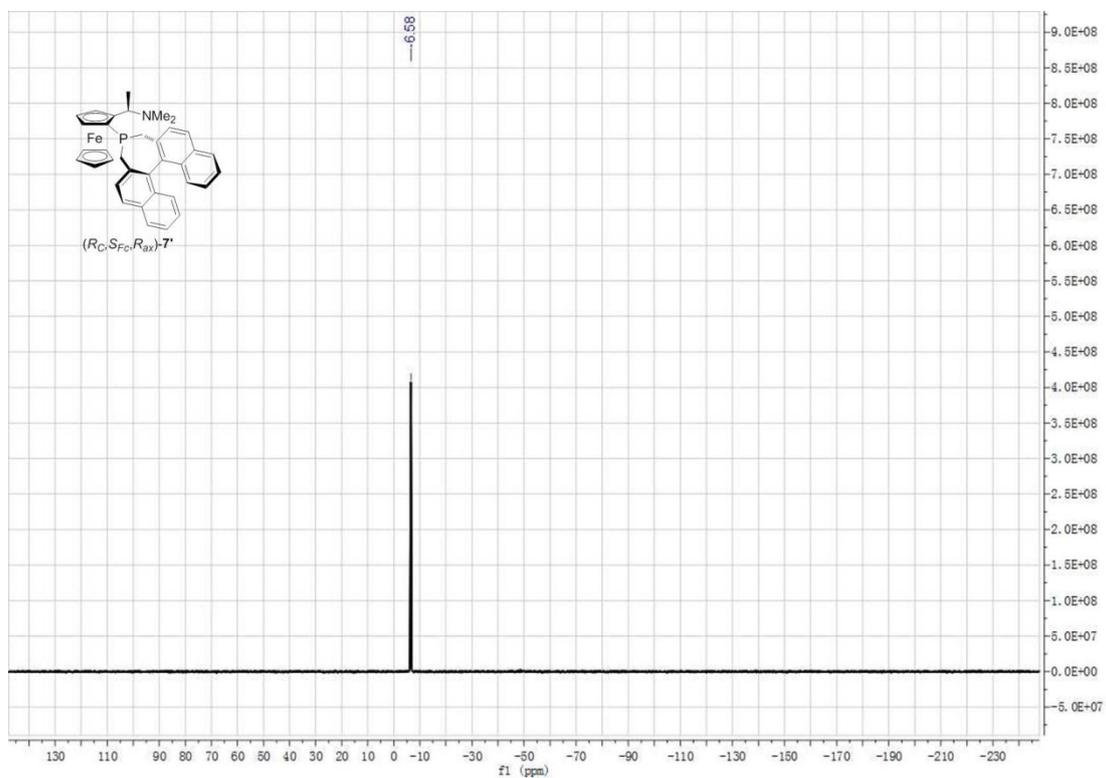
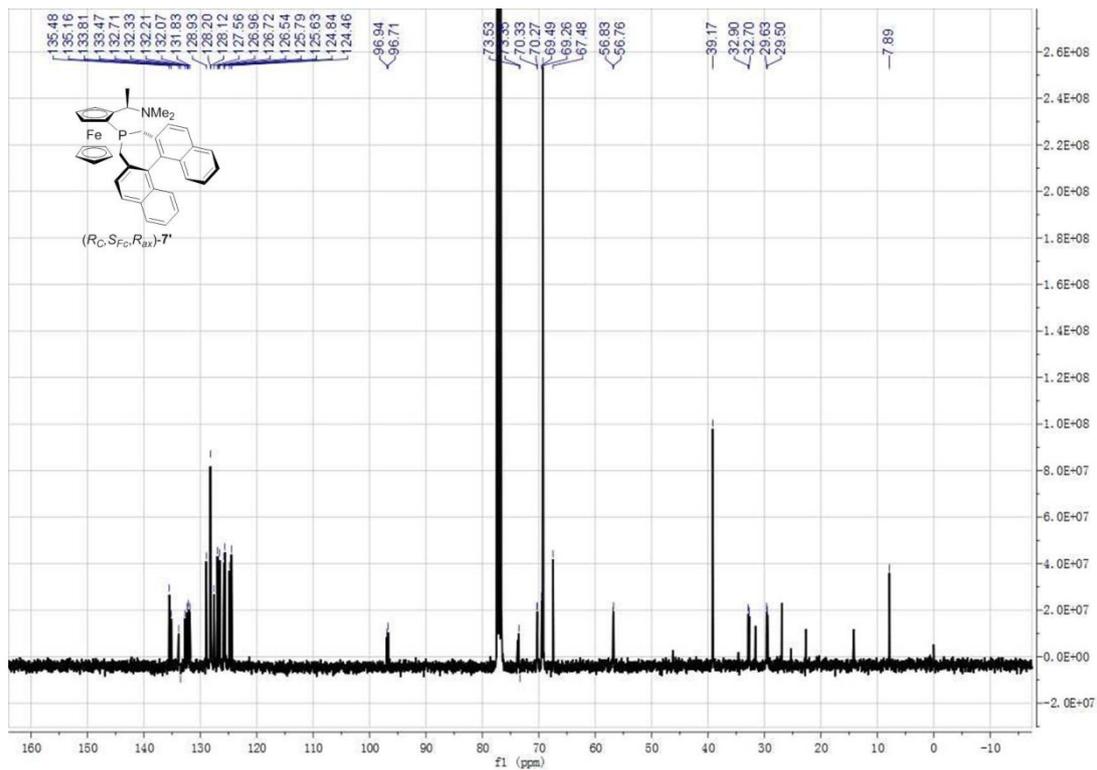
6. NMR spectra and HRMS



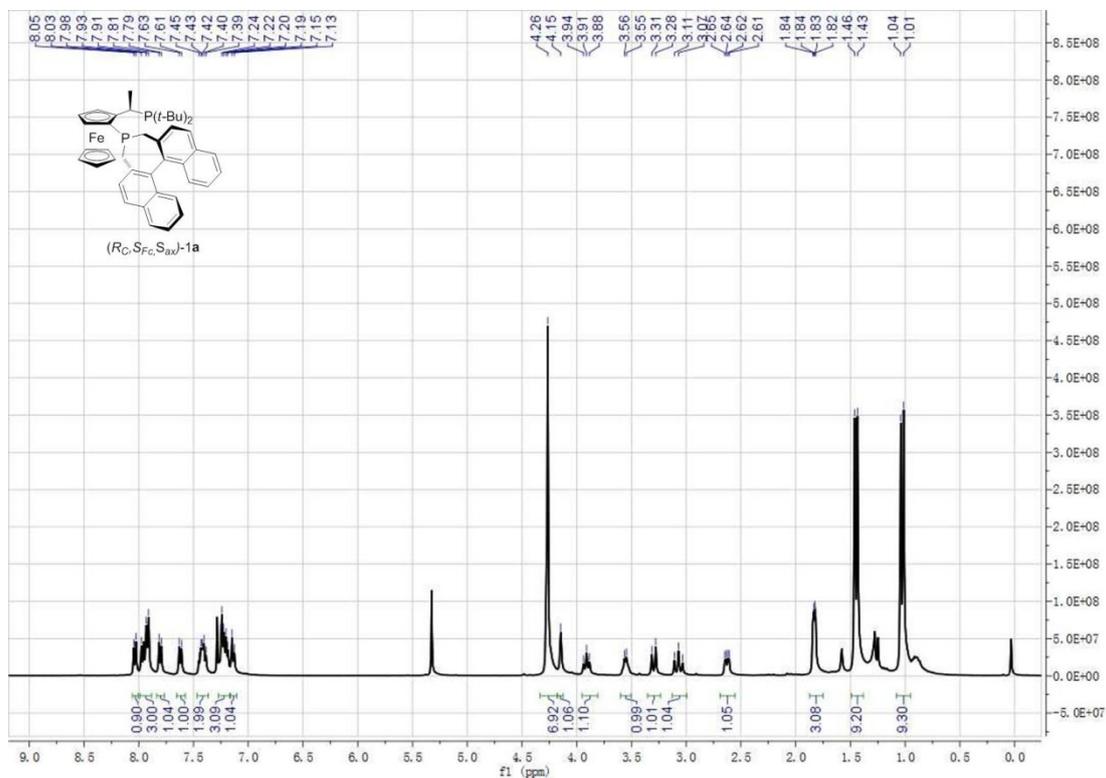
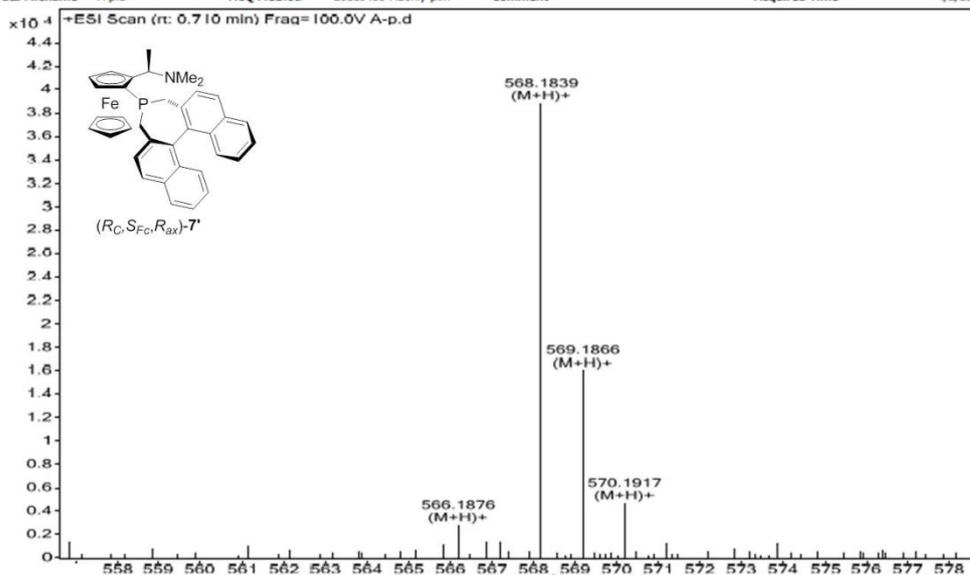


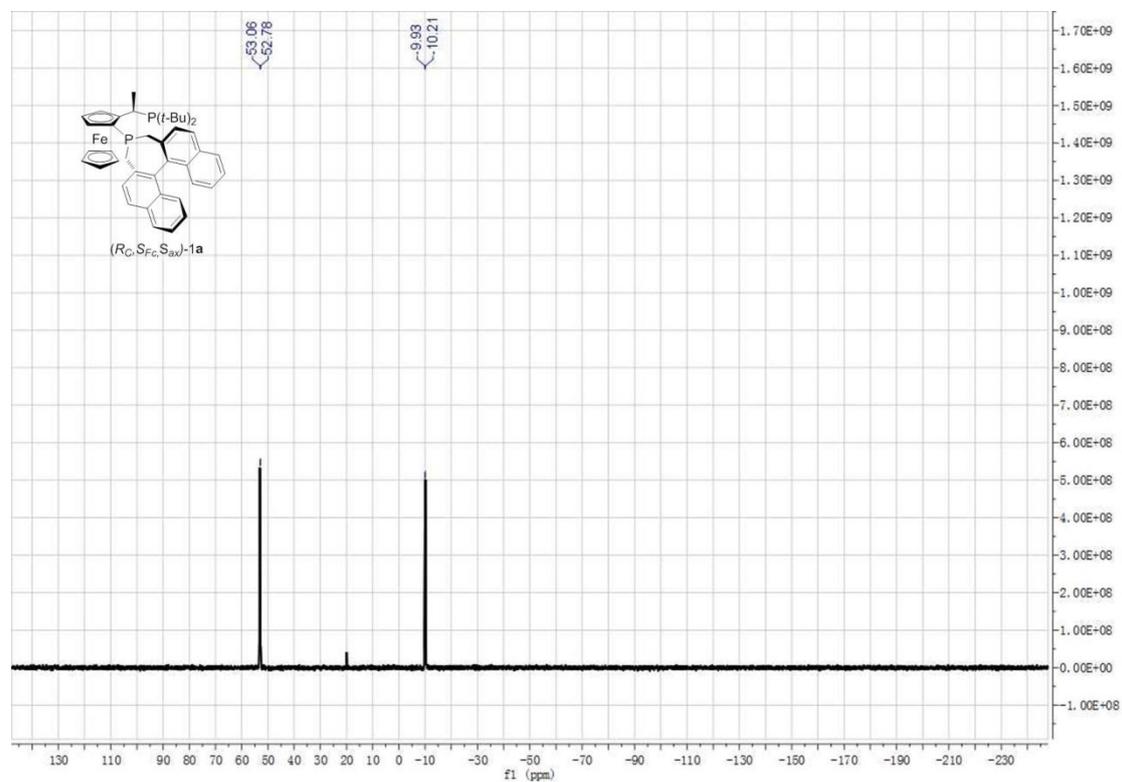
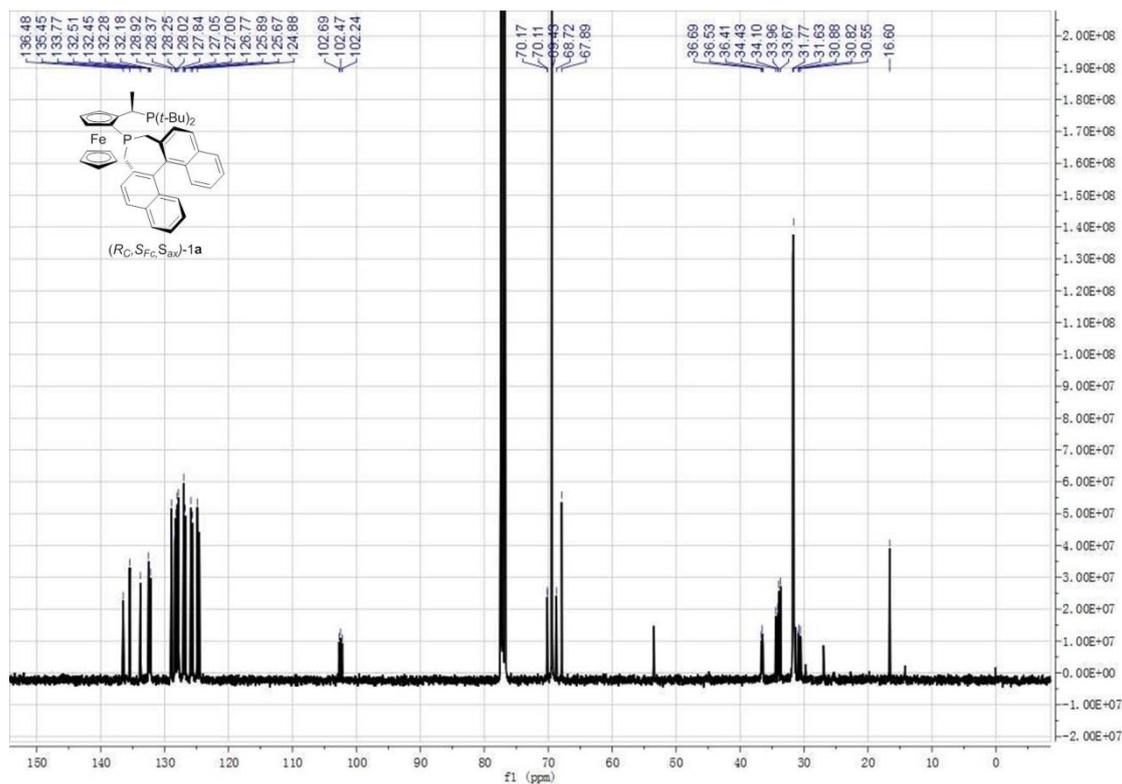
Sample Name	0.1	Position	P2e3	Instrument Name	Instrument 1	User Name	QTOF-PCQTOF
Inj Vol	B-p.d	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	B-p.d	ACQ Method	20110418-MOnly-p.m	Comment		Acquired Time	4/2/2018 4:16:02 PM



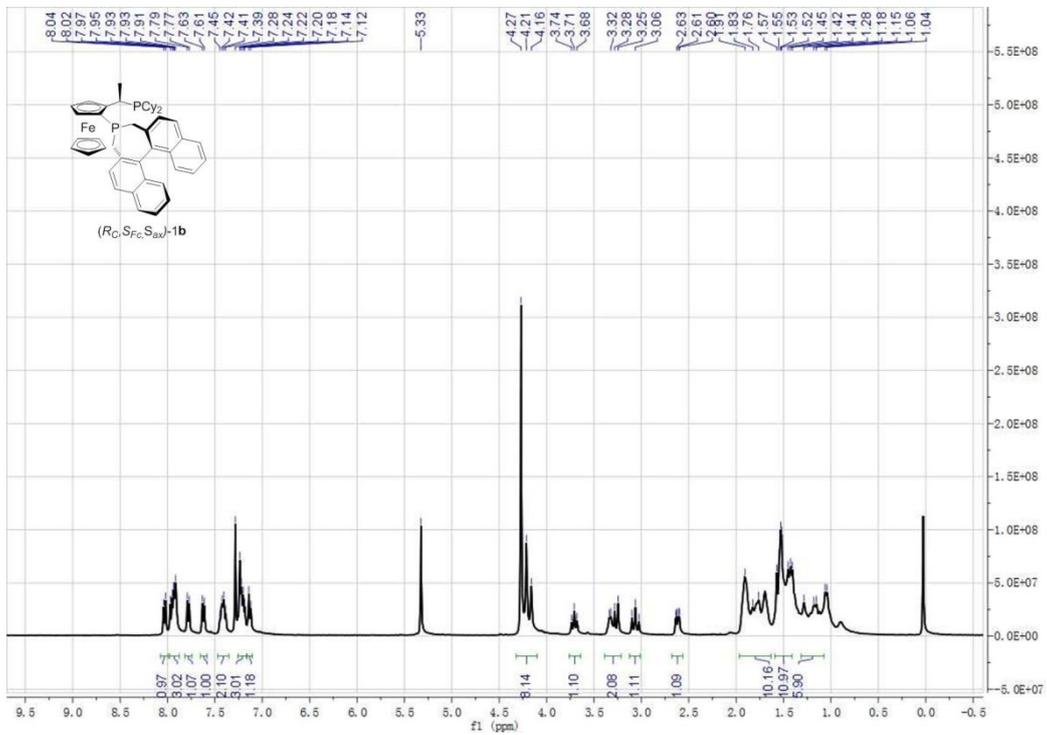
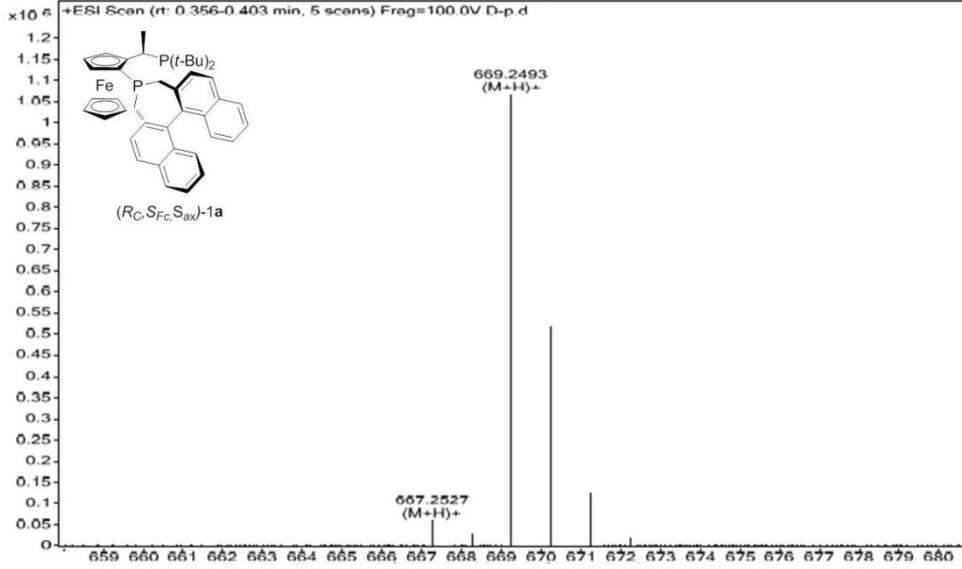


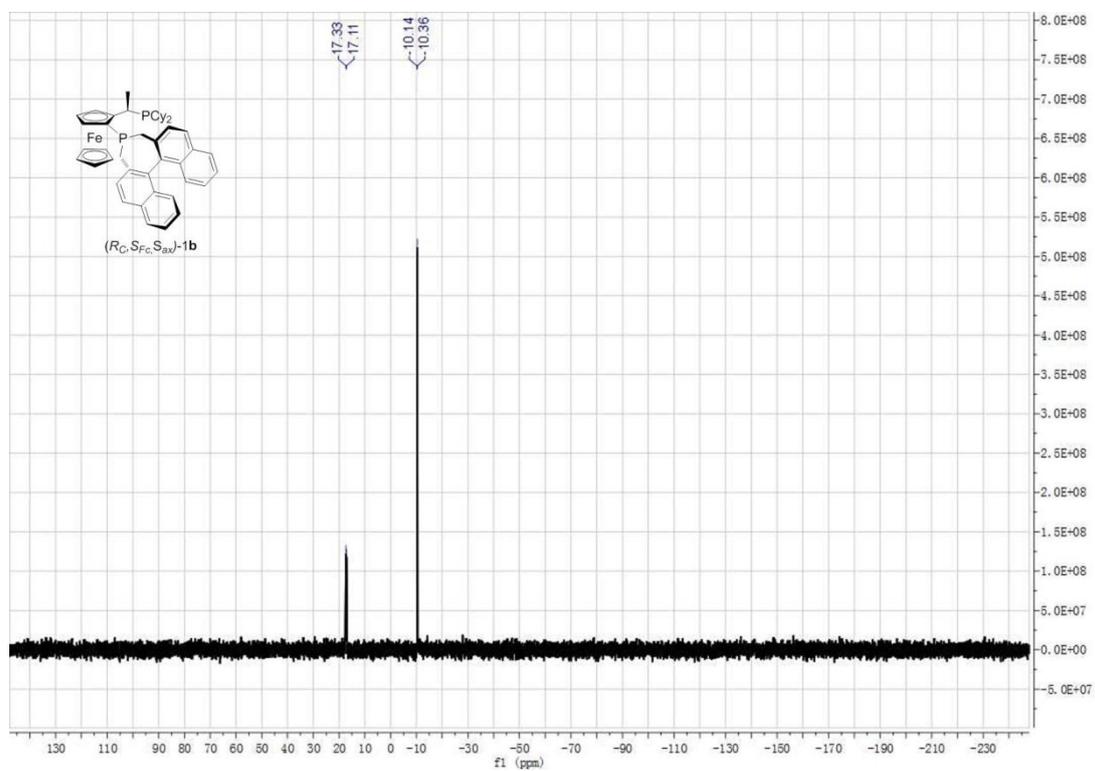
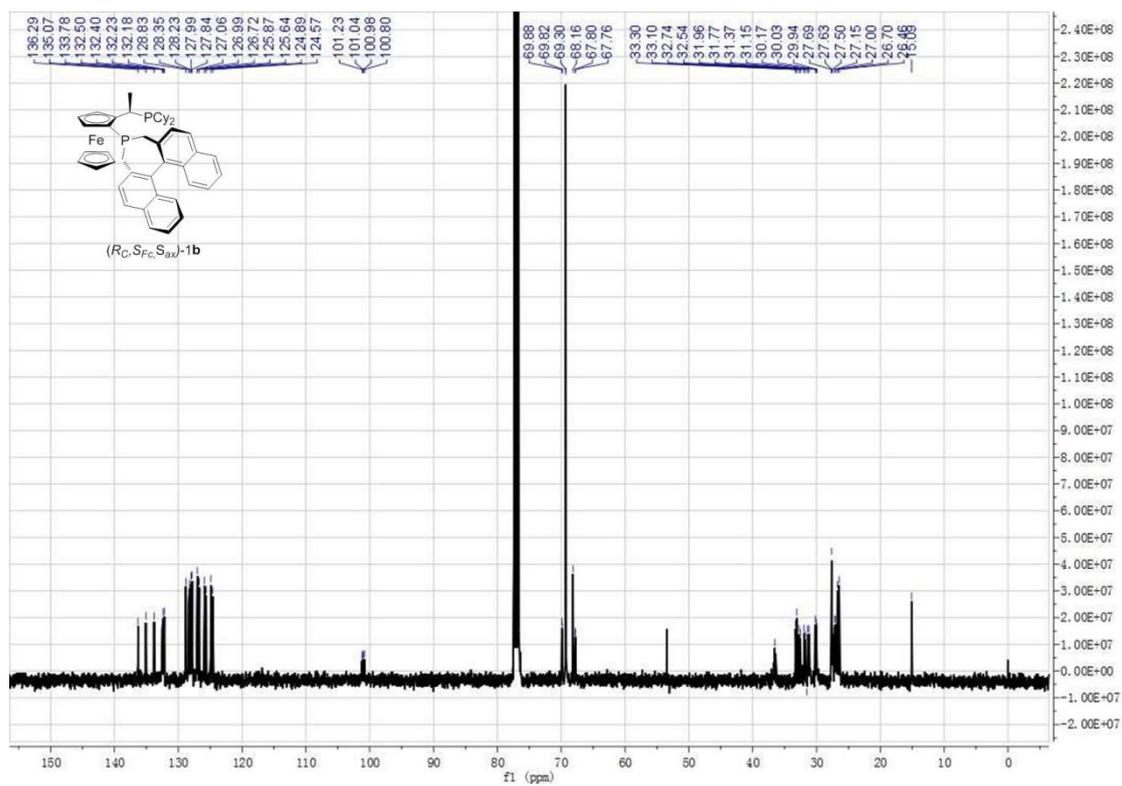
Sample Name		Position	P2e2	Instrument Name	Instrument 1	User Name	QTOF-PC/QTOF
Inj Vol	0.2	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	A-p.d	ACQ Method	20110418-MOnly-p.m	Comment		Acquired Time	4/2/2018 4:25:50 PM



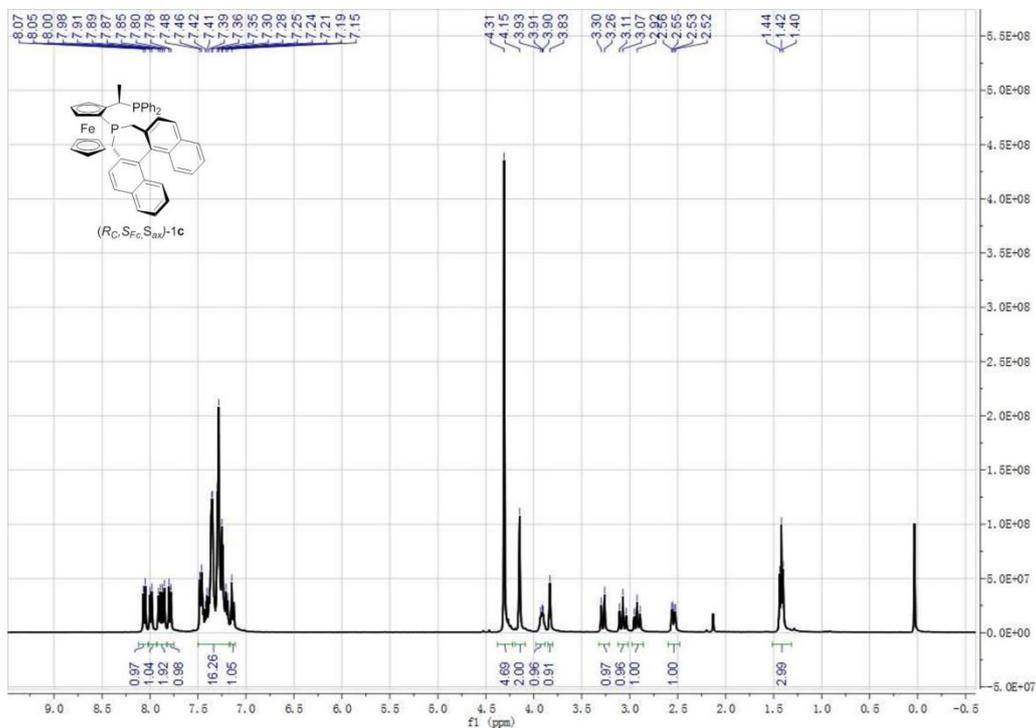
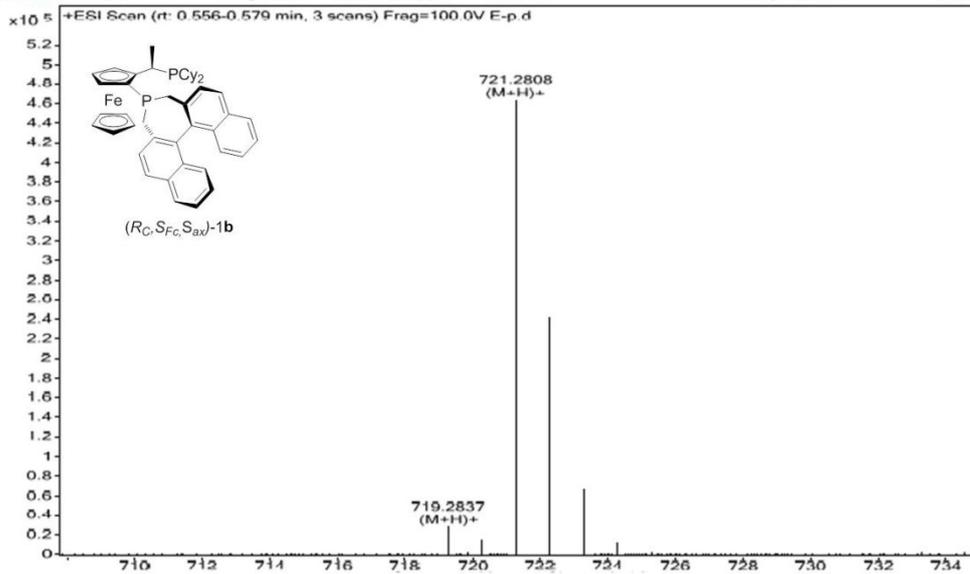


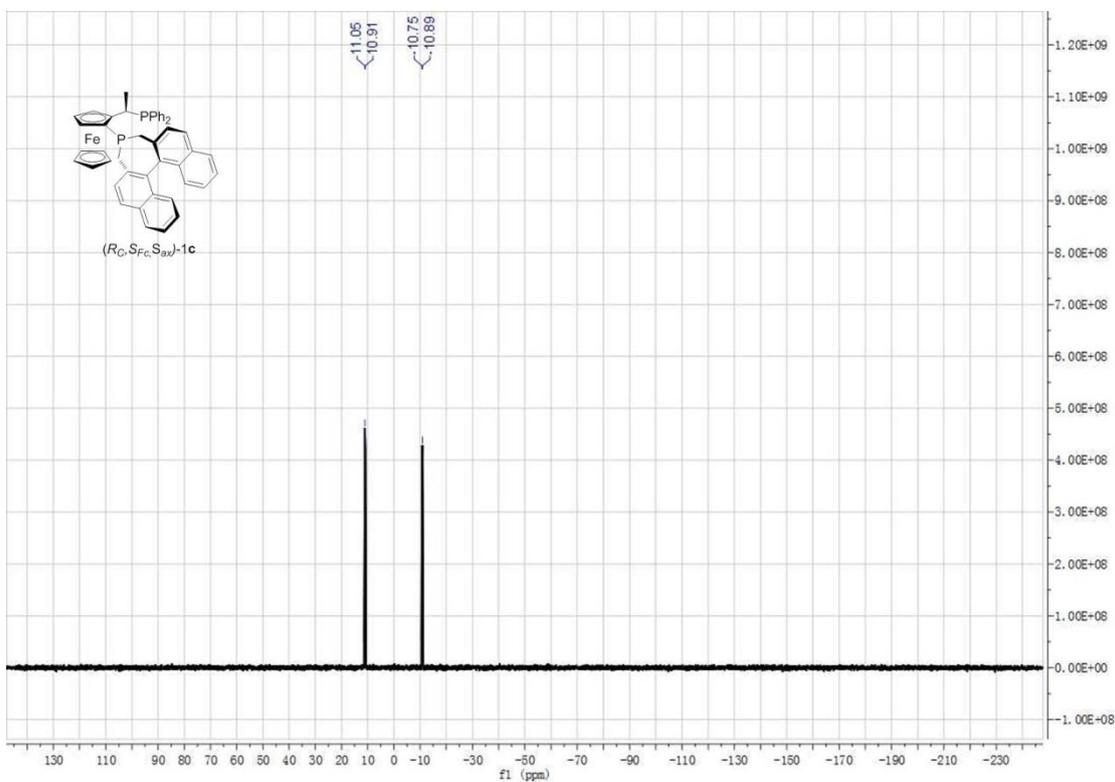
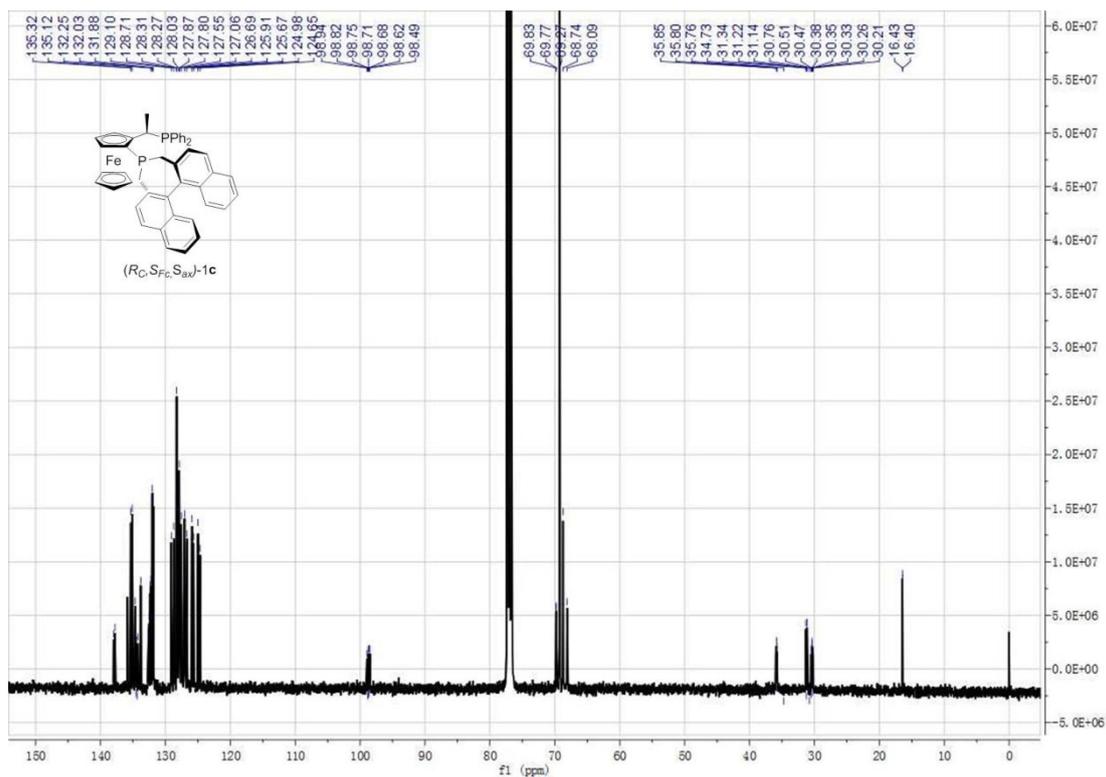
Sample Name	0.1	Position	P2e5	Instrument Name	Instrument 1	User Name	QTOF-PCQTOF
Inj Vol	0.1	Inj Position		Sample Type	Sample	IRM Calibration Status	Success
Data Filename	D-p.d	ACQ Method	20110418-M5only-p.m	Comment		Acquired Time	4/2/2018 4:31:43 PM





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	20110418-MOnly-p.m	Comment	Acquired Time	4/2/2018 4:34:44 PM





Sample Name
User Name
Sample Type
ACQ Method

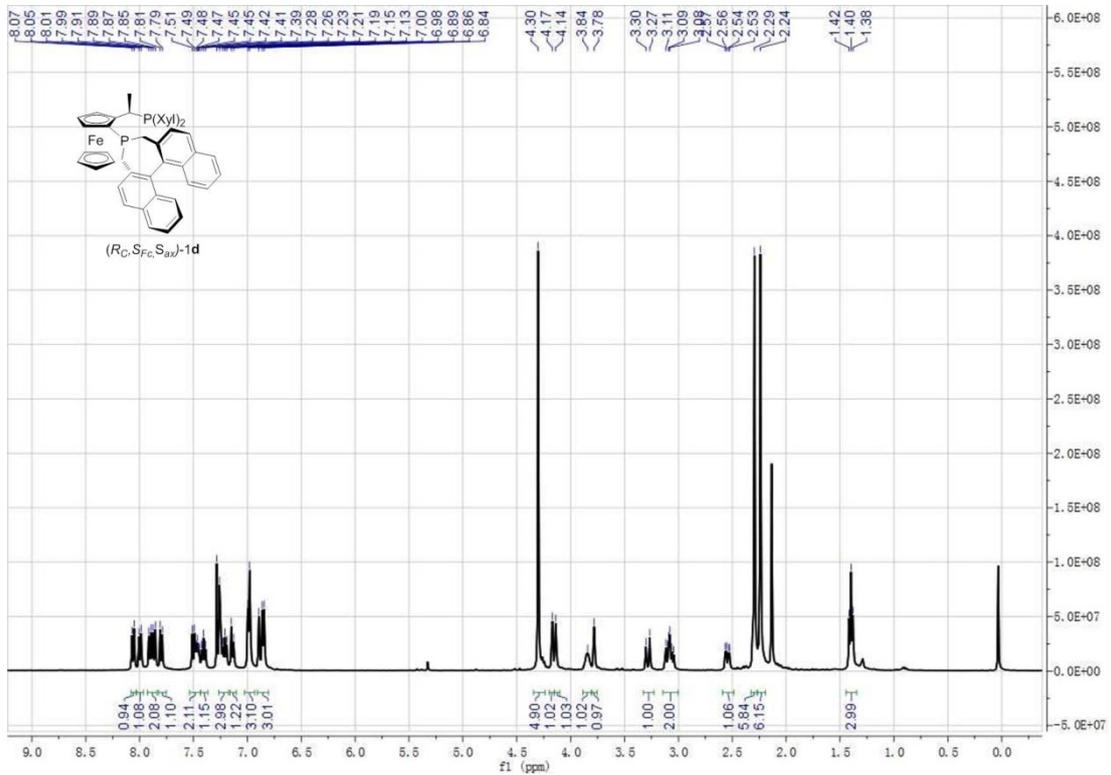
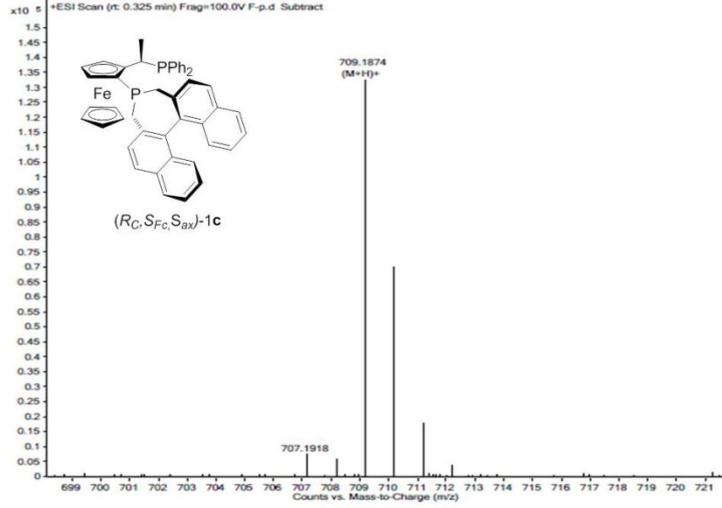
QTOF-PC/QTOF
Sample:
20110418-M50nly-p.m

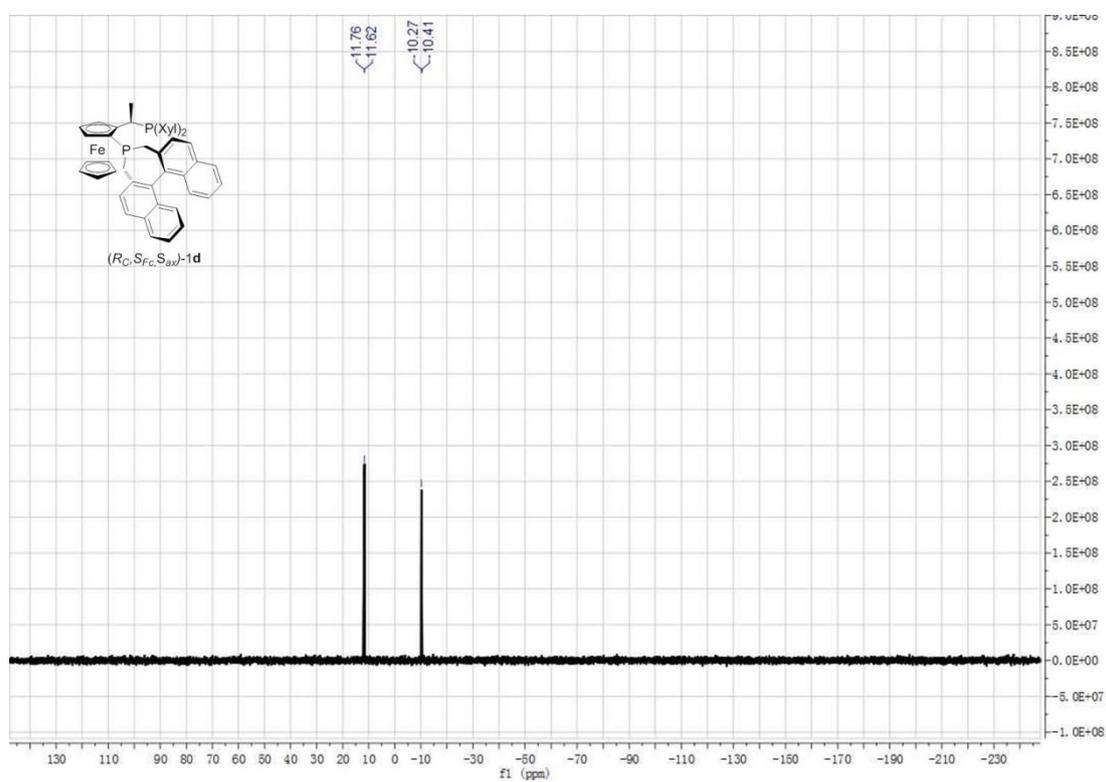
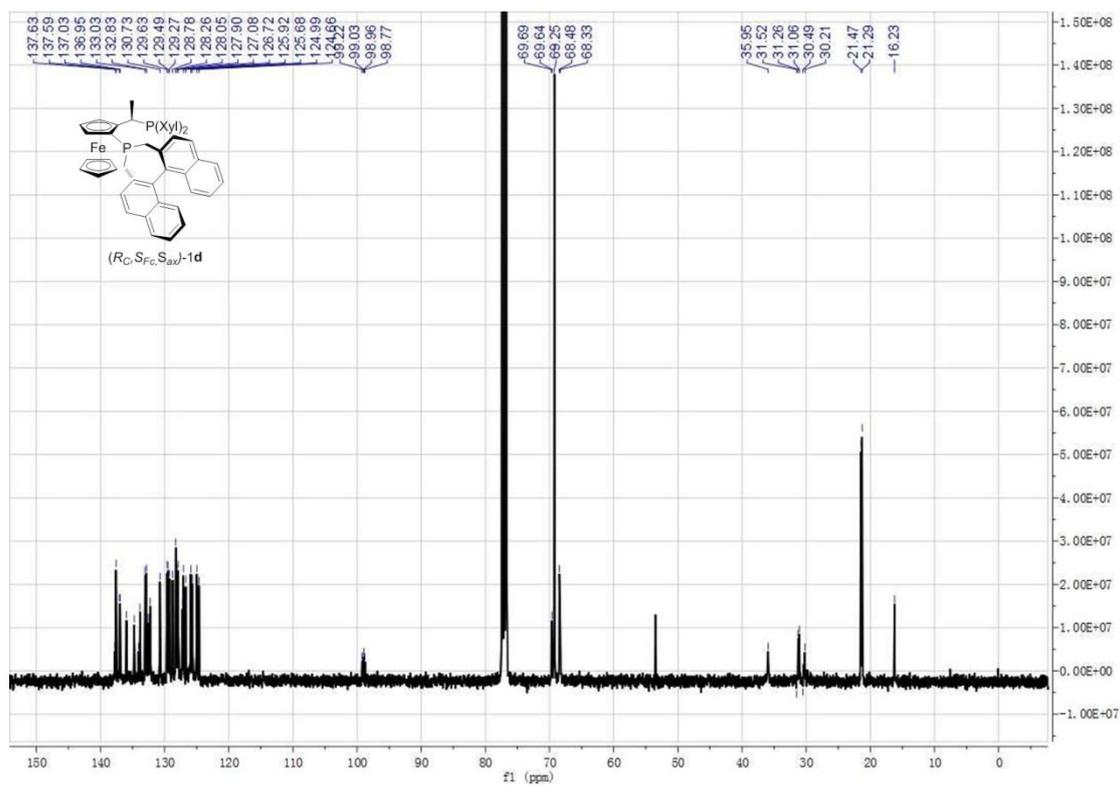
Position
Inj Vol
IRM Calibration Status
Comment

p2E7
0.1
Success

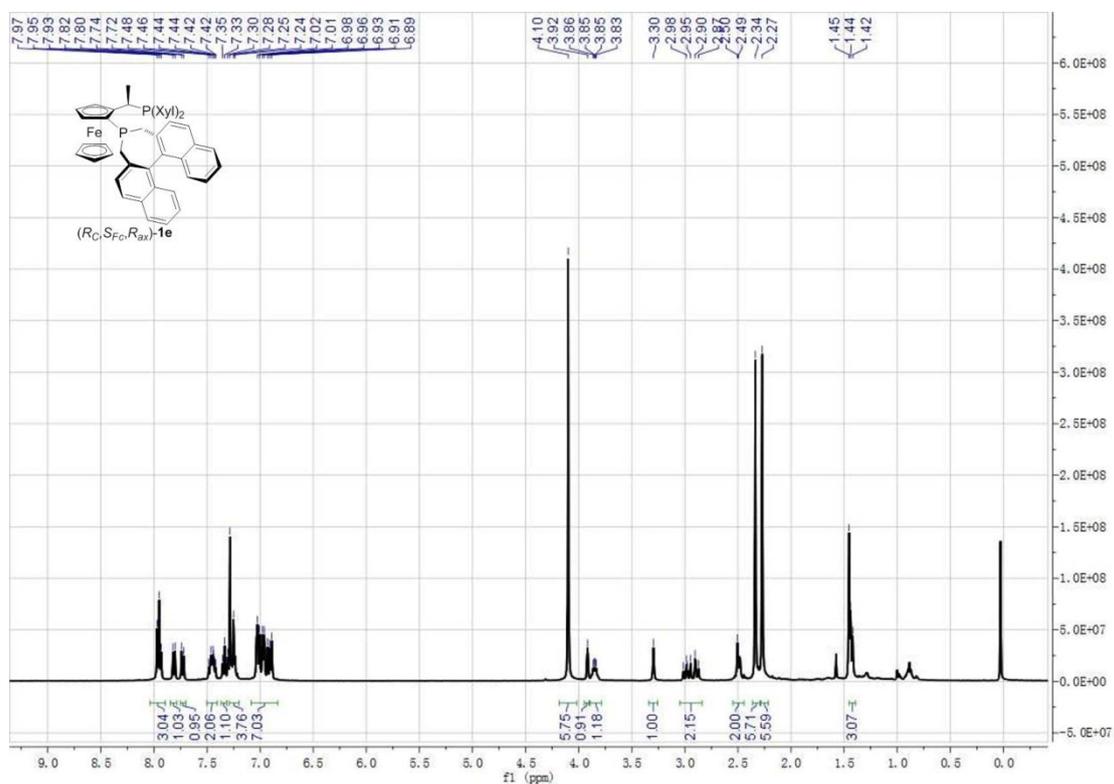
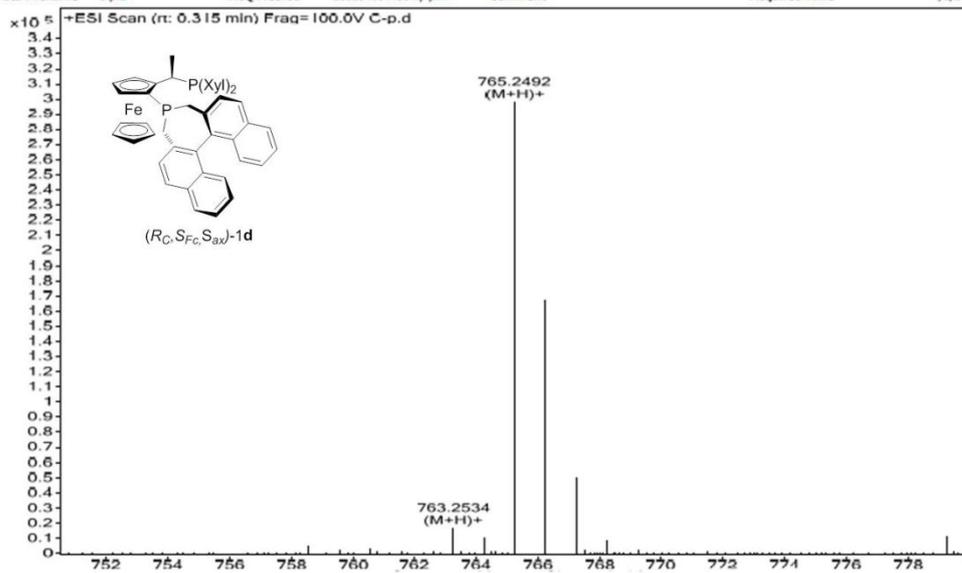
Instrument Name
InjPosition
Data Filename
Acquired Time

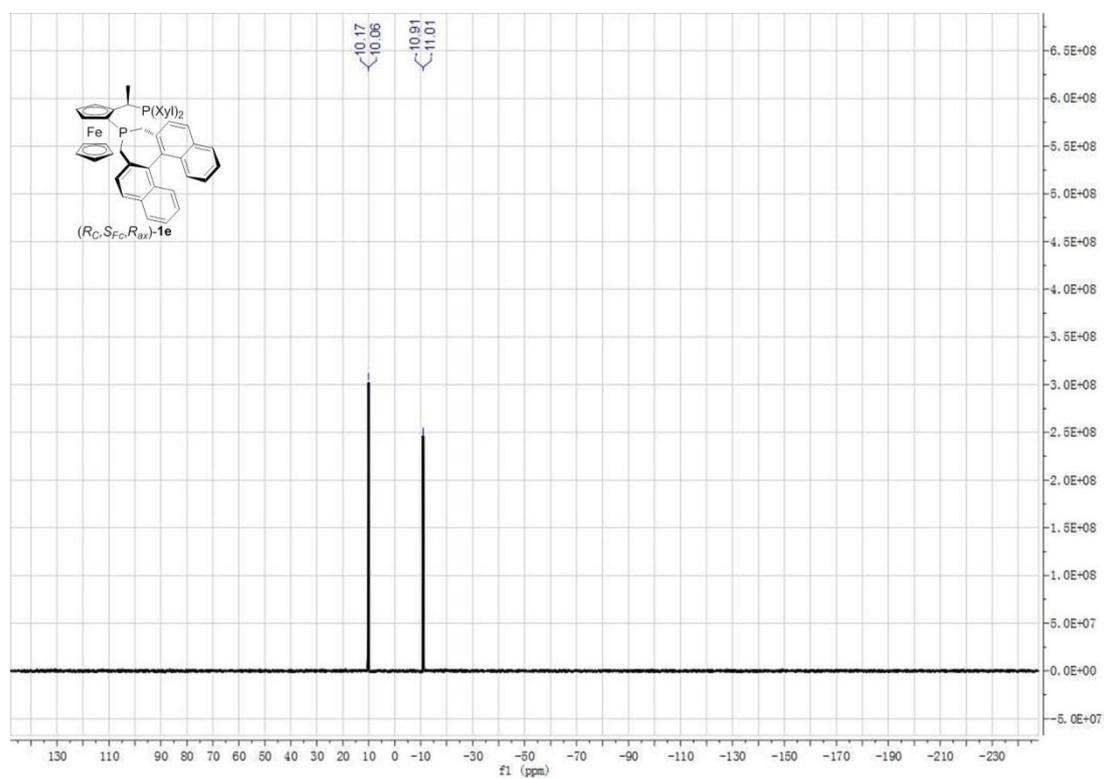
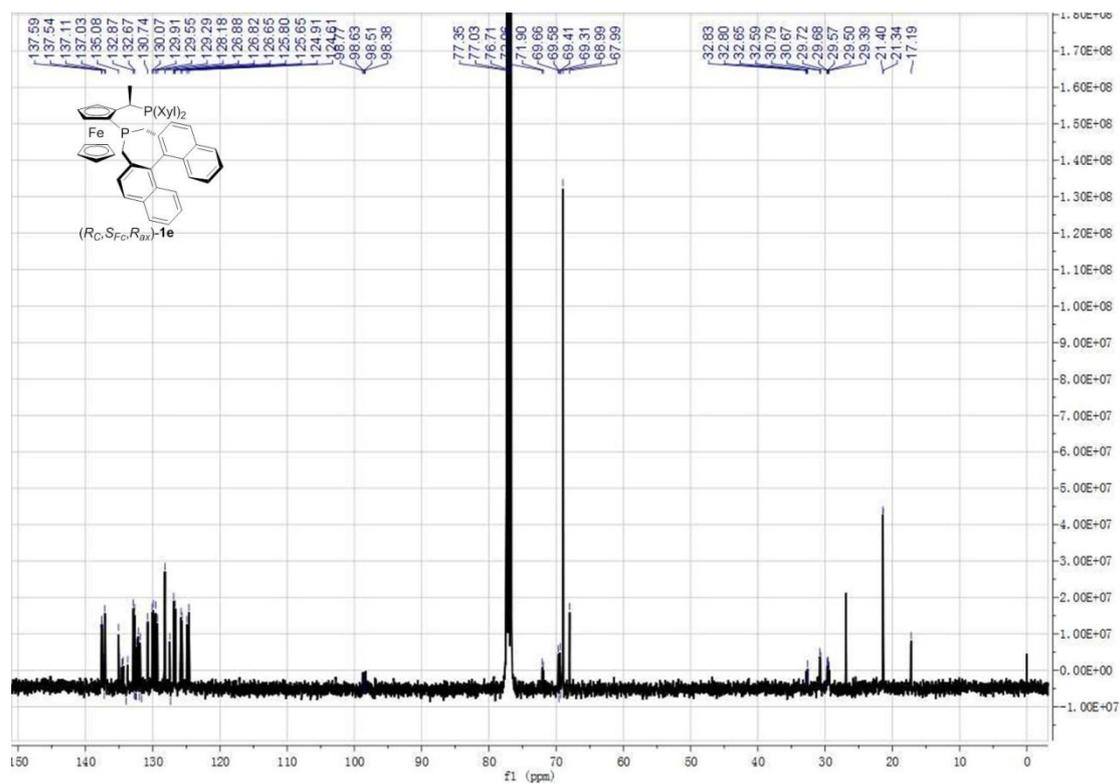
Instrument 1
F-p.d
4/3/2018 9:55:28 AM



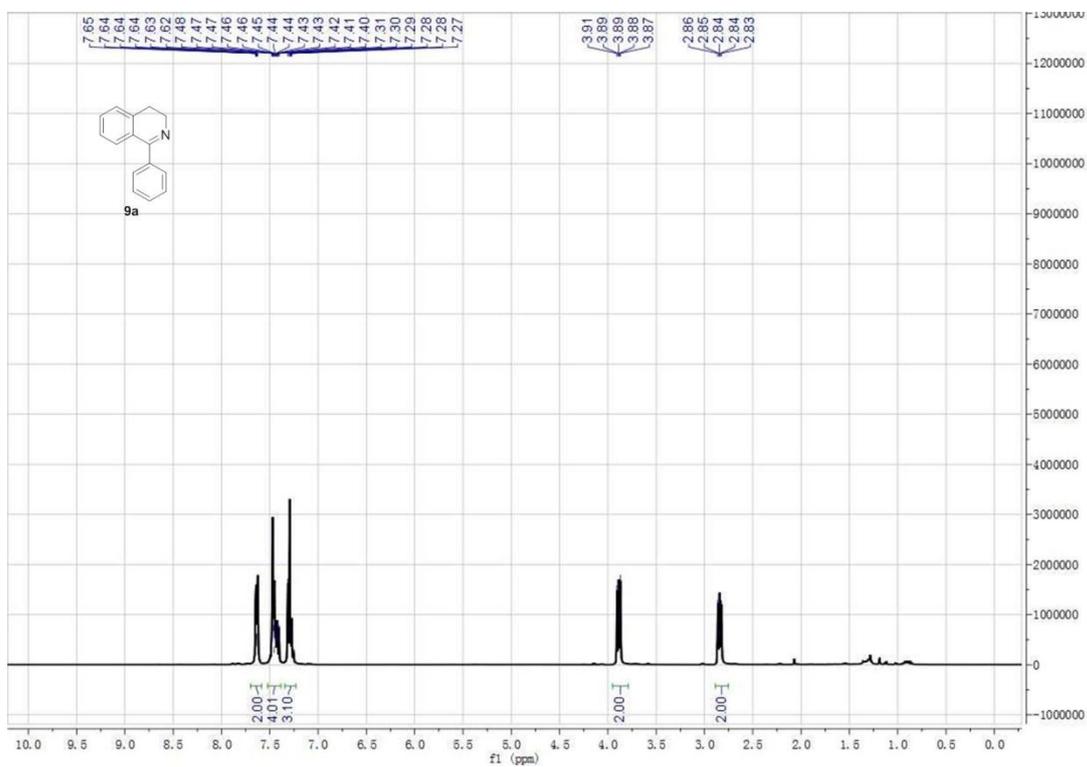
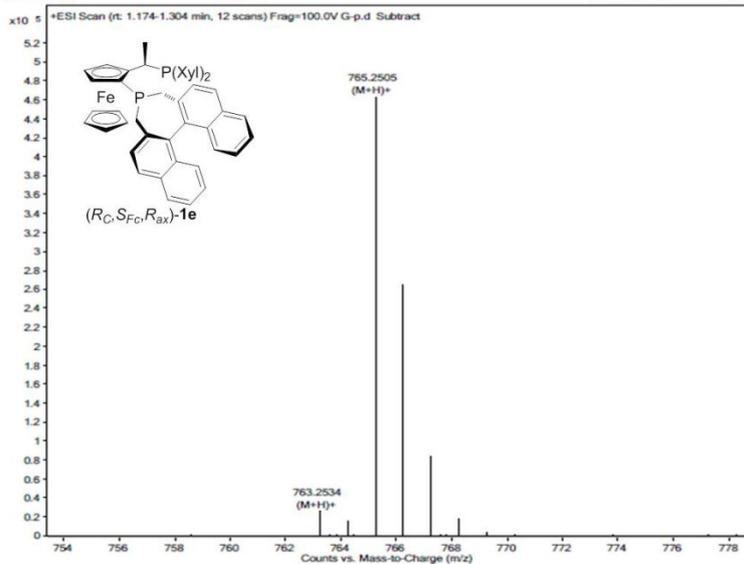


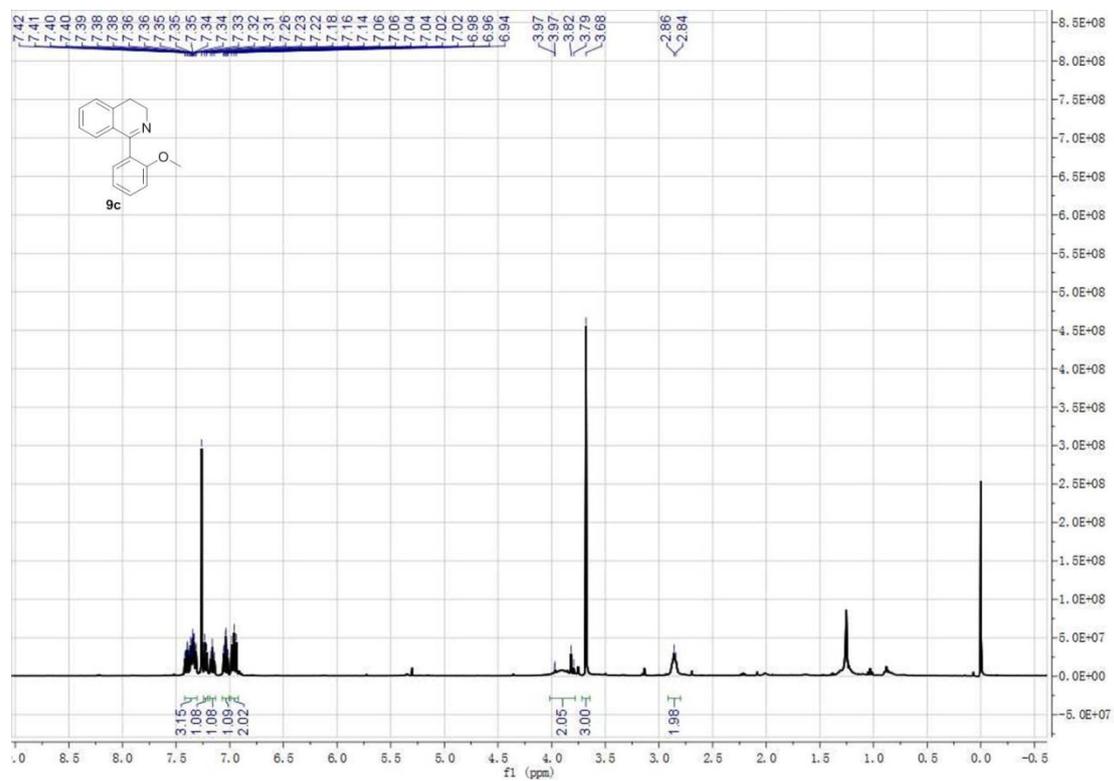
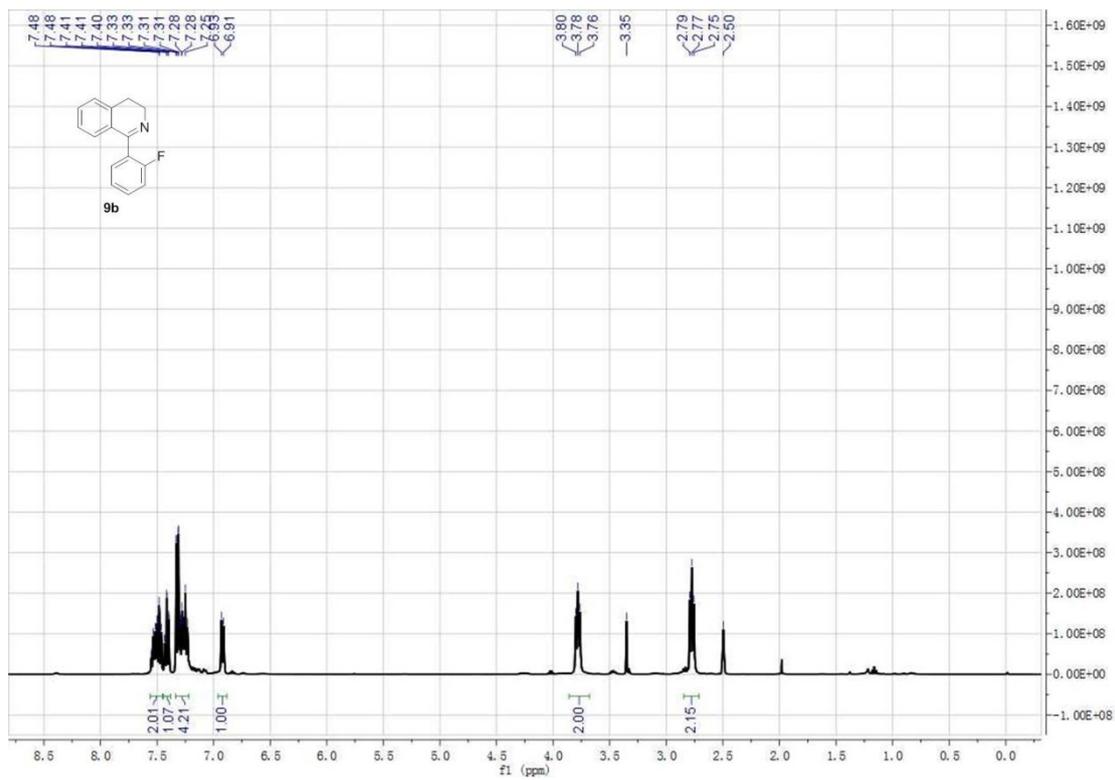
Sample Name	0.1	Position	P2e4	Instrument Name	Instrument 1	User Name	QTOF-PQ/QTOF
Inj Vol	C-p.d	InjPosition	20110418-MSonly-p.m	SampleType	Sample	IRM Calibration Status	Success
Data Filename		ACQ Method		Comment		Acquired Time	4/2/2018 4:28:37 PM

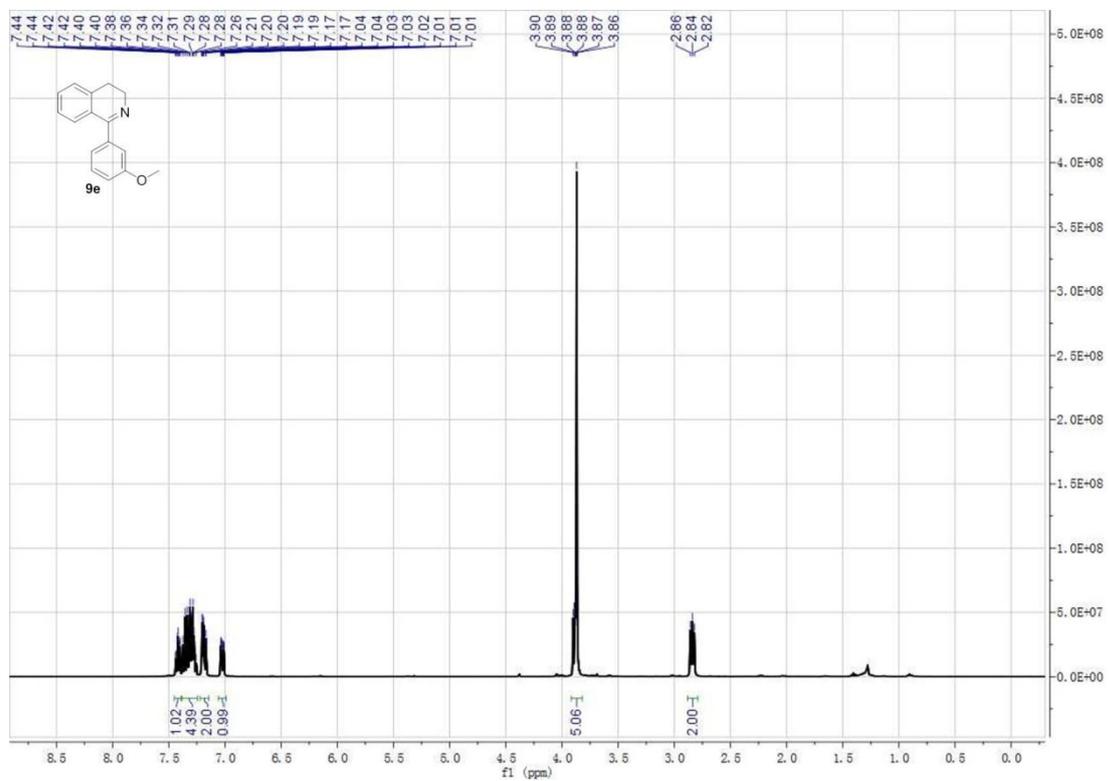
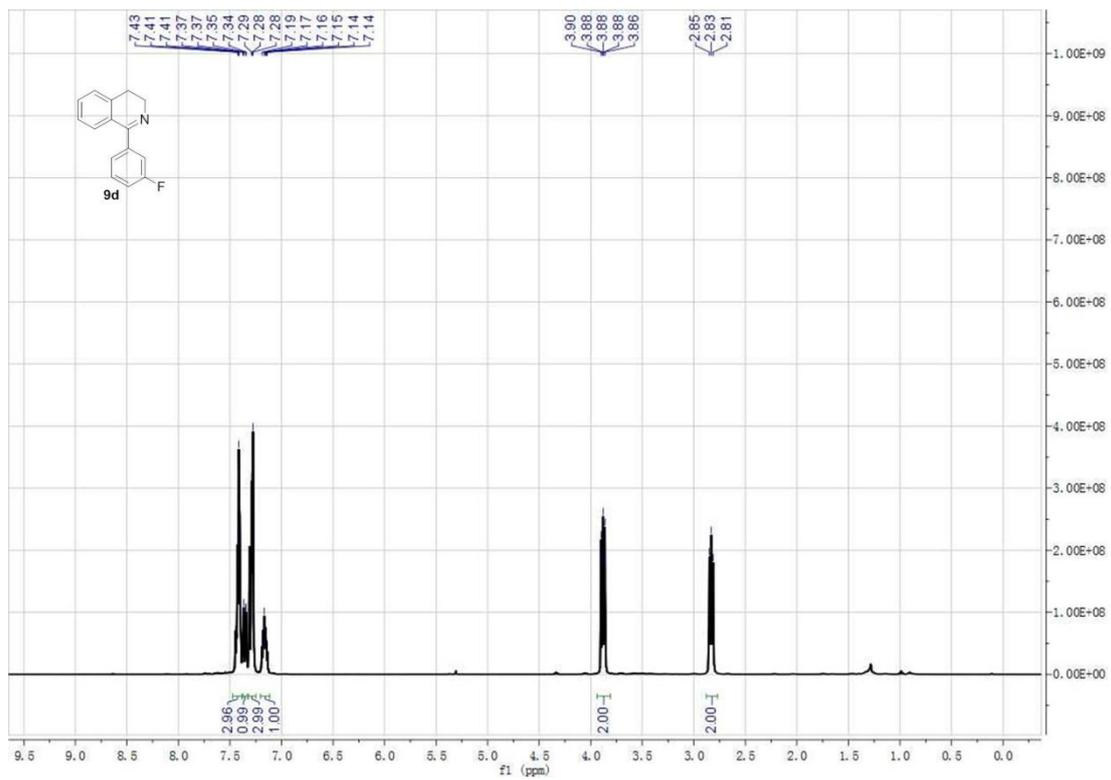


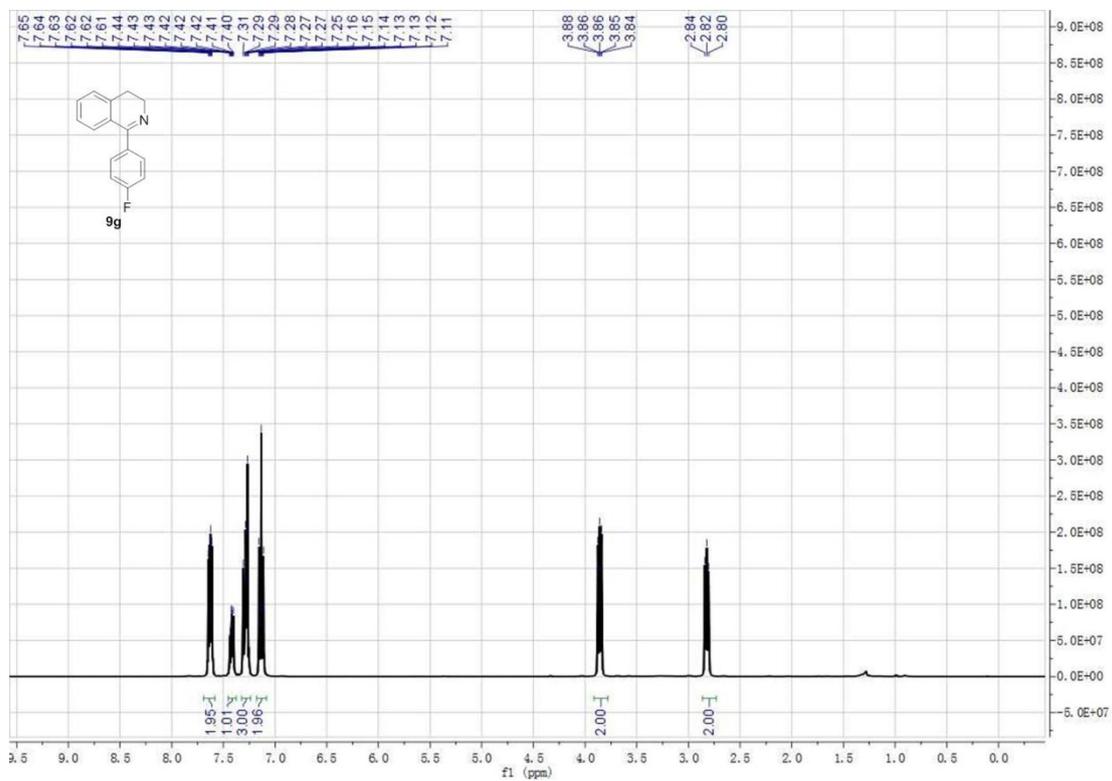
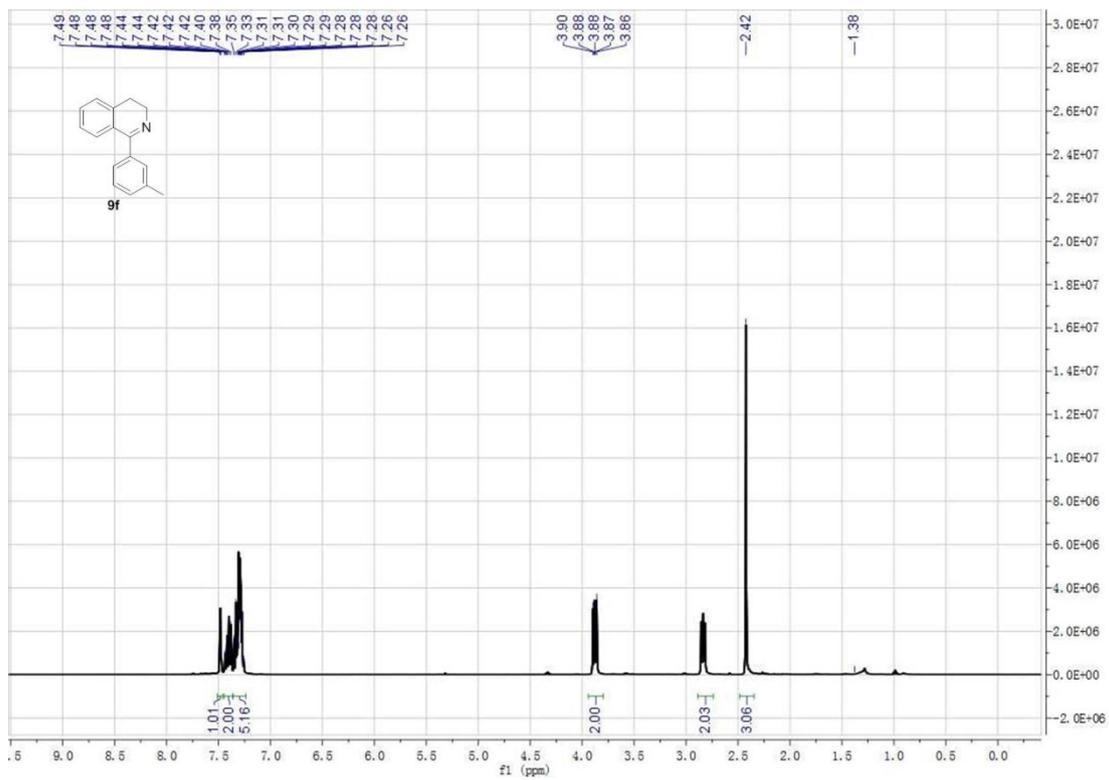


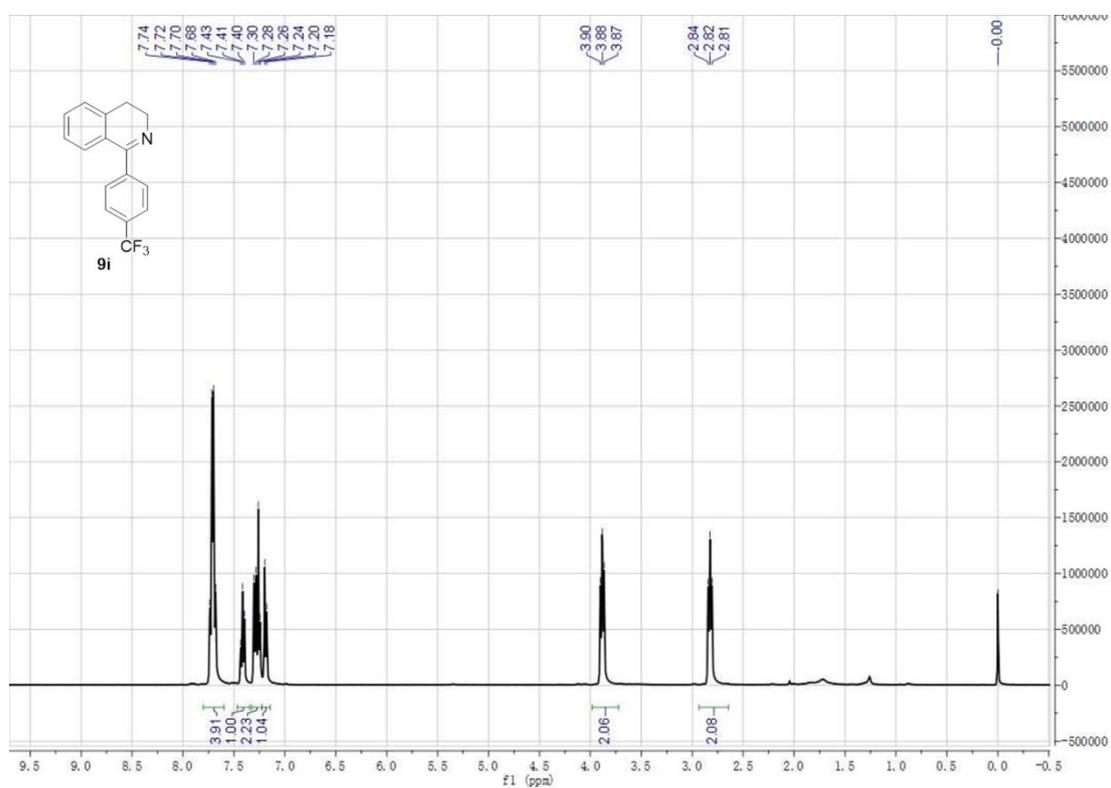
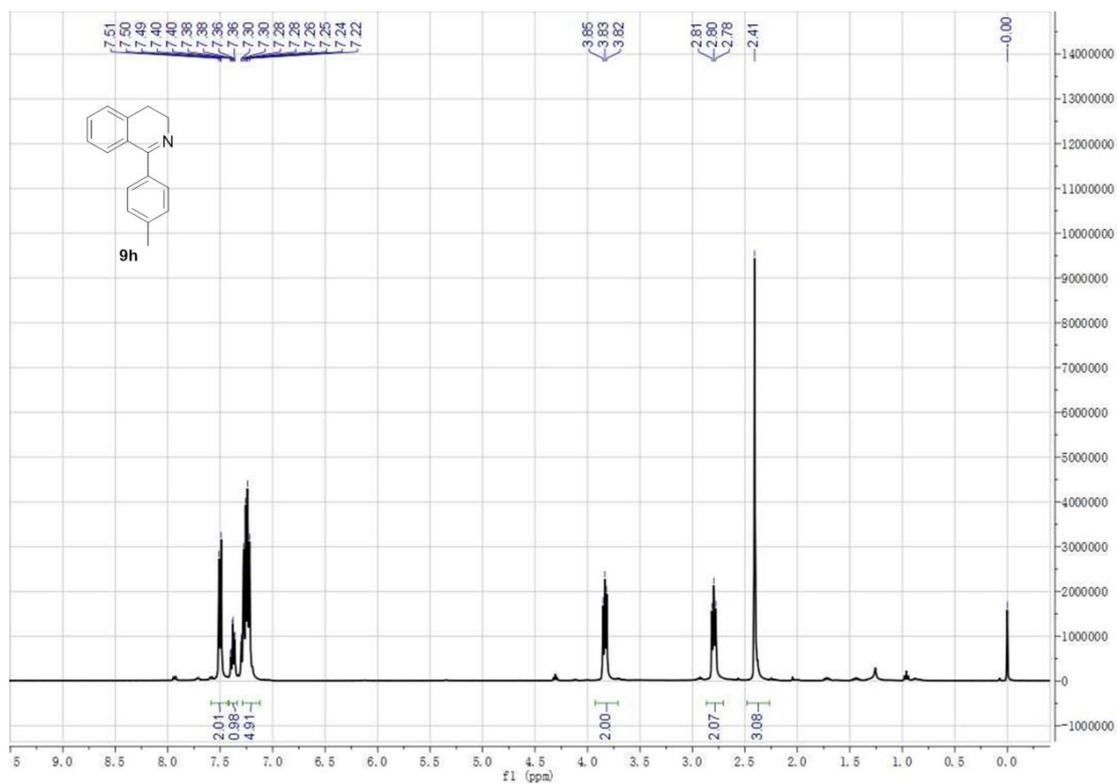
Sample Name	QTQF-PC1QTQF	Position	p2E8	Instrument Name	Instrument 1
User Name	Sample	Inj Vol	0.1	InjPosition	
Sample Type	20110418-M5only-p.m	IRM Calibration Status	Success	Data Filename	G-p.d
ACQ Method		Comment		Acquired Time	4/3/2018 9:58:09 AM

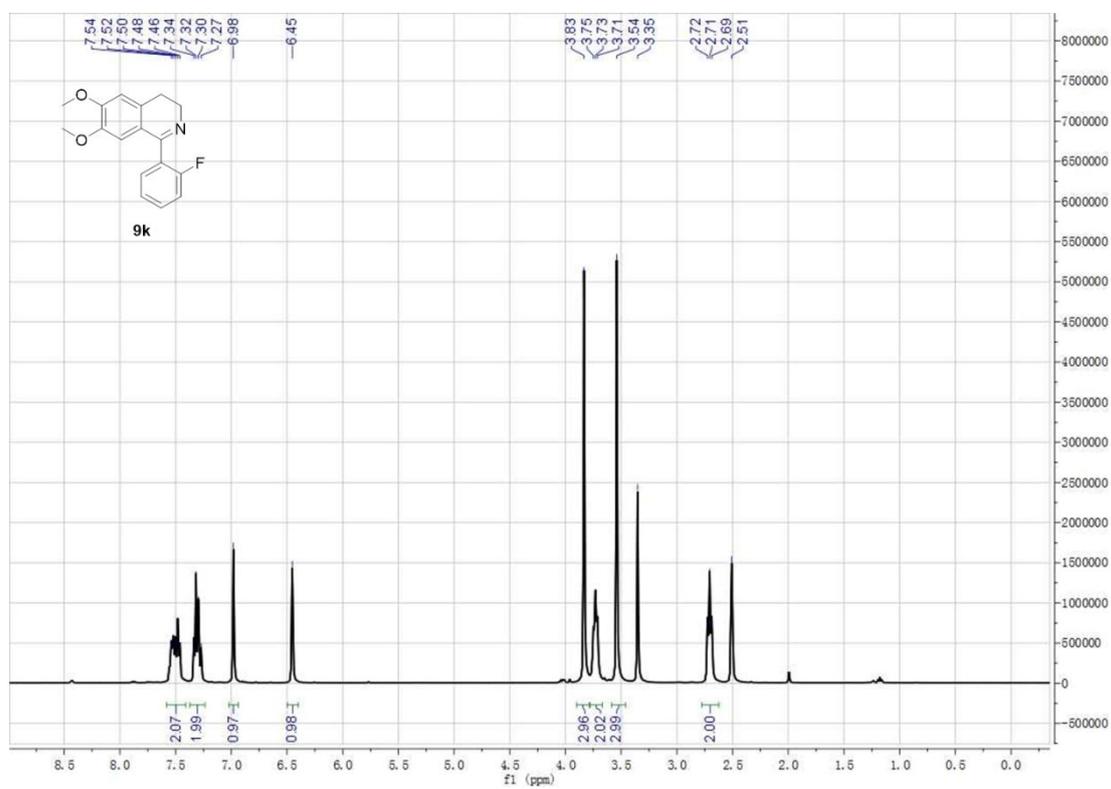
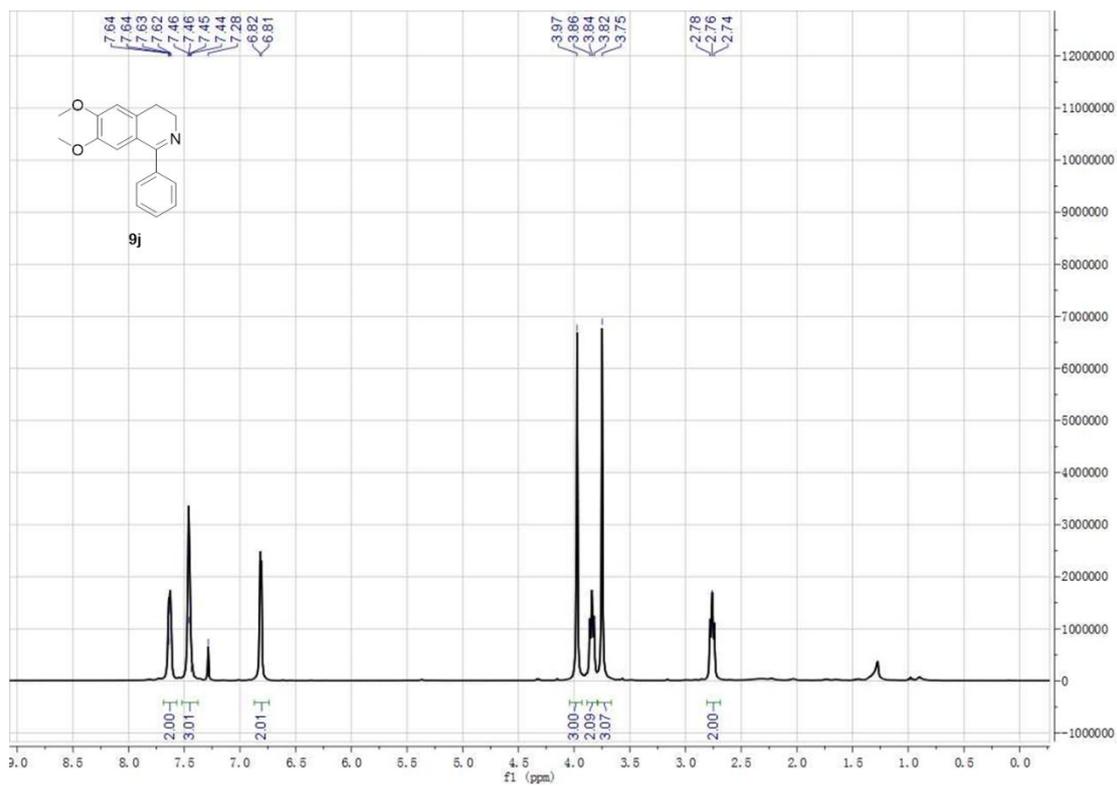


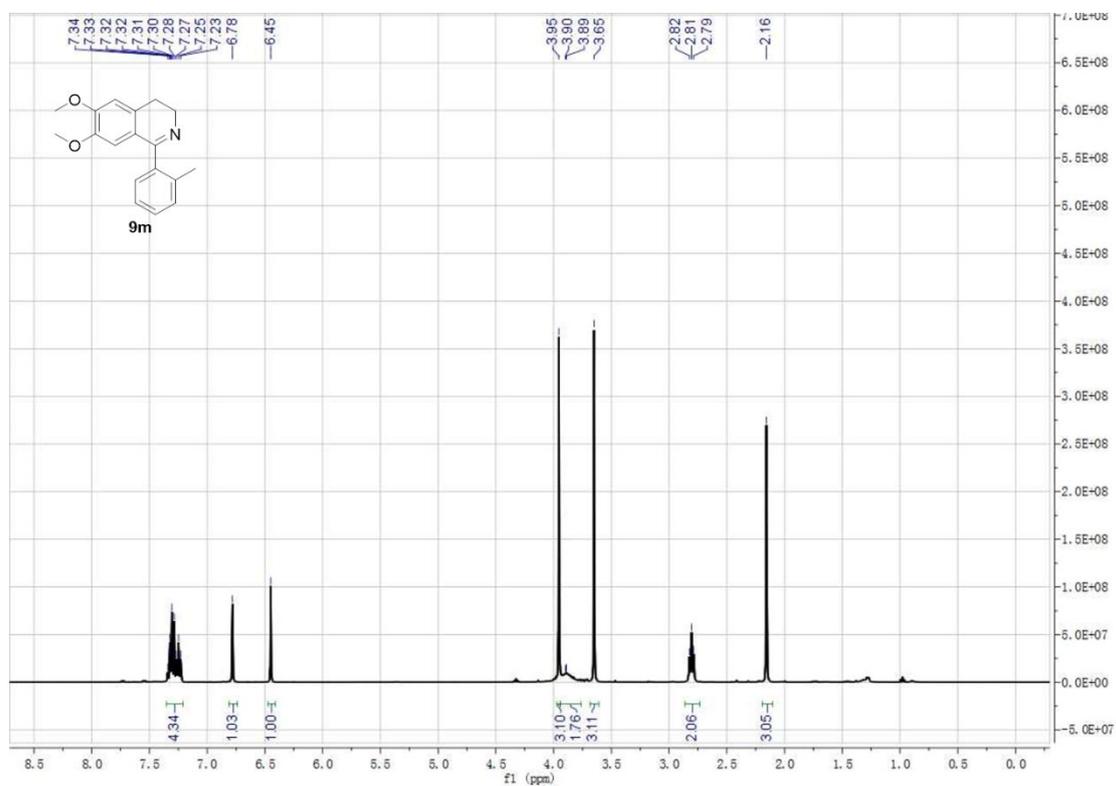
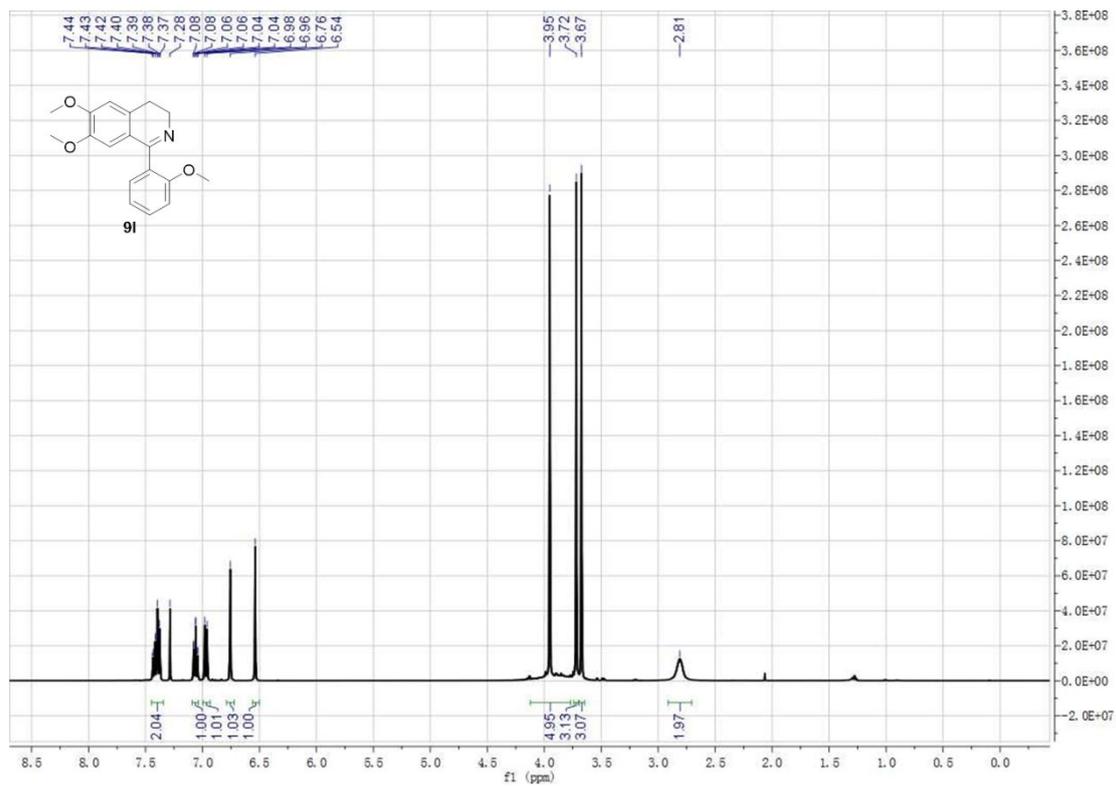


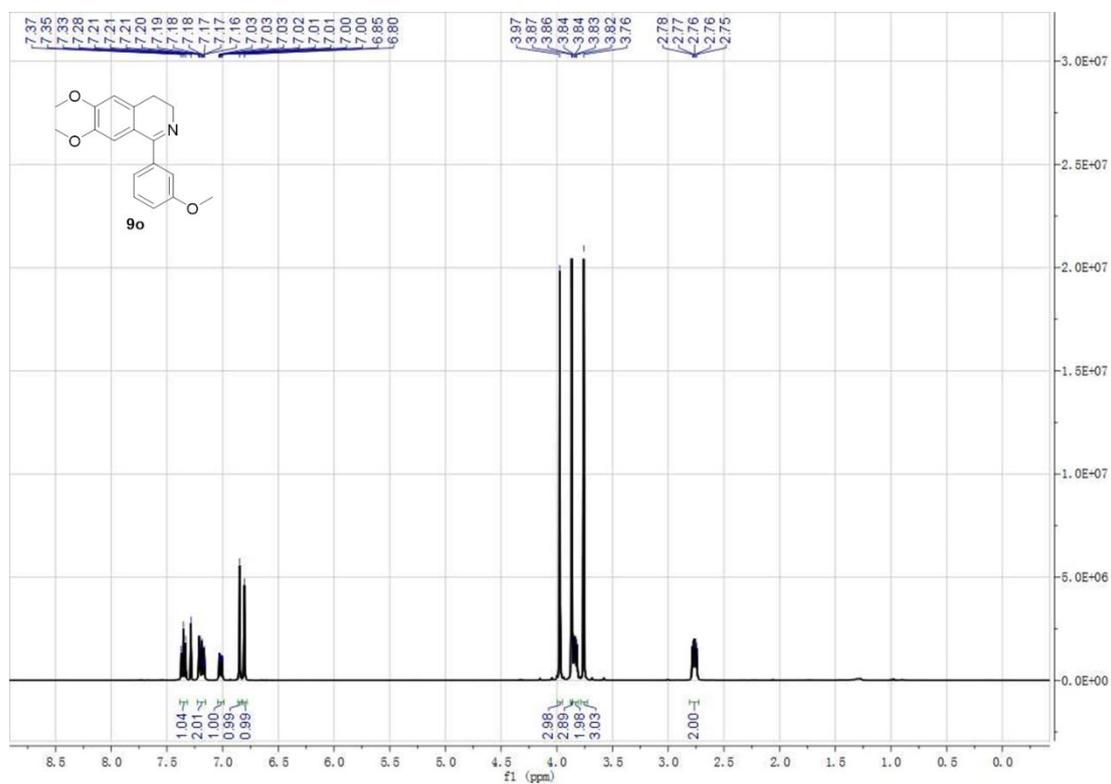
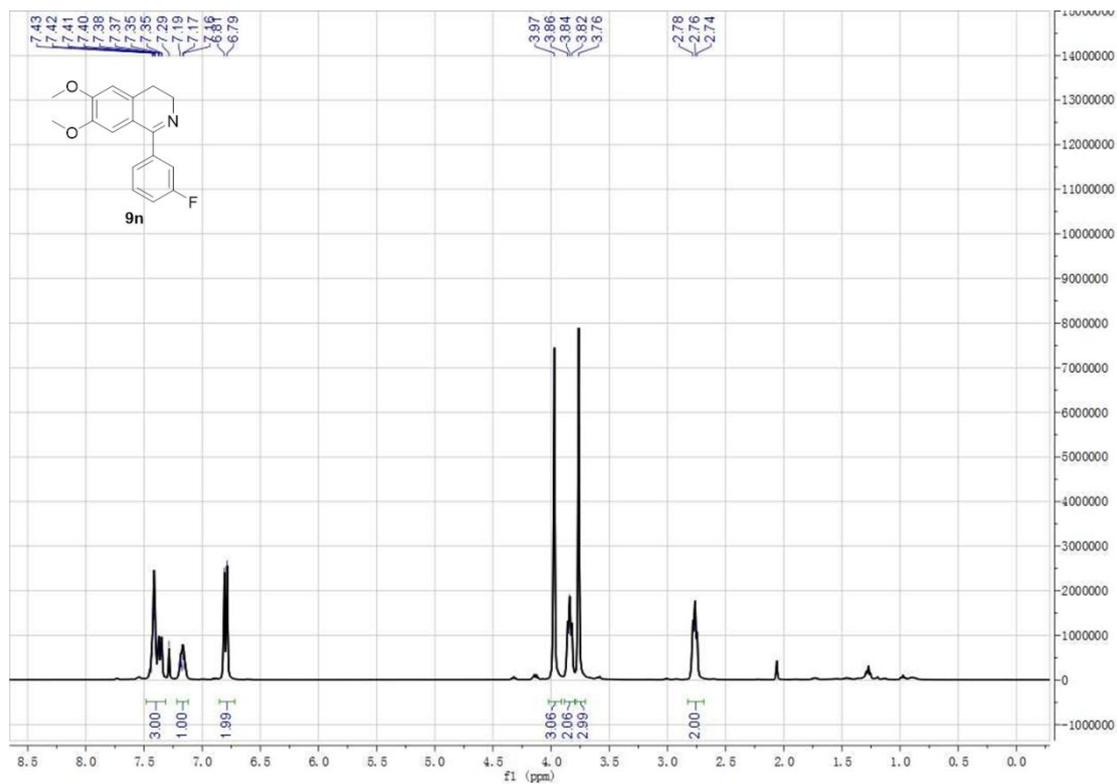


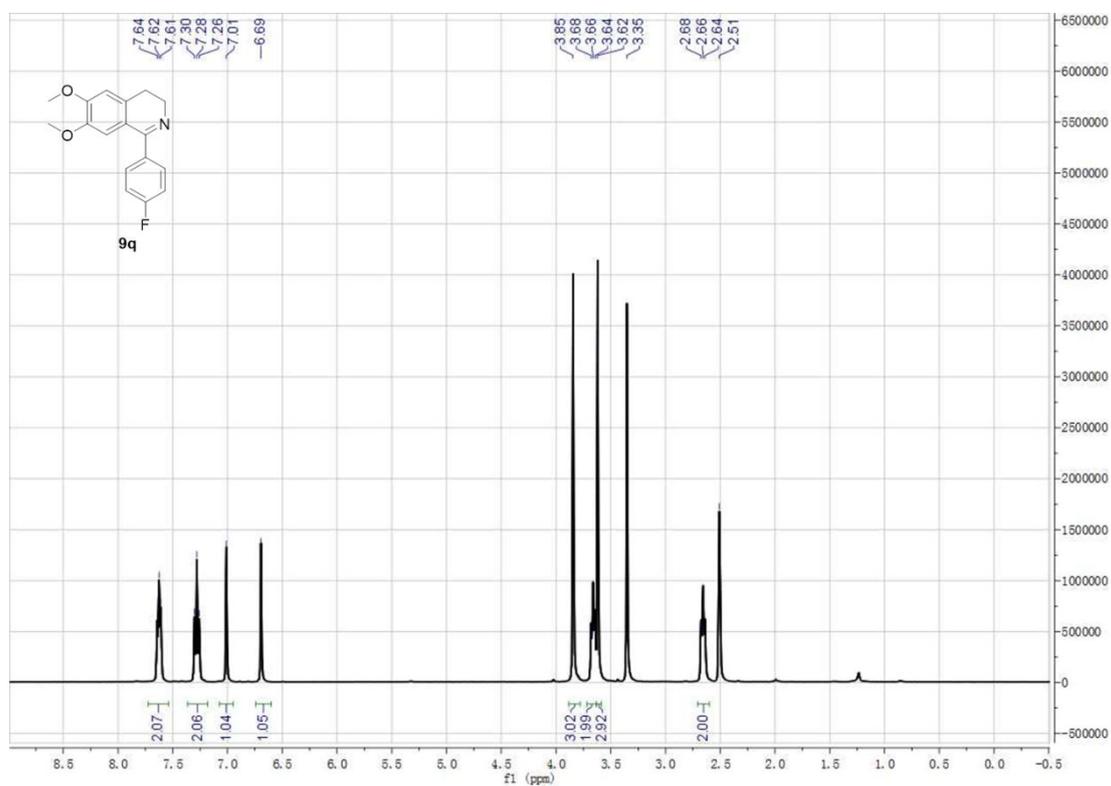
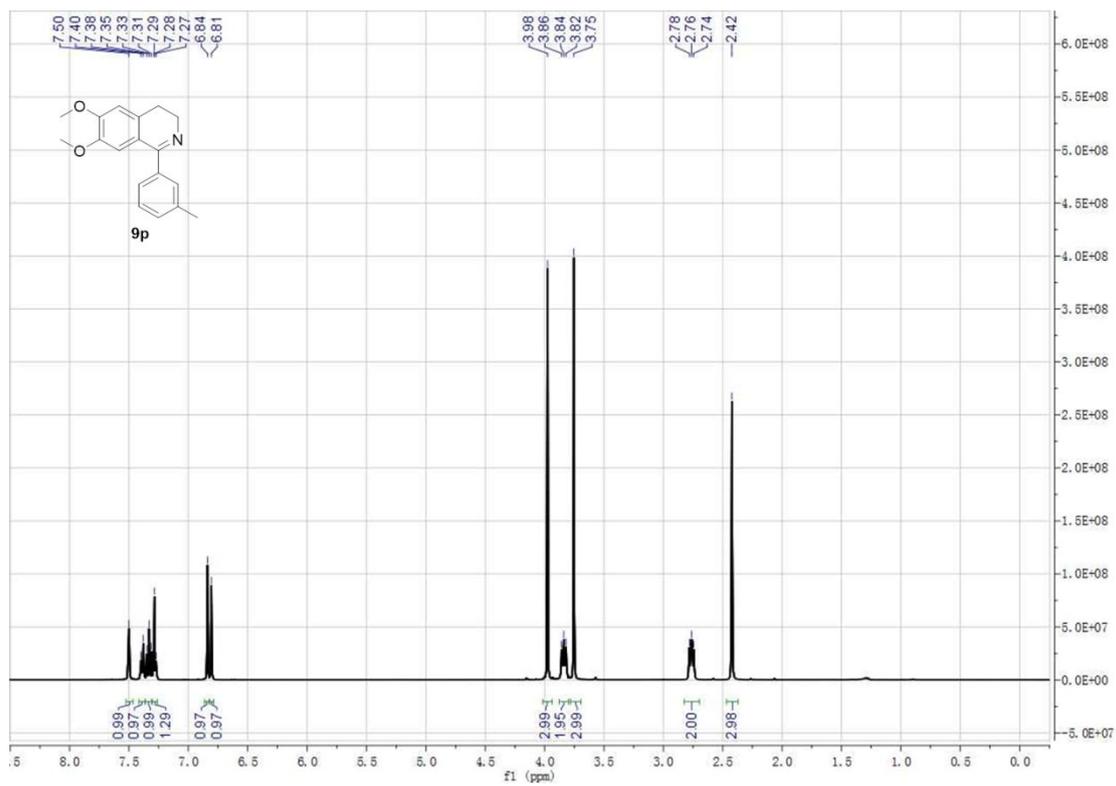


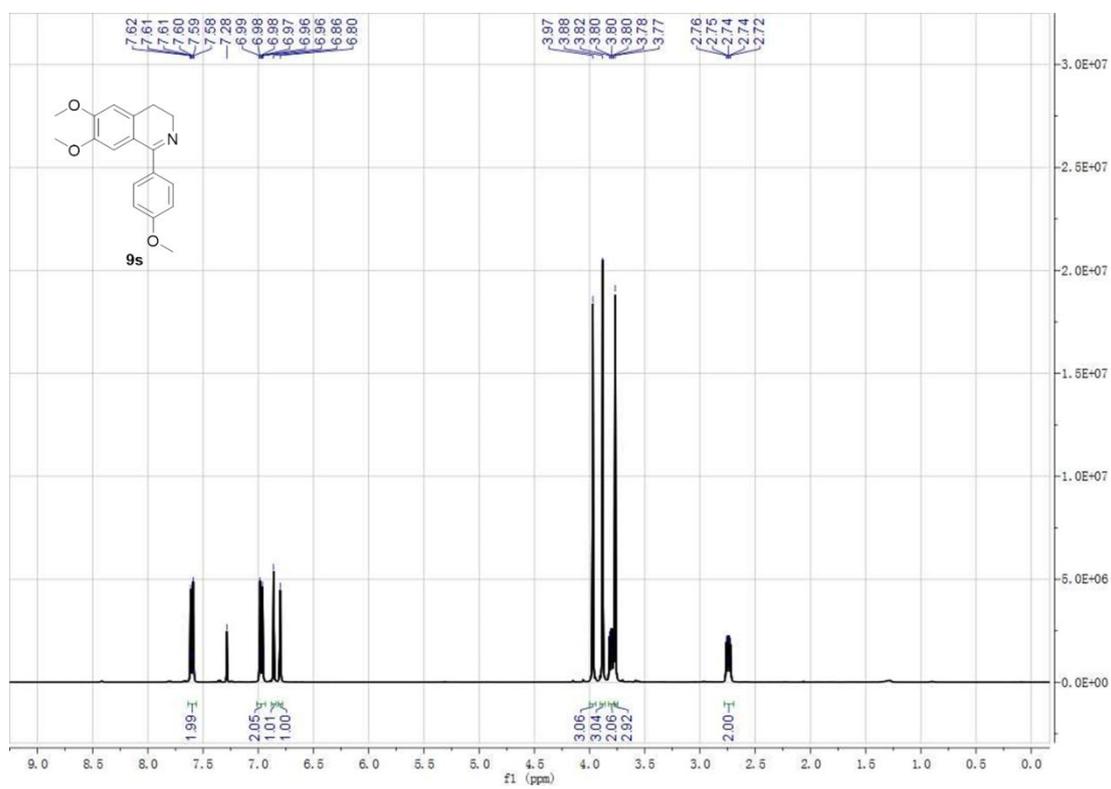
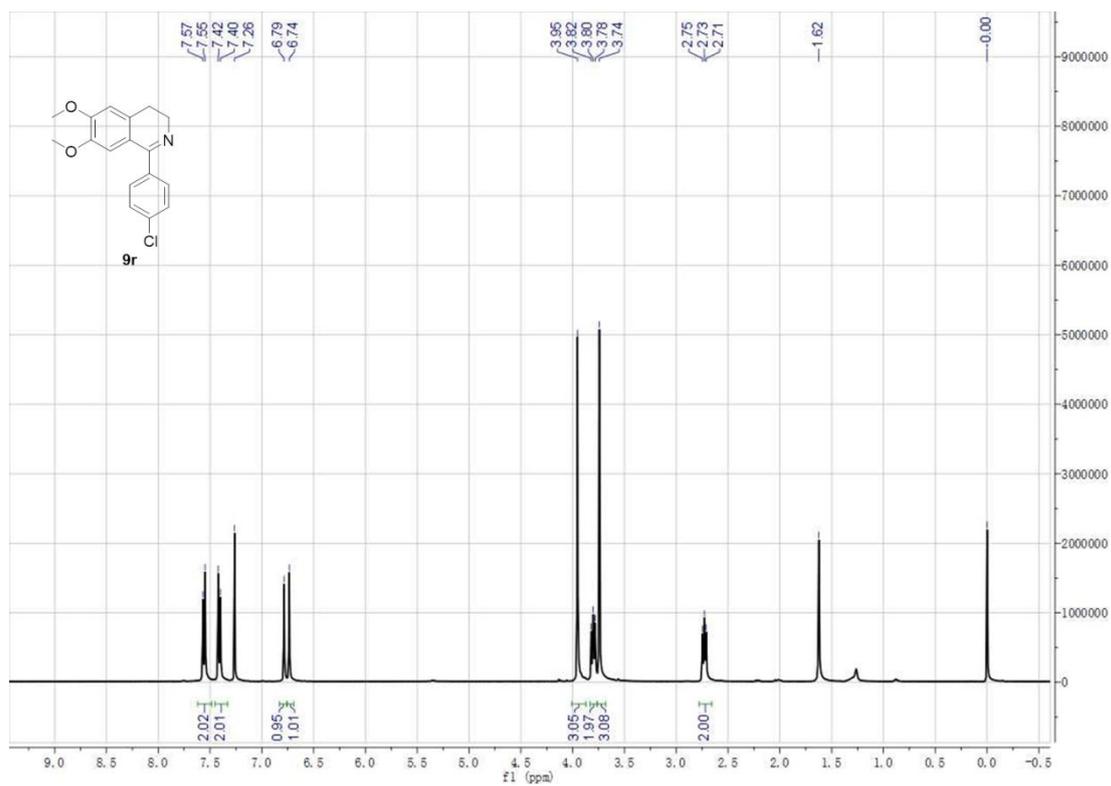


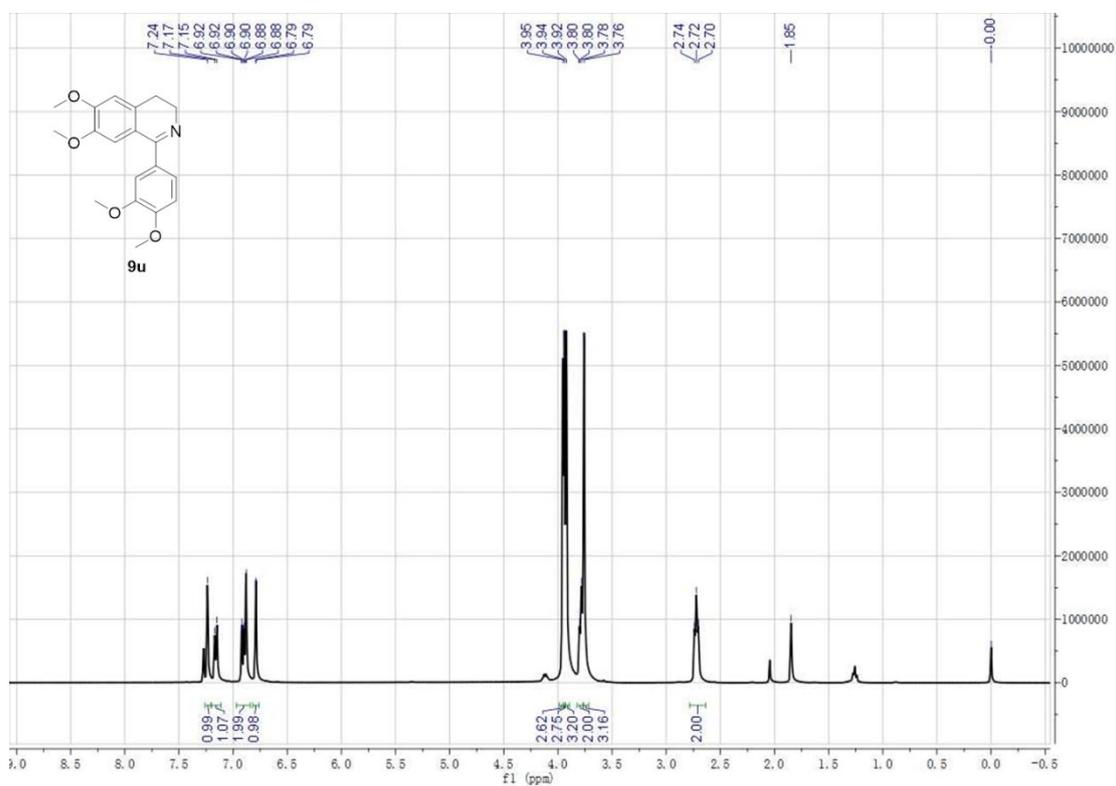
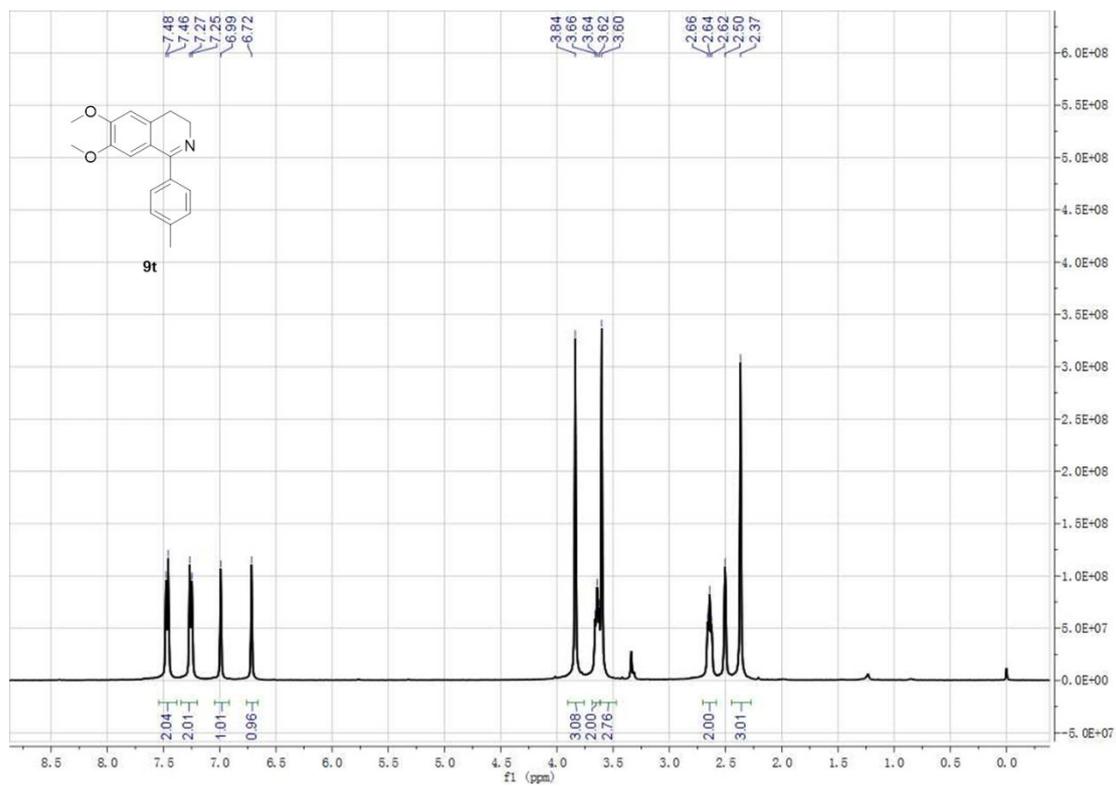


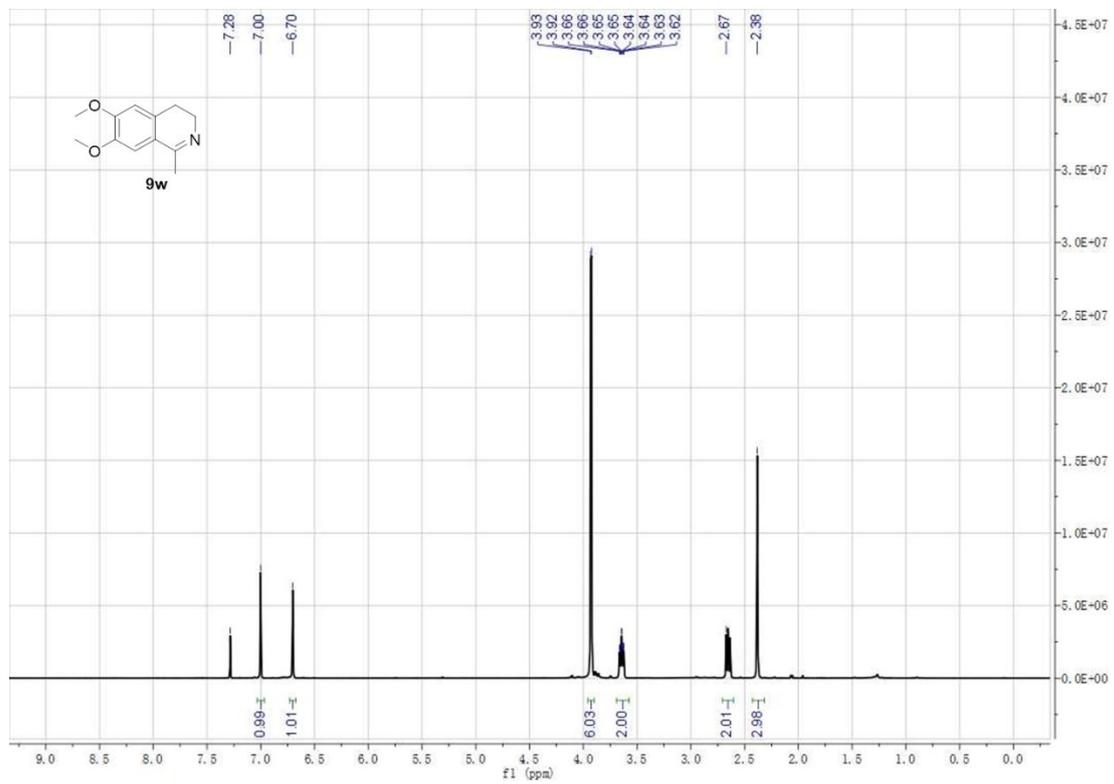
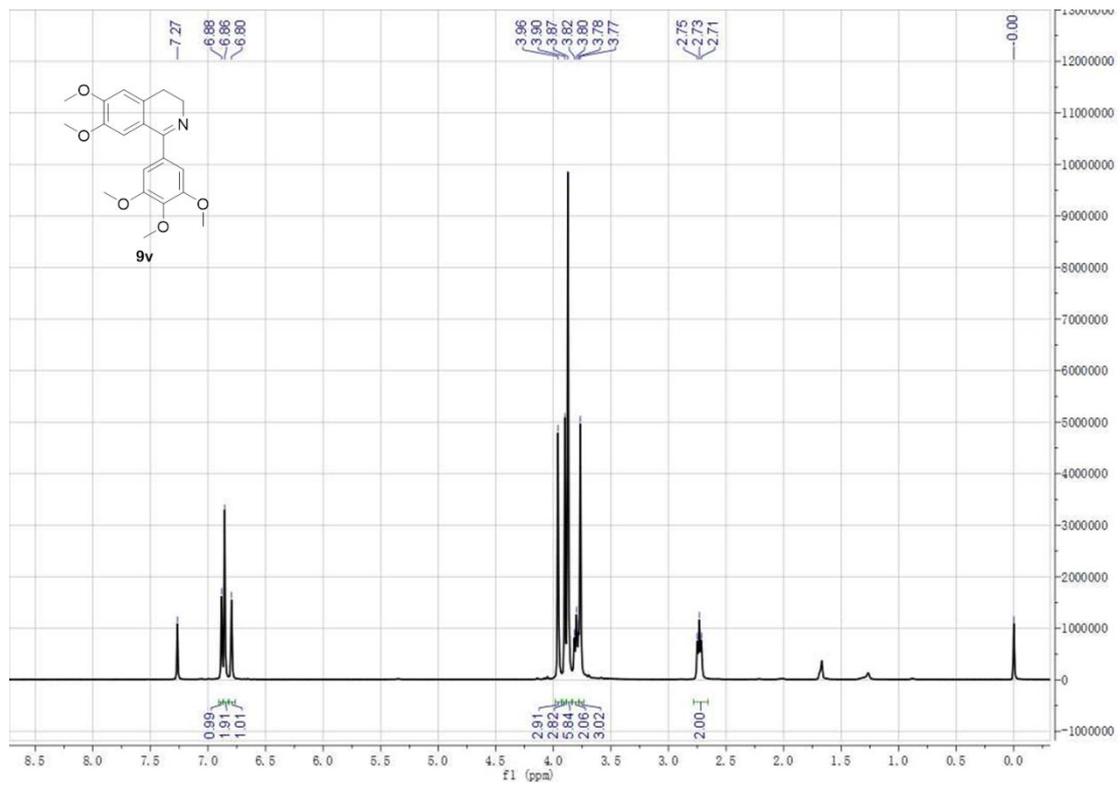


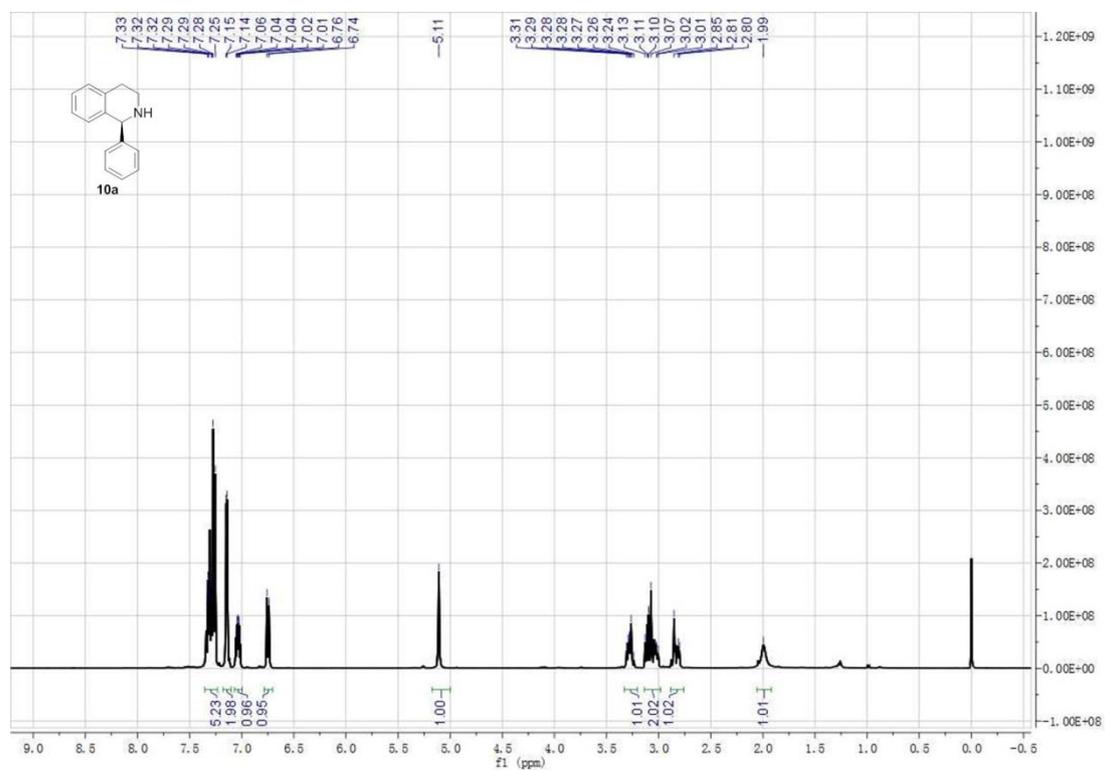
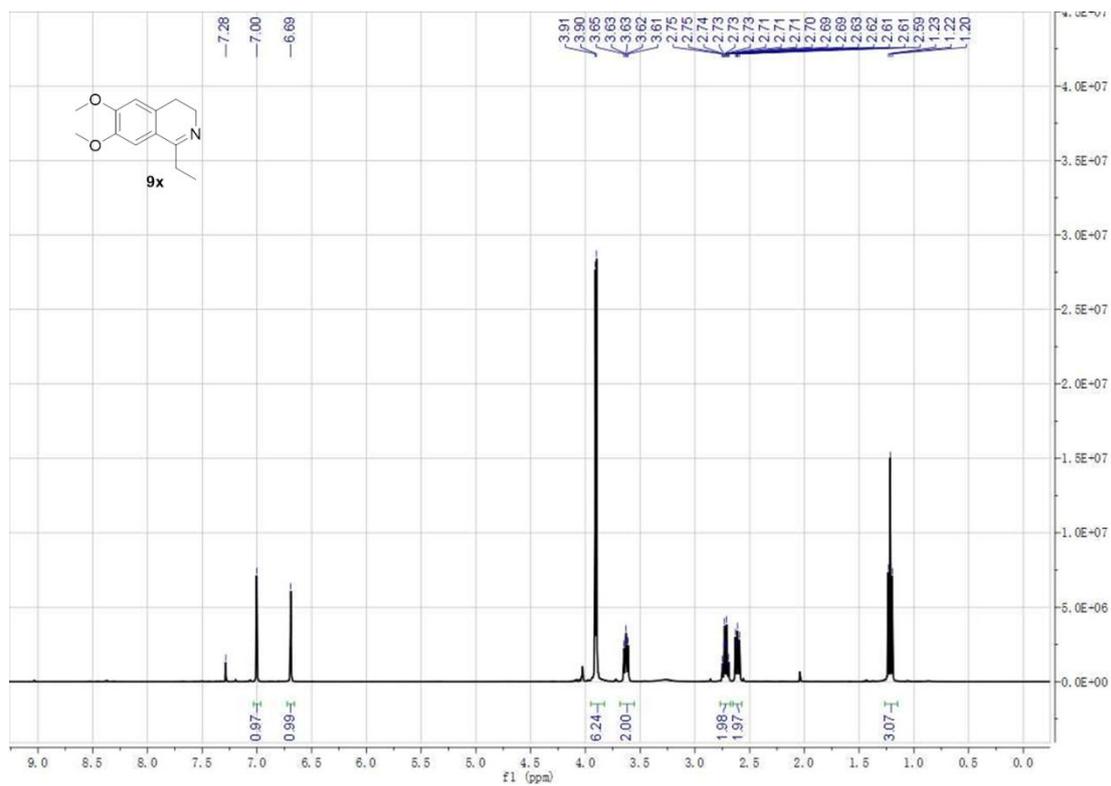


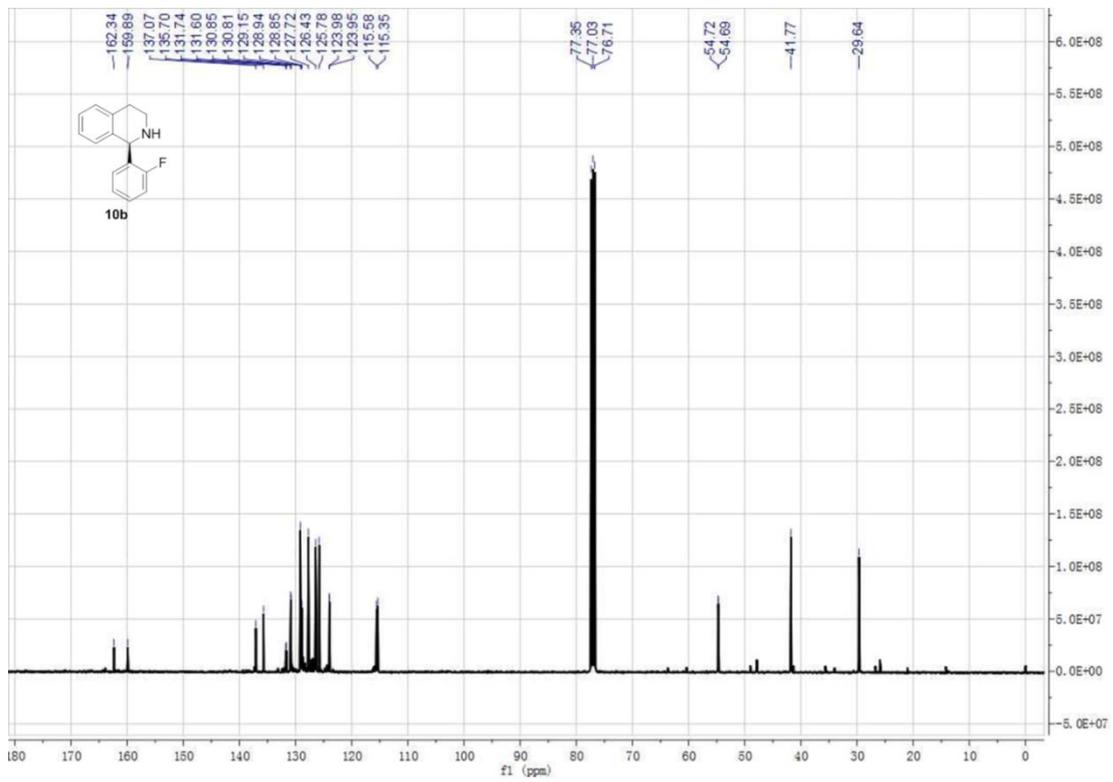
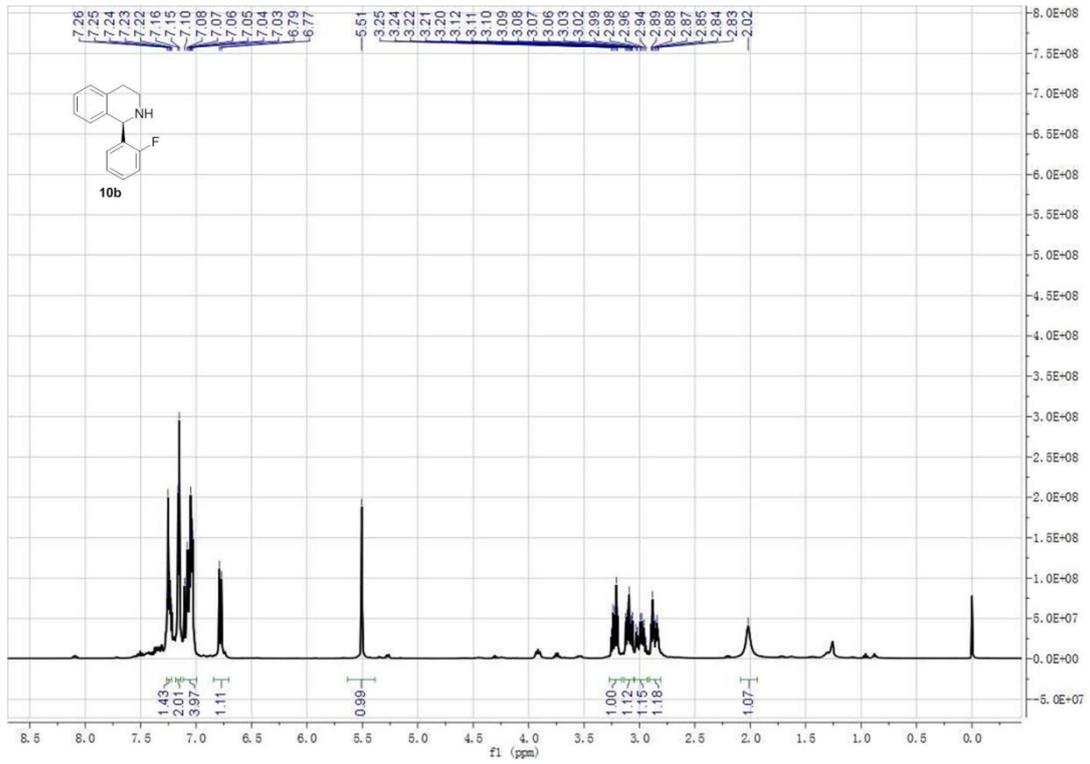




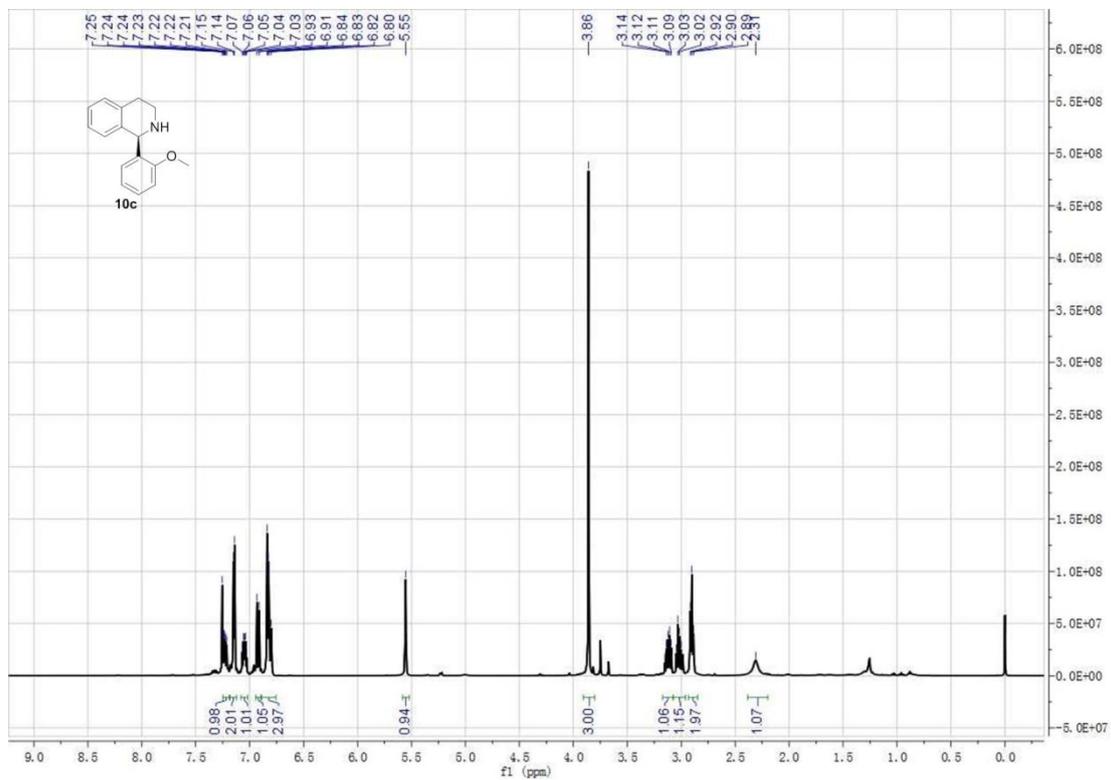
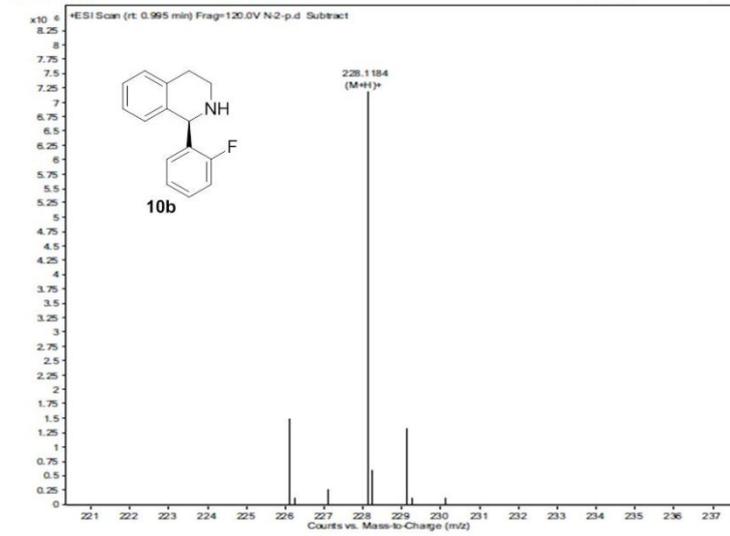


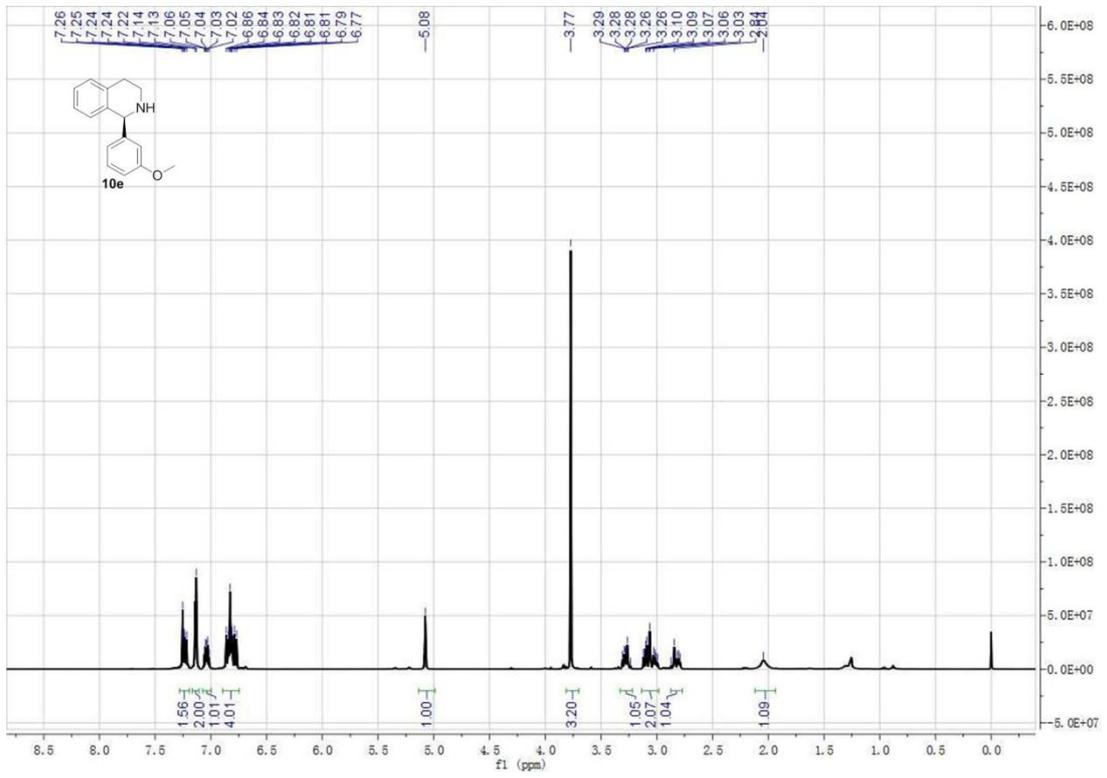
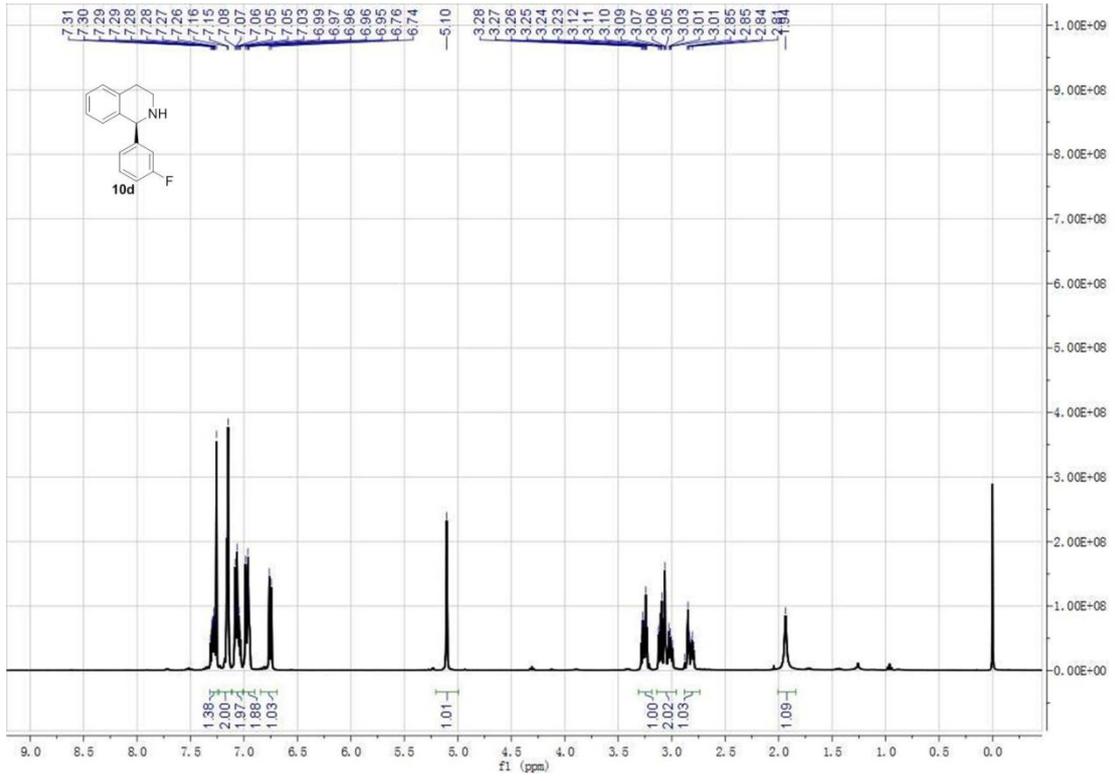


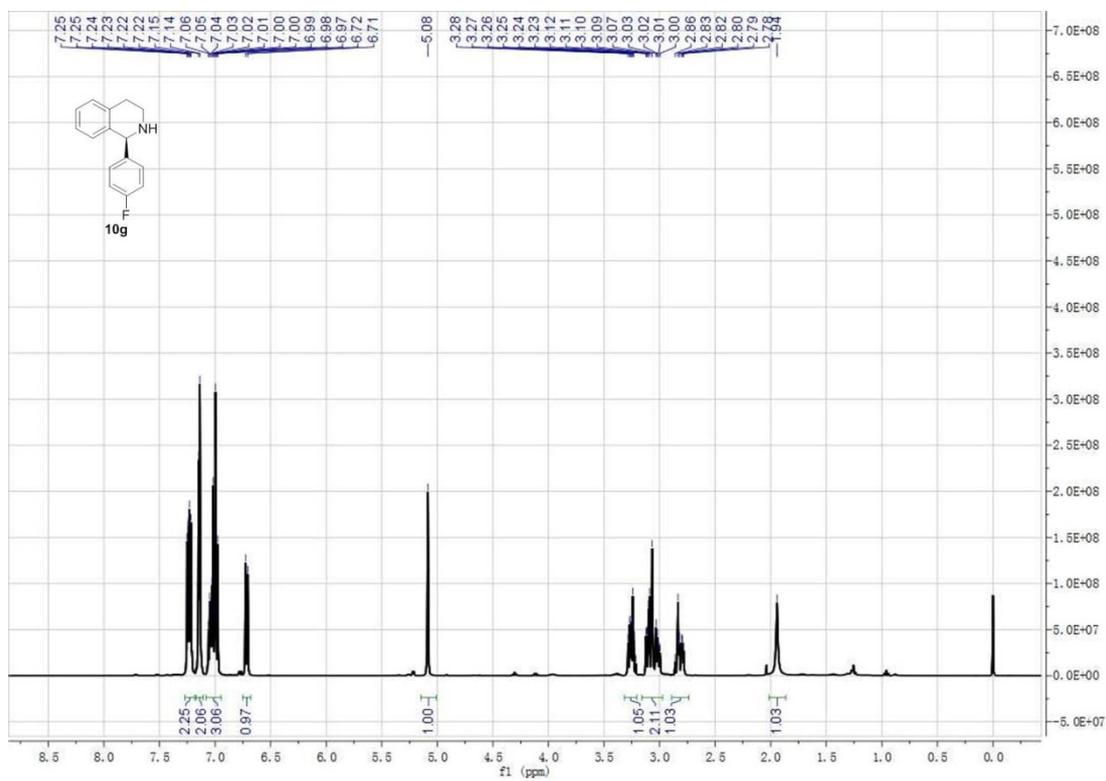
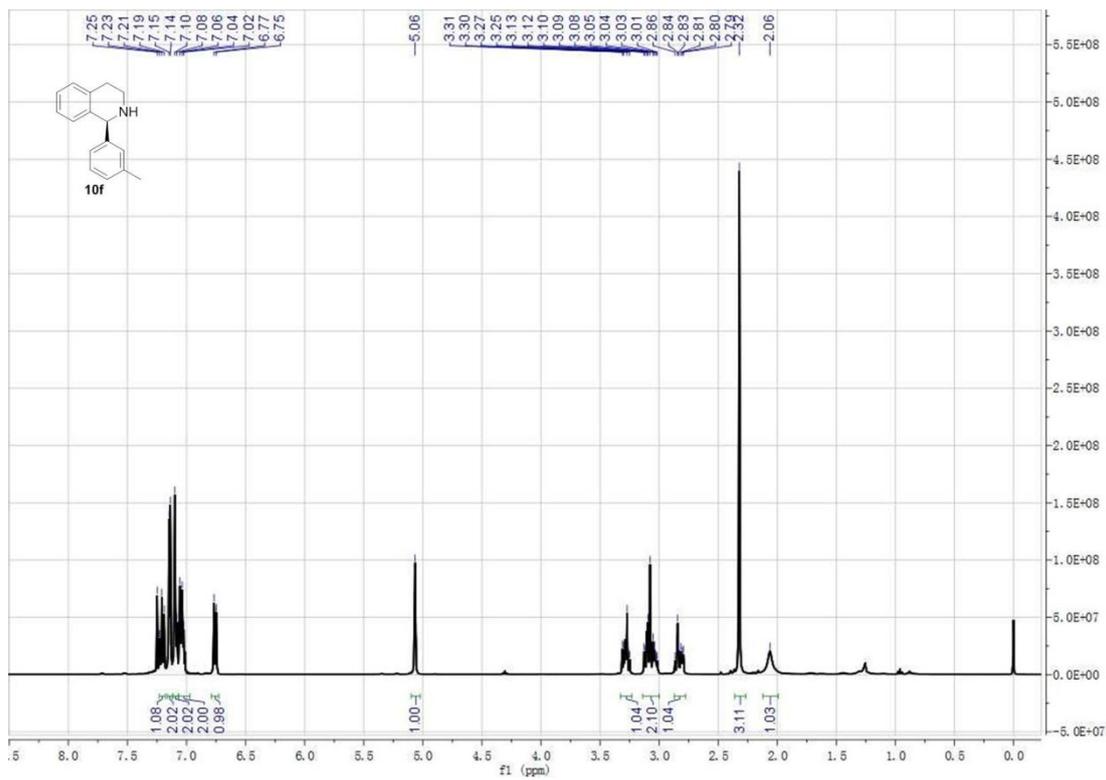


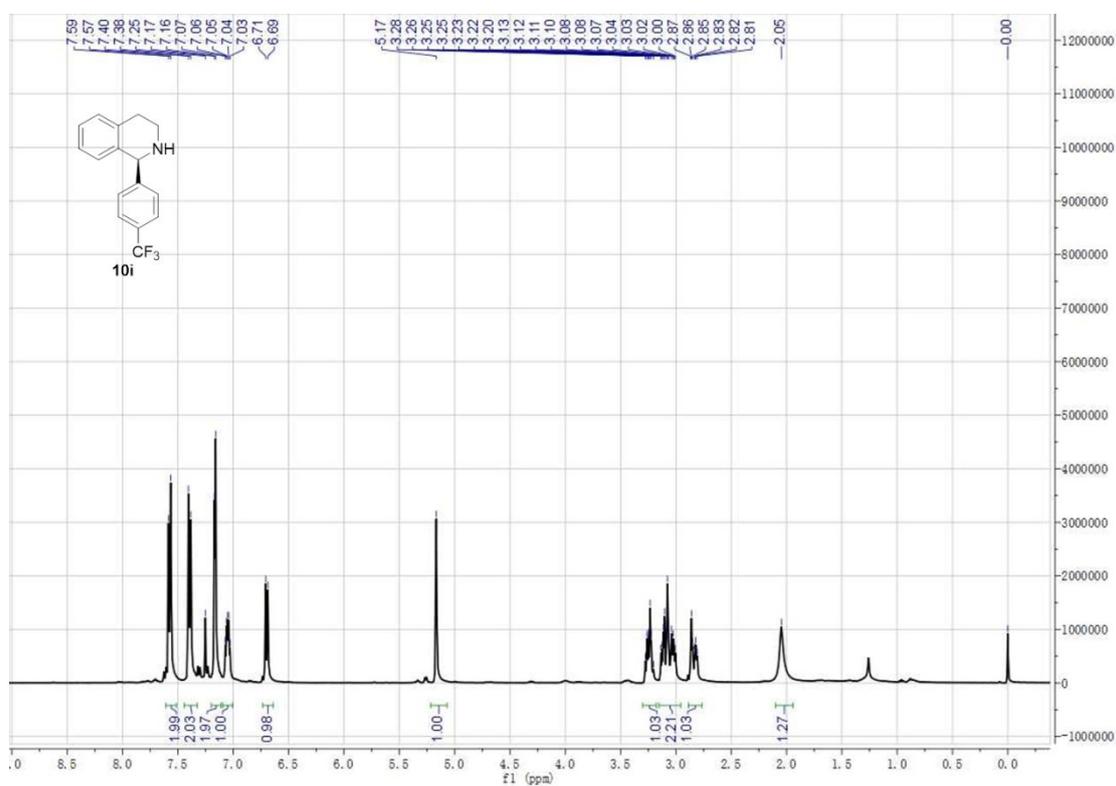
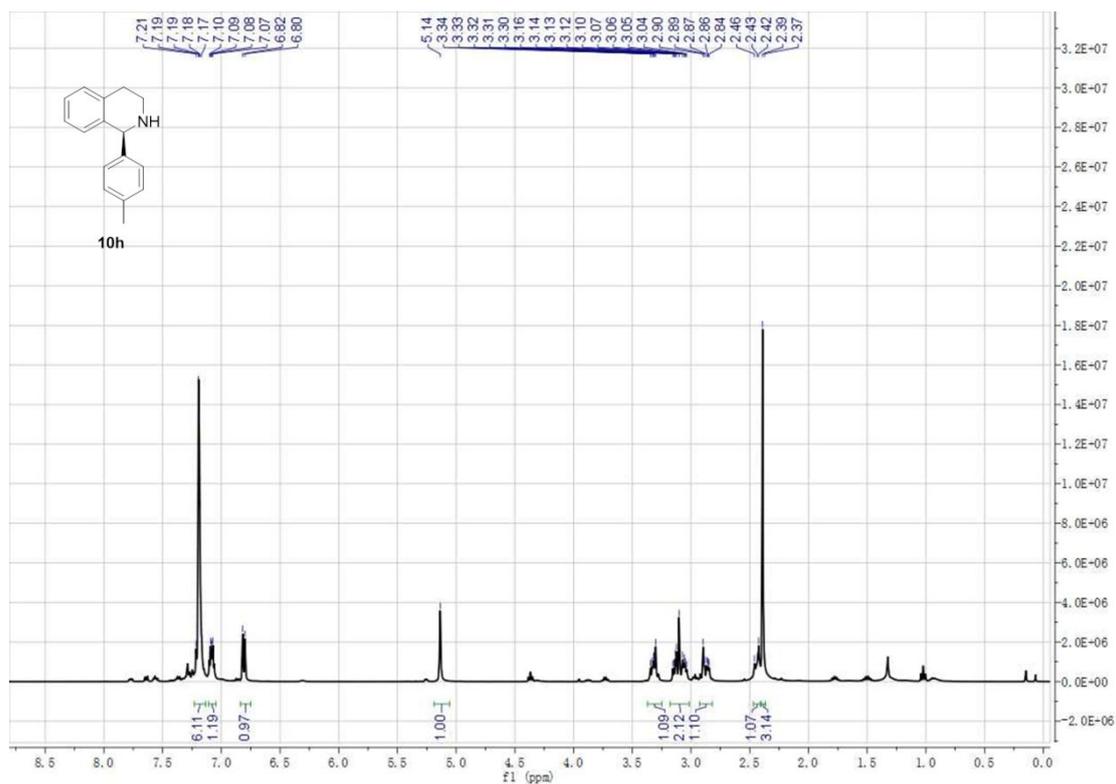


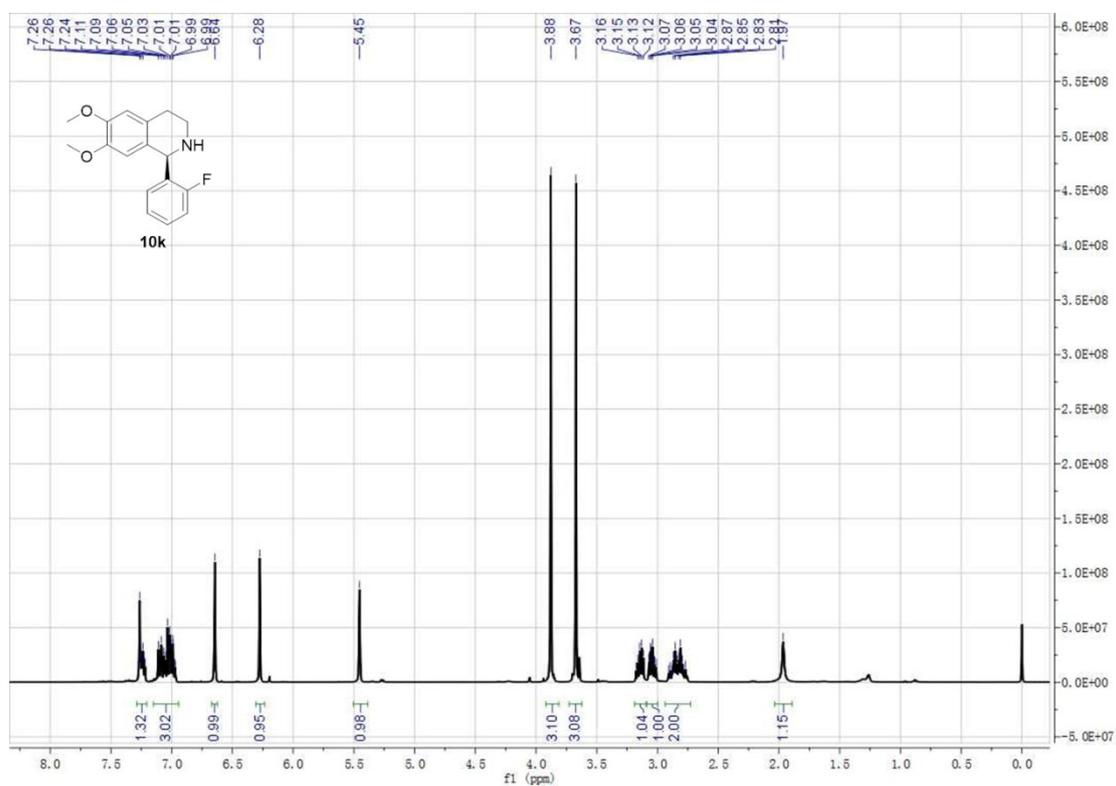
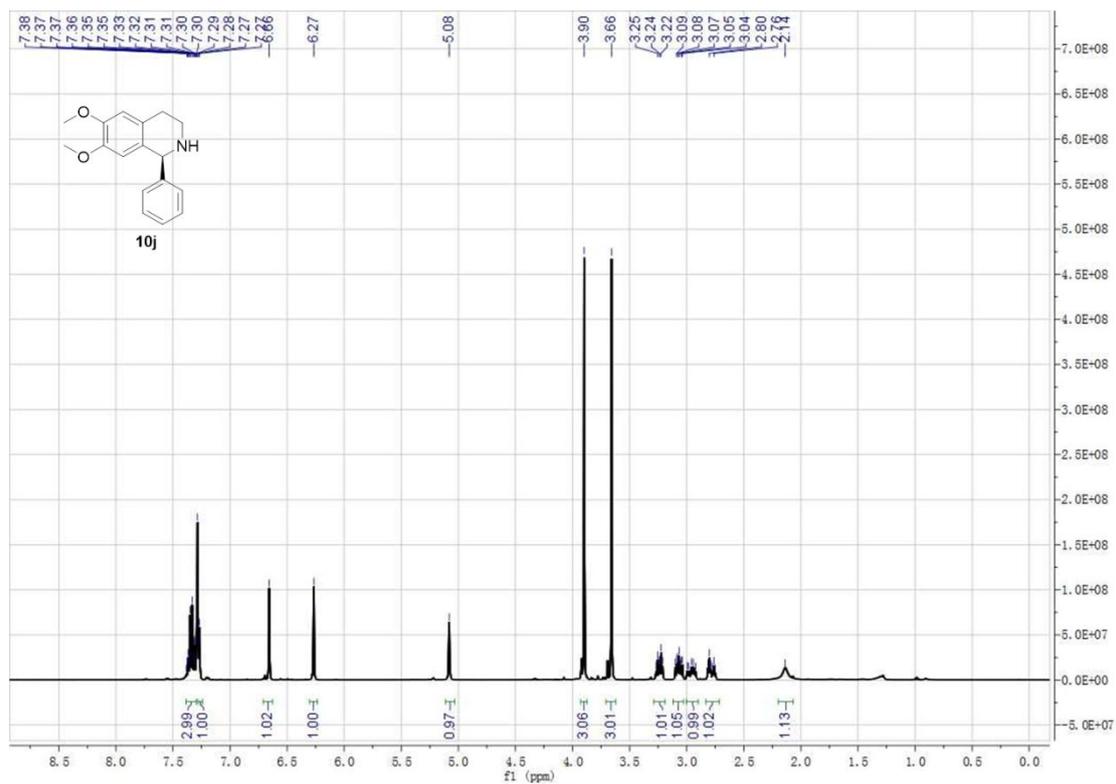
Sample Name	Position	p206	Instrument Name	Instrument 1
User Name	Inj Vol	1	InjPosition	
Sample Type	IRH Calibration Status	Success	Data Filename	N-2-p.d
ACQ Method	Comment		Acquired Time	3/1/2019 1:13:41 PM

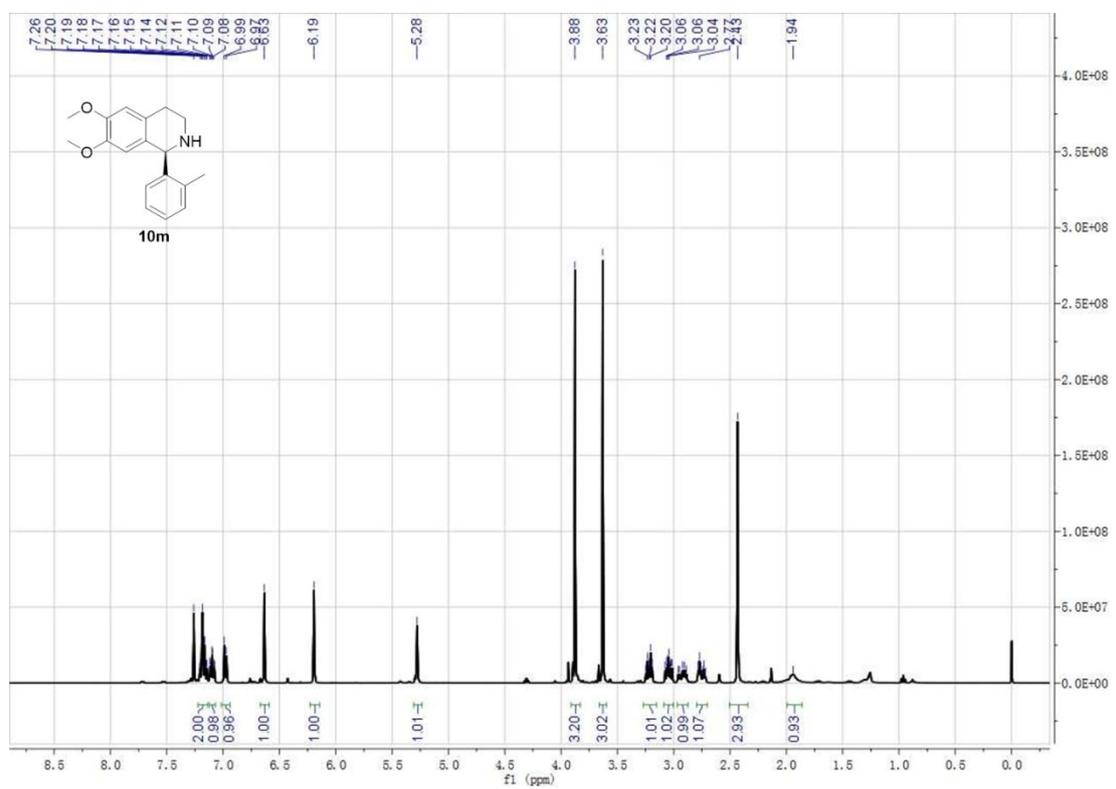
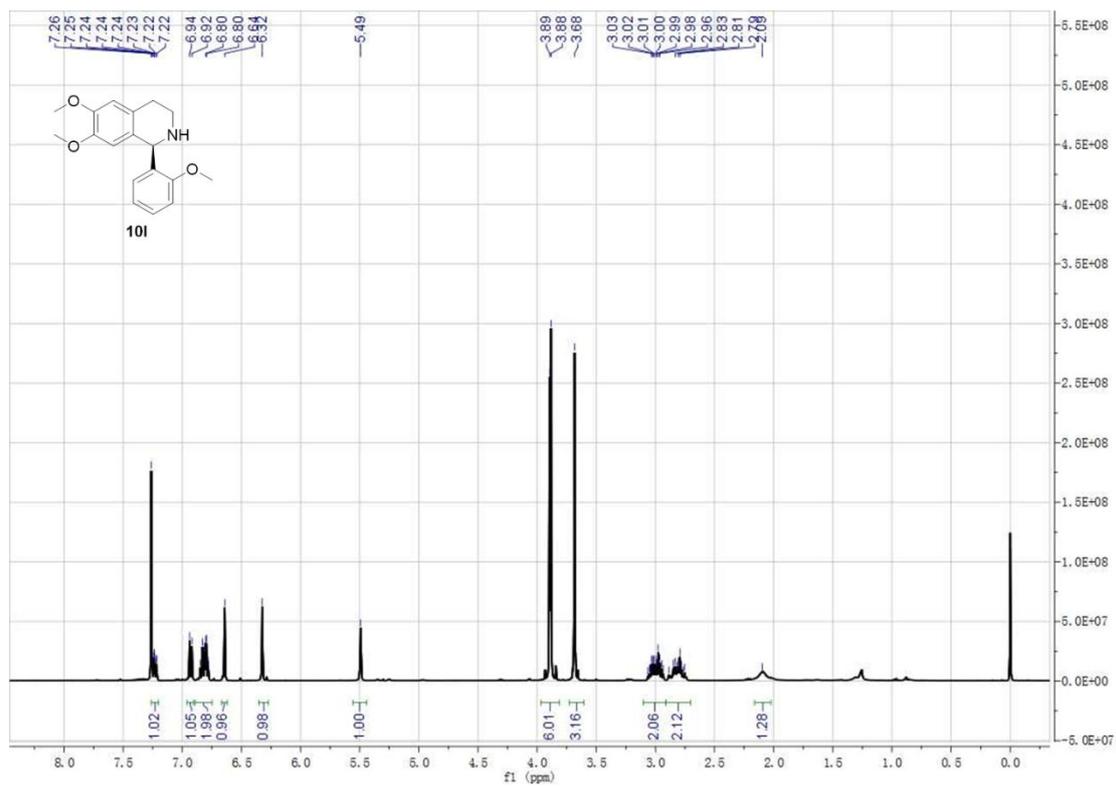


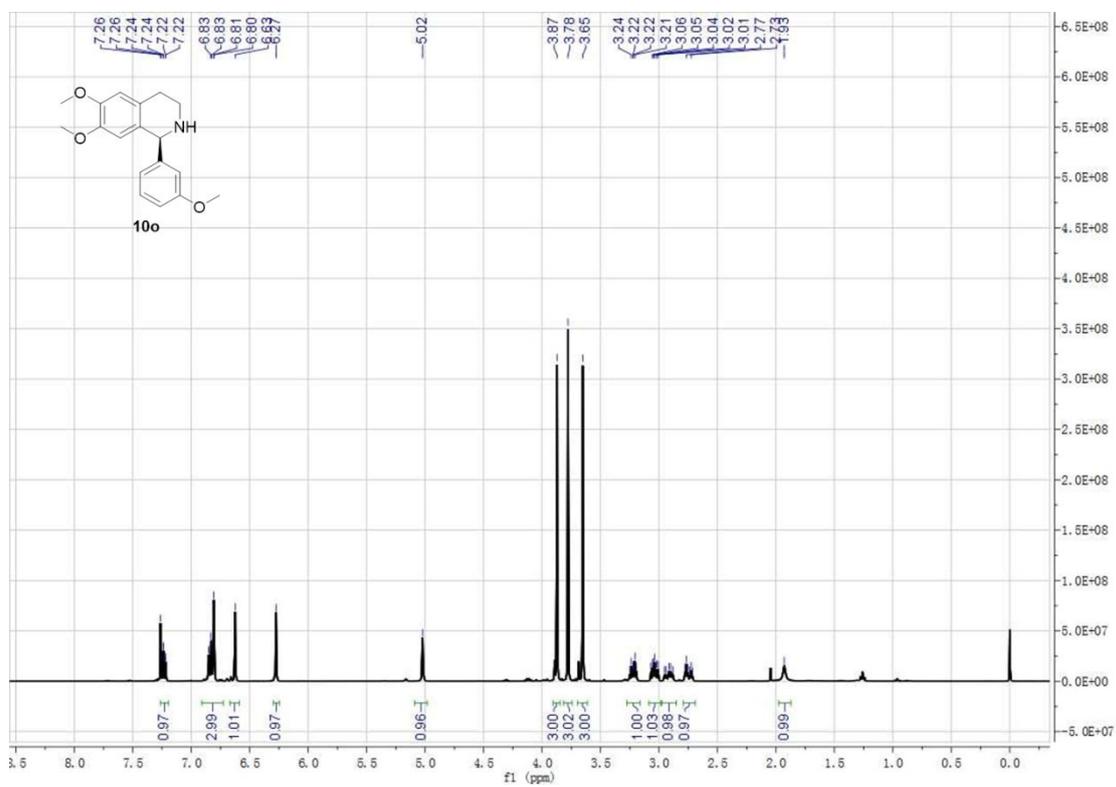
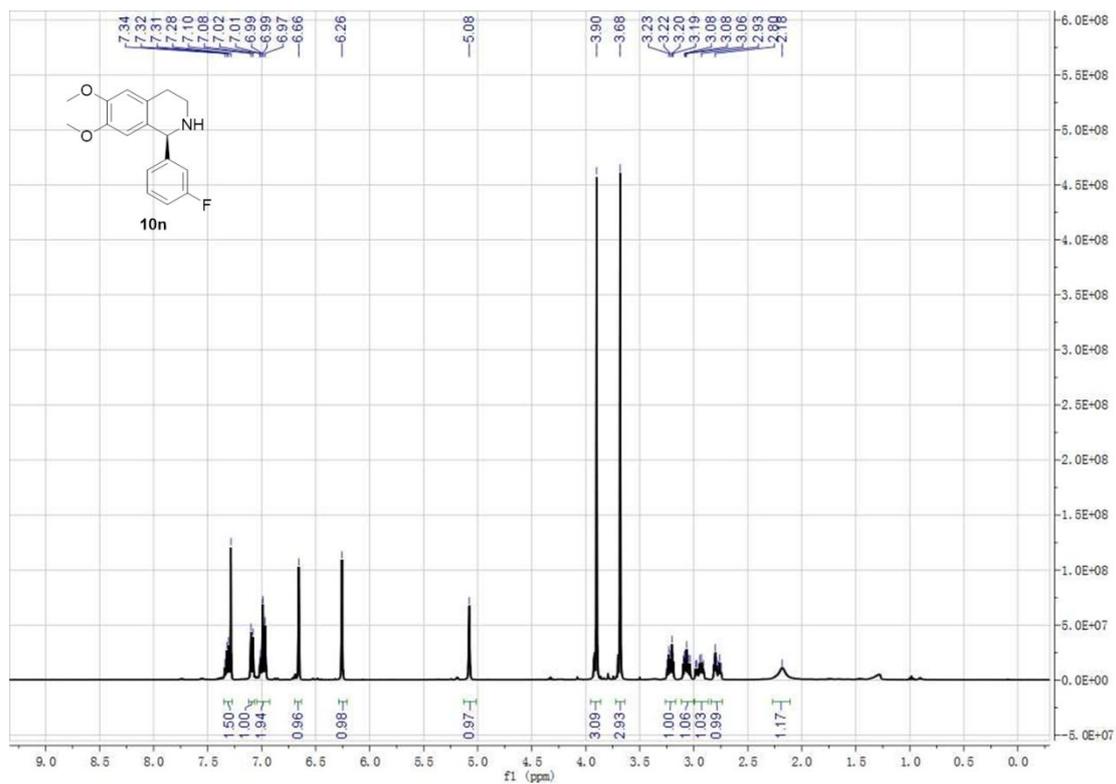


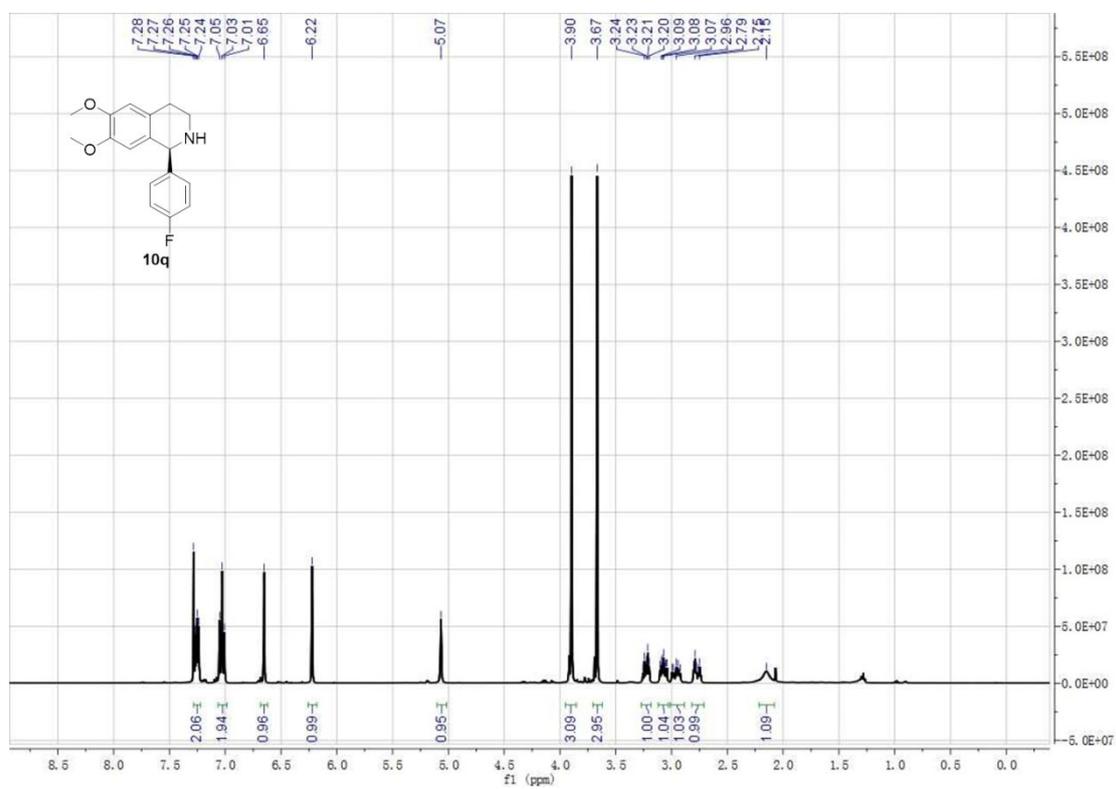
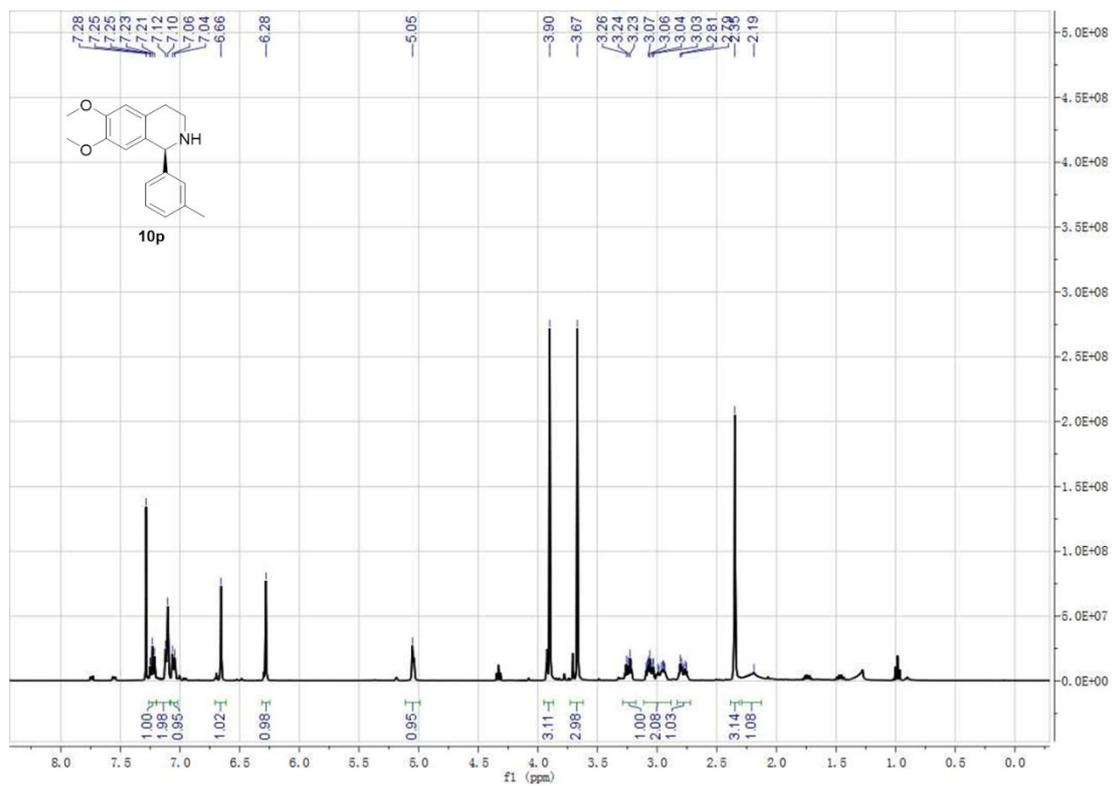


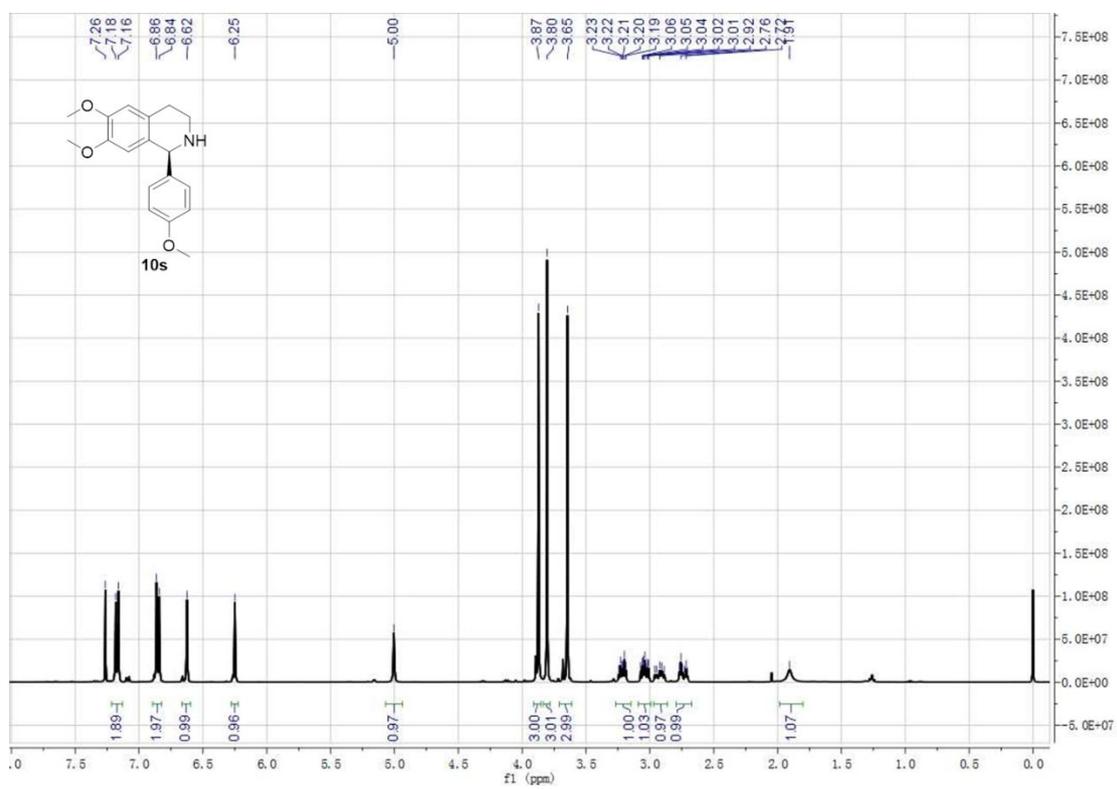
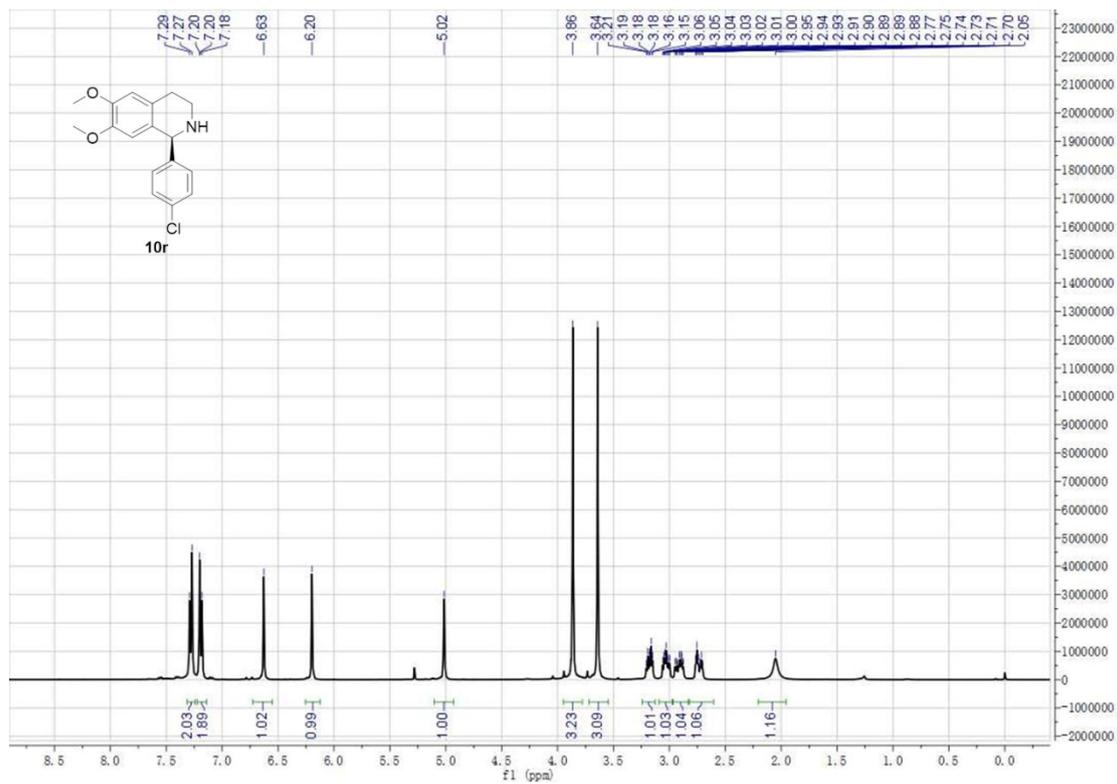


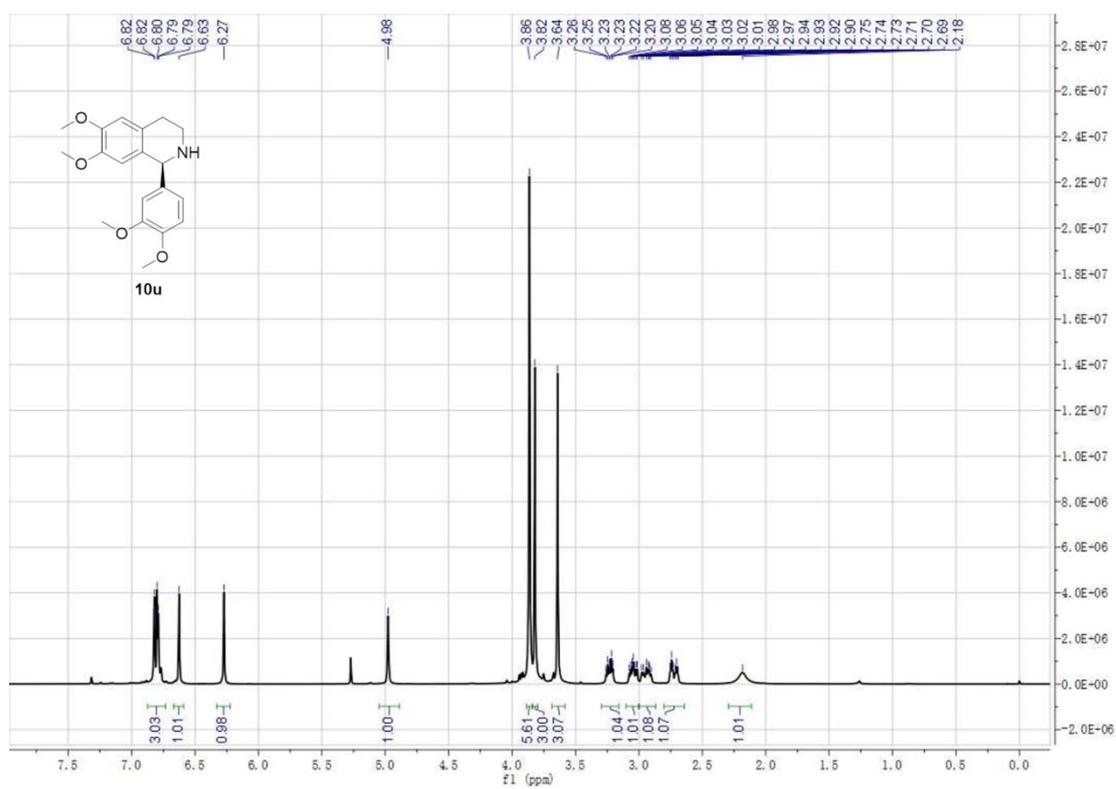
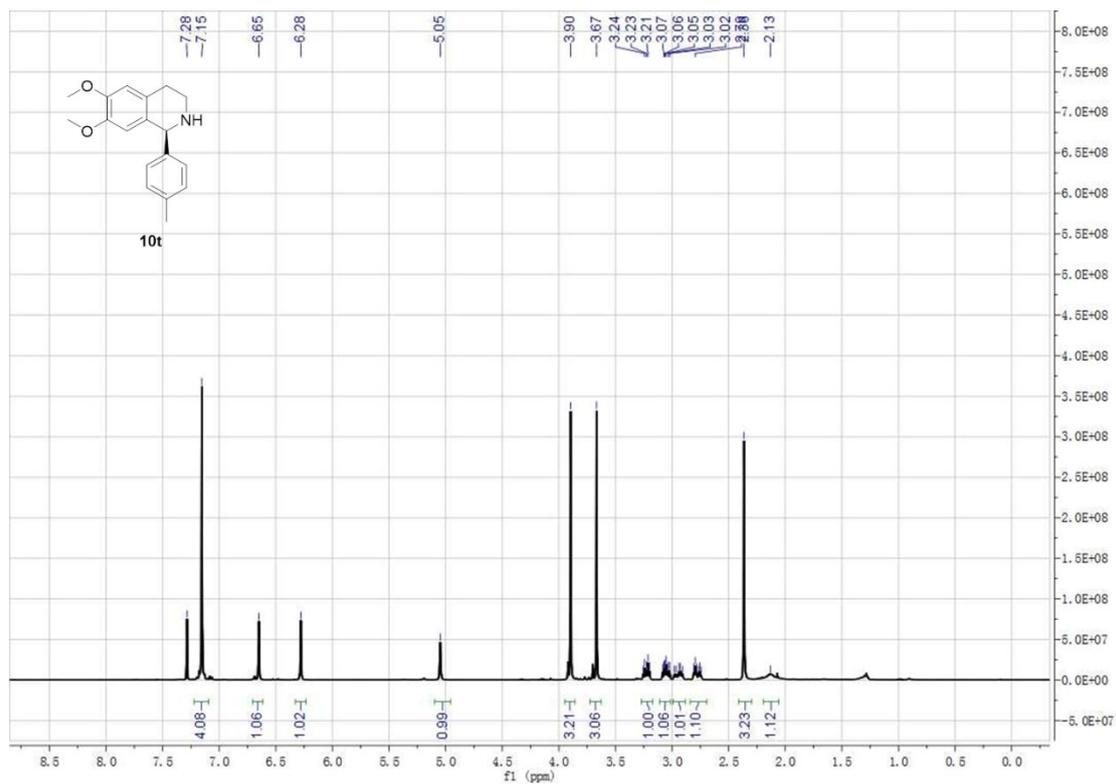


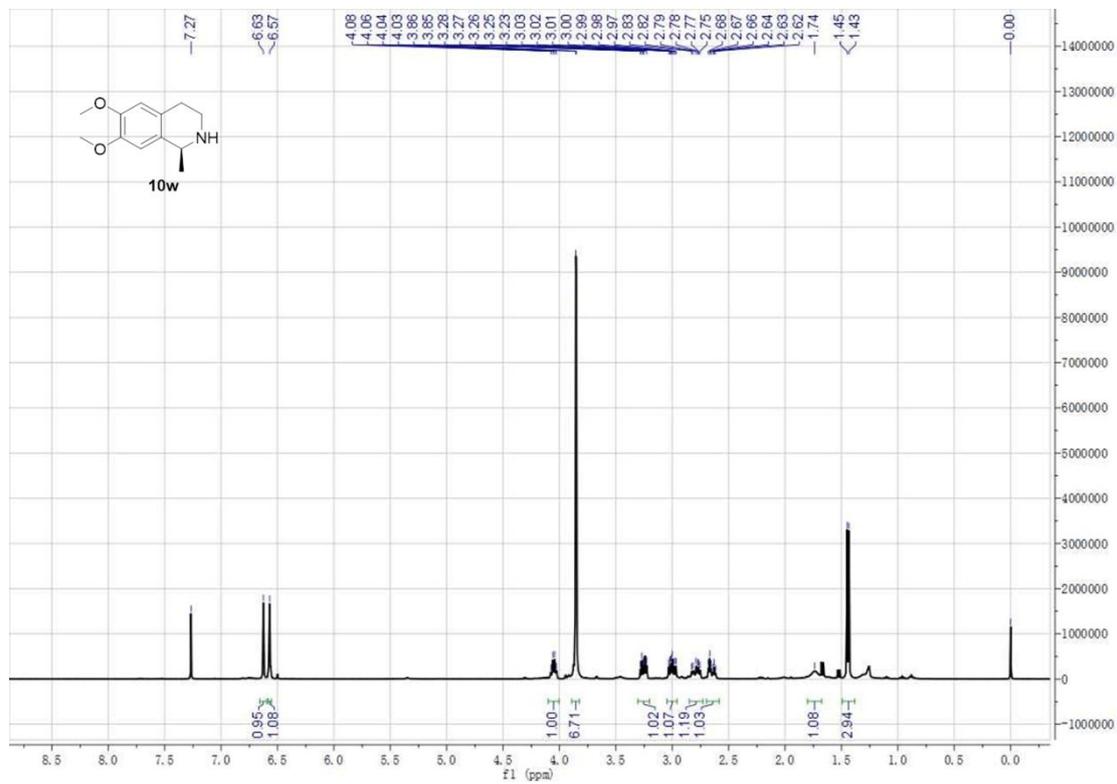
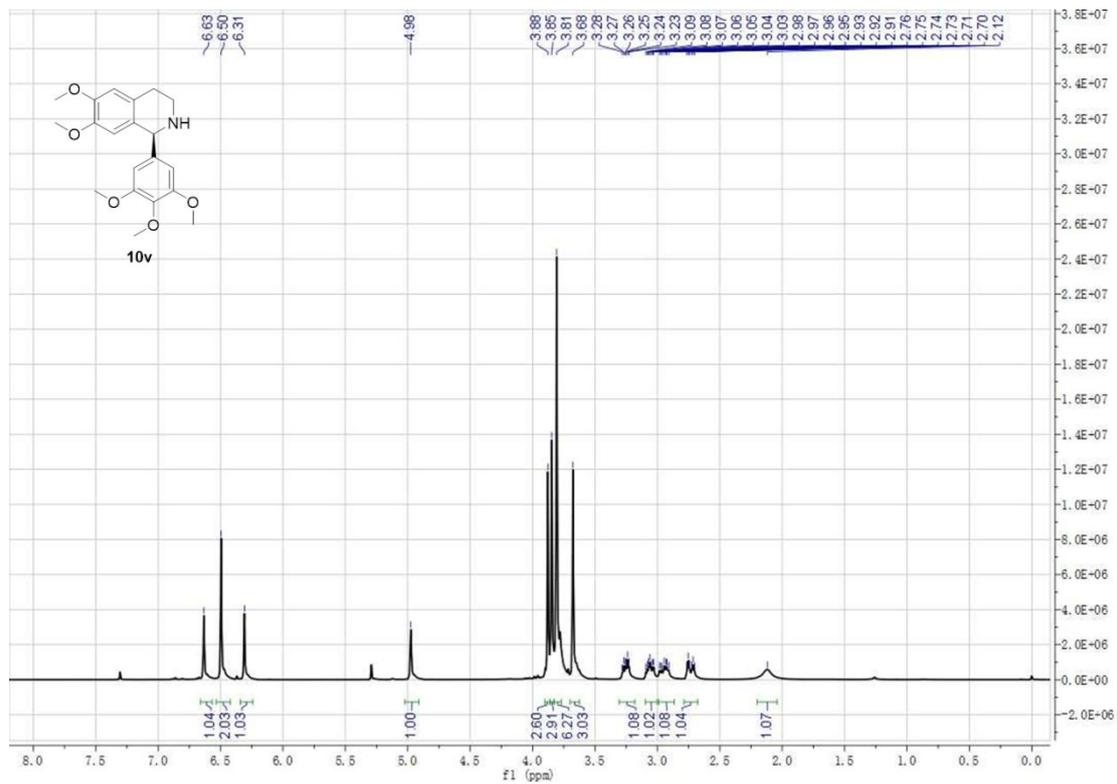


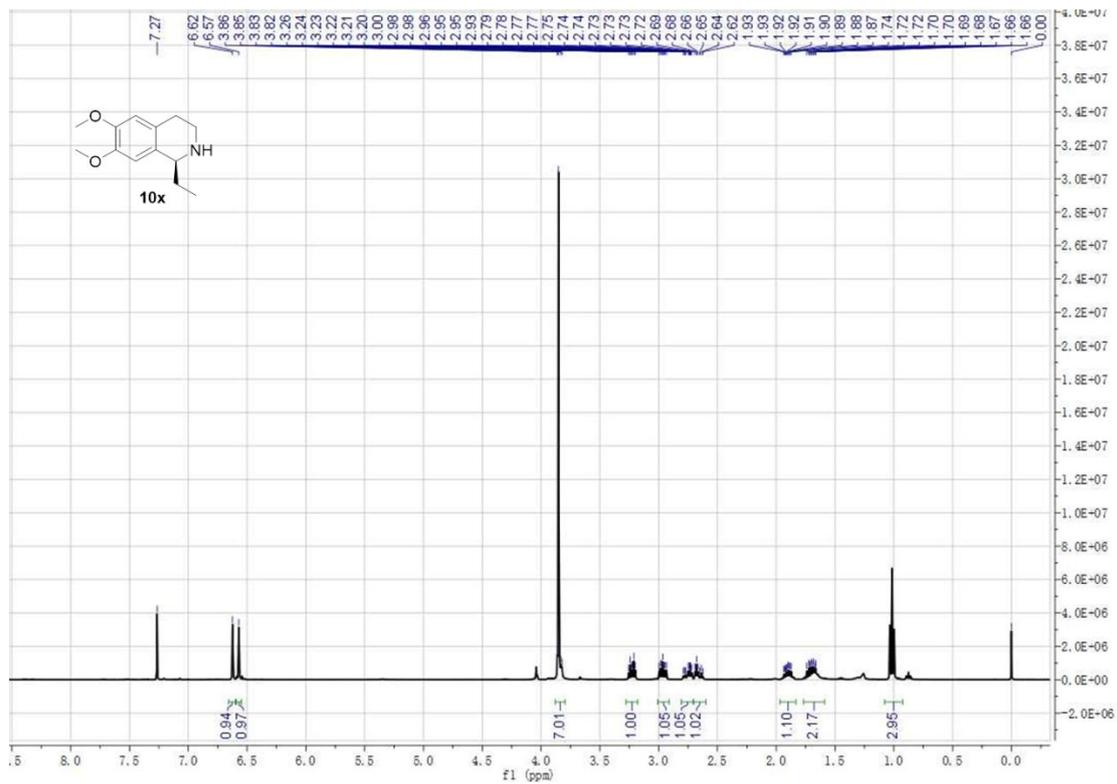




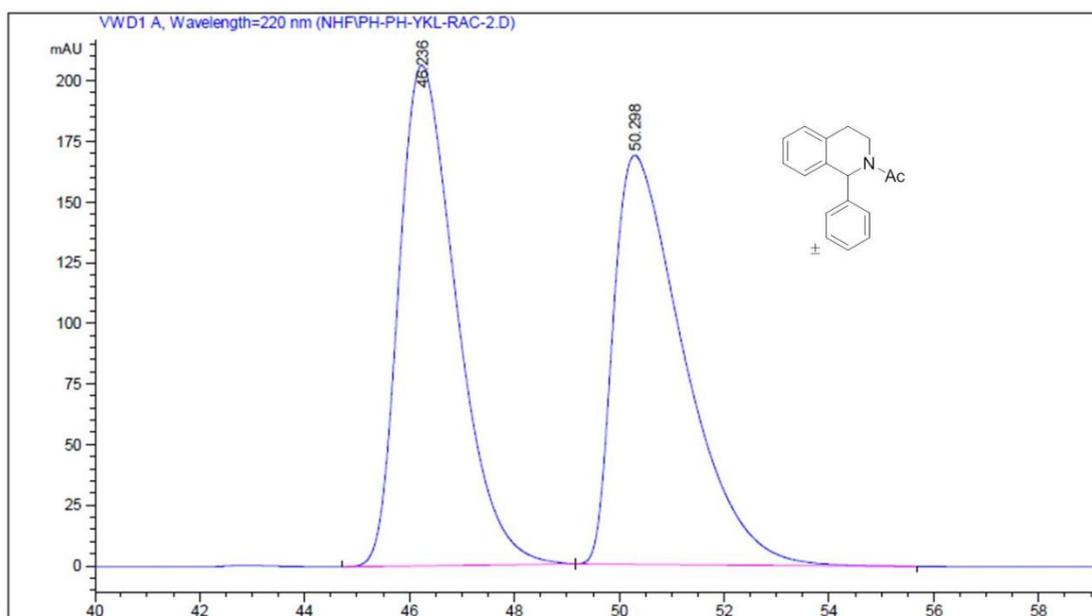




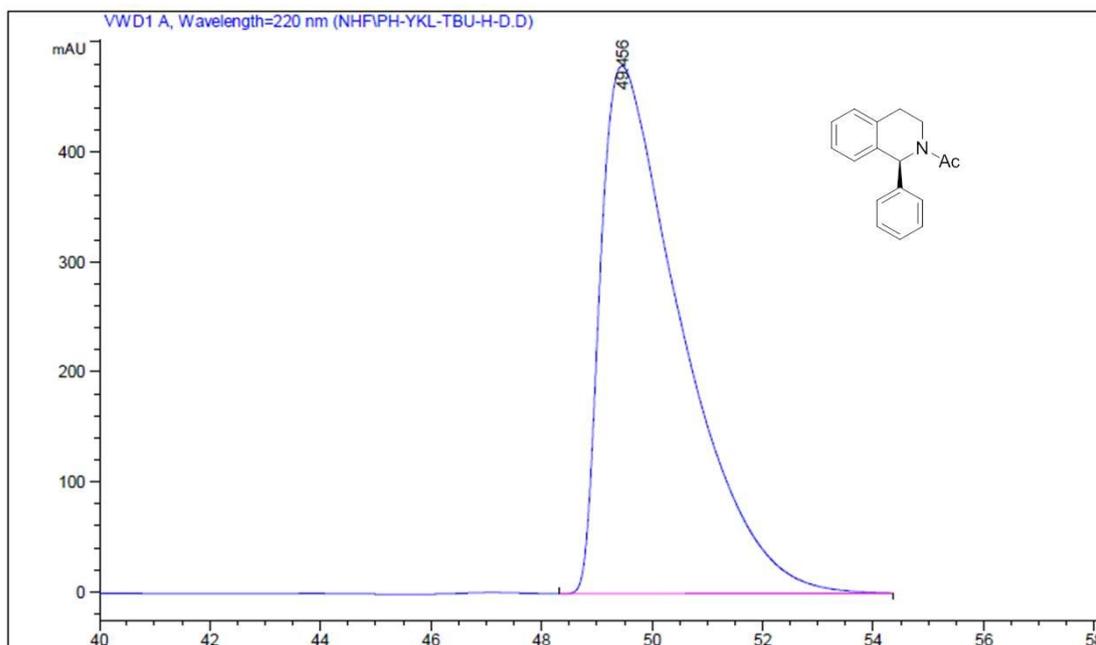




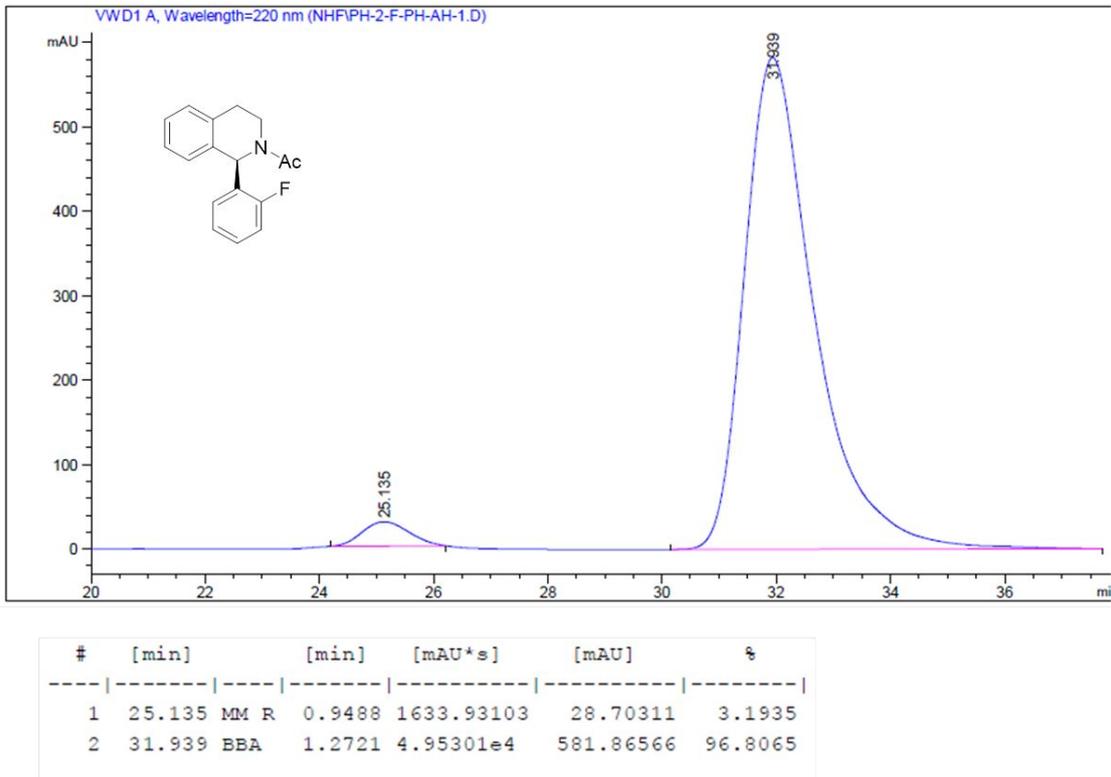
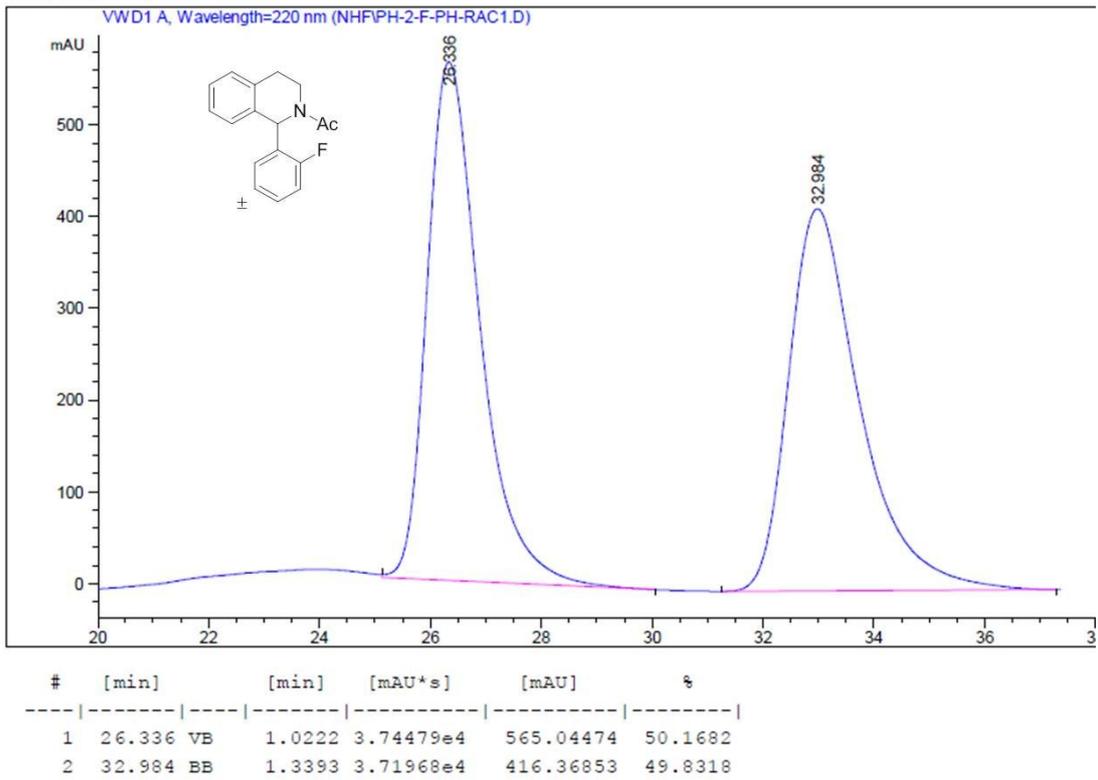
7. HPLC spectra

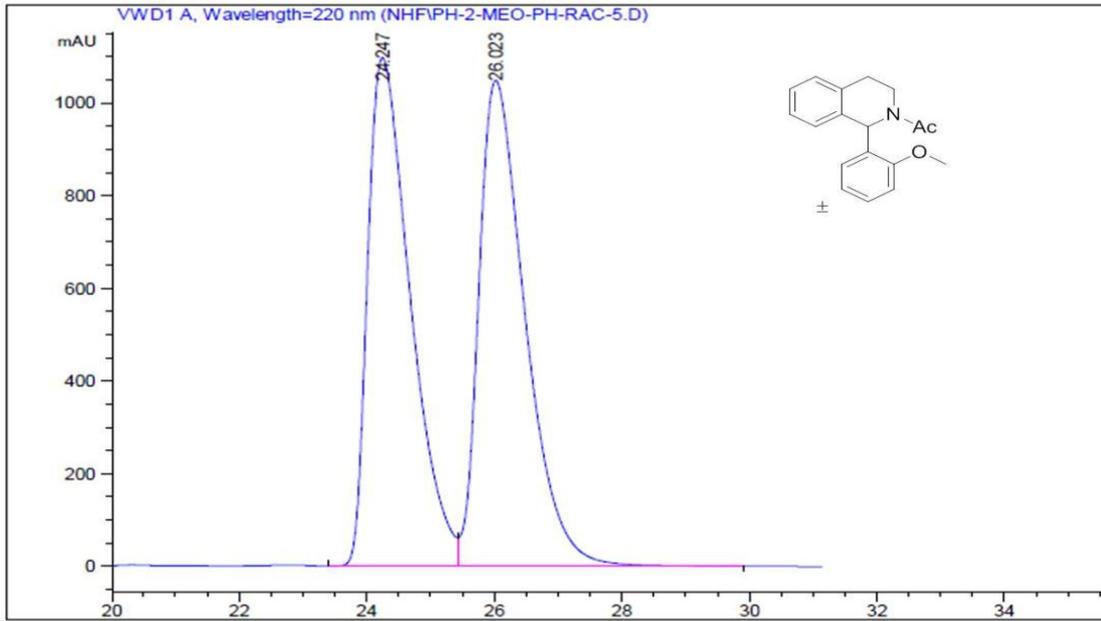


#	[min]	[min]	[mAU*s]	[mAU]	%
1	46.236 BB	1.1801	1.56897e4	206.34862	49.9413
2	50.298 BB	1.4190	1.57266e4	168.63892	50.0587

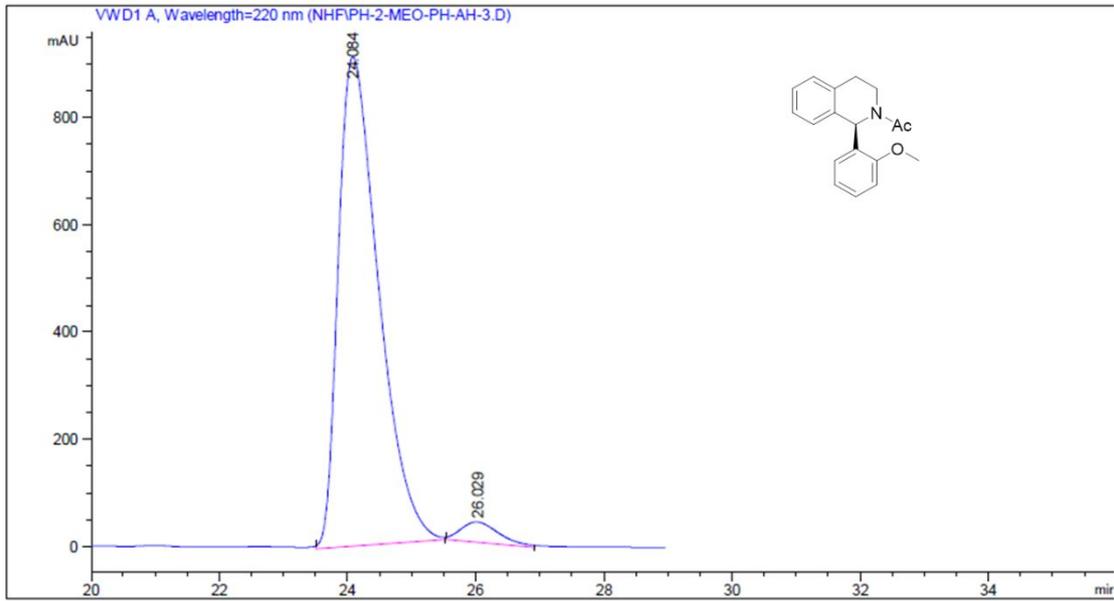


#	[min]	[min]	[mAU*s]	[mAU]	%
1	49.456 BBA	1.4984	4.88430e4	479.90402	100.0000

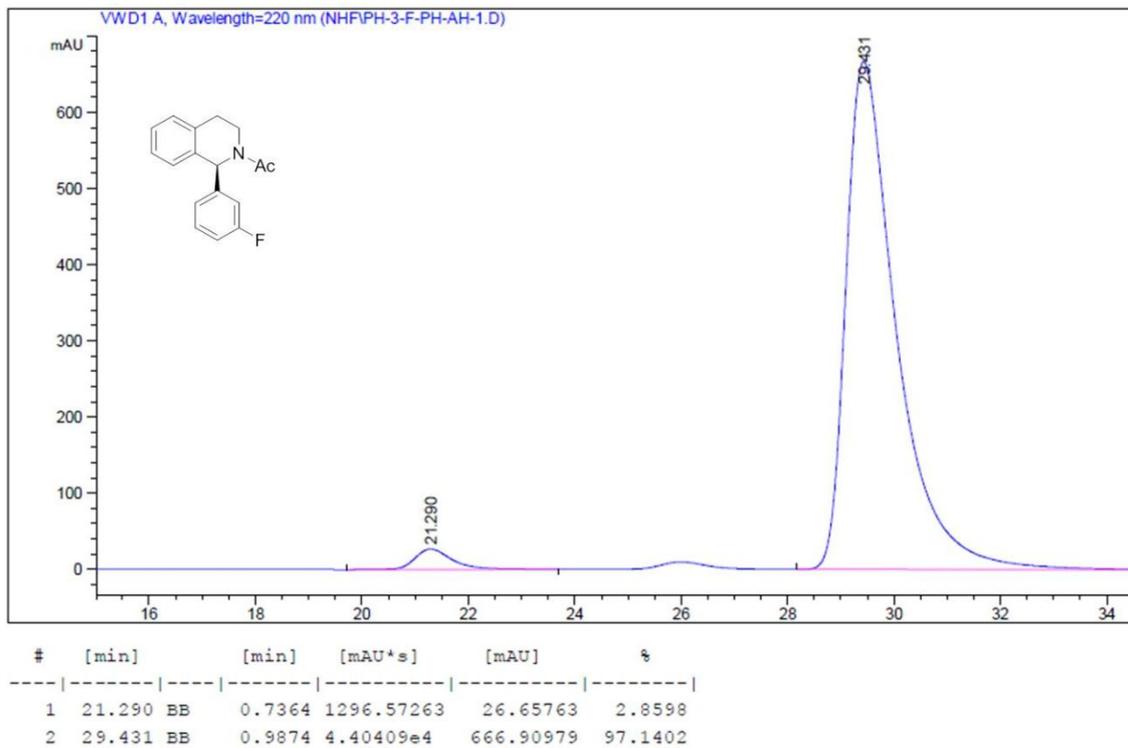
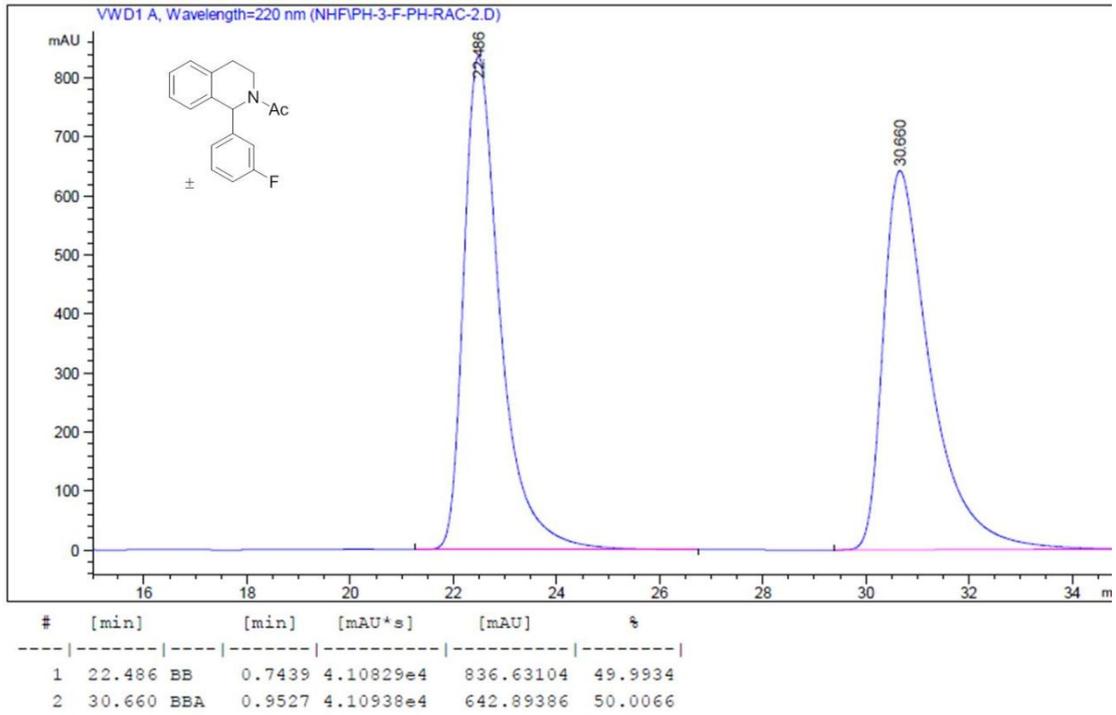


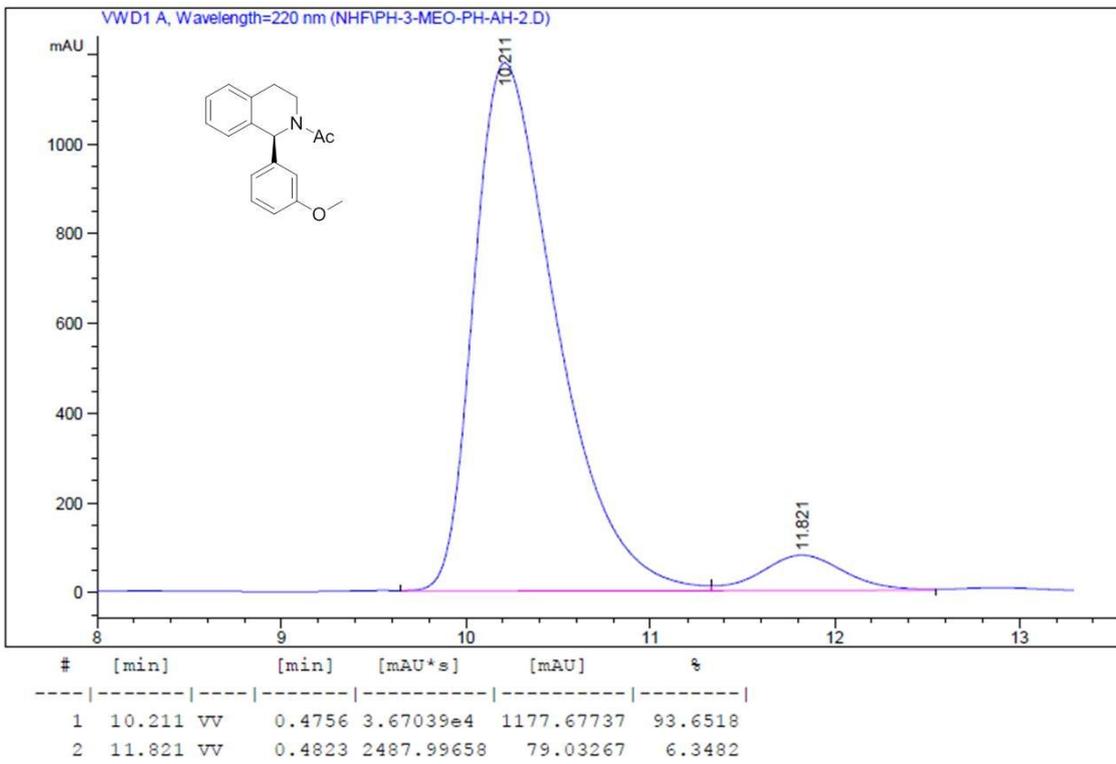
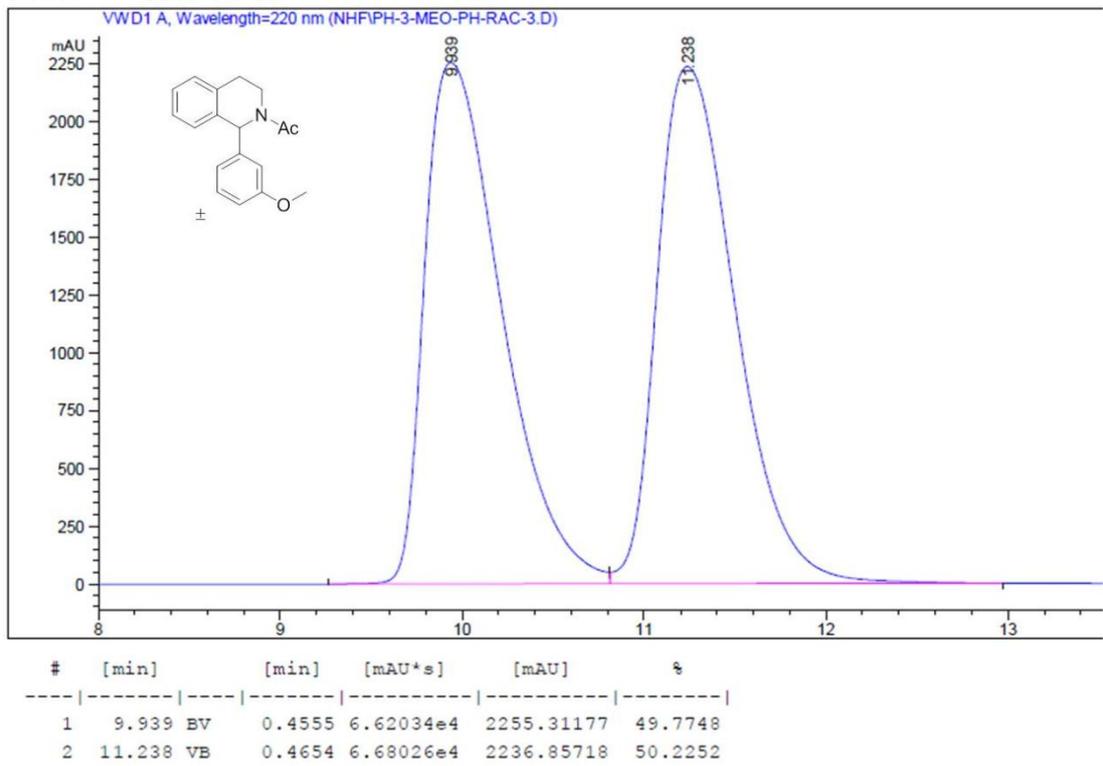


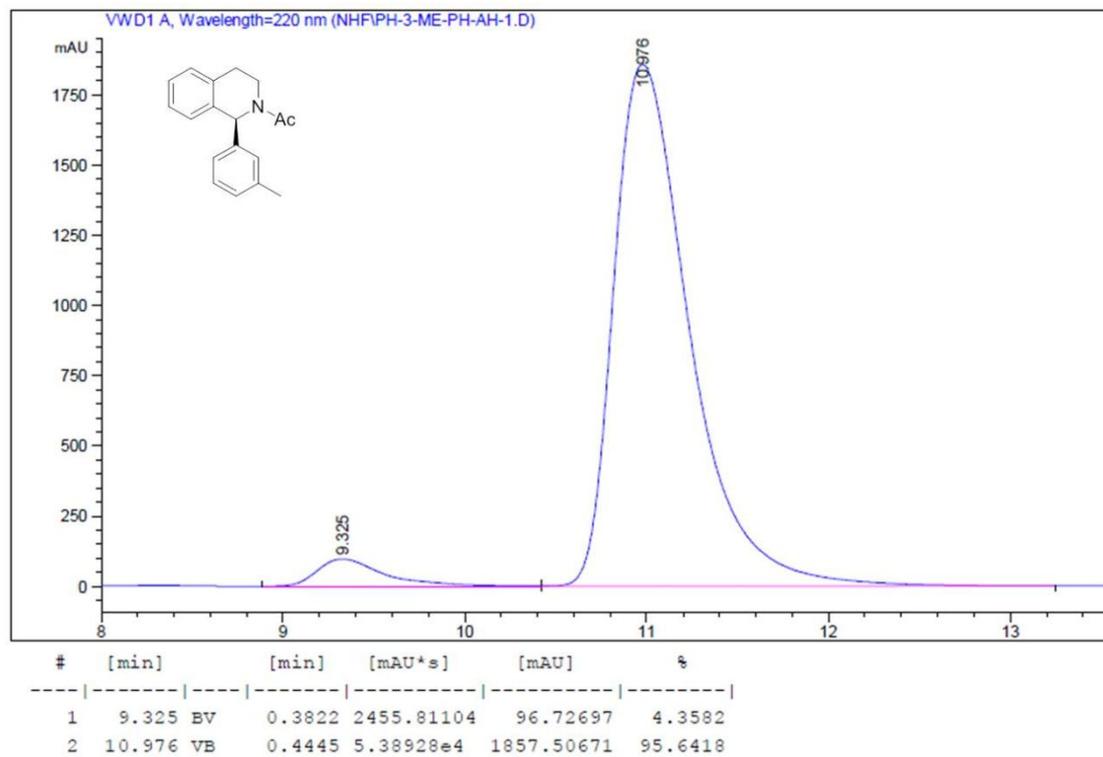
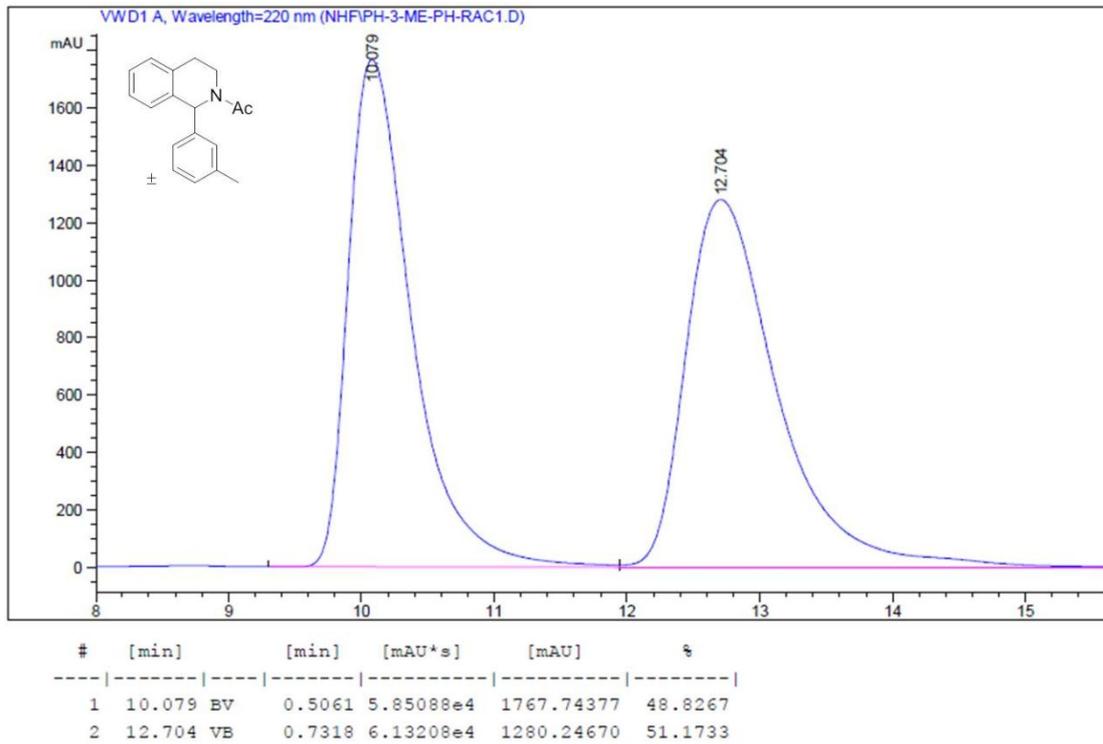
#	[min]	[min]	[mAU*s]	[mAU]	%
1	24.247 BV	0.7124	5.09269e4	1097.37354	49.0640
2	26.023 VB	0.7721	5.28700e4	1048.79651	50.9360

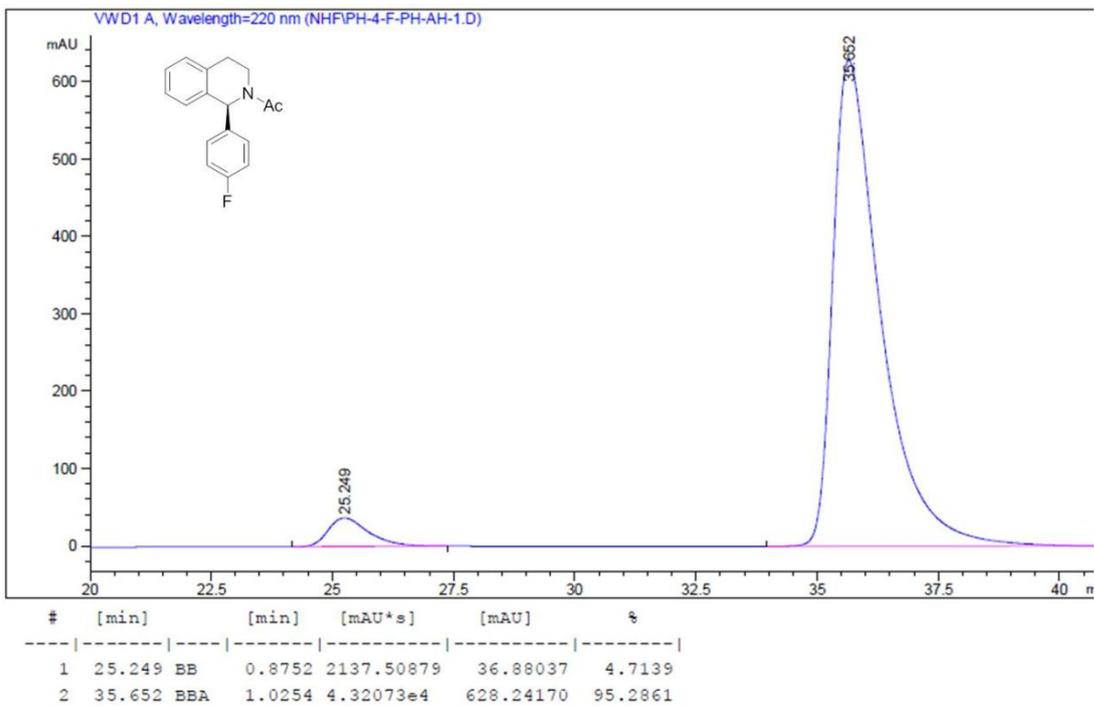
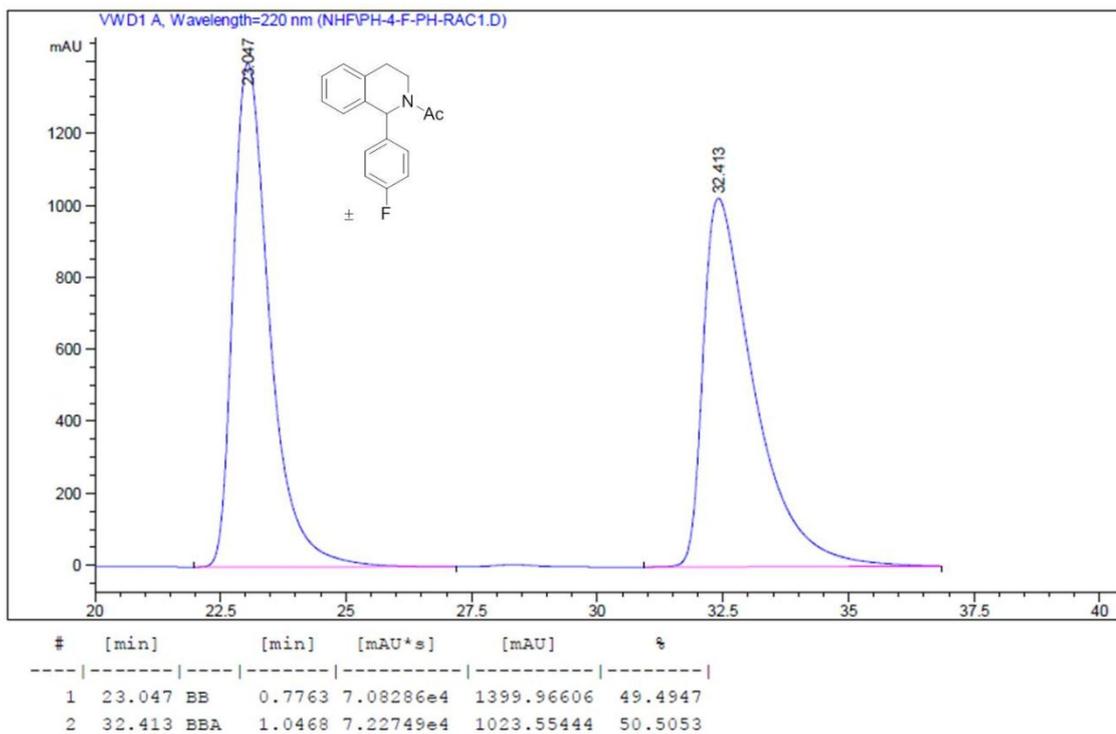


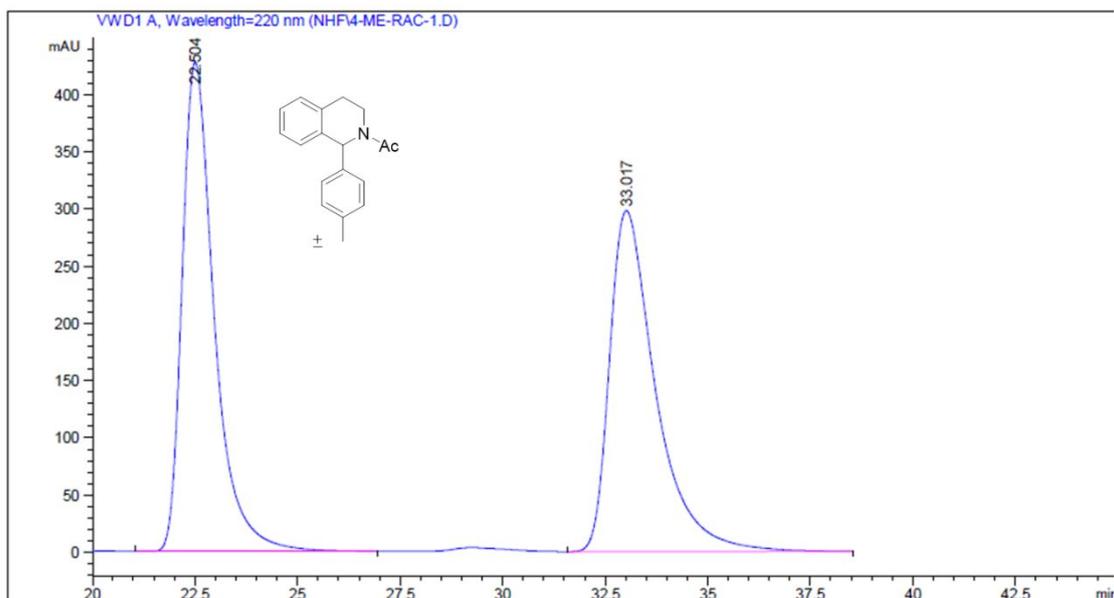
#	[min]	[min]	[mAU*s]	[mAU]	%
1	24.084 MM R	0.7272	3.98355e4	913.01239	96.1868
2	26.029 MM R	0.6969	1579.24353	37.77035	3.8132



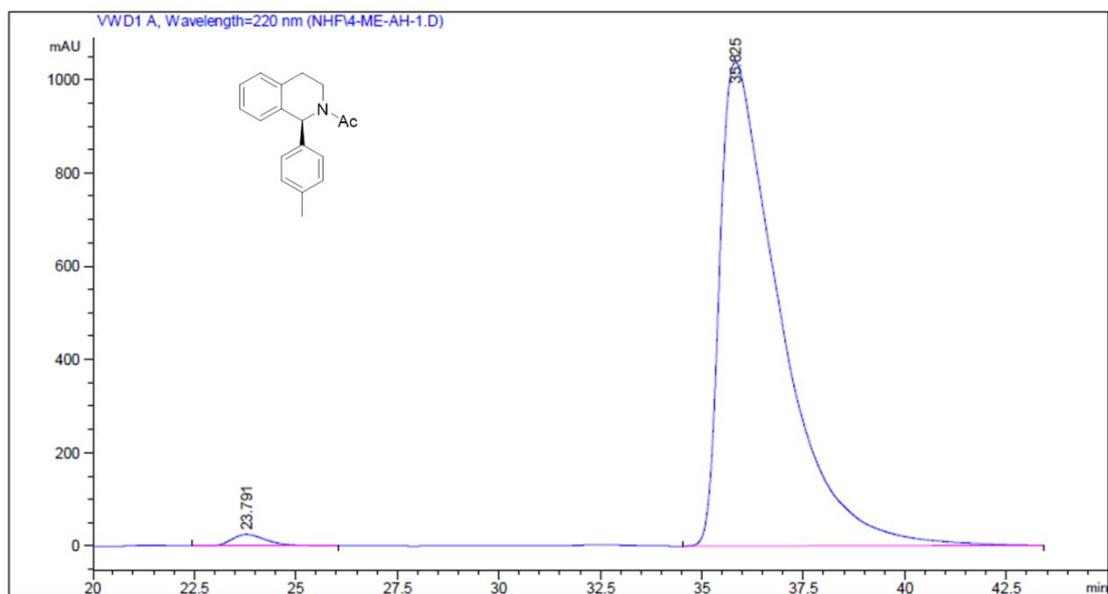




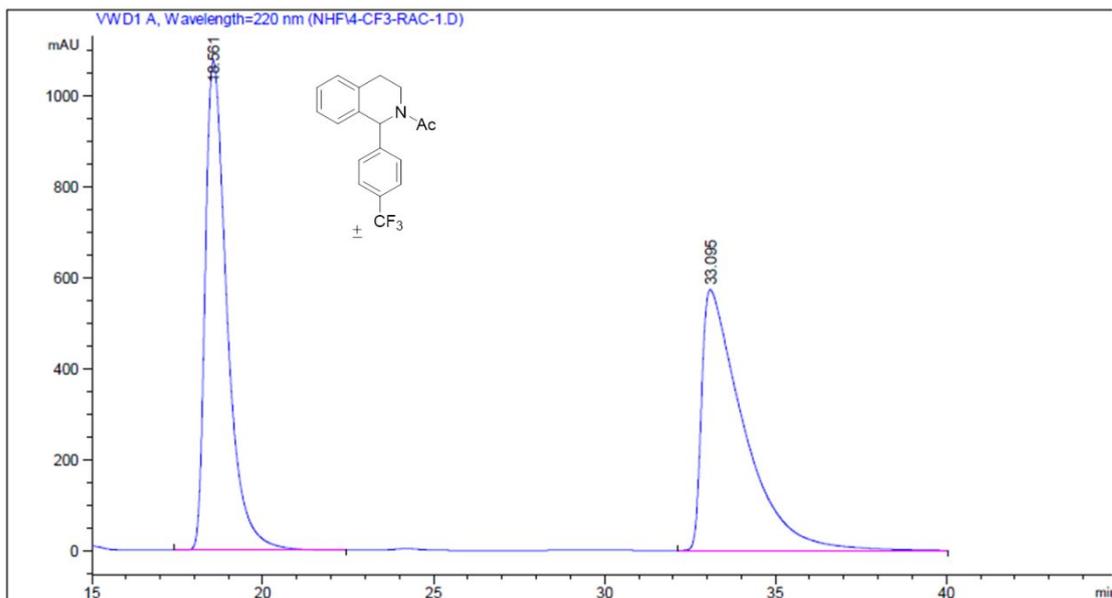




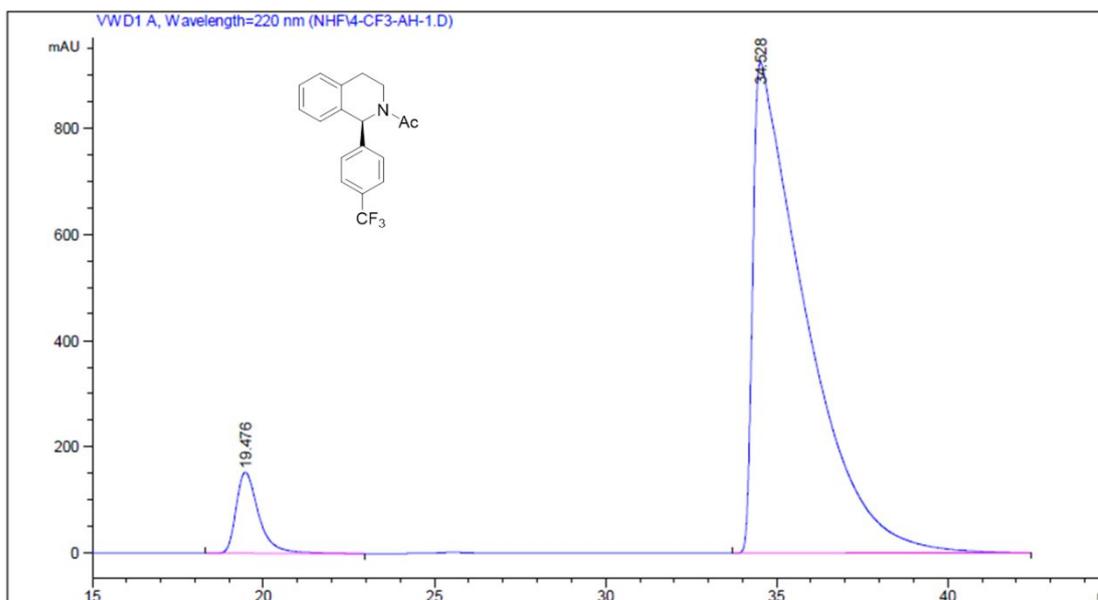
#	[min]	[min]	[mAU*s]	[mAU]	%	
1	22.504	BB	0.8311	2.33117e4	427.53107	50.0365
2	33.017	BBA	1.1869	2.32777e4	298.12299	49.9635



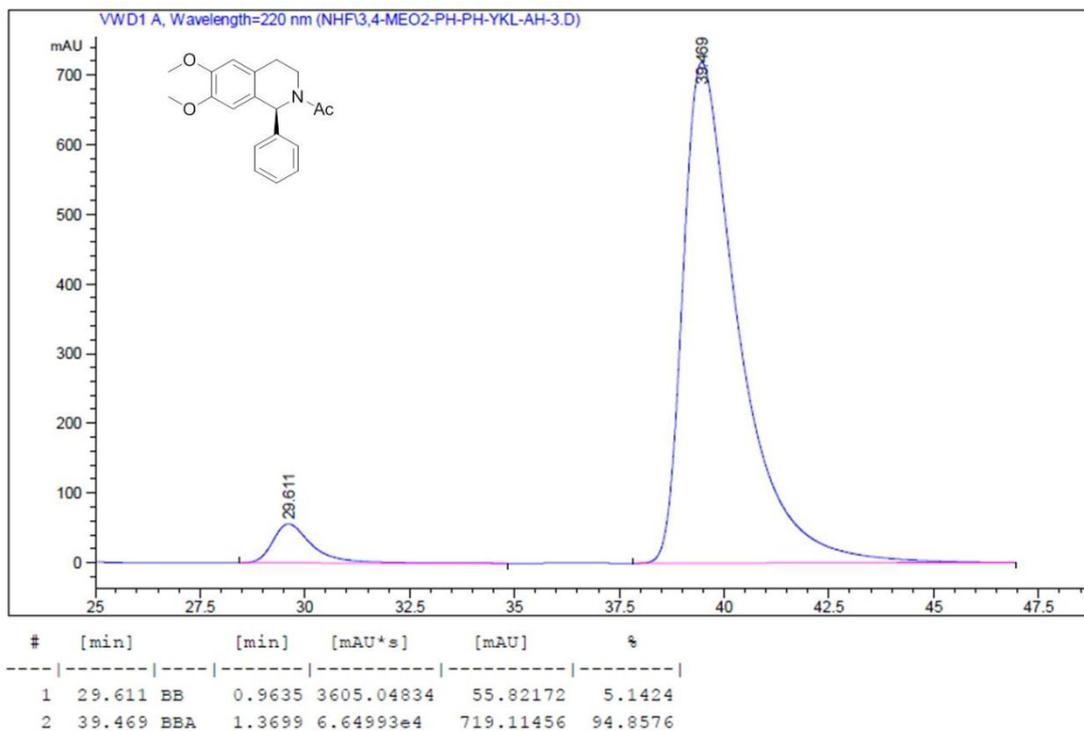
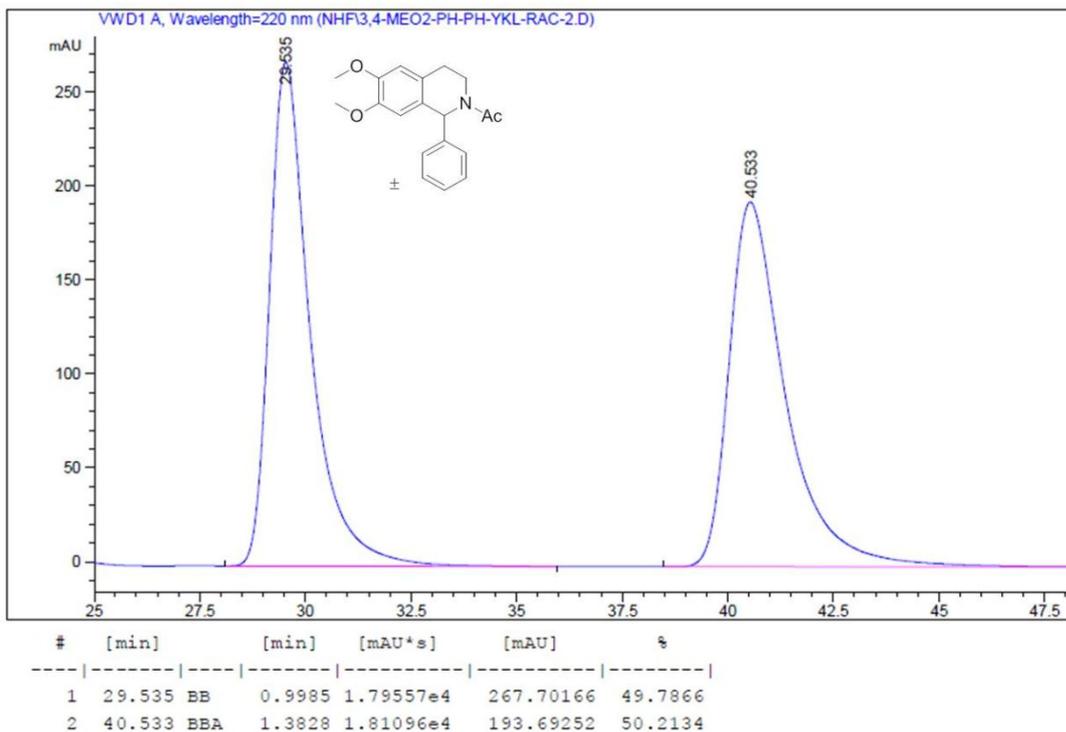
#	[min]	[min]	[mAU*s]	[mAU]	%	
1	23.791	BB	0.9125	1443.49683	24.38996	1.3374
2	35.825	BBA	1.4372	1.06488e5	1038.61377	98.6626

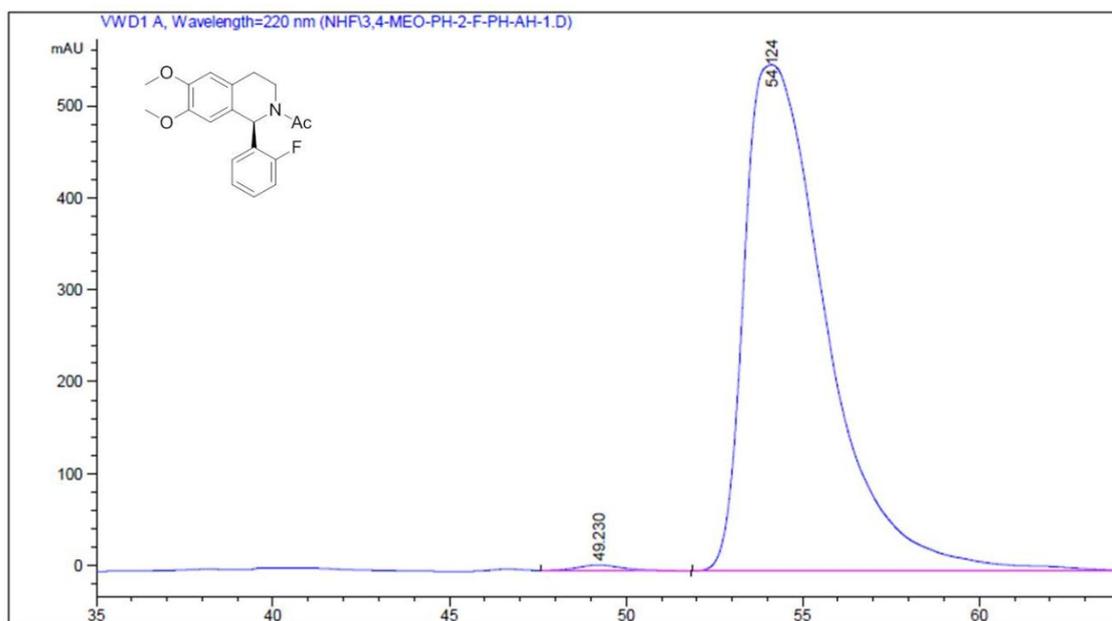
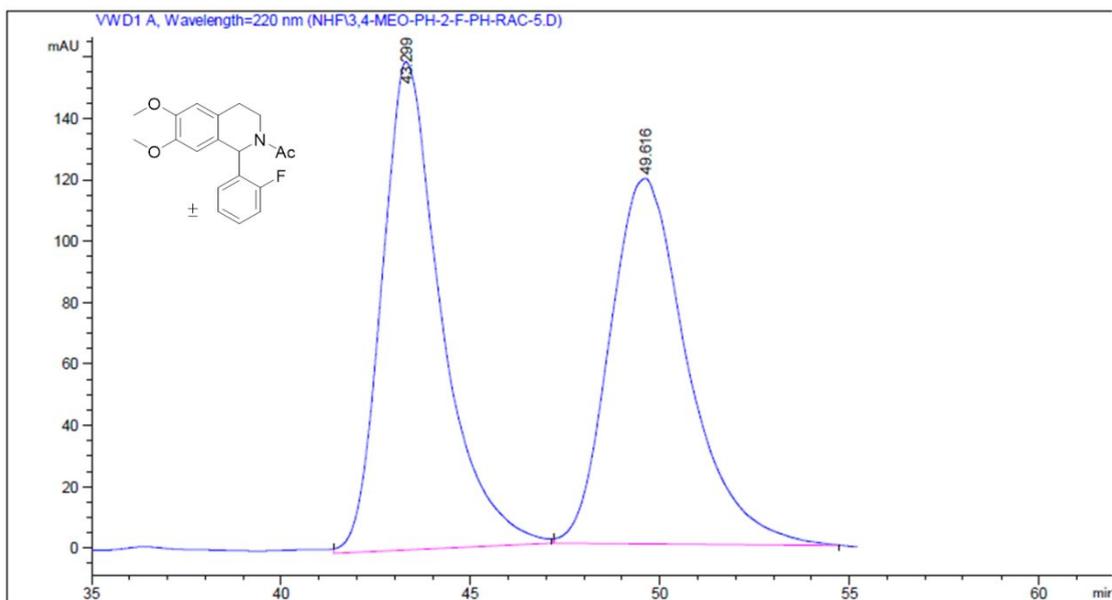


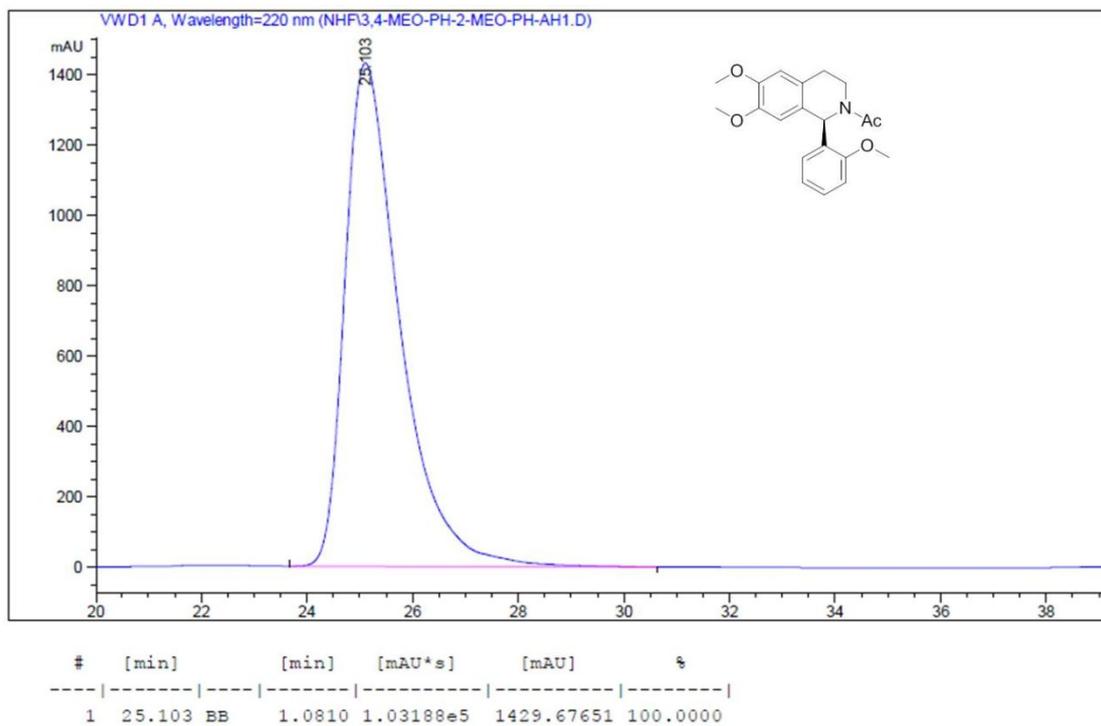
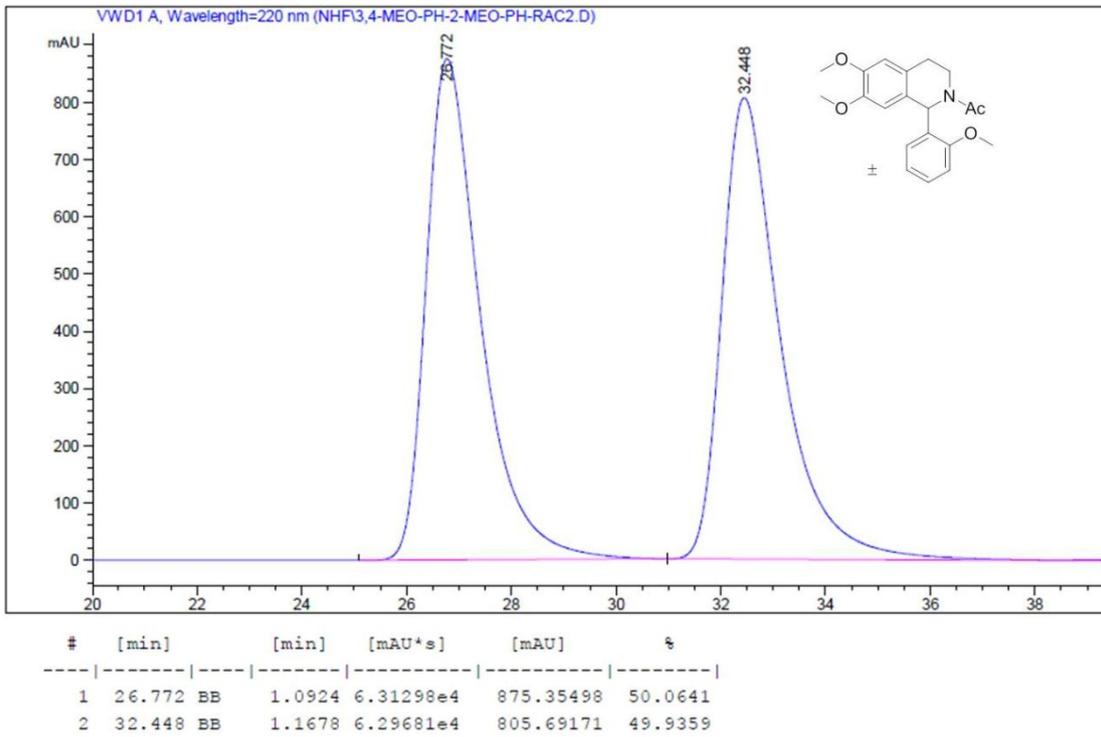
#	[min]	[min]	[mAU*s]	[mAU]	%	
1	18.561	BB	0.6752	4.76625e4	1077.16504	49.4773
2	33.095	BBA	1.2119	4.86695e4	573.62292	50.5227

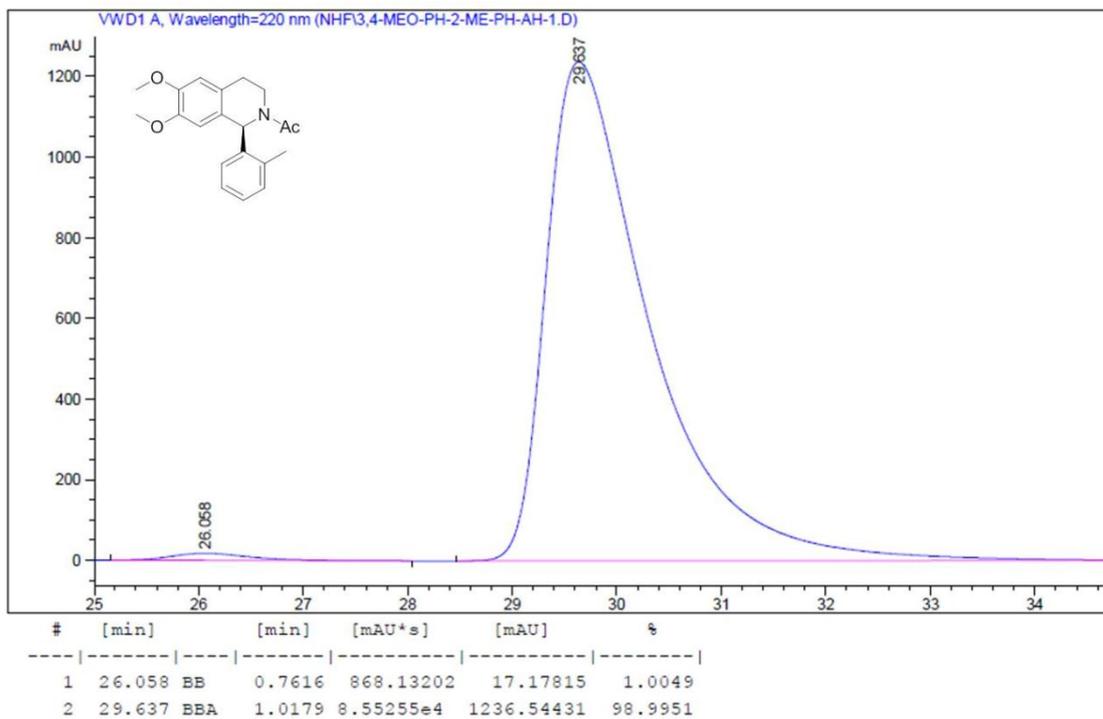
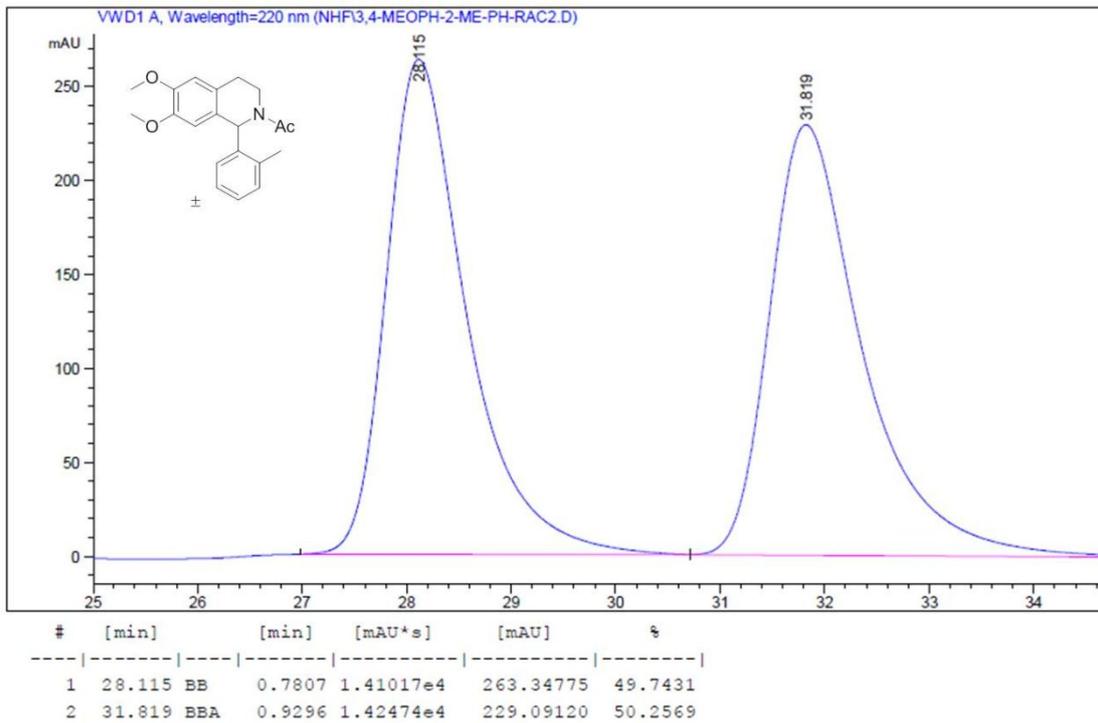


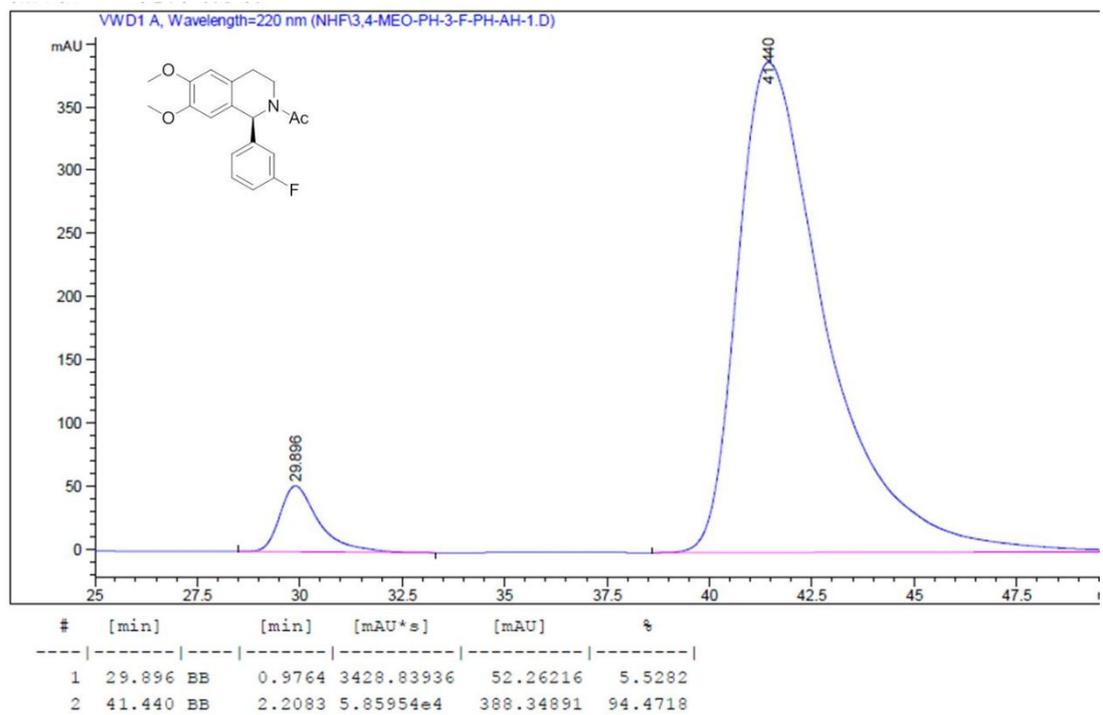
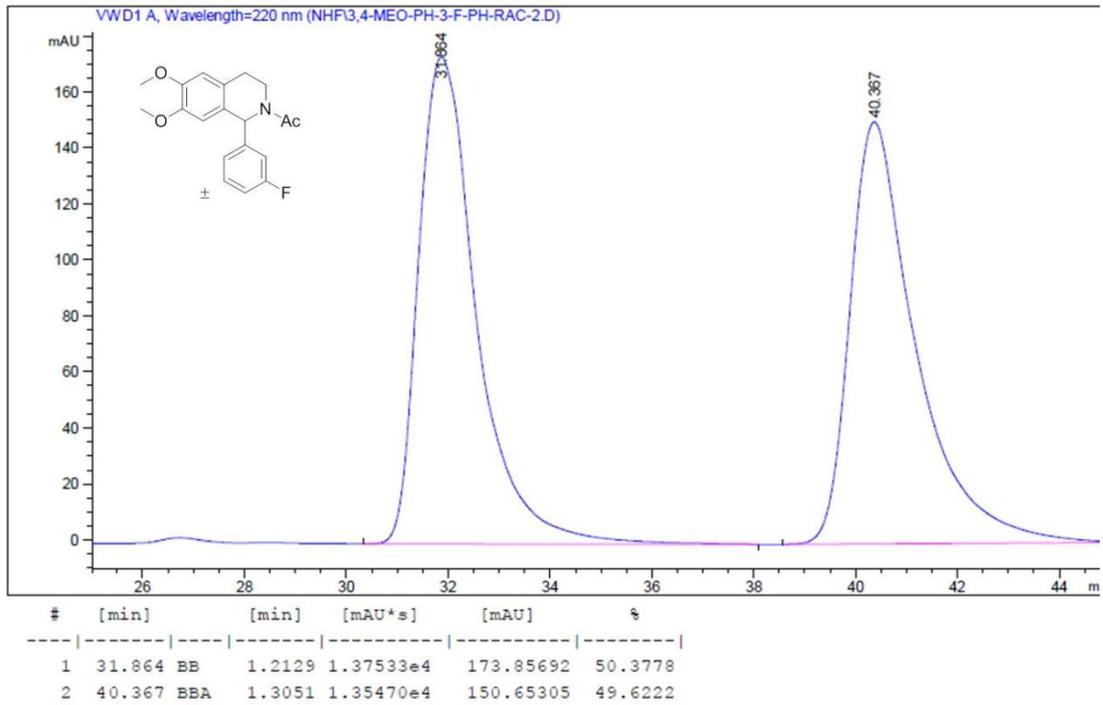
#	[min]	[min]	[mAU*s]	[mAU]	%	
1	19.476	BB	0.7020	6988.89258	152.40936	6.6367
2	34.528	BBA	1.3645	9.83173e4	923.14661	93.3633

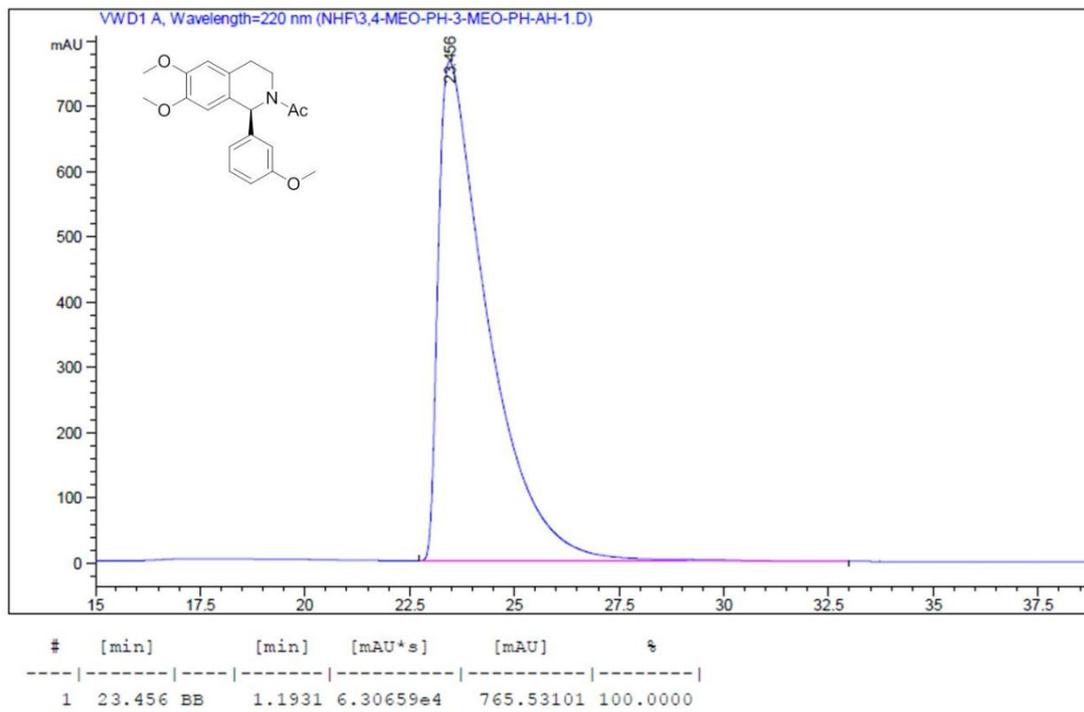
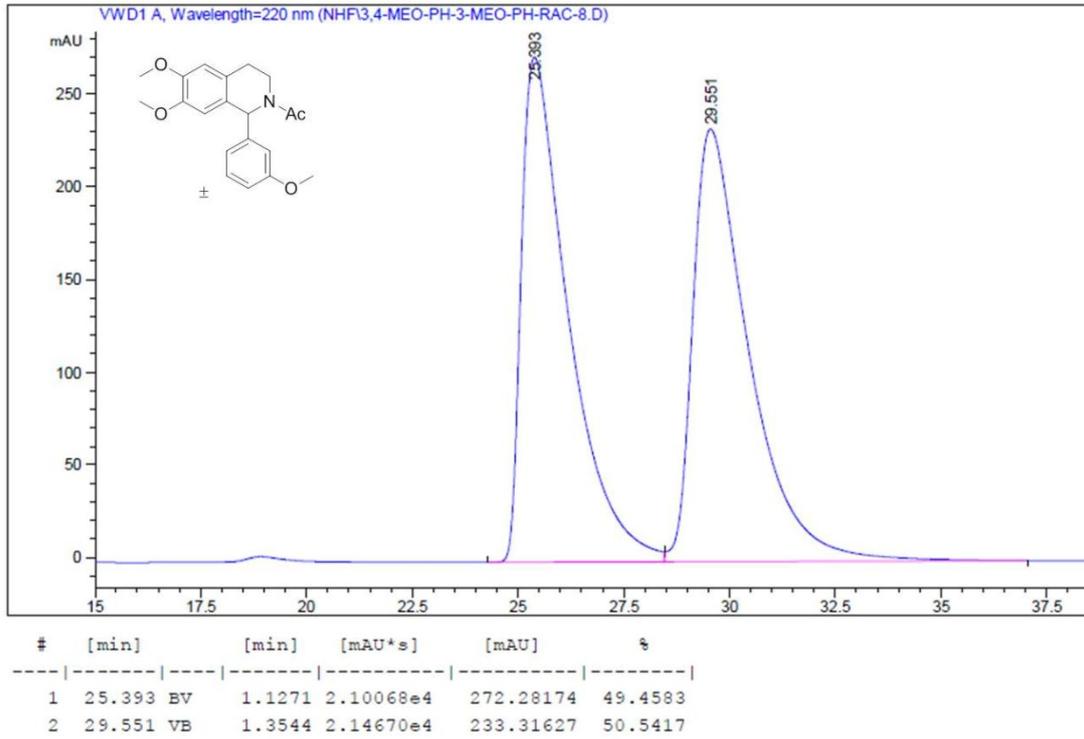


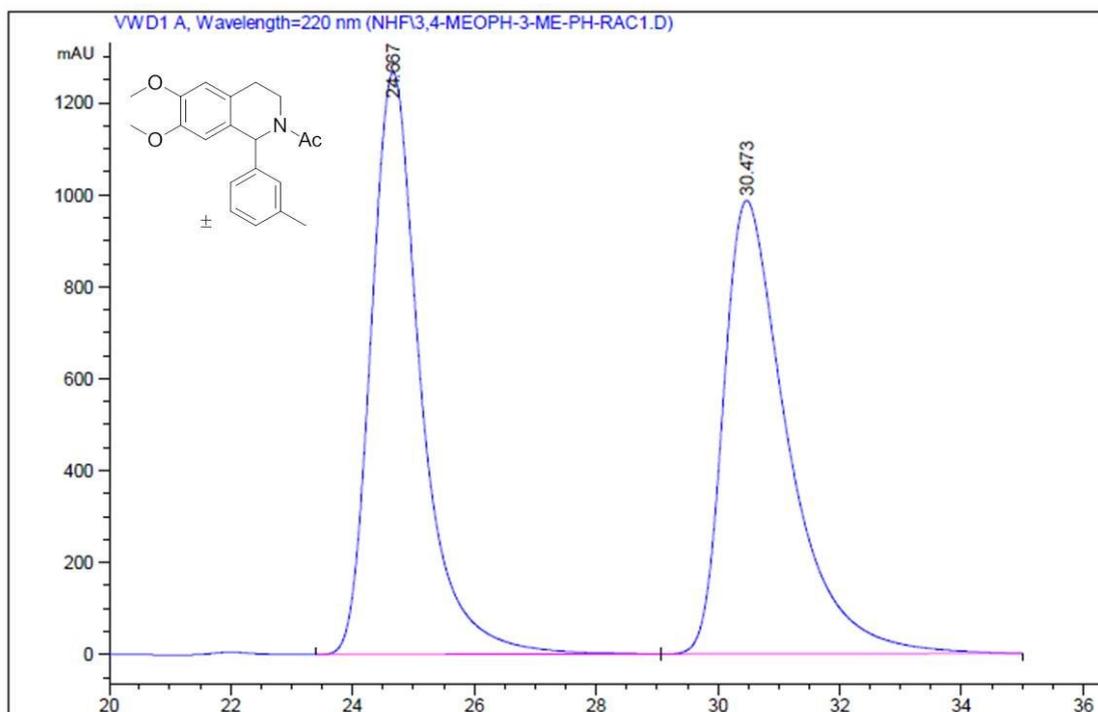




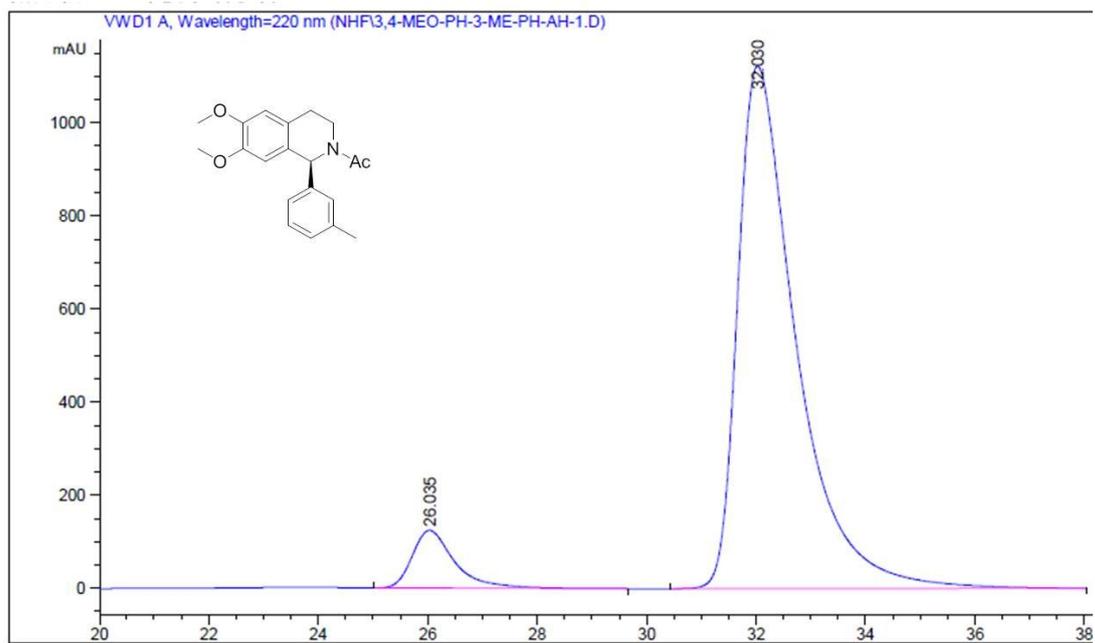




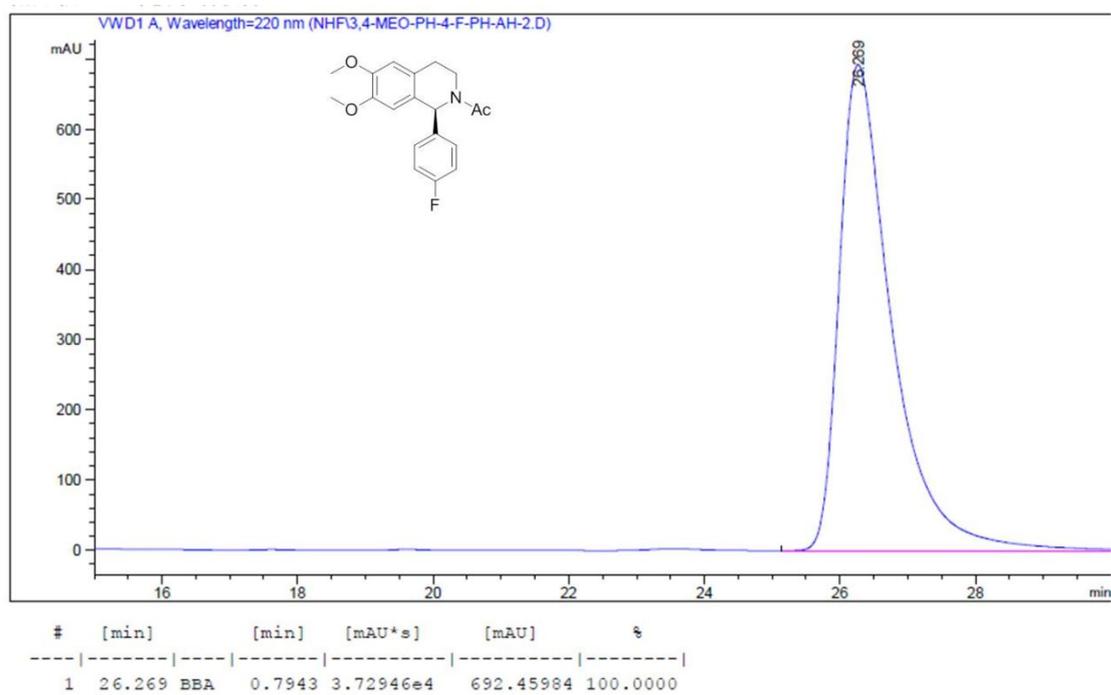
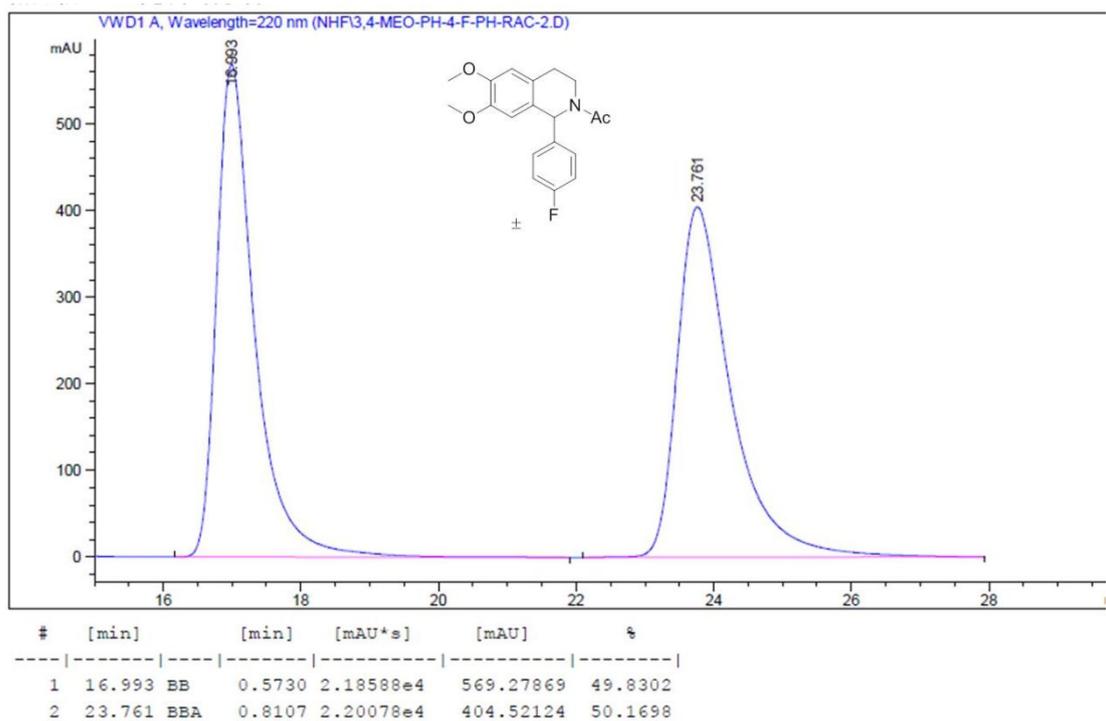


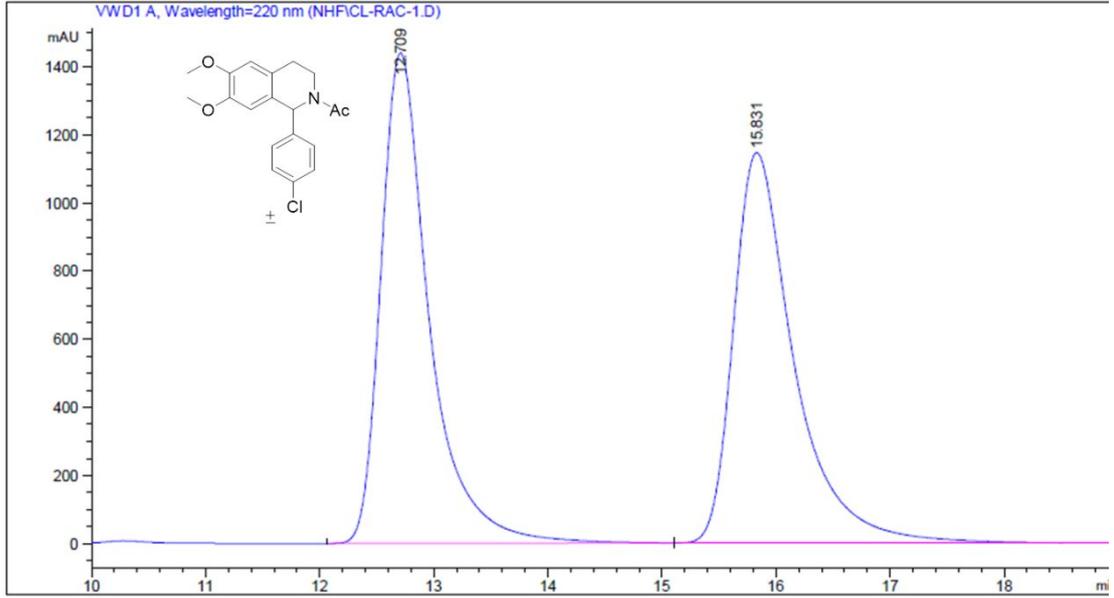


#	[min]	[min]	[mAU*s]	[mAU]	%	
1	24.667	BB	0.8600	7.18416e4	1266.17798	49.8501
2	30.473	BBA	1.0960	7.22736e4	986.21783	50.1499

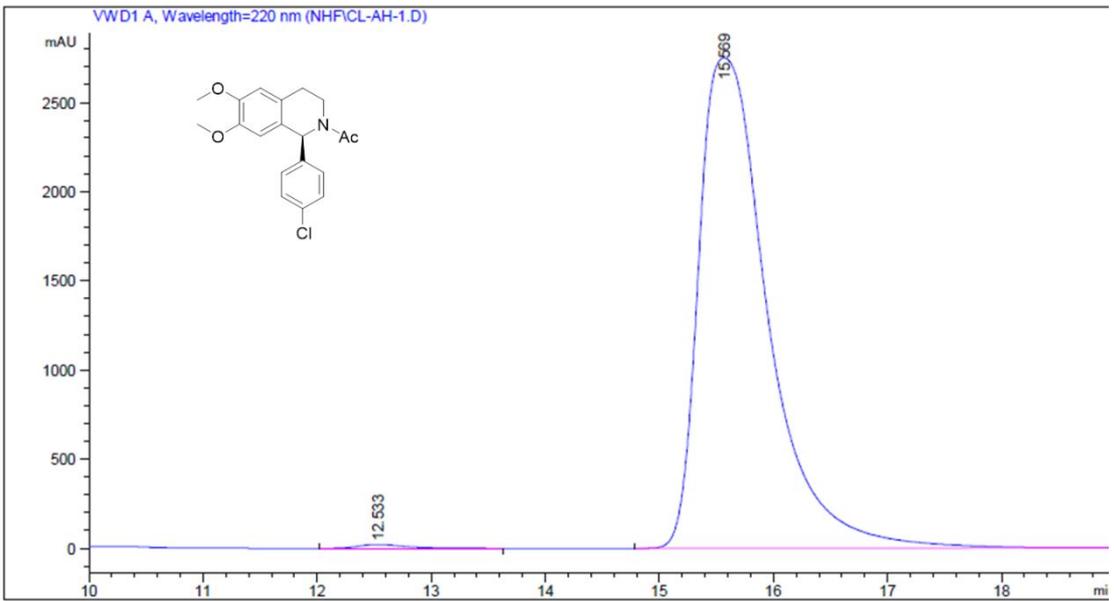


#	[min]	[min]	[mAU*s]	[mAU]	%	
1	26.035	BB	0.8036	6625.61963	123.55285	7.3754
2	32.030	BBA	1.1037	8.32084e4	1122.67004	92.6246

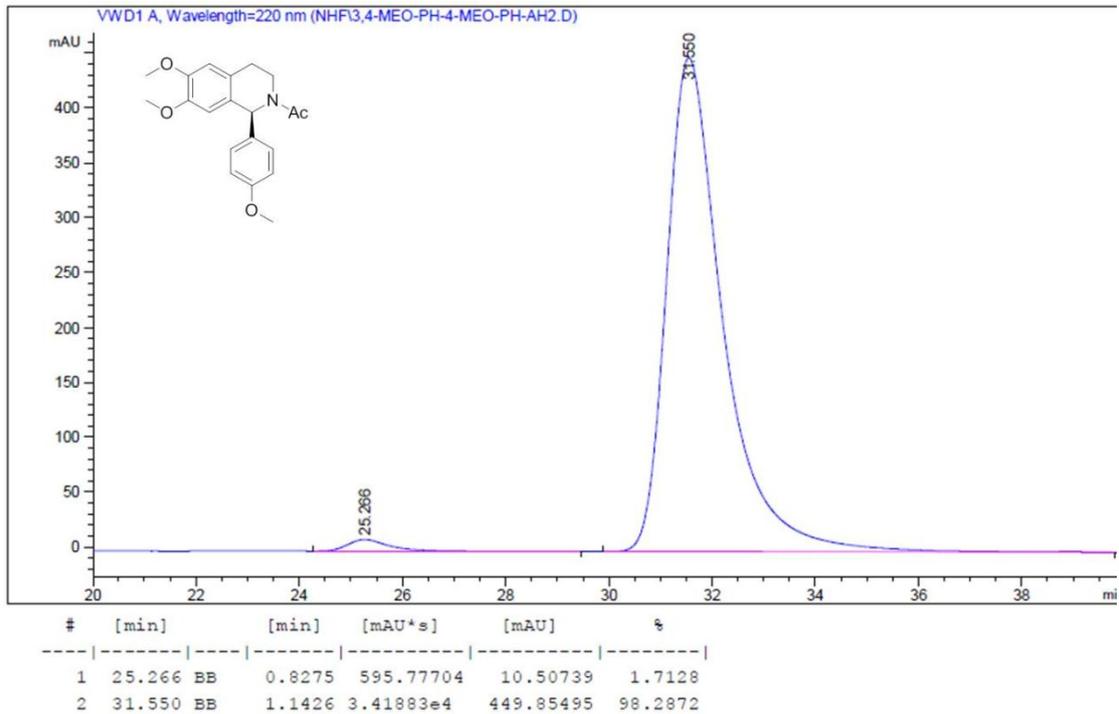
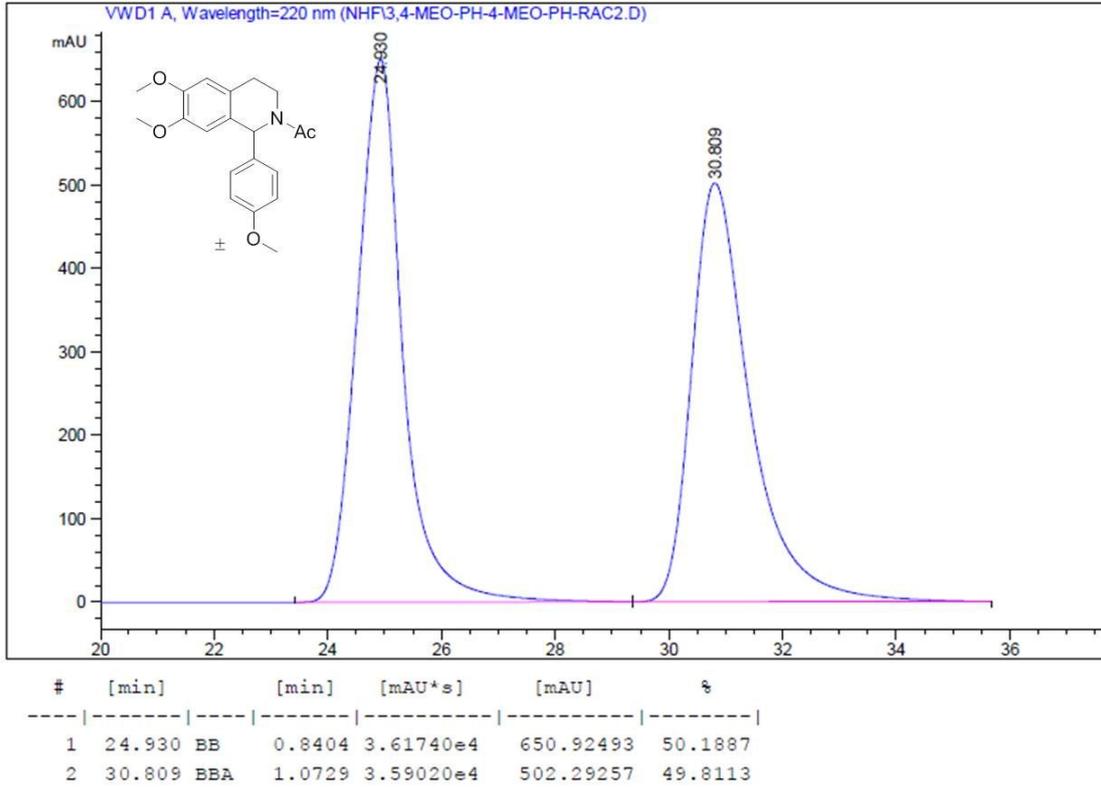


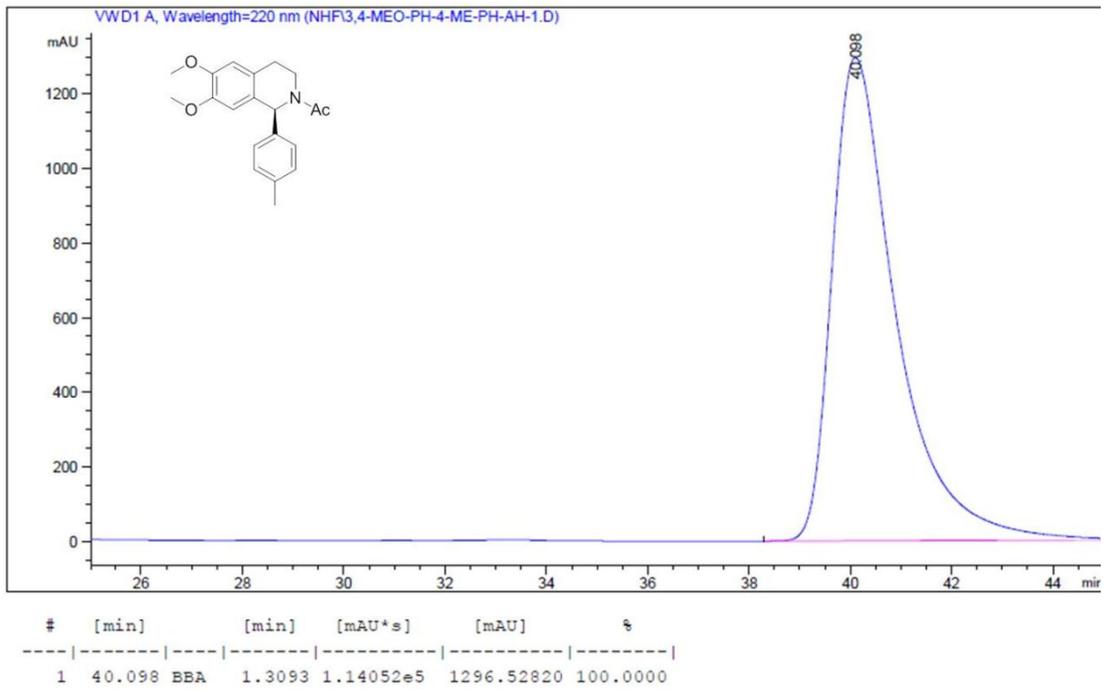
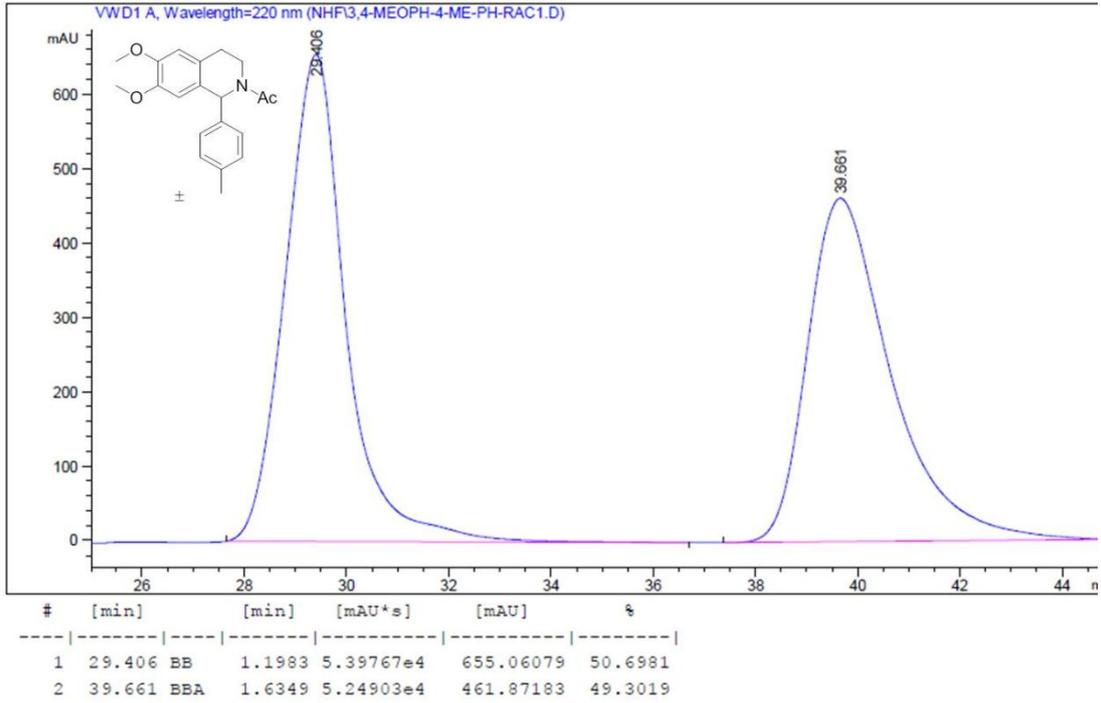


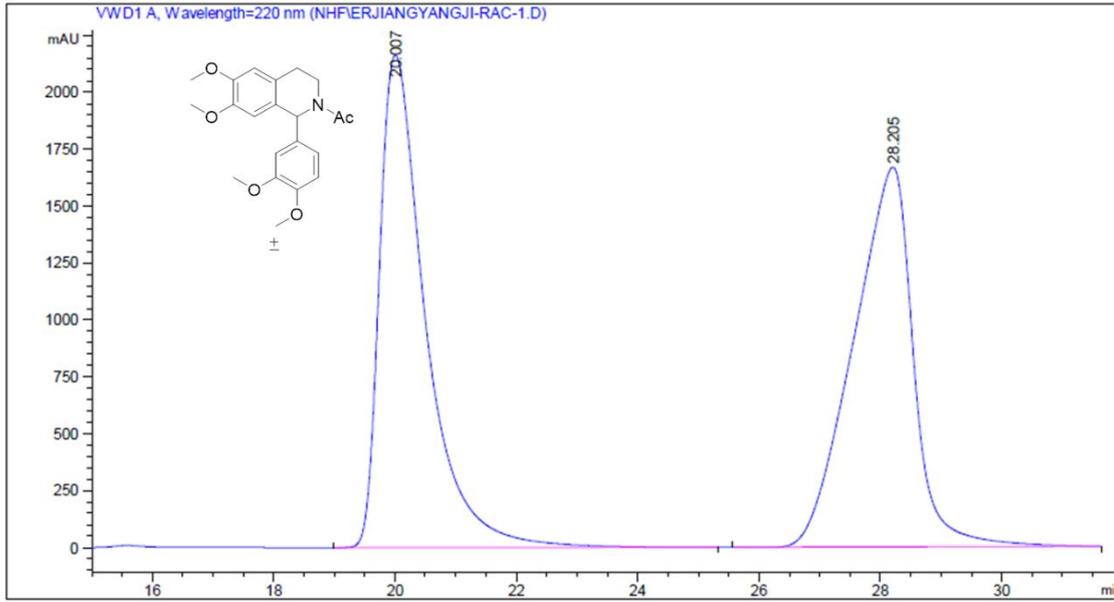
#	[min]	[min]	[mAU*s]	[mAU]	%	
1	12.709	BB	0.4412	4.24983e4	1440.40491	50.0035
2	15.831	BBA	0.5523	4.24923e4	1146.83386	49.9965



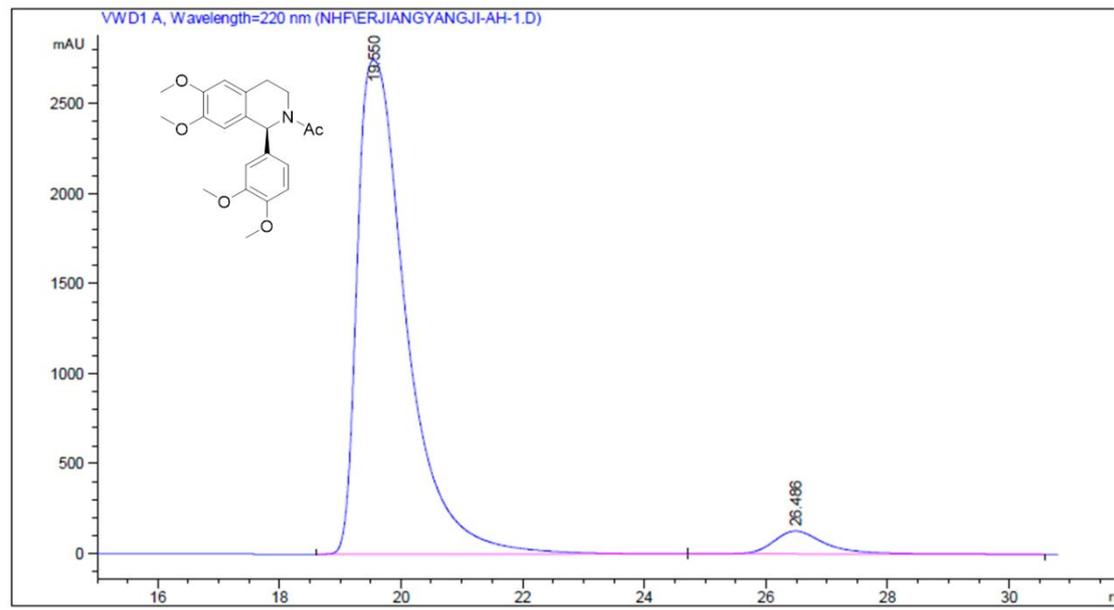
#	[min]	[min]	[mAU*s]	[mAU]	%	
1	12.533	BB	0.4129	577.39880	21.05529	0.4969
2	15.569	BBA	0.6394	1.15621e5	2750.42505	99.5031



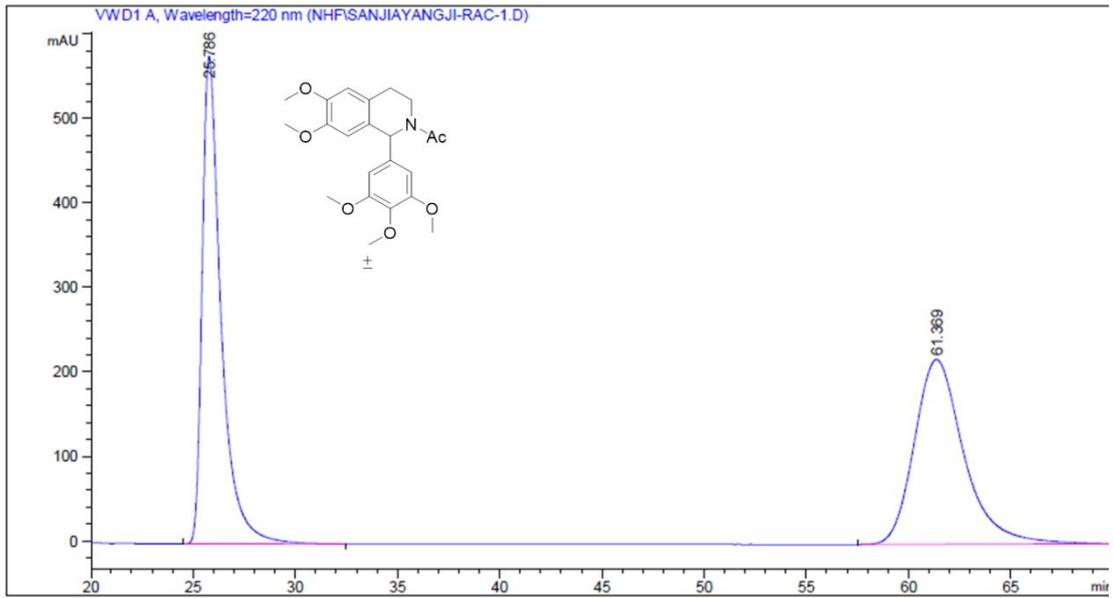




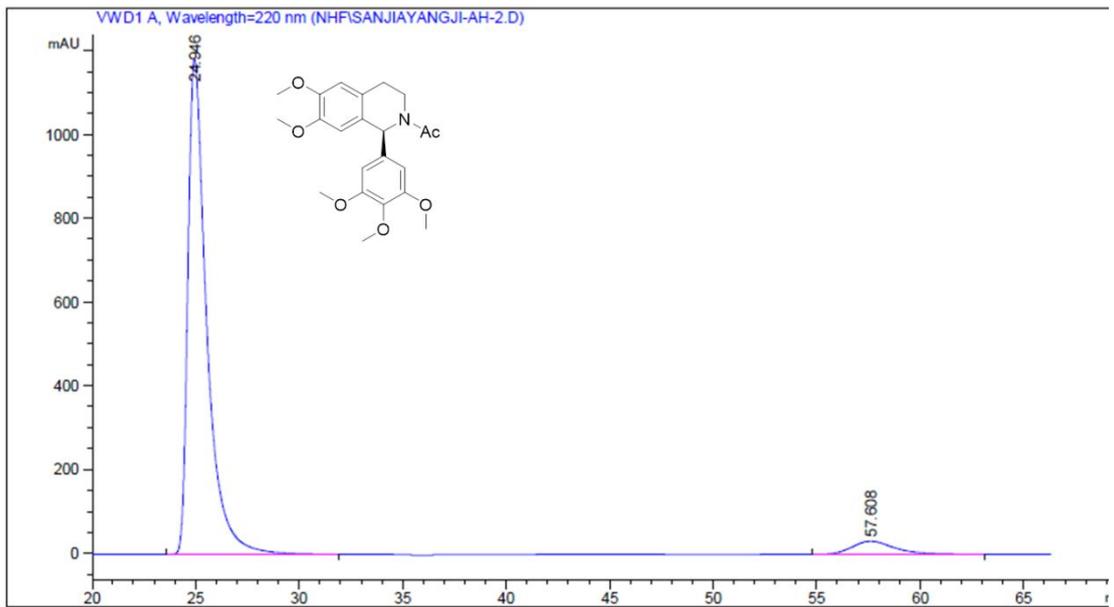
#	[min]	[min]	[mAU*s]	[mAU]	%	
1	20.007	BB	0.7874	1.13575e5	2163.66528	49.7220
2	28.205	BBA	1.0179	1.14844e5	1668.68860	50.2780



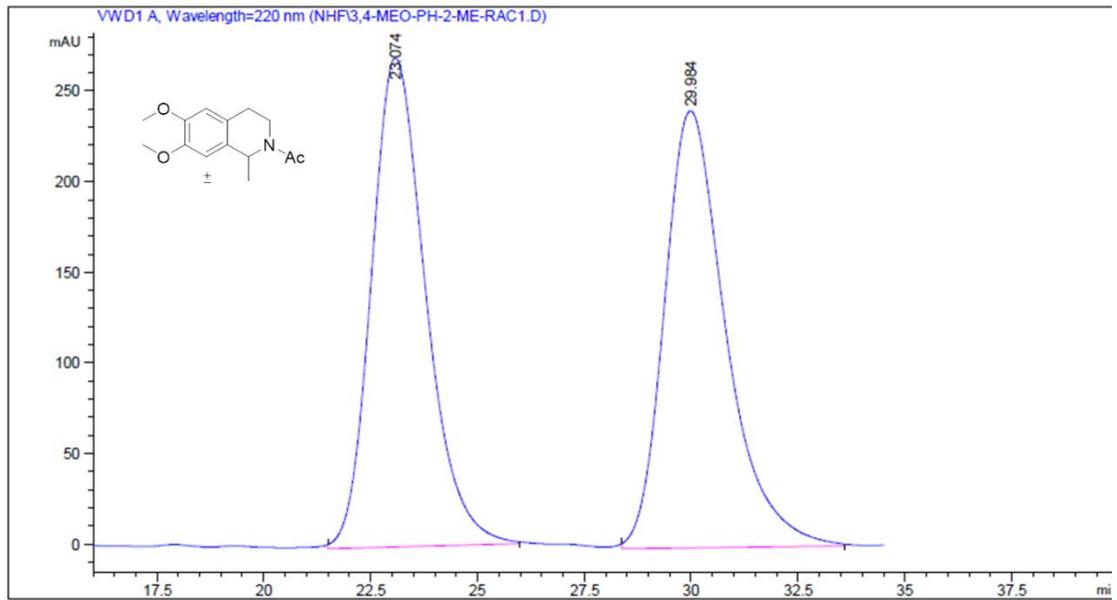
#	[min]	[min]	[mAU*s]	[mAU]	%	
1	19.550	BB	0.8467	1.53505e5	2743.91479	95.2707
2	26.486	BB	0.8909	7620.12305	127.75839	4.7293



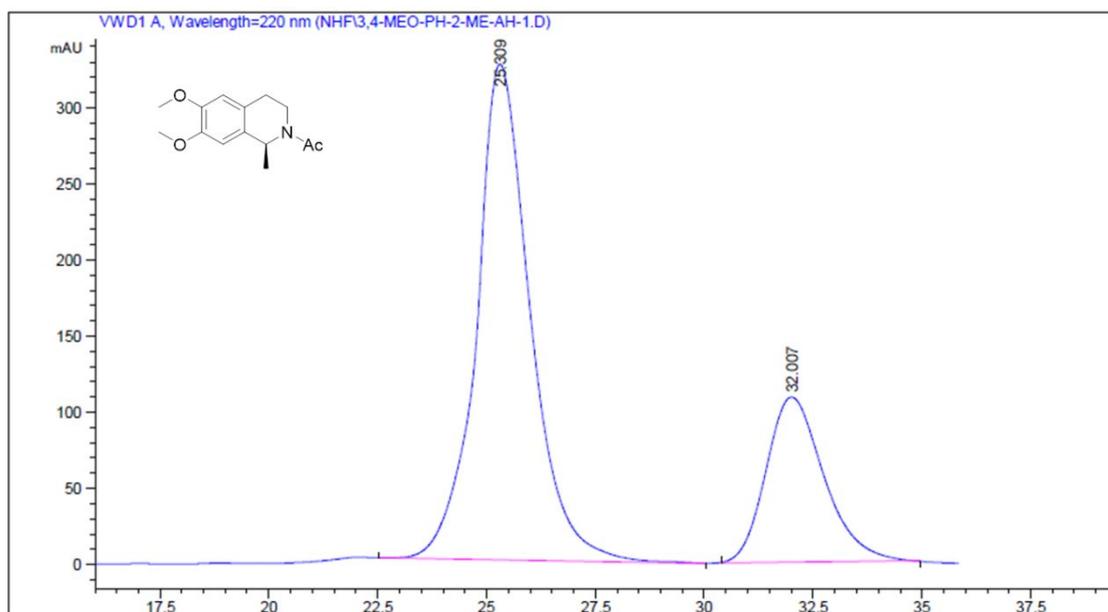
#	[min]	[min]	[mAU*s]	[mAU]	%
1	25.786 BB	0.9635	3.72812e4	576.47546	50.2769
2	61.369 BB	2.5089	3.68706e4	218.58797	49.7231



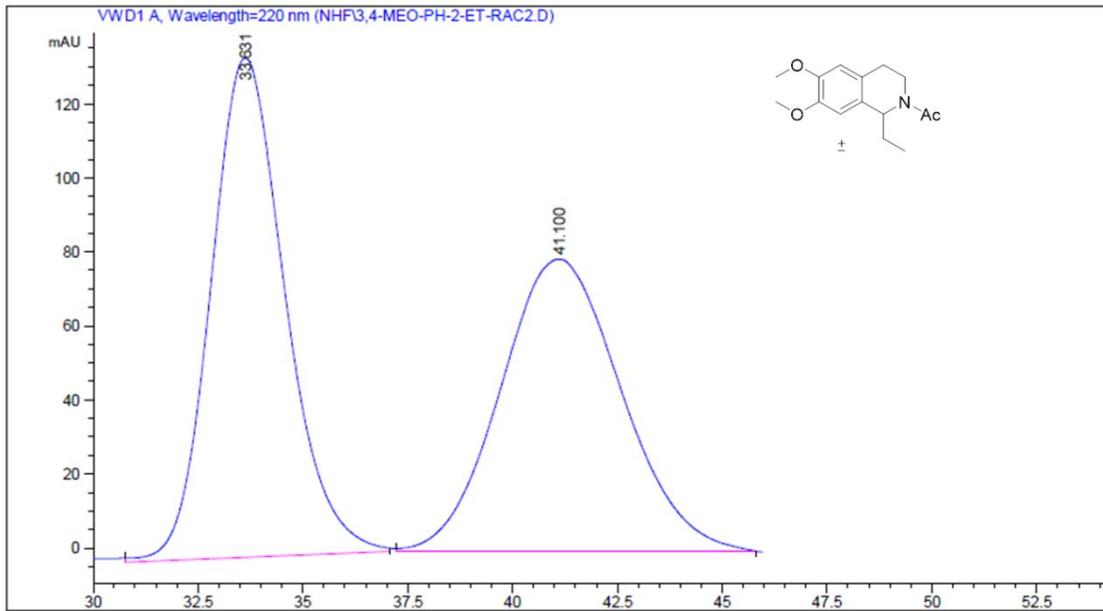
#	[min]	[min]	[mAU*s]	[mAU]	%
1	24.946 BB	0.9406	7.47505e4	1180.68372	94.3256
2	57.608 BB	1.9857	4496.77490	31.21457	5.6744



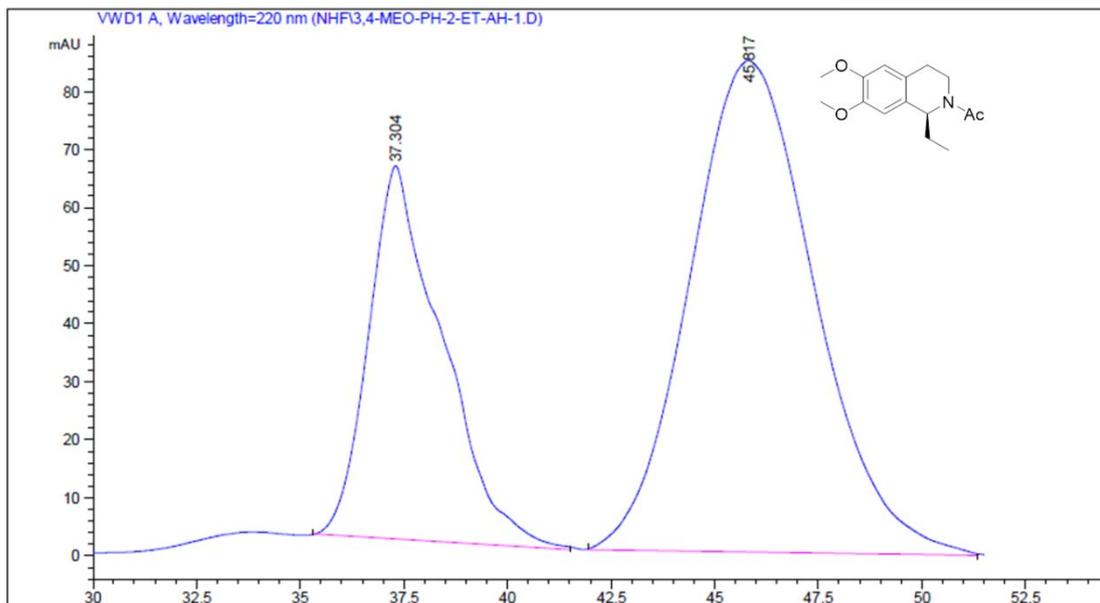
#	[min]	[min]	[mAU*s]	[mAU]	%	
1	23.074	MM R	1.4691	2.38038e4	270.05054	49.6936
2	29.984	MM R	1.6652	2.40974e4	241.18373	50.3064



#	[min]	[min]	[mAU*s]	[mAU]	%	
1	25.309	BB	1.2785	2.79349e4	325.41354	73.6479
2	32.007	MM R	1.5385	9995.47656	108.28092	26.3521



#	[min]	[min]	[min]	[mAU*s]	[mAU]	%	
1	33.631	MM	R	2.0454	1.65474e4	134.83536	51.1626
2	41.100	MM	R	3.3317	1.57954e4	79.01489	48.8374



#	[min]	[min]	[min]	[mAU*s]	[mAU]	%	
1	37.304	MM	R	2.0622	7960.55713	64.33728	30.9884
2	45.817	MM	R	3.4864	1.77282e4	84.75056	69.0116

References

- (1) Enthaler, S.; Erre, G.; Junge, K.; Holz, J.; Alberico, E.; Nieddu, I.; Gladiali, S.; Beller, M. Development of Practical Rhodium Phosphine Catalysts for the Hydrogenation of β -Dehydroamino Acid Derivatives. *Org. Process Res. Dev.* **2007**, *11*, 568-577.
- (2) Nie, H.; Yao, L.; Li, B.; Zhang, S.; Chen, W. Very Simple and Highly Modular Synthesis of Ferrocene-Based Chiral Phosphines with a Wide Variety of Substituents at the Phosphorus Atom(s). *Organometallics* **2014**, *33*, 2109-2114.
- (3) Togni, A.; Breutel, C.; Schnyder, A.; Spindler, F.; Landert, H.; Tijani, A. A Novel Easily Accessible Chiral Ferrocenyldiphosphine for Highly Enantioselective Hydrogenation, Allylic Alkylation, and Hydroboration Reactions. *J. Am. Chem. Soc.* **1994**, *116*, 4062-4066.
- (4) Mohammad, M.; Matthew, D. H. A Versatile Cyclodehydration Reaction for the Synthesis of Isoquinoline and β -Carboline Derivatives. *Org. Lett.* **2008**, *10*, 3485-3488.
- (5) Chang, M.; Li, W.; Zhang, X. A Highly Efficient and Enantioselective Access to Tetrahydroisoquinoline Alkaloids: Asymmetric Hydrogenation with an Iridium Catalyst. *Angew. Chem. Int. Ed.* **2011**, *50*, 10679-10681.
- (6) Péter, Á. B.; Péter, S.; Balázs, V.; László, P.; Mátyás, M. New Synthetic Approach for the Preparation of 1-Aryl-3,4-dihydroisoquinolines by Liebeskind-Srogl Reaction. *Synlett* **2014**, *25*, 2574-2578.
- (7) Zhou, H.; Liu, Y.; Yang, S.; Chang, M. One-Pot N-Deprotection and Catalytic Intramolecular Asymmetric Reductive Amination for the Synthesis of Tetrahydroisoquinolines. *Angew. Chem. Int. Ed.* **2017**, *56*, 2725-2729.
- (8) Perez, M.; Wu, Z.; Scalone, M.; Ayad, T.; Ratovelomanana-Vidal, V. Enantioselective Synthesis of 1-Aryl-Substituted Tetrahydroisoquinolines Through Ru-Catalyzed Asymmetric Transfer Hydrogenation. *Eur. J. Org. Chem.* **2015**, 6503-6514.
- (9) Wu, Z.; Perez, M.; Scalone, M.; Ayad, T.; Ratovelomanana-Vidal, V.

- Ruthenium-Catalyzed Asymmetric Transfer Hydrogenation of 1-Aryl- Substituted Dihydroisoquinolines: Access to Valuable Chiral 1-Aryl- Tetrahydroisoquinoline Scaffolds. *Angew. Chem. Int. Ed.* **2013**, *52*, 4925-4928.
- (10) Santanu, H.; Subhabrata, S. Cerium Chloride Catalyzed, 2-Iodoxybenzoic Acid Mediated Oxidative Dehydrogenation of Multiple Heterocycles at Room Temperature. *Eur. J. Org. Chem.* **2017**, 1277-1280.
- (11) Li, H.; Tian, P.; Xu, J.; Zheng, G. Identification of an Imine Reductase for Asymmetric Reduction of Bulky Dihydroisoquinolines. *Org. Lett.* **2017**, *19*, 3151-3154.
- (12) Rosaria, G.; Roberta, C.; Valerie, O.; Silvana, Q.; Letizia, B. M.; Guido, F.; Emilio, R.; Giovambattista, De S.; Alba, C. Synthesis and anticonvulsant properties of tetrahydroisoquinoline derivatives. *Il Farmaco* **2004**, *59*, 7-12.