

Supporting Information

Enantioselective Synthesis of Tetrahydroisoquinolines via Catalytic Intramolecular Asymmetric Reductive Amination

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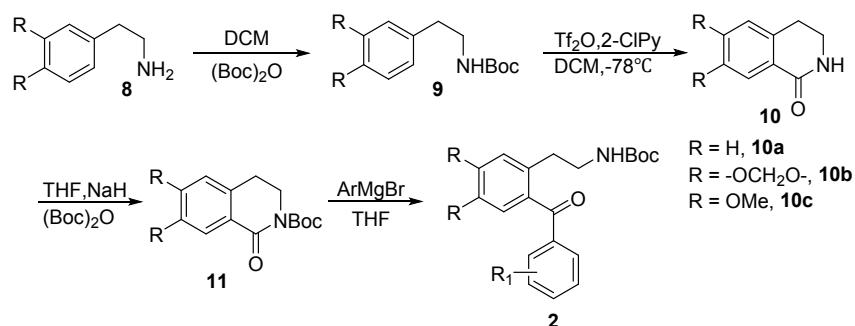
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1. General remarks

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

2. General procedure for synthesis of substrates

Substrates **2a-2f'** were prepared according to literature.¹

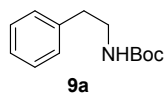


Phenyl ethyl amines **8** (50 mmol, 0.1 equiv) was resolved in DCM (200 mL), after cooling to 0 °C, NEt₃ (100 mmol, 2.0 equiv), DMAP (5 mmol, 0.1 equiv) and (Boc)₂O (55 mmol, 1.1 equiv) were subsequently added, stirred at room temperature for 3 h. Then the reaction was quenched by the addition of a saturated NH₄Cl solution at 0 °C. This solution was extracted with CH₂Cl₂. The organic phase washed with saturated NaCl, dried with anhydrous NaSO₄, filtered, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (Petroleum ether/EtOAc = 5:1) to give the *N*-Boc-carbamate products **9a-c** as a white solid.

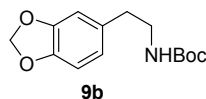
2-chloropyridine (75 mmol, 1.5 equiv) and triflic anhydride (52.5 mmol, 1.05 equiv) was added to a stirred solution of *N*-Boc-carbamate **9** (50 mmol, 1.0 equiv) in CH₂Cl₂ (10 mL) at -78 °C. After 30 min, the reaction mixture was warmed to room temperature. Then the reaction was quenched by the addition of a saturated NaHCO₃ solution at 0 °C. This solution was diluted with CH₂Cl₂, washed with brine, dried with MgSO₄, filtered, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (CH₂Cl₂/MeOH, 20:1) to give the cyclized products **10a-c** as a white solid.

NaH (60 mmol, 2.0 equiv) was slowly added to a solution of **10** (30 mmol, 1.0 equiv) in anhydrous THF (100 mL) at 0 °C. Then the reaction was stirred at this temperature for 1h. A solution of (Boc)₂O (30 mmol, 1.0 equiv) in THF (20 mL) was slowly added to the above mixture. After stirring at room temperature for 12 h, the reaction was quenched with aq. NH₄Cl solution and concentrated under vacuum. Then the reaction mixture was extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine, dried over Na₂SO₄, and concentrated under vacuum. The crude product was purified by recrystallization (EtOAc/Petroleum ether) to provide product **11a-c**.

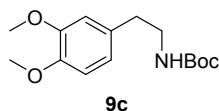
To a solution of the resulting **11** (6 mmol, 1.0 equiv) in THF (20 mL) was added Grignard reagent (9.0 mmol, 1.5 equiv) via syringe dropwise at 0 °C. The reaction was stirred at this temperature for 15 min and slowly warm to room temperature overnight. The reaction was quenched by water and extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine, dried over Na₂SO₄, and concentrated under vacuum. The product **2a-c** was purified by column chromatography or recrystallization (Petroleum ether/EtOAc=5:1).²



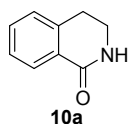
tert-butyl phenethylcarbamate¹ (**9a**): 10.84 g, 98% yield; colorless oil; ¹H NMR (400 MHz, CDCl₃) δ 7.34 - 7.28 (m, 2H), 7.25 - 7.17 (m, 3H), 4.55 (s, 1H), 3.38 (q, *J* = 6.8 Hz, 2H), 2.80 (t, *J* = 7.1 Hz, 2H), 1.43 (s, 9H).



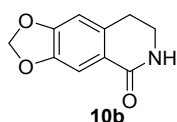
tert-butyl(2-(benzo[d][1,3]dioxol-5-yl)ethyl)carbamate¹ (**9b**): 13.0 g, 98% yield; white solid; ¹H NMR (400 MHz, CDCl₃) δ 6.74 (d, *J* = 7.8 Hz, 1H), 6.68 (s, 1H), 6.63 (d, *J* = 7.7 Hz, 1H), 5.93 (s, 2H), 3.41 - 3.20 (m, 2H), 2.71 (t, *J* = 6.8 Hz, 2H), 1.44 (s, 9H).



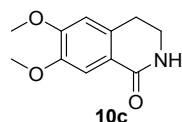
tert-butyl (3,4-dimethoxyphenethyl)carbamate¹ (**9c**): 13.8 g, 98 %yield; white solid; ¹H NMR (400 MHz, CDCl₃) δ 6.81 (d, *J* = 8.0 Hz, 1H), 6.73 (d, *J* = 9.7 Hz, 2H), 4.57 (s,1H), 3.87 (d, *J* = 4.2 Hz, 6H), 3.36 (q, *J* = 6.3 Hz, 2H), 2.75 (t, *J* = 6.9 Hz, 2H), 1.44 (s, 9H).



3,4-dihydroisoquinolin-1(2*H*)-one¹ (**10a**): 5.15 g, 70% yield; white solid; ¹H NMR (400 MHz, CDCl₃) δ 8.07 (d, *J* = 7.6 Hz, 1H), 7.45 (t, *J* = 7.9 Hz, 1H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.23 (d, *J* = 7.5 Hz, 1H), 6.68 (s, 1H), 3.58 (td, *J* = 6.6, 2.9 Hz, 2H), 3.01 (t, *J* = 6.6 Hz, 2H).

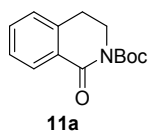


7,8-dihydro-[1,3]dioxolo[4,5-*g*]isoquinolin-5(6*H*)-one¹ (**10b**): 6.59g, 69%yield; white solid; ¹H NMR (400 MHz, CDCl₃) δ 7.51 (s, 1H), 6.62 (d, *J* = 21.5 Hz, 2H), 6.00 (s, 2H), 3.52 (td, *J* = 6.7, 2.8 Hz, 2H), 2.89 (t, *J* = 6.6 Hz, 2H).

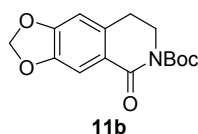


6,7-dimethoxy-3,4-dihydroisoquinolin-1(2*H*)-one¹ (**10c**): 7.77 g, 75% yield; white solid; ¹H NMR (400 MHz, CDCl₃) δ 7.59 (s, 1H), 6.70 (s, 1H), 4.19 (t, *J* = 6.1

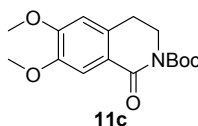
Hz, 2H), 3.97 (s, 3H), 3.92 (s, 3H), 3.12 (t, $J = 6.1$ Hz, 2H).



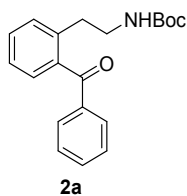
tert-butyl-1-oxo-3,4-dihydroisoquinoline-2(1*H*)-carboxylate¹ (**11a**): 7.05 g, 95% yield; white solid; ¹H NMR (400 MHz, CDCl₃) δ 8.16 (m, 1H), 7.47 (m, 1H), 7.36 (m, 1H), 7.21 (d, $J = 7.7$ Hz, 1H), 4.00 (m, 2H), 3.01 (t, $J = 6.1$ Hz, 2H), 1.59 (s, 9H).



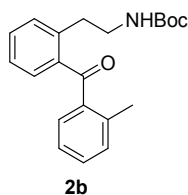
tert-butyl-5-oxo-7,8-dihydro-[1,3]dioxolo[4,5-*g*]isoquinoline-6(5*H*)-carboxylate (**11b**): 7.05 g, 95% yield; white solid; ¹H NMR (400 MHz, CDCl₃) δ 7.58 (s, 1H), 6.62 (s, 1H), 6.01 (s, 2H), 4.05 - 3.83 (m, 2H), 2.95 - 2.86 (m, 2H), 1.58 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 163.34, 153.14, 151.53, 147.17, 135.83, 123.32, 108.90, 106.79, 101.73, 83.04, 44.51, 28.44, 28.11. HRMS (ESI) m/z Calculated for C₁₅H₁₇NO₅ [M+Na]⁺: 314.1004, Found: 314.1003.



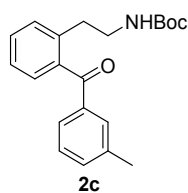
tert-butyl 6,7-dimethoxy-1-oxo-3,4-dihydroisoquinoline-2(1*H*)-carboxylate³ (**10c**): 8.85 g, 96% yield; white solid; ¹H NMR (400 MHz, CDCl₃) δ 7.65 (s, 1H), 6.64 (s, 1H), 3.98 (t, $J = 6.2$ Hz, 2H), 3.93 (s, 3H), 3.91 (s, 3H), 2.94 (t, $J = 6.2$ Hz, 2H), 1.59 (s, 9H).



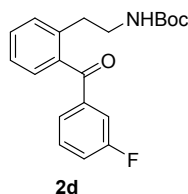
tert-butyl(2-benzoylphenethyl)carbamate² (**2a**): 1.66 g, 85% yield, colorless oil liquid; ¹H NMR (400 MHz, CDCl₃) δ 7.80 (d, $J = 7.6$ Hz, 2H), 7.60 (t, $J = 7.4$ Hz, 1H), 7.47 (t, $J = 7.7$ Hz, 2H), 7.39 (d, $J = 7.7$ Hz, 1H), 7.35 - 7.26 (m, 2H), 5.02 (s, 1H), 3.39 (q, $J = 6.6$ Hz, 2H), 2.86 (t, $J = 6.9$ Hz, 2H), 1.40 (s, 9H).



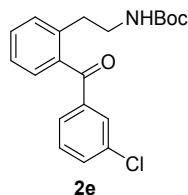
tert-butyl(2-(2-methylbenzoyl)phenethyl)carbamate² (**2b**): 1.77 g, 87% yield, colorless oil liquid; ¹H NMR (400 MHz, CDCl₃) δ 7.50 - 7.34 (m, 3H), 7.34 - 7.23 (m, 3H), 7.21 (q, *J* = 8.1 Hz, 2H), 5.04 (s, 1H), 3.44 (q, *J* = 6.8 Hz, 2H), 3.00 (t, *J* = 7.2 Hz, 2H), 2.45 (s, 3H), 1.41 (s, 9H).



tert-butyl(2-(3-methylbenzoyl)phenethyl)carbamate² (**2c**): 1.77 g, 87% yield, colorless oil liquid; ¹H NMR (400 MHz, CDCl₃) δ 7.64 (s, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.50 - 7.36 (m, 3H), 7.36 - 7.24 (m, 3H), 5.09 (s, 1H), 3.39 (m, 2H), 2.86 (m, 2H), 2.39 (s, 3H), 1.40 (s, 9H).

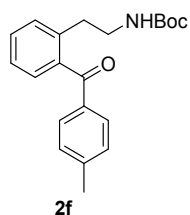


tert-butyl(2-(3-fluorobenzoyl)phenethyl)carbamate² (**2d**): 1.67 g, 81% yield, colorless oil liquid; ¹H NMR (400 MHz, CDCl₃) δ 7.60 - 7.35 (m, 5H), 7.32-7.26 (m, 3H), 4.91 (s, 1H), 3.38 (q, *J* = 6.6 Hz, 2H), 2.86 (t, *J* = 7.0 Hz, 2H), 1.40 (s, 9H). ¹⁹F NMR (376 MHz, Chloroform-*d*) δ -111.74.

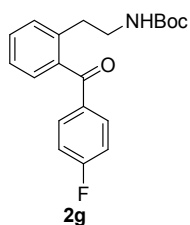


tert-butyl (2-(3-chlorobenzoyl)phenethyl)carbamate² (**2e**): 1.75 g, 81% yield, colorless oil liquid; ¹H NMR (400 MHz, CDCl₃) δ 7.79 (s, 1H), 7.66 (d, *J* = 7.8 Hz, 1H), 7.57 (d, *J* = 8.1 Hz, 1H), 7.51 - 7.45 (m, 1H), 7.44 - 7.36 (m, 2H), 7.31-7.30 (m,

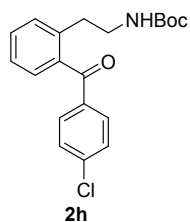
2H), 4.97 (d, $J = 6.7$ Hz, 1H), 3.39 (q, $J = 6.8$ Hz, 2H), 2.87 (t, $J = 7.1$ Hz, 2H), 1.40 (s, 9H).



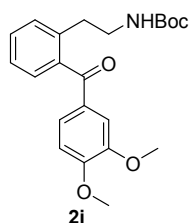
tert-butyl(2-(4-methylbenzoyl)phenethyl)carbamate² (**2f**): 1.77 g, 87% yield, colorless oil liquid; ¹H NMR (400 MHz, CDCl₃) δ 7.83 - 7.60 (m, 2H), 7.52 - 7.41 (m, 1H), 7.37 (d, $J = 7.9$ Hz, 1H), 7.33 - 7.14 (m, 4H), 4.98 (s, 1H), 3.37 (q, $J = 7.2, 6.5$ Hz, 2H), 2.83 (t, $J = 7.1$ Hz, 2H), 2.43 (s, 3H), 1.40 (s, 9H).



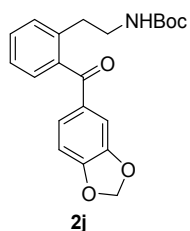
tert-butyl(2-(4-fluorobenzoyl)phenethyl)carbamate² (**2g**): 1.71 g, 83% yield, colorless oil liquid; ¹H NMR (400 MHz, CDCl₃) δ 7.84 (dd, $J = 8.4, 5.5$ Hz, 2H), 7.48-7.44 (m, 1H), 7.39 (d, $J = 7.7$ Hz, 1H), 7.29 (d, $J = 4.3$ Hz, 2H), 7.13 (t, $J = 8.4$ Hz, 2H), 4.96 (s, 1H), 3.37 (q, $J = 6.6$ Hz, 2H), 2.84 (t, $J = 7.0$ Hz, 2H), 1.40 (s, 9H). ¹⁹F NMR (376 MHz, Chloroform-*d*) δ -104.50.



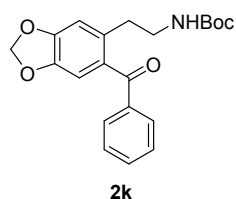
tert-butyl (2-(4-chlorobenzoyl)phenethyl) carbamate² (**2h**): 1.70 g, 79% yield, colorless oil liquid; ¹H NMR (400 MHz, CDCl₃) δ 7.88 - 7.63 (m, 2H), 7.63 - 7.34 (m, 4H), 7.29 (d, $J = 4.1$ Hz, 2H), 4.98 (s, 1H), 3.38 (q, $J = 6.7$ Hz, 2H), 2.85 (t, $J = 7.0$ Hz, 2H), 1.40 (s, 9H).



tert-butyl(2-(3,4-dimethoxybenzoyl)phenethyl)carbamate² (**2i**): 1.96 g, 85% yield, colorless oil liquid; ¹H NMR (400 MHz, CDCl₃) δ 7.58 (s, 1H), 7.47-7.43 (m, 1H), 7.38 (d, *J* = 7.8 Hz, 1H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.24 (d, *J* = 8.7 Hz, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 5.09 (s, 1H), 3.95 (s, 6H), 3.38 (q, *J* = 6.6 Hz, 2H), 2.83 (t, *J* = 7.1 Hz, 2H), 1.40 (s, 9H).



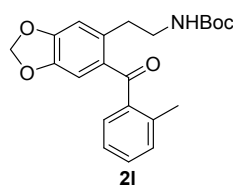
tert-butyl(2-(benzo[d][1,3]dioxole-5-carbonyl)phenethyl) carbamate (**2j**): 1.84 g, 83% yield, colorless oil liquid; ¹H NMR (400 MHz, CDCl₃) δ 7.55 - 7.33 (m, 3H), 7.34 - 7.16 (m, 3H), 6.82 (d, *J* = 8.2 Hz, 1H), 6.07 (s, 2H), 5.04 (s, 1H), 3.36 (q, *J* = 6.6 Hz, 2H), 2.81 (t, *J* = 7.0 Hz, 2H), 1.40 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 196.67, 155.95, 152.21, 148.16, 138.93, 138.06, 132.26, 130.68, 130.25, 128.39, 127.70, 125.66, 109.41, 107.78, 101.99, 78.92, 42.06, 33.05, 28.38. HRMS (ESI) *m/z* Calculated for C₂₁H₂₃NNaO₅ [M+Na]⁺: 392.1474, Found: 392.1471.



tert-butyl(2-(6-benzoylbenzo[d][1,3]dioxol-5-yl)ethyl) carbamate (**2k**): 1.96 g, 85% yield, white solid, *m.p.* 126.6-127.3 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.79-7.77 (m, 2H), 7.66 - 7.53 (m, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 6.85 (s, 1H), 6.79 (s, 1H), 6.01 (s, 2H), 5.10 (s, 1H), 3.36 (q, *J* = 6.5 Hz, 2H), 2.81 (t, *J* = 6.9 Hz, 2H), 1.41 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 196.64, 155.39, 149.02, 144.74, 137.42, 134.17,

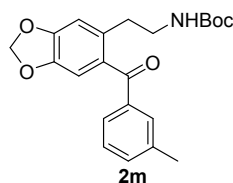
132.43, 131.05, 129.66, 127.77, 110.25, 109.10, 101.00, 78.34, 41.76, 32.50, 27.78.

HRMS (ESI) m/z Calculated for $C_{21}H_{23}NNaO_5$ $[M+Na]^+$: 392.1468, Found: 392.1468.



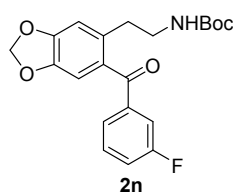
tert-butyl(2-(6-(2-methylbenzoyl)benzo[d][1,3]dioxol-5-yl) ethyl) carbamate (**2l**):

1.91 g, 83% yield, white solid, **m.p.** 102.5-104.3 °C; **1H NMR** (400 MHz, $CDCl_3$) δ 7.38 (t, $J = 7.3$ Hz, 1H), 7.29-7.26 (m, 2H), 7.21 (t, $J = 7.4$ Hz, 1H), 6.84 (s, 1H), 6.73 (s, 1H), 5.99 (s, 2H), 5.11 (s, 1H), 3.41 (q, $J = 6.6$ Hz, 2H), 2.99 (t, $J = 7.1$ Hz, 2H), 2.39 (s, 3H), 1.42 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 199.18, 156.04, 150.22, 145.58, 139.31, 137.65, 136.46, 132.05, 131.26, 130.85, 129.75, 125.38, 111.34, 111.16, 101.72, 78.86, 42.32, 33.64, 28.40, 20.35. **HRMS (ESI) m/z** Calculated for $C_{22}H_{25}NNaO_5$ $[M+Na]^+$: 406.1630, Found: 406.1631.

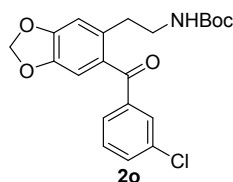


tert-butyl(2-(6-(3-methylbenzoyl)benzo[d][1,3]dioxol-5-yl) ethyl) carbamate

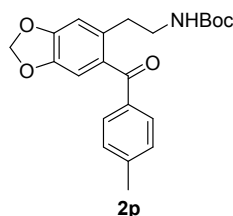
(**2m**): 1.91 g, 83% yield, white solid, **m.p.** 94.7-95.0 °C; **1H NMR** (400 MHz, $CDCl_3$) δ 7.61 (s, 1H), 7.55 (d, $J = 7.6$ Hz, 1H), 7.40 (d, $J = 7.6$ Hz, 1H), 7.34 (d, $J = 7.5$ Hz, 1H), 6.85 (s, 1H), 6.79 (s, 1H), 6.02 (s, 2H), 5.19 (s, 1H), 3.37 (q, $J = 6.6$ Hz, 2H), 2.80 (t, $J = 6.9$ Hz, 2H), 2.40 (s, 3H), 1.41 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 197.40, 156.01, 149.55, 145.29, 138.21, 138.00, 134.68, 133.86, 131.80, 130.59, 128.24, 127.65, 110.79, 109.62, 101.60, 78.80, 42.38, 33.05, 28.38, 21.28. **HRMS (ESI) m/z** Calculated for $C_{22}H_{25}NNaO_5$ $[M+Na]^+$: 406.1630, Found: 406.1628.



tert-butyl(2-(6-(3-fluorobenzoyl)benzo[d][1,3]dioxol-5-yl)ethyl) carbamate (**2n**): 1.93 g, 83% yield, white solid, **m.p.** 132.6-153.4 °C; **¹H NMR** (400 MHz, CDCl₃) δ 7.54 (d, *J* = 7.7 Hz, 1H), 7.50-7.47 (m, 1H), 7.46-7.41 (m, 1H), 7.30-7.28 (m, 1H), 6.85 (s, 1H), 6.78 (s, 1H), 6.03 (s, 2H), 5.02 (s, 1H), 3.36 (q, *J* = 6.6 Hz, 2H), 2.82 (t, *J* = 6.9 Hz, 2H), 1.41 (s, 9H). **¹³C NMR** (100 MHz, CDCl₃) δ 195.69, 162.52 (d, *J* = 248.3 Hz), 155.97, 149.92, 145.42, 140.21 (d, *J* = 6.1 Hz), 135.21, 130.91, 130.05 (d, *J* = 7.6 Hz), 126.11 (d, *J* = 2.9 Hz), 120.00 (d, *J* = 21.4 Hz), 116.76 (d, *J* = 22.3 Hz), 111.03, 109.66, 101.74, 78.95, 42.34, 33.19, 28.36. **¹⁹F NMR** (376 MHz, CDCl₃) δ -111.81. **HRMS (ESI)** *m/z* Calculated for C₂₁H₂₂FNNaO₅ [M+Na]⁺: 410.1380, Found: 410.1380.

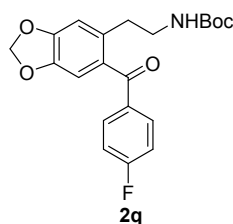


tert-butyl(2-(6-(4-chlorobenzoyl)benzo[d][1,3]dioxol-5-yl)ethyl) carbamate (**2o**): 2.06 g, 85% yield, white solid, **m.p.** 121.0-121.7 °C; **¹H NMR** (400 MHz, CDCl₃) δ 7.76 (s, 1H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.40 (t, *J* = 7.9 Hz, 1H), 6.86 (s, 1H), 6.77 (s, 1H), 6.04 (s, 2H), 5.07 (s, 1H), 3.37 (q, *J* = 6.6 Hz, 2H), 2.81 (d, *J* = 7.1 Hz, 2H), 1.41 (s, 9H). **¹³C NMR** (100 MHz, CDCl₃) δ 195.68, 155.99, 150.00, 145.47, 139.78, 135.34, 134.69, 132.92, 130.80, 130.07, 129.73, 128.38, 111.09, 109.72, 101.76, 79.0, 42.37, 33.23, 28.39. **HRMS (ESI)** *m/z* Calculated for C₂₁H₂₂ClNNaO₅ [M+Na]⁺: 426.1084, Found: 426.1081.

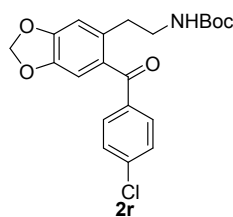


tert-butyl(2-(6-(4-methylbenzoyl)benzo[d][1,3]dioxol-5-yl)ethyl) carbamate (**2p**): 1.93 g, 84% yield, white solid, **m.p.** 102.2-103.7 °C; **¹H NMR** (400 MHz, CDCl₃) δ 7.76 - 7.59 (m, 2H), 7.25 (d, *J* = 8.2 Hz, 2H), 6.84 (s, 1H), 6.78 (s, 1H), 6.01 (s, 2H),

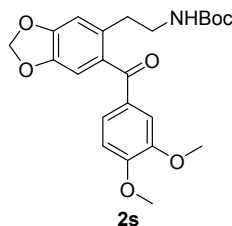
5.12 (s, 1H), 3.35 (q, $J = 6.5$ Hz, 2H), 2.78 (t, $J = 6.9$ Hz, 2H), 2.43 (s, 3H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3) δ 197.03, 156.03, 149.45, 145.35, 144.06, 135.37, 134.35, 132.05, 130.49, 129.13, 110.76, 109.49, 101.58, 78.94, 42.37, 33.02, 28.41, 21.70. HRMS (ESI) m/z Calculated for $\text{C}_{22}\text{H}_{25}\text{NNaO}_5$ $[\text{M}+\text{Na}]^+$: 406.1625, Found: 406.1621.



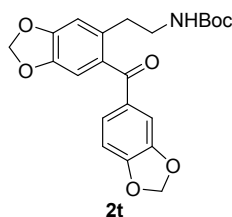
tert-butyl(2-(6-(4-fluorobenzoyl)benzo[d][1,3]dioxol-5-yl)ethyl) carbamate (**2q**): 2.0 g, 86% yield, white solid, **m.p.** 90.7-92.0 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.01 - 7.62 (m, 2H), 7.19 - 7.05 (m, 2H), 6.85 (s, 1H), 6.76 (s, 1H), 6.02 (s, 2H), 5.07 (s, 1H), 3.36 (q, $J = 6.5$ Hz, 2H), 2.79 (t, $J = 6.8$ Hz, 2H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3) δ 195.67, 165.74 (d, $J = 255.4$ Hz), 155.99, 149.71, 145.45, 134.69, 134.33, 132.92 (d, $J = 9.3$ Hz), 131.41, 115.58 (d, $J = 21.9$ Hz), 110.94, 109.41, 101.69, 78.99, 42.36, 33.13, 28.40. ^{19}F NMR (376 MHz, CDCl_3) δ -104.90. HRMS (ESI) m/z Calculated for $\text{C}_{21}\text{H}_{22}\text{FNNaO}_5$ $[\text{M}+\text{Na}]^+$: 410.1380, Found: 410.1378.



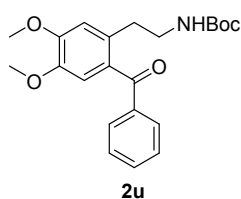
tert-butyl(2-(6-(4-chlorobenzoyl)benzo[d][1,3]dioxol-5-yl)ethyl) carbamate (**2r**): 2.04 g, 84% yield, white solid, **m.p.** 160.0-161.7 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.73 (d, $J = 8.2$ Hz, 2H), 7.44 (d, $J = 8.2$ Hz, 2H), 6.85 (s, 1H), 6.76 (s, 1H), 6.03 (s, 2H), 5.08 (s, 1H), 3.36 (q, $J = 6.7$ Hz, 2H), 2.80 (t, $J = 6.8$ Hz, 2H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3) δ 195.92, 155.99, 149.85, 145.47, 139.58, 136.38, 134.99, 131.66, 131.13, 128.76, 111.02, 109.54, 101.73, 79.02, 42.37, 33.17, 28.40. HRMS (ESI) m/z Calculated for $\text{C}_{21}\text{H}_{22}\text{ClNNaO}_5$ $[\text{M}+\text{Na}]^+$: 426.1084, Found: 426.1085.



tert-butyl(2-(6-(3,4-dimethoxybenzoyl)benzo[d][1,3]dioxol-5-yl)ethyl)carbamate (**2s**): 2.24 g, 87% yield, colorless oil liquid; ¹H NMR (400 MHz, CDCl₃) δ 7.53 (s, 1H), 7.32 - 7.24 (m, 1H), 6.85 (d, *J* = 7.9 Hz, 2H), 6.79 (s, 1H), 6.02 (s, 2H), 5.22 (s, 1H), 3.95 (s, 6H), 3.35 (q, *J* = 6.5 Hz, 2H), 2.76 (t, *J* = 6.9 Hz, 2H), 1.41 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 196.09, 156.00, 153.51, 149.13, 149.04, 145.27, 133.84, 132.11, 130.67, 126.14, 111.51, 110.62, 109.74, 109.10, 101.53, 78.86, 56.09, 55.99, 42.31, 32.91, 28.38. **HRMS (ESI)** *m/z* Calculated for C₂₃H₂₇NNaO₇ [M+Na]⁺: 452.1685, Found: 452.1686.

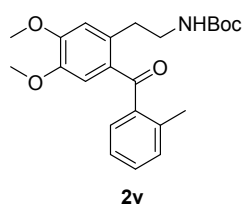


tert-butyl(2-(6-(benzo[d][1,3]dioxole-5-carbonyl)benzo[d][1,3]dioxol-5-yl)ethyl)carbamate (**2t**): 1.88 g, 76% yield, colorless oil liquid; ¹H NMR (400 MHz, CDCl₃) δ 7.39 - 7.24 (m, 2H), 6.98 - 6.79 (m, 2H), 6.77 (s, 1H), 6.07 (s, 2H), 6.02 (s, 2H), 5.17 (s, 1H), 3.34 (q, *J* = 6.7 Hz, 2H), 2.92 - 2.62 (t, *J* = 6.9 Hz, 2H), 1.42 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 195.59, 156.01, 152.03, 149.31, 148.07, 145.33, 133.89, 132.45, 132.05, 127.42, 110.64, 109.56, 109.06, 107.75, 101.97, 101.57, 78.91, 42.30, 32.93, 28.39. **HRMS (ESI)** *m/z* Calculated for C₂₂H₂₃NNaO₇ [M+Na]⁺: 436.1372, Found: 436.1374.

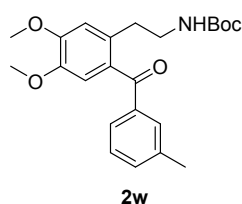


tert-butyl(2-benzoyl-4,5-dimethoxyphenethyl)carbamate (**2u**): 1.83 g, 79% yield,

white solid, **m.p.** 113.3-114.9 °C; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.91-7.70 (m, 2H), 7.64-7.55 (m, 1H), 7.54-7.34 (m, 2H), 6.85 (t, $J = 2.9$ Hz, 2H), 5.11 (s, 1H), 3.96 (s, 3H), 3.78 (s, 3H), 3.42 - 3.38 (m, 2H), 3.07 - 2.62 (t, $J = 6.6$ Hz, 2H), 1.42 (s, 9H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 197.58, 156.08, 151.01, 146.39, 138.32, 133.14, 133.01, 130.34, 130.31, 128.41, 113.49, 113.09, 78.97, 56.12, 56.04, 42.36, 32.97, 28.43. **HRMS (ESI)** m/z Calculated for $\text{C}_{22}\text{H}_{27}\text{NNaO}_5$ $[\text{M}+\text{Na}]^+$: 408.1781, Found: 408.1781.

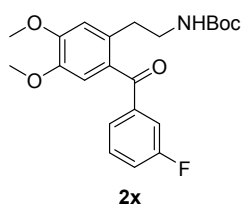


tert-butyl(4,5-dimethoxy-2-(2-methylbenzoyl)phenethyl) carbamate (**2v**): 1.87 g, 78% yield, white solid, **m.p.** 97.9 - 100.3 °C; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.39 (t, $J = 7.4$ Hz, 1H), 7.34 - 7.25 (m, 2H), 7.21 (t, $J = 7.6$ Hz, 1H), 6.83 (s, 1H), 6.79 (s, 1H), 5.07 (s, 1H), 3.95 (s, 3H), 3.70 (s, 3H), 3.43 (q, $J = 6.8$ Hz, 2H), 3.00 (t, $J = 7.2$ Hz, 2H), 2.40 (s, 3H), 1.42 (s, 9H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 199.51, 156.08, 151.61, 146.50, 139.42, 137.75, 134.61, 131.30, 130.85, 130.61, 129.85, 125.34, 114.57, 113.89, 78.93, 56.03, 42.26, 33.46, 28.43, 20.42. **HRMS (ESI)** m/z Calculated for $\text{C}_{23}\text{H}_{29}\text{NNaO}_5$ $[\text{M}+\text{Na}]^+$: 422.1943, Found: 422.1938.

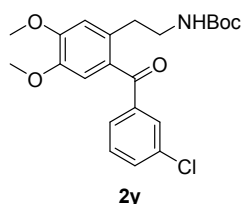


tert-butyl(4,5-dimethoxy-2-(3-methylbenzoyl)phenethyl) carbamate (**2w**): 1.94 g, 81% yield, white solid, **m.p.** 92.5-93.5 °C; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.64 (s, 1H), 7.56 (d, $J = 7.7$ Hz, 1H), 7.41 (d, $J = 7.7$ Hz, 1H), 7.37-7.33 (m, 1H), 6.86-6.85 (m, 2H), 5.19 (s, 1H), 3.96 (s, 3H), 3.79 (s, 3H), 3.40-3.37 (m, 2H), 2.86-2.83 (m, 2H), 2.41 (s, 3H), 1.42 (s, 9H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 197.68, 156.02, 150.81, 146.22, 138.19, 133.74, 132.97, 130.57, 130.40, 128.16, 127.61, 113.32, 112.93, 78.77, 55.99, 55.90, 42.29, 32.81, 28.33, 21.23. **HRMS (ESI)** m/z Calculated for

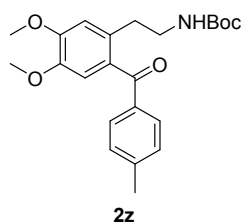
$C_{23}H_{29}NNaO_5$ $[M+Na]^+$: 422.1943, Found: 422.1937.



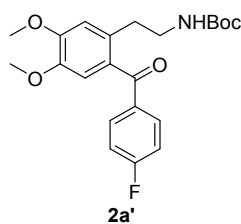
tert-butyl(2-(3-fluorobenzoyl)-4,5-dimethoxyphenethyl) carbamate (**2x**): 1.91 g, 79% yield, white solid, **m.p.** 107.3-107.7 °C; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.57 - 7.47 (m, 2H), 7.47-7.41 (m, 1H), 7.33 - 7.25 (m, 1H), 6.86 (s, 1H), 6.83 (s, 1H), 5.03 (s, 1H), 3.96 (s, 3H), 3.79 (s, 3H), 3.39 (q, $J = 6.6$ Hz, 2H), 2.85 (t, $J = 7.0$ Hz, 2H), 1.41 (s, 9H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 196.04, 162.61 (d, $J = 248.4$ Hz), 156.03, 151.29, 146.45, 140.54 (d, $J = 6.1$ Hz), 133.49, 130.03 (d, $J = 7.6$ Hz), 129.64, 126.11 (d, $J = 2.7$ Hz), 119.96 (d, $J = 21.4$ Hz), 116.79 (d, $J = 22.3$ Hz), 113.62, 113.07, 79.04, 56.10 (d, $J = 8.5$ Hz), 42.33, 33.07, 28.42. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -111.80. **HRMS (ESI)** m/z Calculated for $C_{22}H_{26}FNNaO_5$ $[M+Na]^+$: 426.1693, Found: 426.1690.



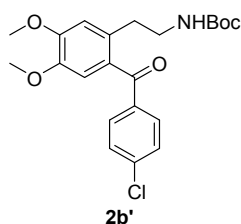
tert-butyl(2-(3-chlorobenzoyl)-4,5-dimethoxyphenethyl) carbamate (**2y**): 2.04 g, 81% yield, white solid, **m.p.** 102.9-103.9 °C; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.79 (s, 1H), 7.65 (d, $J = 7.8$ Hz, 1H), 7.60 - 7.48 (m, 1H), 7.41 (t, $J = 7.9$ Hz, 1H), 6.86 (s, 1H), 6.82 (s, 1H), 5.09 (s, 1H), 3.97 (s, 3H), 3.79 (s, 3H), 3.40 (q, $J = 6.7$ Hz, 2H), 2.85 (d, $J = 7.2$ Hz, 2H), 1.41 (s, 9H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 195.90, 156.00, 151.28, 146.38, 140.02, 134.66, 133.60, 132.79, 130.04, 129.68, 129.42, 128.36, 113.61, 113.05, 78.92, 56.01, 42.30, 33.02, 28.38. **HRMS (ESI)** m/z Calculated for $C_{22}H_{26}ClNNaO_5$ $[M+Na]^+$: 442.1397, Found: 442.1398.



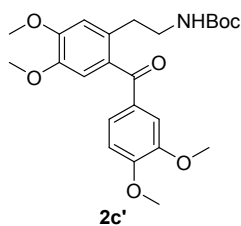
tert-butyl(4,5-dimethoxy-2-(4-methylbenzoyl)phenethyl) carbamate (**2z**): 1.99 g, 83% yield, white solid, **m.p.** 110.4-110.6 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.72-7.69 (m, 2H), 7.28-7.25 (m, 2H), 6.88 – 6.76 (m, 2H), 5.13 (s, 1H), 3.95 (s, 3H), 3.78 (s, 3H), 3.40-3.35 (m, 2H), 2.83 (t, *J* = 7.0 Hz, 2H), 2.43 (s, 3H), 1.41 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 197.34, 156.10, 150.79, 146.36, 143.97, 135.63, 132.75, 130.70, 130.51, 129.14, 113.37, 112.83, 78.93, 56.09, 56.02, 42.36, 32.86, 28.43, 21.70. **HRMS (ESI)** *m/z* Calculated for C₂₃H₂₉NNaO₅ [M+Na]⁺: 422.1938, Found: 422.1937.



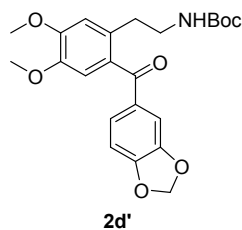
tert-butyl(2-(4-fluorobenzoyl)-4,5-dimethoxyphenethyl) carbamate (**2a'**): 1.86 g, 77% yield, white solid, **m.p.** 84.7 - 85.6 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.83 (m, 2H), 7.14 (t, *J* = 8.4 Hz, 2H), 6.85 (s, 1H), 6.81 (s, 1H), 5.07 (s, 1H), 3.96 (s, 3H), 3.79 (s, 3H), 3.38 (m, 2H), 2.83 (t, *J* = 7.0 Hz, 2H), 1.41 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 196.02, 165.72 (d, *J* = 255.1 Hz), 156.05, 151.08, 146.49, 134.64 (d, *J* = 2.8 Hz), 133.05, 132.91 (d, *J* = 9.3 Hz), 130.12, 115.59 (d, *J* = 21.8 Hz), 113.55, 112.81, 79.00, 56.09 (d, *J* = 8.3 Hz), 42.34, 32.98, 28.43. ¹⁹F NMR (376 MHz, CDCl₃) δ -105.09. **HRMS (ESI)** *m/z* Calculated for C₂₂H₂₆FNO₅ [M+Na]⁺: 426.1693, Found: 426.1689.



tert-butyl(2-(4-chlorobenzoyl)-4,5-dimethoxyphenethyl) carbamate (**2b'**): 2.02 g, 80% yield, white solid, **m.p.** 111.5-111.7 °C; **¹H NMR** (400 MHz, CDCl₃) δ 7.79 - 7.70 (m, 2H), 7.49 - 7.39 (m, 2H), 6.85 (s, 1H), 6.80 (s, 1H), 5.10 (s, 1H), 3.96 (s, 3H), 3.79 (s, 3H), 3.39 (m, 2H), 2.84 (t, *J* = 6.9 Hz, 2H), 1.41 (s, 9H). **¹³C NMR** (100 MHz, CDCl₃) δ 196.19, 156.01, 151.15, 146.41, 139.43, 136.65, 133.30, 131.64, 129.76, 128.72, 113.54, 112.84, 78.96, 56.03, 42.33, 32.98, 28.41. **HRMS (ESI) *m/z*** Calculated for C₂₂H₂₆ClNO₅ [M+Na]⁺: 442.1397, Found: 442.1398.

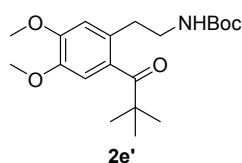


tert-butyl(2-(3,4-dimethoxybenzoyl)-4,5-dimethoxyphenethyl) carbamate (**2c'**): 2.22 g, 83% yield, light yellow solid, **m.p.** 164.7-165.9 °C; **¹H NMR** (400 MHz, CDCl₃) δ 7.54 (s, 1H), 7.34 - 7.25 (m, 1H), 6.86 (d, *J* = 9.0 Hz, 3H), 5.22 (s, 1H), 4.03 - 3.91 (m, 9H), 3.81 (s, 3H), 3.38 (q, *J* = 6.7 Hz, 2H), 2.81 (t, *J* = 7.0 Hz, 2H), 1.42 (s, 9H). **¹³C NMR** (100 MHz, CDCl₃) δ 196.43, 156.09, 153.44, 150.56, 149.05, 146.29, 132.32, 130.95, 130.80, 126.03, 113.23, 112.42, 111.65, 109.77, 78.95, 56.12, 56.10, 56.03, 56.01, 42.34, 32.79, 28.43. **HRMS (ESI) *m/z*** Calculated for C₂₄H₃₁NO₇ [M+Na]⁺: 468.1998, Found: 468.1996.

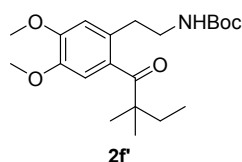


tert-butyl(2-(benzo[d][1,3]dioxole-5-carbonyl)-4,5-dimethoxyphenethyl) carbamate (**2d'**): 2.04 g, 79% yield, white solid, **m.p.** 126.5-127.3 °C; **¹H NMR** (400 MHz, CDCl₃) δ 7.37 (s, 1H), 7.32 (d, *J* = 8.3 Hz, 1H), 6.84-6.82 (m, 3H), 6.08 (s, 2H), 5.16 (s, 1H), 3.95 (s, 3H), 3.81 (s, 3H), 3.39-3.34 (m, 2H), 2.79 (t, *J* = 7.0 Hz, 2H), 1.41 (s, 9H). **¹³C NMR** (100 MHz, CDCl₃) δ 195.96, 156.06, 151.98, 150.61, 148.12, 146.36, 132.73, 132.25, 130.78, 127.36, 113.21, 112.30, 109.57, 107.74, 101.97,

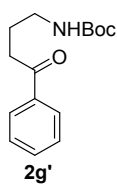
78.92, 56.09, 55.99, 42.28, 32.78, 28.42. **HRMS (ESI) m/z** Calculated for $C_{23}H_{27}NO_7$ $[M+Na]^+$: 452.1685, Found: 452.1677.



tert-butyl(4,5-dimethoxy-2-pivaloylphenethyl)carbamate (**2e'**): 1.52g, 83% yield, colorless oil; 1H NMR (400 MHz, $CDCl_3$) δ 6.77 (s, 1H), 6.75 (s, 1H), 5.10 (s, 1H), 3.90 (s, 3H), 3.86 (s, 3H), 3.34 (q, $J = 6.6$ Hz, 2H), 2.58 (t, $J = 6.9$ Hz, 2H), 1.43 (s, 9H), 1.26 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.74, 156.09, 149.52, 146.34, 132.69, 129.22, 112.88, 108.70, 79.00, 77.27, 56.09, 55.88, 45.02, 42.19, 33.12, 28.45, 27.70. **HRMS (ESI) m/z** Calculated for $C_{20}H_{31}NO_5$ $[M+Na]^+$: 388.2100, Found: 388.2095.



tert-butyl(2-(2,2-dimethylbutanoyl)-4,5-dimethoxyphenethyl)carbamate (**2f'**): 1.48g, 78% yield, colorless oil; 1H NMR (400 MHz, $CDCl_3$) δ 6.77 (s, 2H), 5.15 (s, 1H), 3.90 (s, 3H), 3.86 (s, 3H), 3.36 (q, $J = 6.6$ Hz, 2H), 2.60 (t, $J = 6.9$ Hz, 2H), 1.72 (q, $J = 7.5$ Hz, 2H), 1.43 (s, 9H), 1.20 (s, 6H), 0.92 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 213.24, 156.11, 149.55, 146.32, 132.86, 129.66, 113.03, 108.63, 78.95, 77.30, 56.07, 55.86, 48.59, 42.27, 33.00, 28.45, 25.17, 9.15. **HRMS (ESI) m/z** Calculated for $C_{21}H_{33}NO_5$ $[M+Na]^+$: 402.2256, Found: 402.2255.

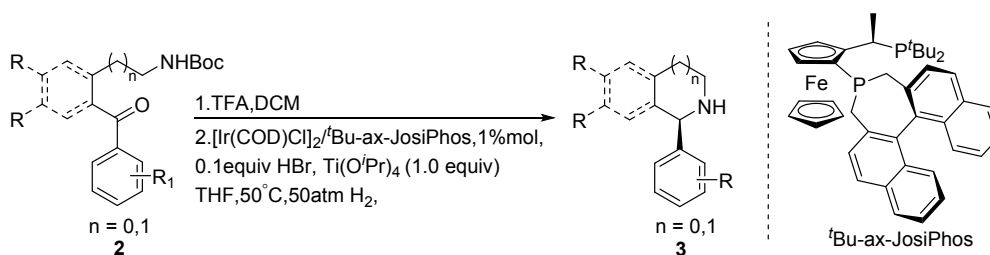


Substrates **2g'** was prepared according to ref 4.

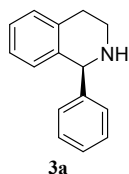
tert-butyl (4-oxo-4-phenylbutyl)carbamate (**2g'**):⁴ 3.21g, 61% yield, white solid;

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.96 (d, $J = 7.3$ Hz, 2H), 7.63 - 7.52 (m, 1H), 7.50 - 7.42 (m, 2H), 3.23 (q, $J = 6.6$ Hz, 2H), 3.03 (t, $J = 7.1$ Hz, 2H), 1.97 - 1.92 (m, 2H), 1.42 (s, 9H).

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

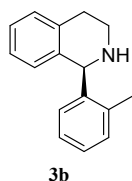


Substrate **2** (0.5 mmol) and TFA (3 mmol) were stirred in CH_2Cl_2 under argon for 3 h, and then all volatiles were removed. In a glass tube equipped with a stir bar, the catalyst (1 mol %) was prepared *in situ* from $[\text{Ir}(\text{COD})\text{Cl}]_2$ (0.0025 mmol, 1.6 mg) and (*R*)-*t*-Bu-ax-Josiphos (0.0055 mmol, 3.4 mg) in anhydrous THF (1 mL) over 30 min. The obtained *N*-Boc deprotected substance was dissolved in THF (1 mL) and then transferred to the above catalyst solution followed by the addition of HBr (0.1 equiv, 40% aq) and $\text{Ti}(\text{O}^i\text{Pr})_4$ (1.0 equiv). The glass tube was then placed into an autoclave, followed by replacing air with H_2 three times. The autoclave was charged with hydrogen to 50 atm, and then the reaction mixture was stirred at 50 °C for 24 h. The resulted solution was neutralized with aqueous sodium bicarbonate solution. The organic phase was concentrated and passed through a short column of silica gel to remove the metal complex to give the chiral tetrahydroisoquinoline product, which was then converted to the corresponding trifluoroacetamide and analyzed by chiral HPLC to determine the enantiomeric excess.

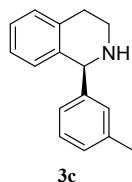


(*S*)-1-phenyl-1,2,3,4-tetrahydroisoquinoline² (**3a**): 103.60 mg, 94% yield, 95% *ee*,

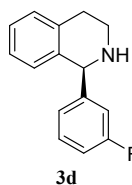
white solid, **m.p.** 95.9-96.9 °C; **¹H NMR** (400 MHz, CDCl₃) δ 7.30 (m, 5H), 7.14 (d, *J* = 4.4 Hz, 2H), 7.04 (m, 1H), 6.75 (d, *J* = 7.8 Hz, 1H), 5.11 (s, 1H), 3.28 (m, 1H), 3.17 - 2.97 (m, 2H), 2.92 - 2.75 (m, 1H), 1.98(s, 1H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 95:5, 1 mL/min, 220 nm, *t_R* = 5.75 min (minor), *t_S* = 10.05 min (major).



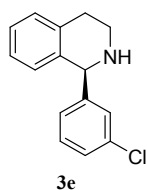
(*S*)-1-(2-methylphenyl)-1,2,3,4-tetrahydroisoquinoline² (**3b**): 102.73 mg, 81% yield, 87% *ee*, light yellow oil; **¹H NMR** (400 MHz, CDCl₃) δ 7.23 - 7.08 (m, 5H), 7.04 (m, 2H), 6.69 (d, *J* = 7.7 Hz, 1H), 5.34 (s, 1H), 3.42 - 3.23 (m, 1H), 3.21 - 2.93 (m, 2H), 2.90 - 2.77 (m, 1H), 2.41 (s, 3H), 1.73(s, 1H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H+AD-H column, Hex/IPA = 95:5, 1 mL/min, 220 nm, *t_R* = 9.89 min (minor), *t_S* = 10.49 min (major).



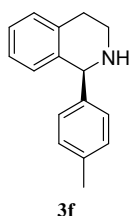
(*S*)-1-(3-methylphenyl)-1,2,3,4-tetrahydroisoquinoline² (**3c**): 110.54 mg, 91% yield, 90% *ee*, white solid, **m.p.** 85.1 - 87.2 °C; **¹H NMR** (400 MHz, CDCl₃) δ 7.21 (t, *J* = 7.9 Hz, 1H), 7.14 (m, 2H), 7.09 (d, *J* = 6.6 Hz, 2H), 7.07 - 6.95 (m, 2H), 6.76 (d, *J* = 7.7 Hz, 1H), 5.06 (s, 1H), 3.36 - 3.21 (m, 1H), 3.15 - 2.95 (m, 2H), 2.88 - 2.73 (m, 1H), 2.32 (s, 3H), 1.92(s, 1H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 95:5, 1 mL/min, 220 nm, *t_R* = 4.68 min (minor), *t_S* = 8.26 min (major).



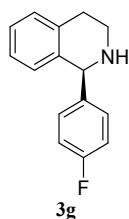
(*S*)-1-(3-fluorophenyl)-1,2,3,4-tetrahydroisoquinoline² (**3d**): 111.37 mg, 94% yield, 94% *ee*, white solid, **m.p.** 78.3 - 88.2 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.28 (m, 1H), 7.15 (m, 2H), 7.06 (m, 2H), 7.01 - 6.86 (m, 2H), 6.75 (d, *J* = 7.7 Hz, 1H), 5.10 (s, 1H), 3.31 - 3.19 (m, 1H), 3.14 - 2.96 (m, 2H), 2.83 (m, 1H), 1.90(s, 1H). ¹⁹F NMR (376 MHz, CDCl₃) δ -113.14. Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 95:5, 1 mL/min, 220 nm, *t_R* = 5.55 min (minor), *t_S* = 9.41 min (major).



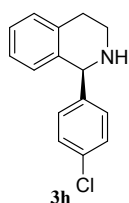
(*S*)-1-(3-chlorophenyl)-1,2,3,4-tetrahydroisoquinoline² (**3e**): 118.21 mg, 92% yield, 91% *ee*, white solid, **m.p.** 88.9 - 90.2 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.31 - 7.21 (m, 3H), 7.16 (m, 3H), 7.06 (dq, *J* = 8.4, 4.3 Hz, 1H), 6.74 (d, *J* = 7.7 Hz, 1H), 5.08 (s, 1H), 3.29 - 3.19 (m, 1H), 3.13 - 2.99 (m, 2H), 2.88 - 2.76 (m, 1H), 1.89(s, 1H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 95:5, 1 mL/min, 220 nm, *t_R* = 5.42 min (minor), *t_S* = 9.80 min (major).



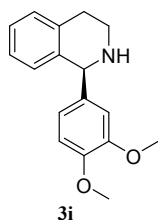
(*S*)-1-(4-methylphenyl)-1,2,3,4-tetrahydroisoquinoline² (**3f**): 109.43 mg, 95% yield, 79% *ee*, white solid, **m.p.** 81.9-83.9 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.26 (s, 2H), 7.14 (s, 6H), 7.03 (m, 1H), 6.76 (d, *J* = 7.8 Hz, 1H), 5.07 (s, 1H), 3.28 (m, 1H), 3.17 - 2.93 (m, 2H), 2.83 (m, 1H), 2.34 (s, 3H), 1.73(s, 1H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 95:5, 1 mL/min, 220 nm, *t_R* = 5.76 min (minor), *t_S* = 8.74 min (major).



(*S*)-1-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinoline² (**3g**): 112.50 mg, 96% yield, 95% *ee*, white solid, **m.p.** 83.5 - 85.5 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.24 (dd, *J* = 8.2, 5.3 Hz, 2H), 7.15 (d, *J* = 4.2 Hz, 2H), 7.09 - 6.91 (m, 3H), 6.72 (d, *J* = 7.8 Hz, 1H), 5.09 (s, 1H), 3.30 - 3.20 (m, 1H), 3.15 - 2.98 (m, 2H), 2.90 - 2.73 (m, 1H), 1.93(s, 1H). ¹⁹F NMR (376 MHz, CDCl₃) δ -115.30. Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 95:5, 1 mL/min, 220 nm, *t_R* = 5.52 min (minor), *t_S* = 9.52 min (major).

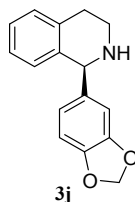


(*S*)-1-(4-chlorophenyl)-1,2,3,4-tetrahydroisoquinoline² (**3h**): 120.65 mg, 95% yield, 89% *ee*, white solid, **m.p.** 104.6 - 106.0 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.29 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.2 Hz, 2H), 7.15 (d, *J* = 3.2 Hz, 2H), 7.04 (dt, *J* = 8.5, 4.3 Hz, 1H), 6.71 (d, *J* = 7.7 Hz, 1H), 5.08 (s, 1H), 3.30 - 3.20 (m, 1H), 3.15 - 2.98 (m, 2H), 2.89 - 2.75 (m, 1H), 1.84(s, 1H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 95:5, 1 mL/min, 220 nm, *t_R* = 5.35 min (minor), *t_S* = 7.54 min (major).

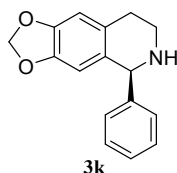


(*S*)-1-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydroisoquinoline² (**3i**): 133.33 mg, 92% yield, 87% *ee*, light yellow solid, **m.p.** 88.4 - 89.0 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.14 (d, *J* = 4.2 Hz, 2H), 7.04 (dt, *J* = 8.6, 4.3 Hz, 1H), 6.85 - 6.68 (m, 4H), 5.04 (s,

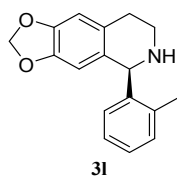
1H), 3.88 (s, 3H), 3.83 (s, 3H), 3.38 - 3.18 (m, 1H), 3.16 - 2.98 (m, 2H), 2.88 - 2.75 (m, 1H), 1.85(s, 1H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 95:5, 1 mL/min, 220 nm, t_R = 7.12 min (minor), t_S = 11.17 min (major).



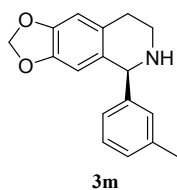
(*S*)-1-(benzo[d][1,3]dioxol-5-yl)-1,2,3,4-tetrahydroisoquinoline (**3j**): 124.12 mg, 81% yield, 89% *ee*, white solid, **m.p.** 72.0 - 73.3 °C; $[\alpha]_D^{25}$ = -34.27 (*c* 0.25, CH₂Cl₂). **¹H NMR** (400 MHz, CDCl₃) δ 7.24 - 7.09 (m, 2H), 7.09 - 6.99 (m, 1H), 6.95 - 6.74 (m, 3H), 6.72 (s, 1H), 5.93 (s, 2H), 5.03 (s, 1H), 3.28 (m, 1H), 3.16 - 2.91 (m, 2H), 2.90 - 2.67 (m, 1H), 1.84(s, 1H). **¹³C NMR** (100 MHz, CDCl₃) δ 129.01, 128.03, 126.27, 125.62, 122.30, 109.19, 107.84, 100.95, 61.82, 42.26, 29.74. **HRMS (ESI)** *m/z* Calculated for C₁₆H₁₆NO₂ [M+H]⁺: 254.1181, Found: 254.1178. Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 90:10, 1 mL/min, 220 nm, t_R = 7.85 min (minor), t_S = 21.04 min (major).



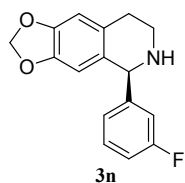
(*S*)-5-phenyl-5,6,7,8-tetrahydro-[1,3]dioxolo[4,5-g]isoquinoline⁵ (**3k**) 120.32 mg, 82% yield, 90% *ee*, white solid, **m.p.** 107.3 - 108.6 °C; $[\alpha]_D^{25}$ = -14.1 (*c* 0.27, CH₂Cl₂). **¹H NMR** (400 MHz, CDCl₃) δ 7.65 - 7.11 (m, 5H), 6.61 (s, 1H), 6.21 (s, 1H), 5.85 (s, 2H), 5.00 (s, 1H), 3.22 (m, 1H), 3.10 - 2.99 (m, 1H), 2.93 (m, 1H), 2.73 (m, 1H), 1.82(s, 1H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 95:5, 1 mL/min, 220 nm, t_R = 12.08 min (minor), t_S = 22.75 min (major).



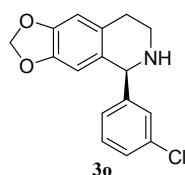
(*S*)-5-(2-methylphenyl)-5,6,7,8-tetrahydro-[1,3]dioxolo[4,5-*g*] isoquinoline (**3l**): 120.30 mg, 78% yield, 94% *ee*, colorless oil liquid; $[\alpha]_D^{25} = -3.4$ (*c* 0.37, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ 7.24 - 7.07 (m, 3H), 7.03 (d, *J* = 7.6 Hz, 1H), 6.61 (s, 1H), 6.16 (s, 1H), 5.86 (s, 2H), 5.24 (s, 1H), 3.24 (m, 1H), 3.04 (m, 1H), 2.94 (m, 1H), 2.73 (m, 1H), 2.41 (s, 3H), 1.88 (s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 145.89, 145.72, 142.34, 136.57, 131.43, 130.80, 129.45, 128.62, 127.26, 125.94, 108.49, 107.49, 100.57, 58.84, 42.36, 29.88, 19.41. HRMS (ESI) *m/z* Calculated for C₁₇H₁₈NO₂ [M+H]⁺: 268.1338, Found: 268.1334. Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 95:5, 1 mL/min, 220 nm, *t_R* = 8.51 min (minor), *t_S* = 9.72 min (major).



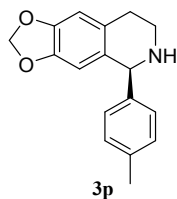
(*S*)-5-(3-methylphenyl)-5,6,7,8-tetrahydro-[1,3]dioxolo[4,5-*g*] isoquinoline (**3m**): 128.32 mg, 85% yield, 91% *ee*, white solid, **m.p.** 116.1 - 117.9 °C; $[\alpha]_D^{25} = -27.1$ (*c* 0.25, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ 7.21 (t, *J* = 7.5 Hz, 1H), 7.16 - 6.87 (m, 3H), 6.60 (s, 1H), 6.22 (s, 1H), 5.85 (s, 2H), 4.95 (s, 1H), 3.31 - 3.18 (m, 1H), 3.09 - 2.88 (m, 2H), 2.71 (m, 1H), 2.33 (s, 3H), 1.85 (s, 1H). ¹³C NMR (100MHz, CDCl₃) δ 145.94, 145.55, 144.70, 138.12, 131.31, 129.47, 128.55, 128.26, 128.19, 125.95, 108.45, 107.97, 100.56, 62.11, 42.25, 29.88, 21.43. HRMS (ESI) *m/z* Calculated for C₁₇H₁₈NO₂ [M+H]⁺: 268.1338, Found: 268.1333. Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 95:5, 1 mL/min, 220 nm, *t_R* = 8.56 min (minor), *t_S* = 19.54 min (major).



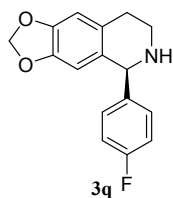
(*S*)-5-(3-fluorophenyl)-5,6,7,8-tetrahydro-[1,3]dioxolo[4,5-*g*] isoquinoline (**3n**): 132.93 mg, 82% yield, 94% *ee*, white solid, **m.p.** 118.0 - 118.5 °C; $[\alpha]_D^{25} = -16.1$ (*c* 0.25, CH₂Cl₂). **¹H NMR** (400 MHz, CDCl₃) δ 7.35 – 7.27 (m, 1H), 7.07 (d, *J* = 7.7 Hz, 1H), 6.97 (t, *J* = 8.9 Hz, 2H), 6.61 (s, 1H), 6.21 (s, 1H), 5.87 (s, 2H), 5.00 (s, 1H), 3.20 (m, 1H), 3.03 (m, 1H), 2.92 (m, 1H), 2.72 (m, 1H), 1.76 (s, 1H). **¹³C NMR** (100 MHz, CDCl₃) δ 162.87 (d, *J* = 246.1 Hz), 147.44 (d, *J* = 6.5 Hz), 146.18, 145.67, 130.38, 129.83 (d, *J* = 8.1 Hz), 128.64, 124.49, 115.70 (d, *J* = 21.4 Hz), 114.34 (d, *J* = 21.2 Hz), 108.60, 107.78, 100.66, 61.45, 41.86, 29.72. **¹⁹F NMR** (376 MHz, CDCl₃) δ -113.08. **HRMS (ESI)** *m/z* Calculated for C₁₆H₁₅FNO₂ [M+H]⁺: 272.1087, Found: 272.1083. Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 95:5, 1 mL/min, 220 nm, *t_R* = 12.50 min (minor), *t_S* = 24.08 min (major).



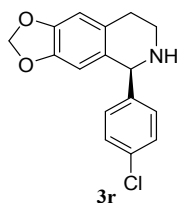
(*S*)-5-(3-chlorophenyl)-5,6,7,8-tetrahydro-[1,3]dioxolo[4,5-*g*] isoquinoline (**3o**): 142.43 mg, 81% yield, 93% *ee*, white solid, **m.p.** 114.3 - 115.9 °C; $[\alpha]_D^{25} = -53.9$ (*c* 0.25, CH₂Cl₂). **¹H NMR** (400 MHz, CDCl₃) δ 7.25 (s, 3H), 7.15 (s, 1H), 6.61 (s, 1H), 6.19 (s, 1H), 5.87 (s, 2H), 4.97 (s, 1H), 3.19 (m, 1H), 3.02 (m, 1H), 2.97 - 2.81 (m, 1H), 2.72 (m, 1H), 1.84 (s, 1H). **¹³C NMR** (100 MHz, CDCl₃) δ 146.89, 146.21, 145.69, 134.28, 130.25, 129.67, 128.94, 128.66, 127.62, 127.09, 108.62, 107.78, 100.67, 61.49, 41.89, 29.71. **HRMS (ESI)** *m/z* Calculated for C₁₆H₁₅ClNO₂ [M+H]⁺: 288.0791, Found: 288.0787. Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 90:10, 1 mL/min, 220 nm, *t_R* = 8.30 min (minor), *t_S* = 15.33 min (major).



(*S*)-5-(4-methylphenyl)-5,6,7,8-tetrahydro-[1,3]dioxolo[4,5-*g*] isoquinoline⁵ (**3p**): 126.98 mg, 90% yield, 85% *ee*, white solid, **m.p.** 81.5 - 83.2 °C; $[\alpha]_D^{25} = -28.7$ (*c* 0.32, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ 7.13 (s, 4H), 6.60 (s, 1H), 6.22 (s, 1H), 5.84 (s, 2H), 4.96 (s, 1H), 3.22 (m, 1H), 3.02 (m, 1H), 2.92 (m, 1H), 2.71 (m, 1H), 2.34 (s, 3H), 1.87 (s, 1H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 95:5, 1 mL/min, 220 nm, *t_R* = 8.97 min (minor), *t_S* = 13.33 min (major).

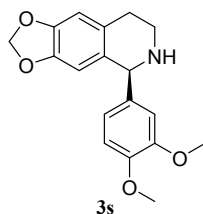


(*S*)-5-(4-fluorophenyl)-5,6,7,8-tetrahydro-[1,3]dioxolo[4,5-*g*] isoquinoline (**3q**): 134.29 mg, 86% yield, 90% *ee*, white solid, **m.p.** 102.9 - 104.1 °C; $[\alpha]_D^{25} = -24.8$ (*c* 0.25, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ 7.44 - 7.12 (m, 2H), 7.00 (t, *J* = 8.5 Hz, 2H), 6.60 (s, 1H), 6.18 (s, 1H), 5.86 (s, 2H), 4.98 (s, 1H), 3.20 (m, 1H), 2.98 (m, 2H), 2.71 (m, 1H), 1.86 (s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 162.13 (d, *J* = 245.6 Hz), 146.11, 145.66, 140.63 (d, *J* = 3.1 Hz), 131.00, 130.41 (d, *J* = 8.0 Hz), 128.64, 115.24 (d, *J* = 21.3 Hz), 108.58, 107.80, 100.65, 61.33, 42.11, 29.81. ¹⁹F NMR (376 MHz, CDCl₃) δ -115.24. **HRMS (ESI)** *m/z* Calculated for C₁₆H₁₅FNO₂ [M+H]⁺: 272.1087, Found: 272.1082. Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 95:5, 1 mL/min, 220 nm, *t_R* = 12.53 min (minor), *t_S* = 22.26 min (major).

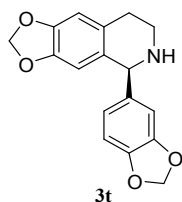


(*S*)-5-(4-chlorophenyl)-5,6,7,8-tetrahydro-[1,3]dioxolo[4,5-*g*] isoquinoline⁵ (**3r**):

142.43 mg, 87% yield, 90% *ee*, white solid, **m.p.** 124.0 - 125.1 °C; $[\alpha]_D^{25} = -41.9$ (*c* 0.34, CH₂Cl₂). **¹H NMR** (400 MHz, CDCl₃) δ 7.29 (d, *J* = 8.7 Hz, 2H), 7.20 (d, *J* = 8.6 Hz, 2H), 6.60 (s, 1H), 6.17 (s, 1H), 5.86 (s, 2H), 4.97 (s, 1H), 3.25 - 3.14 (m, 1H), 3.03 (m, 1H), 2.97 - 2.87 (m, 1H), 2.71 (m, 1H), 1.81 (s, 1H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 95:5, 1 mL/min, 220 nm, *t_R* = 8.73 min (minor), *t_S* = 12.04 min (major).

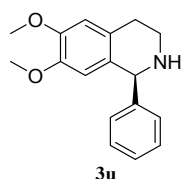


(*S*)-5-(3,4-dimethoxyphenyl)-5,6,7,8-tetrahydro-[1,3]dioxolo[4,5-g]isoquinoline⁵ (**3s**): 148.84 mg, 92% yield, 88% *ee*, white solid, **m.p.** 79.5 - 80.5 °C; $[\alpha]_D^{25} = -40.2$ (*c* 0.50, CH₂Cl₂). **¹H NMR** (400 MHz, CDCl₃) δ 6.94 - 6.72 (m, 3H), 6.60 (s, 1H), 6.23 (s, 1H), 5.86 (s, 2H), 4.93 (s, 1H), 3.86 (d, *J* = 13.6 Hz, 6H), 3.39 - 3.12 (m, 1H), 3.09 - 2.85 (m, 2H), 2.75 - 2.61 (m, 1H), 1.84 (s, 1H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 90:10, 1 mL/min, 220 nm, *t_R* = 16.28 min (minor), *t_S* = 30.78 min (major).

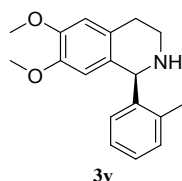


(*S*)-5-(benzo[d][1,3]dioxol-5-yl)-5,6,7,8-tetrahydro-[1,3]dioxolo[4,5-g] isoquinoline (**3t**): 141.22 mg, 82% yield, 92% *ee*, white solid, **m.p.** 136.7 - 139.2 °C; $[\alpha]_D^{25} = -59.9$ (*c* 0.32, CH₂Cl₂). **¹H NMR** (400 MHz, CDCl₃) δ 6.75 (s, 2H), 6.71 (s, 1H), 6.59 (s, 1H), 6.24 (s, 1H), 5.94 (s, 2H), 5.86 (s, 2H), 4.92 (s, 1H), 3.40 - 3.10 (m, 1H), 3.09 - 2.86 (m, 2H), 2.70 (m, 1H), 1.78 (s, 1H). **¹³C NMR** (101 MHz, CDCl₃) δ 147.77, 146.88, 146.05, 145.62, 138.93, 131.26, 128.61, 122.21, 109.10, 108.48, 107.90, 107.89, 100.98, 100.61, 61.80, 42.14, 29.84. **HRMS (ESI)** *m/z* Calculated for C₁₇H₁₆NO₄ [M+H]⁺: 298.1079, Found: 298.1079. Enantiomeric excess was

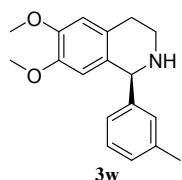
determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 80:20, 1 mL/min, 220 nm, t_R = 11.03 min (minor), t_S = 25.88 min (major).



(*S*)-6,7-dimethoxy-1-phenyl-1,2,3,4-tetrahydroisoquinoline⁶ (**3u**): 133.33 mg, 91% yield, 90% *ee*, white solid, **m.p.** 126.6 - 127.6 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.30 (m, 5H), 6.64 (s, 1H), 6.25 (s, 1H), 5.05 (s, 1H), 3.88 (m, 3H), 3.64 (m, 3H), 3.22 (m, 1H), 3.05 (m, 1H), 2.94 (m, 1H), 2.76 (m, 1H), 1.87(s,1H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 95:5, 1 mL/min, 220 nm, t_S = 10.33 min (major), t_R = 15.97 min (minor).

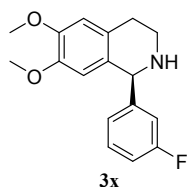


(*S*)-6,7-dimethoxy-1-(2-methylphenyl)-1,2,3,4-tetrahydro isoquinoline⁶ (**3v**): 127.52 mg, 81% yield, 96% *ee*, light yellow oil; ¹H NMR (400 MHz, CDCl₃) δ 7.17 (h, J = 7.0, 6.4 Hz, 2H), 7.12 - 7.04 (m, 1H), 6.98 (d, J = 7.6 Hz, 1H), 6.63 (s, 1H), 6.19 (s, 1H), 5.28 (s, 1H), 3.87 (s, 3H), 3.62 (s, 3H), 3.21 (m, 1H), 3.04 (m, 1H), 2.92 (m, 1H), 2.81 - 2.70 (m, 1H), 2.43 (s, 3H) , 2.06(s,1H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak AD-H column, Hex/IPA = 90:10, 1 mL/min, 220 nm, t_S = 7.47 min (major), t_R = 10.42 min (minor).

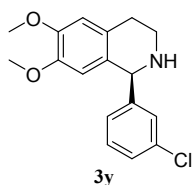


(*S*)-6,7-dimethoxy-1-(3-methylphenyl)-1,2,3,4-tetrahydro isoquinoline⁶ (**3w**): 140.27 mg, 92% yield, 95% *ee*, white solid, **m.p.** 113.4 - 113.6 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.21 (t, J = 7.6 Hz, 1H), 7.09 (d, J = 7.9 Hz, 2H), 7.03 (d, J = 7.5 Hz,

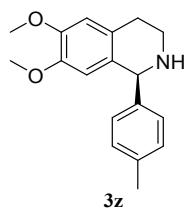
1H), 6.63 (s, 1H), 6.26 (s, 1H), 5.01 (s, 1H), 3.88 (s, 3H), 3.64 (s, 3H), 3.26 - 3.16 (m, 1H), 3.04 (m, 1H), 2.93 (m, 1H), 2.75 (m, 1H), 2.32 (s, 3H), 1.89(s,1H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 95:5, 1 mL/min, 220 nm, $t_S = 7.97$ min (major), $t_R = 9.86$ min (minor).



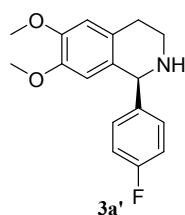
(*S*)-6,7-dimethoxy-1-(3-fluorophenyl)-1,2,3,4-tetrahydro isoquinoline⁶ (**3x**): 142.23 mg, 92% yield, 90% *ee*, white solid, **m.p.** 118.0 - 119.6 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.29 (m, 1H), 7.06 (d, $J = 7.7$ Hz, 1H), 6.97 (t, $J = 8.6$ Hz, 2H), 6.64 (s, 1H), 6.24 (s, 1H), 5.05 (s, 1H), 3.88 (s, 3H), 3.66 (s, 3H), 3.26 - 3.14 (m, 1H), 3.11 - 2.99 (m, 1H), 2.92 (m, 1H), 2.81 - 2.66 (m, 1H), 1.86(s,1H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 95:5, 1 mL/min, 220 nm, $t_S = 10.46$ min (major), $t_R = 14.96$ min (minor).



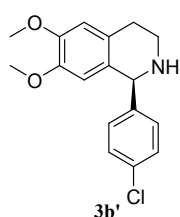
(*S*)-6,7-dimethoxy-1-(3-chlorophenyl)-1,2,3,4-tetrahydro isoquinoline⁷ (**3y**): 147.34 mg, 93% yield, 90% *ee*, white solid, **m.p.** 102.9 - 103.8 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.36 - 7.19 (m, 3H), 7.20 - 7.06 (m, 1H), 6.64 (s, 1H), 6.22 (s, 1H), 5.02 (s, 1H), 3.88 (s, 3H), 3.66 (s, 3H), 3.19 ((m, 1H), 3.04 ((m, 1H), 2.92 ((m, 1H), 2.75 ((m, 1H), 1.89(s,1H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 90:10, 1 mL/min, 220 nm, $t_S = 7.02$ min (major), $t_R = 8.46$ min (minor).



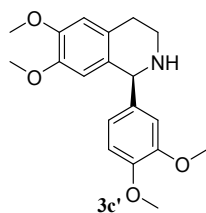
(*S*)-6,7-dimethoxy-1-(4-methylphenyl)-1,2,3,4-tetrahydro isoquinoline⁶ (**3z**): 140.27 mg, 96% yield, 92% *ee*, white solid, **m.p.** 119.2 - 120.7 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.13 (s, 4H), 6.63 (s, 1H), 6.26 (s, 1H), 5.02 (s, 1H), 3.87 (s, 3H), 3.64 (s, 3H), 3.26 - 3.15 (m, 1H), 3.03 (m, 1H), 2.92 (m, 1H), 2.75 (m, 1H), 2.34 (s, 3H), 1.82(s,1H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 95:5, 1 mL/min, 220 nm, *t*_S = 7.56 min (major), *t*_R = 11.07 min (minor).



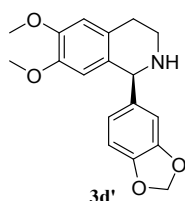
(*S*)-6,7-dimethoxy-1-(4-fluorophenyl)-1,2,3,4-tetrahydro isoquinoline⁶ (**3a'**): 140.79 mg, 95% yield, 85% *ee*, white solid, **m.p.** 132.6 - 133.4 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.26 - 7.17 (m, 2H), 7.01 (t, *J* = 8.1 Hz, 3H), 6.63 (s, 1H), 6.20 (s, 1H), 5.03 (s, 1H), 3.88 (s, 3H), 3.65 (s, 3H), 3.21 (m, 1H), 3.05 (m, 1H), 2.94 (m, 1H), 2.74 (m, 1H), 1.84(s,1H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 95:5, 1 mL/min, 220 nm, *t*_S = 10.62 min (major), *t*_R = 14.54 min (minor).



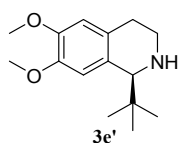
(*S*)-6,7-dimethoxy-1-(4-chlorophenyl)-1,2,3,4-tetrahydro isoquinoline⁶ (**3b'**): 150.37 mg, 94% yield, 87% *ee*, white solid, **m.p.** 122.9 - 130.4 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.35 - 7.24 (m, 2H), 7.20 (d, *J* = 8.6 Hz, 2H), 6.63 (s, 1H), 6.20 (s, 1H), 5.02 (s, 1H), 3.88 (s, 3H), 3.65 (s, 3H), 3.19 (m, 1H), 3.04 (m, 1H), 2.92 (m, 1H), 2.74 (m, 1H), 1.75(s,1H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 90:10, 1 mL/min, 220 nm, *t*_S = 6.73 min (major), *t*_R = 8.45 min (minor).



(*S*)-6,7-dimethoxy-1-(3,4-dimethylphenyl)-1,2,3,4-tetrahydro isoquinoline⁶ (**3c'**): 161.40 mg, 91% yield, 99% *ee*, white solid, **m.p.** 108.0 - 112.3 °C; ¹H NMR (400 MHz, CDCl₃) δ 6.89 - 6.76 (m, 3H), 6.63 (s, 1H), 6.27 (s, 1H), 4.99 (s, 1H), 3.88 (s, 6H), 3.83 (s, 3H), 3.65 (s, 3H), 3.38 - 3.15 (m, 1H), 3.15 - 2.84 (m, 2H), 2.74 (m, 1H), 1.80(s,1H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 90:10, 1 mL/min, 220 nm, *t*_S = 11.85 min (major), *t*_R = 14.74 min (minor).

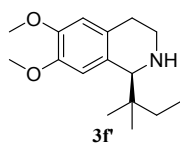


(*S*)-1-(benzo[d][1,3]dioxol-5-yl)-6,7-dimethoxy-1,2,3,4-tetrahydro isoquinoline⁸ (**3d'**): 151.98 mg, 87% yield, 87.5% *ee*, white solid, **m.p.** 117.5 - 118.2 °C; ¹H NMR (400 MHz, CDCl₃) δ 6.83 - 6.67 (m, 3H), 6.62 (s, 1H), 6.27 (s, 1H), 5.94 (s, 2H), 4.97 (s, 1H), 3.87 (s, 3H), 3.67 (s, 3H), 3.27 - 3.16 (m, 1H), 3.03 (m, 1H), 2.92 (m, 1H), 2.73 (m, 1H), 1.86 (s, 1H). Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 90:10, 1 mL/min, 220 nm, *t*_S = 14.68 min (major), *t*_R = 24.34 min (minor).

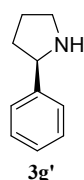


(*S*)-1-(*tert*-butyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline⁹ (**3e'**): 107.2 mg, 86% yield, 98% *ee*, colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 6.67 (s, 1H), 6.58 (s, 1H), 3.85 (d, *J* = 7.9 Hz, 6H), 3.79 (s, 1H), 3.25 (dt, *J* = 9.9, 3.6 Hz, 1H), 2.80-2.63 (m, 2H), 2.52 (dt, *J* = 14.7, 2.8 Hz, 1H), 1.70 (s, 1H), 0.94 (s, 9H). Enantiomeric

excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 80:20, 1 mL/min, 220 nm, t_S = 18.57 min (major), t_R = 33.54 min (minor).

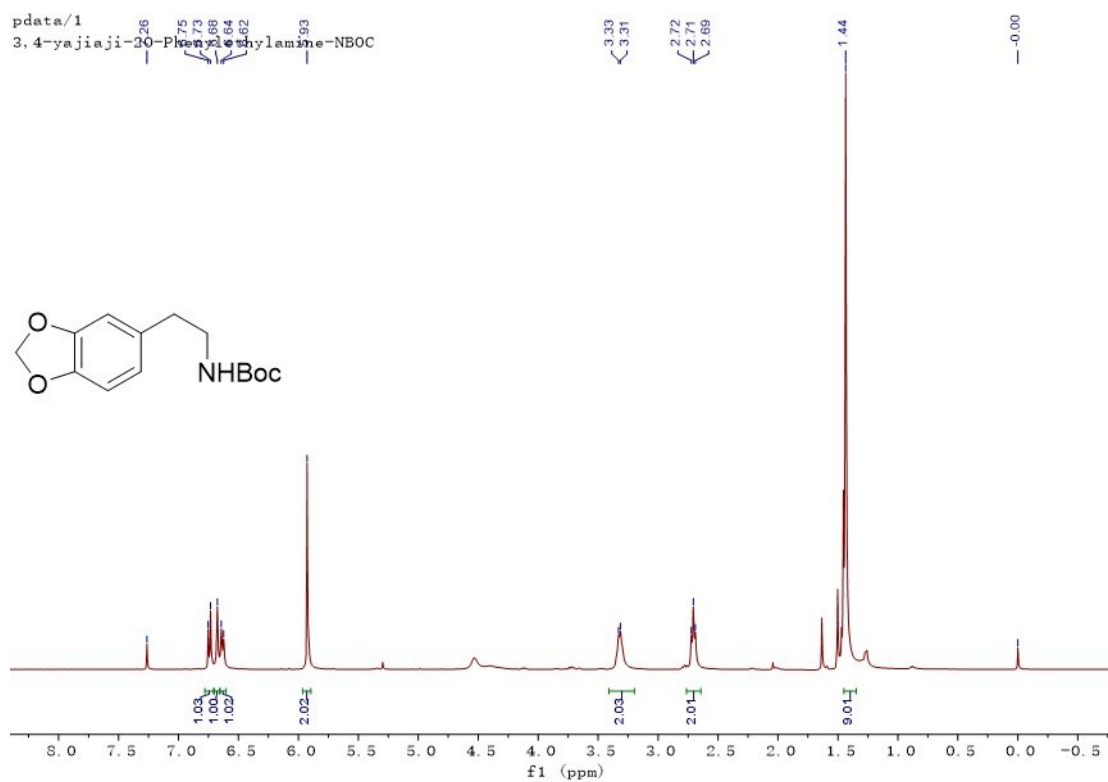
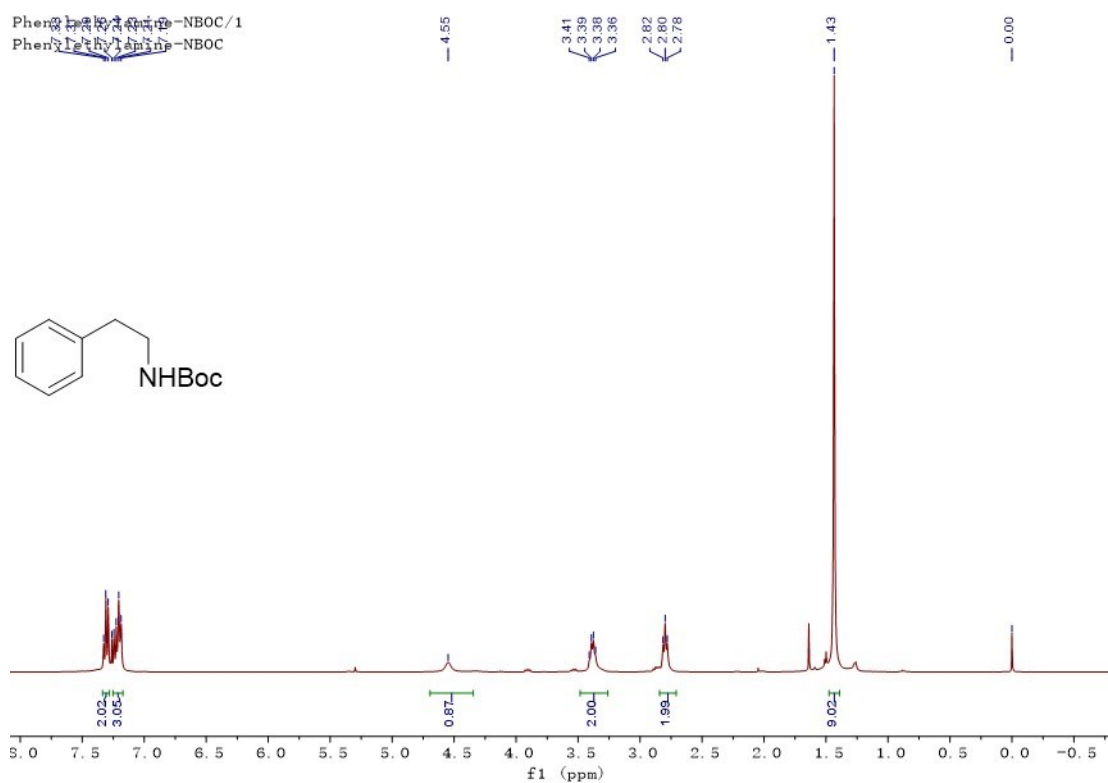


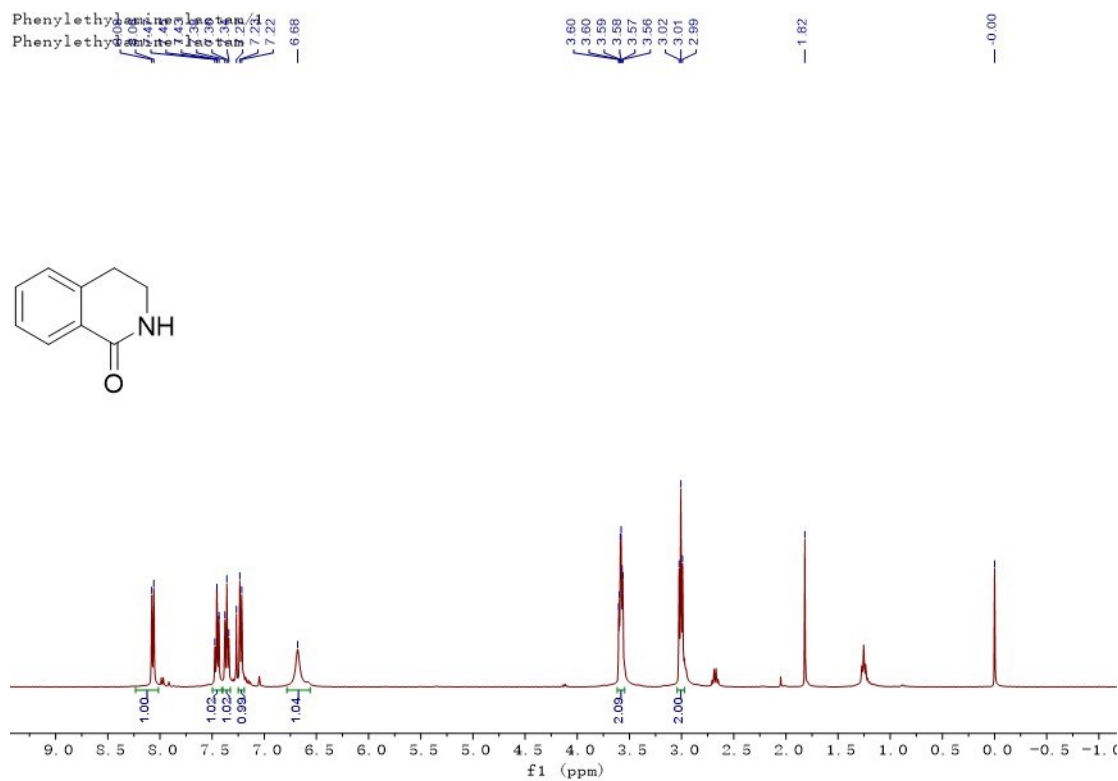
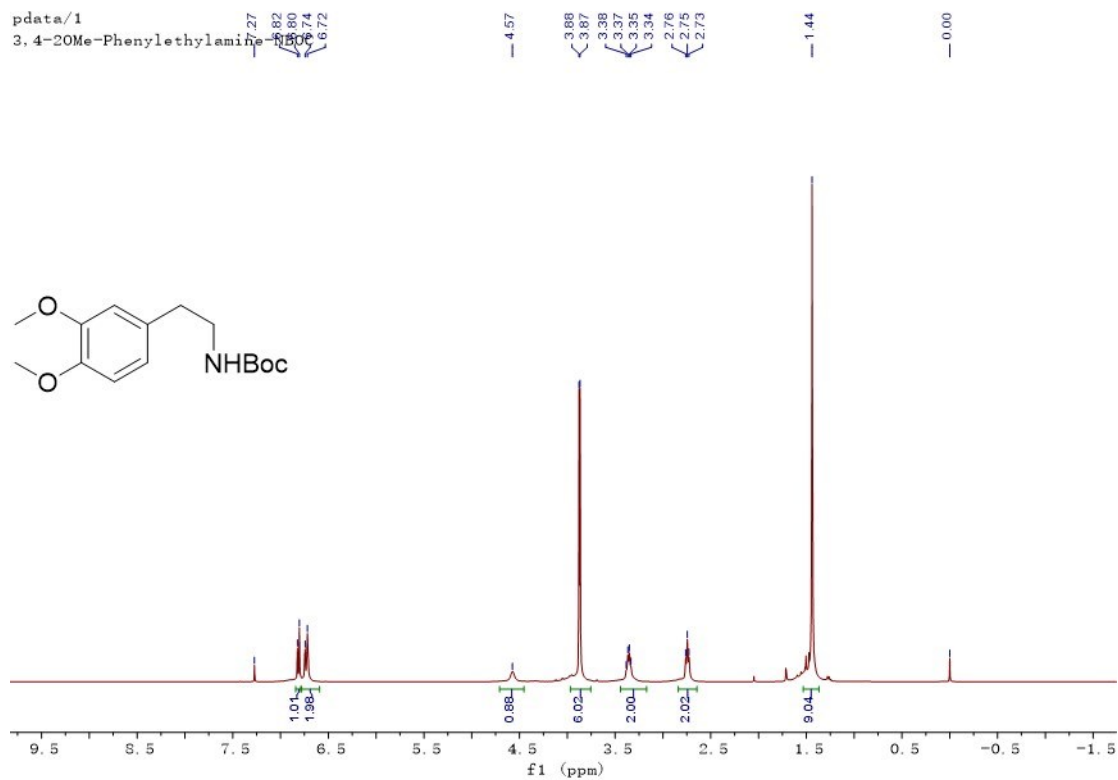
(*S*)-6,7-dimethoxy-1-(*tert*-pentyl)-1,2,3,4-tetrahydroisoquinoline (**3f'**): 114.6 mg, 87% yield, 97% *ee*, colorless oil; $[\alpha]_D^{25}$ = -12.6 (*c* 0.12, CH₂Cl₂). **¹H NMR** (400 MHz, CDCl₃) δ 6.66 (s, 1H), 6.58 (s, 1H), 3.90 (s, 1H), 3.86 (s, 3H), 3.84 (s, 3H), 3.31-3.13 (m, 1H), 2.80 - 2.65 (m, 2H), 2.59 - 2.45 (m, 1H), 1.63 (s, 1H), 1.52 (dq, *J* = 14.8, 7.5 Hz, 1H), 1.25 (dq, *J* = 14.5, 7.5 Hz, 1H), 0.94 - 0.85 (m, 6H), 0.83 (s, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 146.91, 145.99, 131.13, 128.48, 112.78, 111.38, 62.26, 55.94, 55.75, 42.82, 39.79, 31.58, 31.17, 24.81, 23.77, 8.40. **HRMS (ESI) *m/z*** Calculated for C₁₆H₂₅NO₂ [M+H]⁺: 264.1964, Found: 264.1959. Enantiomeric excess was determined by chiral HPLC on a Chiralpak AS-H column, Hex/IPA = 80:20, 1 mL/min, 220 nm, t_S = 17.15 min (major), t_R = 28.67 min (minor).



(*R*)-2-phenylpyrrolidine (**3g'**):⁴ 138.2 mg, 94% yield, 35% *ee*, colourless oil. **¹H NMR** (400 MHz, CDCl₃) δ 7.39 - 7.28 (m, 4H), 7.26 - 7.19 (m, 1H), 4.10 (t, *J* = 7.7 Hz, 1H), 3.24 - 3.14 (m, 1H), 3.04 - 2.94 (m, 1H), 2.25 - 2.11 (m, 1H), 1.98 - 1.81 (m, 3H), 1.74 - 1.57 (m, 1H).

4. NMR spectra and HRMS





3,4-yajiaji-20-lactam. 1. 1. 1r
3,4-yajiaji-20-lactam

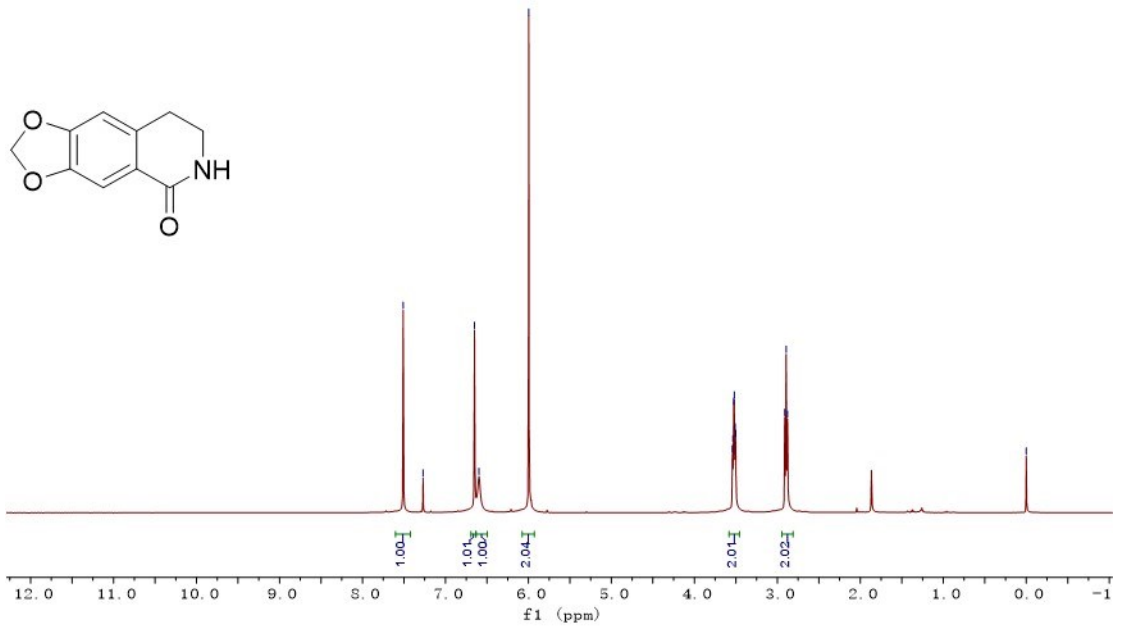
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-6.60

-6.00

3.54
3.54
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3.52
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3.50
2.91
2.89
2.88

-0.00



pdata/1

3,4-20Me-lactam

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-7.27

-6.70

4.21

4.19

4.18

3.97

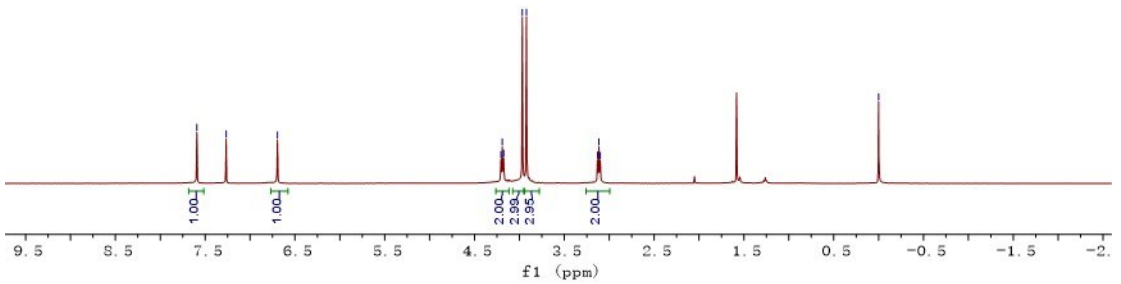
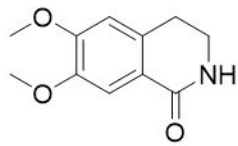
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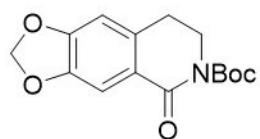
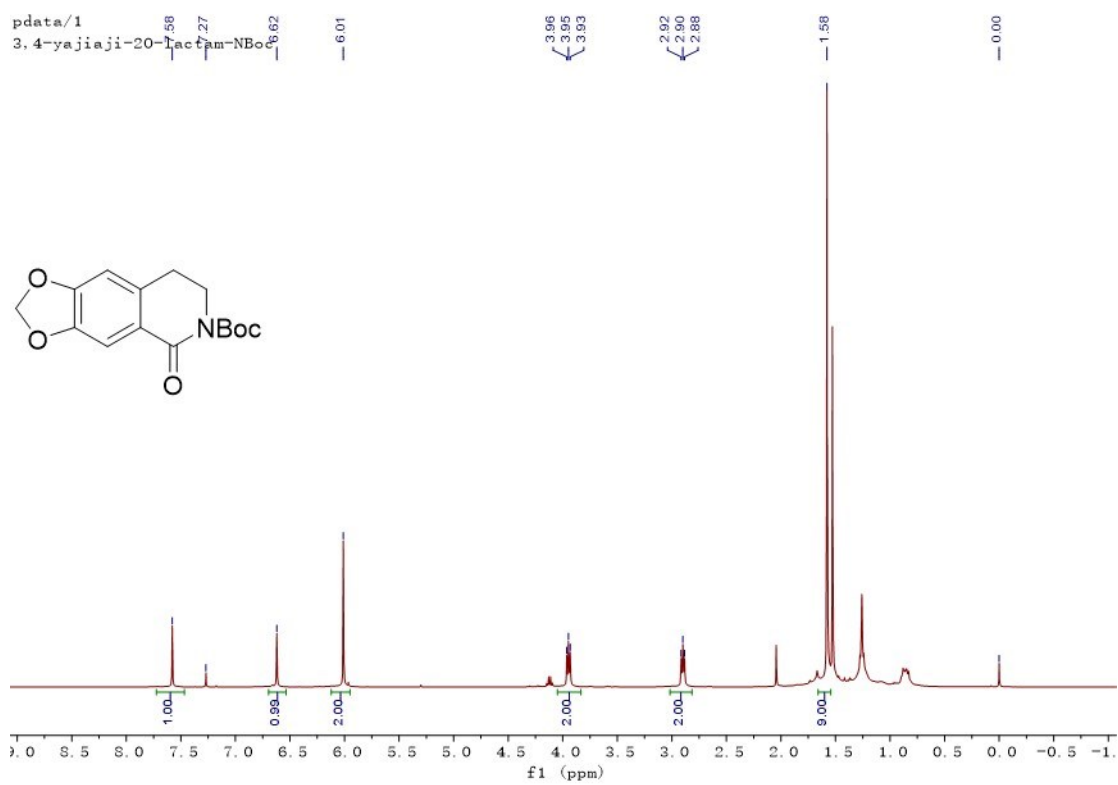
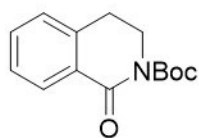
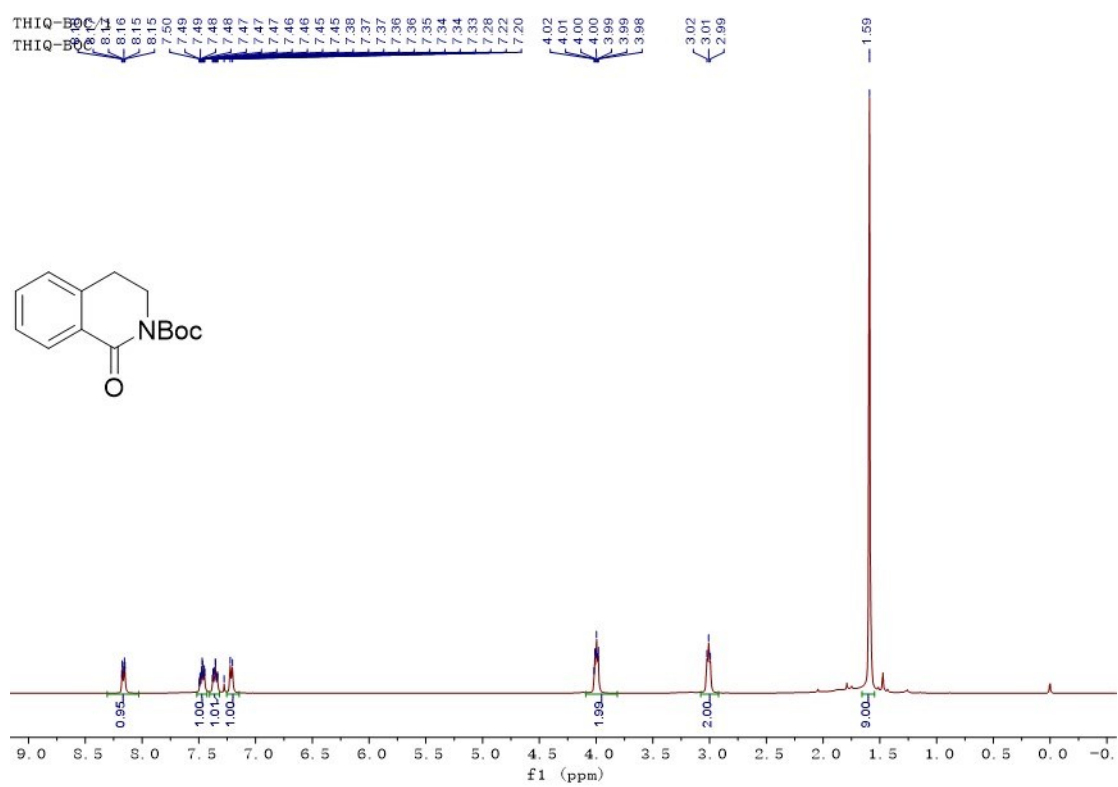
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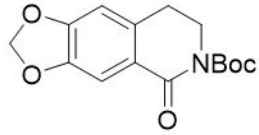
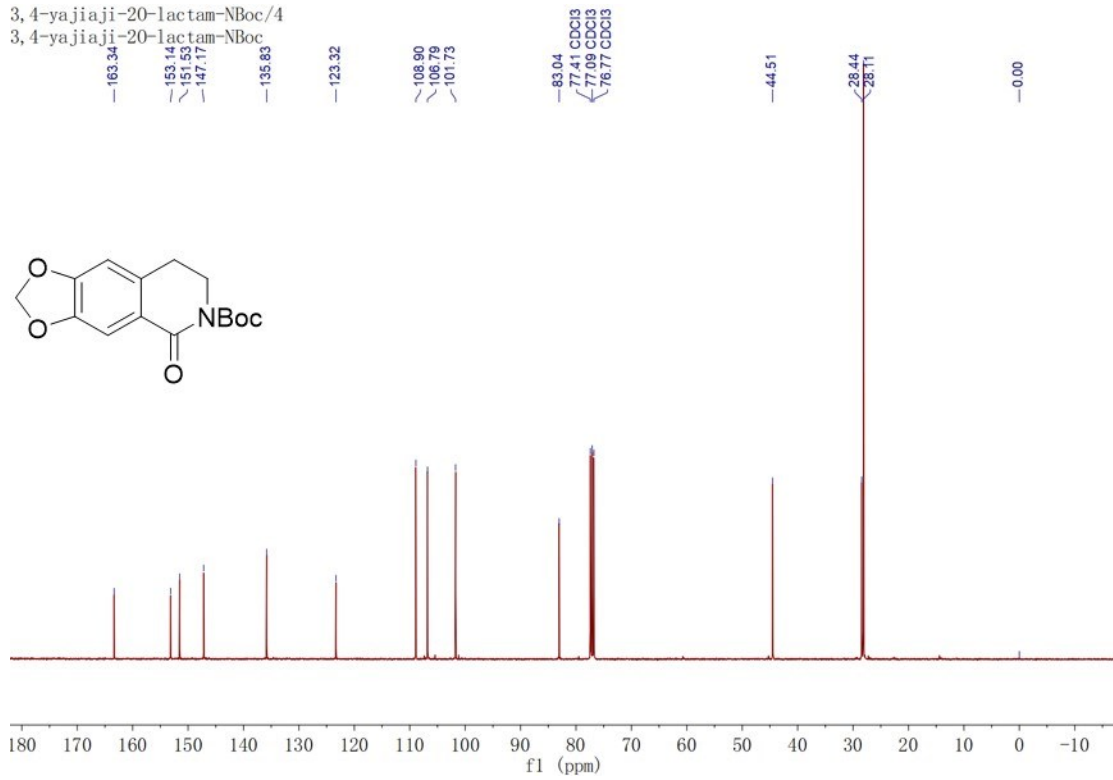
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-0.00

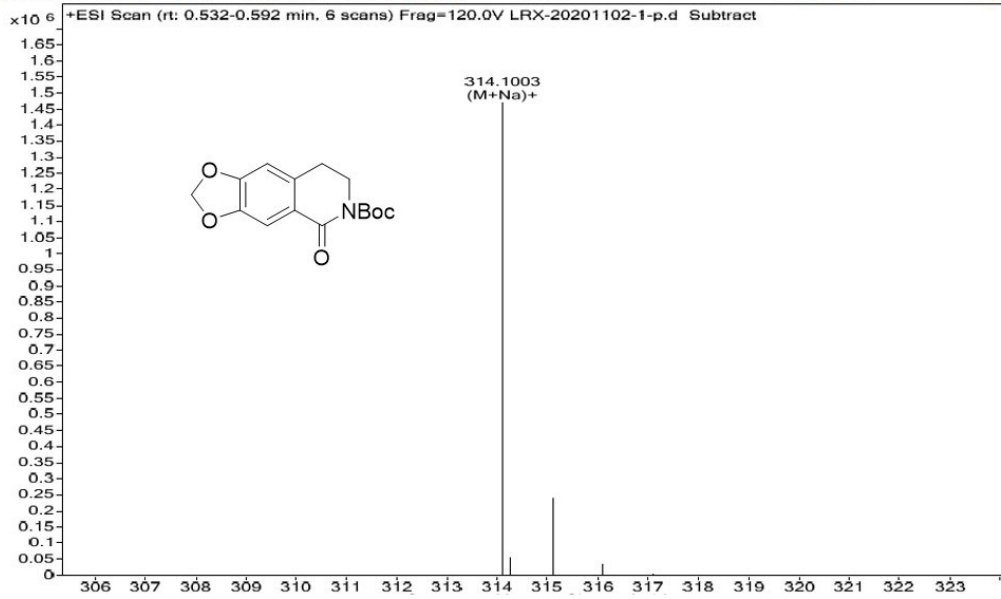


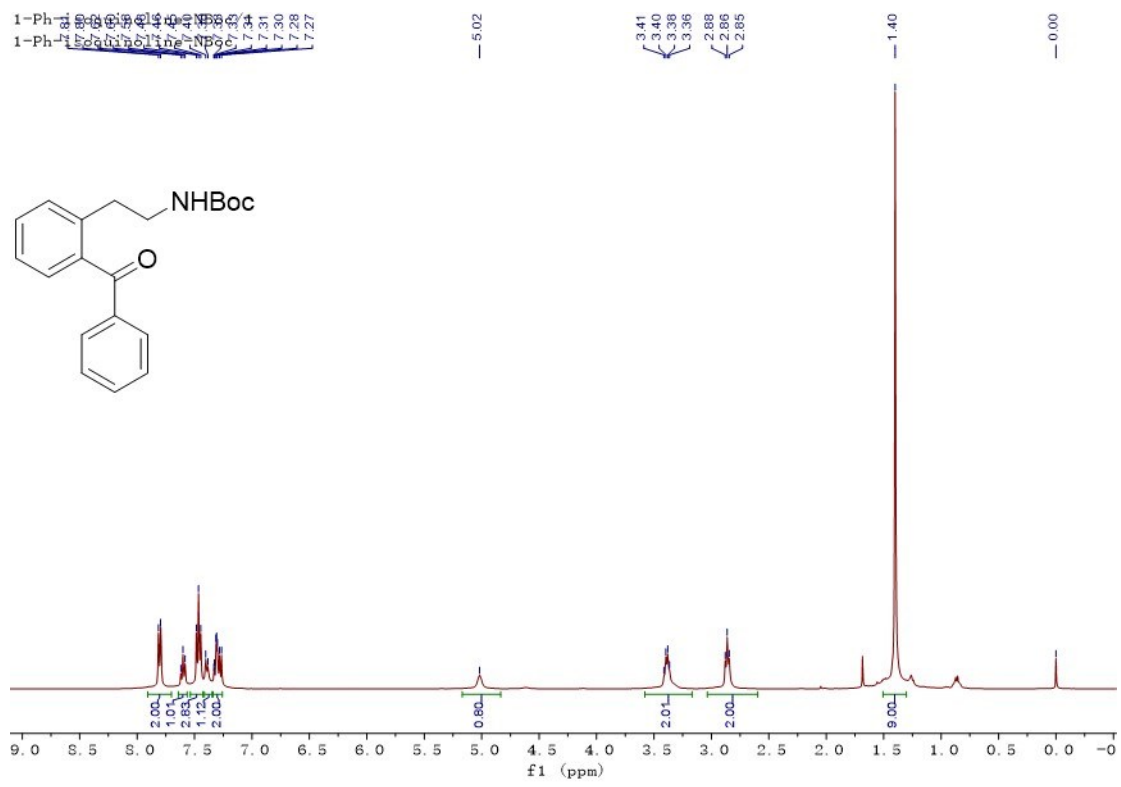
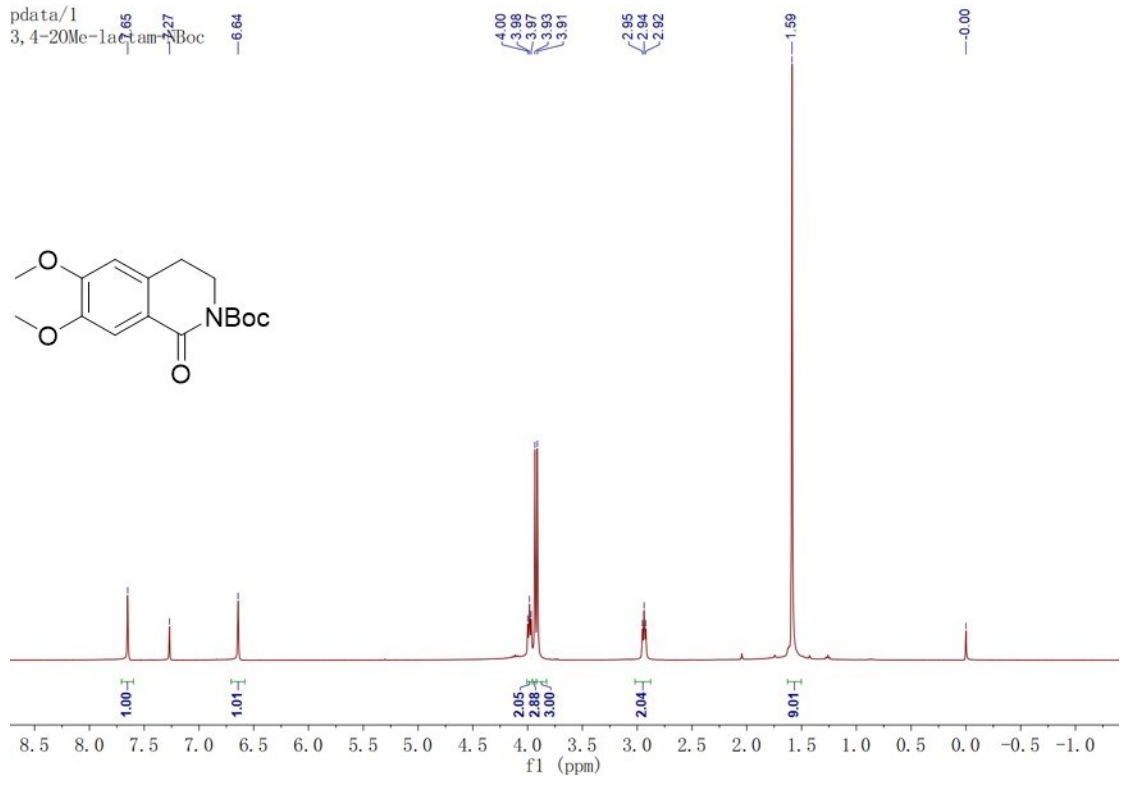


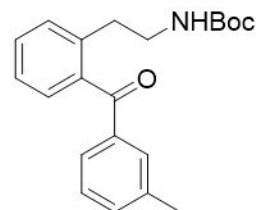
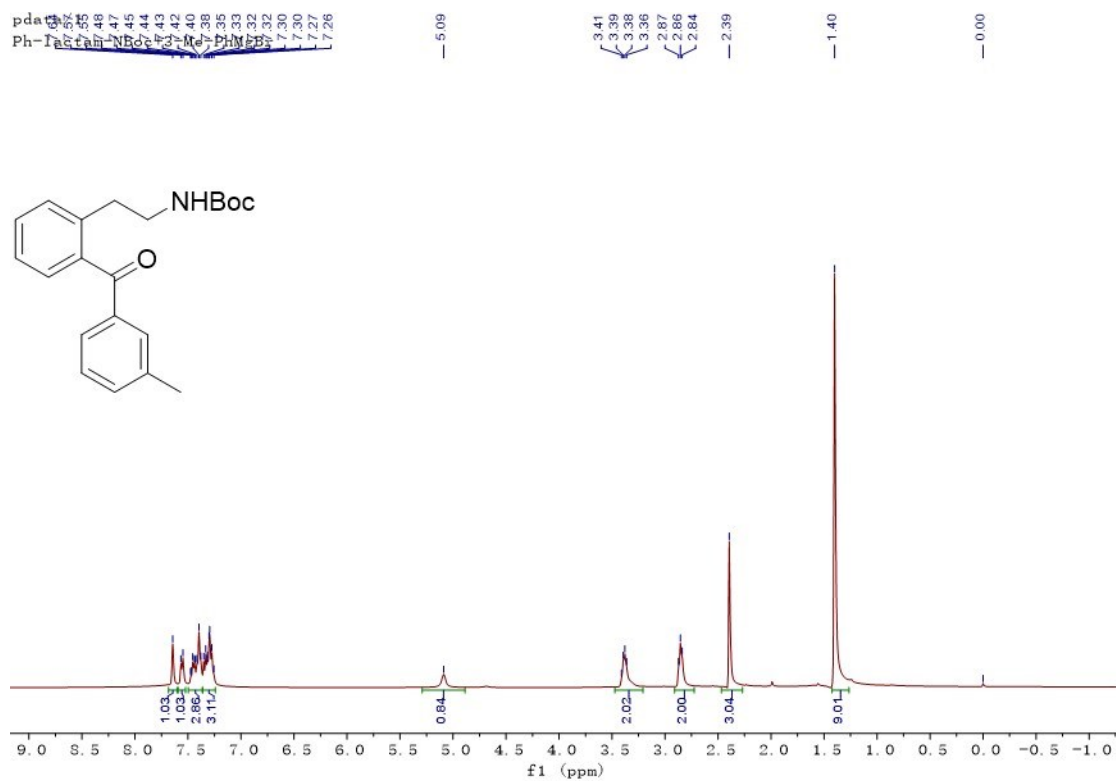
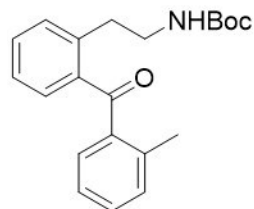
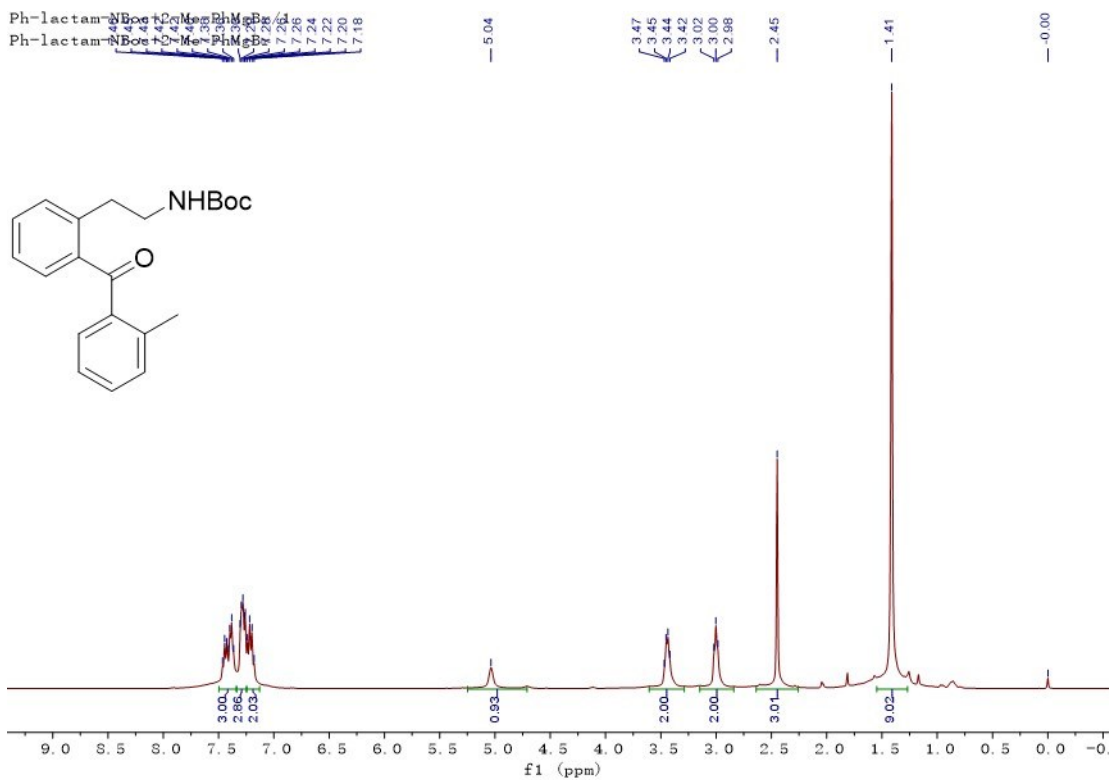
3,4-yajiaji-20-lactam-NBoc/4
 3,4-yajiaji-20-lactam-NBoc

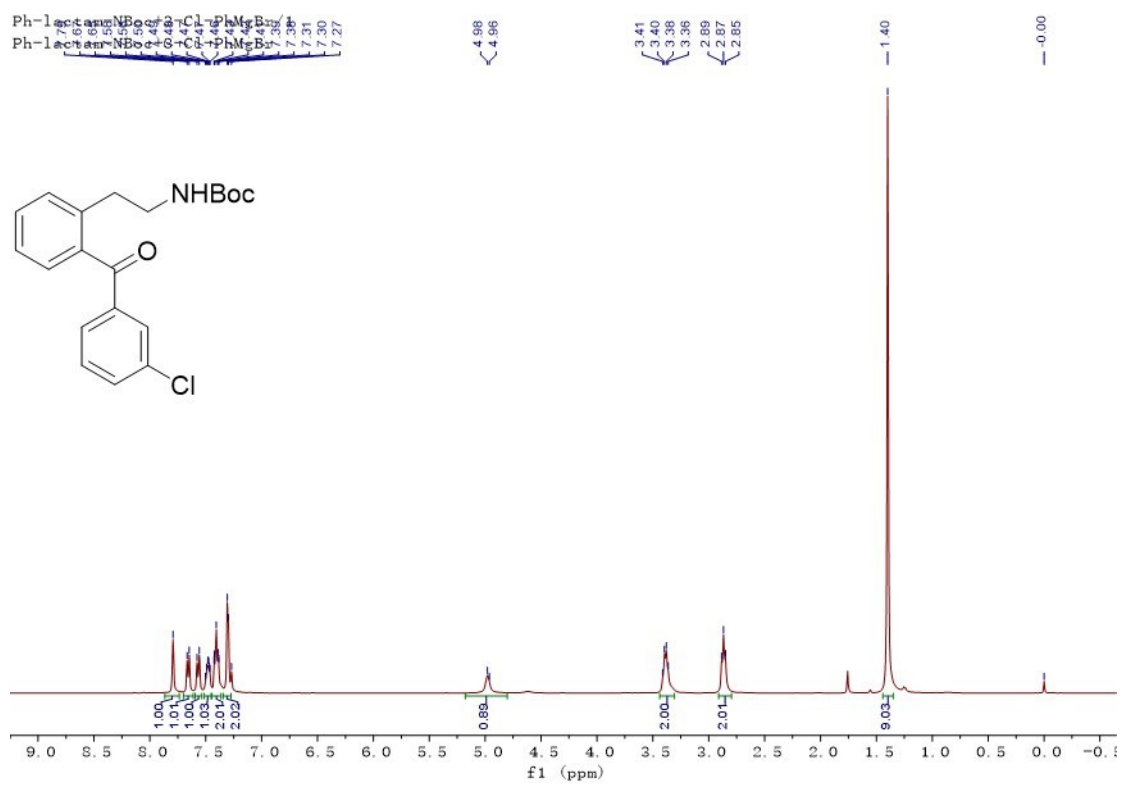
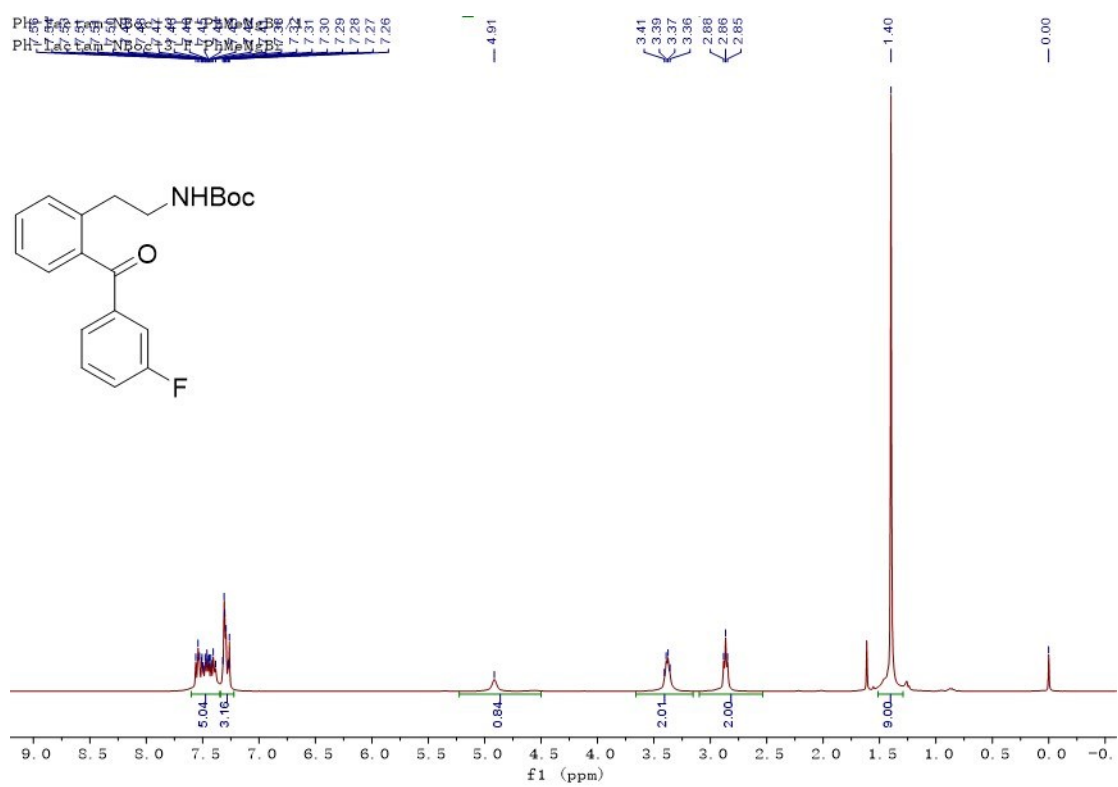


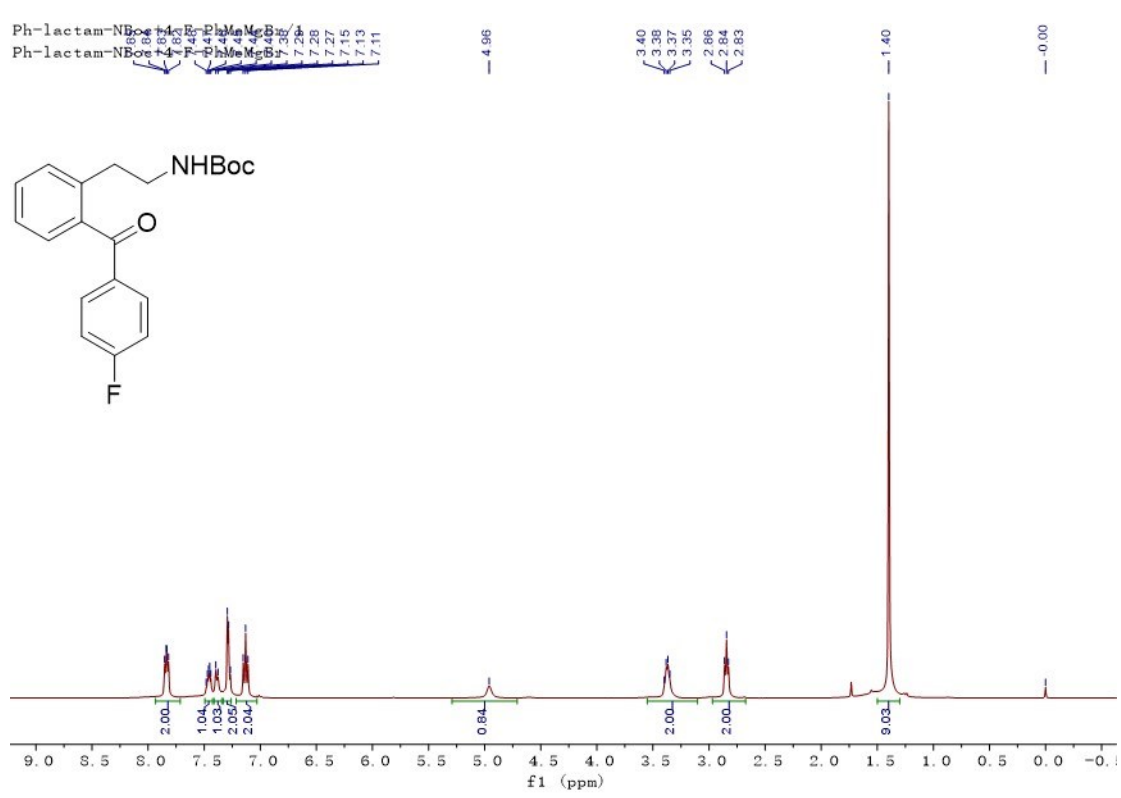
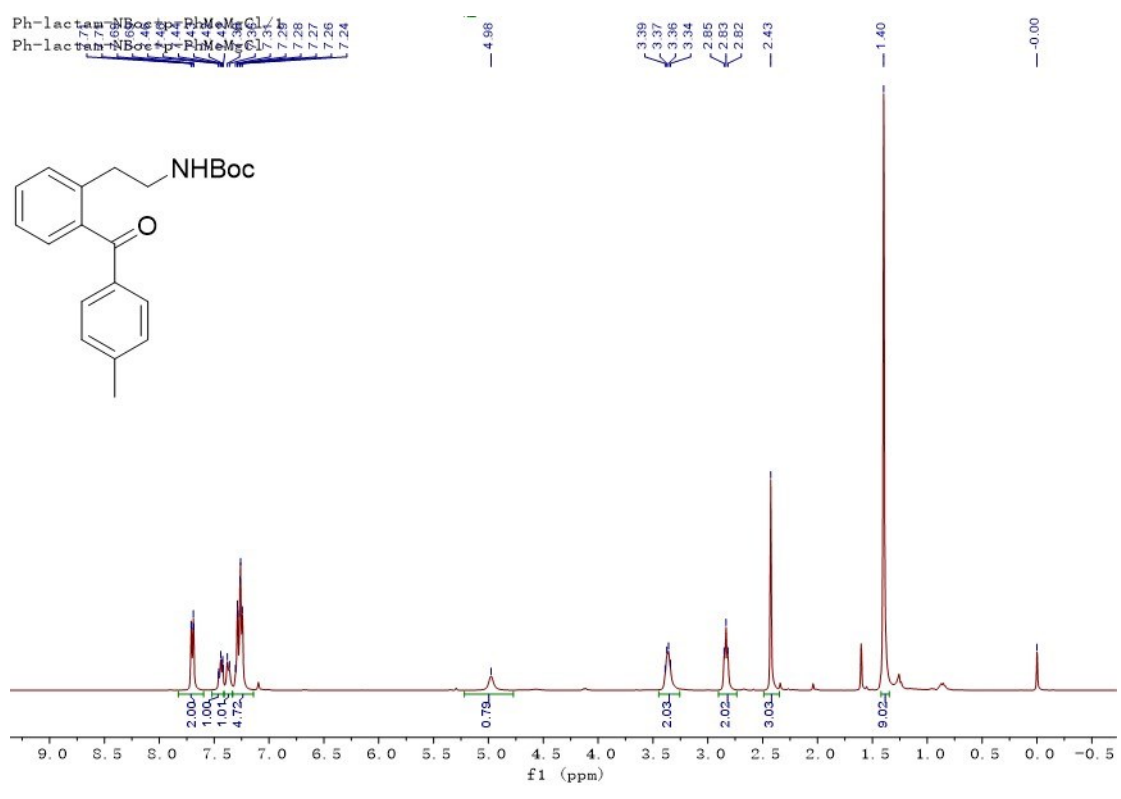
Sample Name	Position	p1C2	Instrument Name	Instrument 1	User Name	G6520B-PC\Admin
Inj Vol	0.1		SampleType	Sample	IRM Calibration Status	Success
Data Filename	LRX-20201102-1-p.d	ACQ Method	20110418-M5only-p.m	Comment	Acquired Time	11/5/2020 1:41:05 PM

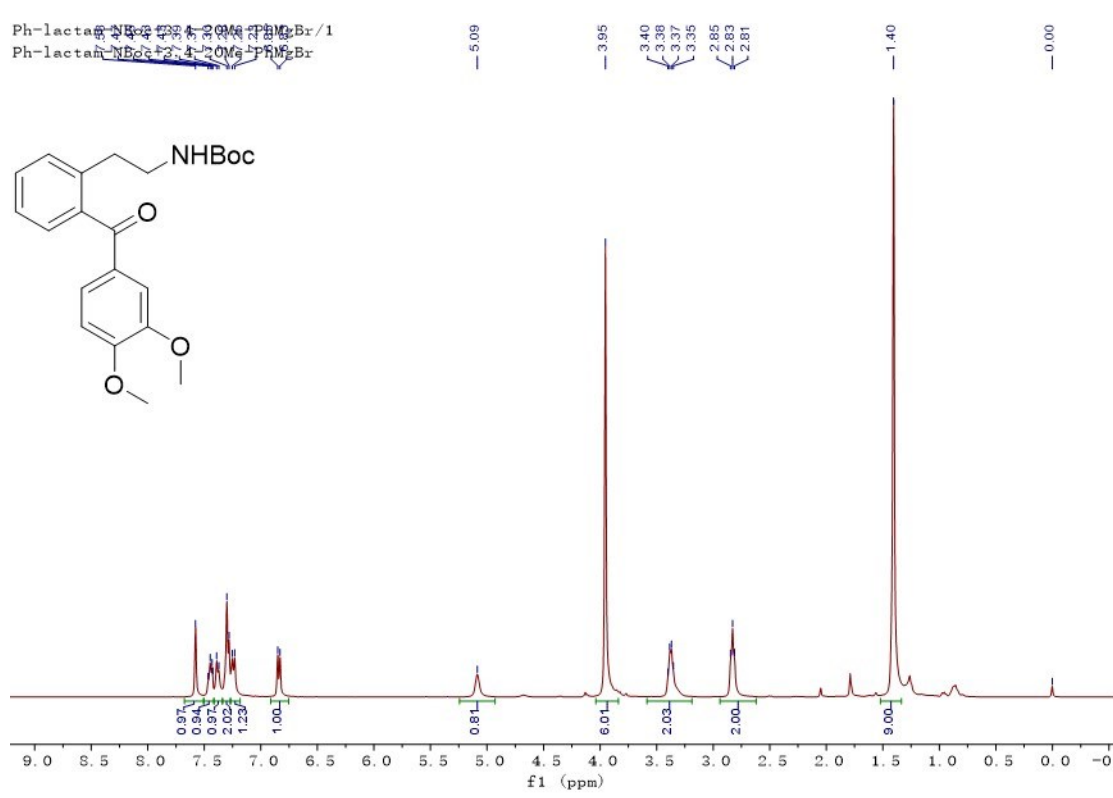
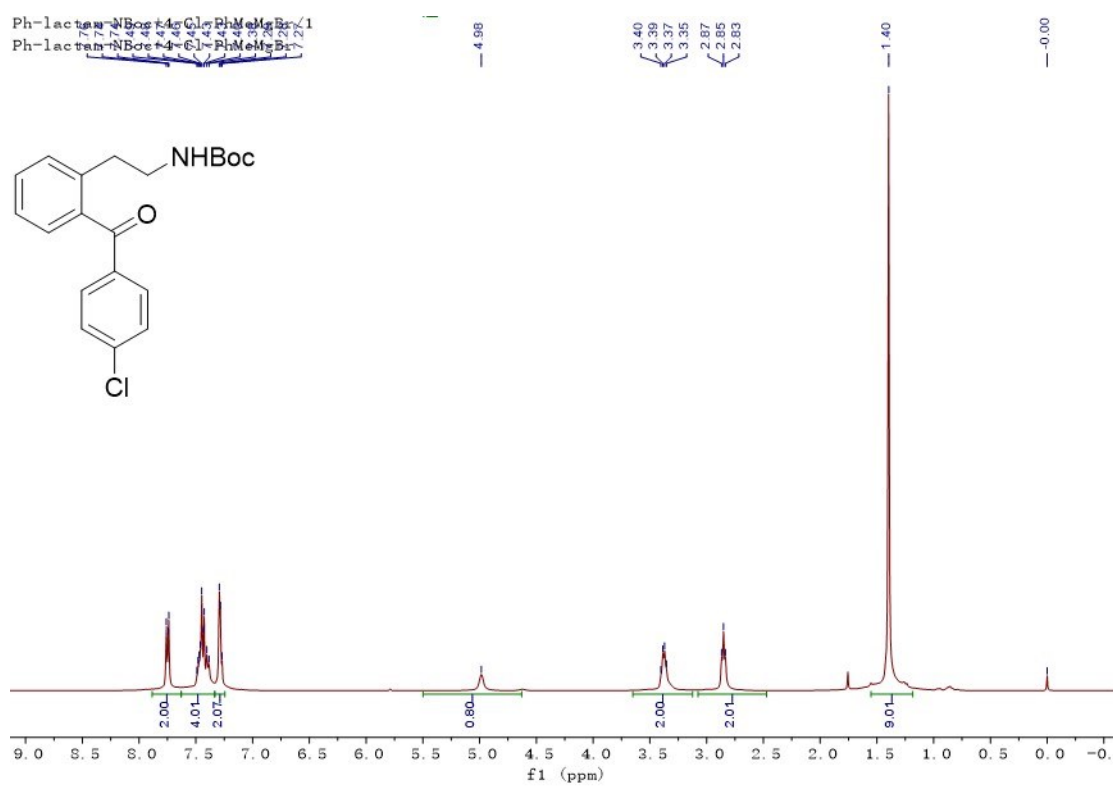


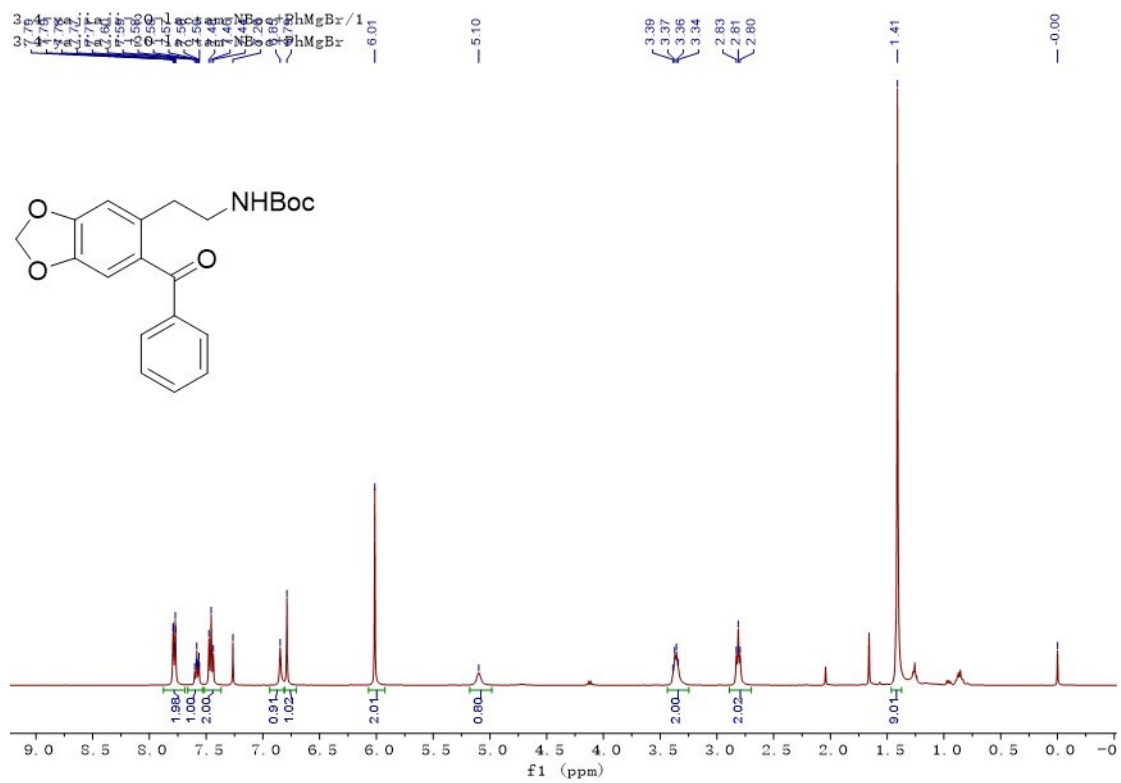
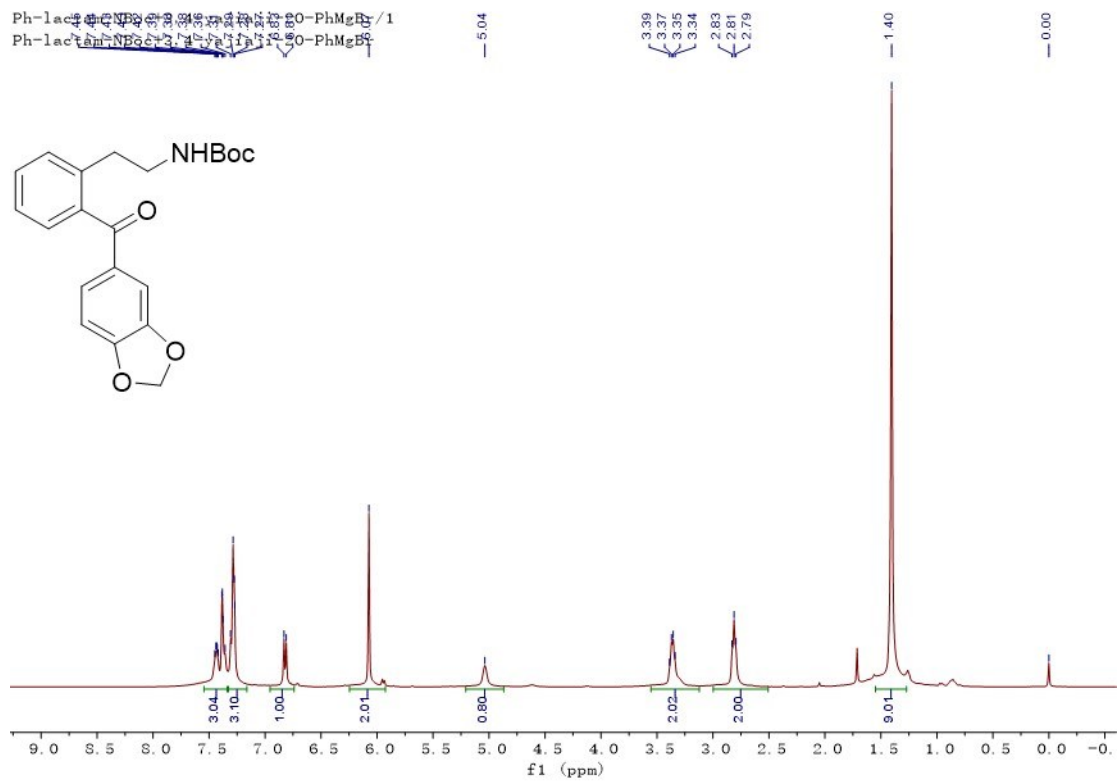


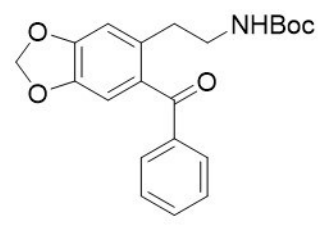
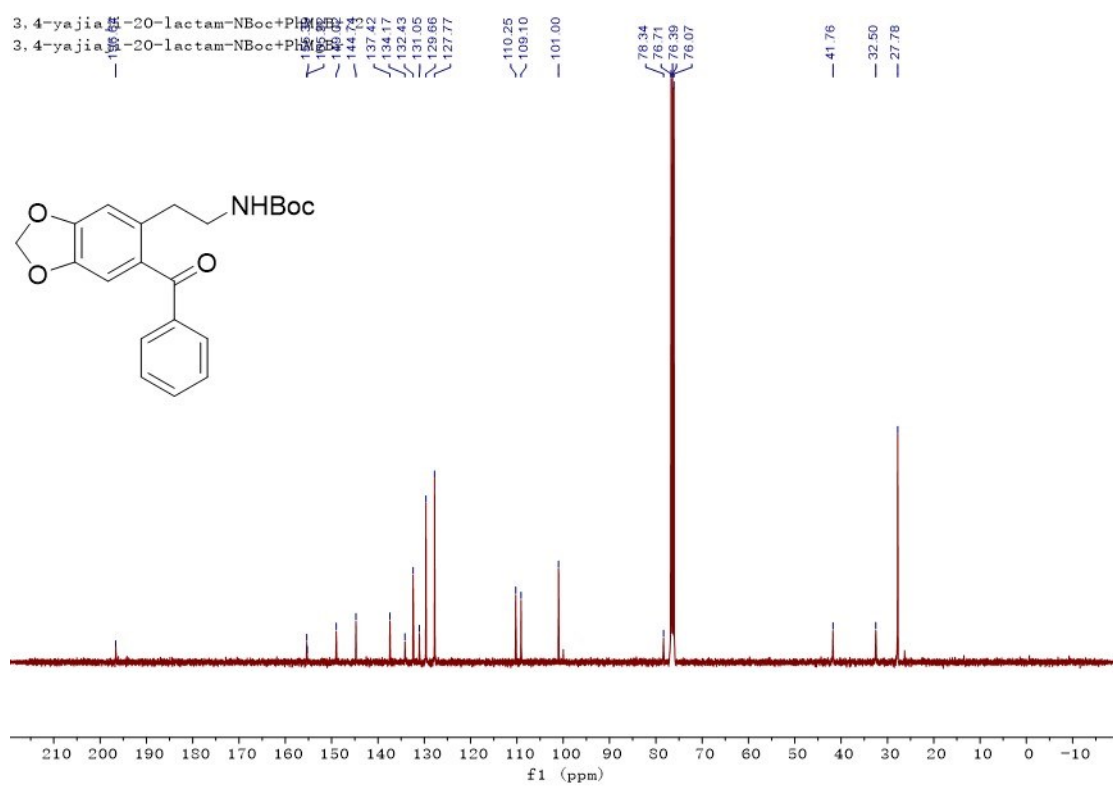




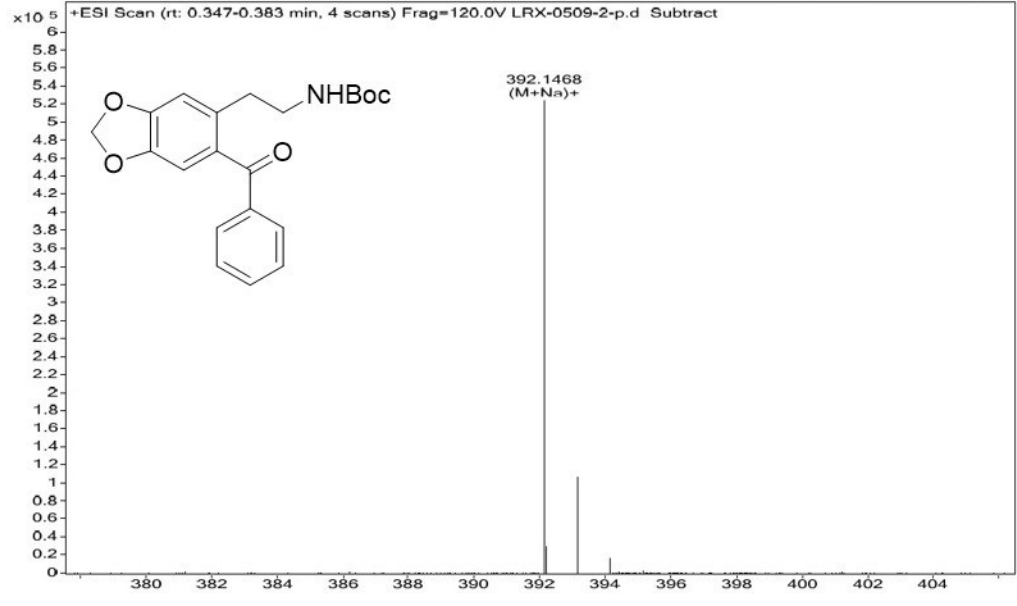


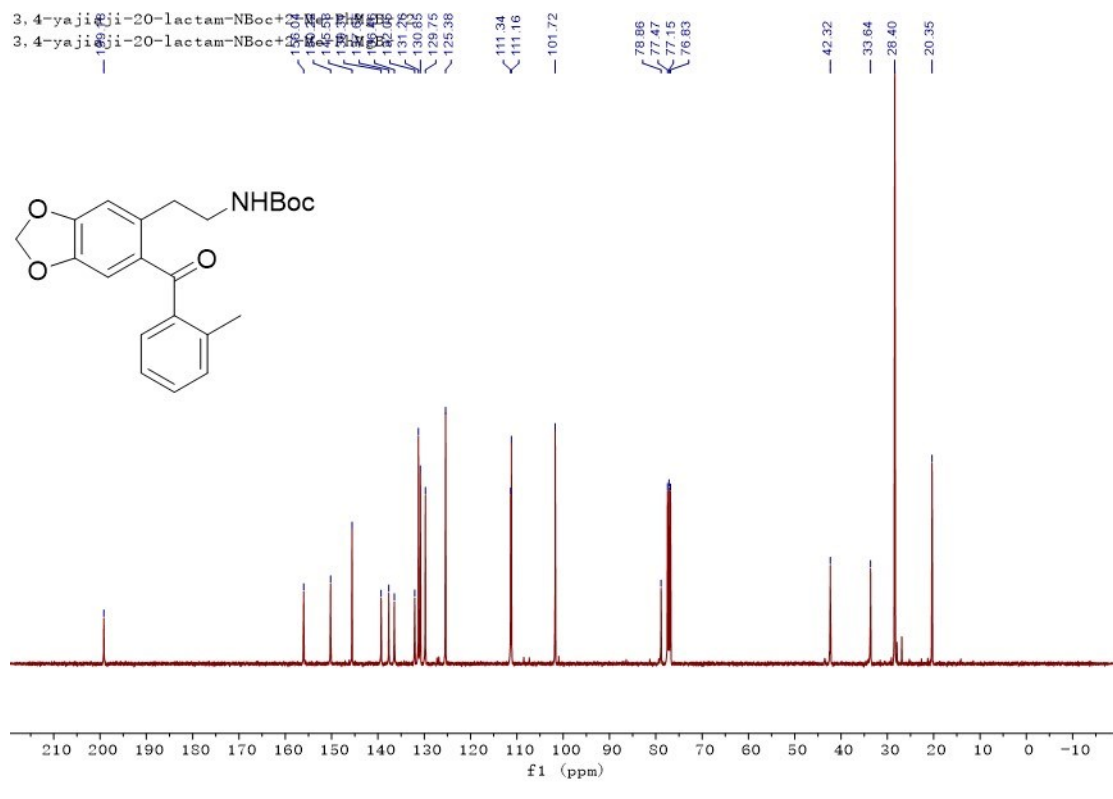
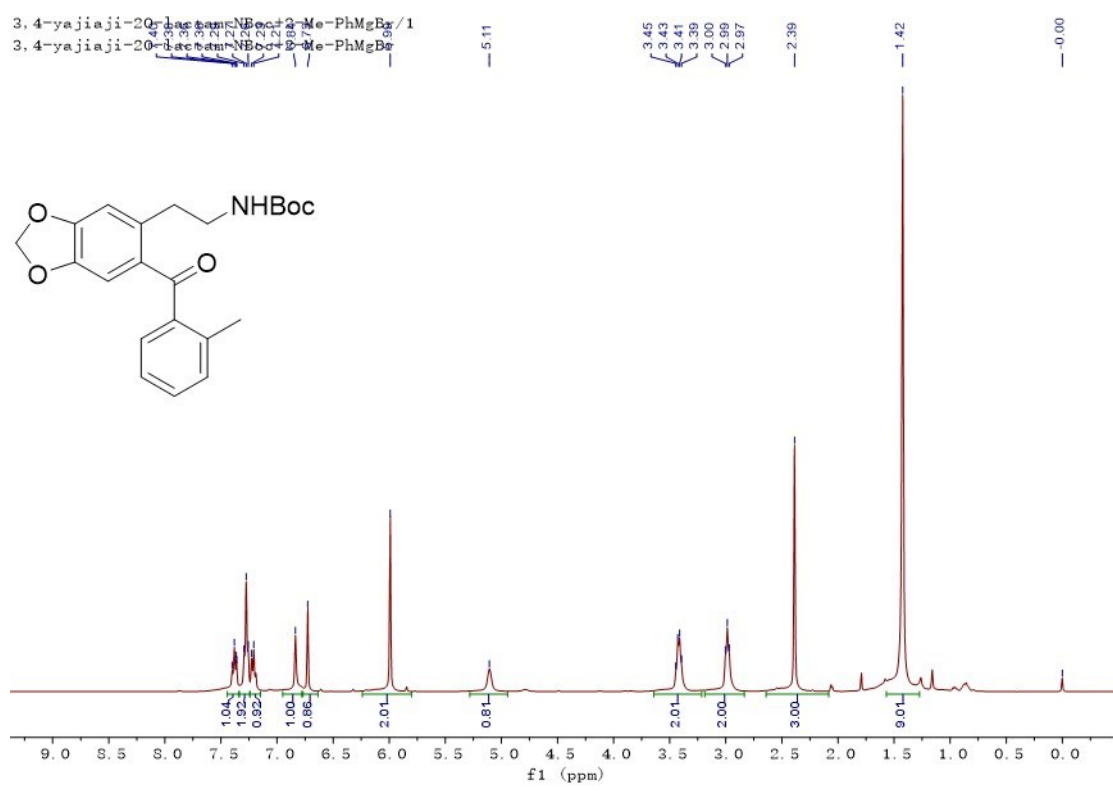




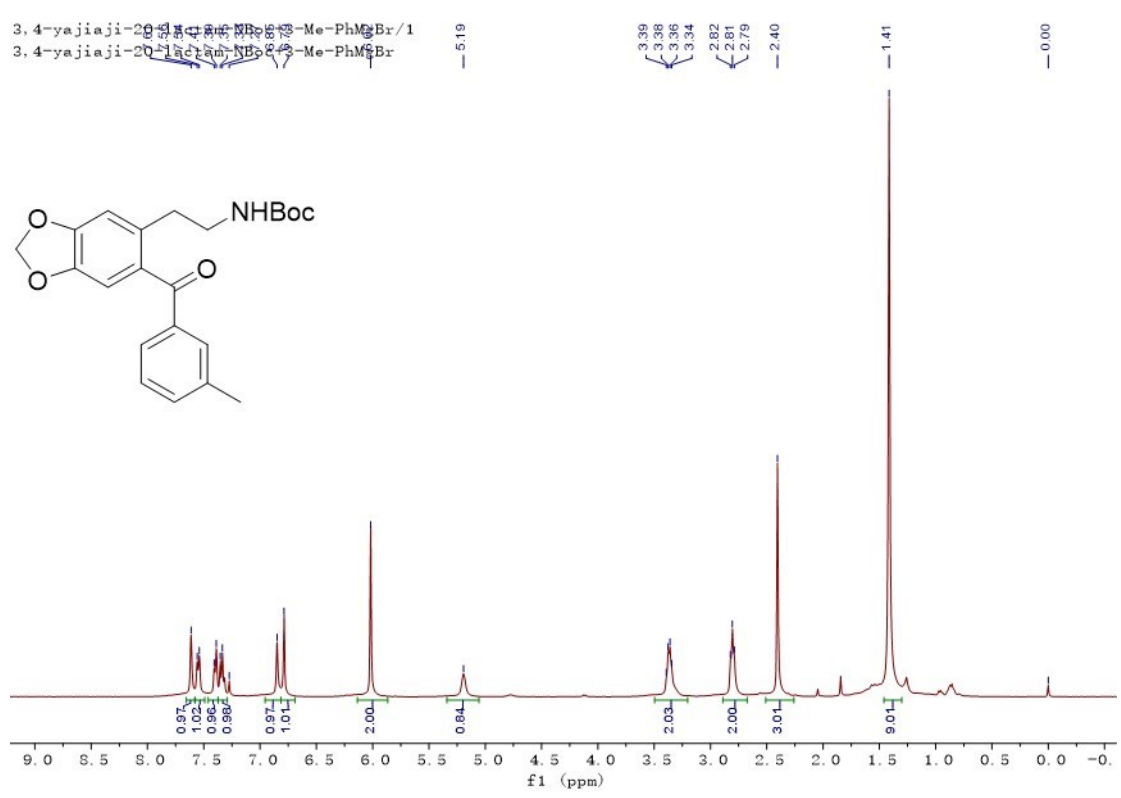
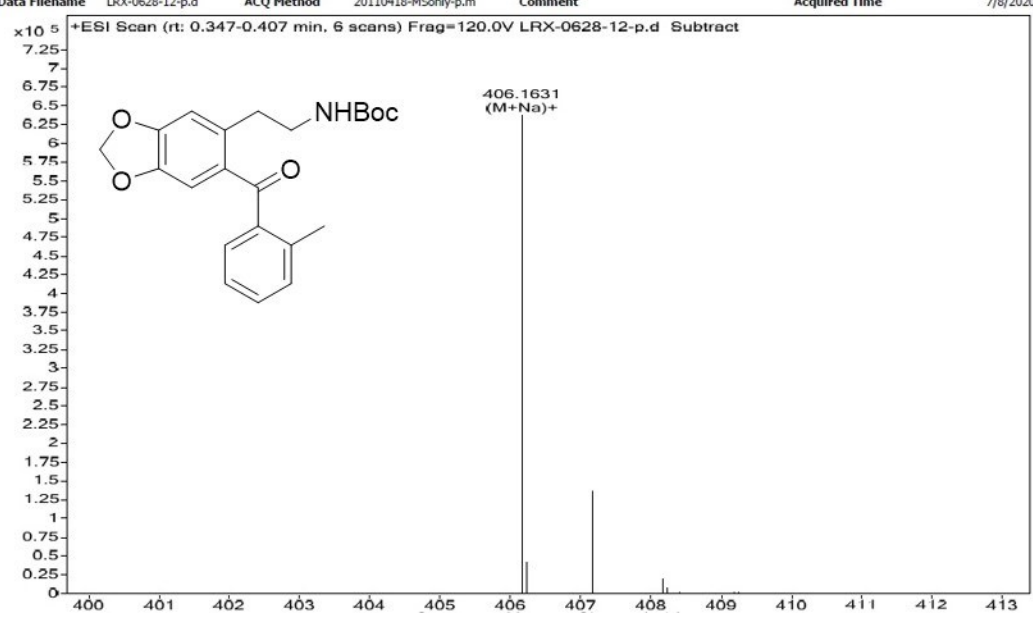


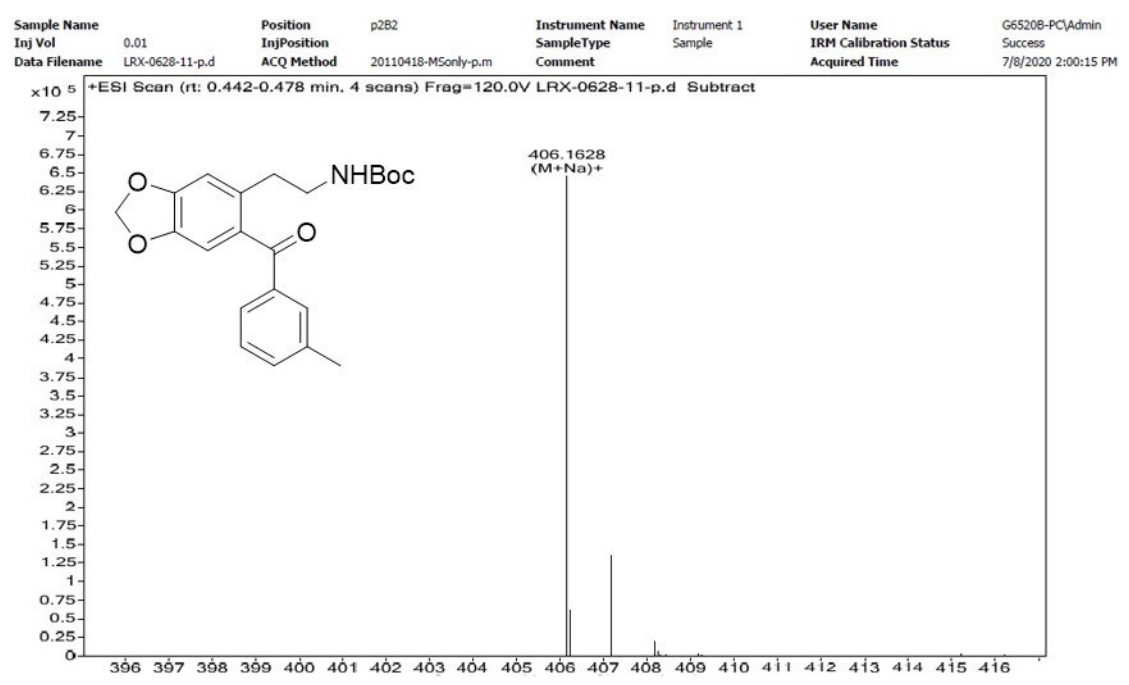
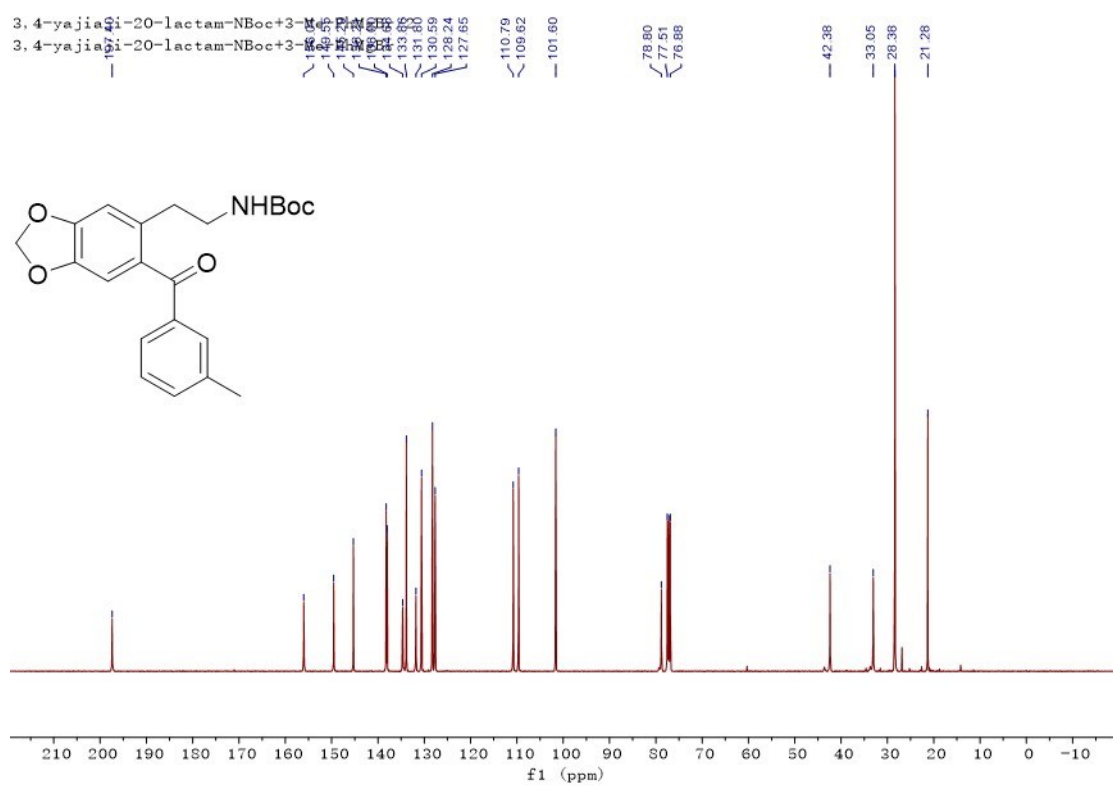
Sample Name	Position	Instrument Name	User Name
0.01	p2C9	Instrument 1	G6520B-PC\Admin
Inj Vol	InjPosition	SampleType	IRM Calibration Status
0.01		Sample	Success
Data Filename	ACQ Method	Comment	Acquired Time
LRX-0509-2-p.d	20110418-MSonly-p.m		5/12/2020 3:36:25 PM



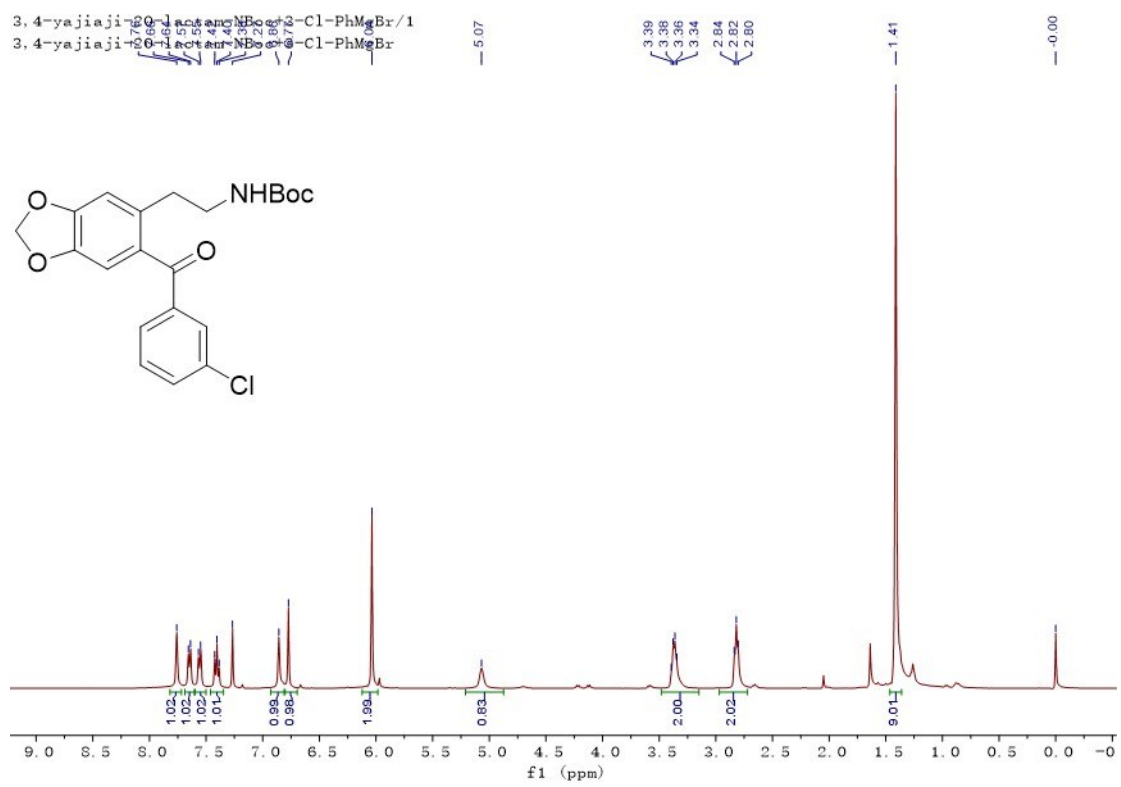
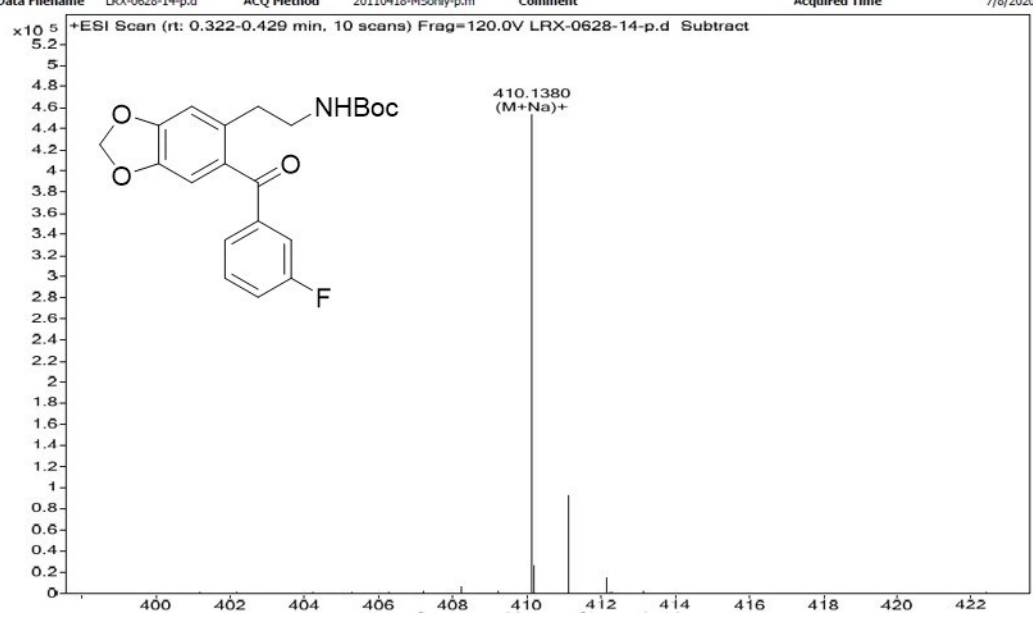


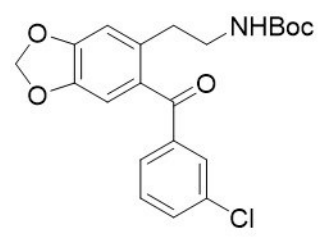
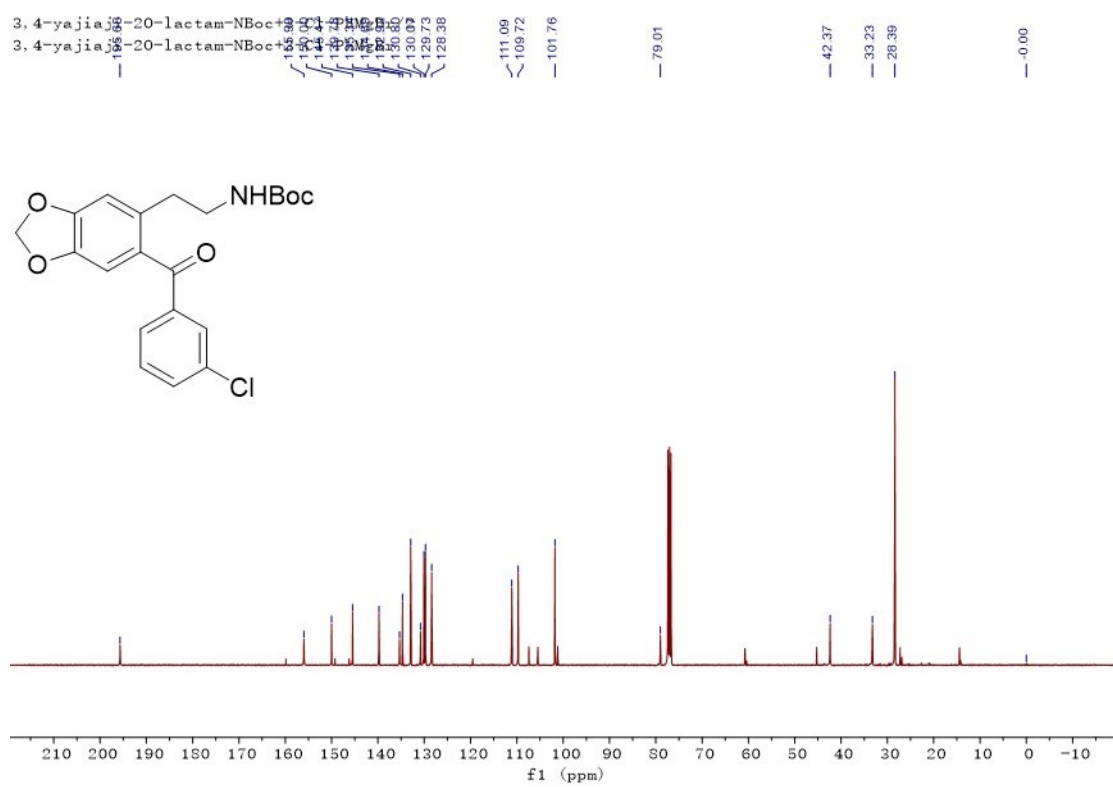
Sample Name	0.01	Position	p283	Instrument Name	Instrument 1	User Name	G65208-PC\Admin
Inj Vol	0.01	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	LRX-0628-12-p.d	ACQ Method	20110418-M5only-p.m	Comment		Acquired Time	7/8/2020 2:02:08 PM



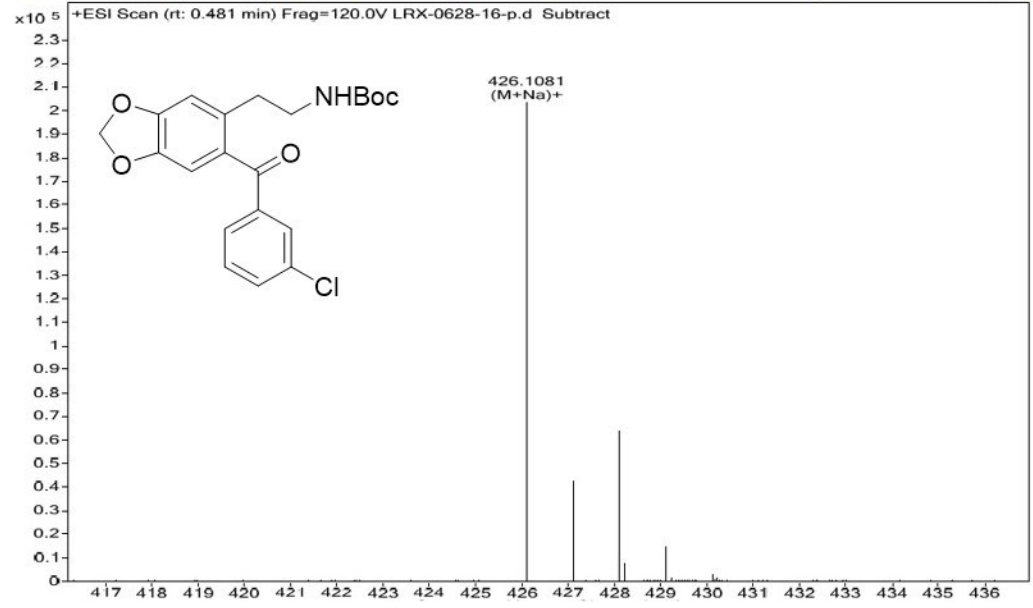


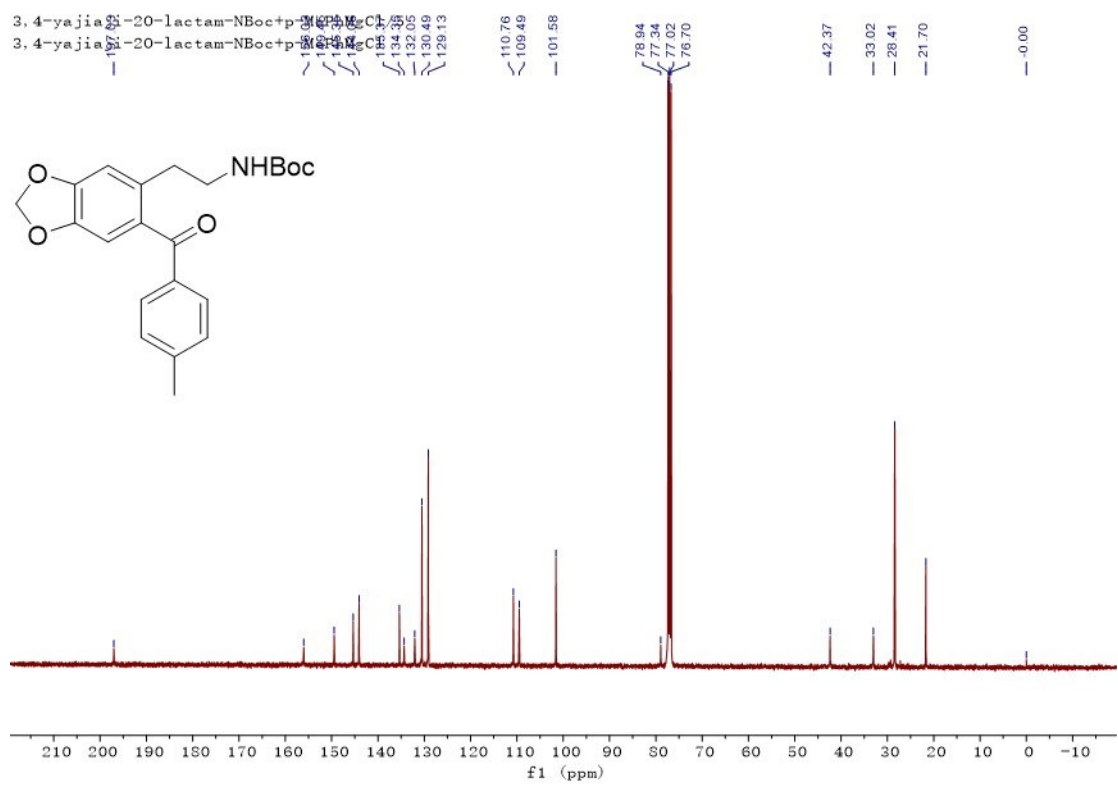
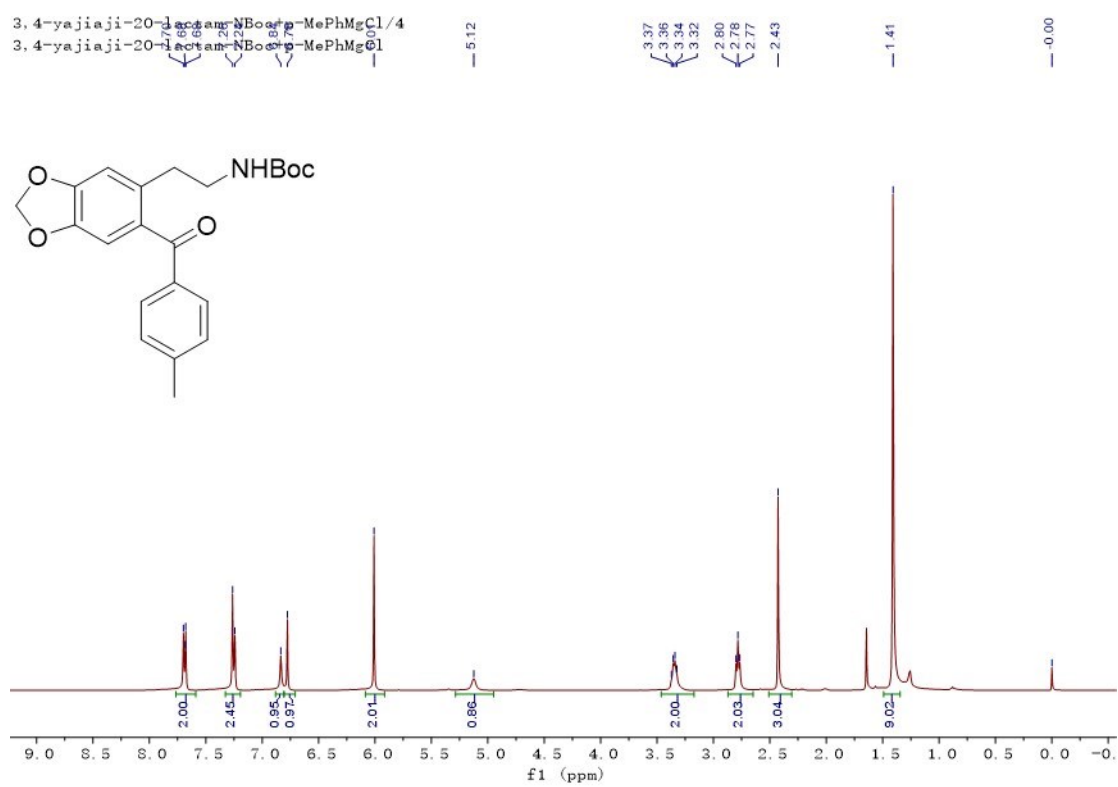
Sample Name	Position	p2B5	Instrument Name	Instrument 1	User Name	G65208-PC\Admin
Inj Vol	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	ACQ Method	20110418-M5only-p.m	Comment		Acquired Time	7/8/2020 2:06:07 PM



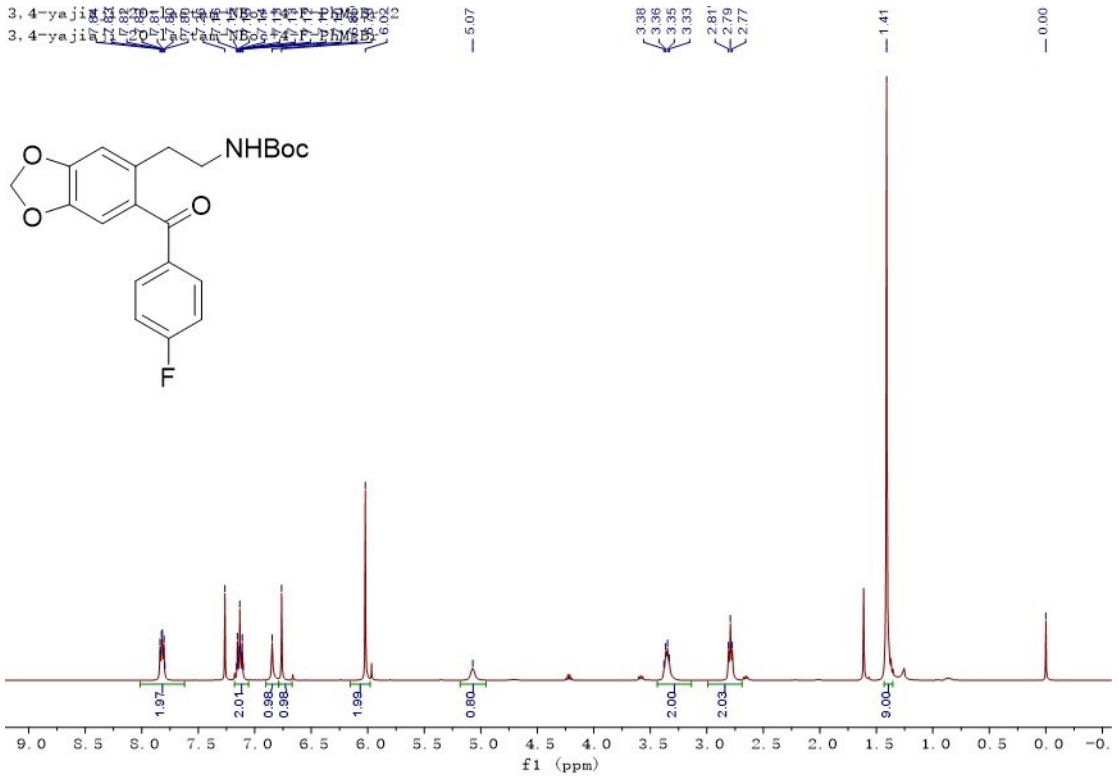
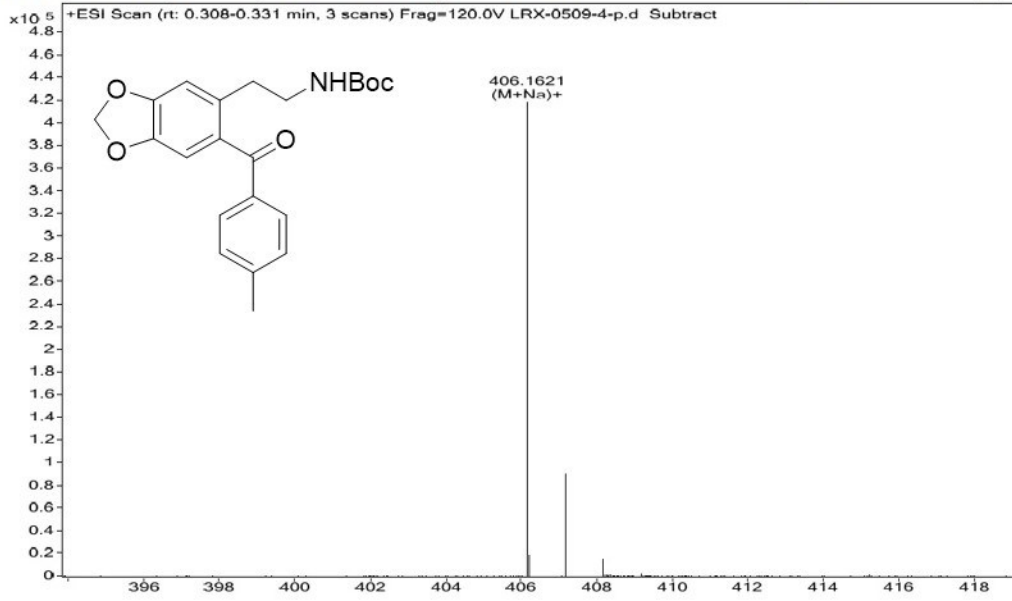


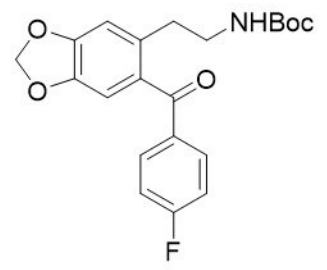
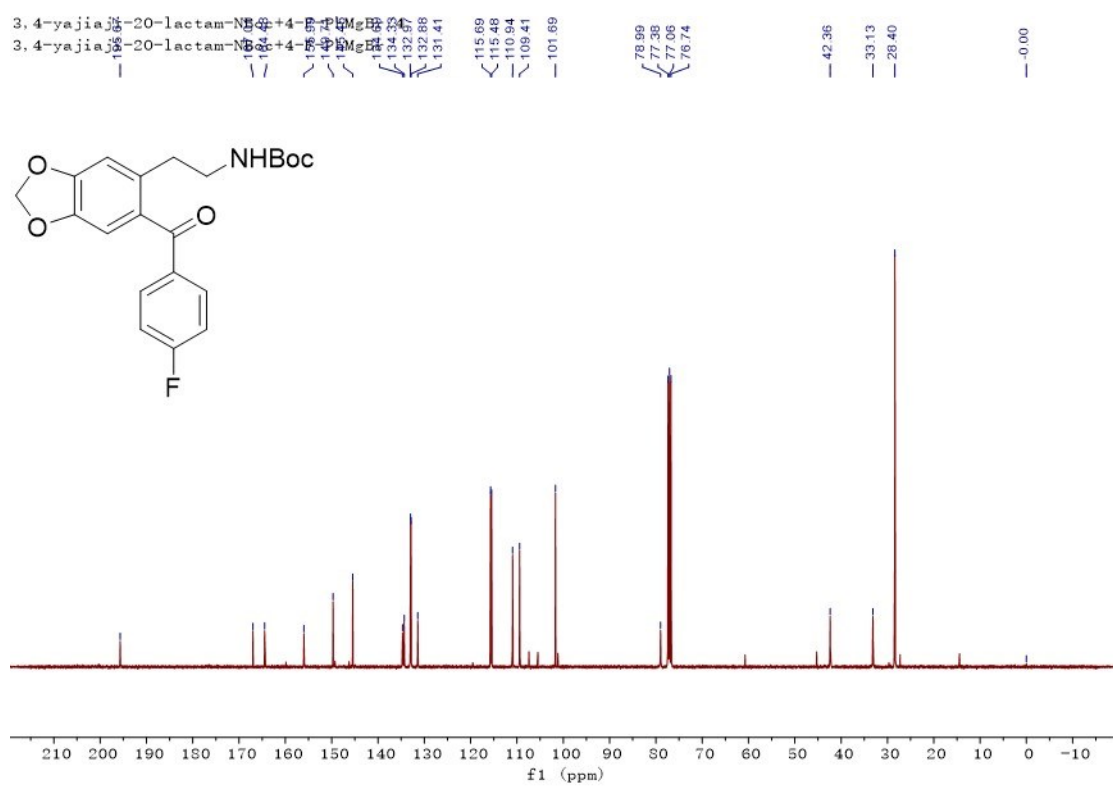
Sample Name	Position	Instrument Name	User Name
LRX-0628-16-p.d	p287	Instrument 1	G65208-PC\Admin
Inj Vol	0.01	Sample	Success
Data Filename	LRX-0628-16-p.d	Comment	7/8/2020 2:09:55 PM



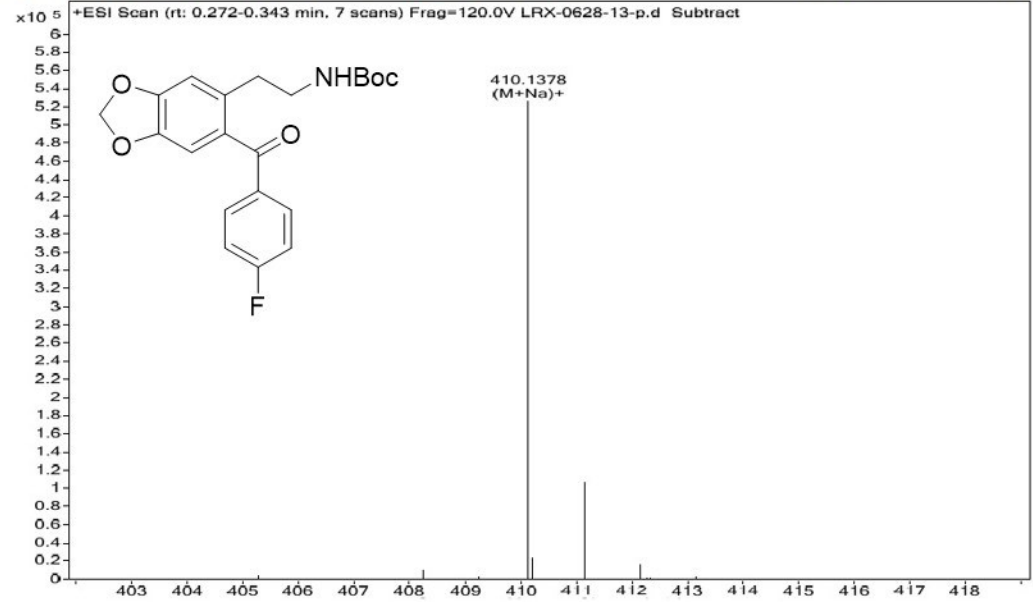


Sample Name	Position	Instrument Name	Instrument 1	User Name	G6520B-PC\Admin
Inj Vol	0.01	p2D2	Sample	IRM Calibration Status	Success
Data Filename	LRX-0509-4-p.d	20110418-MOnly-p.m	Comment	Acquired Time	5/12/2020 3:40:49 PM



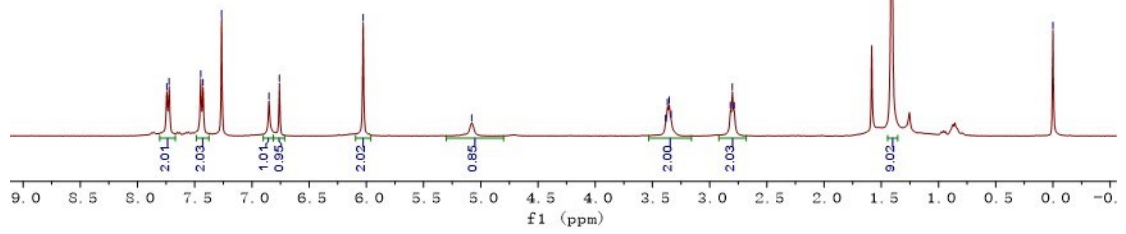
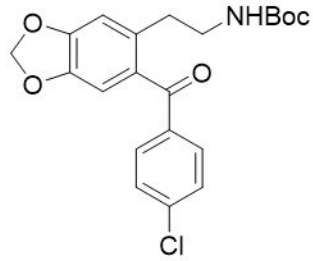


Sample Name	0.01	Position	p2B4	Instrument Name	Instrument 1	User Name	G65208-PC\Admin
Inj Vol		InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	LRX-0628-13-p.d	ACQ Method	20110418-MSonly-p.m	Comment		Acquired Time	7/8/2020 2:04:14 PM



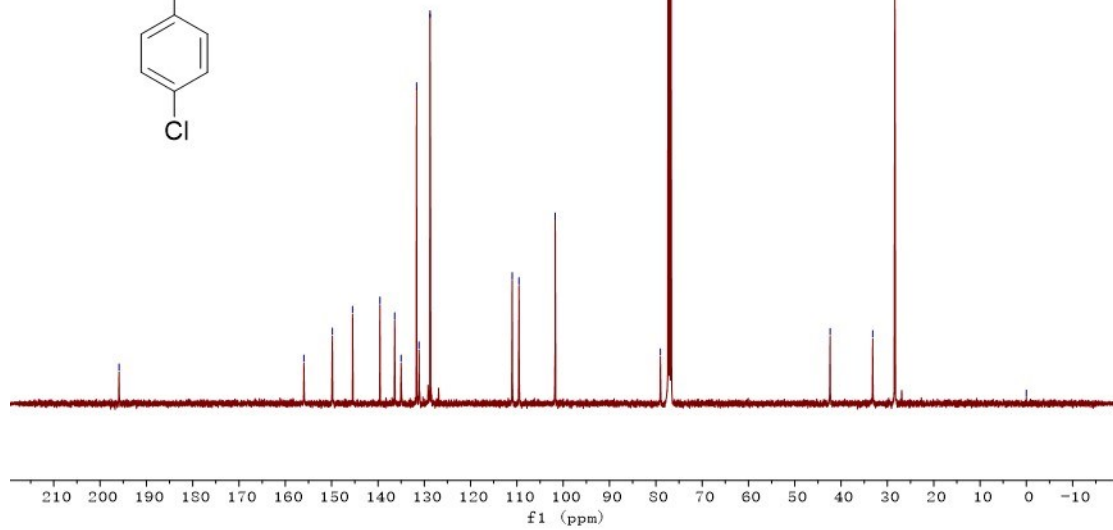
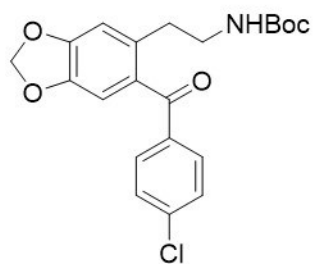
3,4-yajiaji-20-lactam-NBoc+4-Cl-PhMeBr/1
 3,4-yajiaji-20-lactam-NBoc+4-Cl-PhMeBr

5.08 3.39 3.37 3.35 3.34 2.82 2.80 2.78 1.41 0.00

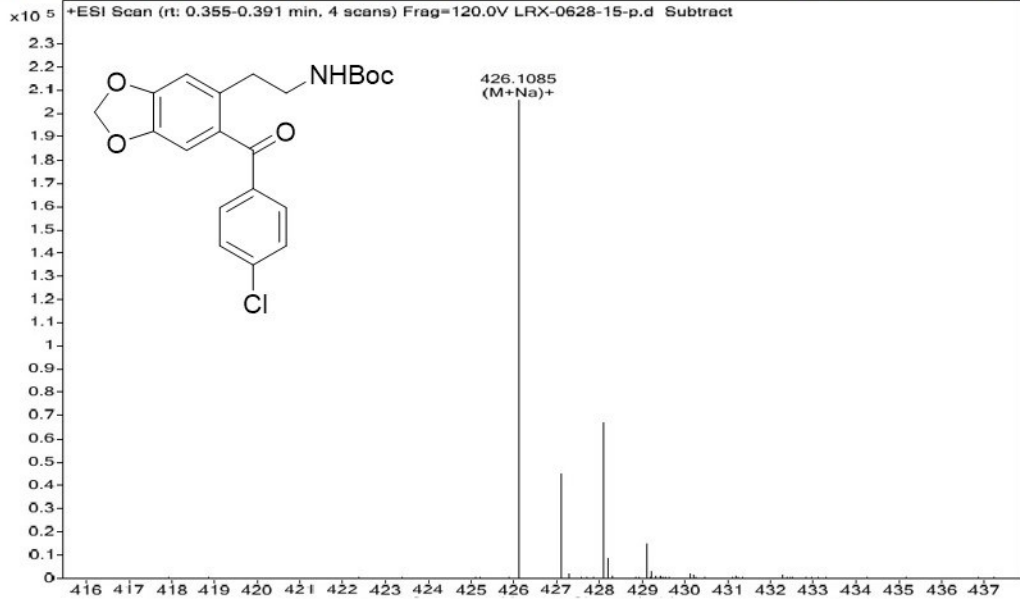


3,4-yajiaji-20-lactam-NBoc+4-Cl-PhMeBr/1
 3,4-yajiaji-20-lactam-NBoc+4-Cl-PhMeBr

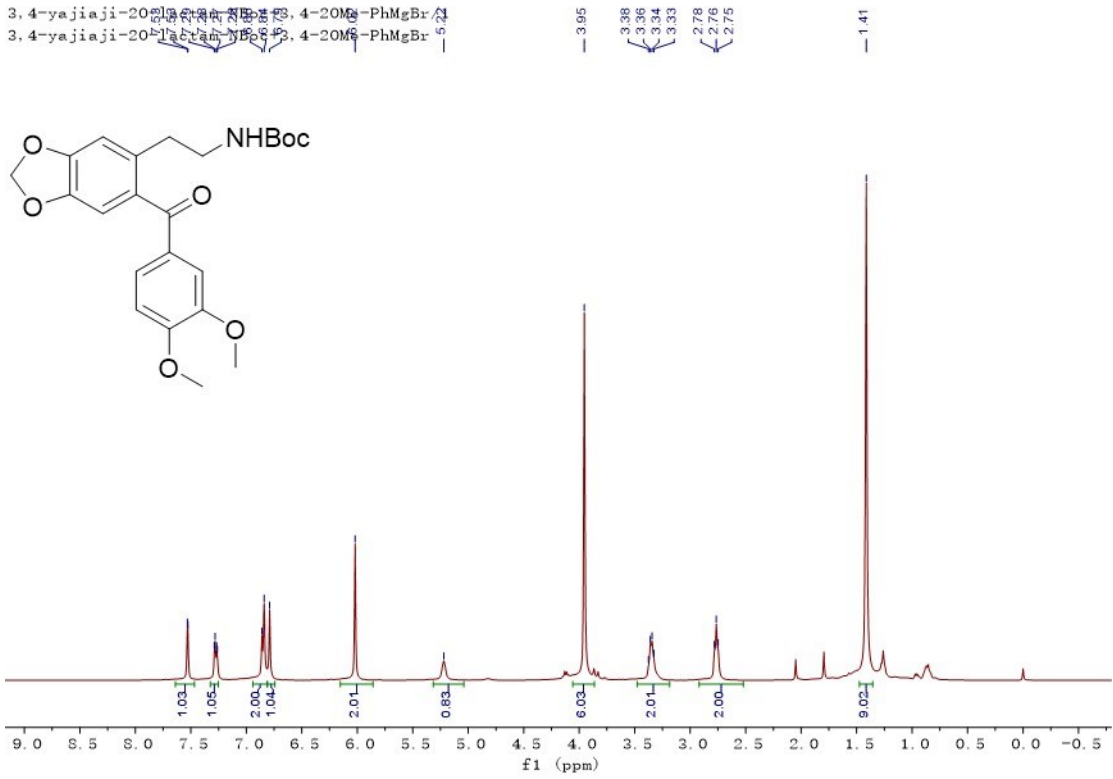
198.33 164.47 151.86 144.84 144.77 131.13 128.76 111.02 109.54 101.73 79.02 77.38 77.04 76.72 42.37 33.17 28.40 0.00

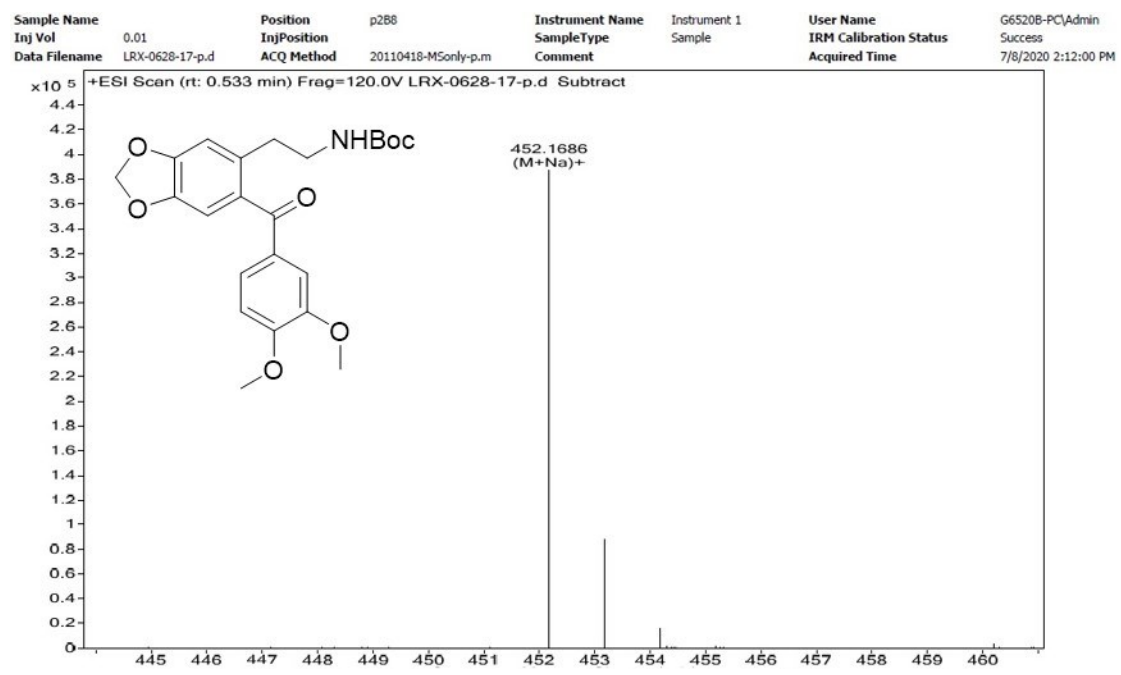
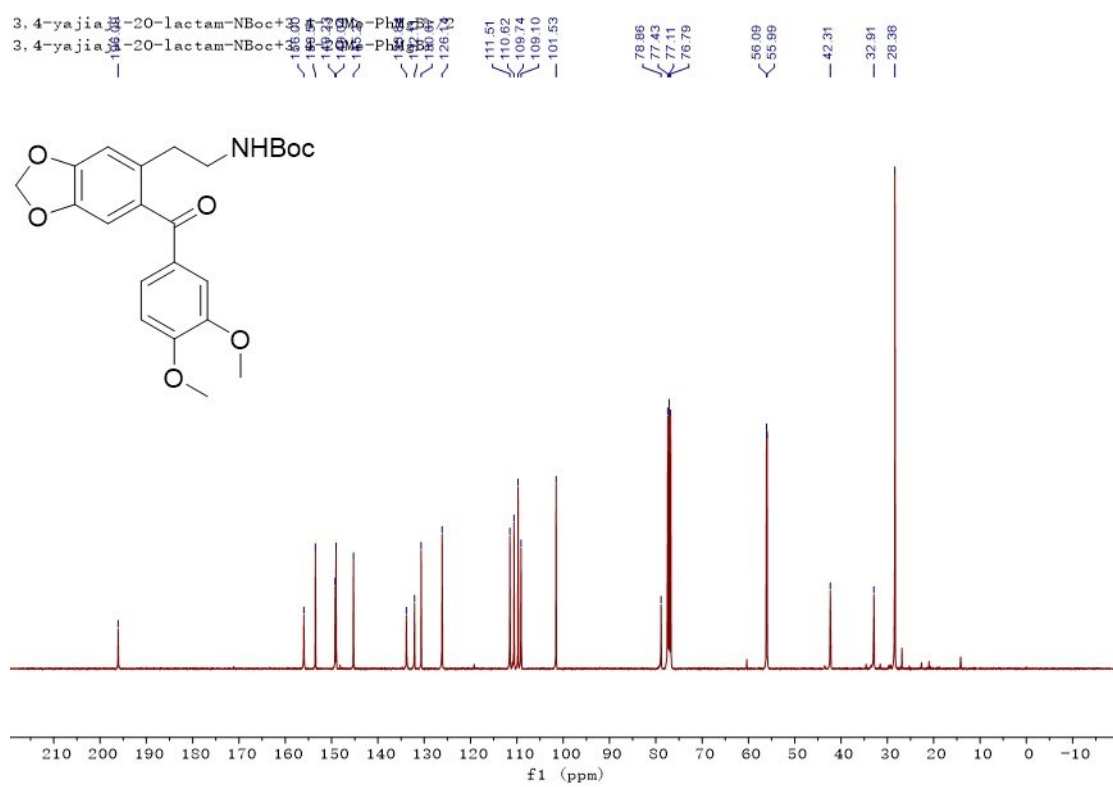


Sample Name	Position	p2B6	Instrument Name	Instrument 1	User Name	G6520B-PC\Admin
Inj Vol	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	ACQ Method	20110418-M5only-p.m	Comment		Acquired Time	7/8/2020 2:08:03 PM

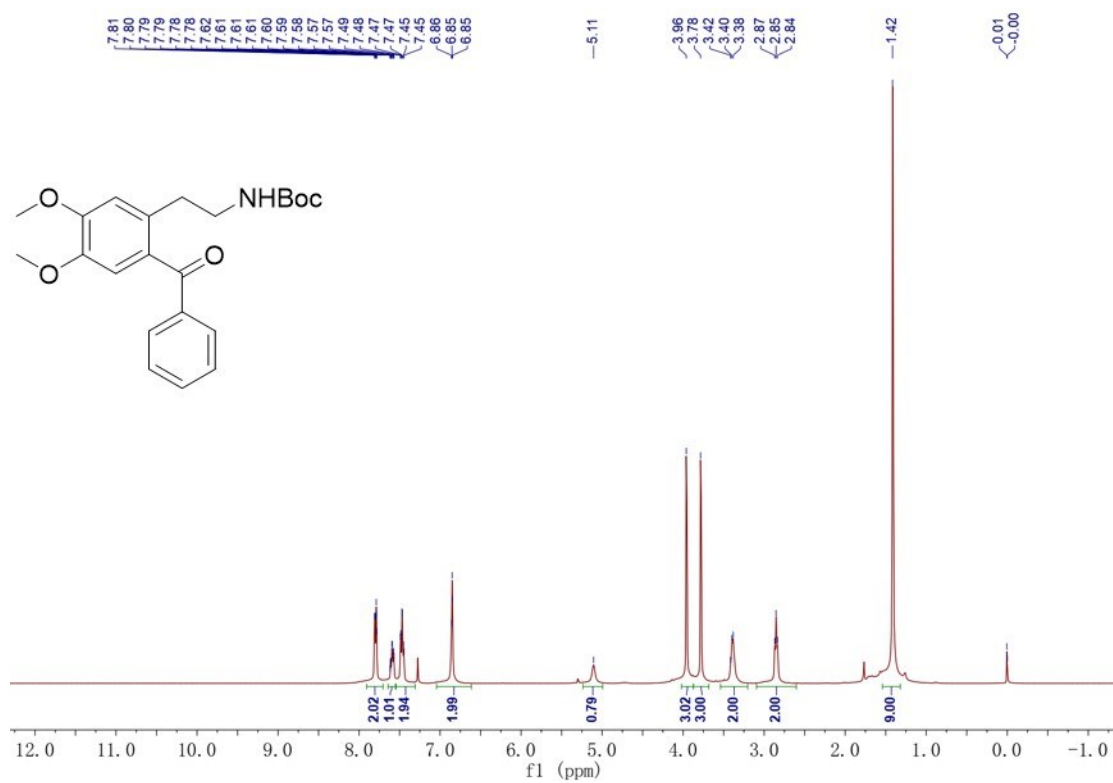
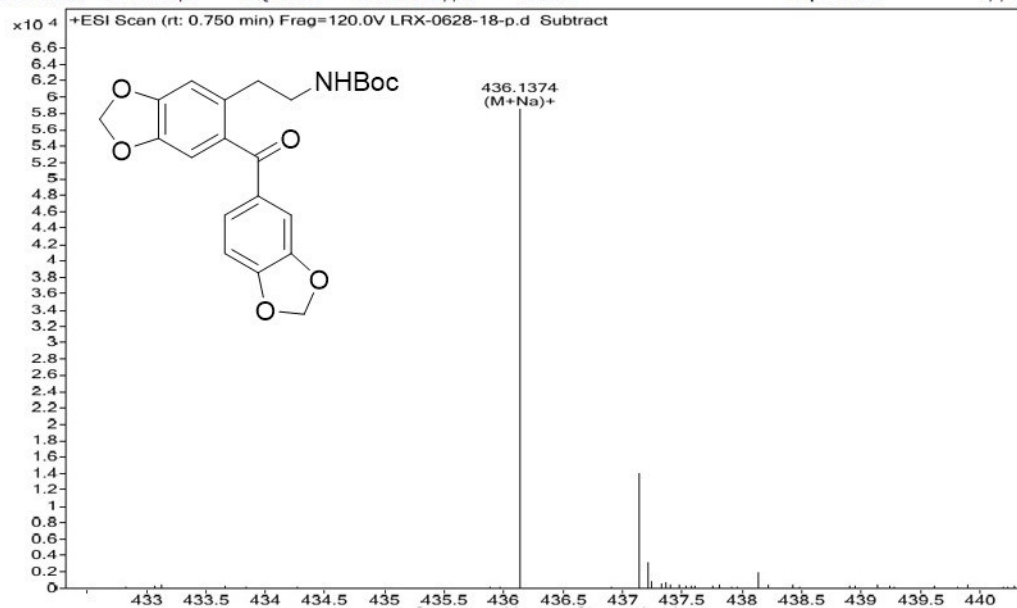


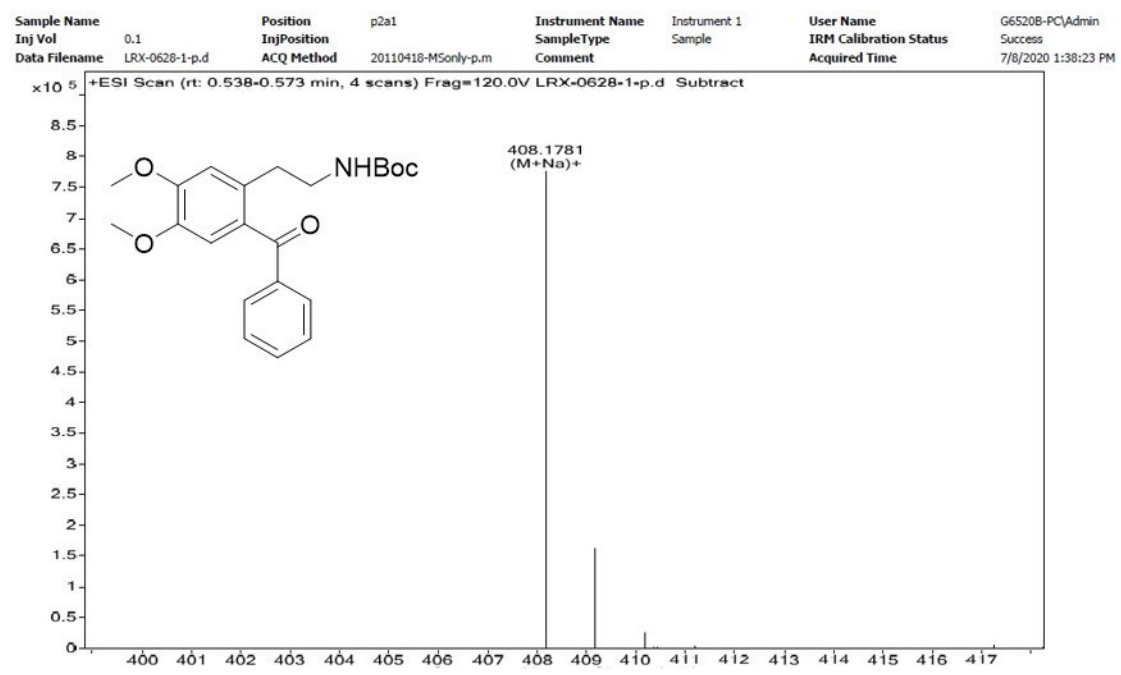
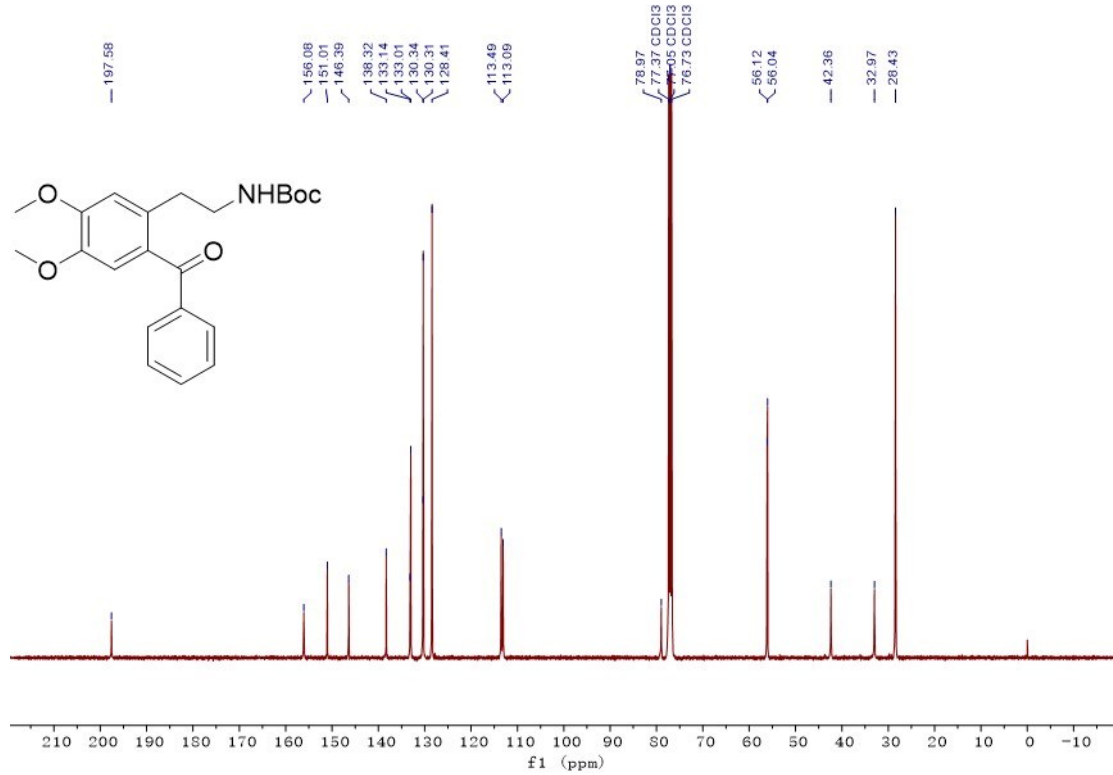
3,4-yajiaji-20201008-181818-3,4-2OMe-PhMgBr
 3,4-yajiaji-20201008-181818-3,4-2OMe-PhMgBr

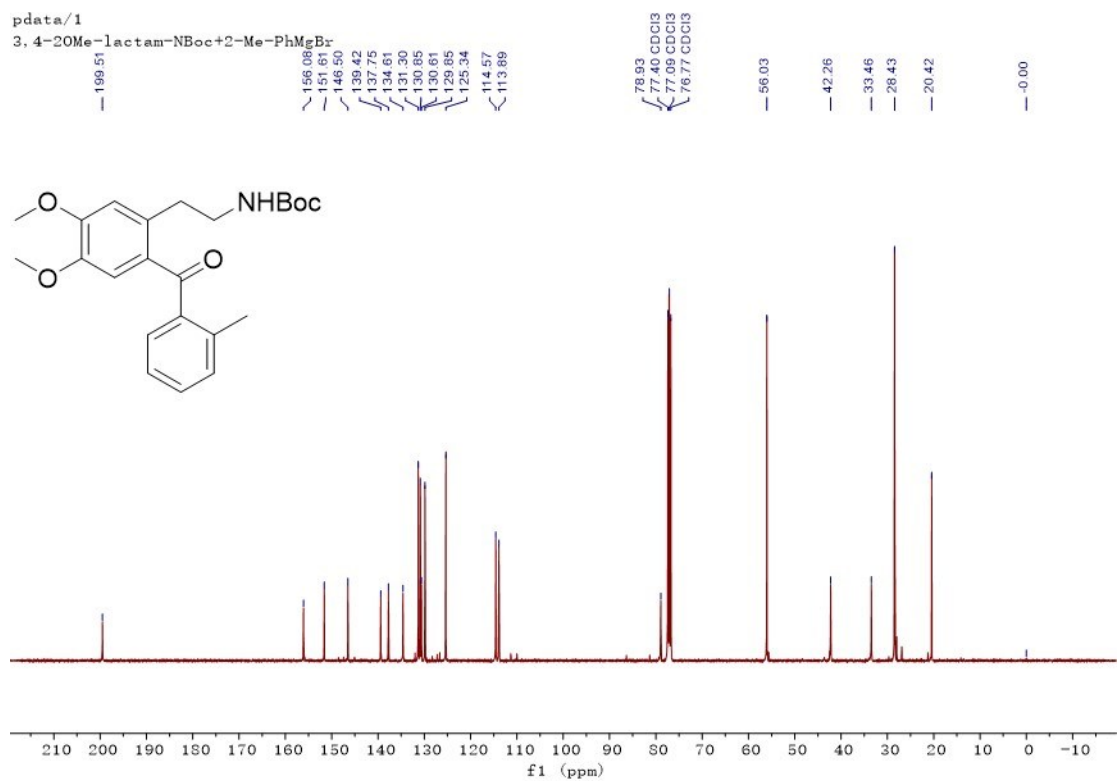
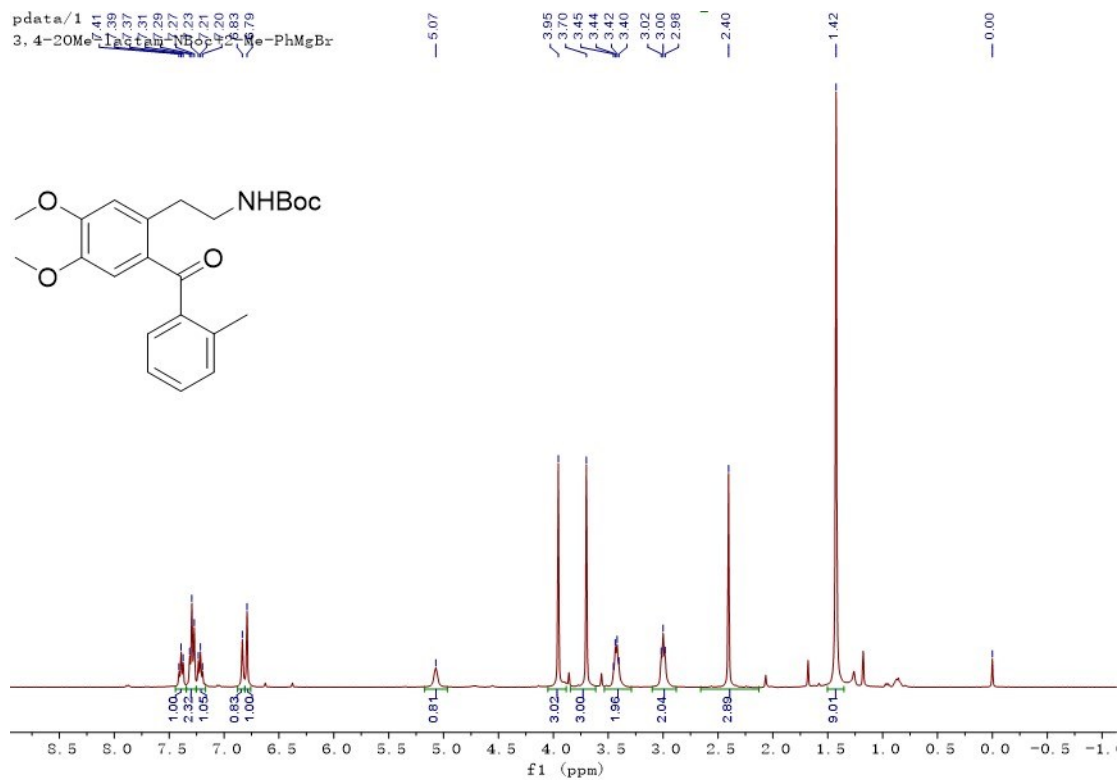




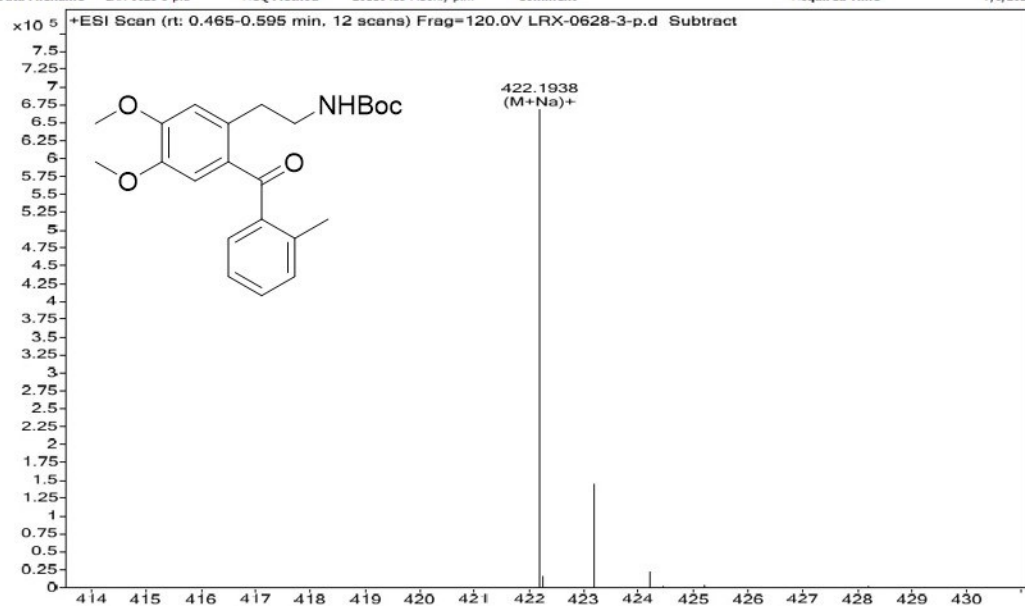
Sample Name	Position	p2B9	Instrument Name	Instrument 1	User Name	G6520B-PC\Admin
Inj Vol	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	ACQ Method	20110418-M5only-p.m	Comment		Acquired Time	7/8/2020 2:14:16 PM



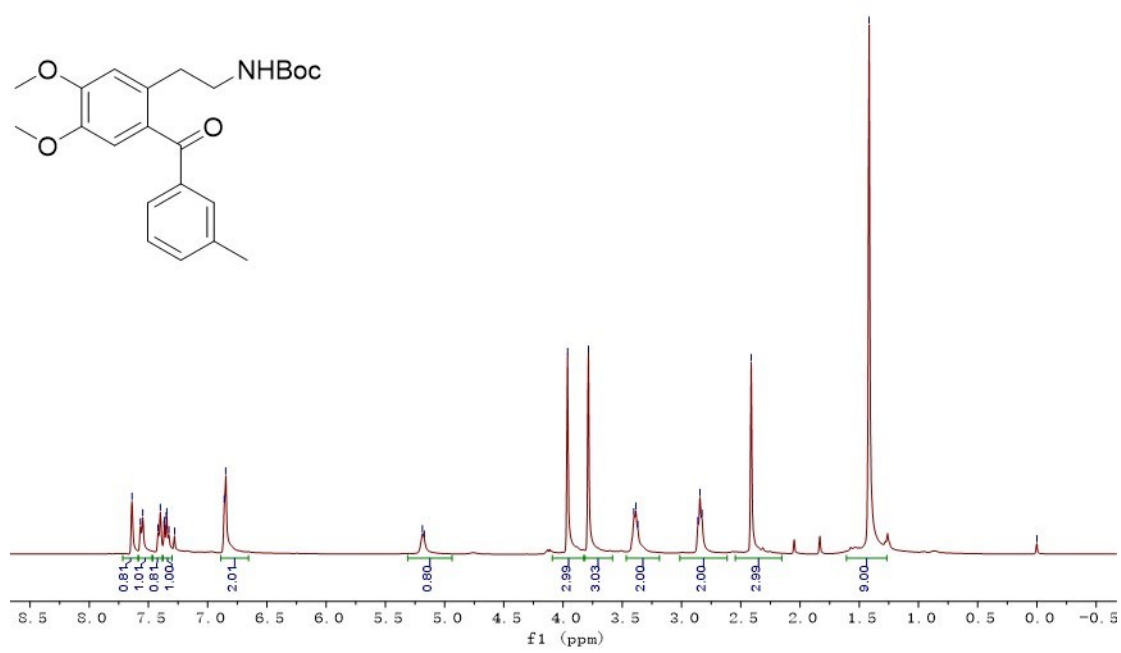


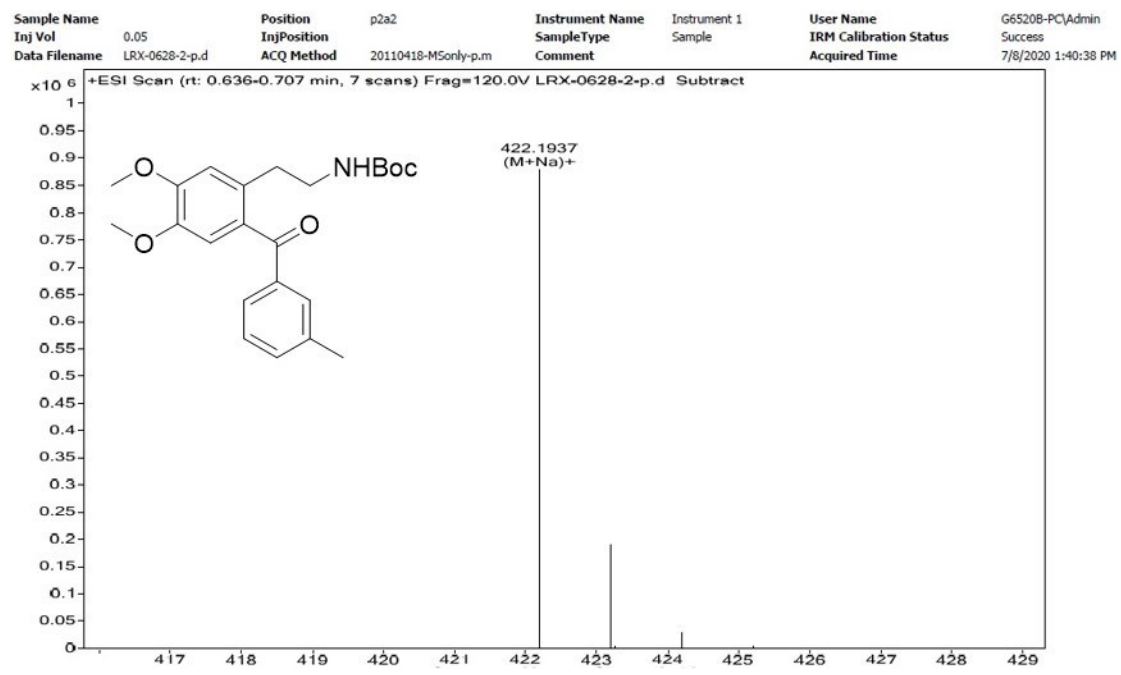
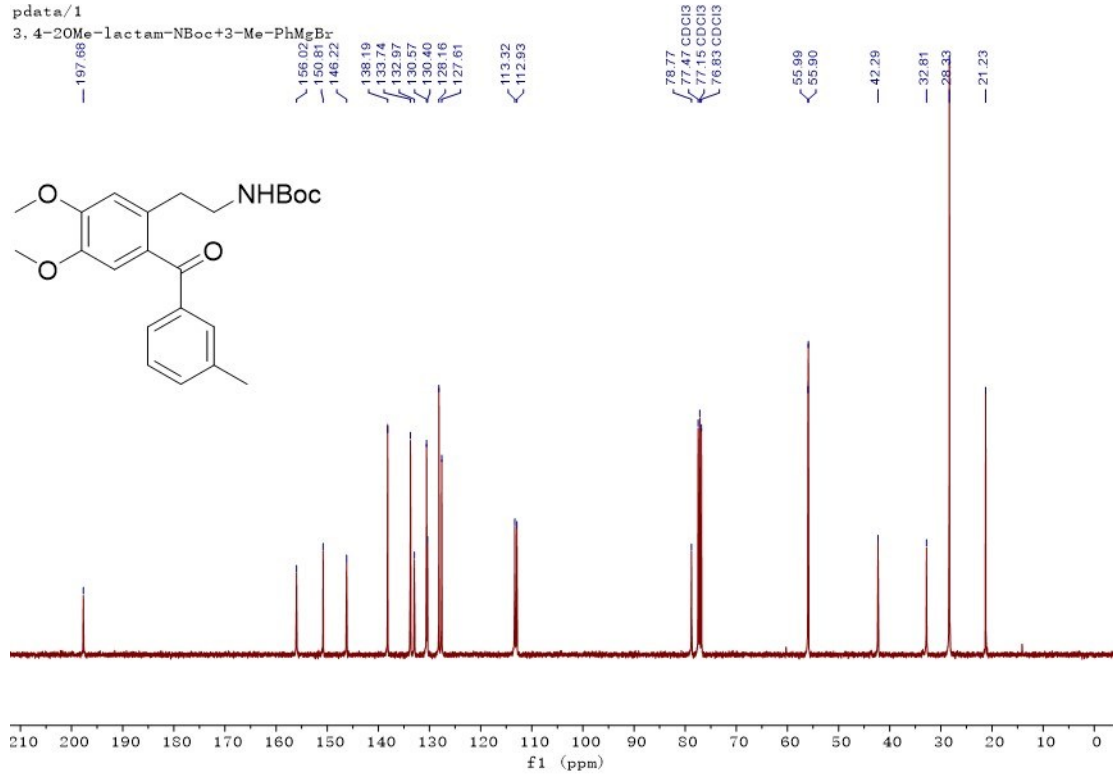


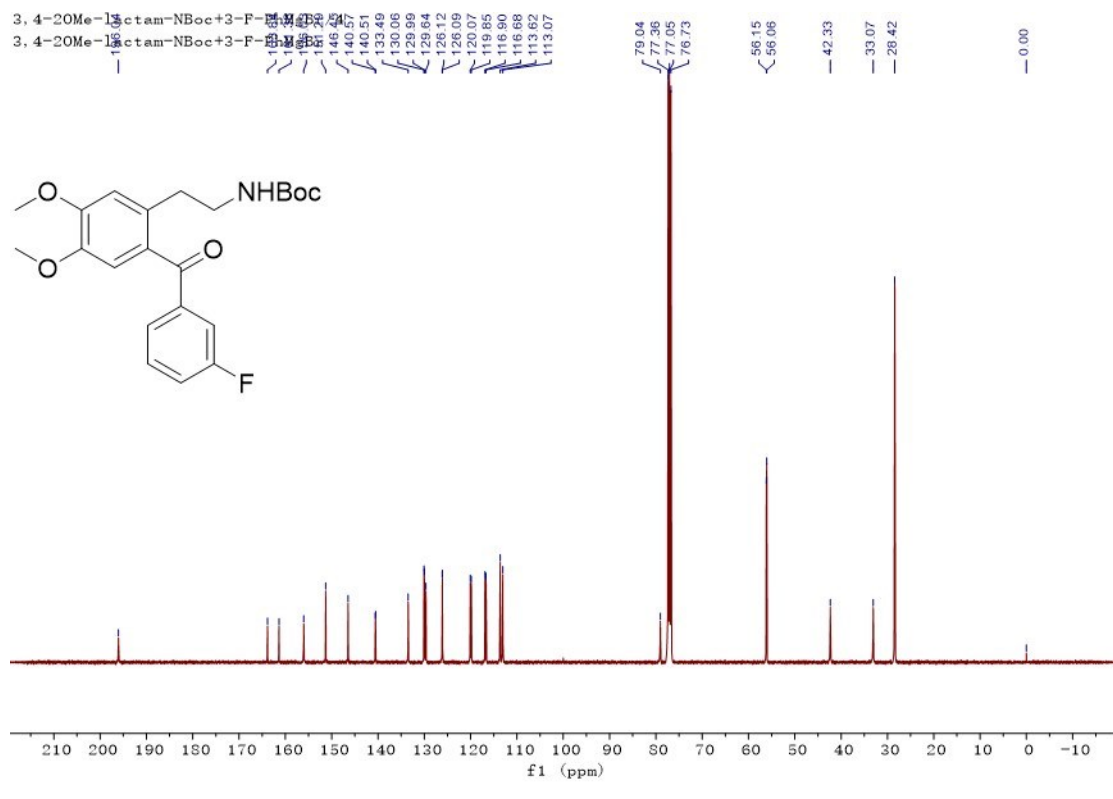
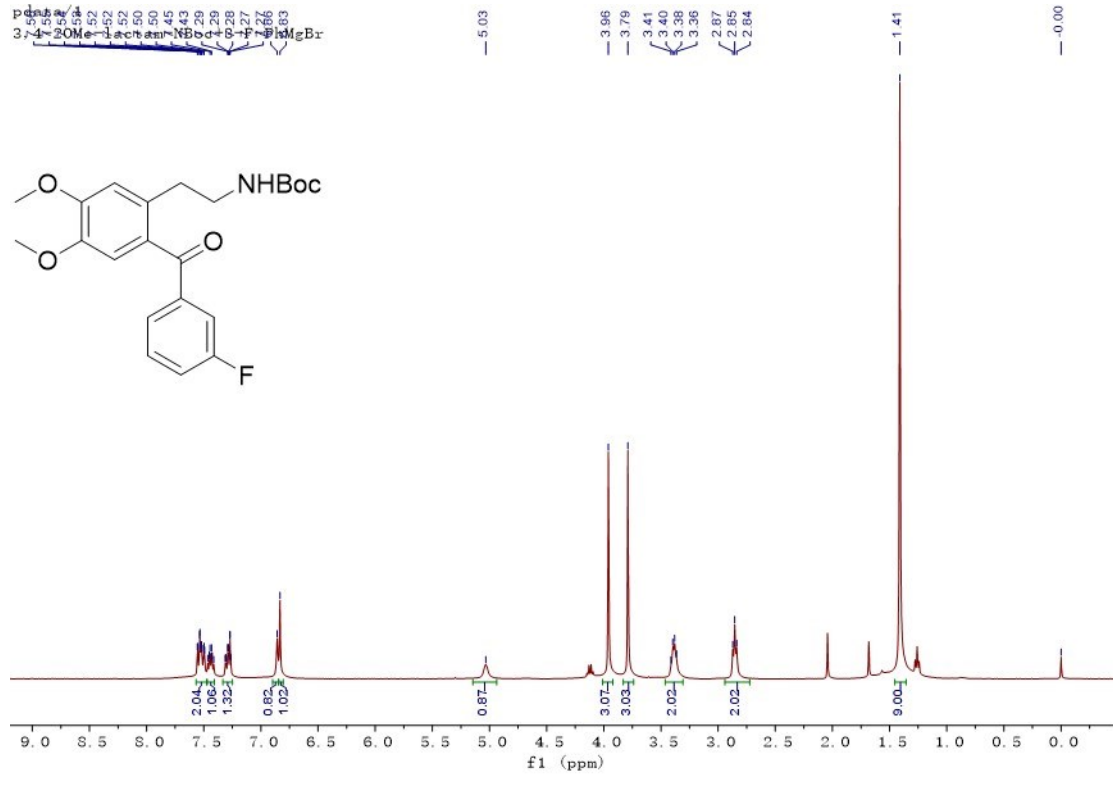
Sample Name	0.02	Position	p2a3	Instrument Name	Instrument 1	User Name	G6520B-PC\Admin
Inj Vol	0.02	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	LRX-0628-3-p.d	ACQ Method	20110418-M5only-p.m	Comment		Acquired Time	7/8/2020 1:43:06 PM



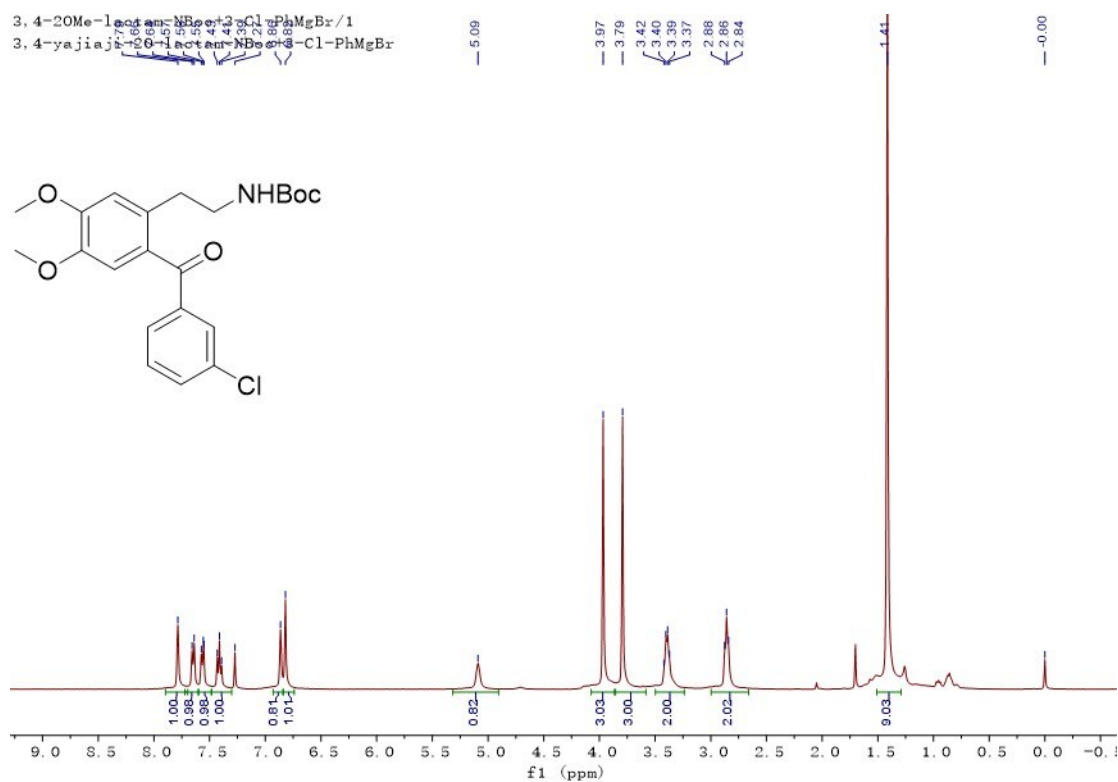
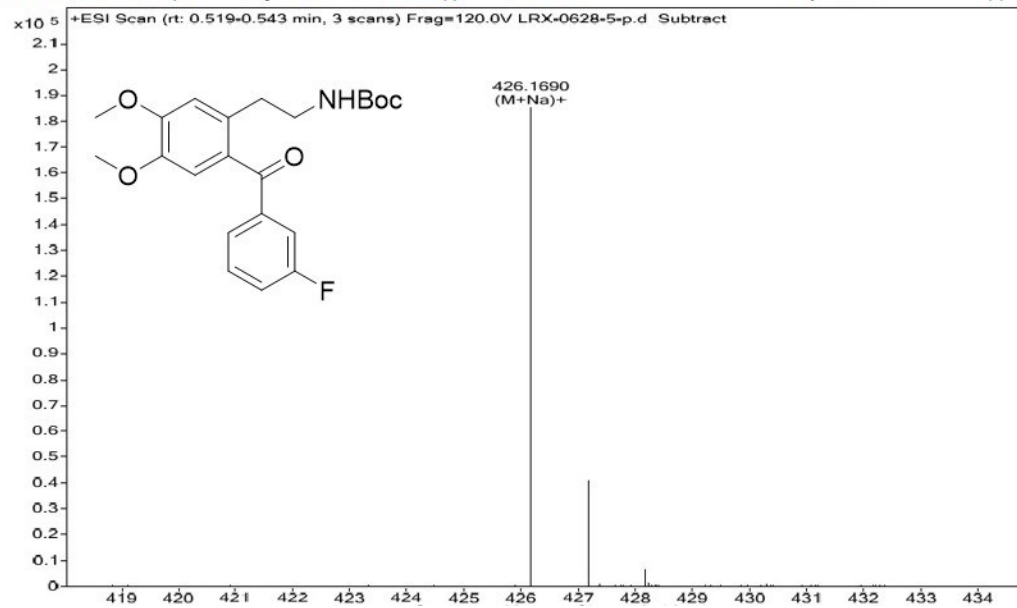
3.41 ppm (OMe), 3.37 ppm (OMe), 3.36 ppm (OMe), 3.34 ppm (OMe), 3.33 ppm (OMe), 3.28 ppm (OMe), 3.26 ppm (OMe), 3.25 ppm (OMe), 3.19 ppm (NH), 3.17 ppm (NH), 3.06 ppm (Me), 3.03 ppm (Me), 3.00 ppm (Me), 2.86 ppm (Me), 2.84 ppm (Me), 2.83 ppm (Me), 2.41 ppm (Me), 1.42 ppm (Me), 0.00 ppm (TMS)

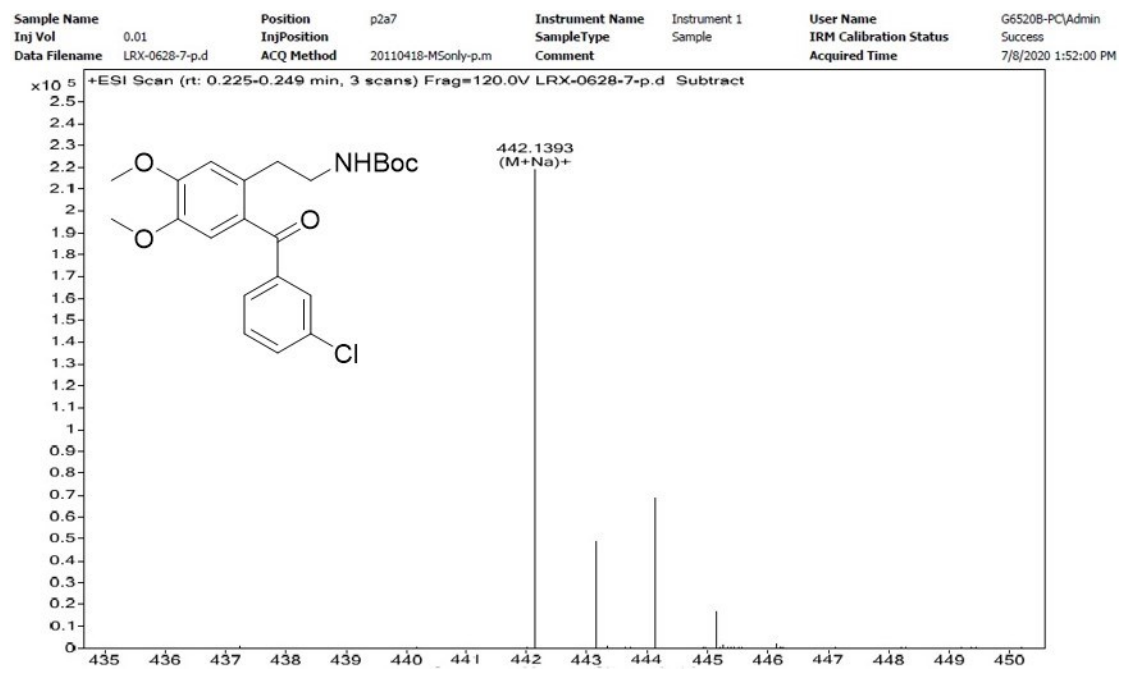
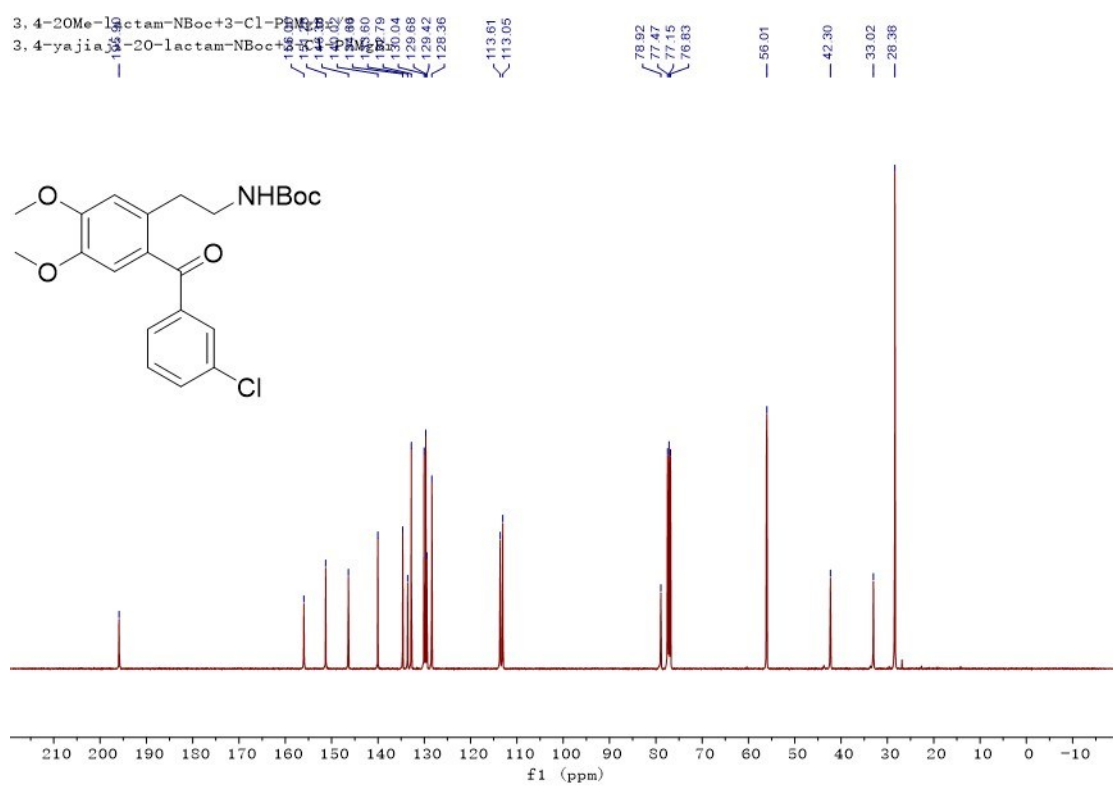


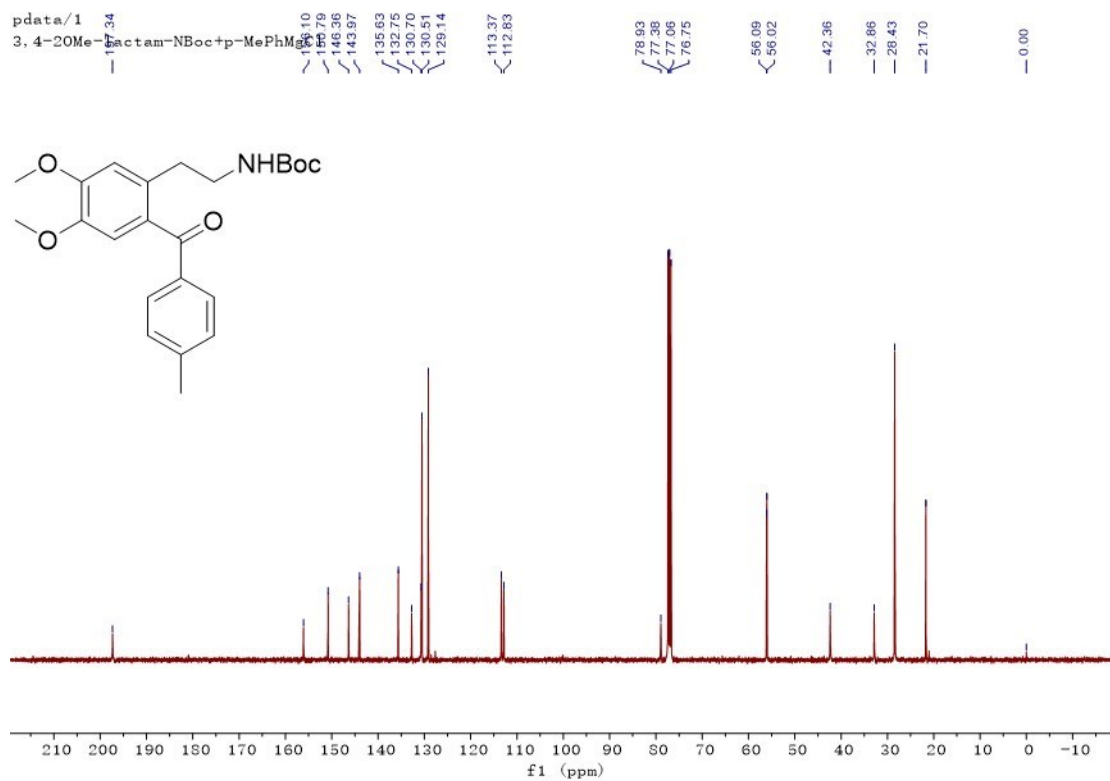
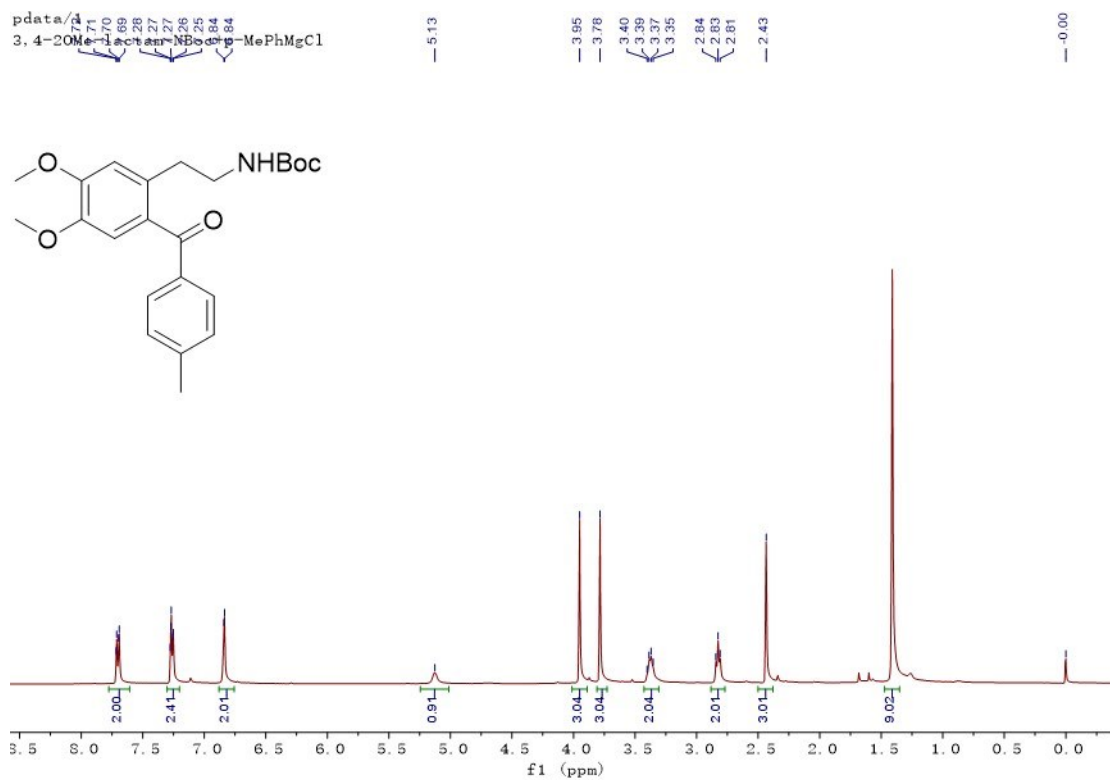




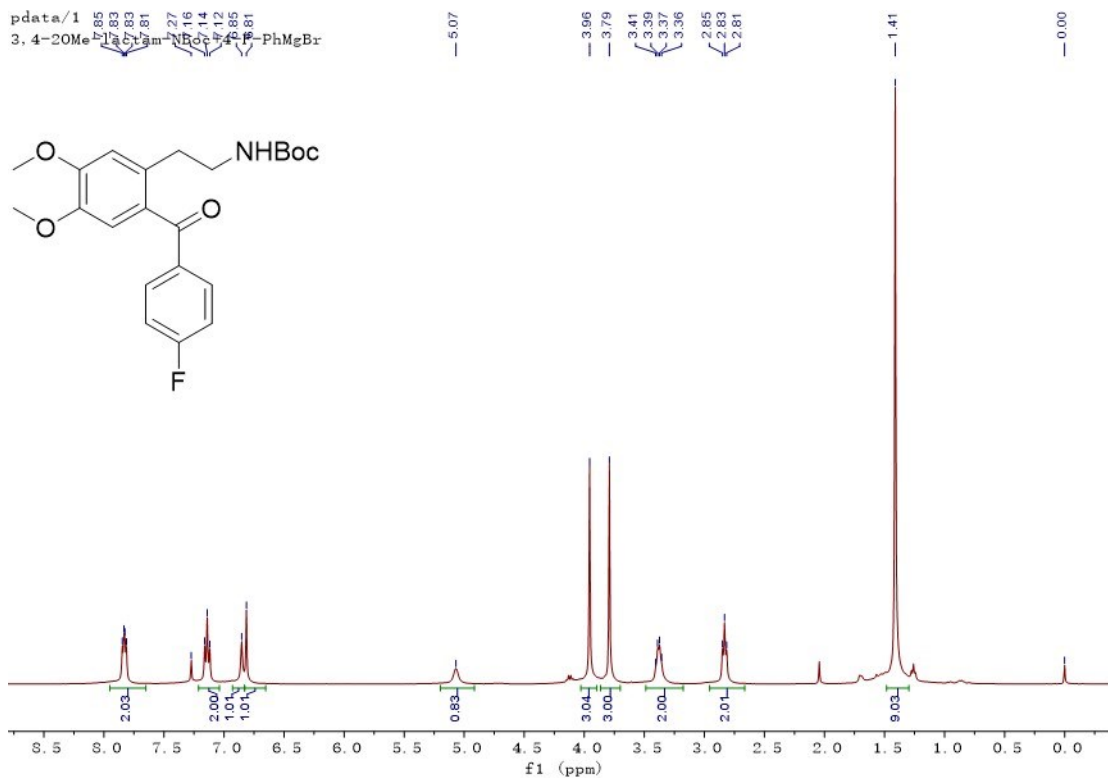
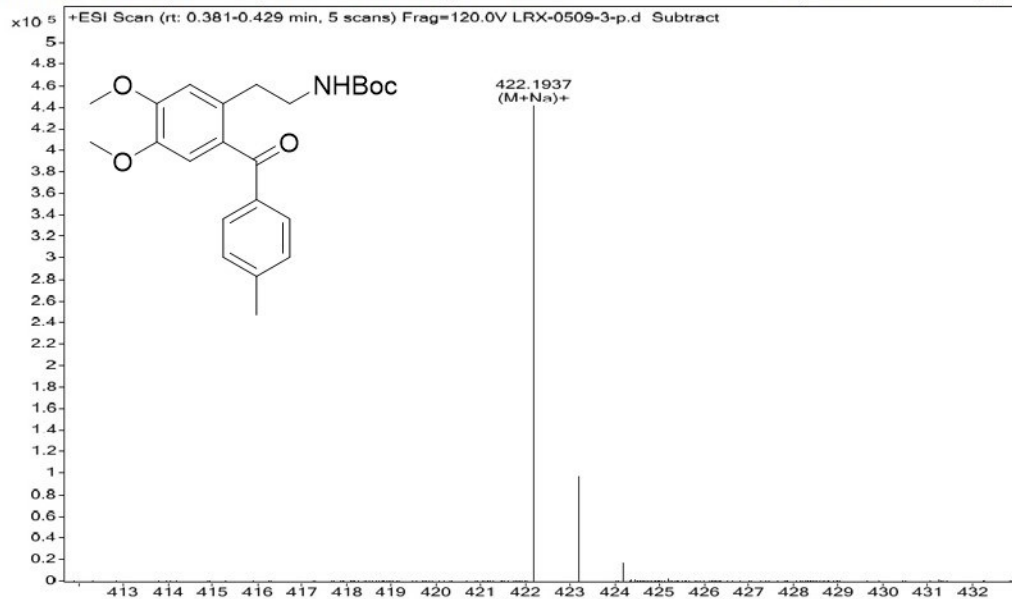
Sample Name	Position	p2a5	Instrument Name	Instrument 1	User Name	G6520B-PC\Admin
Inj Vol	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	ACQ Method	20110418-M5only-p.m	Comment		Acquired Time	7/8/2020 1:47:57 PM

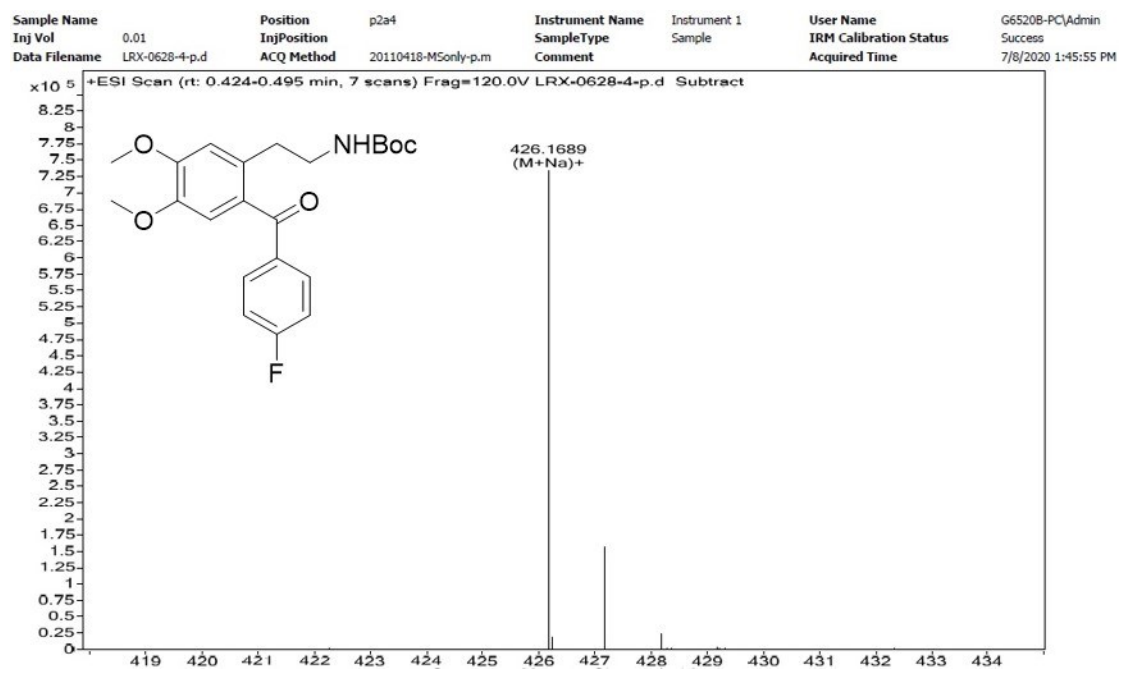
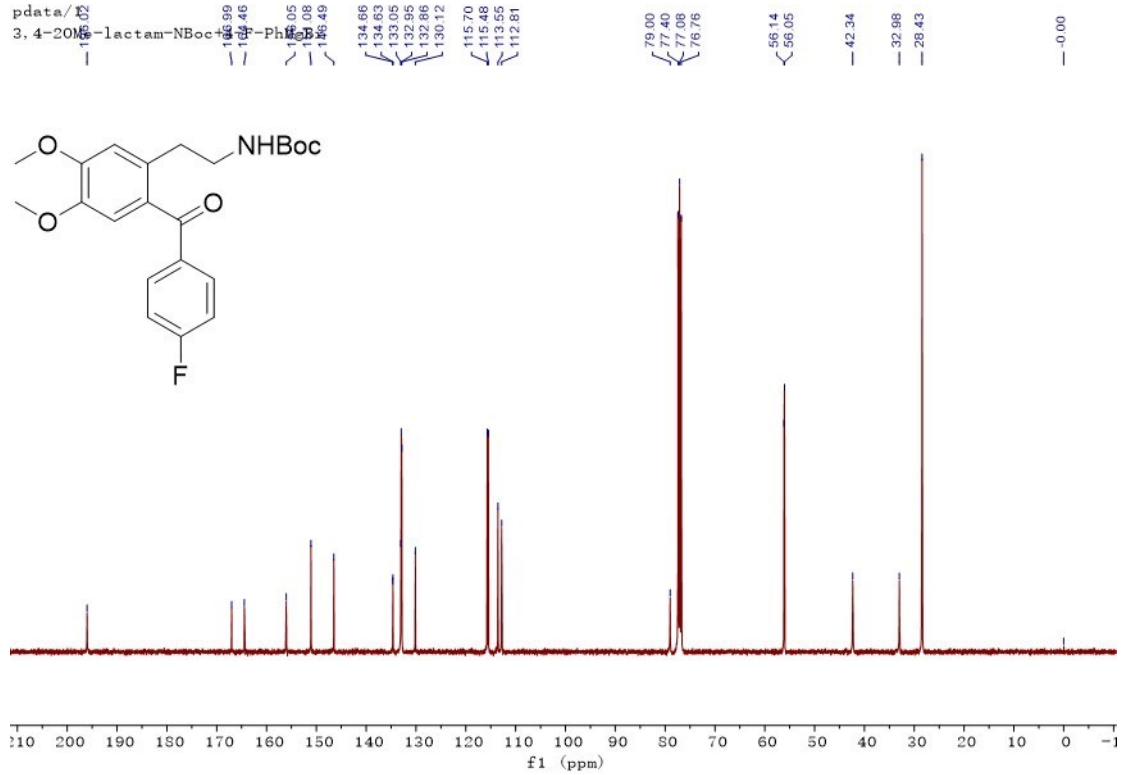


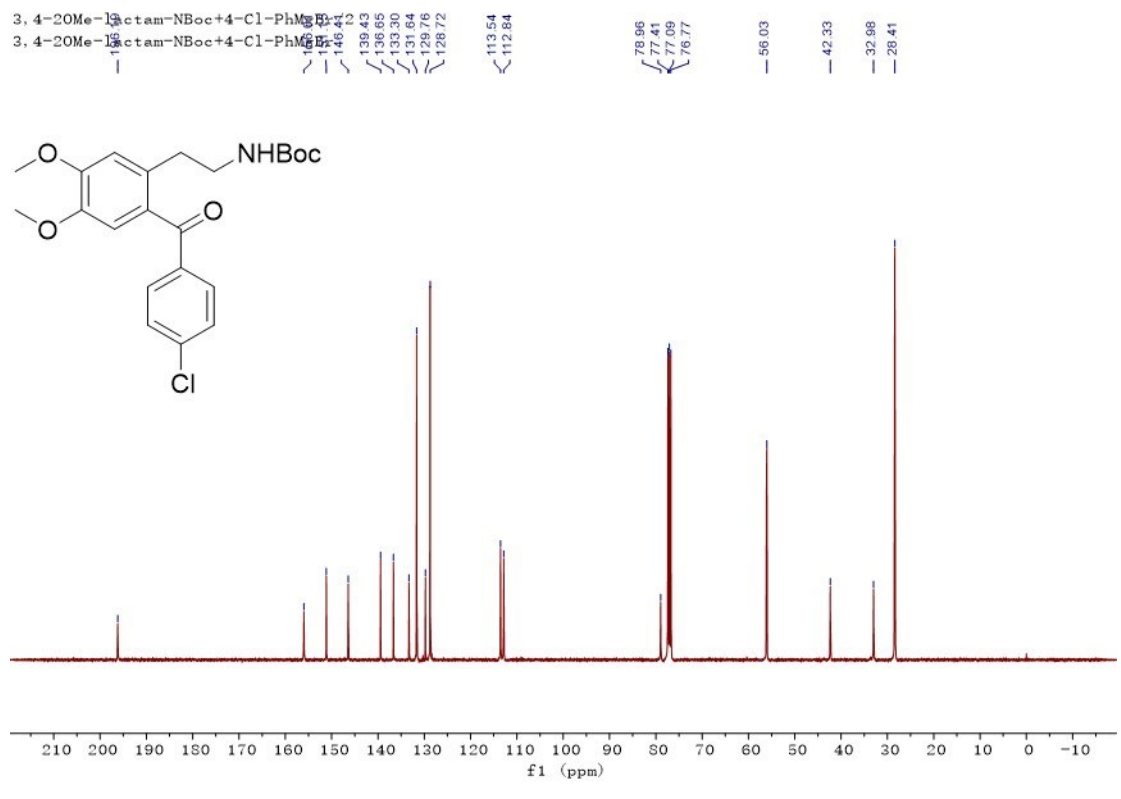
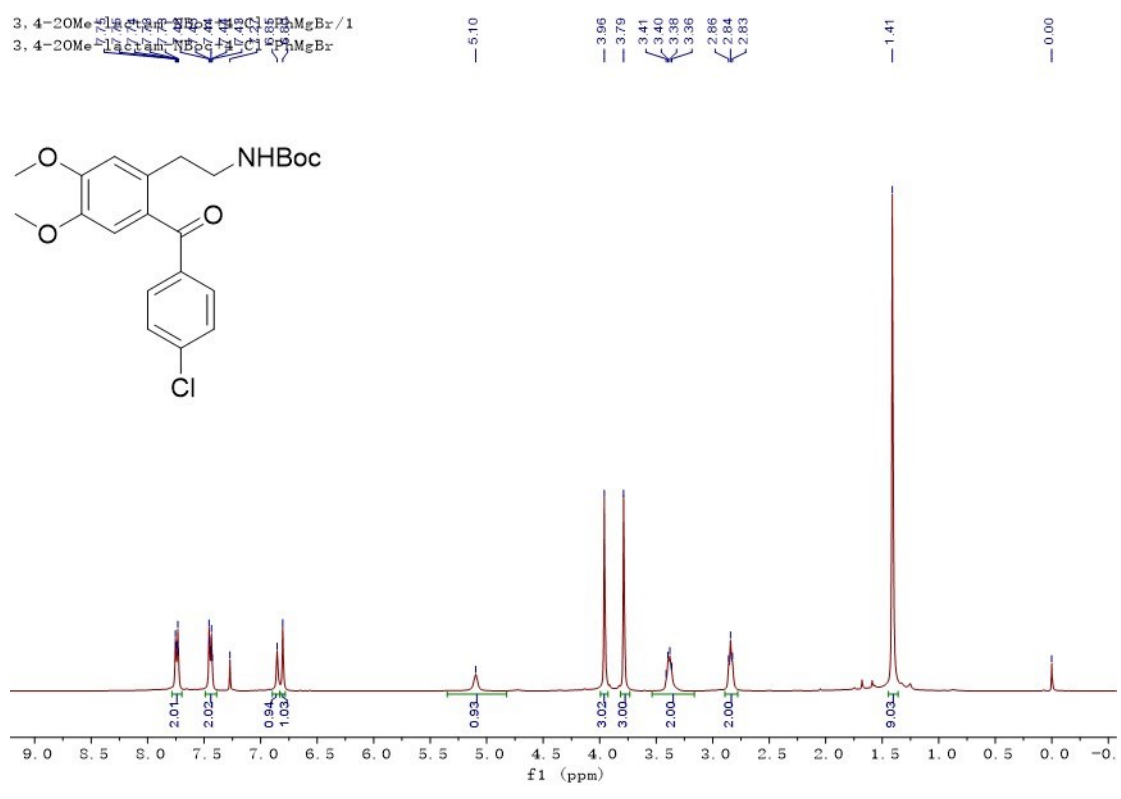




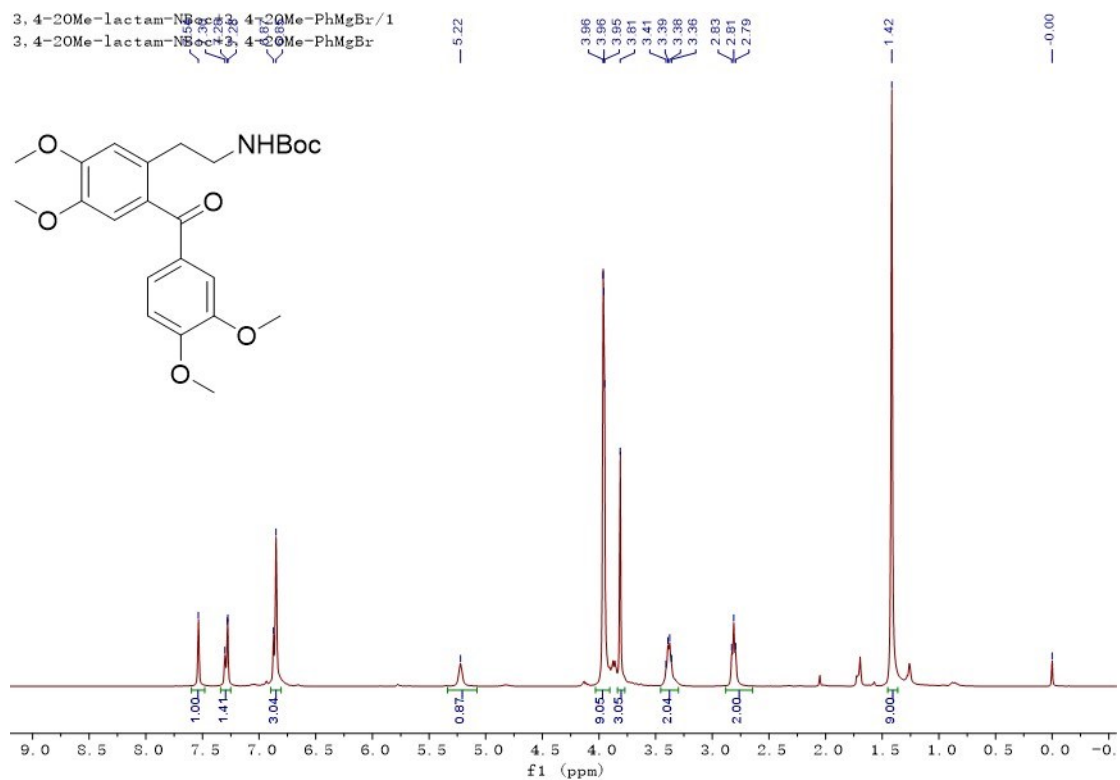
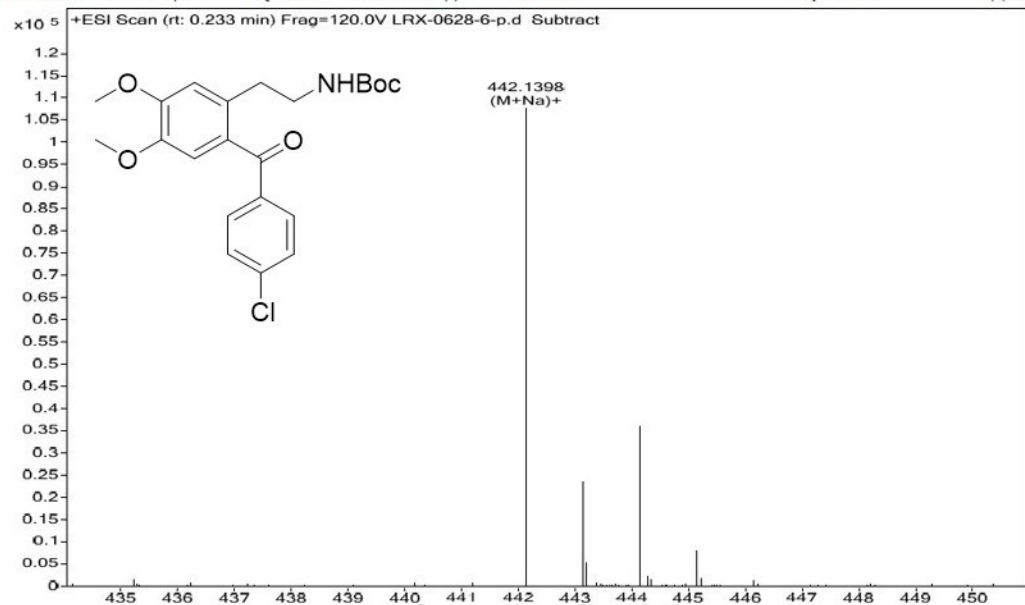
Sample Name	0.01	Position	p2D1	Instrument Name	Instrument 1	User Name	G6520B-PC\Admin
Inj Vol	0.01	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	LRX-0509-3-p.d	ACQ Method	20110418-MSonly-p.m	Comment		Acquired Time	5/12/2020 3:39:04 PM

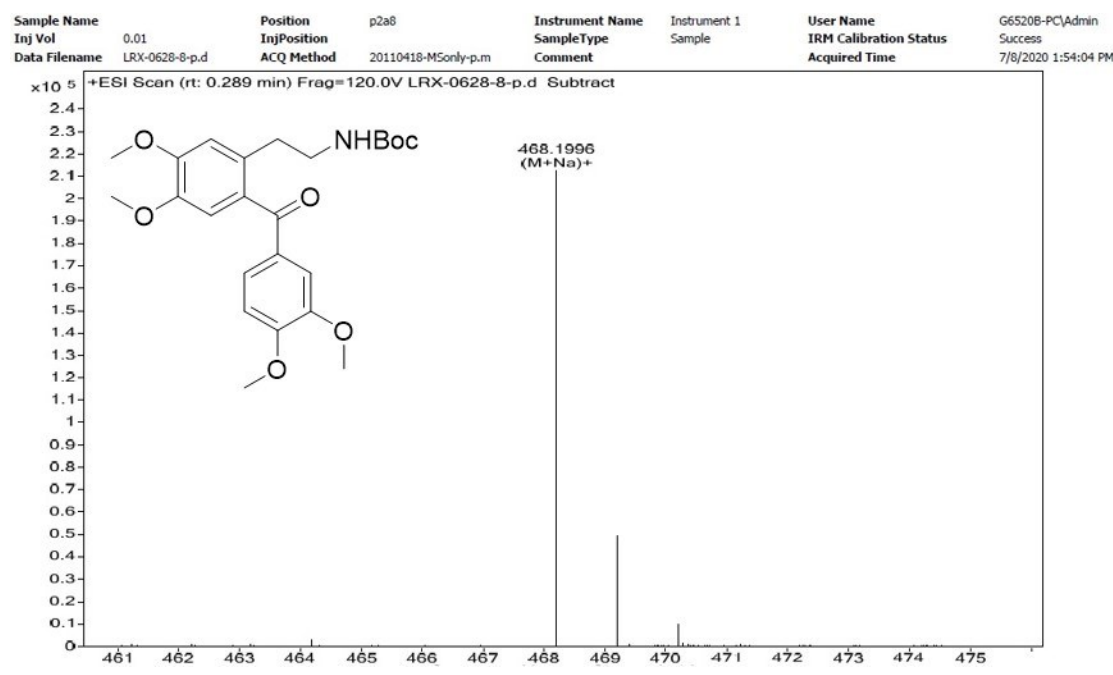
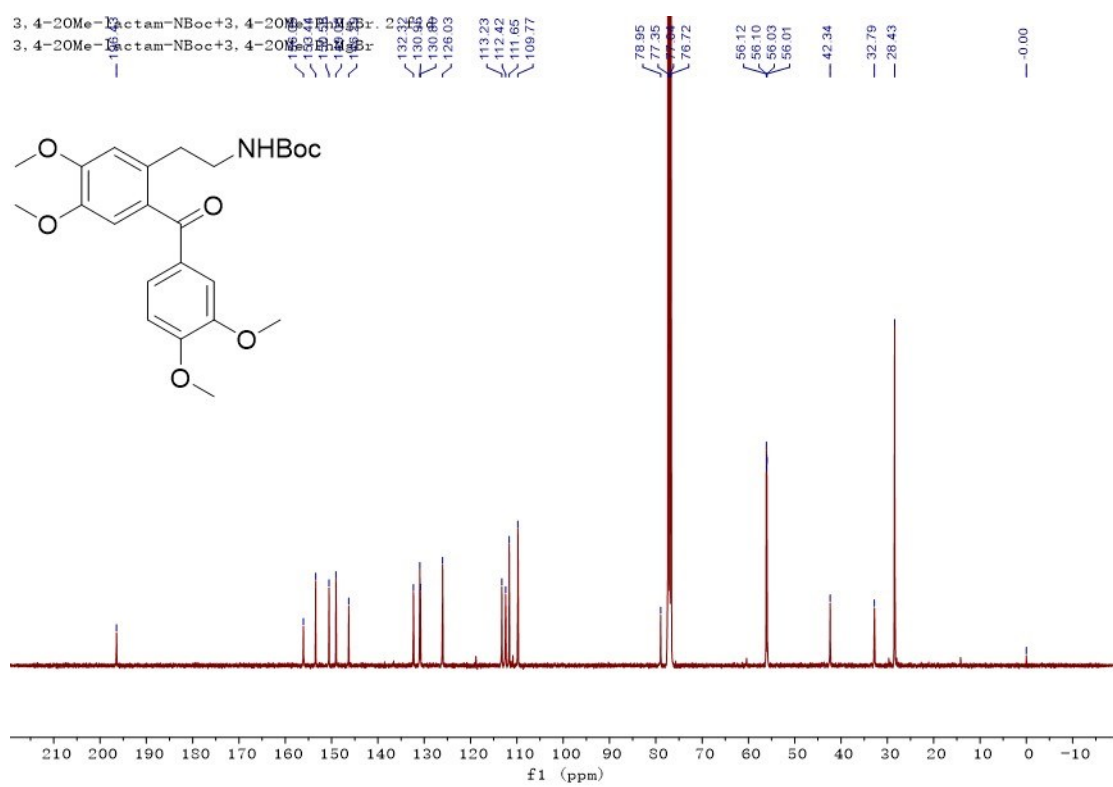


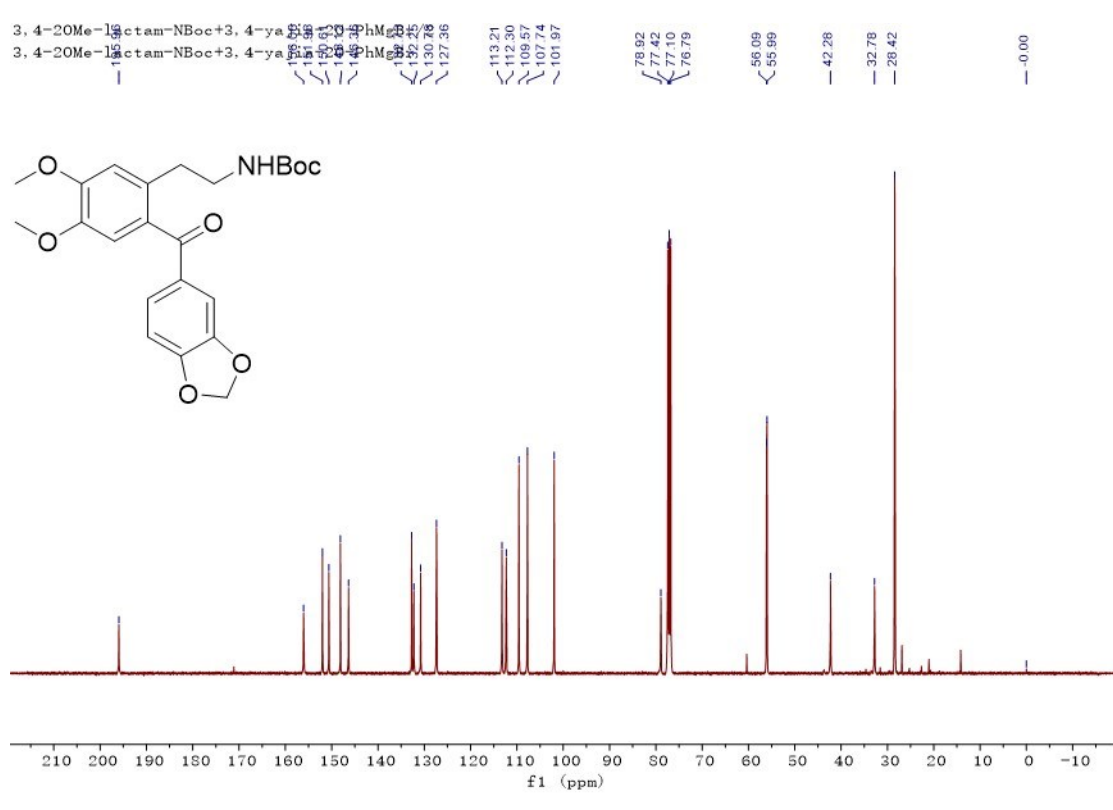
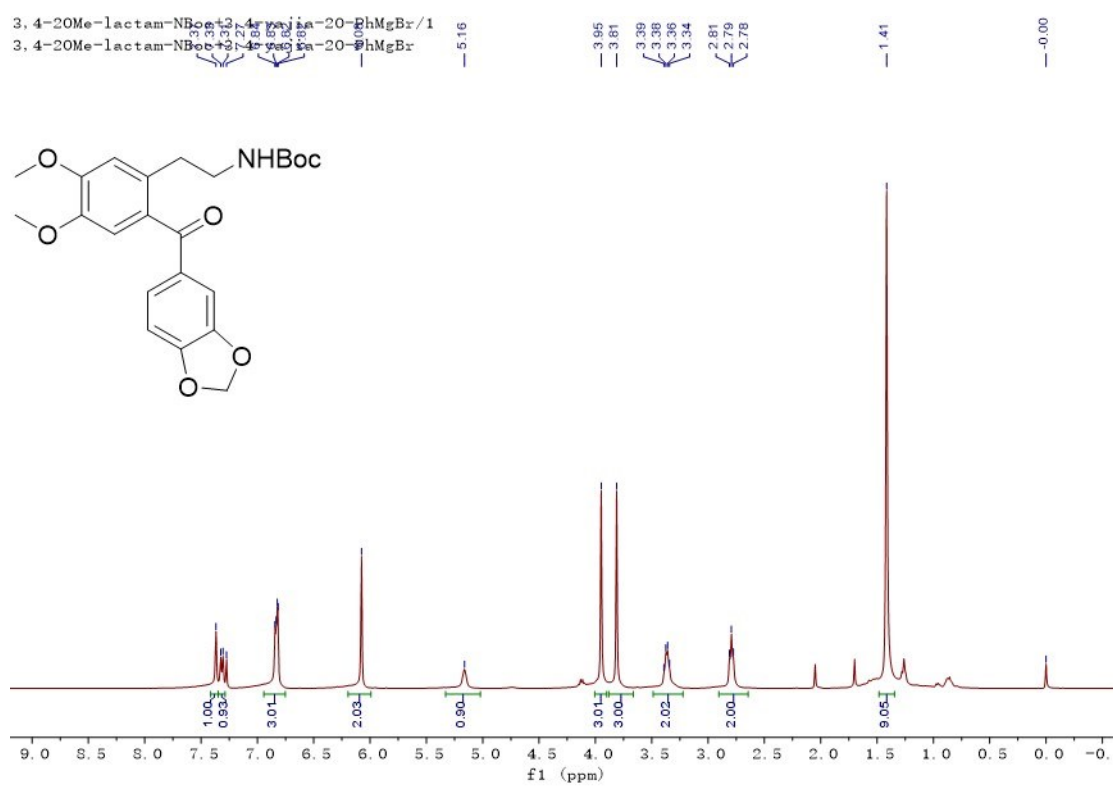




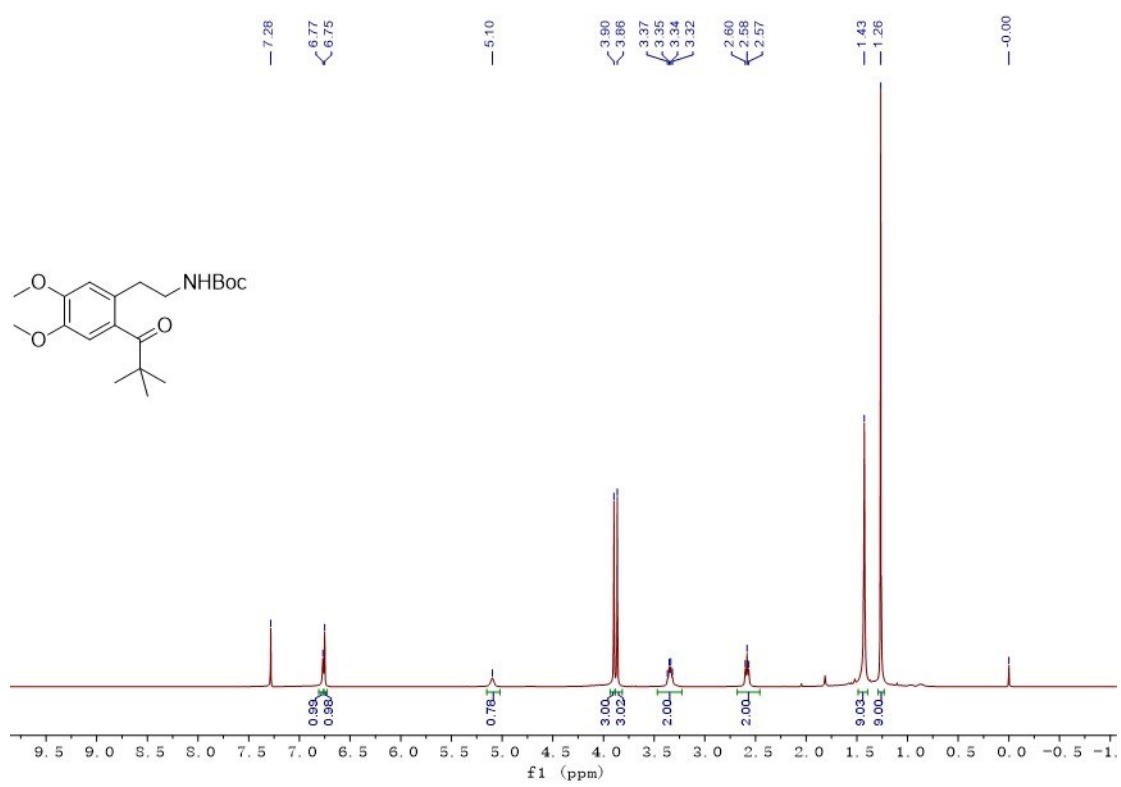
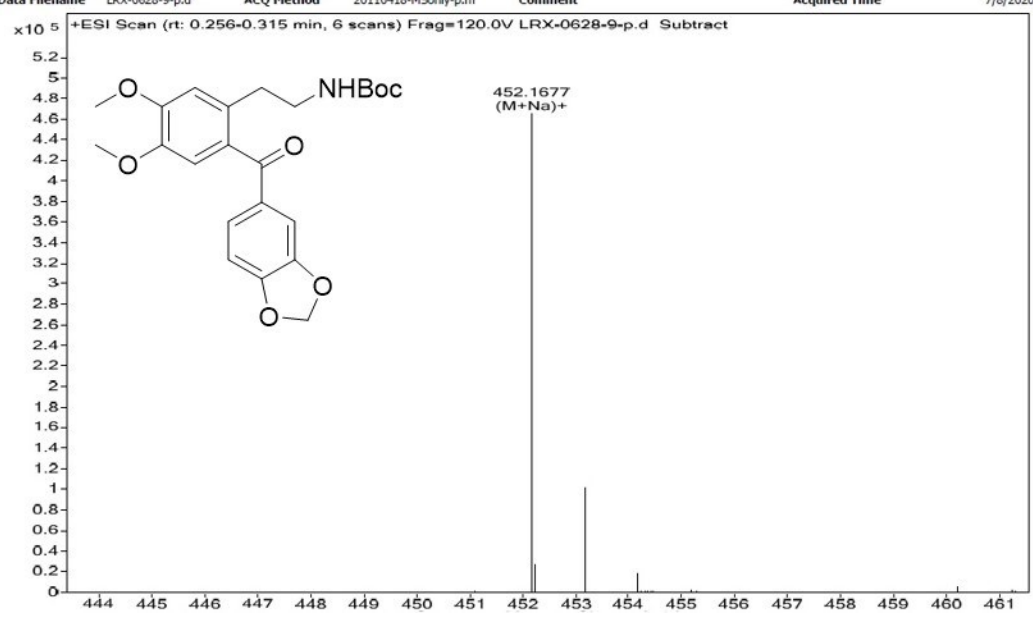
Sample Name	Position	p2a6	Instrument Name	Instrument 1	User Name	G65208-PC\Admin
Inj Vol	0.01	InjPosition	SampleType	Sample	IRM Calibration Status	Success
Data Filename	LRX-0628-6-p.d	ACQ Method	20110418-M5only-p.m	Comment	Acquired Time	7/8/2020 1:49:46 PM

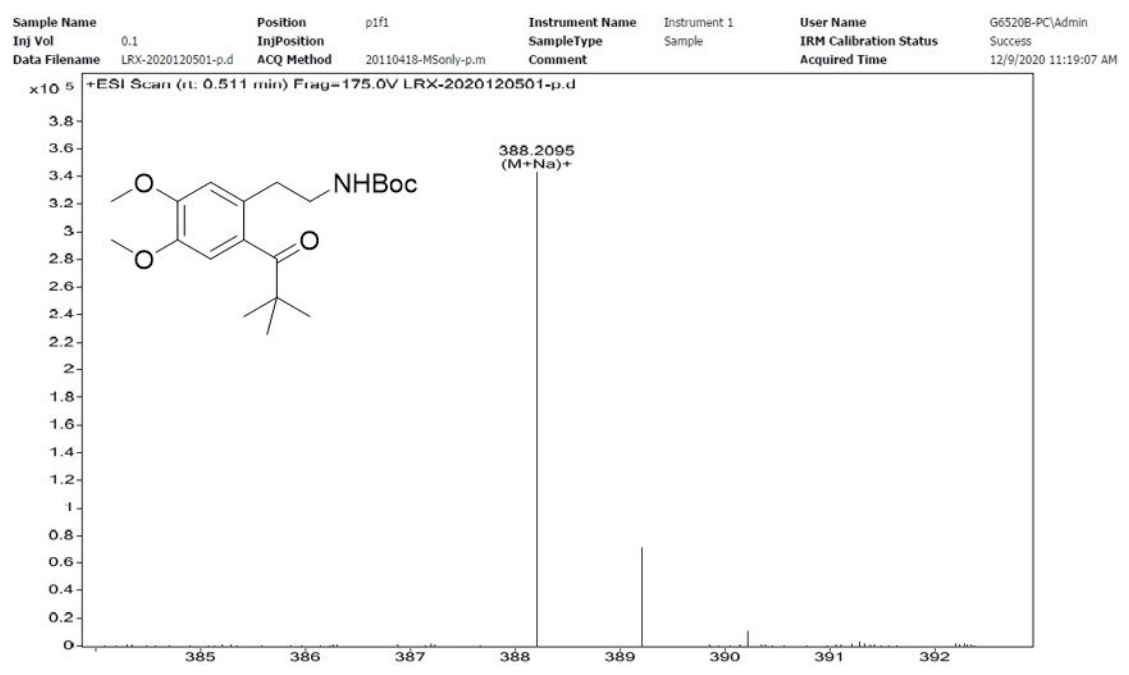
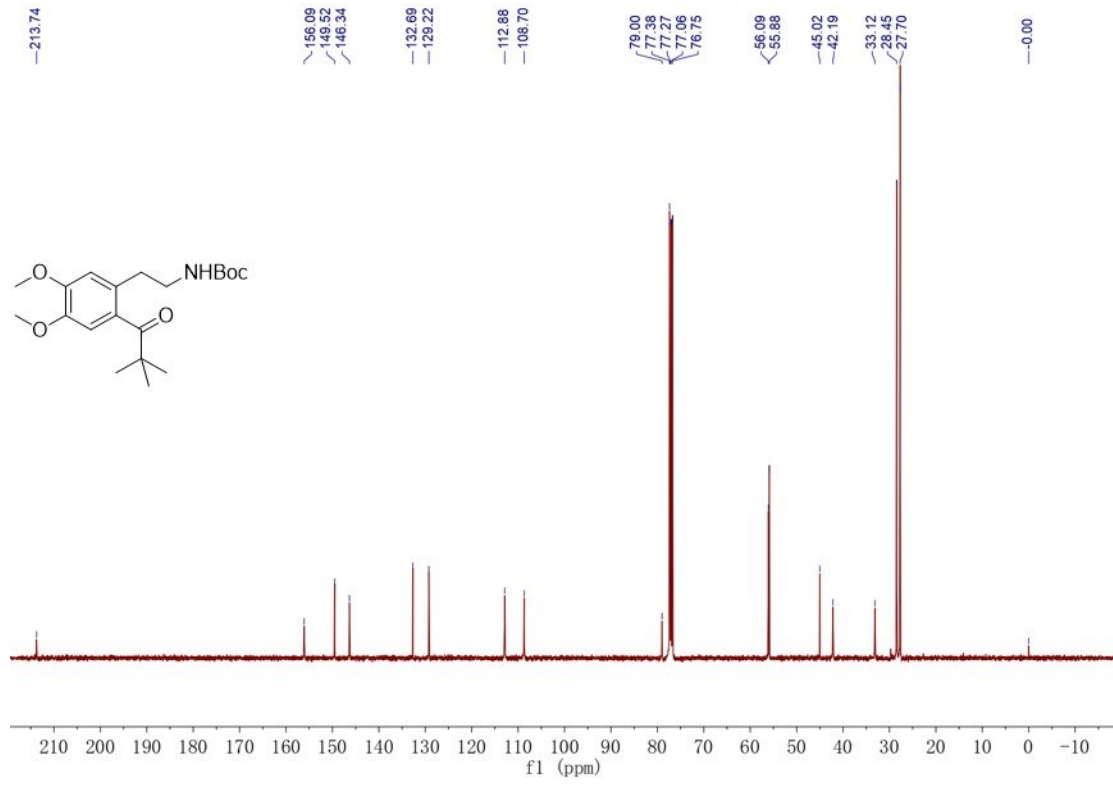


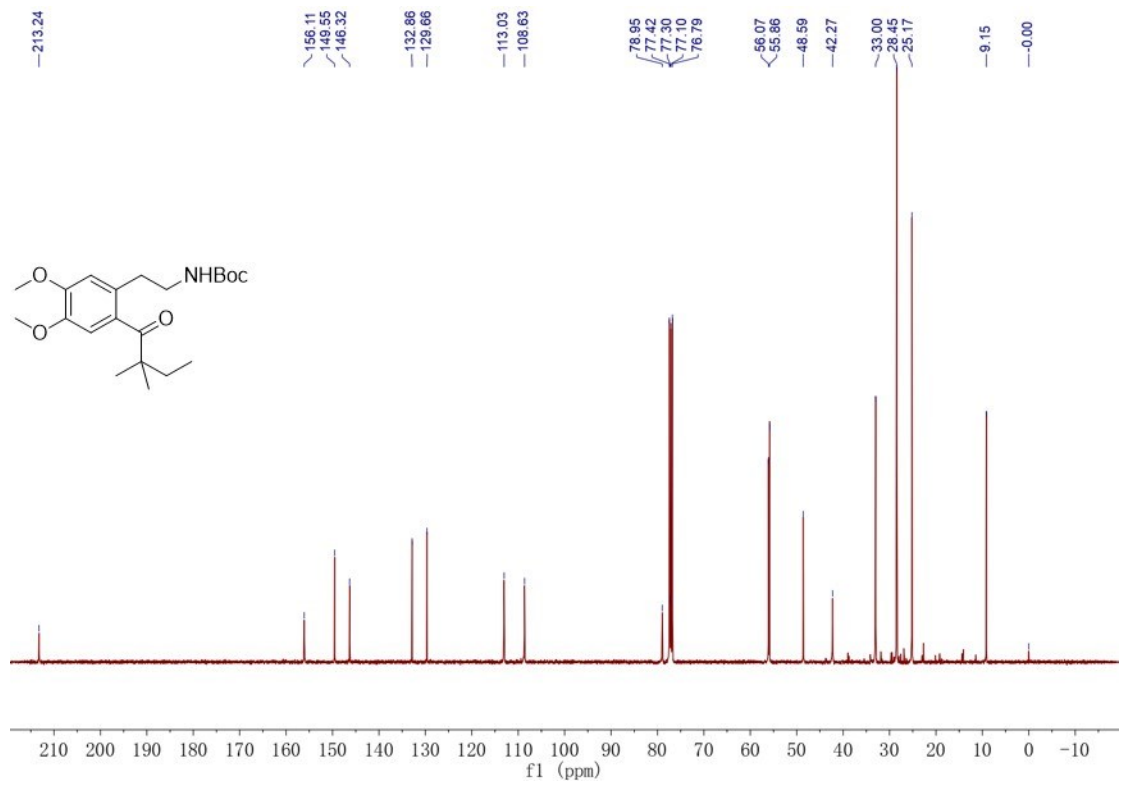
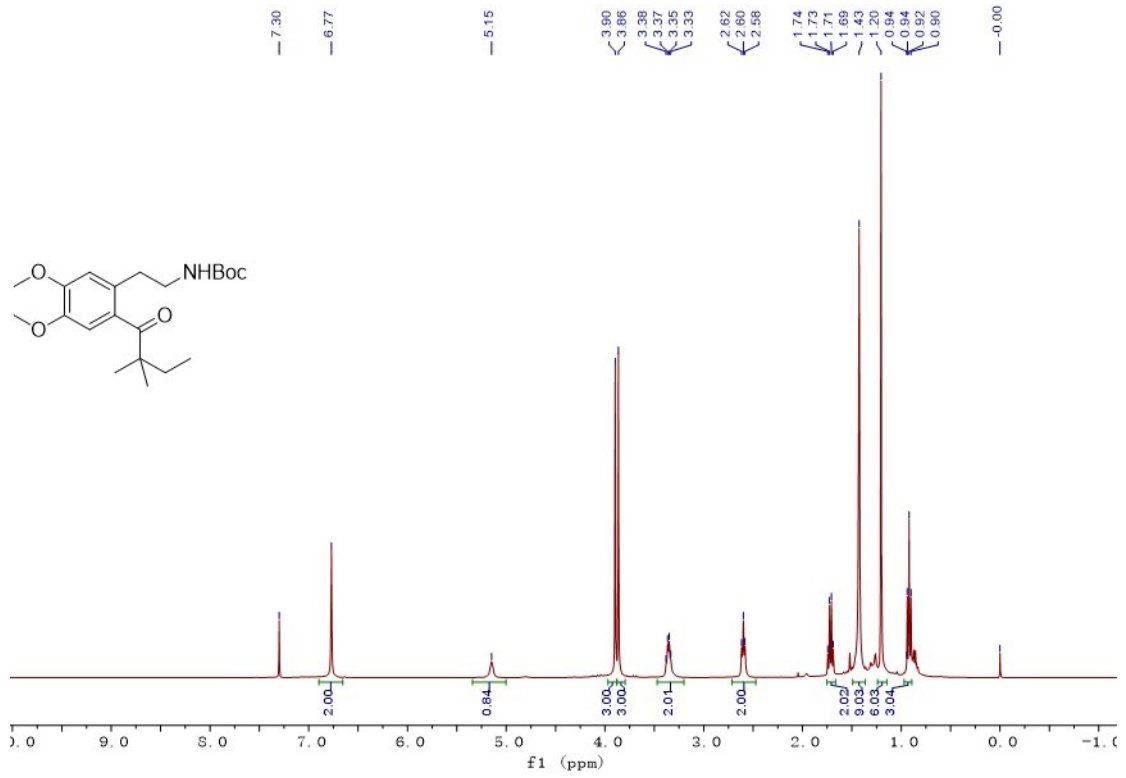




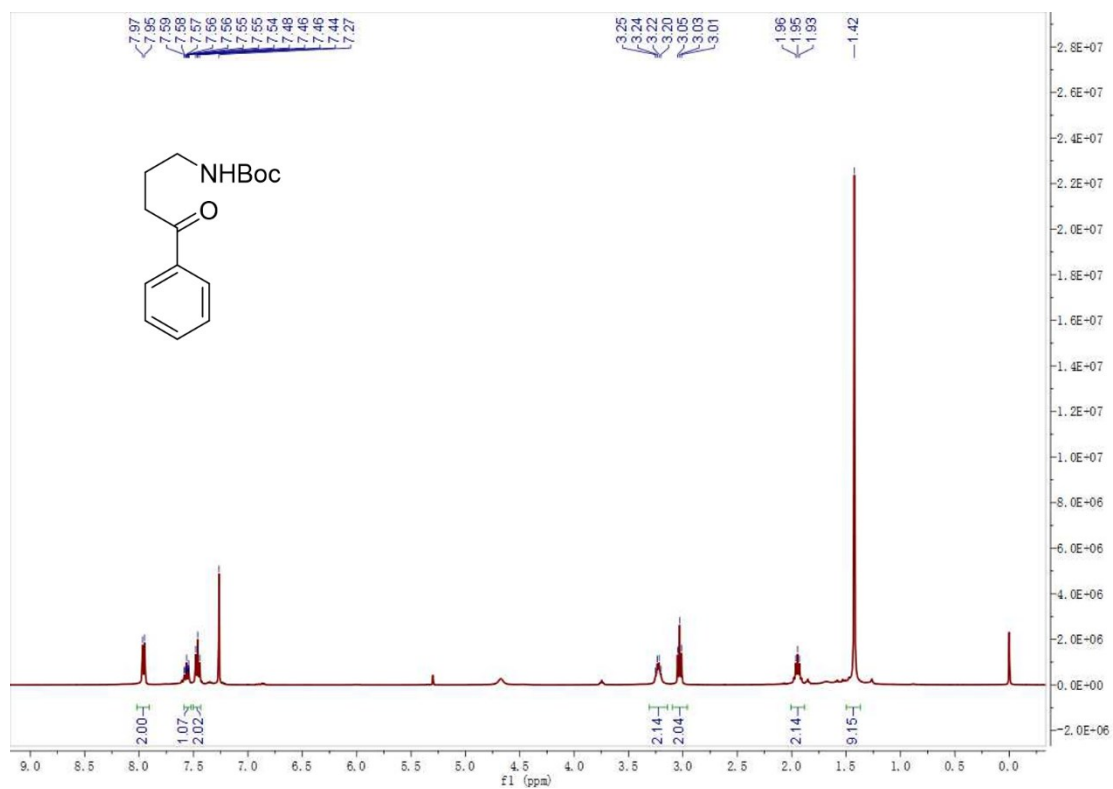
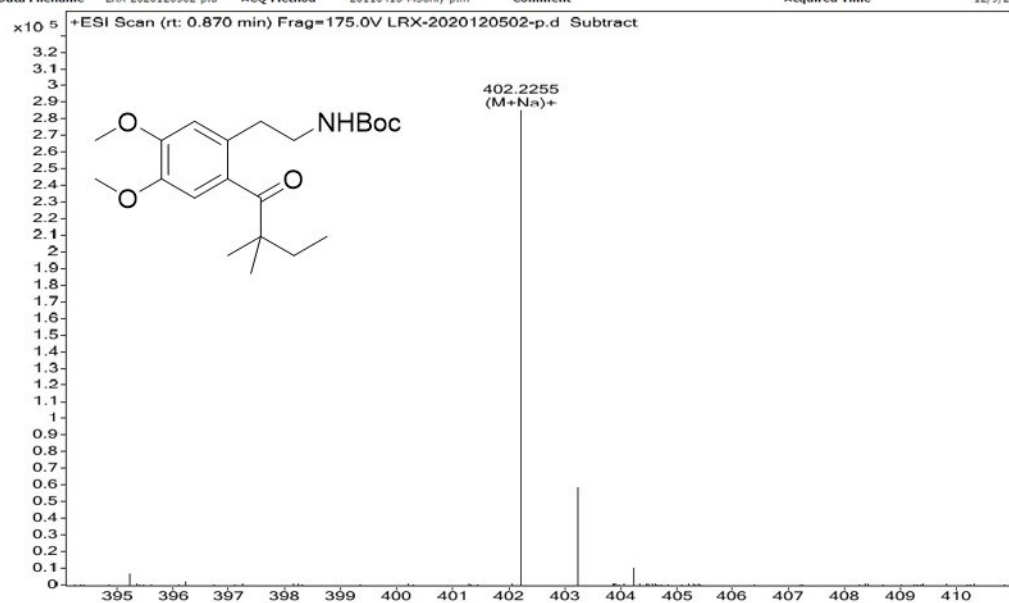
Sample Name	0.01	Position	p2a9	Instrument Name	Instrument 1	User Name	G65208-PC\Admin
Inj Vol	0.01	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	LRX-0628-9-p.d	ACQ Method	20110418-M5only-p.m	Comment		Acquired Time	7/8/2020 1:55:52 PM

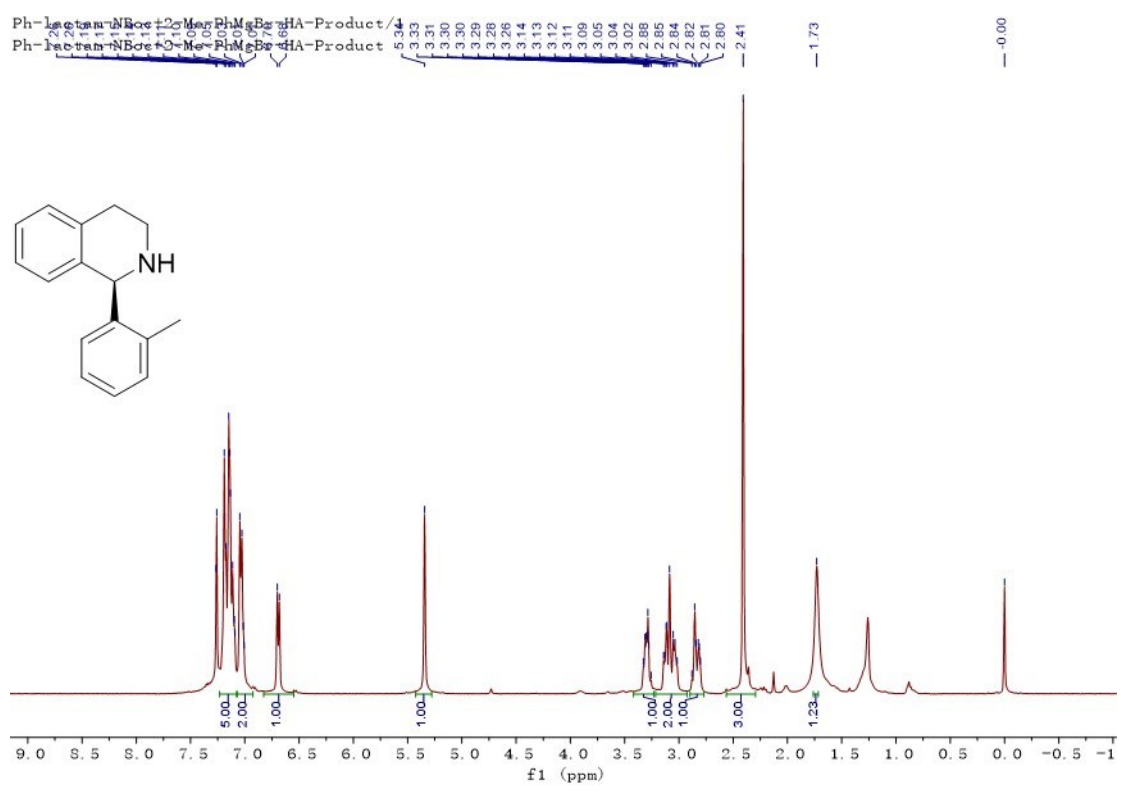
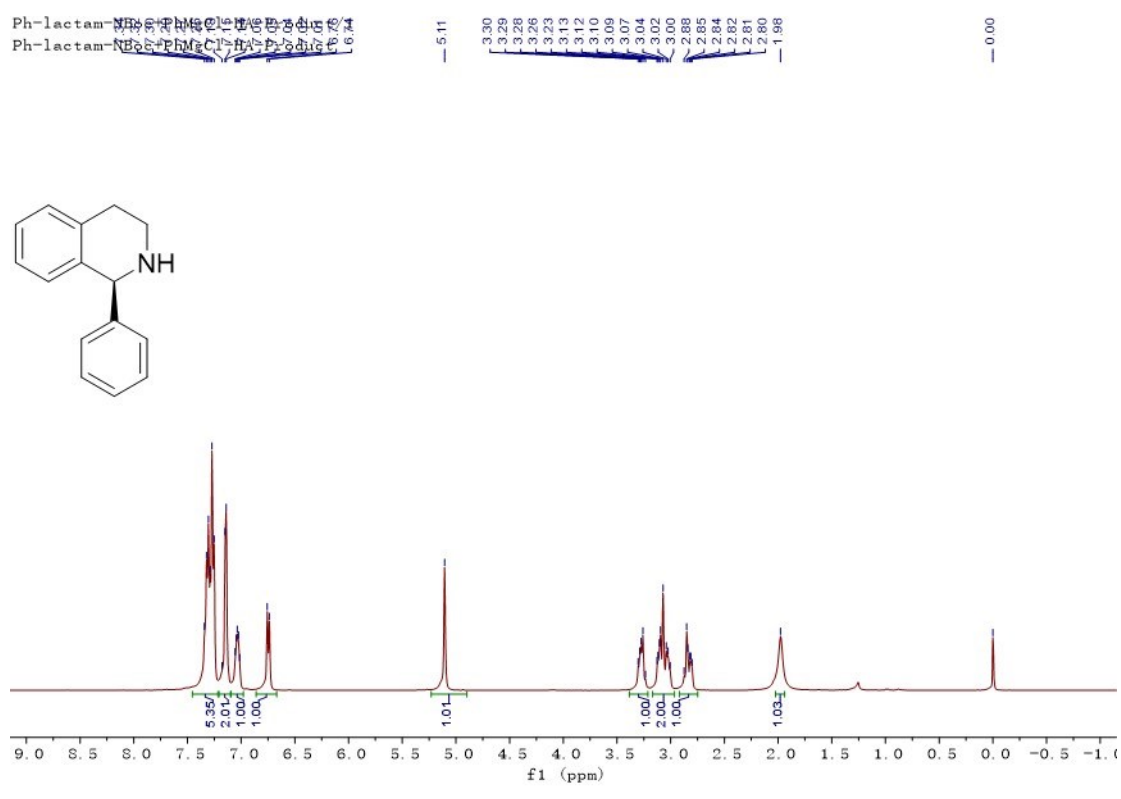


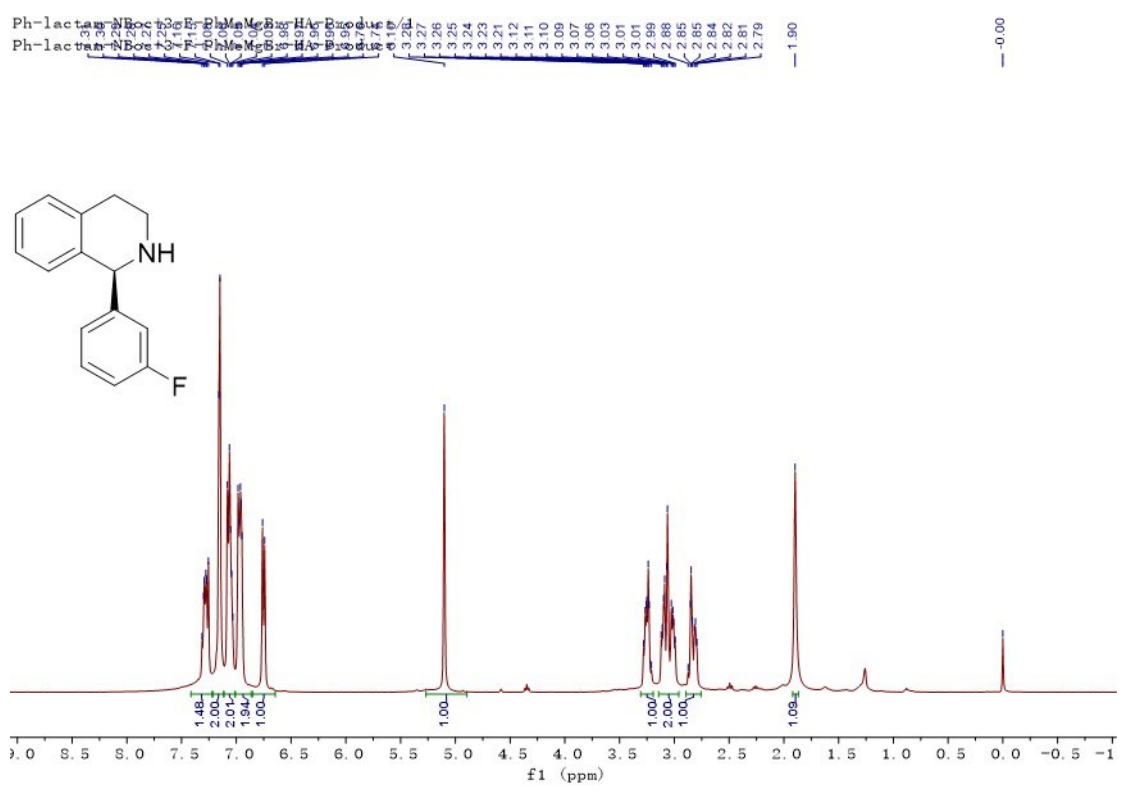
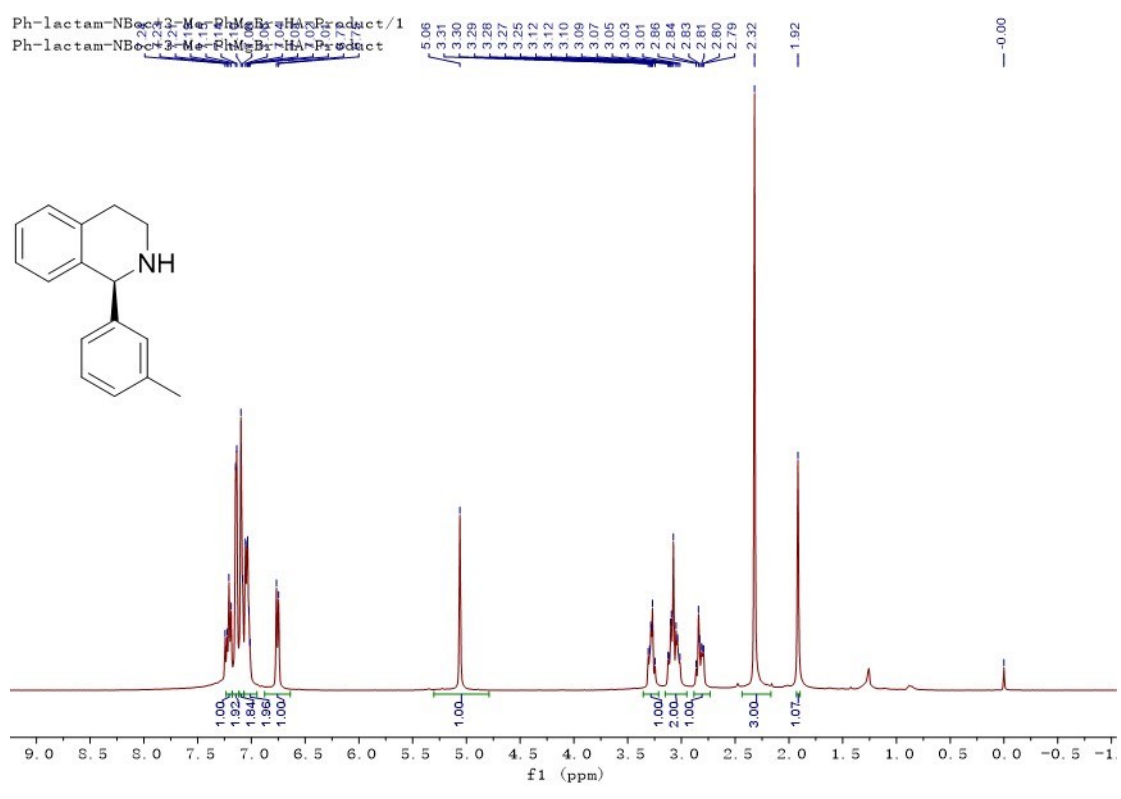


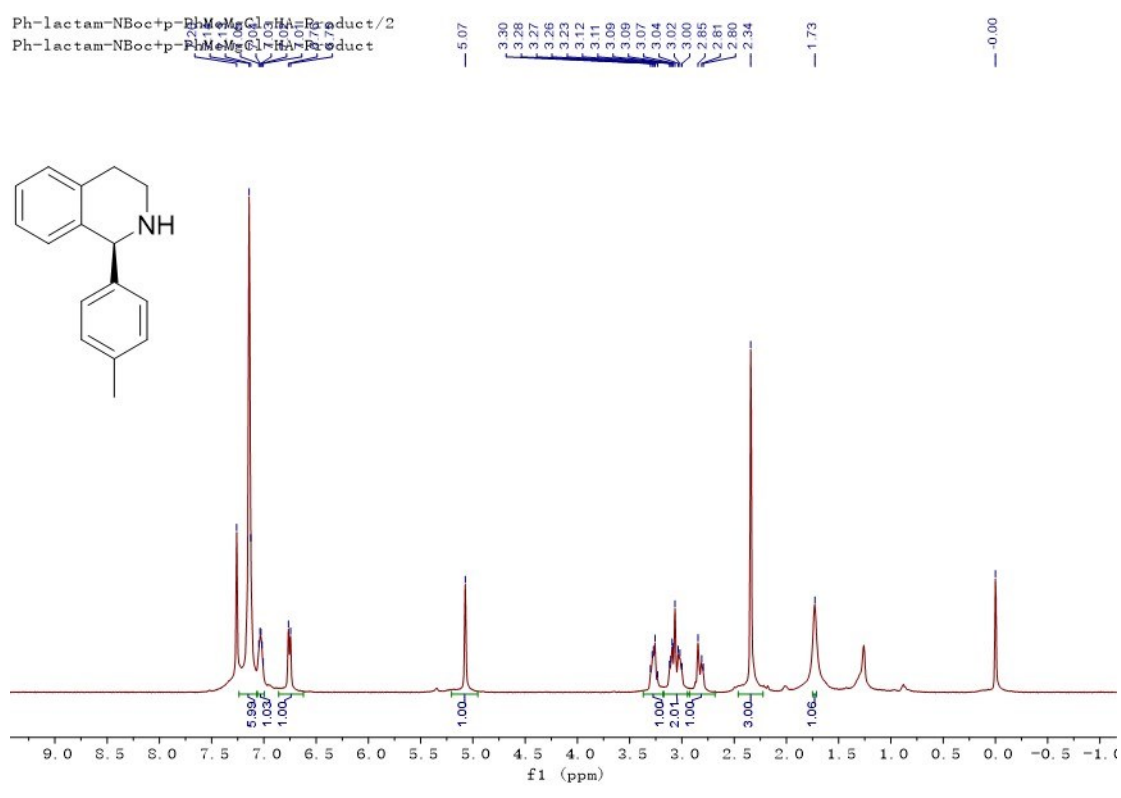
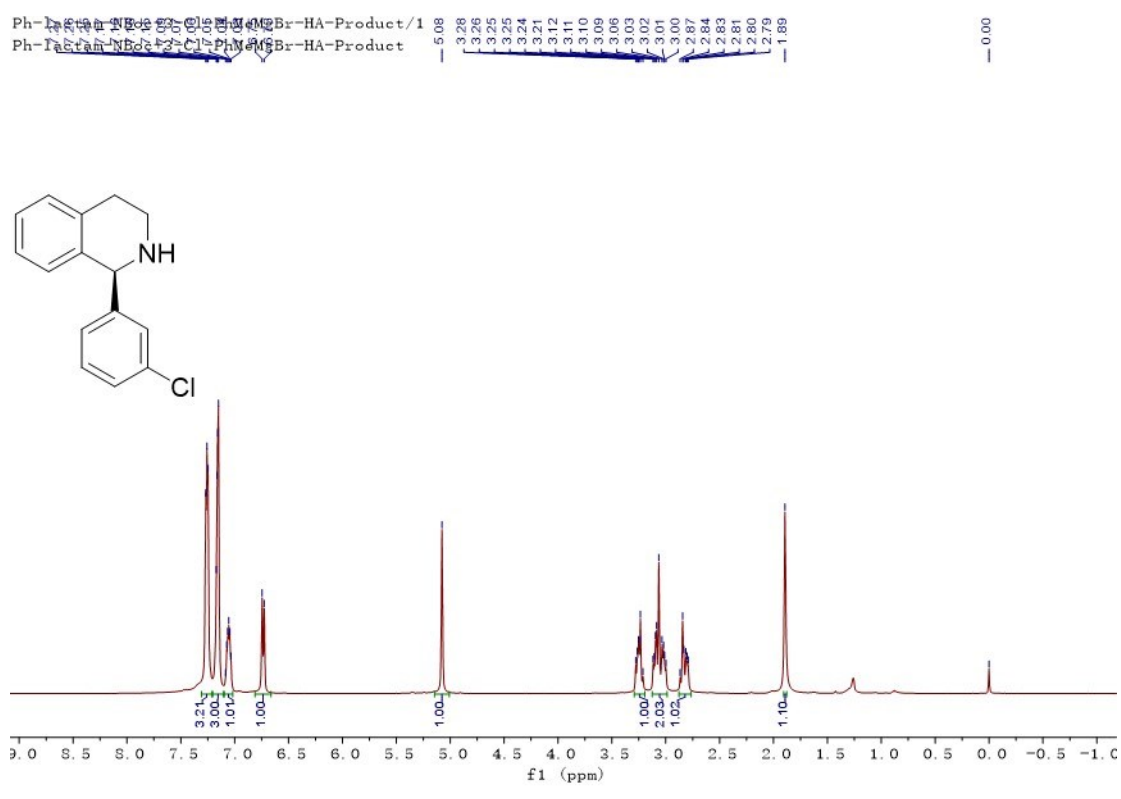


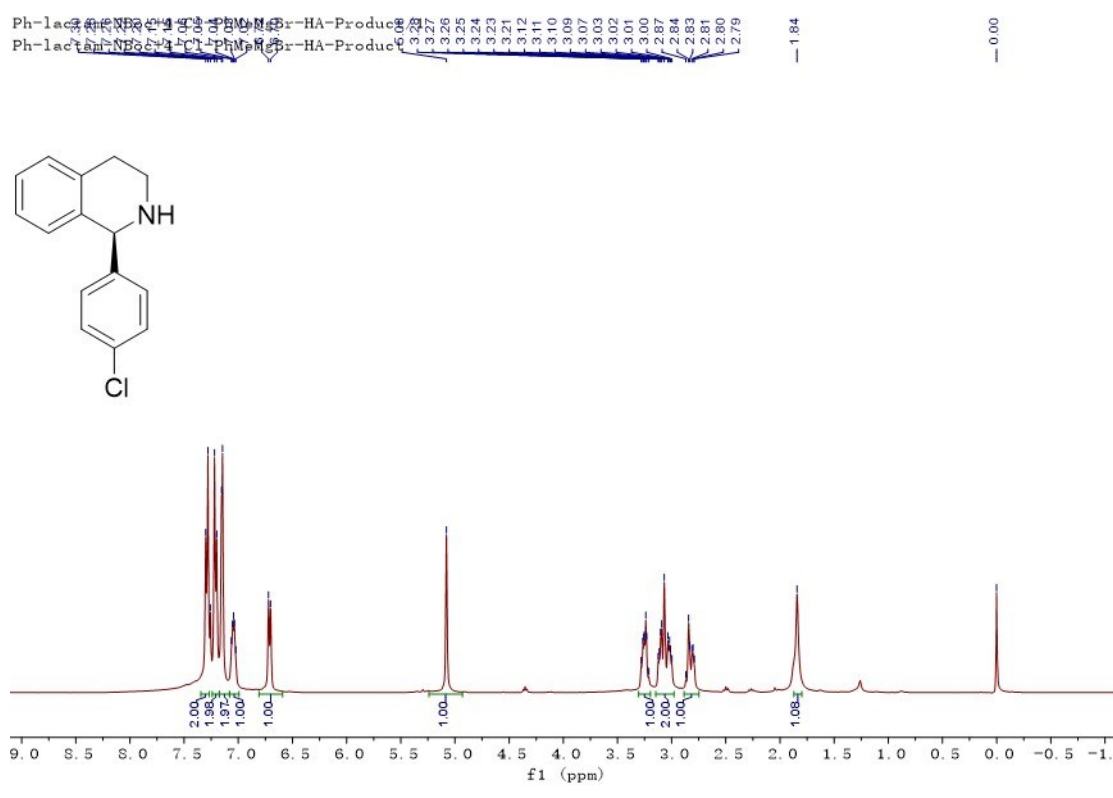
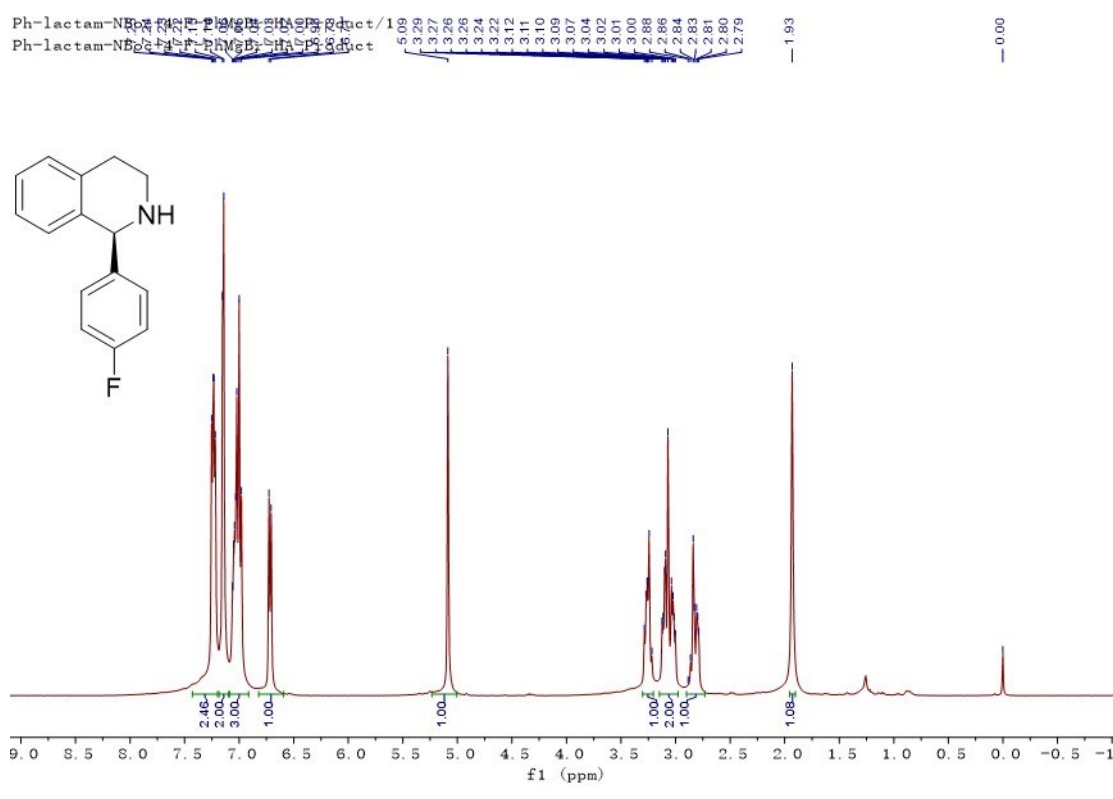
Sample Name: p1f2
 Inj Vol: 0.1
 Data Filename: LRX-2020120502-p.d
 Position: p1f2
 InjPosition: InjPosition
 ACQ Method: 20110418-M5only-p.m
 Instrument Name: Instrument 1
 SampleType: Sample
 Comment:
 User Name: G65208-PC\Admin
 IRM Calibration Status: Success
 Acquired Time: 12/9/2020 11:21:56 AM

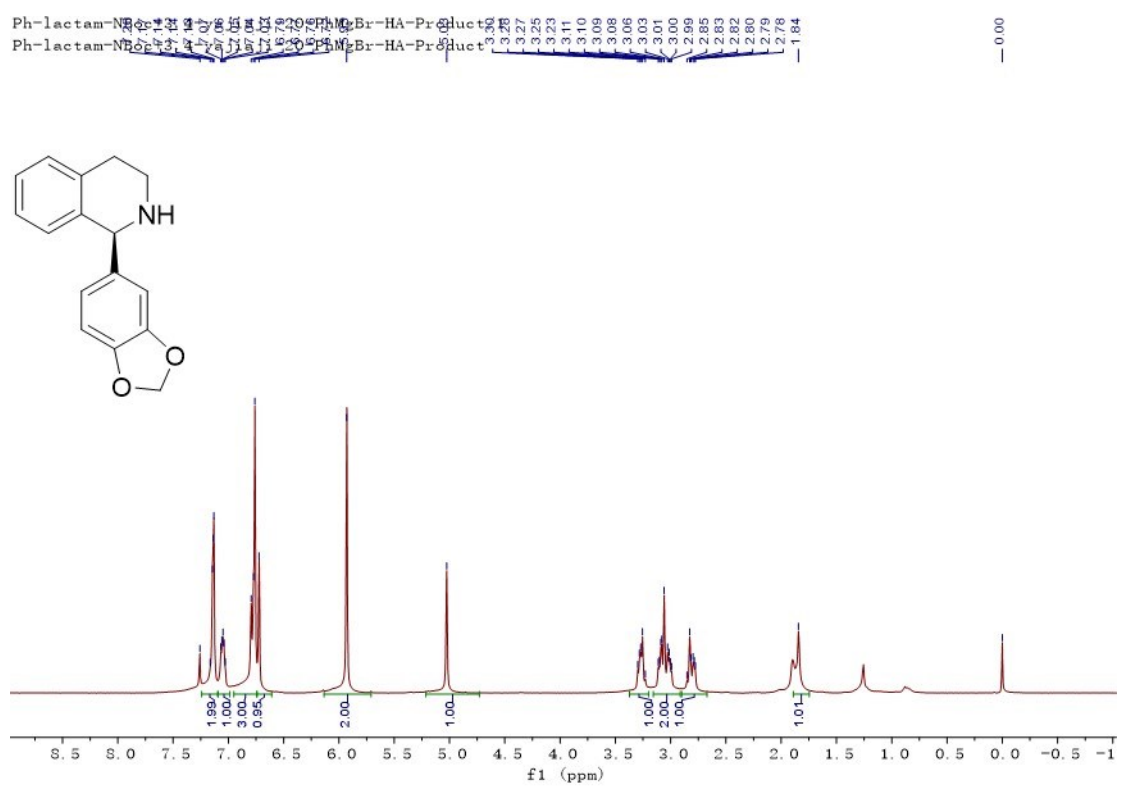
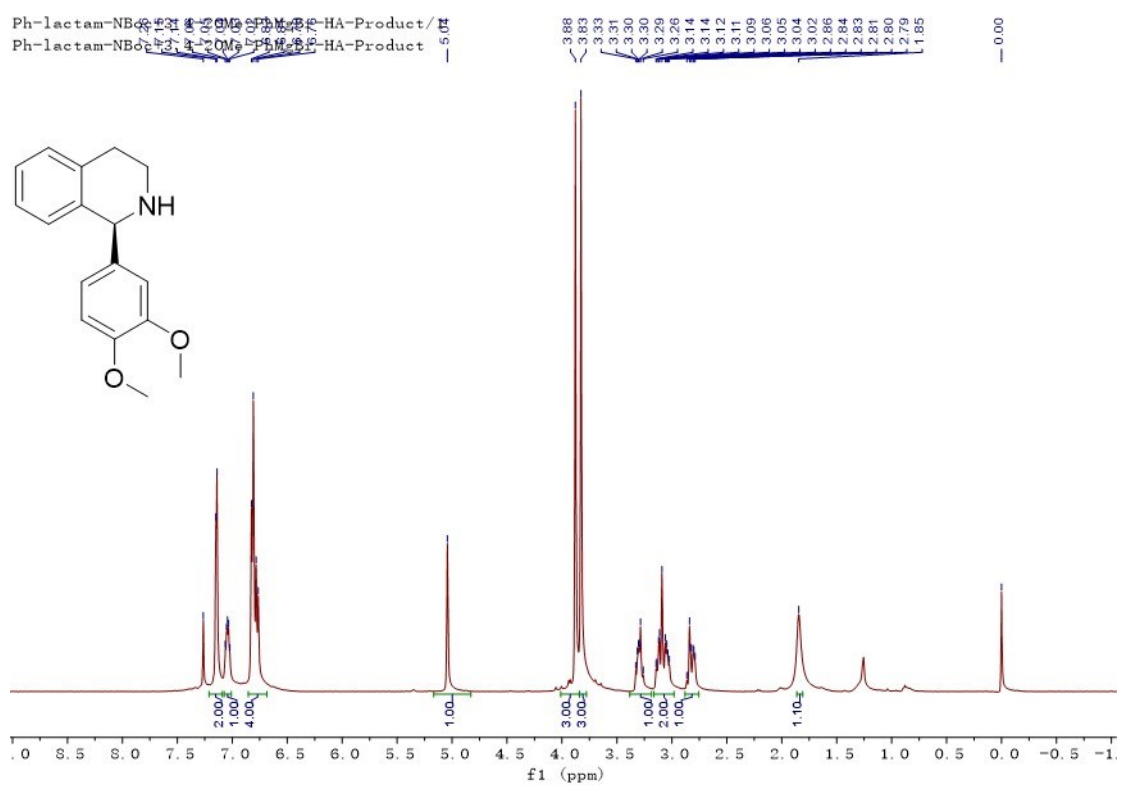


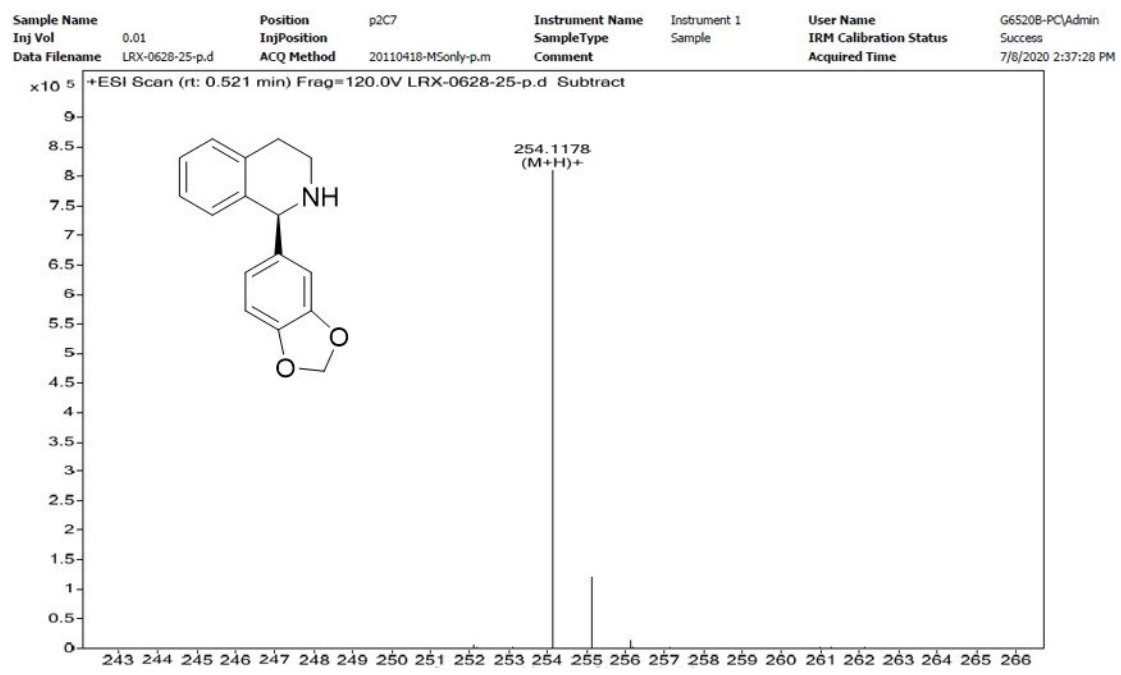
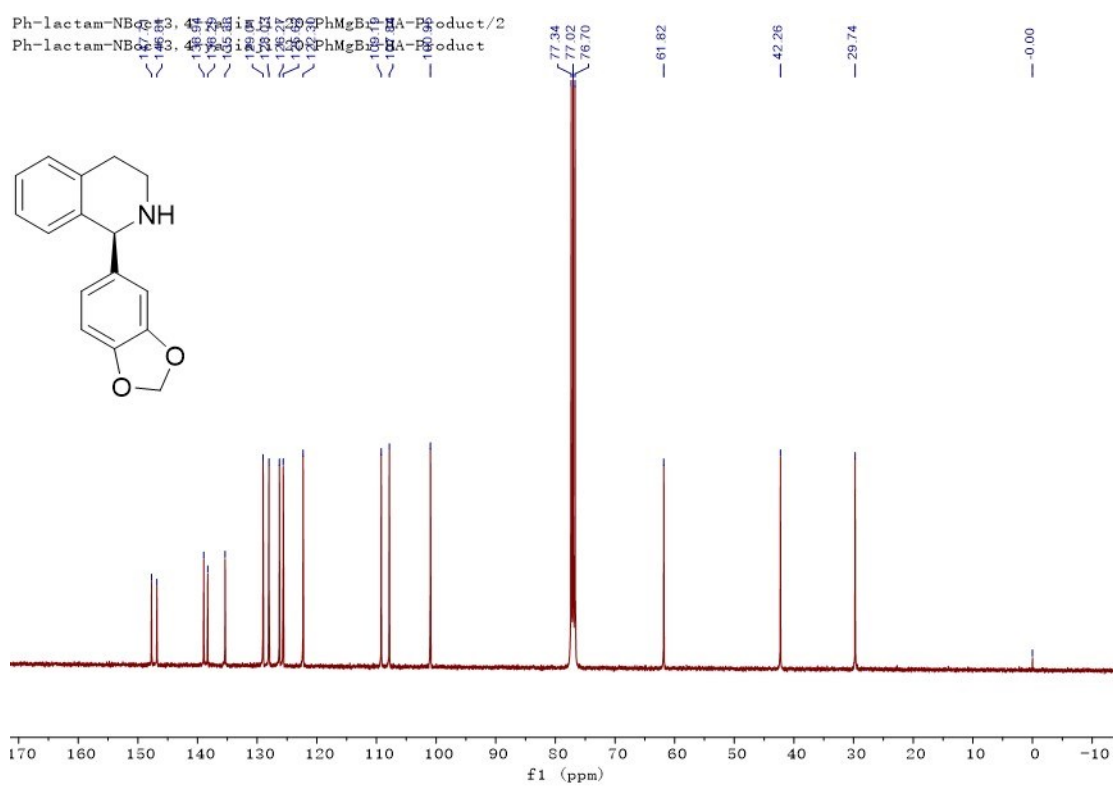


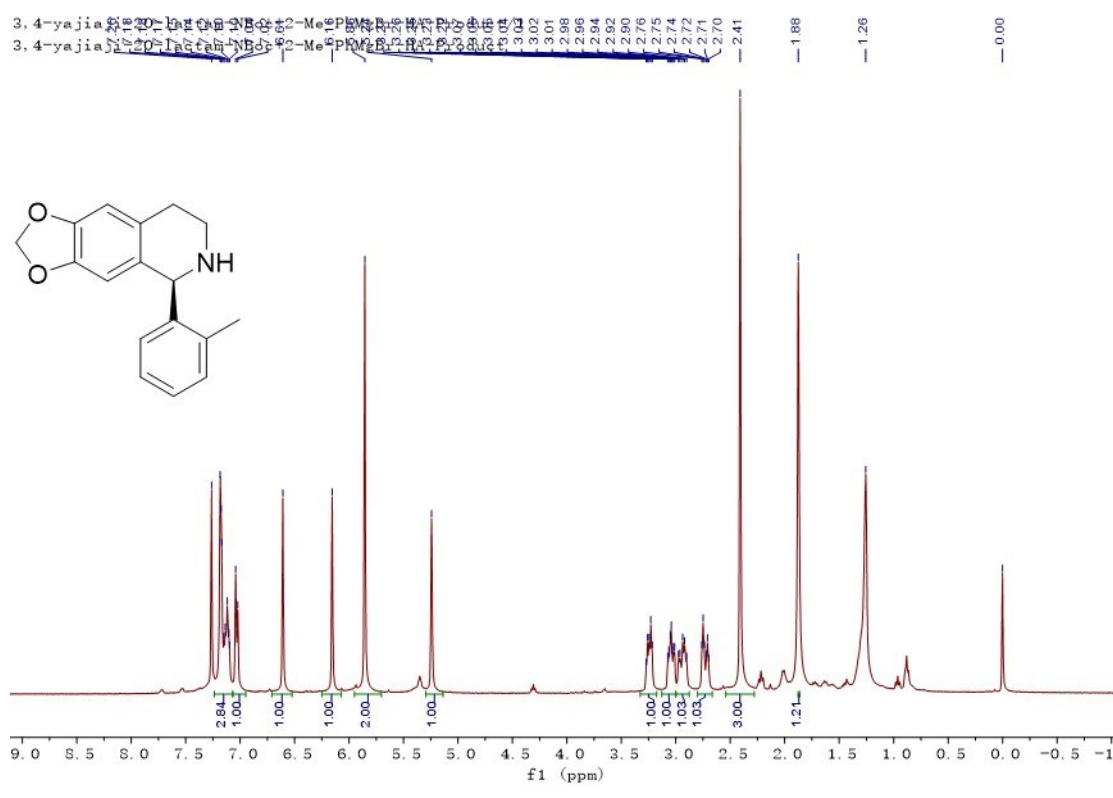
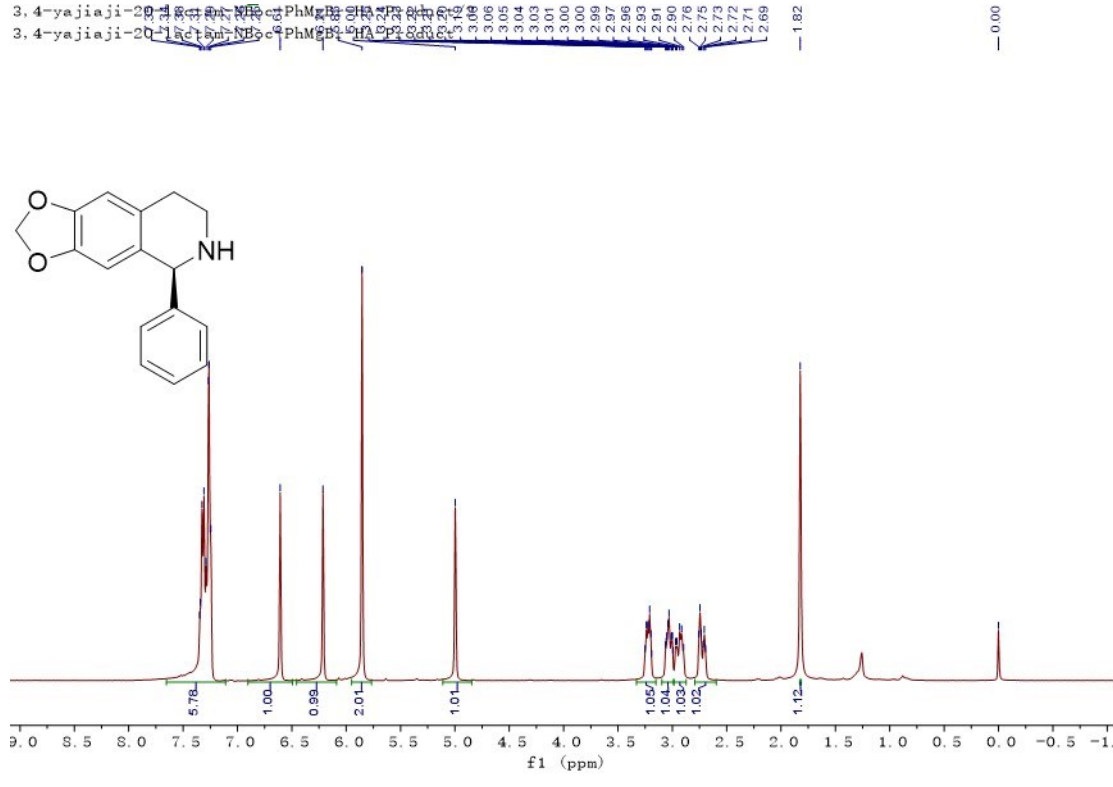


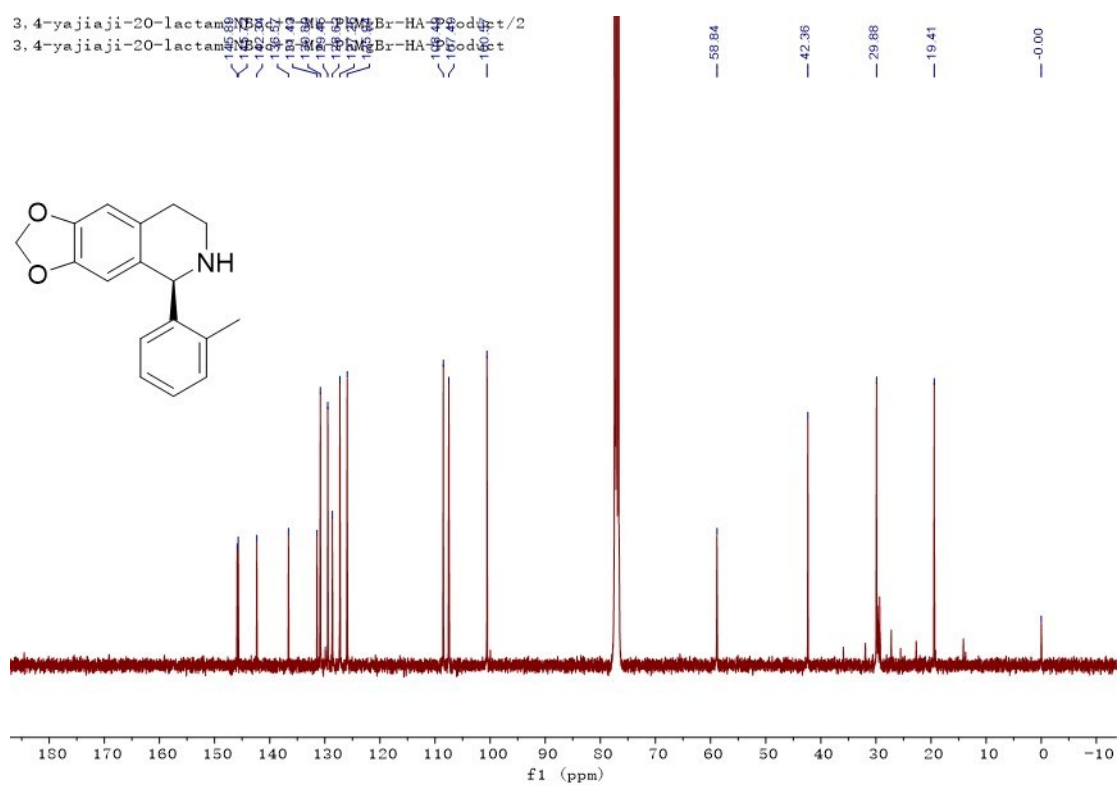




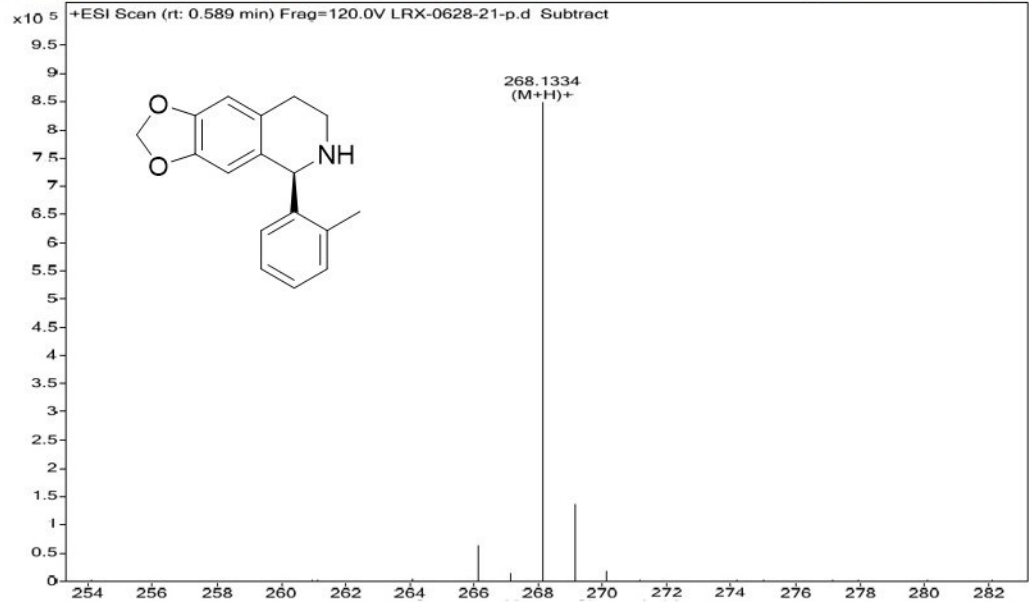




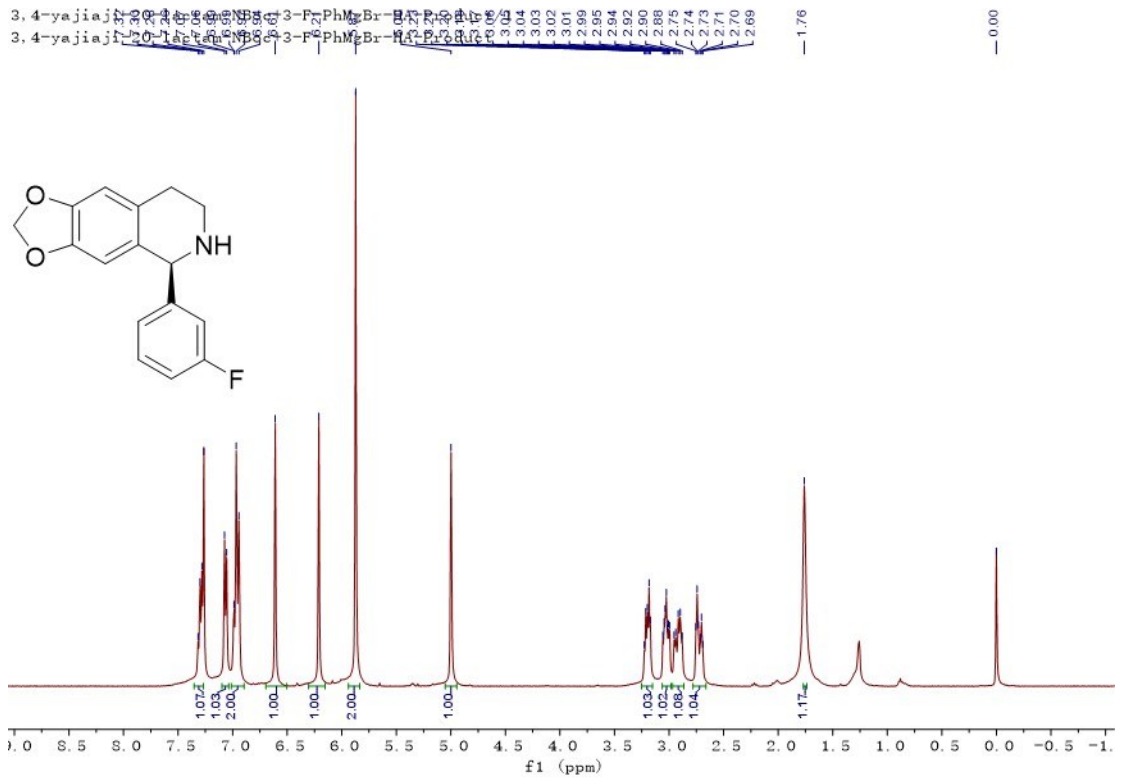
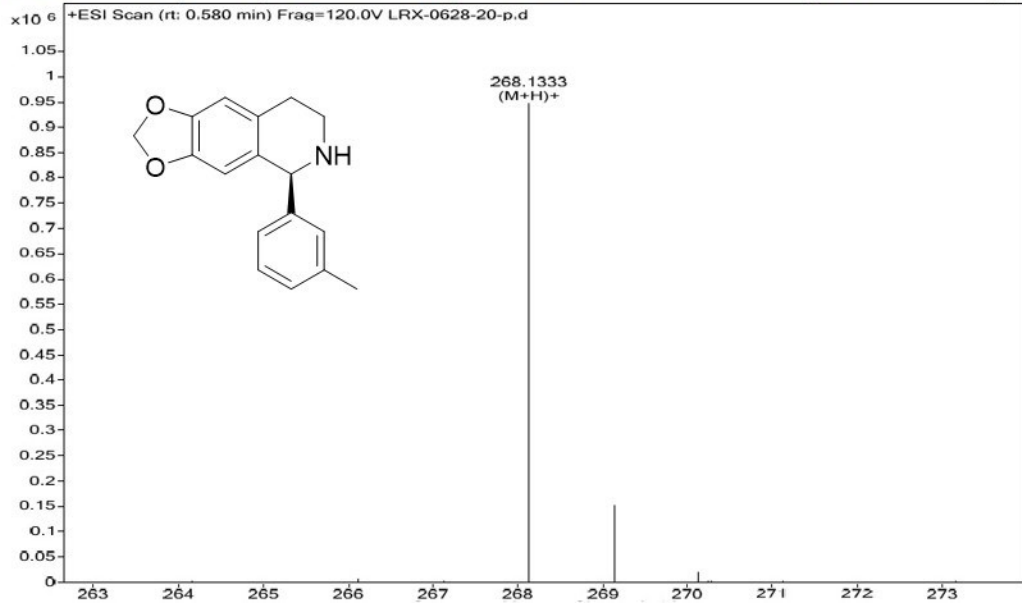


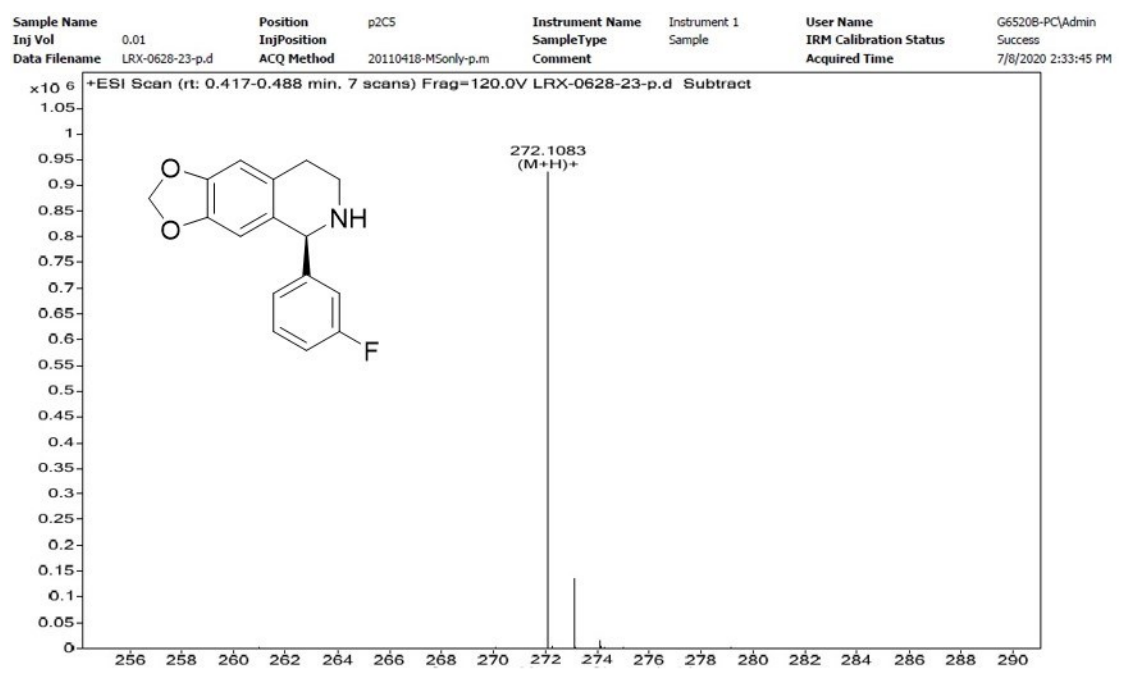
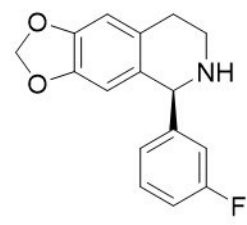
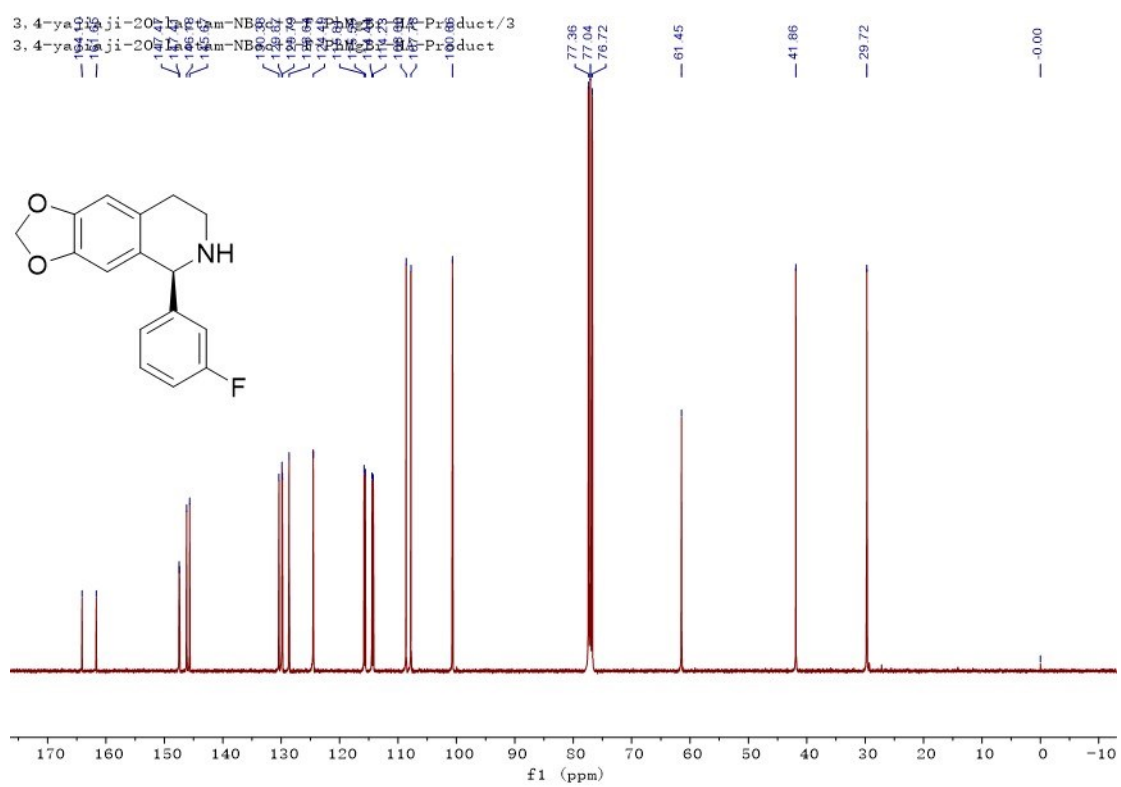


Sample Name	0.01	Position	p2C3	Instrument Name	Instrument 1	User Name	G6520B-PC\Admin
Inj Vol		InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	LRX-0628-21-p.d	ACQ Method	20110418-M5only-p.m	Comment		Acquired Time	7/8/2020 2:29:18 PM

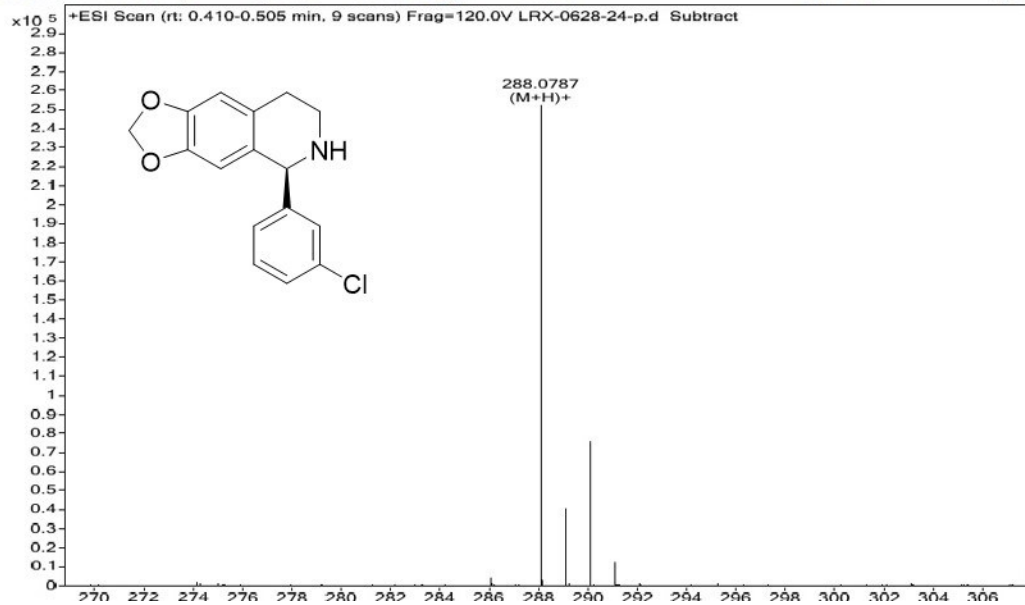


Sample Name	0.01	Position	p2C2	Instrument Name	Instrument 1	User Name	G65208-PC\Admin
Inj Vol	LRX-0628-20-p.d	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename		ACQ Method	20110418-M5only-p.m	Comment		Acquired Time	7/8/2020 2:26:34 PM

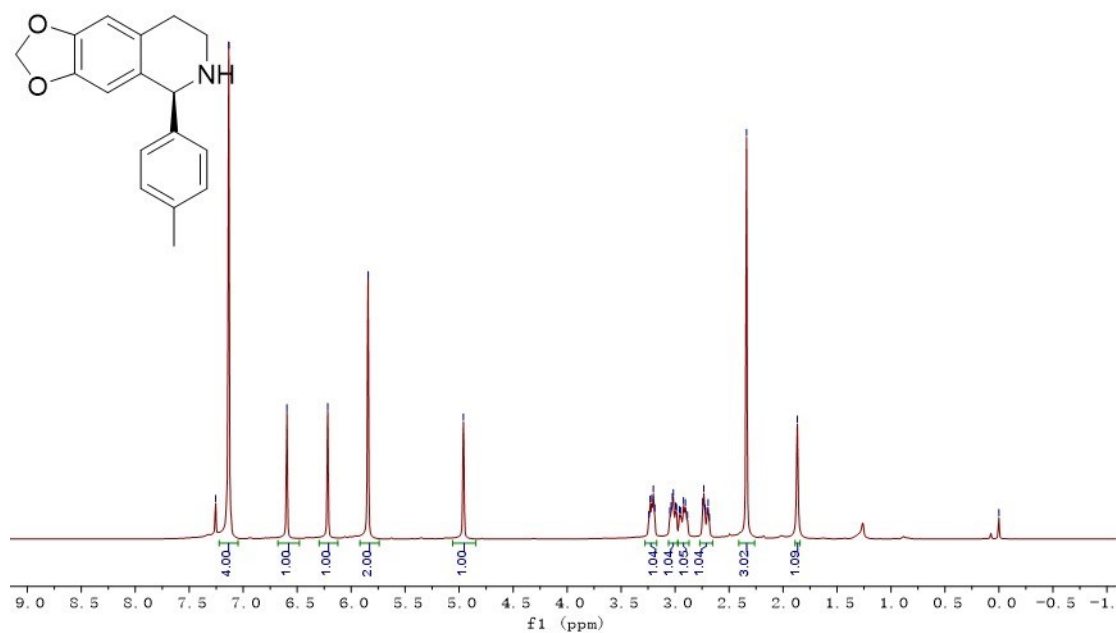


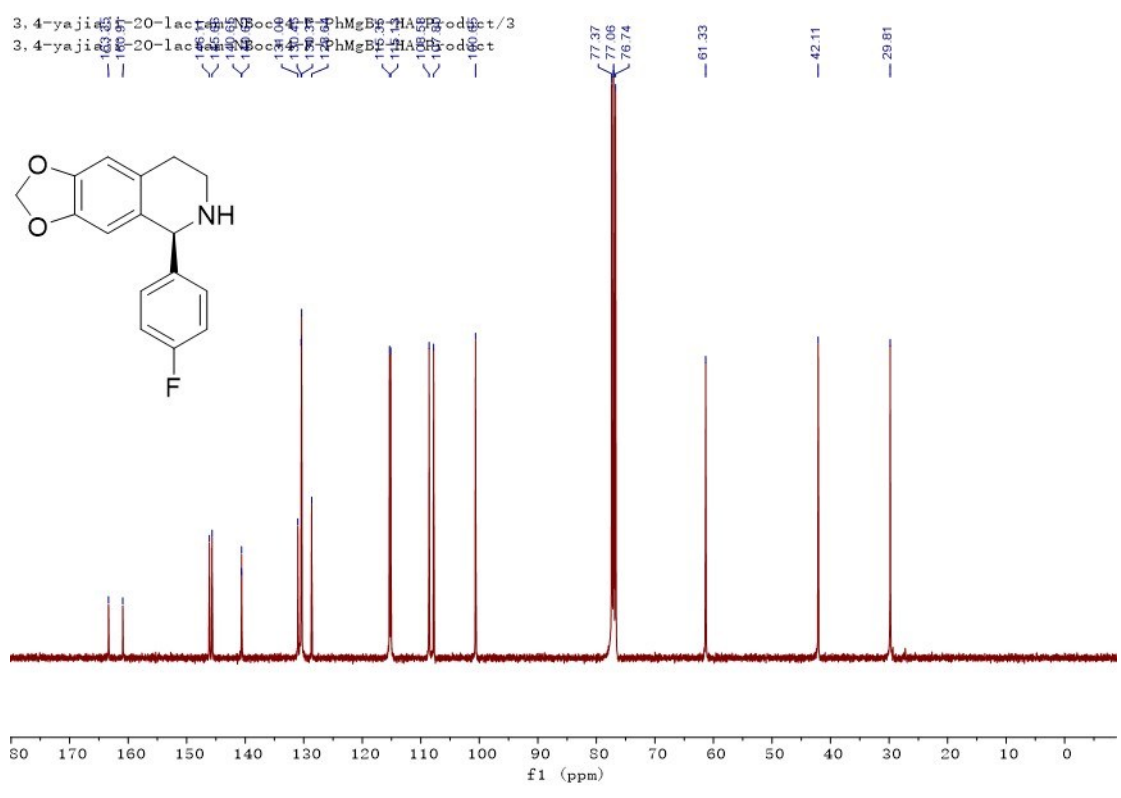
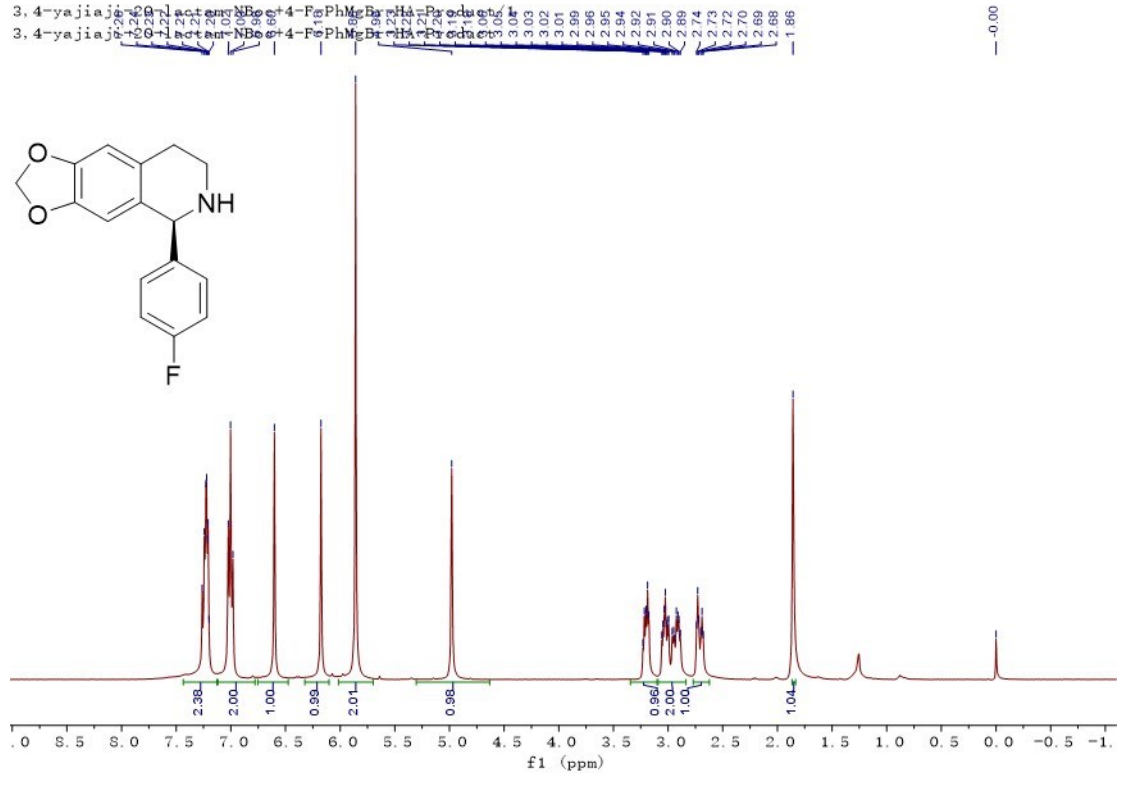


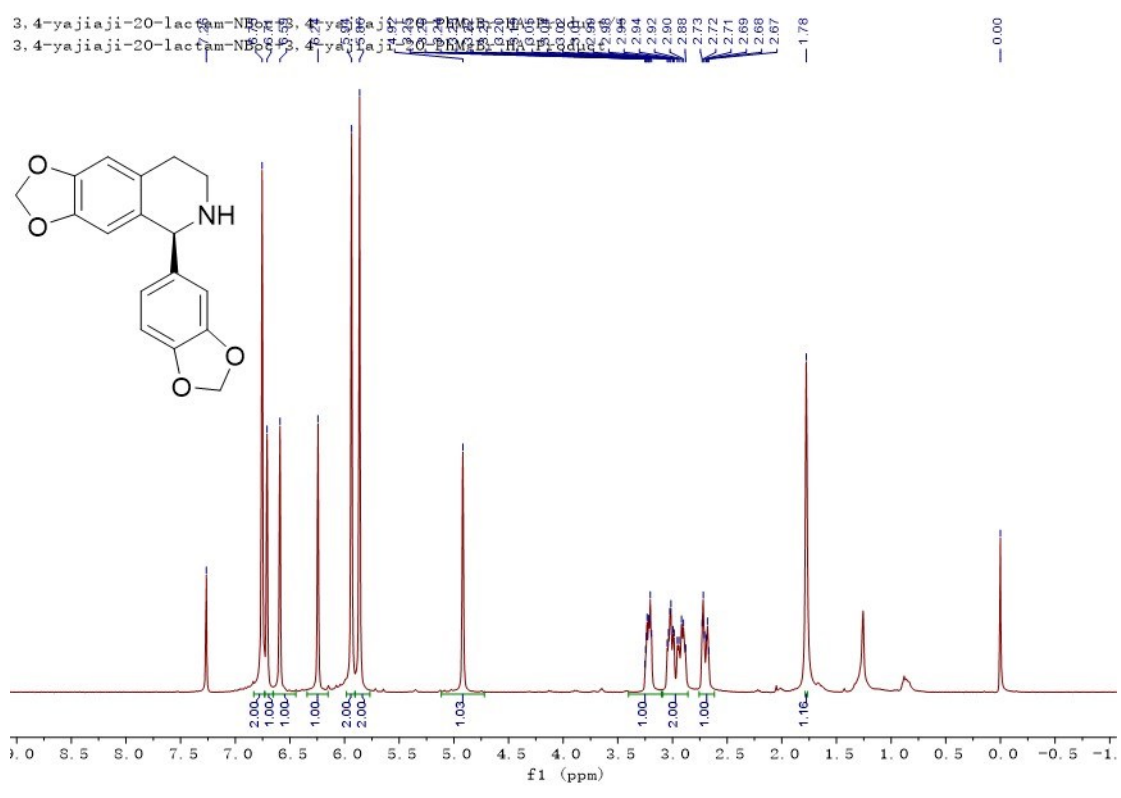
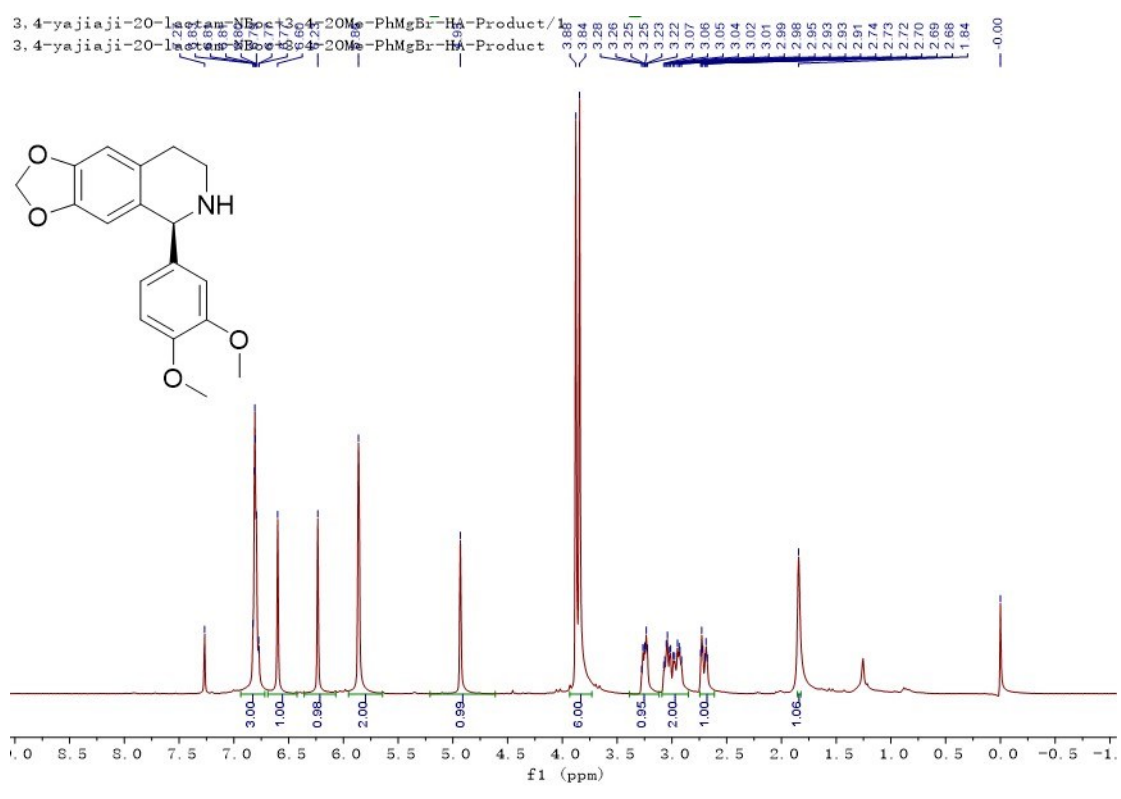
Sample Name	0.01	Position	p2C6	Instrument Name	Instrument 1	User Name	G65208-PC\Admin
Inj Vol	0.01	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	LRX-0628-24-p.d	ACQ Method	20110418-M5only-p.m	Comment		Acquired Time	7/8/2020 2:35:40 PM

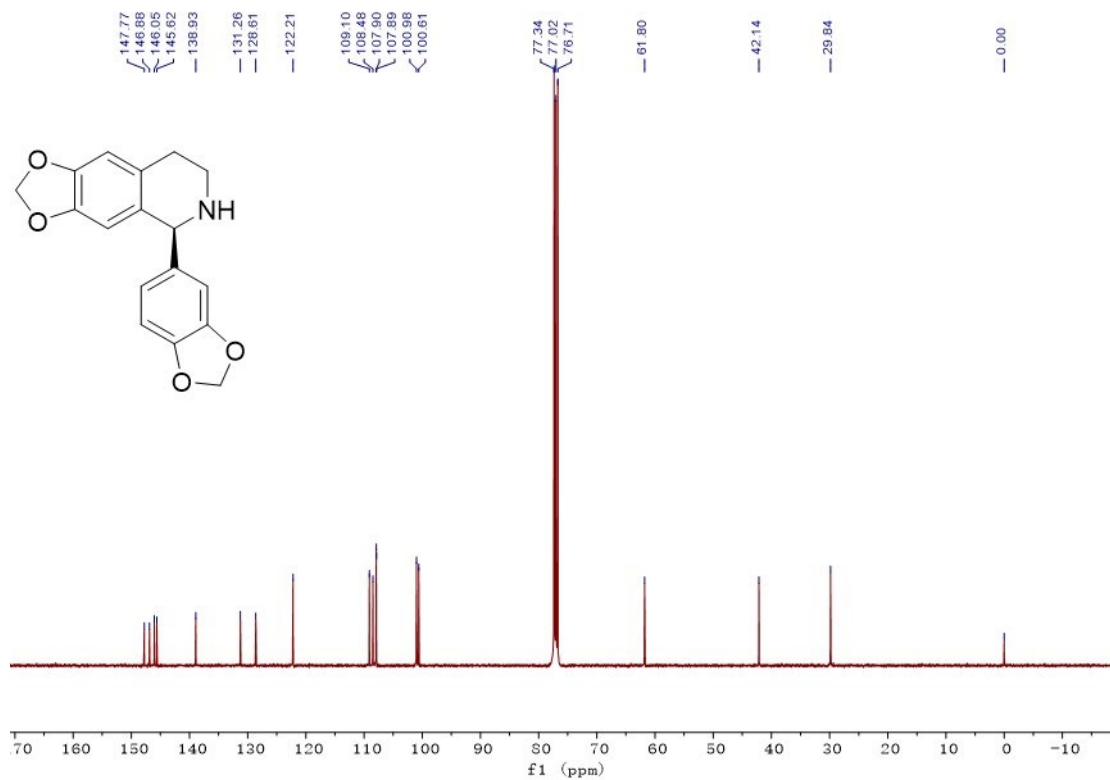


3.4-yajiaji-20-lactam-NBoc-p-MePhMeCl-HA-Product
 3.4-yajiaji-20-lactam-NBoc-p-MePhMeCl-HA-Product

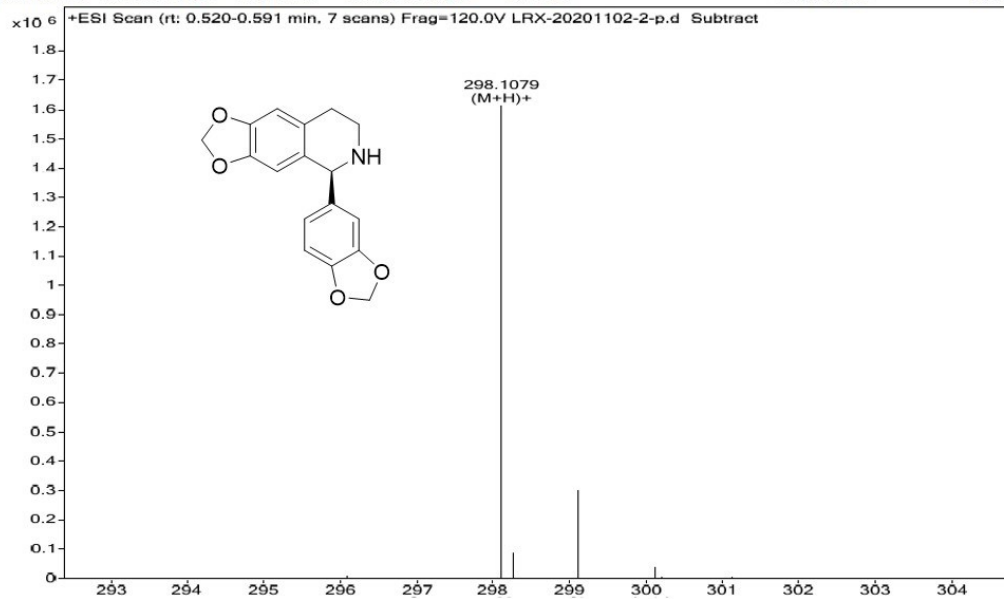




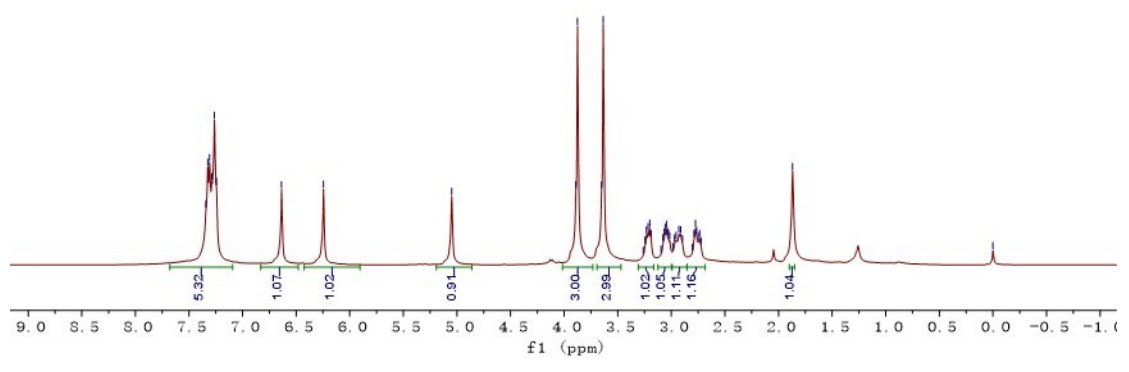
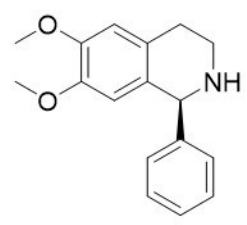




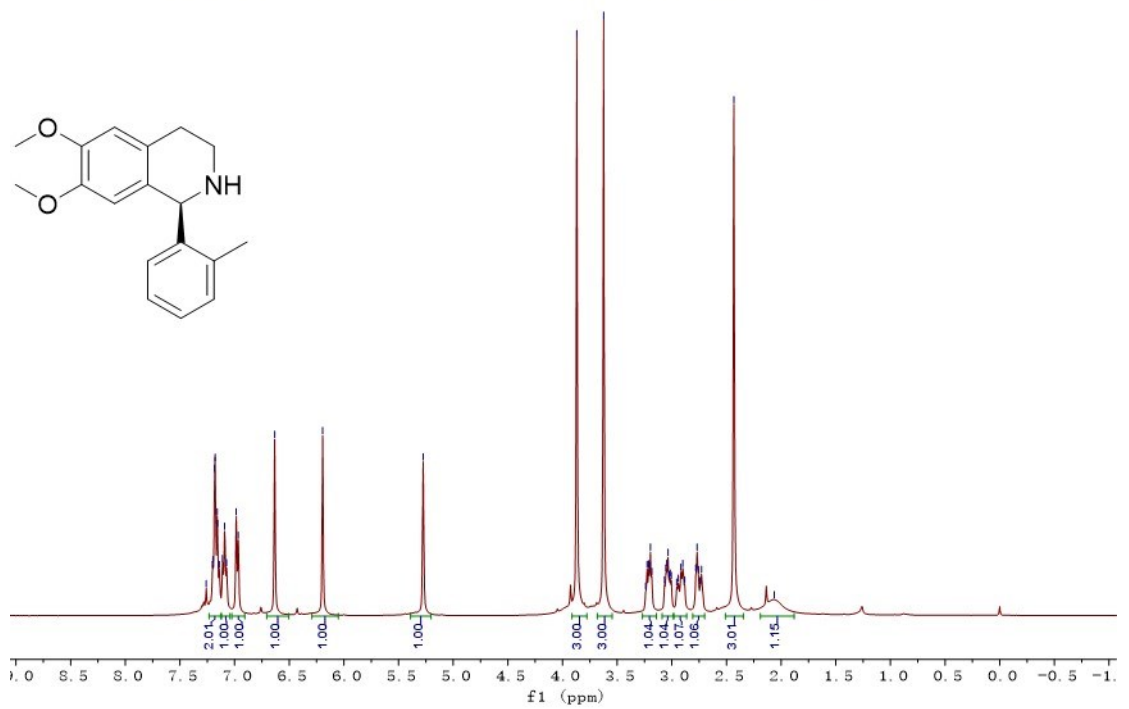
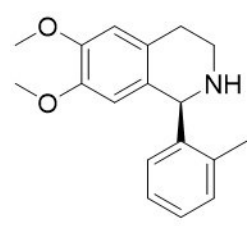
Sample Name	Position	Instrument Name	User Name
Inj Vol	p1C3	Instrument 1	G6520B-PC\Admin
Data Filename	ACQ Method	Sample	IRM Calibration Status
LRX-20201102-2-p.d	20110418-M5only-p.m		Success
			Acquired Time
			11/5/2020 1:44:07 PM

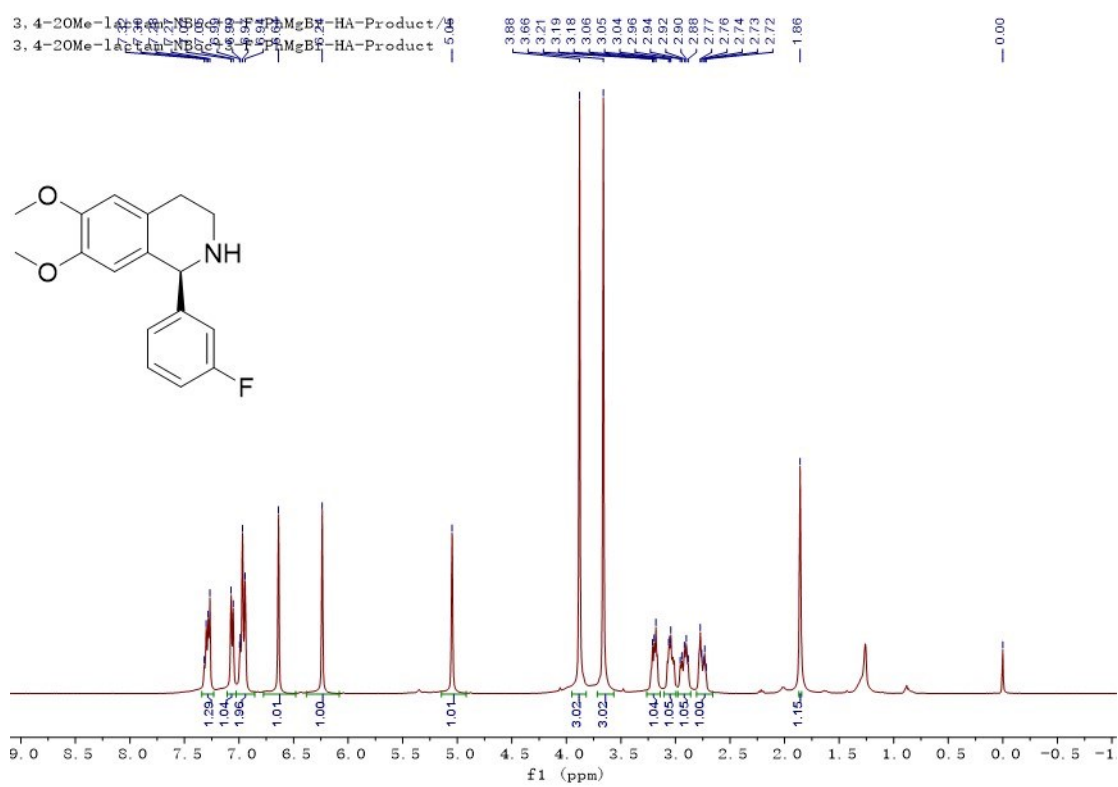
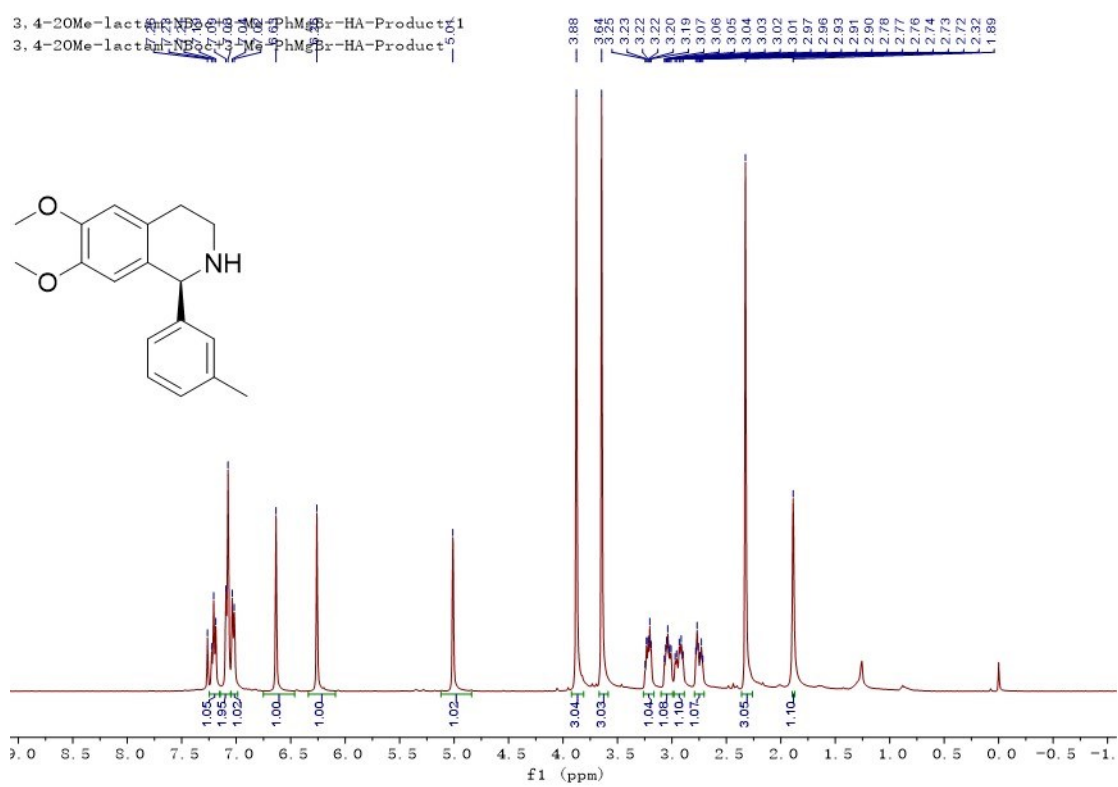


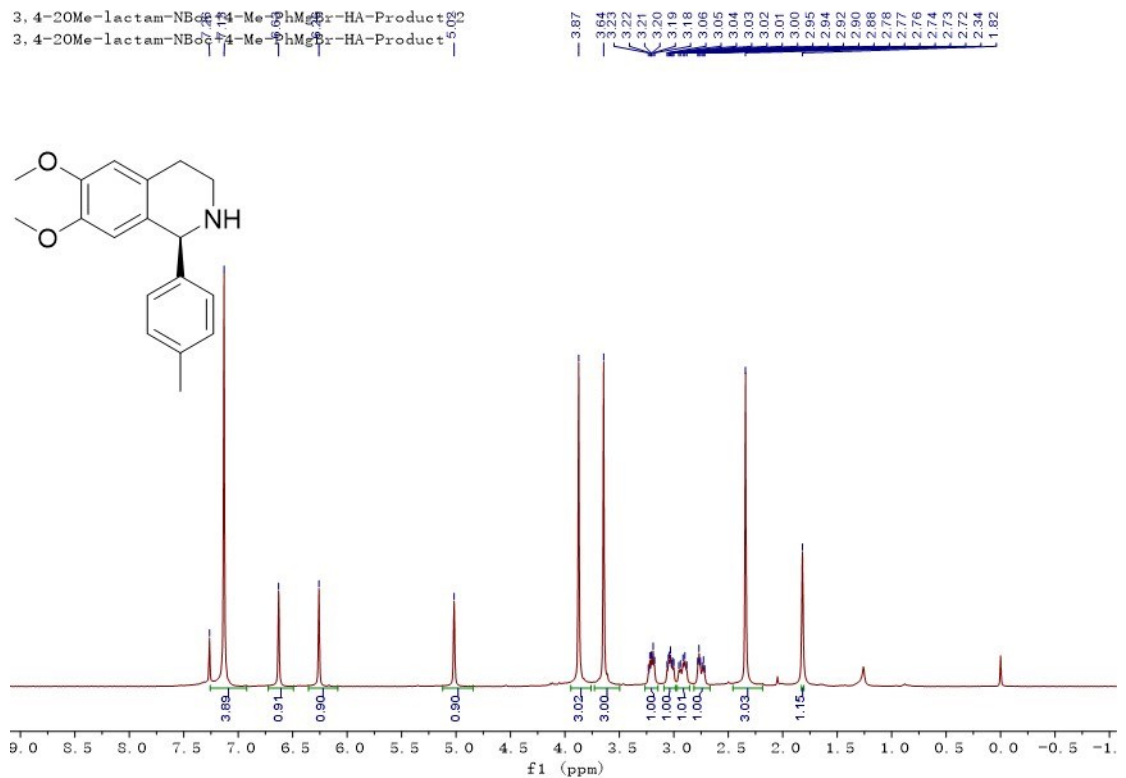
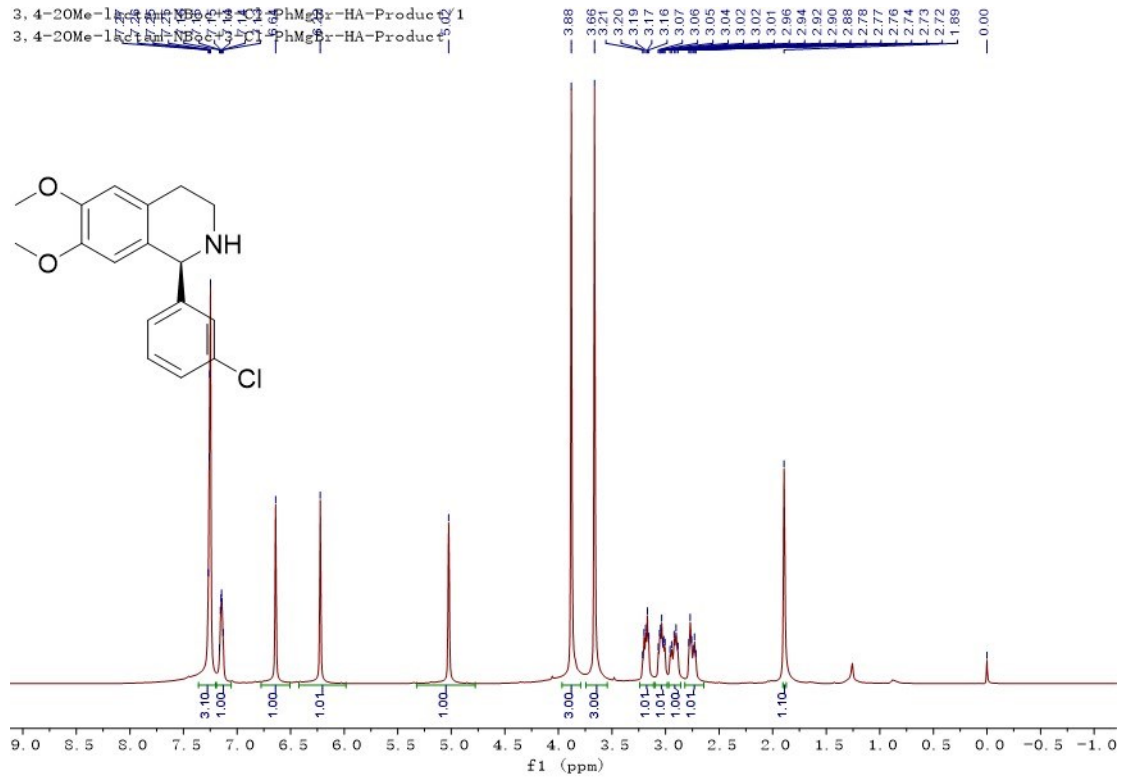
3,4-2OMe-lactam-NB-5-Ph-1-MgBr-HA-Product/2
 3,4-2OMe-lactam-NB-5-Ph-1-MgBr-HA-Product

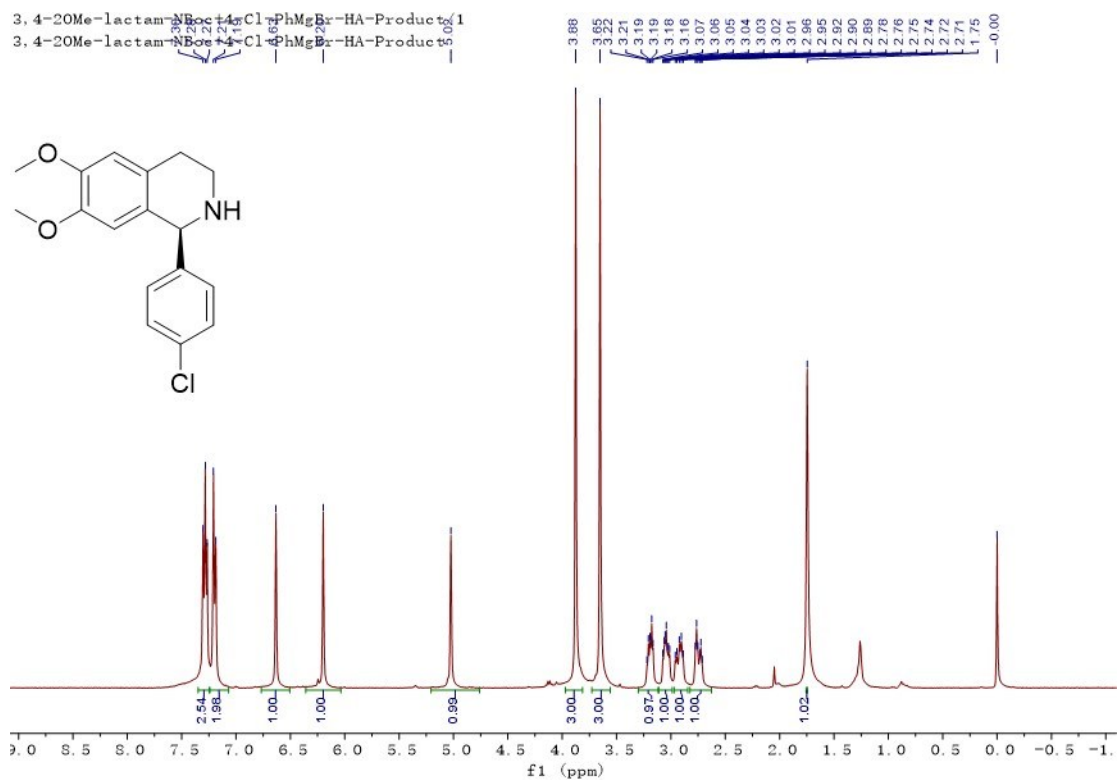
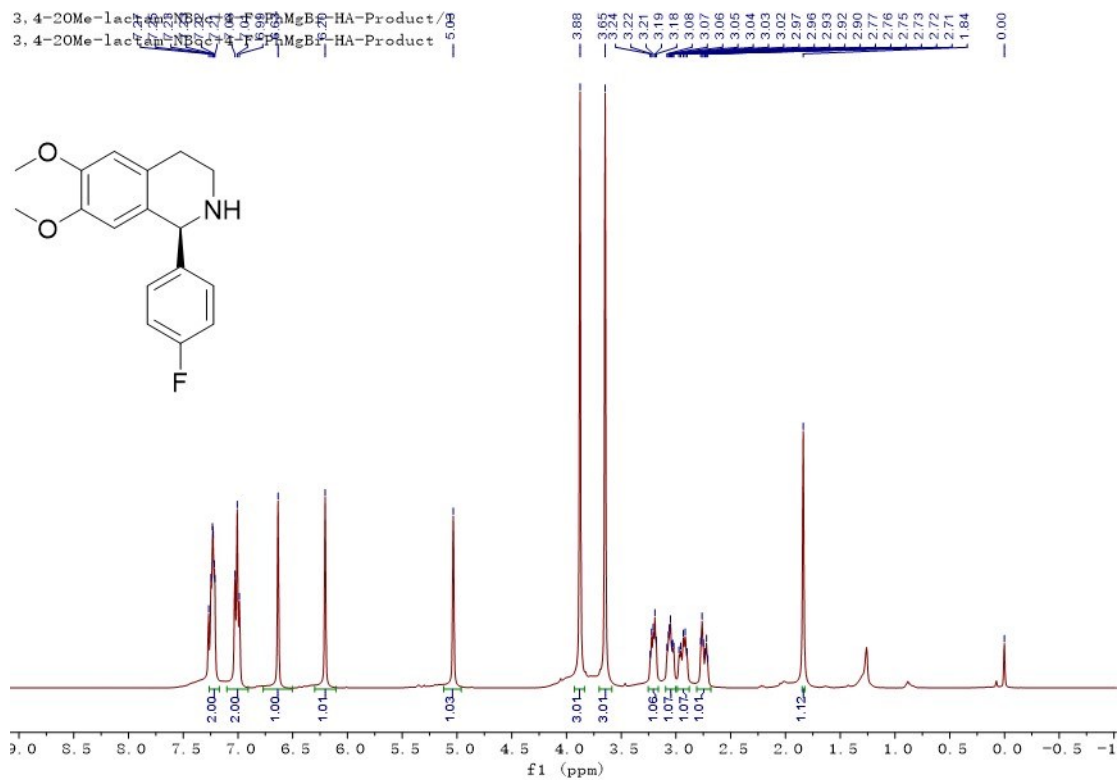


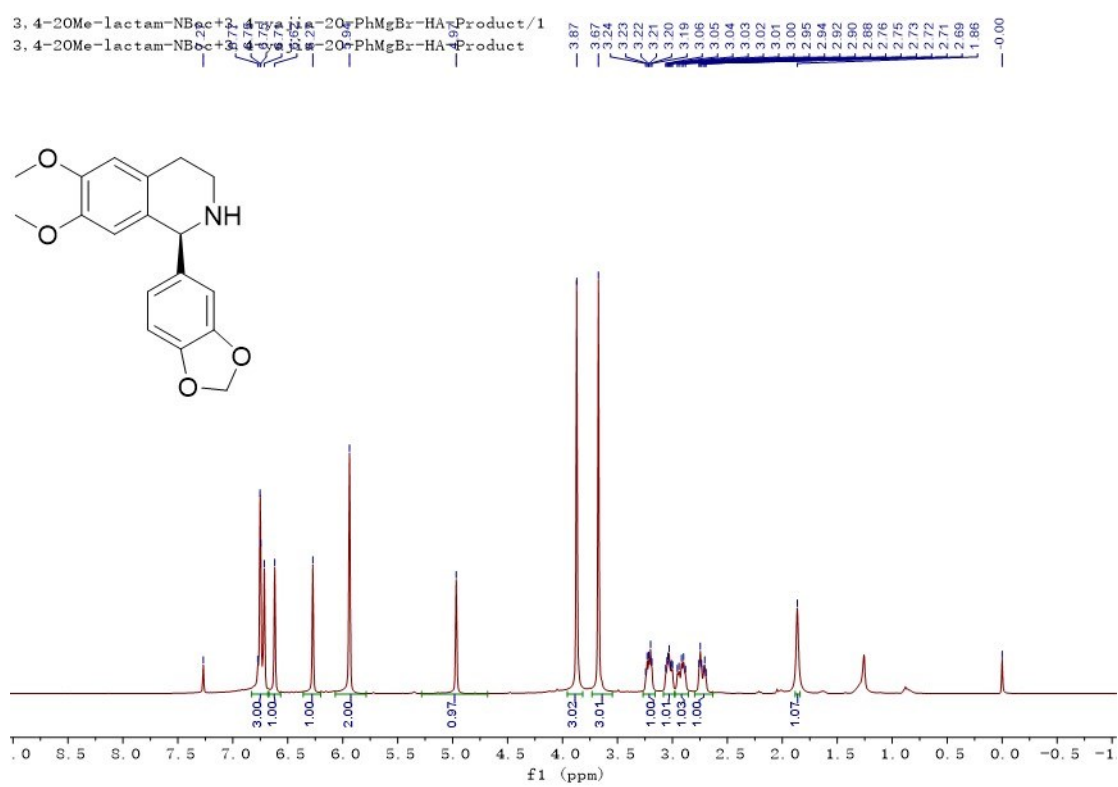
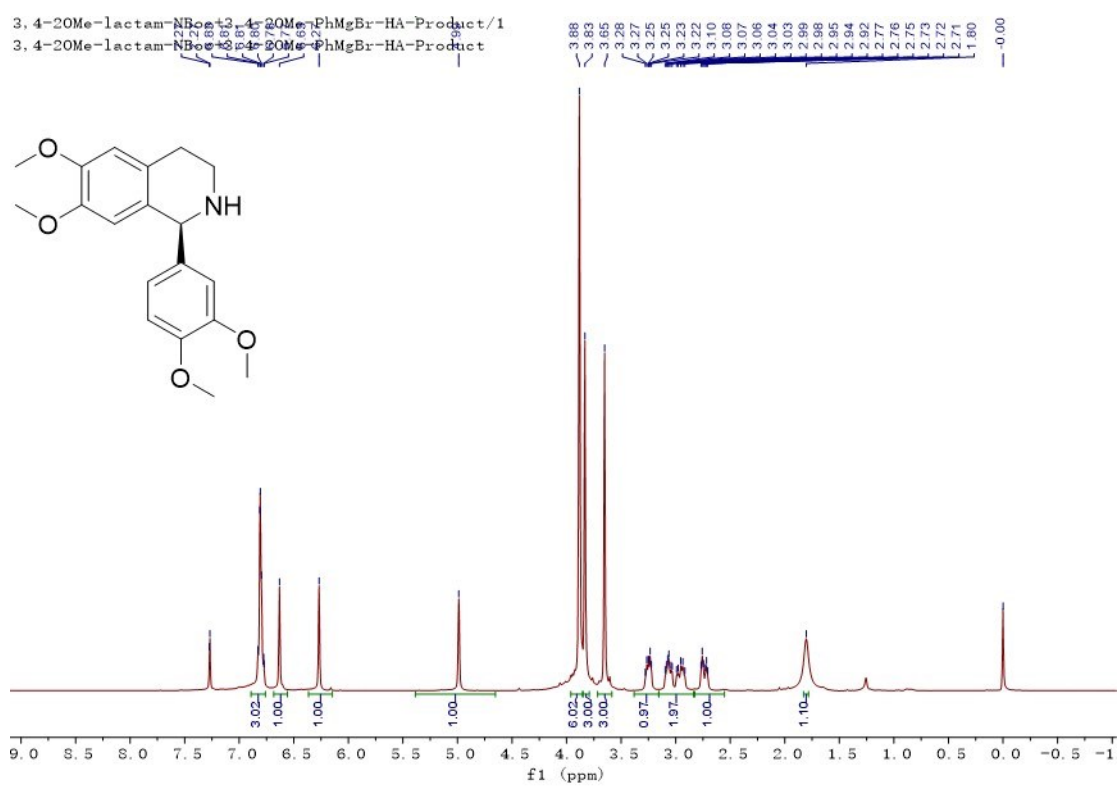
3,4-2OMe-lactam-NB-5-Ph-1-MgBr-HA-Product/1
 3,4-2OMe-lactam-NB-5-Ph-1-MgBr-HA-Product

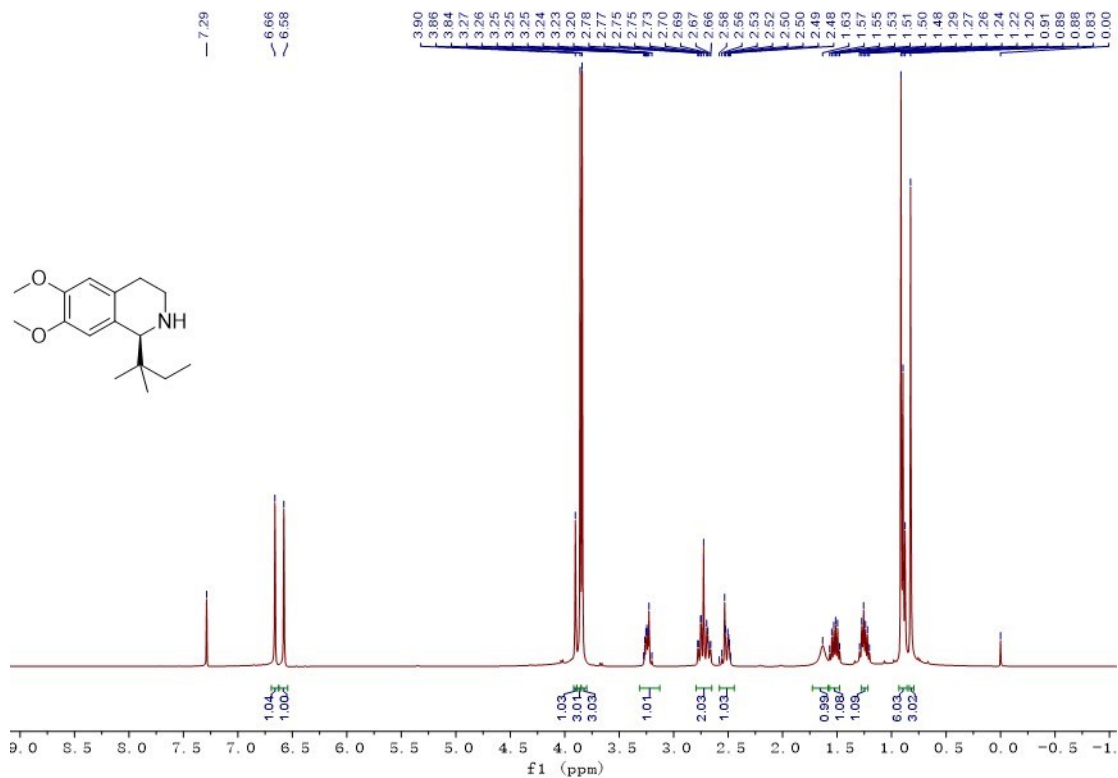
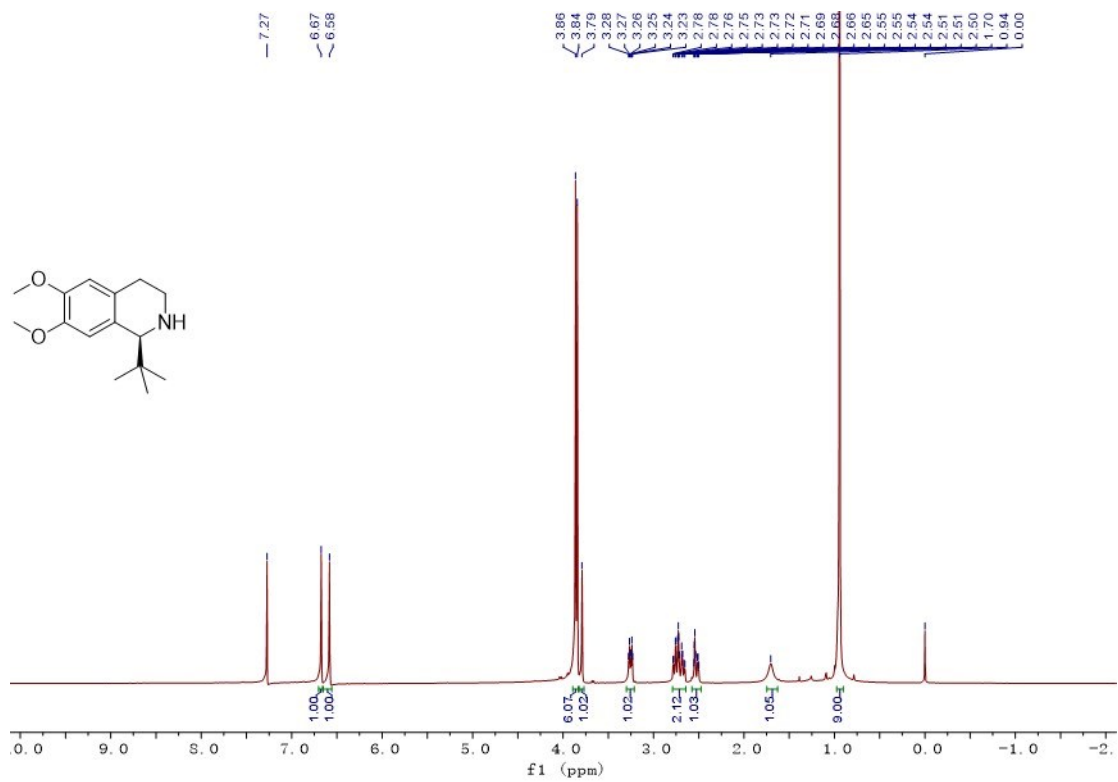


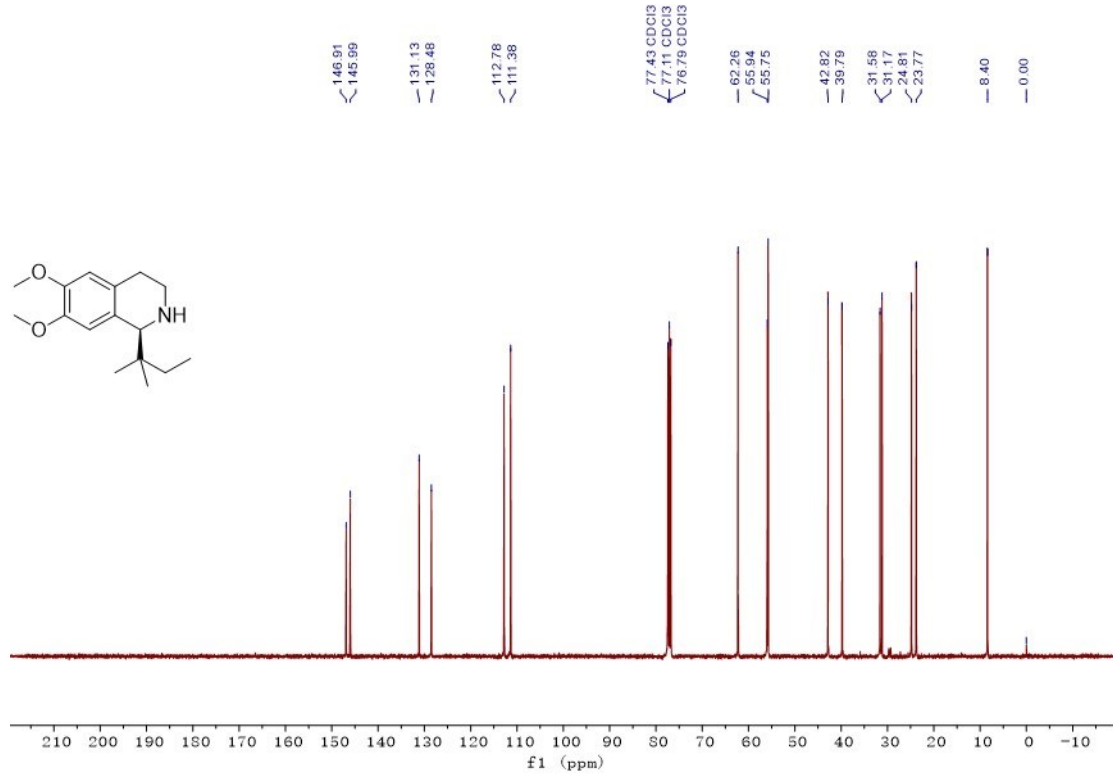








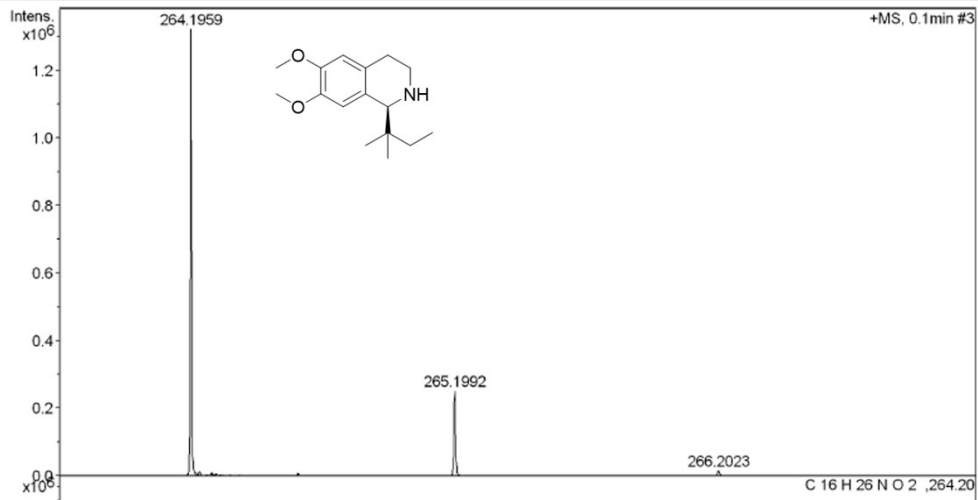


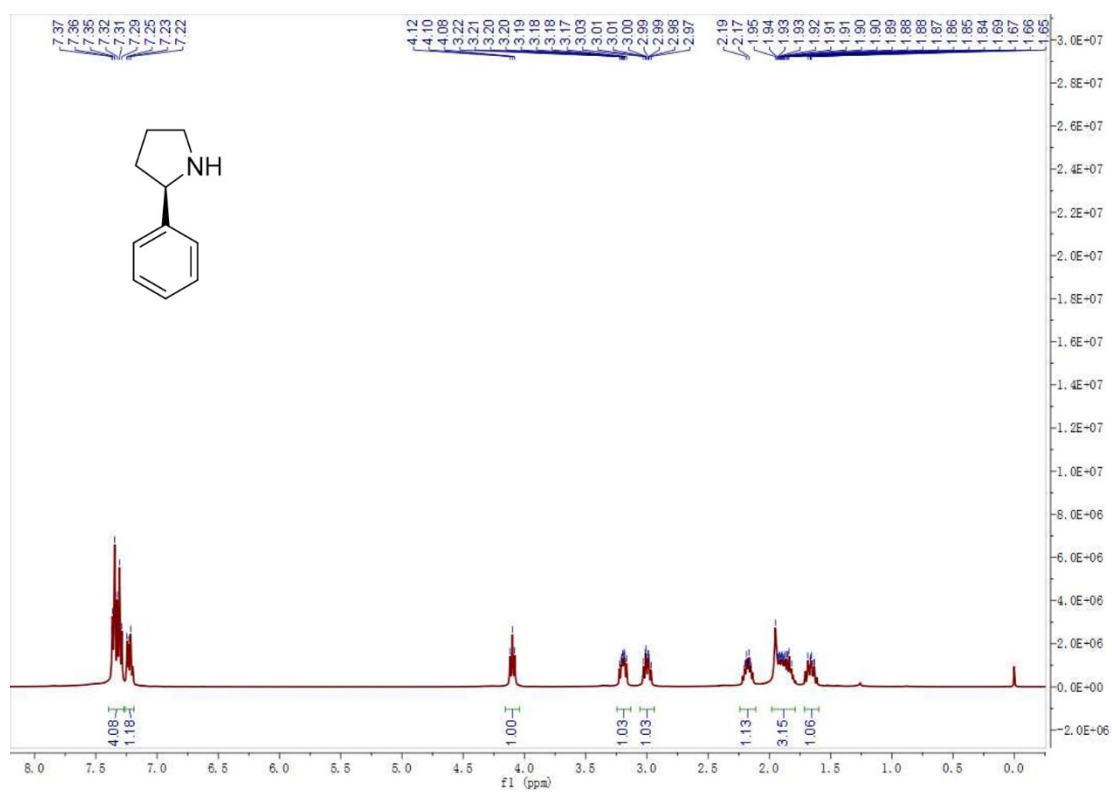


Display Report

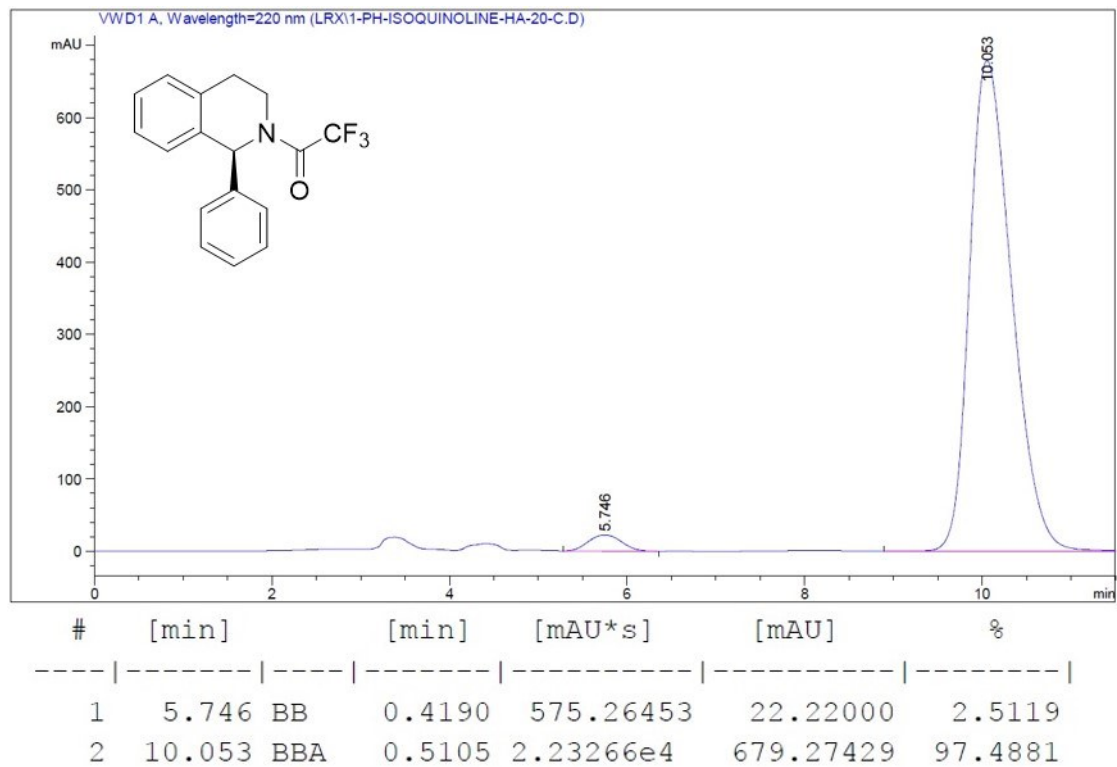
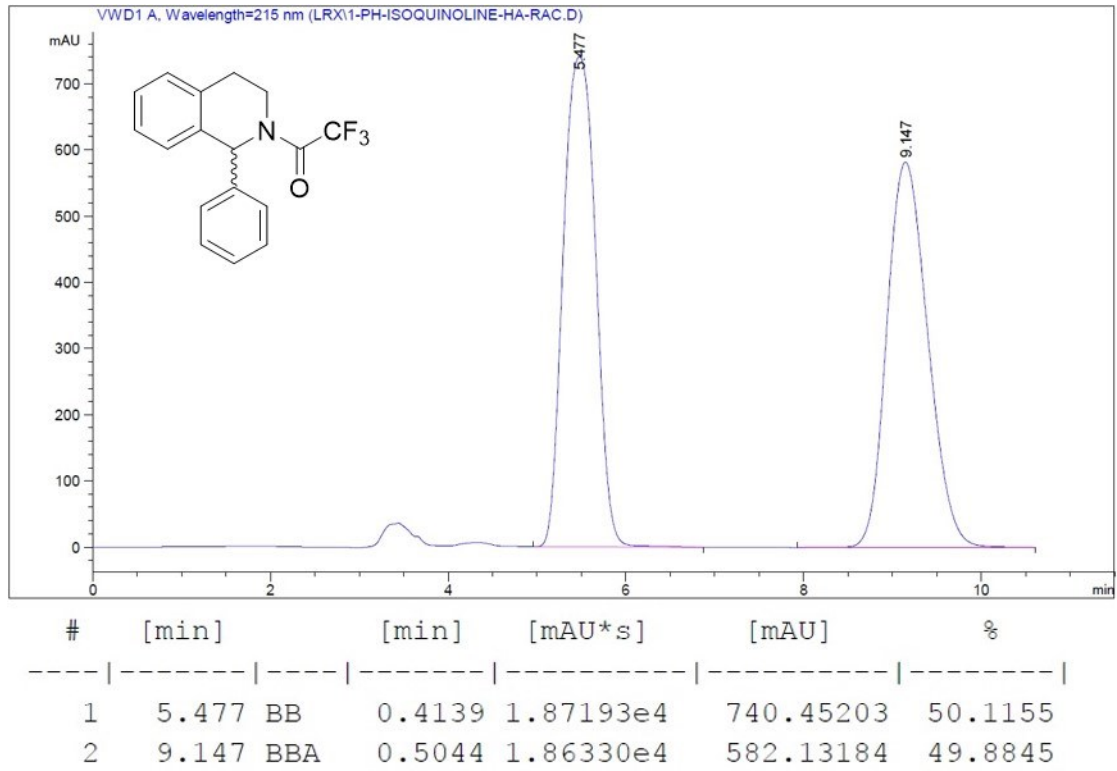
Analysis Info		Acquisition Date	
Analysis Name	D:\Data\2020\12\10\20201209-3.d	12/10/2020 10:56:35 AM	
Method	pos_low-20151116.m	Operator	Fan
Sample Name	niehuifang	Instrument	maXis 10103
Comment			

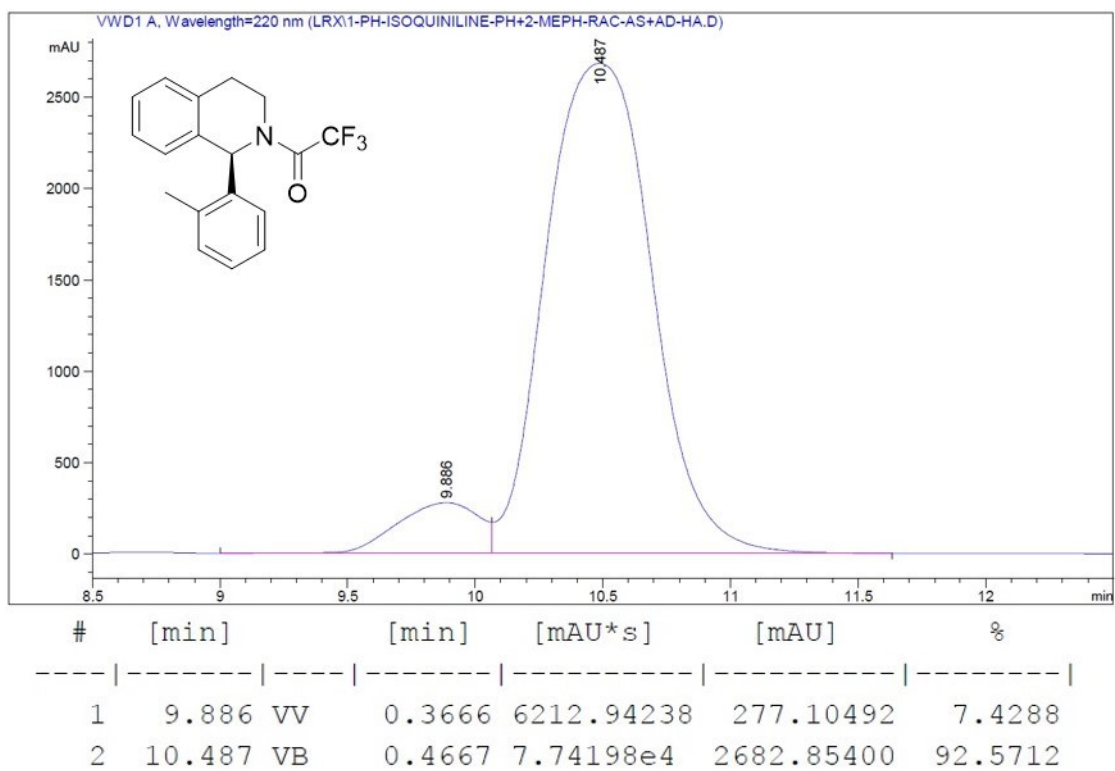
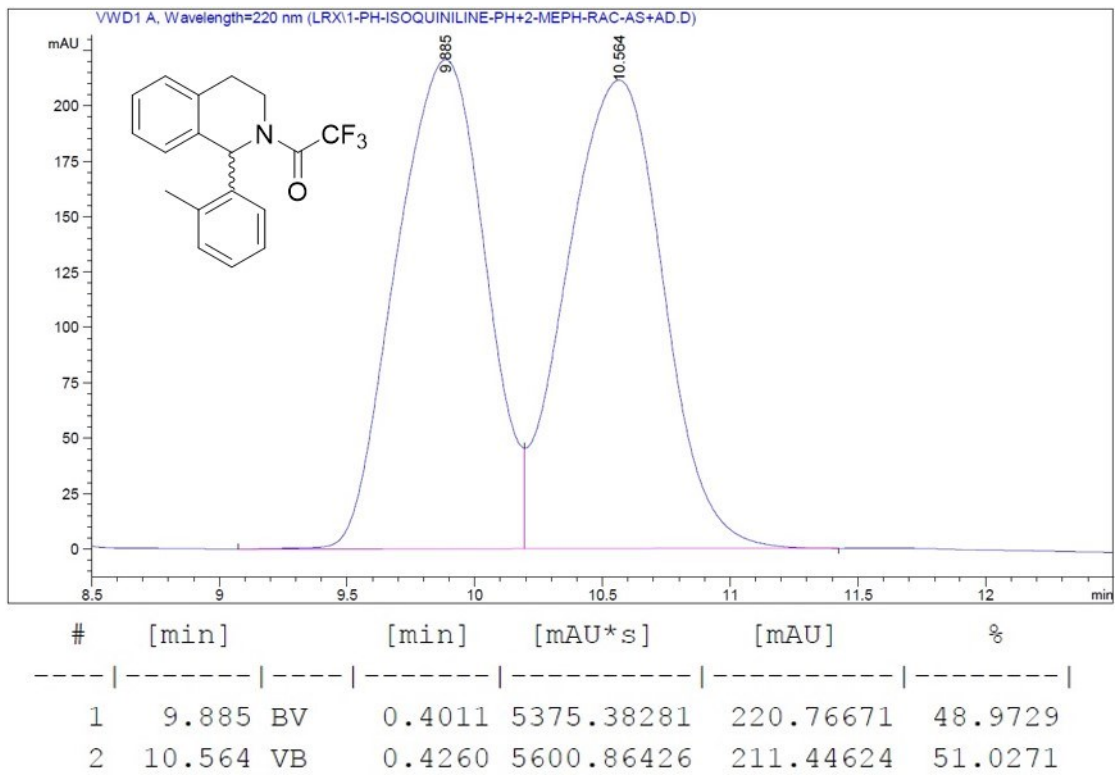
Acquisition Parameter					
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4000 V	Set Dry Heater	180 °C
Scan Begin	100 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1100 m/z	Set Collision Cell RF	200.0 Vpp	Set Divert Valve	Waste

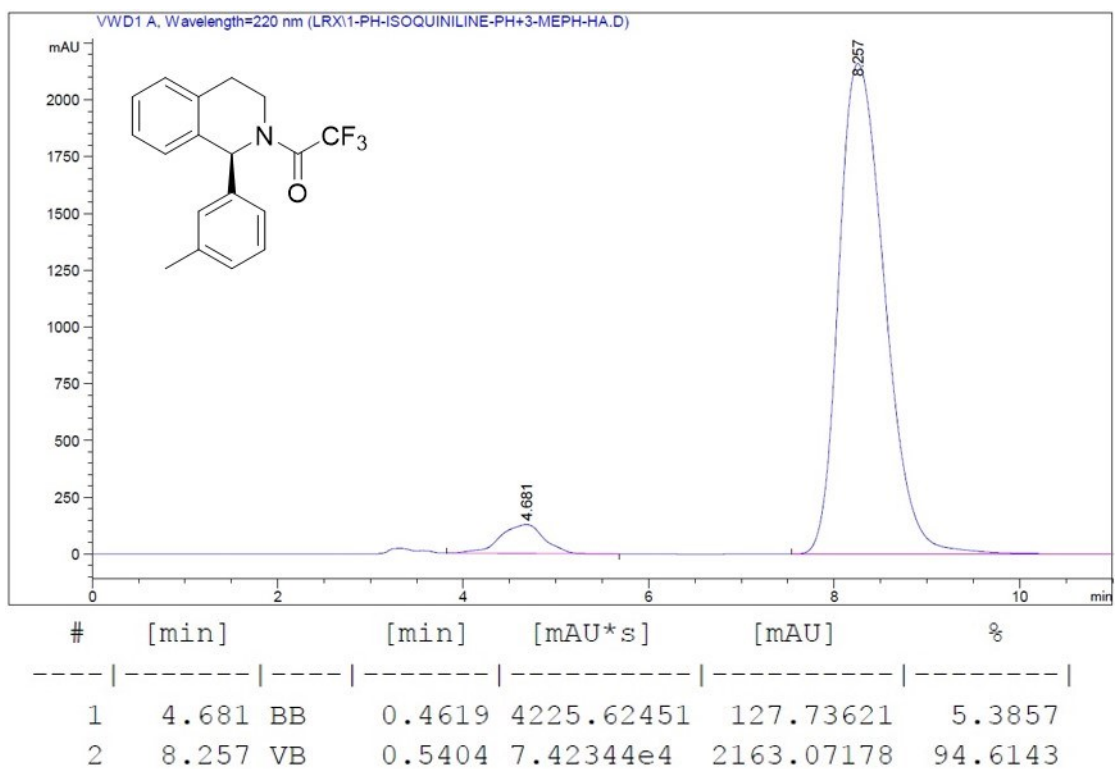
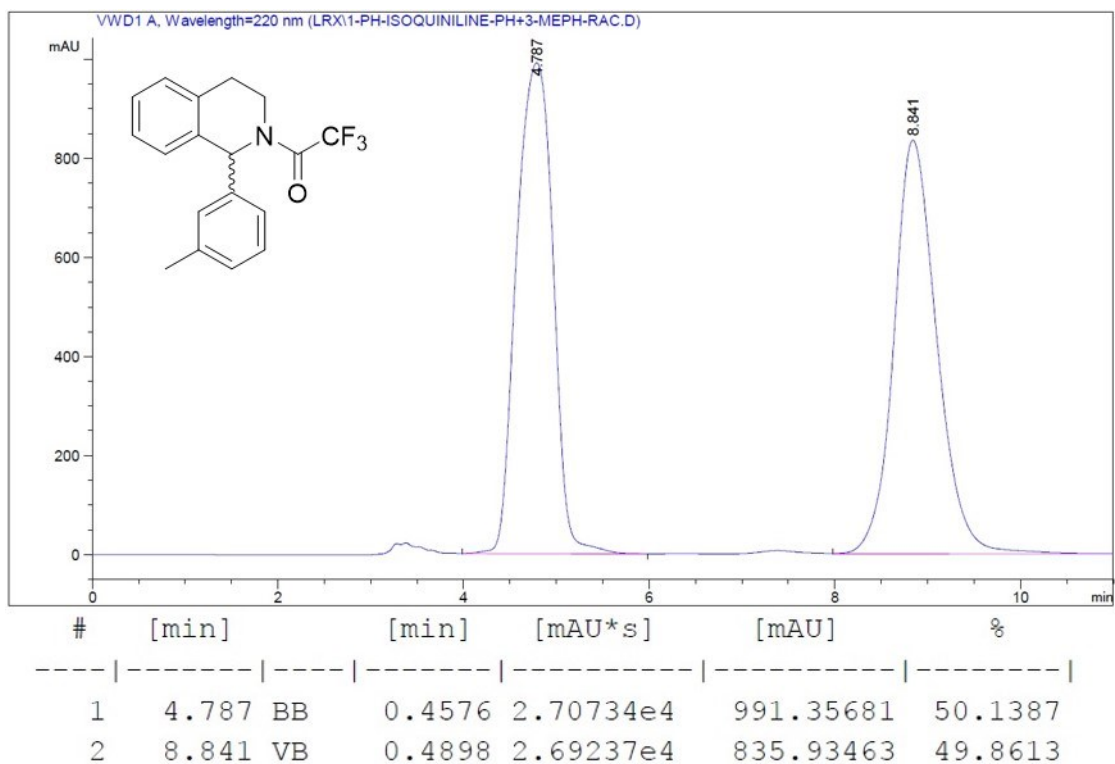


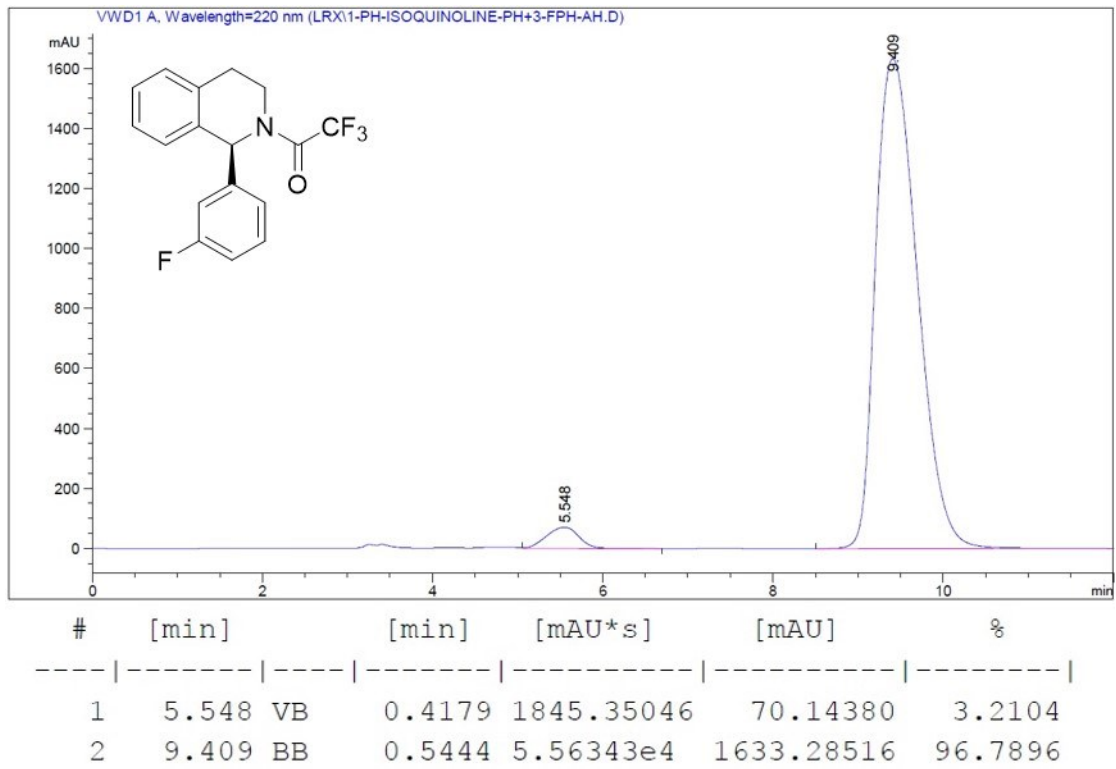
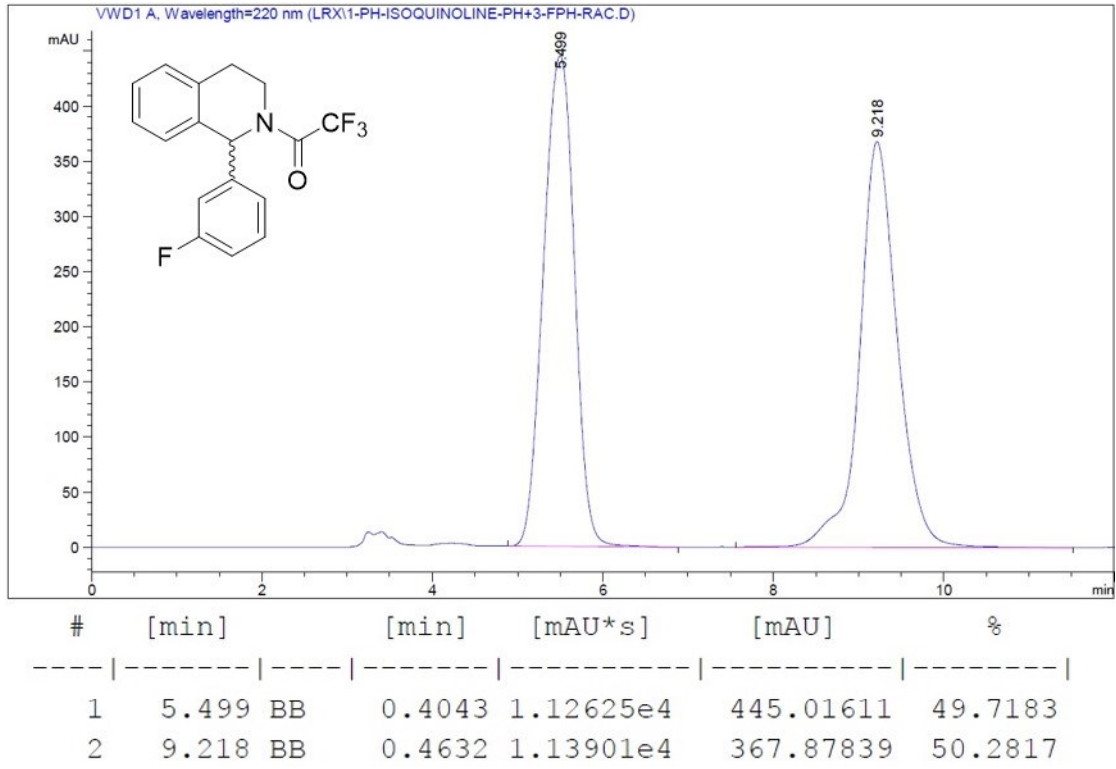


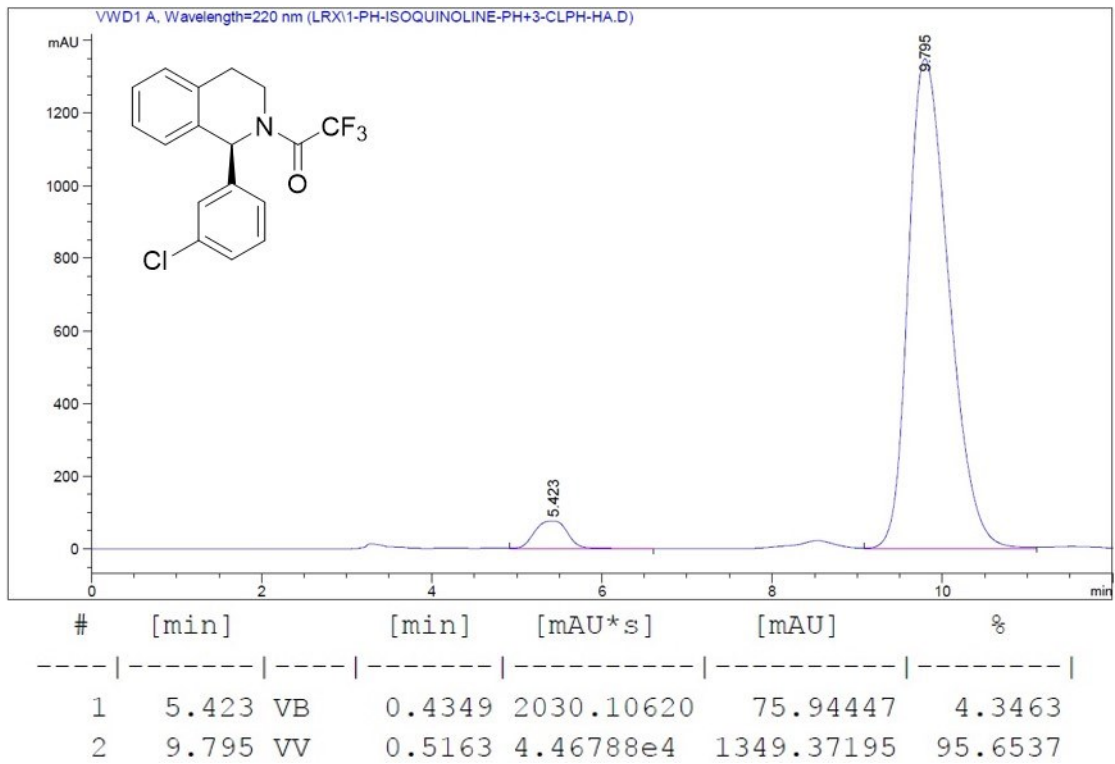
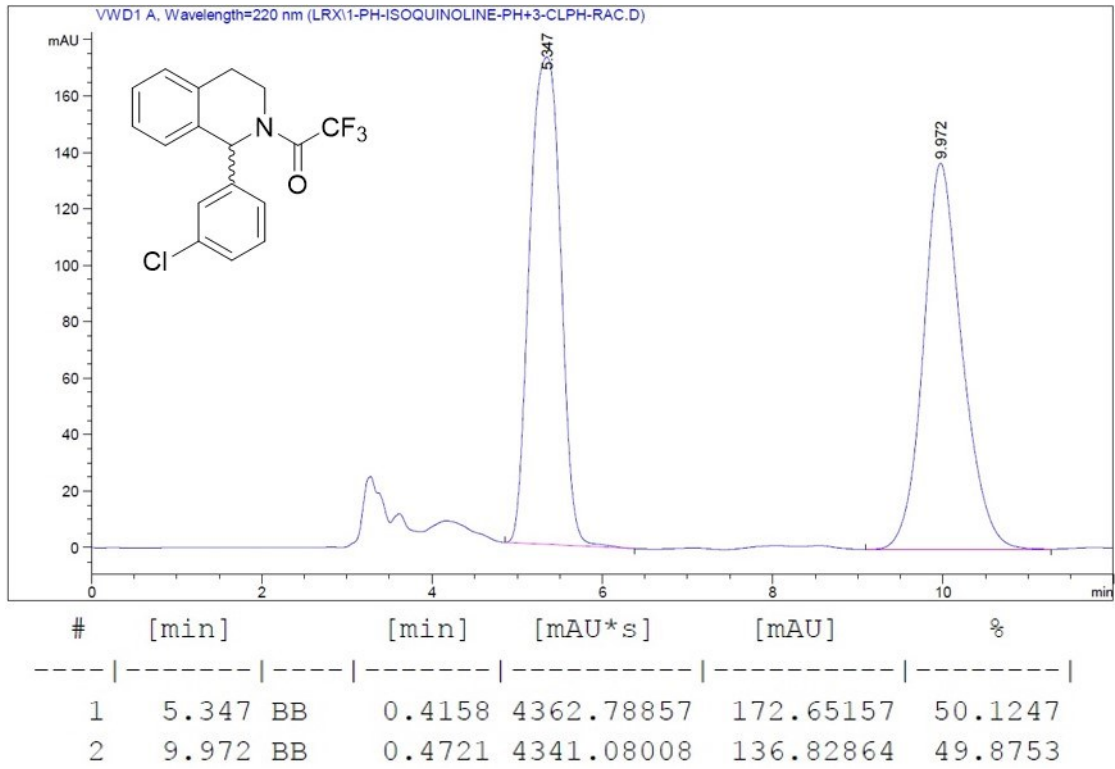
5. HPLC spectra

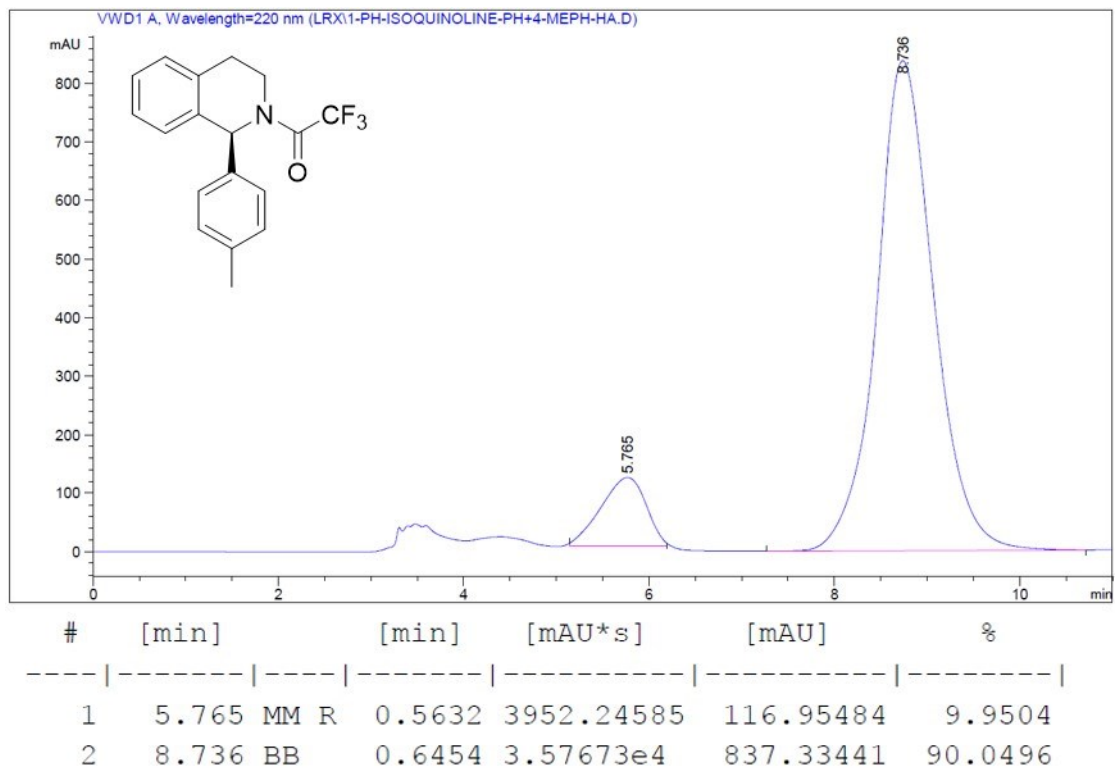
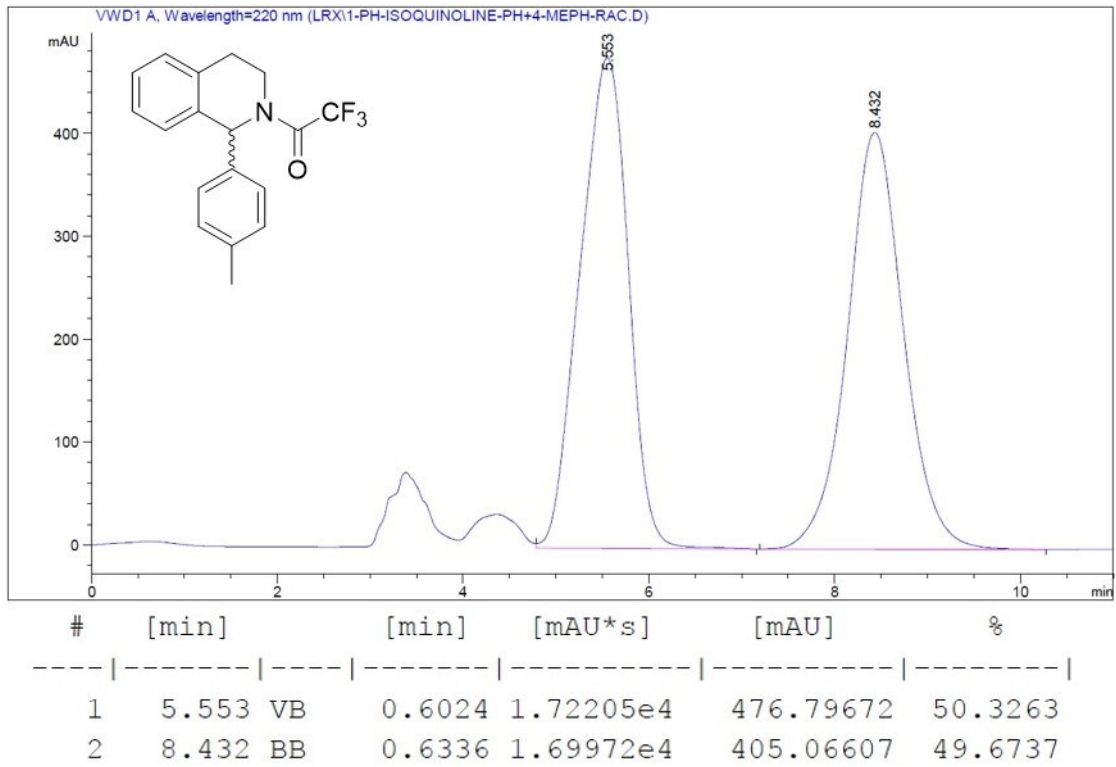


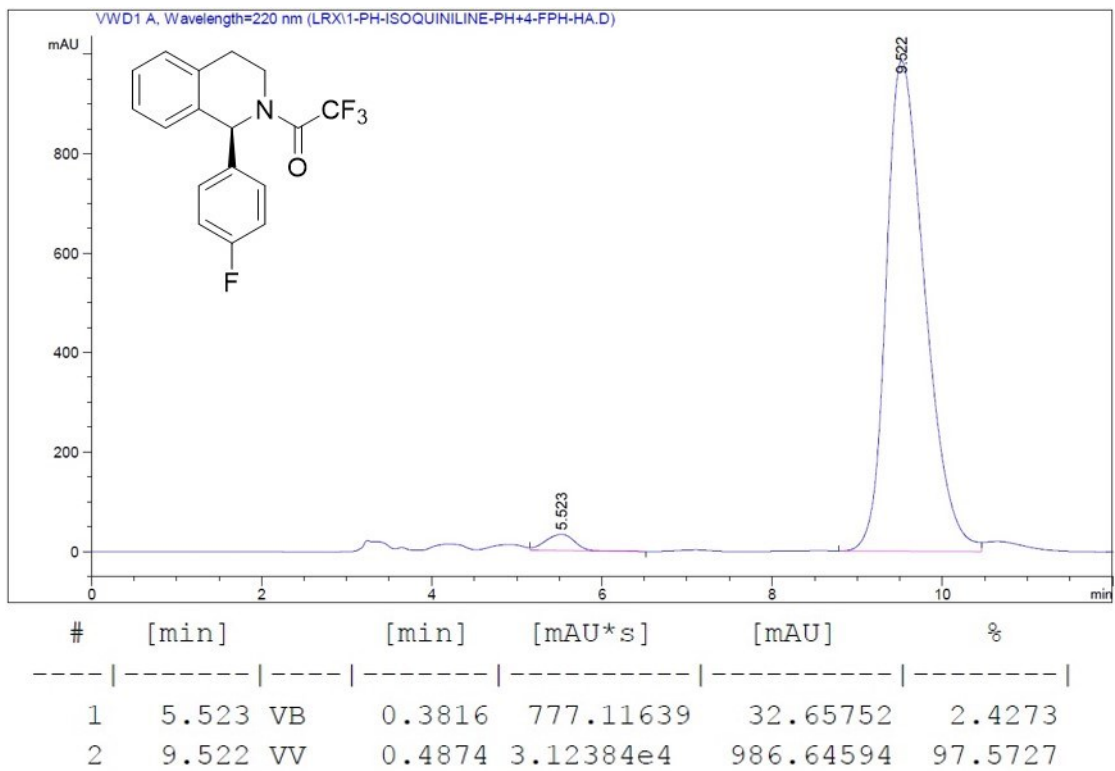
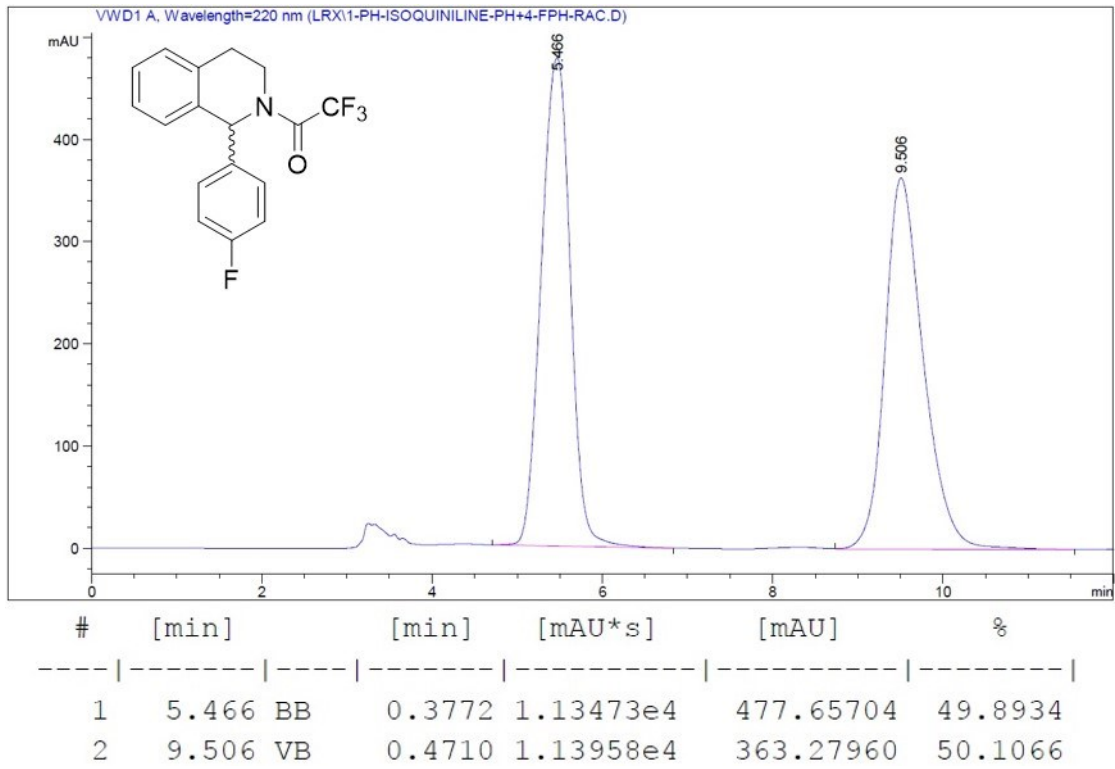


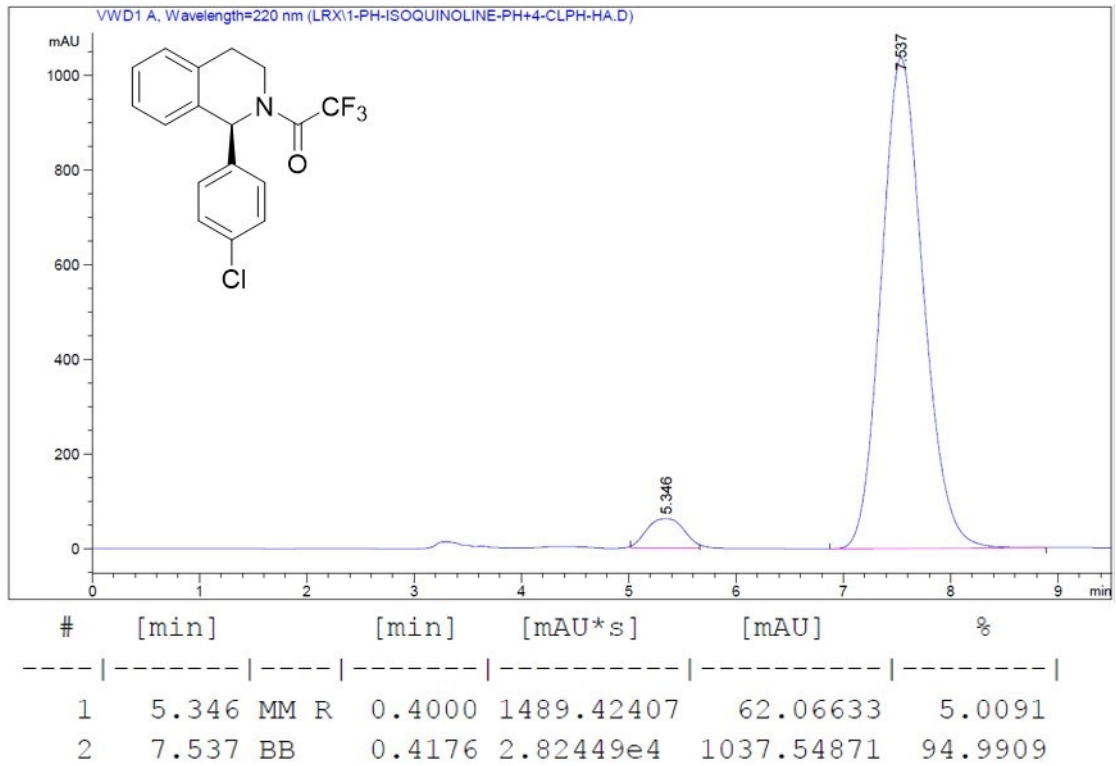
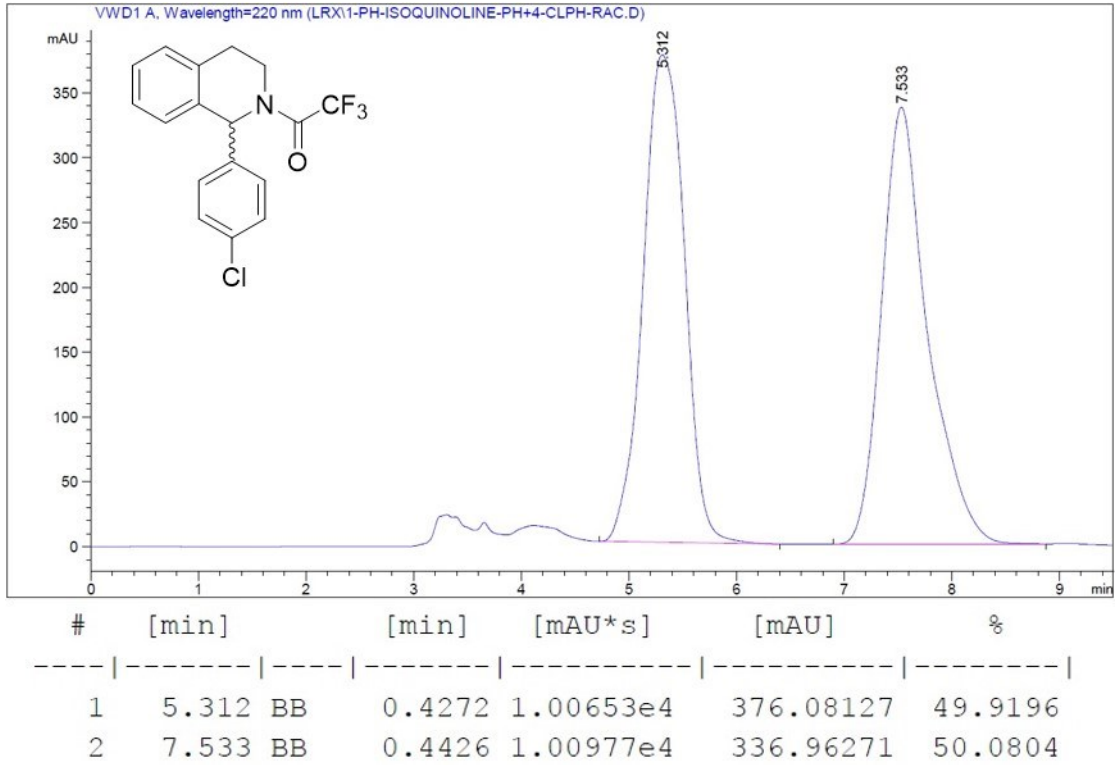


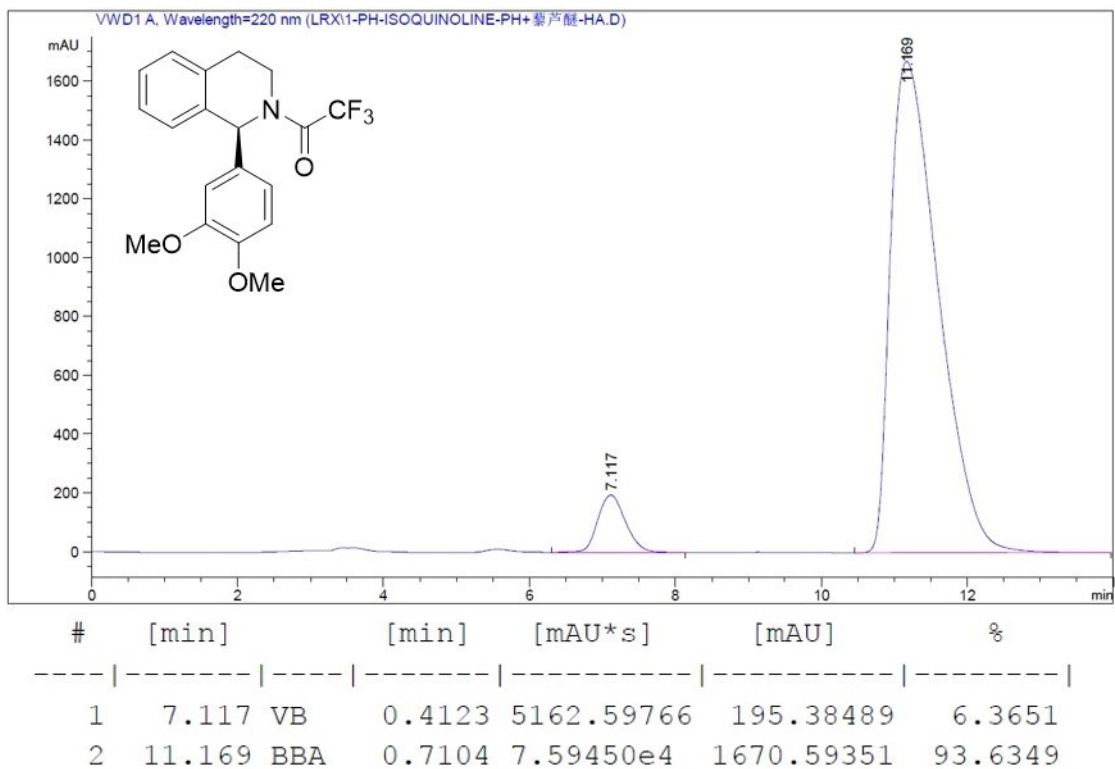
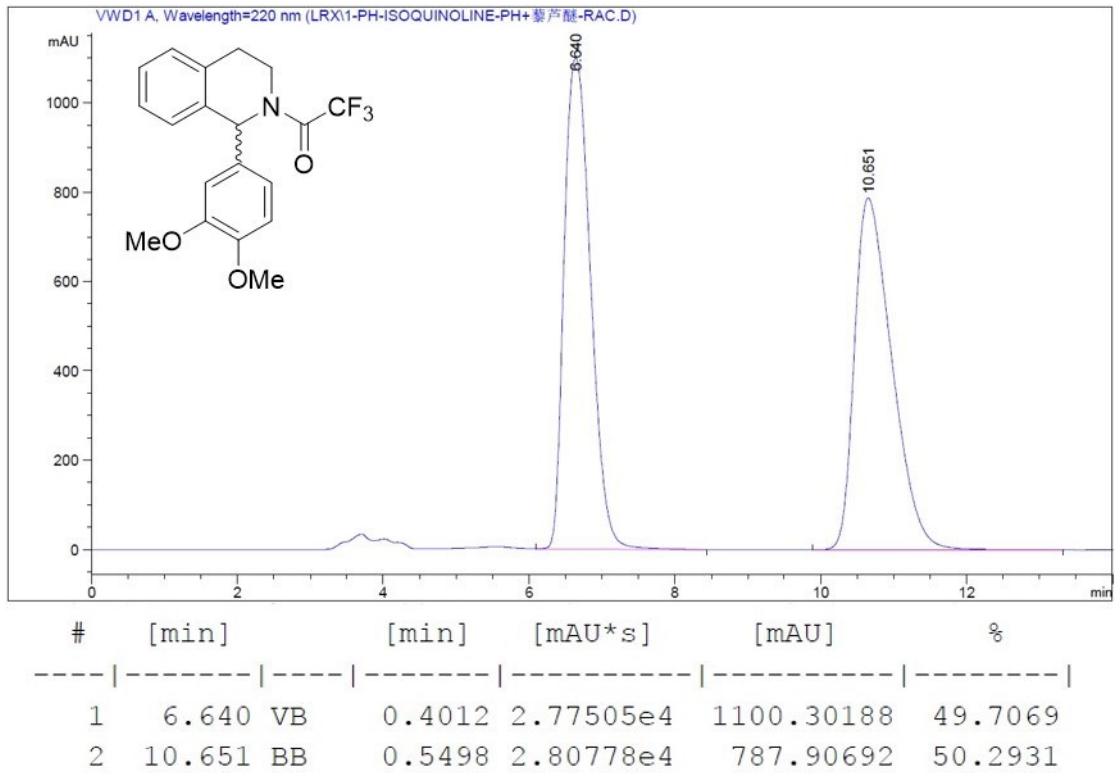


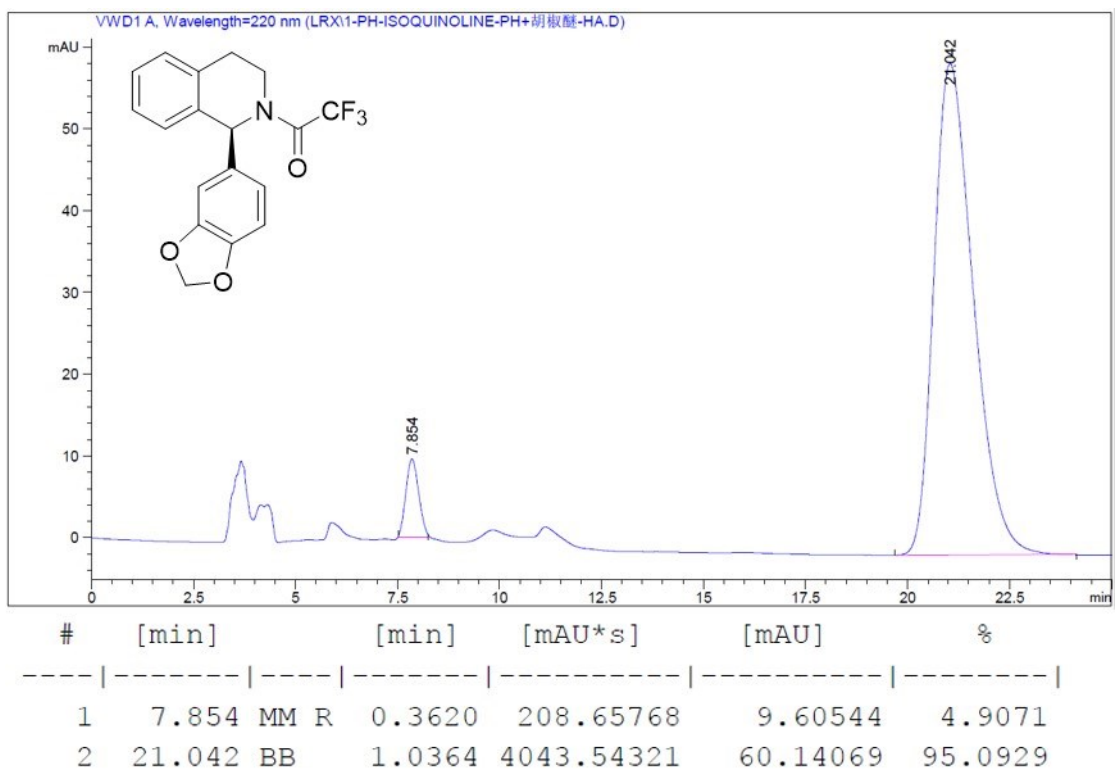
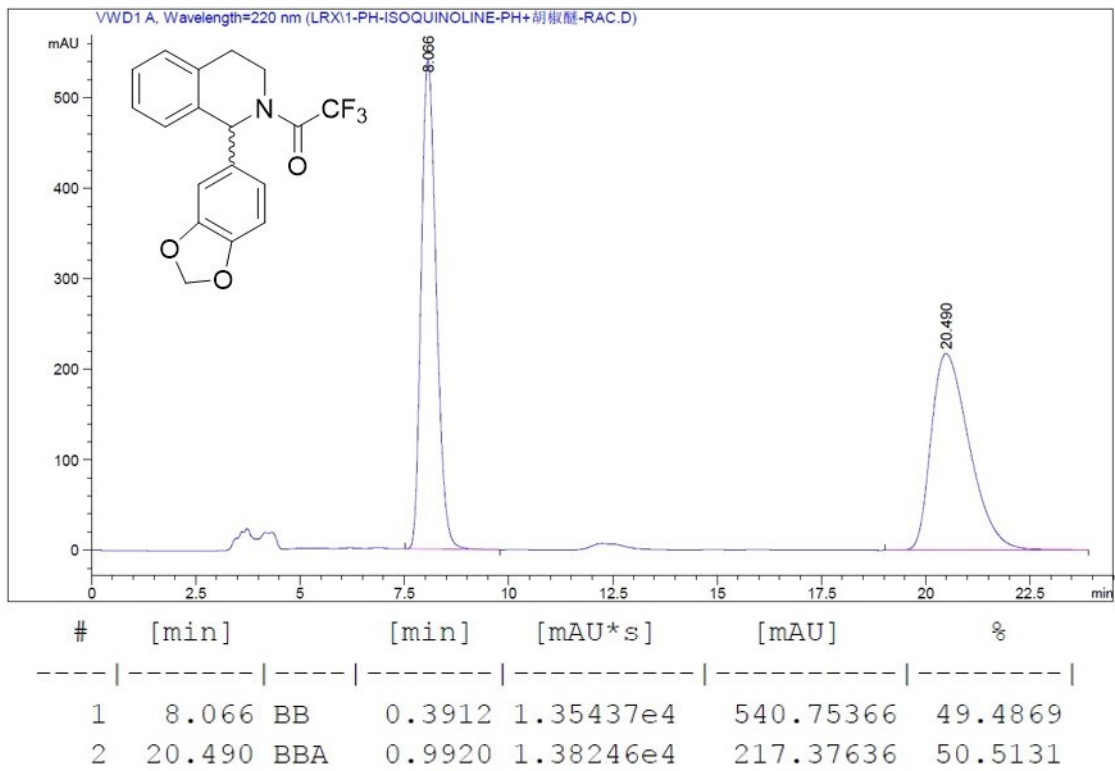


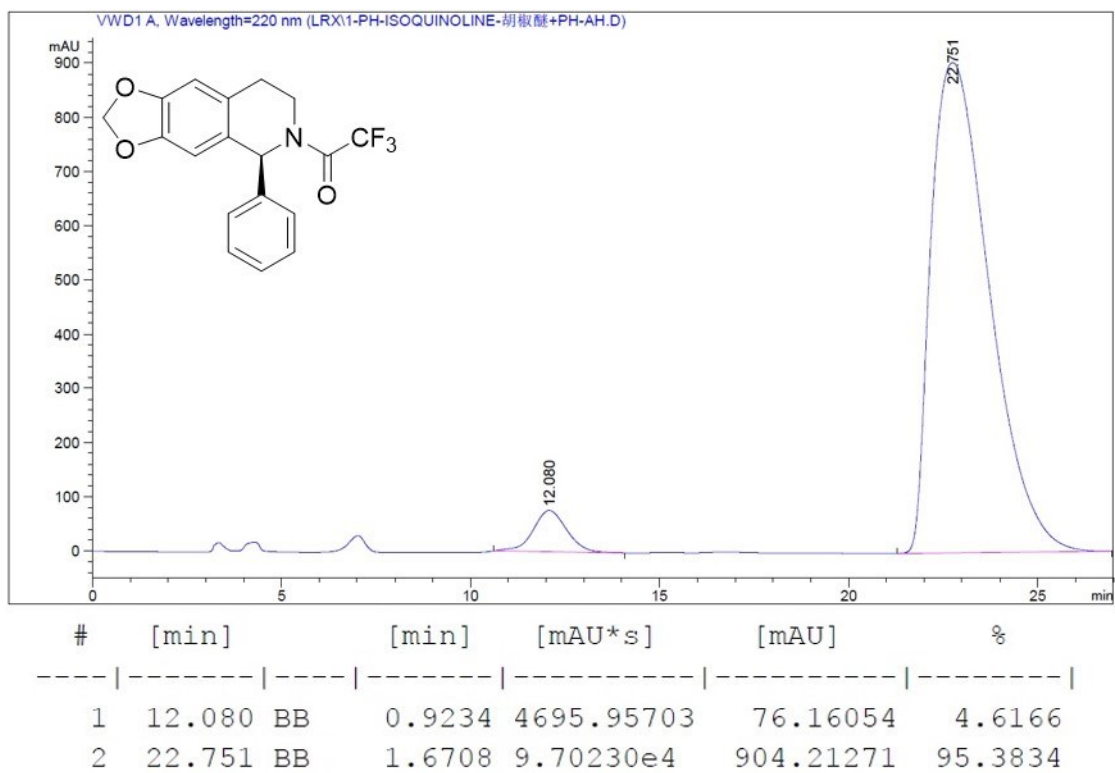
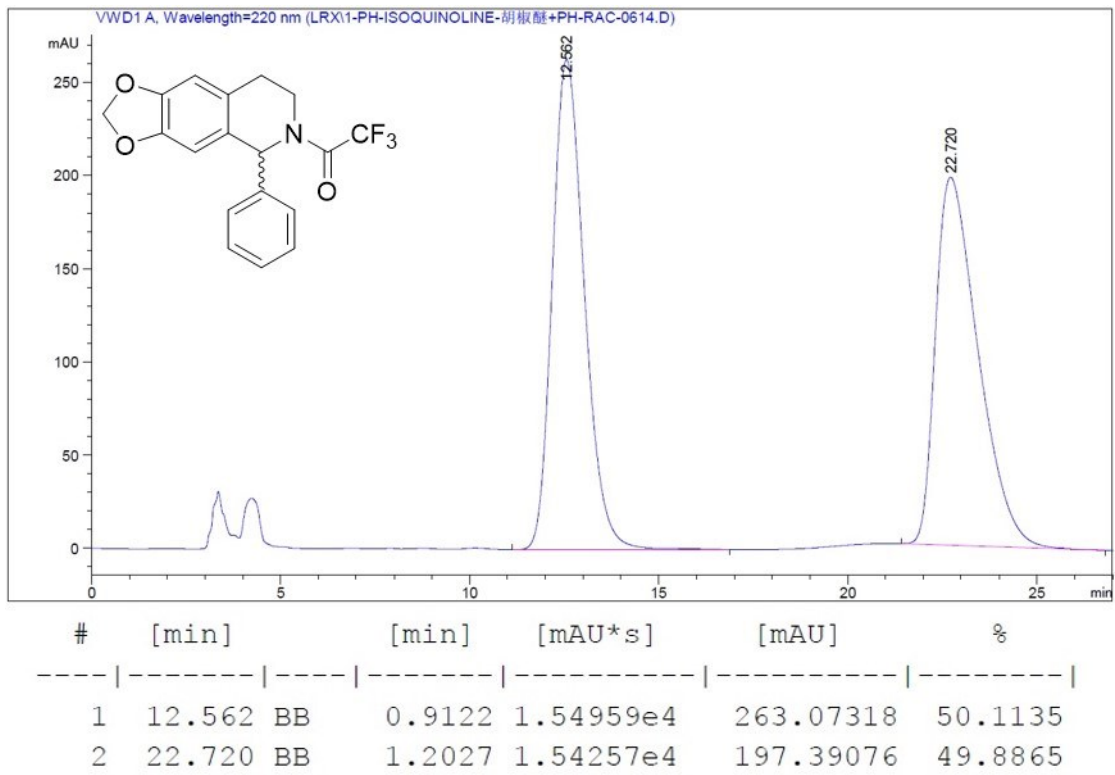


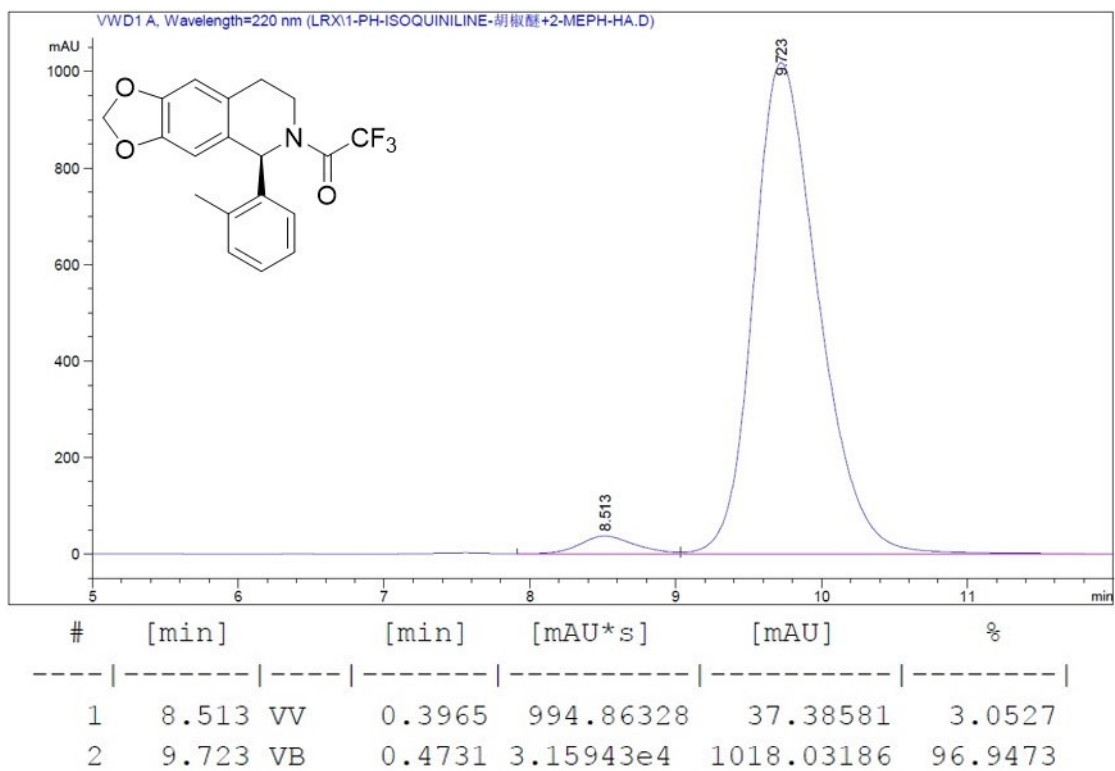
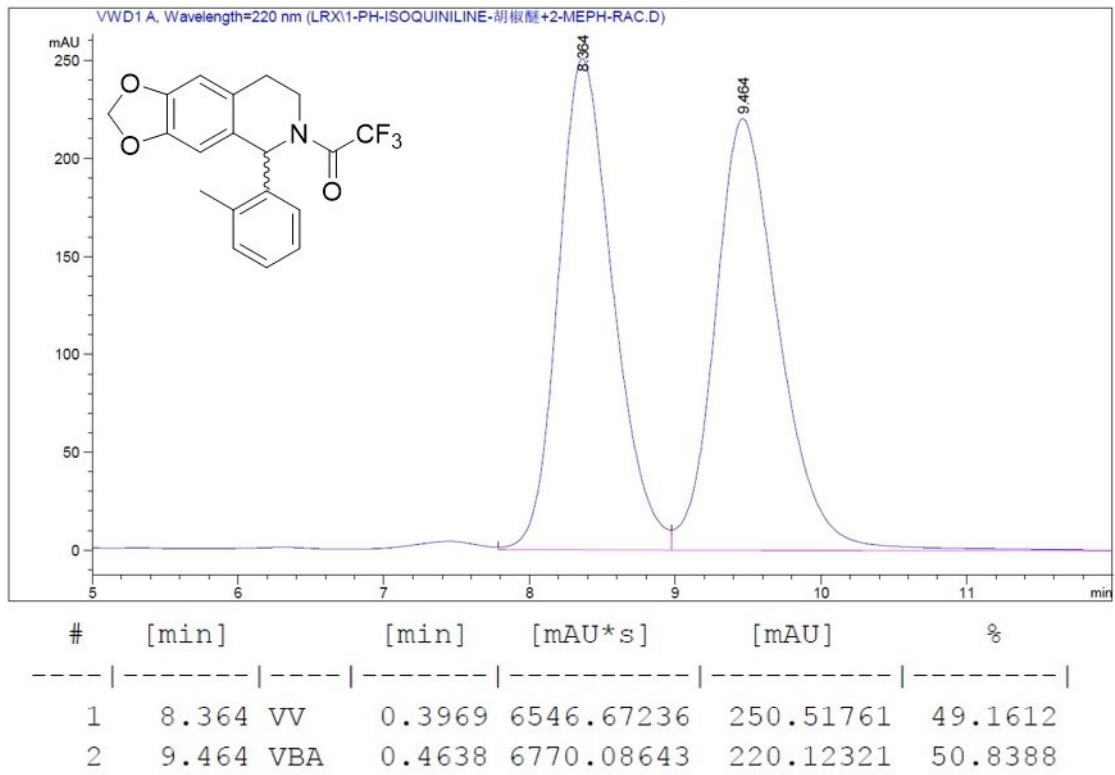


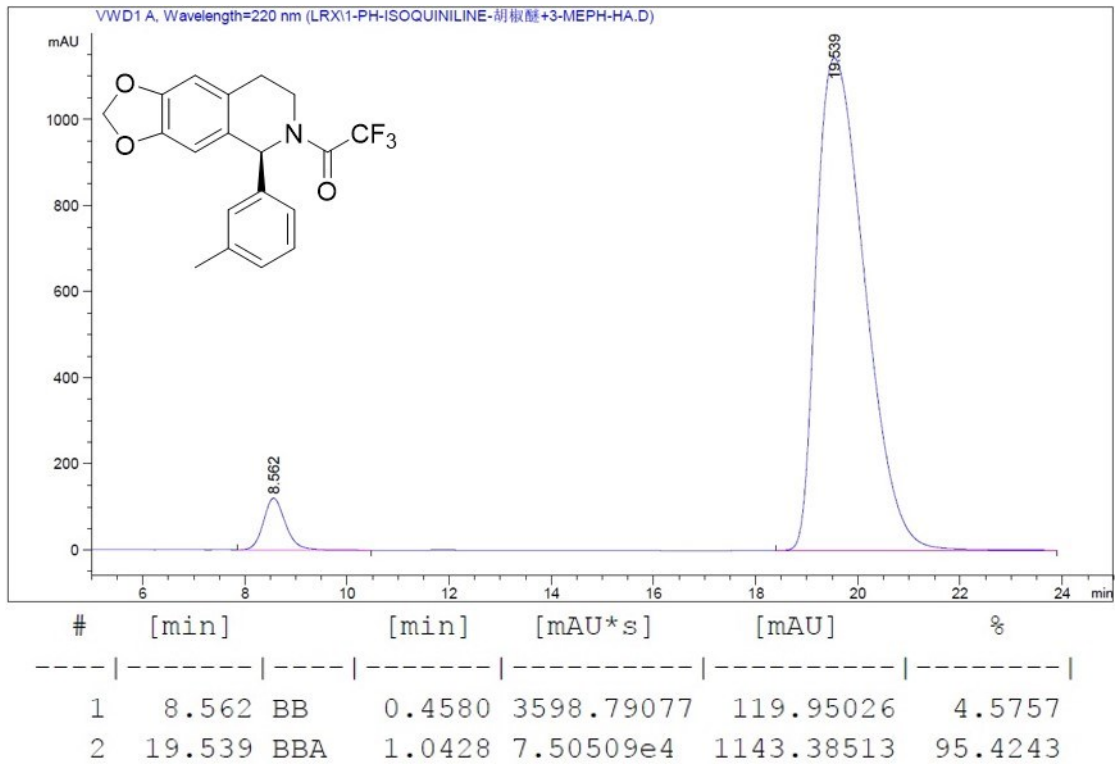
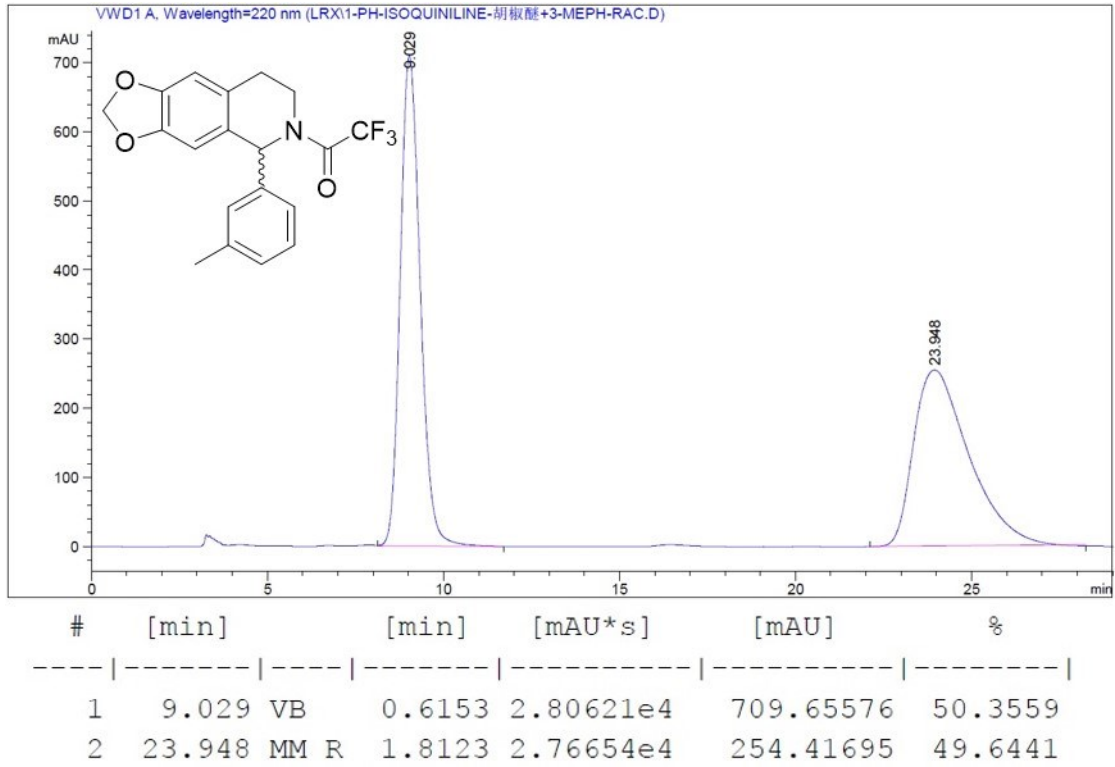


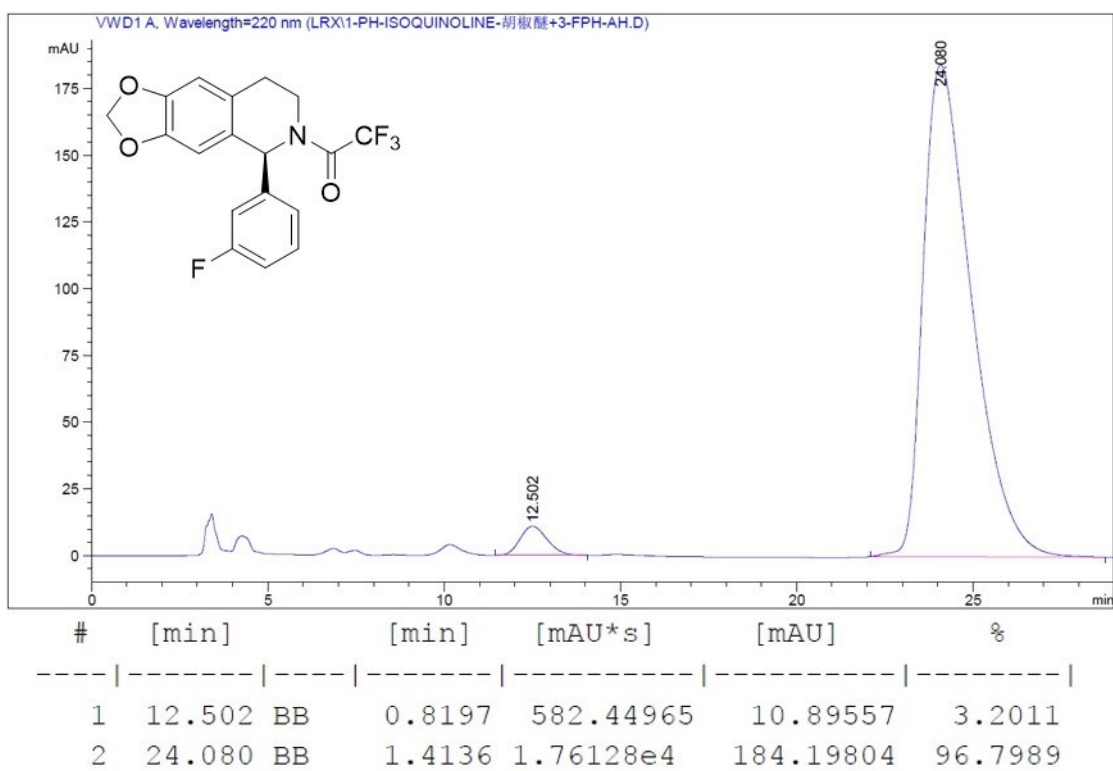
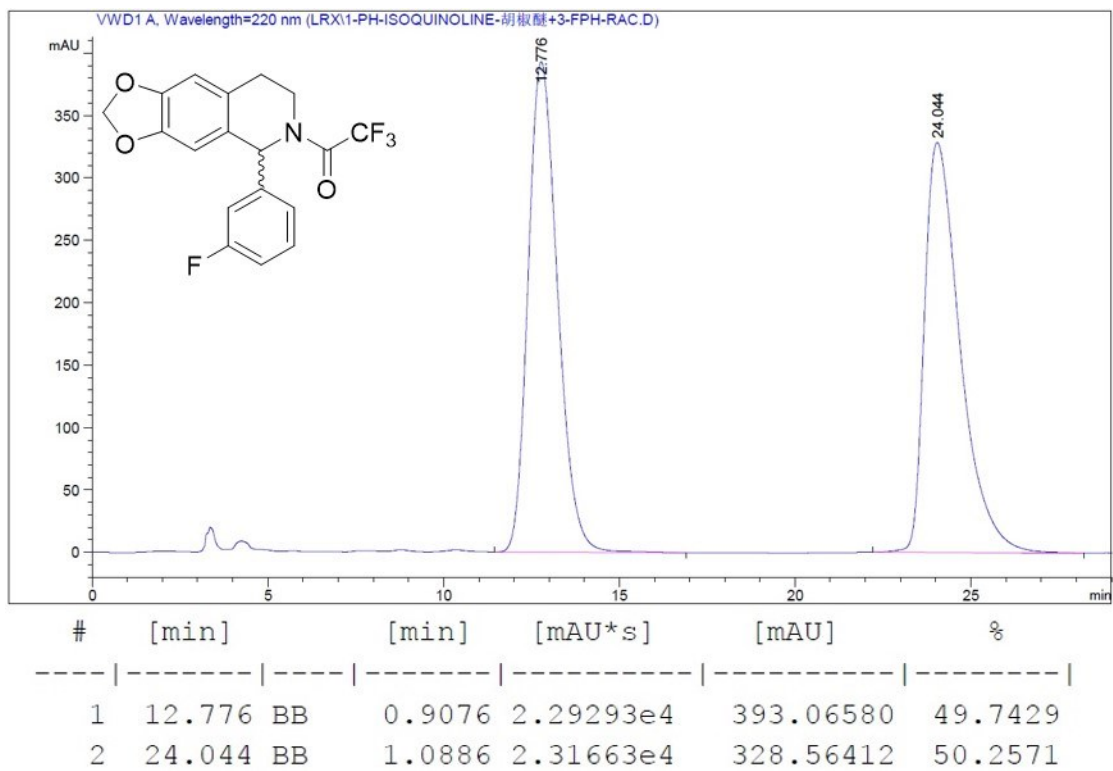


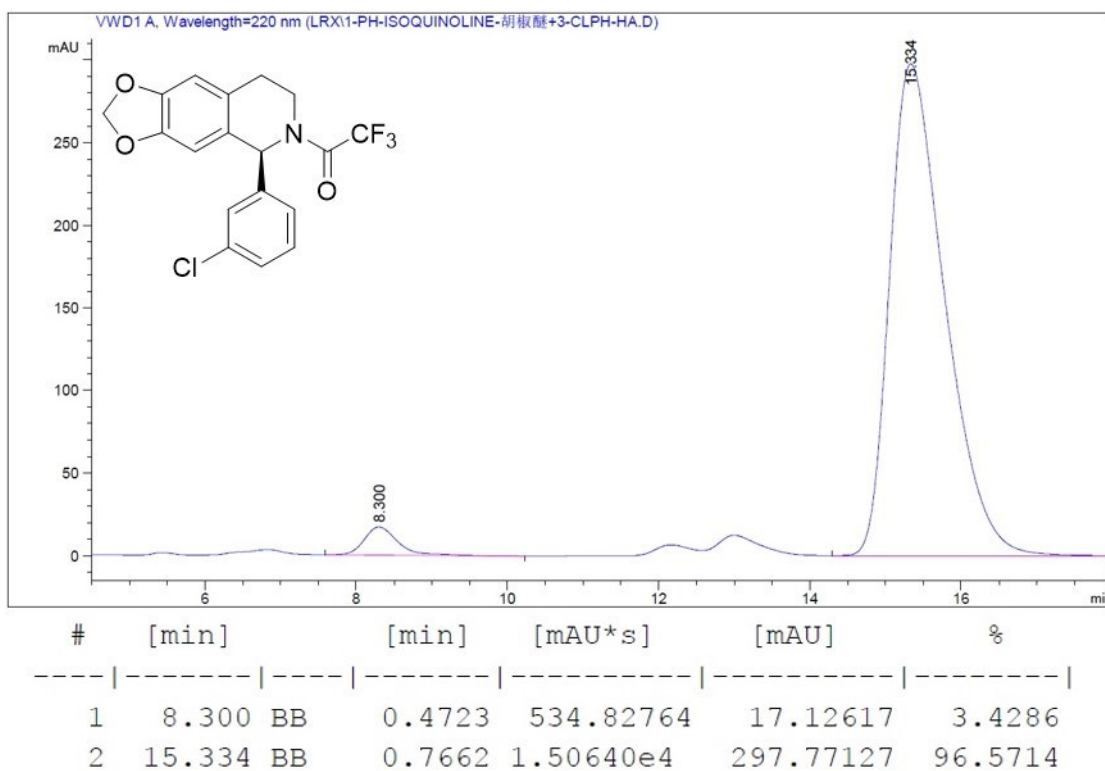
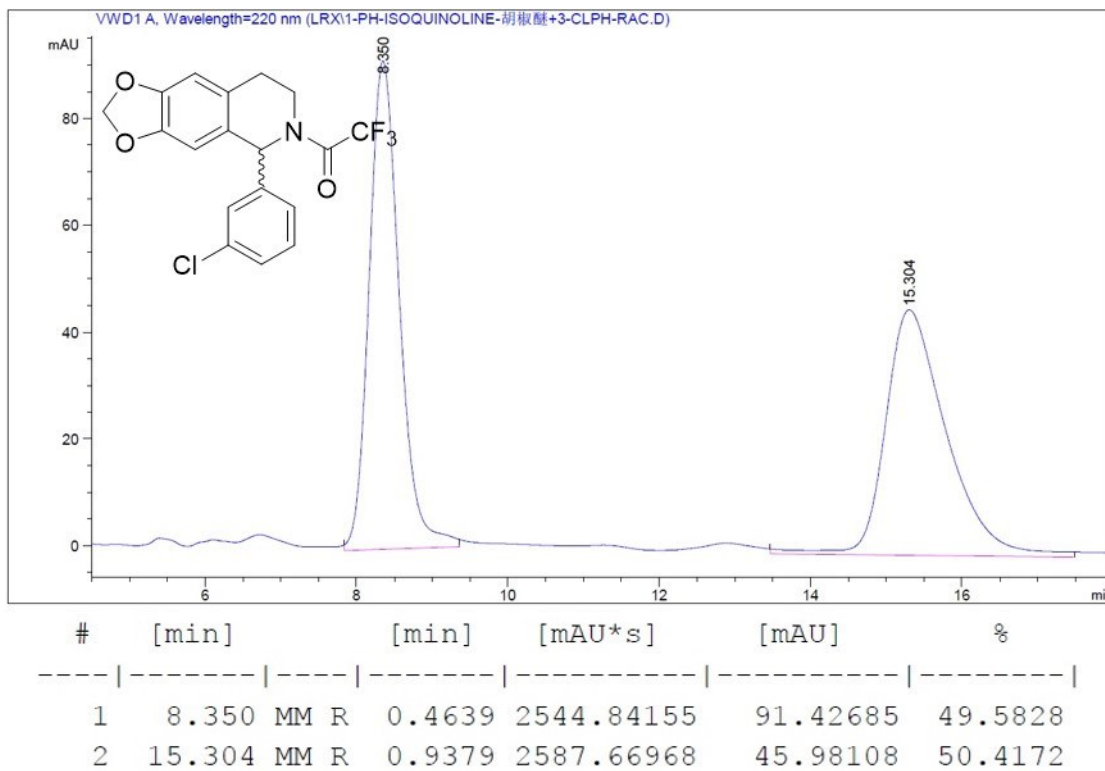


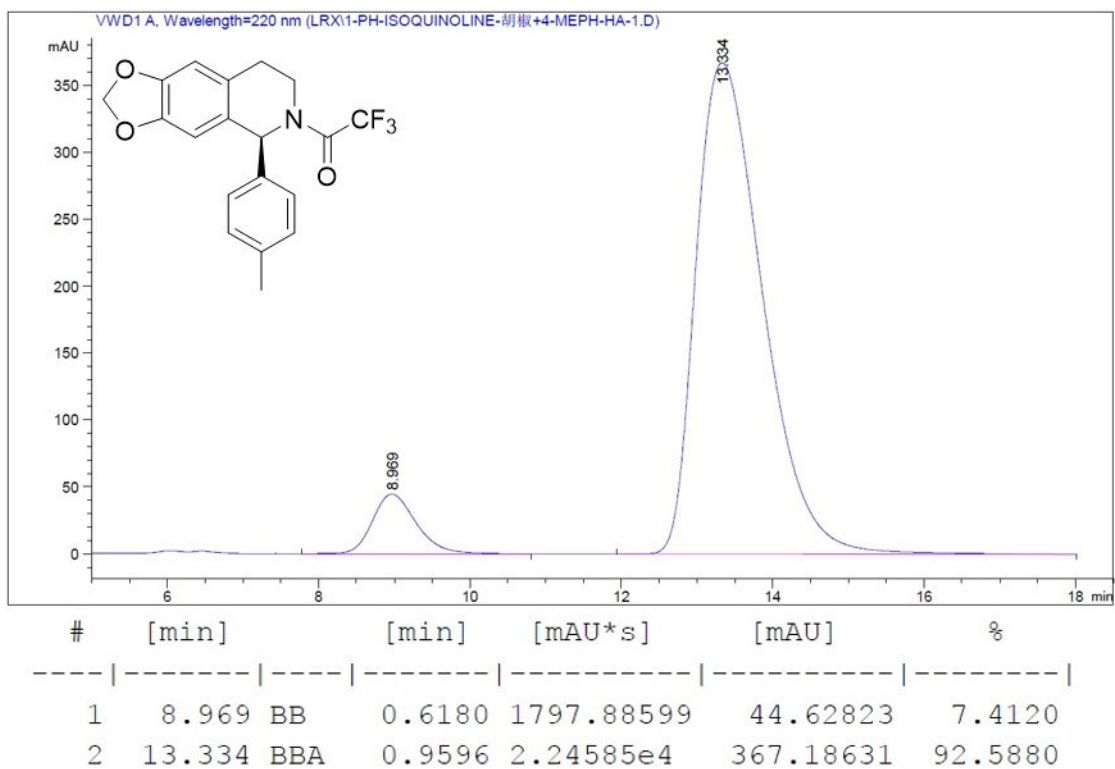
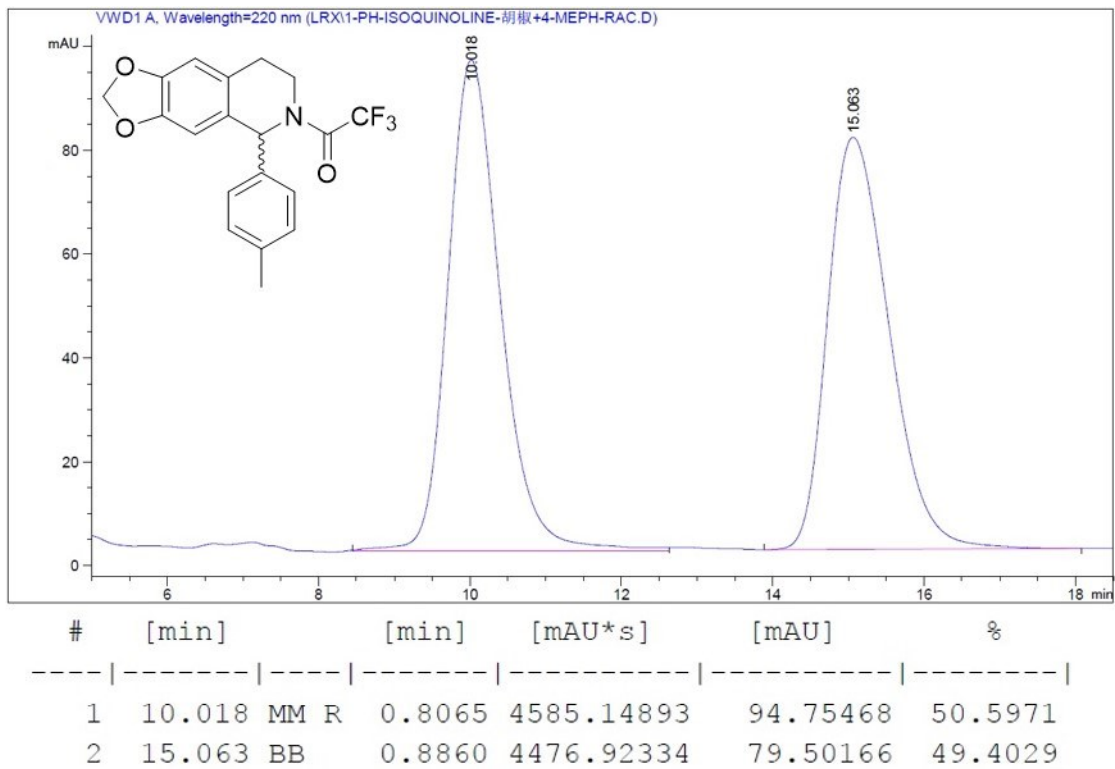


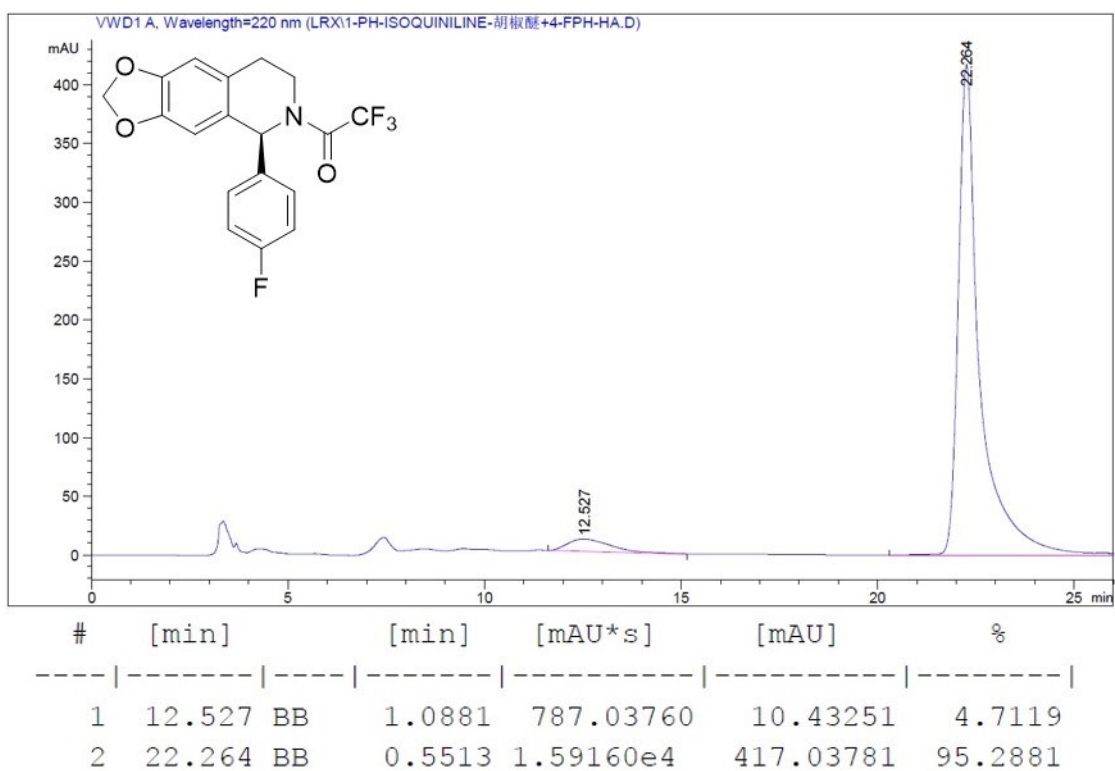
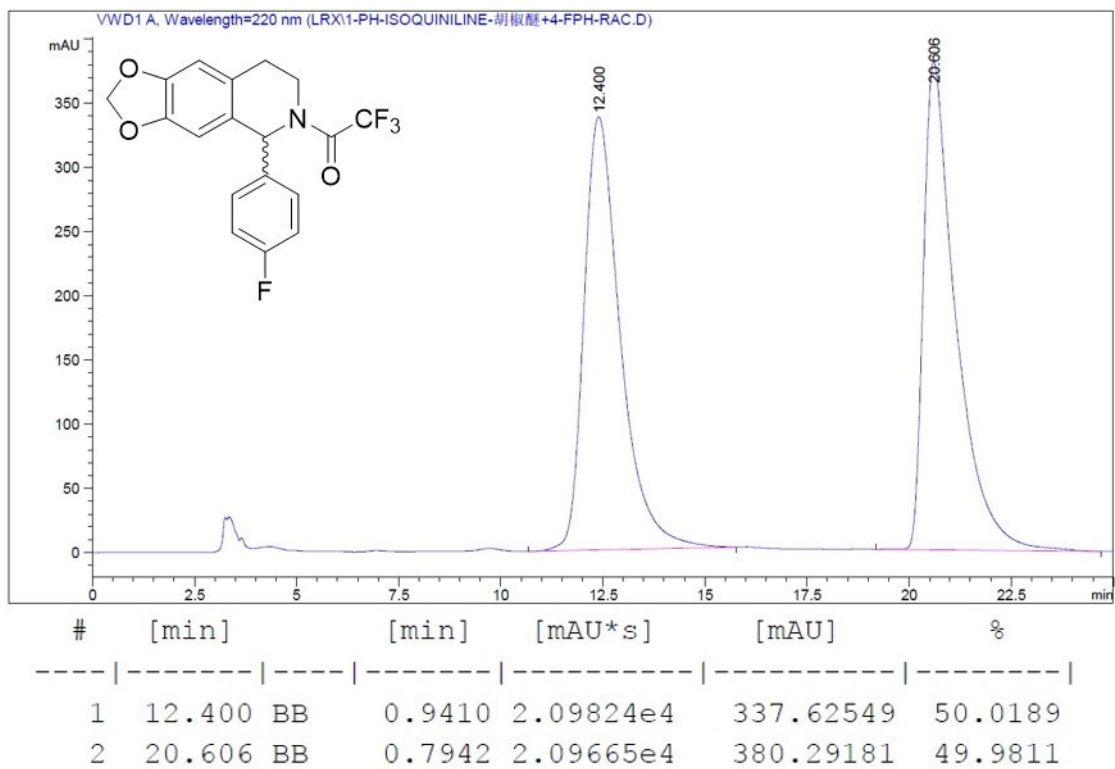


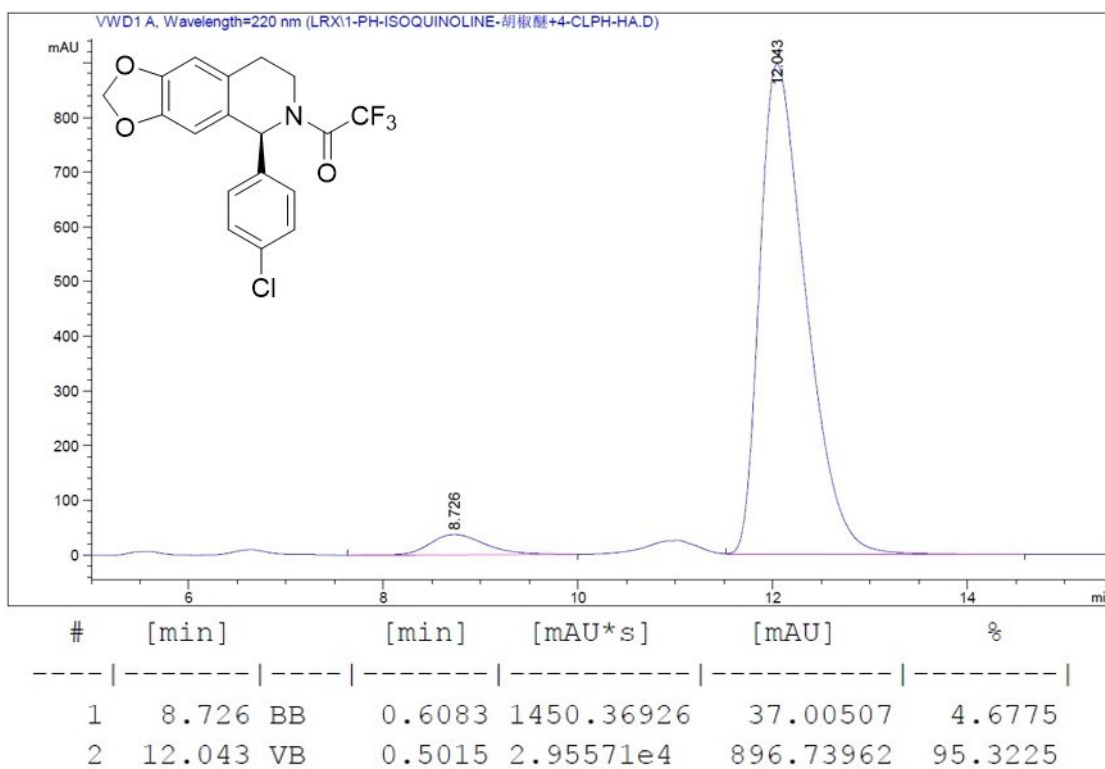
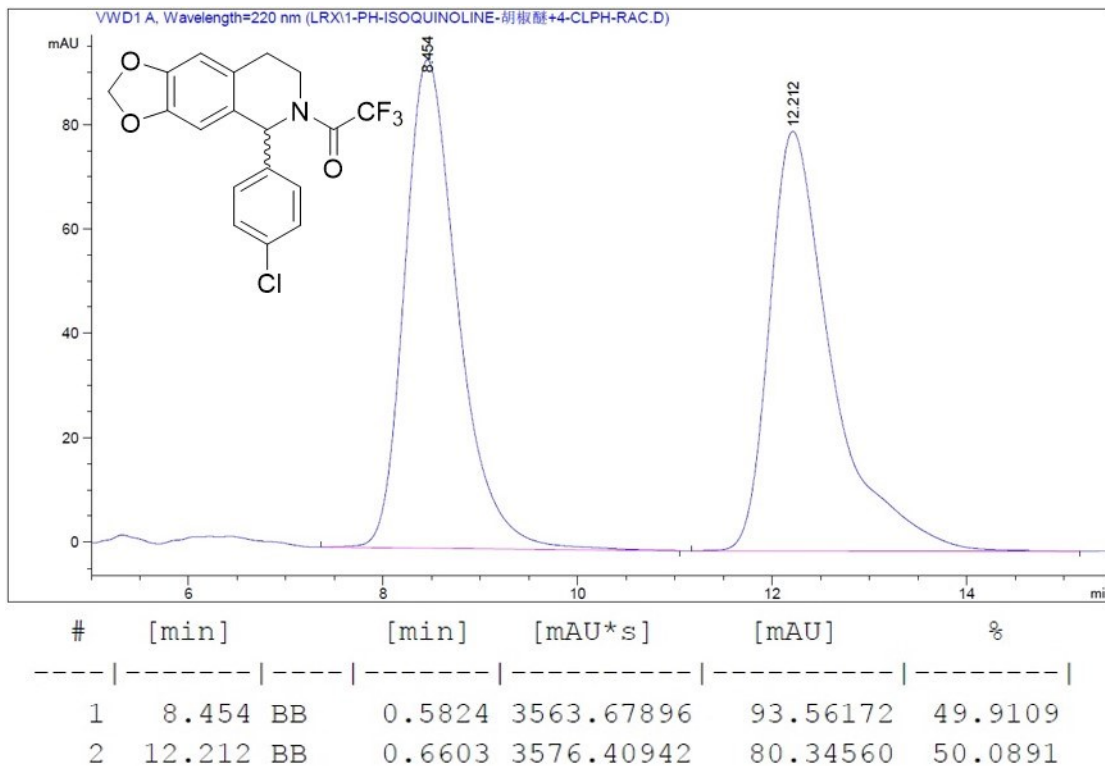


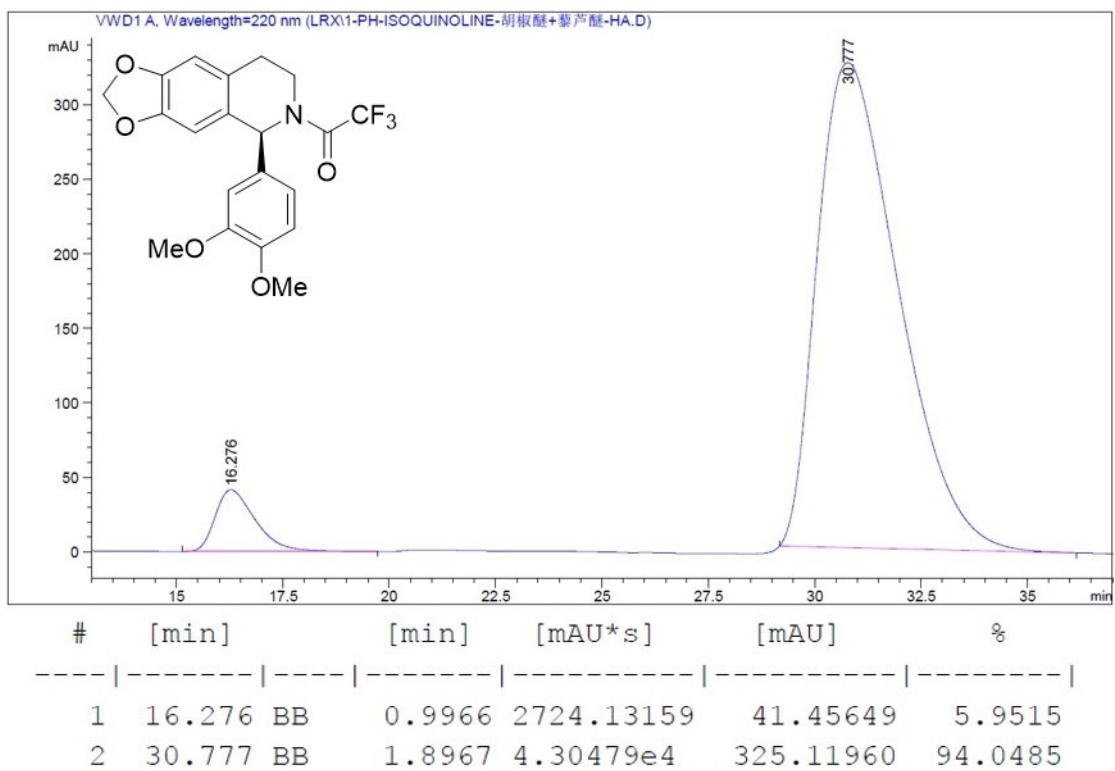
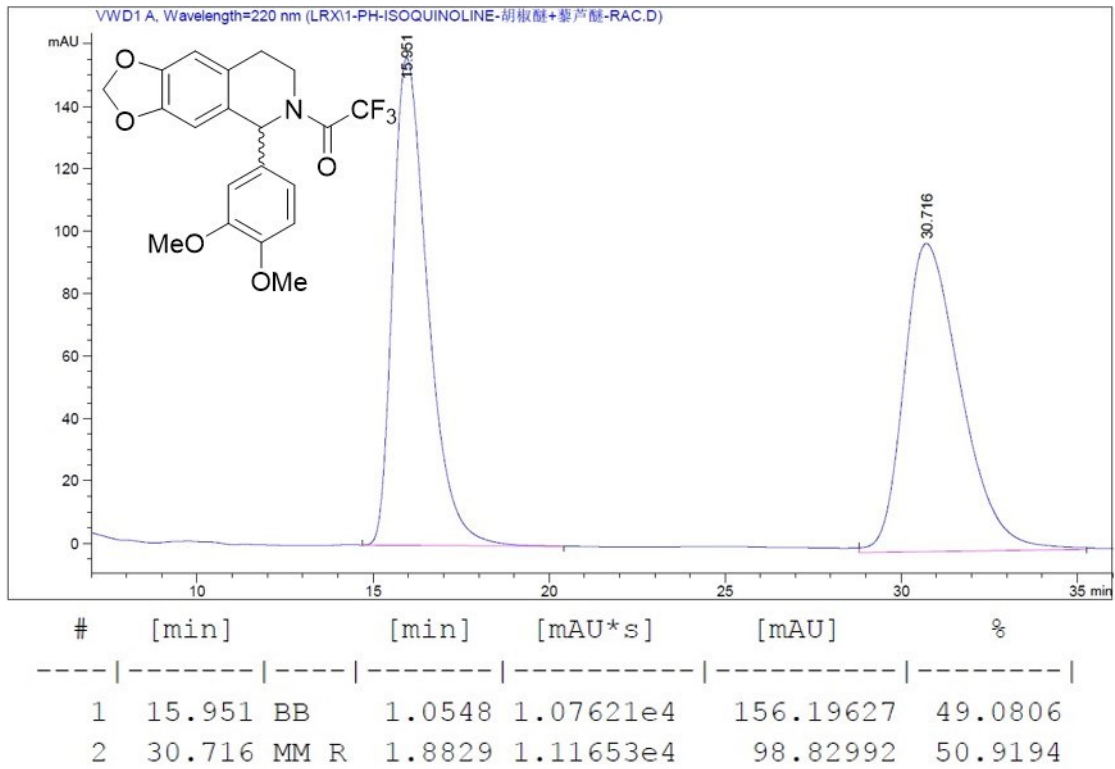


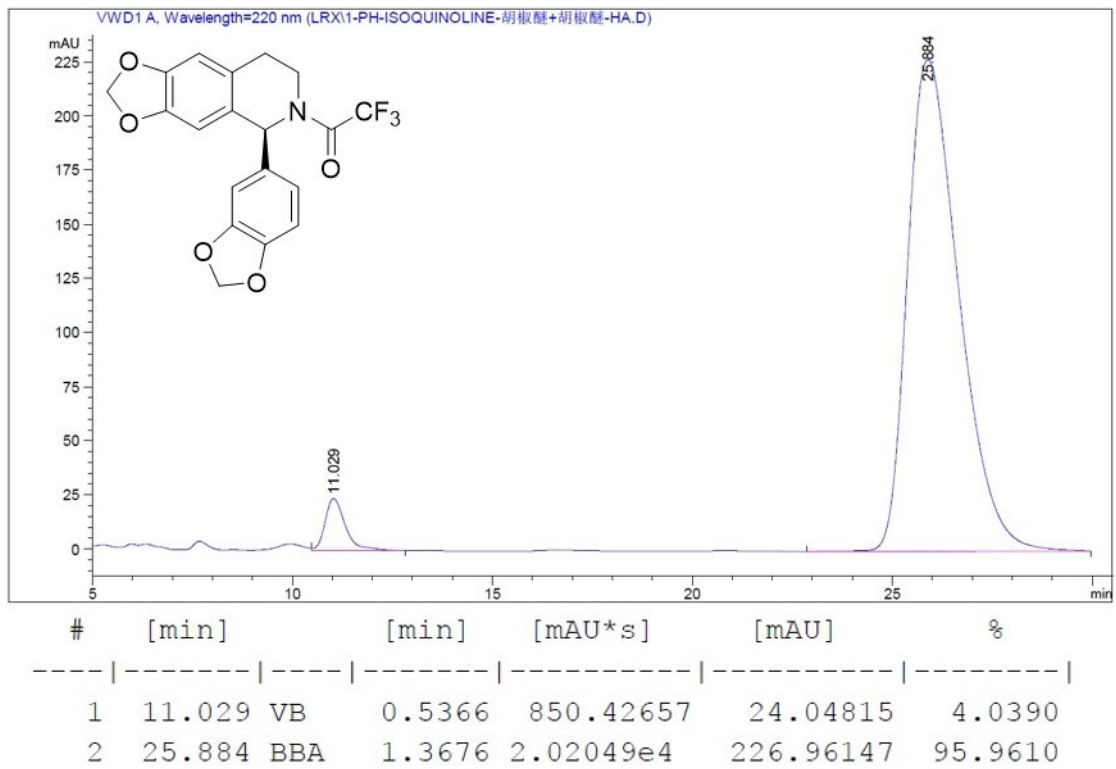
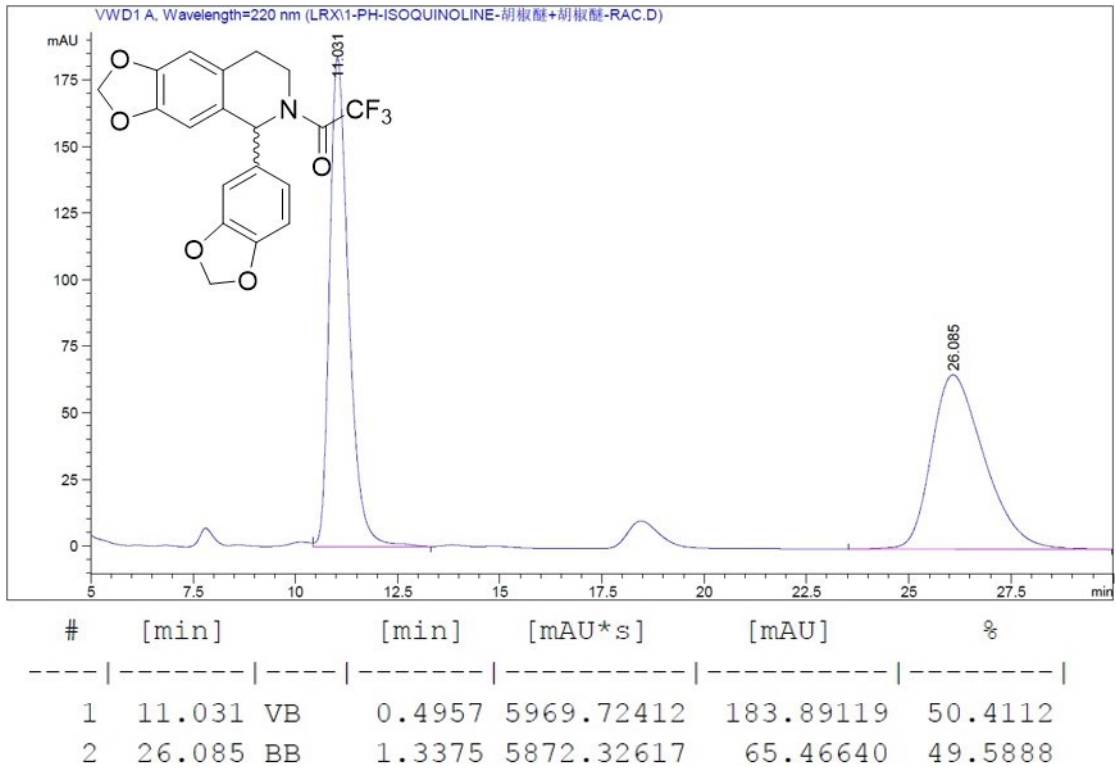


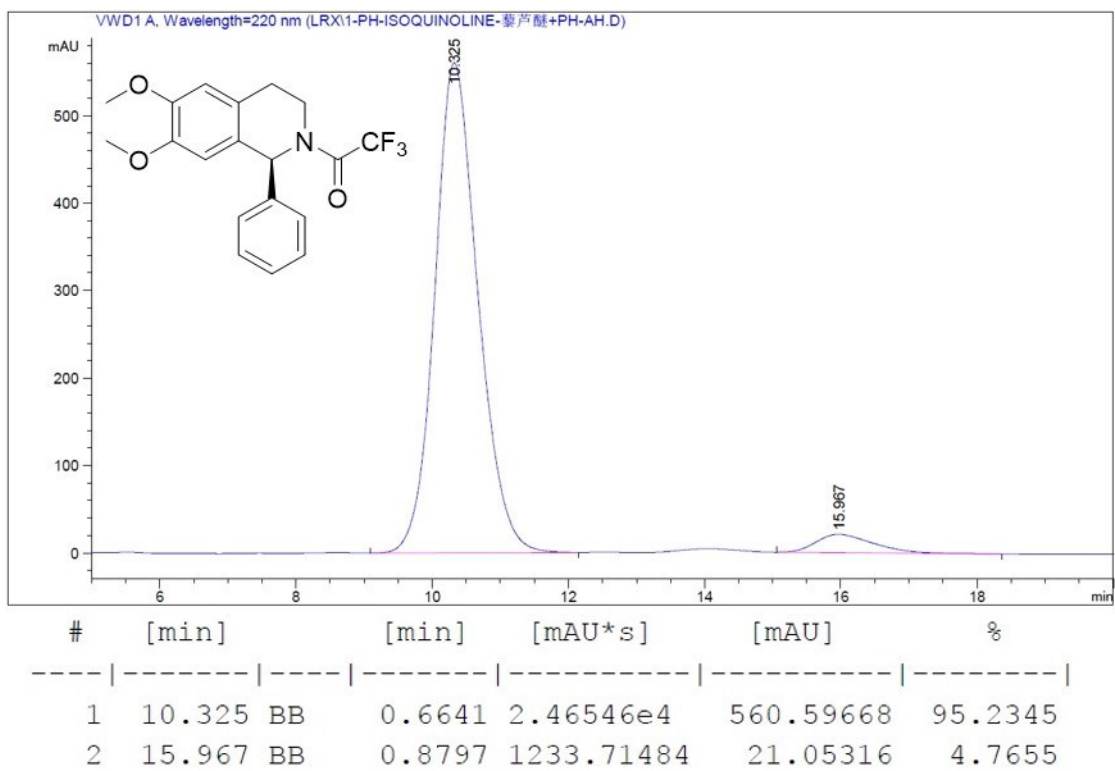
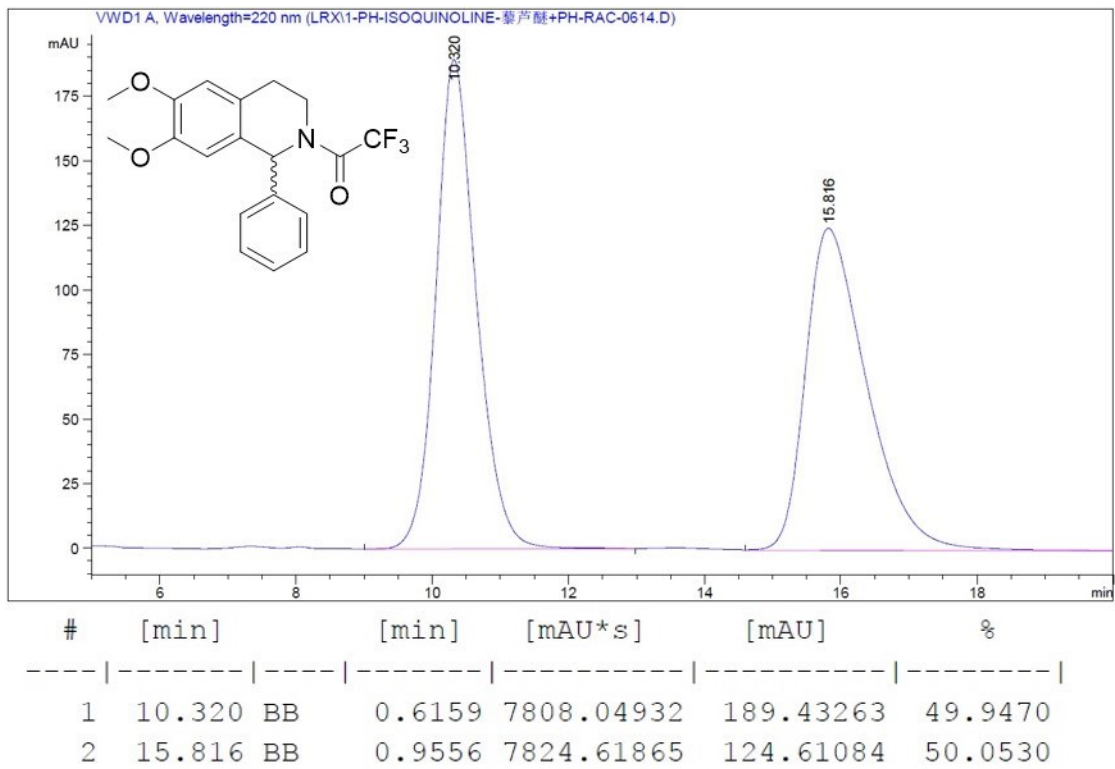


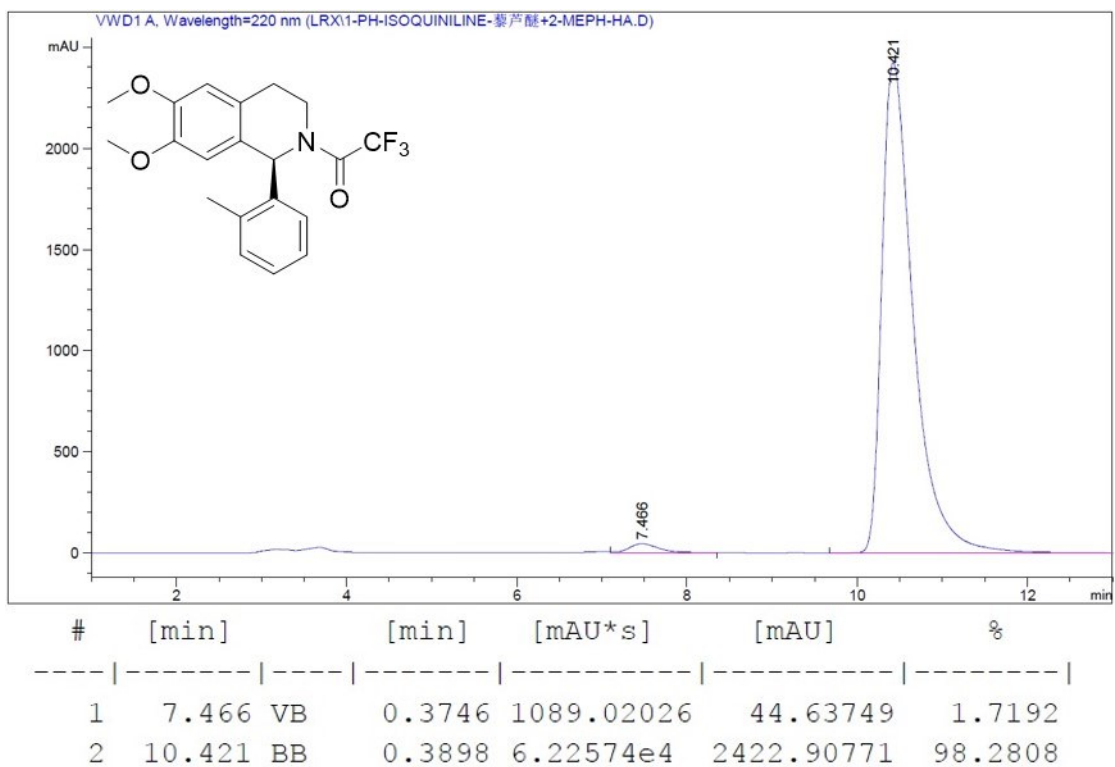
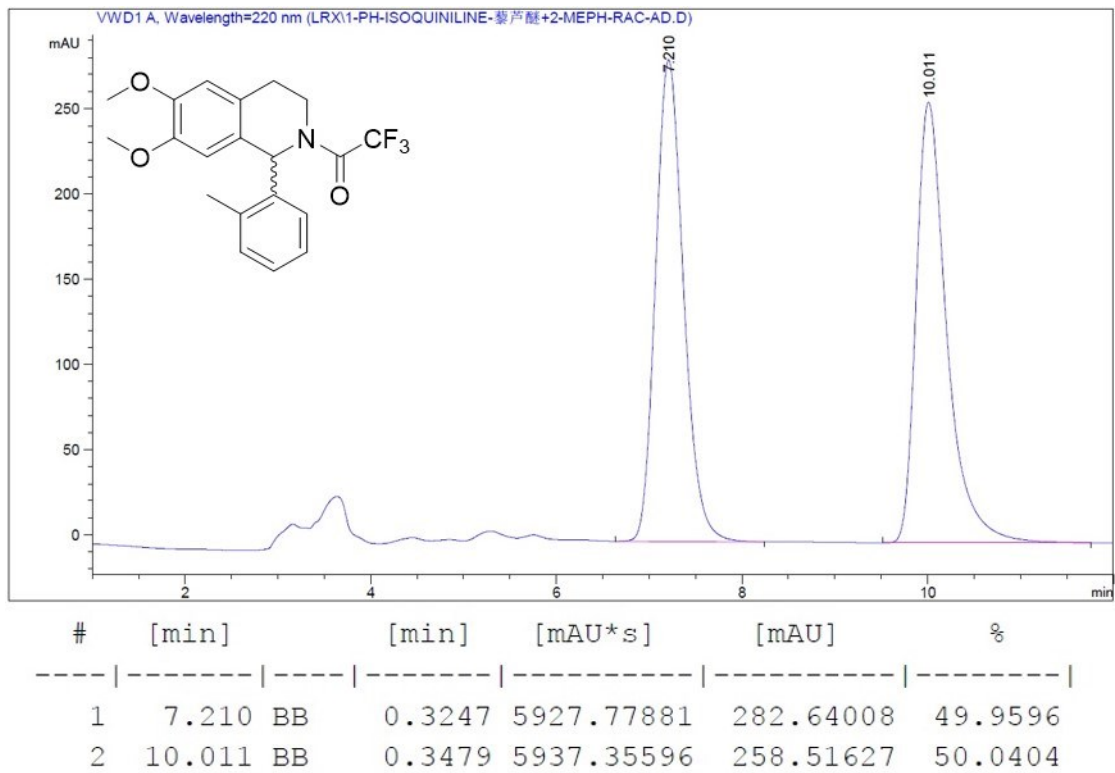


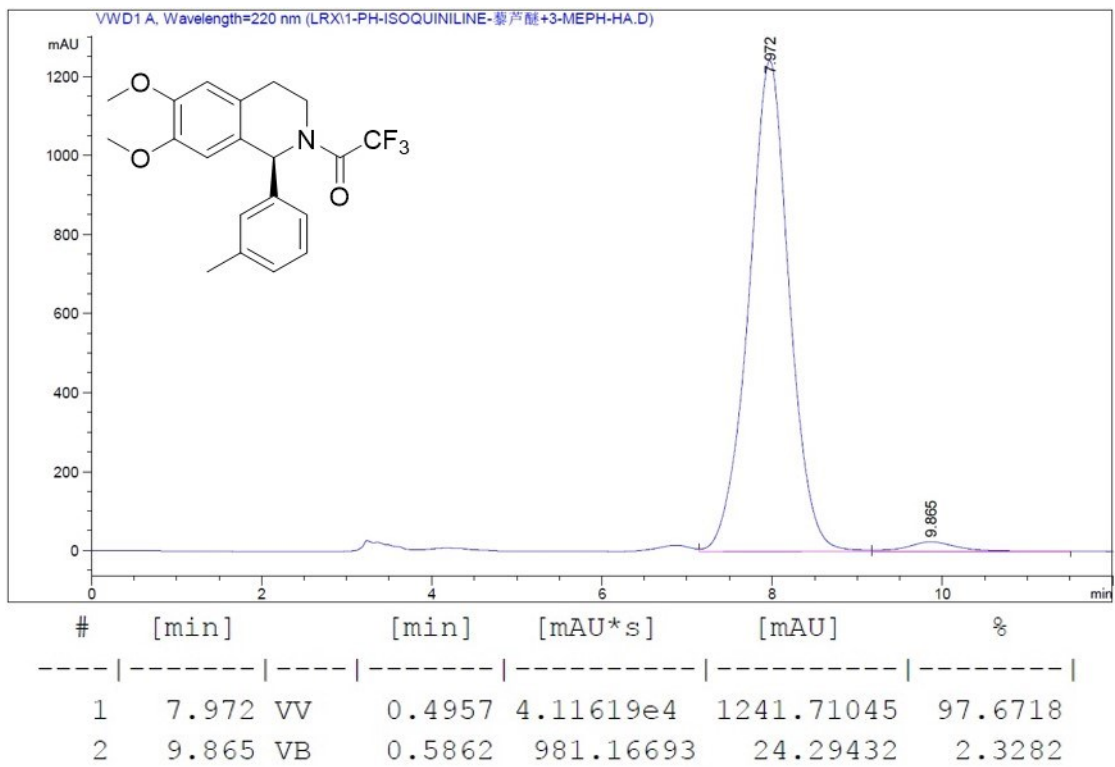
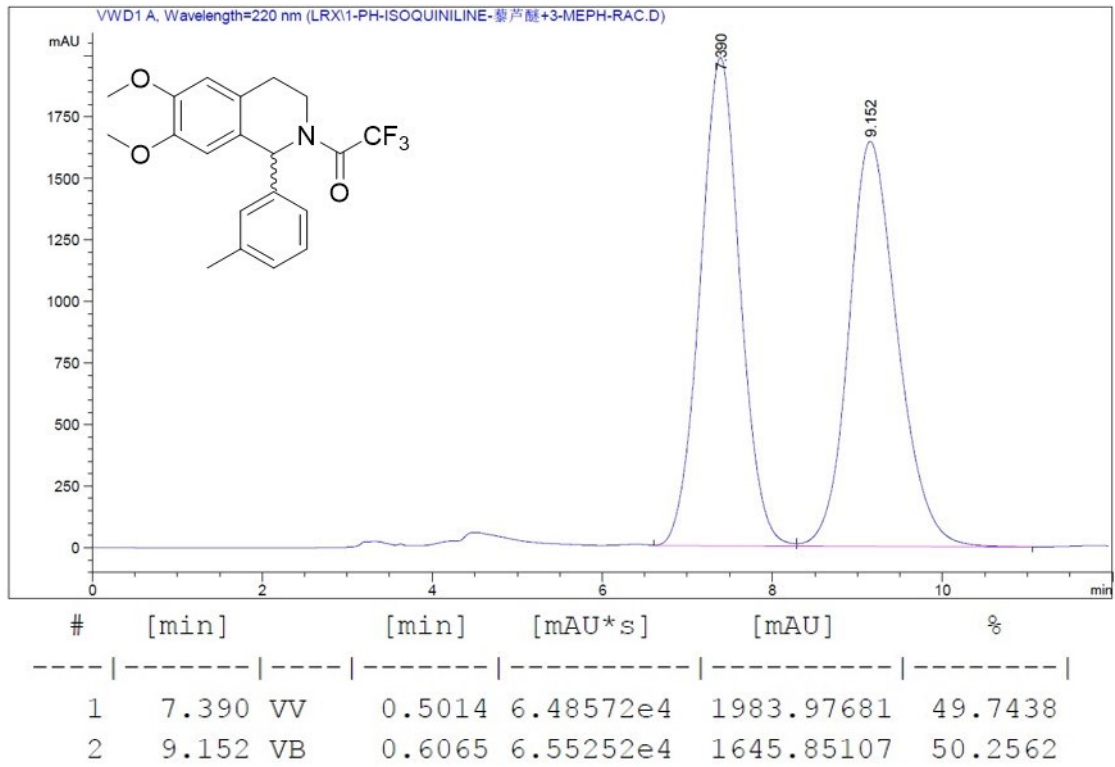


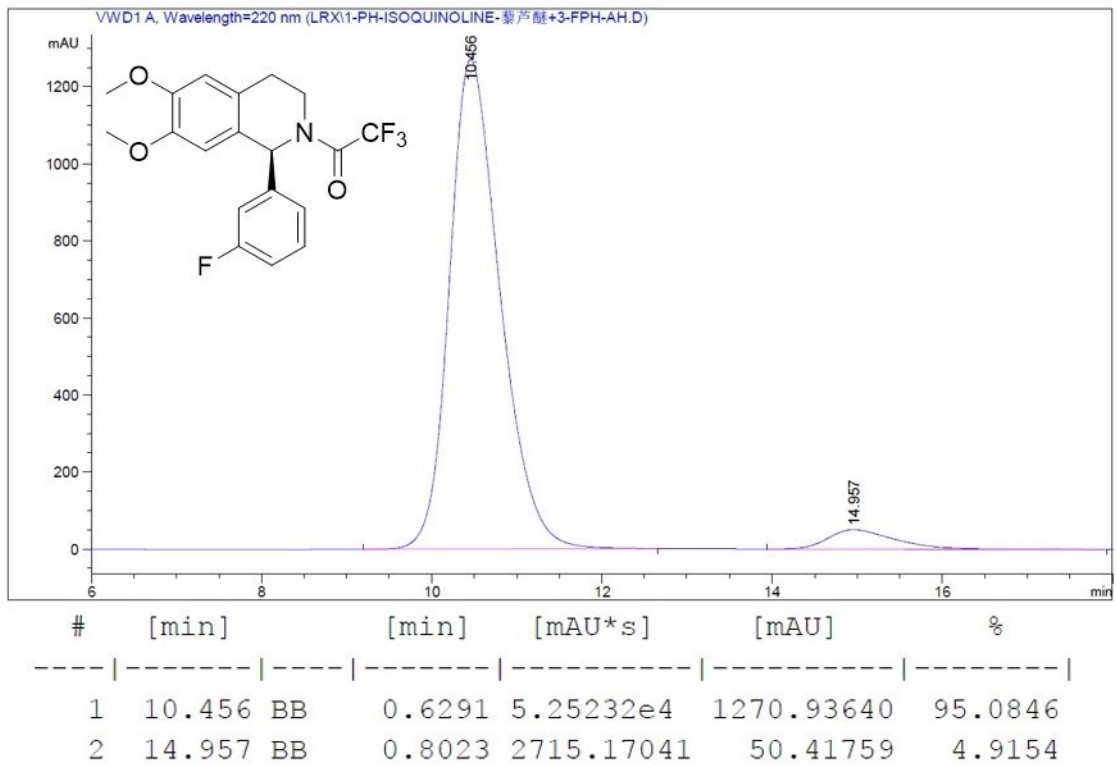
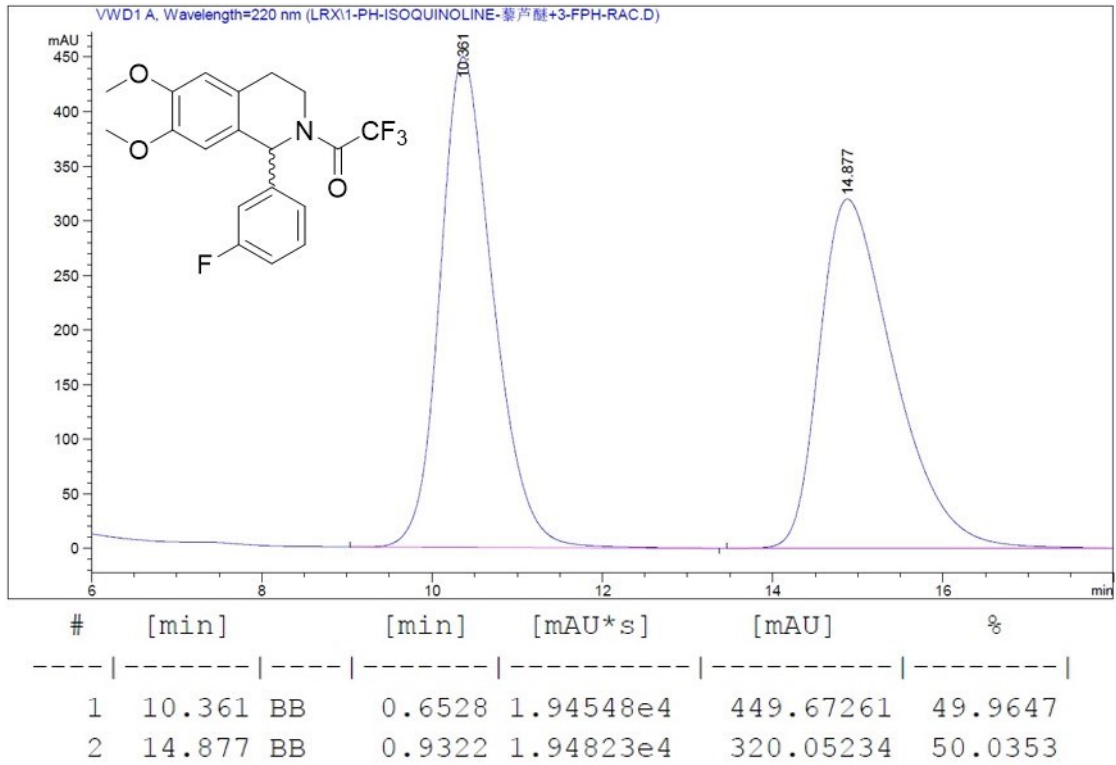


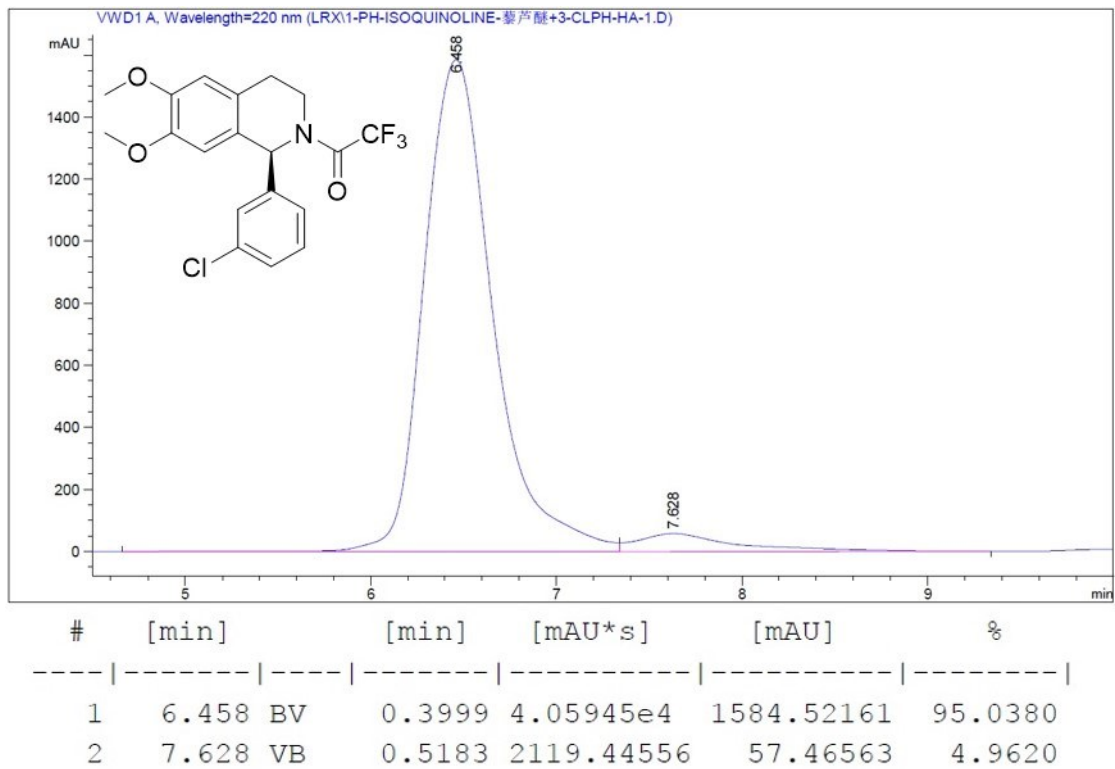
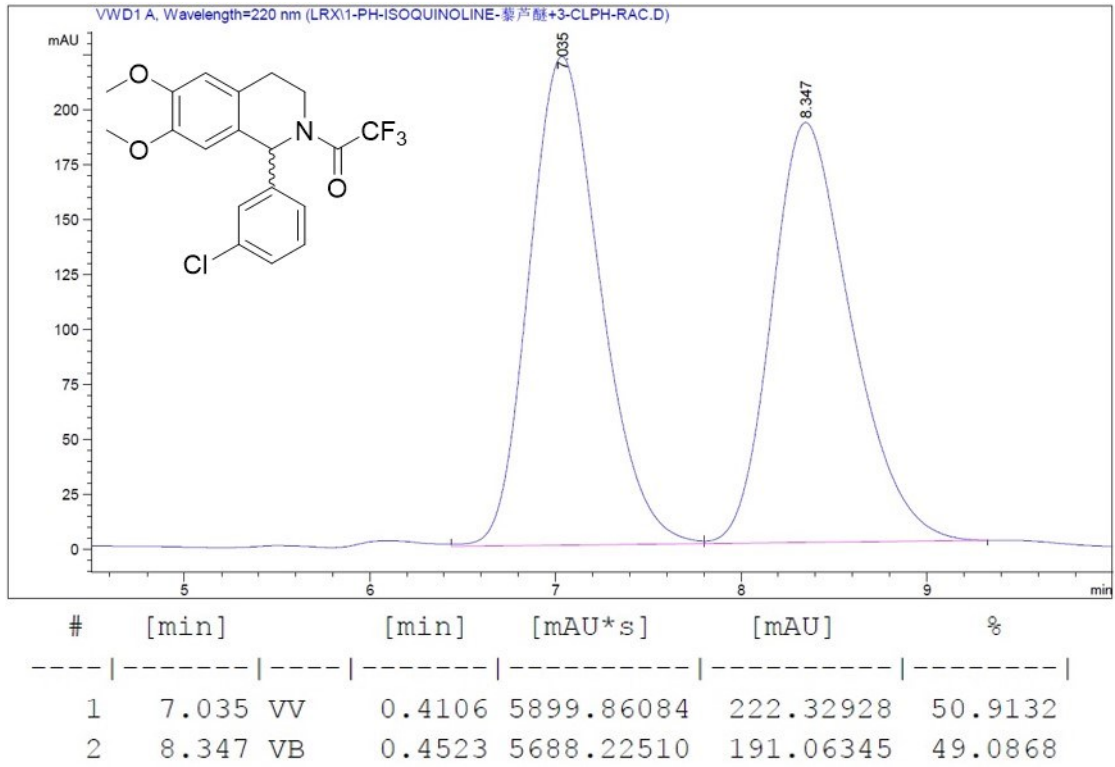


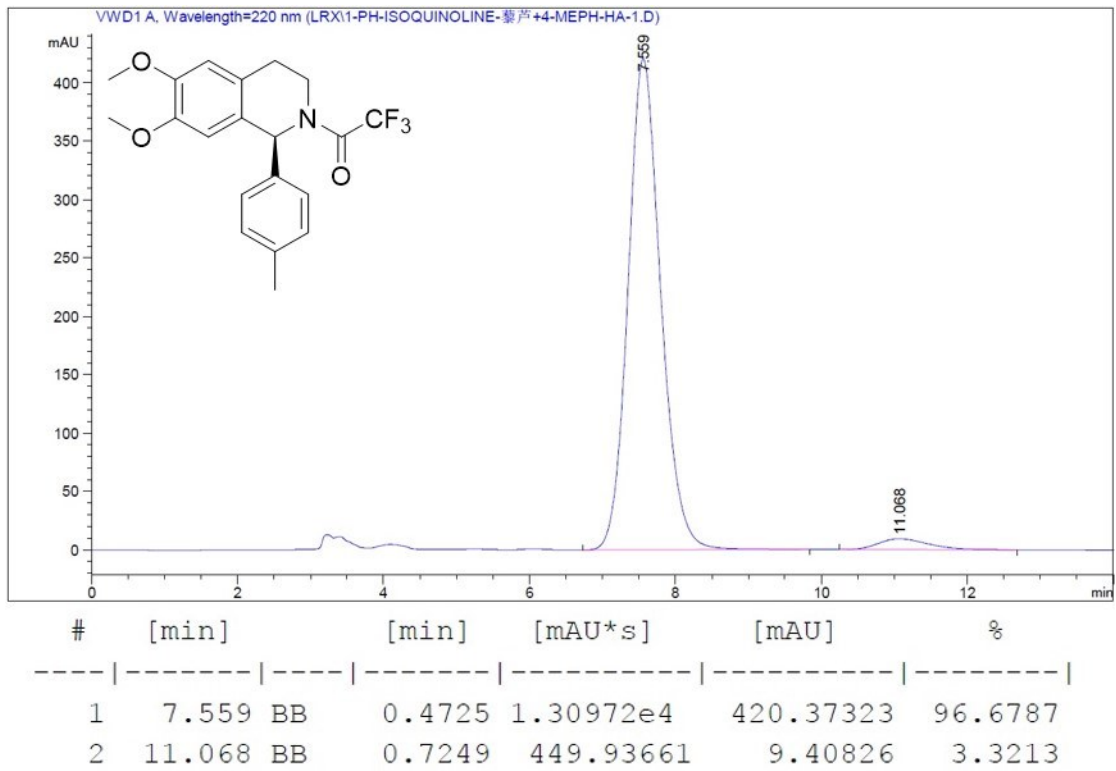
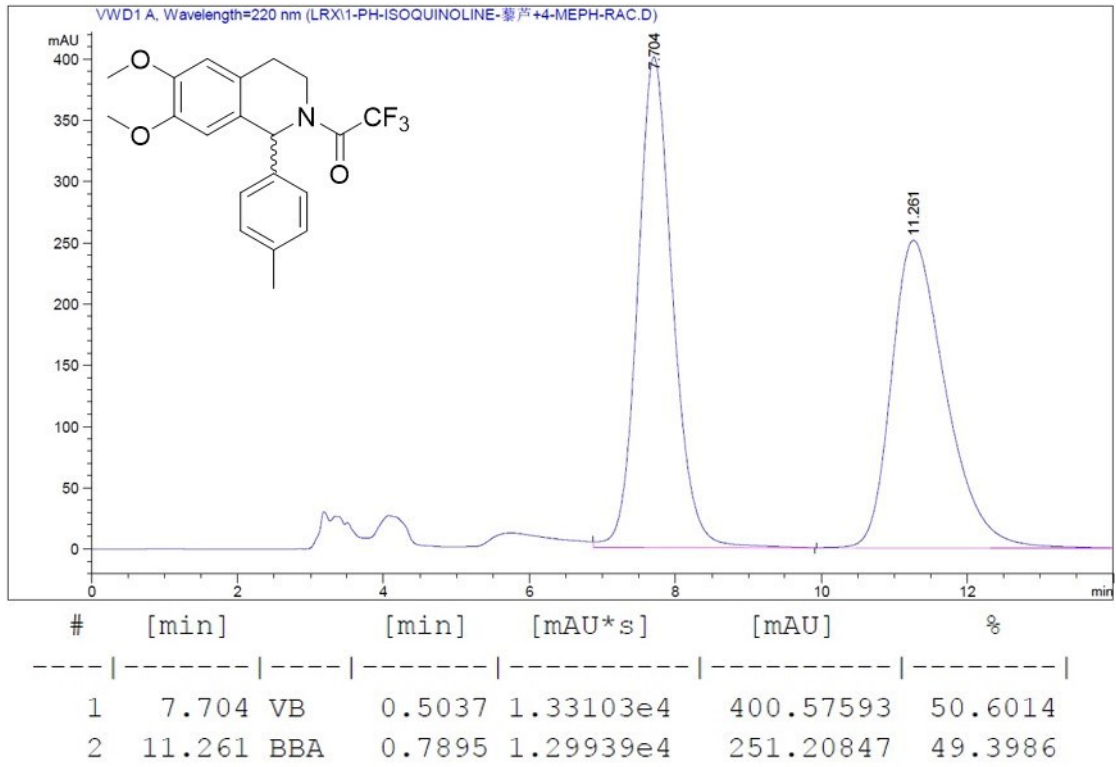


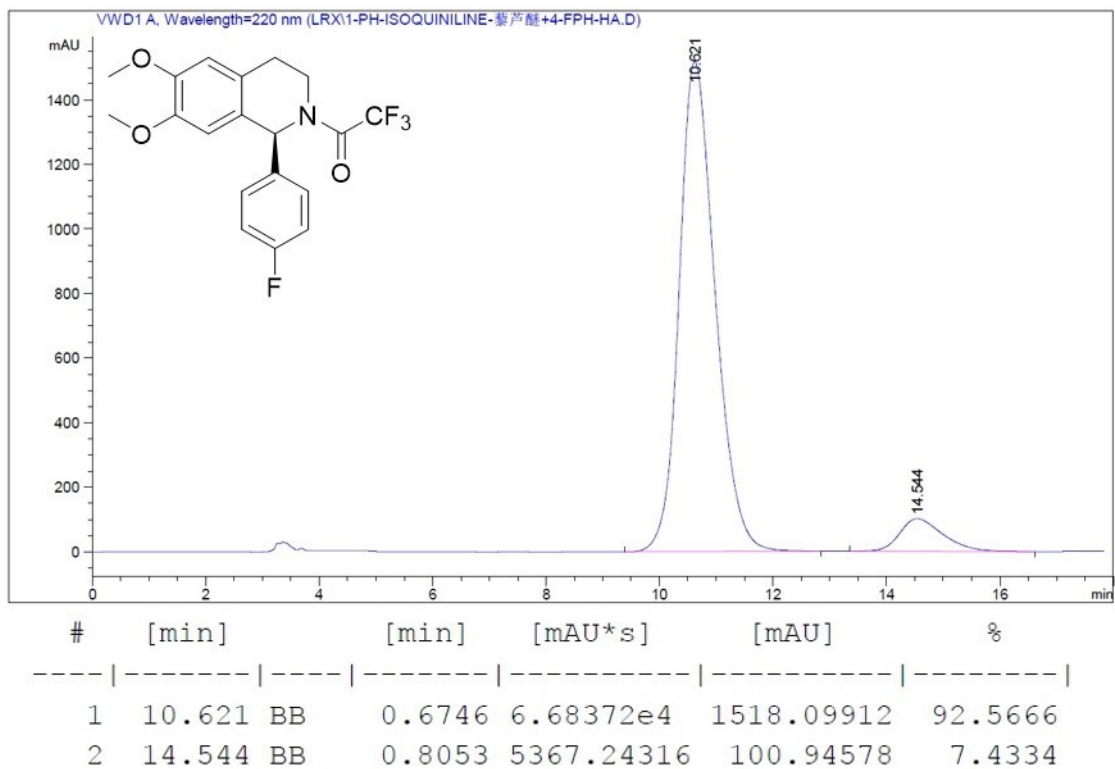
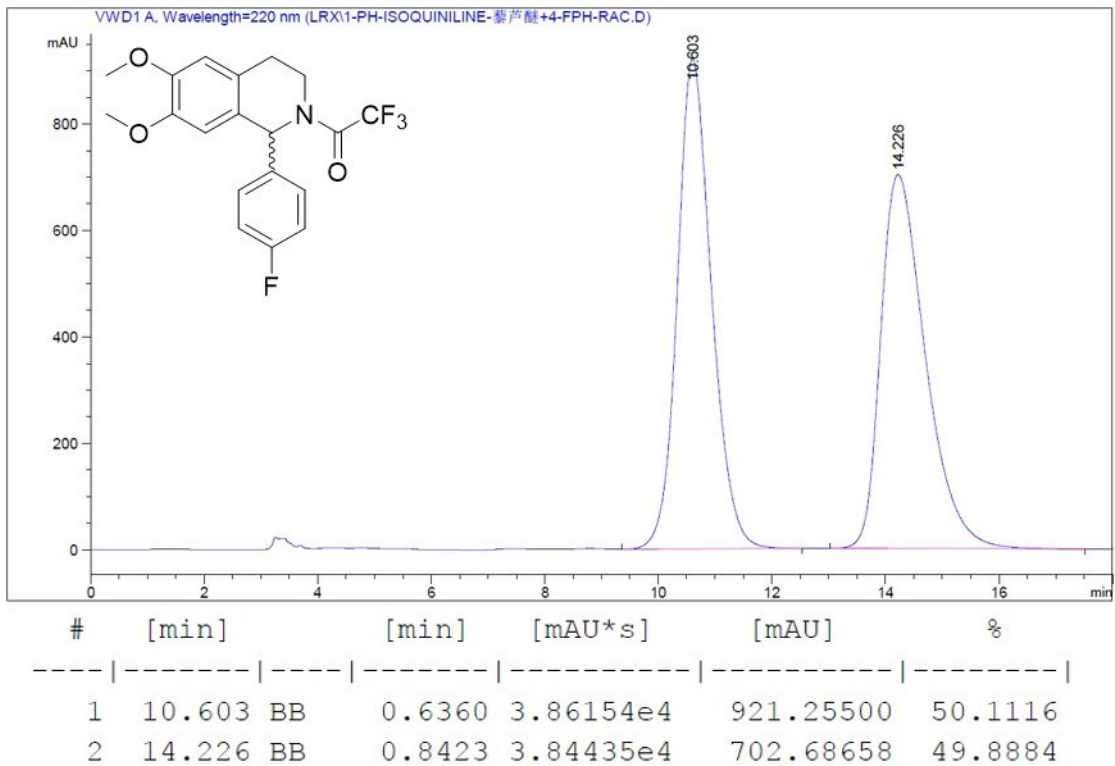


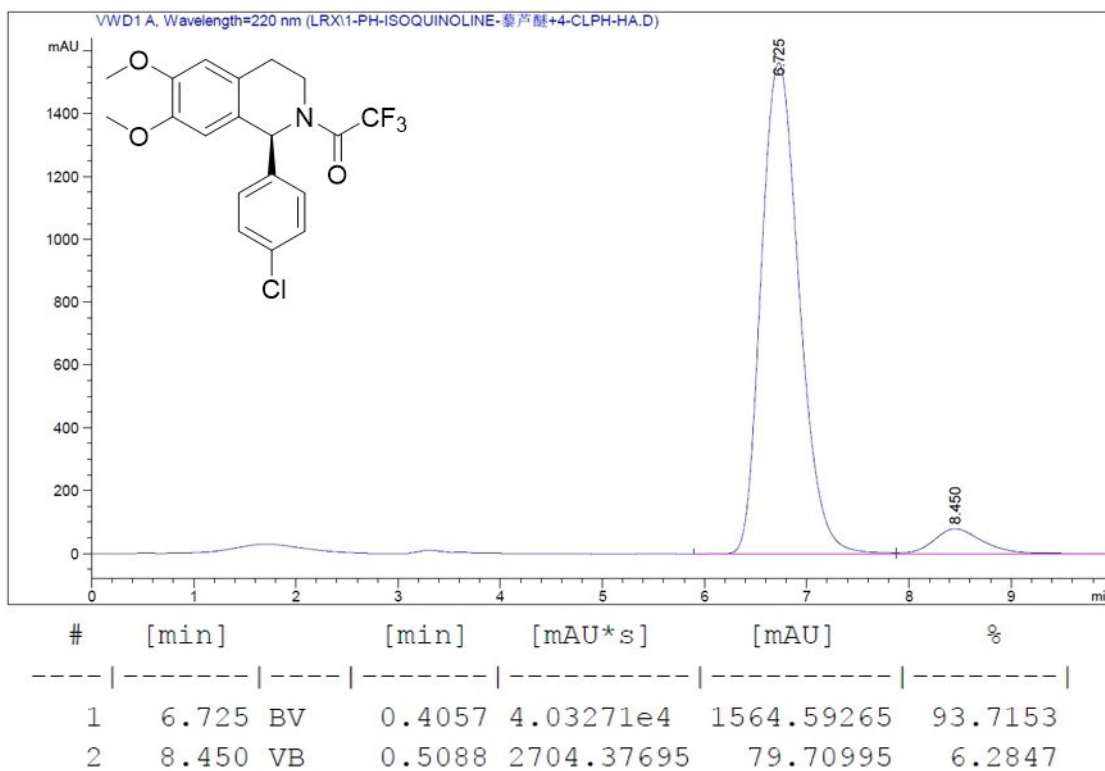
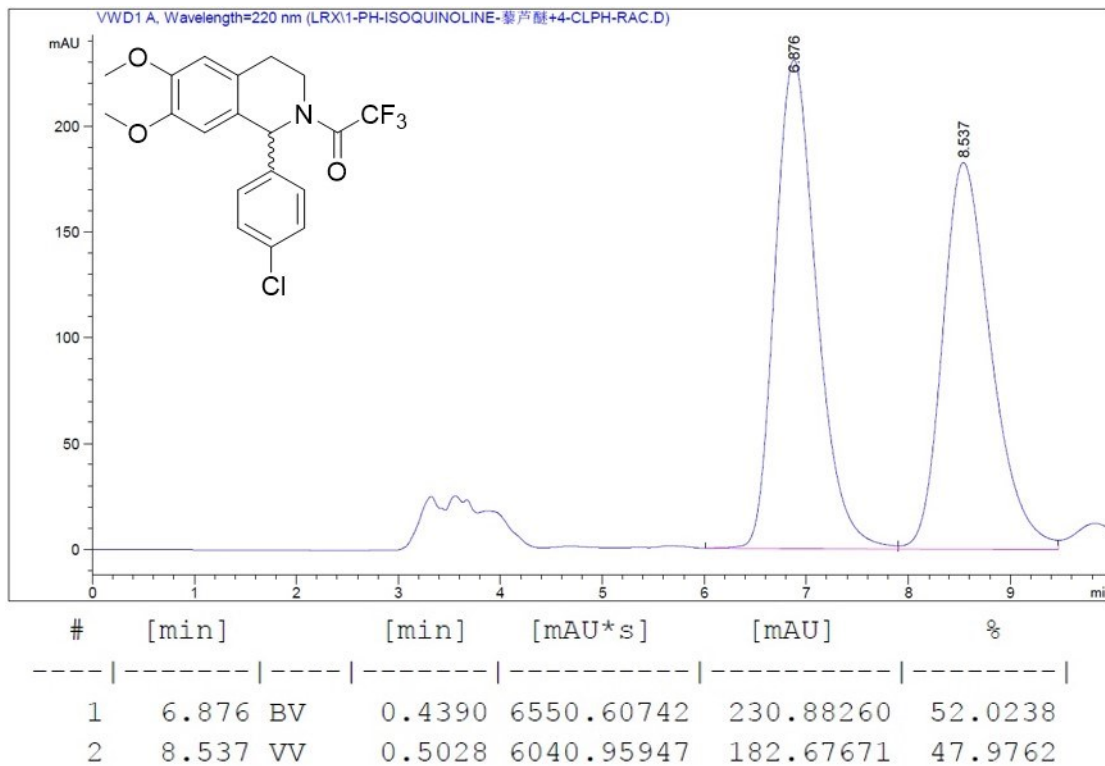


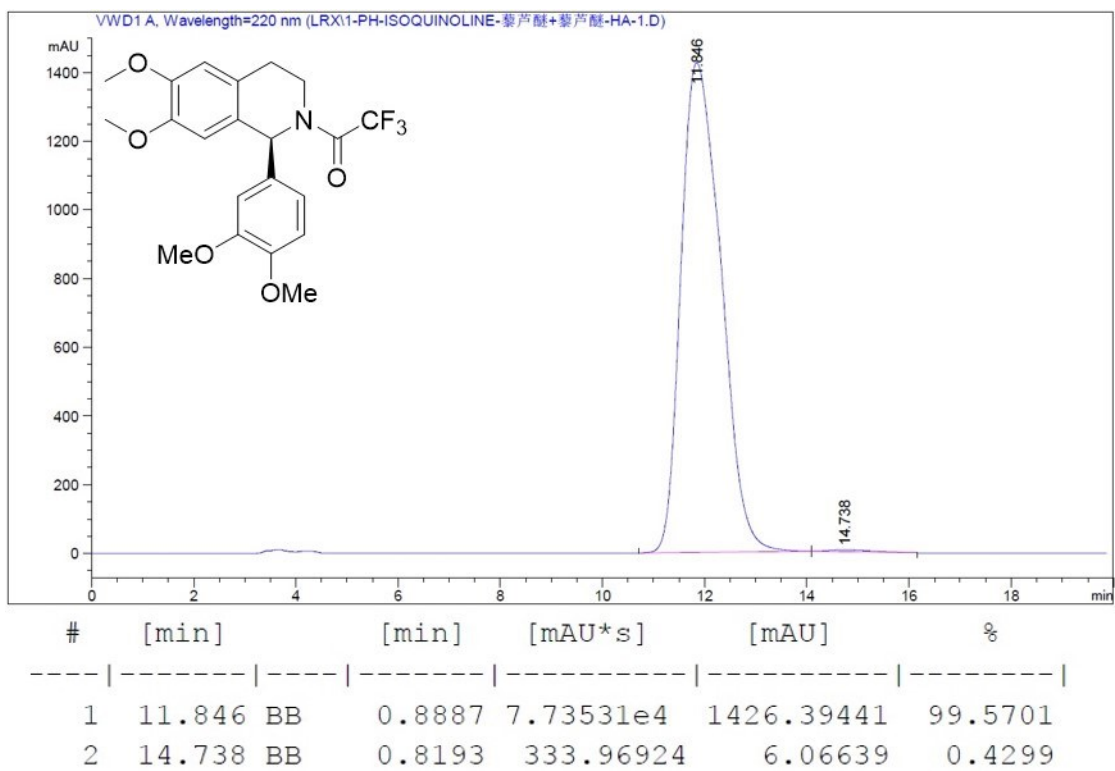
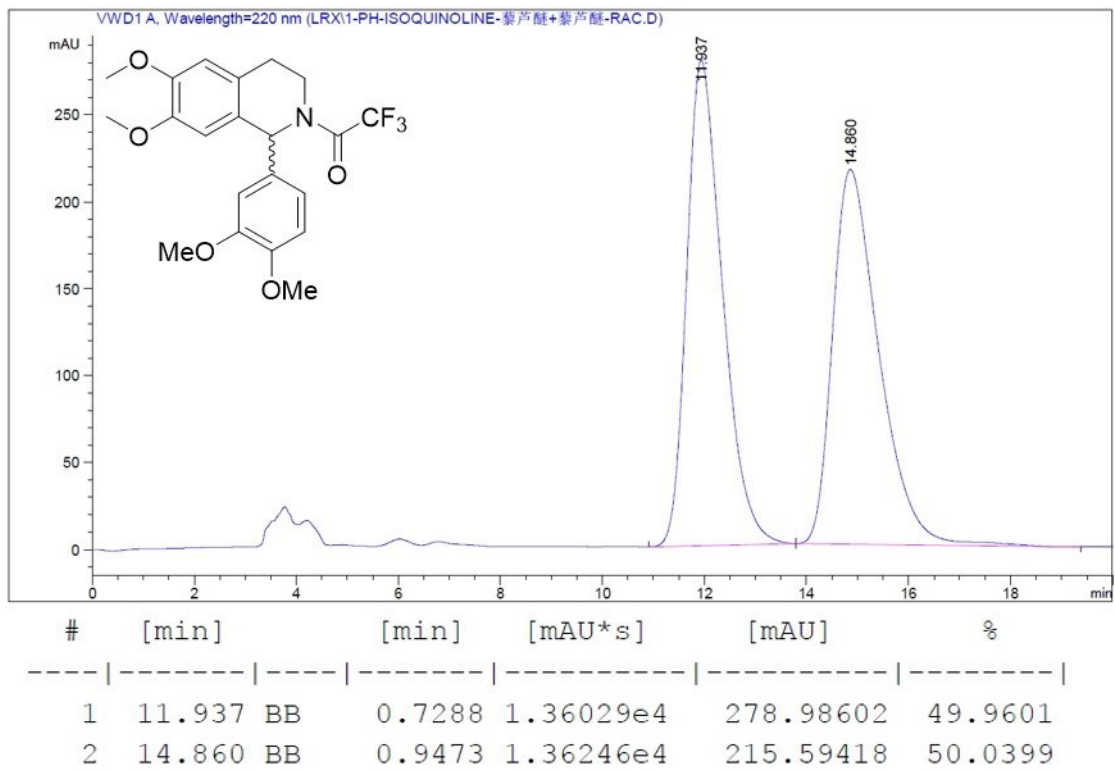


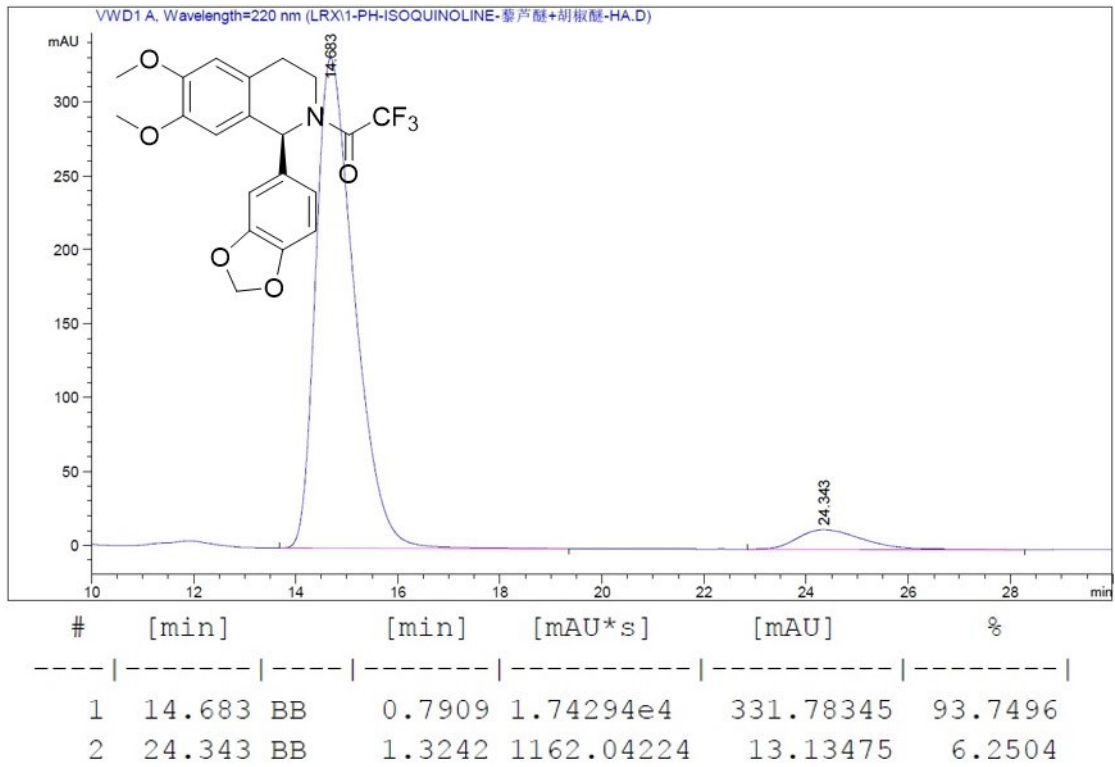
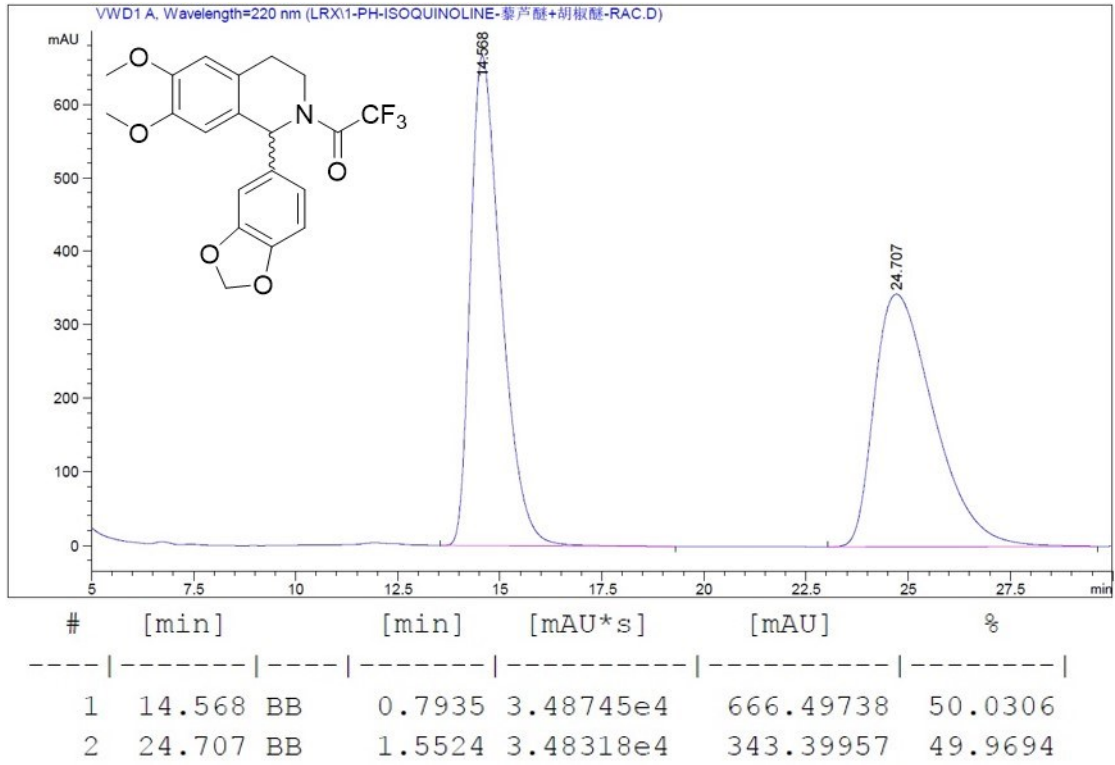


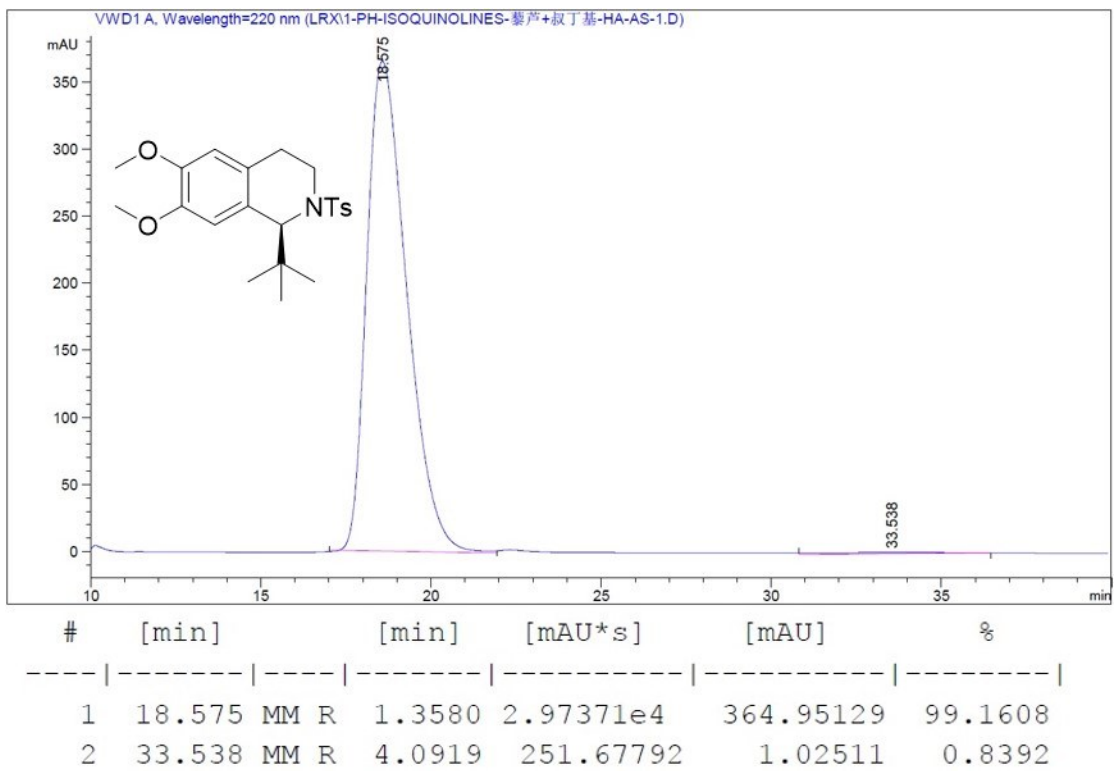
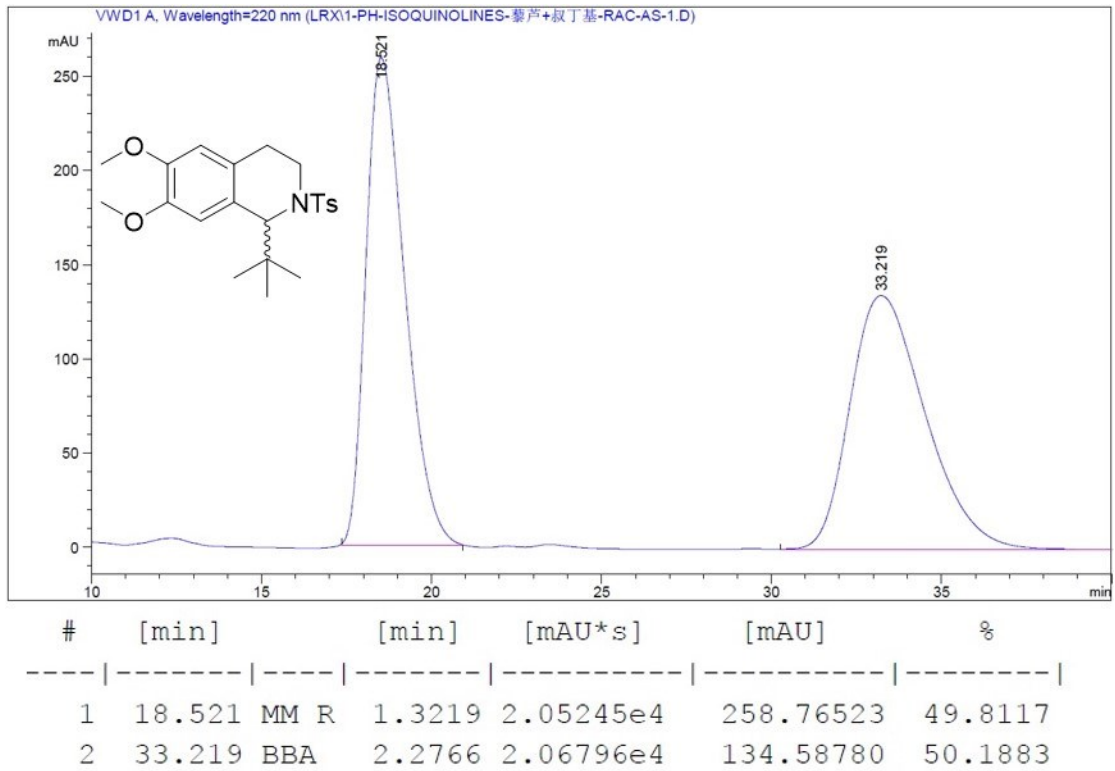


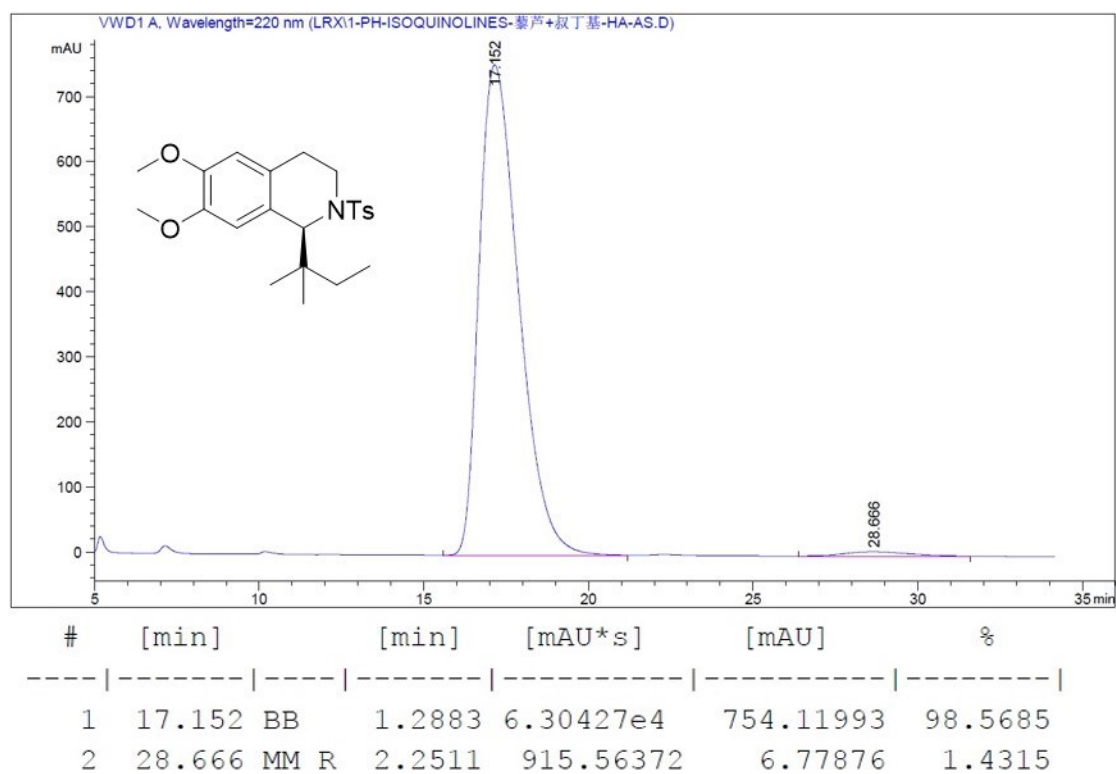
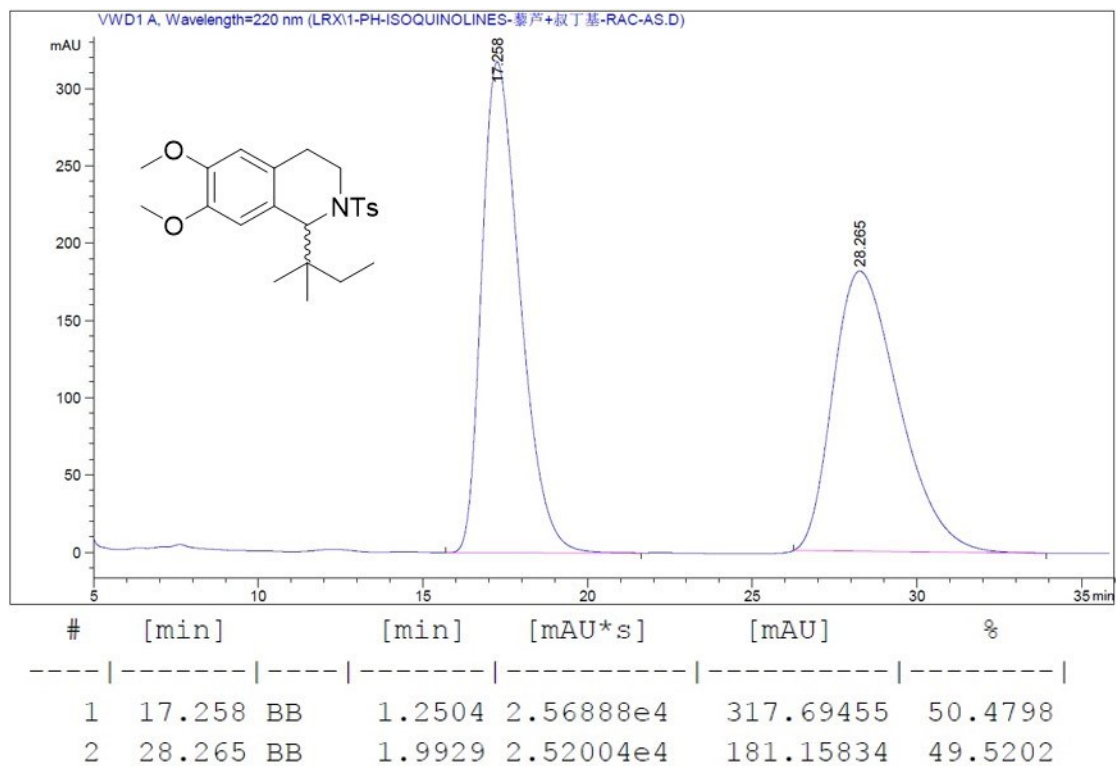


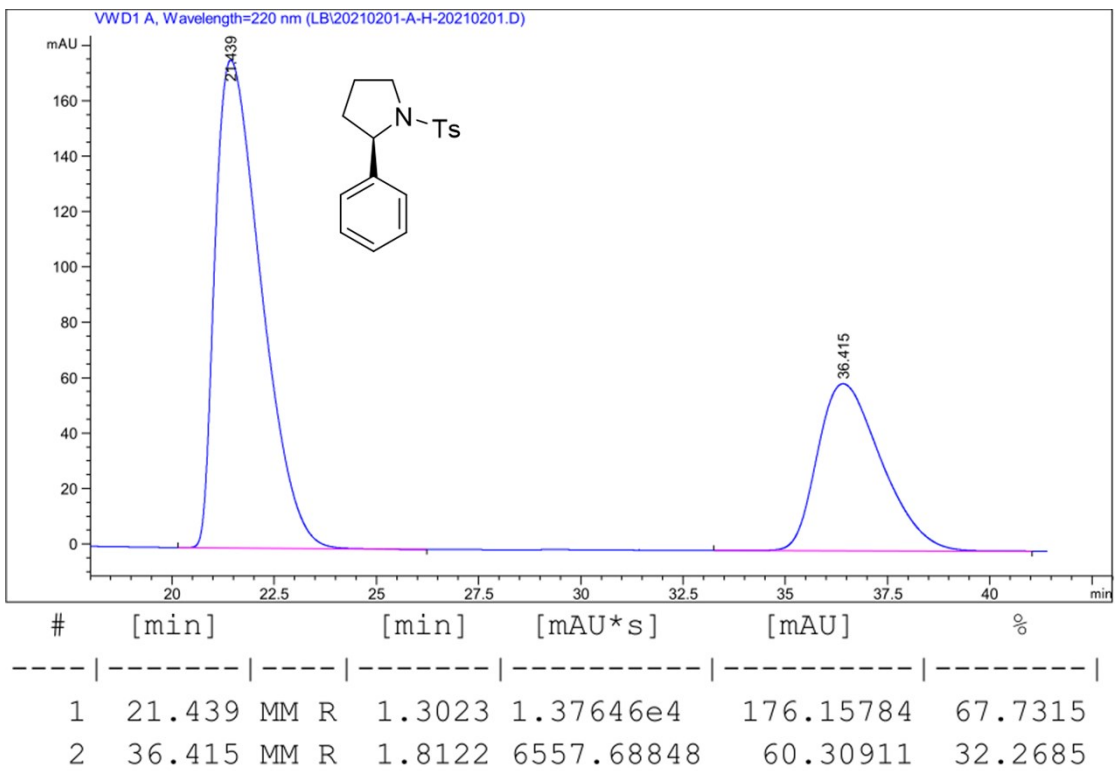
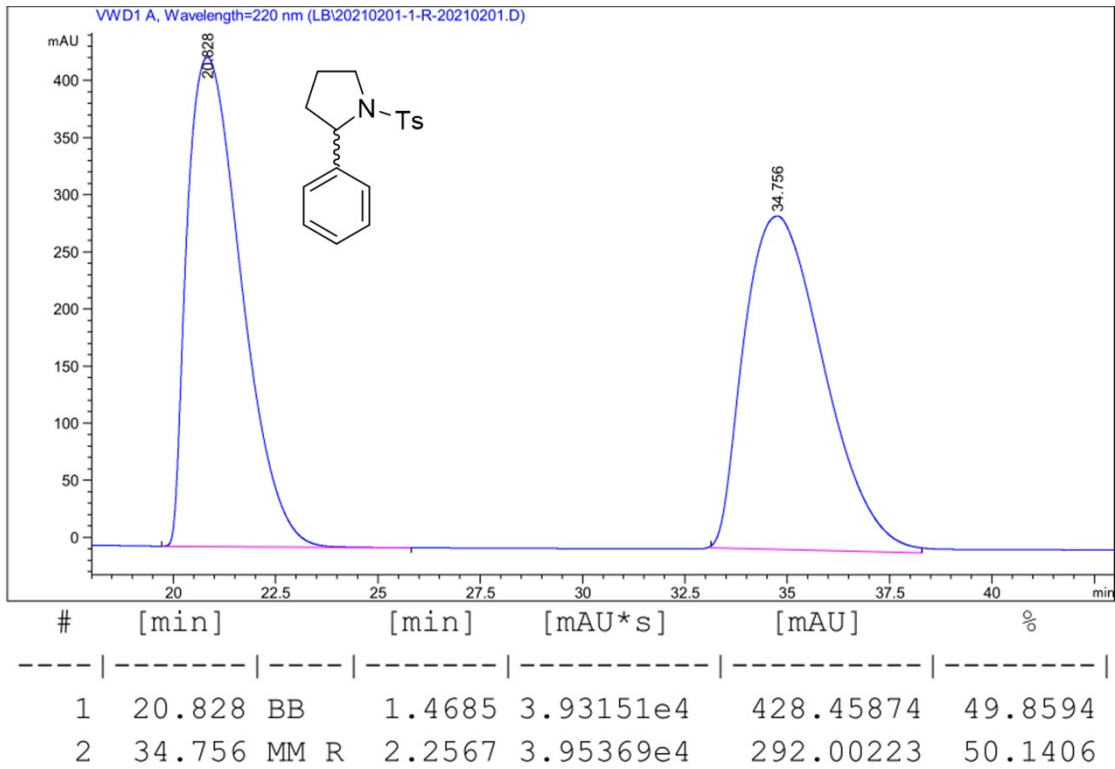












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