Electronic Supplementary Material (ESI) for Chemical Communications

Supporting Information

An Efficient Route to Chiral *N*-Heterocycles Bearing C-F Stereogenic Center *via* Asymmetric Hydrogenation of Fluorinated Isoquinolines

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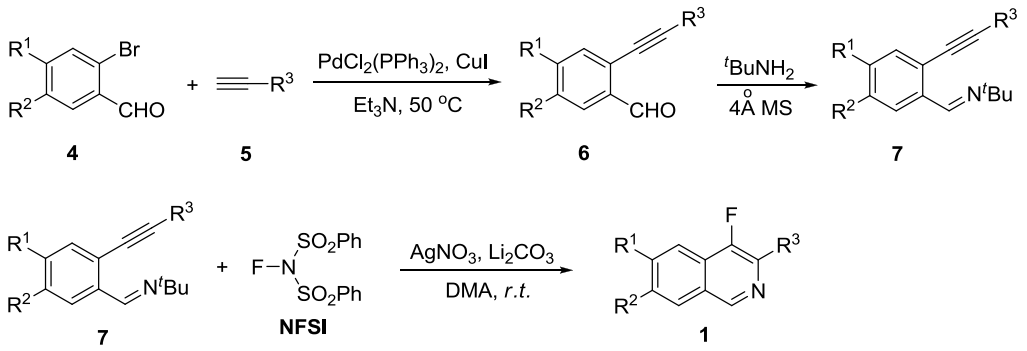
1. General experimental details:

Commercially available reagents were used without further purification. Solvents were treated prior to use according to the standard methods. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded at room temperature in $CDCl_3$ or DMSO-d_6 on 400 MHz instrument with tetramethylsilane (TMS) as internal standard. Enantiomeric excess was determined by HPLC analysis, using chiral column described below in detail. Optical rotations were measured by polarimeter. Flash column chromatography was performed on silica gel (200-300 mesh). All reactions were monitored by TLC or NMR analysis.

2. General Procedure for substituted 4-Fluoroisoquinoline 1

2.1. Synthesis of Substituted 4-Fluoroisoquinoline 1a, 1d-f, 1h-n.

4-Fluoroisoquinoline derivatives can be conveniently synthesized from the easily accessible starting materials 2-bromobenzaldehydes according to the known literature procedure.[1] The compounds 3-butyl-4-fluoroisoquinoline (**1a**), 3-cyclopropyl-4-fluoroisoquinoline (**1e**), 3-butyl-4,7-difluoroisoquinoline (**1j**) are known compounds.



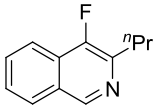
Typical procedure for the syntheses of 4-fluoroisoquinoline derivatives: $PdCl_2(PPh_3)_2$ (0.280 g, 0.40 mmol) and CuI (0.057 g, 0.30 mmol) was added to a solution of 2-Bromo-benzaldehyde (3.700 g, 20.00 mmol) and 1-heptyne (2.308 g, 24.00 mmol) in Et_3N (100 mL), and the resulting mixture was stirred at 50 °C for 5 h. The reaction was filtered, concentrated, and purified by silica gel column chromatography (hexane/EtOAc = 40:1), which furnished 2-(hept-1-ynyl) benzaldehyde (7.41 g, 99% yield) as orange oil.

To a mixture of 4Å MS (2.000 g) and *tert*-butylamine (25 mL) was added 2-(hept-1-ynyl) benzaldehyde at room temperature. The mixture was stirred overnight. Then the mixture was filtered and the filtrate was concentrated to get the pure imine derivative.

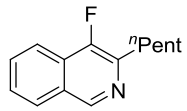
Under N_2, Li_2CO_3 (1.470 g, 19.90 mmol), NFSI (9.41 g, 29.90 mnol), $AgNO_3$ (0.679 g, 4.00 mmol) were dissolved in dry *N*,*N*-dimethyl acetamide (DMA, 50 mL), then the imine derivative was added. The mixture was stirred at room temperature, and the reaction was monitored by thin lay chromatography (TLC). After the reaction completed (5~10 hrs), water was added. The mixture was extracted with Et_2O. The combined organic extracts were concentrated under vacuum and the residue was purified by silica gel column chromatography (hexane/EtOAc = 20:1) affording the product 4-fluoro-3-pentylisoquinoline **1f** (3.157 g, 73% yield) as pale yellow oil.

1. Xu, T.; Liu, G. *Org. Lett.* **2012**, *14*, 5416.

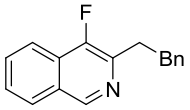
4-Fluoro-3-propylisoquinoline (1d): pale yellow oil, 51% yield, R_f = 0.45 (petroleum ether/EtOAc 20/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (s, 1H), 7.98 (d, *J* = 8.1 Hz, 1H), 7.89 (d, *J* = 6.3 Hz, 1H), 7.66 (m, 1H), 7.52-7.51 (m, 1H), 2.97 (t, *J* = 7.4 Hz, 2H), 1.94-1.74 (m, 2H), 1.01 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.4 (d, $^1J_{FC}$ = 257.1 Hz), 147.3 (d, $^3J_{FC}$ = 6.0 Hz), 140.6 (d, $^2J_{FC}$ = 15.8 Hz), 130.4, 128.9 (d, $^4J_{FC}$ = 2.3 Hz), 127.1, 126.9, 126.6 (d, $^2J_{FC}$ = 16.6 Hz), 119.4 (d, $^3J_{FC}$ = 4.6 Hz), 33.1 (d, $^3J_{FC}$ = 1.6 Hz), 22.4, 14.0; ^{19}F NMR (376 MHz, $CDCl_3$): δ -140.7 (s). HRMS Calculated for $C_{12}H_{13}FN$ $[M+H]^+$ 190.1032, found 190.1024.



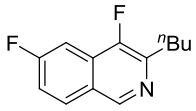
4-Fluoro-3-pentylisoquinoline (1f): pale yellow oil, 72% yield, R_f = 0.40 (petroleum ether/EtOAc 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (s, 1H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.68-7.64 (m, 1H), 7.54-7.50 (m, 1H), 2.97 (td, *J* = 8.1, 1.8 Hz, 2H), 1.87-1.71 (m, 2H), 1.36-1.35 (m, 4H), 0.88 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.4 (d, $^1J_{FC}$ = 257.2 Hz), 147.4 (d, $^3J_{FC}$ = 6.1 Hz), 141.0 (d, $^2J_{FC}$ = 15.8 Hz), 130.5, 129.0 (d, $^4J_{FC}$ = 2.5 Hz), 127.1, 127.0 (d, $^4J_{FC}$ = 1.8 Hz), 126.7 (d, $^2J_{FC}$ = 16.7 Hz), 119.5 (d, $^3J_{FC}$ = 4.6 Hz), 31.8, 31.2 (d, $^4J_{FC}$ = 1.7 Hz), 29.0 (d, $^5J_{FC}$ = 1.2 Hz), 22.7, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$): δ -140.7 (s); HRMS Calculated for $C_{14}H_{17}FN$ $[M+H]^+$ 218.1345, found 218.1333.



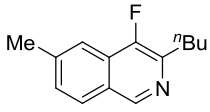
4-Fluoro-3-phenethylisoquinoline (1h): pale yellow oil, 52% yield, R_f = 0.50 (petroleum ether/EtOAc 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (s, 1H), 8.03 (d, *J* = 8.9 Hz, 1H), 7.98 (d, *J* = 8.1 Hz, 1H), 7.75-7.71 (m, 1H), 7.63-7.59 (m, 1H), 7.27 (m, 5H), 7.20 (s, 1H), 3.31 (t, *J* = 7.2 Hz, 2H), 3.12 (t, *J* = 7.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.6 (d, $^1J_{FC}$ = 257.8 Hz), 147.6 (d, $^3J_{FC}$ = 6.1 Hz), 141.8, 139.8 (d, $^2J_{FC}$ = 15.8 Hz), 130.7 (d, $^4J_{FC}$ = 1.5 Hz), 129.2 (d, $^4J_{FC}$ = 2.5 Hz), 128.7, 128.6, 127.4, 127.2 (d, $^4J_{FC}$ = 2.0 Hz), 126.8 (d, $^2J_{FC}$ = 16.5 Hz), 126.2, 119.6 (d, $^3J_{FC}$ = 4.6 Hz), 35.3 (d, $^3J_{FC}$ = 1.4 Hz), 33.1 (d, $^4J_{FC}$ = 1.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ -140.3 (s); HRMS Calculated for $C_{17}H_{15}FN$ $[M+H]^+$ 252.1189, found 252.1182.



3-Butyl-4,6-difluoroisoquinoline (1i): pale yellow oil, 72% yield, R_f = 0.30 (petroleum ether/EtOAc 20/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (s, 1H), 7.98 (ddd, *J* = 8.7, 5.2, 1.5 Hz, 1H), 7.62 (dd, *J* = 9.4, 2.0 Hz, 1H), 7.37-7.32 (m, 1H), 2.99 (td, *J* = 8.0, 2.9 Hz, 2H), 1.83-1.72 (m, 2H), 1.49-1.37 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5 (dd, $^1J_{FC}$ = 253.1 Hz, $^4J_{FC}$ = 1.2 Hz), 152.1 (dd, $^1J_{FC}$ = 257.0, $^4J_{FC}$ = 5.5 Hz), 147.0 (dd, $^4J_{FC}$ = 6.0 Hz, $^5J_{FC}$ = 1.1 Hz), 142.0 (dd, $^2J_{FC}$ = 15.4 Hz, $^5J_{FC}$ = 1.1 Hz), 130.3 (dd, $^3J_{FC}$ = 9.9 Hz, $^4J_{FC}$ = 2.0 Hz), 128.1 (dd, $^2J_{FC}$ = 16.9 Hz, $^3J_{FC}$ = 10.4 Hz), 126.2 (dd, $^3J_{FC}$ = 2.4 Hz, $^4J_{FC}$ = 0.8 Hz), 117.9 (d, $^2J_{FC}$ = 26.1 Hz), 103.6 (dd, $^2J_{FC}$ = 23.4 Hz, $^3J_{FC}$ = 5.0 Hz), 31.3 (d, $^3J_{FC}$ = 1.4 Hz), 30.9 (d, $^4J_{FC}$ = 1.7 Hz)., 22.7, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -105.6 (d, *J* = 5.9 Hz), -140.0 (d, *J* = 5.7 Hz); HRMS Calculated for $C_{13}H_{14}F_2N$ $[M+H]^+$ 222.1094, found 222.1102.

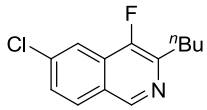


3-Butyl-4-fluoro-6-methylisoquinoline (1k): pale yellow oil, 70% yield, R_f = 0.30 (petroleum ether/EtOAc 20/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (s, 1H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.79 (s, 1H), 7.39 (d, *J* = 8.4 Hz, 1H), 2.98 (td, *J*= 8.2, 2.7 Hz, 2H), 2.56 (s, 3H), 1.82-1.71 (m, 2H), 1.48-1.37 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.2 (d, $^1J_{FC}$ = 256.2 Hz), 147.0 (d, $^3J_{FC}$ = 5.9 Hz), 141.1 (d, $^4J_{FC}$ = 1.5 Hz), 140.9 (d, $^2J_{FC}$ = 15.8 Hz), 129.5, 127.6 (d, $^3J_{FC}$ = 2.8 Hz), 127.0 (d,

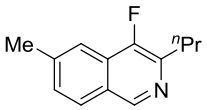


$^{2}J_{FC}$ = 16.2 Hz), 126.9 (d, $^{4}J_{FC}$ = 2.1 Hz), 118.2 (d, $^{3}J_{FC}$ = 4.4 Hz), 31.4 (d, $^{3}J_{FC}$ = 1.5 Hz), 30.9 (d, $^{4}J_{FC}$ = 1.7 Hz), 22.7, 22.4, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -140.1 (s); HRMS Calculated for $C_{14}H_{17}FN$ $[M+H]^+$ 218.1345, found 218.1349.

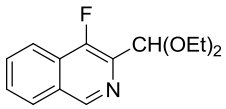
3-Butyl-6-chloro-4-fluoroisoquinoline (1l): pale yellow oil, 54% yield, R_f = 0.30 (petroleum ether/EtOAc 20/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (s, 1H), 8.02 (s, 1H), 7.90 (dd, *J* = 8.8, 1.6 Hz, 1H), 7.52 (dd, *J* = 8.8, 1.7 Hz, 1H), 3.00 (td, *J* = 7.9, 3.0 Hz, 2H), 1.82-1.73 (m, 2H), 1.48-1.37 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5 (d, $^{1}J_{FC}$ = 258.2 Hz), 147.2 (d, $^{3}J_{FC}$ = 6.2 Hz), 142.4 (d, $^{2}J_{FC}$ = 15.6 Hz), 137.2 (d, $^{4}J_{FC}$ = 1.5 Hz), 128.9 (d, $^{4}J_{FC}$ = 1.9 Hz), 128.5 (d, $^{5}J_{FC}$ = 0.5 Hz), 127.5 (d, $^{2}J_{FC}$ = 16.6 Hz), 127.2 (d, $^{4}J_{FC}$ = 2.0 Hz), 118.9 (d, $^{3}J_{FC}$ = 4.8 Hz), 31.3 (d, $^{3}J_{FC}$ = 1.4 Hz), 31.0 (d, $^{4}J_{FC}$ = 1.8 Hz), 22.7, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -141.3 (s); HRMS Calculated for $C_{13}H_{14}FNCl$ $[M+H]^+$ 238.0799, found 238.0791.



4-Fluoro-6-methyl-3-propylisoquinoline (1m): pale yellow oil, 63% yield, R_f = 0.40 (petroleum ether/EtOAc 20/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (s, 1H), 7.82 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.77 (s, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 2.96 (td, *J* = 7.8, 2.9 Hz, 2H), 2.55 (s, 3H), 1.88-1.77 (m, 2H), 1.00 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3 (d, $^{1}J_{FC}$ = 256.3 Hz), 147.1 (d, $^{3}J_{FC}$ = 6.0 Hz), 141.1 (d, $^{4}J_{FC}$ = 1.5 Hz), 140.7 (d, $^{2}J_{FC}$ = 15.8 Hz), 129.5, 127.6 (d, $^{3}J_{FC}$ = 2.8 Hz), 127.0 (d, $^{2}J_{FC}$ = 17.2 Hz), 126.9 (d, $^{4}J_{FC}$ = 2.1 Hz), 118.3 (d, $^{3}J_{FC}$ = 4.4 Hz), 33.2 (d, *J* = 1.8 Hz), 22.6 (d, *J* = 1.4 Hz), 22.4, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -141.3 (s); HRMS Calculated for $C_{13}H_{15}FN$ $[M+H]^+$ 204.1189, found 204.1175.

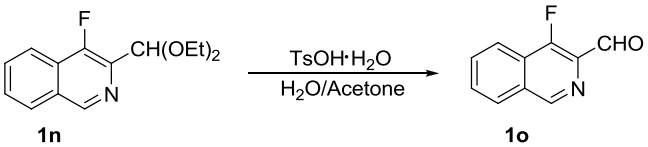


3-(Diethoxymethyl)-4-fluoroisoquinoline (1n): pale yellow oil, 78% yield, R_f = 0.35 (petroleum ether/EtOAc 20/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.12 (s, 1H), 8.12 (d, *J* = 8.4 Hz, 1H), 8.00 (d, *J* = 8.2 Hz, 1H), 7.79-7.75 (m, 1H), 7.69-7.65 (m, 1H), 5.99 (s, 1H), 3.87-3.80 (m, 2H), 3.78-3.68 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.7 (d, $^{1}J_{FC}$ = 263.9 Hz), 148.0 (d, $^{3}J_{FC}$ = 5.8 Hz), 136.0 (d, $^{2}J_{FC}$ = 11.6 Hz), 130.9 (d, $^{4}J_{FC}$ = 1.5 Hz), 130.3 (d, $^{4}J_{FC}$ = 3.0 Hz), 128.5, 127.1 (d, $^{4}J_{FC}$ = 2.0 Hz), 126.9 (d, $^{2}J_{FC}$ = 16.0 Hz), 120.2 (d, $^{3}J_{FC}$ = 4.8 Hz), 98.4, 62.8, 15.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -140.4 (s); HRMS Calculated for $C_{14}H_{16}FNO_2Na$ $[M+Na]^+$ 272.1063, found 272.1071.



2.2. Synthesis of Substituted 4-Fluoroisoquinoline 1b, 1c, 1g

2.2.1. Synthesis of 4-fluoroisoquinoline-3-carbaldehyde 1o[2]



1n **1o**

A mixture of **1n** (7.50 g, 30.00 mmol) and *p*-TsOH·H_2O (0.286 g, 1.50 mmol) in H_2O/acetone (1:1, 150 mL) was heated under reflux for 3 h. After the reaction cooled to room temperature, saturated $NaHCO_3$ was added, and the solution was extracted with diethyl ether (50 mL×3). The organic layer was washed with brine (20 mL), dried (Na_2SO_4). After filtration and

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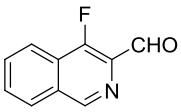
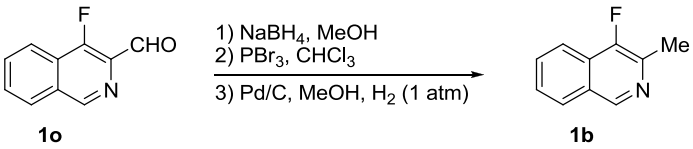
evaporation, the residue was purified by silica gel column chromatography (petroleum ether/EtOAc 10/1) to yield the product **1o**.

4-Fluoroisoquinoline-3-carbaldehyde (1o): 85% yield, pale yellow solid, m.p. 88–89 °C, R_f = 0.30 (petroleum ether/EtOAc 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.48 (s, 1H), 9.18 (s, 1H), 8.29 (d, J = 7.3 Hz, 1H), 8.12 (d, J = 7.2 Hz, 1H), 7.93-7.87 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.6, 158.3 (d, $^1J_{FC}$ = 280.7 Hz), 149.0 (d, $^4J_{FC}$ = 5.4 Hz), 132.4 (d, $^3J_{FC}$ = 4.7 Hz), 132.1 (d, $^2J_{FC}$ = 5.8 Hz), 131.9 (d, $^4J_{FC}$ = 1.5 Hz), 131.5, 127.6 (d, $^4J_{FC}$ = 1.9 Hz), 126.7 (d, $^2J_{FC}$ = 15.9 Hz), 121.7 (d, $^3J_{FC}$ = 5.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ -136.1 (s); HRMS Calculated for $C_{10}H_6FNONa$ $[M+Na]^+$ 198.0331, found 198.0326.



2.2.2. Synthesis of 4-fluoro-3-methylisoquinoline 1b



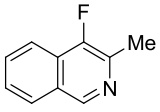
1o **1b**

To a solution of **1o** (0.500 g, 2.85 mmol, 1 eq.) in methanol (15 mL) was added sodium borohydride (0.270 g, 2.5 eq.) at 0 °C. After 30 min, the mixture was allowed to room temperature and stirred for another 1 h. After being quenched by water (10 mL), the solvent was evaporated, and the mixture was extracted by dichloromethane (20 mL×3), then the organic layer was dried ($MgSO_4$), filtered, and concentrated to yield a white powder.

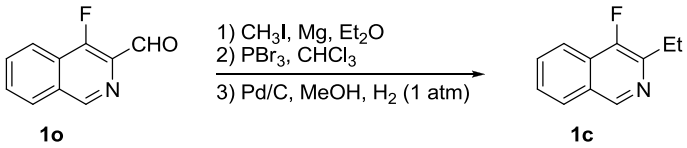
Under N_2, the white powder was dissolved in chloroform (80 mL). To the solution was added phosphorus tribromide (1.6 mL, 6 eq.), then the mixture was heated under reflux for 14 h. After being cooled to 0 °C, the medium was hydrolyzed with saturated $NaHCO_3$ to pH 8. The phases were separated, and the aqueous phase was extracted with dichloromethane (30 mL×3). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated. The crude product was pure enough for further reaction.

To the solution of the crude product in methanol (4 mL) was added Pd/C (4 mol%) and the mixture was stirred under H_2 (1 atm) for 15 h. After carefully releasing the hydrogen, the reaction mixture was neutralised by saturated $NaHCO_3$ and then filtered through Celite. The product was extracted with CH_2Cl_2 (5 mL×3), and the combined organic layer was dried (Na_2SO_4). After filtration and evaporation, the residue was purified by silica gel column chromatography (petroleum ether/EtOAc 10/1) to yield the product **1b**.

4-Fluoro-3-methylisoquinoline (1b): pale yellow oil, 45% yield, R_f = 0.50 (petroleum ether/EtOAc 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.00 (s, 1H), 8.04 (d, J = 8.4 Hz, 1H), 7.96 (d, J = 8.2 Hz, 1H), 7.75-7.71 (m, 1H), 7.61-7.57 (m, 1H), 2.68 (d, J = 3.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.7 (d, $^1J_{FC}$ = 256.8 Hz), 147.3 (d, $^3J_{FC}$ = 6.2 Hz), 136.9 (d, $^2J_{FC}$ = 16.8 Hz), 130.7, 129.1 (d, $^4J_{FC}$ = 2.0 Hz), 127.2, 127.1, 126.7 (d, $^4J_{FC}$ = 2.0 Hz), 119.4 (d, $^3J_{FC}$ = 4.4 Hz), 17.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ -139.0 (s); HRMS Calculated for $C_{10}H_9FN$ $[M+H]^+$ 162.0719, found 162.0698.



2.2.3. Synthesis of 3-ethyl-4-fluoroisoquinoline 1c



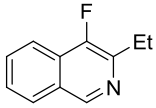
1o **1c**

To a solution of **1o** (0.500 g, 2.85 mmol, 1.0 eq.) in THF/Et_2O (1:1, 20 mL) was added the Et_2O solution of methyl magnesium iodide (1.2 eq.) dropwise at -70 ºC. After 2 h, the mixture was allowed to warm to room temperature and stirred overnight. The reaction was quenched by addition of saturated aqueous NH_4Cl solution. The phases were separated, and the aqueous phase was extracted with dichloromethane (30 mL×3). The combined organic phases were dried ($NaSO_4$), filtered, and concentrated to to yield a pale yellow powder.

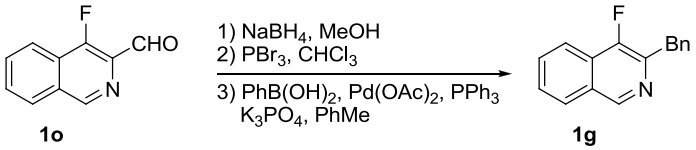
Under N_2, the pale yellow powder was dissolved in chloroform (80 mL). To the solution was added phosphorus tribromide (1.6 mL, 6 eq.), then the mixture was heated under reflux for 14 h. After being cooled to 0 °C, the medium was hydrolyzed with saturated $NaHCO_3$ to pH 8. The phases were separated, and the aqueous phase was extracted with dichloromethane (30 mL×3). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated. The crude product was pure enough for further reaction.

To the solution of the crude product in methanol (4 mL) was added Pd/C (4 mol%) and the mixture was stirred under H_2 (1 atm) for 15 h. After carefully releasing the hydrogen, the reaction mixture was neutralized with saturated $NaHCO_3$ and then filtered through Celite. The product was extracted with CH_2Cl_2 (5 mL×3), and the combined organic layer was dried (Na_2SO_4). After filtration and evaporation, the residue was purified by silica gel column chromatography (petroleum ether/EtOAc 10/1) to yield the product **1c**.

3-Ethyl-4-fluoroisoquinoline (1c): colorless oil, 26% yield, R_f = 0.40 (petroleum ether/EtOAc 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (s, 1H), 7.99 (d, *J* = 8.4 Hz, 1H), 7.90 (d, *J* = 8.3 Hz, 1H), 7.69-7.65 (m, 1H), 7.55-7.51 (m, 1H), 3.01 (qd, *J* = 7.6, 2.8 Hz, 2H), 1.35 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.2 (d, $^1J_{FC}$ = 257.4 Hz),, 147.5 (d, $^3J_{FC}$ = 6.1 Hz), 142.0 (d, $^2J_{FC}$ = 15.7 Hz), 130.5 (d, $^4J_{FC}$ = 1.6 Hz), 129.0 (d, $^4J_{FC}$ = 2.5 Hz), 127.2 (d, $^5J_{FC}$ = 0.7 Hz), 127.1 (d, $^4J_{FC}$ = 2.1 Hz), 126.8 (d, $^2J_{FC}$ = 16.5 Hz), 119.5 (d, $^3J_{FC}$ = 4.6 Hz), 24.5 (d, $^3J_{FC}$ = 1.3 Hz), 13.5 (d, $^4J_{FC}$ = 1.5 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ -141.0 (s); HRMS Calculated for $C_{11}H_{11}FN$ $[M+H]^+$ 176.0876, found 176.0862.



2.2.4. Synthesis of 3-Benzyl-4-fluoroisoquinoline 1g[3]



1o **1g**

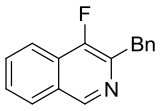
To a solution of **1o** (0.500 g, 2.85 mmol, 1 eq.) in methanol (15 mL) was added sodium borohydride (0.270 g, 2.5 eq.) at 0 °C. After 30 min, the mixture was allowed to room temperature and stirred for another 1 h. After being quenched by water (10 mL), the solvent was evaporated, and the mixture was extracted by dichloromethane (20 mL×3), then the organic layer was dried ($MgSO_4$), filtered, and concentrated to yield a white powder.

3 Monteiro, A. L. et al. *Tetrahedron Lett.* **2004**, *45*, 8225.

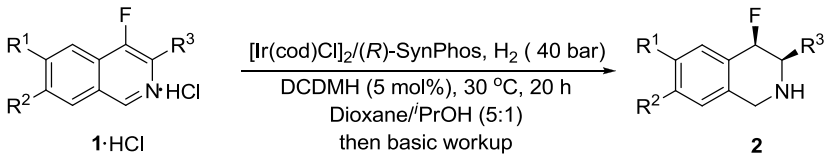
Under N_2, the white powder was dissolved in chloroform (80 mL). To the solution was added phosphorus tribromide (1.6 mL, 6 eq.), then the mixture was heated under reflux for 14 h. After being cooled to 0 °C, the medium was hydrolyzed with saturated $NaHCO_3$ to pH 8. The phases were separated, and the aqueous phase was extracted with dichloromethane (30 mL×3). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated. The crude product was pure enough for further reaction.

To a mixture of the crude product, phenylboronic acids (1.5 eq.), PPh_3 (2.0 mol%), $Pd(OAc)_2$ (1.0 mol%) and K_3PO_4 was added toluene (5 mL). The mixture was stirred for 21 h at 80 °C, filtered through Celite, and the filter cake was washed with CH_2Cl_2 (5 mL×3). The combined organic layers were washed with H_2O and brine, and dried over Na_2SO_4. After filtration, the solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography (petroleum ether/ CH_2Cl_2 1/1) to give the product.

3-Benzyl-4-fluoroisoquinoline (1g): colorless oil, 33% yield, R_f = 0.10 (petroleum ether/ CH_2Cl_2 1/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (s, 1H), 8.05 (d, *J* = 8.4 Hz, 1H), 7.94 (d, *J* = 8.2 Hz, 1H), 7.74-7.70 (m, 1H), 7.60-7.56 (m, 1H), 7.37 (d, *J* = 7.6 Hz, 2H), 7.27 (dd, *J* = 13.4, 6.1 Hz, 2H), 7.20-7.16 (m, 1H), 4.36 (d, *J* = 2.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.6 (d, $^1J_{FC}$ = 258.6 Hz), 147.9 (d, $^2J_{FC}$ = 6.1 Hz), 139.5 (d, $^4J_{FC}$ = 1.2 Hz), 139.4, 130.8 (d, $^4J_{FC}$ = 1.5 Hz), 129.4 (d, $^4J_{FC}$ = 2.4 Hz), 129.2, 128.7, 127.2, 127.2, 127.0 (d, $^2J_{FC}$ = 16.3 Hz), 126.5, 119.7 (d, $^3J_{FC}$ = 4.4 Hz), 37.7 (d, $^3J_{FC}$ = 1.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ -139.4 (s); HRMS Calculated for $C_{16}H_{13}FN$ [M]+ 238.1032, found 229.1019.



3. General Procedure for Asymmetric Hydrogenation of Substituted 4-Fluoroisoquinolinium Salt 1·HCl



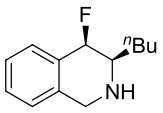
To a stirred solution of the substituted 4-Fluoroisoquinoline **1** (0.500 g, 2.4 mmol) in Et_2O (10 mL) was added 1.0 mL of HCl *conc.* (or 2 N diethylether solution) at room temperature. A white solid formed immediately, and the reaction mixture was stirred at room temperature for around 30 min. All volatiles were removed under reduced pressure to give corresponding 4-fluoroisoquinolinium salt **1**·HCl as a white solid.

In a nitrogen-filled glove box, a mixture of $[Ir(cod)Cl]_2$ (1.3 mg, 0.0020 mmol) and (*R*)-Syn-Phos (2.8 mg, 0.0044 mmol) in 1,4-dioxane/ isopropanol (5:1, V/V, 1.0 mL) was stirred at room temperature for 15-20 min, the mixture was transferred by a syringe to a stainless steel autoclave, in which substrate **1**·HCl (0.20 mmol) and DCDMH (2.0 mg, 0.01 mmol) had been placed beforehand. Dioxane/isopropanol (5:1, V/V, 2.0 mL) was then added to the mixture. The hydrogenation was performed at 30 °C under H_2 (40 bar) for 20 h. After carefully releasing the hydrogen, Et_3N (56 μL, 0.40 mmol) was added and the mixture was stirred for 30 min. The organic layer was separated and extracted with CH_2Cl_2 twice, and the combined organic extracts were dried over Na_2SO_4 and concentrated in vacuo. Purification was performed on a silica gel column eluted with hexane/EtOAc (10:1-2:1) to give the desired product **2**.

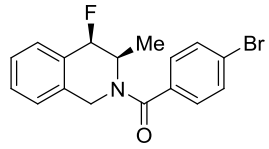
A mixture of 4-bromobenzoyl chloride (66 mg, 0.30 mmol) and Et_3N (56 μL, 0.40 mmol) and **2** dissolved in 3 mL of CH_2Cl_2 was stirred for 30 min. After concentrating in vacuo, the resulting

precipitate was directly purified by column chromatography on silica gel using hexane/EtOAc (20:1-10:1) to give the corresponding *N*-4-bromobenzoyl derivative **3**, the enantiomeric excesses of which was then determined by chiral HPLC.

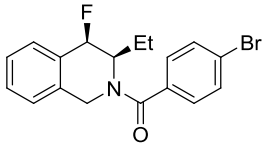
(*3R,4R*)-3-Butyl-4-fluoro-1,2,3,4-tetrahydroisoquinoline (2a): colorless oil, 93% yield, 93% ee, $[\alpha]^{20}_D$ = -71.45 (*c* 0.62, $CHCl_3$), R_f = 0.40 (petroleum ether/EtOAc 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.4 Hz, 1H), 7.35-7.31 (m, 1H), 7.28-7.24 (m, 1H), 7.10 (d, *J* = 7.5 Hz, 1H), 5.20 (d, *J* = 52.1 Hz, 1H), 4.06 (dd, *J* = 30.3, 17.0 Hz, 1H), 4.06 (dd, *J* = 35.4, 17.0 Hz, 1H), 2.84 (dtd, *J* = 28.4, 7.2, 1.2 Hz, 1H), 1.79-1.59 (m, 3H), 1.56-1.46 (m, 2H), 1.46-1.34 (m, 2H), 0.95 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9 (d, $^3J_{FC}$ = 3.7 Hz), 132.2 (d, $^2J_{FC}$ = 17.3 Hz), 131.4 (d, $^4J_{FC}$ = 2.8 Hz), 129.7 (d, $^3J_{FC}$ = 4.3 Hz), 126.8 (d, $^4J_{FC}$ = 3.5 Hz), 126.0 (d, $^5J_{FC}$ = 2.7 Hz), 86.8 (d, $^1J_{FC}$ = 170.3 Hz), 57.3 (d, $^2J_{FC}$ = 20.9 Hz), 48.4, 31.6 (d, $^3J_{FC}$ = 4.7 Hz), 28.6, 23.0, 14.3; ^{19}F NMR (376 MHz, $CDCl_3$): δ -172.5 (s); HRMS Calculated for $C_{13}H_{19}FN$ $[M+H]^+$ 208.1502, found 208.1507; HPLC (corresponding *N*-4-bromobenzoyl derivative): Chiralcel OD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 90/10, flow = 0.8 mL/min, retention time 7.3 min and 8.9 min (maj)..



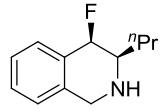
(4-Bromophenyl)((*3R,4R*)-4-fluoro-3-methyl-3,4-dihydroisoquinolin-2(1H)-yl)methanone (3b): colorless oil, 92% yield, 93% ee, $[\alpha]^{20}_D$ = -5.50 (*c* 1.00, $CHCl_3$) R_f = 0.30 (petroleum ether/EtOAc 10/1); ^{1}H NMR (400 MHz, DMSO-d_6, 80 °C) δ 7.88 (d, *J* = 8.0 Hz, 2H), 7.67-7.62 (dd, *J* = 14.3, 6.3 Hz, 3H), 7.59-7.52 (m, 2H), 7.45 (d, *J* = 4.0 Hz, 1H), 6.05 (dd, *J* = 51.1, 5.9 Hz, 1H), 5.07-5.03(m, 1H), 4.91 (brs, 1H), 4.65 (d, *J* = 17.2 Hz, 1H), 1.31 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.01, 134.9 (d, $^2J_{FC}$ = 21.8 Hz), 132.0 (d, $^3J_{FC}$ = 4.2 Hz), 131.7 (d, $^2J_{FC}$ = 18.8 Hz), 131.5 (d, $^3J_{FC}$ = 3.6 Hz), 128.7, 128.1 (d, $^5J_{FC}$ = 1.9 Hz), 127.0 (d, $^4J_{FC}$ = 3.3 Hz), 125.7, 125.6 (d, $^4J_{FC}$ = 2.7 Hz), 123.1 (d, $^2J_{FC}$ = 9.4 Hz), 86.5 (d, $^1J_{FC}$ = 179.6 Hz), 11.2 (d, $^3J_{FC}$ = 2.5 Hz); ^{19}F NMR (376 MHz, DMSO-d_6) δ -186.4 (s); HRMS Calculated for $C_{17}H_{16}BrFNO$ $[M+H]^+$ 348.0399, found 348.0389; HPLC: Chiralcel OD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 90/10, flow = 0.8 mL/min, retention time 12.8 min and 14.3 min (maj).



(4-Bromophenyl)((*3R,4R*)-3-ethyl-4-fluoro-3,4-dihydroisoquinolin-2(1H)-yl)methanone (3c): colorless oil, 94% yield, 93% ee, $[\alpha]^{20}_D$ = +2.10 (*c* 1.00, $CHCl_3$), R_f = 0.35 (petroleum ether/EtOAc 10/1); ^{1}H NMR (400 MHz, DMSO-d_6, 80 °C) δ 7.89 (d, *J* = 8.2 Hz, 2H), 7.68 (d, *J* = 4.7 Hz, 1H), 7.64 (d, *J* = 8.2 Hz, 1H), 7.57-7.52 (m, 2H), 7.44 (s, 1H), 6.14 (dd, *J* = 51.3, 5.4 Hz, 1H), 5.06 (brs, 1H), 4.73 (brs, 1H), 4.57 (d, *J* = 17.9 Hz, 1H), 1.79 (brs, 1H), 1.64-1.53 (m, 1H), 1.09 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.5, 134.8, 131.9 (d, $^3J_{FC}$ = 1.5 Hz), 131.8 (d, $^2J_{FC}$ = 16.6 Hz), 131.3, 128.6, 127.7, 126.7, 125.2, 125.1, 122.8, 86.1 (d, $^1J_{FC}$ = 179.6 Hz), 17.7, 9.5; ^{19}F NMR (376 MHz, DMSO-d_6) δ -187.0 (s); HRMS Calculated for $C_{18}H_{17}BrFNO$ $[M+H]^+$ 362.0556, found 362.0552; HPLC: Chiralpak IC-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 80/20, flow = 0.8 mL/min, retention time 10.5 min and 11.3 min (maj).

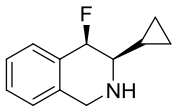


(*3R,4R*)-4-fluoro-3-propyl-1,2,3,4-tetrahydroisoquinoline (2d): colorless oil, 93% yield, 92% ee, $[\alpha]^{20}_D$ = -86.90 (*c* 1.00, $CHCl_3$), R_f = 0.30 (petroleum ether/EtOAc 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.2 Hz, 1H), 7.34-7.30 (m, 1H), 7.27-7.24 (m, 1H), 7.10 (d, *J* = 7.3 Hz, 1H), 5.19 (d, *J* = 52.0 Hz, 1H), 4.11-3.98 (m, 2H), 2.86 (dt, *J* = 28.4, 6.5 Hz, 1H), 1.90 (brs, 1H), 1.79-1.61 (m, 2H), 1.62-1.49 (m, 2H), 1.00 (t,



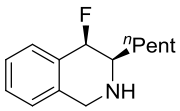
J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.0 (d, $^3J_{FC}$ = 4.0 Hz), 132.3 (d, $^2J_{FC}$ = 17.7 Hz), 131.4 (d, $^4J_{FC}$ = 2.8 Hz), 129.7 (d, $^3J_{FC}$ = 4.3 Hz), 126.8 (d, $^4J_{FC}$ = 3.5 Hz), 126.0 (d, $^5J_{FC}$ = 2.7 Hz), 86.8 (d, $^1J_{FC}$ = 170.3 Hz), 57.0 (d, $^2J_{FC}$ = 21.0 Hz), 48.4 (d, $^4J_{FC}$ = 1.6 Hz), 34.0 (d, $^3J_{FC}$ = 4.7 Hz), 19.6, 14.4; ^{19}F NMR (376 MHz, $CDCl_3$): δ -172.5 (s); HRMS Calculated for $C_{12}H_{17}FN$ $[M+H]^+$ 194.1345, found 194.1337; HPLC (corresponding *N*-4-bromobenzoyl derivative): Chiralcel OD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 90/10, flow = 0.8 mL/min, retention time 8.3 min and 10.3 min (maj).

(*3R,4R*)-3-cyclopropyl-4-fluoro-1,2,3,4-tetrahydroisoquinoline (2e): colorless oil, 79% yield, 90% ee, $[\alpha]^{20}_D$ = -74.68 (*c* 0.32, $CHCl_3$), R_f = 0.30 (petroleum ether/EtOAc 2/1); ^{1}H NMR



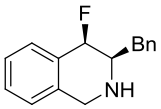
(400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 7.4 Hz, 1H), 7.34-7.30 (m, 1H), 7.28-7.24 (m, 1H), 7.10 (d, *J* = 7.4 Hz, 1H), 5.29 (d, *J* = 51.9 Hz, 1H), 4.07 (dd, *J* = 56.2, 16.6 Hz, 1H), 4.06 (dd, *J* = 62.0, 16.6 Hz, 1H), 2.04 (dd, *J*= 27.7, 9.2 Hz, 1H), 1.94 (brs, 1H), 1.22 (m, 1H), 0.76-0.59 (m, 2H), 0.42-0.30 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.4 (d, $^3J_{FC}$ = 4.1 Hz), 132.2 (d, $^2J_{FC}$ = 17.6 Hz), 131.3 (d, $^4J_{FC}$ = 2.8 Hz), 129.7 (d, $^3J_{FC}$ = 4.3 Hz), 126.9 (d, $^4J_{FC}$ = 3.4 Hz), 126.1 (d, $^5J_{FC}$ = 2.7 Hz), 87.6 (d, $^1J_{FC}$ = 170.8 Hz), 63.2 (d, $^2J_{FC}$ = 19.7 Hz), 48.7, 12.8 (d, $^3J_{FC}$ = 6.7 Hz), 4.1, 2.7; ^{19}F NMR (376 MHz, $CDCl_3$): δ -169.4 (s); HRMS Calculated for $C_{12}H_{15}FN$ $[M+H]^+$ 192.1189, found 192.1182; HPLC (corresponding *N*-4-bromobenzoyl derivative): Chiralcel OD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 90/10, flow = 0.8 mL/min, retention time 9.7 min and 11.8 min (maj).

(*3R,4R*)-4-Fluoro-3-pentyl-1,2,3,4-tetrahydroisoquinoline (2f): colorless oil, 97% yield, 90% ee, $[\alpha]^{20}_D$ = -7.80 (*c* 1.00, $CHCl_3$), R_f = 0.40 (petroleum ether/EtOAc 2/1); ^{1}H NMR (400



MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.5 Hz, 1H), 7.36-7.30 (m, 1H), 7.28-7.24 (m, 1H), 7.11 (d, *J* = 7.5 Hz, 1H), 5.20 (dd, *J* = 52.1, 1.0 Hz, 1H), 4.06 (dd, *J* = 30.5, 17.1 Hz, 1H), 4.06 (dd, *J* = 35.5, 17.0 Hz, 1H), 2.84 (dtd, *J* = 28.4, 7.1, 1.6 Hz, 1H), 1.79-1.58 (m, 3H), 1.53 (dt, *J* = 15.0, 7.7 Hz, 2H), 1.43-1.30 (m, 4H), 0.92 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9 (d, $^3J_{FC}$ = 3.8 Hz), 132.3 (d, $^2J_{FC}$ = 17.6 Hz), 131.4 (d, $^4J_{FC}$ = 2.9 Hz), 129.7 (d, $^3J_{FC}$ = 4.3 Hz), 126.8 (d, $^4J_{FC}$ = 3.6 Hz), 126.0 (d, $^5J_{FC}$ = 2.7 Hz), 86.8 (d, $^1J_{FC}$ = 170.2 Hz), 57.3 (d, $^2J_{FC}$ = 21.1 Hz), 48.4 (d, $^4J_{FC}$ = 1.8 Hz), 32.2, 31.9 (d, $^3J_{FC}$ = 4.7 Hz), 26.1, 22.8, 14.3; ^{19}F NMR (376 MHz, $CDCl_3$): δ -172.5 (s); HRMS Calculated for $C_{14}H_{21}FN$ $[M+H]^+$ 222.1658, found 222.1647; HPLC (corresponding *N*-4-bromobenzoyl derivative): Chiralcel OD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 90/10, flow = 0.8 mL/min, retention time 7.0 min and 8.2 min (maj).

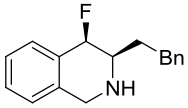
(*3R,4R*)-3-Benzyl-4-fluoro-1,2,3,4-tetrahydroisoquinoline (2g): colorless oil, 95% yield, 93% ee, $[\alpha]^{20}_D$ = -29.50 (*c* 1.00, $CHCl_3$), R_f = 0.20 (petroleum ether/EtOAc 5/1); ^{1}H NMR (400



MHz, $CDCl_3$) δ 7.38-7.29 (m, 6H), 7.29-7.21 (m, 2H), 7.11 (d, *J* = 7.9 Hz, 1H), 5.07 (d, *J* = 52.3 Hz, 1H), 4.08 (dd, *J* = 35.4, 16.8 Hz, 1H), 4.07 (dd, *J* = 40.9, 17.0 Hz, 1H), 3.15 (dt, *J* = 27.1, 7.5 Hz, 1H), 3.01 (d, *J* = 7.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 137.6 (d, $^3J_{FC}$ = 3.9 Hz), 131.9 (d, $^2J_{FC}$ = 17.5 Hz), 131.4 (d, $^4J_{FC}$ = 2.8 Hz), 129.8 (d, $^3J_{FC}$ = 4.3 Hz), 129.6, 128.8, 126.9 (d, $^4J_{FC}$ = 3.6 Hz), 126.7, 126.1 (d, $^5J_{FC}$ = 2.7 Hz), 85.9 (d, $^1J_{FC}$ = 171.0 Hz), 59.1 (d, $^2J_{FC}$ = 20.7 Hz), 48.5 (d, $^4J_{FC}$ = 1.7 Hz), 38.3 (d, $^3J_{FC}$ = 5.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ -171.9 (s); HRMS Calculated for $C_{16}H_{17}FN$ $[M+H]^+$ 242.1345, found 242.1336; HPLC (corresponding *N*-4-bromobenzoyl derivative): Chiralcel OD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 90/10, flow = 0.8 mL/min, retention time 11.0 min

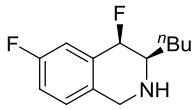
and 15.8 min (maj).

(*3R,4R*)-4-Fluoro-3-phenethyl-1,2,3,4-tetrahydroisoquinoline (2h): colorless oil, 88% yield, 88% ee, $[\alpha]^{20}_{D}$ = -47.66 (*c* 0.90, $CHCl_3$), R_f = 0.25 (petroleum ether/EtOAc 5/1); ^{1}H NMR



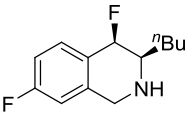
(400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 7.4 Hz, 1H), 7.35-7.22 (m, 6H), 7.22-7.15 (m, 1H), 7.09 (d, *J* = 7.5 Hz, 1H), 5.19 (d, *J* = 52.1 Hz, 1H), 4.04 (dd, *J* = 41.4, 17.1 Hz, 2H), 4.02 (dd, *J* = 46.9, 17.1 Hz, 2H), 2.94-2.74 (m, 3H), 2.12-1.91 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.1, 138.0 (d, $^3J_{FC}$ = 3.9 Hz), 132.2 (d, $^2J_{FC}$ = 17.6 Hz), 131.4 (d, $^4J_{FC}$ = 2.9 Hz), 129.8 (d, $^3J_{FC}$ = 4.2 Hz), 128.7, 128.7, 126.9 (d, $^4J_{FC}$ = 3.6 Hz), 126.1, 126.0 (d, $^5J_{FC}$ = 2.7 Hz), 87.0 (d, $^1J_{FC}$ = 170.3 Hz), 56.4 (d, $^2J_{FC}$ = 20.9 Hz), 48.4 (d, $^4J_{FC}$ = 1.8 Hz), 33.5 (d, $^3J_{FC}$ = 4.6 Hz), 32.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ -172.1 (s); HRMS Calculated for $C_{17}H_{19}FN$ $[M+H]^+$ 256.1502, found 256.1508; HPLC (corresponding *N*-4-bromobenzoyl derivative): Chiralpak IC-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 90/10, flow = 0.8 mL/min, retention time 11.2 min and 15.0 min (maj).

(*3R,4R*)-3-butyl-4,6-difluoro-1,2,3,4-tetrahydroisoquinoline (2i): colorless oil, 99% yield, 91% ee, $[\alpha]^{20}_{D}$ = -82.11 (*c* 0.52, $CHCl_3$), R_f = 0.35 (petroleum ether/EtOAc 2/1); ^{1}H NMR (400



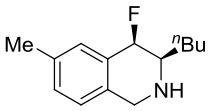
MHz, $CDCl_3$) δ 7.12 -7.00 (m, 3H), 5.15 (d, *J* = 51.8 Hz, 1H), 4.02 (dd, *J* = 39.8, 16.8 Hz, 1H), 4.00 (dd, *J* = 45.5, 16.7 Hz, 1H), 2.82 (dt, *J* = 28.2, 7.1 Hz, 1H), 1.80 (s, 1H), 1.75-1.58 (m, 1H), 1.55-1.46 (m, 1H), 1.45-1.34 (m, 1H), 0.95 (t, *J* = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4 (dd, $^1J_{FC}$ = 245.3 Hz, $^4J_{FC}$ = 4.1 Hz), 134.1 (dd, $^2J_{FC}$ = 17.8 Hz, $^3J_{FC}$ = 7.1 Hz), 133.7-133.5 (m), 127.6 (dd, $^3J_{FC}$ = 7.7 Hz, $^4J_{FC}$ = 2.5 Hz), 117.5 (dd, $^2J_{FC}$ = 20.8 Hz, $^5J_{FC}$ = 2.7 Hz), 117.0 (dd, $^2J_{FC}$ = 21.5 Hz, $^3J_{FC}$ = 4.1 Hz), 86.4 (d, $^1J_{FC}$ = 170.6 Hz), 57.1 (d, $^2J_{FC}$ = 20.9 Hz), 47.9 (d, $^4J_{FC}$ = 1.7 Hz), 31.4 (d, $^3J_{FC}$ = 4.8 Hz), 28.6, 23.0, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$): δ -116.0 (s), -173.7 (s); HRMS Calculated for $C_{13}H_{18}F_2N$ $[M+H]^+$ 226.1407, found 226.1413; HPLC (corresponding *N*-4-bromobenzoyl derivative): Chiralpak IC-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 80/20, flow = 0.8 mL/min, retention time 8.2 min and 9.8 min (maj).

(*3R,4R*)-3-butyl-4,7-difluoro-1,2,3,4-tetrahydroisoquinoline (2j): colorless oil, 93% yield, 91% ee, $[\alpha]^{20}_{D}$ = -70.23 (*c* 0.86, $CHCl_3$), R_f = 0.35 (petroleum ether/EtOAc 2/1); ^{1}H NMR (400



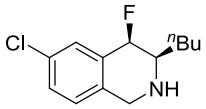
MHz, $CDCl_3$) δ 7.37 (ddd, *J* = 8.1, 5.7, 2.2 Hz, 1H), 6.98-6.93 (m, 1H), 6.81 (d, *J* = 8.9 Hz, 1H), 5.18 (d, *J* = 52.3 Hz, 1H), 4.04 (dd, *J* = 34.1, 17.2 Hz, 1H), 4.02 (dd, *J* = 39.40, 17.2 Hz, 1H), 2.80 (dt, *J* = 27.2, 6.5 Hz, 1H), 1.81-1.58 (m, 3H), 1.56-1.46 (m, 2H), 1.45-1.34 (m, 2H), 0.95 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3 (dd, $^1J_{FC}$ = 249.2 Hz, $^5J_{FC}$ = 4.4 Hz), 140.5 (dd, $^3J_{FC}$ = 7.2, $^3J_{FC}$ = 3.8 Hz), 133.3 (dd, $^3J_{FC}$ = 8.5 Hz, $^3J_{FC}$ = 2.7 Hz), 128.4 (dd, $^2J_{FC}$ = 18.3 Hz, $^4J_{FC}$ = 3.0 Hz), 114.2 (dd, $^2J_{FC}$ = 21.8 Hz, $^4J_{FC}$ = 3.5 Hz), 112.5 (dd, $^2J_{FC}$ = 21.2 Hz, $^4J_{FC}$ = 2.8 Hz), 86.1 (d, $^1J_{FC}$ = 170.7 Hz), 57.4 (d, $^2J_{FC}$ = 21.1 Hz), 48.5 (t, $^4J_{FC}$ = 1.8 Hz), 31.6 (d, $^3J_{FC}$ = 4.7 Hz), 28.6, 23.0, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -111.1 (d, $^6J_{FF}$ = 8.5 Hz), -171.1 (d, $^6J_{FF}$ = 8.4 Hz); HRMS Calculated for $C_{13}H_{18}F_2N$ $[M+H]^+$ 226.1407, found 226.1408; HPLC (corresponding *N*-4-bromobenzoyl derivative): Chiralpak IC-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 90/10, flow = 0.8 mL/min, retention time 8.0 min and 10.8 min (maj).

(*3R,4R*)-3-butyl-4-fluoro-6-methyl-1,2,3,4-tetrahydroisoquinoline (2k): colorless oil, 97% yield, 91% ee, $[\alpha]^{20}_{D}$ = -57.00 (*c* 1.00, $CHCl_3$), R_f = 0.30 (petroleum ether/EtOAc 5/1); ^{1}H NMR



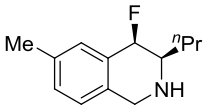
(400 MHz, $CDCl_3$) δ 7.20 (s, 1H), 7.14 (d, *J* = 7.8 Hz, 1H), 7.00 (d, *J* = 7.8 Hz, 1H), 5.16 (d, *J* = 52.2 Hz, 1H), 4.02 (dd, *J* = 32.8, 16.8 Hz, 1H), 4.01 (dd, *J* = 38.3, 16.7 Hz, 1H), 2.82 (dt, *J* = 28.4, 7.0 Hz, 1H), 2.35 (s, 3H), 1.80-1.58 (m, 3H), 1.56-1.45 (m, 2H), 1.45-1.31 (m, 2H), 0.95 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.4 (d, $^4J_{FC}$ = 3.6 Hz), 134.8 (d, $^3J_{FC}$ = 4.0 Hz), 132.1 (d, $^2J_{FC}$ = 17.5 Hz), 131.8 (d, $^4J_{FC}$ = 2.9 Hz), 130.6 (d, $^3J_{FC}$ = 4.3 Hz), 125.9 (d, $^5J_{FC}$ = 2.8 Hz), 87.0 (d, $^1J_{FC}$ = 170.1 Hz), 57.4 (d, $^2J_{FC}$ = 21.0 Hz), 48.2 (d, $^4J_{FC}$ = 1.8 Hz), 31.6 (d, $^3J_{FC}$ = 4.7 Hz), 28.6, 23.0, 21.2, 14.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -172.6 (s); HRMS Calculated for $C_{14}H_{21}FN$ $[M+H]^+$ 222.1658, found 222.1653; HPLC (corresponding *N*-4-bromobenzoyl derivative): Chiralcel OD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 90/10, flow = 0.8 mL/min, retention time 6.9 min and 7.7 min (maj).

(*3R,4R*)-3-butyl-6-chloro-4-fluoro-1,2,3,4-tetrahydroisoquinoline (2l): colorless oil, 90% yield, 93% ee, $[\alpha]^{20}_{D}$ = -55.00 (*c* 0.90, $CHCl_3$), R_f = 0.15 (petroleum ether/EtOAc 2/1); ^{1}H NMR



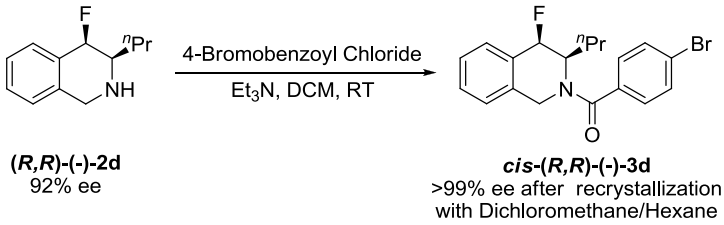
(400 MHz, $CDCl_3$) δ 7.38 (s, 1H), 7.34-7.23 (m, 1H), 7.05 (d, *J* = 8.2 Hz, 1H), 5.15 (d, *J* = 51.6 Hz, 1H), 4.02 (dd, *J* = 40.0, 17.1 Hz, 1H), 4.00 (dd, *J* = 45.4, 17.1 Hz, 1H), 2.81 (dt, *J* = 28.1, 6.9 Hz, 1H), 1.82-1.57 (m, 3H), 1.55-1.45 (m, 2H), 1.45-1.35 (m, 2H), 0.95 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.4 (d, $^4J_{FC}$ = 3.4 Hz), 134.0 (d, $^2J_{FC}$ = 16.8 Hz), 132.3 (d, $^3J_{FC}$ = 3.7 Hz), 131.1 (d, $^4J_{FC}$ = 2.9 Hz), 129.8 (d, $^3J_{FC}$ = 4.1 Hz), 127.5 (d, $^5J_{FC}$ = 2.5 Hz), 86.2 (d, $^1J_{FC}$ = 171.9 Hz), 57.1 (d, $^2J_{FC}$ = 20.9 Hz), 47.9, 31.4 (d, $^3J_{FC}$ = 4.8 Hz), 28.6, 23.0, 14.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -173.7 (s); HRMS Calculated for $C_{13}H_{18}FNCl$ $[M+H]^+$ 242.1112, found 242.1119; HPLC (corresponding *N*-4-bromobenzoyl derivative): Chiralpak IC-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 80/20, flow = 0.8 mL/min, retention time 8.3 min and 9.9 min (maj).

(*3R,4R*)-4-fluoro-6-methyl-3-propyl-1,2,3,4-tetrahydroisoquinoline (2m): colorless oil, 91% yield, 91% ee, $[\alpha]^{20}_{D}$ = -22.86 (*c* 0.97, $CHCl_3$), R_f = 0.30 (petroleum ether/EtOAc 2/1); ^{1}H



NMR (400 MHz, $CDCl_3$) δ 7.20 (s, 1H), 7.14 (d, *J* = 7.8 Hz, 1H), 7.00 (d, *J* = 7.8 Hz, 1H), 5.16 (d, *J* = 52.1 Hz, 1H), 4.02 (dd, *J* = 32.0, 16.8 Hz, 1H), 4.01 (dd, *J* = 37.5, 16.9 Hz, 1H), 2.94-2.74 (m, 1H), 2.35 (s, 3H), 1.82-1.44 (m, 5H), 0.99 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.4 (d, $^4J_{FC}$ = 3.7 Hz), 134.8 (d, $^2J_{FC}$ = 4.0 Hz), 132.1 (d, $^3J_{FC}$ = 17.5 Hz), 131.8 (d, $^4J_{FC}$ = 2.9 Hz), 130.6 (d, $^3J_{FC}$ = 4.3 Hz), 125.9 (d, $^5J_{FC}$ = 2.7 Hz), 87.0 (d, $^1J_{FC}$ = 170.1 Hz), 57.0 (d, $^2J_{FC}$ = 21.0 Hz), 48.1 (d, $^4J_{FC}$ = 1.8 Hz), 34.0 (d, $^3J_{FC}$ = 4.7 Hz), 21.2, 19.6, 14.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -172.6 (s); HRMS Calculated for $C_{13}H_{19}FN$ $[M+H]^+$ 208.1502, found 208.1490; HPLC (corresponding *N*-4-bromobenzoyl derivative): Chiralcel OD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol =90/10, flow = 0.8 mL/min, retention time 7.6 min and 8.6 min (maj).

4. The Determination of Absolute Configuration of 2d



(*R,R*)-(-)-2d
92% ee

***cis*-(*R,R*)-(-)-3d**
>99% ee after recrystallization
with Dichloromethane/Hexane

A solution of 4-bromobenzoyl chloride (0.544 g, 2.48 mmol), Et_3N (0.50 mL, 3.30 mmol) and (-)-**2d** (0.319 g, 1.65 mL) in CH_2Cl_2 (25 mL) was stirred for 30 min. After concentrating in vacuo, the resulting precipitate was directly purified by column chromatography on silica gel to give the corresponding *N*-4-bromobenzoyl derivative of (-)-**3d**.

The *N*-4-bromobenzoyl derivative (-)-**3d** was recrystallized from hexane/dichloromethane twice to give a colorless crystal with 99.8% ee. The structure of (-)-**3d** was determined by X-ray crystallographic analysis which showed that the absolute configuration at the C-3,4 positions are (*3R,4R*). The configurations of the other compounds are proposed by analogy. CCDC 917645 contains the supplementary crystallographic data for this paper. These can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk.

(4-bromophenyl)((*3R,4R*)-4-fluoro-3-propyl-3,4-dihydroisoquinolin-2(1H)-yl)methanone ((-)-3d): colorless solid, 98% yield (before recrystallization), 99.3% ee, $[\alpha]^{20}_D$ = -4.70 (*c* 1.00, $CHCl_3$); R_f = 0.70 (petroleum ether/EtOAc 5/1); ^{1}H NMR (400 MHz, DMSO-d_6, 80 ^{o}C) δ 7.91 (d, *J* = 8.3 Hz, 2H), 7.74-7.68 (m, 1H), 7.66 (d, *J* = 8.3 Hz, 2H), 7.61-7.52 (m, 2H), 7.46 (s, 1H), 6.16 (dd, *J* = 51.2, 5.6 Hz, 1H), 5.06 (brs, 1H), 4.88 (brs, 1H), 4.61 (d, *J* = 17.3 Hz, 1H), 1.68-1.50 (m, 2H), 1.11-1.05 (m, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.3, 134.7, 131.8 (d, $^2J_{FC}$ = 13.0 Hz), 131.8 (d, $^3J_{FC}$ = 4.0 Hz), 131.3, 128.6, 127.7 (d, $^4J_{FC}$ = 1.9 Hz), 126.6, 125.2, 125.1 (d, $^3J_{FC}$ = 8.5 Hz), 122.9, 85.9 (d, $^1J_{FC}$ = 180.7 Hz), 26.4, 18.0, 13.2; ^{19}F NMR (376 MHz, DMSO-d_6) δ -186.9 (s); HRMS Calculated for $C_{19}H_{20}BrFNO$ $[M+H]^+$ 376.0712, found 376.0700; HPLC: Chiralcel OD-H column, 254 nm, 30 ^{o}C, *n*-hexane/*i*-propanol = 90/10, flow = 0.8 mL/min, retention time 8.1 min and 10.1 min (maj).

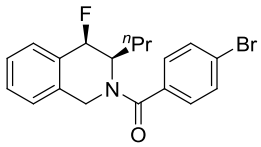
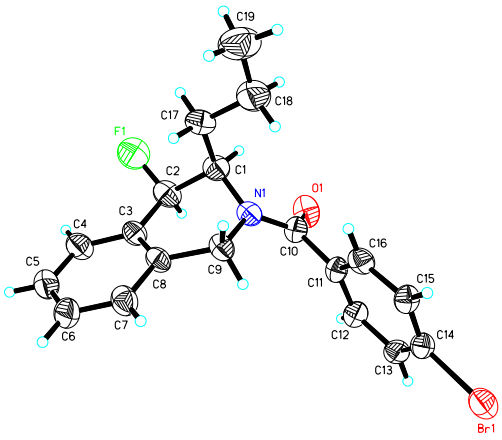
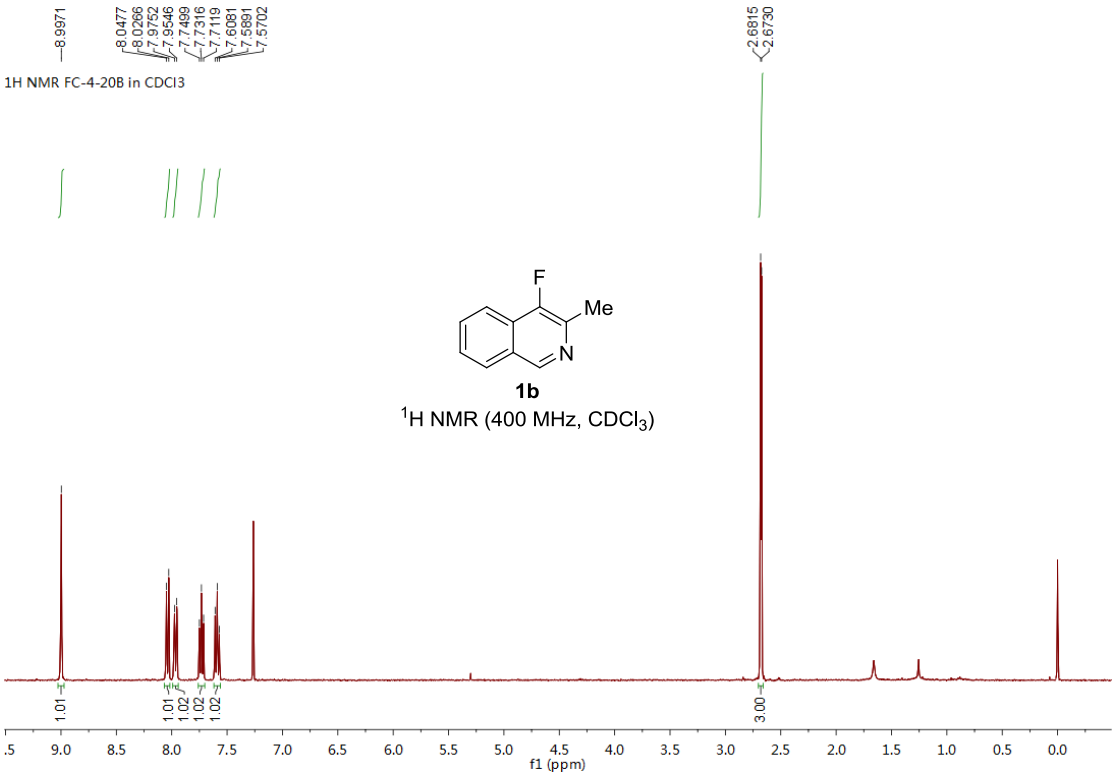


Figure 1. The Absolute Configuration of (-)-**3d**.

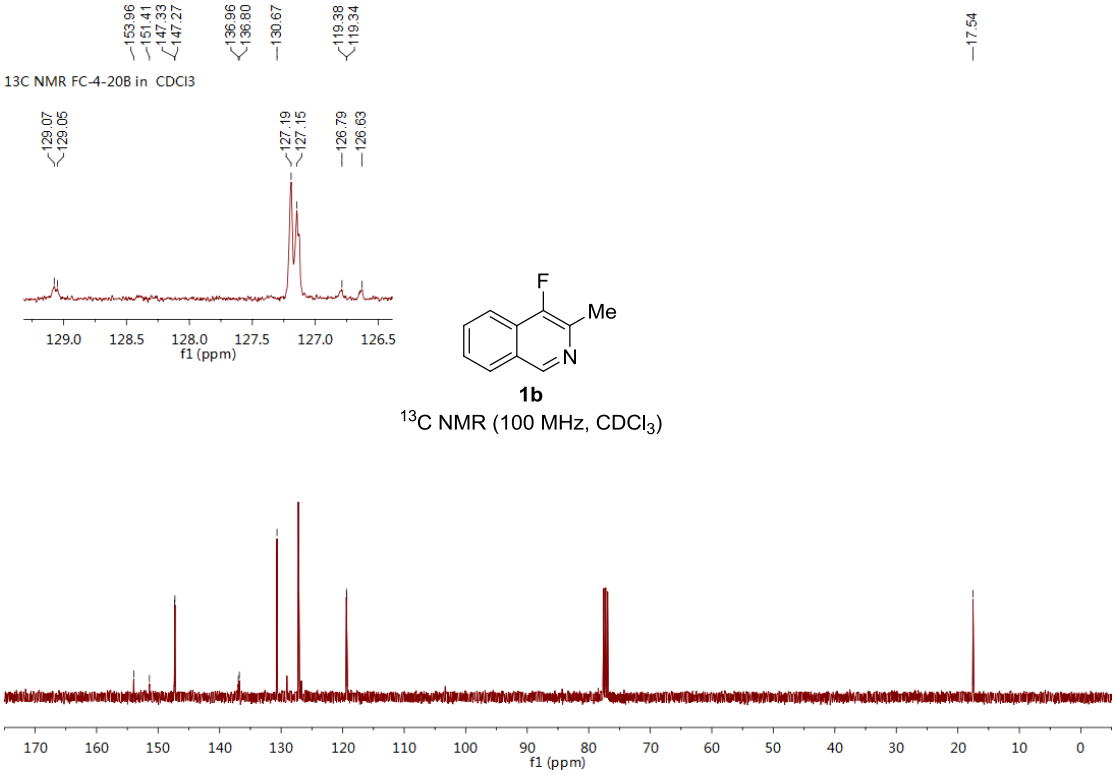


5. Copy of NMR and HPLC for Racemic and Chiral Compounds



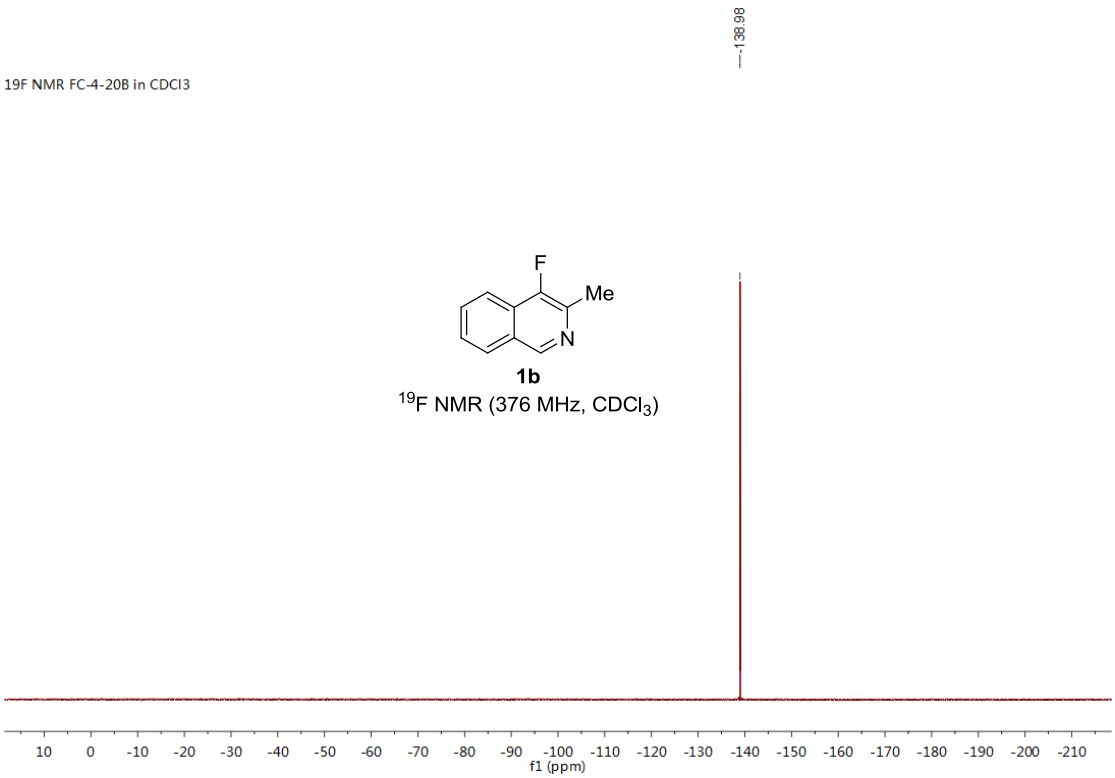
1b

^{1}H NMR (400 MHz, $CDCl_3$)



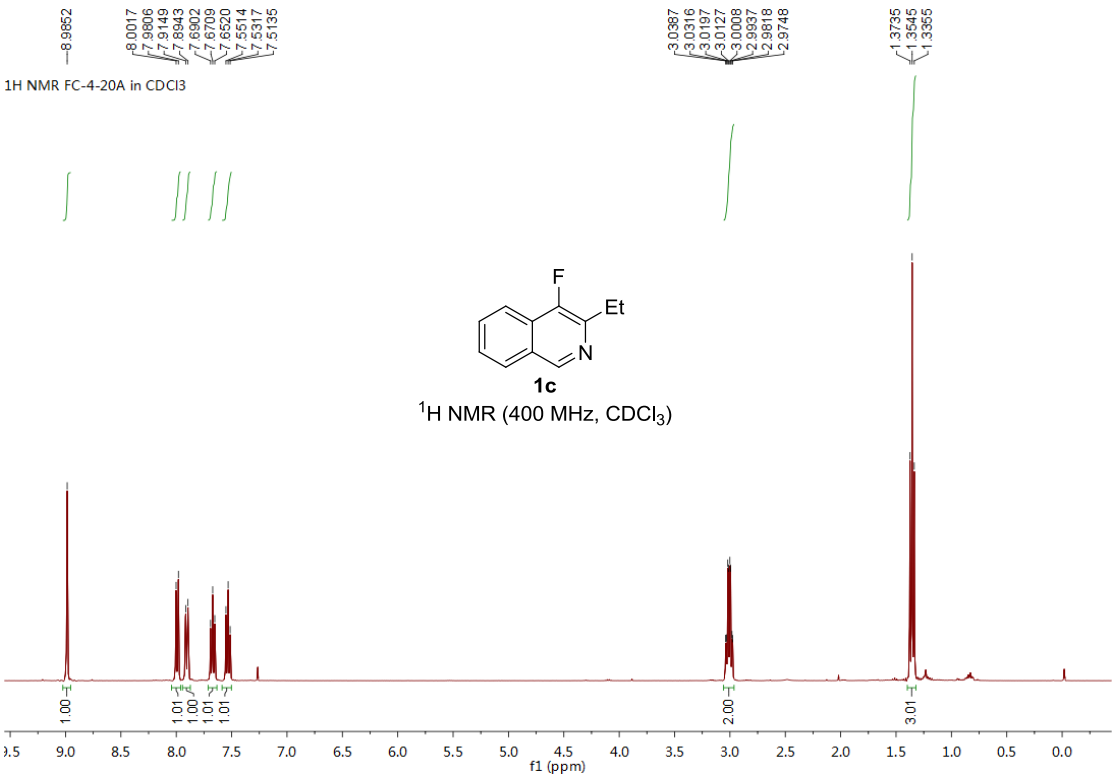
1b

^{13}C NMR (100 MHz, $CDCl_3$)



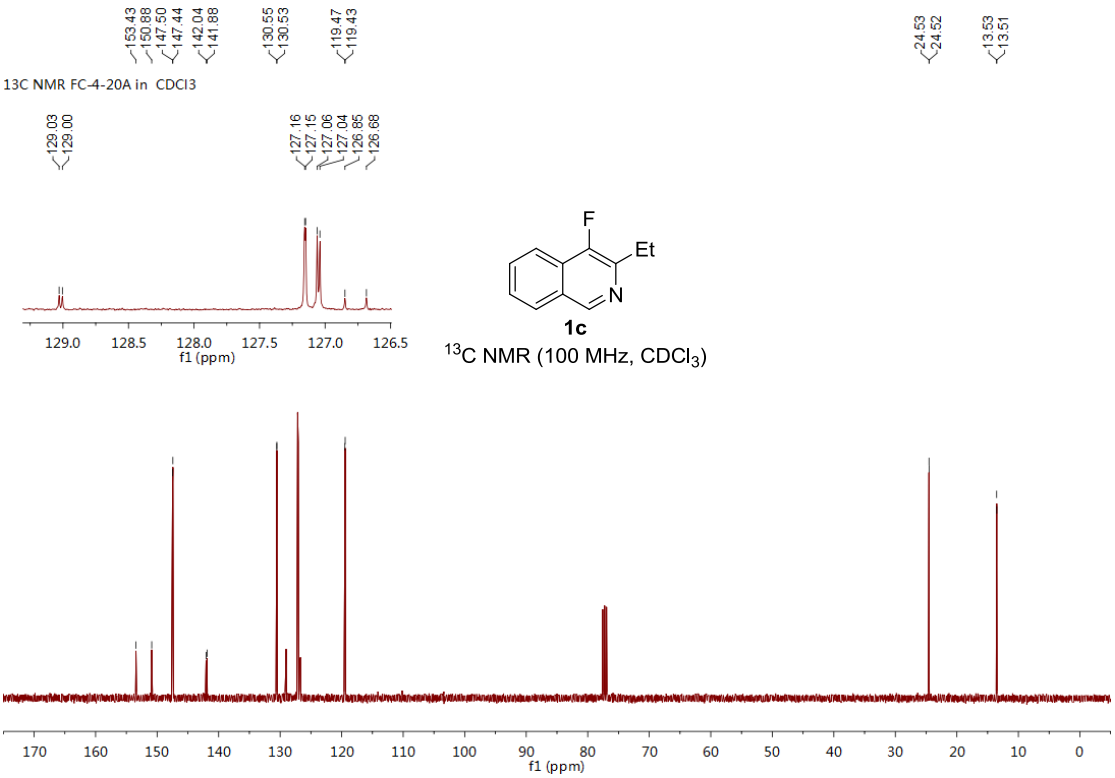
1b

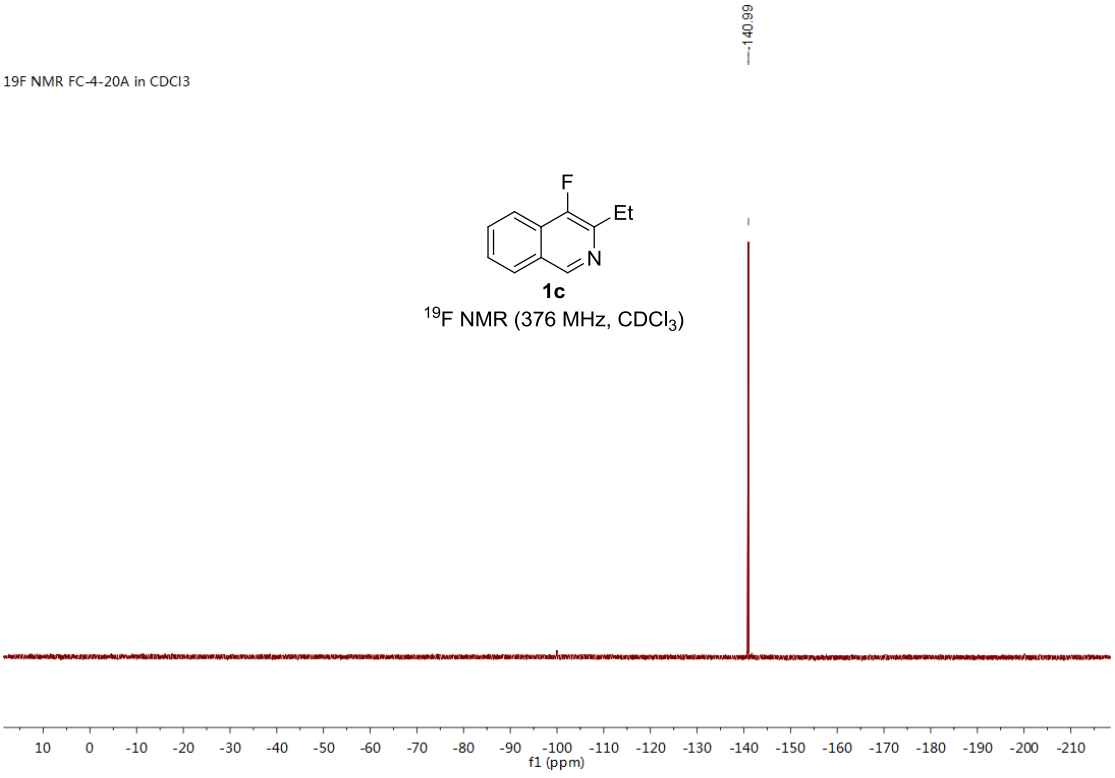
^{19}F NMR (376 MHz, $CDCl_3$)

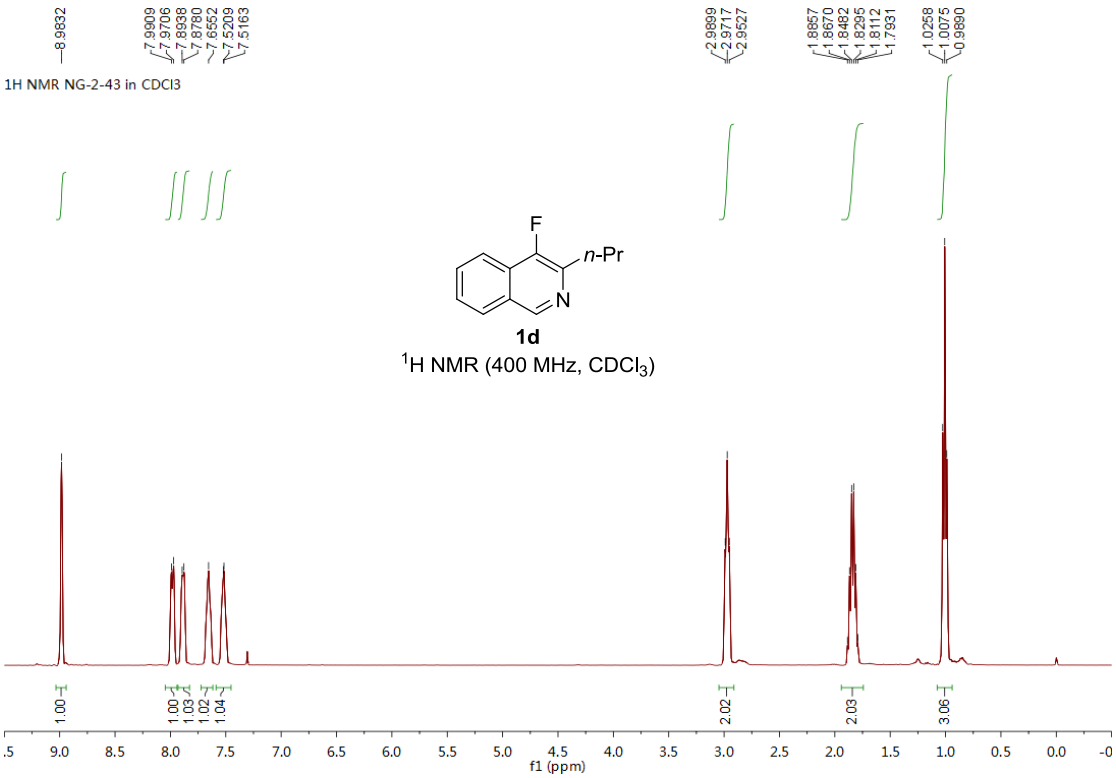


1c

^{1}H NMR (400 MHz, $CDCl_3$)

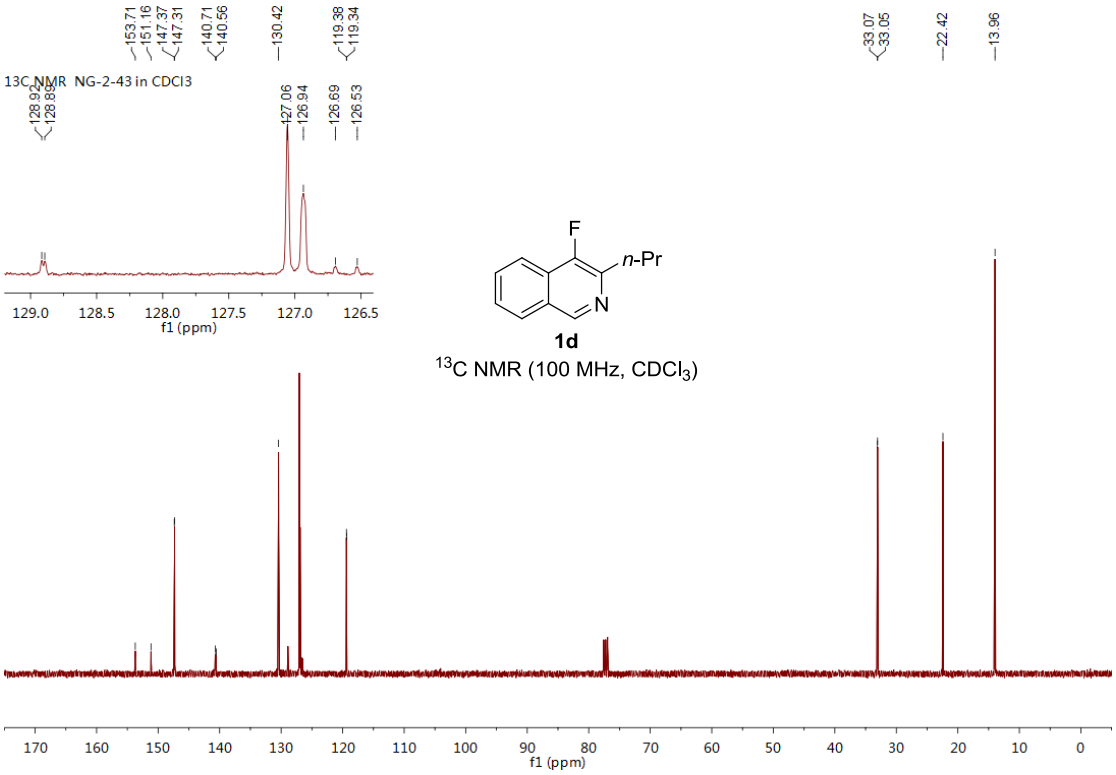

153.43
150.88
147.50
147.44
142.04
141.88
130.55
130.53
119.47
119.43
24.53
24.52
13.53
13.51
13C NMR FC-4-20A in CDCl3
129.03
129.00
127.16
127.15
127.06
127.04
126.85
126.68
129.0
128.5
128.0
127.5
127.0
126.5
f1 (ppm)
F
Et
N
1c
13C NMR (100 MHz, CDCl3)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-140.99
19F NMR FC-4-20A in CDCl3
F
Et
N
1c
19F NMR (376 MHz, CDCl3)
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)



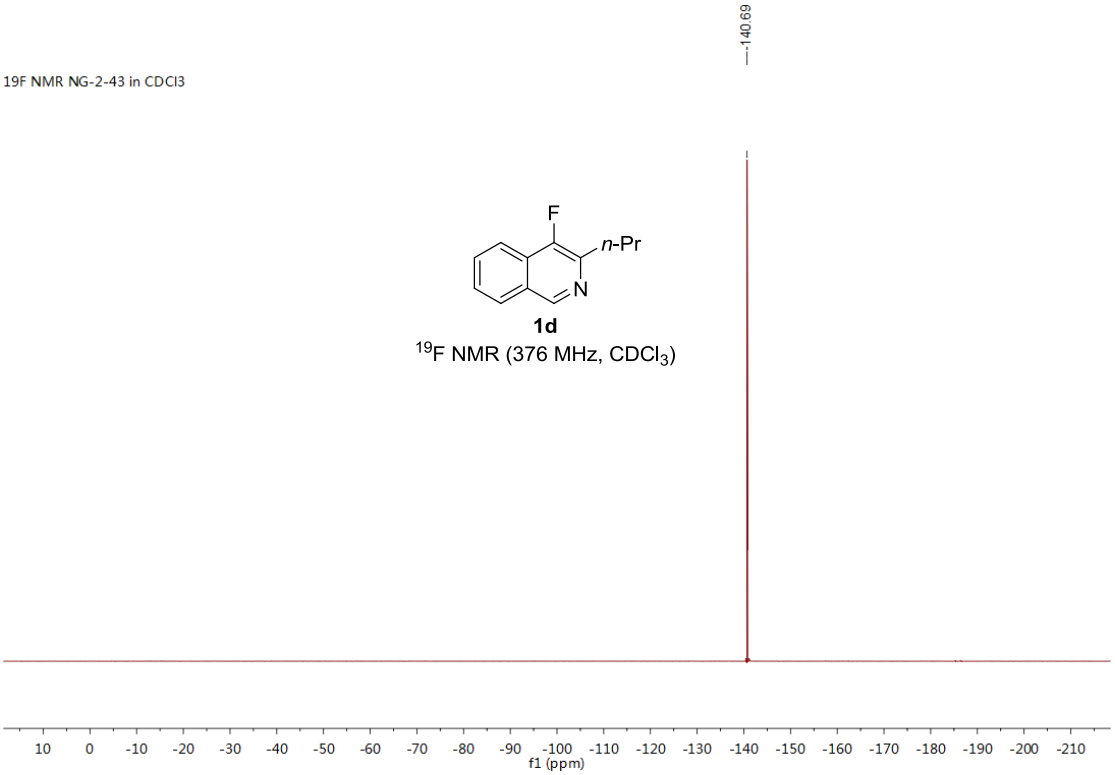
1d

^{1}H NMR (400 MHz, $CDCl_3$)



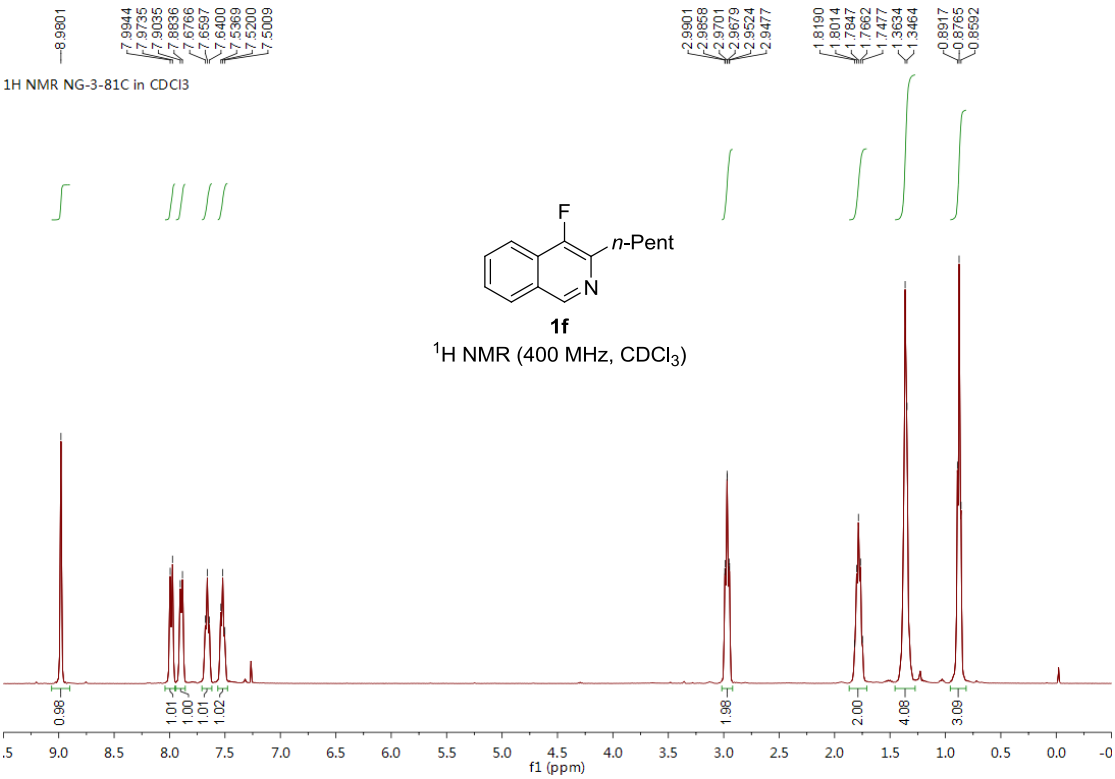
1d

^{13}C NMR (100 MHz, $CDCl_3$)



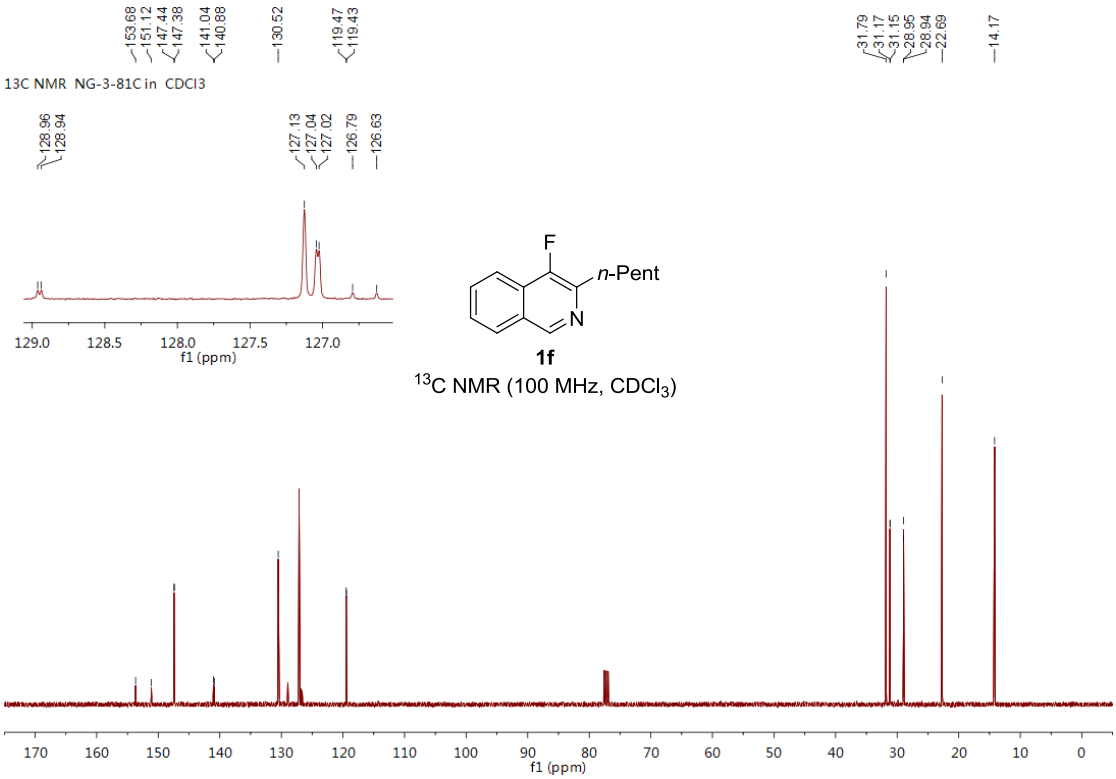
1d

^{19}F NMR (376 MHz, $CDCl_3$)



1f

^{1}H NMR (400 MHz, $CDCl_3$)


153.68
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147.38
141.04
140.88
130.52
119.47
119.43
31.79
31.17
31.15
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28.94
22.69
14.17
13C NMR NG-3-81C in CDCl3
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128.94
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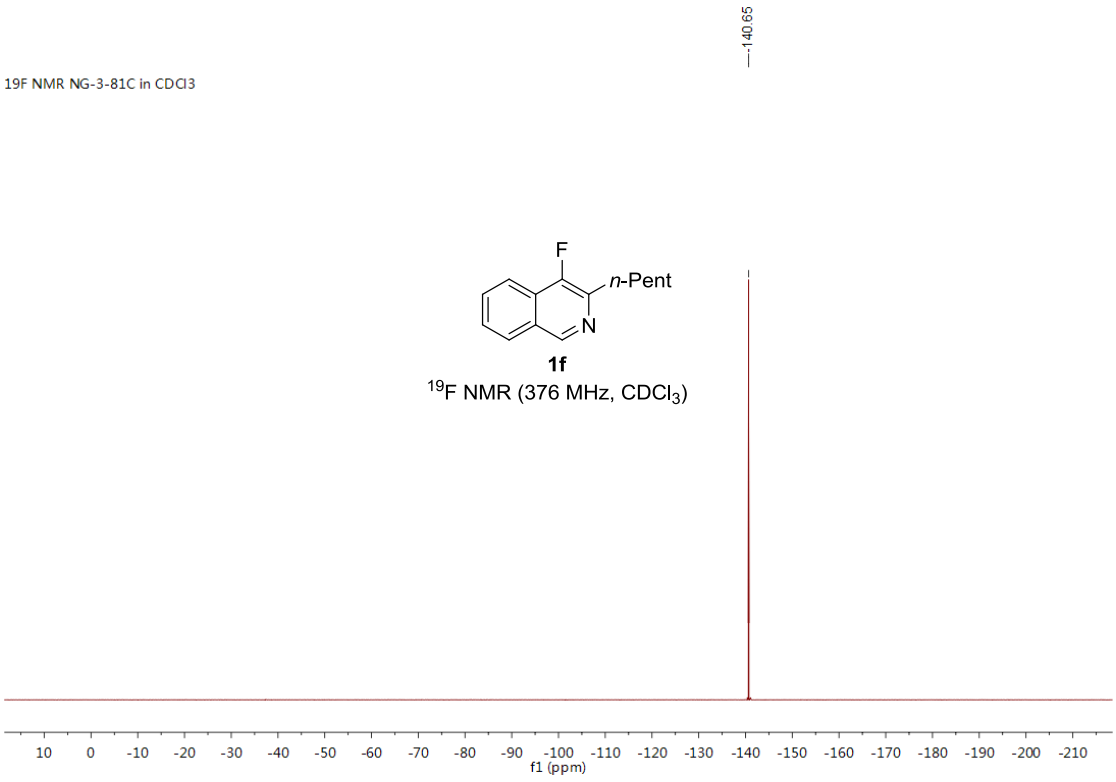
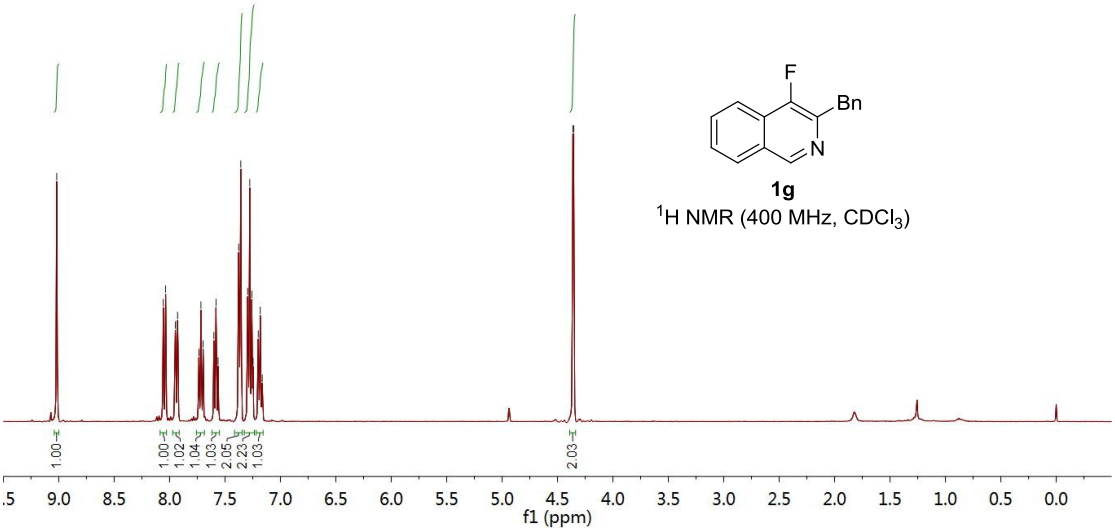
127.04
127.02
126.79
126.63
129.0
128.5
128.0
127.5
127.0
f1 (ppm)
F
n-Pent
N
1f
13C NMR (100 MHz, CDCl3)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


140.65
19F NMR NG-3-81C in CDCl3
F
n-Pent
N
1f
19F NMR (376 MHz, CDCl3)
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

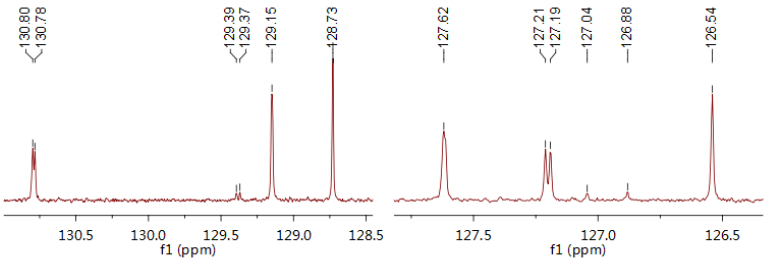
1H NMR FC-3-101 in CDCl3

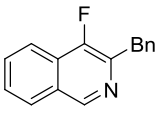


1g

^{1}H NMR (400 MHz, $CDCl_3$)

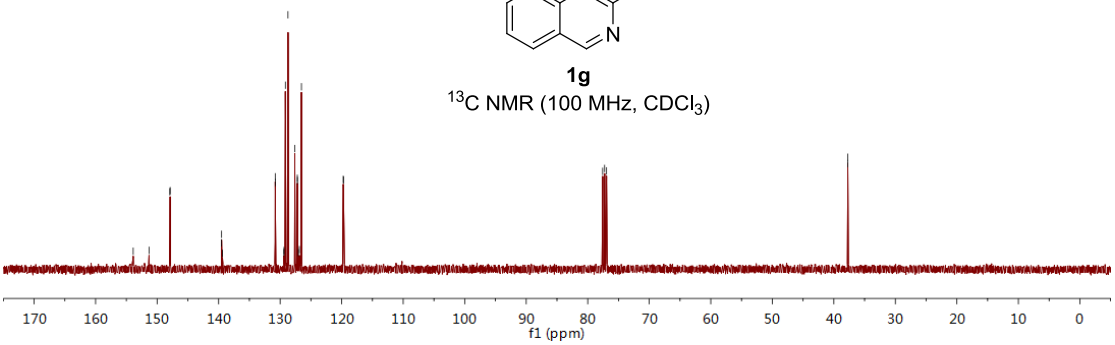
13C NMR FC-3-101 in CDCl3

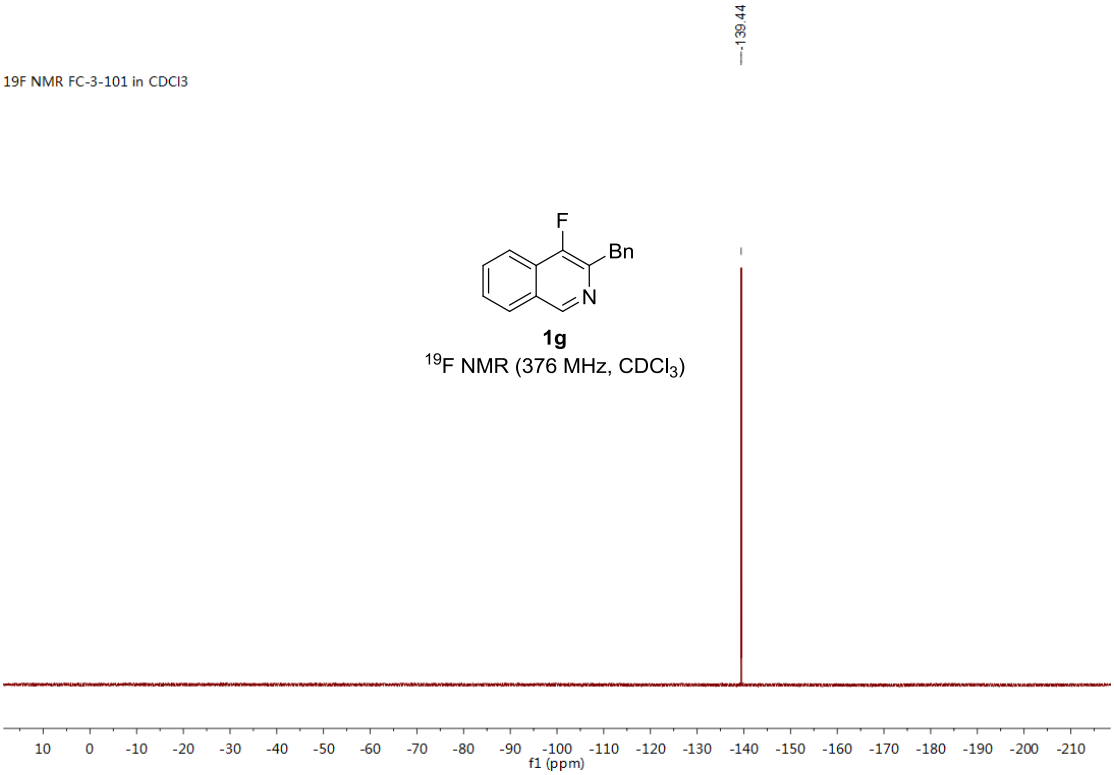




1g

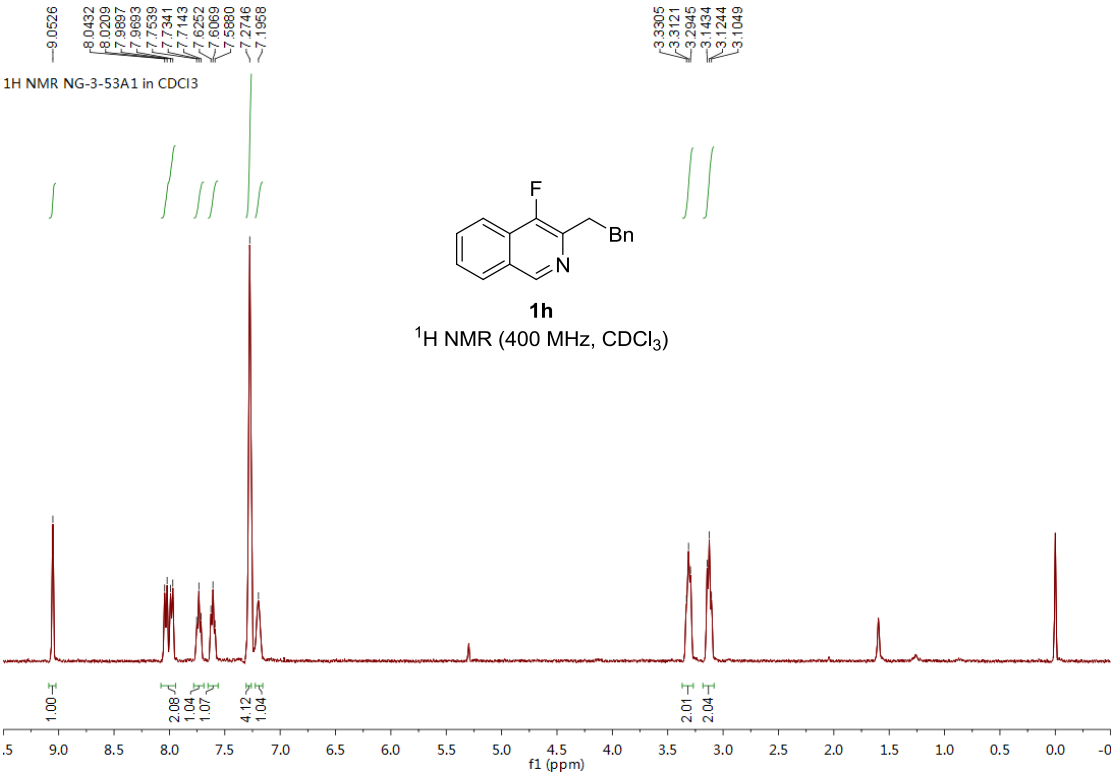
^{13}C NMR (100 MHz, $CDCl_3$)





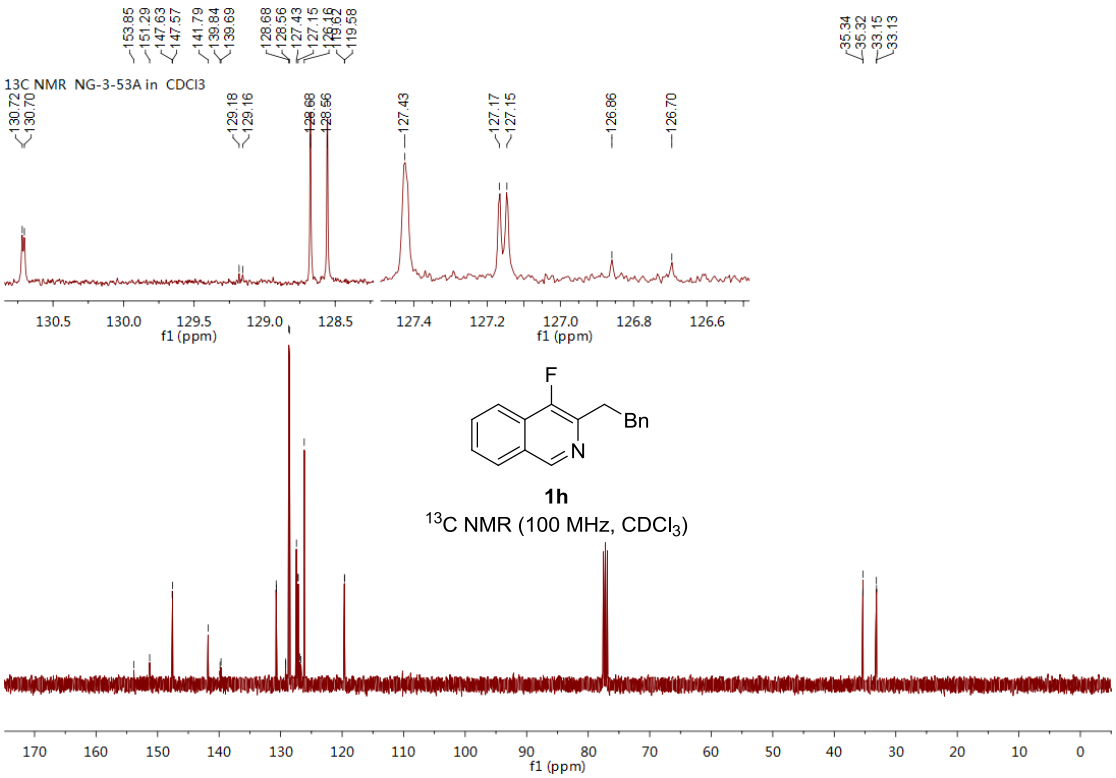
1g

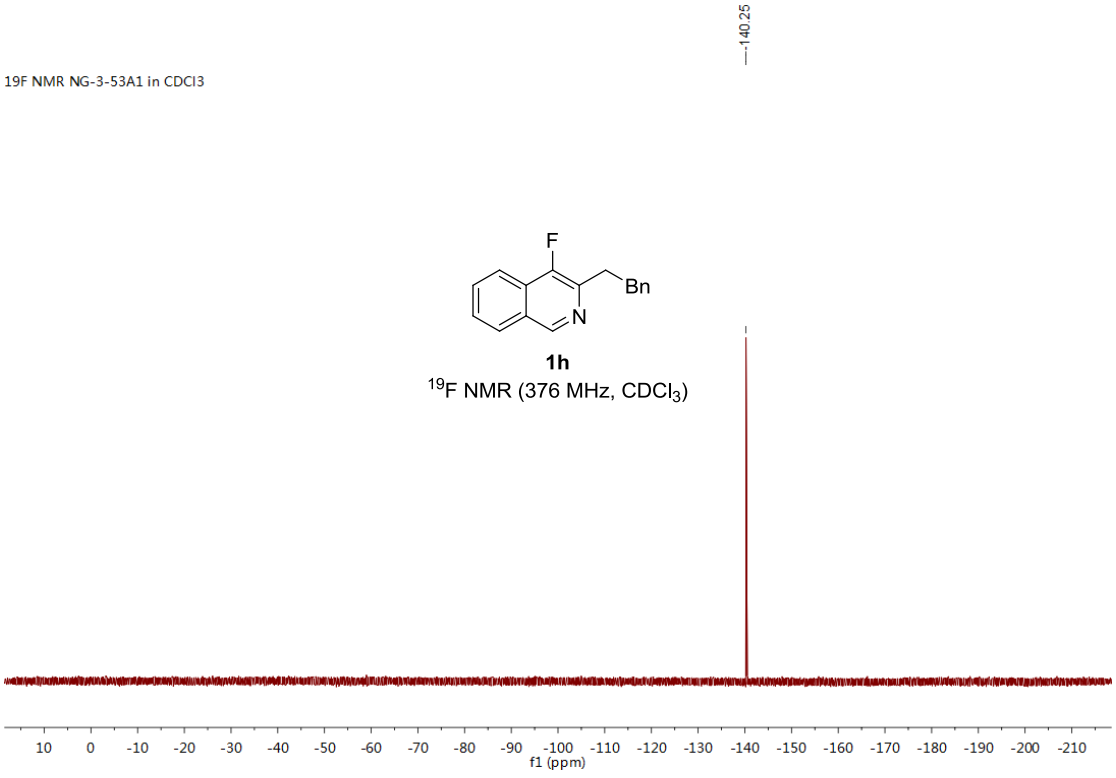
^{19}F NMR (376 MHz, $CDCl_3$)

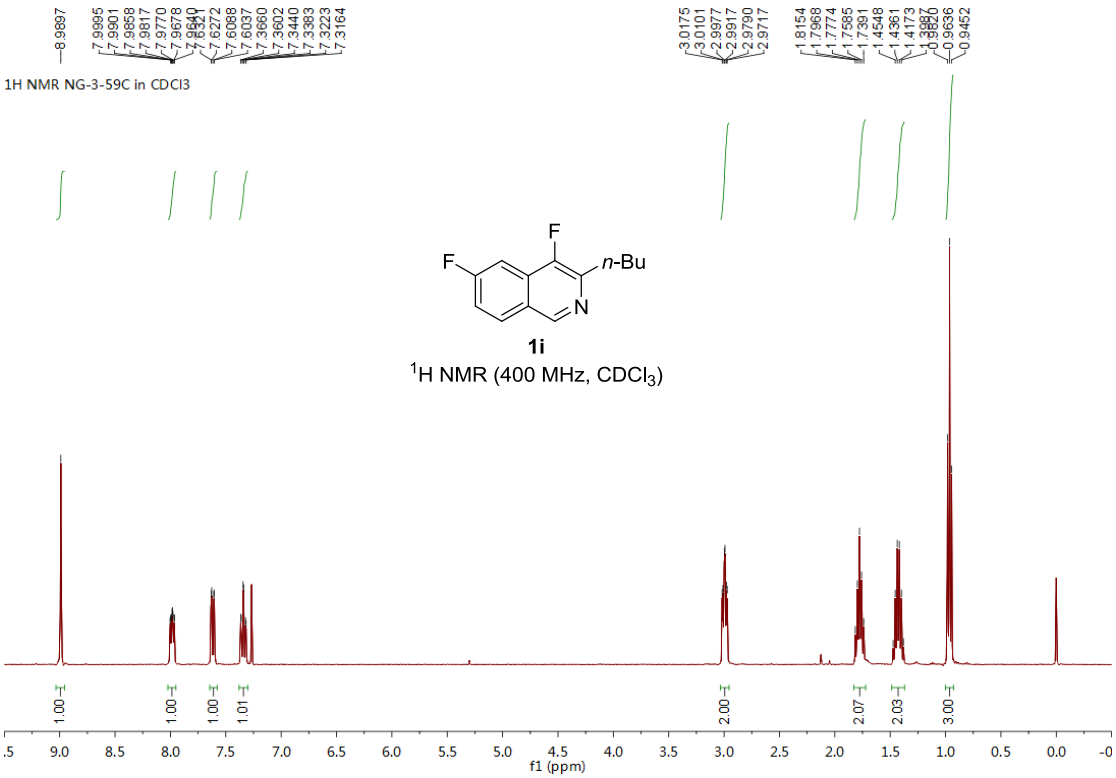


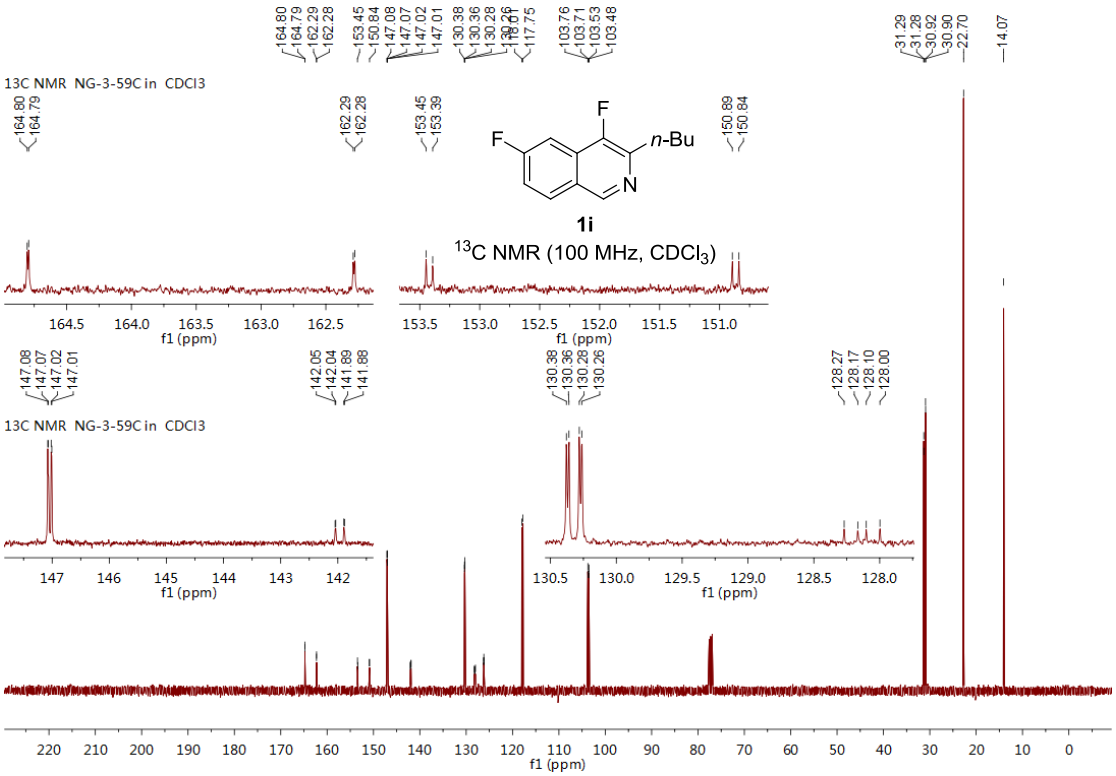
1h

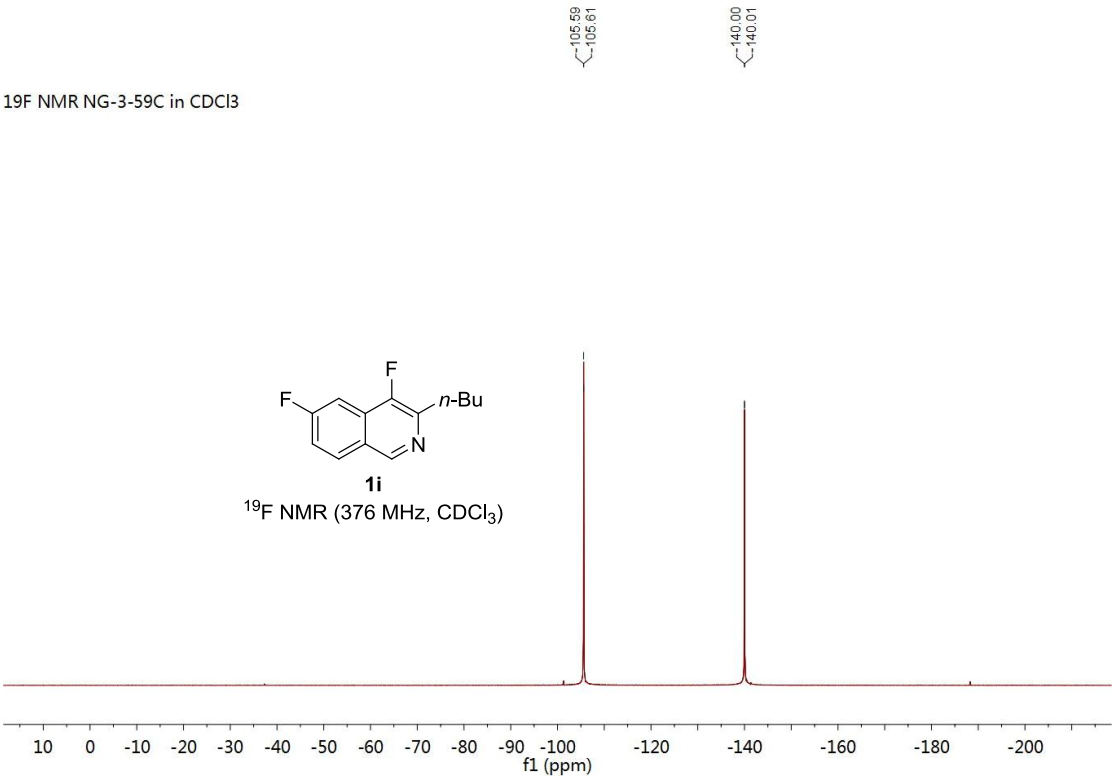
^{1}H NMR (400 MHz, $CDCl_3$)

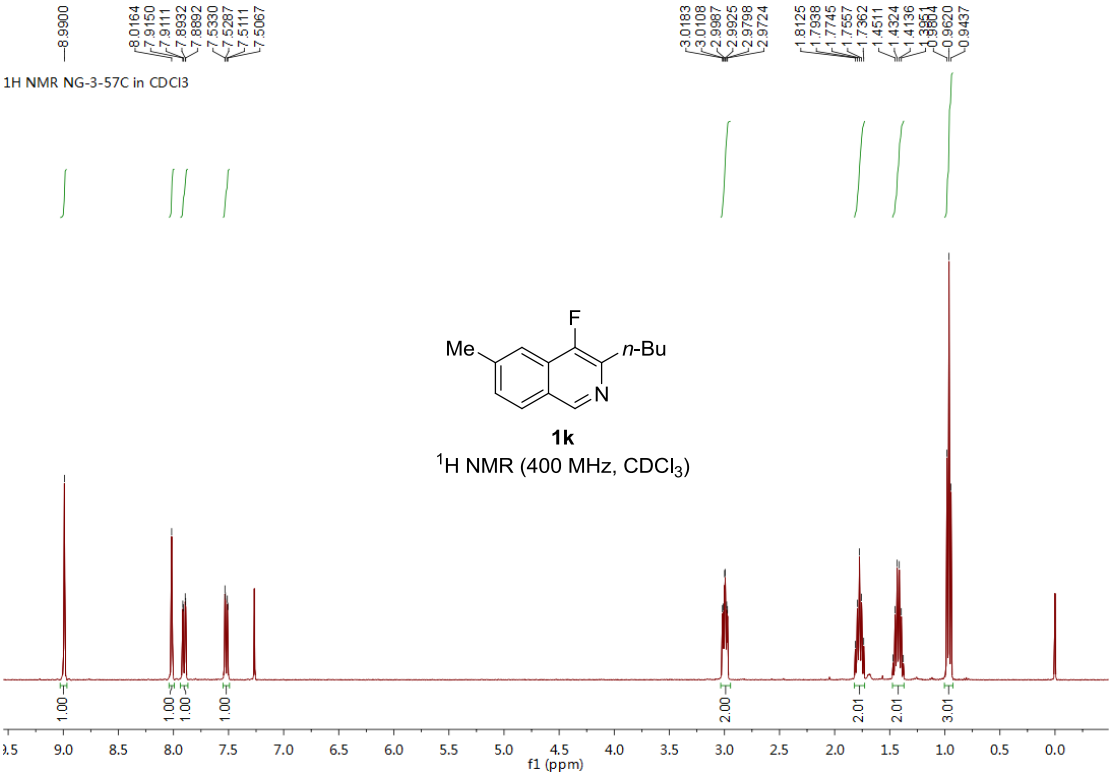

13C NMR NG-3-53A in CDCl3
153.85
151.29
147.63
147.57
141.79
139.84
139.69
128.68
128.56
127.43
127.15
119.58
35.34
35.32
33.15
33.13
130.72
130.70
129.18
129.16
127.43
127.17
127.15
126.86
126.70
f1 (ppm)
F
Bn
N
1h
13C NMR (100 MHz, CDCl3)
f1 (ppm)

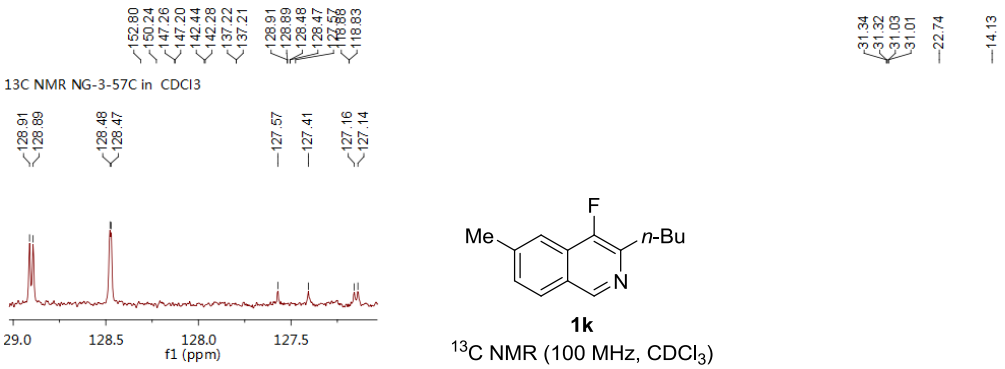

19F NMR NG-3-53A1 in CDCl3
-140.25
F
Bn
N
1h
19F NMR (376 MHz, CDCl3)
f1 (ppm)


1H NMR NG-3-59C in CDCl3
F
F
n-Bu
N
1i
1H NMR (400 MHz, CDCl3)
f1 (ppm)


13C NMR NG-3-59C in CDCl3
F
F
n-Bu
N
1i
13C NMR (100 MHz, CDCl3)
f1 (ppm)

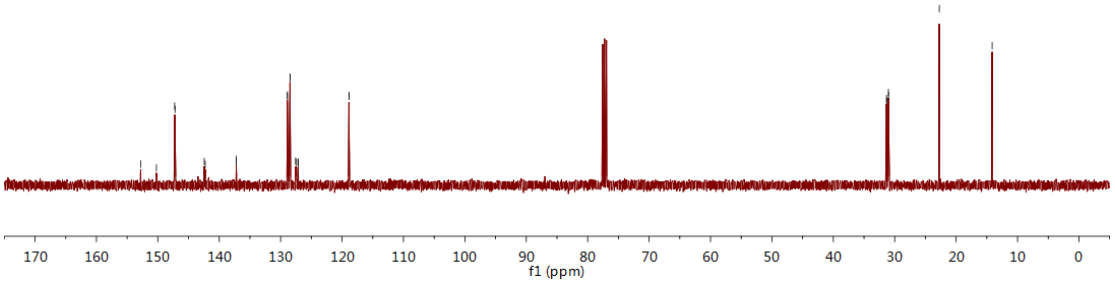

105.59
105.61
140.00
140.01
19F NMR NG-3-59C in CDCl3
F
F
n-Bu
N
1i
19F NMR (376 MHz, CDCl3)
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

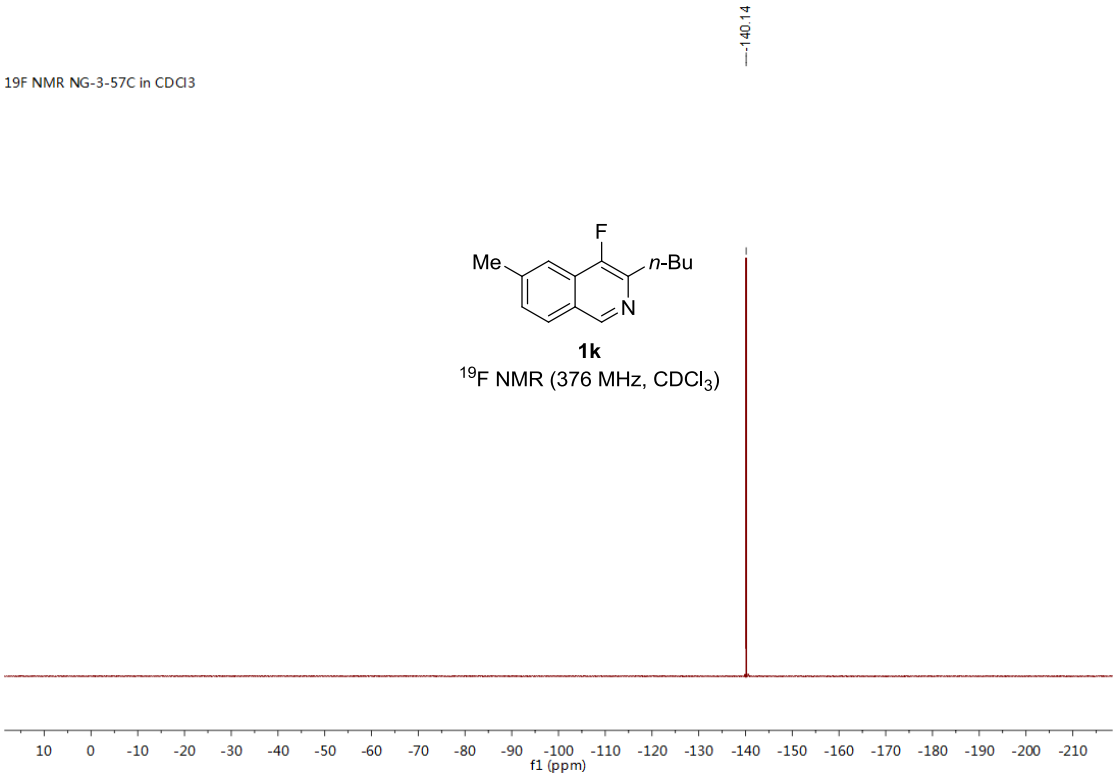

8.9900
8.0164
7.9150
7.9111
7.8932
7.8892
7.5330
7.5287
7.5111
7.5067
3.0183
3.0108
2.9987
2.9925
2.9798
2.9724
1.8125
1.7938
1.7745
1.7557
1.7362
1.4511
1.4324
1.4136
1.3951
0.9620
0.9437
1H NMR NG-3-57C in CDCl3
F
Me
n-Bu
N
1k
1H NMR (400 MHz, CDCl3)
1.00
1.00
1.00
1.00
2.00
2.01
2.01
3.01
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)



1k

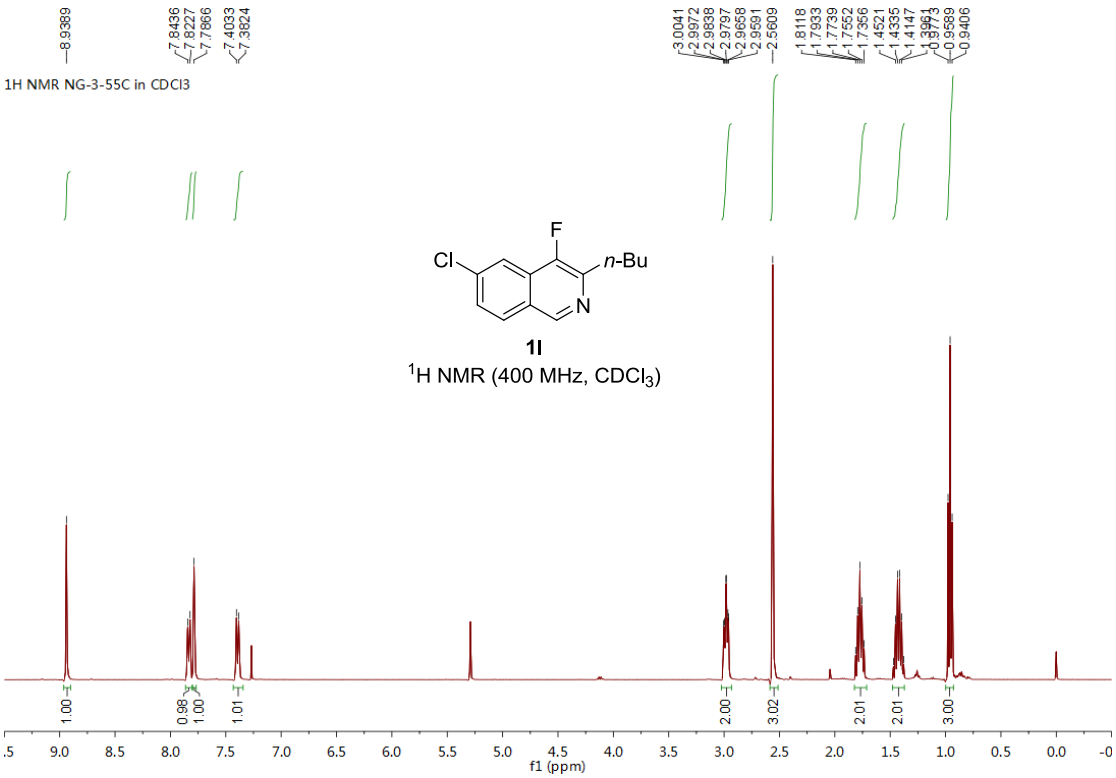
^{13}C NMR (100 MHz, $CDCl_3$)





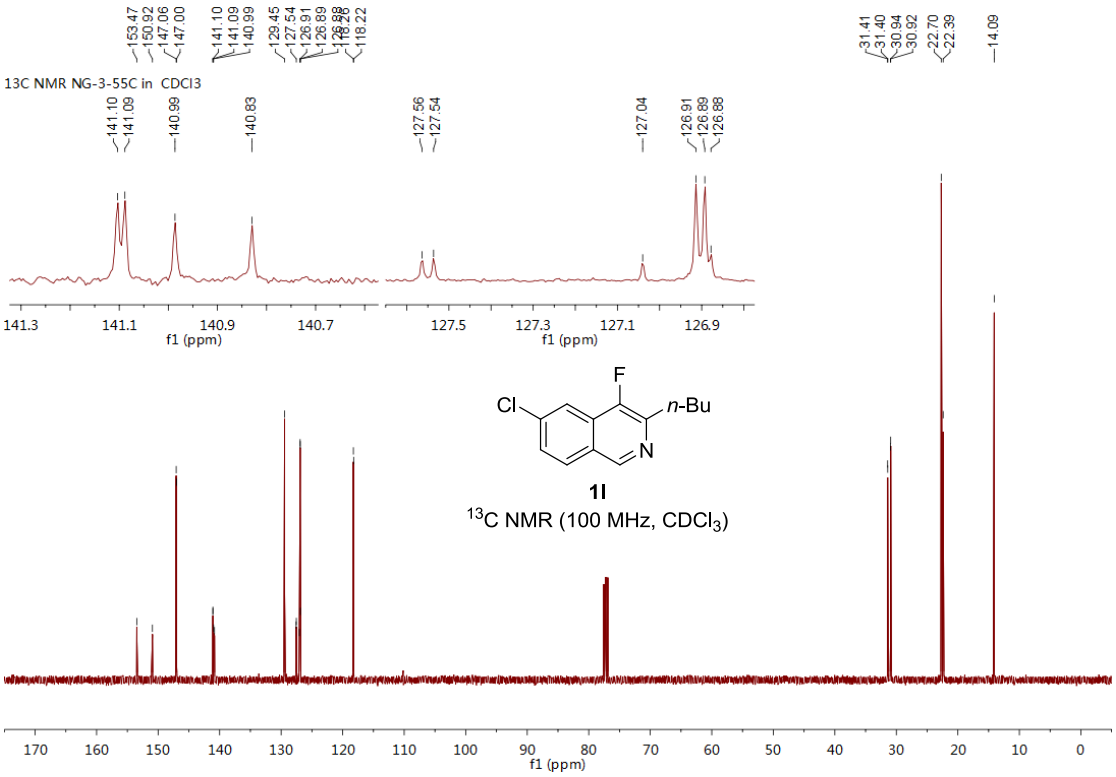
1k

^{19}F NMR (376 MHz, $CDCl_3$)



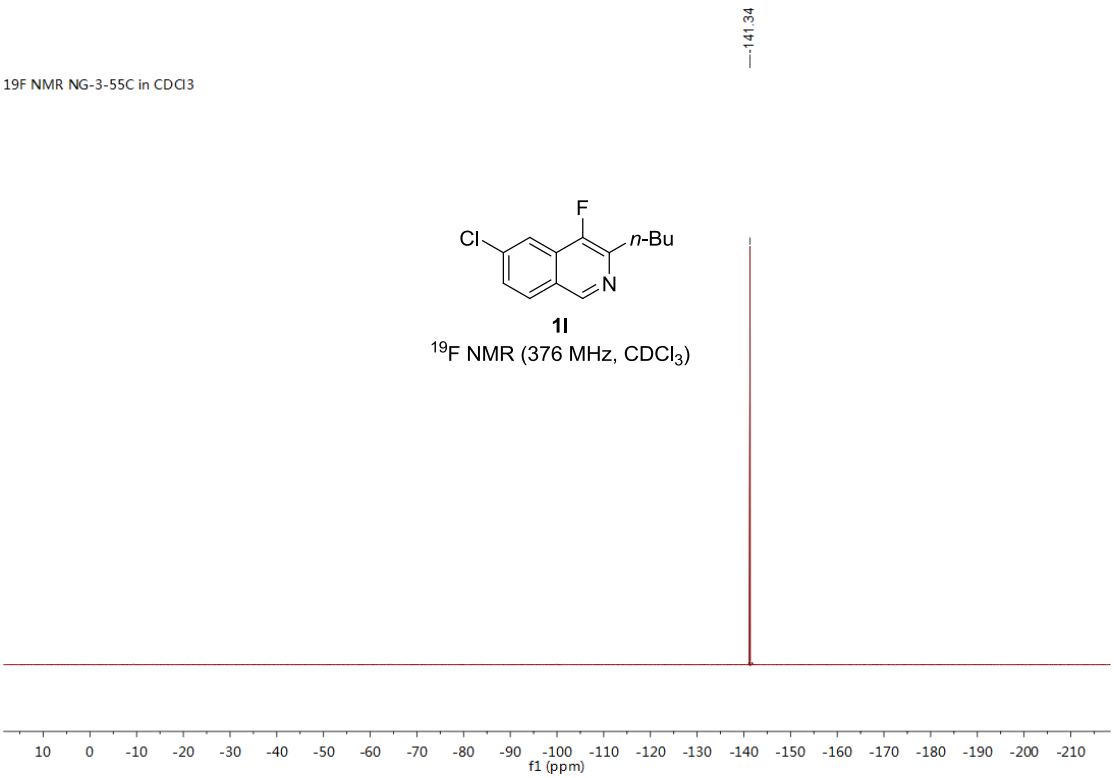
1l

^{1}H NMR (400 MHz, $CDCl_3$)



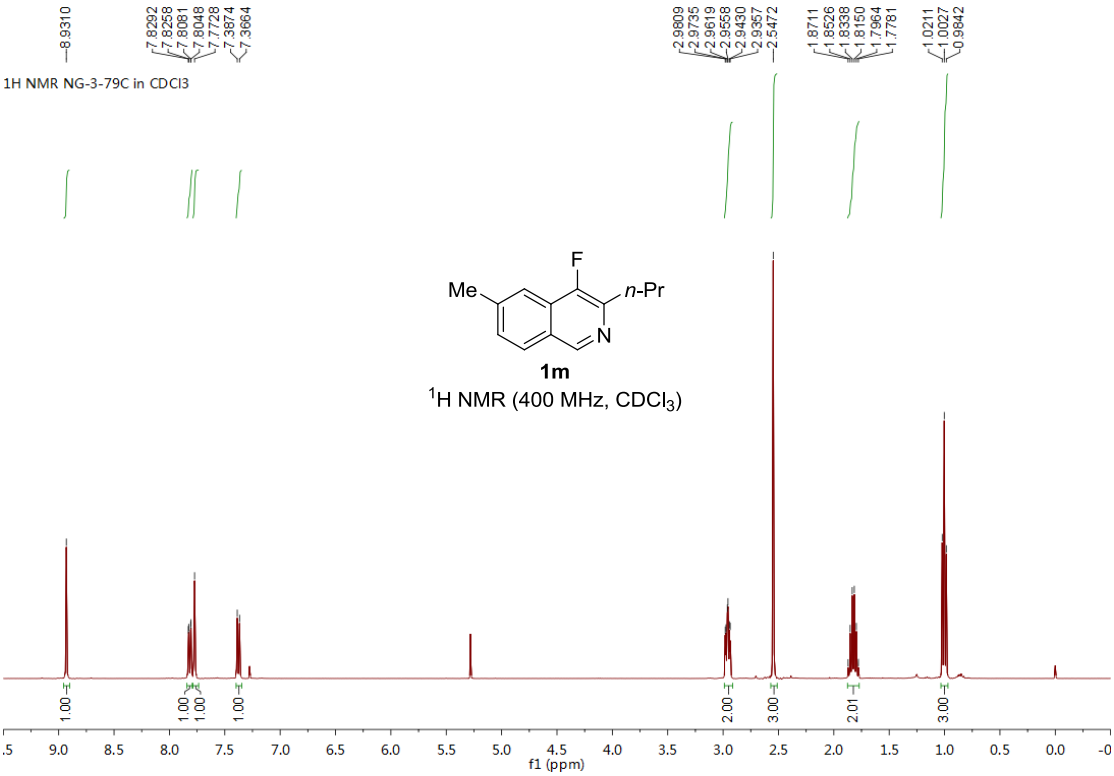
1l

^{13}C NMR (100 MHz, $CDCl_3$)



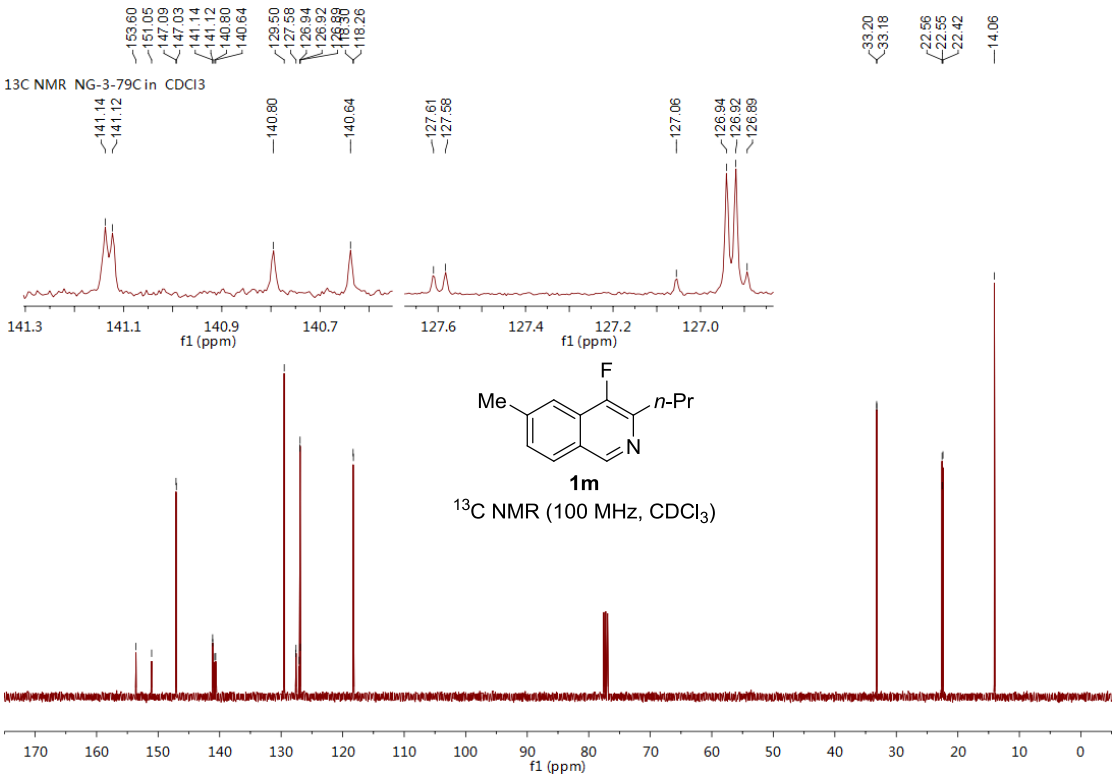
1l

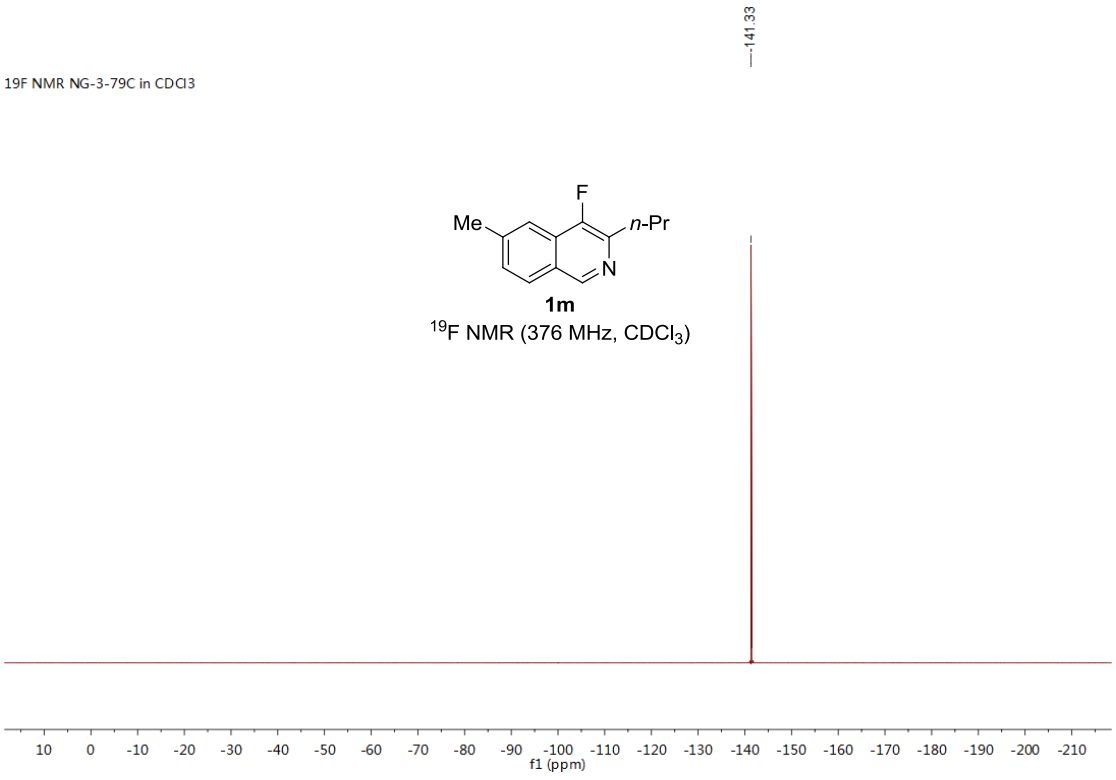
^{19}F NMR (376 MHz, $CDCl_3$)

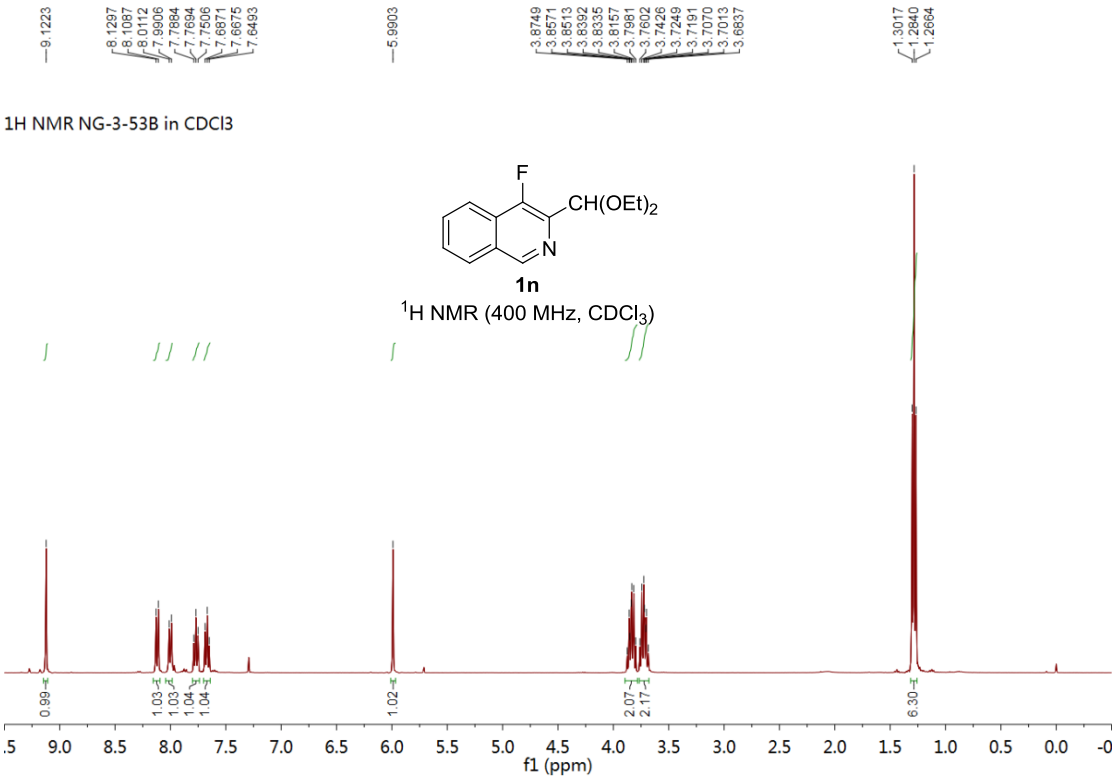


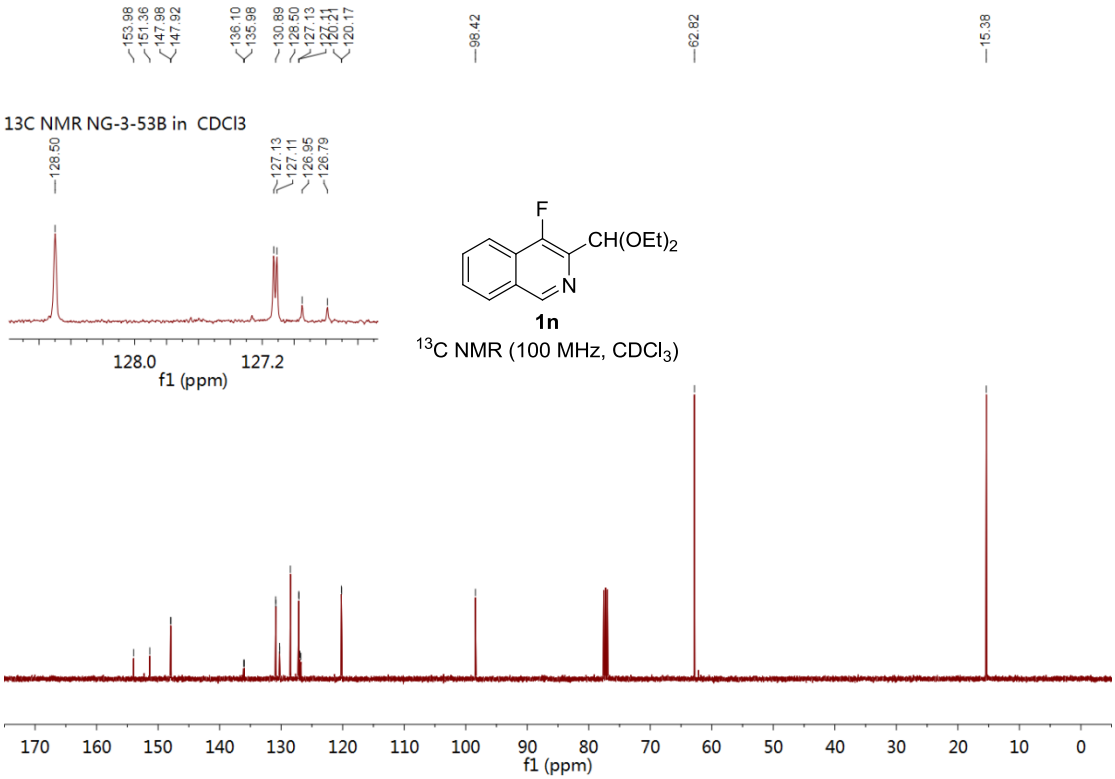
1m

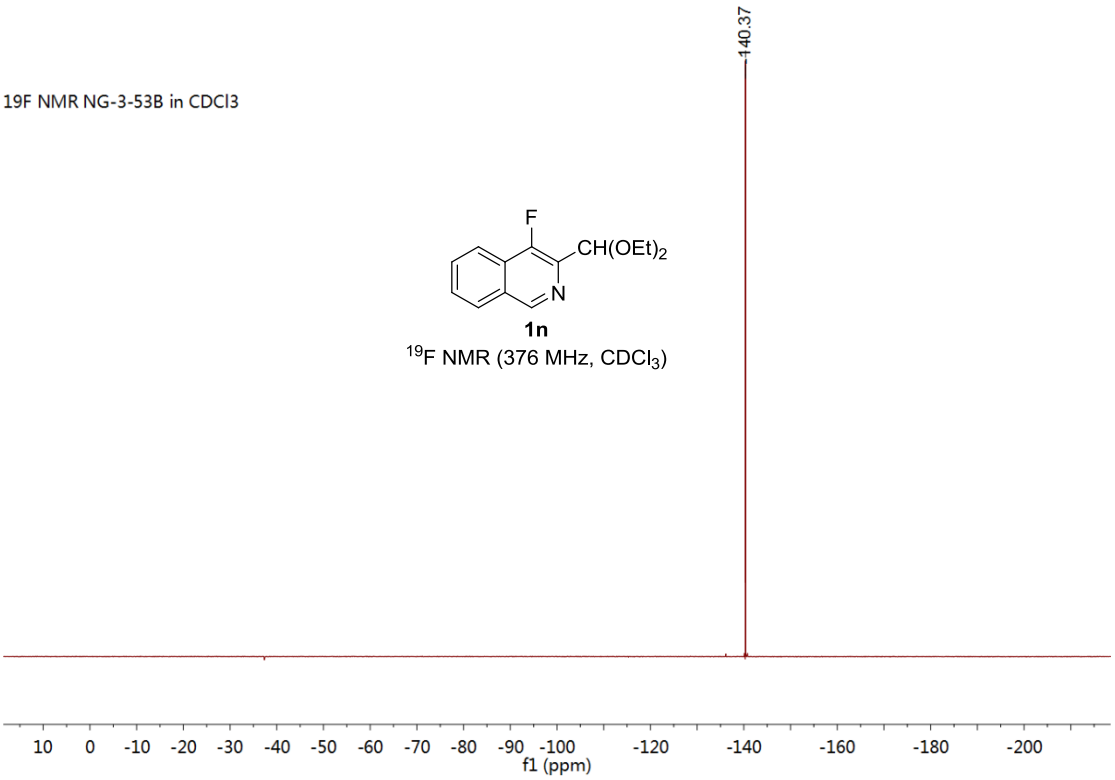
^{1}H NMR (400 MHz, $CDCl_3$)


153.60
151.05
147.09
147.03
141.14
141.12
140.80
140.64
129.50
127.58
126.94
126.92
126.89
118.38
118.26
33.20
33.18
22.56
22.55
22.42
14.06
13C NMR NG-3-79C in CDCl3
141.14
141.12
140.80
140.64
127.61
127.58
127.06
126.94
126.92
126.89
141.3
141.1
140.9
140.7
127.6
127.4
127.2
127.0
f1 (ppm)
F
Me
n-Pr
N
1m
13C NMR (100 MHz, CDCl3)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


141.33
19F NMR NG-3-79C in CDCl3
F
Me
n-Pr
N
1m
19F NMR (376 MHz, CDCl3)
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

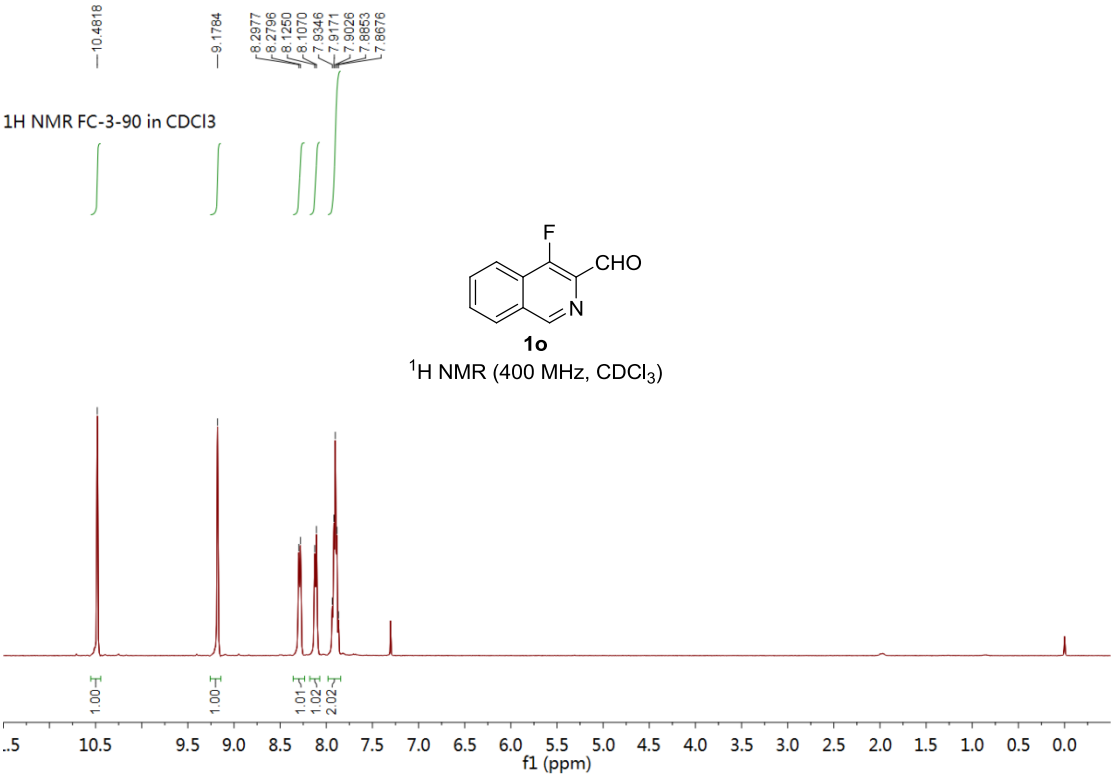

9.1223
8.1297
8.1087
8.0112
7.9906
7.7884
7.7694
7.7506
7.6871
7.6675
7.6493
5.9903
3.8749
3.8571
3.8513
3.8392
3.8335
3.8157
3.7981
3.7602
3.7426
3.7249
3.7191
3.7070
3.7013
3.6837
1.3017
1.2840
1.2664
1H NMR NG-3-53B in CDCl3
F
CH(OEt)2
N
1n
1H NMR (400 MHz, CDCl3)
0.99
1.03
1.03
1.04
1.04
1.02
2.07
2.17
6.30
f1 (ppm)


153.98
151.36
147.98
147.92
136.10
135.98
130.89
128.50
127.13
127.11
126.95
126.79
120.21
120.17
98.42
62.82
15.38
13C NMR NG-3-53B in CDCl3
128.50
127.13
127.11
126.95
126.79
128.0
127.2
f1 (ppm)
F
CH(OEt)2
N
1n
13C NMR (100 MHz, CDCl3)
f1 (ppm)



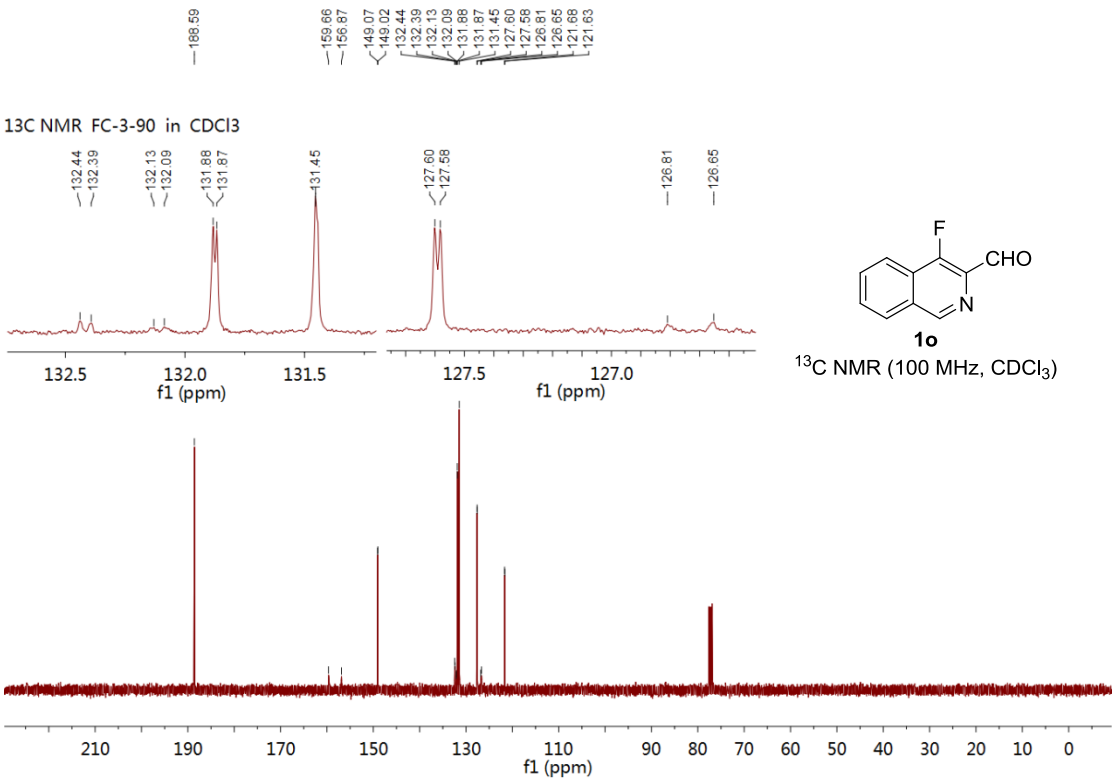
1n

^{19}F NMR (376 MHz, $CDCl_3$)



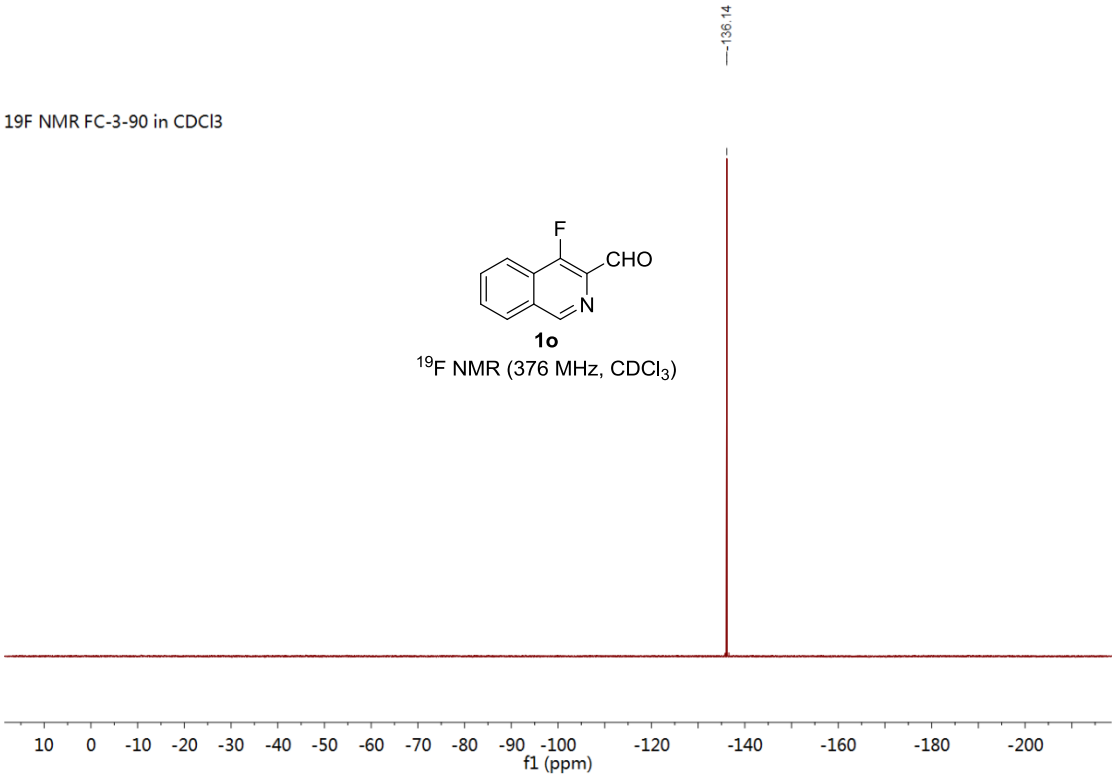
1o

^{1}H NMR (400 MHz, $CDCl_3$)



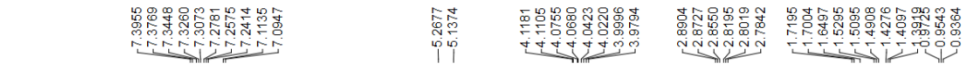
1o

^{13}C NMR (100 MHz, $CDCl_3$)

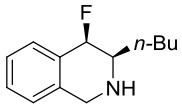


1o

^{19}F NMR (376 MHz, $CDCl_3$)

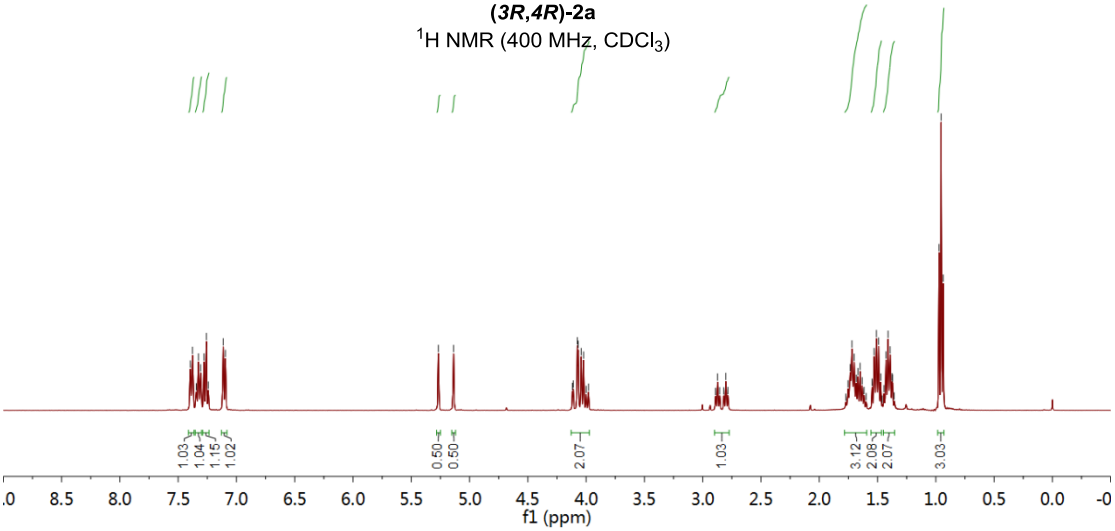


1H NMR NG-3-43A in CDCl3

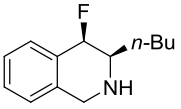


(*3R*,*4R*)-2a

^{1}H NMR (400 MHz, $CDCl_3$)

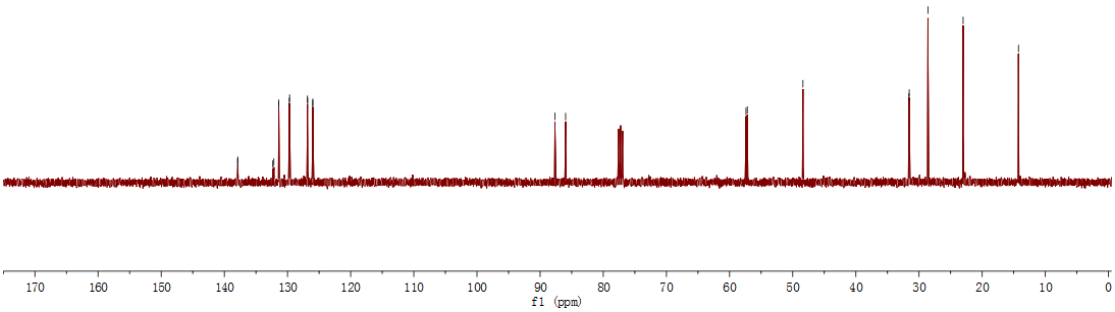


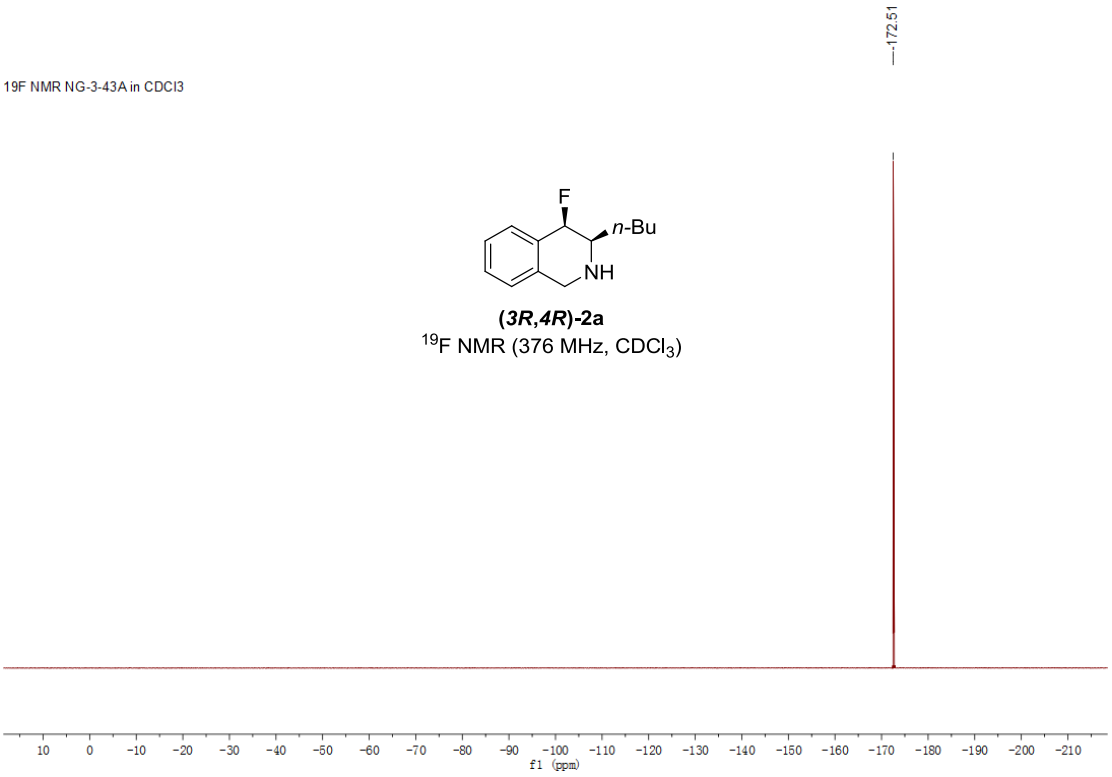
13C NMR NG-3-43A in CDCl3



(*3R*,*4R*)-2a

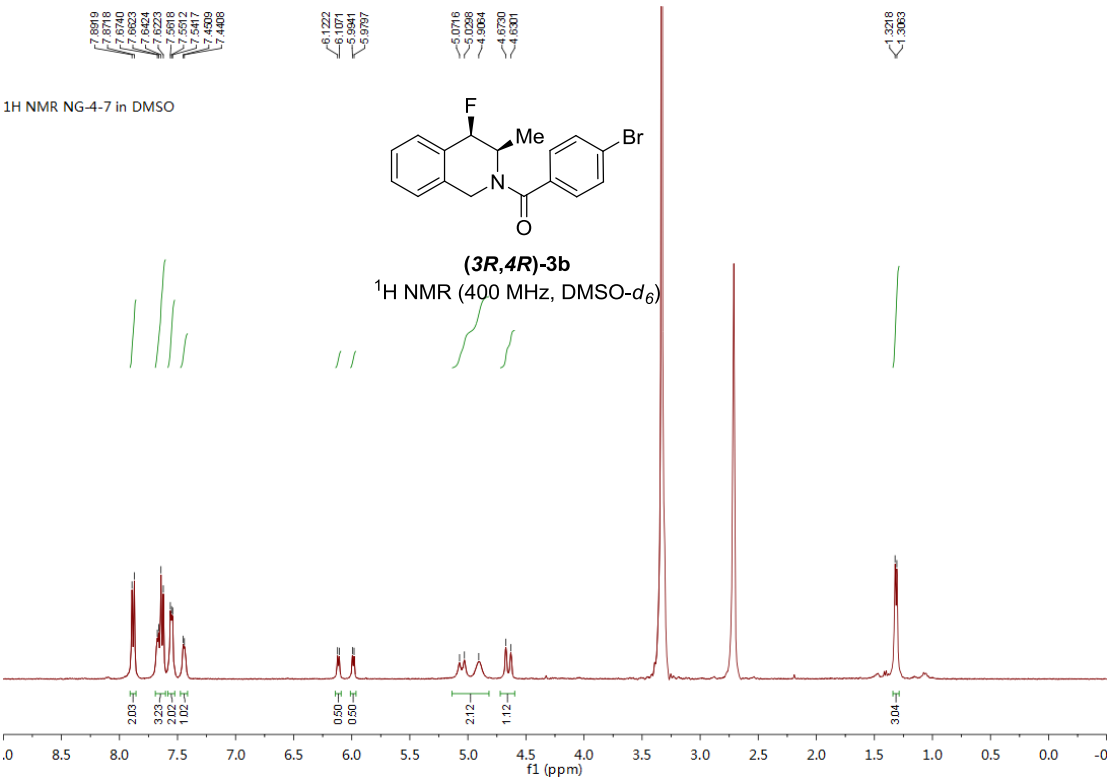
^{13}C NMR (100 MHz, $CDCl_3$)





(*3R*,*4R*)-2a

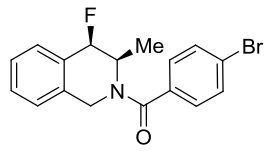
^{19}F NMR (376 MHz, $CDCl_3$)



(*3R*,*4R*)-3b

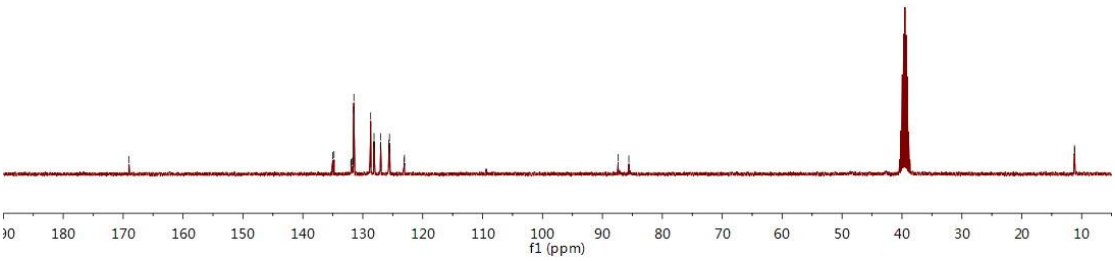
^{1}H NMR (400 MHz, DMSO-d_6)

13C NMR NG-4-7 in DMSO

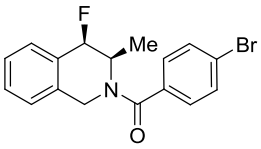


(*3R*,*4R*)-3b

^{13}C NMR (100 MHz, DMSO-d_6)

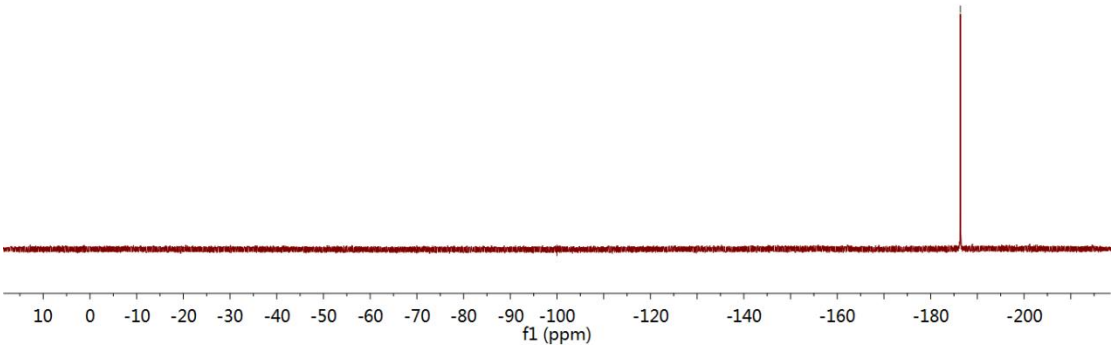


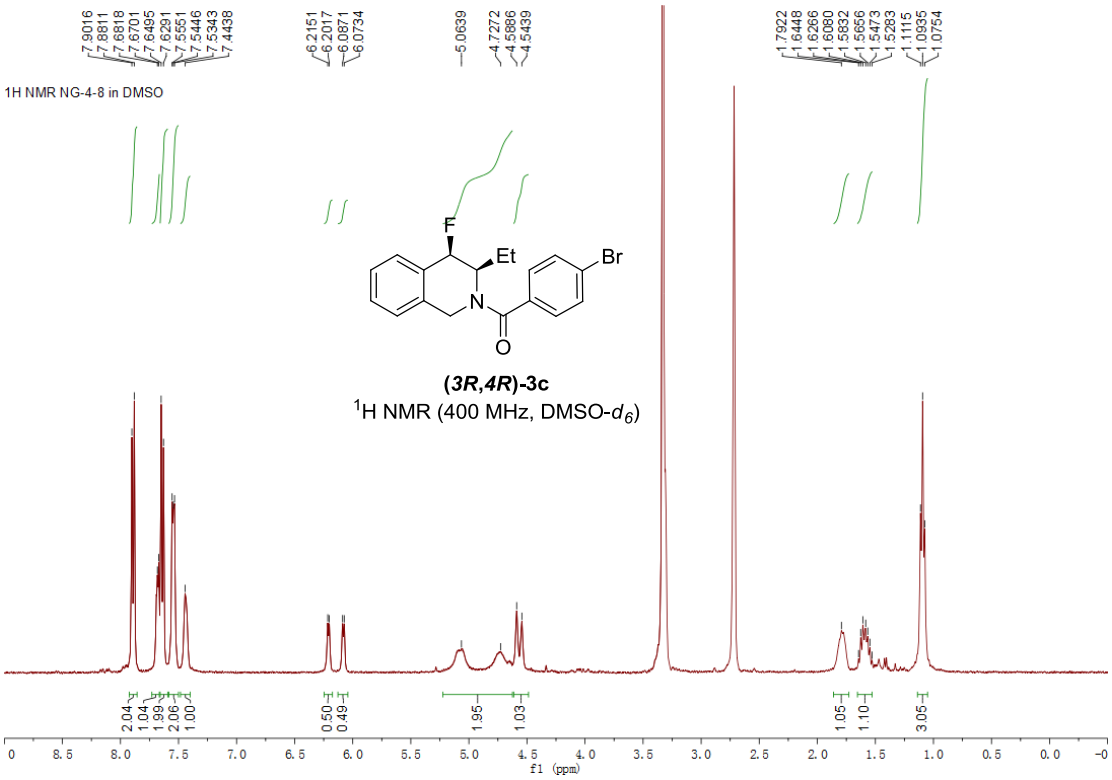
19F NMR NG-4-7 in DMSO



(*3R*,*4R*)-3b

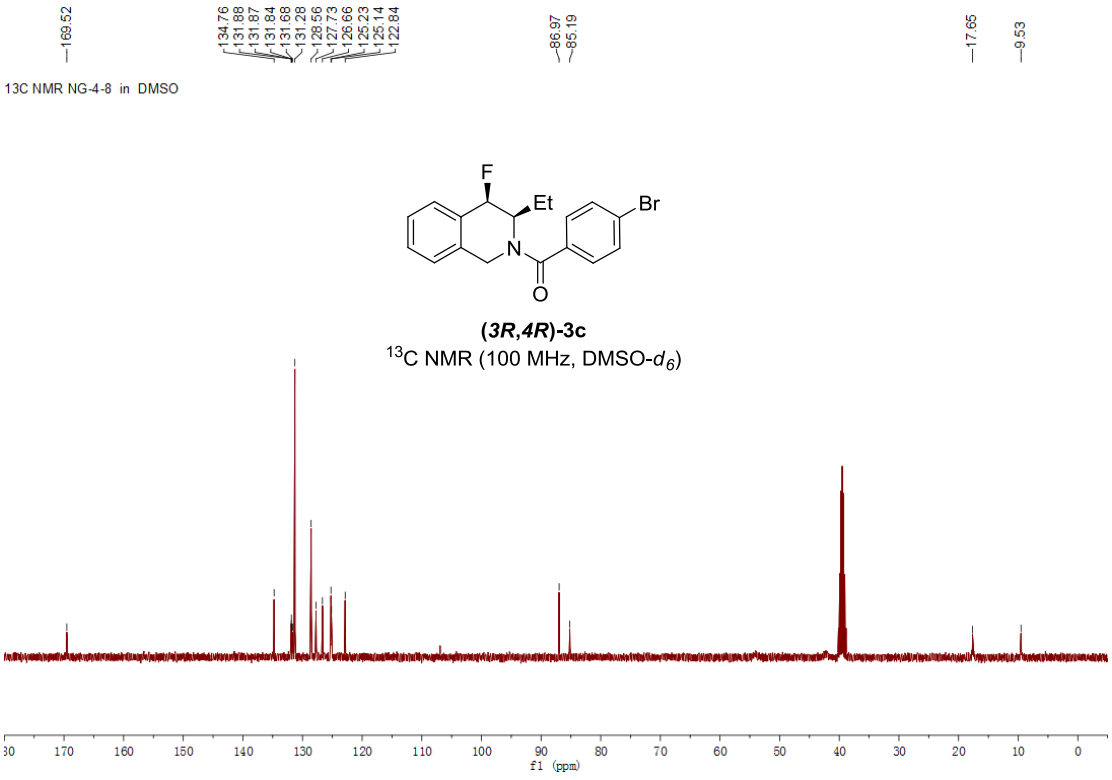
^{19}F NMR (376 MHz, DMSO-d_6)





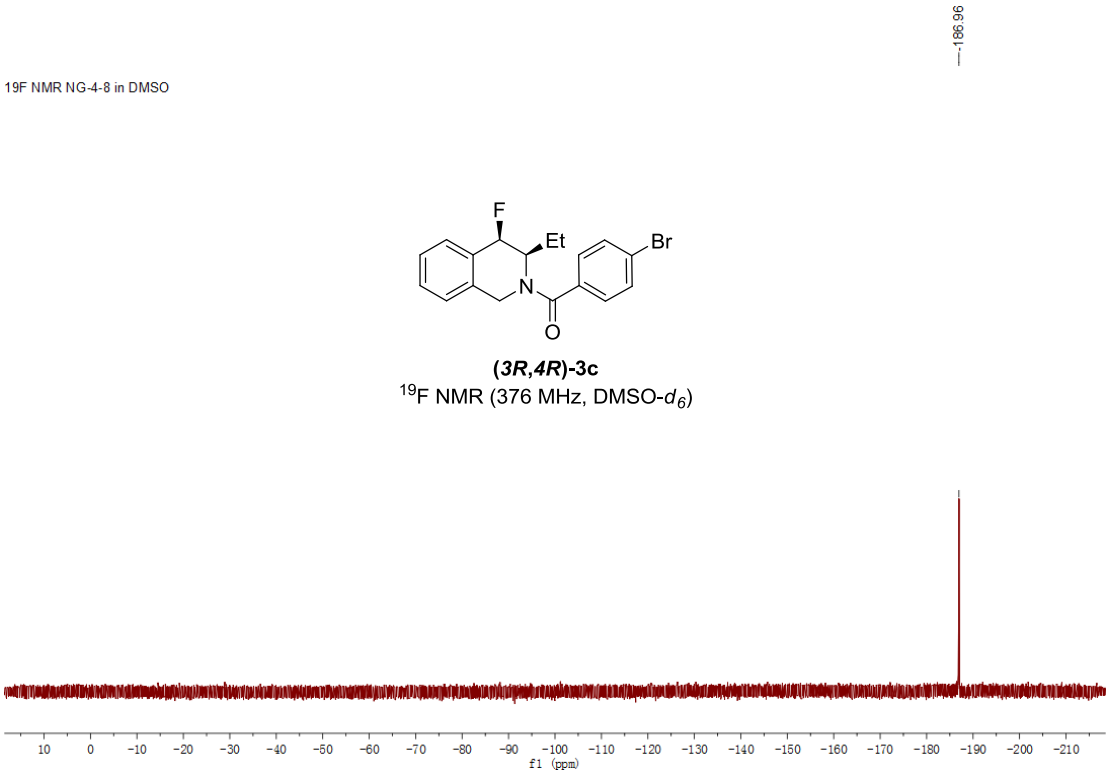
(*3R*,*4R*)-3c

^{1}H NMR (400 MHz, DMSO-d_6)



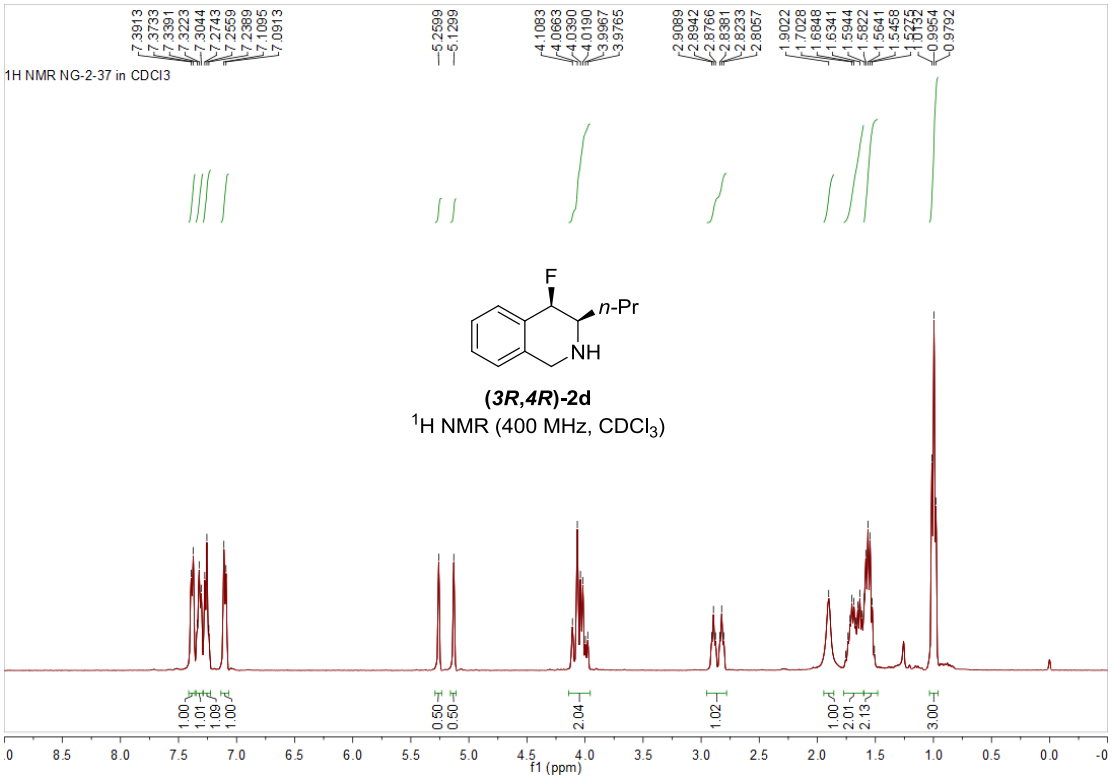
(*3R*,*4R*)-3c

^{13}C NMR (100 MHz, DMSO-d_6)



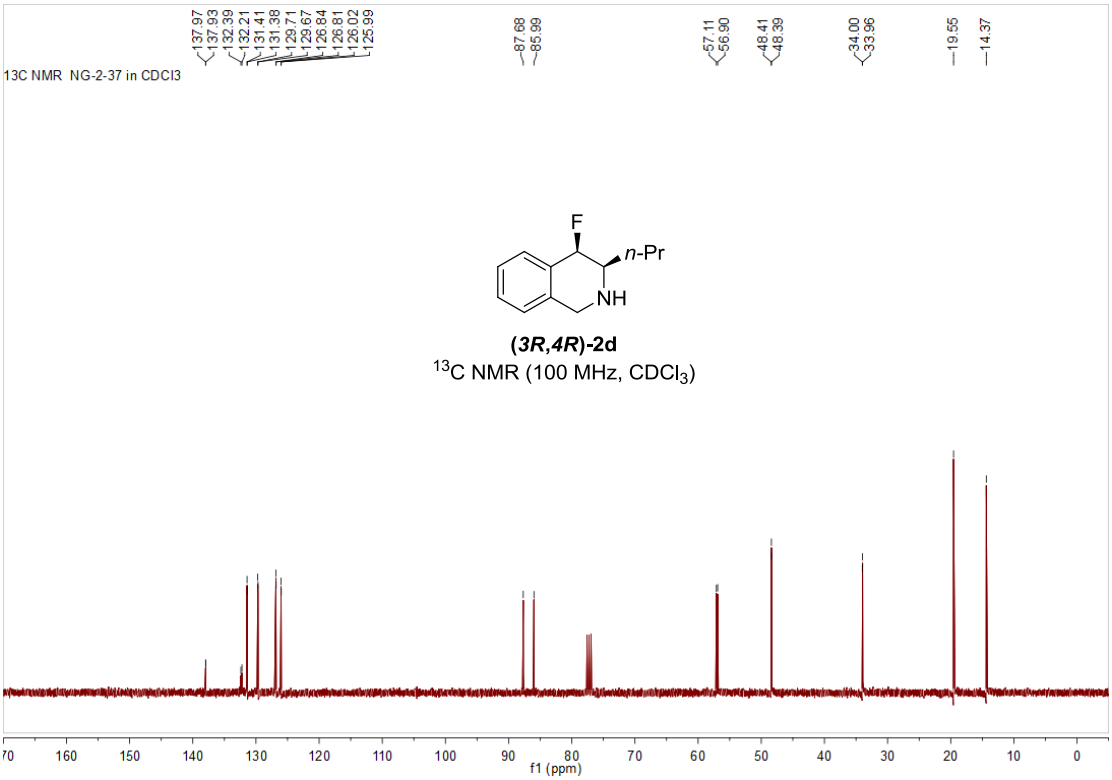
(*3R*,*4R*)-3c

^{19}F NMR (376 MHz, DMSO-d_6)



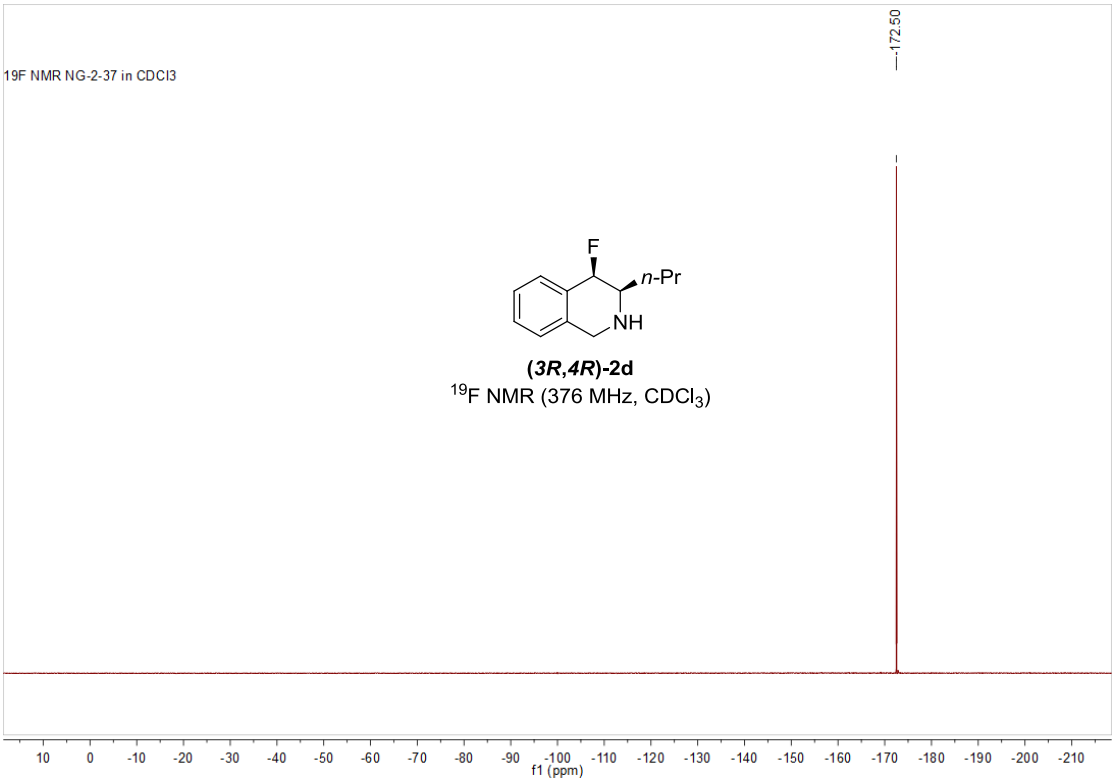
(*3R*,*4R*)-2d

^{1}H NMR (400 MHz, $CDCl_3$)



(*3R*,*4R*)-2d

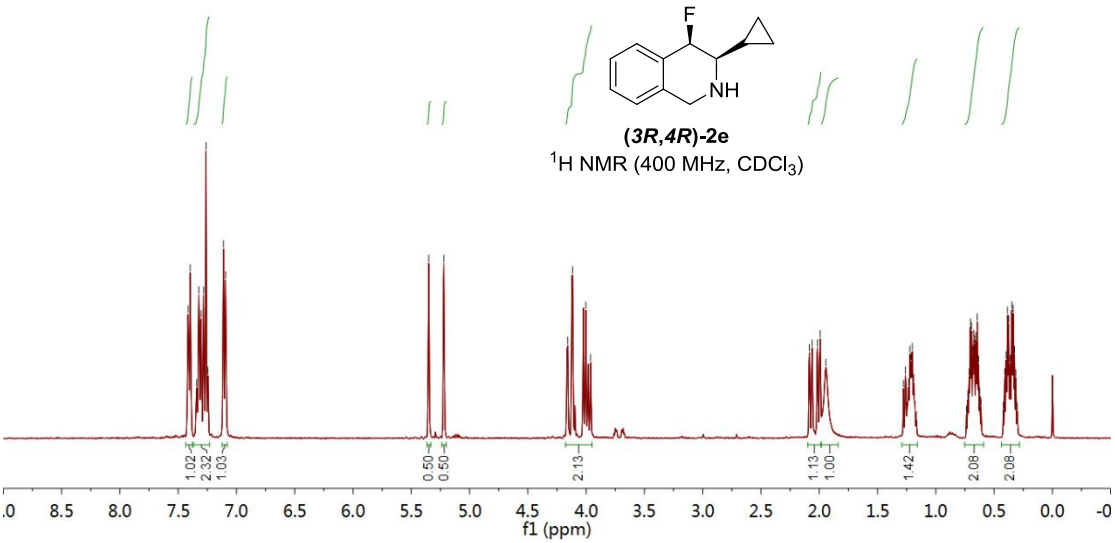
^{13}C NMR (100 MHz, $CDCl_3$)



(*3R*,*4R*)-2d

^{19}F NMR (376 MHz, $CDCl_3$)

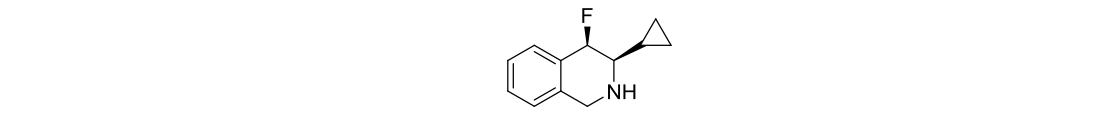
1H NMR NG-3-41B in CDCl3



(*3R*,*4R*)-2e

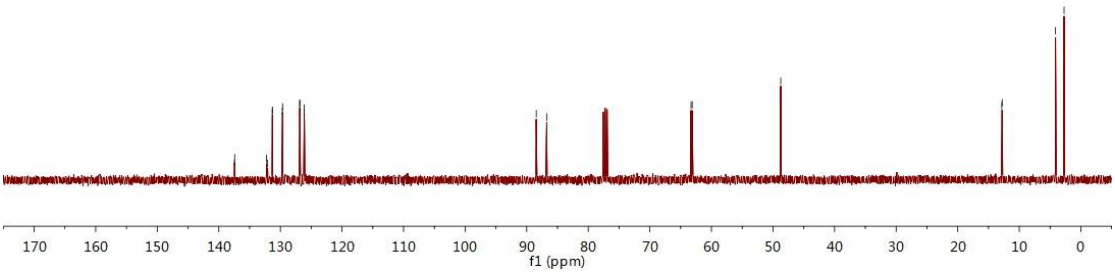
^{1}H NMR (400 MHz, $CDCl_3$)

13C NMR NG-3-41B in CDCl3

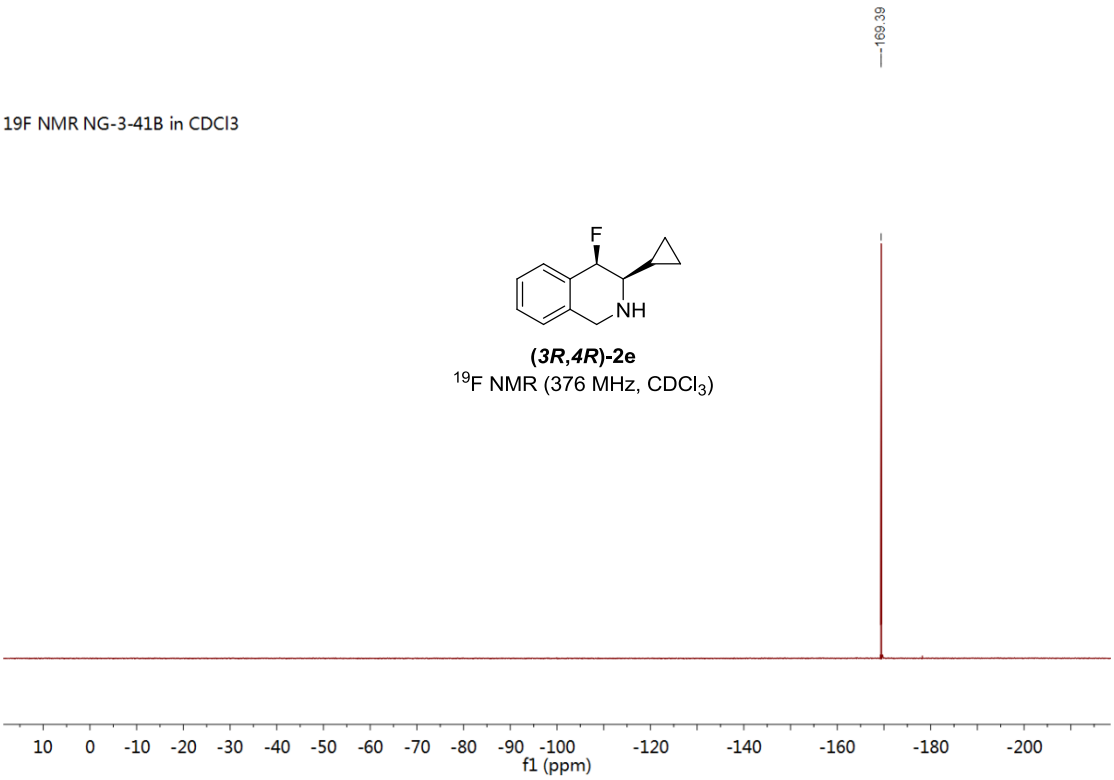


(*3R*,*4R*)-2e

^{13}C NMR (100 MHz, $CDCl_3$)



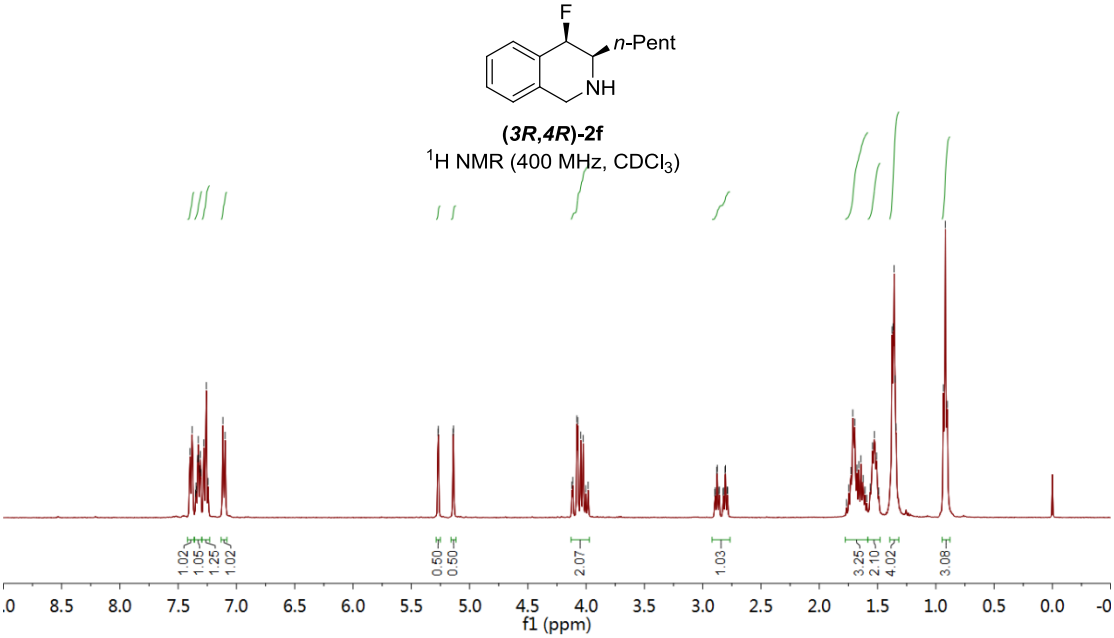
19F NMR NG-3-41B in CDCl3



(*3R,4R*)-2e

^{19}F NMR (376 MHz, $CDCl_3$)

1H NMR NG-3-90C in CDCl3

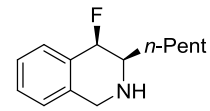


(*3R,4R*)-2f

^{1}H NMR (400 MHz, $CDCl_3$)

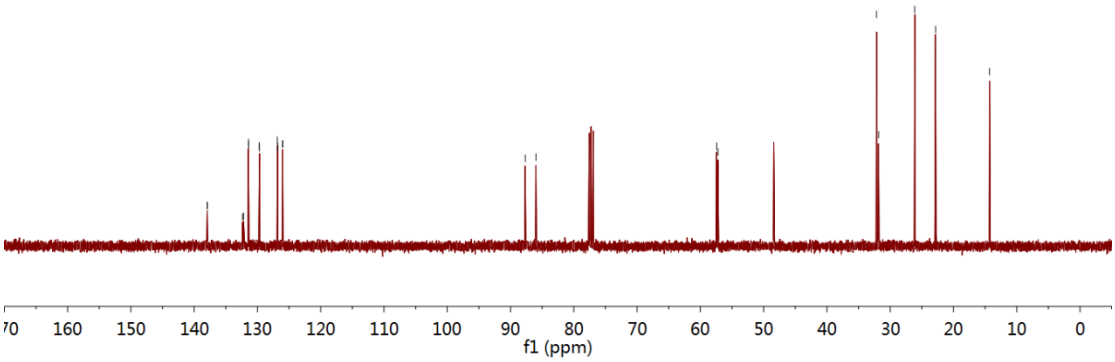
137.95
137.91
132.36
132.18
131.42
131.39
129.73
129.69
126.85
126.82
126.03
126.00
87.67
85.98
57.43
57.22
32.17
31.83
26.11
22.83
14.30

13C NMR NG-3-90C in CDCl3



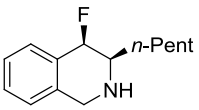
(*3R*,*4R*)-2f

^{13}C NMR (100 MHz, $CDCl_3$)



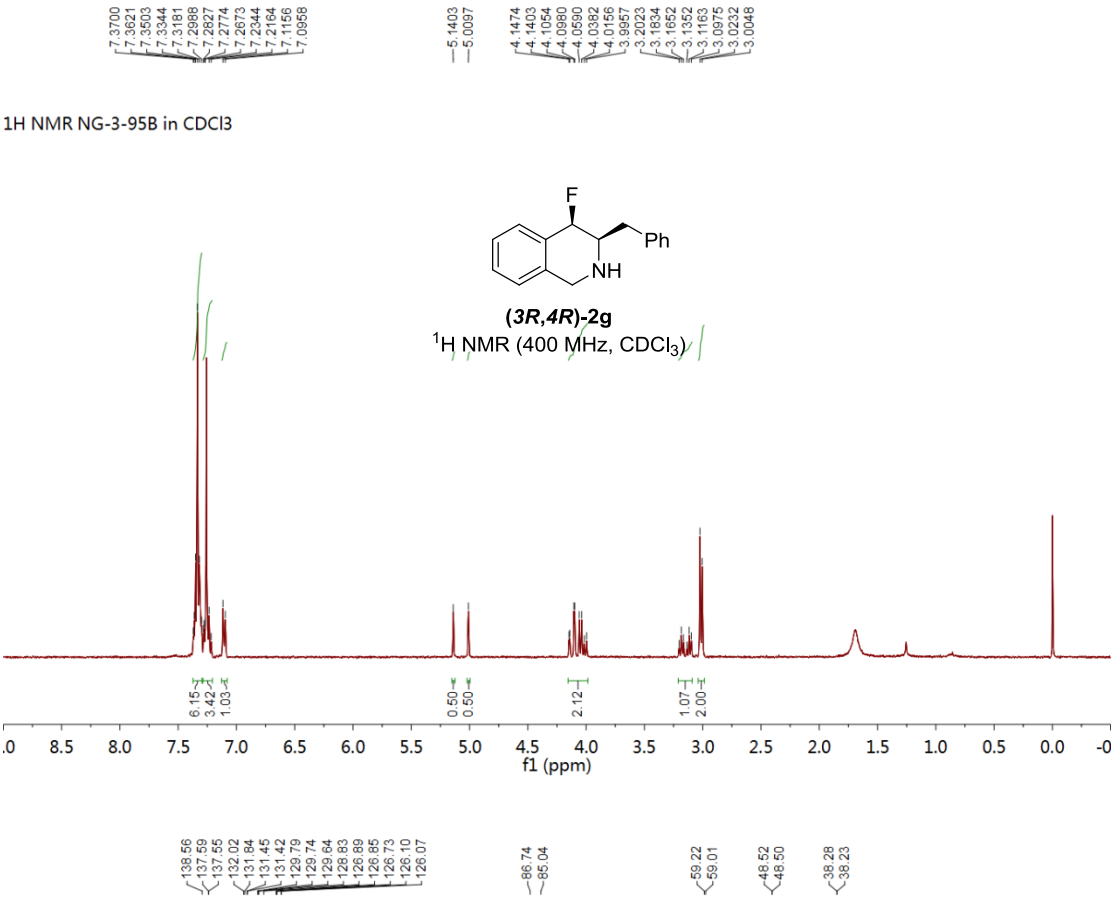
172.53

19F NMR NG-3-90C in CDCl3



(*3R*,*4R*)-2f

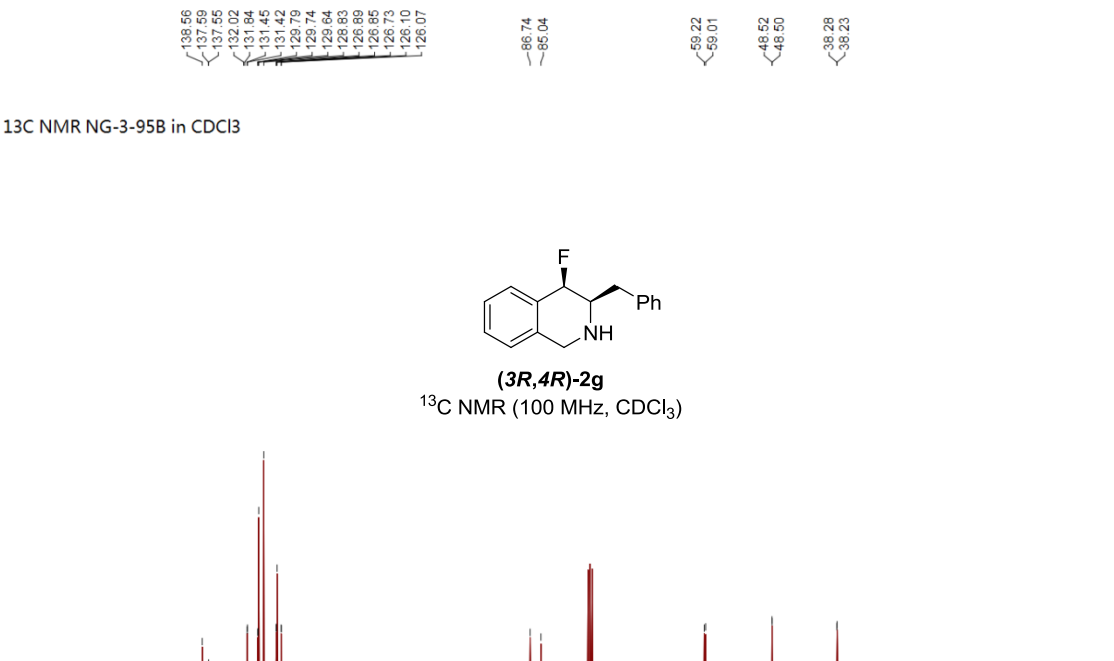
^{19}F NMR (376 MHz, $CDCl_3$)



1H NMR NG-3-95B in CDCl3

(*3R,4R*)-2g

^{1}H NMR (400 MHz, $CDCl_3$)

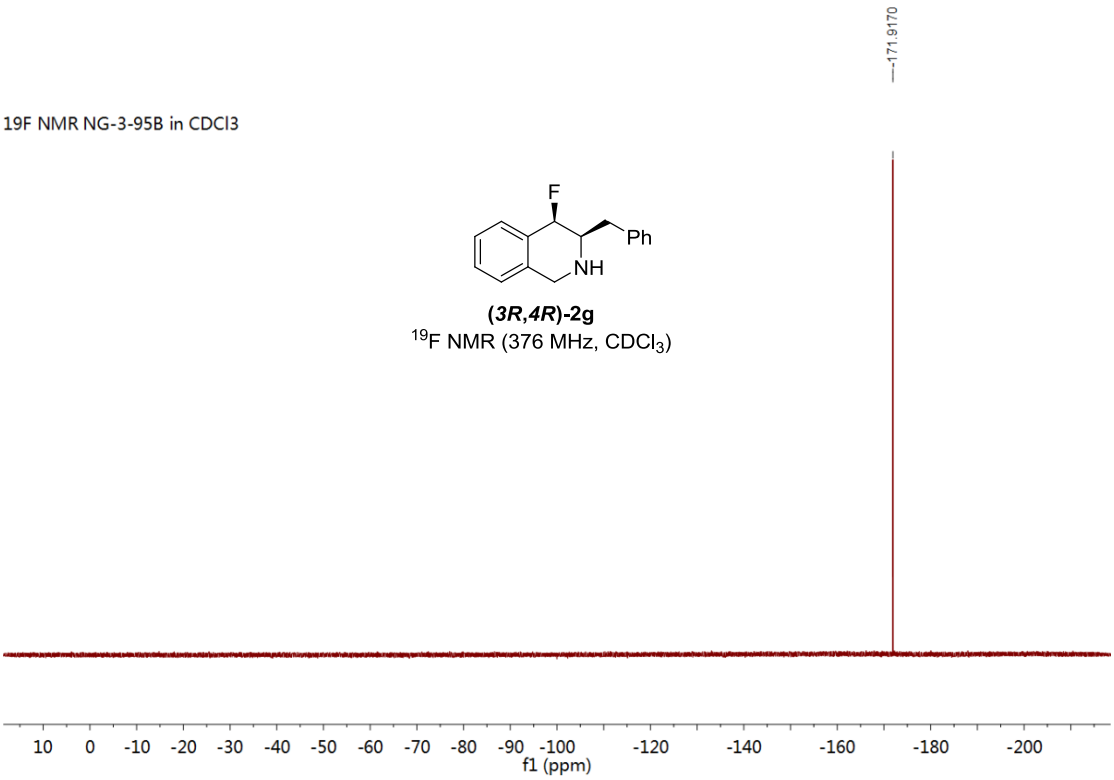


13C NMR NG-3-95B in CDCl3

(*3R,4R*)-2g

^{13}C NMR (100 MHz, $CDCl_3$)

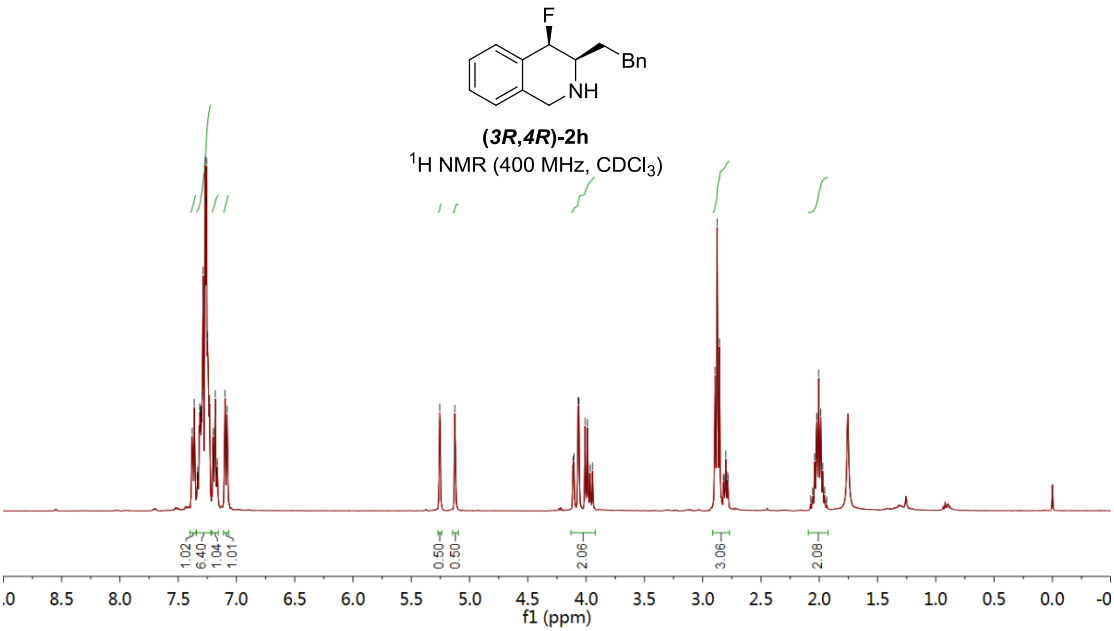
19F NMR NG-3-95B in CDCl3



(*3R*,*4R*)-2g

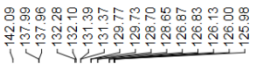
^{19}F NMR (376 MHz, $CDCl_3$)

1H NMR NG-3-74C in CDCl3

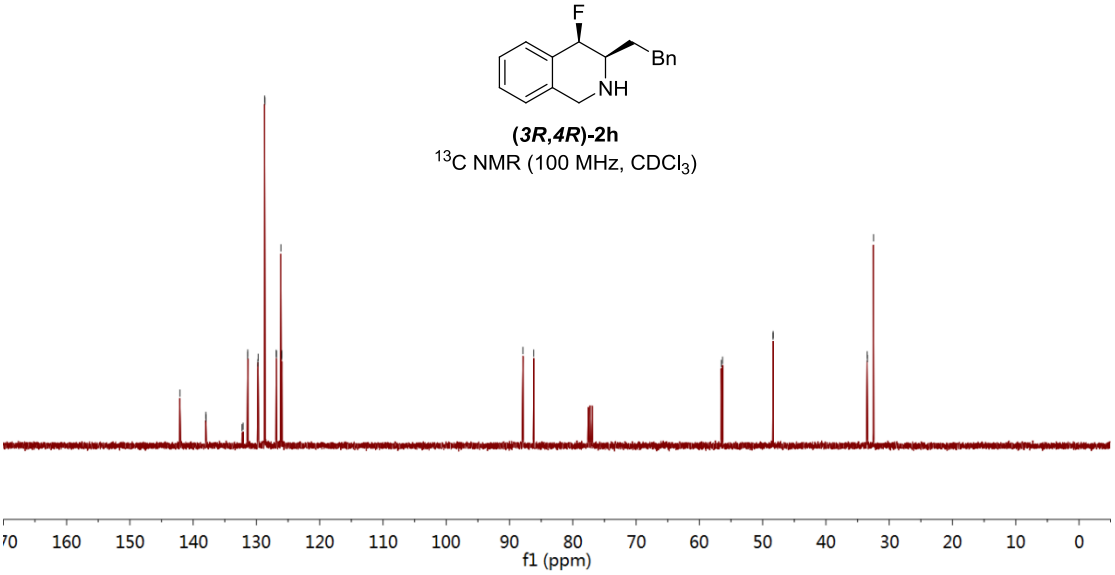


(*3R*,*4R*)-2h

^{1}H NMR (400 MHz, $CDCl_3$)



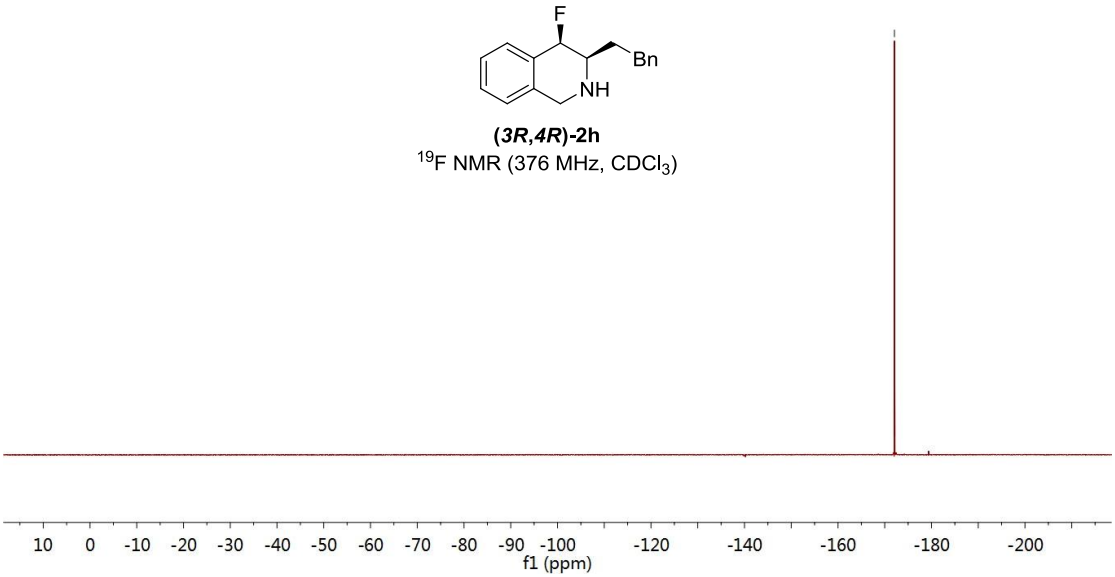
13C NMR NG-3-74C in CDCl3



(*3R*,*4R*)-2h

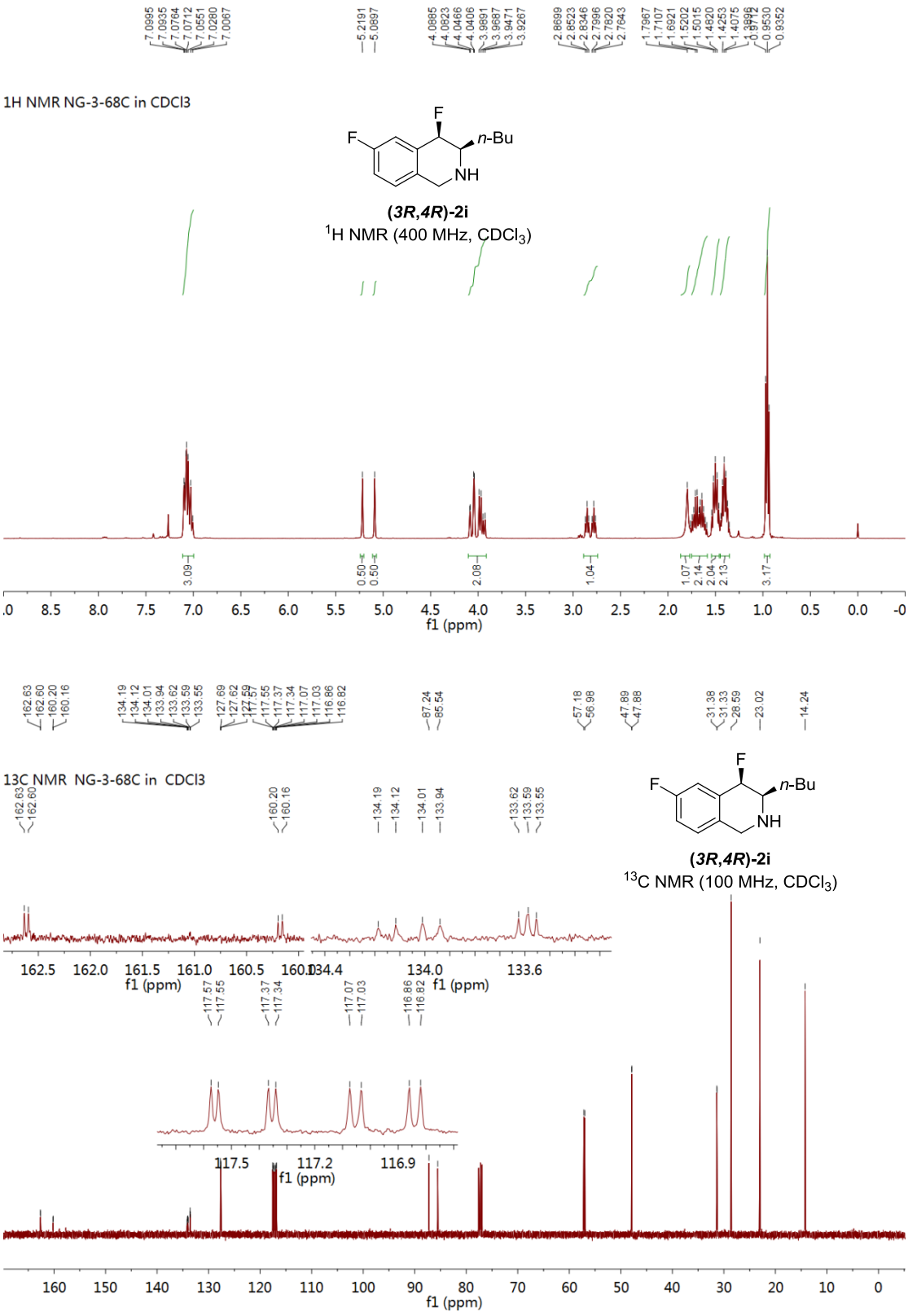
^{13}C NMR (100 MHz, $CDCl_3$)

19F NMR NG-3-74C in CDCl3

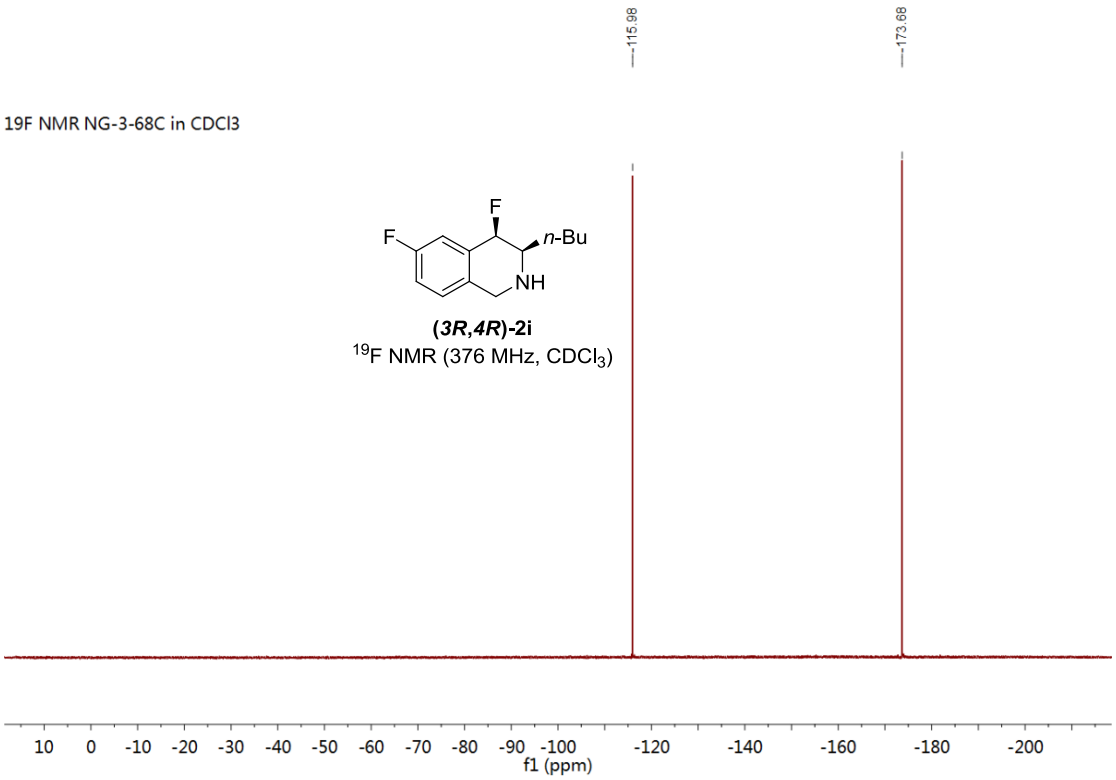


(*3R*,*4R*)-2h

^{19}F NMR (376 MHz, $CDCl_3$)


1H NMR NG-3-68C in CDCl3
F
F
n-Bu
NH
(3R,4R)-2i
1H NMR (400 MHz, CDCl3)
f1 (ppm)
13C NMR NG-3-68C in CDCl3
(3R,4R)-2i
13C NMR (100 MHz, CDCl3)
f1 (ppm)

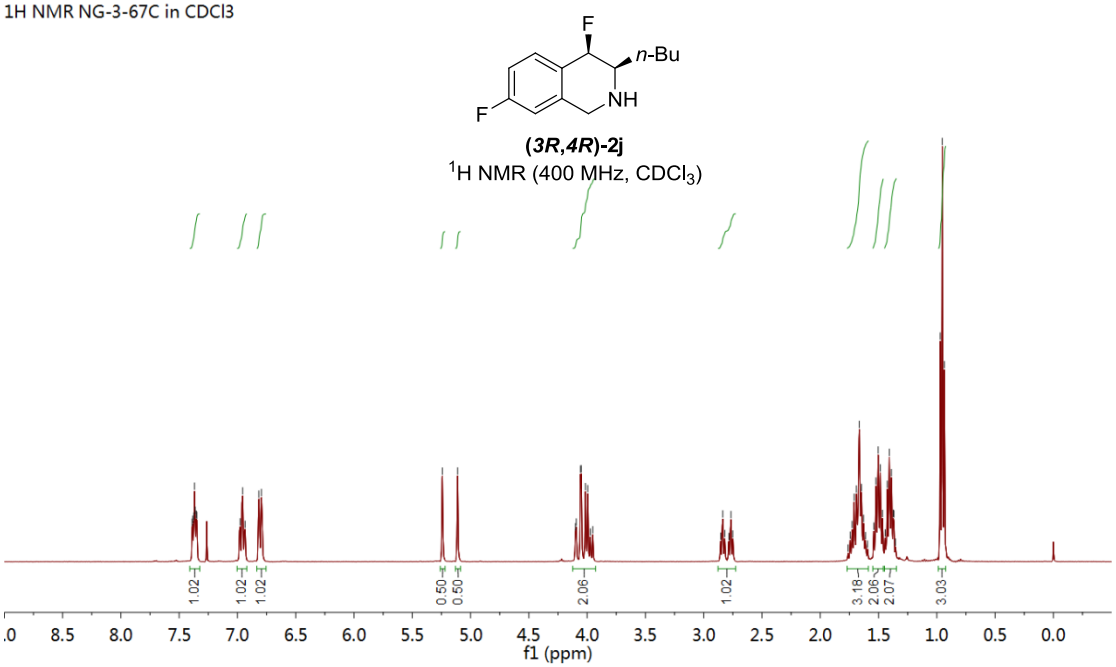
19F NMR NG-3-68C in CDCl3



(3*R*,4*R*)-2i

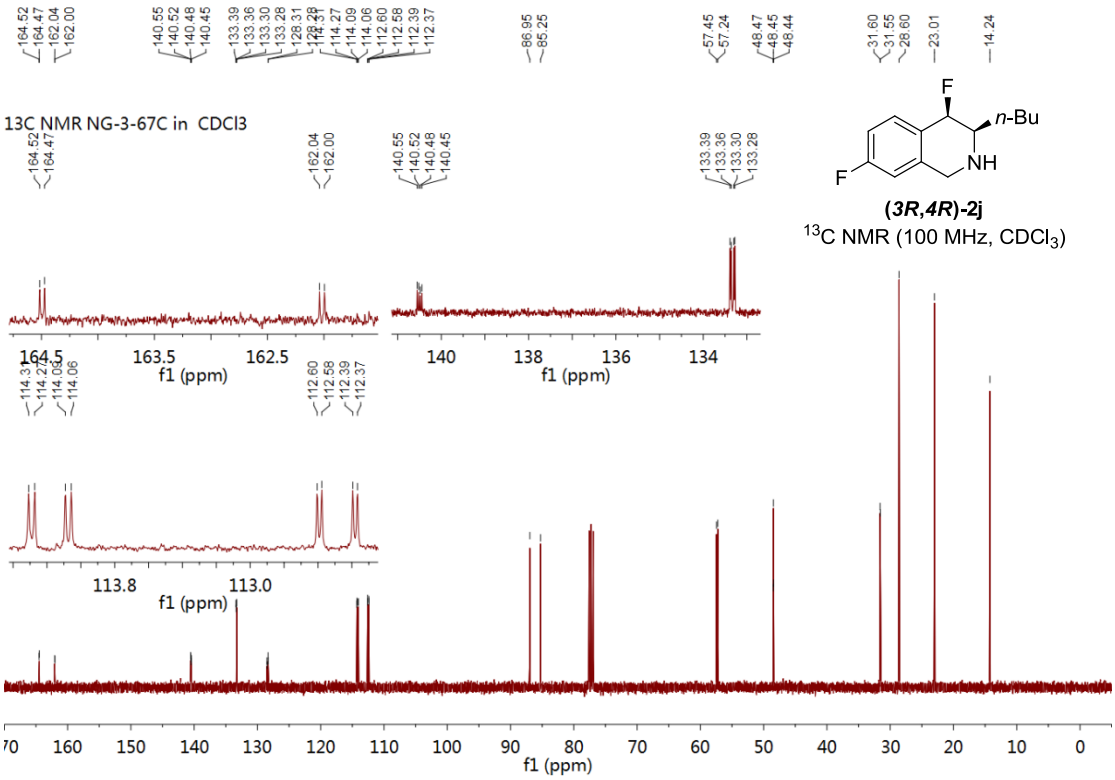
^{19}F NMR (376 MHz, $CDCl_3$)

1H NMR NG-3-67C in CDCl3



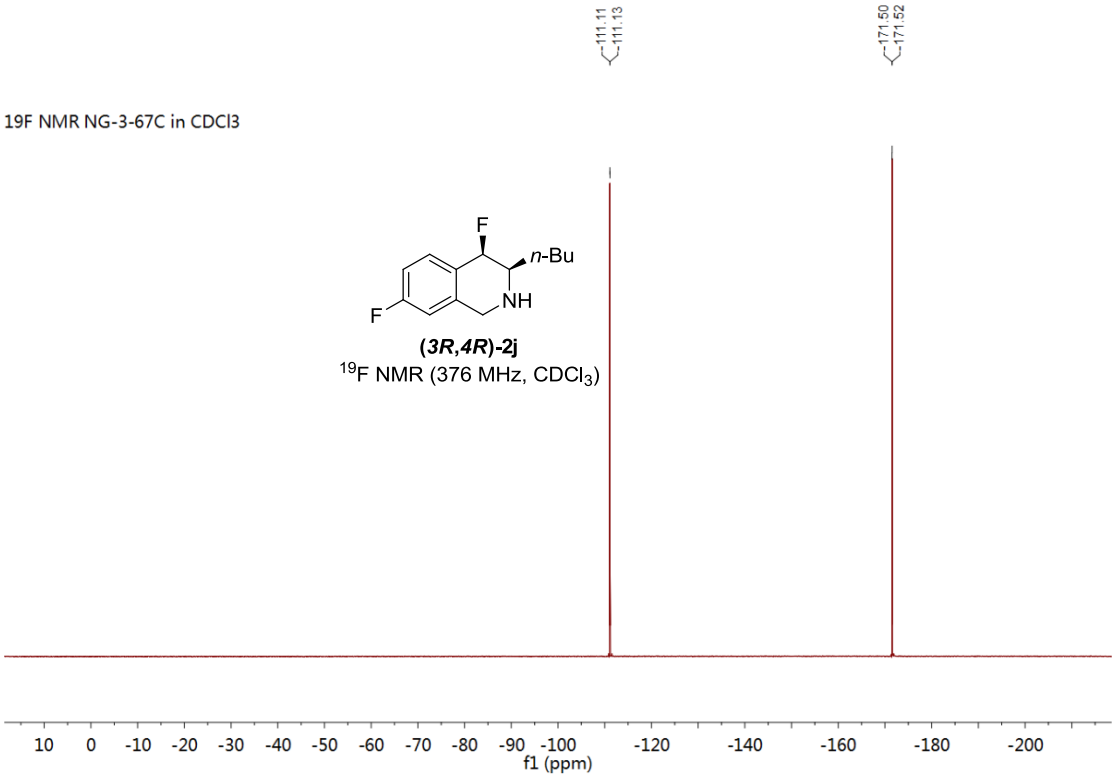
(3*R*,4*R*)-2j

^{1}H NMR (400 MHz, $CDCl_3$)



(*3R*,*4R*)-2j

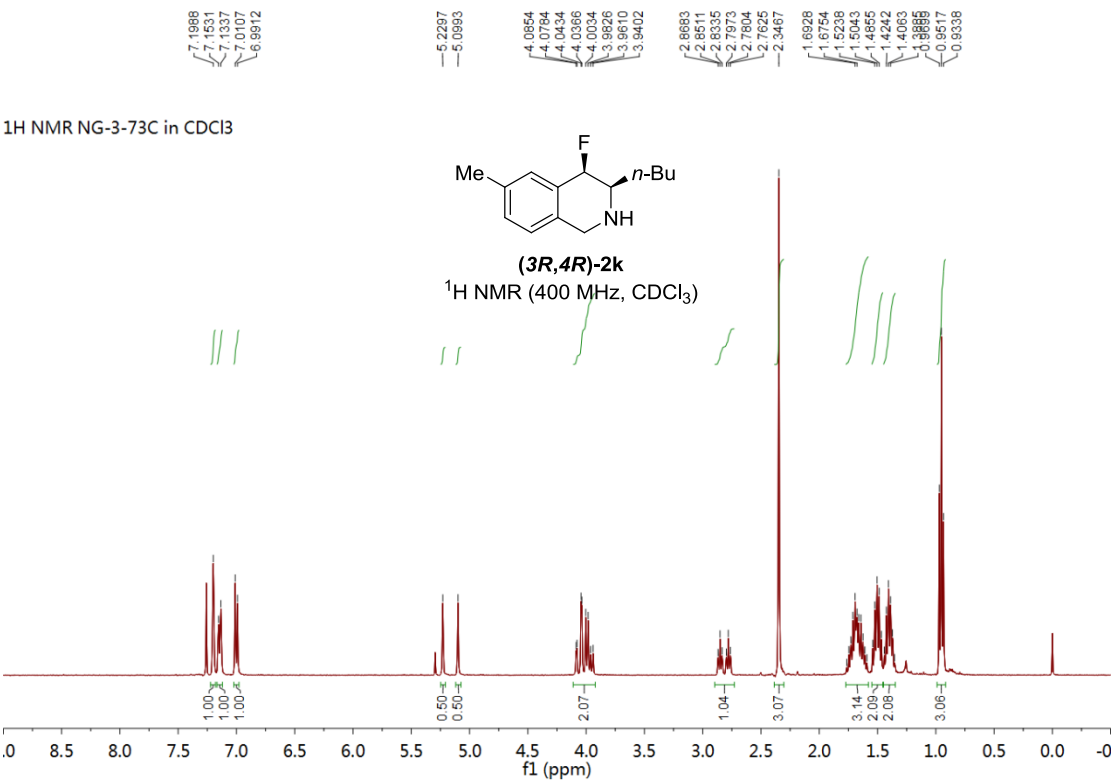
^{13}C NMR (100 MHz, $CDCl_3$)



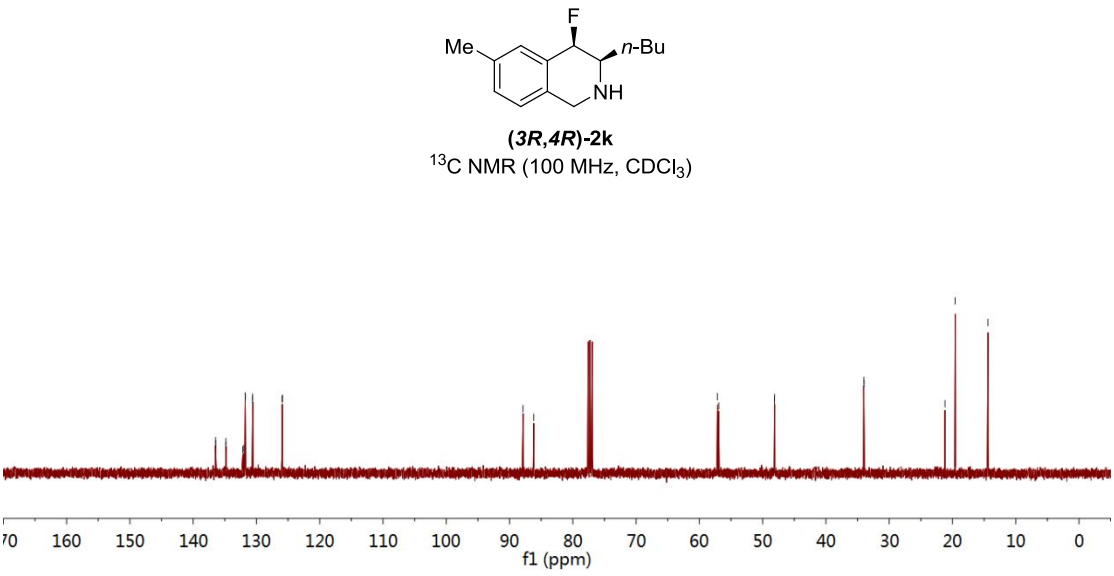
(*3R*,*4R*)-2j

^{19}F NMR (376 MHz, $CDCl_3$)

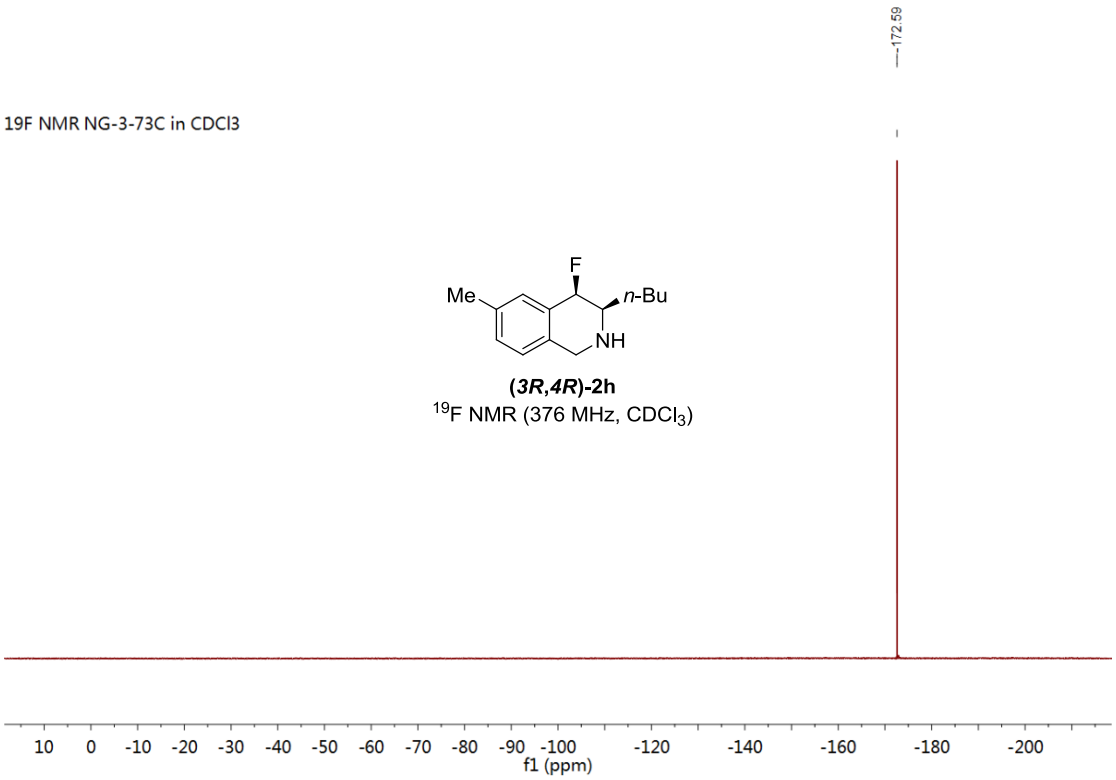
1H NMR NG-3-73C in CDCl3



13C NMR NG-3-89C in CDCl3



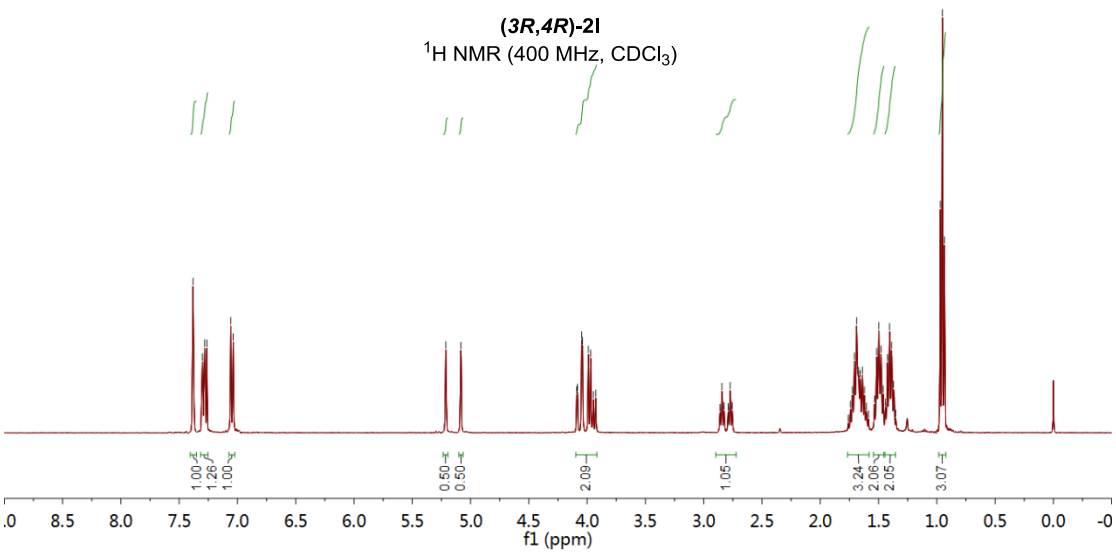
19F NMR NG-3-73C in CDCl3

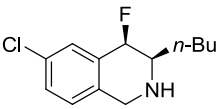


(*3R*,*4R*)-2h

^{19}F NMR (376 MHz, $CDCl_3$)

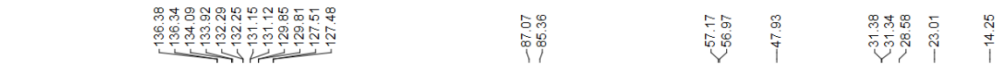
1H NMR NG-3-69C in CDCl3



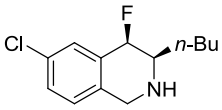


(*3R*,*4R*)-2l

^{1}H NMR (400 MHz, $CDCl_3$)

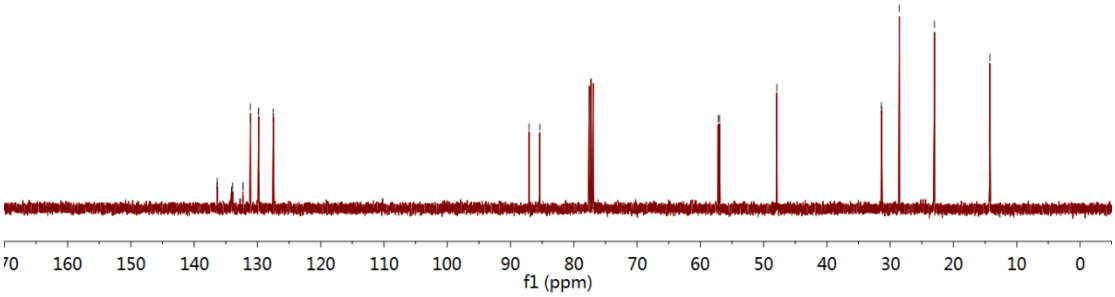


13C NMR NG-3-69C in CDCl3

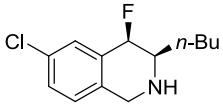


(*3R*,*4R*)-2l

^{13}C NMR (100 MHz, $CDCl_3$)

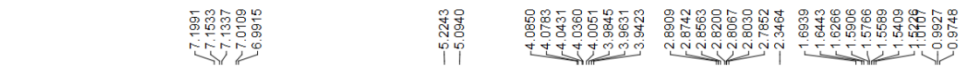


19F NMR NG-3-69C in CDCl3

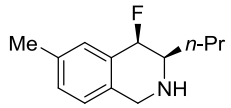


(*3R*,*4R*)-2l

^{19}F NMR (376 MHz, $CDCl_3$)

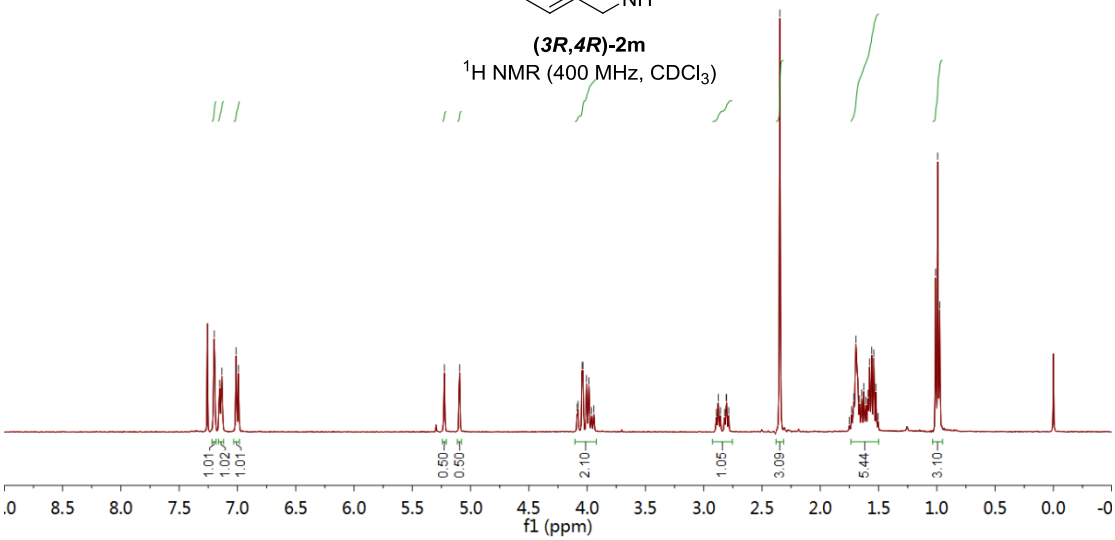


1H NMR NG-3-89C in CDCl3

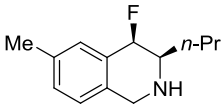


(*3R*,*4R*)-2m

^{1}H NMR (400 MHz, $CDCl_3$)

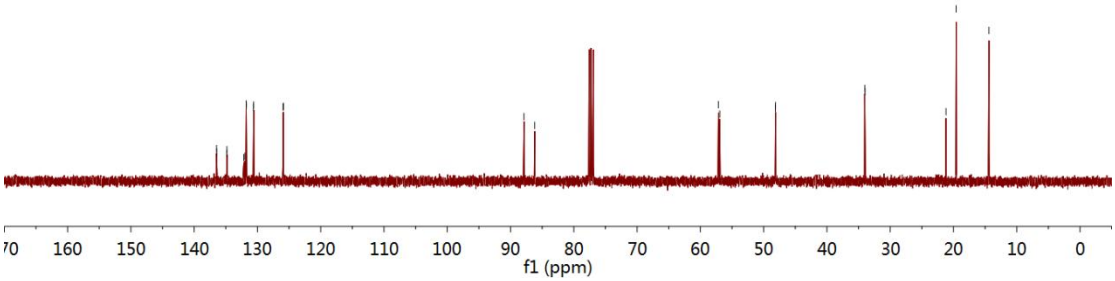


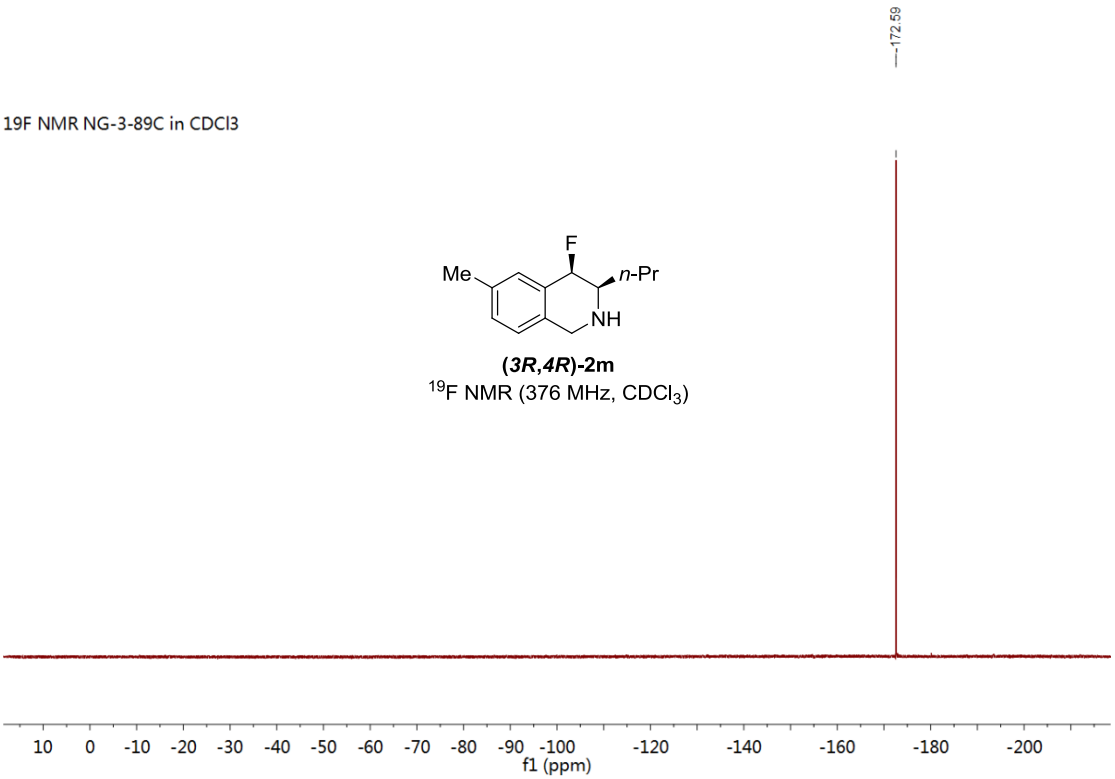
13C NMR NG-3-89C in DMSO



(*3R*,*4R*)-2m

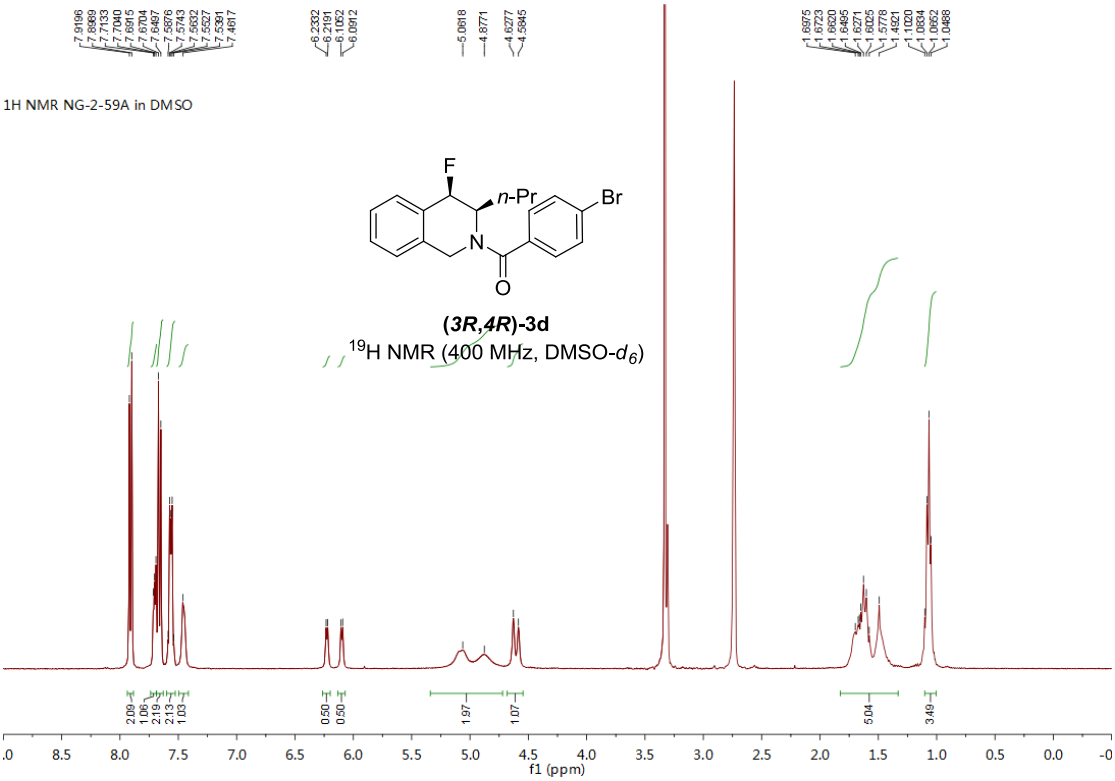
^{13}C NMR (100 MHz, $CDCl_3$)





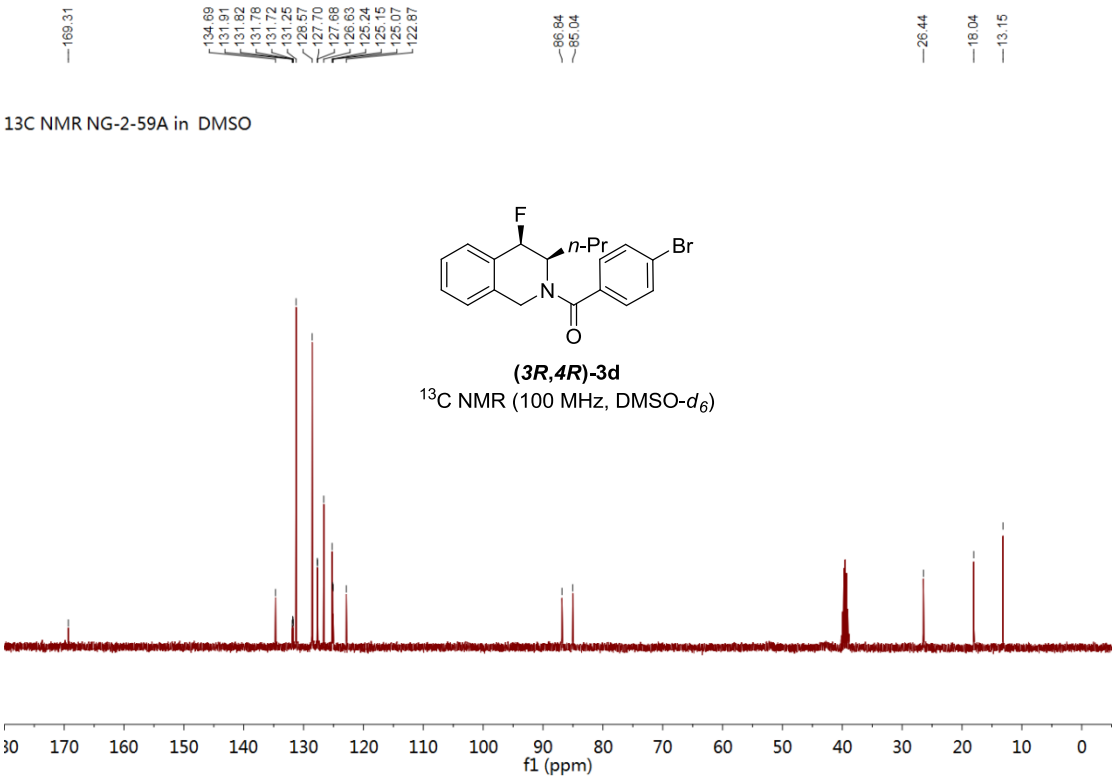
(*3R*,*4R*)-2m

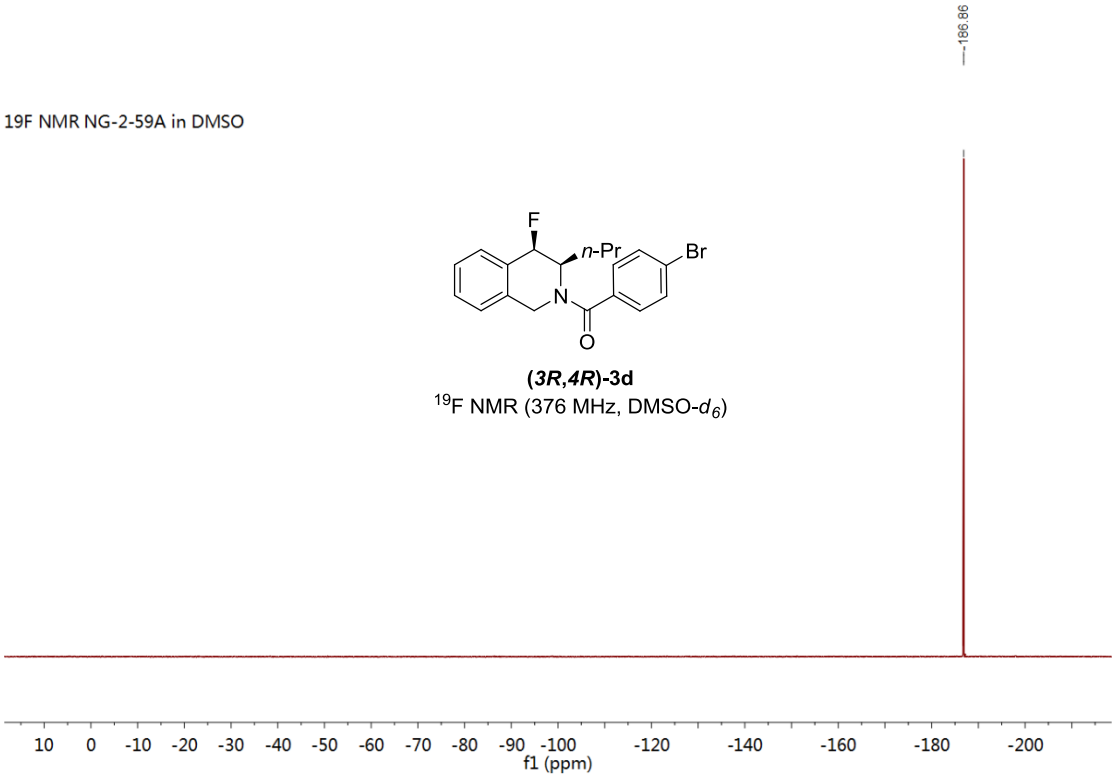
^{19}F NMR (376 MHz, $CDCl_3$)



(*3R*,*4R*)-3d

^{19}H NMR (400 MHz, DMSO-d_6)


169.31
134.69
131.91
131.82
131.78
131.72
131.25
128.57
127.70
127.68
126.63
125.24
125.15
125.07
122.87
86.84
85.04
26.44
18.04
13.15
13C NMR NG-2-59A in DMSO
F
n-Pr
Br
N
O
(3R,4R)-3d
13C NMR (100 MHz, DMSO-d6)
f1 (ppm)


186.86
19F NMR NG-2-59A in DMSO
F
n-Pr
Br
N
O
(3R,4R)-3d
19F NMR (376 MHz, DMSO-d6)
f1 (ppm)

Data File C:\HPCHEM\1\DATA\ZHOU-12\YZ003418.D Sample Name: NG-3-12B
OD-H, H/i-PrOH = 90/10, 0.8 mL/min, 30 oC, 254 nm

```
==========================================================================
Injection Date  : 14/11/2012 09:13:04
Sample Name     : NG-3-12B                      Location : Vial 1
Acq. Operator   : ZX
Acq. Method     : C:\HPCHEM\1\METHODS\SW.M
Last changed    : 14/11/2012 09:07:54  by ZX
                  (modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\SW.M
Last changed    : 13/01/2013 20:11:30  by ZHR
                  (modified after loading)
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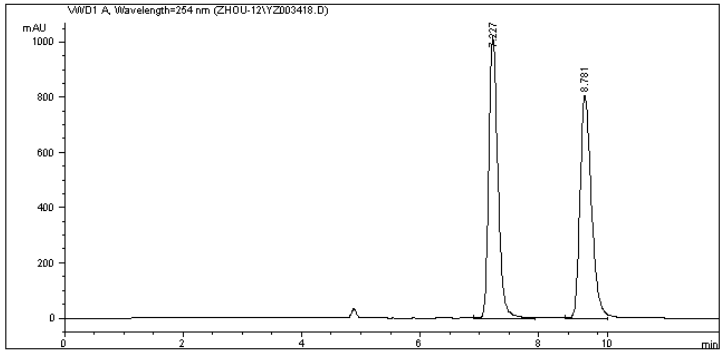


```
==========================================================================
                        Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000

Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|-------|
   1   7.227 VV    0.1645 1.08263e4  1020.63330  49.9854
   2   8.781 VV    0.2094 1.08326e4   805.13129  50.0146

Totals :                 2.16589e4  1825.76459

 Results obtained with enhanced integrator!
==========================================================================
                        *** End of Report ***
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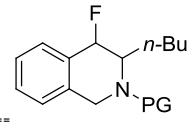

***cis*-(±)-3a**

PG = 4-Bromobenzoyl

Instrument 1 13/01/2013 20:21:01 ZHR Page 1 of 1

Data File C:\CHEM32\1\DATA\ZHOU-12\YZN002067.D
Sample Name: NG-3-37A

```
==========================================================================
Acq. Operator   : ZC
Acq. Instrument : Instrument 1                  Location : Vial 1
Injection Date  : 12/7/2012 3:35:51 PM
Acq. Method     : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 12/7/2012 3:30:57 PM by ZC
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 1/13/2013 8:12:53 PM by WH
                  (modified after loading)
Sample Info     : OD-H, H/i-PrOH = 90/10, 0.8 mL/min, 30 oC, 254nm
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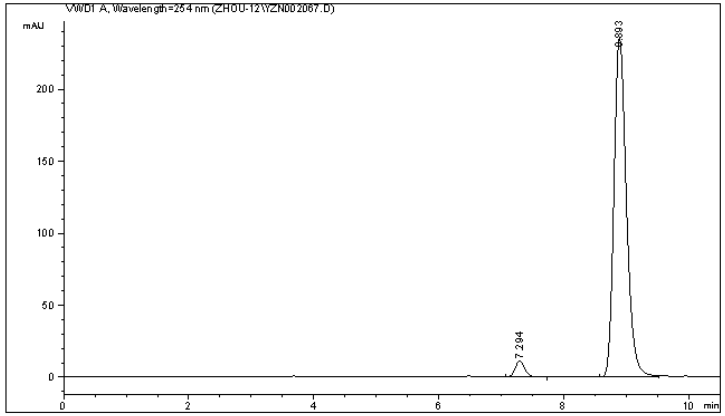


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==========================================================================
                        Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|-------|
   1   7.294 BB    0.1674  121.85497   11.09975   3.6103
   2   8.893 BB    0.2135 3253.32178  235.57579  96.3897

Totals :                 3375.17674  246.67554

==========================================================================
                        *** End of Report ***
```
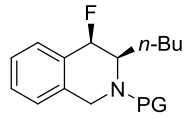



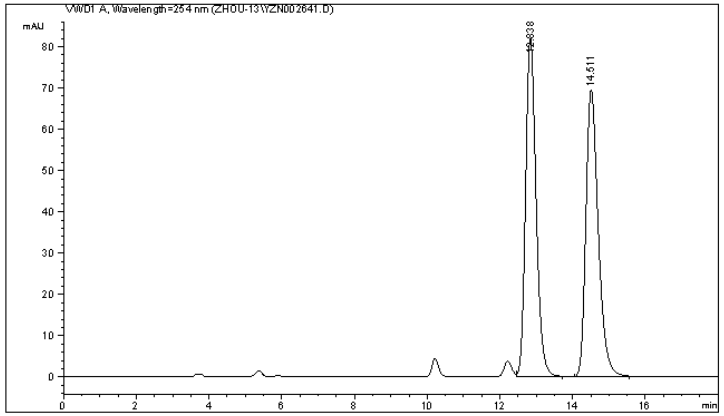
(*3R*,*4R*)-(-)-3a

PG = 4-Bromobenzoyl

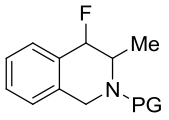
Instrument 1 1/13/2013 8:12:55 PM WH Page 1 of 1

Data File C:\CHEM32\1\DATA\ZHOU-13\YZN002641.D
Sample Name: NG-4-7+-

```
Acq. Operator   : WH
Acq. Instrument : Instrument 1                    Location : Vial 1
Injection Date  : 4/20/2013 3:54:21 PM
Acq. Method     : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 4/20/2013 2:30:38 PM by WH
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 4/21/2013 3:48:23 PM by WH
                  (modified after loading)
Sample Info     : OD-H, H/i-PrOH = 90/10, 0.8 mL/min, 30 oC, 254 nm
```




```
                        Area Percent Report

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]      [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  12.838 VB    0.3077 1640.09741   81.97593  50.0555
   2  14.511 BB    0.3609 1636.45886   69.42700  49.9445

Totals :                  3276.55627  151.40293

                        *** End of Report ***
```

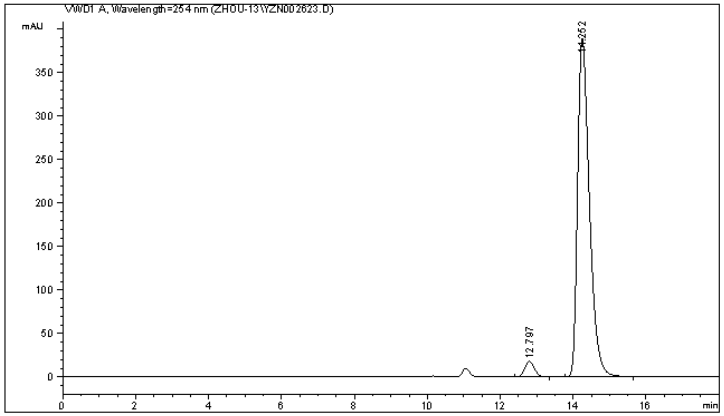


***cis*-(±)-3b**

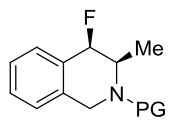
PG = 4-Bromobenzoyl

Data File C:\CHEM32\1\DATA\ZHOU-13\YZN002623.D
Sample Name: NG-4-7

```
Acq. Operator   : WH
Acq. Instrument : Instrument 1                    Location : Vial 1
Injection Date  : 4/16/2013 1:14:10 PM
Acq. Method     : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 4/16/2013 1:12:58 PM by WH
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 4/21/2013 3:48:23 PM by WH
                  (modified after loading)
Sample Info     : OD-H, H/i-PrOH = 90/10, 0.8 mL/min, 30 oC, 254 nm
```




```
                        Area Percent Report

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]      [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  12.797 VB    0.2882  330.77353   17.79214   3.6391
   2  14.252 BB    0.3437 8758.69629  389.77490  96.3609

Totals :                  9089.46982  407.56704

                        *** End of Report ***
```

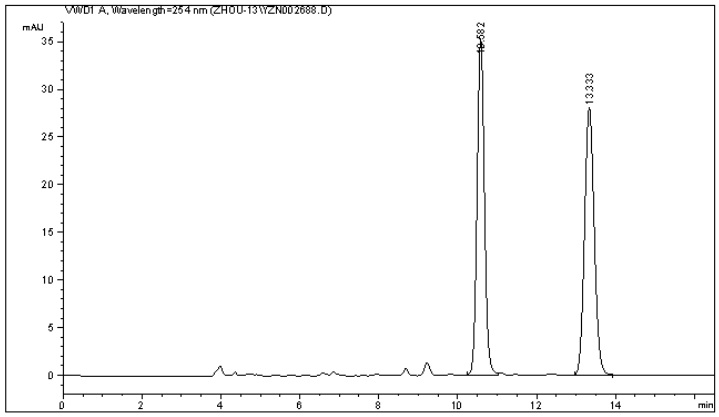


(*3R*,*4R*)-(-)-3b

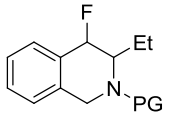
PG = 4-Bromobenzoyl

Data File C:\CHEM32\1\DATA\ZHOU-13\YZN002688.D
Sample Name: NG-4-8+-

```
==========================================================================
Acq. Operator   : WH
Acq. Instrument : Instrument 1                    Location : Vial 1
Injection Date  : 5/6/2013 10:48:12 AM
Acq. Method     : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 5/6/2013 10:23:47 AM by WH
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 5/6/2013 11:12:41 AM by WH
                  (modified after loading)
Sample Info     : IC-H, H/i-PrOH = 80/20, 0.8 mL/min, 30 oC, 254 nm
```




```
==========================================================================
                        Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|---------|---------|-------|
   1  10.582 BB    0.2003  455.74945   35.26851  48.7055
   2  13.333 BB    0.2651  479.97632   28.05778  51.2945

Totals :                  935.72577   63.32629

==========================================================================
                        *** End of Report ***
```

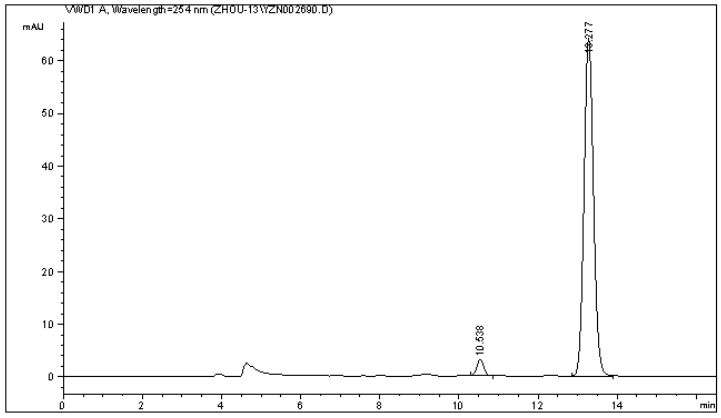


***cis*-(±)-3c**

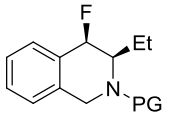
PG = 4-Bromobenzoyl

Data File C:\CHEM32\1\DATA\ZHOU-13\YZN002690.D
Sample Name: NG-4-8

```
==========================================================================
Acq. Operator   : WH
Acq. Instrument : Instrument 1                    Location : Vial 1
Injection Date  : 5/6/2013 11:35:04 AM
Acq. Method     : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 5/6/2013 11:29:22 AM by WH
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 5/6/2013 11:12:41 AM by WH
                  (modified after loading)
Sample Info     : IC-H, H/i-PrOH = 80/20, 0.8 mL/min, 30 oC, 254 nm
```




```
==========================================================================
                        Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|---------|---------|-------|
   1  10.538 BB    0.1919   37.56007    3.04561   3.4023
   2  13.277 BB    0.2583 1066.41125   64.04317  96.5977

Totals :                  1103.97132   67.08878

==========================================================================
                        *** End of Report ***
```

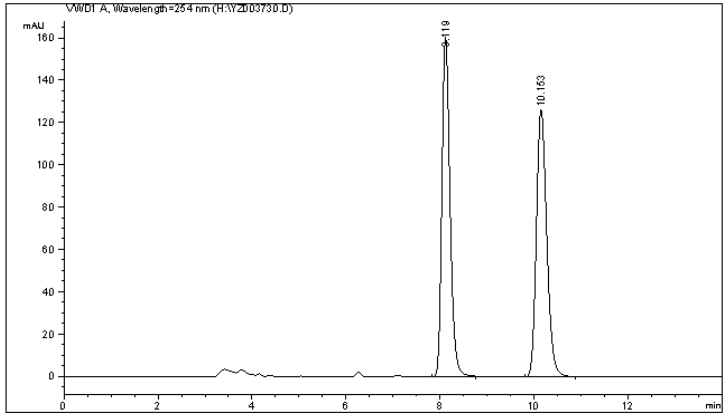


(*3R*,*4R*)-(-)-3c

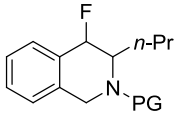
PG = 4-Bromobenzoyl

Data File H:\YZ003730.D
Sample Name: NG-2-59B

```
Acq. Operator   : WH
Acq. Instrument : Instrument 1                    Location : Vial 1
Injection Date  : 1/15/2013 3:21:45 AM
Acq. Method     : C:\HPCHEM\1\METHODS\SW.M
Last changed    : 1/15/2013 3:19:14 AM by WH
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 5/2/2013 9:48:56 AM by WH
                  (modified after loading)
Sample Info     : OD-H, H/i-PrOH = 90/10, 0.8 mL/min, 30 oC, 254 nm
```




```
                        Area Percent Report

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]      [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|-------|
   1   8.119 BB    0.1853 1926.42432  160.39708  49.8410
   2  10.153 BB    0.2373 1938.71204  126.33086  50.1590

Totals :                  3865.13635  286.72794

                        *** End of Report ***
```

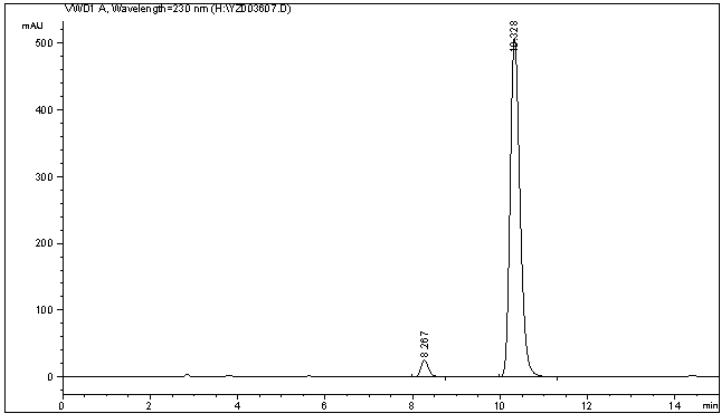


***cis*-(±)-3d**

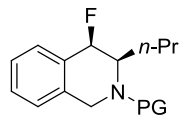
PG = 4-Bromobenzoyl

Data File H:\YZ003607.D
Sample Name: NG-3-48D

```
Acq. Operator   : ZX
Acq. Instrument : Instrument 1                    Location : Vial 1
Injection Date  : 12/23/2012 2:50:11 AM
Acq. Method     : C:\HPCHEM\1\METHODS\SW.M
Last changed    : 12/23/2012 2:48:57 AM by ZX
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 5/2/2013 9:40:44 AM by WH
                  (modified after loading)
Sample Info     : OD-H, H/i-PrOH = 90/10, 0.8 mL/min, 30 oC, 254 nm
```




```
                        Area Percent Report

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]      [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|-------|
   1   8.267 VB    0.1960  324.07059   25.30988   3.9137
   2  10.328 BB    0.2424 7956.32080  508.07111  96.0863

Totals :                  8280.39139  533.38099

                        *** End of Report ***
```

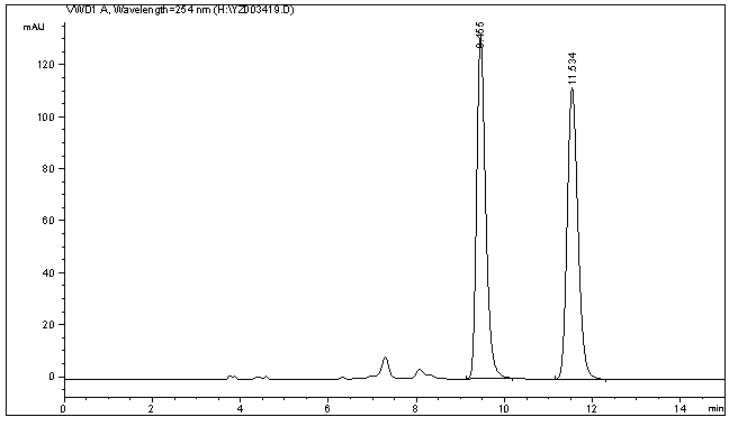


(*3R*,*4R*)-(-)-3d

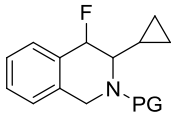
PG = 4-Bromobenzoyl

Data File H:\YZ003419.D
Sample Name: NG-3-12D

```
==================================================================
Acq. Operator   : ZX
Acq. Instrument : Instrument 1                  Location : Vial 1
Injection Date  : 11/15/2012 1:26:32 AM
Acq. Method     : C:\HPCHEM\1\METHODS\SW.M
Last changed    : 11/15/2012 1:23:55 AM by ZX
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 5/2/2013 9:27:48 AM by WH
                  (modified after loading)
Sample Info     : OD-H, H/i-PrOH = 90/10, 0.8 mL/min, 30 oC, 254 nm
```




```
==================================================================
                      Area Percent Report
==================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|---------|---------|-------|
   1   9.455 BB    0.2197 1874.51123  130.69537  49.6595
   2  11.534 BB    0.2621 1900.21362  111.94729  50.3405

Totals :                  3774.72485  242.64266

==================================================================
                      *** End of Report ***
```

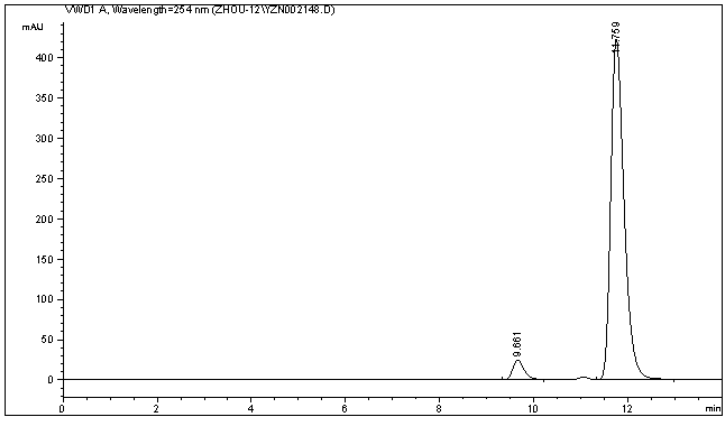


***cis*-(±)-3e**

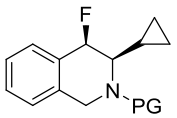
PG = 4-Bromobenzoyl

Data File C:\CHEM32\1\DATA\ZHOU-12\YZN002148.D
Sample Name: NG-3-41B

```
==================================================================
Acq. Operator   : ZC
Acq. Instrument : Instrument 1                  Location : Vial 1
Injection Date  : 12/18/2012 2:53:12 PM
Acq. Method     : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 12/18/2012 2:16:46 PM by ZC
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 1/13/2013 8:15:10 PM by WH
                  (modified after loading)
Sample Info     : OD-H, H/i-PrOH =90/10, 0.8 mL/min, 30 oC, 254 nm
```




```
==================================================================
                      Area Percent Report
==================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|---------|---------|-------|
   1   9.661 BB    0.2596  426.54144   24.88785   4.8966
   2  11.759 VB    0.2999 8284.37402  422.95459  95.1034

Totals :                  8710.91547  447.84244

==================================================================
                      *** End of Report ***
```

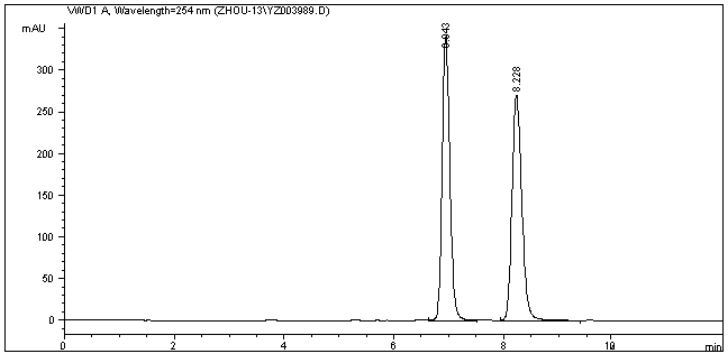


(*3R*,*4R*)-(-)-3e

PG = 4-Bromobenzoyl

Data File C:\HPCHEM\1\DATA\ZHOU-13\YZ003989.D Sample Name: NG-3-90+-
OD-H, H/i-PrOH = 90/10, 0.8 mL/min, 30 oC, 254 nm

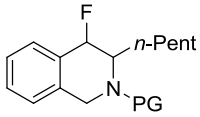
```
Injection Date  : 11/03/2013 22:24:25
Sample Name     : NG-3-90+-                    Location : Vial 1
Acq. Operator   : WH
Acq. Method     : C:\HPCHEM\1\METHODS\SW.M
Last changed    : 11/03/2013 22:22:38  by WH
                  (modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\SW.M
Last changed    : 11/03/2013 22:37:47  by WH
                  (modified after loading)
```



Area Percent Report

```
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000

Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|---------|-------|
   1   6.943 VB    0.1517 3316.77905  339.88205  49.9245
   2   8.228 BB    0.1904 3326.80908  269.83517  50.0755

Totals :                  6643.58813  609.71722

 Results obtained with enhanced integrator!
```

*** End of Report ***



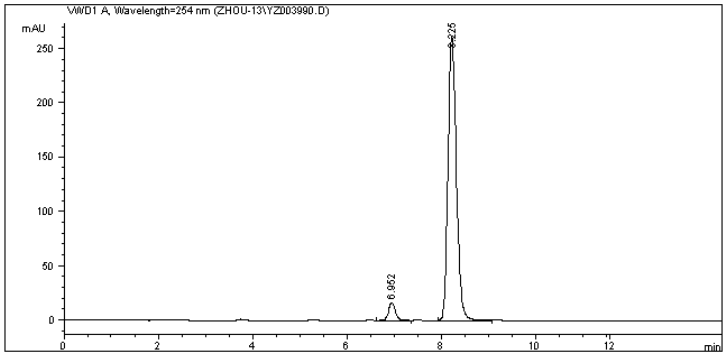
***cis*-(±)-3f**

PG = 4-Bromobenzoyl

Instrument 1 11/03/2013 22:40:59 WH Page 1 of 1

Data File C:\HPCHEM\1\DATA\ZHOU-13\YZ003990.D Sample Name: NG-3-90
OD-H, H/i-PrOH = 90/10, 0.8 mL/min, 30 oC, 254 nm

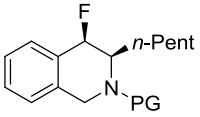
```
Injection Date  : 11/03/2013 22:40:32
Sample Name     : NG-3-90                      Location : Vial 1
Acq. Operator   : WH
Acq. Method     : C:\HPCHEM\1\METHODS\SW.M
Last changed    : 11/03/2013 22:38:29  by WH
                  (modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\SW.M
Last changed    : 11/03/2013 23:00:13  by WH
                  (modified after loading)
```



Area Percent Report

```
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000

Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|---------|-------|
   1   6.952 VV    0.1534  161.13788   16.26775   4.7892
   2   8.225 BB    0.1927 3203.49829  260.98846  95.2108

Totals :                  3364.63617  277.25621

 Results obtained with enhanced integrator!
```

*** End of Report ***



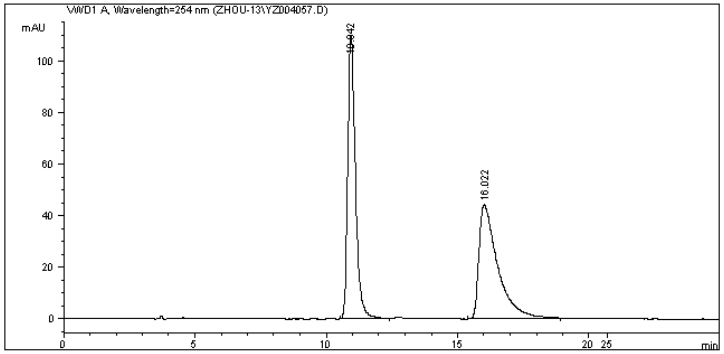
(*3R*,*4R*)-(-)-3f

PG = 4-Bromobenzoyl

Instrument 1 11/03/2013 23:00:49 WH Page 1 of 1

Data File C:\HPCHEM\1\DATA\ZHOU-13\YZ004057.D Sample Name: NG-3-95A
OD-H, H/i-PrOH = 90/10, 0.8 mL/min, 30 oC, 254 nm

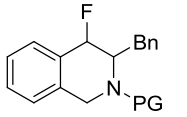
```
Injection Date  : 22/03/2013 17:07:03
Sample Name     : NG-3-95A                    Location : Vial 1
Acq. Operator   : WH
Acq. Method     : C:\HPCHEM\1\METHODS\SW.M
Last changed    : 22/03/2013 17:04:18  by WH
                  (modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\SW.M
Last changed    : 22/03/2013 21:17:52  by WH
                  (modified after loading)
```



Area Percent Report

```
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000

Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|---------|--------|
   1  10.942 BB    0.3110 2238.03955  109.61023  50.5418
   2  16.022 PB    0.7246 2190.06030   44.13142  49.4582

Totals :                  4428.09985  153.74165

 Results obtained with enhanced integrator!
```

*** End of Report ***



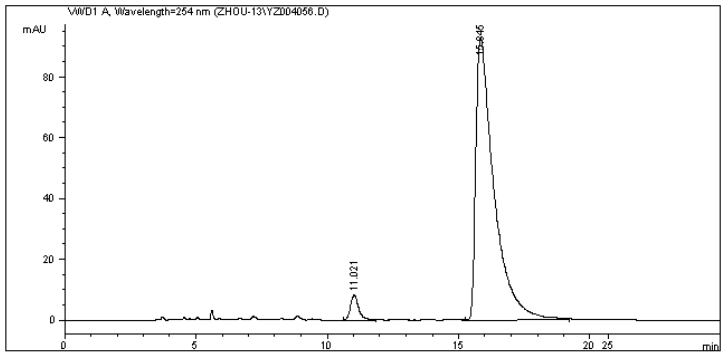
***cis*-(±)-3g**

PG = 4-Bromobenzoyl

Instrument 1 22/03/2013 21:17:55 WH Page 1 of 1

Data File C:\HPCHEM\1\DATA\ZHOU-13\YZ004056.D Sample Name: NG-3-95B
OD-H, H/i-PrOH = 90/10, 0.8 mL/min, 30 oC, 254 nm

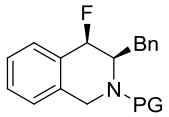
```
Injection Date  : 22/03/2013 16:27:25
Sample Name     : NG-3-95B                    Location : Vial 1
Acq. Operator   : WH
Acq. Method     : C:\HPCHEM\1\METHODS\SW.M
Last changed    : 22/03/2013 16:23:08  by WH
                  (modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\SW.M
Last changed    : 22/03/2013 21:17:56  by WH
                  (modified after loading)
```



Area Percent Report

```
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000

Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|---------|--------|
   1  11.021 BB    0.3212  173.21402    8.13551   3.7411
   2  15.845 VB    0.6916 4456.83936   92.75796  96.2589

Totals :                  4630.05338  100.89346

 Results obtained with enhanced integrator!
```

*** End of Report ***



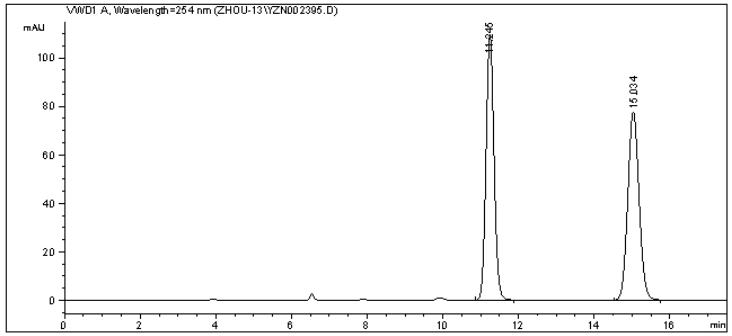
(*3R*,*4R*)-(-)-3g

PG = 4-Bromobenzoyl

Instrument 1 22/03/2013 21:18:59 WH Page 1 of 1

Data File C:\CHEM32\1\DATA\ZHOU-13\YZN002395.D
Sample Name: NG-3-74A

Acq. Operator	: WH
Acq. Instrument	: Instrument 1 Location : Vial 1
Injection Date	: 1/28/2013 10:19:24 PM
Acq. Method	: C:\CHEM32\1\METHODS\DEF LC.M
Last changed	: 1/28/2013 10:10:16 PM by WH (modified after loading)
Analysis Method	: C:\CHEM32\1\METHODS\DEF LC.M
Last changed	: 1/28/2013 11:15:18 PM by WH (modified after loading)
Sample Info	: IC-H, H/i-PrOH = 80/20, 0.8 mL/min, 30 oC, 254 nm



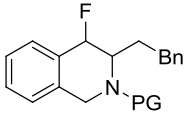
Area Percent Report

Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.245	BB	0.2283	1608.30042	109.36912	49.9648
2	15.034	BB	0.3218	1610.56885	77.73566	50.0352
Totals :				3218.86926	187.10478	

*** End of Report ***



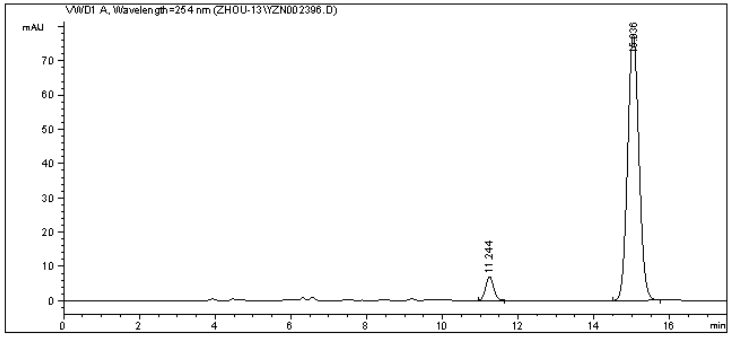
***cis*-(±)-3h**

PG = 4-Bromobenzoyl

Instrument 1 1/28/2013 11:16:43 PM WH Page 1 of 1

Data File C:\CHEM32\1\DATA\ZHOU-13\YZN002396.D
Sample Name: NG-3-74C

Acq. Operator	: WH
Acq. Instrument	: Instrument 1 Location : Vial 1
Injection Date	: 1/28/2013 10:55:05 PM
Acq. Method	: C:\CHEM32\1\METHODS\DEF LC.M
Last changed	: 1/28/2013 10:44:45 PM by WH (modified after loading)
Analysis Method	: C:\CHEM32\1\METHODS\DEF LC.M
Last changed	: 1/28/2013 11:15:18 PM by WH (modified after loading)
Sample Info	: IC-H, H/i-PrOH = 80/20, 0.8 mL/min, 30 oC, 254 nm



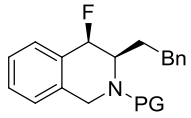
Area Percent Report

Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.244	BB	0.2290	101.29011	6.91893	5.9180
2	15.036	BB	0.3226	1610.25781	77.46608	94.0820
Totals :				1711.54792	84.38501	

*** End of Report ***



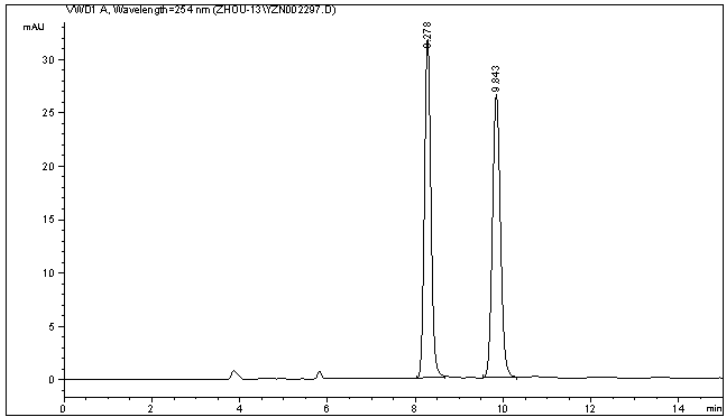
(*3R*,*4R*)-(-)-3h

PG = 4-Bromobenzoyl

Instrument 1 1/28/2013 11:15:23 PM WH Page 1 of 1

Data File C:\CHEM32\1\DATA\ZHOU-13\YZN002297.D
Sample Name: NG-3-68A

```
Acq. Operator   : WH
Acq. Instrument : Instrument 1                    Location : Vial 1
Injection Date  : 1/14/2013 7:15:05 PM
Acq. Method     : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 1/14/2013 6:54:45 PM by WH
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 1/14/2013 8:24:23 PM by WH
                  (modified after loading)
Sample Info     : IC-H, H/i-PrOH = 80/20, 0.8 mL/min, 30 oC, 254 nm
```



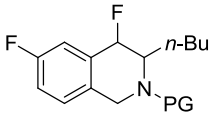
Area Percent Report

Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.278	BB	0.1581	327.08359	31.73967	49.1968
2	9.843	BB	0.1968	337.76309	26.48734	50.8032
Totals :				664.84668	58.22701	

*** End of Report ***



***cis*-(±)-3i**

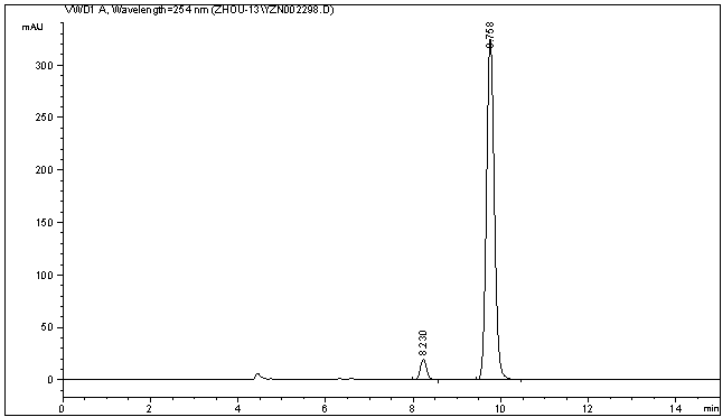
PG = 4-Bromobenzoyl

Instrument 1 1/14/2013 8:24:27 PM WH

Page 1 of 1

Data File C:\CHEM32\1\DATA\ZHOU-13\YZN002298.D
Sample Name: NG-3-68B

```
Acq. Operator   : WH
Acq. Instrument : Instrument 1                    Location : Vial 1
Injection Date  : 1/14/2013 7:42:24 PM
Acq. Method     : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 1/14/2013 7:38:50 PM by WH
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 1/14/2013 8:24:23 PM by WH
                  (modified after loading)
Sample Info     : IC-H, H/i-PrOH = 80/20, 0.8 mL/min, 30 oC, 254 nm
```



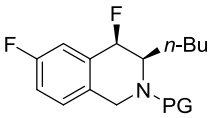
Area Percent Report

Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.230	VB	0.1561	197.85497	19.51814	4.6467
2	9.758	BB	0.1938	4060.07324	324.91684	95.3533
Totals :				4257.92821	344.43498	

*** End of Report ***



(*3R*,*4R*)-(-)-3i

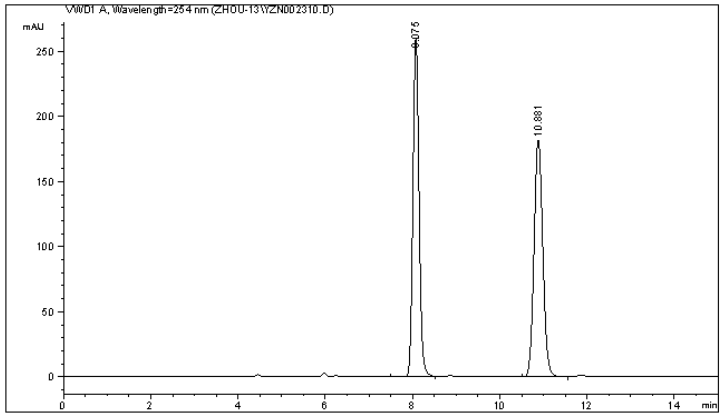
PG = 4-Bromobenzoyl

Instrument 1 1/14/2013 8:27:44 PM WH

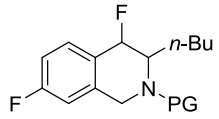
Page 1 of 1

Data File C:\CHEM32\1\DATA\ZHOU-13\YZN002310.D
Sample Name: NG-3-67A

```
Acq. Operator   : WH
Acq. Instrument : Instrument 1                    Location : Vial 1
Injection Date  : 1/16/2013 10:36:44 AM
Acq. Method     : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 1/16/2013 10:20:40 AM by WH
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 1/16/2013 10:58:50 AM by WH
                  (modified after loading)
Sample Info     : IC-H, H/i-PrOH = 80/20, 0.8 mL/min, 30 oC, 254 nm
```




```
                          Area Percent Report

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|---------|---------|-------|
   1   8.075 BV    0.1519 2538.66675  259.77432  49.9056
   2  10.881 VB    0.2171 2548.27051  182.17052  50.0944

Totals :                  5086.93726  441.94484
```



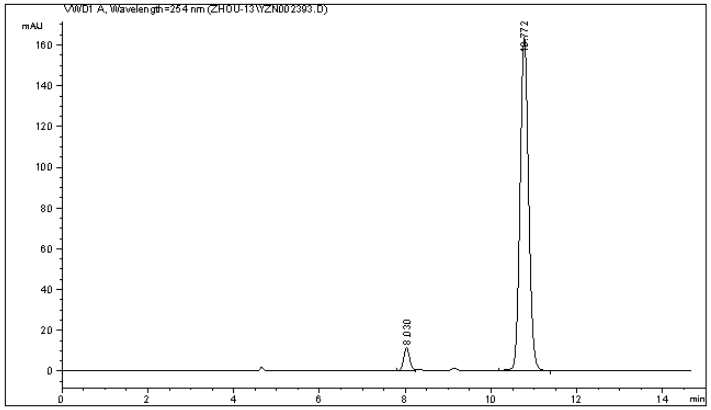
***cis*-(±)-3j**

PG = 4-Bromobenzoyl

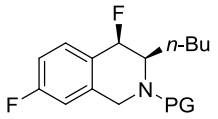
```
                          *** End of Report ***
```


Data File C:\CHEM32\1\DATA\ZHOU-13\YZN002393.D
Sample Name: NG-3-67C

```
Acq. Operator   : WH
Acq. Instrument : Instrument 1                    Location : Vial 1
Injection Date  : 1/28/2013 8:46:10 PM
Acq. Method     : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 1/28/2013 7:54:01 PM by WH
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 1/28/2013 9:02:52 PM by WH
                  (modified after loading)
Sample Info     : IC-H, H/i-PrOH = 80/20, 0.8 mL/min, 30 oC, 254 nm
```




```
                          Area Percent Report

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|---------|---------|-------|
   1   8.030 BV    0.1489  109.94628   11.40597   4.6267
   2  10.772 BB    0.2141 2266.39551  163.56224  95.3733

Totals :                  2376.34179  174.96821
```



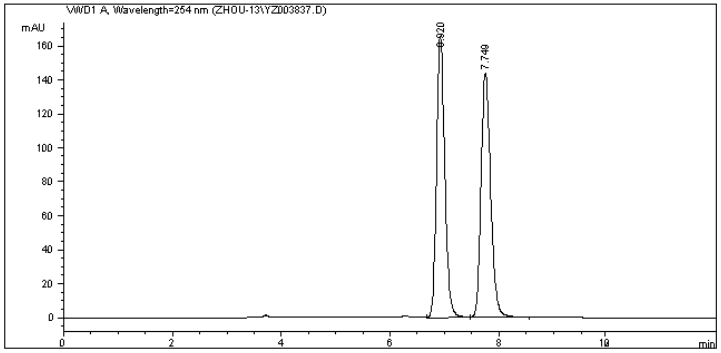
(*3R*,*4R*)-(-)-3j

PG = 4-Bromobenzoyl

```
                          *** End of Report ***
```

Data File C:\HPCHEM\1\DATA\ZHOU-13\YZ003837.D Sample Name: NG-3-73A+-
OD-H, H/i-PrOH = 90/10, 0.8 mL/min, 30 oC, 254 nm

```
Injection Date  : 23/01/2013 22:51:57
Sample Name     : NG-3-73A+-                    Location : Vial 1
Acq. Operator   : WH
Acq. Method     : C:\HPCHEM\1\METHODS\SW.M
Last changed    : 23/01/2013 22:22:35  by WH
                  (modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\SW.M
Last changed    : 24/01/2013 21:57:17  by WH
                  (modified after loading)
```



Area Percent Report

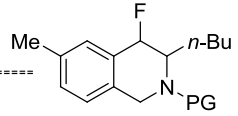
```
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
```

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.920	BV	0.1639	1746.07202	165.50052	49.8992
2	7.749	VB	0.1888	1753.12292	143.85197	50.1008
Totals :				3499.19495	309.35249	

Results obtained with enhanced integrator!

*** End of Report ***



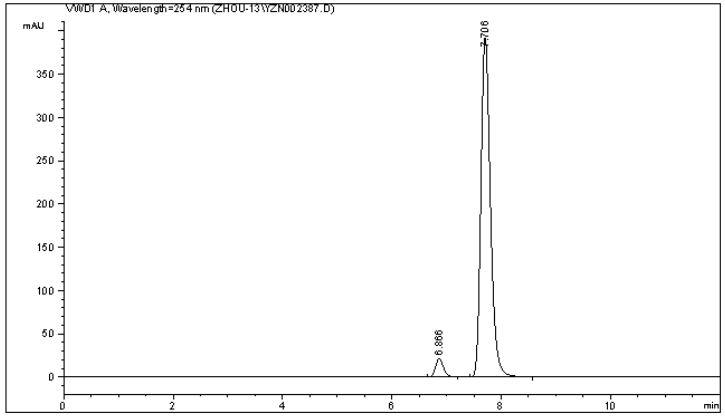
***cis*-(±)-3k**

PG = 4-Bromobenzoyl

Instrument 1 24/01/2013 21:57:20 WH Page 1 of 1

Data File C:\CHEM32\1\DATA\ZHOU-13\YZN002387.D
Sample Name: NG-3-73C

```
Acq. Operator   : WH
Acq. Instrument : Instrument 1                  Location : Vial 1
Injection Date  : 1/26/2013 4:39:17 PM
Acq. Method     : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 1/26/2013 4:37:44 PM by WH
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 1/26/2013 4:38:25 PM by WH
                  (modified after loading)
Sample Info     : OD-H, H/i-PrOH = 90/10, 0.8 mL/min, 30 oC, 254 nm
```



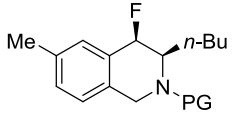
Area Percent Report

```
Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs
```

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.866	BB	0.1583	220.48718	21.35744	4.4492
2	7.706	BB	0.1861	4735.14355	391.98520	95.5508
Totals :				4955.63074	413.34263	

*** End of Report ***



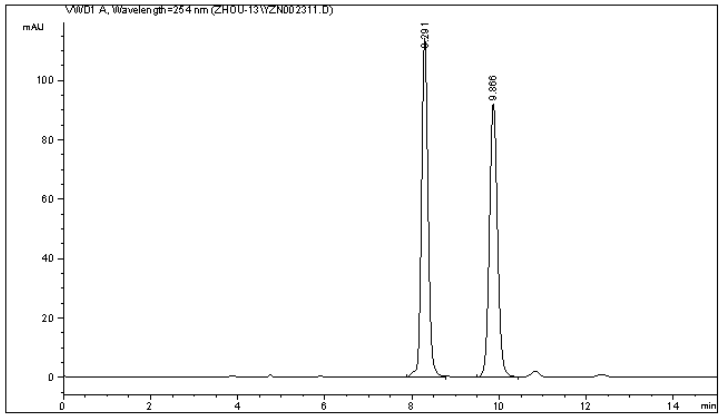
(*3R*,*4R*)-(-)-3k

PG = 4-Bromobenzoyl

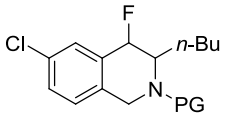
Instrument 1 1/26/2013 4:55:34 PM WH Page 1 of 1

Data File C:\CHEM32\1\DATA\ZHOU-13\YZN002311.D
Sample Name: NG-3-69A

```
    ======================================================================
    Acq. Operator   : WH
    Acq. Instrument : Instrument 1                  Location : Vial 1
    Injection Date  : 1/16/2013 10:53:57 AM
    Acq. Method     : C:\CHEM32\1\METHODS\DEF LC.M
    Last changed    : 1/16/2013 10:52:09 AM by WH
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\DEF LC.M
    Last changed    : 1/16/2013 10:58:50 AM by WH
                      (modified after loading)
    Sample Info     : IC-H, H/i-PrOH = 80/20, 0.8 mL/min, 30 oC, 254 nm
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier:                   :      1.0000
    Dilution:                     :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=254 nm

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]       [min]  mAU   *s   [mAU   ]      %
    ----|-------|----|-------|---------|---------|-------|
       1   8.291 BB    0.1615 1192.84119  113.88027  50.0457
       2   9.866 BB    0.1989 1190.66162   92.09605  49.9543

    Totals :                  2383.50281  205.97632

    ======================================================================
                               *** End of Report ***
```

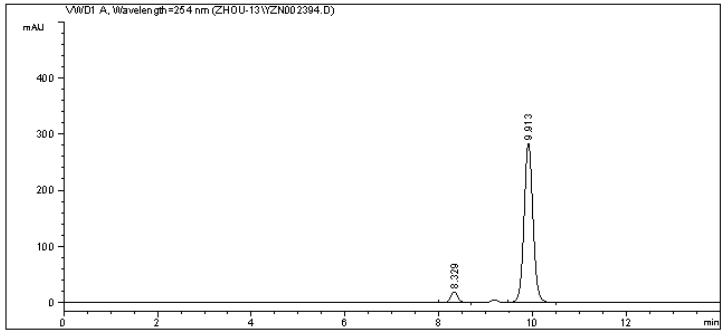


***cis*-(±)-3l**

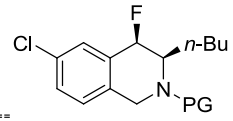
PG = 4-Bromobenzoyl

Data File C:\CHEM32\1\DATA\ZHOU-13\YZN002394.D
Sample Name: NG-3-69C

```
    ======================================================================
    Acq. Operator   : WH
    Acq. Instrument : Instrument 1                  Location : Vial 1
    Injection Date  : 1/28/2013 9:47:37 PM
    Acq. Method     : C:\CHEM32\1\METHODS\DEF LC.M
    Last changed    : 1/28/2013 9:00:54 PM by WH
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\METHODS\DEF LC.M
    Last changed    : 1/28/2013 10:18:19 PM by WH
                      (modified after loading)
    Sample Info     : IC-H, H/i-PrOH = 80/20, 0.8 mL/min, 30 oC, 254 nm

    ======================================================================
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier:                   :      1.0000
    Dilution:                     :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=254 nm

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]       [min]  mAU   *s   [mAU   ]      %
    ----|-------|----|-------|---------|---------|-------|
       1   8.329 BB    0.1622  198.26138   18.82419   5.0200
       2   9.913 BB    0.2037 3751.20581  283.86139  94.9800

    Totals :                  3949.46719  302.68558

    ======================================================================
                               *** End of Report ***
```

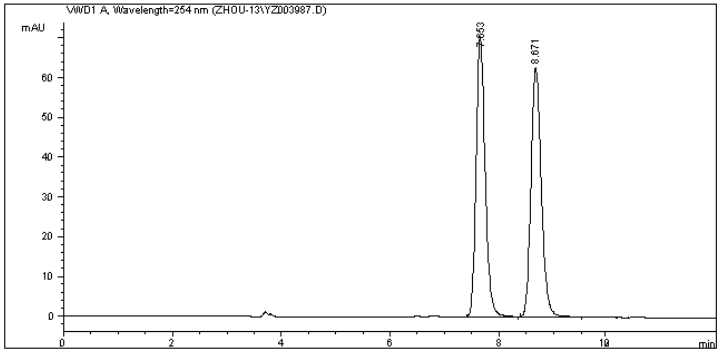


(*3R*,*4R*)-(-)-3l

PG = 4-Bromobenzoyl

Data File C:\HPCHEM\1\DATA\ZHOU-13\YZ003987.D Sample Name: NG-3-89+-
OD-H, H/i-PrOH = 90/10, 0.8 mL/min, 30 oC, 254 nm

```
Injection Date  : 11/03/2013 21:49:01
Sample Name     : NG-3-89+-                    Location : Vial 1
Acq. Operator   : WH
Acq. Method     : C:\HPCHEM\1\METHODS\SW.M
Last changed    : 11/03/2013 21:12:46  by WH
                  (modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\SW.M
Last changed    : 11/03/2013 22:36:57  by WH
                  (modified after loading)
```



Area Percent Report

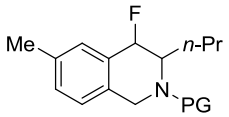
```
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
```

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.653	BB	0.1797	823.67267	70.65521	49.7751
2	8.671	BB	0.2042	831.11646	62.66108	50.2249
Totals :				1654.78912	133.31629	

Results obtained with enhanced integrator!

*** End of Report ***



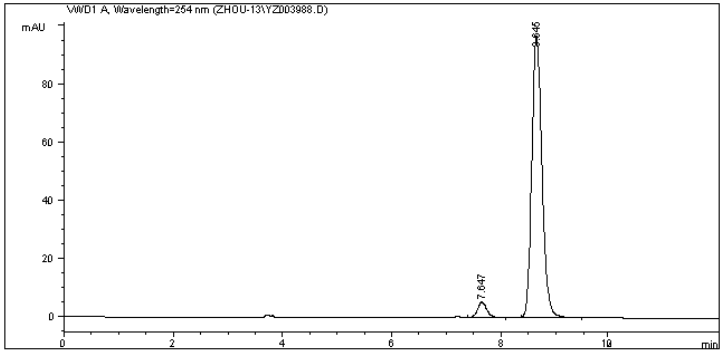
***cis*-(±)-3m**

PG = 4-Bromobenzoyl

Instrument 1 11/03/2013 22:36:59 WH Page 1 of 1

Data File C:\HPCHEM\1\DATA\ZHOU-13\YZ003988.D Sample Name: NG-3-89
OD-H, H/i-PrOH = 90/10, 0.8 mL/min, 30 oC, 254 nm

```
Injection Date  : 11/03/2013 22:06:19
Sample Name     : NG-3-89                      Location : Vial 1
Acq. Operator   : WH
Acq. Method     : C:\HPCHEM\1\METHODS\SW.M
Last changed    : 11/03/2013 22:04:18  by WH
                  (modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\SW.M
Last changed    : 11/03/2013 22:37:39  by WH
                  (modified after loading)
```



Area Percent Report

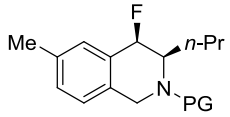
```
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
```

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.647	VB	0.1856	62.28733	5.22785	4.7179
2	8.645	BB	0.2011	1257.94385	96.80502	95.2821
Totals :				1320.23118	102.03288	

Results obtained with enhanced integrator!

*** End of Report ***



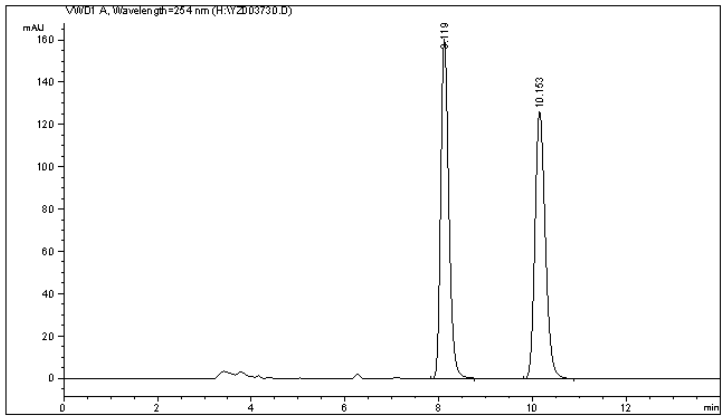
(*3R*,*4R*)-(-)-3m

PG = 4-Bromobenzoyl

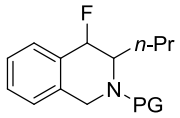
Instrument 1 11/03/2013 22:37:47 WH Page 1 of 1

Data File H:\YZ003730.D
Sample Name: NG-2-59B

```
==========================================================================
Acq. Operator   : WH
Acq. Instrument : Instrument 1                    Location : Vial 1
Injection Date  : 1/15/2013 3:21:45 AM
Acq. Method     : C:\HPCHEM\1\METHODS\SW.M
Last changed    : 1/15/2013 3:19:14 AM by WH
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\DEF LC.M
Last changed    : 5/2/2013 9:48:56 AM by WH
                  (modified after loading)
Sample Info     : OD-H, H/i-PrOH = 90/10, 0.8 mL/min, 30 oC, 254 nm
```




```
==========================================================================
                          Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|---------|---------|-------|
   1   8.119 BB    0.1853 1926.42432  160.39708  49.8410
   2  10.153 BB    0.2373 1938.71204  126.33086  50.1590

Totals :                  3865.13635  286.72794

==========================================================================
                          *** End of Report ***
```

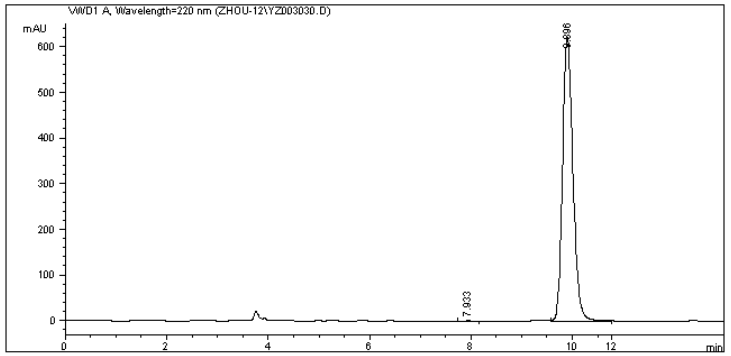


***cis*-(±)-3d**

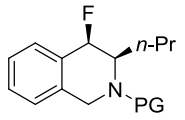
PG = 4-Bromobenzoyl

Data File C:\HPCHEM\1\DATA\ZHOU-12\YZ003030.D
Sample Name: NG-2-59A3
OD-H, H/i-PrOH = 90/10, 0.8 mL/min, 30 oC, 220 nm

```
==========================================================================
Injection Date  : 30/08/2012 21:04:24
Sample Name     : NG-2-59A3                       Location : Vial 1
Acq. Operator   : ZX
Acq. Method     : C:\HPCHEM\1\METHODS\SW.M
Last changed    : 30/08/2012 20:32:02  by ZX
                  (modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\SW.M
Last changed    : 13/01/2013 20:31:08  by ZHR
                  (modified after loading)
==========================================================================
```




```
==========================================================================
                          Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000


Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|---------|---------|-------|
   1   7.933 VV    0.2623    8.47553 4.64741e-1   0.0951
   2   9.896 VV    0.2223 8902.21484  622.07227  99.9049

Totals :                  8910.69037  622.53701

 Results obtained with enhanced integrator!
==========================================================================
                          *** End of Report ***
```



(*3R*,*4R*)-(-)-3d
after recrystallization

PG = 4-Bromobenzoyl