Electronic Supplementary Information

One-pot C(sp^3)-H difluoroalkylation of tetrahydroisoquinolines and isochromans via electrochemical oxidation and organozinc alkylation

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1. General information

All melting points were measured with Yanako MP-J3 and uncorrected. IR spectra were obtained with Shimadzu IRAffinity-1, and absorptions were reported in cm^{-1}. ^{1}H NMR, ^{13}C NMR, and ^{19}F NMR spectra were recorded with Varian NMR System 500PS SN and JEOL JNM-ECZ400R (500 or 400 MHz for ^{1}H NMR, 125 MHz for ^{13}C NMR, 376 MHz for ^{19}F NMR). Chemical shift values are expressed in parts per million relative to internal TMS (δ 0.00 for ^{1}H NMR) or $CDCl_3$ (δ 77.0 for ^{13}C NMR). Abbreviations are as follow: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Mass spectra (MS) and high resolution mass spectra (HRMS) were recorded on JEOL JMS-T100TD (time-of-flight mass spectrometer) with direct analysis in real time (DART) method. Cyclic Voltammetry (CV) was performed with Gamry Reference 600. All reactions were carried out under an argon atmosphere unless otherwise noted.

Chemicals were purchased from Sigma-Aldrich, Tokyo Chemical Industry, FUJIFILM Wako Pure Chemicals, and Nacalai tesque and used as received unless otherwise noted. Dry DMSO, DMF, MeCN, and CH_2Cl_2 were bought from FUJIFILM Wako Pure Chemicals, and dry THF was purchased from Kanto Chemical. AcOEt was distilled and stored over 3Å molecular sieves. Toluene was distilled from sodium benzophenone ketyl under an argon atmosphere. CF_3CH_2OH and EtOH were dried over 3Å molecular sieves before use. Tetrahydroisoquinolines **1a-d**,[1] **1e**,[2] **1f-g**,[3] **1h-i**,[4] **1j**,[5] **1k**,[1] **1m**,[1] **1n**,[2] **1o**,[1] **1q**,[5] **1s**,[6] fluorinated reagents for the preparation of **2b**,[7] **2c**,[8] **2d-e**,[9] **2f**,[7] **2g**,[10] and isochromans **4c-d**[11], **4e**[12] were prepared as reported. The products were isolated by silica gel column chromatography with Fuji Silysia PSQ 60B and PSQ100B.

2. Experimental procedures and characterization data

2.1. Experimental setup for the electrochemical reaction

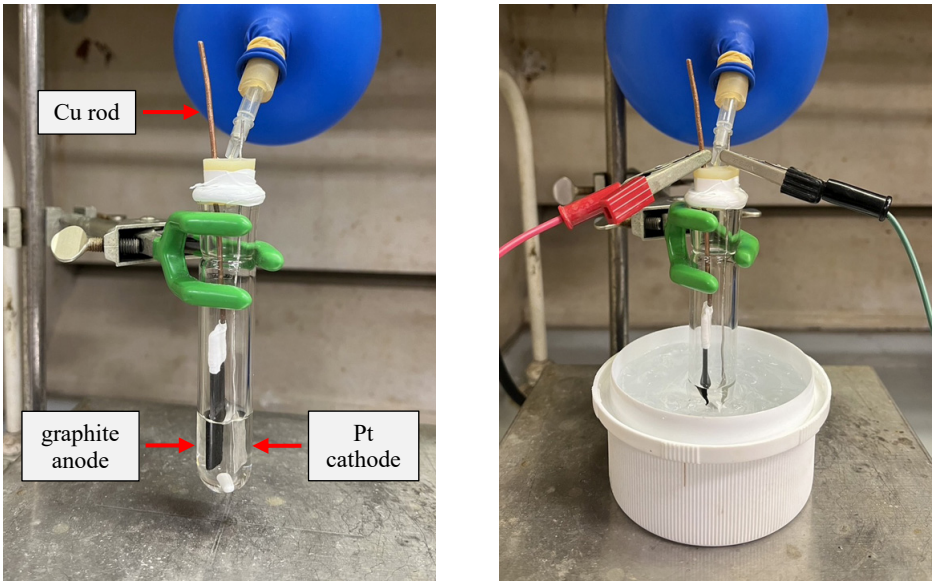


Figure S1. Experimental setup for a small-scale reaction

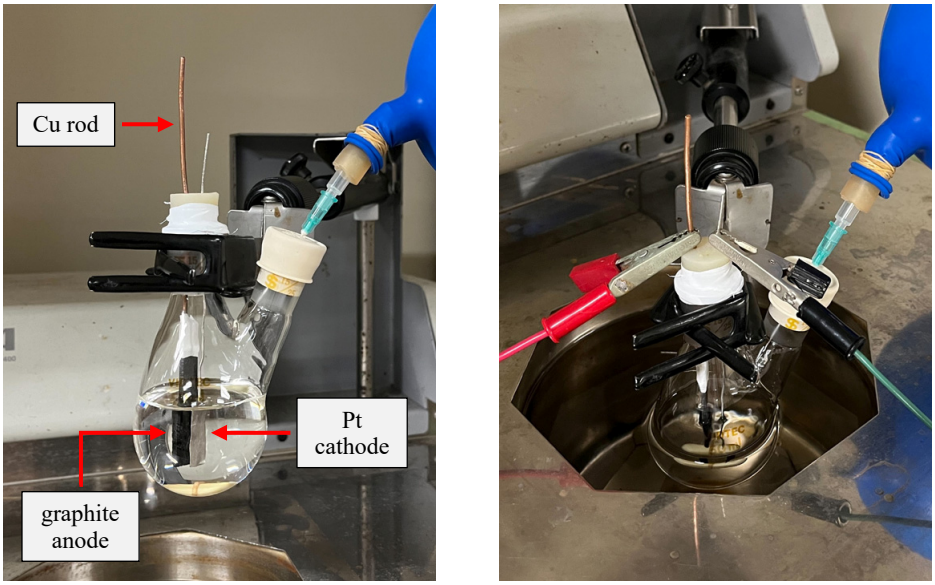


Figure S2. Experimental setup for a gram-scale reaction

2.2. MS analysis of the first step

The reaction was carried out in a cylinder-type undivided cell equipped with a graphite anode (1 x 5 cm^2) and a platinum cathode (1 x 2 cm^2) (distance between the anode and cathode: 1 cm). After the reaction vessel was charged with 2-phenyl-1,2,3,4-tetrahydroisoquinoline (**1a**) (104.6 mg, 0.5 mmol) and Et_4NBr (21.0 mg, 0.1 mmol), dry MeCN (4.0 mL) and CF_3CH_2OH (200.1 mg, 2.0 mmol) were added. Then, a constant current (5 mA, 2.7 F/mol) was supplied at 0 °C with magnetic stirring. After concentration of the reaction mixture, MS analysis was conducted. The detected data was consistent with that of 2-phenyl-1-(2,2,2-trifluoroethoxy)-1,2,3,4-tetrahydroisoquinoline, which could not be isolated by silica gel column chromatography because of its lability. MS (DART) *m/z*: 308 $[M+H]^+$.

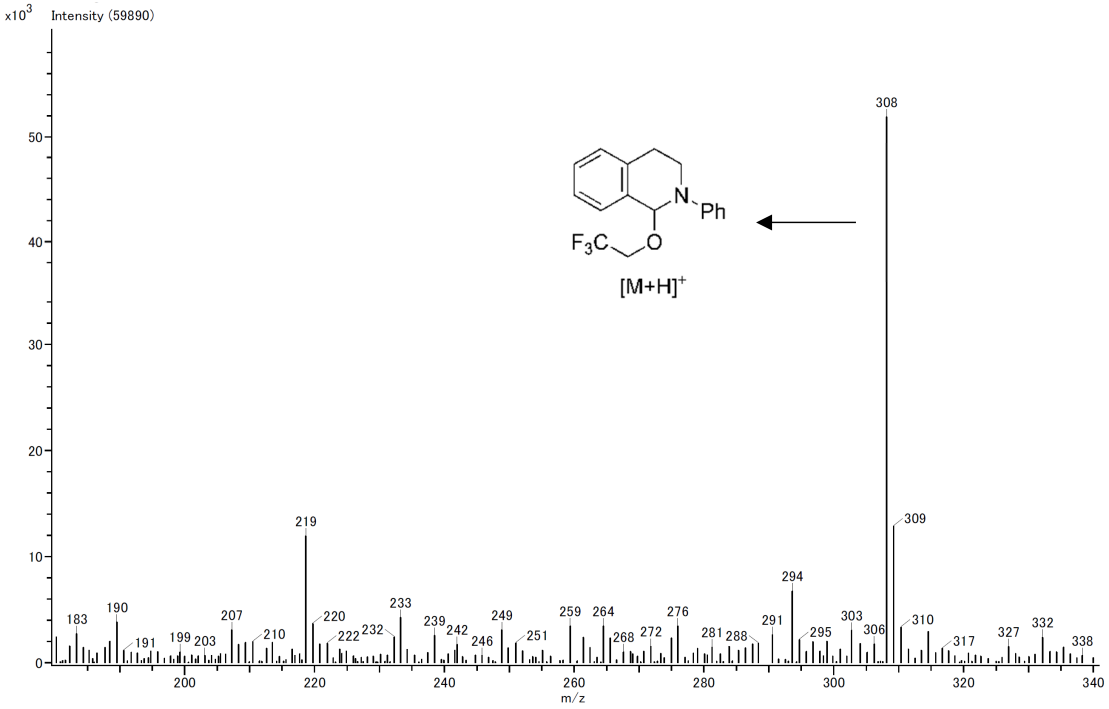


Figure S3. MS analysis of the first step

2.3. Cyclic voltammetry

A glassy carbon electrode (surface area: 0.0201 cm^2), an Au wire electrode, and a Ag/Ag^+ electrode ($AgNO_3$ (10 mM) and Et_4NBF_4 (0.1 M) in MeCN) were used as working, counter, and reference electrodes, respectively. To prevent any leakage of $AgNO_3$ into the sample solution, a double junction configuration was used in constructing the reference electrode. Cyclic voltammetry was performed at 50 mV/s under rt using samples (5 mM) in the electrolyte solution (Et_4NBF_4 (0.1 M) in MeCN). The redox potentials were calibrated with ferrocene as a standard.

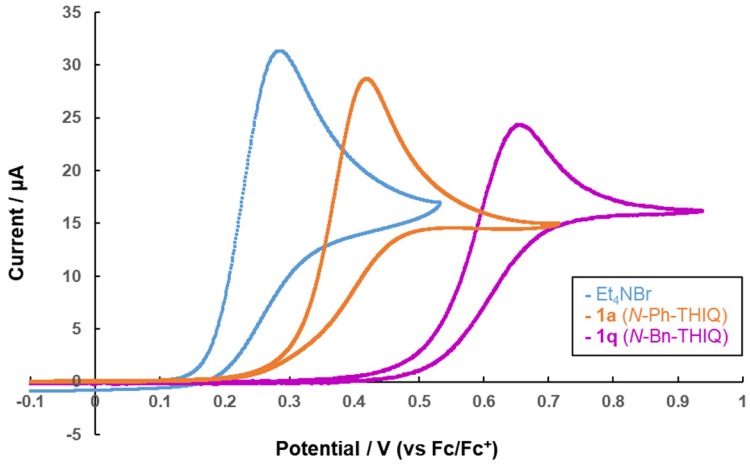
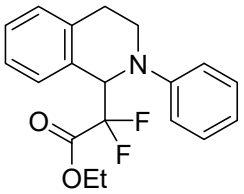


Figure S4. Cyclic voltammograms of Et_4NBr, **1a**, and **1q**

2.4. Typical procedure for the one-pot difluoroalkylation via electrochemical oxidation

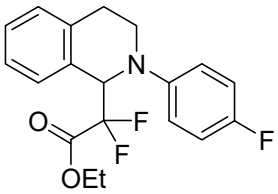
The reactions were carried out in a cylinder-type undivided cell equipped with a graphite anode (1 x 5 cm^2) and a platinum cathode (1 x 2 cm^2) (distance between the anode and cathode: 1 cm). After the reaction vessel was charged with 2-phenyl-1,2,3,4-tetrahydroisoquinoline (**1a**) (104.6 mg, 0.5 mmol) and Et_4NBr (21.0 mg, 0.1 mmol), dry MeCN (4.0 mL) and CF_3CH_2OH (200.1 mg, 2.0 mmol) were added. Then, a constant current (5 mA, 2.7 F/mol) was supplied at 0 °C with magnetic stirring. To the undivided cell was added the organozinc reagent (1.13 mL, 0.78 M in THF) prepared through stirring the mixture of Zn powder (118 mg, 1.8 mmol) and ethyl 2-bromo-2,2-difluoroacetate (406 mg, 2 mmol) in dry THF (2 mL) at rt for 5 min.[13] The reaction mixture was stirred at rt for 6 h. Water was added, and then the resulting mixture was extracted with AcOEt. The combined organic layers were dried over Na_2SO_4. Concentration and purification through silica gel column chromatography gave the desired product **3aa**.

Ethyl 2,2-difluoro-2-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate[14] (3aa)



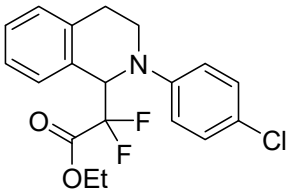
Silica gel column chromatography (hexane/AcOEt = 20/1) gave 133.6 mg (0.403 mmol, 81% yield) of the product as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 6.9 Hz, 1H), 7.29-7.26 (m, 1H), 7.24-7.20 (m, 3H), 7.16 (d, *J* = 7.3 Hz, 1H), 6.95 (d, *J* = 8.2 Hz, 2H), 6.85 (t, *J* = 7.3 Hz, 1H), 5.29 (dd, *J* = 19.7, 10.5 Hz, 1H), 4.26-4.10 (m, 2H), 3.73-3.80 (m, 1H), 3.67-3.64 (m, 1H), 3.00-2.91 (m, 1H), 2.73 (dt, *J* = 16.5, 3.7 Hz, 1H), 1.15 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.9 (dd, *J* = 34.3, 30.5 Hz, C), 149.3 (C), 136.6 (C), 129.15 (CH), 129.13 (CH), 128.5 (C), 128.3 (d, *J* = 4.8 Hz, CH), 128.2 (CH), 126.1 (CH), 120.1 (CH), 117.0 (CH), 116.6 (dd, *J* = 262.3, 258.5 Hz, C), 62.7 (CH_2), 60.7 (dd, *J* = 27.7, 22.9 Hz, CH), 43.4 (d, *J* = 4.8 Hz, CH_2), 25.0 (CH_2), 13.8 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -101.3 (ddd, *J* = 252.2, 10.1, 3.6 Hz, 1F), -111.4 (dd, *J* = 252.2, 19.5 Hz, 1F). IR (ATR): 1760, 1600, 1200, 1070, 740 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{19}H_{20}F_2NO_2$: 332.1462; found: 332.1466.

Ethyl 2,2-difluoro-2-(2-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (3ba)



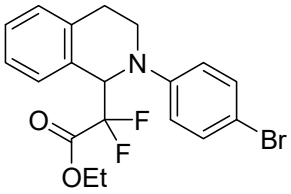
Silica gel column chromatography (hexane/AcOEt = 20/1) gave 134.3 mg (0.384 mmol, 77% yield) of the product as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41-7.39 (m, 1H), 7.31-7.23 (m, 2H), 7.17 (d, *J* = 7.3 Hz, 1H), 6.94-6.85 (m, 4H), 5.13 (dd, *J* = 20.1, 10.1 Hz, 1H), 4.28-4.16 (m, 2H), 3.78-3.71 (m, 1H), 3.54-3.51 (m, 1H), 2.93-2.85 (m, 1H), 2.68 (dt, *J* = 16.5, 3.7 Hz, 1H), 1.16 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.9 (dd, *J* = 29.6, 34.3 Hz, C), 157.5 (d, *J* = 239.4 Hz, C), 146.1 (C), 136.6 (C), 129.2 (CH), 128.32 (d, *J* = 5.7 Hz, CH), 128.27 (CH), 128.2 (C), 126.3 (CH), 119.5 (d, *J* = 7.6 Hz, CH), 116.5 (dd, *J* = 263.2, 258.5 Hz, C), 115.6 (d, *J* = 22.9 Hz, CH), 62.7 (CH_2), 61.1 (dd, *J* = 27.7, 23.8 Hz, CH), 44.7 (d, *J* = 5.7 Hz, CH_2), 24.6 (CH_2), 13.9 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -101.1 (ddd, *J* = 252.9, 10.1, 3.6 Hz, 1F), -112.6 (dd, *J* = 252.9, 20.2 Hz, 1F), -123.3 (s, 1F). IR (ATR): 1770, 1510, 1190, 1070, 750 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{19}H_{19}F_3NO_2$: 350.1368; found: 350.1355.

Ethyl 2-(2-(4-chlorophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-2,2-difluoroacetate (3ca)



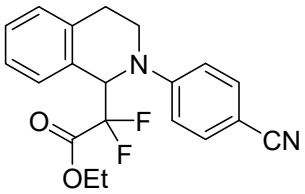
Silica gel column chromatography (hexane/AcOEt = 20/1) gave 144.1 mg (0.394 mmol, 79% yield) of the product as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 6.9 Hz, 1H), 7.31-7.27 (m, 1H), 7.25-7.22 (m, 1H), 7.19-7.16 (m, 3H), 6.87 (d, *J* = 9.2 Hz, 2H), 5.22 (dd, *J* = 18.8, 11.0 Hz, 1H), 4.28-4.13 (m, 2H), 3.80-3.72 (m, 1H), 3.62-3.56 (m, 1H), 2.97-2.89 (m, 1H), 2.76 (dt, *J* = 16.5, 4.1 Hz, 1H), 1.17 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.8 (dd, *J* = 33.4, 30.5 Hz, C), 147.9 (C), 136.4 (C), 129.1 (CH), 129.0 (CH), 128.4 (CH), 128.3 (d, *J* = 4.8 Hz, CH), 128.2 (C), 126.3 (CH), 125.0 (C), 118.0 (CH), 116.4 (dd, *J* = 263.2, 258.5 Hz, C), 62.8 (CH_2), 60.8 (dd, *J* = 27.7, 22.9 Hz, CH), 43.6 (d, *J* = 4.8 Hz, CH_2), 25.0 (CH_2), 13.8 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -101.9 (ddd, *J* = 252.9, 10.8, 2.9 Hz, 1F), -111.2 (dd, *J* = 252.9, 18.8 Hz, 1F). IR (ATR): 1760, 1490, 1210, 1110, 1060, 750 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{19}H_{19}{}^{35}ClF_2NO_2$: 366.1072; found: 366.1081.

Ethyl 2-(2-(4-bromophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-2,2-difluoroacetate (3da)



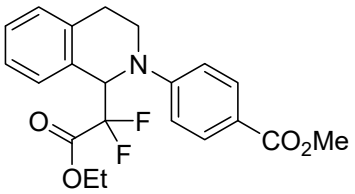
Silica gel column chromatography (hexane/AcOEt = 20/1) gave 150.5 mg (0.367 mmol, 73% yield) of the product as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (d, *J* = 7.1 Hz, 1H), 7.32-7.30 (m, 2H), 7.29-7.27 (m, 1H), 7.25-7.21 (m, 1H), 7.17 (d, *J* = 7.6 Hz, 1H), 6.83 (d, *J* = 8.9 Hz, 2H), 5.23 (dd, *J* = 18.5, 11.0 Hz, 1H), 4.28-4.12 (m, 2H), 3.79-3.72 (m, 1H), 3.62-3.56 (m, 1H), 2.98-2.90 (m, 1H), 2.77 (dt, *J* = 16.5, 4.1 Hz, 1H), 1.18 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.8 (dd, *J* = 33.4, 29.6 Hz, C), 148.3 (C), 136.4 (C), 132.0 (CH), 129.1 (CH), 128.4 (CH), 128.3 (d, *J* = 4.8 Hz, CH), 128.2 (C), 126.3 (CH), 118.4 (CH), 116.3 (dd, *J* = 262.3, 258.5 Hz, C), 112.2 (C), 62.9 (CH_2), 60.8 (dd, *J* = 27.7, 23.8 Hz, CH), 43.5 (d, *J* = 4.8 Hz, CH_2), 25.1 (CH_2), 13.9 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -102.1 (ddd, *J* = 252.9, 10.8, 2.9 Hz, 1F), -111.0 (dd, *J* = 252.9, 18.8 Hz, 1F). IR (ATR): 1760, 1490, 1210, 1060, 750 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{19}H_{19}{}^{79}BrF_2NO_2$: 410.0567; found: 410.0577.

Ethyl 2-(2-(4-cyanophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-2,2-difluoroacetate (3ea)



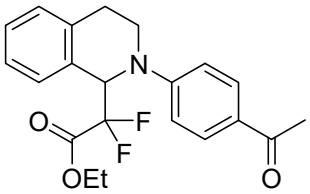
Silica gel column chromatography (hexane/AcOEt = 4/1) gave 104.0 mg (0.292 mmol, 58% yield) of the product as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (d, *J* = 8.9 Hz, 2H), 7.33-7.29 (m, 2H), 7.26-7.21 (m, 2H), 7.00 (d, *J* = 8.9 Hz, 2H), 5.45 (t, *J* = 14.2 Hz, 1H), 4.27-4.11 (m, 2H), 3.87-3.80 (m, 1H), 3.69-3.63 (m, 1H), 3.02 (t, *J* = 6.0 Hz, 2H), 1.19 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.5 (dd, *J* = 32.4, 30.5 Hz, C), 151.6 (C), 136.0 (C), 133.4 (CH), 128.9 (CH), 128.8 (CH), 128.2 (d, *J* = 2.9 Hz, CH), 128.0 (d, *J* = 1.9 Hz, C), 126.4 (CH), 119.6 (C), 115.9 (t, *J* = 260.4 Hz, C), 114.2 (CH), 100.9 (C), 63.1 (CH_2), 60.4 (dd, *J* = 26.7, 23.8 Hz, CH), 42.6 (d, *J* = 2.9 Hz, CH_2), 26.2 (d, *J* = 1.9 Hz, CH_2), 13.7 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -105.6 (dd, *J* = 252.9, 13.7 Hz, 1F), -107.9 (dd, *J* = 252.9, 14.5 Hz, 1F). IR (ATR): 2210, 1750, 1520, 1180, 1110, 750 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{20}H_{19}F_2N_2O_2$: 357.1415; found: 357.1402.

Ethyl 2,2-difluoro-2-(2-(4-(methoxycarbonyl)phenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (3fa)



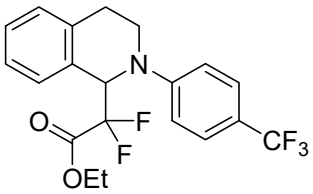
Silica gel column chromatography (hexane/AcOEt = 10/1) gave 128.7 mg (0.331 mmol, 66% yield) of the product as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, *J* = 9.2 Hz, 2H), 7.35-7.28 (m, 2H), 7.25-7.19 (m, 2H), 6.97 (d, *J* = 9.2 Hz, 2H), 5.47 (dd, *J* = 16.5, 12.4 Hz, 1H), 4.25-4.08 (m, 2H), 3.86 (s, 3H), 3.84-3.80 (m, 1H), 3.76-3.70 (m, 1H), 3.06-2.90 (m, 2H), 1.16 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.9 (C), 163.7 (dd, *J* = 33.4, 30.5 Hz, C), 152.3 (C), 136.2 (C), 131.2 (CH), 129.0 (CH), 128.6 (CH), 128.34 (C), 128.31 (CH), 126.3 (CH), 120.3 (C), 116.1 (dd, *J* = 261.3, 259.4 Hz, C), 113.9 (CH), 63.1 (CH_2), 60.4 (dd, *J* = 27.7, 23.8 Hz, CH), 51.7 (CH_3), 42.6 (d, *J* = 3.8 Hz, CH_2), 26.0 (CH_2), 13.8 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -103.8 (ddd, *J* = 252.9, 12.3, 2.2 Hz, 1F), -109.0 (dd, *J* = 252.9, 16.6 Hz, 1F). IR (ATR): 1770, 1710, 1520, 1190, 1110, 740 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{21}H_{22}F_2NO_4$: 390.1517; found: 390.1513.

Ethyl 2-(2-(4-acetylphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-2,2-difluoroacetate (3ga)



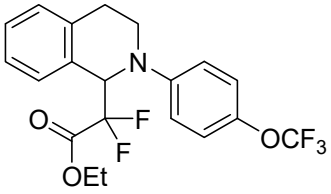
Silica gel column chromatography (hexane/AcOEt = 4/1) gave 123.6 mg (0.331 mmol, 66% yield) of the product as pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, *J* = 8.9 Hz, 2H), 7.34-7.28 (m, 2H), 7.26-7.19 (m, 2H), 6.99 (d, *J* = 8.9 Hz, 2H), 5.49 (dd, *J* = 15.8, 13.0 Hz, 1H), 4.26-4.10 (m, 2H), 3.88-3.81 (m, 1H), 3.77-3.71 (m, 1H), 3.07-2.93 (m, 2H), 2.52 (s, 3H), 1.18 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.4 (C), 163.7 (dd, *J* = 33.4, 30.5 Hz, C), 152.4 (C), 136.2 (C), 130.3 (CH), 129.0 (CH), 128.7 (CH), 128.32 (C), 128.29 (CH), 128.1 (C), 126.4 (CH), 116.1 (t, *J* = 261.3 Hz, C), 113.6 (CH), 63.1 (CH_2), 60.4 (dd, *J* = 27.7, 23.8 Hz, CH), 42.6 (d, *J* = 3.8 Hz, CH_2), 26.1 (CH_2 + CH_3), 13.8 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -104.3 (dd, *J* = 252.9, 13.0 Hz, 1F), -108.6 (dd, *J* = 252.9, 15.9 Hz, 1F). IR (ATR): 1760, 1660, 1520, 1200, 1100, 750 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{21}H_{22}F_2NO_3$: 374.1568; found: 374.1570.

Ethyl 2,2-difluoro-2-(2-(4-(trifluoromethyl)phenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (3ha)



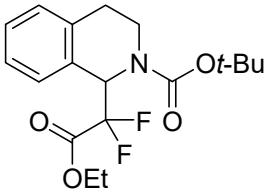
Silica gel column chromatography (hexane/AcOEt = 10/1) gave 162.1 mg (0.406 mmol, 81% yield) of the product as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, *J* = 8.7 Hz, 2H), 7.35-7.33 (m, 1H), 7.29 (d, *J* = 7.3 Hz, 1H), 7.25-7.21 (m, 1H), 7.19 (d, *J* = 7.6 Hz, 1H), 7.02 (d, *J* = 8.7 Hz, 2H), 5.40 (dd, *J* = 16.7, 12.4 Hz, 1H), 4.27-4.11 (m, 2H), 3.86-3.79 (m, 1H), 3.72-3.66 (m, 1H), 3.04-2.97 (m, 1H), 2.91 (dt, *J* = 16.5, 4.8 Hz, 1H), 1.18 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.8 (dd, *J* = 32.4, 30.5 Hz, C), 151.4 (C), 136.2 (C), 129.0 (CH), 128.6 (CH), 128.3 (d, *J* = 3.8 Hz, CH), 128.2 (C), 126.5 (q, *J* = 3.8 Hz, CH), 126.4 (CH), 124.6 (q, *J* = 270.9 Hz, C), 120.9 (q, *J* = 32.4 Hz, C), 116.2 (dd, *J* = 262.3, 259.4 Hz, C), 114,7 (CH), 63.0 (CH_2), 60.7 (dd, *J* = 27.7, 23.8 Hz, CH), 42.8 (d, *J* = 3.8 Hz, CH_2), 25.7 (CH_2), 13.8 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -61.4 (s, 3F), -103.7 (dd, *J* = 252.9, 12.3 Hz, 1F), -109.4 (dd, *J* = 252.9, 16.6 Hz, 1F). IR (ATR): 1770, 1520, 1160, 1110, 750, 710 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{20}H_{19}F_5NO_2$: 400.1336; found: 400.1346.

Ethyl 2,2-difluoro-2-(2-(4-(trifluoromethoxy)phenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (3ia)



Silica gel column chromatography (hexane/AcOEt = 15/1) gave 146.2 mg (0.352 mmol, 70% yield) of the product as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (d, *J* = 6.9 Hz, 1H), 7.31-7.28 (m, 1H), 7.26-7.22 (m, 1H), 7.18 (d, *J* = 7.3 Hz, 1H), 7.09 (d, *J* = 9.1 Hz, 2H), 6.93 (d, *J* = 9.1 Hz, 2H), 5.25 (dd, *J* = 18.5, 11.0 Hz, 1H), 4.25-4.11 (m, 2H), 3.82-3.74 (m, 1H), 3.63-3.57 (m, 1H), 2.99-2.91 (m, 1H), 2.79 (dt, *J* = 16.5, 4.1 Hz, 1H), 1.16 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.9 (dd, *J* = 34.3, 30.5 Hz, C), 148.1 (C), 142.3 (C), 136.4 (C), 129.1 (CH), 128.5 (CH), 128.3 (d, *J* = 3.8 Hz, CH), 128.2 (C), 126.3 (CH), 122.1 (CH), 120.5 (q, *J* = 255.6 Hz, C), 117.5 (CH), 116.3 (dd, *J* = 262.3, 258.5 Hz, C), 62.9 (CH_2), 61.0 (dd, *J* = 27.7, 23.8 Hz, CH), 43.7 (d, *J* = 4.8 Hz, CH_2), 25.2 (CH_2), 13.8 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -58.3 (s, 3F), -102.2 (ddd, *J* = 263.7, 10.8, 2.9 Hz, 1F), -111.1 (dd, *J* = 252.9, 18.1 Hz, 1F). IR (ATR): 1770, 1510, 1250, 1150, 740 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{20}H_{19}F_5NO_3$: 416.1285; found: 416.1289.

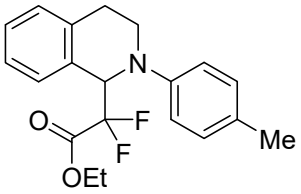
***tert*-Butyl 1-(2-ethoxy-1,1-difluoro-2-oxoethyl)-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (3ja)**



Silica gel column chromatography (hexane/AcOEt = 10/1) gave 67.8 mg (0.191 mmol, 38% yield) of the product as colorless oil. Rotamers were observed. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35-7.27 (m, 2H), 7.23 (d, *J* = 7.1 Hz, 1H), 7.20-7.17 (m, 1H), 5.77-5.62 (m, 1H), 4.38-4.30 (m, 2H), 4.21-4.18 + 3.88-3.85 (m, 1H), 3.63-3.57 + 3.47-3.40 (m, 1H), 2.93-2.82 (m, 2H), 1.46 (s, 9H), 1.40-1.32 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.5 (t, *J* = 32.4 Hz, C), 163.6 (t, *J* = 30.5 Hz, C), 155.0 (C), 154.1 (C), 136.1 (C), 129.3 (CH), 129.1 (d, *J* = 3.8 Hz, CH), 128.8 (CH), 128.4 (CH), 128.1 (C), 127.9 (C), 126.2 (CH), 126.1 (CH), 115.4 (t, *J* = 259.4 Hz, C), 115.0 (t, *J* = 259.4 Hz, C), 81.2 (C), 80.7 (C), 63.0 (CH_2), 56.6 (t, *J* = 25.8 Hz, CH), 55.7 (dd, *J* = 28.6, 23.8 Hz, CH), 39.9 (CH_2), 38.0 (CH_2), 28.2 (CH_3), 27.7 (CH_2), 27.3 (CH_2), 13.9 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -105.1 (dd, *J* = 258.7, 10.8 Hz, 1F), -111.6 (dd, *J* = 258.7, 18.8 Hz, 1F). IR (ATR): 1760, 1610, 1510, 1190, 1100, 750 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$

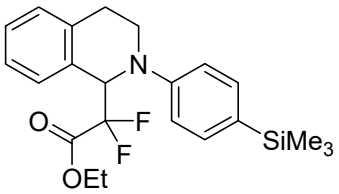
Calcd for $C_{18}H_{24}F_2NO_4$: 356.1673; found: 356.1672.

Ethyl 2,2-difluoro-2-(2-*p*-tolyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (3ka)



Silica gel column chromatography (hexane/AcOEt = 20/1) gave 141.4 mg (0.409 mmol, 82% yield) of the product as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 6.6 Hz, 1H), 7.28-7.21 (m, 2H), 7.15 (d, *J* = 7.1 Hz, 1H), 7.02 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 5.20 (dd, *J* = 20.1, 10.1 Hz, 1H), 4.27-4.12 (m, 2H), 3.77-3.69 (m, 1H), 3.61-3.58 (m, 1H), 2.97-2.88 (m, 1H), 2.67 (dt, *J* = 16.5, 3.4 Hz, 1H), 2.24 (s, 3H), 1.16 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.0 (dd, *J* = 34.3, 30.5 Hz, C), 147.2 (C), 136.7 (C), 129.8 (C), 129.6 (CH), 129.1 (CH), 128.5 (C), 128.3 (d, *J* = 4.8 Hz, CH), 128.1 (CH), 126.1 (CH), 117.6 (CH), 116.6 (dd, *J* = 263.2, 258.5 Hz, C), 62.6 (CH_2), 60.8 (dd, *J* = 27.7, 22.9 Hz, CH), 43.8 (d, *J* = 4.8 Hz, CH_2), 24.7 (CH_2), 20.3 (CH_3), 13.8 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -100.8 (ddd, *J* = 252.2, 10.1, 3.6 Hz, 1F), -112.1 (dd, *J* = 252.2, 20.2 Hz, 1F). IR (ATR): 1760, 1510, 1190, 1100, 750 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{20}H_{22}F_2NO_2$: 346.1619; found: 346.1620.

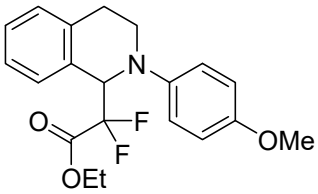
Ethyl 2,2-difluoro-2-(2-(4-(trimethylsilyl)phenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (3la)



Silica gel column chromatography (hexane/AcOEt = 25/1) gave 123.2 mg (0.305 mmol, 61% yield) of the product as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39-7.34 (m, 3H), 7.28-7.19 (m, 2H), 7.15 (d, *J* = 7.3 Hz, 1H), 6.96 (d, *J* = 8.5 Hz, 2H), 5.33 (dd, *J* = 18.8, 11.2 Hz, 1H), 4.27-4.09 (m, 2H), 3.81-3.65 (m, 2H), 3.04-2.95 (m, 1H), 2.77 (dt, *J* = 16.5, 4.1 Hz, 1H), 1.17 (t, *J* = 7.1 Hz, 3H), 0.21 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.0 (dd, *J* = 33.4, 29.6 Hz, C), 149.6 (C), 136.6 (C), 134.4 (CH), 130.1 (C), 129.1 (CH), 128.6 (C), 128.30 (d, *J* = 4.8 Hz, CH), 128.26 (CH), 126.1 (CH), 116.5 (dd, *J* = 262.3, 258.5 Hz, C), 115.7 (CH), 62.8 (CH_2), 60.8 (dd, *J* = 28.6, 23.8 Hz, CH), 42.7 (d, *J* = 4.8 Hz, CH_2), 25.3 (CH_2), 13.8 (CH_3), -1.01 (CH_3).^{19}F NMR (376 MHz, $CDCl_3$): δ -101.5 (ddd, *J* = 252.2, 10.8, 2.9 Hz, 1F), -110.5 (dd, *J* = 252.2, 18.8 Hz, 1F). IR (ATR): 1760, 1600, 1310, 1260, 1100, 850 cm^{-1}. HRMS (DART): *m/z*

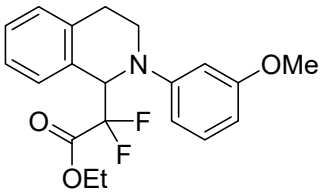
$[M+H]^+$ Calcd for $C_{22}H_{28}F_2NO_2Si$: 404.1857; found: 404.1844.

Ethyl 2,2-difluoro-2-(2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (3ma)



Silica gel column chromatography (hexane/AcOEt = 10/1) gave 139.5 mg (0.386 mmol, 77% yield) of the product as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43-7.41 (m, 1H), 7.30-7.23 (m, 2H), 7.16 (d, *J* = 7.1 Hz, 1H), 6.87-6.84 (m, 2H), 6.78-6.75 (m, 2H), 5.08 (dd, *J* = 21.0, 9.4 Hz, 1H), 4.28-4.14 (m, 2H), 3.74 (s, 3H), 3.72-3.67 (m, 1H), 3.50-3.46 (m, 1H), 2.91-2.83 (m, 1H), 2.62 (dt, *J* = 16.2, 3.4 Hz, 1H), 1.16 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.0 (dd, *J* = 34.3, 29.6 Hz, C), 154.3 (C), 143.8 (C), 136.8 (C), 129.2 (CH), 128.5 (C), 128.3 (d, *J* = 5.7 Hz, CH), 128.1 (CH), 126.2 (CH), 120.3 (CH), 116.6 (dd, *J* = 263.2, 258.5 Hz, C), 114.4 (CH), 62.6 (CH_2), 61.1 (dd, *J* = 27.7, 23.8 Hz, CH), 55.5 (CH_3), 45.1 (d, *J* = 4.8 Hz, CH_2), 24.3 (CH_2), 13.9 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -100.6 (ddd, *J* = 252.1, 9.4, 3.6 Hz, 1F), -113.4 (dd, *J* = 252.2, 21.0 Hz, 1F). IR (ATR): 1770, 1510, 1240, 1100, 1040, 750, cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{20}H_{22}F_2NO_3$: 362.1568; found: 362.1565.

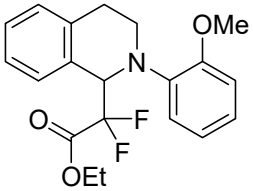
Ethyl 2,2-difluoro-2-(2-(3-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (3na)



Silica gel column chromatography (hexane/AcOEt = 10/1) gave 126.1 mg (0.349 mmol, 70% yield) of the product as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 6.6 Hz, 1H), 7.28-7.20 (m, 2H), 7.16-7.11 (m, 2H), 6.56 (dd, *J* = 8.1, 2.3 Hz, 1H), 6.50 (t, *J* = 2.3 Hz, 1H), 6.40 (dd, *J* = 8.1, 2.3 Hz, 1H), 5.28 (dd, *J* = 19.2, 10.8 Hz, 1H), 4.28-4.12 (m, 2H), 3.77 (s, 3H), 3.78-3.71 (m, 1H), 3.67-3.62 (m, 1H), 3.01-2.93 (m, 1H), 2.74 (dt, *J* = 16.5, 3.9 Hz, 1H), 1.17 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.9 (dd, *J* = 34.3, 30.5 Hz, C), 160.5 (C), 150.6 (C), 136.6 (C), 129.8 (CH), 129.1 (CH), 128.5 (C), 128.3 (d, *J* = 4.8 Hz, CH), 128.2 (CH), 126.1 (CH), 116.5 (dd, *J* = 262.3, 258.5 Hz, C), 109.4 (CH), 104.5 (CH), 103.5 (CH), 62.8 (CH_2), 60.9 (dd, *J* = 27.7, 23.8 Hz, CH), 55.1 (CH_3), 43.2 (d, *J* = 4.8 Hz, CH_2), 25.1 (CH_2), 13.8 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -101.5 (ddd, *J* = 252.1, 10.8, 2.9 Hz, 1F), -111.1 (dd, *J*

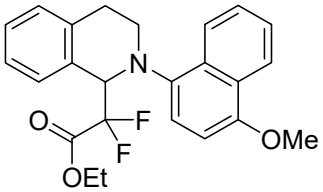
= 252.1, 19.5 Hz, 1F). IR (ATR): 1760, 1490, 1210, 1170, 1060, 730 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{20}H_{22}F_2NO_3$: 362.1568; found: 362.1576.

Ethyl 2,2-difluoro-2-(2-(2-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (3oa)



Silica gel column chromatography (hexane/AcOEt = 10/1) gave 127.9 mg (0.354 mmol, 71% yield) of the product as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46-7.44 (m, 1H), 7.31-7.25 (m, 2H), 7.17 (d, *J* = 7.1 Hz, 1H), 7.02-6.98 (m, 1H), 6.83 (d, *J* = 8.0 Hz, 1H), 6.79-6.74 (m, 2H), 5.05 (dd, *J* = 22.9, 7.8 Hz, 1H), 4.19-4.00 (m, 2H), 3.77 (s, 3H), 3.63-3.55 (m, 1H), 3.44-3.40 (m, 1H), 2.81-2.72 (m, 1H), 2.65-2.60 (m, 1H), 1.09 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.0 (dd, *J* = 34.3, 29.6 Hz, C), 153.3 (C), 139.3 (C), 137.2 (C), 129.3 (C), 129.1 (CH), 128.1 (d, *J* = 5.7 Hz, CH), 127.8 (CH), 126.0 (CH), 124.2 (CH), 123.3 (CH), 120.6 (CH), 116.5 (dd, *J* = 264.2, 258.5 Hz, C), 111.4 (CH), 82.4 (CH_2), 61.2 (dd, *J* = 26.7, 22.9 Hz, CH), 55.1 (CH_3), 44.6 (d, *J* = 3.8 Hz, CH_2), 25.4 (CH_2), 13.6 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -99.1 (ddd, *J* = 252.1, 7.9, 3.6 Hz, 1F), -114.9 (dd, *J* = 252.1, 23.1 Hz, 1F). IR (ATR): 1770, 1500, 1240, 1120, 1070, 750 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{20}H_{22}F_2NO_3$: 362.1568; found: 362.1580.

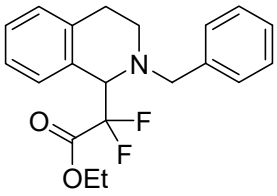
Ethyl 2,2-difluoro-2-(2-(4-methoxynaphthalen-1-yl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (3pa)



Silica gel column chromatography (hexane/AcOEt = 15/1) gave 156.7 mg (0.381 mmol, 76% yield) of the product as pale-orange solids of mp 128-129 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (d, *J* = 8.2 Hz, 1H), 8.05 (d, *J* = 8.2 Hz, 1H), 7.55-7.47 (m, 3H), 7.36-7.30 (m, 2H), 7.22-7.20 (m, 1H), 6.72 (d, *J* = 8.0 Hz, 1H), 6.55 (d, *J* = 8.0 Hz, 1H), 5.02 (dd, *J* = 23.8, 7.1 Hz, 1H), 4.15-4.07 (m, 1H), 3.92 (s, 3H), 3.90-3.83 (m, 1H), 3.77-3.71 (m, 1H), 3.27 (dd, *J* = 14.0, 4.8 Hz, 1H), 2.83-2.75 (m, 1H), 2.53-2.49 (m, 1H), 0.81 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.1 (dd, *J* = 35.3, 29.6 Hz, C), 152.5 (C), 140.5 (C), 137.0 (C), 130.1 (C), 129.3 (CH), 129.1 (C), 128.0 (d, *J* = 6.7 Hz, CH), 127.9 (CH), 126.4 (CH), 126.33 (C), 126.27 (CH),

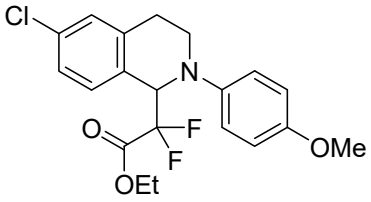
125.4 (CH), 123.1 (CH), 122.3 (CH), 118.6 (CH), 116.6 (dd, J = 262.3, 259.4 Hz, C), 102.9 (CH), 62.6 (dd, J = 26.7, 22.9 Hz, CH), 62.5 (CH_2), 55.3 (CH_3), 45.9 (d, J = 4.8 Hz, CH_2), 23.6 (CH_2), 13.4 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -99.2 (d, J = 254.3 Hz, 1F), -116.3 (dd, J = 254.3, 23.1 Hz, 1F). IR (ATR): 1750, 1590, 1270, 1090, 770, 740 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{24}H_{24}F_2NO_3$: 412.1724; found: 412.1732.

Ethyl 2-(2-benzyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-2,2-difluoroacetate (3qa)



Silica gel column chromatography (hexane/AcOEt = 4/1) gave 122.7 mg (0.355 mmol, 71% yield) of the product as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34-7.27 (m, 5H), 7.25-7.21 (m, 3H), 7.18 (d, J = 7.3 Hz, 1H), 4.44-4.36 (m, 1H), 4.31 (dd, J = 22.2, 9.2 Hz, 1H), 4.26-4.18 (m, 1H), 3.82-3.74 (m, 2H), 3.34-3.27 (m, 1H), 2.99-2.91 (m, 1H), 2.80-2.75 (m 1H), 2.58-2.53 (m, 1H), 1.30 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.3 (dd, J = 33.4, 30.5 Hz, C), 138.3 (C), 136.3 (C), 129.4 (d, J = 4.8 Hz, CH), 129.0 (CH), 128.7 (CH), 128.3 (CH), 127.9 (CH), 127.7 (C), 127.3 (CH), 126.0 (CH), 116.6 (dd, J = 261.3, 254.6 Hz, C), 62.7 (dd, J = 26.7, 22.9 Hz, CH), 62.4 (CH_2), 58.6 (CH_2), 42.6 (d, J = 5.7 Hz, CH_2), 22.4 (CH_2), 13.9 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -100.3 (ddd, J = 252.9, 9.4, 3.6 Hz, 1F), -114.1 (dd, J = 252.9, 22.4 Hz, 1F). IR (ATR): 1760, 1490, 1200, 1060, 750 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{20}H_{22}F_2NO_2$: 346.1619; found: 346.1620.

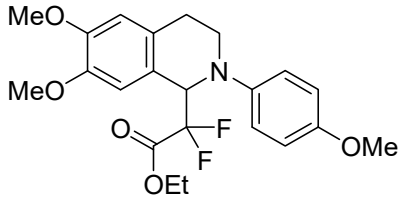
Ethyl 2-(6-chloro-2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-2,2-difluoroacetate (3ra)



Silica gel column chromatography (hexane/AcOEt = 10/1) gave 141.1 mg (0.356 mmol, 71% yield) of the product as pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38-7.35 (m, 1H), 7.23 (dd, J = 8.2, 1.8 Hz, 1H), 7.17 (s, 1H), 6.84-6.81 (m, 2H), 6.78-6.75 (m, 2H), 5.03 (dd, J = 21.3, 8.9 Hz, 1H), 4.28-4.15 (m, 2H), 3.74 (s, 3H), 3.71-3.63 (m, 1H), 3.46 (dd, J = 14.2, 5.0 Hz, 1H), 2.87-2.79 (m, 1H), 2.59-2.55 (m, 1H), 1.16 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.7 (dd, J = 34.3, 29.6 Hz, C), 154.6 (C), 143.4 (C), 138.8 (C), 133.9 (C), 129.6 (d, J = 5.7 Hz, CH), 129.1 (CH), 127.0 (C), 126.5 (CH), 120.6 (CH), 116.3 (dd, J = 263.2, 257.5 Hz, C),

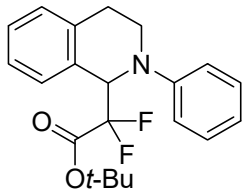
114.4 (CH), 62.7 (CH_2), 60.7 (dd, J = 27.7, 23.8 Hz, CH), 55.5 (CH_3), 44.8 (d, J = 5.7 Hz, CH_2), 13.9 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -100.1 (ddd, J = 252.9, 8.7, 2.9 Hz, 1F), -113.7 (dd, J = 252.9, 21.0 Hz, 1F). IR (ATR): 1770, 1510, 1240, 1100, 1050, 730 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{20}H_{21}{}^{35}ClF_2NO_3$: 396.1178; found: 396.1186.

Ethyl 2-(6,7-dimethoxy-2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-2,2-difluoroacetate (3sa)



Silica gel column chromatography (hexane/AcOEt = 2/1) gave 147.8 mg (0.351 mmol, 70% yield) of the product as colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 6.91 (d, J = 2.7 Hz, 1H), 6.86-6.83 (m, 2H), 6.78-6.75 (m, 2H), 6.63 (s, 1H), 4.98 (dd, J = 21.5, 9.2 Hz, 1H), 4.29-4.16 (m, 2H), 3.90 (s, 3H), 3.87 (s, 3H), 3.74 (s, 3H), 3.70-3.62 (m, 1H), 3.49-3.44 (m, 1H), 2.82-2.74 (m, 1H), 2.50-2.45 (m, 1H), 1.16 (t, J = 7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.0 (dd, J = 34.3, 29.6 Hz, C), 154.4 (C), 148.8 (C), 147.3 (C), 143.8 (C), 129.1 (C), 120.6 (CH), 119.9 (C), 116.6 (dd, J = 263.2, 256.6 Hz, C), 114.3 (CH), 111.5 (CH), 110.8 (d, J = 5.7 Hz, CH), 62.5 (CH_2), 60.8 (dd, J = 27.7, 22.9 Hz, CH), 55.9 (CH_3), 55.7 (CH_3), 55.4 (CH_3), 45.2 (d, J = 5.7 Hz, CH_2), 23.6 (CH_2), 13.9 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -99.8 (ddd, J = 252.2, 8.7, 2.9 Hz, 1F), -114.2 (dd, J = 252.2, 21.7 Hz, 1F). IR (ATR): 1760, 1510, 1220, 1120, 1060, 770 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{22}H_{26}F_2NO_5$: 422.1779; found: 422.1772.

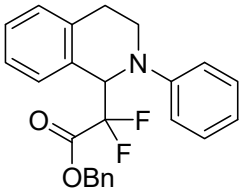
***tert*-Butyl 2,2-difluoro-2-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (3ab)**



In the preparation of the organozinc reagent, the mixture was stirred for 30 min. Silica gel column chromatography (hexane/AcOEt = 20/1) gave 131.5 mg (0.366 mmol, 73% yield) of the product as white solids of mp 92-93 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, J = 6.9 Hz, 1H), 7.28-7.20 (m, 4H), 7.14 (d, J = 7.3 Hz, 1H), 6.95 (d, J = 8.0 Hz, 2H), 6.83 (t, J = 7.3 Hz, 1H), 5.26 (dd, J = 19.7, 10.8 Hz, 1H), 3.81-3.69 (m, 2H), 2.98-2.89 (m, 1H), 2.72-2.66 (m, 1H), 1.37 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.7 (dd, J = 33.4, 28.6 Hz, C), 149.2 (C), 136.6 (C), 129.1 (CH), 128.8 (C), 128.4 (d, J = 4.8 Hz, CH), 128.1 (CH), 126.1 (CH), 119.9 (CH),

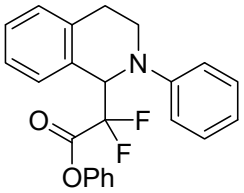
116.7 (CH), 116.3 (dd, J = 262.3, 258.5 Hz, C), 84.4 (C), 60.3 (dd, J = 28.6, 23.8 Hz, CH), 43.3 (d, J = 4.8 Hz, CH_2), 27.6 (CH_3), 24.9 (CH_2). ^{19}F NMR (376 MHz, $CDCl_3$): δ -101.0 (ddd, J = 250.0, 10.8, 2.9 Hz, 1F), -110.7 (dd, J = 250.0, 19.5 Hz, 1F). IR (ATR): 1750, 1590, 1110, 1070, 750 cm^{-1}. HRMS (DART) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{24}F_2NO_2$: 360.1775; found: 360.1791.

Benzyl 2,2-difluoro-2-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (3ac)



In the preparation of the organozinc reagent, the mixture was stirred for 30 min. Silica gel column chromatography (hexane/AcOEt = 20/1) gave 146.7 mg (0.373 mmol, 75% yield) of the product as colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.35-7.33 (m, 1H), 7.31-7.24 (m, 4H), 7.22-7.18 (m, 3H), 7.15-7.13 (m, 3H), 6.89-6.85 (m, 3H), 5.26 (dd, J = 19.7, 10.5 Hz, 1H), 5.22 (d, J = 11.9 Hz, 1H), 5.02 (d, J = 11.9 Hz, 1H), 3.78-3.70 (m, 1H), 3.61-3.58 (m, 1H), 2.96-2.88 (m, 1H), 2.68 (dt, J = 16.5, 3.7 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.9 (dd, J = 34.3, 29.6 Hz, C), 149.4 (C), 136.6 (C), 134.1 (C), 129.23 (CH), 129.16 (CH), 128.74 (CH), 128.66 (CH), 128.5 (CH), 128.4 (C), 128.3 (d, J = 4.8 Hz, CH), 128.2 (CH), 126.2 (CH), 120.4 (CH), 117.4 (CH), 116.7 (dd, J = 263.2, 258.5 Hz, C), 68.4 (CH_2), 60.7 (dd, J = 27.7, 22.9 Hz, CH), 43.6 (d, J = 4.8 Hz, CH_2), 24.8 (CH_2). ^{19}F NMR (376 MHz, $CDCl_3$): δ -100.8 (ddd, J = 252.2, 10.8, 2.9 Hz, 1F), -111.3 (dd, J = 252.2, 19.5 Hz, 1F). IR (ATR): 1770, 1600, 1200, 1070, 740 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{24}H_{22}F_2NO_2$: 394.1619; found: 394.1613.

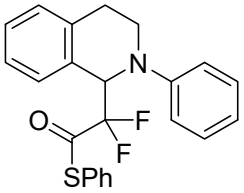
Phenyl 2,2-difluoro-2-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (3ad)



In the preparation of the organozinc reagent, the mixture was stirred for 30 min. Silica gel column chromatography (hexane/AcOEt = 20/1) gave 150.1 mg (0.396 mmol, 79% yield) of the product as white solids of mp 107-108 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.49-7.47 (m, 1H), 7.33-7.18 (m, 8H), 7.01 (d, J = 8.0 Hz, 2H), 6.91-6.88 (m. 1H), 6.87-6.84 (m. 2H), 5.43 (dd, J = 20.1, 10.3 Hz, 1H), 3.88-3.80 (m, 1H), 3.76-3.71 (m, 1H), 3.00-2.92 (m, 1H), 2.72. (dt, J = 16.5, 3.4 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.5 (dd, J = 35.3, 31.5 Hz, C), 149.7 (C), 149.3 (C), 136.7 (C), 129.5 (CH), 129.4 (CH), 129.3 (CH), 128.4 (CH), 128.3 (CH), 128.1 (C), 126.6 (CH), 126.3 (CH), 121.1 (CH), 120.7 (CH), 117.6 (CH), 116.8 (dd, J = 263.2, 259.4 Hz,

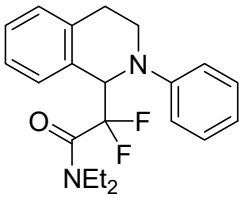
C), 60.7 (dd, J = 28.6, 23.8 Hz, CH), 44.0 (d, J = 5.7 Hz, CH_2), 24.7 (CH_2). ^{19}F NMR (376 MHz, $CDCl_3$): δ -100.2 (ddd, J = 252.2, 10.8, 3.6 Hz, 1F), -111.0 (dd, J = 252.1, 20.2 Hz, 1F). IR (ATR): 1770, 1590, 1480, 1180, 1100, 740 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{23}H_{20}F_2NO_2$: 380.1462; found: 380.1455.

_S_-Phenyl 2,2-difluoro-2-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)ethanethioate (3ae)



In the preparation of the organozinc reagent, the mixture was stirred for 60 min. Silica gel column chromatography (hexane/AcOEt = 15/1) gave 137.8 mg (0.348 mmol, 70% yield) of the product as white solids of mp 110-111 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.45-7.36 (m, 3H), 7.34-7.29 (m, 2H), 7.26-7.20 (m, 6H), 6.98 (d, J = 8.2 Hz, 2H), 6.86 (t, J = 7.3 Hz, 1H), 5.41 (dd, J = 18.1, 12.1 Hz, 1H), 3.92-3.85 (m, 1H), 3.69-3.63 (m, 1H), 3.05-2.98 (m, 1H), 2.91 (dt, J = 16.2, 4.8 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.1 (dd, J = 35.3, 31.5 Hz, C), 149.2 (C), 136.9 (C), 134.6 (CH), 130.0 (CH), 129.4 (CH), 129.2 (CH), 128.9 (CH), 128.7 (C), 128.6 (d, J = 3.8 Hz, CH), 128.4 (CH), 126.2 (CH), 124.9 (C), 119.7 (CH), 118.3 (dd, J = 266.1, 264.2 Hz, C), 116.0 (CH), 60.7 (dd, J = 26.7, 22.9 Hz, CH), 43.5 (d, J = 3.8 Hz, CH_2), 25.7 (CH_2). ^{19}F NMR (376 MHz, $CDCl_3$): δ -100.6 (ddd, J = 251.4, 11.6, 2.2 Hz, 1F), -109.1 (dd, J = 251.4, 18.1 Hz, 1F). IR (ATR): 1700, 1500, 1190, 1070, 740 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{23}H_{20}F_2NOS$: 396.1234; found: 396.1245.

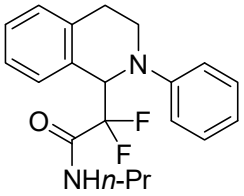
_N_,_N_-Diethyl-2,2-difluoro-2-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetamide[14] (3af)



In the preparation of the organozinc reagent, the mixture was stirred for 60 min. Silica gel column chromatography (hexane/AcOEt = 10/1) gave 127.8 mg (0.357 mmol, 71% yield) of the product as white solid of mp 87-88 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.33 (d, J = 7.6 Hz, 1H), 7.28-7.24 (m, 3H), 7.21-7.16 (m, 2H), 7.02 (d, J = 8.2 Hz, 2H), 6.81 (t, J = 7.3 Hz, 1H), 5.67 (dd, J = 17.8, 10.5 Hz, 1H), 3.88-3.82 (m, 1H), 3.49-3.32 (m, 2H), 3.31-3.15 (m, 2H), 3.13-2.95 (m, 3H), 1.06 (t, J = 7.1 Hz, 3H), 1.02 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.3 (t, J = 27.7 Hz, C), 149.4 (C), 137.0 (C), 129.9 (d, J = 2.9 Hz, C), 129.0 (CH), 128.8 (d, J = 1.9 Hz, CH), 128.1 (CH), 126.0 (CH), 118.8 (t, J = 263.2 Hz, C), 118.4 (CH), 114.3

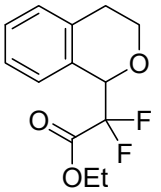
(CH), 61.1 (dd, J = 24.8, 22.9 Hz, CH), 43.9 (CH_2), 42.4 (CH_2), 41.8 (dd, J = 9.5, 4.8 Hz, CH_2), 27.2 (d, J = 2.9 Hz, CH_2), 14.3 (CH_3), 11.8 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -100.7 (dd, J = 255.8, 10.8 Hz, 1F), -104.3 (dd, J = 255.8, 18.1 Hz, 1F). IR (ATR): 1650, 1500, 1130, 1050, 740 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{21}H_{25}F_2N_2O$: 359.1935; found: 359.1941.

2,2-Difluoro-2-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-*N*-propylacetamide (3ag)



In the preparation of the organozinc reagent, the mixture was stirred for 60 min. Silica gel column chromatography (hexane/AcOEt = 5/1) gave 109.2 mg (0.317 mmol, 63% yield) of the product as white solids of mp 101-102 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30-7.24 (m, 4H), 7.20-7.16 (m, 2H), 7.05 (d, J = 8.2 Hz, 2H), 6.82 (t, J = 7.3 Hz, 1H), 6.22 (brs, 1H), 5.56 (dd, J = 17.4, 12.6 Hz, 1H), 3.83-3.77 (m, 1H), 3.56-3.50 (m, 1H), 3.24-3.19 (m, 2H), 3.02-2.99 (m, 2H), 1.50-1.41 (m, 2H), 0.83 (t, J = 7.6 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.0 (t, J = 27.7 Hz, C), 149.6 (C), 136.9 (C), 129.4 (d, J = 2.9 Hz, C), 129.1 (CH), 128.7 (d, J = 2.9 Hz, CH), 128.5 (CH), 128.1 (CH), 126.1 (CH), 118.9 (CH), 117.9 (t, J = 261.3 Hz, C), 114.9 (CH), 60.4 (dd, J = 24.8, 22.9 Hz, CH), 43.5 (d, J = 1.9 Hz, CH_2), 41.2 (CH_2), 26.7 (d, J = 2.9 Hz, CH_2), 22.2 (CH_2), 11.1 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -108.8 (dd, J = 250.0, 12.3 Hz, 1F), -110.9 (dd, J = 250.0, 17.3 Hz, 1F). IR (ATR): 3320, 1680, 1500, 1190, 1040, 760 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{20}H_{23}F_2N_2O$: 345.1778; found: 345.1784.

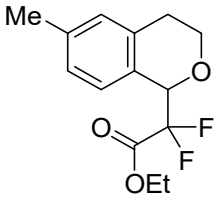
Ethyl 2,2-difluoro-2-(isochroman-1-yl)acetate (5aa)



Silica gel column chromatography (hexane/AcOEt = 10/1) gave 92.6 mg (0361 mmol, 72% yield) of the product as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (d, J = 7.1 Hz, 1H), 7.31-7.23 (m, 2H), 7.18 (d, J = 7.3 Hz, 1H), 5.26 (dd, J = 21.0, 4.8 Hz, 1H), 4.45-4.33 (m, 1H), 4.19-4.14 (m, 1H), 3.85-3.79 (m, 1H), 2.93-2.86 (m, 1H), 2.81 (dt, J = 16.2, 5.3 Hz, 1H), 1.37 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.5 (dd, J = 33.4, 29.6 Hz, C), 135.3 (C), 128.8 (CH), 128.2 (C), 128.0 (CH), 126.7 (d, J = 5.7 Hz, CH), 126.3 (CH), 114.9 (dd, J = 263.2, 253.7 Hz, C), 74.2 (dd, J = 28.6, 24.8 Hz, CH), 63.0 (CH_2), 62.9 (d, J = 1.9 Hz, CH_2), 28.5 (CH_2), 13.9 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -106.7 (dt, J = 257.2, 4.3 Hz, 1F), -119.2

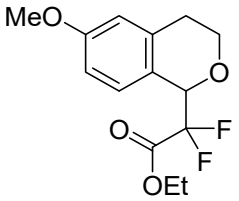
(dd, J = 257.2, 21.0 Hz, 1F). IR (ATR): 1760, 1190, 1110, 1070, 750 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{13}H_{15}F_2O_3$: 257.0989; found: 257.0994.

Ethyl 2,2-difluoro-2-(6-methylisochroman-1-yl)acetate (5ba)



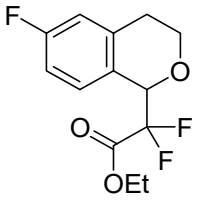
Silica gel column chromatography (hexane/AcOEt = 10/1) gave 92.1 mg (0.341 mmol, 68% yield) of the product as colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.15 (s, 1H), 7.11 (d, J = 8.0 Hz, 1H), 7.07 (d, J = 8.0 Hz, 1H), 5.21 (dd, J = 21.0, 4.8 Hz, 1H), 4.45-4.33 (m, 2H), 4.17-4.12 (m, 1H), 3.82-3.77 (m, 1H), 2.88-2.72 (m, 2H), 2.34 (s, 3H), 1.37 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.6 (dd, J = 33.4, 29.6 Hz, C), 135.9 (C), 132.2 (C), 128.9 (CH), 128.6 (CH), 128.0 (C), 127.1 (d, J = 5.7 Hz, CH), 115.0 (dd, J = 262.3, 254.6 Hz, C), 74.2 (dd, J = 27.7, 23.8 Hz, CH), 63.0 (d, J = 1.9 Hz, CH_2), 62.9 (CH_2), 28.1 (CH_2), 21.2 (CH_3), 14.0 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -106.6 (dt, J = 256.5, 4.3 Hz, 1F), -119.2 (dd, J = 256.5, 21.0 Hz, 1F). IR (ATR): 1770, 1500, 1100, 1070, 750 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{14}H_{17}F_2O_3$: 271.1146; found: 271.1150.

Ethyl 2,2-difluoro-2-(6-methoxyisochroman-1-yl)acetate (5ca)



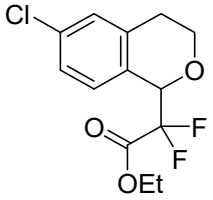
Silica gel column chromatography (hexane/AcOEt = 10/1) gave 95.1 mg (0.332 mmol, 66% yield) of the product as colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.28-7.25 (m, 1H), 6.81 (dd, J = 8.7, 2.4 Hz, 1H), 6.71 (d, J = 2.4 Hz, 1H), 5.21 (dd, J = 20.8, 5.0 Hz, 1H), 4.44-4.33 (m, 2H), 4.17-4.11 (m, 1H), 3.81 (s, 3H), 3.80-3.76 (m, 1H), 2.90-2.83 (m, 1H), 2.77 (dt, J = 16.5, 5.0 Hz, 1H), 1.37 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.6 (dd, J = 34.3, 29.6, Hz, C), 159.2 (C), 136.8 (C), 127.9 (d, J = 5.7 Hz, CH), 120.2 (C), 114.9 (dd, J = 262.3, 252.7, Hz, C), 113.5 (CH), 112.6 (CH), 74.0 (dd, J = 27.7, 23.8, Hz, CH), 62.9 (CH_2), 62.6 (d, J = 1.9 Hz, CH_2), 55.2 (CH_3), 28.8 (CH_2), 13.9 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -107.0 (dt, J = 256.5, 5.1 Hz, 1F), -119.6 (dd, J = 256.5, 21.0 Hz, 1F). IR (ATR): 1770, 1610, 1500, 1250, 1100, 1070, 700 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{14}H_{17}F_2O_4$: 287.1095; found: 287.1089.

Ethyl 2,2-difluoro-2-(6-fluoroisochroman-1-yl)acetate (5da)



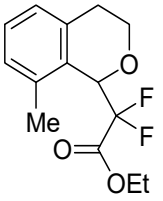
Silica gel column chromatography (hexane/AcOEt = 10/1) gave 95.8 mg (0.349 mmol, 70% yield) of the product as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35-7.30 (m, 1H), 6.98-6.94 (m, 1H), 6.90 (dd, *J* = 9.2, 2.3 Hz, 1H), 5.23 (dd, *J* = 21.0, 4.8 Hz, 1H), 4.45-4.33 (m, 2H), 4.17-4.12 (m, 1H), 3.83-3.77 (m, 1H), 2.92-2.85 (m, 1H), 2.83-2.76 (m, 1H), 1.37 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.4 (dd, *J* = 33.4, 29.6 Hz, C), 162.2 (d, *J* = 248.0 Hz, C), 137.7 (d, *J* = 7.6 Hz, C), 128.5 (dd, *J* = 8.6, 6.7 Hz, CH), 123.9 (d, *J* = 3.1 Hz, C), 115.4 (d, *J* = 21.9 Hz, CH), 114.8 (dd, *J* = 263.2, 253.7 Hz, C), 113.8 (CH), 73.9 (dd, *J* = 28.6, 24.8 Hz, CH), 63.0 (CH_2), 62.4 (d, *J* = 1.9 Hz, CH_2), 28.5 (CH_2), 14.0 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -106.7 (dt, *J* = 257.9, 3.6, Hz, 1F), -113.8 (s, 1F), -119.3 (dd, *J* = 257.9, 21.0 Hz, 1F). IR (ATR): 1770, 1500, 1230, 1100, 1070, 730 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{13}H_{14}F_3O_3$: 275.0895; found: 275.0893.

Ethyl 2-(6-chloroisochroman-1-yl)-2,2-difluoroacetate (5ea)



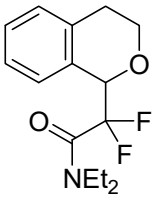
Silica gel column chromatography (hexane/AcOEt = 8/1) gave 98.8 mg (0.340 mmol, 68% yield) of the product as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30-7.28 (m, 1H), 7.24-7.22 (m, 1H), 7.19 (s, 1H), 5.22 (dd, *J* = 21.0, 4.8 Hz, 1H), 4.45-4.33 (m, 2H), 4.17-4.12 (m, 1H), 3.83-3.77 (m, 1H), 2.90-2.75 (m, 2H), 1.37 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.2 (dd, *J* = 33.4, 29.6 Hz, C), 137.2 (C), 133.9 (C), 128.7 (CH), 128.0 (d, *J* = 6.7 Hz, CH), 126.73 (C), 126.66 (CH), 114.7 (dd, *J* = 263.2, 254.6 Hz, C), 73.9 (dd, *J* = 28.6, 24.8 Hz, CH), 63.0 (CH_2) 62.4 (d, *J* = 1.9 Hz, CH_2), 28.3 (CH_2), 13.9 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.6 (dt, *J* = 257.9, 2.9 Hz, 1F), -119.2 (dd, *J* = 257.9, 21.0 Hz, 1F). IR (ATR): 1760, 1490, 1190, 1110, 1070, 720 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{13}H_{14}{}^{35}ClF_2O_3$: 291.0600; found: 291.0594.

Ethyl 2,2-difluoro-2-(8-methylisochroman-1-yl)acetate (5fa)



Silica gel column chromatography (hexane/AcOEt = 10/1) gave 95.3 mg (0.353 mmol, 71% yield) of the product as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23-7.20 (m, 1H), 7.18-7.16 (m, 2H), 5.23 (dd, *J* = 21.3, 5.3 Hz, 1H), 4.45-4.33 (m, 2H), 4.22-4.16 (m, 1H), 3.90-3.84 (m, 1H), 2.72 (t, *J* = 5.7 Hz, 2H), 2.27 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.6 (dd, *J* = 33.4, 29.6 Hz, C), 136.2 (C), 133.6 (C), 129.5 (CH), 128.0 (C), 125.8 (CH), 124.2 (d, *J* = 5.7 Hz, CH), 115.1 (dd, *J* = 263.2, 254.6 Hz, C), 74.3 (dd, *J* = 28.6, 24.8 Hz, CH), 62.9 (CH_2), 62.6 (d, *J* = 1.9 Hz, CH_2), 25.6 (CH_2), 19.0 (CH_3), 14.0 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -105.9 (dt, *J* = 256.5, 5.1 Hz, 1F), -118.2 (dd, *J* = 256.5, 21.0 Hz, 1F). IR (ATR): 1770, 1500, 1100, 1070, 750 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{14}H_{17}F_2O_3$: 271.1146; found: 271.1151.

***N*,*N*-Diethyl-2,2-difluoro-2-(isochroman-1-yl)acetamide (5af)**



Silica gel column chromatography (hexane/AcOEt = 4/1) gave 86.2 mg (0.304 mmol, 61% yield) of the product as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 7.1 Hz, 1H), 7.29-7.22 (m, 2H), 7.17 (d, *J* = 7.1 Hz, 1H), 5.45 (dd, *J* = 19.2, 6.2 Hz, 1H), 4.23-4.18 (m, 1H), 3.77 (dt, *J* = 10.5, 3.4 Hz, 1H), 3.56-3.36 (m, 4H), 3.02-2.94 (m, 1H), 2.72 (dt, *J* = 16.0, 3.4 Hz, 1H), 1.19 (t, *J* = 6.9 Hz, 3H), 1.18 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.7 (t, *J* = 27.7 Hz, C), 135.8 (C), 129.3 (d, *J* = 1.9 Hz, C), 128.6 (CH), 127.7 (CH), 127.1 (d, *J* = 5.7 Hz, CH), 126.2 (CH), 117.1 (dd, *J* = 266.1, 253.7 Hz, C), 75.0 (dd, *J* = 27.7, 24.8 Hz, CH), 63.5 (CH_2), 42.3 (CH_2), 42.2 (dd, *J* = 9.5, 3.8 Hz, CH_2), 29.1 (CH_2), 14.6 (CH_3), 12.3 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ 102.1 (d, *J* = 263.0 Hz, 1F), 113.1 (dd, *J* = 263.0, 18.8 Hz, 1F). IR (ATR): 1650, 1190, 1110, 750 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{15}H_{20}F_2NO_2$: 284.1462; found: 284.1455.

2.5. Gram-scale experiment

The reaction was carried out in a two-necked flask-type undivided cell equipped with a graphite anode (1 x 5 cm^2) and a platinum cathode (1 x 2 cm^2) (distance between the anode and cathode: 1 cm). After the reaction vessel was charged with 2-phenyl-1,2,3,4-tetrahydroisoquinoline (**1a**) (1.05 g, 5 mmol) and Et_4NBr (210 mg, 1 mmol), dry MeCN (40 mL) and CF_3CH_2OH (2.00 g, 20 mmol) were added. Then, a constant current (5 mA, 2.7 F/mol) was supplied at 0 °C with magnetic stirring. To the undivided cell was added the organozinc reagent (11.3 mL, 0.78 M in THF) prepared through stirring the mixture of Zn powder (1.18 g, 18 mmol) and ethyl 2-bromo-2,2-difluoroacetate (4.06 g, 20 mmol) in dry THF (20 mL) at rt for 5 min.[13] The reaction mixture was stirred at rt for 6 h. Water was added, and then the resulting mixture was extracted with AcOEt. The combined organic layers were dried over Na_2SO_4. Concentration and purification through silica gel column chromatography (hexane/AcOEt = 20/1) gave 1.253 g (3.78 mmol, 76% yield) of the desired product **3aa** as colorless oil.

2.6. Synthesis of compound 6

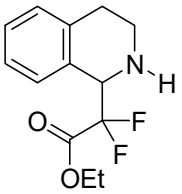
2.6.1. CAN oxidation[15] for 3pa

Ammonium cerium(IV) nitrate (411.2 mg, 0.75 mmol) in H_2O (2.5 mL) was added to the solution of ethyl 2,2-difluoro-2-(2-(4-methoxynaphthalen-1-yl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (**3pa**) (102.9 mg, 0.25 mmol) in MeCN (7.5 mL). After stirring at 0 ºC for 1 h, $NaBH_4$ (47.3 mg, 1.25 mmol) was added at 0 ºC. The mixture was stirred at 0 ºC for 30 min, and water was added. The resulting mixture was filtered through celite, and the celite pad was washed with MeCN and toluene. After the filtrate was extracted with AcOEt, the combined organic layers were dried over Na_2SO_4. Concentration and purification through silica gel column chromatography (hexane/AcOEt = 3/1) gave 47.2 mg (0.185 mmol, 74% yield) of the desired product **6**.

2.6.2. Pd/C-catalyzed reduction for 3qa

To ethyl 2-(2-benzyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-2,2-difluoroacetate (**3qa**) (86.3 mg, 0.25 mmol) in EtOH (4.7 mL) was added Pd/C (23.4 mg, 10% w/w). After stirring under a hydrogen atmosphere at rt for 12 h, the reaction mixture was filtered. Concentration and purification through silica gel column chromatography (hexane/AcOEt = 3/1) gave 62.1 mg (0.243 mmol, 97 % yield) of the desired product **6**.

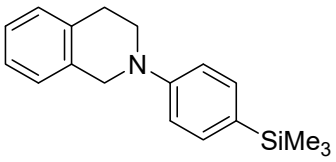
Ethyl 2,2-difluoro-2-(1,2,3,4-tetrahydroisoquinolin-1-yl)acetate (6)



Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (d, *J* = 7.3 Hz, 1H), 7.25-7.18 (m, 2H), 7.15 (d, *J* = 7.3 Hz, 1H), 4.58 (dd, *J* = 20.4, 8.5 Hz, 1H), 4.40-4.28 (m, 2H), 3.26-3.18 (m, 1H), 3.05-2.99 (m, 1H), 2.81-2.69 (m, 2H), 1.76 (brs, 1H), 1.32 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.3 (dd, *J* = 33.4, 31.5 Hz, C), 136.9 (C), 129.33 (C), 129.25 (CH), 128.2 (d, *J* = 4.8 Hz, CH), 127.7 (CH), 125.9 (CH), 116.8 (dd, *J* = 261.3, 254.6 Hz, C), 62.6 (CH_2), 56.5 (dd, *J* = 24.8, 22.9 Hz, CH), 39.6 (d, *J* = 1.9 Hz, CH_2), 29.1 (CH_2), 13.9 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ -102.7 (ddd, *J* = 255.8, 8.8, 2.9 Hz, 1F), -114.5 (dd, *J* = 255.8, 20.2 Hz, 1F). IR (ATR): 3360, 1770, 1190, 1070, 750 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{13}H_{16}F_2NO_2$: 256.1149; found: 256.1148.

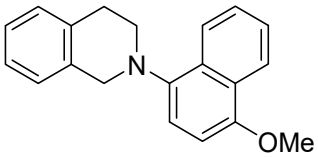
2.7. Synthesis of substrates

2-(4-(Trimethylsilyl)phenyl)-1,2,3,4-tetrahydroisoquinoline (1l)



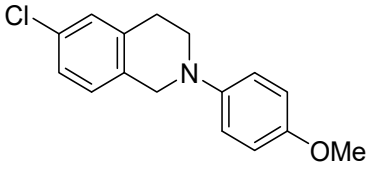
To the solution of 2-(4-bromophenyl)-1,2,3,4-tetrahydroisoquinoline (**1d**) (720.5 mg, 2.5 mmol) in dry THF (10 mL) was added *n*-BuLi (2.0 M in cyclohexane, 1.88 mL, 3.76 mmol) dropwise at -78 ºC. The mixture was stirred at -78 ºC for 2 h. Then, TMSCl (353.1 mg, 3.25 mmol) was added dropwise at -78 ºC. The reaction mixture was gradually warmed to rt and stirred at rt for 6 h. Water was added, and then the resulting mixture was extracted with AcOEt. The combined organic layers were dried over Na_2SO_4. Concentration and purification through silica gel column chromatography (hexane/AcOEt = 20/1) gave 502.3 mg (1.78 mmol, 71% yield) of the desired product as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, *J* =8.1 Hz, 2H), 7.19-7.15 (m, 4H), 6.97 (d, *J* = 8.1 Hz, 2H), 4.44 (s, 2H), 3.59 (t, *J* = 5.7 Hz, 2H), 2.98 (t, *J* = 5.7 Hz, 2H), 0.24 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 150.7 (C), 135.0 (C), 134.5 (CH), 134.4 (C), 128.4 (CH), 128.0 (C), 126.5 (CH), 126.3 (CH), 126.0 (CH), 114.0 (CH), 50.1 (CH_2), 45.8 (CH_2), 29.1 (CH_2), -0.90 (CH_3). IR (ATR): 1590, 1380 1240, 1110, 830 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{18}H_{24}NSi$: 282.1678; found: 282.1686.

2-(4-Methoxynaphthalen-1-yl)-1,2,3,4-tetrahydroisoquinoline (1p)



A reaction tube was charged with BINAP (171.2 mg, 0.275 mmol) and $Pd(OAc)_2$ (56.1 mg, 0.25 mmol), and toluene (12.5 mL) was added. Then, 1-bromo-4-methoxynaphthalene (1186 mg, 5.0 mmol), 1,2,3,4-tetrahydroisoquinoline (799.1 mg, 6.0 mmol), and *t*-BuOK (785.5 mg, 7.0 mmol) was added, and the reaction mixture was stirred at 100 ºC for 4 h. Water was added, and then the resulting mixture was extracted with AcOEt. The combined organic layers were dried over Na_2SO_4. Concentration and purification through silica gel column chromatography (hexane/AcOEt = 20/1) gave 954.9 mg (3.30 mmol, 66% yield) of the desired product as white solids of mp 112-113 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.28-8.25 (m, 2H), 7.52-7.47 (m, 2H), 7.22-7.17 (m, 3H), 7.12-7.09 (m, 2H), 6.76 (d, *J* = 8.3 Hz, 1H), 4.25 (s, 2H), 3.99 (s, 3H), 3.66-2.76 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 152.0 (C), 142.8 (C), 135.6 (C), 134.5 (C), 130.2 (C), 129.0 (CH), 126.5 (C), 126.4 (CH), 126.2 (CH), 126.1 (CH), 125.7 (CH), 125.3 (CH), 123.4 (CH), 122.3 (CH), 115.0 (CH), 103.3 (CH), 55.8 (CH_2), 55.5 (CH_3), 51.6 (CH_2), 29.8 (CH_2). IR (ATR): 1590, 1260, 1090, 1020, 810 cm^{-1}. HRMS (DART) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{20}NO$: 290.1545; found: 290.1546.

6-Chloro-2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (1r)

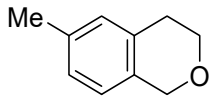


After a flask was charged with 6-chloro-3,4-dihydroisoquinolin-1(2*H*)-one[16] (908.1 mg, 5.0 mmol), 4-iodoanisole (1755 mg, 7.5 mmol), CuI (95.2 mg, 0.5 mmol), and K_3PO_4 (2123 mg, 10 mmol), toluene (5.0 mL) was added. Then, dipivaloylmethane (92.1 mg, 0.5 mmol) was added, and the reaction mixture was refluxed for 24 h. Water was added at rt, and then the resulting mixture was extracted with AcOEt. The combined organic layers were dried over Na_2SO_4. Concentration and purification through silica gel column chromatography (hexane/AcOEt = 4/1) gave 951.2 mg (3.31 mmol, 66% yield) of 6-chloro-2-(4-methoxyphenyl)-3,4-dihydroisoquinoline-1(2*H*)-one as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, *J* = 8.5 Hz, 1H), 7.34 (dd, *J* = 8.5, 2.1 Hz, 1H), 7.30-7.27 (m, 2H), 7.244-7.239 (m, 1H), 6.96-6.92 (m, 2H), 3.94 (t, *J* = 6.4 Hz, 2H), 3.83 (s, 3H), 3.12 (t, *J* = 6.4 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.6 (C), 157.9 (C), 139.9 (C), 137.9 (C), 135.7 (C), 130.3 (CH), 128.2 (C), 127.5 (CH), 126.9 (CH), 126.6 (CH), 114.2 (CH), 55.5 (CH_3), 49.5 (CH_2), 28.4 (CH_2). IR (ATR):

1510, 1250, 1090, 1030, 840 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{16}H_{15}{}^{35}ClNO_2$: 288.0791; found: 288.0781.

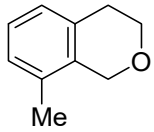
A flask was charged with $LiAlH_4$ (56.9 mg, 1.5 mmol), and dry THF (12 mL) was added. Then, 6-chloro-2-(4-methoxyphenyl)-3,4-dihydroisoquinoline-1(2*H*)-one (287.7 mg, 1.0 mmol) was added at 0 ºC, and the reaction mixture was refluxed for 20 h. Water and aqueous 1M NaOH were added, and then the resulting mixture was extracted with AcOEt. The combined organic layers were dried over Na_2SO_4. Concentration and purification through silica gel column chromatography (hexane/AcOEt = 15/1) gave 167.0 mg (0.61 mmol, 61% yield) of the desired product as colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.15-7.14 (m, 2H), 7.07-7.04 (m, 1H), 6.99-6.95 (m, 2H), 6.89-6.85 (m, 2H), 4.24 (s, 2H), 3.78 (s, 3H), 3.42 (t, *J* = 6.0 Hz, 2H), 2.95 (t, *J* = 6.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 153.7 (C), 145.0 (C), 136.4 (C), 133.1 (C), 131.7 (C), 128.5 (CH), 127.8 (CH), 126.1 (CH), 118.2 (CH), 114.5 (CH), 55.6 (CH_3), 52.3 (CH_2), 48.2 (CH_2), 28.9 (CH_2). IR (ATR): 1510, 1240, 1190, 1090, 1030, 810 cm^{-1}. HRMS (DART) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{17}{}^{35}ClNO$: 274.0999; found: 274.0988.

6-Methylisochroman (4b)



To the solution of 6-bromoisochroman[17] (426.1 mg, 2.0 mmol) in dry THF (8.0 mL) was added *n*-BuLi (2.0 M in cyclohexane, 1.5 mL, 3.0 mmol) dropwise at -78 ºC. The mixture was stirred at -78 ºC for 2 h. Then, dimethyl sulfate (252.3 mg, 2.0 mmol) was added dropwise at -78 ºC. The reaction mixture was gradually warmed to rt and stirred at rt for 6 h. Water was added, and then the resulting mixture was extracted with AcOEt. The combined organic layers were dried over Na_2SO_4. Concentration and purification through silica gel column chromatography (hexane/AcOEt = 15/1) gave 174.1 mg (1.17 mmol, 59% yield) of the desired product as colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.02 (d, *J* = 7.8 Hz, 1H), 6.98 (d, *J* = 7.8 Hz, 1H), 6.80 (s, 1H), 4.74 (s, 2H), 3.96 (t, *J* = 5.7 Hz, 2H), 2.82 (t, *J* = 5.7 Hz, 2H), 2.30 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.5 (C), 134.7 (C), 130.1 (C), 128.7 (CH), 127.1 (CH), 124.8 (CH), 67.9 (CH_2), 65.5 (CH_2), 27.9 (CH_2), 21.0 (CH_3). IR (ATR): 1500, 1230, 1100, 810 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{10}H_{13}O$: 149.0966; found: 149.0972.

8-Methylisochroman (4f)



To the solution of 8-bromoisochroman[17] (426.1 mg, 2.0 mmol) in dry THF (8.0 mL) was added *n*-BuLi (2.0 M in cyclohexane, 1.5 mL, 3.0 mmol) dropwise at -78 ºC. The mixture was stirred

at -78 ºC for 2 h. Then, dimethyl sulfate (252.3 mg, 2.0 mmol) was added dropwise at -78 ºC. The reaction mixture was gradually warmed to rt and stirred at rt for 6 h. Water was added, and then the resulting mixture was extracted with AcOEt. The combined organic layers were dried over Na_2SO_4. Concentration and purification through silica gel column chromatography (hexane/AcOEt = 15/1) gave 186.2 mg (1.26 mmol, 63% yield) of the desired product as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.10-7.03 (m, 2H), 6.84 (d, *J* = 7.3 Hz, 1H), 4.77 (s, 2H), 4.02 (t, *J* = 5.7 Hz, 2H), 2.71 (t, *J* = 5.7 Hz, 2H), 2.23 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 136.4 (C), 134.7 (C), 131.7 (C), 127.6 (CH), 125.6 (CH), 122.0 (CH), 68.2 (CH_2), 65.5 (CH_2), 26.0 (CH_2), 18.8 (CH_3). IR (ATR): 1510, 1230, 1100, 810 cm^{-1}. HRMS (DART): *m/z* $[M+H]^+$ Calcd for $C_{10}H_{13}O$: 149.0966; found: 149.0962.

3. References

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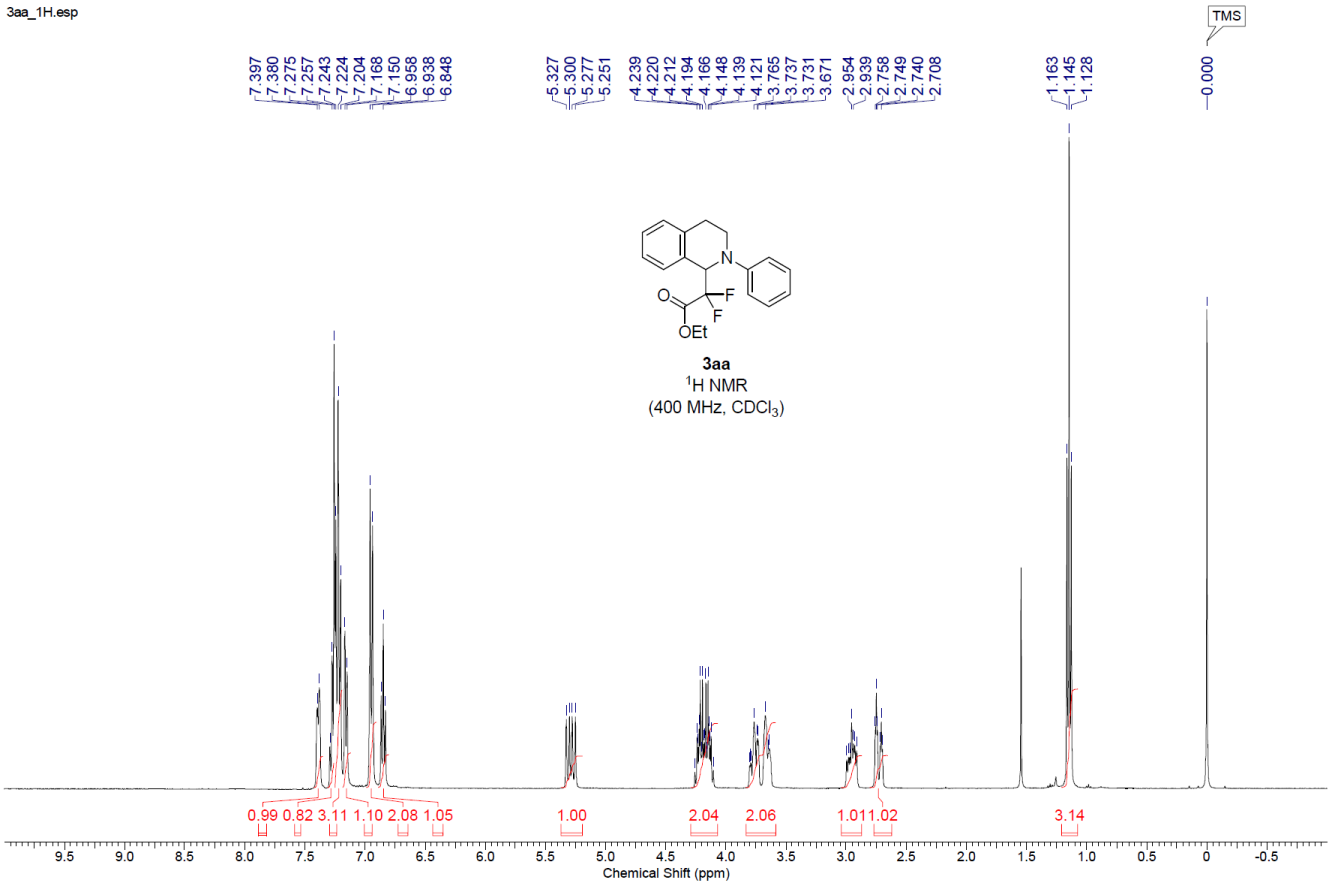
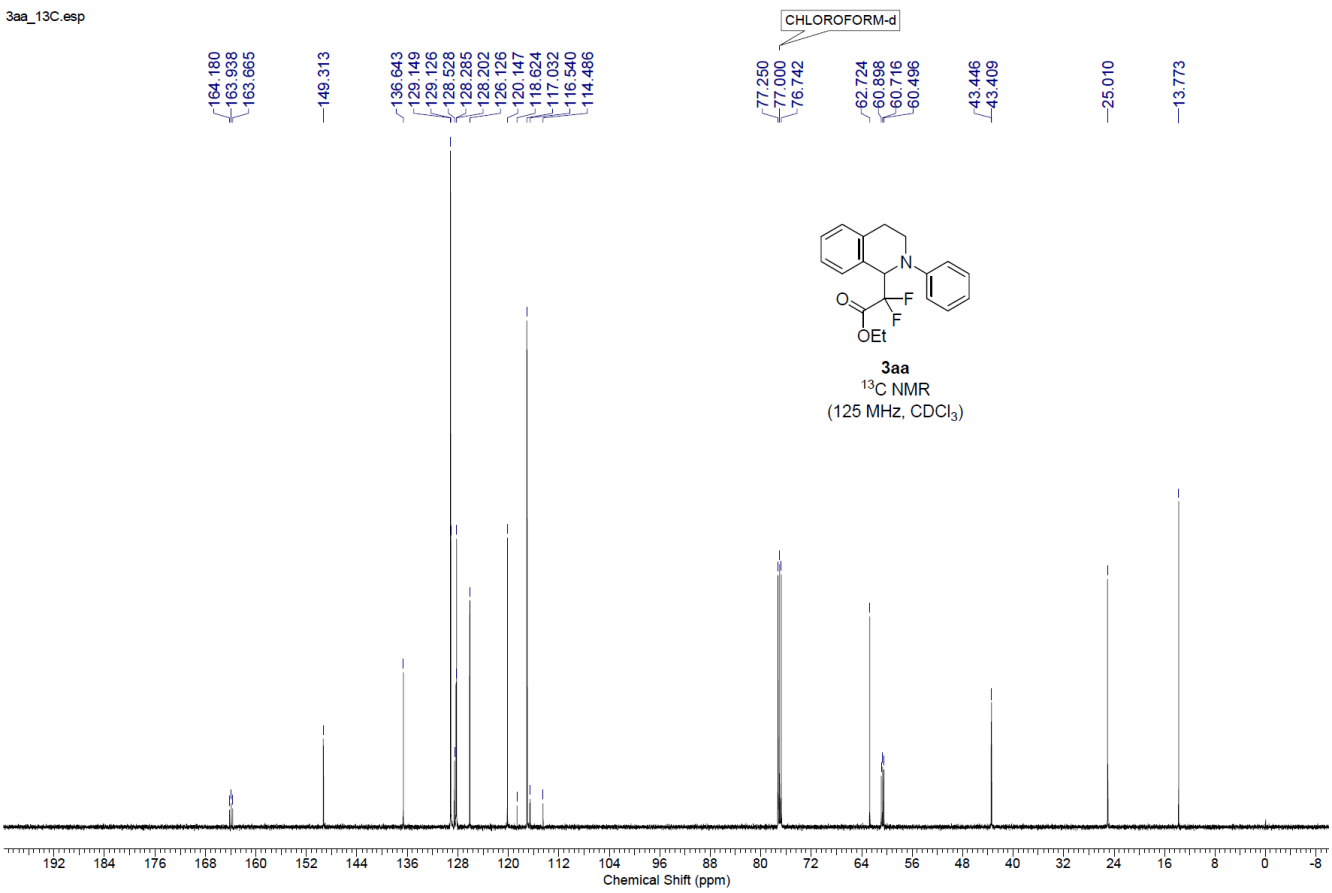
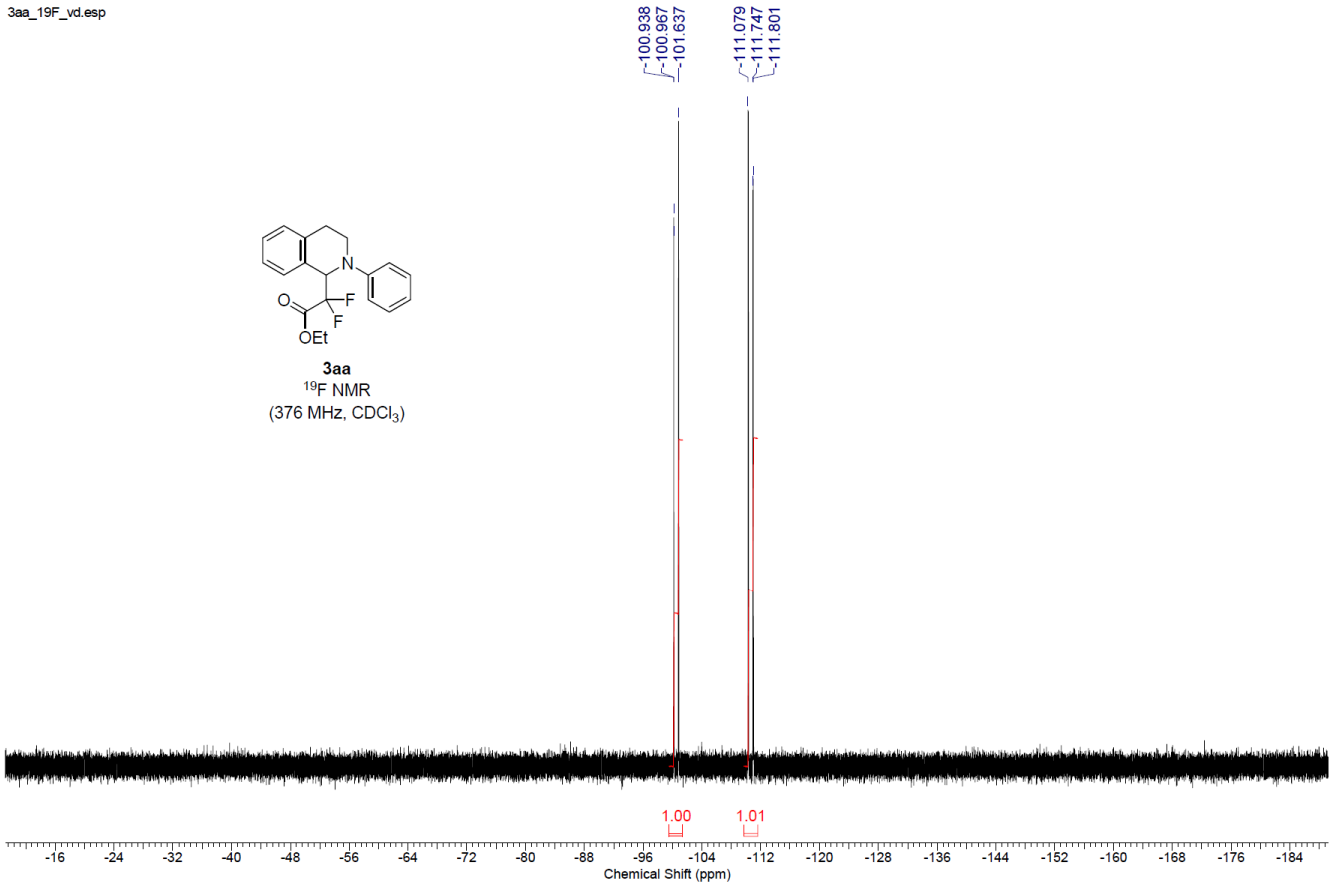
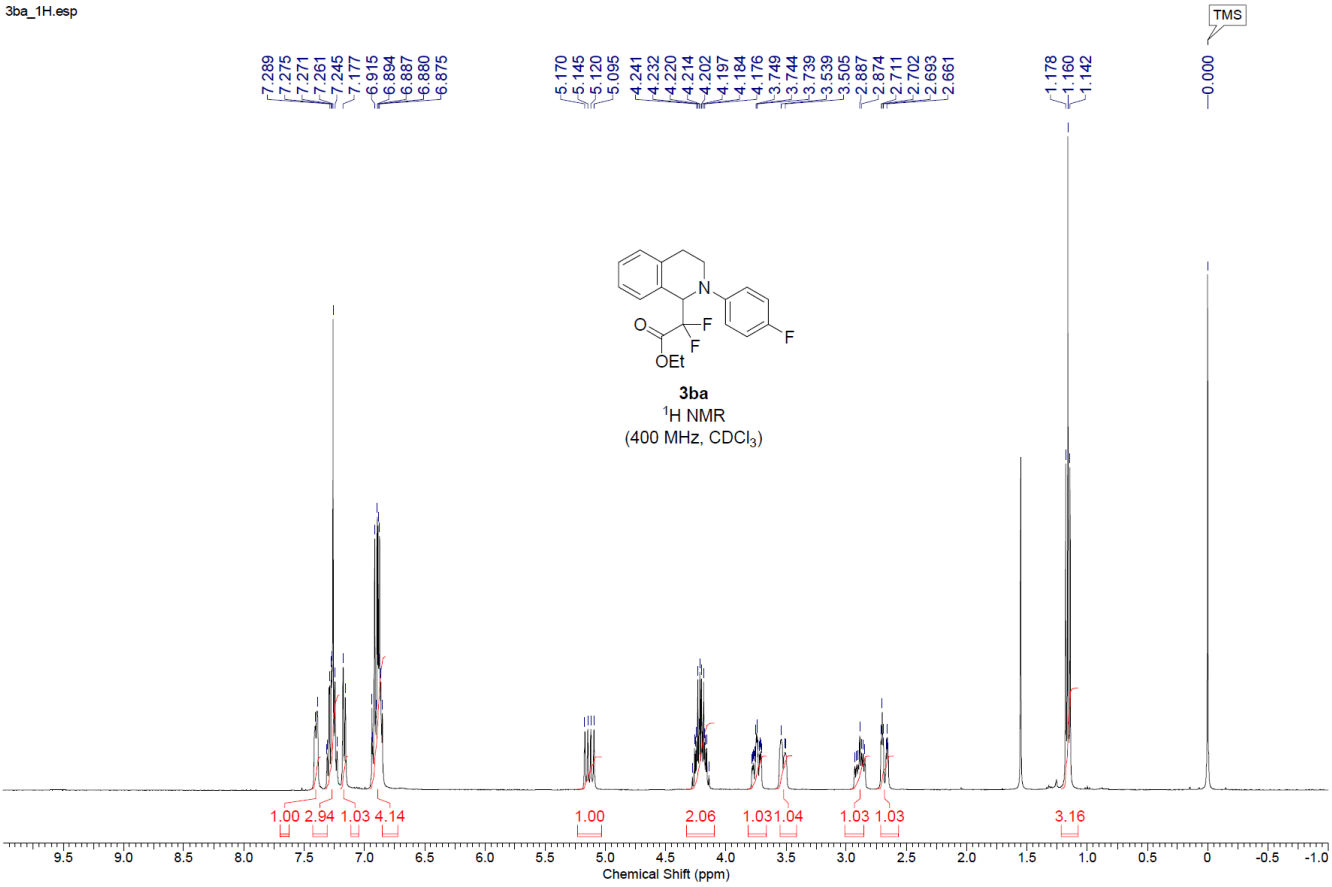


3aa
^{1}H NMR
(400 MHz, $CDCl_3$)

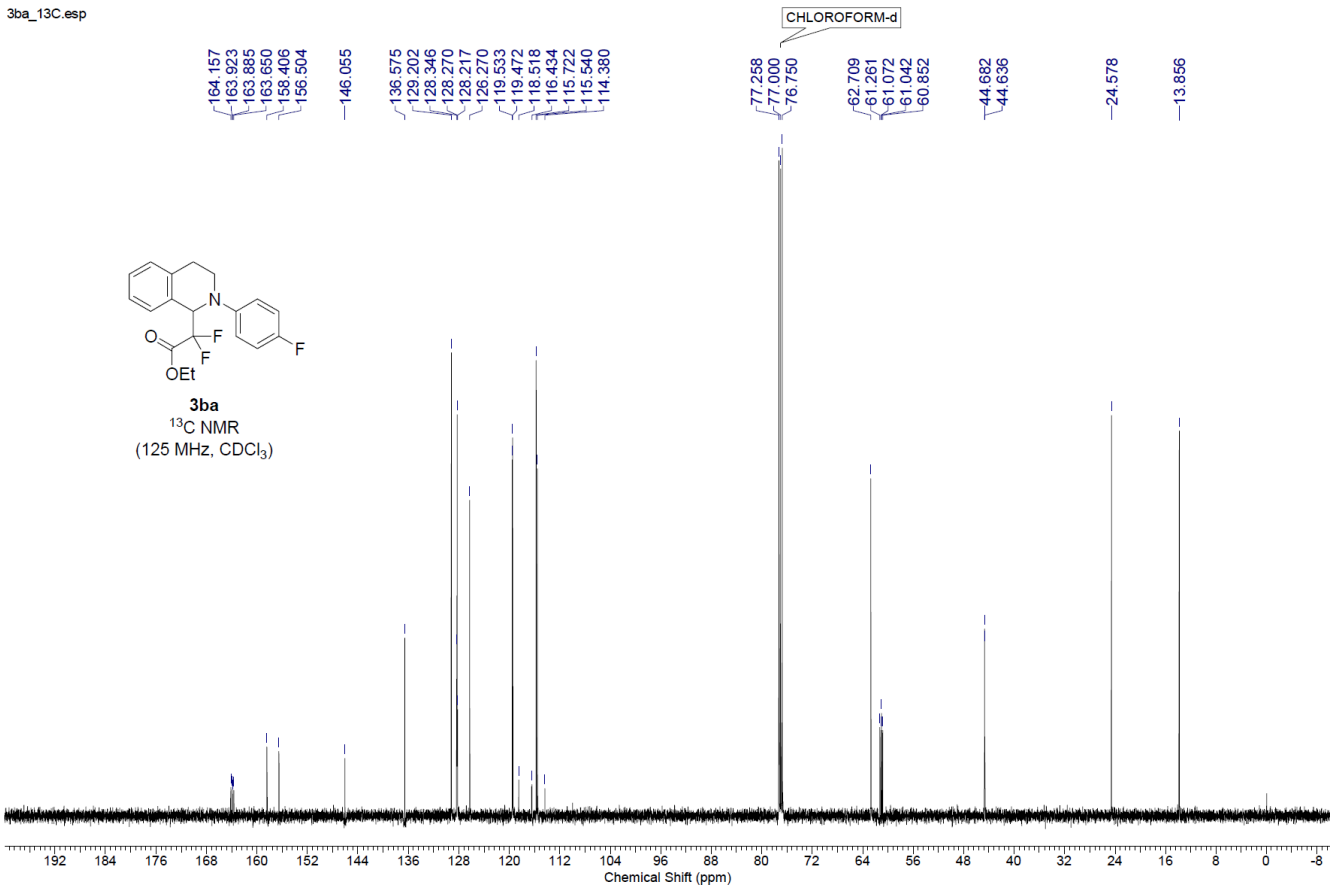


3aa
^{13}C NMR
(125 MHz, $CDCl_3$)

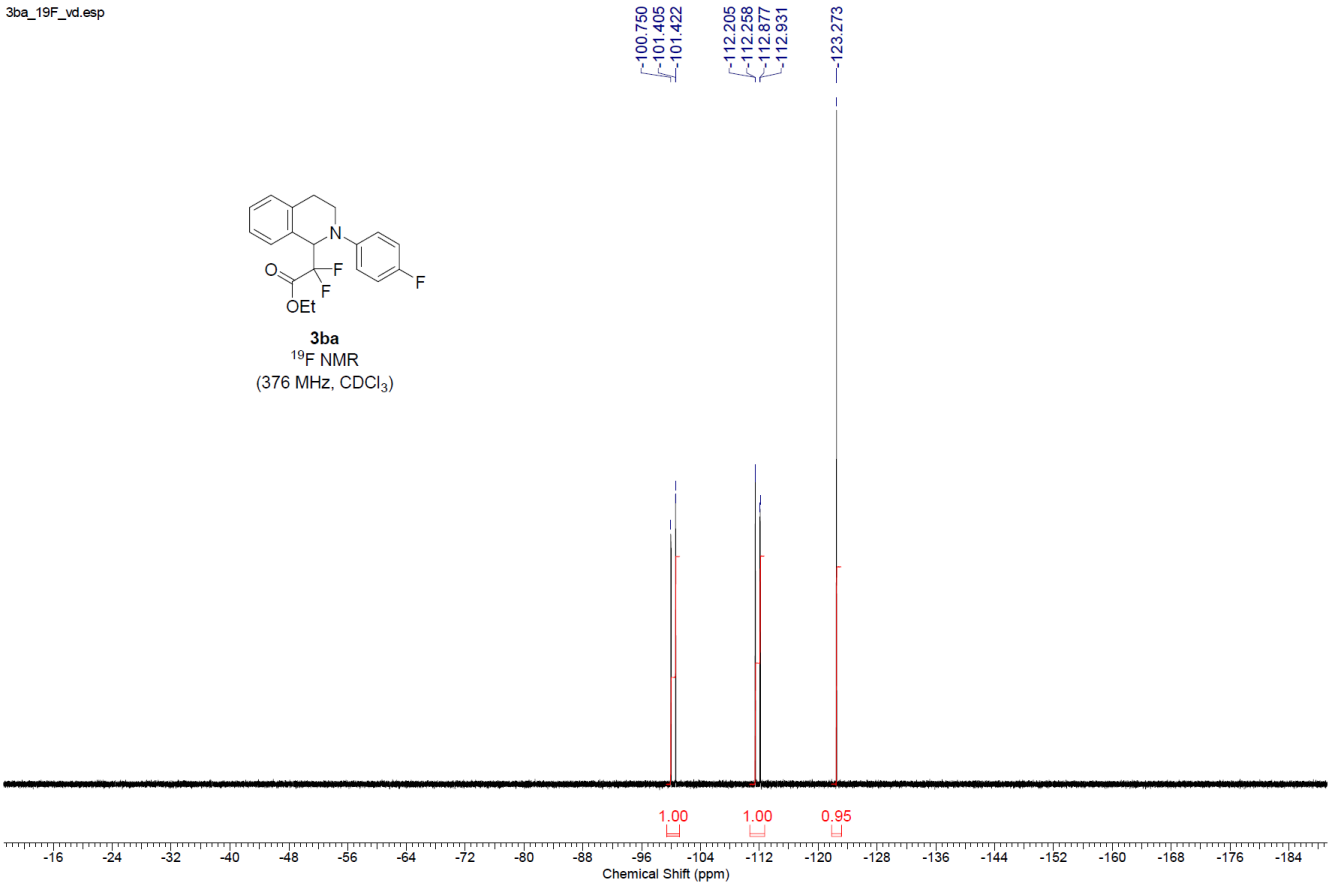

3aa_19F_vd.esp
-100.938
-100.967
-101.637
-111.079
-111.747
-111.801
O
N
F
F
OEt
3aa
19F NMR
(376 MHz, CDCl3)
1.00
1.01
-16
-24
-32
-40
-48
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
-184
Chemical Shift (ppm)



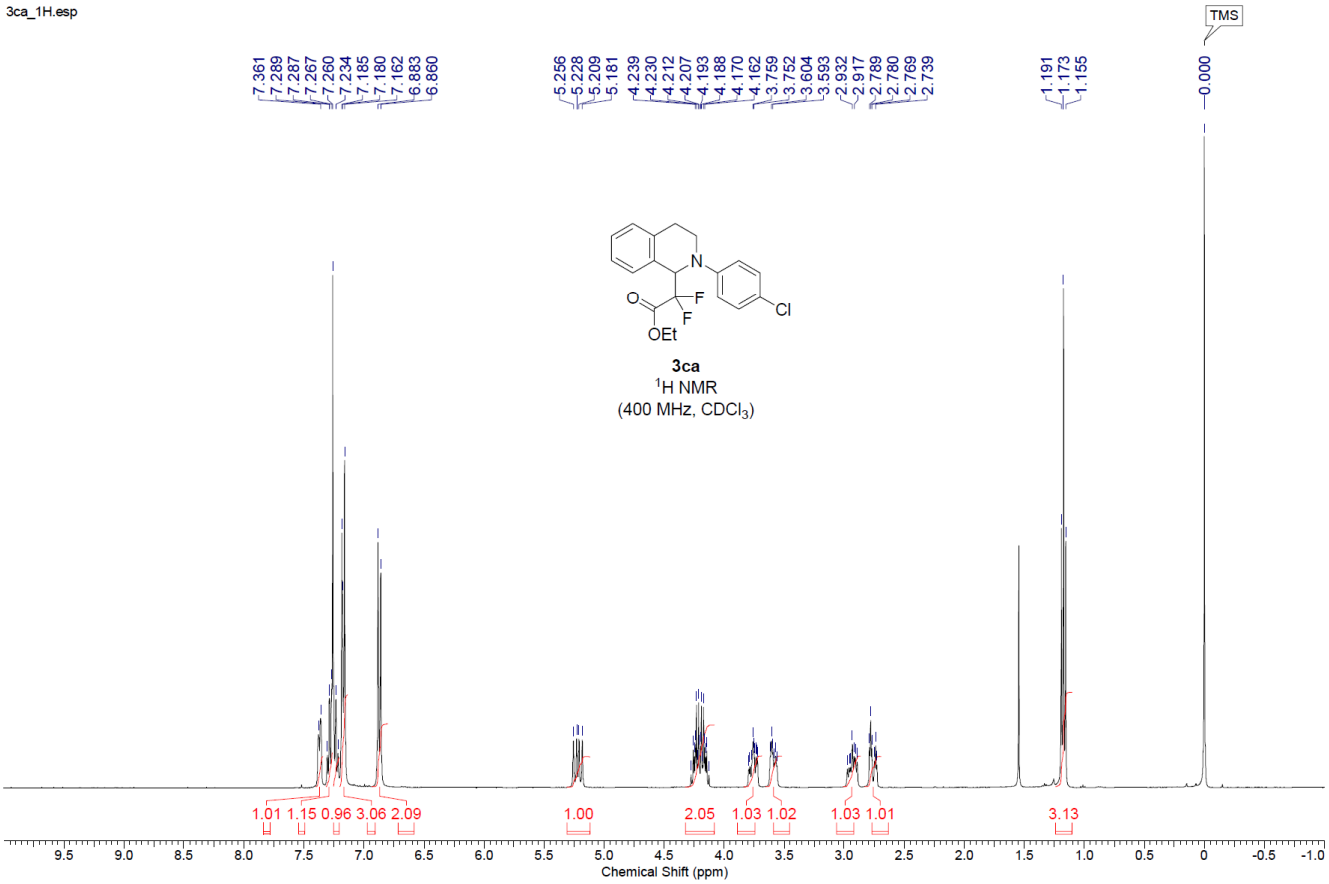
3ba
^{1}H NMR
(400 MHz, $CDCl_3$)



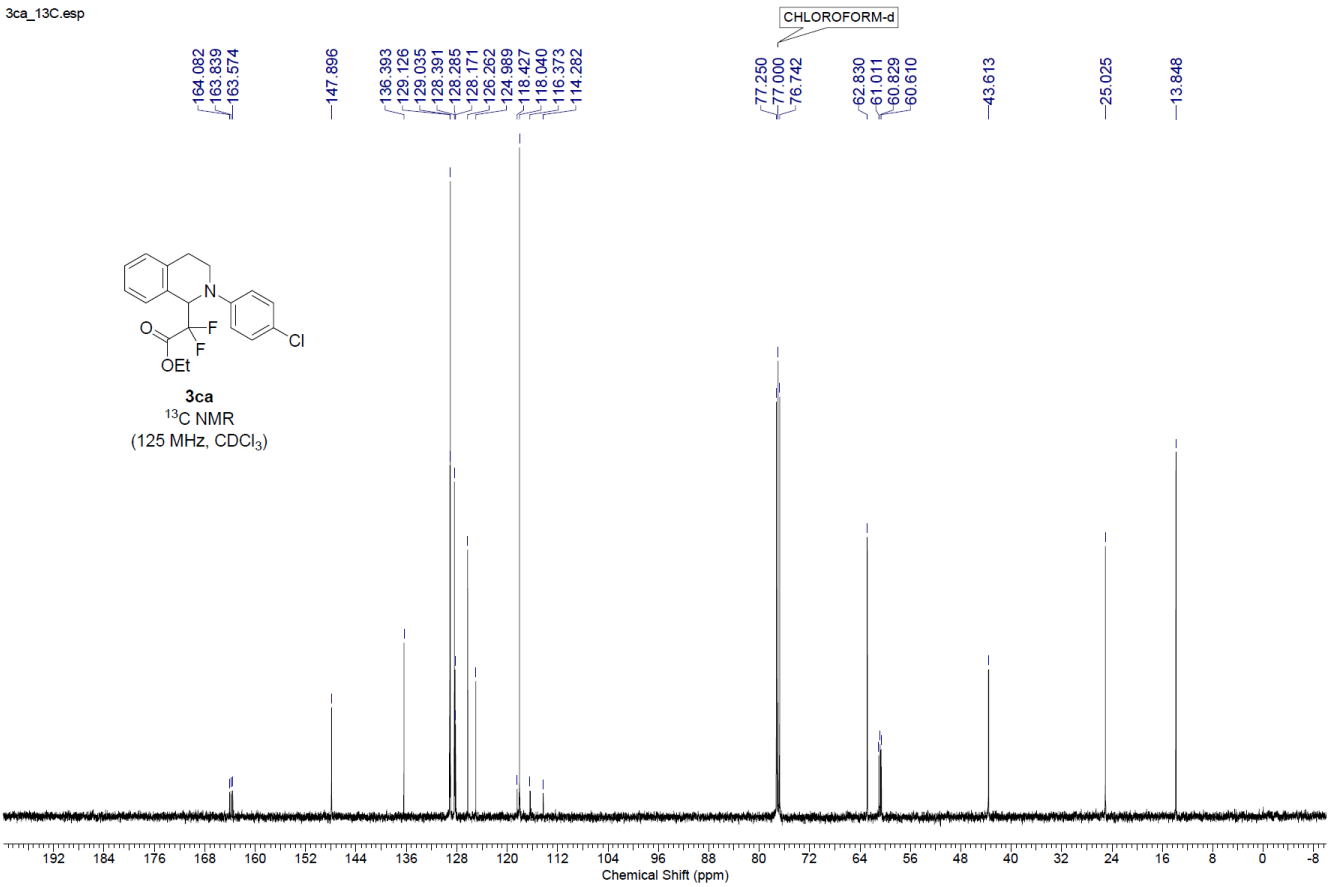
3ba
^{13}C NMR
(125 MHz, $CDCl_3$)



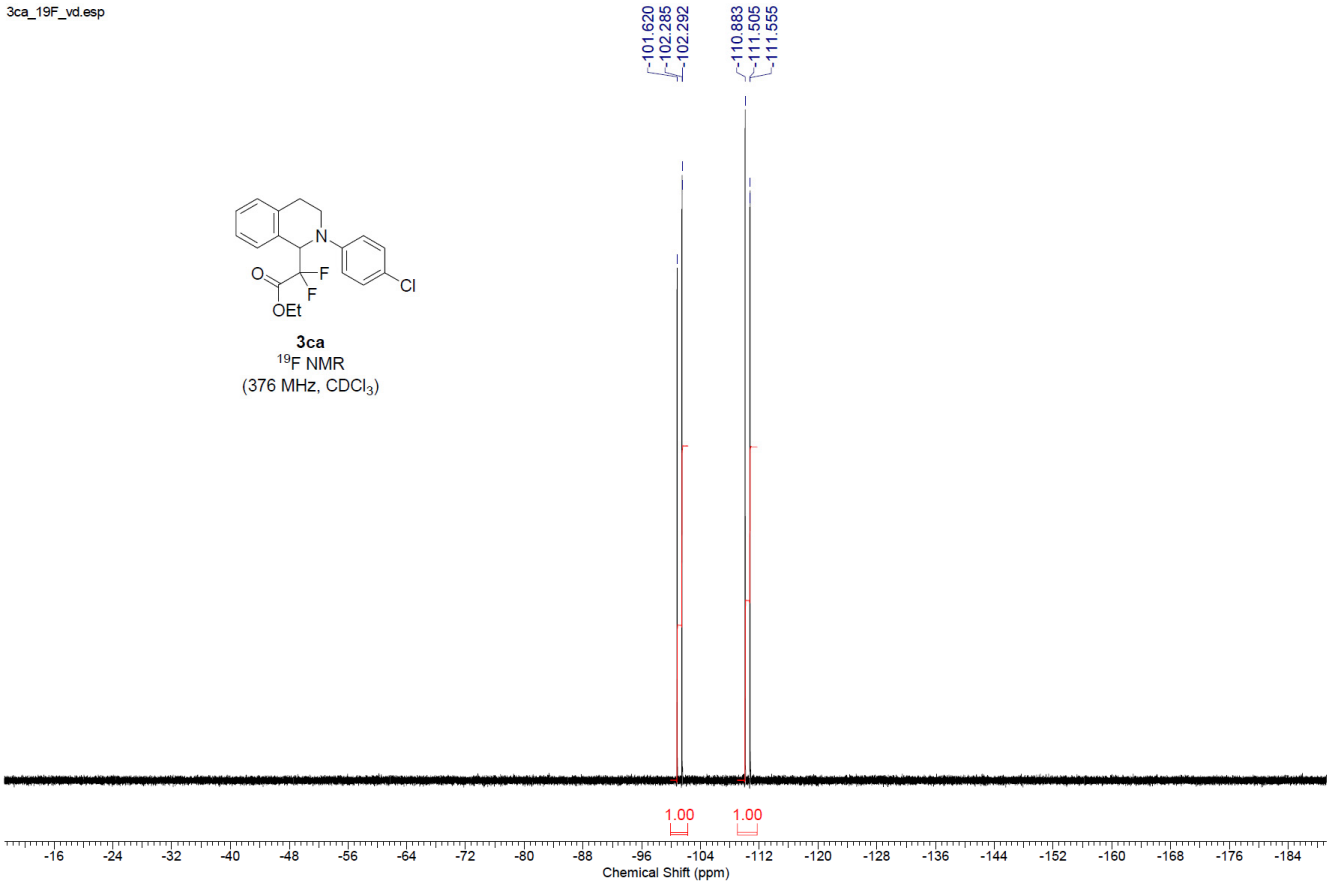
3ba
^{19}F NMR
(376 MHz, $CDCl_3$)

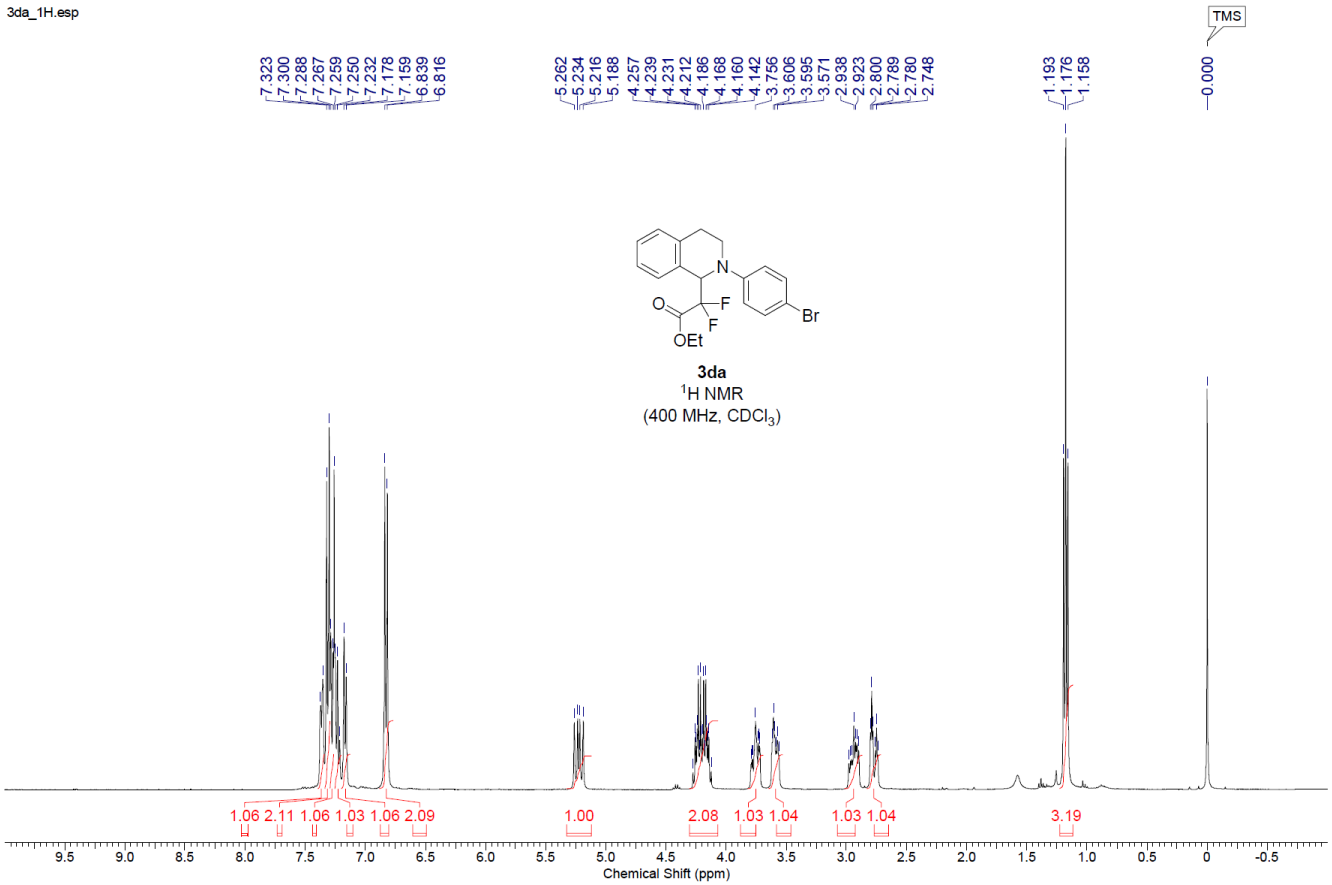


3ca
^{1}H NMR
(400 MHz, $CDCl_3$)



3ca
^{13}C NMR
(125 MHz, $CDCl_3$)


3ca_19F_vd.esp
-101.620
-102.285
-102.292
-110.883
-111.505
-111.555
N
O
F
F
OEt
Cl
3ca
19F NMR
(376 MHz, CDCl3)
1.00
1.00
-16
-24
-32
-40
-48
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
-184
Chemical Shift (ppm)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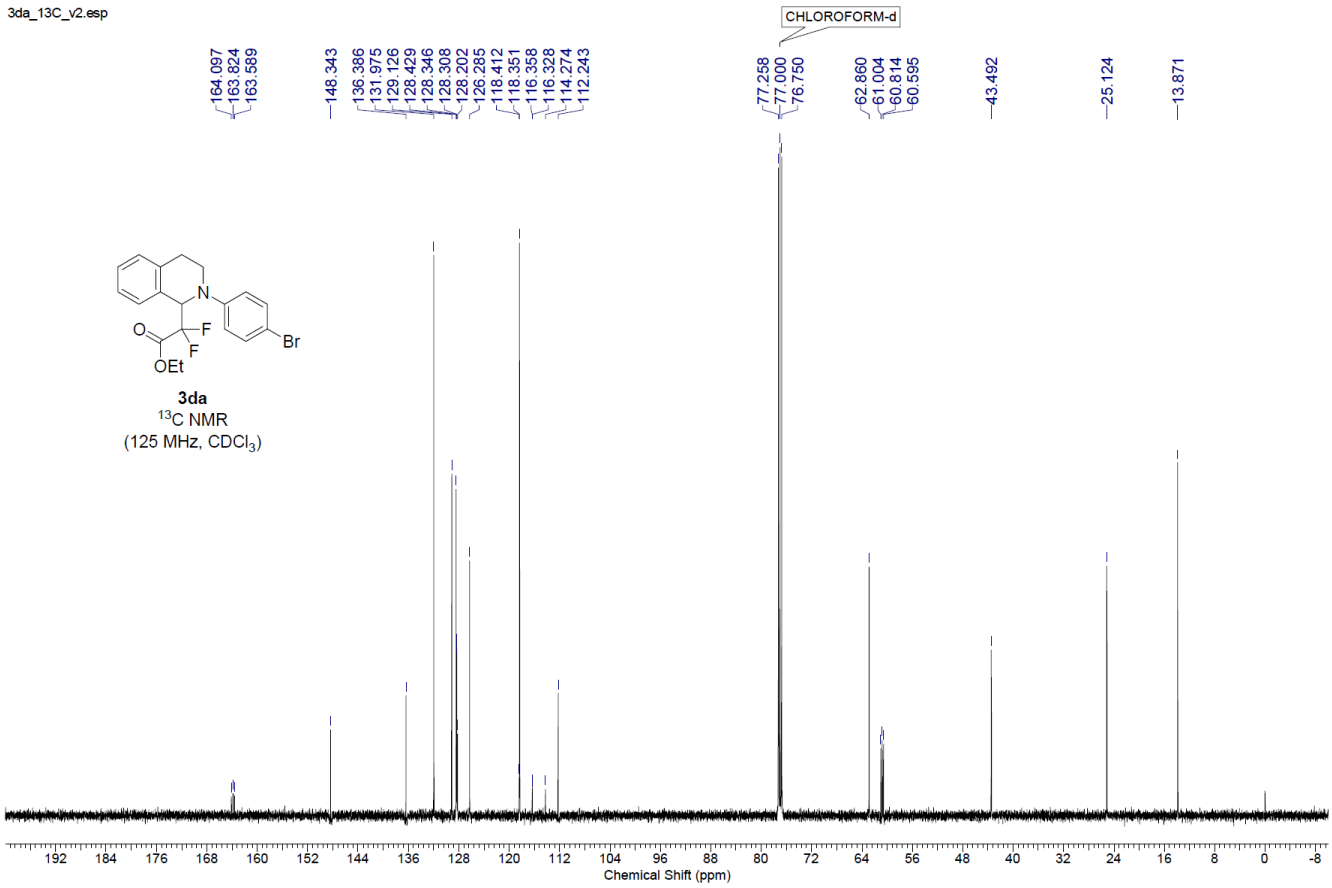
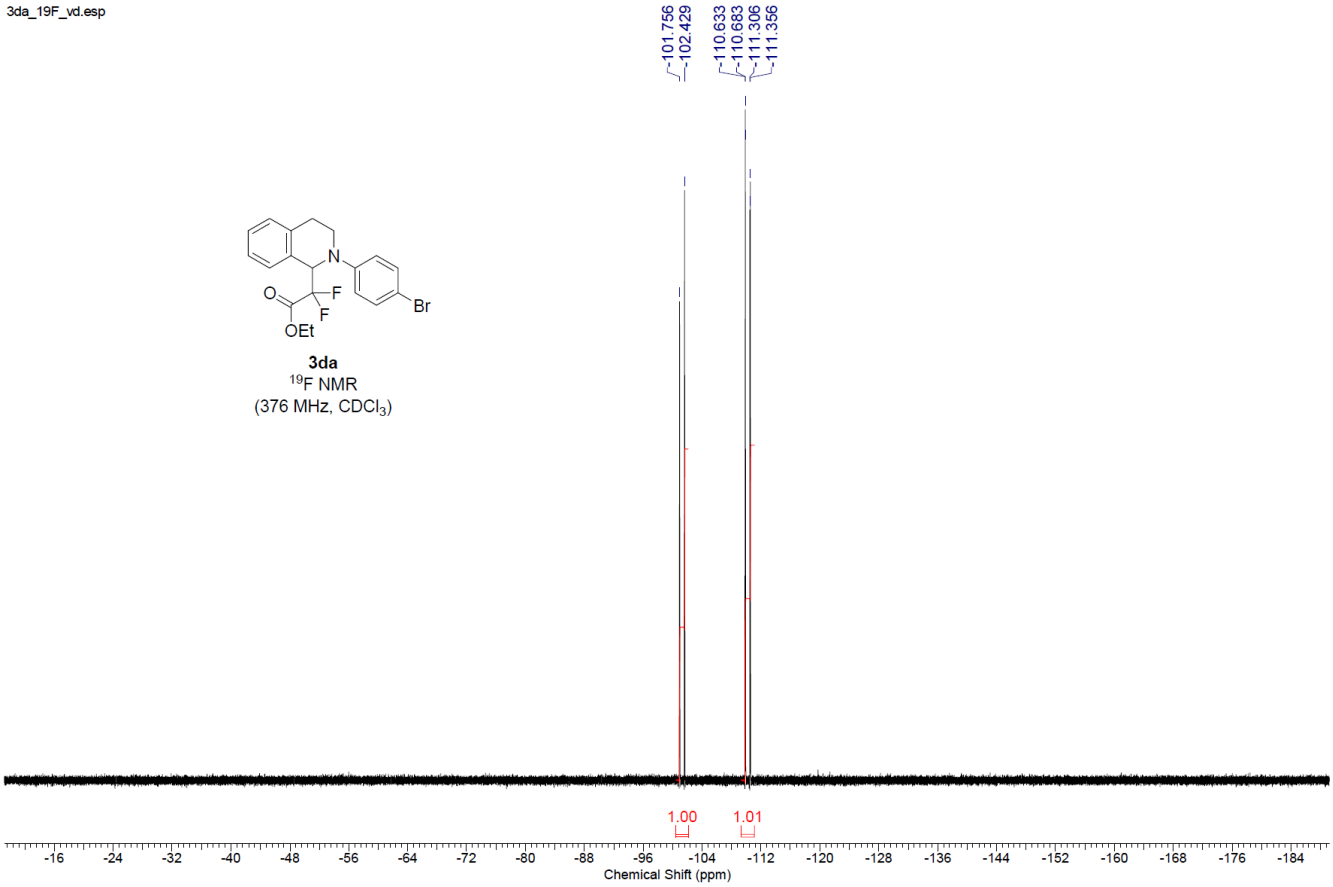
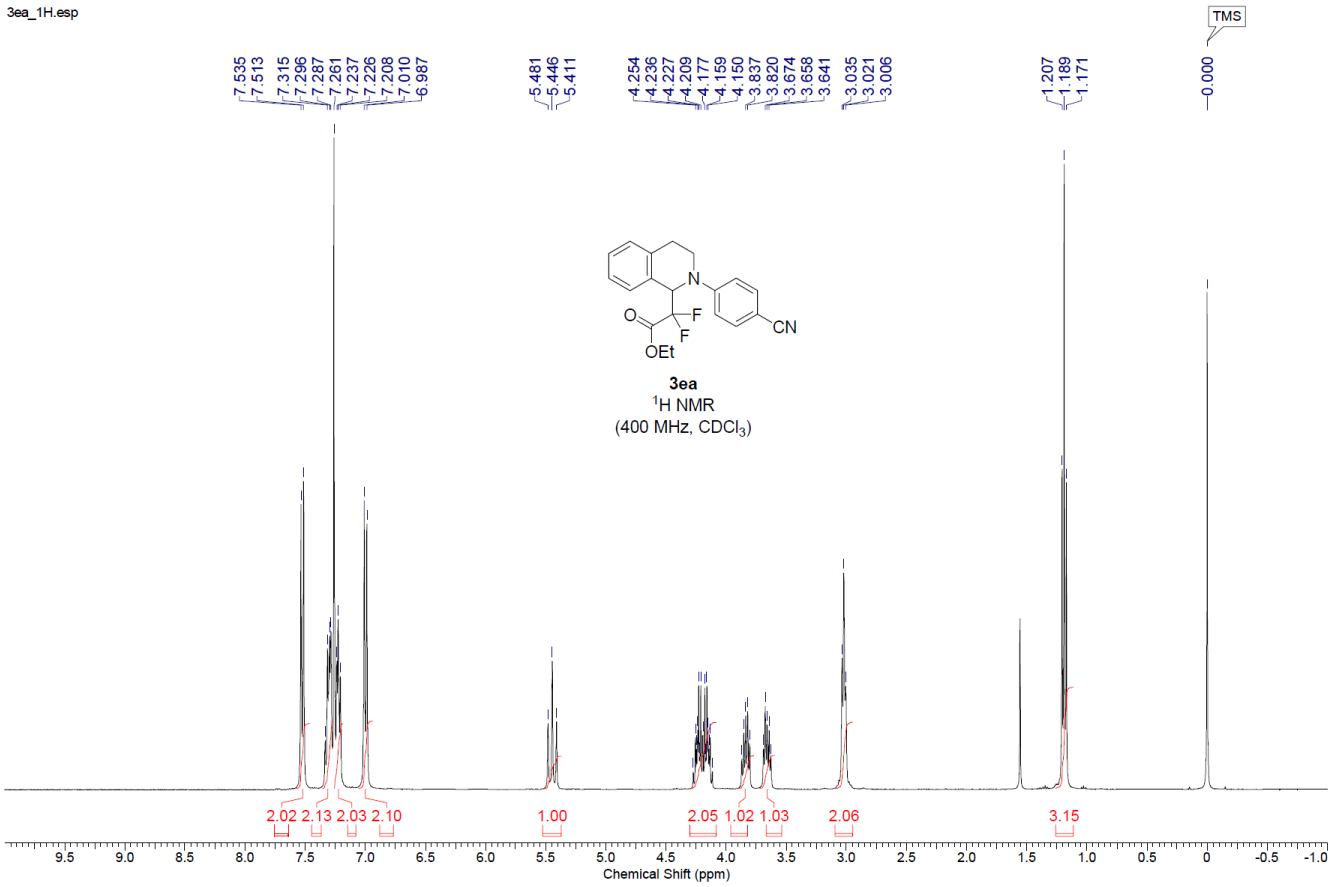
TMS
7.323
7.300
7.288
7.267
7.259
7.250
7.232
7.178
7.159
6.839
6.816
5.262
5.234
5.216
5.188
4.257
4.239
4.231
4.212
4.186
4.168
4.160
4.142
3.756
3.606
3.595
3.571
2.938
2.923
2.800
2.789
2.780
2.748
1.193
1.176
1.158
0.000
N
O
F
F
OEt
Br
3da
1H NMR
(400 MHz, CDCl3)
1.06 2.11 1.06 1.03 1.06 2.09
1.00
2.08
1.03 1.04
1.03 1.04
3.19
Chemical Shift (ppm)


3da_13C_v2.esp
CHLOROFORM-d
164.097
163.824
163.589
148.343
136.386
131.975
129.126
128.429
128.346
128.308
128.202
126.285
118.412
118.351
116.358
116.328
114.274
112.243
77.258
77.000
76.750
62.860
61.004
60.814
60.595
43.492
25.124
13.871
N
O
F
F
OEt
Br
3da
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)


3da_19F_vd.esp
-101.756
-102.429
-110.633
-110.683
-111.306
-111.356
N
O
F
F
OEt
Br
3da
19F NMR
(376 MHz, CDCl3)
1.00
1.01
-16
-24
-32
-40
-48
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
-184
Chemical Shift (ppm)


3ea_1H.esp
TMS
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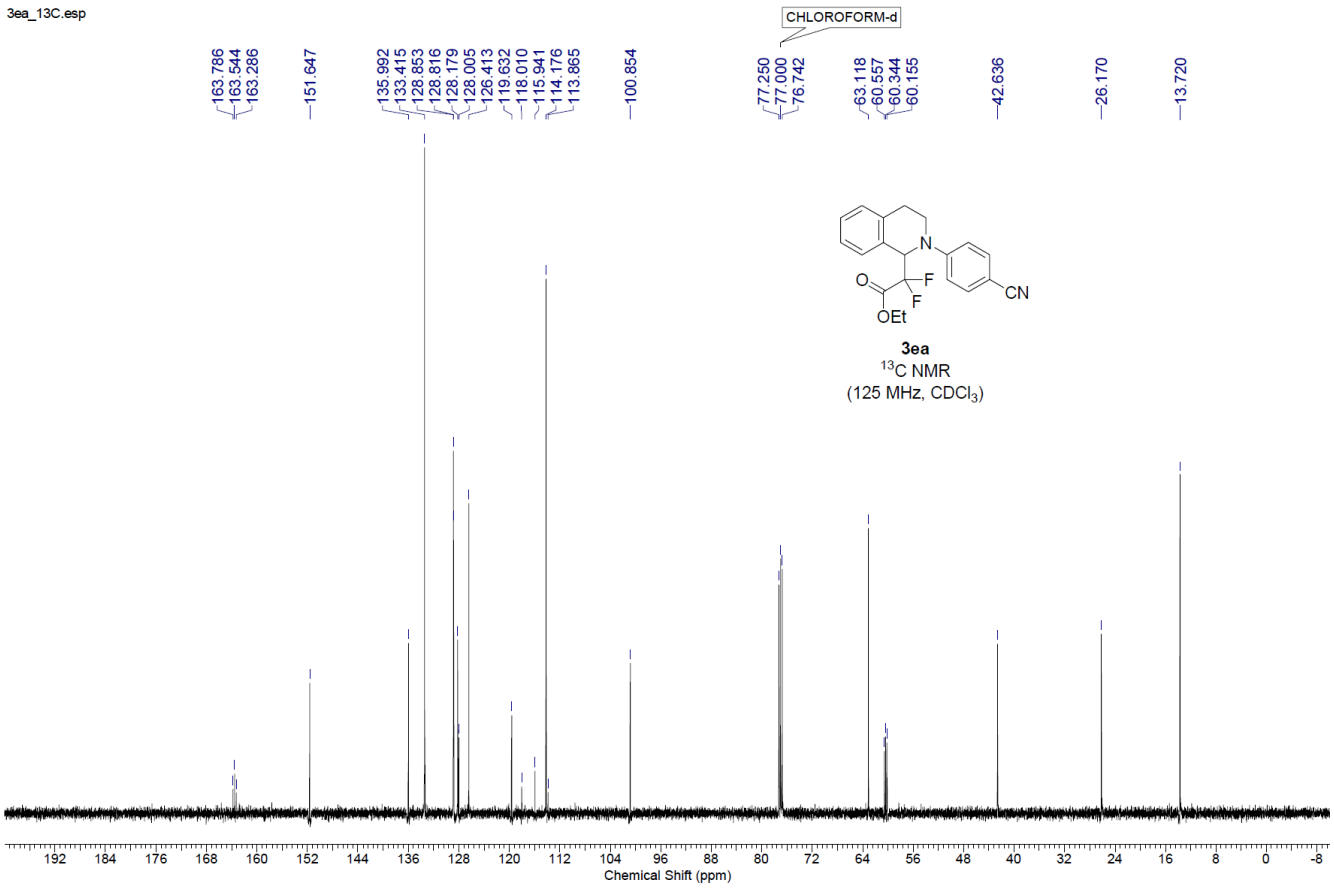
7.513
7.315
7.296
7.287
7.261
7.237
7.226
7.208
7.010
6.987
5.481
5.446
5.411
4.254
4.236
4.227
4.209
4.177
4.159
4.150
3.837
3.820
3.674
3.658
3.641
3.035
3.021
3.006
1.207
1.189
1.171
0.000
O
F
F
N
CN
OEt
3ea
1H NMR
(400 MHz, CDCl3)
2.02 2.13 2.03 2.10
1.00
2.05 1.02 1.03
2.06
3.15
Chemical Shift (ppm)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CHLOROFORM-d
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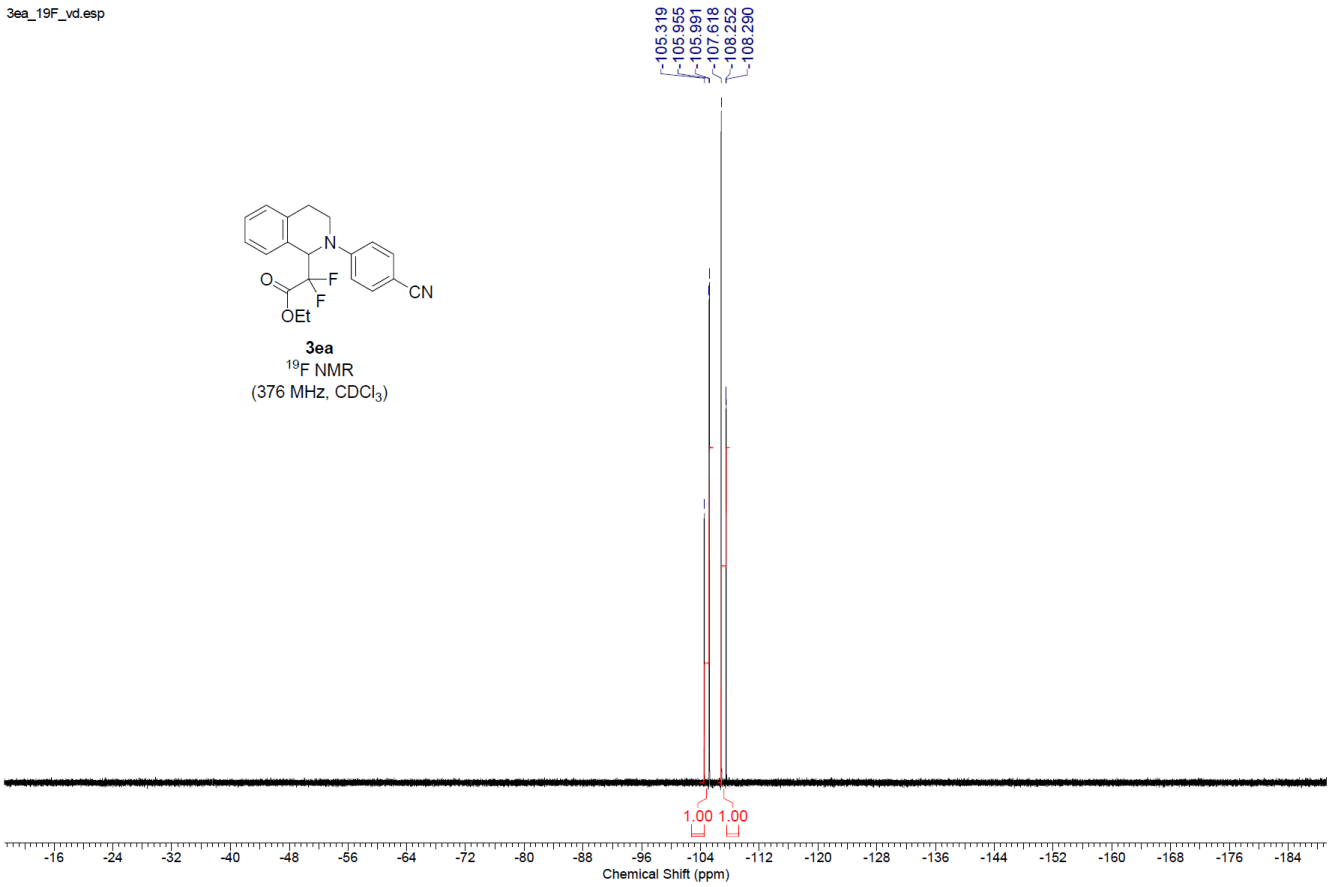
163.544
163.286
151.647
135.992
133.415
128.853
128.816
128.179
128.005
126.413
119.632
118.010
115.941
114.176
113.865
100.854
77.250
77.000
76.742
63.118
60.557
60.344
60.155
42.636
26.170
13.720
O
F
F
N
CN
OEt
3ea
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)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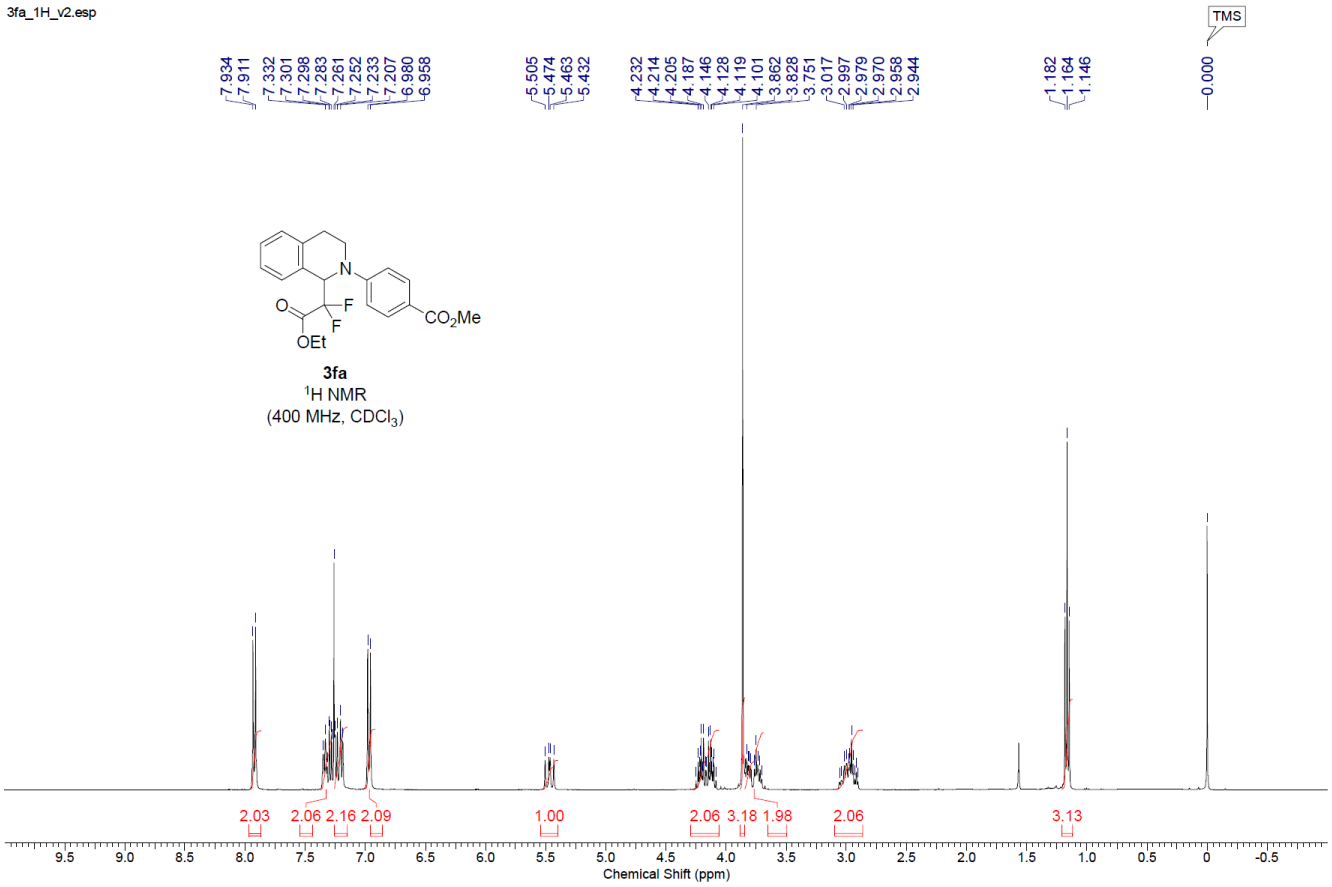
-105.955
-105.991
-107.618
-108.252
-108.290
N
O
F
F
OEt
CN
3ea
19F NMR
(376 MHz, CDCl3)
1.00 1.00
-16 -24 -32 -40 -48 -56 -64 -72 -80 -88 -96 -104 -112 -120 -128 -136 -144 -152 -160 -168 -176 -184
Chemical Shift (ppm)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TMS
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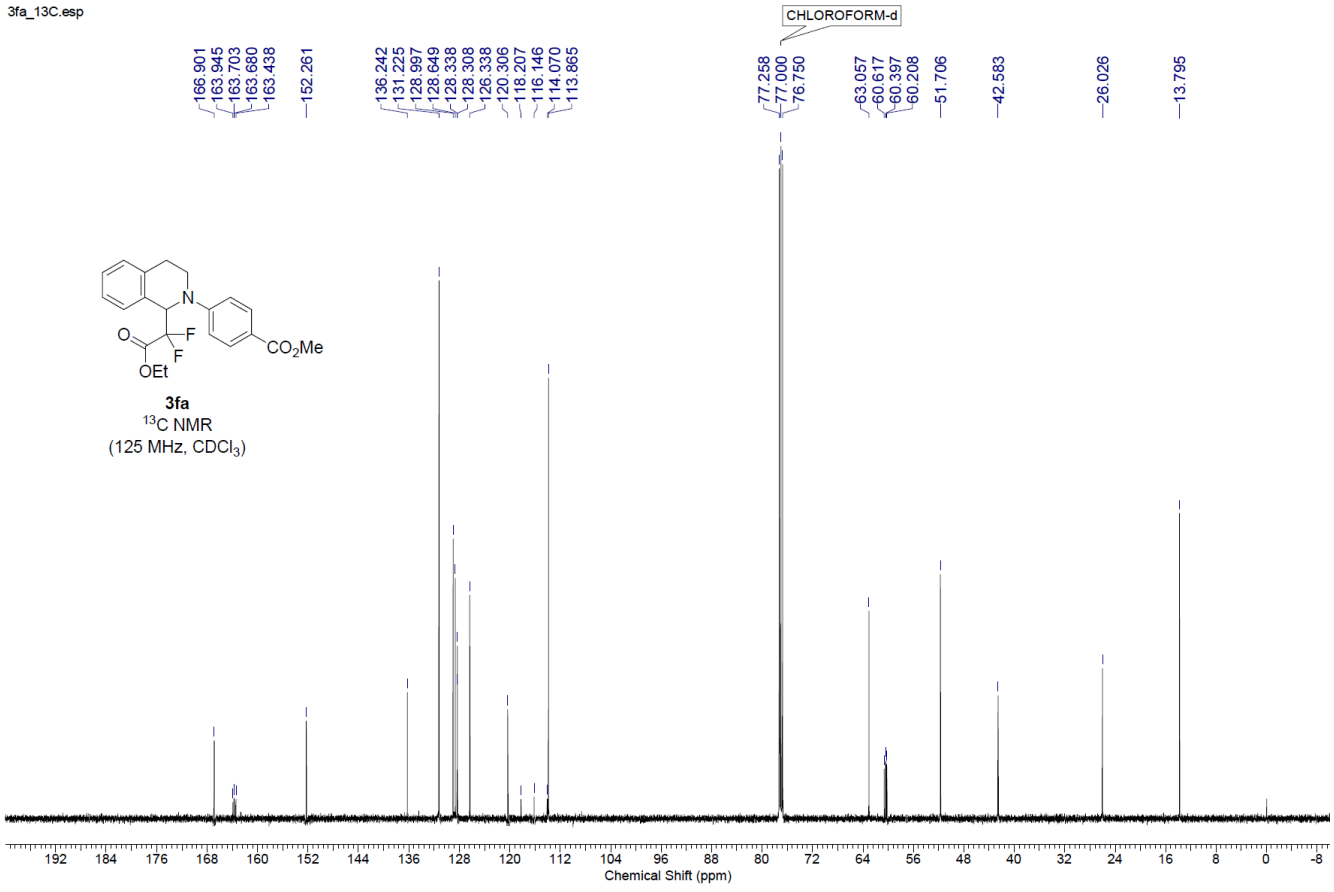
7.911
7.332
7.301
7.298
7.283
7.261
7.252
7.233
7.207
6.980
6.958
5.505
5.474
5.463
5.432
4.232
4.214
4.205
4.187
4.146
4.128
4.119
4.101
3.862
3.828
3.751
3.017
2.997
2.979
2.970
2.958
2.944
1.182
1.164
1.146
0.000
N
O
F
F
OEt
CO2Me
3fa
1H NMR
(400 MHz, CDCl3)
2.03
2.06
2.16
2.09
1.00
2.06
3.18
1.98
2.06
3.13
Chemical Shift (ppm)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CHLOROFORM-d
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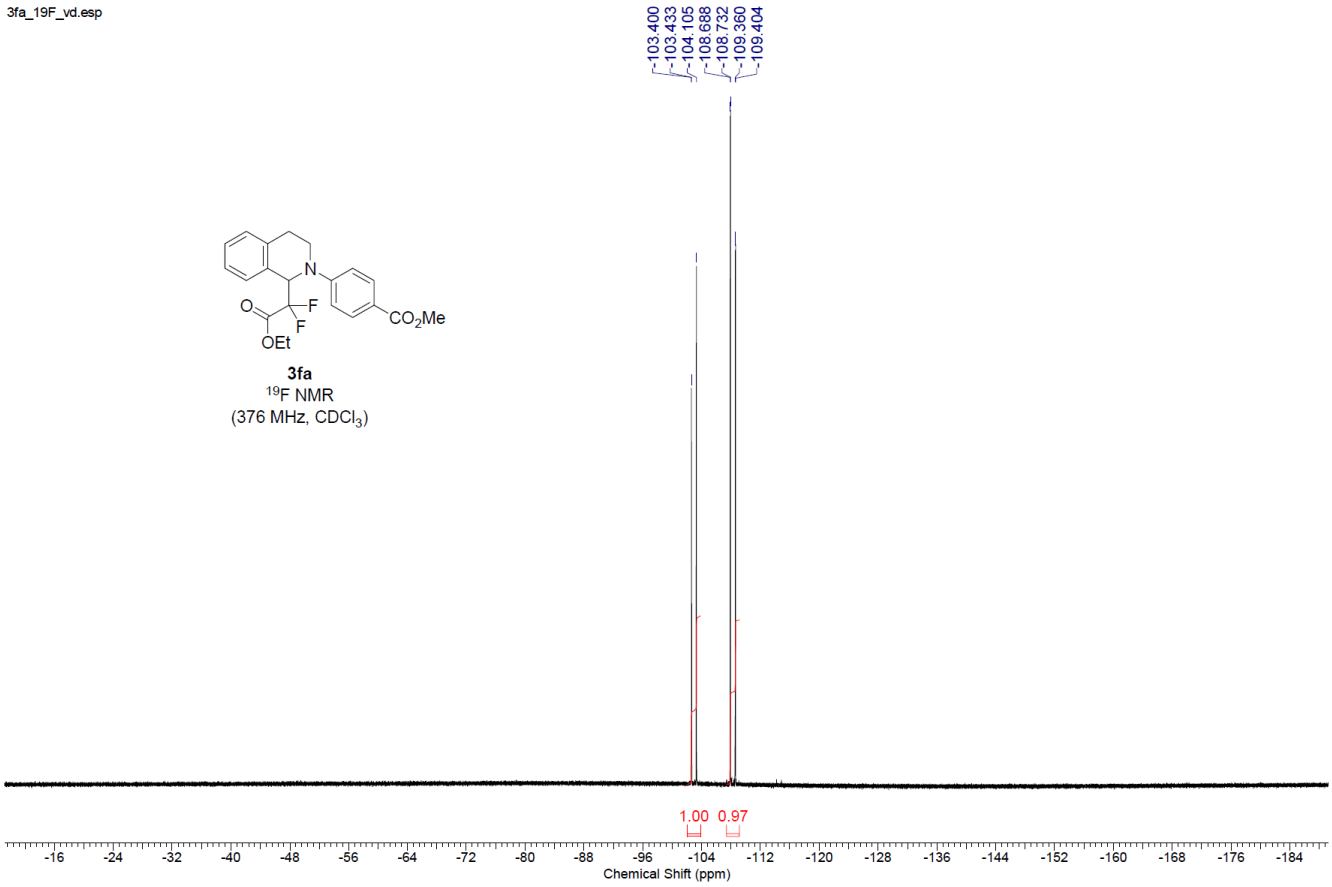
163.945
163.703
163.680
163.438
152.261
136.242
131.225
128.997
128.649
128.338
128.308
126.338
120.306
118.207
116.146
114.070
113.865
77.258
77.000
76.750
63.057
60.617
60.397
60.208
51.706
42.583
26.026
13.795
N
O
F
F
OEt
CO2Me
3fa
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)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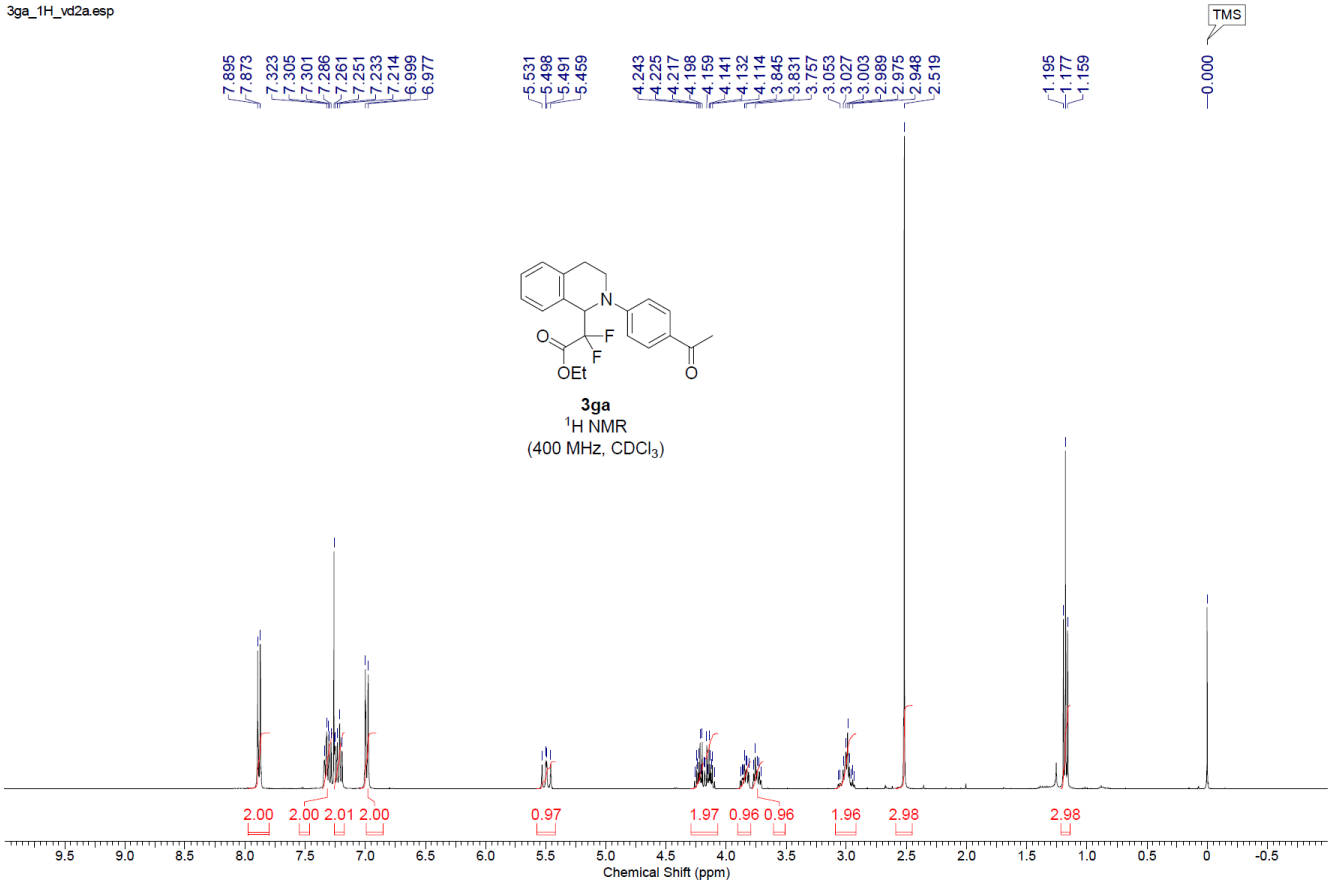
-104.105
-108.688
-108.732
-109.360
-109.404
N
O
F
F
OEt
CO2Me
3fa
19F NMR
(376 MHz, CDCl3)
1.00
0.97
-16
-24
-32
-40
-48
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
-184
Chemical Shift (ppm)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TMS
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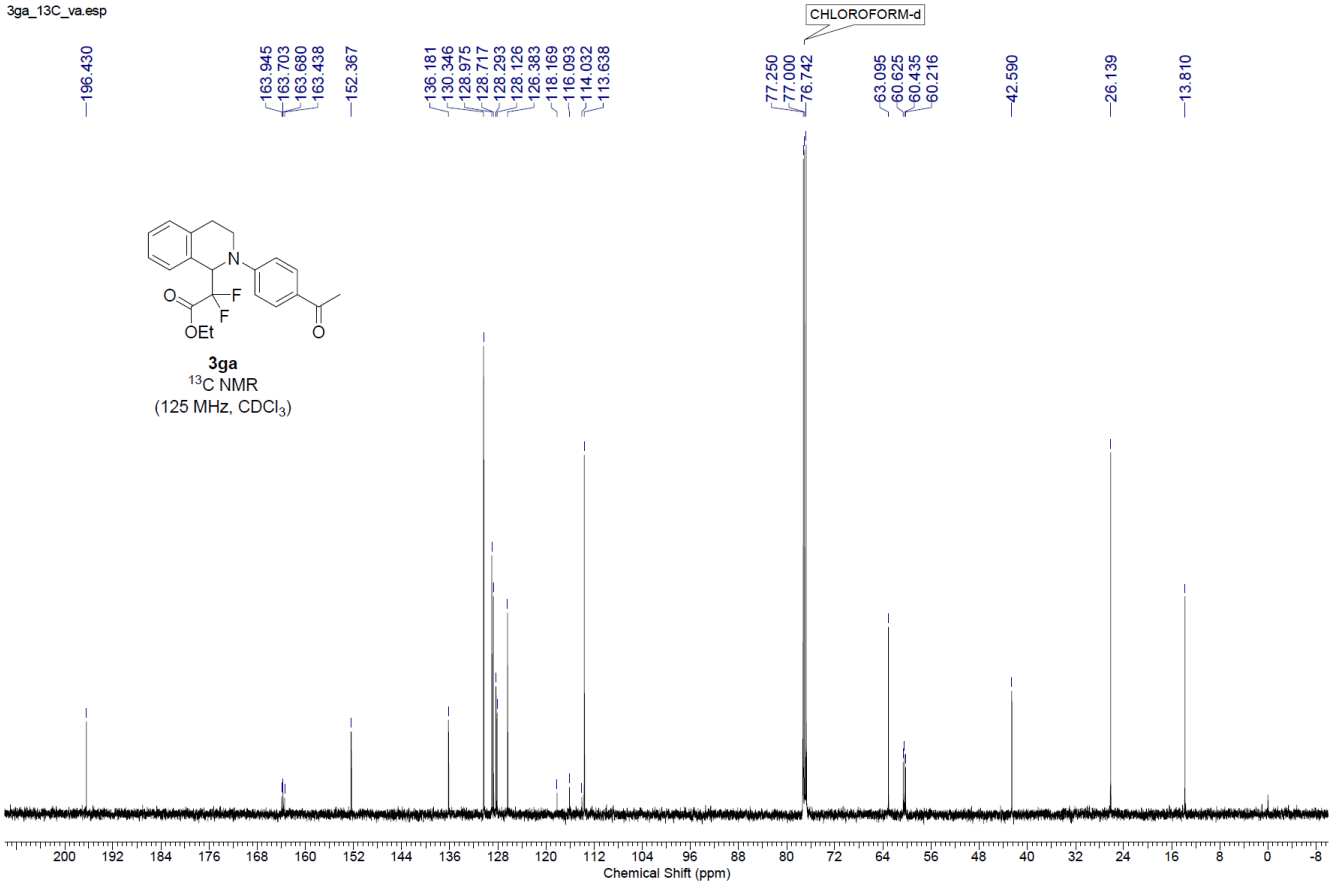
7.873
7.323
7.305
7.301
7.286
7.261
7.251
7.233
7.214
6.999
6.977
5.531
5.498
5.491
5.459
4.243
4.225
4.217
4.198
4.159
4.141
4.132
4.114
3.845
3.831
3.757
3.053
3.027
3.003
2.989
2.975
2.948
2.519
1.195
1.177
1.159
0.000
3ga
1H NMR
(400 MHz, CDCl3)
2.00 2.00 2.01 2.00 0.97 1.97 0.96 0.96 1.96 2.98 2.98
Chemical Shift (ppm)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163.438
152.367
136.181
130.346
128.975
128.717
128.293
128.126
126.383
118.169
116.093
114.032
113.638
77.250
77.000
76.742
63.095
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60.216
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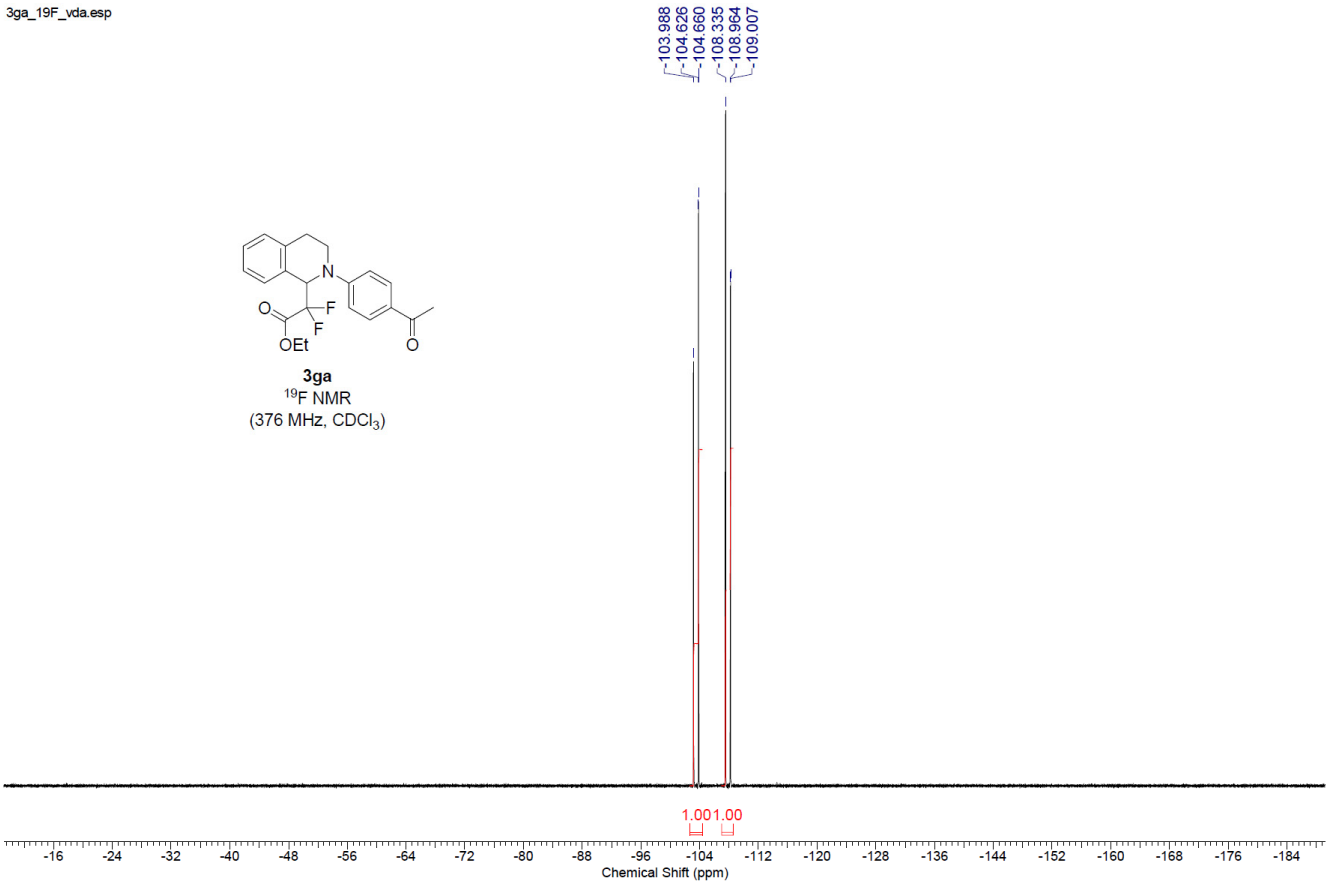
26.139
13.810
3ga
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)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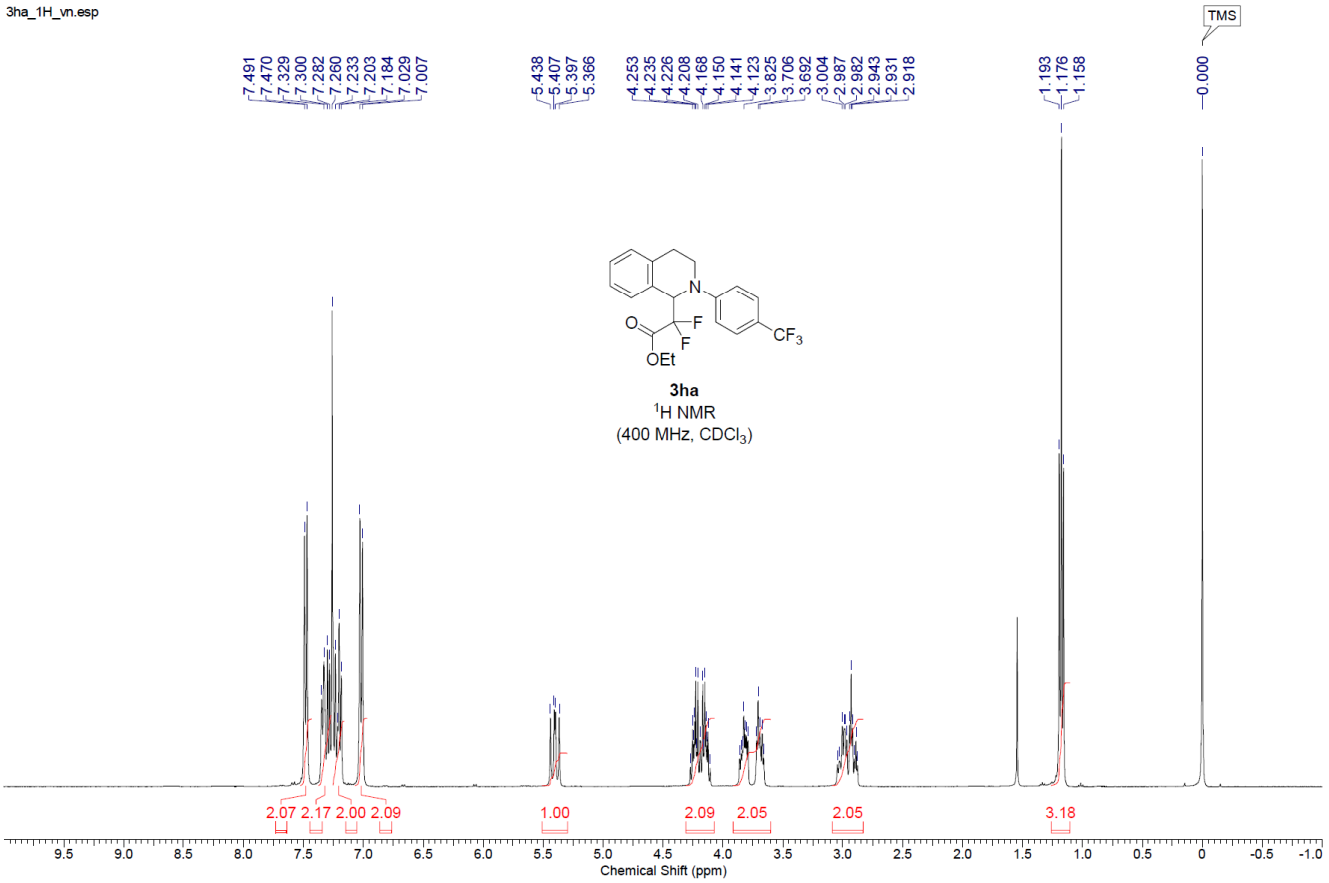
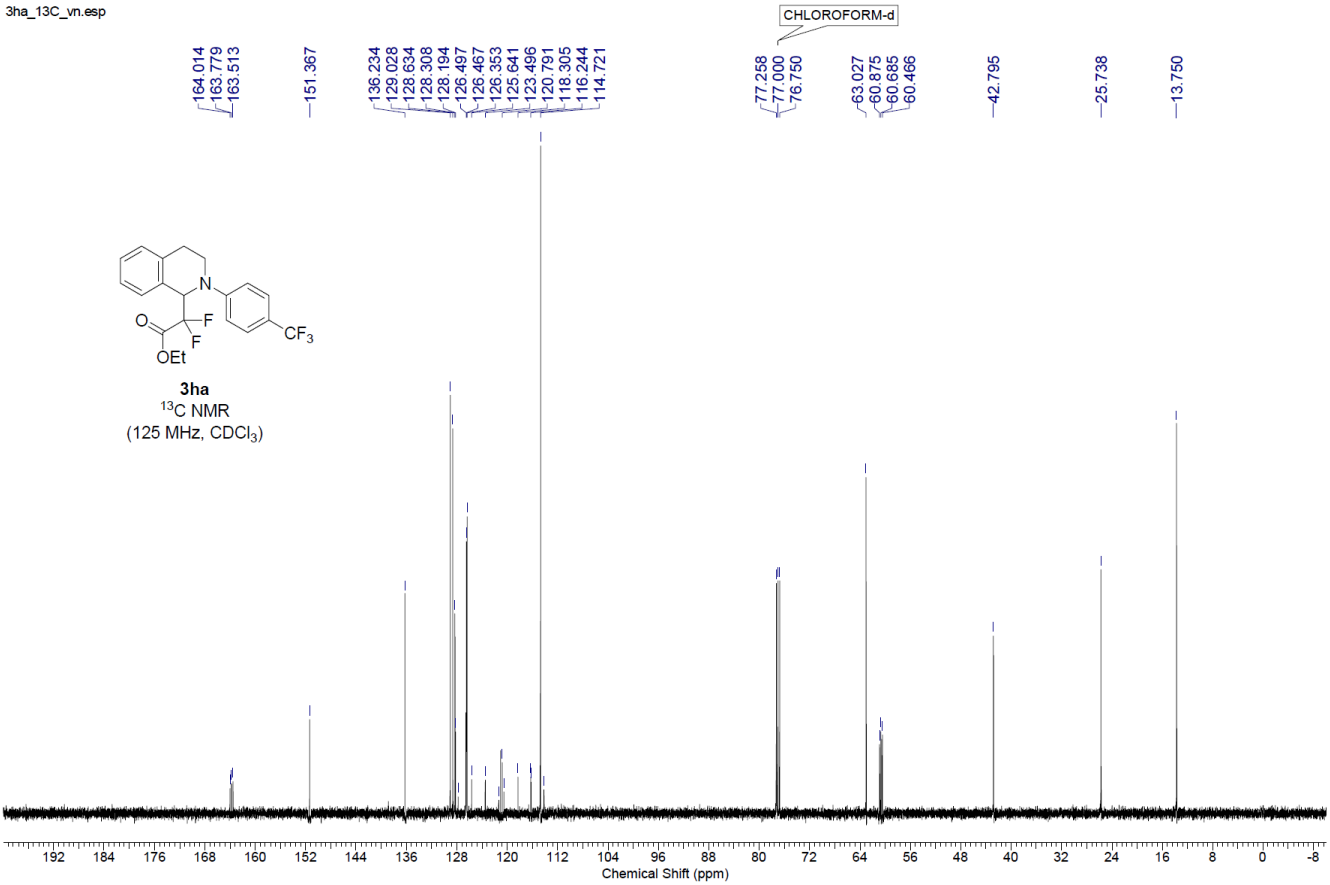
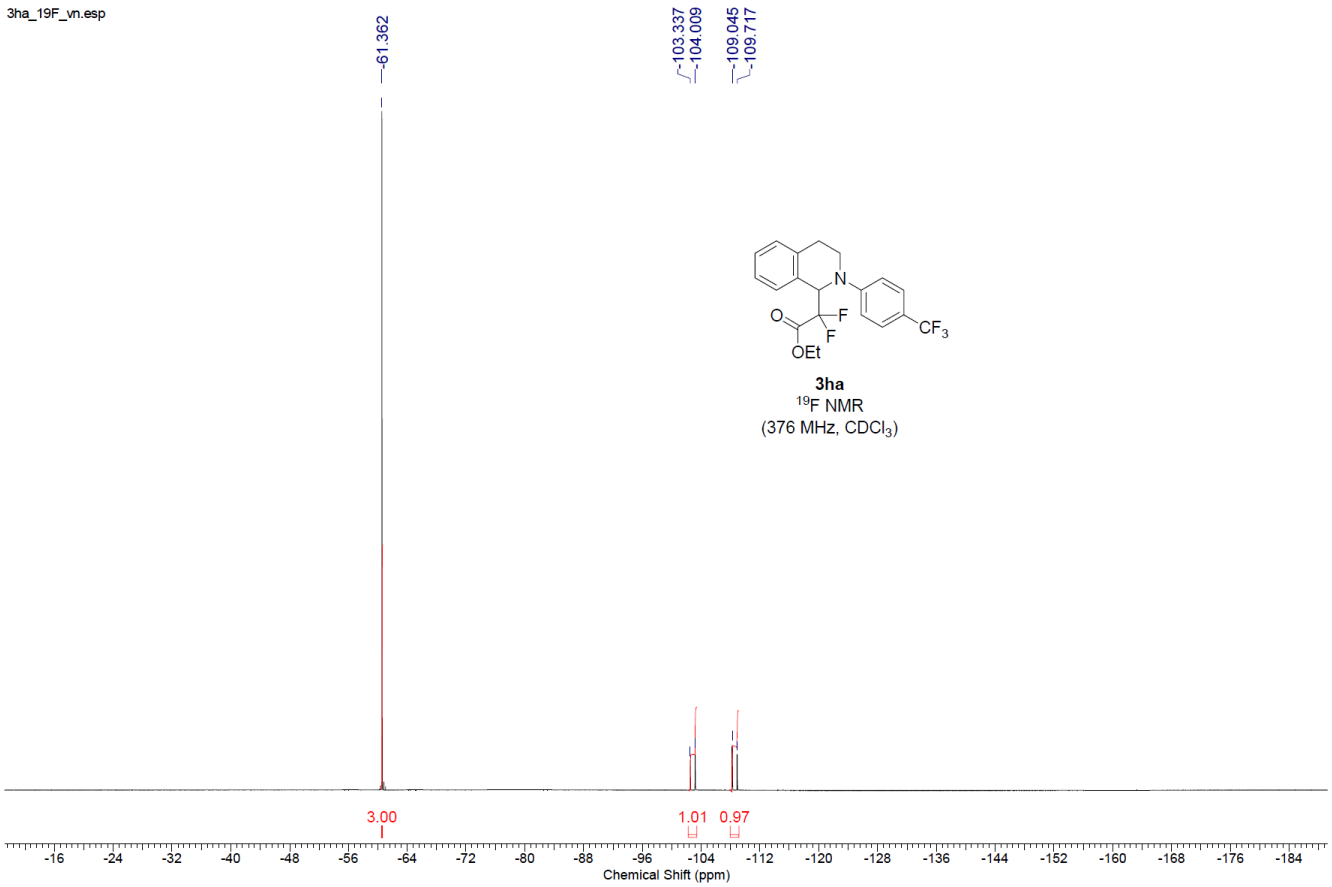
-104.626
-104.660
-108.335
-108.964
-109.007
N
O
F
F
OEt
O
3ga
19F NMR
(376 MHz, CDCl3)
1.00
1.00
-16
-24
-32
-40
-48
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
-184
Chemical Shift (ppm)



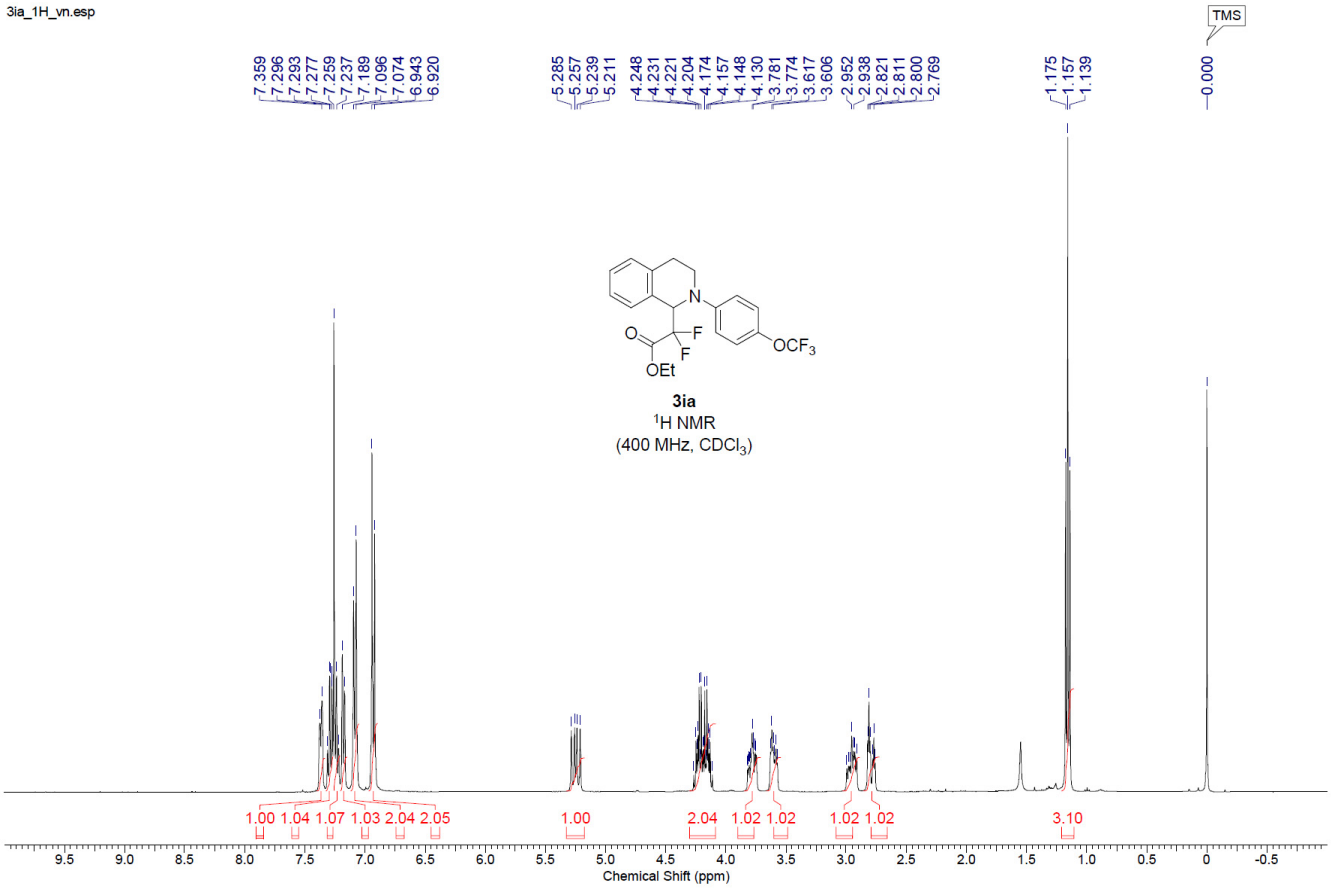
3ha
^{1}H NMR
(400 MHz, $CDCl_3$)



3ha
^{13}C NMR
(125 MHz, $CDCl_3$)



3ha
^{19}F NMR
(376 MHz, $CDCl_3$)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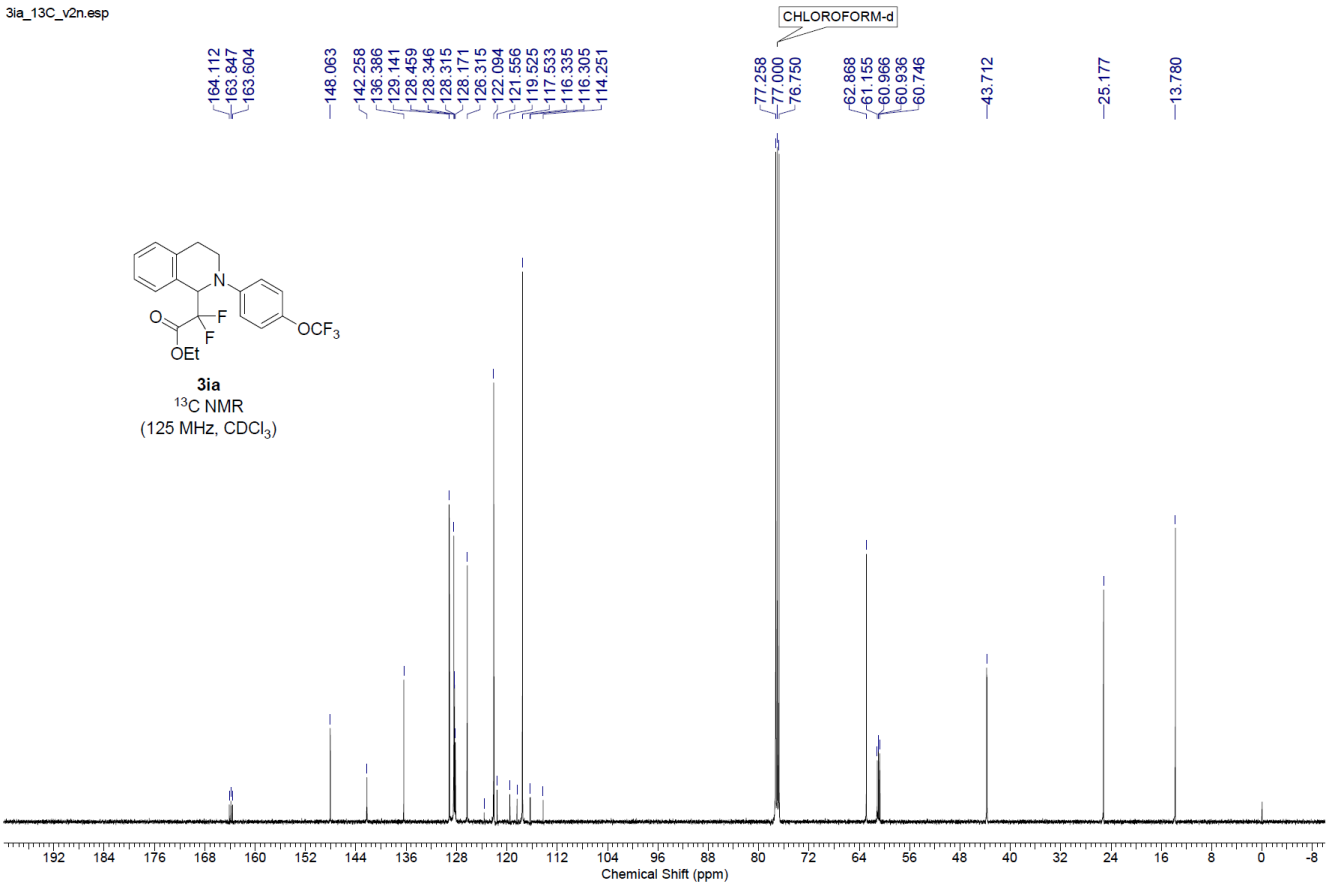
7.189
7.096
7.074
6.943
6.920
5.285
5.257
5.239
5.211
4.248
4.231
4.221
4.204
4.174
4.157
4.148
4.130
3.781
3.774
3.617
3.606
2.952
2.938
2.821
2.811
2.800
2.769
1.175
1.157
1.139
0.000
3ia
1H NMR
(400 MHz, CDCl3)
1.00 1.04 1.07 1.03 2.04 2.05
1.00
2.04
1.02 1.02
1.02 1.02
3.10
Chemical Shift (ppm)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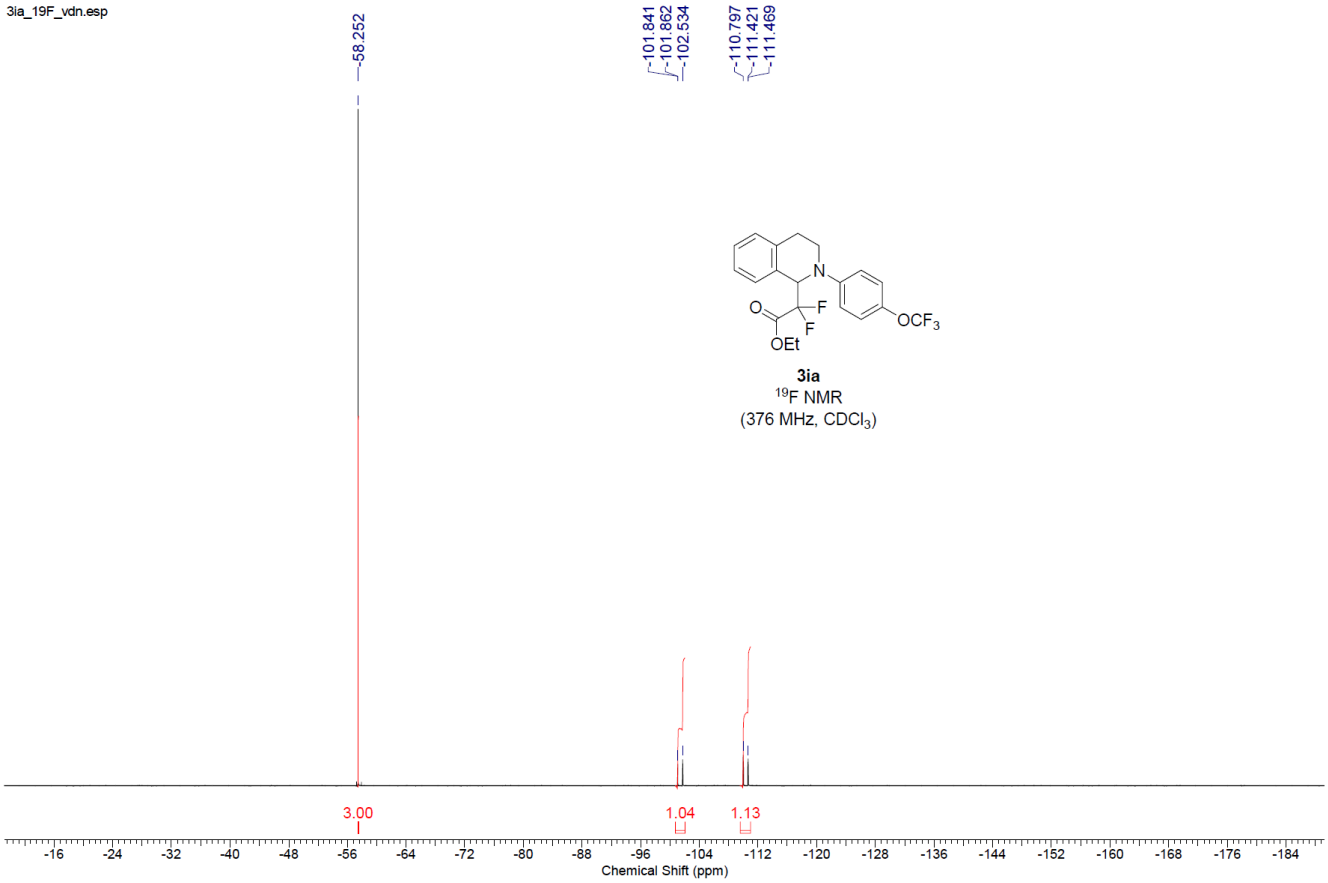
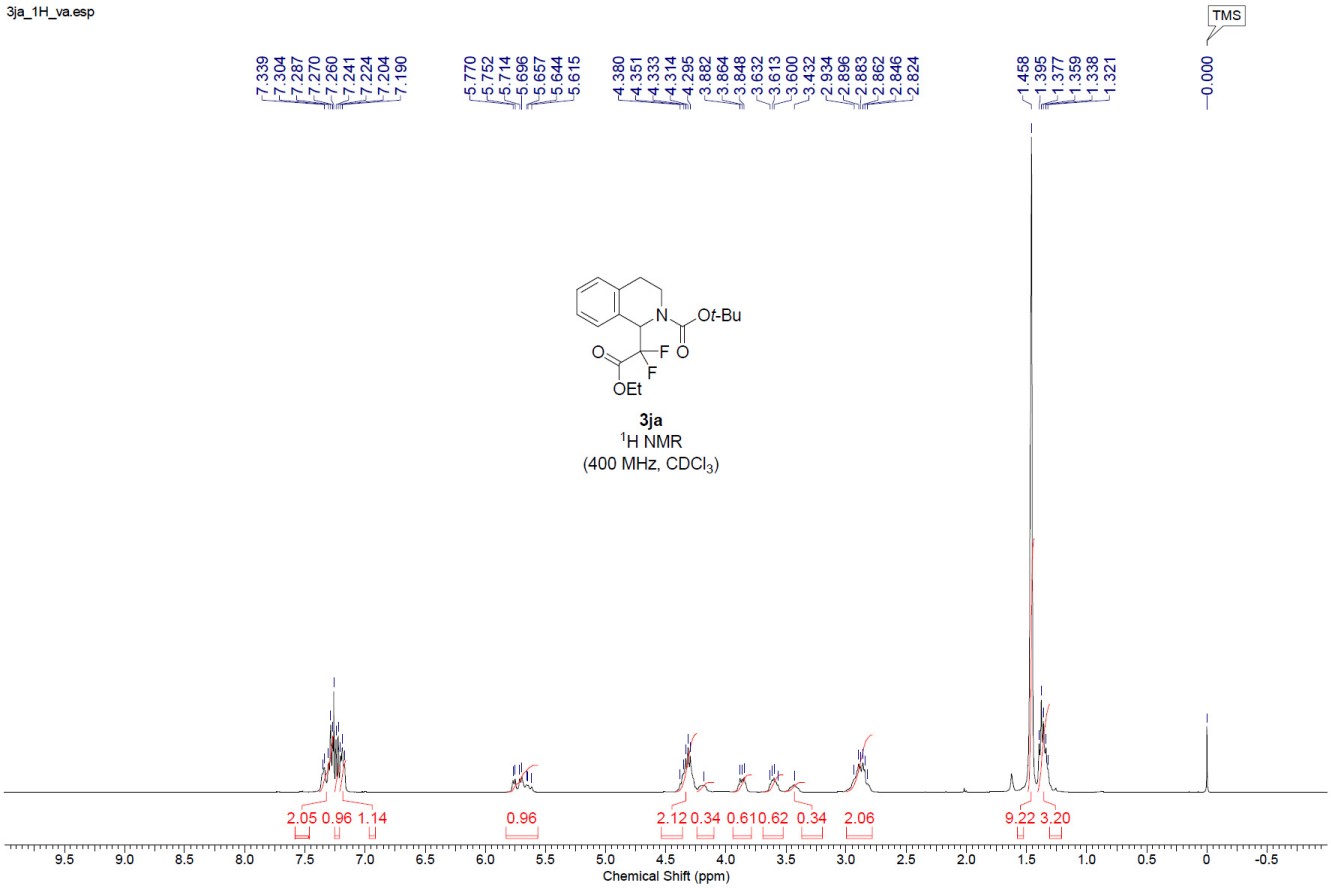
CHLOROFORM-d
164.112
163.847
163.604
148.063
142.258
136.386
129.141
128.459
128.346
128.315
128.171
126.315
122.094
121.556
119.525
117.533
116.335
116.305
114.251
77.258
77.000
76.750
62.868
61.155
60.966
60.936
60.746
43.712
25.177
13.780
3ia
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)



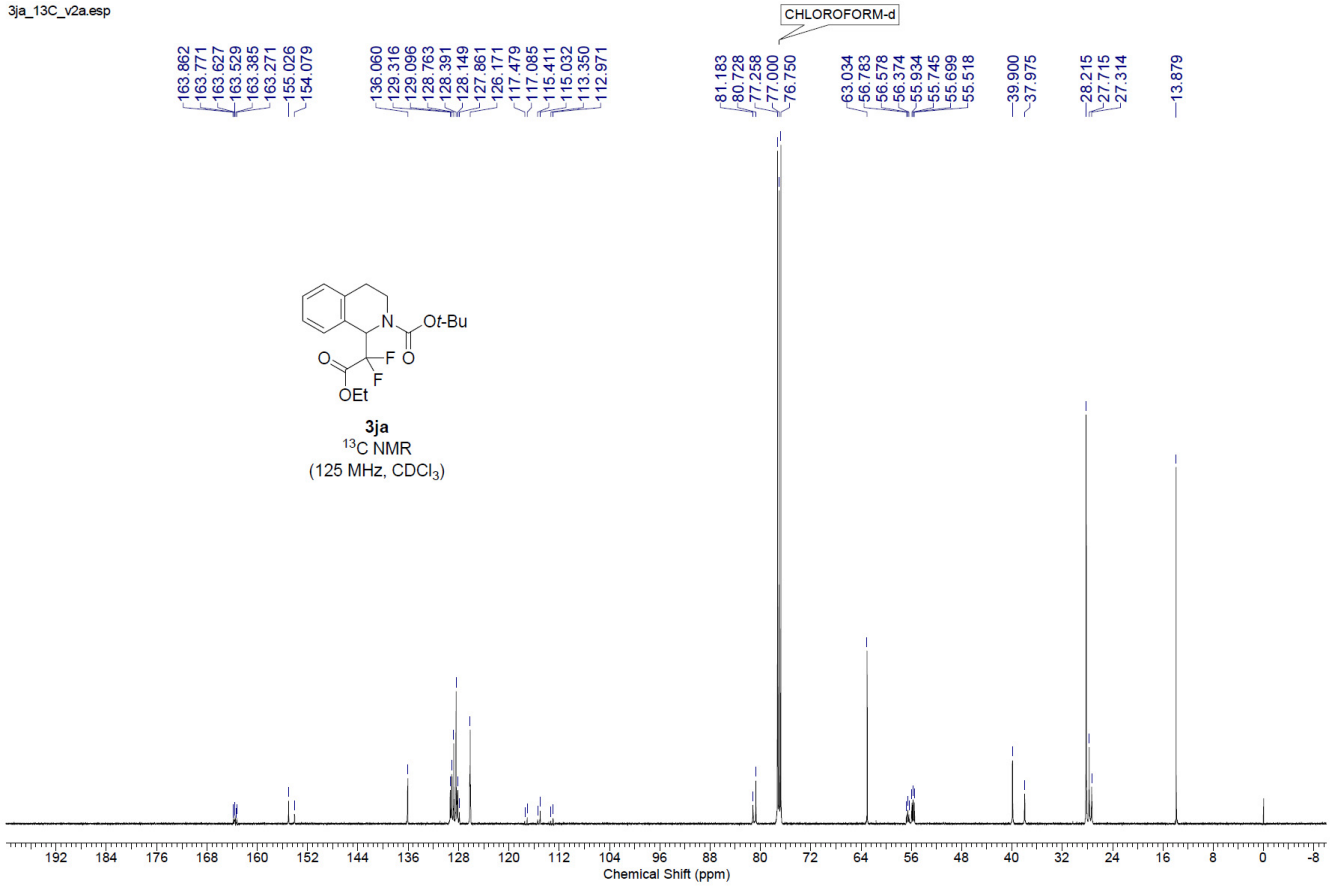
3ia
^{19}F NMR
(376 MHz, $CDCl_3$)

3ja_1H_va.esp

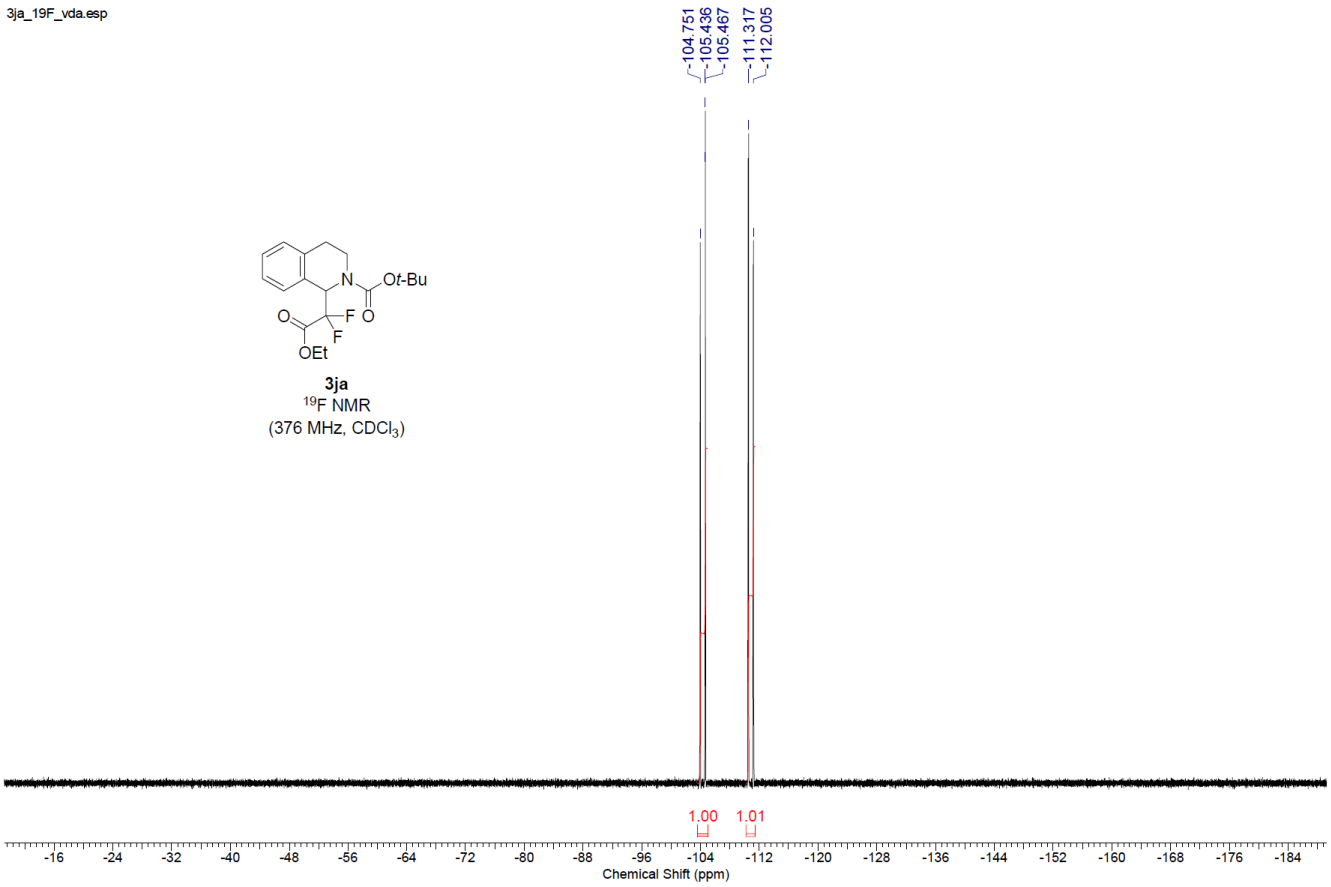


3ja
^{1}H NMR
(400 MHz, $CDCl_3$)

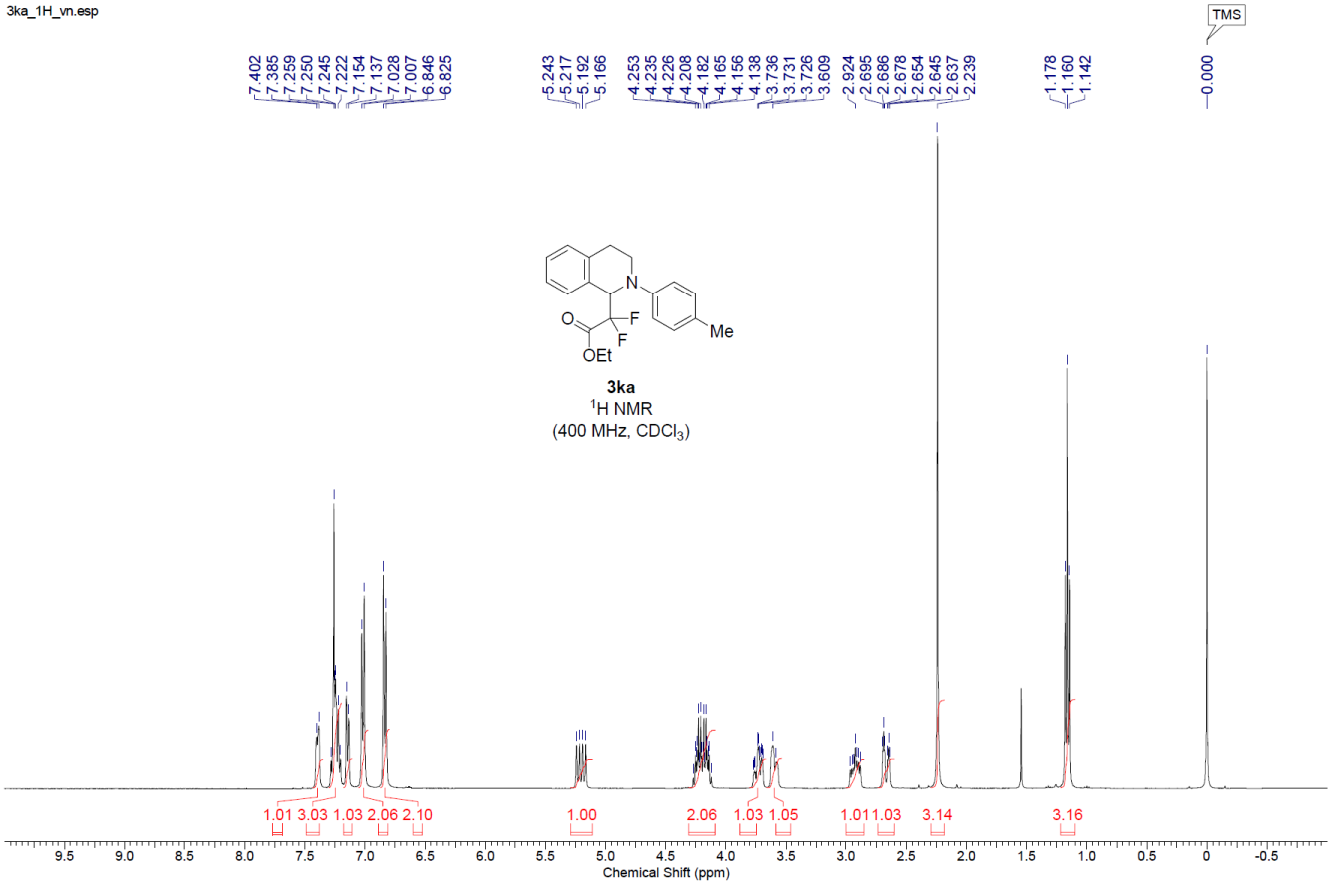
3ja_13C_v2a.esp

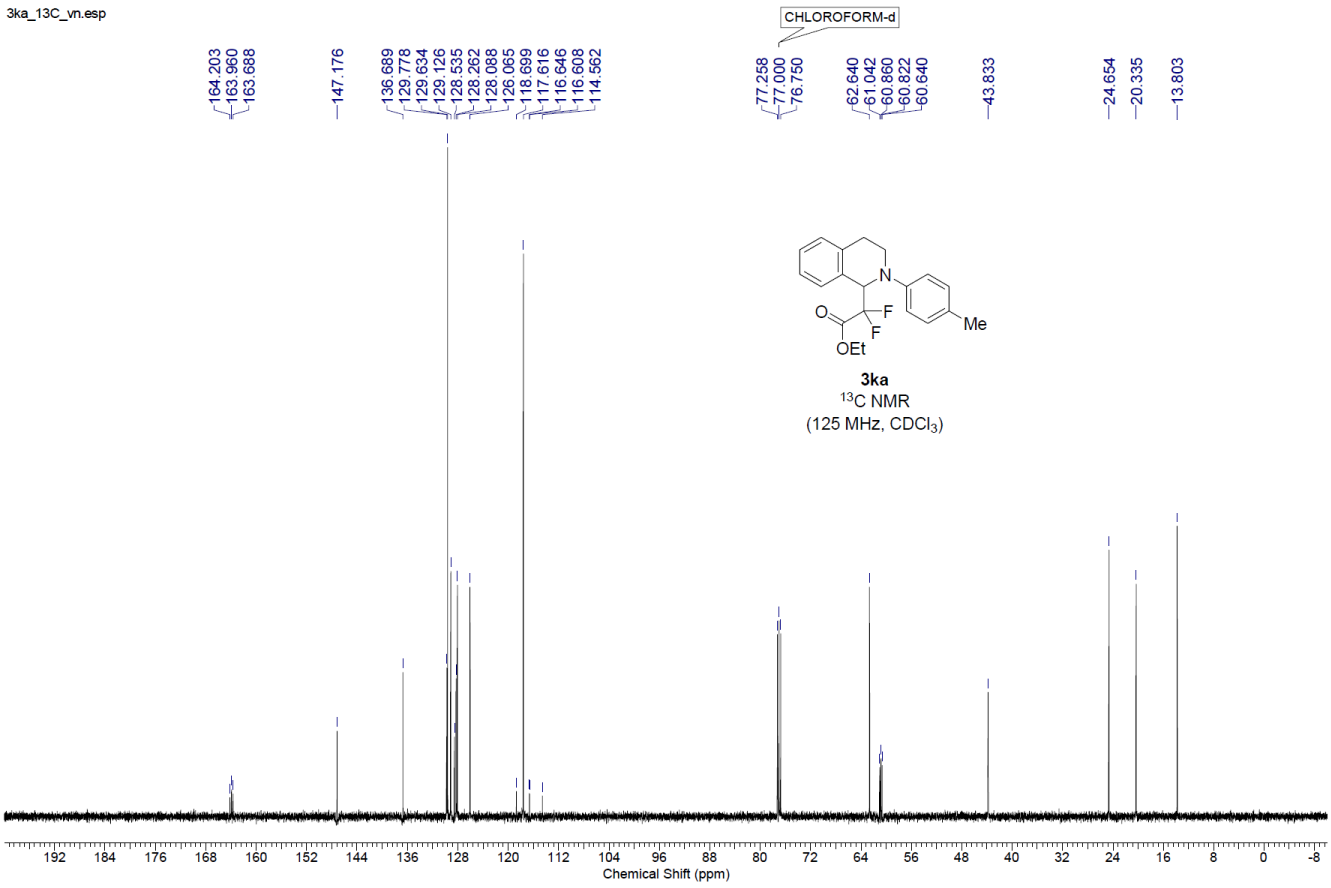


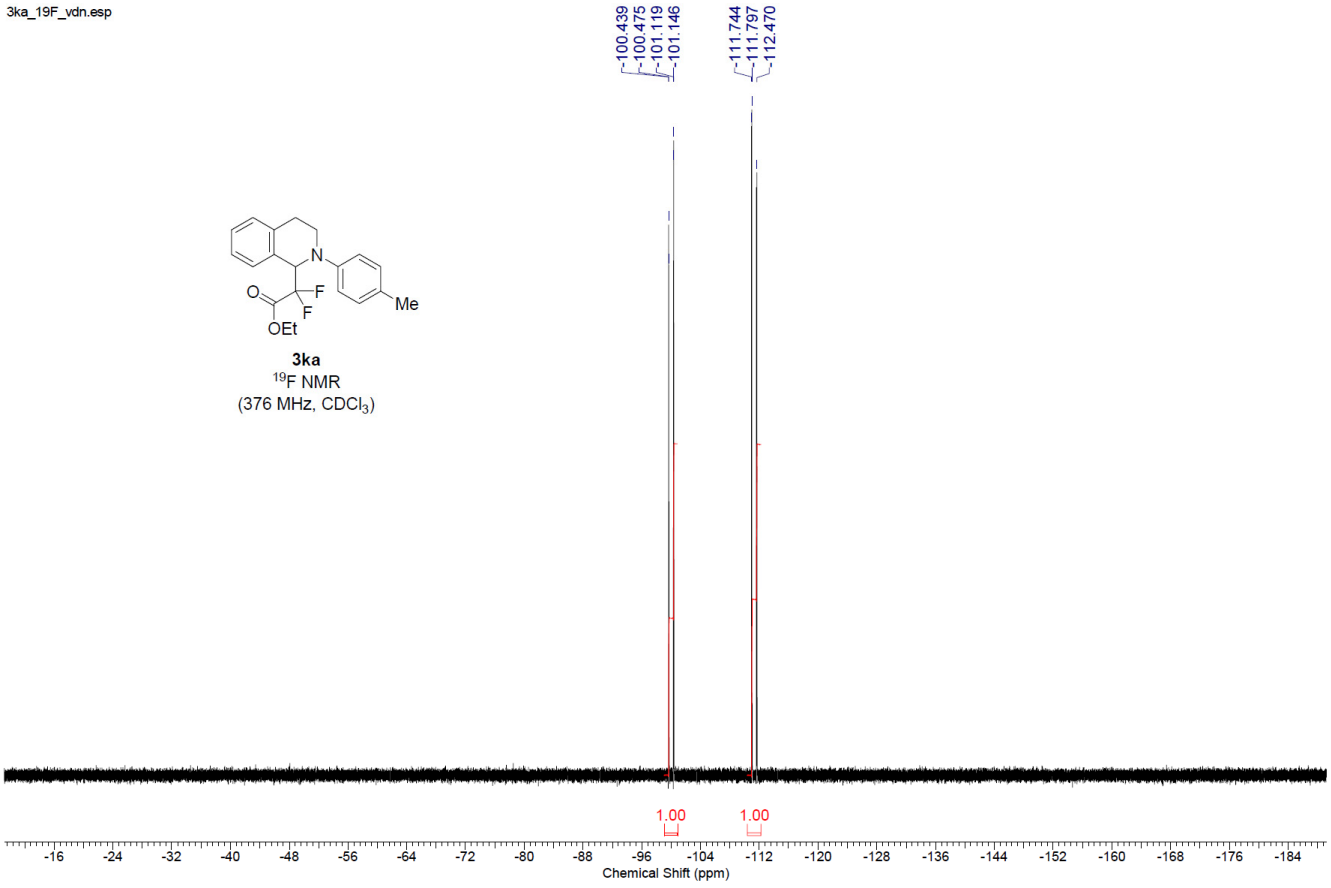
3ja
^{13}C NMR
(125 MHz, $CDCl_3$)



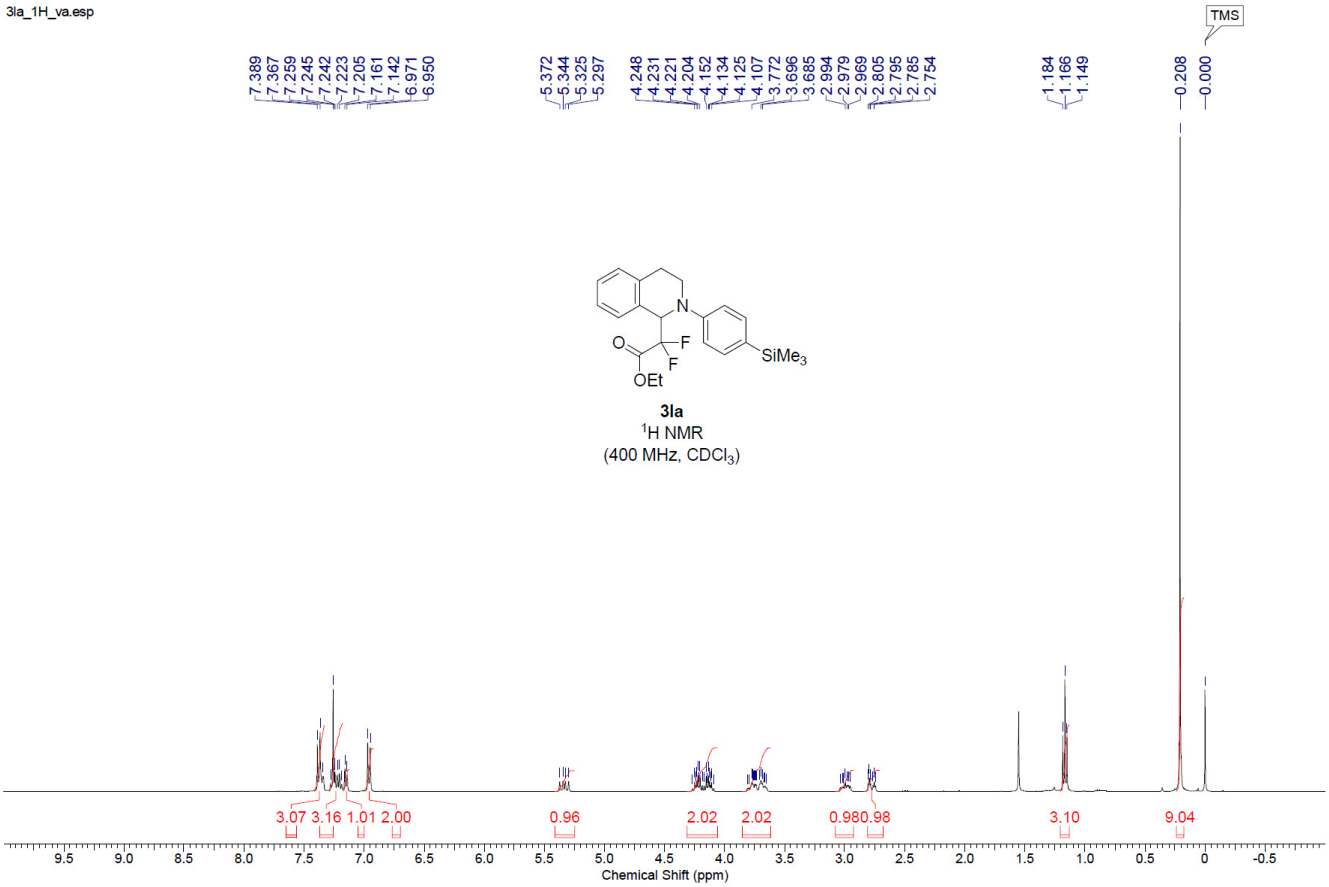
3ja
^{19}F NMR
(376 MHz, $CDCl_3$)


3ka_1H_vn.esp
TMS
7.402
7.385
7.259
7.250
7.245
7.222
7.154
7.137
7.028
7.007
6.846
6.825
5.243
5.217
5.192
5.166
4.253
4.235
4.226
4.208
4.182
4.165
4.156
4.138
3.736
3.731
3.726
3.609
2.924
2.695
2.686
2.678
2.654
2.645
2.637
2.239
1.178
1.160
1.142
0.000
N
O
F
F
OEt
Me
3ka
1H NMR
(400 MHz, CDCl3)
1.01 3.03 1.03 2.06 2.10
1.00
2.06
1.03 1.05
1.01 1.03
3.14
3.16
Chemical Shift (ppm)

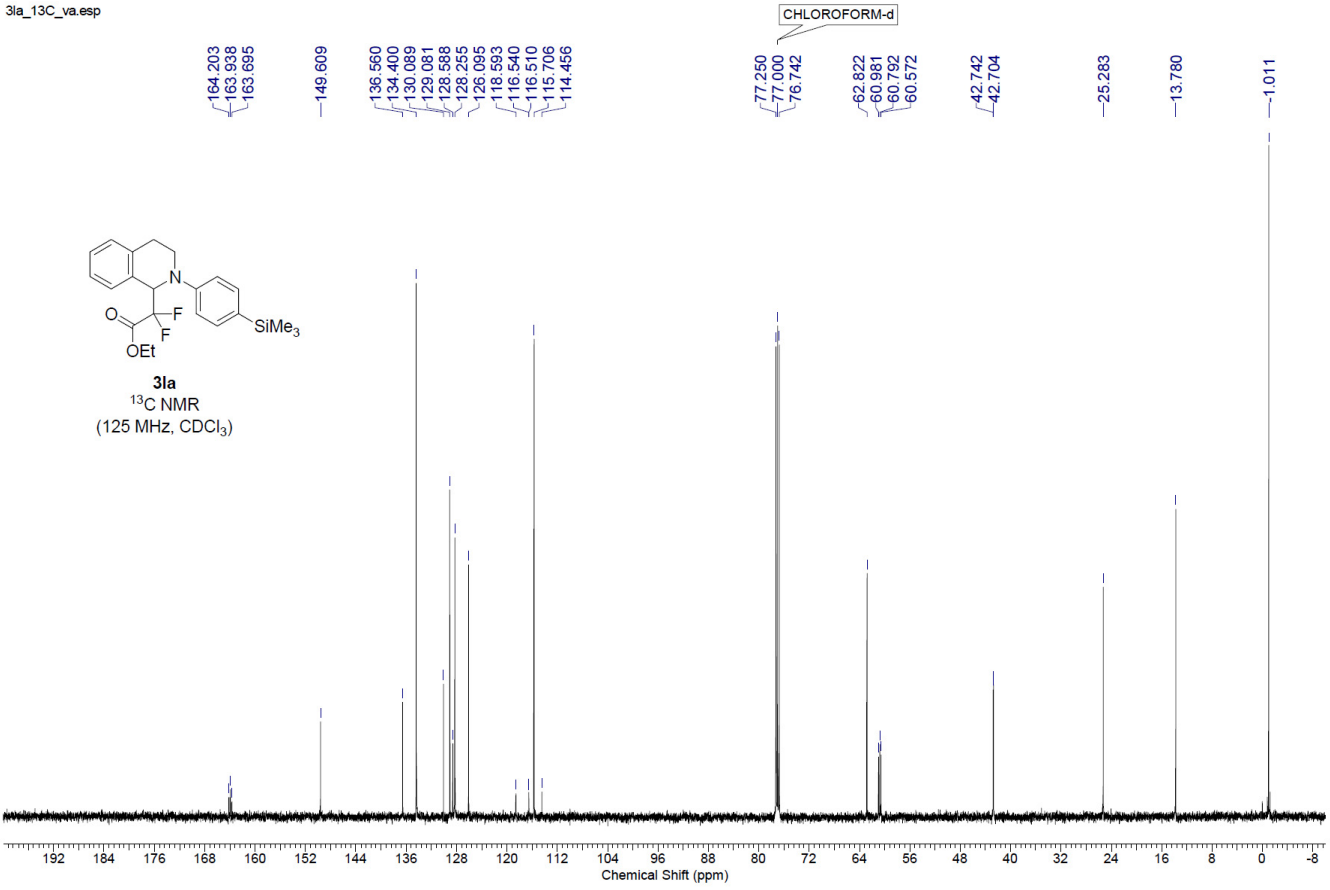

3ka_13C_vn.esp
CHLOROFORM-d
164.203
163.960
163.688
147.176
136.689
129.778
129.634
129.126
128.535
128.262
128.088
126.065
118.699
117.616
116.646
116.608
114.562
77.258
77.000
76.750
62.640
61.042
60.860
60.822
60.640
43.833
24.654
20.335
13.803
N
O
F
F
OEt
Me
3ka
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)



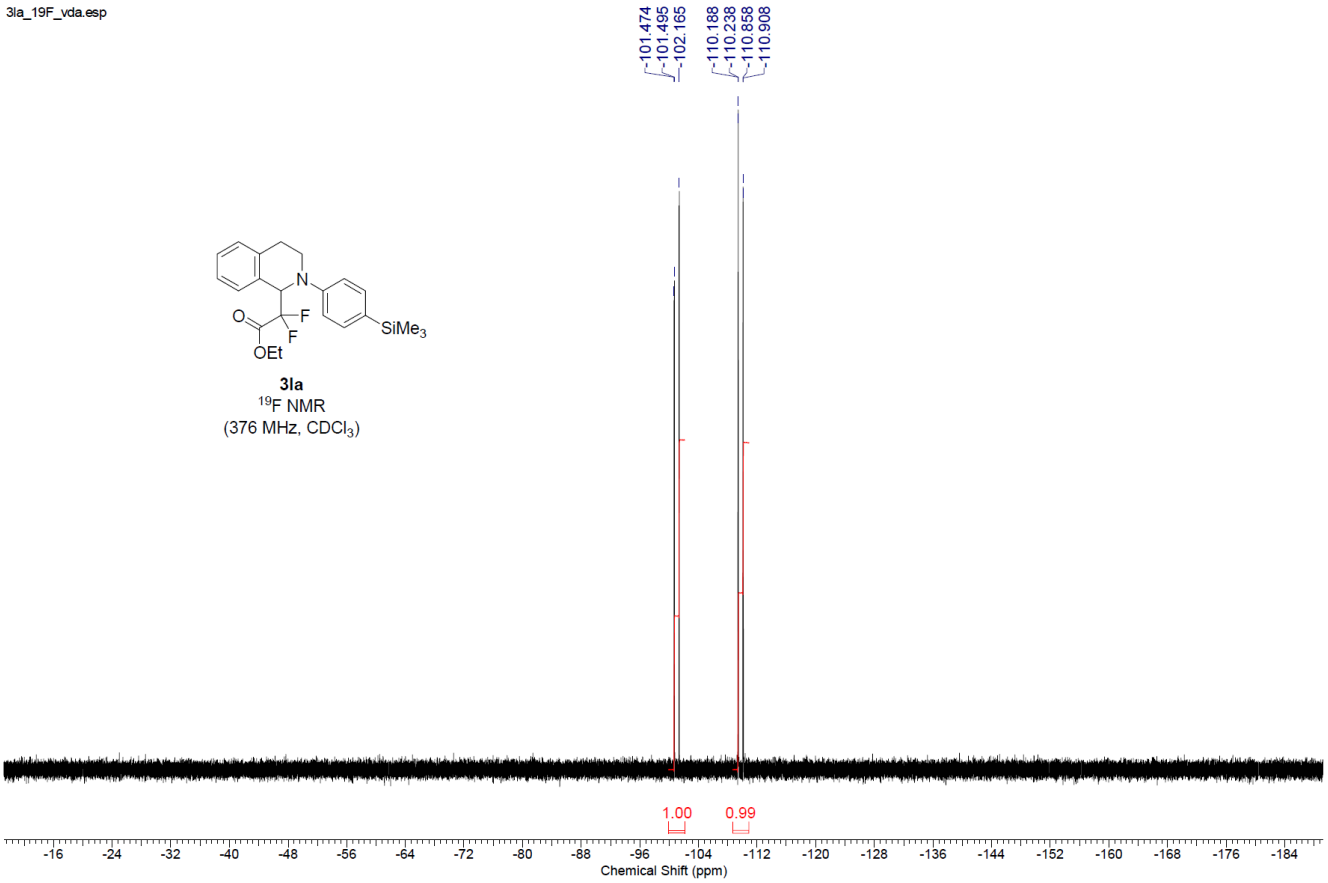
3ka
^{19}F NMR
(376 MHz, $CDCl_3$)

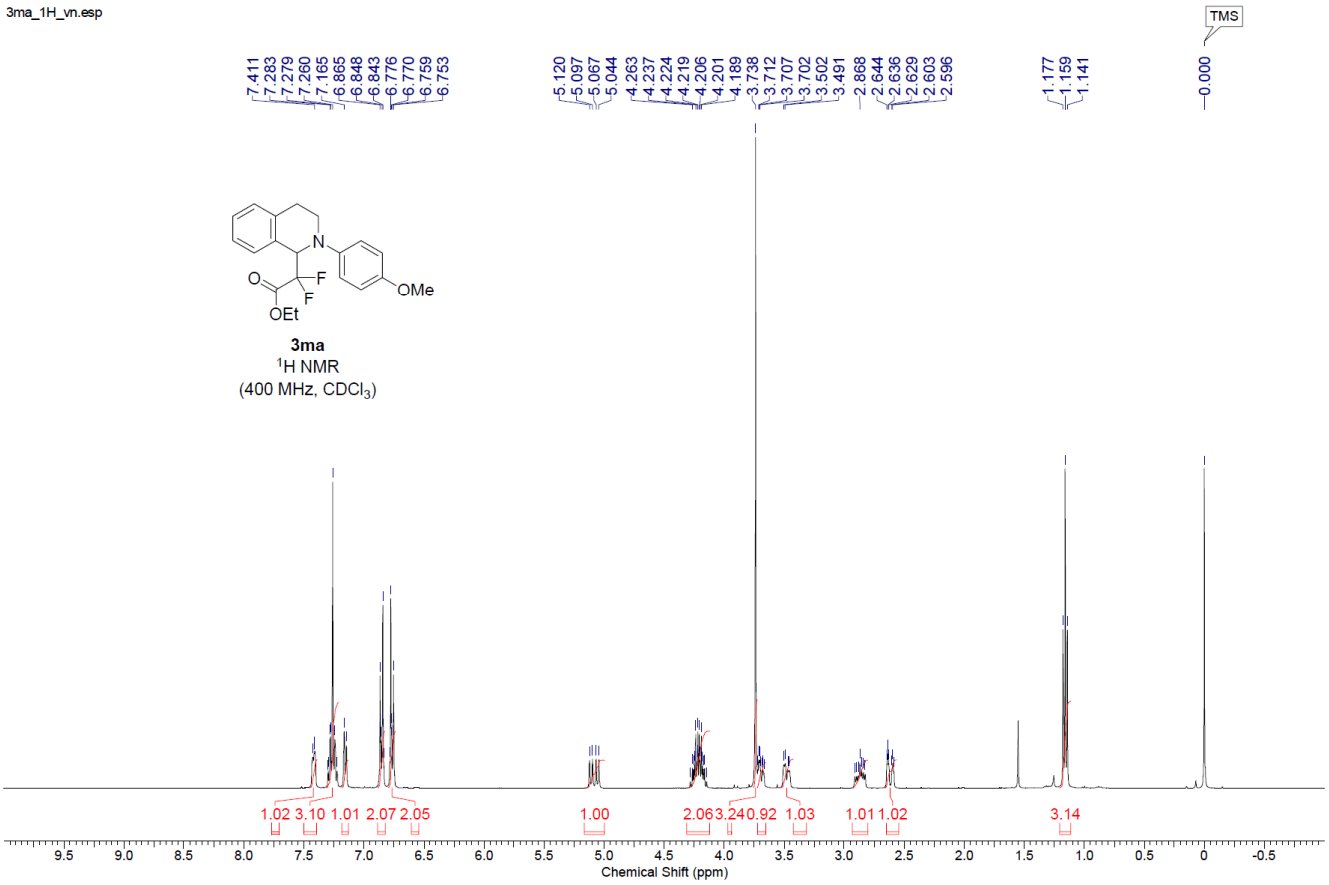


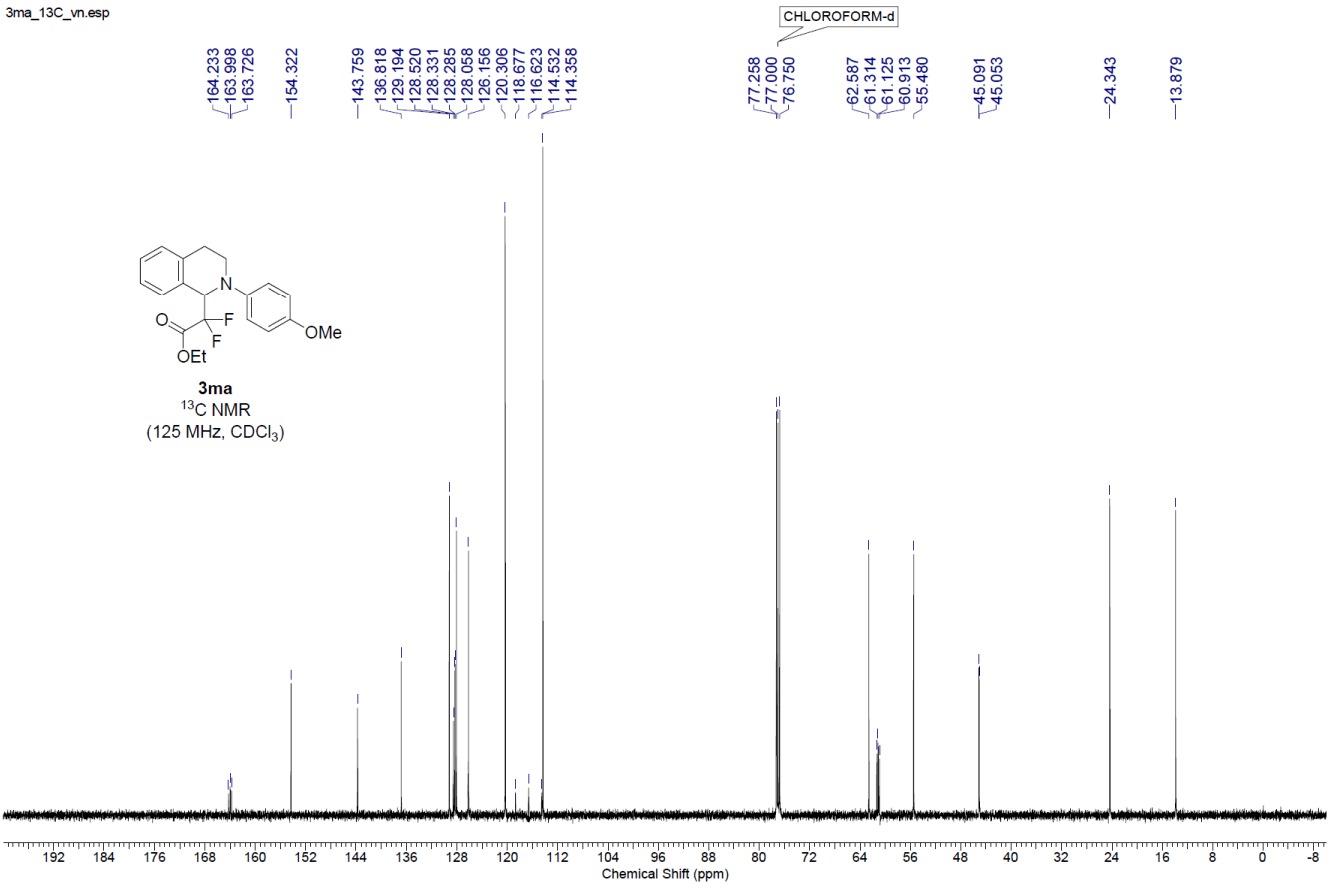
3la
^{1}H NMR
(400 MHz, $CDCl_3$)

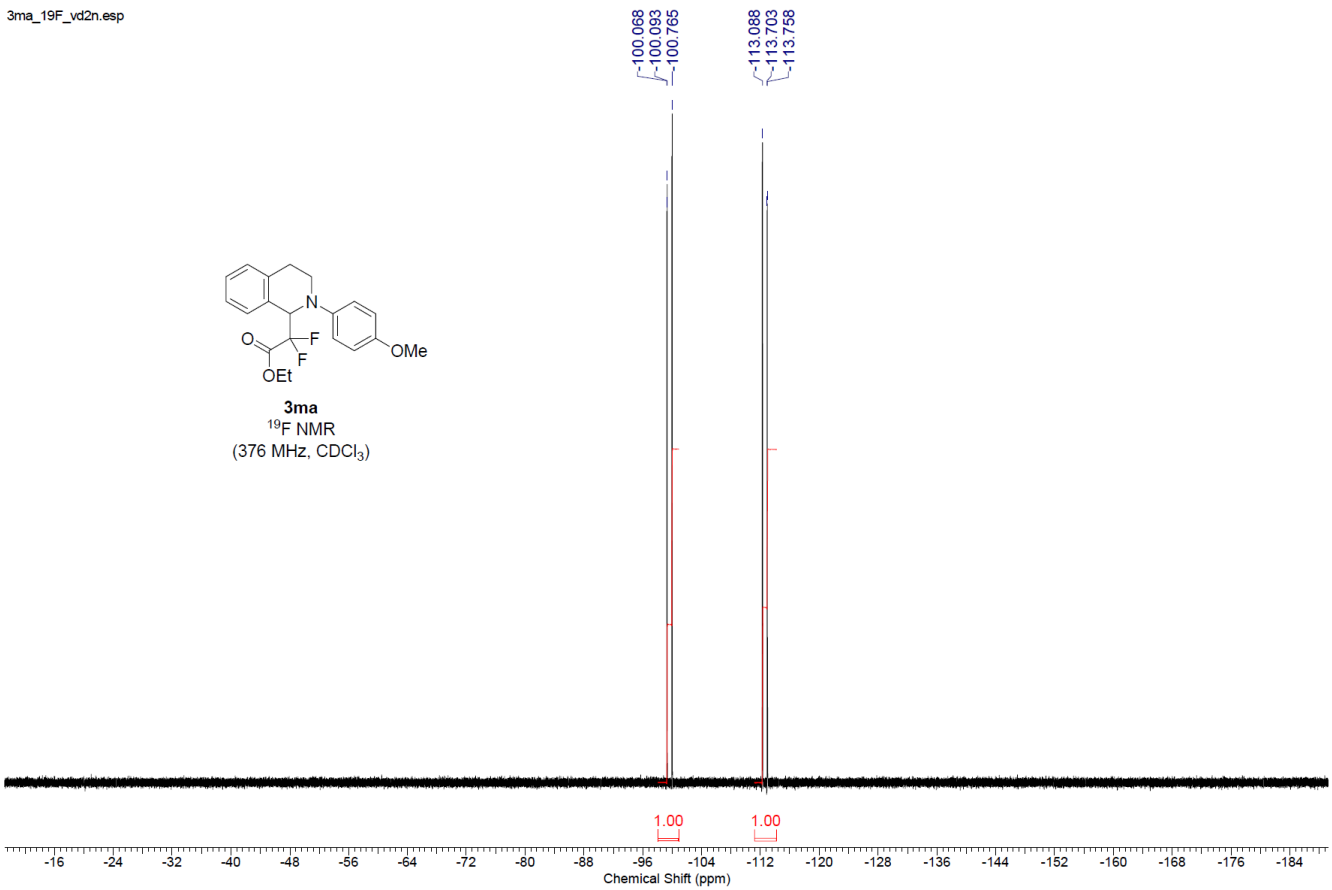


3la
^{13}C NMR
(125 MHz, $CDCl_3$)

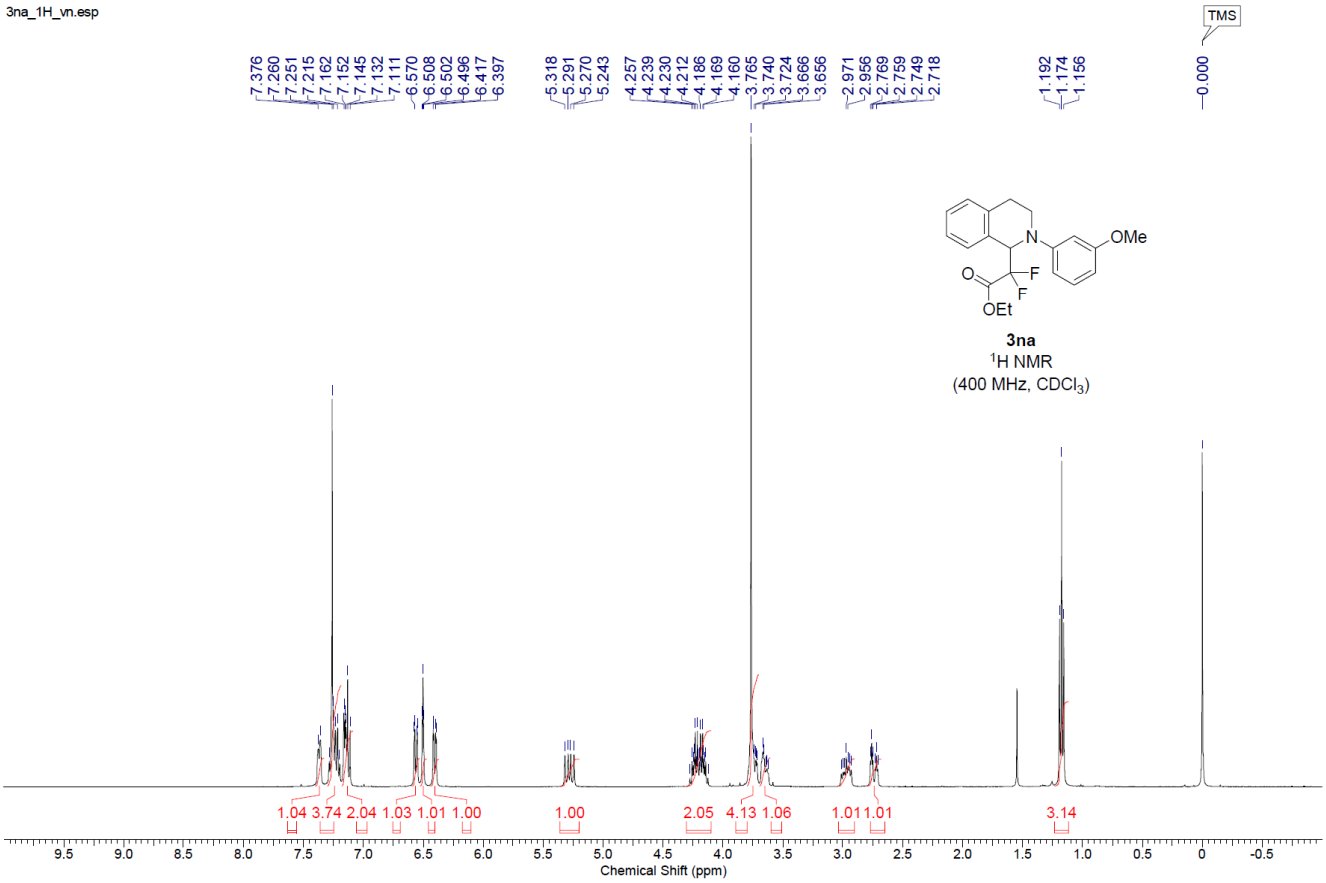

3la_19F_vda.esp
-101.474
-101.495
-102.165
-110.188
-110.238
-110.858
-110.908
O
N
F
F
OEt
SiMe3
3la
19F NMR
(376 MHz, CDCl3)
1.00
0.99
-16
-24
-32
-40
-48
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
-184
Chemical Shift (ppm)

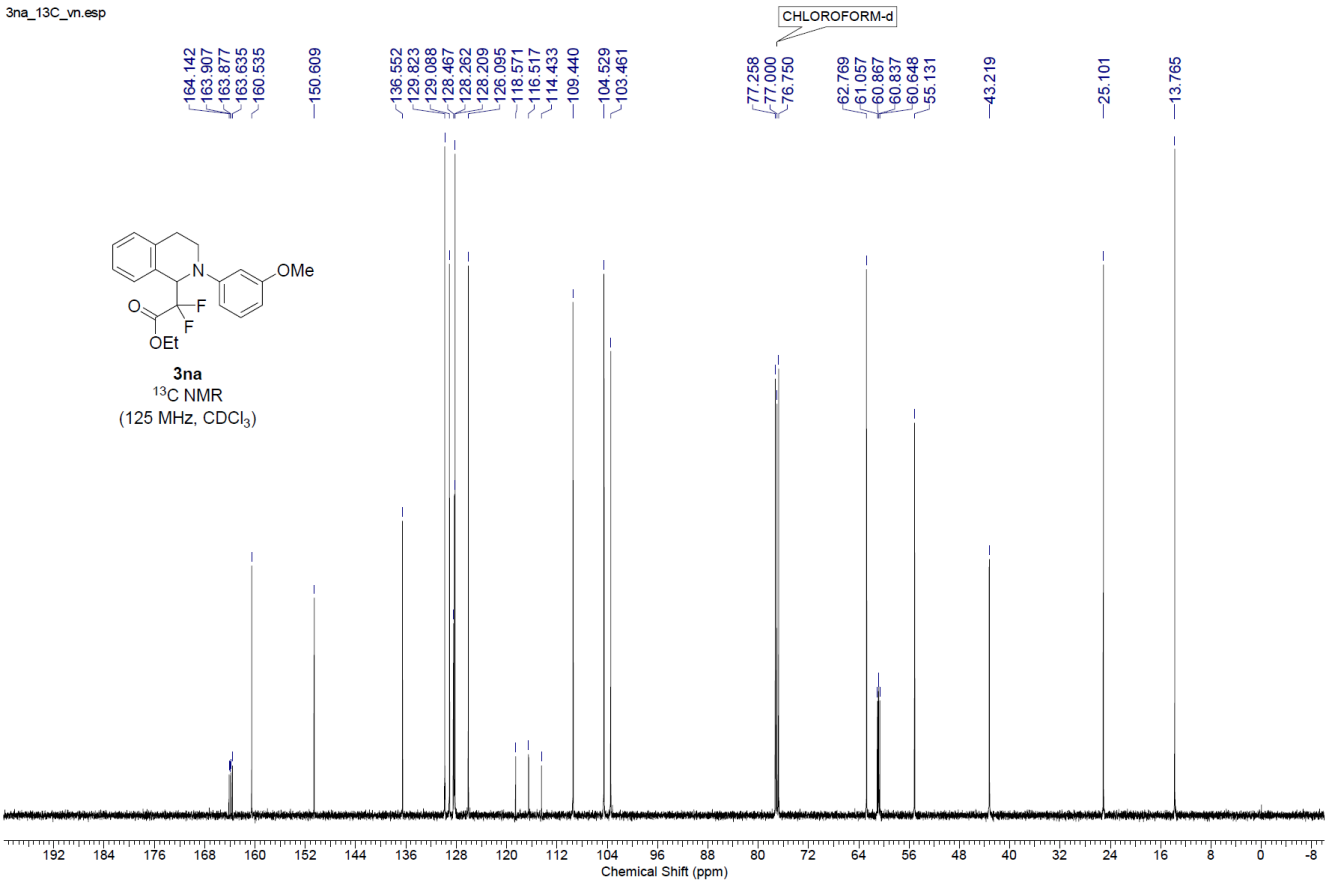

3ma_1H_vn.esp
TMS
7.411
7.283
7.279
7.260
7.165
6.865
6.848
6.843
6.776
6.770
6.759
6.753
5.120
5.097
5.067
5.044
4.263
4.237
4.224
4.219
4.206
4.201
4.189
3.738
3.712
3.707
3.702
3.502
3.491
2.868
2.644
2.636
2.629
2.603
2.596
1.177
1.159
1.141
0.000
N
O
F
F
OEt
OMe
3ma
1H NMR
(400 MHz, CDCl3)
1.02 3.10 1.01 2.07 2.05
1.00
2.06 3.24 0.92 1.03
1.01 1.02
3.14
Chemical Shift (ppm)

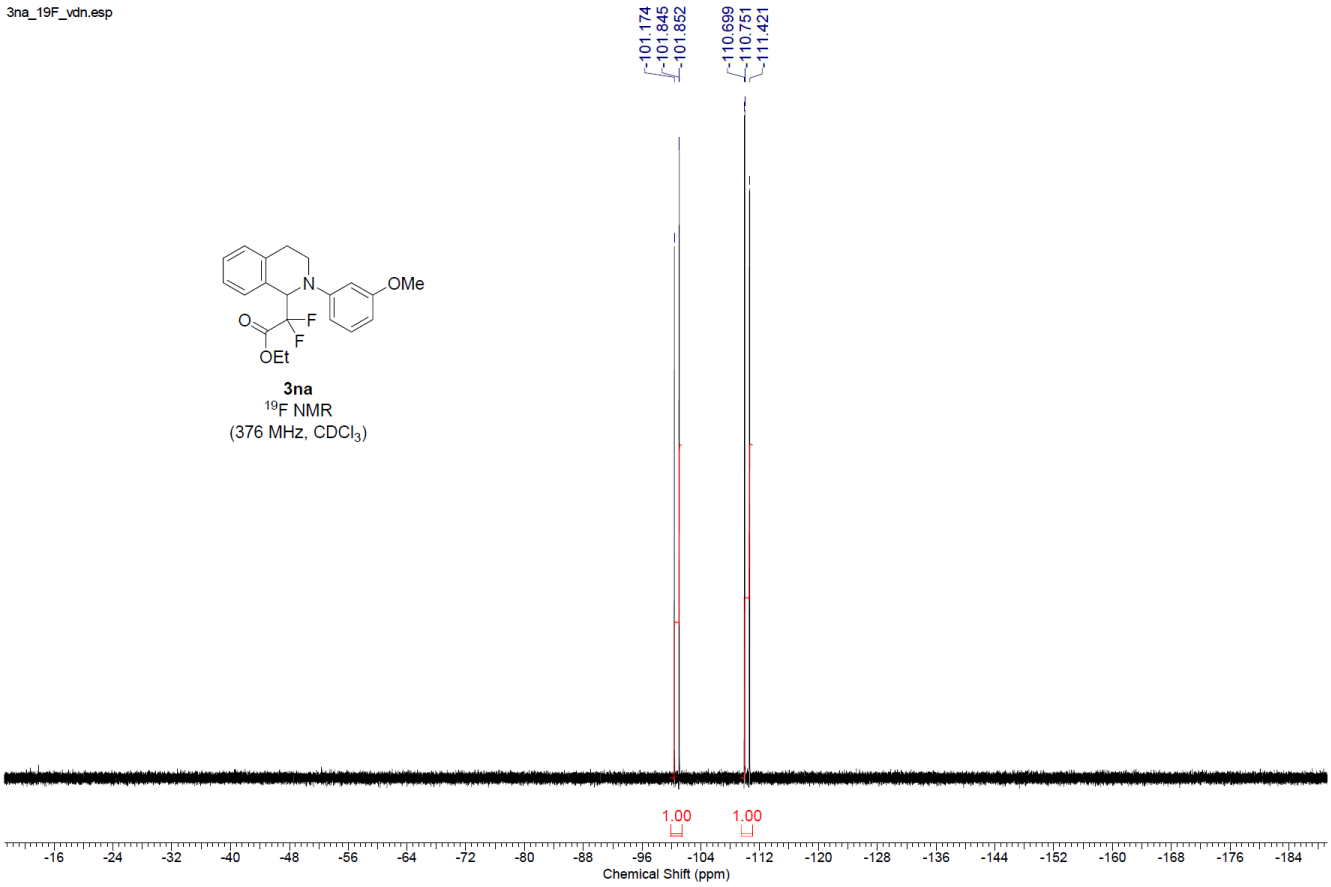

3ma_13C_vn.esp
CHLOROFORM-d
164.233
163.998
163.726
154.322
143.759
136.818
129.194
128.520
128.331
128.285
128.058
126.156
120.306
118.677
116.623
114.532
114.358
77.258
77.000
76.750
62.587
61.314
61.125
60.913
55.480
45.091
45.053
24.343
13.879
N
O
F
F
OEt
OMe
3ma
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)



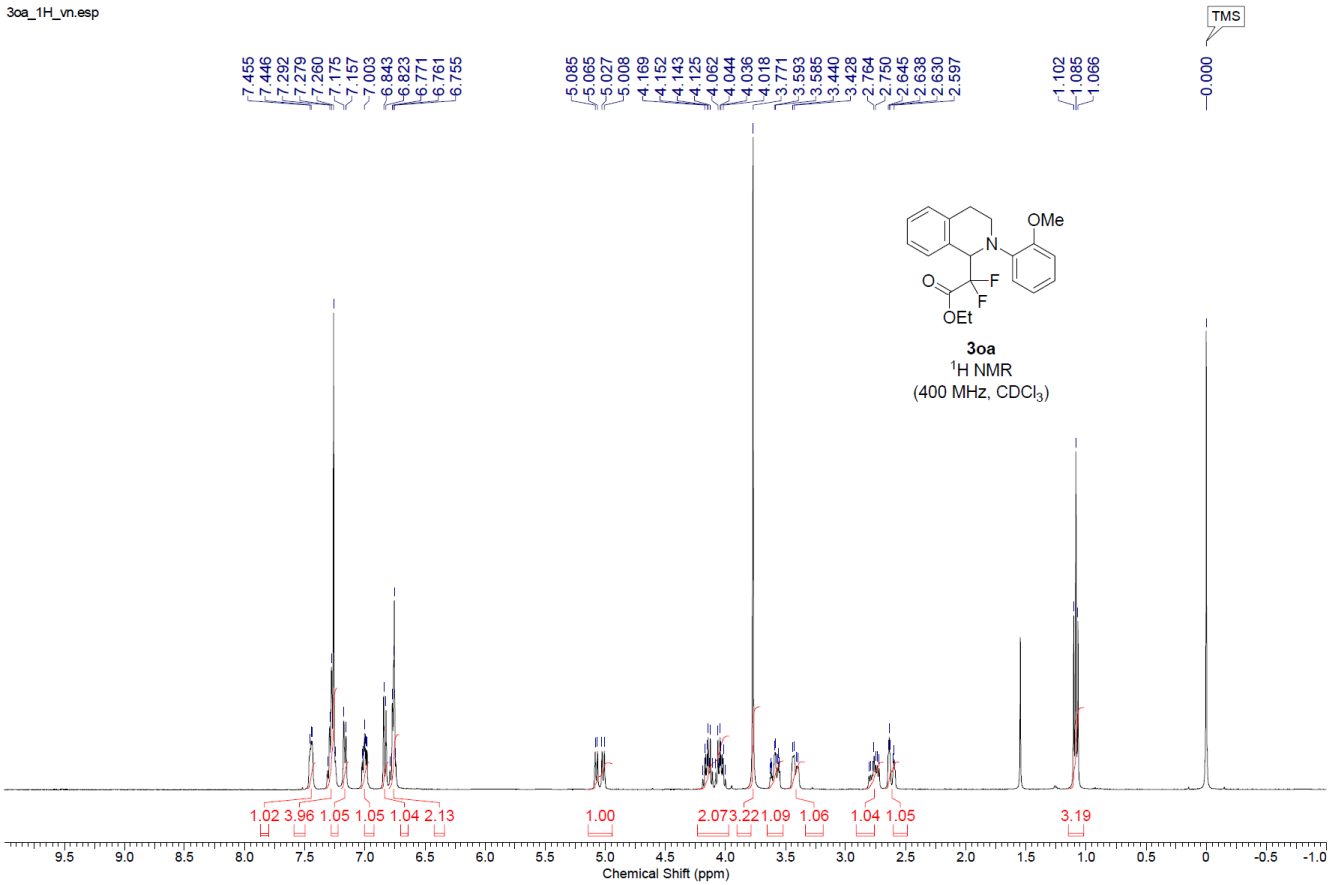
3ma
^{19}F NMR
(376 MHz, $CDCl_3$)

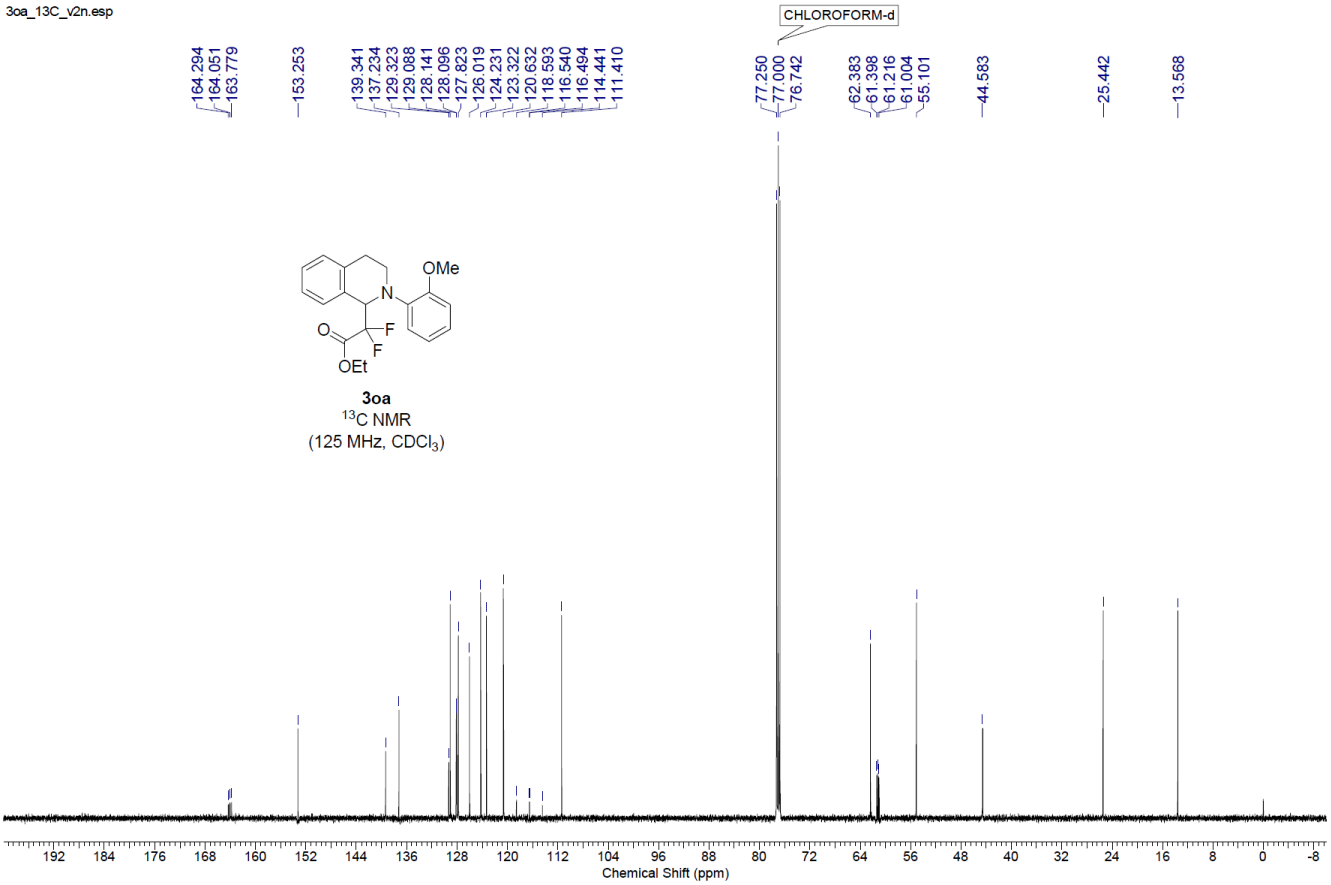

3na_1H_vn.esp
TMS
7.376
7.260
7.251
7.215
7.162
7.152
7.145
7.132
7.111
6.570
6.508
6.502
6.496
6.417
6.397
5.318
5.291
5.270
5.243
4.257
4.239
4.230
4.212
4.186
4.169
4.160
3.765
3.740
3.724
3.666
3.656
2.971
2.956
2.769
2.759
2.749
2.718
1.192
1.174
1.156
0.000
OMe
N
O
F
F
OEt
3na
1H NMR
(400 MHz, CDCl3)
1.04 3.74 2.04 1.03 1.01 1.00
1.00
2.05 4.13 1.06
1.01 1.01
3.14
Chemical Shift (ppm)

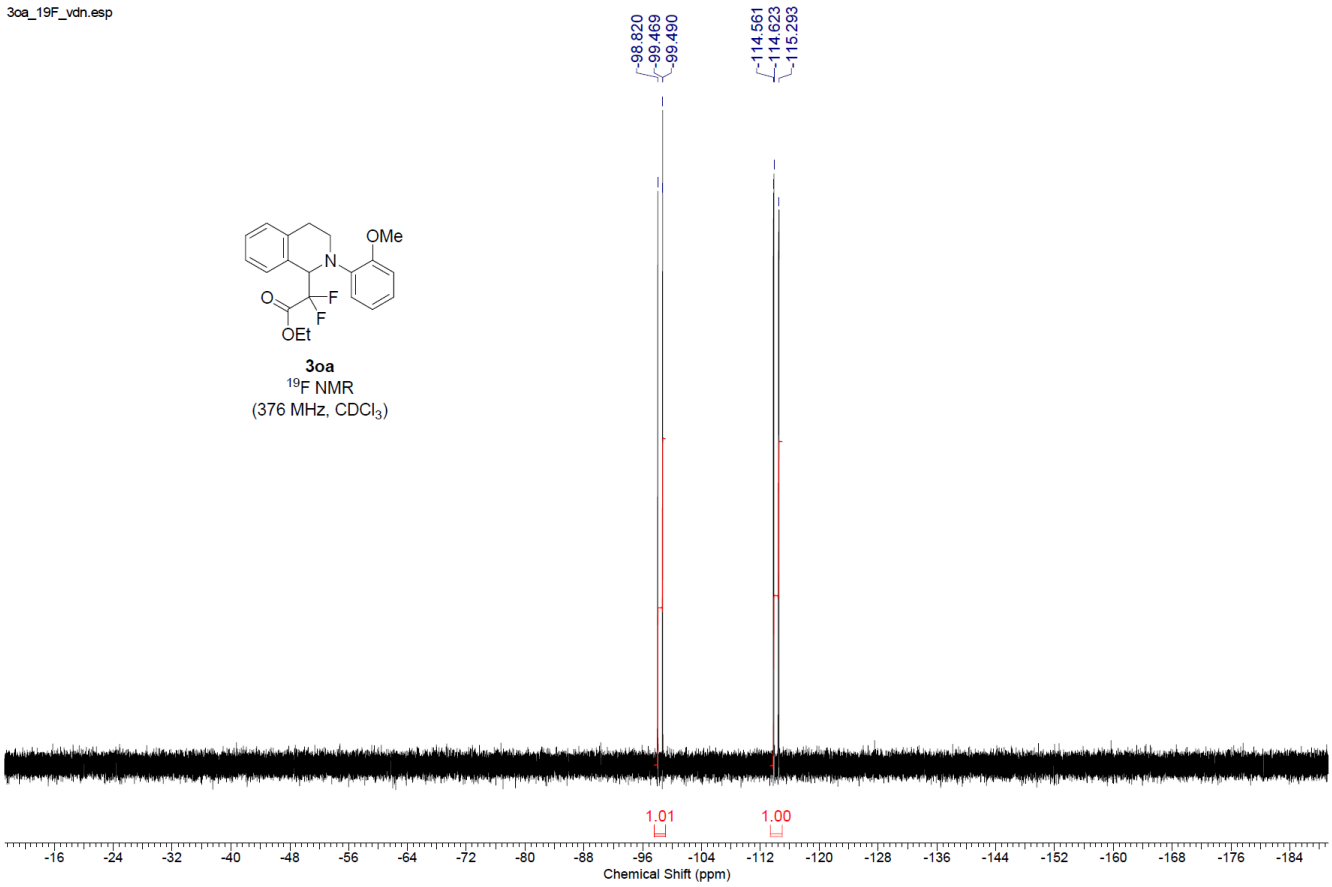

3na_13C_vn.esp
CHLOROFORM-d
164.142
163.907
163.877
163.635
160.535
150.609
136.552
129.823
129.088
128.467
128.262
128.209
126.095
118.571
116.517
114.433
109.440
104.529
103.461
77.258
77.000
76.750
62.769
61.057
60.867
60.837
60.648
55.131
43.219
25.101
13.765
OMe
N
O
F
F
OEt
3na
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)

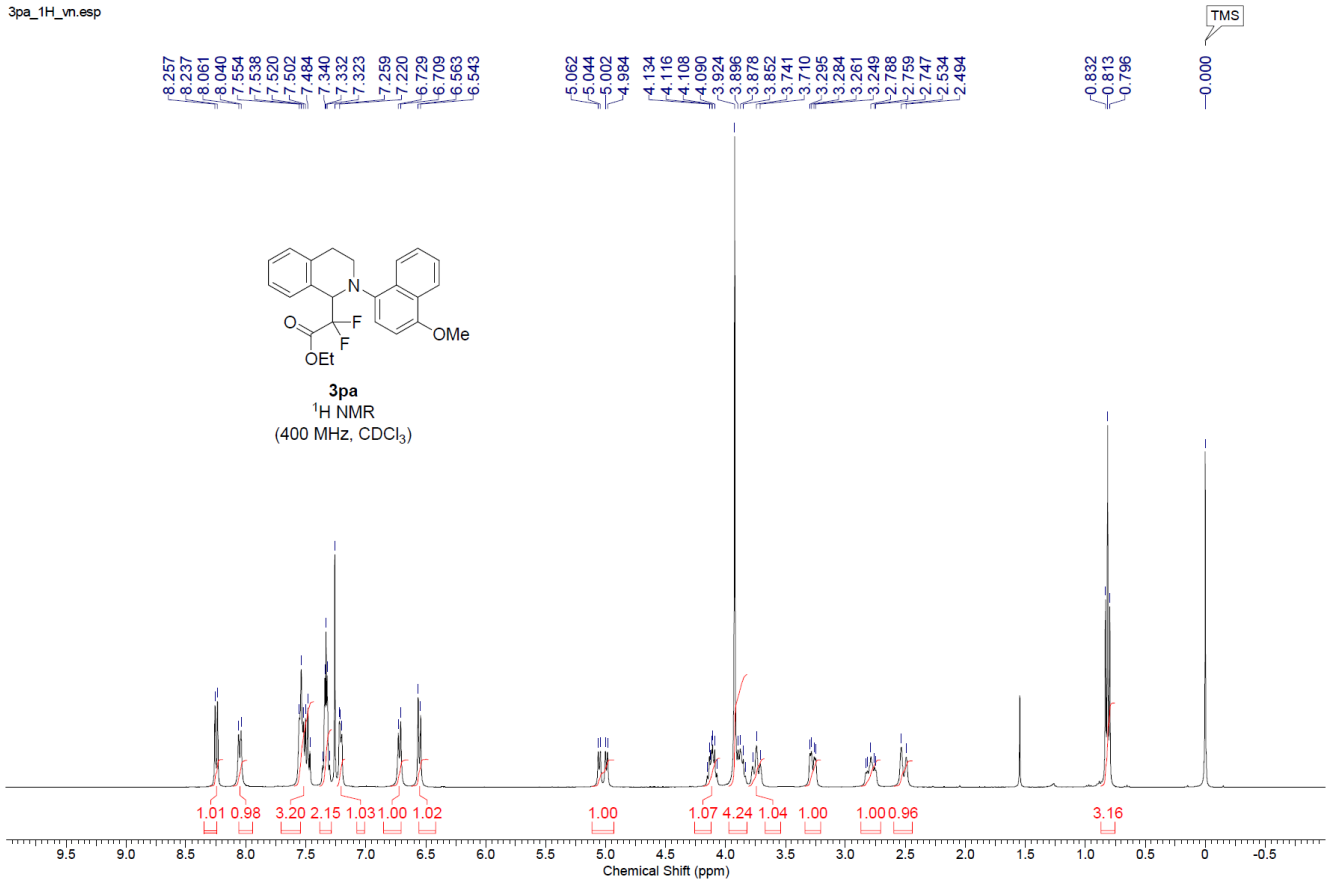


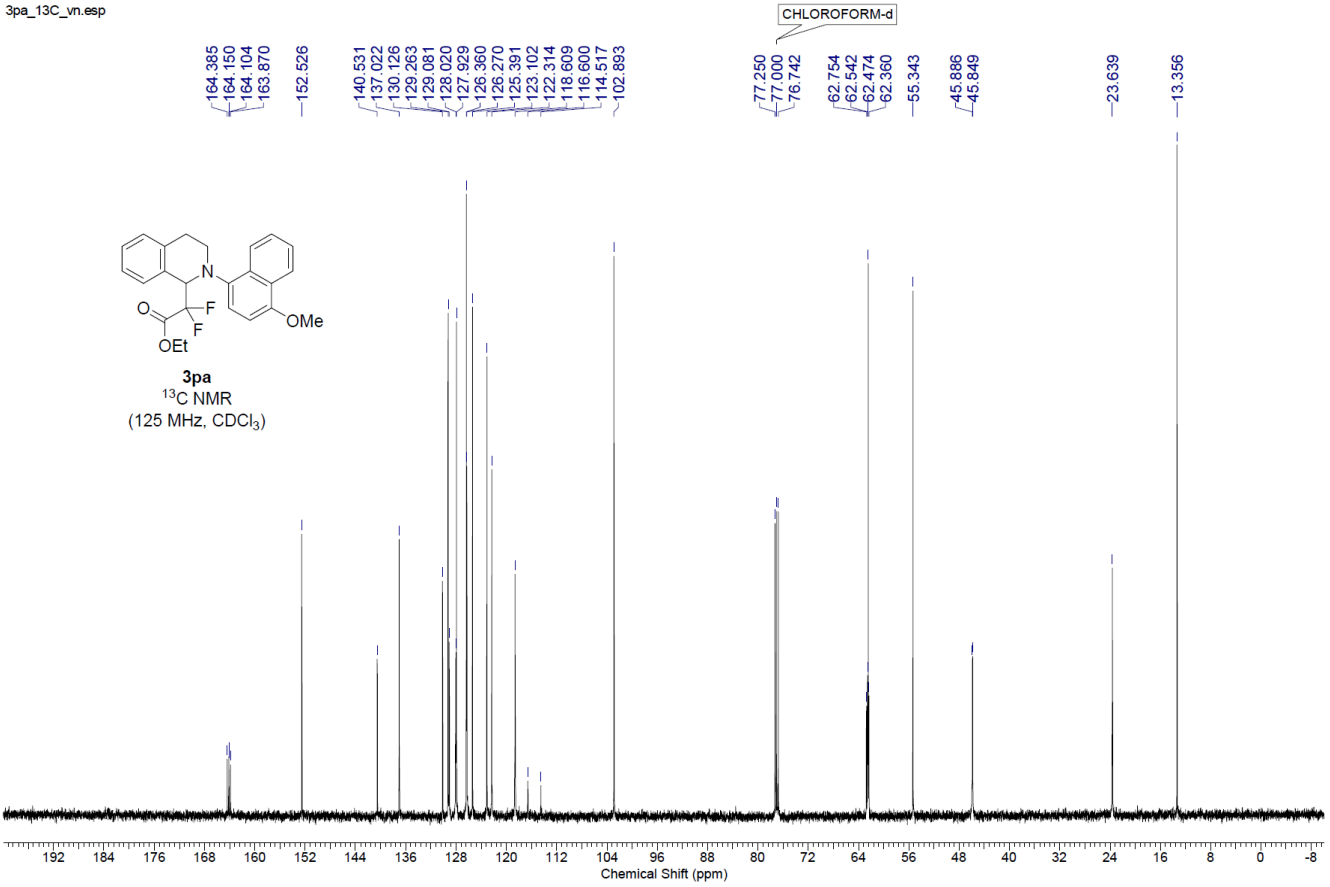
3na
^{19}F NMR
(376 MHz, $CDCl_3$)

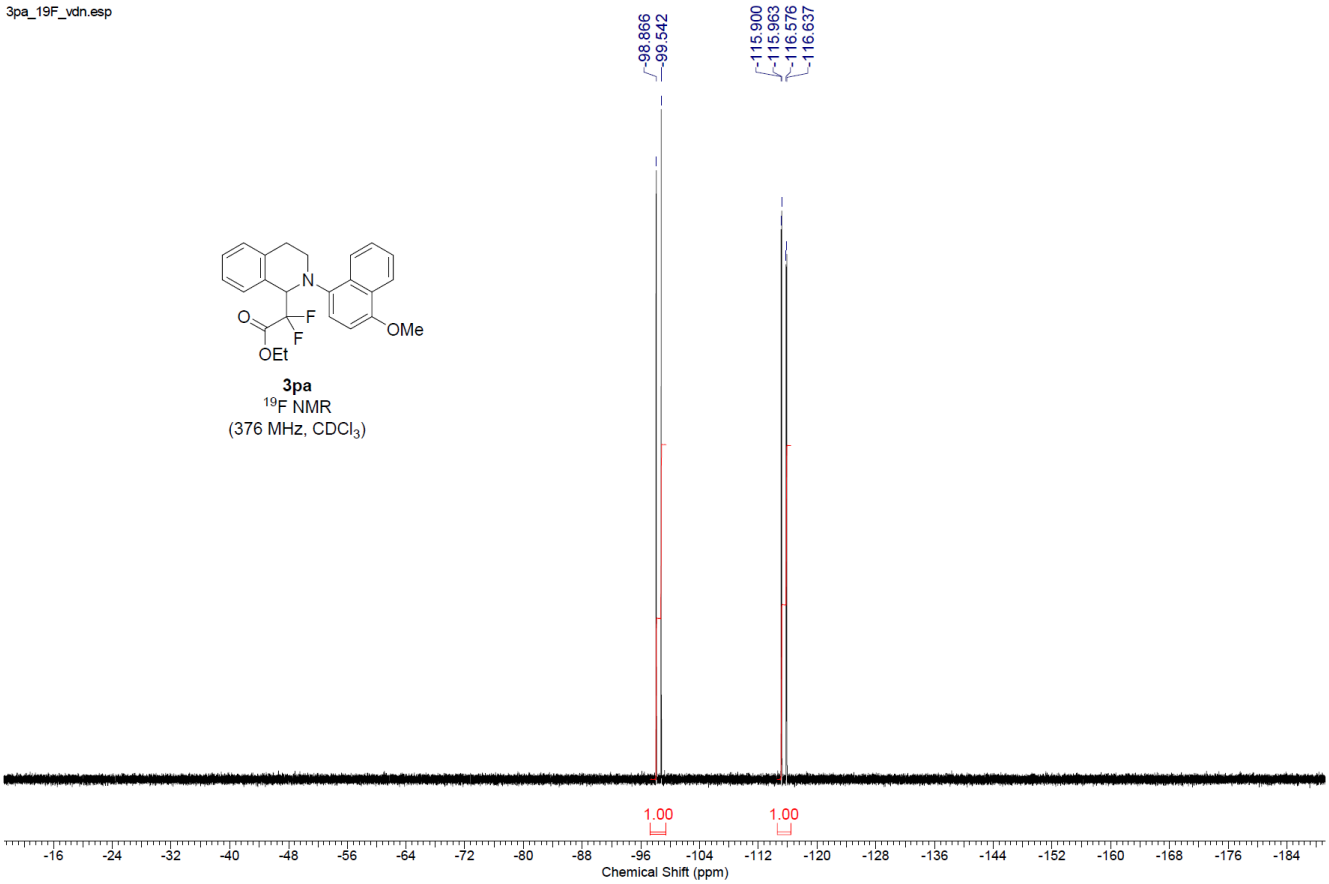

3oa_1H_vn.esp
TMS
7.455
7.446
7.292
7.279
7.260
7.175
7.157
7.003
6.843
6.823
6.771
6.761
6.755
5.085
5.065
5.027
5.008
4.169
4.152
4.143
4.125
4.062
4.044
4.036
4.018
3.771
3.593
3.585
3.440
3.428
2.764
2.750
2.645
2.638
2.630
2.597
1.102
1.085
1.066
0.000
OMe
N
O
F
F
OEt
3oa
1H NMR
(400 MHz, CDCl3)
1.02 3.96 1.05 1.05 1.04 2.13
1.00
2.07 3.22 1.09 1.06
1.04 1.05
3.19
Chemical Shift (ppm)


3oa_13C_v2n.esp
CHLOROFORM-d
164.294
164.051
163.779
153.253
139.341
137.234
129.323
129.088
128.141
128.096
127.823
126.019
124.231
123.322
120.632
118.593
116.540
116.494
114.441
111.410
77.250
77.000
76.742
62.383
61.398
61.216
61.004
55.101
44.583
25.442
13.568
OMe
N
O
F
F
OEt
3oa
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)

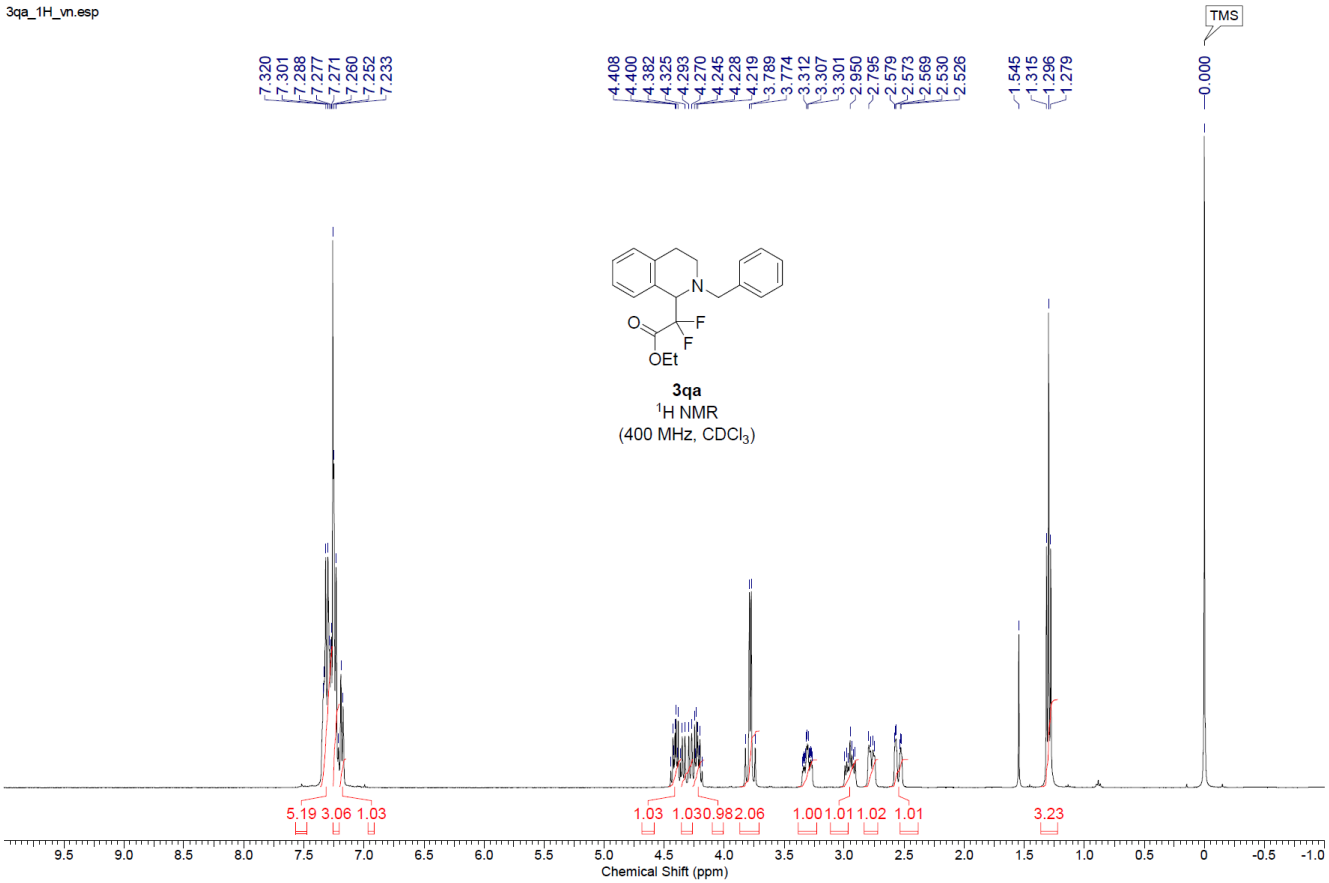

3oa_19F_vdn.esp
-98.820
-99.469
-99.490
-114.561
-114.623
-115.293
OMe
N
O
F
F
OEt
3oa
19F NMR
(376 MHz, CDCl3)
1.01
1.00
-16
-24
-32
-40
-48
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
-184
Chemical Shift (ppm)

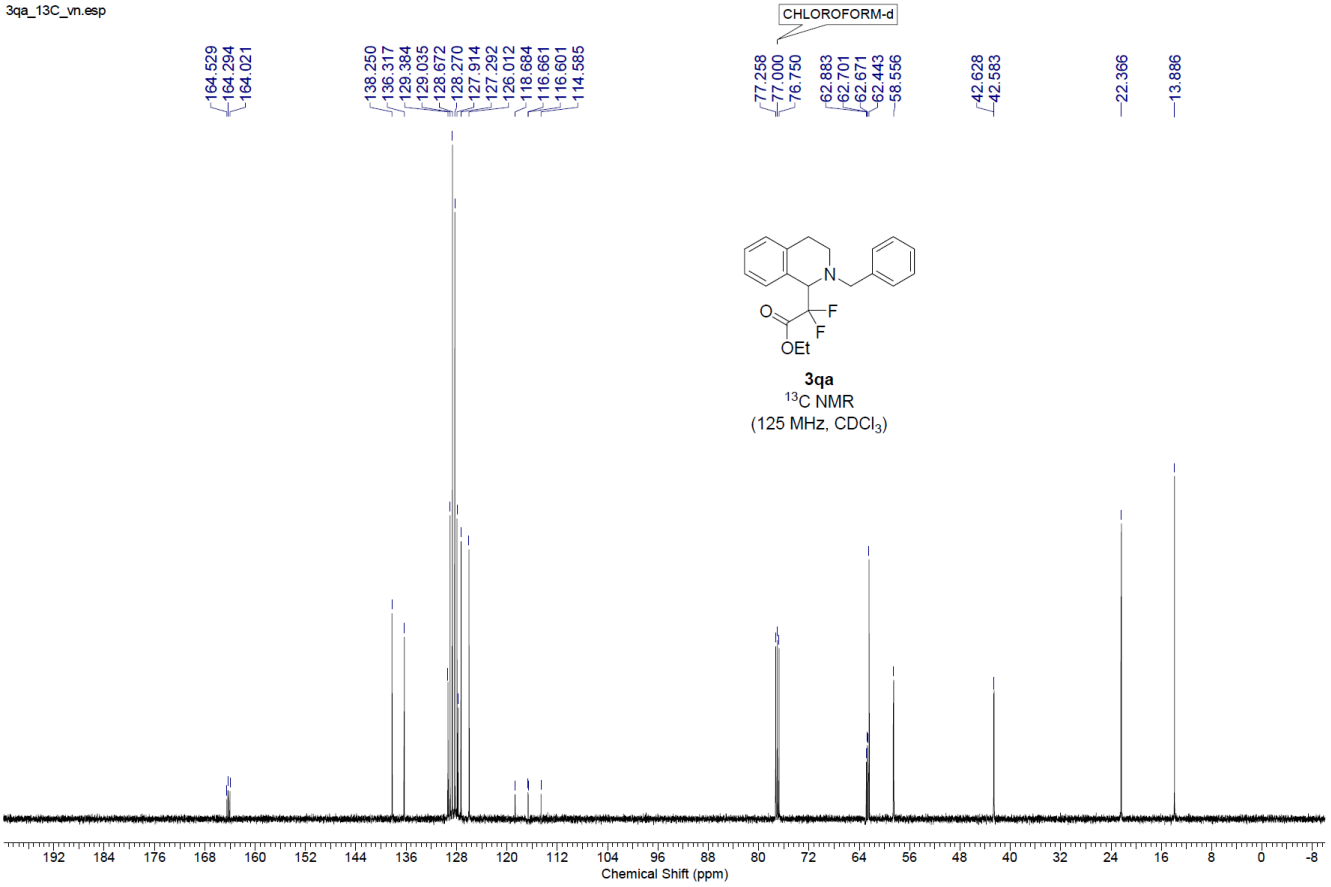

3pa_1H_vn.esp
TMS
8.257
8.237
8.061
8.040
7.554
7.538
7.520
7.502
7.484
7.340
7.332
7.323
7.259
7.220
6.729
6.709
6.563
6.543
5.062
5.044
5.002
4.984
4.134
4.116
4.108
4.090
3.924
3.896
3.878
3.852
3.741
3.710
3.295
3.284
3.261
3.249
2.788
2.759
2.747
2.534
2.494
0.832
0.813
0.796
0.000
N
O
F
F
OEt
OMe
3pa
1H NMR
(400 MHz, CDCl3)
1.01 0.98 3.20 2.15 1.03 1.00 1.02
1.00
1.07 4.24 1.04 1.00
1.00 0.96
3.16
Chemical Shift (ppm)

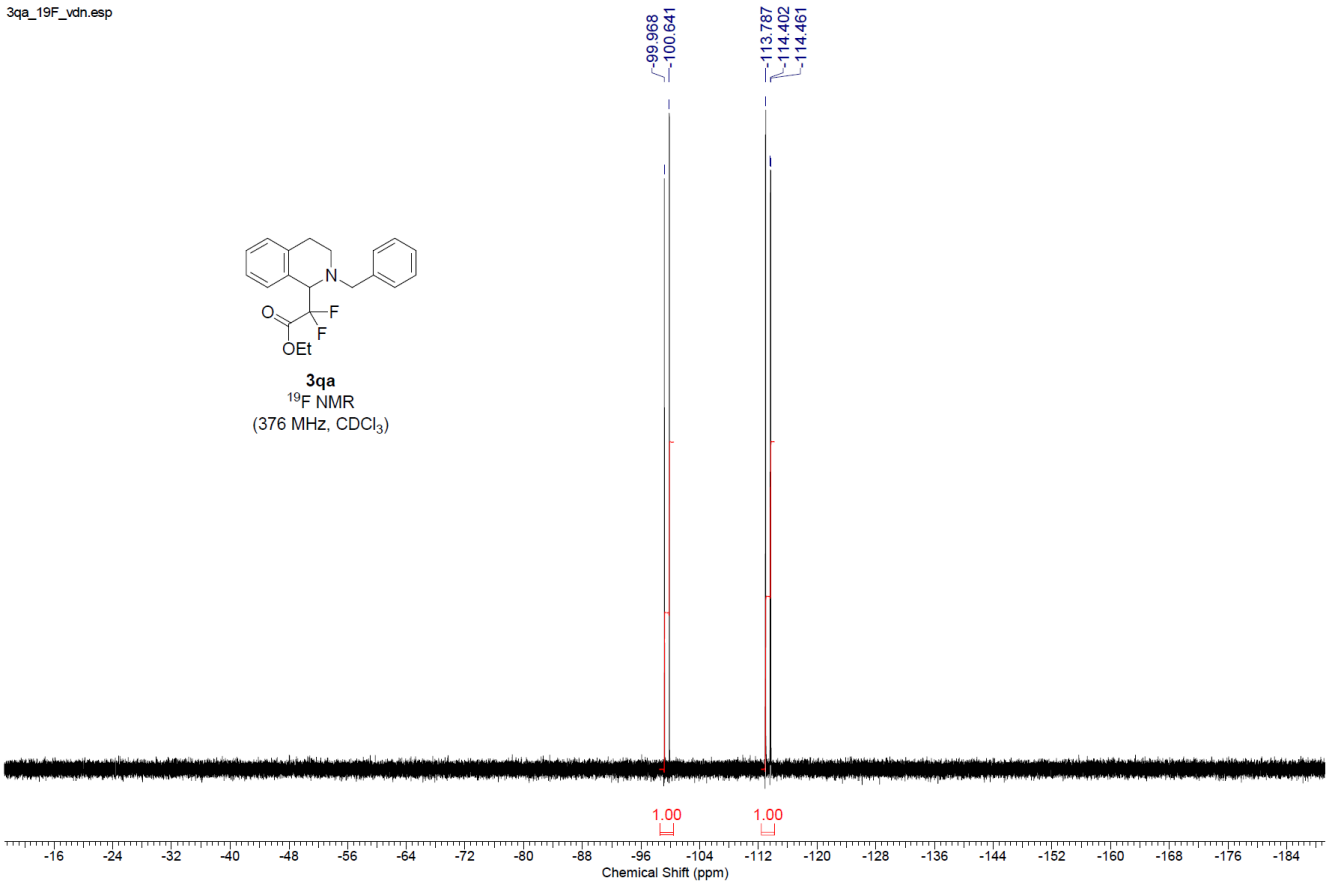

3pa_13C_vn.esp
CHLOROFORM-d
164.385
164.150
164.104
163.870
152.526
140.531
137.022
130.126
129.263
129.081
128.020
127.929
126.360
126.270
125.391
123.102
122.314
118.609
116.600
114.517
102.893
77.250
77.000
76.742
62.754
62.542
62.474
62.360
55.343
45.886
45.849
23.639
13.356
N
O
F
F
OEt
OMe
3pa
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)

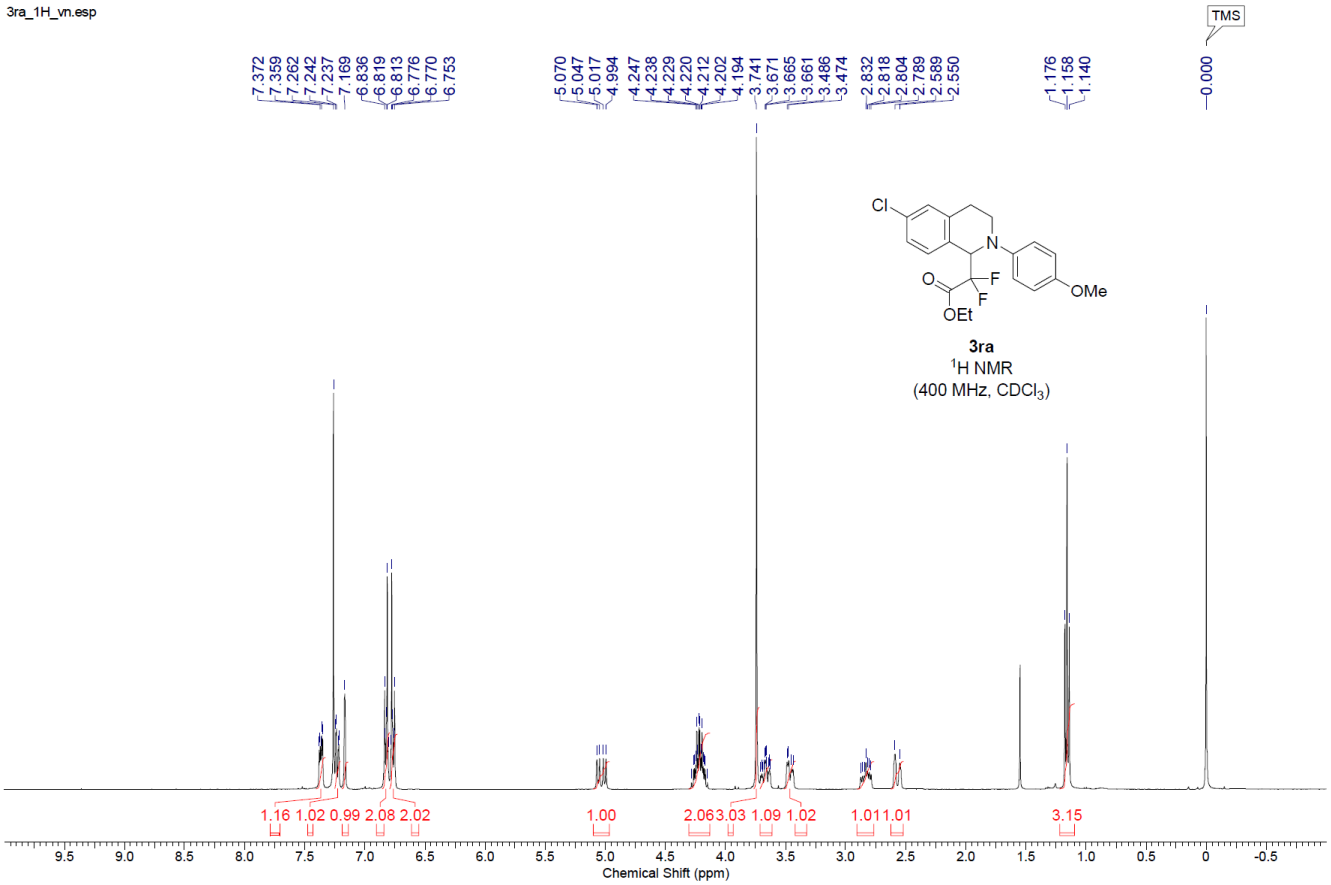


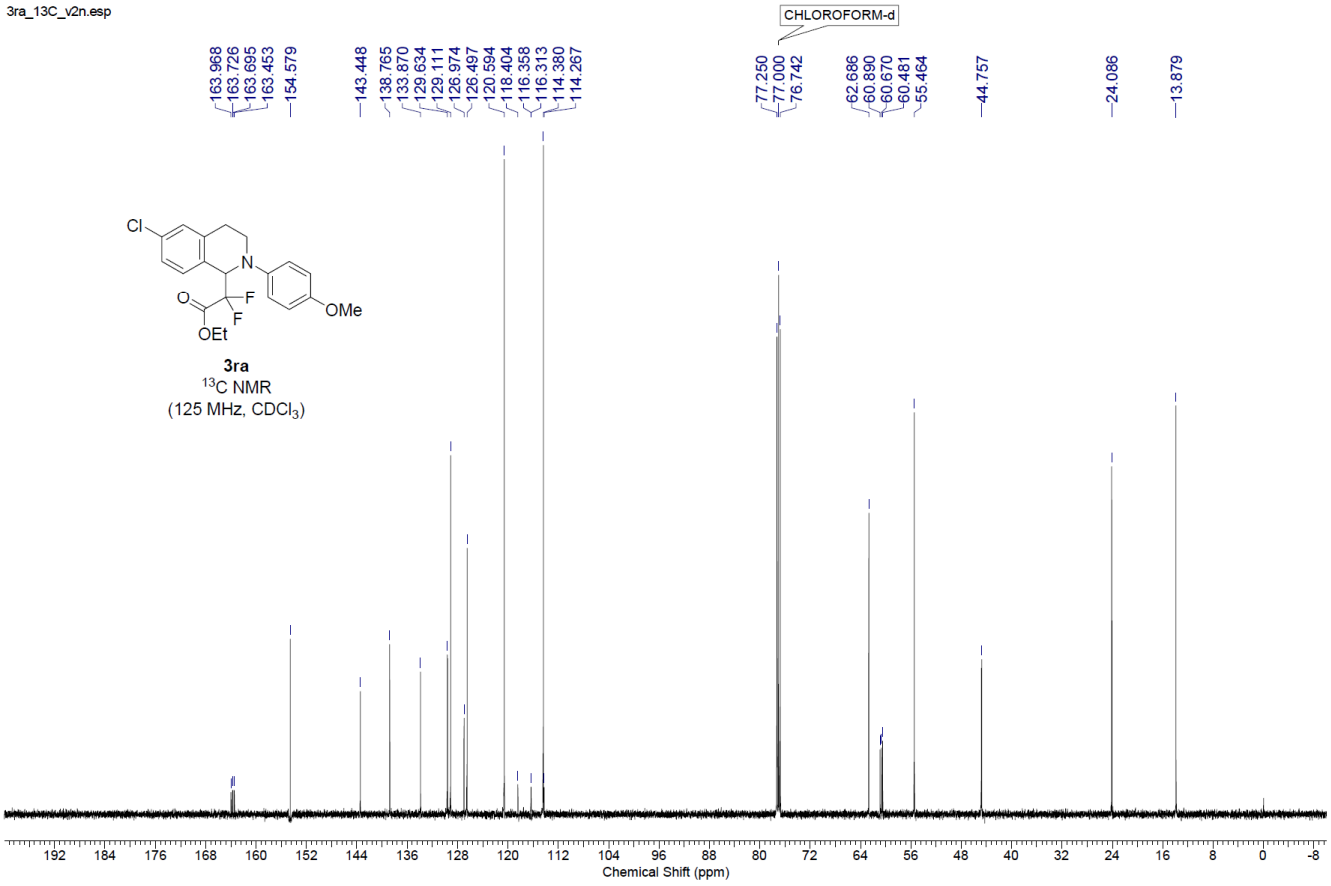
3pa
^{19}F NMR
(376 MHz, $CDCl_3$)

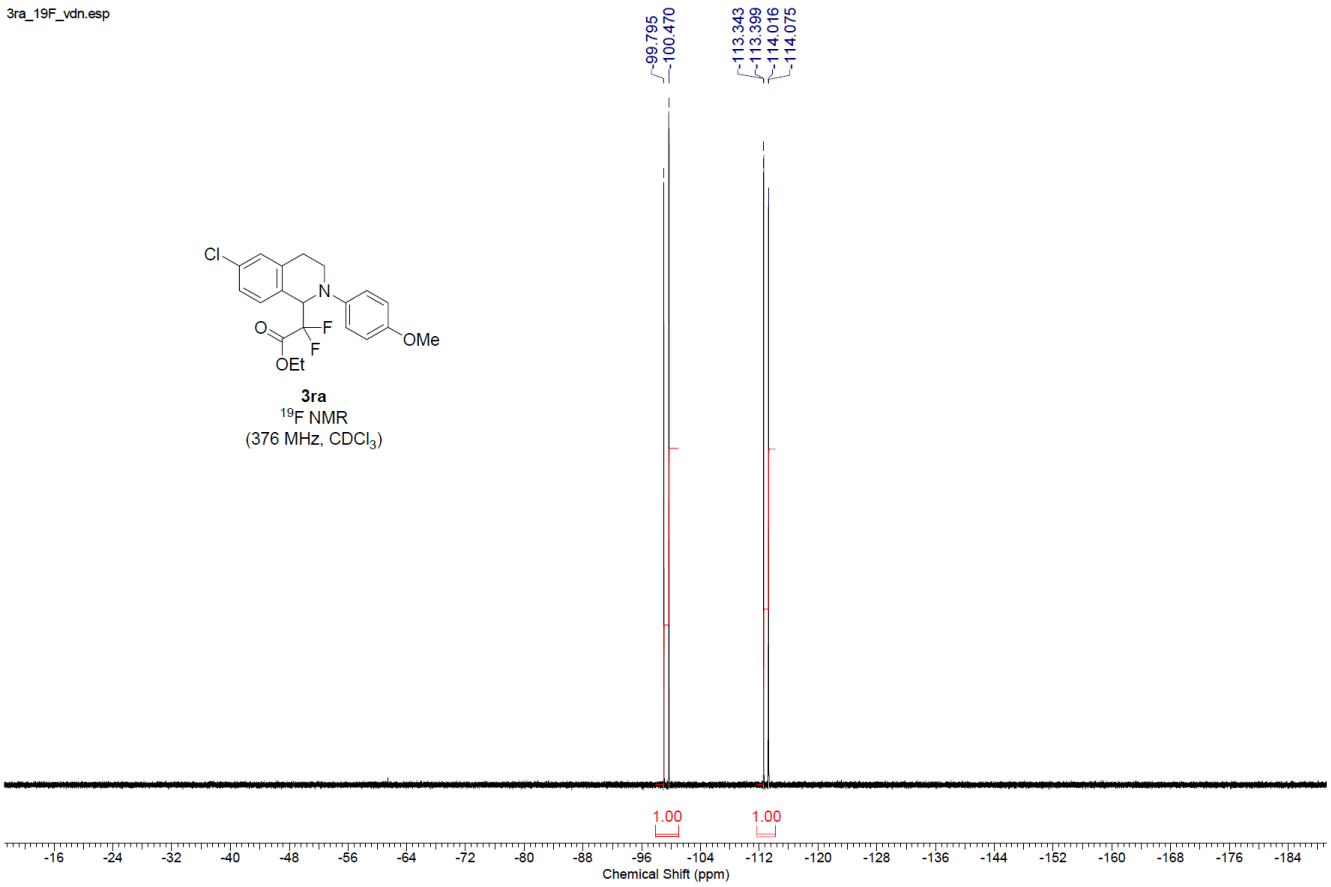

3qa_1H_vn.esp
TMS
7.320
7.301
7.288
7.277
7.271
7.260
7.252
7.233
4.408
4.400
4.382
4.325
4.293
4.270
4.245
4.228
4.219
3.789
3.774
3.312
3.307
3.301
2.950
2.795
2.579
2.573
2.569
2.530
2.526
1.545
1.315
1.296
1.279
0.000
N
O
F
F
OEt
3qa
1H NMR
(400 MHz, CDCl3)
5.19 3.06 1.03
1.03 1.03 0.98 2.06
1.00 1.01 1.02 1.01
3.23
Chemical Shift (ppm)

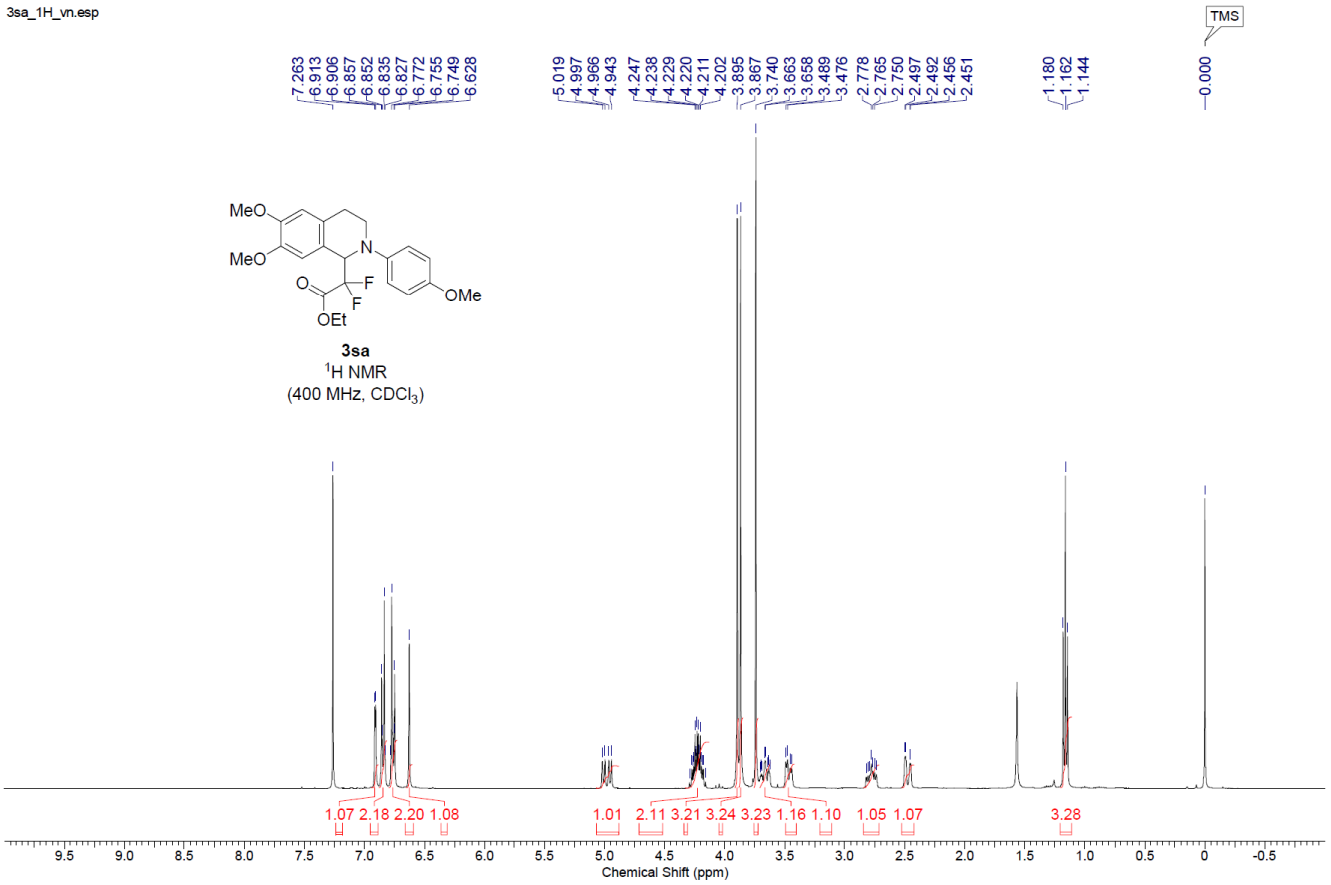

3qa_13C_vn.esp
CHLOROFORM-d
164.529
164.294
164.021
138.250
136.317
129.384
129.035
128.672
128.270
127.914
127.292
126.012
118.684
116.661
116.601
114.585
77.258
77.000
76.750
62.883
62.701
62.671
62.443
58.556
42.628
42.583
22.366
13.886
N
O
F
F
OEt
3qa
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)

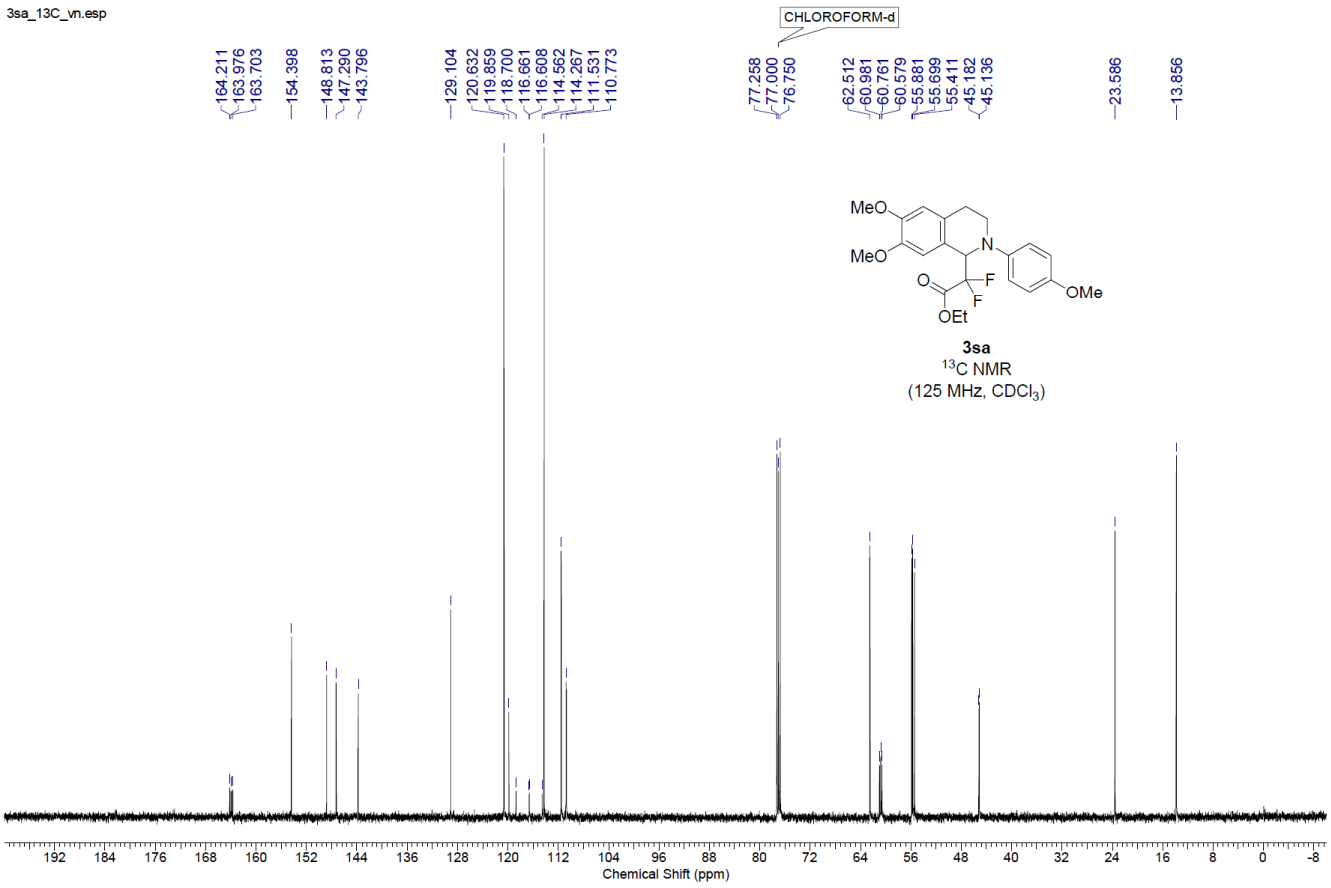

3qa_19F_vdn.esp
-99.968
-100.641
-113.787
-114.402
-114.461
N
O
F
F
OEt
3qa
19F NMR
(376 MHz, CDCl3)
1.00
1.00
-16
-24
-32
-40
-48
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
-184
Chemical Shift (ppm)

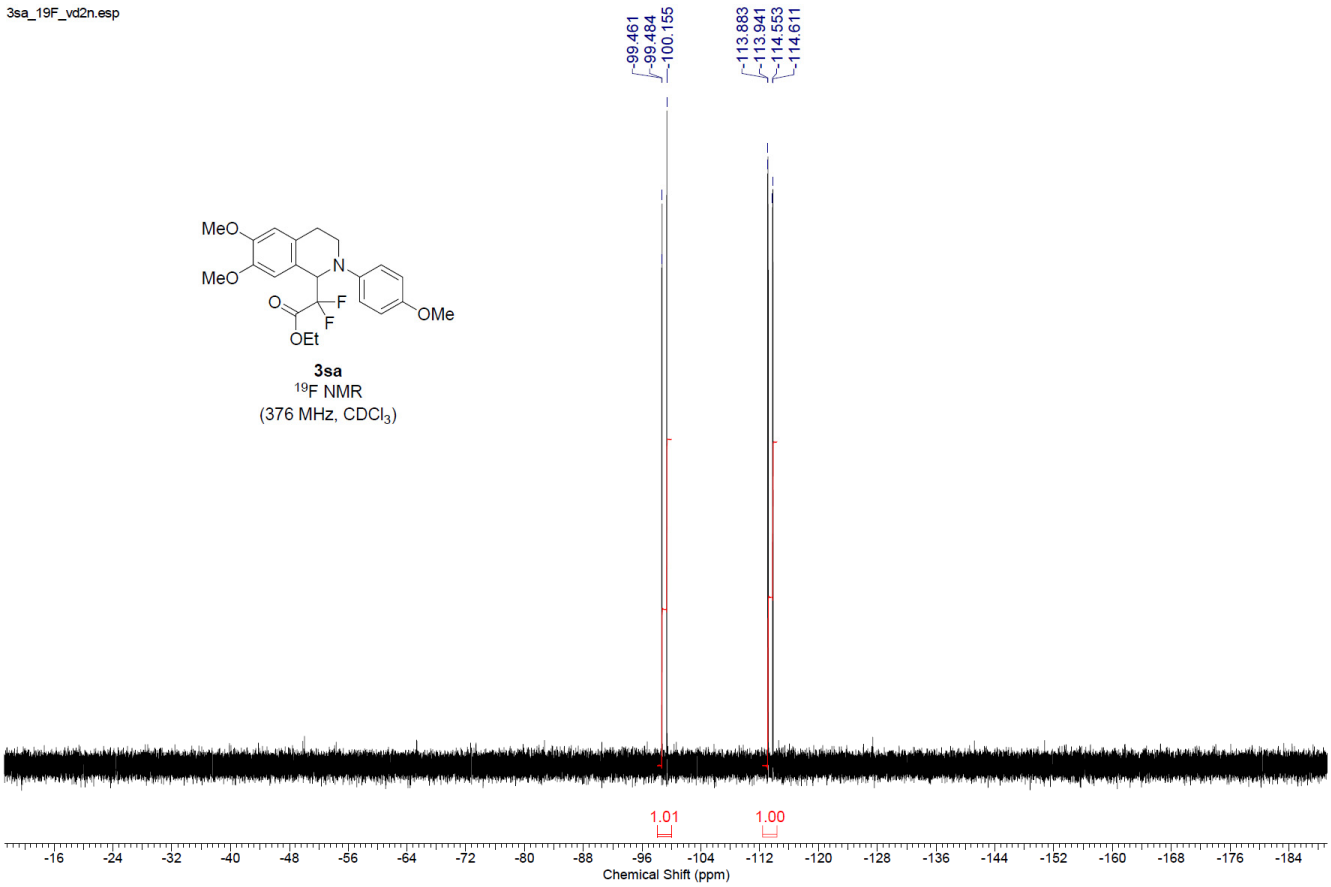

3ra_1H_vn.esp
TMS
7.372
7.359
7.262
7.242
7.237
7.169
6.836
6.819
6.813
6.776
6.770
6.753
5.070
5.047
5.017
4.994
4.247
4.238
4.229
4.220
4.212
4.202
4.194
3.741
3.671
3.665
3.661
3.486
3.474
2.832
2.818
2.804
2.789
2.589
2.550
1.176
1.158
1.140
0.000
Cl
N
O
F
F
OEt
OMe
3ra
1H NMR
(400 MHz, CDCl3)
1.16 1.02 0.99 2.08 2.02
1.00
2.06 3.03 1.09 1.02
1.01 1.01
3.15
Chemical Shift (ppm)

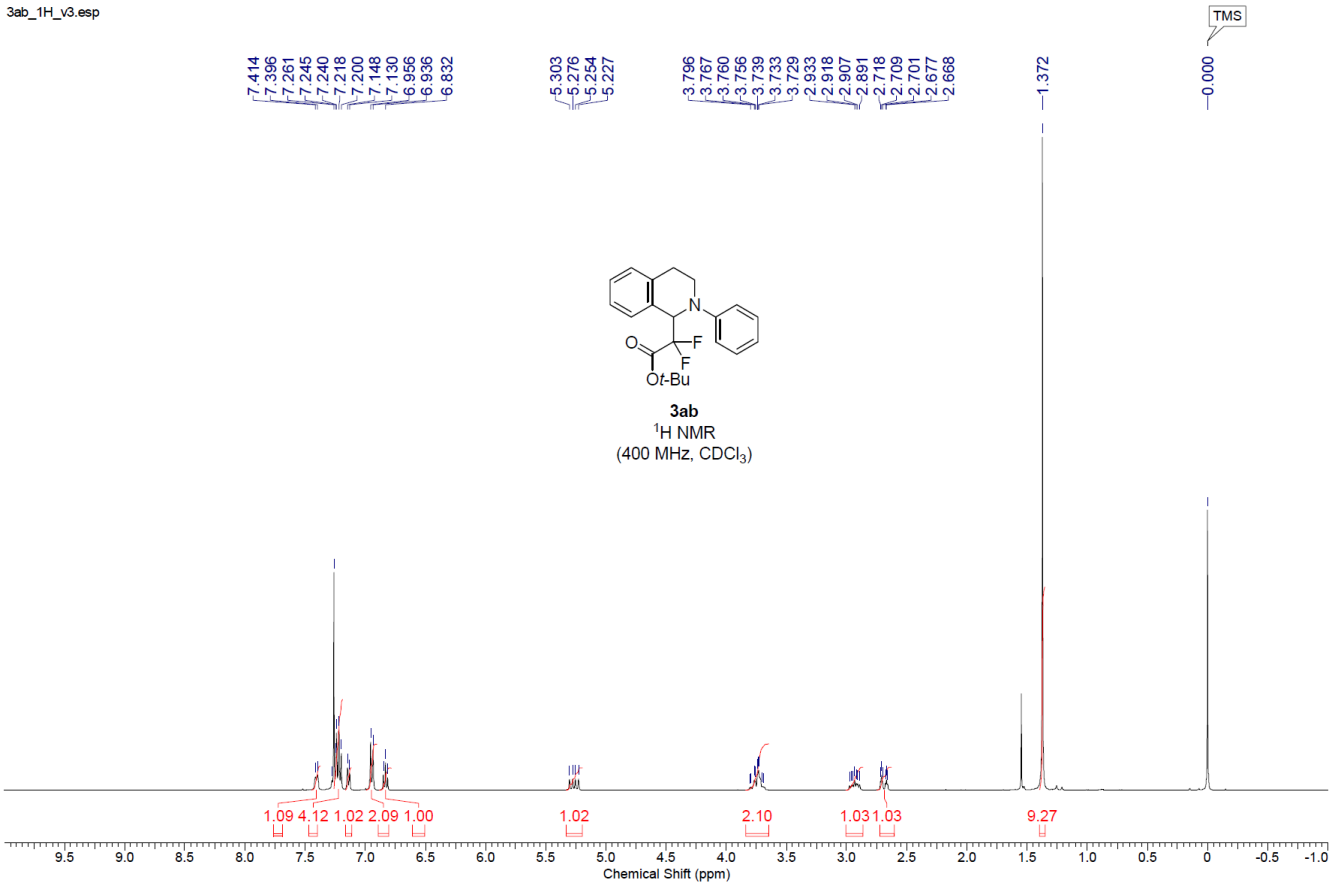

3ra_13C_v2n.esp
CHLOROFORM-d
163.968
163.726
163.695
163.453
154.579
143.448
138.765
133.870
129.634
129.111
126.974
126.497
120.594
118.404
116.358
116.313
114.380
114.267
77.250
77.000
76.742
62.686
60.890
60.670
60.481
55.464
44.757
24.086
13.879
Cl
N
O
F
F
OEt
OMe
3ra
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)


3ra_19F_vdn.esp
-99.795
-100.470
-113.343
-113.399
-114.016
-114.075
Cl
N
O
F
F
OEt
OMe
3ra
19F NMR
(376 MHz, CDCl3)
1.00
1.00
-16
-24
-32
-40
-48
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
-184
Chemical Shift (ppm)

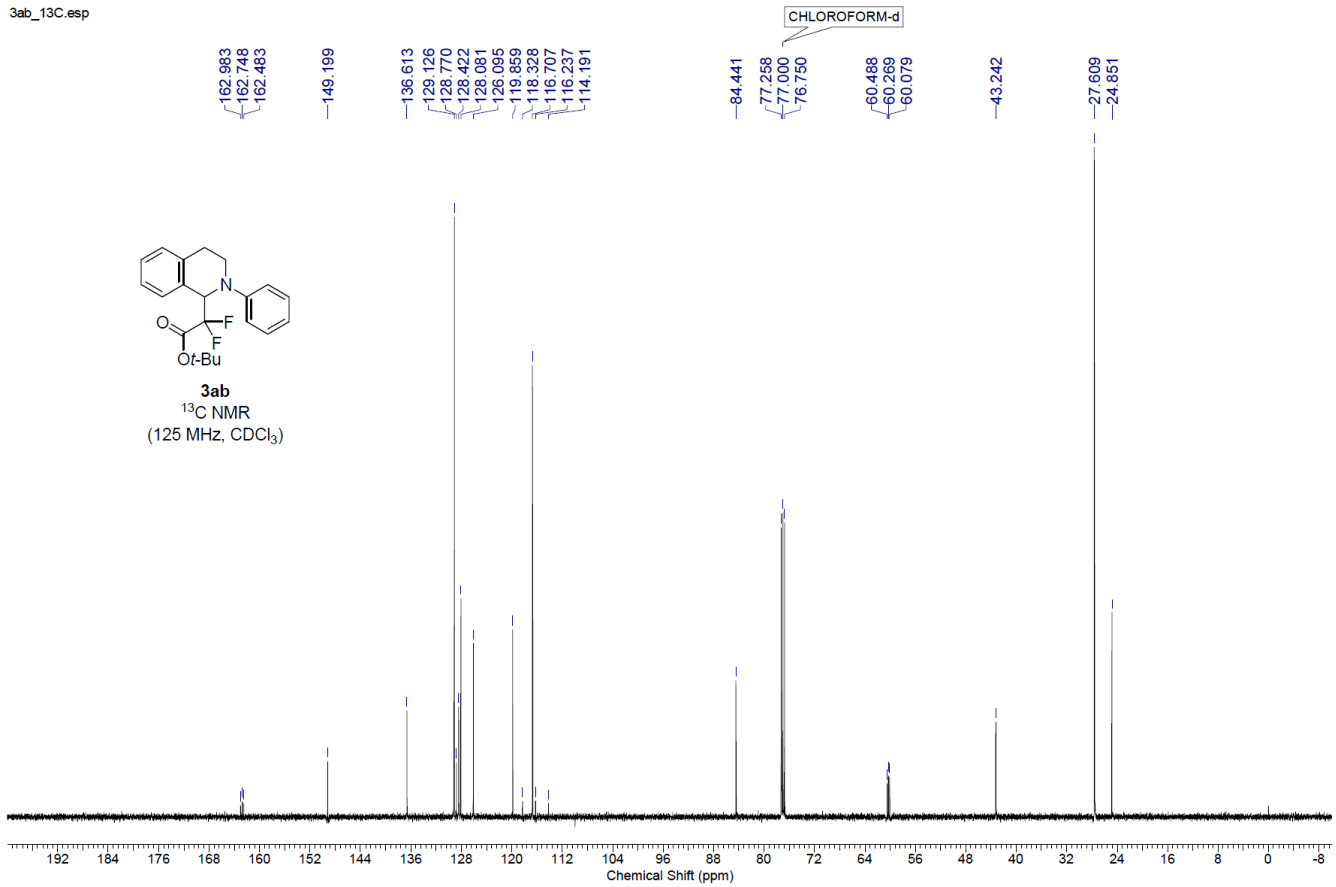

3sa_1H_vn.esp
TMS
7.263
6.913
6.906
6.857
6.852
6.835
6.827
6.772
6.755
6.749
6.628
5.019
4.997
4.966
4.943
4.247
4.238
4.229
4.220
4.211
4.202
3.895
3.867
3.740
3.663
3.658
3.489
3.476
2.778
2.765
2.750
2.497
2.492
2.456
2.451
1.180
1.162
1.144
0.000
MeO
MeO
N
O
F
F
OEt
OMe
3sa
1H NMR
(400 MHz, CDCl3)
1.07 2.18 2.20 1.08
1.01 2.11 3.21 3.24 3.23 1.16 1.10 1.05 1.07
3.28
Chemical Shift (ppm)


3sa_13C_vn.esp
CHLOROFORM-d
164.211
163.976
163.703
154.398
148.813
147.290
143.796
129.104
120.632
119.859
118.700
116.661
116.608
114.562
114.267
111.531
110.773
77.258
77.000
76.750
62.512
60.981
60.761
60.579
55.881
55.699
55.411
45.182
45.136
23.586
13.856
MeO
MeO
N
O
F
F
OEt
OMe
3sa
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)

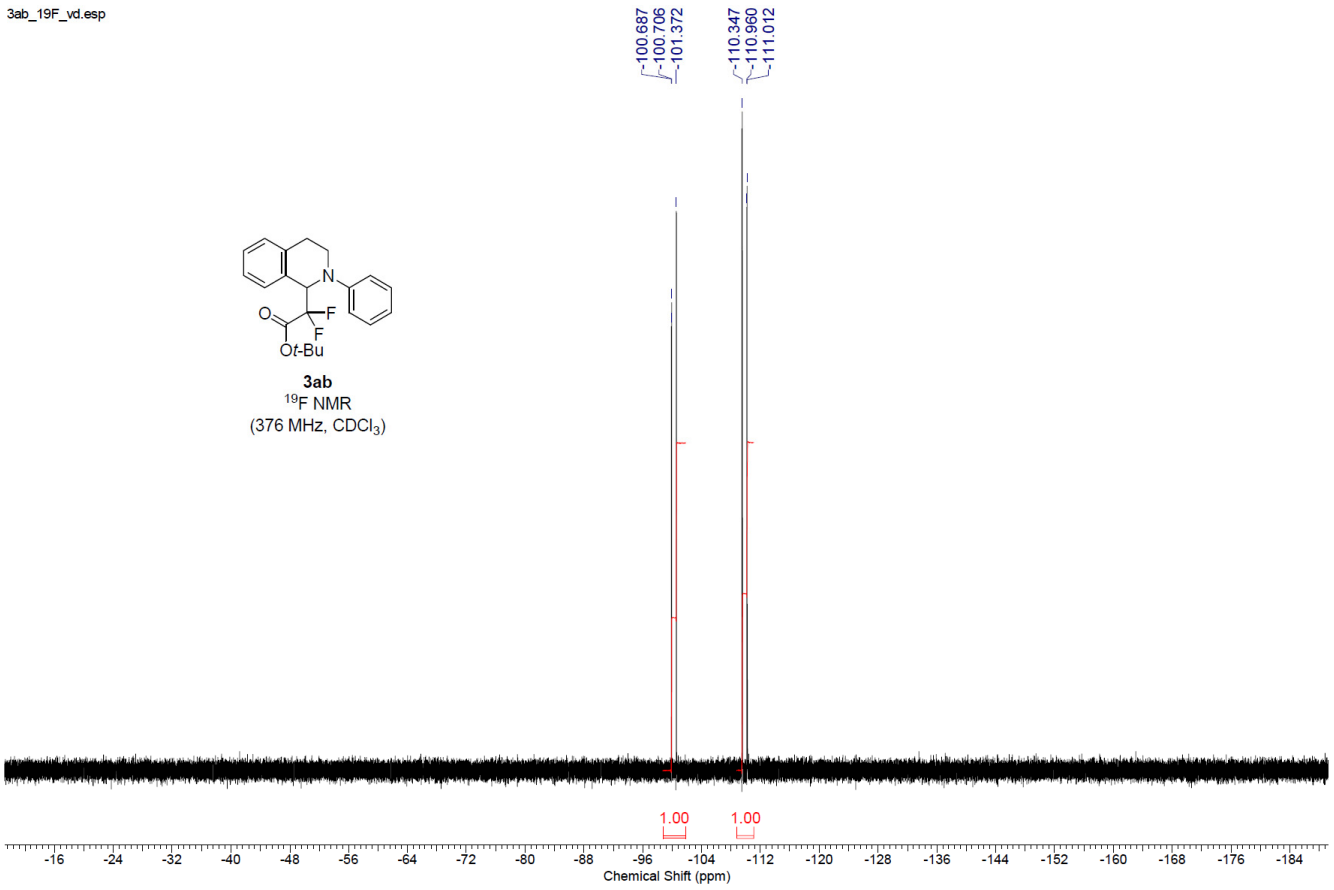

3sa_19F_vd2n.esp
-99.461
-99.484
-100.155
-113.883
-113.941
-114.553
-114.611
MeO
MeO
N
O
F
F
OEt
OMe
3sa
19F NMR
(376 MHz, CDCl3)
1.01
1.00
-16
-24
-32
-40
-48
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
-184
Chemical Shift (ppm)

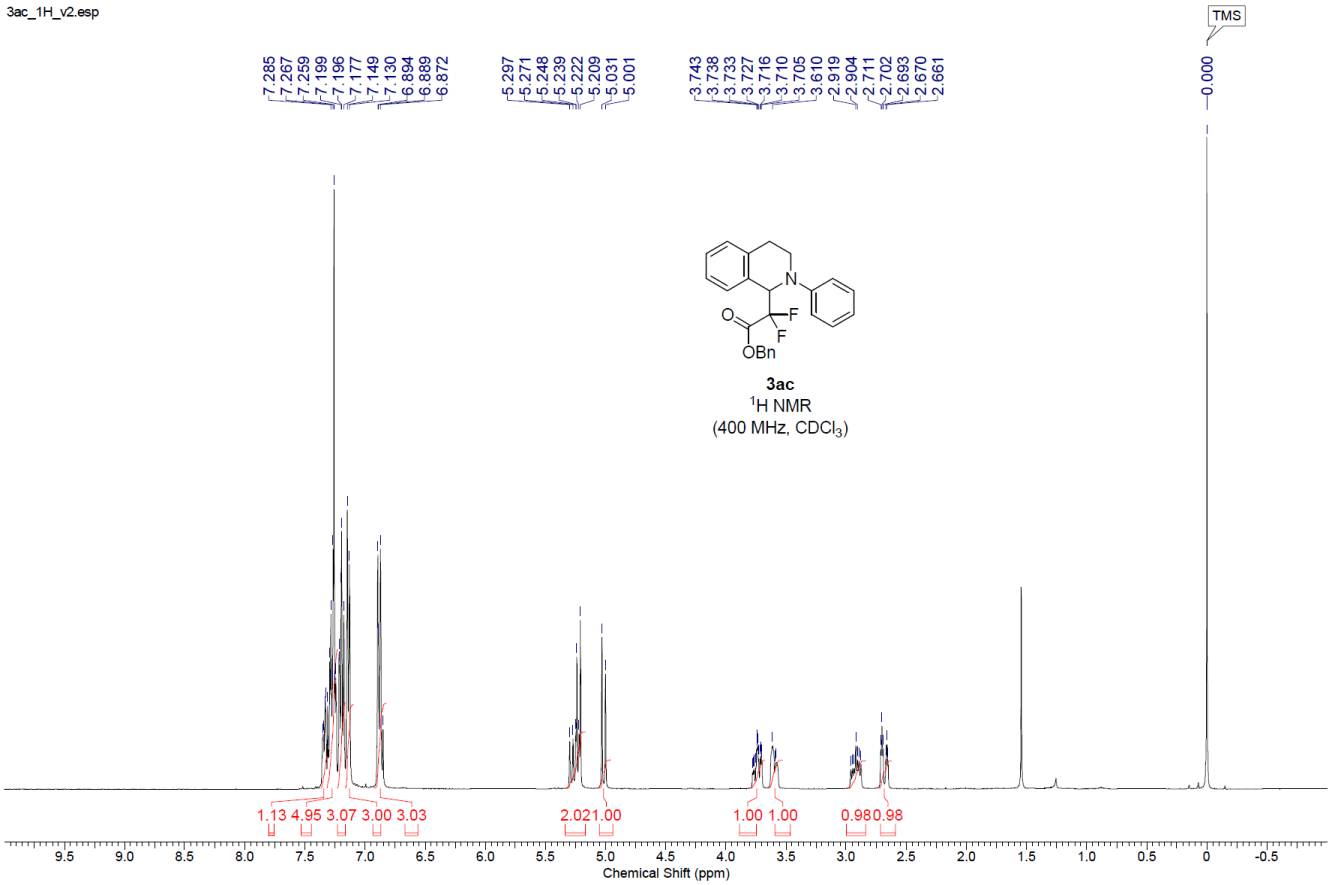


3ab
^{1}H NMR
(400 MHz, $CDCl_3$)

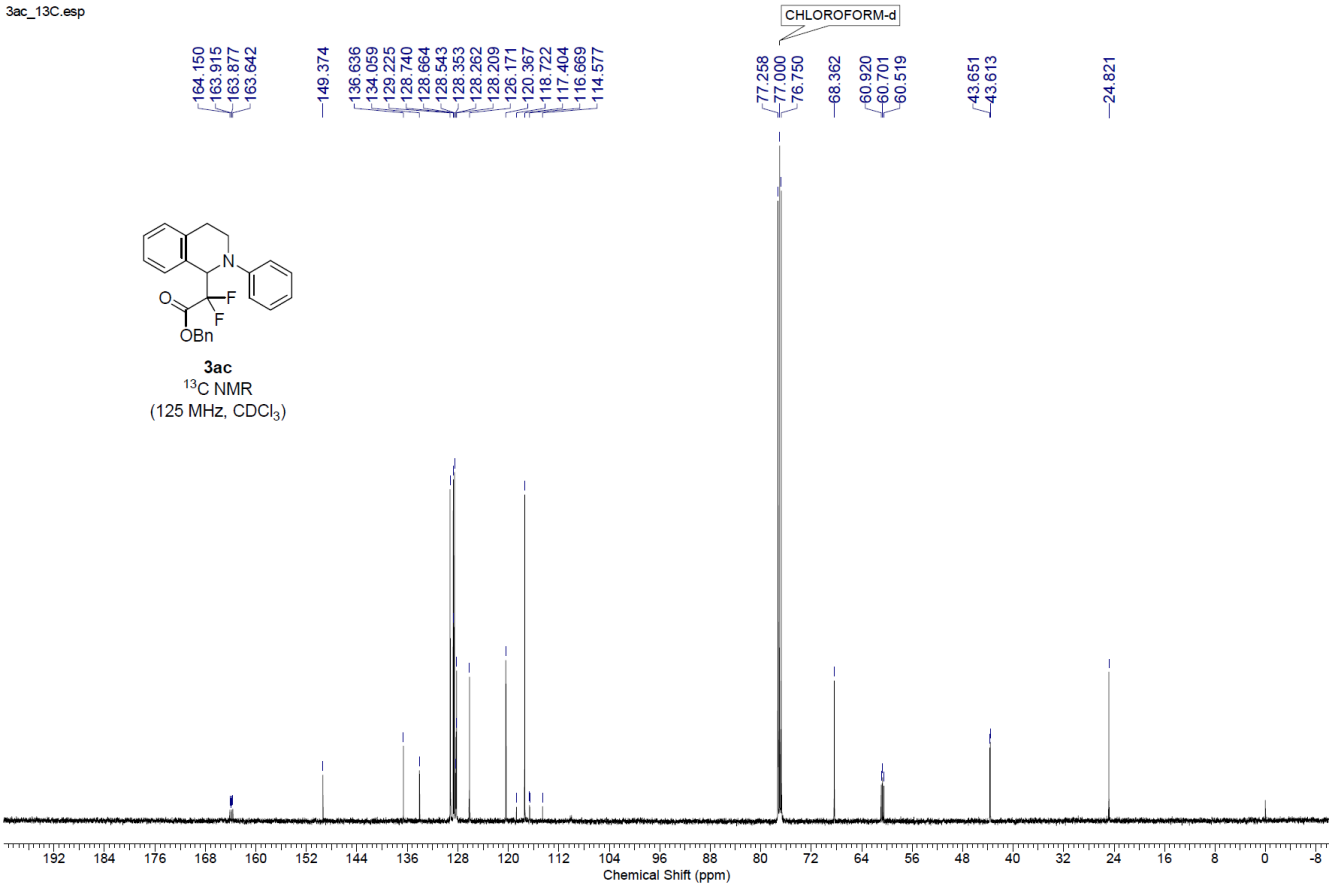


3ab
^{13}C NMR
(125 MHz, $CDCl_3$)

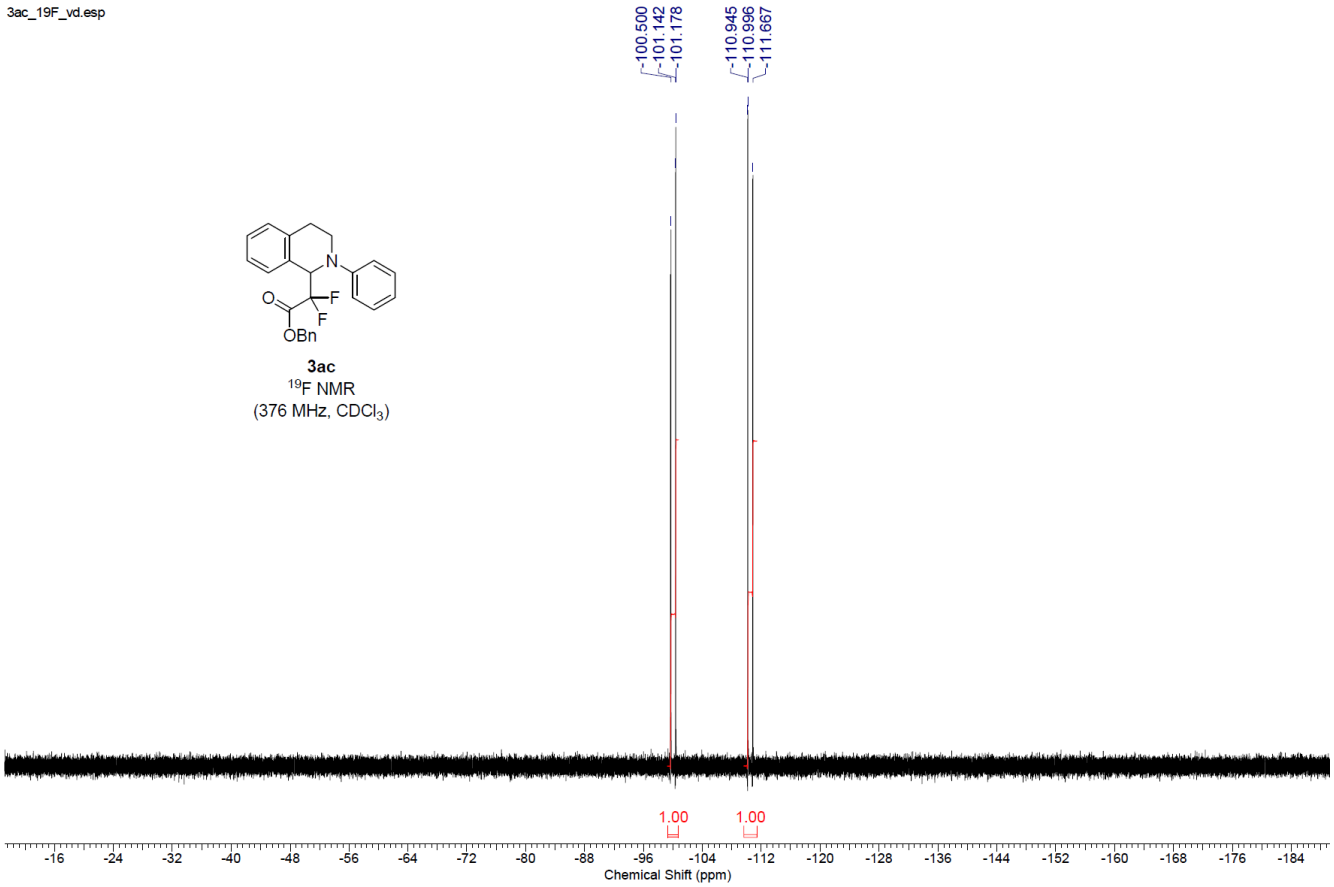

3ab_19F_vd.esp
-100.687
-100.706
-101.372
-110.347
-110.960
-111.012
N
O
F
F
Ot-Bu
3ab
19F NMR
(376 MHz, CDCl3)
1.00
1.00
-16
-24
-32
-40
-48
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
-184
Chemical Shift (ppm)

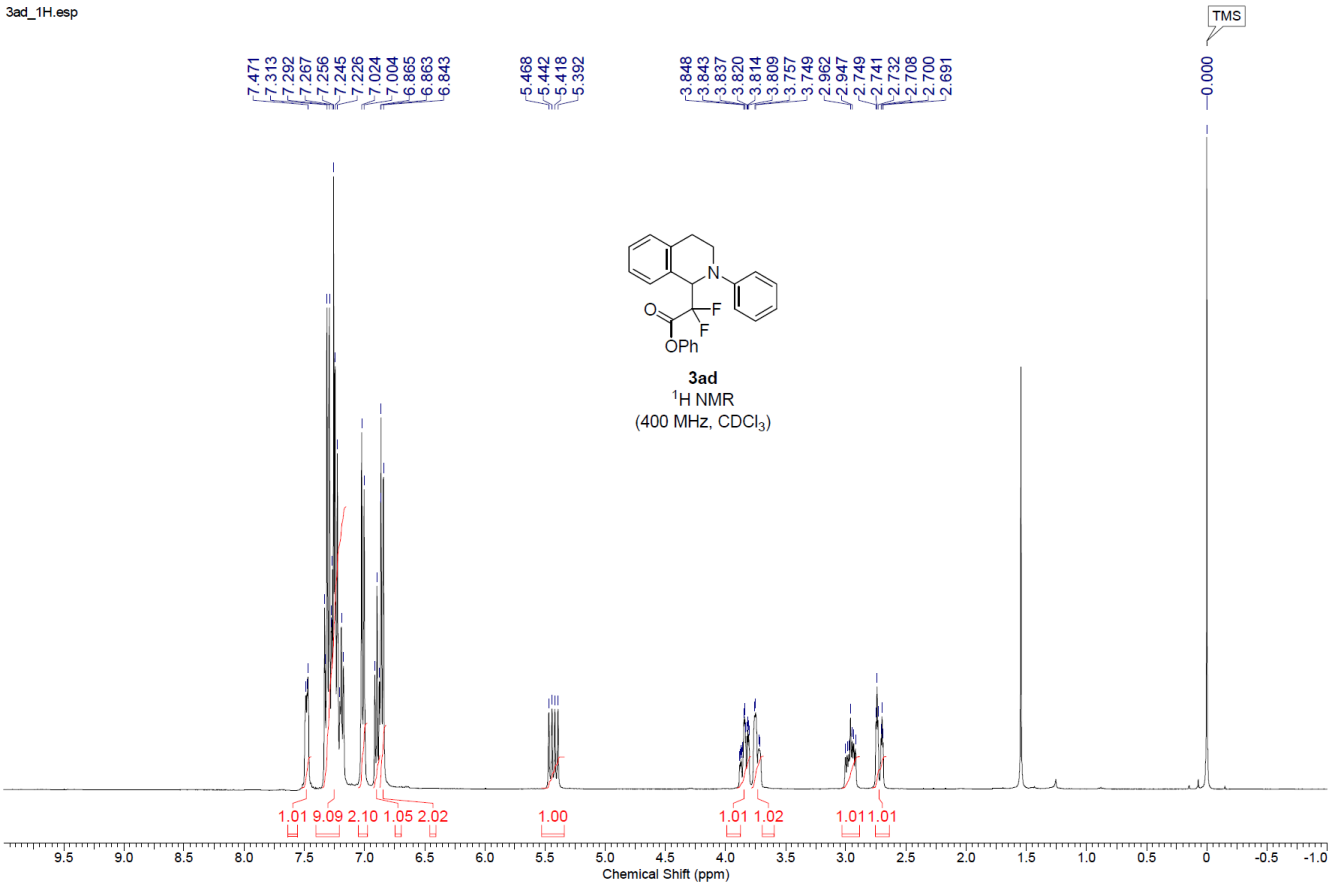


3ac
^{1}H NMR
(400 MHz, $CDCl_3$)

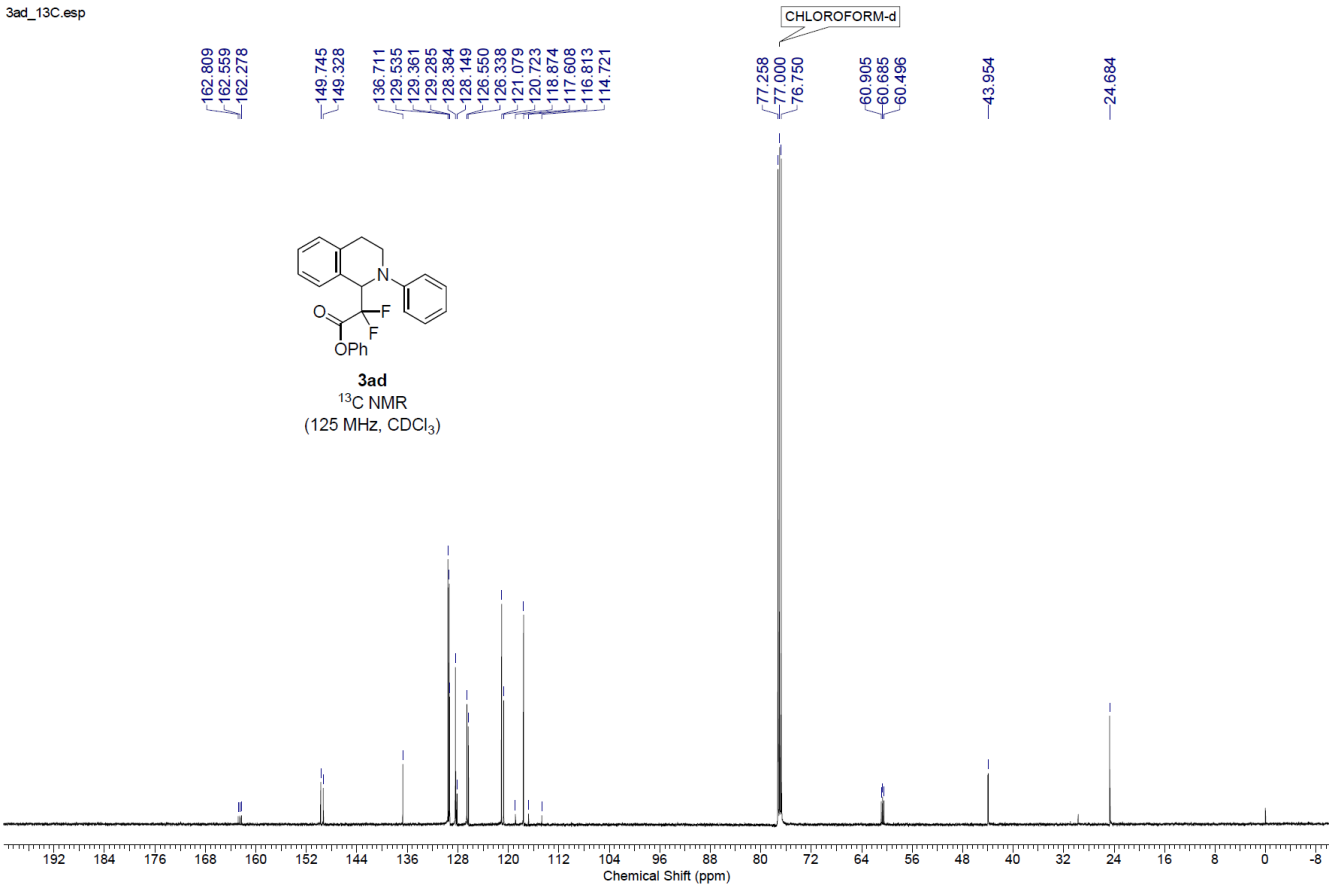


3ac
^{13}C NMR
(125 MHz, $CDCl_3$)

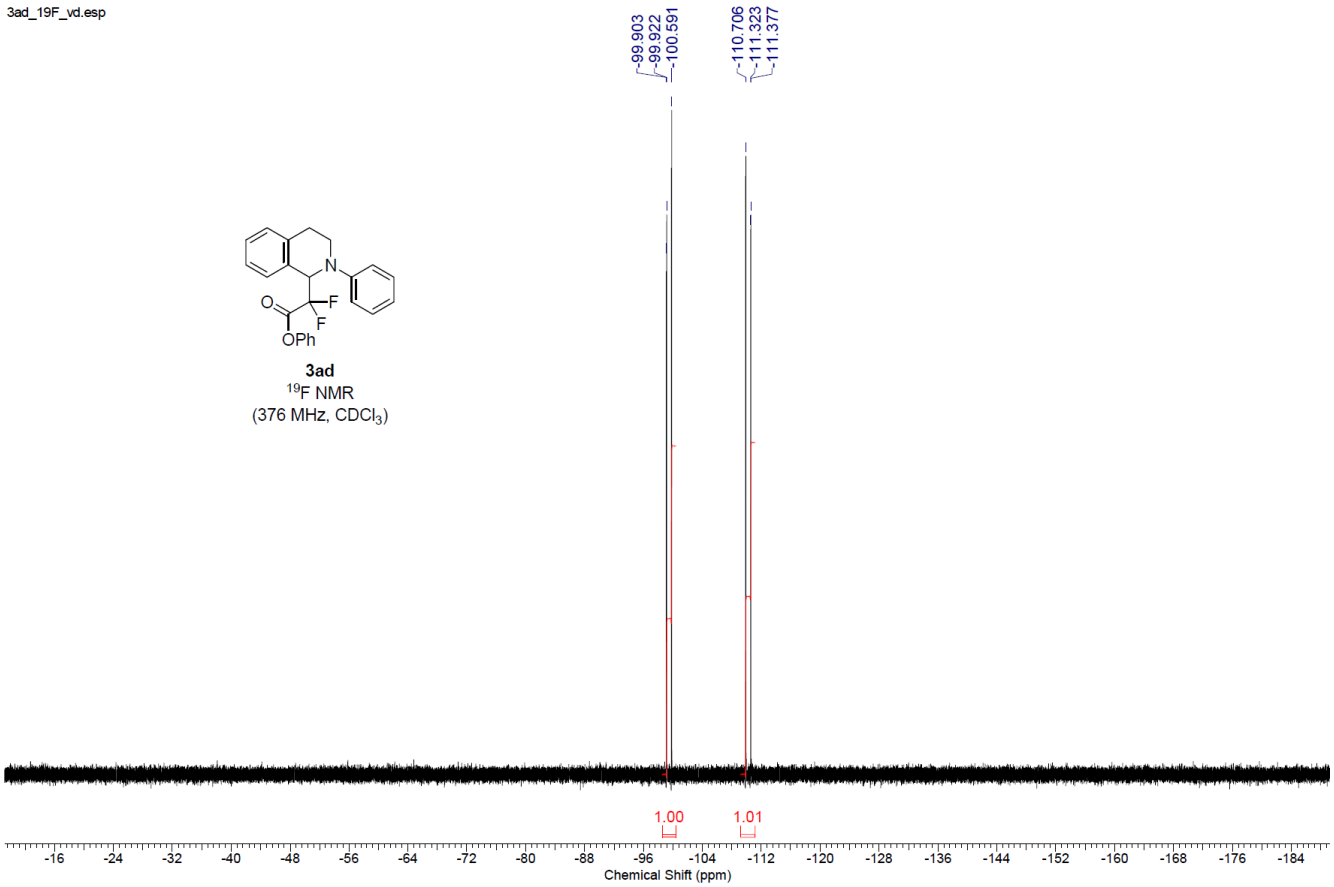

3ac_19F_vd.esp
100.500
101.142
101.178
110.945
110.996
111.667
N
O
F
F
OBn
3ac
19F NMR
(376 MHz, CDCl3)
1.00
1.00
-16
-24
-32
-40
-48
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
-184
Chemical Shift (ppm)

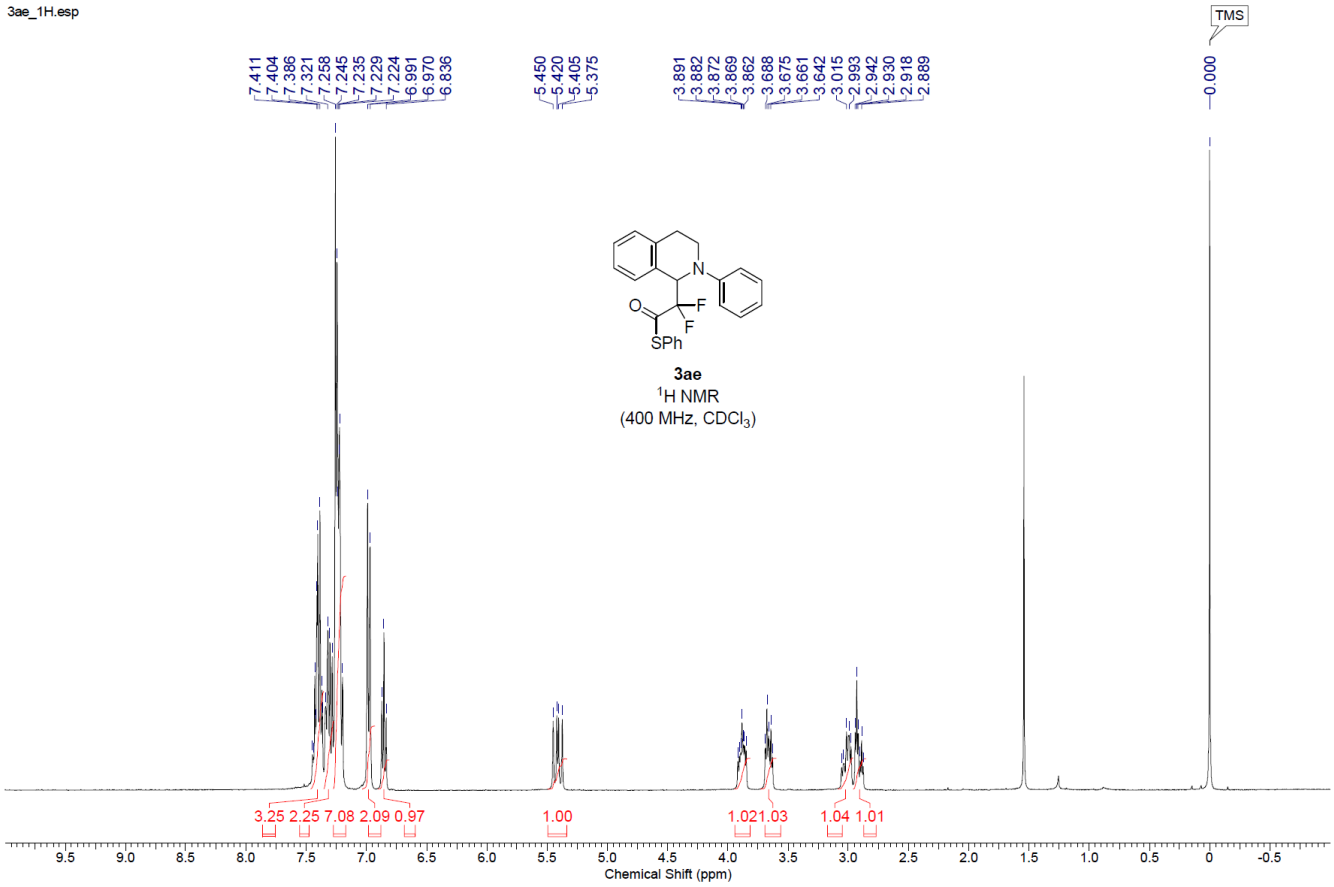


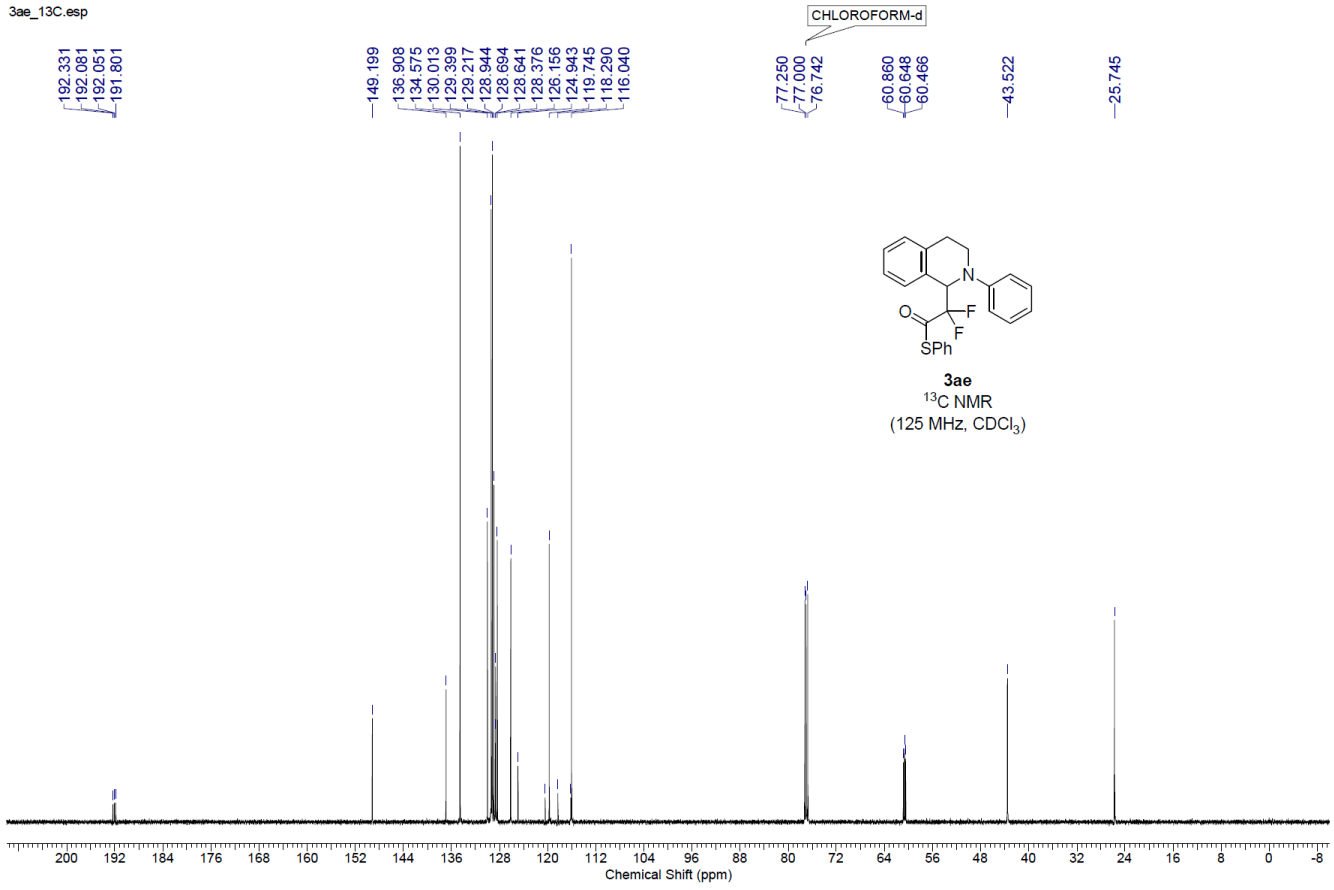
3ad
^{1}H NMR
(400 MHz, $CDCl_3$)

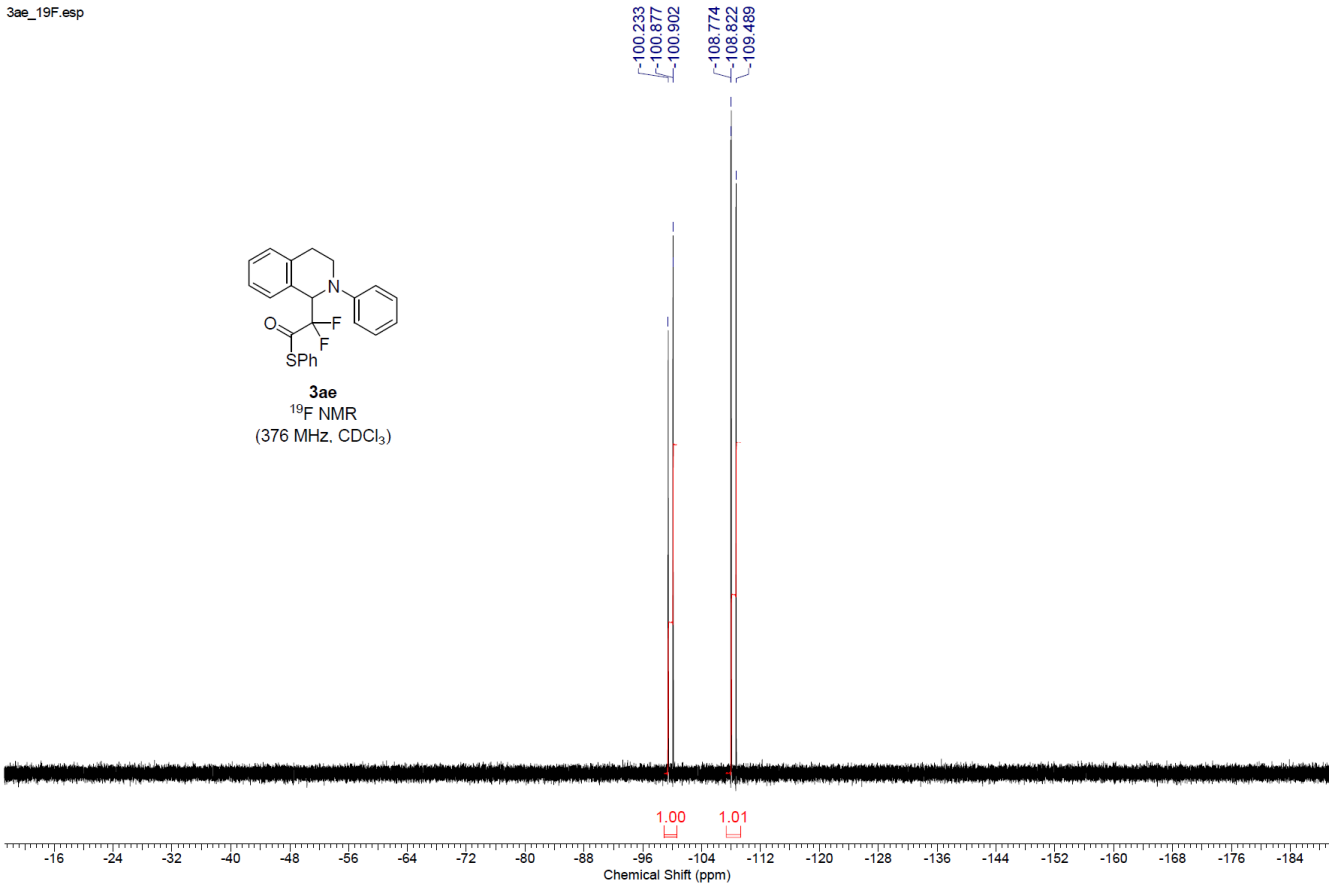


3ad
^{13}C NMR
(125 MHz, $CDCl_3$)

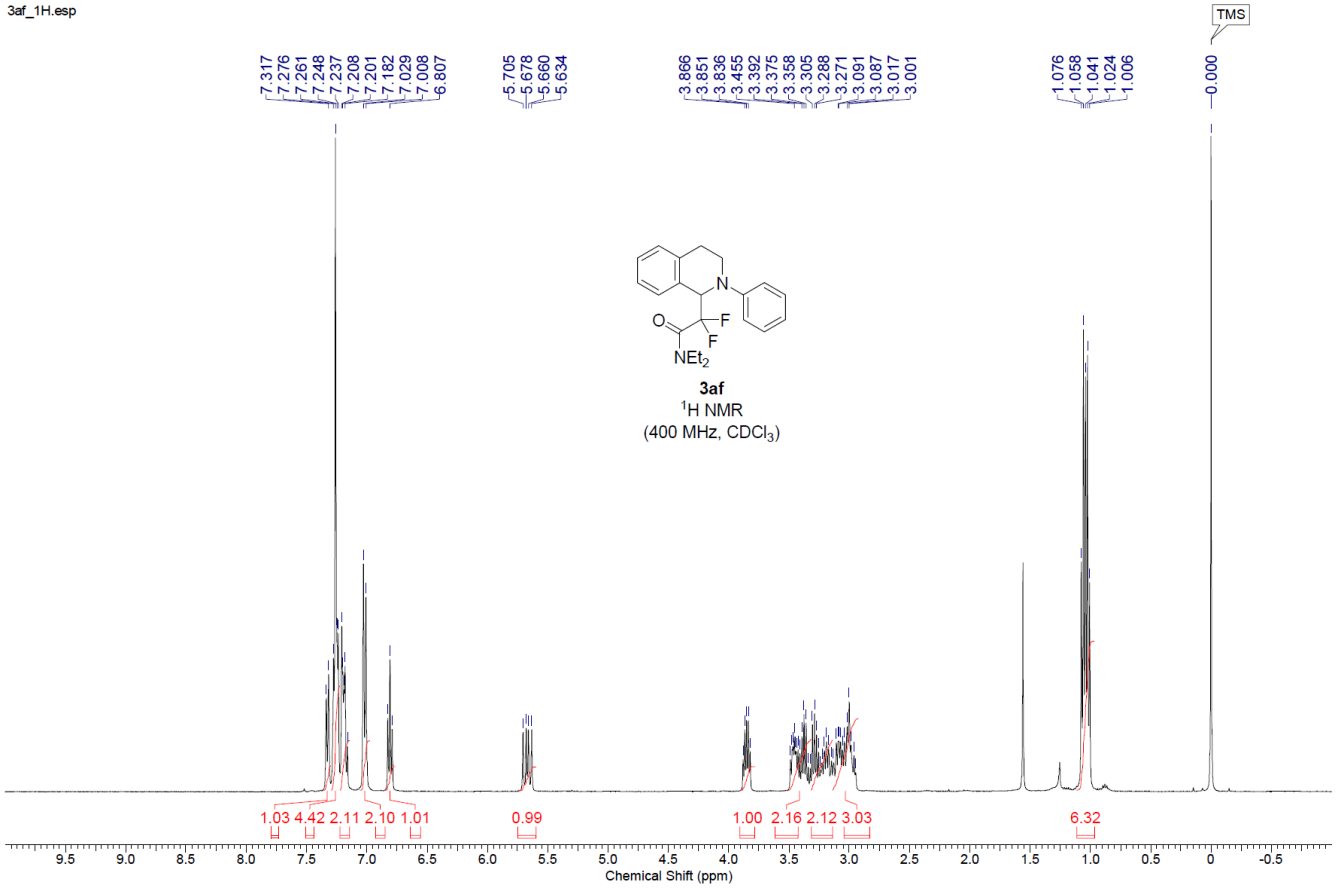

3ad_19F_vd.esp
-99.903
-99.922
-100.591
-110.706
-111.323
-111.377
N
O
F
F
OPh
3ad
19F NMR
(376 MHz, CDCl3)
1.00
1.01
-16
-24
-32
-40
-48
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
-184
Chemical Shift (ppm)


3ae_1H.esp
TMS
7.411
7.404
7.386
7.321
7.258
7.245
7.235
7.229
7.224
6.991
6.970
6.836
5.450
5.420
5.405
5.375
3.891
3.882
3.872
3.869
3.862
3.688
3.675
3.661
3.642
3.015
2.993
2.942
2.930
2.918
2.889
0.000
3ae
1H NMR
(400 MHz, CDCl3)
3.25 2.25 7.08 2.09 0.97
1.00
1.02 1.03
1.04 1.01
Chemical Shift (ppm)

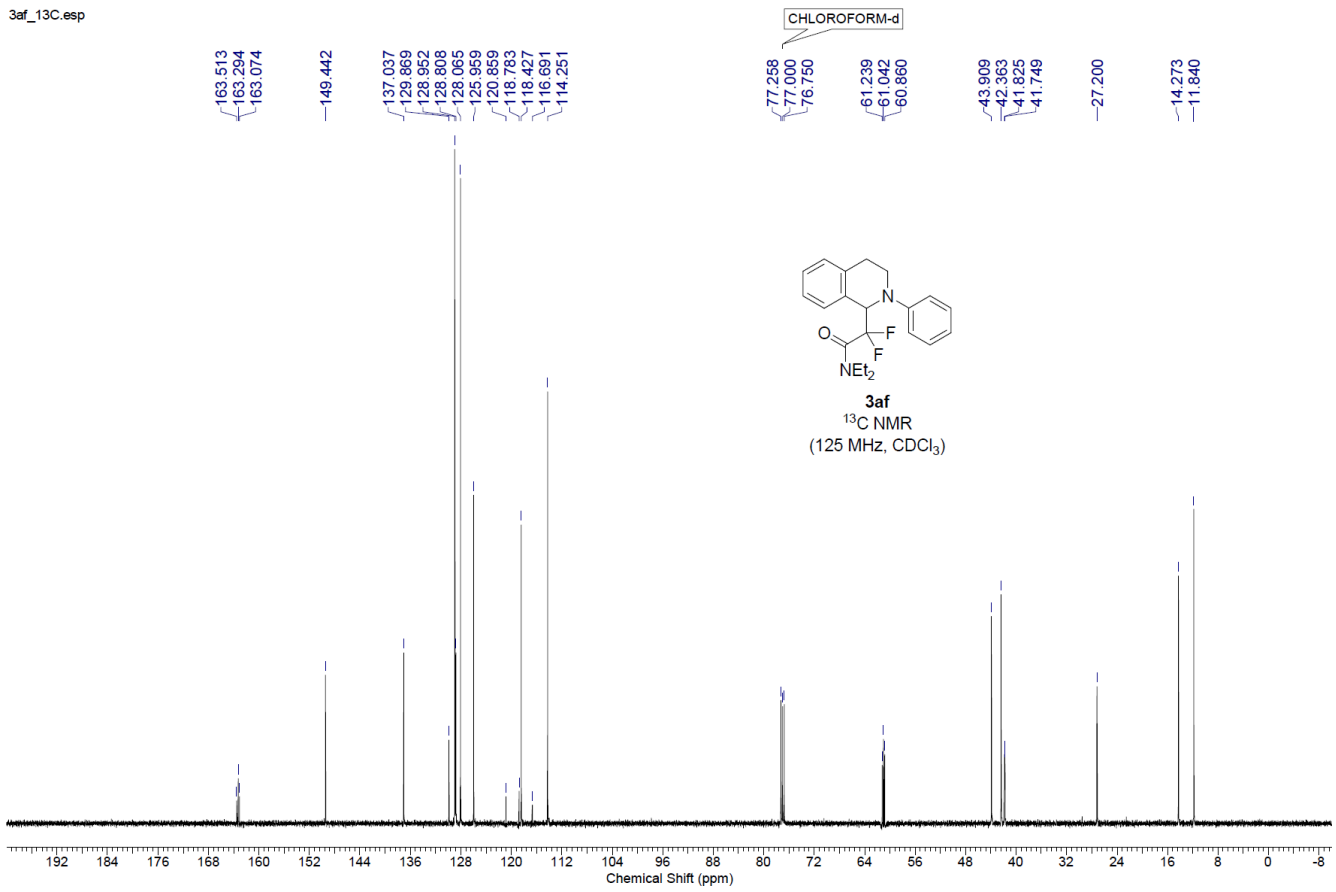

3ae_13C.esp
CHLOROFORM-d
192.331
192.081
192.051
191.801
149.199
136.908
134.575
130.013
129.399
129.217
128.944
128.694
128.641
128.376
126.156
124.943
119.745
118.290
116.040
77.250
77.000
76.742
60.860
60.648
60.466
43.522
25.745
3ae
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)



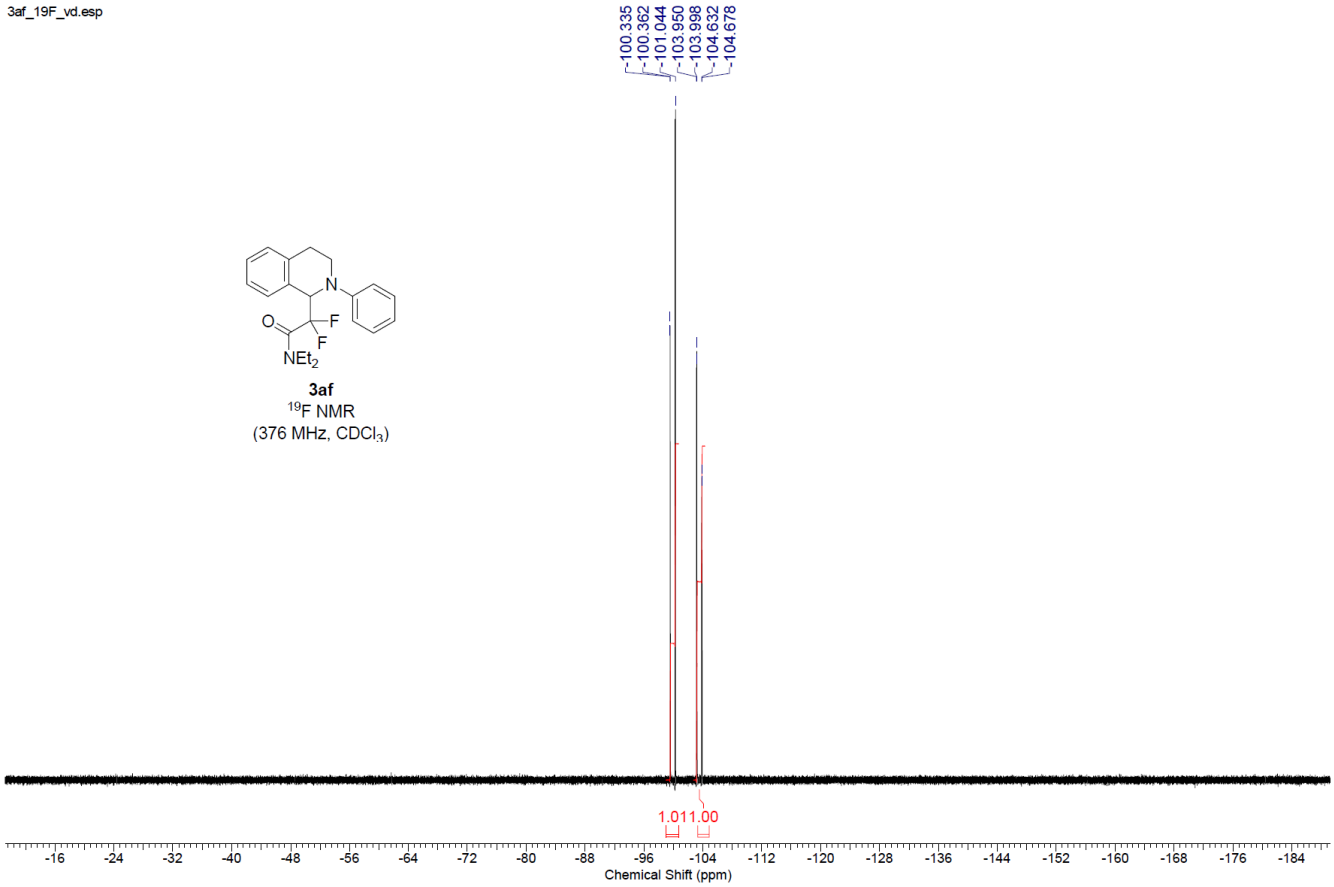
3ae
^{19}F NMR
(376 MHz, $CDCl_3$)

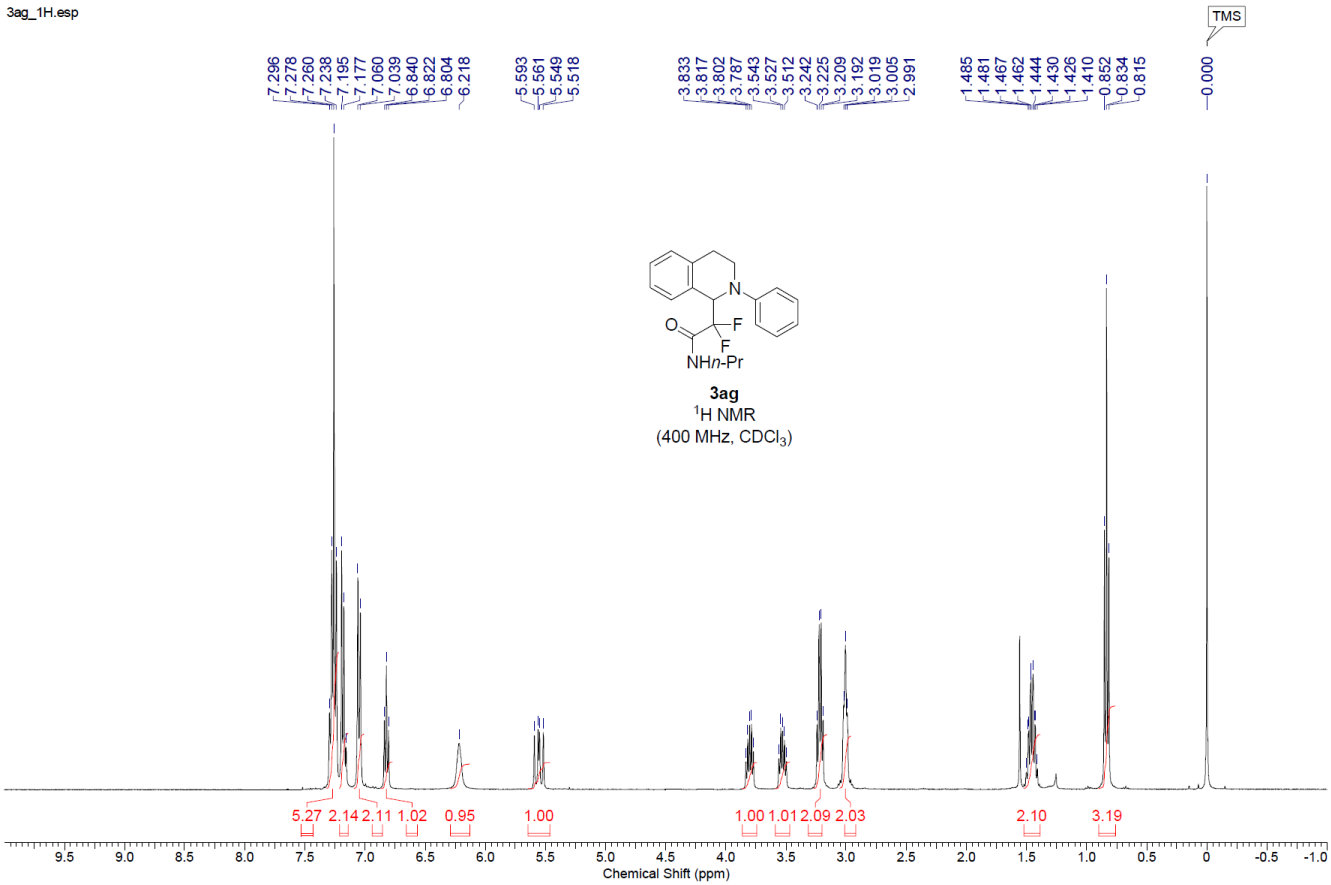


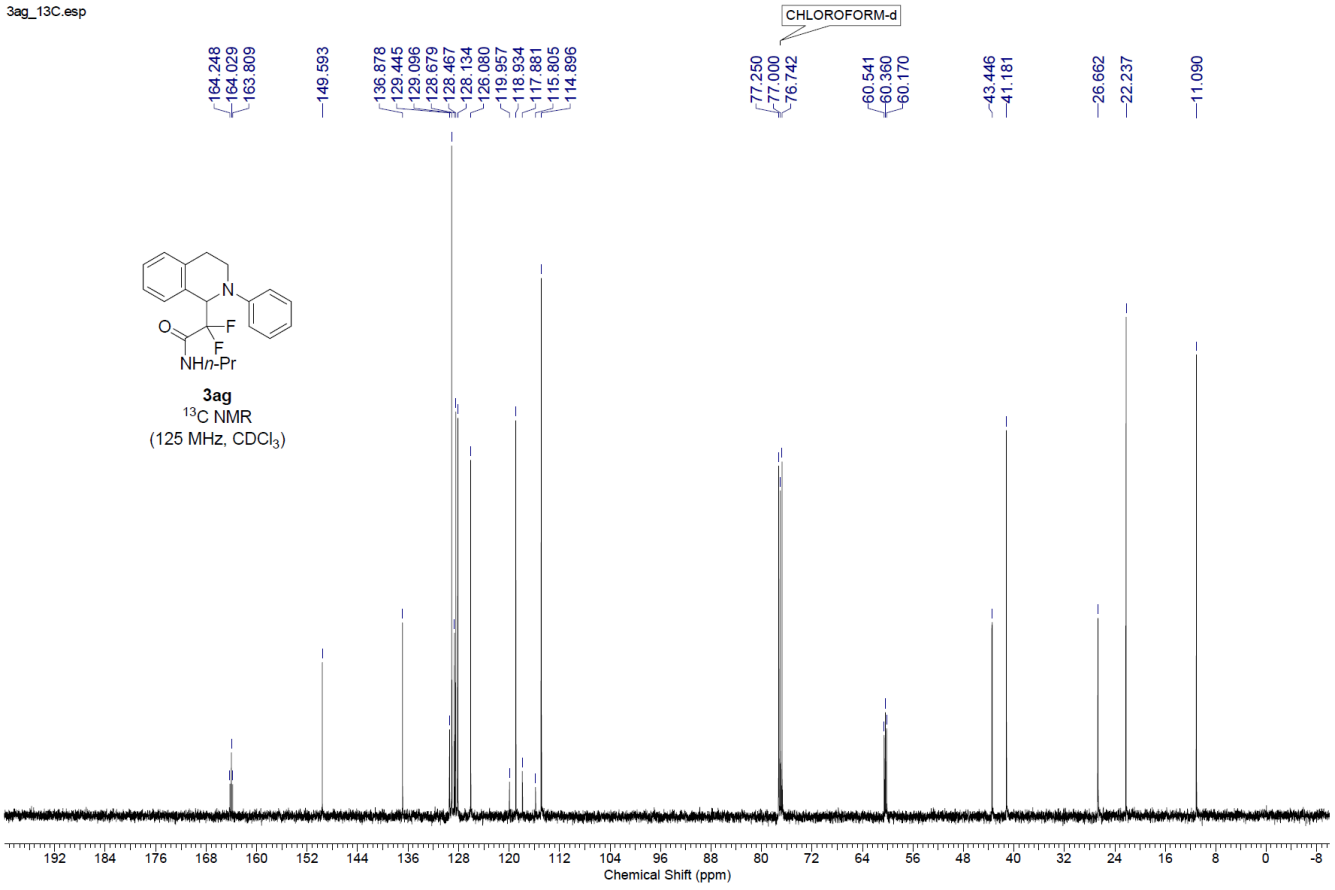
3af
^{1}H NMR
(400 MHz, $CDCl_3$)

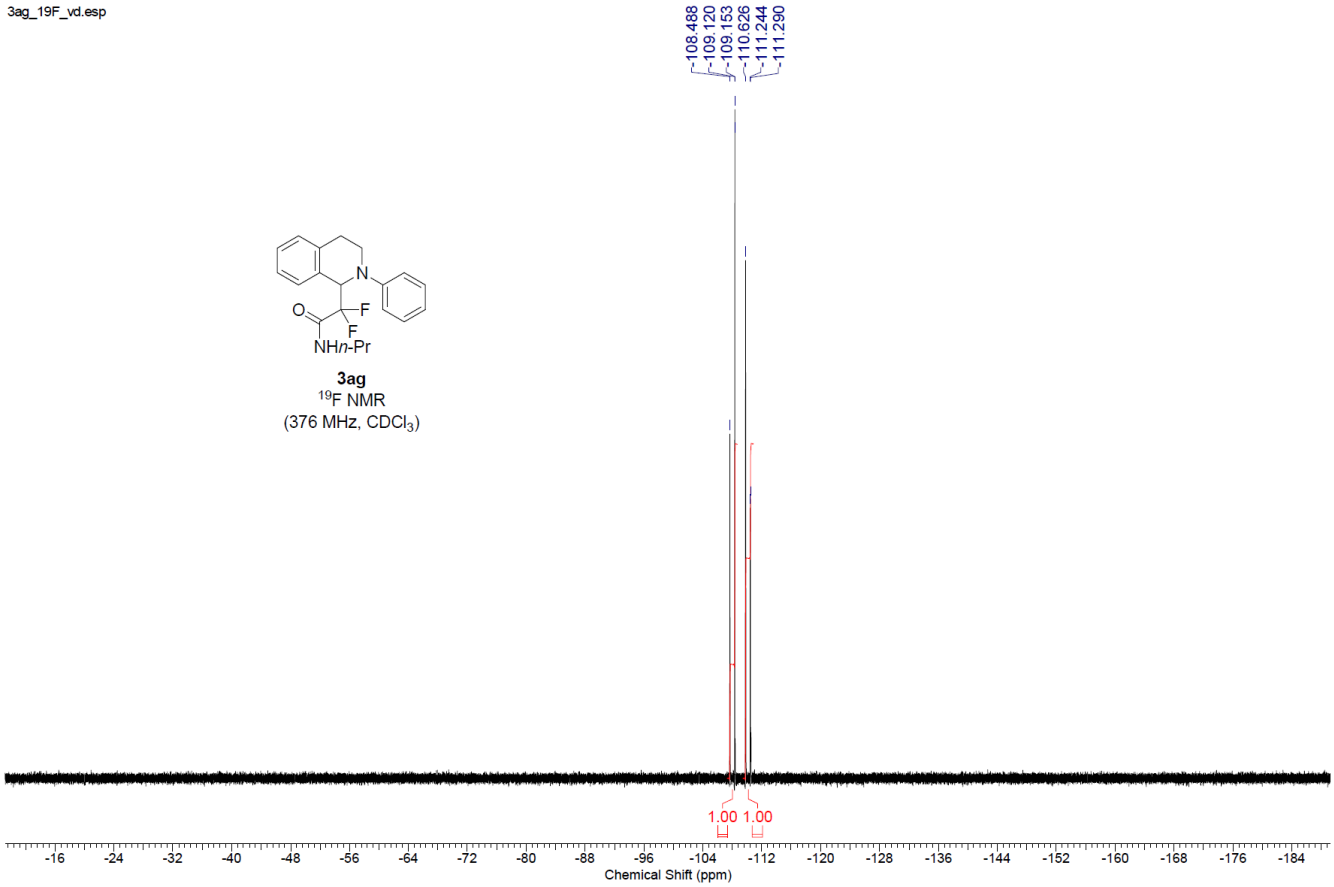


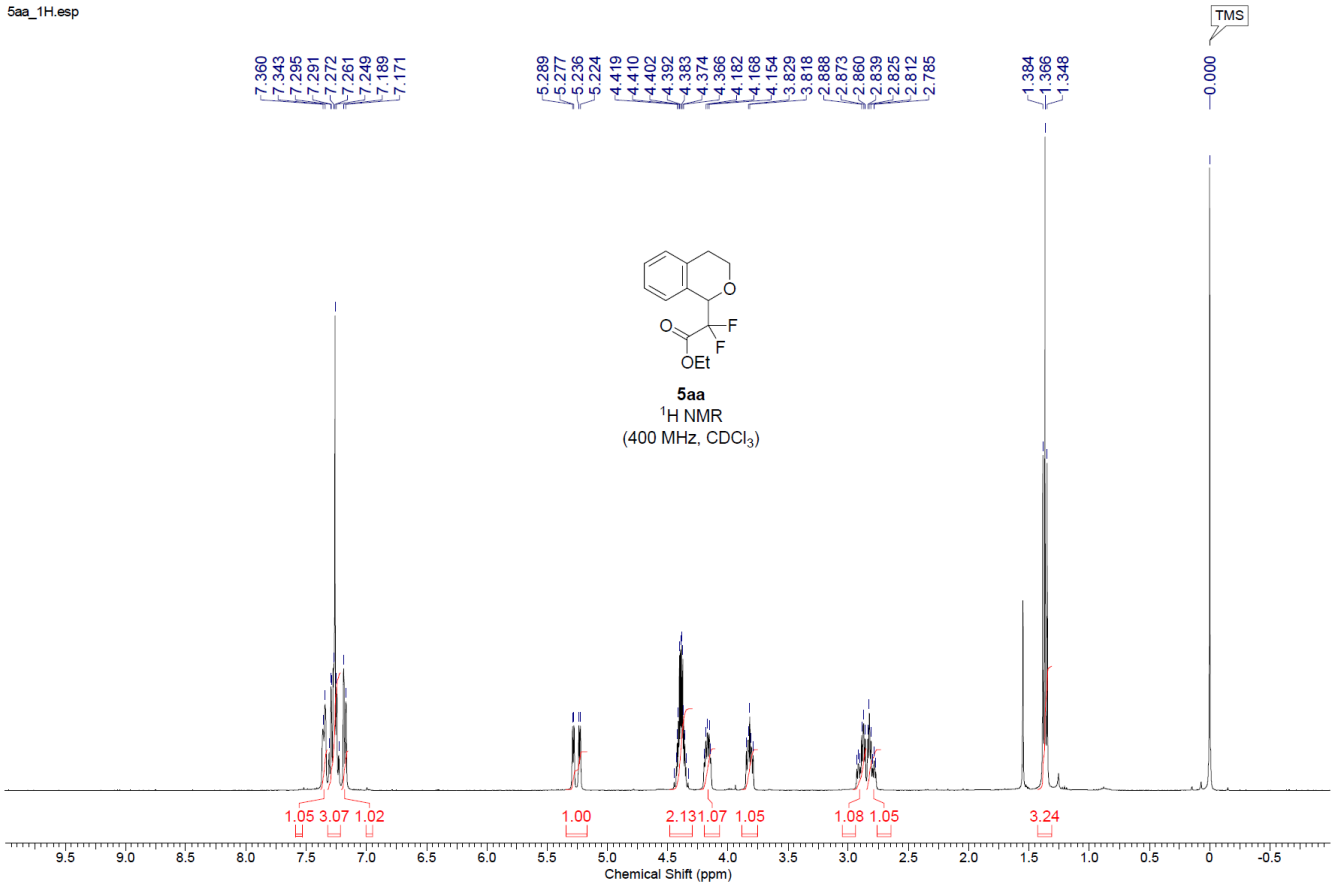
3af
^{13}C NMR
(125 MHz, $CDCl_3$)

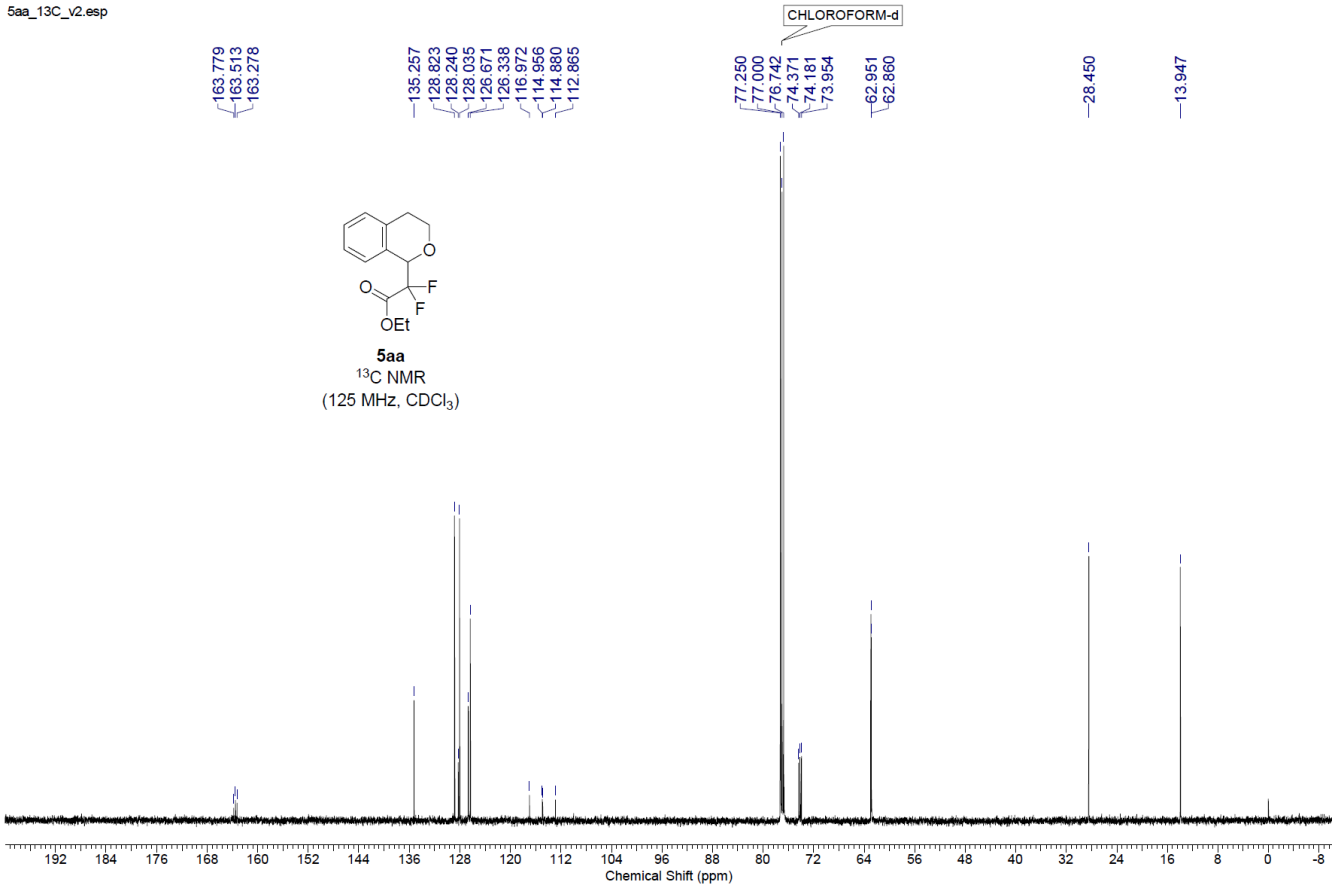

3af_19F_vd.esp
-100.335
-100.362
-101.044
-103.950
-103.998
-104.632
-104.678
N
O
F
F
NEt2
3af
19F NMR
(376 MHz, CDCl3)
1.011.00
-16
-24
-32
-40
-48
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
-184
Chemical Shift (ppm)

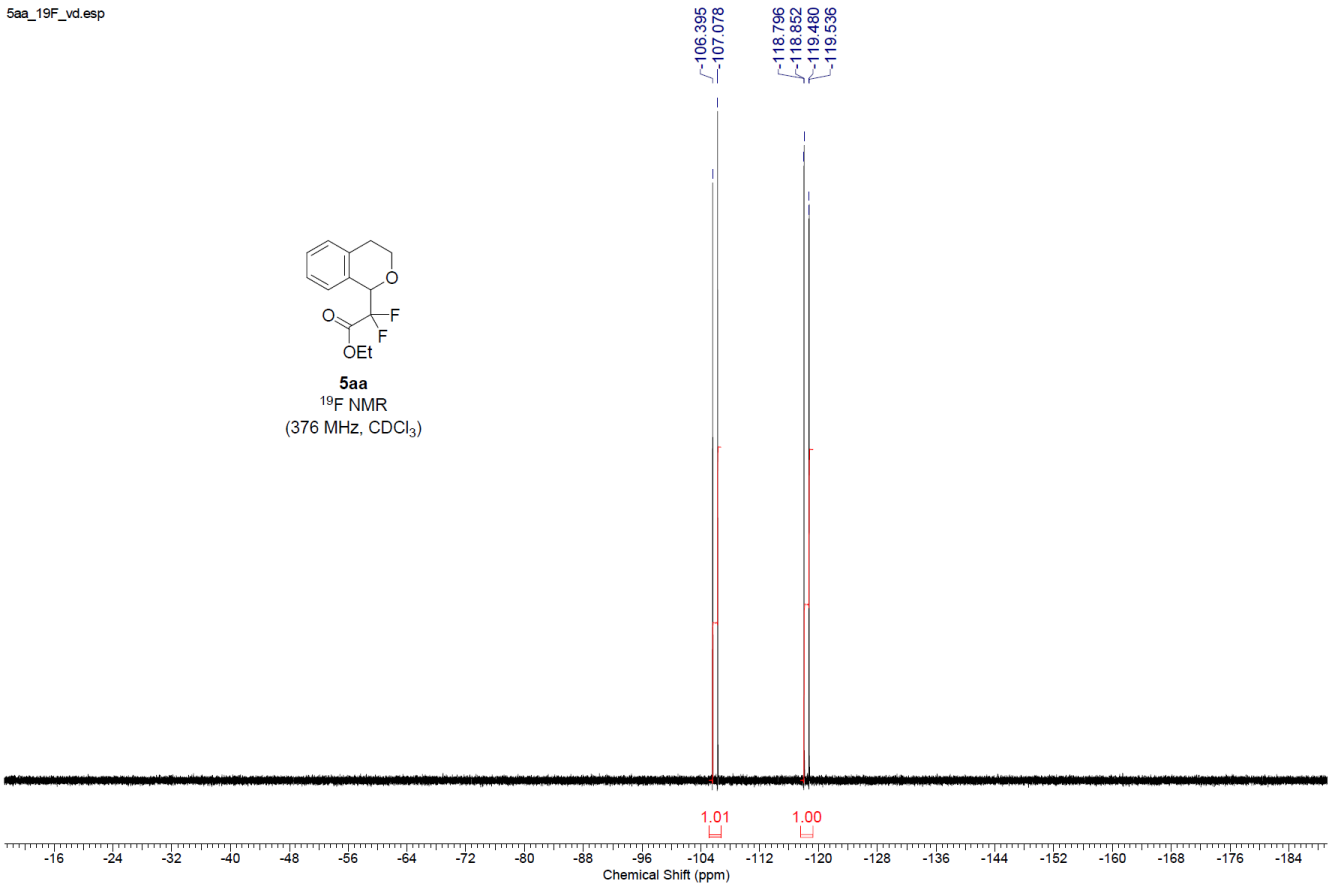

3ag_1H.esp
TMS
7.296
7.278
7.260
7.238
7.195
7.177
7.060
7.039
6.840
6.822
6.804
6.218
5.593
5.561
5.549
5.518
3.833
3.817
3.802
3.787
3.543
3.527
3.512
3.242
3.225
3.209
3.192
3.019
3.005
2.991
1.485
1.481
1.467
1.462
1.444
1.430
1.426
1.410
0.852
0.834
0.815
0.000
N
O
F
F
NHn-Pr
3ag
1H NMR
(400 MHz, CDCl3)
5.27 2.14 2.11 1.02 0.95 1.00 1.00 1.01 2.09 2.03 2.10 3.19
Chemical Shift (ppm)


3ag_13C.esp
CHLOROFORM-d
164.248
164.029
163.809
149.593
136.878
129.445
129.096
128.679
128.467
128.134
126.080
119.957
118.934
117.881
115.805
114.896
77.250
77.000
76.742
60.541
60.360
60.170
43.446
41.181
26.662
22.237
11.090
N
O
F
F
NHn-Pr
3ag
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)

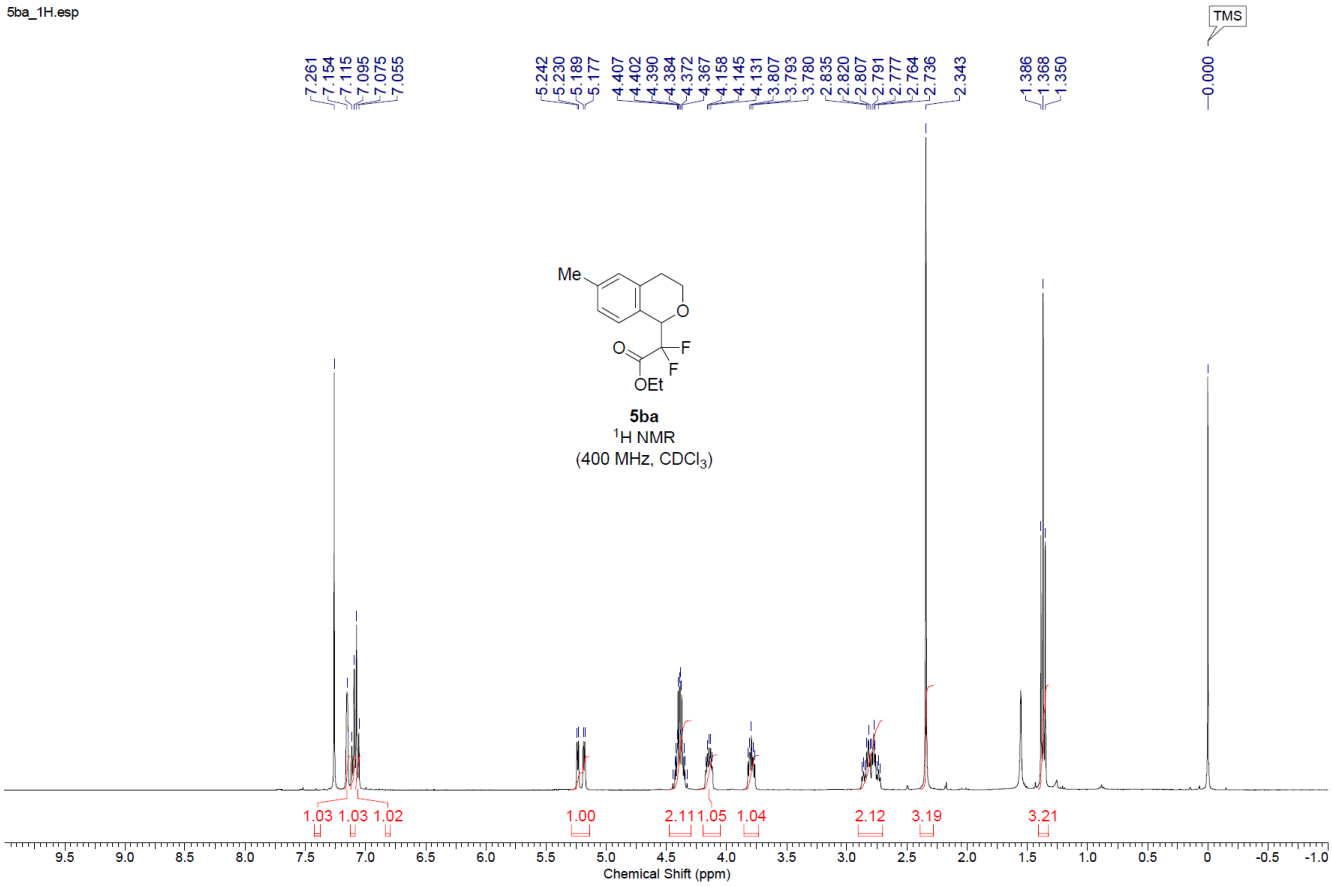

3ag_19F_vd.esp
108.488
109.120
109.153
110.626
111.244
111.290
O
N
F
F
NHn-Pr
3ag
19F NMR
(376 MHz, CDCl3)
1.00 1.00
-16 -24 -32 -40 -48 -56 -64 -72 -80 -88 -96 -104 -112 -120 -128 -136 -144 -152 -160 -168 -176 -184
Chemical Shift (ppm)


5aa_1H.esp
TMS
7.360
7.343
7.295
7.291
7.272
7.261
7.249
7.189
7.171
5.289
5.277
5.236
5.224
4.419
4.410
4.402
4.392
4.383
4.374
4.366
4.182
4.168
4.154
3.829
3.818
2.888
2.873
2.860
2.839
2.825
2.812
2.785
1.384
1.366
1.348
0.000
O
O
F
F
OEt
5aa
1H NMR
(400 MHz, CDCl3)
1.05 3.07 1.02
1.00
2.13 1.07 1.05
1.08 1.05
3.24
Chemical Shift (ppm)


5aa_13C_v2.esp
CHLOROFORM-d
163.779
163.513
163.278
135.257
128.823
128.240
128.035
126.671
126.338
116.972
114.956
114.880
112.865
77.250
77.000
76.742
74.371
74.181
73.954
62.951
62.860
28.450
13.947
O
O
F
F
OEt
5aa
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)

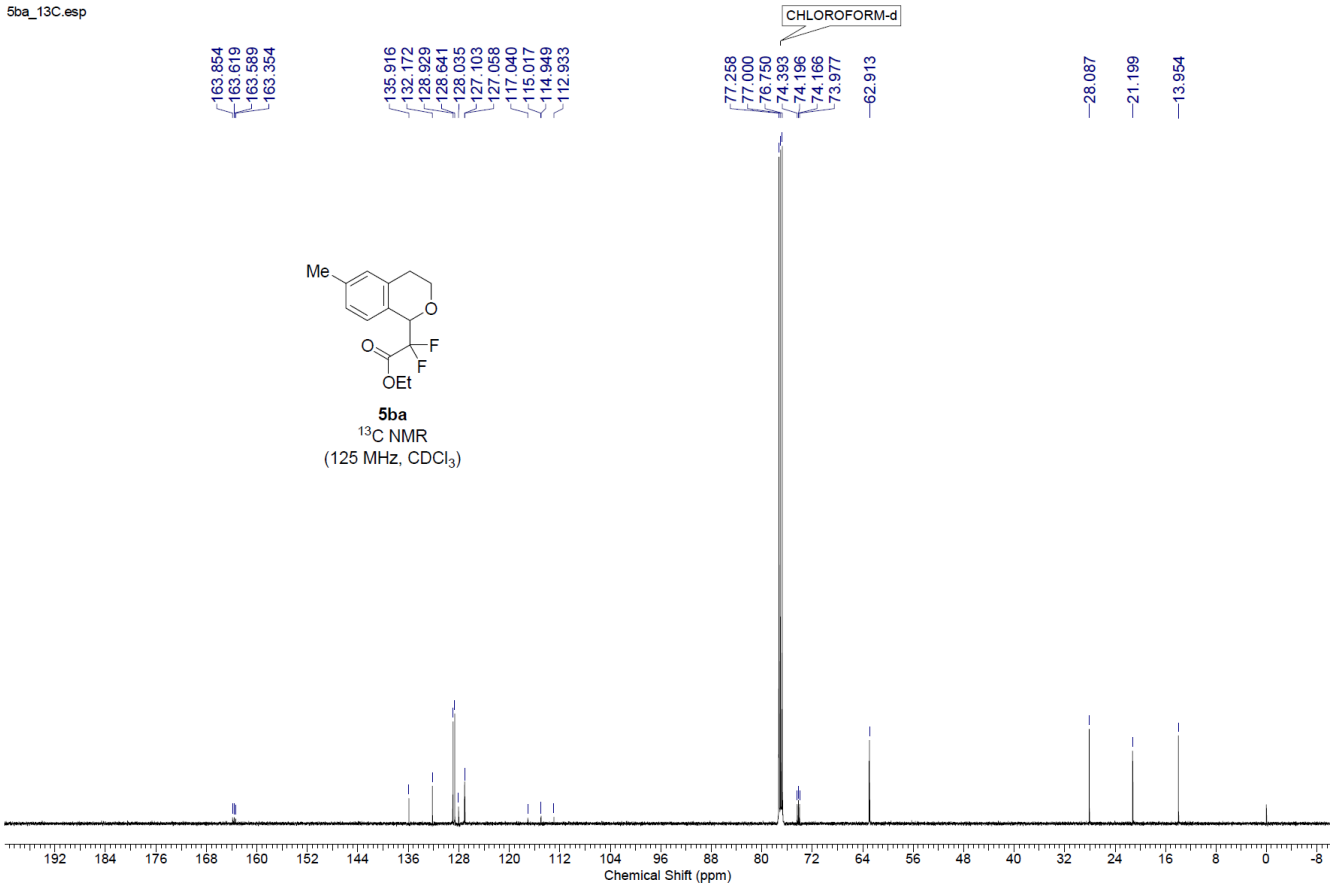

5aa_19F_vd.esp
-106.395
-107.078
-118.796
-118.852
-119.480
-119.536
O
O
F
F
OEt
5aa
19F NMR
(376 MHz, CDCl3)
1.01
1.00
-16
-24
-32
-40
-48
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
-184
Chemical Shift (ppm)

5ba_1H.esp

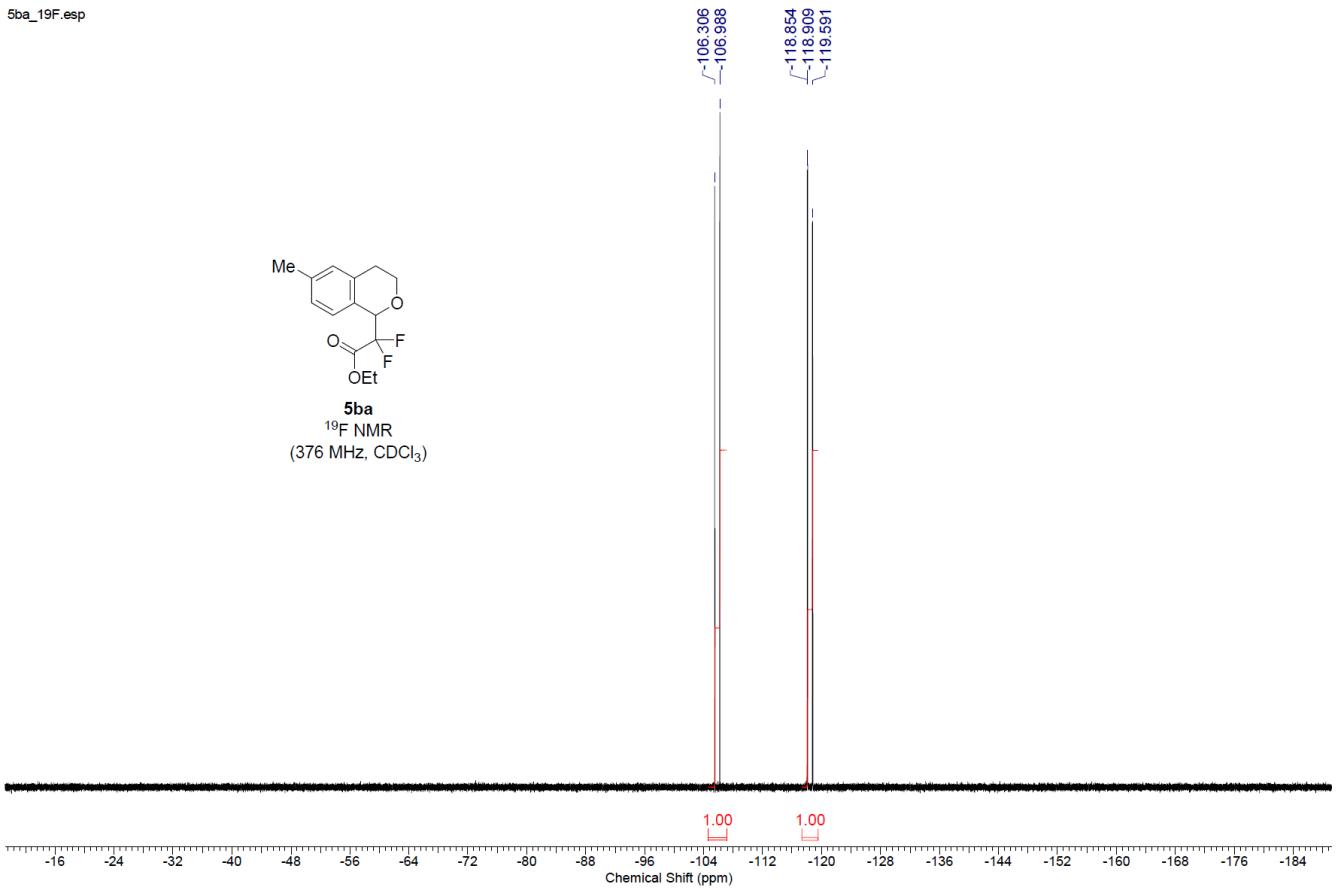


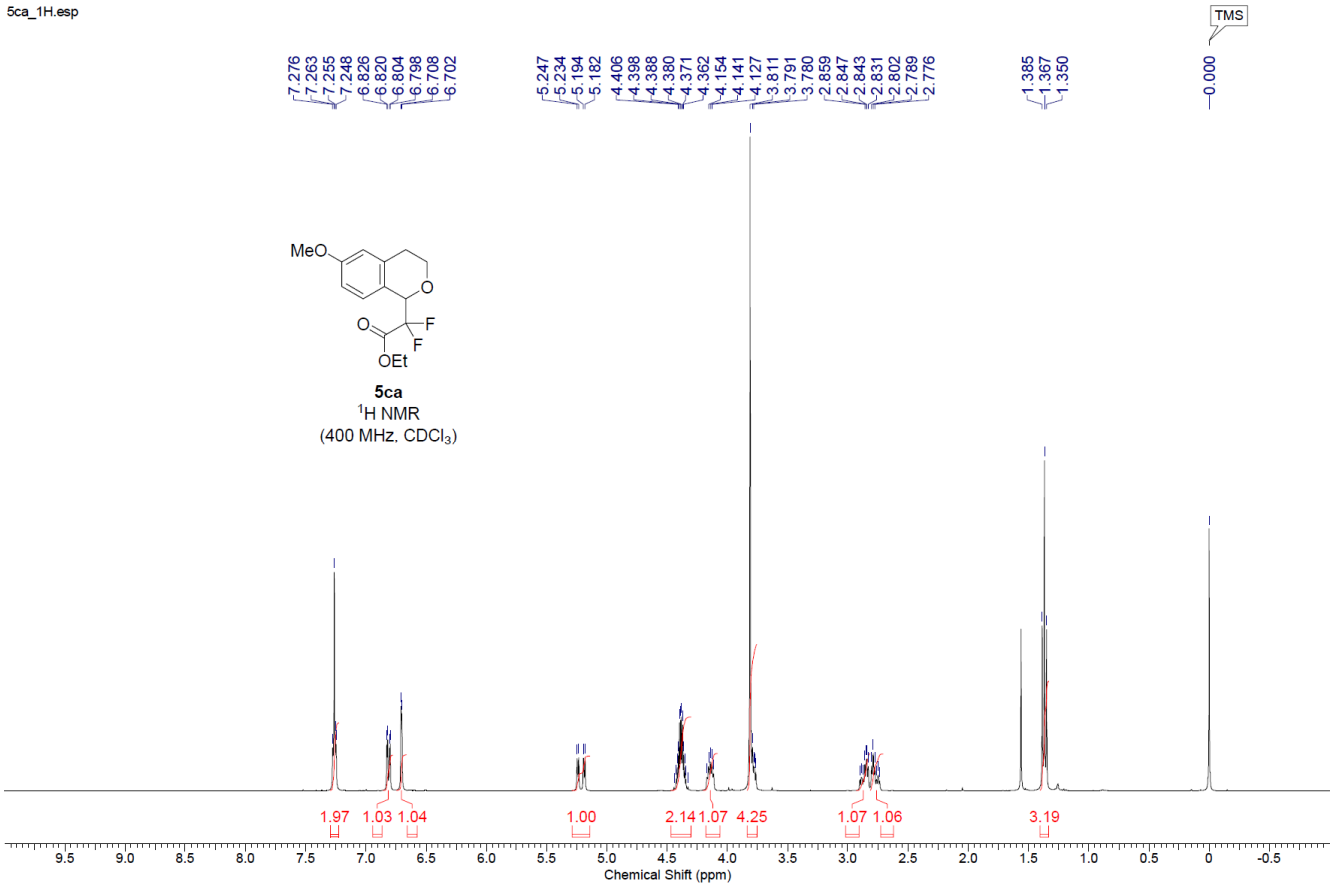
5ba
^{1}H NMR
(400 MHz, $CDCl_3$)

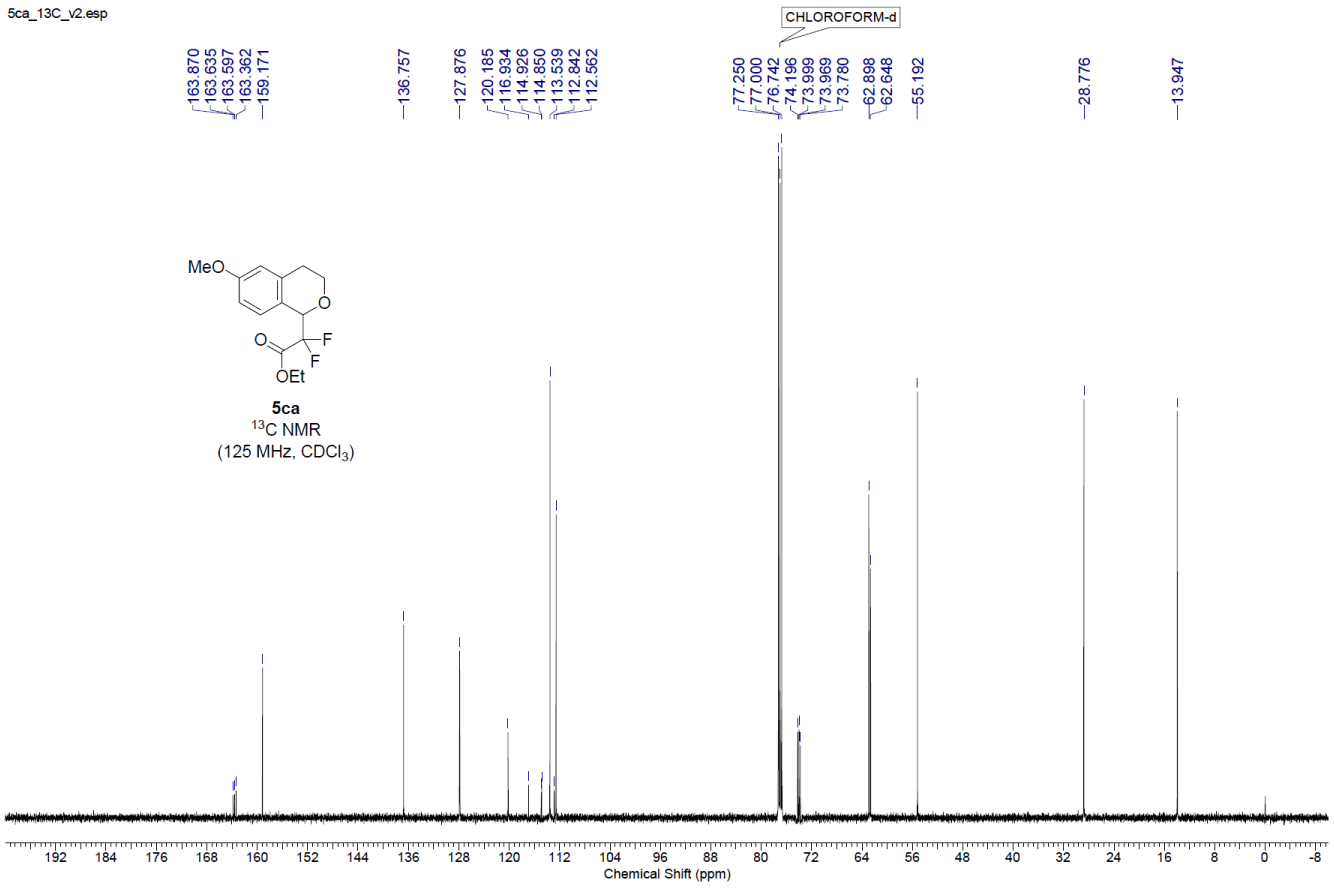
5ba_13C.esp

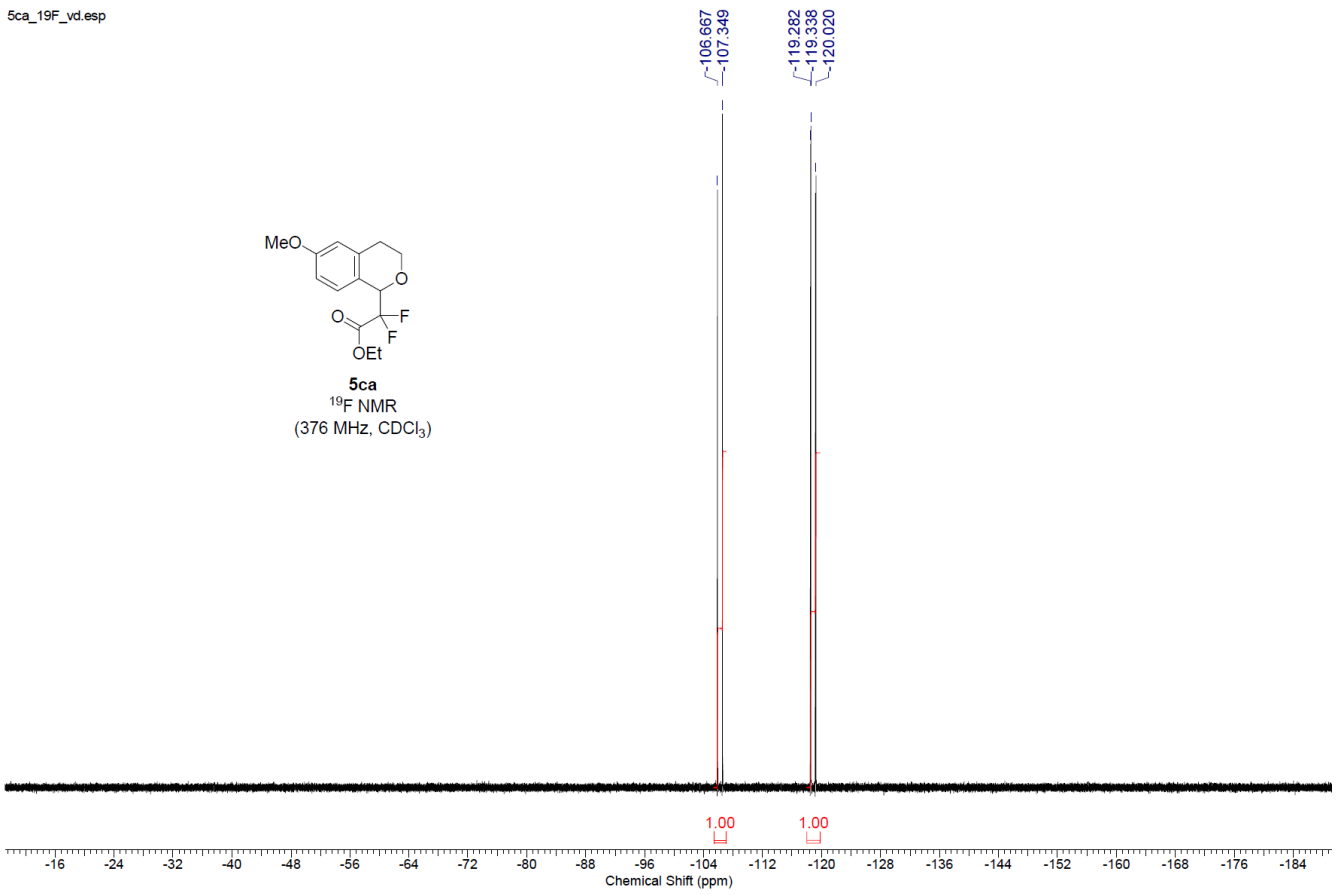


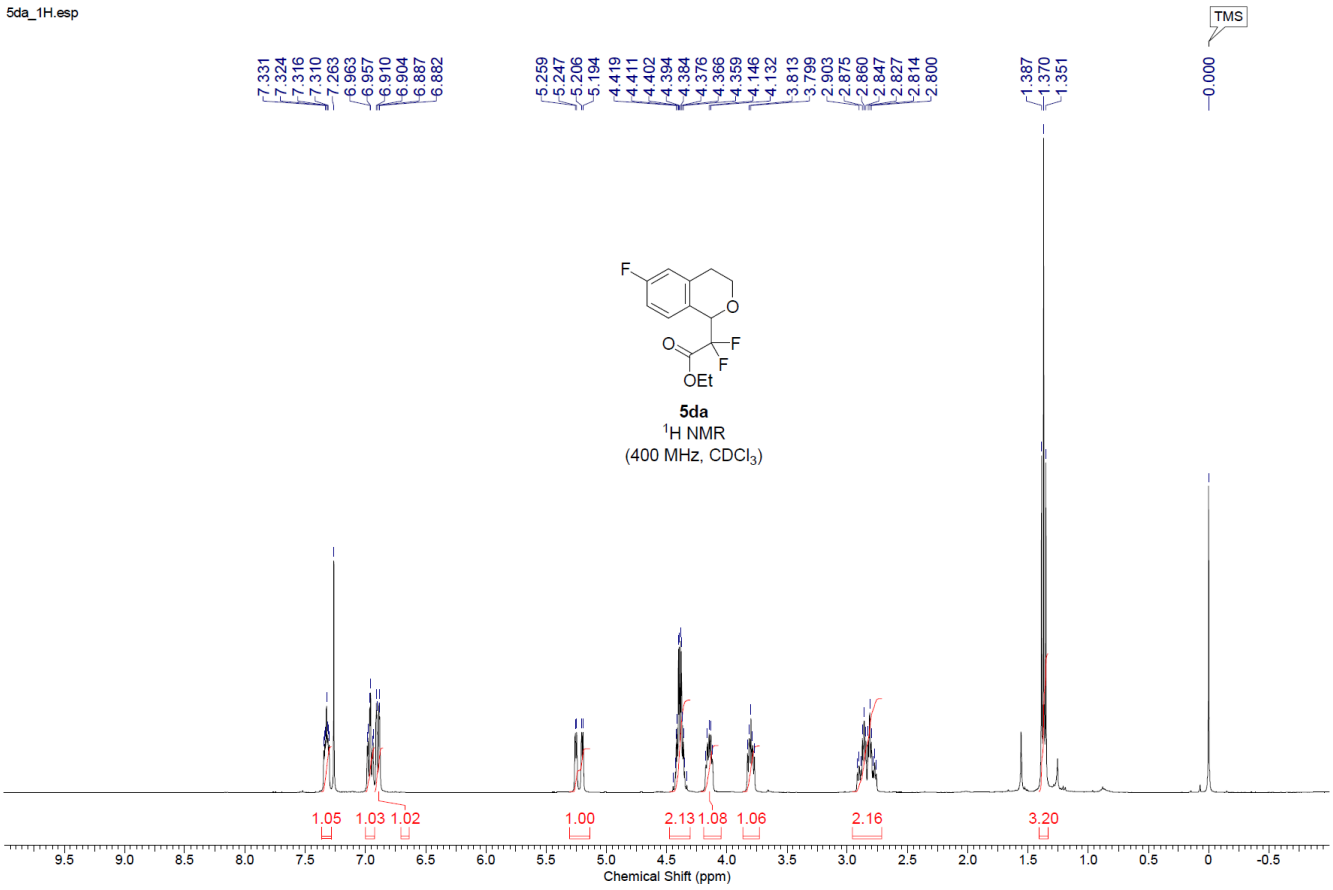
5ba
^{13}C NMR
(125 MHz, $CDCl_3$)

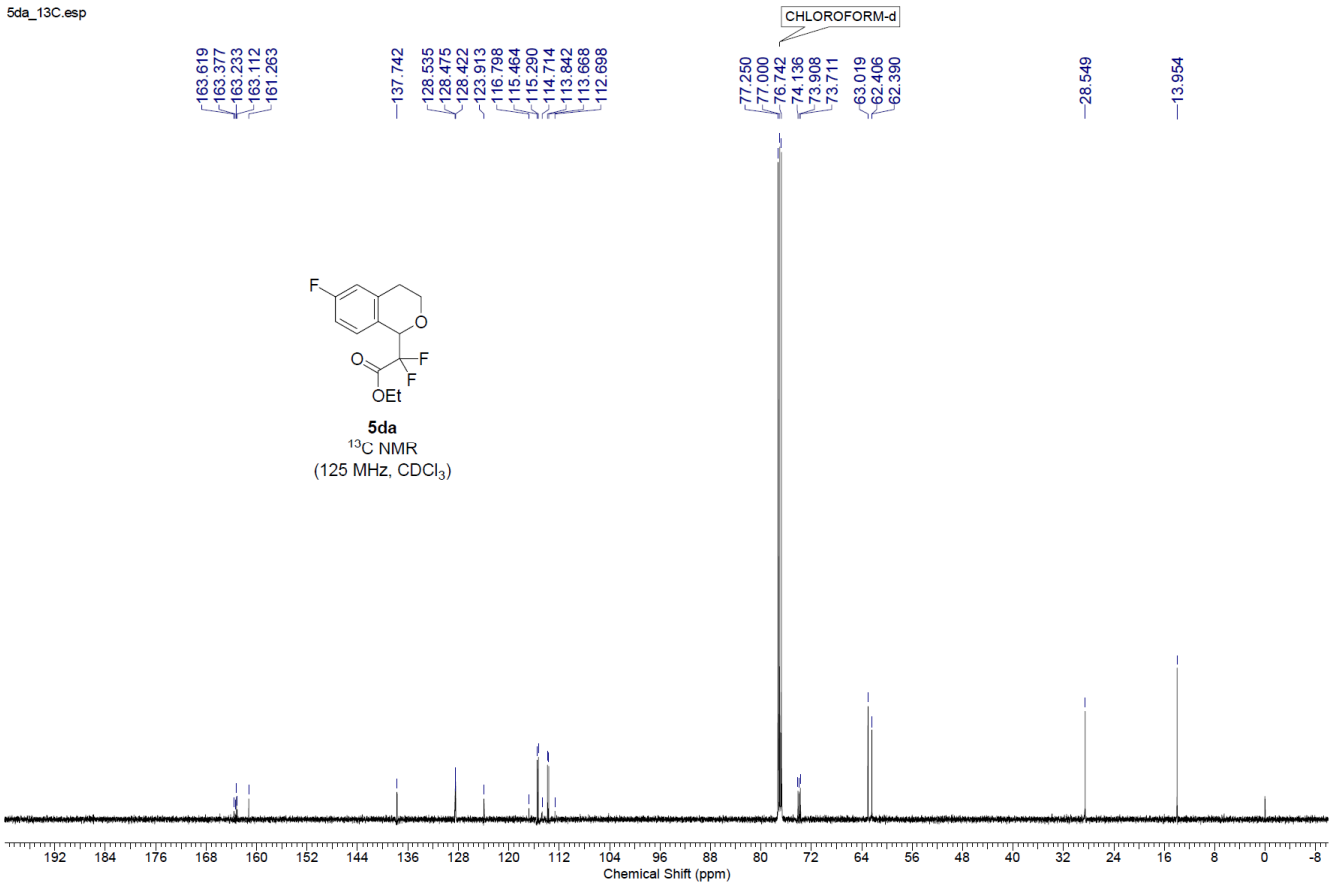

5ba_19F.esp
-106.306
-106.988
-118.854
-118.909
-119.591
Me
O
O
F
F
OEt
5ba
19F NMR
(376 MHz, CDCl3)
1.00
1.00
-16
-24
-32
-40
-48
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
-184
Chemical Shift (ppm)

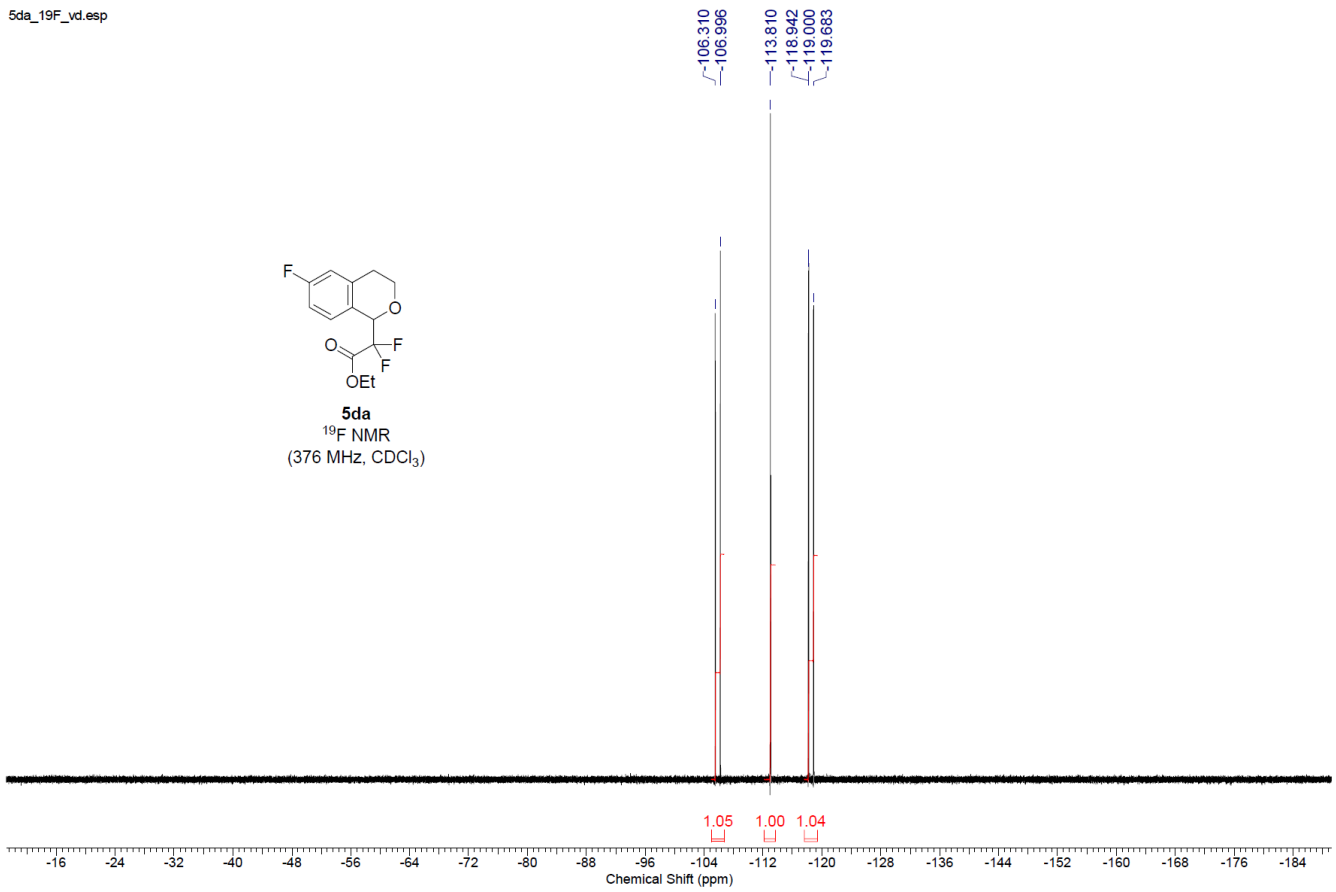

5ca_1H.esp
TMS
7.276
7.263
7.255
7.248
6.826
6.820
6.804
6.798
6.708
6.702
5.247
5.234
5.194
5.182
4.406
4.398
4.388
4.380
4.371
4.362
4.154
4.141
4.127
3.811
3.791
3.780
2.859
2.847
2.843
2.831
2.802
2.789
2.776
1.385
1.367
1.350
0.000
MeO
O
O
F
F
OEt
5ca
1H NMR
(400 MHz, CDCl3)
1.97
1.03
1.04
1.00
2.14
1.07
4.25
1.07
1.06
3.19
Chemical Shift (ppm)

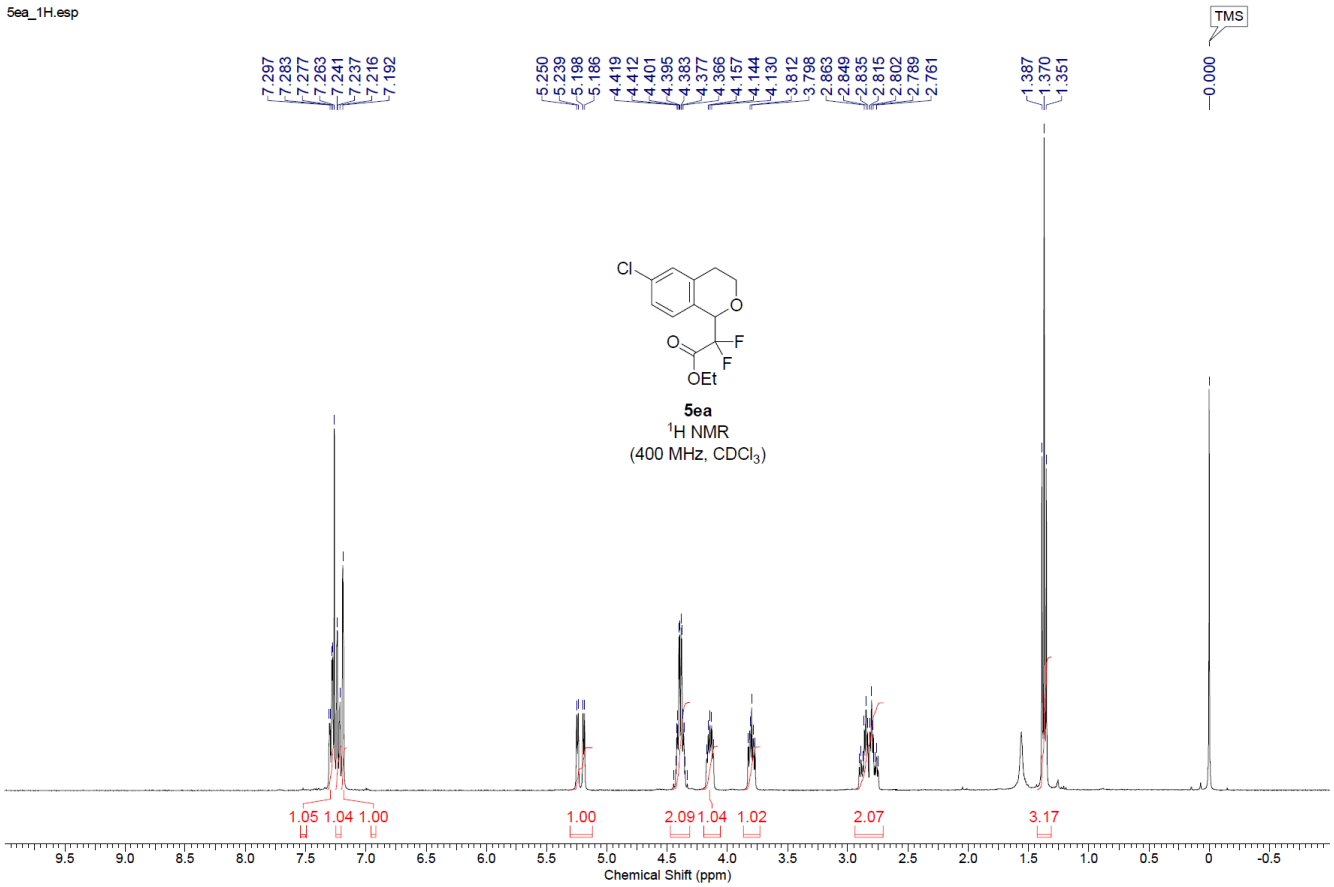

5ca_13C_v2.esp
CHLOROFORM-d
163.870
163.635
163.597
163.362
159.171
136.757
127.876
120.185
116.934
114.926
114.850
113.539
112.842
112.562
77.250
77.000
76.742
74.196
73.999
73.969
73.780
62.898
62.648
55.192
28.776
13.947
MeO
O
O
F
F
OEt
5ca
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)

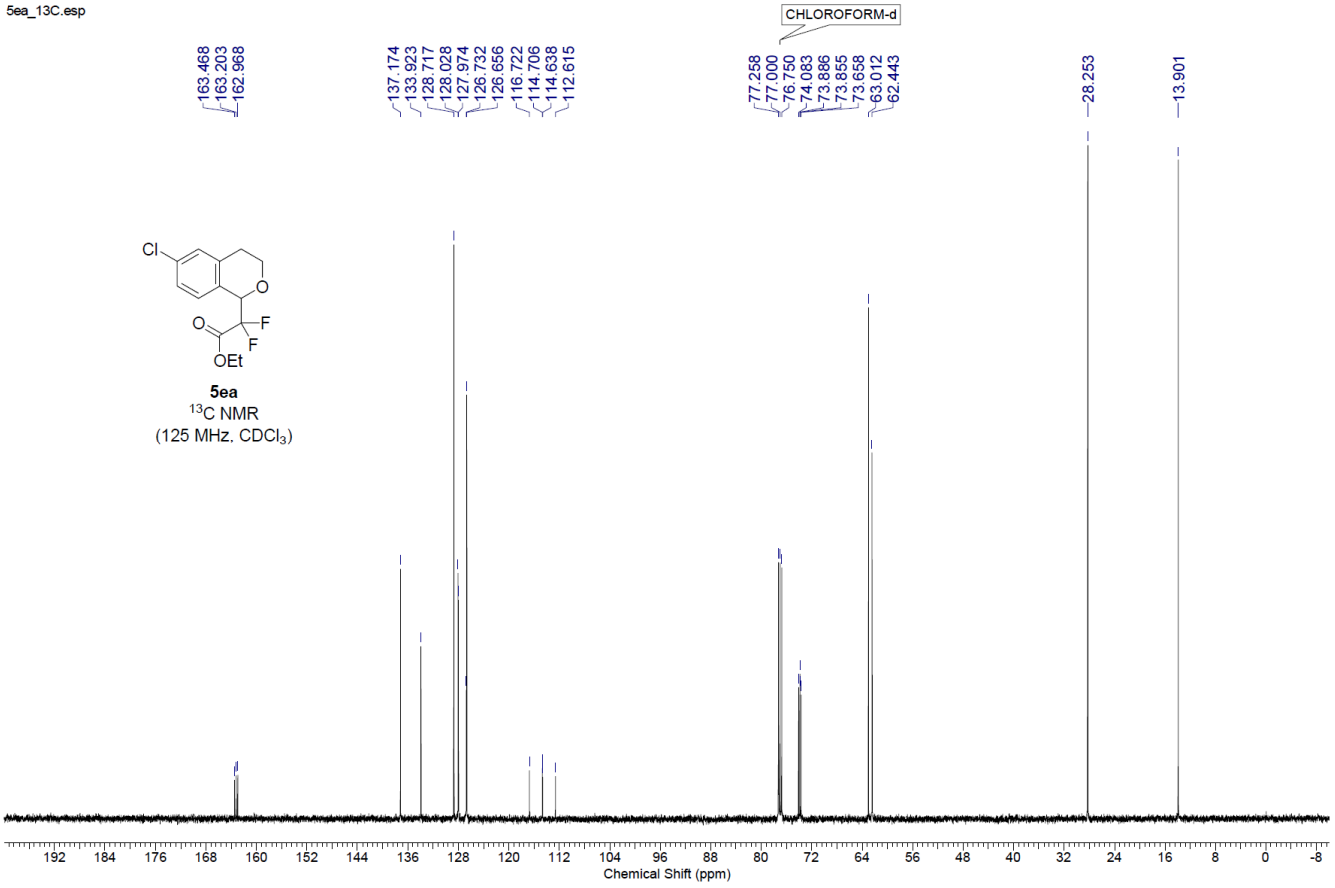

5ca_19F_vd.esp
-106.667
-107.349
-119.282
-119.338
-120.020
MeO
O
O
F
F
OEt
5ca
19F NMR
(376 MHz, CDCl3)
1.00
1.00
-16
-24
-32
-40
-48
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
-184
Chemical Shift (ppm)

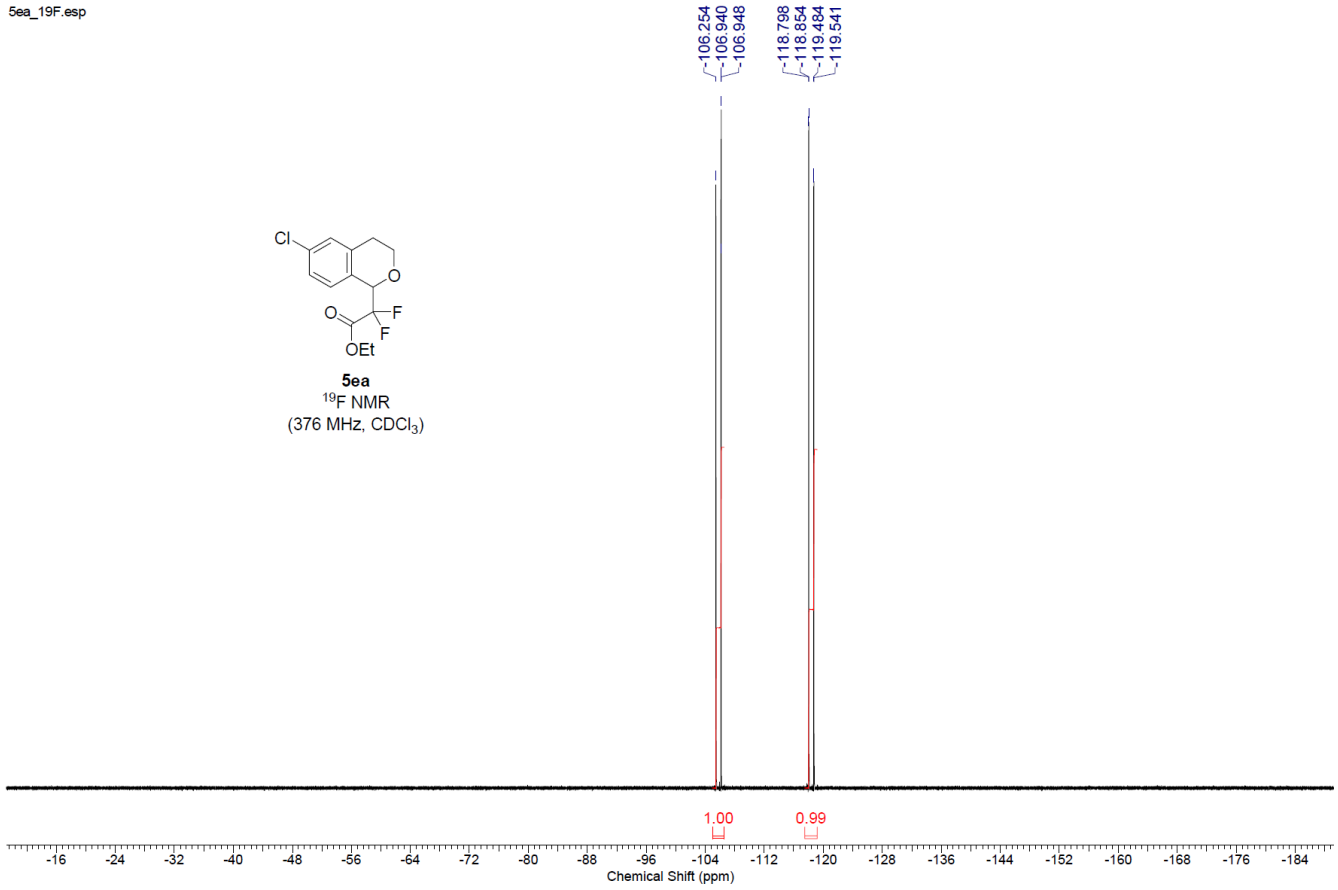

5da_1H.esp
TMS
7.331
7.324
7.316
7.310
7.263
6.963
6.957
6.910
6.904
6.887
6.882
5.259
5.247
5.206
5.194
4.419
4.411
4.402
4.394
4.384
4.376
4.366
4.359
4.146
4.132
3.813
3.799
2.903
2.875
2.860
2.847
2.827
2.814
2.800
1.387
1.370
1.351
0.000
F
O
O
F
F
OEt
5da
1H NMR
(400 MHz, CDCl3)
1.05
1.03
1.02
1.00
2.13
1.08
1.06
2.16
3.20
Chemical Shift (ppm)

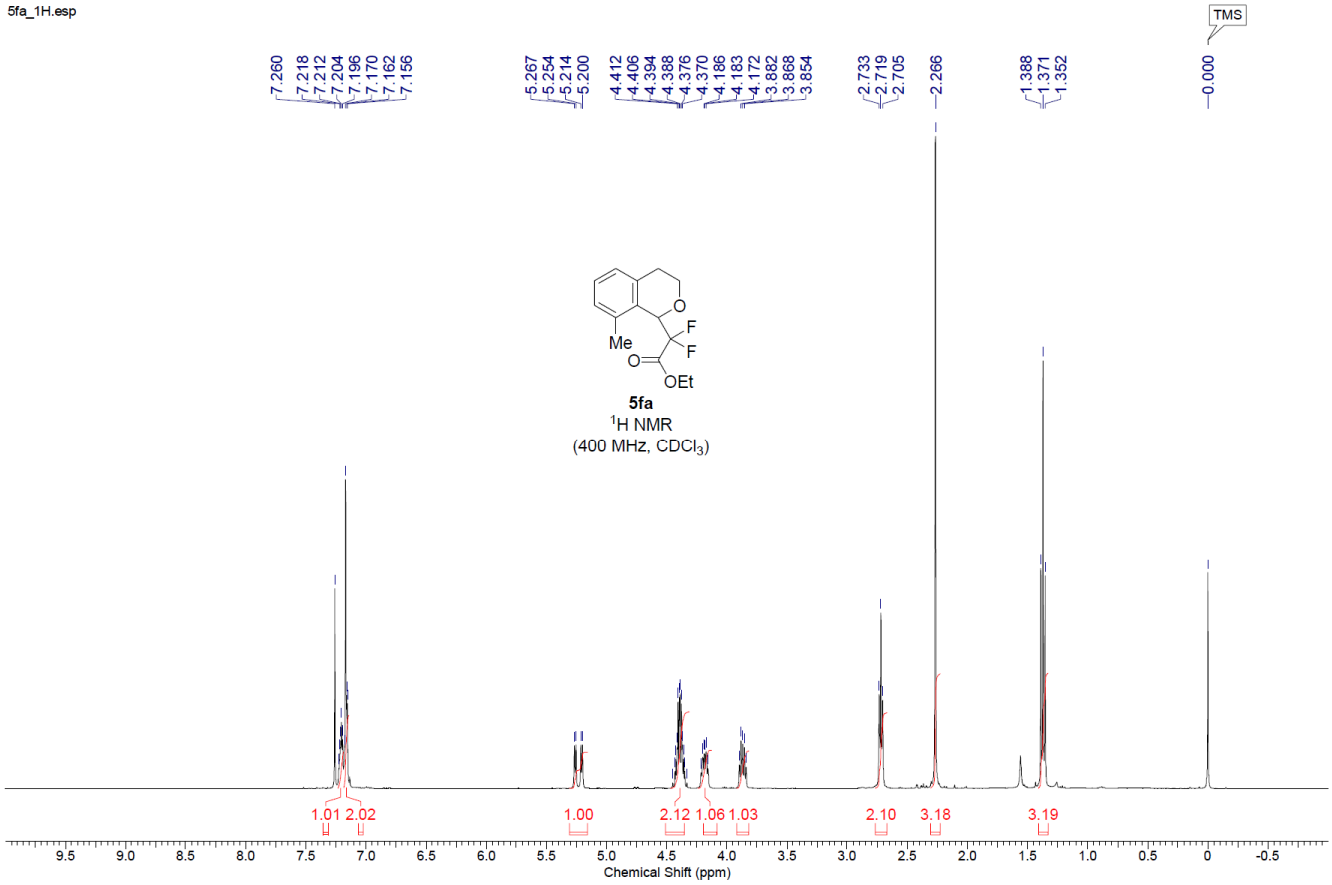

5da_13C.esp
CHLOROFORM-d
163.619
163.377
163.233
163.112
161.263
137.742
128.535
128.475
128.422
123.913
116.798
115.464
115.290
114.714
113.842
113.668
112.698
77.250
77.000
76.742
74.136
73.908
73.711
63.019
62.406
62.390
28.549
13.954
F
O
O
F
F
OEt
5da
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)

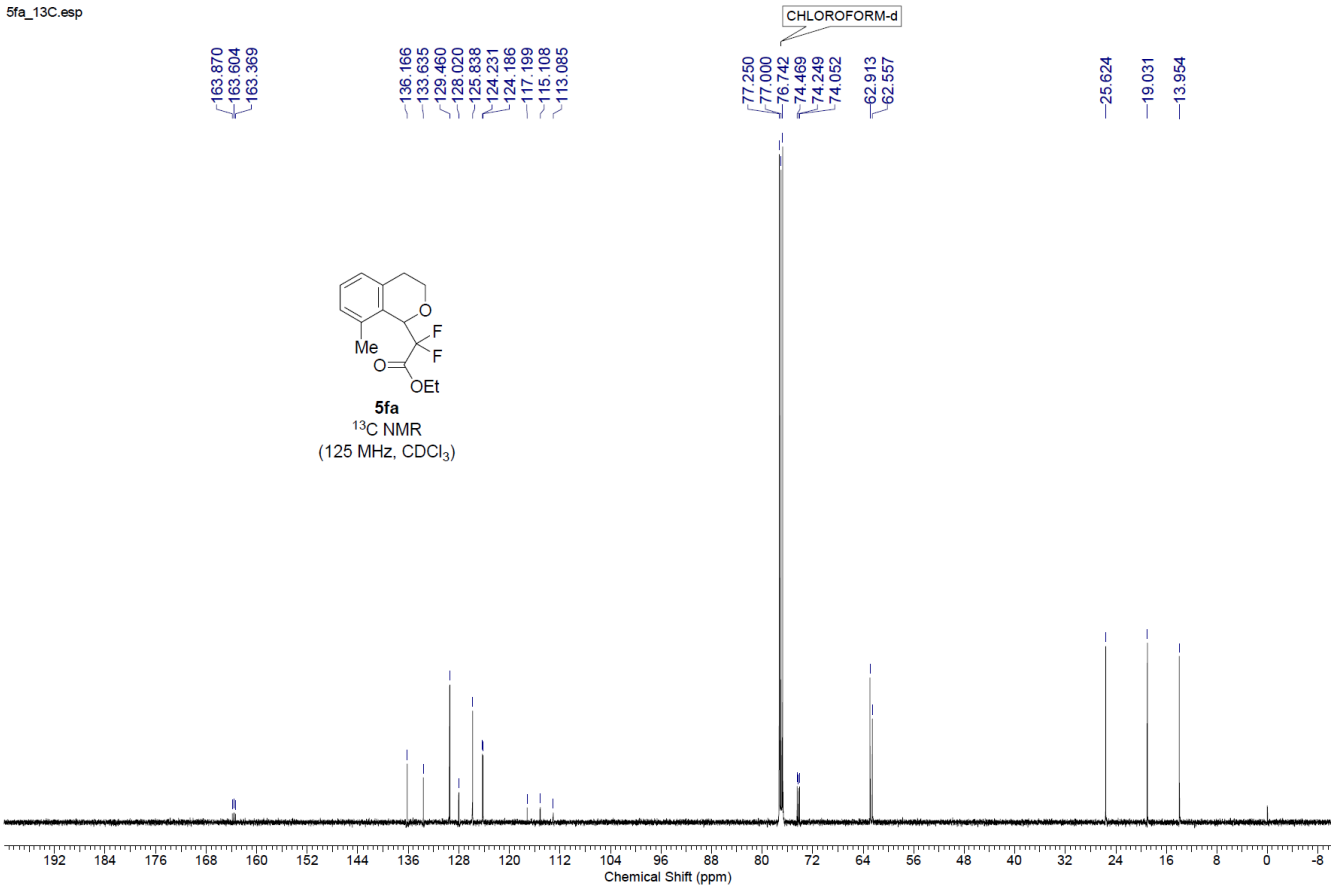

5da_19F_vd.esp
-106.310
-106.996
-113.810
-118.942
-119.000
-119.683
F
O
O
F
F
OEt
5da
19F NMR
(376 MHz, CDCl3)
1.05
1.00
1.04
-16
-24
-32
-40
-48
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
-184
Chemical Shift (ppm)

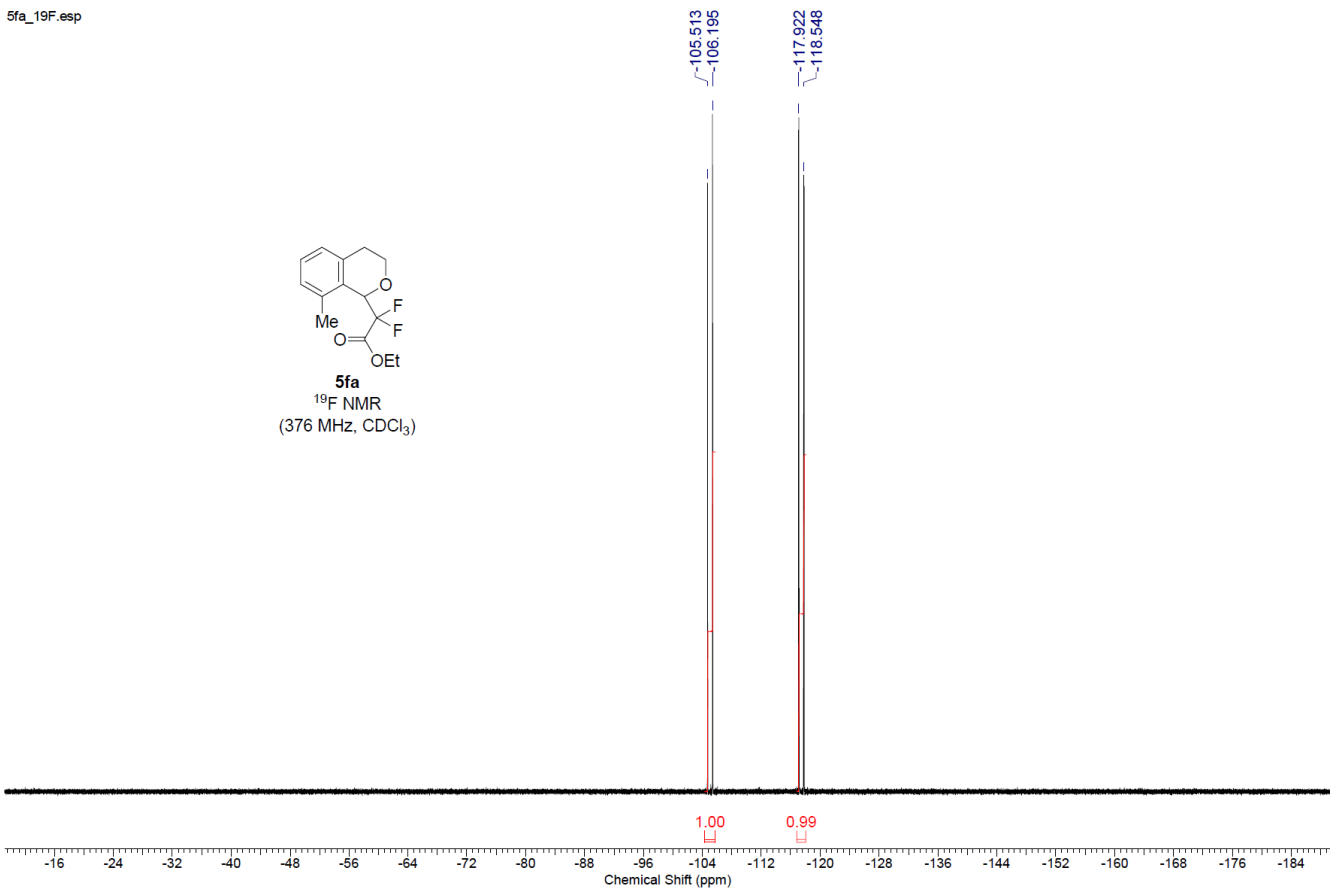

5ea_1H.esp
TMS
7.297
7.283
7.277
7.263
7.241
7.237
7.216
7.192
5.250
5.239
5.198
5.186
4.419
4.412
4.401
4.395
4.383
4.377
4.366
4.157
4.144
4.130
3.812
3.798
2.863
2.849
2.835
2.815
2.802
2.789
2.761
1.387
1.370
1.351
0.000
Cl
O
O
F
F
OEt
5ea
1H NMR
(400 MHz, CDCl3)
1.05 1.04 1.00
1.00
2.09 1.04
1.02
2.07
3.17
Chemical Shift (ppm)

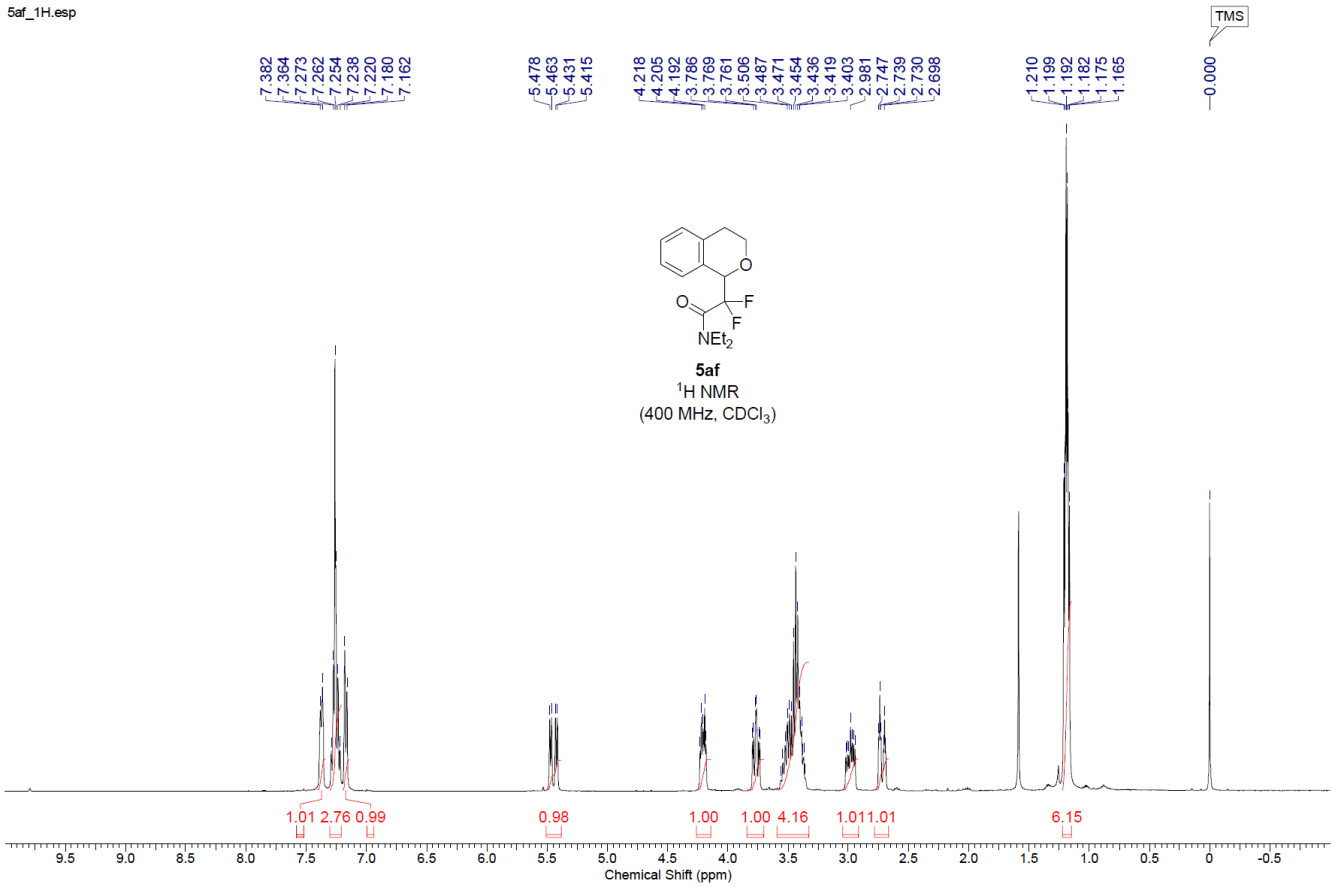

5ea_13C.esp
CHLOROFORM-d
163.468
163.203
162.968
137.174
133.923
128.717
128.028
127.974
126.732
126.656
116.722
114.706
114.638
112.615
77.258
77.000
76.750
74.083
73.886
73.855
73.658
63.012
62.443
28.253
13.901
Cl
O
O
F
F
OEt
5ea
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)

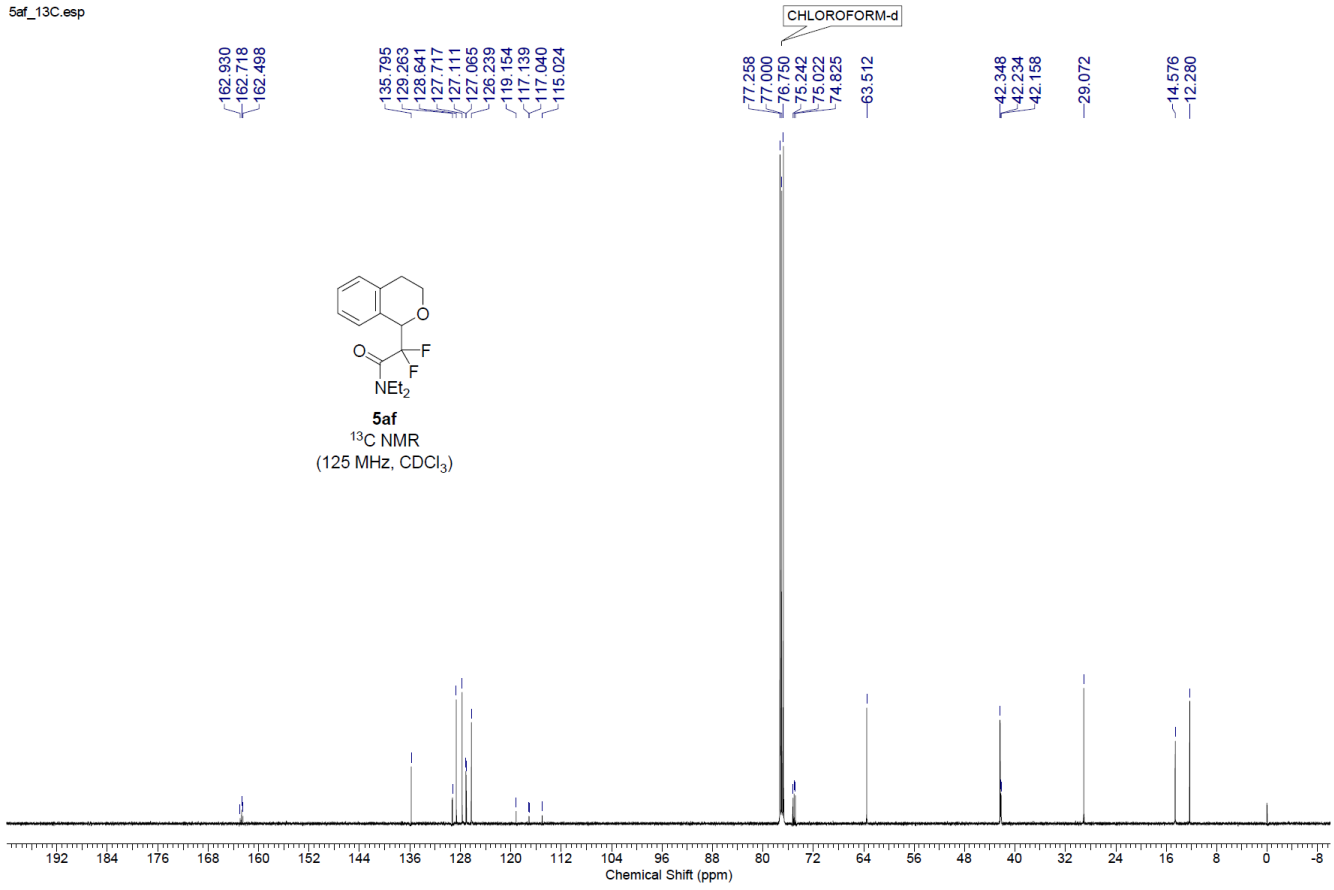

5ea_19F.esp
-106.254
-106.940
-106.948
-118.798
-118.854
-119.484
-119.541
Cl
O
O
F
F
OEt
5ea
19F NMR
(376 MHz, CDCl3)
1.00
0.99
-16
-24
-32
-40
-48
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
-184
Chemical Shift (ppm)

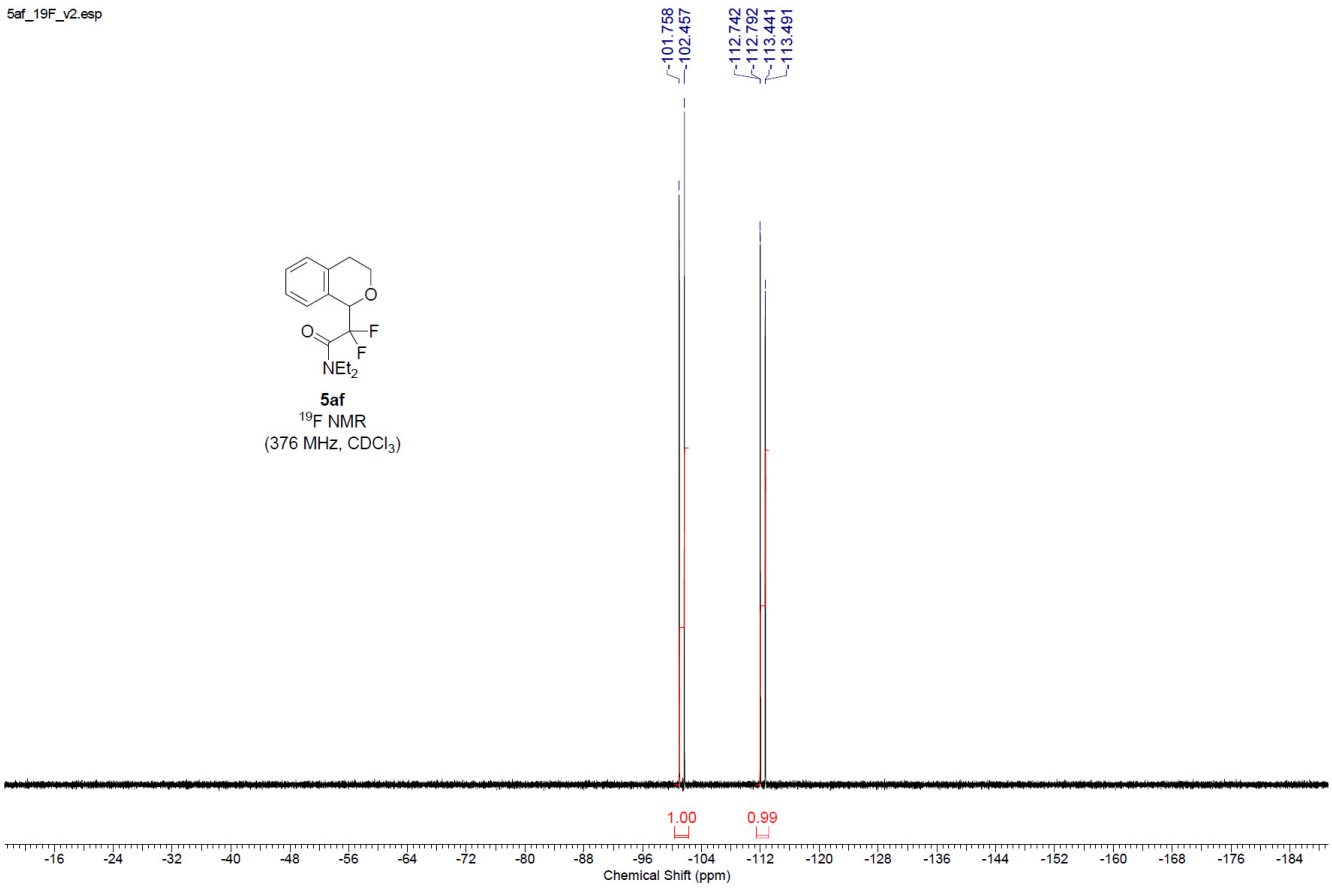

5fa_1H.esp
TMS
7.260
7.218
7.212
7.204
7.196
7.170
7.162
7.156
5.267
5.254
5.214
5.200
4.412
4.406
4.394
4.388
4.376
4.370
4.186
4.183
4.172
3.882
3.868
3.854
2.733
2.719
2.705
2.266
1.388
1.371
1.352
0.000
Me
O
F
F
OEt
5fa
1H NMR
(400 MHz, CDCl3)
1.01 2.02
1.00
2.12 1.06 1.03
2.10
3.18
3.19
Chemical Shift (ppm)

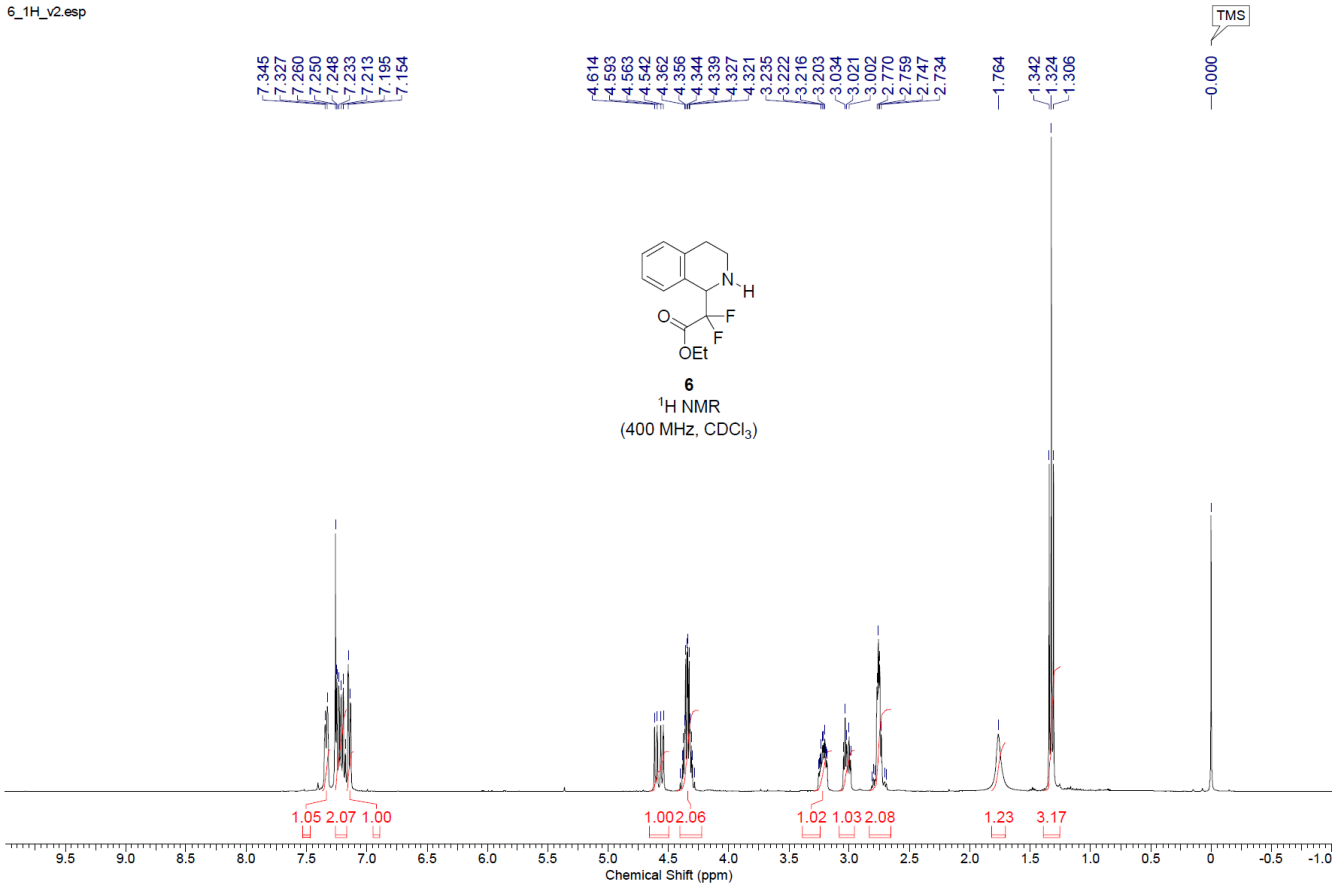

5fa_13C.esp
CHLOROFORM-d
163.870
163.604
163.369
136.166
133.635
129.460
128.020
125.838
124.231
124.186
117.199
115.108
113.085
77.250
77.000
76.742
74.469
74.249
74.052
62.913
62.557
25.624
19.031
13.954
Me
O
F
F
OEt
5fa
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)

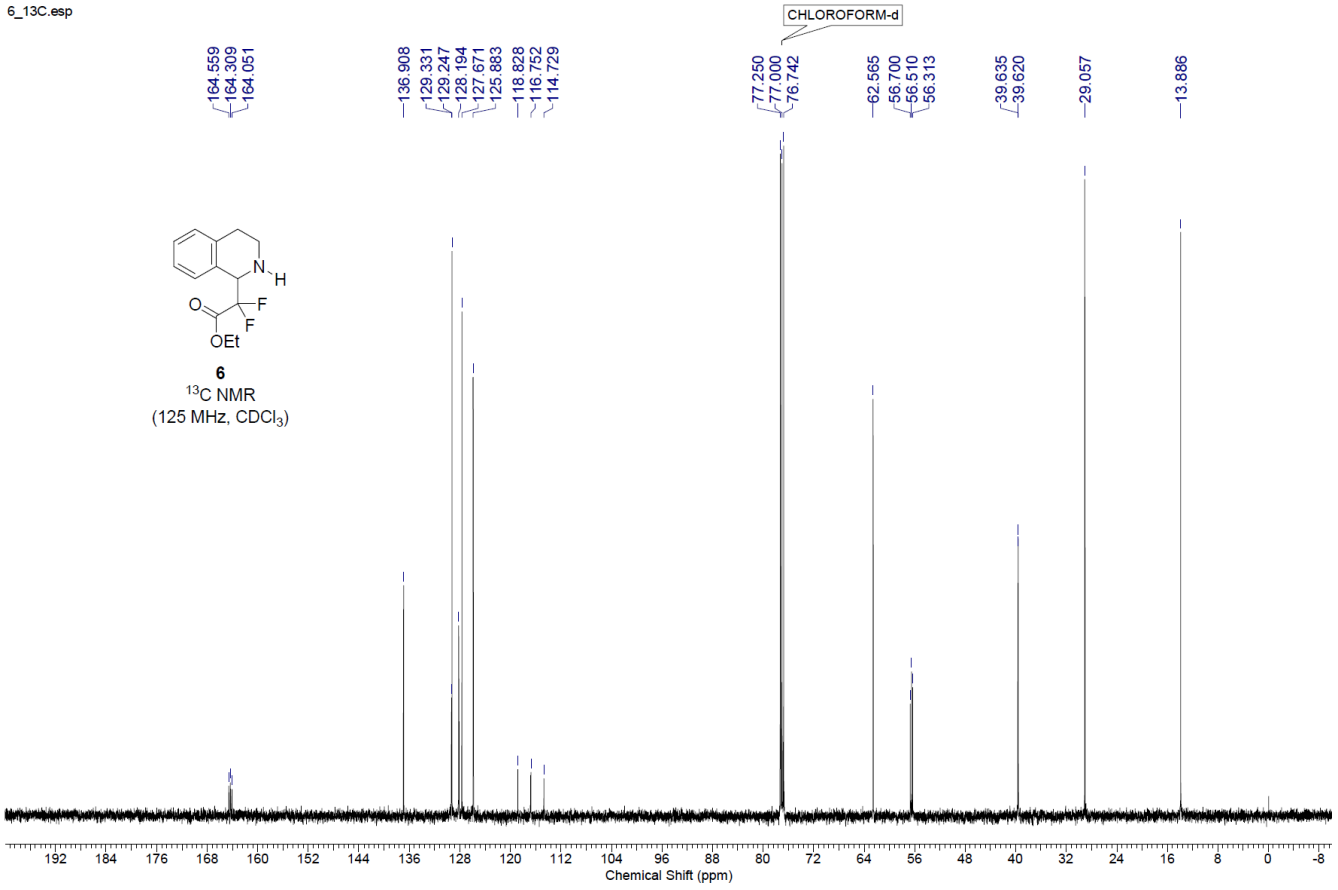

5fa_19F.esp
-105.513
-106.195
-117.922
-118.548
Me
O
F
F
O
OEt
5fa
19F NMR
(376 MHz, CDCl3)
1.00
0.99
-16
-24
-32
-40
-48
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
-184
Chemical Shift (ppm)

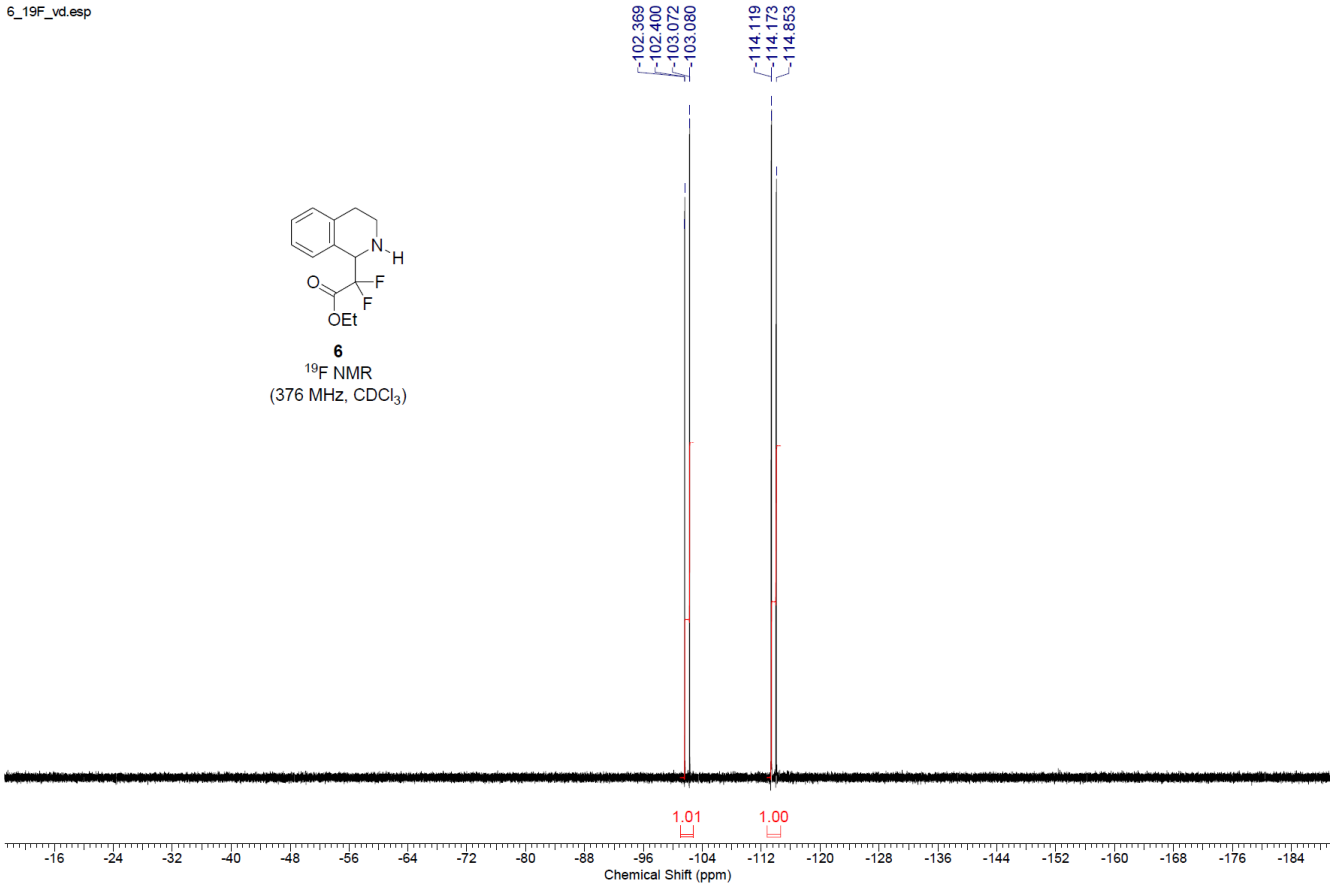

5af_1H.esp
TMS
7.382
7.364
7.273
7.262
7.254
7.238
7.220
7.180
7.162
5.478
5.463
5.431
5.415
4.218
4.205
4.192
3.786
3.769
3.761
3.506
3.487
3.471
3.454
3.436
3.419
3.403
2.981
2.747
2.739
2.730
2.698
1.210
1.199
1.192
1.182
1.175
1.165
0.000
O
O
F
F
NEt2
5af
1H NMR
(400 MHz, CDCl3)
1.01 2.76 0.99
0.98
1.00
1.00 4.16
1.01 1.01
6.15
Chemical Shift (ppm)

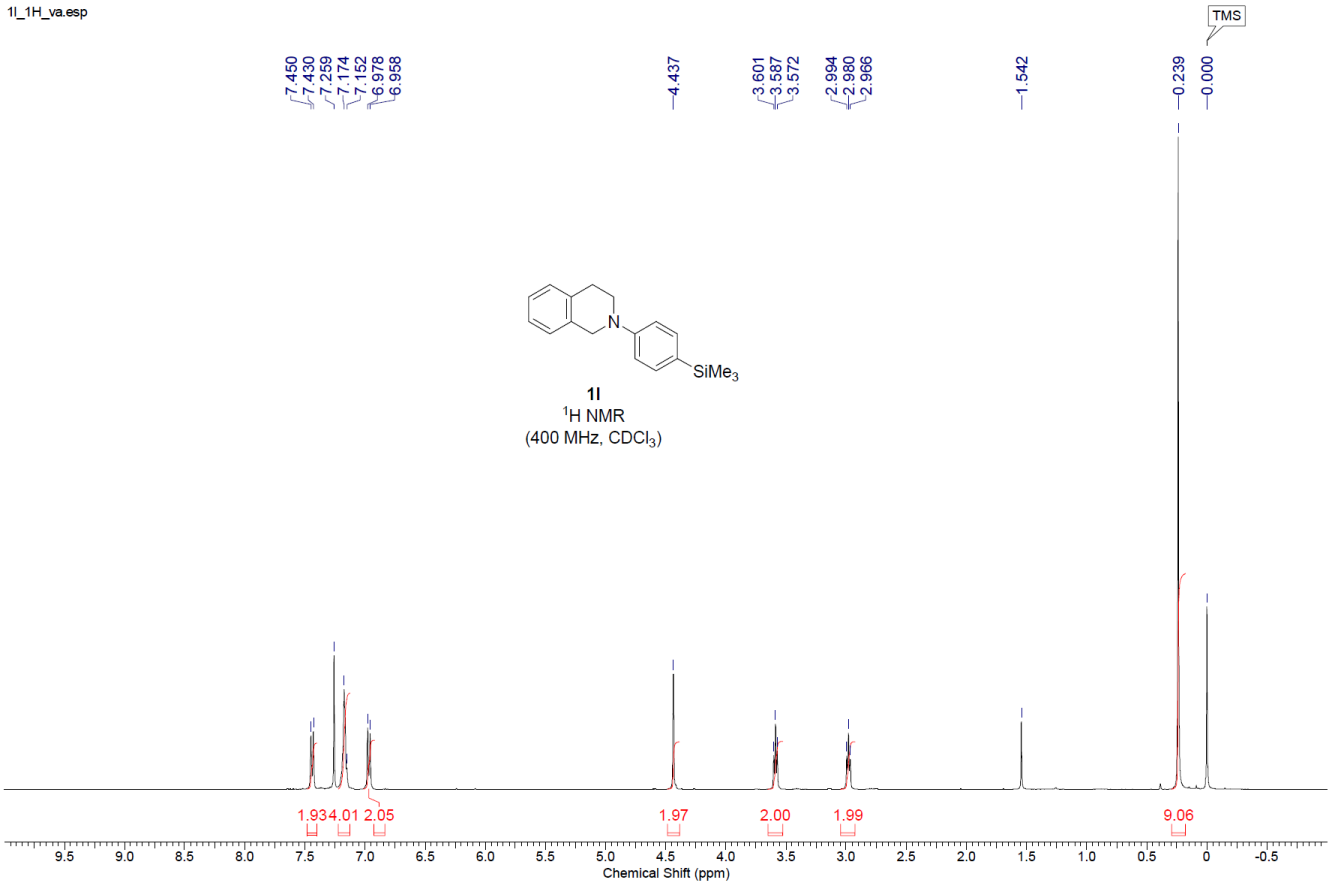

5af_13C.esp
CHLOROFORM-d
162.930
162.718
162.498
135.795
129.263
128.641
127.717
127.111
127.065
126.239
119.154
117.139
117.040
115.024
77.258
77.000
76.750
75.242
75.022
74.825
63.512
42.348
42.234
42.158
29.072
14.576
12.280
O
O
F
F
NEt2
5af
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)

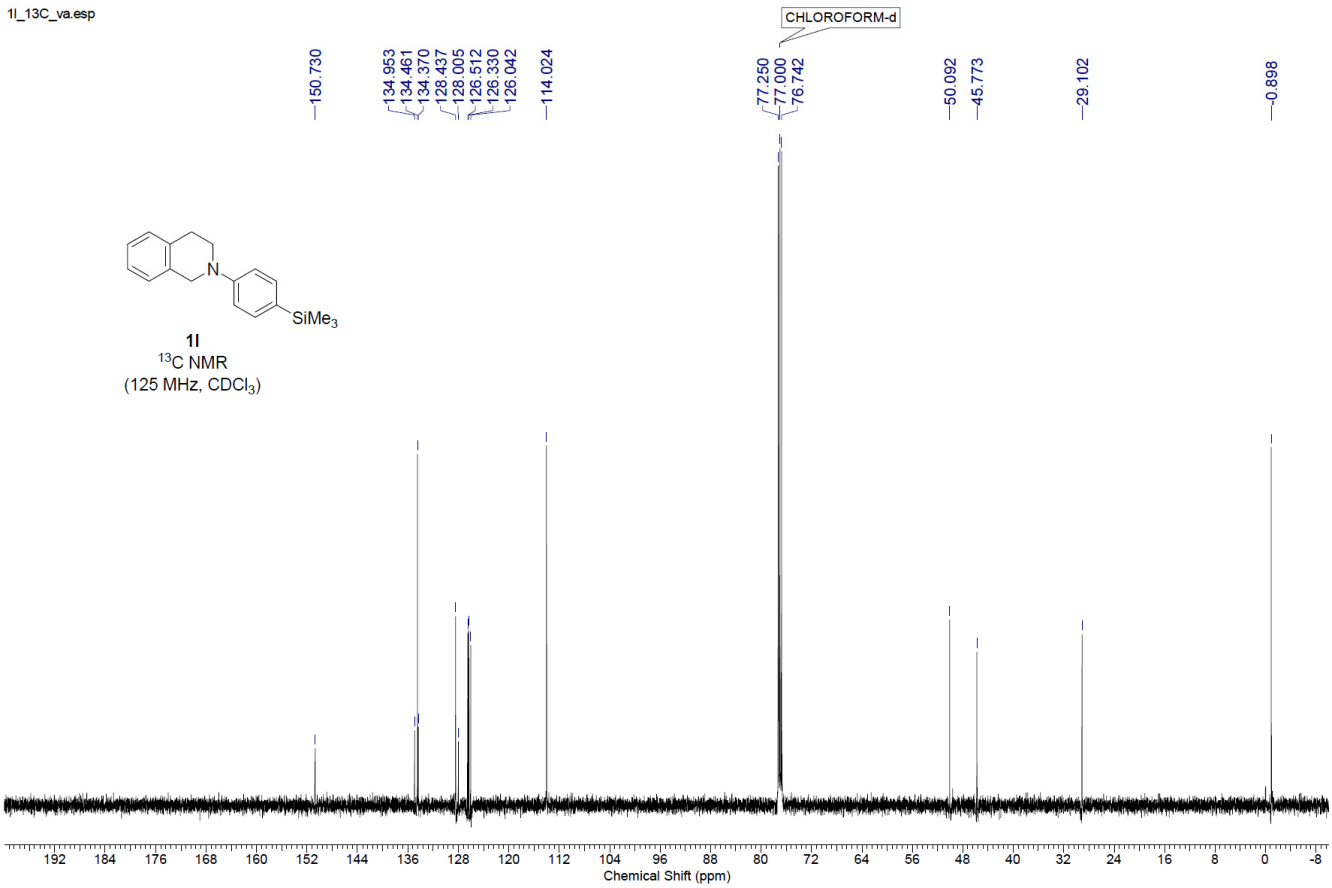

5af_19F_v2.esp
-101.758
-102.457
-112.742
-112.792
-113.441
-113.491
O
O
F
F
NEt2
5af
19F NMR
(376 MHz, CDCl3)
1.00
0.99
-16
-24
-32
-40
-48
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
-184
Chemical Shift (ppm)

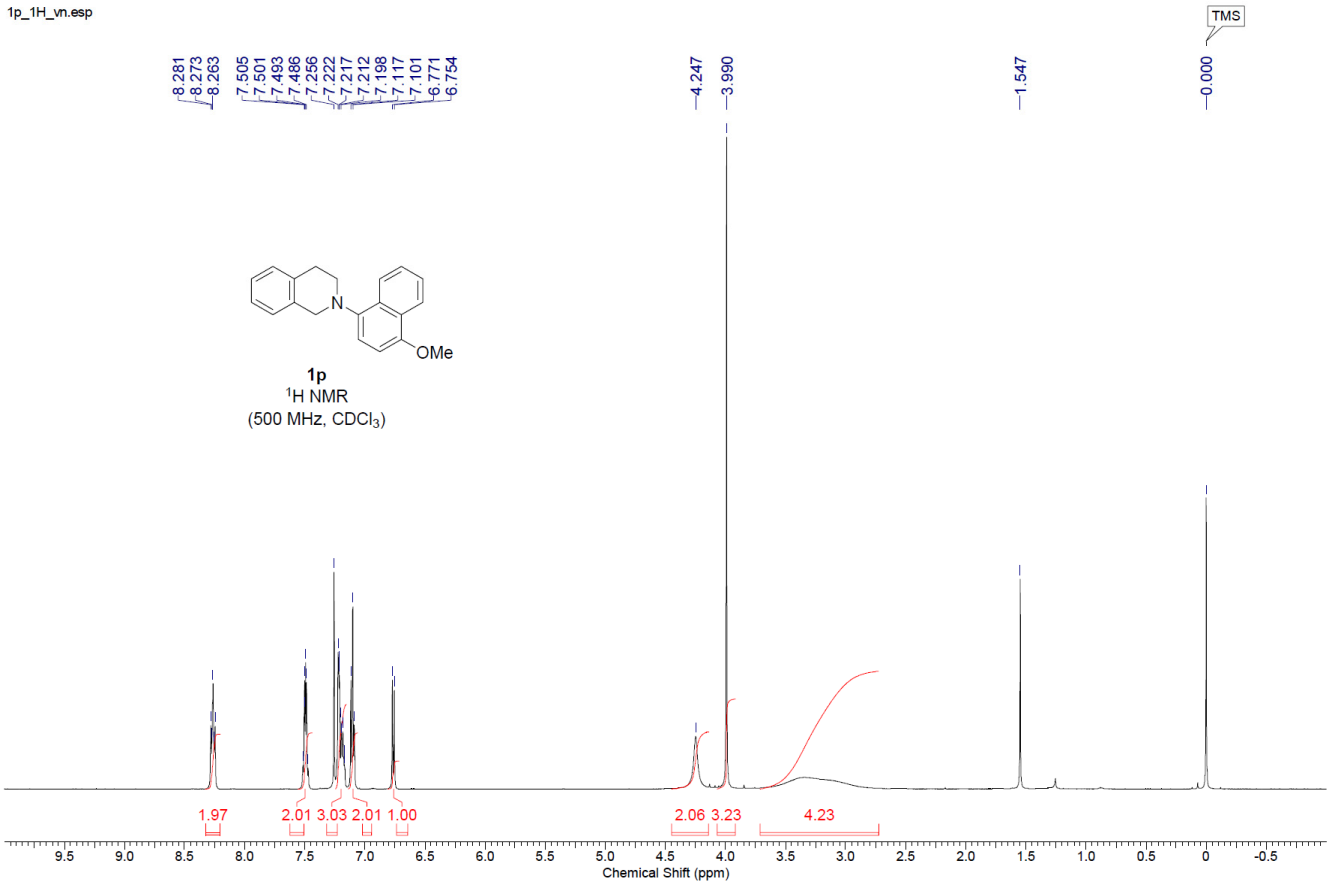

6_1H_v2.esp
TMS
7.345
7.327
7.260
7.250
7.248
7.233
7.213
7.195
7.154
4.614
4.593
4.563
4.542
4.362
4.356
4.344
4.339
4.327
4.321
3.235
3.222
3.216
3.203
3.034
3.021
3.002
2.770
2.759
2.747
2.734
1.764
1.342
1.324
1.306
0.000
N
H
O
F
F
OEt
6
1H NMR
(400 MHz, CDCl3)
1.05 2.07 1.00
1.00 2.06
1.02 1.03 2.08
1.23
3.17
Chemical Shift (ppm)

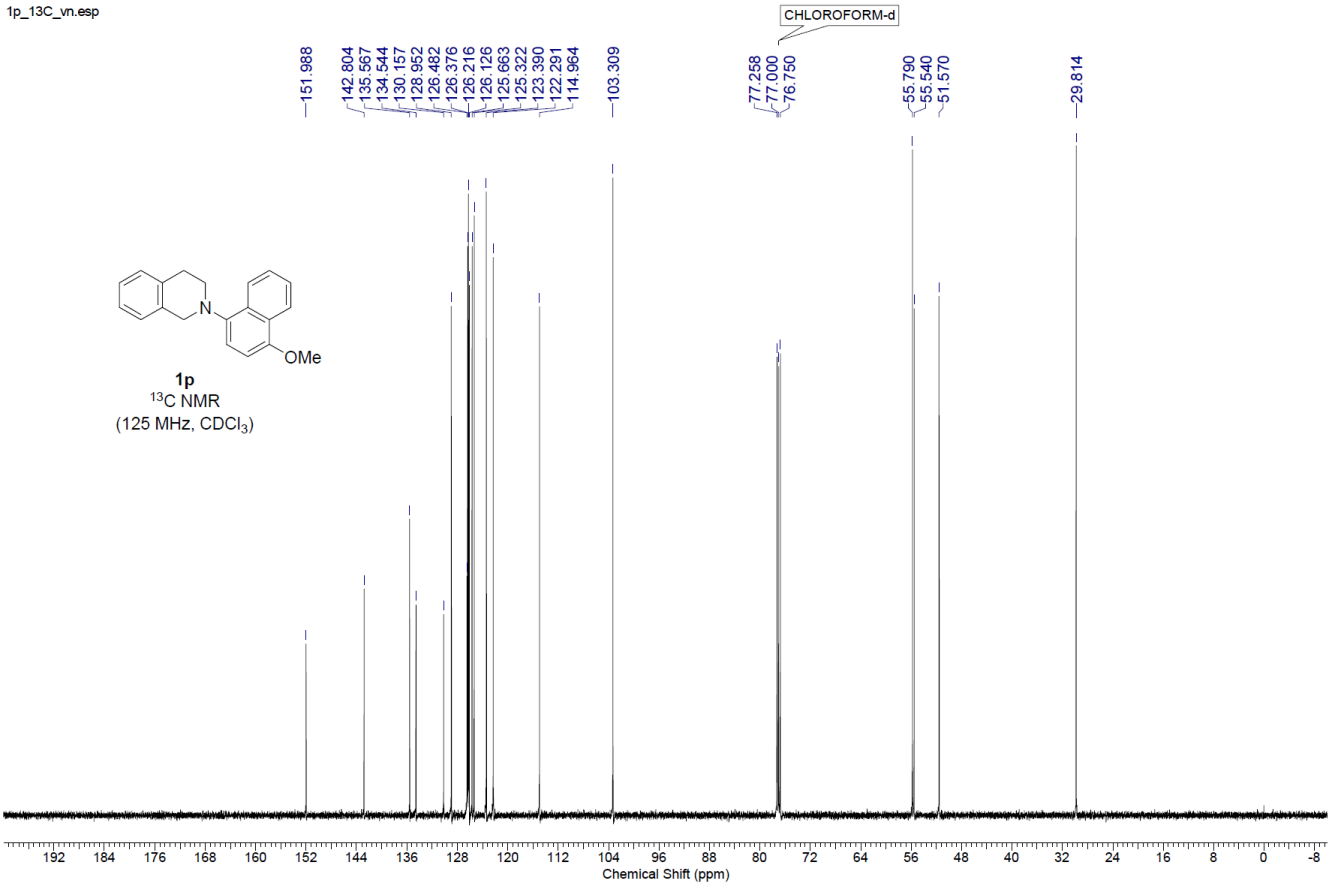

6_13C.esp
CHLOROFORM-d
164.559
164.309
164.051
136.908
129.331
129.247
128.194
127.671
125.883
118.828
116.752
114.729
77.250
77.000
76.742
62.565
56.700
56.510
56.313
39.635
39.620
29.057
13.886
N
H
O
F
F
OEt
6
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)

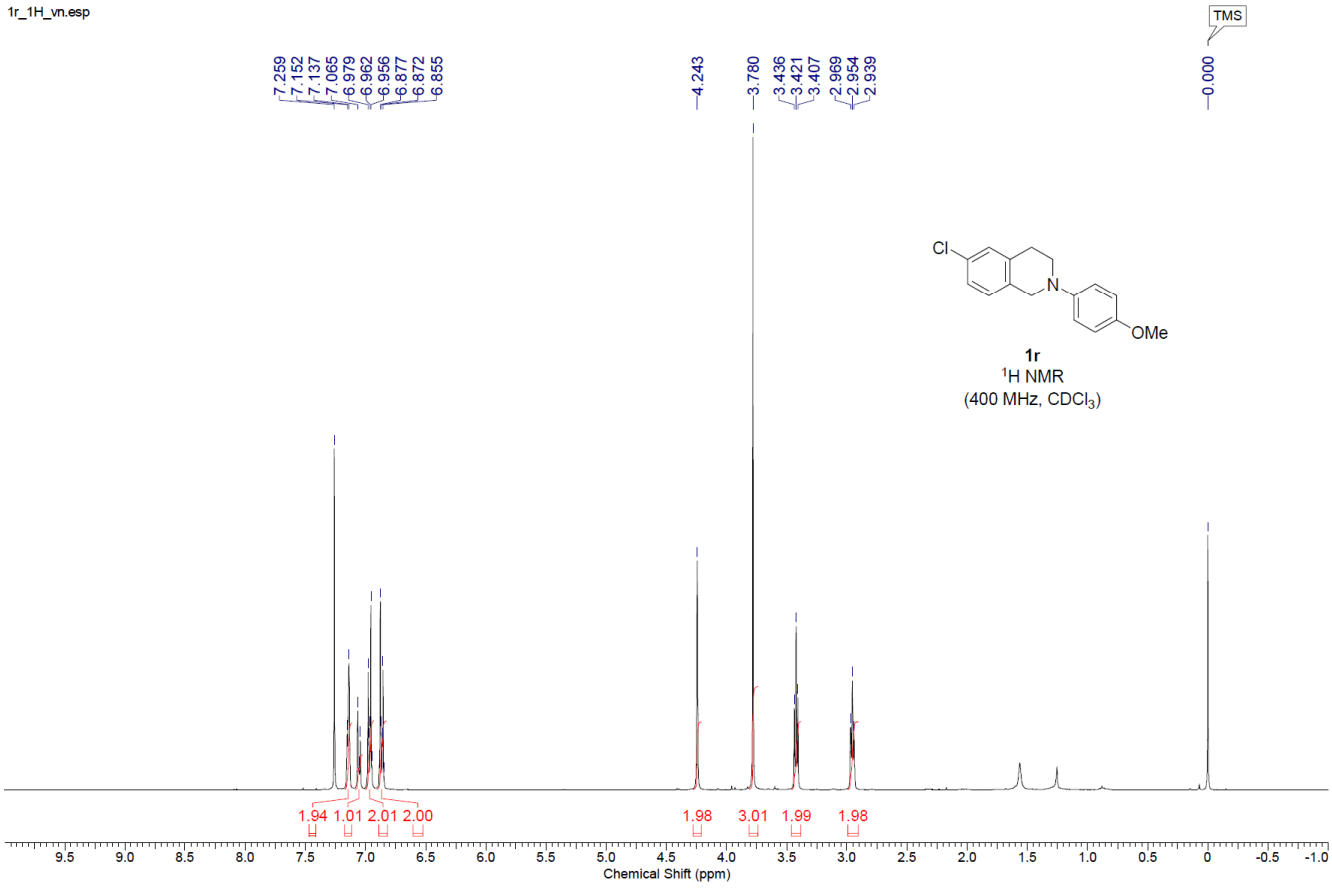

6_19F_vd.esp
-102.369
-102.400
-103.072
-103.080
-114.119
-114.173
-114.853
N
H
O
F
F
OEt
6
19F NMR
(376 MHz, CDCl3)
1.01
1.00
-16
-24
-32
-40
-48
-56
-64
-72
-80
-88
-96
-104
-112
-120
-128
-136
-144
-152
-160
-168
-176
-184
Chemical Shift (ppm)

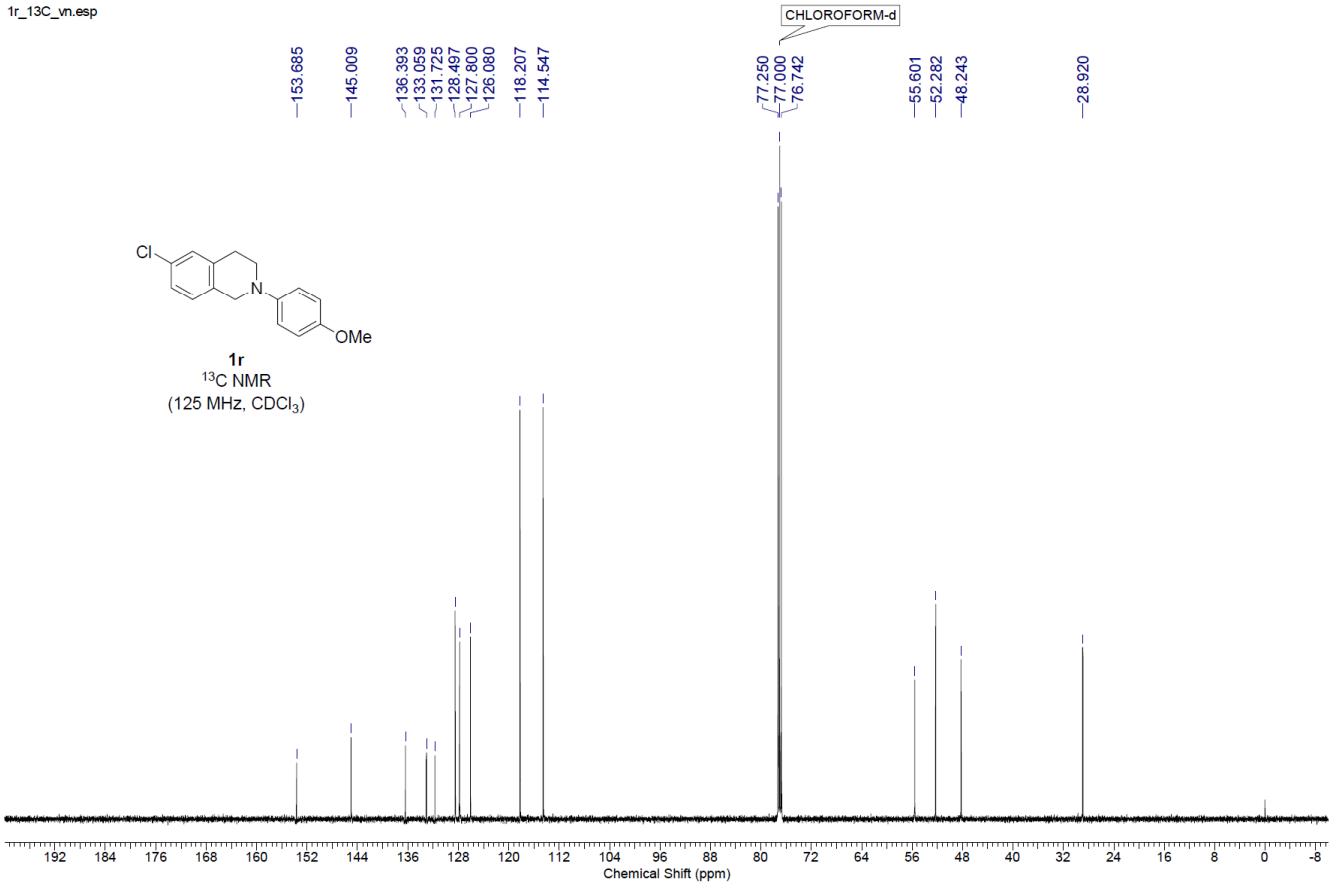

1l_1H_va.esp
TMS
7.450
7.430
7.259
7.174
7.152
6.978
6.958
4.437
3.601
3.587
3.572
2.994
2.980
2.966
1.542
0.239
0.000
SiMe3
1l
1H NMR
(400 MHz, CDCl3)
1.93
4.01
2.05
1.97
2.00
1.99
9.06
Chemical Shift (ppm)

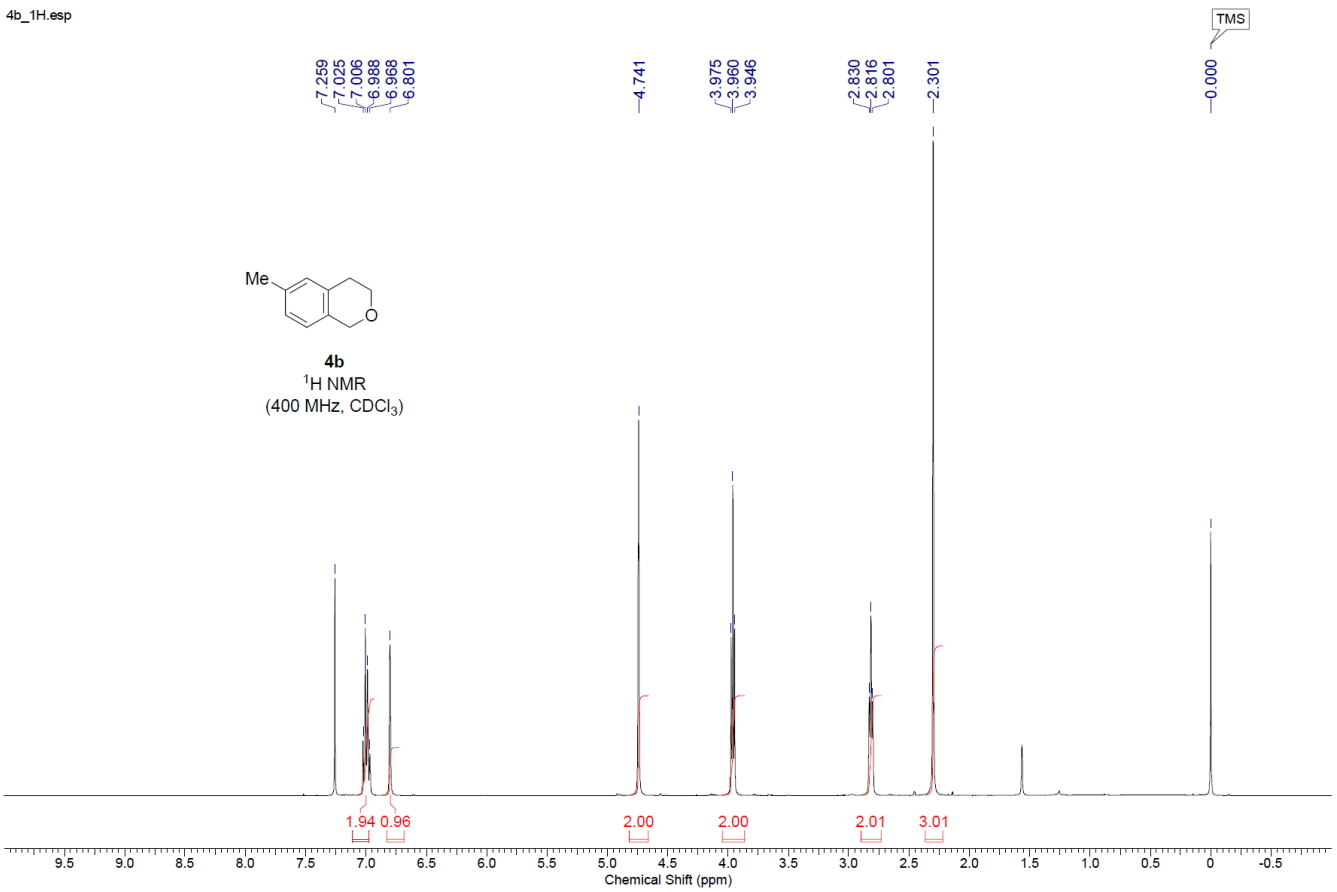

1l_13C_va.esp
CHLOROFORM-d
150.730
134.953
134.461
134.370
128.437
128.005
126.512
126.330
126.042
114.024
77.250
77.000
76.742
50.092
45.773
29.102
0.898
SiMe3
1l
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)

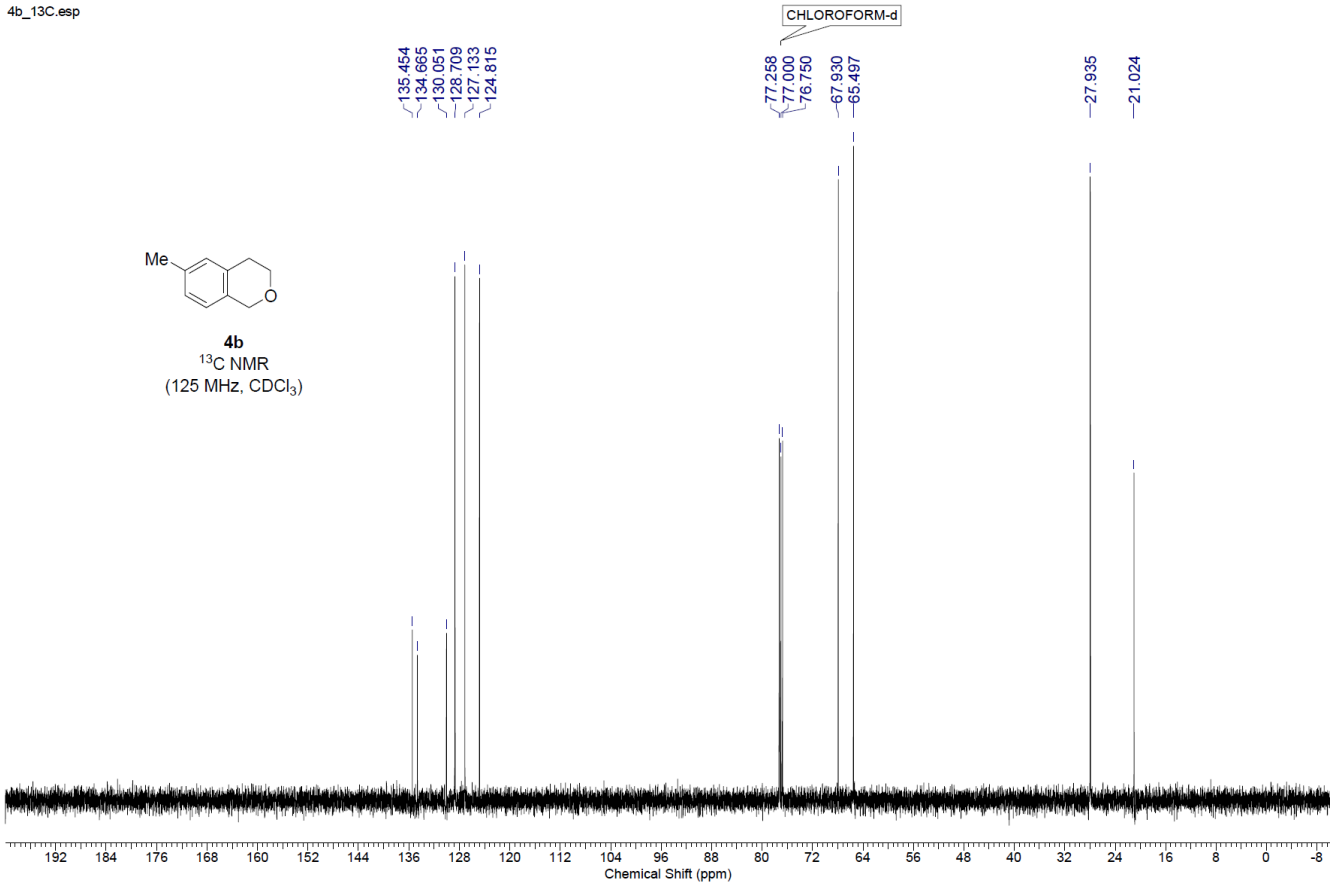

1p_1H_vn.esp
TMS
8.281
8.273
8.263
7.505
7.501
7.493
7.486
7.256
7.222
7.217
7.212
7.198
7.117
7.101
6.771
6.754
4.247
3.990
1.547
0.000
N
OMe
1p
1H NMR
(500 MHz, CDCl3)
1.97
2.01
3.03
2.01
1.00
2.06
3.23
4.23
Chemical Shift (ppm)

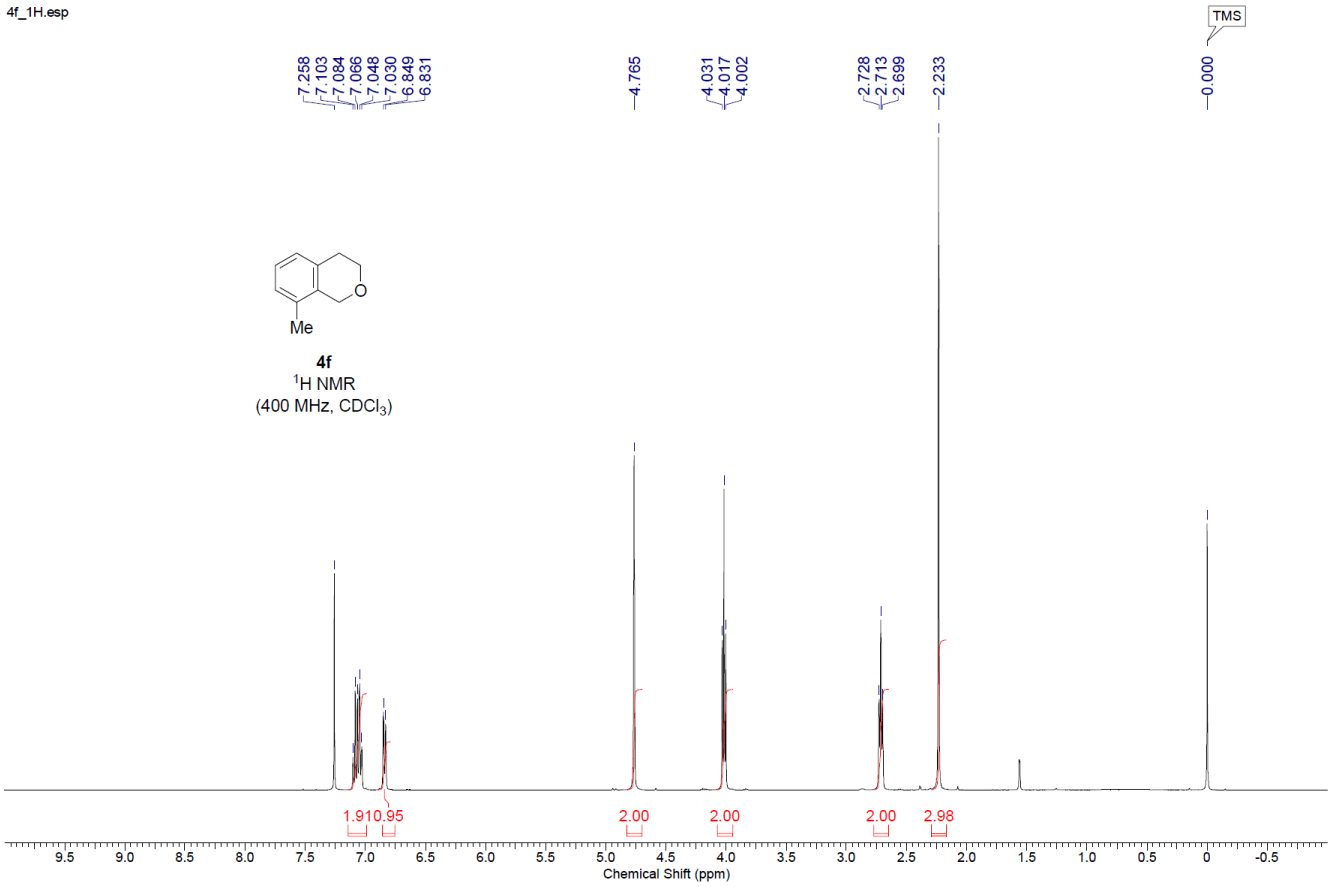

1p_13C_vn.esp
CHLOROFORM-d
151.988
142.804
135.567
134.544
130.157
128.952
128.482
126.376
126.216
126.126
125.663
125.322
123.390
122.291
114.964
103.309
77.258
77.000
76.750
55.790
55.540
51.570
29.814
N
OMe
1p
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)

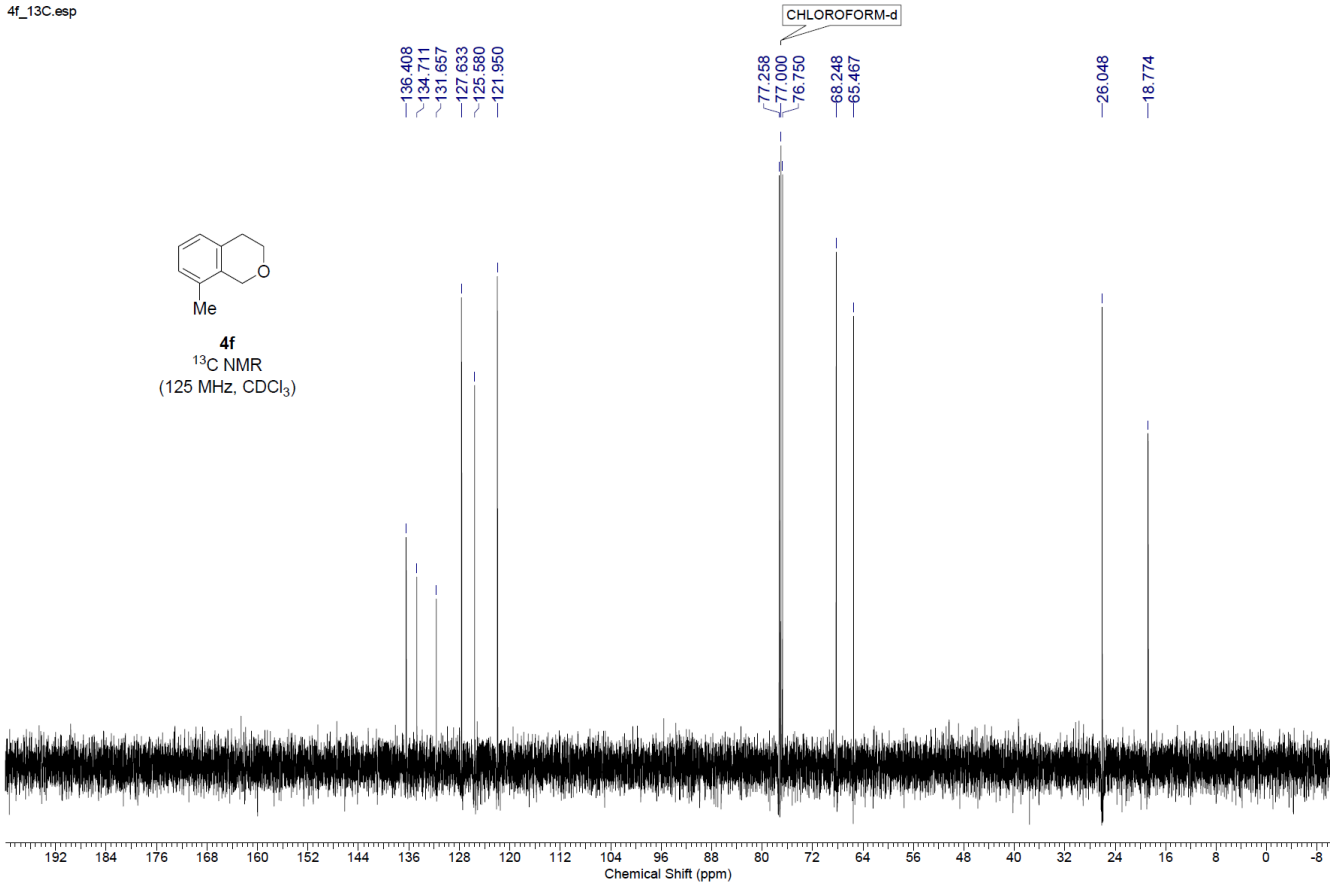

1r_1H_vn.esp
TMS
7.259
7.152
7.137
7.065
6.979
6.962
6.956
6.877
6.872
6.855
4.243
3.780
3.436
3.421
3.407
2.969
2.954
2.939
0.000
Cl
N
OMe
1r
1H NMR
(400 MHz, CDCl3)
1.94 1.01 2.01 2.00
1.98 3.01 1.99 1.98
Chemical Shift (ppm)


1r_13C_vn.esp
CHLOROFORM-d
153.685
145.009
136.393
133.059
131.725
128.497
127.800
126.080
118.207
114.547
77.250
77.000
76.742
55.601
52.282
48.243
28.920
Cl
N
OMe
1r
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)


4b_1H.esp
TMS
7.259
7.025
7.006
6.988
6.968
6.801
4.741
3.975
3.960
3.946
2.830
2.816
2.801
2.301
0.000
Me
O
4b
1H NMR
(400 MHz, CDCl3)
1.94
0.96
2.00
2.00
2.01
3.01
Chemical Shift (ppm)


4b_13C.esp
CHLOROFORM-d
135.454
134.665
130.051
128.709
127.133
124.815
77.258
77.000
76.750
67.930
65.497
27.935
21.024
Me
O
4b
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)


4f_1H.esp
TMS
7.258
7.103
7.084
7.066
7.048
7.030
6.849
6.831
4.765
4.031
4.017
4.002
2.728
2.713
2.699
2.233
0.000
O
Me
4f
1H NMR
(400 MHz, CDCl3)
1.91
0.95
2.00
2.00
2.00
2.98
Chemical Shift (ppm)


4f_13C.esp
CHLOROFORM-d
136.408
134.711
131.657
127.633
125.580
121.950
77.258
77.000
76.750
68.248
65.467
26.048
18.774
O
Me
4f
13C NMR
(125 MHz, CDCl3)
Chemical Shift (ppm)