Supporting Information

Catalytic α-Alkylation of α-Fluoro-α-2-Azaaryl Carbonyl Compounds with Nonconjugated Alkenes

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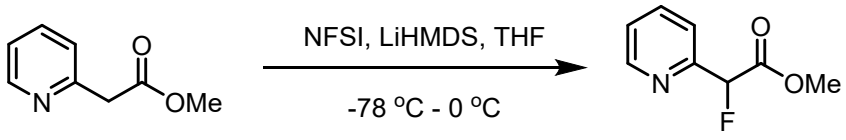
1. General Information

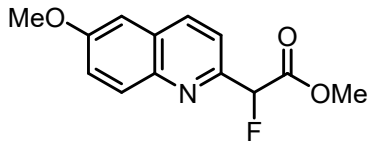
Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. All reactions were carried out at air atmosphere using reaction tubes and were monitored through thin layer chromatography (TLC) on silica gel-precoated glass plates. Reactions were monitored by thin layer chromatography (TLC) using UV light to visualize the course of reaction. Flash column chromatography was performed using Yantai Yinlong flash silica gel (200-300 mesh). Melting points were recorded on an Electrothermal digital melting point apparatus. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on Bruker 400 MHz spectrometer in $CDCl_3$ with tetramethylsilane (TMS) as internal standard. The chemical shifts are expressed in ppm and coupling constants are given in Hz. Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet; d = doublet; t = triplet; q = quarter; p = pentet; m = multiplet; br = broad), coupling constant (Hz), integration. Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm). Data for ^{19}F NMR are reported in terms of chemical shift (δ, ppm). Data for HRMS were obtained by using BRUKER micrOTOF-Q III instrument with ESI source or EI source. IR spectra were recorded on a BRUKER VERTEX 70 spectrophotometer and are reported in terms of frequency of absorption (cm^{-1}).

2. Synthesis of Fluorinated Substrates[1]

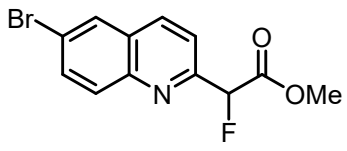


To a solution of LiHMDS (10 mL, 1 M in THF, 10 mmol, 1 equiv) in THF (20 mL) at -78 °C was added methyl 2-pyridylacetate (1.35 mL, 1.51 g, 1 mmol, 1 equiv) in THF (10 mL) dropwise. After being stirred at 0 °C for 40 min, the mixture was cooled to -78 °C. NFSI (3.15 g, 1 mmol, 1 equiv) in THF (30 mL) was added at -78 °C. Thereafter, the mixture was stirred at 0 °C for 1 h. Saturated aqueous NH_4Cl solution (10 mL),

water (40 mL), and EtOAc (30 mL) were added sequentially to the mixture. The organic layer was separated, and the aqueous layer was extracted with EtOAc (40 mL x 2). The organic layers were combined and evaporated under vacuum. The mixture was diluted with Et_2O (40 mL) to afford a cloudy yellow solution, which was then filtered through column of silica gels. The column was flashed with Et_2O (20 mL x 2). After removal of solvent under vacuum, the crude mixture was purified by flash column chromatography (EtOAc/PE = 1/1), to give **1a** as a yellow oil. The fluorinated substrates **1a-1h**, **1k-1m** were known in literature.[1] Characterization of new gem-difluorocyclopropanes **1i, 1j** are listed below.

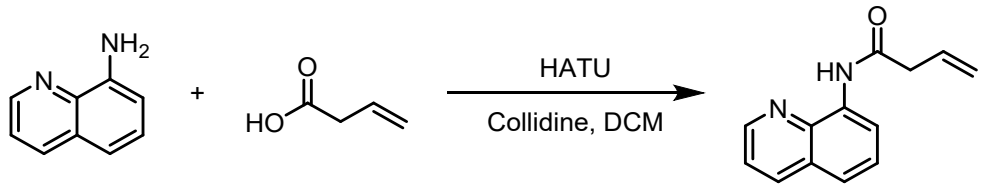


Methyl-2-fluoro-2-(6-methoxyquinolin-2-yl)acetate (1i). **1i** was obtained as a white oil. (2.1 g, 85%). R_f = 0.5 (EtOAc/PE = 2/1); **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.12 (d, *J* = 8.5 Hz, 1H), 8.01 (d, *J* = 9.3 Hz, 1H), 7.56 (d, *J* = 8.5 Hz, 1H), 7.39 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.07 (d, *J* = 2.8 Hz, 1H), 6.05 (d, *J* = 47.7 Hz, 1H), 3.92 (s, 3H), 3.81 (s, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 168.2 (d, *J* = 27.0 Hz), 158.5, 151.0 (d, *J* = 23.5 Hz), 143.6, 136.2, 131.1, 129.3, 123.1, 118.7 (d, *J* = 3.5 Hz), 104.9, 90.8 (d, *J* = 185.8 Hz), 55.6, 52.8. **^{19}F NMR** (376 MHz, Chloroform-d) δ -183.57. **FT-IR** (ATR): 1760, 1620, 1483, 1221, 1070, 1025, 986, 855, 823, 753 cm^{-1}; **HRMS** (ESI^+, m/z): calcd for $C_{13}H_{13}FNO_3^+$ $[M+H]^+$: 250.0874, found:250.0872.



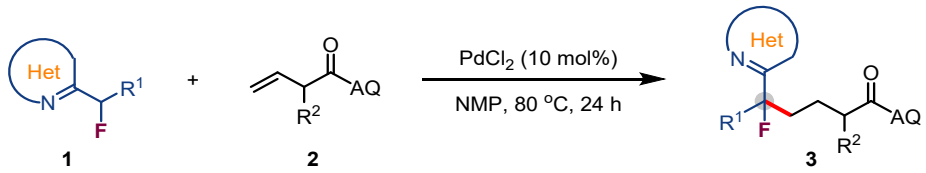
Methyl-2-(6-bromoquinolin-2-yl)-2-fluoroacetate (1j). **1j** was obtained as a white oil. (2.2 g, 75%). R_f = 0.5 (EtOAc/PE = 1/1); **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.14 (d, *J* = 8.5 Hz, 1H), 8.01 – 7.93 (m, 2H), 7.79 (dd, *J* = 9.0, 2.2 Hz, 1H), 7.62 (dd, *J* = 8.6, 0.8 Hz, 1H), 6.05 (d, *J* = 47.7 Hz, 1H), 3.81 (s, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 167.7 (d, *J* = 26.5 Hz), 154.1 (d, *J* = 23.5 Hz), 154.0, 146.0, 136.6, 133.7, 131.4, 129.7, 129.1, 121.5, 119.2 (d, *J* = 3.9 Hz), 90.6 (d, *J* = 186.9 Hz), 52.9. **^{19}F NMR** (376 MHz, Chloroform-d) δ-185.37. **FT-IR** (ATR): 1759, 1593, 1488, 1277, 1178, 1080, 974, 817, 738 cm^{-1}; **HRMS** (ESI^+, m/z): calcd for $C_{12}H_{10}BrFNO_2^+$ $[M+H]^+$: 297.9873, found:297.9860.

3. Synthesis of Alkene Substrates [2]

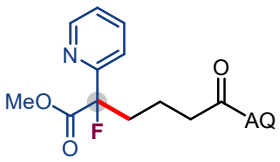


But-3-enoic acid (1.12 mL, 13 mmol) was charged into a flame-dried reaction tube containing 30 mL DCM. 8-Aminoquinoline (1.44 g, 10 mmol), collidine (2.6 mL, 20 mmol), and HATU (4.94 g, 13 mmol) were added sequentially, and the reaction was stirred at ambient temperature for 16 h. The deep brown solution was diluted with EtOAc (200 mL), washed with sat. $NaHCO_3$ (100 mL, ×2) and brine (100 mL, ×1), and purified by column chromatography (EtOAc/PE = 1/10) to afford **2a** as a yellow oil. The Nitroalkanes **2a-2f** were known in literature.[2]

4. General Procedure for the Preparation of 3

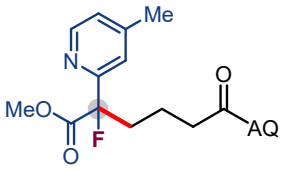


General Procedure: To an 8-mL scintillation vial equipped with a Teflon-coated magnetic stir bar was added **1** (0.15 mmol, 1.5 equiv), **2** (0.1 mmol, 1.0 equiv), $PdCl_2$ (0.0018 g, 0.01 mmol, 0.1 equiv), and NMP (0.2 mL). The vial was sealed with a screw-top septum cap and placed in an oil bath that was preheated to 80 °C. After a time period of 24 h, the reaction vial was allowed cooled to room temperature, and the reaction mixture was dilute with 15 mL ethyl acetate and wash with saturated salt water (3 × 30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash column chromatography (EtOAc/PE = 1/10-1/5) to give **3**.



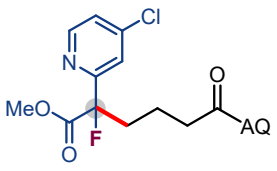
3aa

Methyl-2-fluoro-6-oxo-2-(pyridin-2-yl)-6-(quinolin-8-ylamino)hexanoate (3aa): 63.0 mg, 82% yield, R_f = 0.4 (EtOAc/PE = 1/5), yellow oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.56 (s, 1H), 8.59 - 8.45 (m, 2H), 8.36 (d, *J* = 4.8 Hz, 1H), 7.91 - 7.80 (m, 1H), 7.53 - 7.45 (m, 1H), 7.40 (d, *J* = 7.9 Hz, 1H), 7.28 - 7.12 (m, 3H), 7.00 (dd, *J* = 7.5, 4.8 Hz, 1H), 3.56 (s, 3H), 2.51 - 2.23 (m, 4H), 1.82 - 1.61 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 170.8, 169.5 (d, *J* = 26.3 Hz), 156.8 (d, *J* = 26.7 Hz), 149.1 (d, *J* = 2.1 Hz), 148.1, 138.1, 137.0, 136.2, 134.3, 127.8, 127.2, 123.5, 121.5, 121.4, 120.0 (d, *J* = 8.4 Hz), 116.3, 97.9 (d, *J* = 186.6 Hz), 52.9, 37.4, 35.5 (d, *J* = 20.9 Hz), 19.2 (d, *J* = 3.2 Hz); **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -164.37, (s, 1F); **FT-IR** (ATR): 3349, 2953, 1747, 1682, 1520, 1485, 791, 753 cm^{-1}; **HRMS** (ESI^+, m/z): calcd for $C_{21}H_{20}FN_3O_3Na^+$ $[M+Na]^+$: 404.1381, found: 404.1380.



3ba

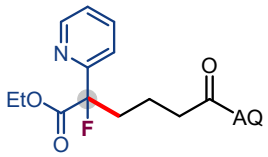
Methyl-2-fluoro-2-(4-methylpyridin-2-yl)-6-oxo-6-(quinolin-8-ylamino)hexanoate (3ba): 59.3 mg, 75% yield, R_f = 0.4 (EtOAc/PE = 1/4), yellow solid. **M.p.** = 100.8 - 102.3 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.77 (s, 1H), 8.83 - 8.71 (m, 2H), 8.44 (d, *J* = 5.0 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.55 - 7.42 (m, 4H), 7.07 - 7.05 (m, 1H), 3.78 (s, 3H), 2.67 - 2.45 (m, 4H), 2.37 (s, 3H), 1.99 - 1.79 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 170.90, 169.7 (d, *J* = 26.5 Hz), 156.5 (d, *J* = 26.5 Hz), 149.0 (d, *J* = 2.2 Hz), 148.4, 148.1, 138.2, 136.3, 134.4, 127.9, 127.3, 124.4, 121.6, 121.4, 120.8(d, *J* = 8.4 Hz), 116.4, 97.9 (d, *J* = 186.3 Hz), 53.0, 37.6, 35.6 (d, *J* = 20.9 Hz), 21.2, 19.33 (d, *J* = 3.3 Hz); **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -164.68 (s, 1F); **FT-IR** (ATR): 2923, 2850, 1753, 1669, 1525, 1486, 829, 793 cm^{-1}; **HRMS** (ESI^+, m/z): calcd for $C_{22}H_{23}FN_3O_3^+$ $[M+H]^+$: 396.1718, found: 396.1704.



3ca

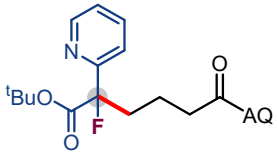
Methyl-2-(4-chloropyridin-2-yl)-2-fluoro-6-oxo-6-(quinolin-8-ylamino)hexanoate (3ca): 54.1 mg, 65% yield, R_f = 0.4 (EtOAc/PE = 1/5), yellow solid. **M.p.** = 94.6 - 96.3 °C;

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.78 (s, 1H), 8.83 - 8.72 (m, 2H), 8.56 - 8.44 (m, 1H), 8.15 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.66 (t, *J* = 1.9 Hz, 1H), 7.56 - 7.43 (m, 3H), 7.29 - 7.25 (m, 1H), 3.79 (s, 3H), 2.68 - 2.44 (m, 4H), 2.00 - 1.77 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 170.7, 169.0 (d, *J* = 26.3 Hz), 158.3 (d, *J* = 27.3 Hz), 150.2 (d, *J* = 2.3 Hz), 148.1, 145.4 (d, *J* = 1.5 Hz), 138.3, 136.4, 134.4, 127.9, 127.4, 123.9, 121.6, 121.5, 120.7 (d, *J* = 9.6 Hz), 116.5, 97.6 (d, *J* = 188.1 Hz), 53.2, 37.5, 35.5 (d, *J* = 20.9 Hz), 19.2 (d, *J* = 3.3 Hz); **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -165.13 (s, 1F); **FT-IR** (ATR): 3338, 2923, 1755, 1524, 1486, 1242, 829, 792 cm^{-1}; **HRMS** (ESI$^+$, m/z): calcd for $C_{21}H_{20}ClFN_3O_3^+$ [M+H]$^+$: 416.1172, found: 416.1172.



3da

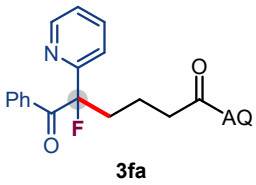
Ethyl-2-fluoro-6-oxo-2-(pyridin-2-yl)-6-(quinolin-8-ylamino)hexanoate (3da): 49.8 mg, 63% yield, R_f = 0.4 (EtOAc/PE = 1/3), yellow oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.76 (s, 1H), 8.77 - 8.72 (m, 2H), 8.62 - 8.53 (m, 1H), 8.11 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.71 (td, *J* = 7.7, 1.8 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.53 - 7.37 (m, 3H), 7.22 (dd, *J* = 7.5, 4.9 Hz, 1H), 4.27 - 4.20 (m, 2H), 2.68 - 2.43 (m, 4H), 2.03 - 1.80 (m, 2H), 1.22 (t, *J* = 7.1 Hz, 3H); **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 170.9, 169.1 (d, *J* = 28.0 Hz), 156.8 (d, *J* = 29.6 Hz), 149.1 (d, *J* = 2.0 Hz), 148.1, 138.3, 137.0, 136.3, 134.4, 127.9, 127.4, 123.4, 121.6, 121.4, 120.1 (d, *J* = 8.4 Hz), 116.4, 97.8 (d, *J* = 186.7 Hz), 62.1, 37.7, 35.5 (d, *J* = 20.9 Hz), 19.3 (d, *J* = 3.2 Hz), 14.1; **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -164.33 (s, 1F); **FT-IR** (ATR): 3351, 2935, 1743, 1683, 1521, 1485, 791, 753 cm^{-1}; **HRMS** (ESI$^+$, m/z): calcd for $C_{22}H_{23}FN_3O_3^+$ [M+H]$^+$: 396.1718, found: 396.1704.



3ea

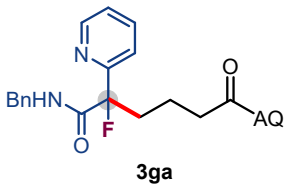
^{t}Butyl-2-fluoro-6-oxo-2-(pyridin-2-yl)-6-(quinolin-8-ylamino)hexanoate (3ea): 63.5 mg, 75% yield, R_f = 0.4 (EtOAc/PE = 1/5), yellow oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.78 (s, 1H), 8.78 - 8.74 (m, 2H), 8.59 - 8.57 (m, 1H), 8.13 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.71 (td, *J* = 7.8, 1.8 Hz, 1H), 7.60 - 7.57 (m,

1H), 7.54 - 7.38 (m, 3H), 7.25 - 7.21 (m, 1H), 2.67 - 2.46 (m, 4H), 2.01 - 1.84 (m, 2H), 1.42 (s, 9H); **^{13}C {^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 171.02, 168.2 (d, *J* = 25.9 Hz), 157.2 (d, *J* = 26.3 Hz), 149.0 (d, *J* = 1.9 Hz), 148.1, 138.3, 136.8, 136.3, 134.5, 127.9, 127.4, 123.2, 121.6, 121.4, 120.1 (d, *J* = 8.0 Hz), 116.4, 97.7 (d, *J* = 186.8 Hz), 82.9, 37.8, 35.2 (d, *J* = 21.1 Hz), 27.8, 19.4 (d, *J* = 3.3 Hz); **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -162.82 (s, 1F); **FT-IR** (ATR): 3352, 2977, 1740, 1324, 1685, 1521, 791, 753 cm^{-1}; **HRMS** (ESI^{+}, m/z): calcd for $C_{24}H_{27}FN_3O_3^{+}$ [M+H]$^{+}$: 424.2031, found: 424.2028.



3fa

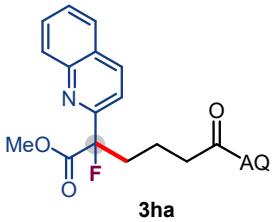
5-Fluoro-6-oxo-6-phenyl-5-(pyridin-2-yl)-N-(quinolin-8-yl)hexanamide (3fa): 68.4 mg, 80% yield, R_f = 0.4 (EtOAc/PE = 1/10), yellow solid. **M.p.** = 106.8 - 108.5 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.57 (s, 1H), 8.59 - 8.48 (m, 2H), 8.33 (d, *J* = 4.8 Hz, 1H), 7.90 - 7.85 (m, 1H), 7.74 - 7.68 (m, 2H), 7.58 - 7.49 (m, 2H), 7.25 - 7.06 (m, 6H), 6.99 - 6.95 (m, 1H), 2.46 - 2.26 (m, 4H), 1.85 - 1.73 (m, 1H), 1.68 - 1.57 (m, 1H); **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 195.4 (d, *J* = 25.9 Hz), 171.1, 157.8 (d, *J* = 25.5 Hz), 149.4 (d, *J* = 2.2 Hz), 148.1, 138.2, 137.3, 137.3, 136.4, 134.6 (d, *J* = 3.2 Hz), 134.4, 133.0, 130.1, 130.0, 128.2, 127.9, 127.3, 123.2, 121.6, 121.5, 119.8 (d, *J* = 7.0 Hz), 116.5, 102.9 (d, *J* = 186.9 Hz), 37.8, 36.9 (d, *J* = 22.1 Hz), 19.3 (d, *J* = 3.9 Hz); **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -161.80 (s, 1F); **FT-IR** (ATR): 3339, 2923, 1747, 1681, 1525, 1486, 789, 748 cm^{-1}; **HRMS** (ESI^{+}, m/z): calcd for $C_{26}H_{22}FN_3O_3Na^{+}$ [M+Na]$^{+}$: 450.1589, found: 450.1590.



3ga

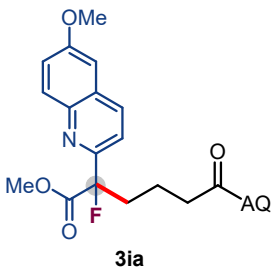
***N1*-Benzyl-2-fluoro-2-(pyridin-2-yl)-*N6*-(quinolin-8-yl)hexanediamide (3ga)**: 63.9 mg, 70% yield, R_f = 0.4 (EtOAc/PE = 1/3), brown solid. **M.p.** = 110.8 - 112.5 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.76 (s, 1H), 8.80 - 8.67 (m, 2H), 8.58 (d, *J* = 4.8 Hz, 1H), 8.09 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.68 (td, *J* = 7.8, 1.8 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.50 - 7.42 (m, 2H), 7.38 (dd, *J* = 8.3, 4.3 Hz, 2H), 7.26

- 7.17 (m, 6H), 4.46 (d, J = 5.8 Hz, 2H), 2.69 - 2.42 (m, 4H), 1.98 - 1.89 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 171.0, 169.2 (d, J = 23.0 Hz), 157.0 (d, J = 24.3 Hz), 149.1 (d, J = 1.5 Hz), 148.1, 138.2, 137.8, 137.1, 136.4, 134.4, 128.7, 127.9, 127.6, 127.5, 127.3, 123.4, 121.6, 121.5, 120.1 (d, J = 7.9 Hz), 116.4, 99.1 (d, J = 187.7 Hz), 43.4, 37.5, 36.7 (d, J = 21.2 Hz), 19.4 (d, J = 3.2 Hz); **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -165.37 (s, 1F); **FT-IR** (ATR): 3344, 2924, 1671, 1520, 1485, 1424, 791, 697 cm^{-1}; **HRMS** (ESI^{+}, m/z): calcd for $C_{27}H_{25}FN_4O_2Na^{+}$ $[M+H]^{+}$: 479.1854, found: 479.1860.



3ha

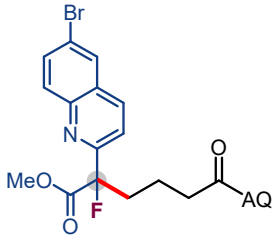
Methyl-2-fluoro-6-oxo-2-(quinolin-2-yl)-6-(quinolin-8-ylamino)hexanoate (3ha): 73.4 mg, 85% yield, R_f = 0.4 (EtOAc/PE = 1/10), yellow oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.78 (s, 1H), 8.81 - 8.70 (m, 2H), 8.19 (d, J = 8.6 Hz, 1H), 8.15 - 8.06 (m, 2H), 7.84 - 7.65 (m, 3H), 7.56 - 7.37 (m, 4H), 3.78 (s, 3H), 2.85 - 2.61 (m, 4H), 2.06 - 1.94 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 170.94, 169.7 (d, J = 26.5 Hz), 156.6 (d, J = 27.0 Hz), 148.1, 147.3, 138.3, 137.3, 136.3, 134.5, 129.8, 129.8, 127.9, 127.7, 127.5, 127.4, 127.1, 121.6, 121.4, 117.6 (d, J = 7.2 Hz), 116.4, 98.5 (d, J = 186.5 Hz), 53.0, 37.7, 35.5 (d, J = 20.9 Hz), 19.5 (d, J = 3.3 Hz); **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -184.9 (s, 1F); **FT-IR** (ATR): 3347, 2951, 1748, 1682, 1520, 1484, 826, 759 cm^{-1}; **HRMS** (ESI^{+}, m/z): calcd for $C_{25}H_{22}FN_3O_3Na^{+}$ $[M+Na]^{+}$: 454.1538, found: 454.1532.



3ia

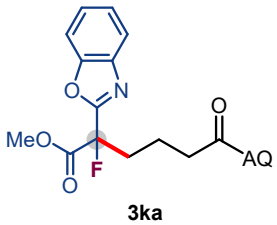
Methyl-2-fluoro-2-(6-methoxyquinolin-2-yl)-6-oxo-6-(quinolin-8-ylamino)hexanoate (3ia): 77.5 mg, 84% yield, R_f = 0.4 (EtOAc/PE = 1/5), white solid. **M.p.** = 110.1 - 112.2 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.64 (s, 1H), 8.70 - 8.53 (m, 2H), 7.97 - 7.80 (m, 3H), 7.59 - 7.48 (m, 1H), 7.35 - 7.15 (m, 4H), 6.86 (d, J = 2.8 Hz, 1H), 3.72 (s, 3H), 3.65 (s, 3H), 2.66 - 2.47 (m, 4H), 1.93 - 1.85 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 170.9, 169.9 (d, J = 26.7

Hz), 158.2, 154.0 (d, J = 26.8 Hz), 148.1, 143.3, 138.2, 136.3, 135.8, 134.4, 131.1, 128.8, 127.8, 127.3, 122.6, 121.6, 121.4, 117.8 (d, J = 7.2 Hz), 116.3, 104.8, 98.4 (d, J = 186.0 Hz), 55.5, 52.9, 37.6, 35.4 (d, J = 21.0 Hz), 19.5 (d, J = 3.3 Hz); **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -161.74 (s, 1F); **FT-IR** (ATR): 3348, 2951, 1748, 1682, 1522, 1484, 825, 790 cm^{-1}; **HRMS** (ESI$^+$, m/z): calcd for $C_{26}H_{25}FN_3O_4^+$ $[M+H]^+$: 462.1824, found: 462.1822.



3ja

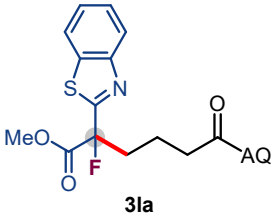
Methyl-2-(6-bromoquinolin-2-yl)-2-fluoro-6-oxo-6-(quinolin-8-ylamino)hexanoate (3ja): 86.8 mg, 85% yield, R_f = 0.4 (EtOAc/PE = 1/7), yellow solid. **M.p.** = 114.8 - 116.3 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.73 (s, 1H), 8.78 - 8.66 (m, 2H), 8.10 - 8.00 (m, 2H), 7.87 (dd, J = 5.7, 3.4 Hz, 2H), 7.72 - 7.65 (m, 2H), 7.50 - 7.33 (m, 3H), 3.77 (s, 3H), 2.81 - 2.57 (m, 4H), 2.08 - 1.88 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 170.8, 169.4 (d, J = 26.5 Hz), 157.1 (d, J = 27.1 Hz), 148.1, 145.8 (d, J = 1.8 Hz), 138.2, 136.3, 136.2, 134.4, 133.2, 131.4, 129.5, 128.7, 127.9, 127.3, 121.6, 121.4, 121.0, 118.4 (d, J = 7.6 Hz), 116.4, 98.4 (d, J = 186.9 Hz), 53.0, 37.6, 35.4 (d, J = 20.8 Hz), 19.4 (d, J = 3.4 Hz); **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -163.1 (s, 1F); **FT-IR** (ATR): 3349, 2946, 1741, 1679, 1524, 1486, 1254, 785 cm^{-1}; **HRMS** (ESI$^+$, m/z): calcd for $C_{25}H_{22}BrFN_3O_3^+$ $[M+H]^+$: 510.0824, found: 510.0824.



3ka

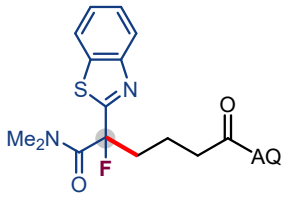
Methyl-2-(benzo[d]oxazol-2-yl)-2-fluoro-6-oxo-6-(quinolin-8-ylamino)hexanoate (3ka): 21.1 mg, 25% yield, R_f = 0.4 (EtOAc/PE = 1/7), cloorless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.82 (s, 1H), 8.82 - 8.74 (m, 2H), 8.16 (dd, J = 8.2, 1.7 Hz, 1H), 7.81 - 7.74 (m, 1H), 7.58 - 7.36 (m, 6H), 3.89 (s, 3H), 2.79 - 2.63 (m, 4H), 2.20 - 1.97 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 170.4, 167.2 (d, J = 27.7 Hz), 160.0 (d, J = 25.3 Hz), 150.8, 148.2, 140.3, 138.3, 136.4, 134.4, 127.9, 127.4, 126.4, 125.0, 121.6, 121.5, 121.0, 116.5, 111.3, 92.4 (d, J = 190.1 Hz), 53.6,

37.2, 34.6 (d, J = 21.2 Hz), 19.2 (d, J = 2.9 Hz); **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -160.26 (s, 1F); **FT-IR** (ATR): 3332, 1658, 1524, 1488, 1396, 782 cm^{-1}; **HRMS** (ESI$^+$, m/z): calcd for $C_{23}H_{21}FN_3O_4^+$ [M+H]$^+$: 422.1511, found: 422.1523.



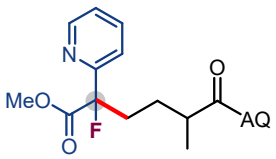
3la

Methyl-2-(benzo[d]thiazol-2-yl)-2-fluoro-6-oxo-6-(quinolin-8-ylamino)hexanoate (3la): 64.8 mg, 74% yield, R_f = 0.4 (EtOAc/PE = 1/7), white solid. **M.p.** = 120.8 - 122.5 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.78 (s, 1H), 8.76 – 8.73 (m, 2H), 8.15 - 8.02 (m, 2H), 7.92 - 7.85 (m, 1H), 7.54 - 7.36 (m, 5H), 3.84 (s, 3H), 2.85 - 2.59 (m, 4H), 2.06 - 1.99 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 170.5, 167.8 (d, J = 26.7 Hz), 166.9 (d, J = 31.0 Hz), 152.9, 148.1, 138.3, 136.4, 135.1, 134.4, 127.9, 127.4, 126.4, 125.9, 123.9, 121.8, 121.6, 121.5, 116.5, 97.0 (d, J = 187.3 Hz), 53.6, 37.3, 36.5 (d, J = 20.6 Hz), 19.3 (d, J = 3.0 Hz); **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -154.10 (s, 1F); **FT-IR** (ATR): 3327, 1647, 1524, 1485, 759 cm^{-1}; **HRMS** (ESI$^+$, m/z): calcd for $C_{23}H_{20}FN_3O_3SNa^+$ [M+Na]$^+$: 460.1102, found: 460.1089.



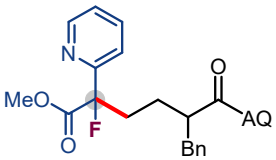
3ma

2-(Benzo[d]thiazol-2-yl)-2-fluoro-*N1*,*N1*-dimethyl-*N6*-(quinolin-8-yl)hexanediamide (3ma): 61.3 mg, 68% yield, R_f = 0.4 (EtOAc/PE = 1/5), white solid. **M.p.** = 120.8 - 122.5 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.77 (s, 1H), 8.80 - 8.70 (m, 2H), 8.18 - 8.05 (m, 2H), 7.89 (dd, J = 8.0, 1.3 Hz, 1H), 7.54 - 7.36 (m, 5H), 3.07 - 2.99 (m, 6H), 2.82 - 2.46 (m, 4H), 2.14 - 1.90 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 170.9, 168.2 (d, J = 27.5 Hz), 166.5 (d, J = 20.5 Hz), 152.8, 148.1, 138.3, 136.3, 134.9, 134.4, 127.9, 127.4, 126.4, 125.7, 123.9, 121.7, 121.6, 121.4, 116.4, 99. 4 (d, J = 192.1 Hz), 39.0, 38.8, 37.7 (d, J = 10.3 Hz), 37.6, 19.6 (d, J = 4.1 Hz); **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -150.78 (s, 1F); **FT-IR** (ATR): 3339, 1751, 1692, 1529, 1259, 790, 760 cm^{-1}; **HRMS** (ESI$^+$, m/z): calcd for $C_{24}H_{23}FN_4O_2SNa^+$ [M+Na]$^+$: 473.1418, found: 473.1415.



3ab

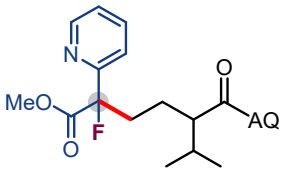
Methyl-2-fluoro-5-methyl-6-oxo-2-(pyridin-2-yl)-6-(quinolin-8-ylamino)hexanoate (3ab): 59.3 mg, 75% yield, R_f = 0.4 (EtOAc/PE = 1/5), yellow oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.85 (d, *J* = 4.4 Hz, 1H), 8.78 - 8.75 (m, 2H), 8.57 - 8.54 (m, 1H), 8.14 - 8.11 (m, 1H), 7.70 (td, *J* = 7.7, 1.7 Hz, 1H), 7.60 - 7.57 (m, 1H), 7.52 - 7.40 (m, 3H), 7.23 - 7.19 (m, 1H), 3.75 (s, 3H), 2.70 - 2.48 (m, 3H), 1.99 - 1.88 (m, 1H), 1.71 - 1.52 (m, 1H), 1.32 (dd, *J* = 11.0, 6.9 Hz, 3H); **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 174.6, 174.5 (isomers), 169.6 (d, *J* = 26.4 Hz), 156.8 (d, *J* = 8.7 Hz), 156.5 (d, *J* = 8.7 Hz) (isomers), 149.2 (d, *J* = 2.1 Hz), 148.1, 138.3, 137.0, 136.4, 134.5, 134.4 (isomers), 127.9, 127.4, 123.5, 121.6, 121.5, 120.1 (d, *J* = 8.5 Hz), 120.0 (d, *J* = 8.4 Hz) (isomers), 116.6, 97.9 (d, *J* = 186.4 Hz), 97.8 (d, *J* = 187.0 Hz) (isomers), 53.0, 42.6, 42.5 (isomers), 34.1 (d, *J* = 20.9 Hz), 33.9 (d, *J* = 21.0 Hz) (isomers), 27.6 (d, *J* = 3.1 Hz), 18.0; **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -164.23, (s, 1F), -164.91 (s, 1F) (isomers); **FT-IR** (ATR): 3350, 2931, 1745, 1682, 1522, 1322, 791, 752 cm^{-1}; **HRMS** (ESI$^+$, m/z): calcd for $C_{22}H_{23}FN_3O_3^+$ [M+H]$^+$: 396.1718, found: 396.1716.



3ac

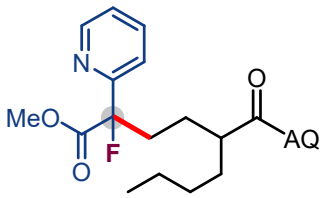
Methyl-5-benzyl-2-fluoro-6-oxo-2-(pyridin-2-yl)-6-(quinolin-8-ylamino)hexanoate (3ac): 69.8 mg, 74% yield, R_f = 0.4 (EtOAc/PE = 1/5), brown solid. **M.p.** = 96.8 - 98.5 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.67 (s, 1H), 8.77 - 8.74 (m, 1H), 8.70 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.55 - 8.53 (m, 1H), 8.10 - 8.07 (m, 1H), 7.69 (td, *J* = 7.7, 1.8 Hz, 1H), 7.57 - 7.55 (m, 1H), 7.51 - 7.42 (m, 2H), 7.38 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.22 - 7.16 (m, 5H), 7.11 - 7.05 (m, 1H), 3.71 (d, *J* = 8.7 Hz, 3H), 3.15 - 3.07 (m, 1H), 2.93 - 2.76 (m, 2H), 2.71 - 2.47 (m, 2H), 2.02 - 1.91 (m, 1H), 1.78 - 1.65 (m, 1H); **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 173.0, 173.0 (isomers), 169.7 (d, *J* = 26.4 Hz), 169.4 (d, *J* = 26.5 Hz) (isomers), 156.6 (d, *J* = 26.7 Hz), 149.2 (t, *J* = 2.7 Hz), 148.0, 139.2, 138.3, 137.0, 136.2, 134.3, 134.2 (isomers), 128.9, 128.9 (isomers), 128.4, 128.4 (isomers), 127.8, 127.3, 126.3, 126.3 (isomers), 123.5, 123.5 (isomers), 121.5, 121.5, 120.1 (d, *J* = 8.4 Hz), 120.0 (d, *J* = 8.5 Hz) (isomers), 116.5, 97.9 (d, *J* =

186.4 Hz), 97.9 (d, *J* = 186.7 Hz) (isomers), 53.0, 52.9 (isomers), 50.7, 50.6 (isomers), 39.0, 34.1 (d, *J* = 20.8 Hz), 33.8 (d, *J* = 20.8 Hz) (isomers), 26.1 (d, *J* = 1.4 Hz), 26.0 (d, *J* = 2.7 Hz) (isomers); **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -164.23, (s, 1F), -164.91 (s, 1F) (isomers); **FT-IR** (ATR): 3344, 2924, 1671, 1520, 1424, 1324, 791, 697 cm^{-1}; **HRMS** (ESI$^+$, m/z): calcd for $C_{28}H_{26}FN_3O_3$ Na^+ $[M+Na]^+$: 494.1851, found: 494.1828.



3ad

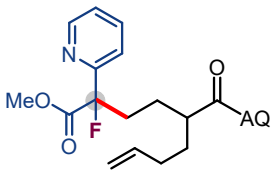
Methyl-2-fluoro-6-methyl-2-(pyridin-2-yl)-5-(quinolin-8-ylcarbamoyl)heptanoate (3ad): 70.3 mg, 83% yield, R_f = 0.4 (EtOAc/PE = 1/5), yellow oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.81 (d, *J* = 6.5 Hz, 1H), 8.84 - 8.71 (m, 2H), 8.56 - 8.46 (m, 1H), 8.09 (dt, *J* = 8.3, 2.2 Hz, 1H), 7.69 - 7.64 (m, 1H), 7.60 - 7.53 (m, 1H), 7.52 - 7.35 (m, 3H), 7.21 - 7.13 (m, 1H), 3.72 (d, *J* = 3.1 Hz, 3H), 2.67 - 2.37 (m, 2H), 2.27 - 2.19 (m, 1H), 2.04 - 1.83 (m, 2H), 1.78 -1.67 (m, 1H), 1.06 - 0.81 (m, 6H); **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 173.4, 173.3 (isomers), 169.7 (d, *J* = 26.3 Hz), 169.6 (d, *J* = 26.7 Hz) (isomers), 156.7 (d, *J* = 26.6 Hz), 149.3 (q, *J* = 2.2 Hz), 148.2, 138.4, 138.4 (isomers), 136.9, 136.9 (isomers), 136.3, 134.4, 134.4 (isomers), 127.9, 127.9 (isomers), 127.3, 127.3 (isomers), 123.5, 123.4 (isomers), 121.6, 121.4, 120.1 (d, *J* = 8.2 Hz), 119.9 (d, *J* = 8.4 Hz) (isomers), 116.4, 98.0 (d, *J* = 186.1 Hz), 97.9 (d, *J* = 187.0 Hz) (isomers), 55.7, 55.7 (isomers), 52.9, 34.4 (d, *J* = 20.7 Hz), 34.1 (d, *J* = 21.3 Hz) (isomers), 31.0, 31.0 (isomers), 23.6 (d, *J* = 3.0 Hz), 23.6 (d, *J* = 3.1 Hz) (isomers), 20.6, 20.4 (d, *J* = 2.5 Hz); **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -163.04 (s, 1F), -165.07 (s, 1F) (isomers); **FT-IR** (ATR): 3352, 2958, 1748, 1680, 1520, 1484, 790, 752 cm^{-1}; **HRMS** (ESI$^+$, m/z): calcd for $C_{24}H_{26}FN_3O_3Na^+$ $[M+Na]^+$: 446.1851, found: 446.1836.



3ae

Methyl-2-fluoro-2-(pyridin-2-yl)-5-(quinolin-8-ylcarbamoyl)nonanoate (3ae): 76.2 mg, 87% yield, R_f = 0.4 (EtOAc/PE = 1/5), yellow oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.84 (d, *J* = 7.6 Hz, 1H), 8.82 - 8.74 (m,

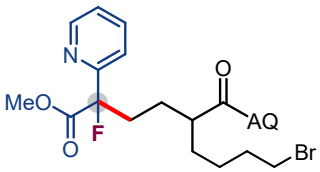
2H), 8.54 (dd, *J* = 11.0, 4.7 Hz, 1H), 8.13 - 8.10 (m, 1H), 7.71 - 7.67 (m, 1H), 7.57 (d, *J* = 7.8 Hz, 1H), 7.52 - 7.39 (m, 3H), 7.24 - 7.16 (m, 1H), 3.74 (d, *J* = 3.9 Hz, 3H), 2.69 - 2.41 (m, 3H), 1.96 - 1.82 (m, 1H), 1.80 - 1.53 (m, 3H), 1.40 - 1.24 (m, 4H), 0.86 - 0.81 (m, 3H); **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 174.1, 174.0 (isomers), 169.6 (d, *J* = 26.2 Hz), 169.6 (d, *J* = 26.6 Hz) (isomers), 156.7 (d, *J* = 26.8 Hz), 156.6 (d, *J* = 26.8 Hz) (isomers), 149.2, 148.2, 138.4, 138.4 (isomers), 137.0, 136.4, 134.4, 134.4 (isomers), 127.9, 127.4, 123.5, 123.5 (isomers), 121.6, 121.5, 120.1 (d, *J* = 8.6 Hz), 120.0 (d, *J* = 8.5 Hz) (isomers), 116.6, 97.9 (d, *J* = 186.3 Hz), 97.9 (d, *J* = 186.8 Hz) (isomers), 53.0, 48.8, 48.8 (isomers), 34.2 (d, *J* = 19.5 Hz), 34.0 (d, *J* = 19.3 Hz) (isomers), 32.7, 32.7 (isomers), 29.6, 29.6 (isomers), 26.4 (d, *J* = 3.0 Hz), 26.4 (d, *J* = 2.9 Hz) (isomers), 22.7, 22.7 (isomers), 13.9; **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -163.87 (s, 1F), -165.05 (s, 1F) (isomers); **FT-IR** (ATR): 3351, 2929, 1749, 1682, 1521, 1484, 791, 753 cm^{-1}; **HRMS** (ESI^{+}, m/z): calcd for $C_{25}H_{29}FN_3O_3^{+}$ $[M+H]^{+}$: 438.2188, found: 438.2179.



3af

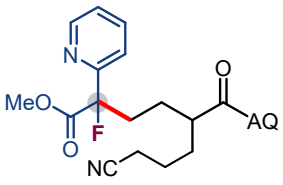
Methyl-2-fluoro-2-(pyridin-2-yl)-5-(quinolin-8-ylcarbamoyl)non-8-enoate (3af): 67.1 mg, 77% yield, R_f = 0.4 (EtOAc/PE = 1/4), colorless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.85 (d, *J* = 6.6 Hz, 1H), 8.85 - 8.72 (m, 2H), 8.61 - 8.45 (m, 1H), 8.13 (dt, *J* = 8.3, 2.1 Hz, 1H), 7.70 (t, *J* = 7.4 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.54 - 7.40 (m, 3H), 7.25 - 7.16 (m, 1H), 5.83 - 5.71 (m, 1H), 5.13 - 4.85 (m, 2H), 3.74 (d, *J* = 3.0 Hz, 3H), 2.67 - 2.40 (m, 3H), 2.22 - 2.04 (m, 2H), 1.97 - 1.83 (m,2H), 1.73 - 1.59 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 173.8, 173.7 (isomers), 169.6 (d, *J* = 26.3 Hz), 156.6 (d, *J* = 26.9 Hz), 156.6 (d, *J* = 26.8 Hz) (isomers), 149.2 (d, *J* = 2.2 Hz), 148.1, 138.3, 137.8, 137.0, 136.4, 134.3, 134.3 (isomers), 127.9, 127.4, 123.5, 123.5 (isomers), 121.6, 121.6, 120.1 (d, *J* = 8.5 Hz), 120.0 (d, *J* = 8.5 Hz) (isomers), 116.7, 115.5, 115.5 (isomers), 97.9 (d, *J* = 186.3 Hz), 97.8 (d, *J* = 186.8 Hz) (isomers), 53.0, 47.9, 34.1 (d, *J* = 20.5 Hz), 33.9 (d, *J* = 20.6 Hz) (isomers), 41.0, 31.9 (isomers), 31.5, 26.3 (d, *J* = 3.0 Hz); **^{19}F NMR** (376 MHz,

Chloroform-*d*) δ -164.05 (s, 1F), -165.09 (s, 1F) (isomers); **FT-IR** (ATR): 3350, 2924, 1748, 1682, 1521, 1484, 791, 753 cm^{-1}; **HRMS** (ESI^+, m/z): calcd for $C_{25}H_{27}FN_3O_3^+$ $[M+H]^+$: 436.2031, found: 436.2026.



3ag

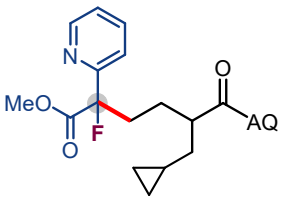
Methyl 9-bromo-2-fluoro-2-(pyridin-2-yl)-5-(quinolin-8-ylcarbamoyl)nonanoate (3ag): 62.4 mg, 80% yield, R_f = 0.4 (EtOAc/PE = 1/5), colorless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.87 (d, *J* = 8.0 Hz, 1H), 8.84 – 8.75 (m, 2H), 8.59 – 8.55 (m, 1H), 8.17 (dt, *J* = 8.2, 1.5 Hz, 1H), 7.73 (td, *J* = 7.8, 1.8 Hz, 1H), 7.61 – 7.58 (m, 1H), 7.56 – 7.44 (m, 3H), 7.27 – 7.21 (m, 1H), 3.76 (d, *J* = 3.0 Hz, 3H), 3.53 – 3.29 (m, 2H), 2.61 – 2.44 m, 3H), 1.94 – 1.76 (m, 4H), 1.68 – 1.46 (m, 4H). **^{13}C{^{1}H}** (101 MHz, Chloroform-*d*) δ 173.7, 173.6 (isomers), 169.6 (d, *J* = 26.6 Hz), 156.6 (d, *J* = 27.1 Hz), 156.5 (d, *J* = 27.1 Hz) (isomers), 149.2, 149.2 (isomers), 148.2, 148.2 (isomers), 138.3, 138.3 (isomers), 137.1, 136.5, 136.5 (isomers), 134.3, 134.2 (isomers), 128.0, 127.4, 123.6, 123.5 (isomers), 121.6, 120.2 (d, *J* = 8.6 Hz), 120.0 (d, *J* = 8.7 Hz) (isomers), 116.8, 116.8 (isomers), 97.9 (d, *J* = 188.3 Hz), 97.8 (d, *J* = 188.8 Hz) (isomers), 53.0, 48.5, 48.5 (isomers), 44.7, 34.1 (d, *J* = 19.1 Hz), 33.9 (d, *J* = 19.0 Hz) (isomers), 32.8, 32.8 (isomers), 32.6, 32.6 (isomers), 32.1, 32.1 (isomers), 32.0, 32.0 (isomers), 26.4, 26.4 (isomers), 26.1, 26.1 (isomers), 24.8, 24.8 (isomers); **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -164.18, (s, 1F), -165.18 (s, 1F) (isomers); **FT-IR** (ATR): 3348, 2935, 1748, 1682, 1522, 1485, 1425, 1323, 1259, 1164, 827, 792, 754, 732 cm^{-1}; **HRMS** (ESI^+, m/z): calcd for $C_{25}H_{28}BrFN_3O_3^+$ $[M+H]^+$: 516.1293, found: 516.1289.



3ah

Methyl 8-cyano-2-fluoro-2-(pyridin-2-yl)-5-(quinolin-8-ylcarbamoyl)octanoate (3ah): 82.4 mg, 92% yield, R_f = 0.4 (EtOAc/PE = 1/3), colorless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.90 (d, *J* = 8.0 Hz, 1H), 8.82 – 8.80 (m, 1H), 8.79 – 8.75 m, 1H), 8.60 – 8.54 (m, 1H), 8.18 – 8.15 m, 1H), 7.73 (td, *J* = 7.8, 1.8 Hz,

1H), 7.61 – 7.58 (m, 1H), 7.55 – 7.50 (m, 2H), 7.48 – 7.45 (m, 1H), 7.27 – 7.21 (m, 1H), 3.76 (d, *J* = 2.2 Hz, 3H), 2.64 – 2.49 (m, 3H), 2.39 – 2.31 (m, 2H), 1.98 – 1.87 (m, 2H), 1.79 – 1.61 (m, 4H); **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 172.9, 172.8 (isomers), 169.5 (d, *J* = 26.5 Hz), 156.5 (d, *J* = 27.2 Hz), 156.4 (d, *J* = 27.0 Hz) (isomers), 149.2, 148.3, 138.4, 137.1, 136.4, 134.1, 134.1 (isomers), 127.9, 127.3, 123.6, 123.6 (isomers), 121.9, 121.7, 120.1 (d, *J* = 8.7 Hz), 120.0 (d, *J* = 8.5 Hz) (isomers), 119.4, 116.7, 97.8 (d, *J* = 188.1 Hz), 97.8 (d, *J* = 188.9 Hz) (isomers), 53.1, 48.0, 34.0, 33.8 (d, *J* = 21.1 Hz), 33.7 (d, *J* = 20.7 Hz) (isomers), 31.8, 31.7 (isomers), 26.5 (d, *J* = 2.9 Hz), 26.4 (d, *J* = 2.9 Hz) (isomers), 23.4, 17.2; **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -164.28, (s, 1F), -165.08 (s, 1F) (isomers); **FT-IR** (ATR): 3343, 2951, 1748, 1682, 1524, 1485, 1425, 1263, 792 cm^{-1}; **HRMS** (ESI^{+}, m/z): calcd for $C_{25}H_{26}FN_4O_3^+$ $[M+H]^+$: 449.1983, found: 449.1988.

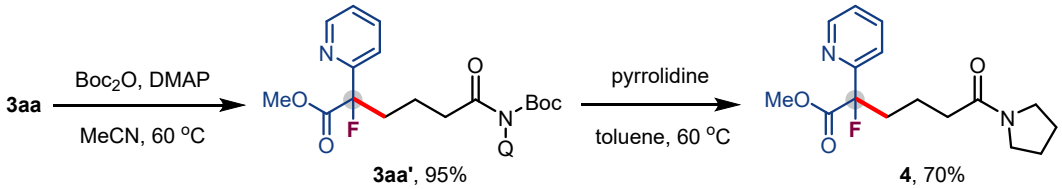


3ai

Methyl 5-(cyclopropylmethyl)-2-fluoro-6-oxo-2-(pyridin-2-yl)-6-(quinolin-8-ylamino)hexanoate (3ai): 71.3 mg, 82% yield, R_f = 0.4 (EtOAc/PE = 1/5), colorless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.84 (d, *J* = 6.3 Hz, 1H), 8.77 – 8.69 (m, 2H), 8.52 – 8.45 (m, 1H), 8.08 – 8.05 (m, 1H), 7.67 – 7.62 (m, 1H), 7.54 – 7.51 (m, 1H), 7.48 – 7.39 (m, 2H), 7.37 (ddd, *J* = 8.3, 4.2, 1.7 Hz, 1H), 7.18 – 7.13 (m, 1H), 3.68 (d, *J* = 2.2 Hz, 3H), 2.58 – 2.39 (m, 3H), 1.91 – 1.81 (m, 1H), 1.70 – 1.54 (m, 2H), 1.43 – 1.33 (m, 1H), 0.76 – (-0.05) (m, 1H); **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 174.0, 173.9 (isomers), 169.6 (d, *J* = 26.5 Hz), 169.6 (d, *J* = 26.9 Hz) (isomers), 156.7 (d, *J* = 27.0 Hz), 156.6 (d, *J* = 27.1 Hz) (isomers), 149.2, 148.2, 138.4, 138.4 (isomers), 137.0, 137.0 (isomers), 136.3, 134.5, 134.5 (isomers), 127.9, 127.9 (isomers), 127.4, 127.4 (isomers), 123.5, 123.5 (isomers), 121.6, 121.41, 120.1 (d, *J* = 8.6 Hz), 120.0 (d, *J* = 8.6 Hz) (isomers), 116.5, 53.0, 49.3, 49.2 (isomers), 38.1, 38.1 (isomers), 34.2 (d, *J* = 20.9 Hz), 34.0 (d, *J* = 20.9 Hz) (isomers), 26.1 (d, *J* = 2.6 Hz), 26.1 (d, *J* = 2.6 Hz) (isomers), 9.2, 4.8, 4.8 (isomers), 4.3, 4.3 (isomers); **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -163.99, (s, 1F), -165.17 (s, 1F) (isomers); **FT-IR** (ATR): 3352,

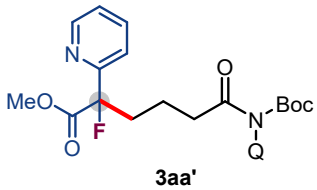
2928, 1749, 1683, 1524, 1485, 1425, 1323, 1262, 905, 729 cm^{-1}; **HRMS** (ESI^+, m/z): calcd for $C_{25}H_{26}FN_3O_3Na^+$ $[M+Na]^+$: 458.1850, found: 458.1843.

3. General Procedure for the Preparation of 4



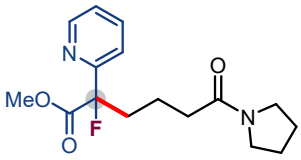
To an 8-mL scintillation vial equipped with a Teflon-coated magnetic stir bar was added **3aa** (38.0 mg, 0.1 mmol), Boc_2O (44 mg, 0.2 mmol) and DMAP (12.2 mg, 0.01 mmol) in CH_3CN (1 mL). The vial was sealed with a screw-top septum cap and placed in an oil bath that was preheated to 60 °C. After a time period of 6 h, the reaction vial was allowed cooled to room temperature, and the reaction mixture was dilute with 15 mL ethyl acetate and wash with saturated salt water (3 × 30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash column chromatography (EtOAc/PE = 1/10-1/3) to give **3aa'**.

To an 8-mL scintillation vial equipped with a Teflon-coated magnetic stir bar was added **3aa'** (48.0 mg, 0.1 mmol) in toluene (1 mL) was added pyrrolidine (11 mg, 0.15 mmol) in one portion at 40 °C under N_2 atmosphere. After a time period of 8 h, the reaction vial was allowed cooled to room temperature, and the reaction mixture was dilute with 15 mL ethyl acetate and wash with saturated salt water (3 × 30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash column chromatography (EtOAc/PE = 1/10-1/5) to give **4**.



Methyl-6-((*tert*-butoxycarbonyl)(quinolin-8-yl)amino)-2-fluoro-6-oxo-2-(pyridin-2-yl)hexanoate (3aa'): 91.5 mg, 95% yield, R_f = 0.4 (EtOAc/PE = 1/7), yellow solid. **M.p.** = 124.6 - 126.3 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.82

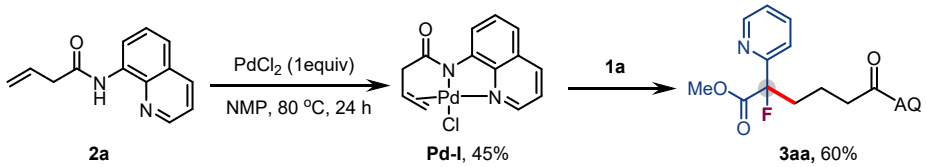
(dd, J = 4.2, 1.7 Hz, 1H), 8.56 (d, J = 4.8 Hz, 1H), 8.08 (dd, J = 8.3, 1.7 Hz, 1H), 7.78 - 7.45 (m, 5H), 7.31 (dd, J = 8.3, 4.2 Hz, 1H), 7.19 (dd, J = 7.5, 4.8 Hz, 1H), 3.73 (s, 3H), 3.28 - 3.15 (m, 2H), 2.70 - 2.47 (m, 2H), 1.96 - 1.79 (m, 2H), 1.22 (s, 9H); **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 175.6, 169.7 (d, J = 26.3 Hz), 156.8 (d, J = 26.5 Hz), 152.8, 150.3, 149.1 (d, J = 2.0 Hz), 144.0, 136.9, 136.8, 136.0, 128.9, 128.8, 128.0, 126.0, 123.5, 121.5, 120.0 (d, J = 8.2 Hz), 97.9 (d, J = 186.3 Hz), 82.5, 52.8, 37.6, 35.6 (d, J = 21.0 Hz), 27.6, 18.7 (d, J = 3.2 Hz); **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -163.90 (s, 1F); **FT-IR** (ATR): 2978, 1736, 1670, 1253, 1152, 1123, 793, 733 cm^{-1}; **HRMS** (ESI^{+}, m/z): calcd for $C_{26}H_{29}FN_3O_5^{+}$ [M+H]$^{+}$: 482.2086, found: 482.2070.



4

Methyl-2-fluoro-6-oxo-2-(pyridin-2-yl)-6-(pyrrolidin-1-yl)hexanoate (4): 21.6 mg, 70% yield, R_f = 0.4 (EtOAc/PE = 1/5), yellow oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.47 (dd, J = 4.9, 1.7 Hz, 1H), 7.63 (td, J = 7.8, 1.8 Hz, 1H), 7.53 - 7.45 (m, 1H), 7.16 - 7.13 (m, 1H), 3.64 (s, 3H), 3.32 - 3.23 (m, 4H), 2.48 - 2.24 (m, 2H), 2.18 (t, J = 8.1 Hz, 2H), 1.85 - 1.78 (m, 2H), 1.75 - 1.55 (m, 4H); **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 170. 7, 169.6 (d, J = 26.4 Hz), 156.6 (d, J = 26.5 Hz), 149.0 (d, J = 2.0 Hz), 136.9 123.4, 120.0 (d, J = 8.4 Hz), 97.9 (d, J = 186.6 Hz), 52.8, 46.4, 45.5, 35.7 (d, J = 20.8 Hz), 34.3, 26.0, 24.3, 18.5 (d, J = 3.2 Hz); **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -164.25 (s, 1F); **FT-IR** (ATR): 2953, 2874, 1748, 1633, 1433, 1260, 994, 754, 733 cm^{-1}; **HRMS** (ESI^{+}, m/z): calcd for $C_{16}H_{21}FN_2O_3Na^{+}$ [M+Na]$^{+}$: 331.1429, found: 331.1423.

5.Control Experiment



2a **Pd-I**, 45% **3aa**, 60%

To an 8-mL scintillation vial equipped with a Teflon-coated magnetic stir bar was added

$PdCl_2$ (18.0 mg, 0.1 mmol, 1.0 equiv), **2a** (21.2 mg, 0.1 mmol, 1.0 equiv), and NMP (0.2 mL). The vial was sealed with a solid screw cap and stirred at 80°C for 24 h. The reaction vial was allowed cooled to room temperature, and the reaction mixture was dilute with 5 mL ethyl acetate and wash with saturated salt water (3 × 30 mL). The combined organic layers were dried ($MgSO_4$), the solvent was removed in vacuo to leave a brown residue, which upon purification by preparative TLC (3:1 hexane:EtOAc) to provide the desired products **Pd-I**[1] as brown solid (14.3 mg, 45% yield). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.17 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.76 (dd, *J* = 7.9, 1.2 Hz, 1H), 8.37 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.56 - 7.50 (m, 2H), 7.43 (dd, *J* = 8.1, 1.2 Hz, 1H), 6.20 - 6.11 (m, 1H), 5.88 - 5.85 (m, 1H), 5.37 (dt, *J* = 15.6, 1.3 Hz, 1H), 3.67 - 3.60 (m, 1H), 3.28 - 3.22 (m, 1H); **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 178.9, 148.2, 146.9, 146.0, 140.3, 130.2, 129.8, 122.97, 120.9, 120.8, 98.1, 92.9, 40.4. **HRMS** (ESI^+, m/z): calcd for $C_{13}H_{11}N_2OPd$ $[M-Cl]^+$: 314.9912, Found: 314.9906.

To an 8-mL scintillation vial equipped with a Teflon-coated magnetic stir bar were added the **Pd-I** (0.1 mmol), **1a** (0.15 mmol), and NMP (0.2 mL). The vial was sealed with a screw-top septum cap and placed in a heating block that was preheated to 80 °C for 24 h, The reaction vial was allowed cooled to room temperature, and the reaction mixture was dilute with 15 mL ethyl acetate and wash with saturated salt water (3 × 30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash column chromatography (EtOAc/PE = 1/10-1/5) to give **3aa** as yellow oil (22.9 mg, 60% yield).

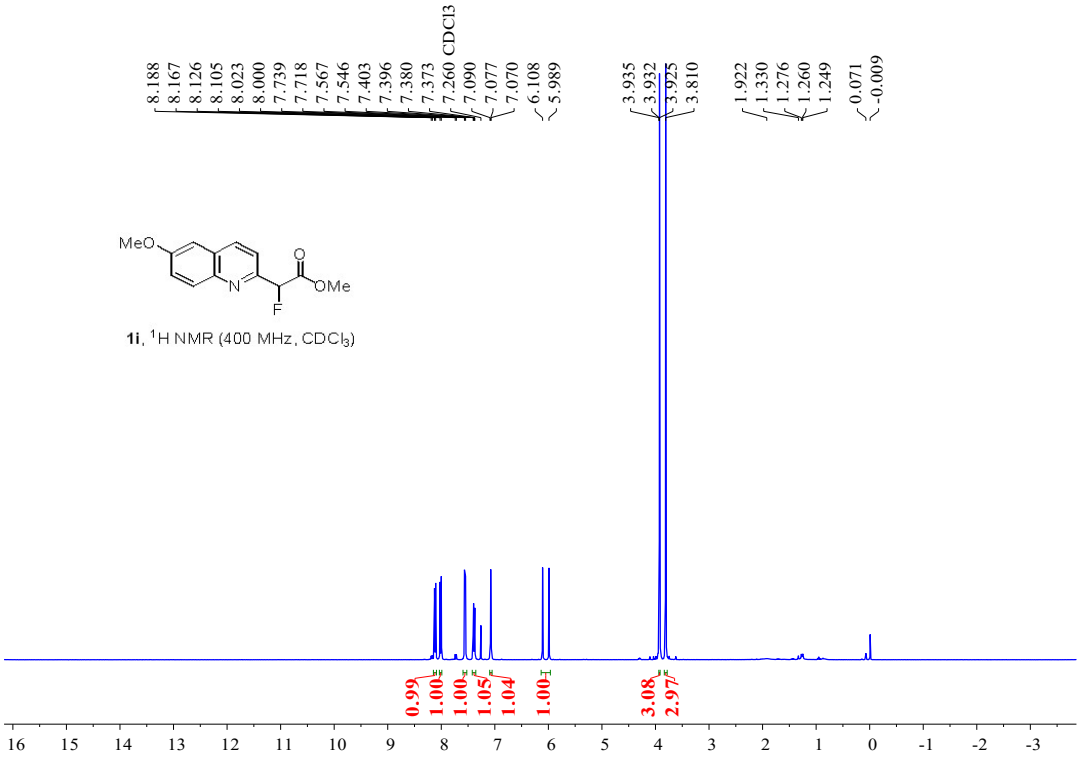
6. Reference

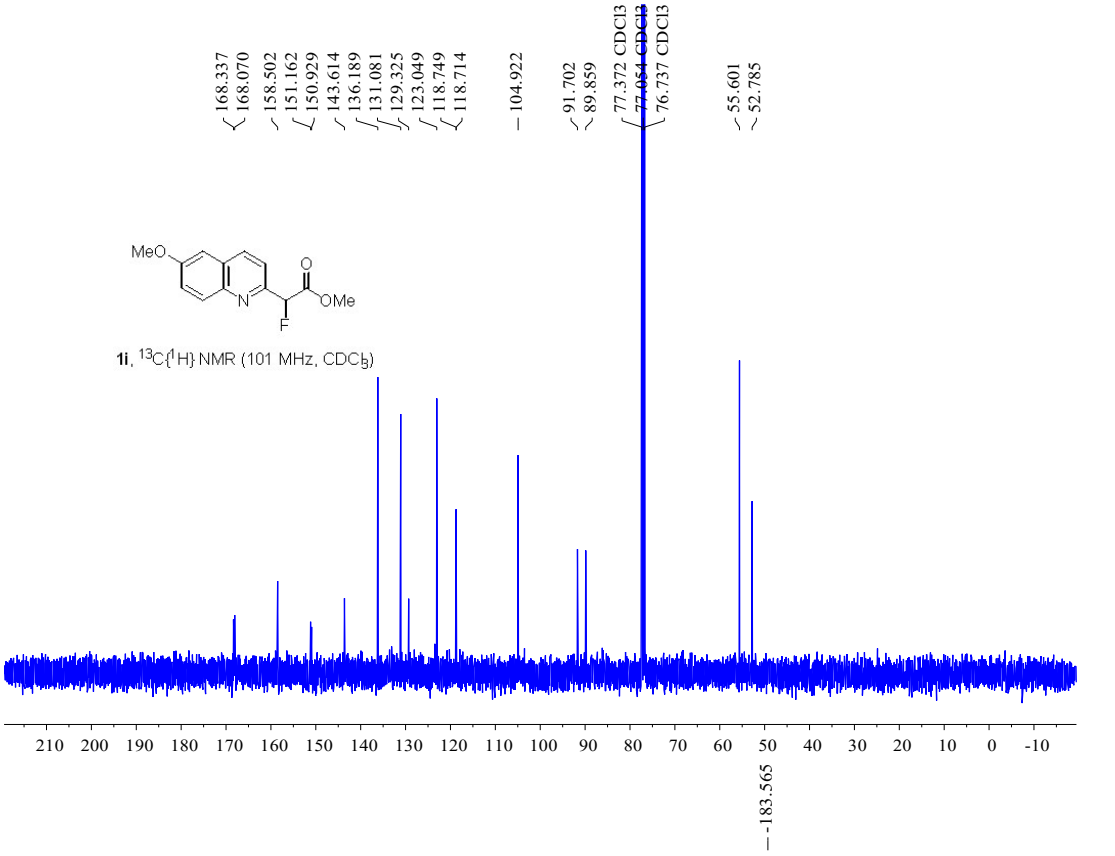
(1) He, Z. T.; Jiang, X.; Hartwig, J. F. Stereodivergent Construction of Tertiary Fluorides in Vicinal Stereogenic Pairs by Allylic Substitution with Iridium and Copper Catalysts. *J. Am. Chem. Soc.*, **2019**, *141*, 13066.

(2) Gurak, Jr. J. A.; Yang, K. S.; Liu, Z.; Engle, K. M. Directed, Regiocontrolled Hydroamination of Unactivated Alkenes via Protodepalladation. *J. Am. Chem. Soc.*, **2016**, *138*, 5805.

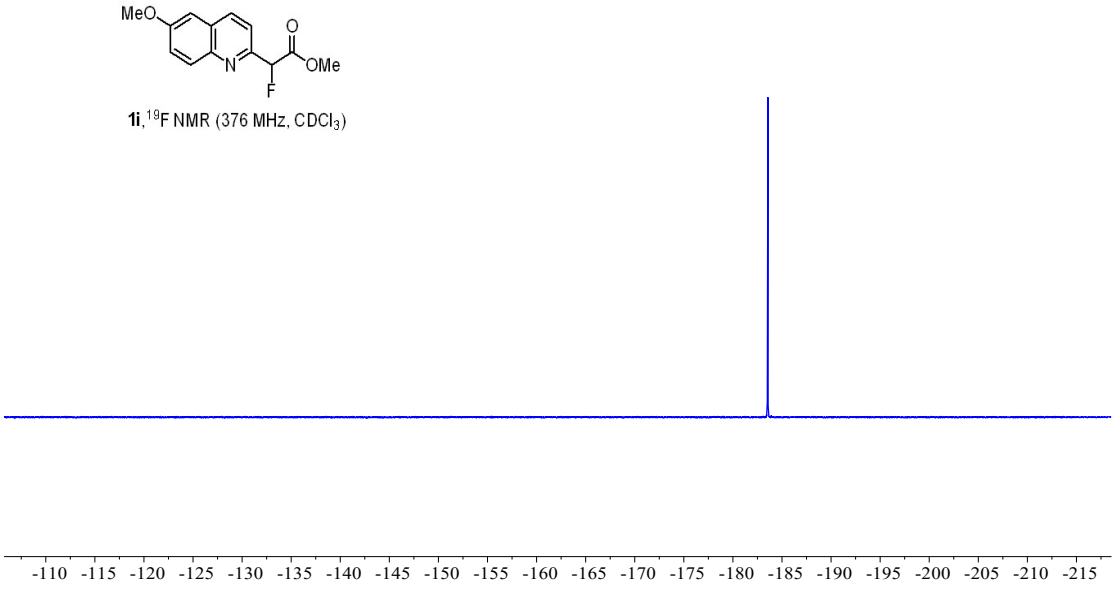
(3) Liu, X. L.; Ji, S. J.; Cai, Z. J. Palladium-catalyzed carbomonofluoromethylation of unactivated alkenes: rapid access to γ-monofluoromethyl carboxylic acid derivatives. *Chem. Commun.*, **2024**, *60*, 730.

7. Copy of NMR spectra

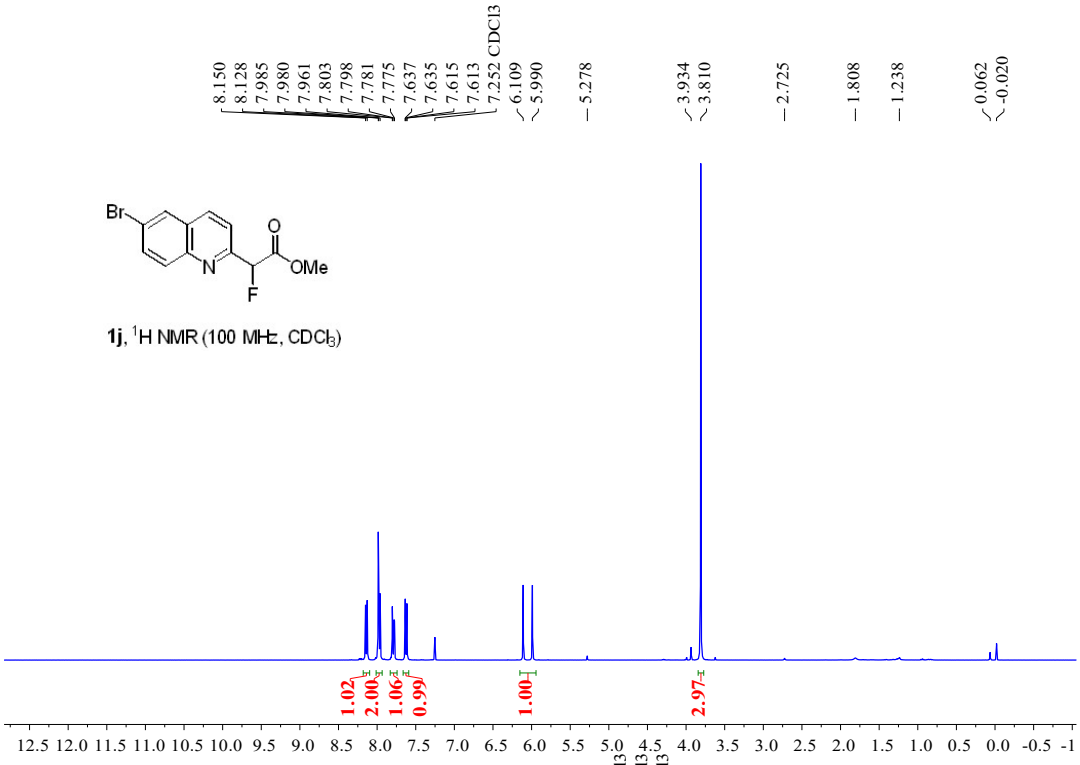




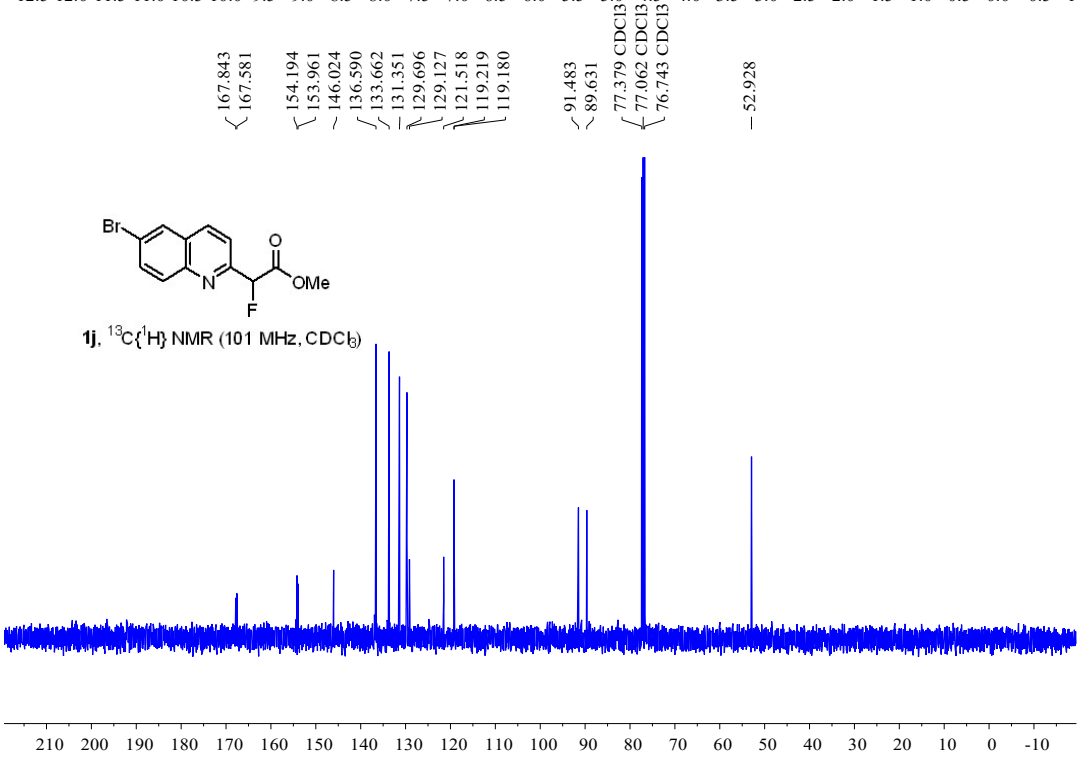
1i, $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)



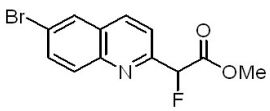
1i, ^{19}F NMR (376 MHz, $CDCl_3$)



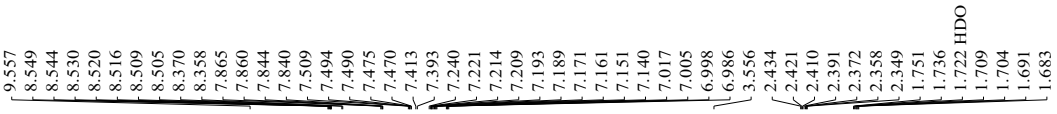
1j, ^{1}H NMR (100 MHz, $CDCl_3$)

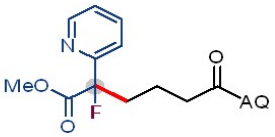


1j, $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)

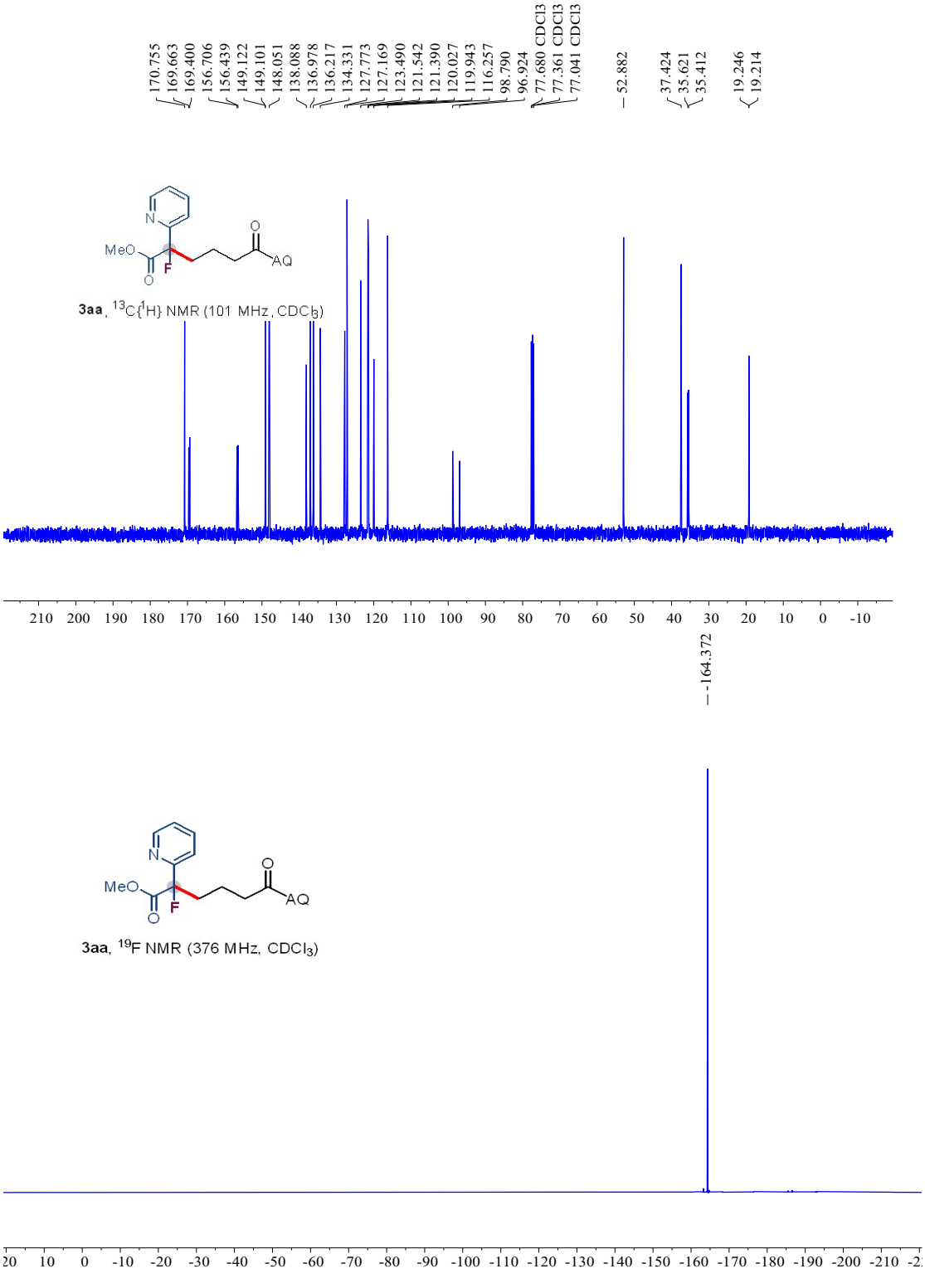


1j,^{19}F NMR (376 MHz, $CDCl_3$)





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


170.755
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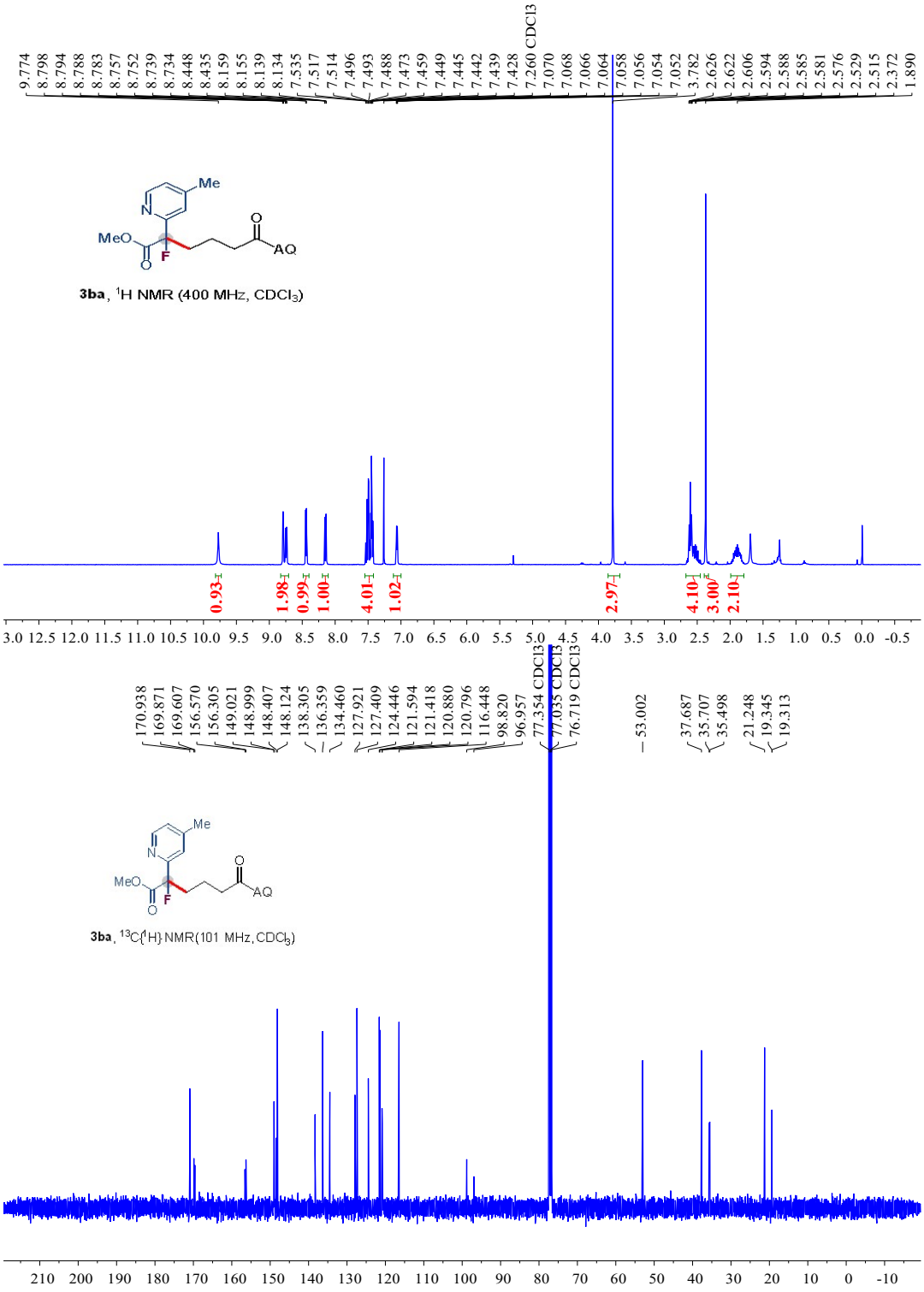
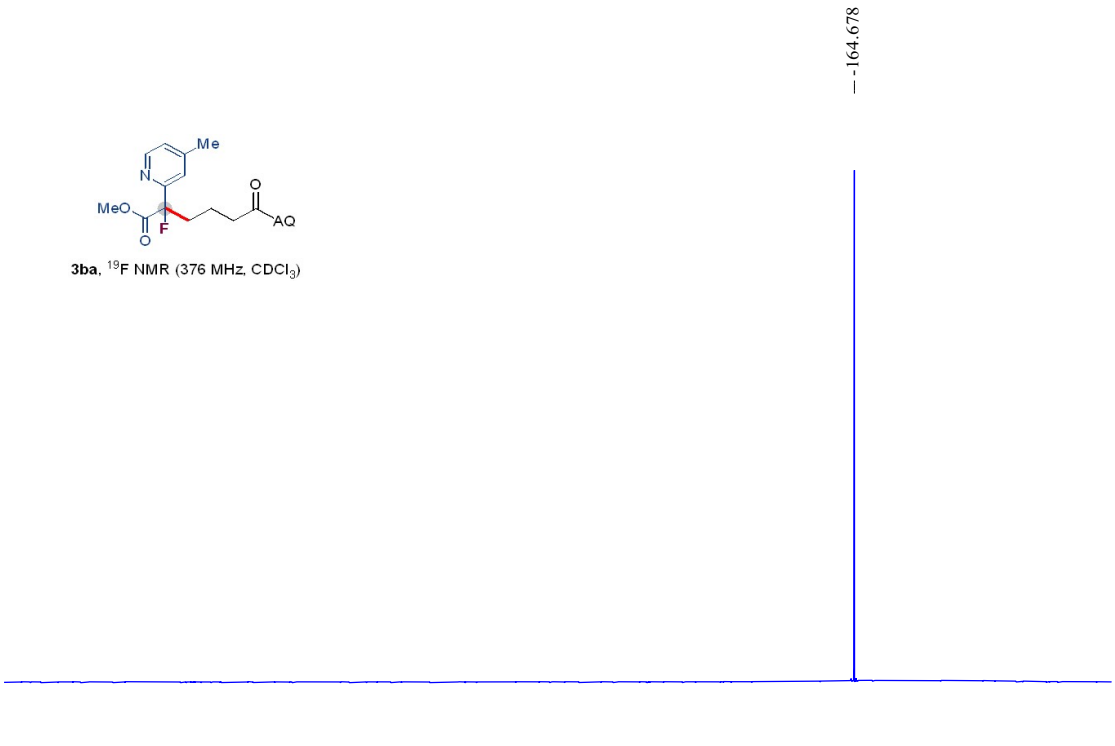
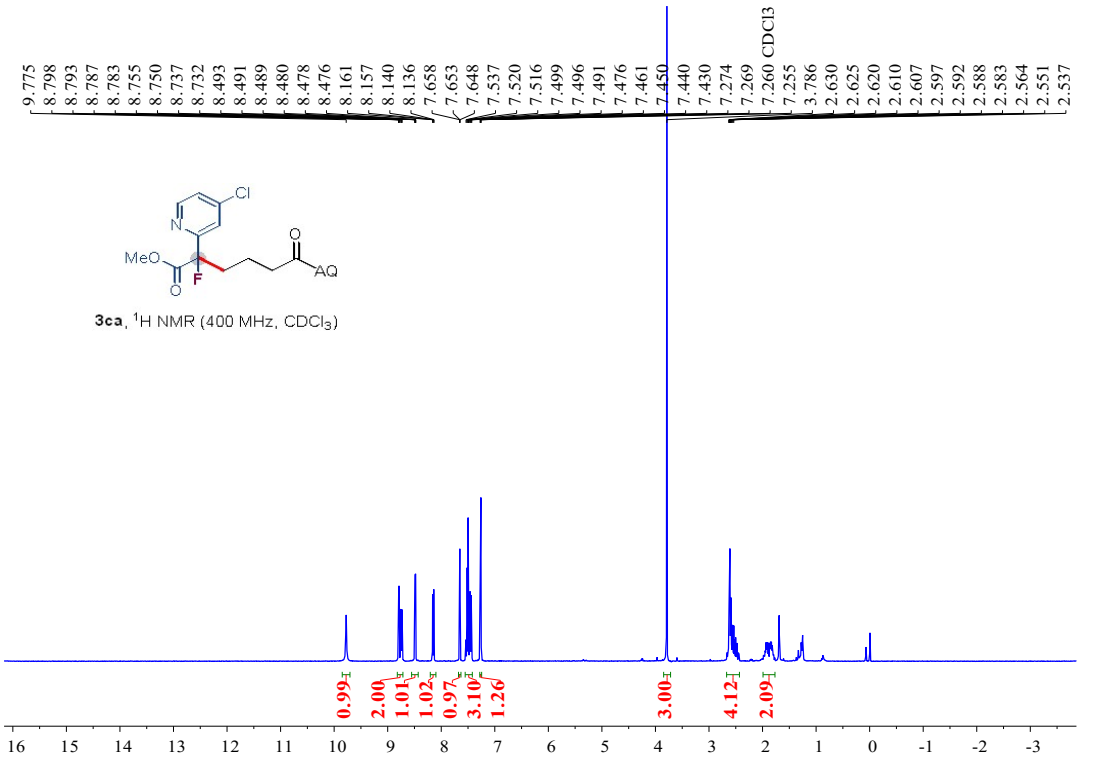
156.706
156.439
149.122
149.101
148.051
138.088
136.978
136.217
134.331
127.773
127.169
123.490
121.542
121.390
120.027
119.943
116.257
98.790
96.924
77.680 CDCl3
77.361 CDCl3
77.041 CDCl3
52.882
37.424
35.621
35.412
19.246
19.214
MeO
F
O
N
AQ
3aa, $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
-164.372
MeO
F
O
N
AQ
3aa, ^{19}F NMR (376 MHz, $CDCl_3$)
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -2

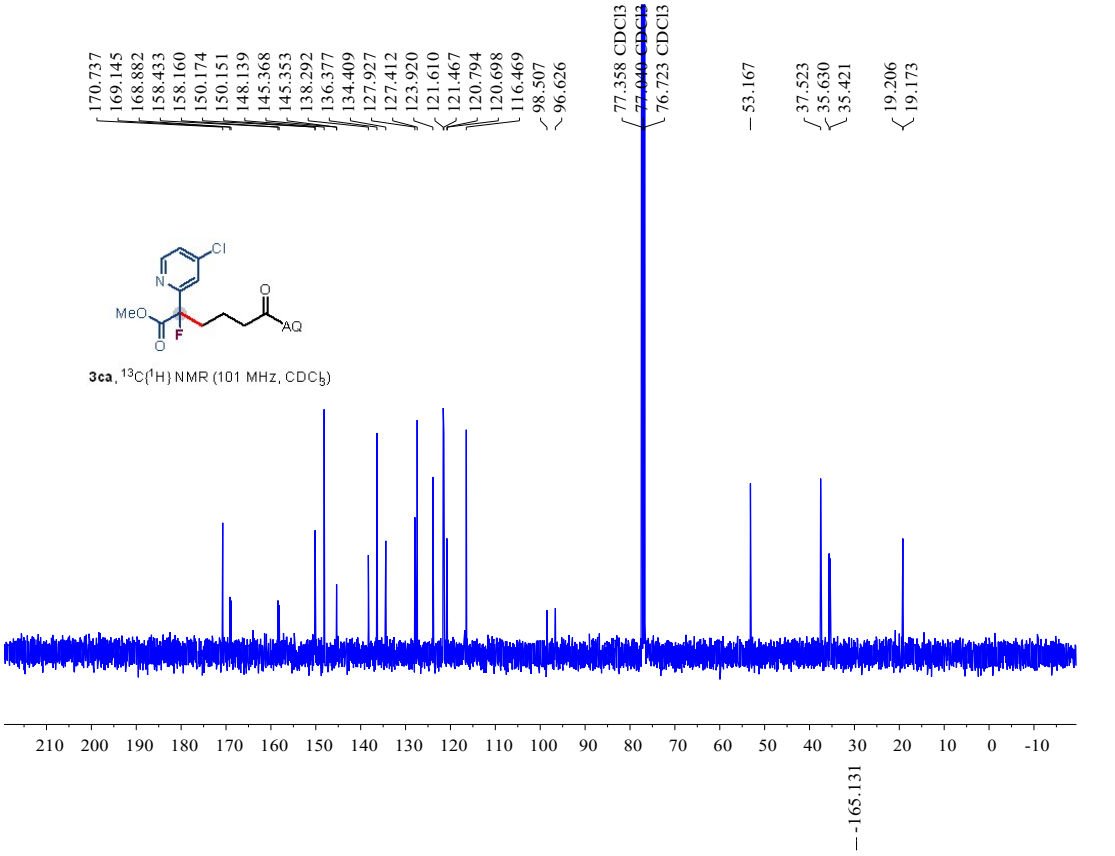

9.774
8.798
8.794
8.788
8.783
8.757
8.752
8.739
8.734
8.448
8.435
8.159
8.155
8.139
8.134
7.535
7.517
7.514
7.496
7.493
7.488
7.473
7.459
7.449
7.445
7.442
7.439
7.428
7.260 CDCl3
7.070
7.068
7.066
7.064
7.058
7.056
7.054
7.052
3.782
2.626
2.622
2.606
2.594
2.588
2.585
2.581
2.576
2.529
2.515
2.372
1.890
Me
N
MeO
O
F
O
AQ
3ba, 1H NMR (400 MHz, CDCl3)
0.93
1.98
0.99
1.00
4.01
1.02
2.97
4.10
3.00
2.10
3.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
170.938
169.871
169.607
156.570
156.305
149.021
148.999
148.407
148.124
138.305
136.359
134.460
127.921
127.409
124.446
121.594
121.418
120.880
120.796
116.448
98.820
96.957
77.354 CDCl3
77.035 CDCl3
76.719 CDCl3
53.002
37.687
35.707
35.498
21.248
19.345
19.313
Me
N
MeO
O
F
O
AQ
3ba, 13C{1H} NMR (101 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10



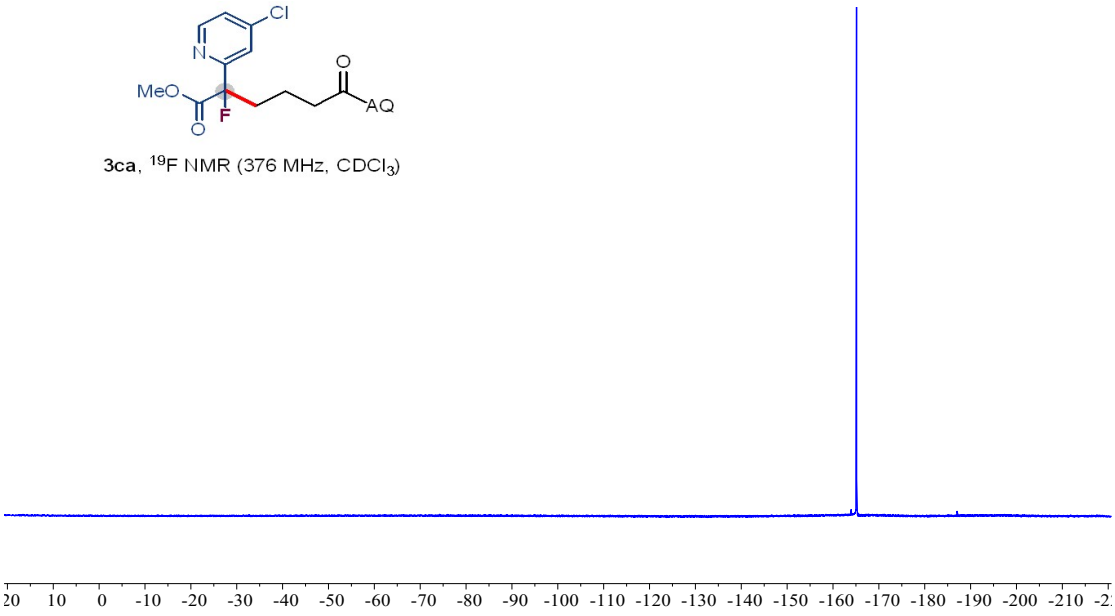
3ba, ^{19}F NMR (376 MHz, $CDCl_3$)



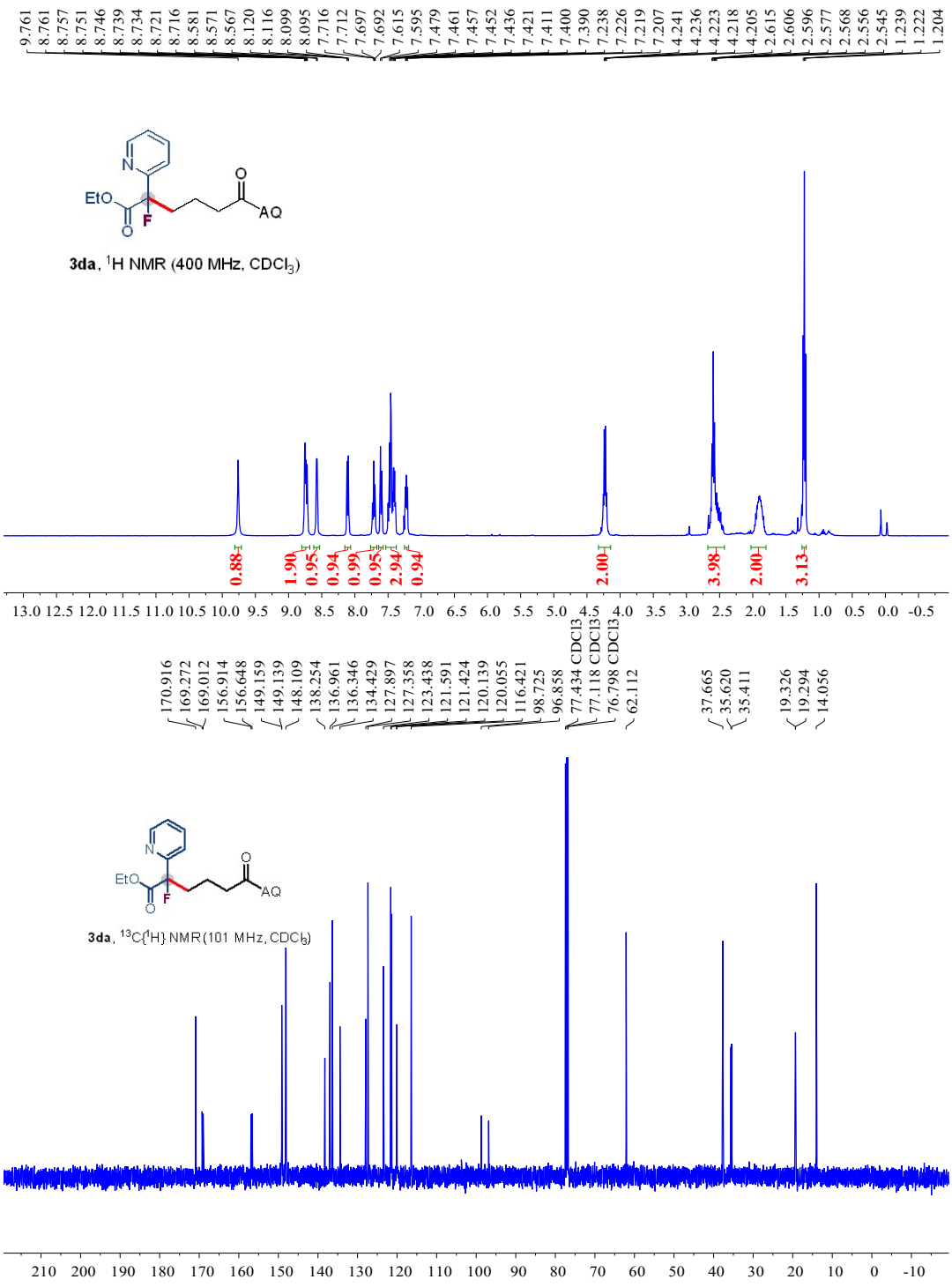
3ca, ^{1}H NMR (400 MHz, $CDCl_3$)

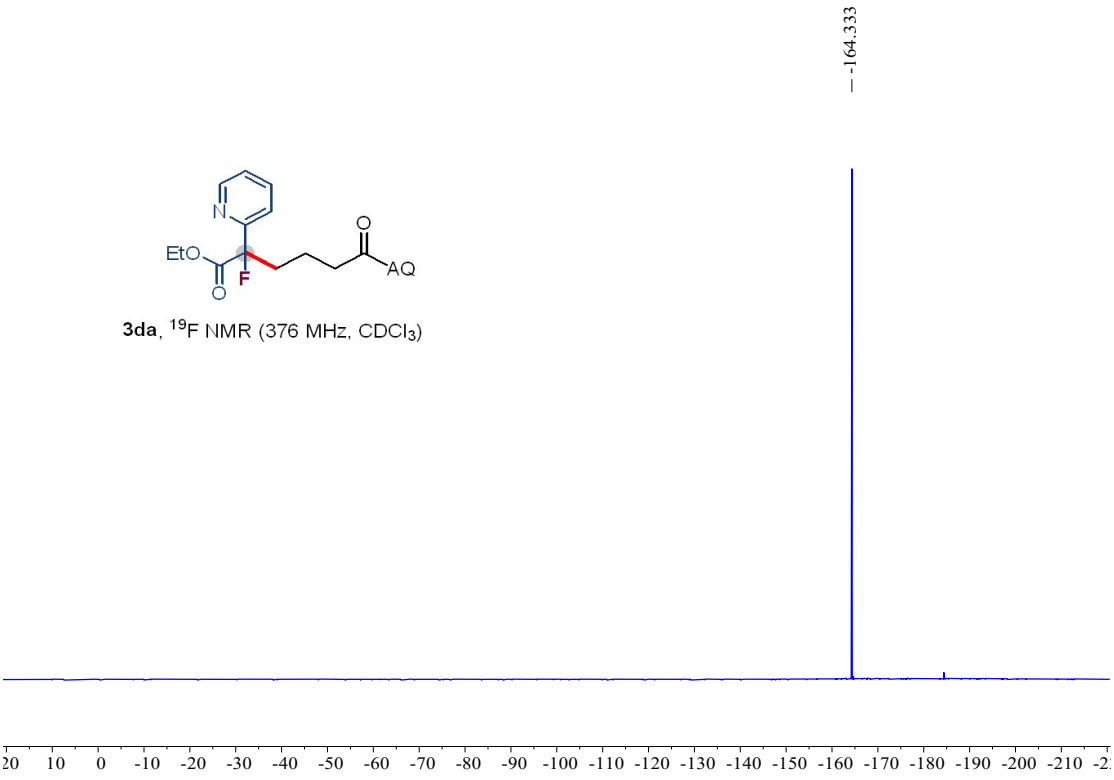


3ca, $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)

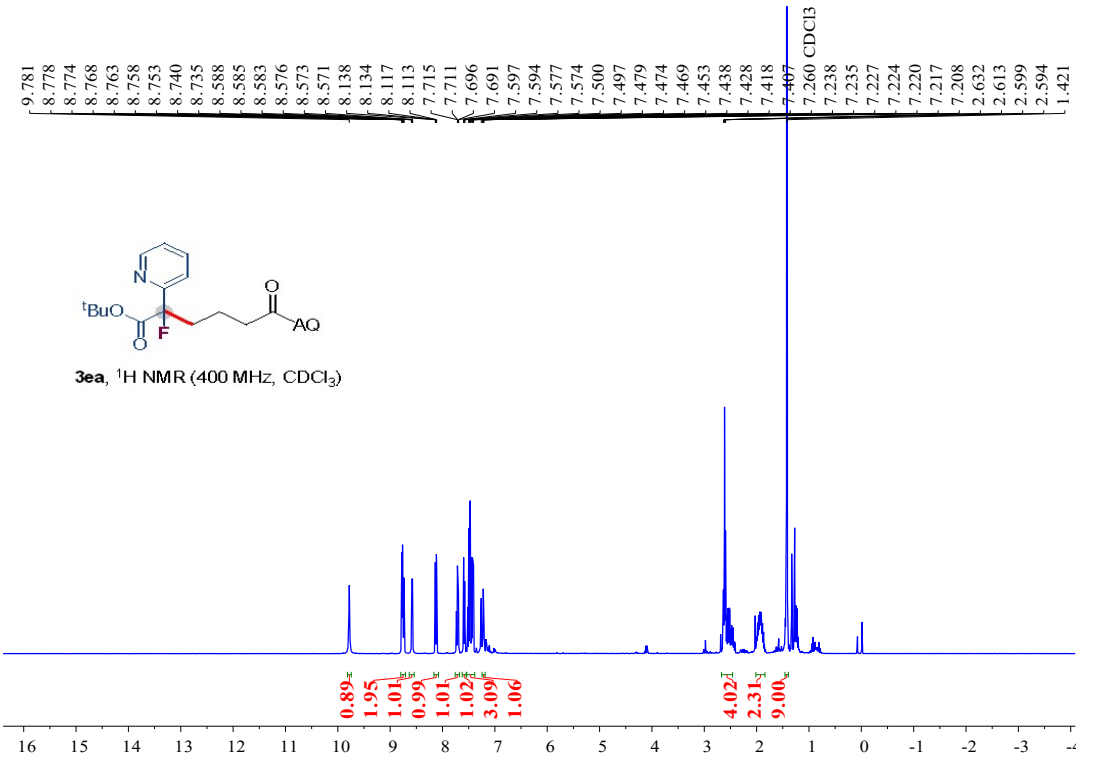


3ca, ^{19}F NMR (376 MHz, $CDCl_3$)

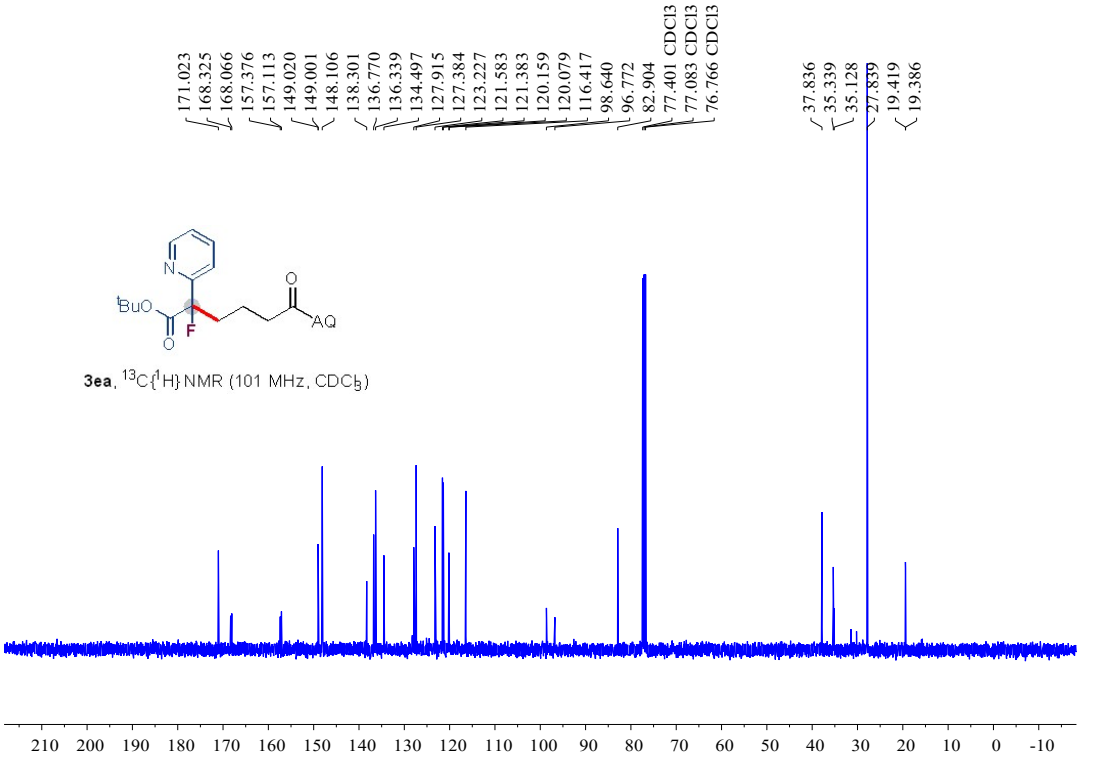

9.761
8.761
8.757
8.751
8.746
8.739
8.734
8.721
8.716
8.581
8.571
8.567
8.120
8.116
8.099
8.095
7.716
7.712
7.697
7.692
7.615
7.595
7.479
7.461
7.457
7.452
7.436
7.421
7.411
7.400
7.390
7.238
7.226
7.219
7.207
4.241
4.236
4.223
4.218
4.205
2.615
2.606
2.596
2.577
2.568
2.556
2.545
1.239
1.222
1.204
EtO
F
O
AQ
3da, ^{1}H NMR (400 MHz, CDCl$_3$)
0.88
1.90
0.95
0.94
0.99
0.95
2.94
0.94
2.00
3.98
2.00
3.13
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
170.916
169.272
169.012
156.914
156.648
149.159
149.139
148.109
138.254
136.961
136.346
134.429
127.897
127.358
123.438
121.591
121.424
120.139
120.055
116.421
98.725
96.858
77.434 CDCl3
77.118 CDCl3
76.798 CDCl3
62.112
37.665
35.620
35.411
19.326
19.294
14.056
3da, ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10



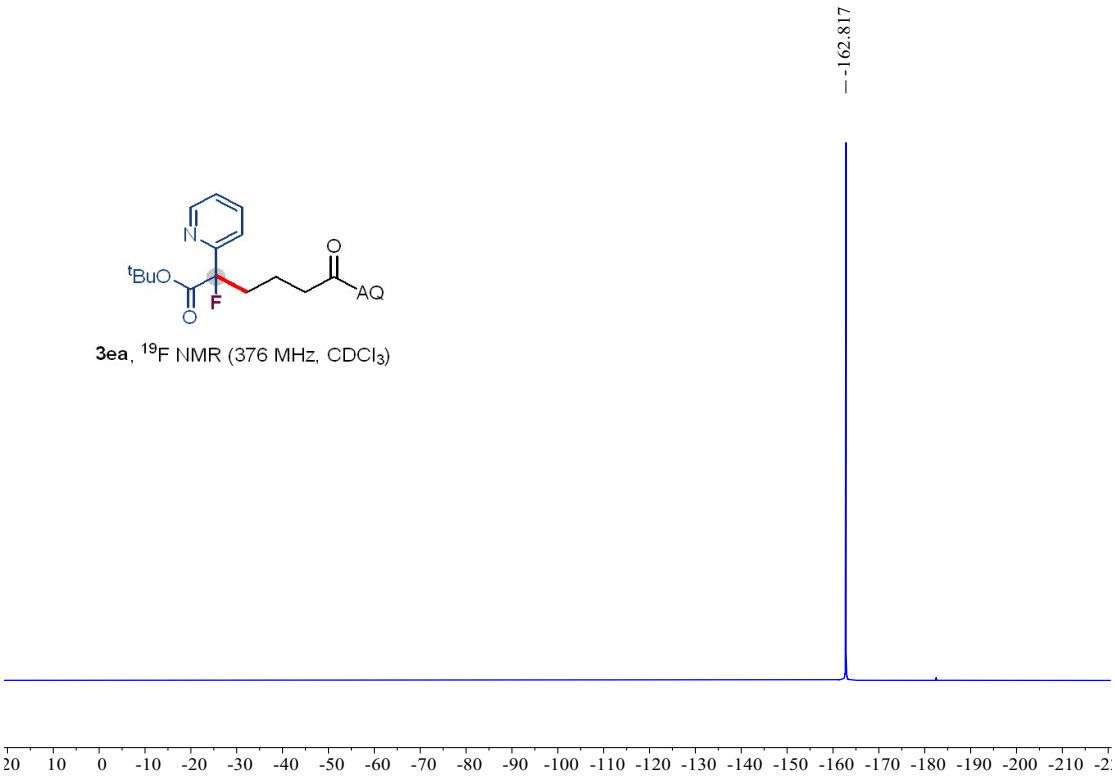
3da, ^{19}F NMR (376 MHz, $CDCl_3$)



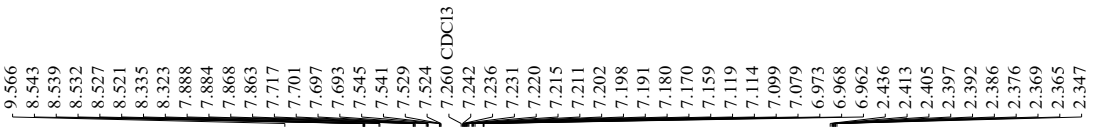
3ea, ^{1}H NMR (400 MHz, $CDCl_3$)

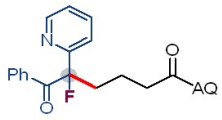


3ea, $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)

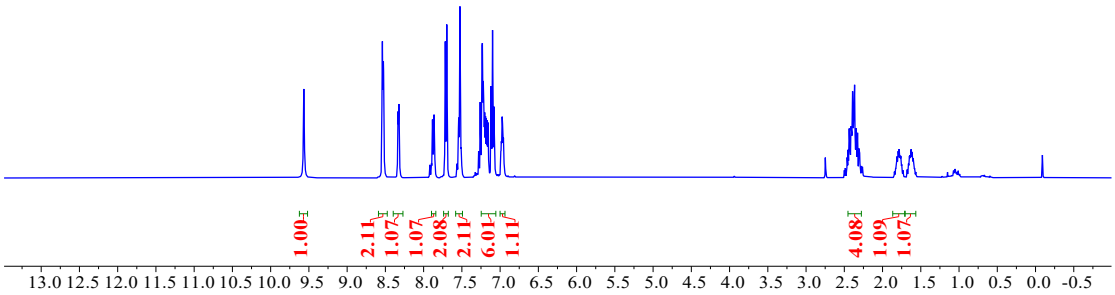


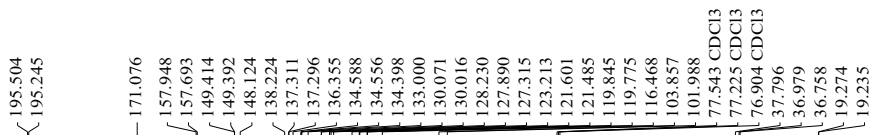
3ea, ^{19}F NMR (376 MHz, $CDCl_3$)

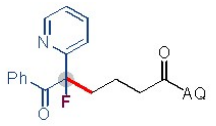




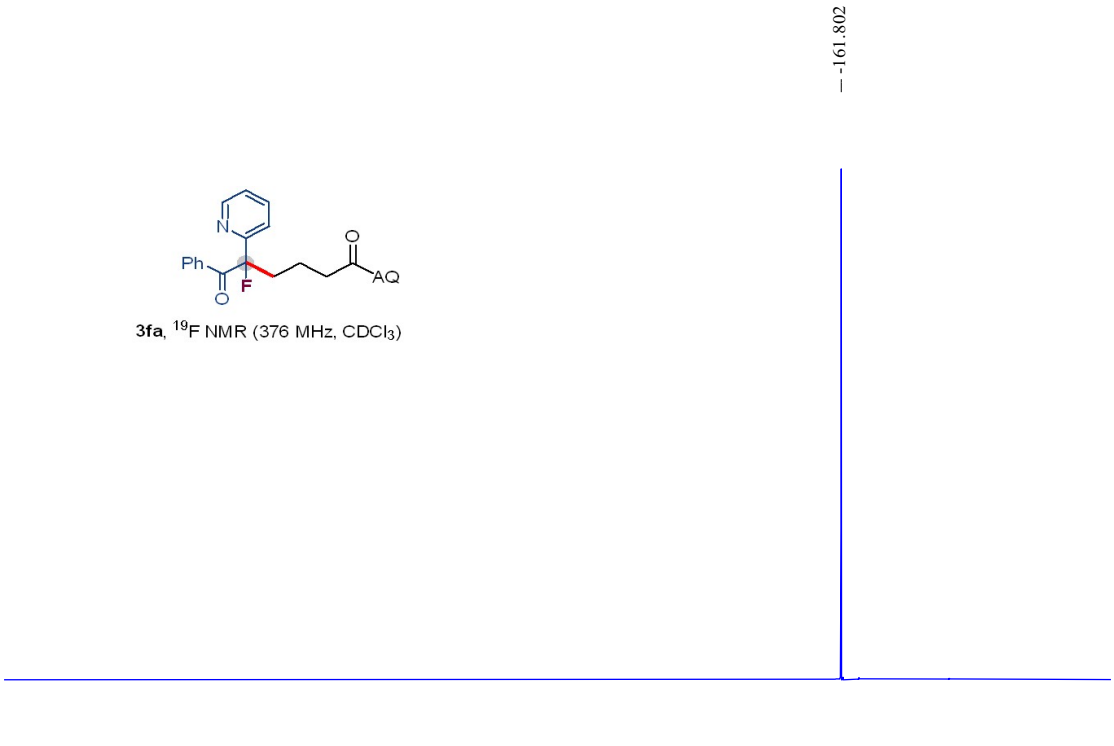
3fa, ^{1}H NMR (400 MHz, $CDCl_3$)



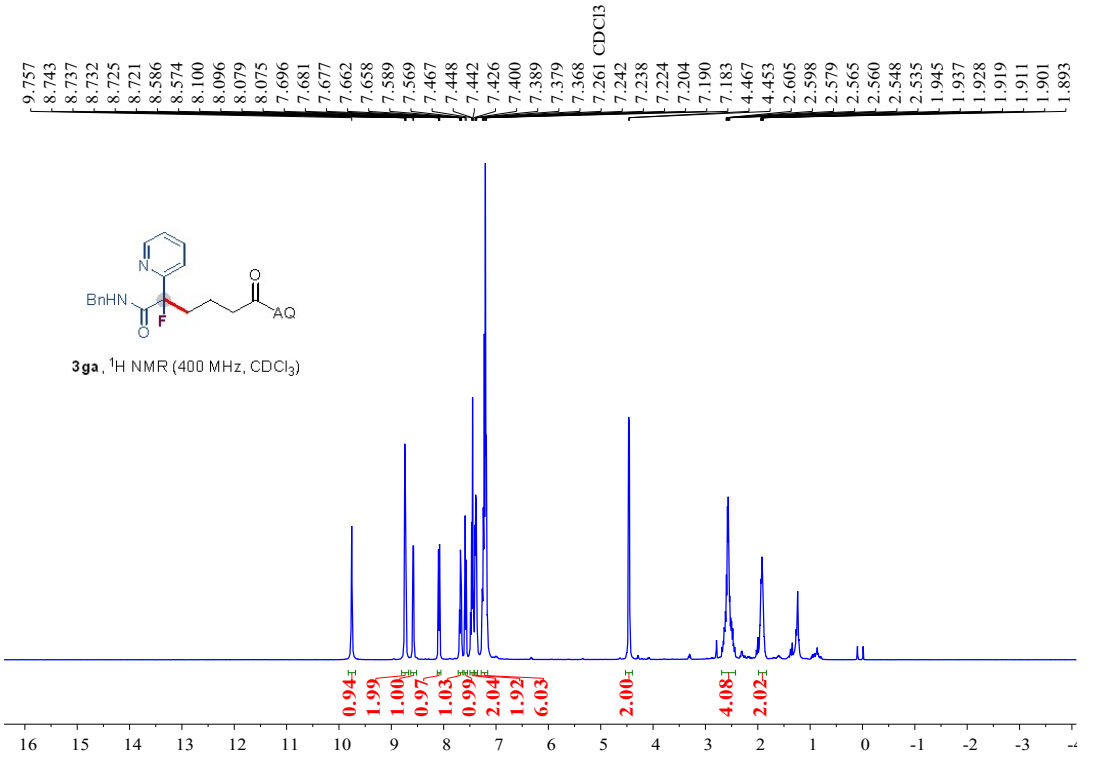




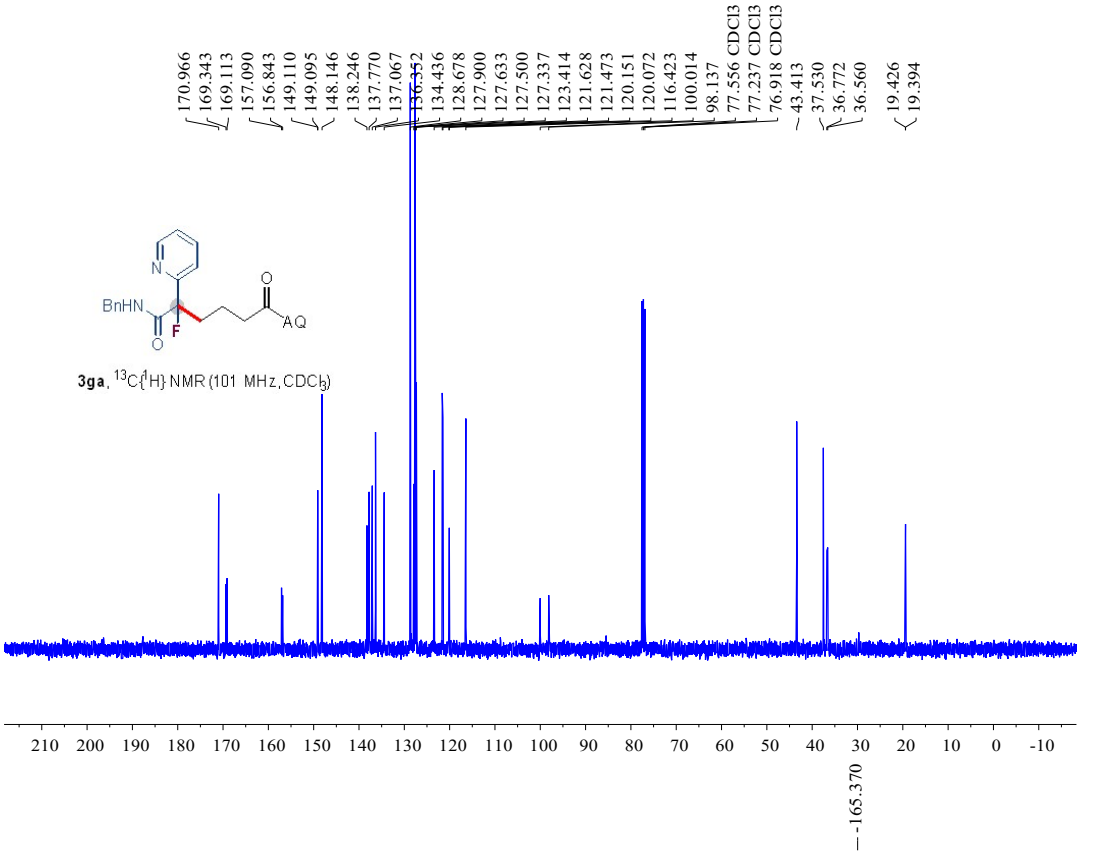
3fa, $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)



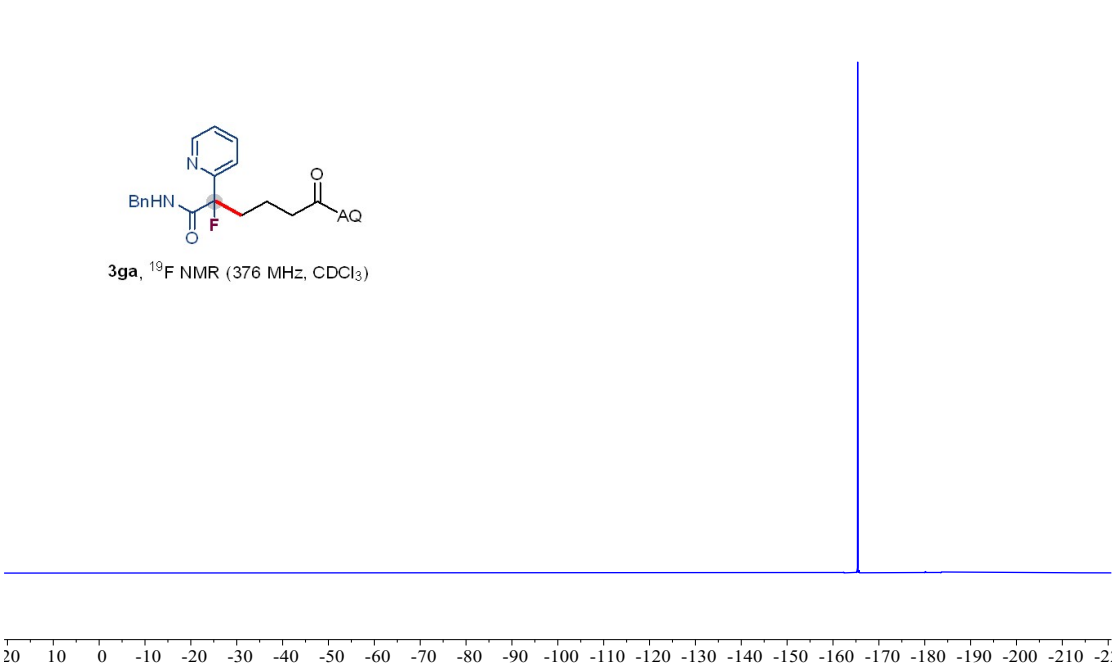
3fa, ^{19}F NMR (376 MHz, $CDCl_3$)



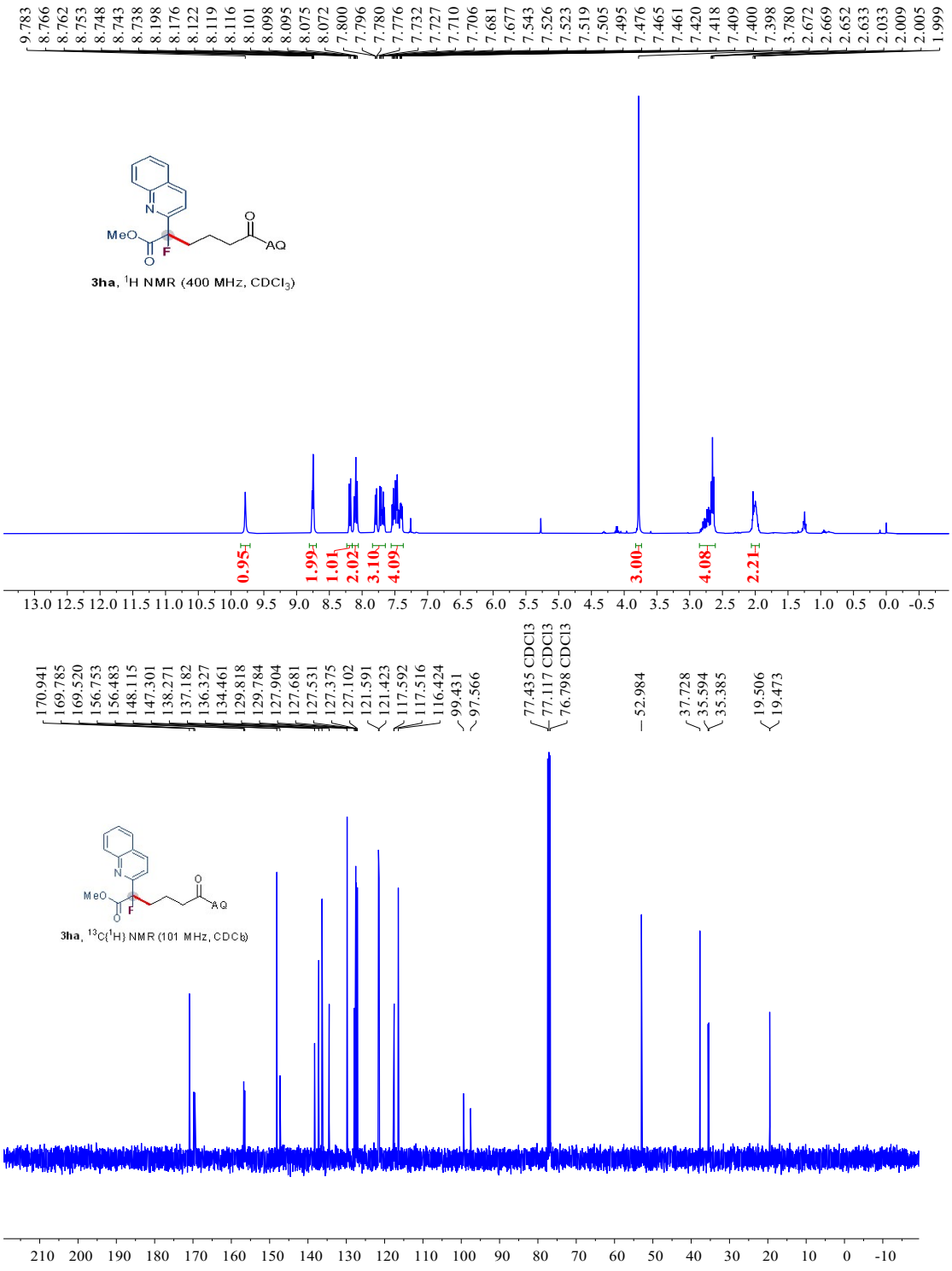
3ga, ^{1}H NMR (400 MHz, $CDCl_3$)

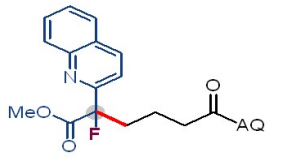


3ga, $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)

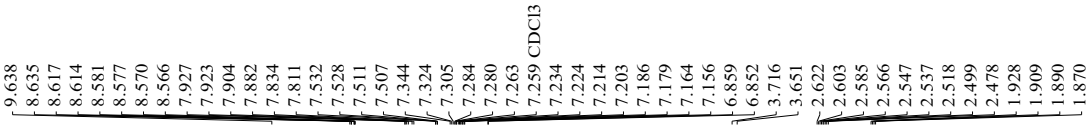


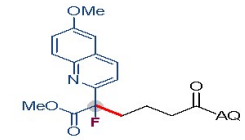
3ga, ^{19}F NMR (376 MHz, $CDCl_3$)


9.783
8.766
8.762
8.753
8.748
8.743
8.738
8.198
8.176
8.122
8.119
8.116
8.101
8.098
8.095
8.075
8.072
7.800
7.796
7.780
7.776
7.732
7.727
7.710
7.706
7.681
7.677
7.543
7.526
7.523
7.519
7.505
7.495
7.476
7.465
7.461
7.420
7.418
7.409
7.400
7.398
3.780
2.672
2.669
2.652
2.633
2.033
2.009
2.005
1.999
MeO
F
O
AQ
3ha, ^{1}H NMR (400 MHz, CDCl$_3$)
0.95
1.99
1.01
2.02
3.10
4.09
3.00
4.08
2.21
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
170.941
169.785
169.520
156.753
156.483
148.115
147.301
138.271
137.182
136.327
134.461
129.818
129.784
127.904
127.681
127.531
127.375
127.102
121.591
121.423
117.592
117.516
116.424
99.431
97.566
77.435 CDCl3
77.117 CDCl3
76.798 CDCl3
52.984
37.728
35.594
35.385
19.506
19.473
3ha, ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

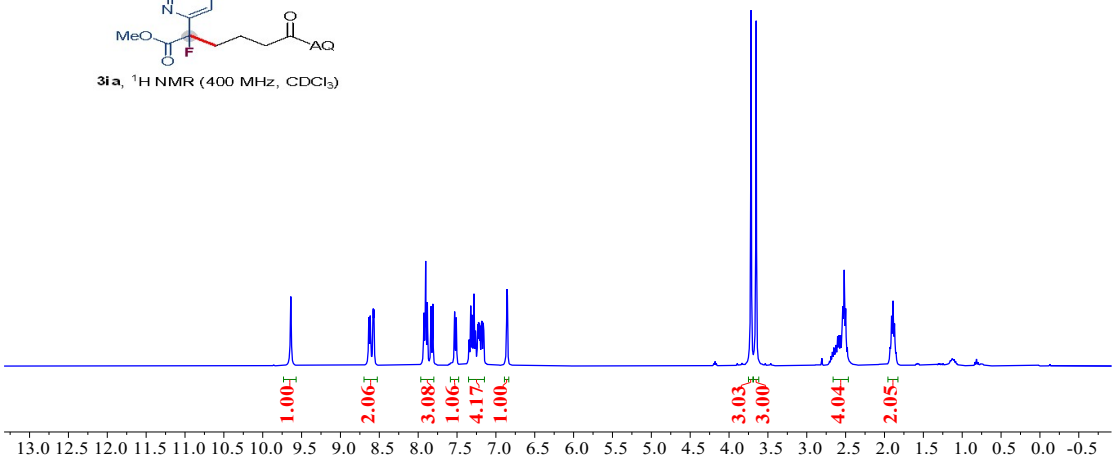


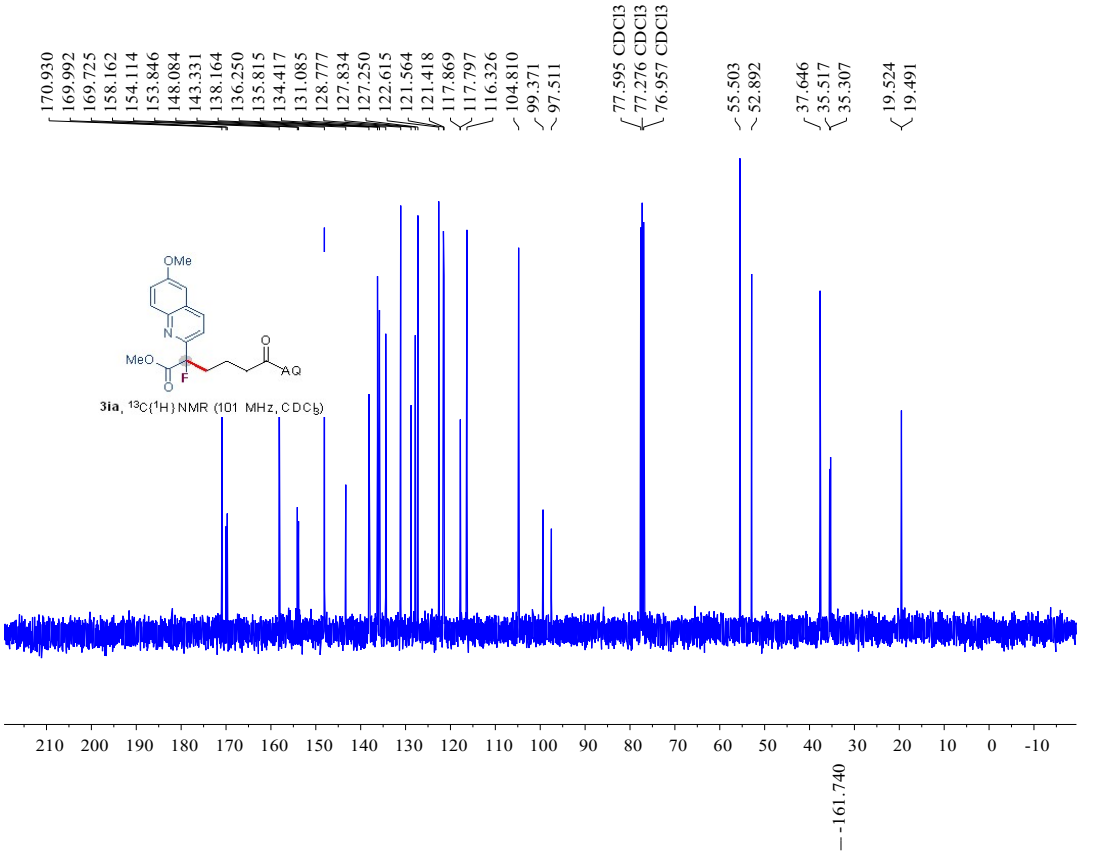
3ha, ^{19}F NMR (376 MHz, $CDCl_3$)



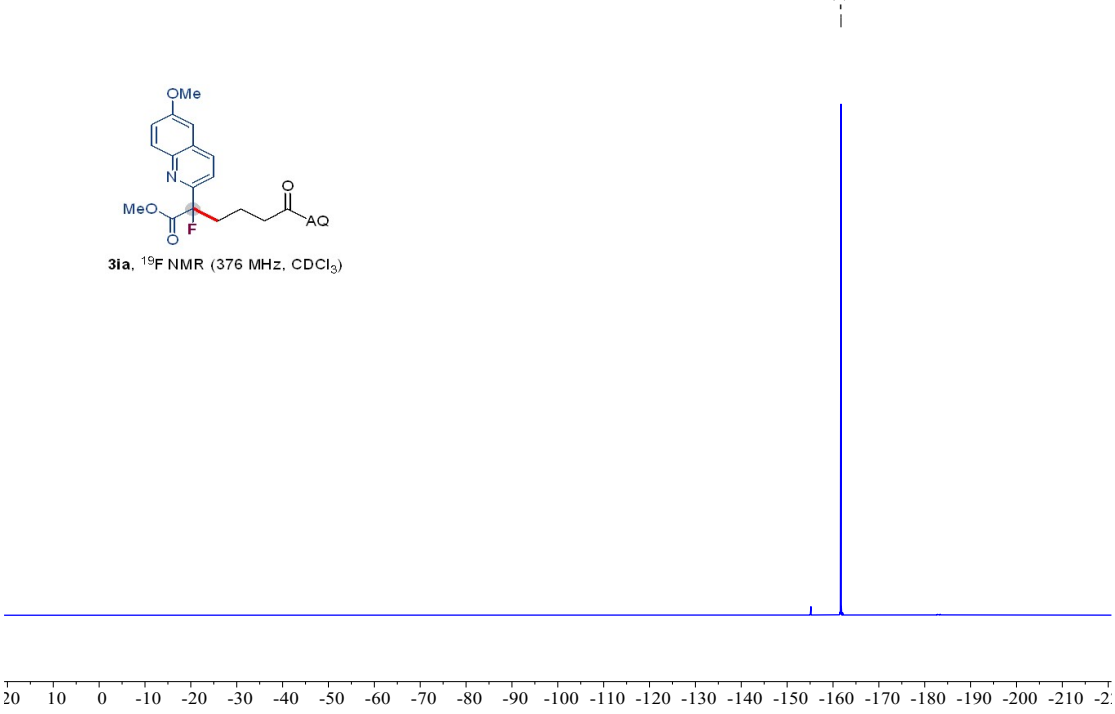


3ia, ^{1}H NMR (400 MHz, $CDCl_3$)

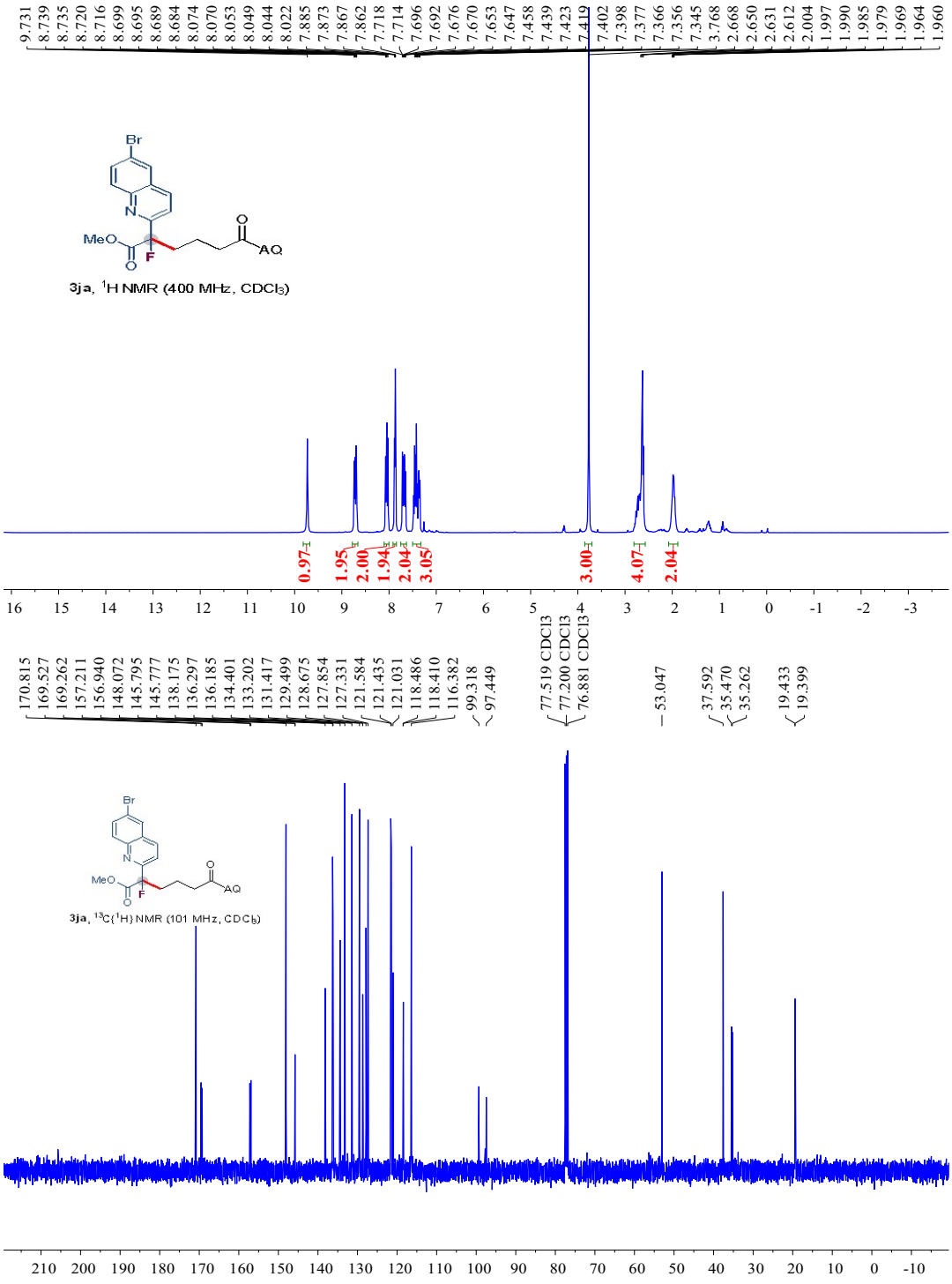


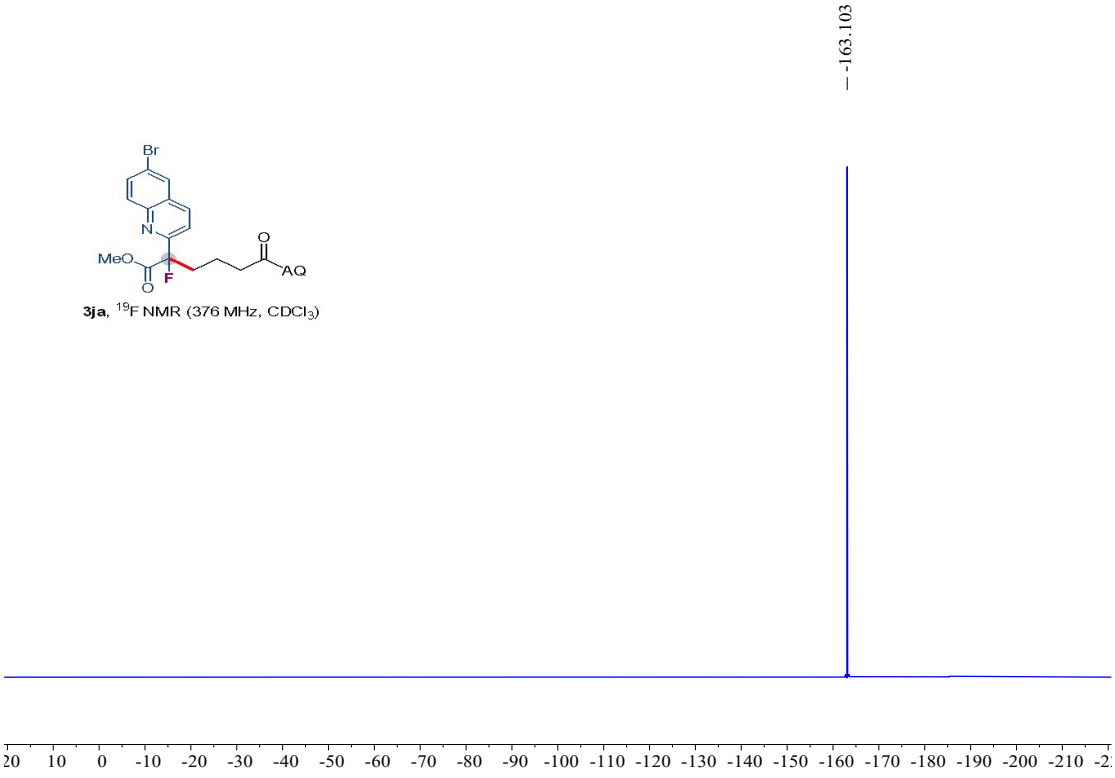


3ia, $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)

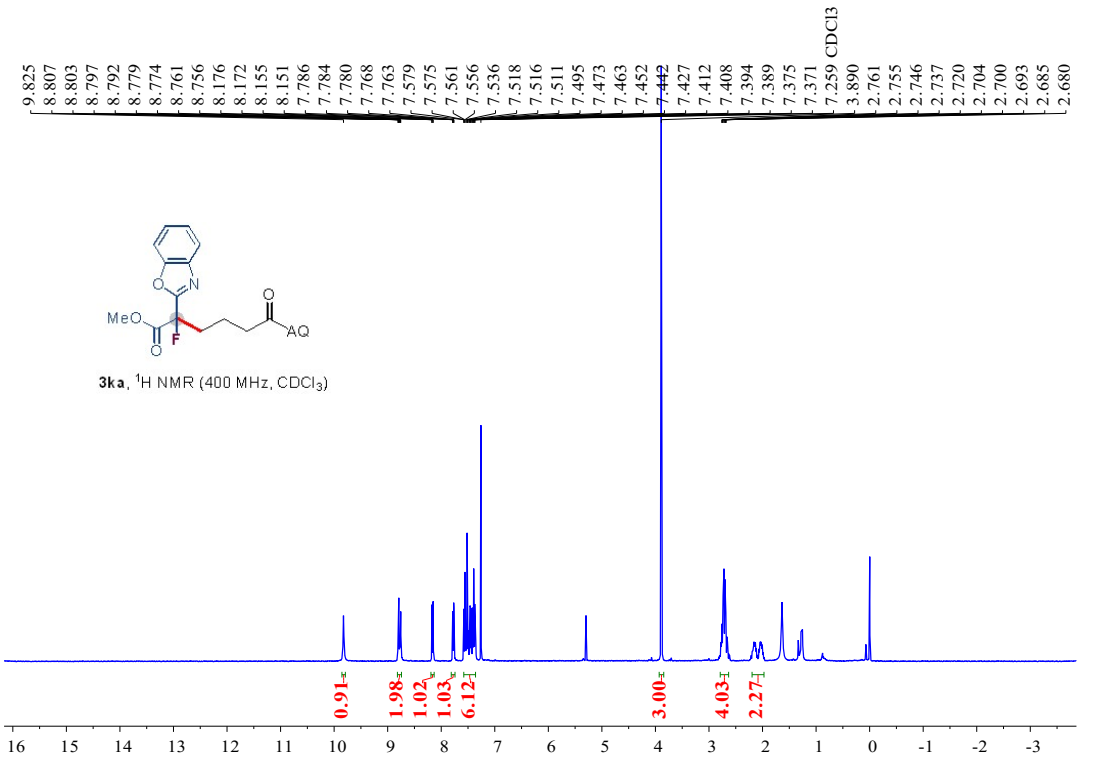


3ia, ^{19}F NMR (376 MHz, $CDCl_3$)

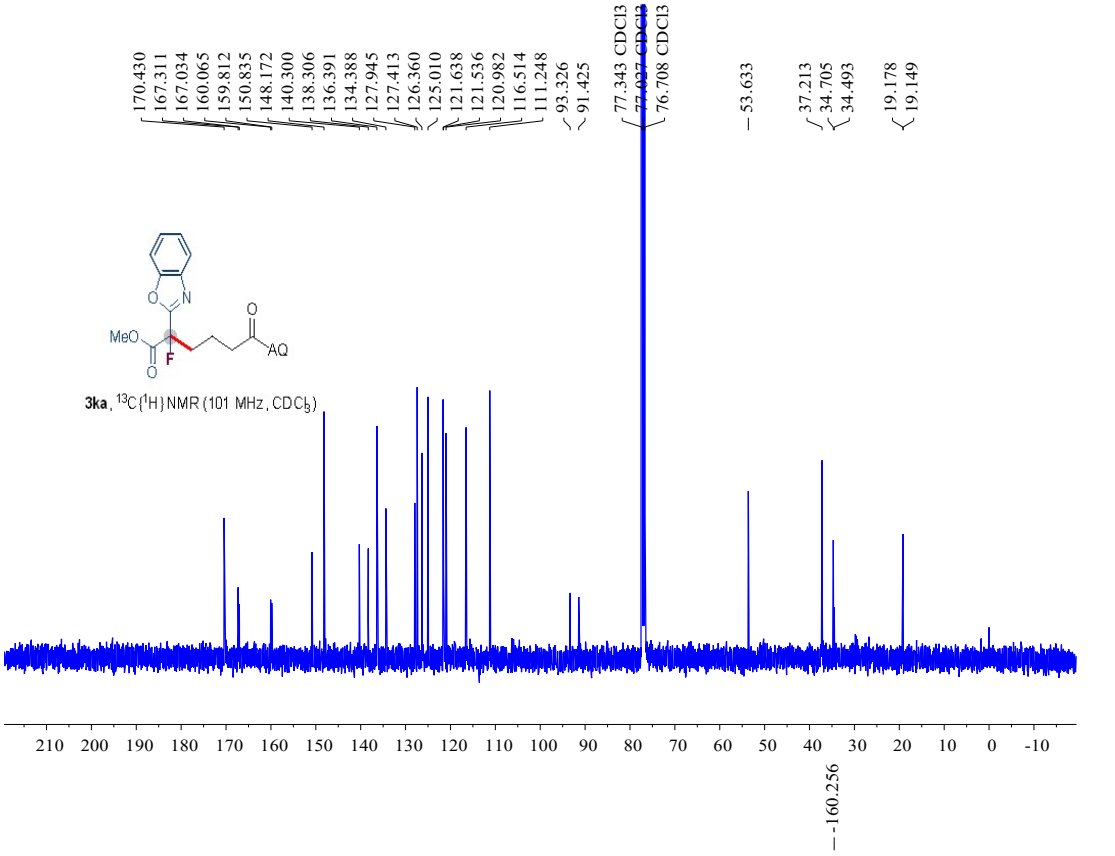

9.731
8.739
8.735
8.720
8.716
8.699
8.695
8.689
8.684
8.074
8.070
8.053
8.049
8.044
8.022
7.885
7.873
7.867
7.862
7.718
7.714
7.696
7.692
7.676
7.670
7.653
7.647
7.458
7.439
7.423
7.419
7.402
7.398
7.377
7.366
7.356
7.345
3.768
2.668
2.650
2.631
2.612
2.004
1.997
1.990
1.985
1.979
1.969
1.964
1.960
Br
N
MeO
O
F
O
AQ
3ja, ^{1}H NMR (400 MHz, CDCl$_3$)
0.97
1.95
2.00
1.94
2.04
3.05
3.00
4.07
2.04
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3
170.815
169.527
169.262
157.211
156.940
148.072
145.795
145.777
138.175
136.297
136.185
134.401
133.202
131.417
129.499
128.675
127.854
127.331
121.584
121.435
121.031
118.486
118.410
116.382
99.318
97.449
77.519 CDCl3
77.200 CDCl3
76.881 CDCl3
53.047
37.592
35.470
35.262
19.433
19.399
Br
N
MeO
O
F
O
AQ
3ja, ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10



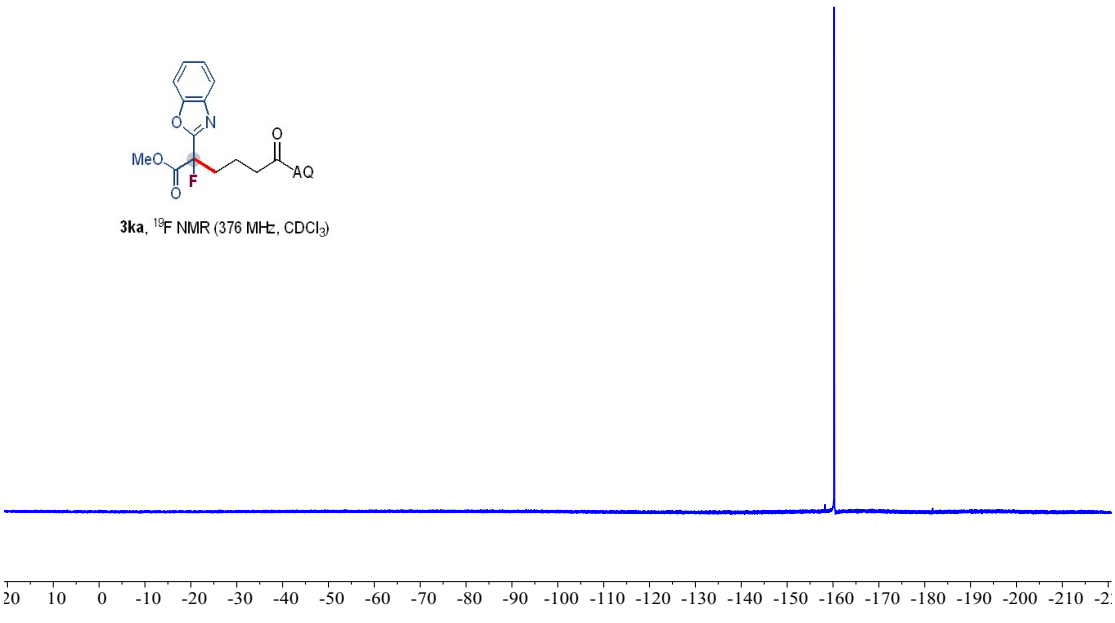
3ja, ^{19}F NMR (376 MHz, $CDCl_3$)



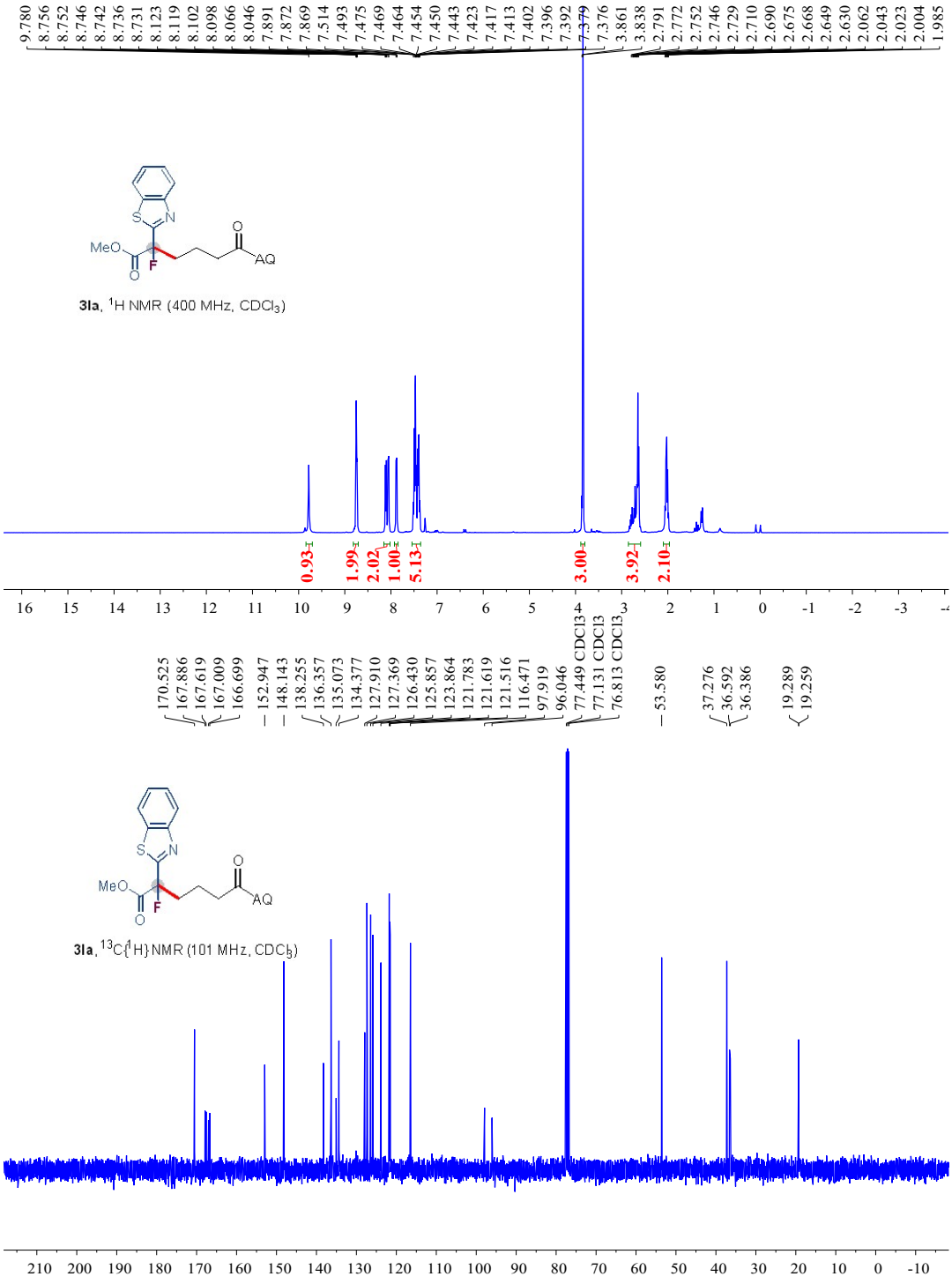
3ka, ^{1}H NMR (400 MHz, $CDCl_3$)

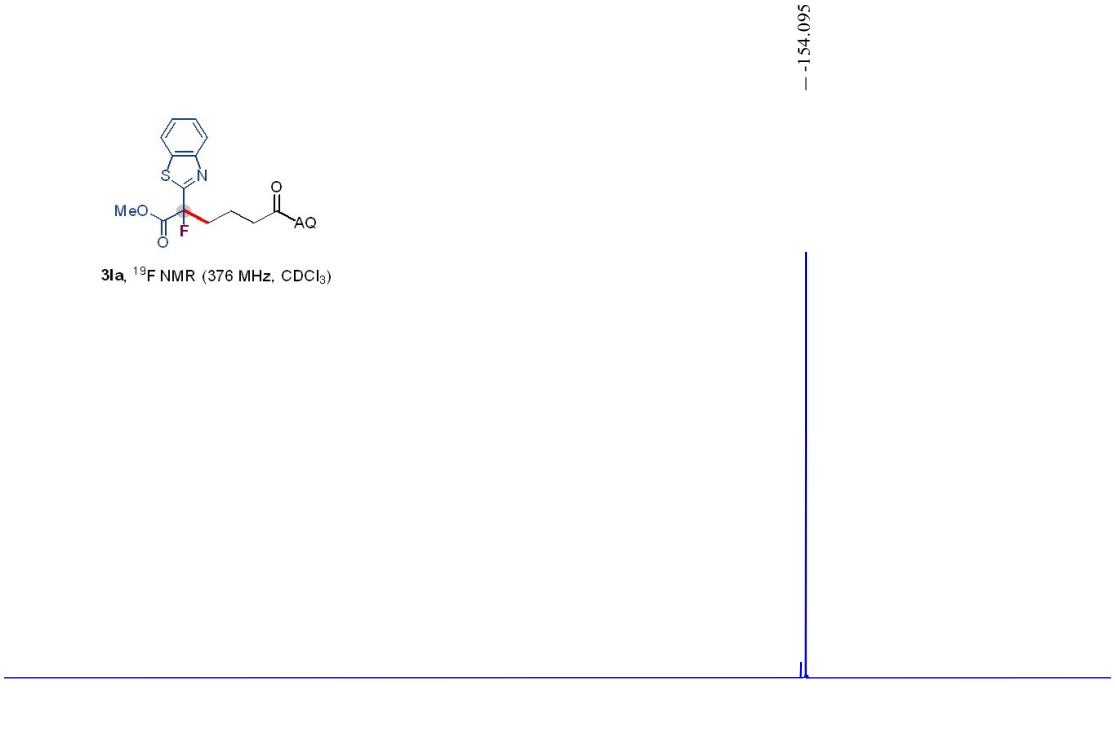


3ka, $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)

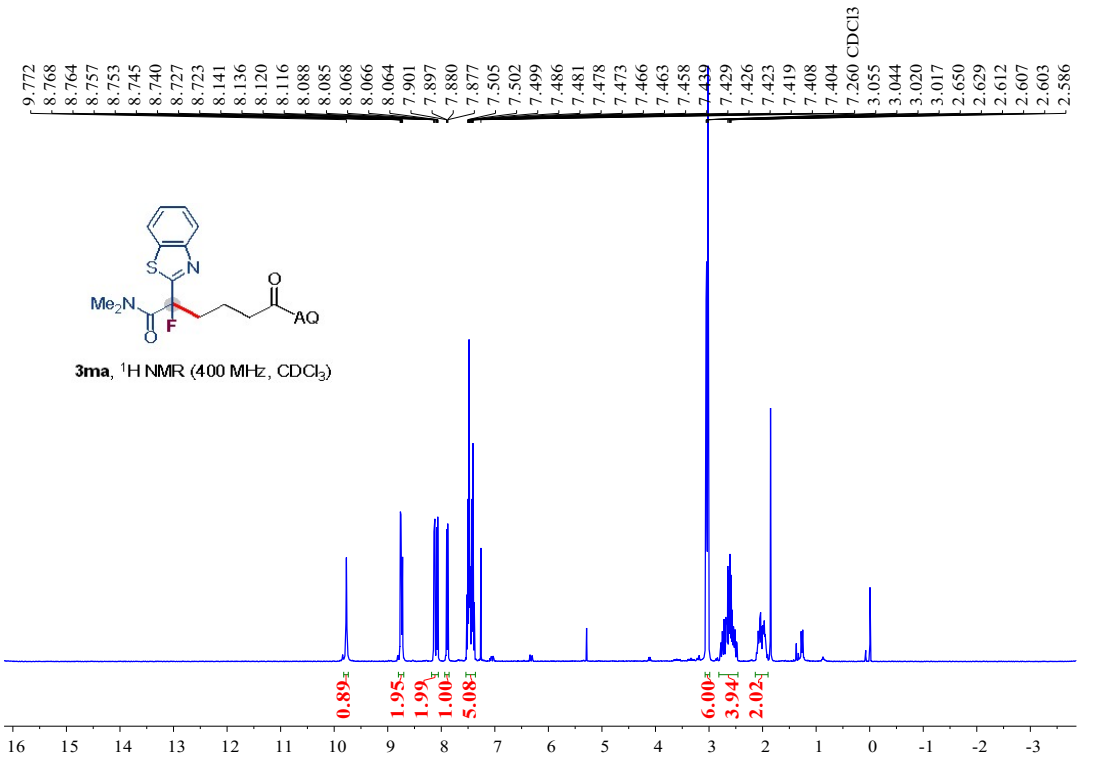


3ka, ^{19}F NMR (376 MHz, $CDCl_3$)

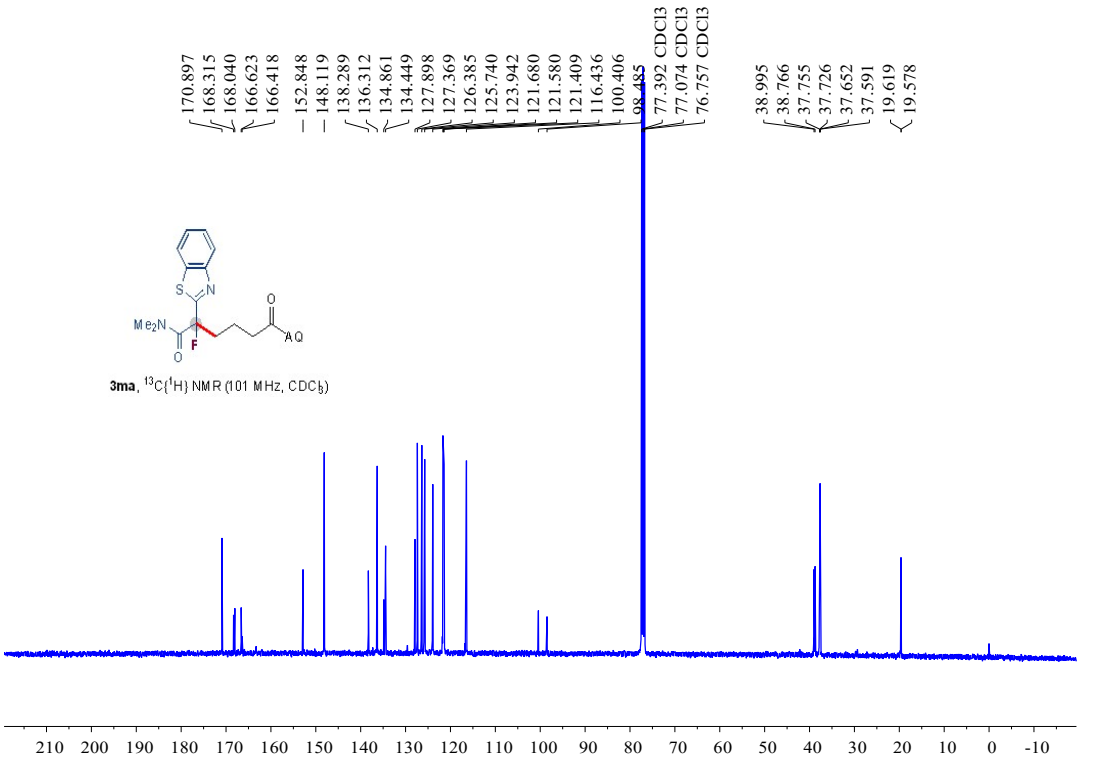

9.780
8.756
8.752
8.746
8.742
8.736
8.731
8.123
8.119
8.102
8.098
8.066
8.046
7.891
7.872
7.869
7.514
7.493
7.475
7.469
7.464
7.454
7.450
7.443
7.423
7.417
7.413
7.402
7.396
7.392
7.379
7.376
3.861
3.838
2.791
2.772
2.752
2.746
2.729
2.710
2.690
2.675
2.668
2.649
2.630
2.062
2.043
2.023
2.004
1.985
MeO
O
F
S
N
O
AQ
3la, ^{1}H NMR (400 MHz, CDCl$_3$)
0.93
1.99
2.02
1.00
5.13
3.00
3.92
2.10
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3
170.525
167.886
167.619
167.009
166.699
152.947
148.143
138.255
136.357
135.073
134.377
127.910
127.369
126.430
125.857
123.864
121.783
121.619
121.516
116.471
97.919
96.046
77.449 CDCl3
77.131 CDCl3
76.813 CDCl3
53.580
37.276
36.592
36.386
19.289
19.259
3la, ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10



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

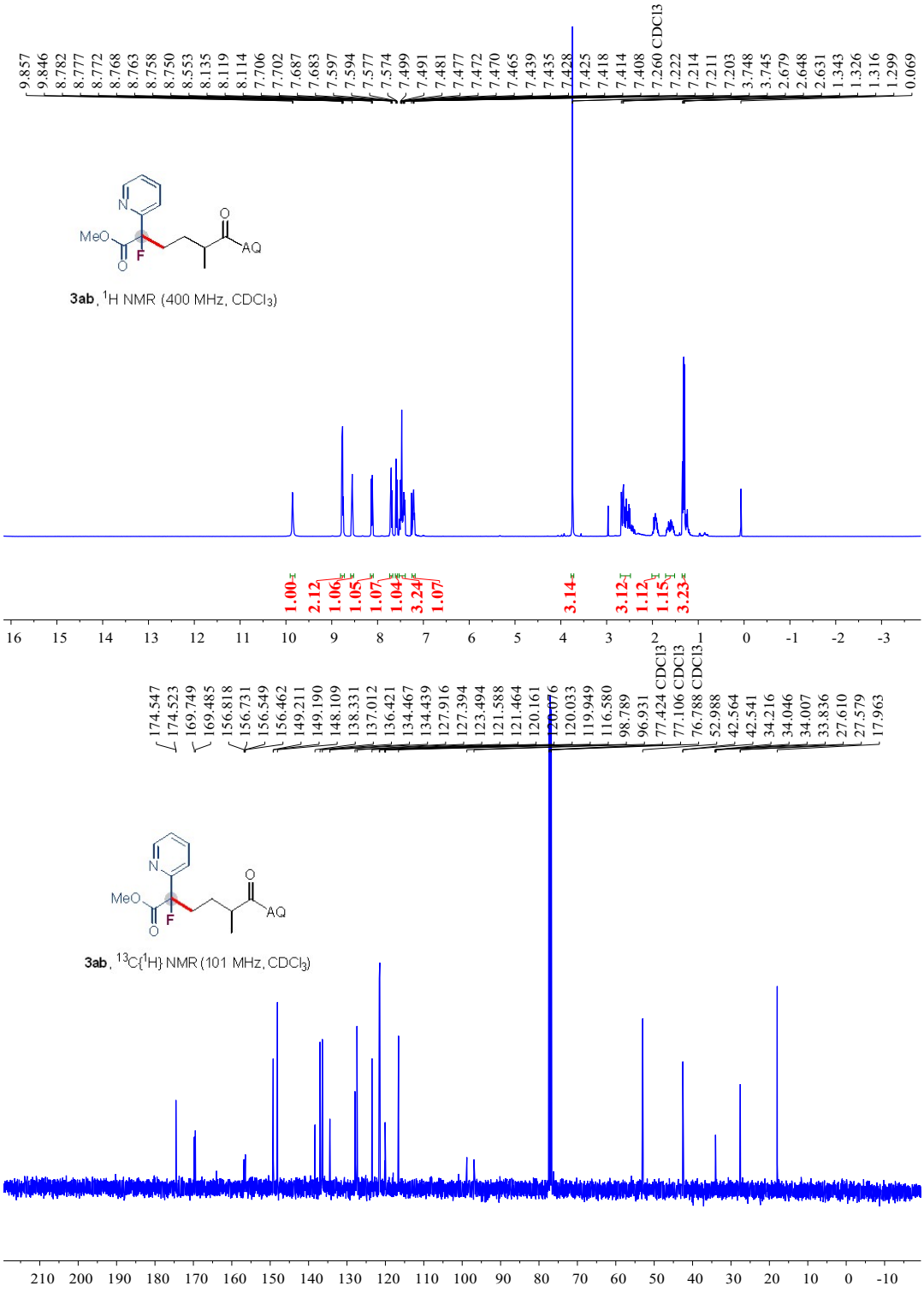


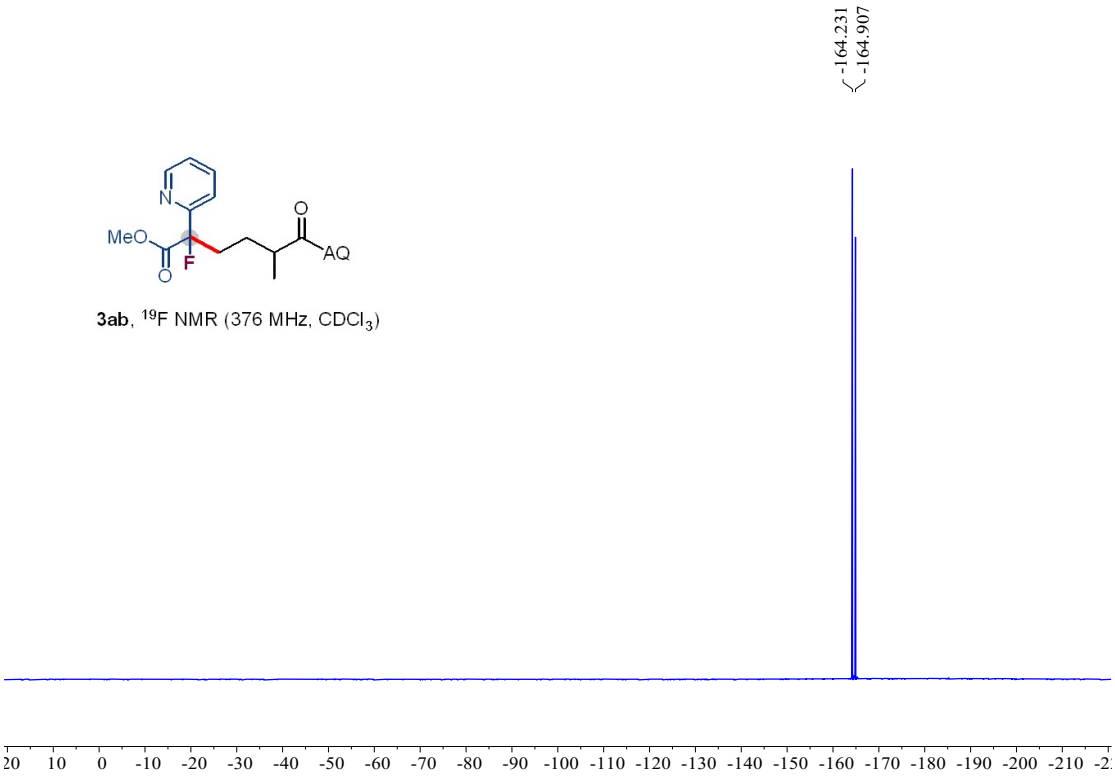
3ma, ^{1}H NMR (400 MHz, $CDCl_3$)



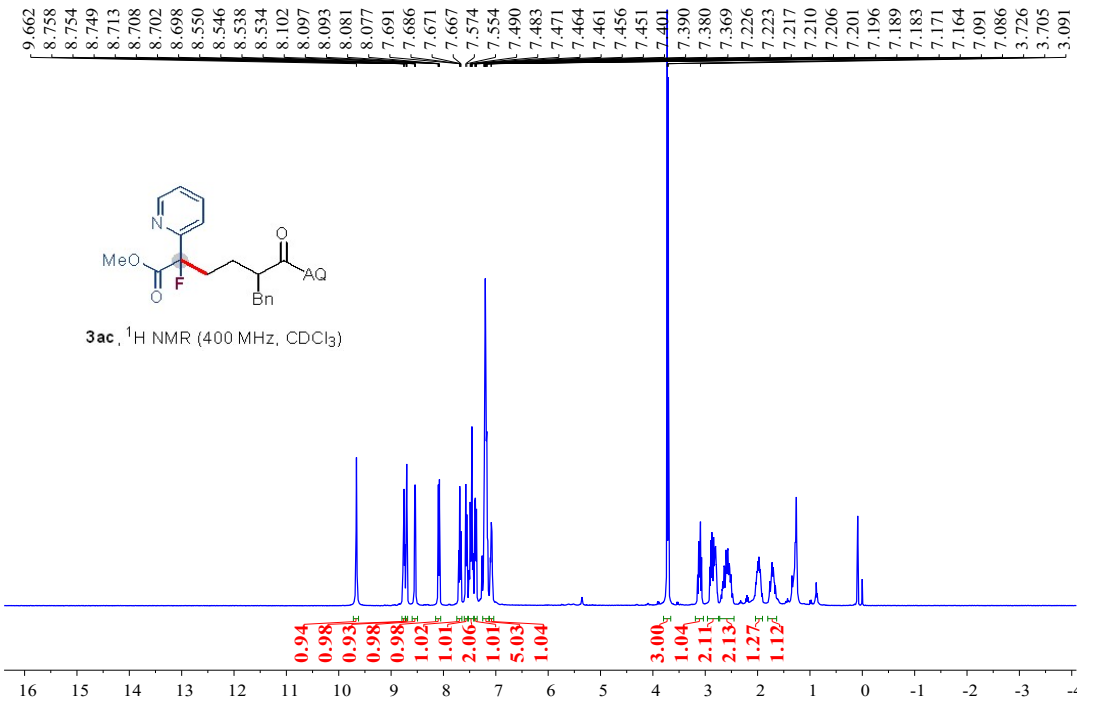
3ma, $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)

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

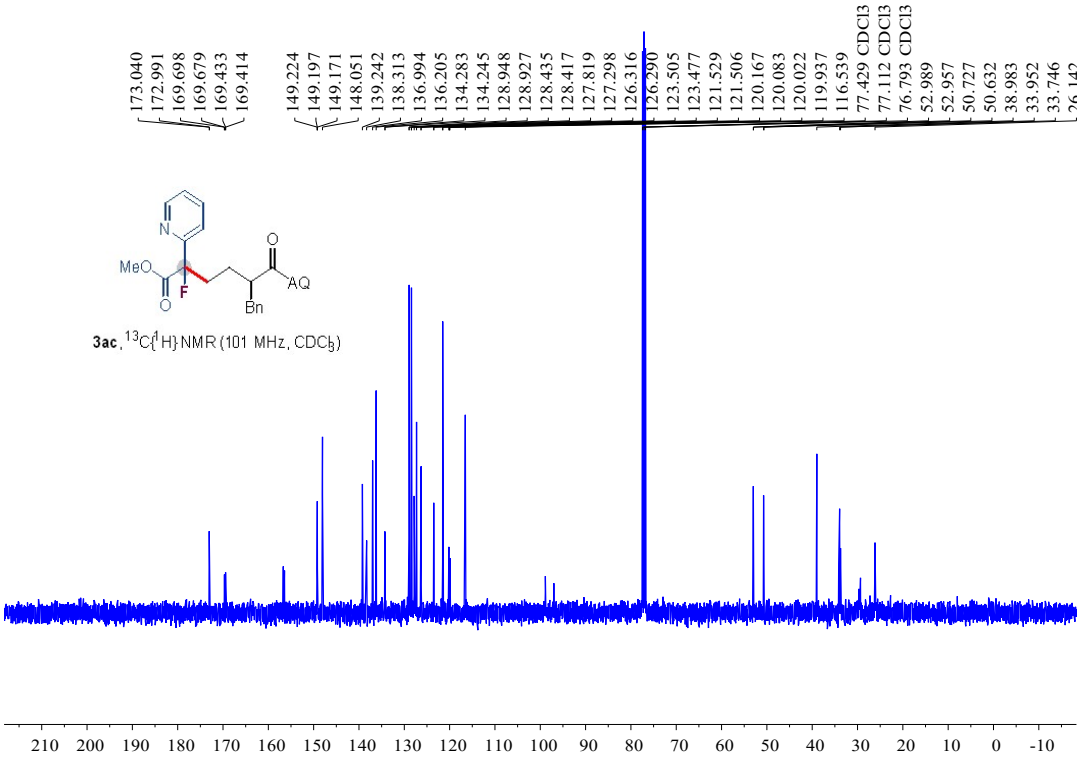

9.857
9.846
8.782
8.777
8.772
8.768
8.763
8.758
8.750
8.553
8.135
8.119
8.114
7.706
7.702
7.687
7.683
7.597
7.594
7.577
7.574
7.499
7.491
7.481
7.477
7.472
7.470
7.465
7.439
7.435
7.428
7.425
7.418
7.414
7.408
7.260 CDCl3
7.222
7.214
7.211
7.203
3.748
3.745
2.679
2.648
2.631
1.343
1.326
1.316
1.299
0.069
MeO
F
O
AQ
3ab, 1H NMR (400 MHz, CDCl3)
1.00
2.12
1.06
1.05
1.07
1.04
3.24
1.07
3.14
3.12
1.12
1.15
3.23
174.547
174.523
169.749
169.485
156.818
156.731
156.549
156.462
149.211
149.190
148.109
138.331
137.012
136.421
134.467
134.439
127.916
127.394
123.494
121.588
121.464
120.161
120.076
120.033
119.949
116.580
98.789
96.931
77.424 CDCl3
77.106 CDCl3
76.788 CDCl3
52.988
42.564
42.541
34.216
34.046
34.007
33.836
27.610
27.579
17.963
MeO
F
O
AQ
3ab, 13C{1H} NMR (101 MHz, CDCl3)



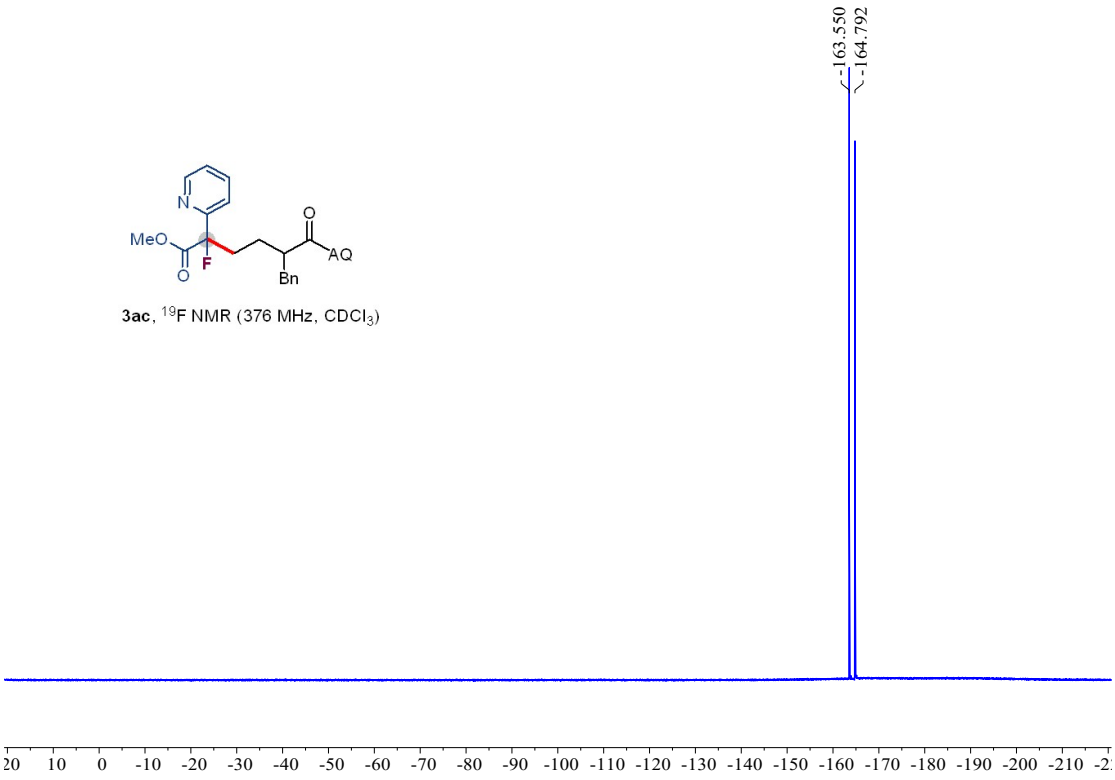
3ab, ^{19}F NMR (376 MHz, $CDCl_3$)



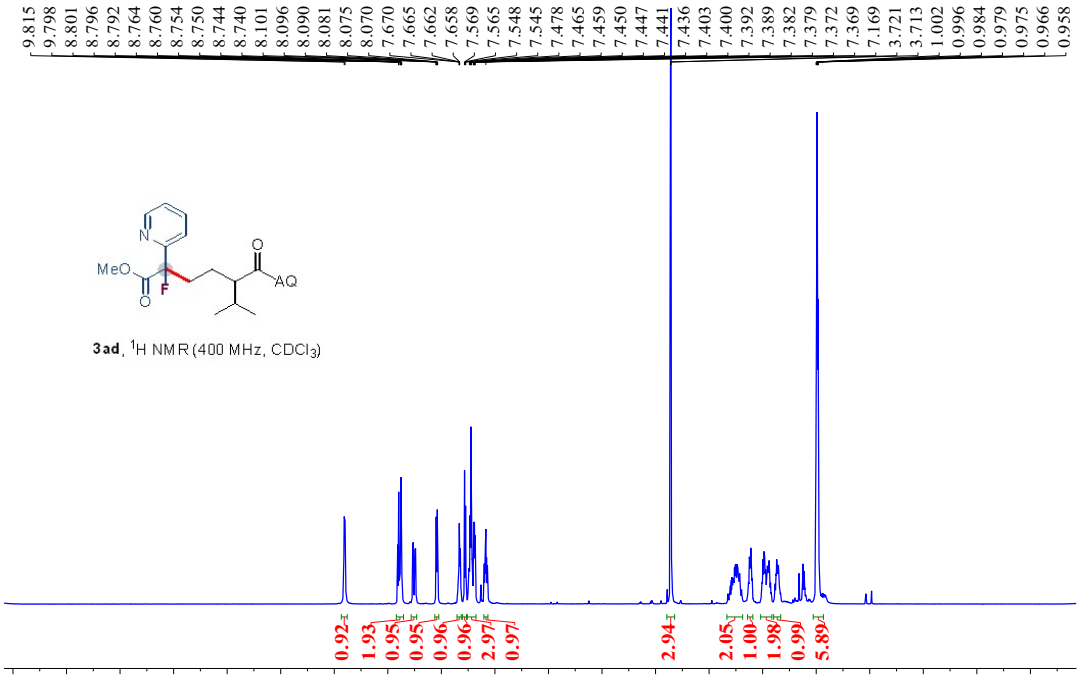
3ac, ^{1}H NMR (400 MHz, $CDCl_3$)

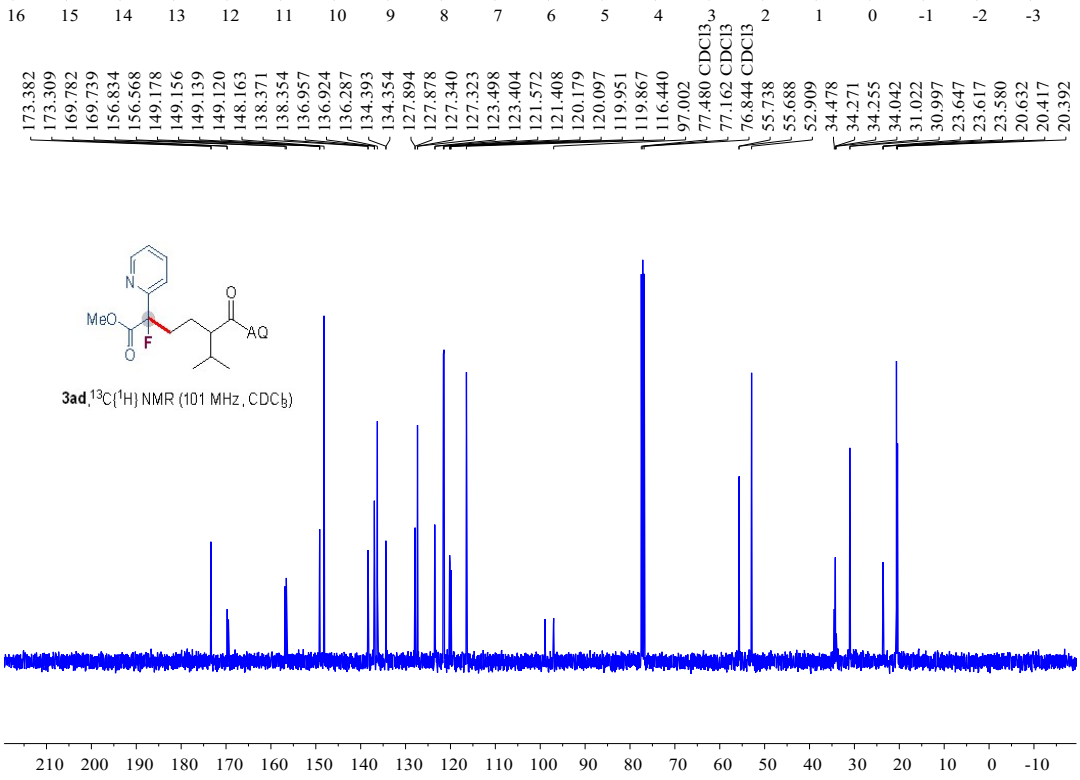


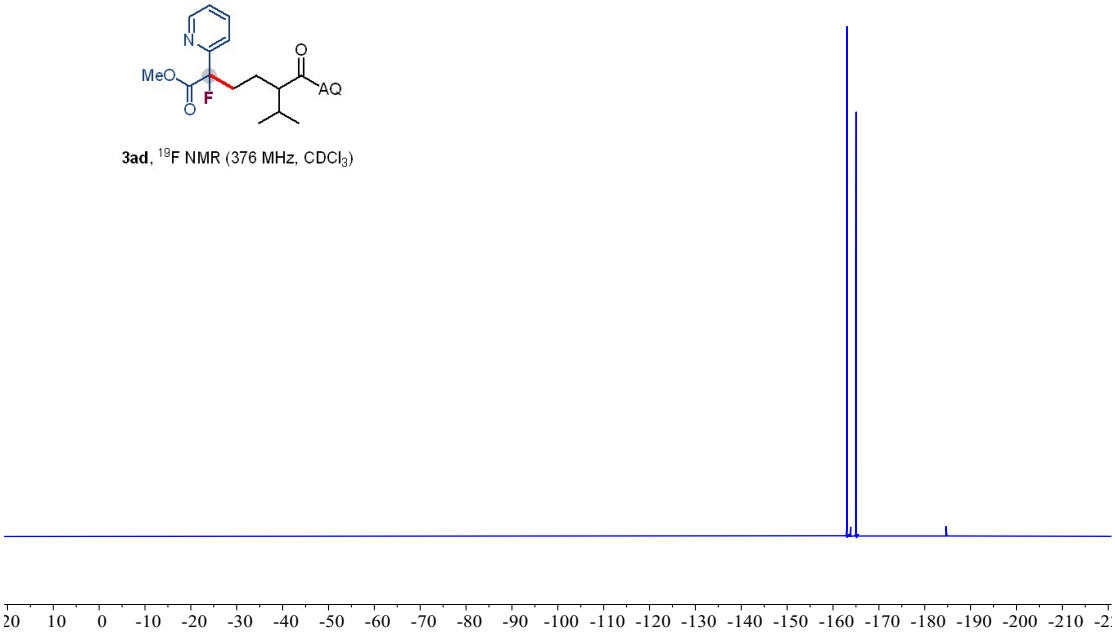
3ac, $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$)



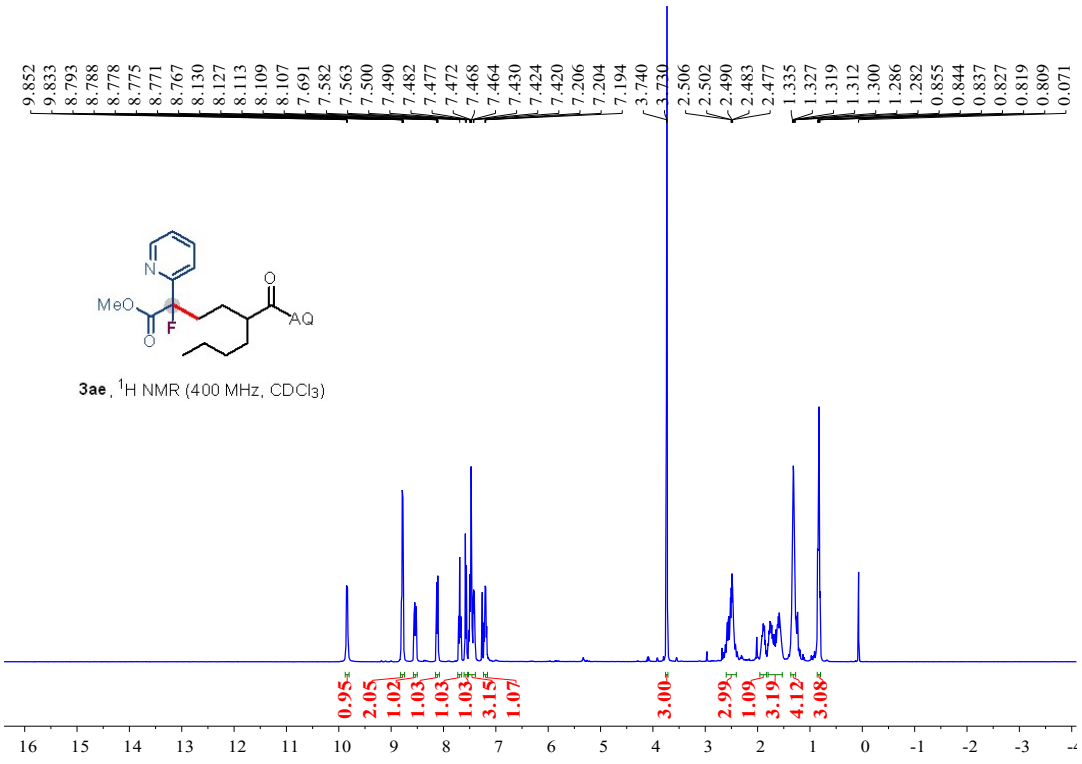
3ac, ^{19}F NMR (376 MHz, $CDCl_3$)


MeO
F
O
N
O
AQ
3ad, 1H NMR (400 MHz, CDCl3)

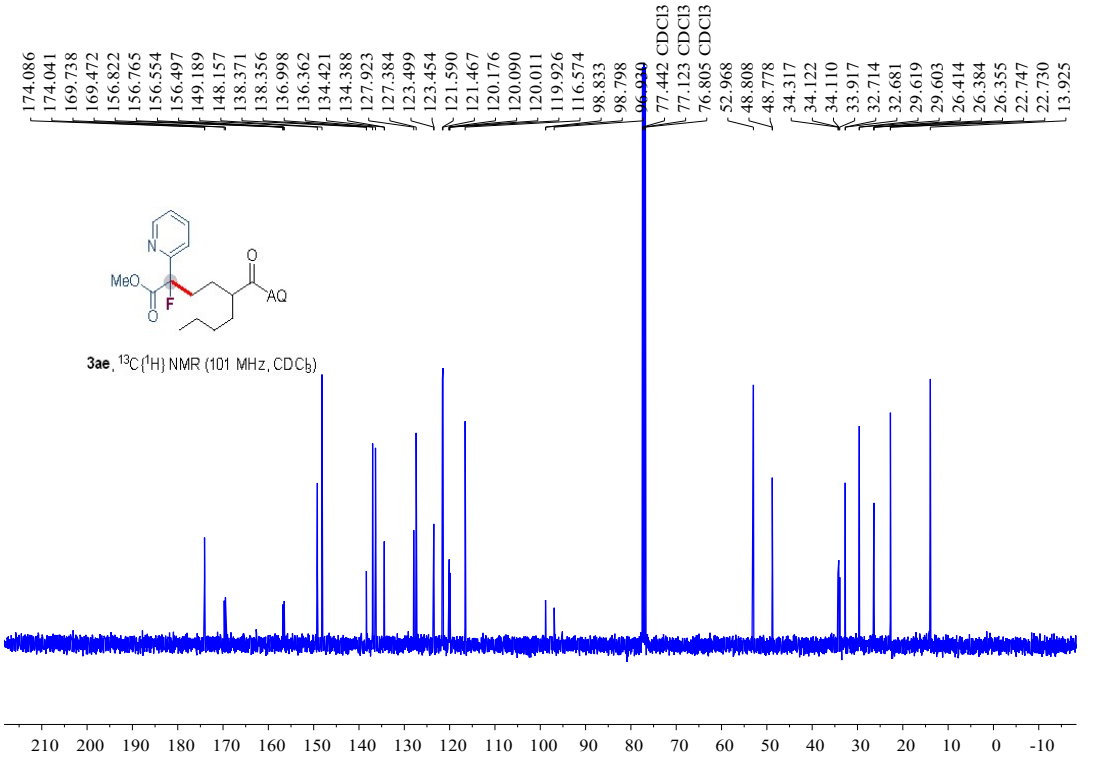

MeO
F
O
N
O
AQ
3ad,13C{1H} NMR (101 MHz, CDCl3)



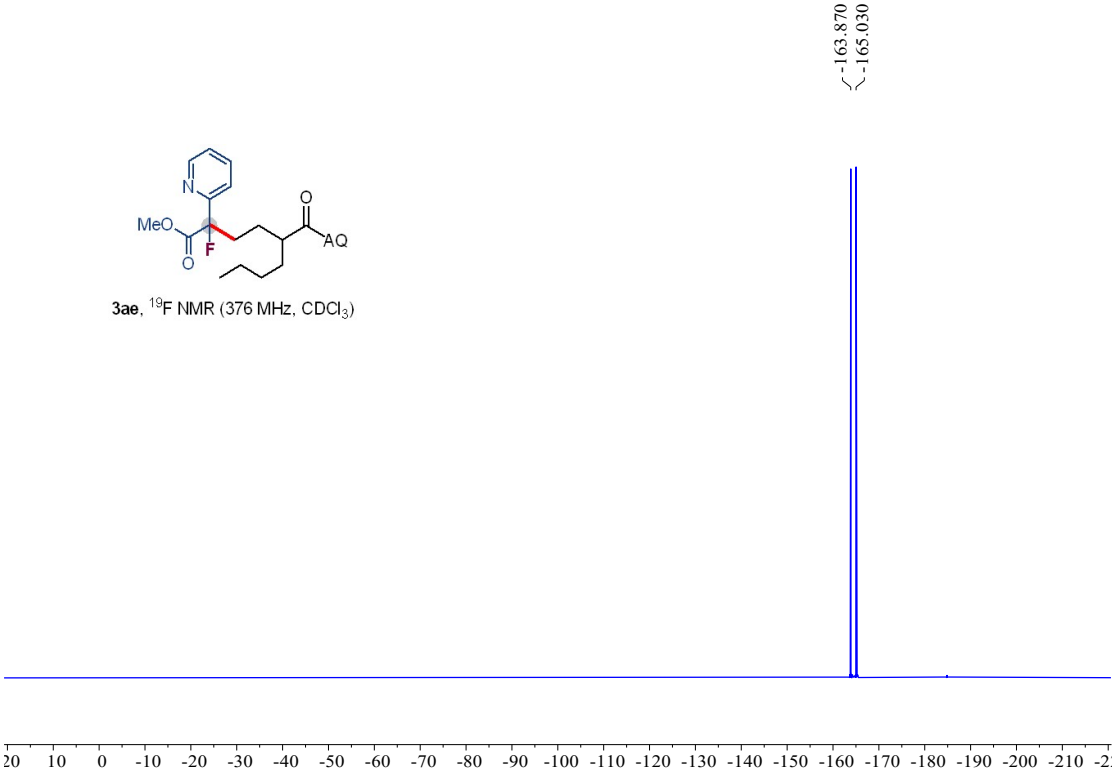
3ad, ^{19}F NMR (376 MHz, $CDCl_3$)



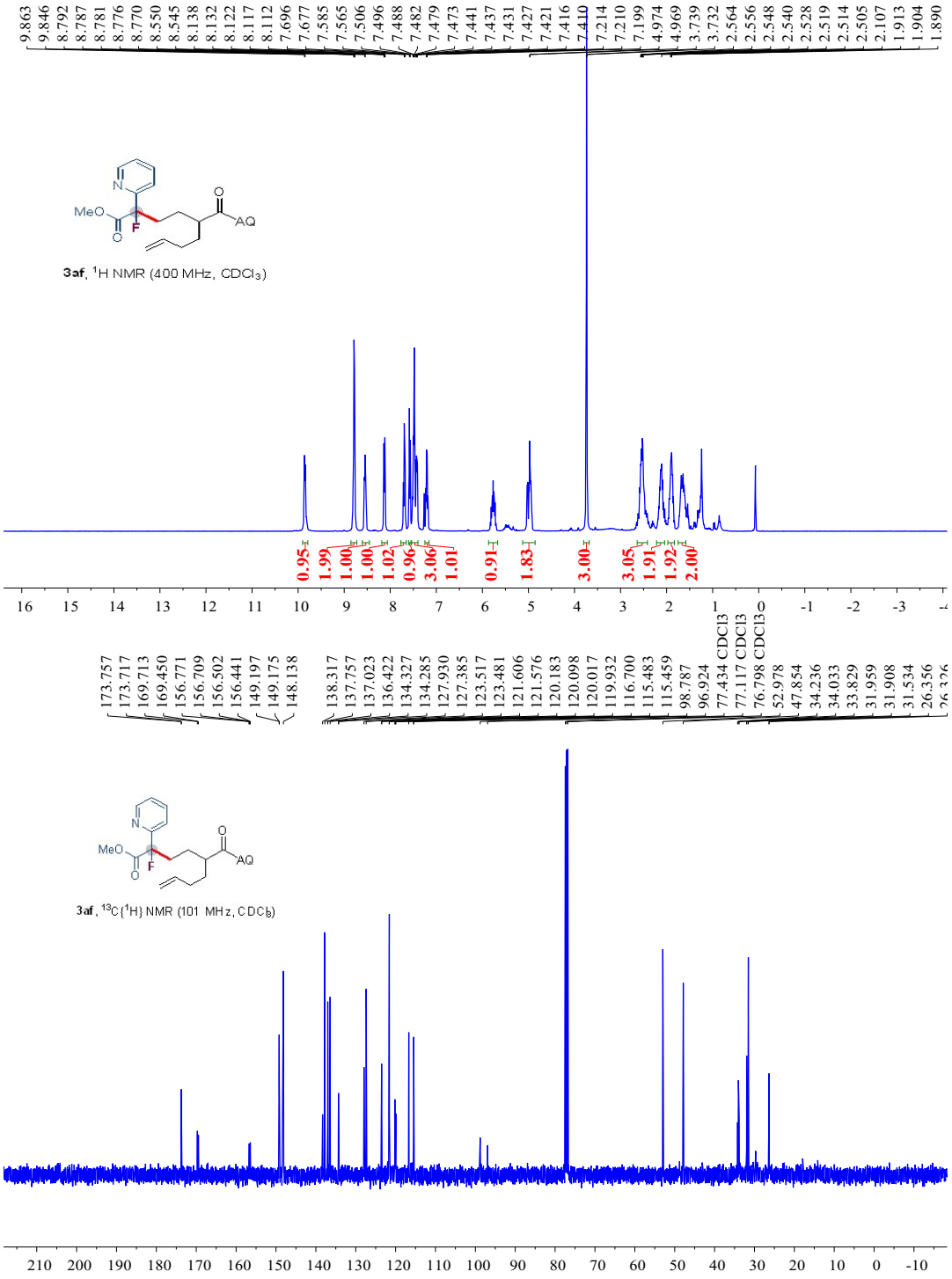
3ae, ^{1}H NMR (400 MHz, $CDCl_3$)

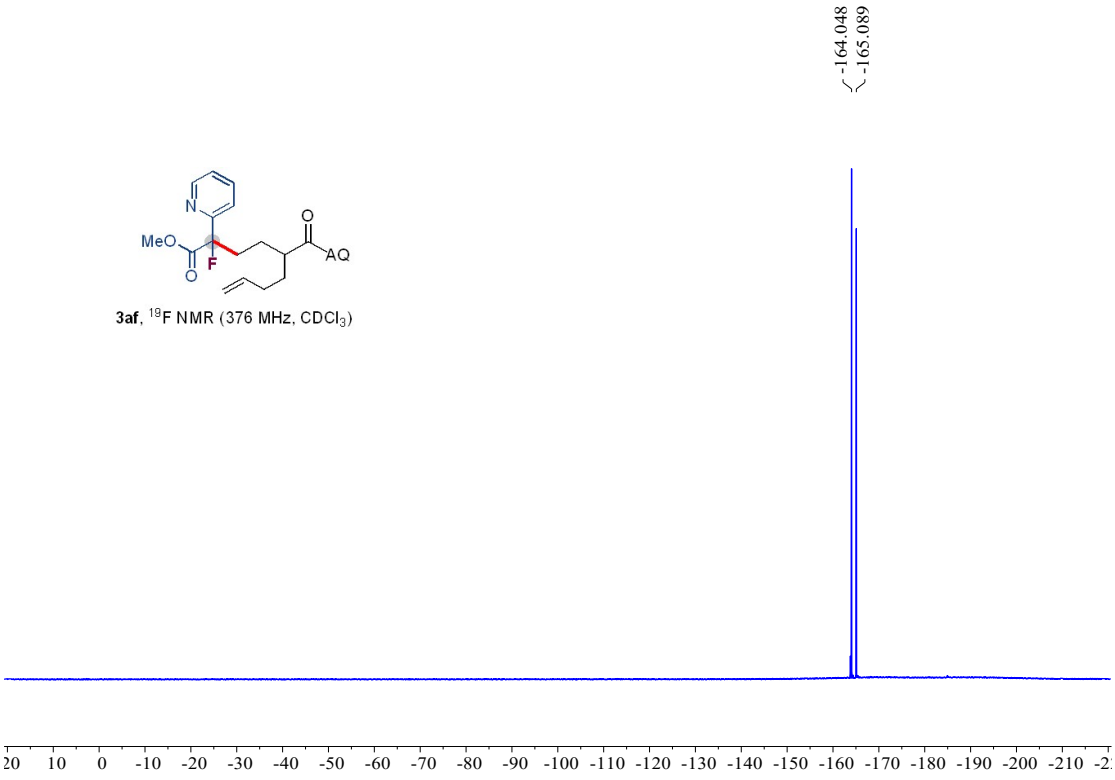


3ae, $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)

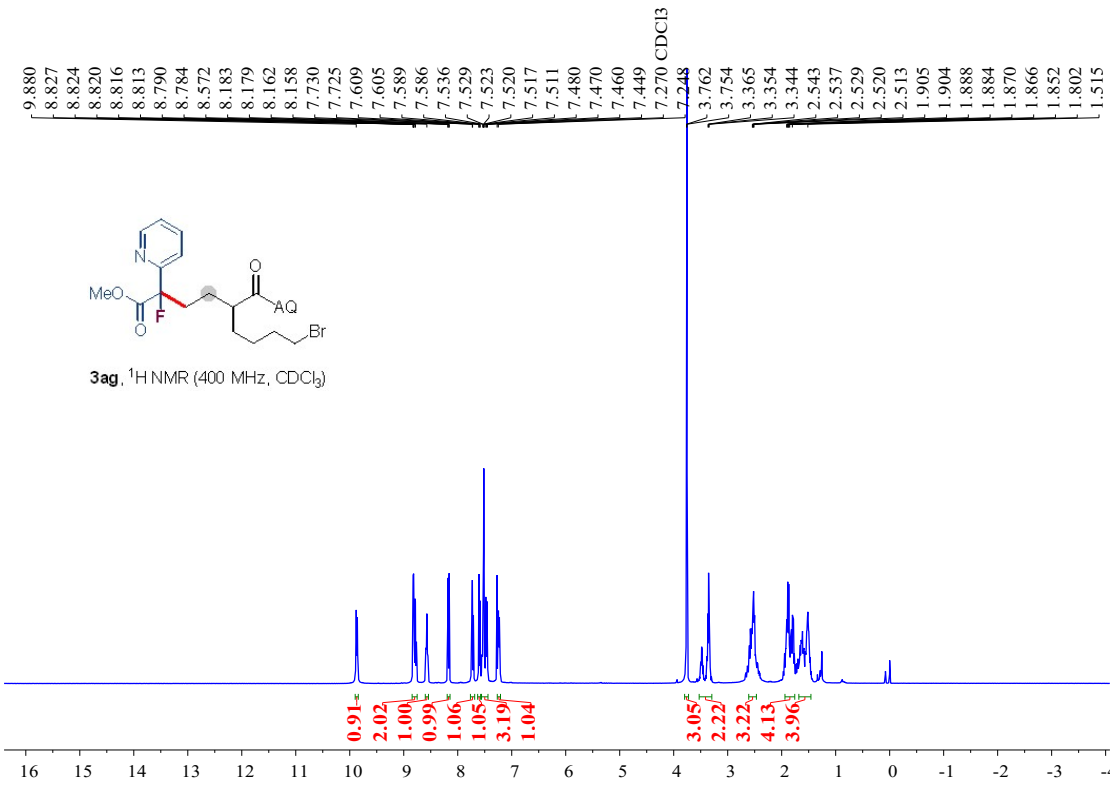


3ae, ^{19}F NMR (376 MHz, $CDCl_3$)

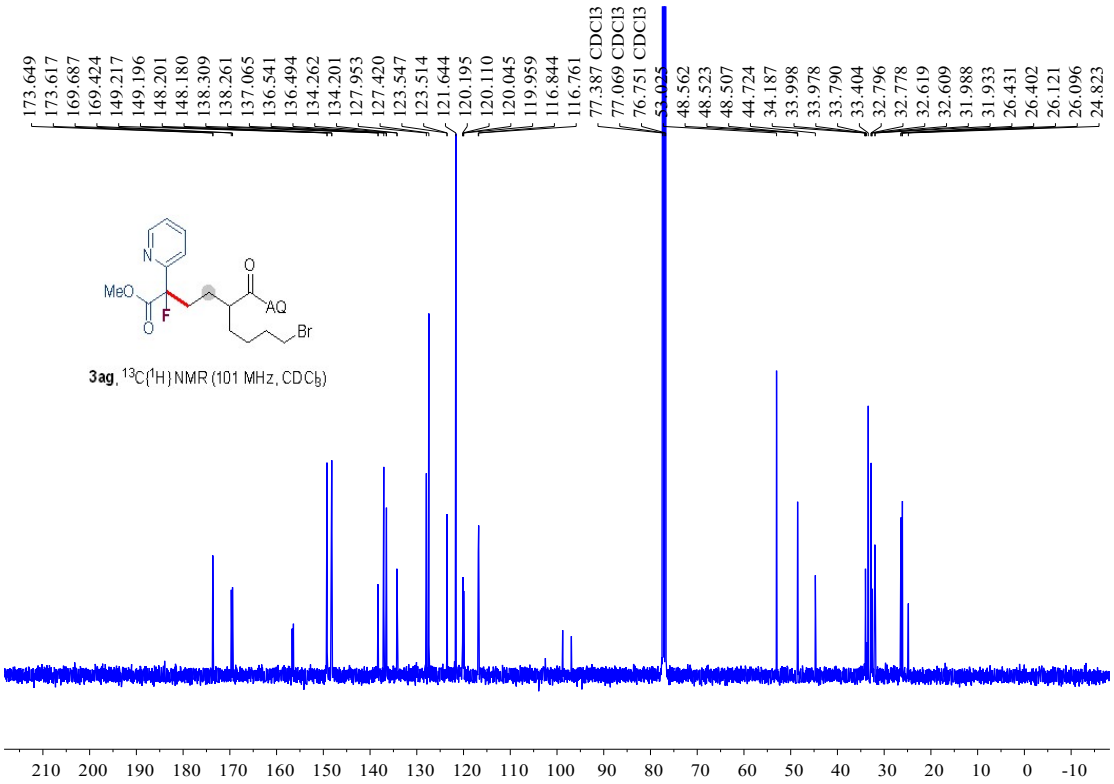

9.863
9.846
8.792
8.787
8.781
8.776
8.770
8.550
8.545
8.138
8.132
8.122
8.117
8.112
7.696
7.677
7.585
7.565
7.506
7.496
7.488
7.482
7.479
7.473
7.441
7.437
7.431
7.427
7.421
7.416
7.410
7.214
7.210
7.199
4.974
4.969
3.739
3.732
2.564
2.556
2.548
2.540
2.528
2.519
2.514
2.505
2.107
1.913
1.904
1.890
MeO
O
F
N
O
AQ
3af, 1H NMR (400 MHz, CDCl3)
0.95
1.99
1.00
1.00
1.02
0.96
3.06
1.01
0.91
1.83
3.00
3.05
1.91
1.92
2.00
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3
173.757
173.717
169.713
169.450
156.771
156.709
156.502
156.441
149.197
149.175
148.138
138.317
137.757
137.023
136.422
134.327
134.285
127.930
127.385
123.517
123.481
121.606
121.576
120.183
120.098
120.017
119.932
116.700
115.483
115.459
98.787
96.924
77.434 CDCl3
77.117 CDCl3
76.798 CDCl3
52.978
47.854
34.236
34.033
33.829
31.959
31.908
31.534
26.356
MeO
O
F
N
O
AQ
3af, 13C{1H} NMR (101 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10



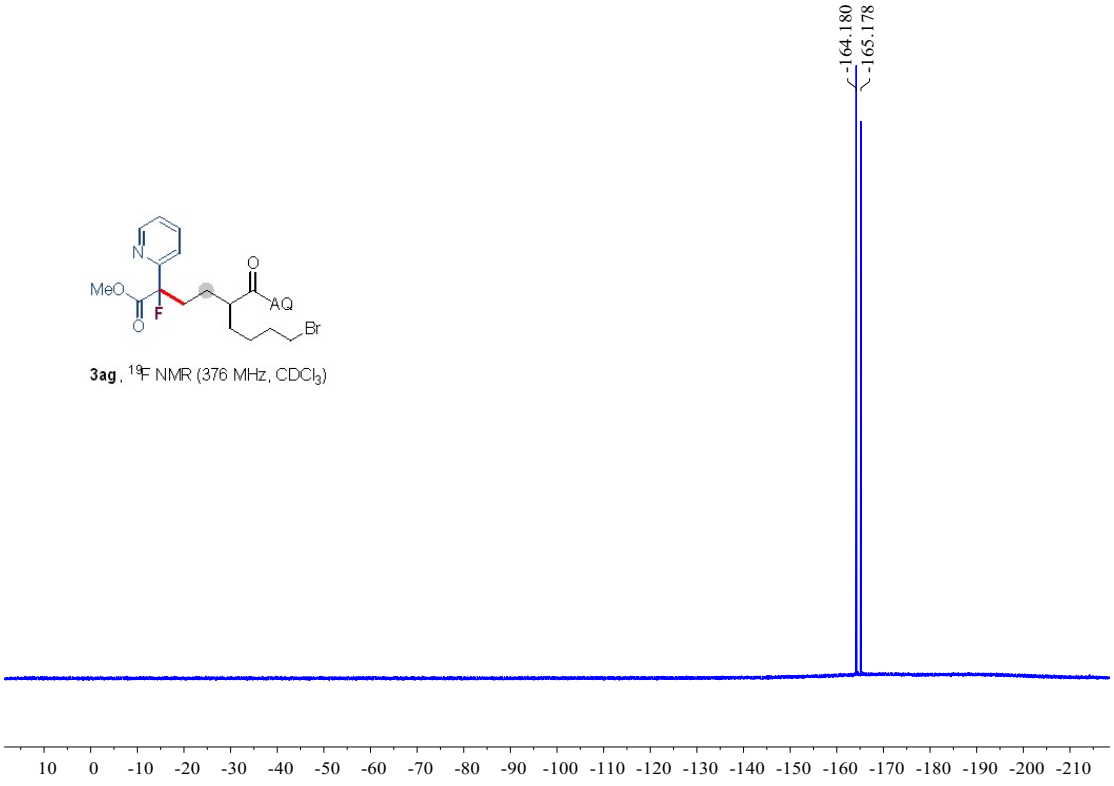
3af, ^{19}F NMR (376 MHz, $CDCl_3$)



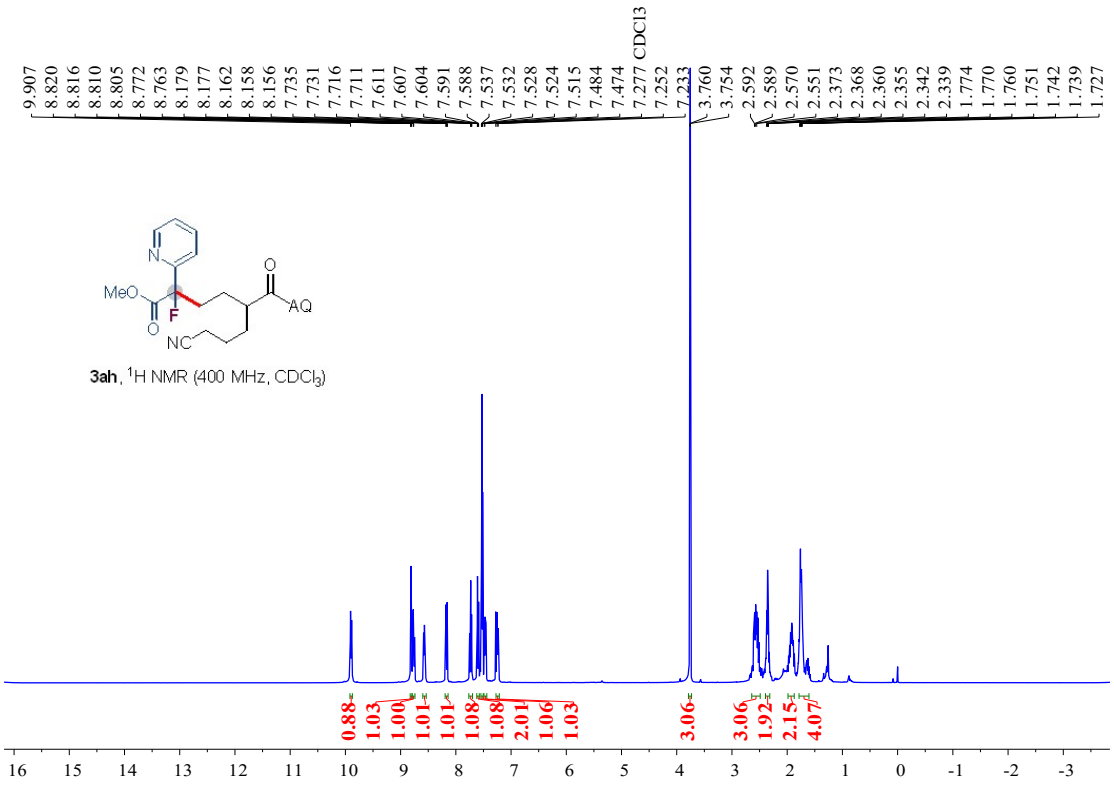
3ag, ^{1}H NMR (400 MHz, $CDCl_3$)



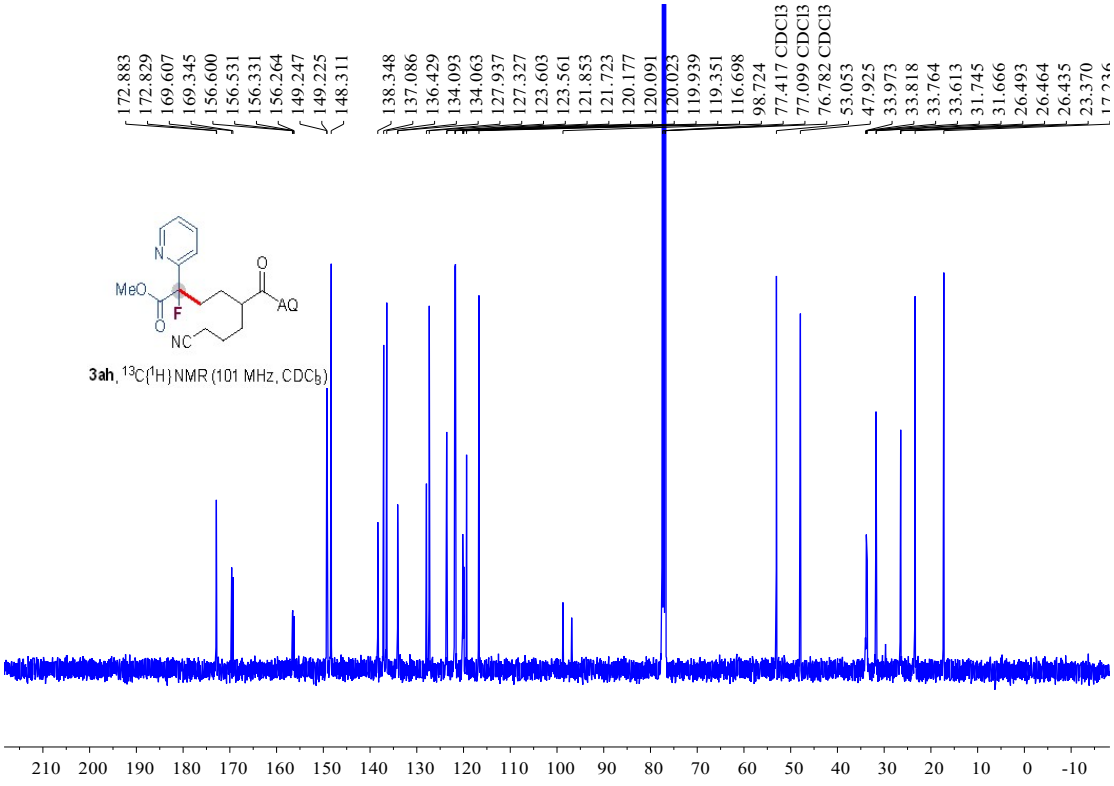
3ag, $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)



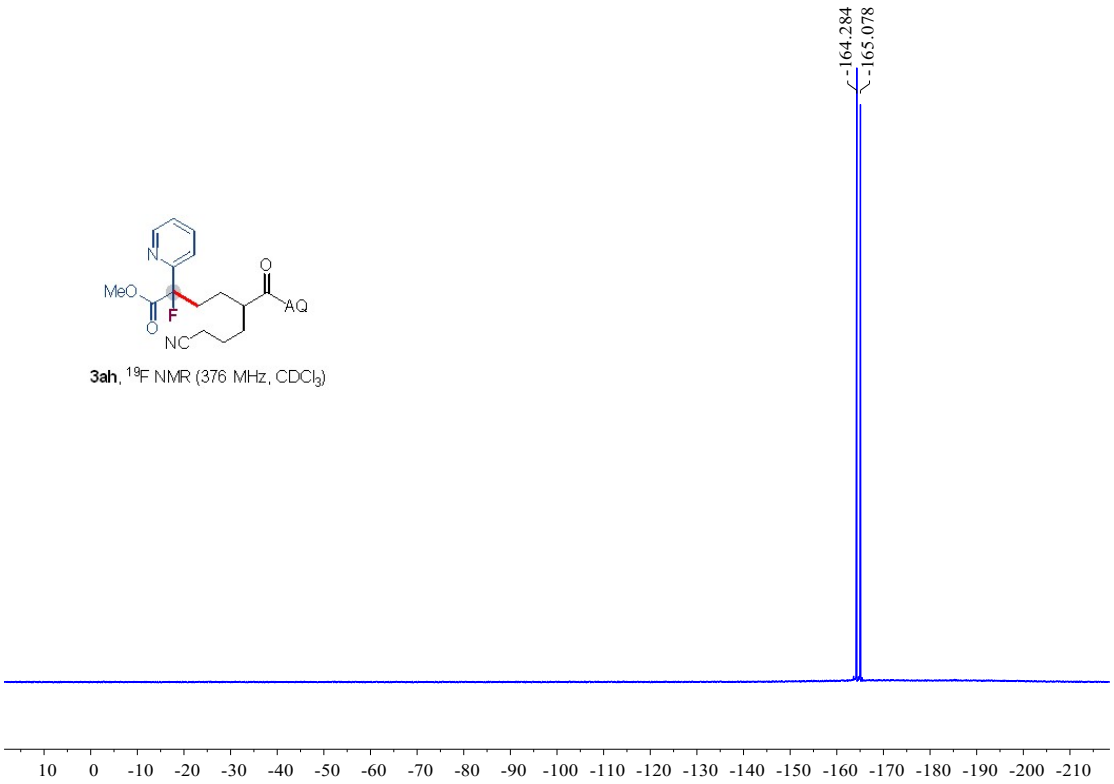
3ag, ^{19}F NMR (376 MHz, $CDCl_3$)



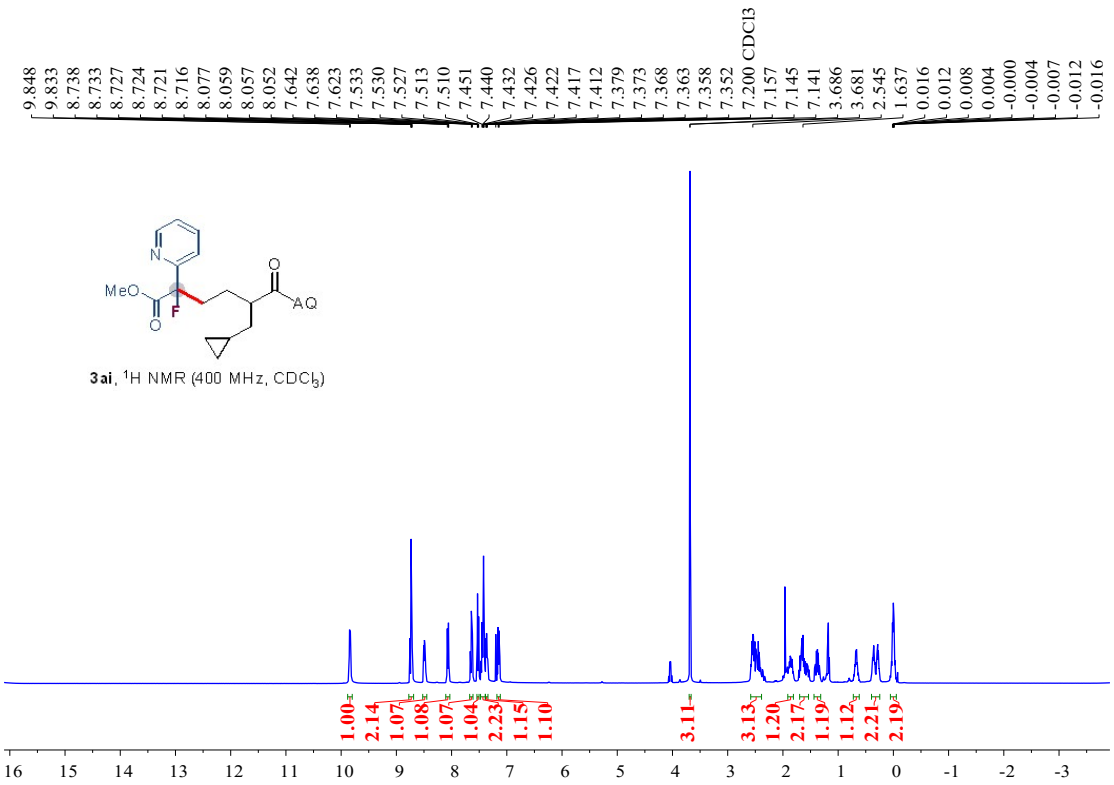
3ah, ^{1}H NMR (400 MHz, $CDCl_3$)



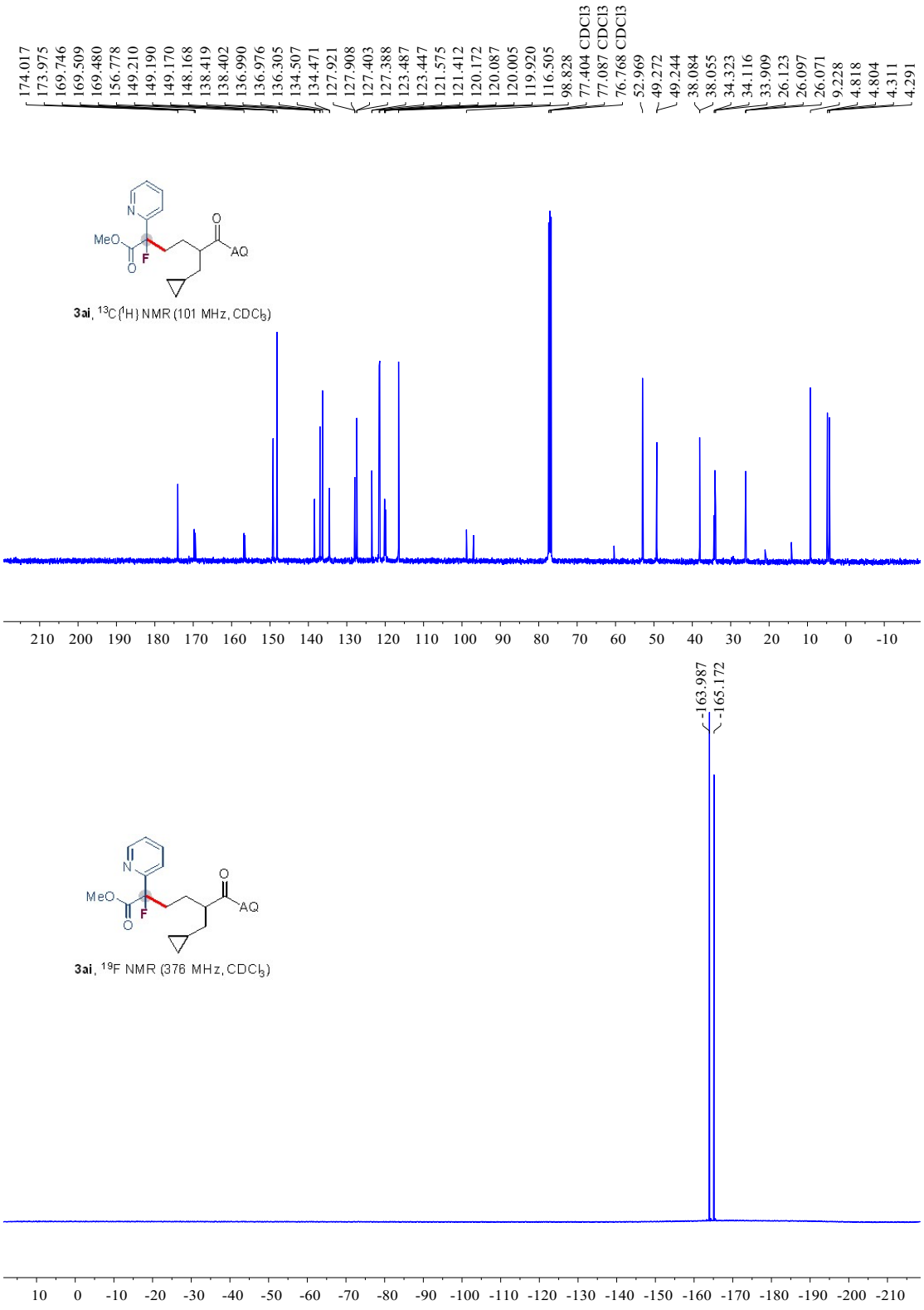
3ah, $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)

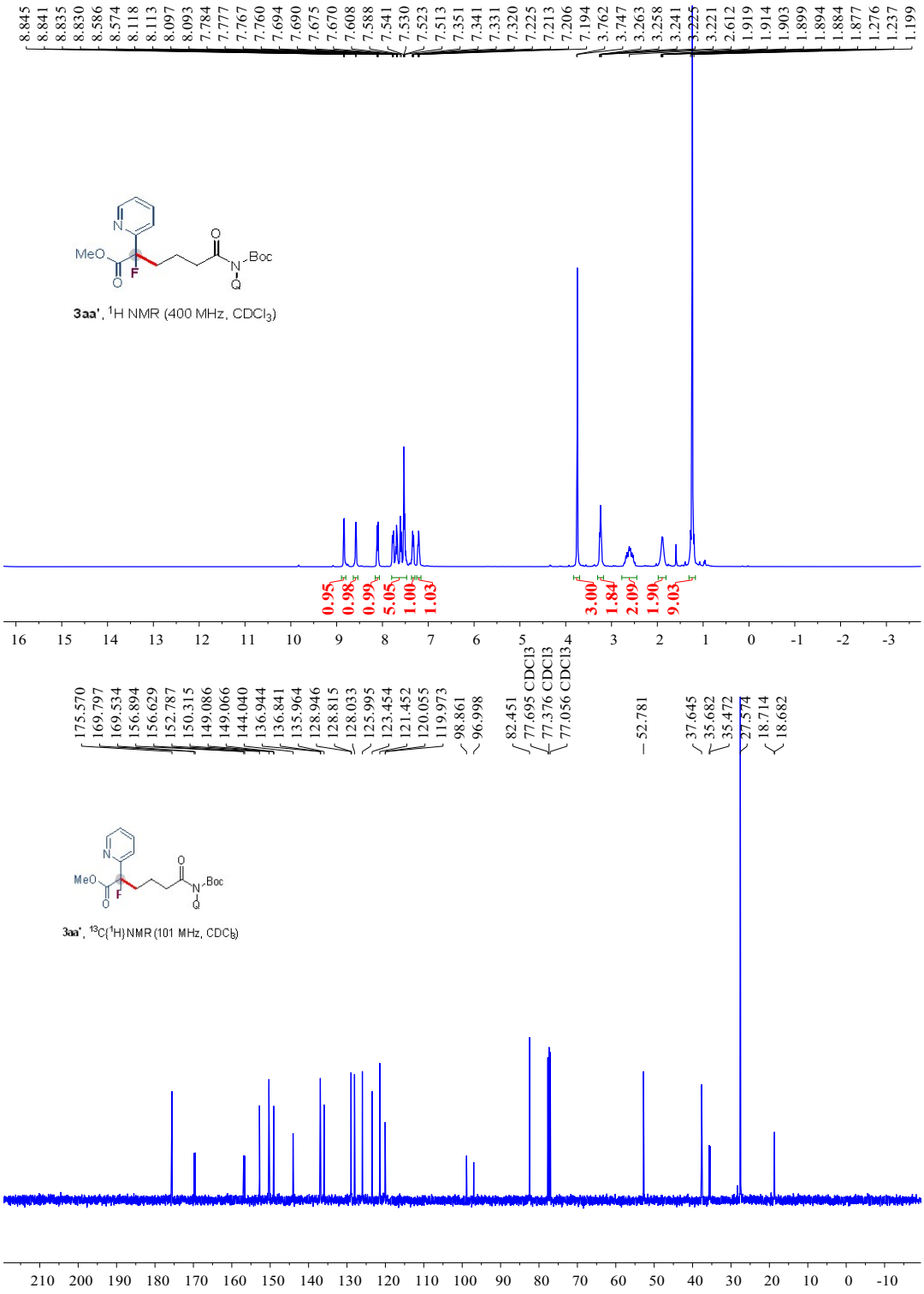


3ah, ^{19}F NMR (376 MHz, $CDCl_3$)

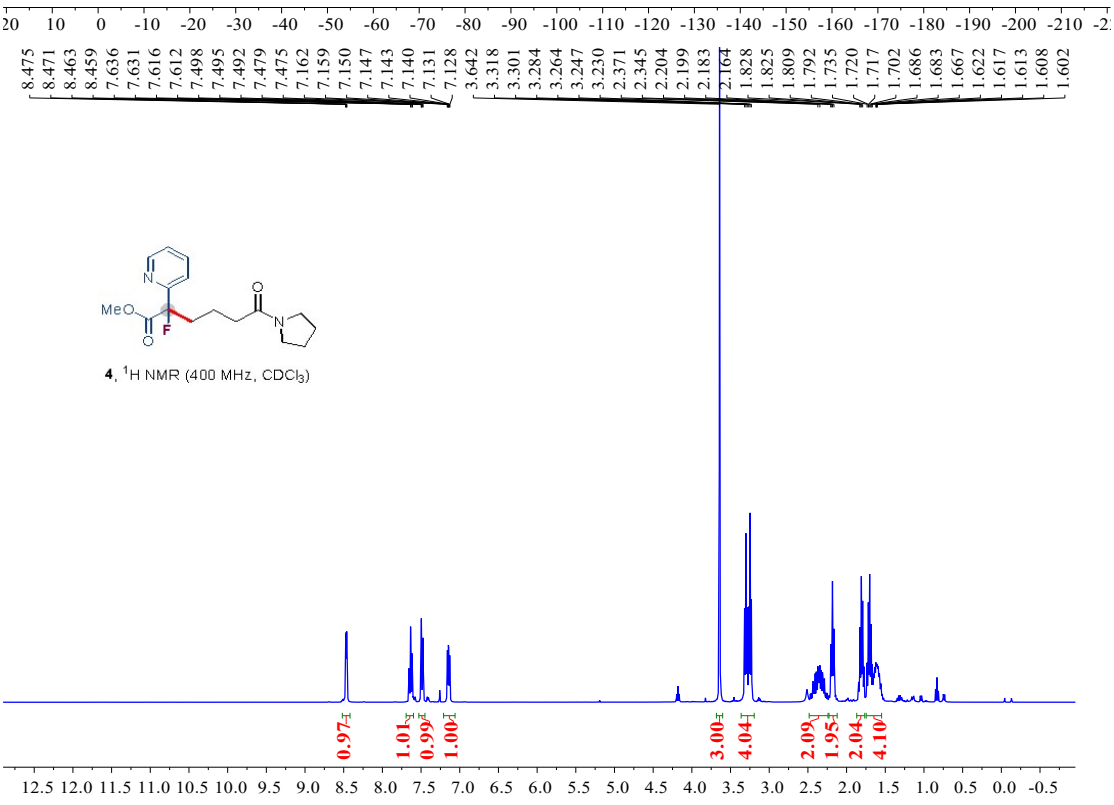


3ai, ^{1}H NMR (400 MHz, $CDCl_3$)

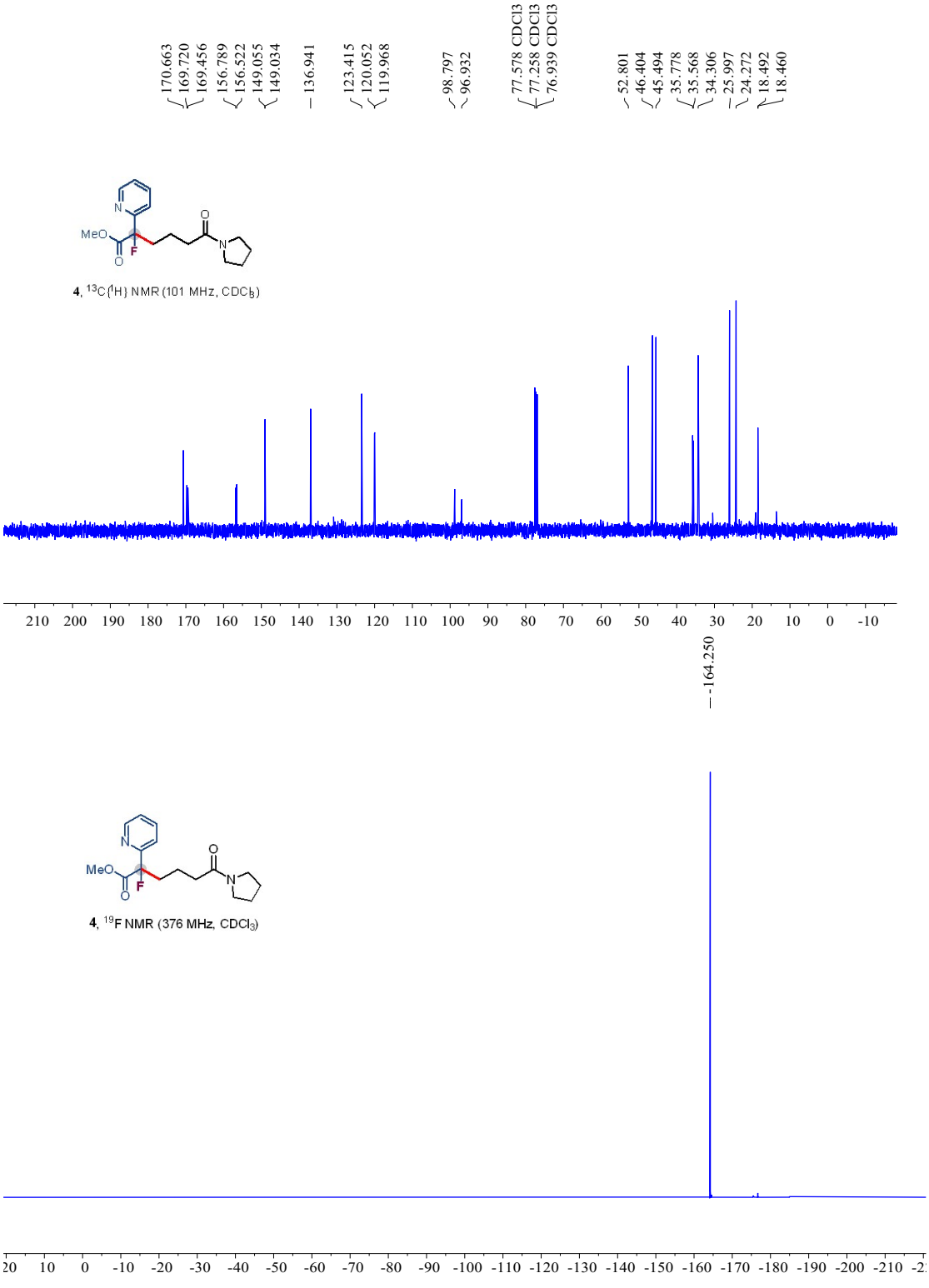

174.017
173.975
169.746
169.509
169.480
156.778
149.210
149.190
149.170
148.168
138.419
138.402
136.990
136.976
136.305
134.507
134.471
127.921
127.908
127.403
127.388
123.487
123.447
121.575
121.412
120.172
120.087
120.005
119.920
116.505
98.828
77.404 CDCl3
77.087 CDCl3
76.768 CDCl3
52.969
49.272
49.244
38.084
38.055
34.323
34.116
33.909
26.123
26.097
26.071
9.228
4.818
4.804
4.311
4.291
MeO
O
F
N
O
AQ
3ai, 13C{1H} NMR (101 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
-163.987
-165.172
MeO
O
F
N
O
AQ
3ai, 19F NMR (376 MHz, CDCl3)
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210

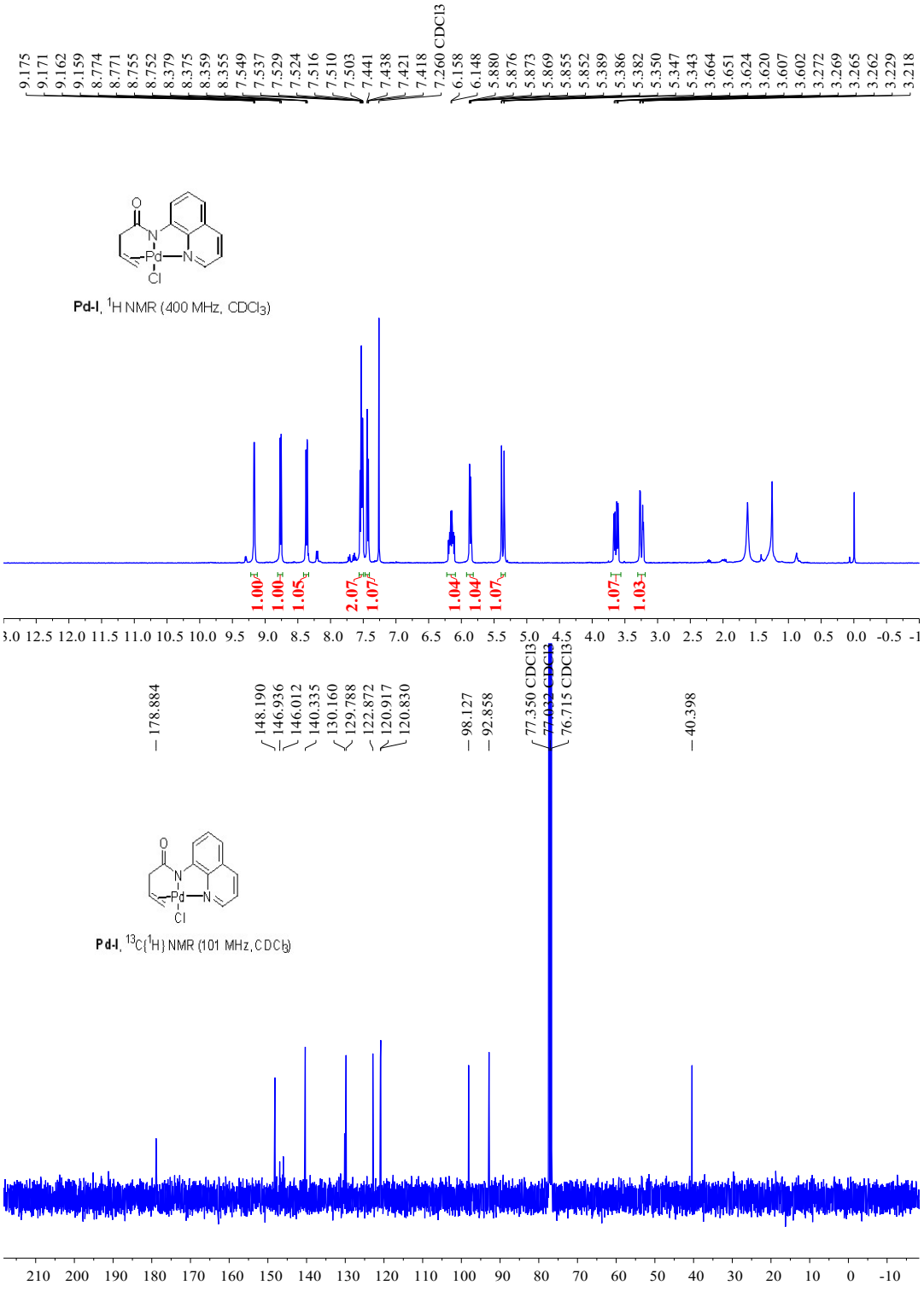

8.845
8.841
8.835
8.830
8.586
8.574
8.118
8.113
8.097
8.093
7.784
7.777
7.767
7.760
7.694
7.690
7.675
7.670
7.608
7.588
7.541
7.530
7.523
7.513
7.351
7.341
7.331
7.320
7.225
7.213
7.206
7.194
3.762
3.747
3.263
3.258
3.241
3.225
3.221
2.612
1.919
1.914
1.903
1.899
1.894
1.884
1.877
1.276
1.237
1.199
MeO
F
O
N
Boc
Q
3aa', 1H NMR (400 MHz, CDCl3)
0.95
0.98
0.99
5.05
1.00
1.03
3.00
1.84
2.09
1.90
9.03
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3
175.570
169.797
169.534
156.894
156.629
152.787
150.315
149.086
149.066
144.040
136.944
136.841
135.964
128.946
128.815
128.033
125.995
123.454
121.452
120.055
119.973
98.861
96.998
82.451
77.695 CDCl3
77.376 CDCl3
77.056 CDCl3
52.781
37.645
35.682
35.472
27.574
18.714
18.682
3aa', 13C{1H} NMR (101 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

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



4, ^{1}H NMR (400 MHz, $CDCl_3$)


170.663
169.720
169.456
156.789
156.522
149.055
149.034
136.941
123.415
120.052
119.968
98.797
96.932
77.578 CDCl3
77.258 CDCl3
76.939 CDCl3
52.801
46.404
45.494
35.778
35.568
34.306
25.997
24.272
18.492
18.460
MeO
F
O
N
4, 13C{1H} NMR (101 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
-164.250
4, 19F NMR (376 MHz, CDCl3)
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210


9.175
9.171
9.162
9.159
8.774
8.771
8.755
8.752
8.379
8.375
8.359
8.355
7.549
7.537
7.529
7.524
7.516
7.510
7.503
7.441
7.438
7.421
7.418
7.260 CDCl3
6.158
6.148
5.880
5.876
5.873
5.869
5.855
5.852
5.389
5.386
5.382
5.350
5.347
5.343
3.664
3.651
3.624
3.620
3.607
3.602
3.272
3.269
3.265
3.262
3.229
3.218
Pd-I, 1H NMR (400 MHz, CDCl3)
1.00
1.00
1.05
2.07
1.07
1.04
1.04
1.07
1.07
1.03
178.884
148.190
146.936
146.012
140.335
130.160
129.788
122.872
120.917
120.830
98.127
92.858
77.350 CDCl3
77.032 CDCl3
76.715 CDCl3
40.398
Pd-I, 13C{1H} NMR (101 MHz, CDCl3)