Supplementary information for

Arene radiofluorination enabled by photoredox-mediated halide interconversion

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1. General information

Methods and materials: Commercially available chemicals reagents and solvents were purchased from Sigma-Aldrich, Alfa Aesar, TCI, Acros, Combi-Blocks,Matrix Scientific, Oakwood Chemical, Chem Impex International, and Fisher Scientific etc. and used as received.

Anhydrous acetonitrile (MeCN), dichloromethane (DCM), tetrahydrofuran (THF) and dimethylformamide (DMF) were dried by an Inert solvent purification system (PS-MD-5).

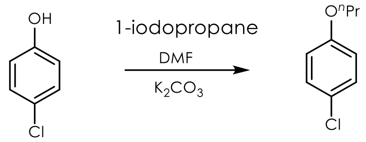
Nuclear magnetic resonance spectra were obtained using a Varian 400 MR or Inova 500 spectrometers. ^{1}H NMR and ^{13}C NMR spectra are referenced to Chloroform-d (^{1}H NMR: 7.26 ppm and ^{13}C NMR: 77.00 ppm), Dimethyl sufoxide-d6 (^{1}H NMR: 2.50 ppm and ^{13}C NMR: 39.63 ppm), D_2O (^{1}H NMR: 4.79 ppm). All spectra are reported as parts per million. ^{1}H, ^{13}C, and ^{19}F NMR data are reported as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, dd = doublet of doublets, td = triplet of doublets, ddd = double of doublet of doublets, m = multiples, app = apparent), coupling constants (Hz), and integration.

High Resolution Mass Spectra (HRMS) were analysed on either ThermoFisher GC Exactive with an Electron Ionization (EI) source or ThermoFisher Q Exactive HF-X (ThermoFisher, Bremen, Germany) mass spectrometer with positive mode electrospray ionization (ESI).

Reverse-phase flash liquid chromatography was performed using a Biotage® Isolera One instrument with a Biotage® SNAP Ultra C18 cartridge.

2. Preparation of arene substrates and fluoroarene standards

Compounds 1-chloro-4-methoxybenzene(**1-Cl**), 1-bromo-4-methoxybenzene(**1-Br**), 1-iodo-4-methoxybenzene(**1-I**), 1-fluoro-4-methoxybenzene(**1-F**), 1-methoxy-4-nitrobenzene (**1-NO_2**), 4-methoxyphenyl trifluoromethanesulfonate (**1-OTf**), 1-bromo-4-(tert-butoxy)benzene （**5-B**r）, 4-chloro-1-methoxy-2-methylbenzene(**6**), 4-fluoro-1-methoxy-2-methylbenzene, 1-chloro-4-methoxy-2-methylbenzene (**7**), 1-fluoro-4-methoxy-2-methylbenzene, 1-bromo-2,4-dimethoxybenzene (**10-Br**), 1-iodo-2,4-dimethoxybenzene(**10-I**), 2,4-dimethoxy-1-nitrobenzene(**10-NO_2**), 1-fluoro-2,4-dimethoxybenzene, 1-chloro-2-methoxybenzene(**17**), 1-fluoro-2-methoxybenzene, 1-chloronaphthalene(**21-Cl**), 1-fluoronaphthalene(**21-F**), 5-chloro-2,3,3-trimethyl-3H-indole(**30-Cl**), 4-fluorobenzo[b]thiophene(**33**), 3-bromo-2,6-dimethoxypyridine(**35**), 6-fluorochroman-4-one(**36**), Cliofibrate(**43**), fluorouracil （**53**）, methyl (S)-2-((tert-butoxycarbonyl)amino)-3-(3,4-dimethoxyphenyl)propanoate(***L*-64**) and other unlabeled reagents were purchased and used directly.

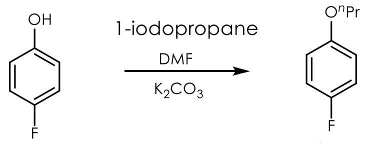


2

1-chloro-4-propoxybenzene (**2**). To a solution of the 4-chlorophenol (386 mg, 3 mmol,1.5 equiv.) in DMF was added anhydrous potassium carbonate (829 mg, 6 mmol, 3 equiv.) follow by the 1-iodopropane (340 mg, 2 mmol, 1 equiv.). The reaction was stirred under room temperature overnight and then extracted with ethyl acetate and water. The organic phase was washed with water, NaOH solution (10%, w/w), water, saturated brine, dried with Na_2SO_4, filtered, and concentrated in vacuo to give the title compound as a colorless liquid (310 mg, 91%) which was used without further purification. Spectral data matched literature data[1]

^{1}H NMR (400 MHz, $CDCl_3$) δ7.25 – 7.18 (m, 2H), 6.86 – 6.78 (m, 2H), 3.89 (t, *J* = 6.6 Hz, 2H), 1.87 – 1.73 (m, 2H), 1.03 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 157.72, 129.22, 125.25, 115.74, 69.79, 22.51, 10.46.



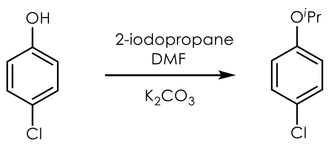
2-F

1-fluoro-4-propoxybenzene (**2-F**). Follow the preparation procedure of compound **2**, the title compound was obtained as a colorless liquid (305 mg, 66%) from with 4-fluorophenol and1-iodopropane.

^{1}H NMR (400 MHz, $CDCl_3$) δ7.03 – 6.91 (m, 2H), 6.89 – 6.77 (m, 2H), 3.88 (t, *J* = 6.6 Hz, 2H), 1.86 – 1.73 (m, 2H), 1.03 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ157.09(d, *J* = 237 Hz), 155.23 (d, *J* = 2.1 Hz), 115.68 (d, *J* = 23Hz), 115.40 (d, *J* = 8Hz), 70.13, 22.59, 10.48.

^{19}F NMR (376 MHz, $CDCl_3$) δ -124.53 (ddd, *J* = 12.5, 8.3, 4.4 Hz).

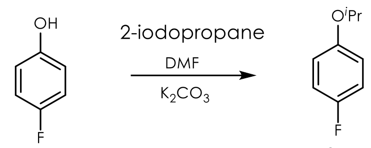


3

1-chloro-4-isopropoxybenzene(**3**). Follow the preparation procedure of compound **2**, the title compound was obtained as a colorless liquid (135 mg, 40%) from 4-chlorophenol and 2-iodopropane.

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.24 – 7.17 (m, 2H), 6.84 – 6.78 (m, 2H), 4.49 (septet, J = 6.0 Hz, 1H), 1.32 (d, J = 6.0 Hz, 6H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 156.46, 129.29, 125.24, 117.17, 70.32, 21.92.



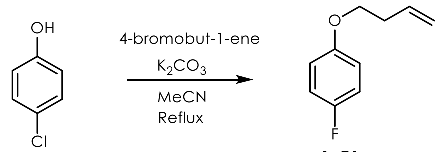
3-F

1-fluoro-4-isopropoxybenzene(**3-F**). Follow the preparation procedure of compound **2**, the title compound was obtained as a colorless liquid from 4-fluorophenol and 2-iodopropane. Spectral data matched literature data[2]

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.00 – 6.89 (m, 2H), 6.87 – 6.78 (m, 2H), 4.45 (septet, *J* = 6 Hz, 1H), 1.31 (d, *J* = 6.0 Hz, 6H).

^{13}C NMR (100 MHz, CDCl$_3$) δ157.14 (d, *J* = 237 Hz), 153.92 (d, *J* = 2.1 Hz), 117.21 (d, *J* = 8.0 Hz), 115.75(d, *J* = 23 Hz), 70.85, 22.00.

^{19}F NMR (376 MHz, CDCl$_3$) δ -124.11 (tt, *J* = 8.5, 4.5 Hz).



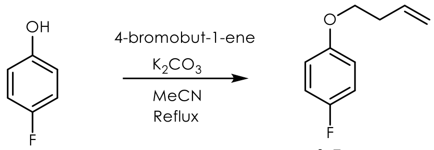
4-Cl

1-(but-3-en-1-yloxy)-4-chlorobenzene (**4-Cl**). To a solution of 4-chlorophenol (257 mg, 2 mmol) in MeCN were added 4-Bromobut-1-ene (540 mg, 4 mmol, 2 equiv.)and potassium carbonate (553 mg, 4 mmol, 2 equiv.). The mixture was stirred under reflux for overnight. The reaction was condensed under reduced pressure and extracted with ethyl acetate and water. The organic phase was washed with NaOH solution (10%, w/w), water, saturated brine, dried with Na_2SO_4, filtered, and concentrated in vacuo and purified by silica gel column with hexane as the eluant to give the title compound as colorless liquid (149 mg, 41%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.25 – 7.20 (m, 2H), 6.86 – 6.79 (m, 2H), 5.89 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H), 5.17 (ddd, *J* = 17.2, 3.2, 1.6 Hz, 1H), 5.14 – 5.09 (m, 1H), 3.98 (t, *J* = 6.7 Hz, 2H), 2.53 (qt, *J* = 6.7, 1.3 Hz, 2H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 157.49, 134.20, 129.27, 125.51, 117.16, 115.82, 67.50, 33.54.

HRMS (EI): Calculated for $C_{10}H_{11}ClO$ $[M]^+$: 182.0498; found: 182.0493.



4-F

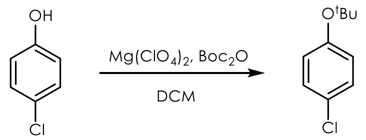
1-(but-3-en-1-yloxy)-4-fluorobenzene (**4-F**). Follow the preparation procedure of compound **4-Cl**, the title compound (**4-F**) was obtained as a colorless liquid (158 mg, 48%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.05 – 6.90 (m, 2H), 6.88 – 6.79 (m, 2H), 5.90 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H), 5.17 (ddd, *J* = 17.2, 3.2, 1.6 Hz, 1H), 5.14 – 5.08 (m, 1H), 3.98 (t, *J* = 6.7 Hz, 2H), 2.53 (qt, *J* = 6.7, 1.3 Hz, 2H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 157.21 (d, *J* = 238.0 Hz), 154.99 (d, *J* = 2.1 Hz), 134.33, 117.06, 115.73 (d, *J* = 23.1 Hz), 115.53 (d, *J* = 7.9 Hz), 67.86, 33.64.

^{19}F NMR (376 MHz, CDCl$_3$) δ -124.12 – -124.26 (m).

HRMS (EI): Calculated for $C_{10}H_{11}FO$ $[M]^+$: 166.0794; found: 166.0789.



5-Cl

1-(tert-butoxy)-4-chlorobenzene (**5-Cl**). The title compound was prepared from reported method[3]. To a solution of 4-chlorophenol (2mmol) and $Mg(ClO_4)_2$ (45 mg, 0.2mmol, 10%) in dichloromethane was added Boc$_2$O (4.6 mmol, 1.0 g, 2.3 equiv.). The resulting solution was heated at 40°C overnight. The solvent was removed under reduce pressure. The residue was extracted with EA and water. The organic phase was washed with 1N HCl, 10% NaOH solution, water, saturated brine in sequence, dried with Na_2SO_4, filtered and concentrated in vacuo to give the product as a colorless liquid (172mg, 47%) which was used without further purification. Spectral data matched literature data[4].

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.25 – 7.19 (m, 2H), 6.96 – 6.88 (m, 2H), 1.33 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 153.94, 128.85, 128.54, 125.44, 78.90, 28.73.

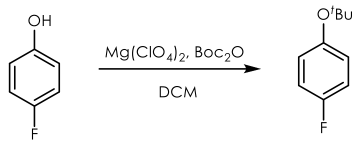
5-I

1-(tert-butoxy)-4-iodobenzene(**5-I**). Follow the same preparation procedure of 1-(tert-butoxy)-4-chlorobenzene(**4-Cl**), the title compound was obtained as a white solid (278 mg, 50%) from

4-iodophenol and purified by silica gel column with ethyl acetate/ hexane (1/20) as the eluant. Spectral data matched literature data[5].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.51 (m, 2H), 6.79 – 6.70 (m, 2H), 1.33 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 155.33, 137.87, 126.34, 86.71, 78.96, 28.75.

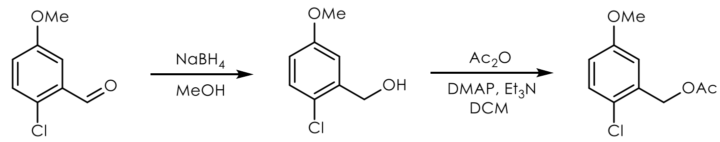


5-F

1-(tert-butoxy)-4-fluorobenzene (**5-F**). The title compound was prepared from the reported literature. Spectral data matched literature data[3]

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95 (d, *J* = 0.5 Hz, 2H), 6.93 (s, 2H), 1.31 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 159.08 (d, *J* = 240 Hz), 151.07 (d, *J* = 2.7 Hz), 125.53 (d, *J* = 8.3 Hz), 115.24 (d, *J* = 22.7 Hz), 78.52 (d, *J* = 1.1 Hz), 28.67.



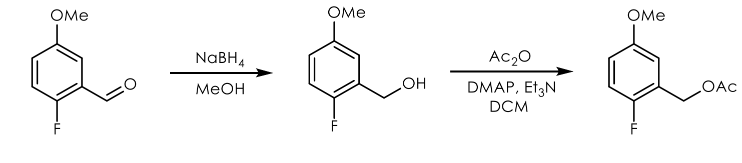
8

2-chloro-5-methoxybenzyl acetate (**8**). To a solution of 2-chloro-5-methoxybenzaldehyde (340 mg, 2 mmol, 1 equiv.) in methanol was added $NaBH_4$ (152 mg, 4 mmol, 2 equiv.) portion-wise. The reaction was stirred under room temperature for 1h and then quenched by the addition of 1N HCl solution. The mixture was extracted with ethyl acetate and water. The organic phase was washed with saturated brine, dried with Na_2SO_4, filtered, and concentrated in vacuo to give the crude intermediate which was then dissolved in dichloromethane followed by the addition of DMAP (12 mg, 0.2 mmol, 0.05 equiv.), triethyl amine (558 μl, 4 mmol, 2 equiv.) acetic anhydride (284 μl, 3 mmol, 1.5 equiv.). The mixture was stirred under room temperature for 2h. Solvent was removed under reduce pressure. The residue was extracted with ethyl acetate and water. The organic phase was washed with 1N HCl, water, saturated brine, dried with Na_2SO_4, filtered, and concentrated in vacuo to give the title compound as a colorless liquid in 86% yield (370 mg) which was used without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.8 Hz, 1H), 6.95 (d, *J* = 3.0 Hz, 1H), 6.80 (dd, *J* = 8.8, 3.0 Hz, 1H), 5.17 (s, 2H), 3.80 (s, 3H), 2.14 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.59, 158.35, 134.47, 130.18, 124.72, 115.32, 114.65, 63.60, 55.53, 20.86.

HRMS (EI): Calculated for $C_{10}H_{11}ClO_3$ $[M]^+$: 214.0397; found: 214.0392.



8-F

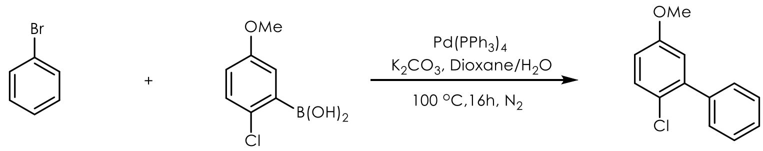
2-fluoro-5-methoxybenzyl acetate(**8-F**). Follow the preparation procedure of compound **8**, the title compound was obtained as a colorless oil (322 mg, 81%) from 2-fluoro-5-methoxybenzaldehyde.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (t, *J* = 9.1 Hz, 1H), 6.89 (dd, *J* = 5.8, 3.2 Hz, 1H), 6.84 – 6.78 (m, 1H), 5.13 (s, 2H), 3.78 (s, 3H), 2.11 (d, *J* = 3.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.69, 155.59 (d, *J* = 2.1 Hz), 155.23 (d, *J* = 239.6 Hz), 123.64 (d, *J* = 16.4 Hz), 115.98 (d, *J* = 23 Hz), 115.28 (d, *J* = 3.7 Hz), 114.90 (d, *J* = 8.0 Hz), 60.21 (d, *J* = 3.9 Hz), 55.76, 20.88.

^{19}F NMR (376 MHz, $CDCl_3$) δ -129.10 (ddd, *J* = 9.6, 5.6, 4.3 Hz).

HRMS (EI): Calculated for $C_{10}H_{11}FO_3$ $[M]^+$: 198.0692; found: 198.0687.



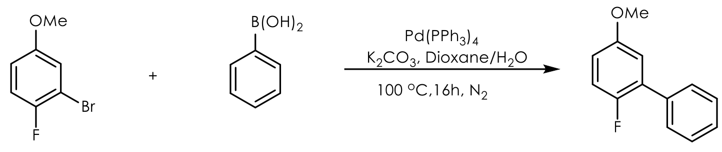
9

2-chloro-5-methoxy-1,1'-biphenyl (**9**). Bromobenzene (0.63 g, 4 mmol, 1.0 equiv.) was weighed in a 100 ml flask with a stir bar. (2-chloro-5-methoxyphenyl)boronic acid (1.83 g, 6 mmol, 1equiv.), potassium carbonate(1.66 g, 12 mmol, 3 equiv.), $Pd(PPh_3)_4$ (462 mg, 0.4 mmol, 0.1 equiv.) were added in sequence. Dioxane and H_2O (3:1, 60 ml) was then added. Vacuumize and refill the mixture with N_2 three times while stirring. The reaction was heated under 100℃ for 16 h under N_2. Most of the solvent was then removed under reduced pressure before ethyl acetate (100 mL) was added to the residue. The solution was passed through a pile of Celatom. Wash the Celatom with additional ethyl acetate (50 mL). The filtration was extracted with water and the organic phase was separated and washed with saturated brine, dried over with Na_2SO_4, filtered and concentrated in vacuo to give crude product which was purified by silica gel column with hexane as the eluant to give the title compound as colorless oil (763 mg, 87%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.43 (m, 4H), 7.43 – 7.39 (m, 1H), 7.38 (d, *J* = 8.8 Hz, 1H), 6.90 (d, *J* = 3.0 Hz, 1H), 6.85 (dd, *J* = 8.7, 3.1 Hz, 1H), 3.82 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 158.18, 141.27, 139.45, 130.55, 129.31, 128.02, 127.65, 123.87, 116.53, 114.30, 55.54.

HRMS (EI): Calculated for $C_{13}H_{11}ClO$ $[M]^+$: 218.0498; found: 202.0493.



9-F

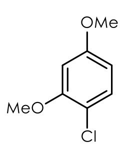
2-fluoro-5-methoxy-1,1'-biphenyl(9-F). 2-bromo-1-fluoro-4-methoxybenzene (205 mg, 1 mmol, 1.0 equiv.) was weighed in a 100 ml flask with a stir bar. Phenylboronic acid (183 mg, 1.5 mmol, 1equiv.), potassium carbonate (414 mg, 3 mmol, 3 equiv.), $Pd(PPh_3)_4$ (58 mg, 0.05 mmol, 0.05 equiv.) were added in sequence. Dioxane and H_2O (3:1, 60 ml) was then added. Vacuumize and refill the mixture with N_2 three times while stirring. The reaction was heated under 100℃ for 16h under N_2. Most of the solvent was then removed under reduced pressure. Ethyl acetate(100ml) was added to the residue. The solution was passed through a pile of Celatom. Washed the Celatom with additional ethyl acetate (50 ml). The filtration was extracted with water and the organic phase was separated and washed with saturated brine, dried over with Na_2SO_4, filtered and concentrated in vacuo to give crude product which was purified by silica gel column with ethyl acetate/ hexane (1/20) as the eluant to give the title compound as colorless oil (176 mg, 87%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.60 – 7.52 (m, 2H), 7.49 – 7.42 (m, 2H), 7.42 – 7.34 (m, 1H), 7.08 (dd, *J* = 9.8, 9.1 Hz, 1H), 6.96 (dd, *J* = 6.3, 3.2 Hz, 1H), 6.84 (dt, *J* = 8.9, 3.5 Hz, 1H), 3.83 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 155.73 (d, *J* = 2.2 Hz), 154.16 (d, *J* = 239 Hz), 135.85 (d, *J* = 1.4 Hz), 129.55 (d, *J* = 15.2 Hz), 128.95 (d, *J* = 3.0 Hz), 128.41, 127.74, 116.57(d, *J* = 24.7 Hz), 115.46 (d, *J* = 3.3 Hz), 113.83 (d, *J* = 8.1 Hz), 55.79.

^{19}F NMR (376 MHz, CDCl$_3$) δ -128.96(m).

HRMS (EI): Calculated for $C_{13}H_{11}FO$ $[M]^+$: 202.0794; found: 202.0789.

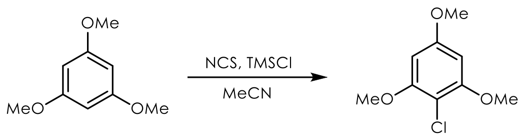


10-Cl

1-chloro-2,4-dimethoxybenzene(10-Cl). The title compound was prepared from reported literature[6].

^{1}H NMR (400 MHz, CDCl$_3$) δ7.24 (d, *J* = 8.7 Hz, 1H), 6.50 (d, *J* = 2.7 Hz, 1H), 6.43 (dd, *J* = 8.7, 2.7 Hz, 1H), 3.87 (s, 3H), 3.79 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 159.44, 155.57, 130.08, 114.09, 105.11, 99.97, 56.01, 55.53.

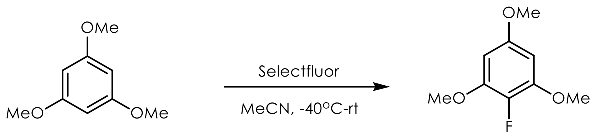


11

2-chloro-1,3,5-trimethoxybenzene (**11**). The title compound was prepared from the reported literature procedure and further purified by stirring in methanol to remove the dechlorinated byproduct. Spectral data matched literature data[7]

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.18 (s, 2H), 3.88 (s, 6H), 3.81 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 159.39, 156.52, 102.68, 91.57, 56.28, 55.52.



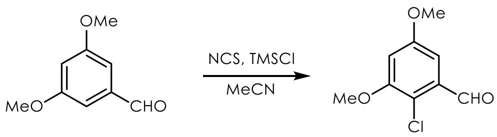
11-F

2-fluoro-1,3,5-trimethoxybenzene(**11-F**). The title compound was prepared from reported literature[8].

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.16 (d, J = 6.2 Hz, 2H), 3.87 (s, 6H), 3.78 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 155.50 (d, J = 3.0 Hz,), 148.59 (d, J = 9.2 Hz), 137.71 (d, J = 235.9 Hz), 92.23, 56.53, 55.65.

^{19}F NMR (376 MHz, CDCl3) δ -168.37 (t, J = 6.1 Hz).



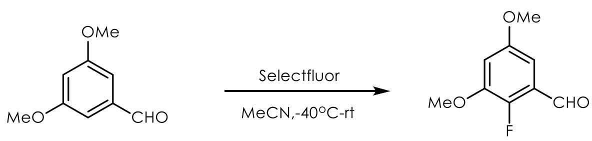
12

2-chloro-3,5-dimethoxybenzaldehyde (**12**). The title compound was prepared from reported chlorination method[7]. The crude solid product after work-up was purified by stirring in methanol. The title compound was obtained as a white solid after filtration.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.49 (s, 1H), 7.01 (d, J = 2.7 Hz, 1H), 6.73 (d, J = 2.8 Hz, 1H), 3.91 (s, 3H), 3.84 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 189.89, 159.07, 156.29, 133.52, 119.59, 106.00, 102.36, 56.50, 55.80.

HRMS (EI): Calculated for $C_9H_9ClO_3$ $[M]^+$: 200.0240; found: 200.0233.



12-F

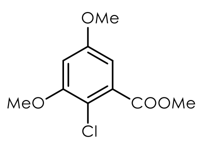
2-fluoro-3,5-dimethoxybenzaldehyde(**12-F**). The title compound was prepared from the same procedure of **11-F**. The product was separated as a white solid which contains ~20% non-fluorinated starting material.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.37 (s, 1H), 6.83 (dd, *J* = 4.1, 3.1 Hz, 1H), 6.77 (dd, *J* = 7.2, 3.0 Hz, 1H), 3.90 (s, 3H), 3.82 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.13, 155.82, 155.53 (d, *J* = 2.0 Hz), 155.39 (d, *J* = 238 Hz), 153.42, 132.65, 130.17, 129.83, 129.30, 124.86 (d, *J* = 16.5 Hz), 124.00, 123.37, 119.11, 118.48, 115.70(d, *J* = 3.8 Hz), 115.46 (d, *J* = 23.9 Hz), 114.50 (d, *J* = 8.0 Hz), 55.63, 44.85 (d, *J* = 3.1 H), 22.11.

^{19}F NMR (376 MHz, $CDCl_3$) δ -154.06 (dd, *J* = 7.3, 4.1 Hz).

HRMS (EI): Calculated for $C_9H_9FO_3$ $[M]^+$: 184.0536; found: 184.0531.



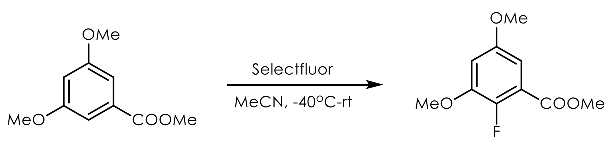
13

methyl 2-chloro-3,5-dimethoxybenzoate(**13**). The title compound was obtained as a colorless oil from the reported chlorination method[7] and purified by flash LC with ethyl acetate/ hexane.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (d, *J* = 2.8 Hz, 1H), 6.61 (d, *J* = 2.8 Hz, 1H), 3.92 (s, 3H), 3.88 (s, 3H), 3.81 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.50, 158.57, 156.35, 132.12, 113.94, 105.80, 102.80, 56.45, 55.69, 52.51.

HRMS (EI): Calculated for $C_{10}H_{11}ClO_4$ $[M]^+$: 230.0346; found: 230.0340.



13-F

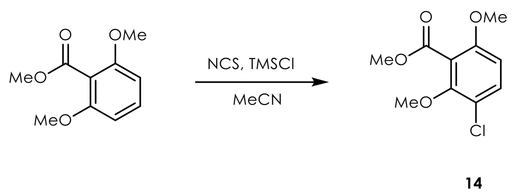
methyl 2-fluoro-3,5-dimethoxybenzoate(**13-F**). The title compound was prepared from the same procedure as **11-F**. white solid was obtained (68 mg, 16%).

^{1}H NMR (400 MHz, CDCl3) δ 6.90 (dd, J = 4.5, 3.1 Hz, 1H), 6.69 (dd, J = 6.6, 3.1 Hz, 1H), 3.93 (s, 3H), 3.87 (s, 3H), 3.81 (s, 3H).

^{13}C NMR (100 MHz, CDCl3) δ 164.99 (d, J = 3.3 Hz), 155.01 (d, J = 2.7 Hz), 149.12 (d, J = 12.3 Hz), 147.09 (d, J = 254.3 Hz), 118.76 (d, J = 8.7 Hz), 105.74 (d, J = 1.8 Hz), 104.05, 56.47, 55.75, 52.39.

^{19}F NMR (376 MHz, CDCl3) δ -141.72 (dd, J = 6.4, 4.7 Hz).

HRMS (EI): Calculated for C10H11FO4 [M]+: 214.0641; found: 214.0636.

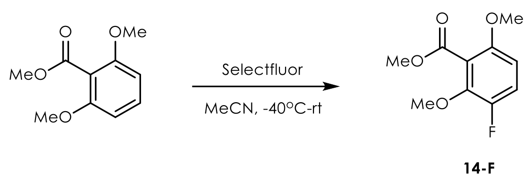


methyl 3-chloro-2,6-dimethoxybenzoate (**14**). The title compound was prepared from reported chlorination method[7]. The crude product was purified by silica gel column using ethyl acetate/ hexane (5% to 10%) to give the title compound as a white solid (190 mg, 83%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.34 (d, *J* = 8.9 Hz, 1H), 6.64 (d, *J* = 8.9 Hz, 1H), 3.93 (s, 3H), 3.89 (s, 3H), 3.81 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 165.81, 155.84, 153.62, 131.51, 119.84, 119.48, 107.73, 61.97, 56.26, 52.62.

HRMS (EI): Calculated for $C_{10}H_{11}ClO_4$ $[M]^+$: 230.0346; found: 230.0342.



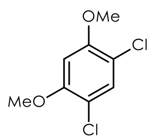
methyl 3-fluoro-2,6-dimethoxybenzoate (**14-F**). Follow the procedure to prepare compound **11-F**, the title compound was obtained as a colorless liquid (146 mg, 68%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.06 (dd, *J* = 11.3, 9.1 Hz, 1H), 6.54 (dd, *J* = 9.1, 3.2 Hz, 1H), 3.94 (d, *J* = 2.1 Hz, 3H), 3.92 (s, 3H), 3.79 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 165.64 (d, *J* = 3.4 Hz), 152.65 (d, *J* = 2.0 Hz), 149.50 (d, *J* = 241.0 Hz), 145.14 (d, *J* = 13.4 Hz), 118.58 (d, *J* = 2.4 Hz), 117.71 (d, *J* = 20.6 Hz), 105.78 (d, *J* = 7.2 Hz), 61.80 (d, *J* = 6.1 Hz), 56.34, 52.58.

^{19}F NMR (376 MHz, CDCl$_3$) δ -139.63 – -139.75 (m)

HRMS (EI): Calculated for $C_{10}H_{11}FO_4$ $[M]^+$: 214.0641; found: 214.0638.

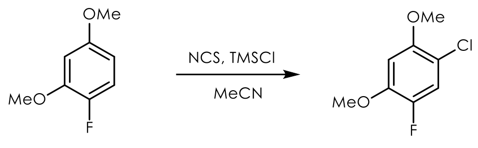


15

1,5-dichloro-2,4-dimethoxybenzene (**15**). The title compound was prepared from reported procedure. Spectral data matched literature data[9].

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.34 (s, 1H), 6.52 (s, 1H), 3.90 (s, 6H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 154.50, 130.47, 113.99, 97.72, 56.49.



15-F

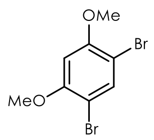
1-chloro-5-fluoro-2,4-dimethoxybenzene(**15-F**). The title compound prepared from reported literature chlorination method[7]. The crude solid product after work-up was purified by silica gel column using ethyl acetate/ hexane (5%) to give the title compound as a white solid (164 mg, 58%) from 1-fluoro-2,4-dimethoxybenzene (234 mg, 1.5 mmol).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.12 (d, *J* = 10.6 Hz, 1H), 6.58 (d, *J* = 7.6 Hz, 1H), 3.90 (s, 3H), 3.88 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 151.53(d, *J* = 25 Hz), 146.72(d, *J* = 11 Hz), 146.38 (d, *J* = 240 Hz), 117.62 (d, *J* = 23 Hz), 113.06 (d, *J* = 8.8 Hz), 99.62 (d, *J* = 2.0 Hz), 56.88.

^{19}F NMR (376 MHz, CDCl$_3$) δ -142.91 (dd, *J* = 10.6, 7.6 Hz).

HRMS (EI): Calculated for $C_8H_8ClFO_2$ $[M]^+$: 190.0197; found: 190.0191.

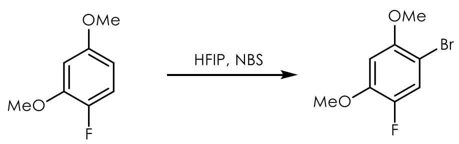


16

1,5-dibromo-2,4-dimethoxybenzene (**16**). The title compound was prepared from reported procedure. Spectral data matched literature data[10].

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.63 (s, 1H), 6.47 (s, 1H), 3.89 (s, 6H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 156.14, 135.86, 102.39, 97.40, 56.51.



16-F

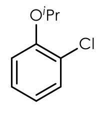
1-bromo-5-fluoro-2,4-dimethoxybenzene(**16-F**). Follow the reported method[11], the title compound was obtained as an off-white solid (225 mg, 64%) from 1-fluoro-2,4-dimethoxybenzene(234 mg, 1.5 mmol).

H NMR (400 MHz, CDCl$_3$) δ 7.27 (d, *J* = 10.4 Hz, 1H), 6.56 (d, *J* = 7.4 Hz, 1H), 3.90 (s, 3H), 3.87 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 152.49 (d, J = 2.6), 147.35 (d, J = 11.4 Hz), 146.64(d, J = 241 Hz), 120.27 (d, J = 22.3 Hz), 100.72 (d, J = 8.1 Hz), 99.30, 56.92, 56.75

^{19}F NMR (376 MHz, $CDCl_3$) δ -142.78 – -143.13 (m).

HRMS (EI): Calculated for $C_8H_8BrFO_2$ $[M]^+$: 190.0197; found: 190.0191.



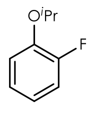
18

1-chloro-2-isopropoxybenzene (**18**). Follow the preparation procedure of compound **2**, the title compound was obtained as a light-yellow liquid (380 mg, 75%) from 2-chlorophenol and 2-iodopropane.

^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (dd, J = 7.6, 1.6 Hz, 1H), 7.22-7.15 (m, 1H), 6.95 (dd, J = 8.4, 1.2Hz, 1H), 6.92-6.85 (m, 1H), 4.55 (septet, J = 6.0 Hz, 1H), 1.38 (d, J = 6.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 153.66, 130.40, 127.48, 124.30, 121.46, 116.13, 72.08, 22.05.

HRMS (EI): Calculated for $C_9H_{11}ClO$ $[M]^+$: 170.0498; found: 170.0490.



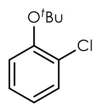
18-F

1-fluoro-2-isopropoxybenzene(**18-F**). Follow the preparation procedure of compound **2**, the title compound was obtained as a colorless liquid (403 mg, 87%) from 2-fluorophenol and 2-iodopropane.

^1H NMR (400 MHz, $CDCl_3$) δ 7.13 – 6.94 (m, 3H), 6.93 – 6.85 (m, 1H), 4.53 (hept, J = 6.1 Hz, 1H), 1.36 (d, J = 6.1 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 153.82 (d, J = 244 Hz), 145.81 (d, J = 10.3 Hz, 2H), 124.15 (d, J = 3.8 Hz), 121.39 (d, J = 7.0 Hz), 117.84 (d, J = 2.1 Hz), 116.37 (d, J = 18.9 Hz), 72.35, 22.07.

^{19}F NMR (376 MHz, $CDCl_3$) δ -133.35 – -133.47 (m).

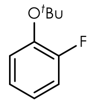


19-Cl

1-(tert-butoxy)-2-chlorobenzene(**19-Cl**). The title compound was prepared from the same procedure as compound **4-Cl** starting with 2-chlorophenol. Colorless liquid (108 mg, 29%) was obtained. Spectral data matched literature data[12].

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.37 (dd, J = 8.0, 1.5 Hz, 1H), 7.20 – 7.08 (m, 2H), 6.99 (ddd, J = 7.9, 7.1, 1.9 Hz, 1H), 1.42 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 152.06, 130.27, 129.22, 127.02, 124.67, 123.94, 81.22, 28.89.



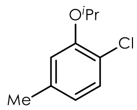
19-F

1-(tert-butoxy)-2-fluorobenzene(**19-F**). The title compound was prepared from the same procedure of compound **4-Cl** from 2-fluorophenol. Colorless liquid (88 mg, 26%) was obtained.

^{1}H NMR (400 MHz, CDCl$_3$) δ7.17 – 6.93 (m, 4H), 1.36 (d, *J* = 0.8 Hz, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 157.09 (d, *J* = 245.2 Hz), 142.72 (d, *J* = 11.6 Hz), 126.95 (d, *J* = 1.5 Hz), 124.42 (d, *J* = 7.3 Hz), 123.77 (d, *J* = 3.9 Hz), 116.43 (d, *J* = 20.2 Hz), 80.48, 28.46 (d, *J* = 1.2 Hz).

^{19}F NMR (376 MHz, CDCl$_3$) δ -127.05 – -127.20.



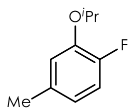
20

1-chloro-2-isopropoxy-4-methylbenzene (**20**). Follow the preparation procedure of compound **2**, the title compound was obtained as a colorless liquid (415 mg, 75%) from 2-chloro-5-methylphenol and 2-iodopropane.

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.22 (d, *J* = 8.0 Hz, 1H), 6.77 (s, 1H), 6.70 (dd, *J* = 8.0, 1.1 Hz, 1H), 4.53 (hept, *J* = 6.1 Hz, 1H), 2.31 (s, 3H), 1.37 (d, *J* = 6.1 Hz, 6H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 153.31, 137.5, 129.8, 122.25, 121.23, 117.16, 72.08, 22.09, 21.28.

HRMS (EI): Calculated for $C_{10}H_{13}ClO$ $[M]^+$: 184.0655; found: 184.0649.



20-F

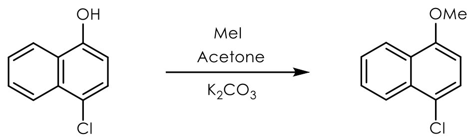
1-fluoro-2-isopropoxy-4-methylbenzene(**20-F**). Follow the preparation procedure of compound **2**, the title compound was obtained as a colorless liquid (304 mg, 90%) from 2-fluoro-5-methylphenol and 2-iodopropane.

^{1}H NMR (400 MHz, CDCl$_3$) δ 6.94 (dd, *J* = 11.3, 8.2 Hz, 1H), 6.79 (dd, *J* = 8.0, 1.6 Hz, 1H), 6.72 – 6.64 (m, 1H), 4.51 (hept, *J* = 6.1 Hz, 1H), 2.29 (s, 3H), 1.35 (d, *J* = 6.1 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 151.97 (d, *J* = 242.4 Hz), 145.26 (d, *J* = 10.7 Hz), 133.81 (d, *J* = 3.9 Hz), 121.70 (d, *J* = 6.8 Hz), 118.69 (d, *J* = 1.9 Hz), 115.85 (d, *J* = 18.8 Hz), 72.35, 22.12, 21.01.

^{19}F NMR (376 MHz, $CDCl_3$) δ -138.18 – -138.31 (m).

HRMS (EI): Calculated for $C_{10}H_{13}FO$ $[M]^+$: 168.0950; found: 168.0944.

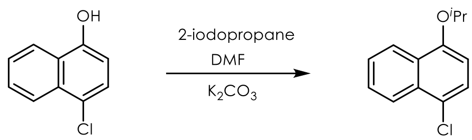


22

1-chloro-4-methoxynaphthalene (**22**). To a solution of the 4-chloro-2-methylphenol (500 mg, 2.81 mmol, 1.0 equiv.) in acetone was added anhydrous potassium carbonate (776 mg, 5.62 mmol) follow by the iodomethane (875 μl, 14.05 mmol, 5 equiv.). The reaction was stirred under room temperature overnight. Solvent was removed under reduce pressure. The residue was then extracted with ethyl acetate and water. The organic phase was washed with water, NaOH solution (10%, w/w), water, saturated brine, dried with Na_2SO_4, filtered, and concentrated in vacuo to give the crude product which was then purified by silica gel column with ethyl acetate/ hexane (1/10) to afford the title compound in 85% yield (462 mg) as a colorless liquid. Spectral data matched literature data[13].

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 – 8.24 (m, 1H), 8.24 – 8.17 (m, 1H), 7.62 (ddd, *J* = 8.4, 6.9, 1.3 Hz, 1H), 7.54 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.46 (d, *J* = 8.2 Hz, 1H), 6.72 (d, *J* = 8.2 Hz, 1H), 3.99 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 154.55, 131.25, 127.44, 126.56, 125.89, 125.72, 124.19, 123.16, 122.38, 103.77, 55.66.



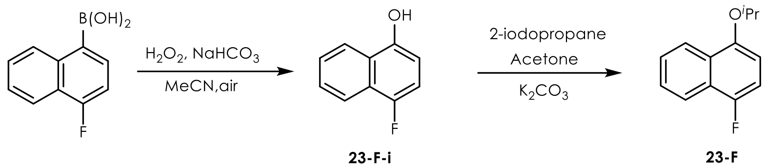
23

1-chloro-4-isopropoxynaphthalene (**23**). To a solution of the 4-chloro-2-methylphenol (356 mg, 2 mmol, 1.0 equiv.) in DMF was added anhydrous potassium carbonate (552 mg, 4 mmol, 2 equiv.), follow by the 2-iodopropane (680 mg, 4 mmol, 2equiv.). The reaction was stirred under room temperature overnight and then extracted with ethyl acetate and water. The organic phase was washed with water, NaOH solution (10%, w/w), water, saturated brine, dried with Na_2SO_4, filtered, and concentrated in vacuo to give the crude product which was then purified by silica gel column with ethyl acetate/ hexane (1/10) to afford the title compound in 70% yield (308 mg) as a colorless oil.

¹H NMR (400 MHz, CDCl₃) δ 8.37 – 8.27 (m, 1H), 8.24 – 8.15 (m, 1H), 7.60 (ddd, *J* = 8.4, 6.8, 1.3 Hz, 1H), 7.52 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.45 (d, *J* = 8.3 Hz, 1H), 6.75 (d, *J* = 8.3 Hz, 1H), 4.72 (hept, *J* = 6.0 Hz, 1H), 1.45 (d, *J* = 6.1 Hz, 7H).

¹³C NMR (100 MHz, CDCl₃) δ 152.76, 131.50, 127.55, 127.31, 125.77, 125.69, 124.14, 122.76, 122.70, 106.26, 70.66, 22.00.

HRMS (EI): Calculated for $C_{13}H_{13}ClO$ $[M]^+$: 220.0655; found: 220.0649.



4-fluoronaphthalen-1-ol(**23-F-i**). The title compound was prepared from reported method[14].

¹H NMR (400 MHz, CDCl₃) δ 8.20 – 8.12 (m, 1H), 8.10-8.03 (m, 1H), 7.62 – 7.50 (m, 2H), 6.98 (dd, *J* = 10.2, 8.2 Hz, 1H), 6.71 (dd, *J* = 8.2, 4.0 Hz, 1H), 5.21 (br, 1H).

¹³C NMR (100 MHz, CDCl₃) δ 153.19 (d, *J* = 243Hz), 147.31 (d, *J* = 3.1 Hz), 126.69 (d, *J* = 1.9 Hz), 126.17 (d, *J* = 0.6 Hz), 125.06 (d, *J* = 4.8 Hz), 124.36 (d, *J* = 18.2 Hz), 121.75 (d, *J* = 2.5 Hz), 120.52 (d, *J* = 4.5 Hz), 108.71(d, *J* = 21.7 Hz), 107.47 (d, *J* = 8.0 Hz).

¹⁹F NMR (376 MHz, CDCl₃) δ -132.40 (ddd, *J* = 10.2, 3.9, 1.8 Hz).

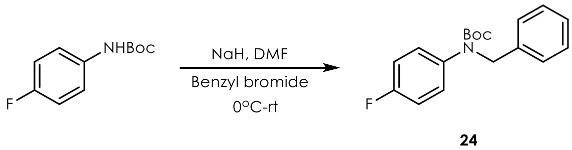
1-fluoro-4-isopropoxynaphthalene(**23-F**). Follow the preparation procedure of compound **23**, the title compound was obtained as a brown oil (134 mg, 66%) from 4-fluoronaphthalen-1-ol and 2-iodopropane.

¹H NMR (400 MHz, CDCl₃) δ 8.35-8.18 (m, 1H), 8.09 – 8.00 (m, 1H), 7.53 (pd, *J* = 6.9, 1.4 Hz, 2H), 7.03 (dd, *J* = 10.3, 8.4 Hz, 1H), 6.72 (dd, *J* = 8.4, 4.0 Hz, 1H), 4.68 (hept, *J* = 6.0 Hz, 1H), 1.44 (d, *J* = 6.1 Hz, 6H).

¹³C NMR (100 MHz, CDCl₃) δ 152.83 (d, *J* = 242 Hz), 149.74 (d, *J* = 3.0 Hz), 127.39 (d, *J* = 4.6 Hz,), 126.51 (d, *J* = 1.8 Hz), 125.91 (d, *J* = 0.5 Hz), 124.46 (d, *J* = 18.1 Hz), 122.48 (d, *J* = 2.4 Hz), 120.23 (d, *J* = 4.6 Hz), 108.62 (d, *J* = 21.4 Hz), 105.81 (d, *J* = 8.0 Hz, 12H), 71.01, 22.08.

¹⁹F NMR (376 MHz, CDCl₃) δ -133.39 (ddd, *J* = 10.3, 3.9, 1.7 Hz).

HRMS (EI): Calculated for $C_{13}H_{13}FO$ $[M]^+$: 204.0950; found: 204.0946.



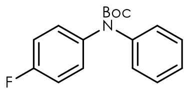
tert-butyl benzyl(4-fluorophenyl) carbamate (**24**). To a solution of tert-butyl (4-fluorophenyl)carbamate (211mg, 1mmol, 1equiv.) in DMF was added NaH (60% wt/wt, 60 mg, 1.5 mmol, 1.5 equiv.) at 0℃. The solution was stirred for additional 15 min. and benzyl bromide (143 μl, 1.2 mmol, 1.2 equiv.) was then added. The reaction was warned to room temperature and stirred for 1h. The solution was then diluted with ethyl acetate and water. The organic phase was washed with water, saturated brine, dried over with Na_2SO_4, filtered and concentrated in vacuo to give the crude product which was purified by silica gel column with ethyl acetate/ hexane (1/20) as the eluant to give the title compound as a white solid (243 mg, 81%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.34 – 7.23 (m, 3H), 7.23 – 7.18 (d, *J* = 6.8 Hz, 2H), 7.17 – 6.99 (s, 2H), 6.94 (t, *J* = 8.6 Hz, 2H), 4.79 (s, 2H), 1.42 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 160.59 (d, *J* = 245.2 Hz), 154.83, 138.60 (d, *J* = 2.5 Hz), 138.27, 128.50, 128.41, 127.59, 127.19, 115.39 (d, *J* = 22.5 Hz), 80.63, 54.03, 28.26.

^{19}F NMR (376 MHz, CDCl$_3$) δ -116.33.

HRMS (EI): Calculated for $C_{18}H_{20}FNO_2$ $[M]^+$: 301.1478; found: 301.1472.



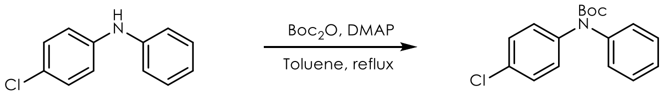
25-F

tert-butyl (4-fluorophenyl)(phenyl)carbamate(**25-F**). The title compound was obtained from our reported method[15].

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.39 – 7.27 (m, 2H), 7.24 – 7.13 (m, 5H), 7.06 – 6.93 (m, 2H), 1.45 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 160.41 (d, *J* = 245.4 Hz), 153.76, 142.88, 139.00 (d, *J* = 3.2 Hz), 128.73, 128.67 (d, *J* = 8.4 Hz), 126.72, 125.67, 115.51 (d, *J* = 22.6 Hz), 81.29, 28.20.

^{19}F NMR (376 MHz, CDCl$_3$) δ -116.61 (s).



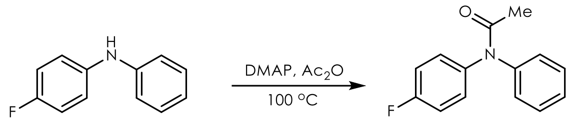
25-Cl

tert-butyl (4-chlorophenyl)(phenyl)carbamate(**25-Cl**). To a solution of the 4-chloro-N-phenylaniline (102 mg, 0.5 mmol, 1.0 equiv.) and DMAP (61mg, 0.5 mmol, 1.0 equiv.) in toluene was added di-tert-butyl dicarbonate (131 mg, 0.6 mmol, 1.2 equiv.). The reaction was stirred under reflux for 1h and then extracted with ethyl acetate and water. The organic phase was washed with 1N HCl solution, saturated brine, dried with Na_2SO_4, filtered, and concentrated in vacuo to give the residue which was purified by silica gel chromatography using ethyl acetate/hexane (0 ~ 1/10) to afford the title compound as a white solid (140 mg, 92%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.35 – 7.28 (m, 2H), 7.28 – 7.23 (m, 2H), 7.22 – 7.10 (m, 5H), 1.44 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 153.54, 142.62, 141.64, 130.95, 128.83, 128.76, 127.99, 127.05, 125.95, 81.49, 28.20.

HRMS (EI): Calculated for $C_{17}H_{18}ClNO_2$ $[M]^+$: 303.1026; found: 303.1020.



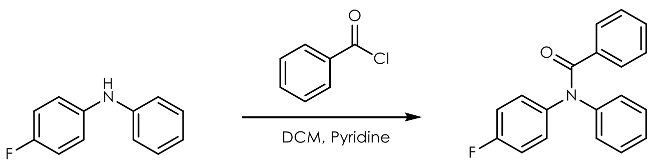
26

N-(4-fluorophenyl)-N-phenylacetamide (**26**). To a solution of 4-fluoro-N-phenylaniline (187 mg, 1 mmol) in 5 ml acetic anhydride was added DMAP (122 mg, 1 mmol, 1equiv.). The solution was stirred under 100℃ for 5h. The solution was poured into water and extracted with ethyl acetate. The organic phase was separated and washed with water, 10% (w/w) NaOH solution, saturated brine, dried with Na_2SO_4, filtered, and concentrated in vacuo to give the crude product which was purified by silica gel chromatography using ethyl acetate/hexane (3/10) to afford the title compound as a light-yellow oil (190 mg, 83%). Spectral data matched literature data[16].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 6.88 (m, 9H), 2.06 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 55 ℃) δ 170.17, 160.96 (d, *J* = 243.7 Hz), 143.08, 139.07, 131.19 – 125.21 (m), 115.87, 23.63 – 23.28 (m).

^{19}F NMR (376 MHz, $CDCl_3$) δ -113.24, -115.98.



27

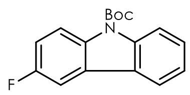
N-(4-fluorophenyl)-N-phenylbenzamide (27). To a solution of 4-fluoro-N-phenylaniline (94 mg, 0.5 mmol, 1 equiv.) in DCM were added pyridine (40 μl, 1 mmol, 2 equiv.) and benzoyl chloride (70 μl, 0.6 mmol, 1.2 equiv.) sequentially. The solution was stirred under room temperature for 3h. The mixture was then extracted with ethyl acetate and water. The organic phase was washed with water, 1N HCl solution, 10% NaOH solution, saturated brine, dried with Na_2SO_4, filtered, and concentrated in vacuo to give the crude product which was purified by stirring in ethyl acetate/ hexane (1/20). The title compound was obtained as an off-white solid after filtration (118 mg, 81%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.40 (m, 2H), 7.32 – 7.26 (m, 2H), 7.24 – 7.17 (m, 3H), 7.17 – 7.09 (m, 4H), 7.05 – 6.93 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.58, 160.72 (d, *J* = 246.8 Hz), 143.76, 139.83 (d, *J* = 3.1 Hz), 135.81, 130.24, 129.17, 129.08, 129.02, 128.93, 127.90, 127.37, 126.44, 116.00 (d, *J* = 22.8 Hz).

^{19}F NMR (376 MHz, CDCl$_3$) δ -115.36.

HRMS (EI): Calculated for $C_{19}H_{14}FNO$ [M]$^+$: 291.1059; found: 291.1056.



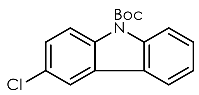
28-F

tert-butyl 3-fluoro-9H-carbazole-9-carboxylate(**28-F**). The title compound was obtained from reported method[15].

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.40 – 8.20 (m, 2H), 7.92 (dd, *J* = 7.7, 0.6 Hz, 1H), 7.61 (dd, *J* = 8.3, 2.6 Hz, 1H), 7.49 (ddd, *J* = 8.5, 7.3, 1.2 Hz, 1H), 7.35 (ddd, *J* = 8.2, 7.5, 0.8 Hz, 1H), 7.18 (td, *J* = 9.0, 2.7 Hz, 1H), 1.77 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 159.26 (d, *J* = 240.6 Hz), 150.87, 139.14, 134.65 (d, *J* = 1.1 Hz), 127.63, 126.84 (d, *J* = 9.5 Hz), 125.09 (d, *J* = 3.6 Hz), 122.99, 119.76, 117.31 (d, *J* = 8.6 Hz), 116.41, 114.25 (d, *J* = 24.2 Hz), 105.54 (d, *J* = 23.9 Hz), 84.09, 28.36.

^{19}F NMR (376 MHz, CDCl$_3$) δ -120.23 (td, *J* = 8.7, 4.6 Hz, 1H).



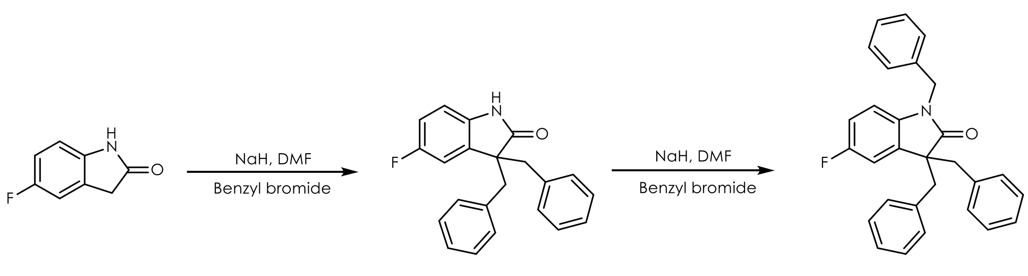
28-Cl

tert-butyl 3-chloro-9H-carbazole-9-carboxylate(**28-Cl**). The title compound was prepared as a white solid from the same procedure of compound **28-F** starting with 3-chloro-9H-carbazole which was synthesized from reported procedure[17].

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.26 (dd, *J* = 14.0, 8.7 Hz, 2H), 7.96 – 7.89 (m, 2H), 7.53 – 7.46 (m, 1H), 7.41 (dd, *J* = 8.9, 2.2 Hz, 1H), 7.36 (td, *J* = 7.8, 0.8 Hz, 1H), 1.76 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 150.81, 138.86, 136.86, 128.56, 127.74, 127.09, 126.98, 124.66, 123.21, 119.75, 119.36, 117.36, 116.37, 84.32, 28.36.

HRMS (EI): Calculated for $C_{12}H_8NCl$ [M]$^+$: 201.0345; found: 201.0340.



29-i **29**

3,3-dibenzyl-5-fluoroindolin-2-one(**29-i**). To a solution of 5-fluoroindolin-2-one (302 mg, 2 mmol, 1equiv.) in DMF was added NaH (60% wt/wt, 160 mg, 4 mmol, 2 equiv.) at 0℃. The solution was stirred for additional 30 min and benzyl bromide were (475 μl, 4 mmol, 2 equiv.) then added. The reaction was warned to room temperature and stirred overnight. The reaction solution was poured into water. The crude solid product was collected by filtration and then stirred in hexane to get the intermediate which was used directly in the next step without further purification (419 mg, 63%).

^{1}H NMR (400 MHz, DMSO-d6) δ 9.95 (s, 1H), 7.43 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.06 – 7.01 (m, 6H), 6.91 – 6.84(m, 4H), 6.75 (td, *J* = 9.7, 2.6 Hz, 1H), 6.30 (dd, *J* = 8.4, 4.4 Hz, 1H), 3.25 – 3.13 (m, 4H).

^{13}C NMR (100 MHz, DMSO-d6) δ 179.81, 157.92 (d, *J* = 235.8 Hz), 138.22 (d, *J* = 1.7 Hz), 136.40, 132.84 (d, *J* = 8.3 Hz), 129.89, 127.89, 126.67, 114.08 (d, *J* = 23.3 Hz), 112.69 (d, *J* = 24.5 Hz), 109.68 (d, *J* = 8.2 Hz), 57.30 (d, *J* = 1.7 Hz), 43.04.

^{19}F NMR (376 MHz, DMSO-d6) δ -122.01 – -122.15 (m).

HRMS (EI): Calculated for $C_{22}H_{18}FNO$ $[M]^+$: 331.1372; found: 331.1369.

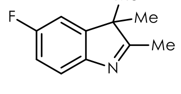
1,3,3-tribenzyl-5-fluoroindolin-2-one (**29**). To a solution of 5-fluoroindolin-2-one （166 mg, 0.5 mmol, 1equiv.） in DMF was added NaH (60% wt/wt, 30 mg, 0.75 mmol, 1.5 equiv.) at 0℃. The solution was stirred for additional 15 min and benzyl bromide were (71 μl, 0.6 mmol, 1.2 equiv.) then added. The reaction was warned to room temperature and stirred for 2 h. The reaction solution was extracted with ethyl acetate and water. The organic phase was washed with water, saturated brine, dried over with Na_2SO_4, filtered and concentrated in vacuo to give the crude solid product which was washed with hexane to get the title compound as a light-yellow solid (125 mg, 60%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.19 – 7.00 (m, 5H), 7.00 – 6.92 (m, 2H), 6.69 – 6.61 (m, 0H), 6.37 (d, *J* = 7.4 Hz, 1H), 6.03 (dd, *J* = 8.5, 4.2 Hz, 0H), 4.54 (d, *J* = 29.1 Hz, 1H), 3.42 (d, *J* = 13.0 Hz, 1H), 3.22 (d, *J* = 13.0 Hz, 1H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 177.78, 158.68 (d, *J* = 240.1 Hz), 138.80 (d, *J* = 1.9 Hz), 135.53, 134.72, 131.97 (d, *J* = 7.8 Hz), 130.12, 128.44, 127.86, 126.97, 126.64, 126.24, 114.11 (d, *J* = 23.4 Hz), 112.00 (d, *J* = 24.5 Hz), 109.48 (d, *J* = 8.1 Hz), 56.98 (d, *J* = 1.7 Hz), 43.62, 43.13.

^{19}F NMR (376 MHz, CDCl$_3$) δ -121.00 – -121.18 (m).

HRMS (EI): Calculated for $C_{29}H_{24}FNO$ $[M]^+$: 421.1842; found: 421.1838.

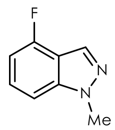


30-F

5-fluoro-2,3,3-trimethyl-3H-indole(**30-F**). The title compound was prepared from reported procedure. Spectra data were in agreement with literature values[18].

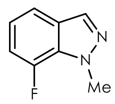
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.46 – 7.40 (m, 1H), 7.00 – 6.92 (m, 2H), 2.24 (s, 3H), 1.28 (s, 6H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 187.62 (d, *J* = 3.5 Hz), 161.12 (d, *J* = 243.6 Hz), 149.57 (d, *J* = 2.2 Hz), 147.55 (d, *J* = 8.5 Hz), 120.40 (d, *J* = 8.8 Hz), 114.01 (d, *J* = 23.6 Hz), 108.99 (d, *J* = 24.3 Hz), 54.09 (d, *J* = 2.2 Hz), 22.94 15.32.
^{19}F NMR (376 MHz, CDCl$_3$) δ -117.75 (tt, *J* = 17.0, 8.5 Hz).



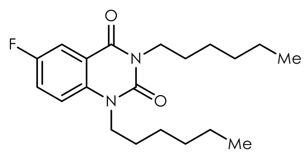
31

4-fluoro-1-methyl-1H-indazole (**31**). The title compound was prepared according to a published procedure; Spectra data were in agreement with literature values[19].
^{1}H NMR (400 MHz, CDCl$_3$) δ 8.04 (s, 1H), 7.36 – 7.23 (m, 1H), 7.15 (d, *J* = 8.4 Hz, 1H), 6.85 – 6.72 (m, 1H), 4.07 (d, *J* = 0.5 Hz, 3H).
^{13}C NMR (100 MHz, CDCl$_3$) δ 155.80 (d, *J* = 252.3 Hz), 142.48 (d, *J* = 9.4 H), 129.15 (d, *J* = 2.0 Hz), 127.09 (d, *J* = 7.7 Hz), 114.29 (d, *J* = 23.4 Hz), 104.93 (d, *J* = 4.2 Hz), 104.65 (d, *J* = 18.6 Hz), 35.79.
^{19}F NMR (376 MHz, CDCl$_3$) δ -118.13 (dd, *J* = 10.0, 4.9 Hz).



32

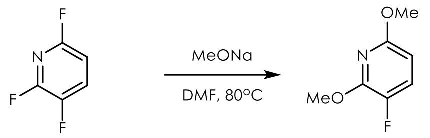
7-fluoro-1-methyl-1H-indazole (**32**). The title compound was prepared from a reported literature method. Spectra data were in agreement with literature values[20].
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.96 (d, *J* = 2.4 Hz, 1H), 7.46 (dd, *J* = 6.2, 2.7 Hz, 1H), 7.06 – 6.97 (m, 2H), 4.26 (d, *J* = 0.9 Hz, 3H).
^{13}C NMR (100 MHz, CDCl$_3$) δ 148.57 (d, *J* = 246.8 Hz,), 133.08 (d, *J* = 1.3 Hz), 129.45 (d, *J* = 12.8 Hz), 128.00 (d, *J* = 4.3 Hz), 120.88 (d, *J* = 5.5 Hz), 116.69 (d, *J* = 4.3 Hz), 110.70 (d, *J* = 17.1 Hz), 38.20 (d, *J* = 4.3 Hz).
^{19}F NMR (376 MHz, CDCl$_3$) δ -135.16 – -135.26 (m).



34

6-fluoro-1,3-dihexylquinazoline-2,4(1H,3H)-dione (**34**). The title compound was prepared from our reported method[21].
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.89 (dd, *J* = 8.2, 3.1 Hz, 1H), 7.37 (ddd, *J* = 9.2, 7.6, 3.1 Hz, 1H), 7.14 (dd, *J* = 9.2, 4.0 Hz, 1H), 4.20 – 3.91 (m, 4H), 1.76 – 1.59 (m, 4H), 1.48 – 1.20 (m, 12H), 0.95 – 0.81 (m, 6H).
^{13}C NMR (100 MHz, CDCl$_3$) δ 160.78 (d, *J* = 2.8 Hz), 158.03 (d, *J* = 244.1 Hz), 150.34, 136.20 (d, *J* = 1.9 Hz), 122.52 (d, *J* = 23.9 Hz), 117.01 (d, *J* = 7.6 Hz), 115.37 (d, *J* = 7.4 Hz), 114.50 (d, *J* = 24.0 Hz), 44.03, 42.13, 31.46, 31.42, 27.68, 27.22, 26.61, 26.42, 22.53, 22.52, 14.00, 13.95.

^{19}F NMR (376 MHz, CDCl$_3$) δ -119.70 (td, *J* = 7.9, 4.0 Hz).



35-F

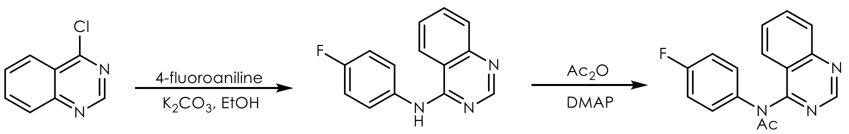
3-fluoro-2,6-dimethoxypyridine(**35-F**). To a solution of 2,3,6-trifluoropyridine (266 mg, 2 mmol, 1equiv.) in anhydrous DMF was added sodium methoxide (648 mg, 12 mmol, 6 equiv.). The solution was stirred at 80°C under N_2 overnight. The reaction was then extracted with ethyl acetate and water. The organic phase was with water, saturated brine, dried over with Na_2SO_4, filtered and concentrated in vacuo to give the title compound as a pale-yellow liquid. (Product is volatile)

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.28 (dd, *J* = 9.5, 8.5 Hz, 1H), 6.20 (dd, *J* = 8.4, 2.0 Hz, 1H), 4.00 (s, 3H), 3.88 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 157.70, 150.58, 141.95 (d, *J* = 244.5 Hz), 126.49 (d, *J* = 18.0 Hz), 99.93 (d, *J* = 2.3 Hz), 53.92, 53.59.

^{19}F NMR (376 MHz, CDCl$_3$) δ -153.92 (dd, *J* = 9.6, 1.8 Hz).

HRMS (EI): Calculated for $C_7H_8FNO_2$ $[M]^+$: 157.0539; found: 157.0534.



37-i **37**

N-(4-fluorophenyl) quinazolin-4-amine (**37-i**). To a solution of 4-chloroquinazoline (2 mmol, 329.2 mg) in EtOH were added 4-fluoroaniline (3 mmol, 333.4 mg, 1.5 equiv.) and potassium carbonate (4 mmol, 553 mg, 2 equiv.). The mixture was stirred under room temperature for 3 h. Water was then added to the reaction solution and solid precipitated. The title compound was obtained as a gray solid after filtration (427 mg, 89%) and used without further purification.

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.74 (s, 1H), 7.95 – 7.85 (m, 2H), 7.86 – 7.73 (m, 1H), 7.72 – 7.61 (m, 2H), 7.61 – 7.49 (m, 2H), 7.17 – 7.06 (m, 2H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 159.76 (d, *J* = 244.5 Hz), 157.69, 154.89, 149.94, 133.96 (d, *J* = 2.9 Hz), 133.02, 128.97, 126.70, 124.15 (d, *J* = 8.0 Hz), 120.28, 115.85 (d, *J* = 22.6 Hz), 114.93.

^{19}F NMR (376 MHz, CDCl$_3$) δ -110.98 – -125.54 (m).

HRMS (EI): Calculated for $C_{14}H_9FN_3$ $[M]^+$: 238.0781; found: 238.0775.

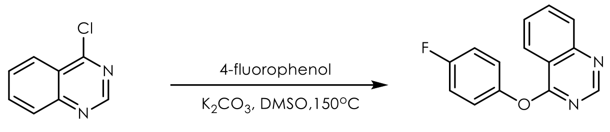
N-(4-fluorophenyl)-N-(quinazolin-4-yl) acetamide (**37**). Follow the literature procedure[22], the title compound was obtained as a colorless oil.

^{1}H NMR (400 MHz, CDCl$_3$) δ 9.24 (s, 1H), 8.11 (d, *J* = 8.4 Hz, 1H), 8.07 – 7.98 (m, 1H), 7.93 (ddd, *J* = 8.4, 7.0, 1.4 Hz, 1H), 7.67 (ddd, *J* = 8.2, 7.0, 1.1 Hz, 1H), 7.46 – 7.36 (m, 2H), 7.14 – 7.04 (m, 2H), 2.17 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 171.07, 162.07, 161.79 (d, *J* = 248.7 Hz), 154.82, 152.75, 136.83 (d, *J* = 3.3 Hz), 134.39, 129.60 (d, *J* = 8.7 Hz), 129.14, 128.73, 124.70, 121.64, 116.49 (d, *J* = 22.8 Hz), 23.58.

^{19}F NMR (376 MHz, CDCl$_3$) δ -112.95.

HRMS (EI): Calculated for $C_{16}H_{12}FN_3O$ $[M]^+$: 281.0964; found: 281.0959.



38

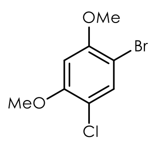
4-(4-fluorophenoxy) quinazoline (**38**). To a solution of 4-chloroquinazoline (329 mg, 2 mmol, 1 equiv.) in DMSO were added 4-flurorophenol (448 mg, 4 mmol, 2 equiv.) and anhydrous potassium carbonate (553 mg, 4 mmol, 2 equiv.). The mixture was stirred at 150℃ for 2 h. Water and ethyl acetate were added to the reaction. The organic phase was separated and washed with water, 10% (w/w) NaOH solution, saturated brine, dried with Na_2SO_4, filtered, and concentrated in vacuo to give the residue which was purified by silica gel chromatography using ethyl acetate/ hexane (1/5 to 1/2) to afford the title compound as a white solid (394 mg, 82%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.77 (s, 1H), 8.38 (dd, *J* = 8.3, 0.8 Hz, 1H), 8.02 (d, *J* = 8.4 Hz, 1H), 7.93 (ddd, *J* = 8.4, 7.0, 1.4 Hz, 1H), 7.68 (ddd, *J* = 8.2, 7.0, 1.1 Hz, 1H), 7.27 – 7.21 (m, 2H), 7.21 – 7.12 (m, 2H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 166.91, 160.32 (d, *J* = 244.6 Hz), 154.10, 151.68, 148.06 (d, *J* = 2.9 Hz,), 134.20, 127.81 (d, *J* = 28.6 Hz), 123.51, 123.36, 123.28, 116.48 (d, *J* = 23.6 Hz), 116.31.

^{19}F NMR (376 MHz, CDCl$_3$) δ -106.15 – -121.21 (m).

HRMS (EI): Calculated for $C_{14}H_9FN_2O$ $[M]^+$: 240.0699; found: 240.0670.

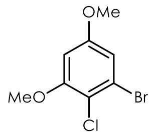


39

1-bromo-5-chloro-2,4-dimethoxybenzene (**39**). The title compound was prepared from reported procedure. Spectral data matched literature data[11].

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.51 (s, 1H), 6.51 (s, 1H), 3.91 (s, 3H), 3.90 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 155.50, 155.18, 133.23, 114.51, 101.92, 97.56, 56.60, 56.45

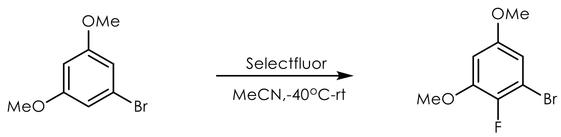


40

1-bromo-2-chloro-3,5-dimethoxybenzene (**40**). The title compound was prepared from the reported literature. Spectral data matched literature data[7].

^{1}H NMR (400 MHz, CDCl$_3$) δ 6.78 (d, *J* = 2.7 Hz, 1H), 6.46 (d, *J* = 2.7 Hz, 1H), 3.87 (s, 3H), 3.79 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 158.96, 156.54, 123.60, 115.36, 109.41, 99.24, 56.43, 55.75.



40-F

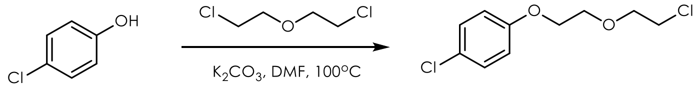
1-bromo-2-fluoro-3,5-dimethoxybenzene(40-F). To a solution of 1-bromo-3,5-dimethoxybenzene (434 mg, 2 mmol) in acetonitrile was added selectfluor (779 mg, 2.2 mmol, 1.1 equiv.) at -40℃. The reaction was stirred at -40℃ for 0.5 h and then stirred overnight at room temperature. The organic phase was washed with water, saturated brine, dried over with Na_2SO_4, filtered and concentrated in vacuo to give the crude product which was purified by flash LC with ethyl acetate / hexane (1/20) as the eluant to give the title compound as a colorless oil (178 mg, 38%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 6.59 (dd, *J* = 4.6, 2.9 Hz, 1H), 6.47 (dd, *J* = 6.6, 2.9 Hz, 1H), 3.86 (s, 3H), 3.76 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 155.86 (d, *J* = 3.0 Hz), 148.86 (d, *J* = 12.6 Hz), 144.63 (d, *J* = 237.8 Hz), 109.23 (d, *J* = 19.5 Hz), 107.54 (d, *J* = 0.9 Hz), 100.63 (d, *J* = 0.6 Hz), 56.42, 55.87.

^{19}F NMR (376 MHz, CDCl$_3$) δ -138.80 (dd, *J* = 6.5, 4.6 Hz).

HRMS (EI): Calculated for $C_8H_8BrFO_2$ $[M]^+$: 233.9692; found: 233.9691



41

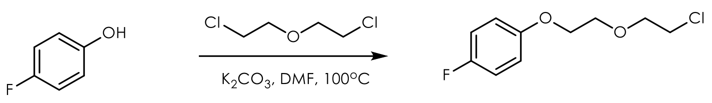
1-chloro-4-(2-(2-chloroethoxy) ethoxy) benzene (**41**). To a solution of the 4-chlorophenol (514 mg, 4 mmol, 1.0 equiv.) in DMF was added anhydrous potassium carbonate (1.1g, 8 mmol, 2.0

equiv.) follow by the 1-1-chloro-2-(2-chloroethoxy) ethane (572 mg, 4 mmol, 1 equiv.). The reaction was heated to 100 ℃ and stirred overnight. The reaction was cooled to room temperature and then extracted with ethyl acetate and water. The organic phase was washed with water, NaOH solution (10%, w/w), water, saturated brine, dried with Na_2SO_4, filtered, and concentrated in vacuo to give the crude product which was purified by flash LC using hexane/ ethyl acetate (0% to 5%) as a colorless oil (581mg, 62%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.20 (m, 2H), 6.89 – 6.81 (m, 2H), 4.11 (dd, *J* = 5.4, 4.1 Hz, 2H), 3.87 (dd, *J* = 5.4, 4.1 Hz, 2H), 3.82 (t, *J* = 5.9 Hz, 2H), 3.65 (t, *J* = 5.8 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 157.22, 129.23, 125.75, 115.86, 71.47, 69.60, 67.67, 42.64.

HRMS (EI): Calculated for $C_{10}H_{12}Cl_2O_2$ $[M]^+$: 234.0214; found: 234.0210



41-F

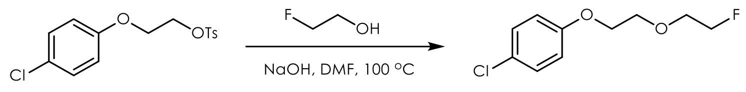
1-chloro-4-(2-(2-chloroethoxy) ethoxy) benzene(**41-F**). The title compound was obtained as a colorless oil (548 mg, 63%) from the same preparation procedure of the compound **41** staring with 4-fluorophenol.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00 – 6.91 (m, 2H), 6.91 – 6.81 (m, 2H), 4.11 – 4.05 (m, 2H), 3.87 – 3.83 (m, 2H), 3.81 (t, *J* = 5.8 Hz, 2H), 3.65 (t, *J* = 5.9 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 157.36 (d, *J* = 238.5 Hz), 154.77 (d, *J* = 2.1 Hz), 115.80 (d, *J* = 17.6 Hz), 115.64 (d, *J* = 2.4 Hz), 71.53, 69.78, 68.10, 42.68.

^{19}F NMR (376 MHz, $CDCl_3$) δ -123.69 – -123.81 (m).

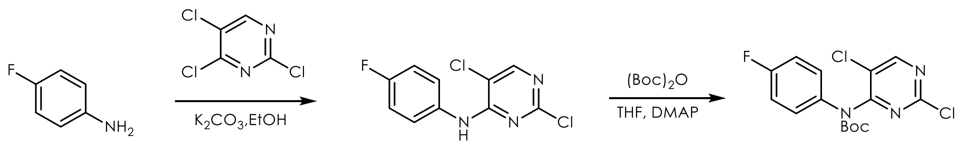
HRMS (EI): Calculated for $C_{10}H_{12}ClFO_2$ $[M]^+$: 218.0510 found: 218.0504



41-F-a

2-(4-chlorophenoxy) ethyl 4-methylbenzenesulfonate(**41-F-a**). To a solution of 2-(4-chlorophenoxy) ethyl 4-methylbenzenesulfonate (164 mg, 0.5 mmol, 1 equiv.) in DMF were added NaOH (49 mg, 1.5 mmol, 3 equiv.) and 2-fluoroethanol (87 μl, 1.5 mmol, 3 equiv.). The reaction was stirred under 100℃ for 1h and then extracted with ethyl acetate and water. The organic phase was washed with water, NaOH solution (10%, w/w), water, saturated brine, dried with Na_2SO_4, filtered, and concentrated in vacuo to give the residue which was purified by silica gel chromatography using ethyl acetate/ hexane (10%) as the eluent to afford the title compound as a colorless oil (72 mg, 66%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.25 – 7.20 (m, 2H), 6.88 – 6.81 (m, 2H), 4.69 – 4.58 (m, 1H), 4.56 – 4.49 (m, 1H), 4.11 (dd, *J* = 5.4, 4.1 Hz, 2H), 3.90 – 3.86 (m, 2H), 3.86 – 3.83 (m, 1H), 3.73 – 3.80 (m, 1H).
^{13}C NMR (100 MHz, CDCl$_3$) δ 157.30, 129.27, 125.78, 115.90, 83.11 (d, *J* = 169.1 Hz), 70.58 (d, *J* = 19.6 Hz), 69.81, 67.74.
^{19}F NMR (376 MHz, CDCl$_3$) δ -222.74 – -223.15 (m).
HRMS (EI): Calculated for $C_{10}H_{12}ClFO_2$ [M]$^+$: 218.0510 found: 218.0505

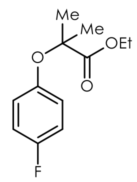


42-i

42

2,5-dichloro-N-(4-fluorophenyl) pyrimidin-4-amine (**42-i**). To a solution of 2,4,5-trichloropyrimidine (1.1 g, 6 mmol, 1.2 equiv.) in ethanol were added potassium carbonate (1.04 g, 7.5 mmol, 1.5 equiv.) and 4-fluoroaniline (555 mg, 5 mmol, 1 equiv.). The mixture was stirred under room temperature for 3 h and then extracted with ethyl acetate and water. The organic phase was washed with 1N HCl solution, saturated brine, dried with Na_2SO_4, filtered, and concentrated in vacuo to give the crude solid which was washed with ethyl acetate/ hexane (1/10) to give the title compound as an off-white solid after filtration (848 mg, 66%).
^{1}H NMR (400 MHz, CDCl$_3$) δ 8.20 (s, 1H), 7.63 – 7.50 (m, 2H), 7.20 (br,1H), 7.14 – 7.05 (m, 2H).
^{13}C NMR (100 MHz, CDCl$_3$) δ 159.95 (d, J = 245.2 Hz), 158.26, 156.47, 154.64, 132.67 (d, J = 3.0 Hz), 123.29 (d, J = 8.1 Hz), 115.96 (d, J = 22.8 Hz), 113.57.
^{19}F NMR (376 MHz, CDCl$_3$) δ -115.03 – -117.87 (m).

tert-butyl (2,5-dichloropyrimidin-4-yl) (4-fluorophenyl) carbamate (**42**). To a solution of the 2,5-dichloro-N-(4-fluorophenyl) pyrimidin-4-amine (129 mg, 0.5 mmol, 1 equiv.) in THF was added DMAP (61 mg, 0.5 mmol, 1equiv.) and followed by the addition of Boc_2O (218 mg, 1 mmol, 2 equiv.). The solution was stirred under room temperature for 2 h. After the solvent was removed, the residue was extracted with ethyl acetate and water. The organic phase was washed with water, 1N HCl solution, saturated brine, dried with Na_2SO_4, filtered, and concentrated in vacuo to give the title compound (146 mg, 82%) as a solid which was used without further purification.
^{1}H NMR (400 MHz, CDCl$_3$) δ 8.61 (s, 1H), 7.30 – 7.24 (m, 12), 7.11 – 7.01 (m, 2H), 1.46 (s, 9H).
^{13}C NMR (100 MHz, CDCl$_3$) δ 161.65 (d, *J* = 248.0 Hz), 159.97, 158.43, 151.52, 135.08 (d, *J* = 3.2 Hz), 129.44 (d, *J* = 8.7 Hz), 126.97, 116.07 (d, *J* = 22.9 Hz), 83.66, 27.92.
^{19}F NMR (376 MHz, CDCl$_3$) δ -113.50 – -113.63 (m).
HRMS (EI): Calculated for $C_{15}H_{14}Cl_2FN_3O_2$ [M]$^+$: 357.0447 found: 357.0443



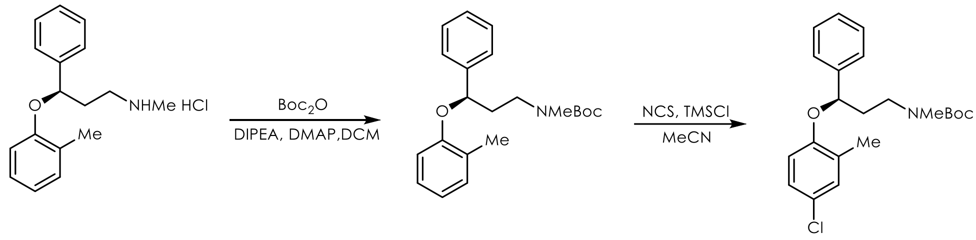
43-F

Ethyl 2-(4-fluorophenoxy)-2-methylpropanoate (**43-F**). The title compound was prepared from reported procedure[23].

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95-6.88, (m, 2H), 6.79-6.87 (m, 2H), 4.22 (q, *J* = 7.2 Hz, 2H), 3.94 (s, 3H), 1.46(s, 6H), 1.26(t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 174.01,158.31 (d, *J* =239 Hz), 151.27 (d, *J* = 2.5 Hz), 121.25 (d, *J* = 8.1 Hz), 115.53 (d, *J* = 22.9 Hz), 79.71, 61.40, 25.25, 14.05.

^{19}F NMR (376 MHz, $CDCl_3$) δ -121.42 (ddd, *J* = 14.7, 8.3,4.6 Hz).



44-i 44

(R)-tert-butyl methyl(3-phenyl-3-(o-tolyloxy) propyl) carbamate(**44-i**). To the solution of atomoxetine hydrochloride (292 mg, 1mmol, 1 equiv.) in dichloromethane were added DIPEA (435 µl, 2.5 mmol, 2.5 equiv.) and DMAP (12.2 mg, 0.1 mmol, 0.1 equiv.) follow by the addition of Boc_2O (262 mg, 1.2 mmol, 1.2 equiv.). The reaction was stirred under room temperature overnight. The reaction was extracted with ethyl acetate and water. The organic phase was washed with 1N HCl, water, saturated brine, dried over with Na_2SO_4, filtered and concentrated in vacuo to give the product as a colorless oil (quantitative yield) which used in the next step without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.27(m, 4H), 7.26-7.21 (m, 1H), 7.11 (d, *J* = 7.3 Hz, 1H), 6.95 – 6.90 (m, 1H), 6.77 (t, *J* = 7.1 Hz, 1H), 6.57 (d, *J* = 8.2 Hz, 1H), 5.15 (d, *J* = 4.4 Hz, 1H), 3.44 (s, 2H), 2.84 (s, 3H), 2.34 (s, 3H), 2.27 – 1.97 (m, 2H), 1.38 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 155.76, 141.78, 130.57, 128.63, 127.49, 126.85, 126.53, 125.58, 120.21, 112.50, 79.33, 77.20, 45.97, 37.30, 34.41, 28.34, 16.52.

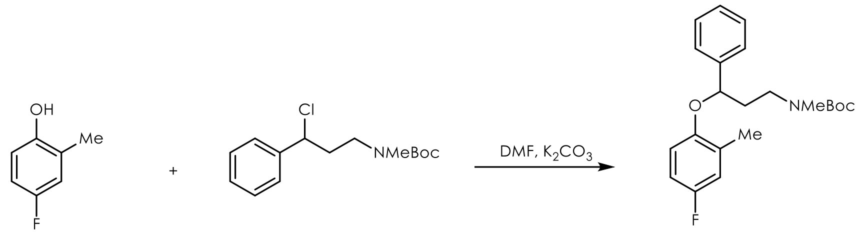
HRMS (ESI): Calculated for $C_{22}H_{30}NO_3$ $(M+H)^+$: 356.2220; found: 356.2216

tert-butyl (R)-(3-(4-chloro-2-methylphenoxy)-3-phenylpropyl) (methyl)carbamate (**44**). Follow the reported method[17], the title compound was purified as a colorless oil (323 mg, 83%) by silica gel column using ethyl acetate/ hexane (1/20).

¹H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.21 (m, 5H), 7.08 (d, *J* = 2.2 Hz, 1H), 6.89 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.47 (d, *J* = 8.7 Hz, 1H), 5.10 (d, *J* = 4.2 Hz, 1H), 3.44 (s, 2H), 2.84 (s, 3H), 2.30 (s, 3H), 2.25 – 2.02 (m, 2H), 1.37 (s, 9H).

¹³C NMR (100 MHz, $CDCl_3$) δ 155.71, 154.33, 141.23, 130.35, 128.73, 127.72, 126.13, 125.56, 124.91, 113.64, 79.40, 77.20, 45.88, 37.20, 34.43, 28.34, 16.40.

HRMS (ESI): Calculated for $C_{22}H_{29}ClNO_3$ $(M+H)^+$: 390.1830; found: 390.1826



44-F

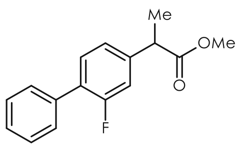
tert-butyl (3-(4-fluoro-2-methylphenoxy)-3-phenylpropyl) (methyl)carbamate (**44-F**). To a solution of tert-butyl (3-chloro-3-phenylpropyl) (methyl)carbamate (284 mg, 1 mmol, 1 equiv.) in DMF were added 4-fluoro-2-methylphenol (256 mg, 2 mmol, 2 equiv.) and potassium carbonate (276 mg, 2 mmol, 2 equiv.). The reaction was stirred under 100℃ overnight and then extracted with ethyl acetate and water. The organic phase was washed with water, NaOH solution (10%, w/w), water, saturated brine, dried with Na_2SO_4, filtered, and concentrated in vacuo to give residue which was purified by silica gel chromatography with ethyl acetate/ hexane (1/20) to afford the title compound as a colorless oil (82 mg, 22%).

¹H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.21 (m, 5H), 6.83 (dd, *J* = 8.9, 2.8 Hz, 1H), 6.61 (td, *J* = 8.5, 3.0 Hz, 1H), 6.47 (dd, *J* = 8.8, 4.6 Hz, 1H), 5.07 (dd, *J* = 8.3, 3.8 Hz, 1H), 3.44 (br, 2H), 2.84 (s, 3H), 2.31 (s, 3H), 2.24 – 1.98 (m, 2H), 1.37 (s, 9H).

¹³C NMR (100 MHz, $CDCl_3$) δ 156.62 (d, *J* = 236.7 Hz), 155.72, 151.80, 141.47, 128.68, 127.65, 125.62, 117.23 (d, *J* = 22.5 Hz), 113.22, 112.15 (d, *J* = 22.4Hz), 79.37, 77.20, 45.90, 37.17, 34.36, 28.33, 16.59.

¹⁹F NMR (376 MHz, $CDCl_3$) δ -124.73.

HRMS (ESI): Calculated for $C_{22}H_{29}FNO_3$ $(M+H)^+$: 374.2126; found: 374.2121

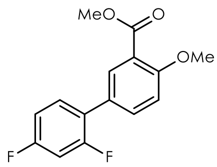


45

methyl 2-(2-fluoro-[1,1'-biphenyl]-4-yl) propanoate (**45**). The title compound was prepared from reported procedure. Spectral data matched literature data[24].

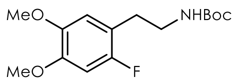
¹H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.52 (m, 2H), 7.49 – 7.34 (m, 4H), 7.20 – 7.12 (m, 2H), 3.79 (q, *J*

= 7.2 Hz,1H), 3.72 (s, 3H), 1.56 (d, *J* = 7.2 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 174.35, 159.62 (d, *J* = 248.4 Hz), 141.75 (d, *J* = 7.7 Hz), 135.42 (d, *J* = 1.2 Hz), 130.76 (d, *J* = 4.0 Hz), 128.87 (d, *J* = 2.9 Hz), 128.37, 127.78 (d, *J* = 13.5 Hz), 127.59, 123.46 (d, *J* = 3.3 Hz), 115.17 (d, *J* = 23.7 Hz), 52.12, 44.84 (d, *J* = 1.3 Hz), 18.37.
^{19}F NMR (376 MHz, $CDCl_3$) δ -117.51 – -117.62 (m, 1H).



46

methyl 2',4'-difluoro-4-methoxy-[1,1'-biphenyl]-3-carboxylate (**46**). The title compound was obtained as a white solid from reported procedure[25]. Spectral data matched literature data.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (dd, *J* = 2.2, 1.0 Hz, 1H), 7.64 – 7.58 (m, 1H), 7.38 (td, *J* = 8.7, 6.5 Hz, 1H), 7.05 (d, *J* = 8.7 Hz, 1H), 6.98 – 6.85 (m, 2H), 3.95 (s, 3H), 3.90 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 166.34, 162.15 (dd, *J* = 249.0, 11.9 Hz), 159.63 (dd, *J* = 250.2, 11.8 Hz), 158.67, 133.83 (d, *J* = 3.4 Hz), 132.01 (d, *J* = 2.4 Hz), 131.08 (dd, *J* = 9.4, 4.8 Hz), 126.90 (d, *J* = 1.2 Hz), 123.93 (dd, *J* = 13.7, 3.9 Hz), 120.11, 112.13, 111.58 (dd, *J* = 21.1, 3.8 Hz), 104.35 (dd, *J* = 26.6, 25.3 Hz), 56.13, 52.11.
^{19}F NMR (376 MHz, $CDCl_3$) δ -111.42 (dt, *J* = 15.4, 7.7 Hz, 1H), -113.74 (dd, *J* = 17.5, 8.8 Hz, 1H).



47-F

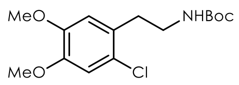
tert-butyl (2-fluoro-4,5-dimethoxyphenethyl) carbamate (**47-F**). To a 25 ml round bottom flask with stir bar was added 2-(2-fluoro-4,5-dimethoxyphenyl) ethan-1-amine (173 mg, 0.87 mmol, 1 equiv.) prepared from reported literature[26] and triethylamine (176 mg, 1.74 mmol, 2 equiv.) dissolved in dichloromethane. The flask was sealed with a rubber septum and cooled to 0℃ for 5 minutes, di-tert-butyl decarbonate (228 mg, 1.04 mmol, 1.2 equiv.) was then added. The reaction was stirred at 0 °C for 15 minutes, then warmed to room temperature and stirred overnight. The reaction was quenched with brine and diluted with dichloromethane. After separation, the aqueous layer was extracted with dichloromethane. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The title compound was isolated as a brown solid (165.4 mg, 64%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.65 (d, *J* = 6.8 Hz, 1H), 6.61 (d, *J* = 11.0 Hz, 1H), 4.58 (s, 1H), 3.89 – 3.74 (m, 6H), 3.33 (q, *J* = 6.0 Hz 2H), 2.76 (t, *J* = 7.0 Hz, 2H), 1.42 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 156.34, 154.92 (d, *J* = 189.0 Hz), 148.31 (d, *J* = 9.2 Hz), 145.09 (d, *J* = 2.6 Hz), 116.13 (d, *J* = 17.6 Hz), 113.12 (d, *J* = 6.6 Hz), 100.09 (d, *J* = 28.5 Hz), 79.22, 56.25 (d, *J* = 28.9 Hz), 40.77, 29.20, 28.38.

^{19}F NMR (376 MHz, CDCl$_3$) δ -125.86 – -126.21 (m).

HRMS (ESI): Calculated for $C_{10}H_{15}FNO_2$ $(M+H)^+$: 200.1081; found: 274.1075



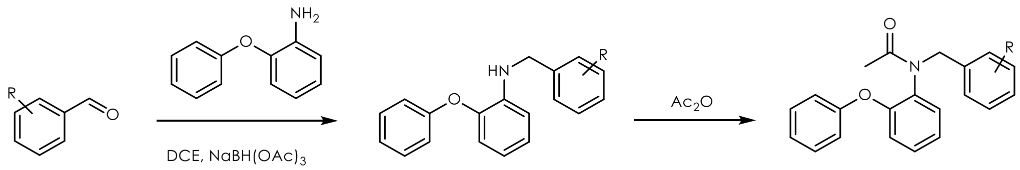
47-Cl

tert-butyl (2-chloro-4,5-dimethoxyphenethyl) carbamate (**47-Cl**). The title compound was obtained as a white solid from reported procedure[14]. Spectral data matched literature value.

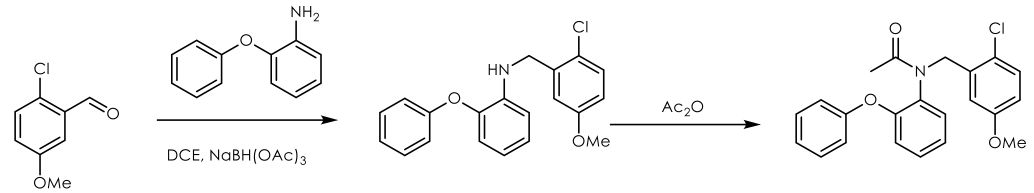
^{1}H NMR (400 MHz, CDCl$_3$) δ 6.85 (s, 1H), 6.71 (s, 1H), 4.77 – 4.17 (m, 1H), 3.85 (s, 3H), 3.85 (s, 3H), 3.36 (d, *J* = 6.7 Hz, 2H), 2.86 (t, *J* = 7.0 Hz, 2H), 1.43 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 155.85, 148.11, 147.76, 128.32, 124.89, 113.38, 112.56, 79.19, 56.10, 56.07, 40.32, 33.53, 28.38.

General procedure to synthesize substrates 48 to 50 and fluorine standards (48-F to 49-F) (General procedure A)



To the solution of the aldehyde (1 mmol, 1 equiv.) in 1,2-dichloroethane (DCE) was added 2-phenoxyaniline (222 mg, 1.2 mmol, 1.2 eq). The solution was stirred under room temperature for 30 min. and $NaBH(OAc)_3$ (424 mg, 2 mmol, 2 equiv.) was then added in portion at 0℃. The resulting solution was warmed to room temperature and stirred for additional 3 h. After fully conversion of the aldehyde (monitored by TLC), 1,2-dichloroethane (DCE) was removed under reduce pressure. The residue was extracted with ethyl acetate and water. The organic phase was washed with 1N HCl, saturated brine, dried with Na_2SO_4, filtered, and concentrated in vacuo to give the crude intermediate which were then dissolved in 5 ml acetic anhydride. This solution was then stirred under room temperature for 5 h. After fully conversion of the amine intermediate, most of the acetic anhydride was removed under reduce pressure. The residue was dissolve in ethyl acetate and washed with 10% (w/w) NaOH solution, 1N HCl, water, saturated brine, dried with Na_2SO_4, filtered, and concentrated in vacuo to give the crude product which was then purified by silica gel column with ethyl acetate/ hexane (20% to 50%) as the eluant to afford the target compound as a colorless oil or white solid.



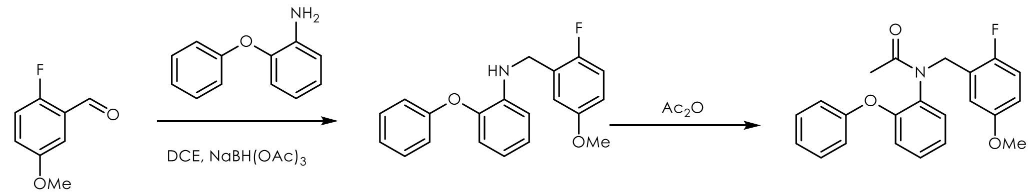
48

N-(2-chloro-5-methoxybenzyl)-N-(2-phenoxyphenyl) acetamide (**48**). Follow the general procedure **A**, the title compound was obtained as a white solid (313 mg, 82%) from 2-chloro-5-methoxybenzaldehyde.

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.38 – 7.28 (m, 2H), 7.21 (ddd, *J* = 8.3, 7.5, 1.8 Hz, 1H), 7.16 – 7.10 (m, 2H), 7.08 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.04 (d, *J* = 3.1 Hz, 1H), 7.00 (td, *J* = 7.6, 1.3 Hz, 1H), 6.93 – 6.88 (m, 2H), 6.86 (dd, *J* = 8.3, 1.3 Hz, 1H), 6.67 (dd, *J* = 8.8, 3.1 Hz, 1H), 5.22 (d, *J* = 15.0 Hz, 1H), 4.79 (d, *J* = 15.0 Hz, 1H), 3.66 (s, 3H), 1.99 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 171.15, 158.30, 155.78, 153.43, 135.85, 132.71, 130.18, 129.85, 129.72, 129.30, 125.12, 124.04, 123.42, 119.16, 118.47, 115.94, 114.55, 55.39, 48.86, 22.08.

HRMS (ESI): Calculated for $C_{22}H_{21}ClNO_3$ $(M+H)^+$: 382.1204; found: 382.1200.



48-F

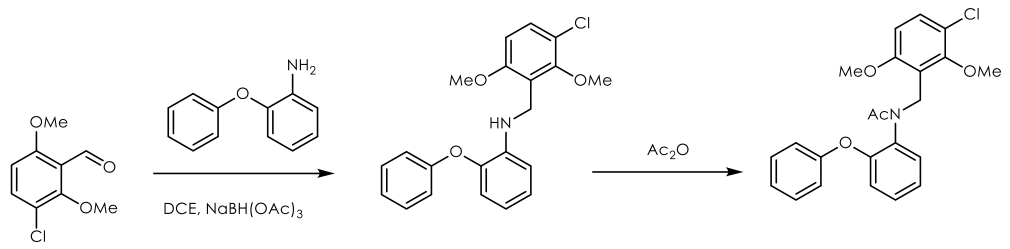
N-(2-fluoro-5-methoxybenzyl)-N-(2-phenoxyphenyl) acetamide(**48-F**). Follow the general procedure **A**, the title compound was obtained as a colorless oil from 2-fluoro-5-methoxybenzaldehyde and gradually solidify after stay (259 mg, 71%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.37 – 7.27 (m, 2H), 7.24 – 7.18 (m, 1H), 7.13 (t, *J* = 7.4 Hz, 1H), 7.06 – 6.97 (m, 2H), 6.96 (dd, *J* = 5.9, 3.2 Hz, 1H), 6.91 – 6.83 (m, 3H), 6.81 (t, *J* = 9.1 Hz, 1H), 6.72 – 6.63 (m, 1H), 5.13 (d, *J* = 14.6 Hz, 1H), 4.72 (d, *J* = 14.6 Hz, 1H), 3.66 (s, 3H), 1.96 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 171.13, 155.82, 155.53 (d, *J* = 2.0 Hz), 155.39 (d, *J* = 238 Hz), 153.42, 132.65, 130.17, 129.83, 129.30, 124.86 (d, *J* = 16.5 Hz), 124.00, 123.37, 119.11, 118.48, 115.70(d, *J* = 3.8 Hz), 115.46 (d, *J* = 23.9 Hz), 114.50 (d, *J* = 8.0 Hz), 55.63, 44.85 (d, *J* = 3.1 H), 22.11.

^{19}F NMR (376 MHz, CDCl$_3$) δ -129.80 – -129.92 (m).

HRMS (ESI): Calculated for $C_{22}H_{21}FNO_3$ $(M+H)^+$: 366.1500; found: 382.1497.



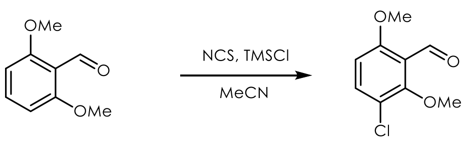
49-i 49

N-(3-chloro-2,6-dimethoxybenzyl)-N-(2-phenoxyphenyl) acetamide (**49**). Follow the general procedure **A**, the title compound was obtained as a colorless oil (362 mg, 88%) from 3-chloro-2,6-dimethoxybenzaldehyde(**49-i)**.

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.36 – 7.28 (m, 2H), 7.17 (d, *J* = 8.9 Hz, 1H), 7.15 – 7.09 (m, 2H), 6.92 – 6.84 (m, 3H), 6.82 (dd, *J* = 7.8, 1.7 Hz, 1H), 6.76 (d, *J* = 8.3 Hz, 1H), 6.42 (d, *J* = 8.9 Hz, 1H), 5.33 (d, *J* = 13.5 Hz, 1H), 4.85 (d, *J* = 13.5 Hz, 1H), 3.69 (s, 3H), 3.50 (s, 3H), 1.90 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 170.23, 158.14, 155.99, 155.72, 154.31, 131.92, 130.82, 129.78, 129.53, 129.00, 124.02, 122.54, 120.56, 119.51, 119.36, 117.49, 106.89, 60.98, 55.60, 39.30, 22.27.

HRMS (ESI): Calculated for $C_{23}H_{23}ClNO_4$ $(M+H)^+$: 412.1310; found: 412.1305.



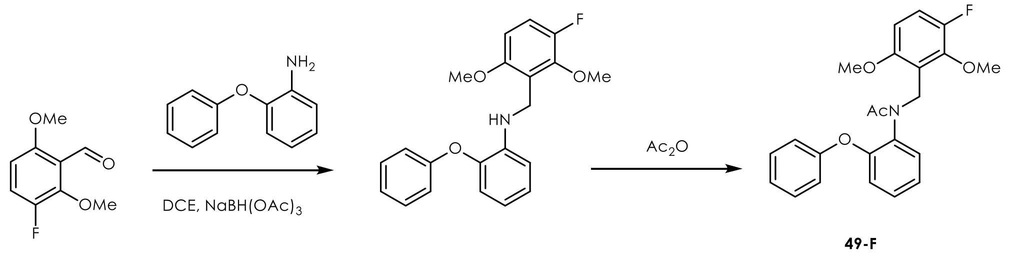
49-i

3-chloro-2,6-dimethoxybenzaldehyde(49-i). The title compound was prepared from reported chlorination procedure[7]. The crude product was purified by silica gel chromatography purification with ethyl acetate/ hexane (1/10) and give the title compound as a light brown solid (476mg, 79%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 10.41 (s, 1H), 7.50 (d, *J* = 9.0 Hz, 1H), 6.72 (d, *J* = 9.0 Hz, 1H), 3.92 (s, 3H), 3.89 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 188.58, 160.46, 157.95, 135.65, 120.44, 120.27 108.17, 62.47, 56.29.

HRMS (ESI): Calculated for $C_9H_{10}ClO_3$ $(M+H)^+$: 201.0313; found: 201.0311.



49-F-i 49-F

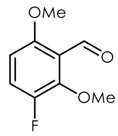
N-(3-fluoro-2,6-dimethoxybenzyl)-N-(2-phenoxyphenyl)acetamide(**49-F**). Follow the general procedure **A**, the title compound was obtained as a colorless oil (253 mg, 64%) from 3-fluoro-2,6-dimethoxybenzaldehyde(**49-F-i**).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.37 – 7.29 (m, 2H), 7.16 – 7.09 (m, 2H), 6.93 – 6.82 (m, 5H), 6.76 (dd, *J* = 8.3, 1.0 Hz, 1H), 6.33 (dd, *J* = 9.1, 3.6 Hz, 1H), 5.28 (d, *J* = 13.3 Hz, 1H), 4.86 (d, *J* = 13.3 Hz, 1H), 3.67 (d, *J* = 2.1 Hz, 3H), 3.52 (s, 3H), 1.90 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 170.14, 155.73, 154.97 (d, *J* = 1.8 Hz), 154.34 (s, 3H), 149.94 (d, *J* = 238 Hz), 147.25 (d, *J* = 11.5 Hz), 132.02, 130.83, 129.77, 128.92, 124.02, 122.49, 119.55, 117.41, 115.54, 115.34, 104.66 (d, *J* = 7.4 Hz), 61.03 (d, *J* = 6.7 Hz), 55.73, 39.03 (d, *J* = 2.2 Hz), 22.28.

^{19}F NMR (376 MHz, CDCl$_3$) δ -139.63 – -139.81 (m).

HRMS (ESI): Calculated for $C_{23}H_{23}FNO_4$ $(M+H)^+$: 396.1606; found: 396.1601



49-F-i

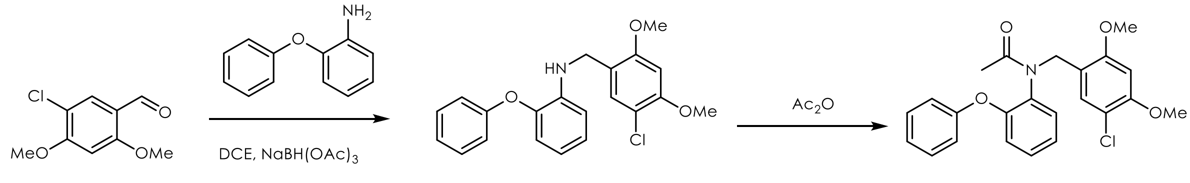
3-fluoro-2,6-dimethoxybenzaldehyde(**49-F-i**). To a solution of 2,6-dimethoxybenzaldehyde (332mg, 2 mmol) in acetonitrile was added selectfluor (779 mg, 2.2 mmol, 1.1 equiv.) at -40 ^{o}C. The solution was stirred overnight and then extracted with ethyl acetate and water. The organic phase was washed with water, saturated brine, dried over with Na_2SO_4, filtered and concentrated in vacuo to give the crude product which was purified by silica gel chromatography with ethyl acetate/hexane (1/4) as the eluant to give the title compound as yellow to brown oil (295 mg, 80%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 10.41 (d, *J* = 1.0 Hz, 1H), 7.24 (dd, *J* = 11.0, 9.2 Hz, 1H), 6.60 (dd, *J* = 9.2, 3.3 Hz, 1H), 4.01 (d, *J* = 2.3 Hz, 3H), 3.87 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 188.77 (d, *J* = 2.7 Hz), 157.25 (d, *J* = 1.8 Hz), 149.56 (d, *J* = 11.6 Hz), 149.42 (d, *J* = 241.4 Hz), 122.17 (d, *J* = 21.0 Hz), 119.17, 105.87 (d, *J* = 6.8 Hz), 62.25 (d, *J* = 6.4 Hz,), 56.31.

^{19}F NMR (376 MHz, CDCl$_3$) δ -139.72 – -139.88 (m).

HRMS (ESI): Calculated for $C_9H_{10}FO_3$ $(M+H)^+$: 185.0608; found: 185.0609.



50-i **50**

N-(5-chloro-2,4-dimethoxybenzyl)-N-(2-phenoxyphenyl) acetamide (**50**). Follow the general procedure **A**, the title compound was obtained as a white solid (311mg, 76%) from 5-chloro-

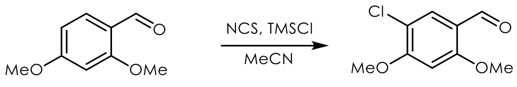
2,4-dimethoxybenzaldehyde(**50-i**).

¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.28 (m, 3H), 7.21 – 7.15 (m, 1H), 7.12 (t, *J* = 7.4 Hz, 1H), 7.04 – 6.95 (m, 2H), 6.89 (dt, *J* = 9.2, 1.9 Hz, 2H), 6.86 (dd, *J* = 8.3, 1.0 Hz, 1H), 6.30 (s, 1H), 4.99 (d, *J* = 14.6 Hz, 1H), 4.70 (d, *J* = 14.6 Hz, 1H), 3.84 (s, 3H), 3.57 (s, 3H), 1.93 (s, 3H).

¹³C NMR (100 MHz, CDCl₃) δ 170.84, 157.13, 155.87, 154.86, 153.42, 133.03, 131.60, 130.30, 129.77, 128.97, 123.88, 123.12, 119.05, 118.66, 118.40, 113.28, 96.18, 56.19, 55.56, 45.22, 22.22.

¹⁹F NMR (376 MHz, CDCl₃) δ -142.91 (dd, *J* = 10.3, 7.3 Hz).

HRMS (ESI): Calculated for $C_{23}H_{23}ClNO_4$ $(M+H)^+$: 412.1310; found: 412.1306.



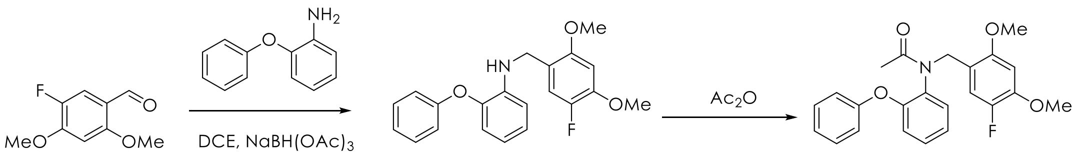
50-i

5-chloro-2,4-dimethoxybenzaldehyde(**50-i**). The title compound was prepared from reported chlorination procedure[7]. The crude product after work-up was purified by stirring in the ethyl acetate/ hexane (1/10) solution. The title compound was obtained as a white solid after filtration (605 mg, 75%).

¹H NMR (400 MHz, CDCl₃) δ 10.25 (s, 1H), 7.83 (s, 1H), 6.47 (s, 1H), 3.98 (s, 3H), 3.95 (s, 3H).

¹³C NMR (100 MHz, CDCl₃) δ 187.18, 162.34, 160.81, 129.71, 118.75, 115.35, 95.65, 56.42, 56.00

HRMS (EI): Calculated for $C_9H_9ClO_3$ $[M]^+$: 200.0240; found: 200.0236



50-F-i **50-F**

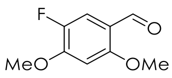
N-(5-fluoro-2,4-dimethoxybenzyl)-N-(2-phenoxyphenyl) acetamide(**50-F**). Follow the general procedure **A**, the title compound was obtained as a colorless oil (359 mg, 91%) from 5-fluoro-2,4-dimethoxybenzaldehyde (**50-F-i**).

¹H NMR (400 MHz, CDCl₃) δ 7.36 – 7.28 (m, 2H), 7.22 – 7.15 (m, 1H), 7.15 – 7.08 (m, 2H), 7.04 – 6.94 (m, 2H), 6.90 (dd, *J* = 9.9, 2.2 Hz, 2H), 6.87 – 6.82 (m, 1H), 6.35 (d, *J* = 7.1 Hz, 1H), 5.01 (d, *J* = 14.6 Hz, 1H), 4.68 (d, *J* = 14.6 Hz, 1H), 3.84 (s, 3H), 3.54 (s, 3H), 1.94 (s, 3H).

¹³C NMR (100 MHz, CDCl₃) δ 170.91, 155.91, 153.76 (d, *J* = 2.1 Hz), 153.39, 146.91 (d, *J* = 11.8 Hz), 146.56 (d, *J* = 236.5 Hz), 133.13, 130.28, 129.79, 128.98, 123.91, 123.16, 119.04, 118.46, 117.85 (d, *J* = 19.9 Hz), 117.83 (d, *J* = 5.7 Hz),98.00 (d, *J* = 1.8 Hz), 56.60, 55.96, 45.30, 22.19.

¹⁹F NMR (376 MHz, CDCl₃) δ -145.34 – -145.45(m).

HRMS (ESI): Calculated for $C_{23}H_{23}FNO_4$ $(M+H)^+$: 396.1606; found: 396.1601



50-F-i

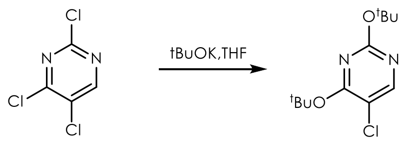
5-fluoro-2,4-dimethoxybenzaldehyde(**50-F-i**). The title compound was prepared from reported literature[27].

^{1}H NMR (400 MHz, CDCl$_3$) δ 10.28 (d, *J* = 3.2 Hz, 1H), 7.54 (d, *J* = 11.2 Hz, 1H), 6.51 (d, *J* = 6.5 Hz, 1H), 3.97 (s, 3H), 3.93 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 188.77 (d, *J* = 2.7 Hz), 157.25 (d, *J* = 1.8 Hz), 149.56 (d, *J* = 11.6 Hz), 149.42 (d, *J* = 241.4 Hz), 122.17 (d, *J* = 21.0 Hz), 119.17 (d, *J* = 1.2 Hz), 105.87 (d, *J* = 6.8 Hz), 62.25 (d, *J* = 6.4 Hz), 56.31.

^{19}F NMR (376 MHz, CDCl$_3$) δ -139.72 – -139.88 (m).

HRMS (ESI): Calculated for $C_9H_{10}FO_3$ $(M+H)^+$: 185.0608; found: 185.0607.

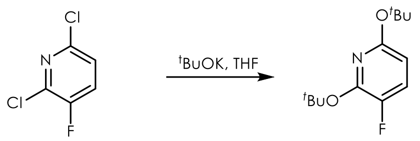


2,4-di-tert-butoxy-5-chloropyrimidine (**51**). To a solution of 2,4,5-trichloropyrimidine (550 mg, 3 mmol, 1equiv.) in anhydrous THF was added potassium tert-butoxide (^{t}BuOK, 1.34 g, 12 mmol, 4 equiv.) portion-wise at 0^{o}C. The reaction was warm to room temperature and stirred for additional 5h. The reaction was quenched by addition of water and extracted with ethyl acetate. The organic phase was washed with water, saturated brine, dried over with Na_2SO_4, filtered and concentrated in vacuo to give the crude product which purified by silica gel chromatography using ethyl acetate/hexane (0% to 5%) to afford the title compound as white solid (498 mg, 64%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.13 (s, 1H), 1.65 (s, 9H), 1.59 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 164.93, 162.14, 156.27, 111.09, 83.19, 80.72, 28.33, 28.29.

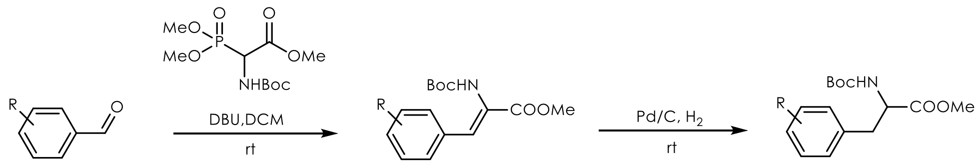
HRMS (ESI): Calculated for $C_{12}H_{20}ClN_2O_2^+$ $(M+H)^+$: 259.1208; found: 259.1204.



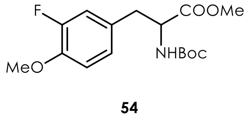
2,4-di-tert-butoxy-5-fluoropyrimidine(**52-F**). Follow the preparation procedure of compound **51**, the title compound was obtained as a colorless liquid (100 mg, 42%) from 2,4-dichloro-5-fluoropyrimidine. Spectral data matched literature data[15].

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.00 (d, *J* = 2.6 Hz, 1H), 1.65 (s, 9H), 1.58 (s, 9H).
^{13}C NMR (100 MHz, CDCl$_3$) δ 158.96 (d, *J* = 3.4 Hz), 158.74 (d, *J* = 10.1 Hz), 143.46 (d, *J* = 252.2 Hz), 142.93 (d, *J* = 20.9 Hz), 83.14, 80.36, 28.37, 28.31.
^{19}F NMR (376 MHz, CDCl$_3$) δ -163.58 (d, *J* = 2.6 Hz).

General procedure to synthesize tyrosine and DOPA derivatives (General procedure B)



Follow the reported procedure[28], to a solution of methyl 2-((*tert*-butoxycarbonyl) amino)-2-(dimethoxyphosphoryl) acetate (713 mg, 2.4 mmol, 1.2 equiv.) in 10 ml dry dichloromethane, was added DBU (358 ml, 2.4 mmol, 1.2 equiv.). The mixture solution was stirred at room temperature for 5 minutes. Then the aldehyde (2 mmol, 1 equiv.) in 5 ml dichloromethane was added dropwise to the solution. The reaction was monitored by TLC. After the reaction is finished (usually in 3 to 4h.), the solution was concentrated and extracted with ethyl acetate and water. The organic phase was separated and washed with 1N HCl, saturated brine, dried with Na_2SO_4, filtered and concentrated in vacuo to give the crude product which was then purified by silica gel column with ethyl acetate/ hexane (10% to 20%) or stirred in the ethyl acetate/ hexane when solid crude products were obtained to give the intermediate in 65-90% yield. To a round bottomed flask equipped with a stir bar was added the intermediate obtained above (1mmol, 1.0 equiv.), which was then dissolved in 20 ml of methanol (THF or EA was added when the material is not soluble in methanol). 10% Pd/C (30-40 mg) was added to the solution and the reaction was placed under N_2. The solution was purged and backfilled with H_2 and then stirred under H_2 atmosphere (1 atm) overnight at room temperature (reaction is typically done in about 2-3 hours). Once the reaction was complete, the solution was passed through a Celite plug and concentrated. The crude mixture was then purified by either silica gel chromatography or flash LC using ethyl acetate/ hexane (1/10 to 2/10) to yield the tyrosine derivatives in 90-98% yield.



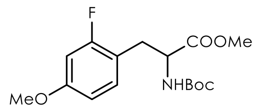
54

methyl 2-((tert-butoxycarbonyl)amino)-3-(3-fluoro-4-methoxyphenyl)propanoate(**54**). Follow the general procedure **B**, the title compound was obtained as a white solid from 3-fluoro-4-methoxybenzaldehyde.

^{1}H NMR (400 MHz, CDCl$_3$) δ 6.99 – 6.67 (m, 3H), 5.10 – 4.65 (m, 1H), 4.58 – 4.28 (m, 1H), 3.86 (s, 3H), 3.72 (s, 3H), 3.15 – 2.76 (m, 1H), 1.42 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 172.10, 154.99, 152.13 (d, *J* = 245.8 Hz), 146.57, 128.93 (d, *J* = 6.1 Hz), 124.96, 116.98 (d, *J* = 18.2 Hz), 113.41 (d, *J* = 2.0 Hz), 80.02, 56.23, 54.36, 52.27, 37.40, 28.26.

^{19}F NMR (376 MHz, CDCl$_3$) δ -134.80 – -135.40 (m).



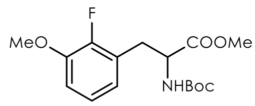
55

methyl 2-((tert-butoxycarbonyl)amino)-3-(2-fluoro-4-methoxyphenyl)propanoate(**55**). Follow the general procedure **B**, the title compound was obtained as a white solid from 2-fluoro-4-methoxybenzaldehyde.

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.02 (t, *J* = 8.5 Hz, 1H), 6.69 – 6.48 (m, 2H), 5.11 – 4.64 (m, 1H), 4.62 – 4.23 (m, 1H), 3.76 (s, 3H), 3.71 (s, 3H), 3.19 – 2.75 (m, 2H), 1.40 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 172.28, 161.82 (d, *J* = 245.1 Hz), 160.03 (d, *J* = 10.6 Hz), 155.00, 131.84 (d, *J* = 6.5 Hz), 114.78 (d, *J* = 16.6 Hz), 109.88 (d, *J* = 3.0 Hz), 101.51 (d, *J* = 26.1 Hz), 79.81, 55.49, 53.74, 52.27, 31.28, 28.25.

^{19}F NMR (376 MHz, CDCl$_3$) δ -115.45 – -115.65 (m).



56

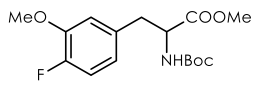
methyl 2-((tert-butoxycarbonyl)amino)-3-(2-fluoro-3-methoxyphenyl)propanoate(**56**). Follow the general procedure **B**, the title compound was obtained as a white solid from 2-fluoro-3-methoxybenzaldehyde.

^{1}H NMR (400 MHz, CDCl$_3$) δ 6.99 (td, *J* = 8.0, 1.4 Hz, 1H), 6.86 (t, *J* = 7.5 Hz, 1H), 6.72 (t, *J* = 6.7 Hz, 1H), 5.15 – 4.70 (m, 1H), 4.64 – 4.37 (m, 1H), 3.86 (s, 3H), 3.73 (s, 3H), 3.26 – 2.86 (m, 2H), 1.40 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 172.15, 155.03, 151.12 (d, *J* = 244.9 Hz), 147.68 (d, *J* = 11.2 Hz), 124.03 (d, *J* = 13.4 Hz), 123.77 (d, *J* = 4.6 Hz), 122.73 (d, *J* = 3.4 Hz), 112.19, 79.88, 56.18, 53.64, 52.35, 31.55, 28.24.

^{19}F NMR (376 MHz, CDCl$_3$) δ -140.36 (t, *J* = 6.9 Hz).

HRMS (ESI): Calculated for $C_{11}H_{15}NO_3F$ $(M+H)^+$: 228.1030; found: 228.1028.



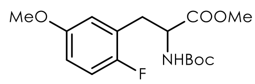
57

methyl 2-((tert-butoxycarbonyl) amino)-3-(4-fluoro-3-methoxyphenyl) propanoate (**57**). Follow the general procedure **B**, the title compound was obtained as a white solid from 4-fluoro-3-methoxybenzaldehyde.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.98 (dd, *J* = 11.2, 8.2 Hz, 1H), 6.72 (dd, *J* = 8.1, 2.0 Hz, 1H), 6.68 – 6.56 (m, 1H), 5.05 – 4.67 (m, 1H), 4.64 – 4.22 (m, 1H), 3.86 (s, 3H), 3.71 (s, 3H), 3.18 – 2.75 (m, 2H), 1.42 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.16, 154.98, 151.60 (d, *J* = 244.9 Hz), 147.43 (d, *J* = 10.6 Hz), 132.29 (d, *J* = 3.9 Hz), 121.47 (d, *J* = 6.8 Hz), 115.90 (d, *J* = 18.4 Hz), 114.37 (d, *J* = 1.9 Hz), 80.02, 56.15, 54.37, 52.26, 38.03, 28.28.

^{19}F NMR (376 MHz, $CDCl_3$) δ -137.52 – -137.94(m).



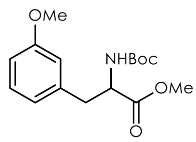
58-F

methyl 2-((tert-butoxycarbonyl)amino)-3-(2-fluoro-5-methoxyphenyl)propanoate(**58-F**). Follow the general procedure **B**, the title compound was obtained as a white solid from 2-fluoro-5-methoxybenzaldehyde. Spectral data matched literature data[28].

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94 (t, *J* = 9.1 Hz, 1H), 6.73 (dt, *J* = 8.9, 3.6 Hz, 1H), 6.65 (dd, *J* = 5.9, 3.1 Hz, 1H), 5.13 – 4.71 (m, 1H), 4.68 – 4.30 (m, 1H), 3.76 (s, 3H), 3.73 (s, 3H), 3.29 – 2.84 (m, 2H), 1.40 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.13, 155.76 (d, *J* = 237.8 Hz), 155.50 (d, *J* = 1.6 Hz), 154.99, 123.77 (d, *J* = 17.8 Hz), 116.39 (d, *J* = 4.1 Hz), 115.74 (d, *J* = 24.3 Hz), 113.66 (d, *J* = 8.1 Hz), 79.90, 55.68, 53.59, 52.34, 32.06, 28.25.

^{19}F NMR (376 MHz, $CDCl_3$) δ -137.52 – -137.94(m).



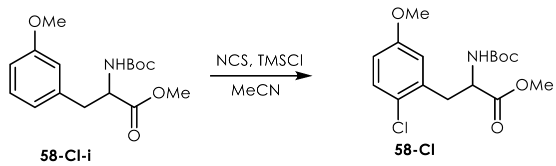
58-Cl-i

methyl 2-((tert-butoxycarbonyl)amino)-3-(3-methoxyphenyl)propanoate(58-Cl-i). The title compound was prepared according to reported procedure. Spectral data matched literature data[28]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (t, *J* = 7.9 Hz, 1H), 6.78 (dd, *J* = 8.2, 2.4 Hz, 1H), 6.71 (d, *J* = 7.5

Hz, 1H), 6.66 (s, 1H), 5.14 – 4.63 (m, J = 57.5 Hz, 1H), 4.63 – 4.27 (m, 1H), 3.78 (s, 3H), 3.72 (s, 3H), 3.16 – 2.76 (m, 2H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 172.28, 159.64, 155.05, 137.47, 129.50, 121.57, 114.93, 112.44, 79.90, 55.11, 54.31, 52.19, 38.29, 28.27.

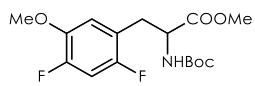


methyl 2-((tert-butoxycarbonyl)amino)-3-(2-chloro-5-methoxyphenyl)propanoate(58-Cl). Follow the reported chlorination method[17], the title compound was obtained as a white solid (234 mg, 68%) from compound **58-Cl-i** (309 mg, 1 mmol) and purified by flash LC using ethyl acetate/ hexane (1/20 to 1/10).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.24 (d, J = 9.3 Hz, 1H), 6.76 – 6.68 (m, 2H), 5.13 – 4.78 (m, 1H), 4.67 – 4.43 (m, 1H), 3.76 (s, 3H), 3.72 (s, 3H), 3.25 (dd, J = 13.8, 5.8 Hz, 1H), 3.12 – 2.80 (m, 1H), 1.38 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 172.28, 158.17, 154.92, 135.08, 130.10, 125.81, 116.56, 114.06, 79.86, 55.43, 53.42, 52.35, 36.25, 28.21.

HRMS (ESI): Calculated for $C_{16}H_{23}ClNO_5$ (M+H)$^+$: 344.1259; found: 344.1255.



59

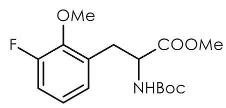
methyl 2-((tert-butoxycarbonyl)amino)-3-(2,4-difluoro-5-methoxyphenyl)propanoate(59). Follow the general procedure **B**, the title compound was obtained as a white solid from 2,4-difluoro-5-methoxybenzaldehyde.

^{1}H NMR (400 MHz, CDCl$_3$) δ 6.90 – 6.76 (m, 1H), 6.77 – 6.64 (m, 1H), 5.15 – 4.68 (m, 1H), 4.63 – 4.29(m, 1H), 3.84 (s, 3H), 3.73 (s, 3H), 3.20 – 2.75 (m, 2H), 1.41 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 171.99, 154.92, 154.47 (dd, J = 240.9, 10.3 Hz), 151.20 (dd, J = 248.6, 12.5 Hz), 143.95 (dd, J = 10.8, 3.0 Hz), 118.31 (dd, J = 17.3, 4.2 Hz), 115.68 (dd, J = 5.4, 2.8 Hz), 104.58 (dd, J = 28.2, 22.4 Hz), 80.01, 56.83, 53.54, 52.42, 31.63, 28.25.

^{19}F NMR (376 MHz, CDCl$_3$) δ -124.12 – -124.28 (m), -131.8 – -132.64(m)

HRMS (ESI): Calculated for $C_{11}H_{14}F_2NO_3$ (M+H)$^+$: 246.0936; found: 246.0934.



60

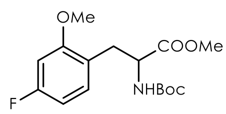
methyl 2-((tert-butoxycarbonyl)amino)-3-(3-fluoro-2-methoxyphenyl)propanoate(**60**). Follow the general procedure **B**, the title compound was obtained as a white solid from 3-fluoro-2-methoxybenzaldehyde.

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.04 – 6.82 (m, 3H), 5.29 – 4.85 (m, 1H), 4.60 – 4.23 (m, 1H), 3.94 (d, *J* = 2.0 Hz, 3H), 3.71 (s, 3H), 3.19 – 2.83 (m, 2H), 1.38 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 172.49, 155.22 (d, *J* = 246.7 Hz), 155.15, 145.97 (d, *J* = 10.4 Hz), 130.70, 126.10 (d, *J* = 3.1 Hz), 123.25 (d, *J* = 8.0 Hz), 115.97 (d, *J* = 19.4 Hz), 79.76, 61.15 (d, *J* = 6.9 Hz), 54.15, 52.21, 32.71, 28.24.

^{19}F NMR (376 MHz, CDCl$_3$) δ -129.90 – -130.40(m)

HRMS (ESI): Calculated for $C_{11}H_{15}FNO_3$ $(M+H)^+$: 228.1030; found: 228.1026.



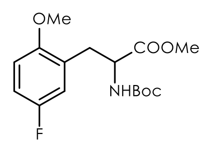
61

methyl 2-((tert-butoxycarbonyl)amino)-3-(4-fluoro-2-methoxyphenyl)propanoate(**61**). Follow the general procedure **B**, the title compound was obtained as a white solid from 4-fluoro-2-methoxybenzaldehyde. Spectral data matched literature data[16].

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.10 – 6.93 (m, 1H), 6.71 – 6.35 (m, 2H), 5.14 – 4.78 (m, 1H), 4.67 – 4.18 (m, 1H), 3.81 (s, 3H), 3.69 (s, 3H), 3.15 – 2.83 (m, 2H), 1.38 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 172.73, 162.87 (d, *J* = 244.9 Hz), 158.64 (d, *J* = 9.8 Hz), 155.11, 131.63 (d, *J* = 9.9 Hz), 120.28 (d, *J* = 3.3 Hz), 106.73 (d, *J* = 21.1 Hz), 98.87 (d, *J* = 25.8 Hz), 79.63, 55.57, 53.73, 52.05, 32.46, 28.24.

^{19}F NMR (376 MHz, CDCl$_3$) δ -112.06 – -112.81 (m).



62

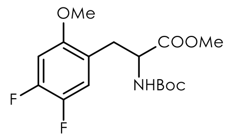
methyl 2-((tert-butoxycarbonyl)amino)-3-(5-fluoro-2-methoxyphenyl)propanoate(**62**). Follow the general procedure **B**, the title compound was obtained as a white solid from 5-fluoro-2-methoxybenzaldehyde. Spectral data matched literature data[21].

^{1}H NMR (400 MHz, CDCl$_3$) δ 6.90 (td, *J* = 8.7, 2.4 Hz, 1H), 6.82 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.77 (dd, *J*

= 8.7, 4.3 Hz, 1H), 5.30 – 4.90 (m, 1H), 4.63 – 4.22 (m, 1H), 3.80 (s, 3H), 3.71 (s, 3H), 3.15 – 2.83 (m, 2H), 1.38 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 172.53, 156.50 (d, *J* = 281.7 Hz), 155.52, 153.75 (d, *J* = 1.8 Hz), 126.36 (d, *J* = 7.3 Hz), 117.83 (d, *J* = 23.3 Hz), 114.07 (d, *J* = 22.7 Hz), 111.08 (d, *J* = 8.3 Hz), 79.68, 55.84, 53.64, 52.11, 32.88, 28.22.

^{19}F NMR (376 MHz, CDCl$_3$) δ -123.69 – -124.43 (m).



63

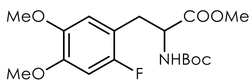
methyl 2-((tert-butoxycarbonyl)amino)-3-(4,5-difluoro-2-methoxyphenyl)propanoate(**63**). Follow the general procedure **B**, the title compound was obtained as a white solid from 4,5-difluoro-2-methoxybenzaldehyde.

^{1}H NMR (400 MHz, CDCl$_3$) δ 6.84 (dd, *J* = 11.3, 6.9 Hz, 1H), 6.66 (dd, *J* = 10.8, 7.1 Hz, 1H), 5.19 – 4.69 (m, 1H), 4.60 – 4.27 (m, 1H), 3.84 (s, 3H), 3.72 (d, *J* = 11.3 Hz, 3H), 3.11 (dd, *J* = 14.0, 5.4 Hz, 1H), 2.95 (dd, *J* = 13.9, 6.2 Hz, 1H), 1.40 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 171.98, 157.01 (dd, *J* = 241.7, 2.5 Hz), 154.92, 148.25 (dd, *J* = 241.8, 2.9 Hz), 147.48 – 147.19 (m), 117.79 (dd, *J* = 20.3, 6.2 Hz), 114.37 (dd, *J* = 18.7, 6.2 Hz), 101.39 (d, *J* = 28.2 Hz), 79.98, 56.37, 53.51, 52.38, 31.21, 28.20.

^{19}F NMR (376 MHz, CDCl$_3$) δ -120.26 – -120.60 (m), -140.17 – -141.11 (m).

HRMS (ESI): Calculated for $C_{11}H_{14}F_2NO_3$ $(M+H)^+$: 246.0936; found: 246.0931.



64-F

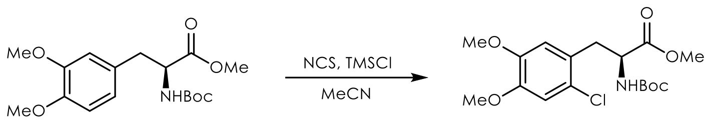
methyl 2-((tert-butoxycarbonyl)amino)-3-(2-fluoro-4,5-dimethoxyphenyl)propanoate(**64-F**). Follow the general procedure **B**, the title compound was obtained as a white solid (341 mg) from 2-fluoro-4,5-dimethoxybenzaldehyde.

^{1}H NMR (400 MHz, CDCl$_3$) δ 6.68 – 6.52 (m, 2H), 5.16 – 4.68 (m, 1H), 4.61 – 4.25 (m, 1H), 3.84 (s, 3H), 3.83 (s, 3H), 3.73 (s, 3H), 3.18 – 2.78 (m, 2H), 1.41 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 172.23, 155.40 (d, *J* = 238.2 Hz), 154.97, 148.86 (d, *J* = 10.8 Hz), 145.06, 113.44 (d, *J* = 6.1 Hz), 113.27 (d, *J* = 17.5 Hz), 99.92 (d, *J* = 28.3 Hz), 79.87, 56.36, 56.07, 53.72, 52.33, 31.44, 28.27.

^{19}F NMR (376 MHz, CDCl$_3$) δ -125.04 (dd, *J* = 10.7, 7.2 Hz).

HRMS (ESI): Calculated for $C_{12}H_{17}FNO_4$ $(M+H)^+$: 258.1136; found: 258.1131.



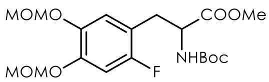
L-64 *L*-64-Cl

methyl (*S*)-2-((tert-butoxycarbonyl)amino)-3-(2-chloro-4,5-dimethoxyphenyl)propanoate(*L*-64-Cl). Follow the reported chlorination method[17], the title compound was prepared as a white solid (190 mg, 42%) from compound ***L*-64** (407 mg, 1.2 mmol) and purified by silica gel chromatography using ethyl acetate/ hexane (1/3) as eluent.

^{1}H NMR (400 MHz, CDCl$_3$) δ 6.85 (s, 1H), 6.67 (s, 1H), 5.20 – 4.70 (m, 1H), 4.72 – 4.35 (m, *J* = 6.6 Hz, 1H), 3.85 (s, 6H), 3.73 (s, 3H), 3.20 (dd, *J* = 14.0, 6.1 Hz, 1H), 3.13 – 2.81 (m, *J* = 14.0, 7.6 Hz, 1H), 1.39 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 172.37, 154.92, 148.50, 147.70, 125.79, 125.49, 113.54, 112.46, 79.89, 56.08, 53.58, 52.37, 35.66, 28.26.

HRMS (ESI): Calculated for $C_{10}H_{12}F_2NO_3$ $(M+H)^+$: 274.0841; found: 274.0831



65

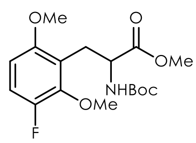
methyl 2-((tert-butoxycarbonyl)amino)-3-(2-fluoro-4,5-bis(methoxymethoxy)phenyl)propanoate(**65**). Follow the general procedure **B**, the title compound was obtained as a white solid from 2-fluoro-4,5-bis(methoxymethoxy)benzaldehyde which obtained from literature procedure[29].

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.00 – 6.73 (m, 2H), 5.19 (s, 2H), 5.14 (q, *J* = 6.7 Hz, 2H), 5.10 – 4.64 (m, 1H), 4.64 – 4.25 (m, 1H), 3.74 (s, 3H), 3.53 – 3.47 (m, 6H), 3.18 – 2.62 (m, 2H), 1.41 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 172.10, 156.32 (d, *J* = 240.5 Hz), 154.97, 147.19 (d, *J* = 10.3 Hz), 143.14, 119.41 (d, *J* = 5.8 Hz), 115.63 (d, *J* = 17.5 Hz), 104.37 (d, *J* = 28.1 Hz), 96.06, 95.38, 79.83, 56.18 (d, *J* = 9.3 Hz), 53.63, 52.28, 31.30, 28.24.

^{19}F NMR (376 MHz, CDCl$_3$) δ -122.51 – -122.91 (m).

HRMS (ESI): Calculated for $C_{19}H_{29}FNO_8$ $(M+H)^+$: 418.1872; found: 418.1869.



66-F

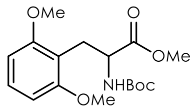
methyl 2-((tert-butoxycarbonyl)amino)-3-(3-fluoro-2,6-dimethoxyphenyl)propanoate(**66-F**). Follow the general procedure **B**, the title compound was obtained as a white solid from 3-fluoro-2,6-dimethoxybenzaldehyde(**49-F-i**).

^{1}H NMR (400 MHz, CDCl$_3$) δ 6.93 (dd, *J* = 11.3, 9.2 Hz, 1H), 6.49 (dd, *J* = 9.1, 3.6 Hz, 1H), 5.38 – 5.04(m, 1H), 4.54 – 4.17 (m, 1H), 3.94 (d, *J* = 2.2 Hz, 3H), 3.80 (s, 3H), 3.73 (s, 3H), 3.02 – 3.21 (m, 1H), 2.97 (dd, *J* = 13.1, 9.6 Hz, 1H), 1.35 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 173.08, 155.39, 154.09, 149.93 (d, *J* = 238.1Hz), 146.42 (d, *J* = 11.2Hz), 118.97, 114.81 (d, *J* = 20.5Hz), 110.00, 104.70 (d, *J* = 7.6 Hz), 79.46, 77.20, 61.15 (d, *J* = 7.2 Hz, 4H), 55.90, 53.59, 52.14, 28.24, 26.31.

^{19}F NMR (376 MHz, CDCl$_3$) δ -139.00 – -139.40 (m).

HRMS (ESI): Calculated for $C_{12}H_{17}FNO_4$ $(M+H)^+$: 258.1136; found: 258.1131.



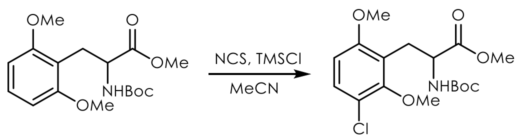
66-Cl-i

methyl 2-((tert-butoxycarbonyl)amino)-3-(2,6-dimethoxyphenyl)propanoate(**66-Cl-i**). Follow the general procedure **B**, the title compound was prepared as a white solid from 2,6-dimethoxybenzaldehyde.

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.16 (t, *J* = 8.3 Hz, 1H), 6.53 (d, *J* = 8.4 Hz, 2H), 5.45 – 5.14 (m, 1H), 4.46 – 4.15 (m, 1H), 3.80 (s, 6H), 3.71 (s, 3H), 3.20 – 2.92 (m, 2H), 1.34 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 173.33, 158.39, 155.43, 128.10, 112.86, 103.49, 79.12, 55.56, 53.72, 51.89, 28.18, 25.17.

HRMS (ESI): Calculated for $C_{12}H_{18}NO_4$ $(M+H)^+$: 240.1230; found: 240.1226.



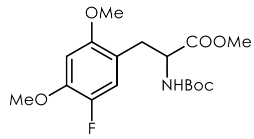
66-Cl-i **66-Cl**

methyl 2-((tert-butoxycarbonyl)amino)-3-(3-chloro-2,6-dimethoxyphenyl)propanoate(**66-Cl**). Follow the reported chlorination method[17], the title compound was obtained as a white solid (284 mg, 76%) from compound **66-Cl-i** (339 mg, 1 mmol) and purified by flash LC using ethyl acetate/ hexane (1/20 to 1/10).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.19 (d, *J* = 8.9 Hz, 1H), 6.58 (d, *J* = 8.9 Hz, 1H), 5.38 – 5.00 (m, 1H), 4.55 – 4.15 (m, 1H), 3.83 (s, 3H), 3.80 (s, 3H), 3.71 (s, 3H), 3.23 – 3.00 (m, 1H), 2.95 (dd, *J* = 13.2, 9.5 Hz, 1H),1.32 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 172.90, 157.27, 155.28, 155.10, 128.83, 120.24, 119.32, 107.01, 79.42, 60.83, 55.81, 53.47, 52.08, 28.14, 26.72.

HRMS (ESI): Calculated for $C_{12}H_{17}ClNO_4$ $(M+H)^+$: 274.0841; found: 274.0836.



67-F

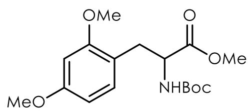
methyl 2-((tert-butoxycarbonyl)amino)-3-(5-fluoro-2,4-dimethoxyphenyl)propanoate(**67-F**). Follow the general procedure **B**, the title compound was obtained as a white solid from 5-fluoro-2,4-dimethoxybenzaldehyde(**50-F-i**).

^{1}H NMR (400 MHz, CDCl$_3$) δ 6.81 (d, *J* = 11.5 Hz, 1H), 6.50 (d, *J* = 7.2 Hz, 1H), 5.31 – 4.87 (m, 1H), 4.56 – 4.18 (m, 1H), 3.89 (s, 3H), 3.81 (s, 3H), 3.71 (s, 3H), 3.10 – 2.78 (m, 2H), 1.39 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 172.62, 155.14, 153.81, 146.79 (d, *J* = 10.8 Hz), 146.48 (d, *J* = 238.2 Hz), 118.25 (d, *J* = 18.7 Hz), 116.58 (d, *J* = 5.8 Hz), 98.20, 79.69, 56.71, 56.03, 53.80, 52.11, 32.16, 28.25.

^{19}F NMR (376 MHz, CDCl$_3$) δ -145.09 – -145.73 (m).

HRMS (EI): Calculated for $C_{12}H_{15}FNO_4$ $[M]^+$: 256.0985; found: 256.0981.



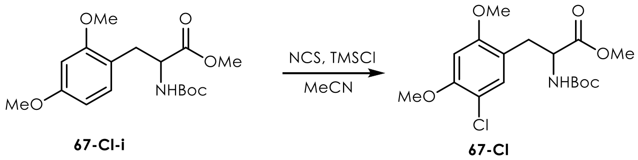
67-Cl-i

methyl 2-((tert-butoxycarbonyl)amino)-3-(2,4-dimethoxyphenyl)propanoate(**67-Cl-i**). Follow the general procedure **B**, the title compound was prepared as a white solid from 2,4-dimethoxybenzaldehyde.

^{1}H NMR (400 MHz, CDCl$_3$) δ 6.98 (d, *J* = 8.0 Hz, 1H), 6.54 – 6.27 (m, 2H), 5.26 – 4.88 (m, 1H), 4.62 – 4.17 (m, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.69 (s, 3H), 3.13 – 2.74 (m, 2H), 1.39 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 172.92, 160.07, 158.49, 155.24, 131.43, 116.93, 104.20, 98.49, 79.49, 55.32, 55.30, 54.18, 51.98, 32.16, 28.28.

HRMS (ESI): Calculated for $C_{12}H_{18}NO_4^+$ $(M+H)^+$: 240.1230; found: 240.1225.



67-Cl-i **67-Cl**

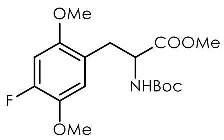
methyl 2-((tert-butoxycarbonyl)amino)-3-(5-chloro-2,4-dimethoxyphenyl)propanoate(**67-Cl**). Follow the reported chlorination method[17], the title compound was prepared as a white solid

(280 mg, 75%) from compound **67-Cl-i** (339 mg, 1 mmol) and purified by flash LC using ethyl acetate/ hexane (5% to 10%)

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.04 (s, 1H), 6.46 (s, 1H), 5.15 – 4.92 (m, 1H), 4.53 – 4.16 (m, 1H), 3.89 (s, 3H), 3.83 (s, 3H), 3.70 (s, 3H), 3.03 (dd, *J* = 13.7, 5.4 Hz, 1H), 2.89 (dd, *J* = 13.6, 7.5 Hz, 1H), 1.38 (s, 9H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 172.60, 157.15, 155.08, 154.78, 131.89, 117.60, 113.24, 96.48, 79.67, 56.28, 55.75, 53.67, 52.08, 32.15, 28.23.

HRMS (ESI): Calculated for $C_{12}H_{17}ClNO_4$ $(M+H)^+$: 274.0841; found: 274.0836.



68

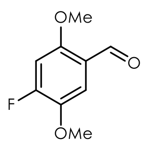
methyl 2-((tert-butoxycarbonyl)amino)-3-(4-fluoro-2,5-dimethoxyphenyl)propanoate(**68**). Follow the general procedure, the title compound was obtained as a white solid from 4-fluoro-2,5-dimethoxybenzaldehyde(**68-i**).

^{1}H NMR (400 MHz, CDCl$_3$) δ 6.74 (d, *J* = 9.4 Hz, 1H), 6.66 (d, *J* = 12.8 Hz, 1H), 3.15 – 2.74 (m, 1H), 4.54 – 4.16 (m, 1H), 3.83 (d, *J* = 0.7 Hz, 3H), 3.77 (s, 3H), 3.71 (s, 3H), 3.15 – 2.74 (m, 2H), 1.39 (s, 10H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 172.64, 155.14, 151.82 (d, *J* = 244.7 Hz), 151.71 (d, *J* = 8.1 Hz), 140.92 (d, *J* = 11.0 Hz), 119.84 (d, *J* = 3.8 Hz), 117.17 (d, *J* = 3.1 Hz), 100.49 (d, *J* = 22.4 Hz), 79.69, 57.25, 56.03, 53.93, 52.12, 32.46, 28.27.

^{19}F NMR (376 MHz, CDCl$_3$) δ -133.20 – -133.76 (m).

HRMS (ESI): Calculated for $C_{12}H_{17}FNO_4$ $(M+H)^+$: 258.1136; found: 258.1130.



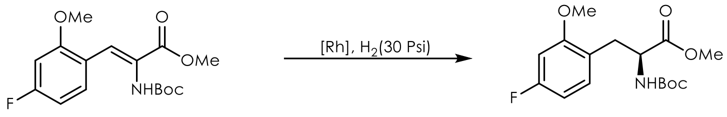
68-i

4-fluoro-2,5-dimethoxybenzaldehyde(68-i). The title compound was prepared from reported procedure[27].

^{1}H NMR (400 MHz, CDCl$_3$) δ 10.36 (s, 1H), 7.44 (d, *J* = 9.7 Hz, 1H), 6.78 (d, *J* = 12.4 Hz, 1H), 3.882 (s, 3H), 3.879 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 188.05 (d, *J* = 1.3 Hz), 157.36 (d, *J* = 9.1 Hz), 157.27 (d, *J* = 256.6 Hz), 142.17 (d, *J* = 11.4 Hz), 120.65 (d, *J* = 3.3 Hz), 112.00 (d, *J* = 4.7 Hz), 101.33 (d, *J* = 22.6 Hz) 56.59, 56.32.

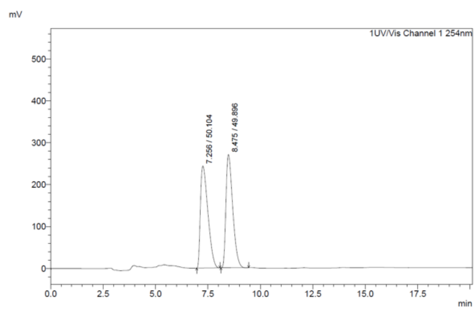
^{19}F NMR (376 MHz, CDCl$_3$) δ -120.04 (dd, *J* = 12.4, 9.7 Hz)



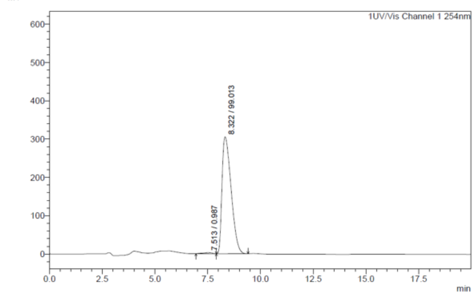
***L*-61**

methyl (*S*)-2-((tert-butoxycarbonyl)amino)-3-(4-fluoro-2-methoxyphenyl)propanoate(*L*-61). To a solution of methyl (Z)-2-((tert-butoxycarbonyl)amino)-3-(4-fluoro-2-methoxyphenyl)acrylate (150 mg, 0.46 mmol) in MeOH was added 1,2-Bis((2S,5S)-2,5-diethylphospholano)benzene(cyclooctadiene)rhodium(I) tetrafluoroborate (10 mg, 0.015mmol, 0.033 equiv.). The solution was purged and backfilled with H_2 and then stirred under H_2 atmosphere (30 psi) for 16 h at room temperature. The reaction solution was then concentrated in vacuo and purified by silica gel chromatography using ethyl acetate/hexane (1/10) to afford the title compound as a white solid (150 mg, 99% yield). Spectral data matched racemic compound **61**. The enantiomeric excess was determined to be 98% by HPLC equipped with a chiral column.

HPLC conditions: Column: Phenomenex, Lux® 5 μm Cellulose-1, 250 x 4.6 mm LC Column. Solvent A: Hexane; Solvent B: isopropanol. Isocratic elution at 10 % solvent B. Flow rate: 1 ml/min.

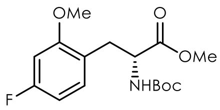


Peak#	Ret. Time	Area	Height	Mark	Area%
1	7.256	6055346	243570	M	50.104
2	8.475	6030190	270479	M	49.896



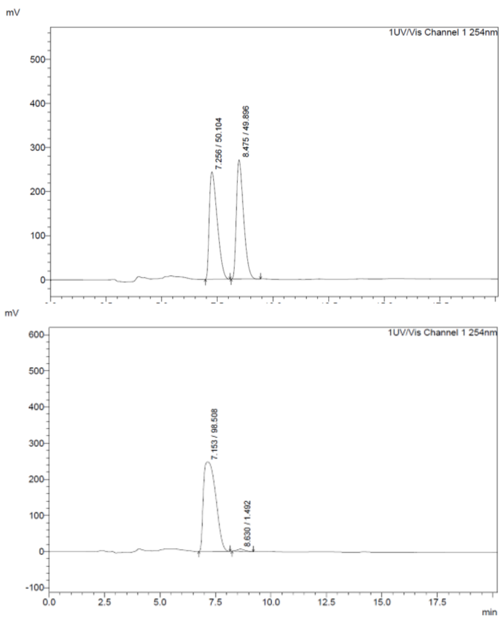
Peak#	Ret. Time	Area	Height	Mark	Area%
1	7.513	91247	3194	M	0.987
2	8.322	9157406	305209	M	99.013

Supplementary Figure1. Determination of enantiomeric excess of ***L*-61**



***D*-61**

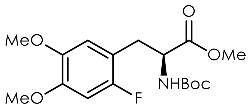
methyl (R)-2-((tert-butoxycarbonyl)amino)-3-(4-fluoro-2-methoxyphenyl)propanoate(***D*-61**). Follow the same preparation procedure of compound ***L*-61**, the title compound was obtained as a white solid (136 mg, 90% yield) with catalyst 1,2-Bis((2R,5R)-2,5-diethylphospholano)benzene(cyclooctadiene)rhodium(I) tetrafluoroborate (10 mg, 3.3% mmol). Spectral data matched racemic compound **61**. The enantiomeric excess was determined to be 97% under the same HPLC conditions with ***L*-61**.



Peak#	Ret. Time	Area	Height	Mark	Area%
1	7.256	6055346	243570	M	50.104
2	8.475	6030190	270479	M	49.896

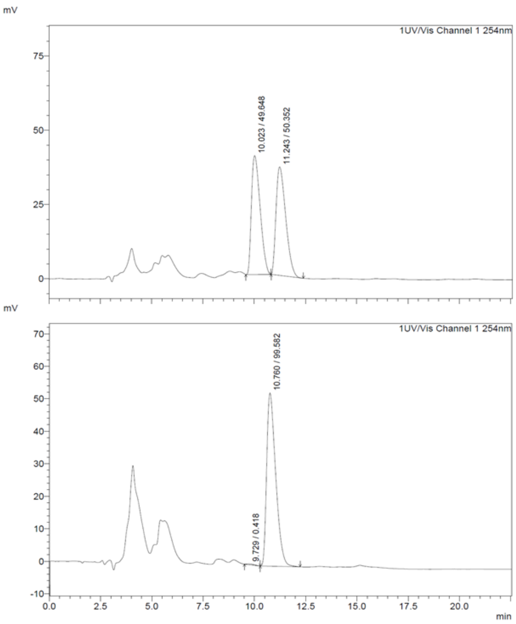
Peak#	Ret. Time	Area	Height	Mark	Area%
1	7.153	9545661	247688	M	98.508
2	8.630	144548	5893	M	1.492

Supplementary Figure 2. Determination of enantiomeric excess of ***D*-61**



***L*-64-F**

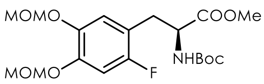
methyl (S)-2-((tert-butoxycarbonyl)amino)-3-(2-fluoro-4,5-dimethoxyphenyl)propanoate(***L*-64-F**). Follow the preparation procedure of compound ***L*-61**, the title compound was obtained as a white solid (168 mg, 93%) from the asymmetric reduction of methyl (Z)-2-((tert-butoxycarbonyl)amino)-3-(2-fluoro-4,5-dimethoxyphenyl)acrylate(180 mg, 0.51 mmol) with the same rhodium catalyst (11 mg, 3.3% mmol). The enantiomeric excess was determined to be 99% under the same HPLC conditions with ***L*-61**. Spectral data matched racemic compound **64.**



Peak#	Ret. Time	Area	Height	Mark	Area%
1	10.023	1183059	40046	M	49.648
2	11.243	1199832	36546	M	50.352

Peak#	Ret. Time	Area	Height	Mark	Area%
1	9.729	6850	260	M	0.418
2	10.760	1632100	53342	M	99.582

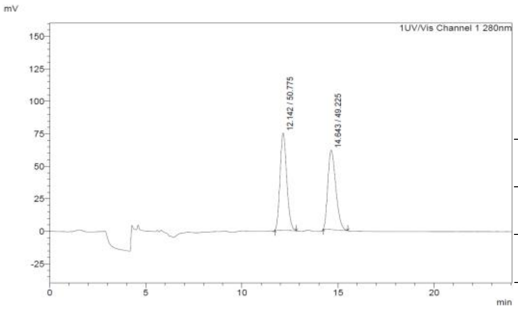
Supplementary Figure 3. Determination of enantiomeric excess of ***L*-64-F**



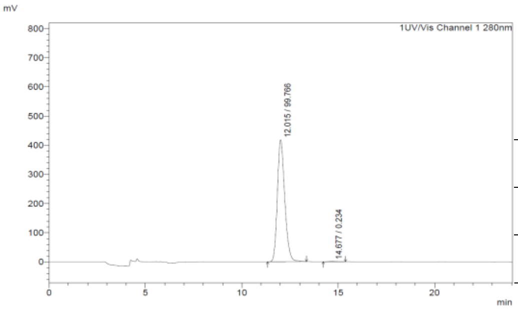
***L*-65**

methyl (*S*)-2-((tert-butoxycarbonyl)amino)-3-(2-fluoro-4,5-bis(methoxymethoxy)phenyl)propanoate(*L*-65). Follow the same preparation procedure of compound ***L*-61**, the title compound was obtained as a colorless oil (478 mg, 95%) from the asymmetric reduction of methyl (Z)-2-((tert-butoxycarbonyl)amino)-3-(2-fluoro-4,5-bis(methoxymethoxy)phenyl)acrylate (500 mg, 1.2 mmol) with the same rhodium catalyst(26 mg, 3.3% mmol). Spectral data matched racemic compound **65.** The enantiomeric excess was determined to be > 99%.

HPLC conditions: Column: Phenomenex, Lux® 5 μm Cellulose-2, 250 x 4.6 mm LC Column. Solvent A: Hexane; Solvent B: isopropanol. Isocratic elution at 10 % solvent B. Flow rate: 1 ml/min.



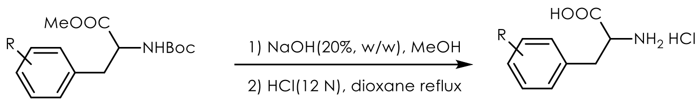
Peak#	Ret. Time	Area	Height	Mark	Area%
1	12.142	1814385	74858	M	50.775
2	14.643	1759011	61159	M	49.225



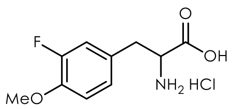
Peak#	Ret. Time	Area	Height	Mark	Area%
1	12.015	11105544	417897	M	99.766
2	14.677	26095	988	M	0.234

Supplementary Figure 4. Determination of enantiomeric excess of ***L*-65**

General procedure for deprotection of tyrosine derivatives (general procedure C)



To a solution of tyrosine derivatives (**54-63**) in methanol (10 ml) was added NaOH solution (20%, 2 ml). The solution was stirred for 4 h and then concentrated to remove the methanol. Water and Et_2O was added to the resulted solution. The aqueous phase was collected and neutralize with HCl (aq. 1N). The solution was extracted with ethyl acetate (3 x15 ml). The organic phase was combined and washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give the hydrolysis product which was dissolved in dioxane (10 ml). After adding HCl (12 N, 2 mL), the solution was refluxed for 2h and then concentrated. The crude product was triturated with Et_2O and filtered to give the amino acid hydrochloride salt.

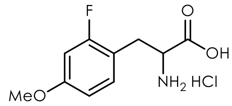


54-F-COOH

2-amino-3-(3-fluoro-4-methoxyphenyl)propanoic acid hydrochloride(54-F-COOH). Follow the general procedure **C**, the title compound was obtained as a white solid (218 mg, 88%) from **54** (327 mg, 1mmol).

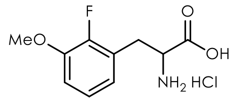
^{1}H NMR (400 MHz, D_2O) δ 7.24 – 6.90 (m, 3H), 4.26 (dt, *J* = 34.2, 17.2 Hz, 1H), 3.85 (s, 3H), 3.24 (dd, *J* = 14.7, 5.6 Hz, 1H), 3.13 (dd, *J* = 14.7, 7.5 Hz, 1H).

^{13}C NMR (100 MHz, D_2O) δ 171.22, 151.72 (d, *J* = 243.4 Hz), 146.26 (d, *J* = 10.6 Hz), 126.92 (d, *J* = 6.5 Hz), 125.61 (d, *J* = 3.5 Hz), 116.60 (d, *J* = 18.6 Hz), 114.13 (d, *J* = 2.0 Hz), 56.03, 53.91, 34.54.
^{19}F NMR (376 MHz, D_2O) δ -103.59 – -161.95 (m).
HRMS (ESI): Calculated for $C_{10}H_{13}FNO_3$ $(M+H)^+$: 214.0874; found: 214.0866.



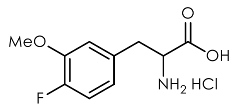
55-F-COOH

2-amino-3-(2-fluoro-4-methoxyphenyl)propanoic acid hydrochloride(55-F-COOH). Follow the general procedure **C**, the title compound was obtained as a light-brown solid (64 mg, 85%) from compound **55** (98 mg, 0.3 mmol).
^1H NMR (400 MHz, D_2O) δ 7.32 – 7.18 (m, 1H), 6.87 – 6.74 (m, 2H), 4.28 (dd, *J* = 7.3, 5.9 Hz, 1H), 3.86 – 3.76 (m, 3H), 3.34 (dd, *J* = 14.8, 5.5 Hz, 1H), 3.19 (dd, *J* = 14.8, 7.3 Hz, 1H).
^{13}C NMR (100 MHz, D_2O) δ 171.43, 161.67 (d, *J* = 244.0 Hz), 160.08 (d, *J* = 10.0 Hz), 132.14 (d, *J* = 6.1 Hz), 112.91 (d, *J* = 16.3 Hz), 110.54 (d, *J* = 2.9 Hz), 101.82 (d, *J* = 25.9 Hz), 55.61, 53.41, 28.87.
^{19}F NMR (376 MHz, D_2O) δ -115.50 – -115.67 (m).
HRMS (ESI): Calculated for $C_{10}H_{13}FNO_3$ $(M+H)^+$: 214.0874; found: 214.0868.



56-F-COOH

2-amino-3-(2-fluoro-3-methoxyphenyl)propanoic acid hydrochloride(56-F-COOH). Follow the general procedure **C**, the title compound was obtained as a light-brown solid (60 mg, 80%) from compound **56** (98 mg, 0.3 mmol).
^1H NMR (400 MHz, D_2O) δ 7.20 – 7.10 (m, 2H), 6.92 (td, *J* = 6.9, 2.3 Hz, 1H), 4.30 (dd, *J* = 7.4, 6.0 Hz, 1H), 3.91 (s, 3H), 3.40 (dd, *J* = 15.1, 5.4 Hz, 1H), 3.32 – 3.16 (m, 1H).
^{13}C NMR (100 MHz, D_2O) δ 171.39, 150.68 (d, *J* = 242.6 Hz), 146.94 (d, *J* = 10.8 Hz), 124.79 (d, *J* = 4.6 Hz,), 122.87 (d, *J* = 3.1 Hz, 16H), 121.80 (d, *J* = 13.1 Hz, 7H), 113.61 (d, *J* = 1.6 Hz, 16H), 56.13 (s, 14H), 53.31 (s, 18H), 29.25 (d, *J* = 3.1 Hz, 17H).
^{19}F NMR (376 MHz, D_2O) δ -140.99 (t, *J* = 6.9 Hz).
HRMS (ESI): Calculated for $C_{10}H_{13}FNO_3$ $(M+H)^+$: 214.0874; found: 214.0867.



57-F-COOH

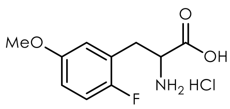
2-amino-3-(4-fluoro-3-methoxyphenyl)propanoic acid hydrochloride(57-F-COOH). Follow the general procedure **C**, the title compound was obtained as a white solid (223 mg, 90%) from compound **57** (327 mg, 1mmol)

^{1}H NMR (400 MHz, D_2O) δ 7.14 (dd, *J* = 11.6, 8.3 Hz, 1H), 7.03 (dd, *J* = 8.2, 1.9 Hz, 1H), 6.94 – 6.80 (m, 1H), 4.31 (dd, *J* = 7.6, 5.7 Hz, 1H), 3.87 (s, 3H), 3.30 (dd, *J* = 14.6, 5.6 Hz, 1H), 3.18 (dd, *J* = 14.7, 7.6 Hz, 1H).

^{13}C NMR (100 MHz, D_2O) δ 171.39, 151.47 (d, *J* = 242.8 Hz), 146.92 (d, *J* = 10.9 Hz), 130.56 (d, *J* = 3.8 Hz,), 122.09 (d, *J* = 7.3 Hz), 116.19 (d, *J* = 18.4 Hz), 114.58, 56.04, 54.07, 35.18.

^{19}F NMR (376 MHz, D_2O) δ -137.79 – -137.93 (m).

HRMS (ESI): Calculated for $C_{10}H_{13}FNO_3$ $(M+H)^+$: 214.0874; found: 214.0868.



58-F-COOH

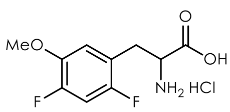
2-amino-3-(2-fluoro-5-methoxyphenyl)propanoic acid hydrochloride(58-F-COOH). Follow the general procedure **C**, the title compound was obtained as a white solid (70 mg, 90%) from compound **58-F** (100 mg, 0.31 mmol).

^{1}H NMR (400 MHz, D_2O) δ 7.13 (t, *J* = 9.3 Hz, 1H), 6.95 (dt, *J* = 9.0, 3.7 Hz, 1H), 6.90 (dd, *J* = 6.0, 3.1 Hz, 1H), 4.32 (t, *J* = 6.6 Hz, 1H), 3.80 (s, 3H), 3.37 (dd, *J* = 14.8, 5.8 Hz, 1H), 3.21 (dd, *J* = 14.7, 7.5 Hz, 1H).

^{13}C NMR (100 MHz, D_2O) δ 171.28, 155.73 (d, *J* = 236.7 Hz), 155.08 (d, *J* = 1.9 Hz), 121.72 (d, *J* = 17.9 Hz), 116.50 (d, *J* = 4.1 Hz), 116.32 (d, *J* = 23.9 Hz), 114.98 (d, *J* = 8.4 Hz), 55.81, 53.27, 29.61.

^{19}F NMR (376 MHz, D_2O) δ -127.93 – -128.46 (m).

HRMS (ESI): Calculated for $C_{10}H_{13}FNO_3$ $(M+H)^+$: 214.0874; found: 214.0867.



59-F-COOH

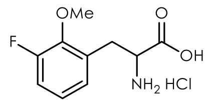
2-amino-3-(2,4-difluoro-5-methoxyphenyl)propanoic acid hydrochloride(59-F-COOH). Follow the general procedure **C**, the title compound was obtained as a light-brown solid (69 mg, 89%) from compound **59** (100 mg, 0.29 mmol).

^{1}H NMR (400 MHz, D_2O) δ 7.13 – 6.99 (m, *J* = 9.6, 2.1 Hz, 2H), 4.30 (dd, *J* = 7.2, 6.0 Hz, 1H), 3.87 (s, 3H), 3.36 (dd, *J* = 14.9, 5.8 Hz, 1H), 3.22 (dd, *J* = 15.0, 7.4 Hz, 1H).

^{13}C NMR (100 MHz, D_2O) δ 171.26, 154.50 (dd, *J* = 239.7, 10.9 Hz), 151.26 (dd, *J* = 246.7, 12.4 Hz), 143.56 (dd, *J* = 10.7, 3.0 Hz), 116.51 (dd, *J* = 17.2, 4.1 Hz), 115.87 (dd, *J* = 5.2, 2.7 Hz), 104.72 (dd, *J* = 28.0, 22.6 Hz), 56.68, 53.32, 29.11.

^{19}F NMR (376 MHz, D$_2$O) δ -123.67 – -124.01 (m), -132.28 (ddd, *J* = 11.4, 9.6, 3.5 Hz).

HRMS (ESI): Calculated for $C_{10}H_{12}F_2NO_3$ $(M+H)^+$: 232.0780; found: 232.0774.



60-F-COOH

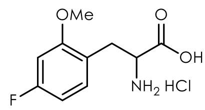
2-amino-3-(3-fluoro-2-methoxyphenyl)propanoic acid hydrochloride(**60-F-COOH**). Follow the general procedure **C**, the title compound was obtained as a white solid (62 mg, 83%) from compound **60** (98 mg, 0.3 mmol).

^{1}H NMR (400 MHz, D$_2$O) δ 7.25 – 7.02 (m, 3H), 4.37 – 4.26 (m, 1H), 3.42 (dd, *J* = 14.4, 6.0 Hz, 1H), 3.24 (dd, *J* = 14.4, 7.4 Hz, 1H).

^{13}C NMR (100 MHz, D$_2$O) δ 171.36, 155.12 (d, *J* = 245.9 Hz), 145.35 (d, *J* = 9.9 Hz), 128.44 (d, *J* = 2.2 Hz), 126.47 (d, *J* = 3.1 Hz), 124.52 (d, *J* = 8.2 Hz), 116.91 (d, *J* = 19.1 Hz), 61.29 (d, *J* = 6.2 Hz), 53.49, 30.48 (d, *J* = 2.5 Hz).

^{19}F NMR (376 MHz, D$_2$O) δ -130.45 – -130.64 (m).

HRMS (ESI): Calculated for $C_{10}H_{13}FNO_3$ $(M+H)^+$: 214.0874; found: 214.0867.



61-F-COOH

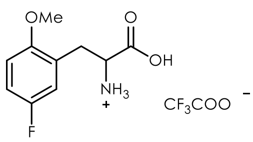
2-amino-3-(4-fluoro-2-methoxyphenyl)propanoic acid hydrochloride(**61-F-COOH**). Follow the general procedure **C**, the title compound was obtained as a white solid (65 mg, 87%) from compound **61** (98 mg, 0.3 mmol).

^{1}H NMR (400 MHz, D$_2$O) δ 7.22 (t, *J* = 7.5 Hz, 1H), 6.86 (dd, *J* = 11.2, 2.3 Hz, 1H), 6.73 (td, *J* = 8.5, 2.4 Hz, 1H), 4.37 – 4.25 (m, 1H), 3.85 (s, 3H), 3.34 (dd, *J* = 14.5, 5.5 Hz, 1H), 3.15 (dd, *J* = 14.5, 7.2 Hz, 1H).

^{13}C NMR (100 MHz, D$_2$O) δ 171.67, 163.27 (d, *J* = 243.7 Hz), 158.69 (d, *J* = 10.4 Hz), 132.09 (d, *J* = 10.3 Hz), 117.77 (d, *J* = 3.1 Hz), 107.03 (d, *J* = 21.4 Hz), 99.47 (d, *J* = 26.3 Hz), 55.41, 53.28, 30.25.

^{19}F NMR (376 MHz, D$_2$O) δ -111.69 – -111.88 (m).

HRMS (ESI): Calculated for $C_{10}H_{13}FNO_3$ $(M+H)^+$: 214.0874; found: 214.0867.



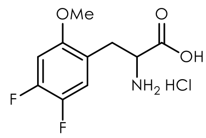
62-F-COOH

2-amino-3-(5-fluoro-2-methoxyphenyl)propanoic acid trifluoroacetic acid(62-F-COOH). The title compound was obtained from our reported procedure[21].

^{1}H NMR (400 MHz, D_2O) δ 7.10 (td, *J* = 8.6, 3.0 Hz, 1H), 7.05 – 6.96 (m, 2H), 4.30 (dd, *J* = 6.9, 5.9 Hz, 1H), 3.84 (s, 3H), 3.36 (dd, *J* = 14.4, 5.5 Hz, 1H), 3.15 (dd, *J* = 14.4, 7.3 Hz, 1H).

^{13}C NMR (100 MHz, D_2O) δ 171.65, 162.87 (q, *J* = 35.5 Hz), 156.51 (d, *J* = 236.5 Hz), 153.69 (d, *J* = 2.1 Hz), 123.64 (d, *J* = 7.7 Hz), 117.75 (d, *J* = 23.7 Hz), 116.24 (q, *J* = 291.7 Hz), 115.25 (d, *J* = 22.8 Hz), 112.20 (d, *J* = 8.5 Hz), 55.62, 53.31, 30.71.

^{19}F NMR (376 MHz, D_2O) δ -75.65, -124.19 (td, *J* = 8.7, 4.6 Hz).



63-F-COOH

2-amino-3-(4,5-difluoro-2-methoxyphenyl)propanoic acid hydrochloride(63-F-COOH). Follow the general procedure **C**, the title compound was obtained as a white solid (68 mg, 88%) from compound **62** (100 mg, 0.29 mmol).

^{1}H NMR (400 MHz, D_2O) δ 7.12 (dd, *J* = 11.6, 7.0 Hz, 1H), 7.00 (dd, *J* = 11.3, 7.2 Hz, 1H), 4.28 (dd, *J* = 7.2, 5.9 Hz, 1H), 3.89 (s, 3H), 3.32 (dd, *J* = 14.9, 5.7 Hz, 1H), 3.17 (dd, *J* = 14.9, 7.2 Hz, 1H).

^{13}C NMR (100 MHz, D_2O) δ 171.27, 157.16 (dd, *J* = 240.5, 2.4 Hz), 148.09 (dd, *J* = 239.3, 2.2 Hz), 147.44 (t, *J* = 12.1 Hz), 117.46 (dd, *J* = 20.8, 6.1 Hz), 112.35 (dd, *J* = 18.6, 6.7 Hz), 102.01 (d, *J* = 29.9 Hz), 56.35, 53.26, 28.67.

^{19}F NMR (376 MHz, D_2O) δ -119.85 – -120.25 (m), -141.09 (ddd, *J* = 15.3, 11.6, 7.3 Hz).

HRMS (ESI): Calculated for $C_{10}H_{12}F_2NO_3$ $(M+H)^+$: 232.0780; found: 232.0774.

3. Radiolabeling experiments

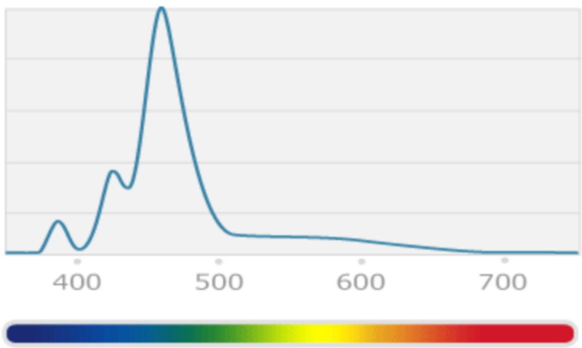
3.1 Reagents and equipment information

All chemicals are analytical grade and used without further purification. Ultrapure water was obtained from a Millipore MilliQ Gradient A10 system. Pre-conditioned Sep-PAK® light QMA cartridge were purchased form ABX Corporation and were flushed with 10 ml of water before use. Photocatalyst **S1** was obtained from our previous reported procedure[21]. Tetrabutylammonium bicarbonate ($TBAHCO_3$) solution (20%, w/w) was prepared by bubbling CO_2 to the tetrabutylammonium hydroxide solution (20%, w/w) diluted from the tetrabutylammonium hydroxide solution (54~56%, w/w) which was purchased from sigma-Aldrich. The pH of the $TBAHCO_3$ solution was in the range of 9.0 to 10.0. $TBAHCO_3$ MeCN solution (~60 mg/ml) was prepared as follows: 300 μl of TBAB solution (20%, w/w) was transferred into a 5 ml V-vial. The water was removed by lyophilization. The $TBAHCO_3$ concentrate was azeotropically dried with anhydrous MeCN (1 ml) under a stream of argon gas at 100℃ and then dissolved in 1ml anhydrous MeCN and stored under N_2 for use.

The 450 nm blue diode laser (MDL-D-450, 450nm, the power rating was set to 3.5W after fiber coupling) used for the labeling reaction was purchased from Changchun New Industries Optoelectronics Tech. Co., Ltd. The blue LED lamp (A160WE TUNA BLUE, 40W) was purchased from Kessil. The irradiation wavelengths observed are centered around 456 nm, 390 nm and 427 nm, with the major irradiation peak centered around 456 nm. (Supplementary Figure 5).

^{18}F activity was counted using a CRC-25 PET detector from Capintec. High- performance liquid chromatography (HPLC) was accomplished on a SHIMADZU chromatography system (Model CBM-20A) and analyzed using LabSolutions software. The λ absorbance detector and the model 2200 scaler ratemeter radiation detector was added to the HPLC system.

[^{18}F]FDOPA scale up synthesis was isolated on a PeakSimple chromatography system using peakSimple software(version 4.44) with a semi-preparation HPLC column.



Supplementary Figure 5. Irradiation profile for A160WE TUNA BLUE lamp.

3.2 General procedure for the preparation of [^{18}F]TBAF

Anhydrous [^{18}F]TBAF was obtained from our reported procedure[15]. [^{18}F]Fluoride was produced via the $^{18}O(p,n)^{18}F$ reaction by proton irradiation (40 μA, 45 min) of [^{18}O]H_2O. The aqueous solution of [^{18}F]fluoride was delivered into a hot cell and passed through a QMA cartridge (water preconditioning) to trap the [^{18}F]fluoride. The [^{18}F]fluoride was eluted into a 5 ml V-vial which sealed with a Teflon-lined septum screw cap with 600 μL solution of 70 μL tetrabutylammonium bicarbonate ($TBAHCO_3$) solution (20%, w/w), 53 μl H_2O and 477 μl MeCN. This solution was azeotropically dried with MeCN (1ml x 3) under stream of Argon at 100℃ and then put under vacuum for 3 min. The resulting residue was diluted with ~1ml anhydrous MeCN to obtain the [^{18}F]TBAF solution (typically1.6 -1.8 Ci) which was used for the labeling reaction.

3.3 General HPLC conditions

General HPLC conditions for crude reaction analysis (Radiochemical conversion calculation)

Column: Phenomenex, Kinetex® 5 μm EVO C18 100 Å, 250 x 4.6 mm LC Column. Solvent A:

0.1%TFA water; Solvent B: 0.1%TFA acetonitrile.

Grad/isocrat: 0 to 2 min: isocratic elution at 5% solvent B, 2 to 22 min: 5% to 95% solvent B, 22 to 28.1 min: isocratic elution at 95% solvent B, 28.1 to 30 min: 95% to 5% solvent B, 30 to 35 min: isocratic elution at 5% solvent B. Flow rate: 1 ml/min.

General HPLC conditions for purification and co-injection

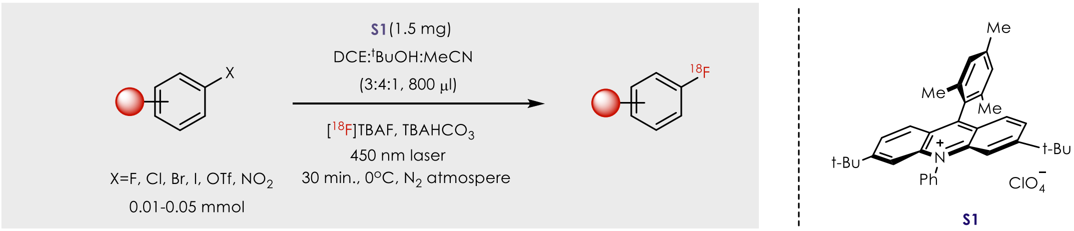
Column: Phenomenex, Kinetex® 5 µm F5 100 Å, 250 x 4.6 mm LC Column. Solvent A: 0.1%TFA water; Solvent B: 0.1%TFA acetonitrile; Isocratic elution at **x %** solvent B. Flow rate: 1 ml/min.

x % = **35%** for **36-¹⁸F**, **38-¹⁸F**; **x %**= **40%** for **1-¹⁸F**, **14-¹⁸F**, **31-¹⁸F**, **32-¹⁸F**, **37-¹⁸F**; **x %**= **45%** for **5-¹⁸F**, **12-¹⁸F**, **41-¹⁸F-a**; **x %**= **50%** for **3-¹⁸F**, **6-¹⁸F**, **8-¹⁸F**, **11-¹⁸F**, **13-¹⁸F**, **26-¹⁸F**, **35-¹⁸F**, **43-¹⁸F**, **47-¹⁸F**, ***L*-64-¹⁸F**; **x %**= **55%** for **2-¹⁸F**, **4-¹⁸F**, **7-¹⁸F**, **15-¹⁸F**, **16-¹⁸F**, **19-¹⁸F**, **27-¹⁸F**, **33-¹⁸F**, **40-¹⁸F**,**41-¹⁸F**, **48-¹⁸F**, **54-¹⁸F**, **55-¹⁸F**, **56-¹⁸F**, **57-¹⁸F**, **58-¹⁸F**, **59-¹⁸F**, **60-¹⁸F**, **61-¹⁸F**, **62-¹⁸F**, **63-¹⁸F**, ***L*-65-¹⁸F**, **66-¹⁸F**, **67-¹⁸F**, **68-¹⁸F**; **x %**= **60%** for **9-¹⁸F**, **20-¹⁸F**, **21-¹⁸F**, **24-¹⁸F**, **25-¹⁸F**, **29-¹⁸F**, **42-¹⁸F**, **45-¹⁸F**, **46-¹⁸F**, **49-¹⁸F**, **50-¹⁸F**; **x %**= **65%** for **52-¹⁸F**; **x %**= **70%** for **23-¹⁸F**, **34-¹⁸F**, **44-¹⁸F**; **x %** = **75%** for **28-¹⁸F**.

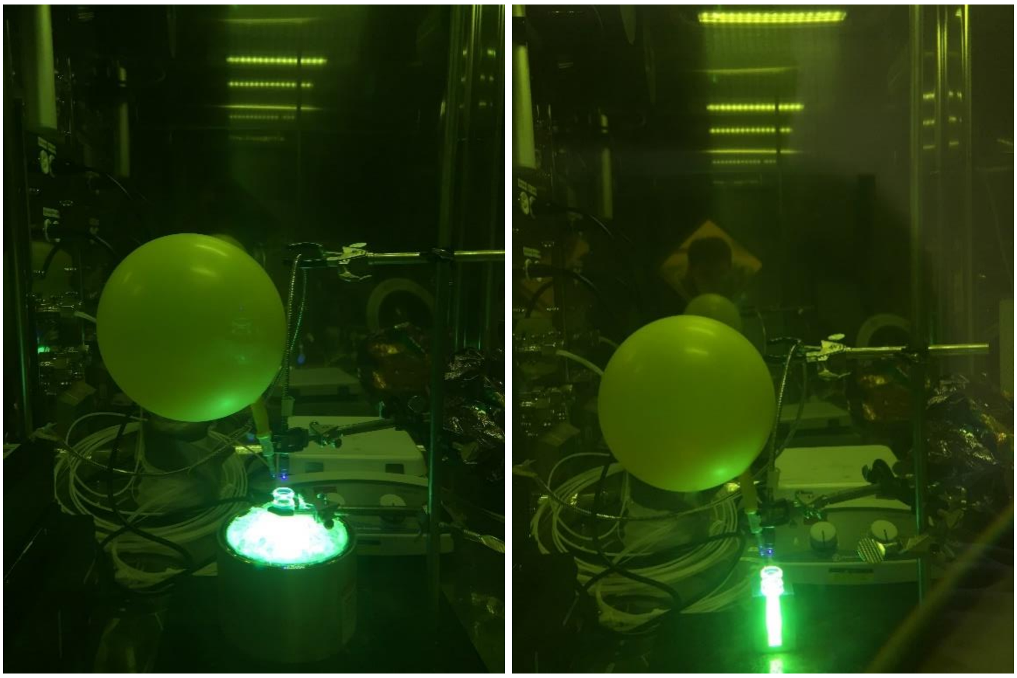
Compound **10-¹⁸F** was purified and characterized by isocratic elution at 30% solvent B using the crude analysis conditions; compound **30-¹⁸F** was purified and characterized using the same condition as the crude analysis HPLC conditions.

All the radiochemical reactions were subjected to radio-HPLC using this general HPLC condition unless otherwise noted.

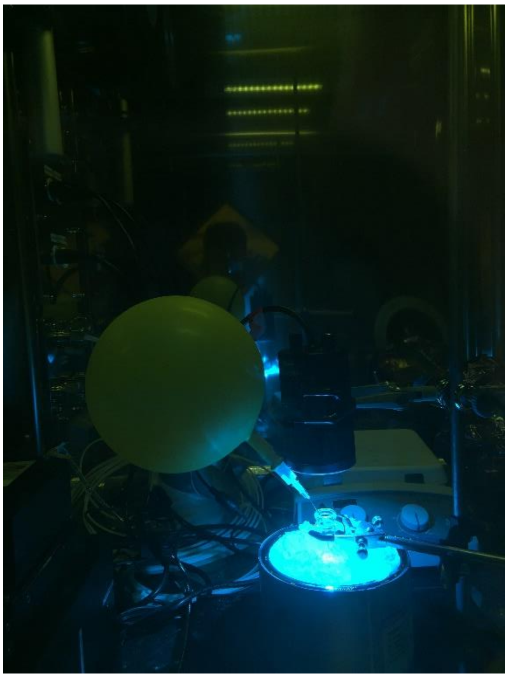
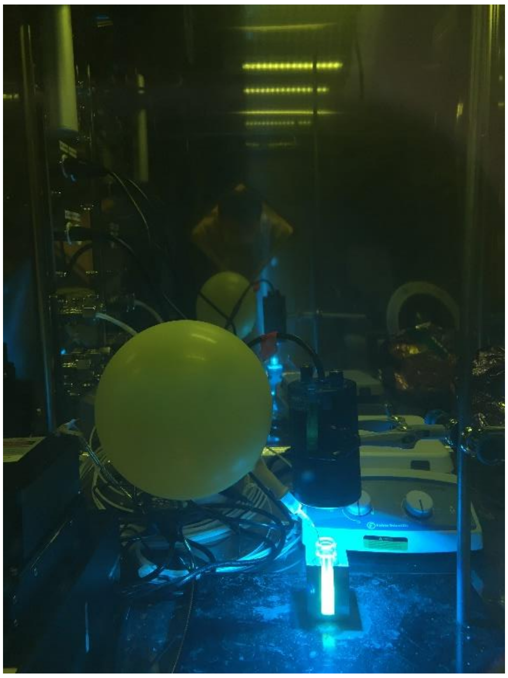
3.4 General procedure for photoredox-mediated halide/¹⁸F interconversion



Follow the modified reported procedure[15], the substrate (0.01 - 0.05 mmol) and photocatalyst (**S1**, 1.5 mg) were weighed into a 1.5 ml eppendorf tube and transferred (with solvent when the substrate is liquid or oil) into a 5 ml V-vial via pipette. DCE (300 µl), anhydrous MeCN (45-65 µl), ᵗBuOH(400 µl) and 25 µl of TBAB in MeCN solution (~60 mg/ml) were sequentially added to the V-vial. Then a 10 - 30 µl aliquot of [¹⁸F]TBAF in MeCN (typically 10-30 mCi) was added to the reaction vial via pipette. The reaction V-vial was then either fixed on an iron support and cooled using an ice bath or on a block without cooling. A needle connected to an N_2 filled balloon was inserted to the bottom of the V-vial and the reaction medium was continuously sparged throughout the entire reaction time. The reaction was then irradiated top-down with a laser (MDL-D-450, 450 nm, 3.5 W after fibre coupling) (Supplementary Figure 6) or a A160WE Tuna Blue Kessil LED lamp (Supplementary Figure 7) for 30 min. The resulting solution was diluted and evenly mixed with MeCN (0.5 -1ml). An aliquot of the reaction mixture (typically 300-1000 μCi) was taken for radio-HPLC analysis. The activity injected into HPLC was measured (this activity was denoted by α) and the time was recorded. The fraction corresponding to radiolabeled product was collected and the activity was measured (this activity was denoted by β) and the time was recorded. The decay-corrected β could be calculated from the recorded isolation time of each substrate. The radiochemical conversion (RCC) was obtained by dividing the decay-corrected β by α. Co-injection of the purified ^{18}F-labeled compound with commercial or synthesized ^{19}F standard via HPLC was used to confirm the identity of the radiolabeled compound.



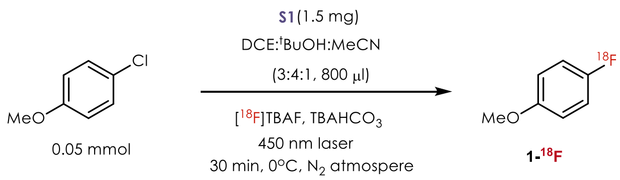
Supplementary Figure 6. Reaction set-up with laser under ice cooling(left) and room temperature(right)

Supplementary Figure 7. Reaction set-up with LED under ice cooling(left) and room temperature(right)

3.5. Radio-HPLC analysis and characterization for ^{18}F-radiolabeled arenes

All ^{18}F-labelling reactions were performed according to general procedure at section 3.4 unless otherwise noted. Each labeling reaction, starting activity ([^{18}F]TBAF), injected and collected activities, isolation time, decay corrected activity and calculated radiochemical conversion (RCC) are summarized in a table for each substrate. All ^{18}F-labeled products were analyzed and characterized according to the general HPLC conditions listed in Section 3.3. Crude radio-HPLC traces of each reaction (labled with reaction number), HPLC traces of purification and co-injection were listed. The collected ^{18}F-labeled product from crude HPLC analysis may require further HPLC-purification before co-injection with its corresponding ^{19}F standard. The red HPLC traces in the following spectra were obtained with a UV signal at 212 nm unless otherwise noted. The black HPLC traces represent the radio signal.

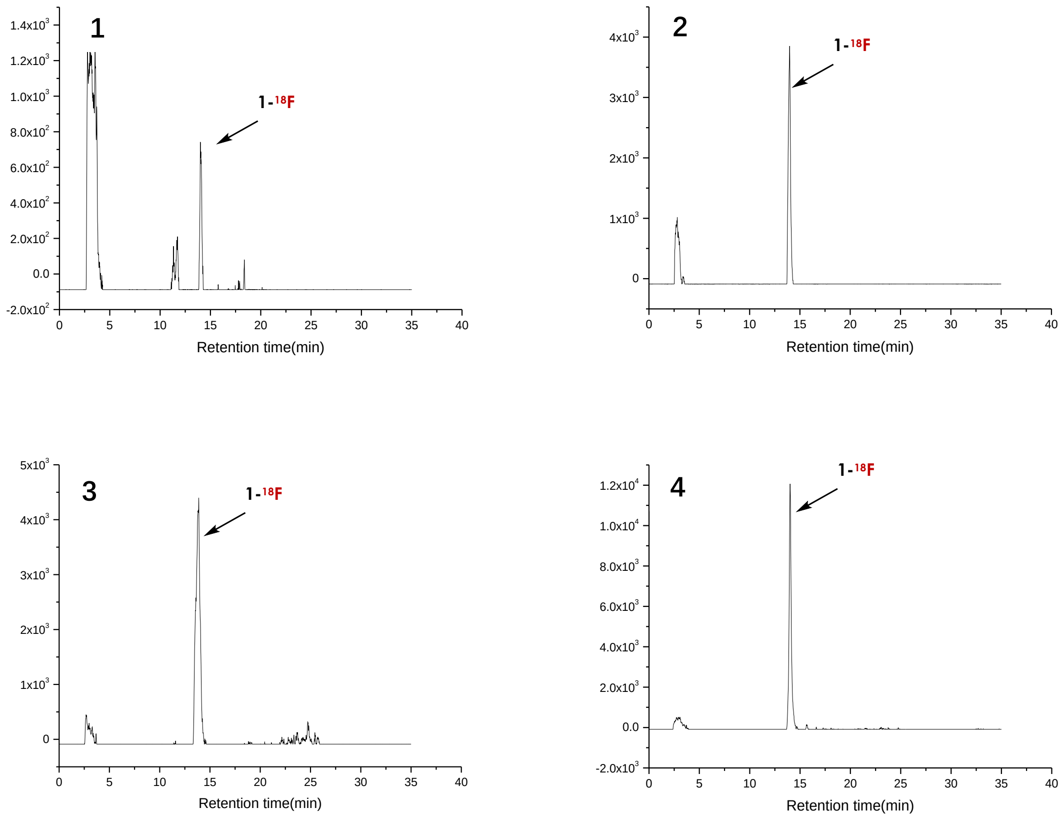


Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)

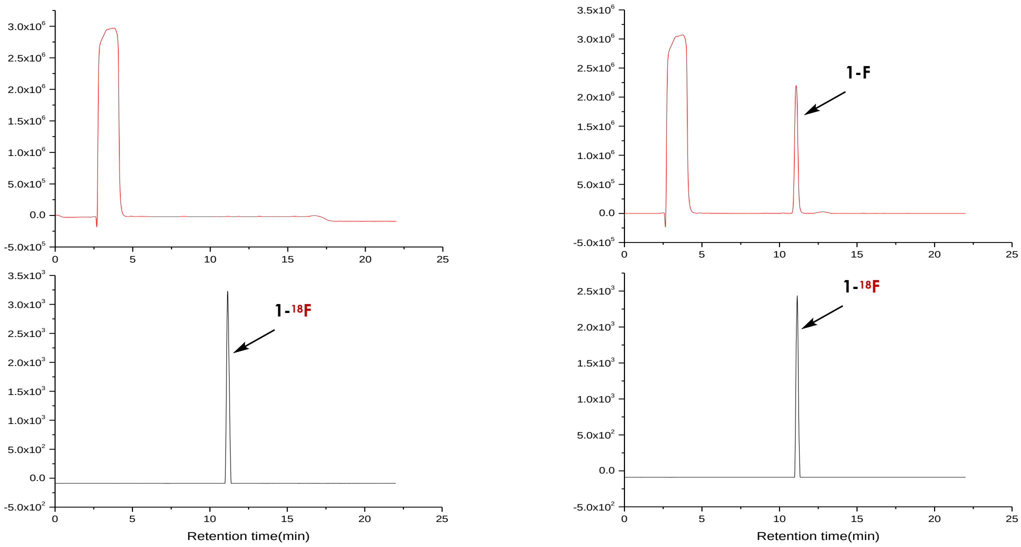
1	**1-Cl**	11.04 mCi	600 µCi	9 µCi	18 min	10.1 µCi	1.7% [a]
2		7.84 mCi	279 µCi	33 µCi	17 min	36.7 µCi	13.2%
3		7.51 mCi	585 µCi	68 µCi	17 min	75.7 µCi	12.9%
4		7.52 mCi	755 µCi	84 µCi	17 min	93.5 µCi	12.4%
Average RCC: **12.8±0.3%** (n=3, N_2)							

[a]Reaction was conducted in the air.

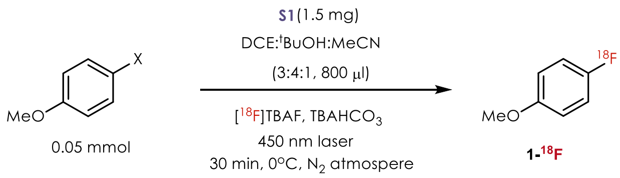
Supplementary Table 1. HPLC-isolated RCCs of **1-^{18}F**



Supplementary Figure 8. Crude radio-HPLC traces from **1-Cl** to **1-^{18}F**



Supplementary Figure 9. Purification(left) and co-injection(right) of **1-^{18}F**

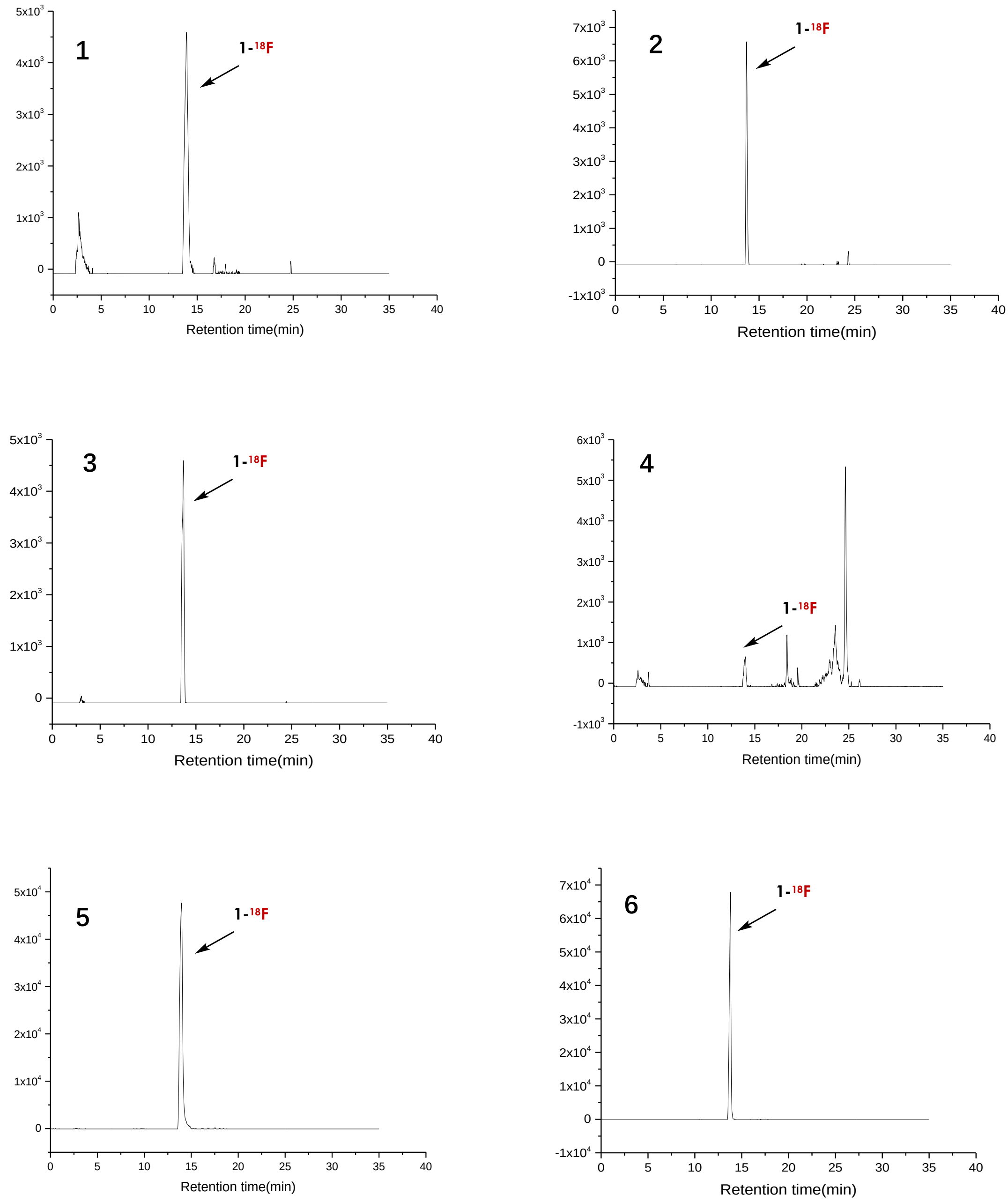


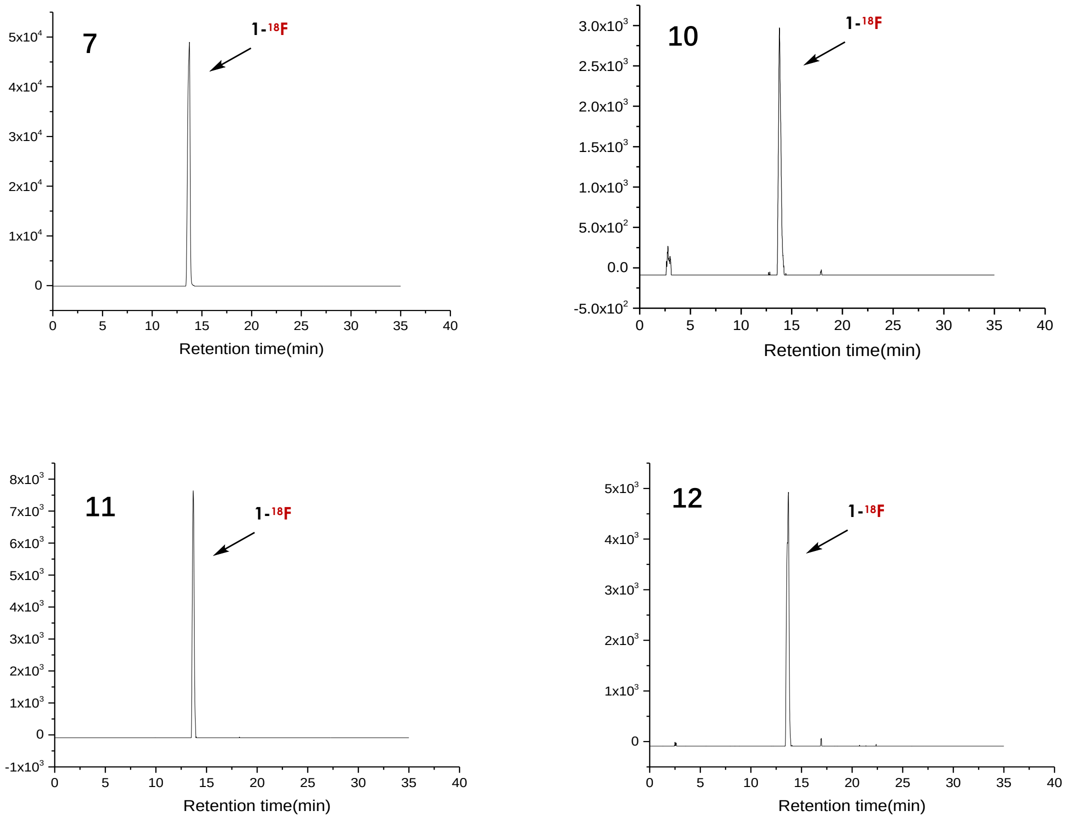
Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1		9.64 mCi	442 μCi	54 μCi	16 min	59.7 μCi	13.5%
2	**1-Br**(X=Br)	8.58 mCi	341 μCi	30 μCi	16 min	33.2 μCi	9.7%
3		7.5 mCi	324 μCi	32 μCi	16 min	35.4 μCi	10.9%
Average RCC of **1-^{18}F** from **1-Br: 11.4±1.6%** (n=3)							
4	**1-I**(X=I)	12.42 mCi	668 μCi	9 μCi	16 min	10 μCi	**1.5%**
5		11.53 mCi	540 μCi	386 μCi	20 min	432.5 μCi	80.1%
6	**1-F**(X=F)	7.14 mCi	432 μCi	304 μCi	17 min	338.4 μCi	78.3%
7		6.93 mCi	426 μCi	309 μCi	17 min	344.0 μCi	80.8%
Average RCC of **1-^{18}F** from **1-F: 79.7±1.1%** (n=3)							
8	**1-NO$_2$**(X=NO$_2$)	12.44 mCi	496 μCi	--	--	--	n.d.
9		16.11 mCi	501 μCi	--	--	--	n.d.
10		8.24 mCi	313 μCi	29 μCi	16 min	32.1 μCi	10.3%
11	**1-OTf**(X=OTf)	12.10 mCi	357 μCi	42 μCi	16 min	46.5 μCi	13.0%
12		12.06 mCi	369 μCi	38 μCi	17 min	42.3 μCi	11.5%

Average RCC of **1-^{18}F** from **1-OTf: 11.6±1.1%** (n=3)

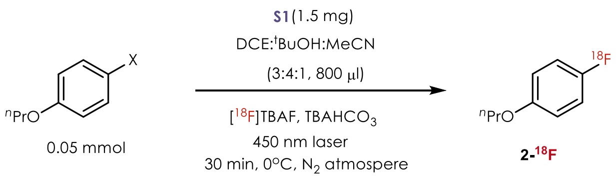
n.d., not detected

Supplementary Table 2. HPLC-isolated RCCs for **1-^{18}F**



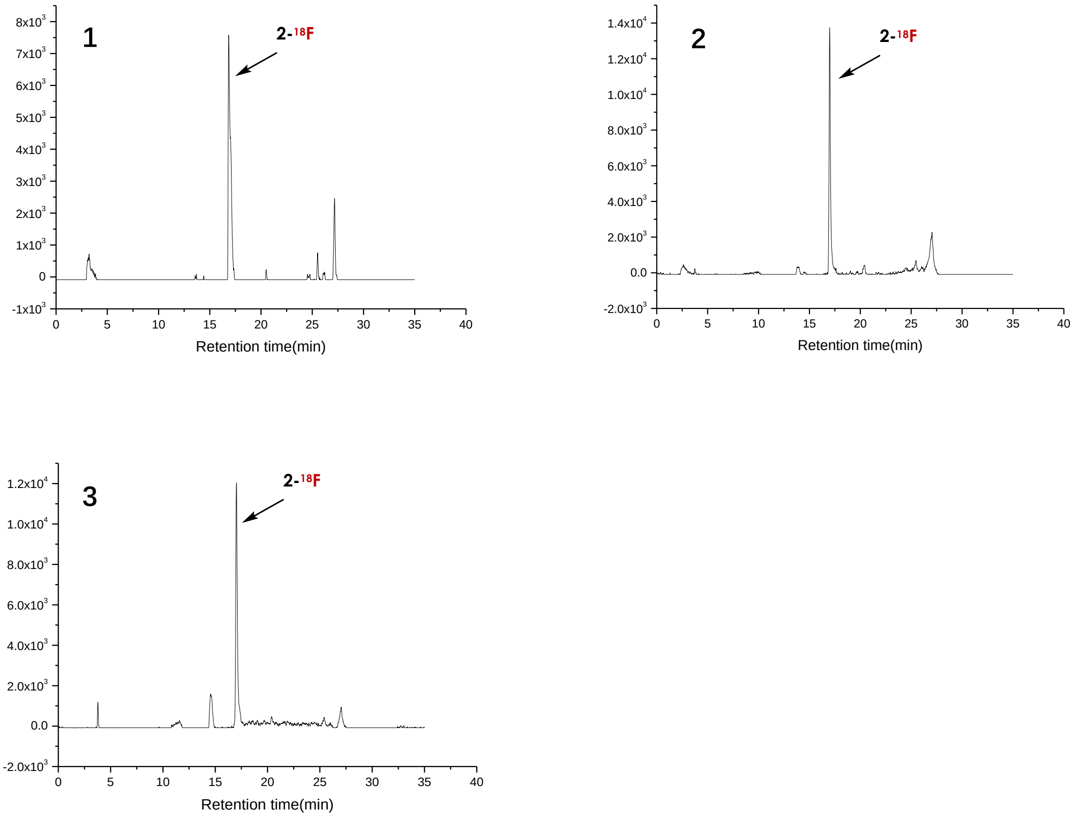


Supplementary Figure 10. Crude radio-HPLC traces from **1-Br,1-I, 1-F,1-OTf** to **1-18F**

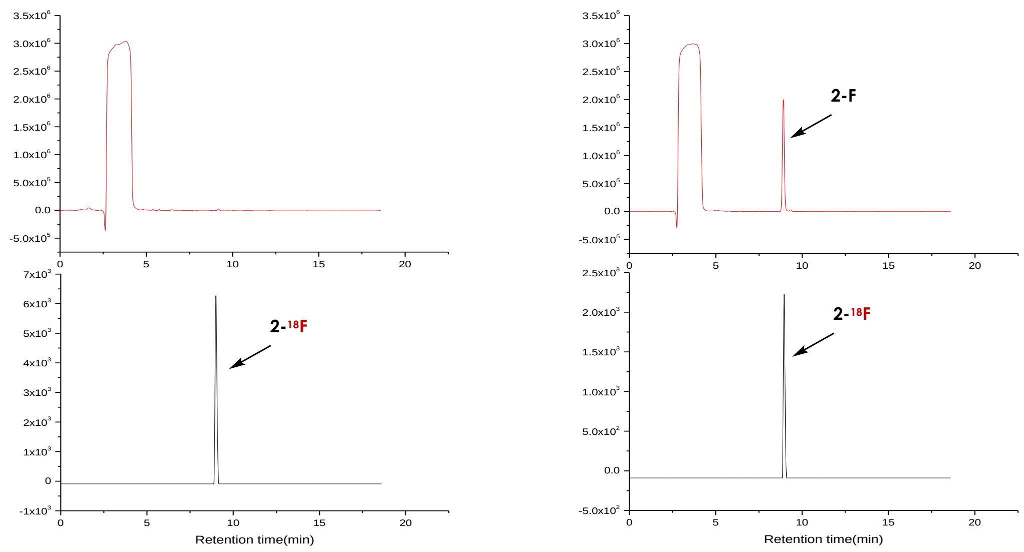


Reaction	Substrate	Activity ([18F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1		10.56 mCi	536 µCi	62 µCi	20 min	70.3 µCi	13.1%
2	**2**	10.76 mCi	482 µCi	64 µCi	21 min	73.1 µCi	15.2%
3		11.39 mCi	679 µCi	68 µCi	20 min	77.2 µCi	11.4%
Average RCC: **13.2±1.6%** (n=3)							

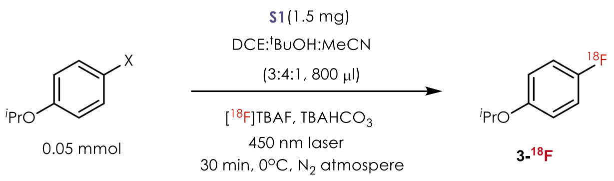
Supplementary Table 3. HPLC-isolated RCCs of **2-18F**



Supplementary Figure 11. Crude radio-HPLC traces from **2** to **2-^{18}F**

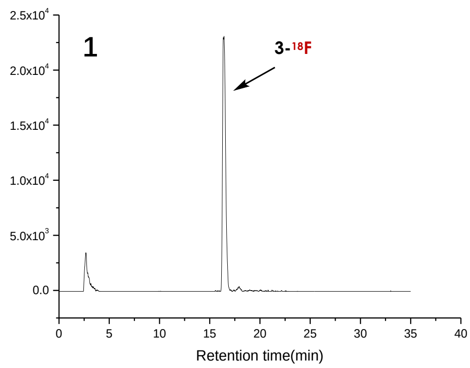


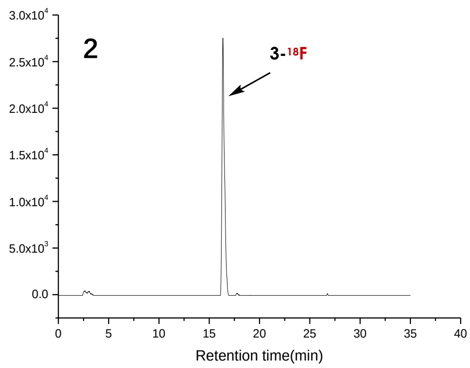
Supplementary Figure 12. Purification (left) and co-injection(right) for **2-^{18}F**

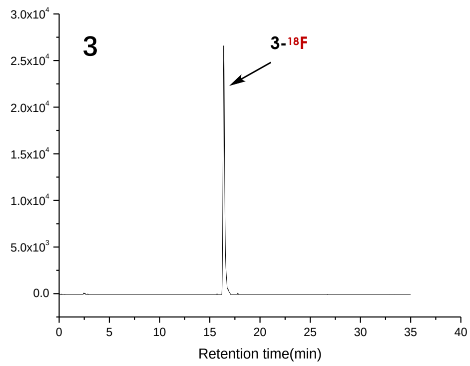


Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**3**	8.42 mCi	867 μCi	212 μCi	20 min	240.5 μCi	27.7%
2		8.97 mCi	619 μCi	201 μCi	20 min	228.1μCi	36.8%
3		13.87 mCi	671 μCi	138 μCi	21 min	157.6 μCi	23.5%
Average RCC: **29.3±5.6%** (n=3)							

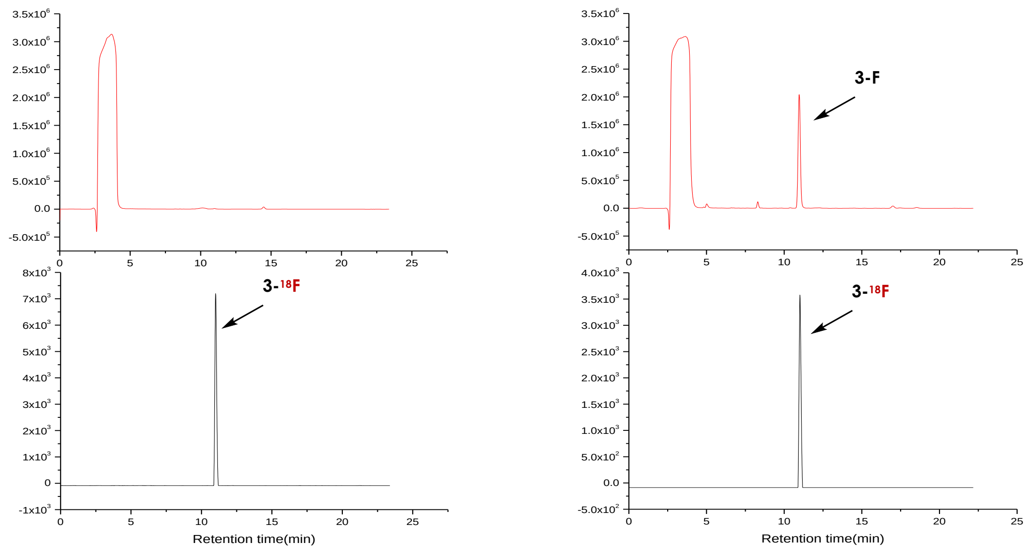
Supplementary Table 4. HPLC-isolated RCCs of **3-^{18}F**



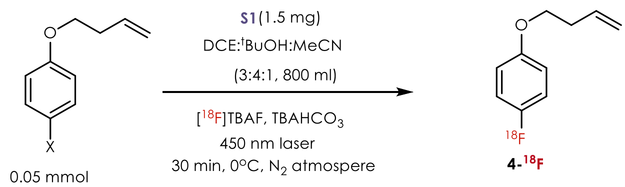




Supplementary Figure 13. Crude radio-HPLC traces from **3** to **3-^{18}F**

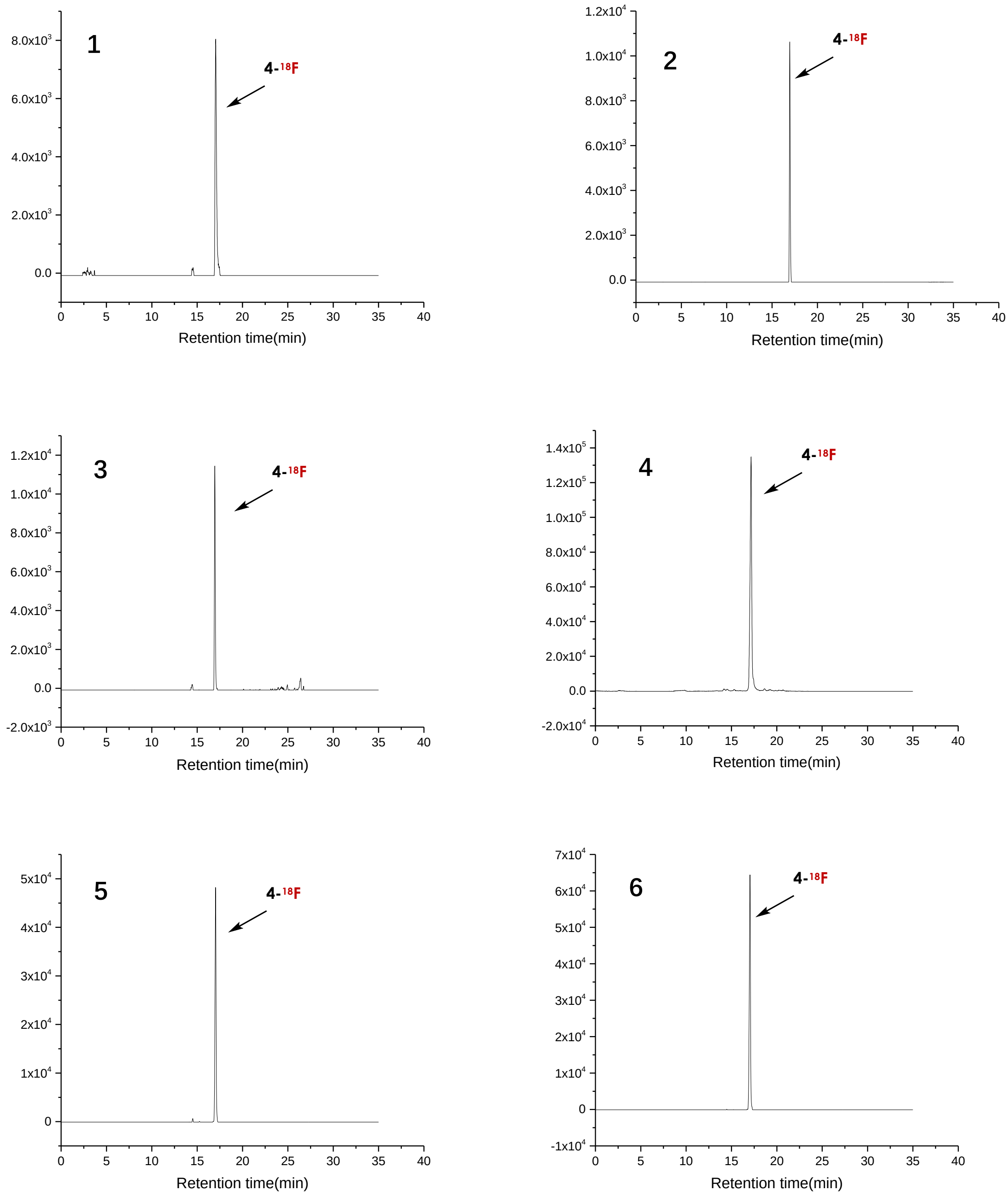


Supplementary Figure 14. Purification (left) and co-injection(right) for **3-^{18}F**

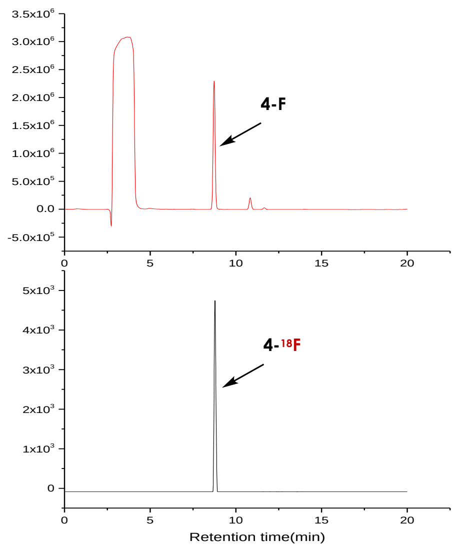


Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**4-Cl (X=Cl)**	8.73 mCi	409 µCi	46 µCi	24 min	53.5 µCi	13.1%
2		9.85 mCi	302 µCi	34 µCi	19 min	38.3 µCi	12.6%
3		8.41 mCi	354 µCi	36 µCi	19 min	40.6 µCi	11.5%
Average RCC of **4-^{18}F** from **4-Cl**: **12.4±0.7%** (n=3)							
4	**4-F (X=F)**	12.99 mCi	811 µCi	577 µCi	21 min	658.8 µCi	81.2%
5		6.82 mCi	235 µCi	156 µCi	20 min	177.0 µCi	75.3%
6		6.79 mCi	310 µCi	216 µCi	20 min	245.1 µCi	79.1%
Average RCC of **4-^{18}F** from **4-F**: **78.5±2.4%** (n=3)							

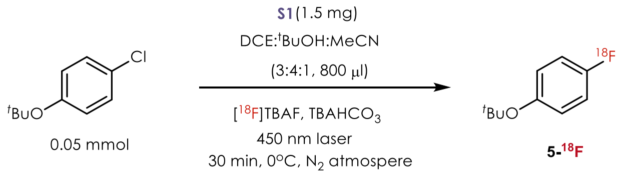
Supplementary Table 5. HPLC-isolated RCCs of **4-^{18}F**



Supplementary Figure 15. Crude radio-HPLC traces from **4-Cl** and **4-F** to **4-^{18}F**



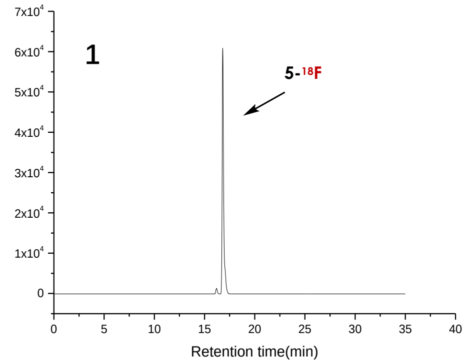
Supplementary Figure 16. HPLC trace of purification of **4-18F** from **4-F**

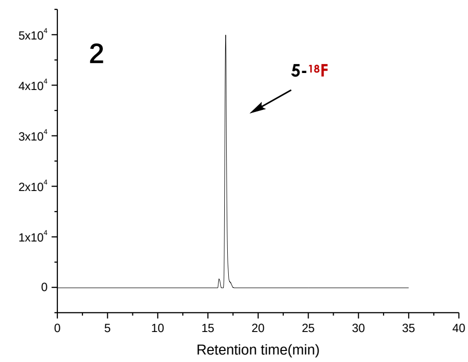


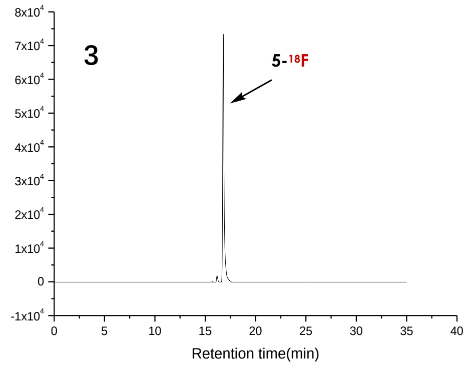
Reaction	Substrate	Activity ([18F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**5-Cl**	11.68 mCi	445 µCi	238 µCi	19 min	268.3 µCi	60.3%
2		11.55 mCi	540 µCi	242 µCi	19 min	272.8 µCi	50.5%
3		10.56 mCi	443 µCi	263 µCi	20 min	298.4 µCi	67.4%
Average RCC: **59.4±6.6%** (n=3)							
4	**5-Cl**[a]	12.03 mCi	747 µCi	165 µCi	20 min	187.2 µCi	25.1%
5		7.99 mCi	374 µCi	166 µCi	20 min	188.3 µCi	50.4%
6		6.70 mCi	348 µCi	113 µCi	19 min	133.0 µCi	38.2%
7		9.35 mCi	348 µCi	130 µCi	18 min	145.6 µCi	41.9%
Average RCC: **38.9±9.1%** (n=4, LED)							

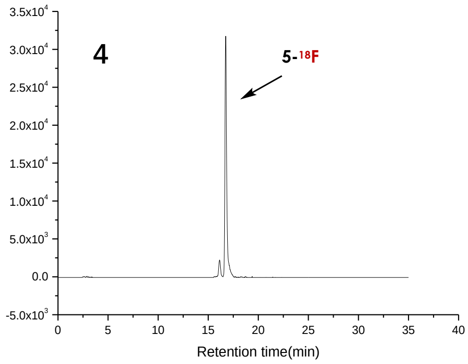
[a]Blue LED was used instead of laser.

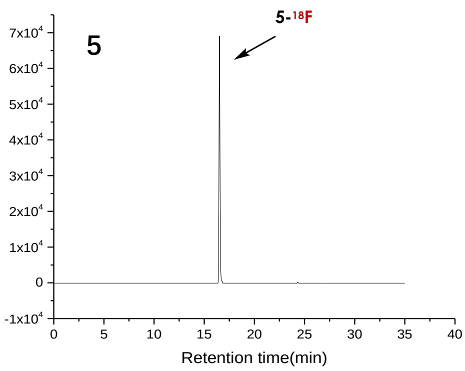
Supplementary Table 6. HPLC-isolated RCCs of **5-18F**

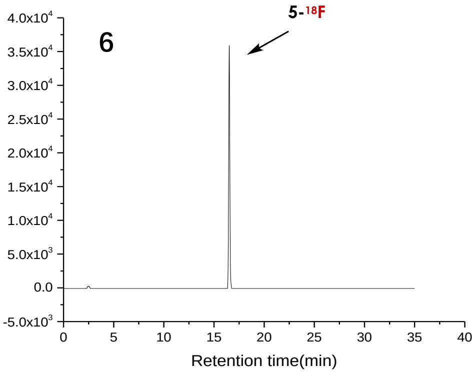

1
5-18F
7x10^4
6x10^4
5x10^4
4x10^4
3x10^4
2x10^4
1x10^4
0
0 5 10 15 20 25 30 35 40
Retention time(min)

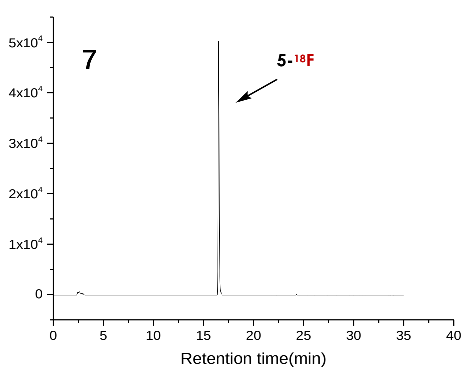

2
5-18F
5x10^4
4x10^4
3x10^4
2x10^4
1x10^4
0
0 5 10 15 20 25 30 35 40
Retention time(min)


3
5-18F
8x10^4
7x10^4
6x10^4
5x10^4
4x10^4
3x10^4
2x10^4
1x10^4
0
-1x10^4
0 5 10 15 20 25 30 35 40
Retention time(min)

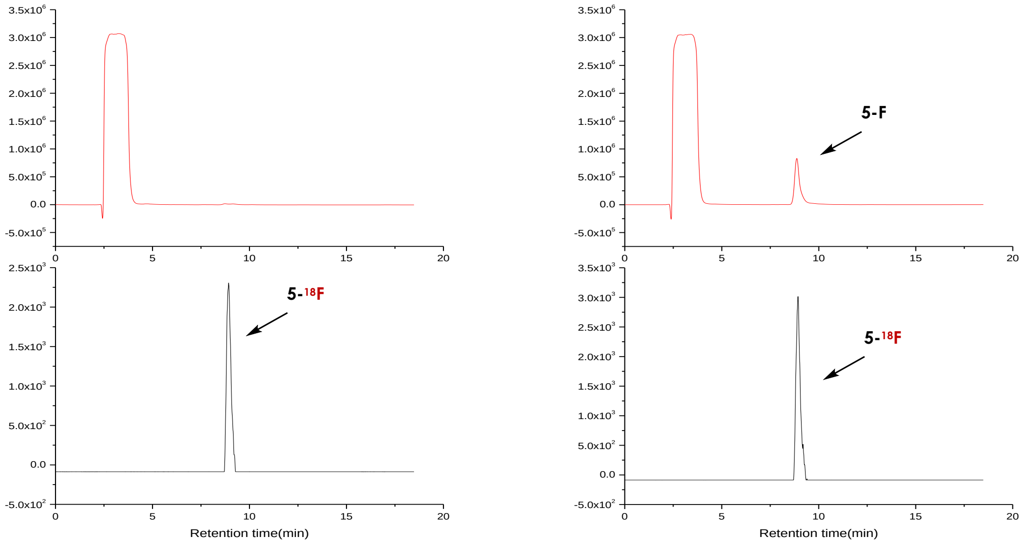

4
5-18F
3.5x10^4
3.0x10^4
2.5x10^4
2.0x10^4
1.5x10^4
1.0x10^4
5.0x10^3
0.0
-5.0x10^3
0 5 10 15 20 25 30 35 40
Retention time(min)


5
5-18F
7x10^4
6x10^4
5x10^4
4x10^4
3x10^4
2x10^4
1x10^4
0
-1x10^4
0 5 10 15 20 25 30 35 40
Retention time(min)

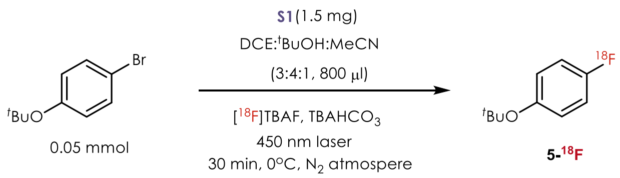

6
5-18F
4.0x10^4
3.5x10^4
3.0x10^4
2.5x10^4
2.0x10^4
1.5x10^4
1.0x10^4
5.0x10^3
0.0
-5.0x10^3
0 5 10 15 20 25 30 35 40
Retention time(min)


7
5-18F
5x10^4
4x10^4
3x10^4
2x10^4
1x10^4
0
0 5 10 15 20 25 30 35 40
Retention time(min)

Supplementary Figure 17. Crude radio-HPLC traces from **5-Cl** to **5-^{18}F**

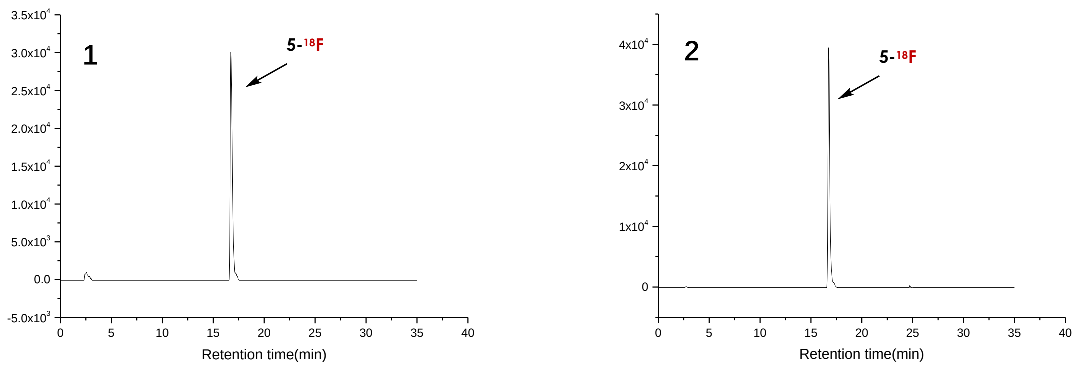


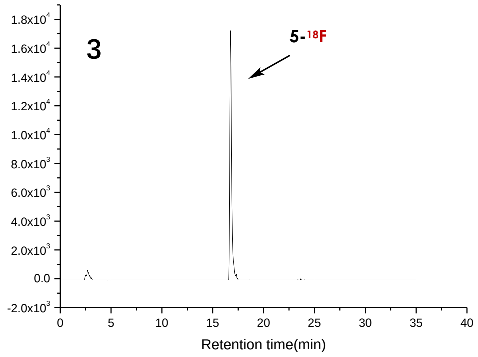
Supplementary Figure 18. Purification (left) and co-injection(right) for **5-^{18}F**



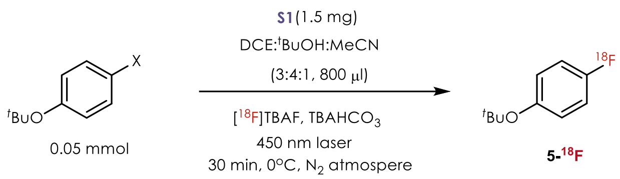
Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1		13.05 mCi	446 μCi	179 μCi	20 min	203.1 μCi	45.5%
2	**5-Br**	9.95 mCi	410 μCi	200 μCi	19 min	225.5 μCi	55%
3		9.2 mCi	273 μCi	93 μCi	21 min	106.2 μCi	38.9%
Average RCC: **46.5±7.0%** (n=3)							

Supplementary Table 7. HPLC-isolated RCCs of **5-^{18}F**





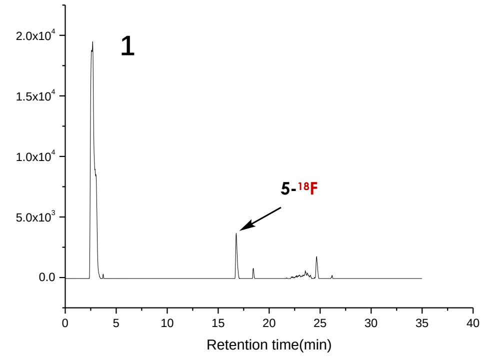
Supplementary Figure 19. Crude radio-HPLC traces from **5-Br** to **5-18F**

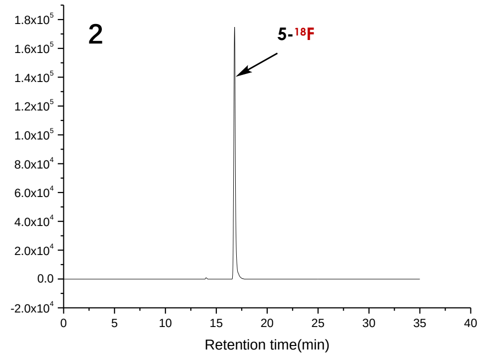


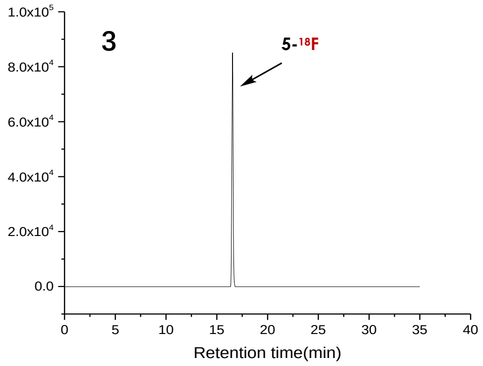
Reaction	Substrate	Activity ([18F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**5-I (X=I)**	14.71 mCi	778 µCi	21 µCi	20 min	23.8 µCi	**3.1%**
2	**5-F (X=F)**	10.68 mCi	775 µCi	599 µCi	20 min	679.6 µCi	87.7%
3		5.90 mCi	336 µCi	268 µCi	19 min	302.2 µCi	89.9%
4		11.98 mCi	489 µCi	366 µCi	20 min	415.3 µCi	84.9%
Average RCC of **5-18F** from **5-F**: **87.5±2.0%** (n=3, laser)							
5	**5-F (X=F)**[a]	11.64 mCi	322uCi	233 uCi	20 min	264.4 uCi	82.1%
6		9.53 mCi	403uCi	301 uCi	19 min	339.4 uCi	84.2%
7		6.52 mCi	435 uCi	298 uCi	20 min	338.1 uCi	77.7%
Average RCC of **5-18F** from **5-F**: **81.3±2.7%** (n=3, LED)							

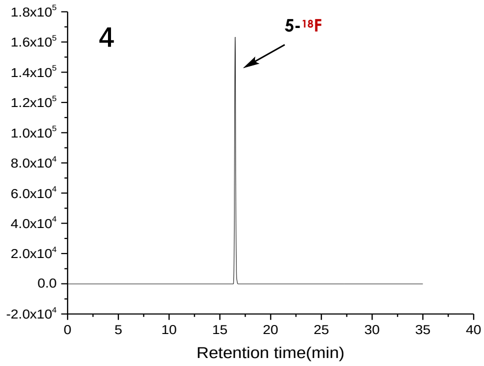
[a]Blue LED was used instead of laser.

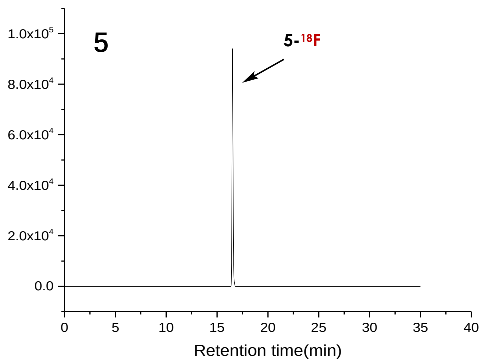
Supplementary Table 8. HPLC-isolated RCCs of **5-18F**

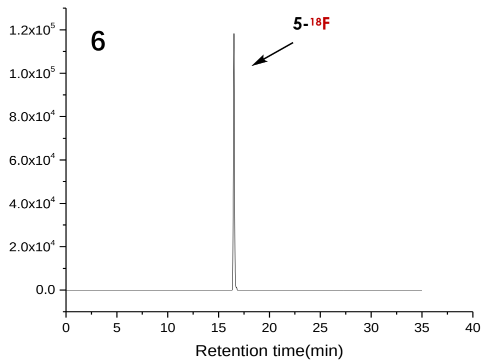

1
5-18F
2.0x10^4
1.5x10^4
1.0x10^4
5.0x10^3
0.0
0 5 10 15 20 25 30 35 40
Retention time(min)

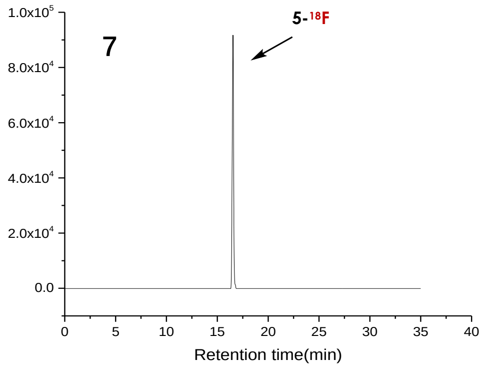

2
5-18F
1.8x10^5
1.6x10^5
1.4x10^5
1.2x10^5
1.0x10^5
8.0x10^4
6.0x10^4
4.0x10^4
2.0x10^4
0.0
-2.0x10^4
0 5 10 15 20 25 30 35 40
Retention time(min)


3
5-18F
1.0x10^5
8.0x10^4
6.0x10^4
4.0x10^4
2.0x10^4
0.0
0 5 10 15 20 25 30 35 40
Retention time(min)

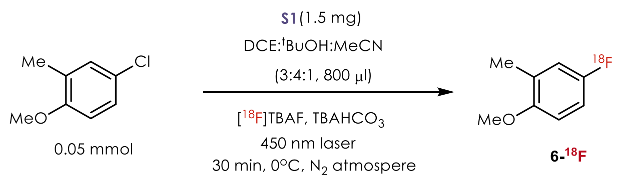

4
5-18F
1.8x10^5
1.6x10^5
1.4x10^5
1.2x10^5
1.0x10^5
8.0x10^4
6.0x10^4
4.0x10^4
2.0x10^4
0.0
-2.0x10^4
0 5 10 15 20 25 30 35 40
Retention time(min)


5
5-18F
1.0x10^5
8.0x10^4
6.0x10^4
4.0x10^4
2.0x10^4
0.0
0 5 10 15 20 25 30 35 40
Retention time(min)


6
5-18F
1.2x10^5
1.0x10^5
8.0x10^4
6.0x10^4
4.0x10^4
2.0x10^4
0.0
0 5 10 15 20 25 30 35 40
Retention time(min)

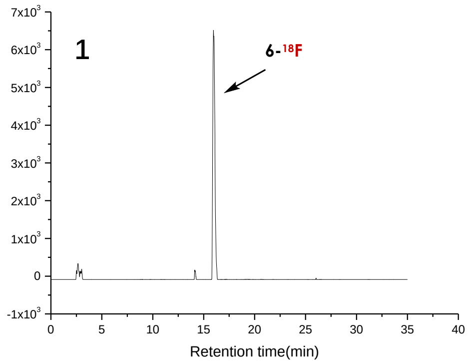

7
5-18F
1.0x10^5
8.0x10^4
6.0x10^4
4.0x10^4
2.0x10^4
0.0
0 5 10 15 20 25 30 35 40
Retention time(min)

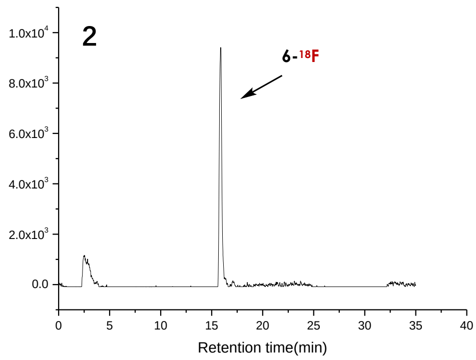
Supplementary Figure 20. Crude radio-HPLC traces from **5-I** and **5-F** to **5-18F**

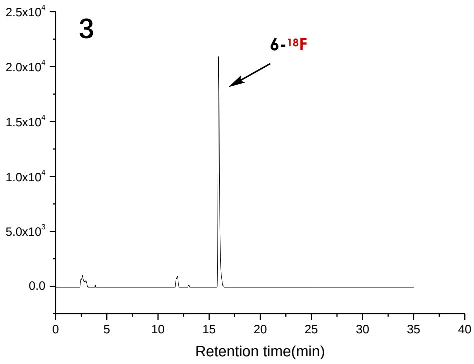


Reaction	Substrate	Activity ([18F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**6**	10.89 mCi	344 μCi	46 μCi	19 min	51.9 μCi	15.1%
2		10.97 mCi	588 μCi	75 μCi	19 min	84.6 μCi	14.4%
3		21.2 mCi	611 μCi	87 μCi	19 min	98.1 μCi	16.1%
Average RCC: **15.2±0.7%** (n=3)							

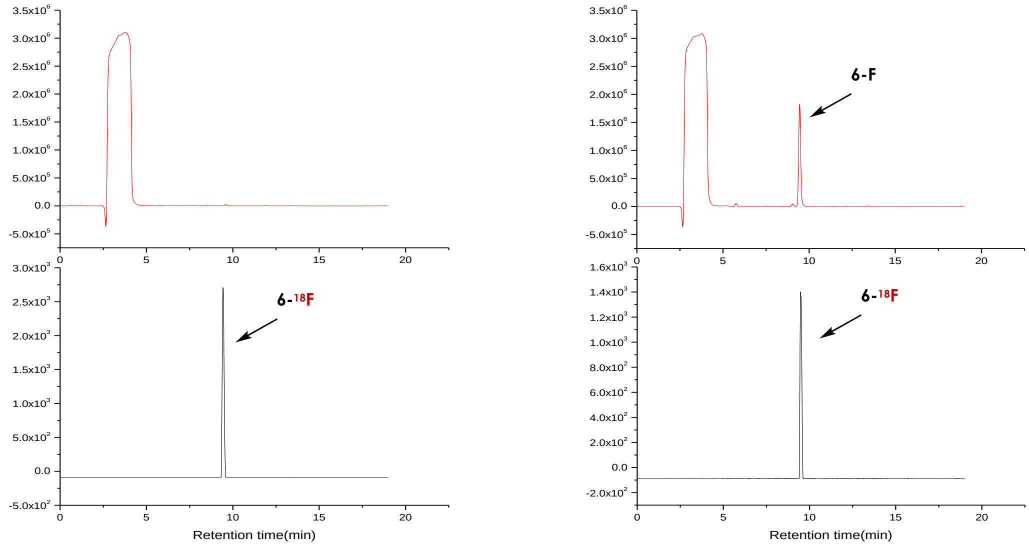
Supplementary Table 9. HPLC-isolated RCCs of **6-18F**



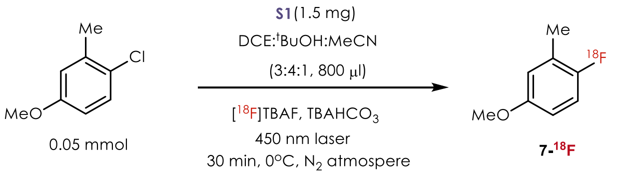




Supplementary Figure 21. Crude radio-HPLC traces from **6** to **6-18F**

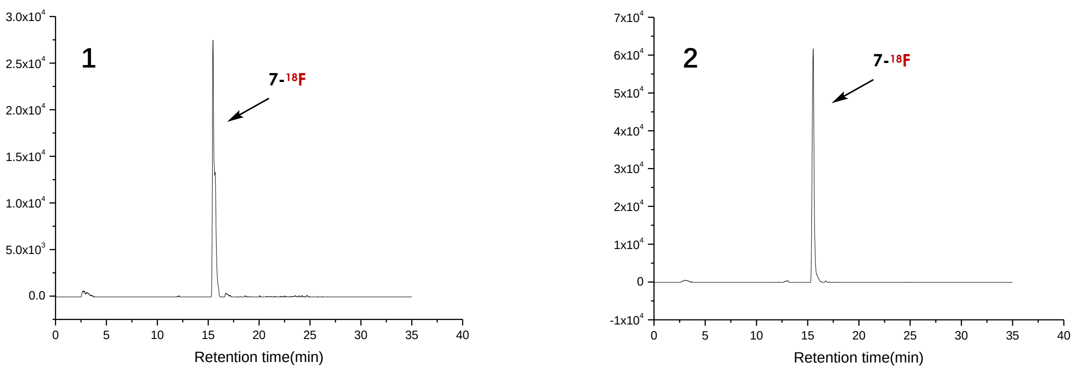


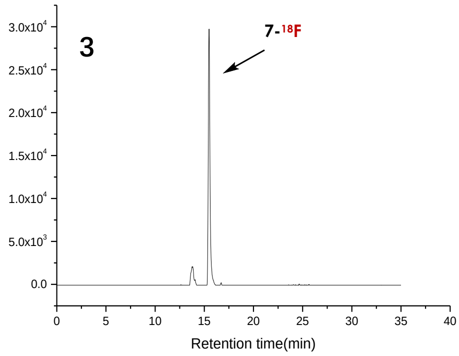
Supplementary Figure 22. Purification (left) and co-injection(right) for **6-18F**



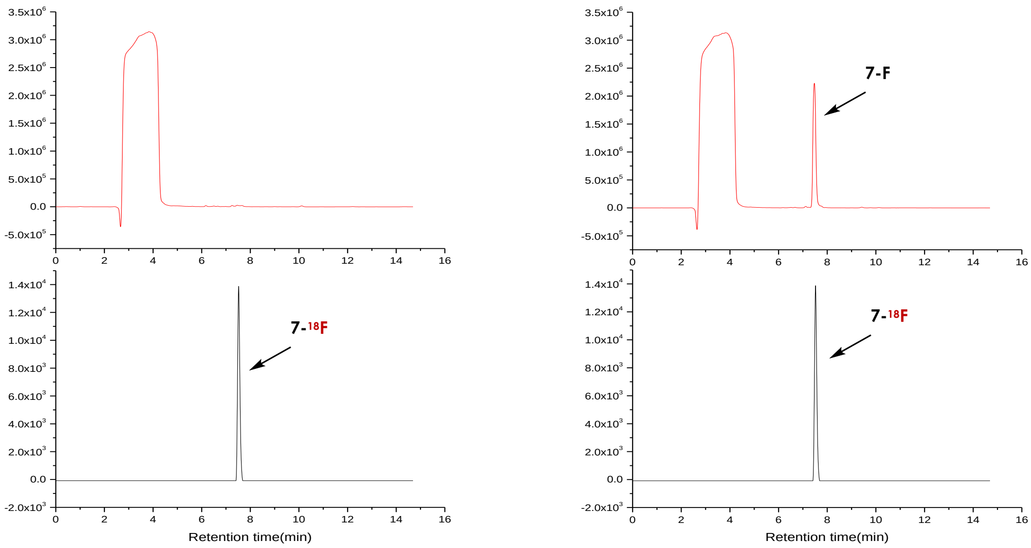
Reaction	Substrate	Activity ([18F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**7**	9.38 mCi	524 μCi	172 μCi	19 min	193.9 μCi	37%
2		9.01 mCi	784 μCi	310 μCi	18 min	347.3 μCi	44.3%
3		15.32 mCi	538 μCi	155 μCi	18 min	173.7 μCi	32.3%
Average RCC:**37.9±5.0%** (n=3)							

Supplementary Table 10. HPLC-isolated RCCs of **7-18F**

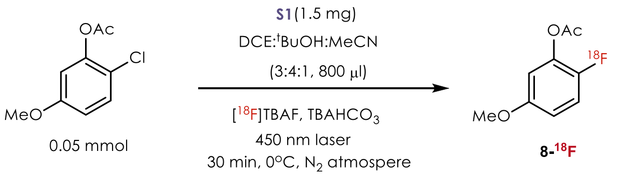




Supplementary Figure 23. Crude radio-HPLC traces from **7** to **7-^{18}F**

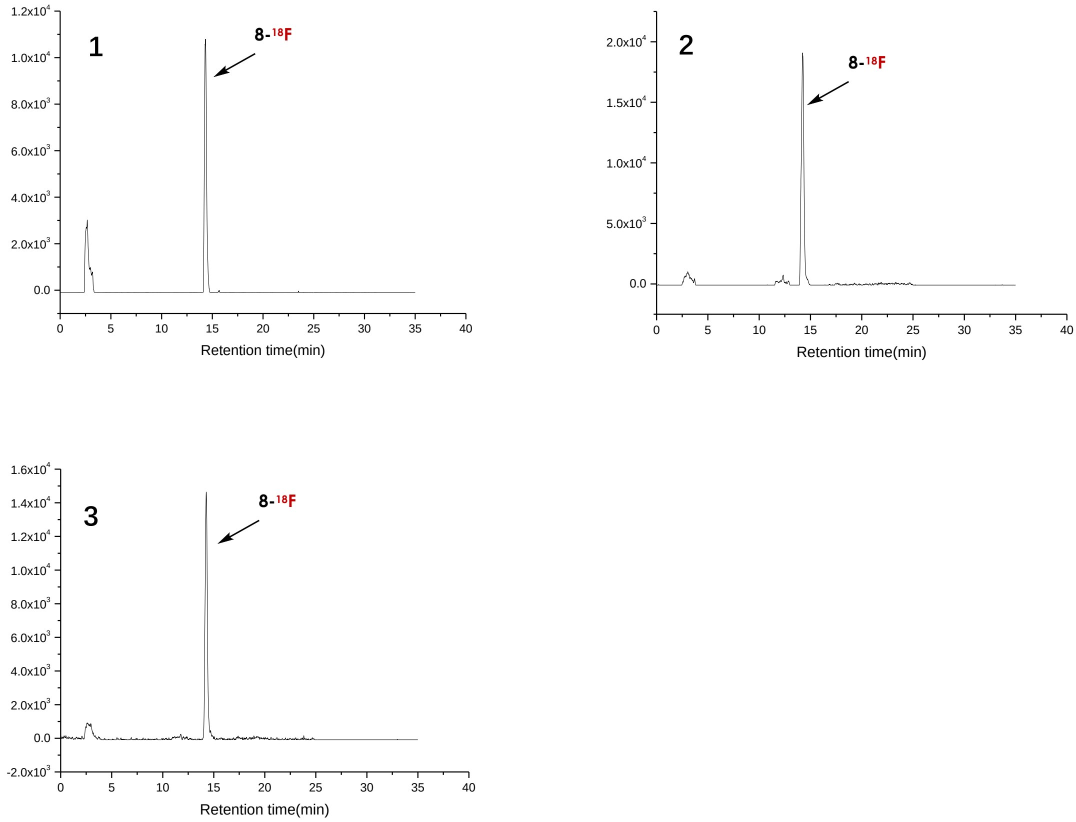


Supplementary Figure 24. Purification (left) and co-injection(right) for **7-^{18}F**

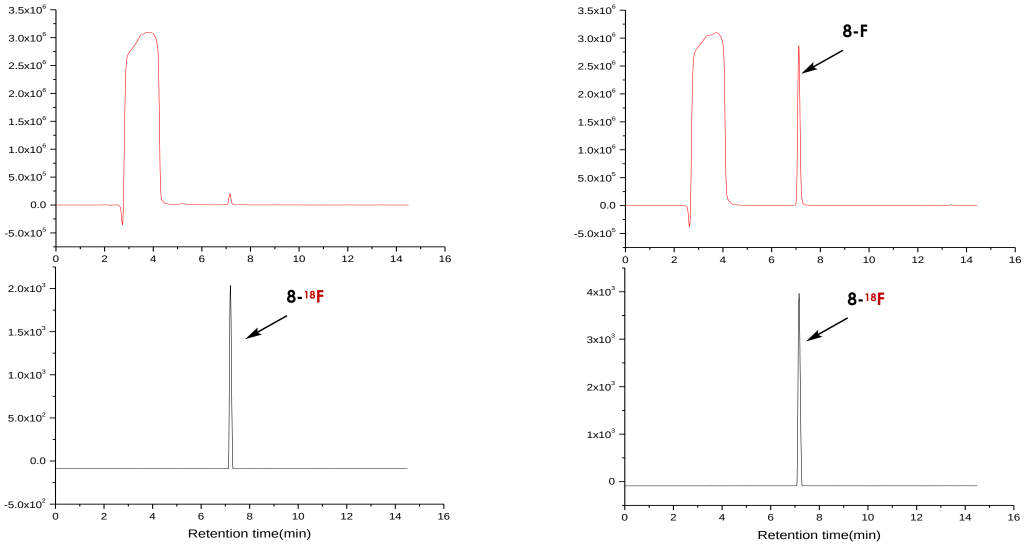


Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**8**	10.94 mCi	463 μCi	74 μCi	17 min	82.4 μCi	17.8%
2		11.43 mCi	932 μCi	151 μCi	16 min	167.1 μCi	17.9%
3		8.47 mCi	412 μCi	100 μCi	16 min	110.6 μCi	26.8%
Average RCC: **20.8±4.0%** (n=3)							

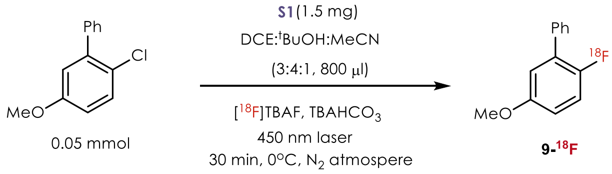
Supplementary Table 11. HPLC-isolated RCCs of **8-^{18}F**



Supplementary Figure 25. Crude radio-HPLC traces from **8** to **8-^{18}F**

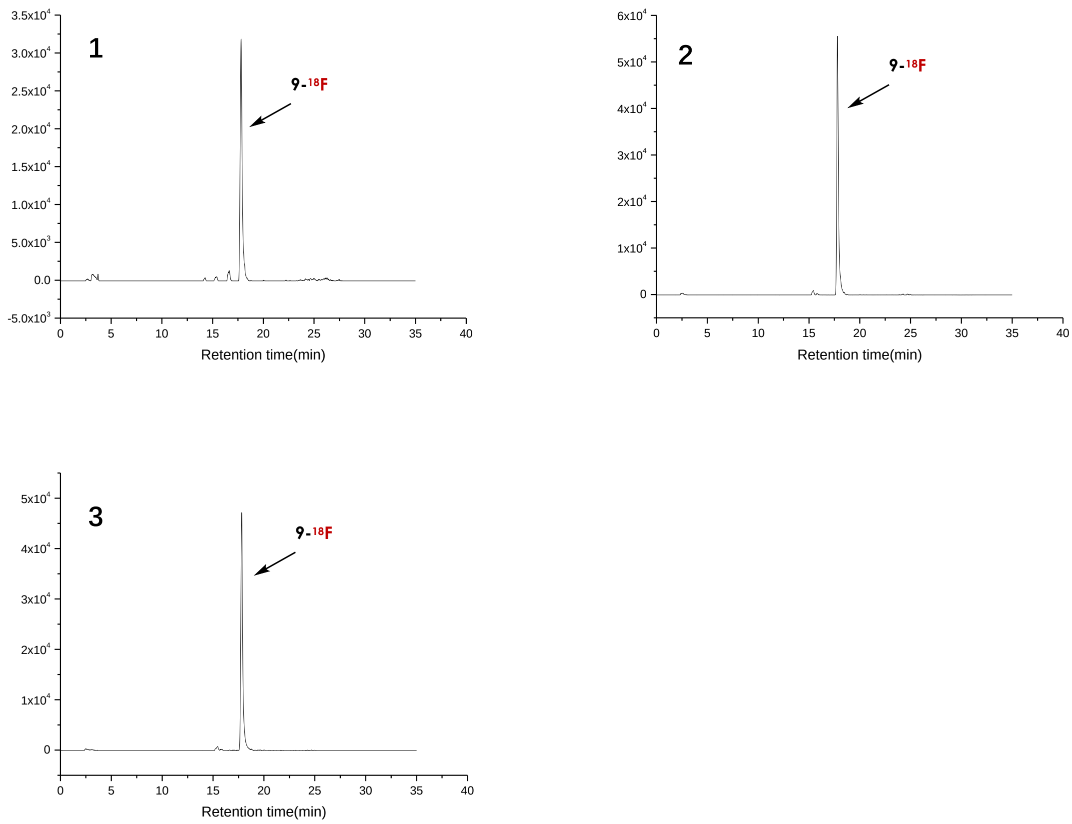


Supplementary Figure 26. Purification (left) and co-injection(right) for **8-^{18}F**

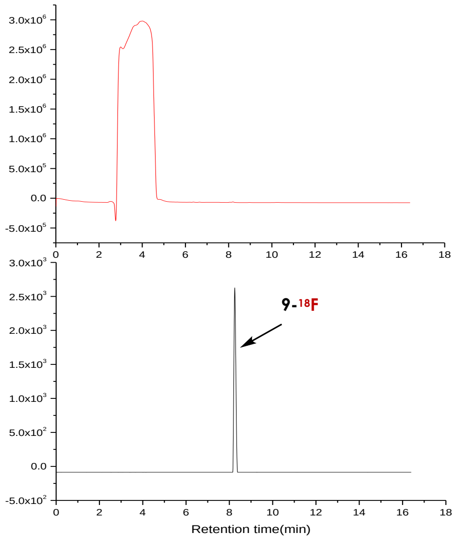


Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**9**	12.07 mCi	518 μCi	180 μCi	22 min	206.8 μCi	39.9%
2		11.84 mCi	702 μCi	244 μCi	22 min	280.4 μCi	39.9%
3		10.21 mCi	668 μCi	240 μCi	21 min	274.0 μCi	41.0%
Average RCC: **40.3±0.5%** (n=3)							

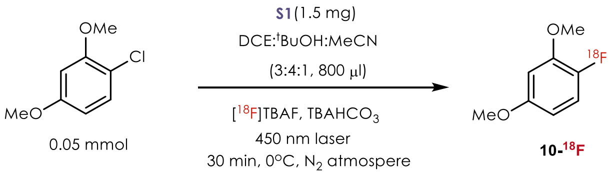
Supplementary Table 12. HPLC-isolated RCCs of **9-^{18}F**



Supplementary Figure 27. Crude radio-HPLC traces from **9** to **9-^{18}F**

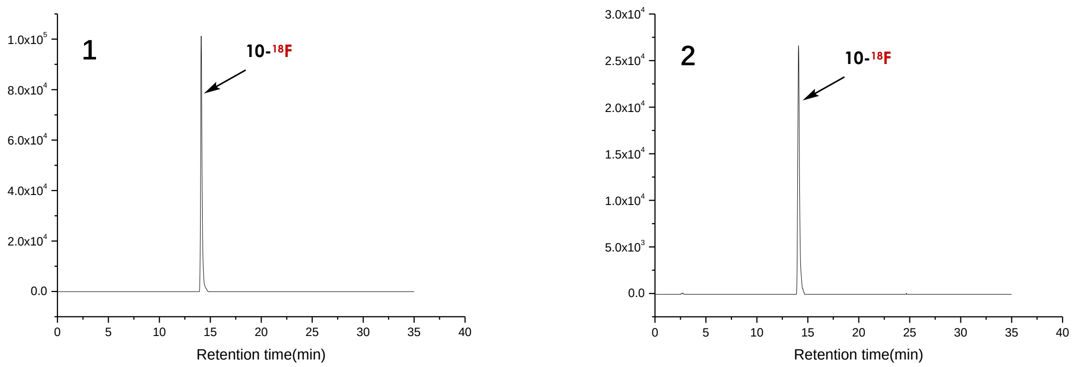


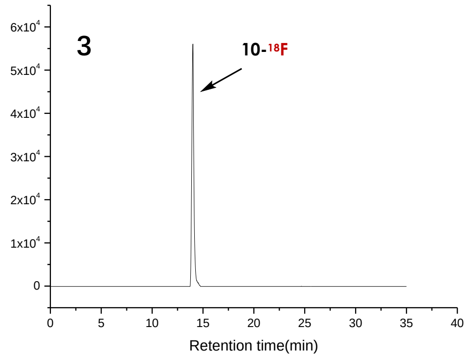
Supplementary Figure 28. Purification (left) and co-injection(right) for **9-18F**



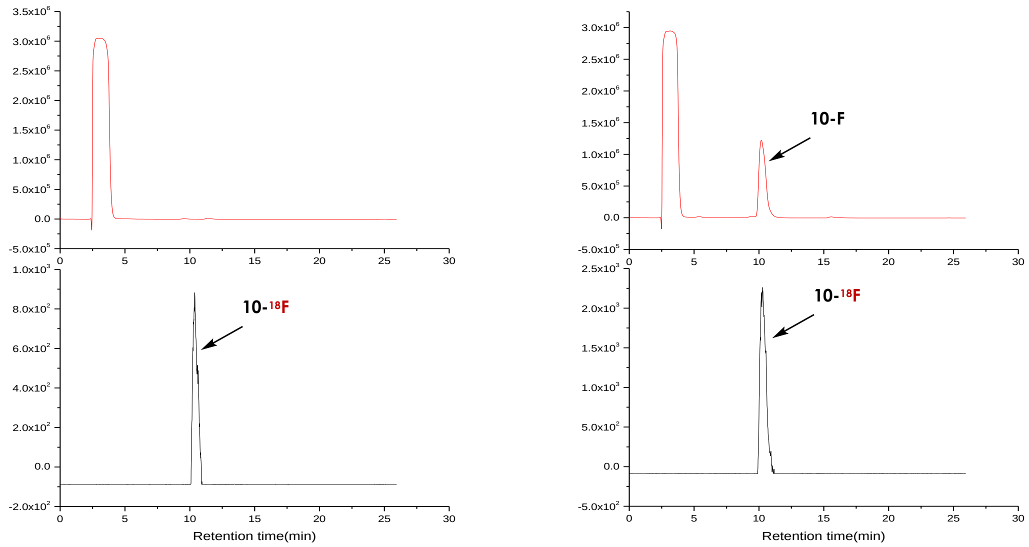
Reaction	Substrate	Activity ([18F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**10-Cl**	12.32 mCi	506 μCi	364 μCi	17 min	405.2 μCi	80.1%
2		9.82 mCi	520 μCi	336 μCi	17 min	225.5 μCi	71.9%
3		14.71 mCi	450 μCi	301 μCi	16 min	333.0 μCi	74.0%
Average RCC: **75.3±3.5%** (n=3)							

Supplementary Table 13. HPLC-isolated RCCs of **10-18F**

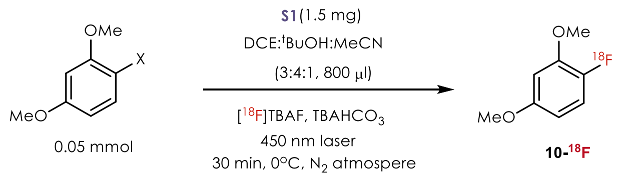




Supplementary Figure 29. Crude radio-HPLC traces from **10-Cl** to **10-^{18}F**



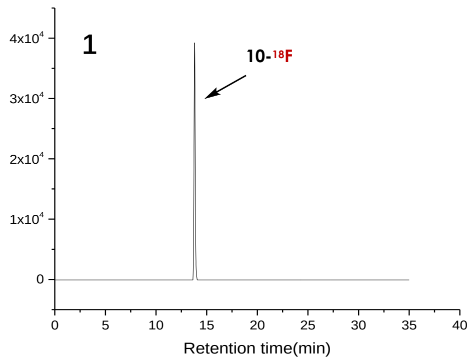
Supplementary Figure 30. Purification (left) and co-injection(right) for **10-^{18}F**

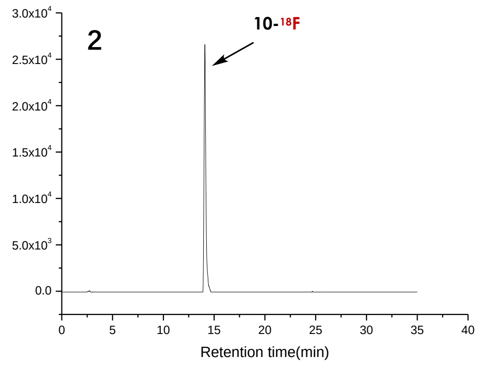


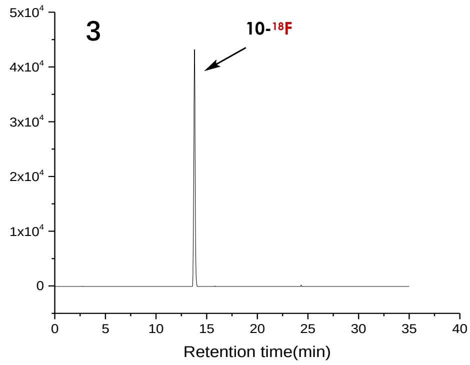
Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1		8.93 mCi	386 μCi	140 μCi	17 min	155.9 μCi	40.4%
2	**10-Br (X=Br)**	11.93 mCi	377 μCi	126 μCi	15 min	138.5 μCi	36.7%
3		8.98 mCi	415 μCi	154 μCi	16 min	170.4 μCi	41.1%
Average RCC of **10-^{18}F** from **10-Br**:**39.4±1.9%** (n=3)							
4	**10-I (X=I)**	12.52 mCi	346 μCi	16 μCi	17 min	17.8 μCi	**5.1%**

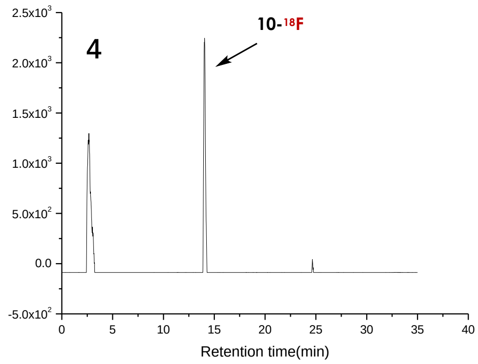
5		12.48 mCi	712 μCi	315 μCi	17 min	432.5 μCi	49.3%
6	**10-NO_2 (X=NO_2)**	11.28 mCi	333 μCi	134 μCi	16 min	148.2 μCi	44.5%
7		16.05 mCi	412 μCi	192 μCi	16 min	212.4 μCi	51.2%
Average RCC of **10-^{18}F** from **10- NO_2**: **48.3±2.8%** (n=3)							

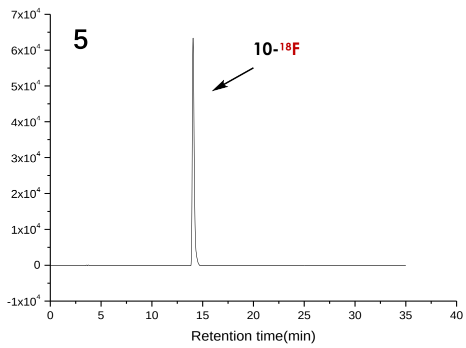
Supplementary Table 14. HPLC-isolated RCCs of **10-^{18}F**

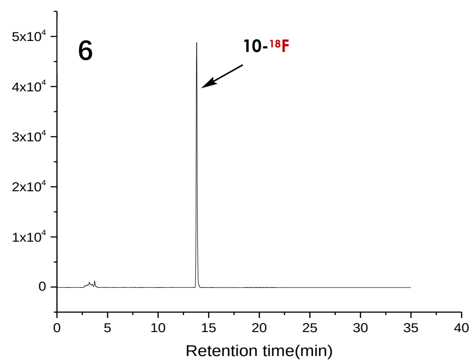


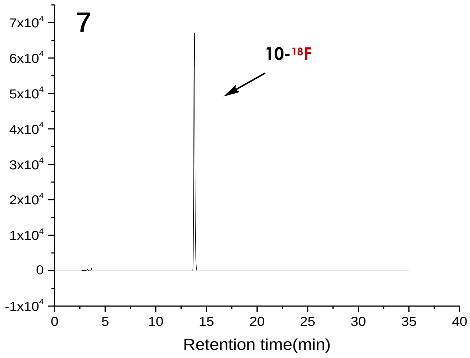




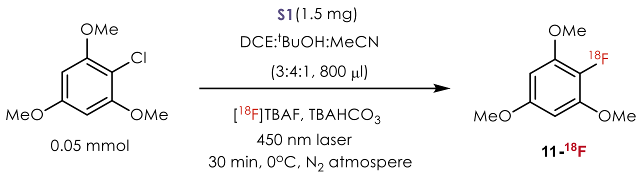






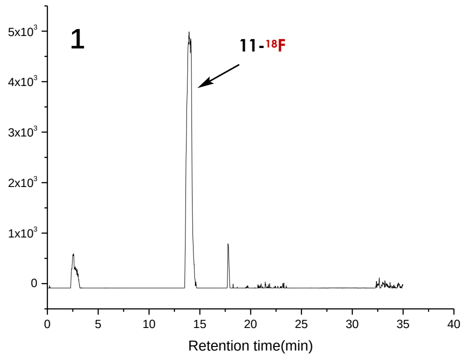


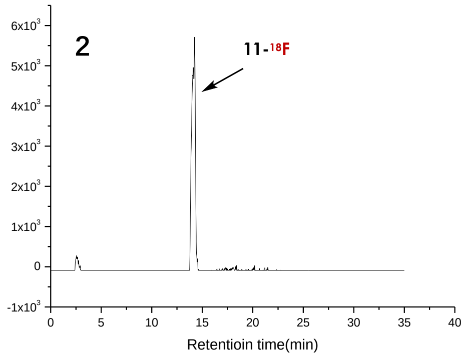
Supplementary Figure 31. Crude radio-HPLC traces from **10-Br, 10-I, 10-NO_2** to **10-^{18}F**

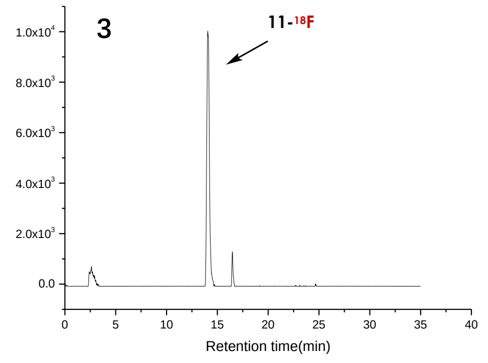


Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**11**	10.66 mCi	491 μCi	71 μCi	18 min	79.5 μCi	16.2%
2		9.53 mCi	526 μCi	84 μCi	16 min	92.9 μCi	17.7%
3		11.79 mCi	736 μCi	81 μCi	16 min	90.8 μCi	12.3%
Average RCC: **15.4±2.3%** (n=3)							

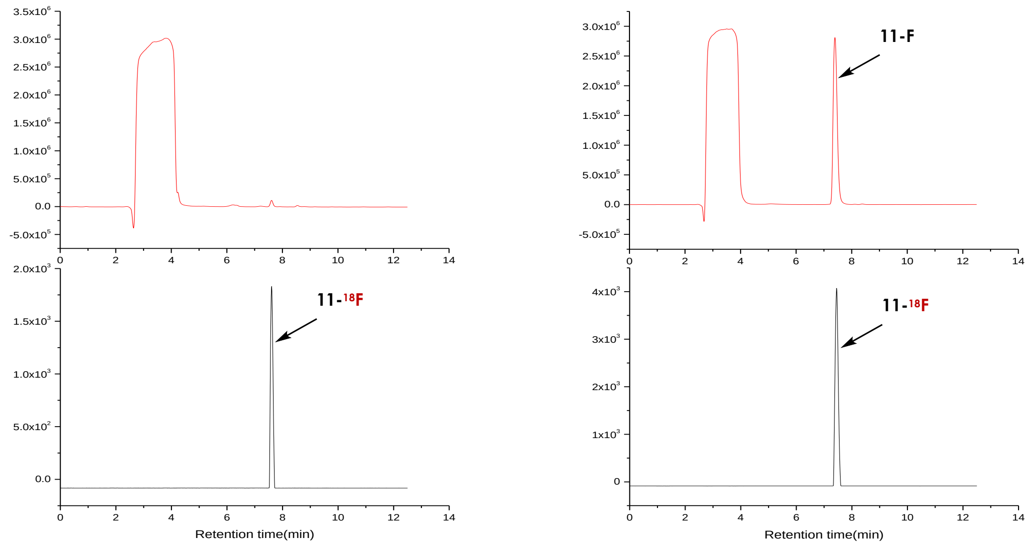
Supplementary Table 15. HPLC-isolated RCCs of **11-^{18}F**



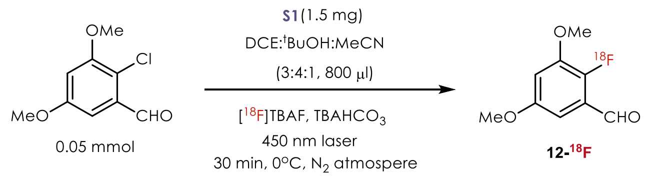




Supplementary Figure 32. Crude radio-HPLC traces from **11** to **11-18F**

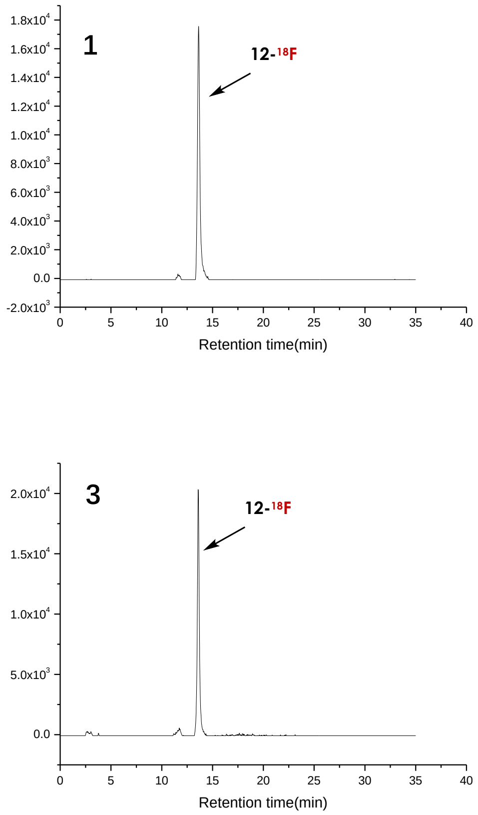


Supplementary Figure 33. Purification (left) and co-injection for **11-18F**

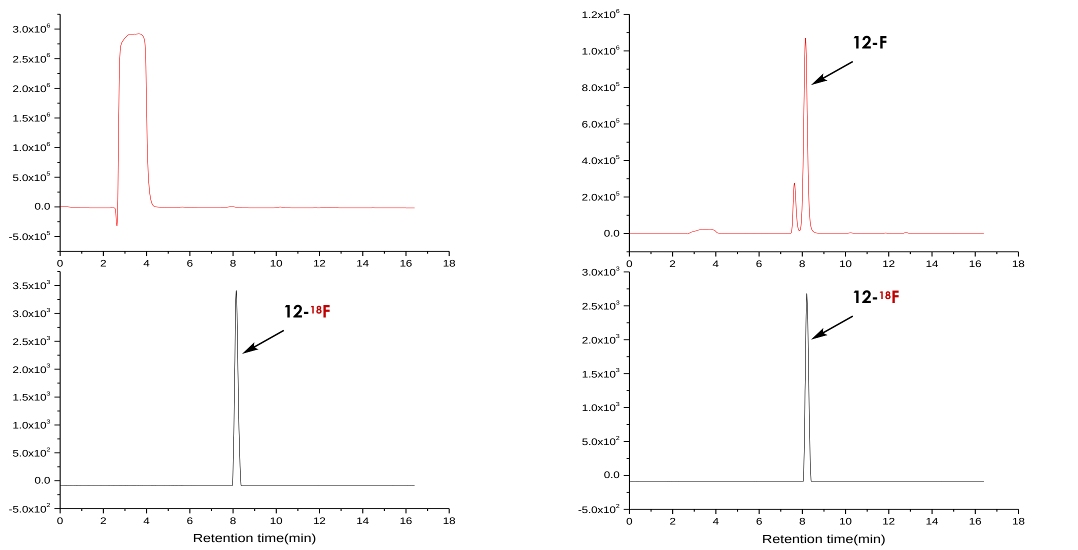


Reaction	Substrate	Activity ([18F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**12**	9.95 mCi	372 μCi	135 μCi	17 min	150.3 μCi	40.4%
2		11.22 mCi	355 μCi	129 μCi	17 min	143.6 μCi	40.5%
3		9.64 mCi	451 μCi	127 μCi	17 min	141.4 μCi	31.4%
Average RCC: **37.4±4.3%** (n=3)							

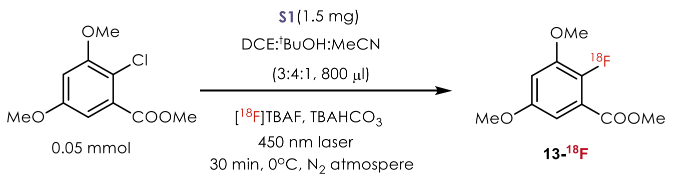
Supplementary Table 16. HPLC-isolated RCCs of **12-18F**



Supplementary Figure 34. Crude radio-HPLC traces from **12** to **12-^{18}F**

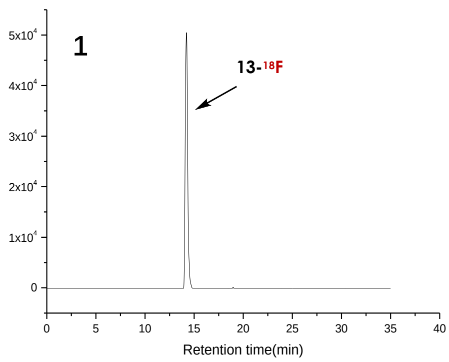


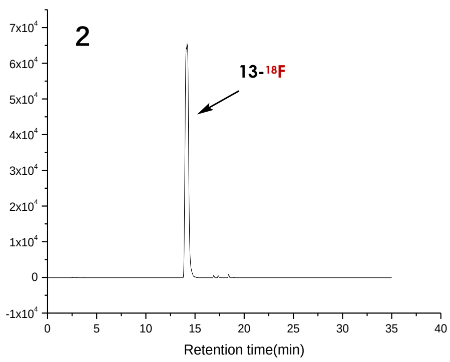
Supplementary Figure 35. Purification (left) and co-injection(right) for **12-^{18}F**

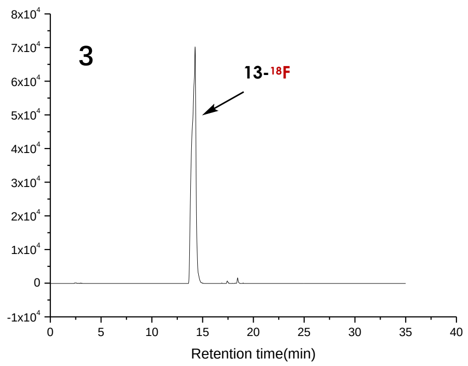


Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**13**	12.18 mCi	503 μCi	328 μCi	16 min	362.9 μCi	72.1%
2		8.98 mCi	800 μCi	565 μCi	17 min	629.0 μCi	78.6%
3		13.71 mCi	902 μCi	688 μCi	17 min	766.0 μCi	84.9%
Average RCC: **78.5±5.2%** (n=3)							

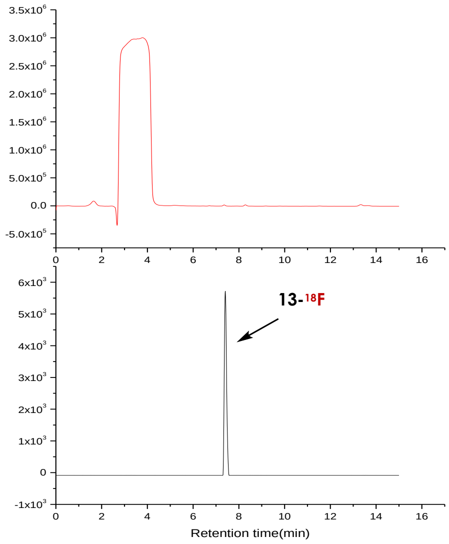
Supplementary Table 17. HPLC-isolated RCCs of **13-^{18}F**



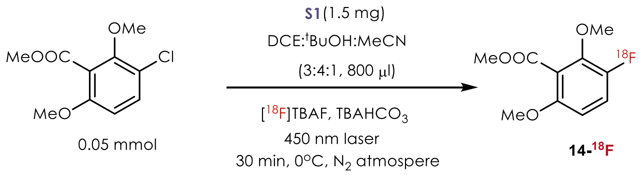




Supplementary Figure 36. Crude radio-HPLC traces from **13** to **13-^{18}F**

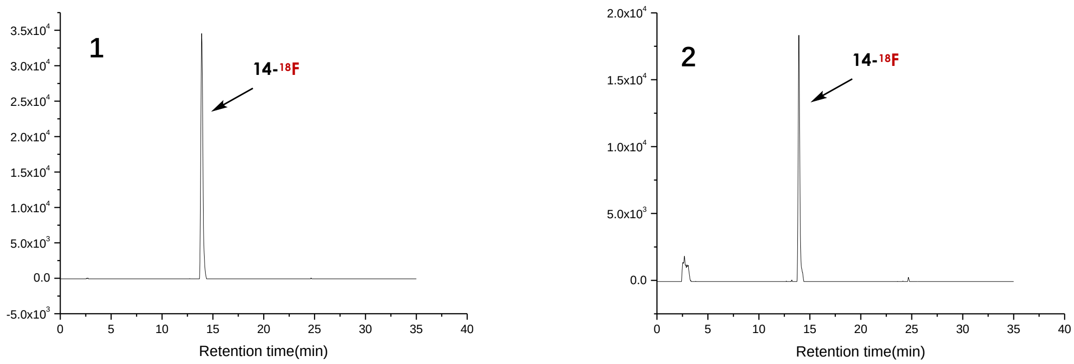


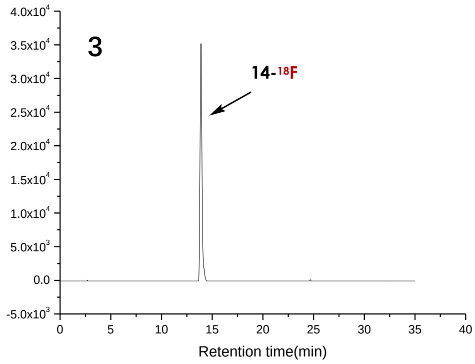
Supplementary Figure 37. Purification (left) and co-injection(right) for **13-18F**



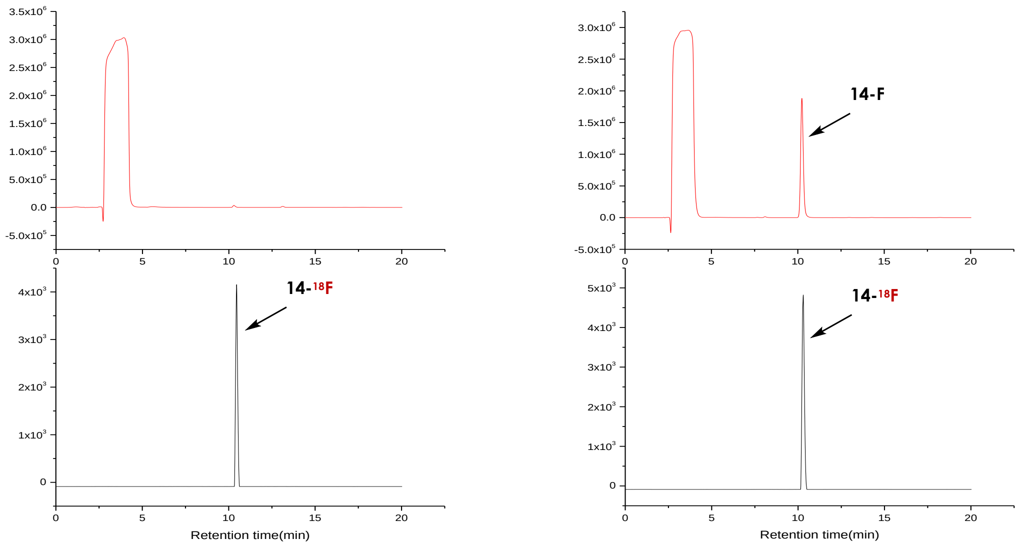
Reaction	Substrate	Activity ([18F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1		13.02 mCi	524 µCi	214 µCi	16 min	236.8 µCi	45.2%
2	**14**	8.35 mCi	308 µCi	92 µCi i	16 min	101.8 µCi	33%
3		6.68 mCi	476 µCi	192 µCi	17 min	213.8 µCi	44.9%
Average RCC: **41.0±4.7%** (n=3)							

Supplementary Table 18. HPLC-isolated RCCs of **14-18F**

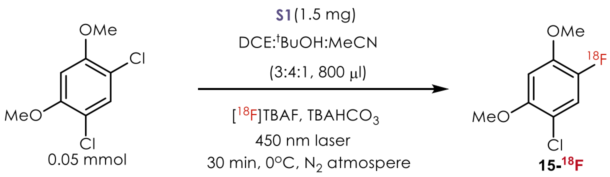




Supplementary Figure 38. Crude radio-HPLC traces from **14** to **14-^{18}F**

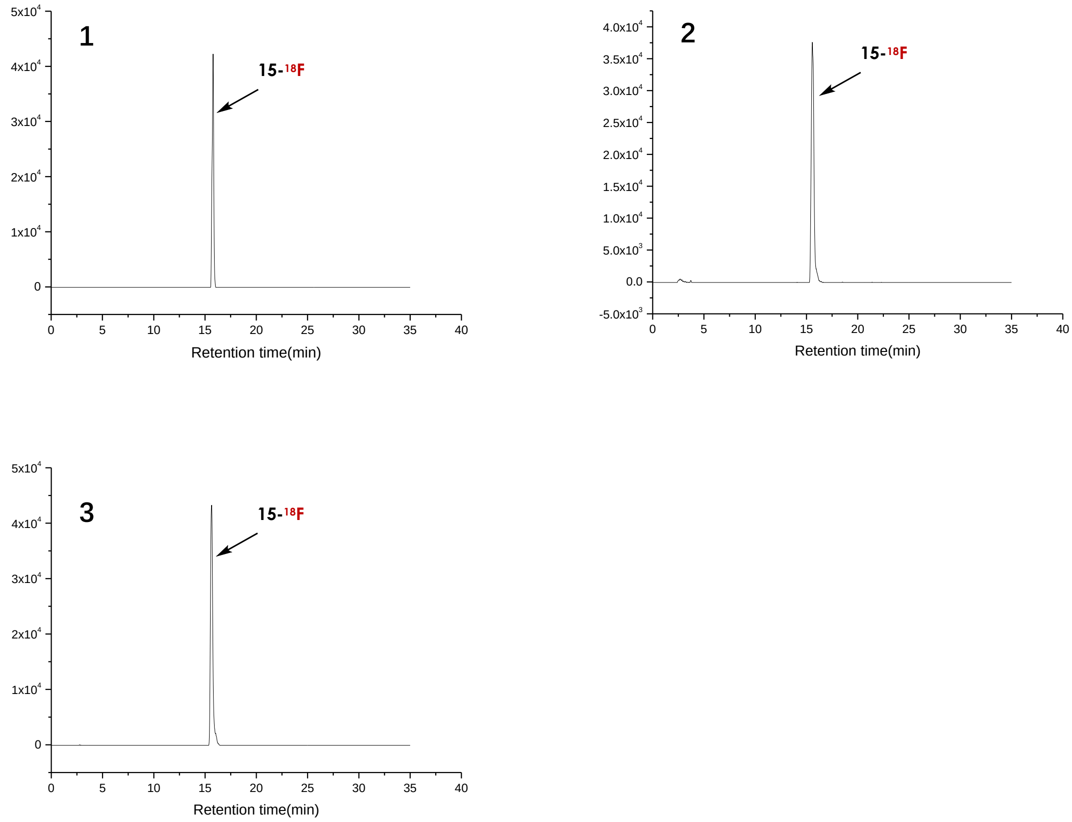


Supplementary Figure 39. Purification (left) and co-injection(right) for **14-^{18}F**

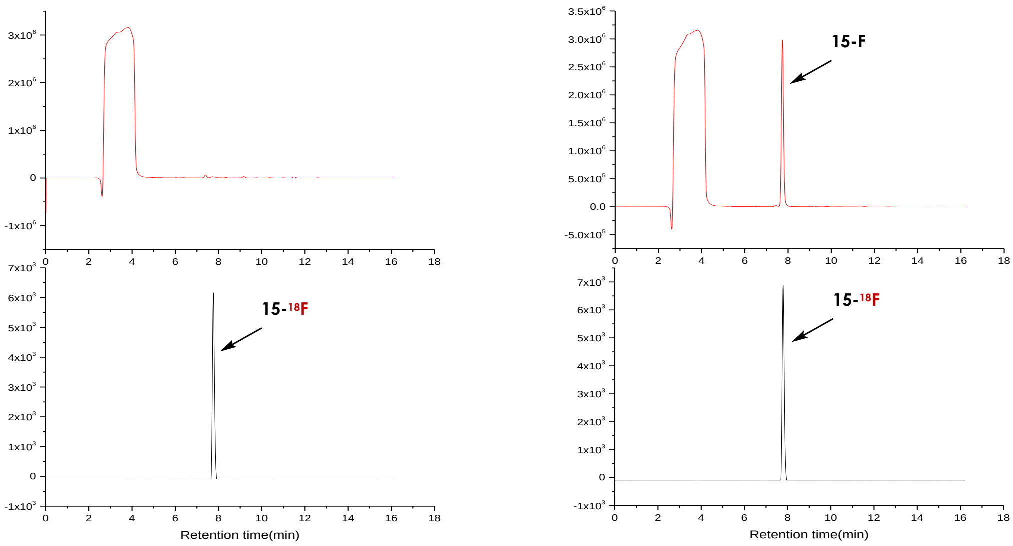


Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	15	9.79 mCi	328 μCi	187 μCi	19 min	210.8 μCi	64.3%
2		8.91 mCi	566 μCi	283 μCi	19 min	319.1 μCi	56.4%
3		12.10 mCi	520 μCi	271 μCi	19 min	305.5 μCi	58.8%
Average RCC: **59.8±3.3%** (n=3)							

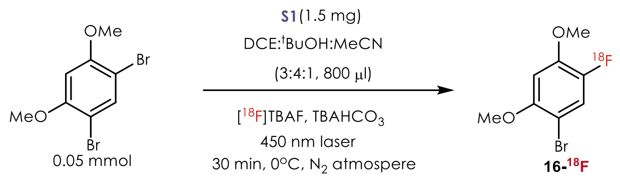
Supplementary Table 19. HPLC-isolated RCCs of **15-^{18}F**



Supplementary Figure 40. Crude radio-HPLC traces from **15** to **15-18F**



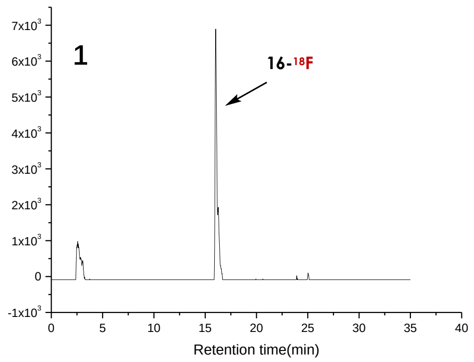
Supplementary Figure 41. Purification (left) and co-injection(right) for **15-18F**

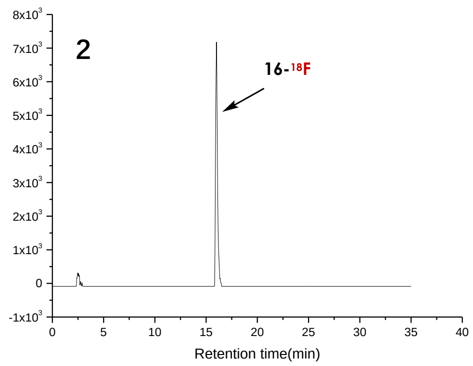


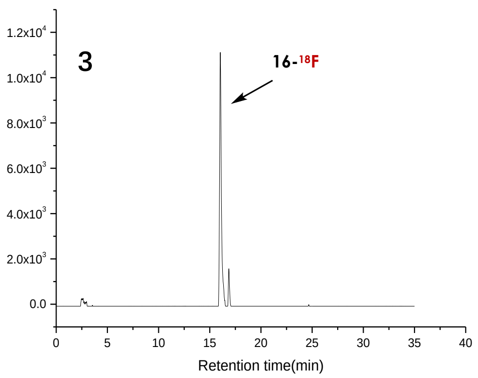
Reaction	Substrate	Activity ([18F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1		10.09 mCi	477 μCi	48 μCi	19 min	54.1 μCi	11.3%
2	**16**[a]	11.26 mCi	350 μCi	44 μCi	19 min	49.6 μCi	14.2%
3		9.13 mCi	395 μCi	64 μCi	18 min	71.7 μCi	18.2%
Average RCC: **14.6±2.8%** (n=3)							

[a]Substrate precipitated out during the reaction.

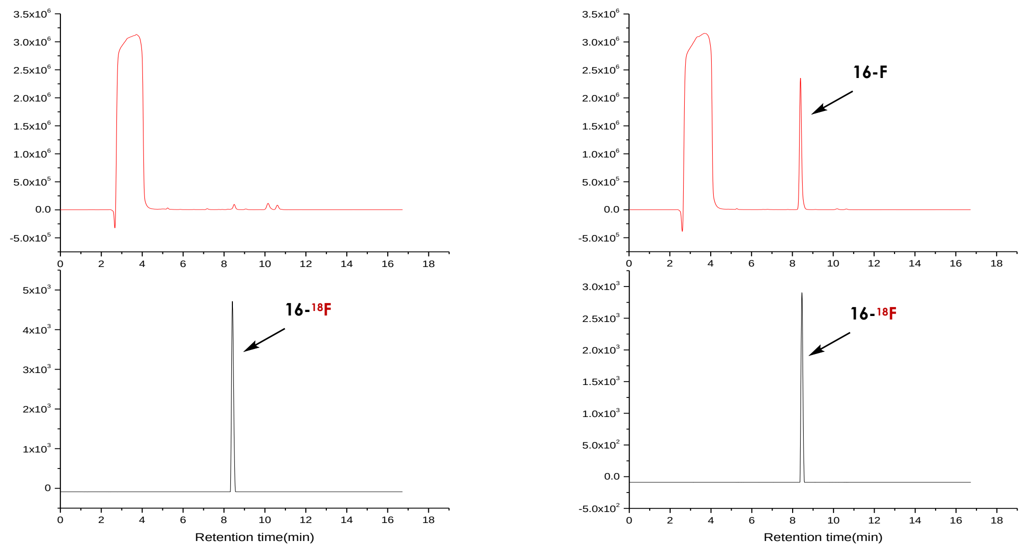
Supplementary Table 20. HPLC-isolated RCCs of **16-^{18}F**



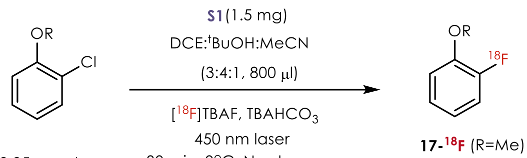




Supplementary Figure 42. Crude radio-HPLC traces from **16** to **16-^{18}F**



Supplementary Figure 43. Purification (left) and co-injection(right) for **16-18F**

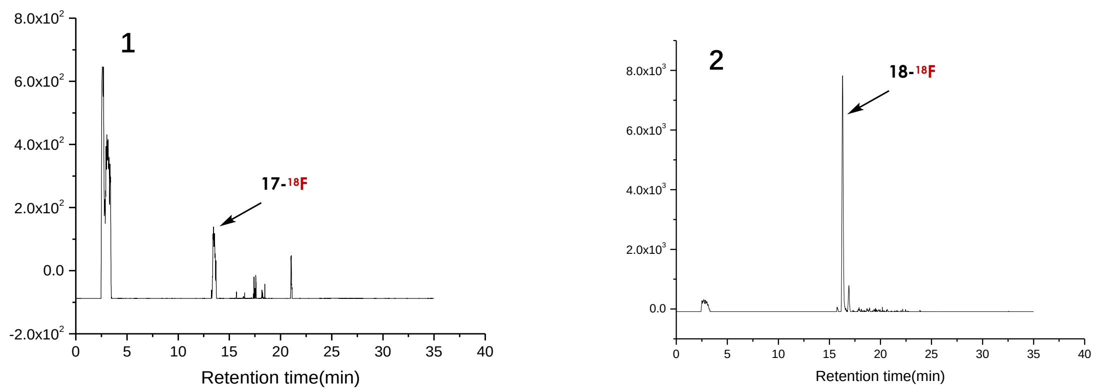


0.05 mmol

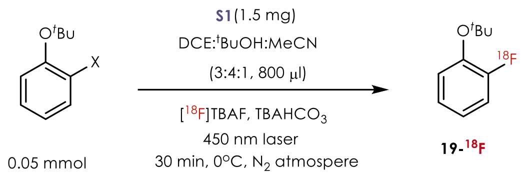
17-18F (R=Me)
18-18F (R=^{i}Pr)

Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**17** (R=Me)	12.69 mCi	533 µCi	---	---	---	**trace**
2	**18** (R=^{i}Pr)	9.39 mCi	519 µCi	33 µCi	19 min	37.2 µCi	**7.2%**

Supplementary Table 21. HPLC-isolated RCCs of **17-18F**, **18-18F**

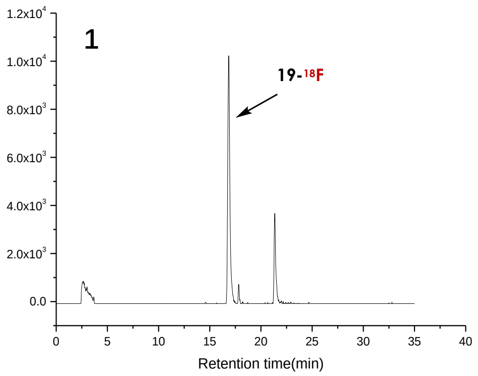


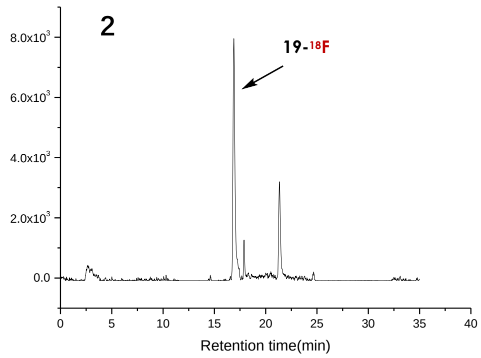
Supplementary Figure 44. Crude radio-HPLC traces from **17**,**18** to **17-18F**, **18-18F**.

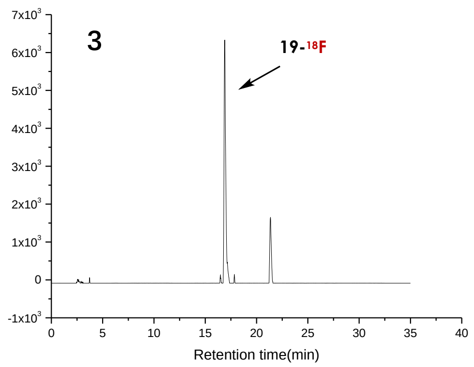


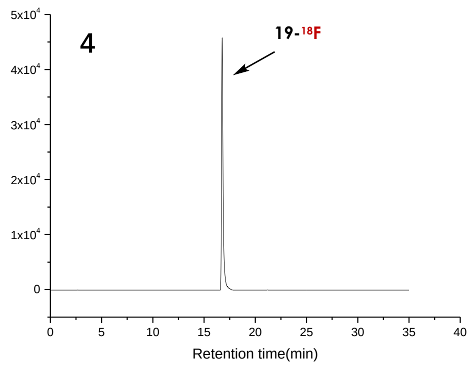
Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**19-Cl**	9.21mCi	729 μCi	68 μCi	19 min	77.2 μCi	10.5%
2		9.40 mCi	837 μCi	53 μCi	20 min	60.1 μCi	7.2%
3		9.83 mCi	451 μCi	37 μCi	19 min	41.7 μCi	9.2%
Average RCC of **19-^{18}F** from **19-Cl**: **9.0±1.4%** (n=3)							
4	**19-F**[a] (X=F, R=^{t}Bu)	15.13 mCi	624 μCi	183 μCi	20 min	207.6 μCi	33.3%
5		11.71mCi	726 μCi	237 μCi	19 min	267.2 μCi	36.8%
6		9.45 mCi	285 μCi	71 μCi	19 min	80.1 μCi	28.1%
Average RCC of **19-^{18}F** from **19-F**: **32.7±3.6%** (n=3)							

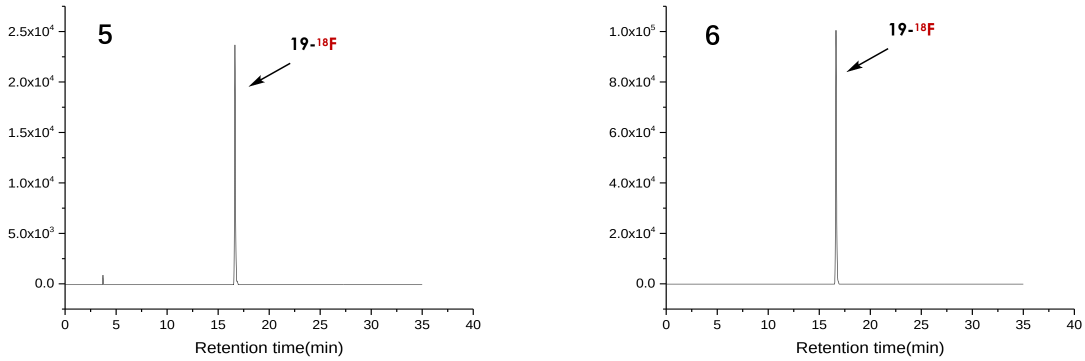
Supplementary Table 22. HPLC-isolated RCCs of **19-^{18}F**



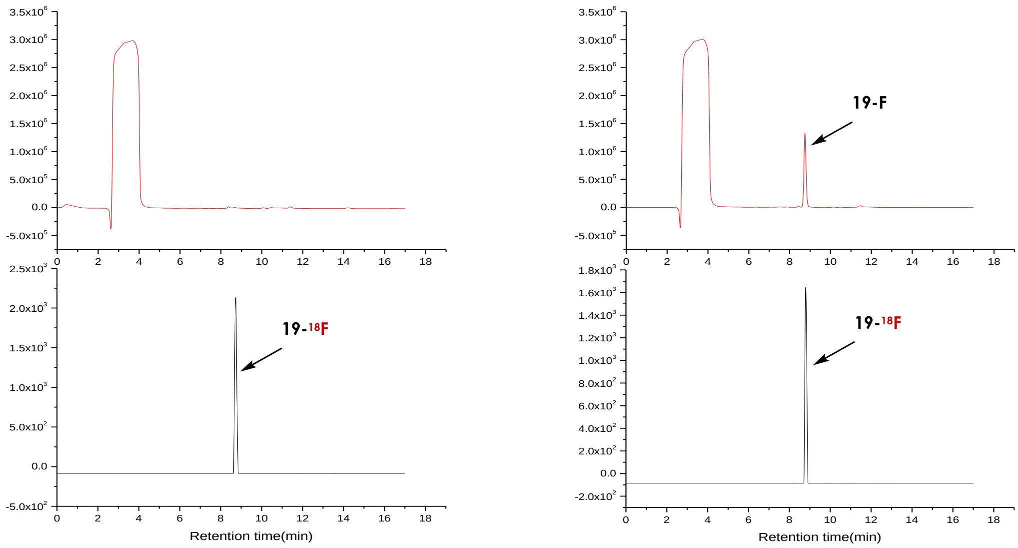




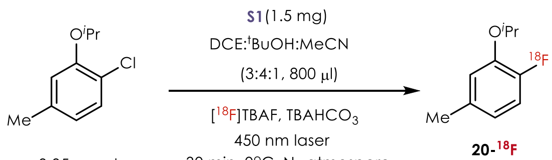




Supplementary Figure 45. Crude radio-HPLC traces from **19-Cl** to **19-18F**

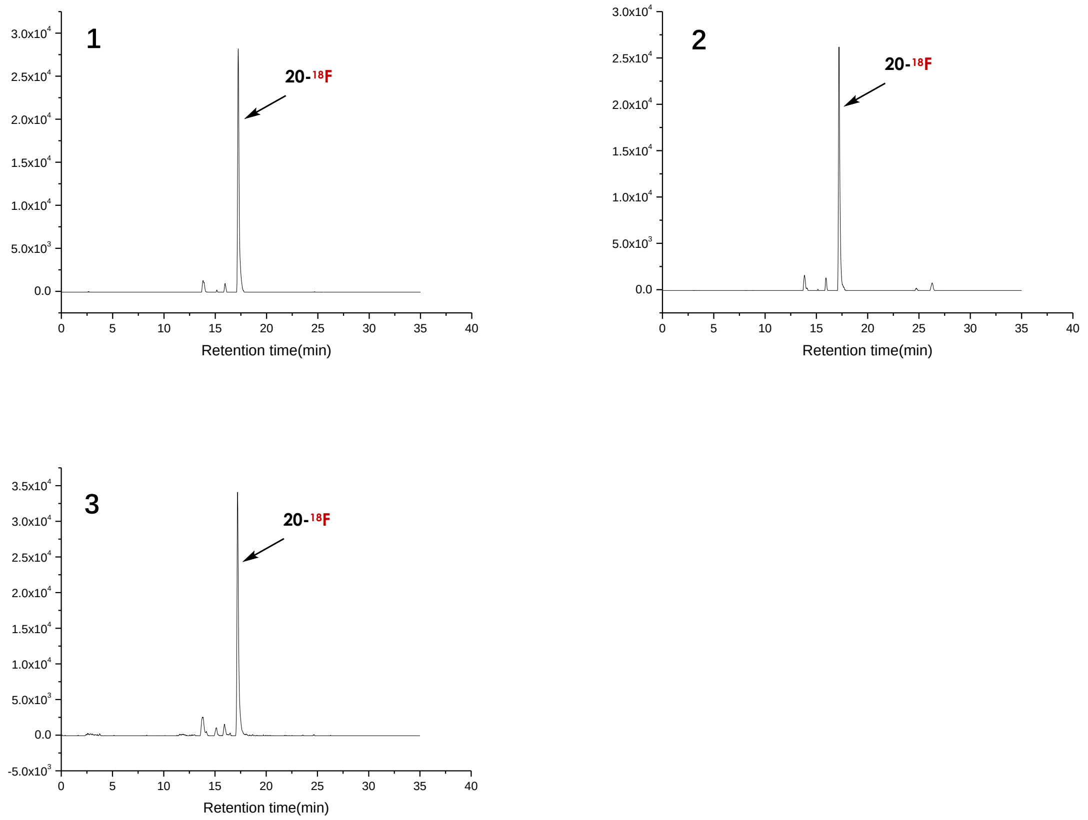


Supplementary Figure 46. Purification (left) and co-injection(right) for **19-18F**

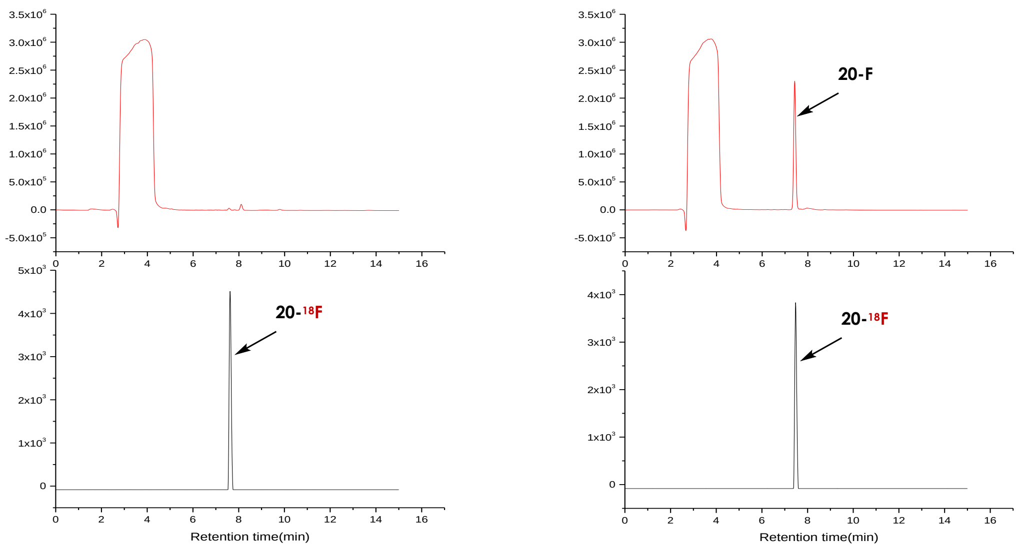


Reaction	Substrate	Activity ([18F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**20**	9.55 mCi	437 μCi	119 μCi	20 min	135 μCi	30.9%
2		10.96 mCi	459 μCi	110 μCi	21 min	125.6 μCi	27.4%
3		8.89 mCi	609 μCi	159 μCi	21 min	181.5 μCi	29.8%
Average RCC: **29.4±1.5%** (n=3)							

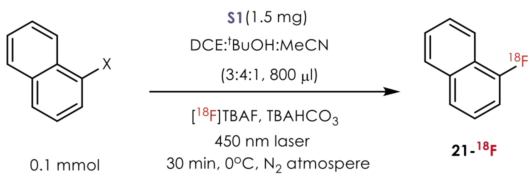
Supplementary Table 23. HPLC-isolated RCCs of **20-18F**



Supplementary Figure 47. Crude radio-HPLC traces from **20** to **20-18F**



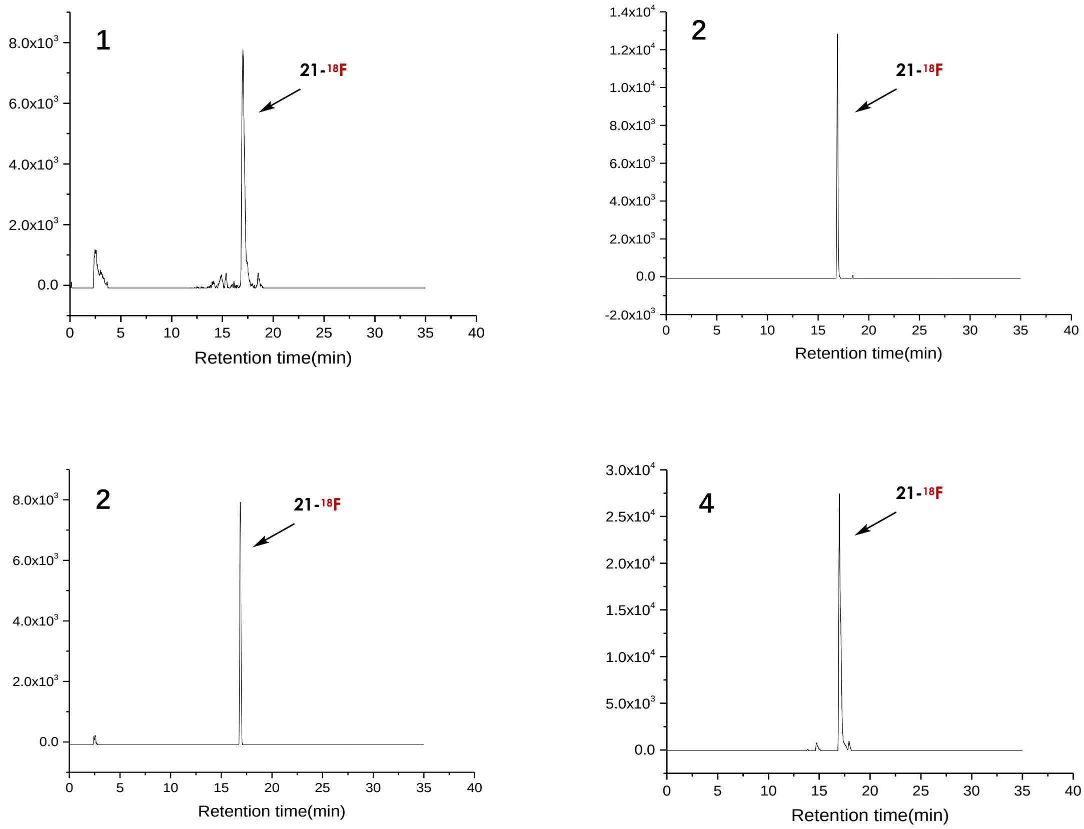
Supplementary Figure 48. Purification (left) and co-injection for **20-18F**

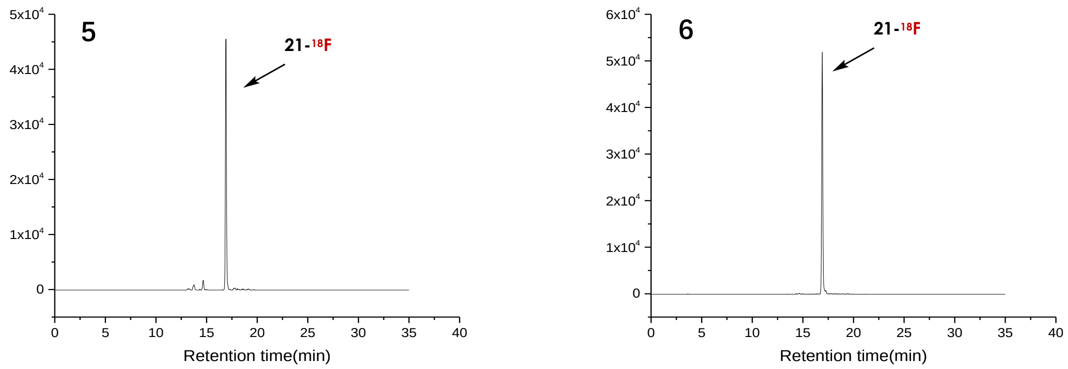


Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**21-Cl** (X=Cl)	12.59 mCi	541 μCi	72 μCi	20 min	81.7 μCi	15.1%
2		12.06 mCi	415 μCi	43 μCi	20 min	48.8 μCi	11.8%
3		10.86 mCi	355 μCi	35 μCi	19 min	39.5 μCi	11.1%
Average RCC of **21-^{18}F** from **21-Cl**: **12.7±1.7%** (n=3)							
4	**21-F**[a] (X=F)	5.23 mCi	300 μCi	150 μCi	20 min	170.2 μCi	56.7%
5		6.67 mCi	329 μCi	138 μCi	20 min	156.6 μCi	47.6%
6		10.79 mCi	338 μCi	151 μCi	20 min	171.3 μCi	50.7%
Average RCC of **21-^{18}F** from **21-F**: **51.7±3.8%** (n=3)							

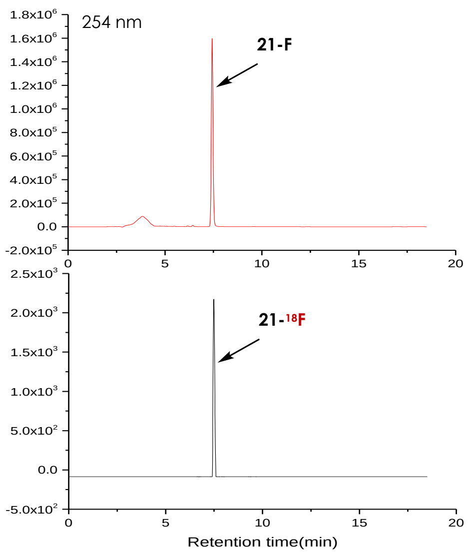
[a]0.02 mmol substrate.

Supplementary Table 24. HPLC-isolated RCCs of **21-^{18}F**

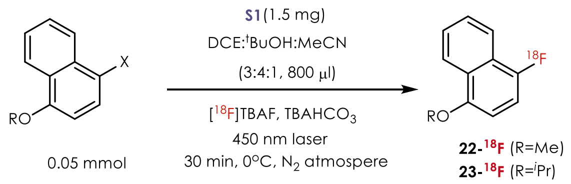




Supplementary Figure 49. Crude radio-HPLC traces from **21-Cl** and **21-F** to **21-^{18}F**



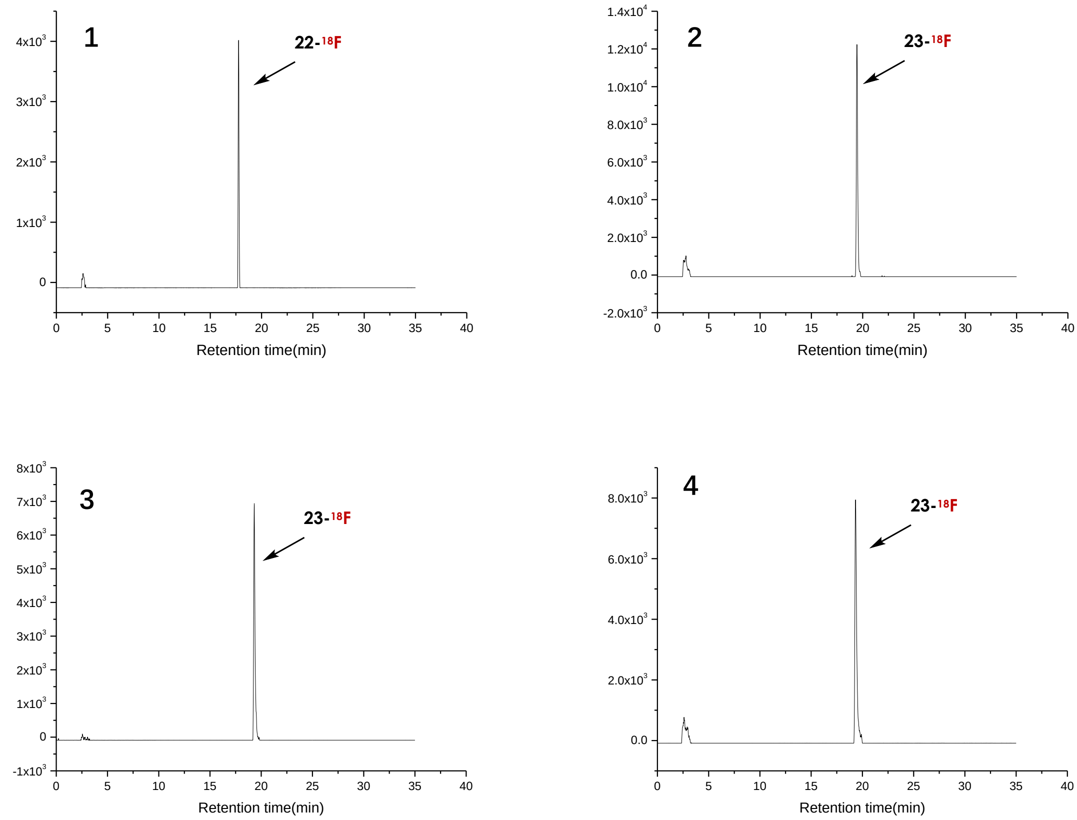
Supplementary Figure 50. Purification of **21-^{18}F**



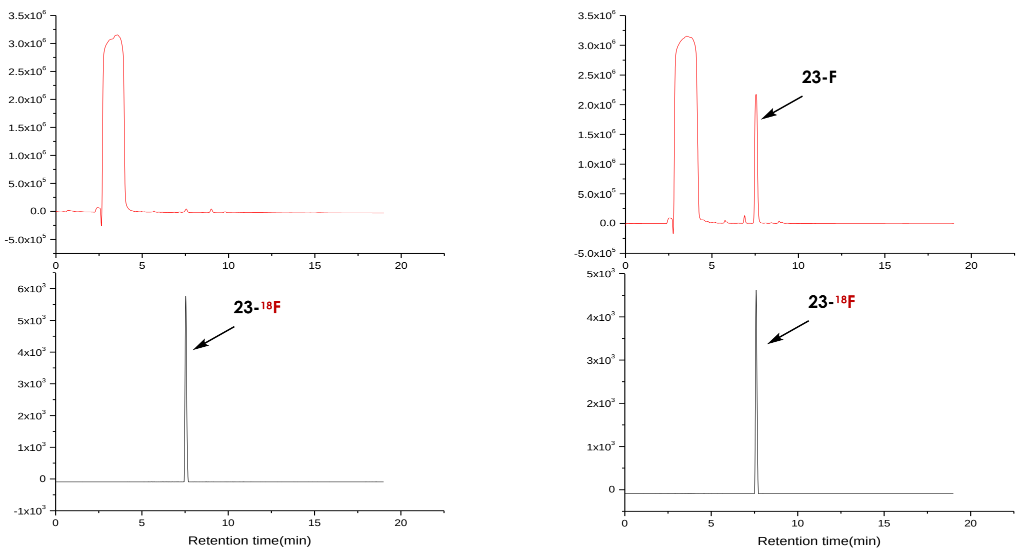
Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**22(R=Me)**	12.07 mCi	321 μCi	13 μCi	21 min	37.2 μCi	**4.6%**
2		13.69 mCi	374 μCi	51 μCi	22 min	58.6 μCi	15.7%
3	**23(R=^{i}Pr)**	11.28 mCi	307 μCi	34 μCi	22 min	39.1 μCi	12.7%
4		10.20 mCi	439 μCi	47 μCi	22 min	54.0 μCi	12.3%

Average RCC (**23-¹⁸F**):**13.6±1.5%** (n=3)

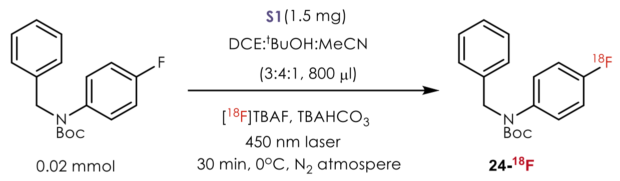
Supplementary Table 25. HPLC-isolated RCCs of **22-^{18}F** and **23-^{18}F**



Supplementary Figure 51. Crude radio-HPLC traces from **22** and **23** to **22-^{18}F** and **23-^{18}F**

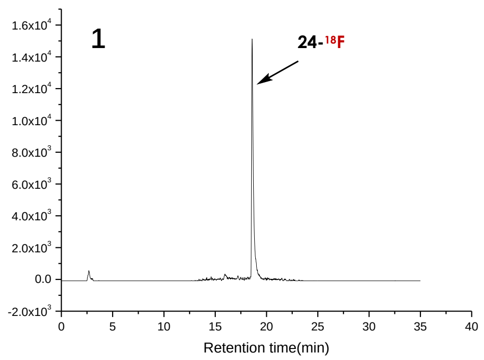


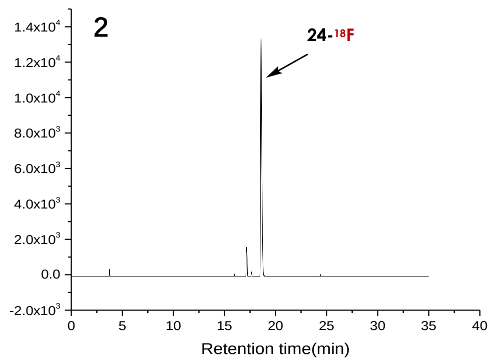
Supplementary Figure 52. Purification (left) and co-injection(right) for **23-^{18}F**

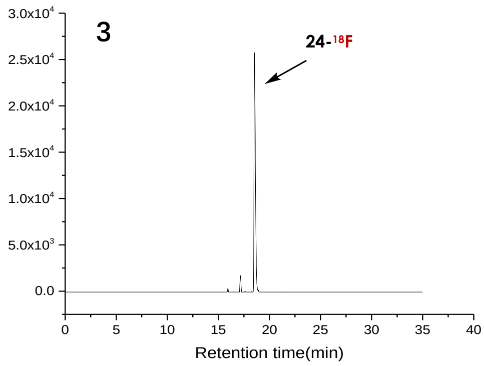


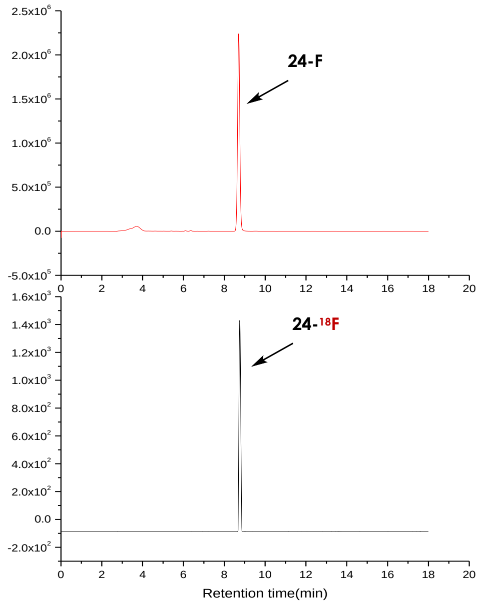
Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**24-F**	9.33 mCi	725 μCi	87 μCi	21 min	99.3 μCi	13.2%
2		12.11 mCi	362 μCi	44 μCi	20 min	49.9 μCi	13.8 %
3		12.26 mCi	492 μCi	101 μCi	20 min	114.6 μCi	23.3%
Average RCC:**16.8±4.6%** (n=3)							

Supplementary Table 26. HPLC-isolated RCCs of **24-^{18}F**

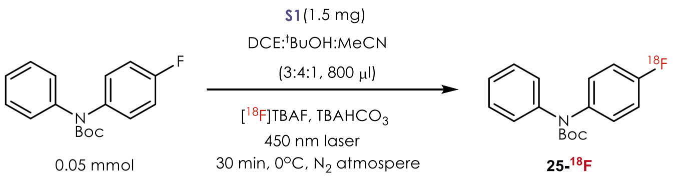








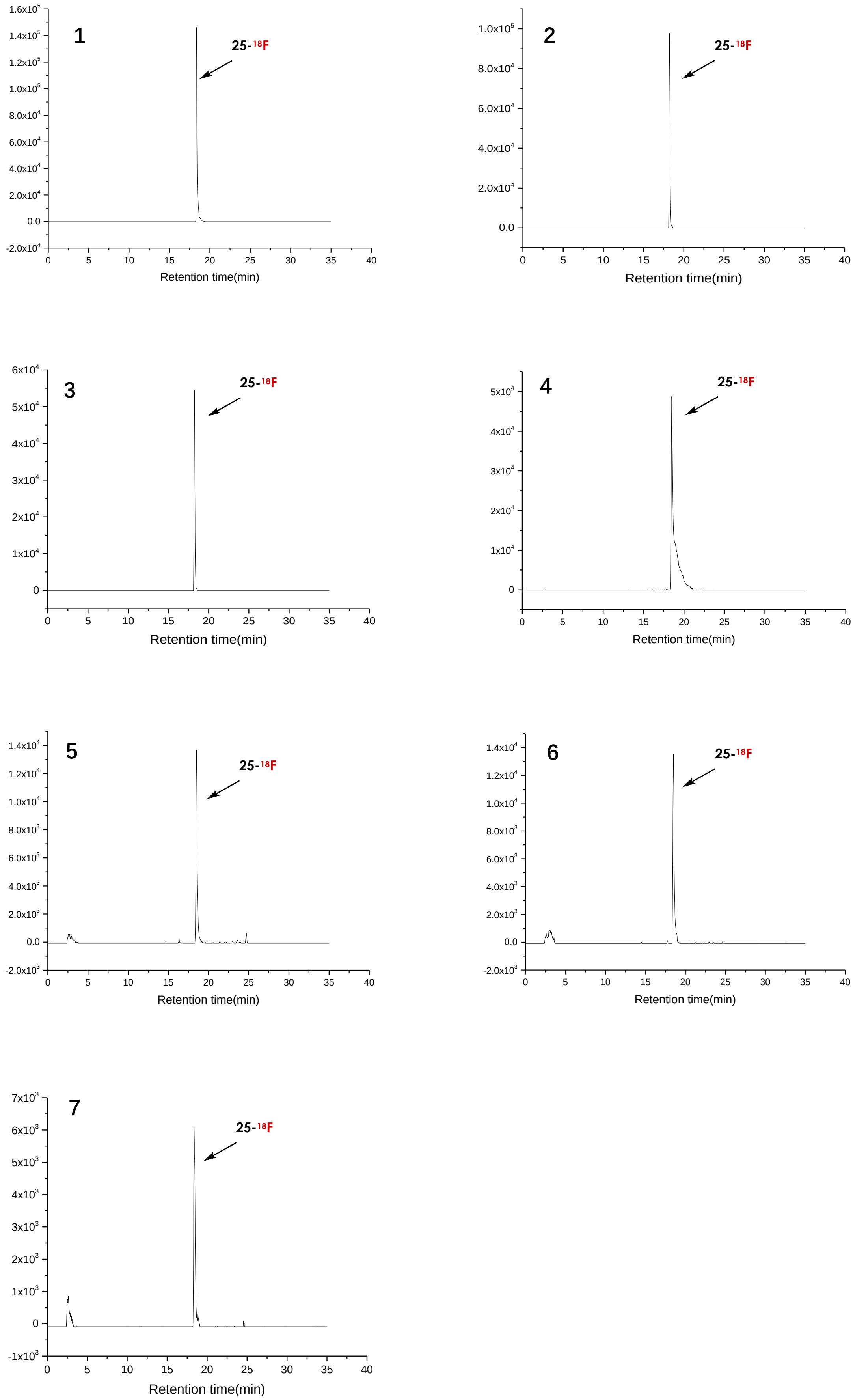
Supplementary Figure 53. Crude radio-HPLC traces and purification of **24-^{18}F**



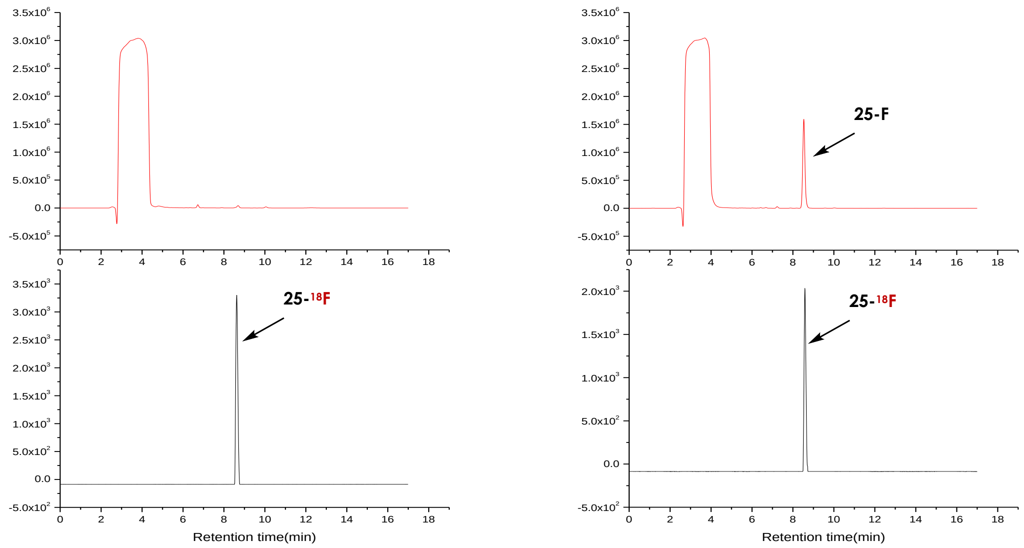
Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1[a]	**25-F (X-F)**	16.00 mCi	920 μCi	425 μCi	21 min	485.3 μCi	52.7%
2[a]		6.59 mCi	396 μCi	259 μCi	21 min	295.7 μCi	74.7%
3[a]		5.94 mCi	314 μCi	162 μCi	21min	185.0 μCi	58.9%
4		11.21 mCi	749 μCi	491 μCi	23 min	567.7 μCi	75.8%
Average RCC of 25-^{18}F from 25-F:**62.1±9.2%** (n=3)							
5	**25-Cl (X=Cl)**	8.75 mCi	641 μCi	74 μCi	21 min	84.5 μCi	13.2%
6		12.55 mCi	976 μCi	77 μCi	21min	87.9 μCi	9.0%
7		16.47 mCi	733 μCi	69 μCi	22 min	79.3 μCi	10.8%
Average RCC of 25-^{18}F from 25-Cl:**11.0%±1.7%** (n=3)							

[a]0.01 mmol substrate.

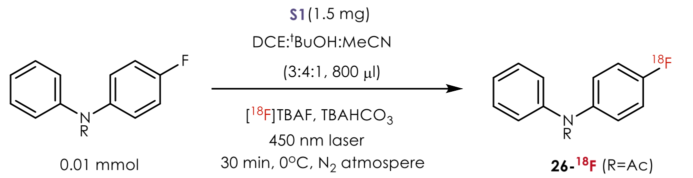
Supplementary Table 27. HPLC-isolated RCCs of **25-^{18}F**


1
2
3
4
5
6
7
25-18F
Retention time(min)

Supplementary Figure 54. Crude radio-HPLC traces from **25-Cl** and **25-F** to **25-^{18}F**



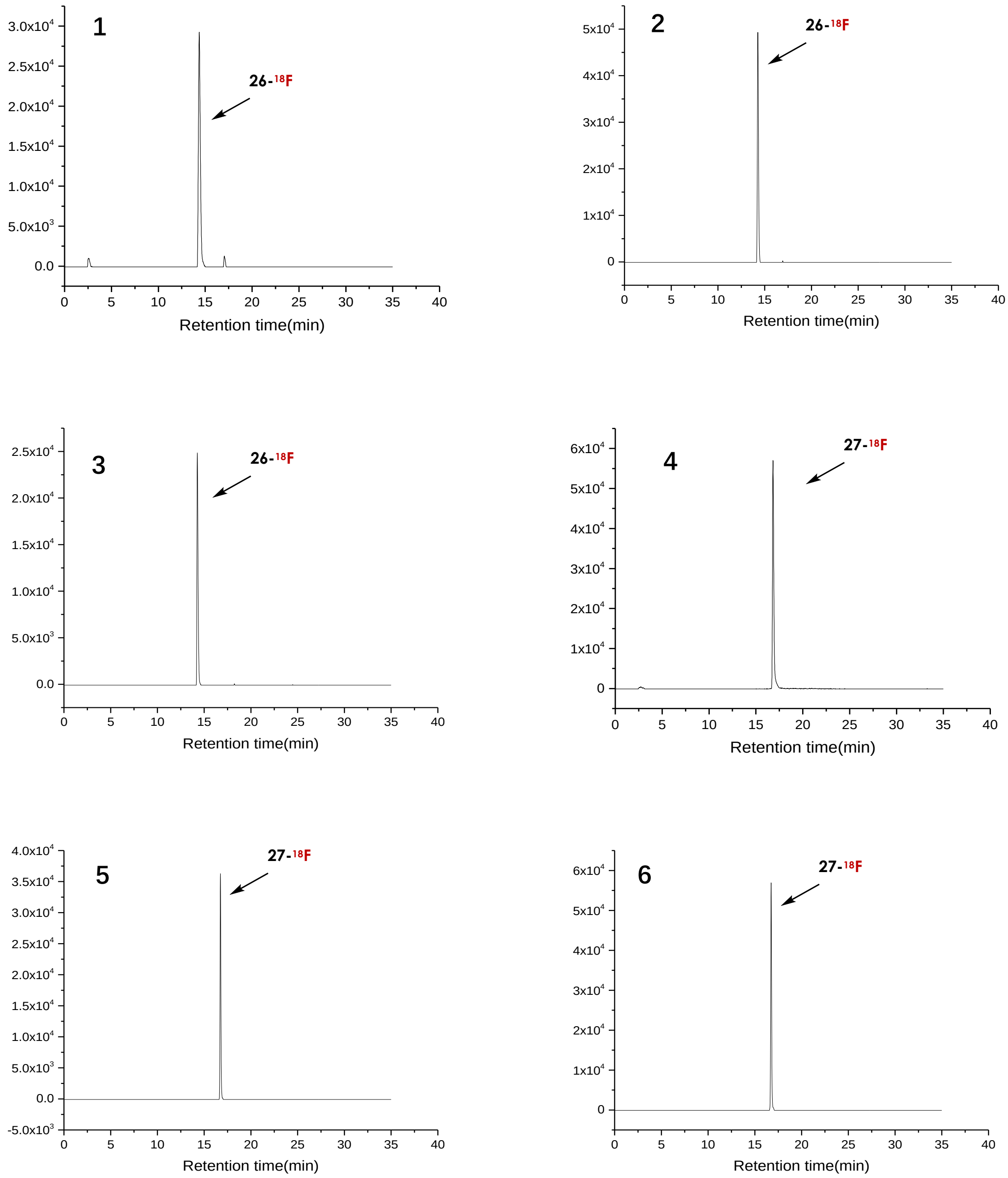
Supplementary Figure 55. Purification (left) and co-injection(right) for **25-^{18}F**



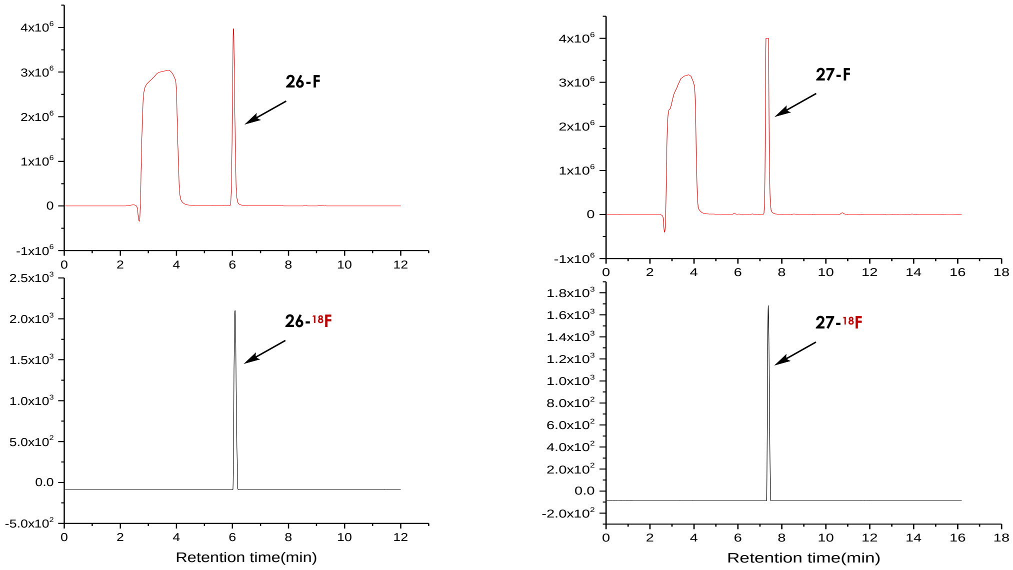
26-^{18}F (R=Ac)
27-^{18}F (R=C(O)Ph)

Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**26** (R=Ac)	8.59 mCi	492 μCi	178 μCi	17 min	198.2 μCi	40.3%
2		10.61 mCi	427 μCi	164 μCi	16 min	181.4 μCi	42.5%
3		7.67 mCi	308 μCi	90 μCi	16 min	99.6 μCi	32.3%
Average RCC of **26-^{18}F**: **38.4%±4.4%** (n=3)							
4	**27** (R=COPh)	16.61 mCi	750 μCi	217 μCi	20 min	246.2 μCi	32.8%
5		17.46 mCi	523 μCi	104 μCi	21 min	118.7 μCi	22.7%
6		11.55 mCi	396 μCi	147 μCi	19 min	165.7 μCi	41.8%
Average RCC of **27-^{18}F:32.4%±7.8%** (n=3)							

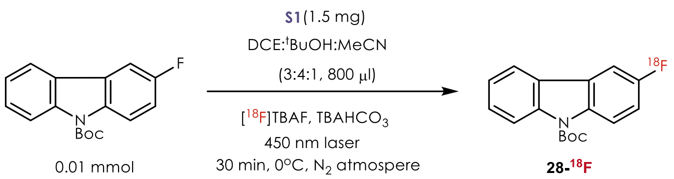
Supplementary Table 28. HPLC-isolated RCCs of **26-^{18}F** and **27-^{18}F**



Supplementary Figure 56. Crude radio-HPLC traces for **26-^{18}F** and **27-^{18}F**



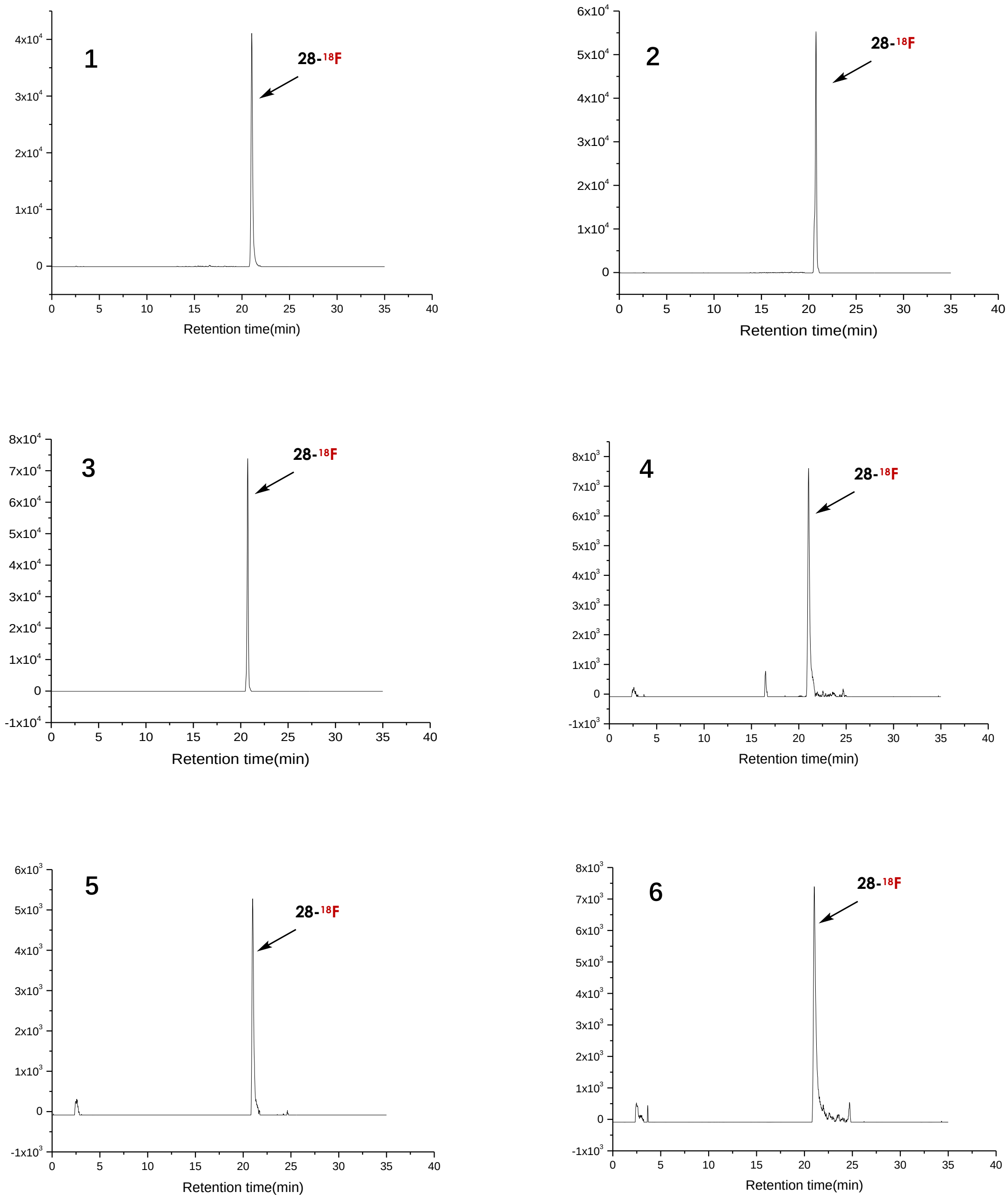
Supplementary Figure 57. HPLC traces of purification of **26-^{18}F** and **27-^{18}F**



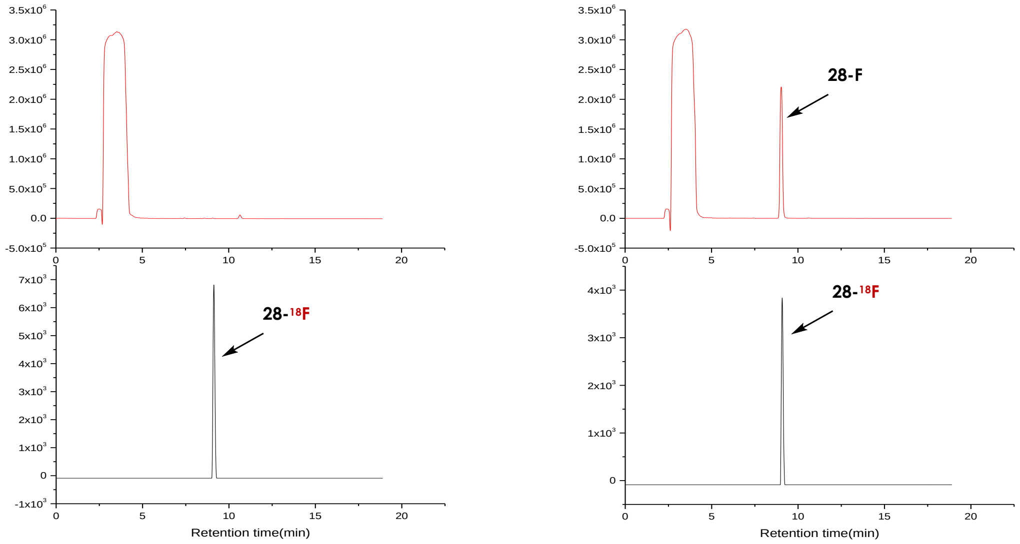
Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1		15.18mCi	558 μCi	205 μCi	25 min	240.1 μCi	43.0%
2	**28-F**[a] (X=F)	8.98 mCi	535 μCi	224 μCi	24 min	260.7 μCi	48.7%
3		7.03 mCi	472 μCi	238 μCi	23 min	275.2 μCi	58.3%
Average RCC of **28-^{18}F** from **28-F**: **50.0%±6.3%** (n=3)							
4		9.88 mCi	602 μCi	54 μCi	25 min	63.2 μCi	10.5%
5	**28-Cl** (X=Cl)	10.68 mCi	499 μCi	39 μCi	25 min	45.7 μCi	9.2%
6		15.66 mCi	742 μCi	77 μCi	25 min	90.2 μCi	12.2%
Average RCC of **28-^{18}F** from **28-Cl**: **10.7±1.2%** (n=3)							

[a]0.01 mmol substrate.

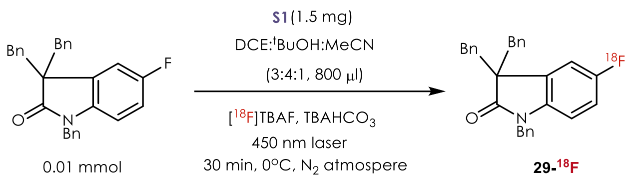
Supplementary Table 29. HPLC-isolated RCCs of **28-^{18}F**



Supplementary Figure 58. Crude radio-HPLC traces from **28-F** and **28-Cl** to **28-^{18}F**

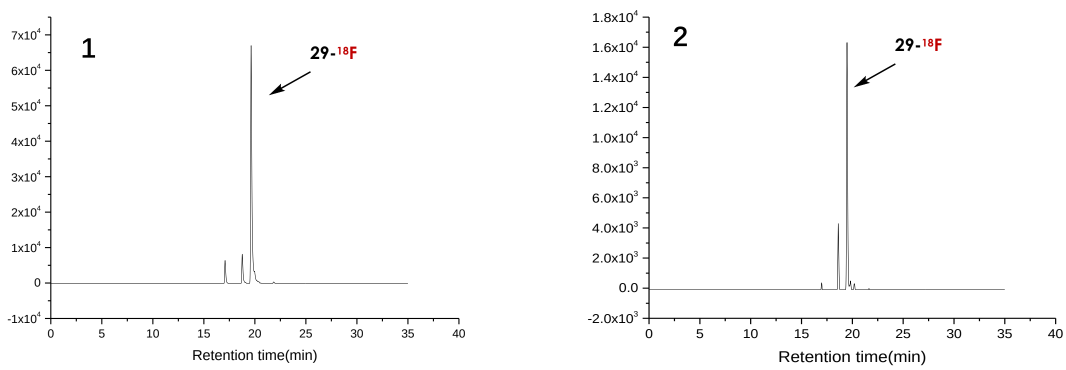


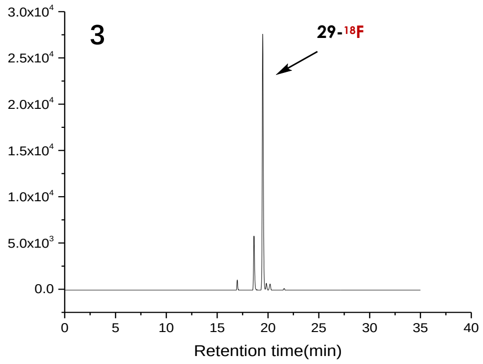
Supplementary Figure 59. Purification (left) and co-injection(right) for **28-18F**

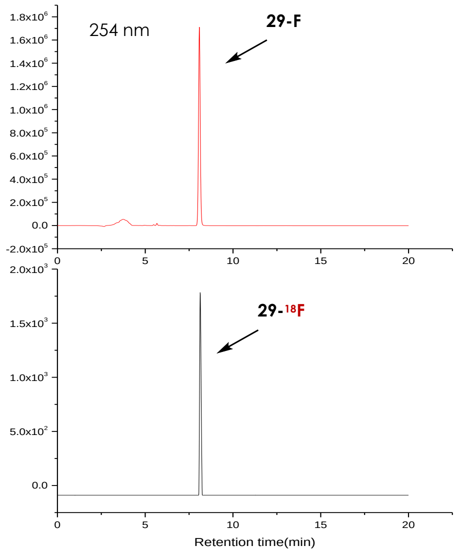


Reaction	Substrate	Activity ([18F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1		14.86 mCi	555 μCi	188 μCi	25 min	220.1 μCi	39.7%
2	**29**	9.16 mCi	298 μCi	75 μCi	22 min	86.2 μCi	28.9%
3		10.37 mCi	382 μCi	108 μCi	23 min	124.9 μCi	32.7%
Average RCC: **33.8±4.5%** (n=3)							

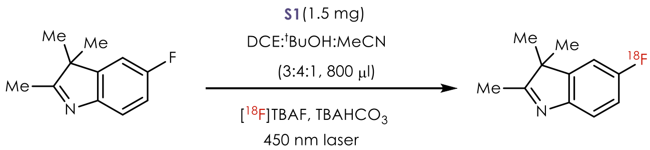
Supplementary Table 30. HPLC-isolated RCCs of **29-18F**







Supplementary Figure 60. Radio-HPLC traces and purification of **29-^{18}F**



0.01 mmol

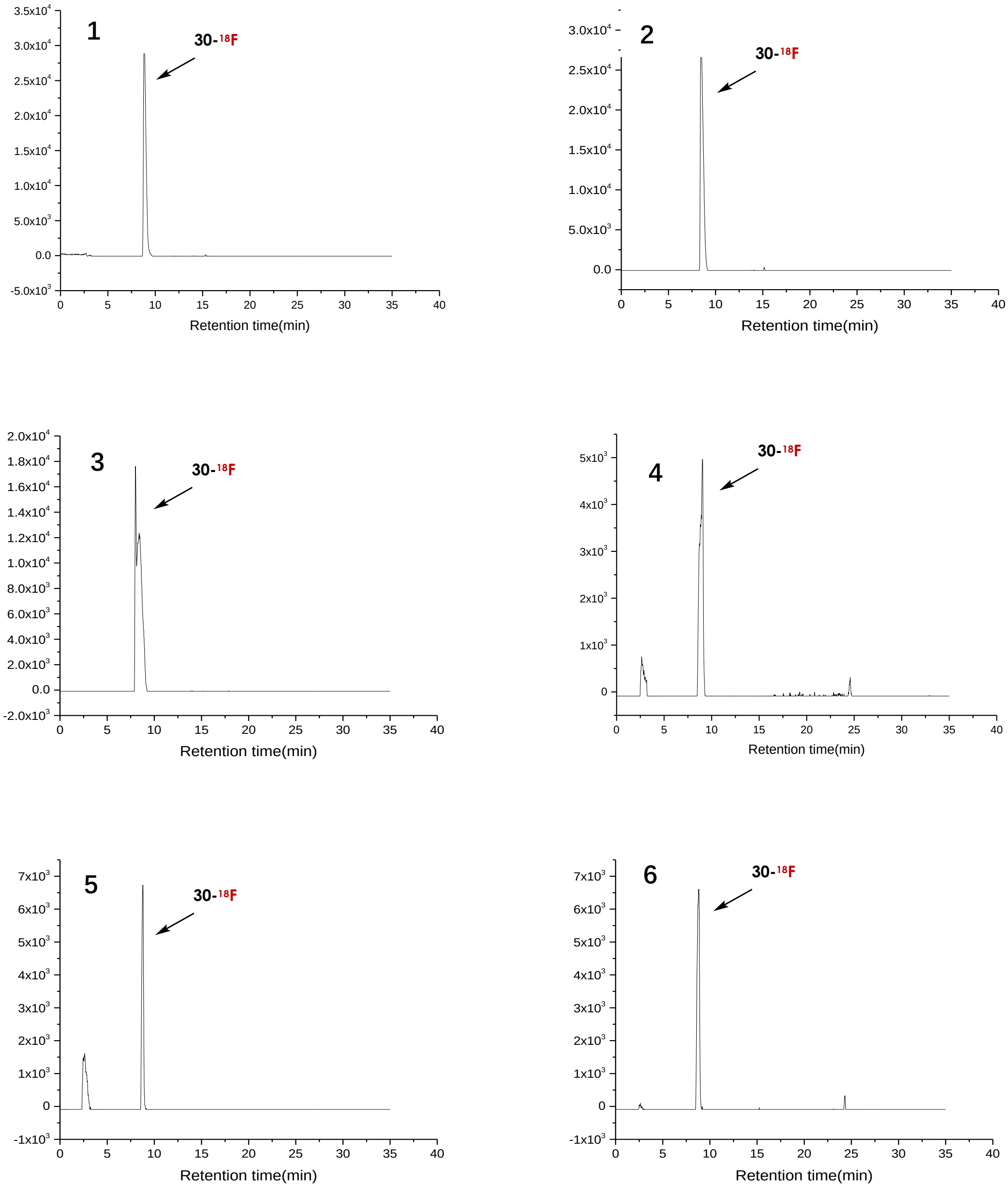
30-^{18}F

Reaction	**Substrate**	**Activity ([^{18}F]TBAF)**	**Injected dose**	**Collected dose**	**Isolation time**	**Decay corrected dose**	**Radiochemical conversion (RCC)**
1	**30-F** (X=F)	15.66 mCi	349 μCi	231 μCi	12 min	249.2 μCi	71.4%
2		11.33 mCi	405 μCi	260 μCi	12 min	280.5 μCi	69.3%
3		9.28 mCi	459 μCi	266 μCi	14 min	290.6 μCi	63.3%
Average RCC of **30-^{18}F** from **30-F**: **68.0%±3.4%** (n=3)							
4	**30-Cl**[a] (X=Cl)	12.81 mCi	449 μCi	59 μCi	12 min	63.6 μCi	14.2%
5		6.59 mCi	286 μCi	42 μCi	12 min	46.5 μCi	16.1%

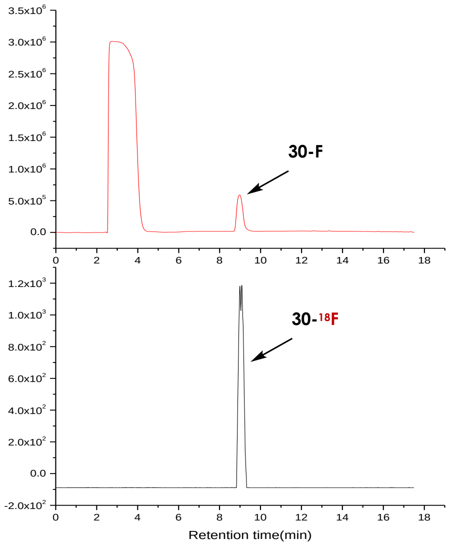
6		11.87 mCi	338 µCi	57 µCi	11 min	61.1 µCi	18.1%
Average RCC of **30-^{18}F** from **30-Cl**: **16.1%±1.6%** (n=3)							

[a]0.05 mmol substrate.

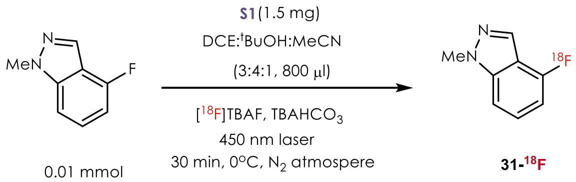
Supplementary Table 31. HPLC-isolated RCCs of **30-^{18}F**



Supplementary Figure 61. Radio-HPLC traces from **30-F** and **30-Cl** to **30-^{18}F**

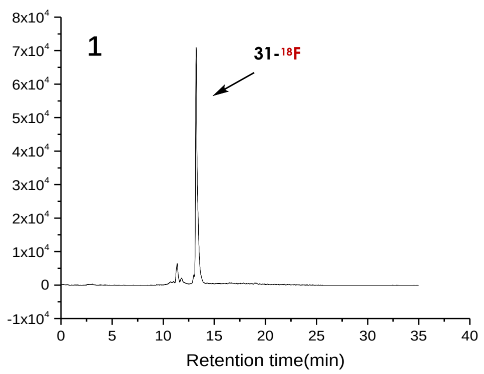


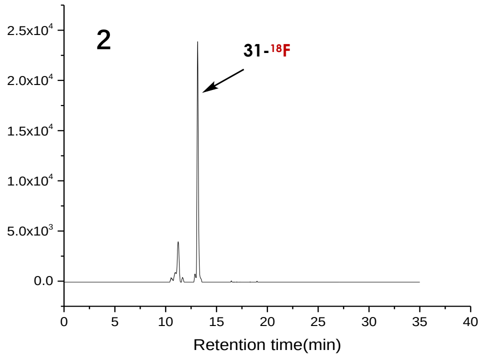
Supplementary Figure 62. Purification of **30-18F**

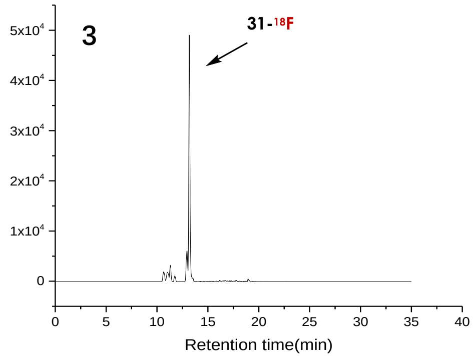


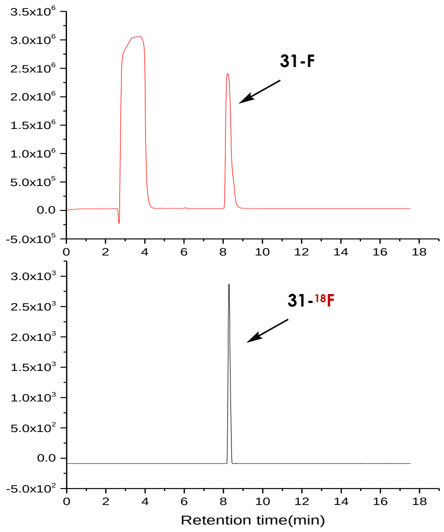
Reaction	Substrate	Activity ([18F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1		16.44 mCi	863 μCi	361 μCi	15 min	396.9 μCi	46%
2	**31**	5.91 mCi	339 μCi	106 μCi	15 min	116.5 μCi	34.4%
3		12.62 mCi	489 μCi	149 μCi	16 min	164.8 μCi	33.7%
Average RCC: **38.0%±5.6%** (n=3)							

Supplementary Table 32. HPLC-isolated RCCs of **31-18F**

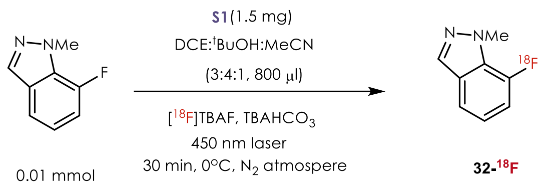






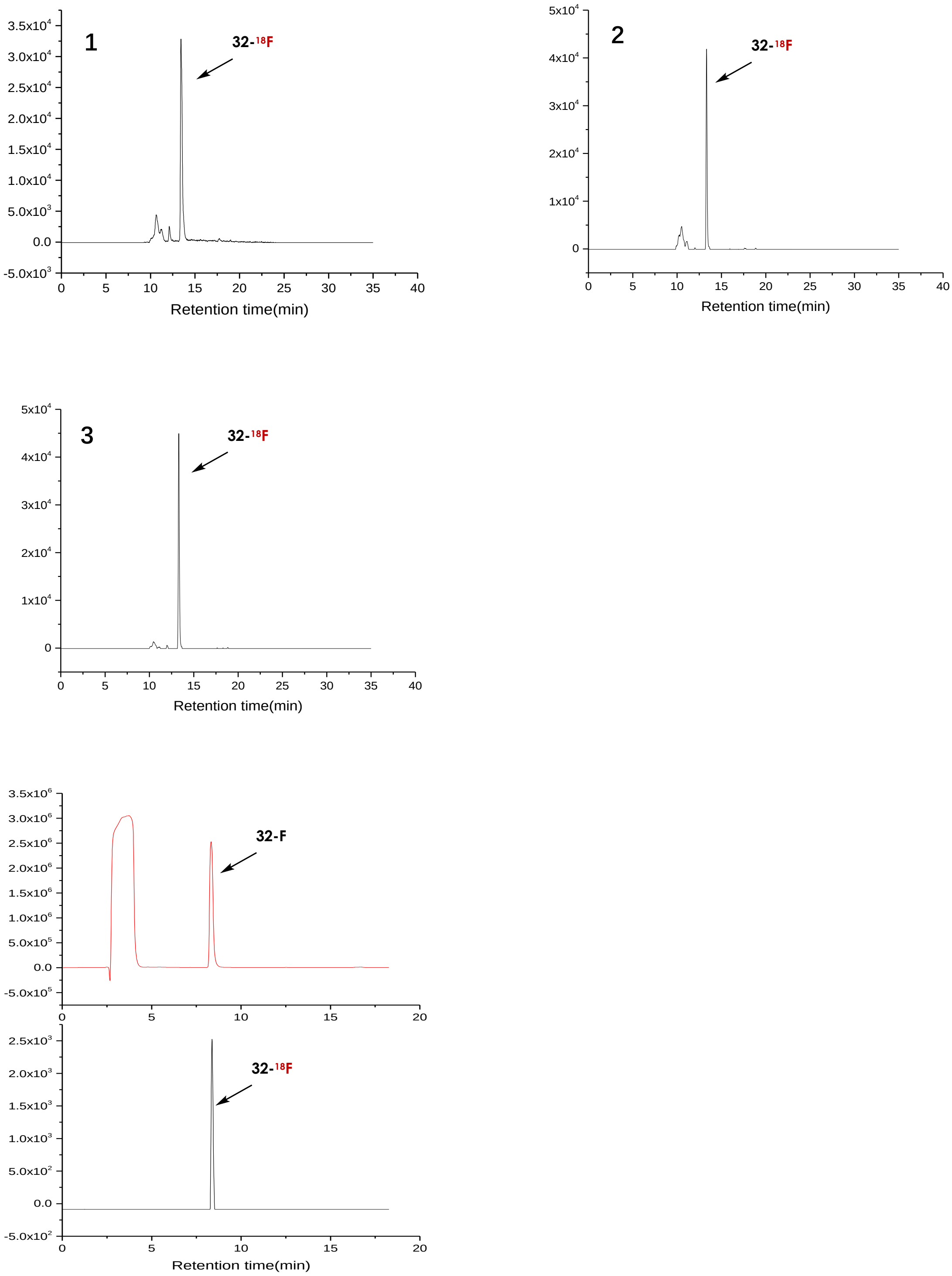


Supplementary Figure 63. Radio-HPLC traces and purification of **31-^{18}F**

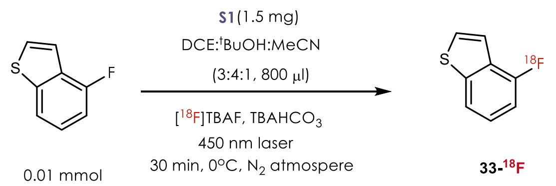


Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1		9.54 mCi	528 µCi	189 µCi	17 min	210.4 µCi	39.9%
2	**32**	7.95 mCi	448 µCi	133 µCi	16 min	147.1 µCi	32.8%
3		6.39 mCi	366 µCi	149 µCi	16 min	164.8 µCi	45.0%
Average RCC: **39.2%±5.0%** (n=3)							

Supplementary Table 33. HPLC-isolated RCCs of **32-^{18}F**

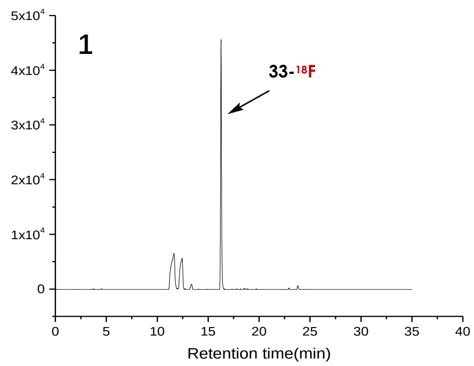


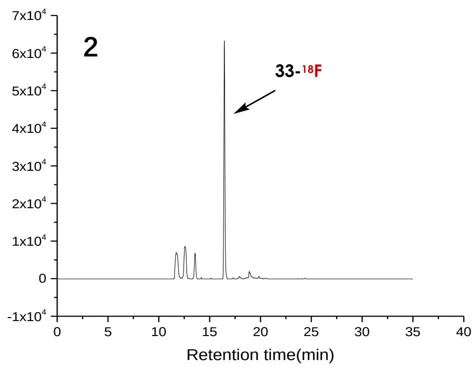
Supplementary Figure 64. Crude radio-HPLC traces and purification of **32-^{18}F**

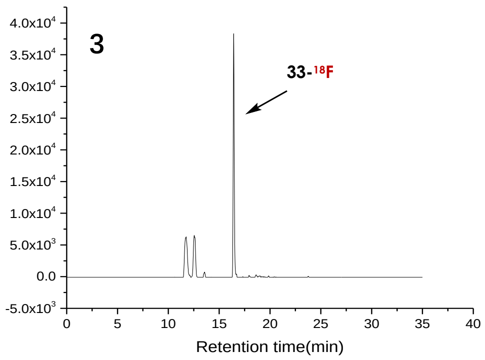


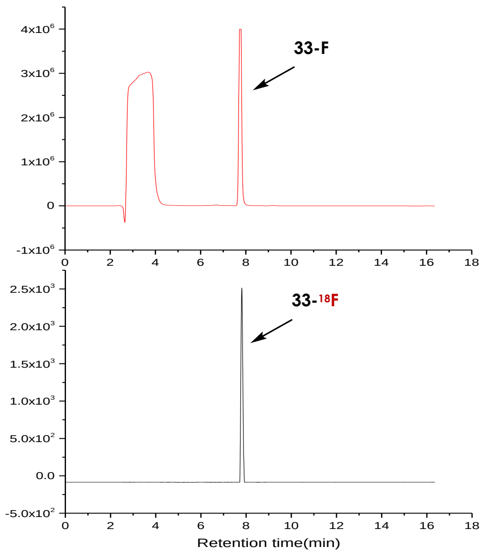
Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**33**	10.94 mCi	421 μCi	108 μCi	19 min	121.8 μCi	28.9%
2		14.56 mCi	638 μCi	171 μCi	19 min	192.8 μCi	30.2%
3		8.05 mCi	364 μCi	110 μCi	19 min	124.0 μCi	34.1%
Average RCC: **31.1%±2.2%** (n=3)							

Supplementary Table 34. HPLC-isolated RCCs of **33-^{18}F**

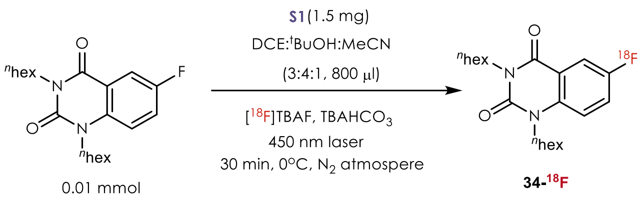






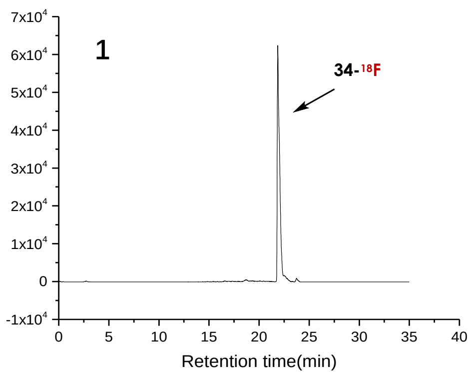


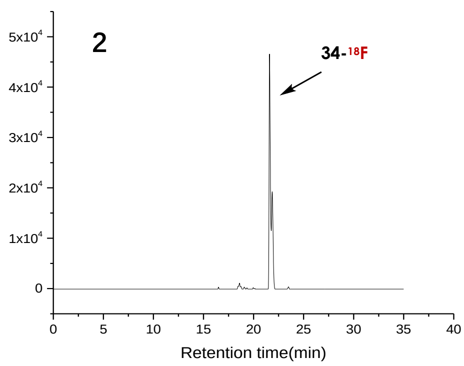
Supplementary Figure 65. Crude radio-HPLC traces and purification of **33-18F**

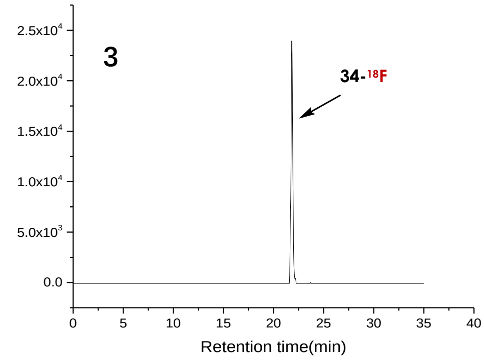


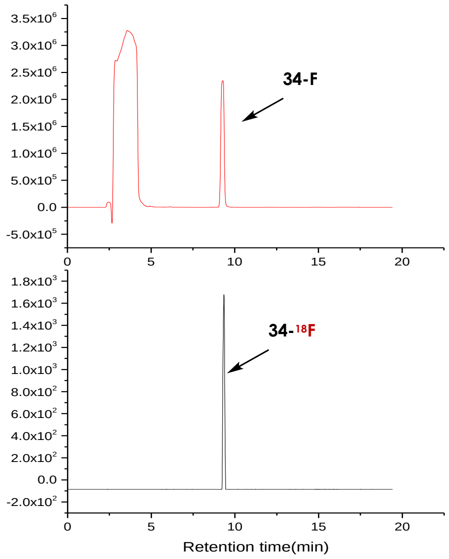
Reaction	Substrate	Activity ([18F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1		15.81 mCi	903 µCi	369 µCi	25 min	432.1 µCi	47.9%
2	**34**	11.04 mCi	493 µCi	255 µCi	24 min	296.7 µCi	60.2%
3		9.16 mCi	317 µCi	129 µCi	24 min	150.1 µCi	47.4%
Average RCC: **51.8%±5.9%** (n=3)							

Supplementary Table 35. HPLC-isolated RCCs of **34-18F**

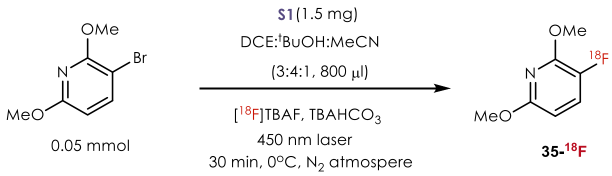






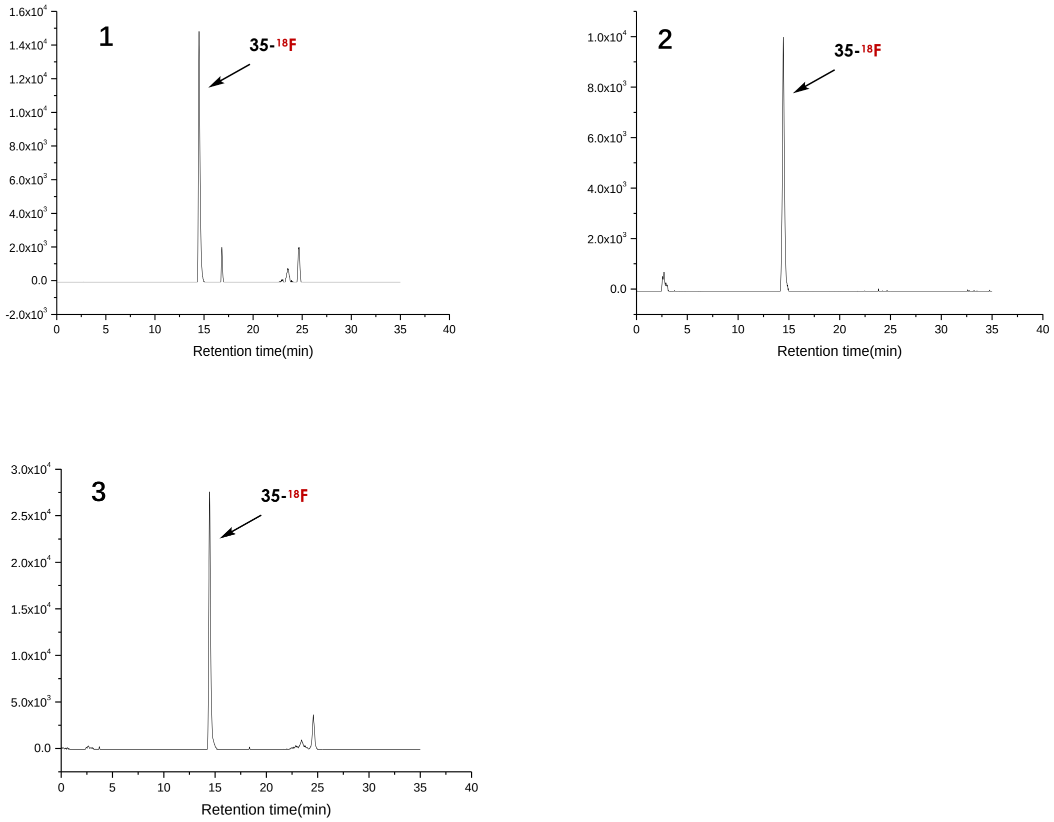


Supplementary Figure 66. Crude radio-HPLC traces and purification of **34-18F**

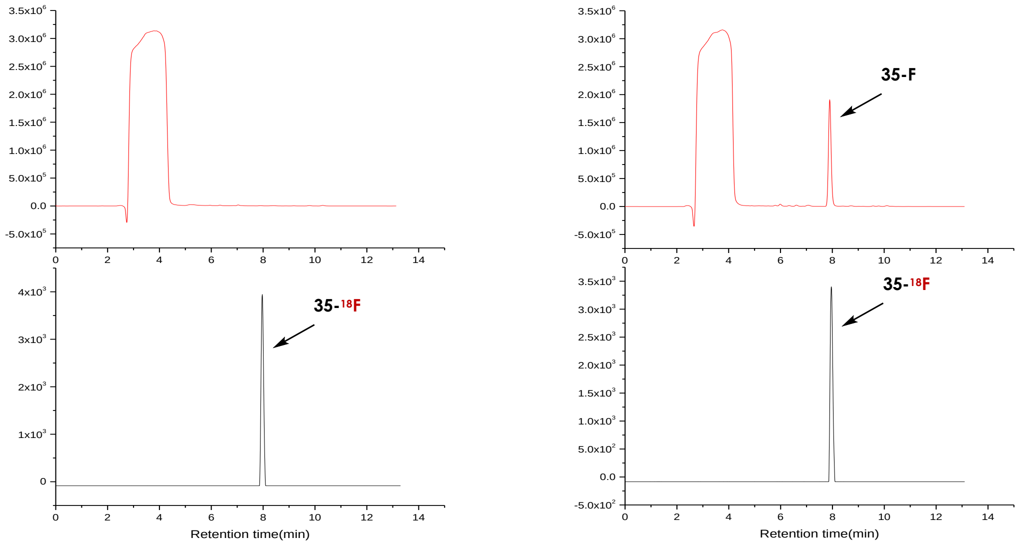


Reaction	Substrate	Activity ([18F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	35	10.08 mCi	463 µCi	72 µCi	17 min	80.2 µCi	17.3%
2		9.22 mCi	465 µCi	68 µCi	17 min	75.7 µCi	16.3%
3		11.48 mCi	636 µCi	147 µCi	17 min	163.7 µCi	25.7%
Average RCC: **19.8±4.2%** (n=3)							

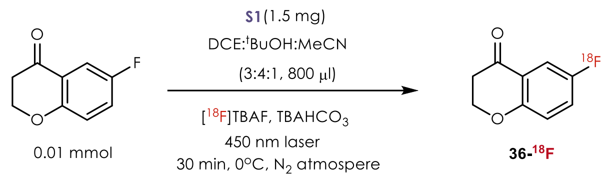
Supplementary Table 36. HPLC-isolated RCCs of **35-18F**



Supplementary Figure 67. Crude radio-HPLC traces from **35** to **35-^{18}F**



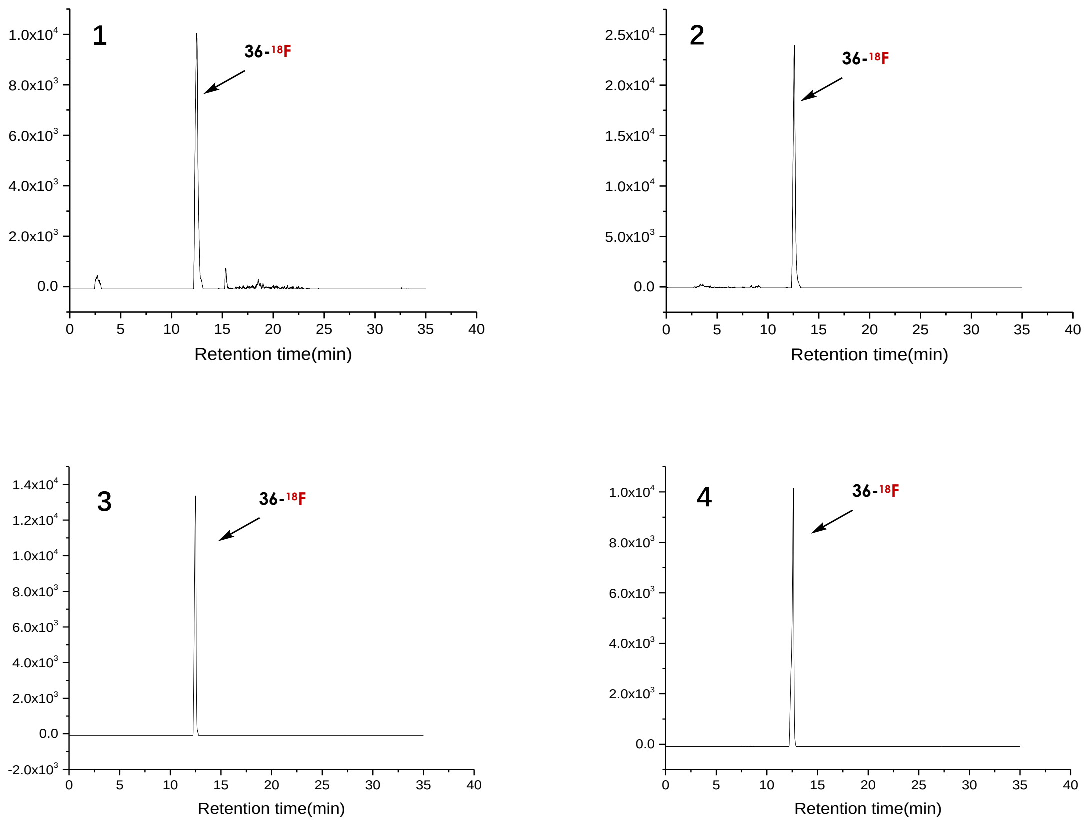
Supplementary Figure 68. Purification (left) and co-injection for **35-^{18}F**



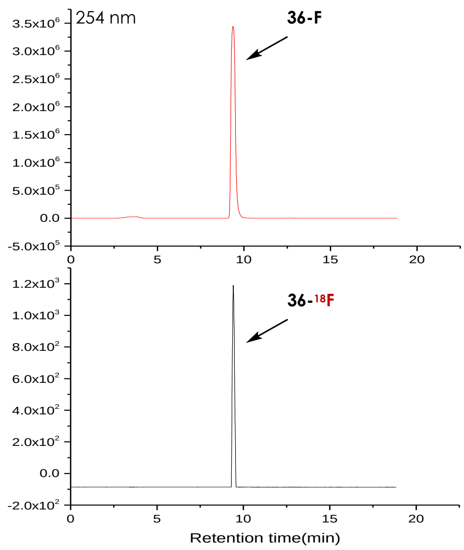
Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**36**	17.33 mCi	821 μCi	86 μCi	15 min	94.5 μCi	**11.5%**
2[a]		13.30 mCi	600 μCi	150 μCi	16 min	165.9 μCi	27.7%
3[a]		8.74 mCi	352 μCi	72 μCi	15 min	79.2 μCi	22.5%
4[a]		3.36 mCi	218 μCi	65 μCi	15 min	71.5 μCi	32.8%
Average RCC from 0.05mmol substrate: **27.7±4.2%** (n=3)							

[a]0.05 mmol substrate.

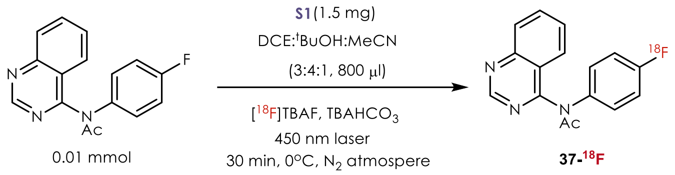
Supplementary Table 37. HPLC-isolated RCCs of **36-^{18}F**



Supplementary Figure 69. Crude radio-HPLC traces from **36** to **36-^{18}F**

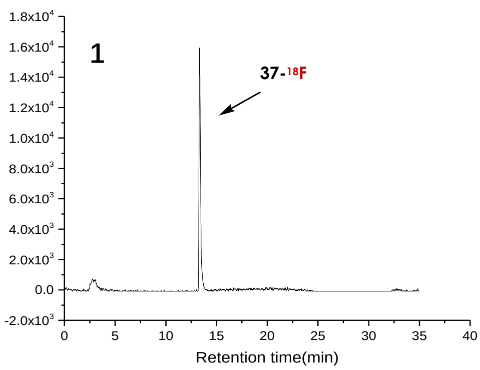


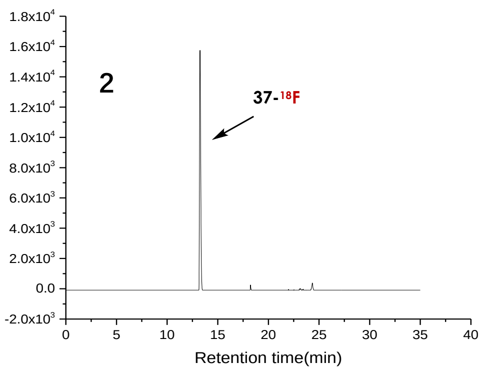
Supplementary Figure 70. Purification of **36-18F**

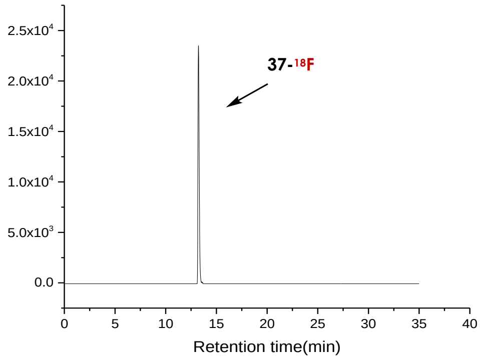


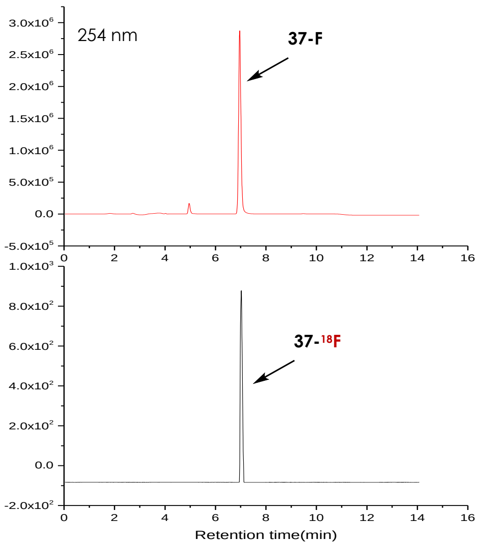
Reaction	Substrate	Activity ([18F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**37**	20.0 mCi	584 μCi	76 μCi	16 min	84.1 μCi	14.4%
2		12.36 mCi	508 μCi	61 μCi	16 min	67.5 μCi	13.3 %
3		8.18 mCi	437 μCi	87 μCi	16 min	96.2 μCi	22.0%
Average RCC: **16.6±3.9%** (n=3)							

Supplementary Table 38. HPLC-isolated RCC of **37-18F**

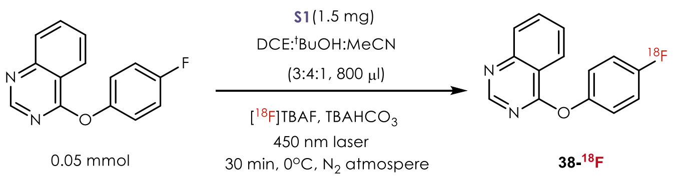








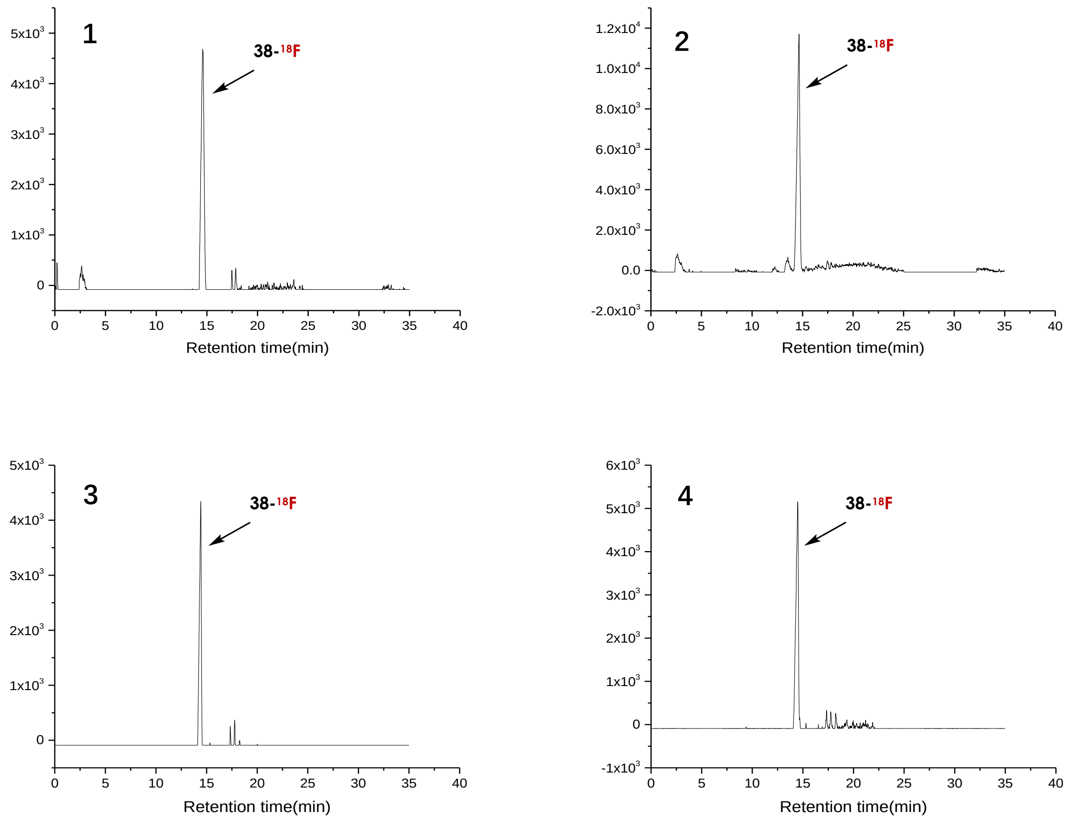
Supplementary Figure 71. Crude radio-HPLC traces and purification of **37-18F**



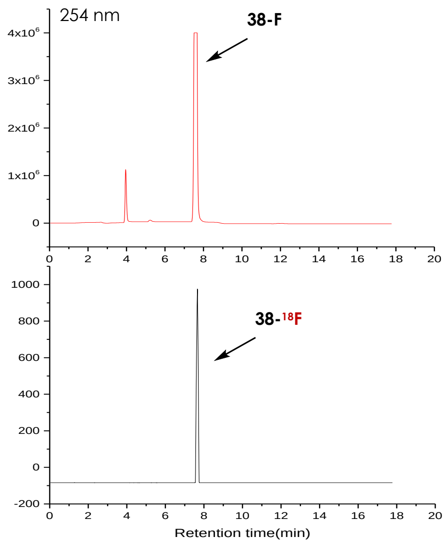
Reaction	Substrate	Activity ([18F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**38**	16.32 mCi	848 μCi	46 μCi	18 min	51.5 μCi	6.1%
2[a]		12.65 mCi	833 μCi	103 μCi	18 min	115.4 μCi	13.9%
3[a]		10.01 mCi	350 μCi	33 μCi	17 min	36.7 μCi	10.5%
4[a]		8.35 mCi	427 μCi	47 μCi	16 min	52.0 μCi	12.2%
Average RCC: **12.2±1.4%** (n=3)							

[a]reaction was performed under air.

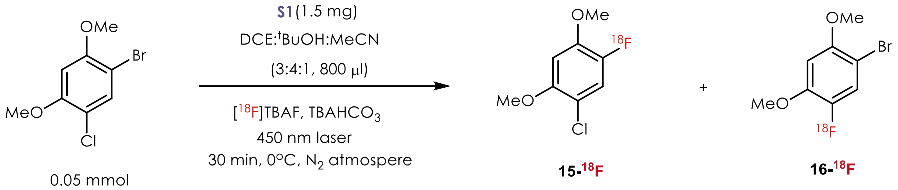
Supplementary Table 39. HPLC-isolated RCCs of **38-¹⁸F**



Supplementary Figure 72. Crude radio-HPLC traces from **38** to **38-¹⁸F**

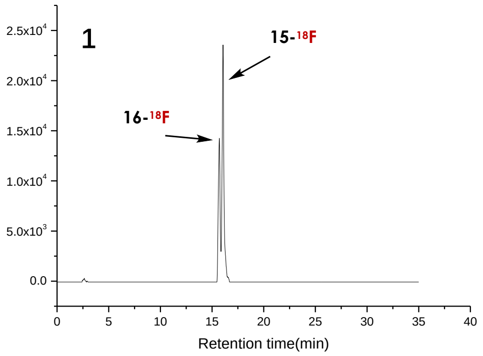


Supplementary Figure 73. Purification for **38-¹⁸F**

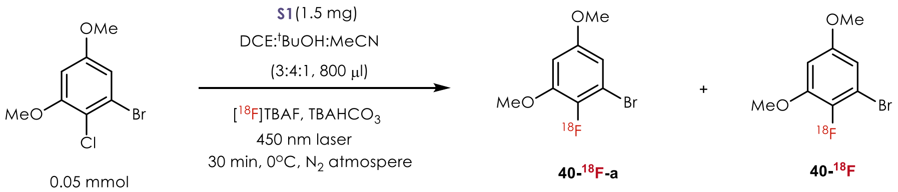


Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	39	12.93 mCi	456 μCi	121 μCi	19 min	136.4 μCi	**29.9%** (**16-^{18}F**)
				85 μCi	20 min	96.4 μCi	**21.1%** (**15-^{18}F**)

Supplementary Table 40. HPLC-isolated RCCs of **16-^{18}F** and **15-^{18}F**

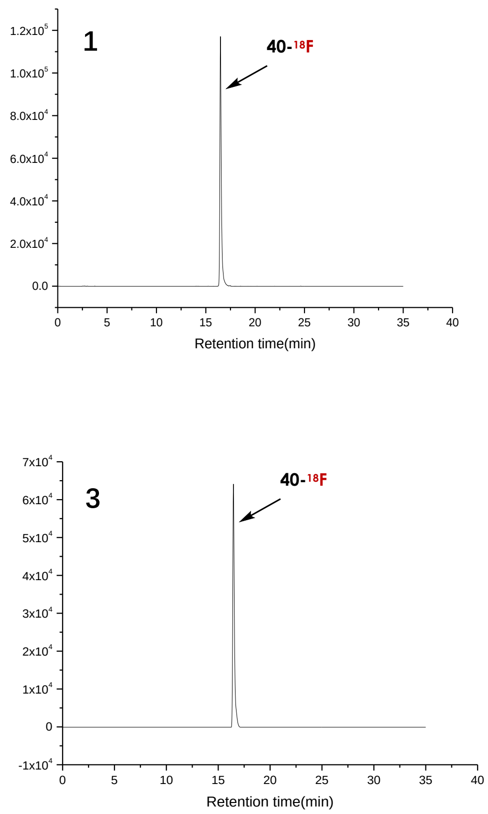


Supplementary Figure 74. Crude radio-HPLC trace from **40** to **16-^{18}F** and **15-^{18}F**

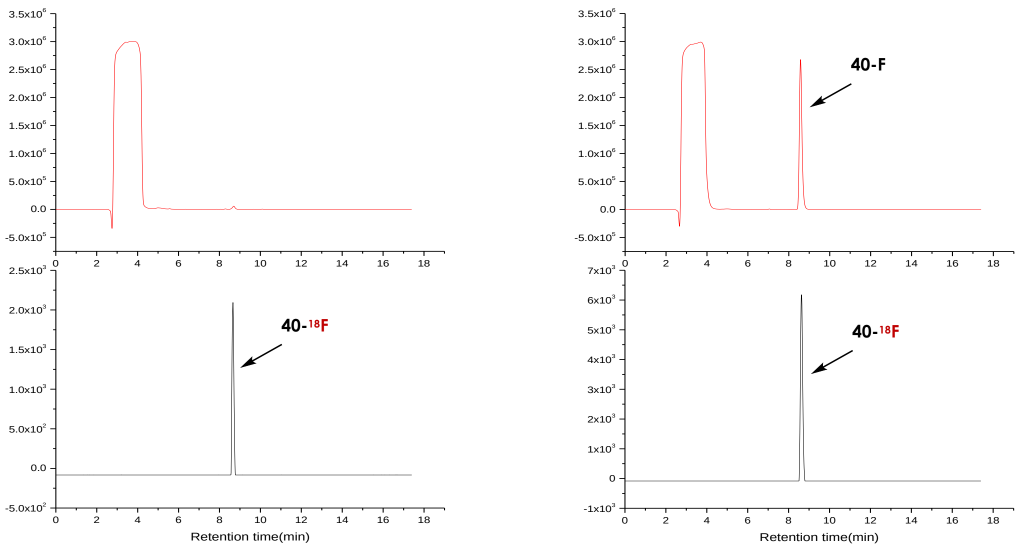


Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	40	9.10 mCi	650 μCi	408 μCi	20 min	462.9 μCi	71.2%
2		12.68 mCi	581 μCi	403 μCi	19 min	454.4 μCi	78.2%
3		9.06 mCi	408 μCi	263 μCi	19 min	296.5 μCi	72.7%
Average RCC: **74.0±3.0%** (n=3)							

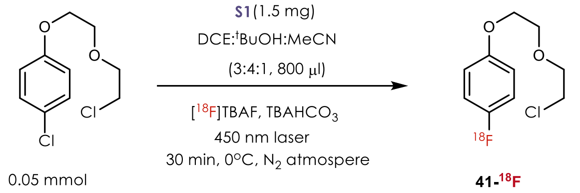
Supplementary Table 41. HPLC-isolated RCCs of **40-^{18}F-a**



Supplementary Figure 75. Crude radio-HPLC traces from **40** to **40-**^{18}**F**

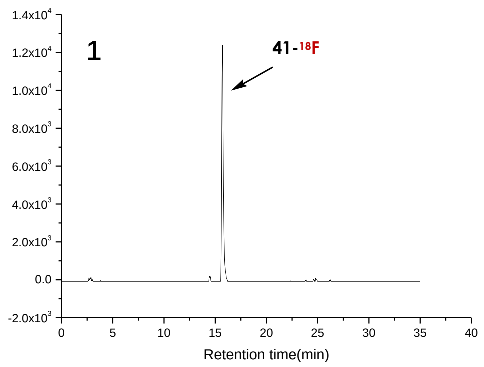


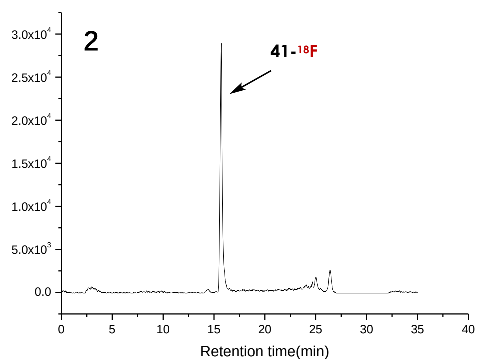
Supplementary Figure 76. Purification (left) and co-injection(right) for **40-**^{18}**F**

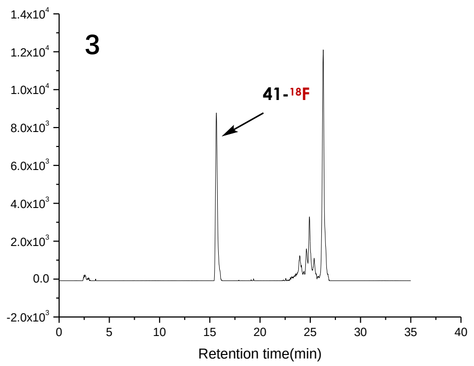


Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1		10.20 mCi	480 μCi	62 μCi	18 min	69.5 μCi	14.5%
2	**41**	9.32 mCi	1332 μCi	188 μCi	20 min	213.3 μCi	16%
3		10.11 mCi	481 μCi	57 μCi	18 min	63.9 μCi	13.3%
Average RCC: **14.6±1.1%** (n=3)							

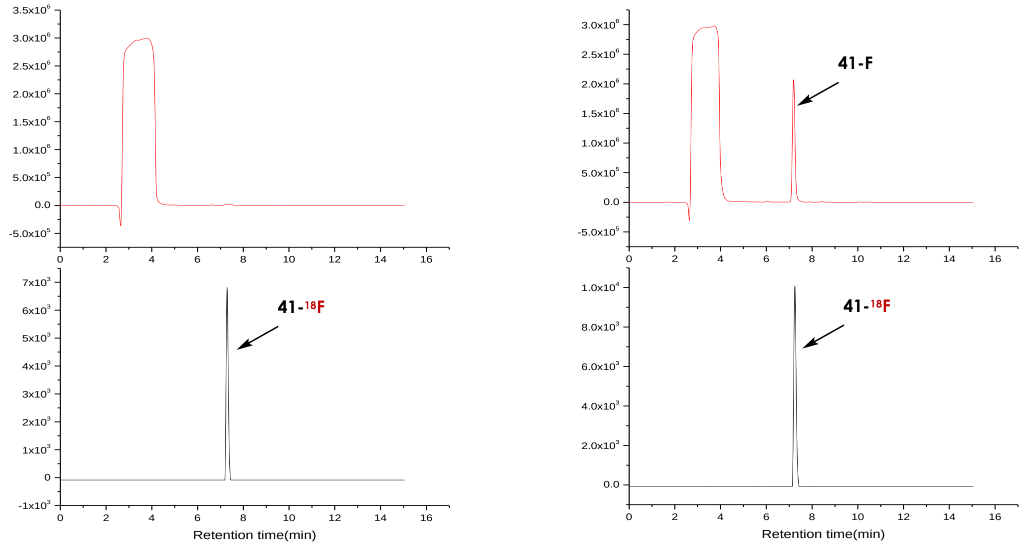
Supplementary Table 42. HPLC-isolated RCCs of **41-^{18}F**



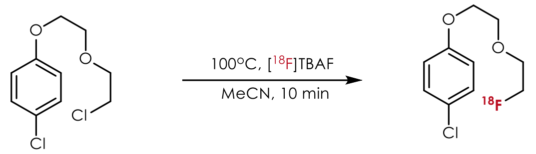




Supplementary Figure 77. Crude radio-HPLC traces from **41** to **41-^{18}F**



Supplementary Figure 78. Purification (left) and co-injection for **41-^{18}F**



41-^{18}F-a

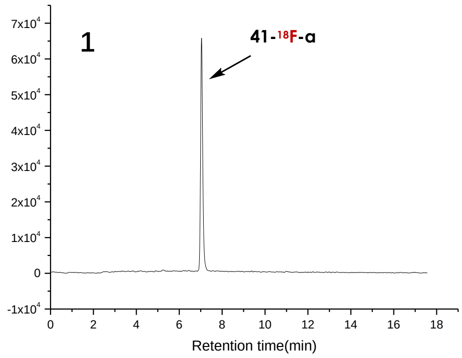
The MeCN solution (~200 µl) of compound **41** (11.7 mg, 0.05 mmol) and [^{18}F][TBAF] (21 mCi) were added to a 5 mL v-vial which was sealed with a Teflon-lined septum screw cap. The vial was heated in a heating block under 100°C for 10 min. The reaction was then diluted with MeCN and analyzed on HPLC. The data were summarized below.

HPLC condition:

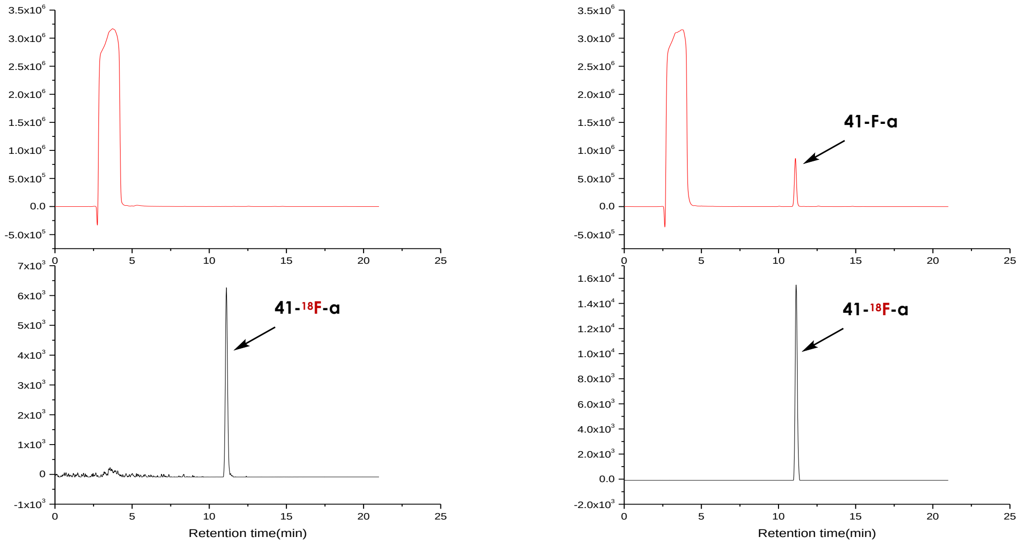
Column: Phenomenex, Kinetex® 5 µm F5 100 Å, 250 x 4.6 mm LC Column. Solvent A: 0.1%TFA water; Solvent B: 0.1%TFA acetonitrile; Isocratic elution at **55%** solvent B. Flow rate: 1 mL/min.

Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	41	21 mCi	417 µCi	149 µCi	10 min	158.7 µCi	38.1%

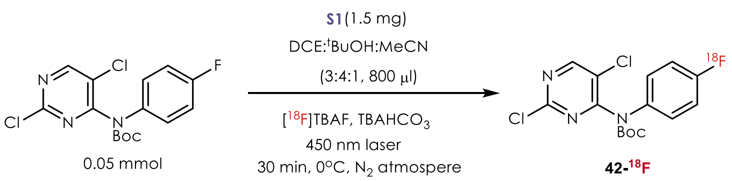
Supplementary Table 43. HPLC-isolated RCC of **41-^{18}F-a**



Supplementary Figure 79. Crude radio-HPLC traces from **41** to **41-^{18}F-a**

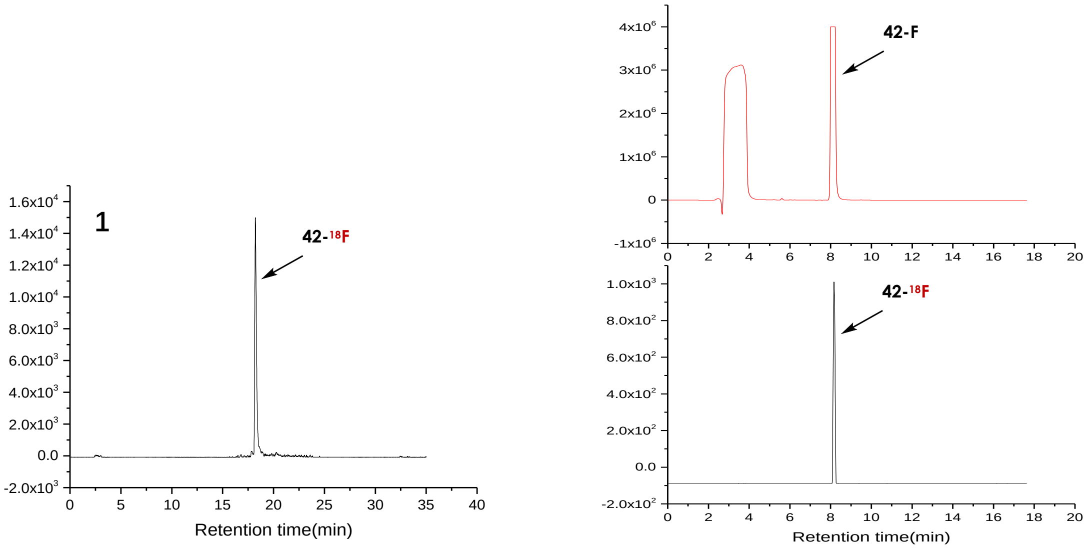


Supplementary Figure 80. Purification (left) and co-injection(right) for **41-^{18}F-a**

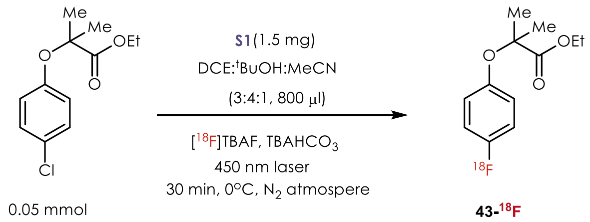


Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**42**	15.98 mCi	777 μCi	83 μCi	22 min	95.4 μCi	12.3%

Supplementary Table 44. HPLC-isolated RCC of **42-^{18}F**

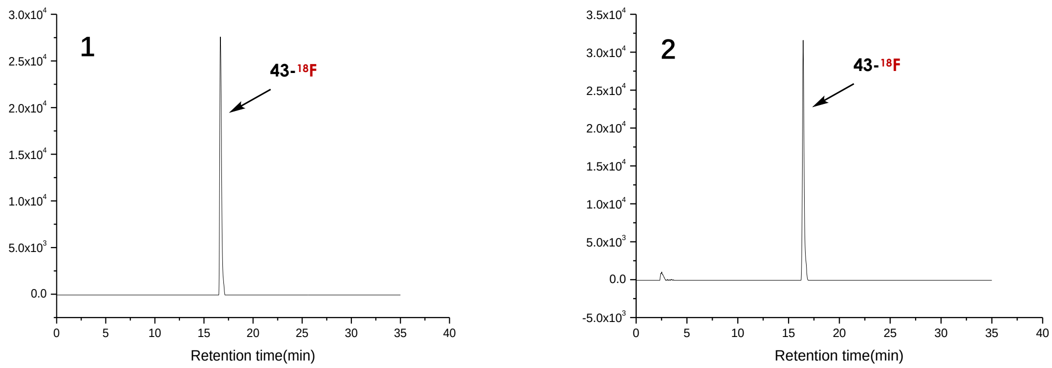


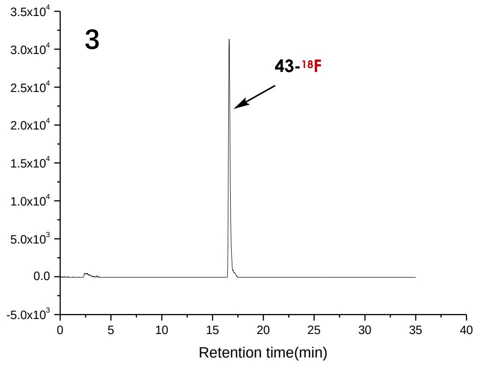
Supplementary Figure 81. Crude radio-HPLC trace(left) and purification (right)of **42-18F**



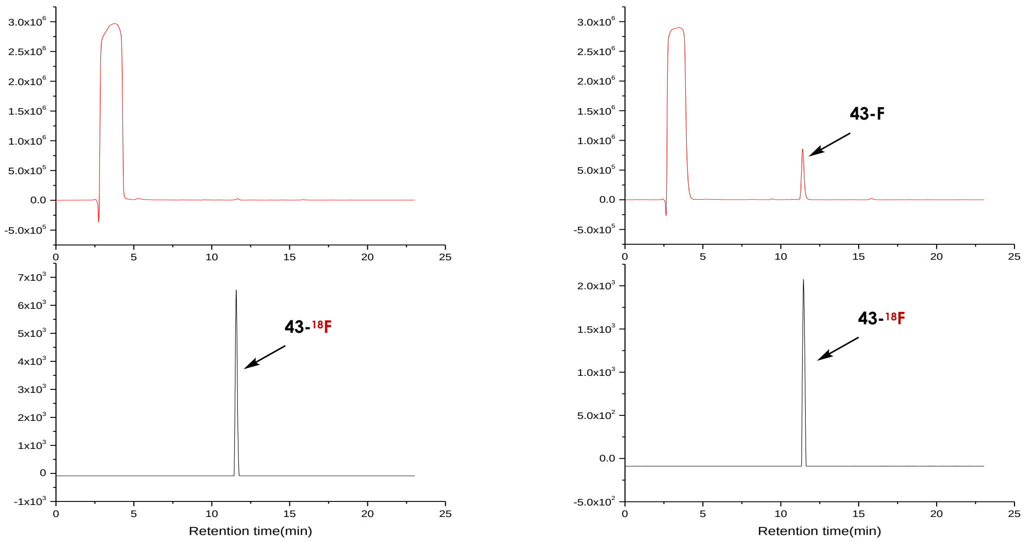
Reaction	Substrate	Activity ([18F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**43**	12.48 mCi	396 μCi	150 μCi	20 min	170.2 μCi	43%
2		12.12 mCi	488 μCi	158 μCi	20 min	179.3 μCi	36.7%
3		8.81 mCi	478 μCi	164 μCi	20 min	186.1μCi	38.9%
Average RCC: **39.5±2.6%** (n=3)							

Supplementary Table 45. HPLC-isolated RCCs of **43-18F**

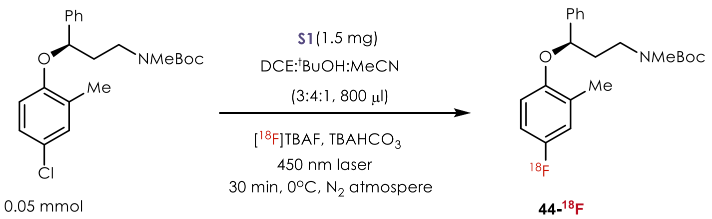




Supplementary Figure 82. Crude radio-HPLC traces from **43** to **43-^{18}F**

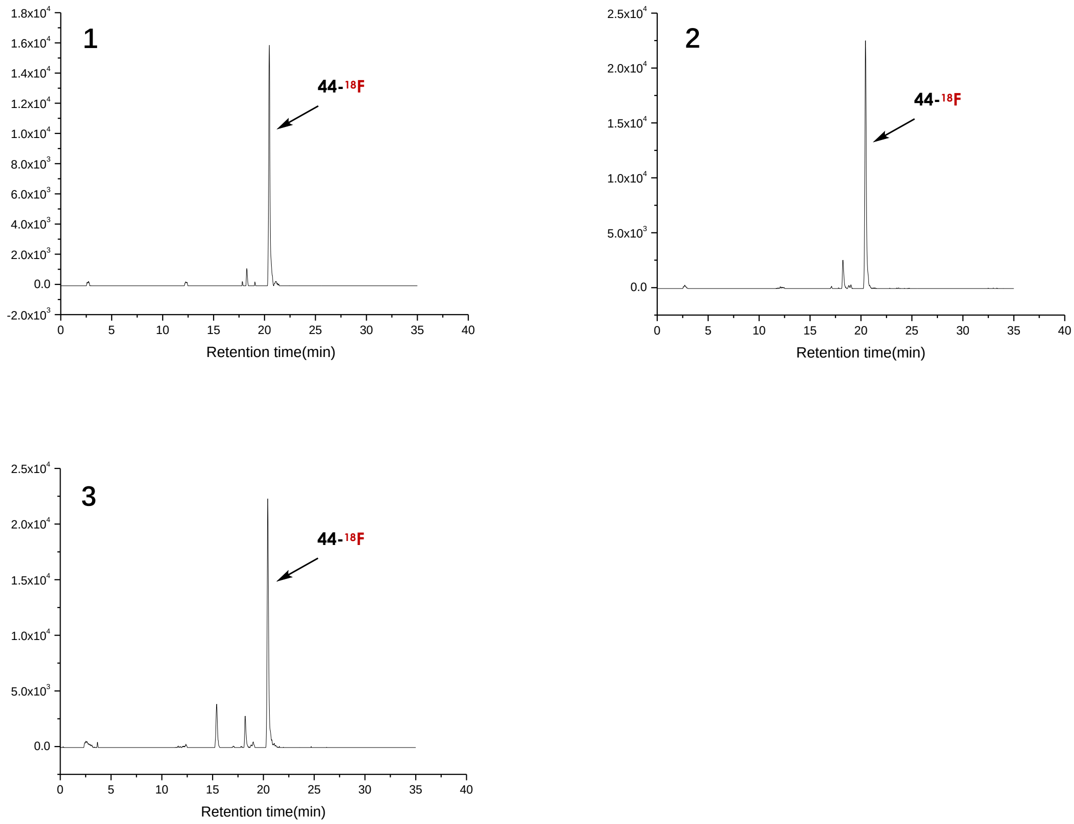


Supplementary Figure 83. Purification (left) and co-injection(right) for **43-^{18}F**

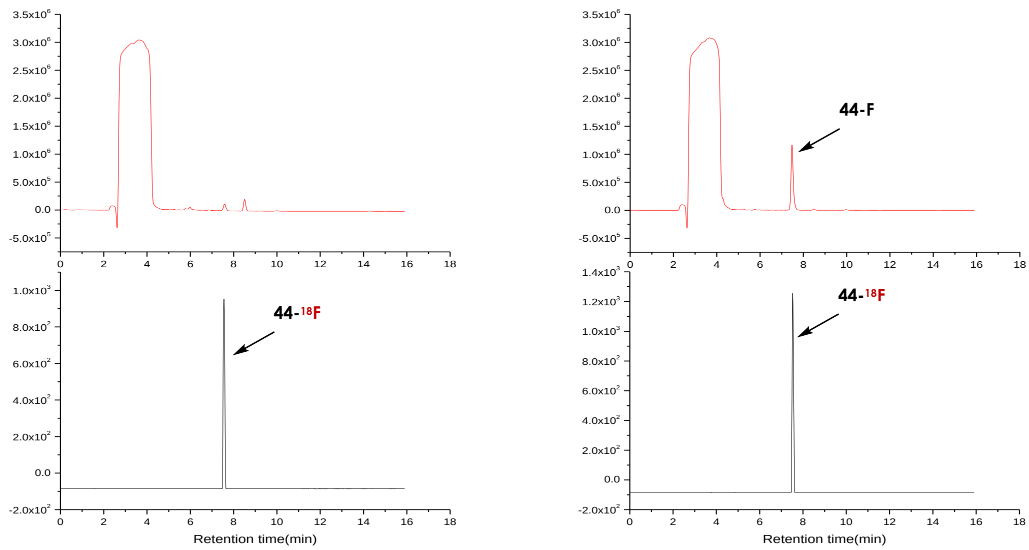


Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**44**	15.46 mCi	419 µCi	68 µCi	26 min	80.1 µCi	19.1%
2		10.42 mCi	781 µCi	99 µCi	23 min	114.5 µCi	14.7%
3		13.22 mCi	604 µCi	102 µCi	23 min	117.9 µCi	19.5%
Average RCC: **17.8±2.2%** (n=3)							

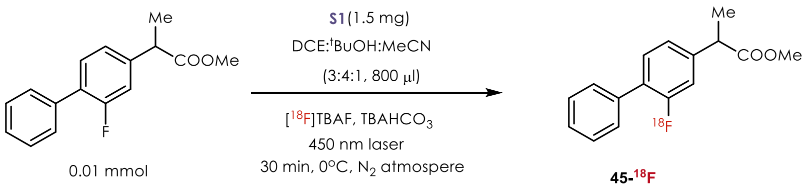
Supplementary Table 46. HPLC-isolated RCCs of **44-^{18}F**



Supplementary Figure 84. Crude radio-HPLC traces from **44** to **44-^{18}F**

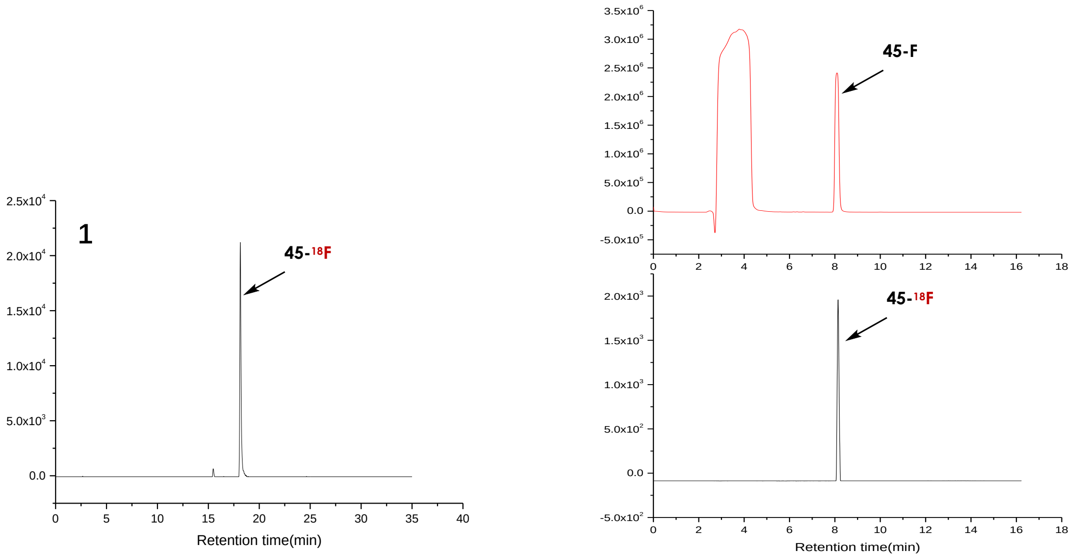


Supplementary Figure 85. Purification (left) and co-injection(right) for **44-^{18}F**

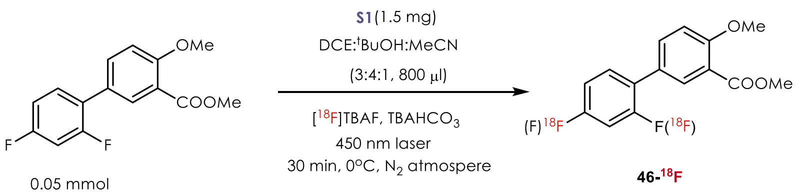


Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**45**	11.36 mCi	545 μCi	79 μCi	20 min	89.6 μCi	**16.4%**

Supplementary Table 47. HPLC-isolated RCC of **45-^{18}F**

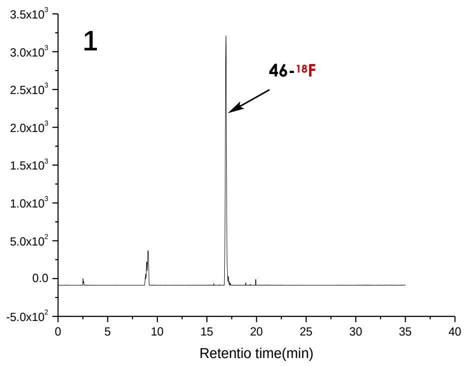


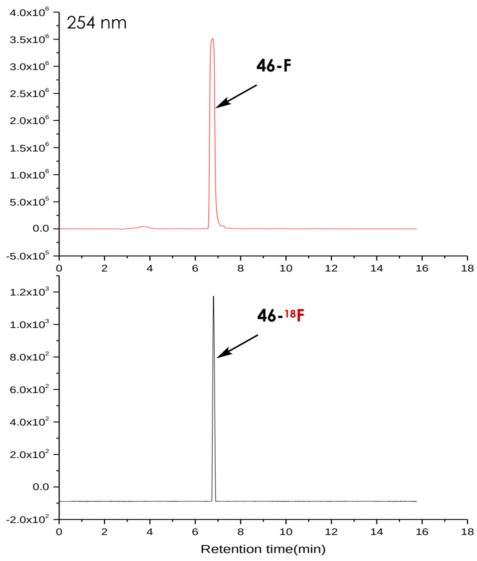
Supplementary Figure 86. Crude radio-HPLC trace(left) and Purification (right)of **45-^{18}F**



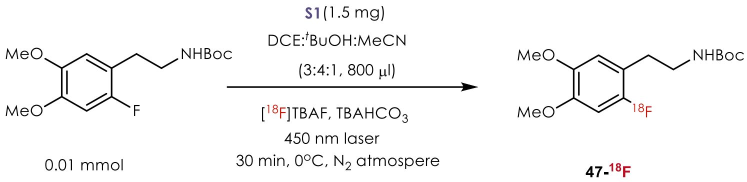
Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**47**	11.48 mCi	665 μCi	59 μCi	20 min	66.9 μCi	**10.1%**

Supplementary Table 48. HPLC-isolated RCC of **46-^{18}F**





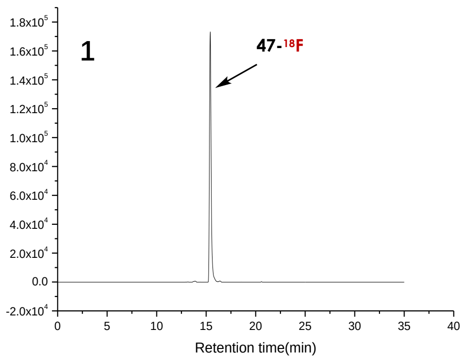
Supplementary Figure 87. Crude radio-HPLC trace(left) and purification (right)of **46-18F**

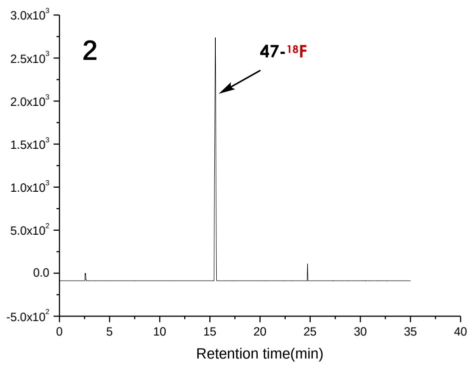


Reaction	Substrate	Activity ([18F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**47-F** (X=F)	14.46 mCi	984 μCi	632 μCi	18 min	708.1 μCi	**72%**
2[a]	**47-Cl** (X=Cl)	9.93 mCi	317 μCi	11 μCi	18 min	12.3 μCi	**3.9%**

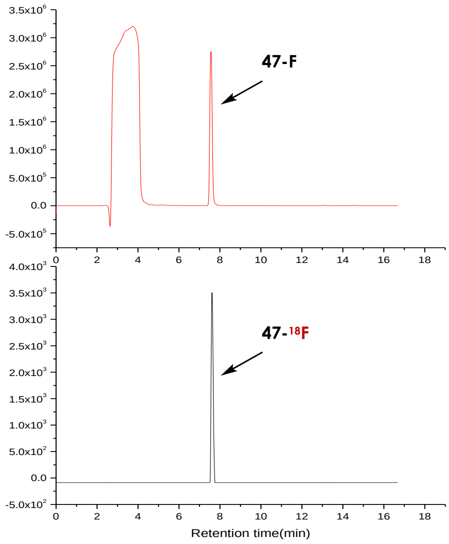
a0.05 mmol substrate were used.

Supplementary Table 49. HPLC-isolated RCCs of **47-18F**

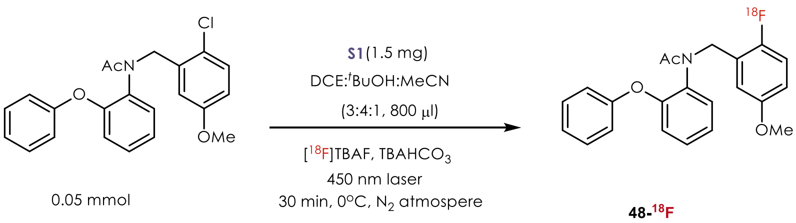




Supplementary Figure 88. Crude radio-HPLC traces from **48-F** and **48-Cl** to **47-18F**

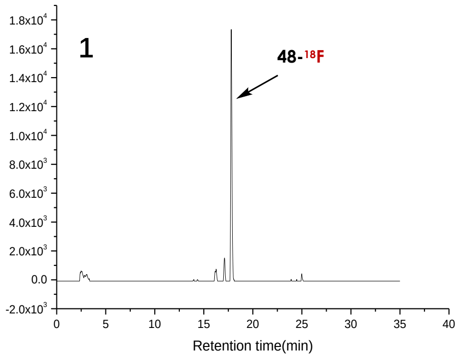


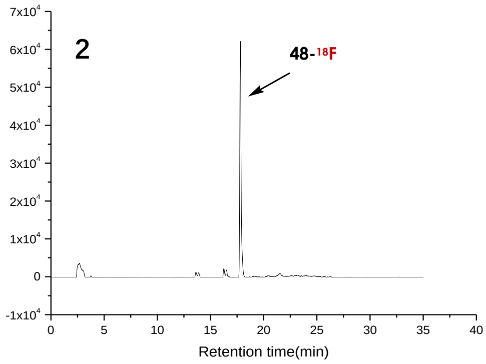
Supplementary Figure 89. Purification of **47-18F**

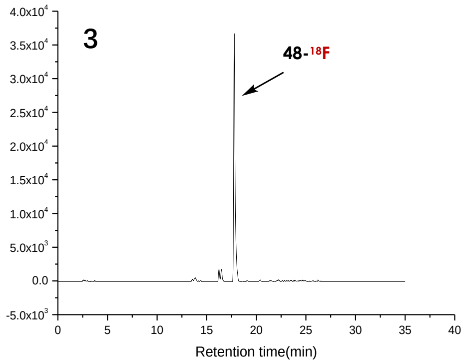


Reaction	Substrate	Activity ([18F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1		19.6 mCi	483 μCi	62 μCi	20 min	70.3 μCi	14.6%
2	**48**	47.7 mCi	1306 μCi	203 μCi	21 min	231.8 μCi	17.7%
3		48.4 mCi	662 μCi	145 μCi	20 min	164.5 μCi	24.9%
Average RCC: **19.1±4.3%** (n=3)							

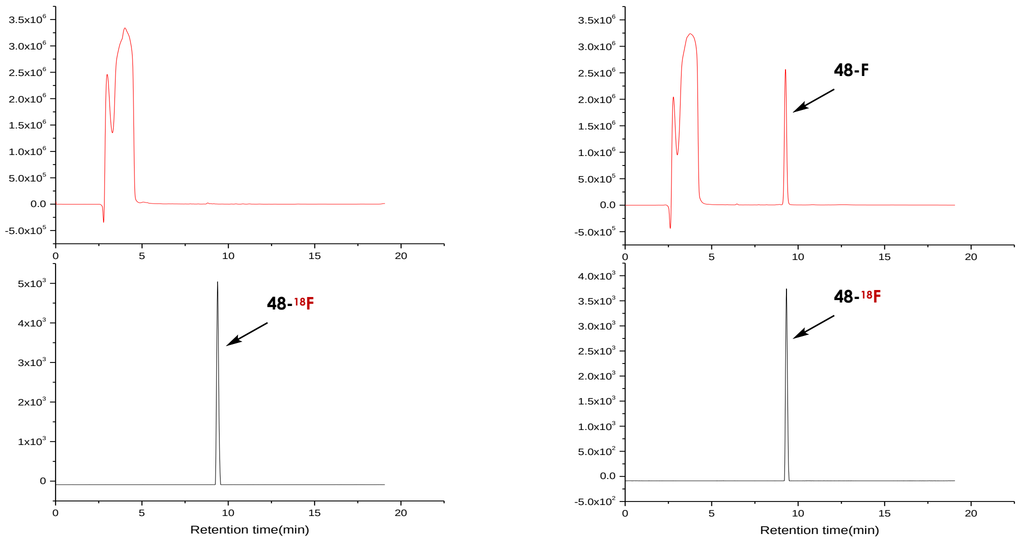
Supplementary Table 50. HPLC-isolated RCCs of **48-18F**



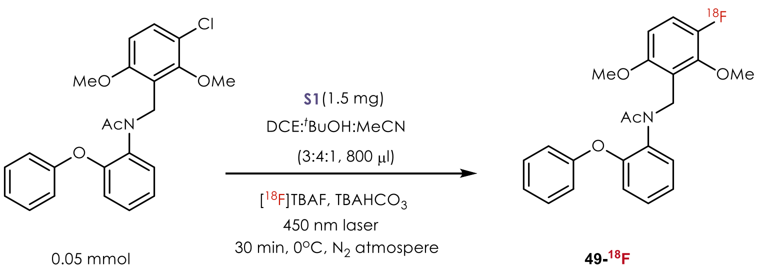




Supplementary Figure 90. Crude radio-HPLC traces from **48** to **48-^{18}F**

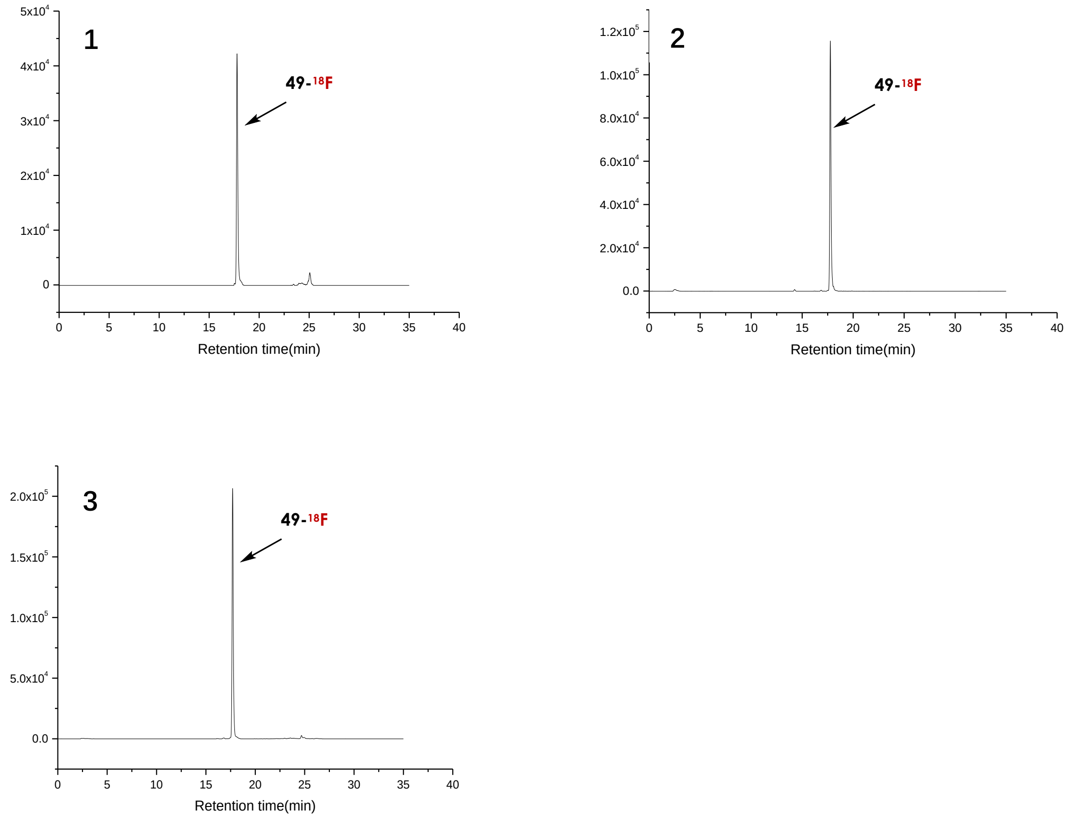


Supplementary Figure 91. Purification (left) and co-injection(right) for **48-^{18}F**

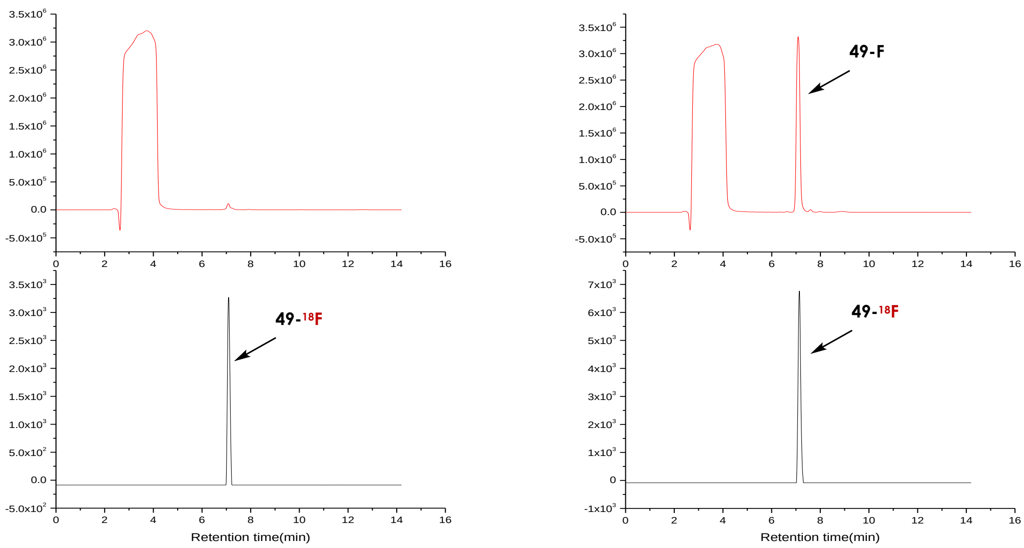


Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1		9.89 mCi	452 μCi	165 μCi	21 min	188.4 μCi	41.7%
2	49	10.63 mCi	979 μCi	318 μCi	21 min	363.1 μCi	37.1%
3		11.90 mCi	1161 μCi	542 μCi	20 min	615 μCi	53%
Average RCY (decay-corrected):**43.9±6.6%** (n=3)							

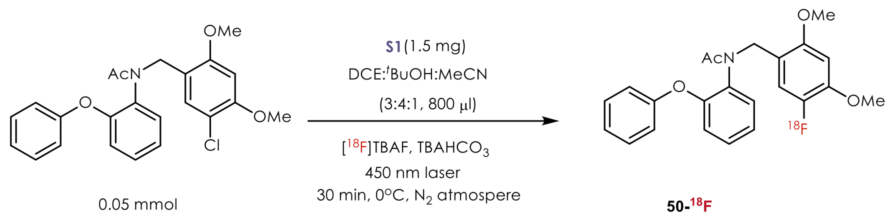
Supplementary Table 51. HPLC-isolated RCYs of **49-^{18}F**



Supplementary Figure 92. Crude radio-HPLC traces from **49** to **49-^{18}F**

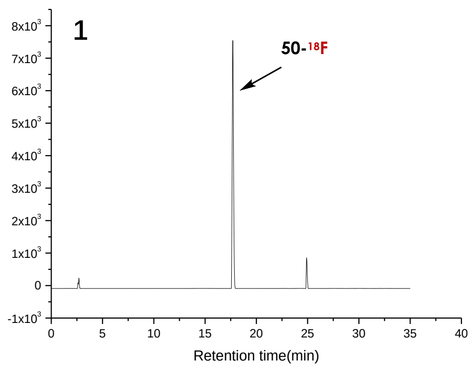


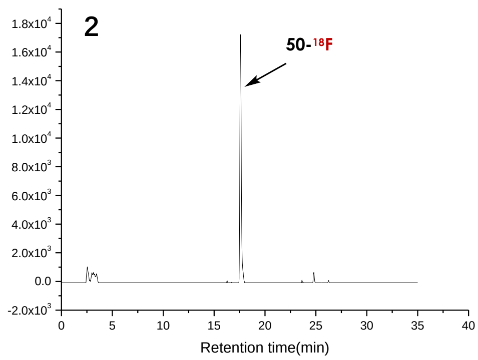
Supplementary Figure 93. Purification (left) and co-injection(right) for **49-^{18}F**

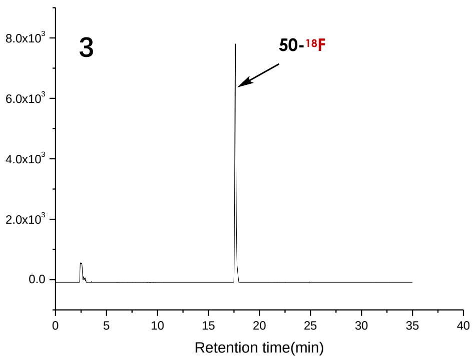


Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	50	15.59 mCi	409 μCi	33 μCi	21 min	37.7 μCi	9.2%
2		11.67 mCi	617 μCi	75 μCi	21 min	85.6 μCi	13.9%
3		10.46 mCi	465 μCi	35 μCi	21 min	40 μCi	8.6%
Average RCC: **10.6±2.4%** (n=3)							

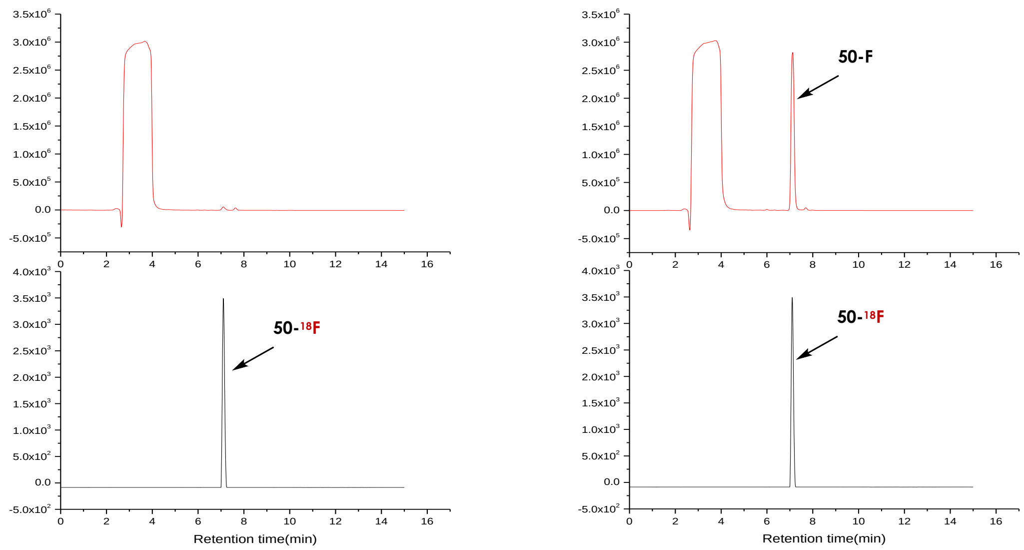
Supplementary Table 52. HPLC-isolated RCCs of **50-^{18}F**



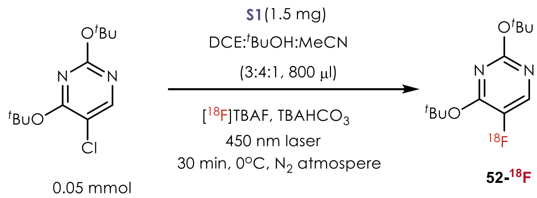




Supplementary Figure 94. Crude radio-HPLC traces from **50** to **50-^{18}F**

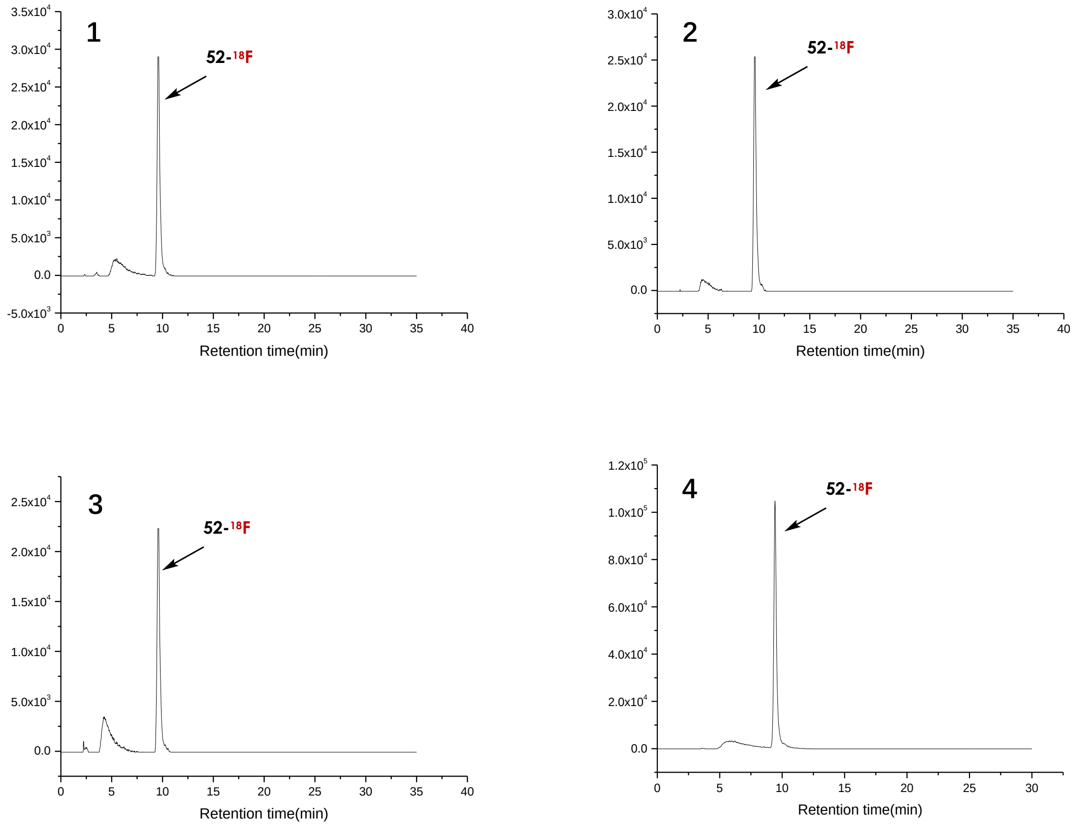


Supplementary Figure 95. Purification (left) and co-injection (right) for **50-18F**

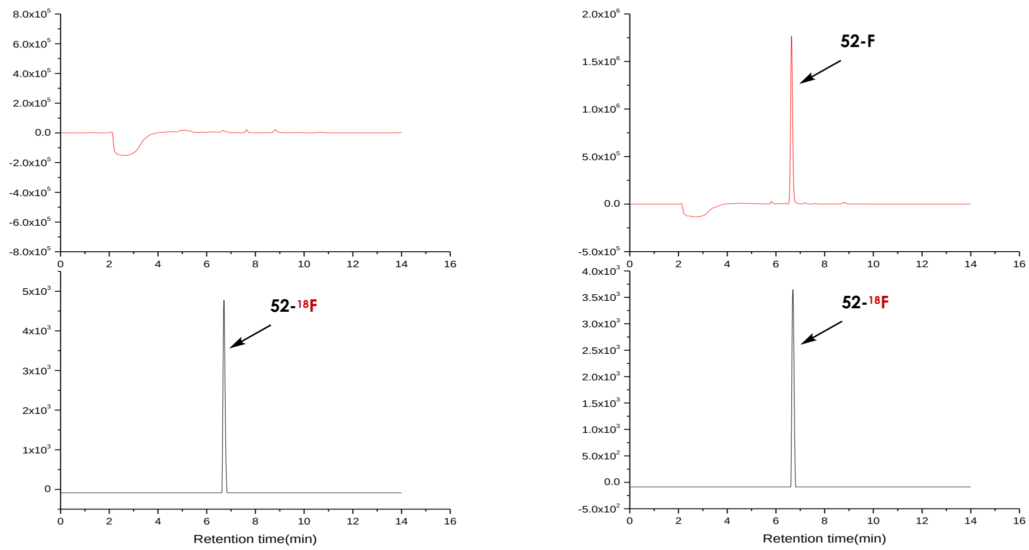


Reaction	Substrate	Activity ([18F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**51**	17.95 mCi	455 μCi	235 μCi	13 min	255.1 μCi	56.1%
2		6.09 mCi	337 μCi	203 μCi	12 min	219 μCi	65%
3		5.7 mCi	425 μCi	198 μCi	13 min	214.9 μCi	50.6%
4		26.4 mCi	1082 μCi	558 μCi	14 min	609.6 μCi	56.3%
Average RCC: **57.0±5.2%** (n=4)							

Supplementary Table 53. HPLC-isolated RCCs of **52-18F**

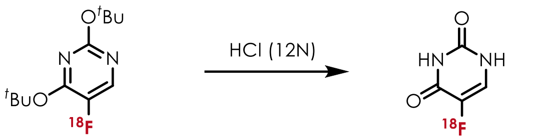


Supplementary Figure 96. Crude radio-HPLC traces from **52** to **52-^{18}F**



Supplementary Figure 97. Purification (left) and co-injection(right) for **52-^{18}F**

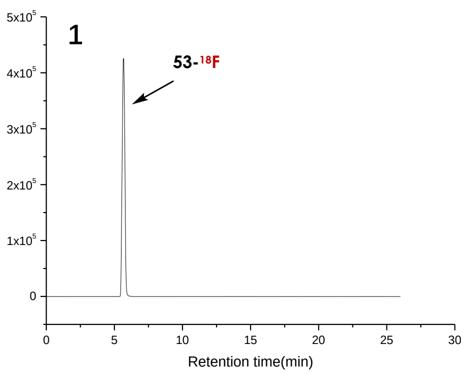
Deprotection of 52-^{18}F to 53-^{18}F ([^{18}F]fluoroursail)



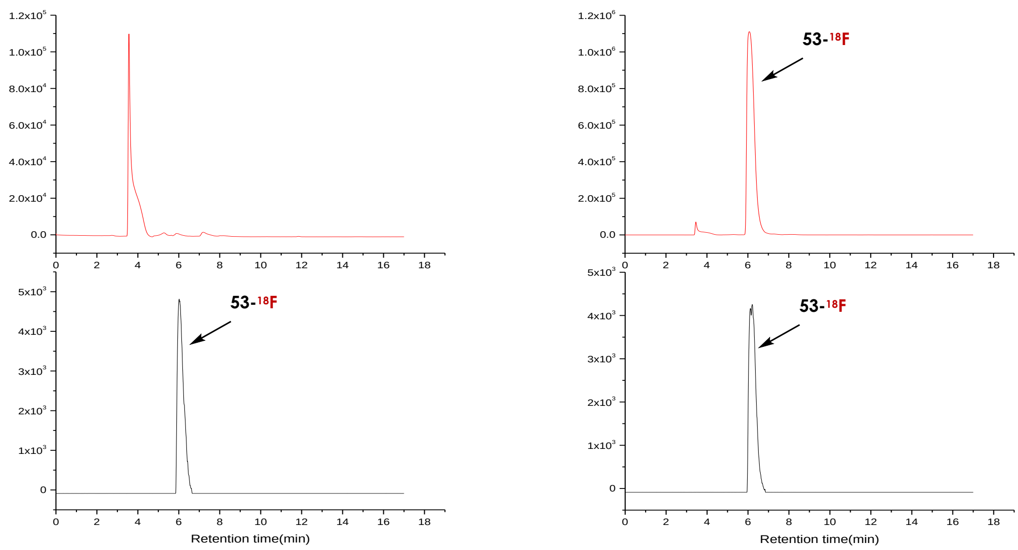
Follow our reported procedure[15], the [18F]fluorouracil(**53-18F)** was obtained in 95.8% RCC from deprotection of **52-18F**.

Reaction	Substrate	Activity ([18F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**52-18F**	1.6 mCi	1225 μCi	1102 μCi	10 min	1173.8 μCi	**95.8%**

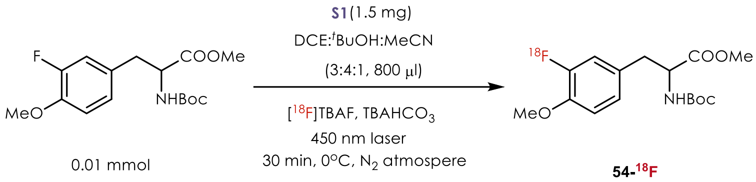
Supplementary Table 54. HPLC-isolated RCC of **53-18F**



Supplementary Figure 98. Crude radio-HPLC traces from **52-18F** to **53-18F**



Supplementary Figure 99. Purification (left) and co-injection(right) for **53-18F**

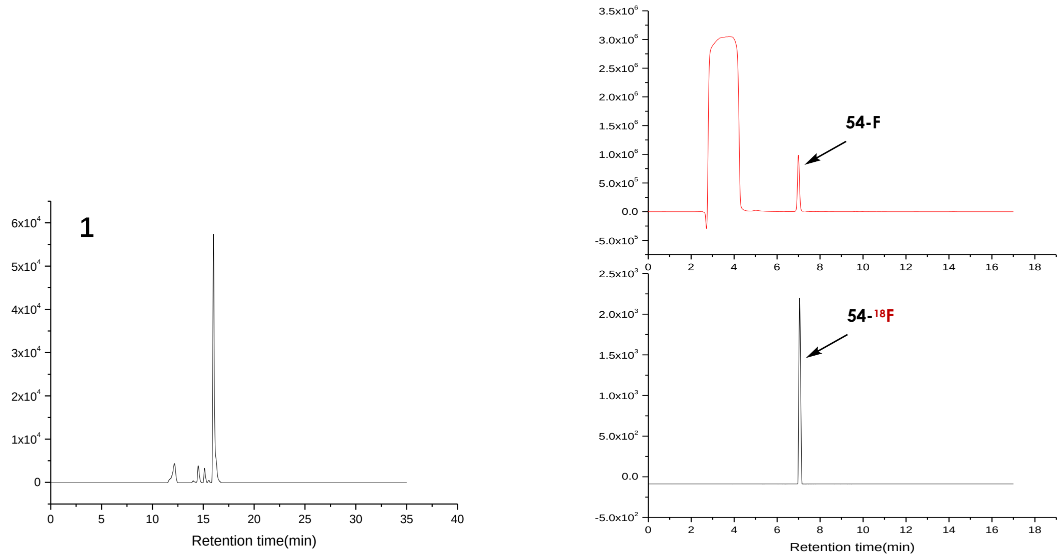


0.01 mmol

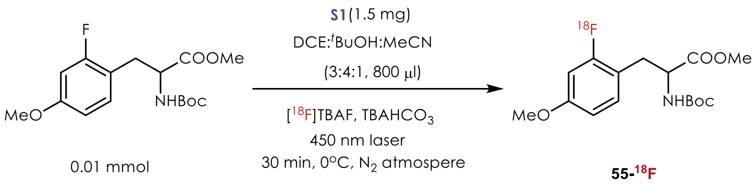
54-^{18}F

Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**54**	13.59 mCi	593 μCi	206 μCi	19 min	232.3 μCi	**39.2%**

Supplementary Table 55. HPLC-isolated RCC of **54-^{18}F**



Supplementary Figure 100. Crude radio-HPLC trace(left) and purification (right)of **54-^{18}F**

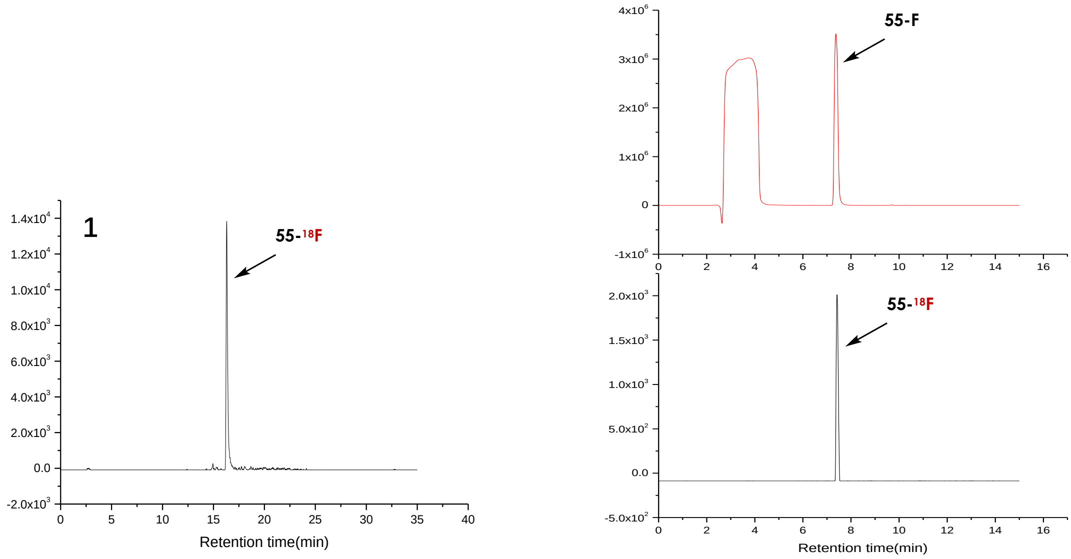


0.01 mmol

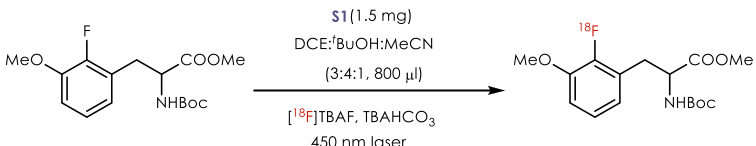
55-^{18}F

Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**55**	9.83 mCi	696 μCi	78 μCi	20 min	88.5 μCi	**12.7%**

Supplementary Table 56. HPLC-isolated RCC of **55-^{18}F**



Supplementary Figure 101. Crude radio-HPLC trace(left) and purification (right)of **57-18F**

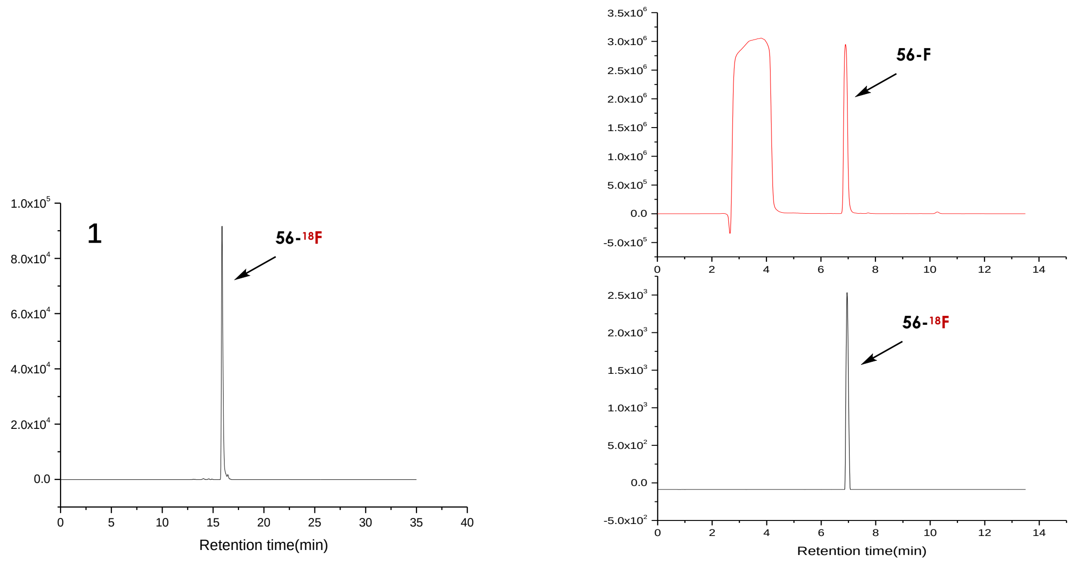


0.01 mmol

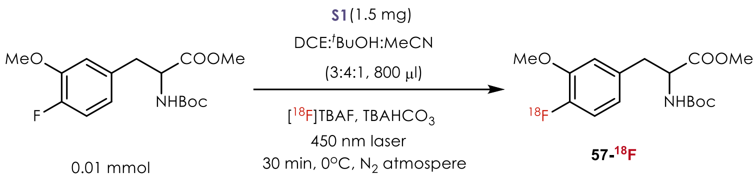
56-18F

Reaction	Substrate	Activity ([18F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**56**	5.57 mCi	512 µCi	356 µCi	19 min	401.4 µCi	**78.4%**

Supplementary Table 57. HPLC-isolated RCCof **56-18F**

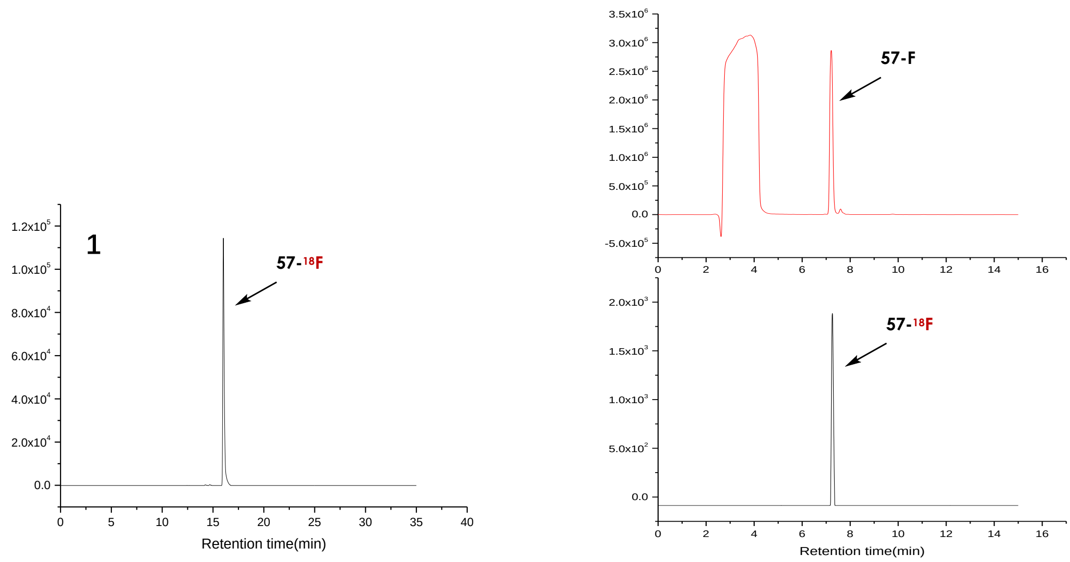


Supplementary Figure 102. Crude radio-HPLC trace(left) and purification (right)of **56-18F**

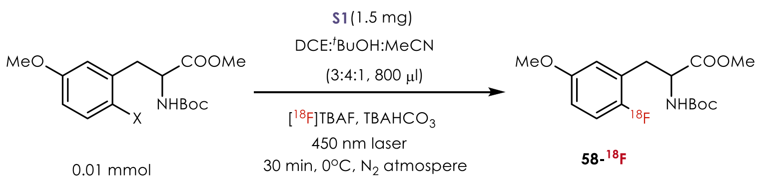


Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**57**	12.08 mCi	560 μCi	376 μCi	18 min	421.3 μCi	**75.2%**

Supplementary Table 58. HPLC-isolated RCC of **57-^{18}F**



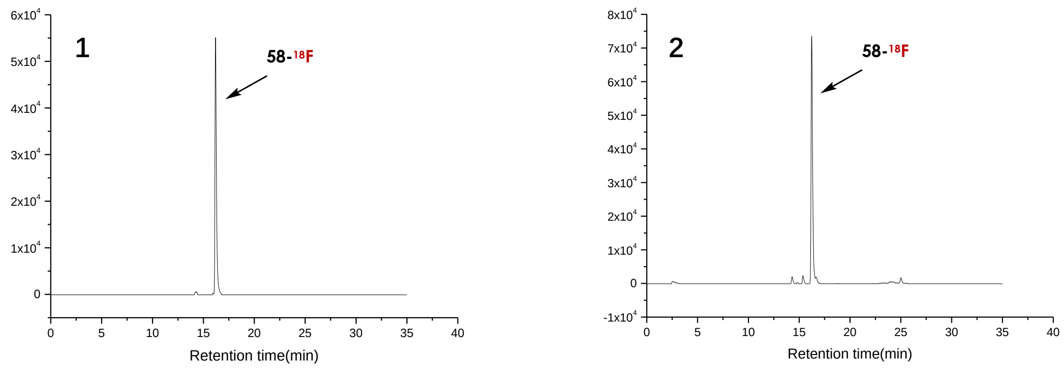
Supplementary Figure 103. Crude radio-HPLC trace(left) and purification (right)of **57-^{18}F**



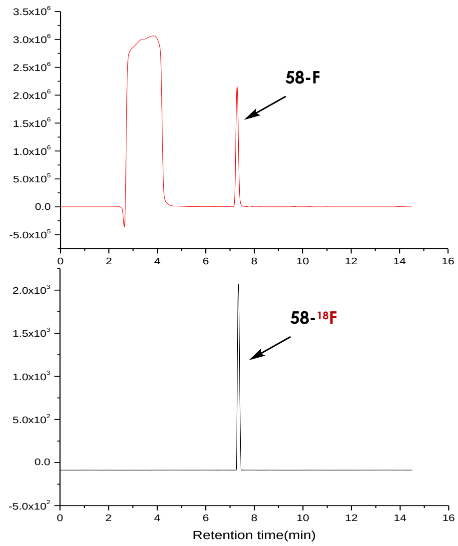
Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**58-F** (X=F)	11.95 mCi	998 μCi	675 μCi	20 min	765.9 μCi	**76.7%**
2	**58-Cl** (X=Cl)[a]	9.54 mCi	890 μCi	290 μCi	19 min	327 μCi	**36.7%**

[a]0.05 mmol substrate.

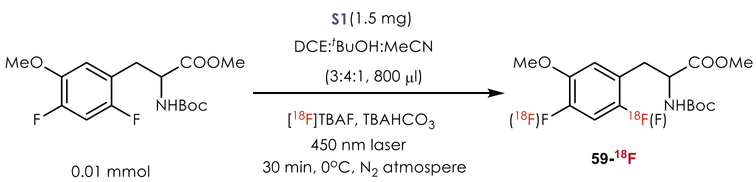
Supplementary Table 59. HPLC-isolated RCCs of **58-^{18}F**



Supplementary Figure 104. Crude radio-HPLC traces from **58-F** and **58-Cl** to **58-^{18}F**

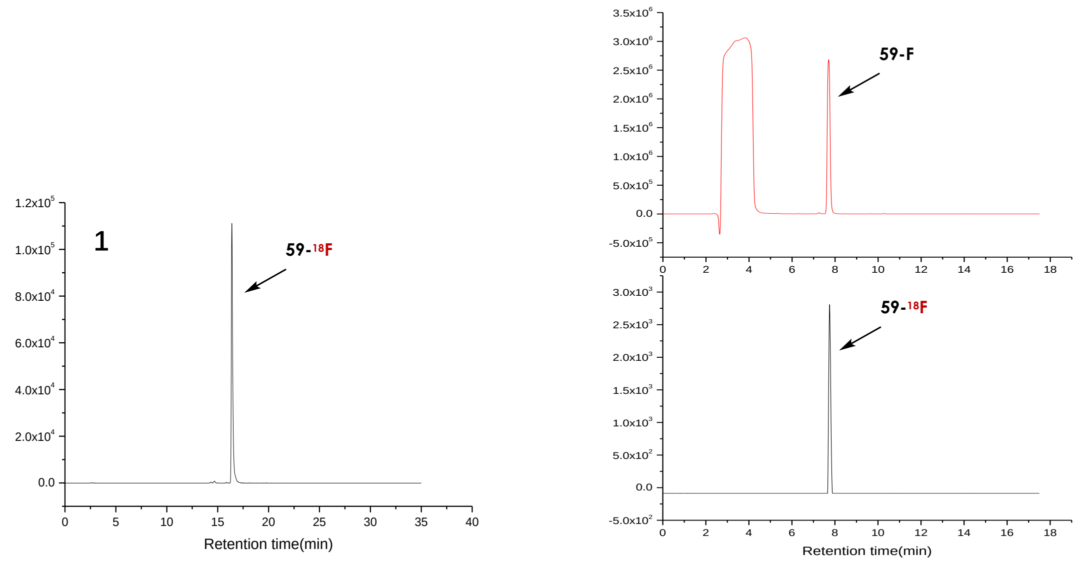


Supplementary Figure 105. HPLC traces of purification of **58-^{18}F** from reaction **1.**

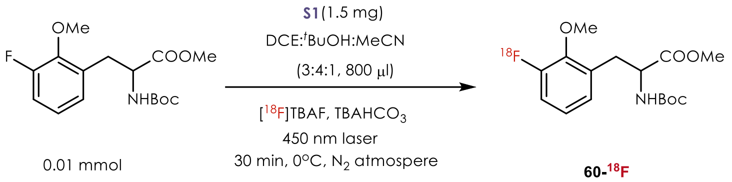


Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**59**	5.95 mCi	495 µCi	367 µCi	20 min	416.4 µCi	**84.1%**

Supplementary Table 60. HPLC-isolated RCC of **59-^{18}F**

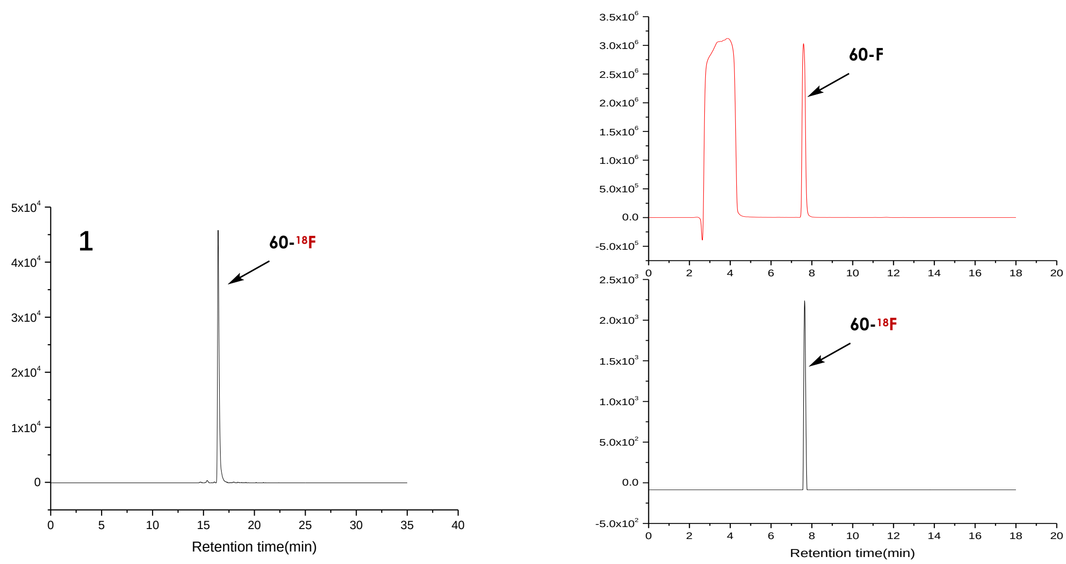


Supplementary Figure 106. Crude radio-HPLC trace(left) and purification (right)of **59-18F**

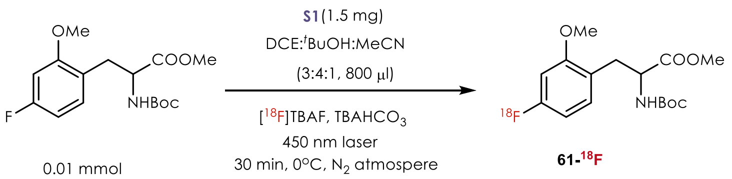


Reaction	Substrate	Activity ([18F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**60**	7.69 mCi	612 µCi	207 µCi	19 min	233.4 µCi	**38.1%**

Supplementary Table 61. HPLC-isolated RCC of **60-18F**

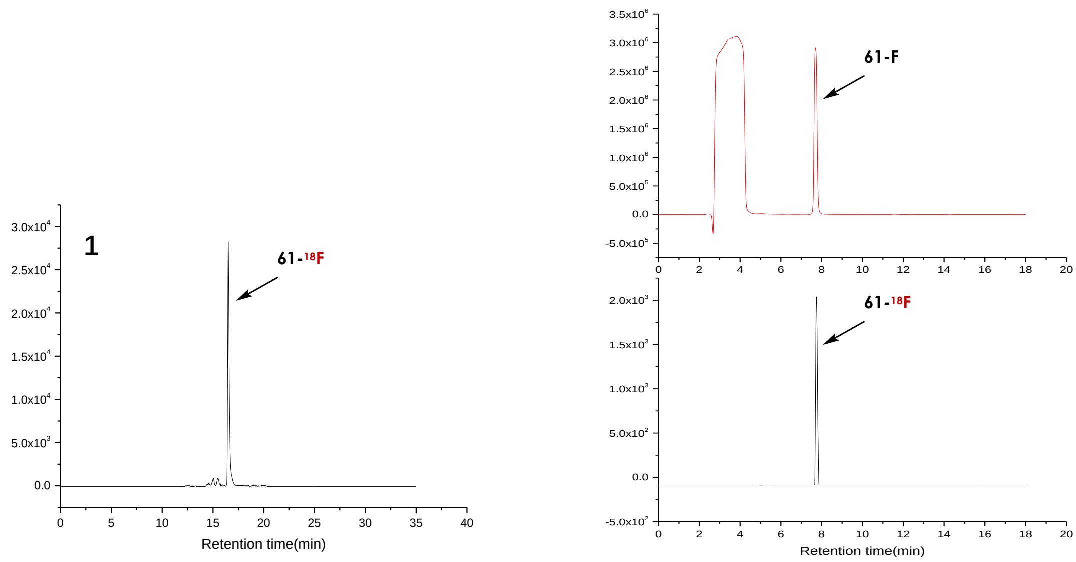


Supplementary Figure 107. Crude radio-HPLC trace(left) and purification (right)of **60-18F**

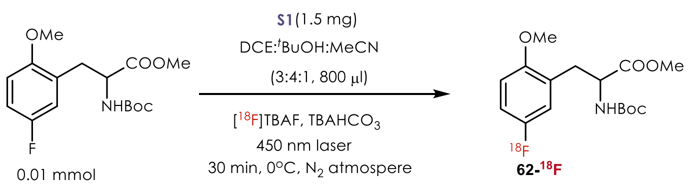


Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**61**	6.47 mCi	577 μCi	124 μCi	19 min	139.8 μCi	**24.2%**

Supplementary Table 62. HPLC-isolated RCC of **61-^{18}F**

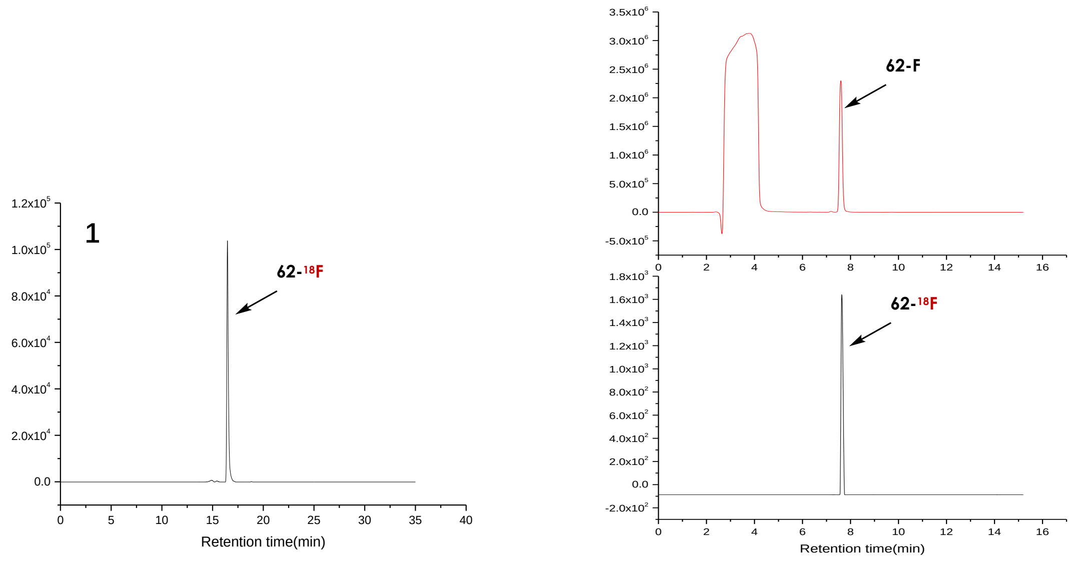


Supplementary Figure 108. Crude radio-HPLC trace(left) and purification (right)of **61-^{18}F**

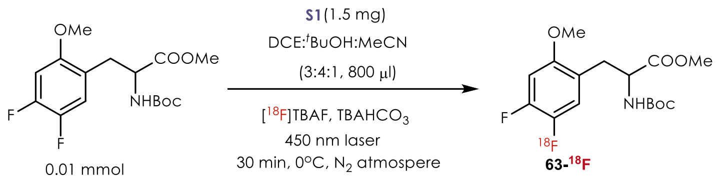


Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**62**	8.05 mCi	550 μCi	389 μCi	20 min	441.4 μCi	**80.2%**

Supplementary Table 63. HPLC-isolated RCC of **62-^{18}F**

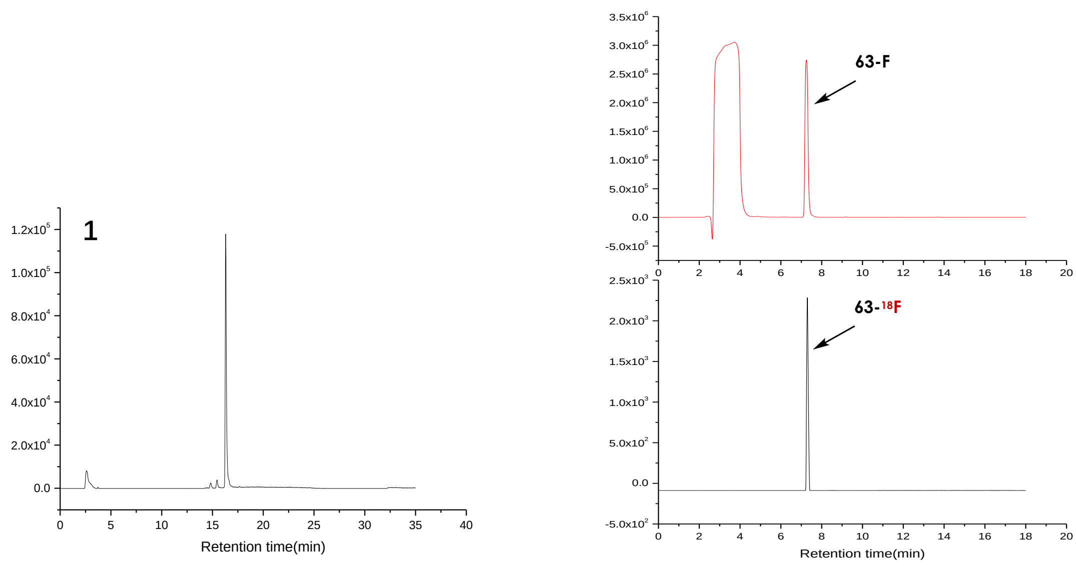


Supplementary Figure 109. Crude radio-HPLC trace(left) and Purification (right)of **62-^{18}F**



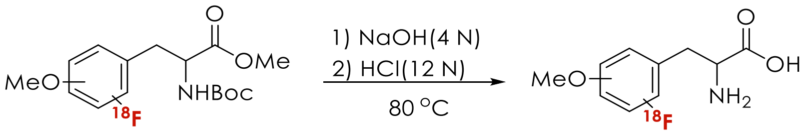
Reaction	Substrate	Activity ([^{18}F]TBAF)	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	**63**	31.4 mCi	2009 μCi	328 μCi	20 min	372.2 μCi	**18.5%**

Supplementary Table 64. HPLC-isolated RCC of **63-^{18}F**



Supplementary Figure 110. Crude radio-HPLC trace(left) and purification (right)of **63-^{18}F**

3.6 General procedure for deprotection of ^{18}F-labeled tyrosine derivatives

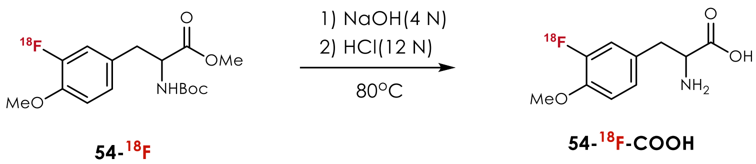


The ^{18}F-fluorinated tyrosine derivatives (**54-^{18}F** to **63-^{18}F**) from the ^{19}F/^{18}F isotopic exchange reactions were isolated on radio-HPLC and directly transferred into a 5 ml V-vial. 200 μl of 4N NaOH solution was added to the vial. The V-vial was then sealed with a Teflon-lined septum screw cap equipped with a vent needle. The solution was heated at 80°C with a positive argon flow for 5 min. Argon flow was then stopped and the vent needle was removed. 300 μl of concentrated HCl was then added via a syringe and the solution was kept at 80℃ for 2 min. The solution was diluted with DI H_2O before being analyzed and purified on HPLC. The ^{18}F-fluorinated tyrosines were collected and the acetonitrile from the mobile phase was removed under reduced pressure. The resulting water solution was neutralized to pH 7 by adding NaOH (1N) and phosphate-buffered saline (PBS, 10X). The tracers were eventually reformulated in a 1X PBS solution for use in the following PET imaging studies.

Note: For compound ***D*-64-^{18}F** and ***L*-64-^{18}F**, 200 μl con. HCl (12 N) was employed only for the deprotection under 120℃ for 10 min. to avoid potential racemization.

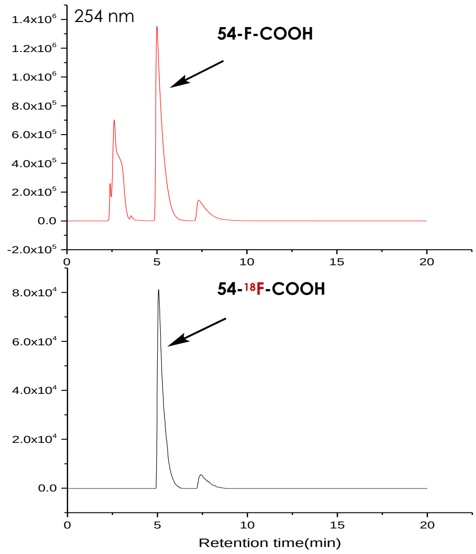
HPLC condition:

Column: Phenomenex, Kinetex® 5 μm EVO C18 100 Å, 250 x 4.6 mm LC Column. Solvent A: 0.1%TFA water; Solvent B: 0.1%TFA acetonitrile. Isocratic elution at 10% solvent B. Flow rate: 1 mL/min.

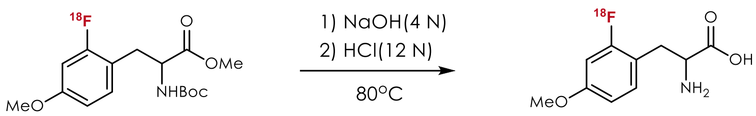


Tracer	Activity (54-^{18}F)	Injected dose	Collected dose	Isolation time	Decay corrected	Radiochemical conversion (RCC)
54-^{18}F-COOH	948 μCi	815 μCi	**619** μCi	11 min	663.5 μCi	**81.4%**

Supplementary Table 65. HPLC-isolated RCC of **54-^{18}F-COOH**



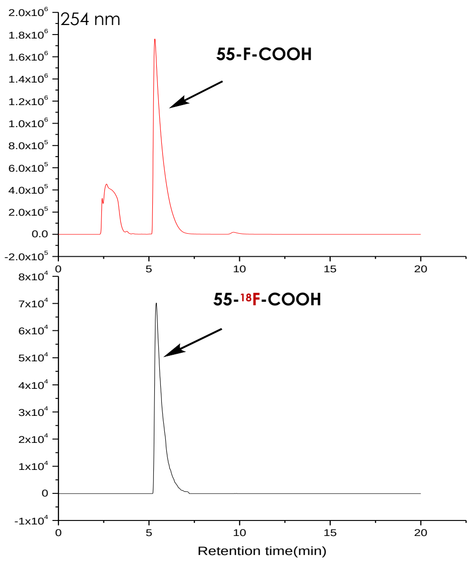
Supplementary Figure 111. HPLC trace of isolation of **54-^{18}F-COOH**



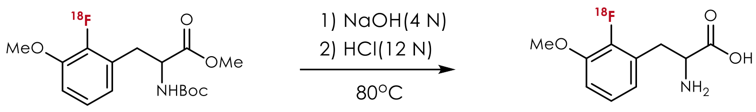
55-^{18}F **55-^{18}F-COOH**

Tracer	Activity (55-^{18}F)	Injected dose	Collected dose	Isolation time	Decay corrected	Radiochemical conversion (RCC)
55-^{18}F-COOH	1.15 mCi	826 μCi	751 μCi	9 min	794.9 μCi	**96.2%**

Supplementary Table 66. HPLC-isolated RCC of **55-^{18}F-COOH**



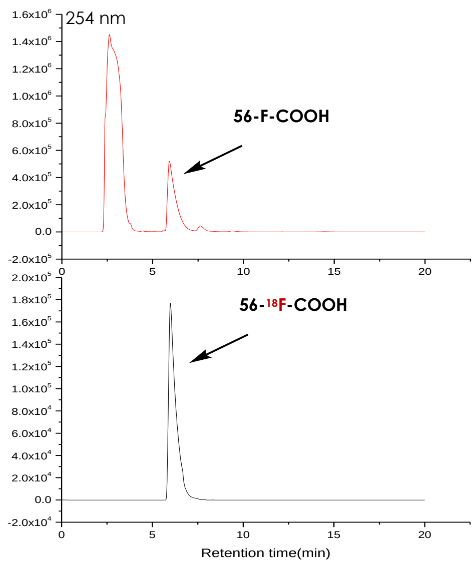
Supplementary Figure 112. HPLC trace of isolation of **55-^{18}F-COOH**



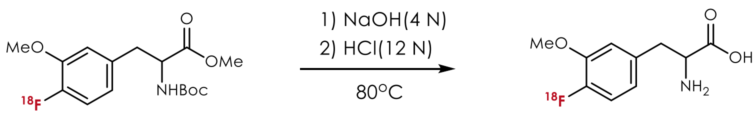
56-^{18}F **56-^{18}F-COOH**

Tracer	Activity (56-^{18}F)	Injected dose	Collected dose	Isolation time	Decay corrected	Radiochemical conversion (RCC)
56-^{18}F-COOH	2.04 mCi	1678 µCi	**1534 µCi**	10 min	1634 µCi	**97.4%**

Supplementary Table 67. HPLC-isolated RCC of **56-^{18}F-COOH**



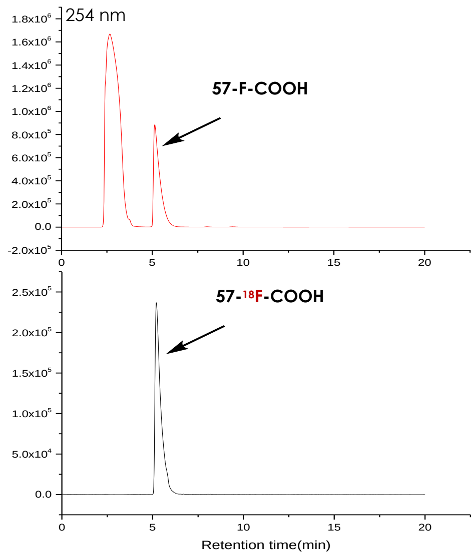
Supplementary Figure 113. HPLC trace of isolation of **56-^{18}F-COOH**



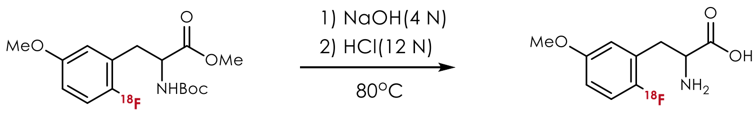
57-^{18}F **57-^{18}F-COOH**

Tracer	Activity (57-^{18}F)	Injected dose	Collected dose	Isolation time	Decay corrected	Radiochemical conversion (RCC)
57-^{18}F-COOH	2.0 mCi	1675 µCi	**1536 µCi**	10 min	1636.1 µCi	**97.7%**

Supplementary Table 68. HPLC-isolated RCC of **57-^{18}F-COOH**



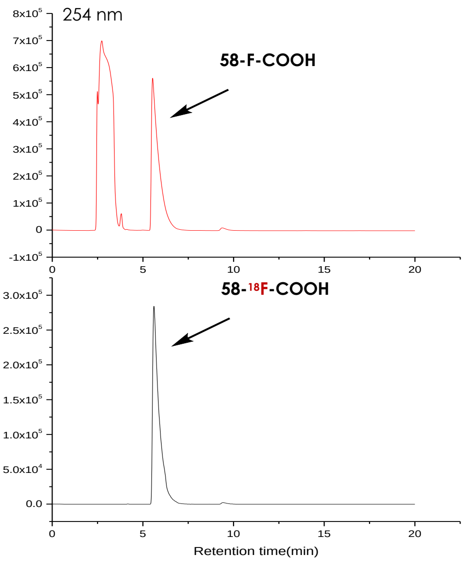
Supplementary Figure 114. HPLC trace of isolation of **57-18F-COOH**



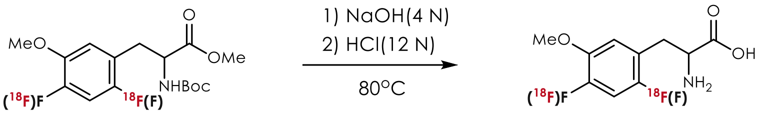
58-18F **58-18F-COOH**

Tracer	Activity (58-18F)	Injected dose	Collected dose	Isolation time	Decay corrected	Radiochemical conversion (RCC)
58-18F-COOH	2.51 mCi	2110 μCi	**1940** μCi	9 min	2053.4 μCi	**97.8%**

Supplementary Table 69. HPLC-isolated RCC of **58-18F-COOH**



Supplementary Figure 115. HPLC trace of isolation of **58-18F-COOH**

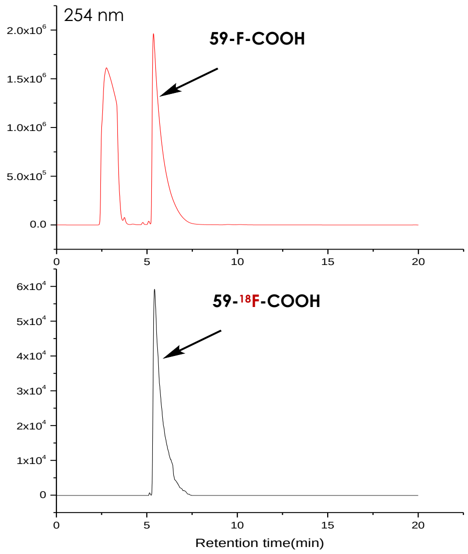


59-^{18}F

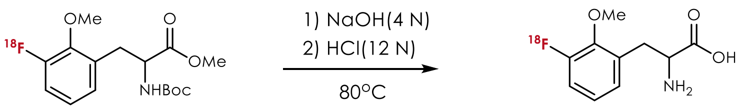
59-^{18}F-COOH

Tracer	Activity (59-^{18}F)	Injected dose	Collected dose	Isolation time	Decay corrected	Radiochemical conversion (RCC)
59-^{18}F-COOH	1.721mCi	1434 μCi	**1323 μCi**	10 min	1409.2 μCi i	**98.3%**

Supplementary Table 70. HPLC-isolated RCC of **59-^{18}F-COOH**



Supplementary Figure 116. HPLC trace of isolation of **59-^{18}F-COOH**

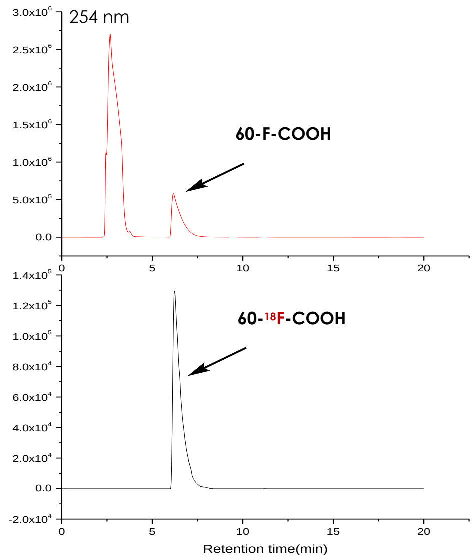


60-^{18}F

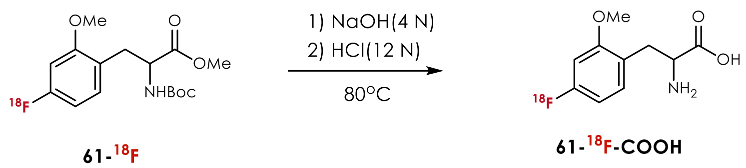
60-^{18}F-COOH

Tracer	Activity (60-^{18}F)	Injected dose	Collected dose	Isolation time	Decay corrected	Radiochemical conversion (RCC)
60-^{18}F-COOH	965 μCi	787 μCi	**688 μCi**	8 min	723.6 μCi	**92%**

Supplementary Table 71. HPLC-isolated RCC of **60-^{18}F-COOH**

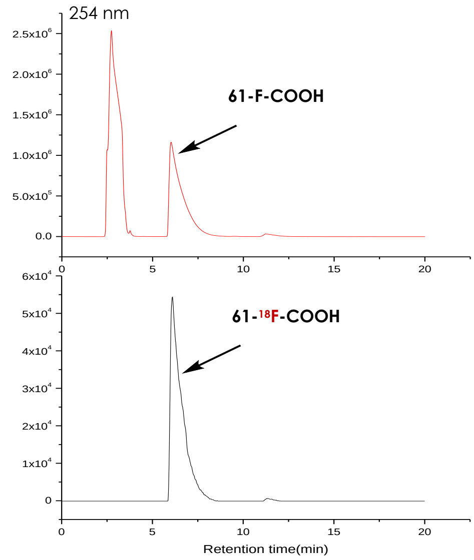


Supplementary Figure 117. HPLC trace of isolation of **60-^{18}F-COOH**

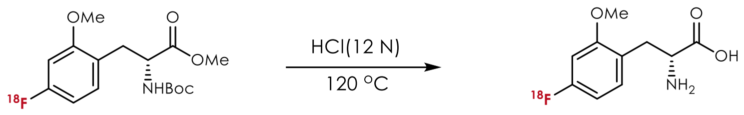


Tracer	Activity (61-^{18}F)	Injected dose	Collected dose	Isolation time	Decay corrected	Radiochemical conversion
61-^{18}F-COOH	1.183 mCi	997 μCi	**901 μCi**	12 min	971.9 μCi	**97.5%**

Supplementary Table 72. HPLC-isolated RCC of **61-^{18}F-COOH**



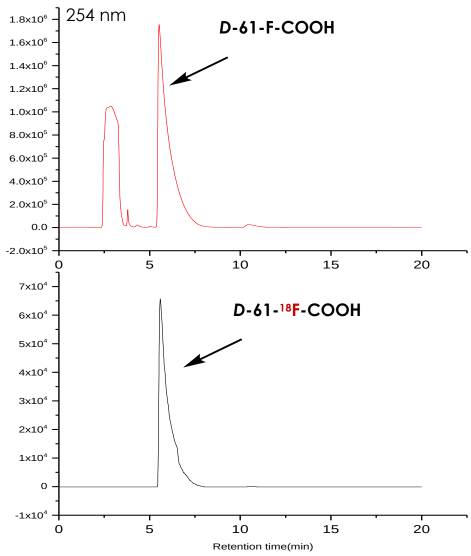
Supplementary Figure 118. HPLC trace of isolation of **61-^{18}F-COOH**



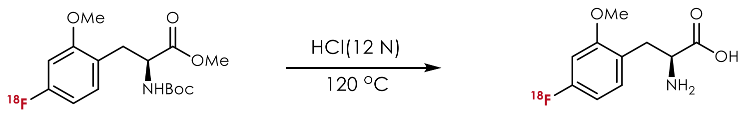
***D*-61-^{18}F** ***D*-61-^{18}F-COOH**

Tracer	Activity (*D*-61-^{18}F)	Injected dose	Collected dose	Isolation time	Decay corrected	Radiochemical conversion
***D*-61-^{18}F-COOH**	1.315 mCi	946 μCi	**853 μCi**	10 min	908.6 μCi	**96%**

Supplementary Table 73. HPLC-isolated RCC of ***D*-61-^{18}F-COOH**



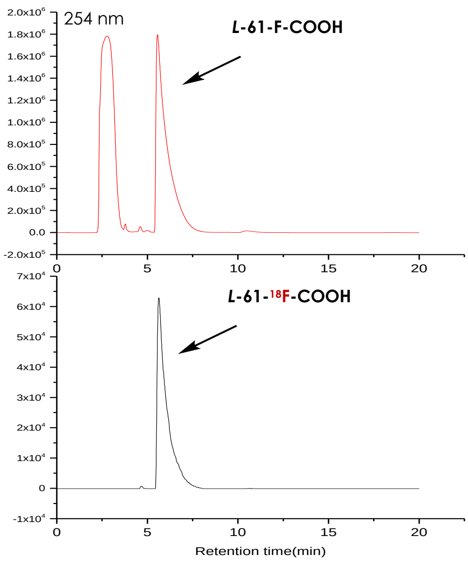
Supplementary Figure 119. HPLC trace of isolation of ***D*-61-^{18}F-COOH**



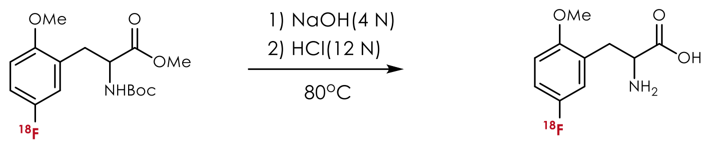
***L*-61-^{18}F** ***L*-61-^{18}F-COOH**

Tracer	Activity (*L*-61-^{18}F)	Injected dose	Collected dose	Isolation time	Decay corrected	Radiochemical conversion
***L*-61-^{18}F-COOH**	1.281 mCi	943 μCi	**835 μCi**	10 min	889.4 μCi	**94.3%**

Supplementary Table 74. HPLC-isolated RCC of ***L*-61-^{18}F-COOH**



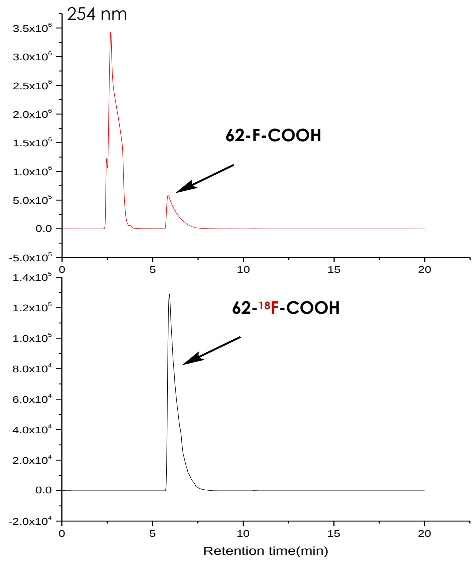
Supplementary Figure 120. HPLC trace of isolation of ***L*-61-^{18}F-COOH**



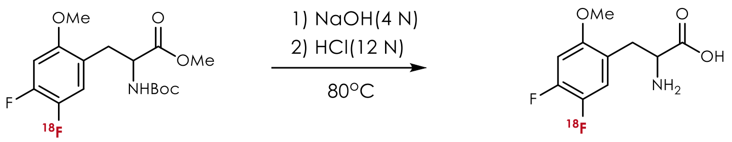
62-^{18}F **62-^{18}F-COOH**

Tracer	Activity (62-^{18}F)	Injected dose	Collected dose	Isolation time	Decay corrected	Radiochemical conversion
62-^{18}F-COOH	1.847 mCi	1541 µCi	**1416 µCi**	11 min	1517.9 µCi	**98.5%**

Supplementary Table 75. HPLC-isolated RCC of **62-^{18}F-COOH**



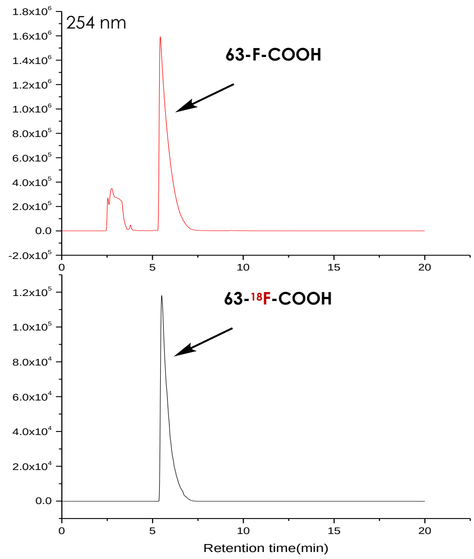
Supplementary Figure 121. HPLC trace of isolation of **62-^{18}F-COOH**



63-^{18}F **63-^{18}F-COOH**

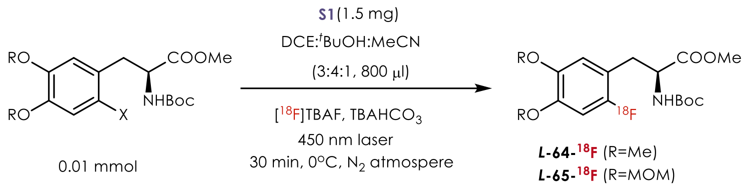
Tracer	Activity (63-^{18}F)	Injected dose	Collected dose	Isolation time	Decay corrected	Radiochemical conversion
63-^{18}F-COOH	1.52 mCi	1230 μCi	**1089 μCi**	10 min	1160 μCi	**94.3%**

Supplementary Table 76. HPLC-isolated RCC of **63-^{18}F-COOH**



Supplementary Figure 122. HPLC trace of isolation of **63-^{18}F-COOH**

3.7 Synthesis of ^{18}F-labeled DOPAs via halide/^{18}F interconversion



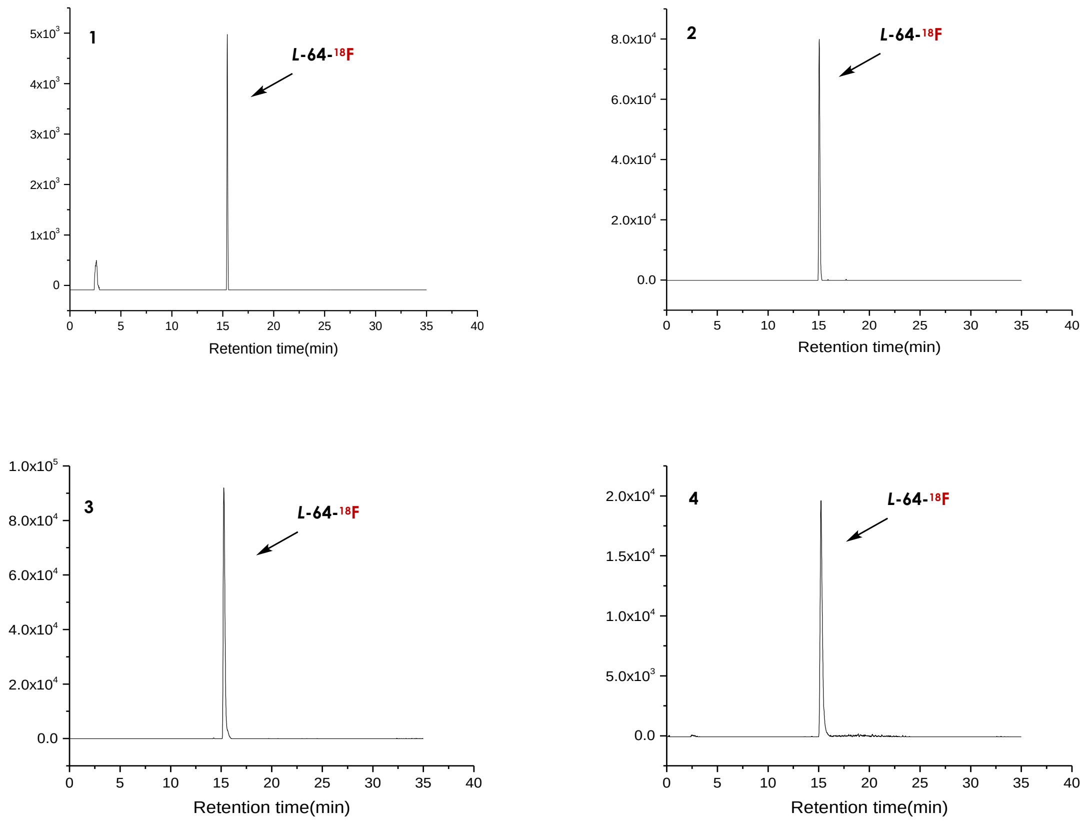
***L*-64-^{18}F** (R=Me)
***L*-65-^{18}F** (R=MOM)

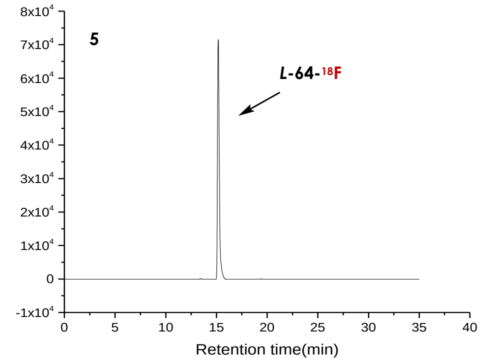
Reaction	Substrate	Activity [^{18}F]TBAF	Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
1	***L*-64-Cl (R=Me, X=Cl)**	13.75 mCi	368 μCi	14 μCi	17 min	15.6 μCi	4.2%
2	***L*-64-F (R=Me, X=F)**	7.86 mCi	332 μCi	216 μCi	19 min	243.5 μCi	73.4%
3		22.9 mCi	998 μCi	388 μCi	17 min	432 μCi	43.3%[a]
4		12.59 mCi	712 μCi	133 μCi	19 min	150 μCi	21.1%[b]
5		7.64 mCi	485 μCi	318 μCi	18 min	356.3 μCi	73.5%[c, d]

6		12.39 mCi	399 μCi	256 μCi	15 min	281.4 μCi	70.5%[c, d, e, g]
7		13.46 mCi	311 μCi	212 μCi	14 min	231.6 μCi	74.4%[c, f, g]
8		10.18 mCi	247 μCi	93 μCi	14 min	101.6 μCi	41.1%[a, c, f, g]
9		28.1mCi	1678 μCi	700 μCi	20 min	794.2 μCi	47.3%[h]
10	***L*-65-F (R=MOM, X=F)**	18.33 mCi	505 μCi	324 μCi	18 min	363 μCi	71.9%
11		13.68 mCi	554 μCi	335 μCi	18 min	40.3 μCi	67.7%[c, d]

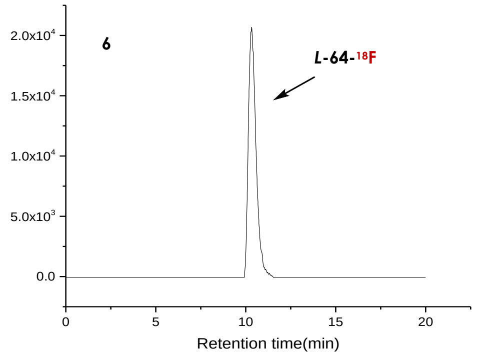
[a]Blue LED was used instead of laser. [b]No DCE were added in the reaction. [c]No ice cooling and 500 μl DCE were used. [d]Reaction ran 20 min. [e]0.005 mmol substrate. [f]Reaction ran 5 min. [g]Isolated under isocratic elution of 35% MeCN. [h]Air bubbling instead of N_2.

Supplementary Table 77. HPLC-isolated RCCs of ***L*-64-^{18}F** and ***L*-65-^{18}F**

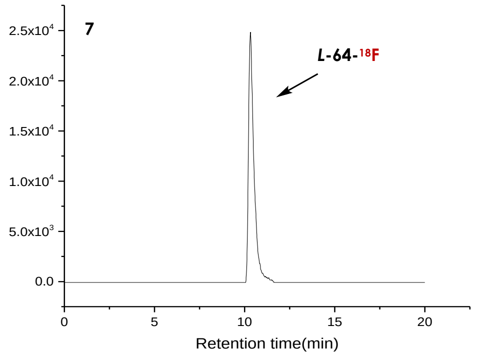




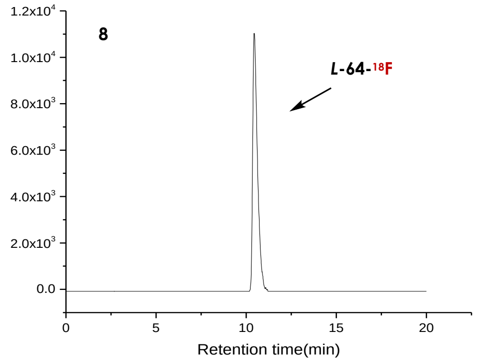
5
L-64-18F
Retention time(min)



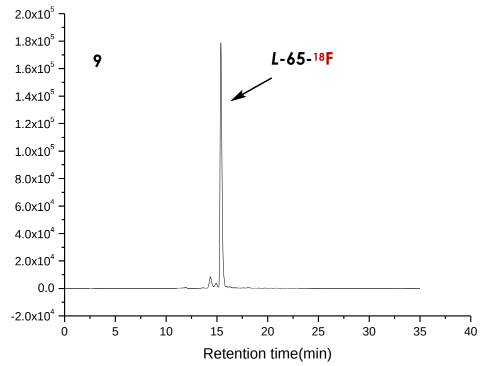
6
L-64-18F
Retention time(min)



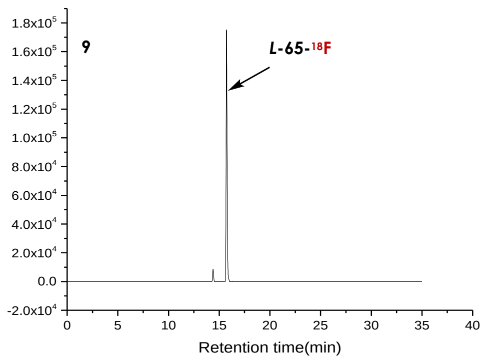
7
L-64-18F
Retention time(min)



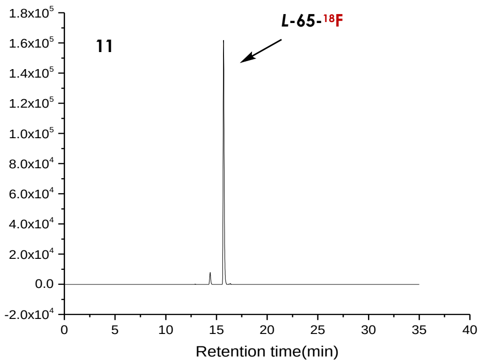
8
L-64-18F
Retention time(min)



9
L-65-18F
Retention time(min)

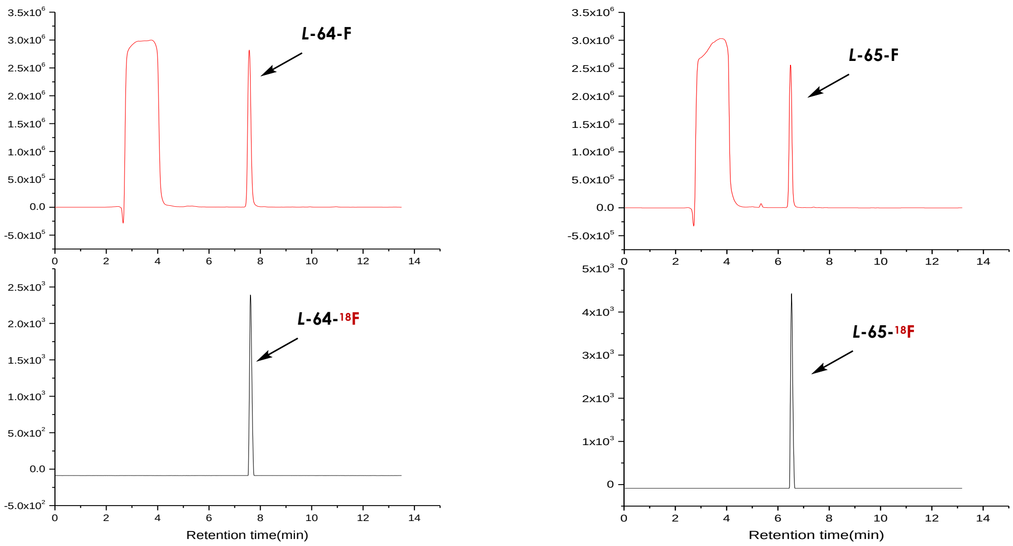


9
L-65-18F
Retention time(min)



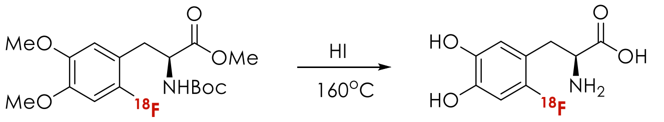
11
L-65-18F
Retention time(min)

Supplementary Figure 123. Crude radio-HPLC traces of synthesis of ***L*-64-18F** and ***L*-65-18F**



Supplementary Figure 124. HPLC traces of purification of ***L*-64-18F** (left) **and *L*-65-18F**(right)

Deprotection of *L*-64-18F to [18F]FDOPA

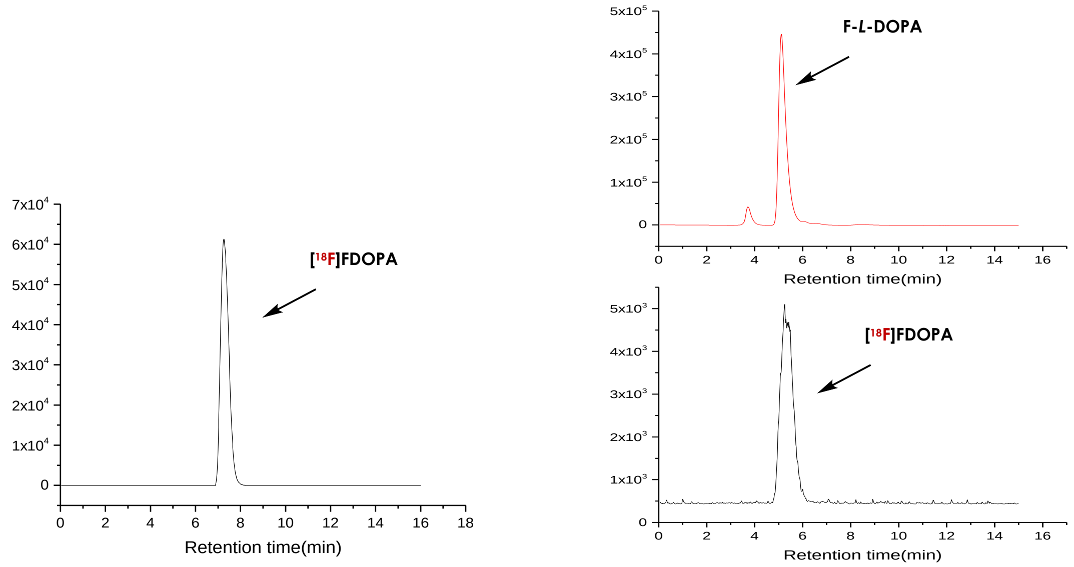


***L*-64-18F** **[18F]FDOPA**

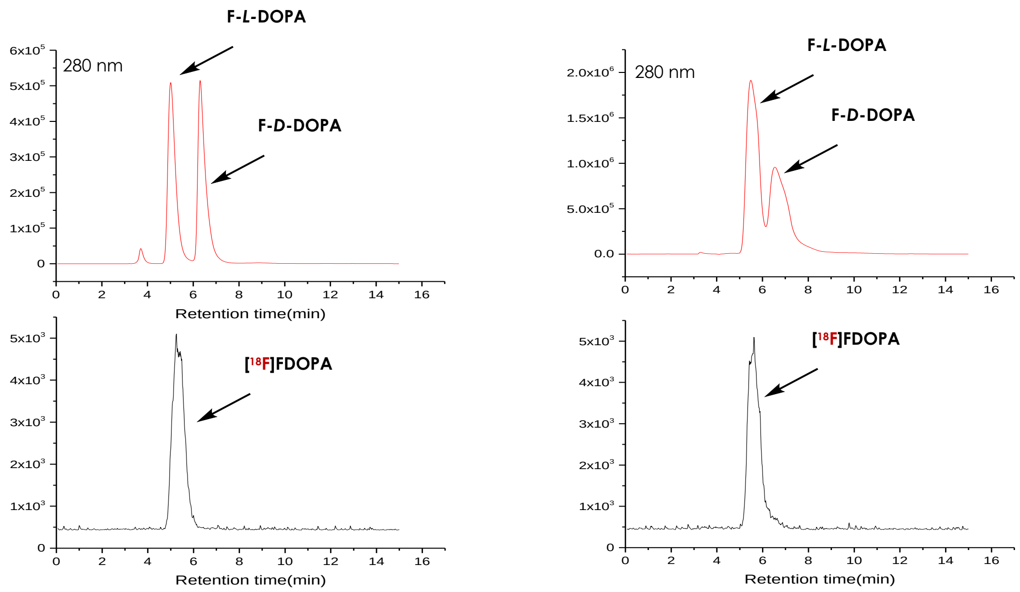
The isolated ***L*-64-18F** from the labeling reaction above was transferred into a 5 ml v-vial and caped with a Teflon-lined septum screw cap equipped with a vent needle. The solvent was removed under 80oC with argon stream. Argon flow was then stopped and the vent needle was removed. 100 µl HI (57 wt.% in H_2O) was then added into the V-vial via syringe and the mixture was heated under 160℃ for 10 min. The V-vial was cooled. The cap was then removed and saturated $NaHCO_3$ (200 µl) solution was added to the V-vial. The resulted aqueous solution was then purified on the radio-HPLC to afford the **[18F]FDOPA** in 97.1% RCC. The **[18F]FDOPA** was then analyzed on the radio-HPLC with a chiral column. The **[18F]FDOPA** was confirmed by comparison of the radio-HPLC trace with the UV HPLC traces of F-*L*-DOPA and > 99% ee was further confirmed by comparison and co-injection of the **[18F]FDOPA** with racemic FDOPA on a chiral column.

Injected dose	Collected dose	Isolation time	Decay corrected dose	Radiochemical conversion (RCC)
510 µCi	**465 µCi**	10 min	495.3 µCi	**97.1%**

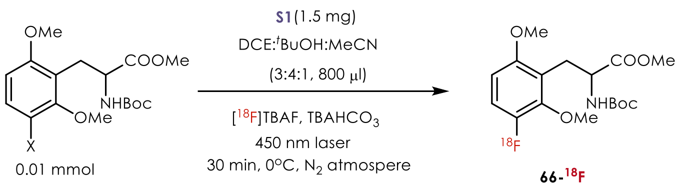
Supplementary Table 78. HPLC-isolated RCC of deprotection of ***L*-64-18F** to **[18F]FDOPA**



Supplementary Figure 125. Crude radio-HPLC trace of **[18F]FDOPA** (left) and comparison of the **[18F]FDOPA** with **F-*L*-DOPA** (right) on chiral column.



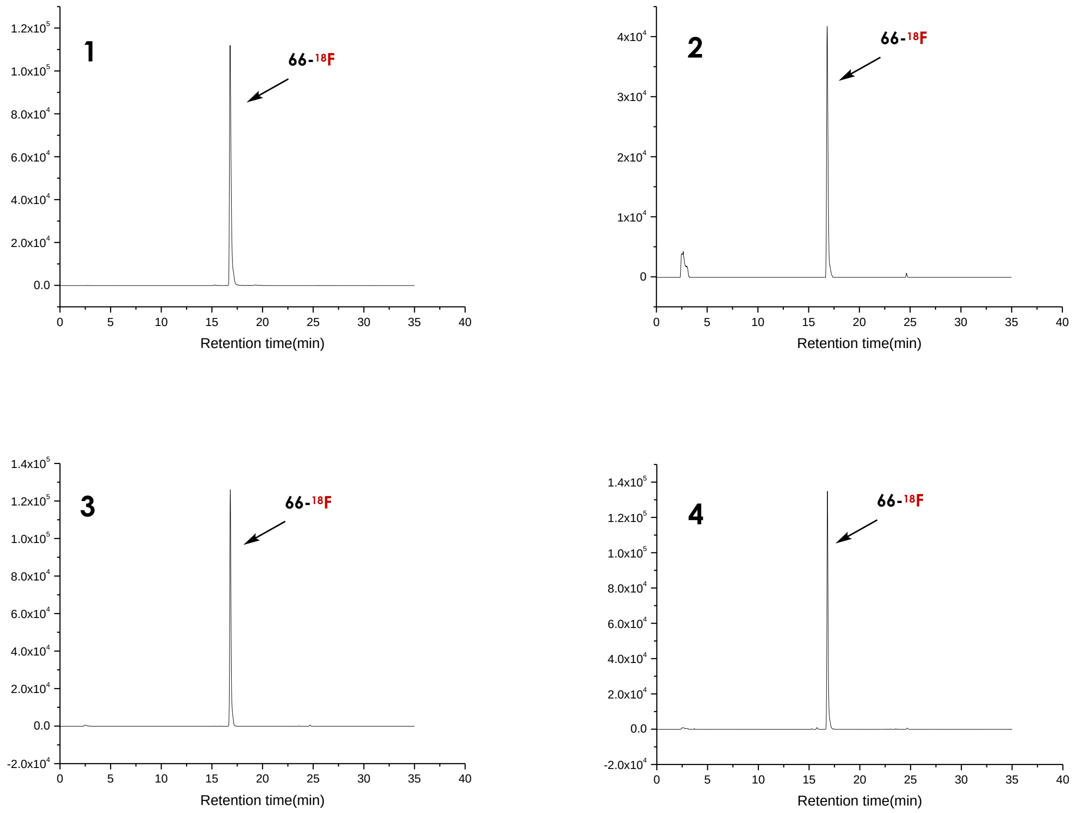
Supplementary Figure 126. Comparison(left) and co-injection (right)of **18F]FDOPA** with racemic FDOPA.



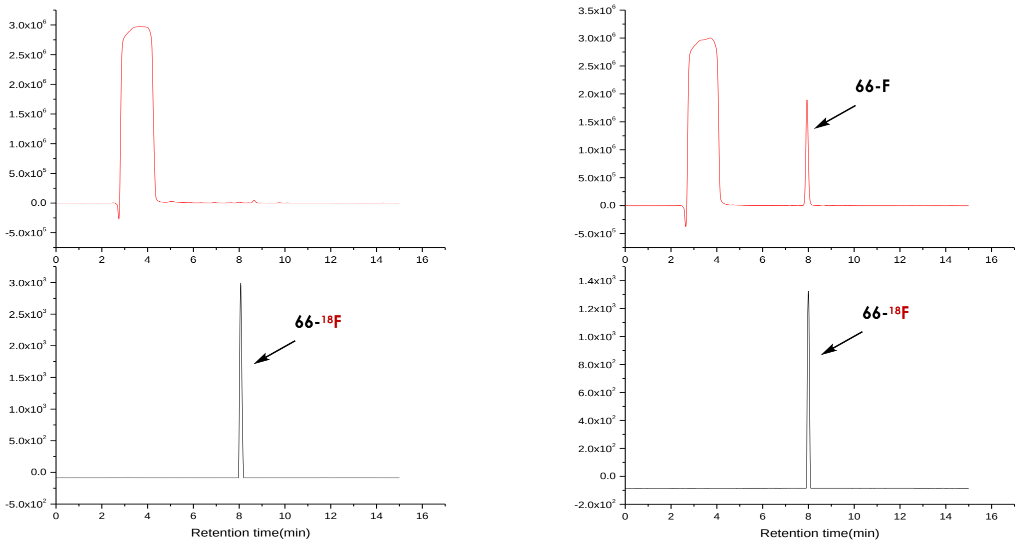
Reaction	Substrate	Activity	Injected dose	Collected dose	Isolation time	Decay corrected	Radiochemical conversion (RCC)
1	**66-F (X=F)**	11.91 mCi	618 μCi	437 μCi	20 min	495.8 μCi	**80.2%**
2	**66-Cl (X=Cl)**[a]	18.99 mCi	478 μCi	163 μCi	20 min	184.9 μCi	38.7%
3		10.11 mCi	784 μCi	357 μCi	19 min	402.5 μCi	51.3%
4		14.65 mCi	781 μCi	352 μCi	20 min	399.4 μCi	51.1%
Average RCC from **66-Cl** to **66-18F**: **47.0±5.9%** (n=3)							

Note: *a*. 0.05 mmol substrate.

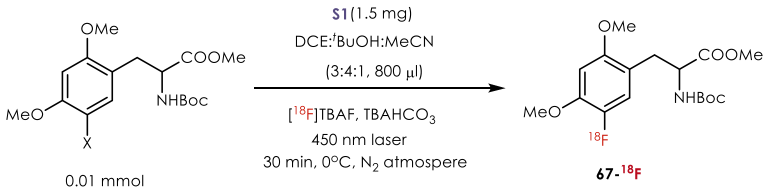
Supplementary Table 79. HPLC-isolated RCCs of **66-18F**



Supplementary Figure 127. Crude radio-HPLC traces from **66-F** and **66-Cl** to **66-18F**



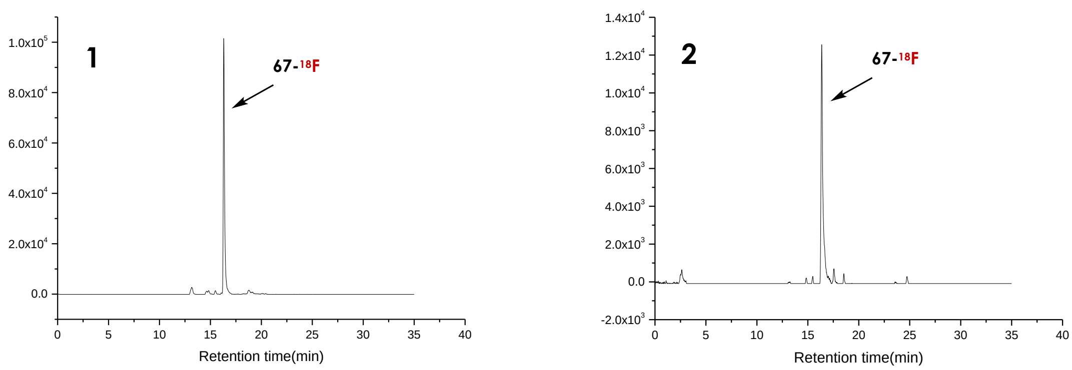
Supplementary Figure 128. Purification (left) and co-injection(right) for **66-^{18}F**

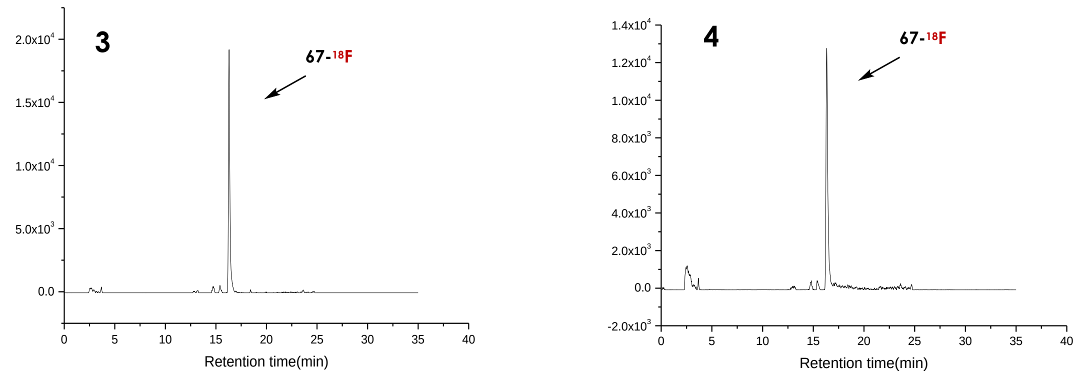


Reaction	Substrate	Activity	Injected dose	Collected dose	Isolation time	Decay corrected	Radiochemical conversion
1	**67-F (X=F)**	12.32 mCi	489 μCi	297 μCi	20 min	337 μCi	**68.9%**
2	**67-Cl (X=Cl)**[a]	13.33 mCi	507 μCi	81 μCi	18 min	90.8 μCi	17.9%
3		11.35 mCi	517 μCi	88 μCi	19 min	99.2 μCi	19.2%
4		9.86 mCi	591 μCi	81 μCi	21 min	92.5 μCi	15.6%
Average RCC from **67-Cl** to **67-^{18}F**:**17.6±1.5%** (n=3)							

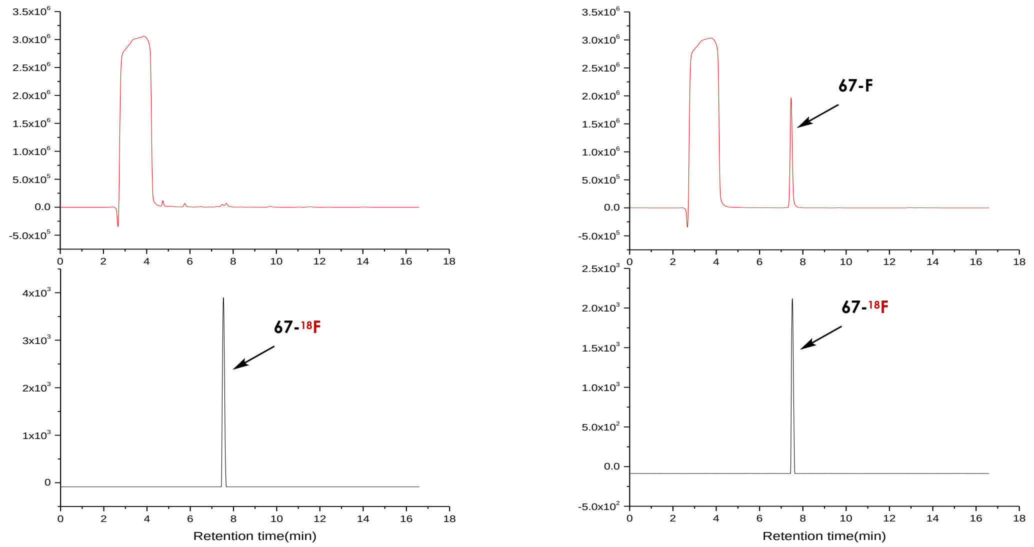
[a]0.05 mmol substrate.

Supplementary Table 80. HPLC-isolated RCCs of **67-^{18}F**

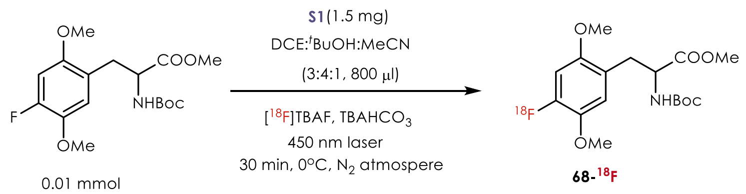




Supplementary Figure 129. Crude radio-HPLC traces from **67-F** and **67-Cl** to **67-18F**

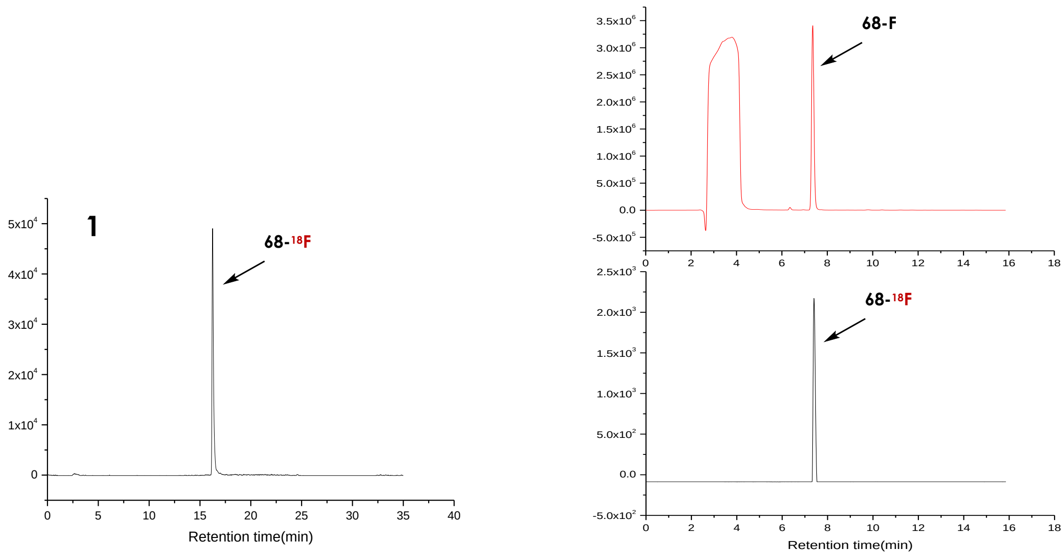


Supplementary Figure 130. Purification (left) and co-injection (right)for **67-18F**



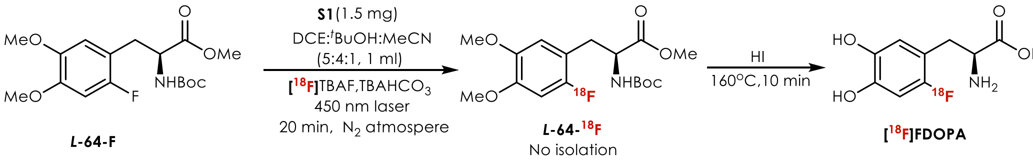
Reaction	Substrate	Activity	Injected dose	Collected dose	Isolation time	Decay corrected	Radiochemical conversion (RCC)
1	68	11.13 mCi	737 μCi	192 μCi	19 min	216.5 μCi	**29.4%**

Supplementary Table 81. HPLC-isolated RCC of **68-18F**



Supplementary Figure 131. Crude radio-HPLC trace(left) and purification (right)of **68-^{18}F**

3.8 Small scale synthesis of [^{18}F]FDOPA from preformed [^{18}F]TBAF



The FDOPA precursor ***L*-64-F** (0.01 or 0.005 mmol) and Photocatalyst **SI** (1.5 mg) were dissolved in the DCE/^{t}BuOH/MeCN in a 5 ml V-vial. After addition of the [^{18}F]TBAF and $TBAHCO_3$ (25 μl), the solution was top-down irradiated for 20 min under 450 nm laser (450 nm, 3.5 W after fibre coupling) with a N_2 balloon sparge at room temperature. The resulting reaction solution was diluted with 1 mL MeCN and passed through an aluminum cartridge (preconditioned with 5 mL DI water) to remove the unconverted ^{18}F-fluoride. Rinse the reaction vial with another 1 mL MeCN which was then passed through the same aluminum cartridge. The elution was collected in another 5 mL V-Vial and caped with a Teflon-lined septum screw cap equipped with a vent needle. The solvent was removed under 100℃ with argon stream. Ar flow was then stopped and the vent needle was removed. 200 μl HI (57 wt.% in H_2O) were then added into the V-vial and the mixture was heated under 160°C for 10 min. A vent needle was then equipped before water (300 μl) and saturated $NaHCO_3$ solution (400 μl) was slowly added to the V-vial. The resulting aqueous solution was passed through a HPLC filter to remove the insoluble catalyst residue. The collected solution was then purified on HPLC to give the product [^{18}F]**FDOPA**.

HPLC isolation condition for reaction 1 and 2:

Column: Phenomenex, Kinetex® 4 µm Synergi 80 Å, 250 x 10.00 mm LC Column. Solvent: 10 mM KH_2PO_4. Flow rate: 5 mL/min.

HPLC condition for QC of reaction 1:

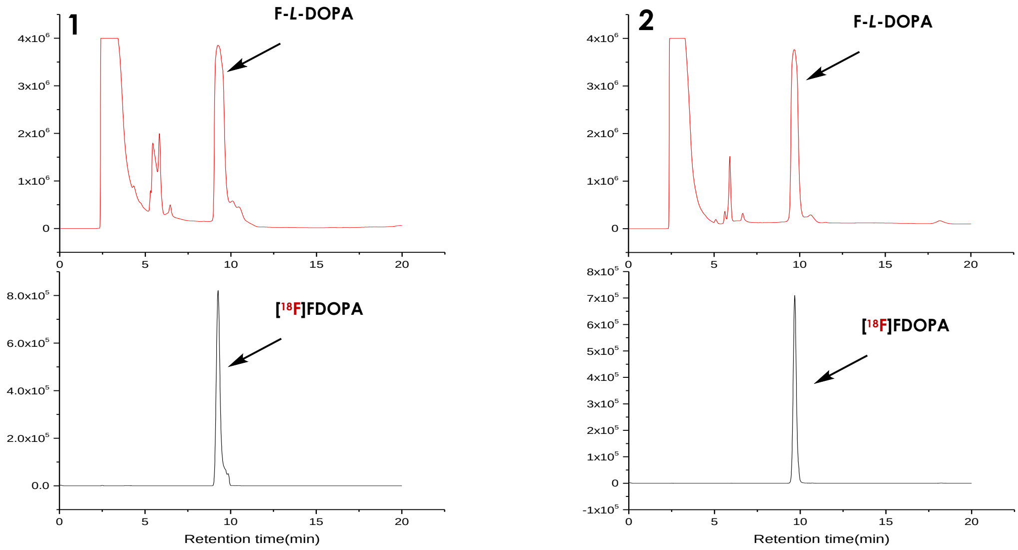
Column: Phenomenex, Kinetex® 4 µm Synergi 80 Å, 250 x 10.00 mm LC Column. Solvent: 10 mM KH_2PO_4. Flow rate: 5 mL/min.

HPLC condition for QC of reaction 2:

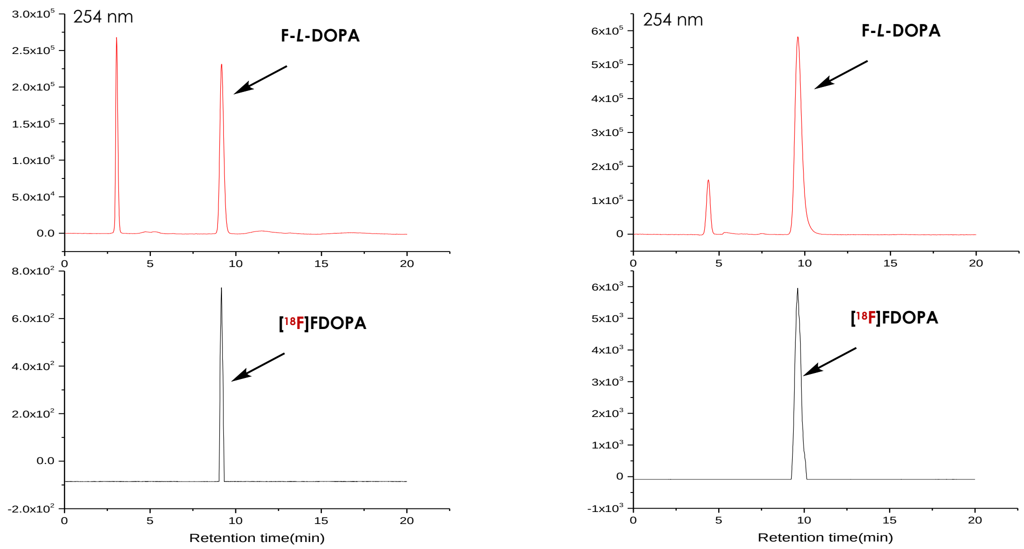
Column: Phenomenex, Kinetex® 10 µm Synergi 80 Å, 250 x 10.00 mm LC Column. Solvent: 10 mM KH_2PO_4. Flow rate: 3 mL/min.

Reaction	Substrate	Activity ([^{18}F]TBAF)	Activity (Isolated [^{18}F]FDOPA)	n.d.c RCY	Total synthesis time
1	***L*-64-F** (0.01 mmol)	30.3 mCi	12.74 mCi	42%	67 min
2	***L*-64-F** (0.005 mmol)	25.5mCi	9.65 mCi	37.8%	66 min

Supplementary Table 82. HPLC-isolated n.d.c. RCYs of **[^{18}F]FDOPA**

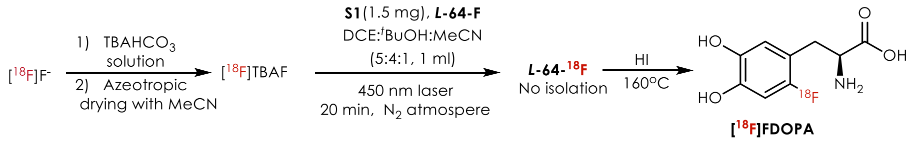


Supplementary Figure 132. Crude HPLC trace of isolation of **[^{18}F]FDOPA** from reaction **1** and **2**



Supplementary Figure 133. HPLC trace of isolated **[18F]FDOPA** from reaction **1** and **2**

3.9 Scale-up synthesis of [18F]FDOPA from [18F]F⁻



The aqueous solution of [18F]F⁻ fluoride produced via the ¹⁸O(p,n)¹⁸F reaction by proton irradiation (40 μA) was delivered to a hot cell equipped with manipulators and collected in a 5 ml V-vial containing 5 μl TBAB (20%) water solution . This aqueous solution was azeotropically dried with anhydrous MeCN (1 ml × 5) under a stream of Argon at 100°C. After removing the water, the V-vial was removed from the heater. The solution of precursor ***L*-64-F** (0.01 mmol) and photocatalyst (**S1**, 1.5 mg) in DCE/ᵗBuOH/MeCN (5/4/1, 1 ml) was then added into the V-vial. A needle connected to a N_2 filled balloon was inserted into the bottom of the V-vial and the reaction medium was continuously sparged with N_2 for the entire reaction time. The reaction was then irradiated top-down with an optic fiber of an OEM diode laser (450 nm, 3.5 W after fibre coupling) for 20 min. The resulting reaction was diluted with 1 ml MeCN and passed through an aluminum cartridge (preconditioned with 5 ml DI water) to remove the unconverted ¹⁸F-fluoride. Rinse the reaction vial with another 1 ml MeCN which was then passed through the same aluminum cartridge. The elution was collected in another 5 ml V-Vial and caped with a Teflon-lined septum screw cap equipped with a vent needle. The solvent was removed under 100°C with argon stream. Ar flow was then stopped and the vent needle was removed. 200 μl HI (57 wt.% in H_2O) were then added into the V-vial and the mixture was heated under 160°C for 10 min. A vent needle was then equipped before water (300 μl) and saturated $NaHCO_3$ solution (400 μl) was slowly added to the V-vial. The resulting aqueous solution was passed through a HPLC filter to remove the insoluble catalyst residue. The collected solution was then purified on HPLC to give the product [^{18}F]**FDOPA**. (Note: all these operation were conducted in the hot cell) .

The isolated [^{18}F]**FDOPA** (> 99% ee) was confirmed by HPLC traces comparison with the racemic FDOPA.

Synthesis data were summarized in the table (Supplementary Table 83) below.

HPLC isolation conditions:

Column: Phenomenex, Kinetex® 4 μm Synergi 80 Å, 250 x 10.00 mm LC Column. Mobile phase: 10 mM KH_2PO_4. Flow rate: 5 mL/min.

HPLC conditions for comparison isolated [^{18}F]FDOPA with racemic FDOPA:

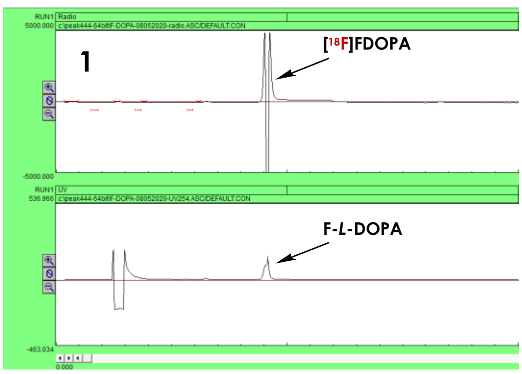
Column: Astec CHIROBIOTICR T Chiral HPLC Column, 5 μm particle size, 250 mm x 4.6 mm, SUPELCO. Mobile phase: 0.2 mL formic acid in 700 ml MeOH and 300 mL water (Ph=3.5).

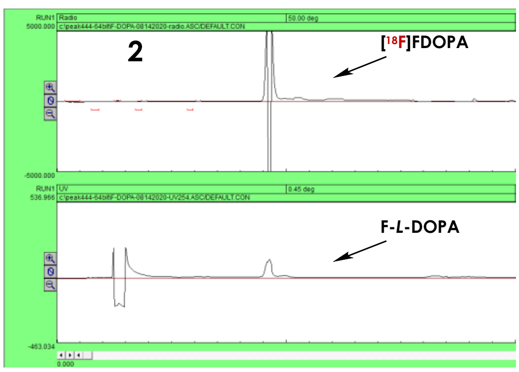
Flow rate: 1 ml/min

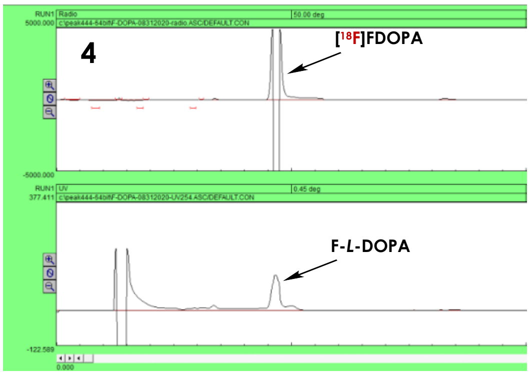
Reaction	**Activity ([^{18}F]F^-)**	**Substrate**	**Activity (Isolated [^{18}F]FDOPA)**	**n.d.c RCY**	**Total synthesis time**
1[a]	1.023 Ci	***L*-64-F** (0.01 mmol)	**197 mCi**	19.3%[a]	93 min
2	1.12 Ci	***L*-64-F** (0.008 mmol)	**259 mCi**	23.1%	87 min
3[b]	1.024 Ci	***L*-64-F** (0.01 mmol)	**310 mCi**	30.2%	87 min
4	1.07 Ci	***L*-64-F** (0.01 mmol)	**348 mCi**	32.5%	98 min

[a]100 μl HI was used (incomplete deprotection). [b]Fail to record the isolation HPLC trace.

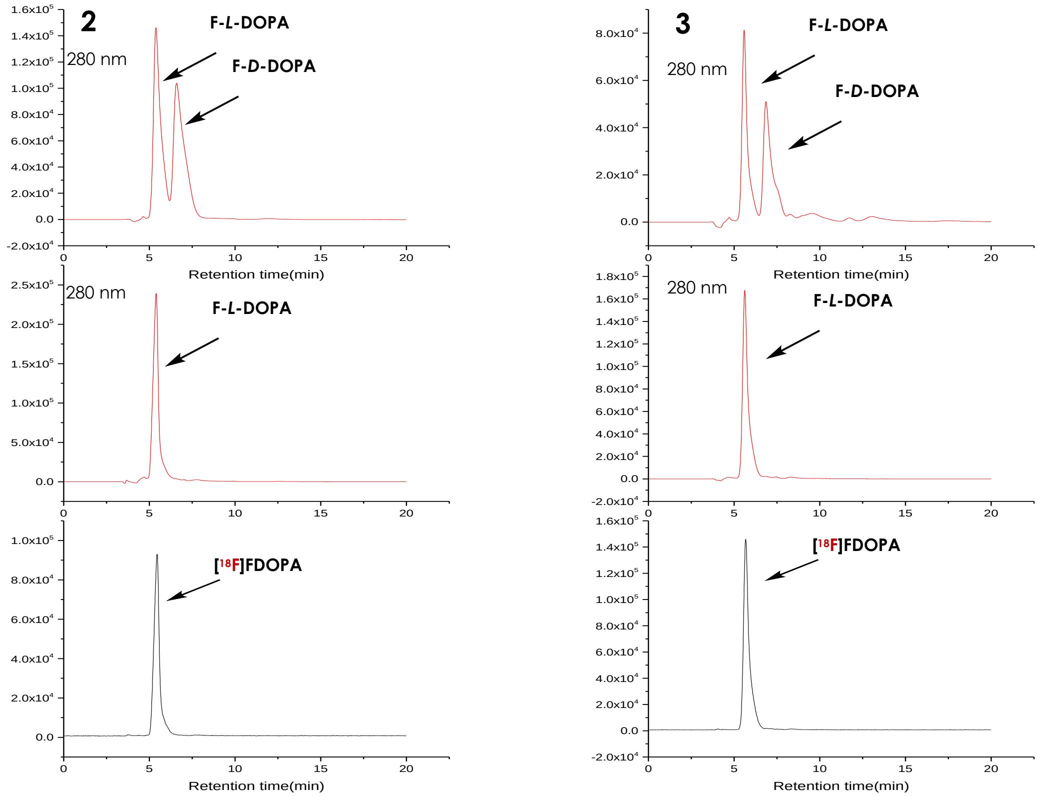
Supplementary Table 83. HPLC-isolated n.d.c. RCYs of **[^{18}F]FDOPA**

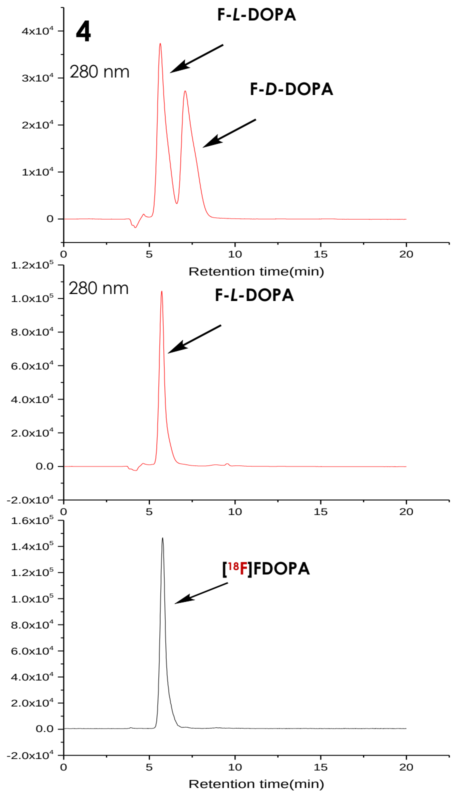






Supplementary Figure 134. HPLC traces of isolation of **[18F]FDOPA** from reaction **1**, **2** and **4**





Supplementary Figure 135. HPLC traces of comparison of isolated **[^{18}F]FDOPA** from reaction **2**, **3** and **4** with racemic FDOPA

3.10. Molar activity calculation

Molar activity calculation for [^{18}F]1-fluoro-4-methoxybenzene (1-^{18}F) obtained from labeling of 1-Cl (Cl/^{18}F exchange).

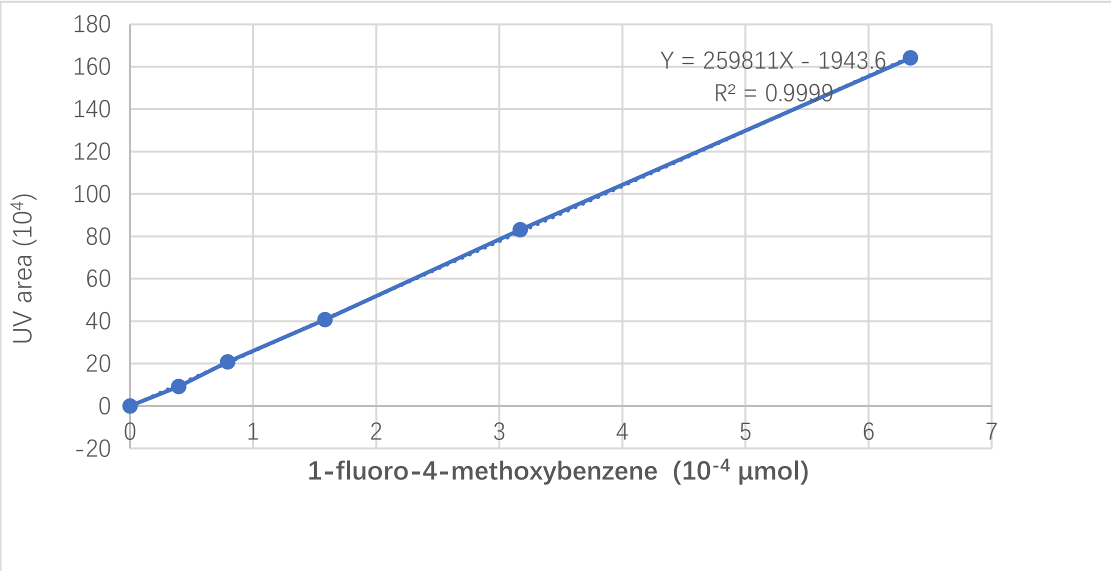
Molar activity was calculated using a standard curve of the corresponding fluorinated arene. A ^{19}F standard curve [Y axis = UV area, X axis = mole number (μmol)] was created from the HPLC trace from a standard solution of 1-fluoro-4-methoxybenzene (**1-F**). The radiolabeled product from the labeling reaction was collected and purified via HPLC; the UV area overlapping with the radio peak was then recorded. The standard curve was used to calculate mole number. Dividing the product decay corrected activity by the mole number gives the molar activity in GBq/μmol. In this example, the isolated product **[^{18}F]1-fluoro-4-methoxybenzene** has a molar activity of 71.25 ± 4.18 GBq/μmol, which is decay corrected to the end of bombardment (EOB).

a

1-fluoro-4-methoxybenzene (10^{-4} μmol)	UV area (10^4)
0	0

3.96	9.1876
7.93	20.8663
15.86	40.6923
31.71	83.1809
79.28	164.1623

b



c

Entry	Decay corrected (EOS) Activity (10^{-4} GBq)	UV area (10^4)	1-fluoro-4-methoxybenzene (10-4 μmol)	Molar activity (GBq/μmol)
1	133	4.8396	1.94	68.56
2	125	4.0045	1.62	77.16
3	100	3.6343	1.47	68.03

Average molar activity: 71.25 ± 4.18 GBq/μmol

Supplementary Figure 136. a and **b**, Standard curve data for **1-F**; **c**, the average molar activity for **1-^{18}F** calculated from parts **a** and **b**.

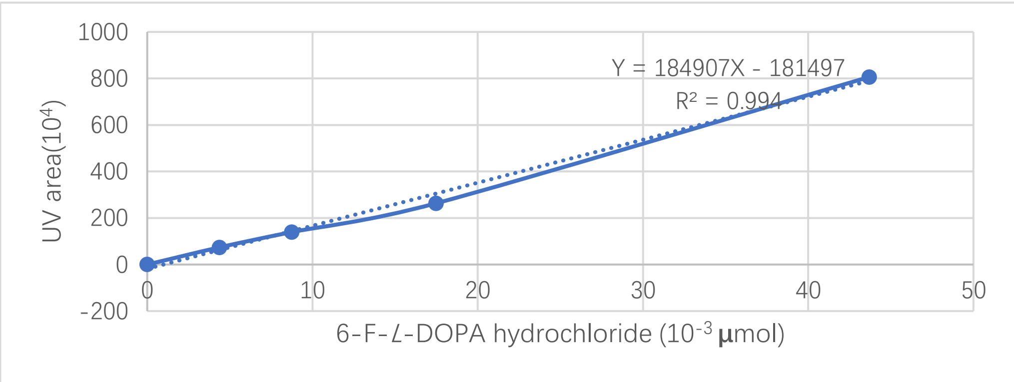
Molar activity calculation for [^{18}F]FDOPA

Follow the same procedure to calculate the molar activity of **[^{18}F]1-fluoro-4-methoxybenzene(1-^{18}F)** above, the standard curve was prepared from the 6-Fluoro-L-FDOPA hydrochloride (purchased from ABX). The dose decay corrected back to end of synthesis of purified **[^{18}F]FDOPA** and corresponding UV area integration were recorded. **[^{18}F]FDOPA** has a molar activity of 1.51GBq/μmol at end of synthesis.

a

6-Fluoro-L-FDOPA hydrochloride (10^{-3} μmol)	UV area (10^4)
0	0
4.37	73.8691
8.74	139.4975
17.48	263.2771
43.7	806.2787

b

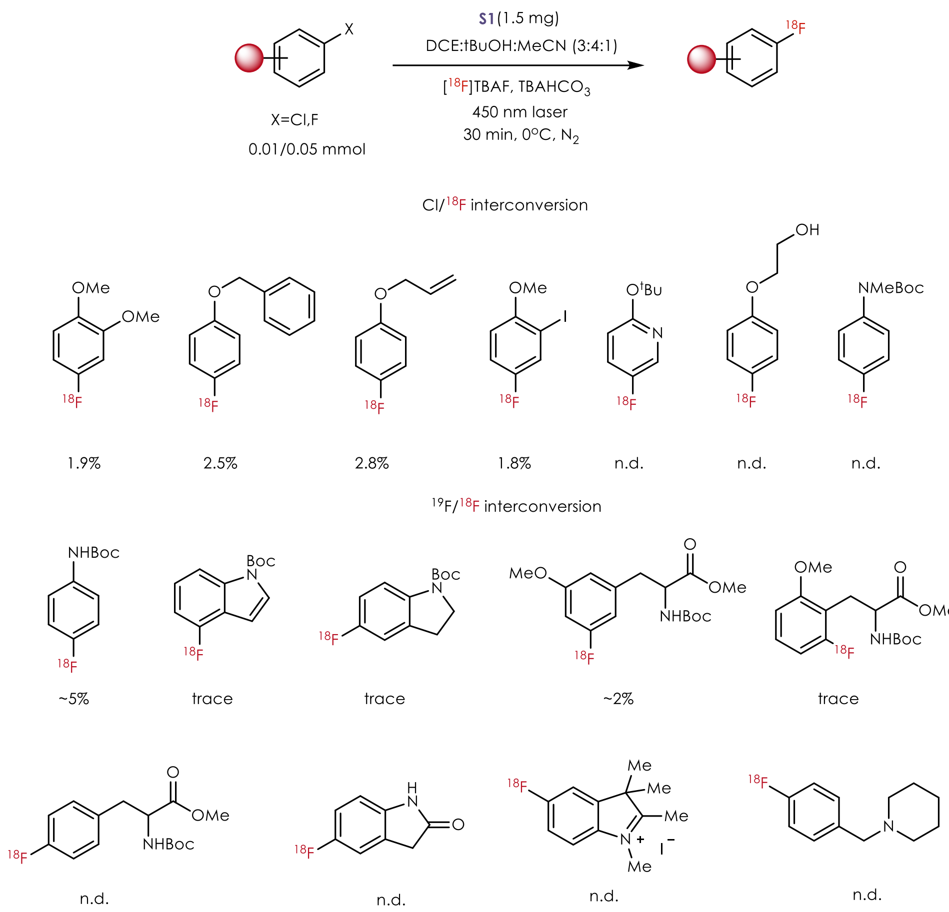


c

Entry	**Decay corrected (EOS) Activity** (10^{-3} GBq)	**UV area** (10^4)	**FDOPA** (10^{-3} μmol)	**Molar activity** (GBq/μmol)
1	21.9	249.2604	14.5	1.51

Supplementary Figure 137. **a** and **b,** Standard curve data for FDOPA; **c,** molar activity for **[^{18}F]FDOPA** calculated from parts **a** and **b**.

3.11. **Less effective substrates for photoredox-mediated halide/^{18}F interconversion**



Supplementary Figure 138. Less effective substrates for photoredox-mediated halide/^{18}F interconversion. All reactions were performed according to the general procedure at section 3.4. n.d., not detected.

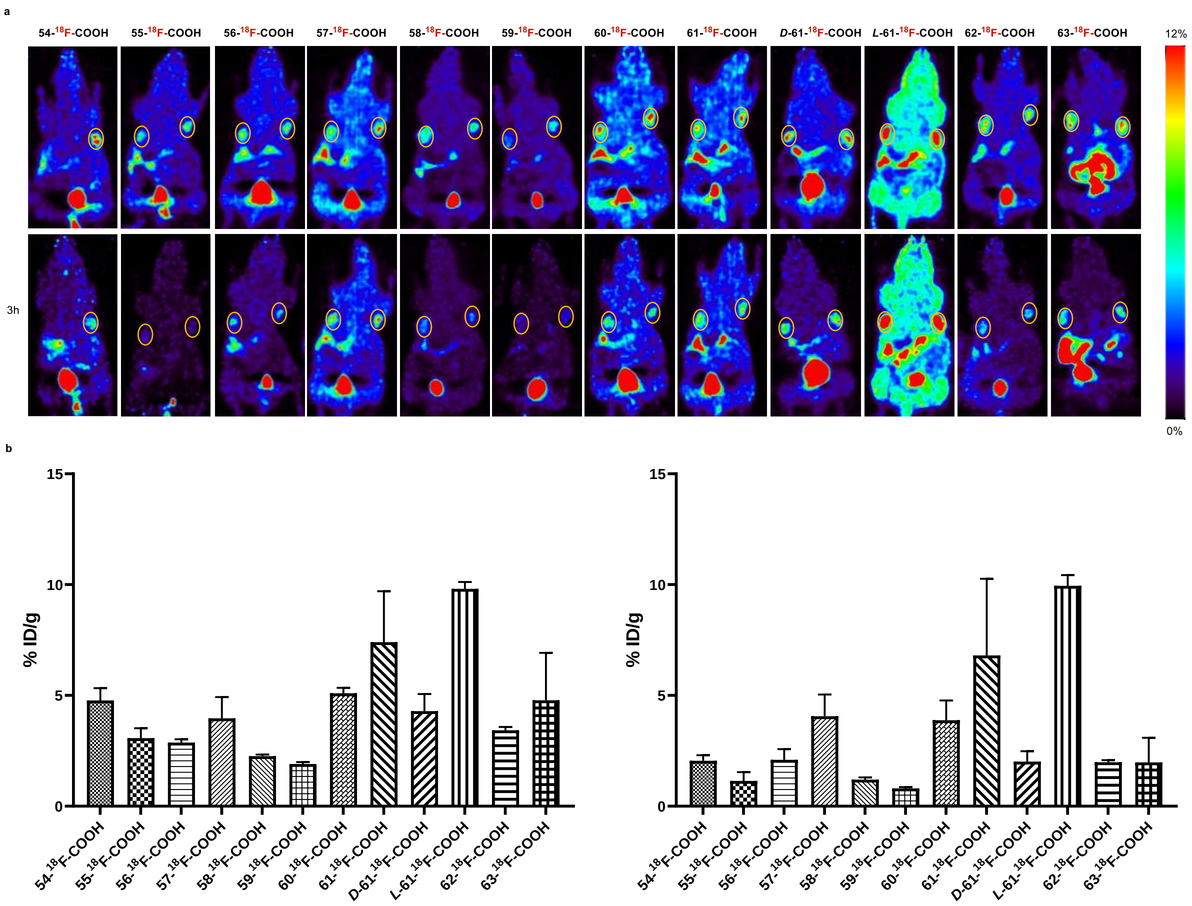
4. Positron emission tomography (PET) Imaging Study

In Vivo PET Imaging in MCF-7 breast cancer xenografts in nude mice

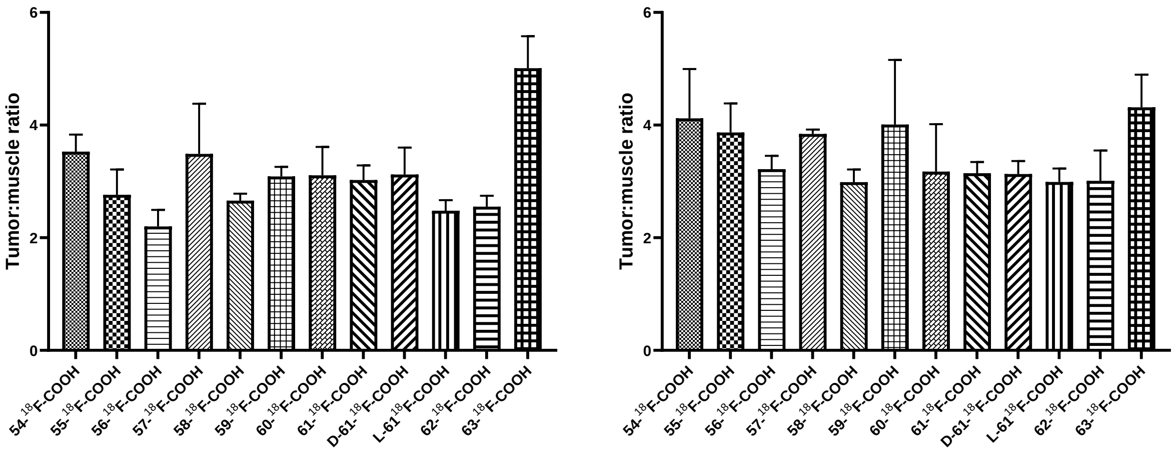
Materials and methods: All animal studies were conducted in compliance with the protocol approved by the University of North Carolina Institutional Animal Care and Use Committee. Human breast cancer cells line MCF-7 was obtained from American Type Culture (Manassas, VA, USA) and cultured in Eagle's Minimum Essential Medium (EMEM) (Gibco, Grand Island, NY, USA) supplemented with 10% fetal bovine serum (FBS) (SAFC Bioscience, Lenexa, KS). MCF-7 xenograft was established in 4- to 6-weeks old female nude mice (Division of Comparative Medicine, the University of North Carolina at Chapel Hill) as described (PMID: 31221856). Mice were group housed (no more than five mice per cage) with air temperature 24 ± 3°C, humidity 60 ± 4%, and a 12-hours light/12-hours dark cycle. Food and water were provided ad libitum. The PET imaging studies were conducted when the tumor size was between 250-750 mm^3. ^{18}F PET tracers were prepared from section 3.6

Results of *in vivo* PET Imaging

The MCF-7 tumor-bearing mice received an intravenous injection of the ^{18}F-PET agent (~8.2 MBq). At 1 h and 3 h post-injection, the animals were anesthetized using 2% isoflurane and subjected to 10 min static PET scan (SuperArgus 4R, SEDECAL, Madrid, Spain). The uptake values (percentage injected dose per gram) were calculated and reported as mean ± SD averaged over n(n≥3) tumors. PET images were reconstructed into a single frame by OSEM 3D with random and scatter correction. The reconstructed PET images were analyzed using AMIDE (http://amide.sourceforge.net/) software (Supplementary Figure 139). Most of the PET tracers demonstrated initial prominent tumor uptake at 1h post-injection followed by washout at 3h while few tracers (**57-^{18}F-COOH**, **60-^{18}F-COOH**, **61-^{18}F-COOH**) showed high and persistent retention in the MCF-7 tumor model. The *L*-configuration isomer (***L*-61-^{18}F-COOH**) shows higher tumor uptake and longer retention time than the *D*-isomer (***D*-61-^{18}F-COOH**). Besides the tumor accumulation of each tracer at a different time point, we calculated the tumor to muscle ratio to reflect the signal to noise for each tracer. All the ^{18}F-labeled tyrosine analogs show similar uptake ratio between tumor and muscle except tracer **63-^{18}F-COOH** which demonstrates relatively higher uptake ratio, especially at 1h post-injection, comparing to other tracers (Supplementary Figure 140).



Supplementary Figure 139. PET imaging study. a, PET imaging of ^{18}F-labeled tyrosines in the MCF7 tumor model system (tumors were circled in the pictures). **b**, Tumor uptake (percentage injected dose per gram) of each tracer at 1h post-injection (left) and 3h post-injection (right). Tumor uptake of the each tracer from **54-^{18}F-COOH** to **63-^{18}F-COOH** at 1h and 3h post-injection are 4.77±0.55% (n=3), 2.05±0.25% (n=3); 3.07±0.44% (n=4), 1.14±0.39% (n=4); 2.87±0.15% (n=4), 2.09±0.49% (n=4); 3.96±0.96% (n=7), 4.06±0.98% (n=4); 2.26±0.07% (n=4), 1.20±0.10% (n=3); 1.91±0.08% (n=4), 0.80±0.06% (n=4); 5.10±0.25% (n=4), 3.88±0.90% (n=4); 7.41±2.29% (n=10), 6.80±3.46% (n=10); 4.29±0.77% (n=6), 2.02±0.47% (n=6); 9.81±0.30% (n=6), 9.95±0.48% (n=6); 3.43±0.15% (n=3), 1.98±0.10% (n=3); 4.78±2.14% (n=6), 1.98±1.11% (n=6), respectively.



Supplementary Figure 140. Tracer uptake ratio between tumor and muscle of each tracer at 1h (left) and 3h (right) post-injection. The ratios were calculated and reported as mean ± SD averaged over n (n ≥ 3) tumors and muscles. The ratios from **54-^{18}F-COOH** to **63-^{18}F-COOH** at 1h and 3h post-injection are 3.53±0.30 (n=3), 4.12±0.88 (n=3); 2.76±0.45 (n=4), 3.87±0.52 (n = 4); 2.20±0.29 (n = 4), 3.22±0.24 (n=4) ; 3.49 ± 0.89 (n=7), 3.84 ± 0.08 (n=4); 2.66 ± 0.12 (n=4), 2.99 ± 0.23 (n=3); 3.09±0.17 (n=4), 4.01±1.15 (n=4); 3.11±0.50, 3.17±0.84 (n=4); 2.81±0.34(n=10), 3.04±0.49 (n=10); 3.12±0.48 (n=6), 3.13±0.23(n=6); 2.45±0.19 (n=6), 2.99±0.24 (n=6); 2.55±0.19 (n=3), 3.01±0.54 (n=4); 5.01±0.57 (n=6) 4.32±0.58 (n=6), respectively.

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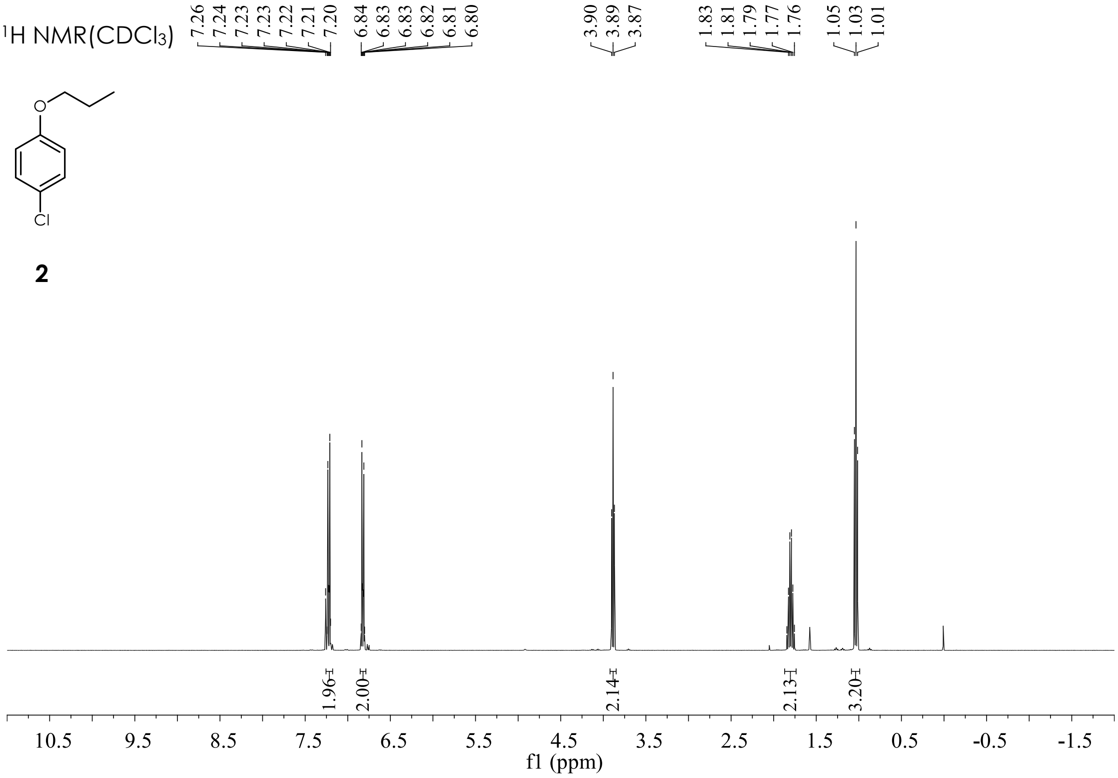
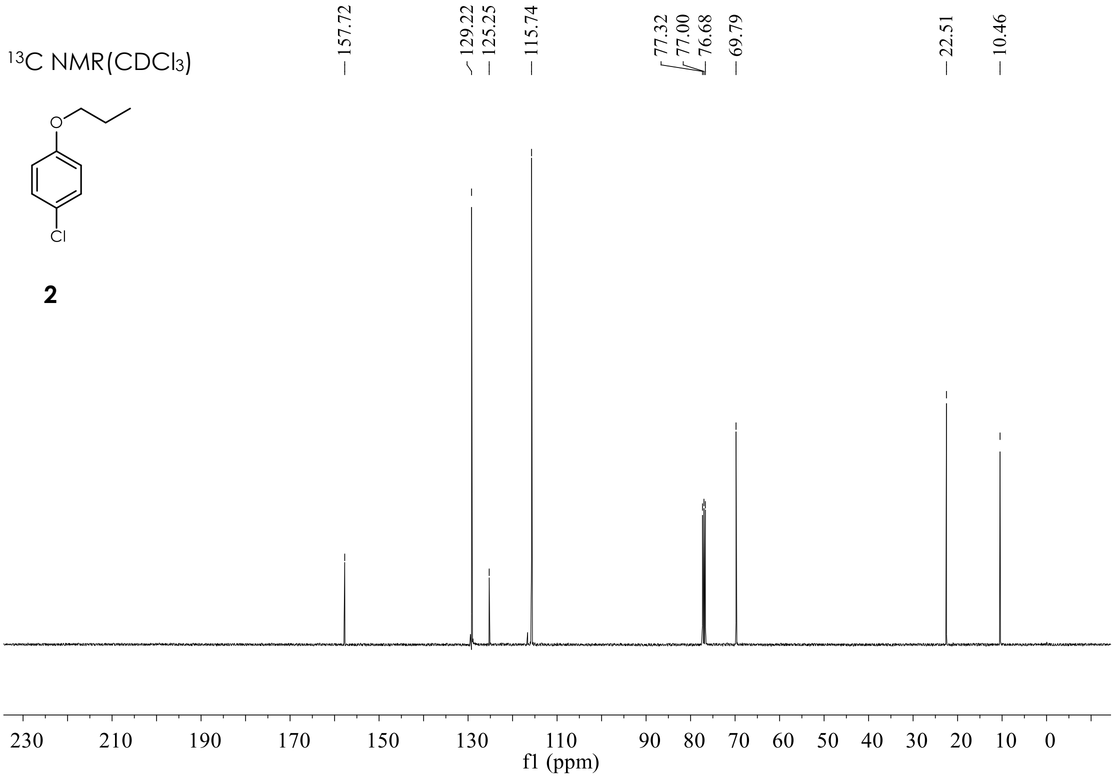
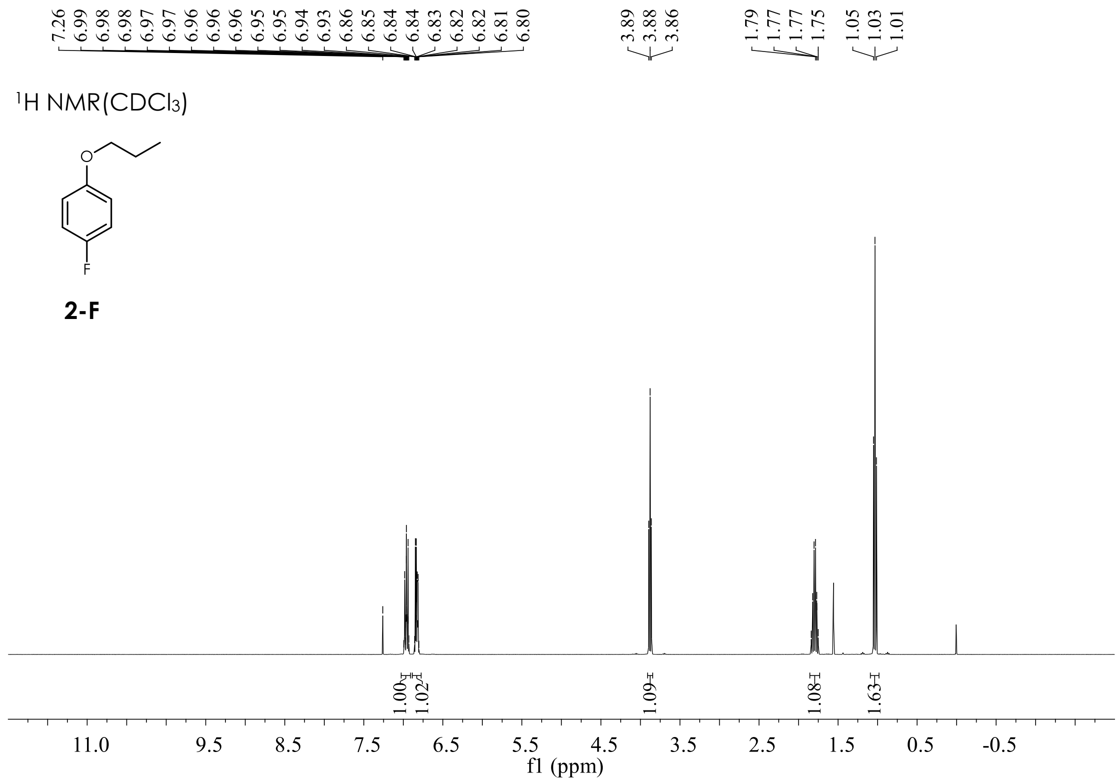
6. NMR spectra (^{1}H NMR, ^{13}C NMR, ^{19}F NMR)



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1.77
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1.01
¹H NMR(CDCl₃)
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1.08
1.63
11.0
9.5
8.5
7.5
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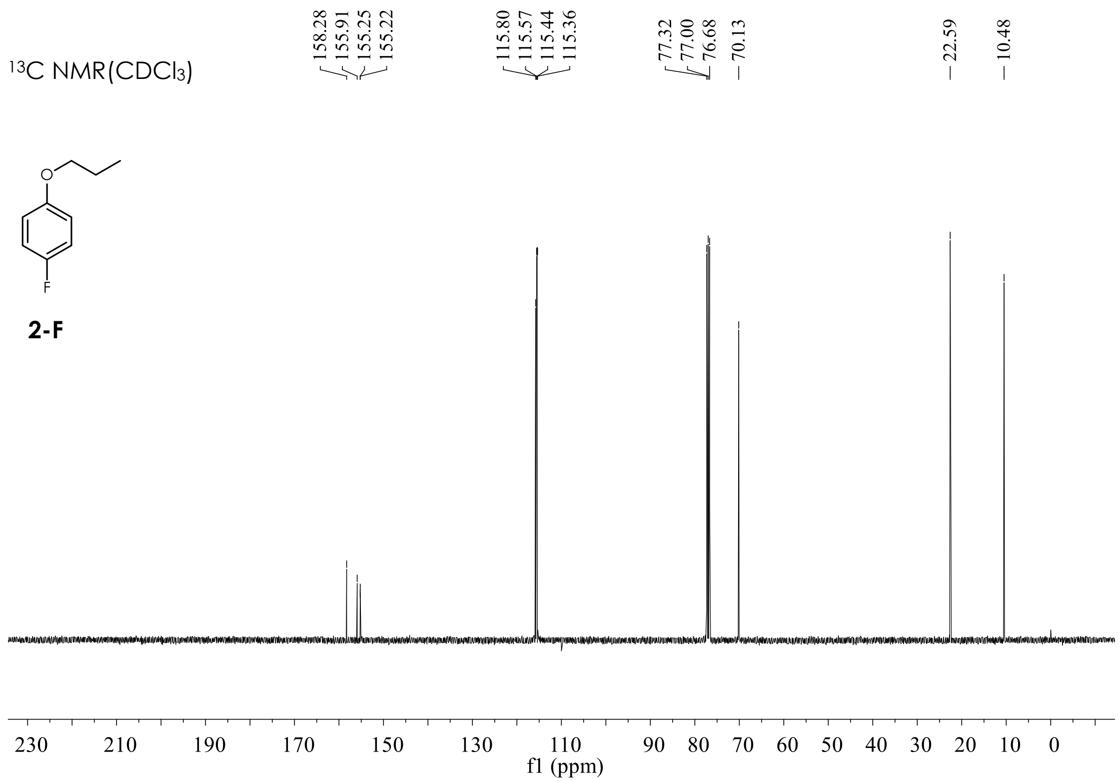
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)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O
F
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150
130
110
90
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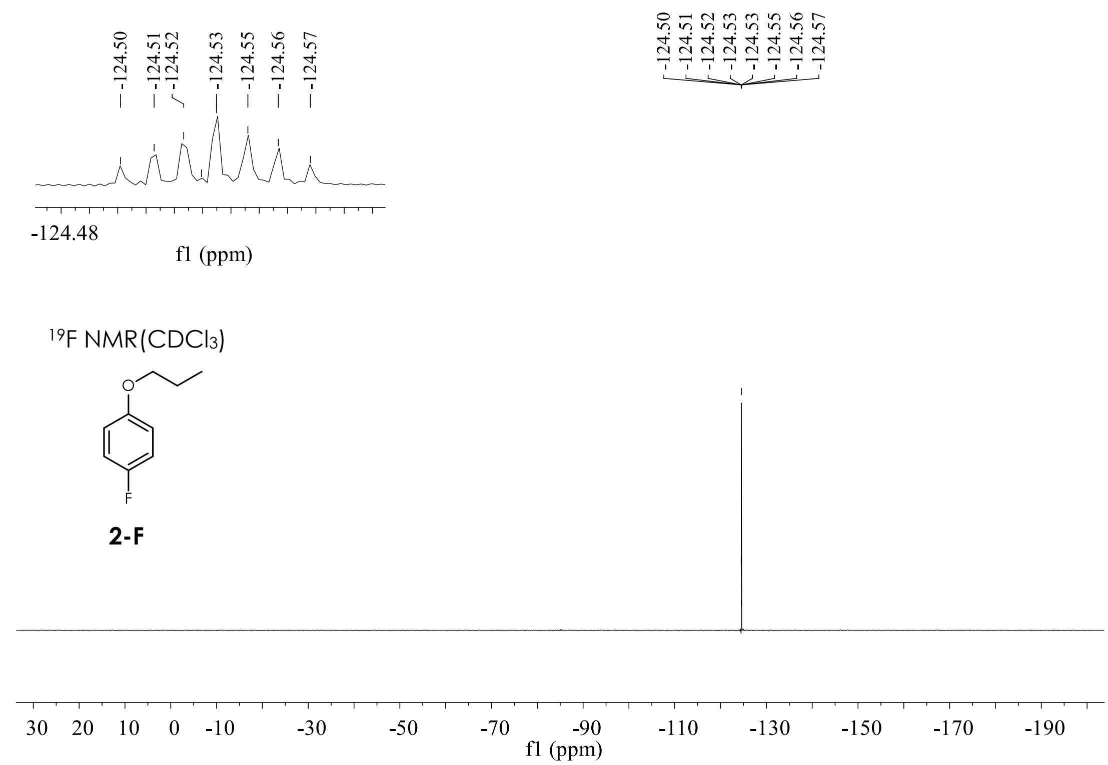
70
60
50
40
30
20
10
0
f1 (ppm)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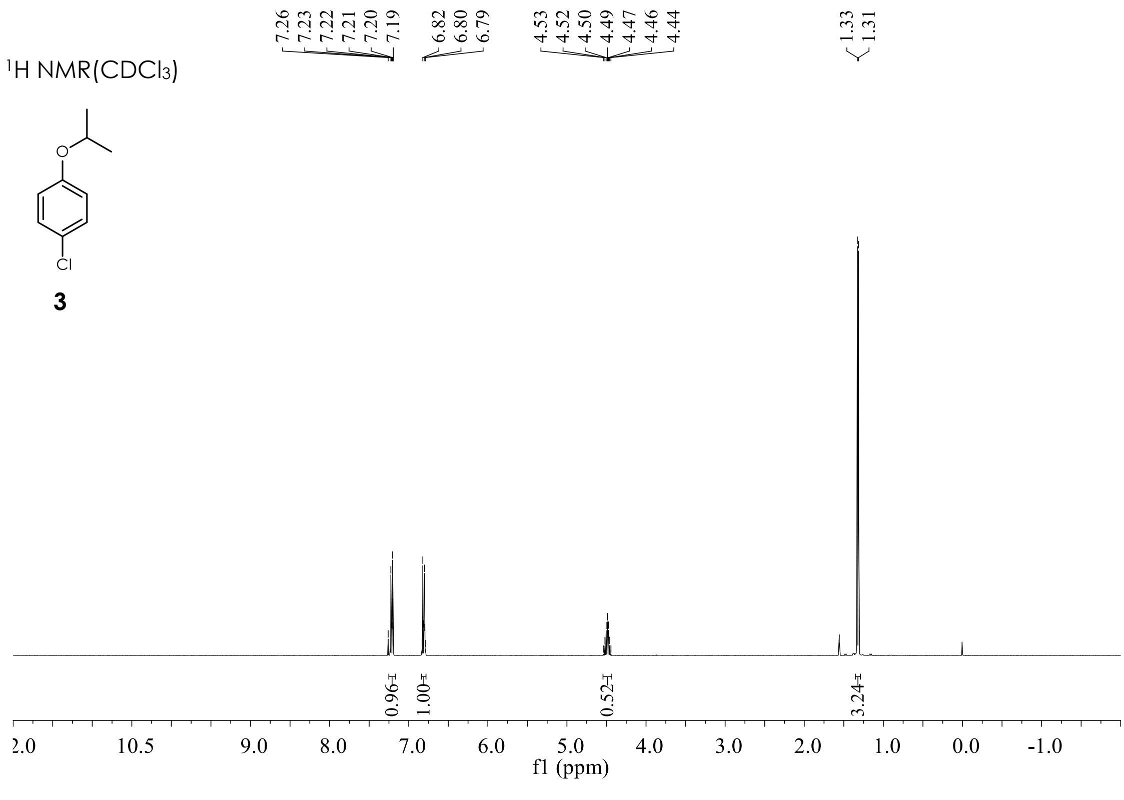
F
2-F
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)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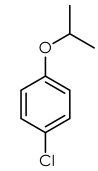
4.49
4.47
4.46
4.44
1.33
1.31
^{1}H NMR(CDCl$_3$)
O
Cl
3
0.96
1.00
0.52
3.24
2.0 10.5 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0
f1 (ppm)

^{13}C NMR($CDCl_3$)



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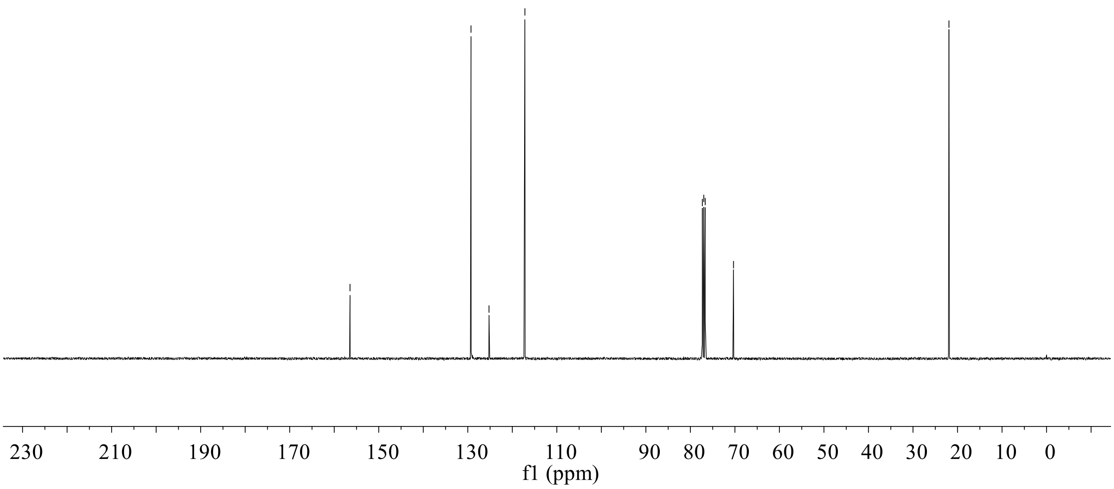
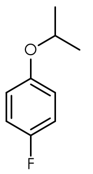
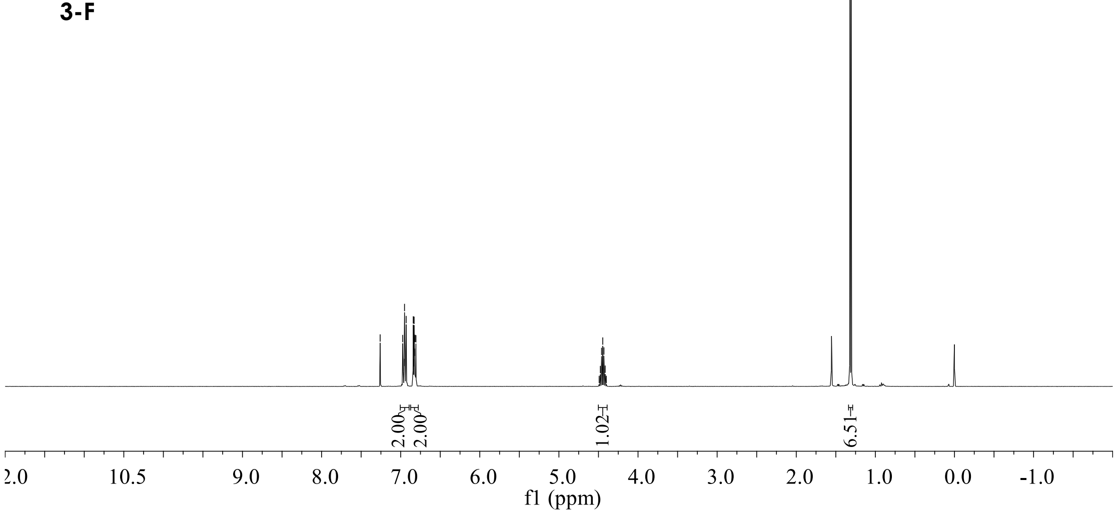


^{1}H NMR($CDCl_3$)

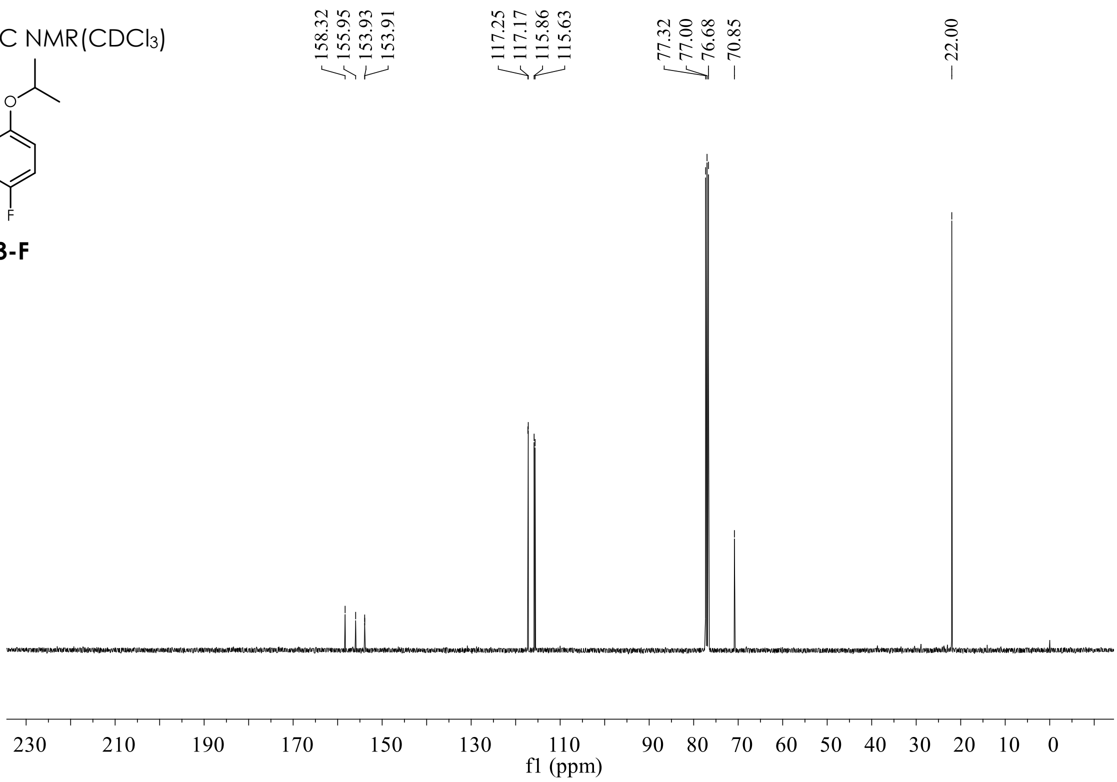


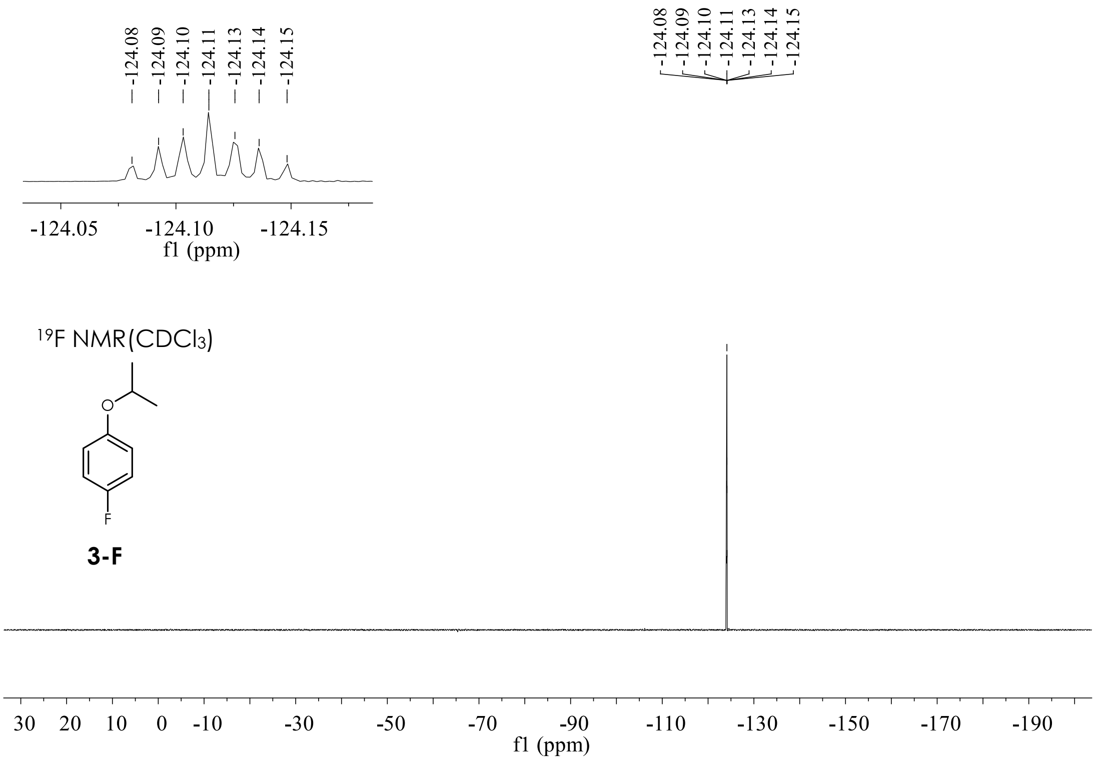
3-F



^{13}C NMR($CDCl_3$)

3-F

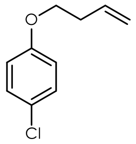




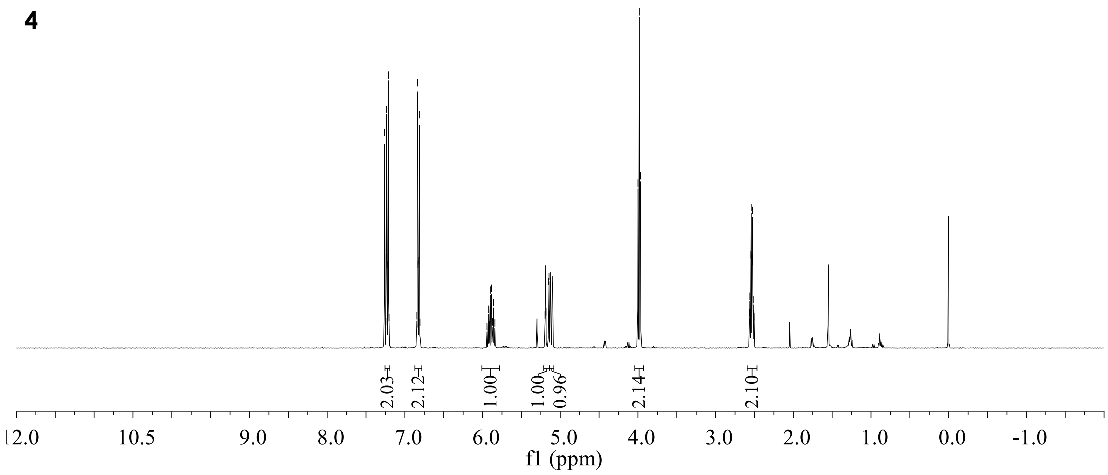
^{19}F NMR($CDCl_3$)

3-F

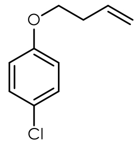
^{1}H NMR($CDCl_3$)



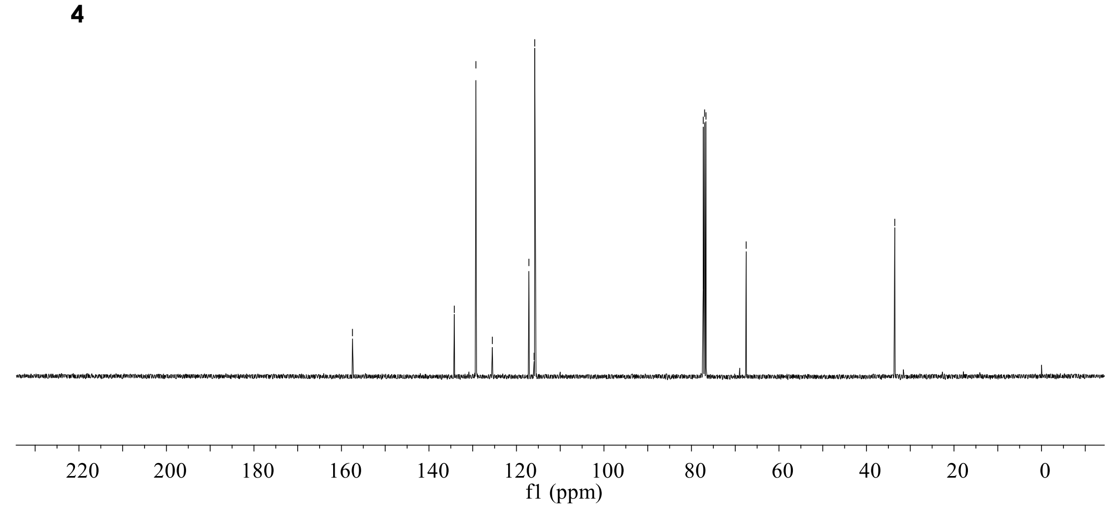
4



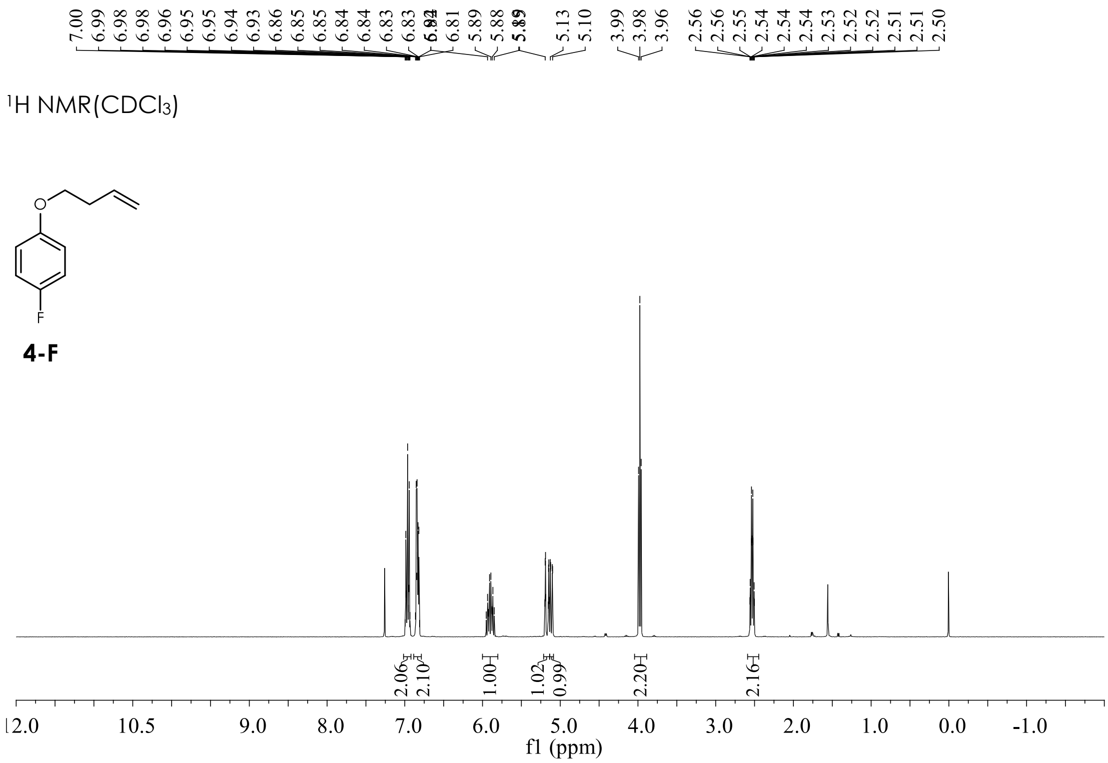
^{13}C NMR($CDCl_3$)



4

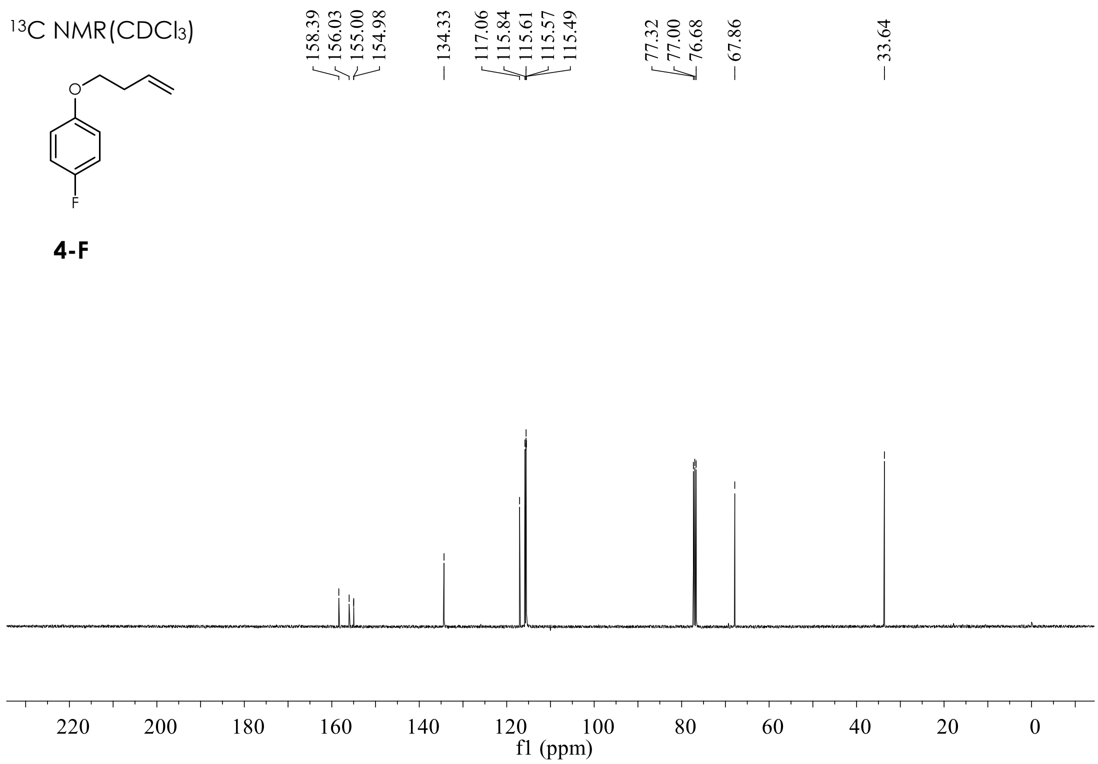


^1H NMR($CDCl_3$)

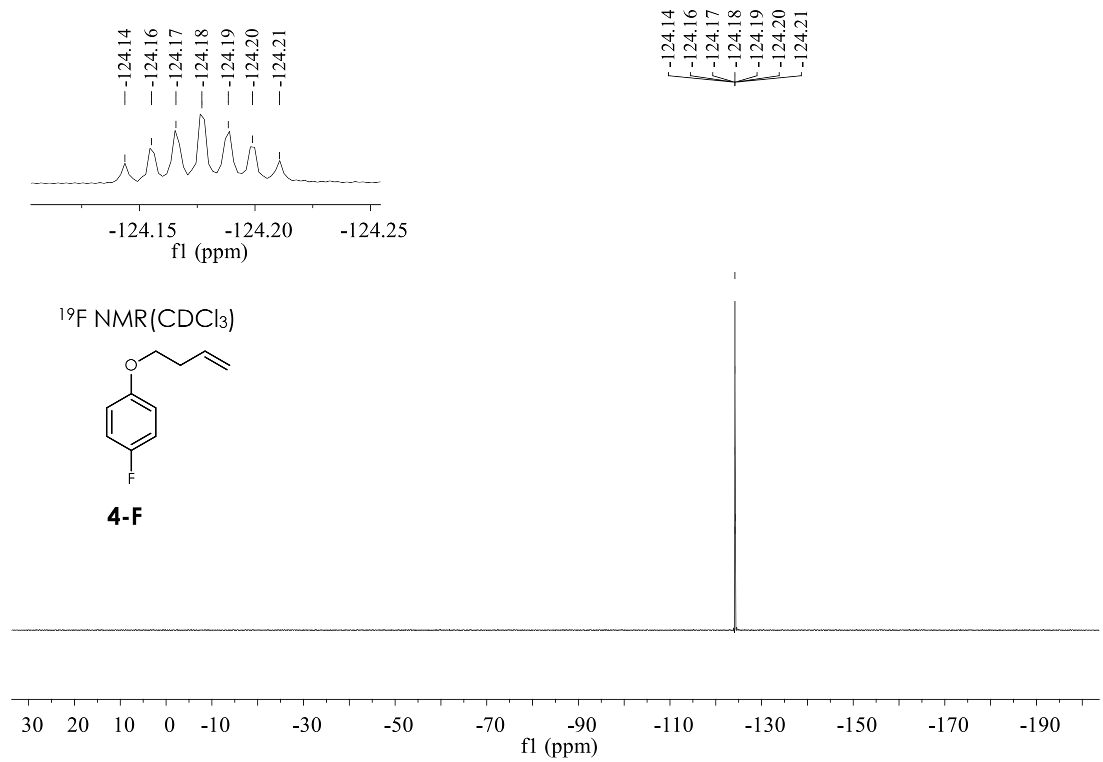


4-F

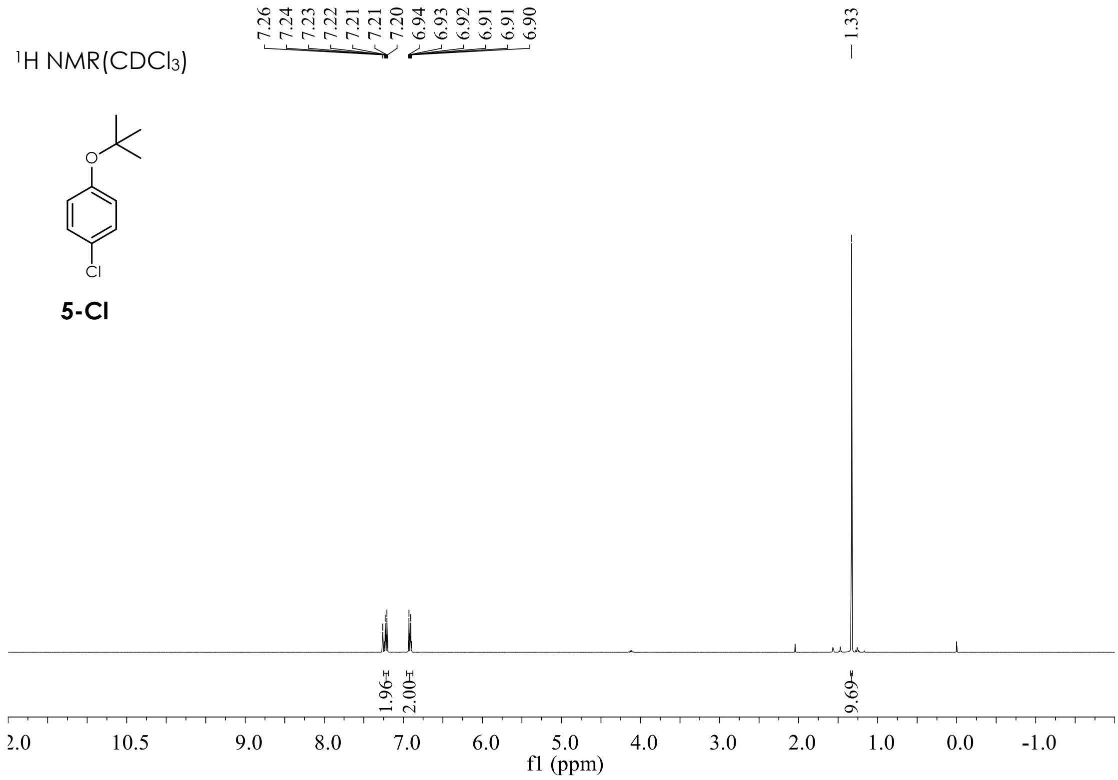
^{13}C NMR($CDCl_3$)



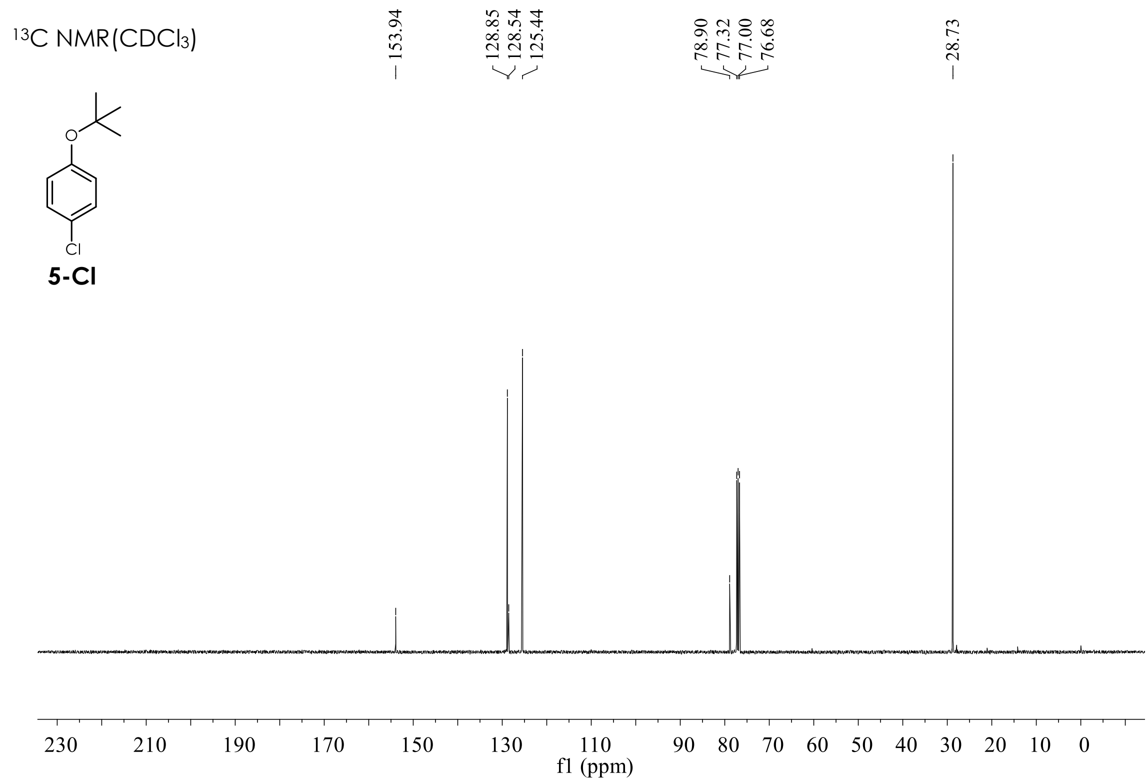
4-F



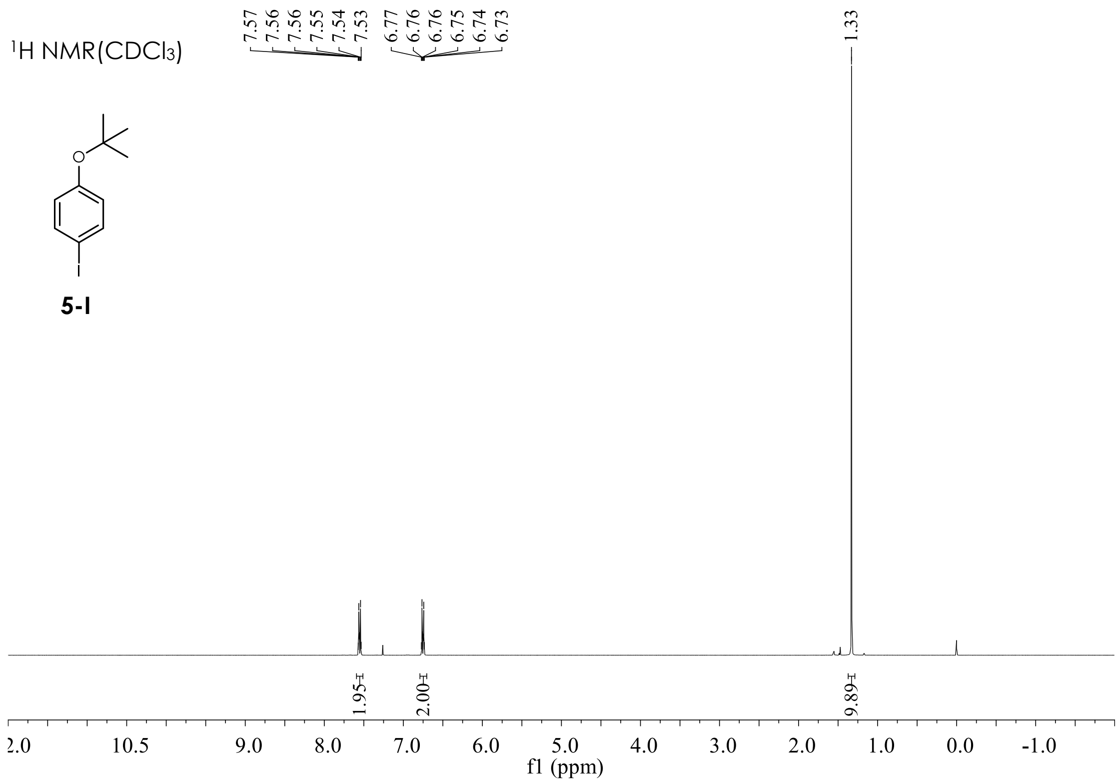
-124.14
-124.16
-124.17
-124.18
-124.19
-124.20
-124.21
-124.15 -124.20 -124.25
f1 (ppm)
^{19}F NMR($CDCl_3$)
O
F
4-F
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)



7.26
7.24
7.23
7.22
7.21
7.21
7.20
6.94
6.93
6.92
6.91
6.91
6.90
1.33
^1H NMR($CDCl_3$)
O
Cl
5-Cl
1.96
2.00
9.69
2.0 10.5 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0
f1 (ppm)

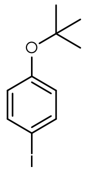


13C NMR(CDCl3)
153.94
128.85
128.54
125.44
78.90
77.32
77.00
76.68
28.73
O
Cl
5-Cl
230 210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

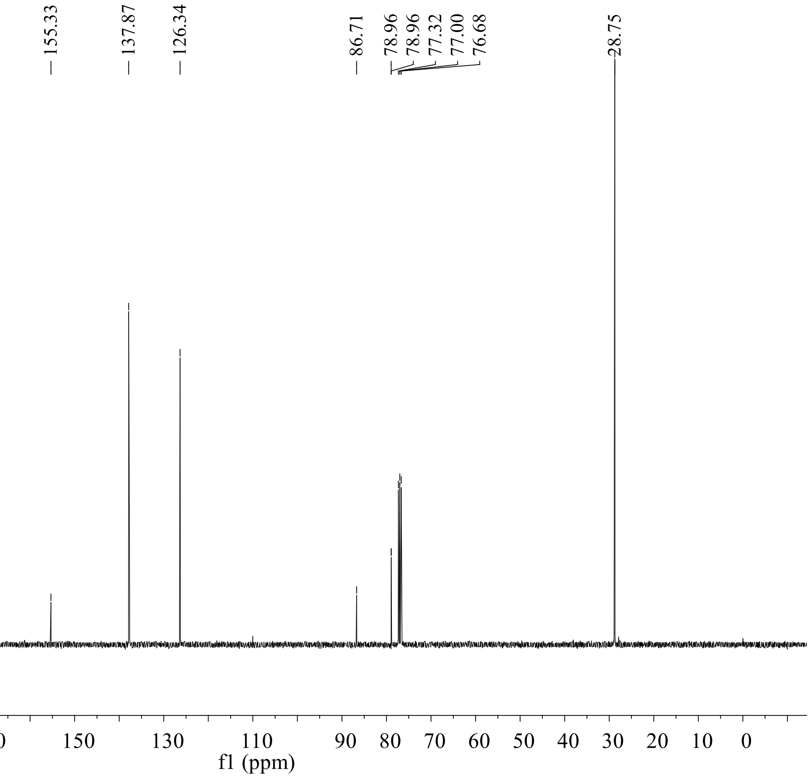


1H NMR(CDCl3)
7.57
7.56
7.56
7.55
7.54
7.53
6.77
6.76
6.76
6.75
6.74
6.73
1.33
O
I
5-I
1.95
2.00
9.89
2.0 10.5 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0
f1 (ppm)

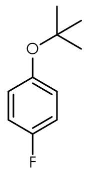
^{13}C NMR($CDCl_3$)



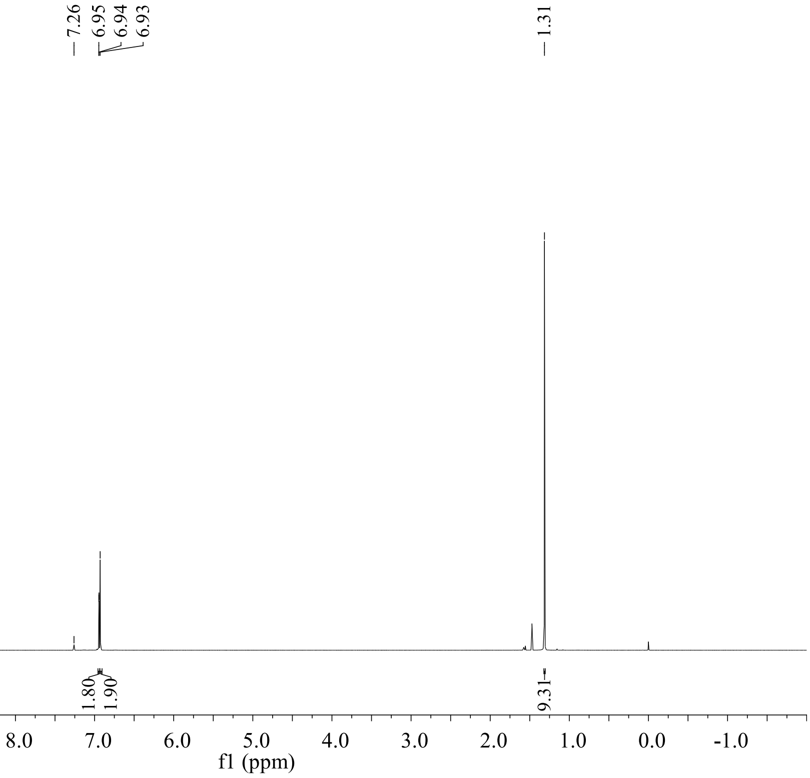
5-I

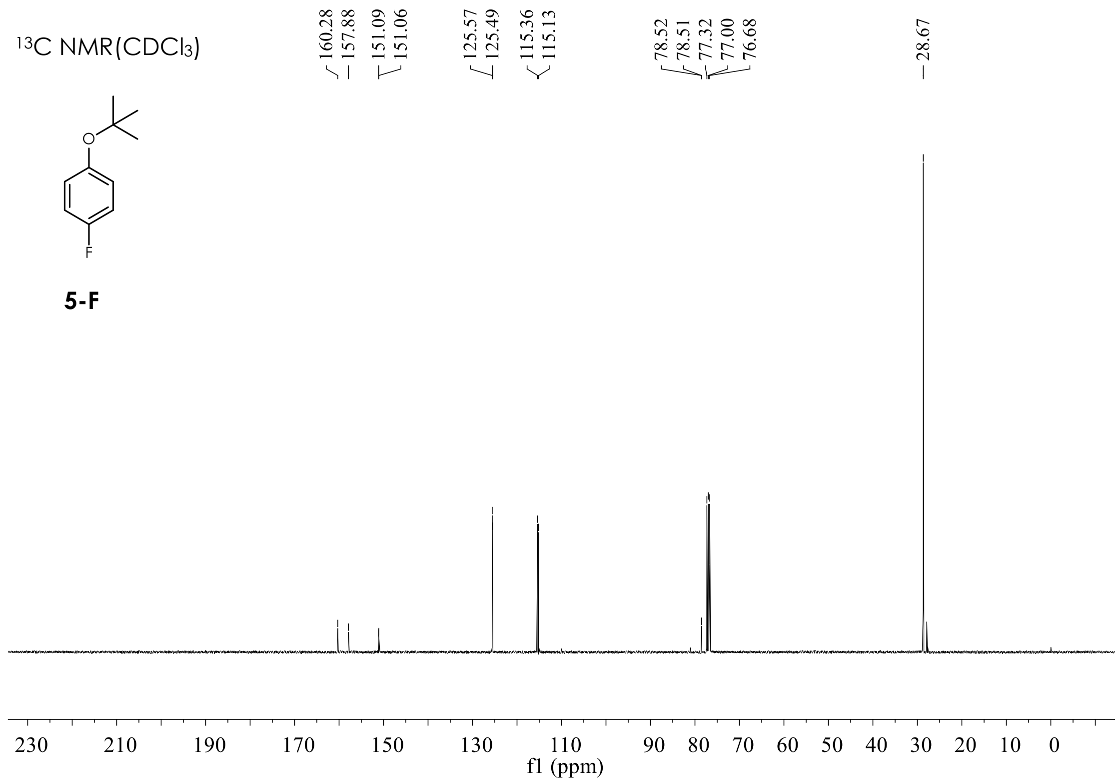


^{1}H NMR($CDCl_3$)

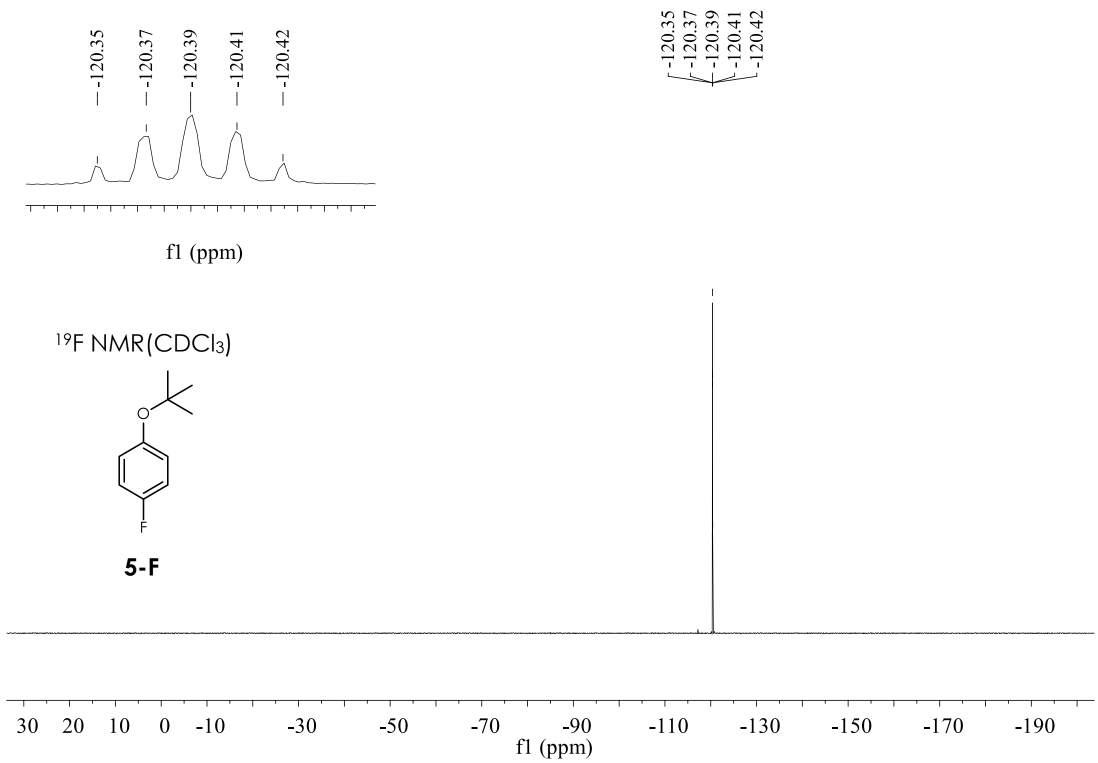


5-F



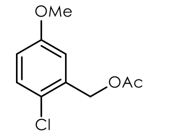


13C NMR(CDCl3)
5-F
160.28
157.88
151.09
151.06
125.57
125.49
115.36
115.13
78.52
78.51
77.32
77.00
76.68
28.67
230 210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



-120.35
-120.37
-120.39
-120.41
-120.42
f1 (ppm)
19F NMR(CDCl3)
5-F
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)

^1H NMR($CDCl_3$)



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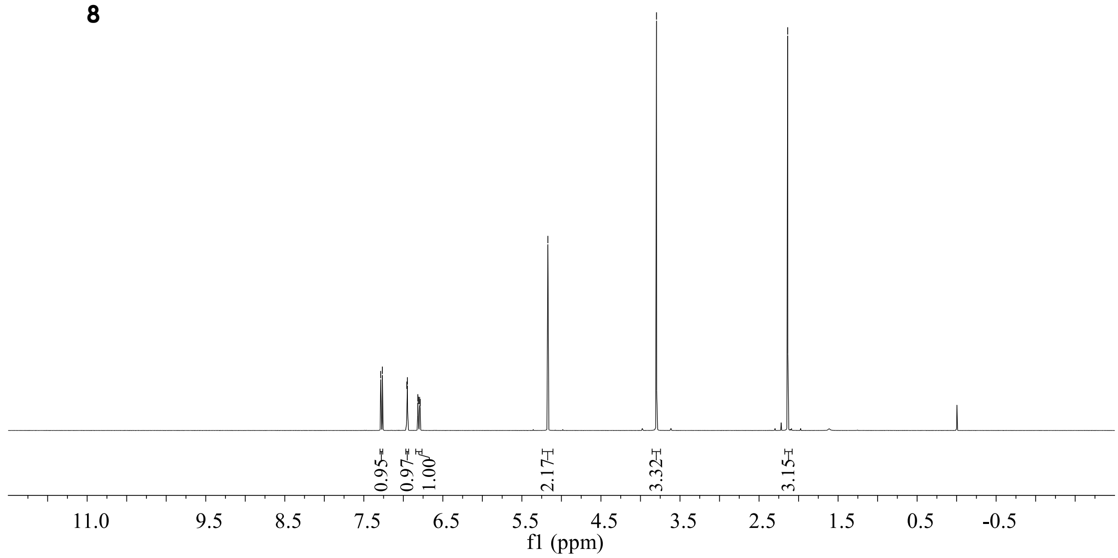
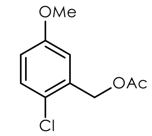
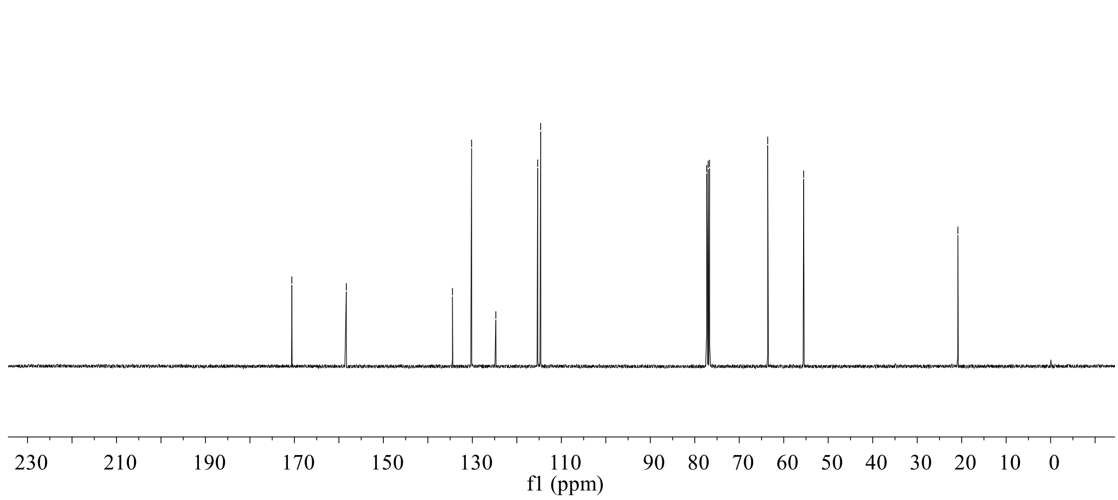
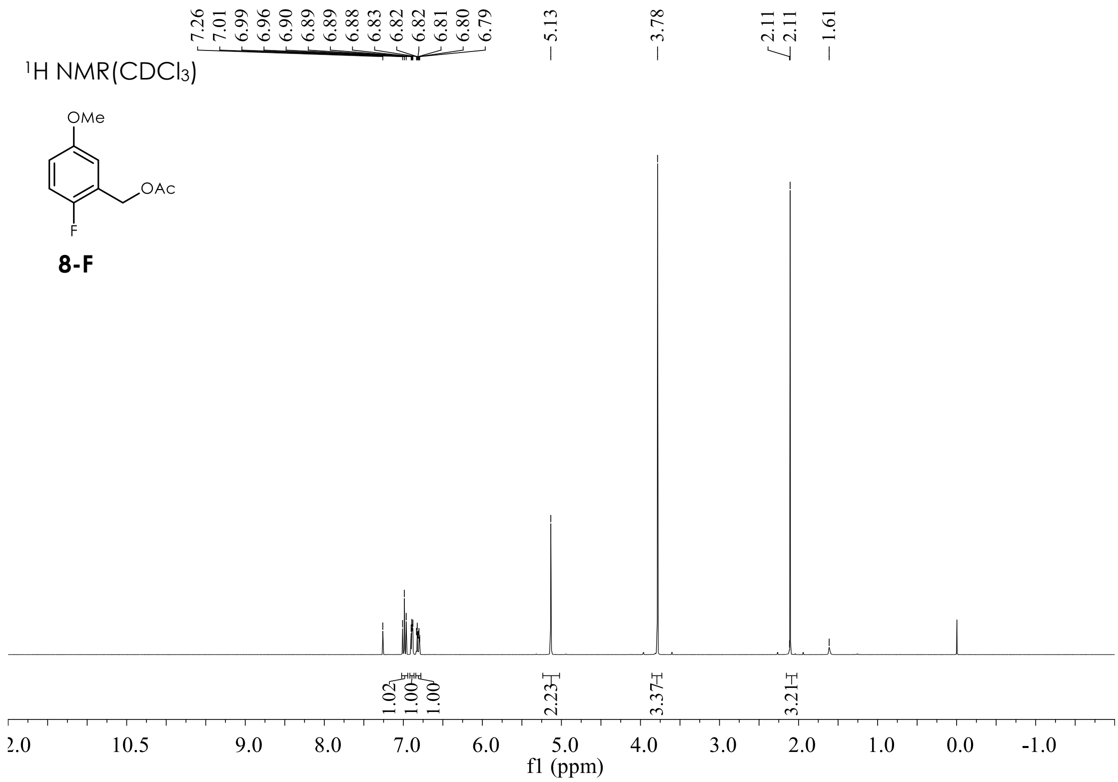


^{13}C NMR($CDCl_3$)



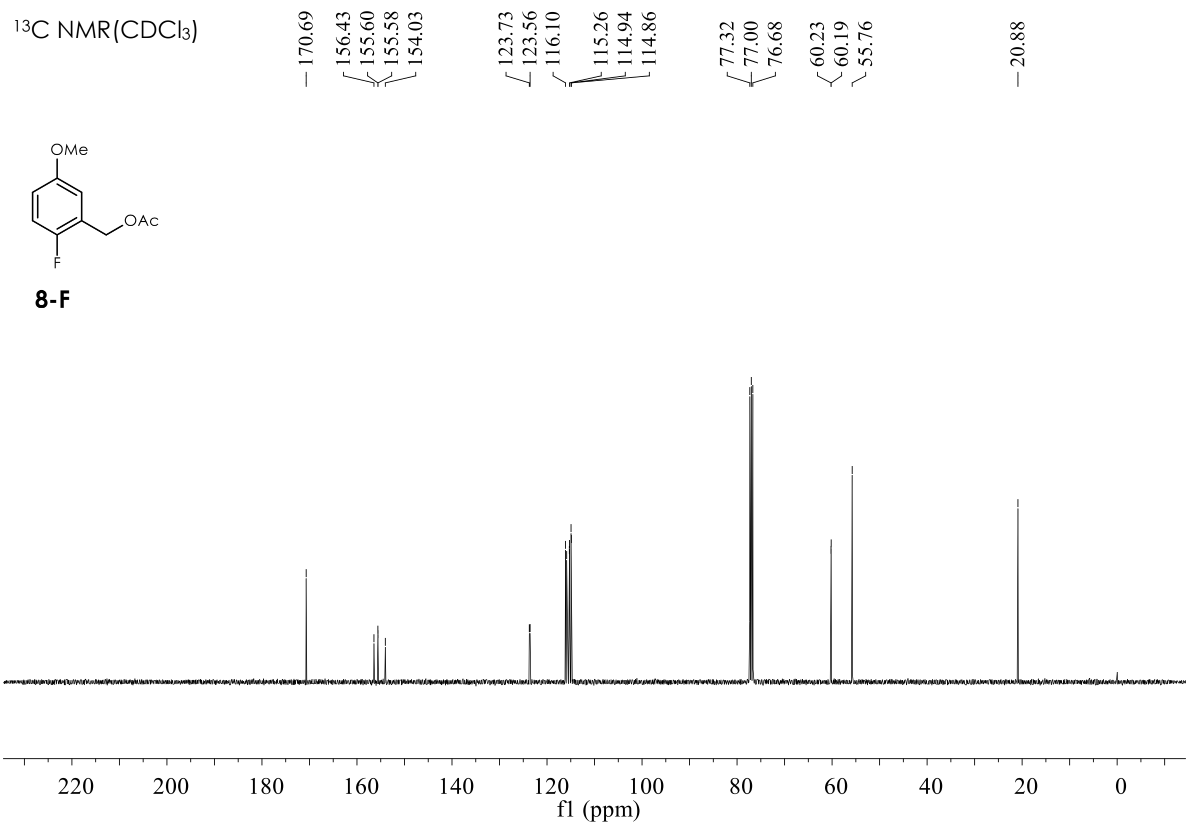
8





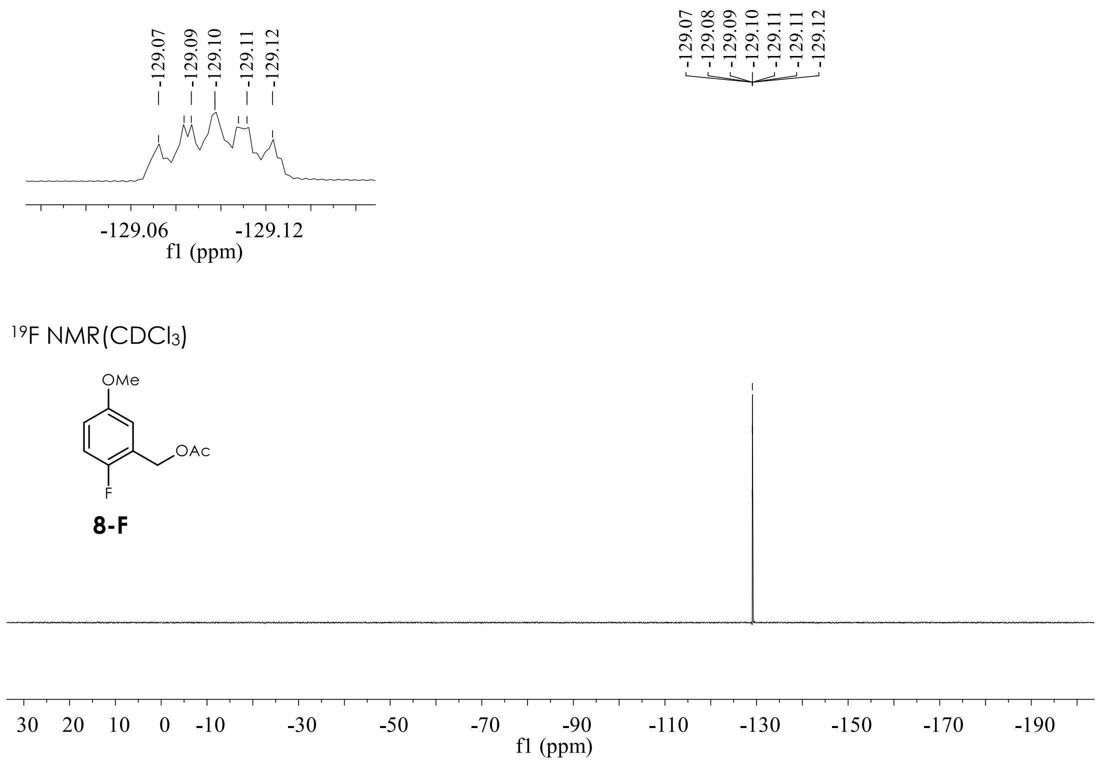
^{1}H NMR(CDCl$_3$)
7.26
7.01
6.99
6.96
6.90
6.89
6.89
6.88
6.83
6.82
6.82
6.81
6.80
6.79
5.13
3.78
2.11
2.11
1.61
OMe
OAc
F
1.02
1.00
1.00
2.23
3.37
3.21
f1 (ppm)

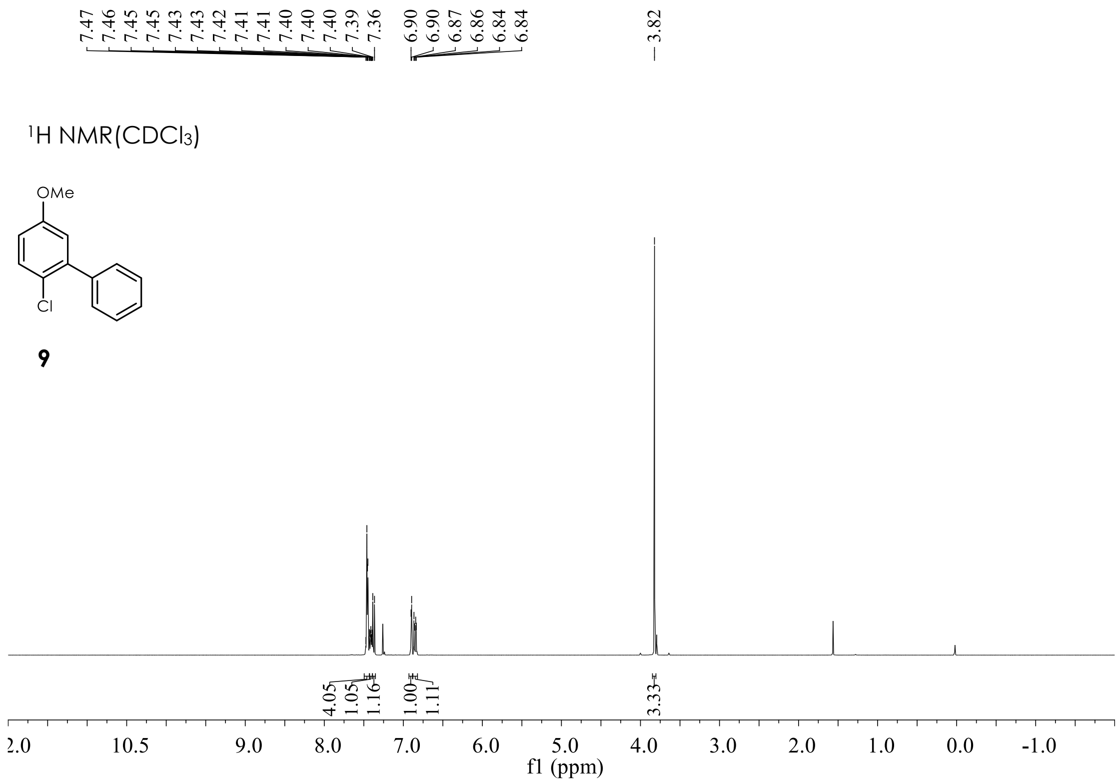
8-F



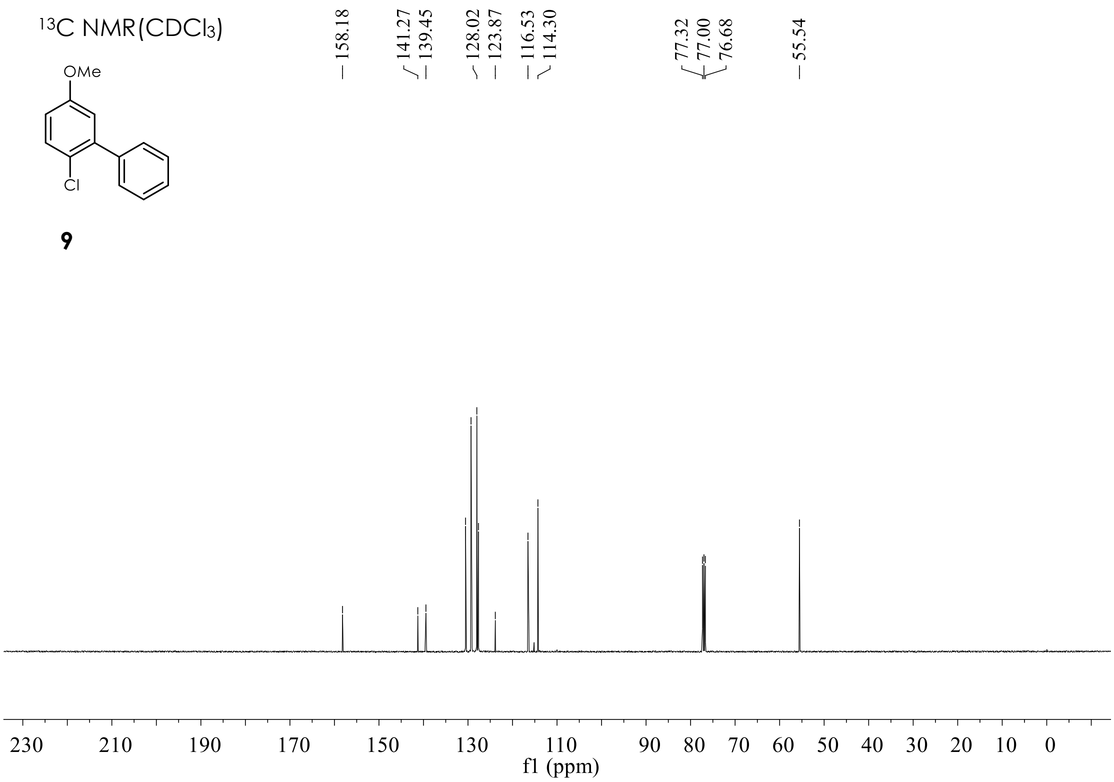
^{13}C NMR(CDCl$_3$)
170.69
156.43
155.60
155.58
154.03
123.73
123.56
116.10
115.26
114.94
114.86
77.32
77.00
76.68
60.23
60.19
55.76
20.88
OMe
OAc
F
f1 (ppm)

8-F


-129.07
-129.09
-129.10
-129.11
-129.12
-129.06
-129.12
f1 (ppm)
-129.07
-129.08
-129.09
-129.10
-129.11
-129.11
-129.12
^{19}F NMR(CDCl3)
OMe
OAc
F
8-F
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)

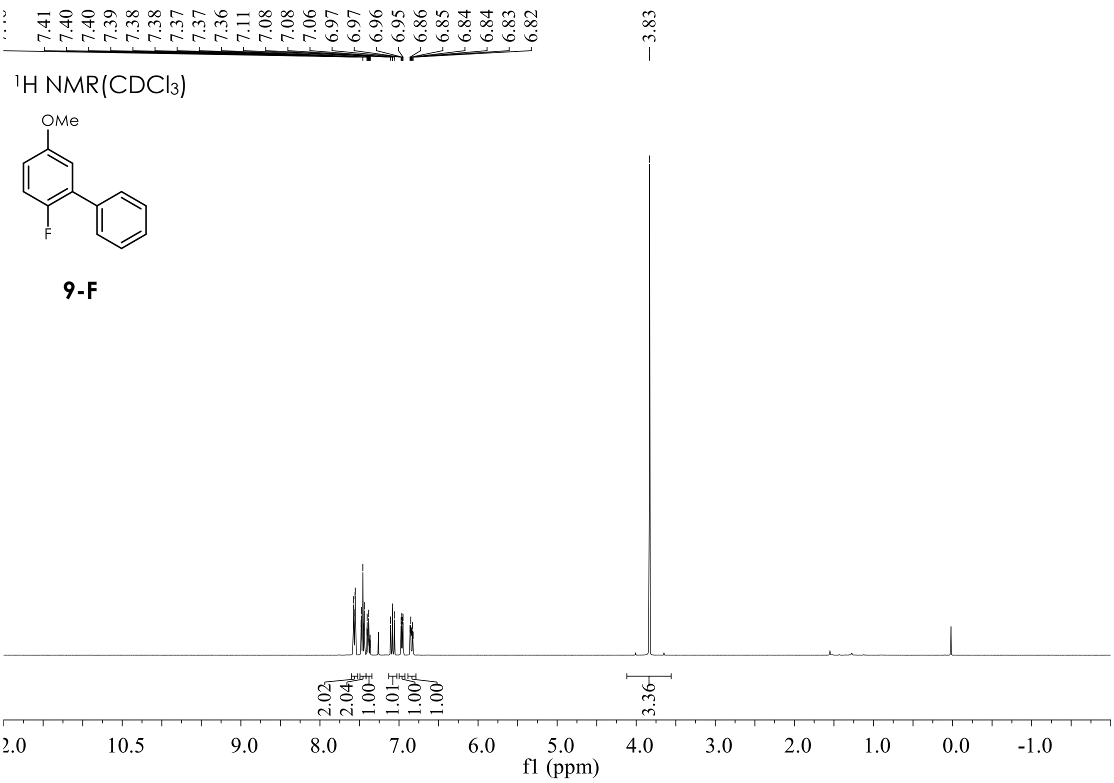

7.47
7.46
7.45
7.45
7.43
7.43
7.42
7.41
7.41
7.40
7.40
7.40
7.39
7.36
6.90
6.90
6.87
6.86
6.84
6.84
3.82
^{1}H NMR(CDCl3)
OMe
Cl
9
4.05
1.05
1.16
1.00
1.11
3.33
2.0 10.5 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0
f1 (ppm)

^{13}C NMR($CDCl_3$)

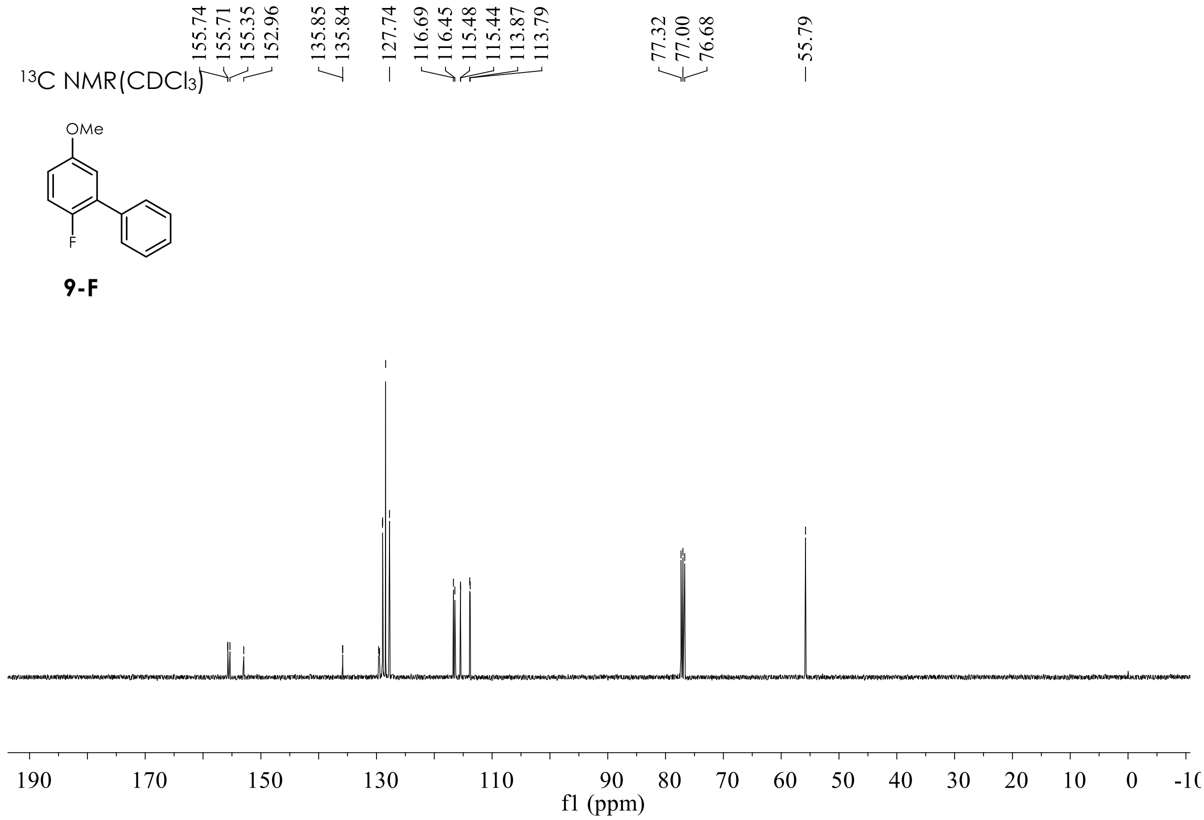


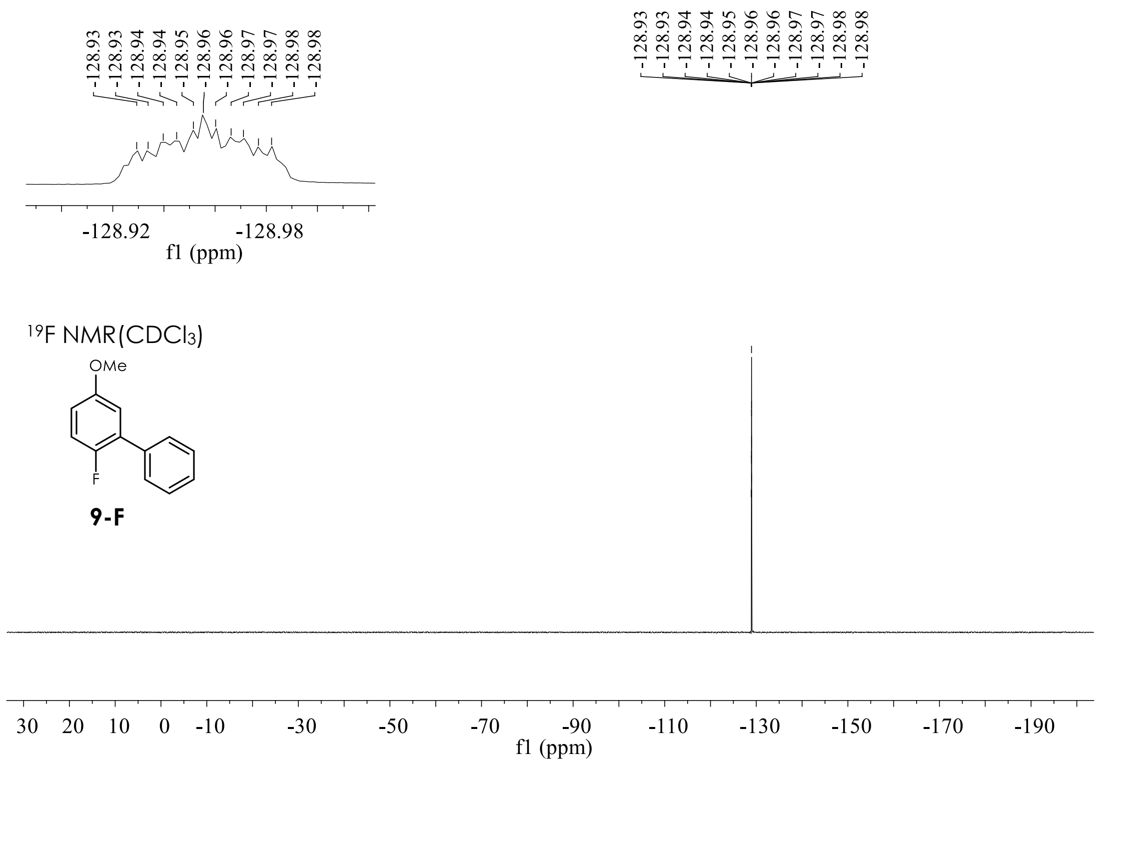
9

^{1}H NMR($CDCl_3$)

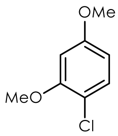


9-F

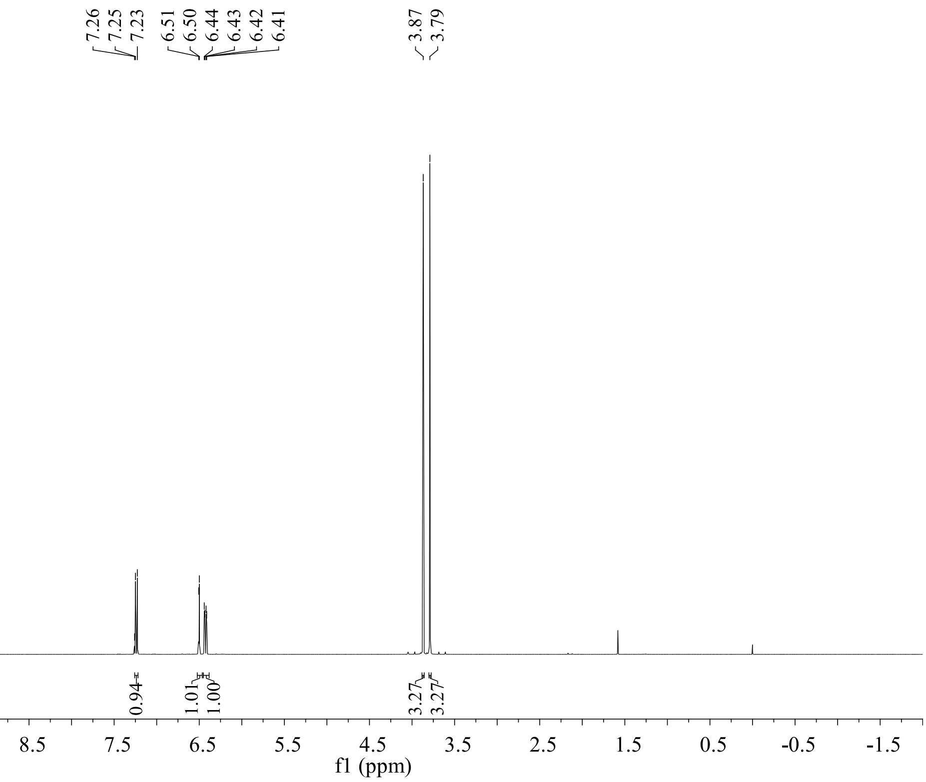

13C NMR(CDCl3)
155.74
155.71
155.35
152.96
135.85
135.84
127.74
116.69
116.45
115.48
115.44
113.87
113.79
77.32
77.00
76.68
55.79
OMe
F
9-F
190 170 150 130 110 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-128.93
-128.93
-128.94
-128.94
-128.95
-128.96
-128.96
-128.97
-128.97
-128.98
-128.98
-128.92 -128.98
f1 (ppm)
19F NMR(CDCl3)
OMe
F
9-F
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)

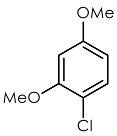
^1H NMR($CDCl_3$)



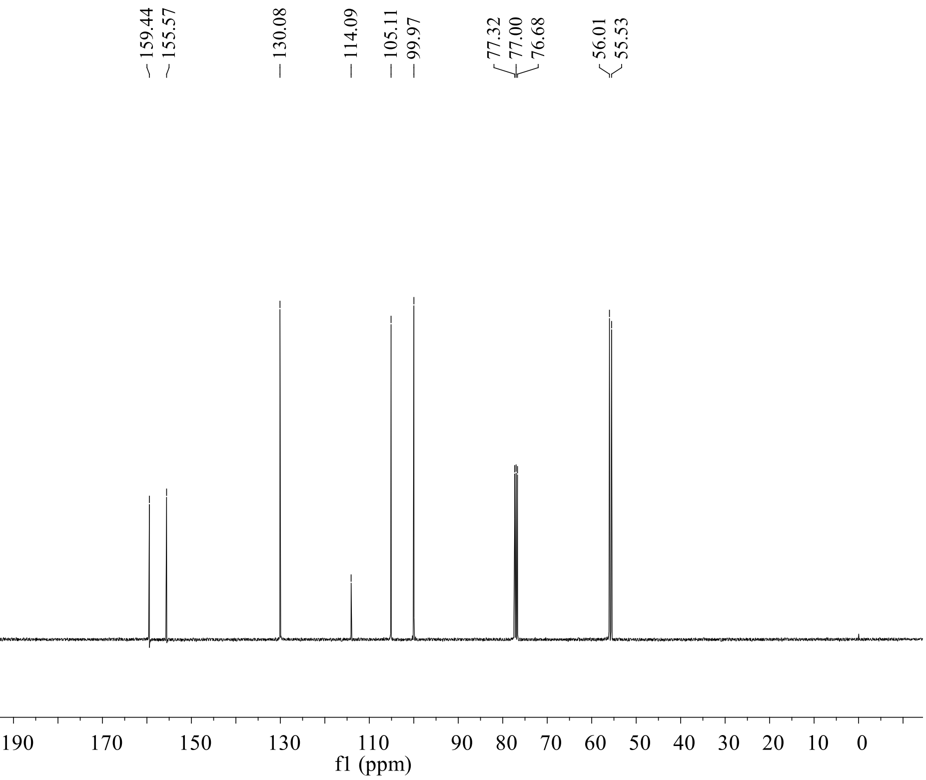
10-Cl



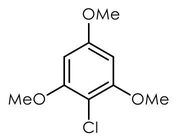
^{13}C NMR($CDCl_3$)



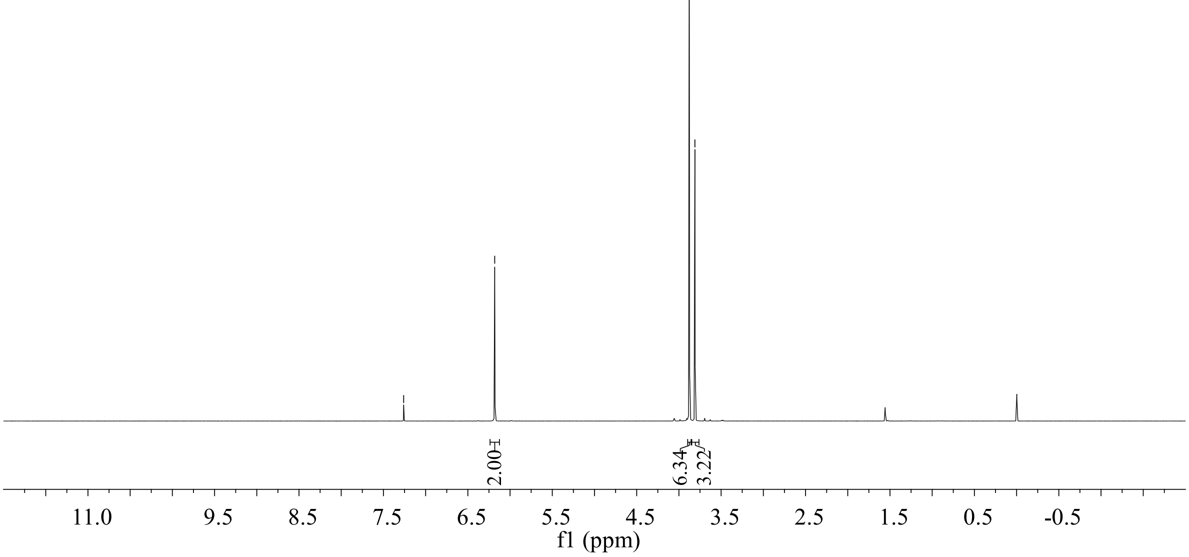
10-Cl



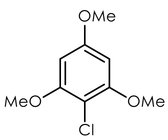
^{1}H NMR($CDCl_3$)



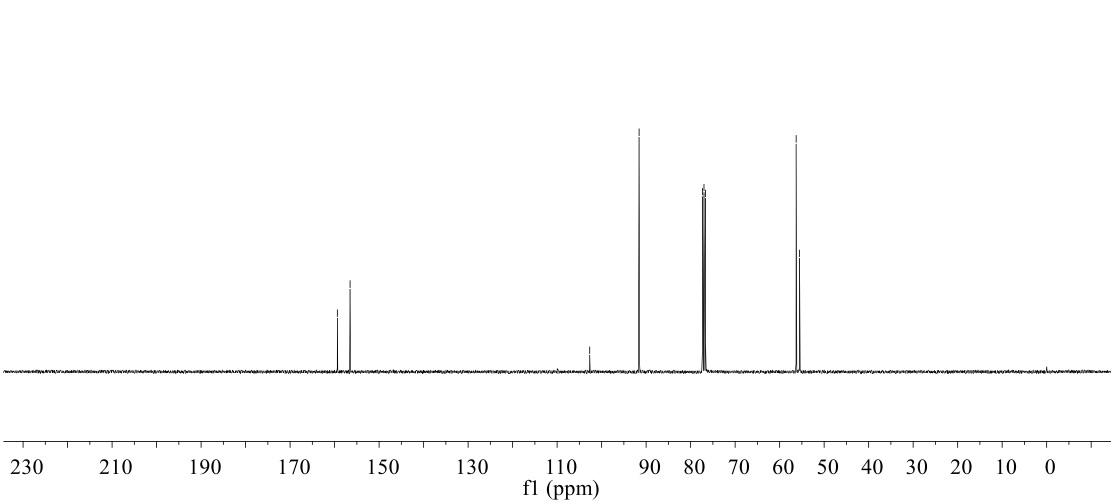
11



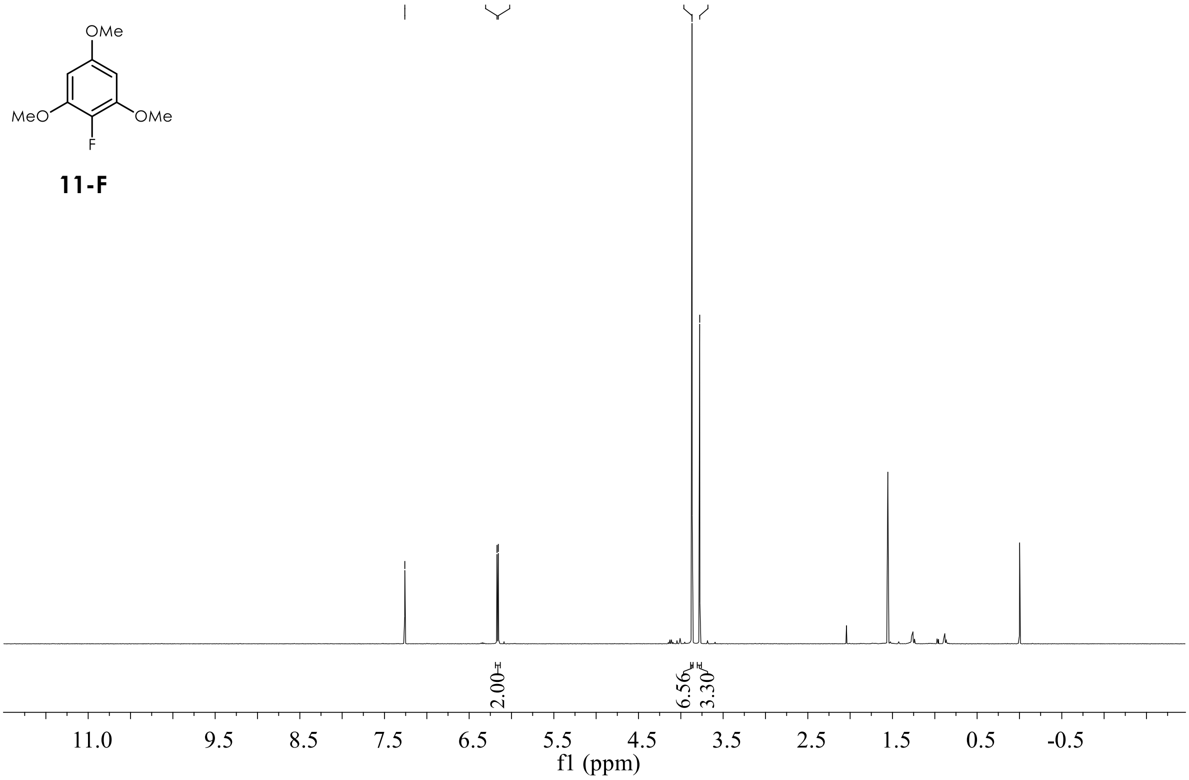
^{13}C NMR($CDCl_3$)



11

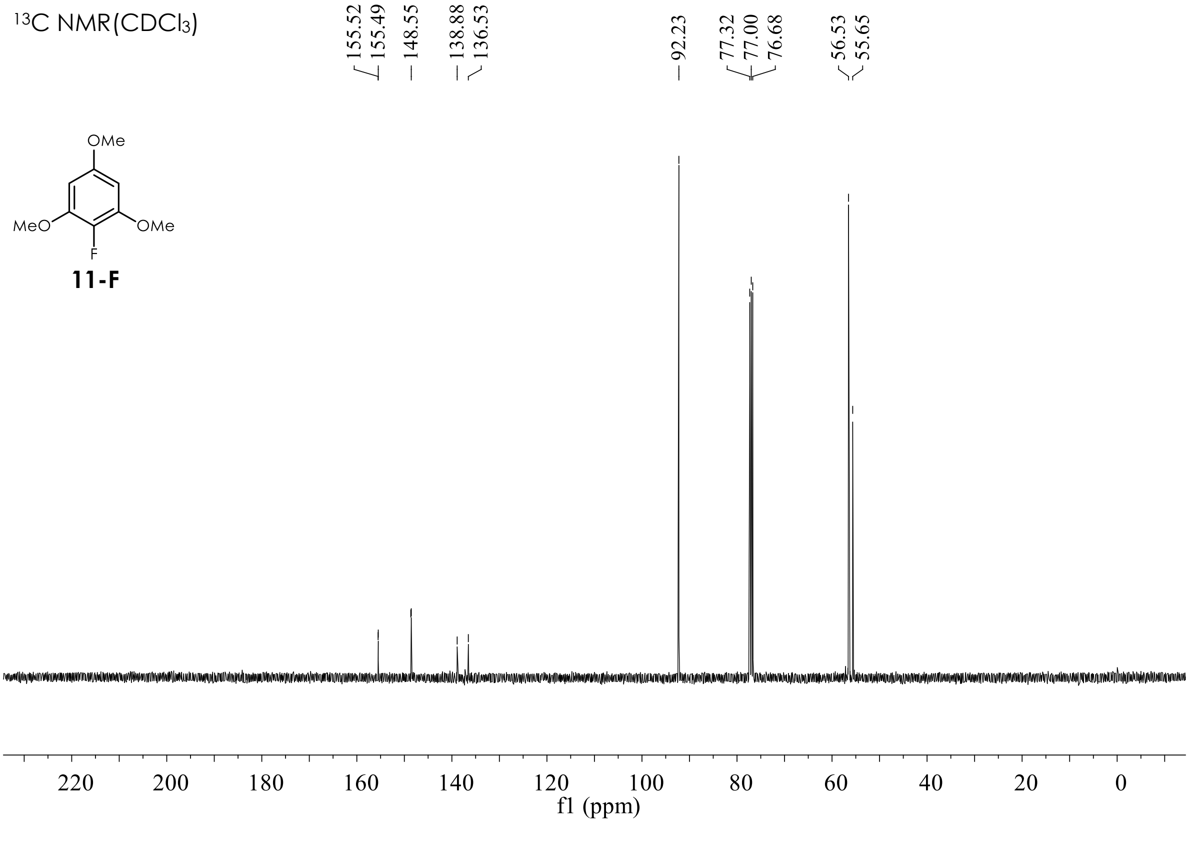


^{1}H NMR($CDCl_3$)

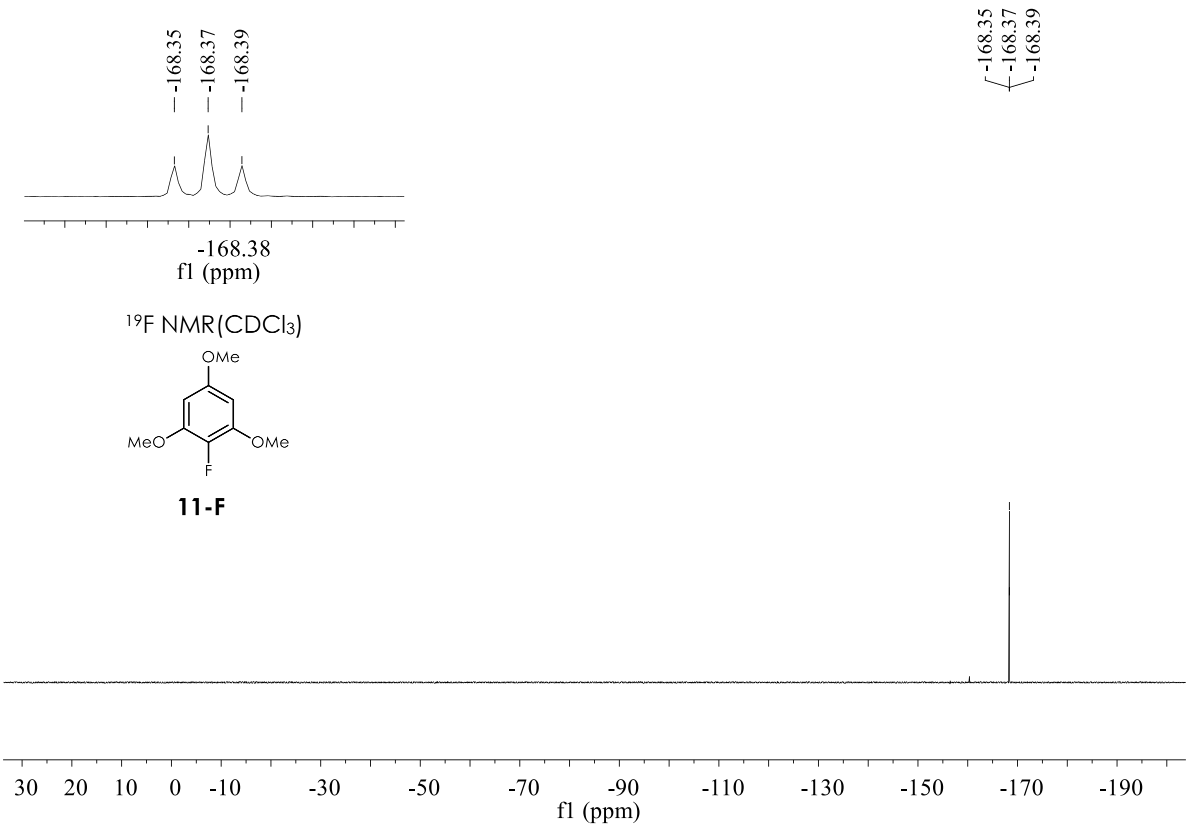


11-F

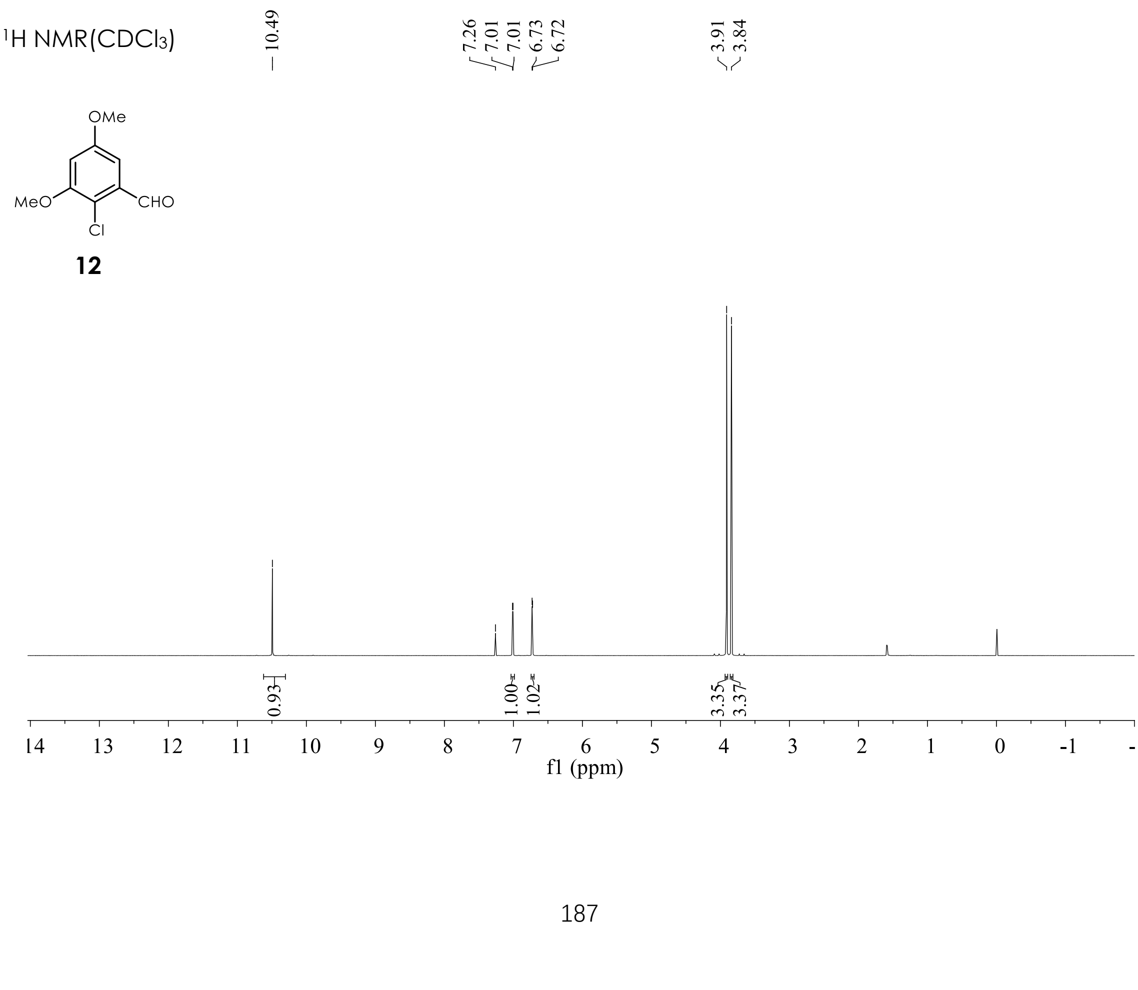
^{13}C NMR($CDCl_3$)



11-F

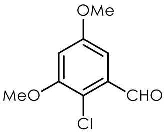

-168.35
-168.37
-168.39
-168.38
f1 (ppm)
19F NMR(CDCl3)
OMe
MeO
OMe
F
-168.35
-168.37
-168.39
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)

11-F

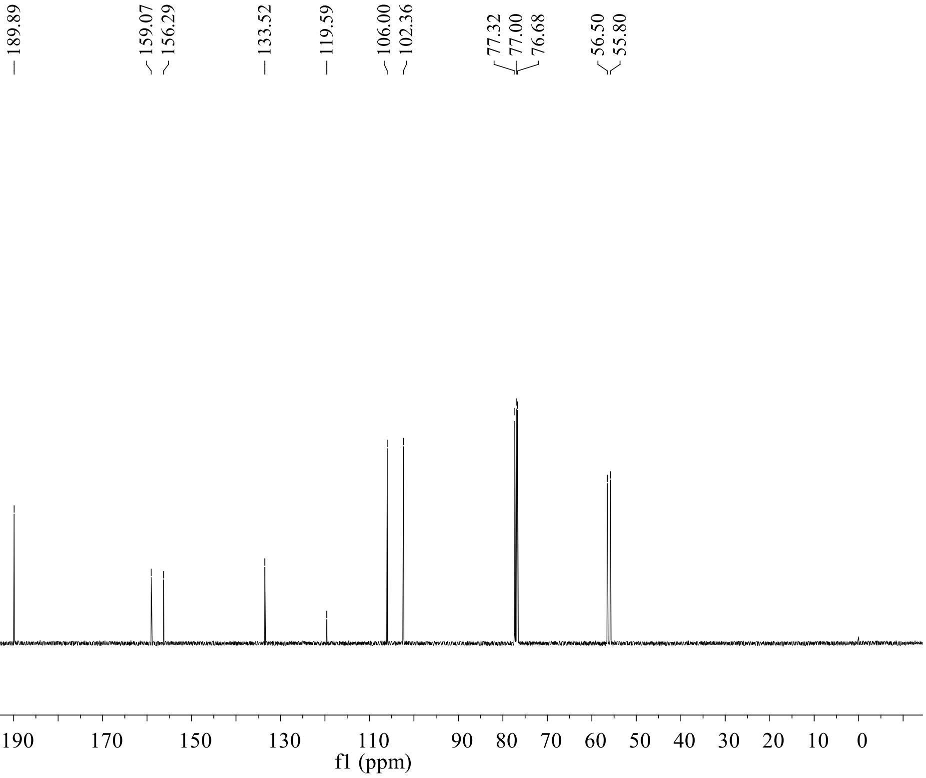

1H NMR(CDCl3)
10.49
7.26
7.01
7.01
6.73
6.72
3.91
3.84
OMe
MeO
CHO
Cl
0.93
1.00
1.02
3.35
3.37
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)

12

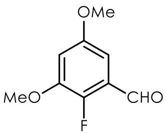
^{13}C NMR($CDCl_3$)



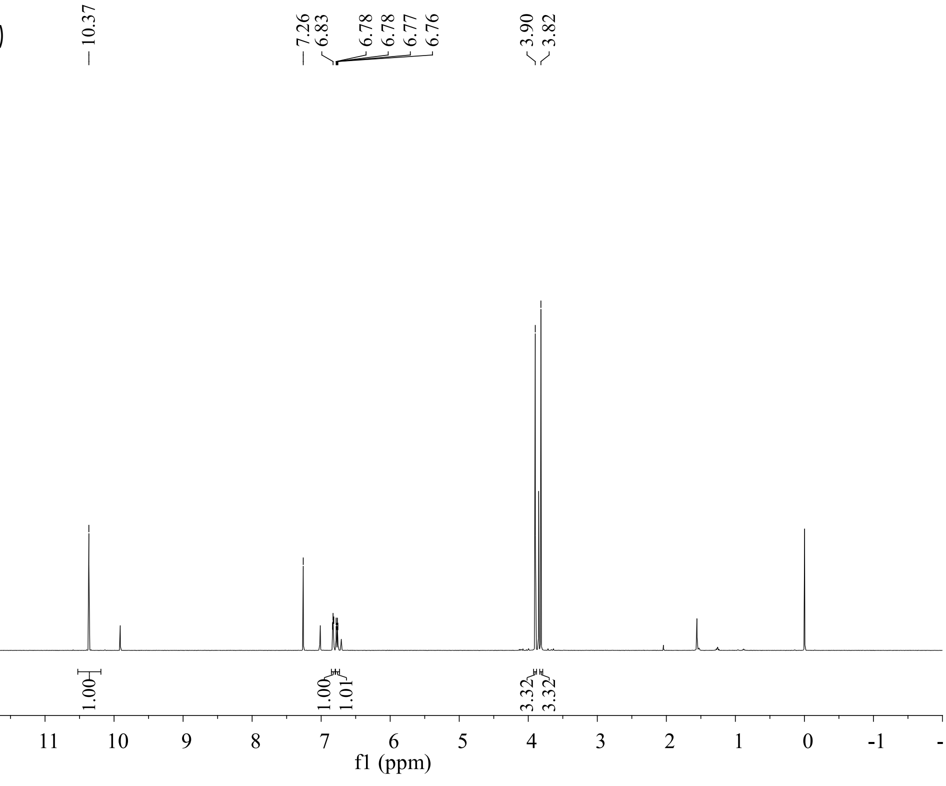
12

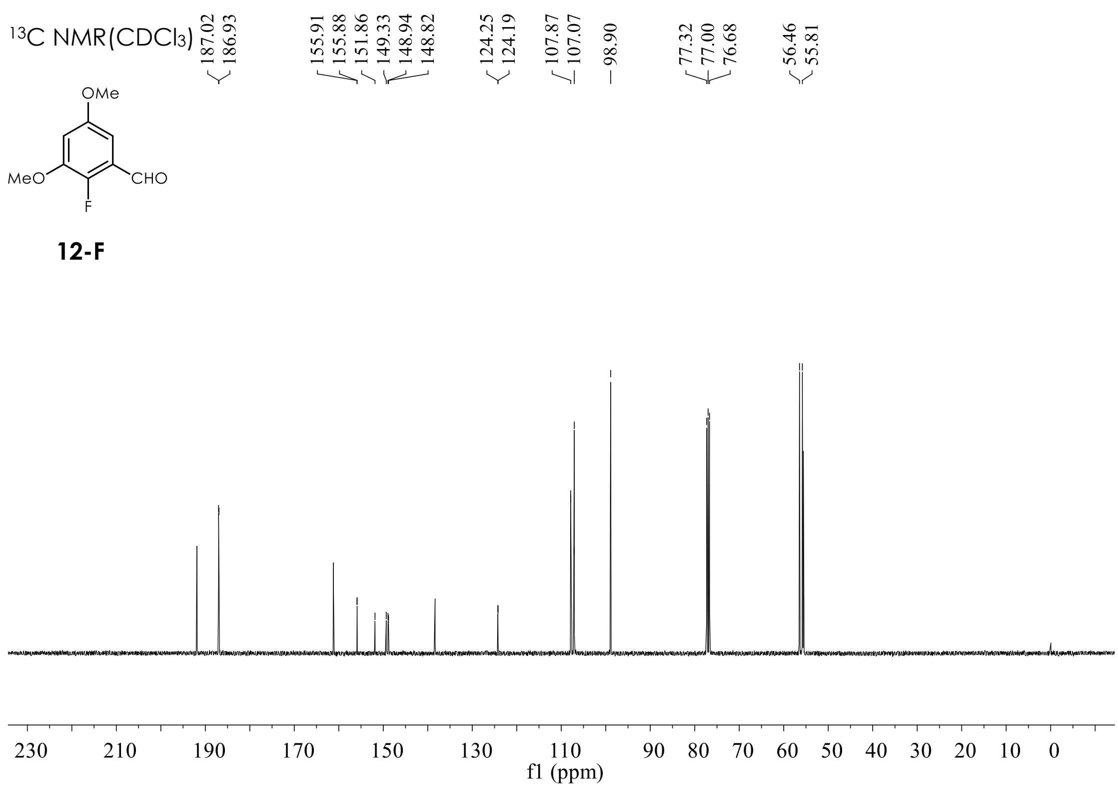


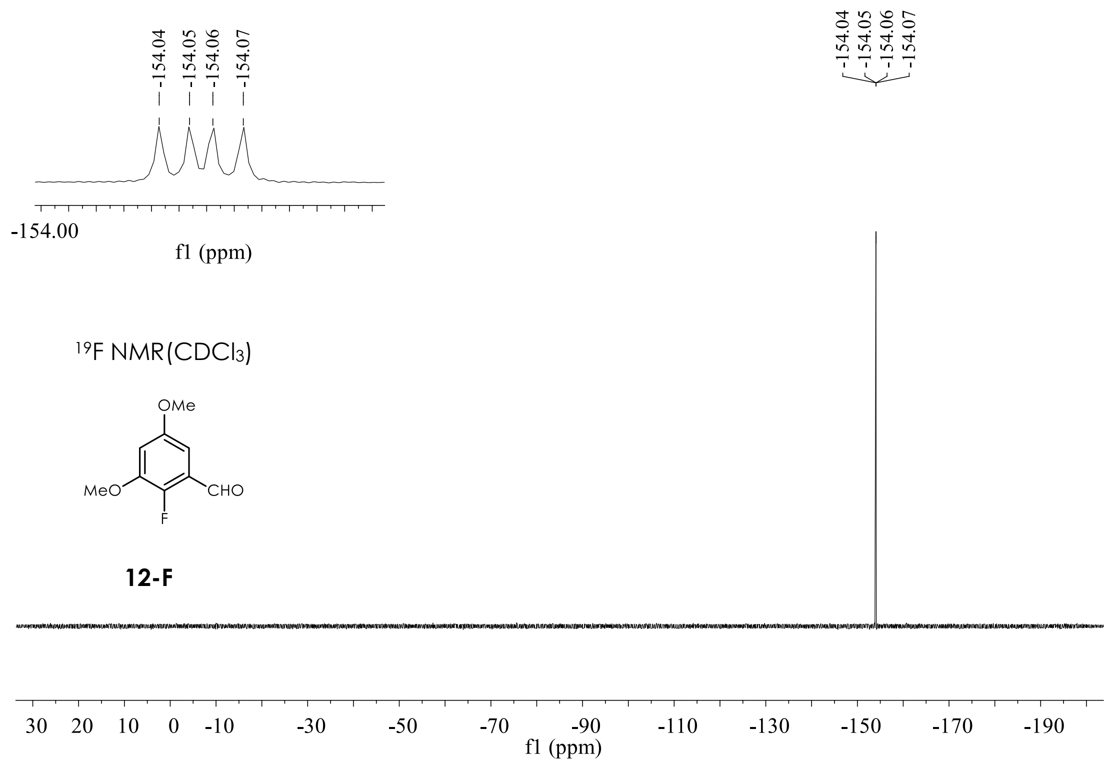
^{1}H NMR($CDCl_3$)



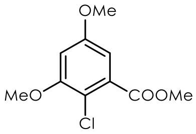
12-F



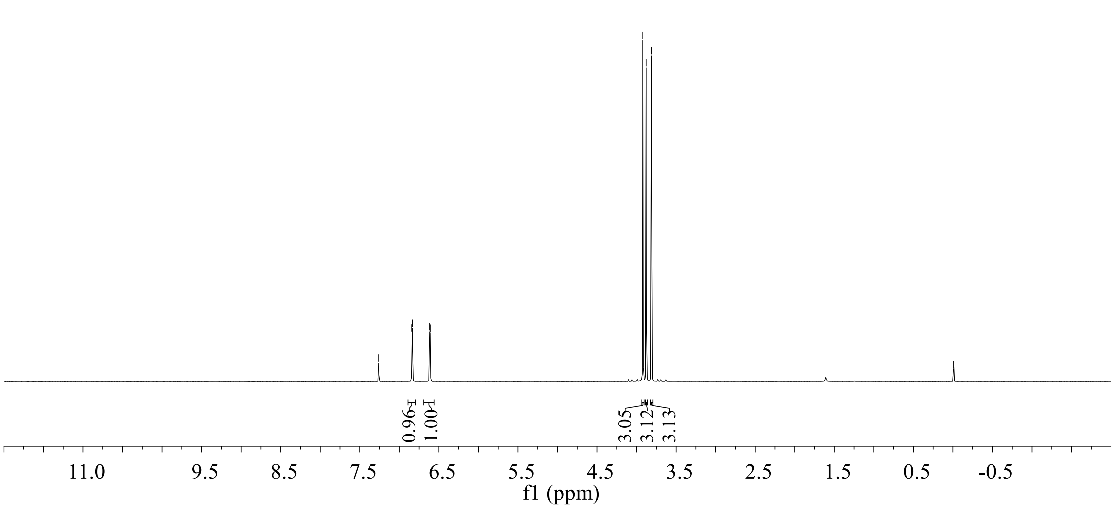

13C NMR(CDCl3)
187.02
186.93
155.91
155.88
151.86
149.33
148.94
148.82
124.25
124.19
107.87
107.07
98.90
77.32
77.00
76.68
56.46
55.81
OMe
MeO
CHO
F
12-F
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-154.04
-154.05
-154.06
-154.07
-154.00
f1 (ppm)
19F NMR(CDCl3)
OMe
MeO
CHO
F
12-F
30
20
10
0
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
f1 (ppm)

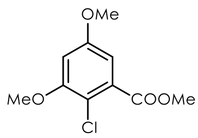
[1]H NMR($CDCl_3$)



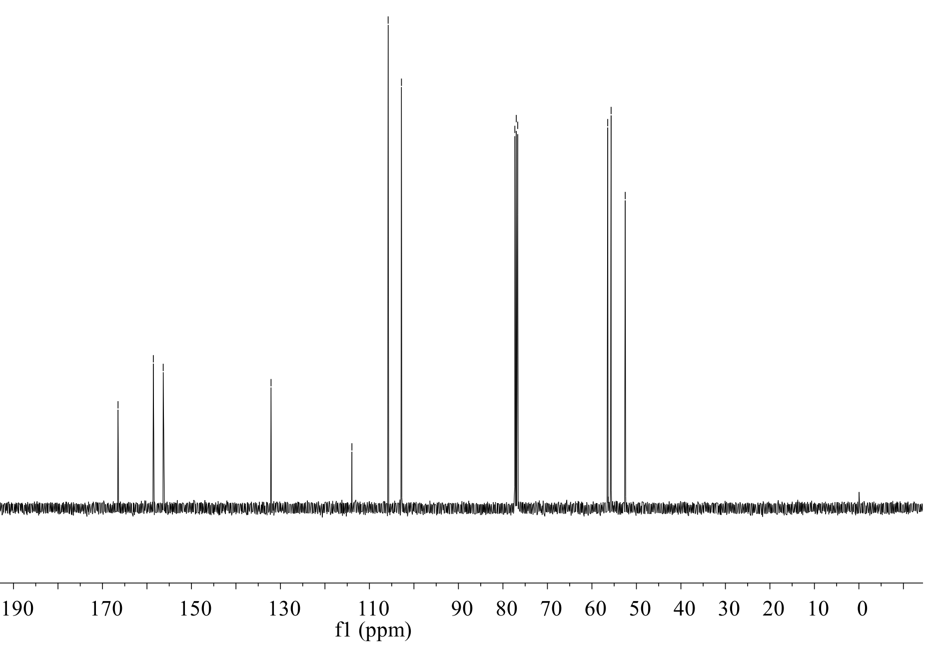
13



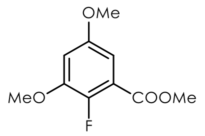
[13]C NMR($CDCl_3$)



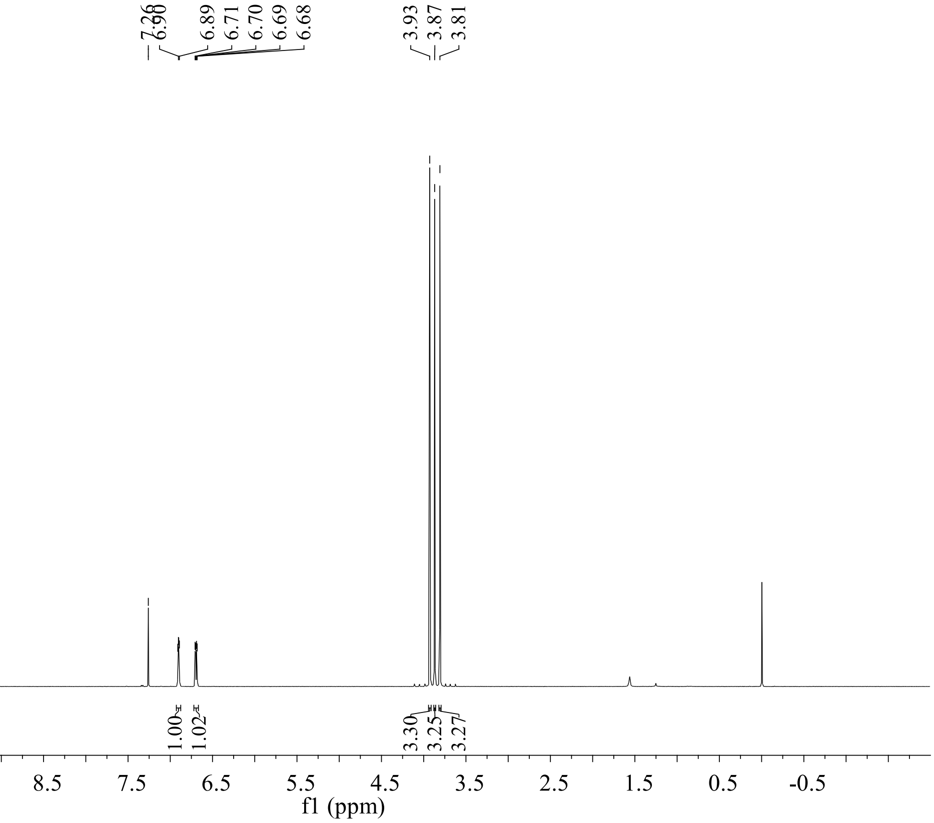
13



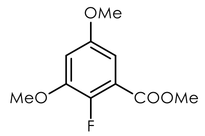
^{1}H NMR($CDCl_3$)



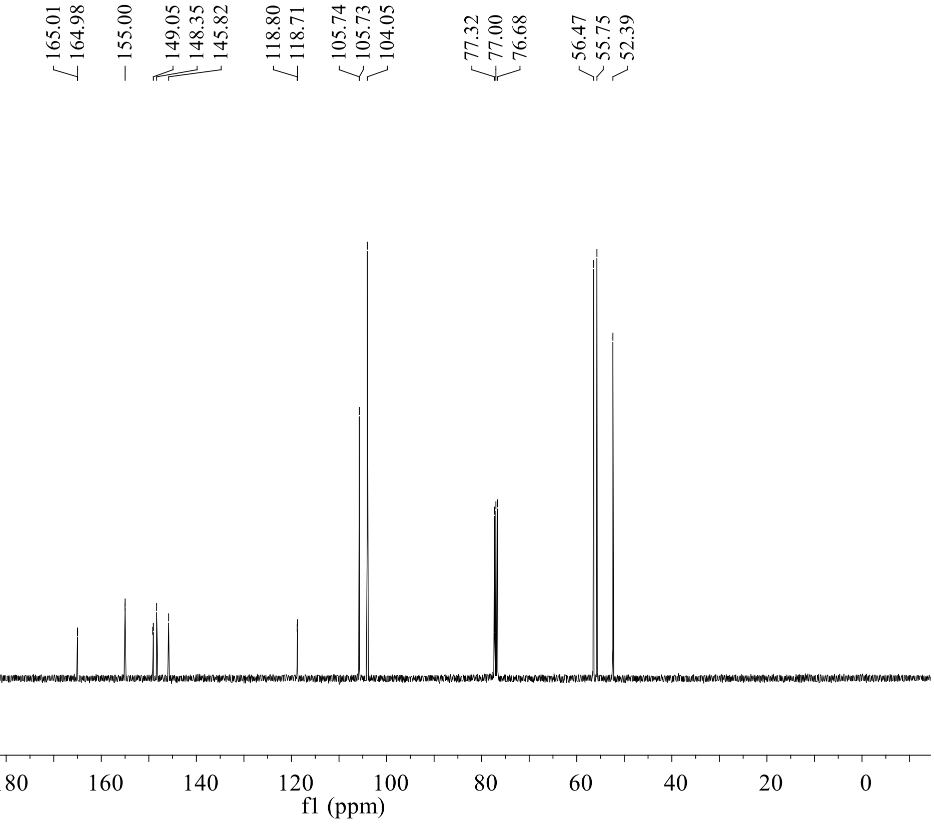
13-F

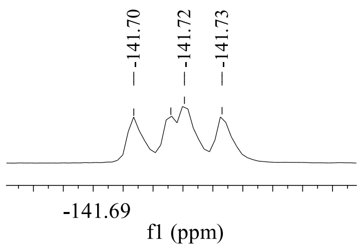


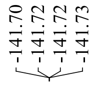
^{13}C NMR($CDCl_3$)



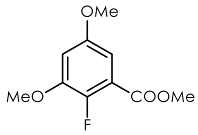
13-F



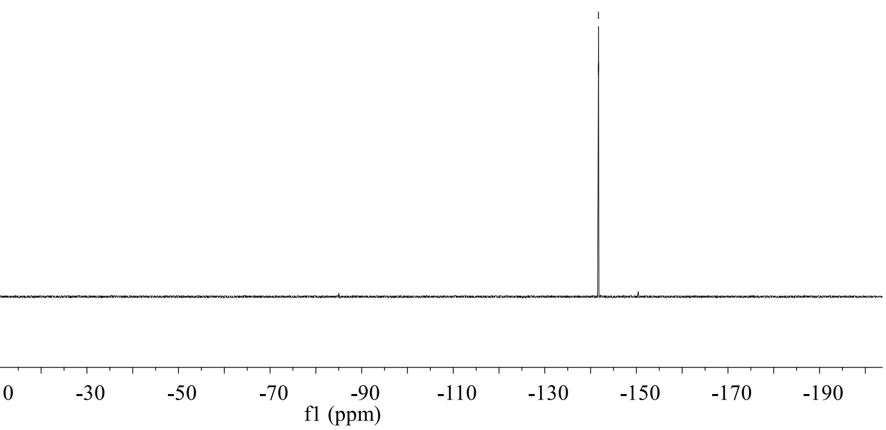




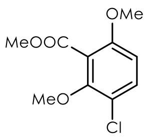
^{19}F NMR($CDCl_3$)



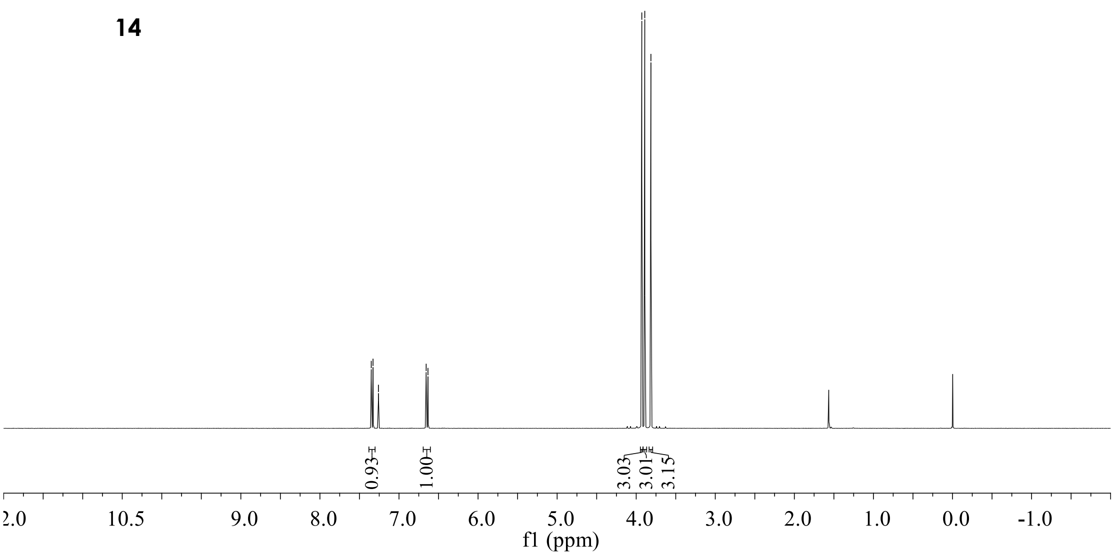
13-F



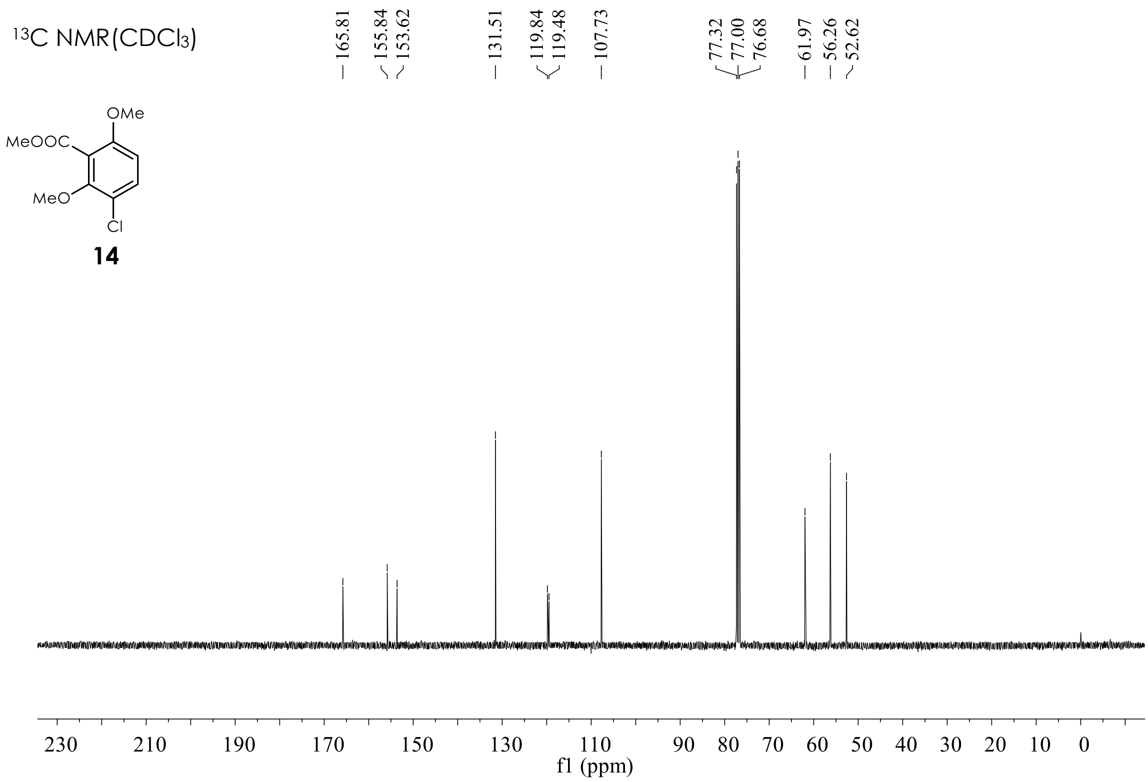
^1H NMR($CDCl_3$)



14

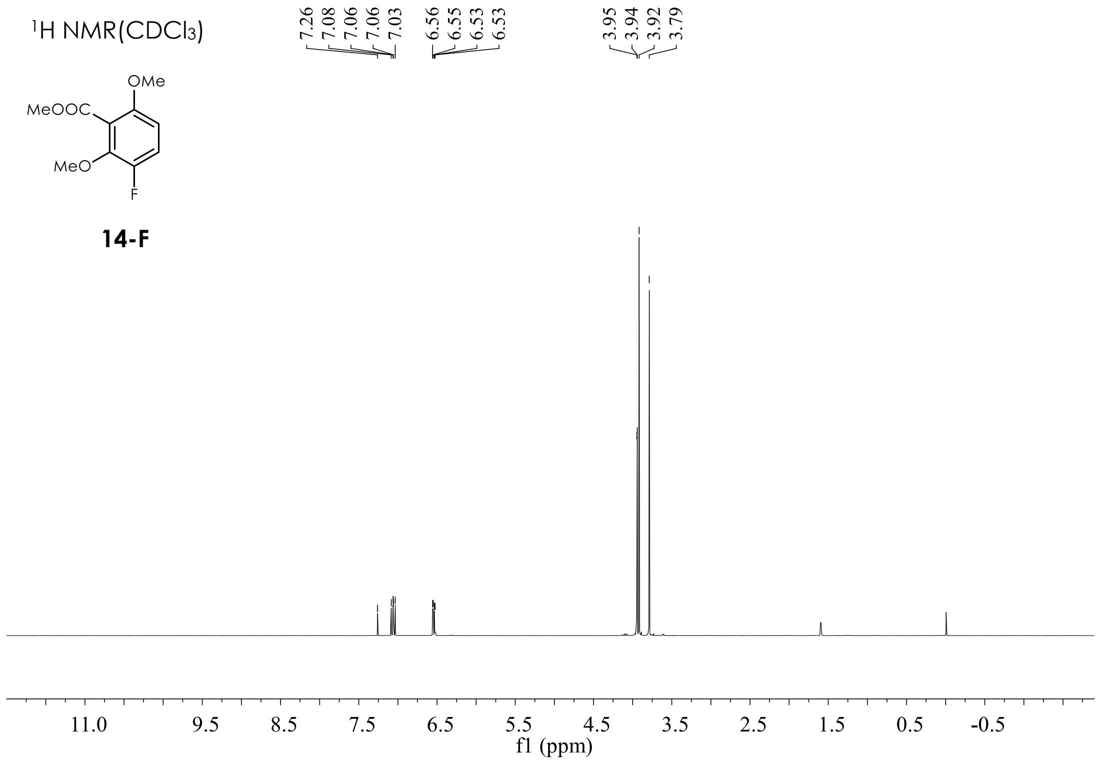


^{13}C NMR($CDCl_3$)



14

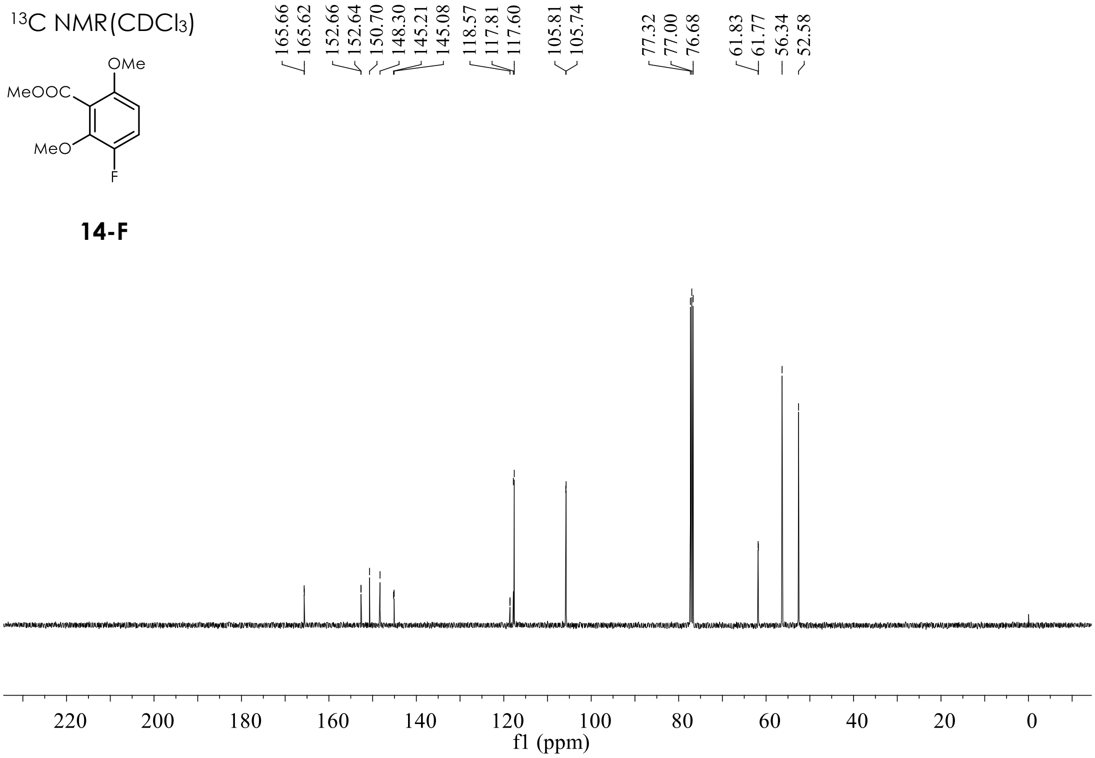
^{1}H NMR($CDCl_3$)

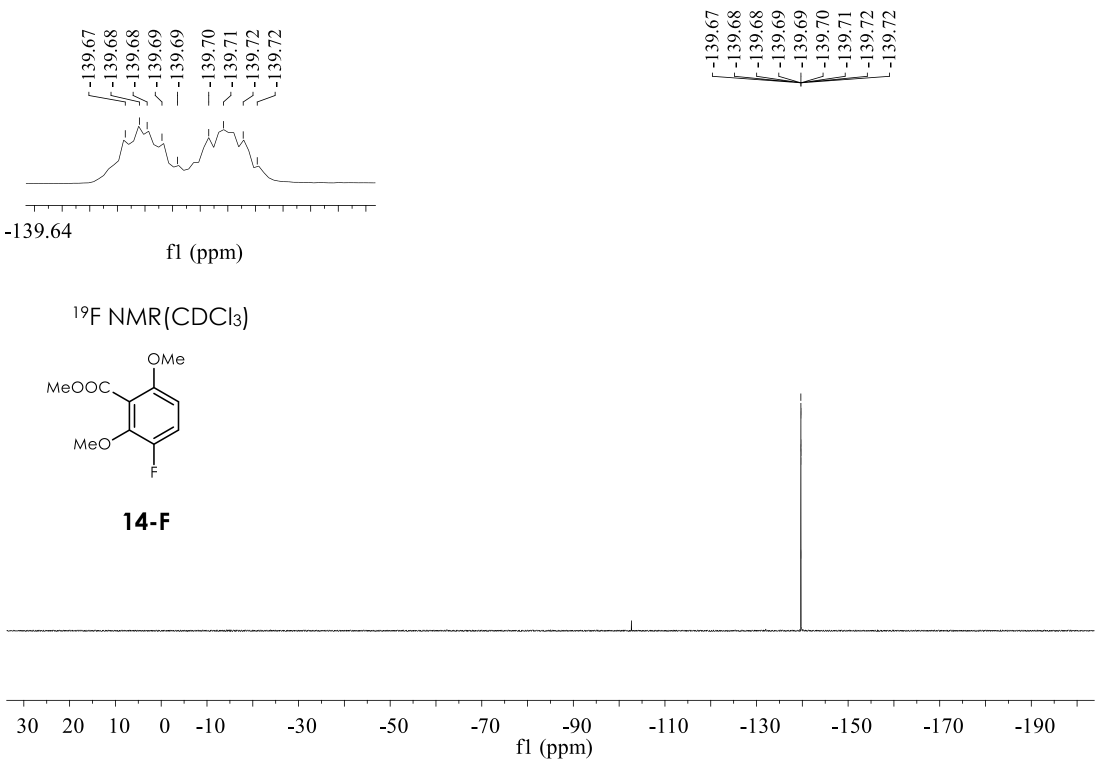


14-F

^{13}C NMR($CDCl_3$)

14-F

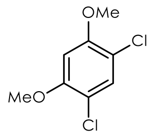




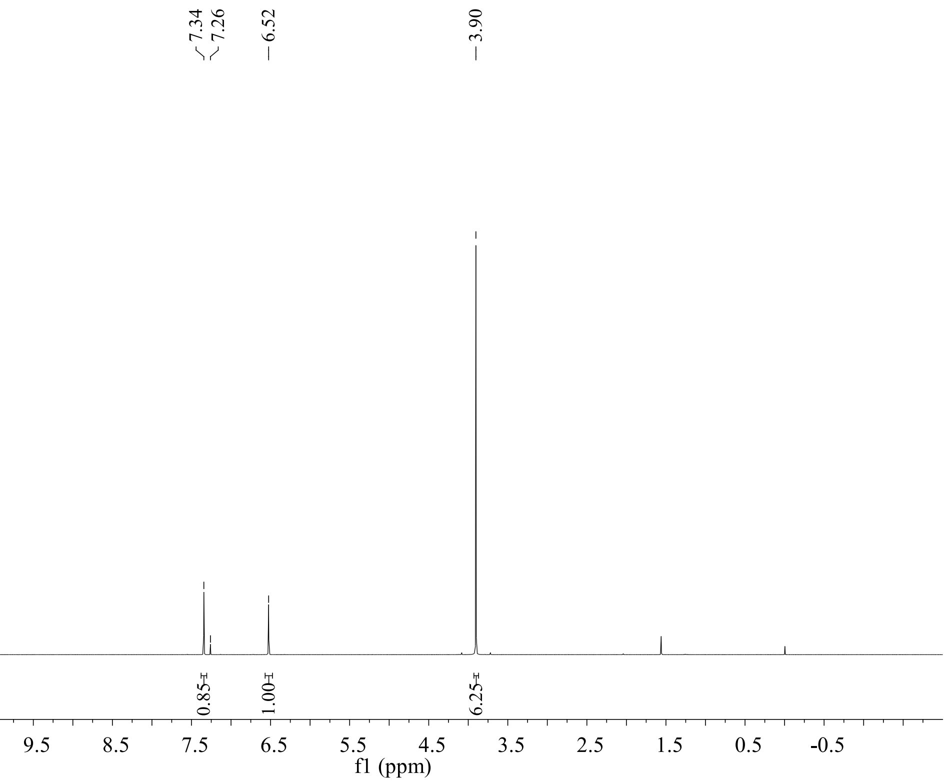
^{19}F NMR($CDCl_3$)

14-F

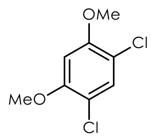
^{1}H NMR($CDCl_3$)



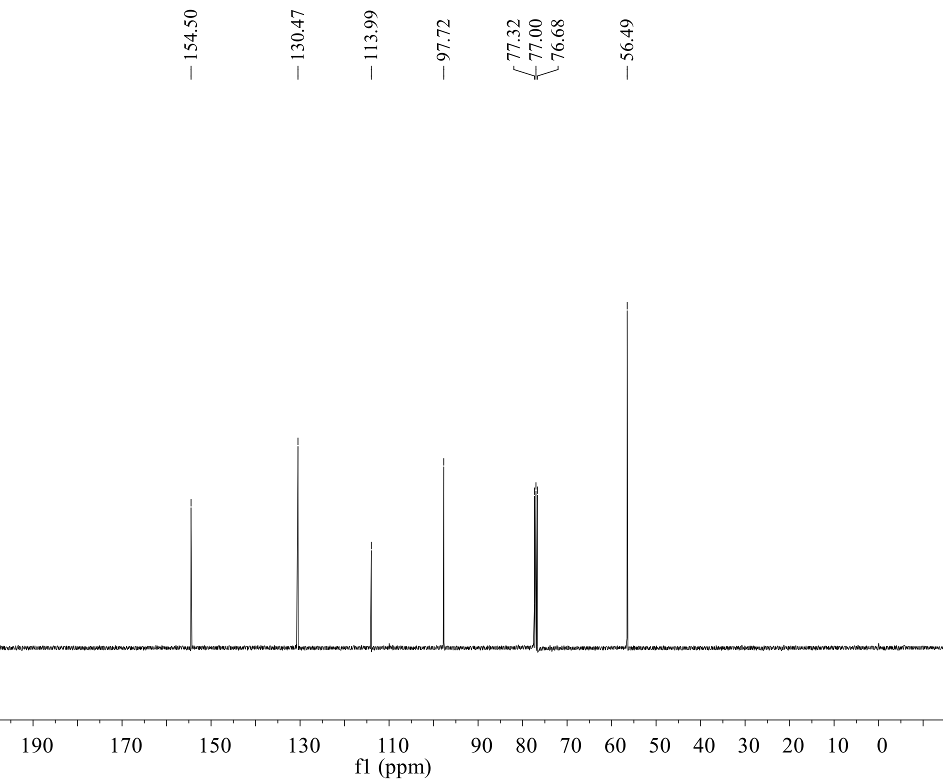
15



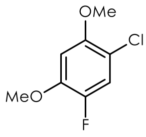
^{13}C NMR($CDCl_3$)



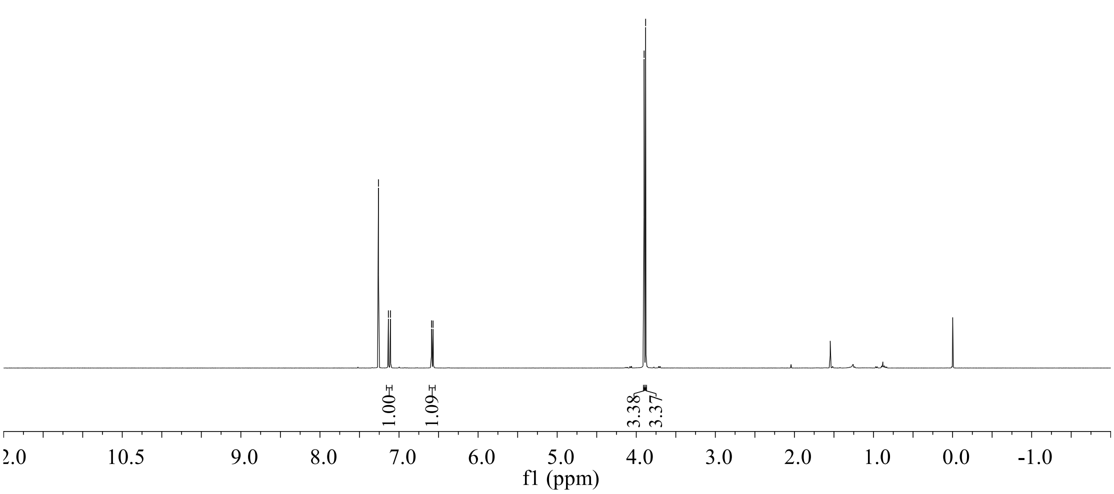
15



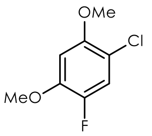
^{1}H NMR($CDCl_3$)



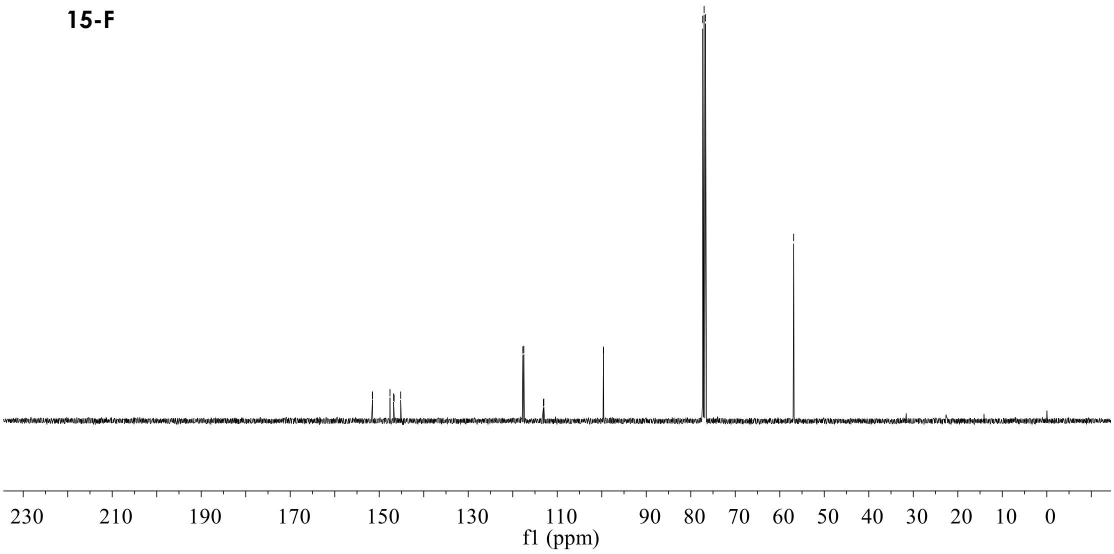
15-F

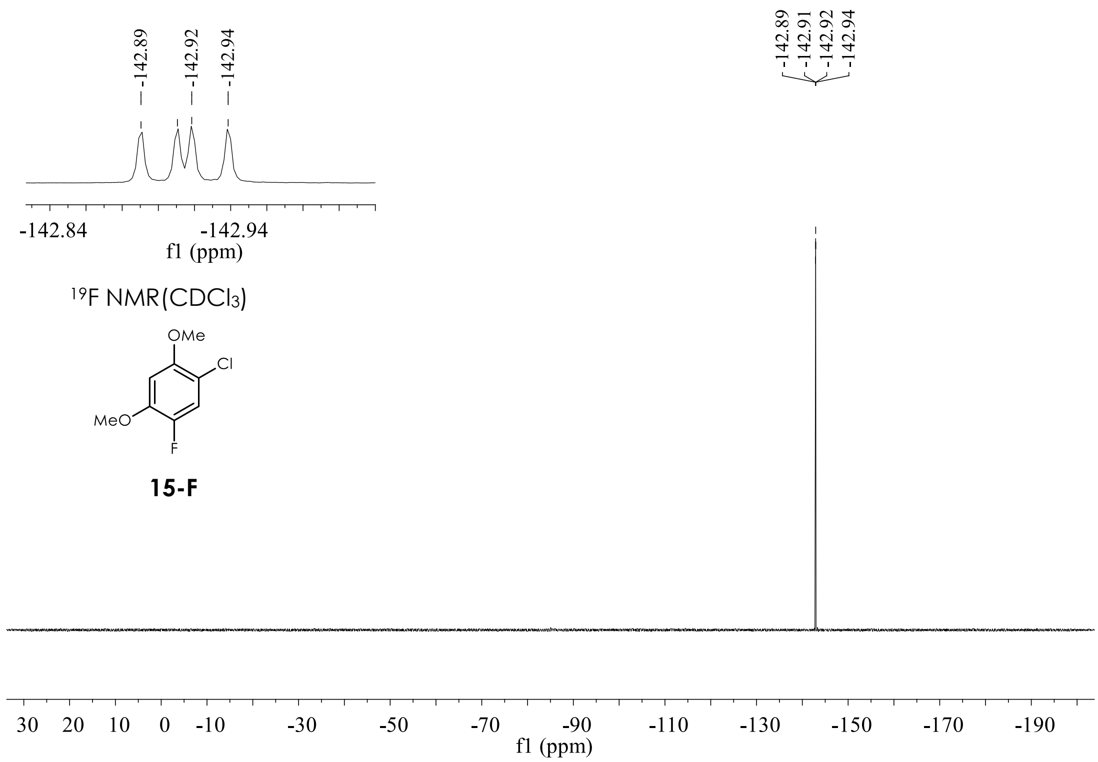


^{13}C NMR($CDCl_3$)

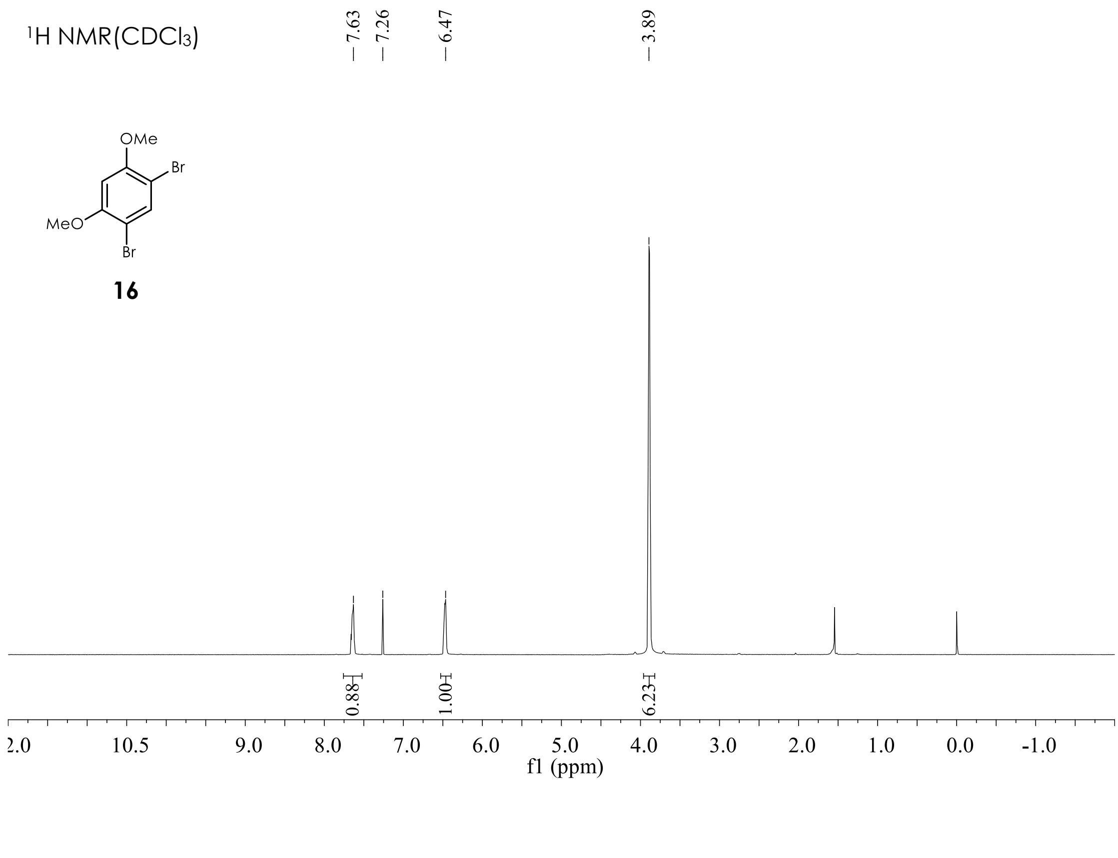


15-F



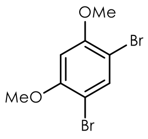


-142.89
-142.92
-142.94
-142.84
-142.94
f1 (ppm)
¹⁹F NMR(CDCl₃)
OMe
Cl
MeO
F
15-F
-142.89
-142.91
-142.92
-142.94
30
20
10
0
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
f1 (ppm)

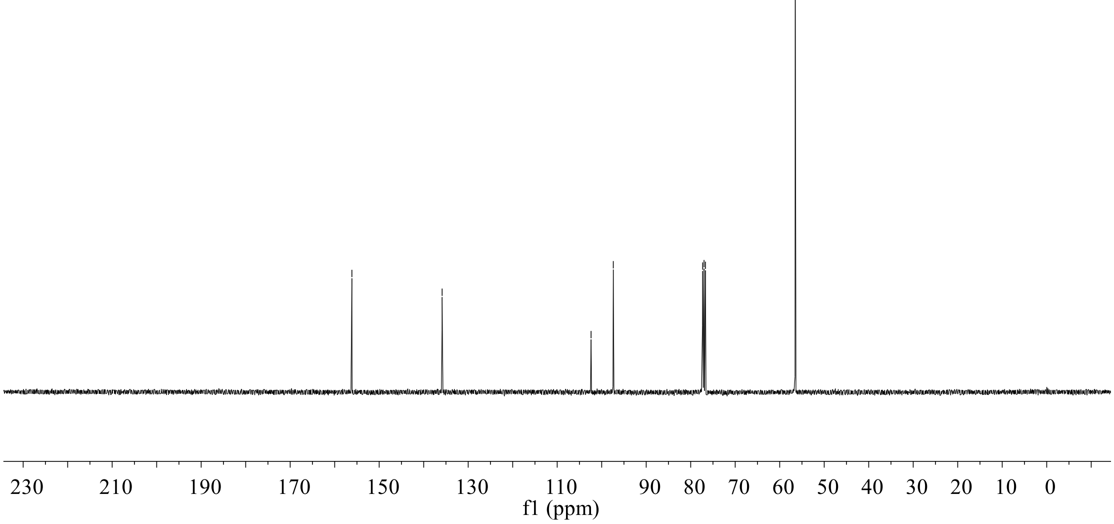


¹H NMR(CDCl₃)
7.63
7.26
6.47
3.89
OMe
Br
MeO
Br
16
0.88
1.00
6.23
2.0
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
f1 (ppm)

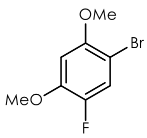
^{13}C NMR($CDCl_3$)



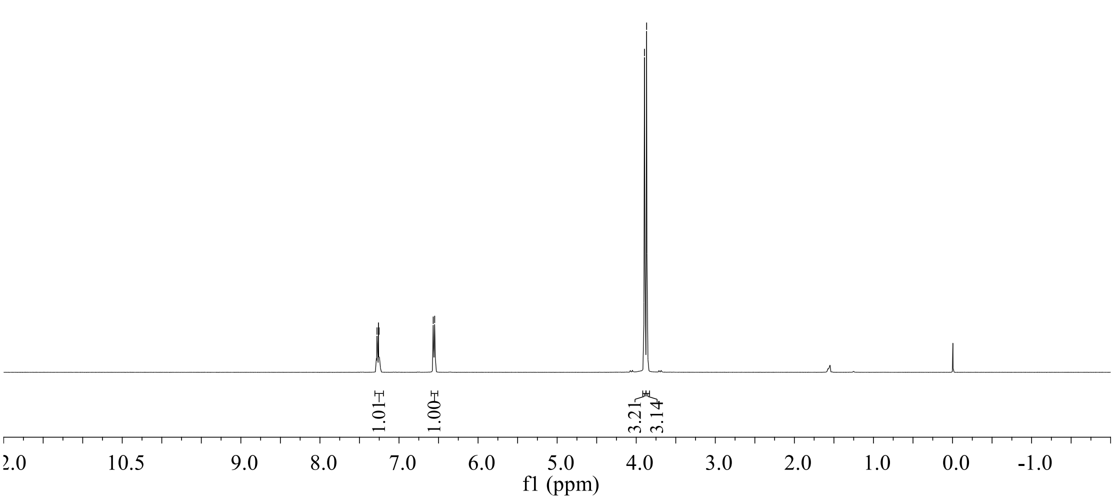
16



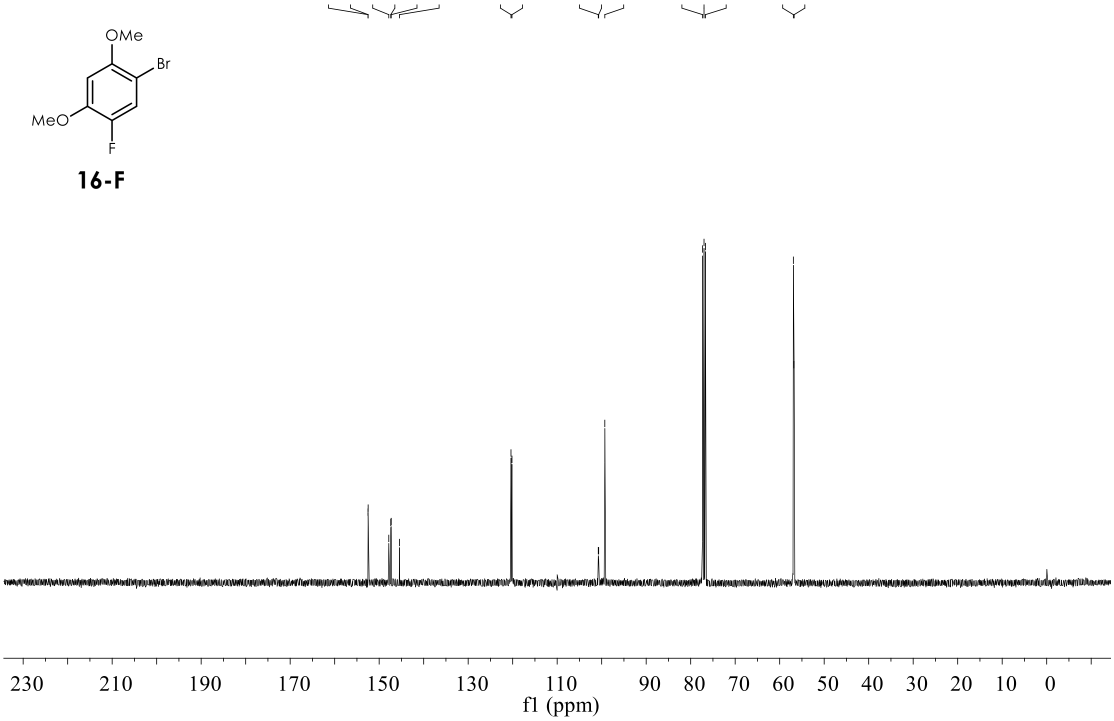
^{1}H NMR($CDCl_3$)



16-F

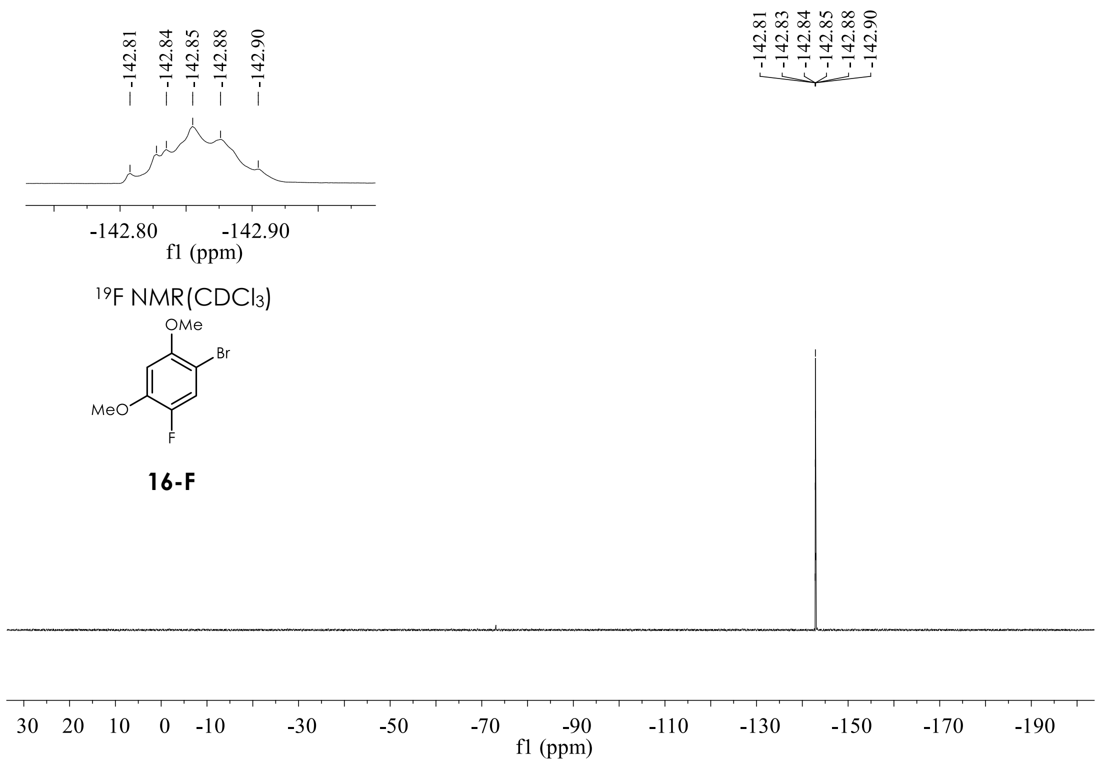


13C NMR(CDCl3)

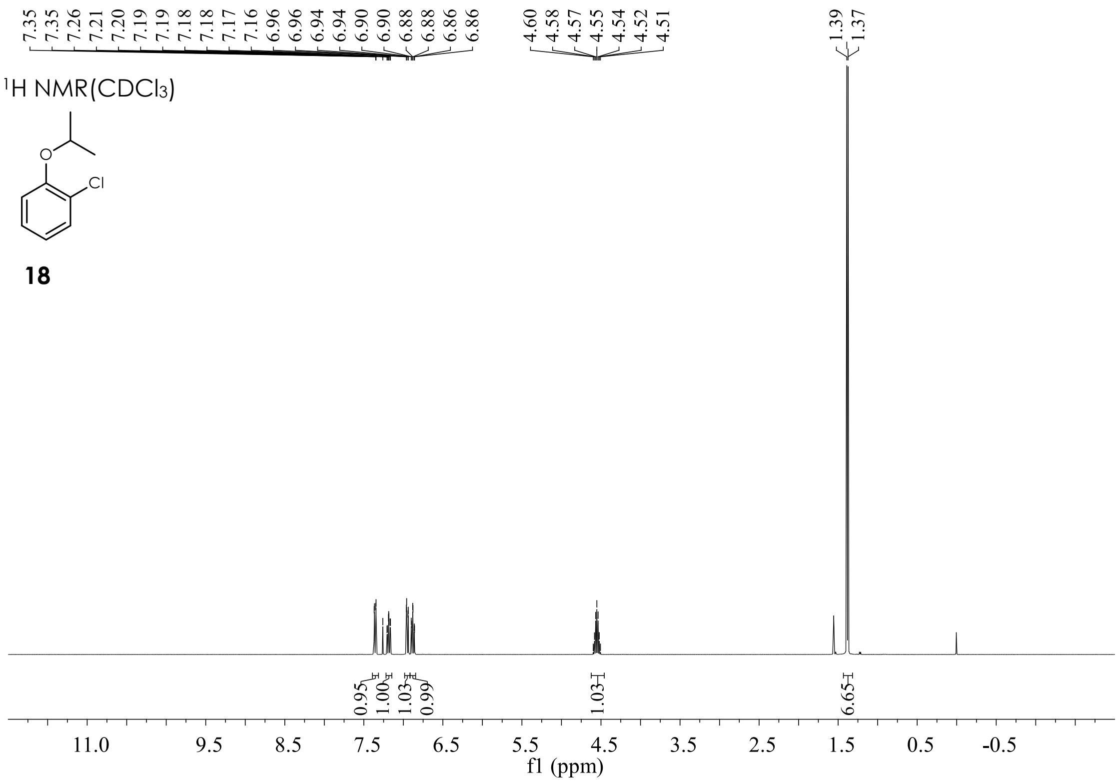


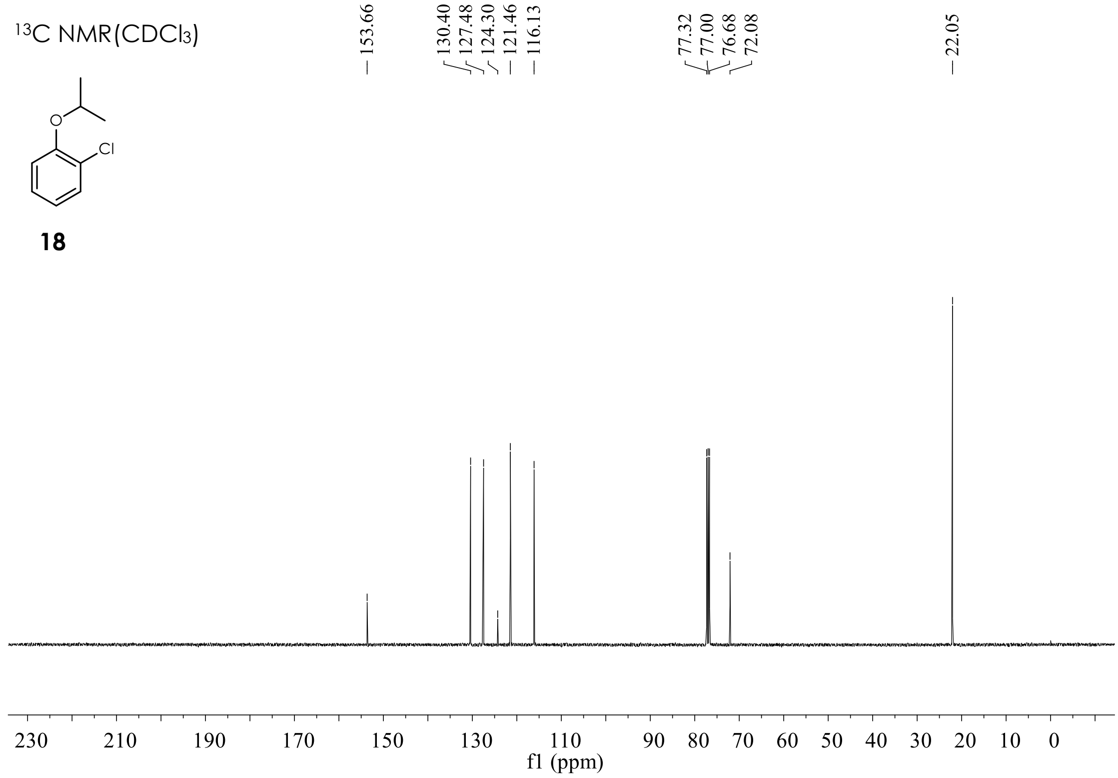
16-F

19F NMR(CDCl3)

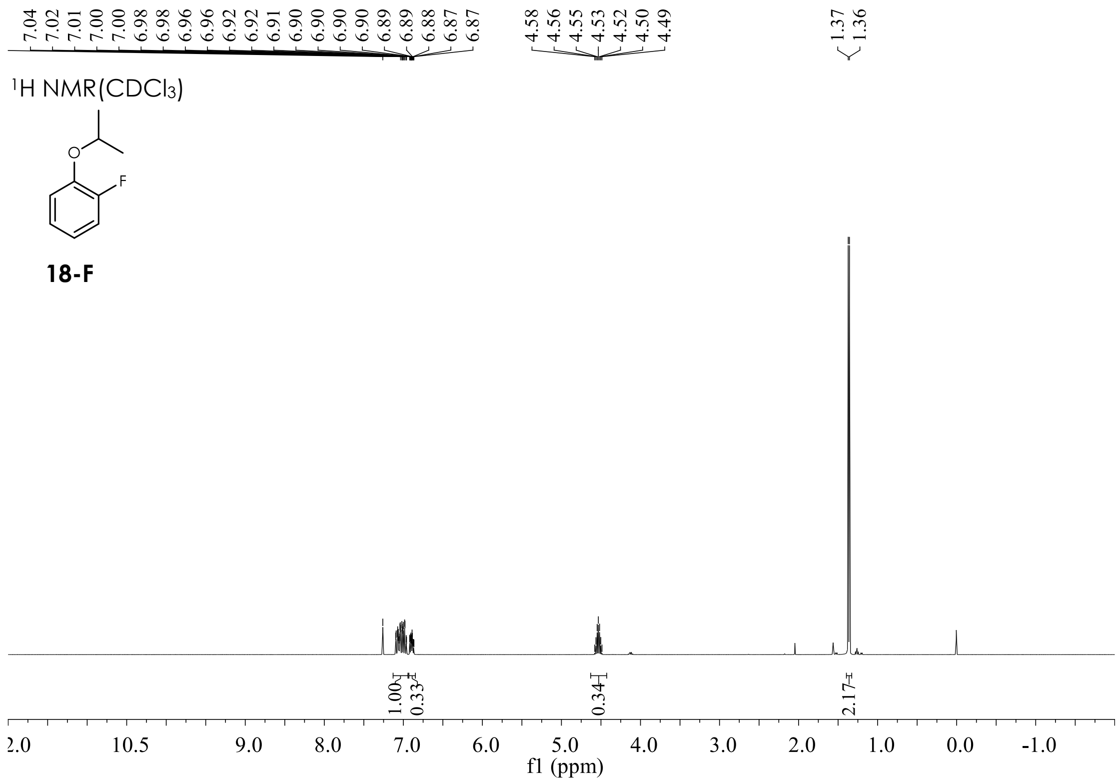


16-F


7.35 7.35 7.26 7.21 7.20 7.19 7.19 7.18 7.18 7.17 7.16 6.96 6.96 6.94 6.94 6.90 6.90 6.88 6.88 6.86 6.86
4.60 4.58 4.57 4.55 4.54 4.52 4.51
1.39 1.37
1H NMR(CDCl3)
O
Cl
18
0.95 1.00 1.03 0.99
1.03
6.65
11.0 9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5 -0.5
f1 (ppm)

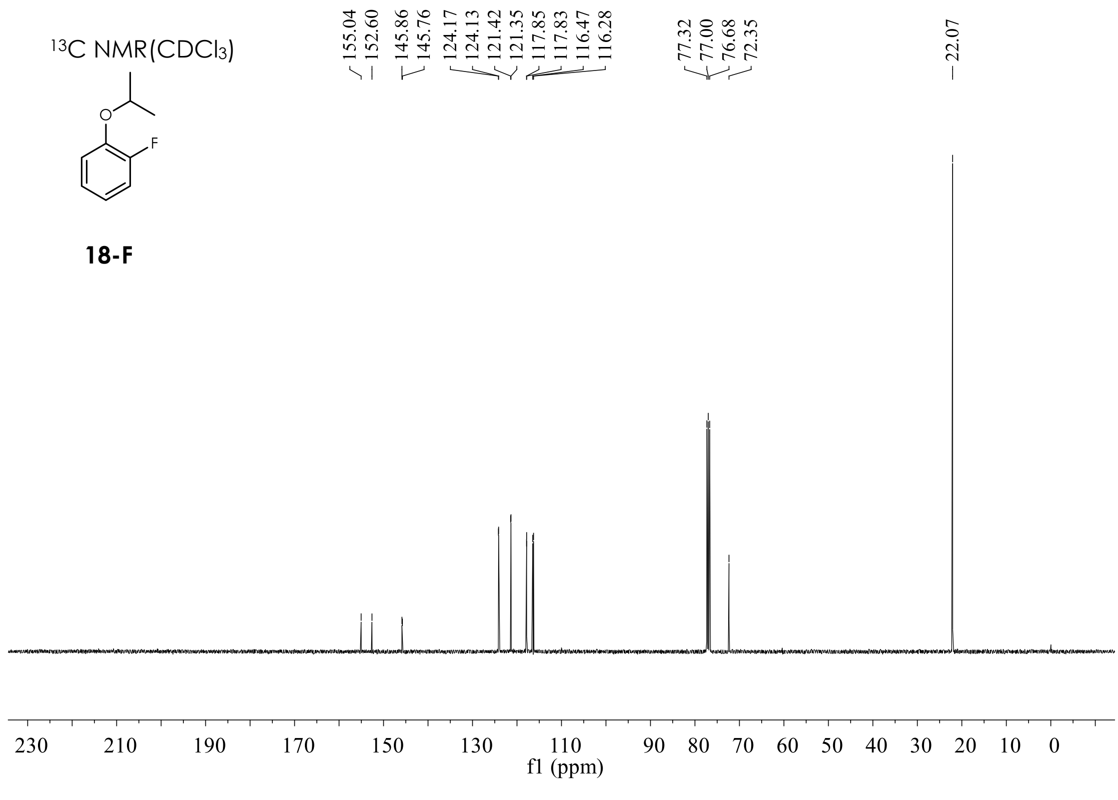

13C NMR(CDCl3)
153.66
130.40 127.48 124.30 121.46 116.13
77.32 77.00 76.68 72.08
22.05
O
Cl
18
230 210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

¹H NMR($CDCl_3$)

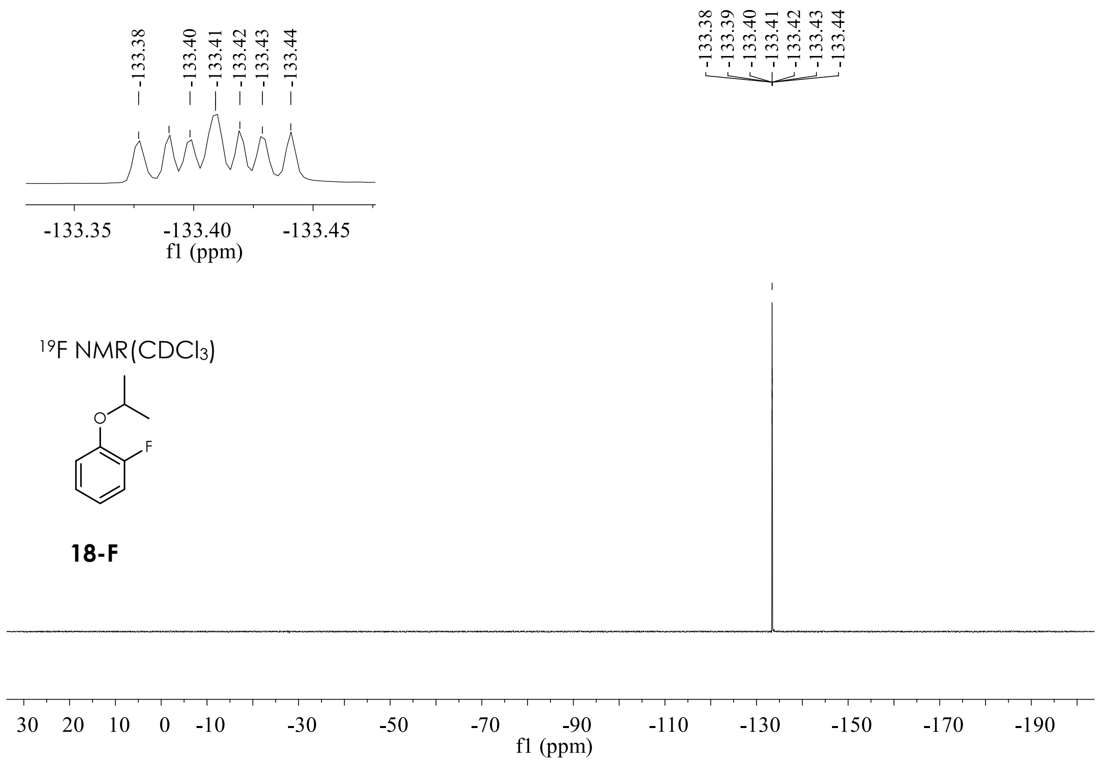


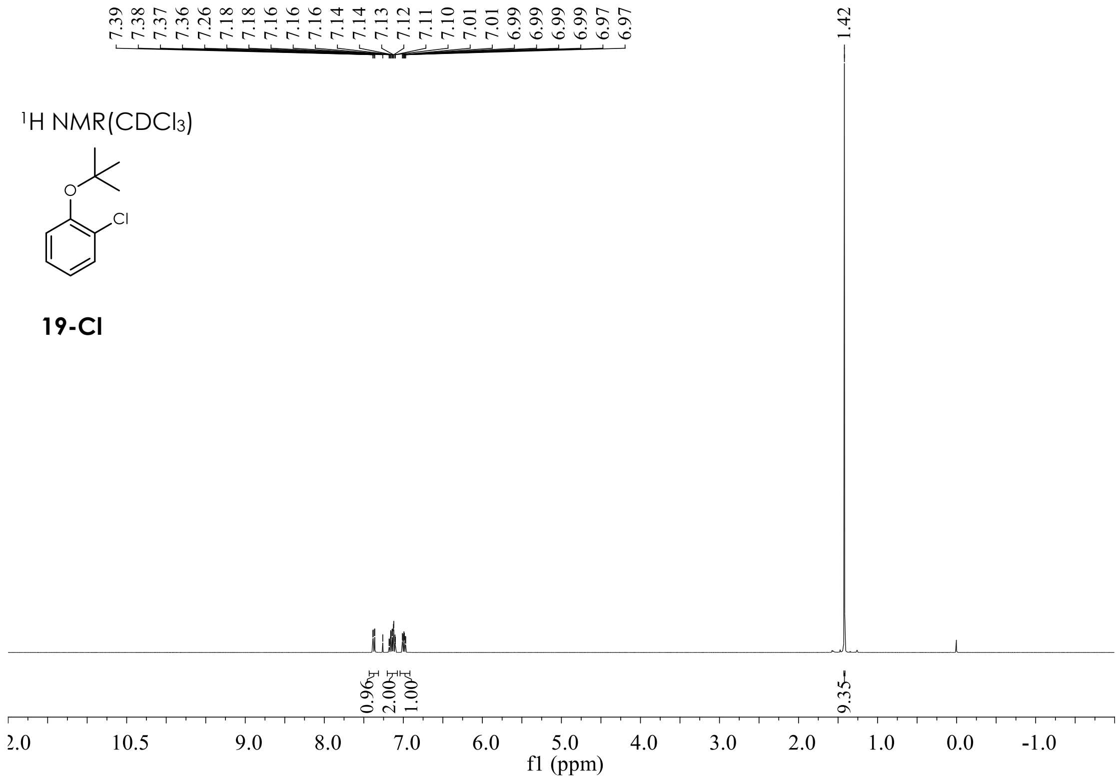
18-F

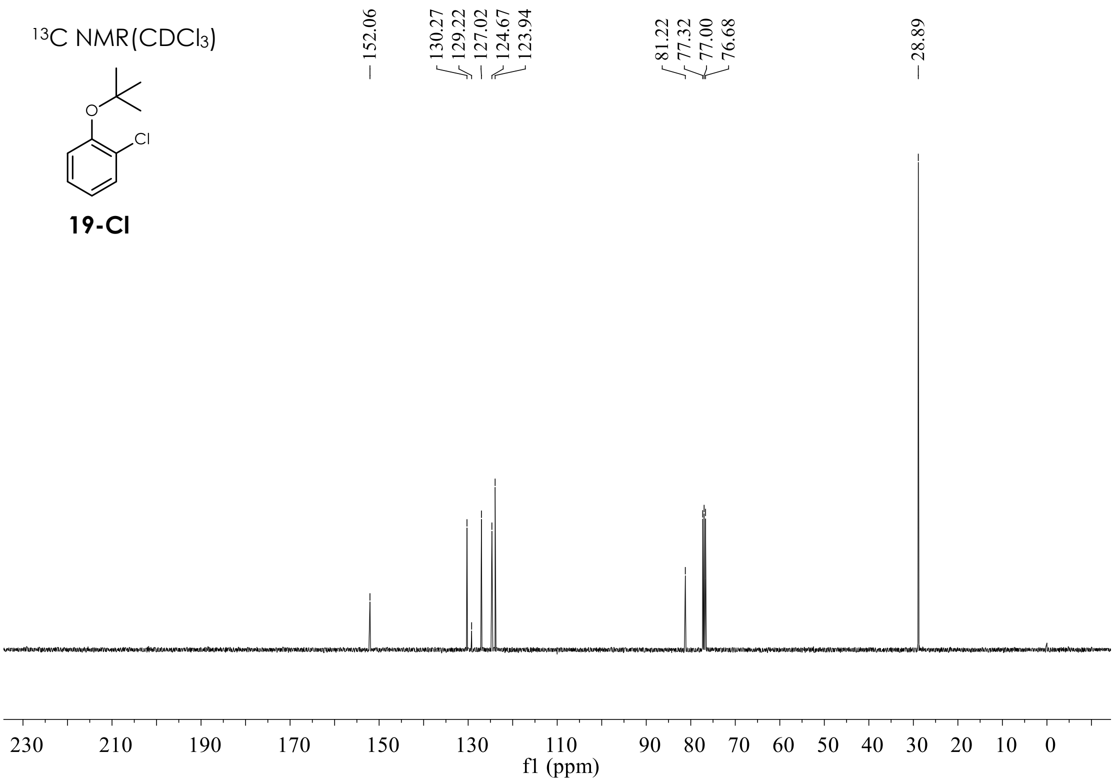
¹³C NMR($CDCl_3$)



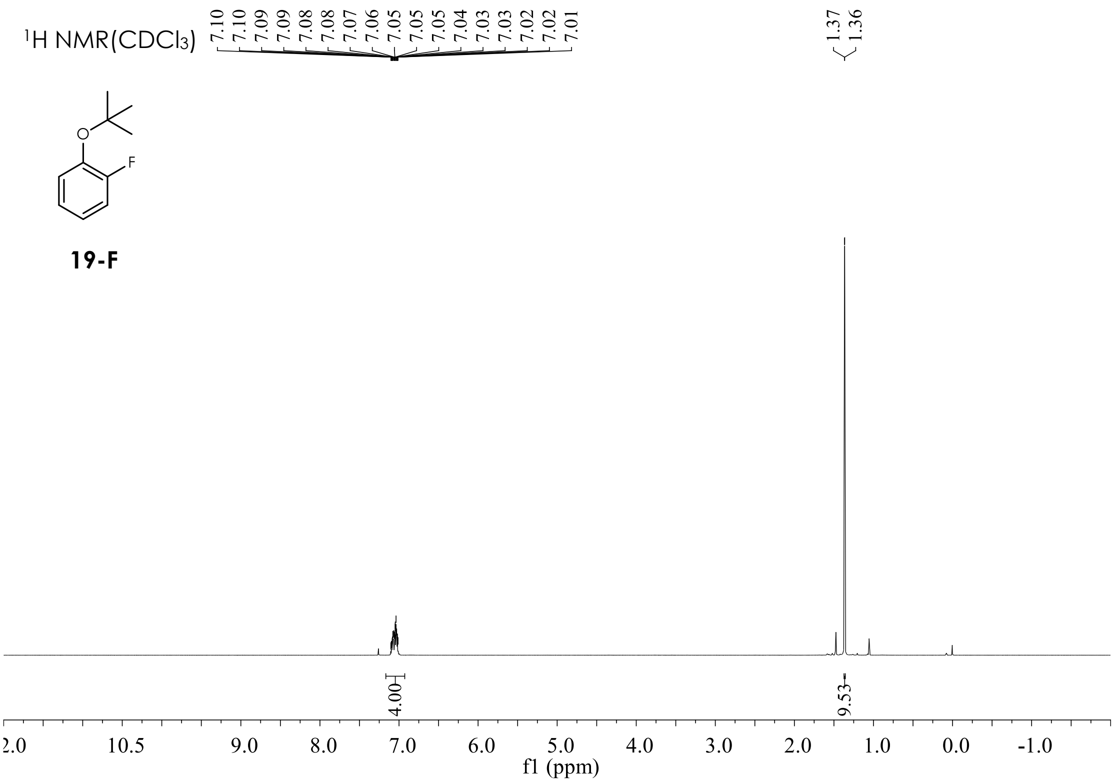
18-F


19F NMR(CDCl3)
18-F
f1 (ppm)

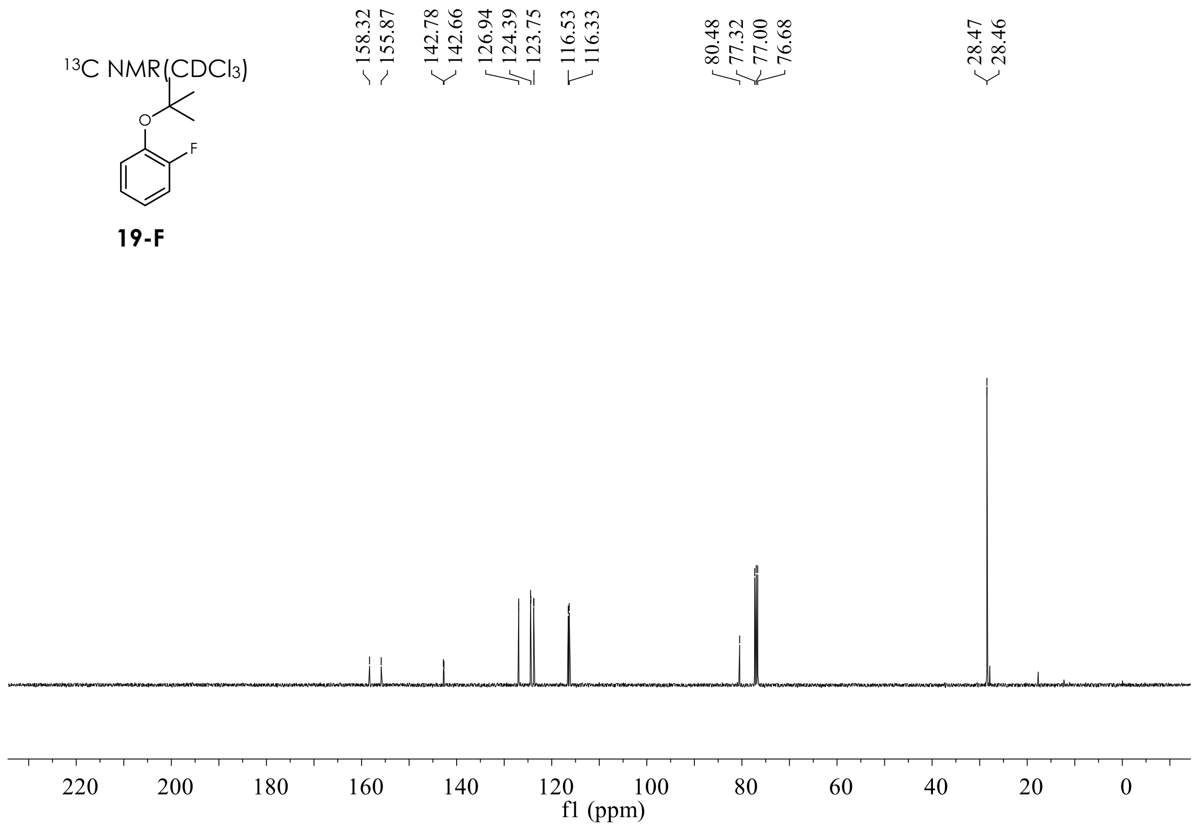

1H NMR(CDCl3)
19-Cl
f1 (ppm)

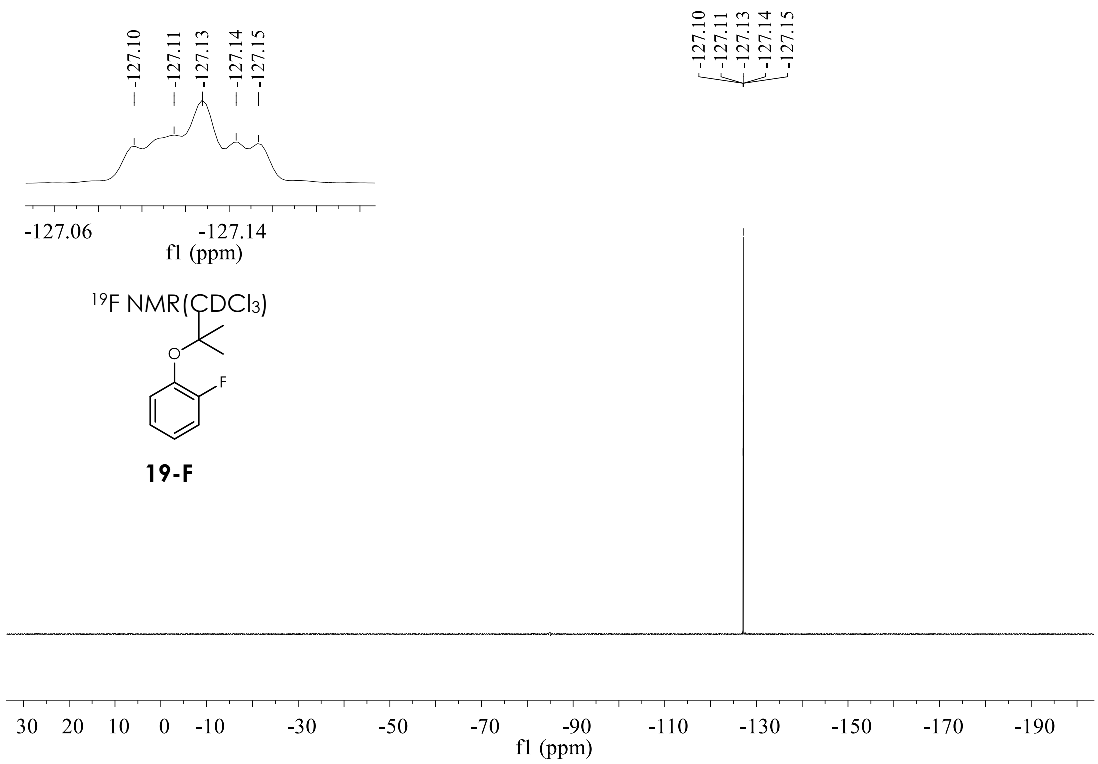


13C NMR(CDCl3)
19-Cl
Cl
O
152.06
130.27
129.22
127.02
124.67
123.94
81.22
77.32
77.00
76.68
28.89
230 210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

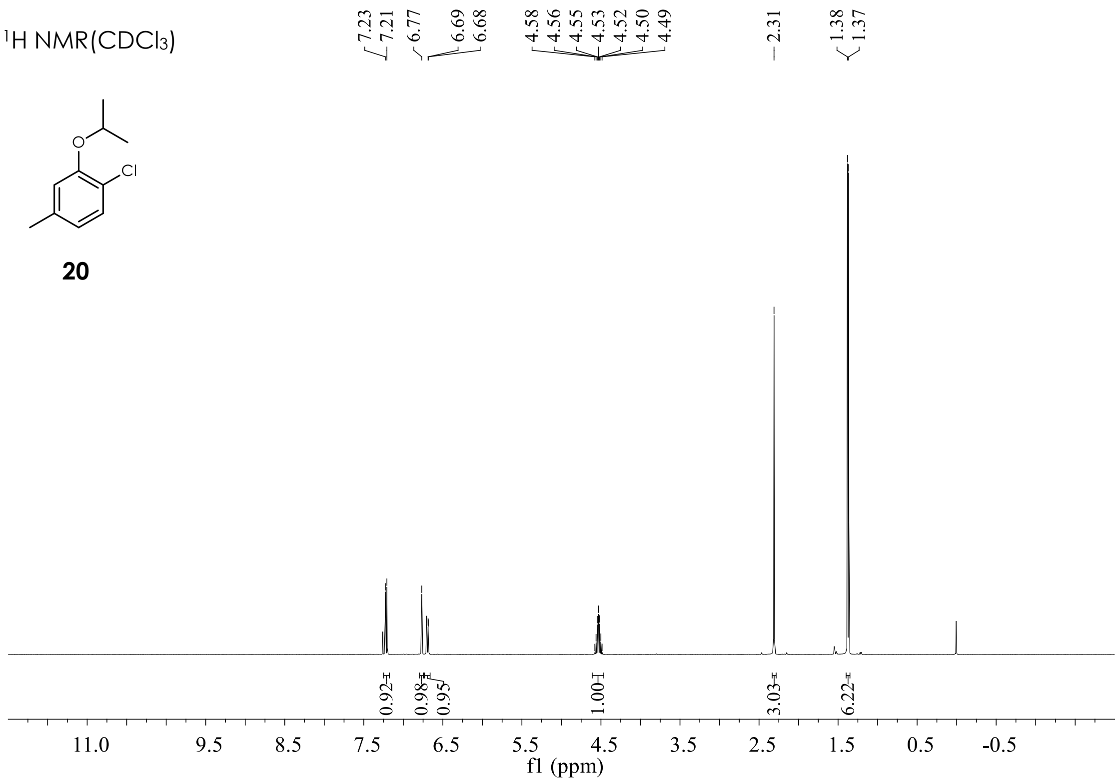


1H NMR(CDCl3)
19-F
F
O
7.10
7.10
7.09
7.09
7.08
7.08
7.07
7.06
7.05
7.05
7.05
7.04
7.03
7.03
7.02
7.02
7.01
1.37
1.36
4.00
9.53
2.0 10.5 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0
f1 (ppm)


^{13}C NMR(CDCl$_3$)
F
O
19-F
158.32
155.87
142.78
142.66
126.94
124.39
123.75
116.53
116.33
80.48
77.32
77.00
76.68
28.47
28.46
220 200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)

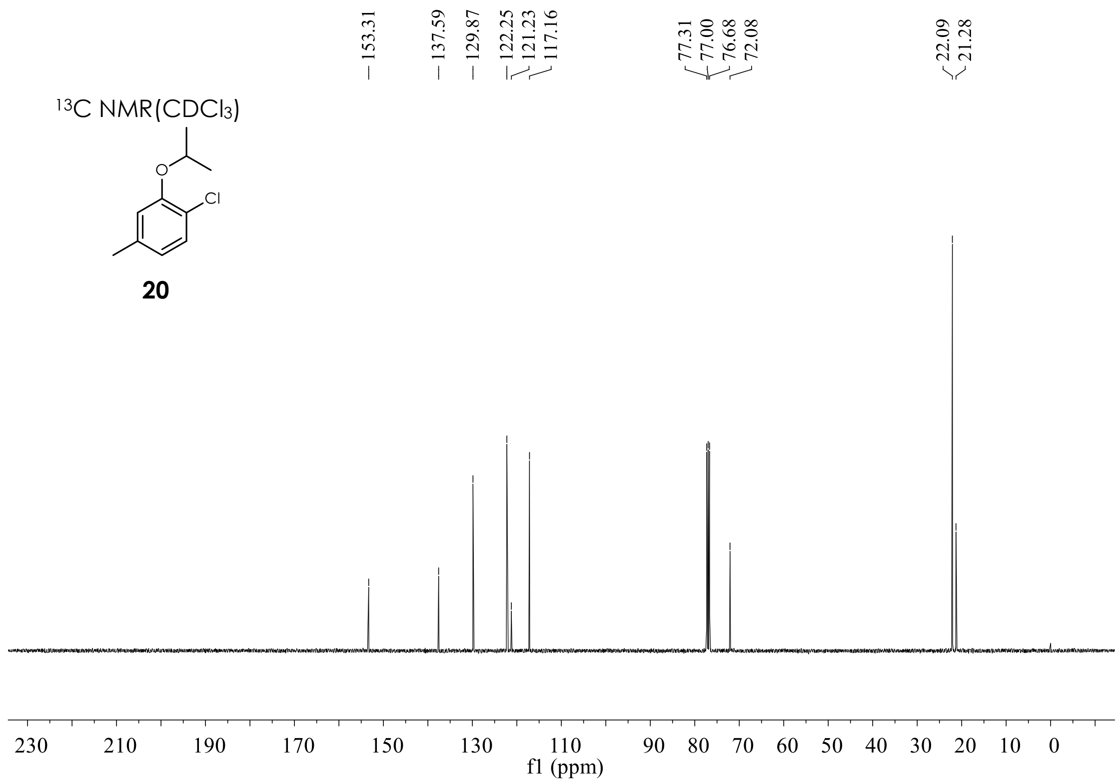

-127.10
-127.11
-127.13
-127.14
-127.15
-127.06
-127.14
f1 (ppm)
^{19}F NMR(CDCl$_3$)
F
O
19-F
-127.10
-127.11
-127.13
-127.14
-127.15
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)

^{1}H NMR($CDCl_3$)



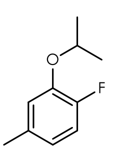
20

^{13}C NMR($CDCl_3$)

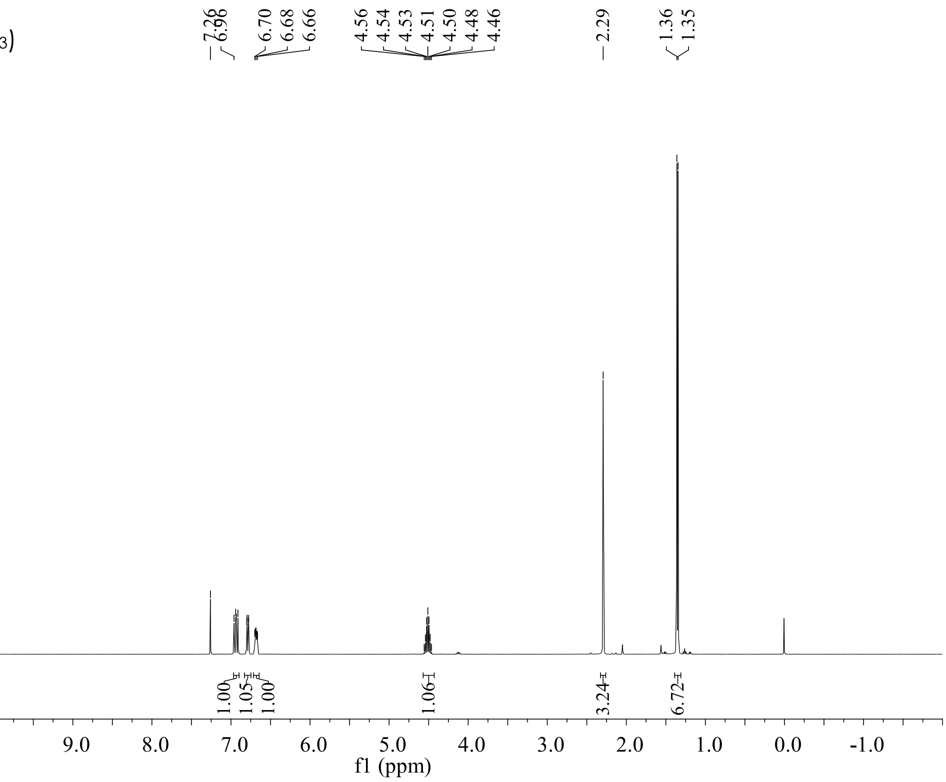


20

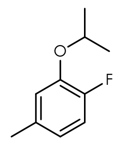
^{1}H NMR($CDCl_3$)



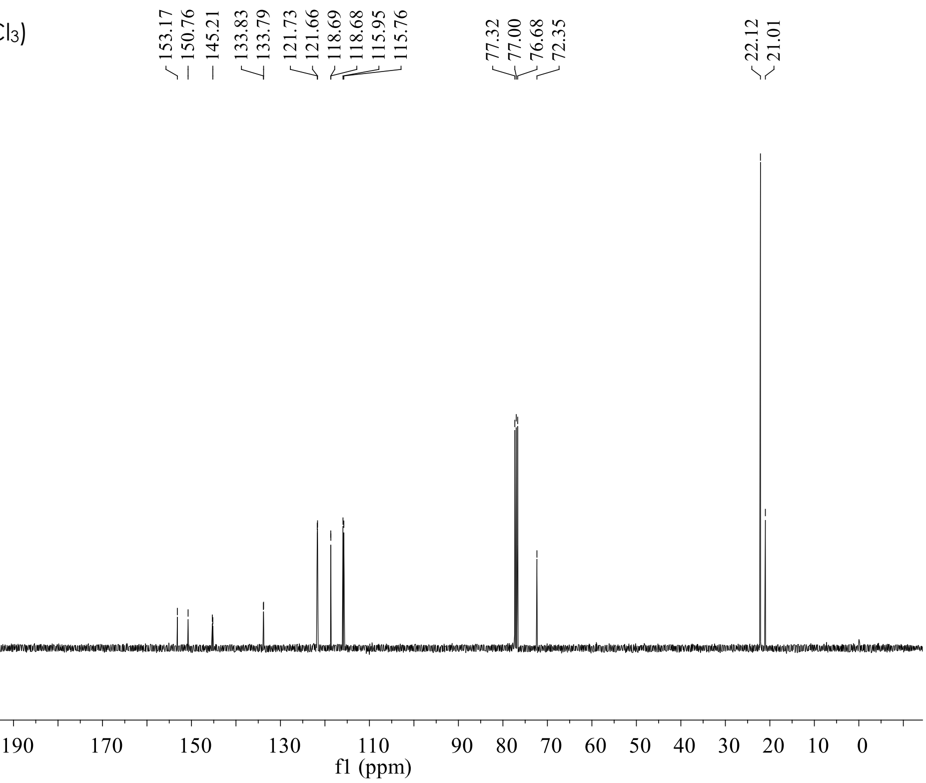
20-F

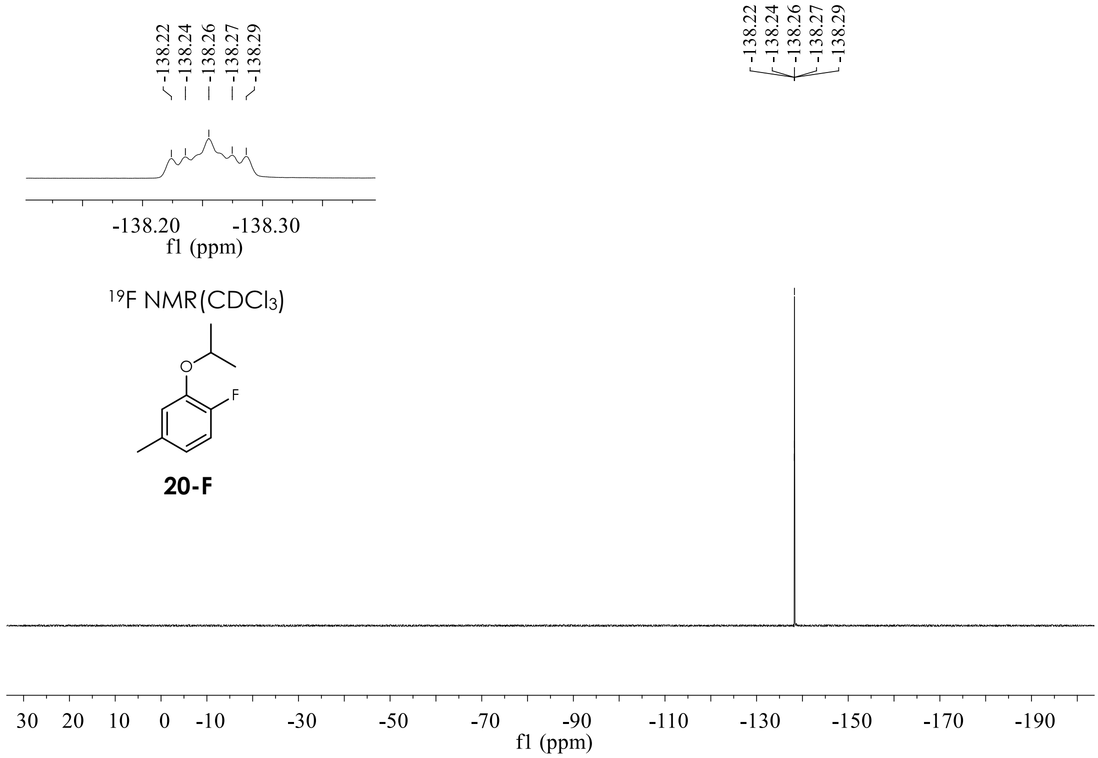


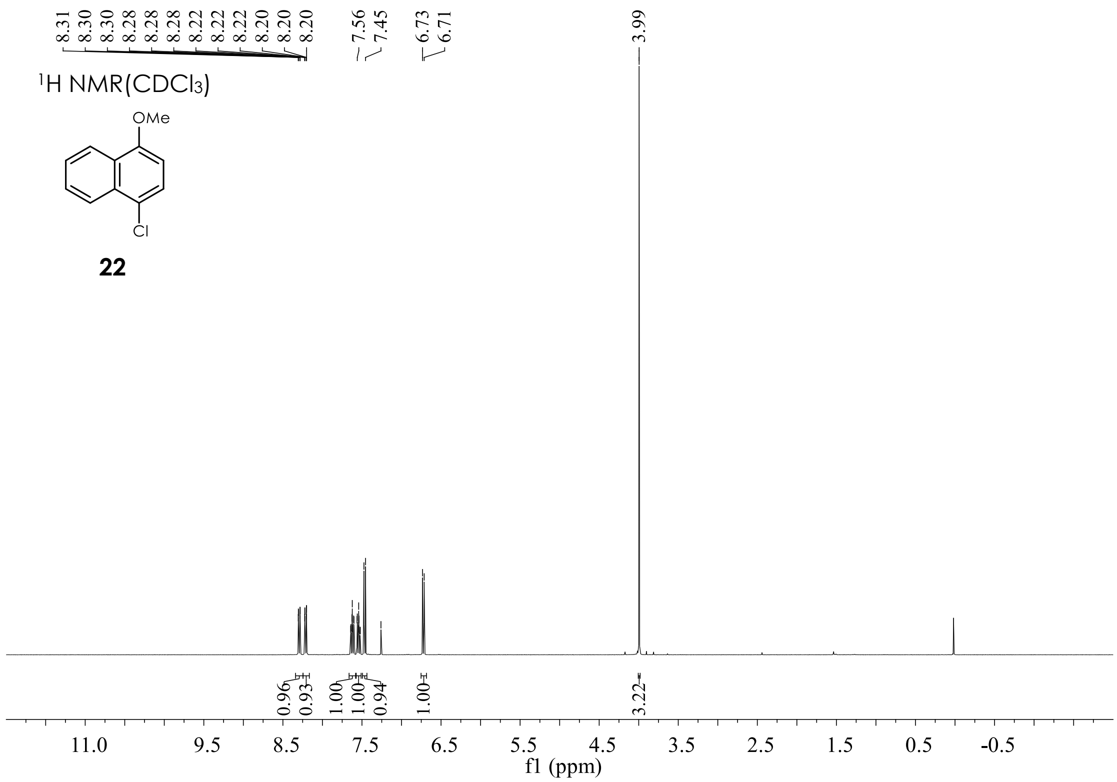
^{13}C NMR($CDCl_3$)



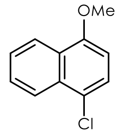
20-F



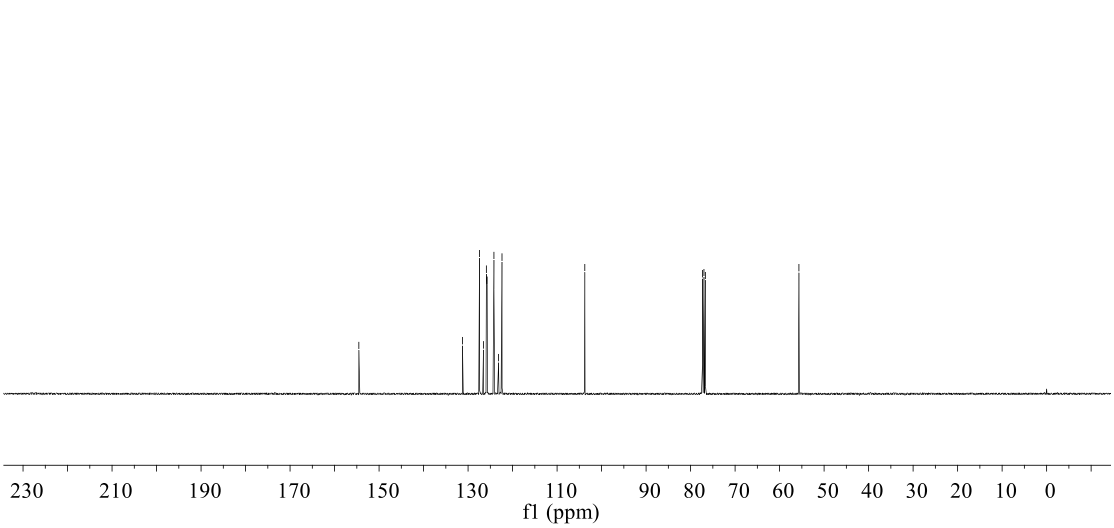

-138.22
-138.24
-138.26
-138.27
-138.29
-138.20
-138.30
f1 (ppm)
19F NMR(CDCl3)
O
F
20-F
30
20
10
0
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
f1 (ppm)


8.31
8.30
8.30
8.28
8.28
8.28
8.22
8.22
8.22
8.20
8.20
8.20
7.56
7.45
6.73
6.71
3.99
1H NMR(CDCl3)
OMe
Cl
22
0.96
0.93
1.00
1.00
0.94
1.00
3.22
11.0
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

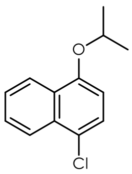
^{13}C NMR($CDCl_3$)



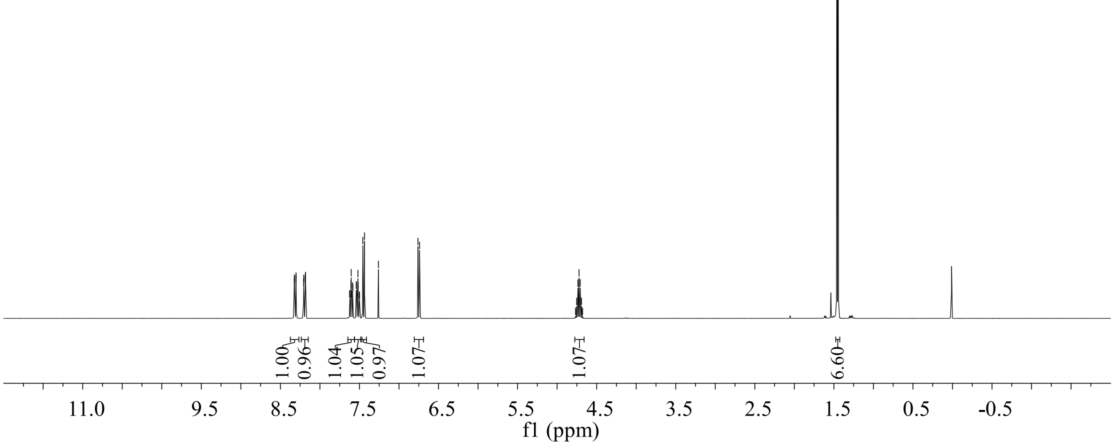
22

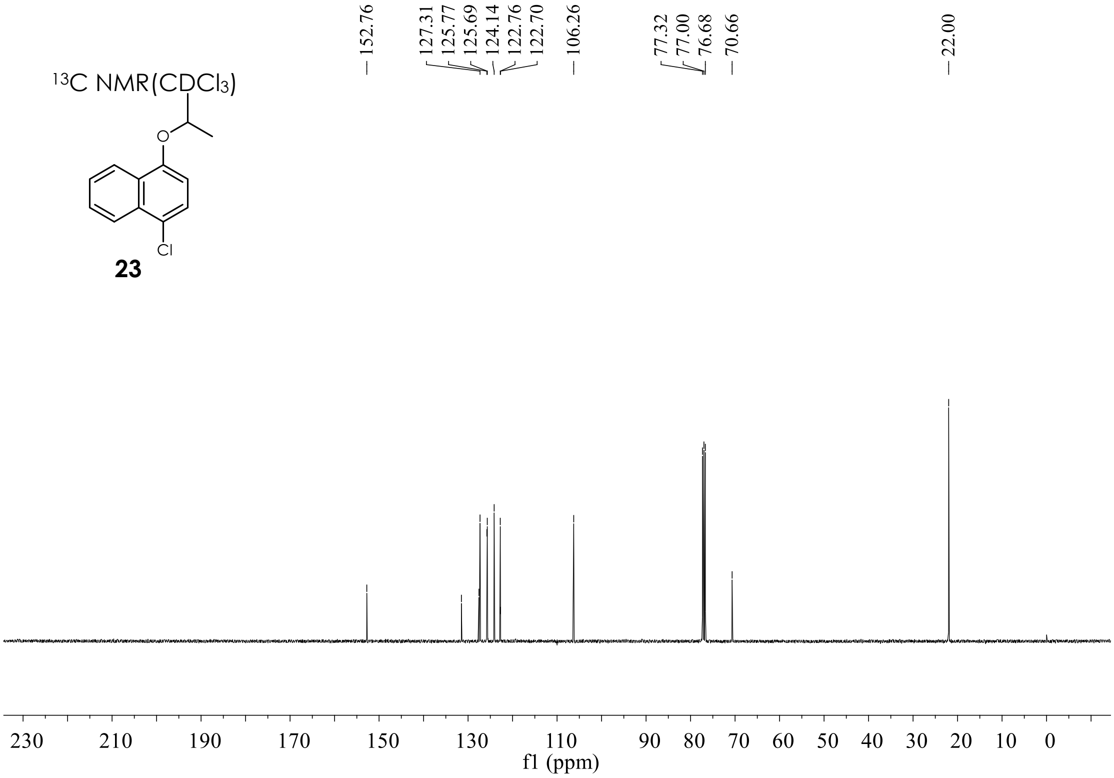


^{1}H NMR($CDCl_3$)

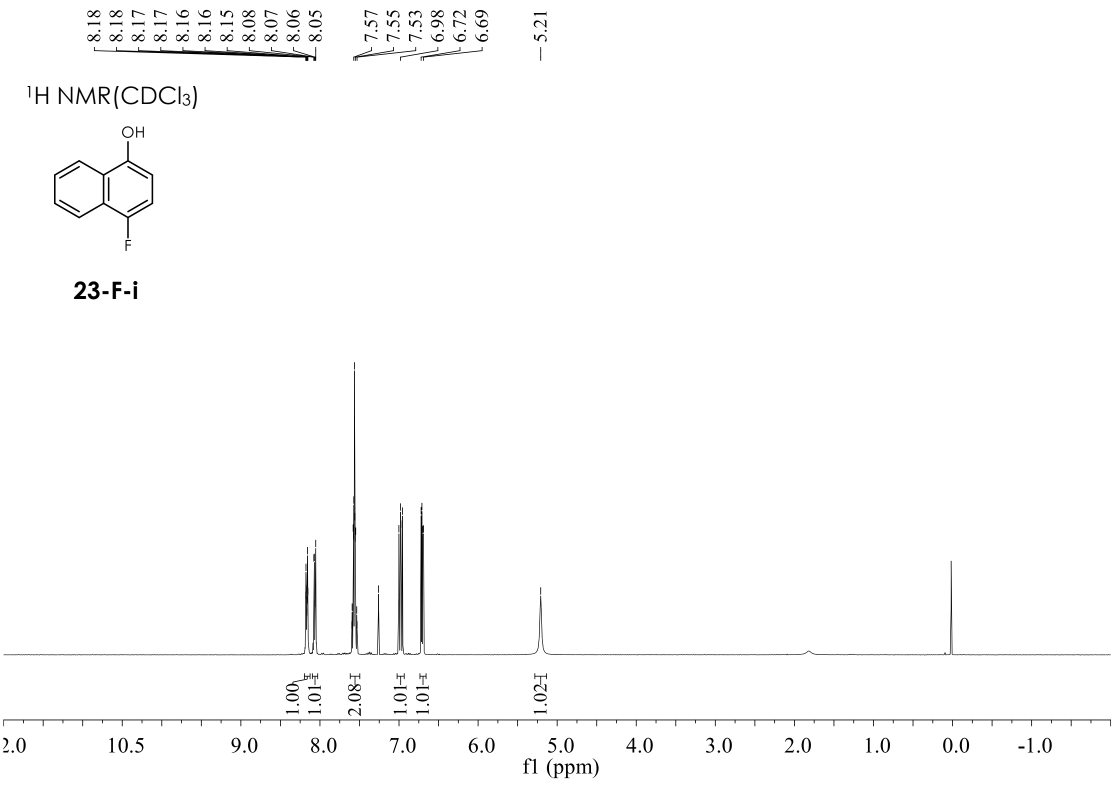


23



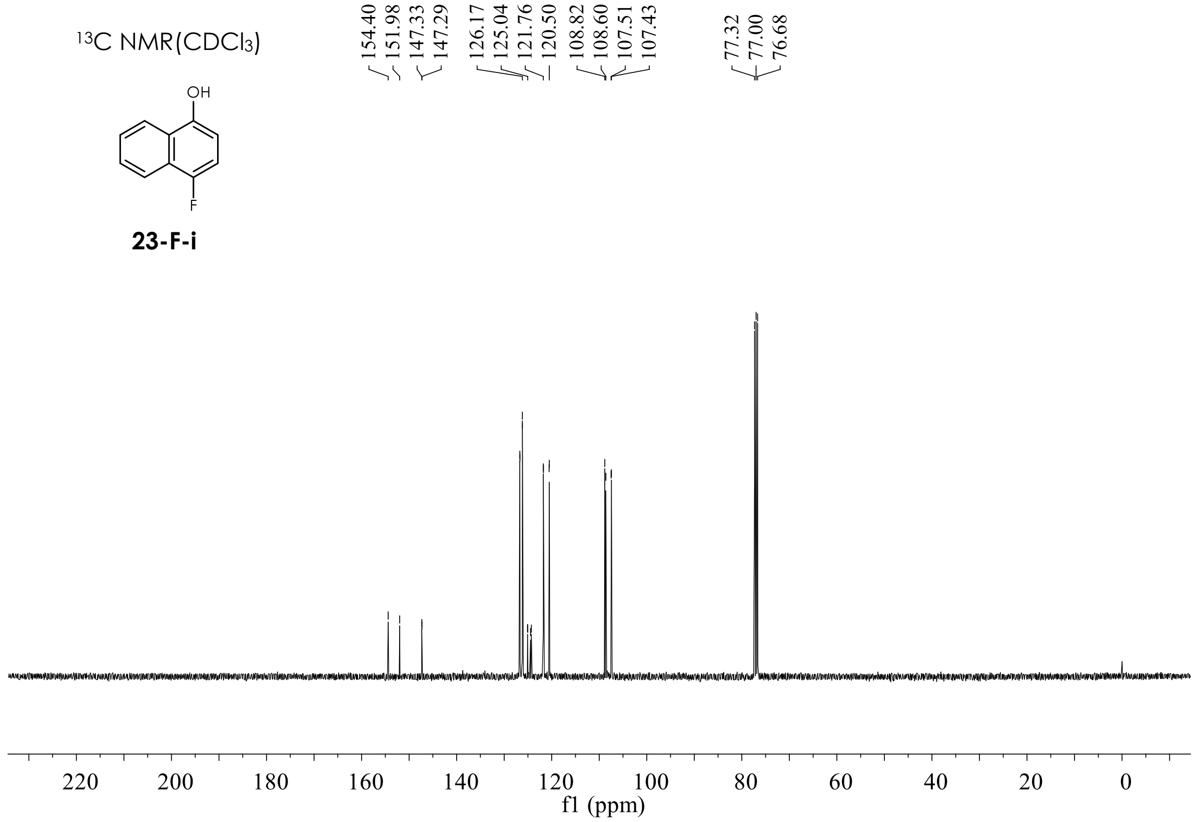


^{13}C NMR($CDCl_3$)
23
Cl
O
152.76
127.31
125.77
125.69
124.14
122.76
122.70
106.26
77.32
77.00
76.68
70.66
22.00
230 210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



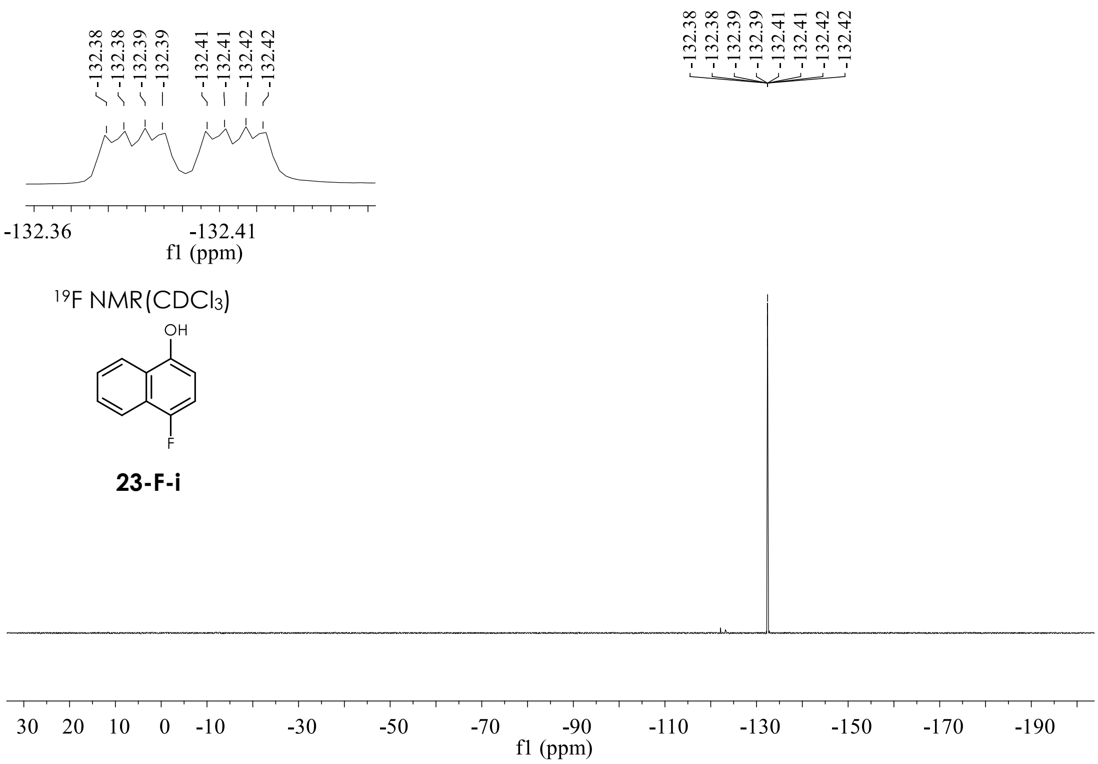
^{1}H NMR($CDCl_3$)
23-F-i
OH
F
8.18
8.18
8.17
8.16
8.16
8.15
8.08
8.07
8.06
8.05
7.57
7.55
7.53
6.98
6.72
6.69
5.21
1.00
1.01
2.08
1.01
1.01
1.02
2.0 10.5 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0
f1 (ppm)

^{13}C NMR($CDCl_3$)

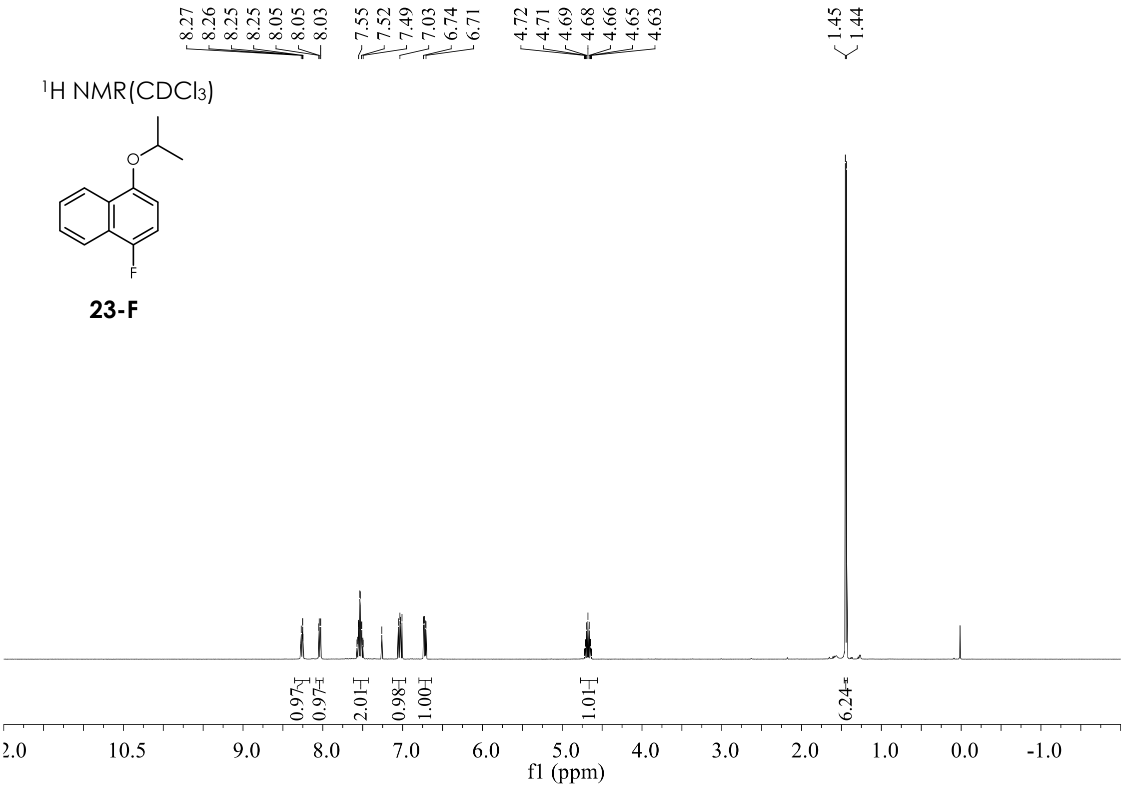


23-F-i

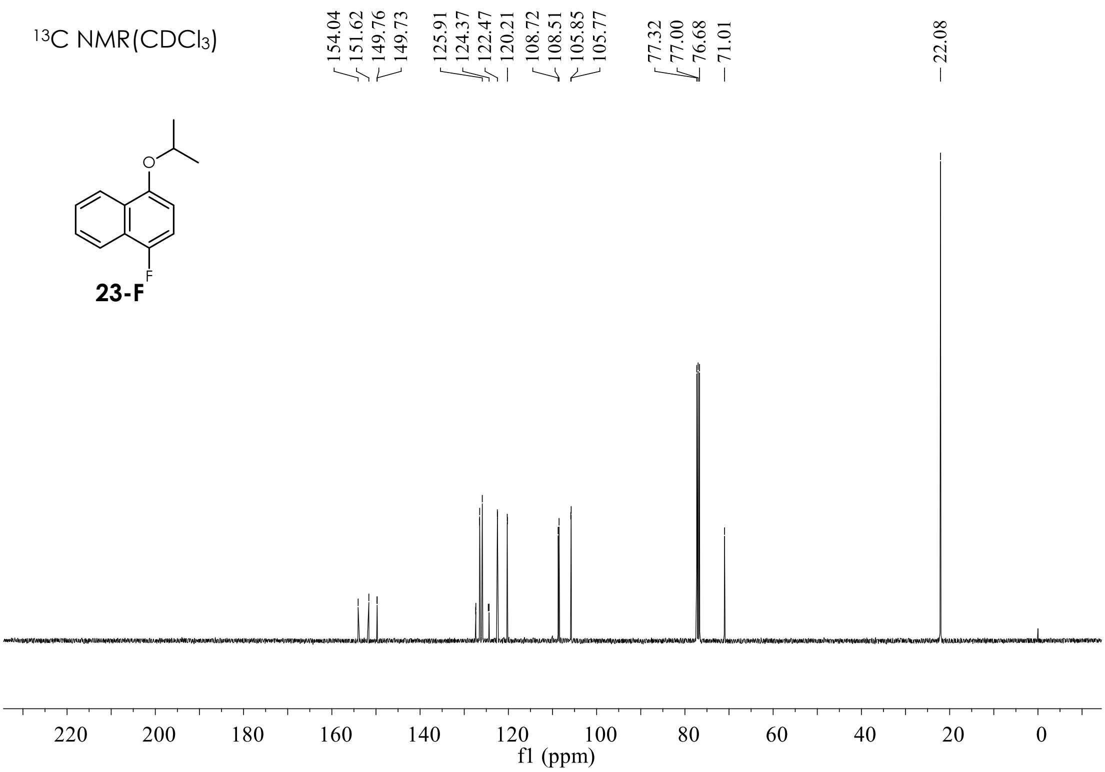
^{19}F NMR($CDCl_3$)



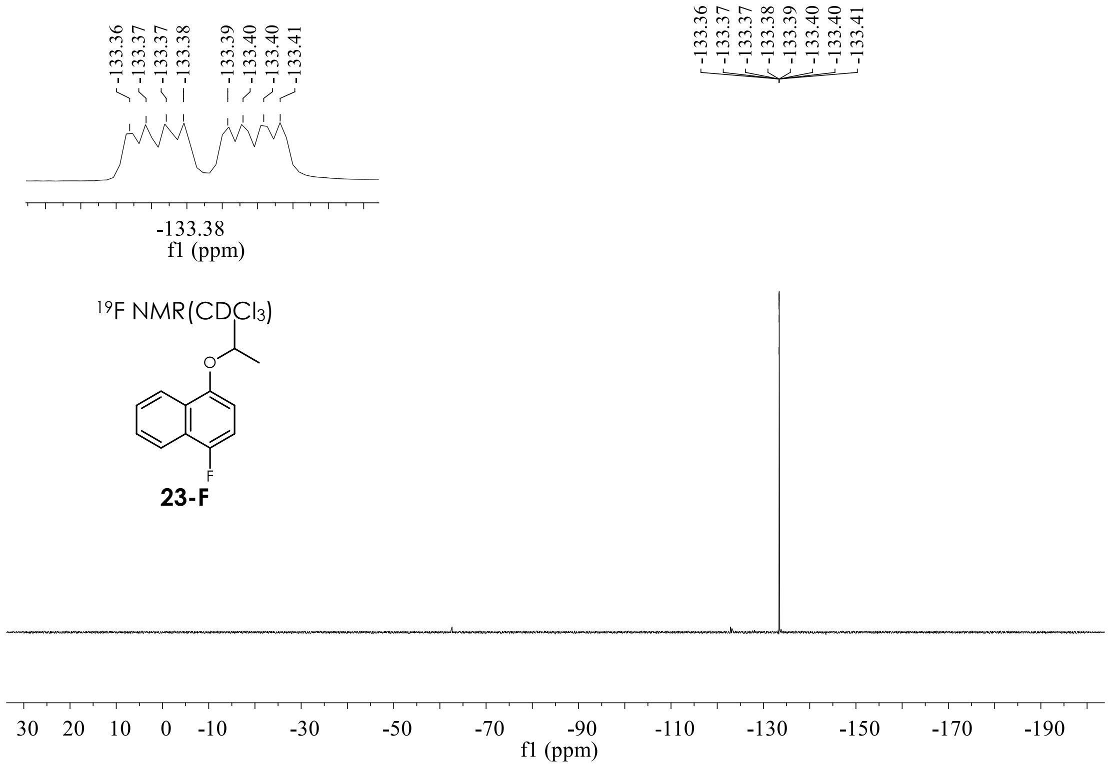
23-F-i



8.27 8.26 8.25 8.25 8.05 8.05 8.03
7.55 7.52 7.49 7.03 6.74 6.71
4.72 4.71 4.69 4.68 4.66 4.65 4.63
1.45 1.44
1H NMR(CDCl3)
O
F
23-F
0.97 0.97 2.01 0.98 1.00
1.01
6.24
2.0 10.5 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0
f1 (ppm)

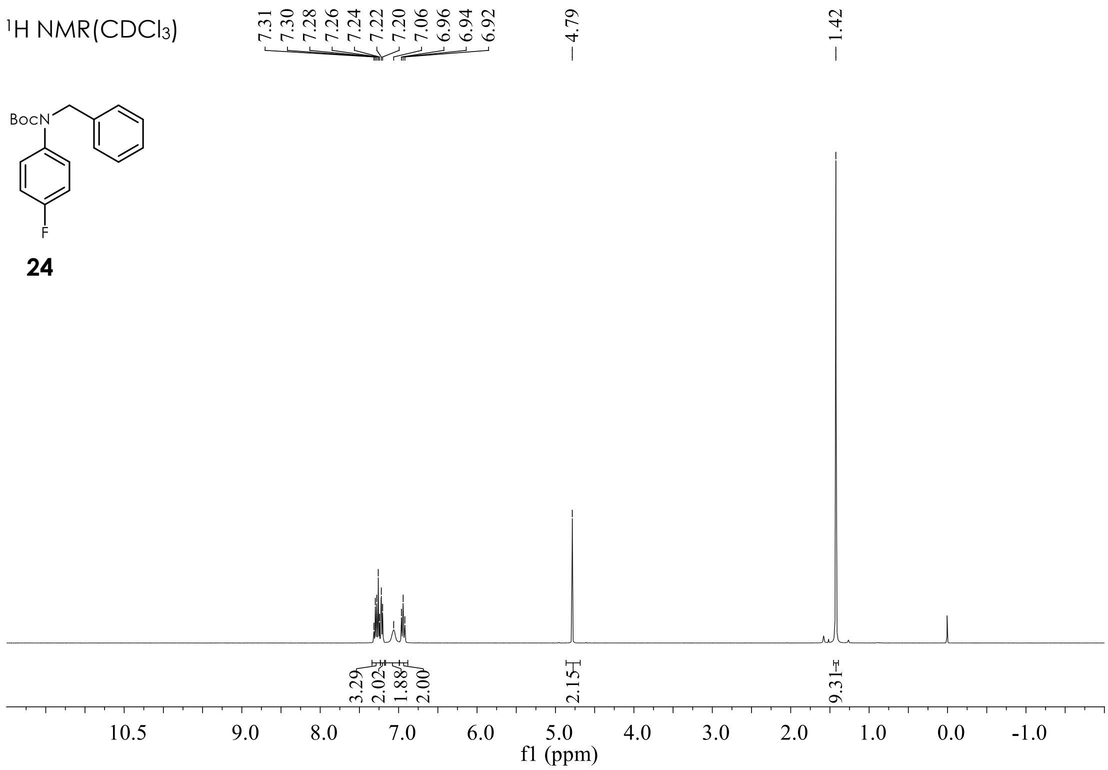


13C NMR(CDCl3)
154.04 151.62 149.76 149.73
125.91 124.37 122.47 120.21
108.72 108.51 105.85 105.77
77.32 77.00 76.68
71.01
22.08
O
F
23-F
220 200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)



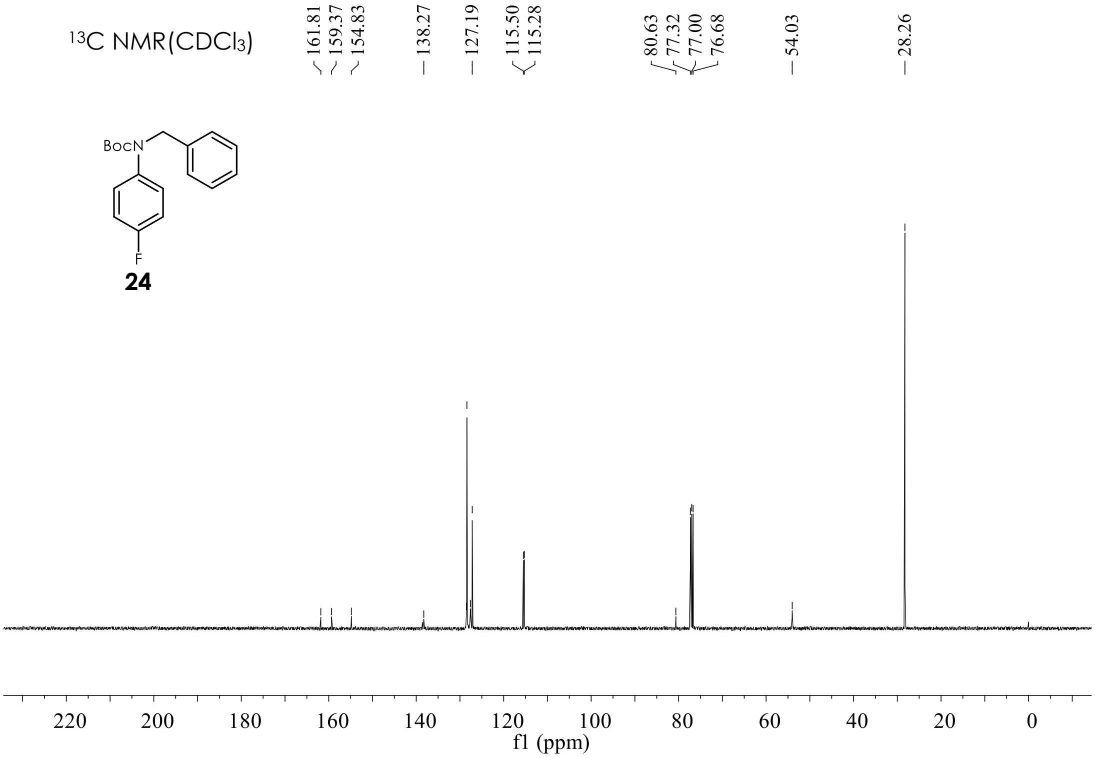
^{19}F NMR($CDCl_3$)

23-F

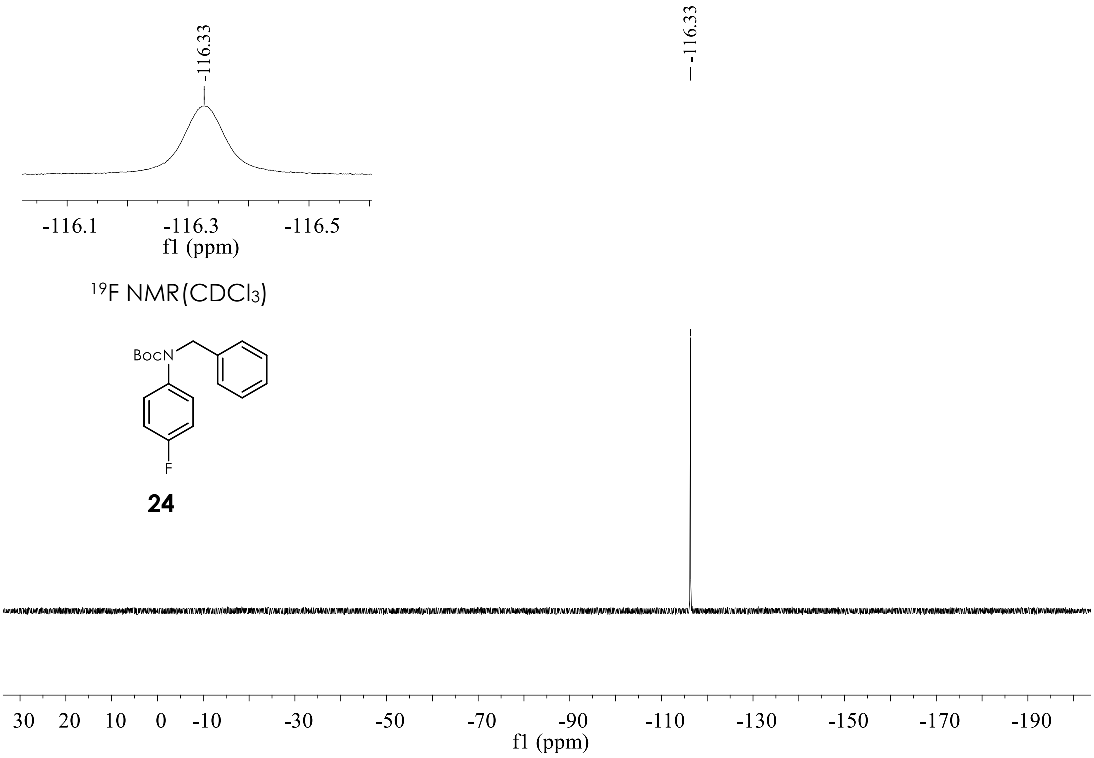


^{1}H NMR($CDCl_3$)

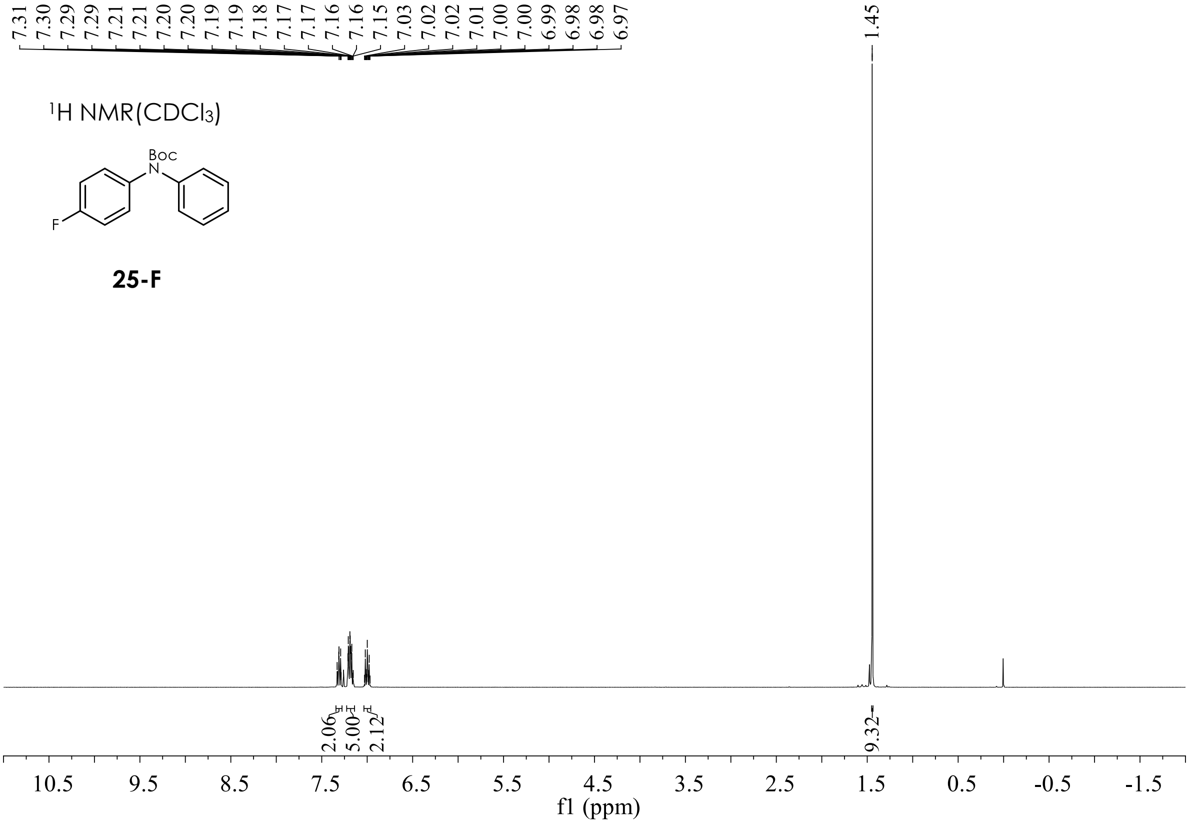
24



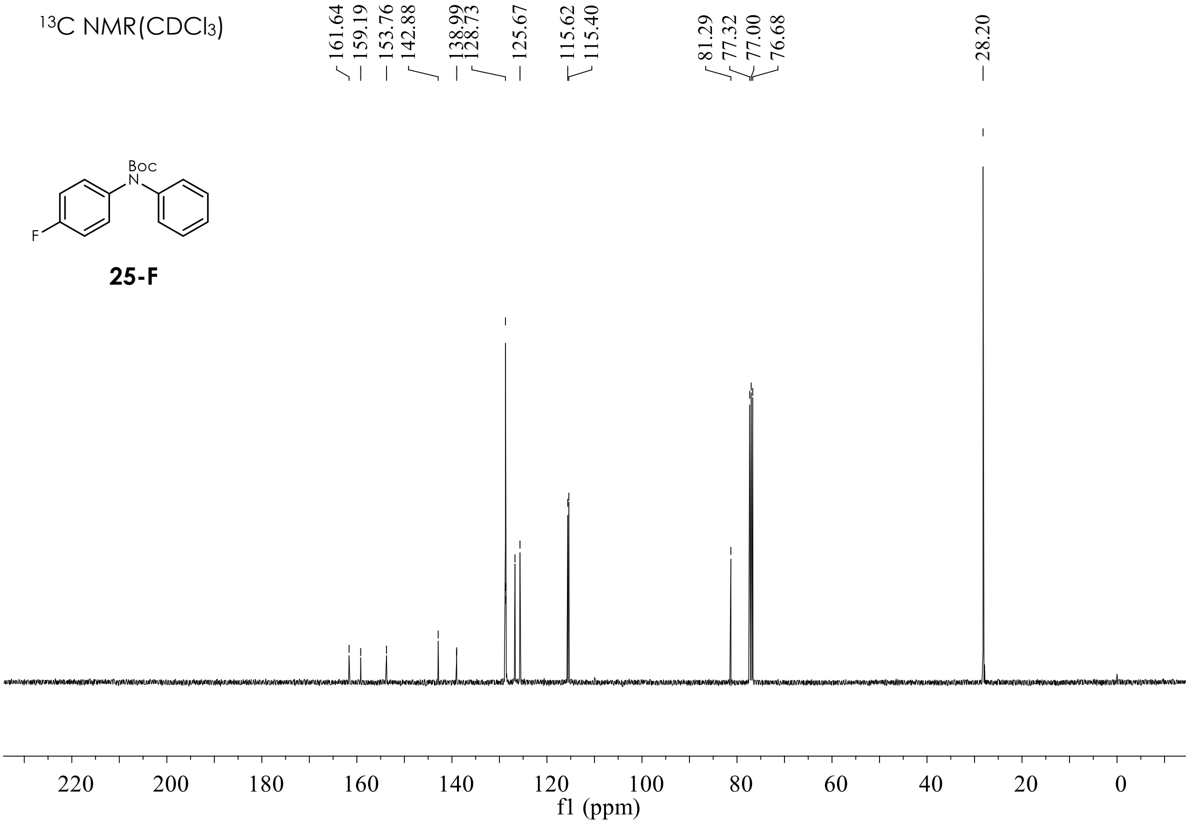
^{13}C NMR($CDCl_3$)
161.81
159.37
154.83
138.27
127.19
115.50
115.28
80.63
77.32
77.00
76.68
54.03
28.26
BocN
F
24
220 200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)



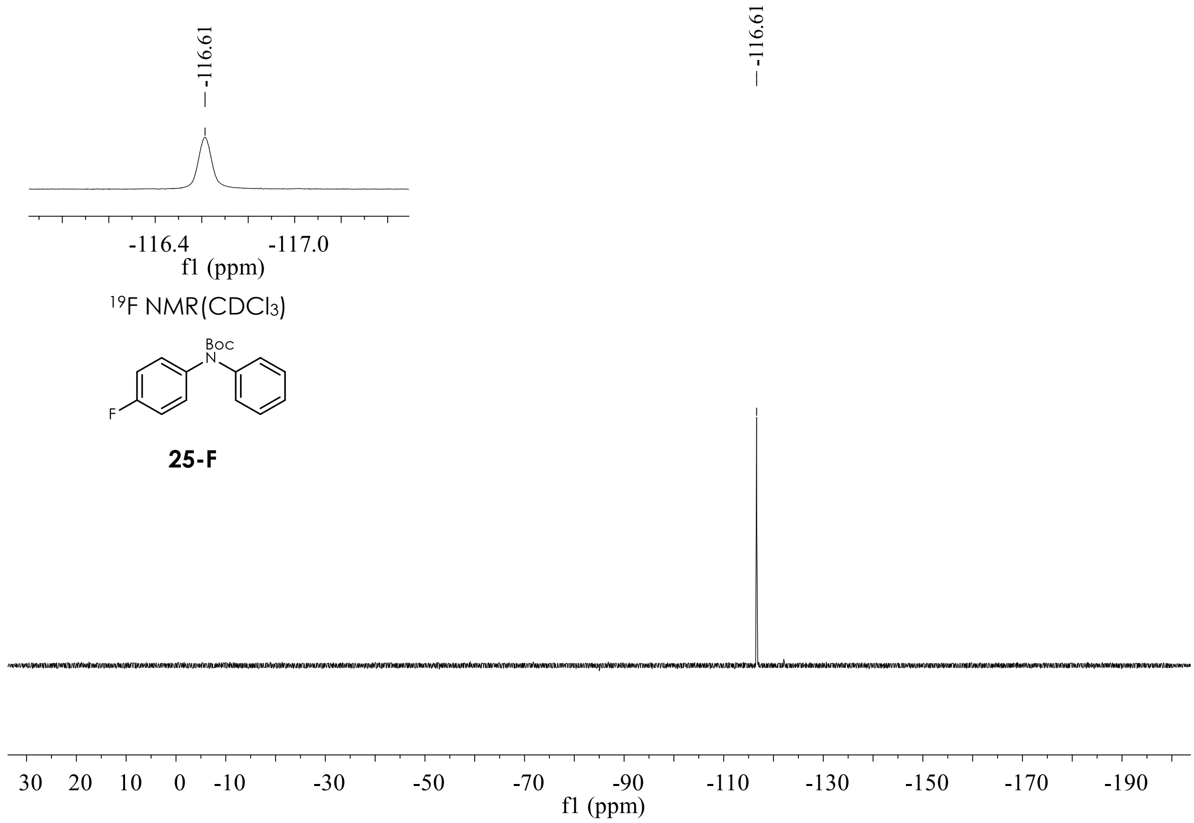
-116.33
-116.1 -116.3 -116.5
f1 (ppm)
^{19}F NMR($CDCl_3$)
-116.33
BocN
F
24
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)

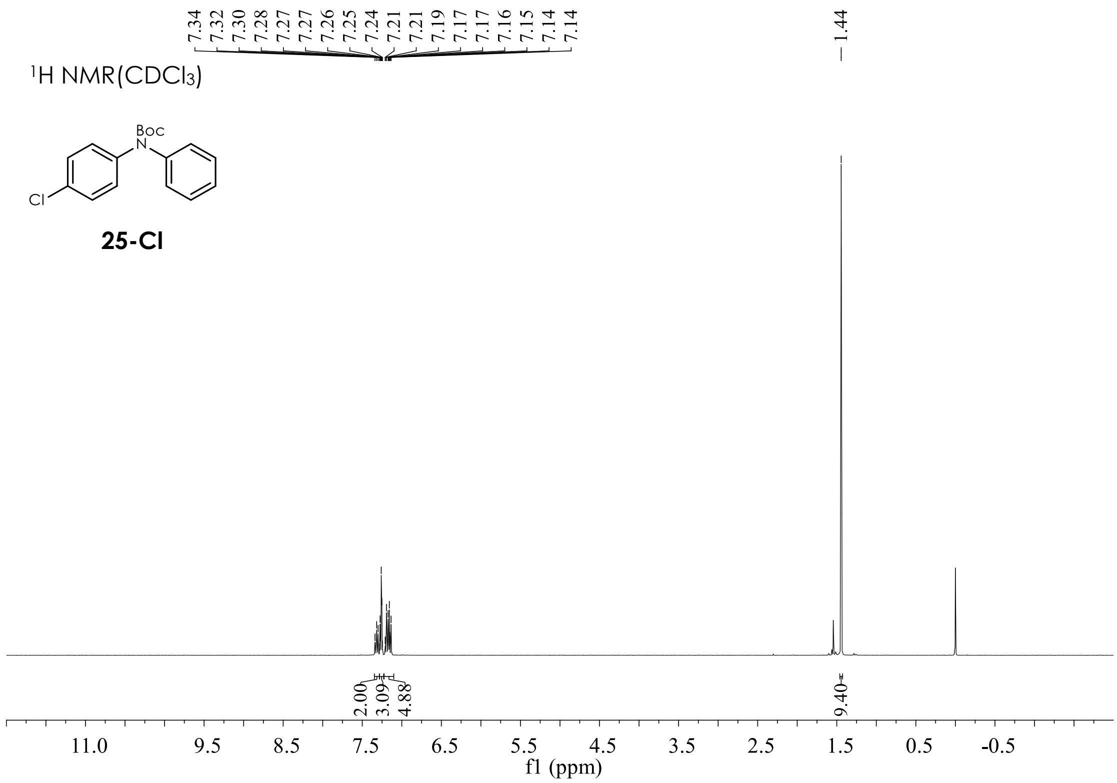


7.31 7.30 7.29 7.29 7.21 7.21 7.20 7.20 7.19 7.19 7.18 7.17 7.17 7.16 7.16 7.15 7.03 7.02 7.02 7.01 7.00 7.00 6.99 6.98 6.98 6.97
1.45
^1H NMR($CDCl_3$)
Boc
N
F
25-F
2.06
5.00
2.12
9.32
10.5 9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5 -0.5 -1.5
f1 (ppm)



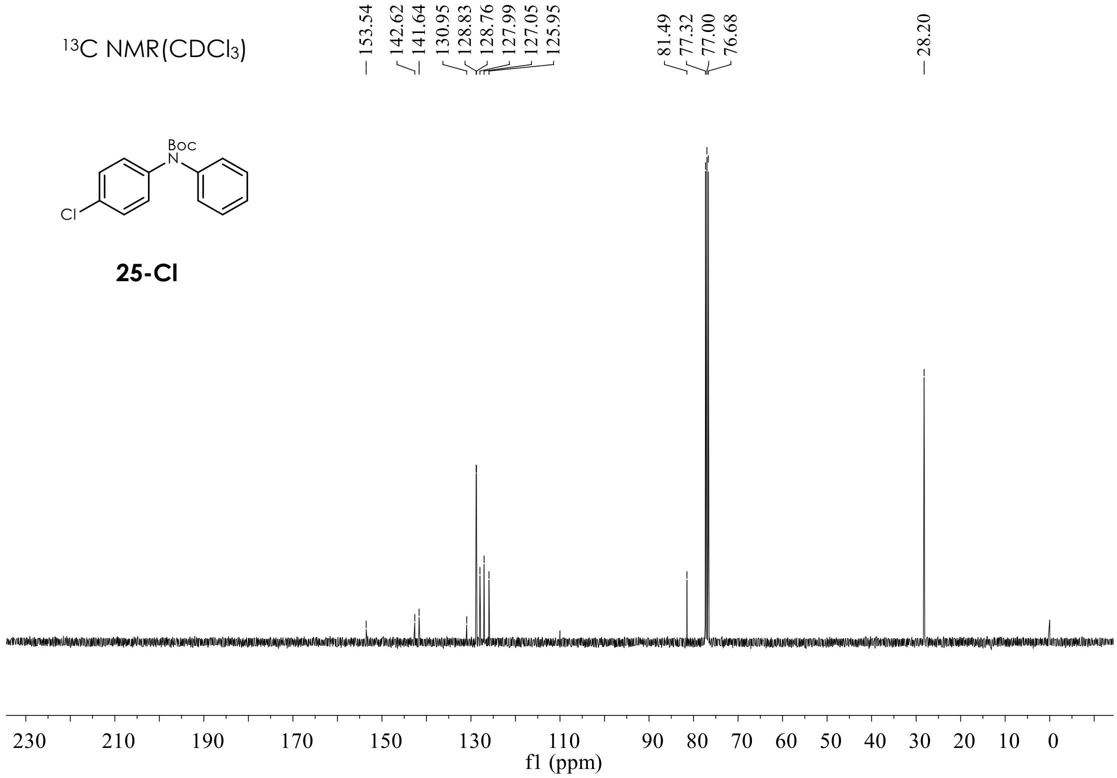
^{13}C NMR($CDCl_3$)
161.64 159.19 153.76 142.88 138.99 128.73 125.67 115.62 115.40
81.29 77.32 77.00 76.68
28.20
Boc
N
F
25-F
220 200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)


-116.61
-116.61
-116.4
-117.0
f1 (ppm)
^{19}F NMR(CDCl$_3$)
Boc
N
F
25-F
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)


7.34 7.32 7.30 7.28 7.27 7.27 7.26 7.25 7.24 7.21 7.21 7.19 7.17 7.17 7.16 7.15 7.14 7.14
1.44
^{1}H NMR(CDCl$_3$)
Boc
N
Cl
25-Cl
2.00
3.09
4.88
9.40
11.0 9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5 -0.5
f1 (ppm)

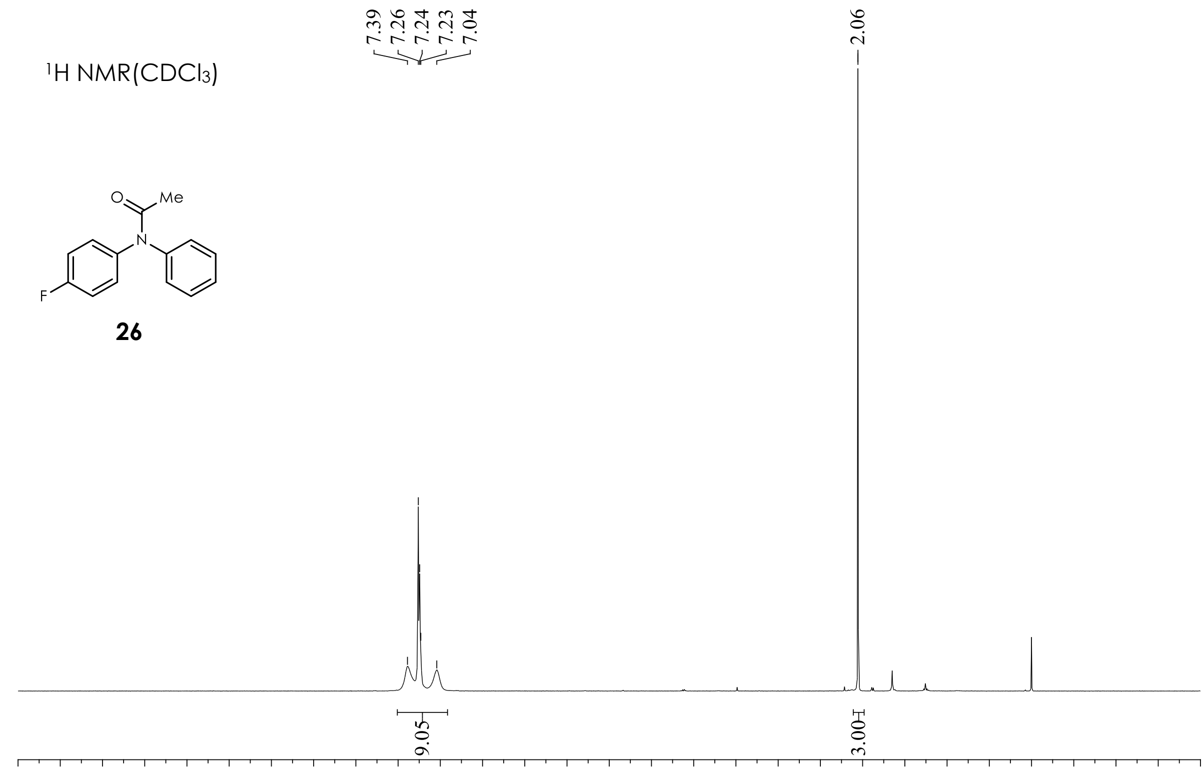
^{13}C NMR($CDCl_3$)

25-Cl

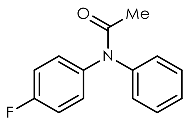


^{1}H NMR($CDCl_3$)

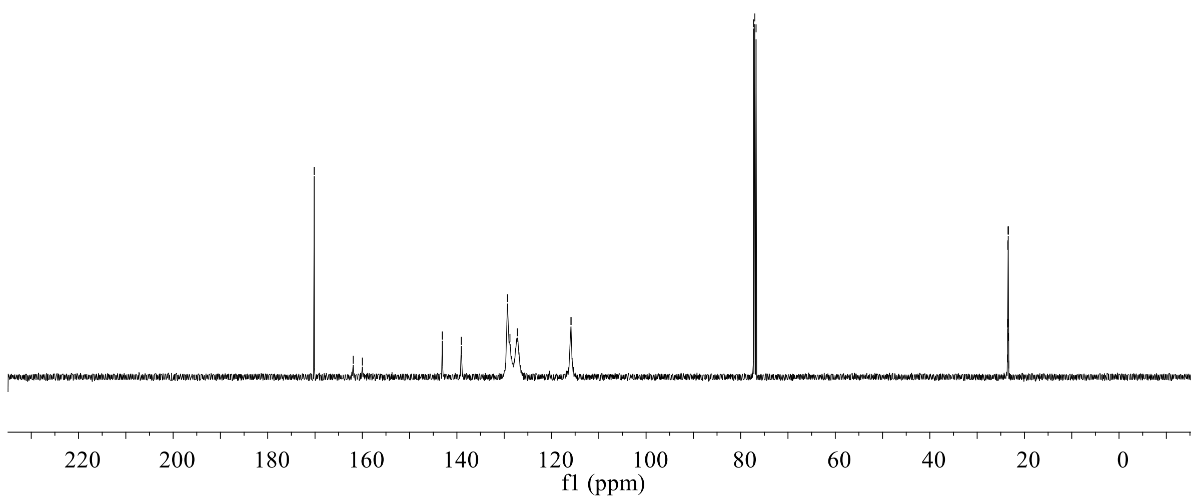
26

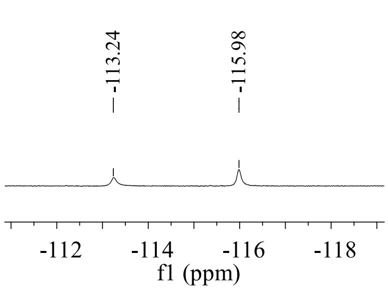


^{13}C NMR(CDCl$_3$)

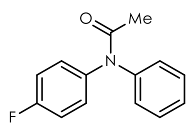


26

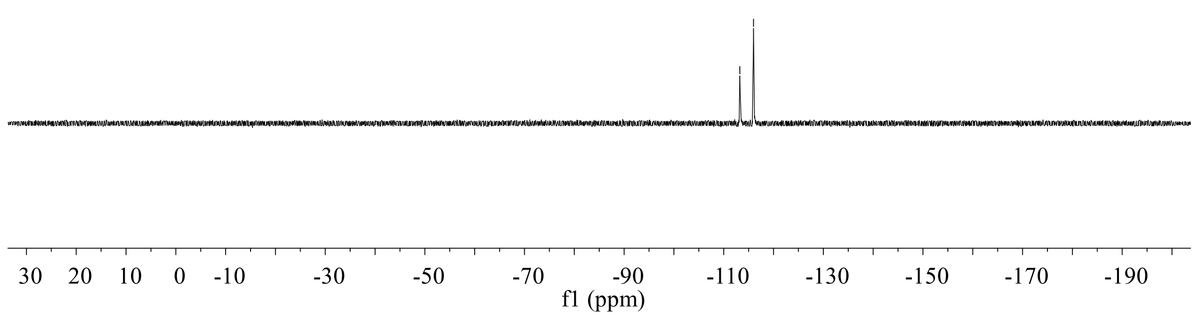




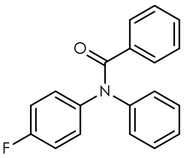
^{19}F NMR(CDCl$_3$)



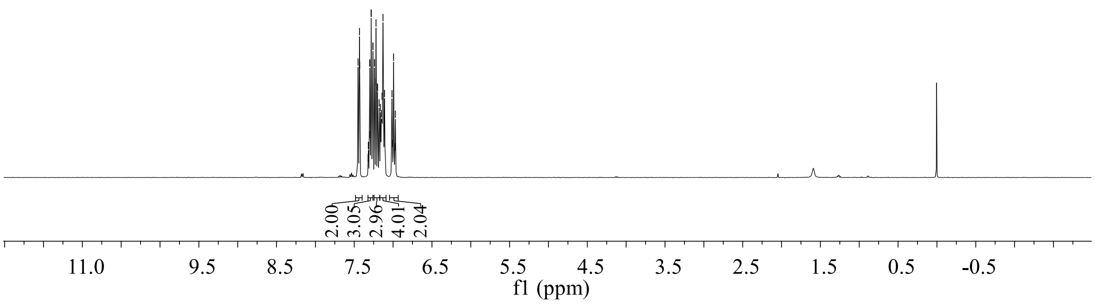
26



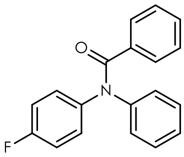
^{1}H NMR($CDCl_3$)



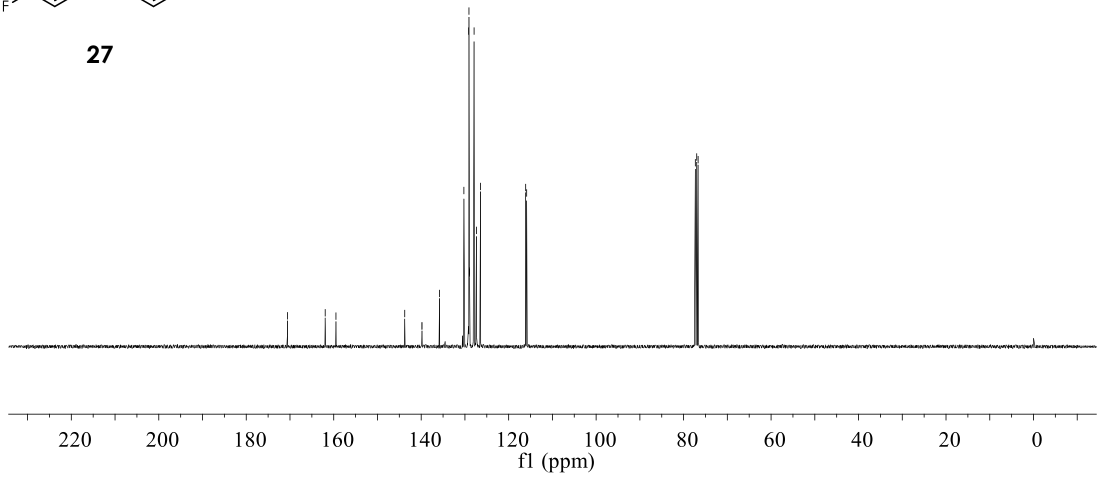
27

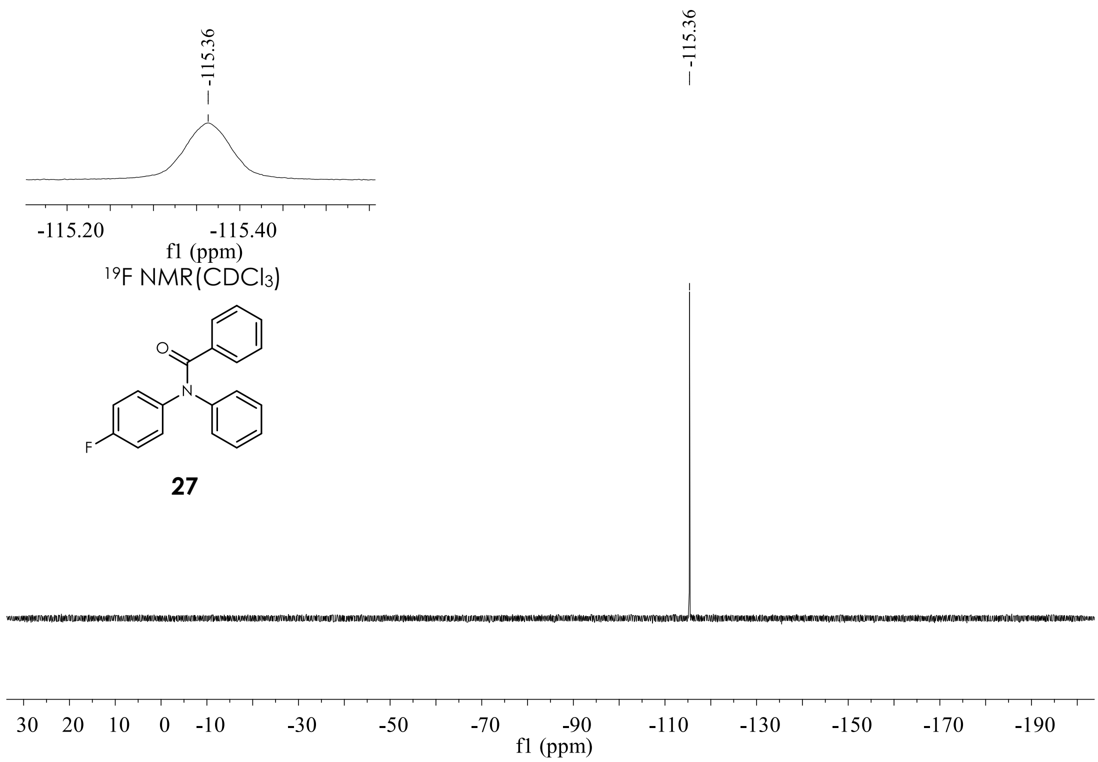


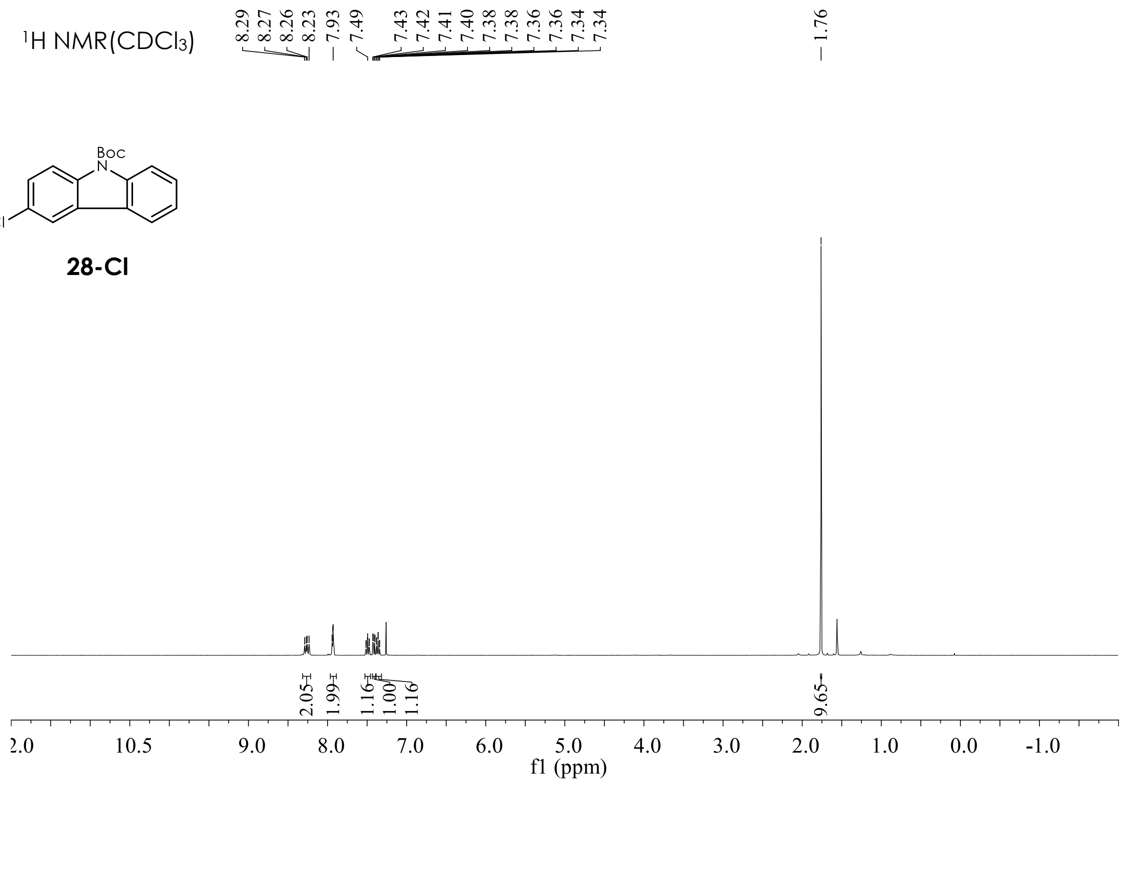
^{13}C NMR($CDCl_3$)

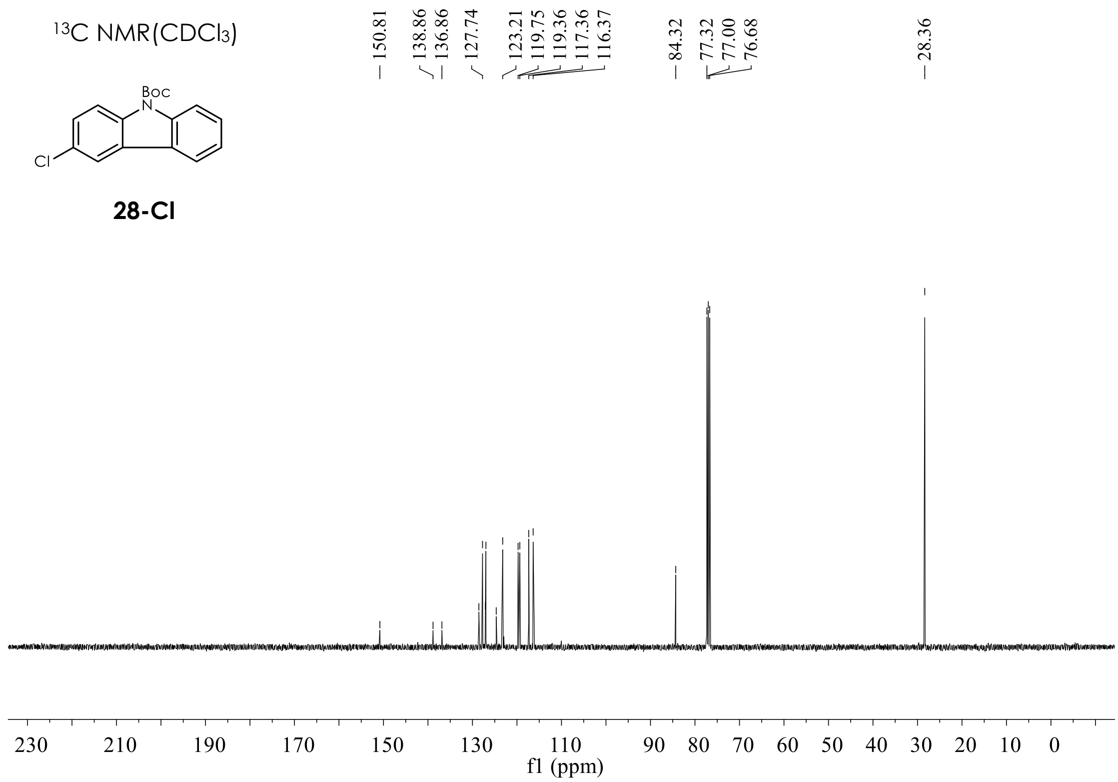


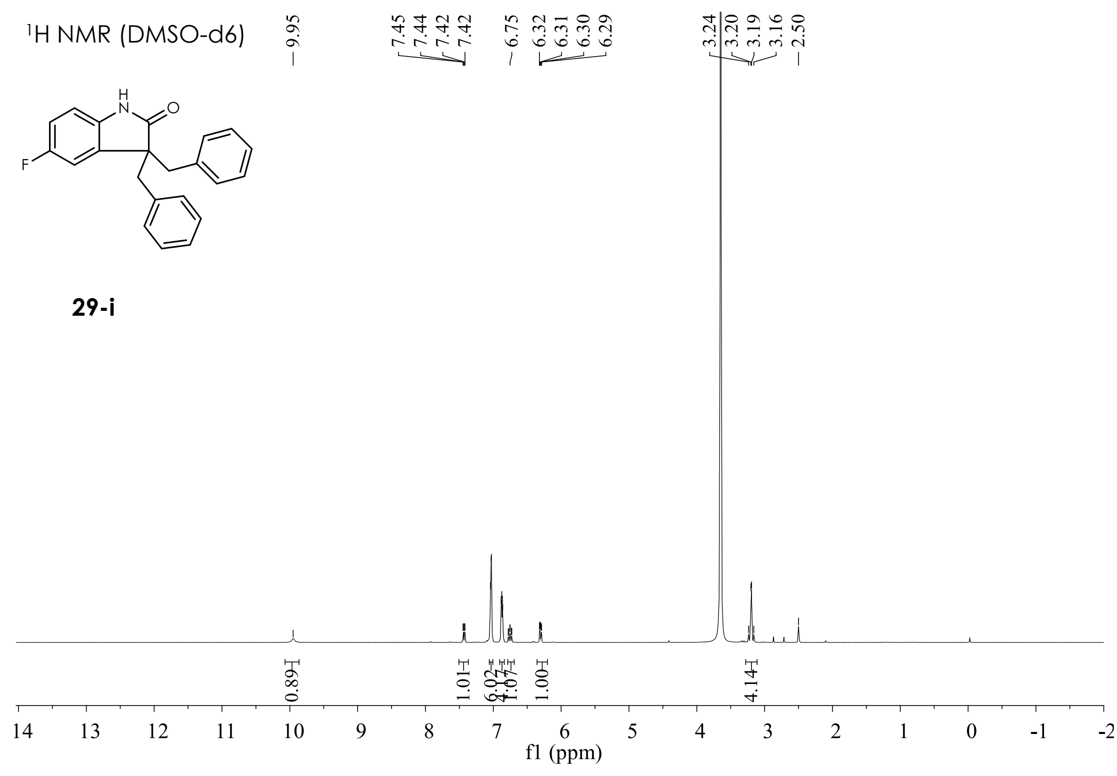
27



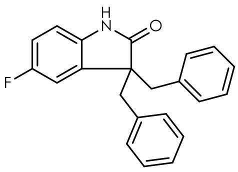

-115.36
-115.36
-115.20
-115.40
f1 (ppm)
19F NMR(CDCl3)
O
N
F
27
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)


1H NMR(CDCl3)
8.29 8.27 8.26 8.23 7.93 7.49 7.43 7.42 7.41 7.40 7.38 7.38 7.36 7.36 7.34 7.34
1.76
Boc
N
Cl
28-Cl
2.05 1.99 1.16 1.00 1.16
9.65
2.0 10.5 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0
f1 (ppm)

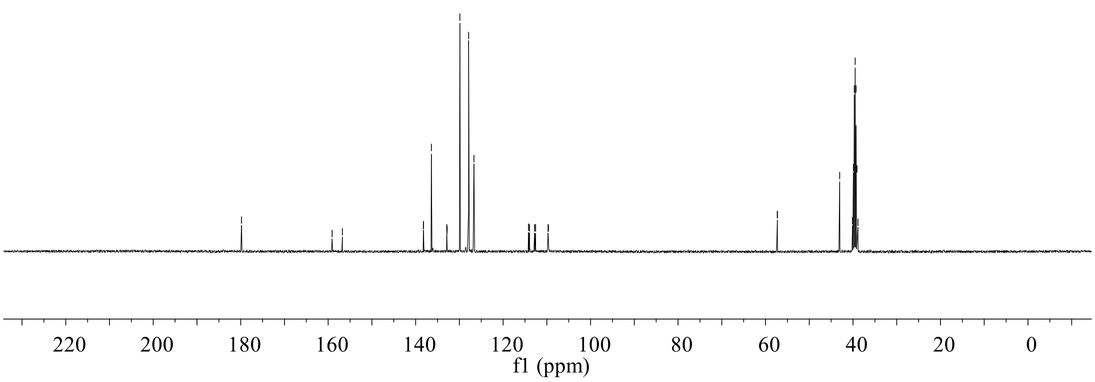

13C NMR(CDCl3)
Boc
N
Cl
28-Cl
150.81
138.86
136.86
127.74
123.21
119.75
119.36
117.36
116.37
84.32
77.32
77.00
76.68
28.36
230 210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

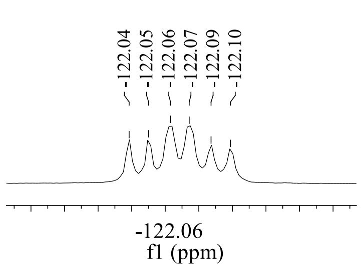

1H NMR (DMSO-d6)
H
N
O
F
29-i
9.95
7.45
7.44
7.42
7.42
6.75
6.32
6.31
6.30
6.29
3.24
3.20
3.19
3.16
2.50
0.89
1.01
6.02
1.00
4.14
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
f1 (ppm)

^{13}C NMR (DMSO-d6)

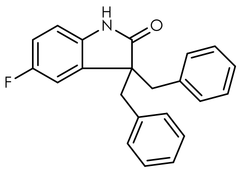


29-i

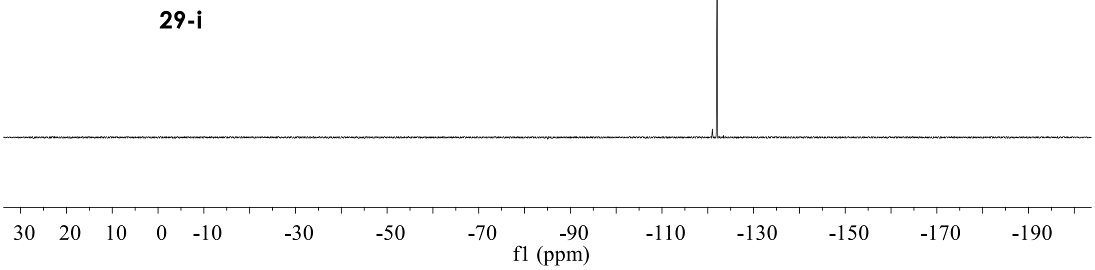




^{19}F NMR (DMSO-d6)

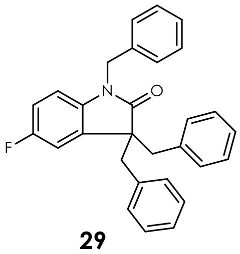


29-i

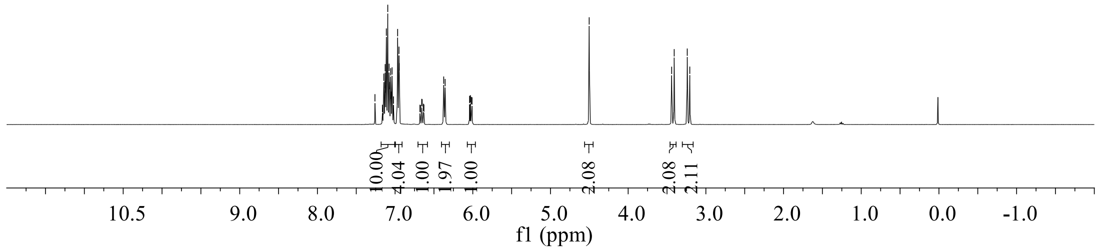


7.13 7.11 7.09 7.08 7.07 7.06 7.05 7.04 7.02 6.97 6.95 6.95 6.68 6.67 6.66 6.65 6.64 6.63 6.37 6.36 6.03 6.02 6.01 4.50 3.44 3.41 3.24 3.21

^{1}H NMR(CDCl$_3$)

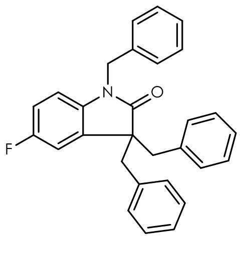


29

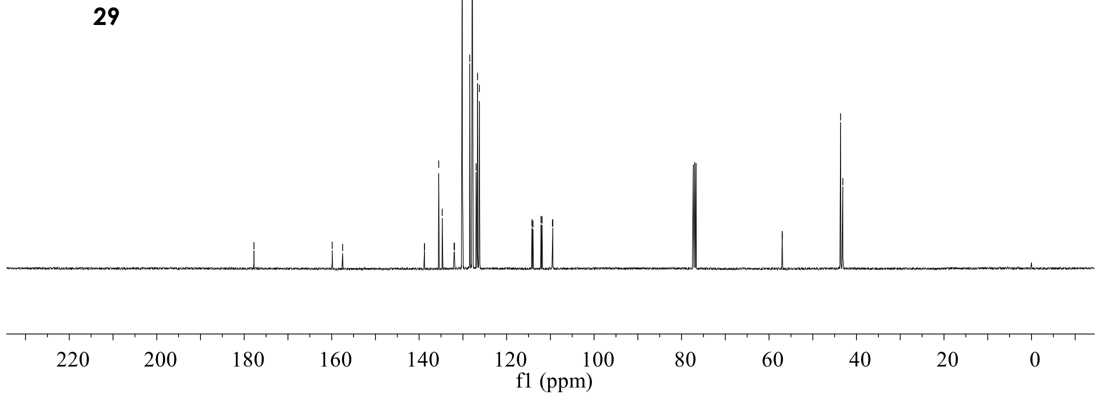


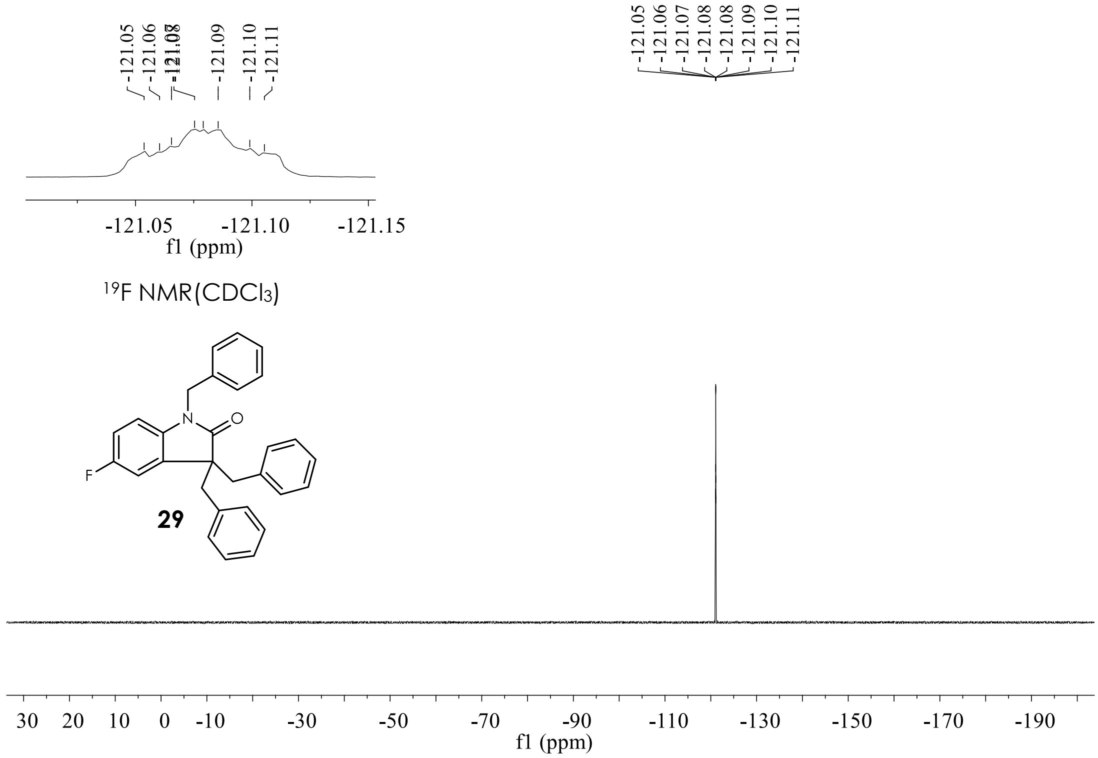
^{13}C NMR(CDCl$_3$)

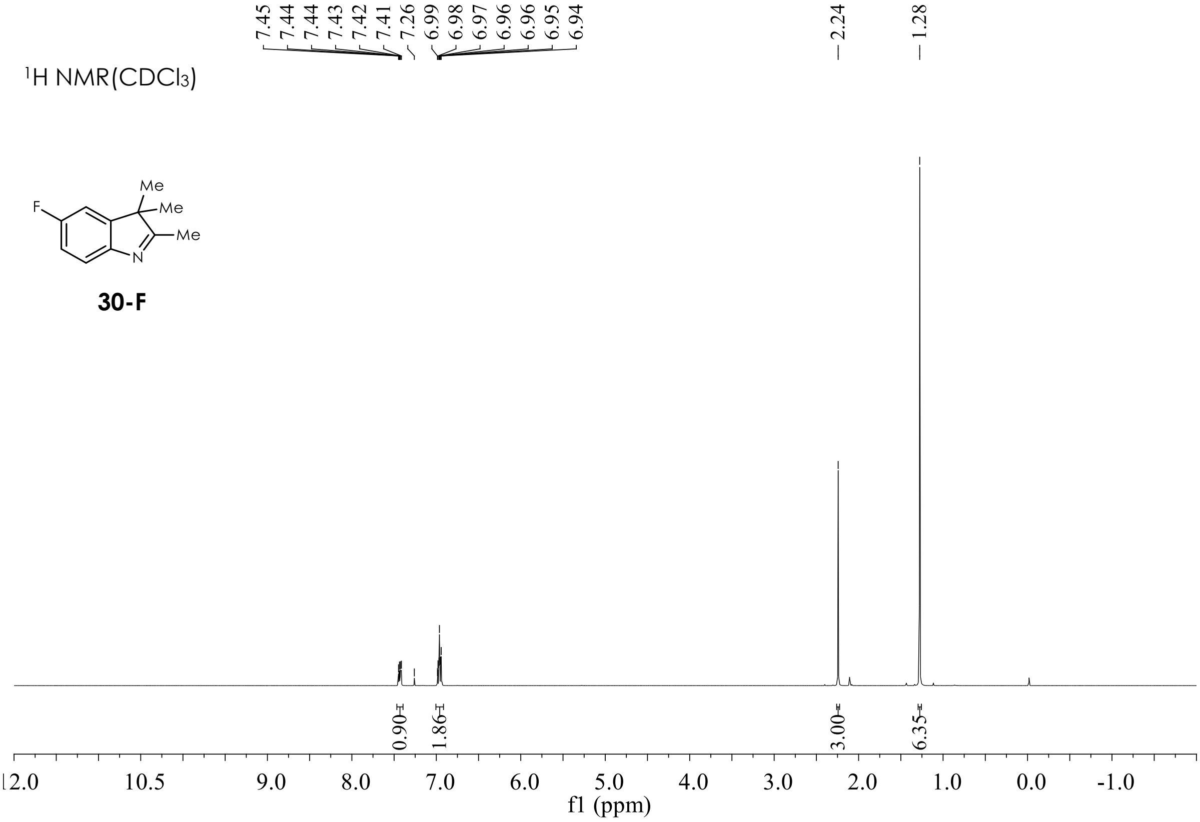
177.78 159.88 157.49 134.72 131.93 128.44 126.97 126.24 114.22 113.99 112.13 111.88 109.52 109.44 56.99 56.97 43.62 43.13

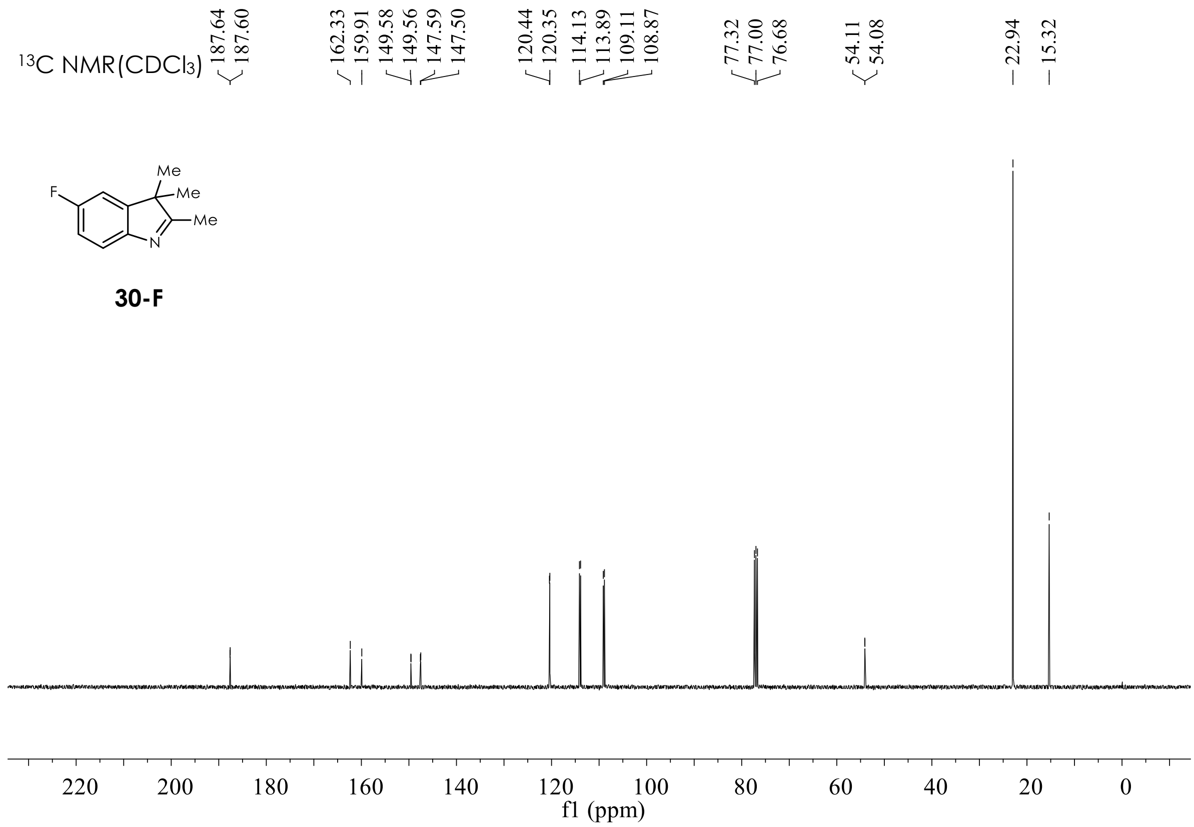


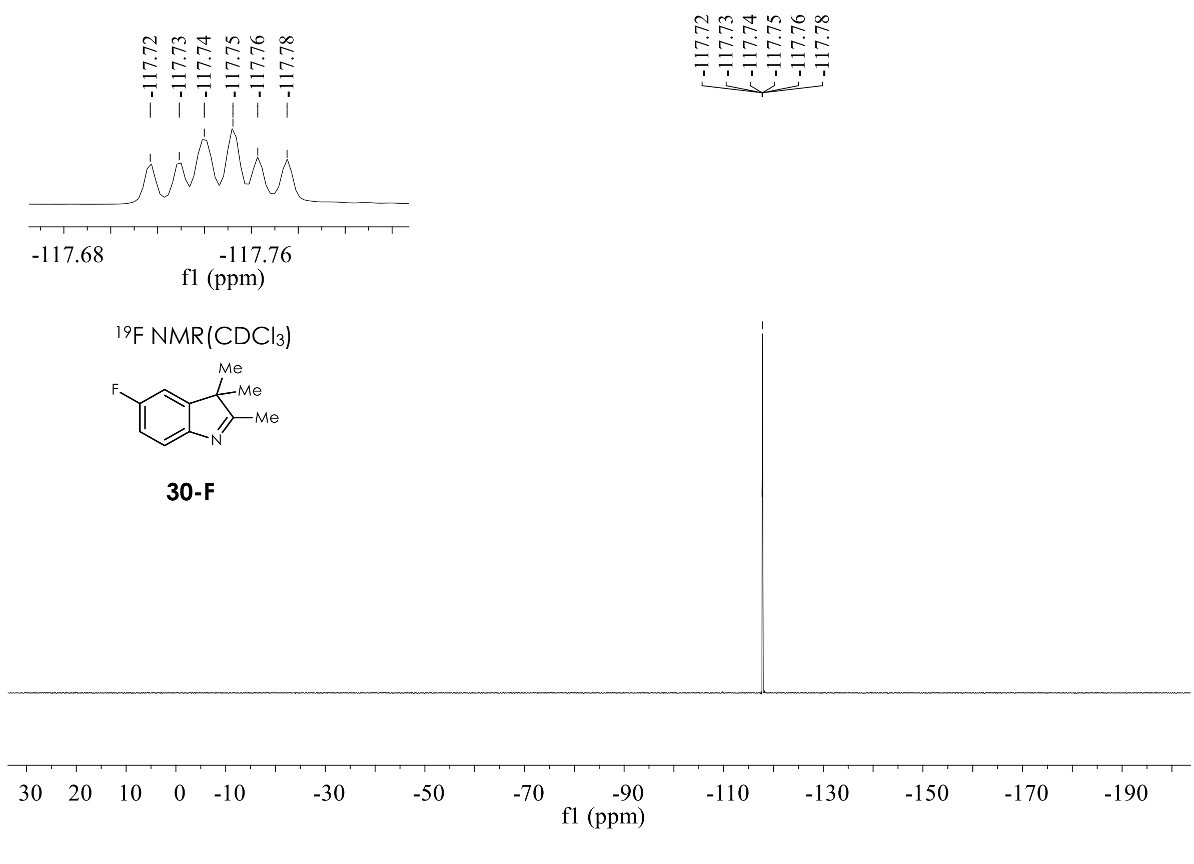
29



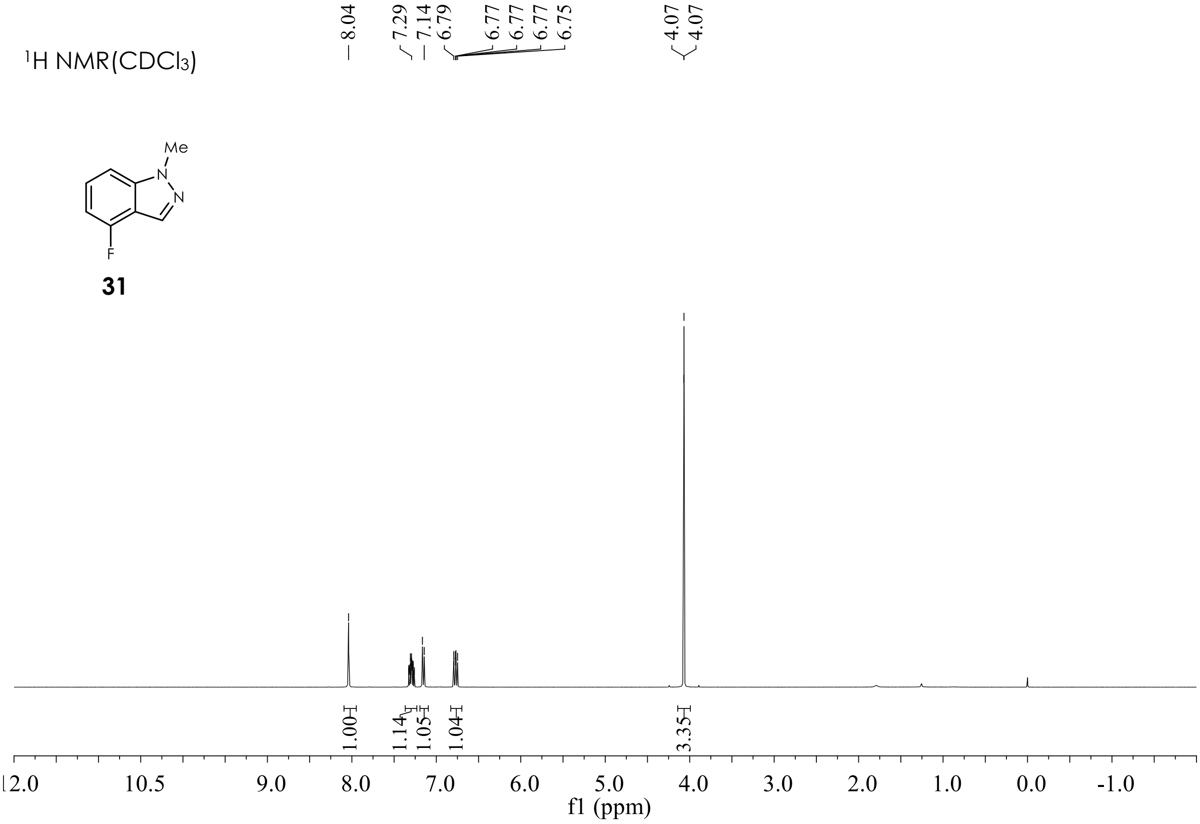

-121.05
-121.06
-121.07
-121.08
-121.08
-121.09
-121.10
-121.11
-121.05 -121.10 -121.15
f1 (ppm)
^{19}F NMR(CDCl$_3$)
F
N
O
29
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)


7.45
7.44
7.44
7.43
7.42
7.41
7.26
6.99
6.98
6.97
6.96
6.96
6.95
6.94
2.24
1.28
^{1}H NMR(CDCl$_3$)
F
Me
Me
Me
N
30-F
0.90
1.86
3.00
6.35
12.0 10.5 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0
f1 (ppm)

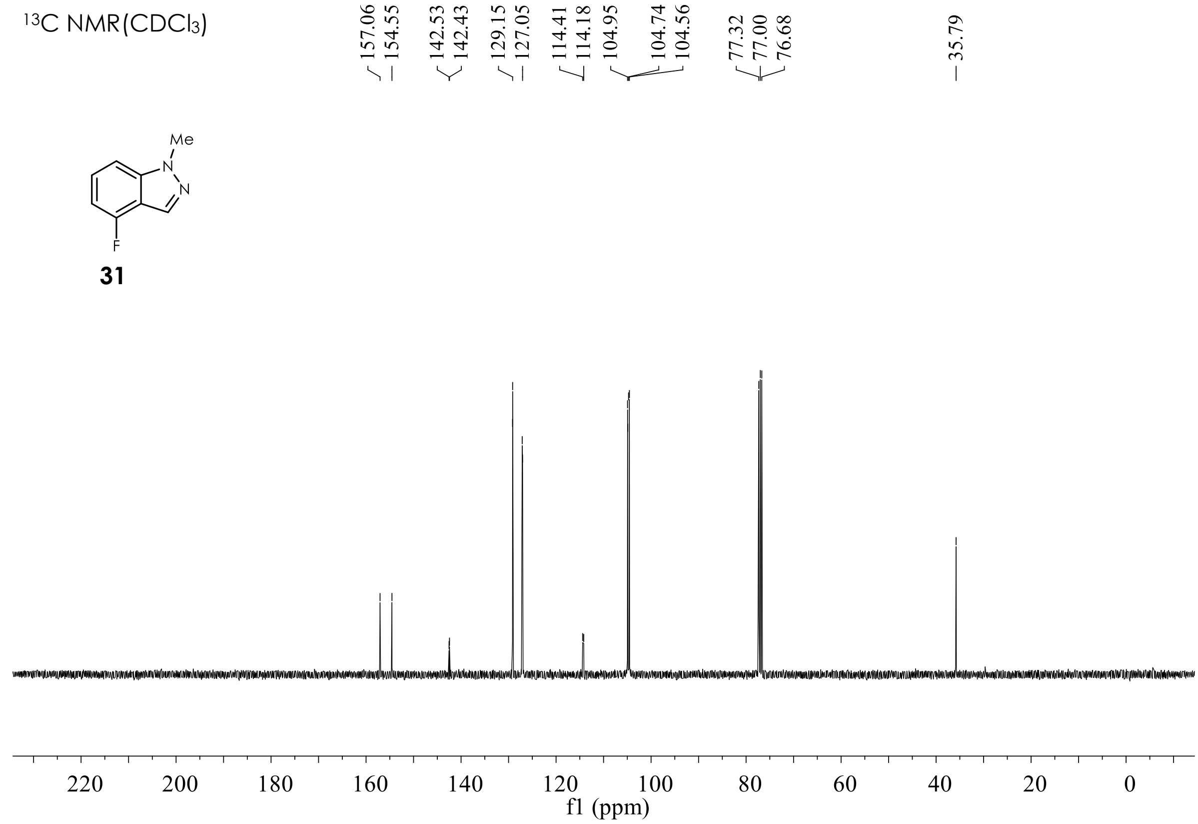

13C NMR(CDCl3)
187.64
187.60
162.33
159.91
149.58
149.56
147.59
147.50
120.44
120.35
114.13
113.89
109.11
108.87
77.32
77.00
76.68
54.11
54.08
22.94
15.32
Me
Me
Me
F
N
30-F
220
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

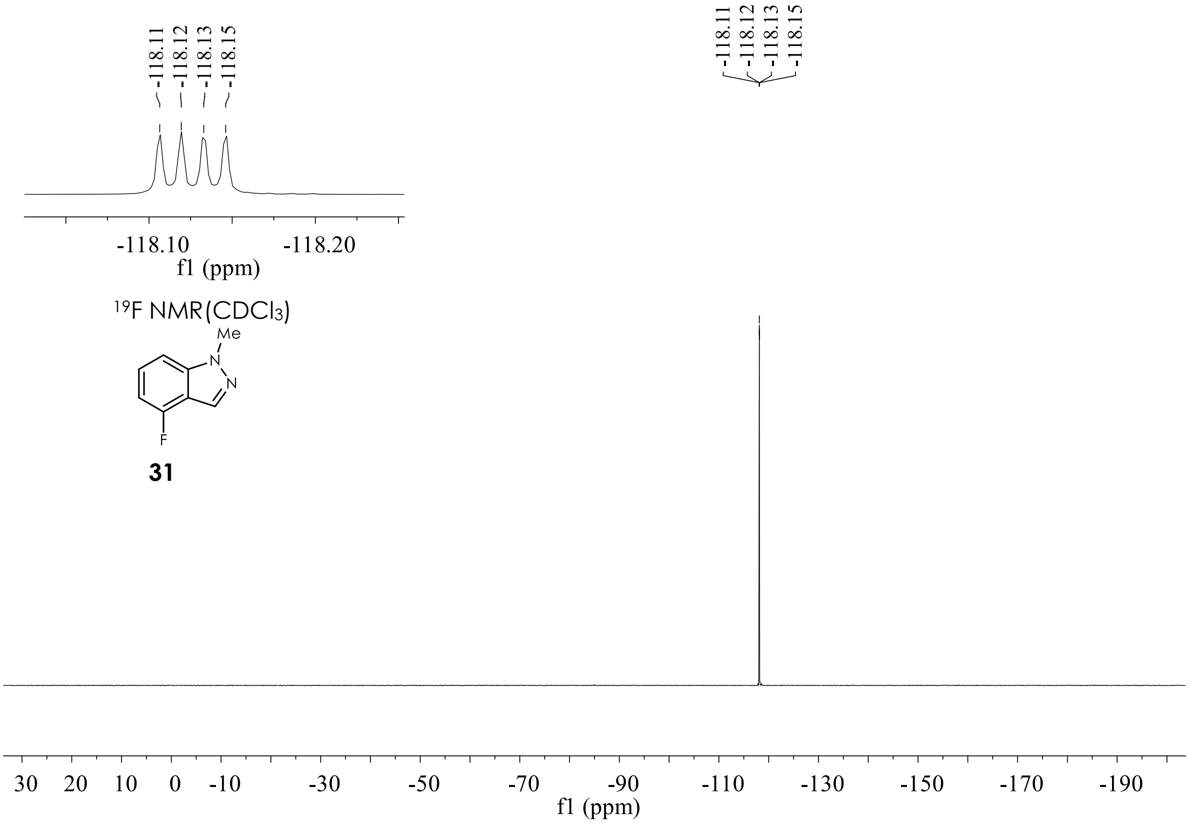

-117.72
-117.73
-117.74
-117.75
-117.76
-117.78
-117.68
-117.76
f1 (ppm)
19F NMR(CDCl3)
Me
Me
Me
F
N
30-F
30
20
10
0
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
f1 (ppm)

[1]H NMR($CDCl_3$)



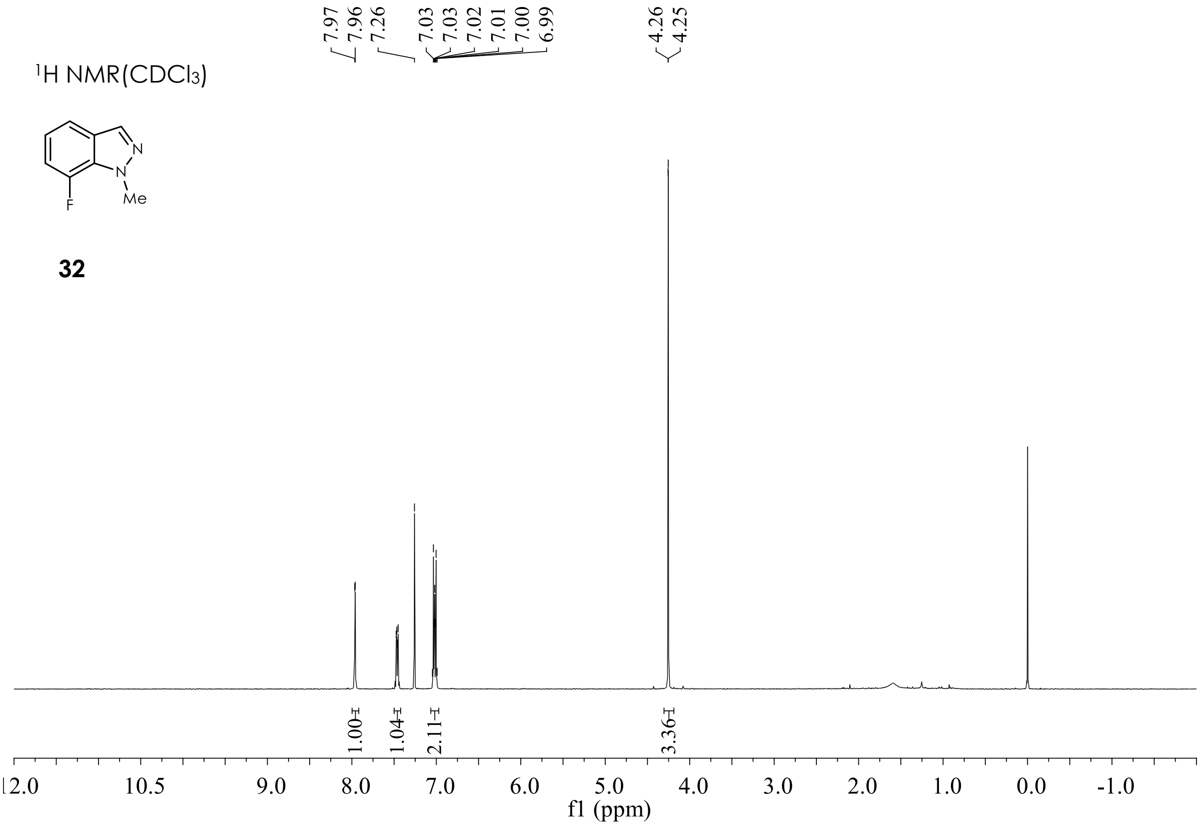
[13]C NMR($CDCl_3$)





^{19}F NMR($CDCl_3$)

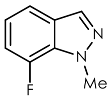
31



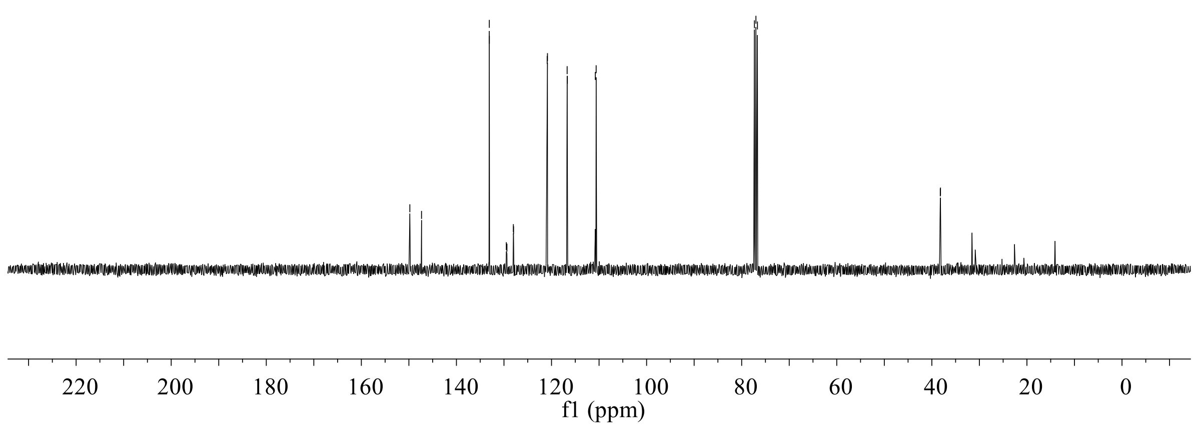
^{1}H NMR($CDCl_3$)

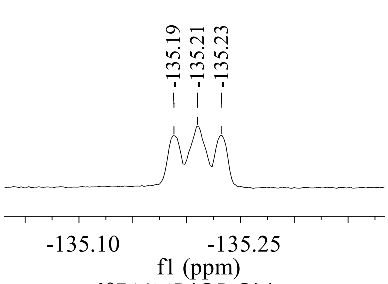
32

^{13}C NMR($CDCl_3$)

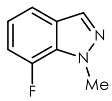


32

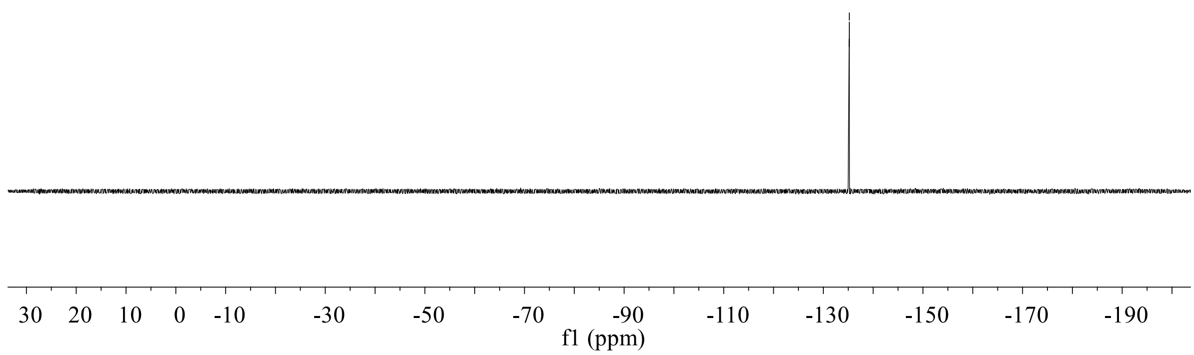




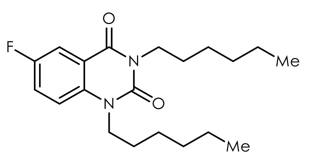
^{19}F NMR($CDCl_3$)



32



^1H NMR($CDCl_3$)



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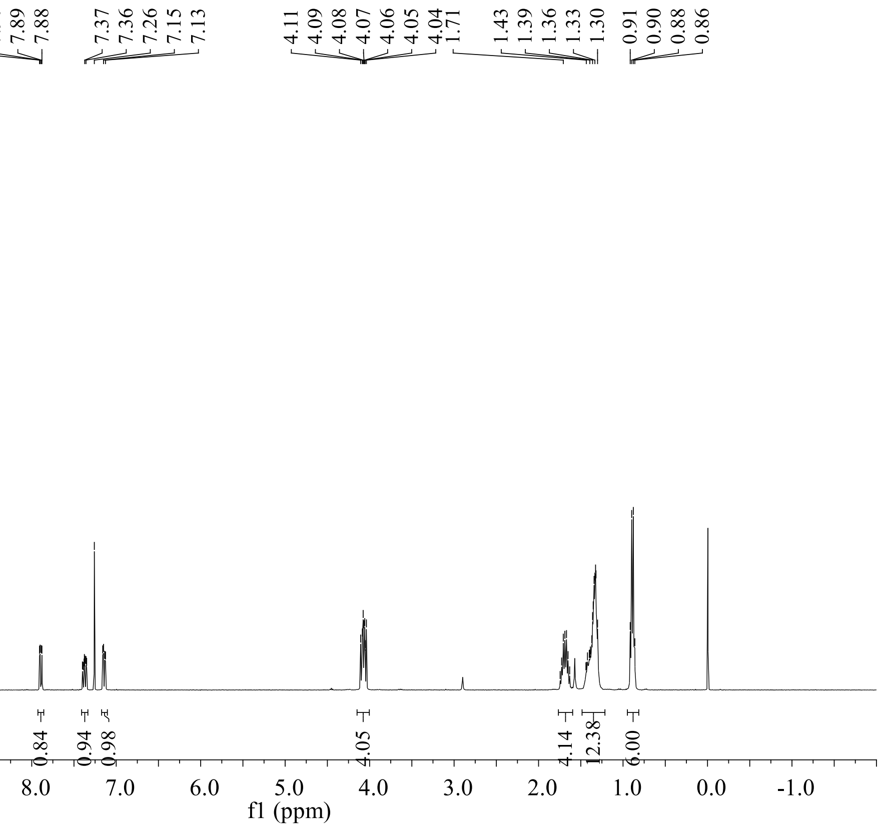
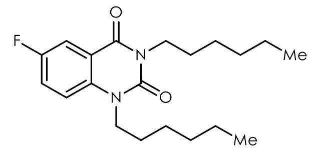
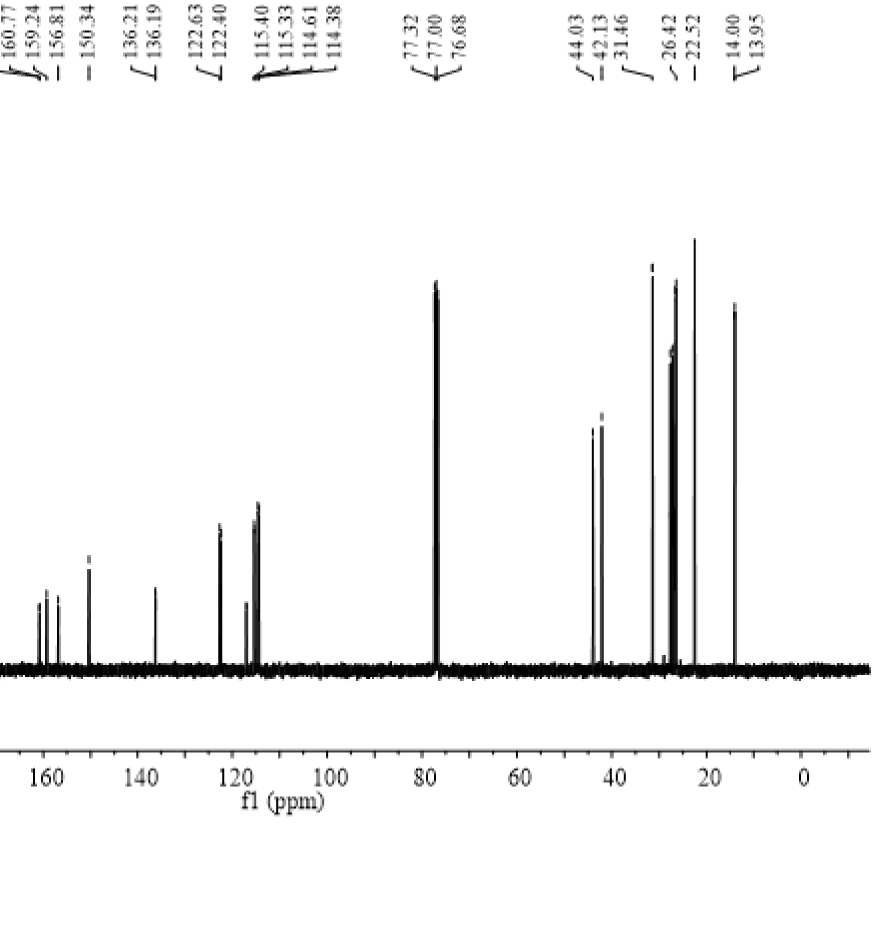
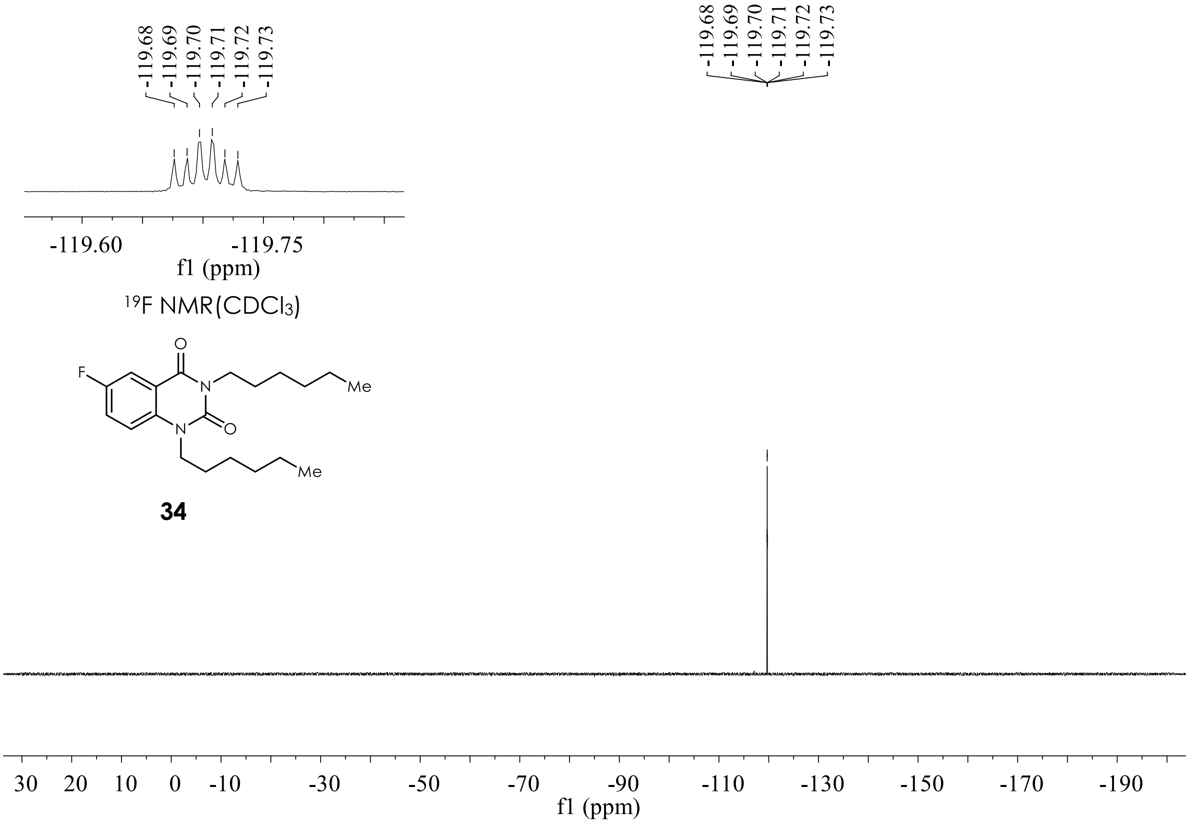


^{13}C NMR($CDCl_3$)



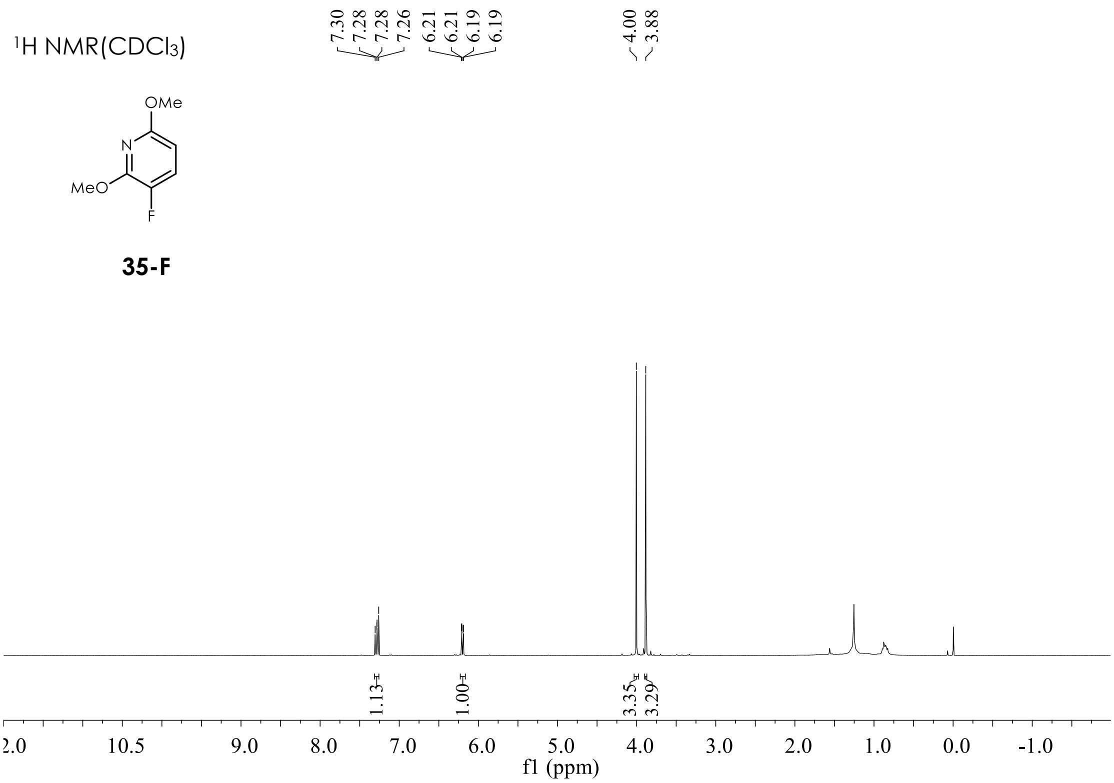
34





^{19}F NMR($CDCl_3$)

34

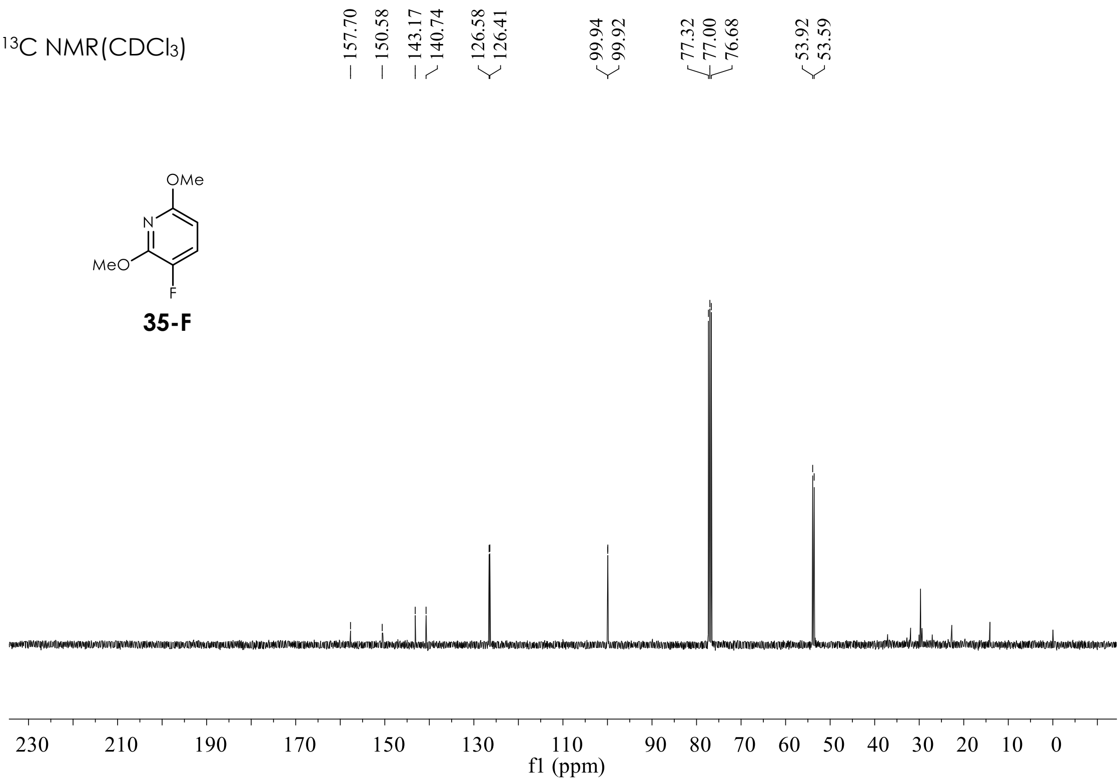


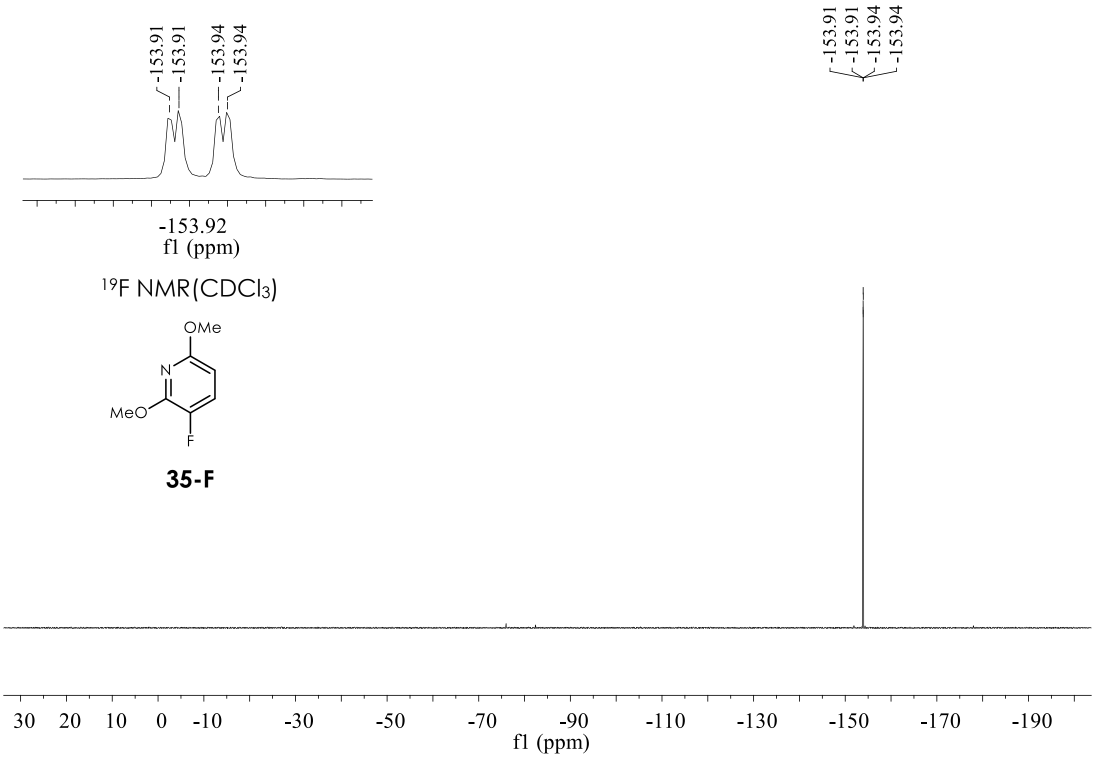
^{1}H NMR($CDCl_3$)

35-F

^{13}C NMR($CDCl_3$)

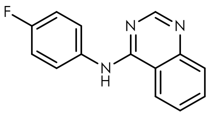
35-F



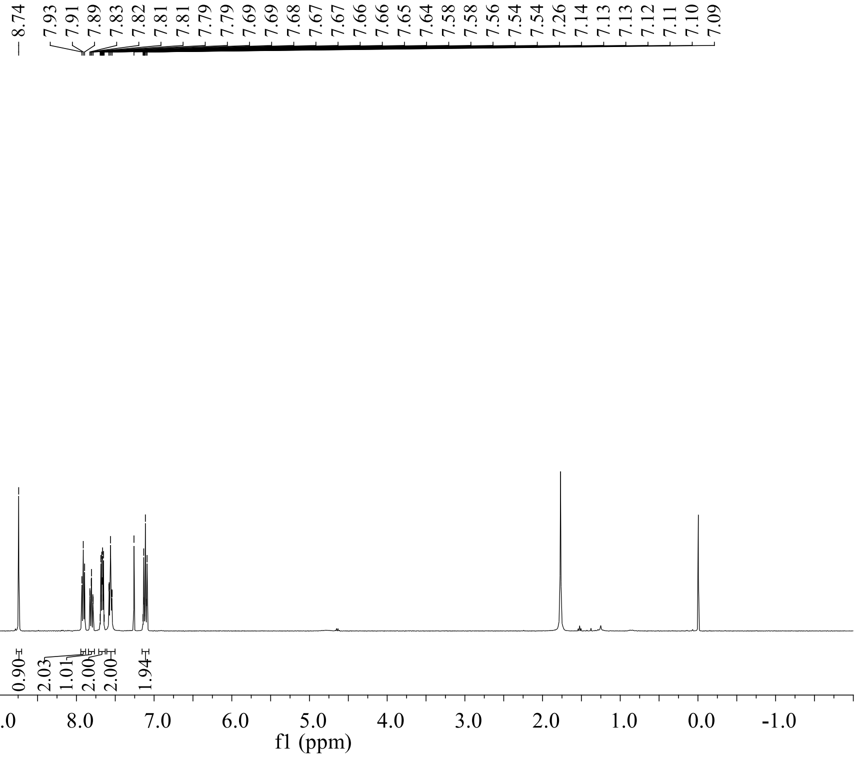


35-F

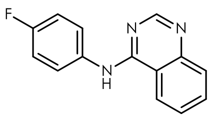
^{1}H NMR($CDCl_3$)



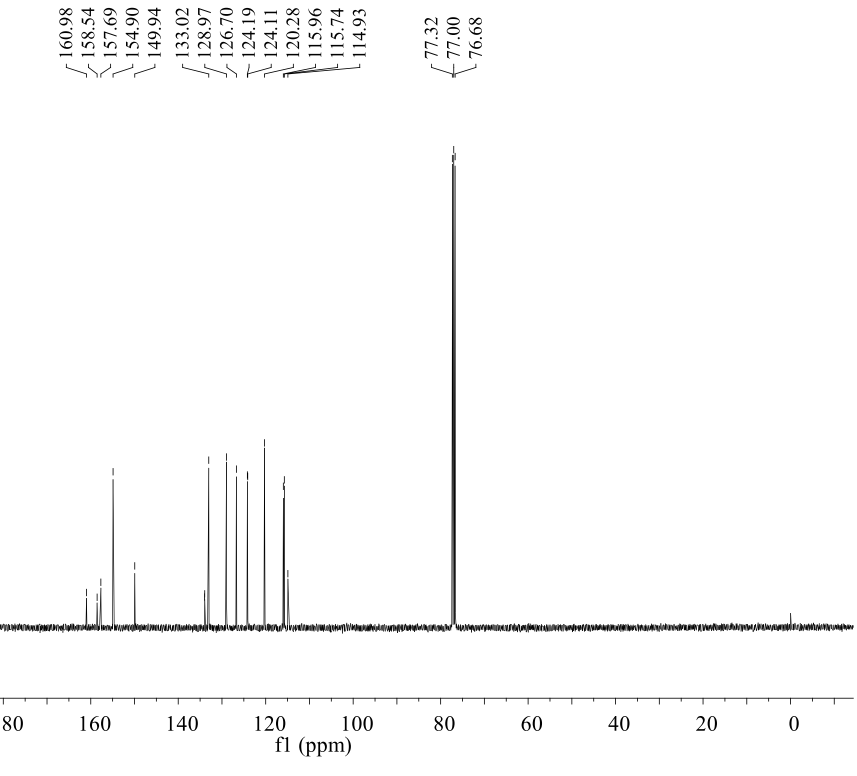
37-i



^{13}C NMR($CDCl_3$)

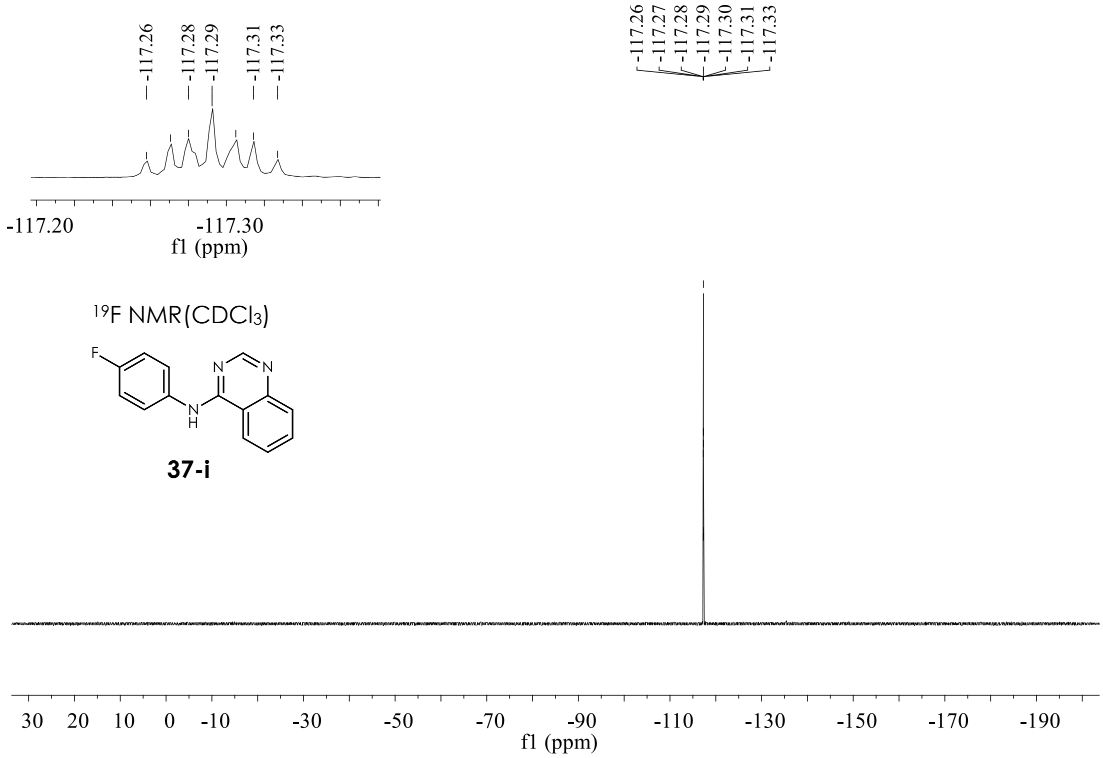


37-i



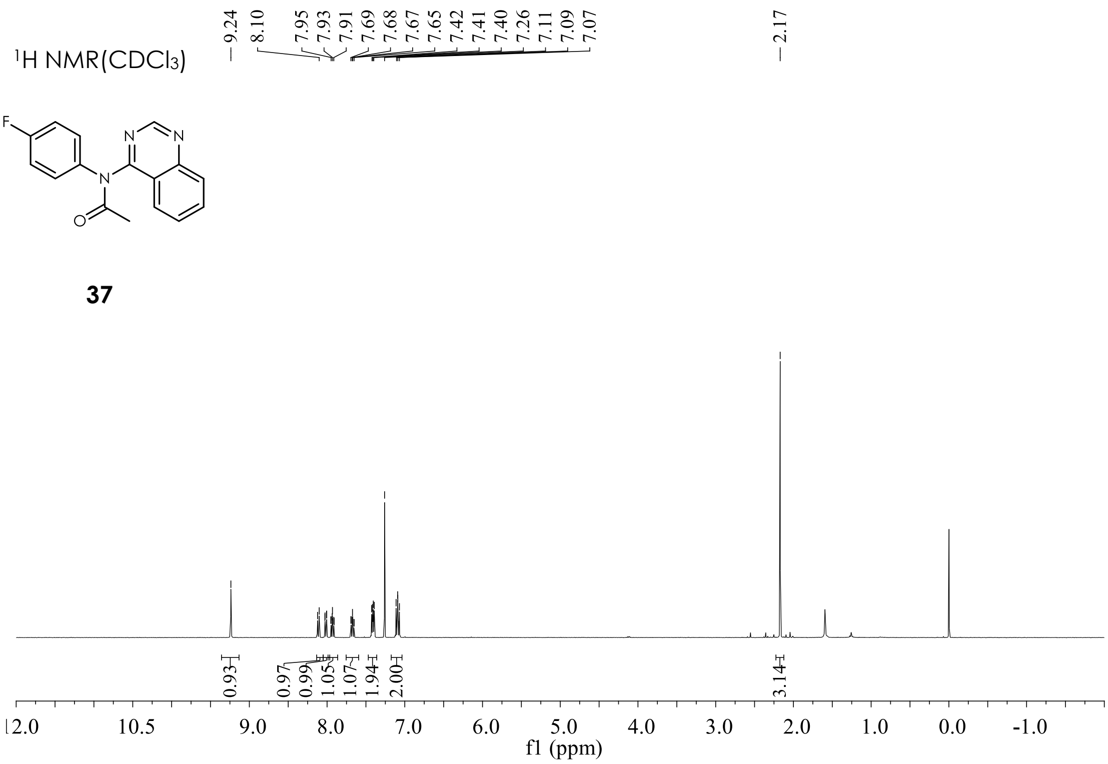
^{19}F NMR($CDCl_3$)

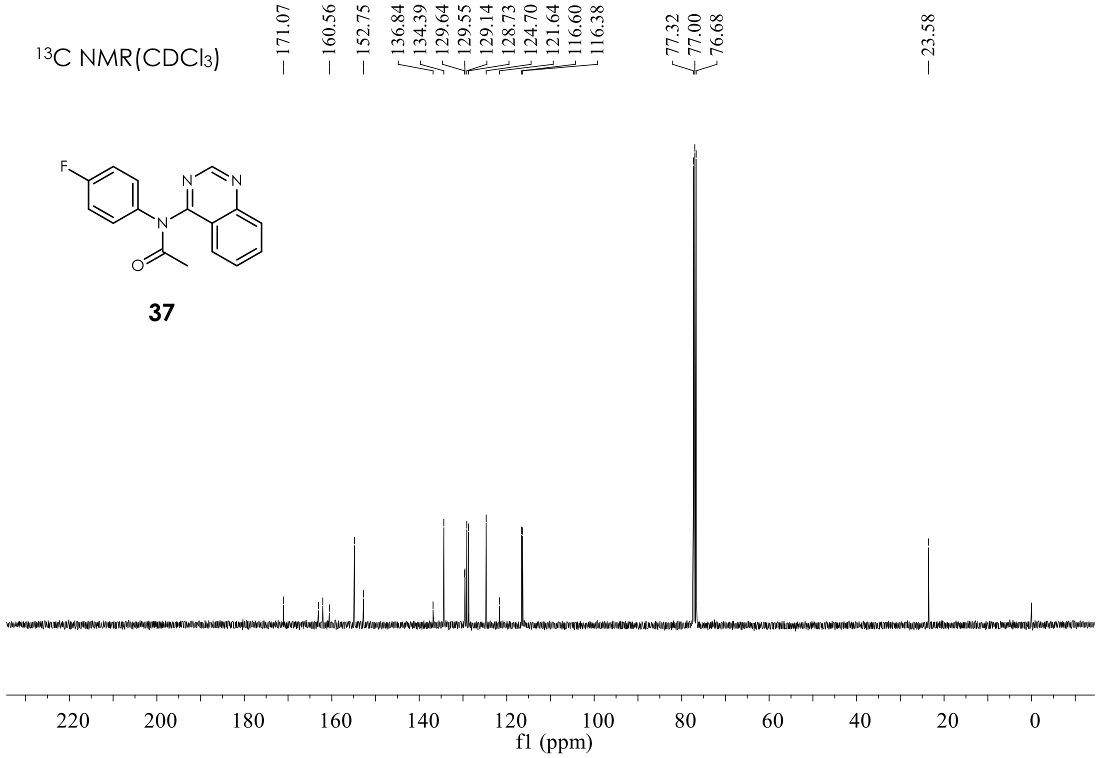
37-i



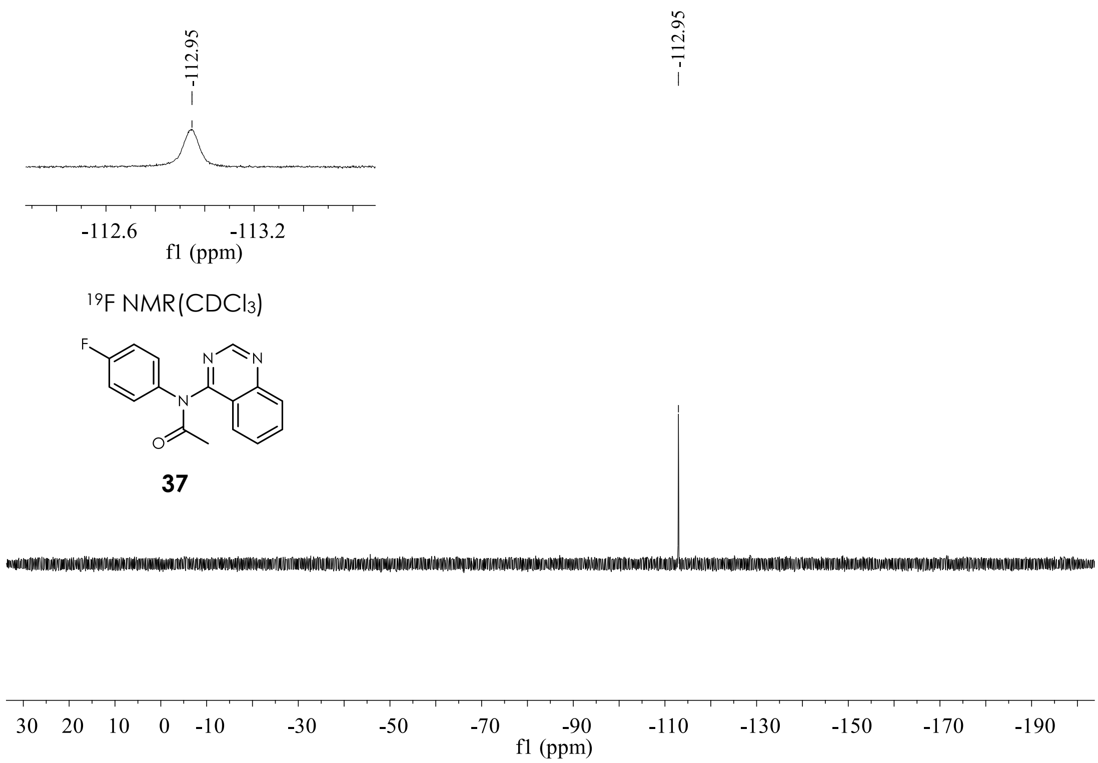
^{1}H NMR($CDCl_3$)

37



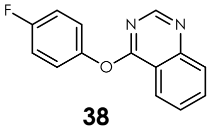


^{13}C NMR(CDCl3)
171.07
160.56
152.75
136.84
134.39
129.64
129.55
129.14
128.73
124.70
121.64
116.60
116.38
77.32
77.00
76.68
23.58
37
220 200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)

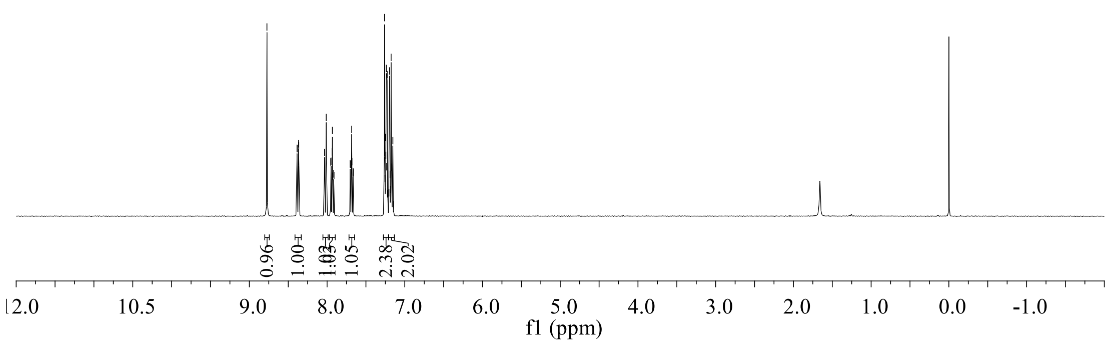


-112.95
-112.6 -113.2
f1 (ppm)
^{19}F NMR(CDCl3)
37
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)

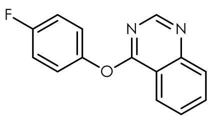
^1H NMR($CDCl_3$)



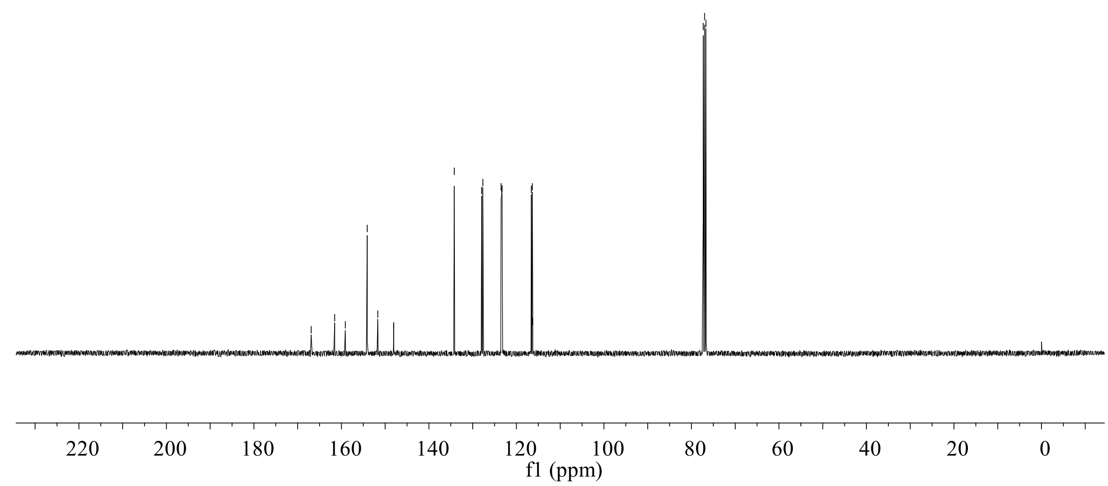
38

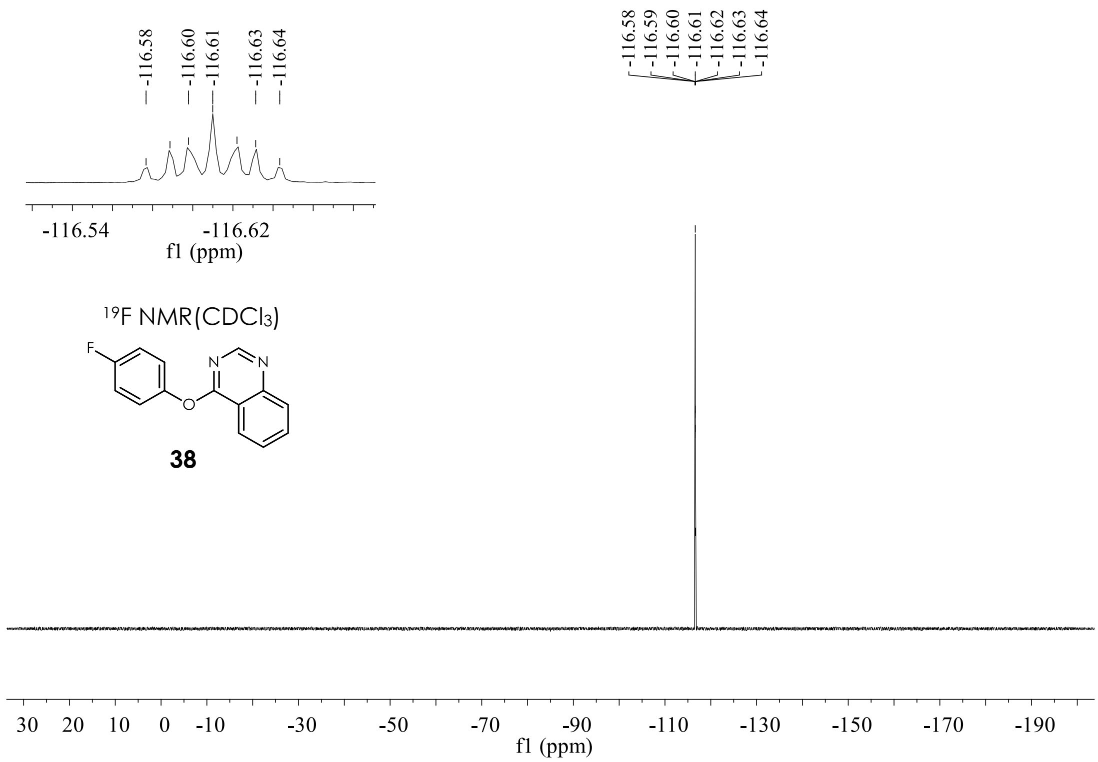


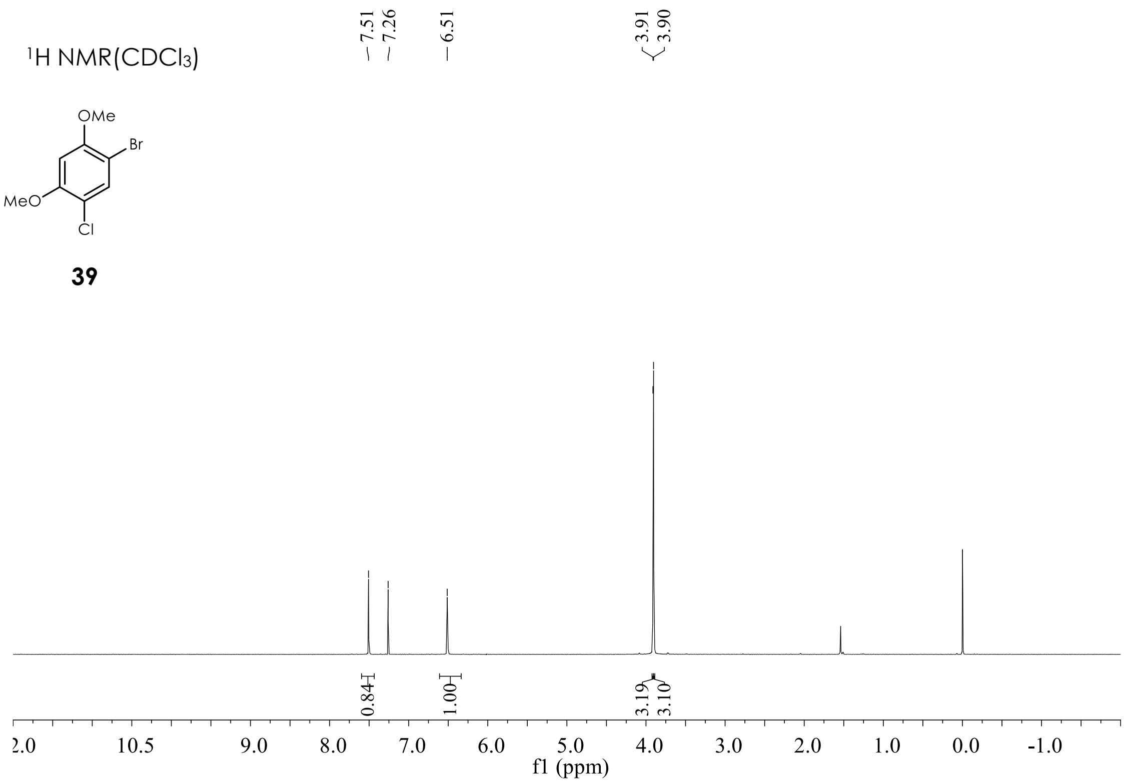
^{13}C NMR($CDCl_3$)



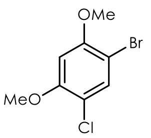
38



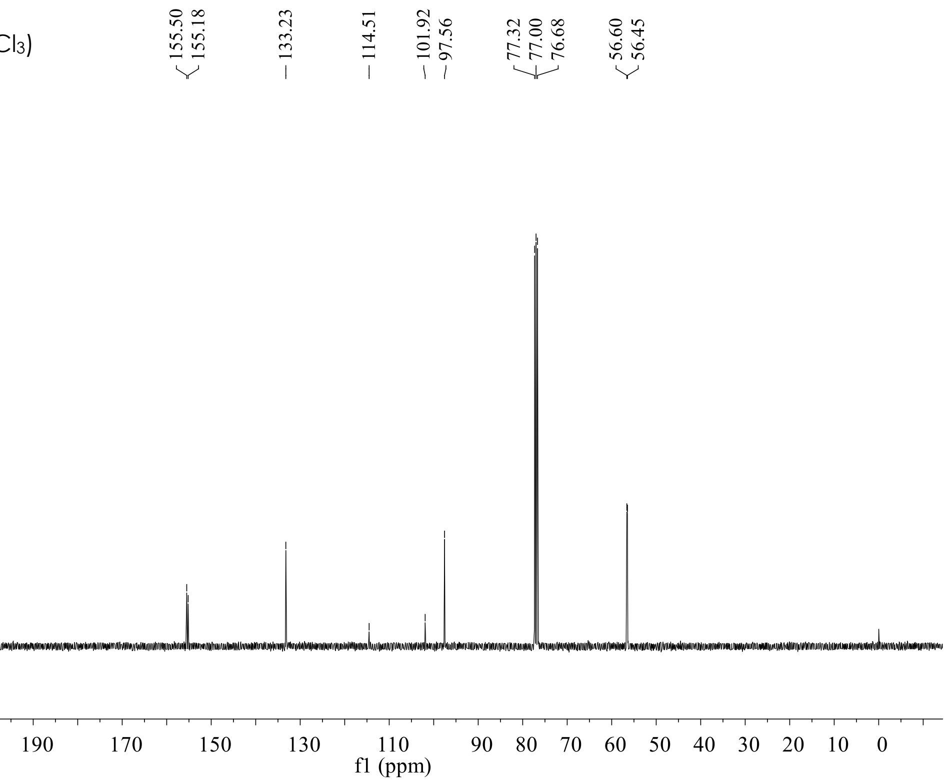

-116.58
-116.60
-116.61
-116.63
-116.64
-116.54
-116.62
f1 (ppm)
19F NMR(CDCl3)
38
-116.58
-116.59
-116.60
-116.61
-116.62
-116.63
-116.64
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)


1H NMR(CDCl3)
OMe
Br
MeO
Cl
39
7.51
7.26
6.51
3.91
3.90
0.84
1.00
3.19
3.10
2.0 10.5 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0
f1 (ppm)

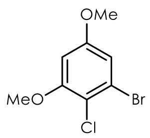
^{13}C NMR($CDCl_3$)



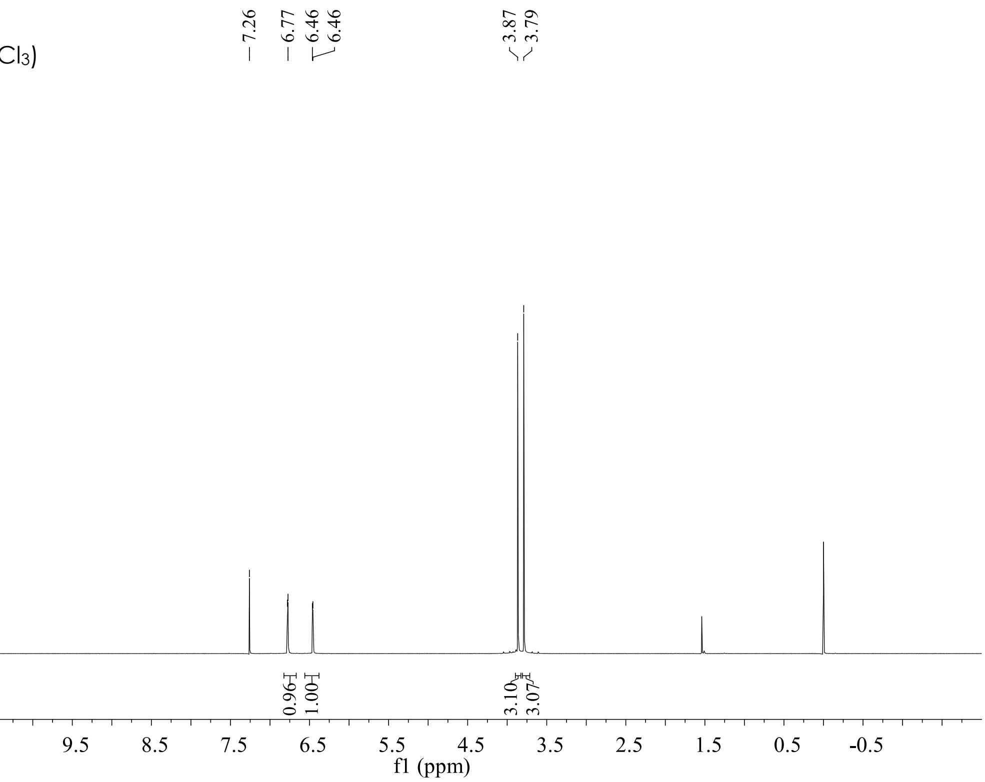
39



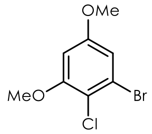
^{1}H NMR($CDCl_3$)



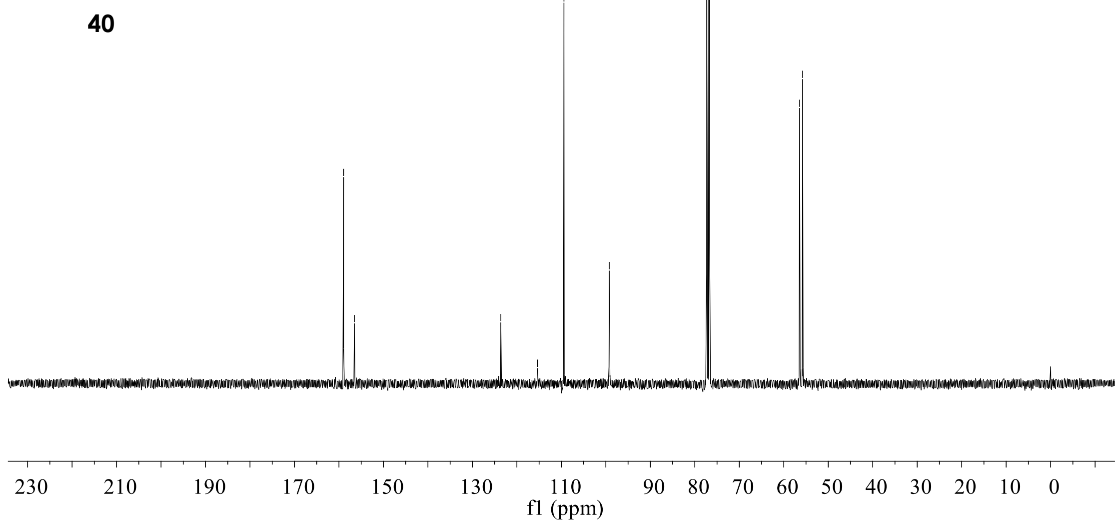
40



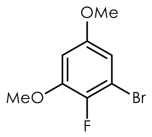
^{13}C NMR($CDCl_3$)



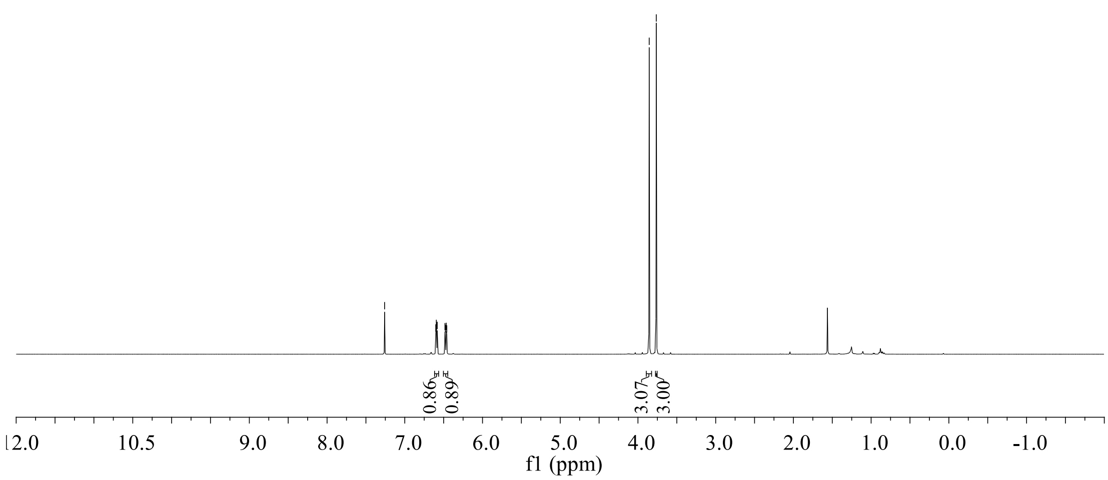
40

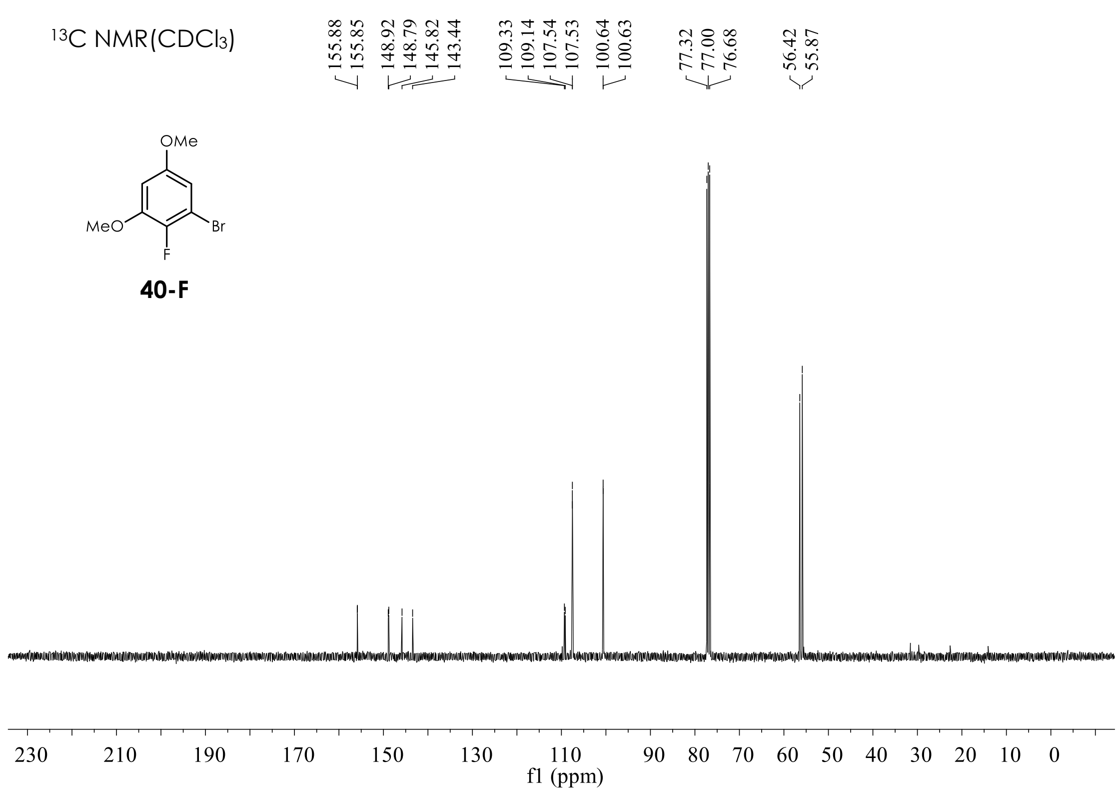


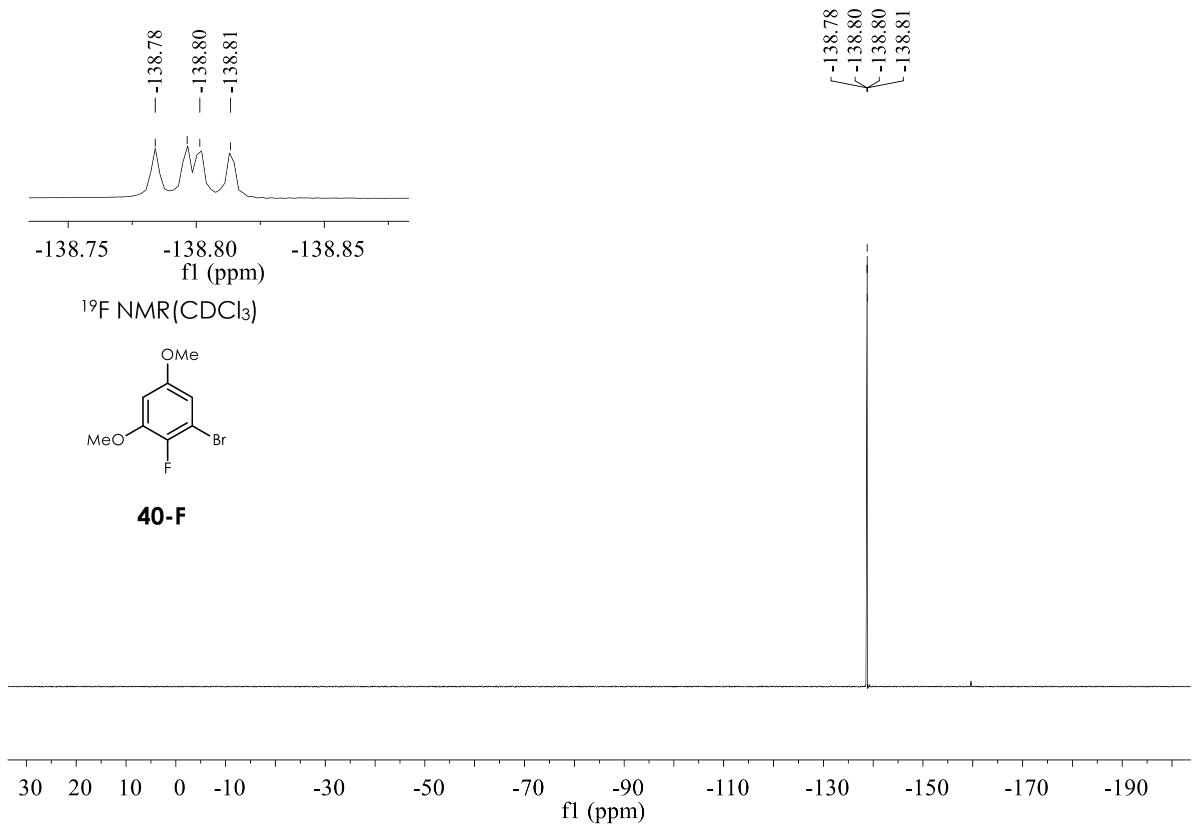
^{1}H NMR($CDCl_3$)



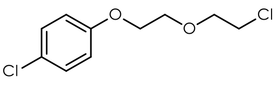
40-F



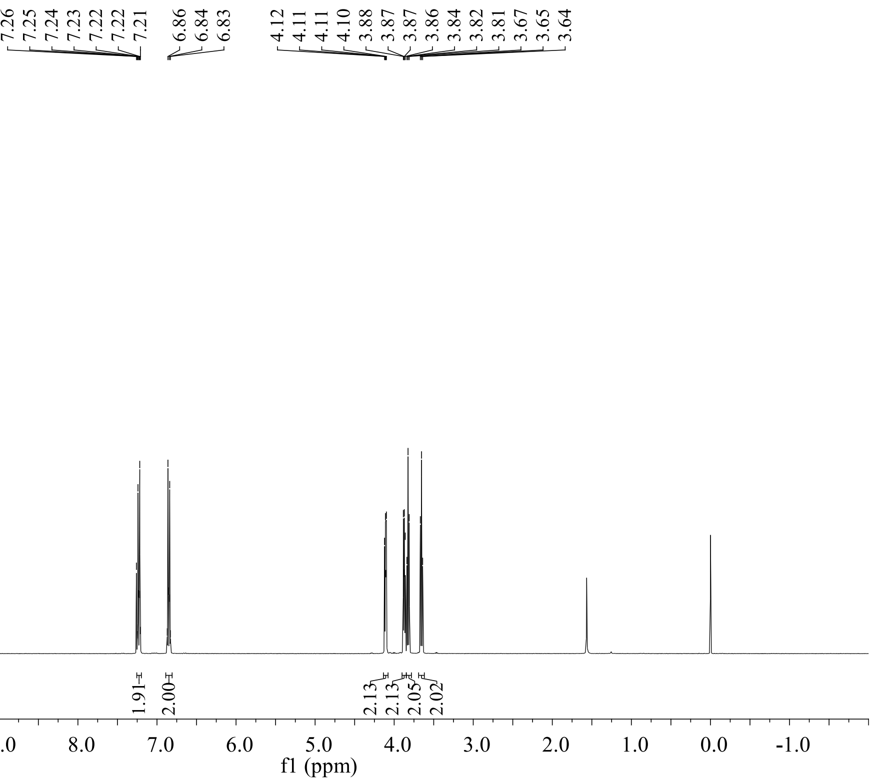

13C NMR(CDCl3)
155.88
155.85
148.92
148.79
145.82
143.44
109.33
109.14
107.54
107.53
100.64
100.63
77.32
77.00
76.68
56.42
55.87
OMe
MeO
Br
F
40-F
230 210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-138.78
-138.80
-138.81
-138.75 -138.80 -138.85
f1 (ppm)
19F NMR(CDCl3)
-138.78
-138.80
-138.80
-138.81
OMe
MeO
Br
F
40-F
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)

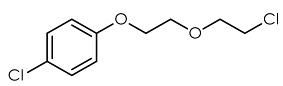
^{1}H NMR($CDCl_3$)



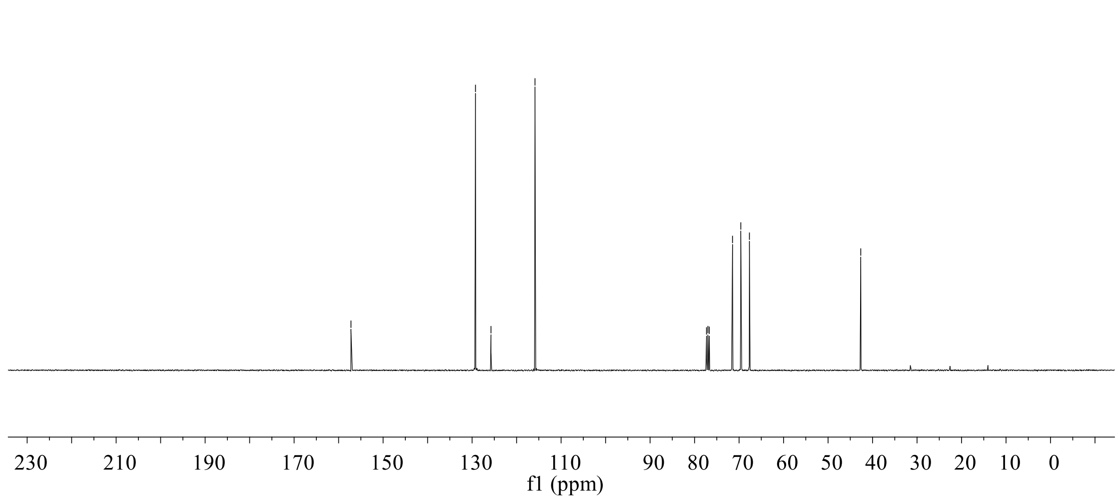
41



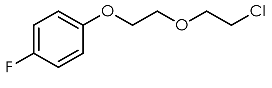
^{13}C NMR($CDCl_3$)



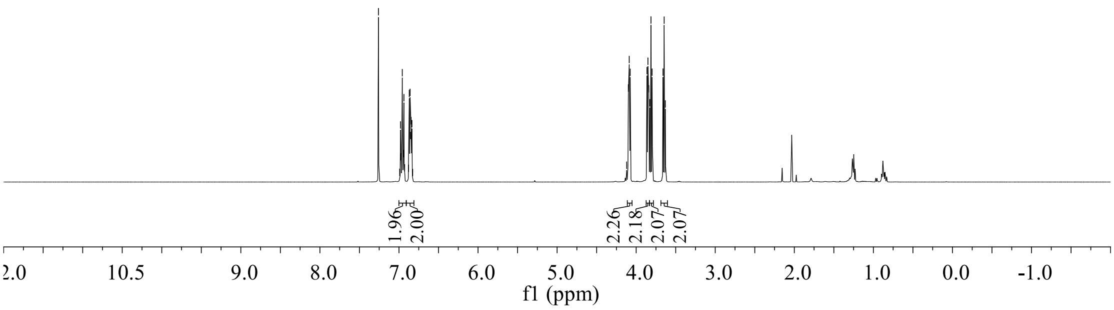
41



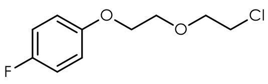
[1]H NMR($CDCl_3$)



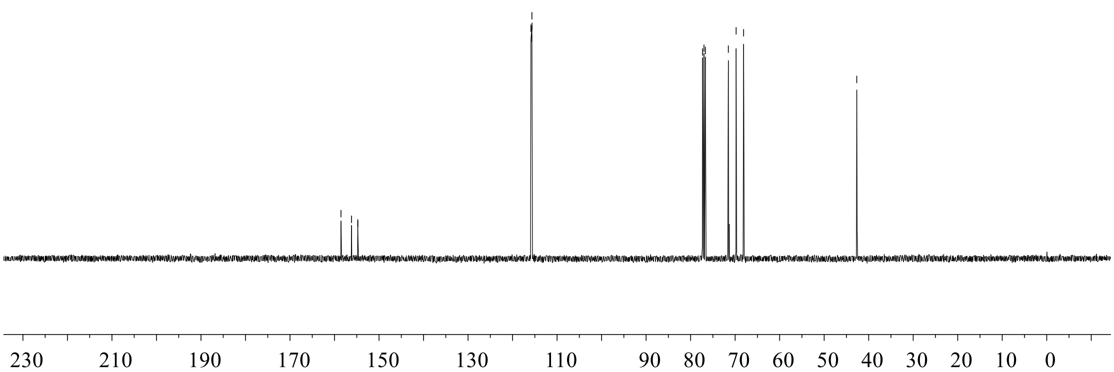
41-F

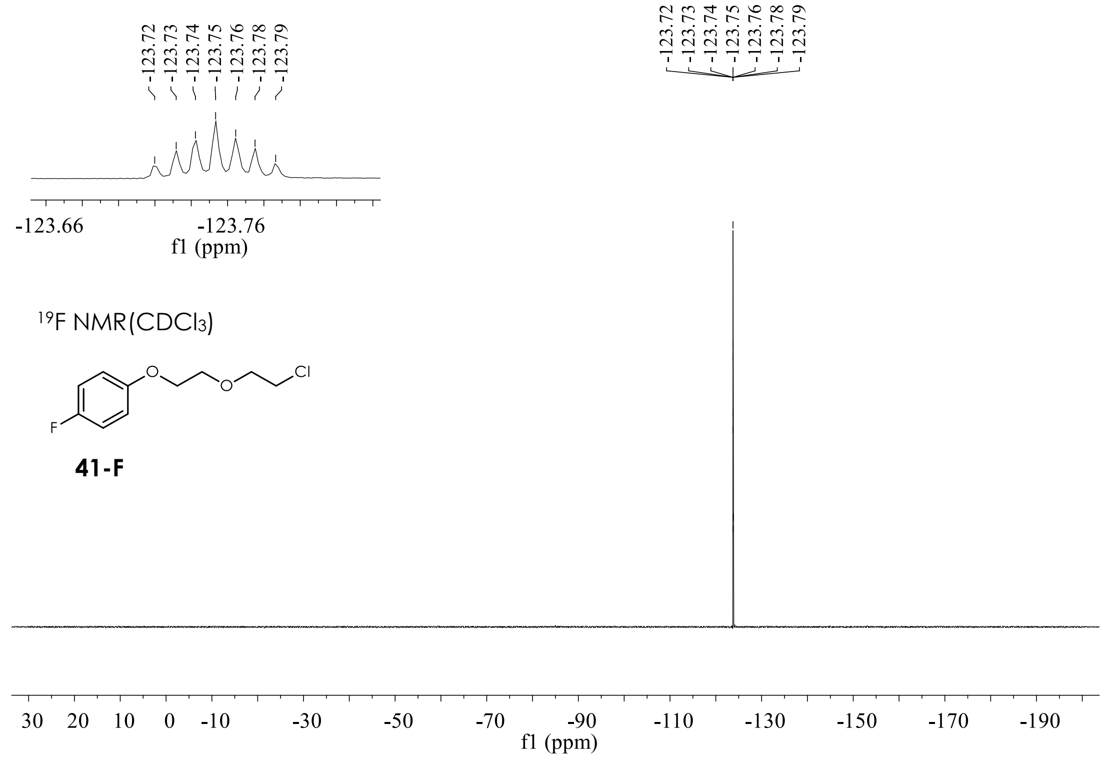


[13]C NMR($CDCl_3$)



41-F

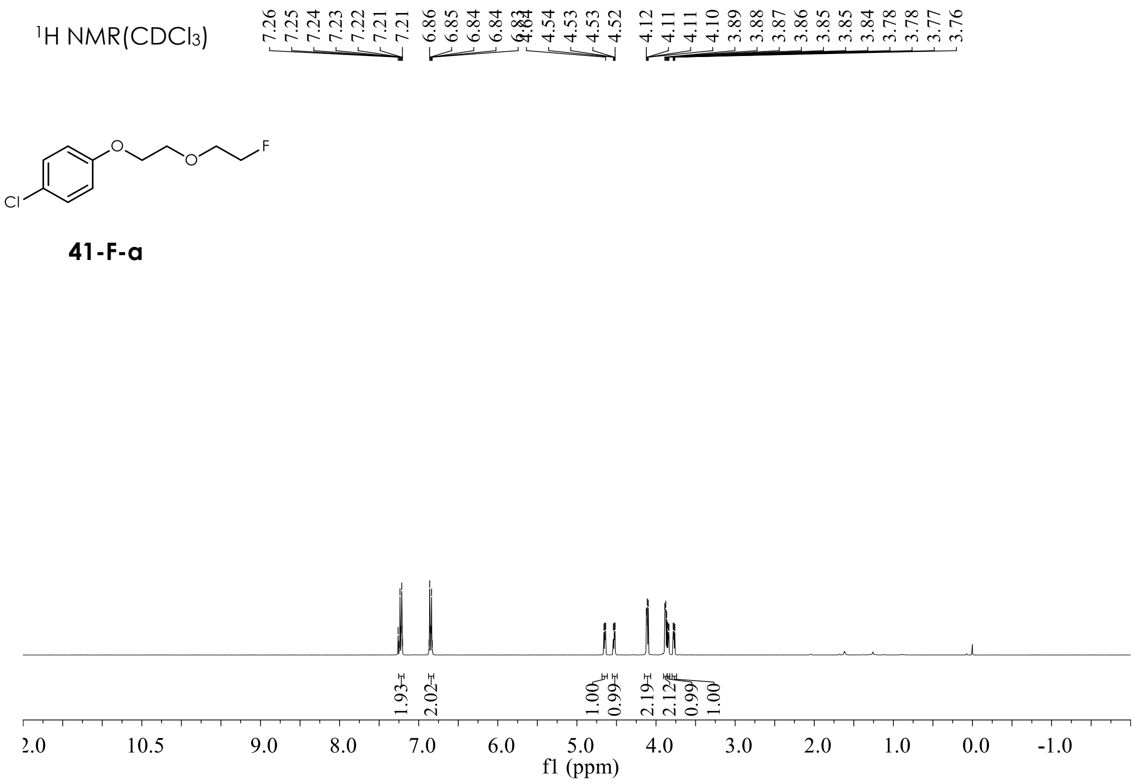




^{19}F NMR($CDCl_3$)

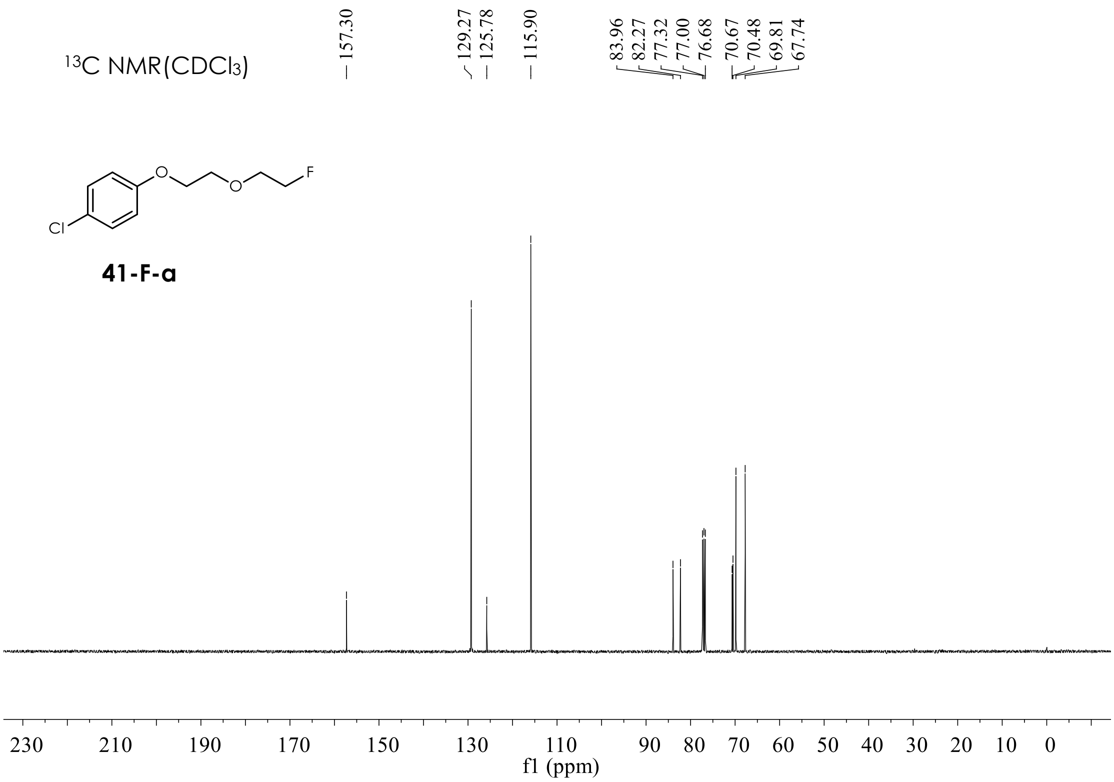
41-F

^{1}H NMR($CDCl_3$)



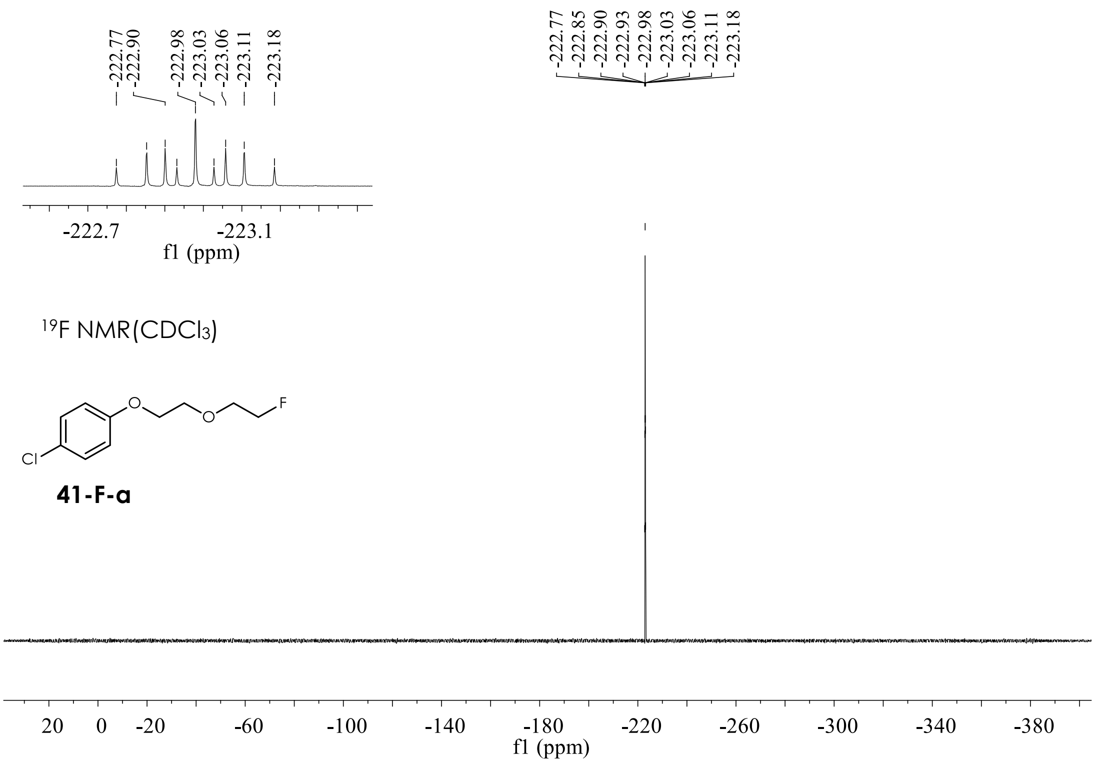
41-F-a

^{13}C NMR($CDCl_3$)



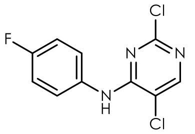
41-F-a

^{19}F NMR($CDCl_3$)

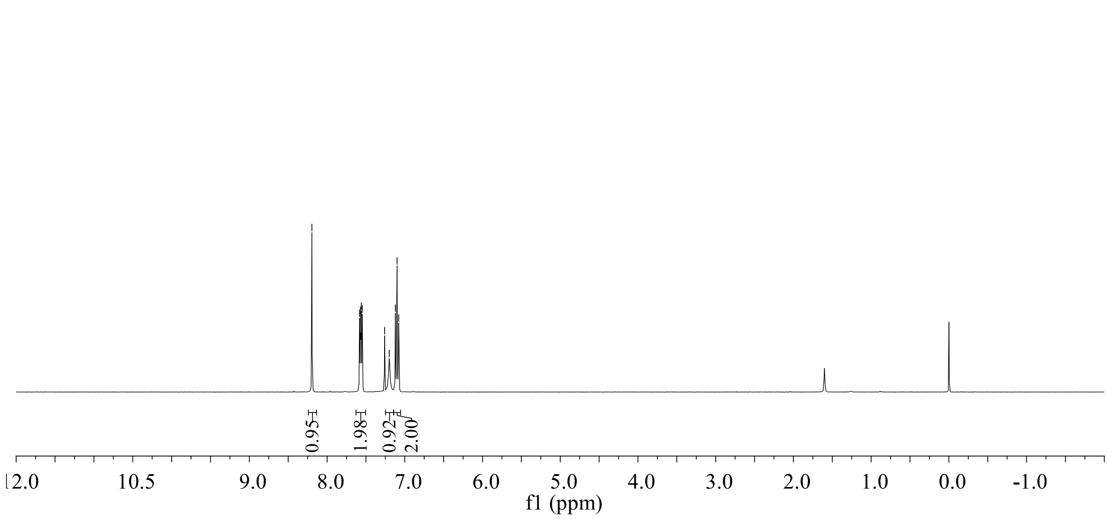


41-F-a

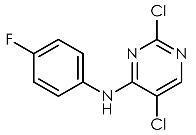
^{1}H NMR($CDCl_3$)



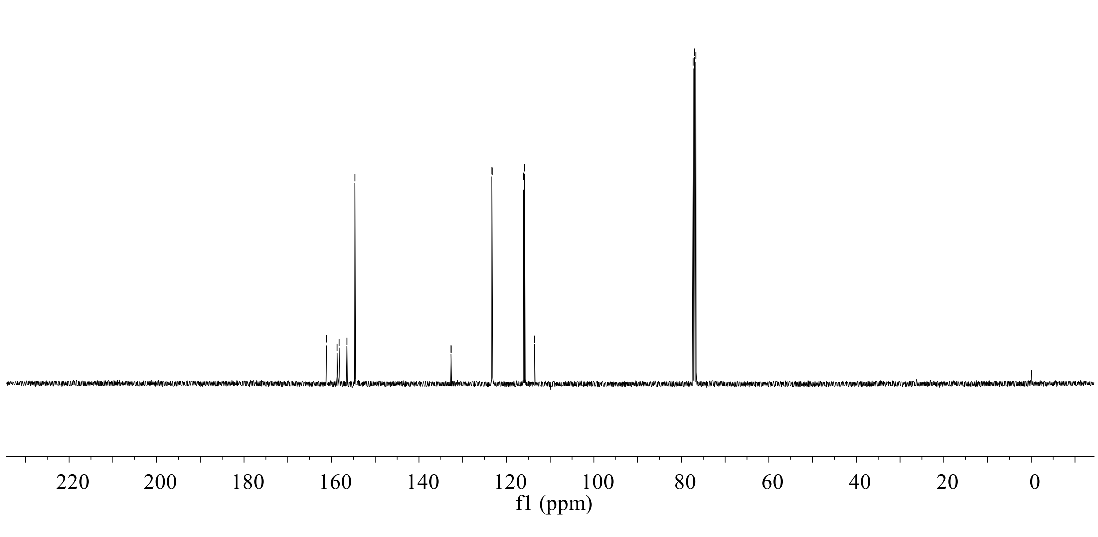
42-i

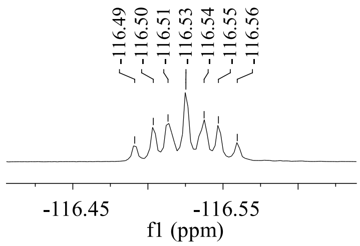


^{13}C NMR($CDCl_3$)

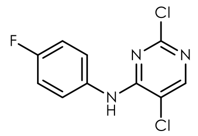


42-i

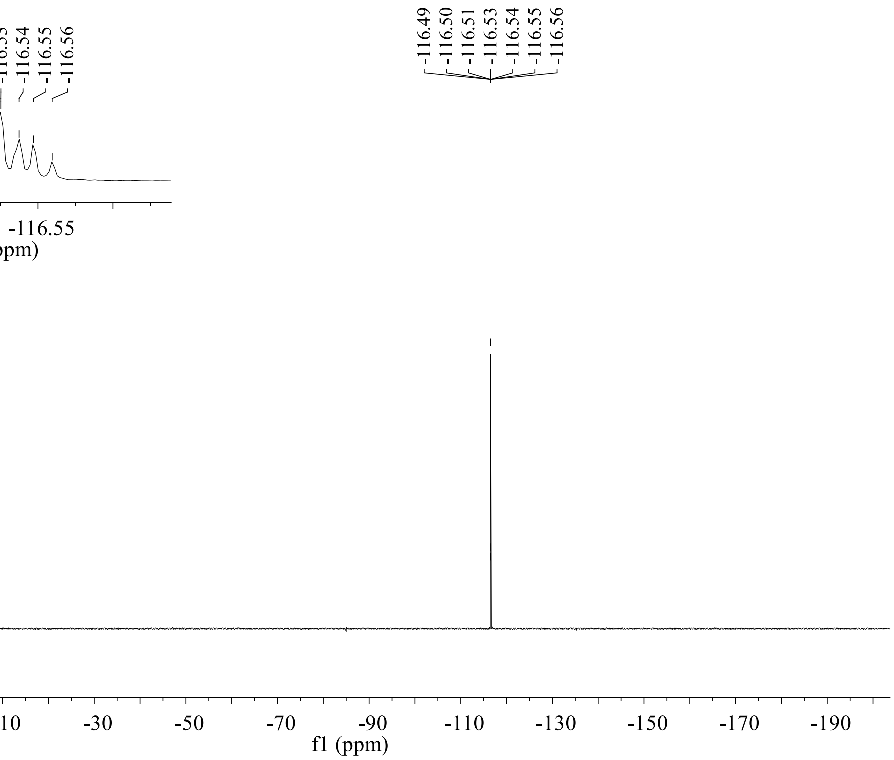




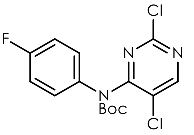
^{19}F NMR($CDCl_3$)



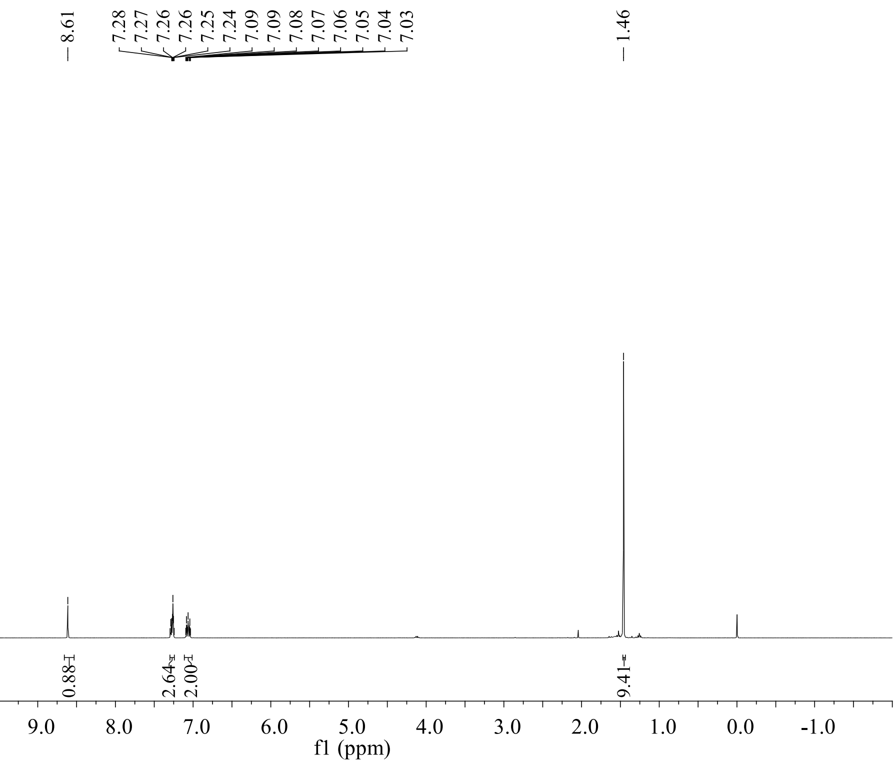
42-i



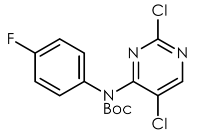
^{1}H NMR($CDCl_3$)



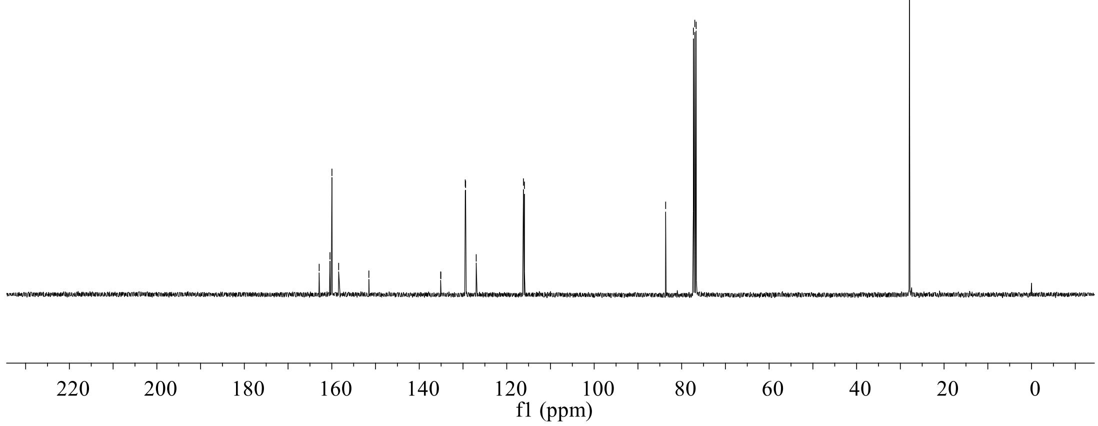
42

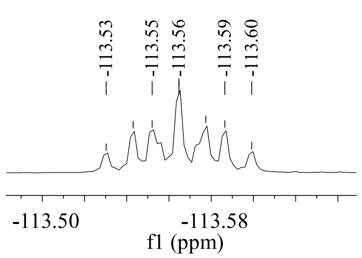
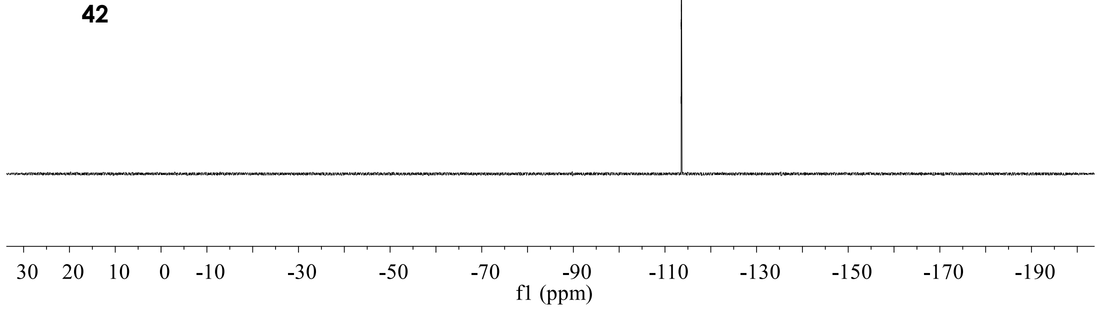


^{13}C NMR($CDCl_3$)

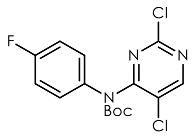


42



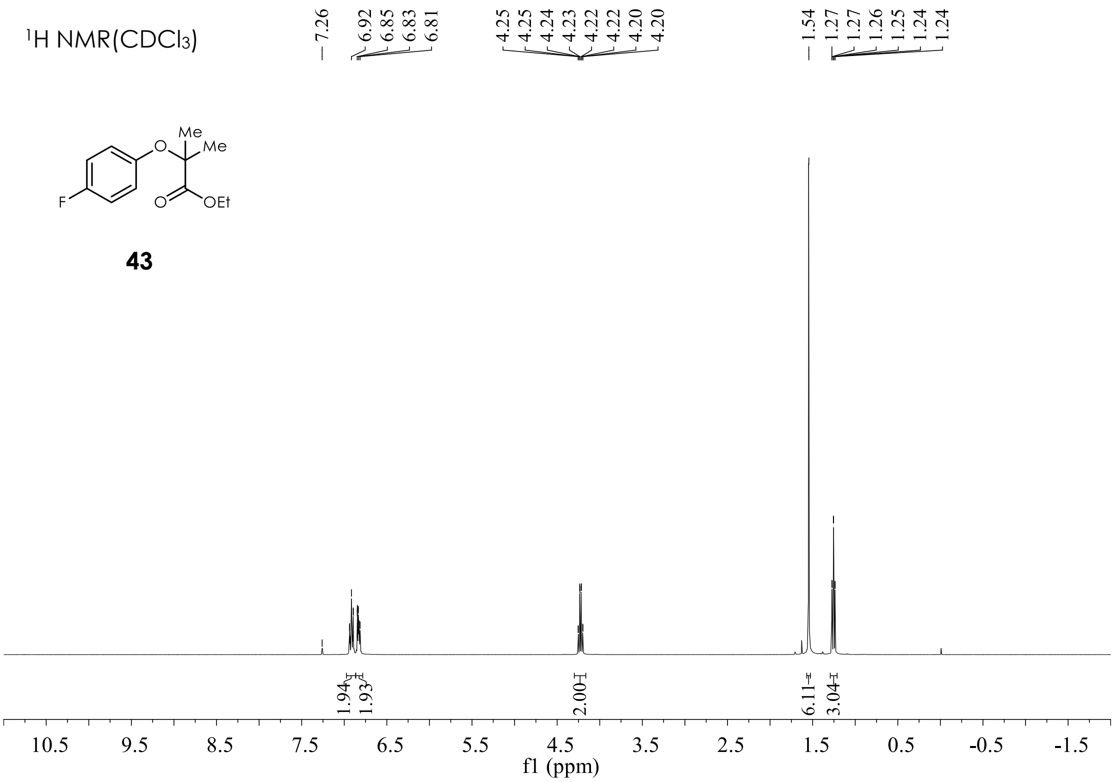



^{19}F NMR($CDCl_3$)



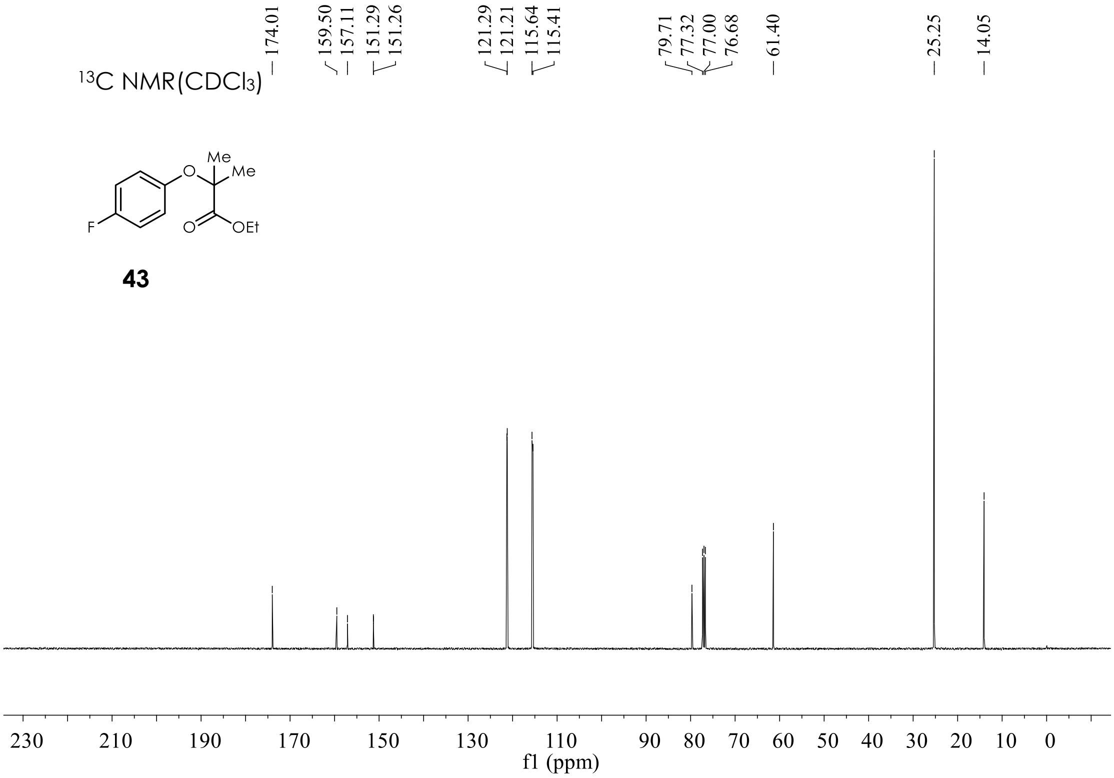
42

[1]H NMR(CDCl3)

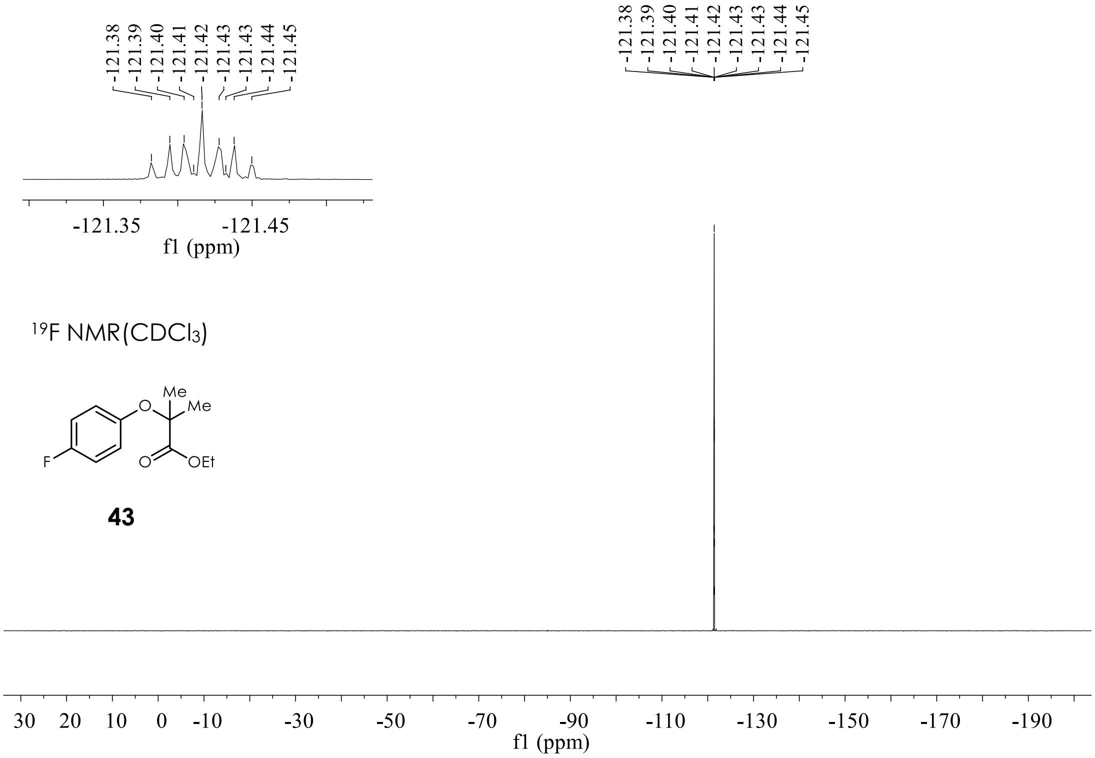


43

[13]C NMR(CDCl3)

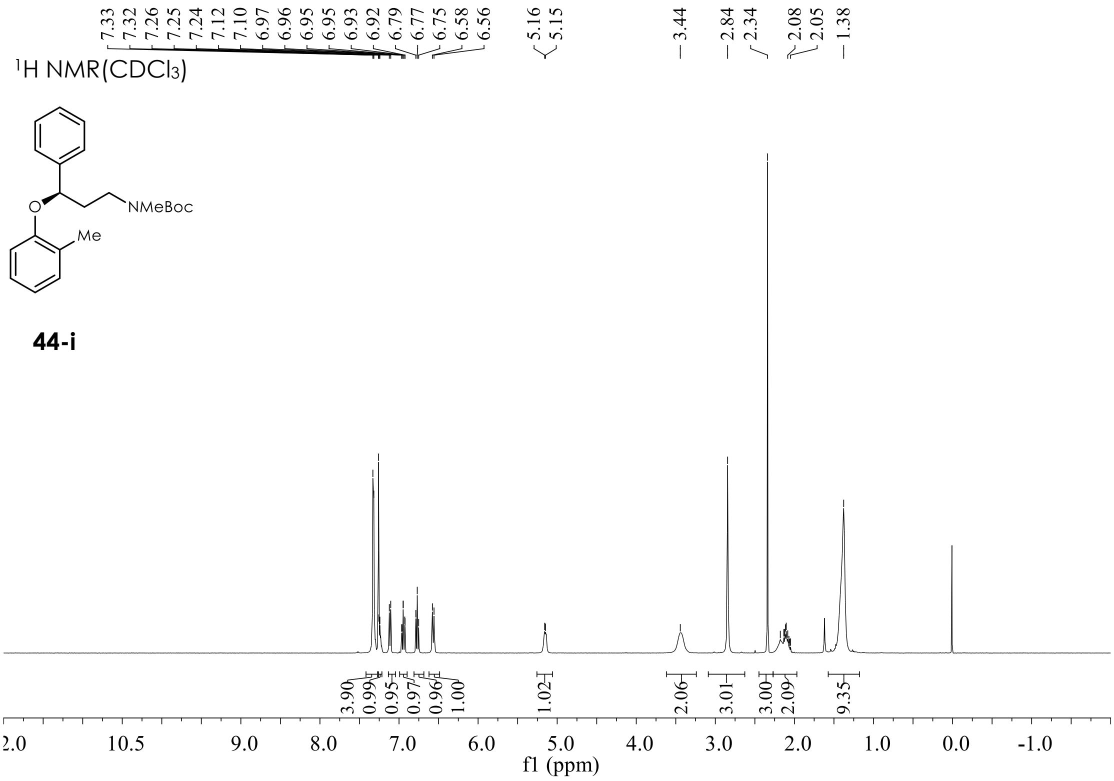


43



^{19}F NMR($CDCl_3$)

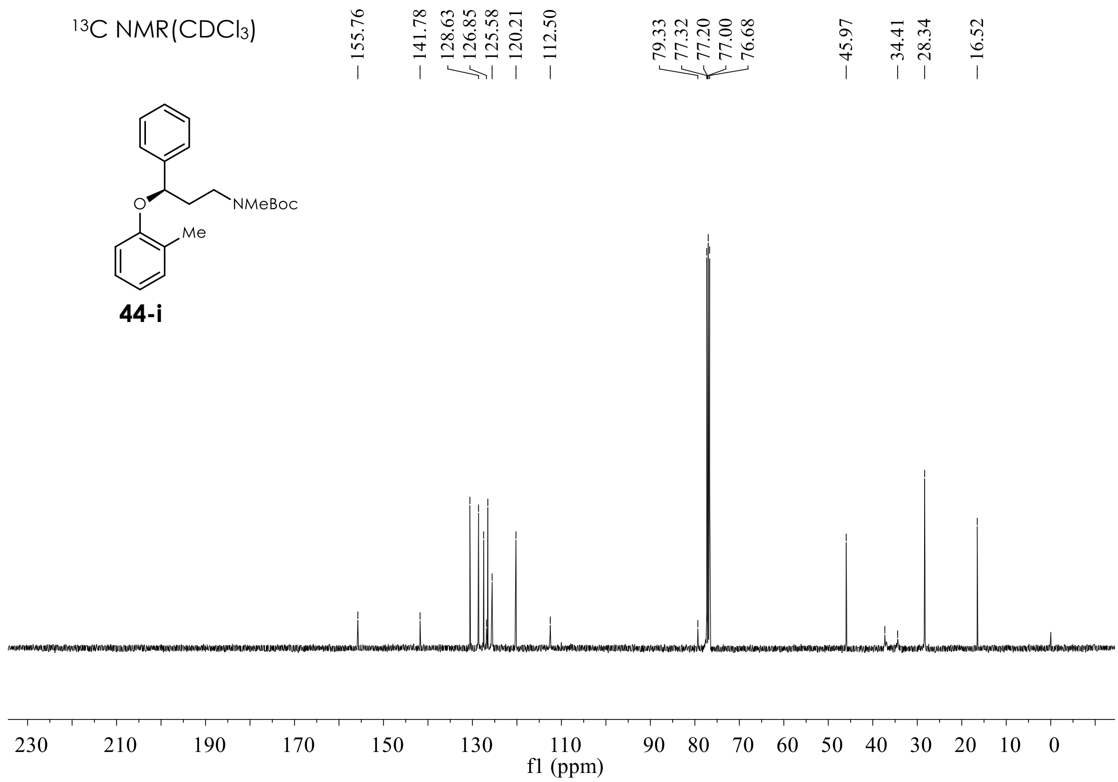
43



^{1}H NMR($CDCl_3$)

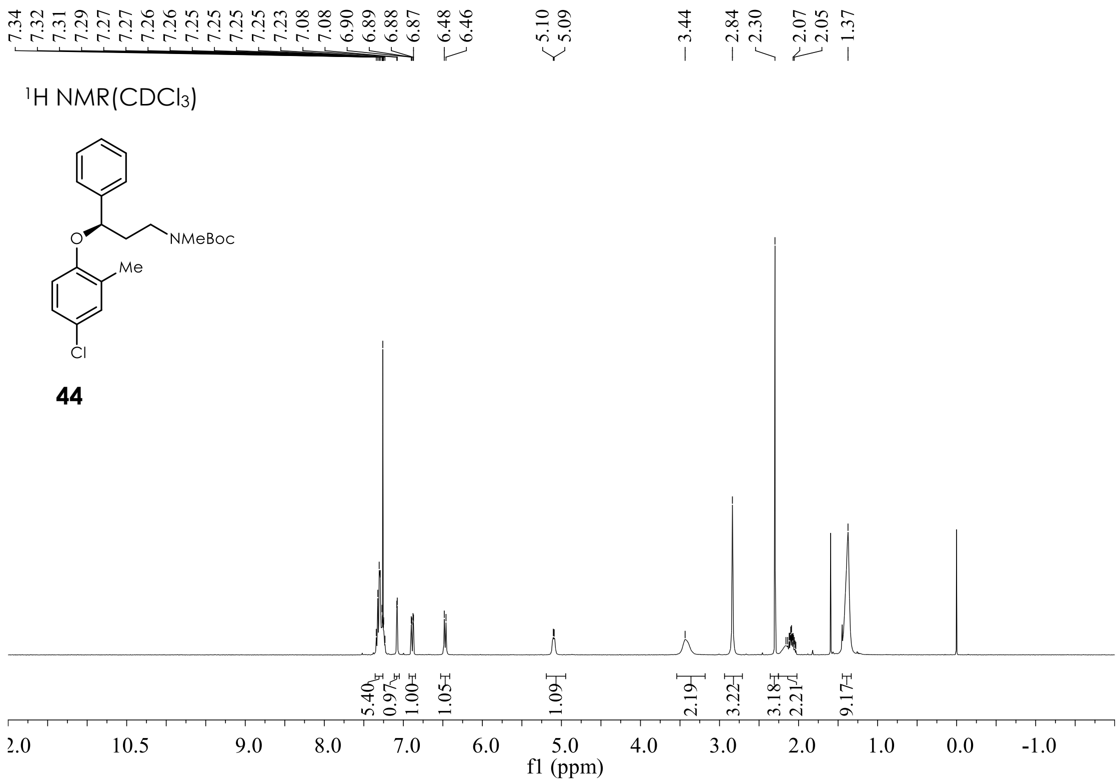
44-i

^{13}C NMR($CDCl_3$)

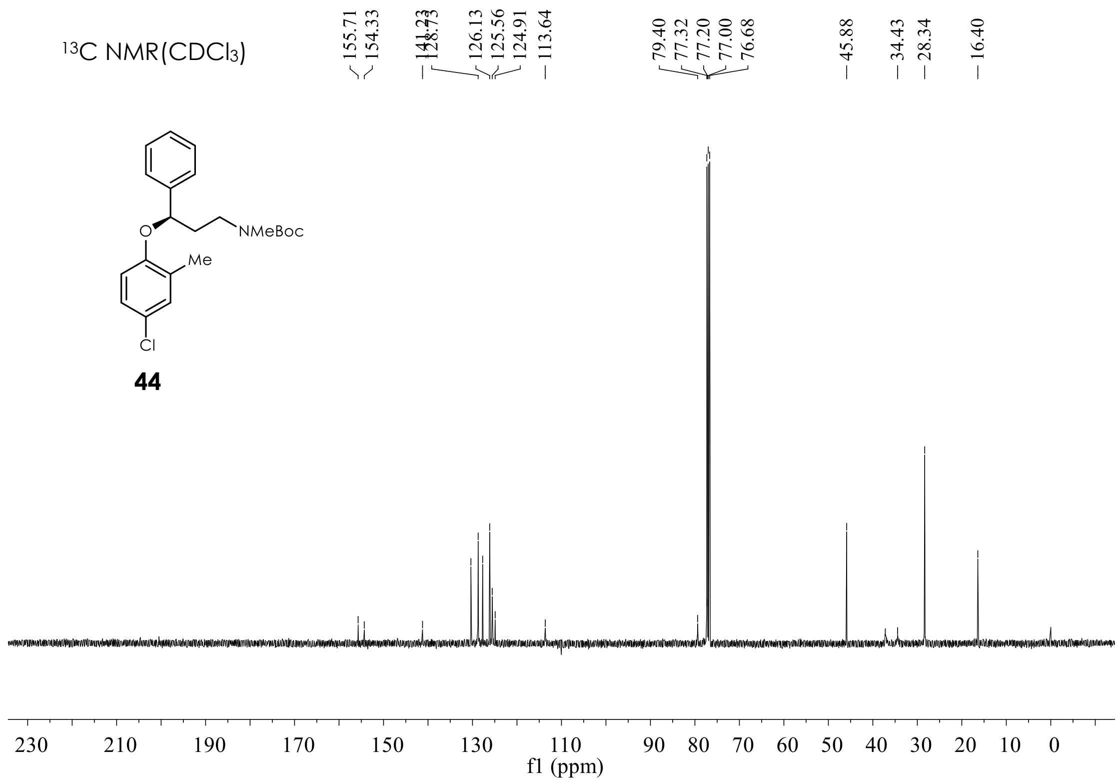


44-i

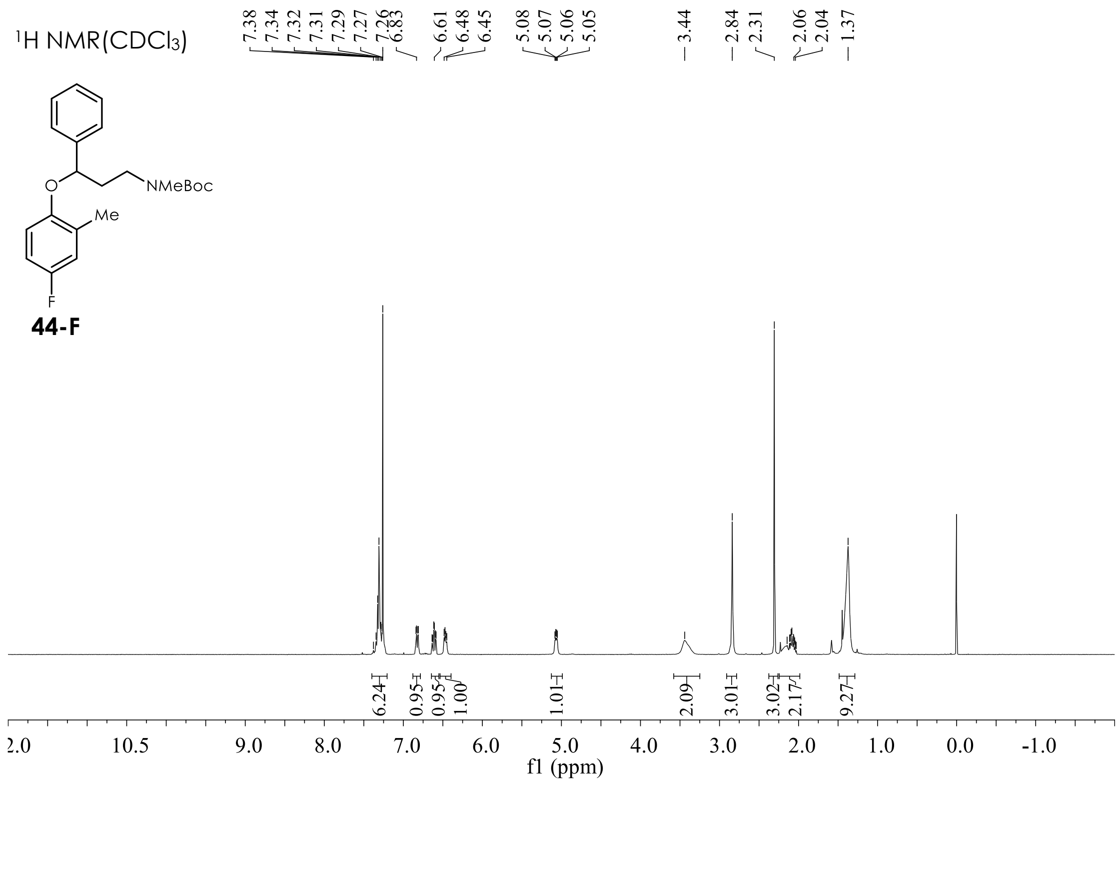
^{1}H NMR($CDCl_3$)



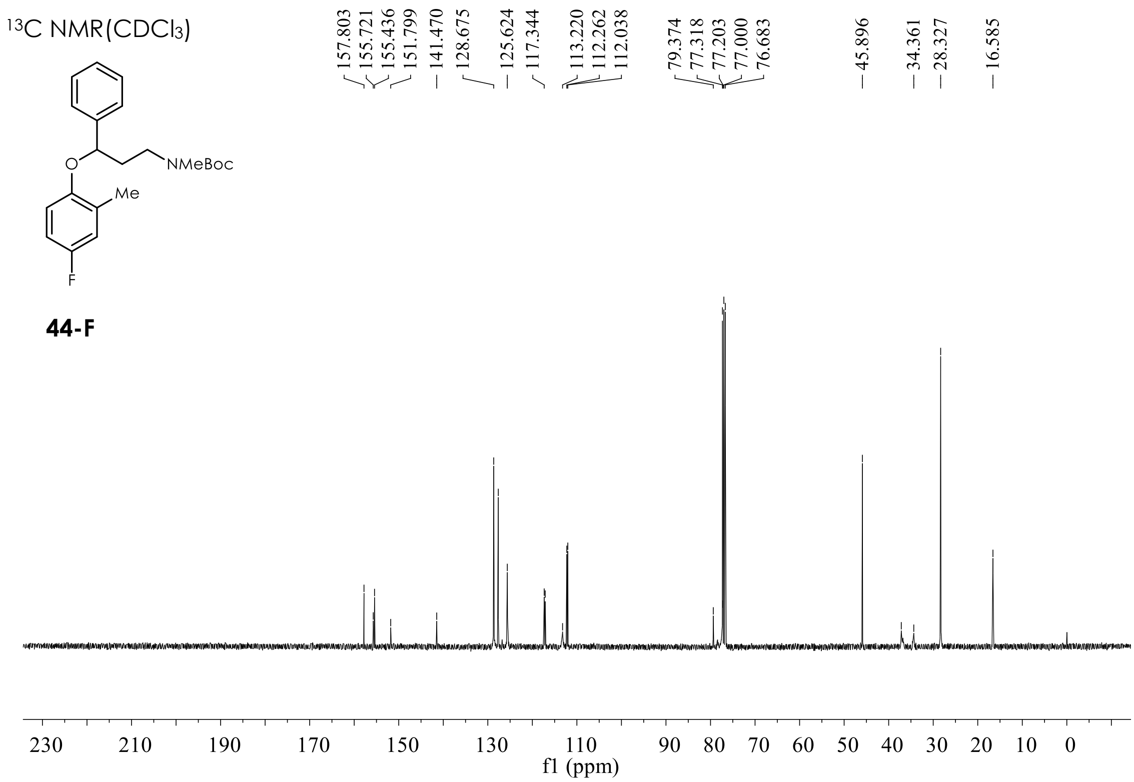
44

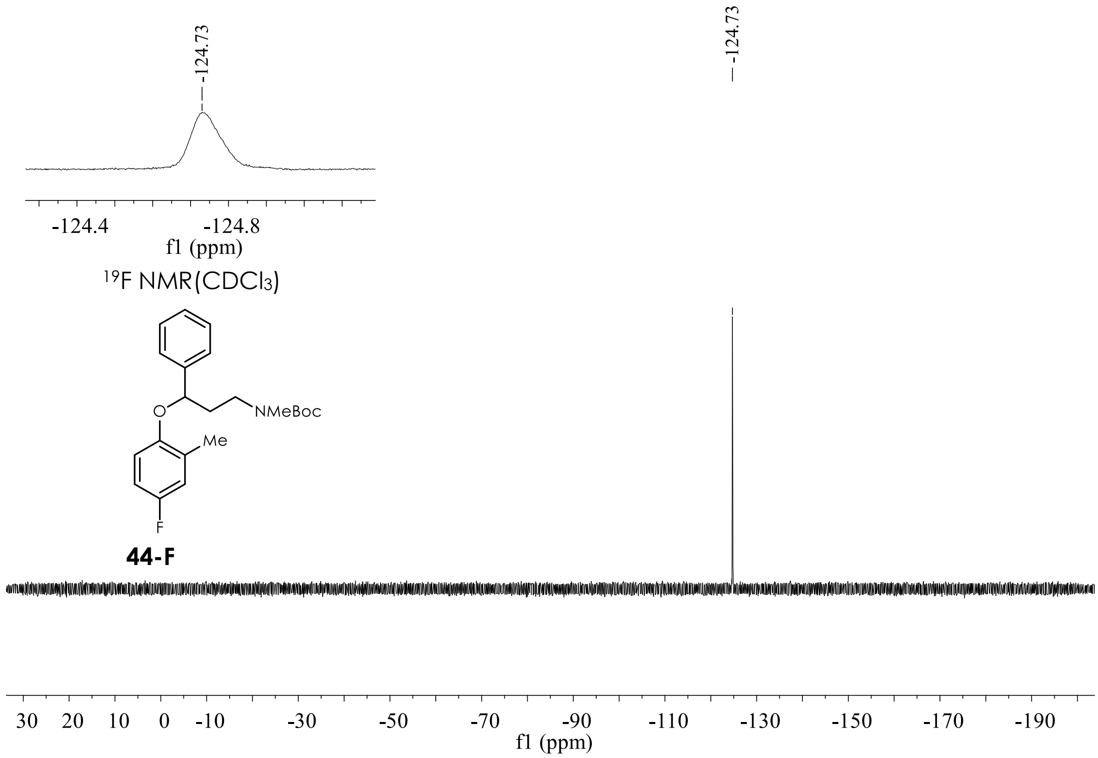


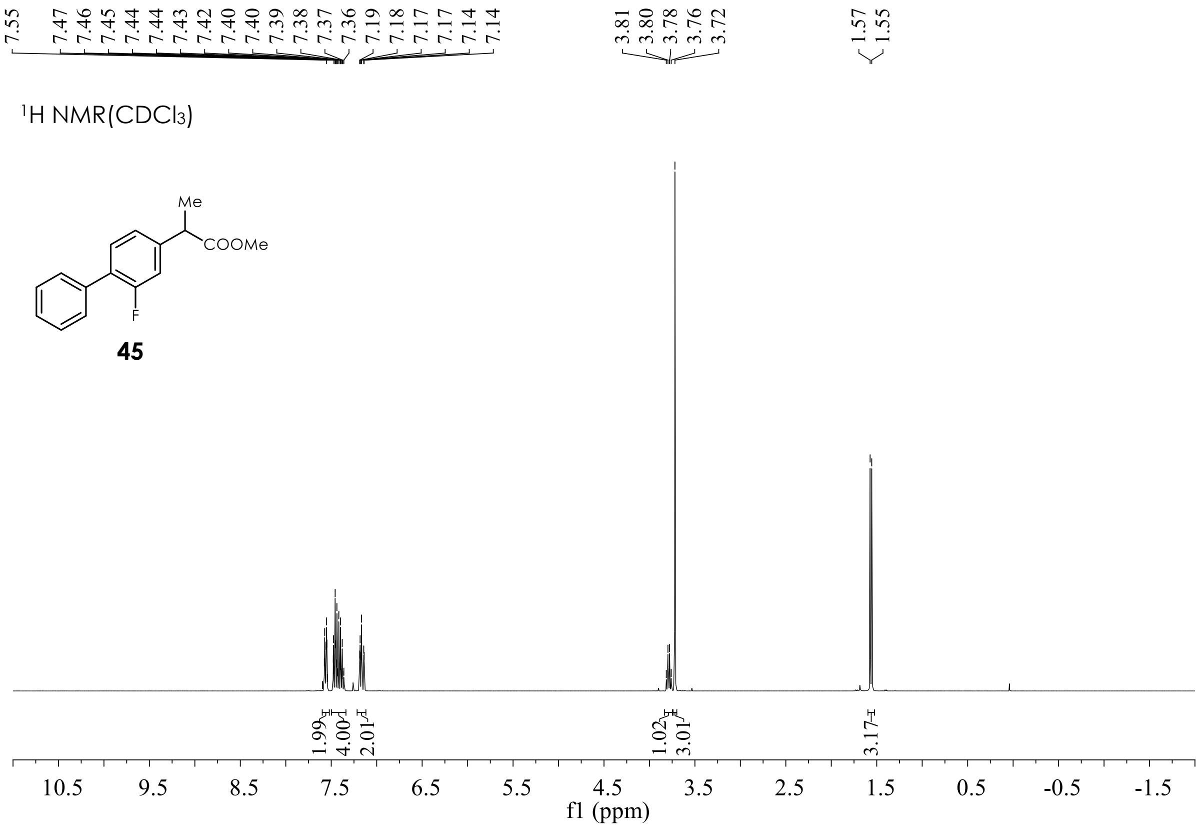
^{13}C NMR(CDCl$_3$)
155.71
154.33
141.23
128.73
126.13
125.56
124.91
113.64
79.40
77.32
77.20
77.00
76.68
45.88
34.43
28.34
16.40
NMeBoc
Me
Cl
44
230 210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

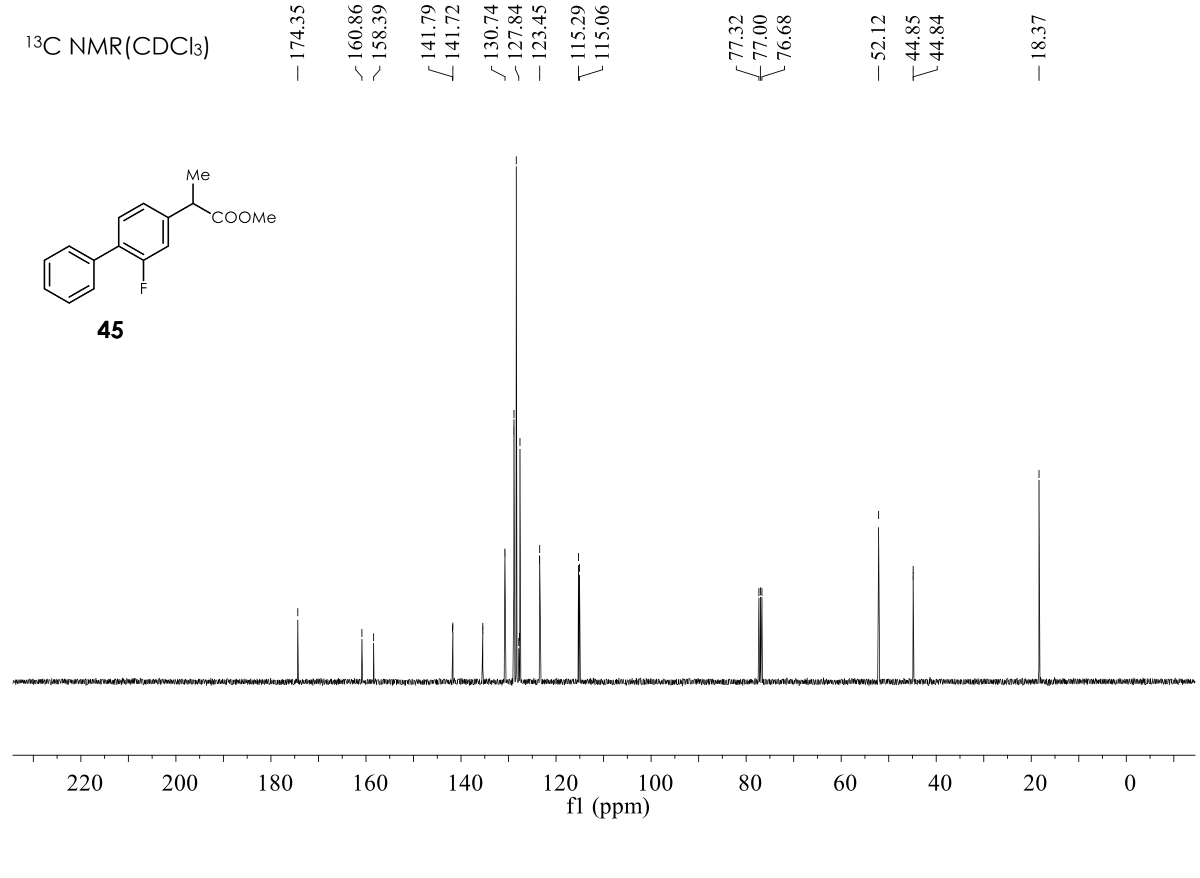


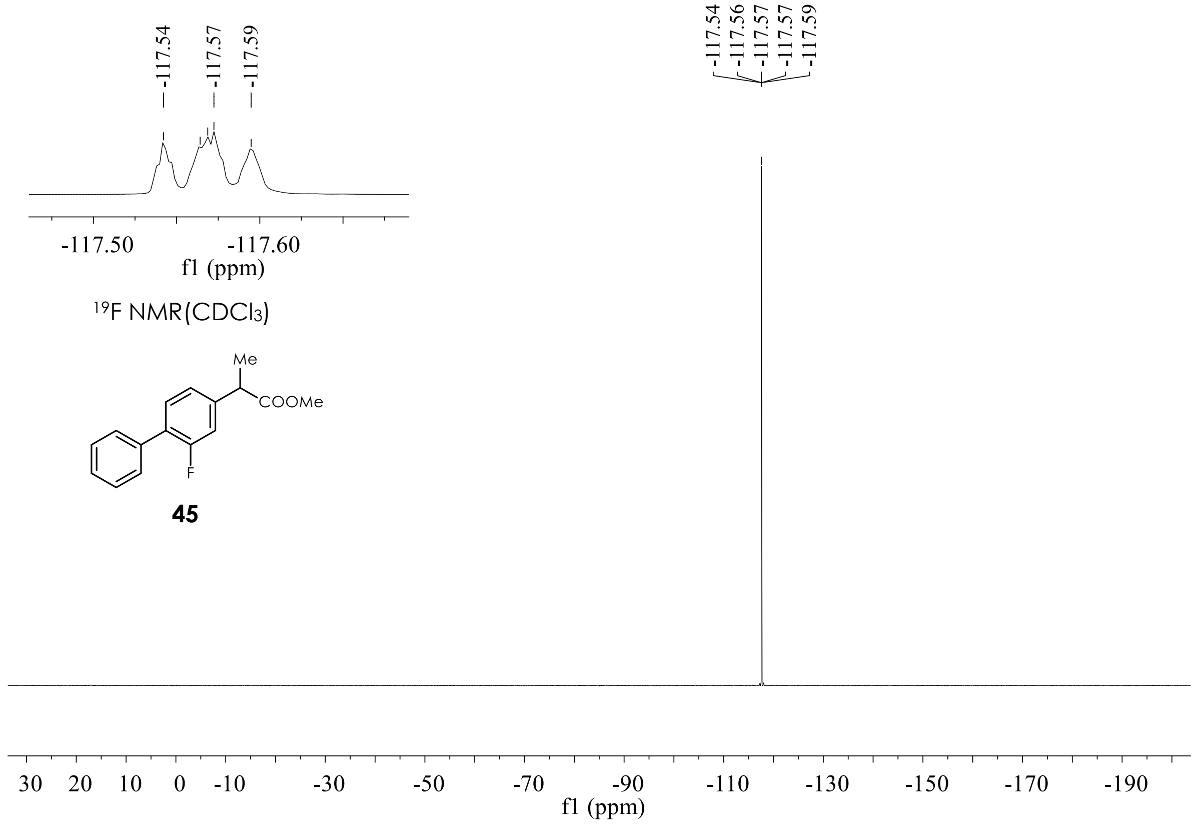
^{1}H NMR(CDCl$_3$)
7.38
7.34
7.32
7.31
7.29
7.27
7.26
6.83
6.61
6.48
6.45
5.08
5.07
5.06
5.05
3.44
2.84
2.31
2.06
2.04
1.37
NMeBoc
Me
F
44-F
6.24
0.95
0.95
1.00
1.01
2.09
3.01
3.02
2.17
9.27
2.0 10.5 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0
f1 (ppm)


13C NMR(CDCl3)
NMeBoc
Me
F
44-F
157.803
155.721
155.436
151.799
141.470
128.675
125.624
117.344
113.220
112.262
112.038
79.374
77.318
77.203
77.000
76.683
45.896
34.361
28.327
16.585
230 210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-124.73
-124.4
-124.8
f1 (ppm)
19F NMR(CDCl3)
NMeBoc
Me
F
44-F
-124.73
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)


1H NMR(CDCl3)
7.55 7.47 7.46 7.45 7.44 7.44 7.43 7.42 7.40 7.40 7.39 7.38 7.37 7.36 7.19 7.18 7.17 7.17 7.14 7.14
3.81 3.80 3.78 3.76 3.72
1.57 1.55
Me
COOMe
F
45
1.99
4.00
2.01
1.02
3.01
3.17
10.5 9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5 -0.5 -1.5
f1 (ppm)

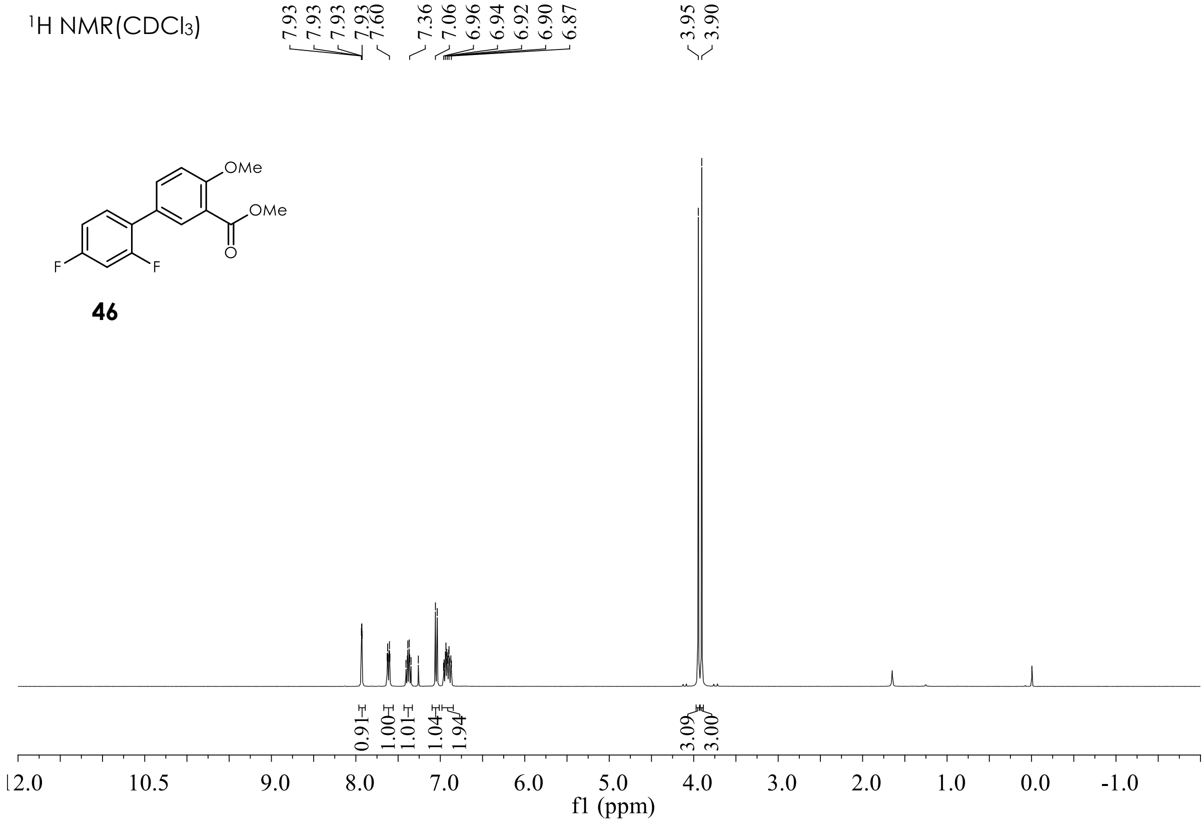

13C NMR(CDCl3)
174.35
160.86 158.39
141.79 141.72
130.74 127.84 123.45
115.29 115.06
77.32 77.00 76.68
52.12
44.85 44.84
18.37
Me
COOMe
F
45
220 200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)



^{19}F NMR($CDCl_3$)

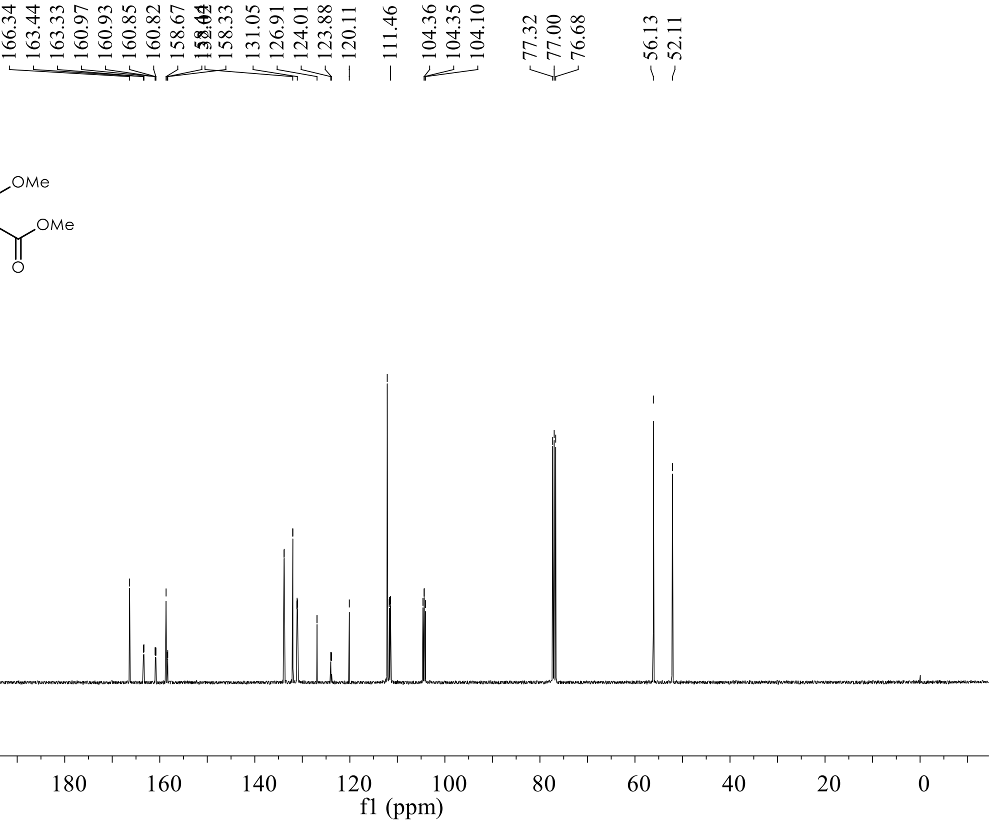
45

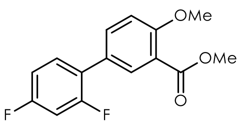
^{1}H NMR($CDCl_3$)



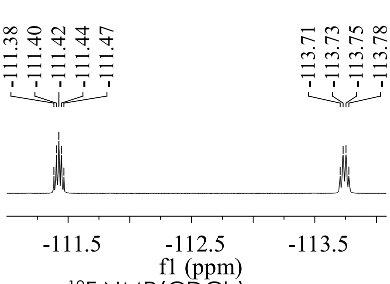
46

^{13}C NMR($CDCl_3$)

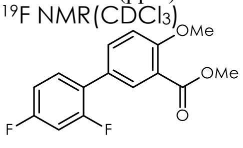




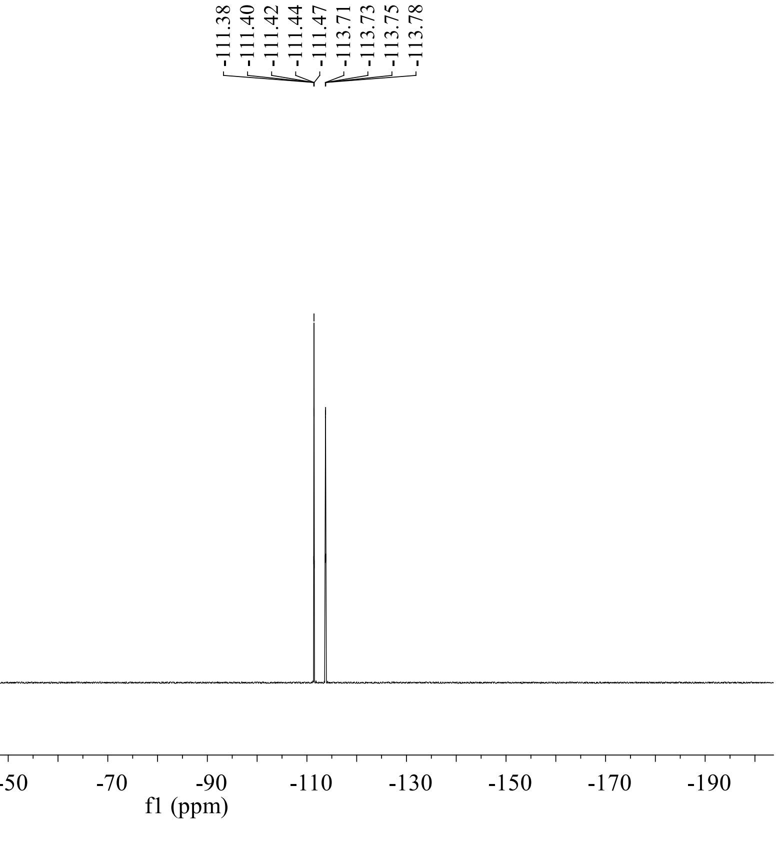
46



^{19}F NMR($CDCl_3$)

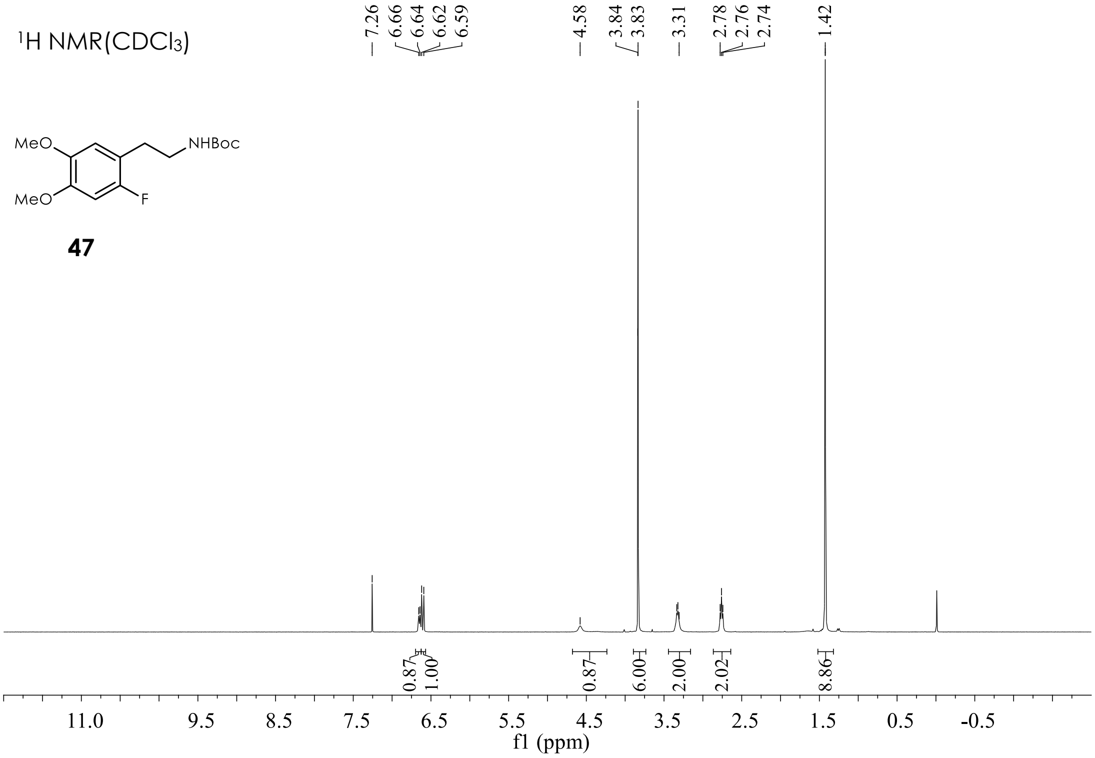


46



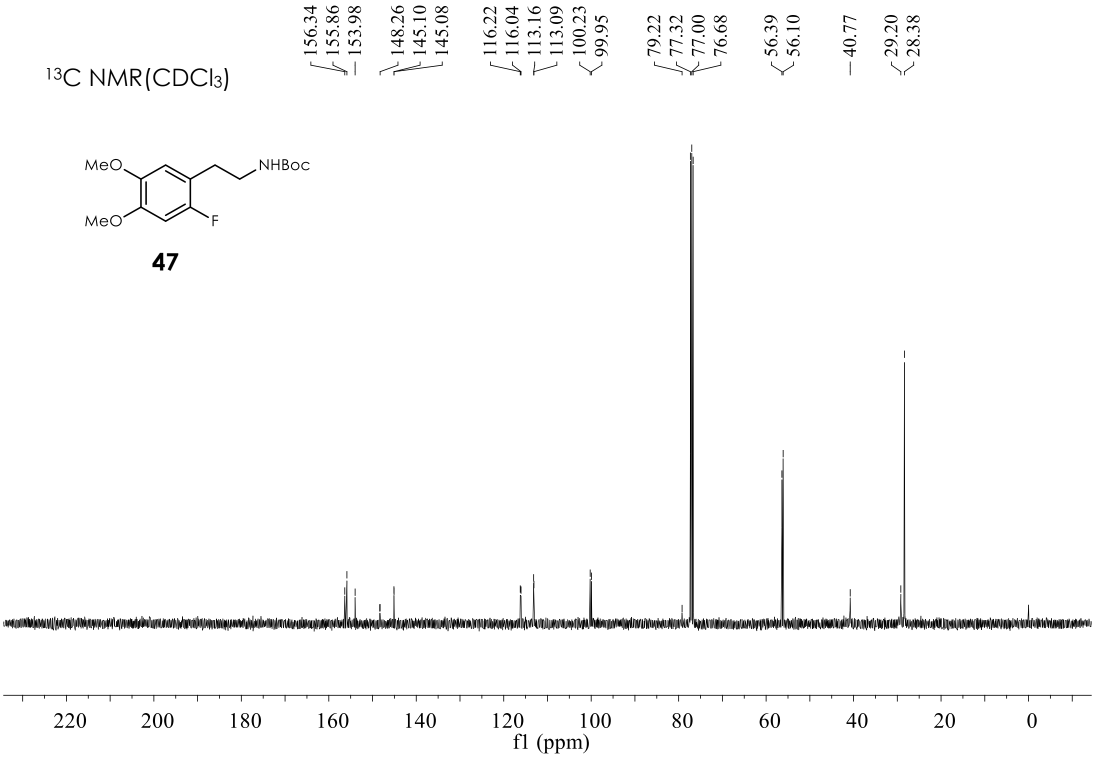
^{1}H NMR($CDCl_3$)

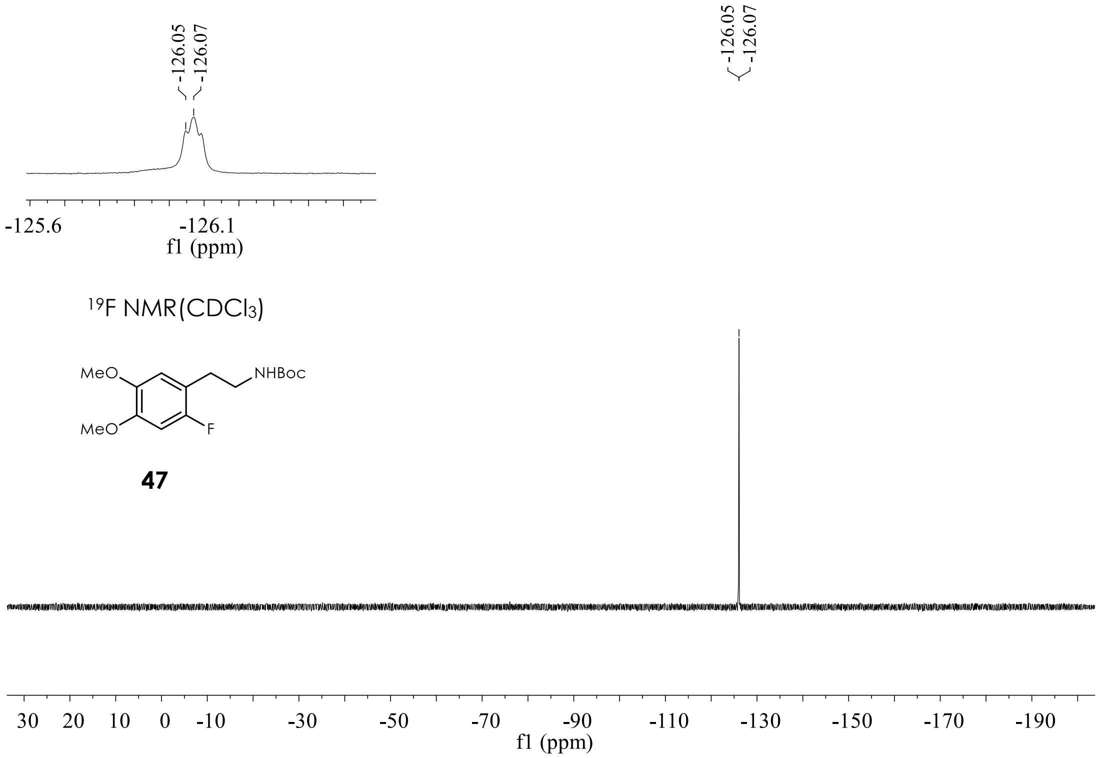
47



^{13}C NMR($CDCl_3$)

47

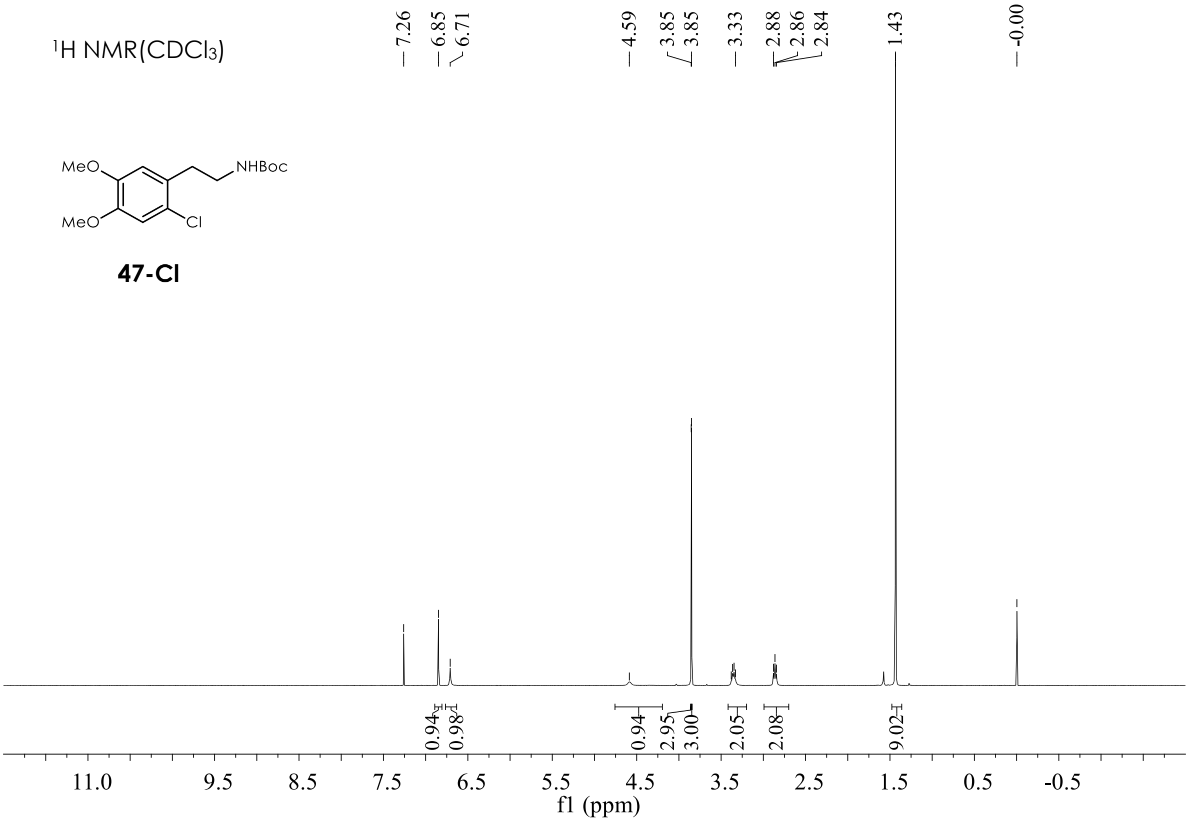




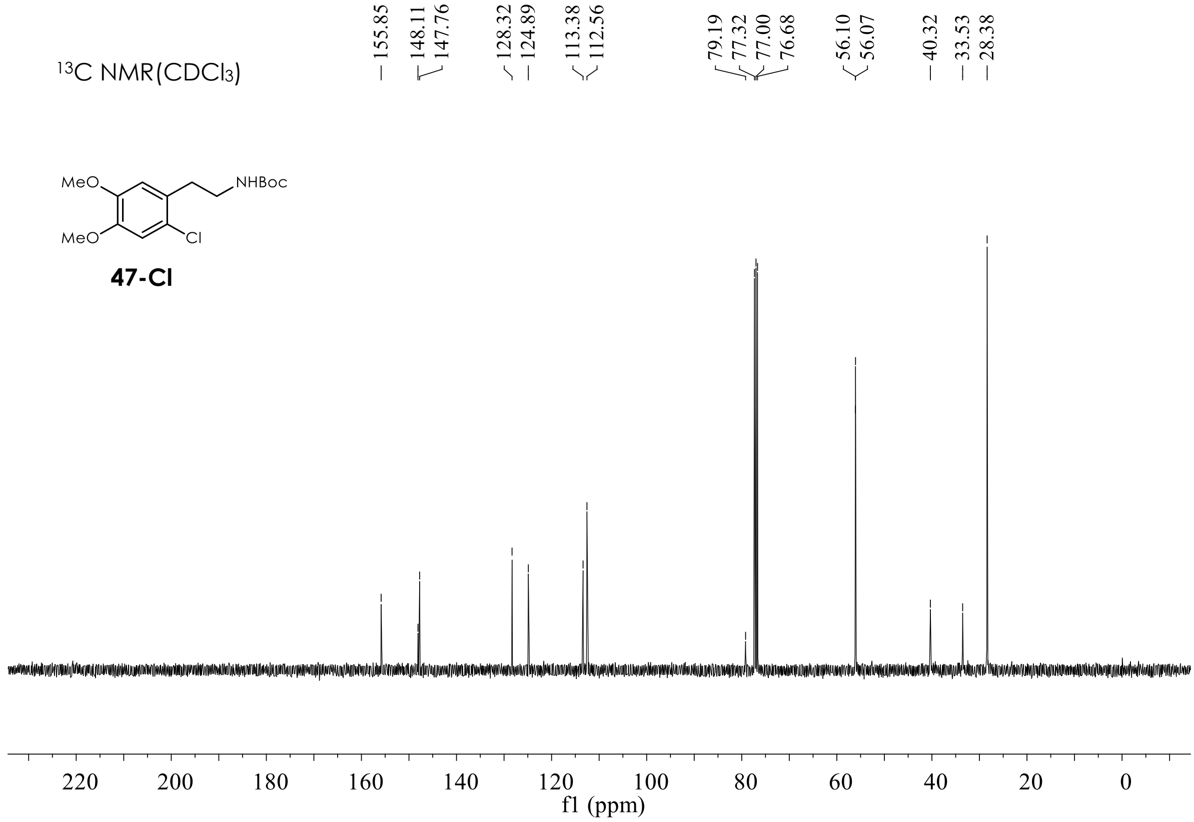
^{19}F NMR($CDCl_3$)

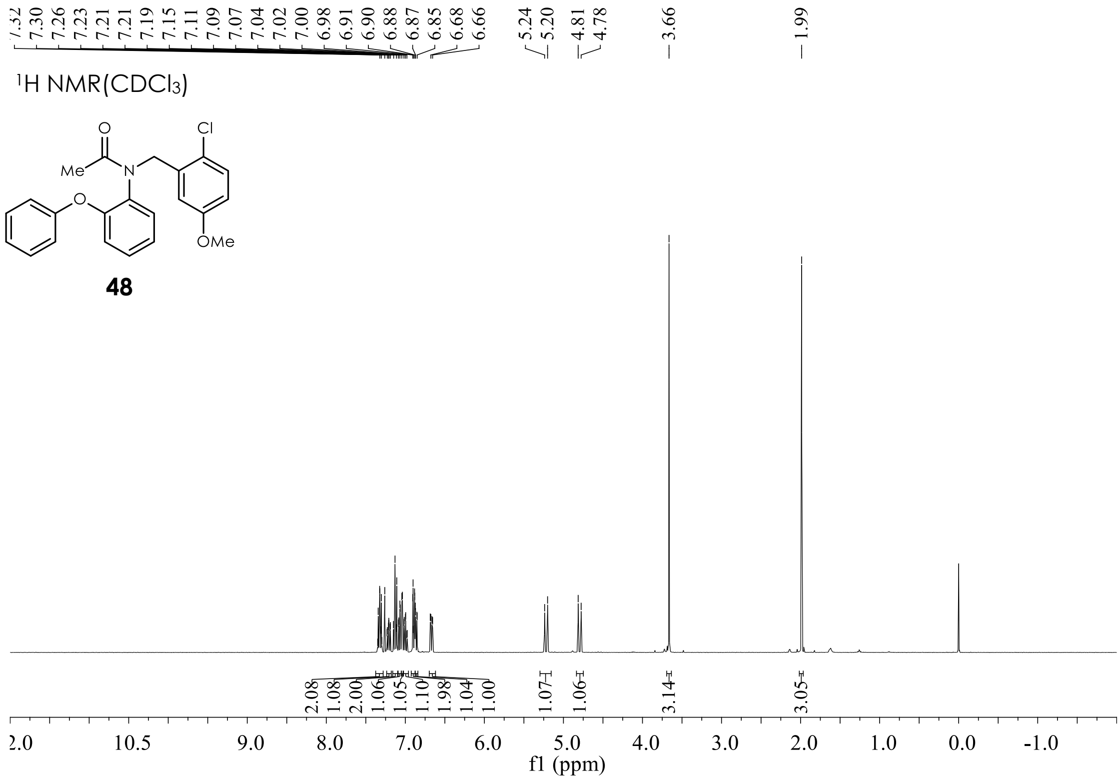
47

^{1}H NMR($CDCl_3$)

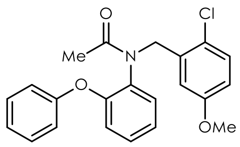


47-Cl

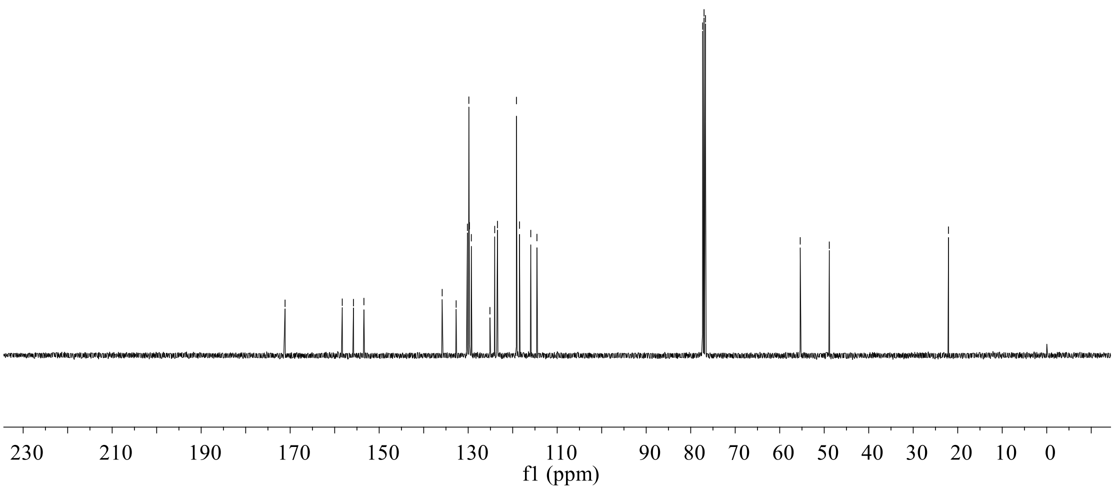

13C NMR(CDCl3)
155.85
148.11
147.76
128.32
124.89
113.38
112.56
79.19
77.32
77.00
76.68
56.10
56.07
40.32
33.53
28.38
MeO
MeO
NHBoc
Cl
47-Cl
220 200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)


7.32
7.30
7.26
7.23
7.21
7.21
7.19
7.15
7.11
7.09
7.07
7.04
7.02
7.00
6.98
6.91
6.90
6.88
6.87
6.85
6.68
6.66
5.24
5.20
4.81
4.78
3.66
1.99
1H NMR(CDCl3)
O
Me
N
Cl
O
OMe
48
2.08
1.08
2.00
1.06
1.05
1.10
1.98
1.04
1.00
1.07
1.06
3.14
3.05
2.0 10.5 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0
f1 (ppm)

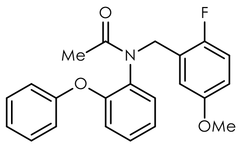
¹³C NMR(CDCl₃)



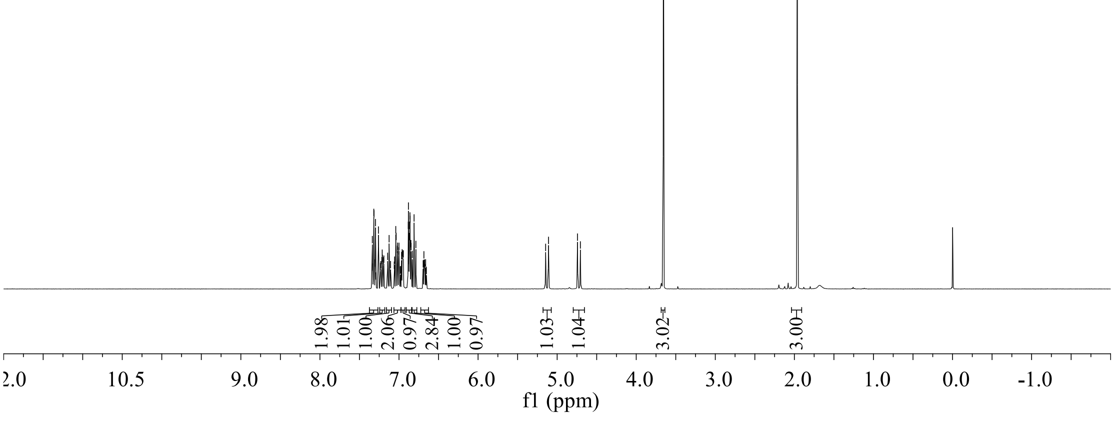
48

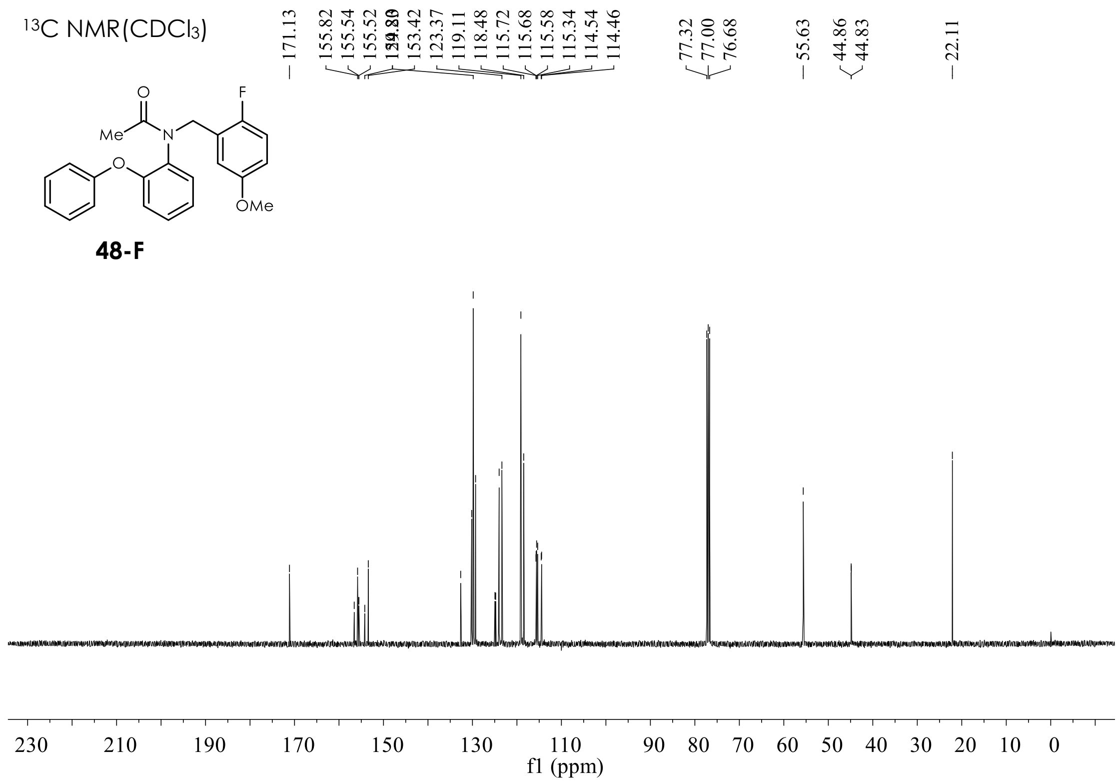


¹H NMR(CDCl₃)

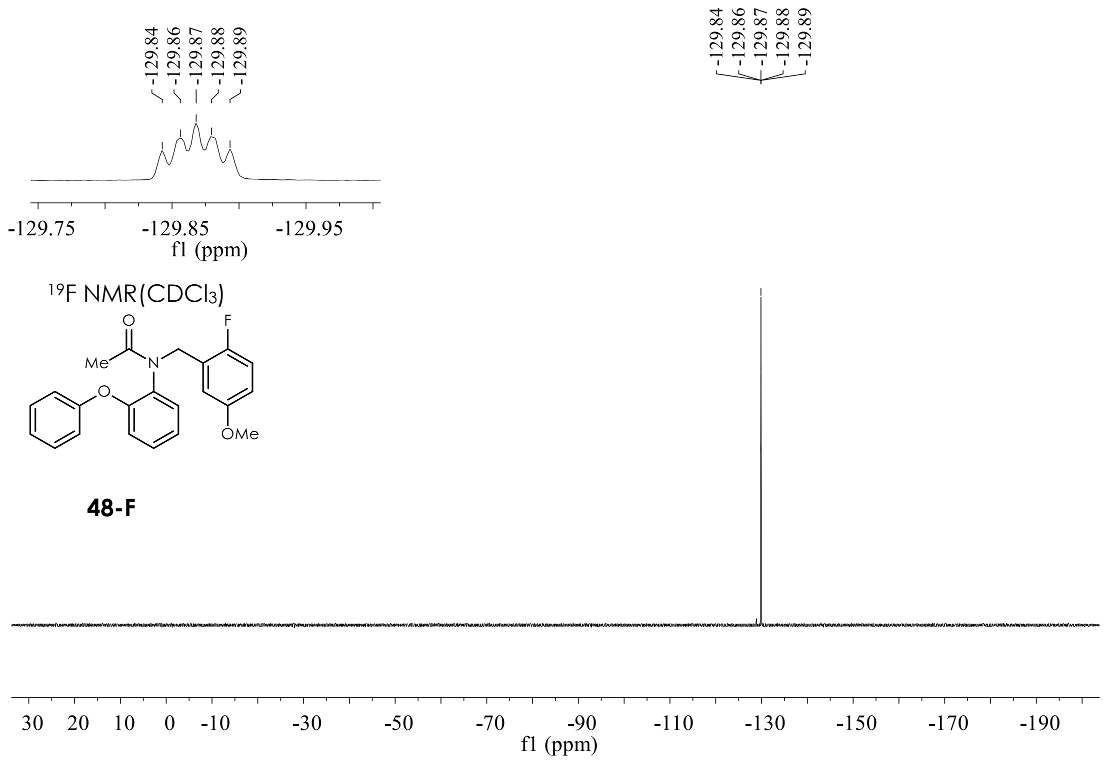


48-F

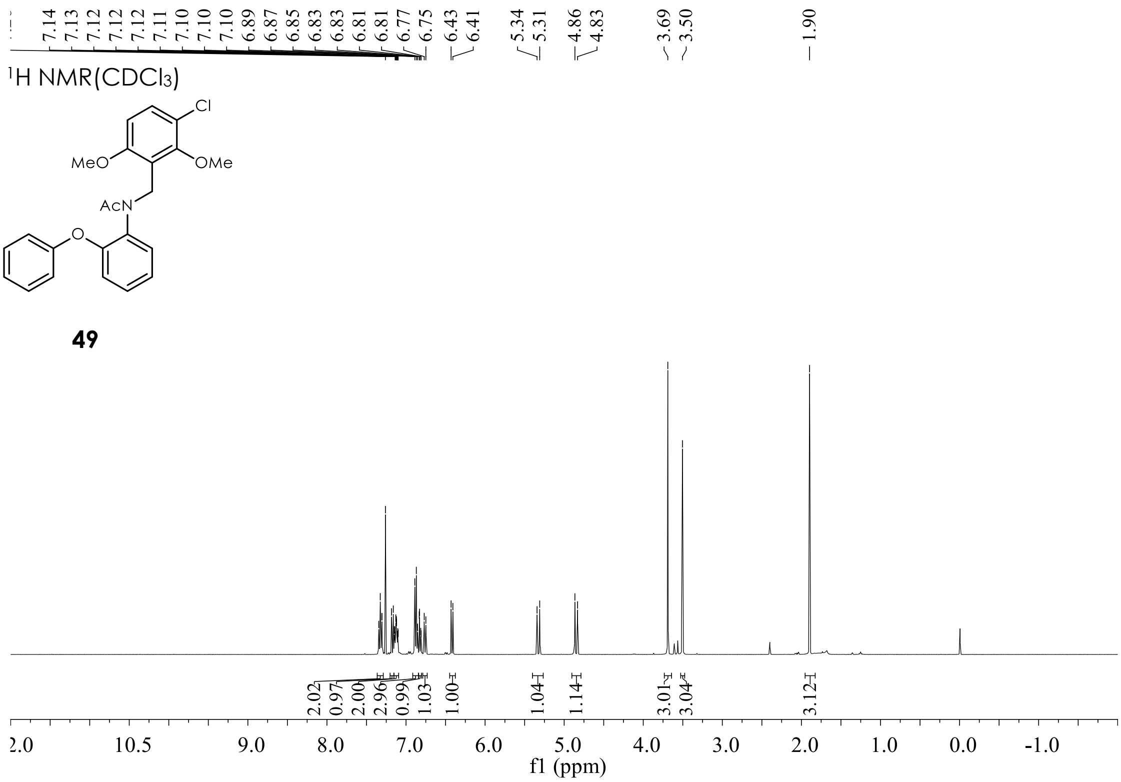




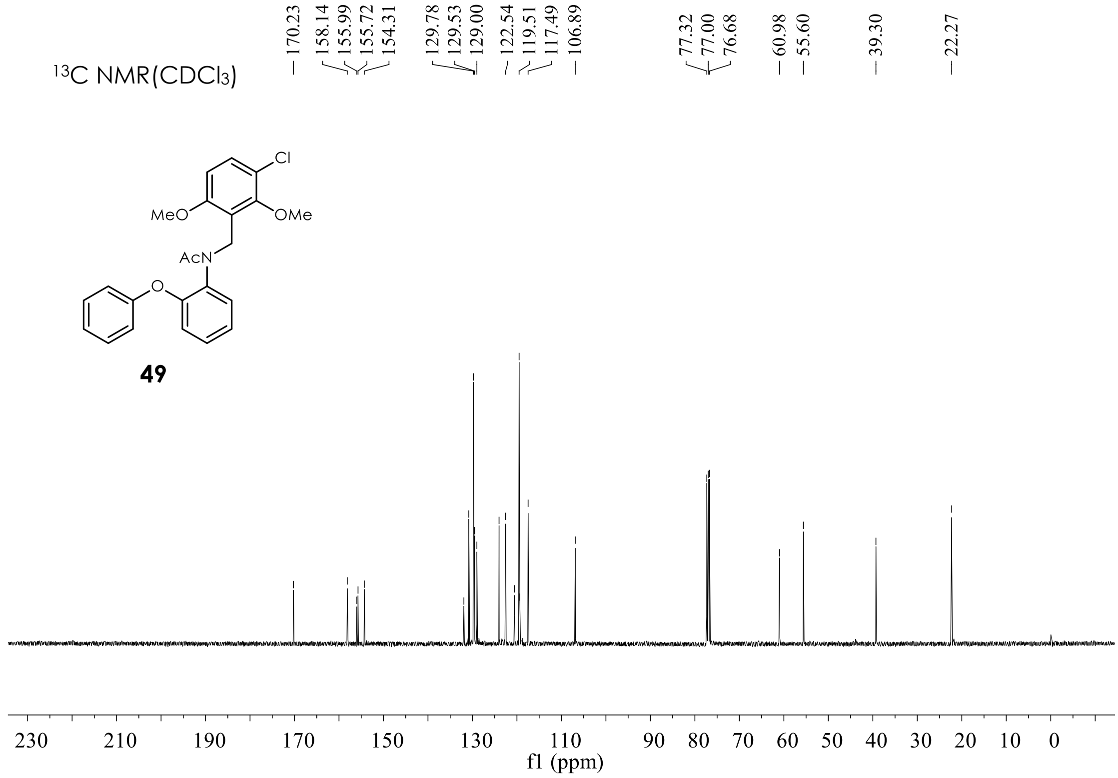
13C NMR(CDCl3)
171.13
155.82
155.54
155.52
153.42
123.37
119.11
118.48
115.72
115.68
115.58
115.34
114.54
114.46
77.32
77.00
76.68
55.63
44.86
44.83
22.11
O
Me
N
F
O
OMe
48-F
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



-129.84
-129.86
-129.87
-129.88
-129.89
-129.75
-129.85
-129.95
f1 (ppm)
19F NMR(CDCl3)
O
Me
N
F
O
OMe
48-F
30
20
10
0
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
f1 (ppm)

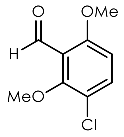


7.14
7.13
7.12
7.12
7.12
7.11
7.10
7.10
7.10
6.89
6.87
6.85
6.83
6.83
6.81
6.81
6.77
6.75
6.43
6.41
5.34
5.31
4.86
4.83
3.69
3.50
1.90
^{1}H NMR(CDCl$_3$)
Cl
MeO
OMe
AcN
O
49
2.02
0.97
2.00
2.96
0.99
1.03
1.00
1.04
1.14
3.01
3.04
3.12
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
f1 (ppm)

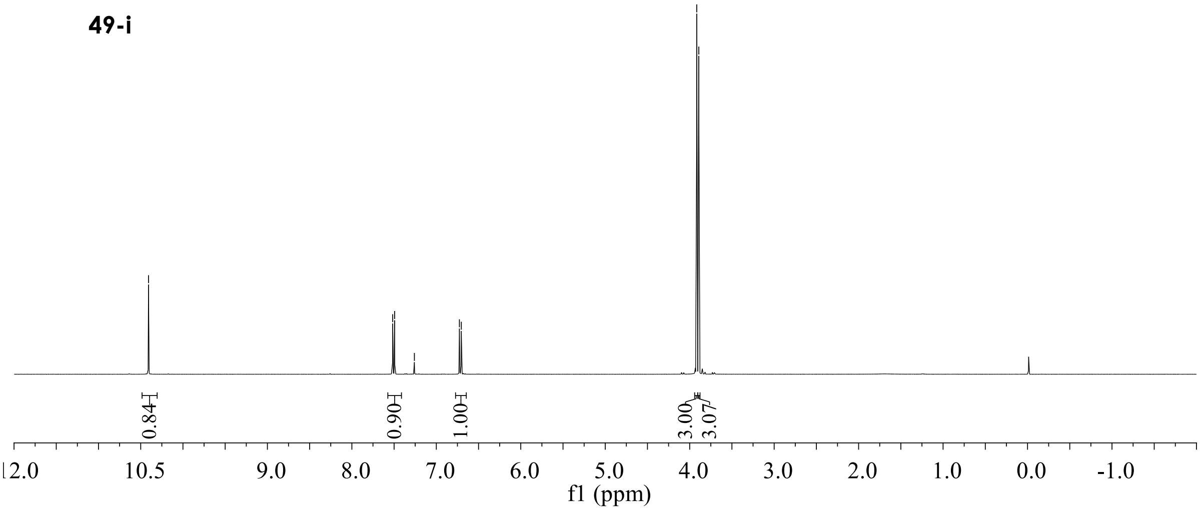


170.23
158.14
155.99
155.72
154.31
129.78
129.53
129.00
122.54
119.51
117.49
106.89
77.32
77.00
76.68
60.98
55.60
39.30
22.27
^{13}C NMR(CDCl$_3$)
Cl
MeO
OMe
AcN
O
49
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

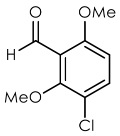
^{1}H NMR($CDCl_3$)



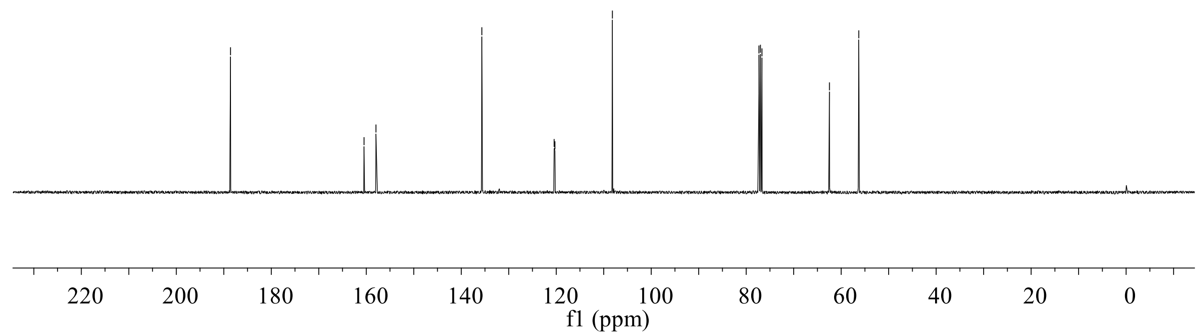
49-i

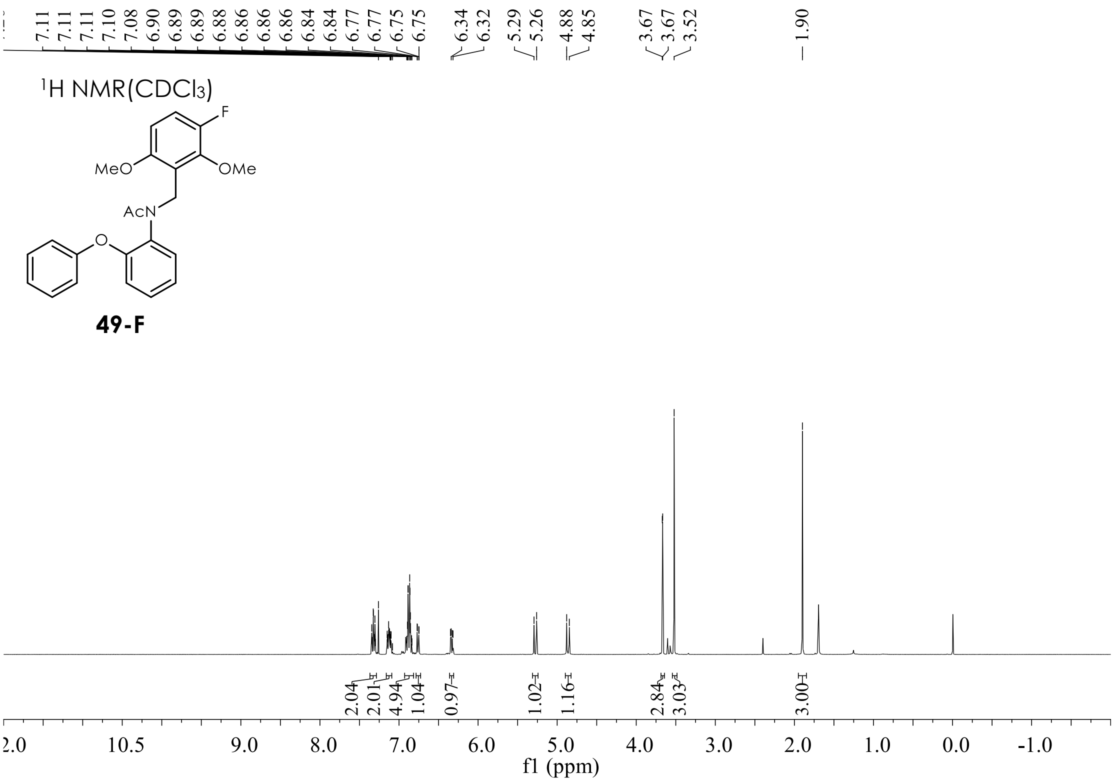


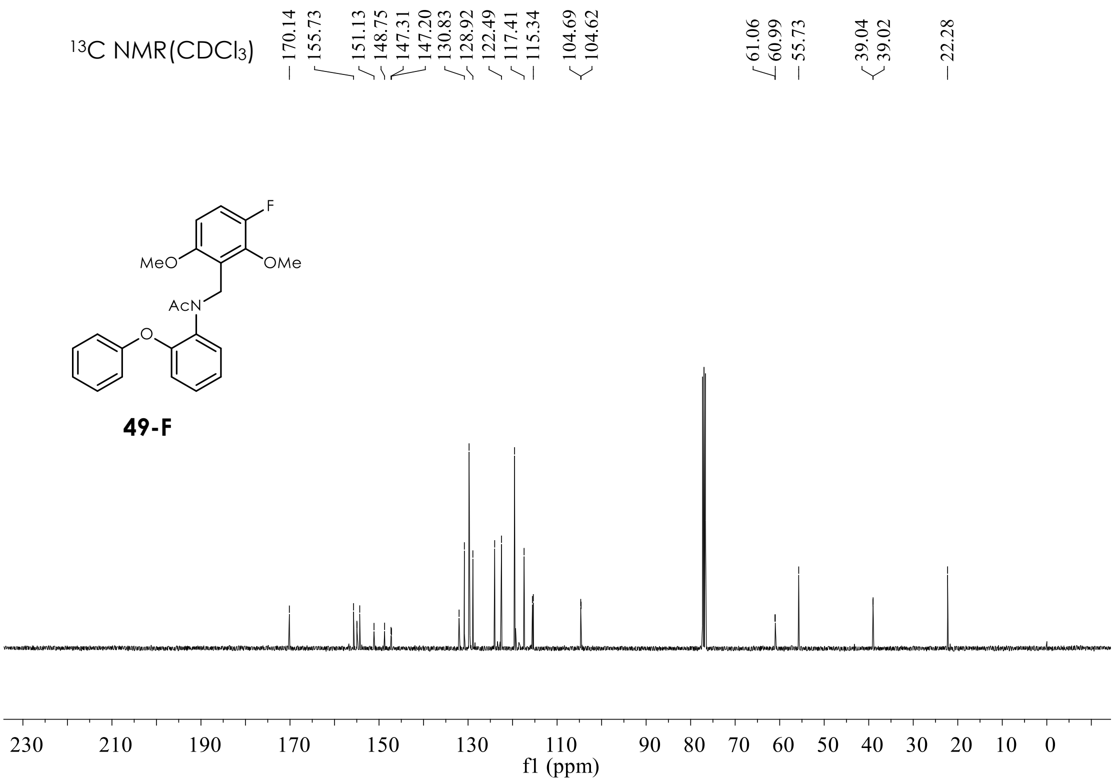
^{13}C NMR($CDCl_3$)

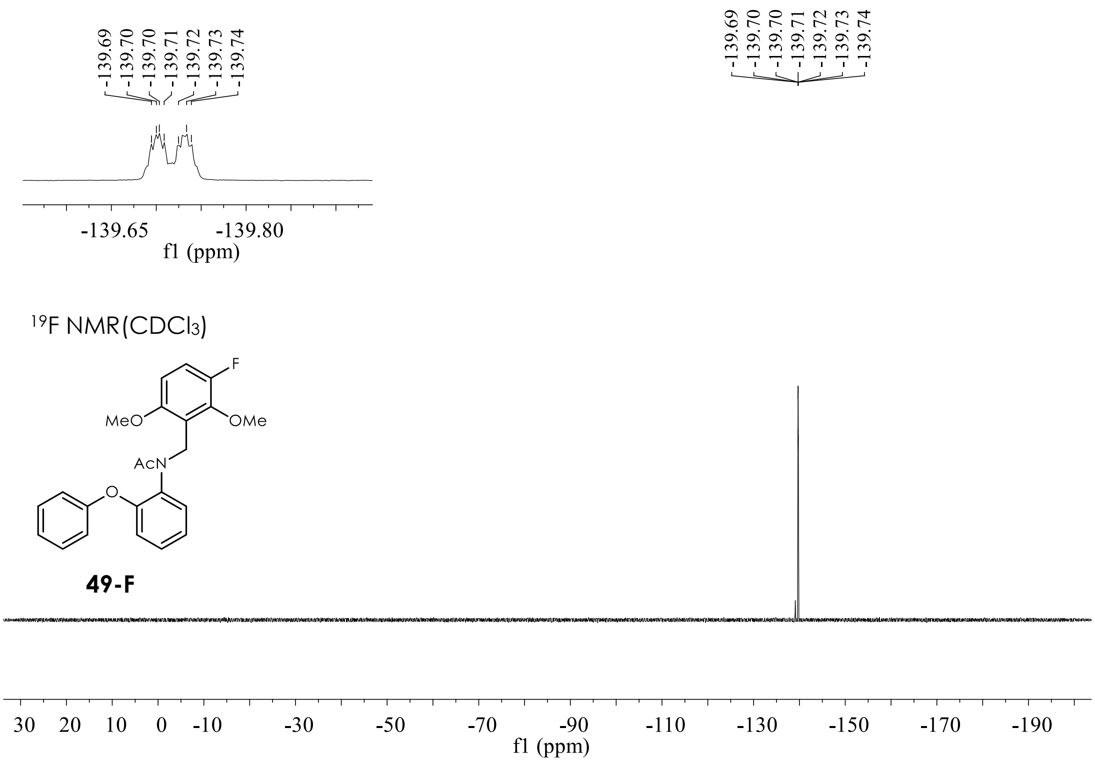


49-i

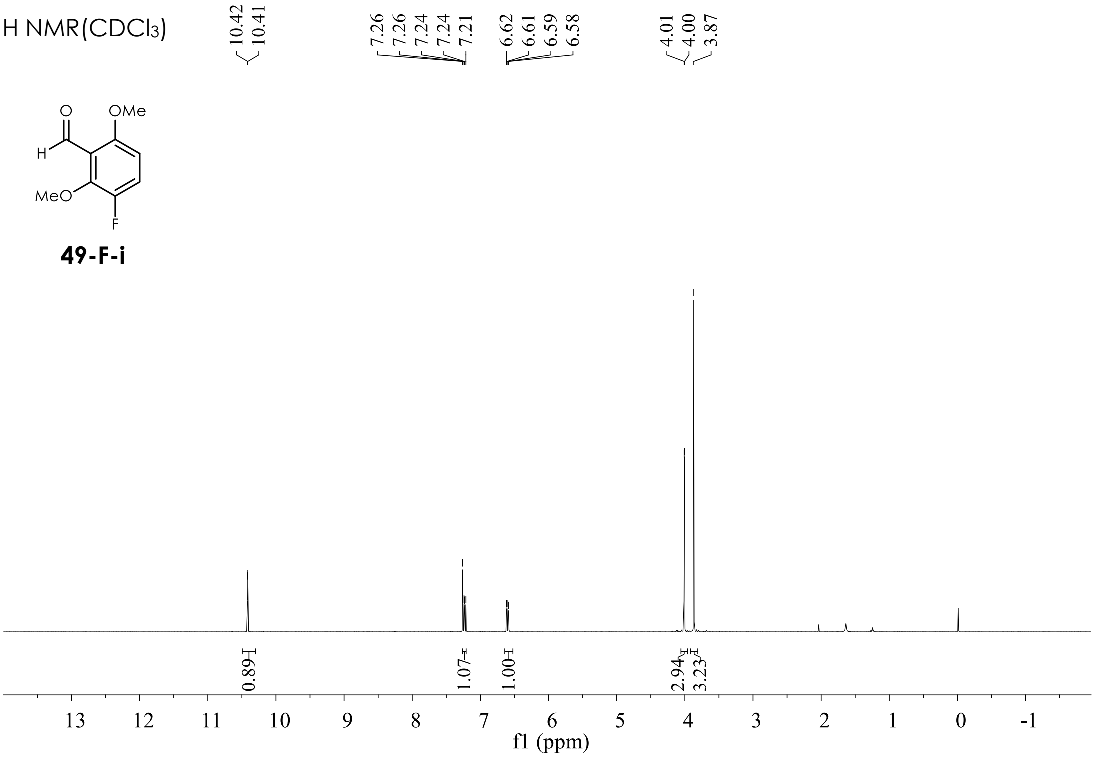



1H NMR(CDCl3)
49-F

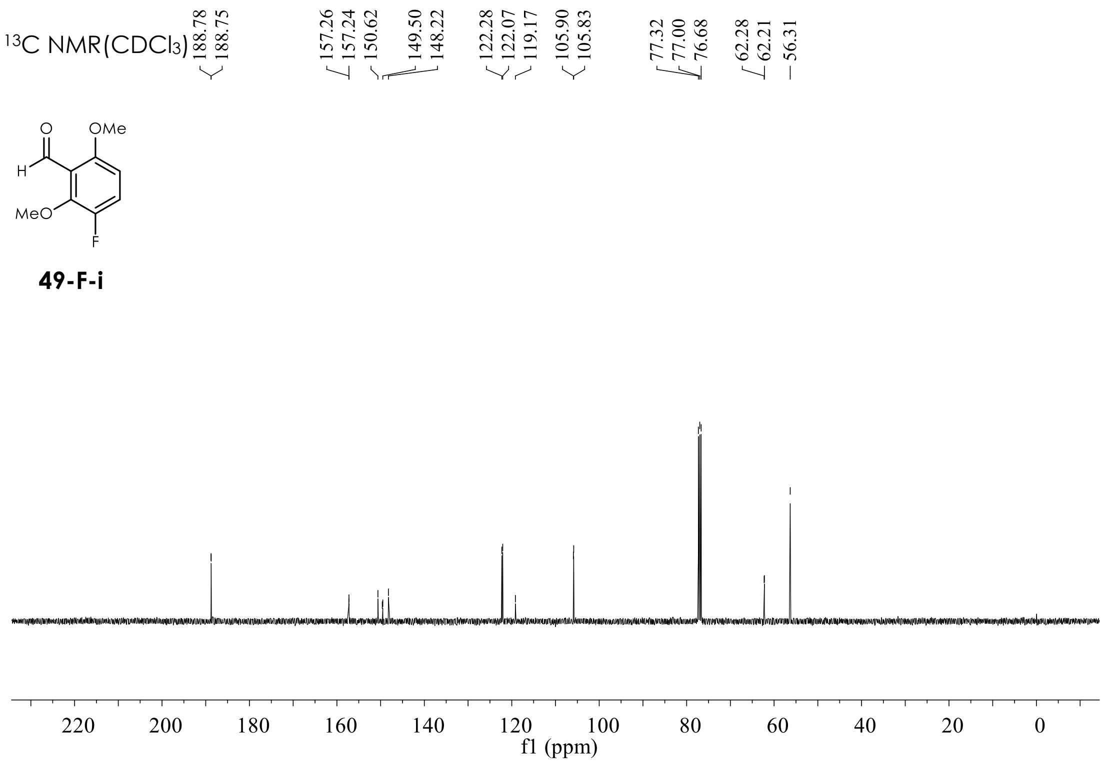

13C NMR(CDCl3)
49-F

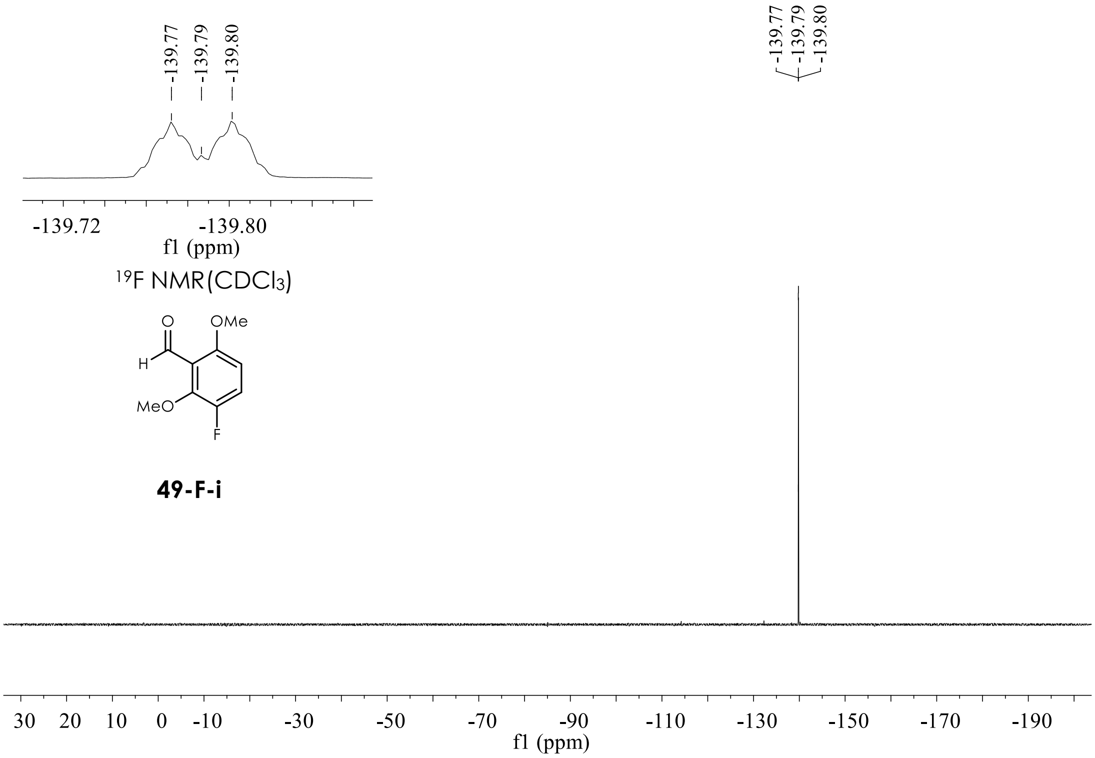


-139.69
-139.70
-139.70
-139.71
-139.72
-139.73
-139.74
-139.65
-139.80
f1 (ppm)
^{19}F NMR(CDCl$_3$)
F
MeO
OMe
AcN
O
49-F
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)

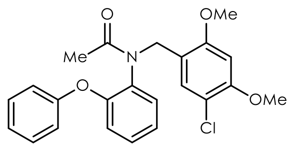


^{1}H NMR(CDCl$_3$)
10.42
10.41
7.26
7.26
7.24
7.24
7.21
6.62
6.61
6.59
6.58
4.01
4.00
3.87
O
OMe
H
MeO
F
49-F-i
0.89
1.07
1.00
2.94
3.23
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)

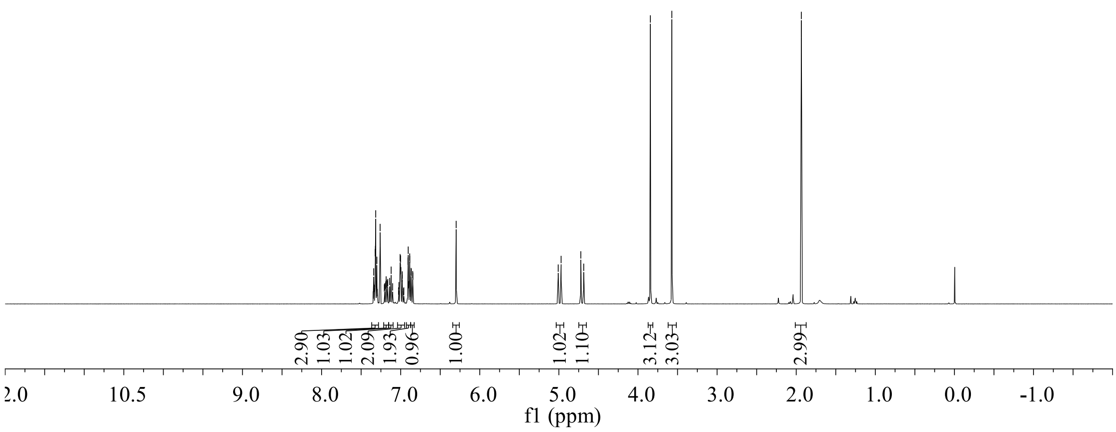

13C NMR(CDCl3)
188.78
188.75
157.26
157.24
150.62
149.50
148.22
122.28
122.07
119.17
105.90
105.83
77.32
77.00
76.68
62.28
62.21
56.31
O
OMe
H
MeO
F
49-F-i
220 200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)


-139.77
-139.79
-139.80
-139.72
-139.80
f1 (ppm)
19F NMR(CDCl3)
O
OMe
H
MeO
F
49-F-i
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)

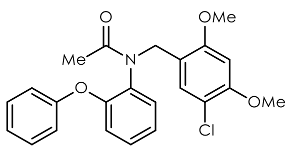
^{1}H NMR($CDCl_3$)



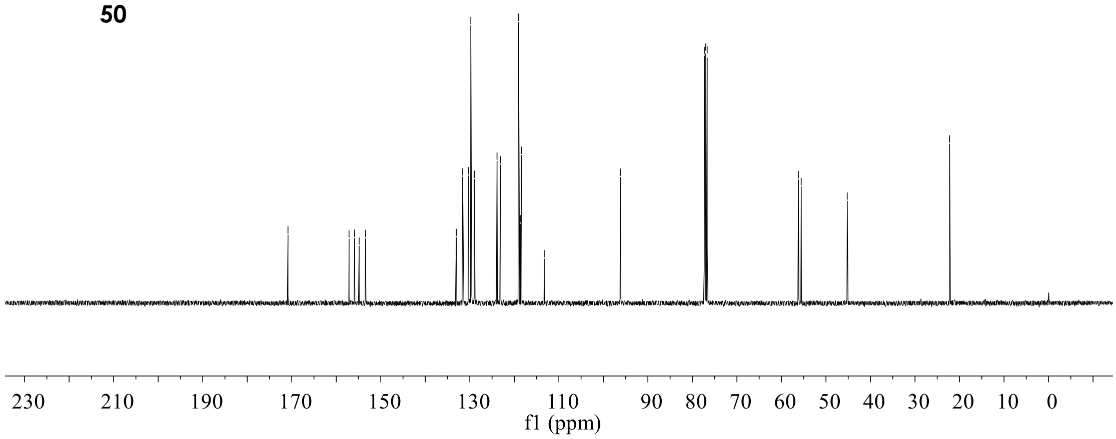
50



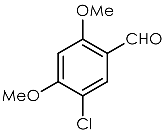
^{13}C NMR($CDCl_3$)



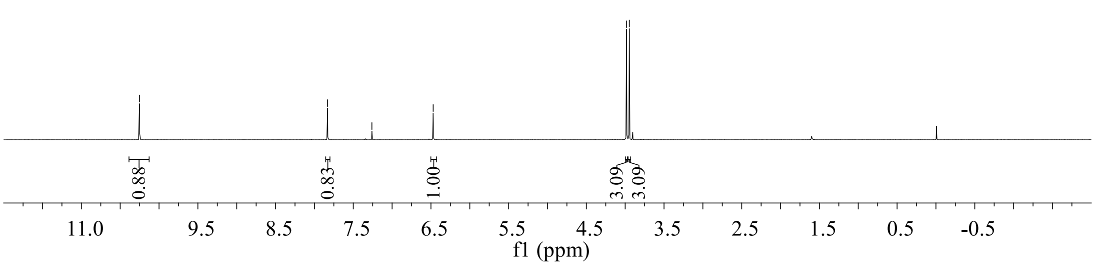
50



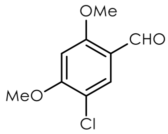
[1]H NMR($CDCl_3$)



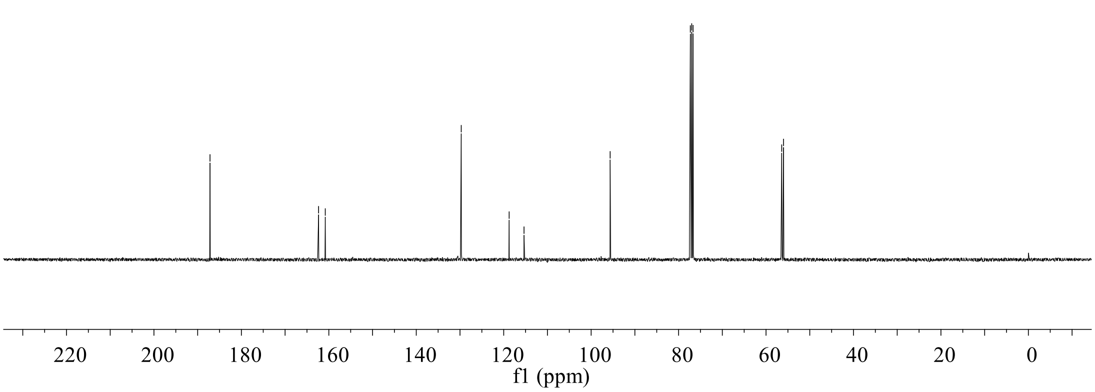
50-i

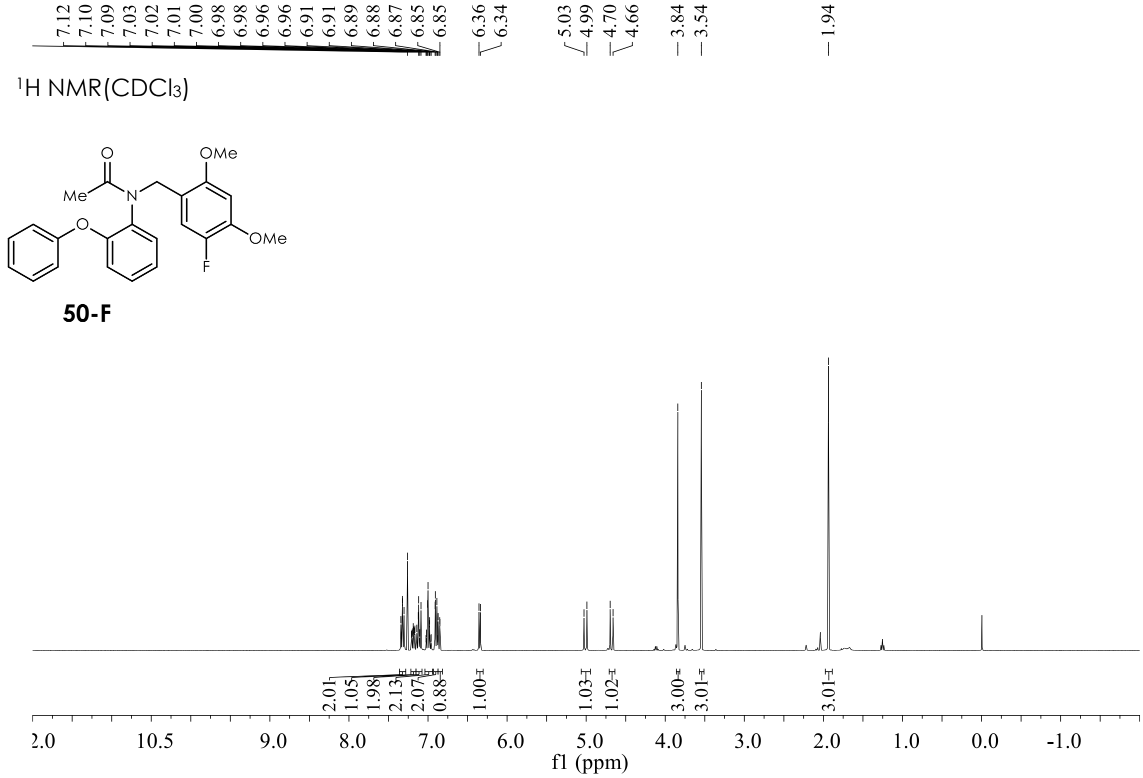


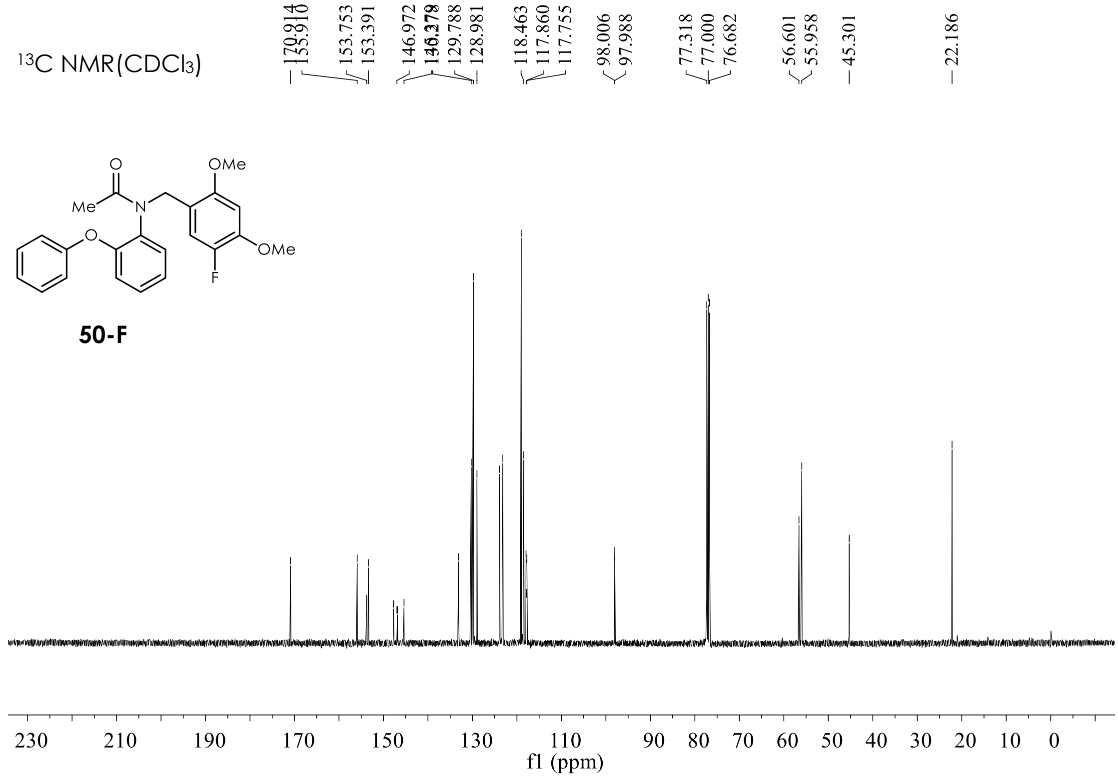
[13]C NMR($CDCl_3$)

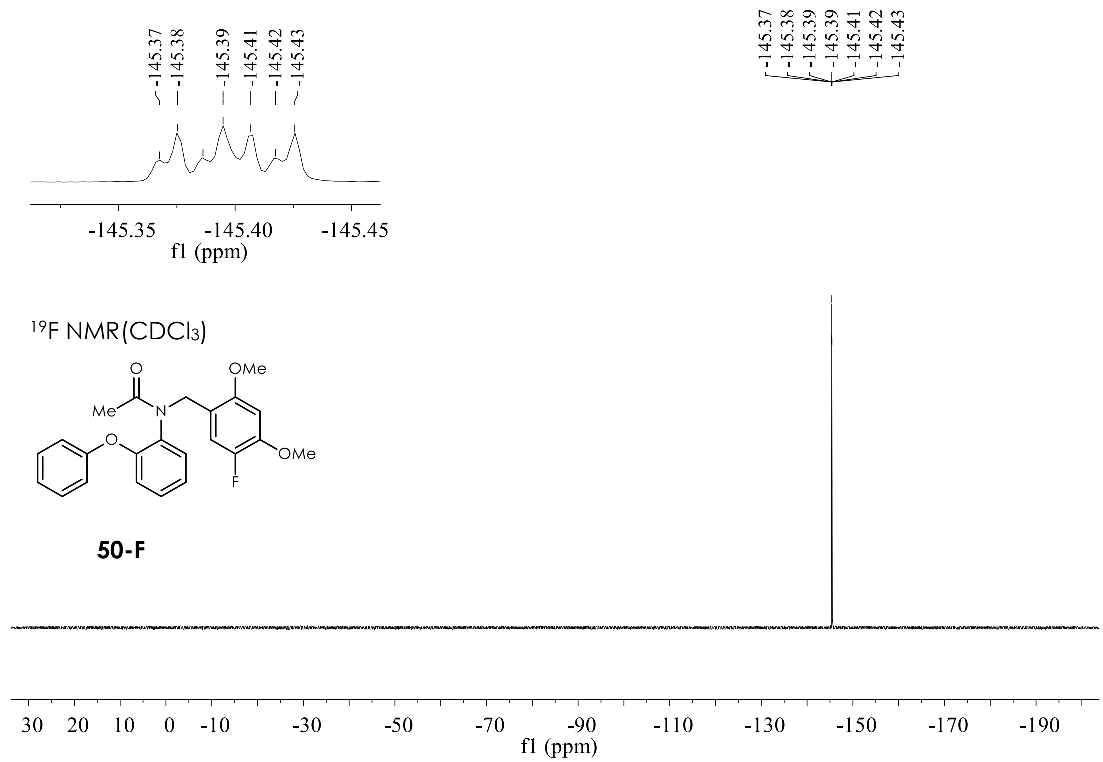


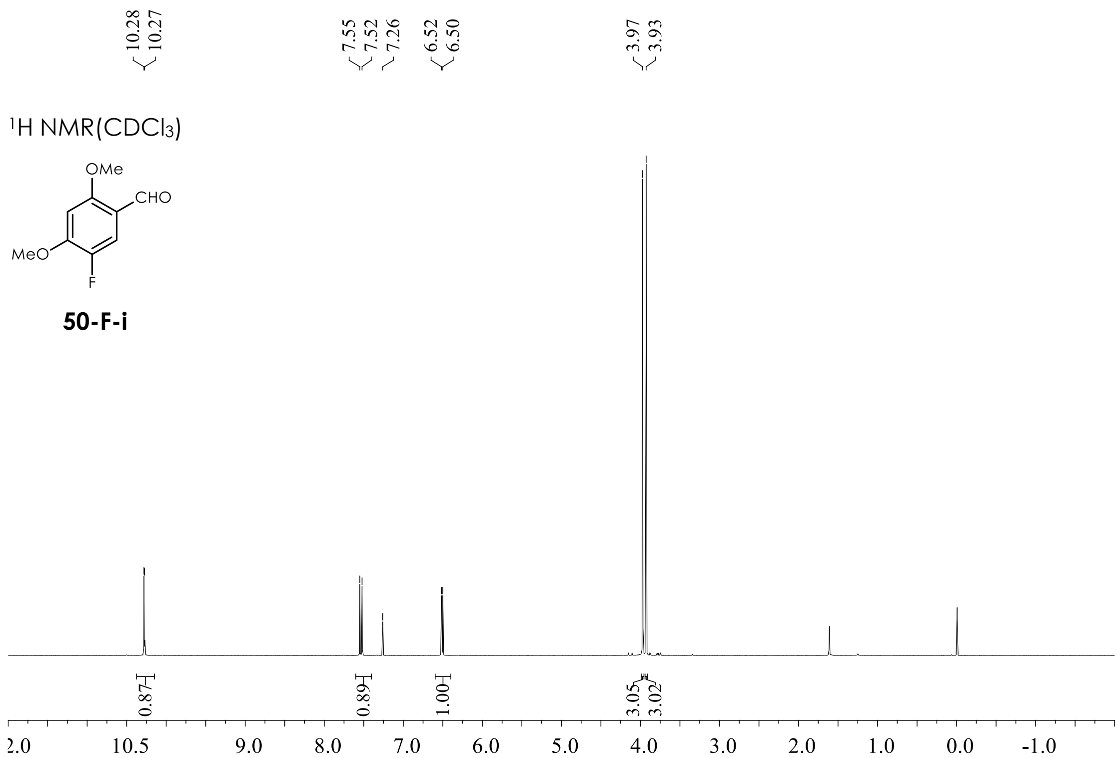
50-i

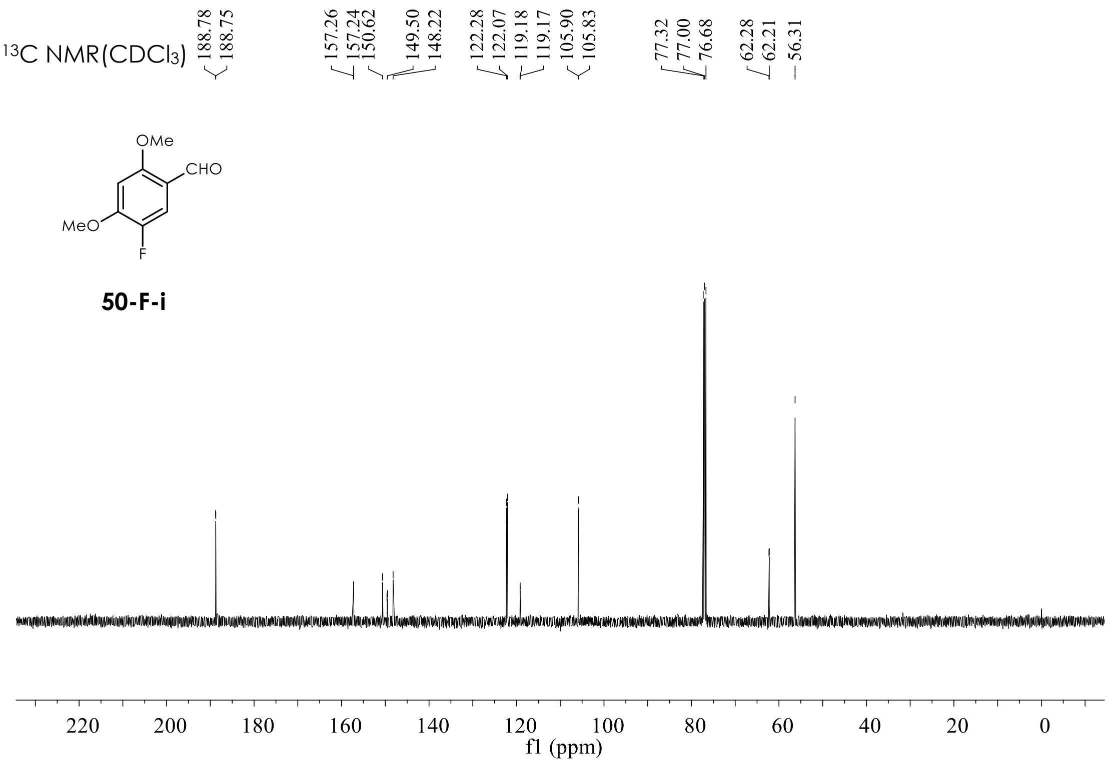


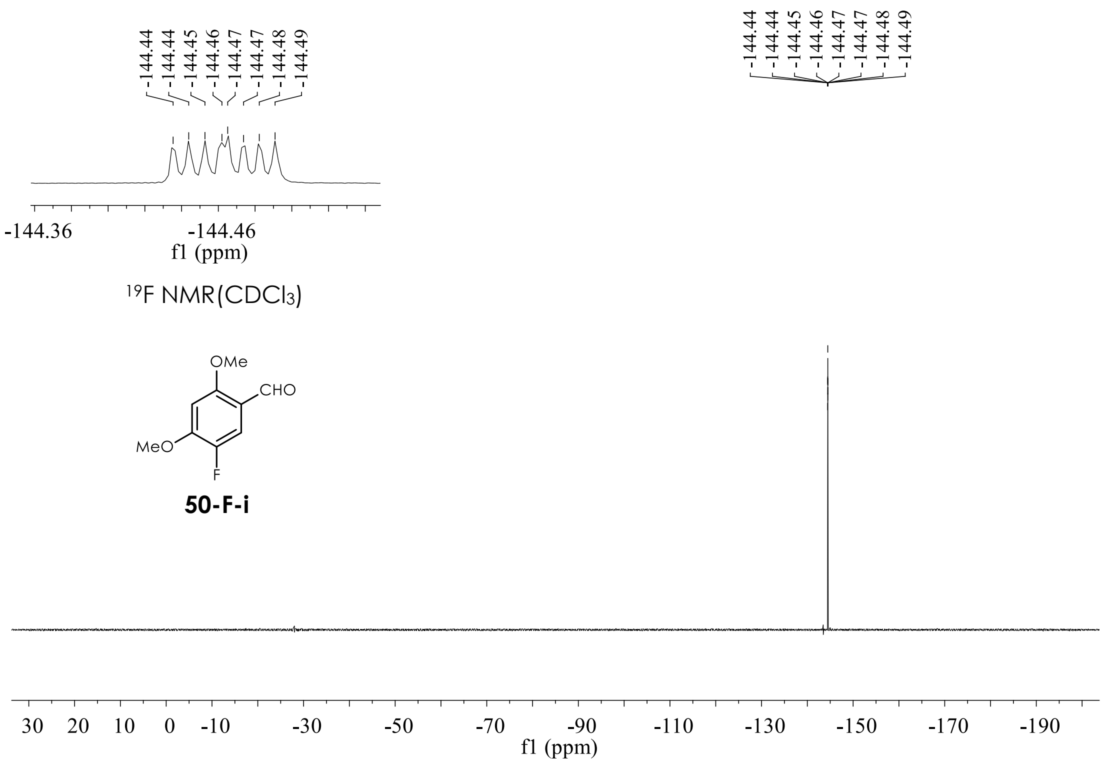

7.12 7.10 7.09 7.03 7.02 7.01 7.00 6.98 6.98 6.96 6.96 6.91 6.91 6.89 6.88 6.87 6.85 6.85
6.36 6.34
5.03 4.99 4.70 4.66
3.84
3.54
1.94
1H NMR(CDCl3)
OMe
Me
O
N
O
OMe
F
50-F
2.01 1.05 1.98 2.13 2.07 0.88
1.00
1.03
1.02
3.00
3.01
3.01
2.0 10.5 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0
f1 (ppm)

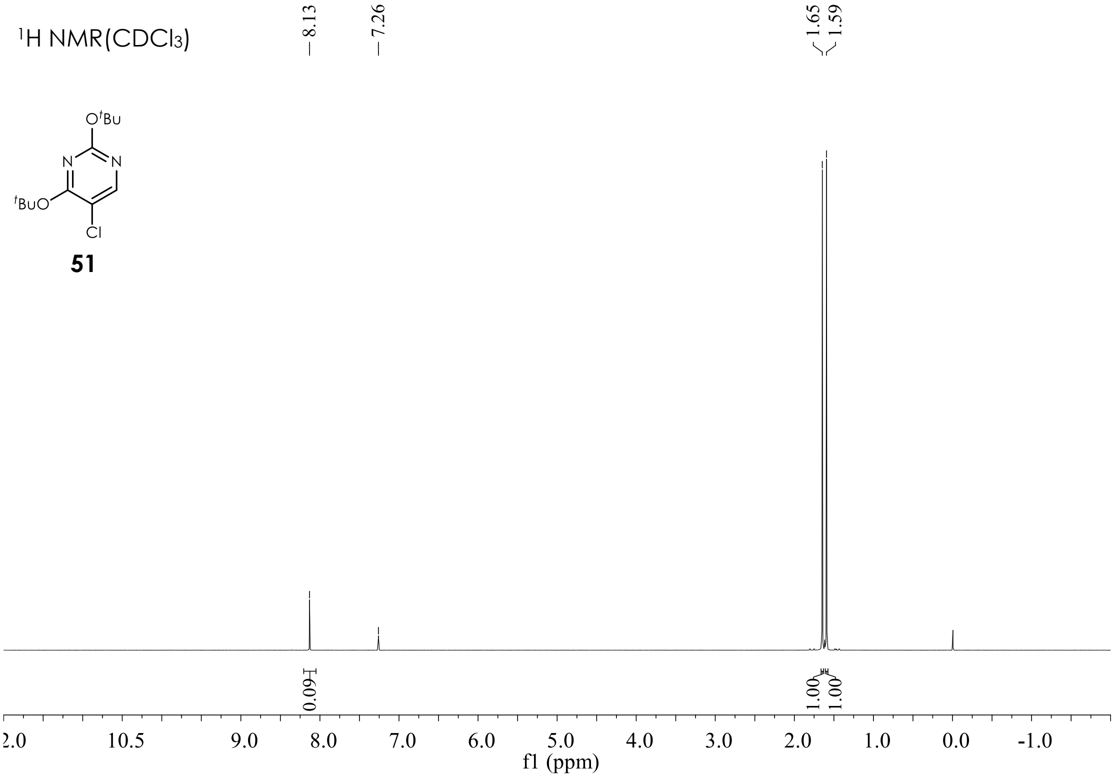

13C NMR(CDCl3)
155.910
153.753 153.391
146.972
129.788 128.981
118.463 117.860 117.755
98.006 97.988
77.318 77.000 76.682
56.601 55.958
45.301
22.186
OMe
Me
O
N
O
OMe
F
50-F
230 210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-145.37
-145.38
-145.39
-145.41
-145.42
-145.43
-145.35
-145.40
-145.45
f1 (ppm)
-145.37
-145.38
-145.39
-145.39
-145.41
-145.42
-145.43
19F NMR(CDCl3)
O
Me
N
OMe
O
OMe
F
50-F
30
20
10
0
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
f1 (ppm)

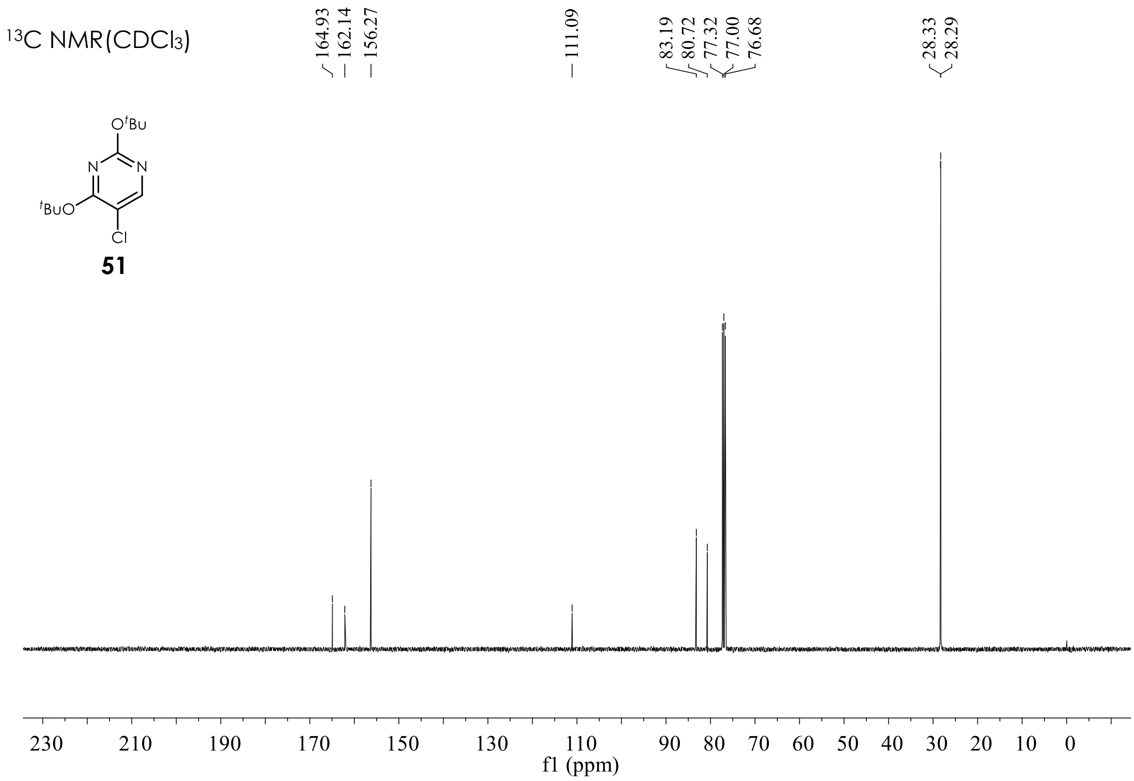

10.28
10.27
7.55
7.52
7.26
6.52
6.50
3.97
3.93
1H NMR(CDCl3)
OMe
CHO
MeO
F
50-F-i
0.87
0.89
1.00
3.05
3.02
2.0
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
f1 (ppm)


^{13}C NMR(CDCl$_3$)
188.78
188.75
157.26
157.24
150.62
149.50
148.22
122.28
122.07
119.18
119.17
105.90
105.83
77.32
77.00
76.68
62.28
62.21
56.31
OMe
CHO
MeO
F
50-F-i
220 200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)


-144.44
-144.44
-144.45
-144.46
-144.47
-144.47
-144.48
-144.49
-144.36
-144.46
f1 (ppm)
^{19}F NMR(CDCl$_3$)
OMe
CHO
MeO
F
50-F-i
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)

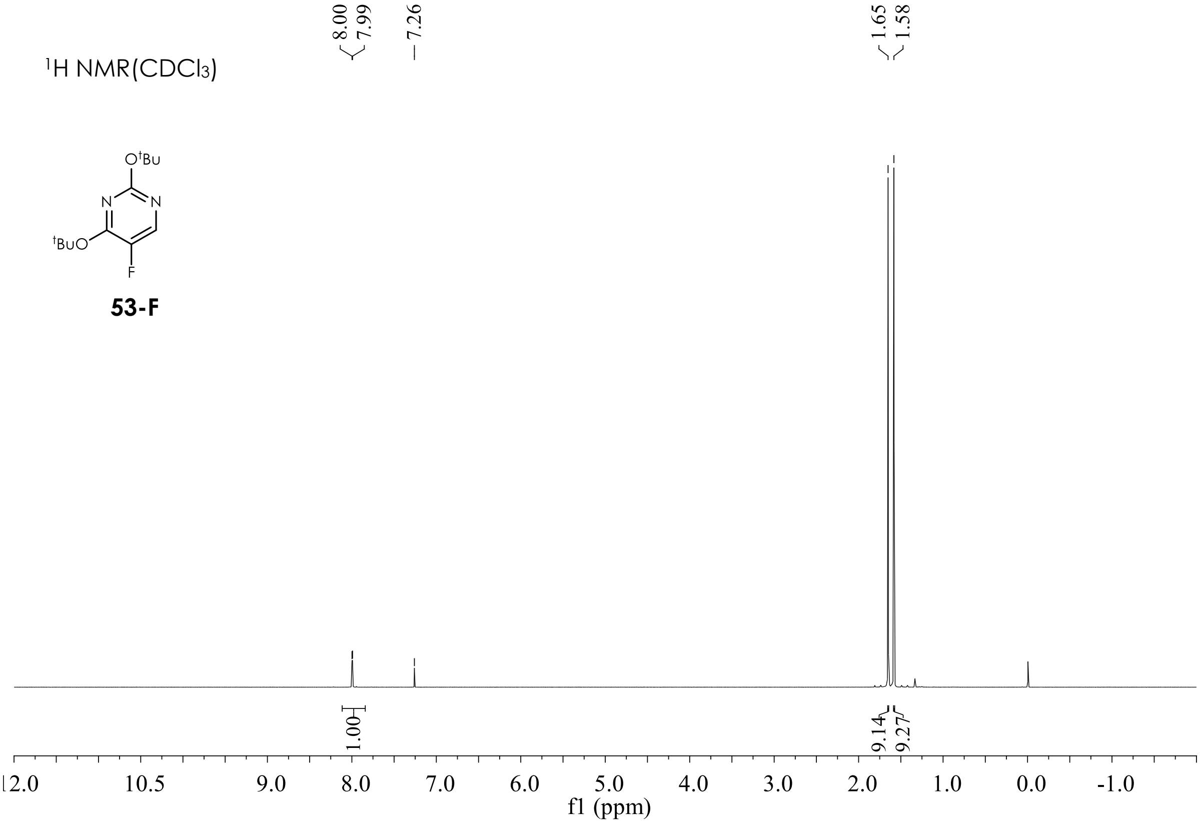


^{1}H NMR(CDCl$_3$)
8.13
7.26
1.65
1.59
O^{t}Bu
N
N
^{t}BuO
Cl
51
0.09
1.00
1.00
2.0 10.5 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0
f1 (ppm)



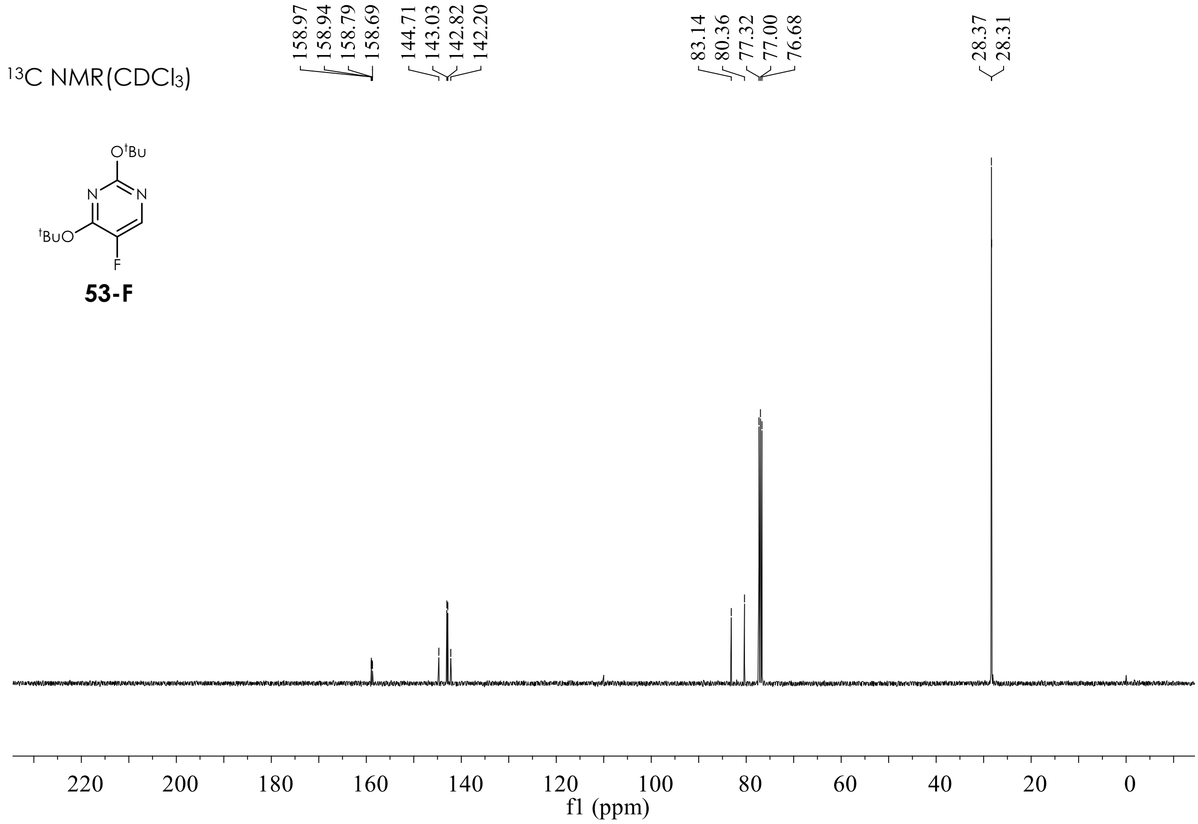
^{13}C NMR(CDCl$_3$)
164.93
162.14
156.27
111.09
83.19
80.72
77.32
77.00
76.68
28.33
28.29
O^{t}Bu
N
N
^{t}BuO
Cl
51
230 210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

^{1}H NMR($CDCl_3$)

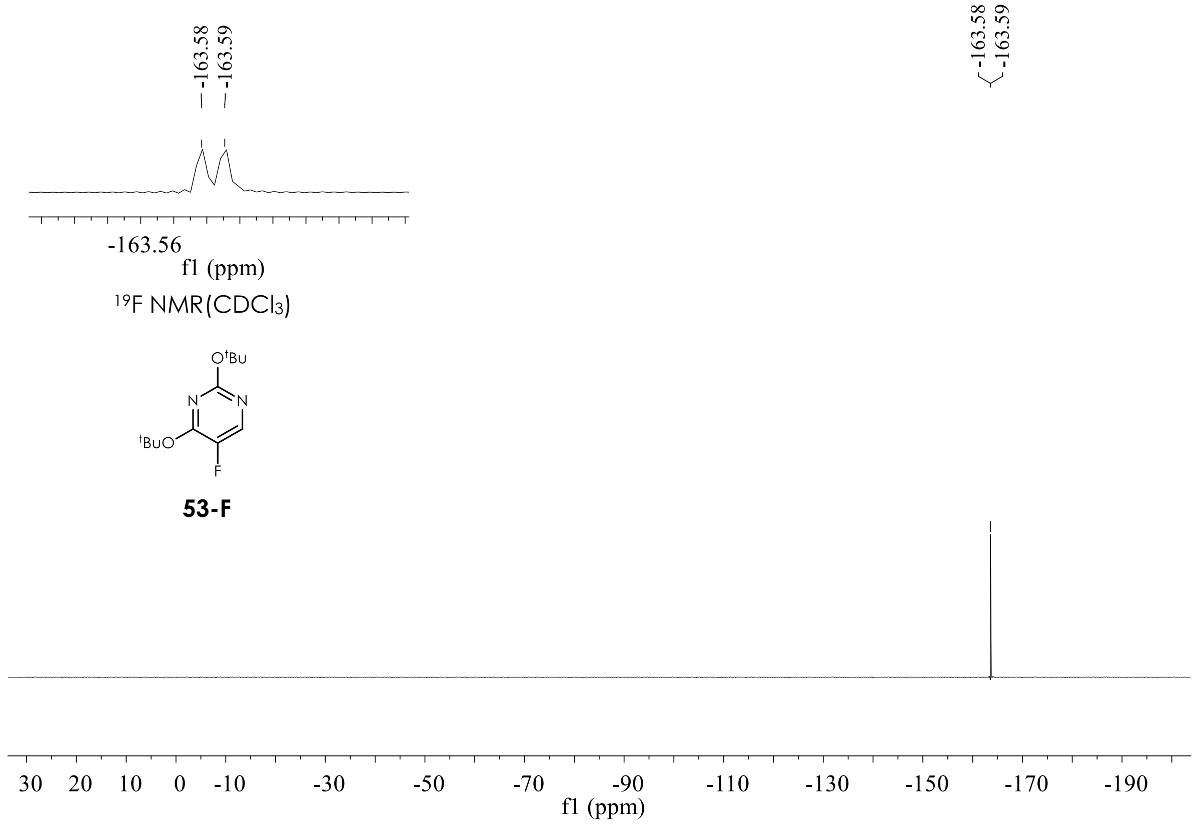


53-F

^{13}C NMR($CDCl_3$)



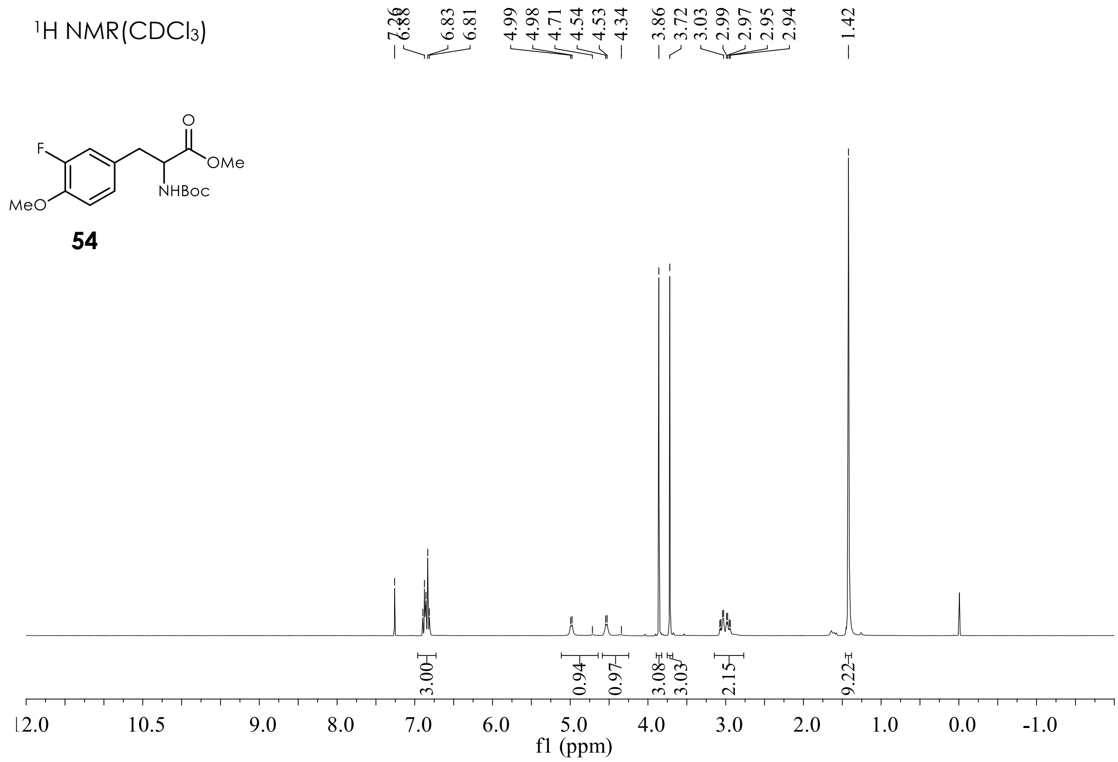
53-F



^{19}F NMR(CDCl$_3$)

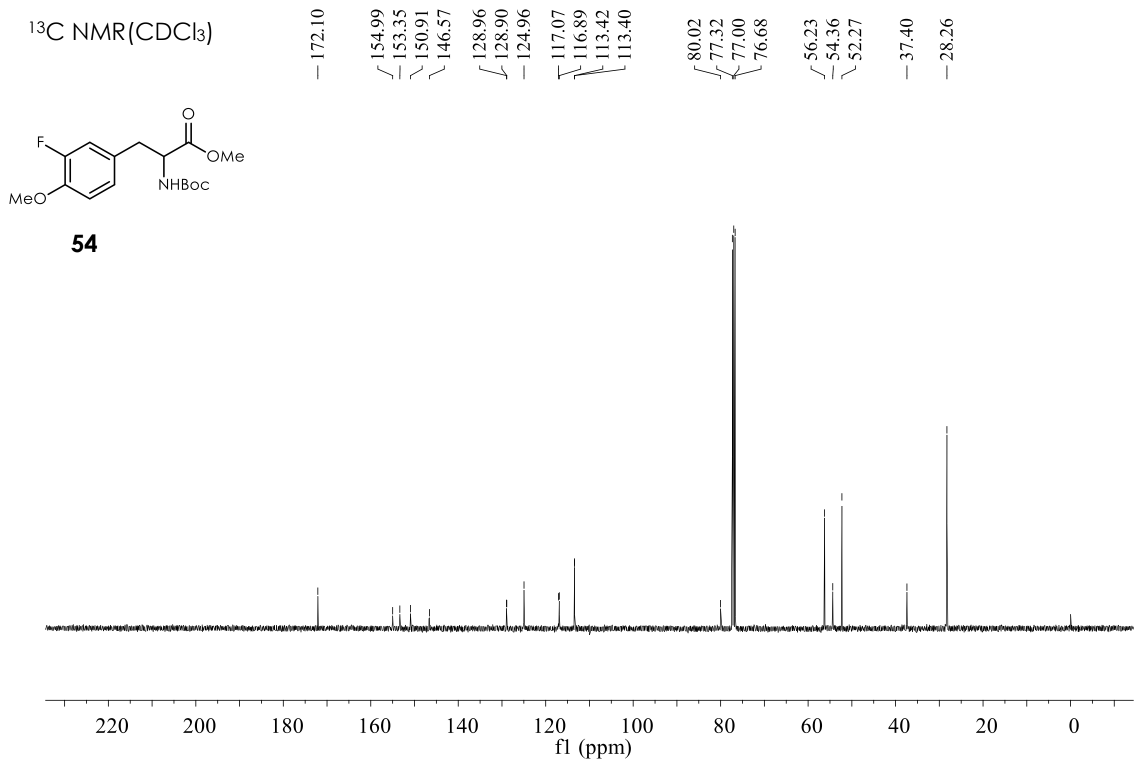
53-F

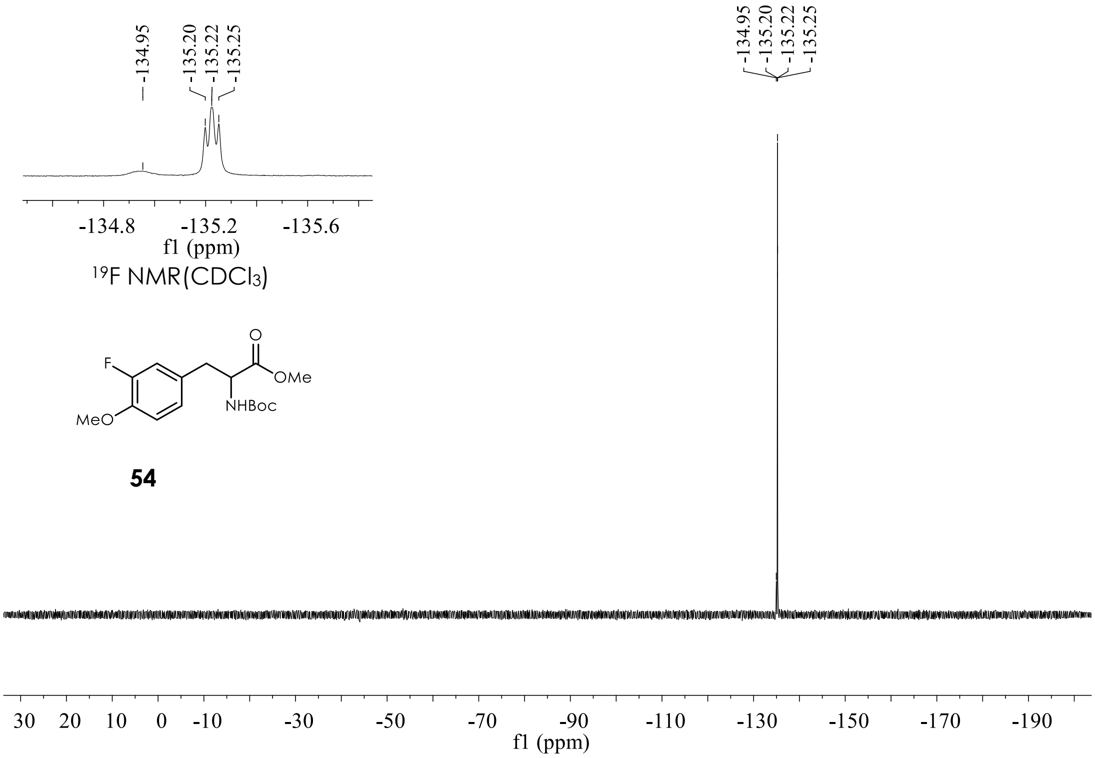
^{1}H NMR(CDCl$_3$)



54

^{13}C NMR(CDCl$_3$)

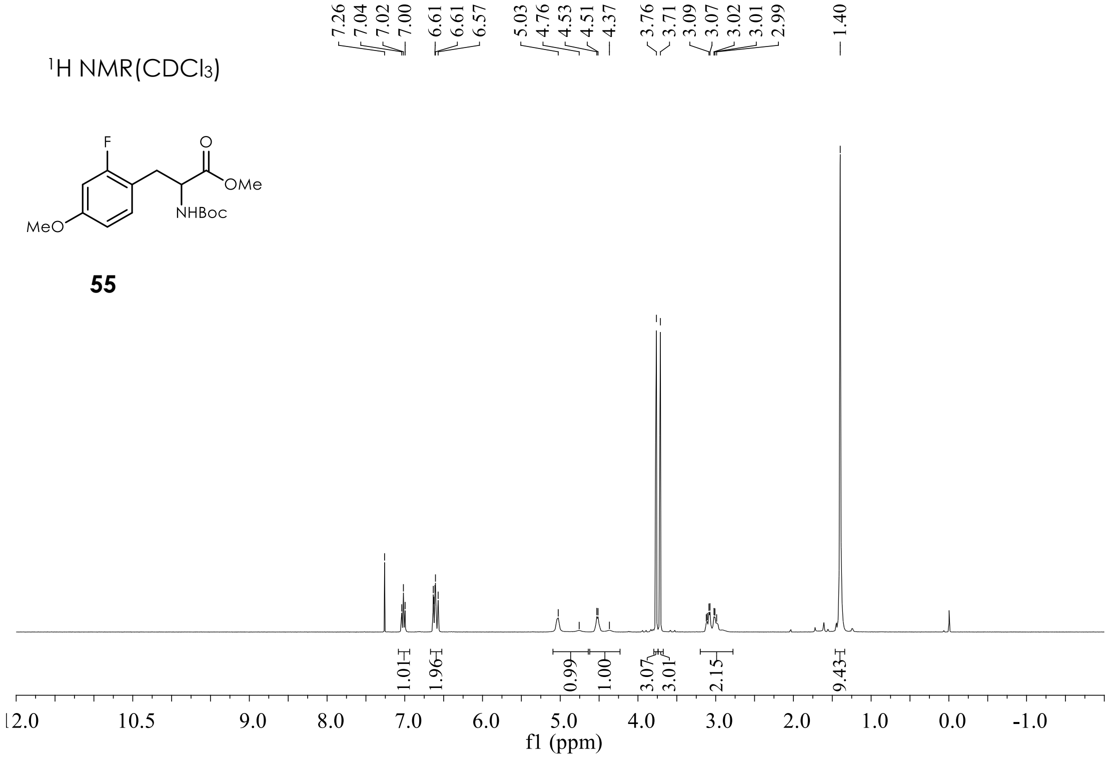




^{19}F NMR(CDCl$_3$)

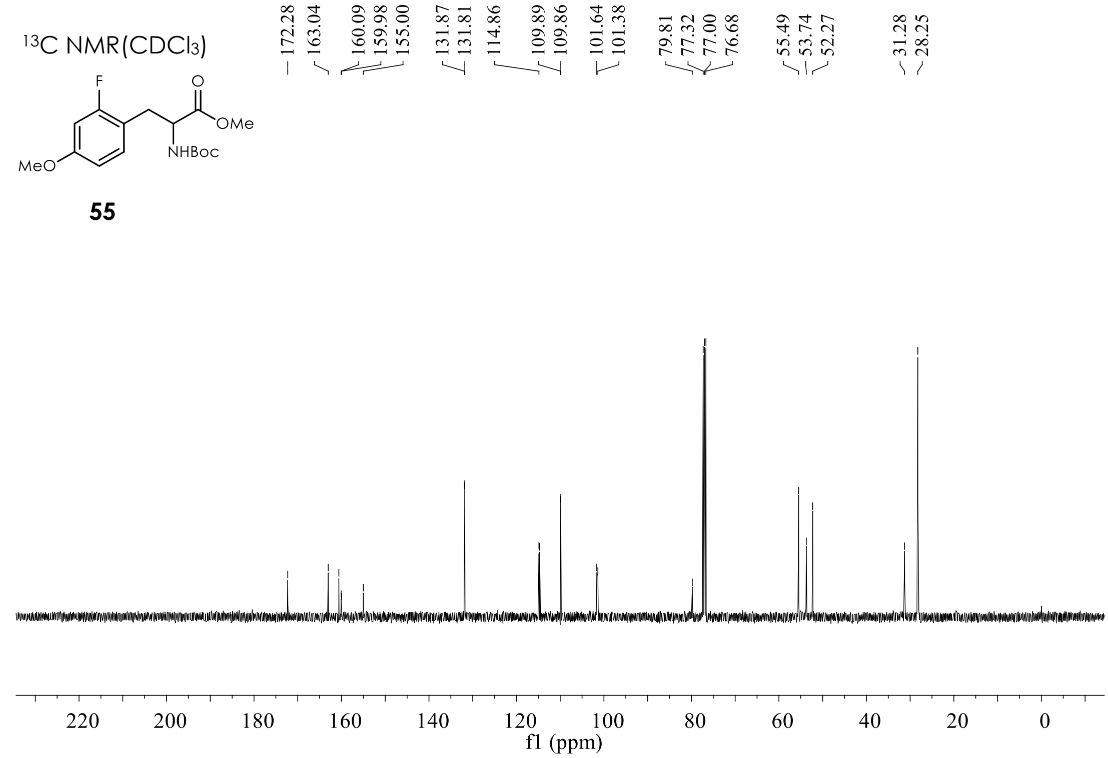
54

^{1}H NMR($CDCl_3$)

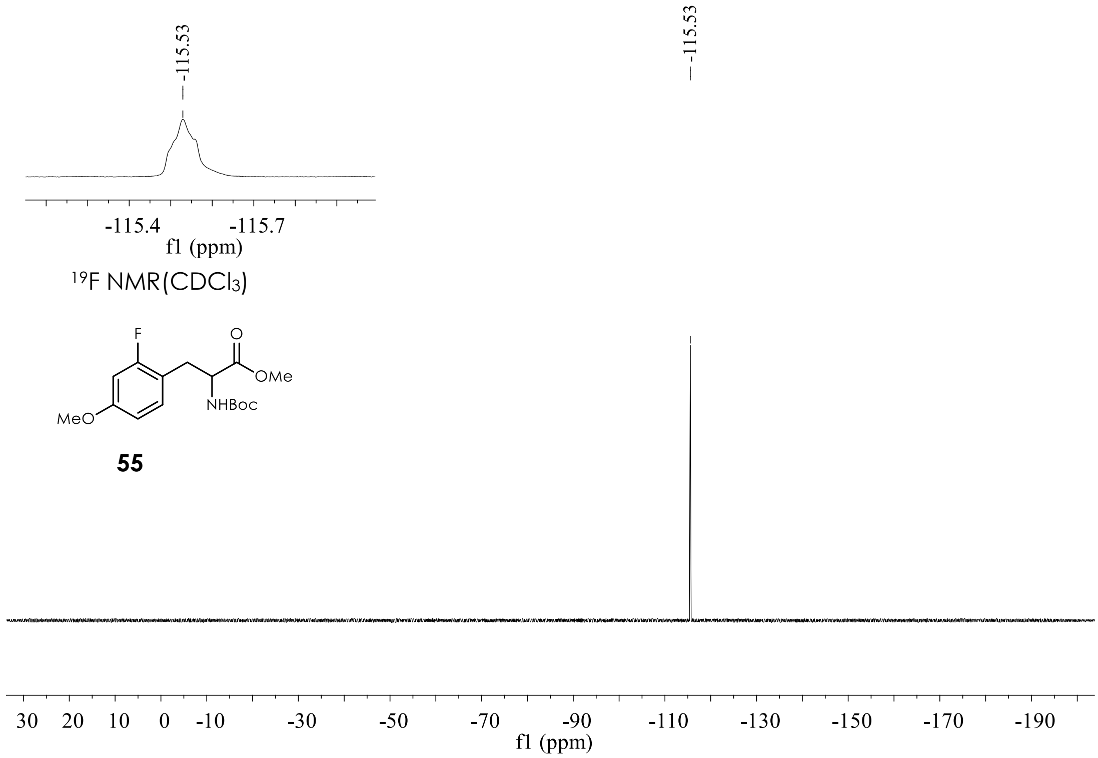


55

^{13}C NMR($CDCl_3$)



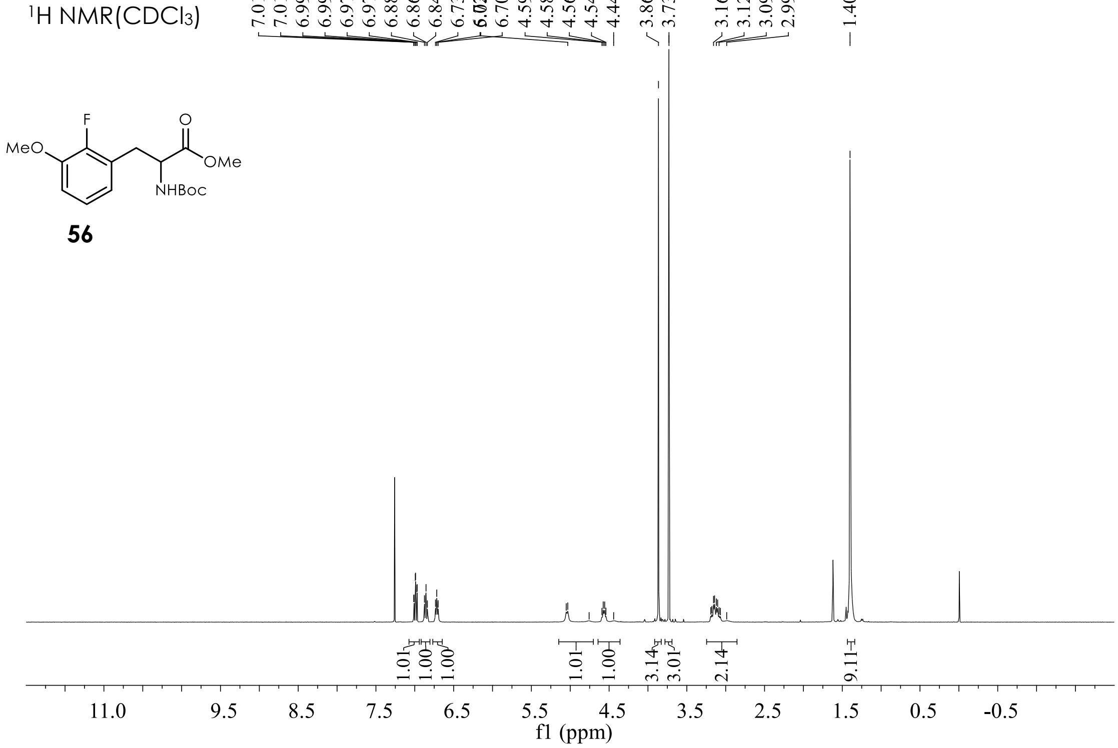
55



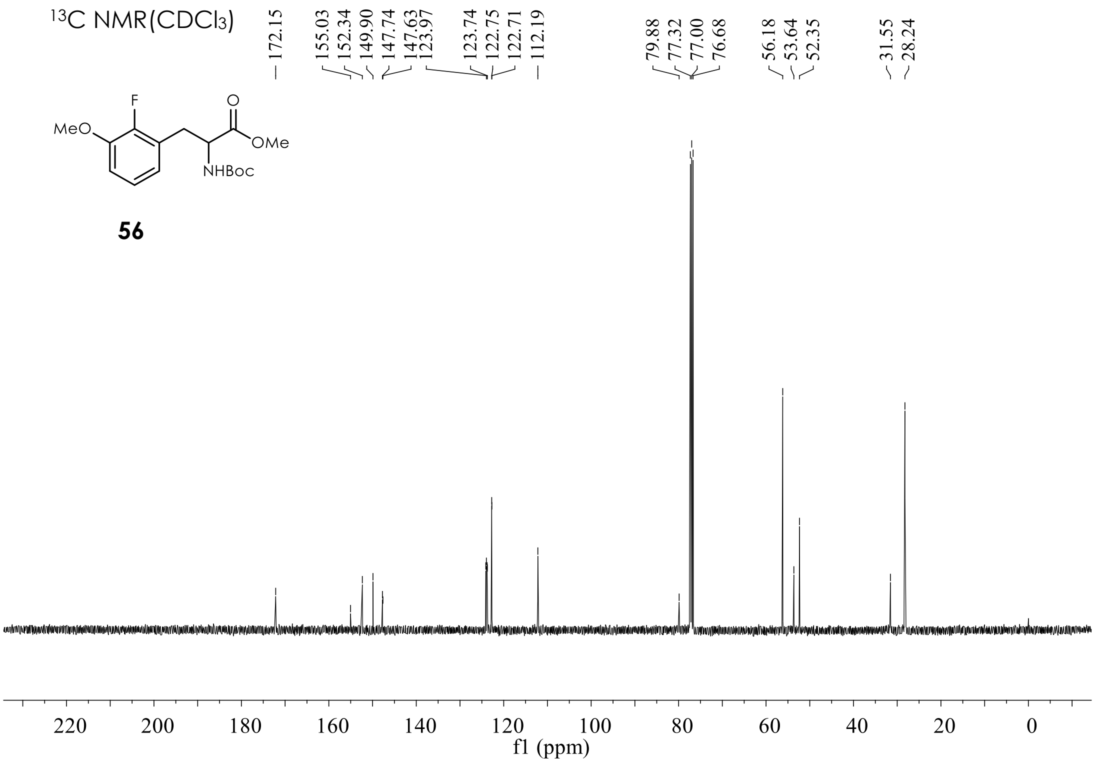
^{19}F NMR($CDCl_3$)

55

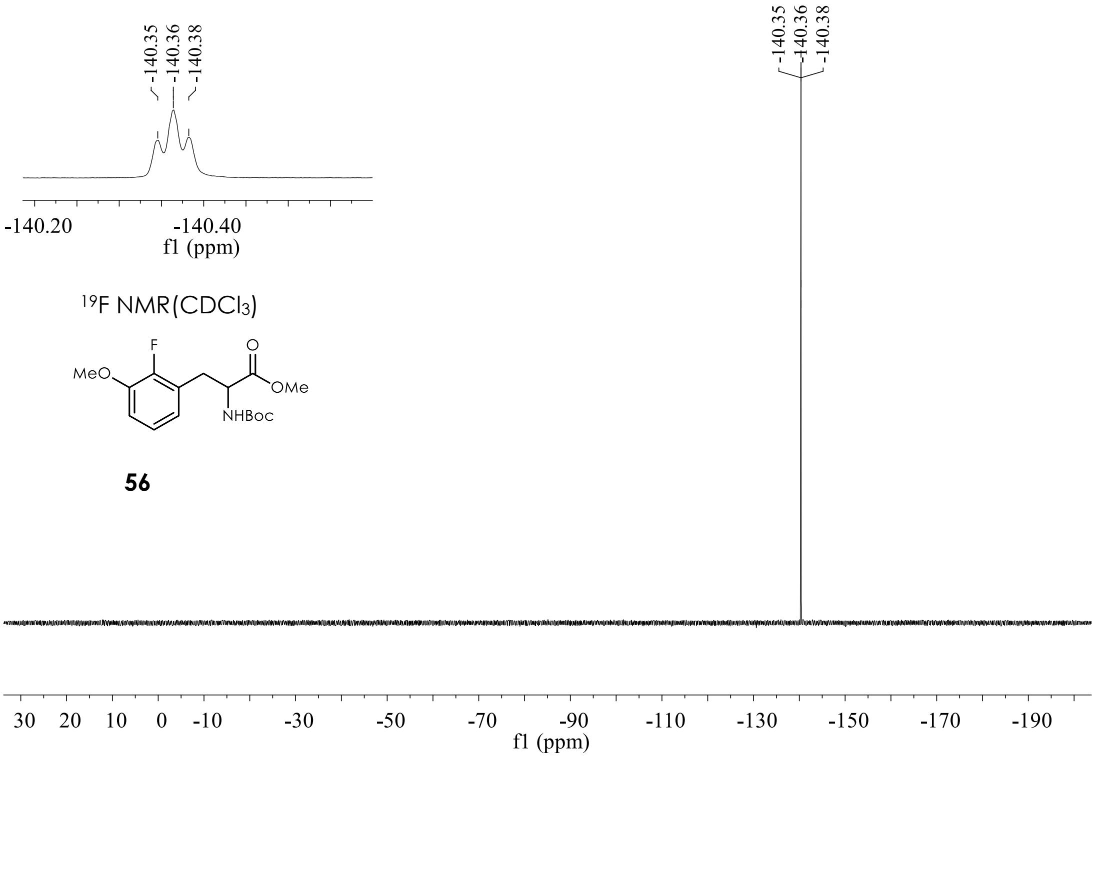
^{1}H NMR($CDCl_3$)



56

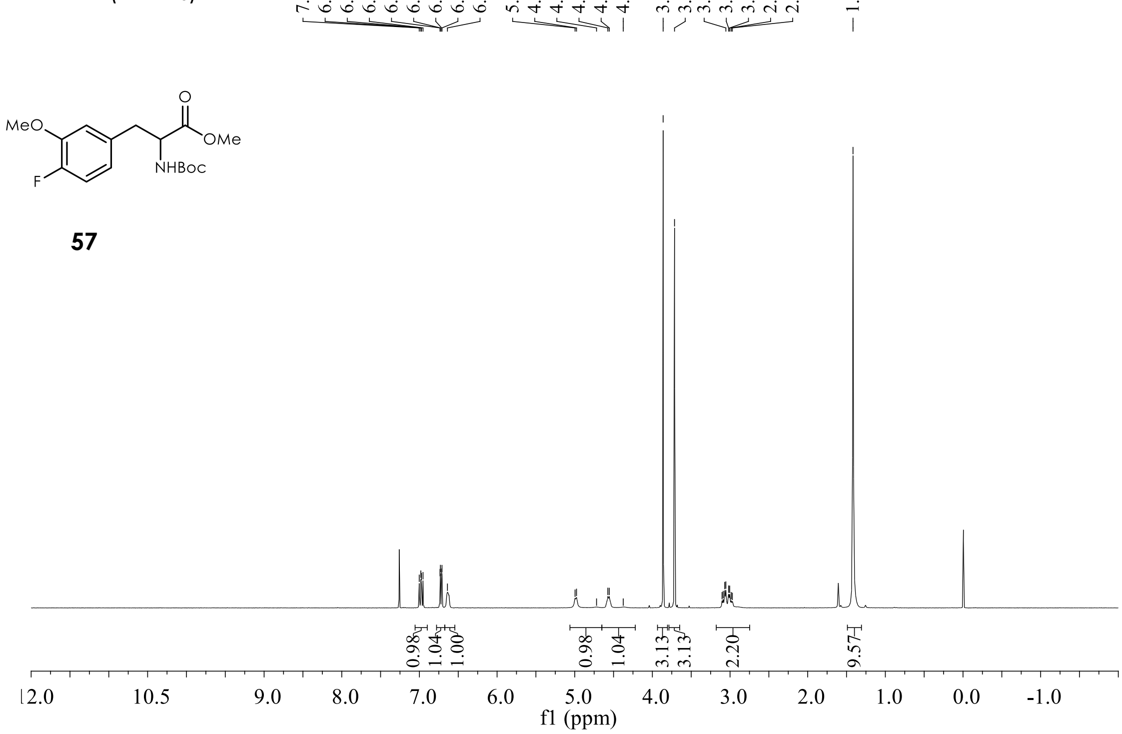

13C NMR(CDCl3)
172.15
155.03
152.34
149.90
147.74
147.63
123.97
123.74
122.75
122.71
112.19
79.88
77.32
77.00
76.68
56.18
53.64
52.35
31.55
28.24
MeO
F
O
OMe
NHBoc
220 200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)

56

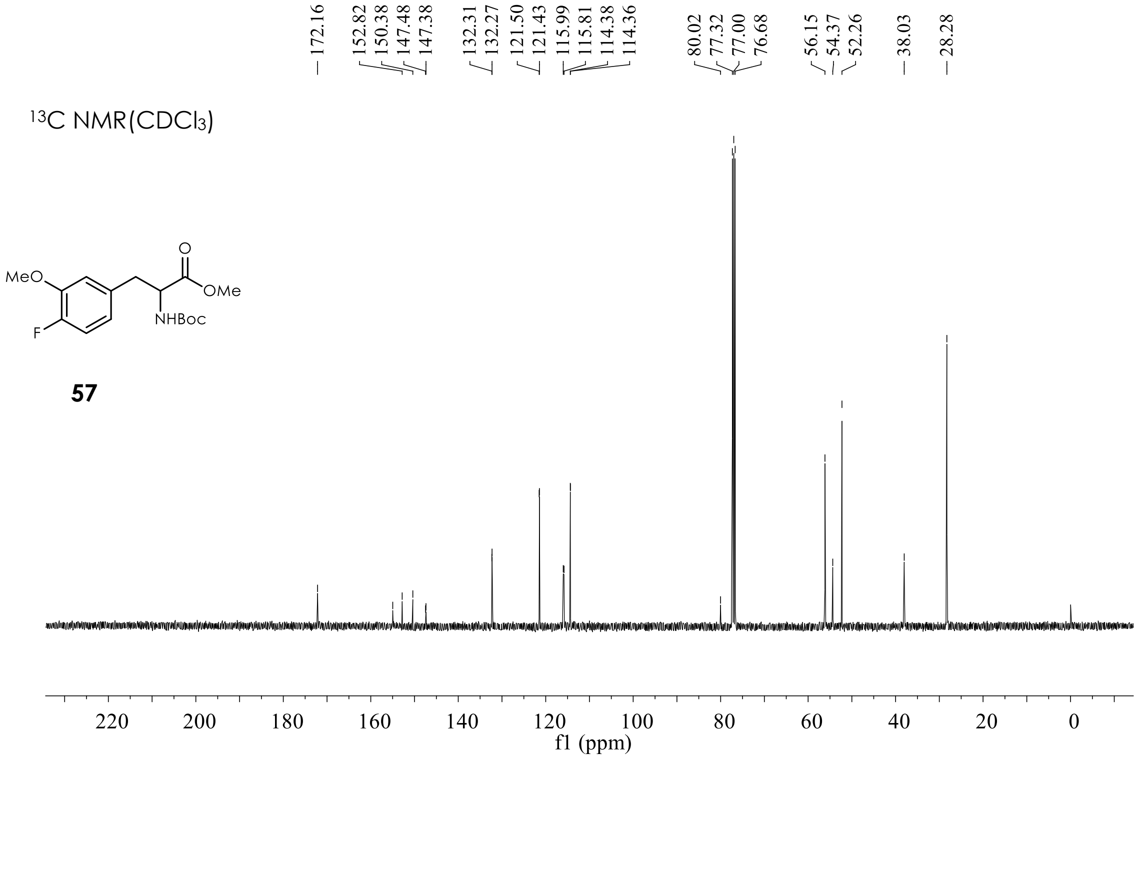

-140.35
-140.36
-140.38
-140.20
-140.40
f1 (ppm)
19F NMR(CDCl3)
MeO
F
O
OMe
NHBoc
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)

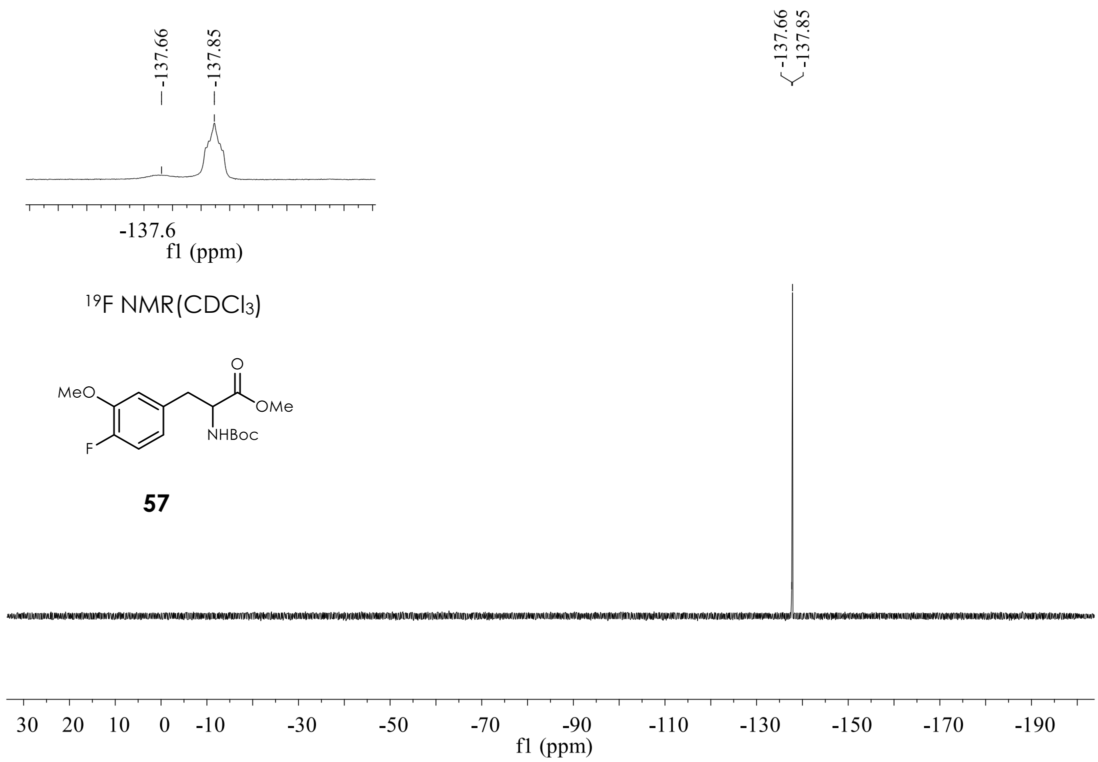
56

^{1}H NMR($CDCl_3$)

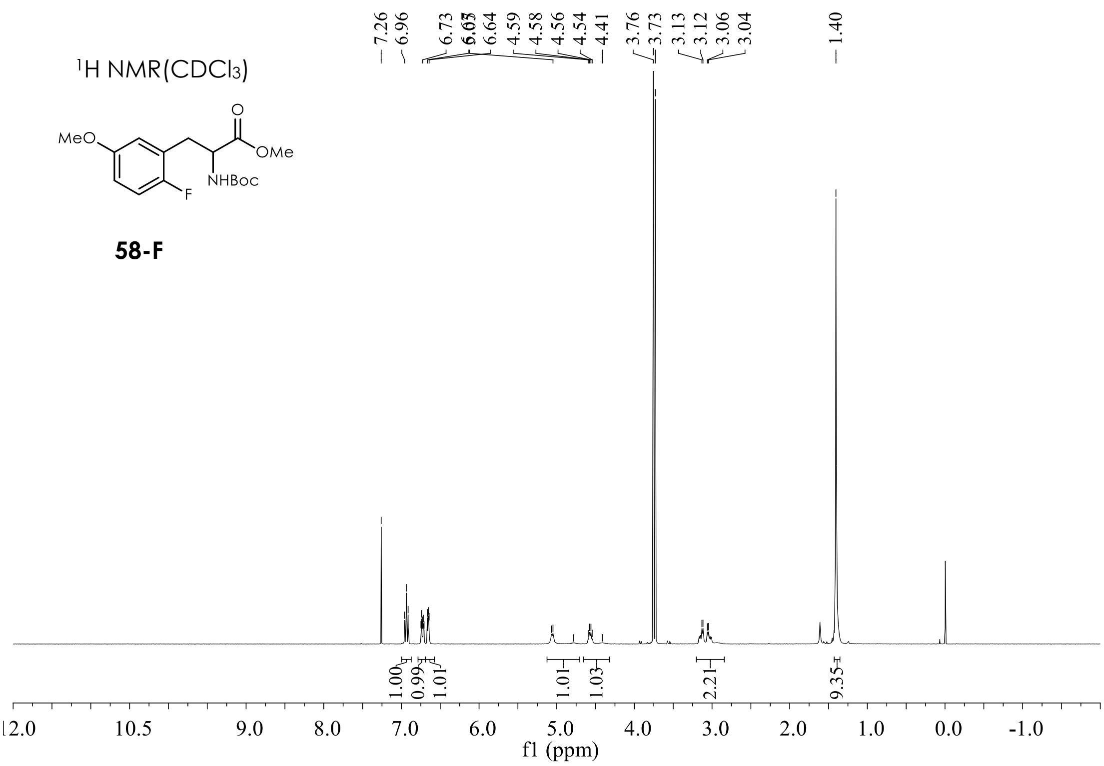


^{13}C NMR($CDCl_3$)

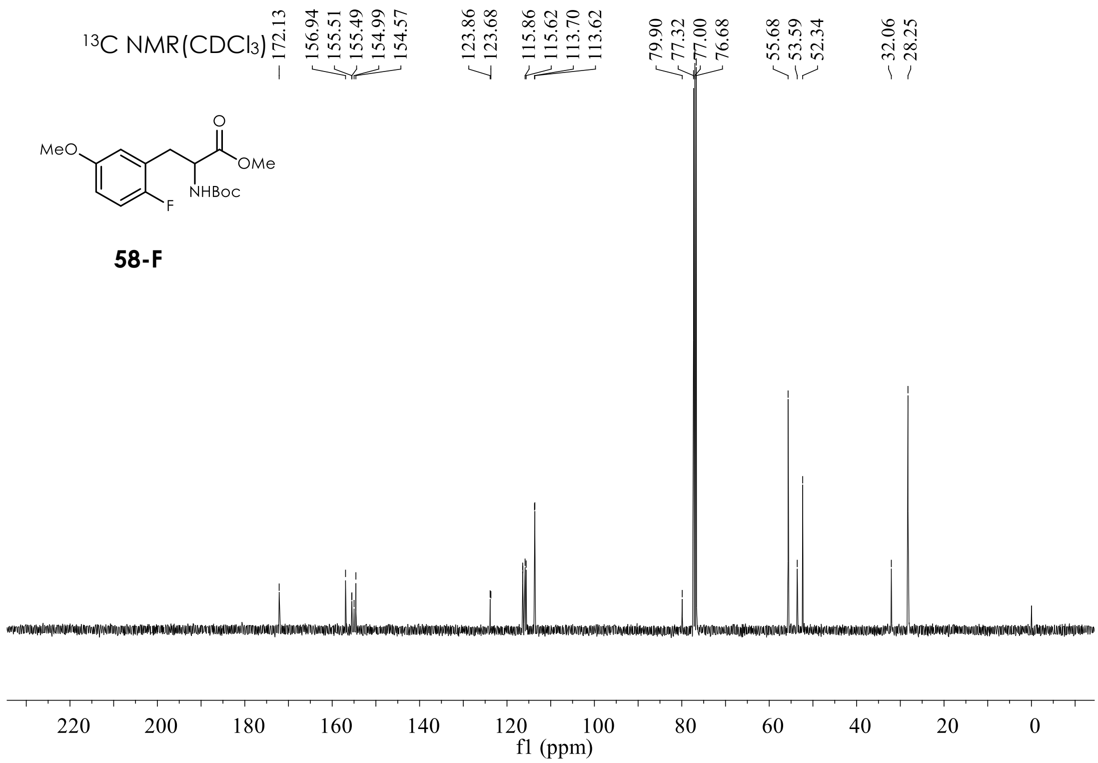


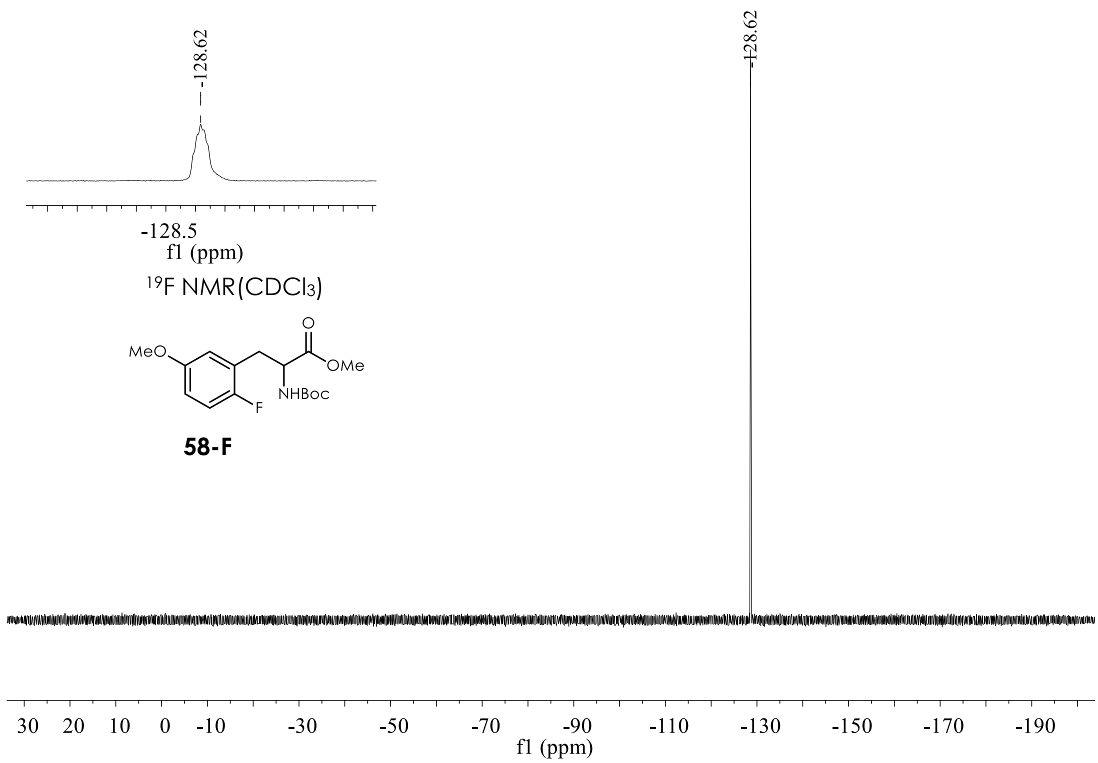

-137.66
-137.85
-137.6
f1 (ppm)
19F NMR(CDCl3)
MeO
O
OMe
NHBoc
F
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)

57

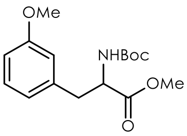

7.26
6.96
6.73
6.67
6.64
4.59
4.58
4.56
4.54
4.41
3.76
3.73
3.13
3.12
3.06
3.04
1.40
1H NMR(CDCl3)
MeO
O
OMe
NHBoc
F
1.00
0.99
1.01
1.01
1.03
2.21
9.35
12.0 10.5 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0
f1 (ppm)

58-F

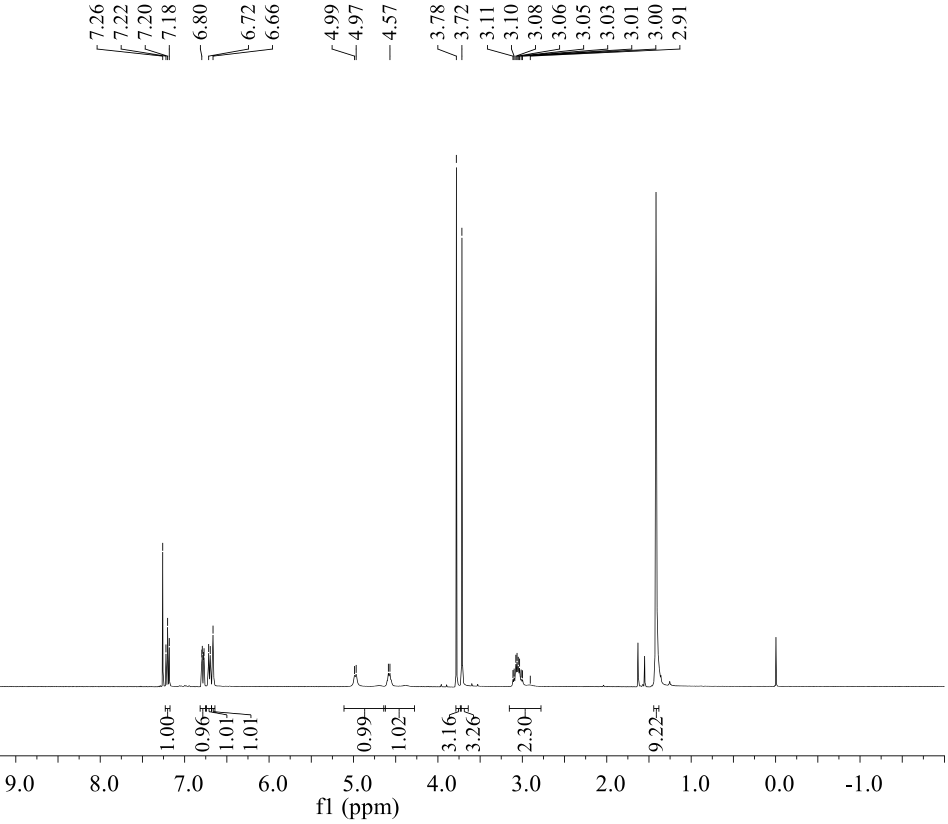

^{13}C NMR($CDCl_3$)
172.13
156.94
155.51
155.49
154.99
154.57
123.86
123.68
115.86
115.62
113.70
113.62
79.90
77.32
77.00
76.68
55.68
53.59
52.34
32.06
28.25
MeO
O
OMe
NHBoc
F
58-F
220 200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)


-128.62
-128.5
f1 (ppm)
^{19}F NMR($CDCl_3$)
MeO
O
OMe
NHBoc
F
58-F
-128.62
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)

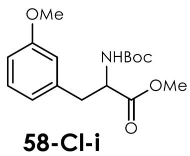
^{1}H NMR($CDCl_3$)



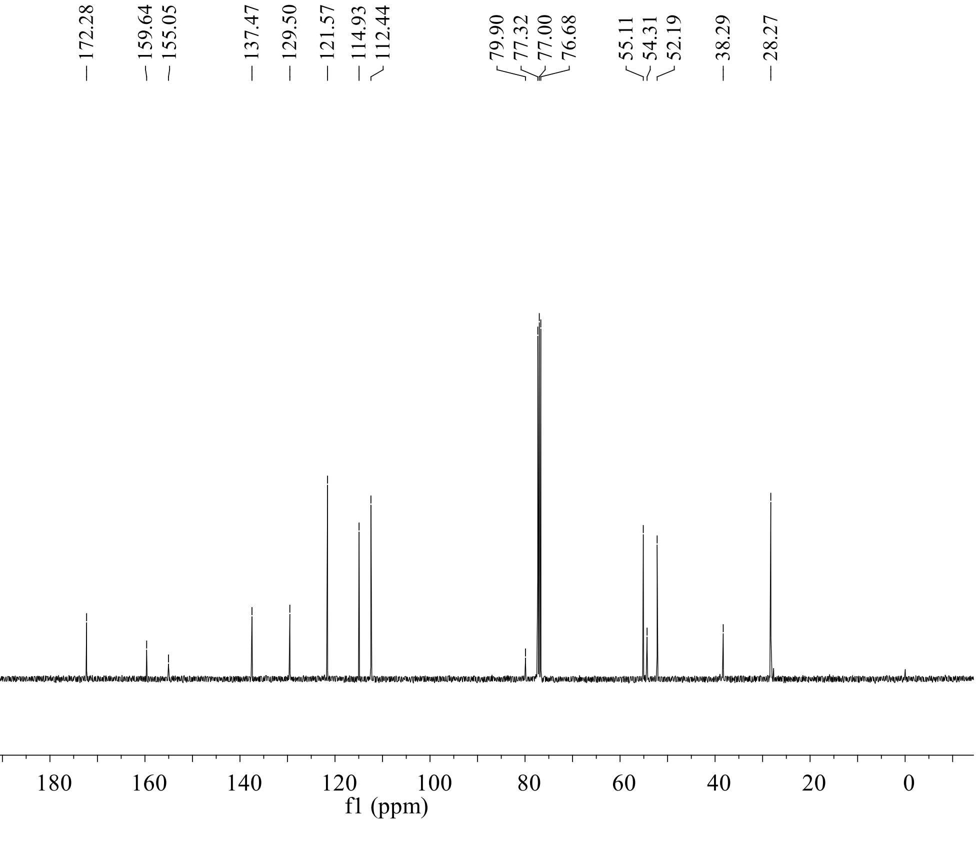
58-Cl-i



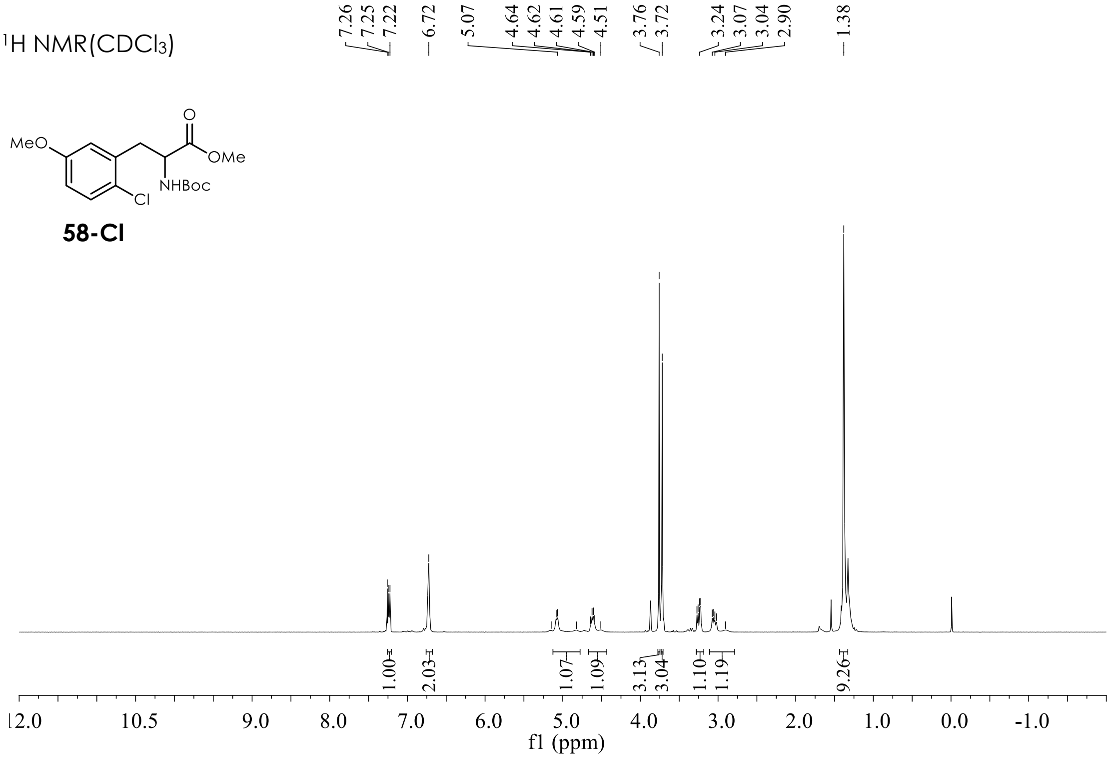
^{13}C NMR($CDCl_3$)



58-Cl-i

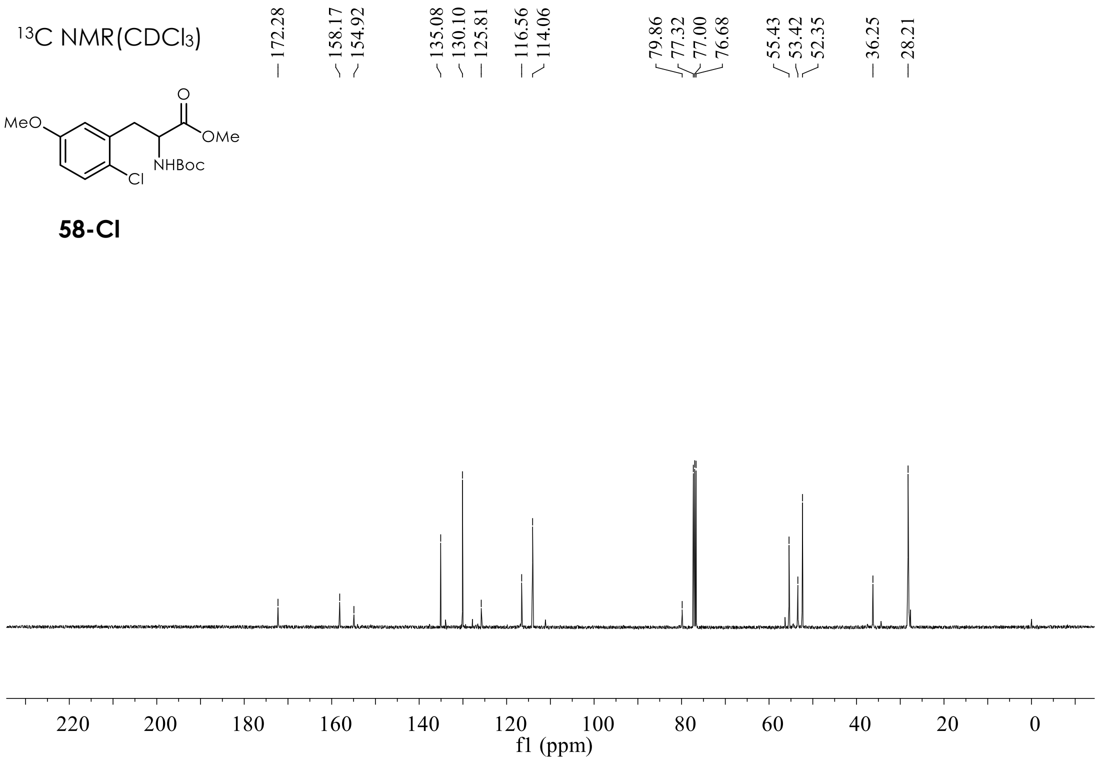


^{1}H NMR($CDCl_3$)



58-Cl

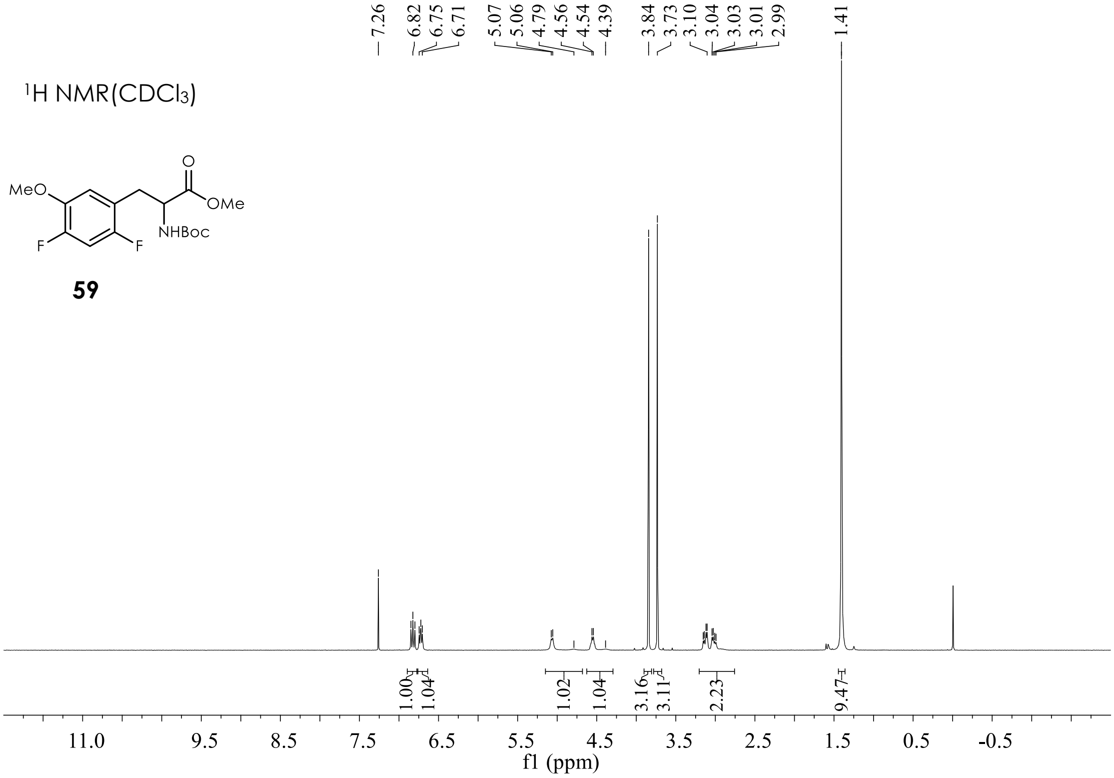
^{13}C NMR($CDCl_3$)



58-Cl

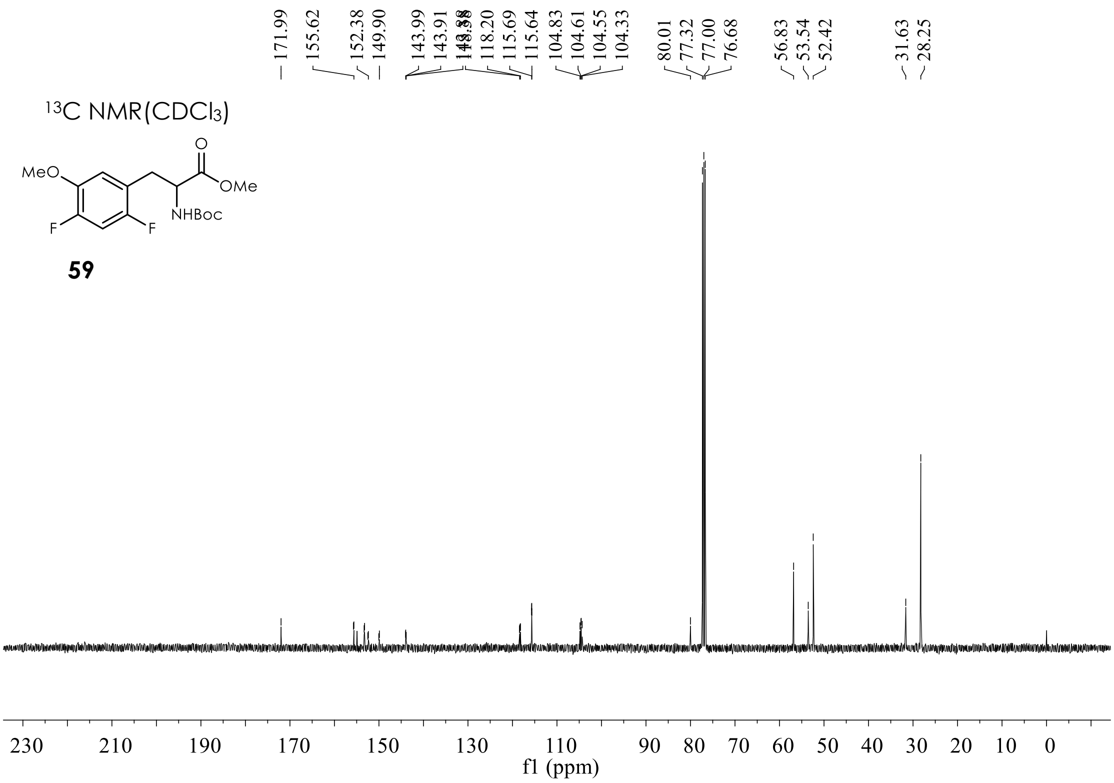
^1H NMR($CDCl_3$)

59

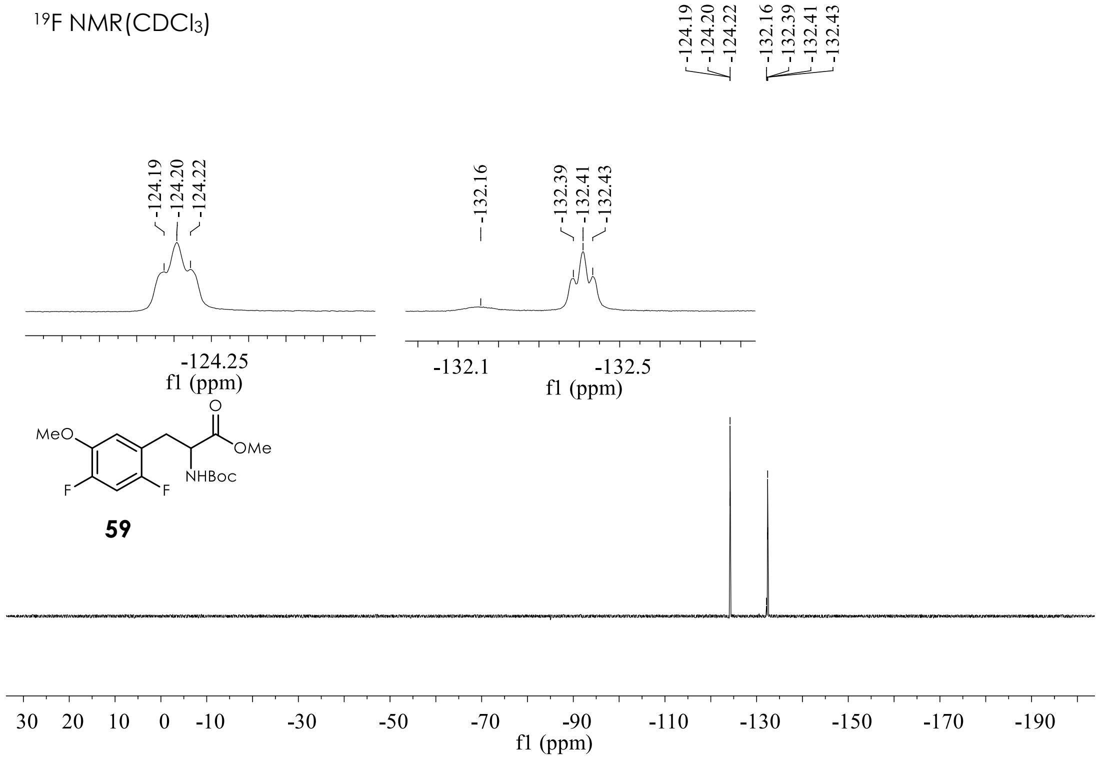


^{13}C NMR($CDCl_3$)

59

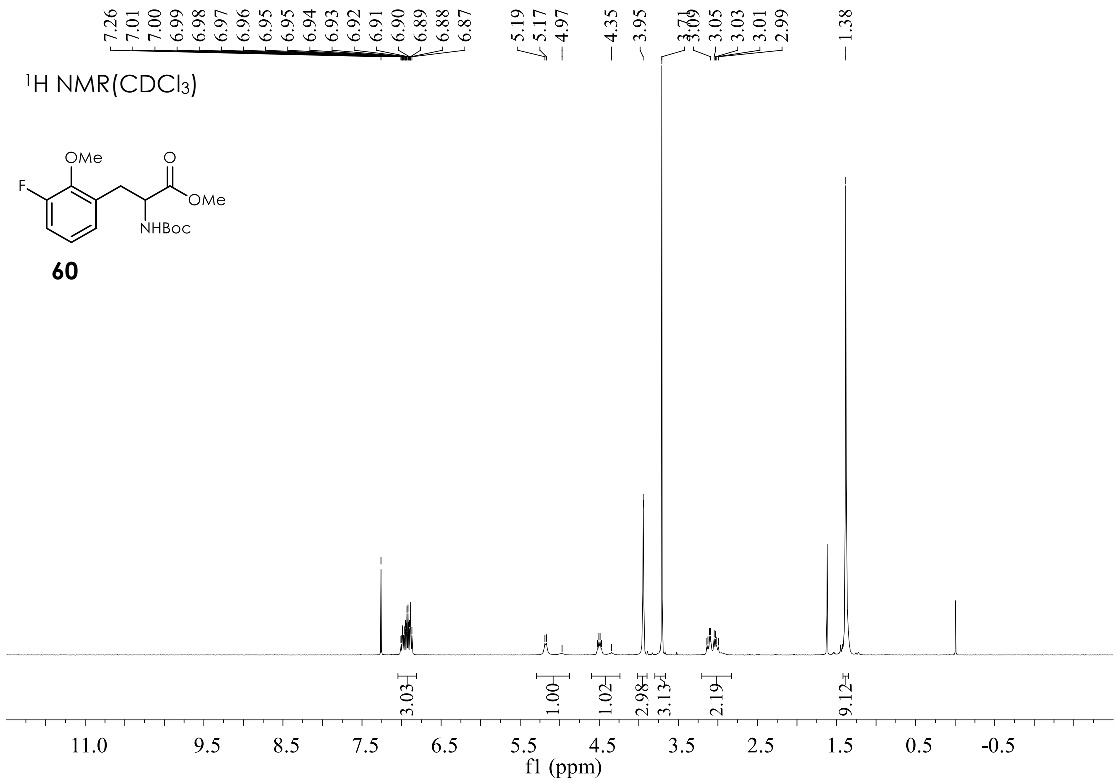


^{19}F NMR(CDCl$_3$)

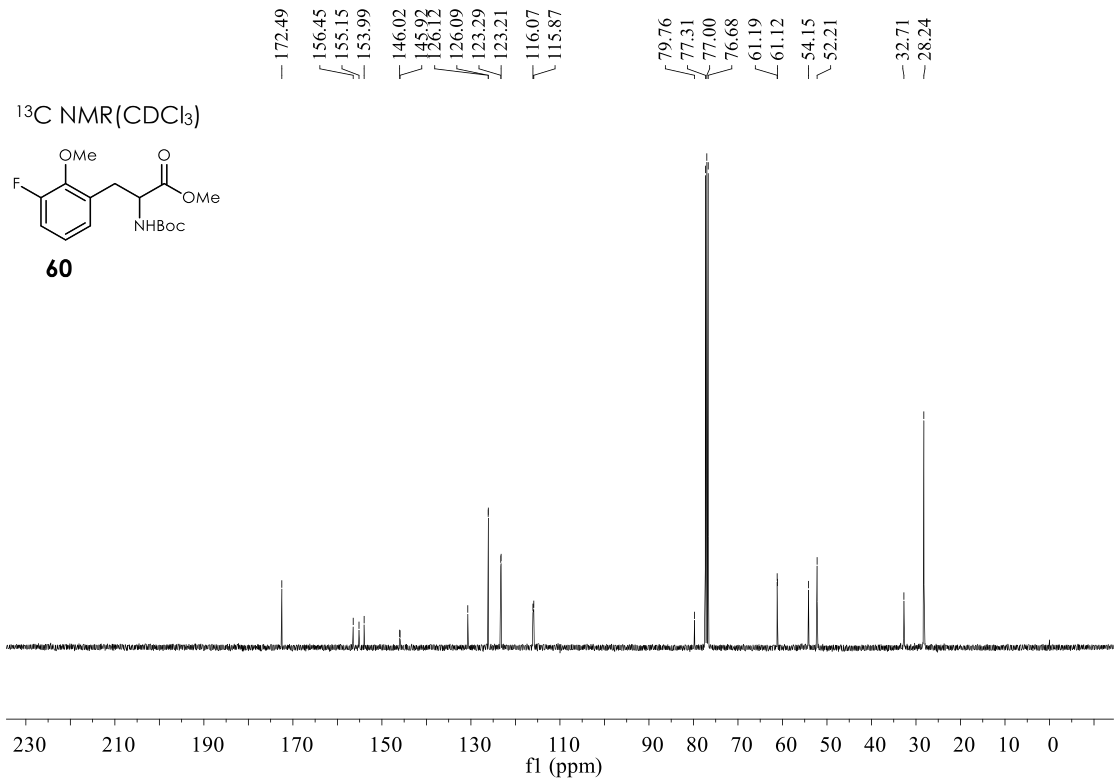


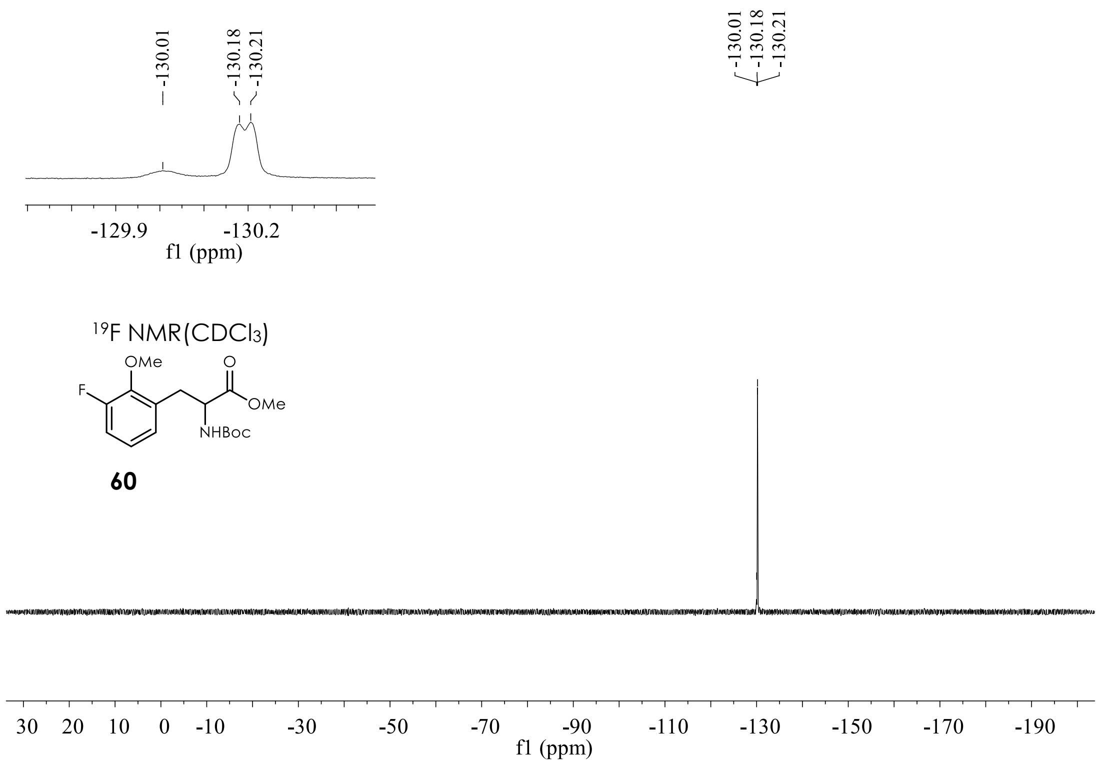
59

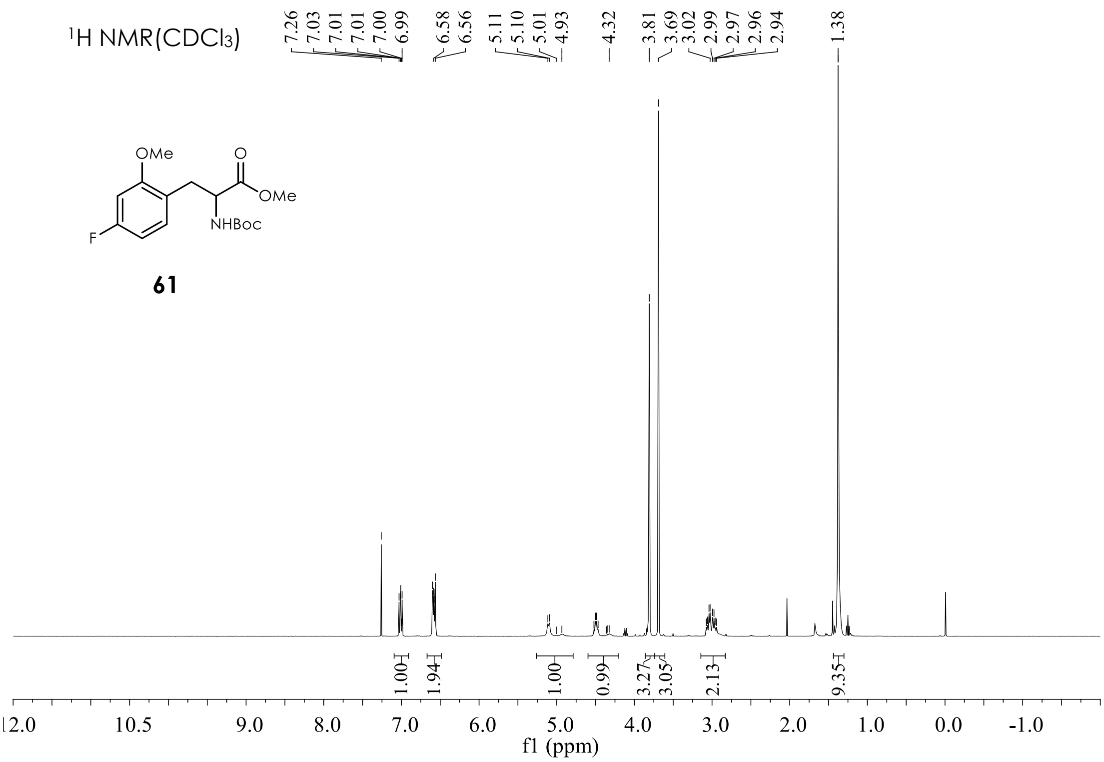
^{1}H NMR(CDCl$_3$)



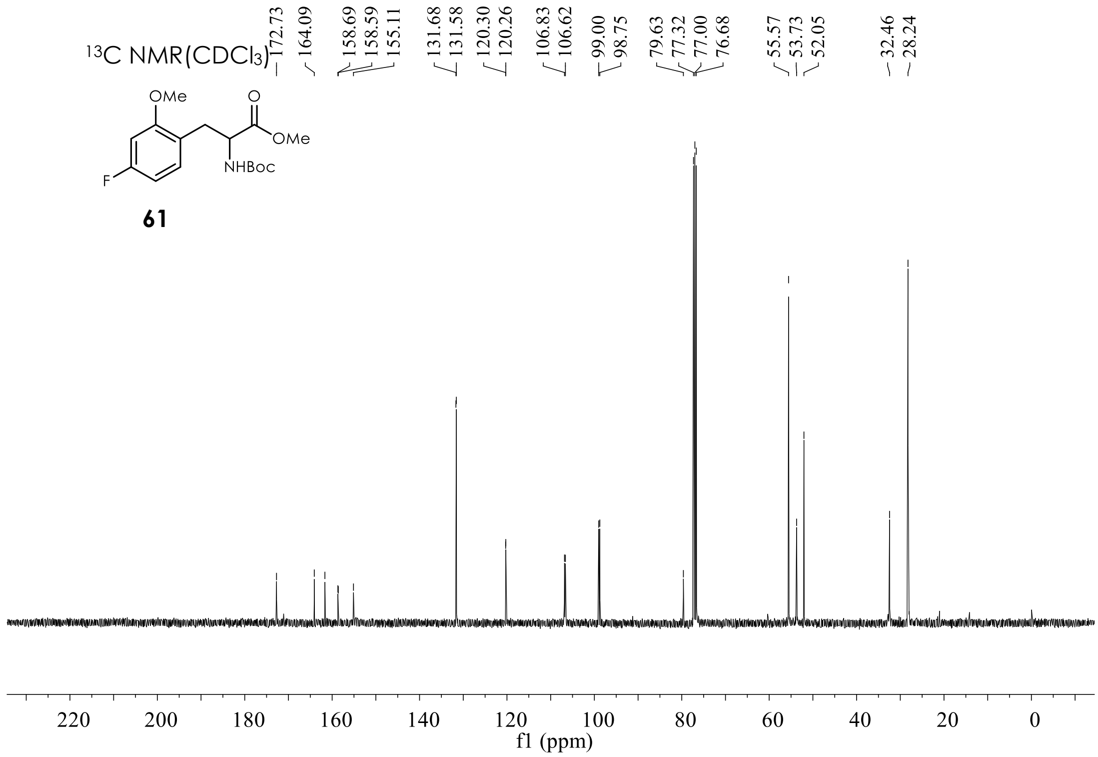
60


172.49
156.45
155.15
153.99
146.02
145.92
126.12
126.09
123.29
123.21
116.07
115.87
79.76
77.31
77.00
76.68
61.19
61.12
54.15
52.21
32.71
28.24
^{13}C NMR(CDCl$_3$)
OMe
F
O
OMe
NHBoc
60
230 210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

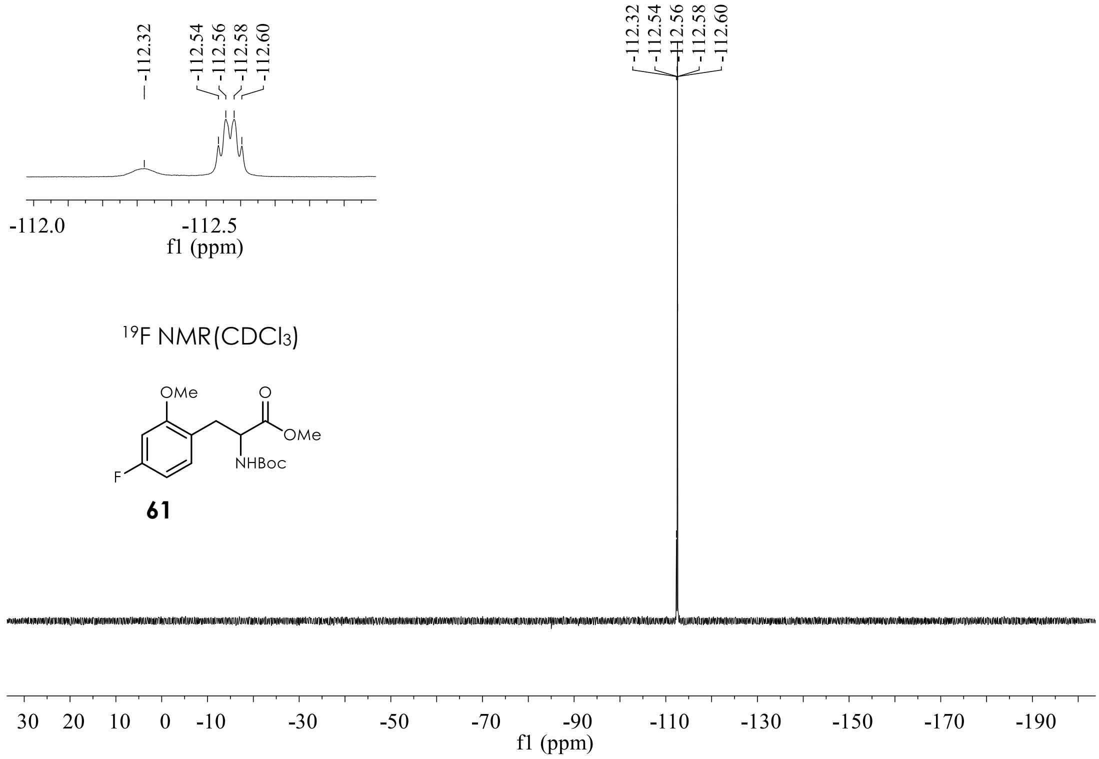

-130.01
-130.18
-130.21
-129.9
-130.2
f1 (ppm)
^{19}F NMR(CDCl$_3$)
OMe
F
O
OMe
NHBoc
60
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)



^{1}H NMR(CDCl$_3$)
7.26 7.03 7.01 7.01 7.00 6.99 6.58 6.56 5.11 5.10 5.01 4.93 4.32 3.81 3.69 3.02 2.99 2.97 2.96 2.94 1.38
OMe
O
OMe
NHBoc
F
61
1.00 1.94 1.00 0.99 3.27 3.05 2.13 9.35
12.0 10.5 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0
f1 (ppm)



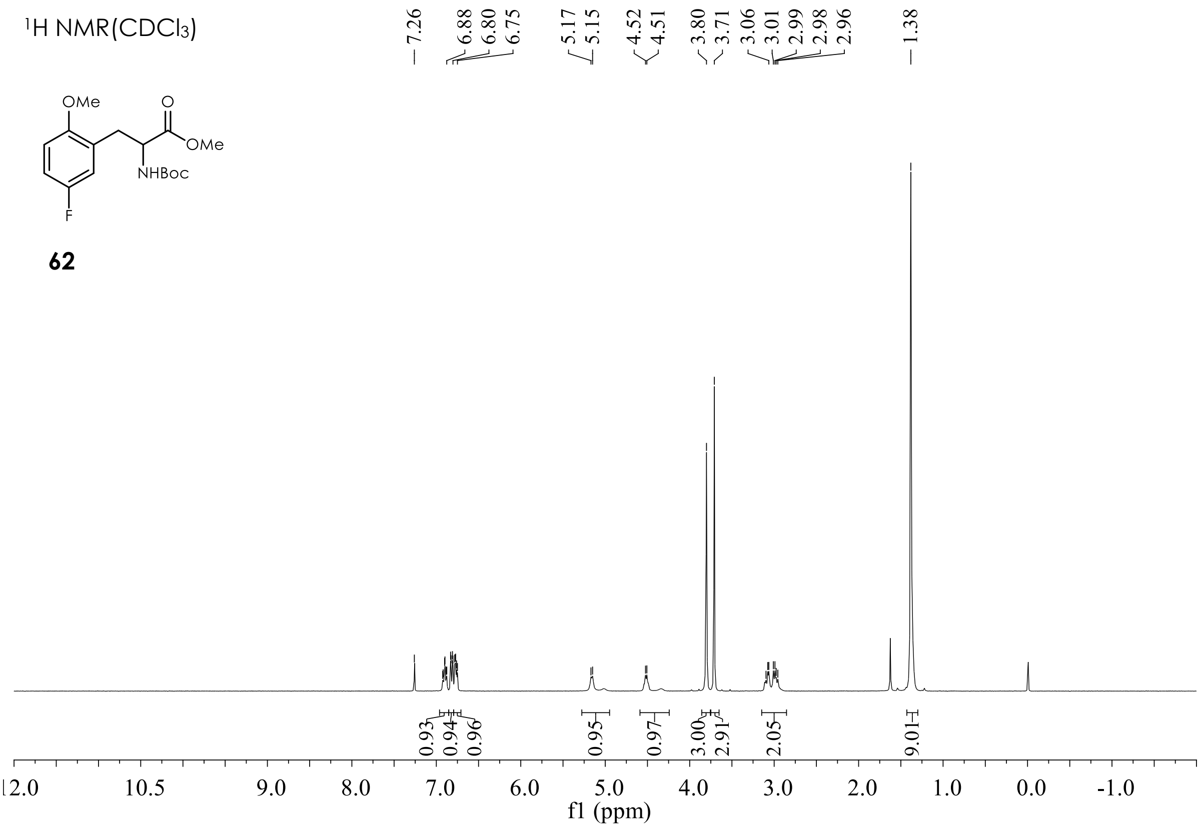
^{13}C NMR(CDCl$_3$)
172.73 164.09 158.69 158.59 155.11 131.68 131.58 120.30 120.26 106.83 106.62 99.00 98.75 79.63 77.32 77.00 76.68 55.57 53.73 52.05 32.46 28.24
OMe
O
OMe
NHBoc
F
61
220 200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)



^{19}F NMR(CDCl$_3$)

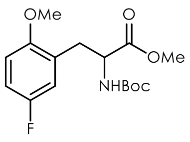
61

^{1}H NMR(CDCl$_3$)

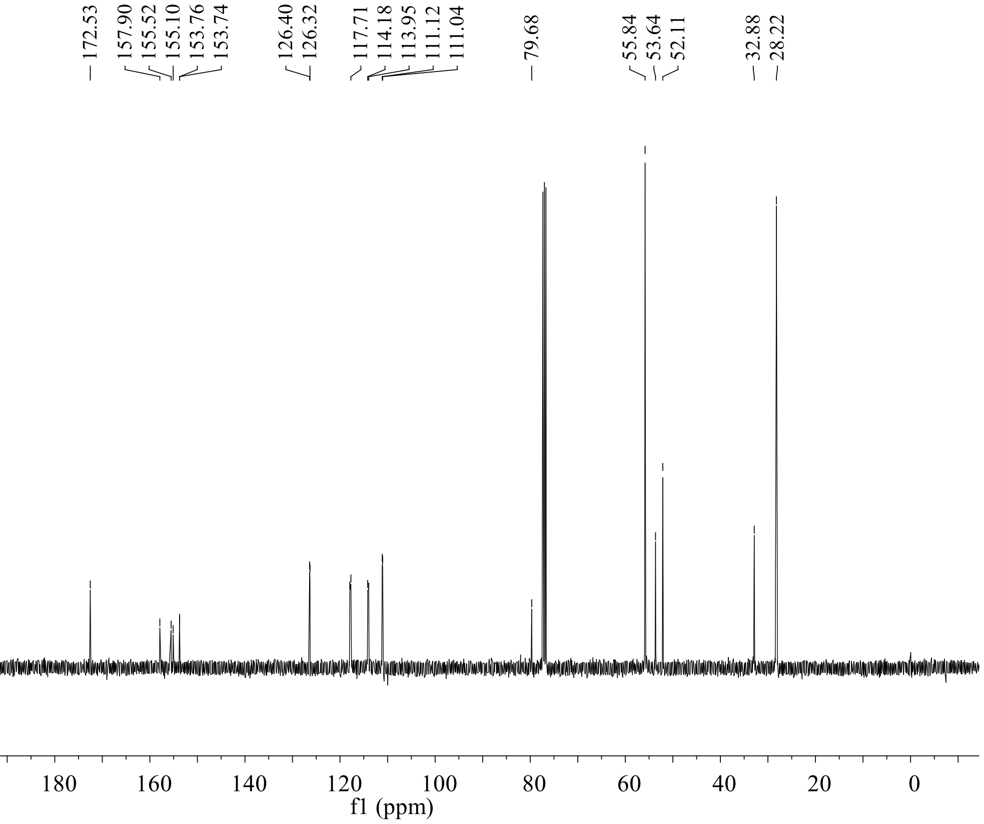


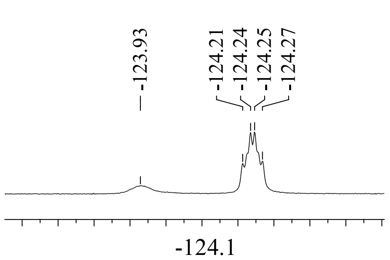
62

13C NMR(CDCl3)

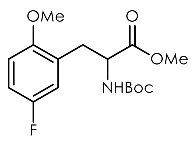


62

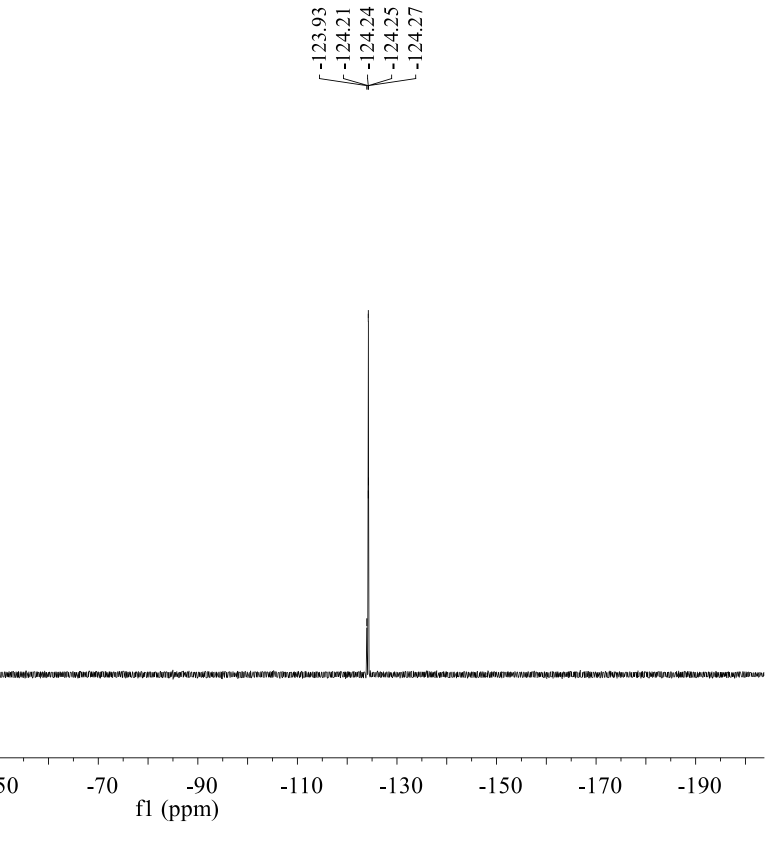




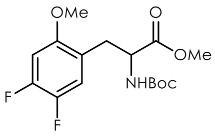
19F NMR(CDCl3)



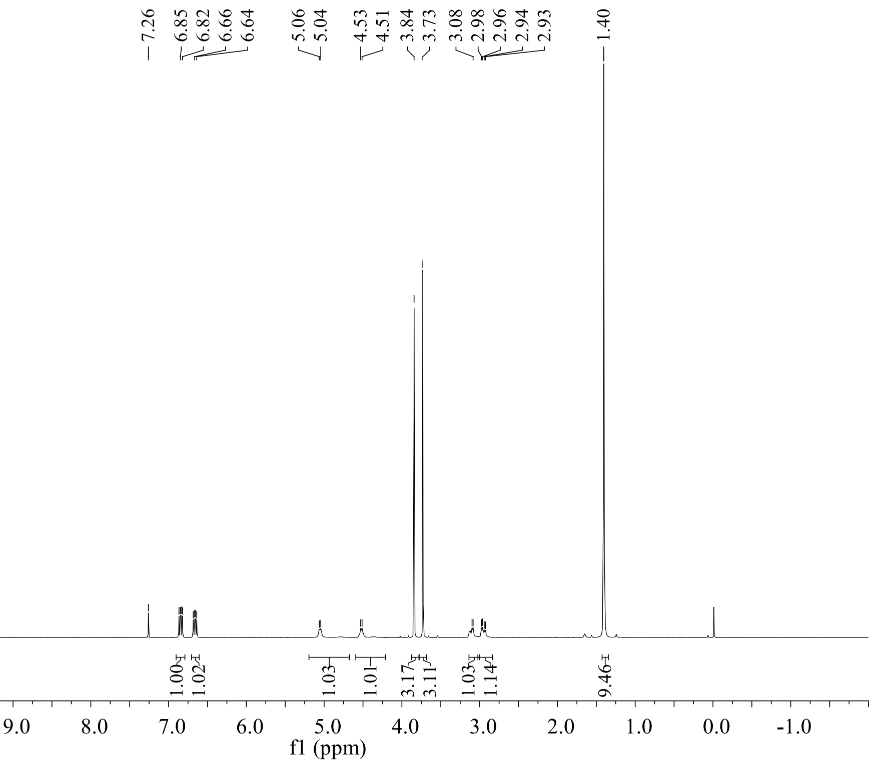
62



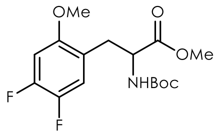
^{1}H NMR(CDCl$_3$)



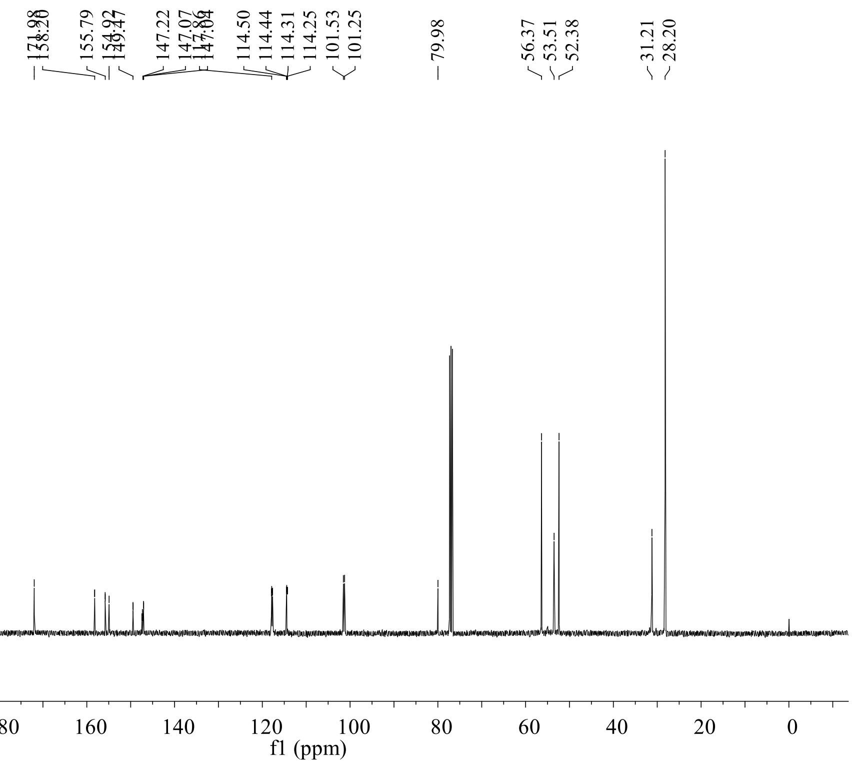
63

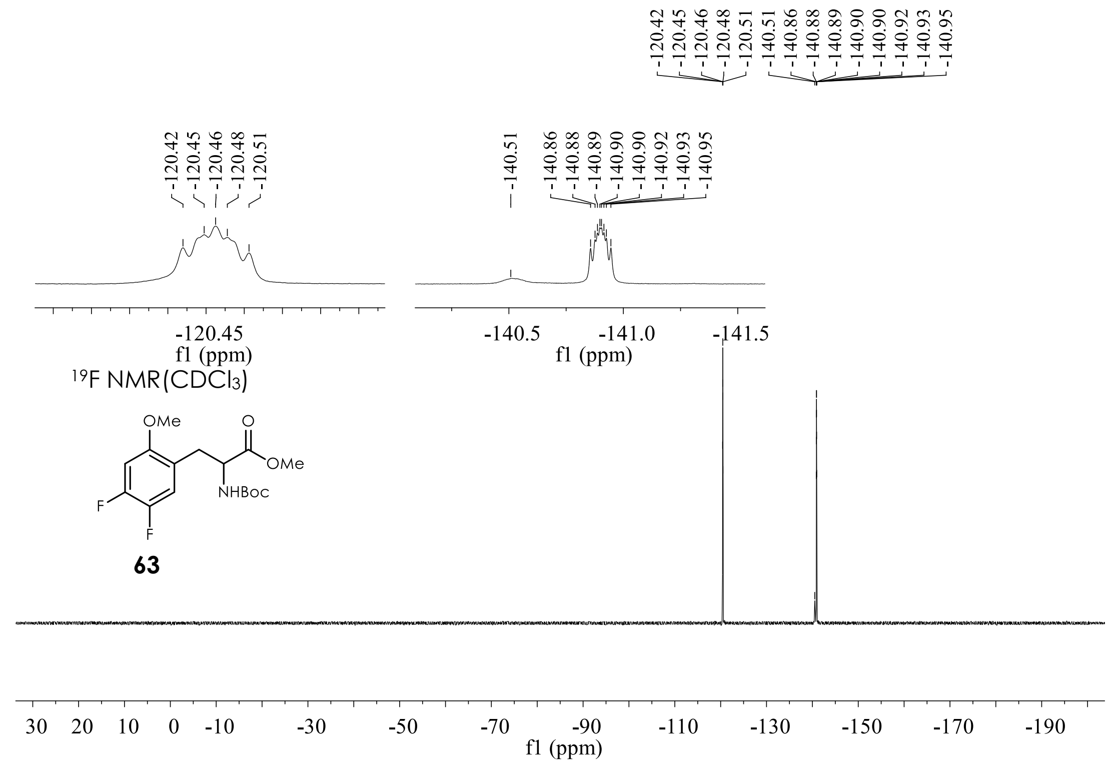


^{13}C NMR(CDCl$_3$)

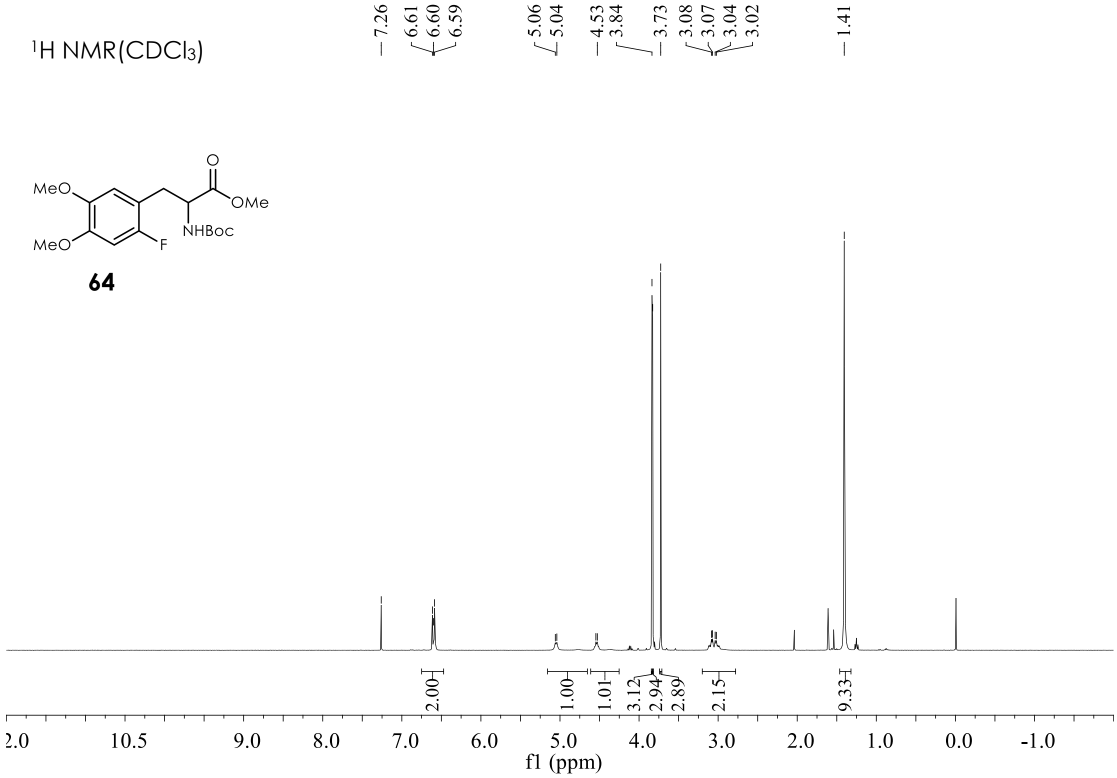


63



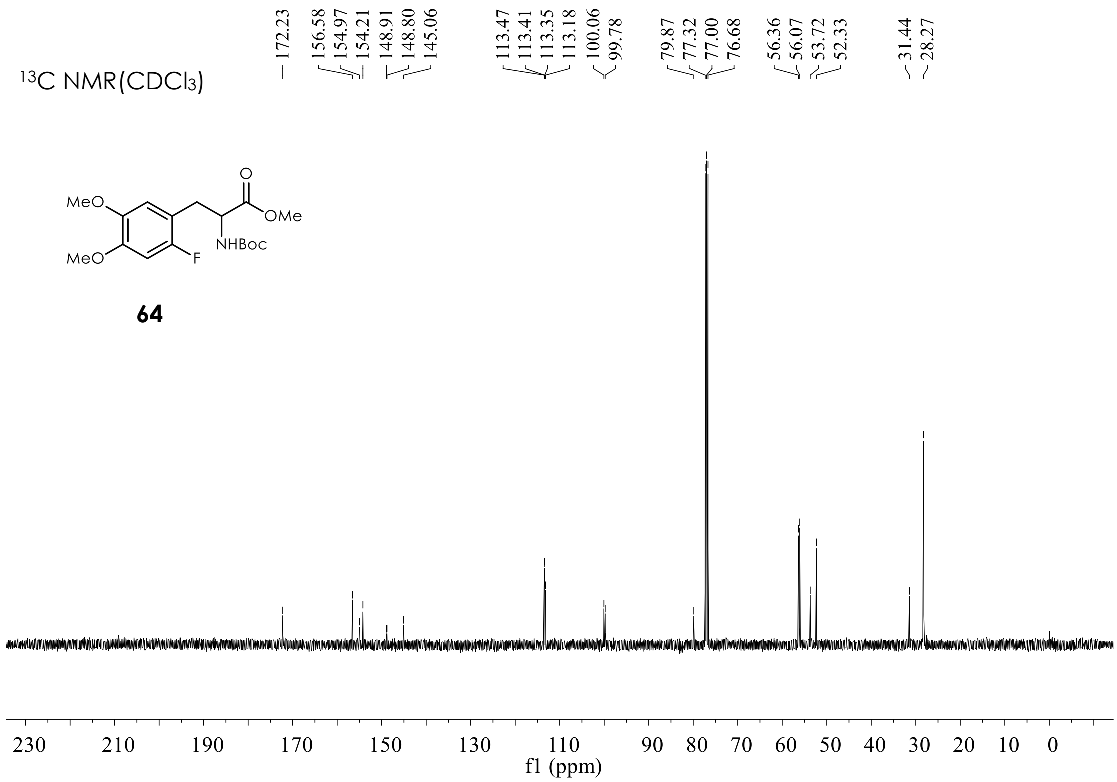

-120.42
-120.45
-120.46
-120.48
-120.51
-140.51
-140.86
-140.88
-140.89
-140.90
-140.90
-140.92
-140.93
-140.95
-120.45
f1 (ppm)
-140.5
-141.0
-141.5
f1 (ppm)
19F NMR(CDCl3)
OMe
O
OMe
NHBoc
F
F
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)

63

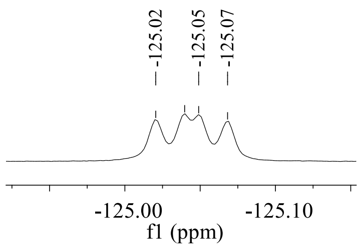

1H NMR(CDCl3)
7.26
6.61
6.60
6.59
5.06
5.04
4.53
3.84
3.73
3.08
3.07
3.04
3.02
1.41
MeO
MeO
O
OMe
NHBoc
F
2.00
1.00
1.01
3.12
2.94
2.89
2.15
9.33
2.0 10.5 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0
f1 (ppm)

64

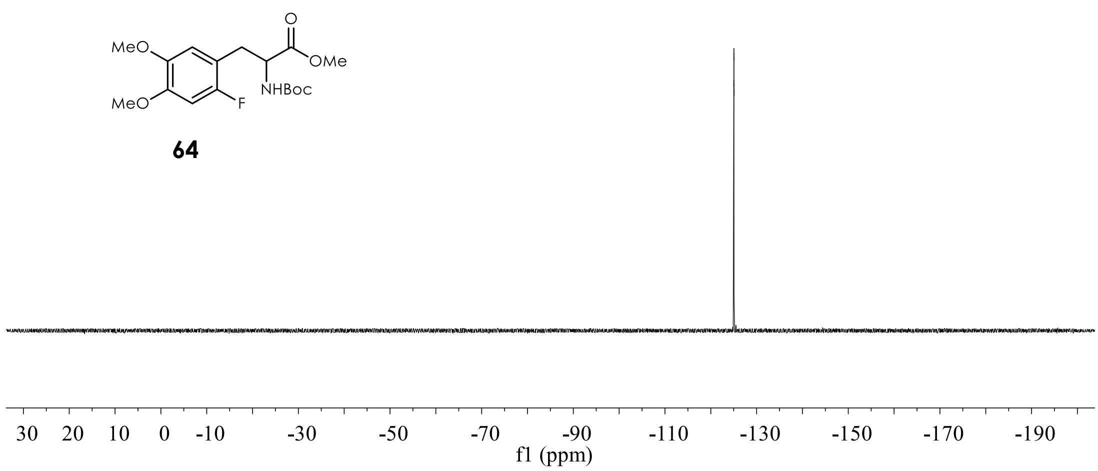
^{13}C NMR($CDCl_3$)



64

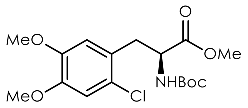


^{19}F NMR($CDCl_3$)

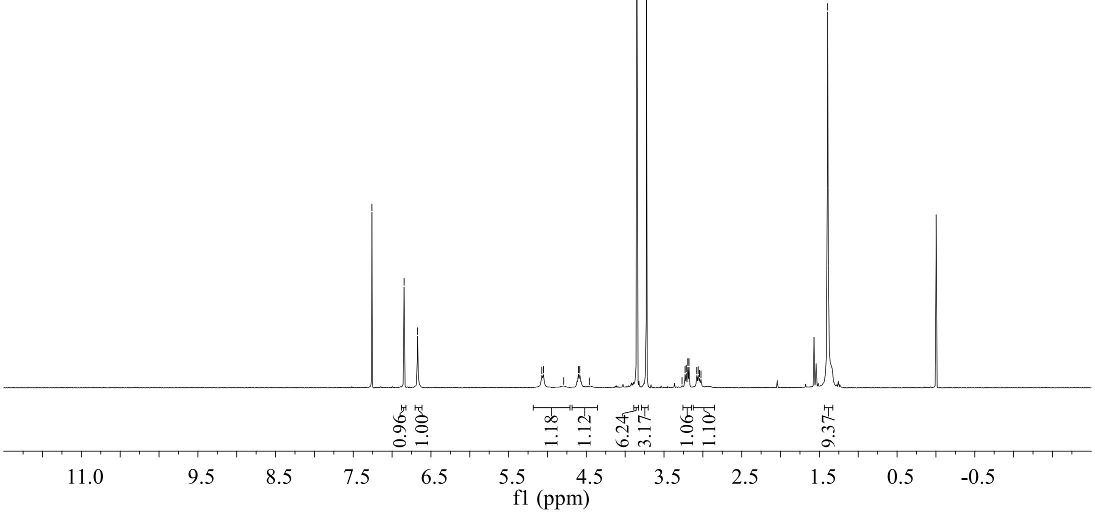


64

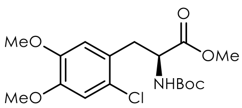
[1]H NMR($CDCl_3$)



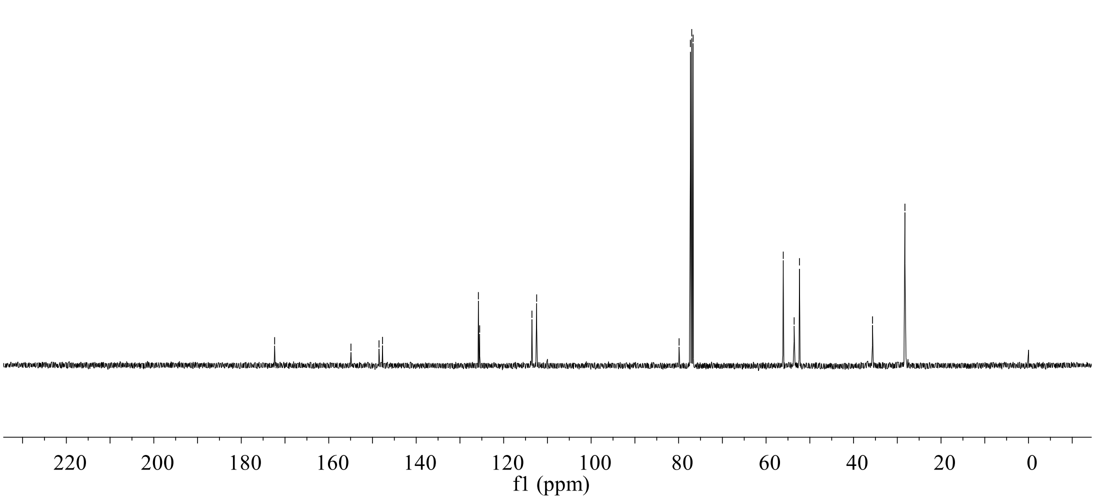
***L*-64-Cl**



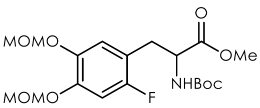
[13]C NMR($CDCl_3$)



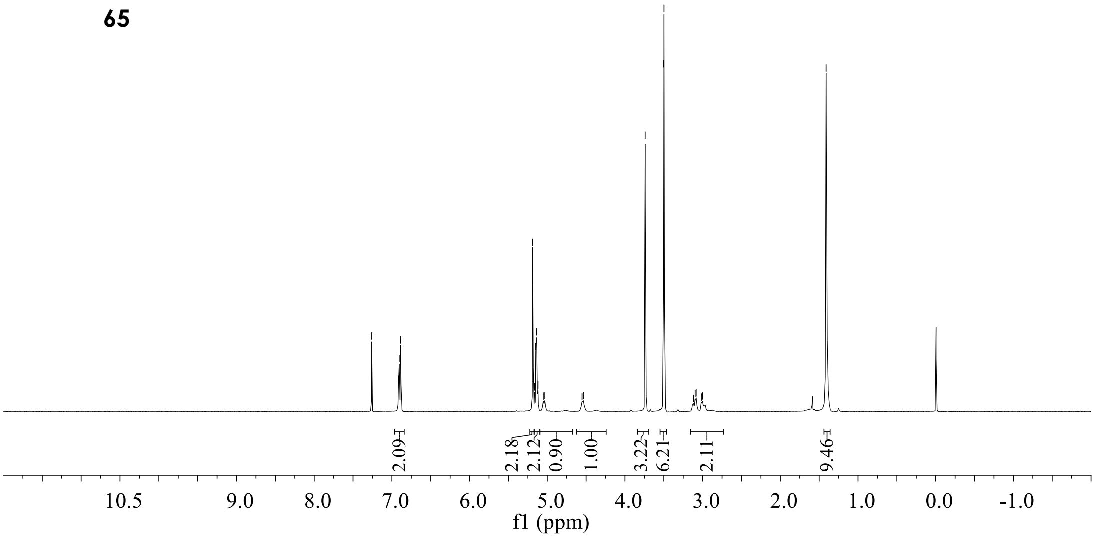
***L*-64-Cl**



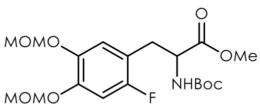
^{1}H NMR($CDCl_3$)



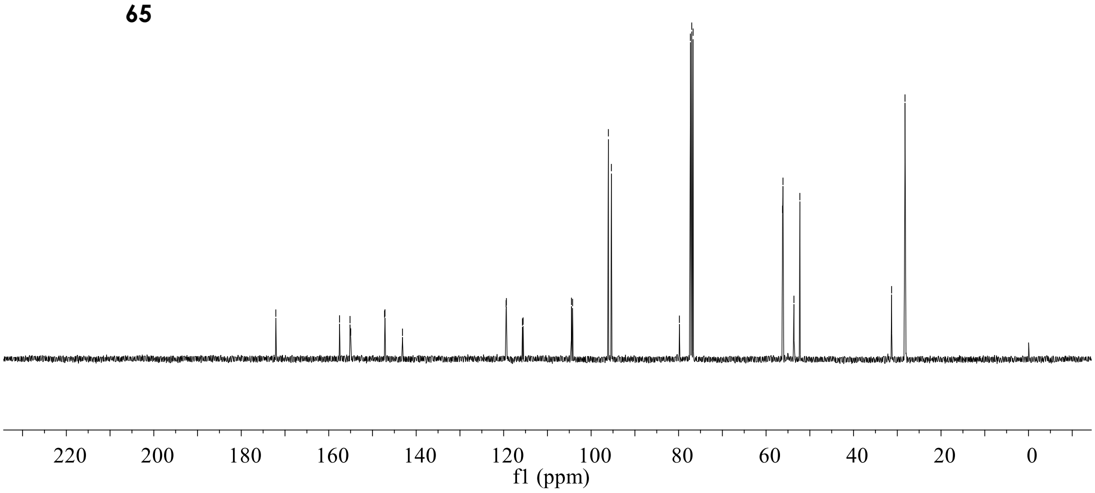
65

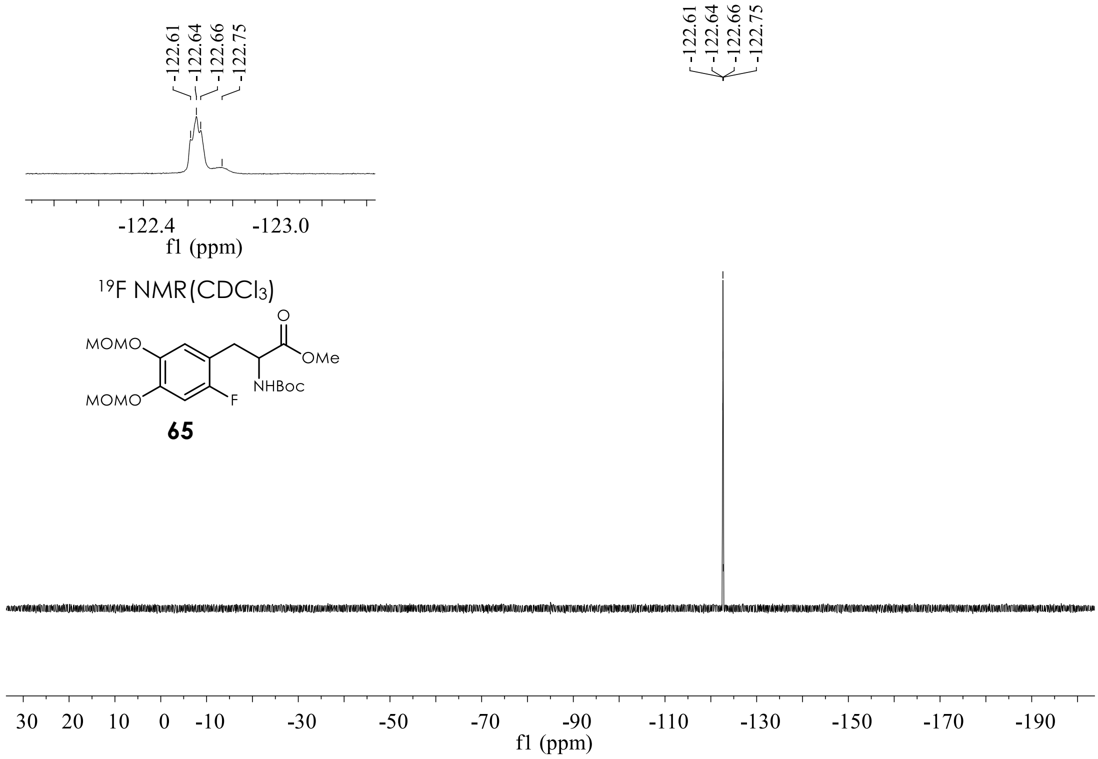


^{13}C NMR($CDCl_3$)



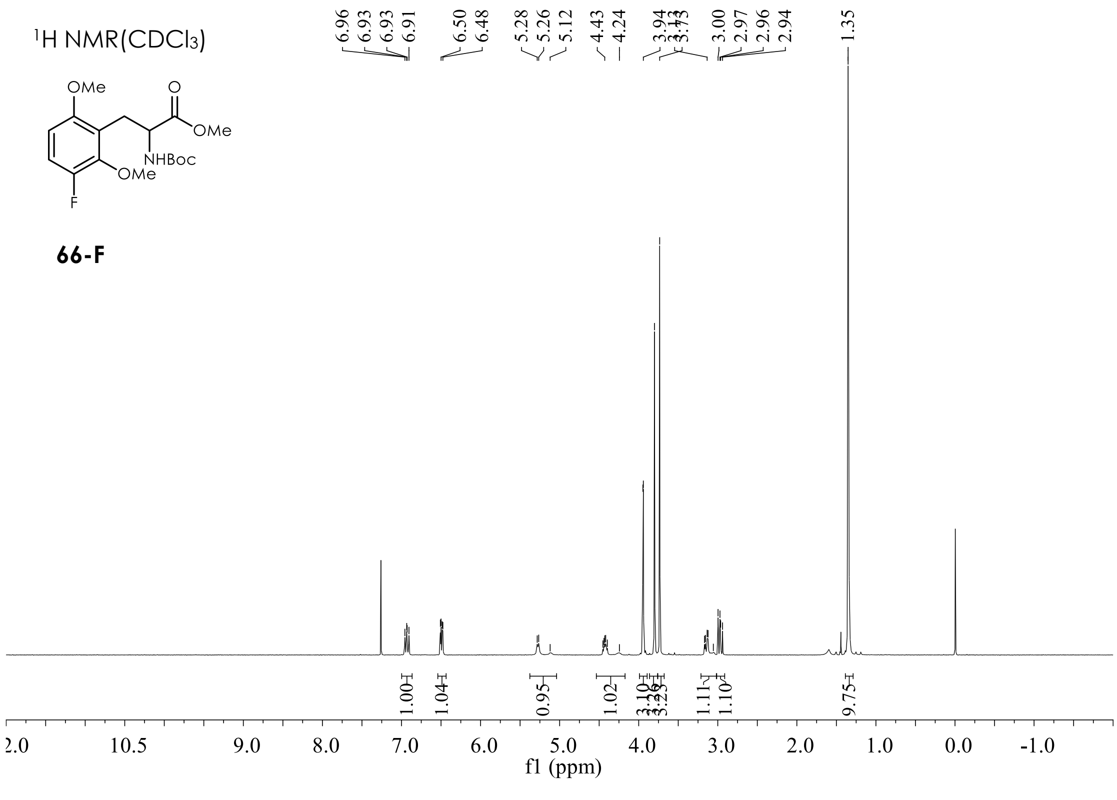
65





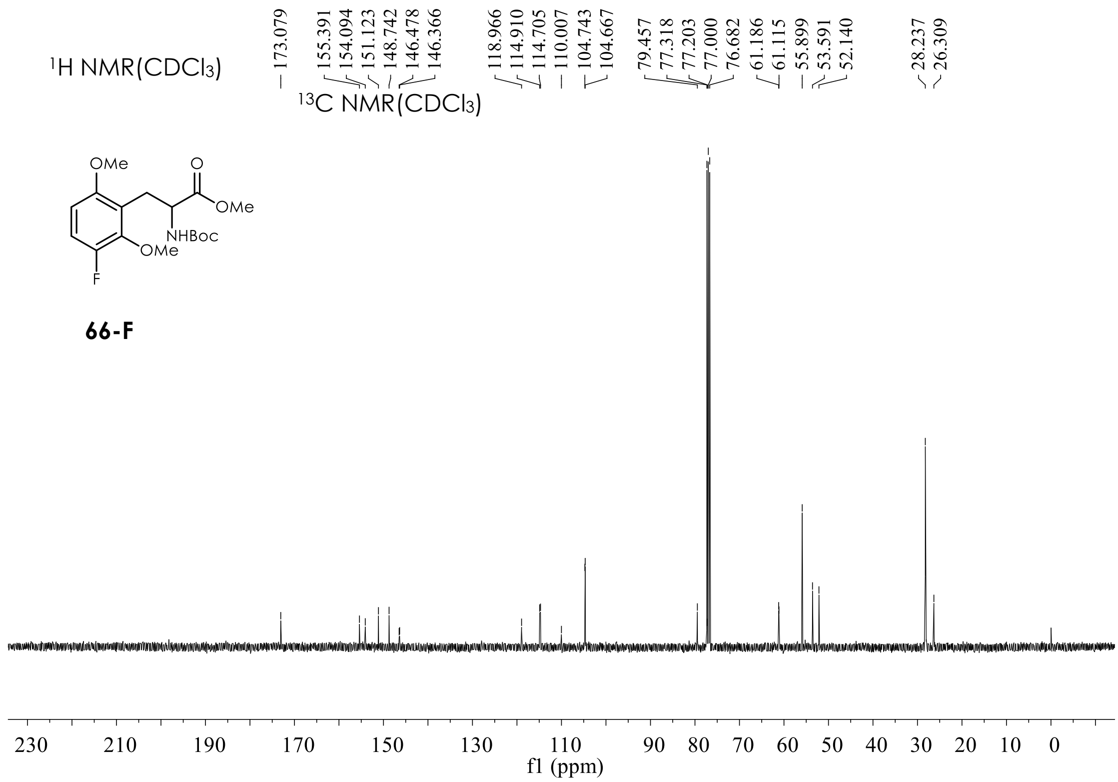
^{19}F NMR($CDCl_3$)

65

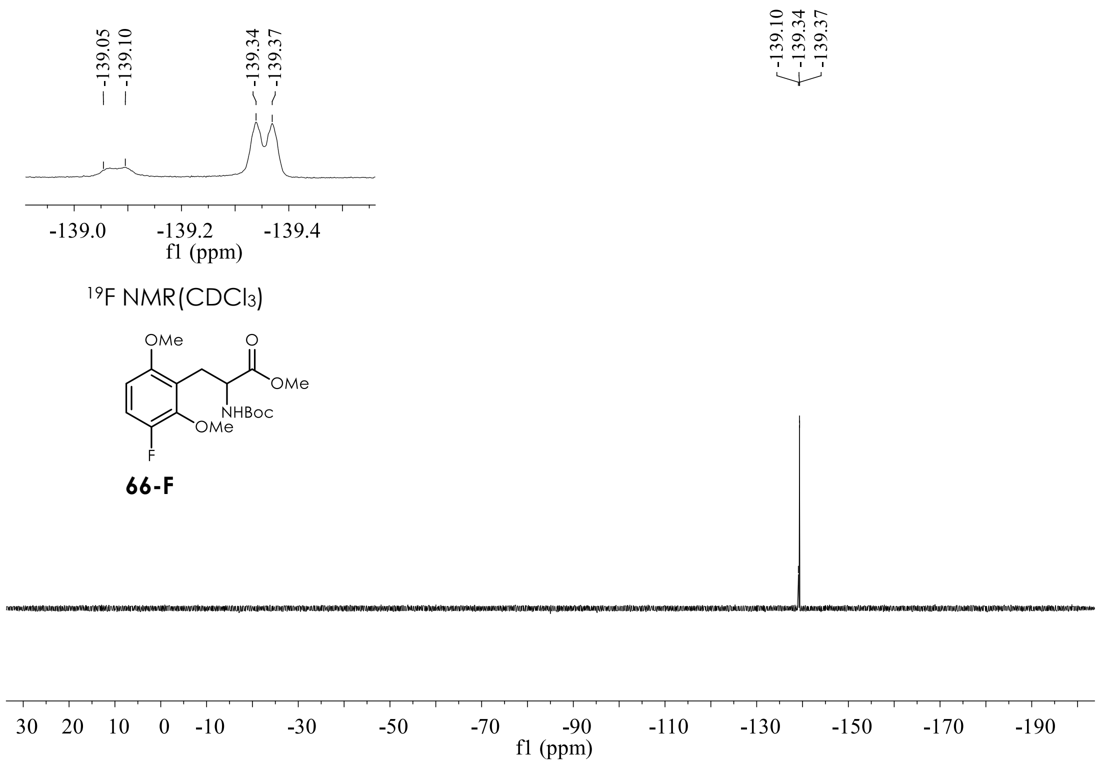


^{1}H NMR($CDCl_3$)

66-F

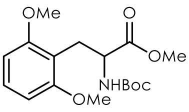

1H NMR(CDCl3)
13C NMR(CDCl3)
173.079
155.391
154.094
151.123
148.742
146.478
146.366
118.966
114.910
114.705
110.007
104.743
104.667
79.457
77.318
77.203
77.000
76.682
61.186
61.115
55.899
53.591
52.140
28.237
26.309
OMe
O
OMe
NHBoc
OMe
F
230 210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

66-F

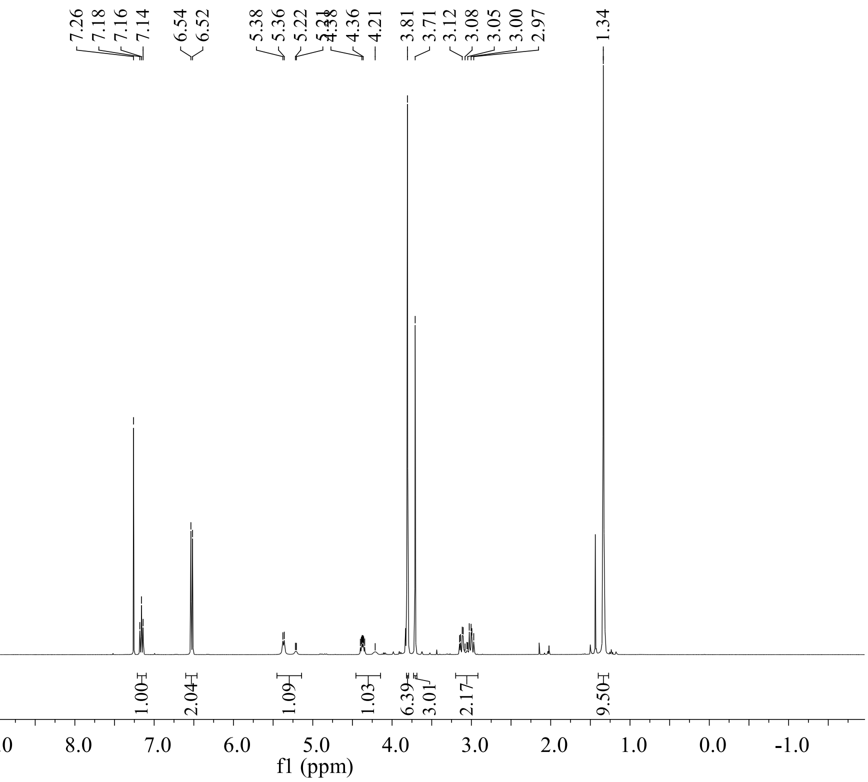

-139.05
-139.10
-139.34
-139.37
-139.0
-139.2
-139.4
f1 (ppm)
19F NMR(CDCl3)
OMe
O
OMe
NHBoc
OMe
F
-139.10
-139.34
-139.37
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)

66-F

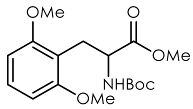
^{13}C NMR($CDCl_3$)



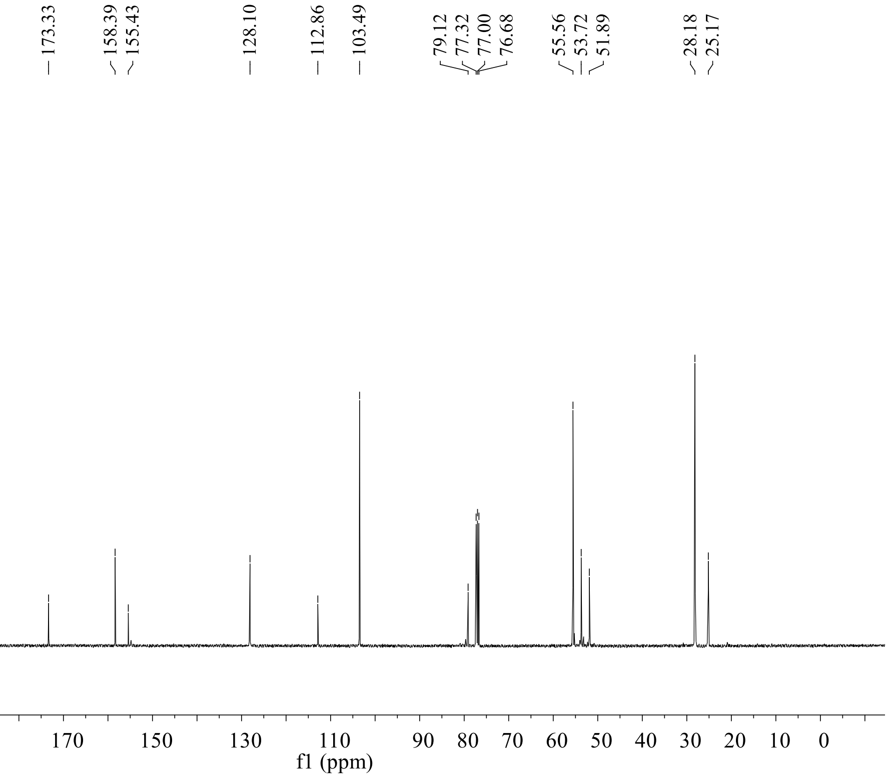
66-Cl-i



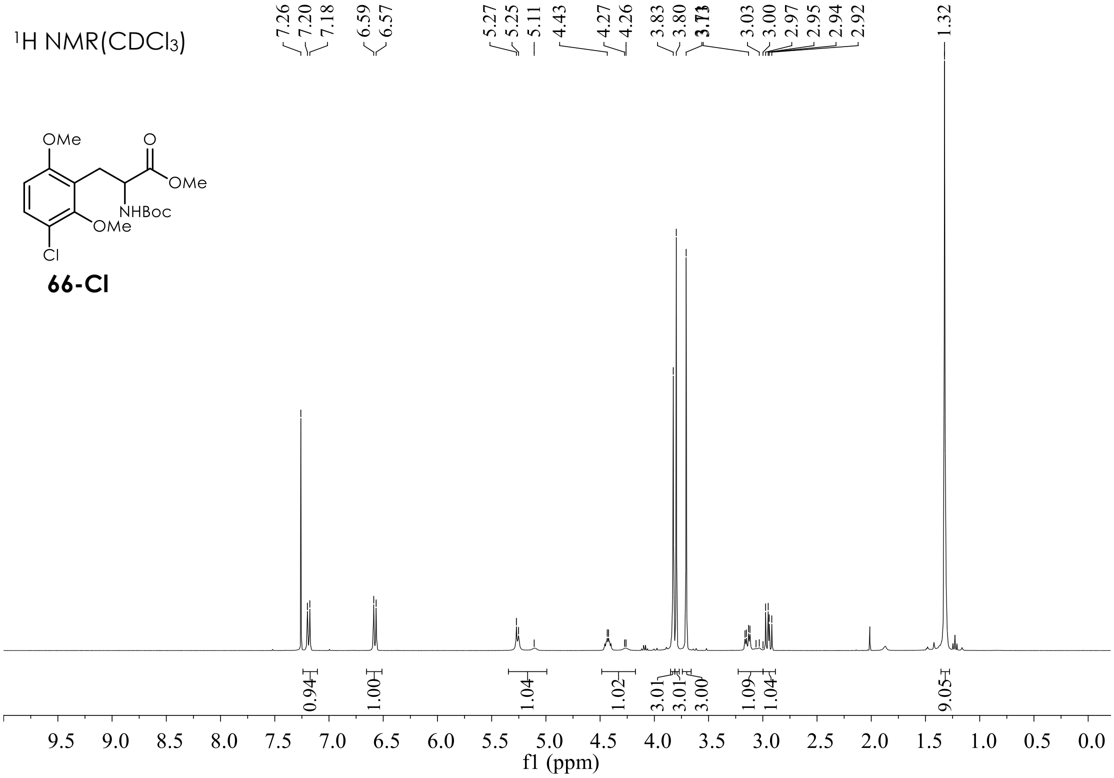
^{13}C NMR($CDCl_3$)



66-Cl-i

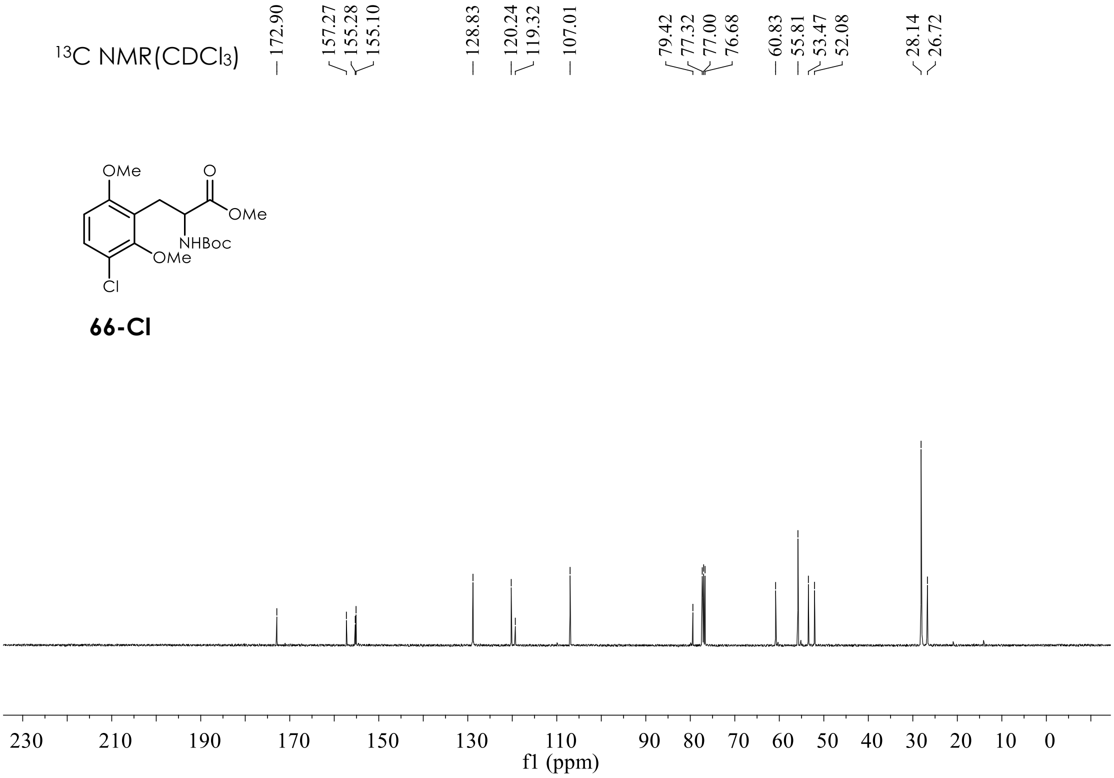


^{1}H NMR($CDCl_3$)

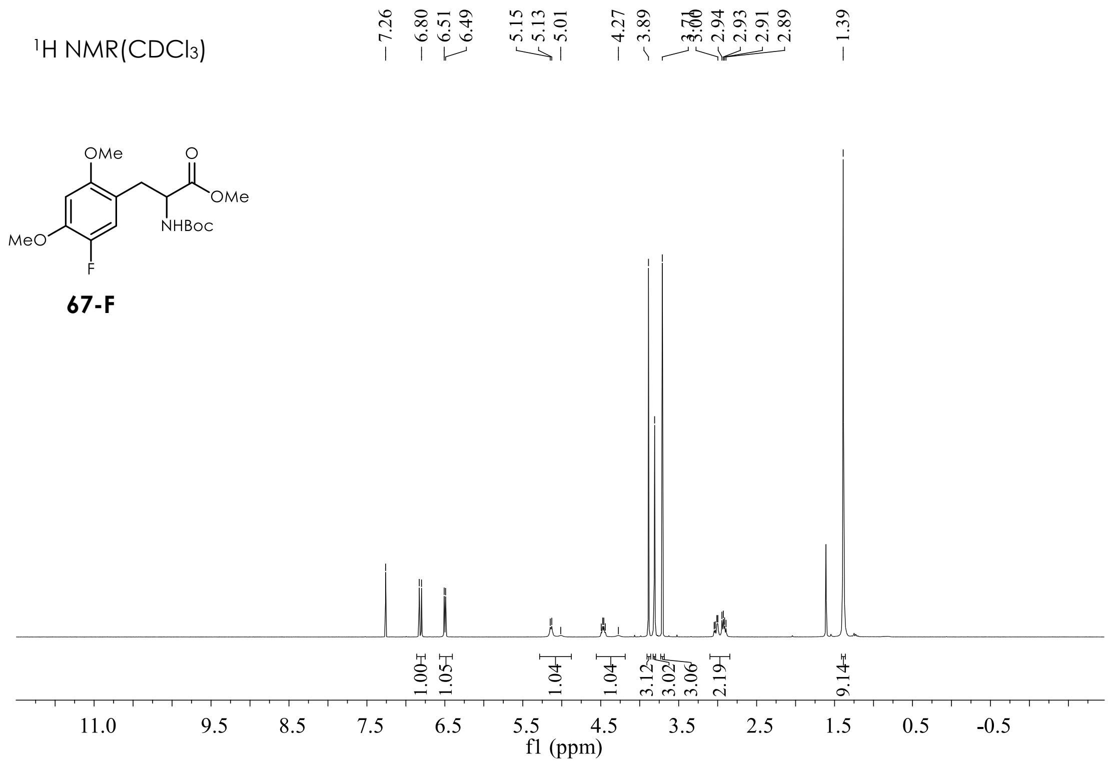


66-Cl

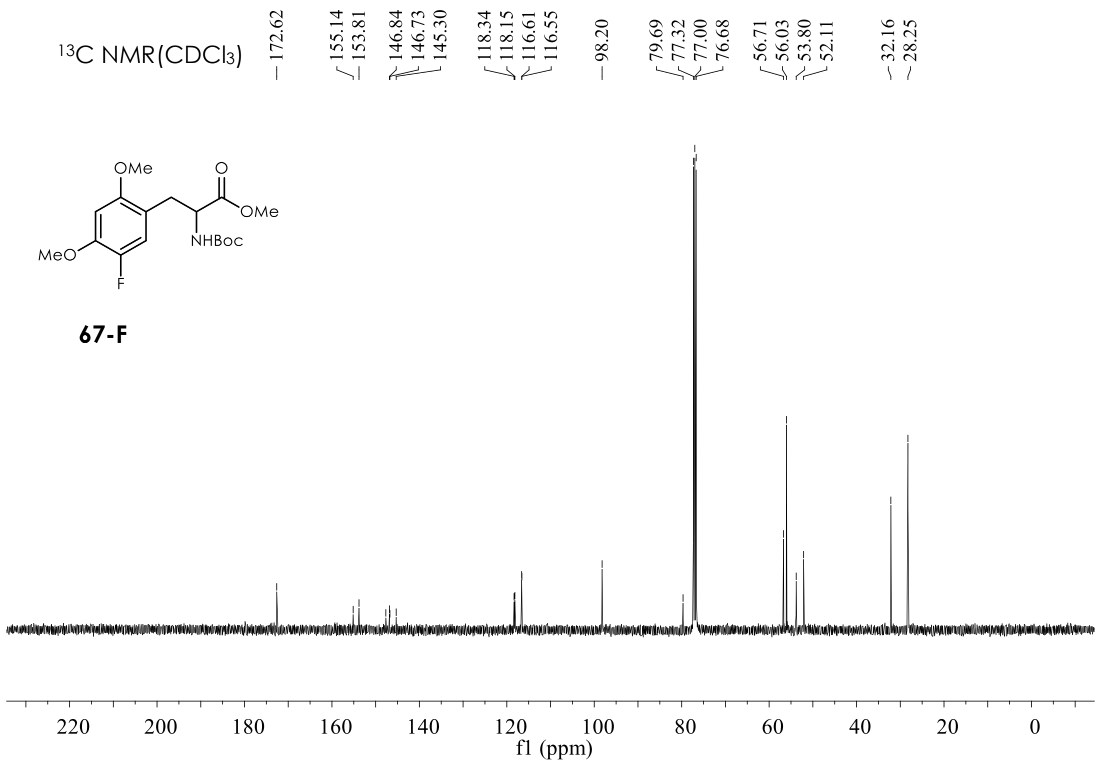
^{13}C NMR($CDCl_3$)



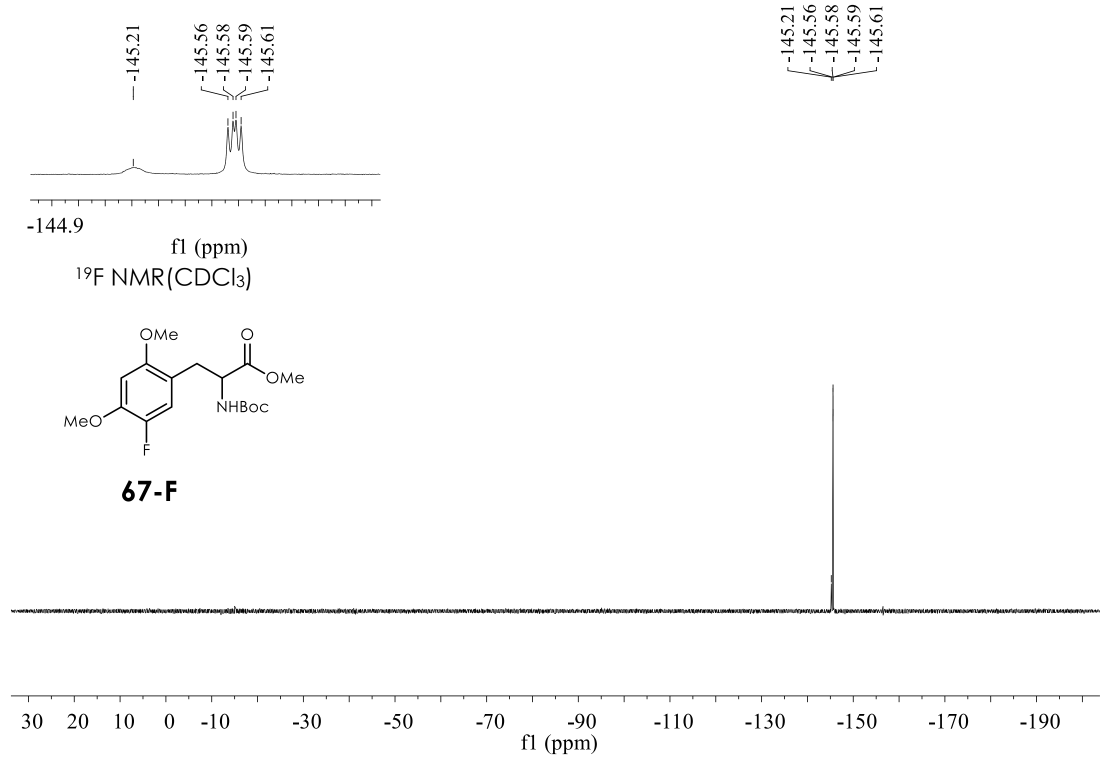
66-Cl

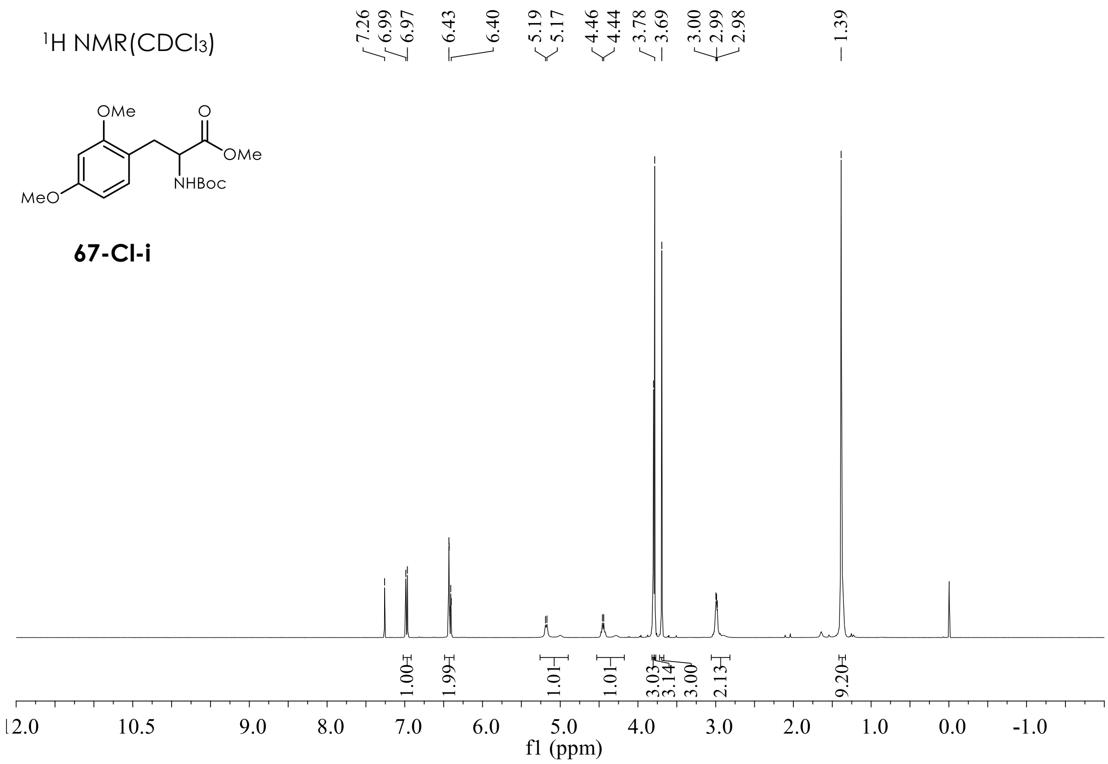


^{1}H NMR($CDCl_3$)
OMe
OMe
NHBoc
MeO
F
67-F
f1 (ppm)

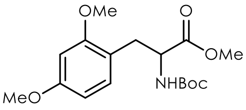


^{13}C NMR($CDCl_3$)
OMe
OMe
NHBoc
MeO
F
67-F
f1 (ppm)

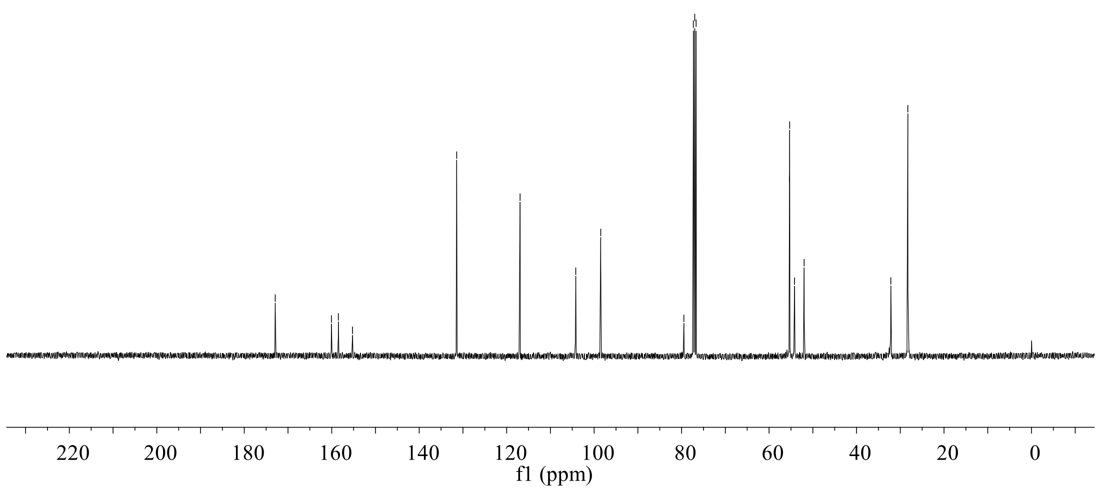

-145.21
-145.56
-145.58
-145.59
-145.61
-144.9
f1 (ppm)
19F NMR(CDCl3)
OMe
O
OMe
MeO
NHBoc
F
67-F
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)


1H NMR(CDCl3)
7.26
6.99
6.97
6.43
6.40
5.19
5.17
4.46
4.44
3.78
3.69
3.00
2.99
2.98
1.39
OMe
O
OMe
MeO
NHBoc
67-Cl-i
1.00
1.99
1.01
1.01
3.03
3.14
3.00
2.13
9.20
12.0 10.5 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0
f1 (ppm)

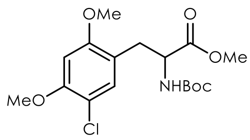
^{13}C NMR(CDCl$_3$)



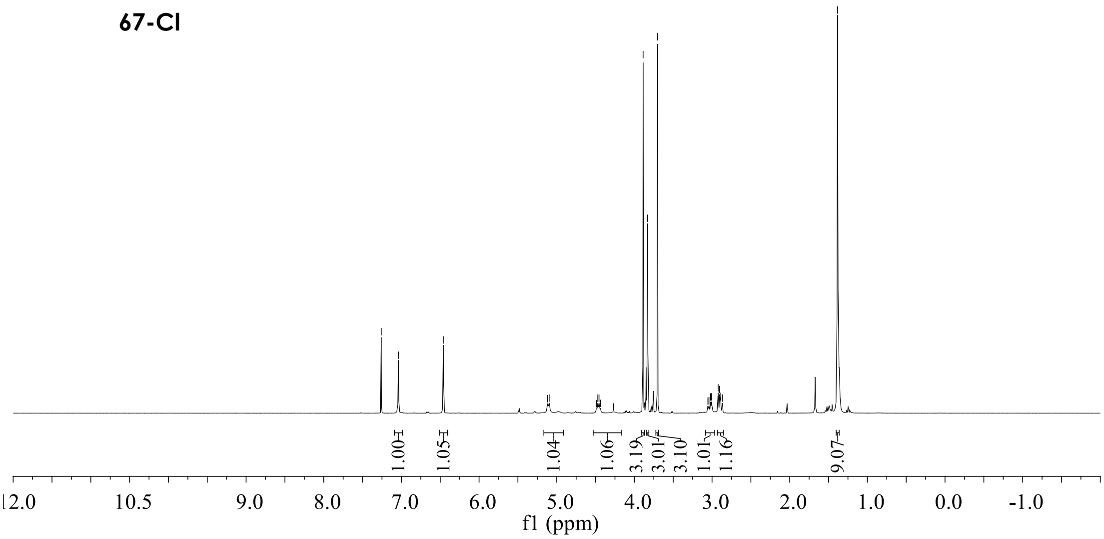
67-Cl-i



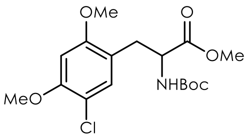
^{1}H NMR(CDCl$_3$)



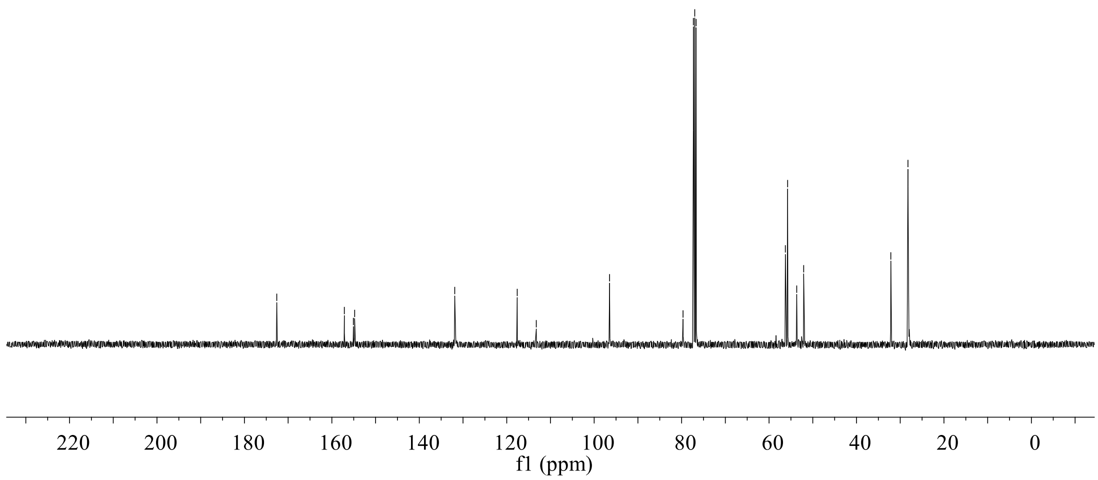
67-Cl



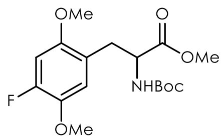
^{13}C NMR($CDCl_3$)



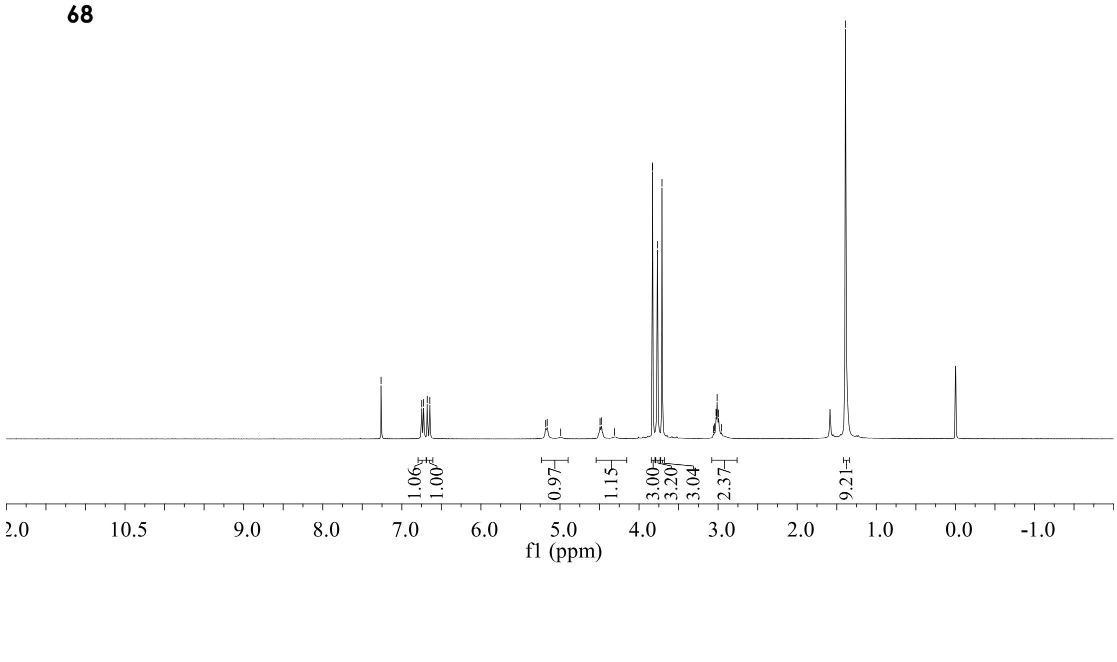
67-Cl



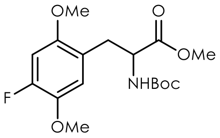
^{1}H NMR($CDCl_3$)



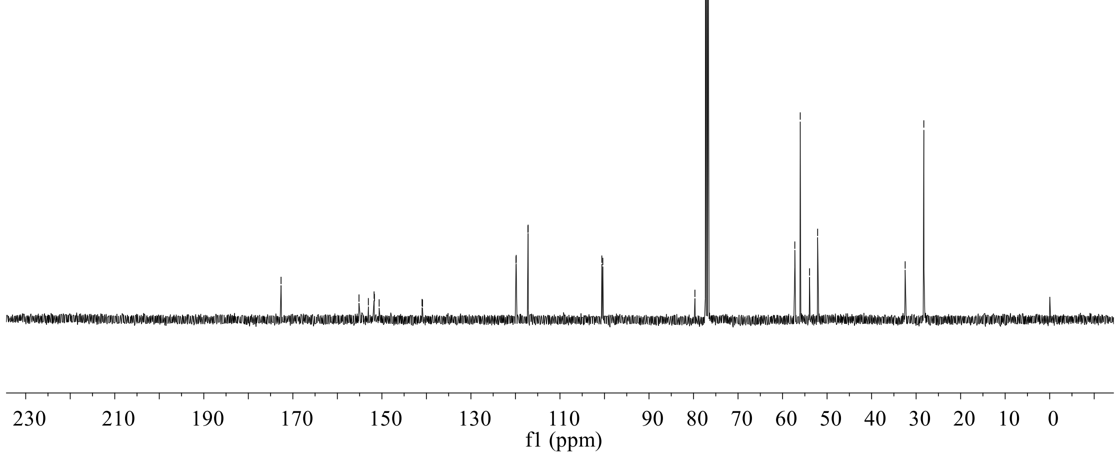
68

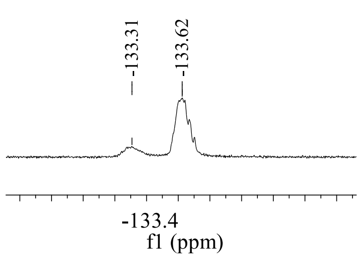


^{13}C NMR(CDCl$_3$)

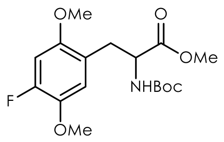


68

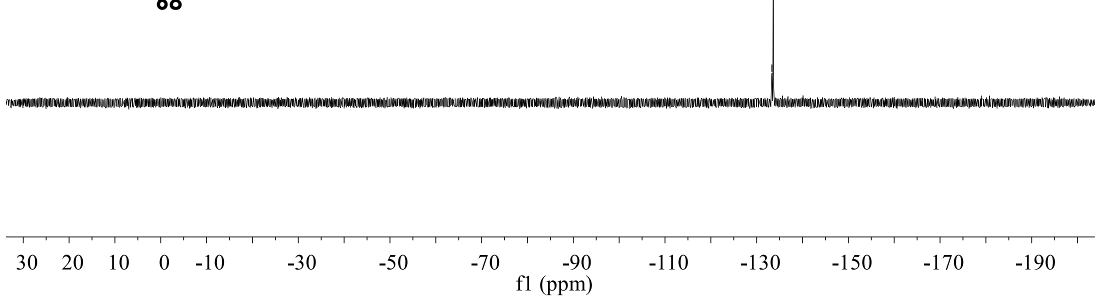




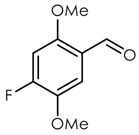
^{19}F NMR(CDCl$_3$)



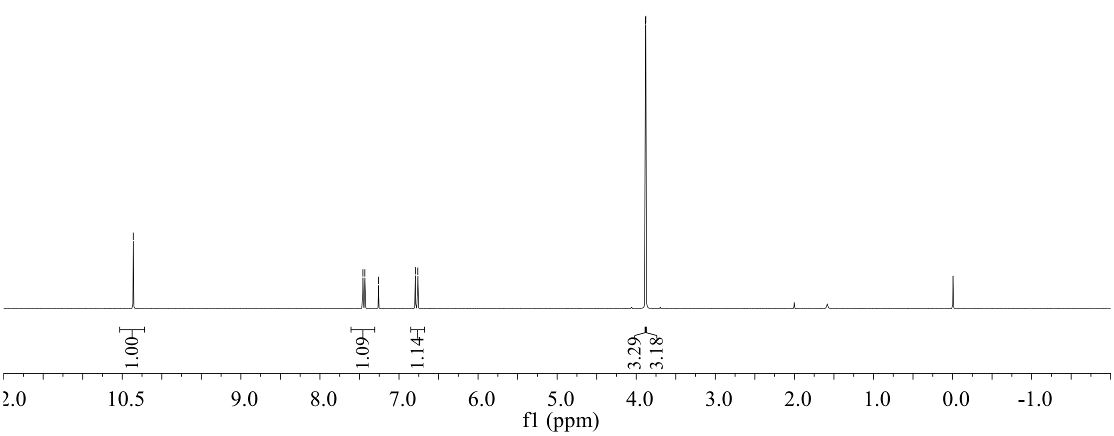
68



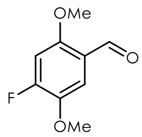
^1H NMR($CDCl_3$)



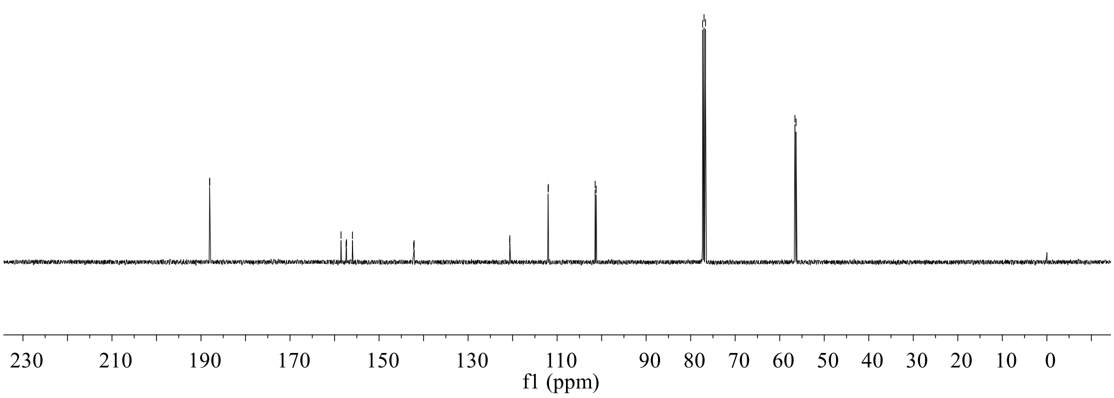
68-i

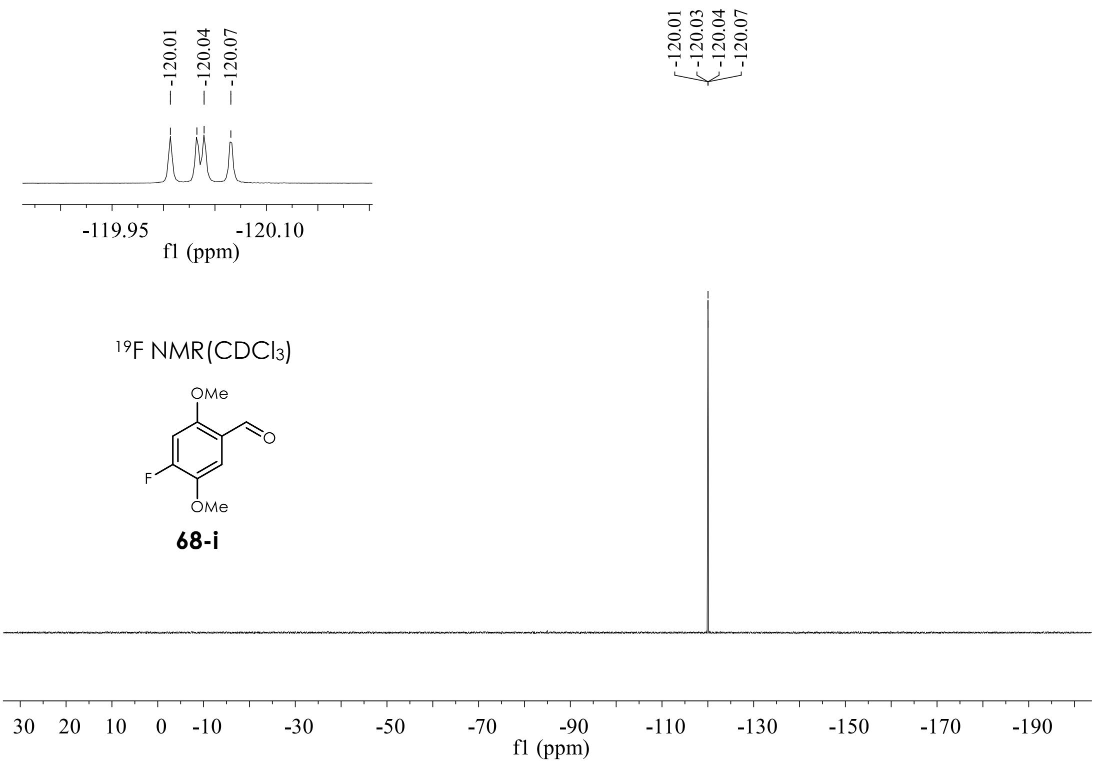


^{13}C NMR($CDCl_3$)



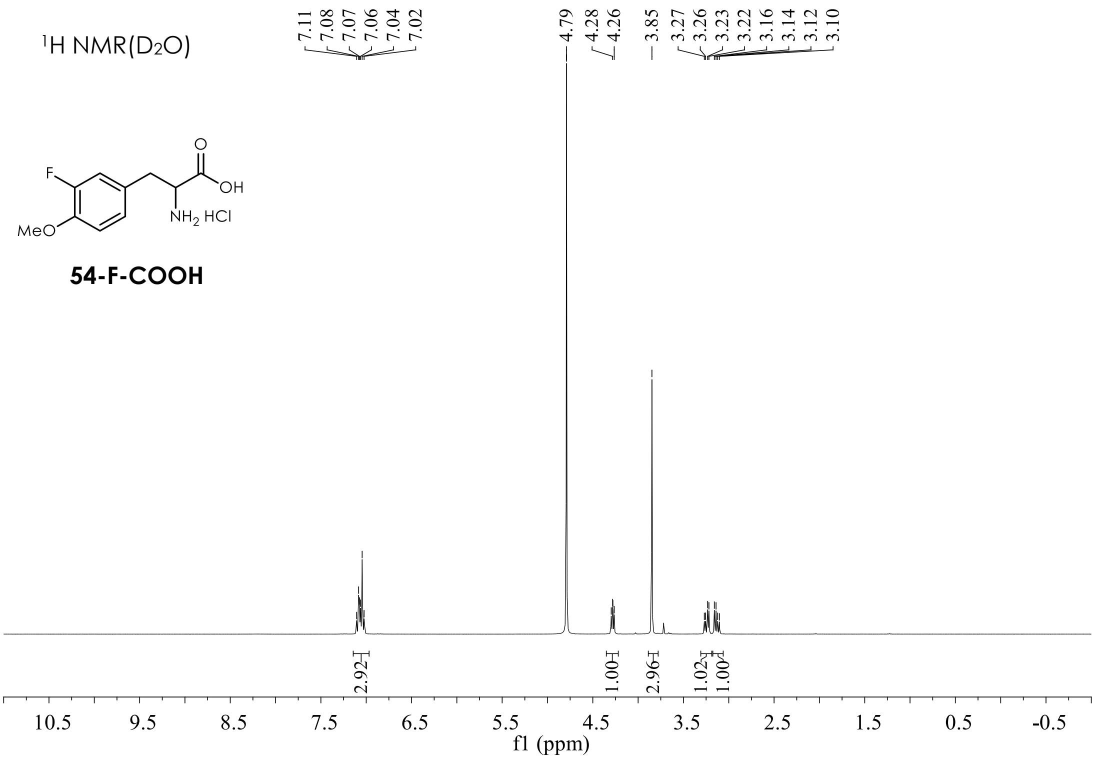
68-i





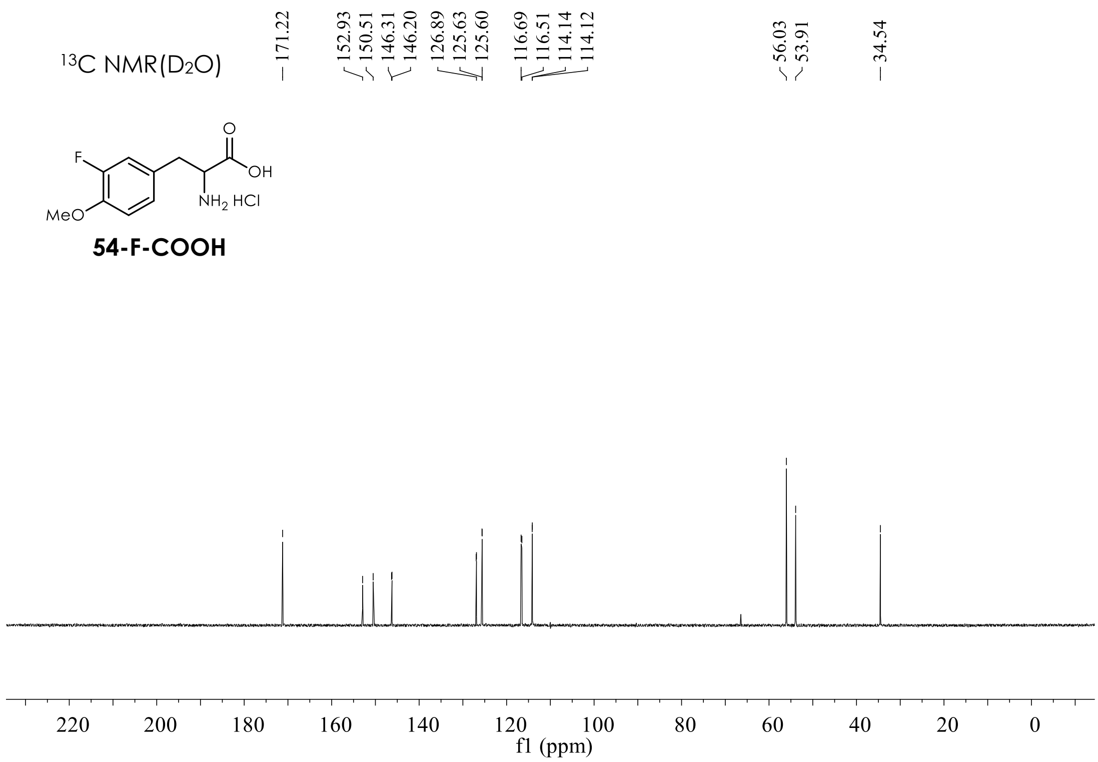
-120.01
-120.04
-120.07
-119.95
-120.10
f1 (ppm)
^{19}F NMR(CDCl$_3$)
OMe
O
F
OMe
-120.01
-120.03
-120.04
-120.07
30
20
10
0
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
f1 (ppm)

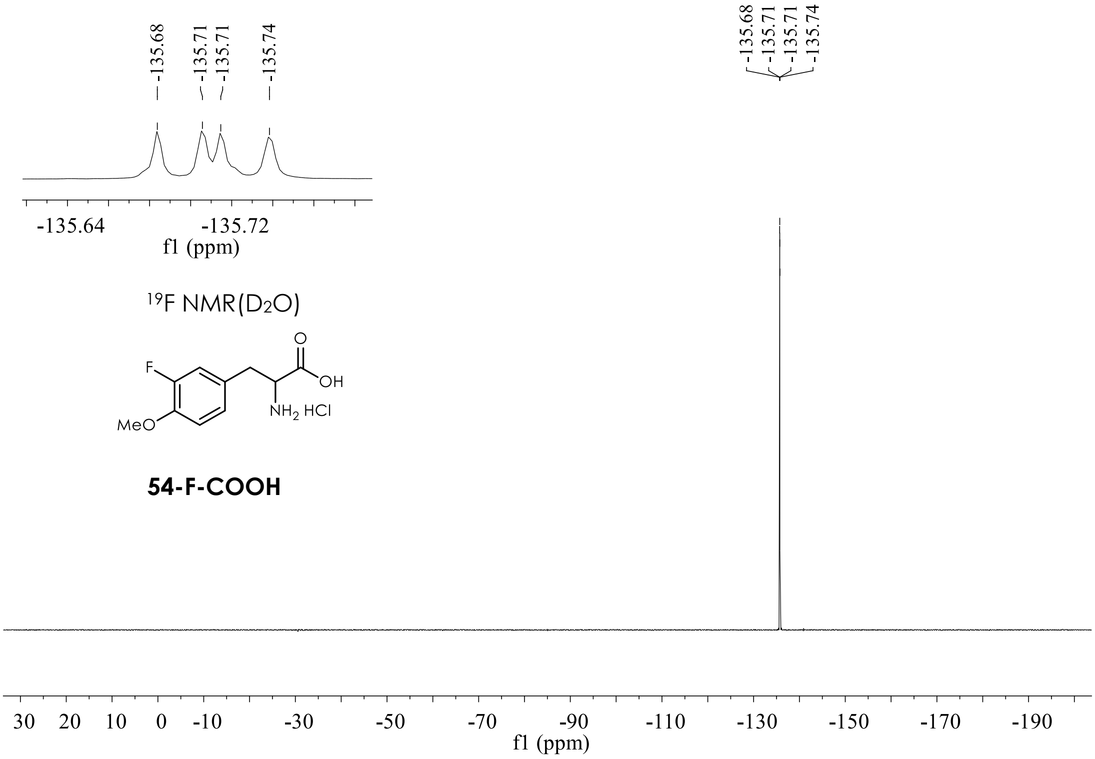
68-i

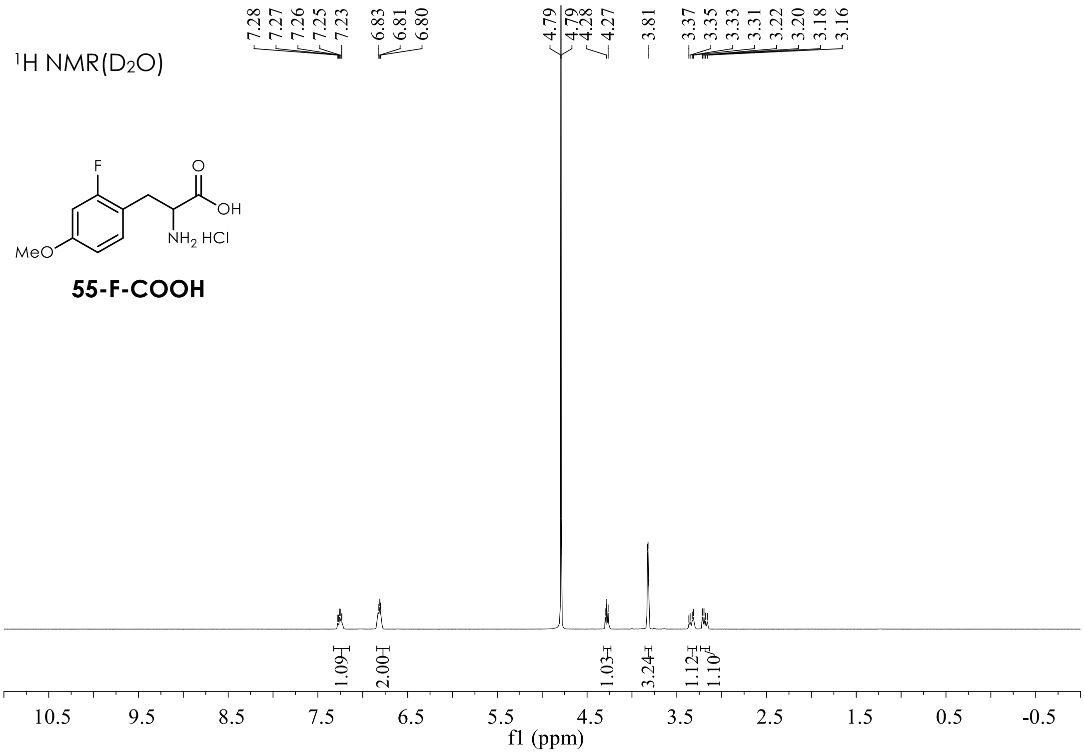


^{1}H NMR(D$_2$O)
7.11
7.08
7.07
7.06
7.04
7.02
4.79
4.28
4.26
3.85
3.27
3.26
3.23
3.22
3.16
3.14
3.12
3.10
F
MeO
O
OH
NH$_2$ HCl
2.92
1.00
2.96
1.02
1.00
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

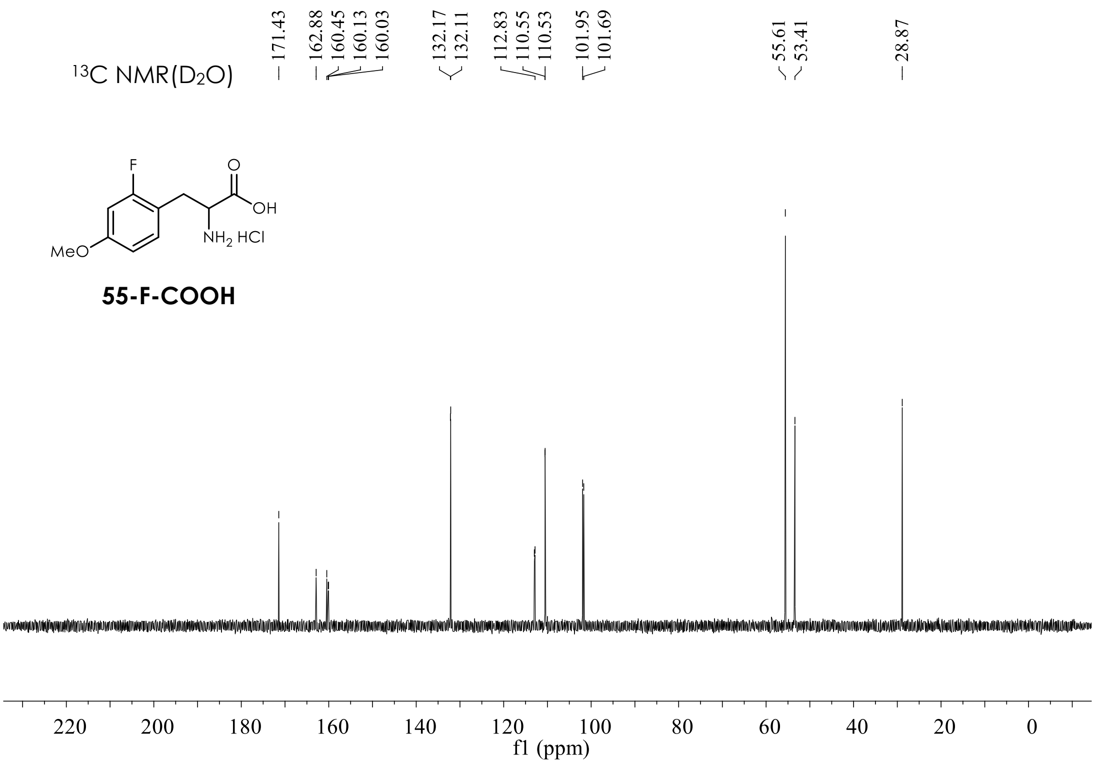
54-F-COOH


13C NMR(D2O)
171.22
152.93
150.51
146.31
146.20
126.89
125.63
125.60
116.69
116.51
114.14
114.12
56.03
53.91
34.54
F
MeO
O
OH
NH2 HCl
54-F-COOH
220
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

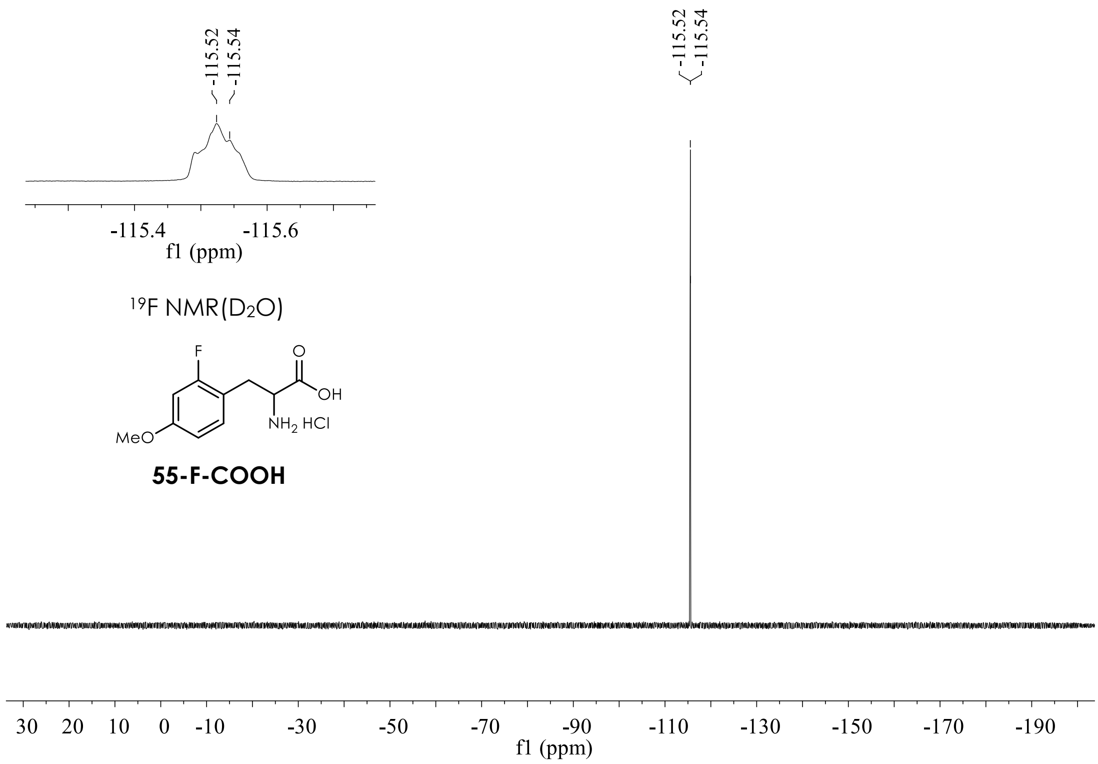

-135.68
-135.71
-135.71
-135.74
-135.64
-135.72
f1 (ppm)
19F NMR(D2O)
F
MeO
O
OH
NH2 HCl
54-F-COOH
30
20
10
0
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
f1 (ppm)



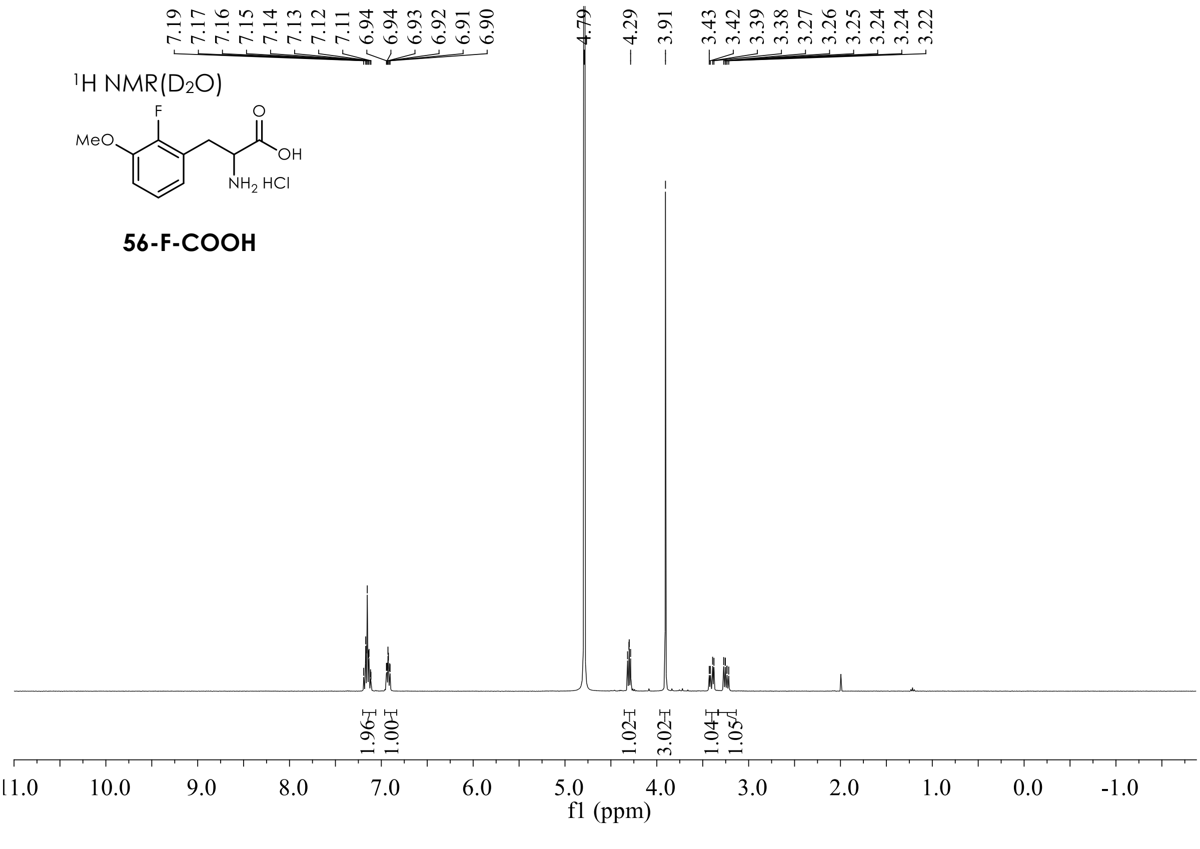
1H NMR(D2O)
7.28
7.27
7.26
7.25
7.23
6.83
6.81
6.80
4.79
4.79
4.28
4.27
3.81
3.37
3.35
3.33
3.31
3.22
3.20
3.18
3.16
F
O
OH
MeO
NH2 HCl
55-F-COOH
1.09
2.00
1.03
3.24
1.12
1.10
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)



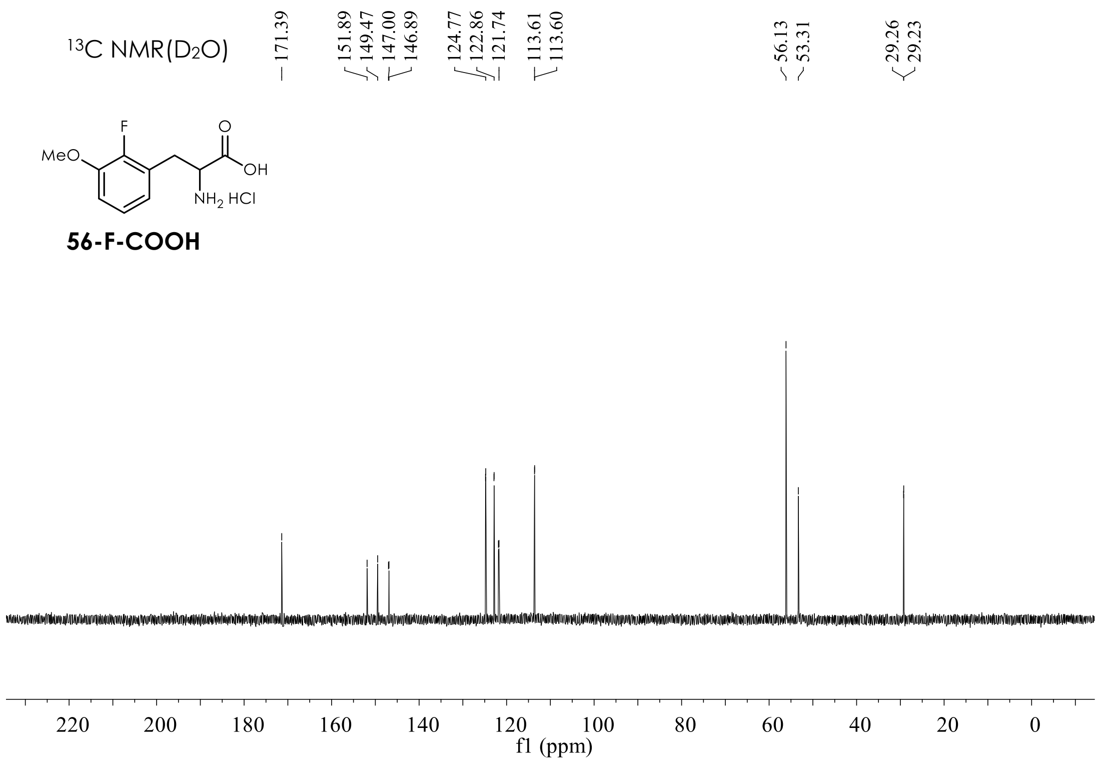
13C NMR(D2O)
171.43
162.88
160.45
160.13
160.03
132.17
132.11
112.83
110.55
110.53
101.95
101.69
55.61
53.41
28.87
F
O
OH
MeO
NH2 HCl
55-F-COOH
220
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)



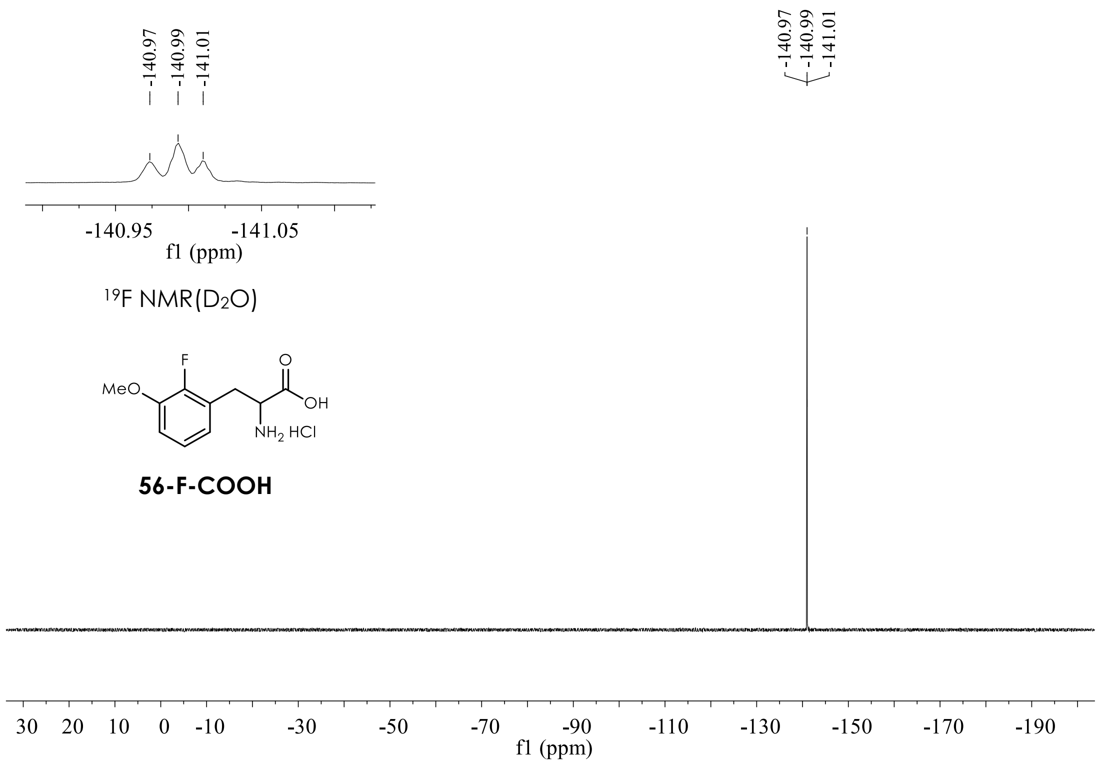
-115.52
-115.54
-115.4
-115.6
f1 (ppm)
^{19}F NMR(D$_2$O)
F
O
OH
MeO
NH$_2$ HCl
55-F-COOH
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)



7.19 7.17 7.16 7.15 7.14 7.13 7.12 7.11 6.94 6.94 6.93 6.92 6.91 6.90
4.79
4.29
3.91
3.43 3.42 3.39 3.38 3.27 3.26 3.25 3.24 3.24 3.22
^{1}H NMR(D$_2$O)
F
MeO
O
OH
NH$_2$ HCl
56-F-COOH
1.96
1.00
1.02
3.02
1.04
1.05
11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0
f1 (ppm)



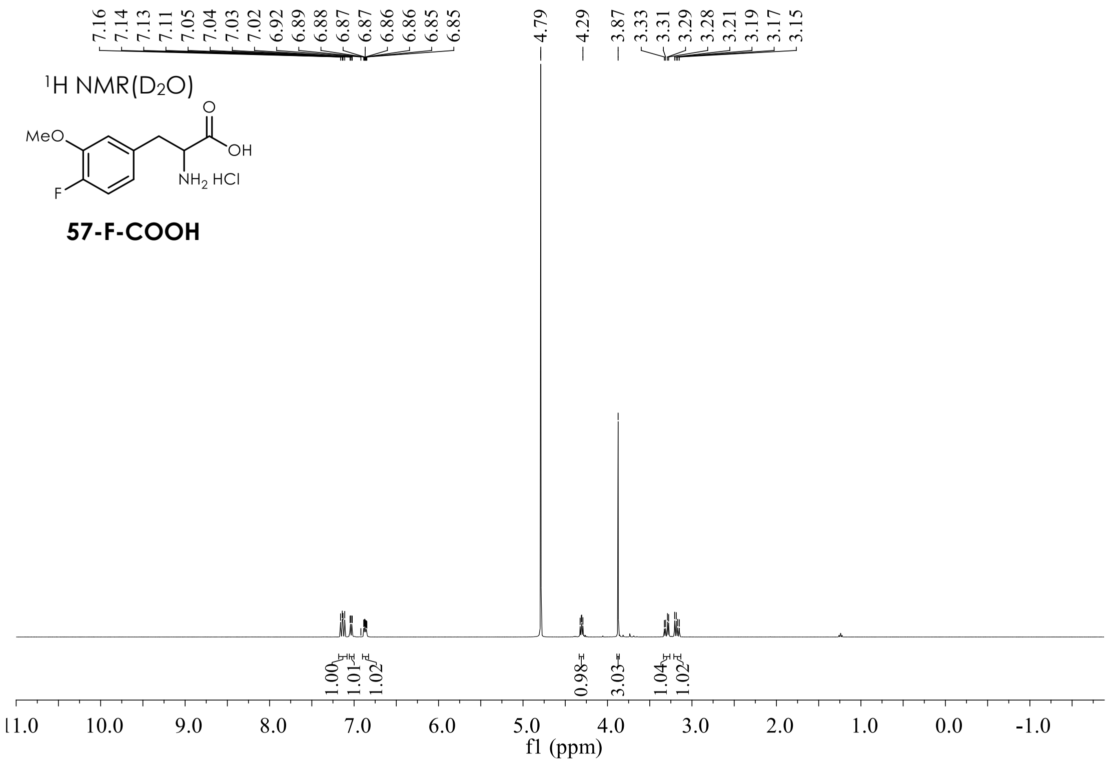
^{13}C NMR(D_2O)
171.39
151.89
149.47
147.00
146.89
124.77
122.86
121.74
113.61
113.60
56.13
53.31
29.26
29.23
MeO
F
O
OH
NH_2 HCl
56-F-COOH
220 200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)



-140.97
-140.99
-141.01
-140.95
-141.05
f1 (ppm)
^{19}F NMR(D_2O)
MeO
F
O
OH
NH_2 HCl
56-F-COOH
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)

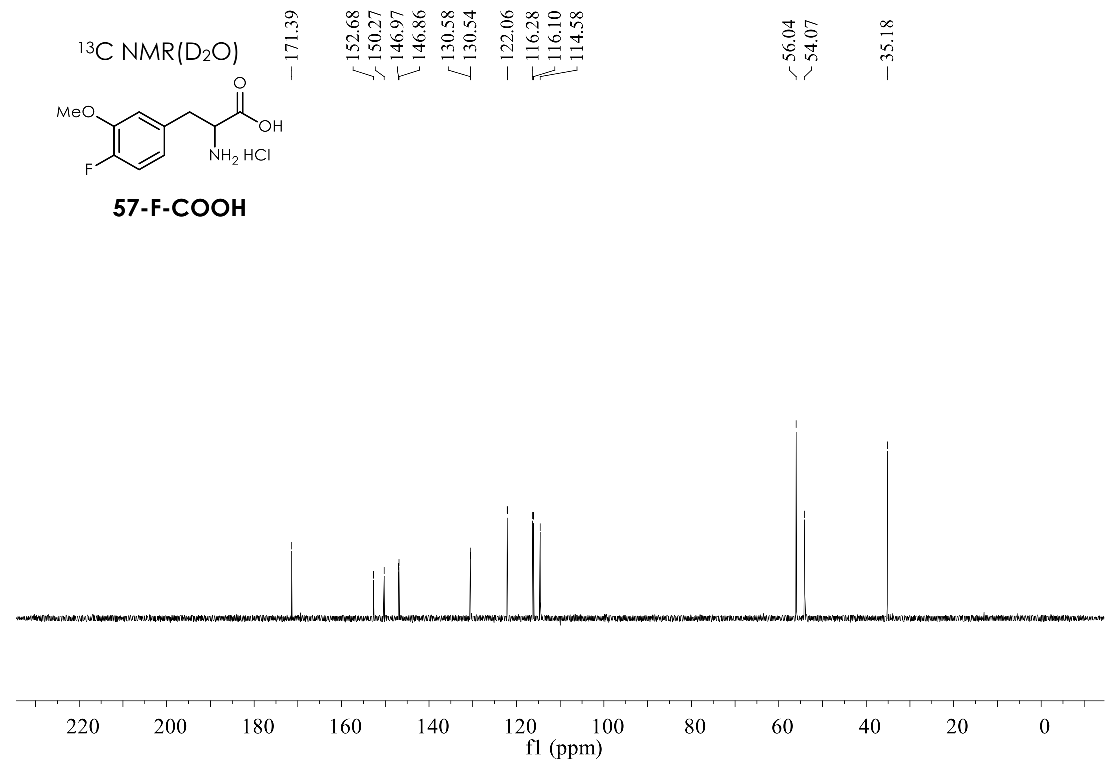
^{1}H NMR(D_2O)

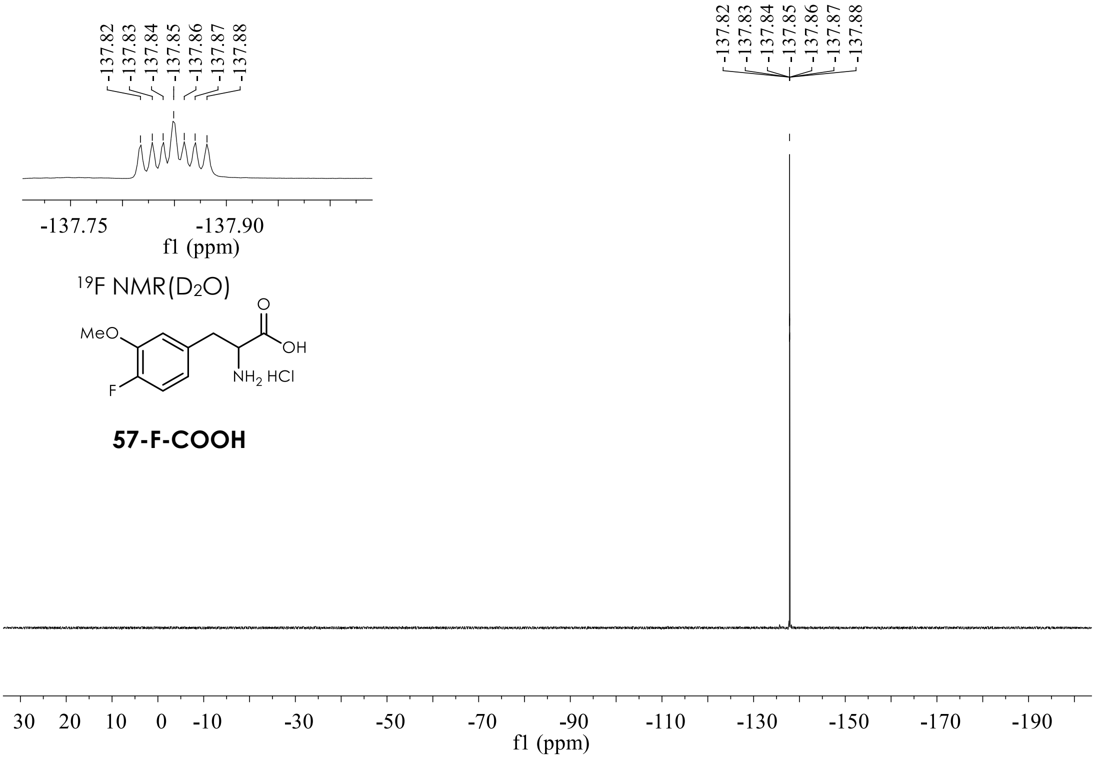
57-F-COOH



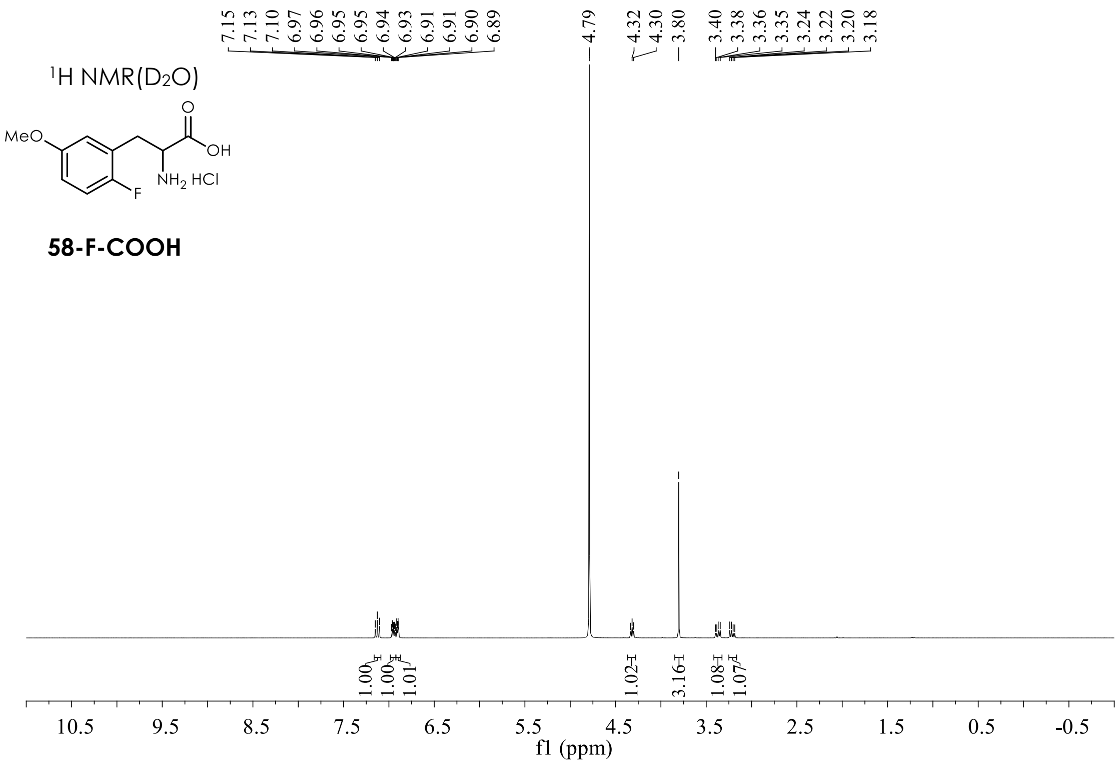
^{13}C NMR(D_2O)

57-F-COOH

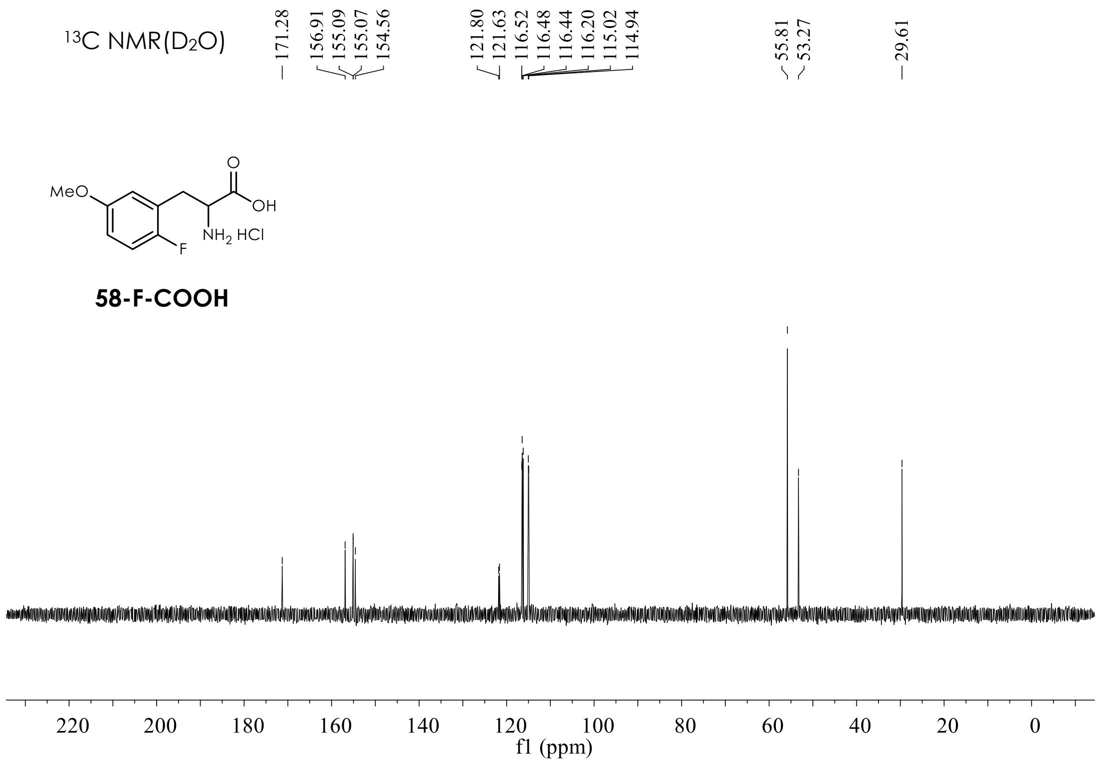


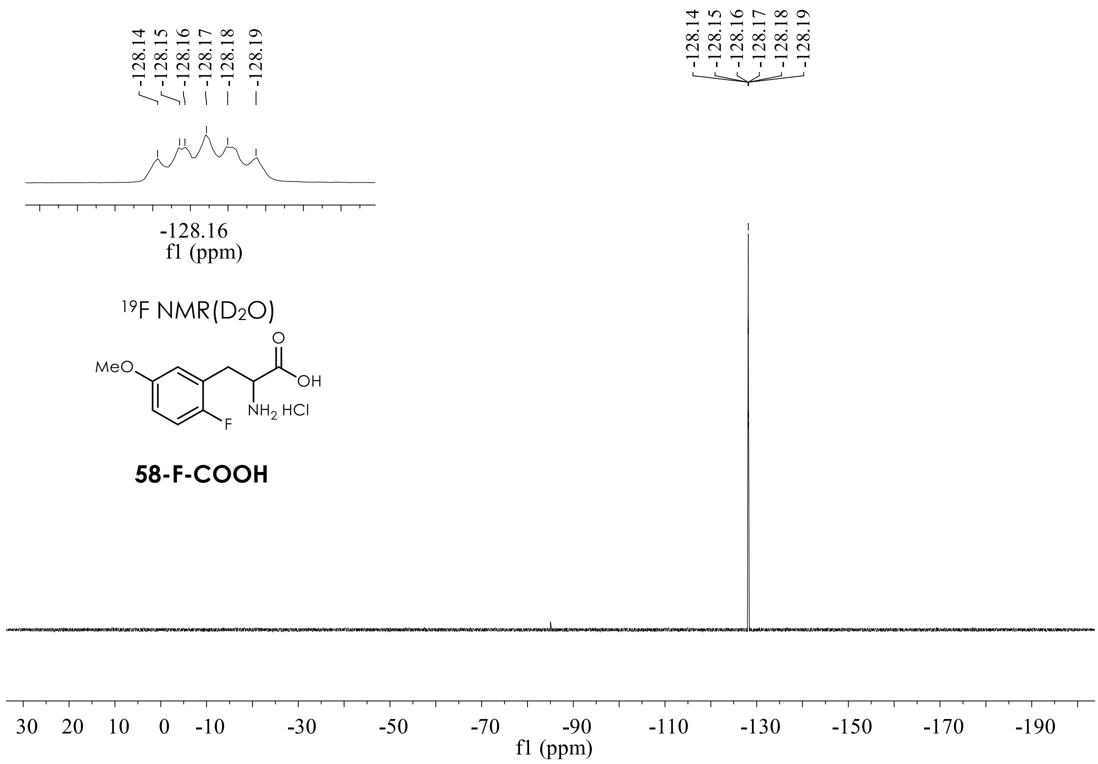


57-F-COOH



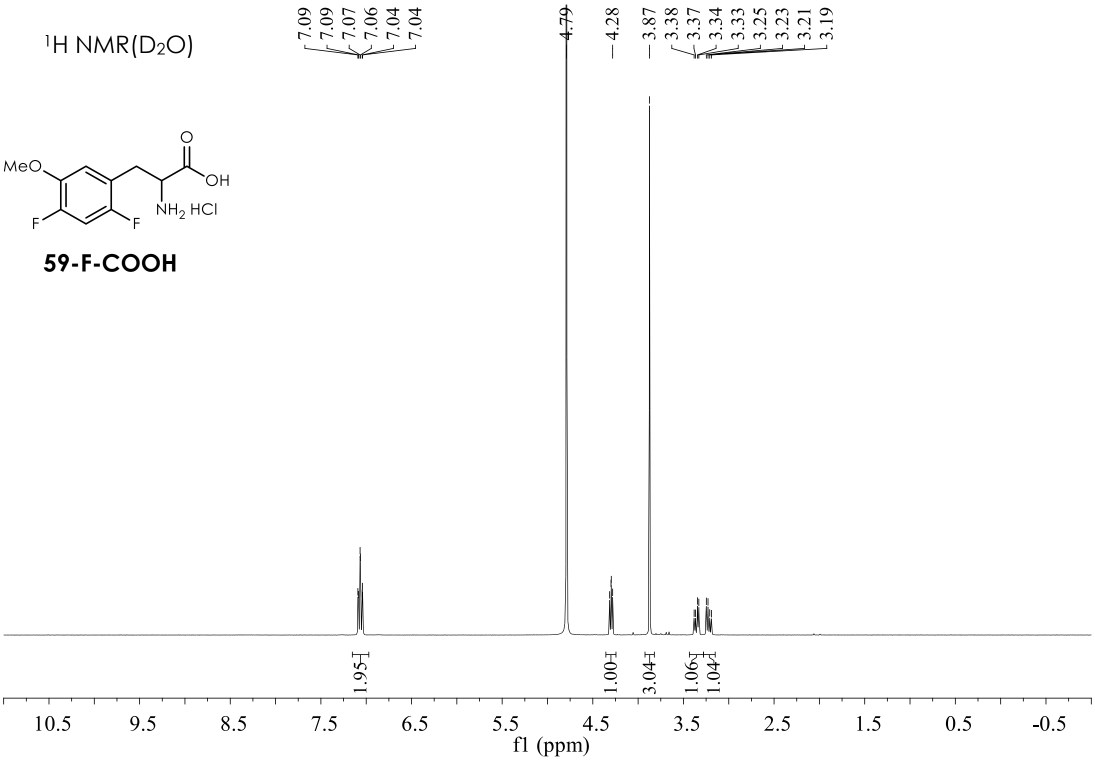
58-F-COOH


^{13}C NMR(D_2O)
171.28
156.91
155.09
155.07
154.56
121.80
121.63
116.52
116.48
116.44
116.20
115.02
114.94
55.81
53.27
29.61
MeO
O
OH
NH_2 HCl
F
58-F-COOH
220 200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)


-128.14
-128.15
-128.16
-128.17
-128.18
-128.19
-128.16
f1 (ppm)
^{19}F NMR(D_2O)
MeO
O
OH
NH_2 HCl
F
58-F-COOH
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)

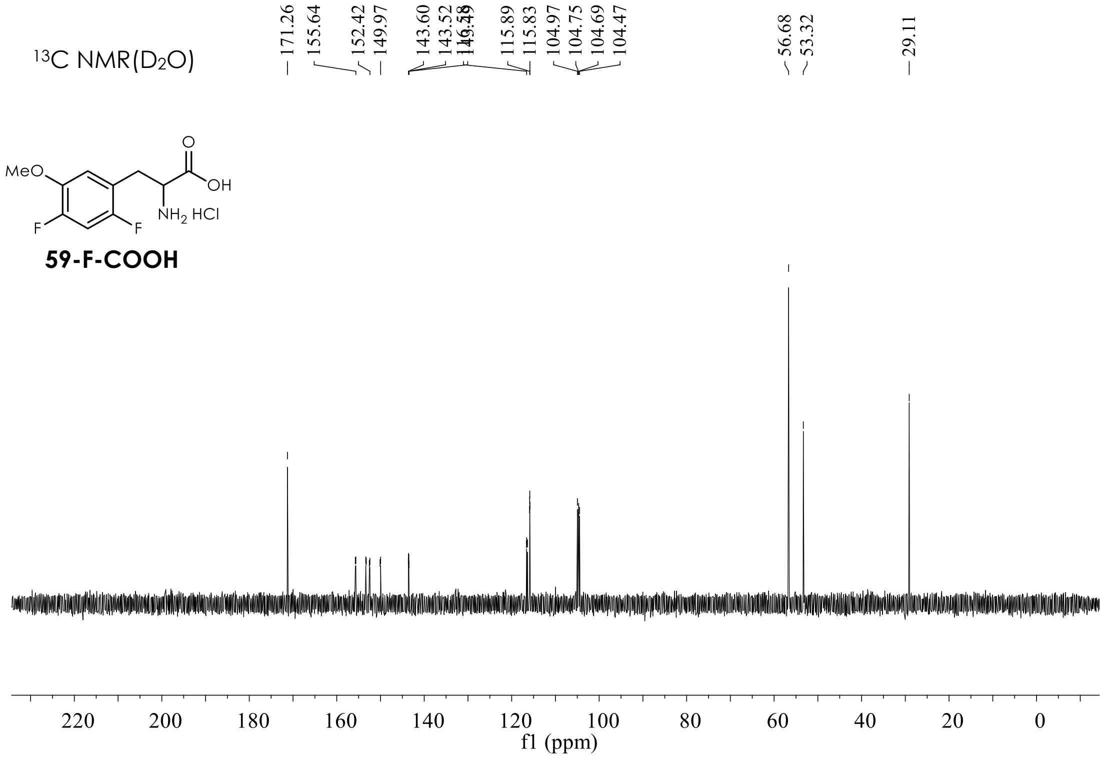
^1H NMR(D_2O)

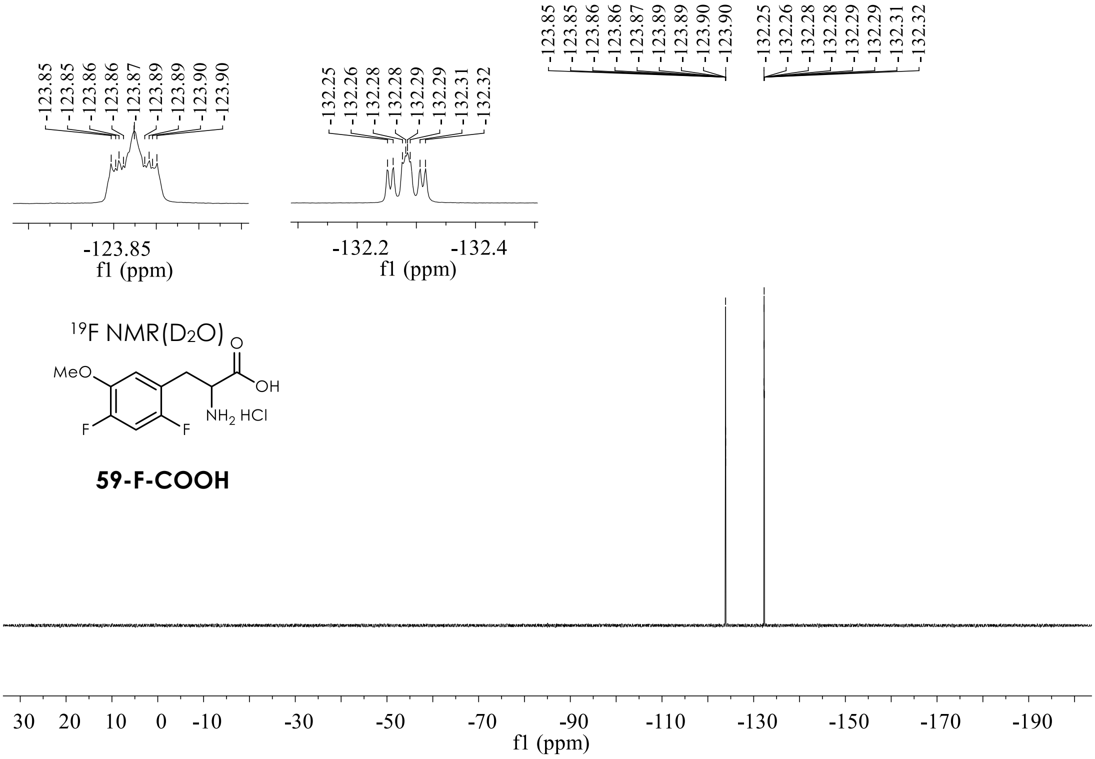
59-F-COOH



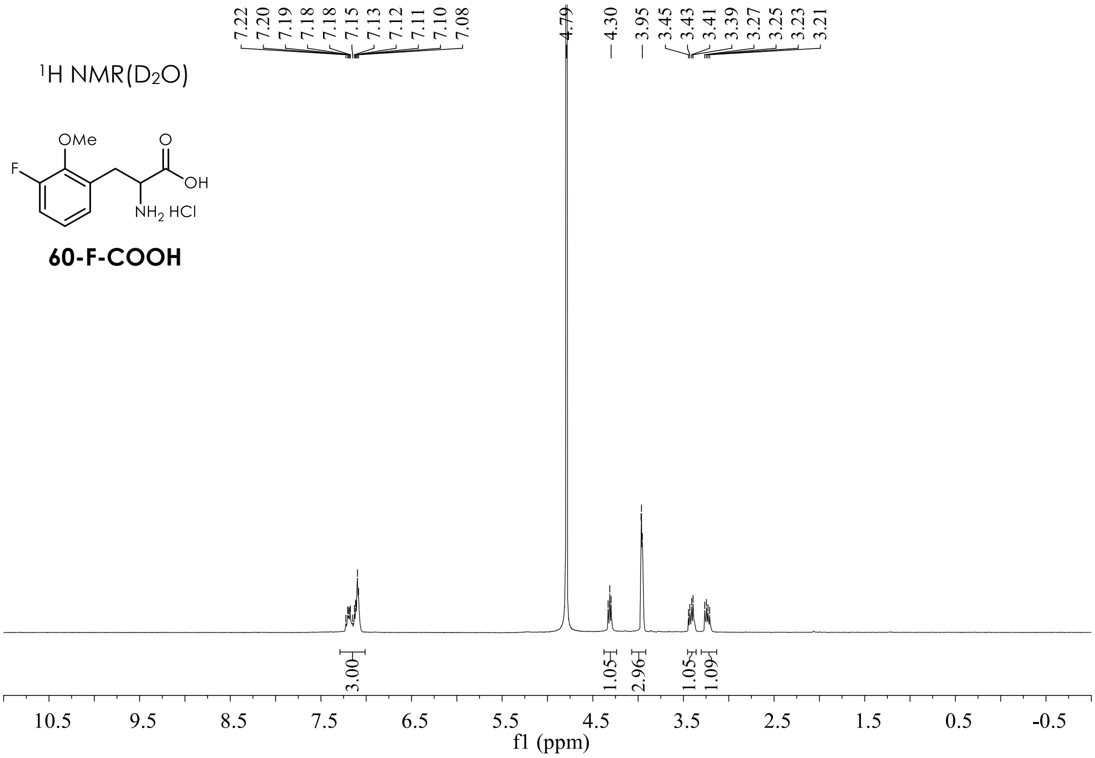
^{13}C NMR(D_2O)

59-F-COOH

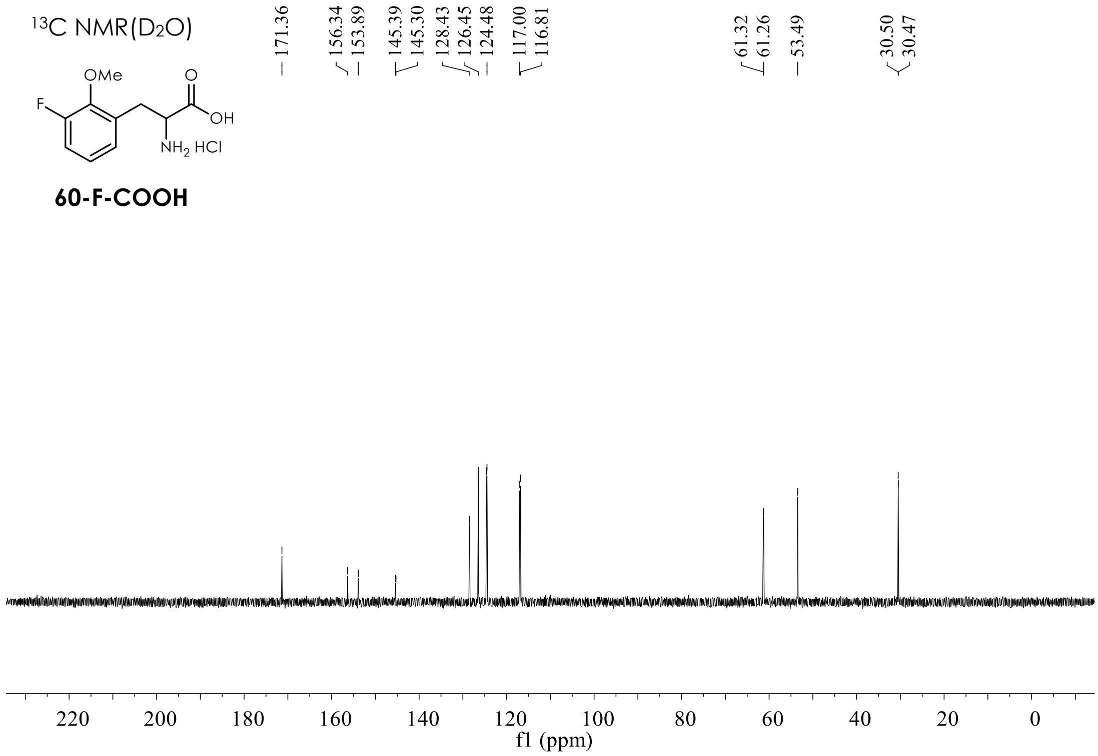


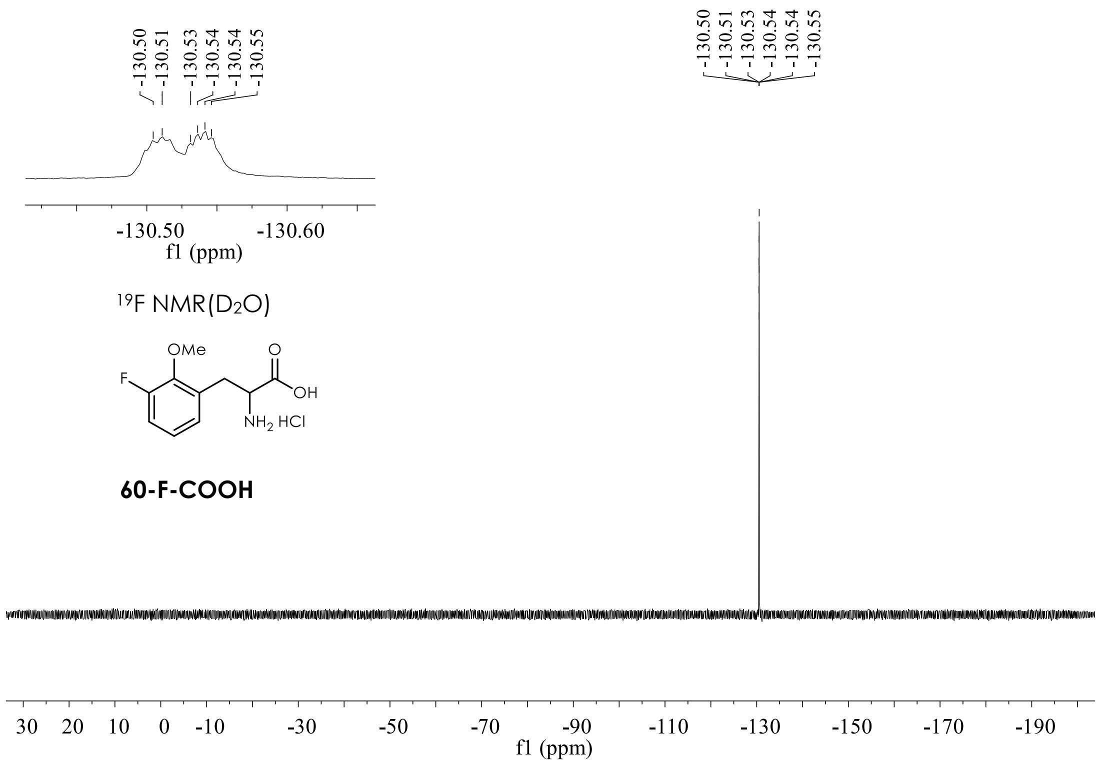


-123.85
-123.85
-123.86
-123.86
-123.87
-123.89
-123.89
-123.90
-123.90
-132.25
-132.26
-132.28
-132.28
-132.29
-132.29
-132.31
-132.32
-123.85
f1 (ppm)
-132.2
-132.4
f1 (ppm)
19F NMR(D2O)
MeO
O
OH
NH2 HCl
F
F
59-F-COOH
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)

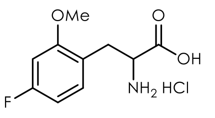


7.22
7.20
7.19
7.18
7.18
7.15
7.13
7.12
7.11
7.10
7.08
4.79
4.30
3.95
3.45
3.43
3.41
3.39
3.27
3.25
3.23
3.21
1H NMR(D2O)
OMe
F
O
OH
NH2 HCl
60-F-COOH
3.00
1.05
2.96
1.05
1.09
10.5 9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5 -0.5
f1 (ppm)

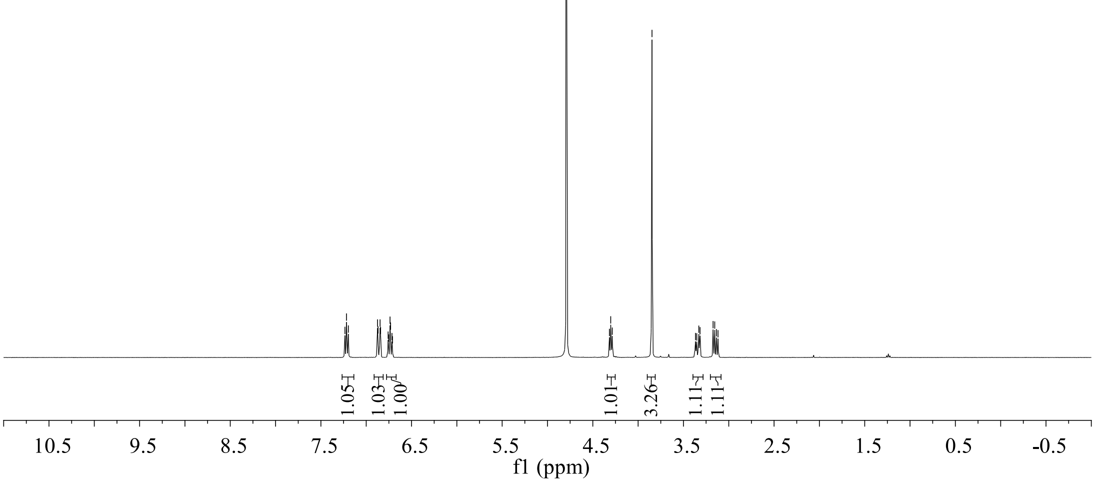

13C NMR(D2O)
OMe
F
O
OH
NH2 HCl
60-F-COOH
171.36
156.34
153.89
145.39
145.30
128.43
126.45
124.48
117.00
116.81
61.32
61.26
53.49
30.50
30.47
220 200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)


-130.50
-130.51
-130.53
-130.54
-130.54
-130.55
-130.50 -130.60
f1 (ppm)
19F NMR(D2O)
OMe
F
O
OH
NH2 HCl
60-F-COOH
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)

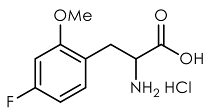
^{1}H NMR(D_2O)



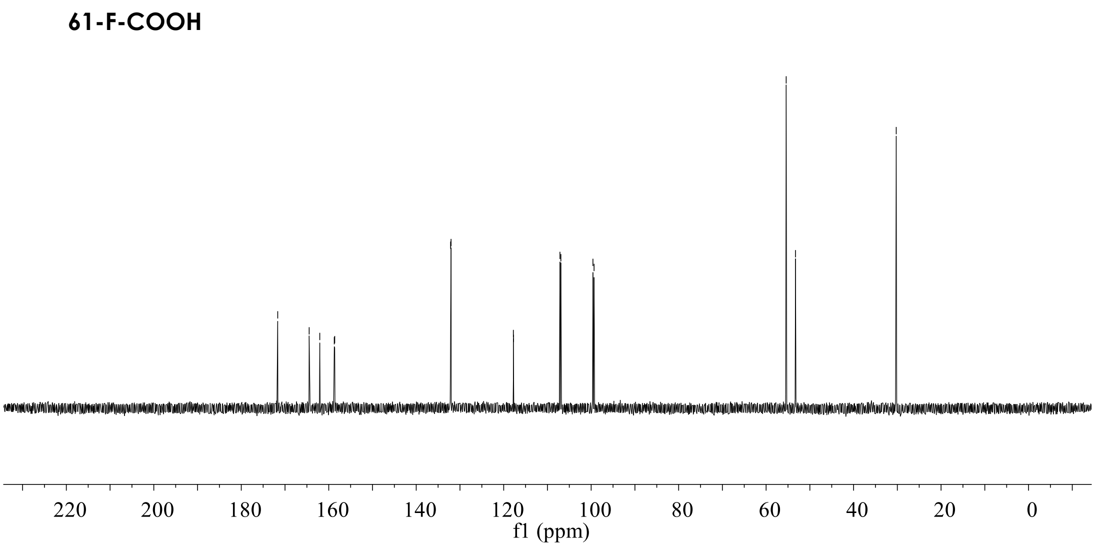
61-F-COOH

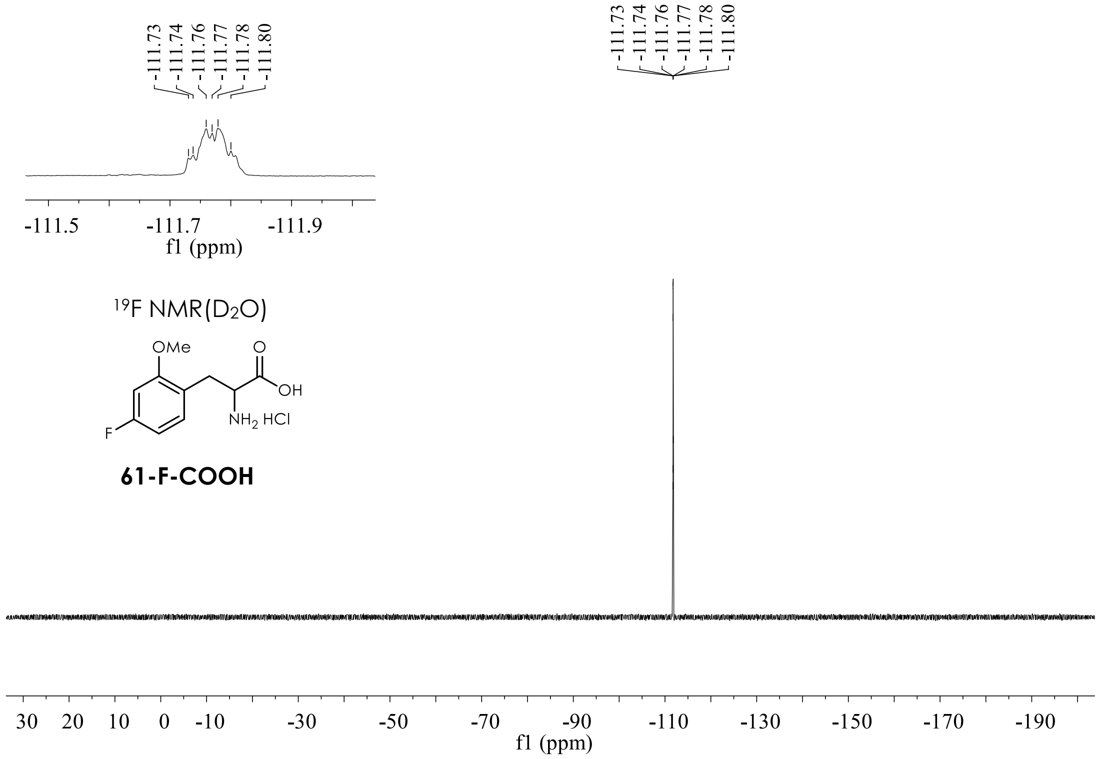


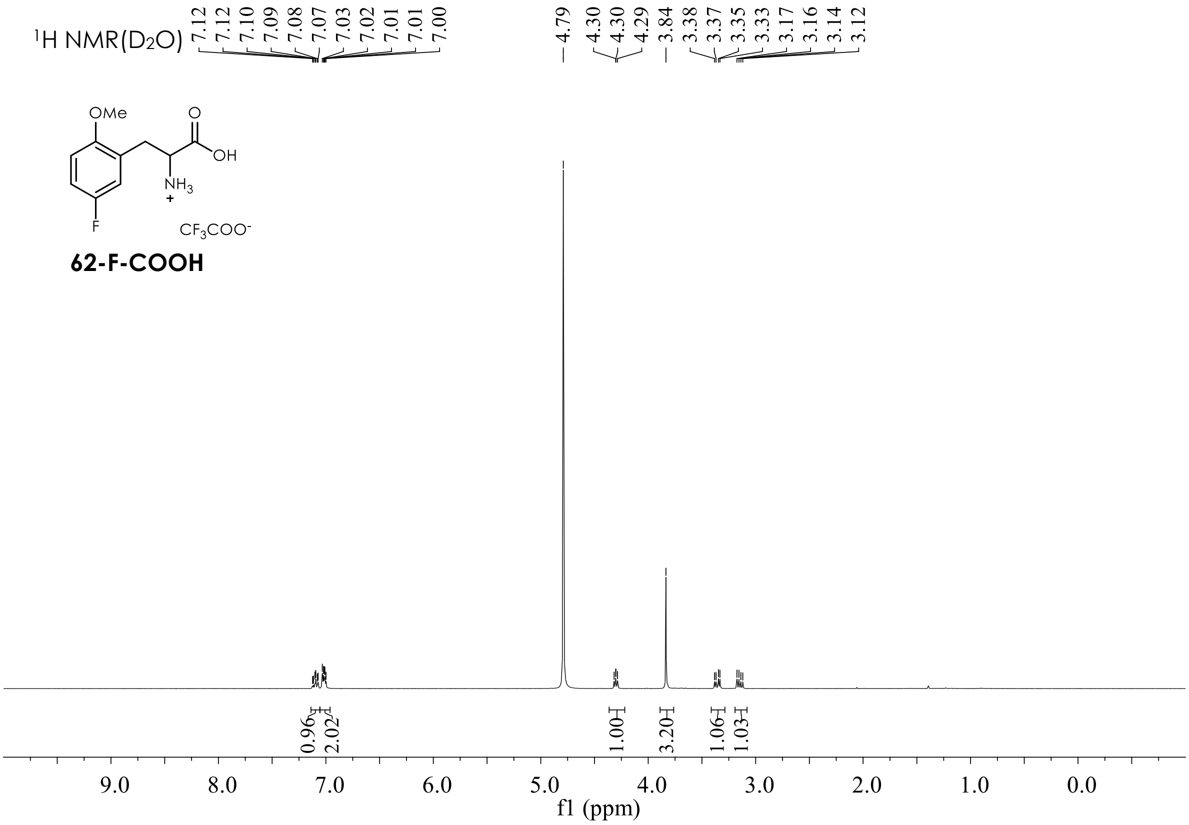
^{13}C NMR(D_2O)

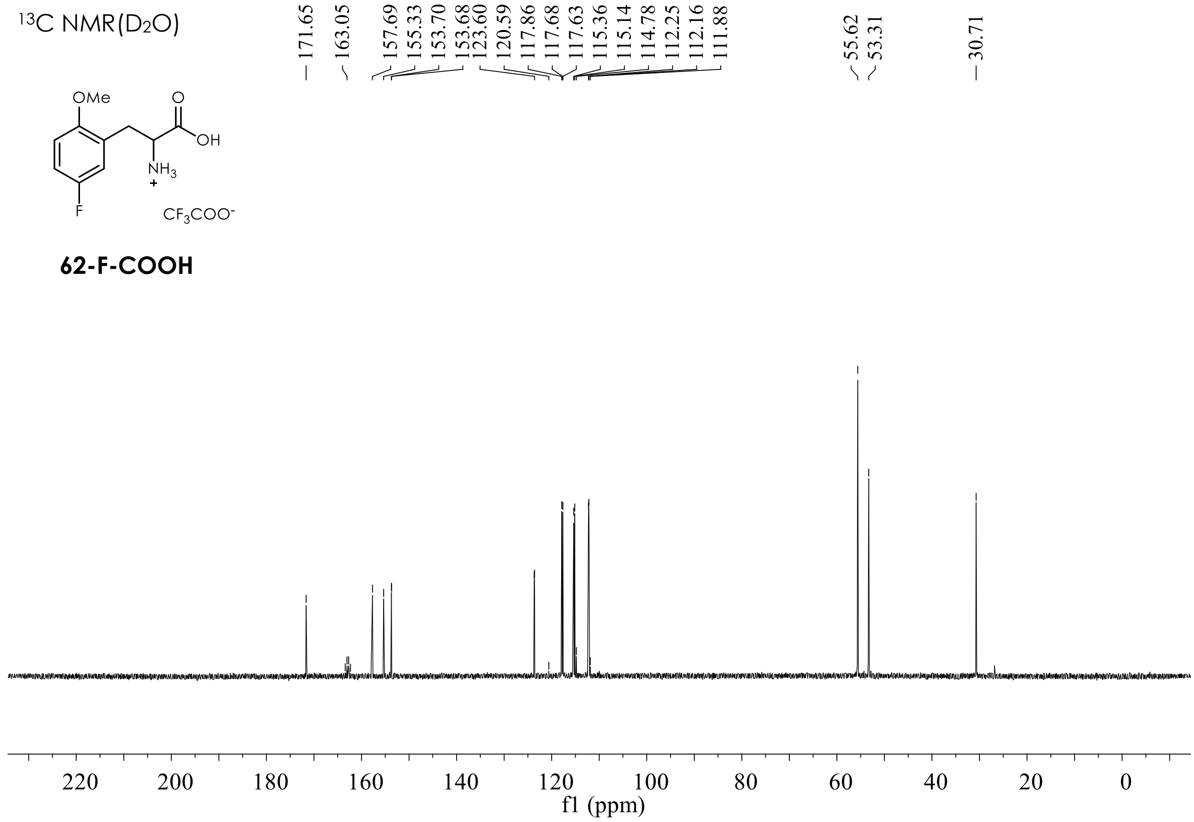


61-F-COOH

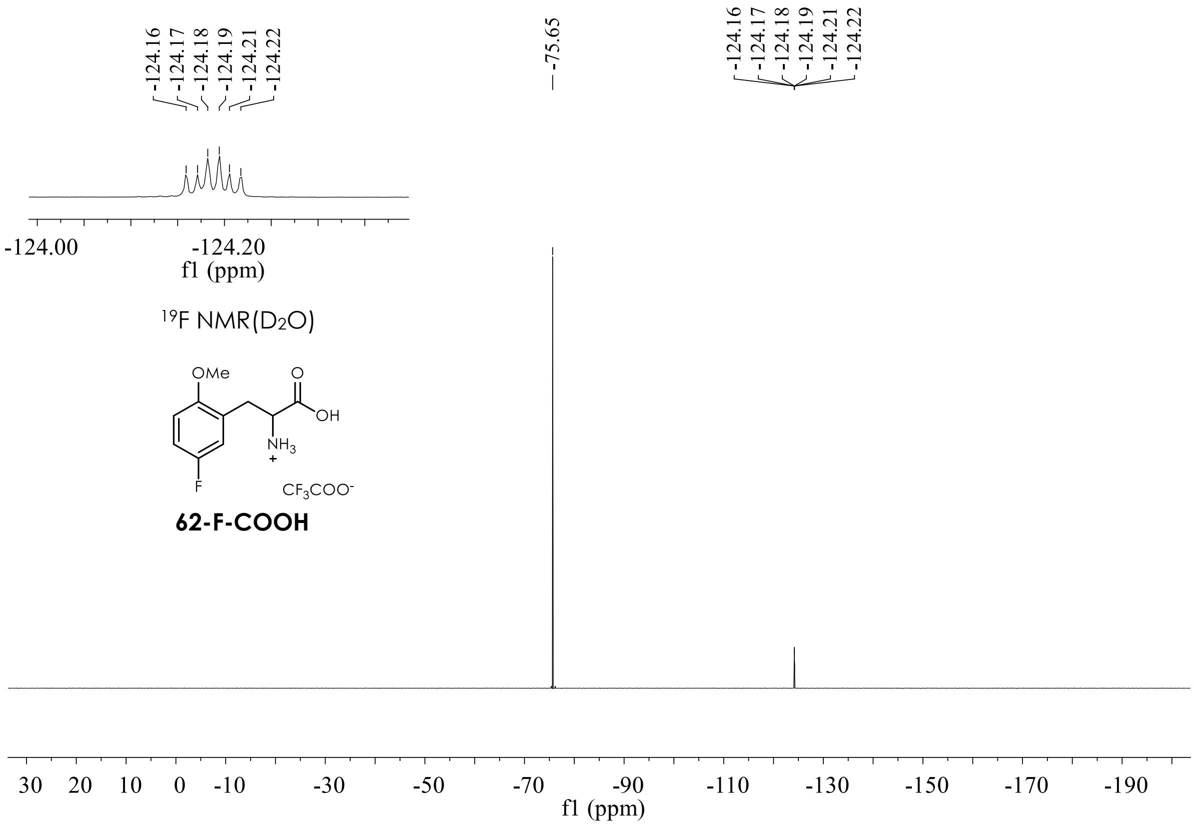



-111.73
-111.74
-111.76
-111.77
-111.78
-111.80
-111.5
-111.7
-111.9
f1 (ppm)
19F NMR(D2O)
OMe
O
OH
F
NH2 HCl
61-F-COOH
30
20
10
0
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
f1 (ppm)


1H NMR(D2O)
7.12
7.12
7.10
7.09
7.08
7.07
7.03
7.02
7.01
7.01
7.00
4.79
4.30
4.30
4.29
3.84
3.38
3.37
3.35
3.33
3.17
3.16
3.14
3.12
OMe
O
OH
NH3
+
F
CF3COO-
62-F-COOH
0.96
2.02
1.00
3.20
1.06
1.03
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

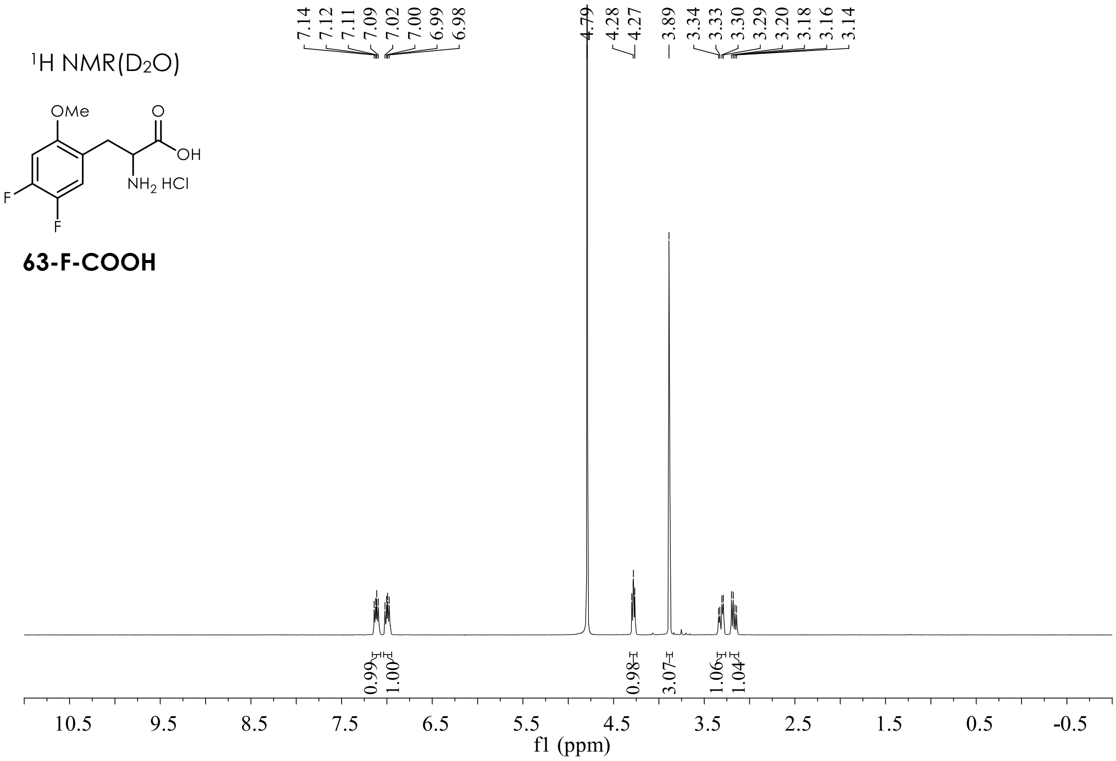


^{13}C NMR(D$_2$O)
OMe
O
OH
NH$_3$
+
F
CF$_3$COO$^-$
62-F-COOH
171.65
163.05
157.69
155.33
153.70
153.68
123.60
120.59
117.86
117.68
117.63
115.36
115.14
114.78
112.25
112.16
111.88
55.62
53.31
30.71
220 200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)



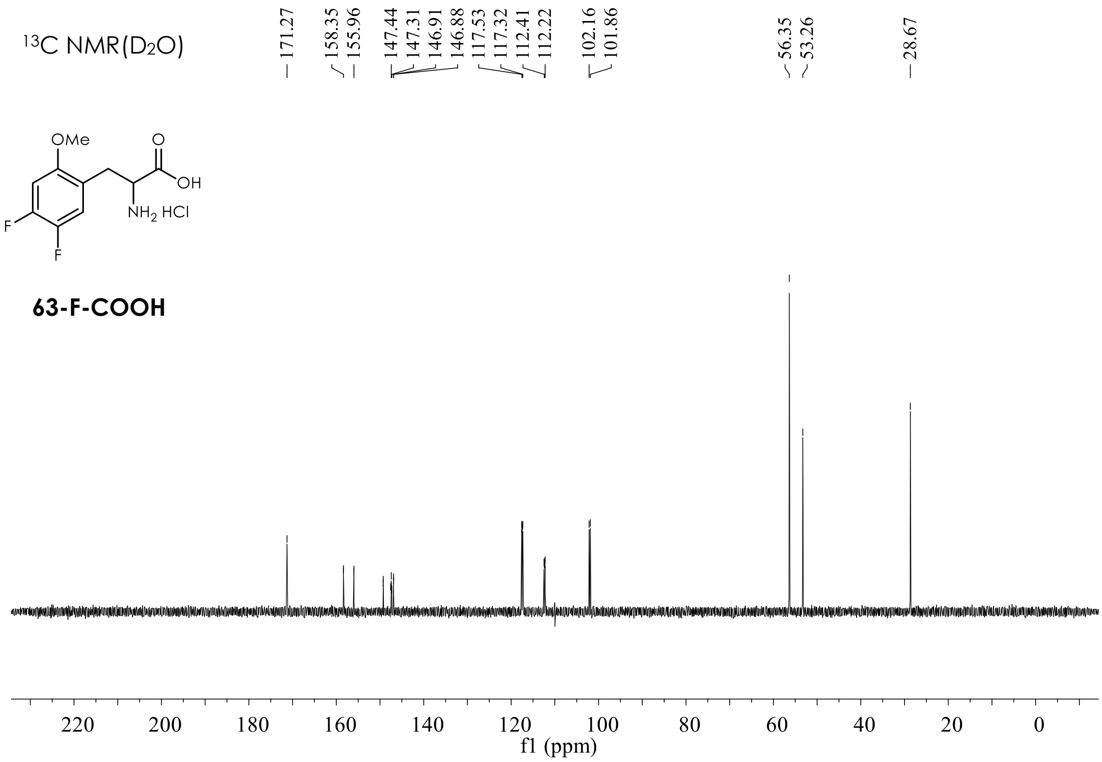
-124.16
-124.17
-124.18
-124.19
-124.21
-124.22
-124.00
-124.20
f1 (ppm)
^{19}F NMR(D$_2$O)
OMe
O
OH
NH$_3$
+
F
CF$_3$COO$^-$
62-F-COOH
-75.65
-124.16
-124.17
-124.18
-124.19
-124.21
-124.22
30 20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190
f1 (ppm)

^1H NMR(D_2O)

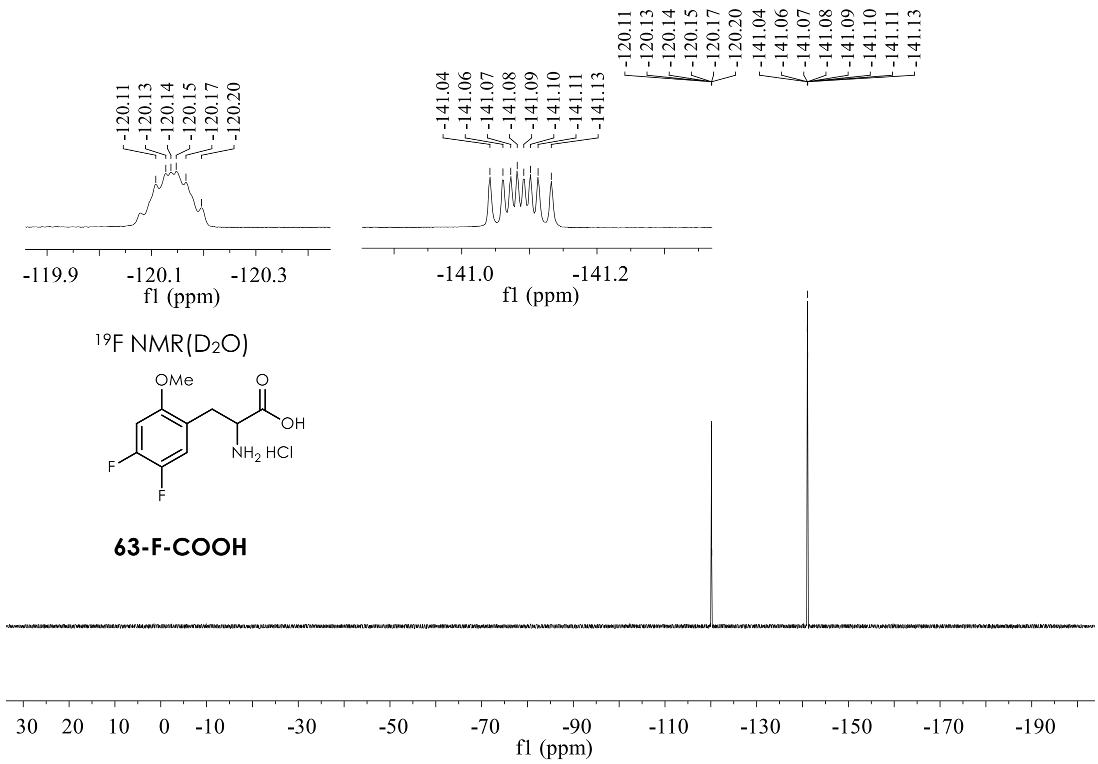


63-F-COOH

^{13}C NMR(D_2O)



63-F-COOH


-120.11
-120.13
-120.14
-120.15
-120.17
-120.20
-141.04
-141.06
-141.07
-141.08
-141.09
-141.10
-141.11
-141.13
-119.9
-120.1
-120.3
f1 (ppm)
-141.0
-141.2
f1 (ppm)
^{19}F NMR(D_2O)
OMe
O
OH
NH_2 HCl
F
F
63-F-COOH
30
20
10
0
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
f1 (ppm)