Supplementary information for

Simplified radiolabeling process toward rapid photoredox-catalyzed aryl ^{18}F-fluorination and PET tracer development

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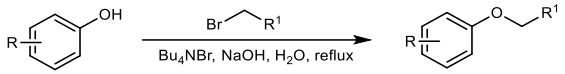
1. General information

Methods and materials: Commercially available chemicals reagents purchased from Sigma-Aldrich, TCI, Acros, J&K Scientific, Bidepharmatech, *etc* and used directly without further purification. Nuclear magnetic resonance spectra were obtained on a Bruker nuclear magnetic resonance spectrometer. 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), coupling constants (Hz), and integration. High-resolution mass spectra (HRMS) were analysed on a high-resolution quadrupole-orbitrap tandem mass spectrometer (Q-Exactive; Thermo Fisher Scientific, Waltham, MA, USA) with an electrospray ionisation (ESI) probe operated in the positive-ion mode.

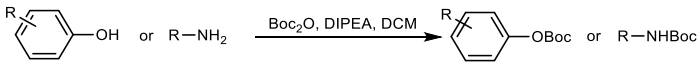
2. Preparation of arene substrates and standards

General procedures for alkyl aryl ethers (A)



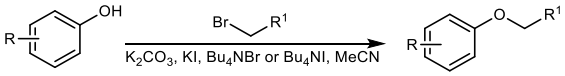
To a solution of the phenols (1 equiv.), tetrabutylammonium bromide (0.05 equiv.), NaOH (2.0 equiv.) in H_2O (15 mL) was added to the alkyl bromide (4 equiv.). The mixture was stirred under reflux overnight. The reaction was extracted with dichloromethane or ethyl acetate. The organic phase was washed with 1M NaOH solution, water, saturated brine, dried with Na_2SO_4, filtered, and concentrated in vacuo and purified by silica gel column with hexane/ethyl acetate as the eluent to give the alkyl aryl ethers.

General procedure for Boc protection of phenol or amine (B)



To a solution of phenol or amine (1.0 equiv.) in DCM (10 mL) was added DIPEA (1.5 equiv.) and di-tert-butyl 2ptimized2o (1.2 equiv.). The reaction was stirred under room temperature for 2 h and then extracted with ethyl acetate and water. The organic phase was washed with water and sat. NaCl solution, dried with Na_2SO_4, filtered, and concentrated in vacuo to give the crude product, which was purified by silica gel column with PE/EA as the eluant to give the Boc-protected phenols or amines

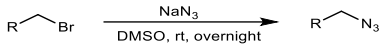
General procedures for the synthesis of alkyl aryl ethers ©



To a solution of phenol (1.0 equiv.) in MeCN (10 mL) was added K_2CO_3 (1.8 equiv.), KI (10%), Bu_4NBr (10%), and alkyl

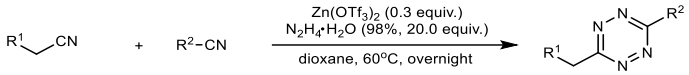
bromide or alkyl chloride (1.2 equiv.). The reaction was stirred under 80 ºC overnight and then extracted with ethyl acetate and water. The organic phase was dried with Na_2SO_4, filtered, and concentrated in vacuo to give the crude product, which was purified by a silica gel column with PE/EA as the eluant to give the alkyl aryl ethers.

General procedure for the synthesis of azides (D)



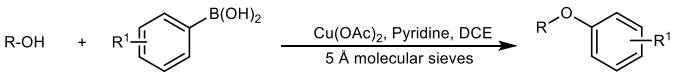
To the solution of alkyl bromide (1.0 equiv.) in DMSO (2.0 mL) was added sodium azide (1.2 equiv.). The reaction mixture was stirred at room temperature overnight. After reaction completion, as monitored by TLC, the reaction mixture was extracted with Et_2O (3 × 15 mL) and washed with brine. The combined organic extracts were dried with anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure, and the residue was purified by silica gel column chromatography (PE : EA = 30:1 to 20:1) to afford the corresponding azide products.

General procedure for the synthesis of tetrazines ©

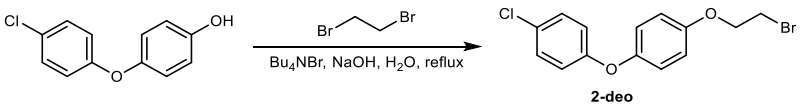


To the mixture of alkyl nitrile (1.0 equiv.), aryl nitrile (3–15 equiv.), and $Zn(Otf_3)_2$ (922 mg, 6.798 mmol, 0.3 equiv.) in 1,4-dioxane (12 mL) was added hydrazine hydrate (98%, 20.0 equiv.). The mixture was stirred at 60 °C overnight. After reaction completion, as monitored by TLC, the reaction mixture was cooled with ice water, and added DCM as cosolvent. An ice water solution of sodium nitrite (20.0 equiv.) was slowly added into the reaction mixture, followed by a slow addition of 1M HCl, during which the solution was stirred intensely and turned bright red, and gas evolved. Addition of 1M HCl continued until gas evolution ceased and the pH value was 3–4. Then, the reaction mixture was extracted with DCM (3 × 20 mL). The extract was combined, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure, and the residue was purified by silica gel column chromatography (PE : EtOAc = 20:1) to afford corresponding tetrazine as a red solid.

General procedure for the copper-catalyzed coupling of aryl boronic acid and alcohol (F)



To a solution of pyridine (1 equiv.) in DCE (2 mL) were added $Cu(Oac)_2$ (30% mmol) and 5 Å molecular sieves (300 mg). The mixture was stirred at room temperature for 5 mins. (4-fluorophenyl)boronic acid (2 equiv.) and (2S,3R,4S,5R,6R)-6-(hydroxymethyl)tetrahydro-2H-pyran-2,3,4,5-tetrayl tetraacetate (1 equiv.) were then added to the reaction. The reaction was stirred overnight at room temperature. The citric acid aqueous solution (5 mL, 1M) was added, and the reaction was extracted with dichloromethane. The organic layers were combined and washed with saturated sodium chloride aqueous solution, dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (PE: EA = 5:1) to obtain the O-arylated compounds[1]



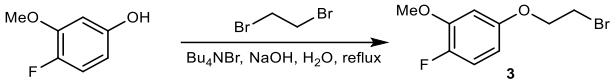
2-deo

1-(2-bromoethoxy)-4-(4-chlorophenoxy)benzene (2-deo). To a solution of 4-(4-Chlorophenoxy)phenol (1.0 g, 4.5 mmol, 1.0 equiv.), tetrabutylammonium bromide (70 mg, 0.225 mmol, 0.05 equiv.), NaOH (360 mg, 9 mmol, 2.0 equiv.) in H_2O (15 mL) was added 1,2-dibromoethane (1.56 mL, 18.1 mmol, 4 equiv.). The mixture was stirred under reflux overnight. The reaction was extracted with dichloromethane (3 × 15 mL). The organic phase was washed with 1M NaOH solution, water, saturated brine, dried with Na_2SO_4, filtered, and concentrated in vacuo and purified by silica gel column with hexane/ethyl acetate (40:1 to 20:1) as the eluent to give the **2-deo** as a white solid (0.88g, 59.3 %).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.26 – 7.24 (m, 2H), 6.96 (d, *J* = 9.1 Hz, 2H), 6.90 (d, *J* = 9.1 Hz, 2H), 6.87 (d, *J* = 8.9 Hz, 2H), 4.28 (t, *J* = 6.2 Hz, 2H), 3.64 (t, *J* = 6.2 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.09, 154.71, 150.67, 129.74, 127.71, 120.93, 119.09, 116.22, 68.62, 29.25.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{13}BrClO_2^+$: 326.9782; Found: 326.9782.



3

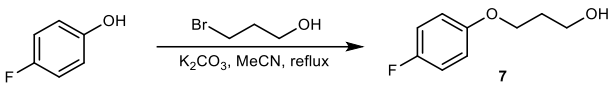
4-(2-bromoethoxy)-1-fluoro-2-methoxybenzene (**3**). To a solution of the 4-fluoro-3-methoxyphenol (1.42 g，10 mmol，1.0 equiv.) in H_2O (20 mL) was added Bu_4NBr (142 mg，10%), sodium hydroxide (800 mg，20 mmol，2.0 equiv.) and 1,2-dibromoethane (3.6 mL，80 mmol，4.0 equiv.). The reaction was stirred under reflux overnight and then extracted with ethyl acetate and water. The organic phase was dried with Na_2SO_4, filtered, and concentrated in vacuo to give the crude product, which was purified by silica gel column with PE/EA =7/1 as the eluant to give the title compound as a white solid (1.72 g, 69.1%)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.97 (dd, *J* = 11.0, 8.9 Hz, 1H), 6.57 (dd, *J* = 7.2, 2.9 Hz, 1H), 6.36 (dt, *J* = 8.9, 3.1 Hz, 1H), 4.25 (t, *J* = 6.1 Hz, 2H), 3.86 (s, 3H), 3.62 (t, *J* = 6.2 Hz, 2H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 154.62 (d, *J* = 2.3 Hz), 148.29 (d, *J* = 12.0 Hz), 147.69 (d, *J* = 238.8 Hz), 115.78 (d, *J* = 19.7 Hz), 104.60 (d, *J* = 6.6 Hz), 102.20, 68.53, 56.23, 29.12.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -144.44.

HRMS (ESI): $[M+H]^+$ Calcd for $C_9H_{11}BrFO_2^+$: 248.9921; Found: 248.9922.



7

3-(4-fluorophenoxy)propan-1-ol (7). To a solution of 4-fluorophenol (336 mg，3.0 mmol，1.0 equiv.) and 3-bromopropan-1-ol (500 mg，3.6 mmol，1.2 equiv.) in MeCN (10 mL) was added K_2CO_3 (621 mg，4.5 mmol，1.5 equiv.). The reaction

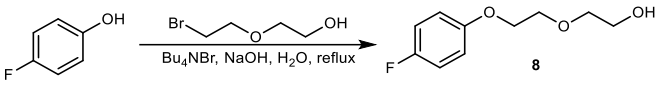
was stirred under reflux overnight and then extracted with ethyl acetate and water. The organic phase was dried with Na_2SO_4, filtered, and concentrated in vacuo to give the crude product, which was purified by silica gel column with PE/EA =5/1 as the eluant to give the title compound as a colorless oil (502 mg, 98.4%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.01 – 6.92 (m, 2H), 6.89 – 6.80 (m, 2H), 4.09 (t, *J* = 6.0 Hz, 2H), 3.86 (t, *J* = 5.9 Hz, 2H), 2.04 (p, *J* = 5.9 Hz, 2H), 1.73 (br, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 157.32 (d, *J* = 238.3 Hz), 154.90 (d, *J* = 2.1 Hz), 115.82 (d, *J* = 23.1 Hz), 115.46 (d, *J* = 8.0 Hz), 66.33, 60.38, 32.00.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -123.89.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_9H_{12}FO_2^+$: 171.0816; Found: 171.0806.



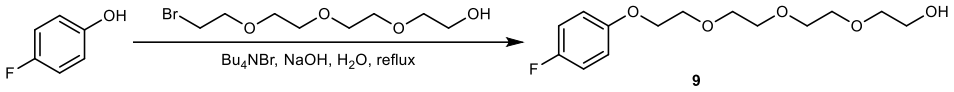
2-(2-(4-fluorophenoxy)ethoxy)ethan-1-ol (8). Following the general preparation procedure **A**, the title compound was obtained as a colourless oil (216 mg, 36%) from 4-fluorophenol (336 mg，3.0 mmol，1.0 equiv.) and 2-(2-bromoethoxy)ethan-1-ol (1.3 ml，12.0 mmol，4.0 equiv.).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.99 – 6.95 (m, 2H), 6.91 – 6.80 (m, 2H), 4.10 (dd, *J* = 5.6, 3.7 Hz, 2H), 3.86 (dd, *J* = 6.0, 3.4 Hz, 2H), 3.81 – 3.73 (m, 2H), 3.67 (t, *J* = 4.4 Hz, 2H), 2.09 (br, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 157.43 (d, *J* = 238.4 Hz), 154.79 (d, *J* = 2.1 Hz), 115.85 (d, *J* = 23.1 Hz), 115.67 (d, *J* = 8.0 Hz), 72.58, 69.70, 68.08, 61.80.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -123.62.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{10}H_{13}FO_3Na^+$: 223.0741; Found: 223.0739.



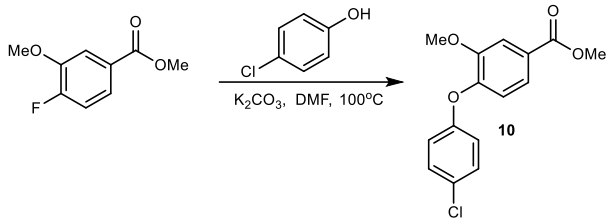
2-(2-(2-(2-(4-fluorophenoxy)ethoxy)ethoxy)ethoxy)ethan-1-ol (**9**). Following the general preparation procedure **A**, the title compound was obtained from 4-fluorophenol (336 mg，3.0 mmol，1.0 equiv.) and 2-(2-(2-(2-bromoethoxy)ethoxy)ethoxy)ethan-1-ol (921 mg，12.0 mmol，4.0 equiv.) as a colorless oil (283 mg, 32.7%).

^{1}H NMR (400 MHz, Chloroform-d) δ 7.01 – 6.91 (m, 2H), 6.90 – 6.82 (m, 2H), 4.12 – 4.07 (m, 2H), 3.86 – 3.82 (m, 2H), 3.77 – 3.65 (m, 11H), 3.63 – 3.59 (m, 2H).

^{13}C NMR (100 MHz, Chloroform-d) δ 157.36 (d, *J* = 238.1 Hz), 154.87 (d, *J* = 2.2 Hz), 115.79 (d, *J* = 18.0 Hz), 115.64 (d, *J* = 2.9 Hz), 72.55, 70.80, 70.66, 70.59, 70.32, 69.76, 68.07, 61.75.

^{19}F NMR (376 MHz, Chloroform-d) δ -123.88.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{21}FO_5Na^+$: 311.1265; Found: 311.1262.

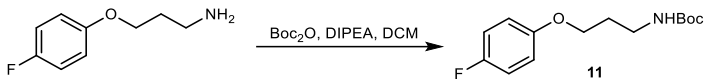


methyl 4-(4-chlorophenoxy)-3-methoxybenzoate (10). To a solution of methyl 4-fluoro-3-methoxybenzoat (920 mg，5.0 mmol，1.0 equiv.) and 4-chlorophenol (775 mg，6.0 mmol，1.2 equiv.) in DMF (10 mL) was added K_2CO_3 (1.25 g，9.0 mmol，1.8 equiv.). The reaction was stirred under 100 °C overnight and then extracted with ethyl acetate and water. The organic phase was washed with water and sat. NaCl solution dried with Na_2SO_4, filtered, and concentrated in vacuo to give the crude product, which was purified by silica gel column with PE/EA =10/1 as the eluant to give the title compound as a white solid (192 mg, 13.2%). Spectra data matched the reported literature.[2]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 (d, *J* = 1.9 Hz, 1H), 7.62 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.32 – 7.27 (m, 2H), 6.95 – 6.88 (m, 3H), 3.92 (s, 3H), 3.91 (s, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 166.51, 155.26, 150.52, 149.50, 129.77, 128.68, 126.32, 123.14, 119.67, 118.91, 113.62, 56.12, 52.24.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{14}ClO_4^+$: 293.0575; Found: 293.0573.



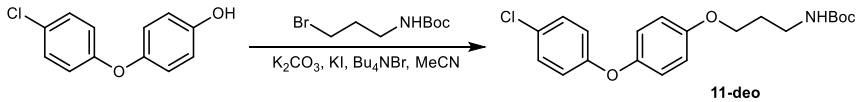
tert-butyl (3-(4-fluorophenoxy)propyl)carbamate (11). The title compound was prepared according to the general procedure **B** and obtained as a colourless oil (310 mg, 97.5%) from 3-(4-fluorophenyl) propane-1-amine (200 mg，1.2 mmol).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.96 (t, *J* = 8.6 Hz, 2H), 6.82 (dd, *J* = 9.2, 4.2 Hz, 2H), 4.75 (br, 1H), 3.98 (t, *J* = 6.0 Hz, 2H), 3.32 (q, *J* = 6.5 Hz, 2H), 1.96 (p, *J* = 6.4 Hz, 2H), 1.44 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 157.29 (d, *J* = 238.3 Hz), 156.01, 154.90 (d, *J* = 2.2 Hz), 115.92, 115.69, 115.48, 115.40, 79.26, 66.45, 38.01, 29.60, 28.41.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -123.96.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{20}FNO_3Na^+$: 292.1319; Found: 292.1319.



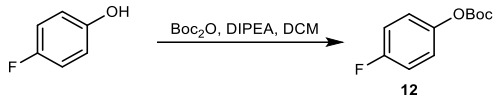
tert-butyl (3-(4-(4-chlorophenoxy)phenoxy)propyl)carbamate (11-deo). The title compound was prepared according to the

general procedure **C** and obtained as a white solid (671mg, 86.9%) from4-(4-chlorophenoxy)phenol (450 mg，2.05 mmol).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 – 7.18 (m, 2H), 7.00 – 6.91 (m, 2H), 6.91 – 6.81 (m, 4H), 4.77 (br, 1H), 4.00 (t, *J* = 6.0 Hz, 2H), 3.33 (q, *J* = 6.4 Hz, 2H), 1.98 (p, *J* = 6.3 Hz, 2H), 1.44 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 157.17, 156.01, 155.35, 149.92, 129.56, 127.40, 120.83, 118.80, 115.60, 79.26, 66.32, 38.05, 29.62, 28.43.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{24}ClNO_4Na^+$: 400.1286; Found: 400.1283.



12

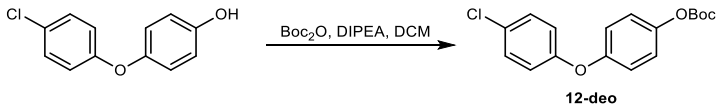
tert-butyl (4-fluorophenyl) carbonate (12). The title compound was prepared according to the general procedure **B** and obtained as a white solid (415, 97%) from 4-fluorophenol (224 mg，2.0 mmol)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.13 (ddt, *J* = 8.1, 5.9, 2.9 Hz, 2H), 7.09 – 7.00 (m, 2H), 1.55 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 160.16 (d, *J* = 244.1 Hz), 151.91, 146.96 (d, *J* = 2.9 Hz), 122.71 (d, *J* = 8.4 Hz), 115.99 (d, *J* = 23.6 Hz), 83.77, 27.68.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -117.14.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{11}H_{14}FO_3^+$: 213.0921; Found: 213.0932.



12-deo

tert-butyl (4-(4-chlorophenoxy)phenyl) carbonate(12-deo). The title compound was prepared according to the general procedure **B** and obtained as a white solid (305 mg, 95.3%) from 4-(4-chlorophenoxy)phenol (220 mg，1.0 mmol).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.26 (m, 2H), 7.17 – 7.11 (m, 2H), 7.01 – 6.96 (m, 2H), 6.96 – 6.89 (m, 2H), 1.56 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 155.98, 154.27, 152.06, 146.87, 129.77, 128.36, 122.65, 119.91, 119.70, 83.72, 27.71.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{17}ClO_4Na^+$: 343.0708; Found: 343.0701.

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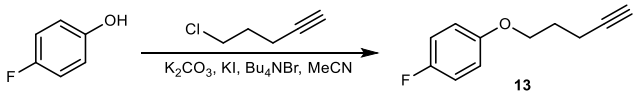


13

5- fluoro-4-(pent-4-yn-1-yloxy)benzene (13). Following the general preparation procedure of C, the title compound was obtained as a yellow liquid (152 mg, 42.7%) from 4-fluorophenol (224 mg，2.0 mmol，1.0 equiv.) and 5-chloropent-1-yne (245 mg，2.4 mmol，1.2 equiv.).

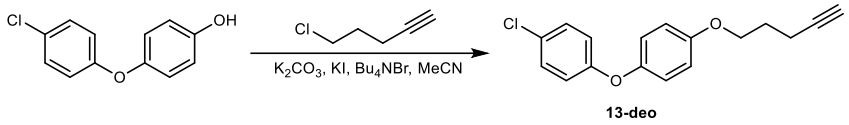
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.01 – 6.91 (m, 2H), 6.90 – 6.78 (m, 2H), 4.02 (t, *J* = 6.1 Hz, 2H), 2.40 (td, *J* = 7.0, 2.6 Hz, 2H), 2.05 – 1.97 (m, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 157.26 (d, *J* = 238.0 Hz), 155.02 (d, *J* = 2.0 Hz), 115.90, 115.67, 115.53, 115.45, 83.41,

68.92, 66.78, 28.18, 15.15.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -124.09.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{11}H_{12}FO^+$: 179.0867; Found: 179.0869.



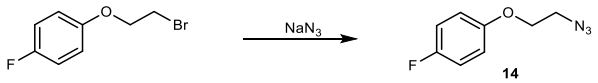
13-deo

5- chloro-4-(4-(pent-4-yn-1-yloxy)phenoxy)benzene (13-deo). Following the general preparation procedure C, the title compound was obtained from 4-(4-chlorophenoxy)phenol (450 mg，2.05 mmol，1.0 equiv.) and 5-chloropent-1-yne (251 mg，2.46 mmol，1.2 equiv.) as a white solid (420 mg, 71.8%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.24 (dd, *J* = 9.0, 2.3 Hz, 2H), 6.98 – 6.92 (m, 2H), 6.91 – 6.83 (m, 4H), 4.05 (t, *J* = 6.1 Hz, 2H), 2.42 (td, *J* = 7.0, 2.6 Hz, 2H), 2.05 – 1.98 (m, 2H), 1.97 (d, *J* = 2.6 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 157.21, 155.46, 149.85, 129.55, 127.37, 120.83, 118.79, 115.64, 83.45, 68.92, 66.63, 28.21, 15.19.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{16}ClO_2^+$: 287.0833; Found: 287.0830.



14

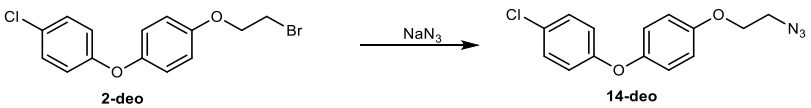
1-(2-azidoethoxy)-4-fluorobenzene (**14**). The title compound was prepared according to the general procedure **D** from 1-(2-bromoethoxy)-4-fluorobenzene (65.7 mg, 0.30 mmol, 1.0 equiv.) and obtained as a colourless oil (52.5 mg, 0.29 mmol, 97%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.04 – 6.93 (m, 2H), 6.86 (dd, *J* = 9.2, 4.3 Hz, 2H), 4.14 – 4.07 (m, 2H), 3.58 (t, *J* = 5.0 Hz, 2H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 157.62 (d, *J* = 239.0 Hz), 154.38 (d, *J* = 2.2 Hz), 116.07, 115.84, 115.76, 115.68, 67.67, 50.18.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -123.12.

HRMS (ESI) m/z: $[M]^+$ Calcd for $C_8H_8FN_3O^+$: 181.0651; Found: 181.0660.



2-deo 14-deo

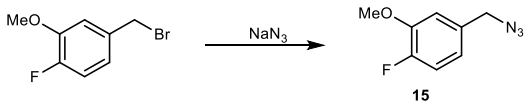
1-(2-azidoethoxy)-4-(4-chlorophenoxy)benzene (**14-deo**). The title compound was prepared according to the general procedure **D** from compound **2-deo** (98.3 mg, 0.30 mmol, 1.0 equiv.) and obtained as a colourless oil (85.2 mg, 98%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 – 7.20 (m, 2H), 7.01 – 6.93 (m, 2H), 6.93 – 6.83 (m, 4H), 4.13 (t, *J* = 5.0 Hz, 2H),

3.59 (t, *J* = 5.0 Hz, 2H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 157.01, 154.74, 150.45, 129.61, 127.55, 120.82, 118.94, 115.84, 67.53, 50.21.

HRMS (ESI) m/z: $[M]^+$ Calcd for $C_{14}H_{12}ClN_3O_2^+$: 289.0618; Found: 289.0622.



15

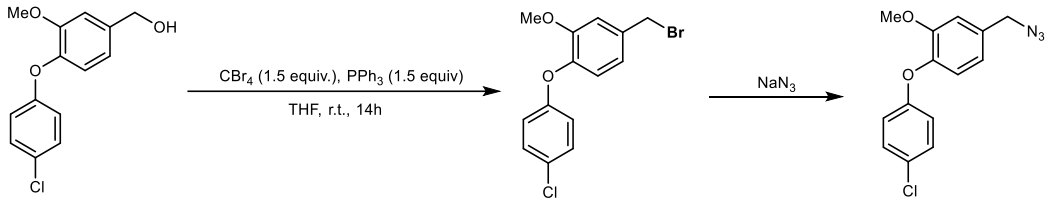
4-(azidomethyl)-1-fluoro-2-methoxybenzene (15). The title compound was prepared according to the general procedure **D** from 4-(bromomethyl)-1-fluoro-2-methoxybenzene (65.7 mg, 0.30 mmol, 1.0 equiv.) and obtained as a colourless oil (52.2 mg, 96%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.99 (dd, *J* = 11.1, 8.2 Hz, 1H), 6.84 (dd, *J* = 8.1, 2.1 Hz, 1H), 6.76 (ddd, *J* = 8.3, 4.3, 2.1 Hz, 1H), 4.22 (s, 2H), 3.83 (s, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 151.27 (d, J = 246.7 Hz), 146.91 (d, J = 11.0 Hz), 130.69 (d, J = 3.9 Hz), 119.57 (d, J = 7.2 Hz), 115.17 (d, J = 18.6 Hz), 112.23 (d, J = 2.2 Hz), 55.22, 53.41.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -135.52.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_8H_8FN_3Ona^+$: 204.0544; Found: 204.0547.



15-deo-i 15-deo-ii 15-deo

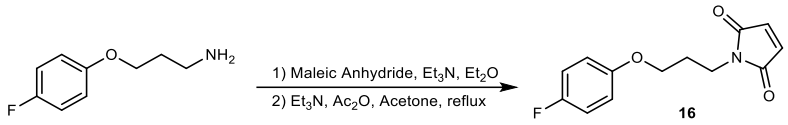
4-(bromomethyl)-1-(4-chlorophenoxy)-2-methoxybenzene (15-deo-ii). The THF (1.5 ml) solution of **15-deo-i**[2] (50.0 mg, 0.188 mmol, 1.0 equiv.), CBr_4 (93.5 mg, 0.282 mmol, 1.5 equiv.) and PPh_3 (74.0 mg, 0.282 mmol, 1.5 equiv.) were stirred at room temperature for 14 h under an argon atmosphere. After reaction completion, as monitored by TLC, the reaction mixture was poured into petroleum ether (PE, 10 mL), filtered, and concentrated under reduced pressure and the residue was purified by silica gel column chromatography (PE : EtOAc = 10:1) to afford the title compound as a colourless oil (59.2 mg, 96%).

4-(azidomethyl)-1-(4-chlorophenoxy)-2-methoxybenzene (**15-deo**). The title compound was prepared according to the general procedure **D** from compound **15-deo-ii** (49.1 mg, 0.15 mmol, 1.0 equiv.) and obtained as a colourless oil (41.7 mg, 0.144 mmol, 96%

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 – 7.20 (m, 2H), 6.96 (d, *J* = 7.6 Hz, 2H), 6.91 – 6.83 (m, 3H), 4.34 (s, 2H), 3.85 (s, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 156.38, 151.54, 144.71, 132.50, 129.53, 127.65, 121.08, 120.88, 118.47, 112.63, 56.03, 54.62.

HRMS (ESI) m/z: $[M]^+$ Calcd for $C_{14}H_{12}ClN_3O_2^+$: 289.0618; Found: 289.0624.



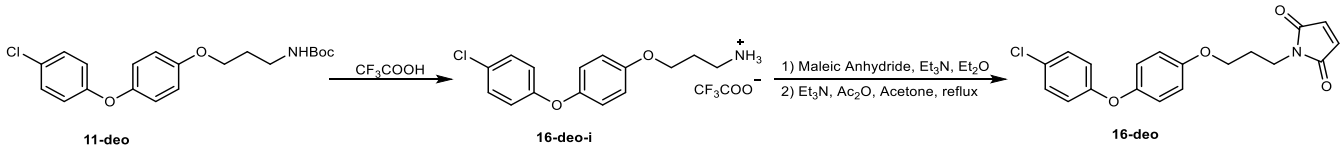
1-(3-(4-fluorophenoxy)propyl)-1H-pyrrole-2,5-dione(**16**). 3-(4-fluorophenoxy)propylamine (340 mg, 2.0 mmol, 1.0 equiv.) was dissolved in ether (10 mL) and cooled to 0°C. Triethylamine (420 μL, 2.4 mmol, 1.2 equiv.) and maleic anhydride (235 mg, 2.4 mmol, 1.2 equiv.) in ether solution (10 mL) were added, and the reaction was allowed to proceed at room temperature for 3 hours. The reaction mixture was filtered, and the filtrate was dissolved in acetone (10 mL). Triethylamine (420 μL, 2.4 mmol, 1.2 equiv.) and acetic anhydride (283 μL, 3.0 mmol, 1.5 equiv.) were added to the reaction mixture, and the reaction was stirred under reflux for 20 hours. The solvent was evaporated, and the residue was dissolved in ethyl acetate (30 mL). The solution was successively washed with saturated sodium bicarbonate, 1 M hydrochloric acid, and saturated saline solution, dried over anhydrous sodium sulfate, filtered, and the solvent was evaporated under reduced pressure. The product was purified by silica gel column chromatography (DCM: MeOH = 30:1) to yield the title compound as a white solid (365 mg, 52.8%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.01 – 6.90 (m, 2H), 6.84 – 6.75 (m, 2H), 6.70 (s, 2H), 3.93 (t, *J* = 6.0 Hz, 2H), 3.74 (t, *J* = 6.9 Hz, 2H), 2.14 – 1.99 (m, 2H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.76, 157.34 (d, *J* = 238.3 Hz), 154.83 (d, *J* = 2.2 Hz), 134.19, 115.90, 115.67, 115.58, 115.50, 66.17, 35.32, 28.29.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -123.88.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{13}H_{13}FNO_3^+$: 250.0874; Found: 250.0871.



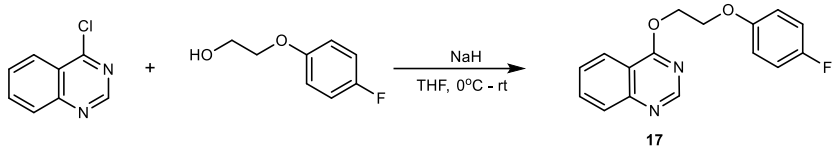
1-(3-(4-(4-chlorophenoxy)phenoxy)propyl)-1H-pyrrole-2,5-dione (**16-deo**). To a solution of compound **11-deo** (300 mg，0.79 mmol，1.0 equiv.) in DCM (20 mL), TFA (5ml) was added. The solution was stirred at room temperature for 5h. The solvent and TFA were evaporated under reduced pressure. The residue was dissolved in ether (20 mL) and cooled to 0°C. Triethylamine (625 μl, 3.57 mmol, 1.5 equiv.) and maleic anhydride (280 mg, 2.86 mmol, 1.2 equiv.) in ether solution (10 mL) were added, and the reaction was allowed to proceed at room temperature for 4 hours. The reaction mixture was filtered, and the filtrate was dissolved in acetone (10 ml). Triethylamine (420 μl, 2.4 mmol, 1.2 equiv.) and acetic anhydride (283 μl, 3.0 mmol, 1.5 equiv.) were added to the reaction mixture, and the reaction was stirred under reflux for 20 hours. The solvent was evaporated, and the residue was dissolved in ethyl acetate (30 ml). The solution was successively washed with saturated sodium bicarbonate, 1 M hydrochloric acid, and saturated saline solution, dried over anhydrous sodium sulfate, filtered, and the solvent was evaporated under reduced pressure. The product was purified by silica gel column chromatography (DCM : MeOH = 30:1)

to yield the title compound as a white solid (407 mg, 47.8%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 – 7.20 (m, 2H), 6.96 – 6.90 (m, 2H), 6.89 – 6.81 (m, 4H), 6.71 (s, 2H), 3.96 (t, *J* = 6.0 Hz, 2H), 3.75 (t, J = 6.9 Hz, 2H), 2.13 – 2.05 (m, 2H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.77, 157.14, 155.26, 149.97, 134.20, 129.55, 127.39, 120.77, 118.84, 115.68, 66.04, 35.36, 28.32.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{16}ClNO_4Na^+$: 380.0660; Found: 380.0658.



17

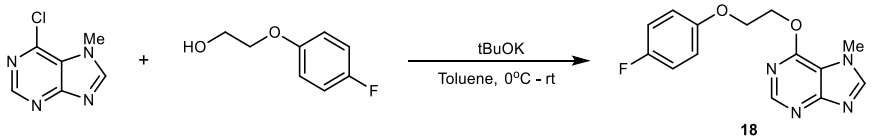
4-(2-(4-fluorophenoxy)ethoxy)quinazoline (17). A solution of 2-(4-Fluorophenoxy)ethanol (117 mg, 0.75 mmol, 1 equiv.) in dry THF (10 mL) was stirred at 0 °C for 15 min. Then, NaH (0.08g，3 mmol，4 equiv.) was added. The mixture was stirred at room temperature for 40 min. The mixture was cooled down to 0 °C, and 4-chloroquinozoline (123 mg, 0.75 mmol，1 equiv.) in dry THF (5 mL) was added. The reaction was stirred at room temperature overnight. The reaction was quenched with saturated aqueous NH_4Cl and extracted with EtOAc (3 × 15mL). The organic phase was washed with saturated brine, dried with Na_2SO_4, filtered, and concentrated in vacuo and purified by silica gel column with hexane/ethyl acetate (6:1) as the eluent to give the title compound as a white solid (130 mg, 61.0%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.81 (s, 1H), 8.17 (d, *J* = 9.1 Hz, 1H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.83 (t, *J* = 8.4 Hz, 1H), 7.55 (t, *J* = 8.1 Hz, 1H), 7.03 – 6.96 (m, 2H),6.92 – 6.89 (m, 2H), 4.92 (t, *J* = 4.7 Hz, 2H), 4.40 (t, *J* = 4.7 Hz, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.59, 157.65 (d, *J* = 238.8 Hz), 154.87 (d, *J* = 2.1 Hz), 154.28, 151.19, 133.83, 127.84, 127.26, 123.71, 116.64, 116.07 (d, *J* = 17.3 Hz), 115.92 (d, *J* = 2.1 Hz), 66.86, 65.52.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -123.30.

HRMS (ESI): Calculated for $C_{16}H_{14}FN_2O_2^+$ $[M+H]^+$: 285.1034; Found:285.1033.



18

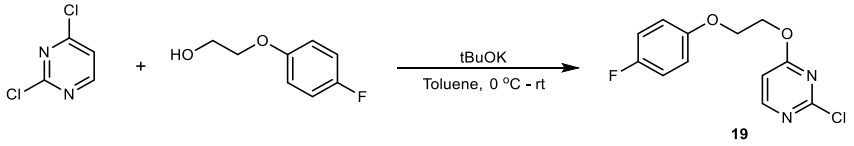
6-(2-(4-fluorophenoxy)ethoxy)-7-methyl-7H-purine (**18**). A mixture of potassium *tert*-butoxide (160 mg，1.4 mmol，2 equiv.) in toluene (6 ml) was treated with 2-(4-Fluorophenoxy)ethanol（109 mg,0.7 mmol, 1equiv.）dropwise at 0 °C. After 5 min, 6-chloro-7-methylpurine (118 mg,0.7 mmol, 1 equiv.) was added to the mixture. The reaction mixture was stirred at room temperature for 5 h. The reaction was quenched with saturated aqueous NH_4Cl and extracted with EtOAc (3 × 15mL). The organic phase was washed with saturated brine, dried with Na_2SO_4, filtered, and concentrated in vacuo, and purified by silica gel column with DCM/MeOH (40:1 to 15:1) as the eluent to give the title compound as a white solid (137 mg, 67.9 %).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.62 (s, 1H), 7.97 (s, 1H), 7.01 – 6.94 (m, 2H), 6.91 – 6.85 (m, 2H), 4.91 (t, *J* = 4.6 Hz, 3H), 4.37 (t, *J* = 4.6 Hz, 3H), 4.00 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 161.99,157.60 (d, *J* = 239.0 Hz), 156.88, 154.77 (d, *J* = 2.1 Hz), 152.13, 146.25, 116.06 (d, *J* = 23.2 Hz), 115.77 (d, *J* = 8.0 Hz)., 113.62, 66.80, 65.25, 34.17.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -123.18.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{14}FN_4O_2^+$: 289.1095; Found:289.1094.



19

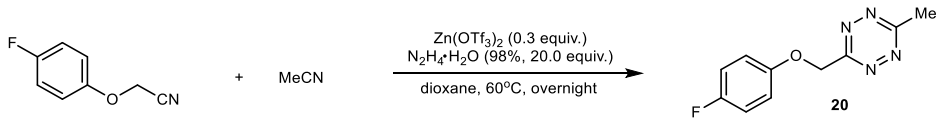
2-chloro-4-(2-(4-fluorophenoxy)ethoxy)pyrimidine (19). Following the same preparation procedure of compound **18**, the title compound was obtained as a yellow solid (0.063 g,31.3 %) from 2-(4-Fluorophenoxy)ethanol (117 mg, 0.75mmol, 1 equiv.) and 2,4-dichloropyrimidine (134 mg, 0.9 mmol,1.2 equiv.).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.32 (d, *J* = 5.7 Hz, 1H), 7.03 – 6.95 (m, 2H), 6.91 – 6.85 (m, 2H), 6.73 (d, *J* = 5.7 Hz, 1H), 4.74 (t, *J* = 4.9 Hz, 3H), 4.28 (t, *J* = 4.7 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.20, 160.26, 159.16,157.69 (d, *J* = 239.0 Hz), 154.62 (d, *J* = 2.1 Hz), 116.07 (d, *J* = 23.2 Hz), 115.84 (d, *J* = 8.0 Hz), 107.49, 66.48, 65.80.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -123.17.

HRMS (ESI): Calculated for $C_{12}H_{11}ClFN_2O_2^+$ $[M+H]^+$: 269.0488 Found: 269.0488.



20

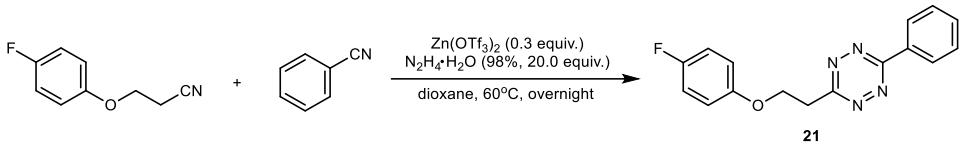
3-((4-fluorophenoxy)methyl)-6-methyl-1,2,4,5-tetrazine (**20**). The title compound was prepared according to the general procedure E from 2-(4-fluorophenoxy)acetonitrile (682 mg, 4.51 mmol, 1.0 equiv.) and MeCN (3.5 mL, 67.65 mmol, 15.0 equiv.). The title compound was obtained as a red solid (29.8 mg, 3%)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.93 (s, 2H), 6.92 – 6.88 (m, 2H), 5.54 (s, 2H), 3.03 (s, 3H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.77, 164.49, 156.92 (d, J = 240.0 Hz), 153.00 (d, J = 2.3 Hz), 115.24 (d, *J* = 8.3 Hz), 67.49, 20.31.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -122.18.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{10}H_{10}FN_4O^+$: 221.0833 ; Found: 221.0835.



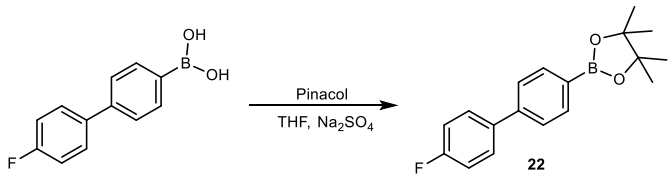
3-(2-(4-fluorophenoxy)ethyl)-6-phenyl-1,2,4,5-tetrazine (**21**). The title compound was prepared according to the general procedure **E** from compound 3-(4-fluorophenoxy)propanenitrile[3] (661 mg, 4.0 mmol, 1.0 equiv.) and benzonitrile (1.2 mL, 12.0 mmol, 3.0 equiv.). The compound **21** was obtained as a red solid (23.8 mg, 2%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.57 – 8.49 (m, 2H), 7.53 (ddt, *J* = 11.1, 8.7, 4.8 Hz, 3H), 6.92 – 6.82 (m, 2H), 6.81 – 6.71 (m, 2H), 4.54 (t, *J* = 6.4 Hz, 2H), 3.75 (t, *J* = 6.3 Hz, 2H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 166.38, 163.51, 156.49 (d, *J* = 238.8 Hz), 153.44 (d, *J* = 2.2 Hz), 131.75, 130.61, 128.26, 127.03, 114.90 (d, *J* = 12.4 Hz) 114.74 (d, *J* = 2.7 Hz), 64.83, 33.97.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -123.25.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{14}FN_4O^+$: 297.1146 ; Found: 297.1144.



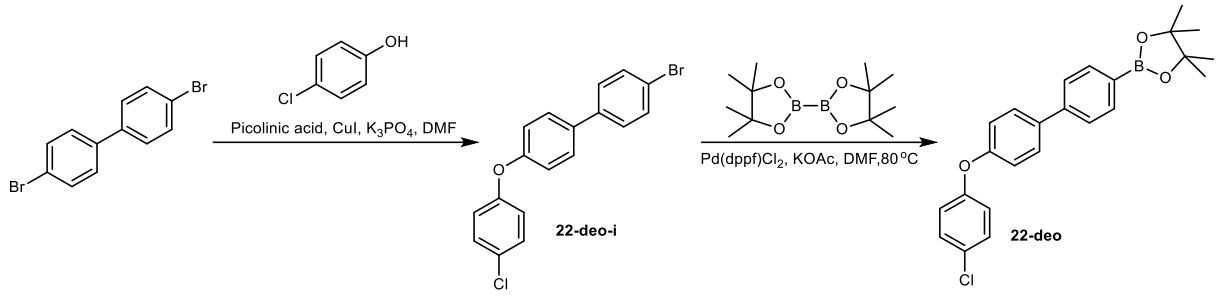
2-(4'-fluoro-[1,1'-biphenyl]-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (22). To a solution of 4-(4-fluorophenyl)phenylboronic acid (200 mg, 1.0 equiv.) in 5 mL of anhydrous tetrahydrofuran was added pinacol (110 mg, 1.0 equiv.) add anhydrous sodium sulfate (238 mg, 1.8 equiv.). The mixture was stirred at room temperature overnight under nitrogen. After the reaction was completed, as monitored by the thin layer chromatography, the reaction was concentrated under reduced pressure and purified by silica gel column chromatography (petroleum ether: ethyl acetate = 8:1) to give the title compound as a white solid (149 mg, 53.7%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.87 (d, *J* = 7.8 Hz, 2H), 7.59 – 7.52 (m, 4H), 7.12 (t, *J* = 8.6 Hz, 2H), 1.36 (s, 12H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 162.66 (d, *J* = 246.7 Hz), 142.88, 137.14 (d, *J* = 3.2 Hz), 135.33, 128.81 (d, *J* = 8.0 Hz), 126.31, 115.66 (d, *J* = 21.4 Hz), 83.88, 24.90.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -115.31.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{21}BFO_2^+$: 299.1613 ; Found: 299.1613 .



4-bromo-4'-(4-chlorophenoxy)-1,1'-biphenyl (22-deo-i). 4,4'-Dibromobiphenyl (1.0 g, 3.21 mmol, 1.0 equiv.), 4-chlorophenol (495 mg, 3.85 mmol, 1.2 equiv.), 2-formylpyridine (473 mg, 3.85 mmol, 1.2 equiv.), cuprous iodide (366 mg, 1.93 mmol, 0.5 equiv.), copper powder (197 mg, 3.08 mmol, 0.8 equiv.), and potassium phosphate (816 mg, 3.85 mmol, 1.2 equiv.) were dissolved in DMF (20 ml) under nitrogen protection. The reaction mixture was then heated at 100 °C overnight. After the reaction mixture was cooled to room temperature, water (20 ml) was added and extracted with ethyl acetate. The combined organic layers were washed with a saturated sodium chloride solution, dried over anhydrous sodium sulfate, filtered, and the solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (PE: EA = 10:1) to yield the title compound as a white solid (395 mg, 34.3%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60 – 7.48 (m, 4H), 7.46 – 7.39 (m, 2H), 7.35 – 7.28 (m, 2H), 7.09 – 7.03 (m, 2H), 7.02 – 6.93 (m, 2H).

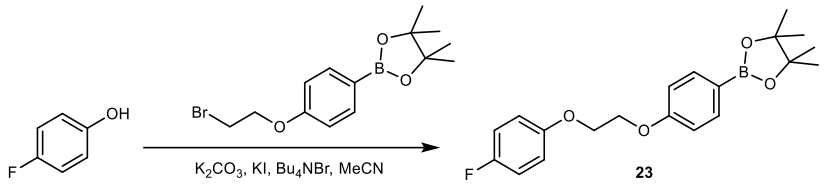
^{13}C NMR (100 MHz, Chloroform-*d*) δ 156.81, 155.68, 139.32, 135.42, 131.93, 129.83, 129.78, 128.83, 128.56, 128.50, 128.39, 127.16, 126.93, 121.39, 120.27, 120.17, 119.15, 119.12.

2-(4'-(4-chlorophenoxy)-[1,1'-biphenyl]-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (22-deo). Compound **22-deo-©** (100 mg, 0.28 mmol, 1.0 equiv.), boronic acid pinacol ester (269 mg, 1.12 mmol, 4.0 equiv.), $Pd(dppf)Cl_2$ (20 mg, 0.028 mmol, 0.1 equiv.) and potassium acetate (136 mg, 1.4 mmol, 5.0 equiv.) were dissolved in DMF (5 ml) under nitrogen protection. The reaction mixture was then heated at 100°C overnight. After cooling the reaction to room temperature, water was added, and the mixture was extracted with ethyl acetate. The combined organic layers were washed with a saturated sodium chloride solution, dried over anhydrous sodium sulfate, filtered, and the solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (PE: EA = 15:1) to yield the title compound as a milky white solid (76 mg, 67.3%).

^{1}H NMR (400 MHz, Chloroform-d) δ 7.90 – 7.85 (m, 2H), 7.61 – 7.56 (m, 4H), 7.34 – 7.27 (m, 2H), 7.08 – 7.04 (m, 2H), 7.01 – 6.95 (m, 2H), 1.36 (s, 12H).

^{13}C NMR (100 MHz, Chloroform-d) δ 156.69, 155.83, 143.03, 136.49, 135.33, 129.79, 128.66, 128.41, 126.20, 120.18, 119.12, 83.86, 24.90.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{24}H_{25}BClO_3^+$: 407.1580 ; Found: 407.1576.



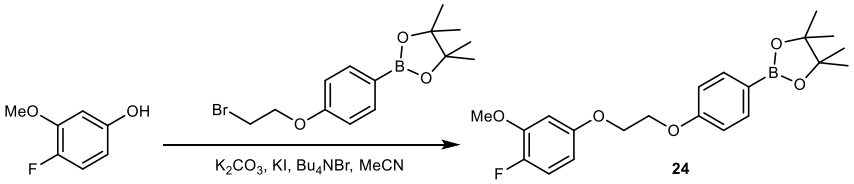
2-(4-(2-(4-fluorophenoxy)ethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**23**). The title compound was prepared according to the general procedure **C** from 4-fluorophenol (112 mg，1.0 mmol，1.0 equiv.) and 2-(4-(2-bromoethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (392 mg，1.2 mmol，1.2 equiv.), and obtained as a white liquid (215 mg, 55.4%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.79 – 7.72 (m, 2H), 7.02 – 6.91 (m, 4H), 6.91 – 6.85 (m, 2H), 4.37 – 4.23 (m, 4H), 1.33 (s, 12H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 161.16, 157.50 (d, *J* = 238.6 Hz), 154.77 (d, *J* = 2.2 Hz), 136.57, 121.08, 115.98, 115.87, 115.79, 115.75, 113.99, 83.62, 67.22, 66.28, 24.88.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -123.48.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{24}BFO_4Na^+$: 381.1644; Found: 381.1642.



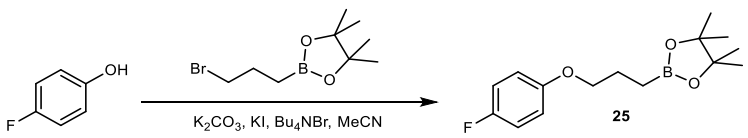
2-(4-(2-(4-fluoro-3-methoxyphenoxy)ethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**24**). The title compound was prepared according to the general procedure **C** from the 4-fluoro-3-methoxyphenol (71 mg，0.5 mmol，1.0 equiv.) and 2-(4-(2-bromoethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (196 mg，0.6 mmol，1.2 equiv.), and obtained as a white liquid (113 mg, 58.5%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.80 – 7.73 (m, 2H), 7.01 – 6.90 (m, 3H), 6.60 (dd, *J* = 7.2, 2.9 Hz, 1H), 6.41 (dt, *J* = 8.9, 3.1 Hz, 1H), 4.33 (dd, *J* = 6.2, 3.7 Hz, 2H), 4.28 (dd, *J* = 5.7, 3.4 Hz, 2H), 3.85 (s, 3H), 1.33 (s, 12H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 161.12, 155.14 (d, *J* = 2.2 Hz), 148.18 (d, *J* = 12.0 Hz), 147.51 (d, *J* = 238.3 Hz), 136.62, 136.56, 121.43, 115.69 (d, *J* = 19.7 Hz), 113.98, 104.44 (d, *J* = 6.6 Hz), 102.12 (d, *J* = 1.7 Hz), 83.61, 67.13, 66.25, 56.18, 24.86.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -145.00.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{26}BFO_5Na^+$: 411.1750; Found: 411.1750.



2-(3-(4-fluorophenoxy)propyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (25). The title compound was prepared according

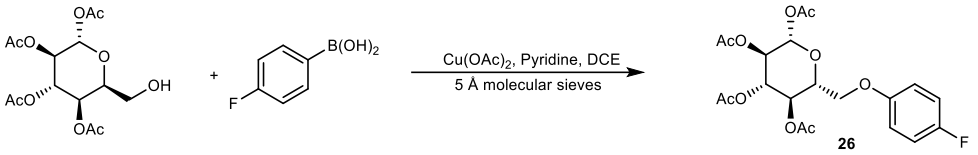
to the general procedure **C** from 4-fluorophenol (112 mg，1.0 mmol，1.0 equiv.) and 2-(3-bromopropyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (298 mg，1.2 mmol，1.2 equiv.), and obtained as a colorless liquid (108 mg, 38.5%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.99 – 6.90 (m, 2H), 6.87 – 6.77 (m, 2H), 3.89 (t, *J* = 6.7 Hz, 2H), 1.94 – 1.81 (m, 2H), 1.25 (s, 12H), 0.91 (t, *J* = 7.8 Hz, 2H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 157.08 (d, *J* = 237.6 Hz), 155.30 (d, *J* = 2.1 Hz), 115.77, 115.56, 115.54, 115.48, 83.12, 70.29, 53.43, 24.84, 23.76.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -124.61.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{23}BFO_3^+$: 281.1719; Found: 281.1723.



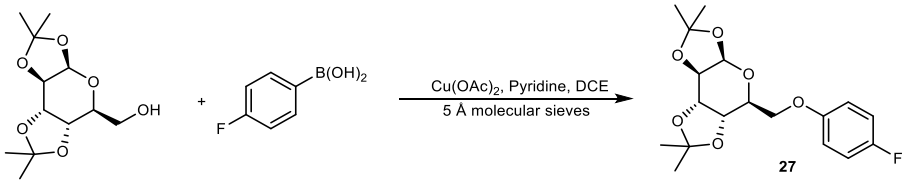
(2S,3R,4S,5R,6R)-6-((4-fluorophenoxy)methyl)tetrahydro-2H-pyran-2,3,4,5-tetrayl tetraacetate(**26**). The title compound was prepared according to the general procedure **F** from (2S,3R,4S,5R,6R)-6-(hydroxymethyl)tetrahydro-2H-pyran-2,3,4,5-tetrayl tetraacetate (157 mg，0.45 mmol, 1 equiv.) and (4-fluorophenyl)boronic acid (126 mg, 0.90 mmol, 2 equiv.), and obtained as a white solid (36 mg, 19.0%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.99 – 6.91 (m, 2H), 6.86 – 6.79 (m, 2H), 5.76 (d, J = 8.2 Hz, 1H), 5.33 – 5.25 (m, 2H), 5.21 – 5.13 (m, 1H), 4.12 – 4.05 (m, 1H), 4.00 – 3.93 (m, 2H), 2.11 (s, 3H), 2.04 (s, 3H), 2.03 (s, 3H), 2.01 (s, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.18, 169.39, 169.26, 169.02, 157.66 (d, *J* = 239.1 Hz), 154.42 (d, *J* = 2.2 Hz), 116.00 (d, *J* = 3.2 Hz), 115.84 (d, J = 18.3 Hz), 91.76, 73.23, 72.87, 70.31, 68.58, 67.25, 20.82, 20.61, 20.58.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -123.01.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{23}FO_{10}Na^+$: 465.1167; Found: 465.1164.



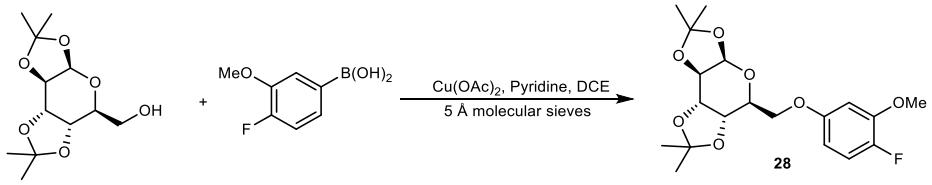
(3aR,5S,5aS,8aS,8bR)-5-((4-fluorophenoxy)methyl)-2,2,7,7-tetramethyltetrahydro-5H-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran(27). The title compound was prepared according to the general procedure **F** from ((3aR,5S,5aS,8aS,8bR)-2,2,7,7-tetramethyltetrahydro-5H-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran-5-yl)methanol (117 mg，0.45 mmol) and (4-fluorophenyl)boronic acid (126 mg，0.90 mmol), and obtained as a white solid (43 mg, 24.1%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.00 – 6.92 (m, 2H), 6.92 – 6.84 (m, 2H), 5.57 (d, *J* = 5.0 Hz, 1H), 4.65 (dd, *J* = 7.9, 2.5 Hz, 1H), 4.39 – 4.30 (m, 2H), 4.21 – 4.01 (m, 3H), 1.51 (s, 3H), 1.47 (s, 3H), 1.36 (s, 3H), 1.34 (s, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 157.41 (d, *J* = 238.2 Hz), 154.72 (d, *J* = 2.1 Hz), 115.92 (d, *J* = 8.0 Hz), 115.72 (d, *J* = 23.0 Hz), 109.49, 108.75, 96.39, 70.99, 70.65, 70.60, 67.37, 66.17, 26.03, 26.00, 24.95, 24.46.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -123.83.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{23}FO_6Na^+$: 377.1371; Found: 377.1366.



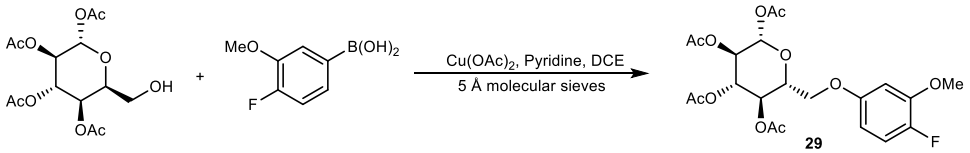
(3aR,5S,5aS,8aS,8bR)-5-((4-fluoro-3-methoxyphenoxy)methyl)-2,2,7,7-tetramethyltetrahydro-5H-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran (28). The title compound was prepared according to the general procedure **F** from ((3aR,5S,5aS,8aS,8bR)-2,2,7,7-tetramethyltetrahydro-5H-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran-5-yl)methanol (117 mg，0.45 mmol) and (4-fluoro-3-methoxyphenyl)boronic acid (153 mg，0.90 mmol), and obtained as a white solid (52 mg, 27.2%)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.95 (dd, *J* = 11.1, 8.9 Hz, 1H), 6.61 (dd, *J* = 7.2, 2.9 Hz, 1H), 6.41 (dt, *J* = 8.9, 3.1 Hz, 1H), 5.58 (d, *J* = 5.0 Hz, 1H), 4.65 (dd, *J* = 7.9, 2.4 Hz, 1H), 4.40 – 4.30 (m, 2H), 4.19 – 4.02 (m, 3H), 3.86 (s, 3H), 1.52 (s, 3H), 1.47 (s, 3H), 1.36 (s, 3H), 1.35 (s, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 155.11, 155.09, 148.06 (d, *J* = 12.0 Hz), 147.39 (d, *J* = 237.9 Hz), 115.60 (d, *J* = 19.6 Hz), 109.51, 108.76, 104.68 (d, *J* = 6.6 Hz), 102.12 (d, *J* = 1.7 Hz), 96.41, 71.02, 70.66, 70.57, 67.31, 66.21, 56.17, 26.04, 26.00, 24.94, 24.47.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -145.39.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{26}FO_7^+$: 385.1657; Found: 385.1652.



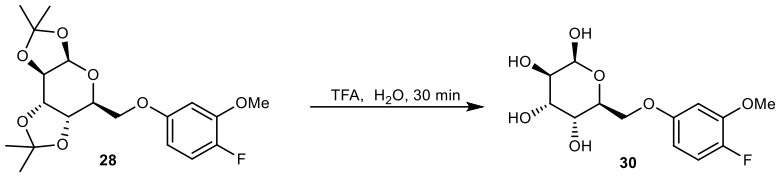
(2S,3R,4S,5R,6R)-6-((4-fluoro-3-methoxyphenoxy)methyl)tetrahydro-2H-pyran-2,3,4,5-tetrayl tetraacetate(29). The title compound was prepared according to the general procedure **F** from (2S,3R,4S,5R,6S)-6-(hydroxymethyl)tetrahydro-2H-pyran-2,3,4,5-tetrayl tetraacetate (157 mg，0.45 mmol) and (4-fluoro-3-methoxyphenyl)boronic acid (153 mg，0.90 mmol), and obtained as a white solid (29 mg, 21.3%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.94 (dd, *J* = 11.0, 8.9 Hz, 1H), 6.56 (dd, *J* = 7.2, 2.9 Hz, 1H), 6.31 (dt, *J* = 8.9, 3.1 Hz, 1H), 5.76 (d, *J* = 8.2 Hz, 1H), 5.37 – 5.24 (m, 2H), 5.23 – 5.11 (m, 1H), 4.12 – 4.04 (m, 1H), 4.01 – 3.91 (m, 2H), 3.86 (s, 3H), 2.11 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H), 2.01 (s, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.17, 169.39, 169.26, 169.02, 154.82 (d, *J* = 2.3 Hz), 148.18 (d, *J* = 12.1 Hz), 147.69 (d, *J* = 238.8 Hz), 115.63 (d, *J* = 19.8 Hz), 104.52 (d, *J* = 6.7 Hz), 102.34 (d, *J* = 1.6 Hz), 91.77, 73.23, 72.89, 70.27, 68.46, 67.07, 56.19, 20.82, 20.63, 20.60, 20.57.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -144.53.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{25}FO_{11}Na^+$: 495.1273; Found: 495.1272.



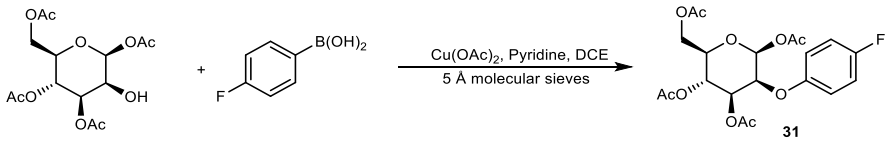
(2S,3R,4S,5R,6S)-6-((4-fluoro-3-methoxyphenoxy)methyl)tetrahydro-2H-pyran-2,3,4,5-tetraol(**30**). The compound **28** (30 mg，0.05 mmol) was dissolved in 1 mL 80% TFA. The solution was stirred under room temperature for 30 min. The reaction was condensed under reduced pressure and co-evaporated with water and ethyl acetate three times to give the title compound as a white solid (16 mg, 84%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.96 (ddd, *J* = 10.4, 8.8, 1.4 Hz, 1H), 6.67 (dt, *J* = 7.2, 2.1 Hz, 1H), 6.49 – 6.39 (m, 1H), 4.53 – 4.43 (m, 1H), 4.20 – 4.06 (m, 2H), 3.95 – 3.92 (m, 1H), 3.89 – 3.76 (m, 4H), 3.54 – 3.47 (m, 2H).

^{13}C NMR (100 MHz, Methanol-d_4) δ 155.46 (d, *J* = 2.3 Hz), 148.15 (d, *J* = 12.0 Hz), 147.26 (d, *J* = 237.1 Hz), 115.19 (d, *J* = 19.8 Hz), 104.63 (d, *J* = 6.5 Hz), 101.46, 97.43, 73.52, 73.20, 72.33, 69.03, 67.68, 55.25.

^{19}F NMR (376 MHz, Methanol-d_4) δ -147.34.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{13}H_{17}FO_7Na^+$: 327.0851; Found: 327.0848.



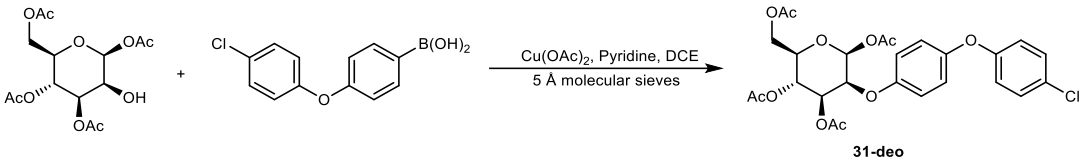
(2S,3S,4S,5R,6R)-6-(acetoxymethyl)-3-(4-fluorophenoxy)tetrahydro-2H-pyran-2,4,5-triyl triacetate (**31**). The title compound was prepared according to the general procedure **F** from (2S,3S,4R,5R,6R)-6-(acetoxymethyl)-3-hydroxytetrahydro-2H-pyran-2,4,5-triyl triacetate (157 mg，0.45 mmol) and (4-fluorophenyl)boronic acid (126 mg，0.90 mmol), and obtained as a white solid (29 mg, 14.9%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.01 – 6.90 (m, 4H), 5.87 (d, *J* = 1.2 Hz, 1H), 5.54 (t, *J* = 9.9 Hz, 1H), 5.06 (dd, *J* = 10.0, 3.1 Hz, 1H), 4.72 (dd, *J* = 3.1, 1.1 Hz, 1H), 4.34 (dd, *J* = 12.4, 5.3 Hz, 1H), 4.20 (dd, *J* = 12.4, 2.4 Hz, 1H), 3.83 (ddd, *J* = 9.9, 5.3, 2.4 Hz, 1H), 2.11 (s, 3H), 2.07 (s, 3H), 2.06 (s, 3H), 1.88 (s, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.77, 170.27, 169.50, 168.66, 158.12 (d, *J* = 240.8 Hz), 155.52 (d, *J* = 2.5 Hz), 118.86 (d, *J* = 8.3 Hz), 115.87 (d, *J* = 23.2 Hz), 91.71, 76.23, 73.37, 72.72, 65.47, 62.15, 20.80, 20.77, 20.71, 20.48.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -121.19.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{23}FO_{10}Na^+$: 465.1167; Found: 465.1164.

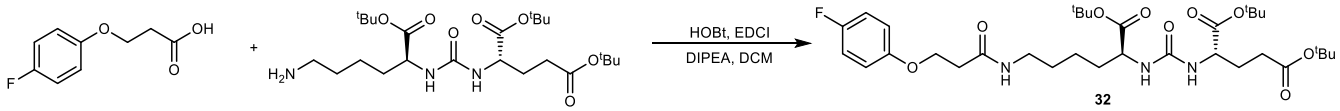


(2S,3S,4S,5R,6R)-6-(acetoxymethyl)-3-(4-(4-chlorophenoxy)phenoxy)tetrahydro-2H-pyran-2,4,5-triyl triacetate (**31-deo**). The title compound was prepared according to the general procedure **F** from (2S,3S,4R,5R,6R)-6-(acetoxymethyl)-3-hydroxytetrahydro-2H-pyran-2,4,5-triyl triacetate (157 mg，0.45 mmol) and (4-(4-chlorophenoxy)phenyl)boronic acid (223 mg，0.90 mmol), and obtained as a white solid (55 mg, 22.2%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 – 7.23 (m, 2H), 7.02 – 6.97 (m, 2H), 6.95 – 6.90 (m, 2H), 6.89 – 6.84 (m, 2H), 5.89 (d, *J* = 1.1 Hz, 1H), 5.55 (t, *J* = 9.9 Hz, 1H), 5.08 (dd, *J* = 10.0, 3.1 Hz, 1H), 4.77 – 4.72 (m, 1H), 4.35 (dd, *J* = 12.4, 5.3 Hz, 1H), 4.21 (dd, *J* = 12.4, 2.4 Hz, 1H), 3.84 (ddd, *J* = 9.9, 5.2, 2.4 Hz, 1H), 2.12 (s, 3H), 2.07 (s, 6H), 1.90 (s, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.80, 170.28, 169.52, 168.68, 156. 59, 155.72, 151.45, 129.68, 127.88, 120.32, 119.22, 118.91, 91.73, 76.09, 73.39, 72.72, 65.53, 62.18, 20.82, 20.72, 20.56.

HRMS (ESI): Calculated for $C_{26}H_{27}ClO_{11}Na^+$ $[M+Na]^+$: 573.1134 Found: 573.1129.



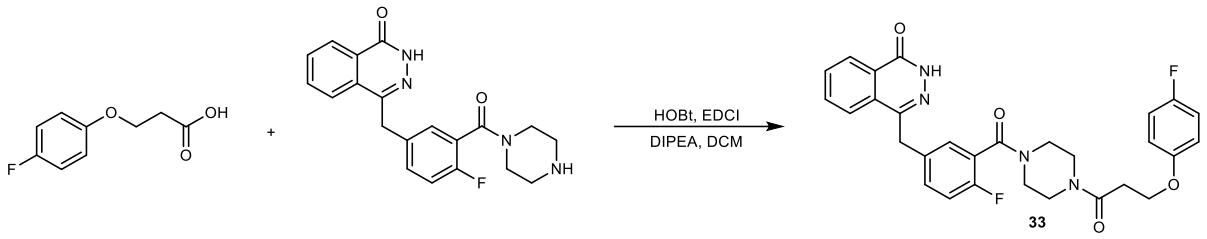
di-tert-butyl (((S)-1-(tert-butoxy)-6-(3-(4-fluorophenoxy)propanamido)-1-oxohexan-2-yl)carbamoyl)-L-glutamate (**32**). The 3-(4-fluorophenoxy)propanoic acid (32 mg, 0.17 mmol, 1.0 equiv.), EDCI (36 mg, 0.19 mmol, 1.1 equiv.) and HOBT (26 mg, 0.19 mmol, 1.1 equiv.) were dissolved in DCM (3 mL). The solution was stirred at room temperature for 0.5h, followed by the addition of DIPEA (92 μl，0.51 mmol, 3.0 equiv.) and di-tert-butyl (((S)-6-amino-1-(tert-butoxy)-1-oxohexan-2-yl)carbamoyl)-L-glutamate (94 mg, 0.19 mmol, 1.1 equiv.). The reaction was stirred overnight. The solution was then washed with 1M citric acid aqueous solution, saturated $NaHCO_3$ solution, water, and saturated NaCl solution, dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (DCM : MeOH = 25 : 1) to yield the title compound as a light-yellow oil (106 mg, 93.3%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.02 – 6.91 (m, 2H), 6.91 – 6.80 (m, 2H), 6.74 – 6.67 (m, 1H), 5.56 (q, *J* = 7.9 Hz, 1H), 5.44 – 5.33 (m, 1H), 4.32 (td, *J* = 8.4, 4.8 Hz, 1H), 4.26 – 4.21 (m, 3H), 3.34 – 3.18 (m, 2H), 2.68 (t, *J* = 6.3 Hz, 2H), 2.40 – 2.20 (m, 2H), 2.10 – 2.02 (m, 1H), 1.89 – 1.70 (m, 2H), 1.60 – 1.50 (m, 3H), 1.49 – 1.39 (m, 27H), 1.36 – 1.28 (m, 2H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.17 (d, *J* = 4.9 Hz), 172.42, 172.27, 170.61, 157.38 (d, *J* = 238.5 Hz), 157.25 (d, *J* = 2.1 Hz), 154.69 (d, *J* = 2.2 Hz), 115.85 (d, *J* = 13.7 Hz), 115.70 (d, *J* = 1.3 Hz), 82.38, 81.64 (d, *J* = 1.4 Hz), 80.62, 65.08, 53.46 (d, *J* = 1.7 Hz), 53.08, 39.04, 36.50, 32.40, 31.62, 28.81, 28.14, 28.06, 28.01, 22.73 (d, *J* = 3.1 Hz).

^{19}F NMR (376 MHz, Chloroform-*d*) δ -123.69.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{33}H_{53}FN_3O_9^+$: 654.3760; Found: 654.3755.



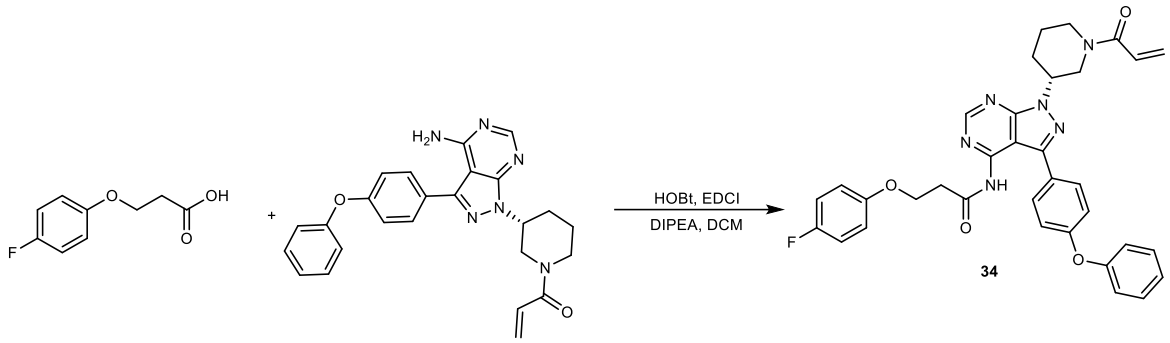
4-(4-fluoro-3-(4-(3-(4-fluorophenoxy)propanoyl)piperazine-1-carbonyl)benzyl)20ptimized20o-1(2H)-on (**33**). Following the preparation procedure of compound **32**, the title compound was obtained from 3-(4-fluorophenoxy)propanoic acid (92 mg, 0.50 mmol, 1.0 equiv.) and 4-(4-fluoro-3-(piperazine-1-carbonyl)benzyl)20ptimized20o-1(2H)-one (202 mg, 0.55 mmol, 1.1 equiv.) as a white solid (212 mg, 79.6%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 11.31 (d, *J* = 33.6 Hz, 1H), 8.50 – 8.47 (m, 1H), 7.88 – 7.64 (m, 3H), 7.39 – 7.32 (m, 2H), 7.05 (t, *J* = 9.0 Hz, 1H), 6.98 – 6.92 (m, 2H), 6.89 – 6.77 (m, 2H), 4.36 – 4.22 (m, 4H), 3.93 – 3.44 (m, 6H), 3.42 – 3.27 (m, 2H), 2.82 (dt, *J* = 29.7, 6.4 Hz, 2H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 169.17 (d, *J* = 19.6 Hz), 165.16 (d, *J* = 23.5 Hz), 160.78 (d, *J* = 4.4 Hz), 157.39 (d, *J* = 238.6 Hz), 157.01 (d, *J* = 247.4 Hz), 154.59 (d, *J* = 2.1 Hz), 145.50, 134.49 (d, *J* = 3.4 Hz), 133.69 (d, *J* = 3.3 Hz), 131.80 (d, *J* = 8.1 Hz), 131.64, 129.55, 129.30 (m), 128.31, 127.20, 125.00, 123.61 (dd, *J* = 17.8, 9.5 Hz), 116.00 (2C), 115.77 (2C), 115.51 (dd, *J* = 8.2, 2.7 Hz), 64.89 (d, *J* = 4.3 Hz), 46.94 (d, *J* = 32.9 Hz), 45.65 (d, *J* = 45.5 Hz), 42.11 (d, *J* = 29.7 Hz), 41.58 (d, *J* = 49.8 Hz), 37.68 (d, *J* = 6.2 Hz), 33.01.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -117.66 (d, *J* = 18.4 Hz), -123.52 (d, *J* = 24.0 Hz).

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{29}H_{27}F_2N_4O_4^+$: 533.1995; Found: 533.1998.



©-N-(1-(1-acryloylpiperidin-3-yl)-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-3-(4-fluorophenoxy)propenamide (**34**). Following the preparation procedure of compound **32**, the title compound was obtained from 3-(4-fluorophenoxy)propanoic acid (92 mg, 0.50 mmol, 1.0 equiv.) and Ibrutinib (243 mg, 0.55 mmol, 1.1 equiv.) as a white solid (76 mg, 25.1%).

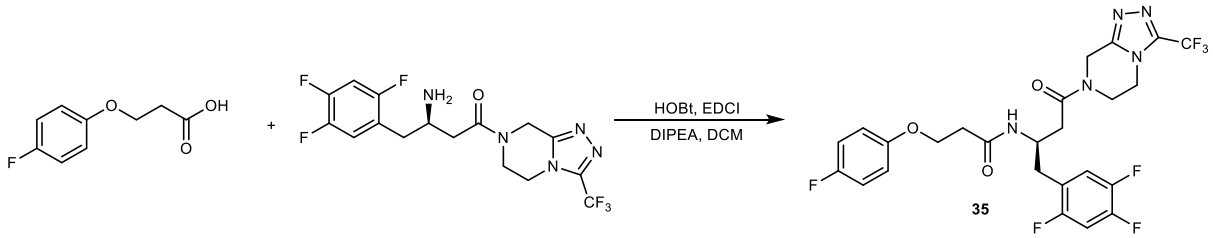
^{1}H NMR (400 MHz, DMSO-d_6) δ 11.06 (s, 1H), 8.83 (s, 1H), 7.66 (d, *J* = 8.1 Hz, 2H), 7.44 – 7.32 (m, 2H), 7.18 – 7.05 (m, 5H), 7.03 – 6.96 (m, 2H), 6.93 – 6.71 (m, 3H), 6.12 (dd, *J* = 23.6, 16.6 Hz, 1H), 5.66 (dd, *J* = 48.8, 10.5 Hz, 1H), 4.96 – 4.80 (m, 1H), 4.67 – 4.59 (m, 0.5H), 4.40 – 4.17 (m, 1H), 4.11 – 4.08 (m, 0.5H), 3.96 (t, *J* = 6.4 Hz, 2H), 3.76 (t, *J* = 11.7 Hz, 0.5H),

3.28 – 3.20 (m, 1H), 3.04 (d, *J* = 9.7 Hz, 0.5H), 2.78 (t, *J* = 6.4 Hz, 2H), 2.33 (d, *J* = 11.9 Hz, 1H), 2.25 – 2.13 (m, 1H), 1.95 (d, *J* = 13.4 Hz, 1H), 1.70 – 1.55 (m, 1H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 168.91, 164.04, 156.13, 155.96, 155.94 (d, *J* = 236.0 Hz), 154.11, 154.05, 153.96 (d, *J* = 1.9 Hz), 152.23, 144.16 (d, *J* = 10.7 Hz), 129.48, 128.76, 128.47, 127.68 (d, *J* = 10.7 Hz), 126.88 (d, *J* = 18.2 Hz), 123.00, 117.93 (d, *J* = 5.3 Hz), 115.21 (d, *J* = 22.5 Hz), 115.06 (d, *J* = 7.7 Hz), 103.80, 62.97, 52.20 (d, *J* = 69.2 Hz), 46.82 (d, *J* = 351.8 Hz), 42.77 (d, *J* = 360.6 Hz), 34.93, 28.89 (d, *J* = 10.5 Hz), 23.51 (d, *J* = 157.3 Hz).

^{19}F NMR (376 MHz, DMSO-d_6) δ -123.81.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{34}H_{32}FN_6O_4^+$: 607.2464; Found: 607.2464.



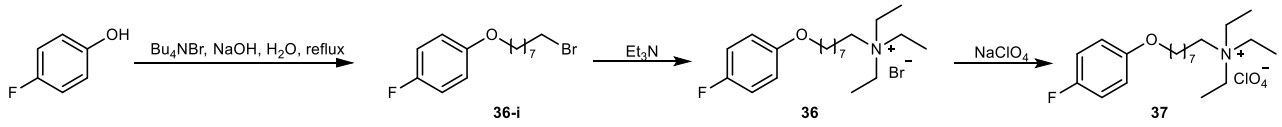
©-3-(4-fluorophenoxy)-N-(4-oxo-4-(3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)-1-(2,4,5-trifluorophenyl)butan-2-yl)propenamide (35). Following the preparation procedure of compound **32**, the title compound was obtained from 3-(4-fluorophenoxy)propanoic acid (92 mg, 0.50 mmol, 1.0 equiv.) and Sitagliptin (75 mg, 0.55 mmol, 1.1 equiv.) as a white solid (146 mg, 51.2%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.98 (dd, *J* = 8.7, 5.4 Hz, 1H), 7.50 – 7.30 (m, 2H), 7.08 (td, *J* = 8.8, 1.9 Hz, 2H), 6.84 (ddd, *J* = 9.2, 4.4, 1.6 Hz, 2H), 5.07 – 4.91 (m, 1H), 4.90 – 4.79 (m, 1H), 4.34 – 4.30 (m, 1H), 4.29 – 4.20 (m, 1H), 4.08 – 3.87 (m, 5H), 2.92 – 2.87 (m, 1H), 2.81 – 2.60 (m, 3H), 2.39 (dt, *J* = 22.5, 6.2 Hz, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 169.69 (d, *J* = 10.4 Hz), 169.51, 157.54 (d, *J* = 8 Hz), 156.94 (d, *J* = 235.8 Hz), 155.14 (d, *J* = 1.9 Hz), 151.37 (d, *J* = 13.1 Hz), 147.16 (dd, *J* = 22.3, 13.1 Hz), 146.40 (m), 142.87 (dd, *J* = 38.9, 18.5 Hz), 122.97, 119.53 (dd, *J* = 19.2, 6.2 Hz), 118.92 (d, *J* = 269.9 Hz), 116.20 (d, *J* = 20.5 Hz), 116.04 (d, *J* = 5.8 Hz), 105.93 (dd, *J* = 29.3, 20.9 Hz), 64.98 (d, *J* = 7.5 Hz), 46.47, 43.70 (d, *J* = 63.4 Hz), 42.04 (d, *J* = 90.0 Hz), 38.60 (d, *J* = 43.1 Hz), 37.82 (d, *J* = 14.5 Hz), 35.83 (d, *J* = 8.7 Hz), 32.77 (d, *J* = 12.4 Hz). *Note*: The spectrum data was not perfectly assigned due to too many C-F couplings in the compound.

^{19}F NMR (376 MHz, DMSO-d_6) δ -61.92 (d, *J* = 18.6 Hz), -118.52 (td, *J* = 14.5, 13.4, 3.5 Hz), -124.04 (d, *J* = 3.1 Hz), -137.37 (ddd, *J* = 22.3, 18.0, 3.3 Hz), -144.07 (dt, *J* = 22.9, 16.5 Hz).

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{25}H_{23}F_7N_5O_3^+$: 574.1684; Found: 574.1682.



1-((8-bromooctyl)oxy)-4-fluorobenzene (36-i). The title compound was prepared according to the general procedure **A** from 4-chlorophenol (1.0g，8.92 mmol, 1.0 equiv.) and 1,8-dibromo octane (6.6 ml, 35.7 mmol, 4 equiv.), and obtained as a colourless oil (1.6 g, 59.2 %).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.99 – 6.92 (m, 2H), 6.85 – 6.79 (m, 2H), 3.90 (t, *J* = 6.5 Hz, 2H), 3.41 (t, *J* = 6.8 Hz, 2H), 1.90 – 1.82 (m, 2H), 1.81 – 1.71 (m, 2H), 1.50 – 1.31 (m, 8H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.25 (d, *J* = 237.8 Hz), 155.35 (d, *J* = 2.0 Hz), 115.84 (d, *J* = 23.0 Hz), 115.52 (d, *J* = 7.9 Hz), 68.67, 34.10, 32.91, 29.37, 29.31, 28.81, 28.22, 26.07.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -124.43.

N,N,N-triethyl-8-(4-fluorophenoxy)octan-1-aminium bromide (36). The solution of **36-©** (152 mg, 0.5 mmol) and triethylamine (0.5mL) in MeCN (2 ml) was stirred under 80 ℃ overnight. The reaction was cooled to room temperature, and then the solvent was evaporated under vacuum. The residue was washed three times with ether to obtain the title compound as a white solid (168 mg, 83%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.96 (t, *J* = 8.7 Hz, 2H), 6.85 – 6.80 (m, 2H), 3.91 (t, *J* = 6.4 Hz, 2H), 3.52 (q, *J* = 7.3 Hz, 6H), 3.33 – 3.26 (m, 2H), 1.79 – 1.76 (m, 2H), 1.74 – 1.70 (m, 2H), 1.49 – 1.38 (m, 17H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.08 (d, *J* = 237.8 Hz), 155.19 (d, *J* = 2.0 Hz), 115.71 (d, *J* = 23.0 Hz), 115.42 (d, *J* = 7.9 Hz), 68.44, 57.58, 53.58, 29.15, 29.09, 29.08, 26.41, 25.84, 22.13, 8.14.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -124.38.

HRMS (ESI) m/z: $[M\text{-}Br]^+$ Calcd for $C_{20}H_{35}FNO^+$: 324.2697 ; Found: 324.2692 .

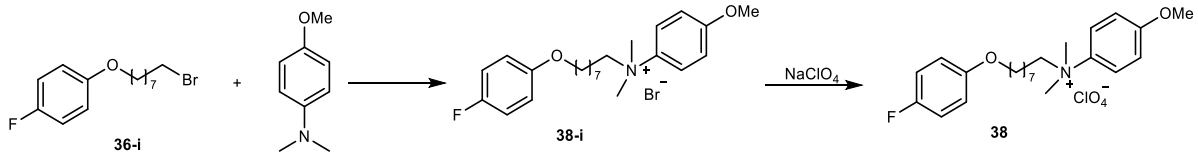
N,N,N-triethyl-8-(4-fluorophenoxy)octan-1-aminium perchlorate (37). To a solution of **36** (50 mg, 0.124 mmol) in deionised water (7.5 mL), $NaClO_4$ (0.5 g) was added. The mixture was stirred at room temperature overnight. Then the residue was extracted with EtOAc (5 × 7 mL). The organic phase was dried with Na_2SO_4, filtered, and concentrated in a vacuum to give the **37** as a white solid (40 mg, 76.4%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.00 – 6.91 (m, 2H), 6.86 – 6.79 (m, 2H), 3.91 (t, *J* = 6.4 Hz, 2H), 3.33 (q, *J* = 7.3 Hz, 6H), 3.19 – 3.10 (m, 2H), 1.75 (p, *J* = 6.6 Hz, 2H), 1.70 – 1.64 (m, 2H), 1.49 – 1.42 (m, 2H), 1.41 – 1.30 (m, 15H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.22 (d, *J* = 237.7 Hz), 155.35 (d, *J* = 2.0 Hz), 115.86 (d, *J* = 23.0 Hz), 115.58 (d, *J* = 7.9 Hz), 68.59, 57.43, 53.30, 29.26, 29.15, 29.09, 26.38, 25.93, 21.89, 7.74.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -124.43.

HRMS (ESI) m/z: $[M\text{-}ClO_4]^+$ Calcd for $C_{20}H_{35}FNO^+$: 324.2697 ; Found: 324.2695 .



N-(8-(4-fluorophenoxy)octyl)-4-methoxy-N,N-dimethylbenzenaminium bromide (38-i) To a solution of **36-©** (0.5 mmol,

152 mg) and (4-methoxy-phenyl)-dimethyl-amine (2 mmol, 300 mg) in MeCN (2ml) was stirred under 80℃ overnight. The reaction was cooled to room temperature, and then the solvent was evaporated under vacuum. The residue was washed three times with ether to obtain the title compound (100 mg, 44%), which was used in the next step without further purification.

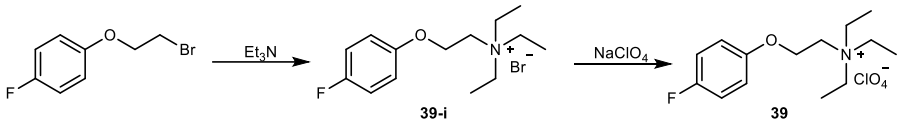
N-(8-(4-fluorophenoxy)octyl)-4-methoxy-N,N-dimethylbenzenaminium perchlorate (38). To a solution of **38-©** (70 mg, 0.154 mmol) in 23ptimized water (7 mL) was added $NaClO_4$ (500 mg). The mixture was stirred at room temperature overnight. Then the residue was extracted with EtOAc (5 × 7mL). The organic phase was dried with Na_2SO_4, filtered, and concentrated in a vacuum to give the title compound as a white solid (62 mg, 84.9%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 9.3 Hz, 2H), 7.05 (d, *J* = 9.3 Hz, 2H), 6.94 (t, *J* = 8.7 Hz, 2H), 6.79 (m, 2H), 3.94 – 3.85 (m, 4H), 3.84 (s, 3H), 3.63 (s, 6H), 1.69 (dt, *J* = 14.5, 6.6 Hz, 2H), 1.45 – 1.24 (m, 10H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.49, 157.09 (d, *J* = 237.7 Hz), 155.20 (d, *J* = 2.0 Hz), 136.45, 121.67, 115.72 (d, *J* = 22.9 Hz), 115.71, 115.43 (d, *J* = 7.9 Hz), 69.53, 68.48, 55.83, 55.00, 29.10, 28.90, 28.82, 25.74, 25.70, 23.46.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -124.44.

HRMS (ESI) m/z: $[M\text{-}ClO_4]^+$ Calcd for $C_{23}H_{33}FNO_2^+$: 374.2490 ; Found: 374.2484 .



39-i 39

N,N,N-triethyl-2-(4-fluorophenoxy)ethan-1-aminium bromide (39-i). A solution of 1-(2-bromoethoxy)-4-fluorobenzene (110 mg, 0.5 mmol) and triethylamine (0.5 mL) in MeCN (2 ml) was stirred under 80℃ overnight. The reaction was cooled to room temperature, and then the solvent was evaporated under vacuum. The residue was washed three times with ether to obtain the title compound (150 mg, 93.7 %), which was used in the next step without further purification.

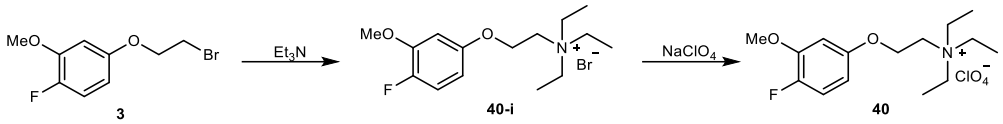
N,N,N-triethyl-2-(4-fluorophenoxy)ethan-1-aminium perchlorate (39). To a solution of **39-©** (150 mg, 0.468 mmol) in deionised water (8 mL), $NaClO_4$ (0.5g) was added. The mixture was stirred at room temperature overnight. Then the residue was extracted with EtOAc (5 × 7 mL). The organic phase was dried with Na_2SO_4, filtered, and concentrated in a vacuum to give the title compound as a colourless liquid (40 mg, 27%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.18 (t, *J* = 8.8 Hz, 2H), 7.05 – 6.97 (m, 2H), 4.39 – 4.33 (m, 3H), 3.69 – 3.63 (m, 3H), 3.37 (q, *J* = 7.4 Hz, 6H), 1.22 (t, *J* = 7.1 Hz, 9H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 157.43 (d, *J* = 236.5 Hz), 154.22 (d, *J* = 2.0 Hz), 116.52 (d, *J* = 2.8 Hz), 116.36 (d, *J* = 12.3 Hz), 62.02, 55.64, 53.38, 7.76.

^{19}F NMR (376 MHz, DMSO-d_6) δ -123.02.

HRMS (ESI) m/z: $[M\text{-}ClO_4]^+$ Calcd for $C_{14}H_{23}FNO^+$: 240.1758 ; Found: 240.1755 .



N,N,N-triethyl-2-(4-fluoro-3-methoxyphenoxy)ethan-1-aminium bromide (40-i). The solution of compound **3** (125 mg, 0.5 mmol) and triethylamine (0.5 mL) in MeCN (2 ml) was stirred overnight at 80 ºC. The reaction was cooled to room temperature, and the solvent was evaporated under vacuum. The residue was washed three times with ether to obtain the title compound (160 mg, 92%), which was used in the next step without further purification.

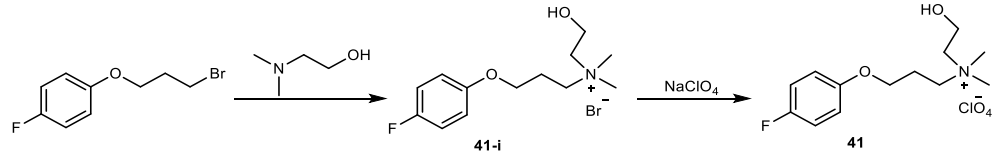
N,N,N-triethyl-2-(4-fluoro-3-methoxyphenoxy)ethan-1-aminium perchlorate (40). To a solution of **40-©** (35 mg g, 0.10 mmol) in deionized water (7.5 mL), $NaClO_4$ (0.5 g) was added. The mixture was stirred at room temperature overnight. Then the residue was extracted with EtOAc (5 × 7mL). The organic phase was dried with Na_2SO_4, filtered, and concentrated in a vacuum to give the **40** as a white solid (30 mg, 81.2%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.17 (dd, J = 11.4, 8.9 Hz, 1H), 6.77 (dd, J = 7.3, 2.9 Hz, 1H), 6.53 (dt, J = 9.0, 3.1 Hz, 1H), 4.37 (t, J = 4.8 Hz, 2H), 3.85 (s, 3H), 3.66 (t, J = 4.8 Hz, 2H), 3.38 (q, J = 7.2 Hz, 6H), 1.24 (t, J = 7.1 Hz, 9H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 154.61 (d, J = 2.0 Hz), 148.18 (d, J = 11.9 Hz), 147.17 (d, J = 236.7 Hz), 116.30 (d, J = 19.4 Hz),105.74 (d, J = 6.6 Hz), 102.11 (d, J = 1.2 Hz), 62.04, 56.60, 55.60, 53.38, 7.77.

^{19}F NMR (376 MHz, DMSO-d_6) δ -144.49.

HRMS (ESI) m/z: $[M\text{-}ClO_4]^+$ Calcd for $C_{15}H_{25}FNO_2^+$: 270.1864; Found: 270.1863.



3-(4-fluorophenoxy)-N-(2-hydroxyethyl)-N,N-dimethylpropan-1-aminium bromide (41-i). The solution of 1-(3-bromopropoxy)-4-fluorobenzene (117 mg, 0.5 mmol) and 2-dimethylaminoethanol triethylamine (0.5 ml) in MeCN (2 ml) was stirred under 80℃ overnight. The reaction was cooled to room temperature, then the solvent was evaporated under vacuum. The residue was washed three times with ether to obtain the title compound (100 mg, 61.9%), which was used in the next step without further purification.

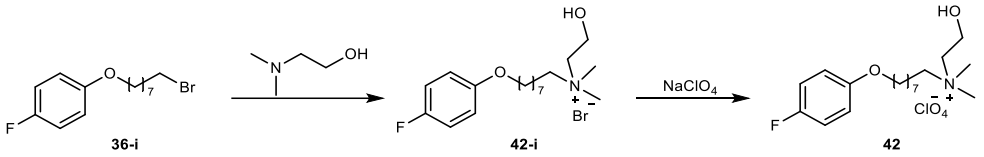
3-(4-fluorophenoxy)-N-(2-hydroxyethyl)-N,N-dimethylpropan-1-aminium perchlorate (41). To a solution **41-©** (100 mg, 0.31 mmol) in deionised water (7.5 mL), $NaClO_4$ (500 mg) was added. The mixture was stirred at room temperature overnight. Then the residue was extracted with EtOAc (5 × 7 mL). The organic phase was dried with Na_2SO_4, filtered, and concentrated in a vacuum to give the title compound as a white solid (70 mg, 66.1%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.15 (t, J = 8.8 Hz, 2H), 6.99 – 6.94 (m, 2H), 5.30 (t, J = 4.9 Hz, 1H), 4.03 (t, J = 6.0 Hz, 2H), 3.90 – 3.78 (m, 2H), 3.57 – 3.49 (m, 2H), 3.47 – 3.40 (m, 3H), 3.11 (s, 6H), 2.18 (dq, J = 11.8, 5.9 Hz, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 156.67 (d, J = 236.0 Hz), 154.52 (d, J = 1.9 Hz), 115.95 (d, J = 14.0 Hz), 115.80, 65.35, 64.79, 64.76, 64.74, 61.66, 61.64, 61.61, 54.95, 51.03, 51.00, 50.96, 22.30.

^{19}F NMR (376 MHz, DMSO-d_6) δ -123.58.

HRMS (ESI) m/z: $[M\text{-}ClO_4]^+$ Calcd for $C_{13}H_{21}FNO_2^+$: 242.1551 ; Found: 242.1550 .



8-(4-fluorophenoxy)-N-(2-hydroxyethyl)-N,N-dimethyloctan-1-aminium bromide (42-i). The solution of **36-©** (0.152g, 0.5 mmol) and 2-dimethylaminoethanol triethylamine (0.5 ml) in MeCN (2 ml) was stirred under 80℃ overnight. The reaction was cooled to room temperature, and the solvent was evaporated under vacuum. The residue was washed three times with ether to obtain the title compound (189 mg, 96.6%), which was used in the next step without further purification.

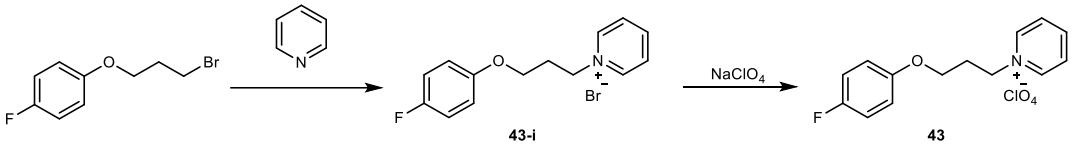
8-(4-fluorophenoxy)-N-(2-hydroxyethyl)-N,N-dimethyloctan-1-aminium perchlorate (42) To a solution of **42-©** (0.06 g,0.153mmol) in deionized water (7.5 mL) was added $NaClO_4$ (0.5g). The mixture was stirred at room temperature overnight. Then the residue was extracted with EtOAc (5 × 7mL). The organic phase was dried with Na_2SO_4, filtered, and concentrated in a vacuum to give the **42** as a white solid (28 mg, 44.5%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.99 – 6.92 (m, 2H), 6.85 – 6.79 (m, 2H), 4.10 (s, 2H), 3.90 (t, *J* = 6.5 Hz, 2H), 3.64 – 3.49 (m, 3H), 3.40 – 3.31 (m, 2H), 3.17 (s, 6H), 1.74 (m, 6H), 1.44 (m, 2H), 1.37 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.10 (d, *J* = 237.6 Hz), 155.22 (d, *J* = 2.1 Hz), 115.76 (d, *J* = 23.0 Hz), 115.51 (d, *J* = 7.9 Hz), 68.54, 66.21, 65.55, 56.39, 51.65, 29.15, 29.00, 28.92, 26.06, 25.81, 22.63.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -124.33.

HRMS (ESI) m/z: $[M\text{-}ClO_4]^+$ Calcd for $C_{18}H_{31}FNO_2^+$: 312.2333; Found:312.2332.



1-(3-(4-fluorophenoxy)propyl) 25 ptimize-1-ium bromide (43-i). The solution of 1-(3-bromopropoxy)-4-fluorobenzene (0.117 g, 0.5 mmol) and pyridine (0.5 mL) in MeCN (2 ml) was stirred under 80℃ overnight. The reaction was cooled to room temperature, and the solvent was evaporated under vacuum. The residue was washed three times with ether to obtain the **1-(3-(4-fluorophenoxy)propyl)25ptimize-1-ium bromide** (0.101 g, 65 %), which was used in the next step without further purification.

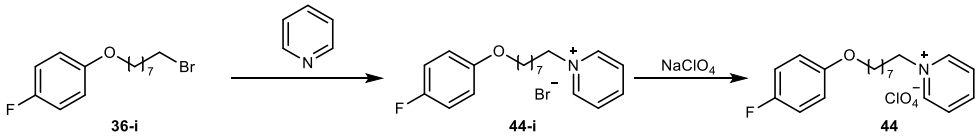
1-(3-(4-fluorophenoxy)propyl)25ptimize-1-ium perchlorate (43). To a solution of **43-©** (0.05 g,0.160 mmol) in 25ptimized water (7.5 mL), NaClO4 (0.5g) was added. The mixture was stirred overnight at room temperature. Then the residue was extracted with EtOAc (5 × 7 mL). The organic phase was dried with Na_2SO_4, filtered, and concentrated in a vacuum to give the title compound as a white solid (48 mg, 90.4%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.12 (d, J = 5.6 Hz, 2H), 8.61 (t, J = 7.8 Hz, 1H), 8.61 (t, J = 4.1 Hz, 2H), 7.13 – 7.06 (m, 2H), 6.83 – 6.76 (m, 2H), 4.79 (t, J = 6.8 Hz, 2H), 4.05 (t, J = 5.7 Hz, 2H), 2.42 (p, J = 6.4 Hz, 2H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 157.09 (d, J = 236.0 Hz), 154.73 (d, J = 1.8 Hz), 146.07, 145.53, 128.43,116.31 (d, J = 23.0 Hz), 116.04 (d, J = 8.1 Hz), 65.86, 59.39, 30.35.

^{19}F NMR (376 MHz, DMSO-d_6) δ -123.67.

HRMS (ESI) m/z: $[M\text{-}ClO_4]^+$ Calcd for $C_{14}H_{15}FNO^+$: 232.1132 ; Found: 232.1129 .



36-i 44-i 44

1-(8-(4-fluorophenoxy)octyl)26ptimize-1-ium bromide (44-i). The MeCN (2 ml) solution of **36-©** (152 mg, 0.5 mmol) and pyridine (0.5 mL) was stirred under 80℃ overnight. The reaction was cooled to room temperature; then, the solvent was evaporated under vacuum. The residue was washed three times with ether to obtain the title compound (149 mg, 78% yield), which was used in the next step without further purification.

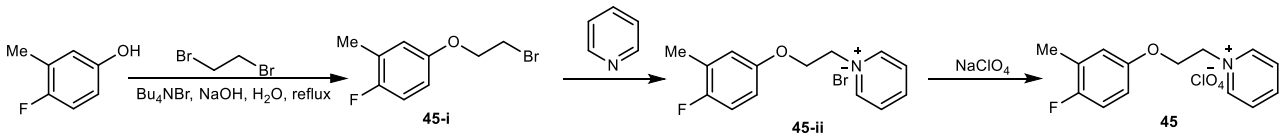
1-(8-(4-fluorophenoxy)octyl)26ptimize-1-ium perchlorate (44). To a solution of **44-©** (0.05 g, 0.131 mmol) in 26ptimized water (7.5 mL) was added $NaClO_4$ (0.5 g). The mixture was stirred at room temperature overnight. Then the residue was extracted with EtOAc (5 × 7 mL). The organic phase was dried with Na_2SO_4, filtered, and concentrated in a vacuum to give the title compound as a white solid (20 mg, 38.0% yield).

^{1}H NMR (400 MHz, Chloroform-d) δ 8.84 (d, J = 5.7 Hz, 2H), 8.48 (t, J = 7.8 Hz, 1H), 8.05 (t, J = 7.1 Hz, 2H), 6.95 (t, J = 8.7 Hz, 2H), 6.85 – 6.78 (m, 2H), 4.65 (t, J = 7.6 Hz, 2H), 3.88 (t, J = 6.5 Hz, 2H), 2.07 – 1.96 (m, 2H), 1.72 (m, 2H), 1.48 – 1.31 (m, 8H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.09 (d, J = 237.7 Hz), 155.21 (d, J = 2.1 Hz), 145.48, 144.51, 128.64, 115.74 (d, J = 23.1 Hz), 115.46 (d, J = 7.8 Hz), 68.49, 62.60, 31.54, 29.15, 28.94, 28.79, 25.93, 25.81.

^{19}F NMR (376 MHz, Chloroform-d) δ -124.38.

HRMS (ESI) m/z: $[M\text{-}ClO_4]^+$ Calcd for $C_{19}H_{25}FNO^+$: 302.1915 ; Found: 302.1909 .



45-i 45-ii 45

4-(2-bromoethoxy)-1-fluoro-2-methylbenzene (45-i). The title compound was prepared according to general procedure **A** from 4-fluoro-3-methylphenol (1.0g, 4.5 mmol, 1.0 equiv.) and 1,2-dibromoethane (1.56 mL, 18 mmol, 4 equiv.). It was obtained as a colourless liquid (80 mg, 43.3%).

^{1}H NMR (400 MHz, Chloroform-d) δ 6.91 (t, J = 9.0 Hz, 1H), 6.73 (dd, J = 6.2, 3.1 Hz, 1H), 6.67 (dt, J = 8.5, 3.5 Hz, 1H), 4.23 (t, J = 6.3 Hz, 2H), 3.61 (t, J = 6.3 Hz, 2H), 2.25 (d, J = 1.8 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.29 (d, *J* = 237.7 Hz), 153.87 (d, *J* = 2.2 Hz), 125.85 (d, *J* = 18.9 Hz), 117.74 (d, *J* = 4.8 Hz), 115.43 (d, *J* = 24.1 Hz), 112.97 (d, *J* = 8.0 Hz), 68.57, 29.17, 14.80 (d, *J* = 3.3 Hz).

^{19}F NMR (376 MHz, Chloroform-*d*) δ -127.12.

HRMS (ESI) m/z: $[M-Br]^+$ Calcd for $C_9H_{10}FO^+$: 153.0710 ; Found: 153.0707.

1-(2-(4-fluoro-3-methylphenoxy)ethyl)27ptimize-1-ium bromide (45-ii). The solution of **45-©** (117 mg, 0.5 mmol) and pyridine (0.5 mL) in MeCN (2 ml) was stirred under 80℃ overnight. The reaction was cooled to room temperature, and then the solvent was evaporated under vacuum. The residue was washed three times with ether to obtain the title compound (108 mg, 69.4%), which was used in the next step without further purification.

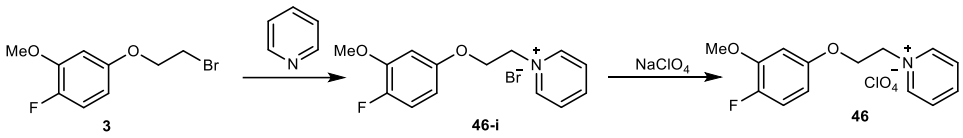
1-(2-(4-fluoro-3-methylphenoxy)ethyl)27ptimize-1-ium perchlorate (45). To a solution of **45-ii** (70 mg, 0.224 mmol) in deionized water (7 mL) was added $NaClO_4$ (0.5g). The mixture was stirred at room temperature overnight. Then the residue was extracted with EtOAc (5 × 7 mL). The organic phase was dried with Na_2SO_4, filtered, and concentrated in a vacuum to give the title compound as a yellow viscous liquid (66 mg, 88.7 %).

^{1}H NMR (400 MHz, Methanol-d_4) δ 9.06 (d, *J* = 5.4 Hz, 2H), 8.64 (t, *J* = 7.8 Hz, 1H), 8.15 ((t, *J* = 7.2 Hz, 2H), 6.90 (t, *J* = 9.1 Hz, 1H), 6.79 (dd, *J* = 6.1, 3.1 Hz, 1H), 6.71 (dt, *J* = 8.7, 3.5 Hz, 1H), 5.04 (t, *J* = 4.8 Hz, 2H), 4.47 (t, *J* = 4.9 Hz, 2H), 2.20 (d, *J* = 2.0 Hz, 3H).

^{13}C NMR (101 MHz, Methanol-d_4) δ 157.76 (d, *J* = 237.1 Hz), 154.97 (d, *J* = 2.3 Hz), 147.46, 146.65, 129.33, 126.99 (d, *J* = 19.0 Hz), 118.45 (d, *J* = 4.7 Hz), 116.40 (d, *J* = 24.6 Hz), 114.06 (d, *J* = 8.0 Hz), 67.97, 62.30, 14.59 (d, *J* = 3.6 Hz).

^{19}F NMR (376 MHz, Methanol-d_4) δ -128.93.

HRMS (ESI) m/z: $[M-ClO_4]^+$ Calcd for $C_{14}H_{15}FNO^+$: 232.1132 ; Found: 232.1129 .



1-(2-(4-fluoro-3-methoxyphenoxy)ethyl)27ptimize-1-ium bromide (46-i). The solution of **3** (0.125g, 0.5 mmol) and pyridine (0.5 mL) in MeCN (2 ml) was stirred under 80℃ overnight. The reaction was cooled to room temperature; then the solvent was evaporated under vacuum. The residue was washed three times with ether to give the title compound (130 mg, 81.4%), which was used in the next step without further purification.

1-(2-(4-fluoro-3-methoxyphenoxy)ethyl)27ptimize-1-ium perchlorate (46). To a solution of **46-©** (70 mg,0.219 mmol) in 27ptimized water (8 ml) and acetone (3 ml) was added $NaClO_4$ (0.5g). The mixture was stirred at room temperature overnight. Then the residue was extracted with EtOAc (5 × 7 mL). The organic phase was dried with Na_2SO_4, filtered, and concentrated in vacuum to give the title compound as a yellow viscous liquid (30 mg, 39.5 %).

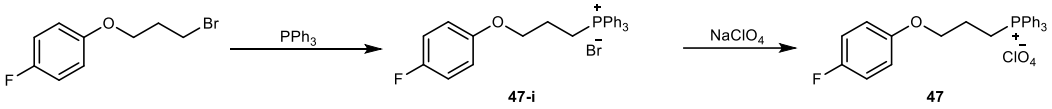
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.13 (d, *J* = 5.6 Hz, 2H), 8.65 (t, *J* = 7.8 Hz, 1H), 8.20 (t, *J* = 7.2 Hz, 2H), 7.11 (dd, *J* = 11.3,

8.9 Hz, 1H), 6.70 (dd, *J* = 7.3, 2.9 Hz, 1H), 6.45 (dt, *J* = 8.9, 3.1 Hz, 1H), 5.03 (t, *J* = 4.9 Hz, 2H), 4.50 (t, *J* = 4.9 Hz, 2H), 3.79 (s, 3H).

^{13}C NMR (101 MHz, DMSO) δ 154.17 (d, *J* = 2.0 Hz),147.68 (d, *J* = 11.9 Hz), 146.68 (d, *J* = 236.9 Hz), 146.10, 145.43, 127.94, 115.81 (d, *J* = 19.4 Hz), 105.09 (d, *J* = 6.7 Hz), 101.78 (d, *J* = 1.3 Hz), 66.70, 59.98, 56.05.

^{19}F NMR (376 MHz, DMSO-d_6) δ -144.34.

HRMS (ESI) m/z: $[M\text{-}ClO_4]^+$ Calcd for $C_{14}H_{15}FNO_2^+$: 248.1081 ; Found: 248.1077 .



47-i 47

(3-(4-fluorophenoxy)propyl)triphenylphosphonium bromide (47-i). The solution of 1-(3-bromopropoxy)-4-fluorobenzene (117 mg, 0.5 mmol) and triphenylphosphine (0.5 g, 1.9 mmol) in MeCN (2 ml) was stirred under 80℃ overnight. The reaction was cooled to room temperature, then the solvent was evaporated under vacuum. The residue was washed three times with ether to give the title compound (0.108 g, 43.7 %) which was used in the next step without further purification.

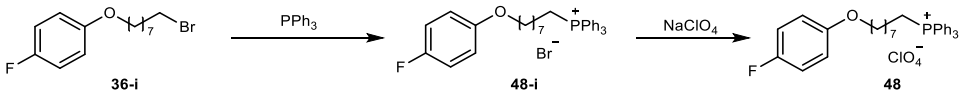
(3-(4-fluorophenoxy)propyl)triphenylphosphonium perchlorate (47). To a solution of **47-©** (70 mg, 0.141 mmol) in 28ptimized water (2 ml) and acetone (6 ml) was added $NaClO_4$ (0.5 mg). The mixture was stirred at room temperature overnight. Then the residue was extracted with EtOAc (5 × 7 ml). The organic phase was dried with Na_2SO_4, filtered, and concentrated in vacuum to give the title compound as a white solid (60 mg, 39.5 %).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.83 – 7.78 (m, 3H), 7.76 – 7.67 (m, 12H), 6.94 – 6.87 (m, 2H), 6.84 – 6.78 (m, 2H), 4.17 (t, *J* = 5.5 Hz, 2H), 3.58 – 3.46 (m, 2H), 2.19 – 2.10 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.51 (d, *J* = 238.5 Hz), 154.35 (d, *J* = 2.0 Hz), 135.42 (d, *J* = 3.0 Hz), 133.58 (d, *J* = 10.0 Hz), 130.75 (d, *J* = 12.6 Hz), 117.94 (d, *J* = 86.5 Hz), 115.92 (d, *J* = 34.6 Hz), 115.85 (d, *J* = 3.5 Hz), 67.09 (d, *J* = 16.9 Hz), 22.89 (d, *J* = 3.5 Hz), 19.38 (d, *J* = 54.1 Hz).

^{19}F NMR (376 MHz, Chloroform-*d*) δ -123.50.

HRMS (ESI) m/z: $[M\text{-}ClO_4]^+$ Calcd for $C_{27}H_{25}FOP^+$: 415.1622 ; Found: 415.1618 .



36-i 48-i 48

(8-(4-fluorophenoxy)octyl)triphenylphosphonium bromide (48-i). The solution of **36-©** (0.152 g, 0.5mmol) and triphenylphosphine (0.5 g,1.9mmol) in MeCN (2 ml) was stirred under 80 ℃ overnight. The reaction was cooled to room temperature, then the solvent was evaporated under vacuum. The residue was washed three times with ether to give the title compound (0.144 g, 51.1 %) which was used in the next step without further purification.

(8-(4-fluorophenoxy)octyl)triphenylphosphonium perchlorate (48). To a solution of **48-©** (0.070 g,0.124 mmol) in

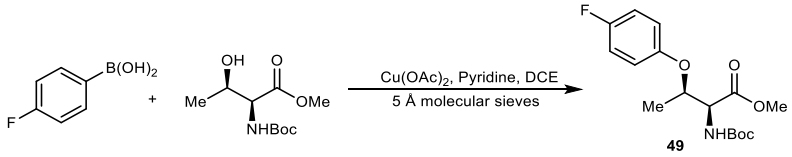
29ptimized water (2 ml) and acetone (6 ml) was added $NaClO_4$ (0.5 g). The mixture was stirred at room temperature overnight. Then the residue was extracted with EtOAc (5 × 7mL). The organic phase was dried with Na_2SO_4, filtered, and concentrated in vacuum to give the title compound as a colourless oil (54 mg, 74.5% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.84 – 7.75 (m, 3H), 7.75 – 7.65 (m, 12H), 6.92 (t, *J* = 8.7 Hz, 2H), 6.81 – 6.77 (m, 2H), 3.86 (t, *J* = 6.5 Hz, 2H), 3.30 – 3.23 (m, 2H), 1.69 (p, *J* = 6.8 Hz, 2H), 1.44 – 1.34 (m, 2H), 1.35 – 1.21 (m, 8H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.15 (d, *J* = 237.5 Hz), 155.33 (d, *J* = 2.0 Hz), 135.32 (d, *J* = 3.2 Hz), 133.54 (d, *J* = 9.9 Hz), 130.71 (d, *J* = 12.6 Hz), 118.18 (d, *J* = 86.0 Hz), 115.78 (d, *J* = 22.9 Hz), 115.53 (d, *J* = 7.9 Hz), 68.62, 30.36 (d, *J* = 15.9 Hz), 29.80, 29.10 (d, *J* = 21.9 Hz), 28.96, 25.87, 22.65 (d, *J* = 4.4 Hz), 22.25 (d, *J* = 51.1 Hz).

^{19}F NMR (376 MHz, Chloroform-*d*) δ -124.53.

HRMS (ESI) m/z: $[M-ClO_4]^+$ Calcd for $C_{32}H_{35}FOP^+$: 485.2404 ; Found: 485.2402 .



49

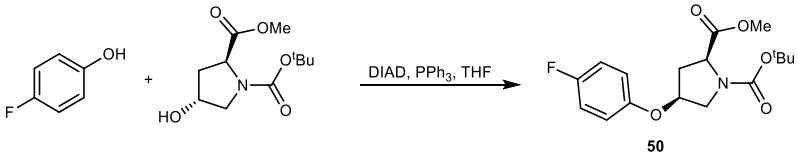
methyl N-(tert-butoxycarbonyl)-O-(4-fluorophenyl)-L-threoninate (49). The title compound was prepared according to the general procedure **F** from (4-fluorophenyl)boronic acid (252 mg，1.8 mmol) and methyl (tert-butoxycarbonyl)-*L*-threoninate (210 mg，0.90 mmol) and obtained as a colourless oil (69 mg, 23.5%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.01 – 6.90 (m, 2H), 6.87 – 6.77 (m, 2H), 5.37 (d, *J* = 9.8 Hz, 1H), 4.85 (qd, *J* = 6.2, 2.4 Hz, 1H), 4.49 (dd, *J* = 9.7, 2.4 Hz, 1H), 3.68 (s, 3H), 1.49 (s, 9H), 1.32 (d, *J* = 6.3 Hz, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.01, 157.83 (d, *J* = 239.9 Hz), 156.10, 153.19 (d, *J* = 2.4 Hz), 117.97 (d, *J* = 8.1 Hz), 115.95 (d, *J* = 23.2 Hz), 80.22, 75.62, 57.87, 52.51, 28.32, 16.23.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -122.22.

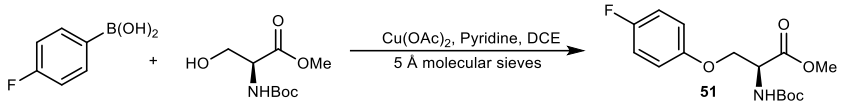
HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{22}FNO_5Na^+$: 350.1374; Found: 350.1370.



50

1-(tert-butyl) 2-methyl (2S,4S)-4-(4-fluorophenoxy)pyrrolidine-1,2-dicarboxylate (**50**). The 4-fluorophenol (200 mg，1.79 mmol，1.0 equiv.) and PPh_3 (525 mg，1.97 mmol，1.1 equiv.) were dissolved in THF(10 ml). The solution was cooled to 0℃, to which the *N*-Boc-trans-4-Hydroxy-*L*-proline methyl ester (483 mg，1.97 mmol，1.1 equiv.) and DIAD (393 μl，1.97 mmol，1.1 equiv.) were added. The solution was stirred at room temperature overnight and then extracted with ethyl acetate and water. The organic phase was dried with Na_2SO_4, filtered, and concentrated in vacuo to give the crude product which was purified by silica gel column with PE/EA =5/1 as the eluant to give the title compound as a white solid (400 mg, 65.9%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.99 – 6.93 (m, 2H), 6.77 – 6.73 (m, 2H), 4.88 – 4.77 (m, 1H), 4.56 – 4.41 (m, 1H), 3.80 – 3.59 (m, 5H), 2.50 – 2.36 (m, 2H), 1.46 (d, J = 17.9 Hz, 9H). The spectra data matched the reported literature [4]



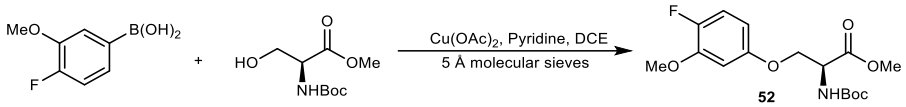
methyl N-(tert-butoxycarbonyl)-O-(4-fluorophenyl)-L-serinate (**51**). The title compound was prepared according to the general procedure **F** from (4-fluorophenyl)boronic acid (252 mg，1.8 mmol) and methyl (tert-butoxycarbonyl)-L-serinate (197 mg，0.90 mmol), and obtained as a colorless oil (83 mg, 29.5%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.01 – 6.91 (m, 2H), 6.86 – 6.77 (m, 2H), 5.48 (d, *J* = 8.7 Hz, 1H), 4.65 (dd, *J* = 7.7, 3.9 Hz, 1H), 4.35 (dd, *J* = 9.2, 3.0 Hz, 1H), 4.17 (dd, *J* = 9.3, 3.2 Hz, 1H), 3.77 (s, 3H), 1.46 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.51, 157.65 (d, *J* = 239.3 Hz), 155.37, 154.36 (d, *J* = 1.8 Hz), 115.91 (d, *J* = 23.0 Hz), 115.76 (d, *J* = 7.9 Hz), 80.33, 68.98, 53.55, 52.72, 28.30.

^{19}F N MR (376 MHz, Chloroform-*d*) δ -122.91.

HRMS (ESI) m/z: $[M+ Na]^+$ Calcd for $C_{15}H_{20}FNO_5Na^+$: 336.1218; Found: 336.1217.



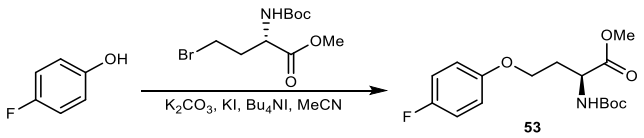
methyl N-(tert-butoxycarbonyl)-O-(4-fluoro-3-methoxyphenyl)-L-serinate (**52**). The title compound was prepared according to the general procedure **F** from (4-fluoro-3-methoxyphenyl)boronic acid (153 mg，0.90 mmol) and methyl (tert-butoxycarbonyl)-L-serinate (99 mg，0.45 mmol), and obtained as a light yellow oil (38 mg, 24.5%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.96 (dd, *J* = 11.0, 8.9 Hz, 1H), 6.52 (dd, *J* = 7.1, 2.9 Hz, 1H), 6.34 (dt, *J* = 8.9, 3.1 Hz, 1H), 5.48 (d, *J* = 8.8 Hz, 1H), 4.64 (dd, *J* = 8.0, 3.6 Hz, 1H), 4.35 (dd, *J* = 9.3, 3.0 Hz, 1H), 4.17 (dd, *J* = 9.3, 3.2 Hz, 1H), 3.86 (s, 3H), 3.78 (s, 3H), 1.46 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.52, 155.37, 154.72 (d, *J* = 2.4 Hz), 148.20 (d, *J* = 12.0 Hz), 147.65 (d, *J* = 238.9 Hz), 115.74 (d, *J* = 19.8 Hz), 104.40 (d, *J* = 6.7 Hz), 101.88, 80.36, 68.85, 56.22, 53.51, 52.75, 28.31.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -144.47.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{22}FNO_6Na^+$: 366.1323; Found: 366.1320.



methyl N-(tert-butoxycarbonyl)-O-(4-fluorophenyl)-L-homoserinate (53). The title compound was prepared according to the general procedure **C** from 4-fluorophenol (60 mg，0.54 mmol，1.0 equiv.) and methyl (S)-4-bromo-2-((tert-

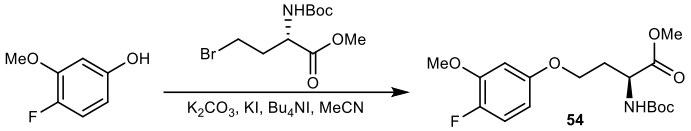
butoxycarbonyl)amino)butanoate (190 mg，0.65 mmol，1.2 equiv.), and obtained as a colourless oil (138 mg, 78.8%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.01 – 6.90 (m, 2H), 6.84 – 6.76 (m, 2H), 5.38 – 5.22 (m, 1H), 4.50 (q, *J* = 6.6 Hz, 1H), 4.00 (t, *J* = 6.0 Hz, 2H), 3.76 (s, 3H), 2.37 – 2.14 (m, 2H), 1.43 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.76, 157.42 (d, *J* = 238.6 Hz), 155.33, 154.60 (d, *J* = 2.2 Hz), 115.82 (d, *J* = 23.2 Hz), 115.56 (d, *J* = 7.9 Hz), 80.04, 64.73, 52.40, 51.21, 31.83, 28.29.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -123.63.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{22}FNO_5Na^+$: 350.1374; Found: 350.1370.



54

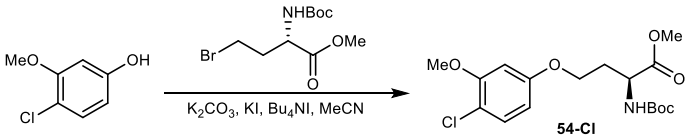
methyl N-(tert-butoxycarbonyl)-O-(4-fluoro-3-methoxyphenyl)-L-homoserinate (54). The title compound was prepared according to the general procedure **C** from 4-fluoro-3-methoxyphenol (76 mg，0.53 mmol，1.0 equiv.) and methyl (S)-4-bromo-2-((tert-butoxycarbonyl)amino)butanoate (188 mg，0.64 mmol，1.2 equiv.), and obtained as a white foamy solid(152 mg, 79.6%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.96 (dd, *J* = 11.0, 8.8 Hz, 1H), 6.51 (dd, *J* = 7.2, 2.9 Hz, 1H), 6.34 (dt, *J* = 8.9, 3.1 Hz, 1H), 5.27 – 5.25 (m, 1H), 4.52 – 4.50 (m, 1H), 4.00 (t, *J* = 6.0 Hz, 2H), 3.86 (s, 3H), 3.76 (s, 3H), 2.40 – 2.27 (m, 1H), 2.21 – 2.16 (m, 1H), 1.44 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.77, 155.34, 155.02 (d, *J* = 2.2 Hz), 148.12 (d, *J* = 12.0 Hz), 147.46 (d, *J* = 238.2 Hz), 115.73 (d, *J* = 19.6 Hz), 104.59 (d, *J* = 6.7 Hz), 101.77, 80.07, 64.73, 56.21, 52.42, 51.17, 31.92, 28.29.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -145.08.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{24}FNO_6Na^+$: 380.1480; Found: 380.1477.



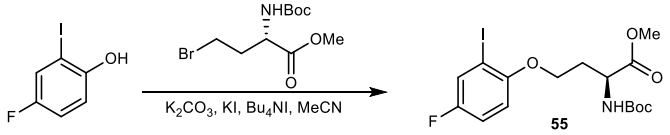
54-Cl

methyl N-(tert-butoxycarbonyl)-O-(4-chloro-3-methoxyphenyl)-L-homoserinate (54-Cl). The title compound was prepared according to the general procedure **C** from 4-chloro-3-methoxyphenol (84 mg, 0.53 mmol, 1.0 equiv.) and methyl (S)-4-bromo-2-((tert-butoxycarbonyl)amino)butanoate (188 mg, 0.64 mmol, 1.2 equiv.), and obtained as a white foamy solid (143 mg, 72.2%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.23 (d, *J* = 8.7 Hz, 1H), 6.48 (d, *J* = 2.6 Hz, 1H), 6.40 (dd, *J* = 8.7, 2.7 Hz, 1H), 5.26 – 5.19 (m, 1H), 4.55 – 4.43 (m, 1H), 4.03 (t, *J* = 6.0 Hz, 2H), 3.87 (s, 3H), 3.76 (s, 3H), 2.37 – 2.29 (m, 1H), 2.26 – 2.10 (m, 1H), 1.43 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.73, 158.35, 155.64, 130.16, 114.54, 105.96, 100.51, 80.13, 64.47, 56.09, 52.45, 51.12, 31.91, 28.29.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{24}ClNO_6Na^+$: 396.1184; Found: 396.1182.



55

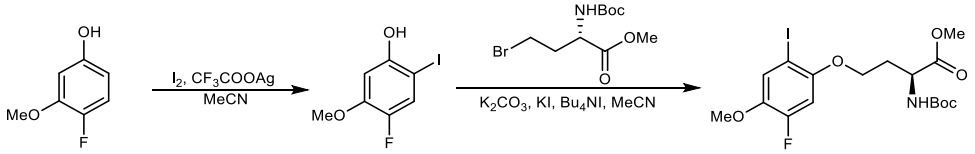
methyl N-(tert-butoxycarbonyl)-O-(4-fluoro-2-iodophenyl)-L-homoserinate (**55**). The title compound was prepared according to the general procedure **C** from 4-fluoro-2-iodophenol (125 mg, 0.53 mmol, 1.0 equiv.) and methyl (S)-4-bromo-2-((tert-butoxycarbonyl)amino)butanoate (188 mg，0.64 mmol，1.2 equiv.), and obtained as a colourless oil (172 mg, 72.3%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.50 (dd, *J* = 7.6, 3.0 Hz, 1H), 7.01 (ddd, *J* = 9.0, 7.8, 3.1 Hz, 1H), 6.73 (dd, *J* = 9.1, 4.6 Hz, 1H), 5.59 – 5.50 (m, 1H), 4.52 – 4.57 (m, 1H), 4.11 – 4.00 (m, 2H), 3.76 (s, 3H), 2.48 – 2.16 (m, 2H), 1.43 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.52, 157.00 (d, *J* = 244.1 Hz), 155.52, 153.86 (d, *J* = 2.6 Hz), 126.16 (d, *J* = 25.1 Hz), 115.65 (d, *J* = 22.6 Hz), 112.29 (d, *J* = 8.3 Hz), 85.88 (d, *J* = 8.0 Hz), 79.97, 66.74, 52.53, 51.75, 31.61, 28.32.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -121.61.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{21}FINO_5Na^+$: 476.0341; Found: 476.0340.



56-i 56

4-fluoro-2-iodo-5-methoxyphenol(56-i). To a solution of 4-fluoro-3-methoxyphenol (284 mg，2.0 mmol，1.0 equiv.) in MeCN were added I_2（610 mg，2.4 mmol，1.2 equiv.）and CF_3COOAg (57 mg, 20%). The solution was stirred at room temperature for 36 h and then quenched with saturated $Na_2S_2O_3$ solution. The reaction was extracted with ethyl acetate and water. The organic phase was dried with Na_2SO_4, filtered, and concentrated in vacuo to give the crude product, which was purified by silica gel column with PE/EA =15/1 as the eluant to give the title compound as a white solid (194 mg, 46.8%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 (d, *J* = 10.2 Hz, 1H), 6.67 (d, *J* = 7.5 Hz, 1H), 5.08 (s, 1H), 3.85 (s, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 151.74 (d, *J* = 2.6 Hz), 149.21 (d, *J* = 11.7 Hz), 146.84 (d, *J* = 243.1 Hz), 123.65 (d, *J* = 22.0 Hz), 100.24 (d, *J* = 1.6 Hz), 70.95 (d, *J* = 7.7 Hz), 56.26.

methyl N-(tert-butoxycarbonyl)-O-(5-fluoro-2-iodo-4-methoxyphenyl)-L-homoserinate (**56**). The title compound was prepared according to the general procedure **C** from compound **56-©** (143 mg，0.53 mmol，1.0 equiv.) and methyl (S)-4-bromo-2-((tert-butoxycarbonyl)amino)butanoate (188 mg，0.64 mmol，1.2 equiv.) as a brown foamy solid (121 mg, 72.3%).

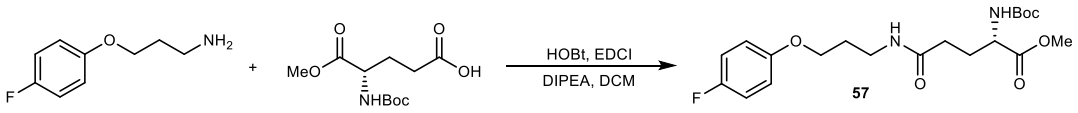
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 (d, *J* = 10.4 Hz, 1H), 6.51 (d, *J* = 7.3 Hz, 1H), 5.65 – 5.47 (m, 1H), 4.64 – 4.476 (m, 1H), 4.13 – 4.00 (m, 2H), 3.88 (s, 3H), 3.77 (s, 3H), 2.45 – 2.37 (m, 1H), 2.31 – 2.16 (m, 1H), 1.44 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.53, 155.33, 154.09, 148.36 (d, *J* = 11.6 Hz), 147.42 (d, *J* = 243.8 Hz), 125.60 (d, *J*

= 21.7 Hz), 99.73, 80.01, 73.09 (d, *J* = 7.2 Hz), 67.11, 56.66, 52.57, 51.67, 31.78, 28.32.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -141.88.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{23}FINO_6Na^+$: 506.0446; Found: 506.0447.



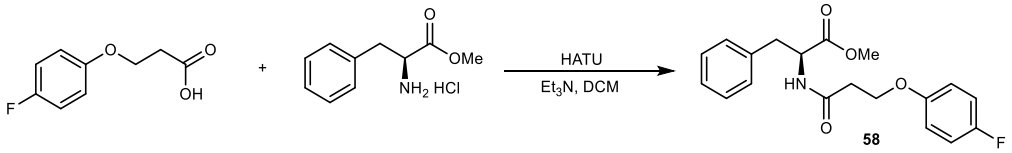
methyl N2-(tert-butoxycarbonyl)-N5-(3-(4-fluorophenoxy)propyl)-L-glutaminate (57). Following the preparation procedure of compound **32**, the title compound was obtained from (S)-4-((tert-butoxycarbonyl)amino)-5-methoxy-5-oxopentanoic acid (131 mg, 0.50 mmol, 1.0 equiv.) and 3-(4-fluorophenoxy)propan-1-amine (93 mg, 0.55 mmol, 1.1 equiv.) as a white solid (172 mg, 83.5%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.04 – 6.90 (m, 2H), 6.90 – 6.75 (m, 2H), 6.39 (br, 1H), 5.33 (d, *J* = 8.3 Hz, 1H), 4.28 (td, *J* = 8.9, 4.2 Hz, 1H), 4.00 (t, *J* = 6.0 Hz, 2H), 3.73 (s, 3H), 3.46 (qd, *J* = 6.7, 4.7 Hz, 2H), 2.27 (dd, *J* = 8.1, 6.3 Hz, 2H), 2.18 (ddd, *J* = 19.2, 10.5, 5.7 Hz, 1H), 2.00 (p, *J* = 6.4 Hz, 2H), 1.92 (dd, *J* = 21.8, 7.2 Hz, 1H), 1.43 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.72, 171.97, 157.32 (d, *J* = 238.3 Hz), 155.89, 154.83 (d, *J* = 2.0 Hz), 115.95, 115.72, 115.49, 115.41, 80.18, 66.60, 52.93, 52.45, 37.12, 32.68, 29.21, 29.08, 28.28.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -123.85.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{30}FN_2O_6^+$: 413.2082; Found: 413.2079.



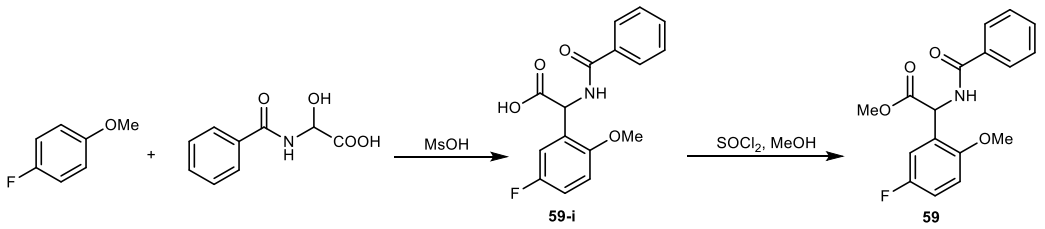
methyl (3-(4-fluorophenoxy)propanoyl)-L-phenylalaninate (**58**). To a solution of 3-(4-fluorophenoxy)propanoic acid (92 mg, 0.50 mmol, 1.0 equiv.) and D-Phenylalanine methyl ester hydrochloride in DCM (5 mL) were added Et_3N（200 μl，1.5 mmol）and HATU (230 mg, 0.60 mmol, 1.2 equiv.). The reaction was stirred at room temperature for 3h. The solution was then washed with 1M citric acid aqueous solution, saturated $NaHCO_3$ solution, water, and saturated NaCl solution, dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (PE: EA= 2:1) to yield the title compound as a colourless oil (113 mg, 65.3%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.22 (dd, *J* = 5.0, 1.9 Hz, 3H), 7.12 – 7.03 (m, 2H), 7.01 – 6.91 (m, 2H), 6.82 – 6.75 (m, 2H), 6.41 (d, *J* = 7.8 Hz, 1H), 4.95 – 4.90 (m, 1H), 4.20 – 4.12 (m, 2H), 3.73 (s, 3H), 3.23 – 3.04 (m, 2H), 2.65 (dd, *J* = 6.6, 5.4 Hz, 2H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.88, 170.00, 157.56 (d, *J* = 238.9 Hz), 154.33 (d, *J* = 2.1 Hz), 135.73, 129.27, 128.54, 127.12, 115.88 (d, *J* = 20.4 Hz), 115.73 (d, *J* = 5.2 Hz), 64.70, 53.11, 52.36, 37.81, 36.52.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -123.52.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{21}FNO_4^+$: 346.1449; Found: 346.1446.



2-benzamido-2-(5-fluoro-2-methoxyphenyl)acetic acid (**59-i**). 1-fluoro-4-methoxybenzene (969 mg，17.68 mmol，1.0 equiv.) and α-hydroxyhippuricacid (1.5 g，7.68 mmol) were added to a round bottom flask containing 6 mL methanesulfonic acid at 0 ºC. The solution was stirred at room temperature for 1h and poured into ice water. The precipitate was collected after filtration and washed with water. After drying, the solid (1.82 g, 78.1%) was used for the next step without further purification.

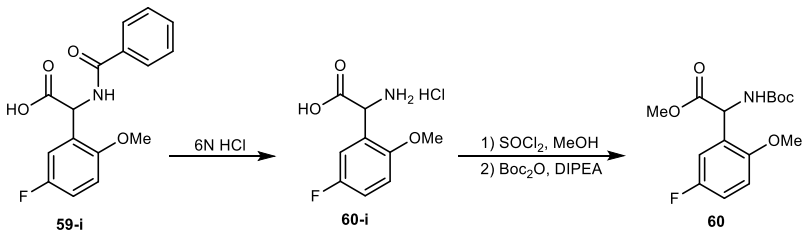
Methyl 2-benzamido-2-(5-fluoro-2-methoxyphenyl)acetate (**59**). To a solution of **59-©** in MeOH, $SOCl_2$ was added (265 μl，3.68 mmol，9.2 equiv.) at 0 ºC. The solution was warmed to room temperature and stirred for 24 h. The reaction was quenched by the addition of 1 ml water. After removal of the solvent, the crude product was dissolved in 10 ml DCM and washed with water and saturated NaCl solution, dried over anhydrous sodium sulfate, filtered, and the solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (PE: EA = 5:1) to yield the title compound as a white solid (95 mg, 75.4%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.85 – 7.76 (m, 2H), 7.54 – 7.46 (m, 1H), 7.47 – 7.39 (m, 2H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.18 (dd, *J* = 8.3, 3.1 Hz, 1H), 7.00 (ddd, *J* = 8.9, 7.9, 3.1 Hz, 1H), 6.85 (dd, *J* = 9.0, 4.3 Hz, 1H), 5.92 (d, *J* = 8.0 Hz, 1H), 3.85 (s, 3H), 3.74 (s, 3H).

^{13}C NMR (100 MHz, Chloroform-d) δ 171.11, 166.58, 156.89 (d, *J* = 240.2 Hz), 153.28 (d, *J* = 2.3 Hz), 133.86, 131.78, 128.58, 127.17,126.92 (d, *J* = 7.2 Hz), 117.58 (d, *J* = 24.0 Hz), 115.73 (d, *J* = 22.8 Hz), 112.20 (d, *J* = 8.0 Hz), 56.32, 53.29 (d, *J* = 1.4 Hz), 52.88.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -122.69.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{17}FNO_4^+$: 318.1136; Found: 318.1133.



2-amino-2-(5-fluoro-2-methoxyphenyl)acetic acid hydrochloride (60-i). The compound **59-©** (500 mg, 1.65 mmol, 1.0

equiv.) was dissolved in 30 mL 6N HCl. The mixture was stirred under reflux for 24 h. The solution was cooled to temperature and washed with EA. The aqueous solution was concentrated to give the title compound as a white solid (285 mg, 86.9%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 13.78 (br, 1H), 8.80 (br, 2H), 7.35 (dd, J = 9.0, 3.1 Hz, 1H), 7.27 (td, J = 8.6, 3.1 Hz, 1H), 7.12 (dd, J = 9.1, 4.5 Hz, 1H), 5.14 (s, 1H), 3.80 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 169.58, 156.24 (d, J = 236.7 Hz), 153.87 (d, J = 2.0 Hz), 123.33 (d, J = 7.9 Hz), 117.46 (d, J = 7.8 Hz), 117.23 (d, J = 9.9 Hz), 113.53 (d, J = 8.2 Hz), 56.87, 51.21.

^{19}F NMR (376 MHz, DMSO-d_6) δ -123.33.

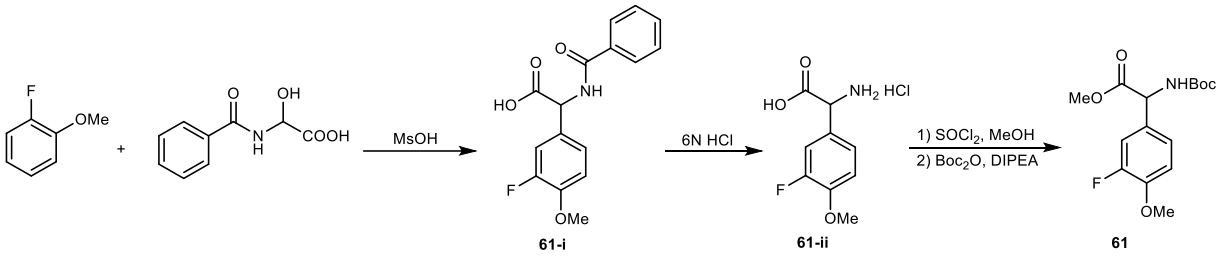
methyl 2-((tert-butoxycarbonyl)amino)-2-(5-fluoro-2-methoxyphenyl)acetate (**60**). The solution of compound **60-©** was cooled to 0°C, and $SOCl_2$ (1.0 ml，13.89 mmol，9.2 equiv.) was added. The solution was warmed to room temperature and stirred for 24 h. The reaction was quenched with 1 mL water and then concentrated under reduced pressure to give the methyl ester. The intermediate was dissolved in dioxane. DIPEA (657 μl，3.78 mmol，2.5 equiv.) and Boc_2O (395 mg，1.81 mmol，1.2 equiv.) were added to the solution. The solution was stirred at room temperature for 2h and diluted with EA. The solution was washed with water and saturated NaCl solution. The organic phase was dried with Na_2SO_4, filtered, and concentrated in vacuo to give the crude product, which was purified by silica gel column with PE/EA =10/1 as the eluant to give the title compound as a white solid (310 mg, 65.5%)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.05 (dd, J = 8.4, 3.1 Hz, 1H), 6.98 (ddd, J = 9.0, 8.0, 3.1 Hz, 1H), 6.81 (dd, J = 9.0, 4.3 Hz, 1H), 5.66 (d, J = 8.9 Hz, 1H), 5.44 (d, J = 8.8 Hz, 1H), 3.81 (s, 3H), 3.70 (s, 3H), 1.44 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.40, 156.81 (d, J = 239.8 Hz), 155.17, 153.13, 127.38 (d, J = 7.1 Hz), 117.09 (d, J = 23.7 Hz), 115.48 (d, J = 22.8 Hz), 111.96 (d, J = 8.0 Hz), 80.11, 56.14, 54.14, 52.69, 28.34.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -123.03.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{15}H_{20}FNO_5Na^+$: 336.1218; Found: 336.1214.



2-benzamido-2-(3-fluoro-4-methoxyphenyl)acetic acid (**61-i**). Following the preparation procedure of compound **59-©**, the title compound was obtained from 1-fluoro-2-methoxybenzene (646 mg，5.13 mmol，1.0 equiv.) and α-hydroxyhippuricacid (1.0 g，5.13 mmol, 1.0 equiv.) as a white solid (1.32 g, 85.2%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.95 (br, 1H), 9.01 (d, J = 7.5 Hz, 1H), 7.91 (dt, J = 7.1, 1.4 Hz, 2H), 7.58 – 7.51 (m, 1H),

7.47 (dd, *J* = 8.2, 6.7 Hz, 2H), 7.38 (dd, *J* = 12.6, 2.1 Hz, 1H), 7.31 – 7.25 (m, 1H), 7.17 (t, *J* = 8.7 Hz, 1H), 5.57 (d, *J* = 7.5 Hz, 1H), 3.84 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 172.27, 166.73, 151.58 (d, *J* = 243.7 Hz), 147.29 (d, *J* = 10.5 Hz), 134.18, 131.98, 1130.38 (d, *J* = 6.3 Hz), 128.69, 128.13, 125.14 (d, *J* = 3.3 Hz), 116.08 (d, *J* = 19.0 Hz), 114.09 (d, *J* = 2.0 Hz), 56.51, 56.37.

^{19}F NMR (376 MHz, DMSO-d_6) δ -135.37.

2-amino-2-(3-fluoro-4-methoxyphenyl)acetic acid hydrochloride(61-ii). Following the preparation procedure of compound **60-I**, the title compound was obtained as a white solid (585 mg, 89.3%).

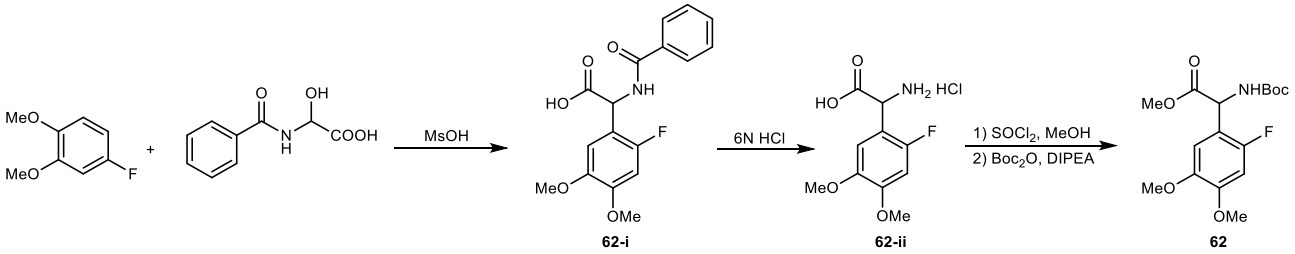
Methyl 2-((tert-butoxycarbonyl)amino)-2-(3-fluoro-4-methoxyphenyl)acetate (61). Following the preparation procedure of compound **60**, the title compound was obtained from **61-ii** as a white solid (415 mg, 87.7%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.11 (t, J = 2.7 Hz, 1H), 7.08 (d, J = 1.2 Hz, 1H), 6.93 (t, J = 8.4 Hz, 1H), 5.56 (d, J = 7.0 Hz, 1H), 5.24 (d, J = 7.3 Hz, 1H), 3.88 (s, 3H), 3.73 (s, 3H), 1.43 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.35, 154.73, 152.35 (d, J = 247.1 Hz), 147.75 (d, J = 10.6 Hz), 129.91, 123.09, 114.88 (d, J = 19.7 Hz), 113.53 (d, J = 2.1 Hz), 80.31, 56.70, 56.28, 52.82, 28.29.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -133.94.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{15}H_{20}FNO_5Na^+$: 336.1218; Found: 336.1217.



2-benzamido-2-(2-fluoro-4,5-dimethoxyphenyl)acetic acid (62-i). Following the preparation procedure of compound **59-©**, the title compound was obtained as a white solid (2.0 g, 47%) from 4-fluoro-1,2-dimethoxybenzene (2.0 g，12.8 mmol，1.0 equiv.) and α-hydroxyhippuricacid (2.5 g, 12.8 mmol, 1.0 equiv.).

2-amino-2-(2-fluoro-4,5-dimethoxyphenyl)acetic acid hydrochloride (62-ii). Following the preparation procedure of compound **60-I**, the title compound was obtained as a white solid (200 mg, 29%) from **62-©** (1.0 g, 3.0 mmol).

Methyl 2-((tert-butoxycarbonyl)amino)-2-(2-fluoro-4,5-dimethoxyphenyl)acetate (62). Following the preparation procedure of compound **60**, the title compound was obtained as a white solid (84 mg, 39.4%) from **62-ii** (150 mg, 0.65 mmol).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.78 (d, *J* = 6.8 Hz, 1H), 6.64 (d, *J* = 11.2 Hz, 1H), 5.57 (d, *J* = 7.6 Hz, 1H), 5.46 (d, *J* = 7.8 Hz, 1H), 3.86 (s, 6H), 3.73 (s, 3H), 1.44 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.24, 154.89, 154.69 (d, *J* = 242.0 Hz), 149.94 (d, *J* = 9.8 Hz), 145.52, 114.99 (d, *J* = 16.1 Hz), 111.02, 100.30 (d, *J* = 25.2 Hz), 80.28, 56.47, 56.18, 52.89, 52.09, 28.30.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -124.84.

HRMS (ESI) m/z: $[M+K]^+$ Calcd for $C_{16}H_{22}FNO_6K^+$: 382.1063 ; Found: 382.1060.

63

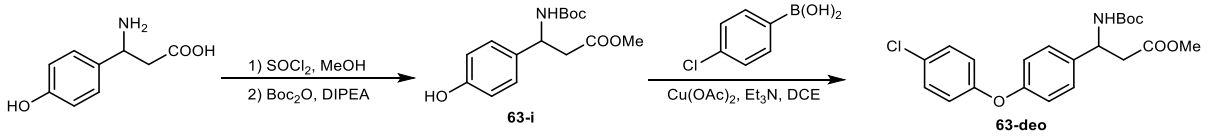
methyl 3-((tert-butoxycarbonyl)amino)-3-(4-fluorophenyl)propanoate (63). Following the preparation procedure for compound **60**, the title compound was obtained as a white solid (283 mg, 42.0%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 – 7.24 (m, 2H), 7.06 – 6.96 (m, 2H), 5.27 (d, *J* = 165.7 Hz, 2H), 3.62 (s, 3H), 2.81 (td, *J* = 15.4, 14.0, 6.1 Hz, 2H), 1.42 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ171.27, 162.08 (d, *J* = 245.8 Hz), 154.98, 127.79 (d, *J* = 8.1 Hz), 115.49 (d, *J* = 21.5 Hz), 79.89, 51.83, 50.61, 40.71, 28.33

^{19}F NMR (376 MHz, Chloroform-*d*) δ -115.14.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{15}H_{20}FNO_4Na^+$: 320.1269; Found: 320.1265.



63-i

63-deo

methyl 3-((tert-butoxycarbonyl)amino)-3-(4-hydroxyphenyl)propanoate (63-i). Following the preparation procedure for compound **60**, the title compound was obtained as a white solid (209 mg, 46%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.05 (d, *J* = 8.5 Hz, 2H), 6.69 – 6.59 (m, 2H), 6.48 (s, 1H), 5.53 (s, 1H), 5.00 (s, 1H), 3.61 (s, 3H), 2.80 (qd, *J* = 15.3, 6.2 Hz, 2H), 1.43 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.72, 155.56, 155.36, 132.49, 127.27, 115.53, 80.12, 51.87, 50.88, 40.95, 28.38.

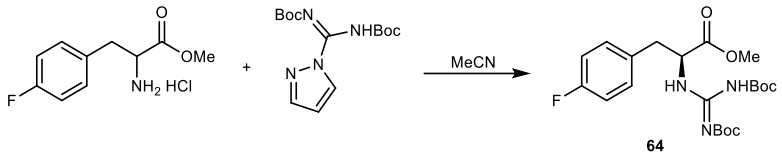
HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{15}H_{21}NO_5Na^+$: 318.1312; Found: 318.1310.

methyl 3-((tert-butoxycarbonyl)amino)-3-(4-(4-chlorophenoxy)phenyl)propanoate (63-deo). To a solution of compound **63-©** (102 mg, 0.35 mmol) in 30 mL DCM, p-chlorophenylboronic acid (110 mg, 0.70 mmol), copper acetate (84 mg, 0.42 mmol) and triethylamine (53 mg, 0.53 mmol) were added. The reaction was stirred under room temperature overnight. 30 mL of water was added to the reaction, and the solution was extracted with DCM. The organic layer was washed with saturated brine and dried with anhydrous sodium sulfate, filtered and concentrated to give the residue, which was then separated and refined by silica gel column chromatography (petroleum ether: ethyl acetate =10:1) to give the title compound as a colourless oil (44 mg, 31.0%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.25 (m, 4H), 7.00 – 6.85 (m, 4H), 5.47 (s, 1H), 5.08 (s, 1H), 3.63 (s, 3H), 2.84 (qd, *J* = 15.4, 6.2 Hz, 2H), 1.43 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.36, 156.25, 155.73, 155.03, 129.75, 128.39, 127.68, 120.17, 118.89, 51.84, 29.71, 28.36.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{24}ClNO_5Na^+$: 428.1235; Found: 428.1234.



64

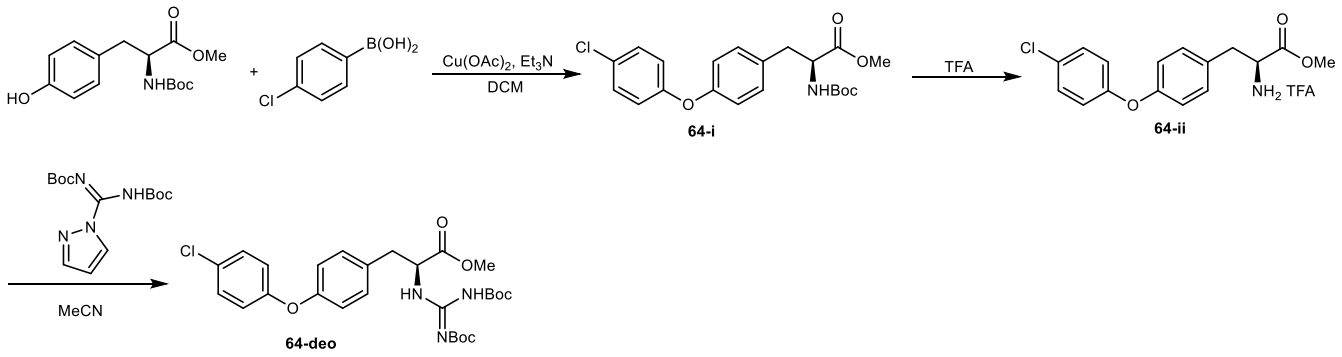
methyl (S,Z)-2-(2,3-bis(tert-butoxycarbonyl)guanidino)-3-(4-fluorophenyl)propanoate (**64**). To a solution of Methyl 2-amino-3-(4-fluorophenyl)propanoate hydrochloride (233 mg，1.00 mmol，1.0 equiv.) and N,N'-Di-Boc-1H-pyrazole-1-carboximidamide (341 mg，1.10 mmol，1.1 equiv.) in MeCN (10 ml) was added K_2CO_3 (345 mg，2.50 mmol，1.5 equiv.). The solution was stirred at room temperature for 24 h and then quenched by the addition of water (20 ml). The reaction was extracted with ethyl acetate. The organic layers were combined and washed with saturated sodium chloride aqueous solution, dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (PE: EA = 15:1) to obtain the title compound as a white solid (153 mg, 34.8%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 11.37 (s, 1H), 8.77 (d, *J* = 7.5 Hz, 1H), 7.18 – 7.07 (m, 2H), 7.04 – 6.91 (m, 2H), 5.06 (dt, *J* = 7.5, 5.9 Hz, 1H), 3.71 (s, 3H), 3.22 – 3.03 (m, 2H), 1.49 (s, 18H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.46, 163.28, 162.06 (d, *J* = 246.0 Hz), 155.40, 152.79, 131.58 (d, *J* = 3.3 Hz), 130.97, 130.89, 115.44, 115.23, 83.34, 79.37, 54.51, 52.33, 37.27, 28.27, 28.01.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -115.83.

HRMS (ESI): Calculated for $C_{21}H_{31}FN_3O_6Na^+$ $[M+H]^+$: 440.2191 Found: 440.2186.



64-i　　64-ii　　64-deo

methyl (S)-2-((tert-butoxycarbonyl)amino)-3-(4-(4-chlorophenoxy)phenyl)propanoate (**64-i**). To a solution of Boc-*L*-Tyrosine methyl ester (1.2 g，4.07 mmol，1.0 equiv.) and (4-chlorophenyl)boronic acid (699 mg，4.48 mmol，1.1 equiv.) were added $Cu(Oac)_2$ (896 mg，4.48 mmol，1.1 equiv.) and Et_3N (847 μl，6.11 mmol，1.5 equiv.). The solution was stirred at room temperature for 24h and then quenched by the addition of 1M citric acid (40 mL). The reaction was extracted with dichloromethane. The organic layers were combined and washed with saturated sodium chloride aqueous solution, dried over

anhydrous sodium sulfate, filtered, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (PE: EA = 15:1) to obtain the title compound as a white solid (396 mg, 24%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.24 (m, 2H), 7.13 – 7.06 (m, 2H), 6.95 – 6.89 (m, 4H), 5.01 (d, J = 8.4 Hz, 1H), 4.58 (q, J = 6.6 Hz, 1H), 3.73 (s, 3H), 3.11 (dd, J = 13.9, 5.6 Hz, 1H), 3.01 (dd, J = 13.9, 6.3 Hz, 1H), 1.42 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.28, 155.97, 155.87, 155.05, 131.33, 130.74, 129.73, 128.28, 120.07, 118.92, 80.00, 54.46, 52.28, 37.74, 28.31.

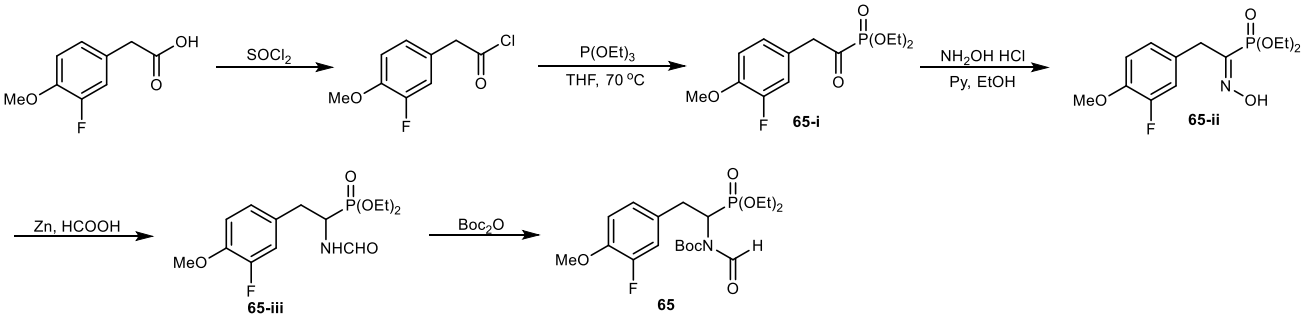
methyl (S)-2-amino-3-(4-(4-chlorophenoxy)phenyl)propanoate trifluoroacetic acid (**64-ii**). To a solution of **64-©** (320 mg，0.79 mmol) in DCM, TFA (2 ml) was added. The solution was stirred at room temperature for 5h. After removing the solvent, the crude product was used in the next step without further purification.

Methyl(S,Z)-2-(2,3-bis(tert-butoxycarbonyl)guanidino)-3-(4-(4-chlorophenoxy)phenyl)propanoate (**64**). To a solution of **64-ii** (331 mg，0.79 mmol，1.0 equiv.) and N,N'-Di-Boc-1H-pyrazole-1-carboximidamide (269 mg，0.87 mmol，1.1 equiv.) in MeCN (10 mL) were added K_2CO_3 (275 mg，1.98 mmol，2.5 equiv.). The solution was stirred at room temperature for 24h and then quenched by the addition of water (20 ml). The reaction was extracted with ethyl acetate. The organic layers were combined and washed with saturated sodium chloride aqueous solution, dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (PE: EA = 15:1) to obtain the title compound as a white solid (353 mg, 81.5%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 11.38 (s, 1H), 8.76 (d, J = 7.5 Hz, 1H), 7.30 – 7.24 (m, 2H), 7.16 – 7.08 (m, 2H), 6.96 – 6.86 (m, 4H), 5.07 (dt, J = 7.6, 5.9 Hz, 1H), 3.72 (s, 3H), 3.24 – 3.04 (m, 2H), 1.49 (s, 9H), 1.48 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.56, 163.31, 156.00, 155.93, 155.45, 152.80, 131.15, 130.90, 129.69, 128.14, 119.95, 118.97, 83.30, 79.37, 54.50, 52.33, 37.27, 28.28, 28.02.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{35}ClN_3O_7^+$: 548.2158; Found: 548.2162.



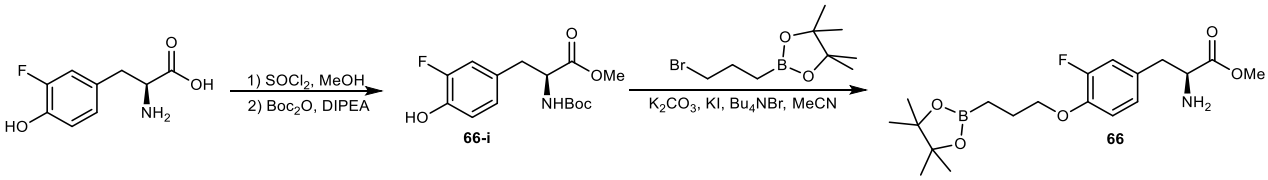
tert-butyl (1-(diethoxyphosphoryl)-2-(3-fluoro-4-methoxyphenyl)ethyl)(formyl)carbamate (65). The title compound was prepared according to a modified literature procedure[5]. 2-(3-fluoro-4-methoxyphenyl)acetic acid (0.92 g, 5 mmol) was dissolved in thionyl chloride (10 mL) and refluxed for 2 h. The reaction mixture was concentrated in vacuo to give the crude phenylacetyl chloride as a yellow liquid which was dissolved in dry tetrahydrofuran (10 mL) and cooled to 0 °C. Triethyl phosphite (0.83 g, 5 mmol) was then added dropwise. Then, the mixture was stirred at 70 °C for 30 min. The resulting solution

was concentrated to remove volatile compounds. The crude α-keto phosphonate and hydroxylamine hydrochloride (0.42 g, 6 mmol) were added to the mixture of dry pyridine (1 ml) and dry ethanol (10 ml). The mixture was stirred at room temperature for 12 h and then concentrated in vacuo. The crude product was dissolved in dichloromethane (30 mL) and washed with 2 N HCl (3 × 10 mL) and water (10 ml). The organic layer was dried with anhydrous $MgSO_4$, filtered, and concentrated to obtain the crude oxime. Finally, the crude oxime was added to a suspension of zinc (1.3 g, 20 mmol) in anhydrous formic acid (10 mL), and the mixture was refluxed overnight under nitrogen. The suspension was filtered, and the filtrate was concentrated. The crude formamide was dissolved in THF (10 mL), and to it was added Boc_2O (1.9 g, 5 mmol). The mixture was stirred under reflux for 4 h and cooled to room temperature. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography using DCM/MeOH (20:1) to give the title compound (mixture of 2 rotamers) as a yellow oil (360 mg, 17% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.1 (s, 0.32H), 8.95 (s, 0.57H), 6.91 – 6.80 (m, 3H), 5.09 (ddd, J = 20.4, 11.3, 5.6 Hz, 0.58H), 4.89 – 4.72 (m, 0.42H), 4.37 – 4.01 (m, 4H), 3.84 (s, 3H), 3.33 (dt, J = 13.8, 11.1 Hz, 1H), 3.11 (dd, J = 28.3, 13.8 Hz, 1H), 1.36 – 1.29 (m, 9H).

^{19}F NMR (100 MHz, $CDCl_3$): δ -135.29 (m).

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{29}FNO_7Pna^+$: 456.1558; Found: 456.1559.



methyl (S)-2-amino-3-(3-fluoro-4-hydroxyphenyl)propanoate hydrochloride (66-i). Following the preparation procedure of compound **60**，the title compound was obtained from 3-fluoro-*L*-tyrosine (120 mg，0.6 mmol，1.0 equiv.) as a white solid (135 mg, 90.6%).

Methyl (S)-2-((tert-butoxycarbonyl)amino)-3-(3-fluoro-4-hydroxyphenyl)propanoate (66-i). Following the preparation procedure of compound **60**, the title compound was obtained from 3-fluoro-*L*-tyrosine as a white solid (89 mg, 83.9%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.90 (t, *J* = 8.6 Hz, 1H), 6.85 (dd, *J* = 11.4, 2.1 Hz, 1H), 6.78 (dd, *J* = 8.7, 2.1 Hz, 1H), 5.30 (br, 1H), 5.00 (d, *J* = 8.3 Hz, 1H), 4.54 (q, *J* = 6.5 Hz, 1H), 3.72 (s, 3H), 3.10 – 2.82 (m, 2H), 1.43 (s, 9H).

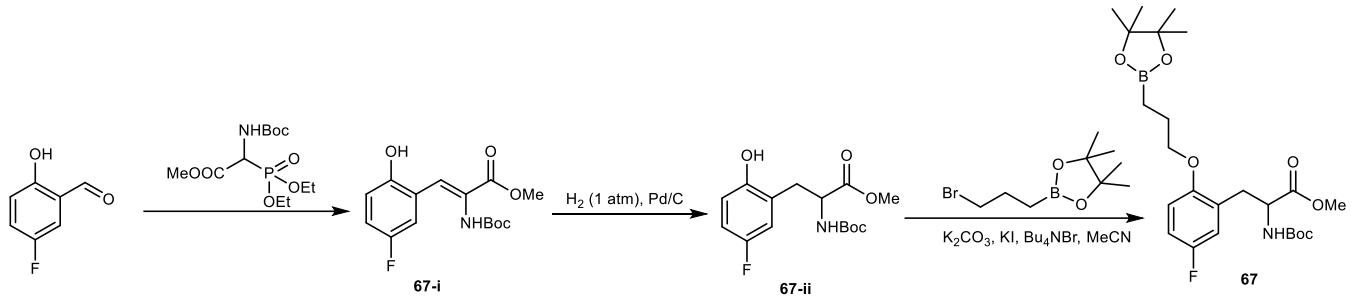
Methyl(S)-2-amino-3-(3-fluoro-4-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propoxy)phenyl)propanoate (66). The title compound was prepared according to the general procedure **C** from **66-©** (80 mg，0.26 mmol，1.0 equiv.) and 2-(3-bromopropyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (78 mg, 0.31 mmol, 1.2 equiv.), and obtained as a colorless oil (65 mg, 52.0%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.89 (t, J = 8.4 Hz, 1H), 6.86 – 6.75 (m, 2H), 4.98 (d, J = 8.3 Hz, 1H), 4.53 (q, J = 6.6 Hz, 1H), 3.98 (t, J = 6.8 Hz, 2H), 3.72 (s, 3H), 3.00 (qd, J = 14.0, 5.8 Hz, 2H), 1.98 – 1.86 (m, 2H), 1.42 (s, 9H), 1.25 (s, 12H), 0.92 (t, J = 7.8 Hz, 2H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.17, 155.04, 152.46 (d, J = 246.0 Hz), 146.19 (d, J = 10.9 Hz), 128.71 (d, J = 6.2 Hz), 124.88, 117.02 (d, J = 18.5 Hz), 114.94 (d, J = 2.3 Hz), 83.13, 80.01, 71.05, 54.39, 52.27, 37.40, 28.29, 24.83, 23.70,7.00.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -134.19.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{24}H_{37}BFNO_7Na^+$: 504.2539; Found: 504.2541.



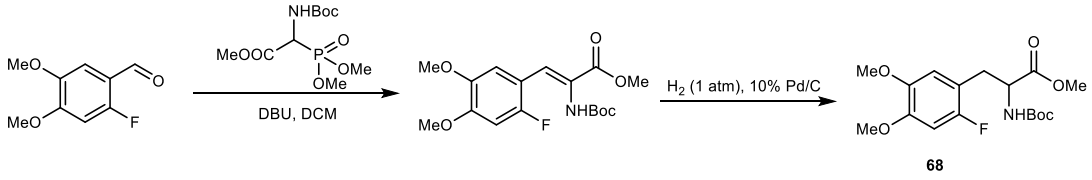
methyl 2-((tert-butoxycarbonyl)amino)-3-(5-fluoro-2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propoxy)phenyl)propanoate (67). Following the preparation procedure of compound **66**, the title compound was obtained from compound **67-ii** (120 mg，0.38 mmol，1.0 equiv.) and 2-(3-bromopropyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (115 mg, 0.46 mmol, 1.2 equiv.) as a white solid (85 mg, 46.4%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.87 (td, J = 8.4, 3.1 Hz, 1H), 6.82 (dd, J = 8.8, 3.1 Hz, 1H), 6.78 (dd, J = 8.9, 4.5 Hz, 1H), 5.40 (d, J = 7.9 Hz, 1H), 4.48 (td, J = 8.0, 4.8 Hz, 1H), 3.93 (q, J = 7.3 Hz, 2H), 3.71 (s, 3H), 3.11 (dd, J = 13.6, 4.9 Hz, 1H), 2.96 (dd, J = 13.6, 8.2 Hz, 1H), 1.98 – 1.88 (m, 2H), 1.39 (s, 9H), 1.25 (s, 12H), 0.97 – 0.88 (m, 2H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.56, 156.68 (d, J = 238.5 Hz), 155.26, 153.17, 126.75 (d, J = 7.2 Hz), 117.68 (d, J = 23.1 Hz), 114.09 (d, J = 22.8 Hz), 112.22 (d, J = 8.2 Hz), 83.17, 79.62, 70.49, 54.24, 52.13, 32.80, 28.27, 24.85, 23.67, 7.21.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -124.25.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{24}H_{37}BFNO_7Na^+$: 504.2539; Found: 504.2542.



methyl 2-((tert-butoxycarbonyl)amino)-3-(2-fluoro-4,5-dimethoxyphenyl)propanoate (68). The title compound was prepared according to the reported procedure. The spectra data matched the reported literature[6].

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.63 – 6.35 (m, 2H), 4.99 (d, *J* = 8.3 Hz, 1H), 4.47 (q, *J* = 6.8 Hz, 1H), 3.77 (d, *J* = 3.4 Hz, 6H), 3.66 (s, 3H), 2.99 (qd, *J* = 14.0, 6.1 Hz, 2H), 1.34 (s, 9H).

3. Radiolabeling experiments

3.1 Reagents and equipment information

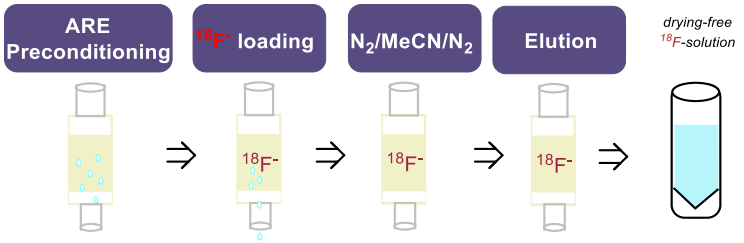
All chemicals are analytical grade and used without further purification. ^{18}F was produced in an HM-10 cyclotron (Sumitomo Heavy Industries, Ltd., Japan) *via* $^{18}O(p, n)$ ^{18}F nuclear reaction. Sep-PAK® light QMA cartridges, Alumina N Cartridges, and Sep-Pak light C18 Cartridges were purchased from Waters. KT-101 anion exchange resins were purchased from Huayi Isotopes (https://nucmedcor.com/sup18supf-separation-cartridge-pshco3). Photocatalyst **S1** was purchased from Acmec Biochemical and used directly. Tetrabutylammonium bicarbonate MeCN solution was prepared according to the reported procedure[6]. Analytic grades of solvents used for the ^{18}F-labeling reaction were purchased and used as received. Acetonitrile (MeCN) was purchased from Chron Chemicals; dichloroethane (DCE) was purchased from Aladdin Biochemical; tert-butyl alcohol (t-BuOH) was purchased from J&K Scientific; dichloromethane (DCM) was purchased from Titan Sci. Tetrabutylammonium perchloride (TBAP) was purchased from Sigma-Aldrich. The solid TBAP salt was dissolved in MeCN to obtain a solution (0.1mg/μl) for labeling reactions (0.1mg/μl), and 30 μl of the solution (3 mg TBAP) was used to prepare the eluent for the full-batch labeling reaction.

The blue LED lamp (A160WE TUNA BLUE) was purchased from Kessil, and the irradiation wavelengths observed are centered around 456 nm. The automatic radiosynthesis module (AllinOne 4530) and ^{18}F-FDOPA production cassette were purchased from Trasis. The LED reactor (ProBox, Model No. PR486-450) was purchased from LED RADIOFLUIDICS. ^{18}F activity was counted using a CRC-25 PET detector. High-performance liquid chromatography (HPLC) was accomplished on an Agilent chromatography system (Model 1260), collecting a radiation detector (Bioscan flow-count FC3200).

3.2 General procedure for anion-exchange resin preconditioning

The anion-exchange resin (KT-101, HCO_3^-) was washed with 10 ml water and then directly used for the $^{18}F^-$ capture, or the resin was washed with 10 ml 1M basic solution (K_2CO_3 or K_3PO_4 or K_2HPO_4) and followed by 10 ml water.

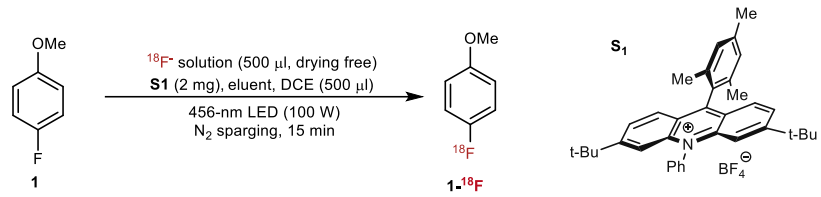
3.3. Preparation of azeotropic drying-free $^{18}F^-$ solution



Supplementary Figure 1. Illustration of azeotropic drying-free $^{18}F^-$ solution preparation

The aqueous $^{18}F^-$ solution produced by the cyclotron was loaded on a preconditioned anion-exchange resin (KT-101). After the loading, the resin was flushed under N_2 flow for 10 seconds to remove most of the water, then washed with 5 ml MeCN and flushed with N_2 for another 5 min. The $^{18}F^-$ was then eluted in a 5 ml v-vial with eluents listed in Supplementary Table **1** to provide the azeotropic drying-free $^{18}F^-$ solution for labelling (Supplementary Figure **1**). The $^{18}F^-$ eluted in the v-vial and left on the resin were recorded to calculate the elution efficiency.

3.4 Aryl ^{18}F-fluorination optimization with a portion of the drying-free ^{18}F$^-$ solution



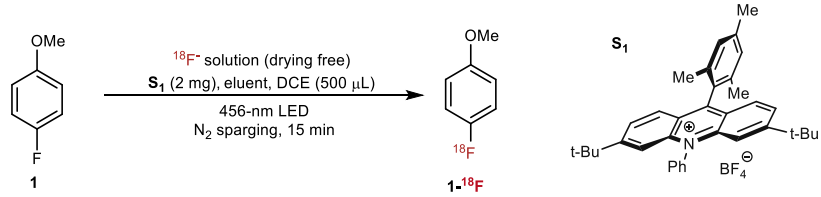
Fluoro-4-methoxybenzene (2 μL), photocatalyst S1 (2 mg), were dissolved in 1,2-dichloroethane (DCE, 500 μL) in a 5 ml v-vial. The drying-free ^{18}F$^-$ solution (500 μL) obtained at section **3.3** was added into the reaction v-vial, which was then irradiated with a 456-nm LED light for 15 min under an N_2 balloon sparging. After dilution with 1 ml MeCN, an aliquot of the reaction solution was analysed on a radio-HPLC to obtain the RCC with a basic mobile phase to avoid the unconverted ^{18}F-fluoride being trapped on the C18 HPLC column. The ^{18}F$^-$ eluted in the v-vial and left on the resin were recorded to calculate the elution efficiency (**Supplementary Table 1**).

Entry	AER-formation	eluent			EE (%)	RCC (%)
		solvent (0.5 ml)	base	salt		
1	Sep-Pak Light QMA-CO_3^{2-}	^{t}BuOH	TBAB (20%, 20 μL)	none	-	-
2	**KT-101**-HCO_3^-	^{t}BuOH/MeCN (4/1)	TBAB (20%, 20 μL)	none	65	61.8 ± 5.2 (n = 3)
3	**KT-101**-HCO_3^-	EtOH/MeCN (4/1)	TBAB (20%, 20 μL)	none	75	31.8
4	**KT-101**-HCO_3^-	^{t}BuOH/MeCN (4/1)	TBAB (20%, 20 μL)	TBAP (5 mg)	82	63.1 ± 7.2 (n = 3)
5	**KT-101**-HCO_3^-	^{t}BuOH/MeCN (4/1)	TBAOH (20%, 20 μL)	none	66	70.4 ± 12.9 (n = 3)
6	**KT-101**-HCO_3^-	^{t}BuOH/MeCN (1/1)	TBAOH (20%, 20 μL)	none	60	75.0 ± 0.2 (n = 3)
7	**KT-101**-HCO_3^-	^{t}BuOH/MeCN (4/1)	TBAOH (40%,10 μL)	none	78	72.0 ± 1.7 (n = 3)
8	**KT-101**-HCO_3^-	^{t}BuOH/MeCN (4/1)	TBAOH (40%,10 μL)	TBAP (3 mg)	88	75.6 ± 4.6 (n = 3)
9[a]	**KT-101**-HCO_3^-	^{t}BuOH/MeCN (4/1)	TBAOH (40%, 10 μL)	TBAP (2 mg)	99.5	78
10[a]	**KT-101**-HCO_3^-	^{t}BuOH/MeCN (4/1)	TBAOH (40%, 4 μL)	TBAP (5 mg)	99.3	68
11[a]	**KT-101**-HCO_3^-	^{t}BuOH/MeCN (4/1)	none	TBAP (10 mg)	98.8	68
12[a,b]						39
13[a,c]	**KT-101**-HCO_3^-	^{t}BuOH/MeCN (4/1)	none	TBAP (10 mg)	97%	Trace
14[a,d]						25
15[a,e]						61

Aryl ^{18}F-fluorination conditions: ^{18}F$^-$ (0.19 -1.11 GBq), substrate **1** (2 μL), photocatalyst **S1** (2 mg), DCE (500 μL), 456-nm LED, rt, 15-min irradiation, N_2 atmosphere. 500 μL drying-free ^{18}F$^-$ solution was used for each reaction. All RCCs were calculated by HPLC integration with a basic mobile phase to avoid the unconverted ^{18}F$^-$ fluoride being trapped on the C18 HPLC column. [a]The AER was slowly eluted with the eluent in 1min.[b]MeCN (500 μL) was used as the solvent. [c]DMF (500 μL) was used as the solvent. [d]Ethyl acetate (500 μL) was used as the solvent. [e]DCM (600 μL) was used as the solvent.

Supplementary Table 1. Drying-free aryl ^{18}F-fluorination development and optimization

3.5 Full-batch aryl ^{18}F-fluorination optimization.



With different kinds of eluents listed in the Supplementary Table **2**, the ^{18}F$^-$ trapped on the preconditioned anion-exchange resin (KT-101) was directly eluted in a 5 ml v-vial preloaded with 1-fluoro-4-methoxybenzene **1** (2 μl) and photocatalyst $\mathbf{S_1}$ (2 mg) in 0.5 ml 1,2-dichloroethane. The solution was irradiated with a 456-nm LED light for 15 min under a nitrogen balloon sparging.

After dilution with 1 ml MeCN, an aliquot of the reaction solution was analysed on a radio-HPLC to obtain the RCC with a basic mobile phase to avoid the unconverted ^{18}F-fluoride being trapped on the C18 HPLC column. The $^{18}F^-$ eluted in the v-vial and left on the resin were recorded to calculate the elution efficiency (Supplementary Table **2**)

entry	AER-formation	eluent			EE (%)	RCC (%)
		solvent (2.5 ml)	base	salt		
1	**KT-101**-HCO_3^-	^{t}BuOH/MeCN (4/1)	TBAOH (40%, 2 µL)	TBAP (1 mg)	47 ± 0.82 (n = 3)	56.7 ± 7.6 (n = 3)
2	**KT-101**-HCO_3^-	^{t}BuOH/MeCN (4/1)	TBAOH (40%, 2 µL)	TBAT (1 mg)	54	59
3	**KT-101**-HCO_3^-	^{t}BuOH/MeCN (4/1)	TBAOH (40%, 4 µL)	none	35	62
4	**KT-101**-HCO_3^-	^{t}BuOH/MeCN (4/1)	TBAOH (40%, 4 µL)	TBAP (1 mg)	37	66
5	**KT-101**-HCO_3^-	^{t}BuOH/MeCN (4/1)	TBAOH (1M MeOH solution, 10 µL)	none	56	53
6	**KT-101**-HCO_3^-	^{t}BuOH/MeCN (4/1)	TPAOH (40%, 4 µL)	none	40.5	57
7[a]	**KT-101**-HCO_3^-	^{t}BuOH/MeCN (4/1)	none	TBAP (3 mg)	81 ± 4.3 (n = 3)	56.3 ± 3.3 (n = 3)
8[a]	**KT-101**-CO_3^{2-}	^{t}BuOH/MeCN (4/1)	none	TBAP (3 mg)	90.5 ± 1.1 (n = 3)	60.3 ± 6.6 (n = 3)
9[a]	**KT-101**-PO_4^{3-}	^{t}BuOH/MeCN (4/1)	none	TBAP (3 mg)	76.7 ± 8.7 (n = 10)	71.2 ± 3.5 (n = 10)
10[a]	**KT-101-HPO_4^{2-}**	**^{t}BuOH/MeCN (4/1)**	**none**	**TBAP (3 mg)**	**96 ± 1.7 (n = 9)**	**66.9 ± 4.8 (n = 9)**
11[a,b]	**KT-101**-HPO_4^{2-}	^{t}BuOH/MeCN (4/1)	none	TBAP (3 mg)	92.3 ± 1.2 (n = 3)	73 ± 1.1 (n = 3)
12[a,c]	**KT-101**-HPO_4^{2-}	^{t}BuOH/MeCN (4/1)	none	TBAP (3 mg)	98	66.7

Aryl ^{18}F-fluorination conditions: $^{18}F^-$ (0.19 -1.11 GBq), substrate **1** (2 µL), photocatalyst **S1** (2 mg), DCE (500 µl), 456-nm LED, rt, 15-min irradiation, N_2 atmosphere. All RCCs were calculated by HPLC integration with a basic mobile phase to avoid the unconverted $^{18}F^-$ fluoride being trapped on the C18 HPLC column. [a]The AER was slowly eluted with the eluent in 1min. [b] used AER. [c]DCM (600 µL) was used instead of DCE.

Supplementary Table 2. Full-batch azeotropic drying-free aryl ^{18}F-fluorination optimization

3.6 General HPLC conditions

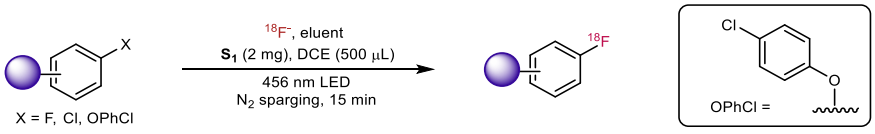
General HPLC conditions for crude reaction analysis and radiochemical conversion (RCC) calculation.

Column A: Agilent ZORBAX SB-C18 column (5 µm, 4.6 × 250 mm). Column B: Phenomenex Gemini® C18 110Å column (5 µm, 4.6 × 250 mm). Solvent A: Phosphate buffer (pH = 8); Solvent B: Acetonitrile. Isocratic elution at 20% to 70 % solvent B. Flow rate: 1 ml/min. The phosphate buffer was prepared by mixing K_2HPO_4. $3H_2O$ (7.332 g) and KH_2PO_4 (0.41 g) in 1L water. All the radiochemical reactions were subjected to radio-HPLC using this general HPLC condition with column A unless otherwise noted.

3.7 Preparation of standard eluent

The optimized eluent (tBuOH-MeCN-TBAP) for the full-batch photoredox-catalysed aryl ^{18}F-labelling reaction was prepared by mixing 400 µL tBuOH, 100 µl MeCN and 30 µL of the TBAP MeCN solution (0.1 mg/ µL).

3.8 General procedure for the photoredox-mediated azeotropic drying-free aryl ^{18}F-fluorination.

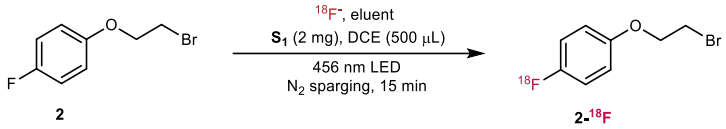


The aqueous $^{18}F^-$ solution (0.19 – 3.7 GBq) produced by the cyclotron was loaded on an anion-exchange resin (KT-101) preconditioned with 10 ml K_2HPO_4 (1 M) and 10 ml water. The resin was flushed under N_2 flow for 10 seconds to remove most of the water, then washed with 5 ml MeCN and flushed with N_2 for another 5 min. With the eluent prepared at section **3.7**, the

$^{18}F^-$ was slowly eluted in a 5 ml v-vial preloaded with aryl substrates (0.01 mmol, unless otherwise noted), photocatalyst **S1** (2 mg), and 1,2-dichloroethane (0.5 ml) for around 1 minute. The solution was irradiated with a 456-nm LED light for 15 min under a nitrogen balloon sparging. After dilution with 1 ml MeCN, an aliquot of the reaction solution was analysed on a radio-HPLC to obtain the RCC with a basic mobile phase (pH = 8) to avoid the unconverted ^{18}F-fluoride being trapped on the C18 HPLC column. The $^{18}F^-$ eluted in the v-vial and left on the resin were recorded to calculate the elution efficiency. Co-injection or comparison of the ^{19}F standard with the labelling crude via HPLC was used to confirm the identity of the radiolabeled compounds.

3.9 Radio-HPLC analysis and RCC calculation of the ^{18}F-radiolabeled arenes

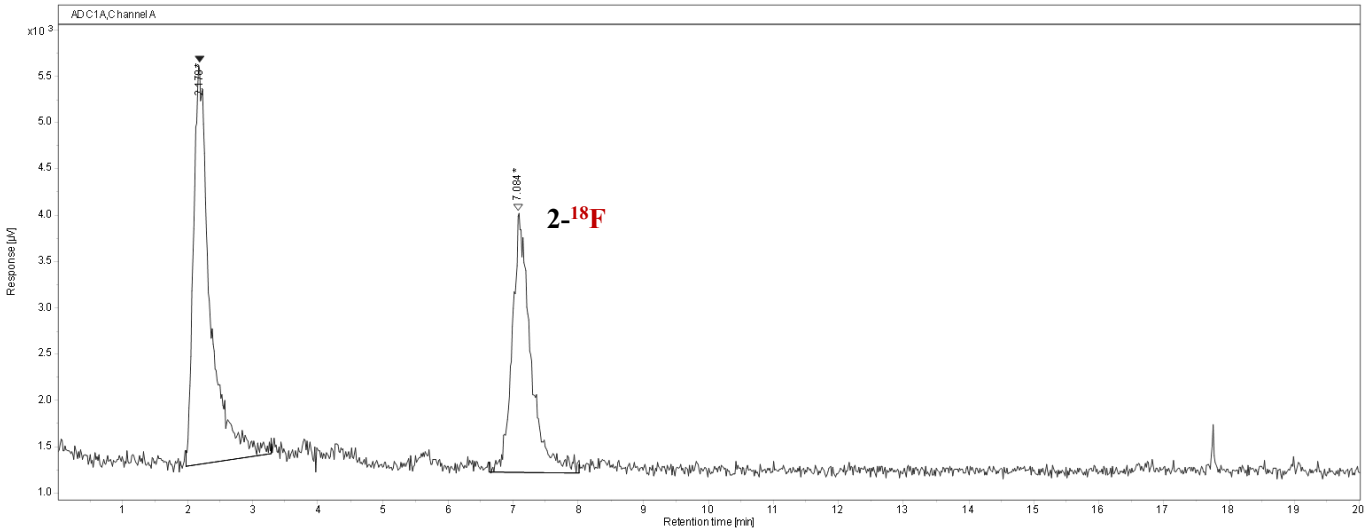
All ^{18}F-labelling reactions were performed according to the general procedure in section **3.8** unless otherwise noted. The elution efficiency (EE) which was calculated by division of the $^{18}F^-$ eluted in the reaction v-vial by the whole $^{18}F^-$ ($^{18}F^-$ in the v-vial and $^{18}F^-$ left on the resin), HPLC analysis condition, RCC, copy of the HPLC traces and integration information were listed for each substrate. All ^{18}F-labelling reactions were analysed according to the general HPLC conditions listed in Section **3.6**. Crude radio and UV (210 nm) HPLC traces were listed. The black HPLC traces represent the radio signal. The blue HPLC traces were obtained with a UV signal at 210 nm. For all the labelling reactions, the trapping efficiencies are >97%.

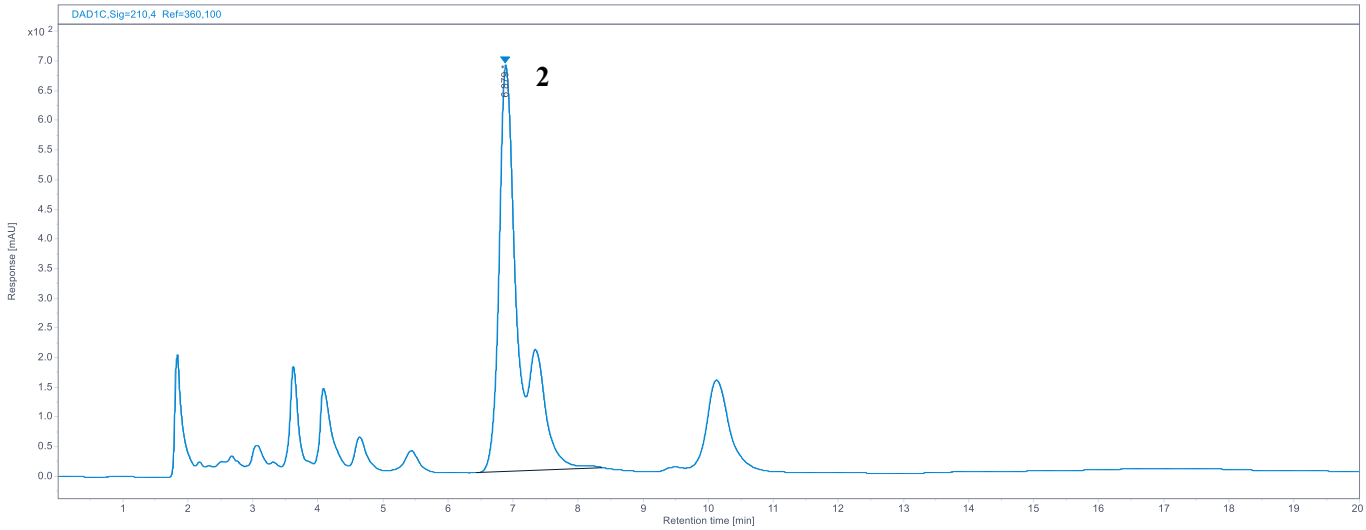


2 **2-^{18}F**

Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
2	**2-^{18}F**	8.9 mCi/(8.9 + 0.3) mCi = 97%	60% MeCN	42%

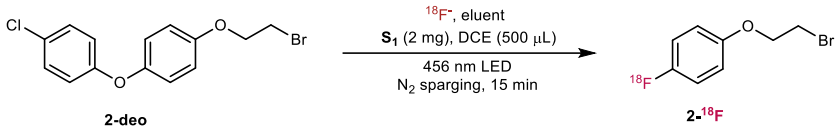
Supplementary Table 3. Elution efficiency and RCC calculation of **2-^{18}F**





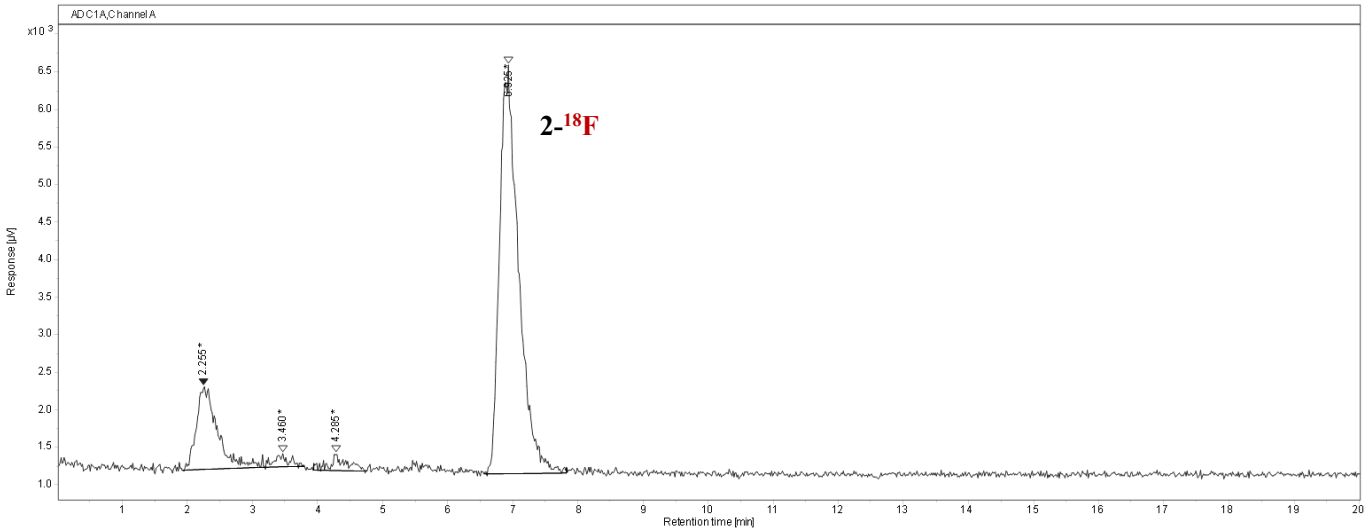
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.178	77624.558	58.147	4327.269	60.66	1.973	3.282
2	7.084	55872.088	**41.853**	2806.295	39.34	6.637	8.014

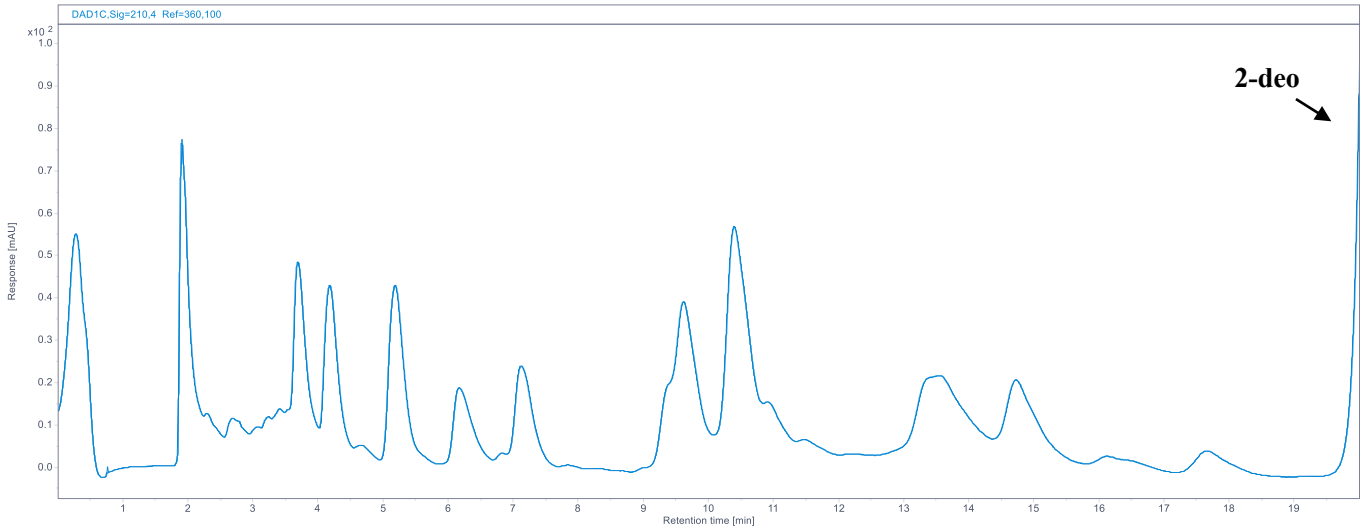
Supplementary Figure 2. Radio-HPLC analysis of **2-^{18}F**



Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
2-deo	**2-^{18}F**	5.45 mCi/(5.45 + 0.28) mCi= 95%	60% MeCN	78%[a]

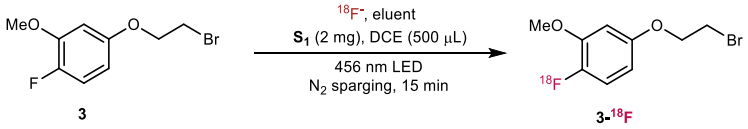
Supplementary Table 4. Elution efficiency and RCC calculation of **2-^{18}F** from **2-deo**. a.0.02 mmol substrate.





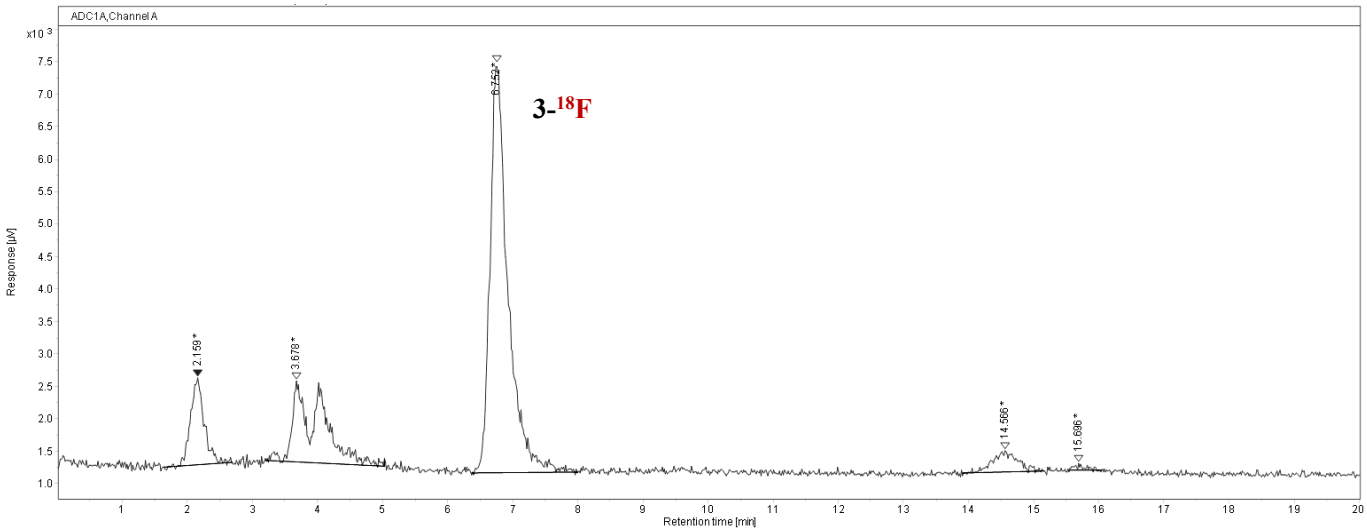
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.255	24936.265	17.602	1103.443	15.90	1.927	3.182
2	3.460	2455.481	1.733	171.086	2.47	3.182	3.800
3	4.285	3525.850	2.489	218.735	3.15	3.941	4.751
4	6.925	110746.154	**78.175**	5446.464	78.48	6.558	7.819

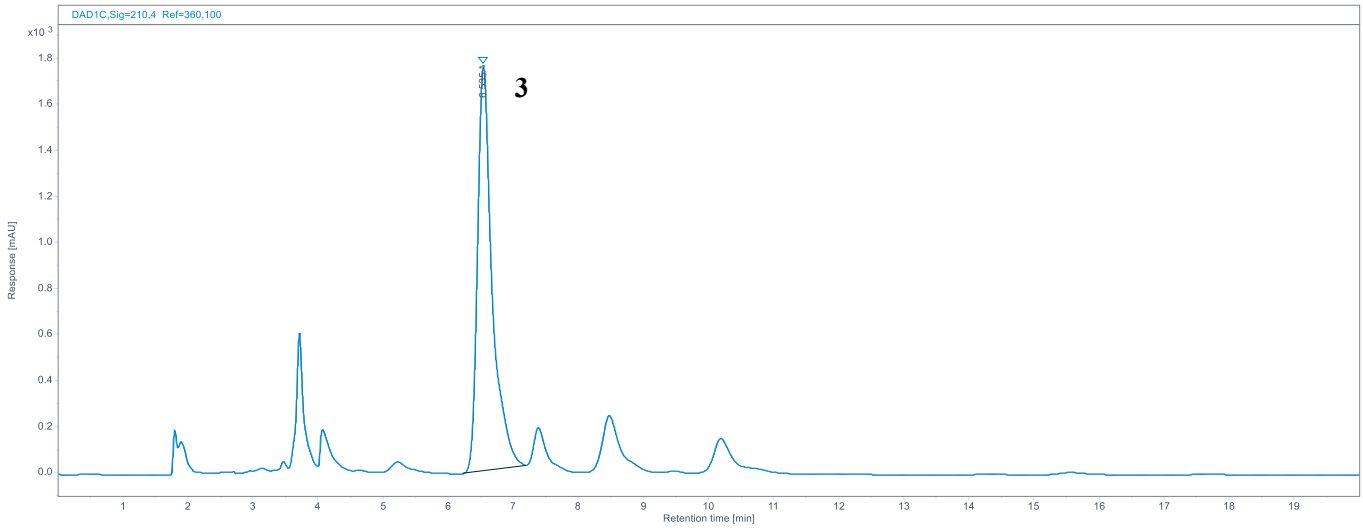
Supplementary Figure 3. Radio-HPLC analysis of **2-^{18}F**



Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
3	**3-^{18}F**	6.78 mCi/(6.78 + 0.2) mCi = 97%	60% MeCN	65%

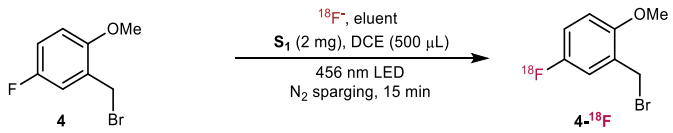
Supplementary Table 5. Elution efficiency and RCC calculation of **3-^{18}F**.





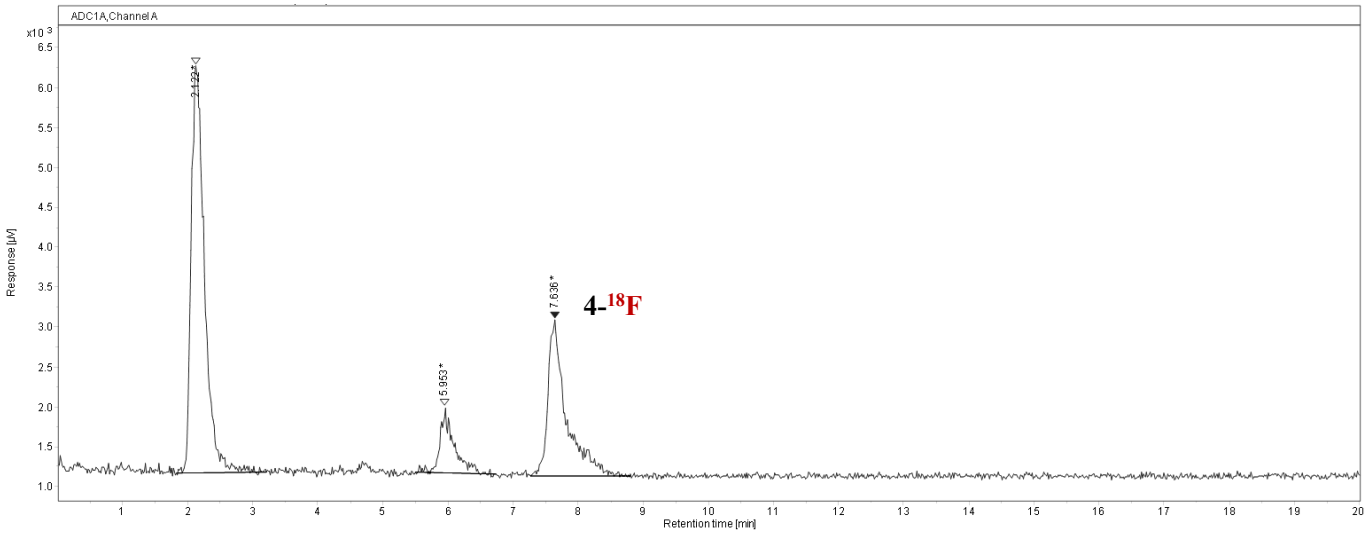
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.159	19794.517	10.649	1336.218	14.36	1.641	2.692
2	3.678	37302.848	20.068	1242.002	13.35	3.203	5.036
3	6.752	119925.627	**64.516**	6295.510	67.68	6.371	8.005
4	14.566	7874.177	4.236	320.342	3.44	13.901	15.151
5	15.696	987.089	0.531	107.874	1.16	15.535	16.046

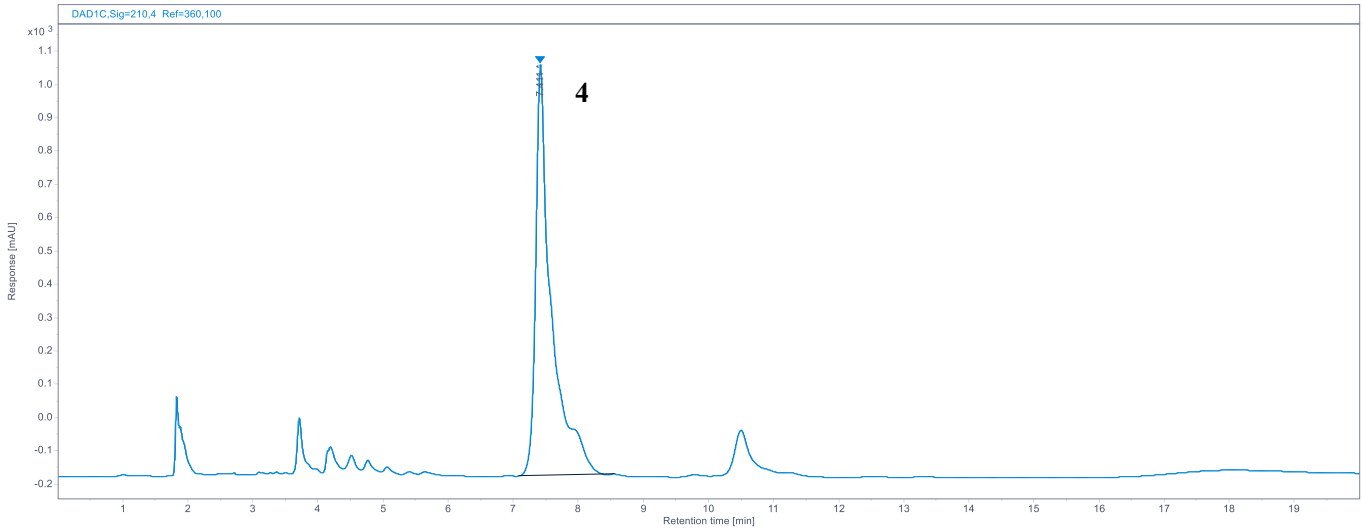
Supplementary Figure 4. Radio-HPLC analysis of **3**-^{18}F



Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
4	**4**-^{18}F	9.04 mCi/(9.04 + 0.44) mCi = 97%	60% MeCN	31%

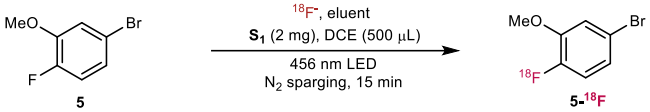
Supplementary Table 6. Elution efficiency and RCC calculation of **4**-^{18}F.





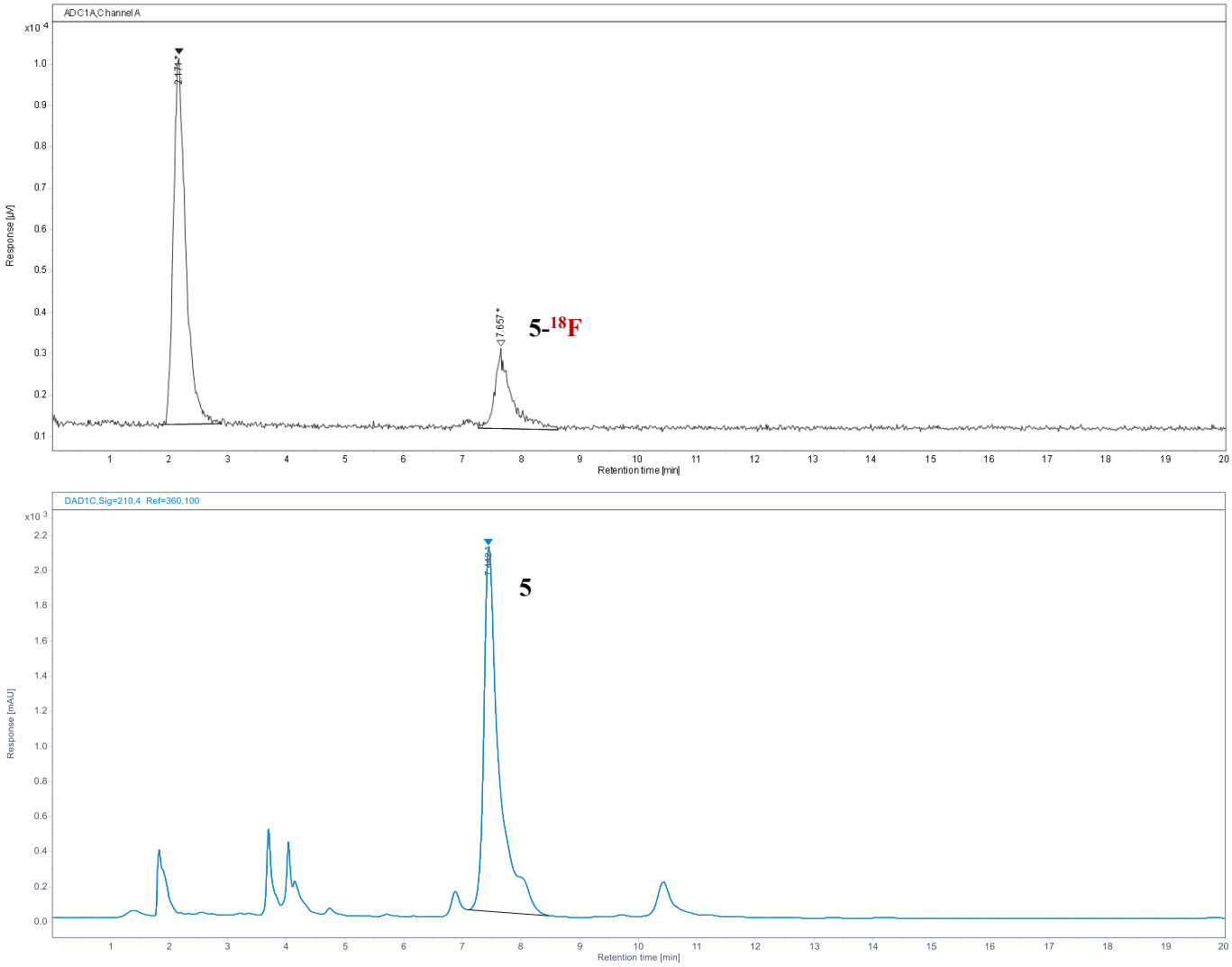
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.122	72932.867	59.225	5102.921	64.74	1.843	3.205
2	5.953	12073.636	9.804	823.738	10.45	5.507	6.729
3	7.636	38138.396	**30.970**	1955.954	24.81	7.269	8.795

Supplementary Figure 5. Radio-HPLC analysis of **4-**^{18}**F**



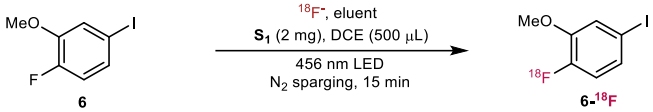
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
5	**5-^{18}F**	6.0 mCi/(6.0 + 0.22) mCi = 96%	60% MeCN	22%

Supplementary Table 7. Elution efficiency and RCC calculation of **5-^{18}F**.



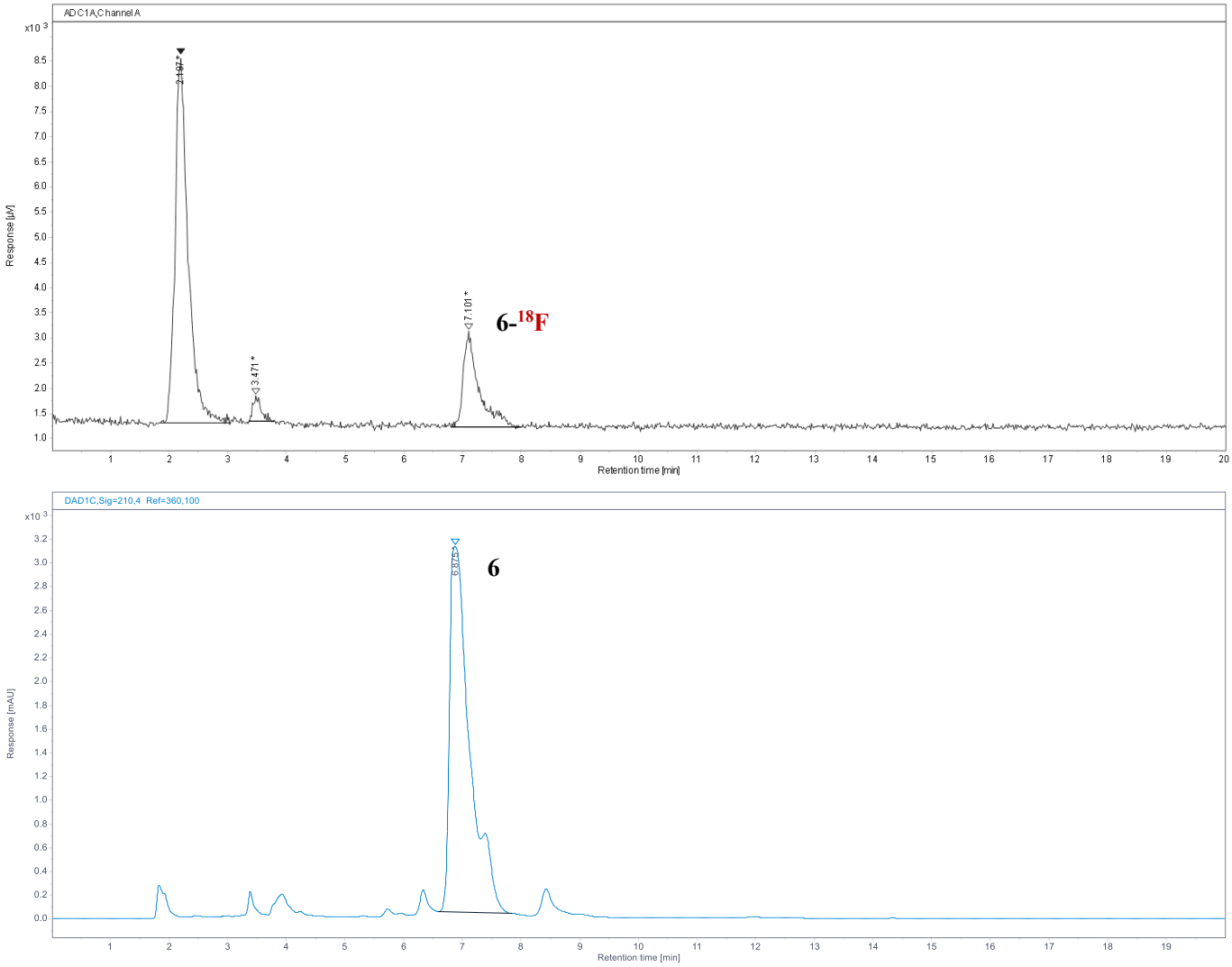
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.171	129226.923	77.661	8910.713	82.03	1.869	2.897
2	7.657	37171.524	**22.339**	1951.603	17.97	7.279	8.631

Supplementary Figure 6. Radio-HPLC analysis of **5-^{18}F**



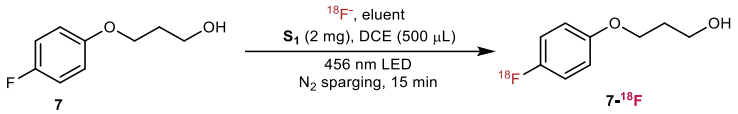
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
6	**6-^{18}F**	7.95 mCi/(7.95 + 0.24) mCi = 97%	65% MeCN	23%[a]

Supplementary Table 8. Elution efficiency and RCC calculation of **6-^{18}F**.a.0.02 mmol substrate.



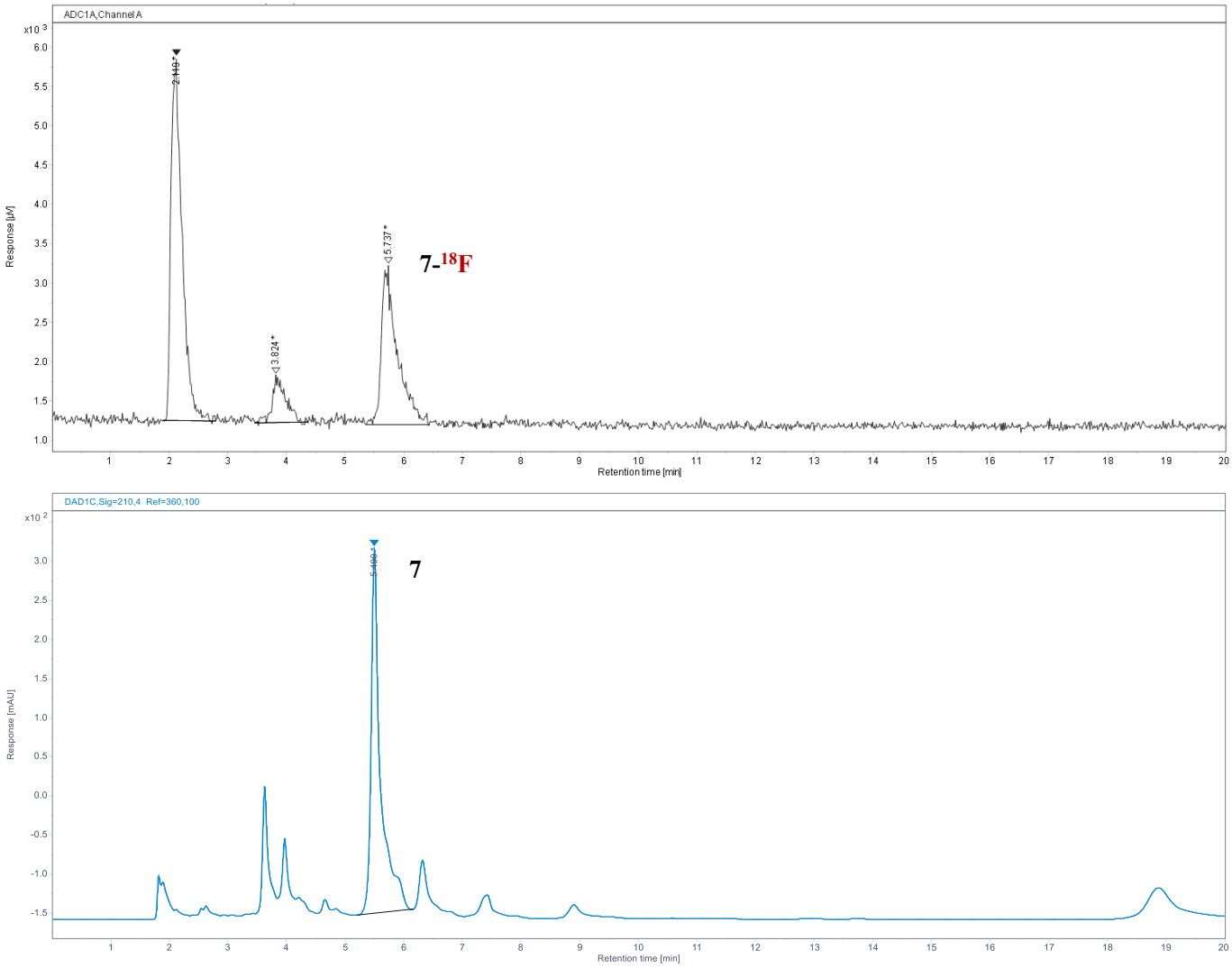
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.197	111758.209	73.948	7286.081	75.13	1.856	3.044
2	3.471	4666.438	3.088	501.223	5.17	3.360	3.783
3	7.101	34705.779	**22.964**	1910.724	19.70	6.800	7.997

Supplementary Figure 7. Radio-HPLC analysis of **6-^{18}F**



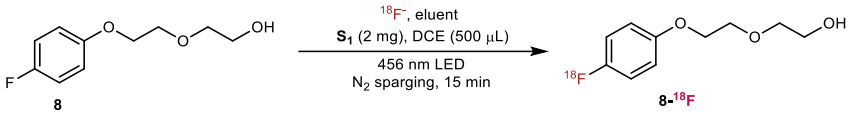
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
7	7-^{18}F	10.34 mCi/(10.34 + 0.27) mCi = 97%	45% MeCN	35%

Supplementary Table 9. Elution efficiency and RCC calculation of 7-^{18}F.



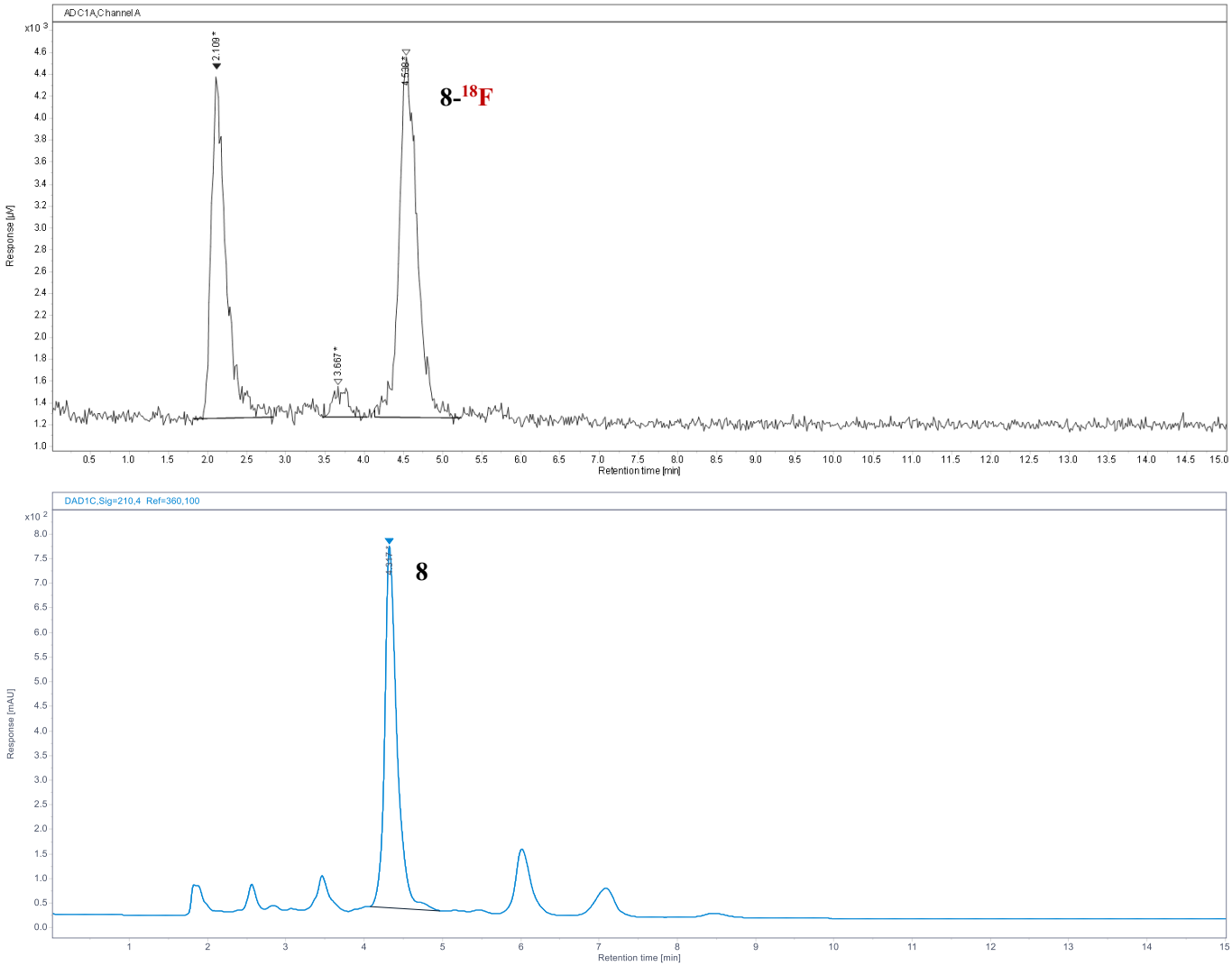
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.119	60248.389	56.271	4626.664	63.67	1.904	2.791
2	3.824	9347.097	8.730	609.044	8.38	3.463	4.374
3	5.737	37473.132	**34.999**	2031.356	27.95	5.352	6.436

Supplementary Figure 8. Radio-HPLC analysis of **7-^{18}F**



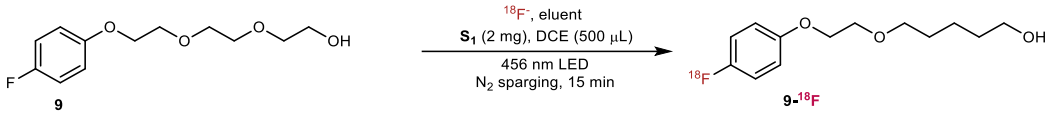
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
8	**8-^{18}F**	6.60 mCi/(6.60 + 0.21) mCi = 96%	45% MeCN	54%

Supplementary Table 10. Elution efficiency and RCC calculation of **8-^{18}F**.



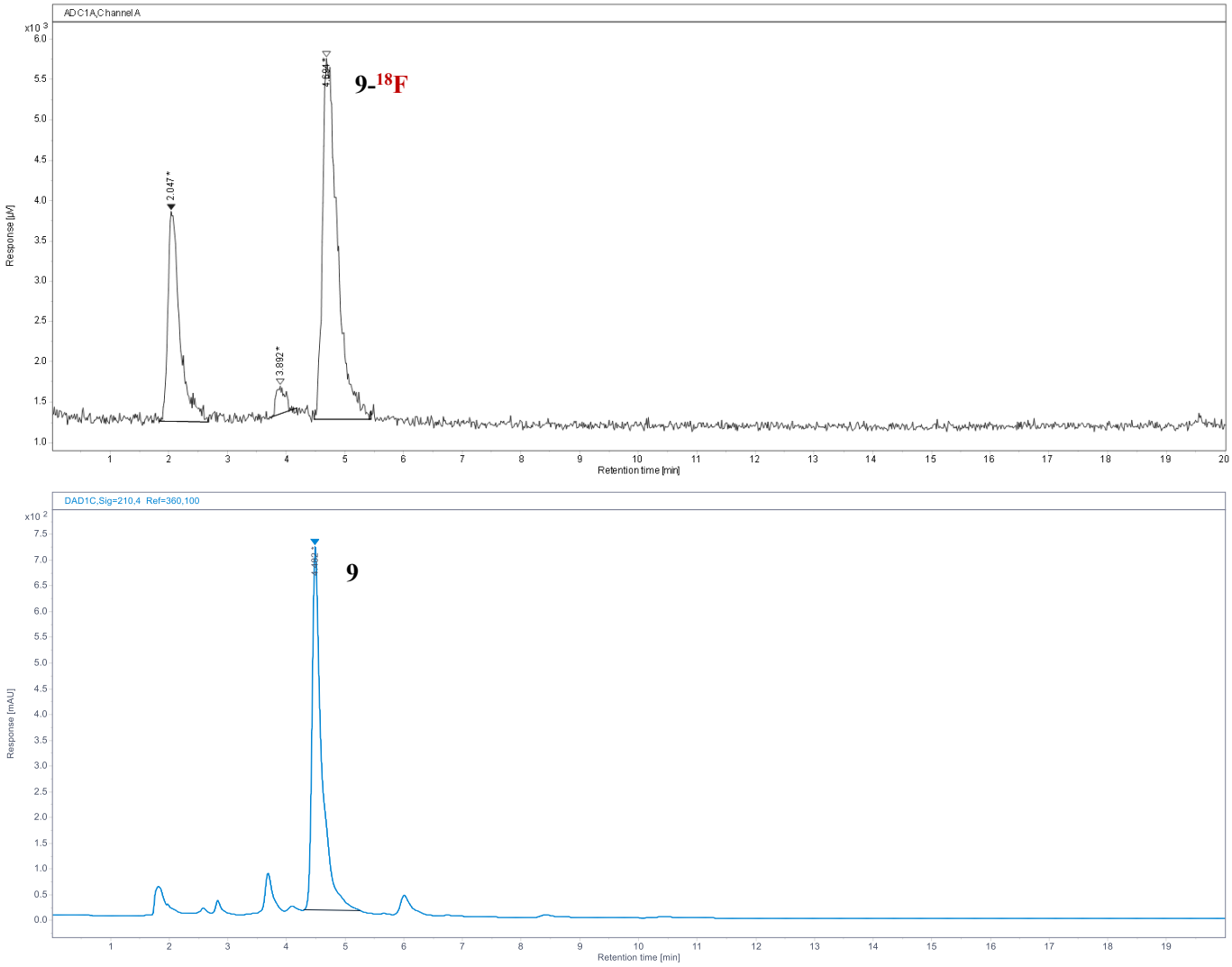
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.109	41044.450	42.260	3170.582	47.03	1.821	2.835
2	3.667	3566.132	3.672	279.393	4.14	3.462	4.034
3	4.538	52513.791	**54.069**	3291.871	48.83	4.127	5.234

Supplementary Figure 9. Radio-HPLC analysis of **8-^{18}F**



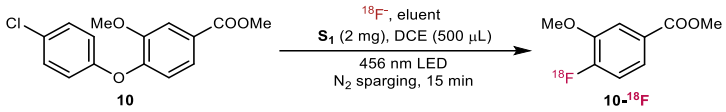
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
9	**9-^{18}F**	8.97 mCi/(8.97+0.54) mCi = 94%	45% MeCN	66%

Supplementary Table 11. Elution efficiency and RCC calculation of **9-^{18}F**.



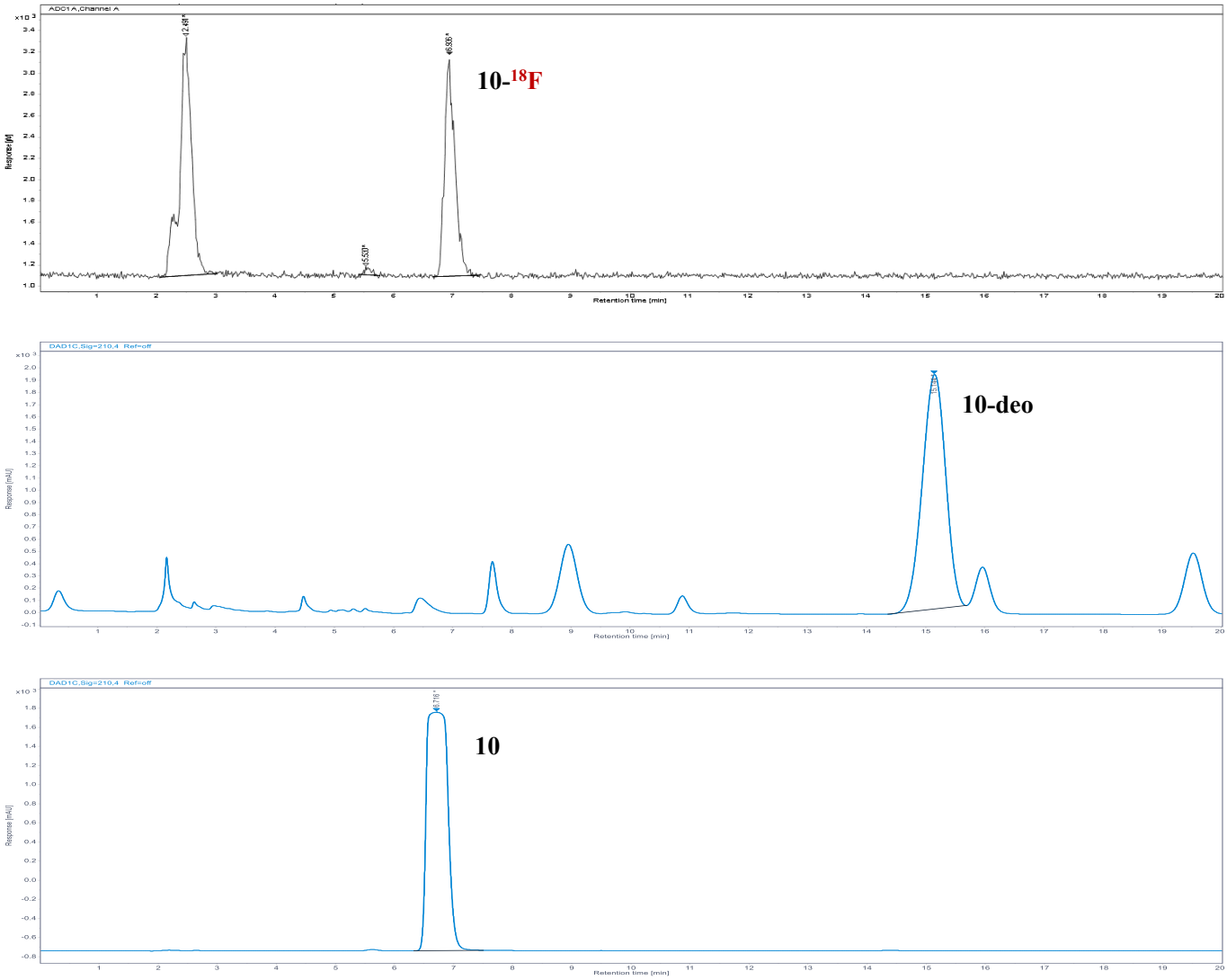
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.047	37264.208	31.235	2601.713	35.05	1.835	2.676
2	3.892	3507.337	2.940	352.220	4.75	3.720	4.176
3	4.694	78531.543	**65.825**	4467.886	60.20	4.478	5.448

Supplementary Figure 10. Radio-HPLC analysis of **9-^{18}F**



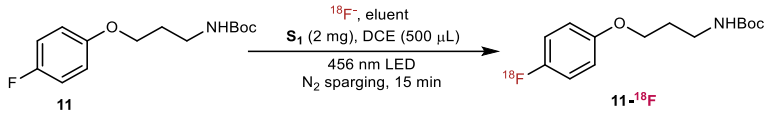
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
10-deo	**10-^{18}F**	6.4 mCi/(6.4 + 1.9) mCi = 77%	60% MeCN	44%

Supplementary Table 12. Elution efficiency and RCC calculation of **10-^{18}F**.



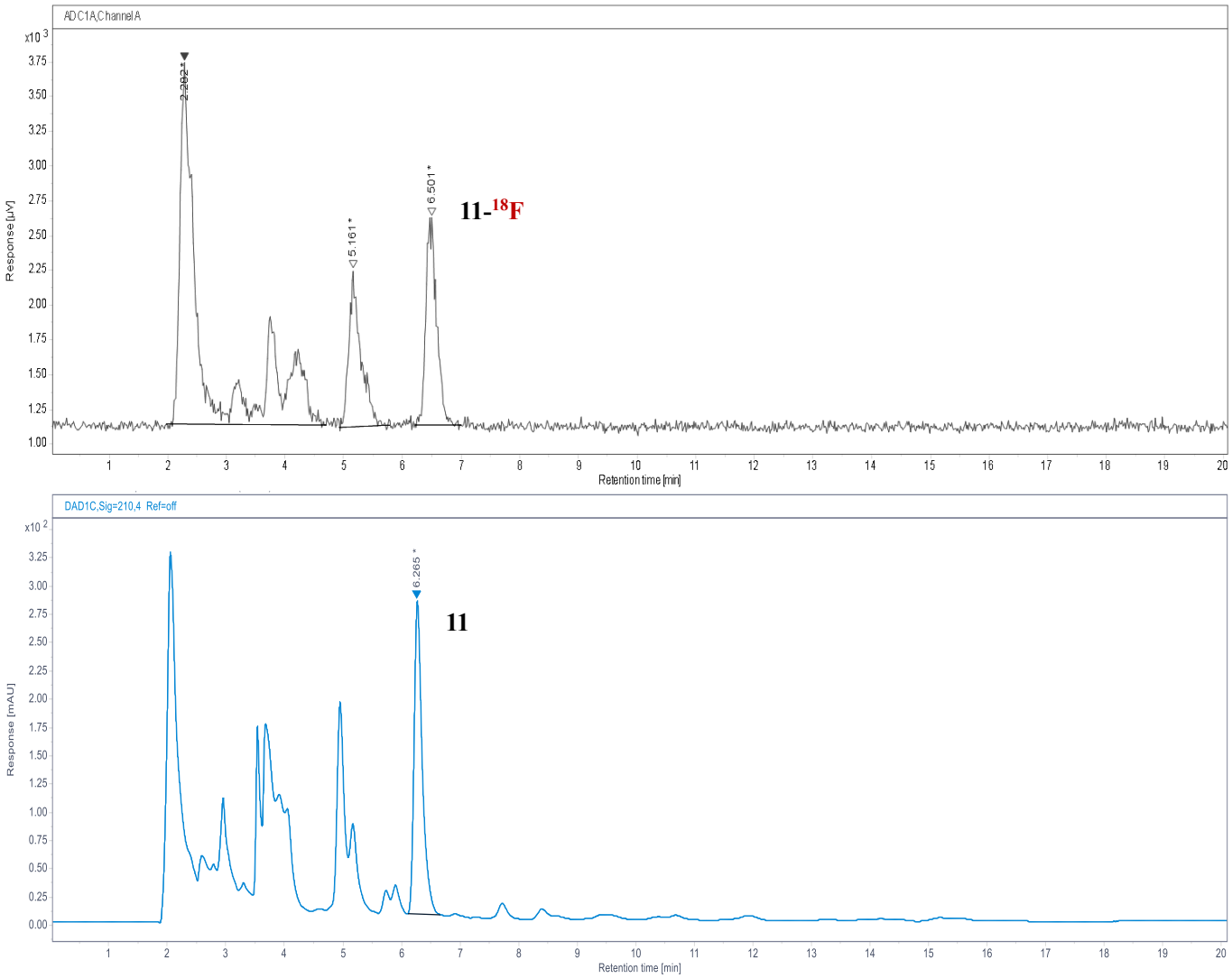
#	RT (min)	Area (µV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.491	31602.544	55.483	2243.407	51.05	2.039	3.016
2	5.530	492.414	0.865	77.460	1.76	5.411	5.762
3	6.936	24864.414	**43.653**	2073.815	47.19	6.662	7.455

Supplementary Figure 11. Radio-HPLC analysis of **10-^{18}F**



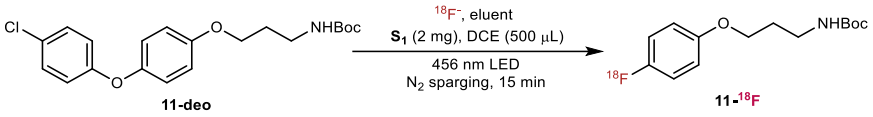
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
11	**11-^{18}F**	9.57 mCi/(9.57 + 2.57) mCi = 79%	40% MeCN	19%

Supplementary Table 13. Elution efficiency and RCC calculation of **11-^{18}F**.



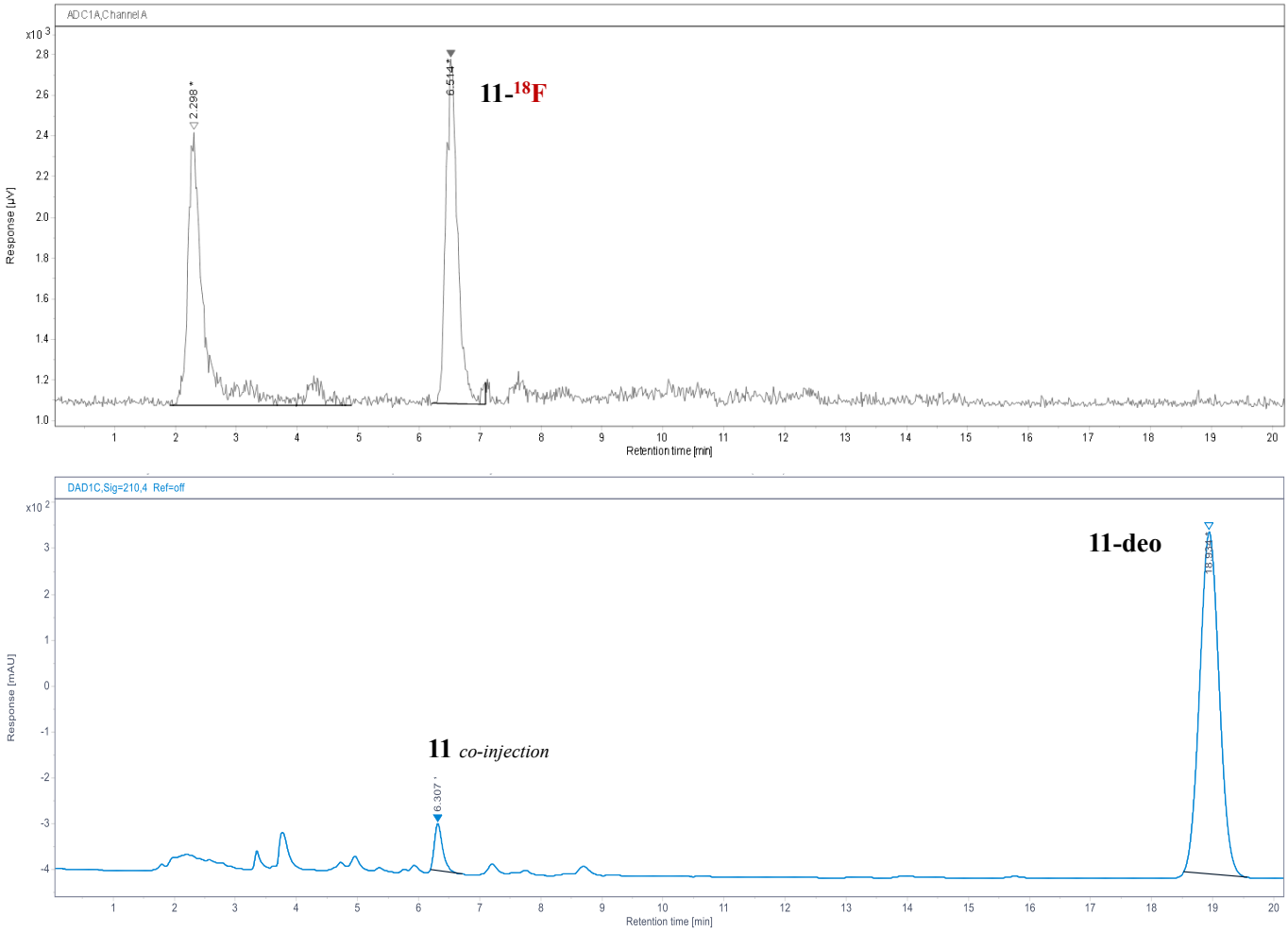
#	RT (min)	Area (μV·s)	Area%	Height (μV)	Height%	Start time (min)	End time(min)
1	2.282	65500.523	65.382	2602.948	49.81	1.967	4.693
2	5.161	15749.092	15.720	1126.969	21.56	4.926	5.793
3	6.501	18932.394	**18.898**	1496.098	28.63	6.211	7.001

Supplementary Figure 12. Radio-HPLC analysis of **11-^{18}F**



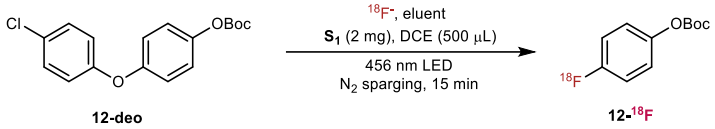
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
11-deo	**11-^{18}F**	11.5 mCi/(11.5 + 1.88) mCi = 86%	40% MeCN	46%

Supplementary Table 14. Elution efficiency and RCC calculation of **11-^{18}F** from **11-deo**.



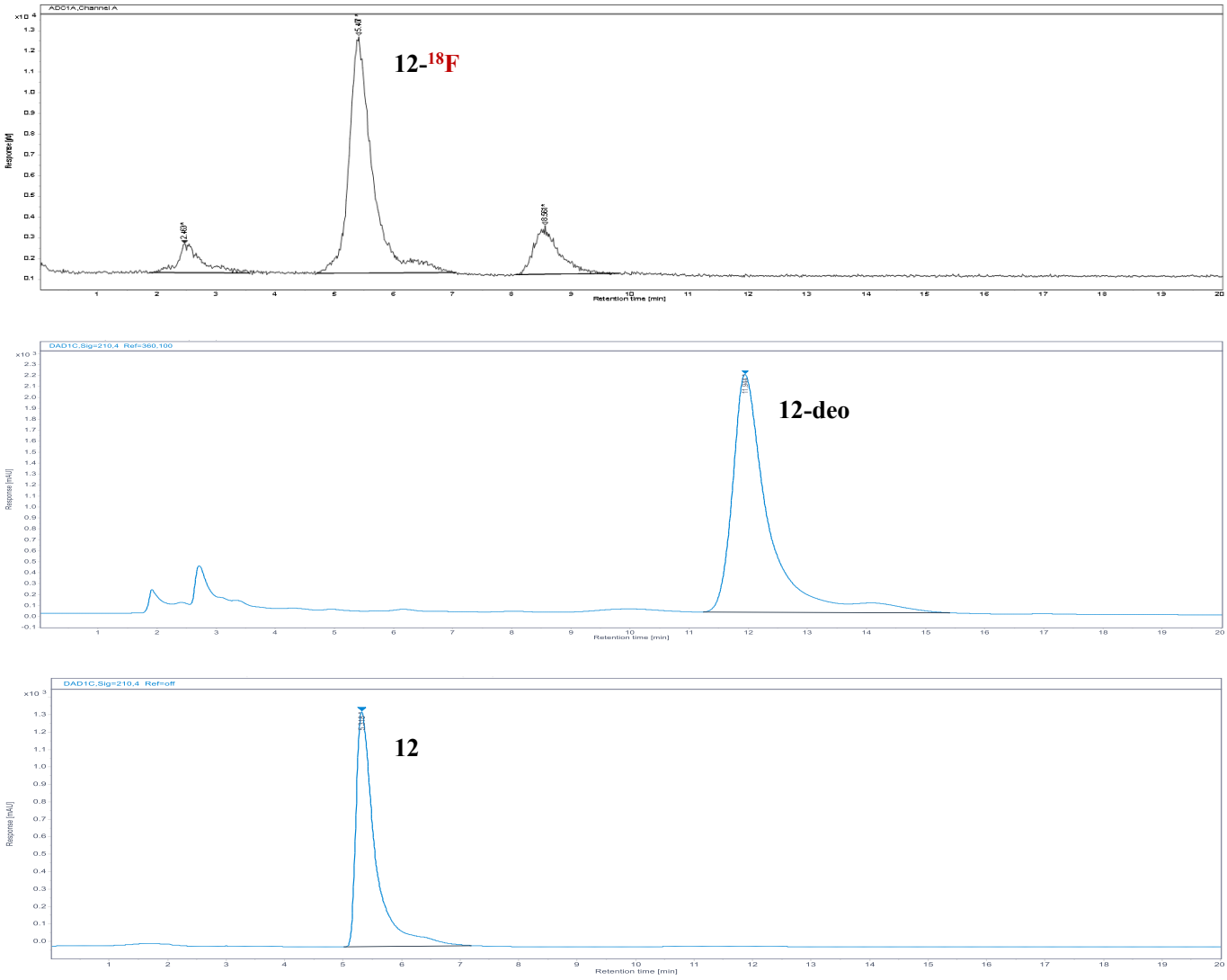
#	RT (min)	Area (µV·s)	Area%	Height (µV)	Height%	Start time (min)	End time (min)
1	2.298	26789.781	53.845	1345.158	44.25	1.911	4.885
2	6.514	22963.429	**46.155**	1694.656	55.75	6.211	7.083

Supplementary Figure 13. Radio-HPLC analysis of **11-^{18}F**



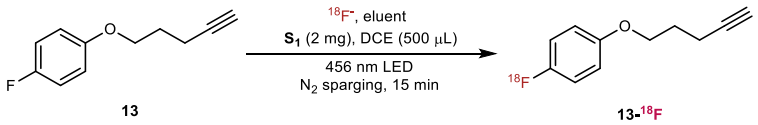
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
12-deo	**12-^{18}F**	27.3 mCi/(27.3 + 1.6) mCi = 95%	45% MeCN	75%

Supplementary Table 15. Elution efficiency and RCC calculation of **12-^{18}F** from **12-deo**.



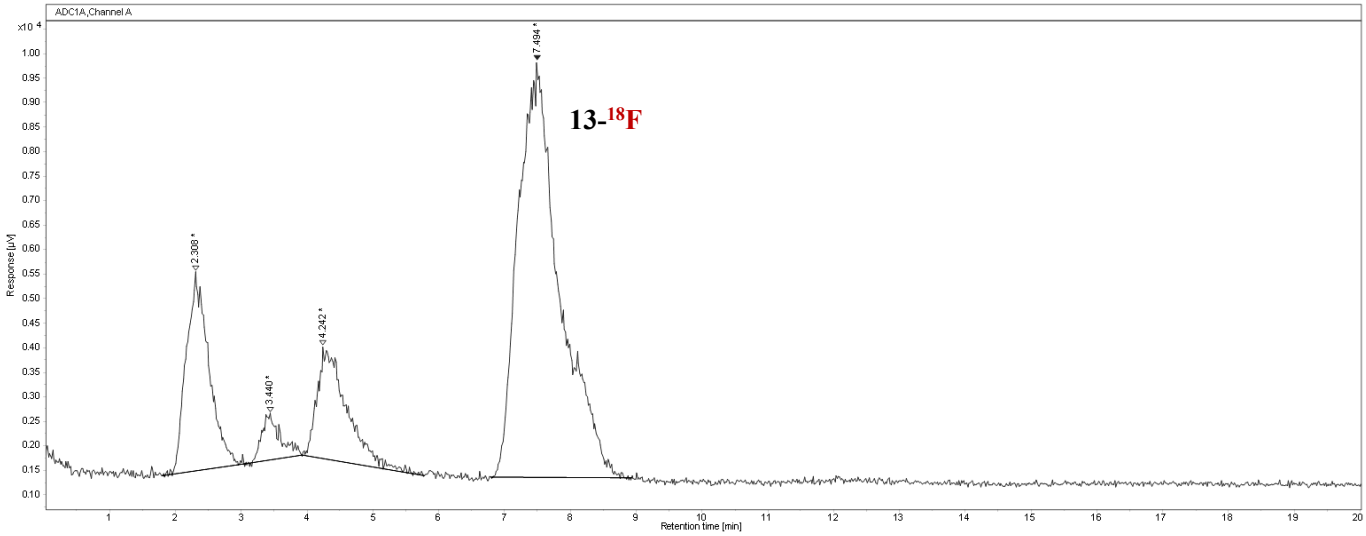
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.463	39818.942	9.471	1394.764	9.20	1.875	3.552
2	5.407	314206.738	**74.736**	11432.658	75.40	4.696	7.047
3	8.561	66397.611	15.793	2334.941	15.40	8.058	9.806

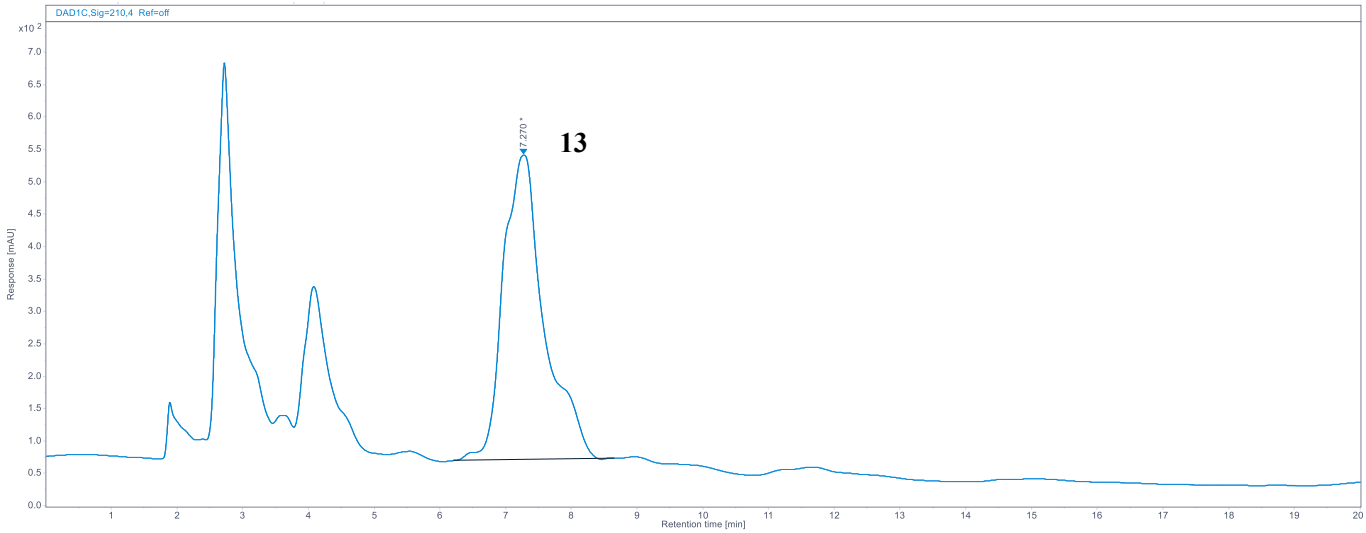
Supplementary Figure 14. Radio-HPLC analysis of **12-^{18}F**



Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
13	**13-^{18}F**	33 mCi/(33 + 2.5) mCi = 93%	60% MeCN	67%

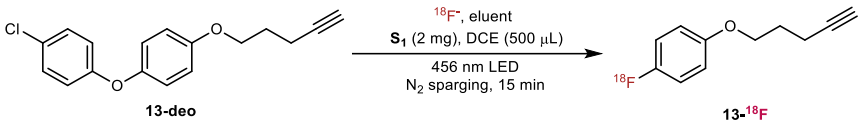
Supplementary Table 16. Elution efficiency and RCC calculation of **13-^{18}F**.





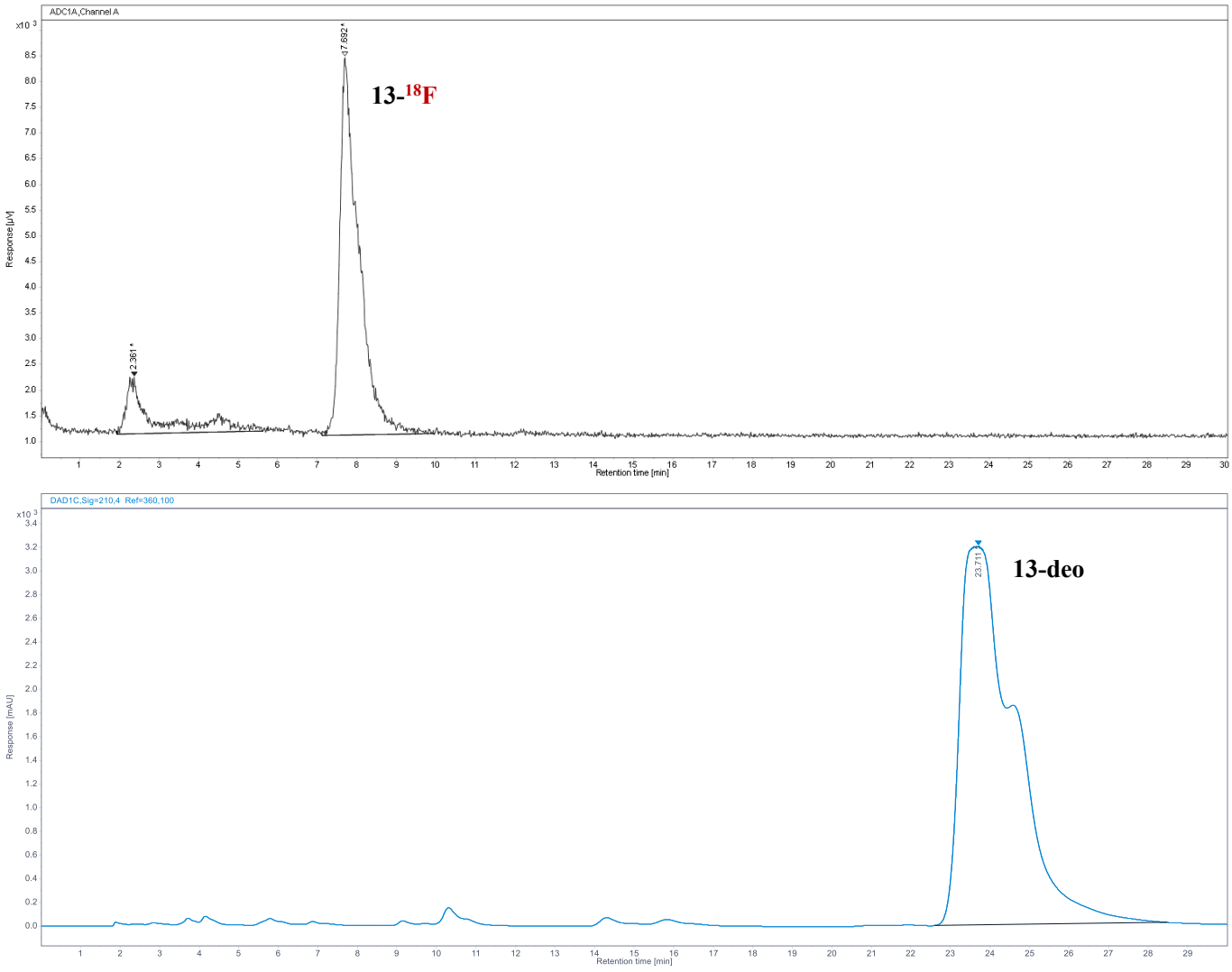
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.308	96802.592	17.423	4057.725	25.73	1.804	3.079
2	3.440	17963.870	3.233	944.674	5.99	3.079	3.929
3	4.242	71327.400	12.838	2281.407	14.47	3.929	5.781
4	7.494	369517.160	**66.506**	8486.968	53.81	6.790	8.931

Supplementary Figure 15. Radio-HPLC analysis of **13-^{18}F**



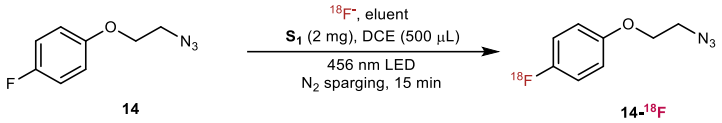
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
13-deo	**13-^{18}F**	25.05 mCi/(25.05 + 3.25) mCi= 89%	60% MeCN	83%

Supplementary Table 17. Elution efficiency and RCC calculation of **11-^{18}F** from **13-deo**.



#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.361	52106.956	17.371	1103.031	13.04	1.929	5.627
2	7.692	247850.271	**82.629**	7356.385	86.96	7.119	9.961

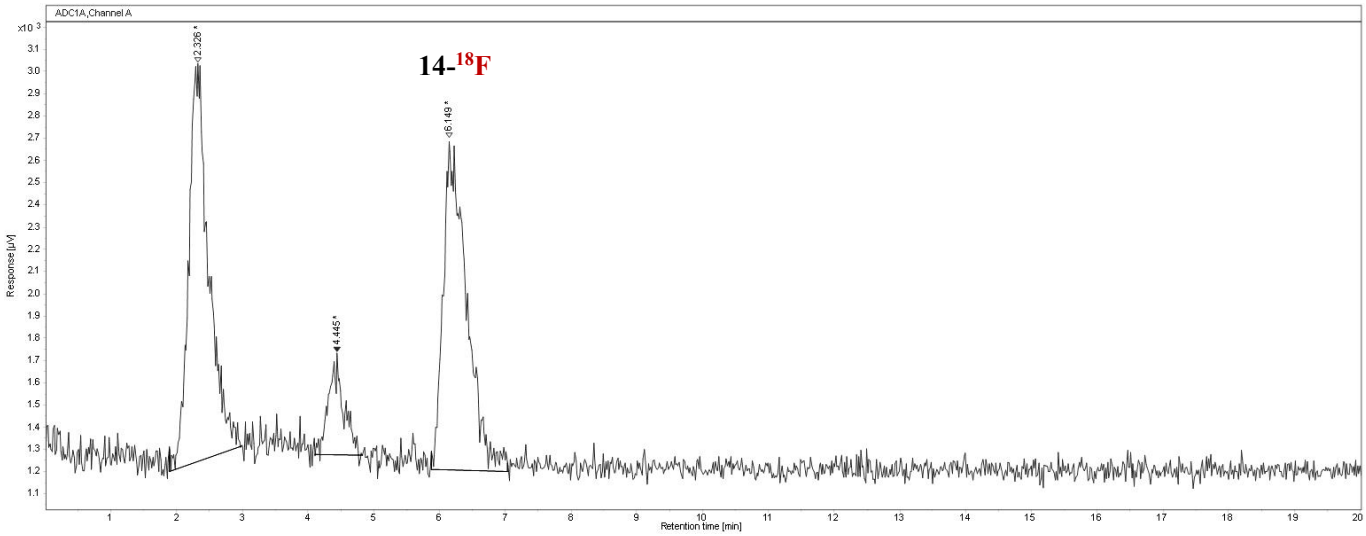
Supplementary Figure 16. Radio-HPLC analysis of **13-^{18}F**

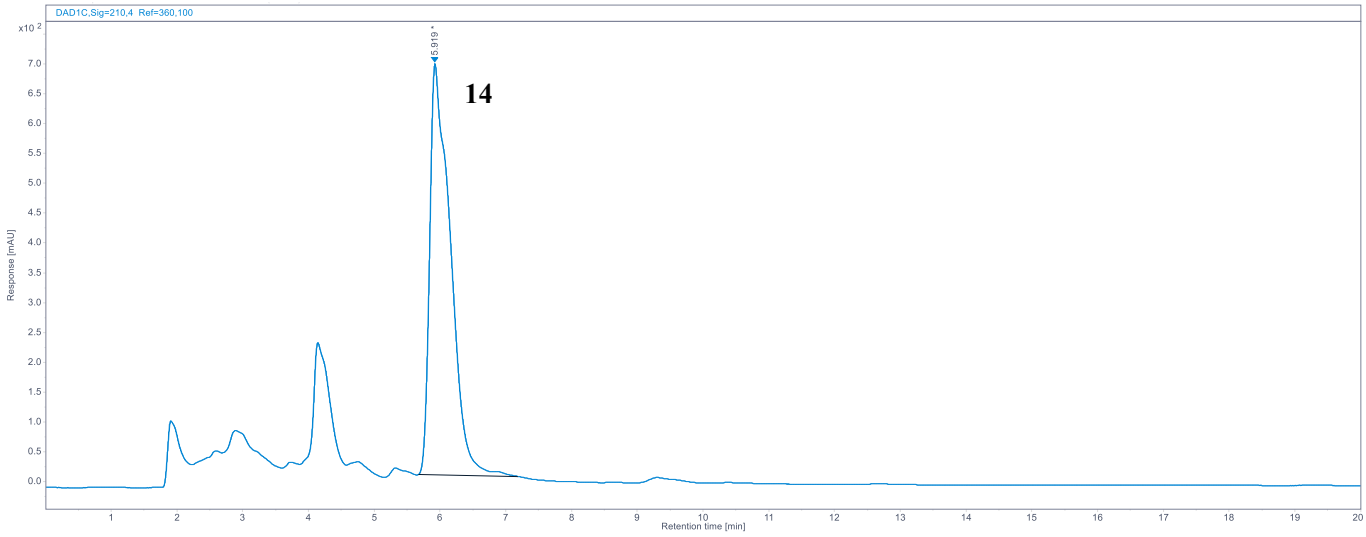


14 14-^{18}F

Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
14	**14-^{18}F**	6.82 mCi/(6.82 + 0.26) mCi = 96%	60% MeCN	45%

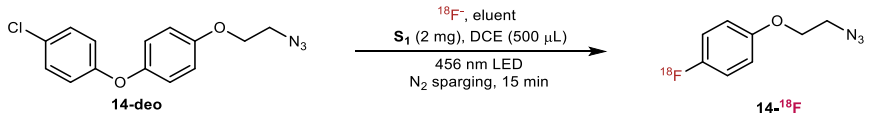
Supplementary Table 18. Elution efficiency and RCC calculation of **14-^{18}F**.





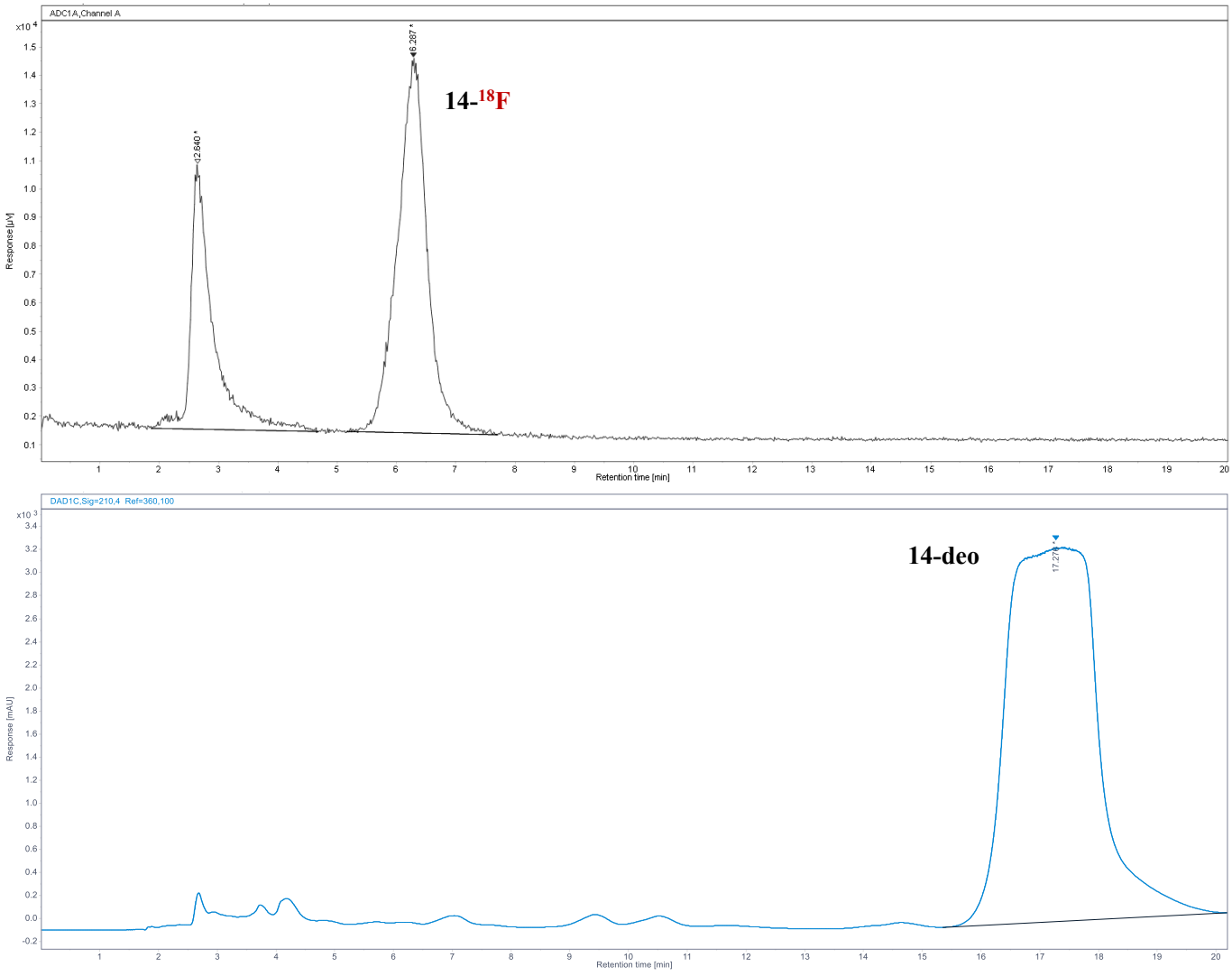
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.326	38151.666	46.658	1789.667	47.90	1.891	2.999
2	4.445	7025.865	8.592	458.212	12.26	4.108	4.824
3	6.149	36591.794	**44.750**	1488.721	39.84	5.878	7.032

Supplementary Figure 17. Radio-HPLC analysis of **14-^{18}F**



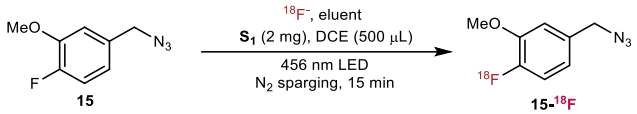
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
14-deo	**14-^{18}F**	11.42 mCi/(11.42 + 0.63) mCi = 95%	60% MeCN	66%

Supplementary Table 19. Elution efficiency and RCC calculation of **14-^{18}F** from **14-deo**.



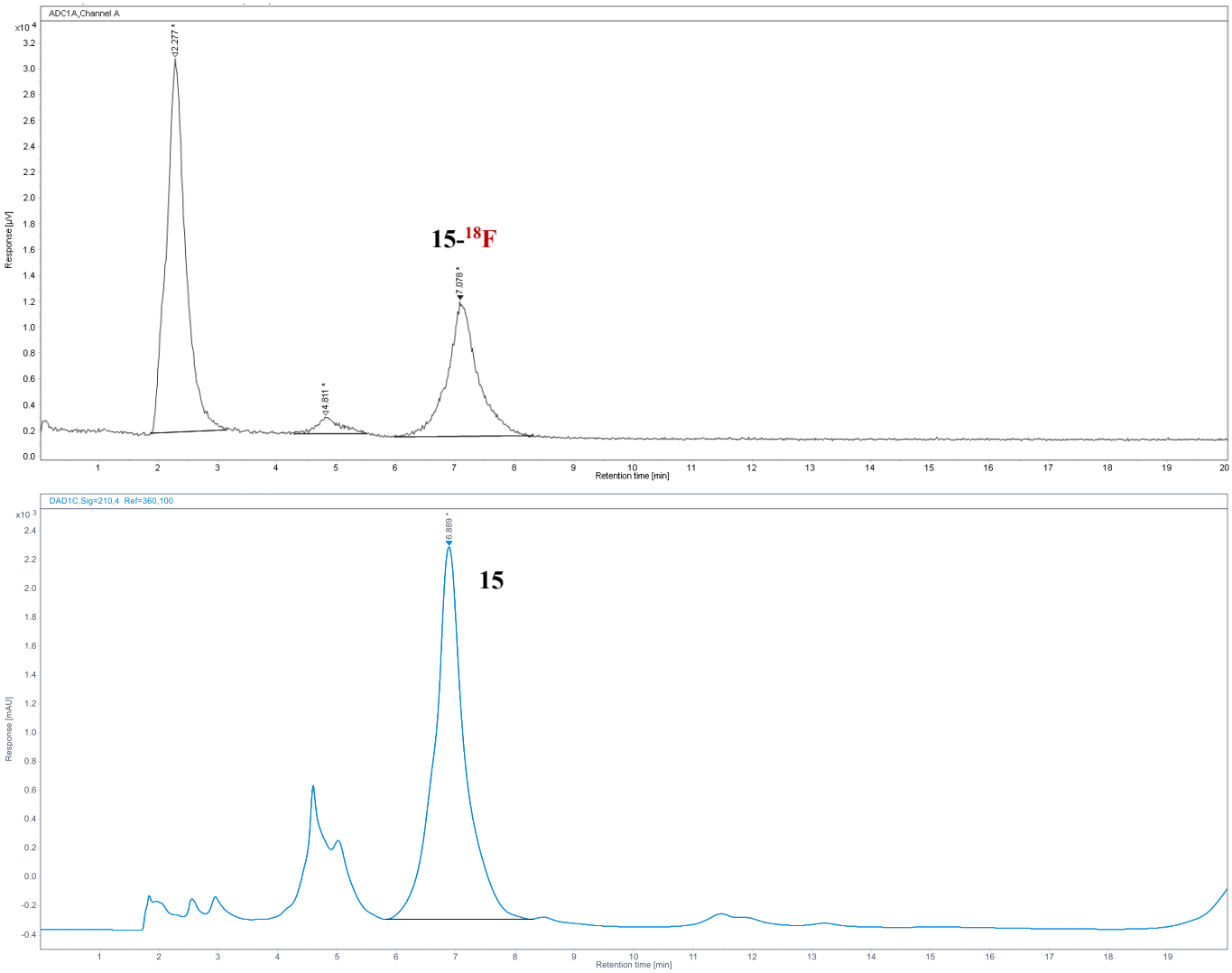
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.640	241937.155	34.508	9318.917	41.40	1.870	4.673
2	6.287	459163.951	**65.492**	13192.681	58.60	5.163	7.698

Supplementary Figure 18. Radio-HPLC analysis of **14-^{18}F**



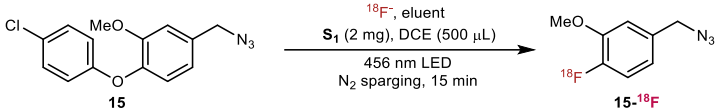
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
15	**15-^{18}F**	10.11 mCi/(10.11 + 0.38) mCi = 96%	55% MeCN	35%

Supplementary Table 20. Elution efficiency and RCC calculation of **15-^{18}F**.



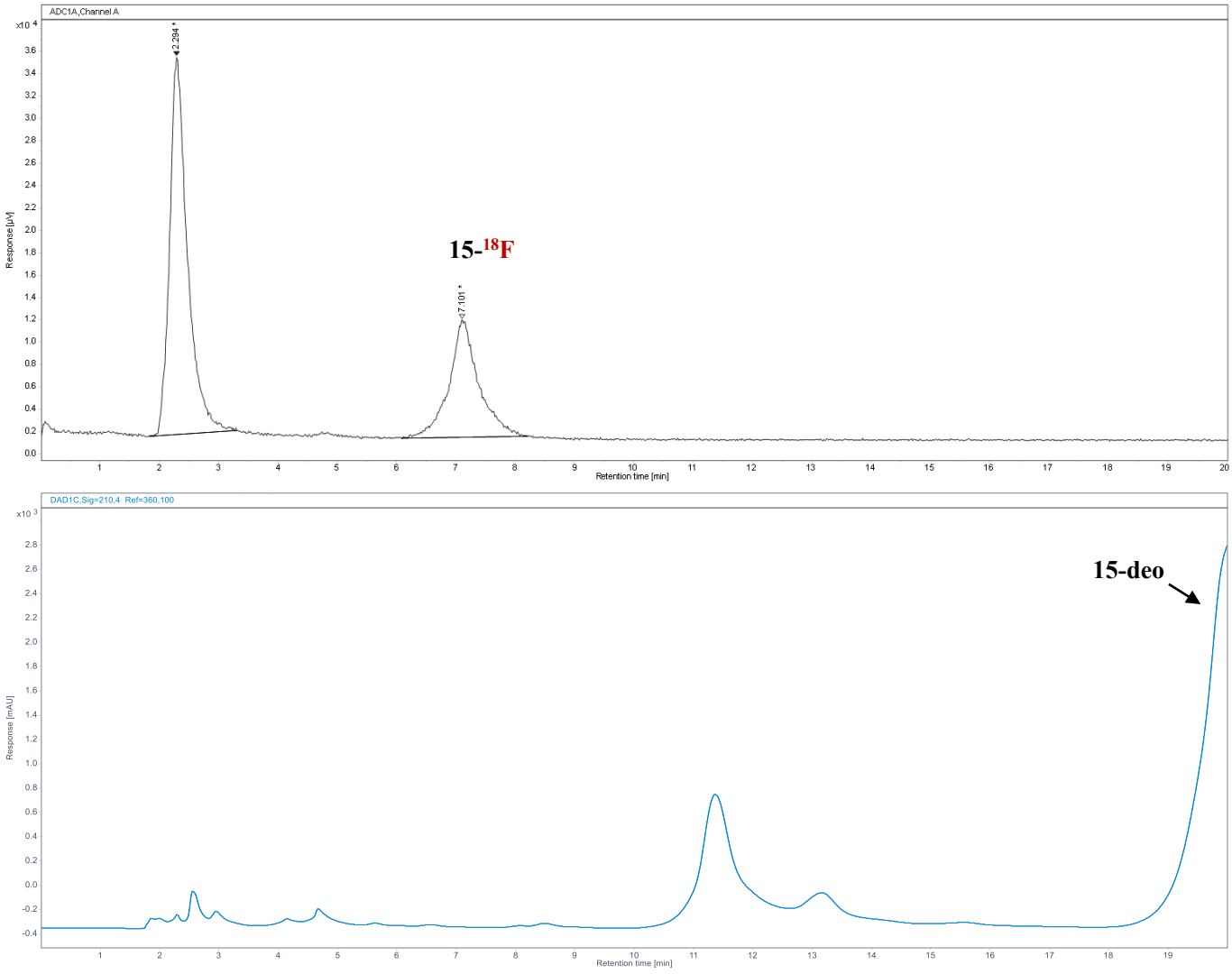
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.277	650040.587	61.414	28955.263	71.01	1.869	3.141
2	4.811	36572.667	3.455	1306.397	3.20	4.284	5.510
3	7.078	371842.684	**35.131**	10511.859	25.78	5.966	8.316

Supplementary Figure 19. Radio-HPLC analysis of **15-^{18}F**



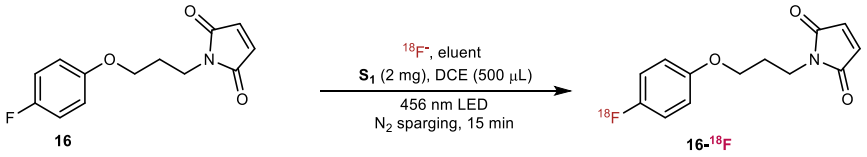
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
15-deo	**15-^{18}F**	12.68 mCi/(12.68 + 0.28) mCi = 98%	55% MeCN	34%[a]

Supplementary Table 21. Elution efficiency and RCC calculation of **15-^{18}F** from **15-deo**. A.0.02 mmol substrate.



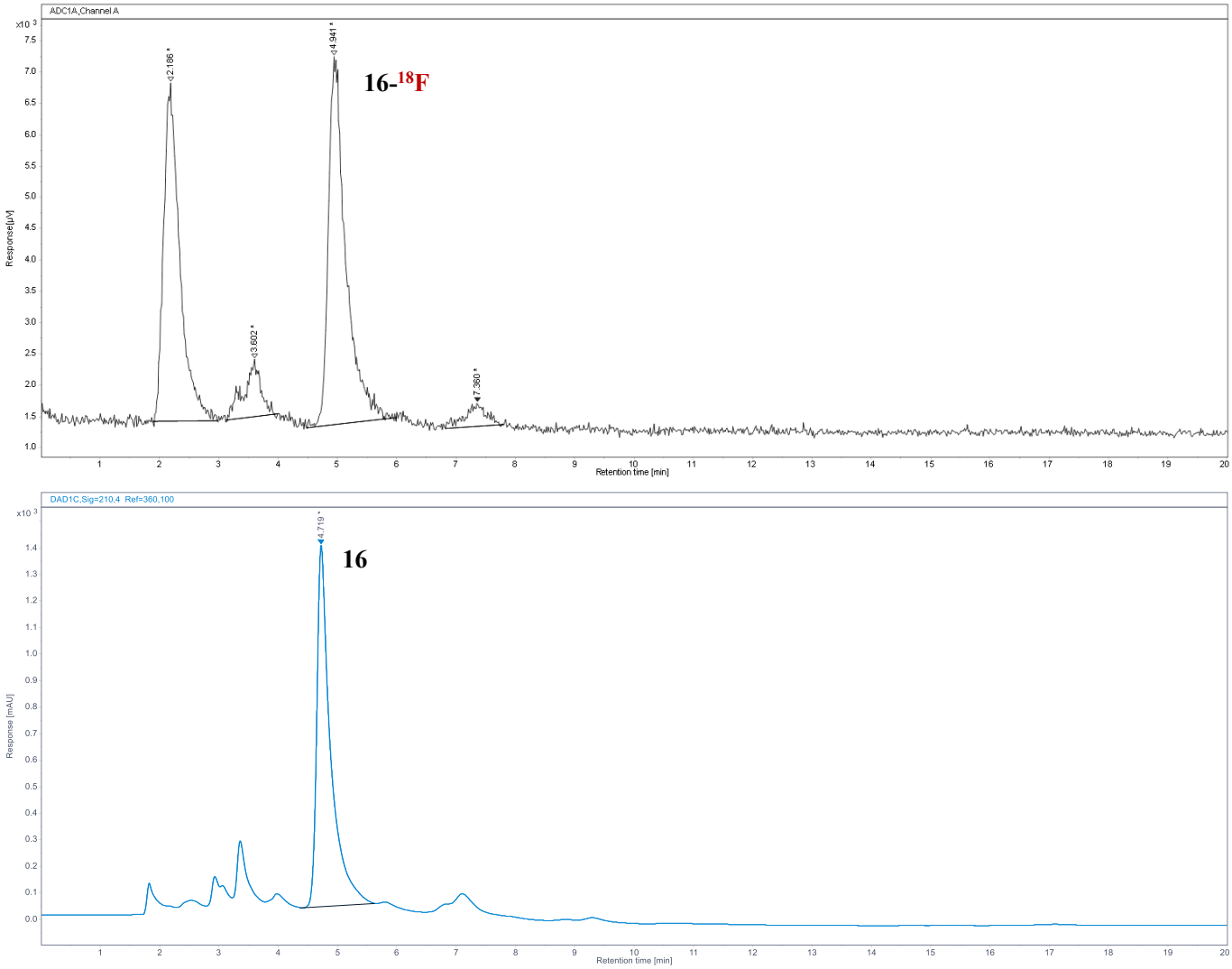
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.294	700929.354	65.731	33621.792	76.18	1.830	3.304
2	7.101	365436.580	**34.269**	10510.163	23.82	6.083	8.202

Supplementary Figure 20. Radio-HPLC analysis of **15-^{18}F**



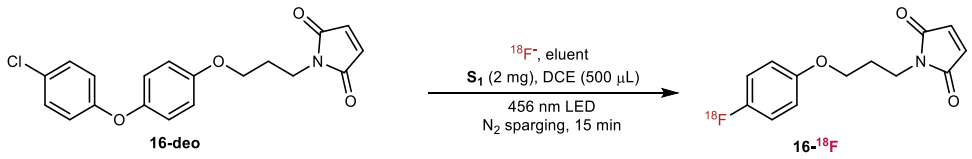
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
16	**16-^{18}F**	13.8 mCi/(13.8 + 0.92) mCi = 94%	60% MeCN	48%

Supplementary Table 22. Elution efficiency and RCC calculation of **16-^{18}F**.



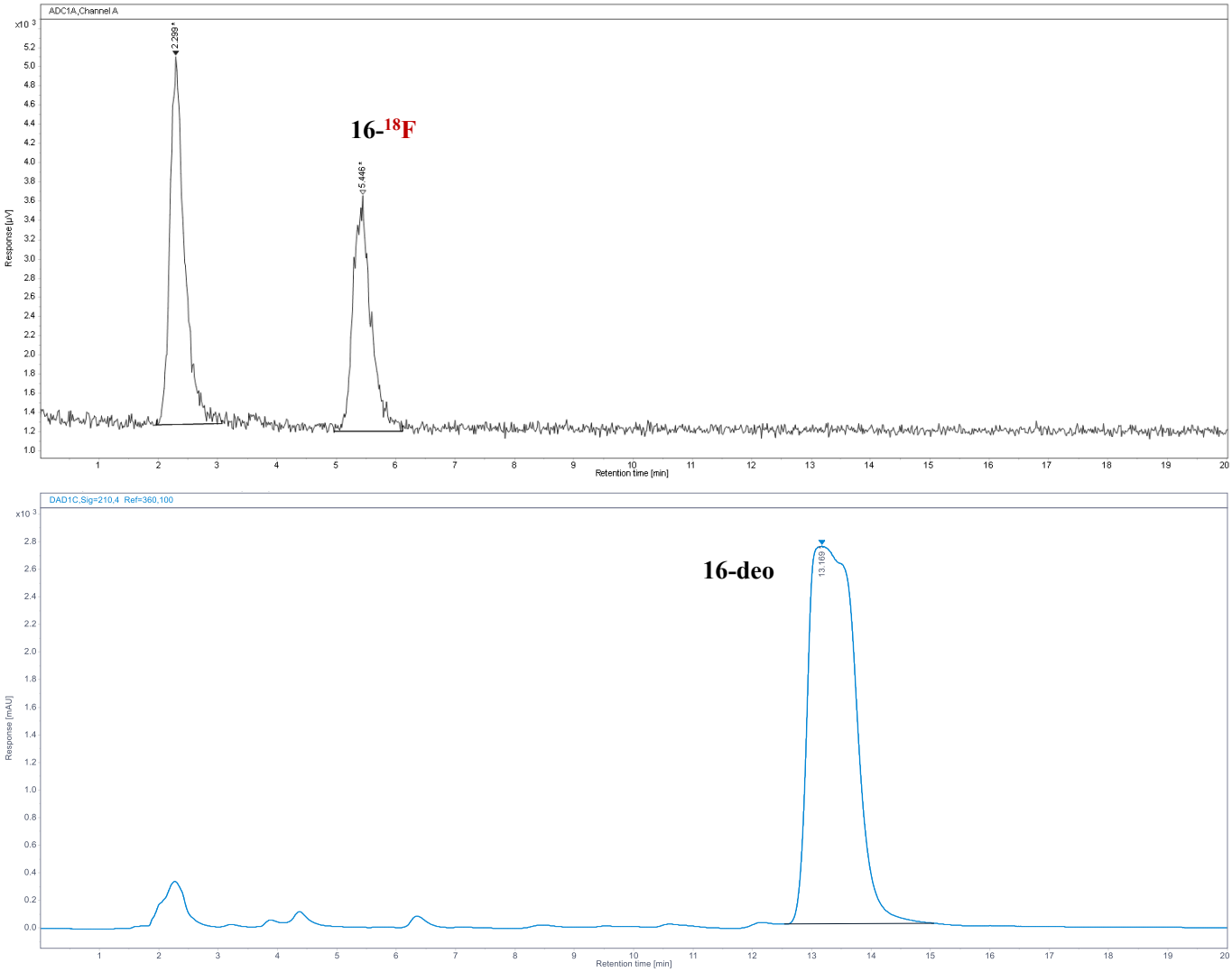
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.186	102802.378	41.204	5414.293	42.98	1.885	2.979
2	3.602	17606.580	7.057	919.978	7.30	3.116	4.016
3	4.941	120181.345	**48.169**	5890.231	46.76	4.484	5.996
4	7.360	8908.195	3.570	371.533	2.95	6.817	7.796

Supplementary Figure 21. Radio-HPLC analysis of **16-^{18}F**



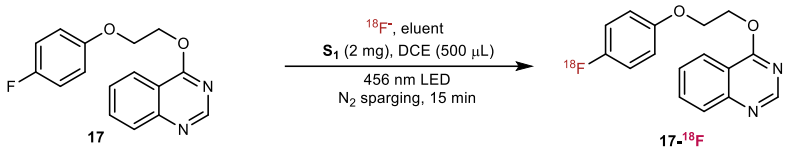
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
16-deo	**16-^{18}F**	3.4 mCi/(3.4 + 0.17) mCi = 95%	60% MeCN	44%[a]

Supplementary Table 23. Elution efficiency and RCC calculation of **16-^{18}F** from **16-deo**. A.0.02 mmol substrate.



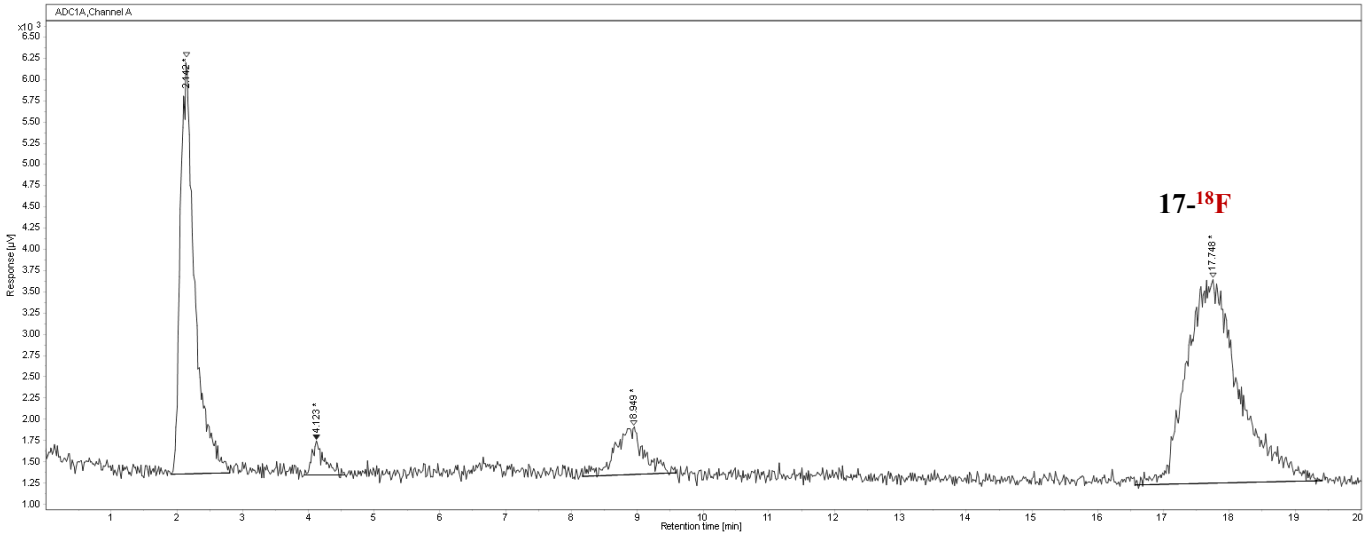
#	RT (min)	Area (µV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.299	65623.798	56.487	3830.354	60.98	1.976	3.076
2	5.446	50551.753	**43.513**	2450.686	39.02	4.958	6.118

Supplementary Figure 22. Radio-HPLC analysis of **16-^{18}F**



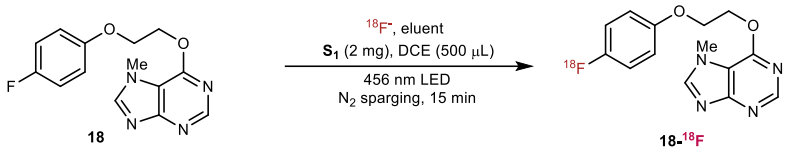
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
17	**17-^{18}F**	10.32 mCi/(10.32 + 0.51) mCi = 95%	60% MeCN	58%

Supplementary Table 24. Elution efficiency and RCC calculation of **17-^{18}F**.



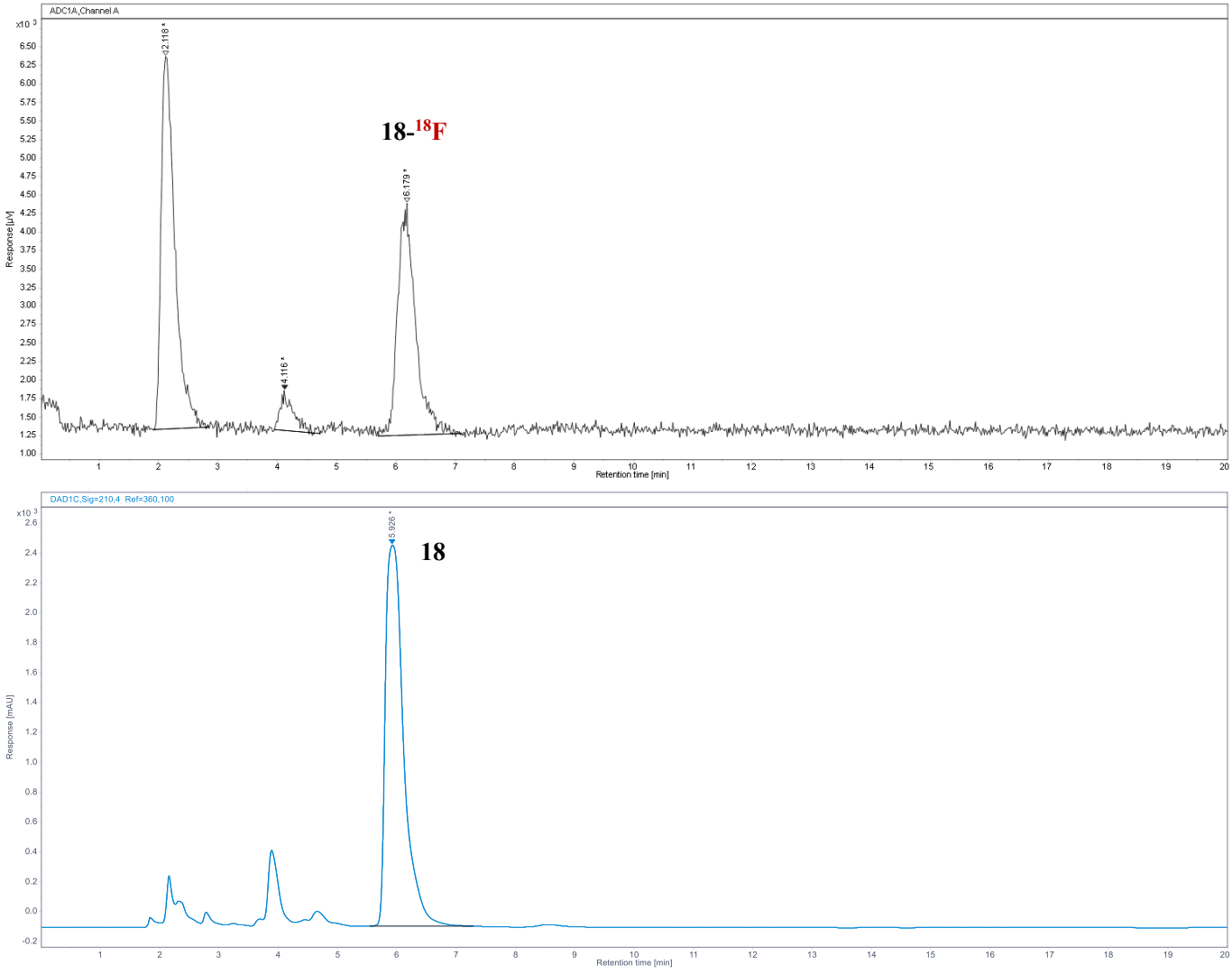
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.142	74298.428	32.482	4888.739	59.26	1.906	2.803
2	4.123	5077.350	2.220	400.591	4.86	3.934	4.554
3	8.949	16893.403	7.386	559.410	6.78	8.168	9.589
4	17.748	132466.345	**57.912**	2401.066	29.10	16.568	19.410

Supplementary Figure 23. Radio-HPLC analysis of **17-^{18}F**



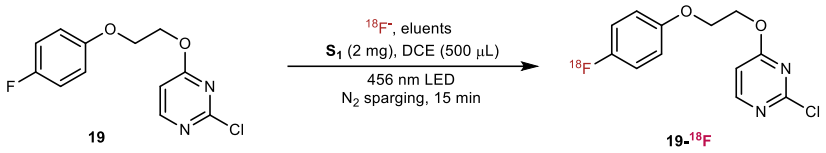
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
18	**18-^{18}F**	7.92 mCi/(7.92 + 0.57) mCi = 93%	50% MeCN	42%

Supplementary Table 25. Elution efficiency and RCC calculation of **18-^{18}F**.



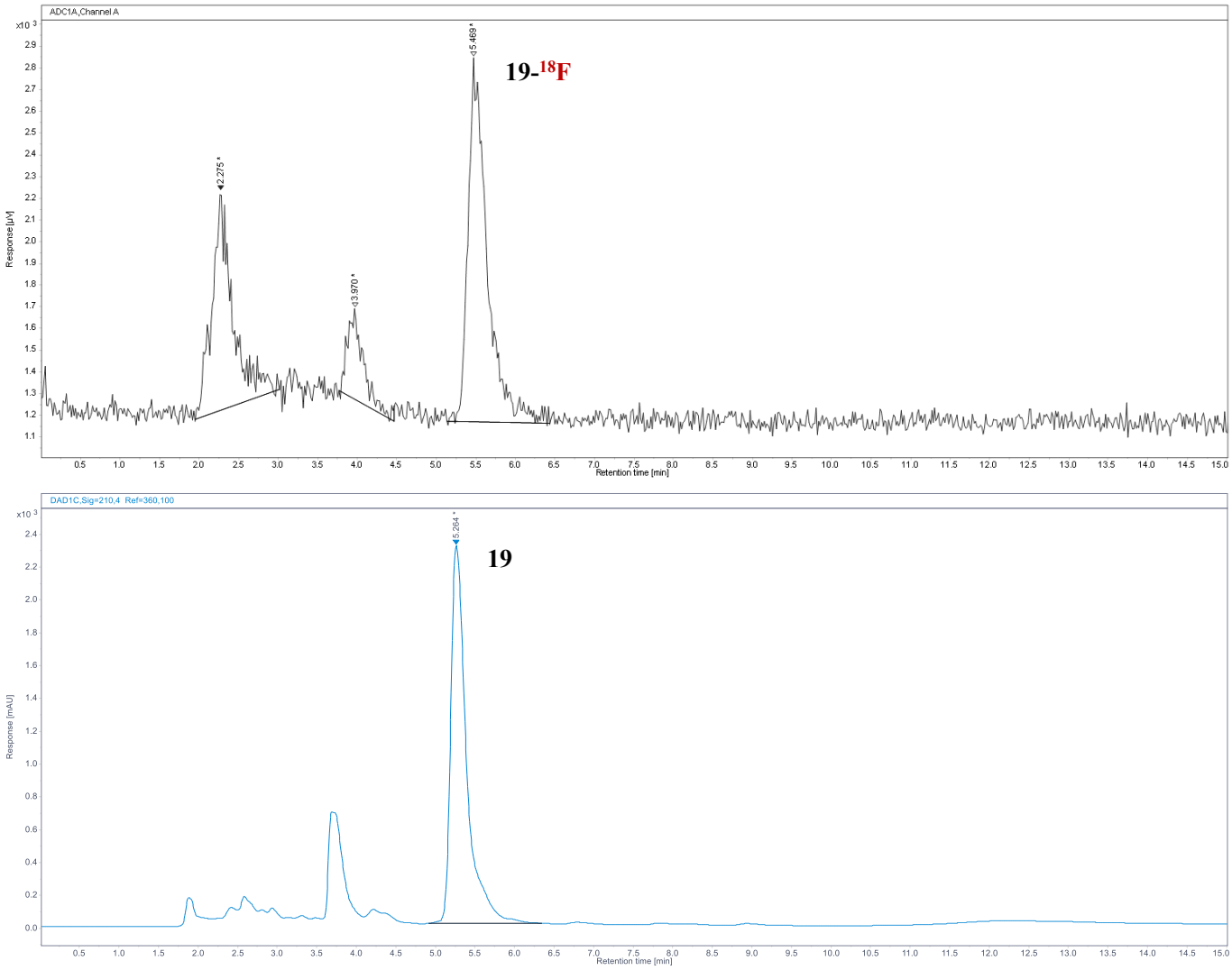
#	RT (min)	Area (µV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.118	81454.533	52.603	5033.862	57.83	1.904	2.842
2	4.116	8045.685	5.196	535.578	6.15	3.945	4.718
3	6.179	65347.047	**42.201**	3134.890	36.02	5.697	7.104

Supplementary Figure 24. Radio-HPLC analysis of **18-^{18}F**



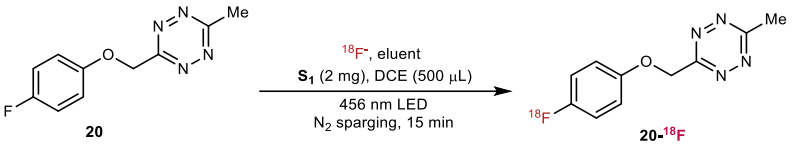
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
19	**19-^{18}F**	30.9 mCi/(30.9 + 2.1) mCi = 94%	65% MeCN	54%

Supplementary Table 26. Elution efficiency and RCC calculation of **19-^{18}F**.



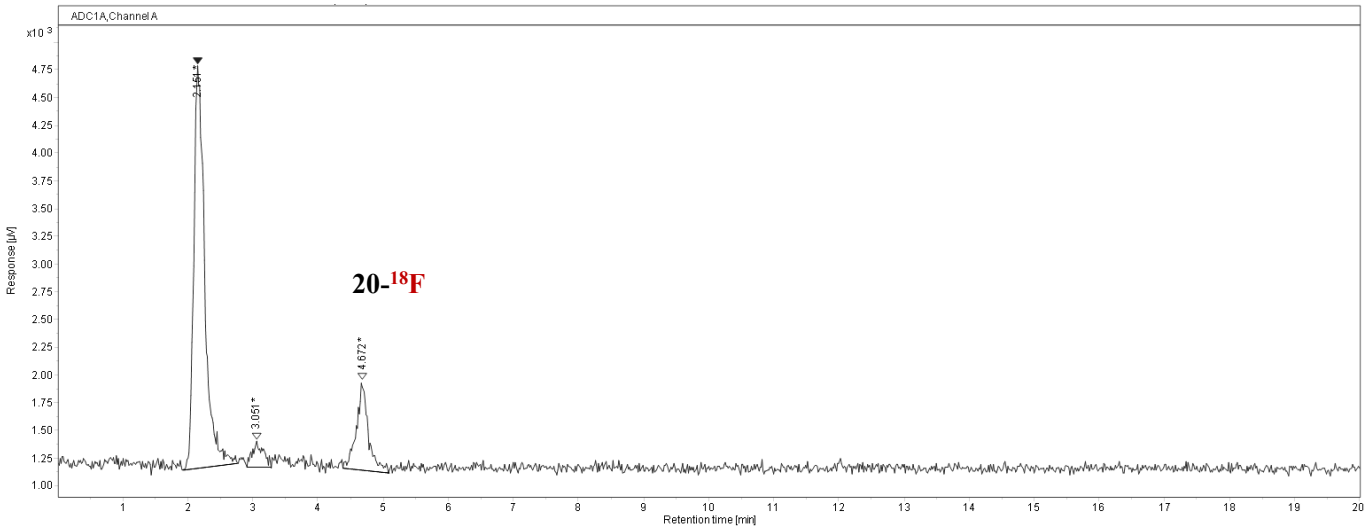
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.275	18241.605	35.128	1007.116	32.42	1.947	3.018
2	3.970	5821.588	11.211	421.286	13.56	3.767	4.469
3	5.469	27866.232	**53.662**	1678.136	54.02	5.137	6.439

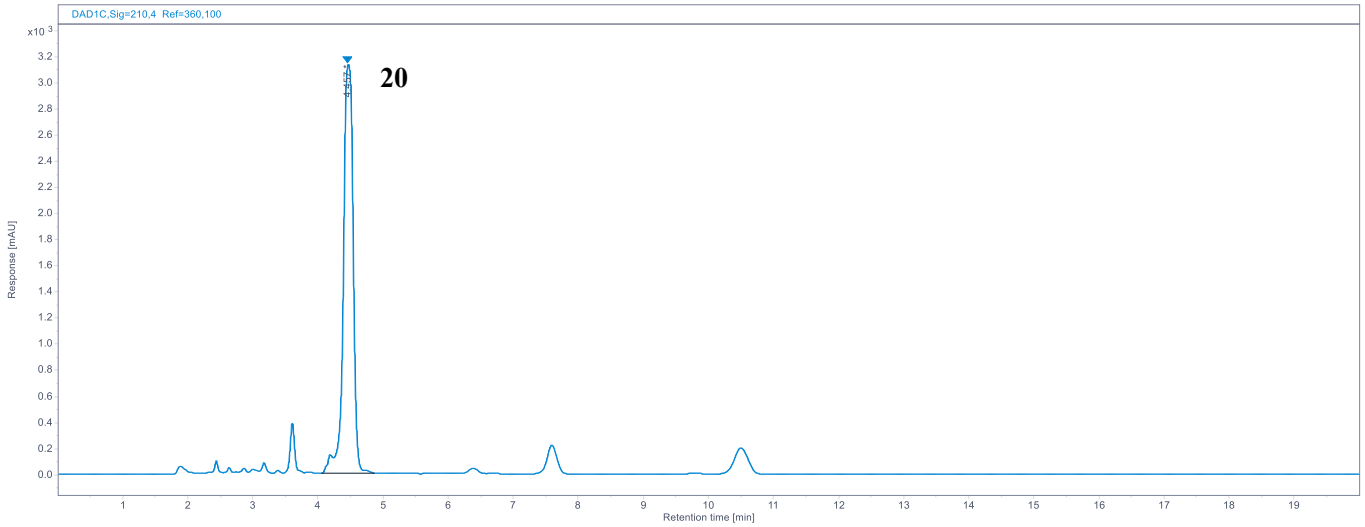
Supplementary Figure 25. Radio-HPLC analysis of **19-^{18}F**.



Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
20	**20-^{18}F**	7.82 mCi /(7.82 + 0.23) mCi = 97%	60% MeCN	18%[a]

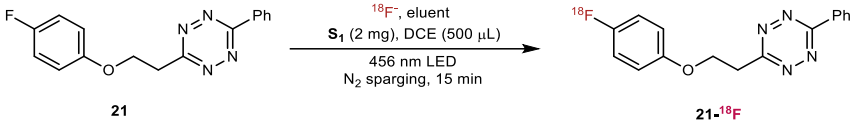
Supplementary Table 27. Elution efficiency and RCC calculation of **20-^{18}F**. [a]0.02 mmol substrate was used.





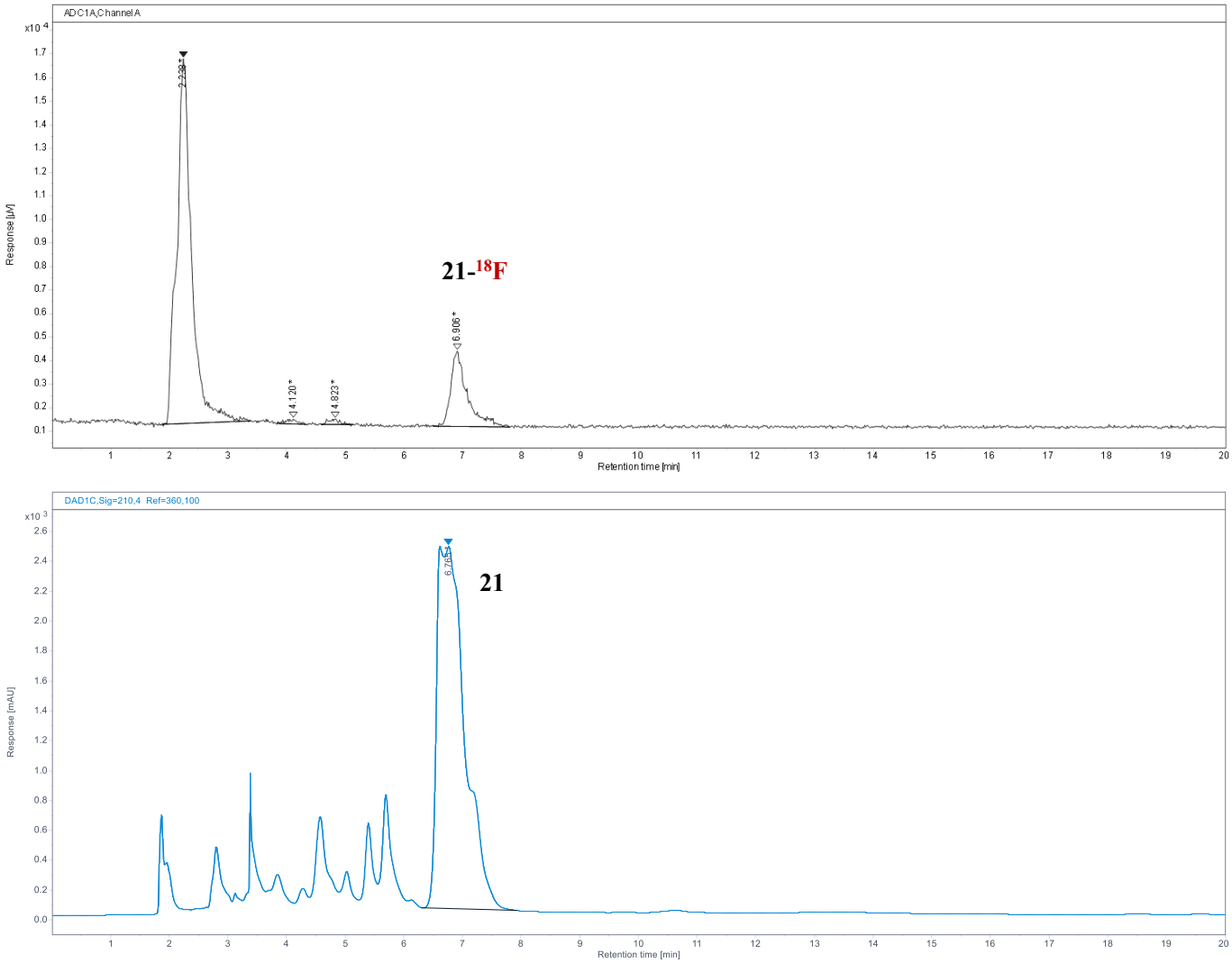
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.151	42564.037	76.994	3627.583	77.89	1.929	2.762
2	3.051	2683.414	4.854	229.807	4.93	2.901	3.286
3	4.672	10034.751	**18.152**	799.777	17.17	4.384	5.086

Supplementary Figure 26. Radio-HPLC analysis of **20-^{18}F**.



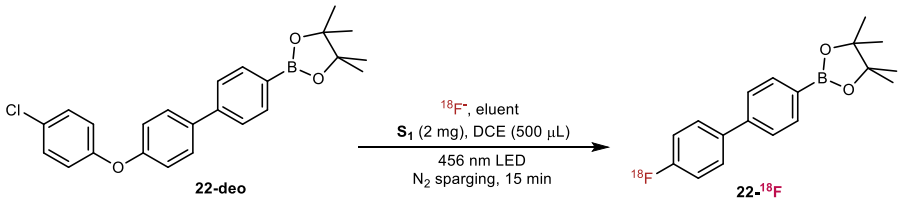
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
21	**21-^{18}F**	9.39 mCi/(9.39 + 0.25) mCi=97%	70% MeCN	18%[a]

Supplementary Table 28. Elution efficiency and RCC calculation of **21-^{18}F**. [a]0.02 mmol substrate was used.



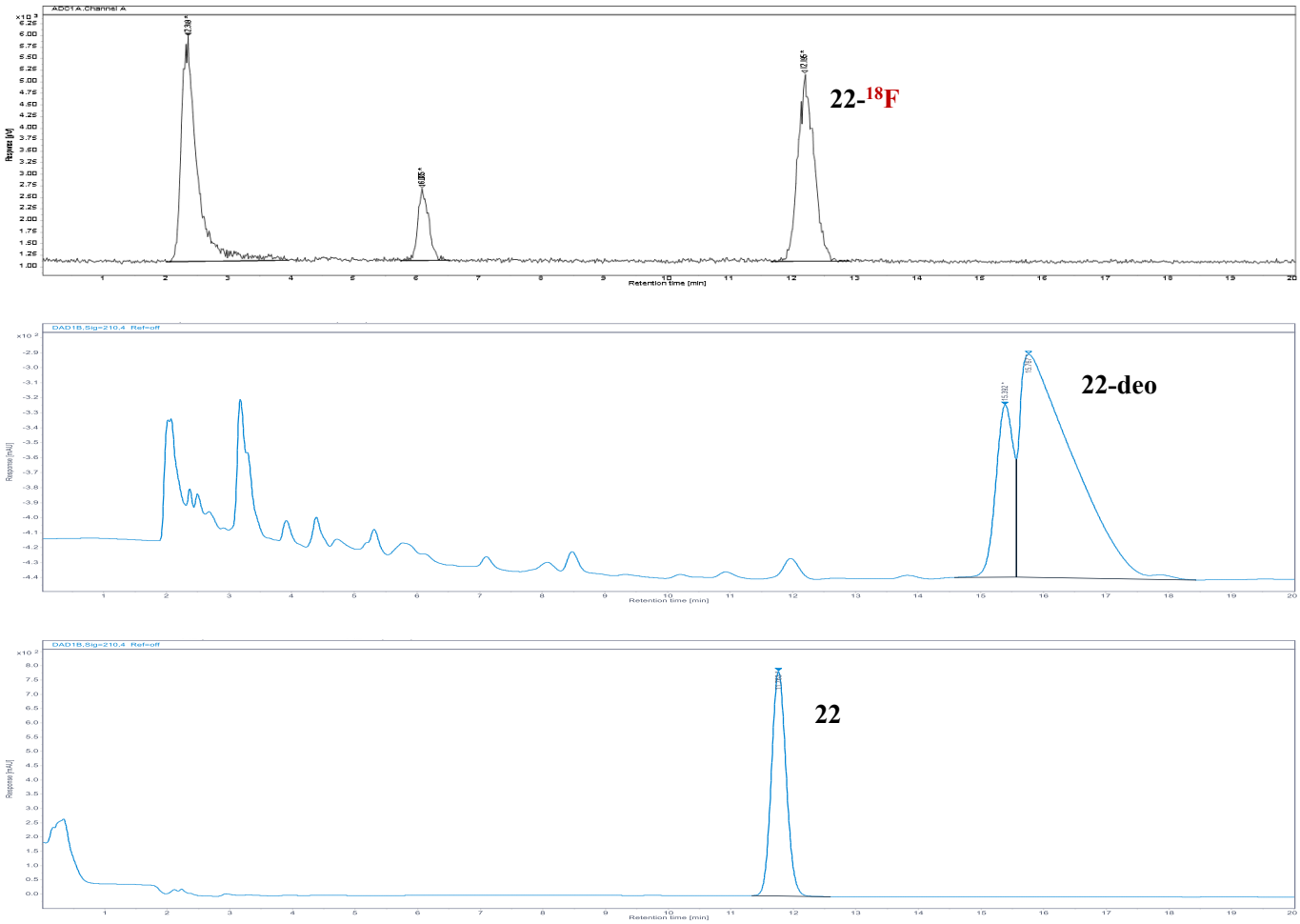
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.238	269865.439	80.327	15473.357	81.03	1.880	3.400
2	4.120	2438.460	0.726	214.414	1.12	3.845	4.317
3	4.823	2862.743	0.852	244.135	1.28	4.586	5.124
4	6.906	60791.349	**18.095**	3163.832	16.57	6.496	7.803

Supplementary Figure 27. Radio-HPLC analysis of **21-^{18}F**.



Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
22-deo	**22-^{18}F**	9.82 mCi/(9.82 + 2.87) mCi = 77%	70% MeCN	41%

Supplementary Table 29. Elution efficiency and RCC calculation of **22-^{18}F from 22-deo**.

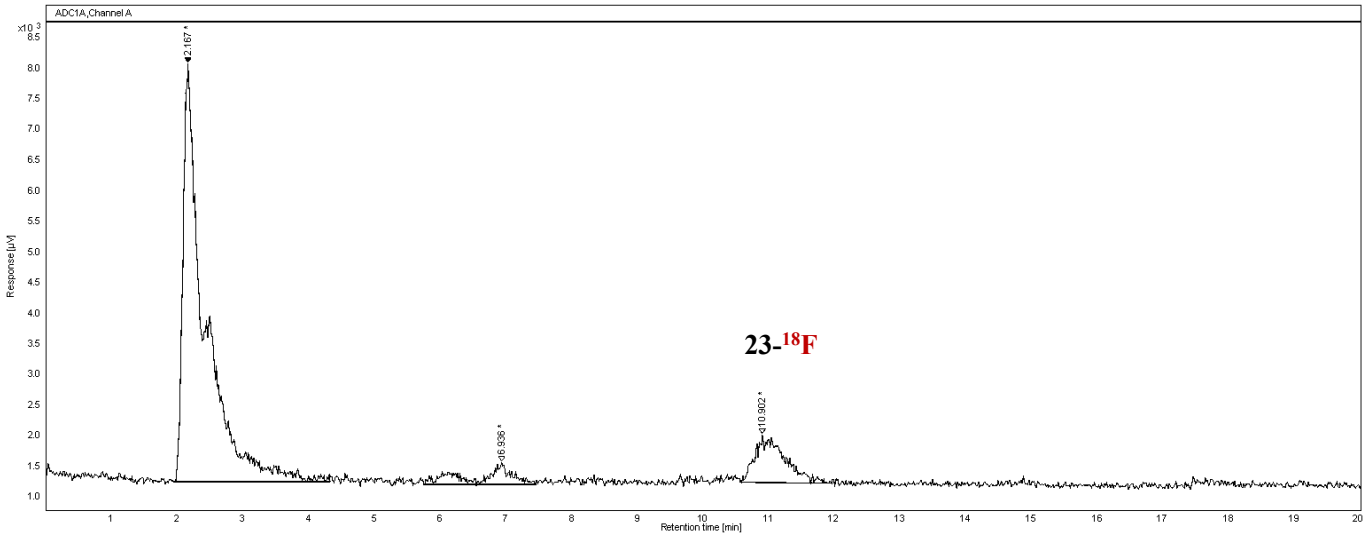


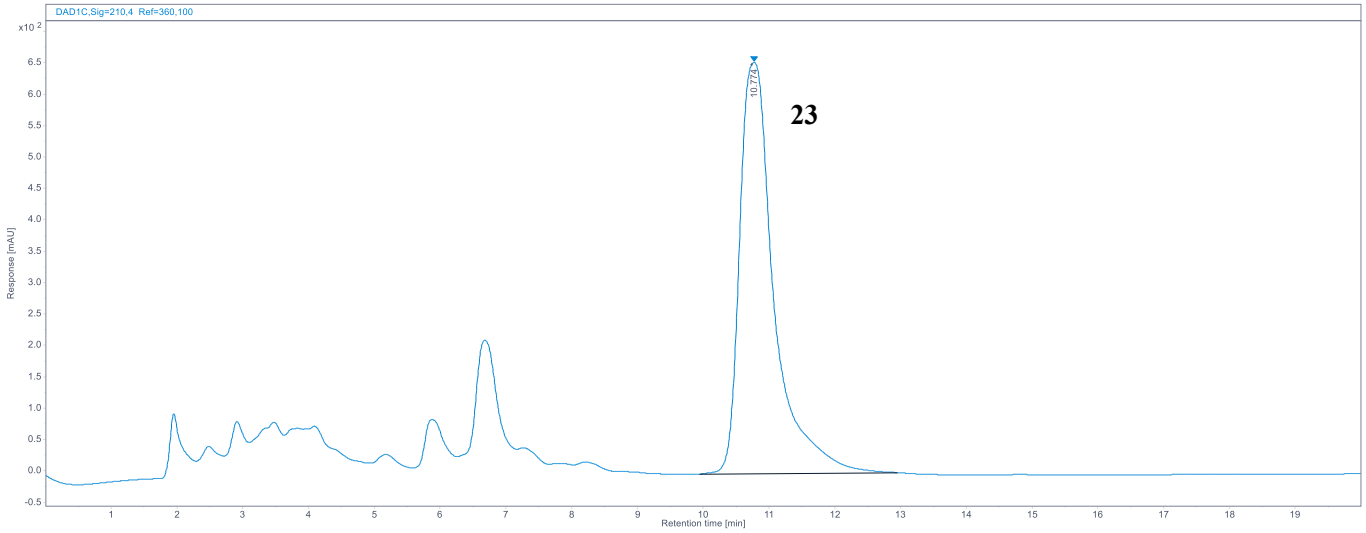
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.349	85386.472	48.289	4864.557	46.45	2.007	3.947
2	6.085	18702.693	10.577	1558.694	14.88	5.745	6.529
3	12.195	72735.810	**41.134**	4048.518	38.66	11.654	12.900

Supplementary Figure 27. Radio-HPLC analysis of **22-^{18}F**.

Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
23	**23-^{18}F**	8.92 mCi/(8.92 + 0.43) mCi = 95%	70% MeCN	13%

Supplementary Table 30. Elution efficiency and RCC calculation of **23-^{18}F**.



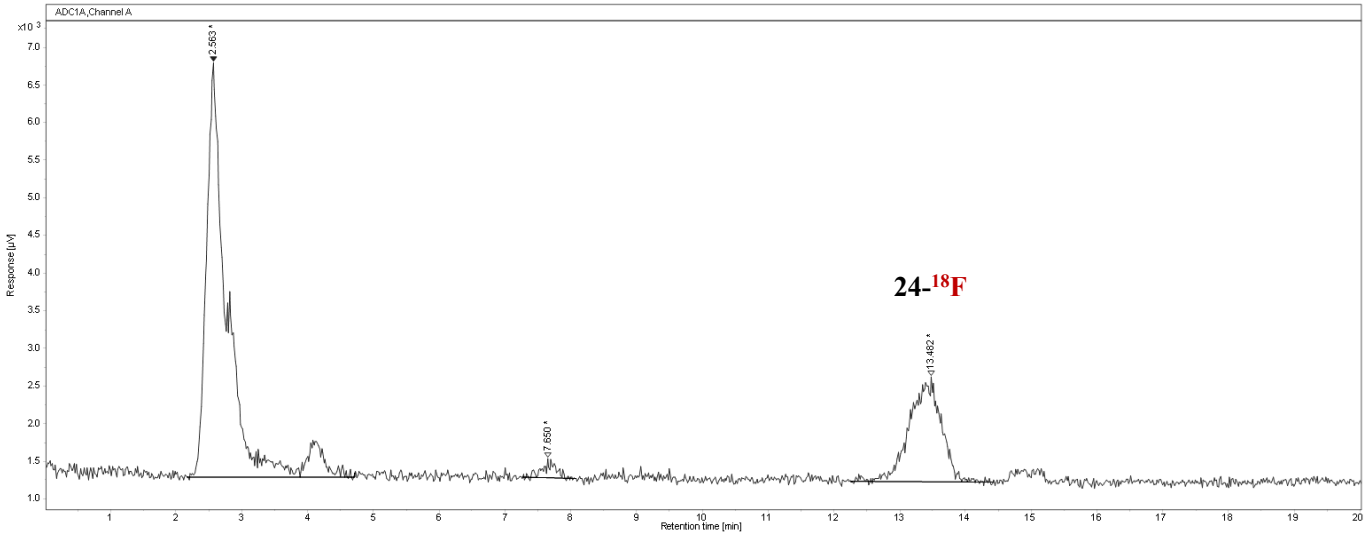


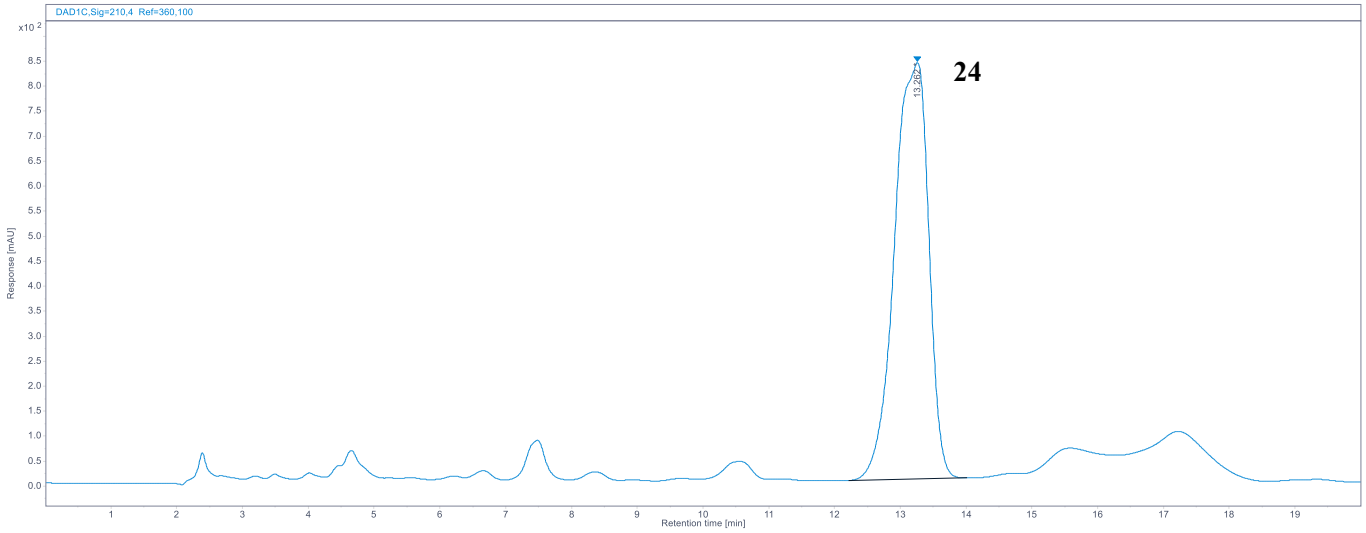
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.167	156557.134	81.269	6824.923	85.76	1.953	4.322
2	6.936	11974.361	6.216	354.728	4.46	5.761	7.455
3	10.902	24109.563	**12.515**	778.259	9.78	10.565	11.945

Supplementary Figure 28. Radio-HPLC analysis of **23-^{18}F**.

Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
24	**24-^{18}F**	7.6 mCi/(7.6 + 0.52) mCi = 94%	65% MeCN (column B)	27%

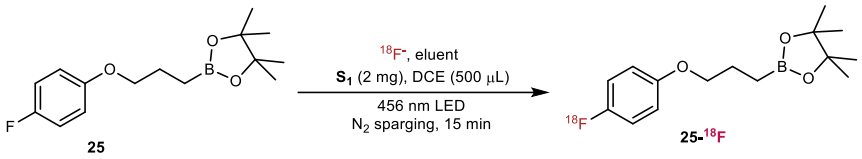
Supplementary Table 31. Elution efficiency and RCC calculation of **24-^{18}F**.





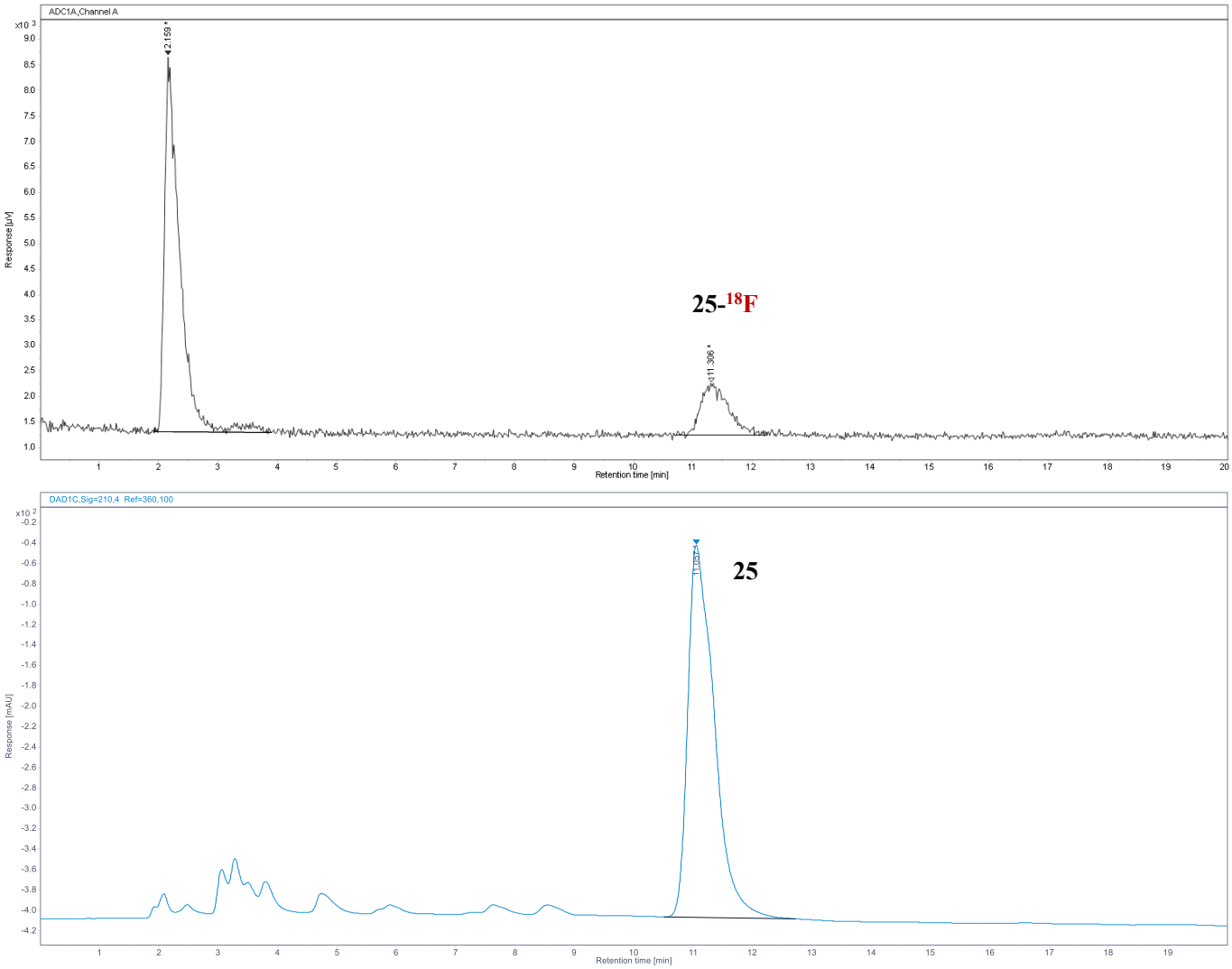
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.563	123192.173	71.510	5502.308	77.00	2.166	4.718
2	7.650	3262.465	1.894	253.539	3.55	7.269	8.074
3	13.482	45818.485	**26.596**	1389.788	19.45	12.258	14.419

Supplementary Figure 29. Radio-HPLC analysis of **24-^{18}F**.



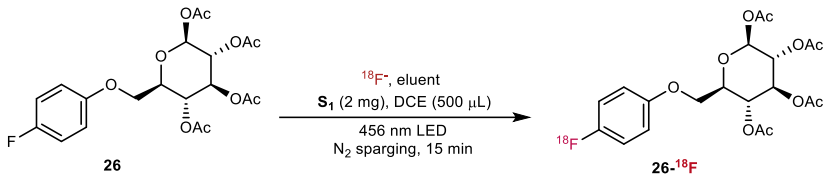
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
25	**25-^{18}F**	9.64 mCi/(9.64 + 0.34) mCi = 97%	65% MeCN	20%[a]

Supplementary Table 32. Elution efficiency and RCC calculation of **25-^{18}F**. a.0.02 mmol substrate.



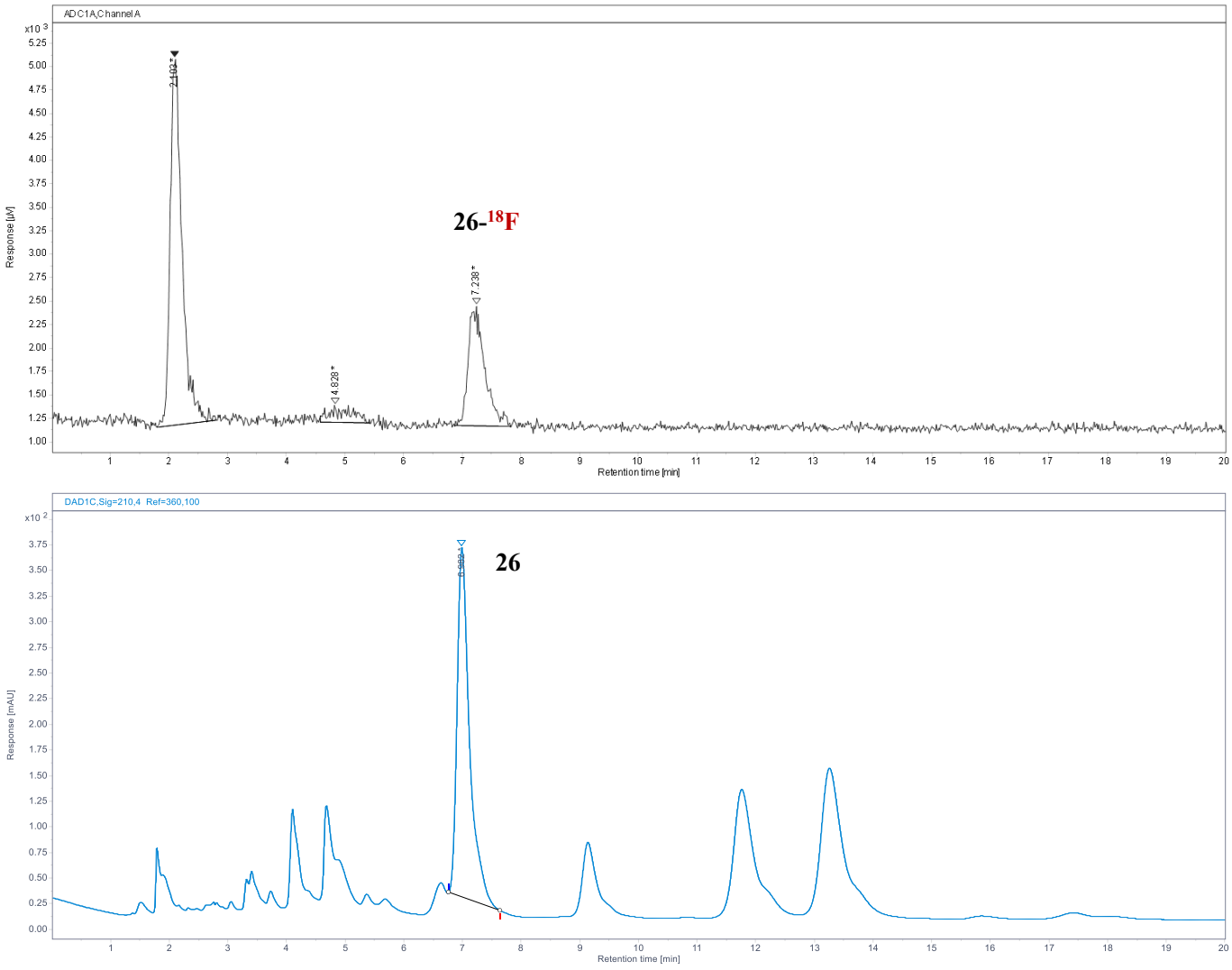
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.159	131316.125	80.004	7369.335	87.78	1.936	3.894
2	11.306	32821.755	**19.996**	1026.155	12.22	10.699	12.248

Supplementary Figure 30. Radio-HPLC analysis of **25-^{18}F**.



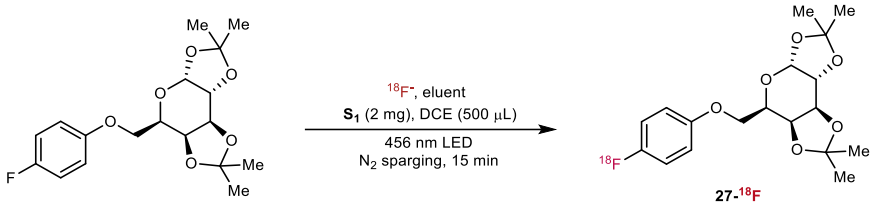
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
26	**26-^{18}F**	7.6 mCi/(7.6 + 0.11) mCi = 99%	55% MeCN	29%

Supplementary Table 33. Elution efficiency and RCC calculation of **26-^{18}F**.



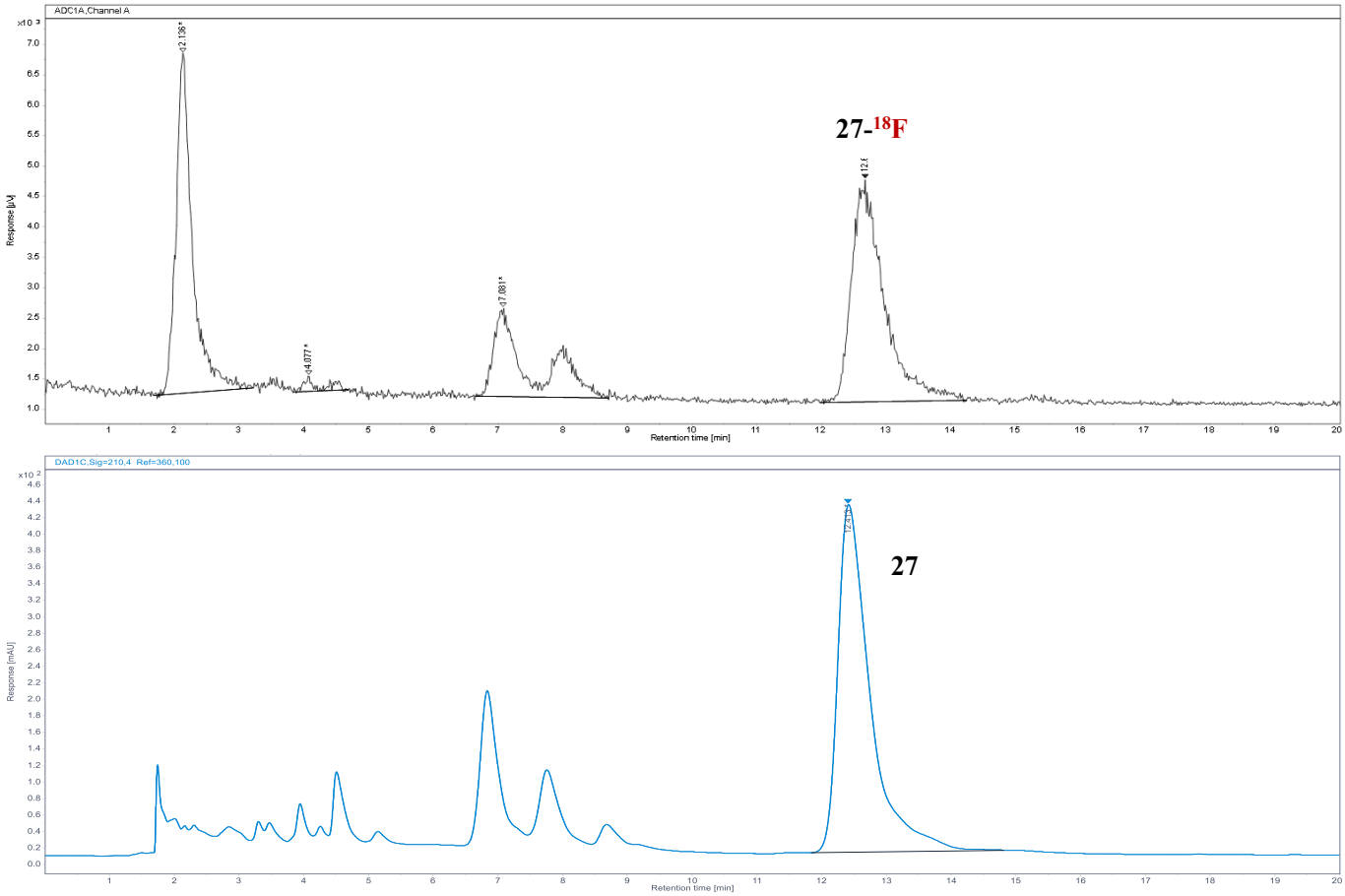
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.103	55048.549	65.441	3911.379	72.82	1.794	2.803
2	4.828	4372.555	5.198	179.297	3.34	4.577	5.433
3	7.238	24698.884	**29.361**	1280.725	23.84	6.868	7.833

Supplementary Figure 31. Radio-HPLC analysis of **26-^{18}F**.



Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
27	**27-^{18}F**	10.8 mCi/(10.48 + 0.45) mCi = 96%	55% MeCN	45%

Supplementary Table 34. Elution efficiency and RCC calculation of **27-^{18}F**.

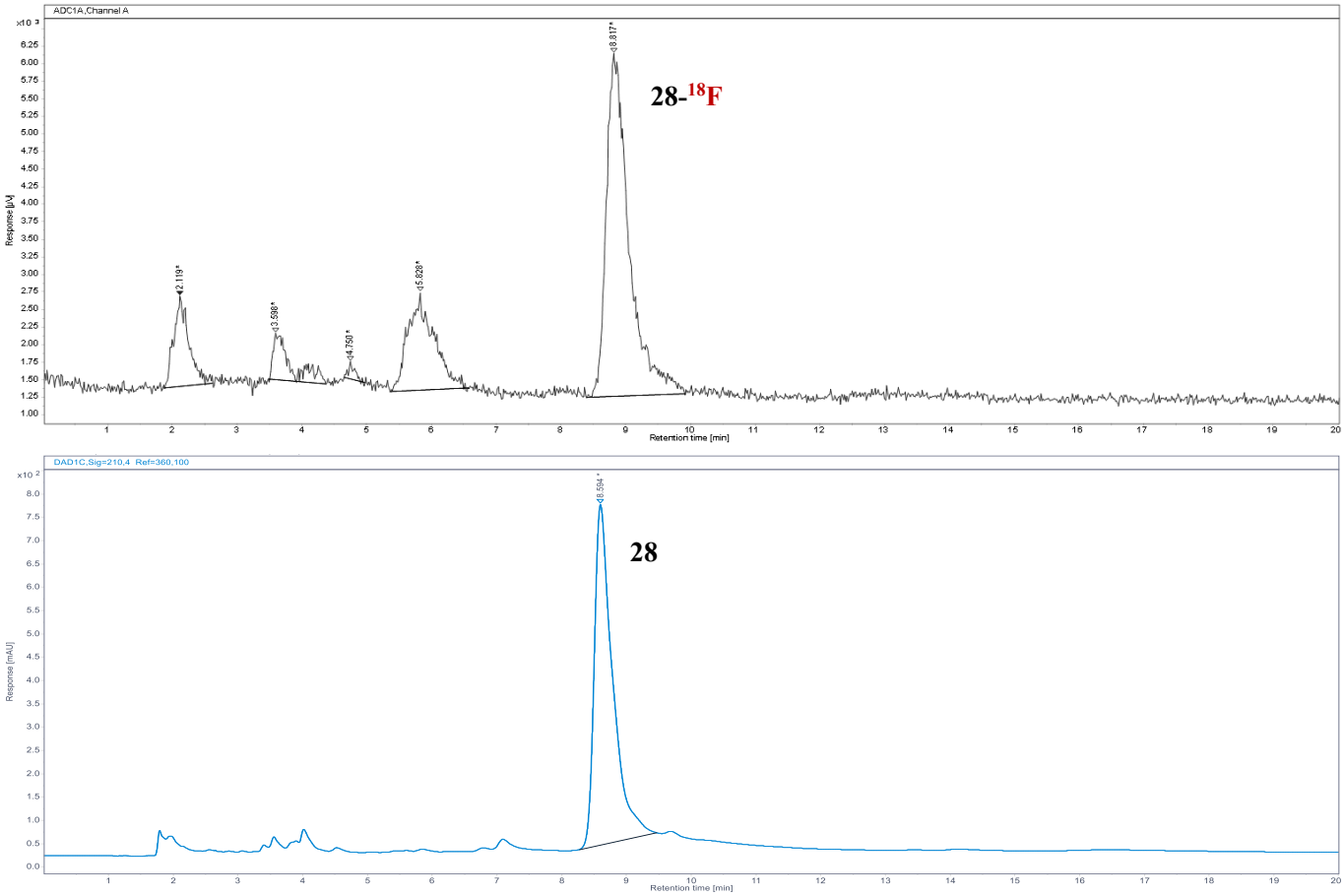


#	RT (min)	Area (µV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.136	98669.333	34.775	5584.544	50.95	1.685	3.216
2	4.077	3831.479	1.350	256.179	2.34	3.836	4.692
3	7.081	54424.362	19.181	1459.018	13.31	6.650	8.705
4	12.665	126814.889	**44.694**	3661.634	33.40	11.974	14.236

Supplementary Figure 32. Radio-HPLC analysis of **27-^{18}F**.

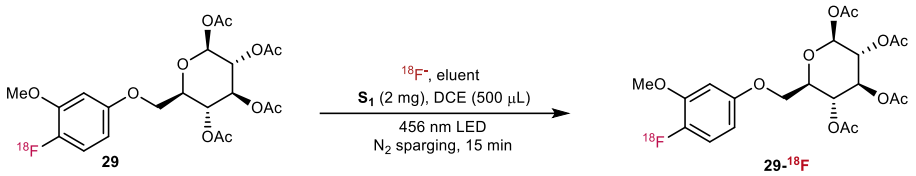
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
28	**28-^{18}F**	12.18 mCi / (12.18 + 0.41) mCi = 97%	60% MeCN	62%

Supplementary Table 35. Elution efficiency and RCC calculation of **28-^{18}F**.



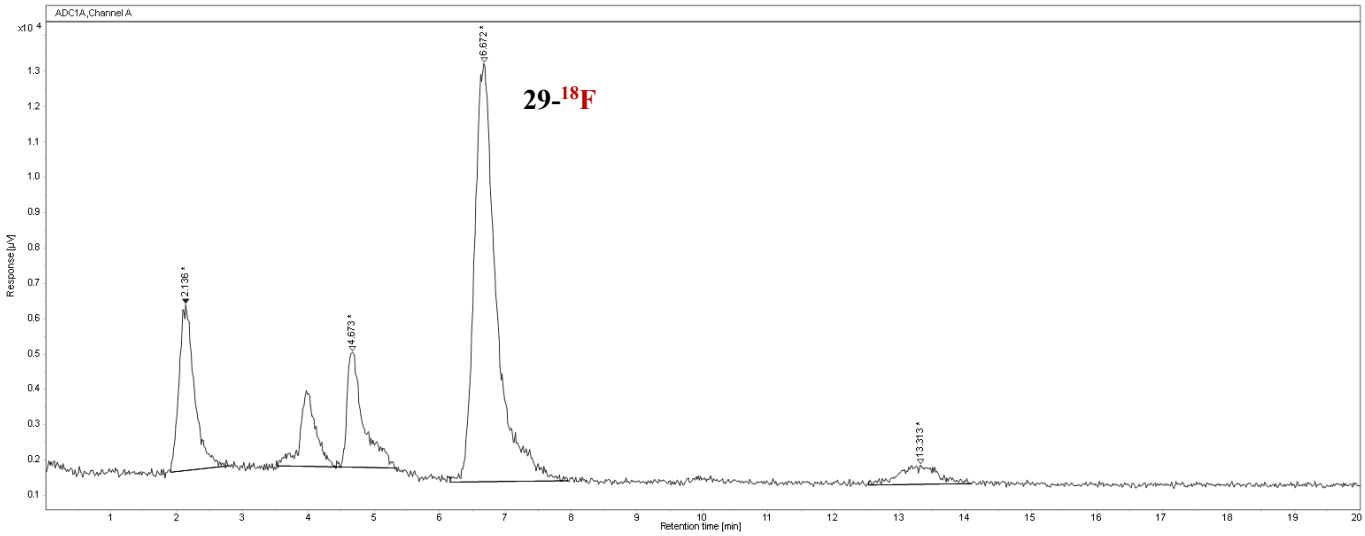
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.119	20880.602	10.876	1288.180	15.20	1.879	2.627
2	3.598	12375.068	6.445	658.876	7.78	3.485	4.363
3	4.750	1518.560	0.791	247.124	2.92	4.652	4.971
4	5.828	37968.432	19.776	1399.080	16.51	5.371	6.568
5	8.817	119253.337	**62.112**	4880.962	57.60	8.403	9.920

Supplementary Figure 33. Radio-HPLC analysis of **28-^{18}F**.



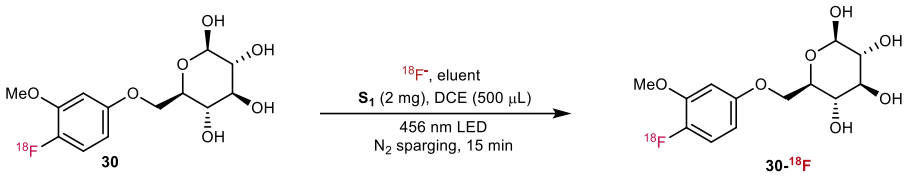
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
29	**29-^{18}F**	14.89 mCi/(14.89 + 0.57) mCi = 96%	55% MeCN	59%

Supplementary Table 36. Elution efficiency and RCC calculation of **29-^{18}F**.



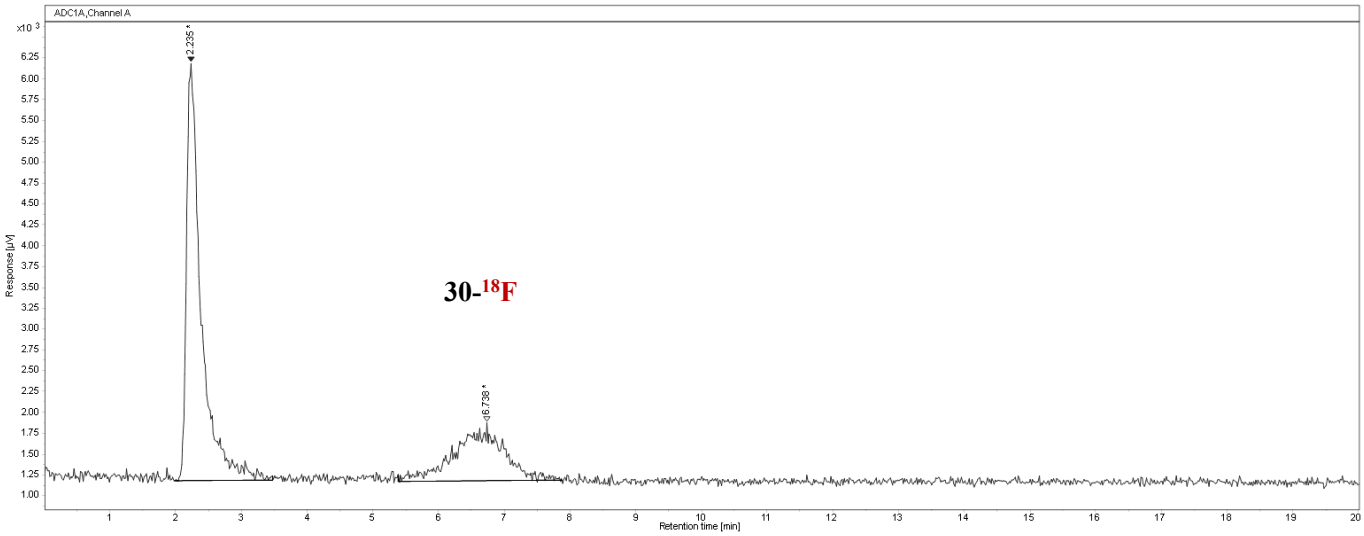
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.136	76767.715	16.364	4694.308	23.10	1.902	2.785
2	4.673	93745.296	19.982	3252.394	16.00	3.540	5.329
3	6.672	276663.439	**58.973**	11829.061	58.21	6.158	7.946
4	13.313	21962.396	4.681	546.394	2.69	12.533	14.097

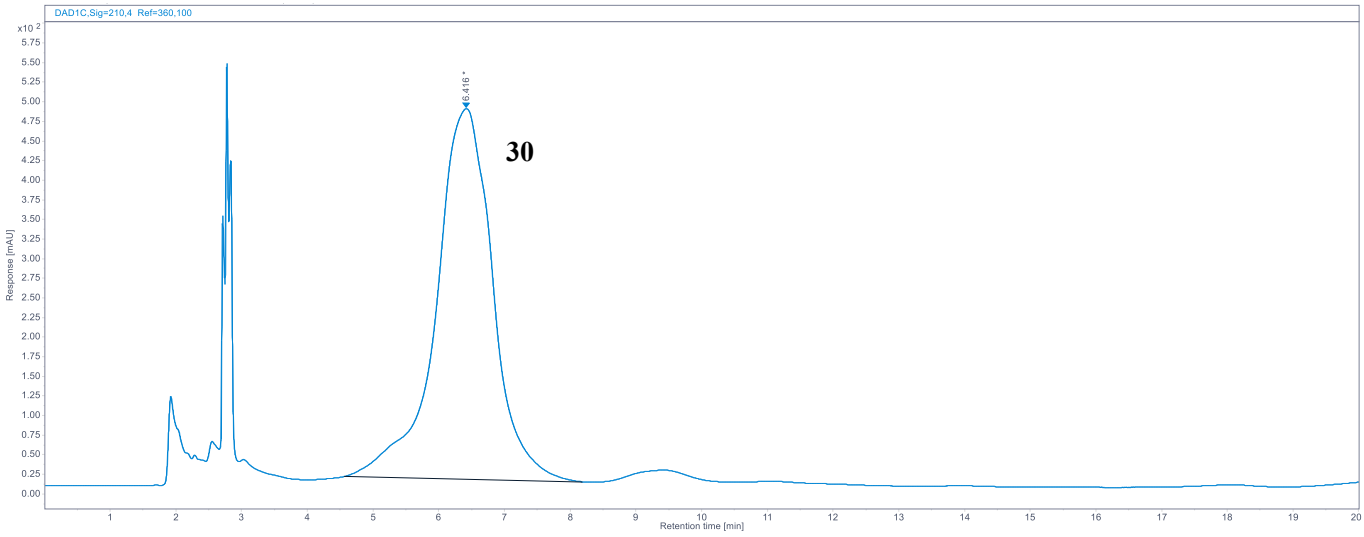
Supplementary Figure 34. Radio-HPLC analysis of **29-^{18}F**.



Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
30	**30-^{18}F**	3.1 mCi/(3.1 + 0.09) mCi = 97%	20% MeCN	30%

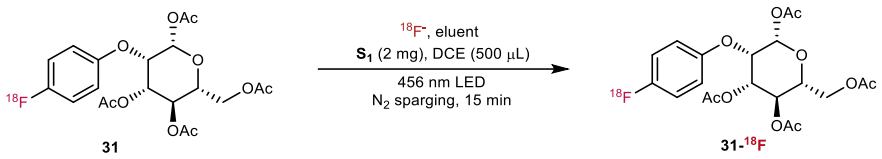
Supplementary Table 37. Elution efficiency and RCC calculation of **30-^{18}F**.





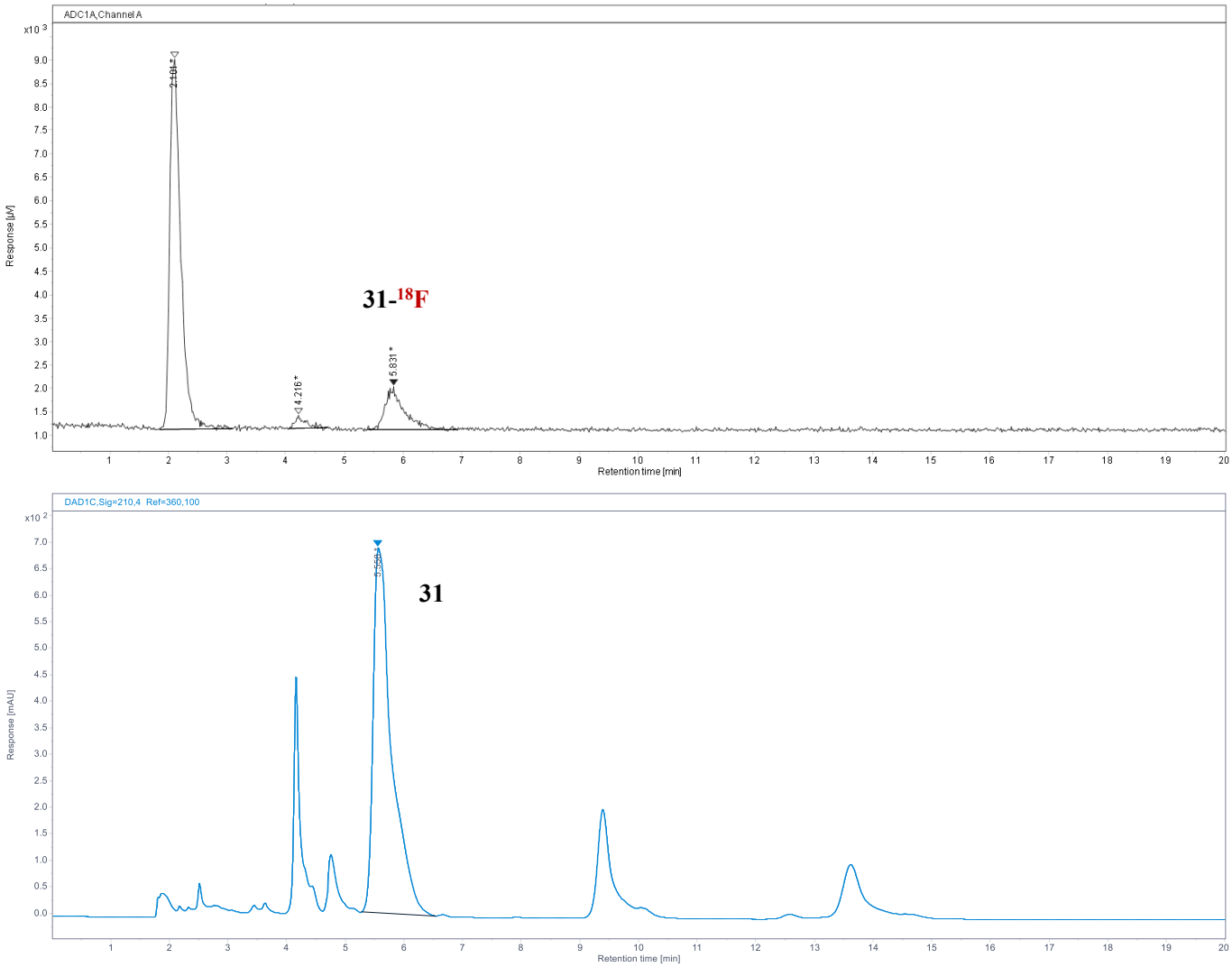
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.235	78096.010	69.981	5014.881	87.87	1.982	3.471
2	6.738	33499.844	**30.019**	692.027	12.13	5.385	7.877

Supplementary Figure 35. Radio-HPLC analysis of **30-^{18}F**.



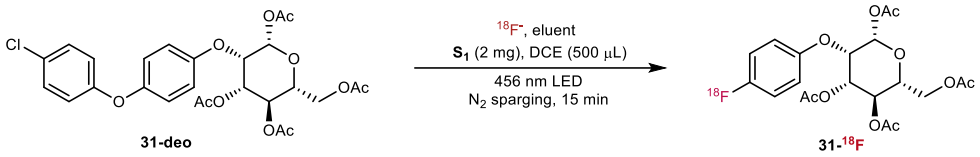
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
31	**31-^{18}F**	5.7 mCi/(5.7 + 0.8) mCi = 88%	55% MeCN	16%

Supplementary Table 38. Elution efficiency and RCC calculation of **31-^{18}F**.



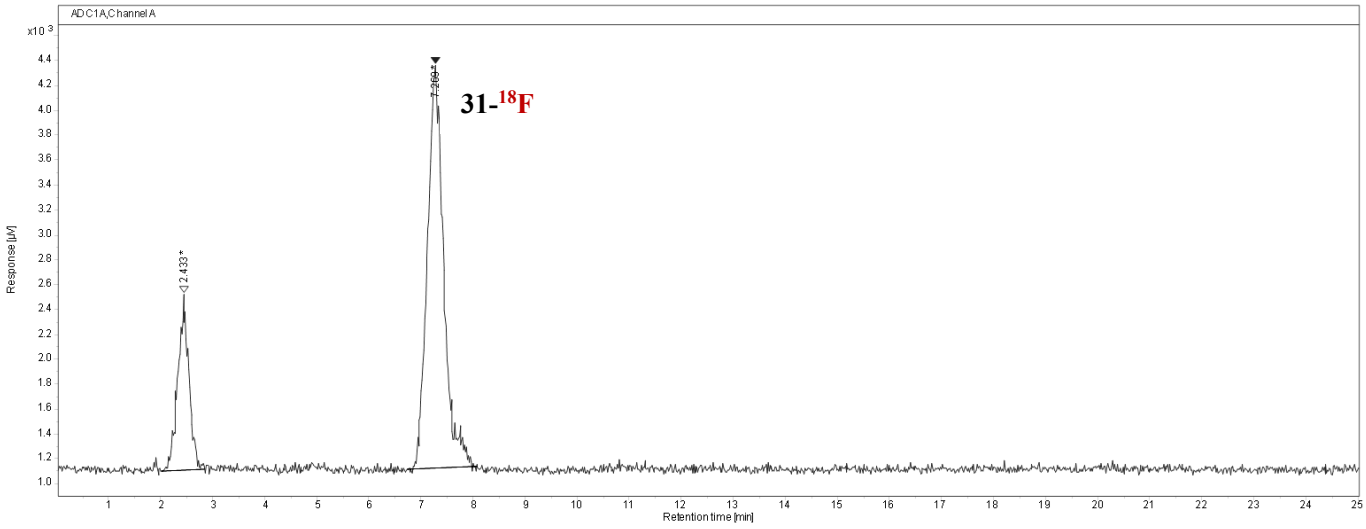
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.101	102954.392	81.610	7872.019	86.86	1.855	3.086
2	4.216	3273.419	2.595	284.953	3.14	4.049	4.709
3	5.831	19926.457	**15.795**	906.414	10.00	5.386	6.920

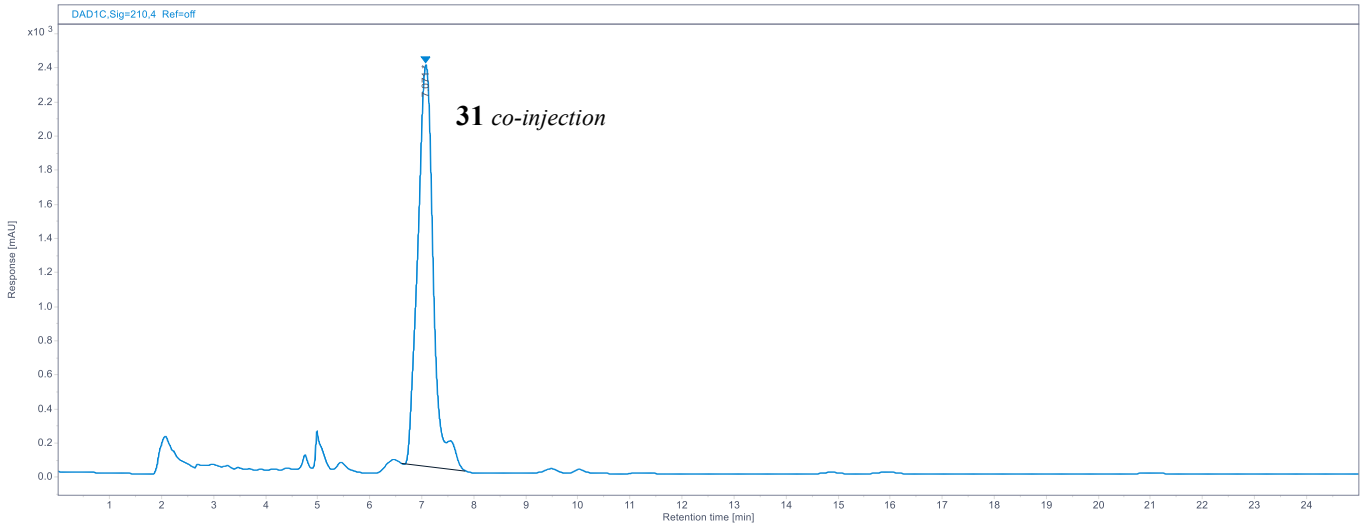
Supplementary Figure 36. Radio-HPLC analysis of **31-^{18}F**.



Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
31-deo	**31-^{18}F**	16.9 mCi/ (16.9 + 1.8) mCi = 90%	50% MeCN	77%

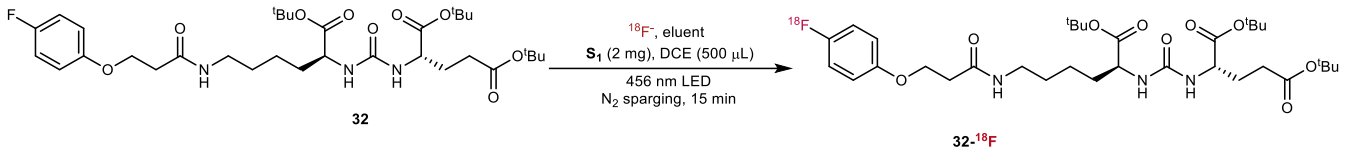
Supplementary Table 39. Elution efficiency and RCC calculation of **31-^{18}F** from **31-deo**.





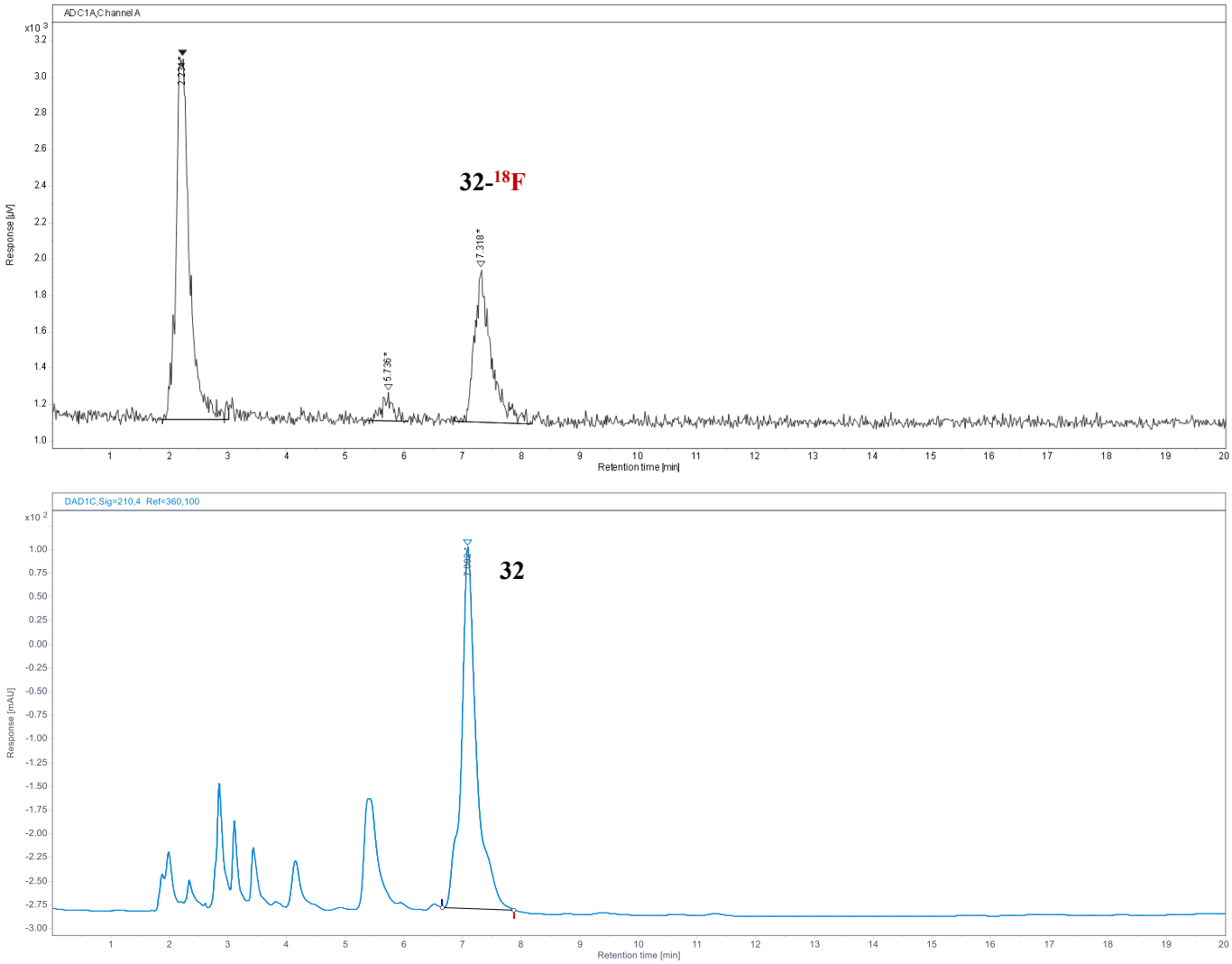
#	RT (min)	Area (μV·s)	Area%	Height (μV)	Height%	Start time (min)	End time (min)
1	2.433	20759.180	22.807	1413.636	30.39	2.022	2.840
2	7.269	70263.120	**77.193**	3238.768	69.61	6.740	8.077

Supplementary Figure 37. Radio-HPLC analysis of **31-^{18}F**.



Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
32	**32-^{18}F**	4.76 mCi/ (4.76 + 0.04) mCi = 99%	70% MeCN	33%

Supplementary Table 40. Elution efficiency and RCC calculation of **32-^{18}F**.



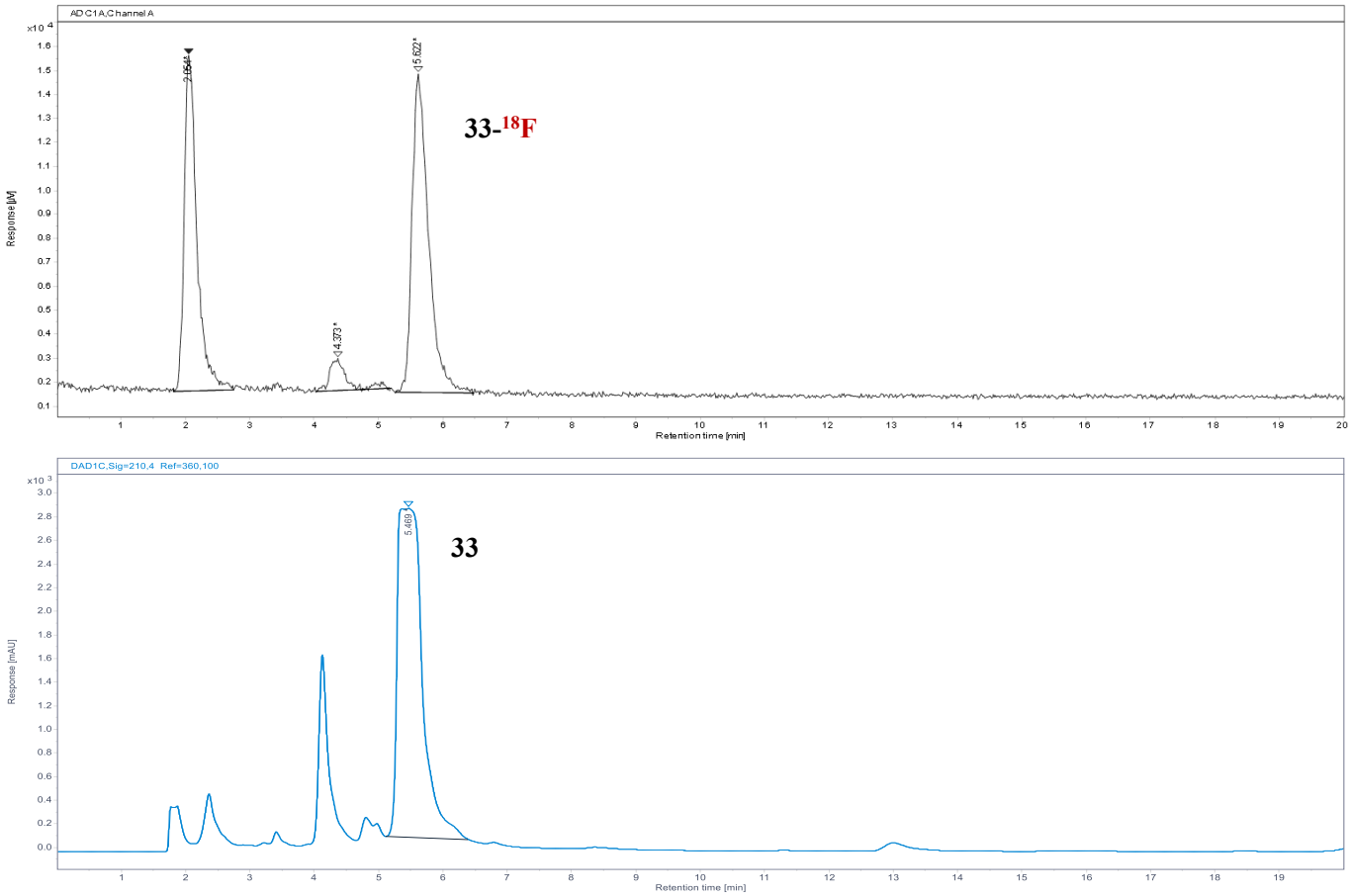
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.234	32025.617	63.742	1994.086	6.48	1.859	3.015
2	5.736	1860.540	3.703	159.983	5.33	5.370	6.070
3	7.318	16356.180	**32.555**	845.402	28.19	6.855	8.170

Supplementary Figure 38. Radio-HPLC analysis of **32-^{18}F**.

33 33-^{18}F

Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
33	**33-^{18}F**	16.01 mCi/(16.01 + 0.57) mCi = 97%	50% MeCN	52%

Supplementary Table 41. Elution efficiency and RCC calculation of **33-^{18}F**.

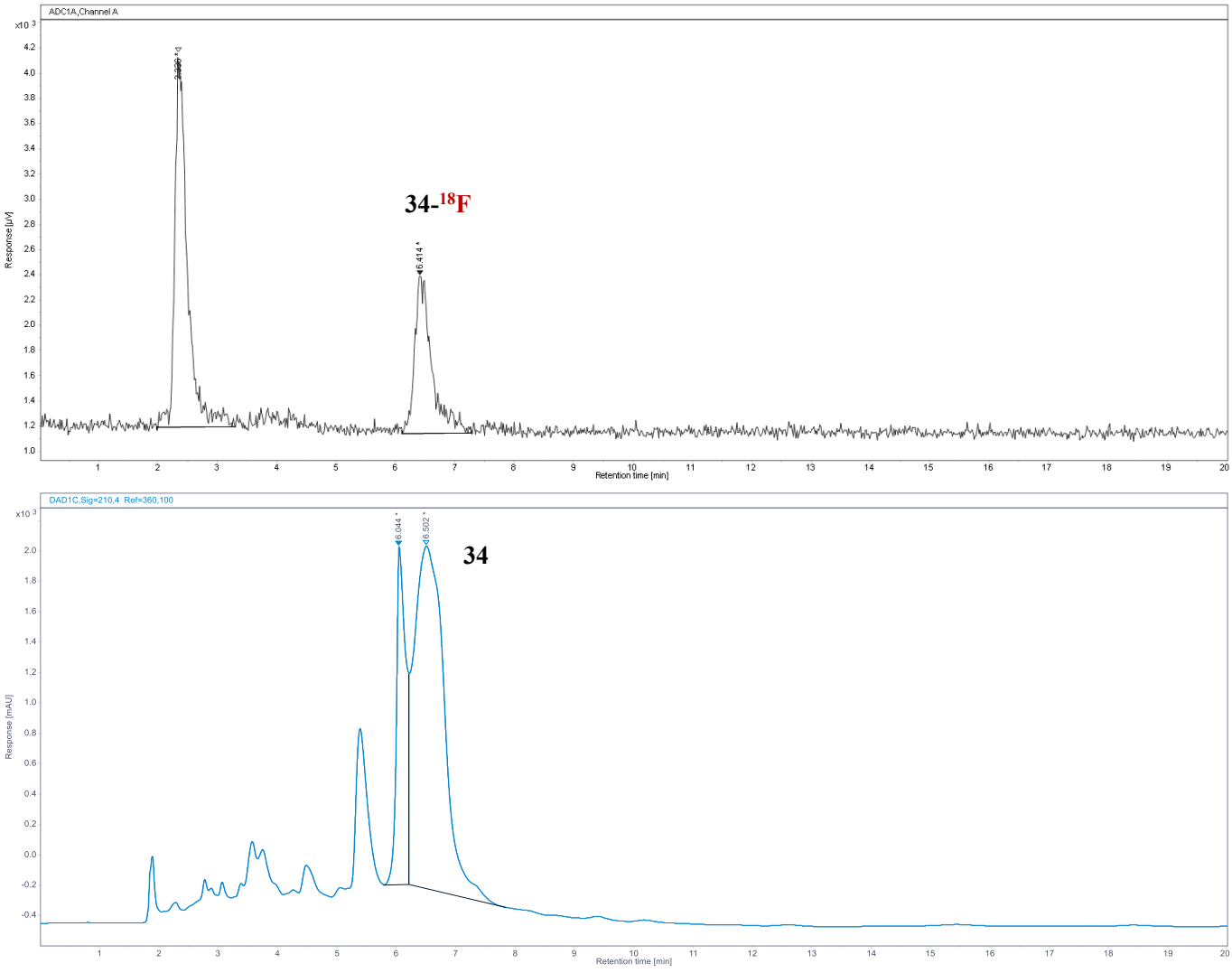


#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.054	192831.022	42.688	14000.744	48.91	1.811	2.756
2	4.373	24105.993	5.336	1334.936	4.66	4.032	5.204
3	5.622	234786.161	**51.976**	13289.138	46.43	5.264	6.480

Supplementary Figure 39. Radio-HPLC analysis of **33-^{18}F**.

Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
34	**34-^{18}F**	12.8 mCi /(12.8 + 0.73) mCi = 95%	70% MeCN	37%

Supplementary Table 42. Elution efficiency and RCC calculation of **34-^{18}F**.

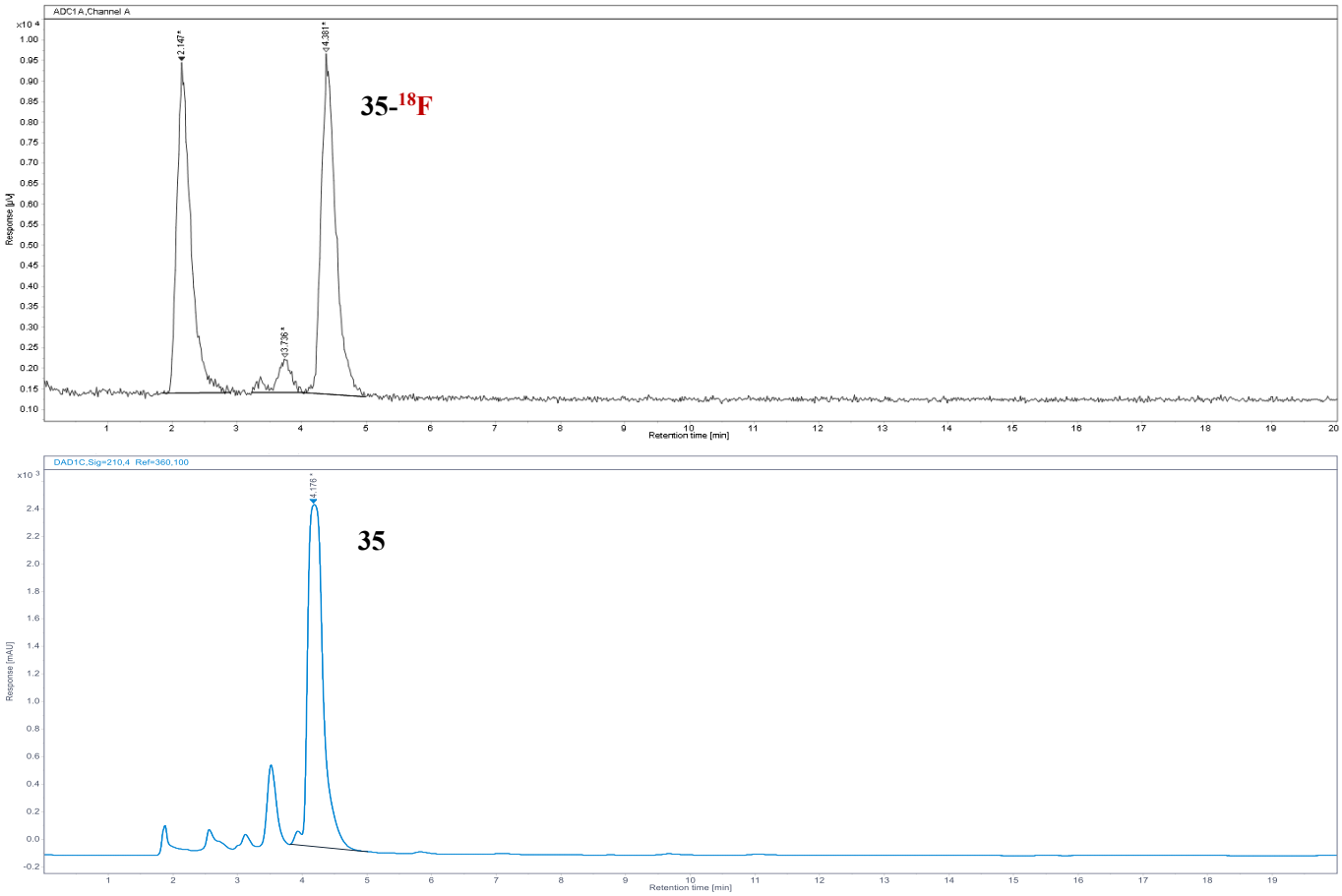


#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.336	43755.415	63.488	2965.759	70.37	1.978	3.301
2	6.414	25163.537	**36.512**	1248.516	29.63	6.107	7.271

Supplementary Figure 40. Radio-HPLC analysis of **34-^{18}F**.

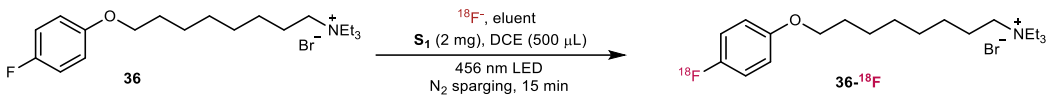
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
35	**35-^{18}F**	10.1 mCi/(10.1+0.61) mCi = 94%	60% MeCN	49%

Supplementary Table 43. Elution efficiency and RCC calculation of **35-^{18}F**.



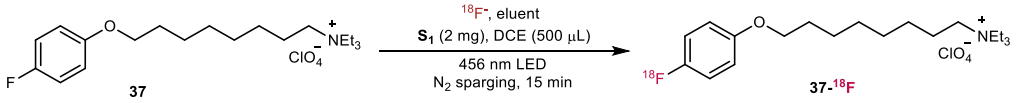
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.147	119558.478	45.544	8063.640	46.84	1.849	2.887
2	3.736	14201.080	5.410	834.112	4.85	3.224	4.016
3	4.381	128749.656	**49.046**	8316.193	48.31	4.016	4.982

Supplementary Figure 41. Radio-HPLC analysis of **35-^{18}F**.



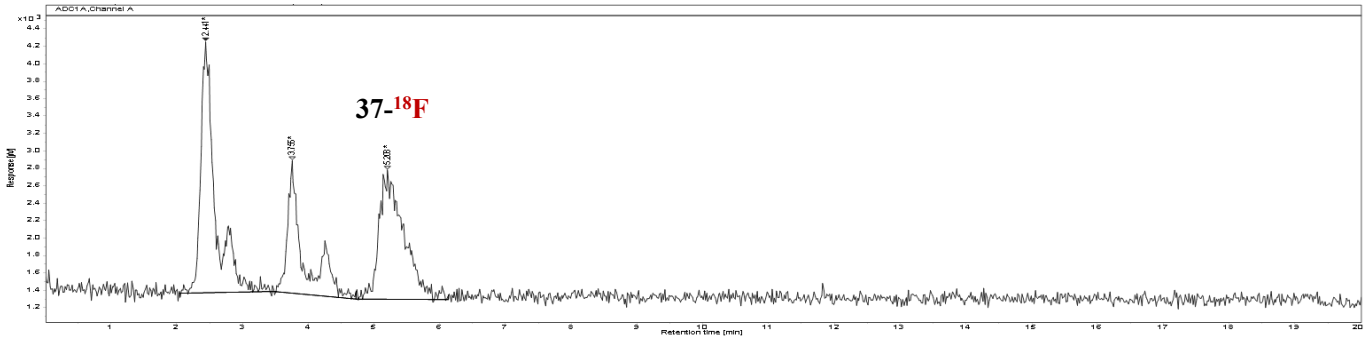
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
36	**36-^{18}F**	8.57 mCi/(8.57 + 0.46) mCi = 95%	65% MeCN	Trace

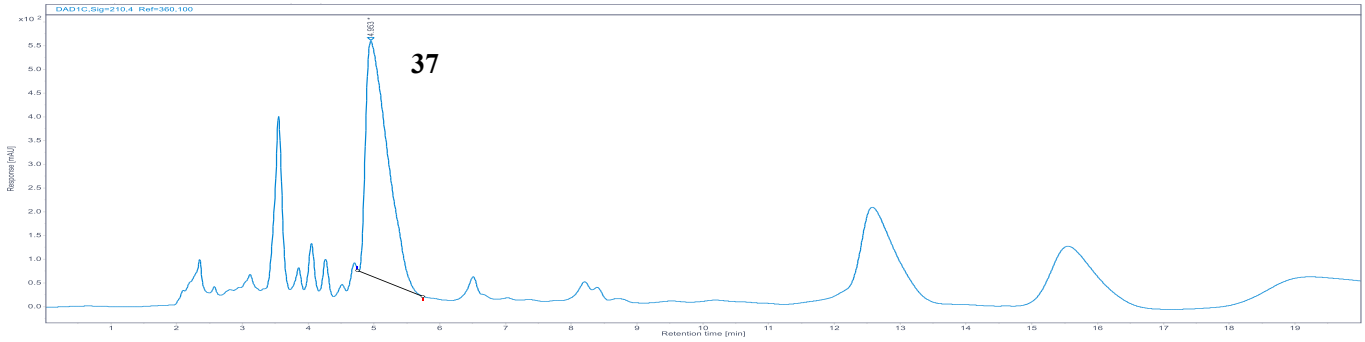
Supplementary Table 44. Elution efficiency and RCC calculation of **36-^{18}F**.



Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
37	**37-^{18}F**	12.23 mCi/(12.23 + 0.81) mCi = 94%	65% MeCN	36%

Supplementary Table 45. Elution efficiency and RCC calculation of **37-^{18}F**.



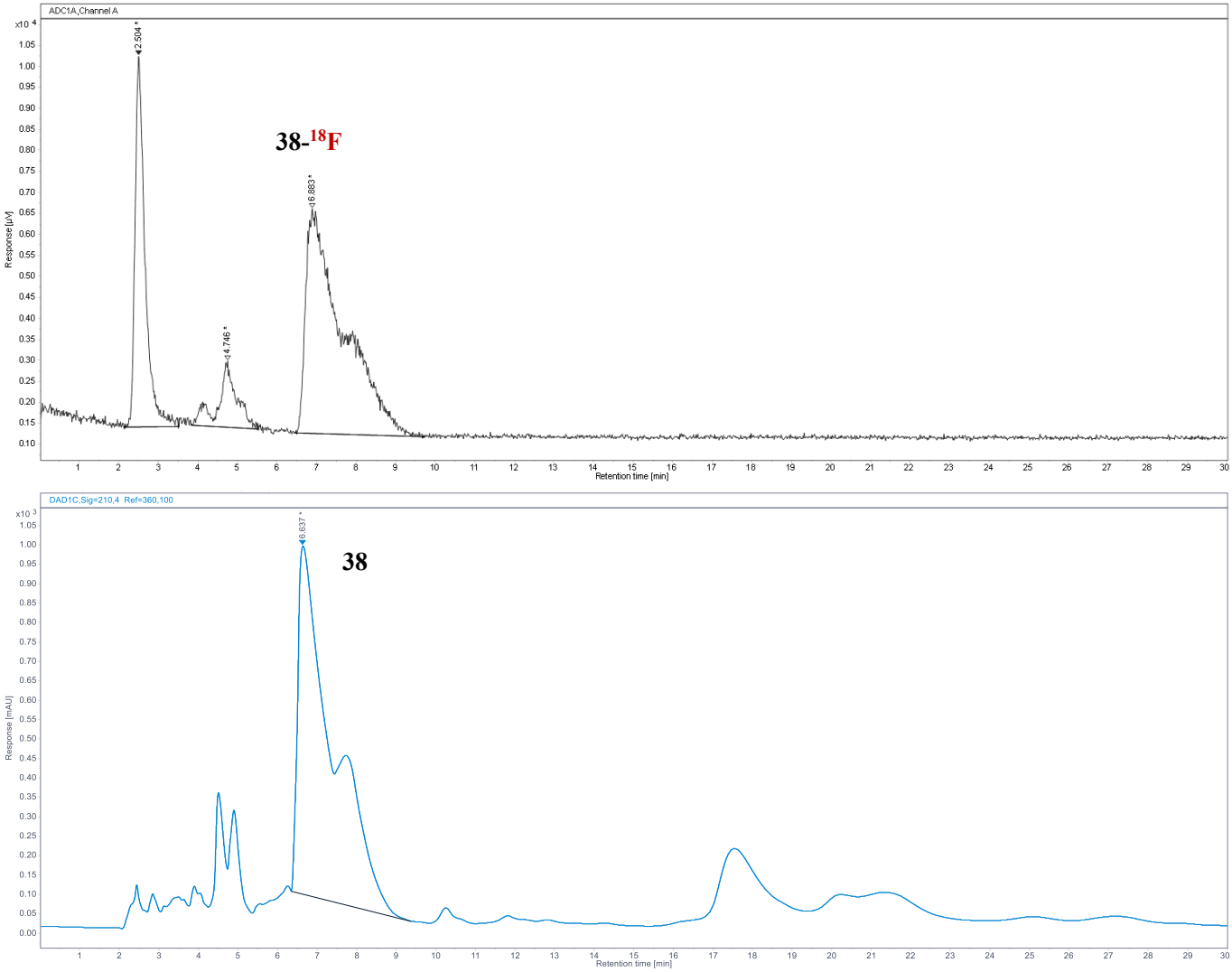


#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.441	44096.707	41.014	2886.001	48.93	2.045	3.480
2	3.755	24884.132	23.145	1525.153	25.86	3.480	4.731
3	5.208	38534.568	**35.841**	1487.368	25.22	4.731	6.133

Supplementary Figure 42. Radio-HPLC analysis of **37-^{18}F**.

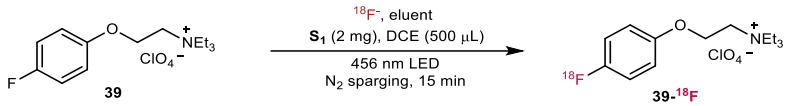
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
38	**38-^{18}F**	9.48 mCi/(9.48 + 0.2) mCi = 98%	60% MeCN (column B)	62%

Supplementary Table 46. Elution efficiency and RCC calculation of **37-^{18}F**.



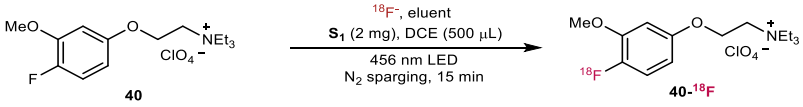
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.504	158693.334	28.555	8835.954	56.04	2.136	3.528
2	4.746	50597.145	9.104	1585.133	10.05	3.835	5.537
3	6.883	346461.274	**62.341**	5344.961	33.90	6.440	9.741

Supplementary Figure 43. Radio-HPLC analysis of **38-^{18}F**.



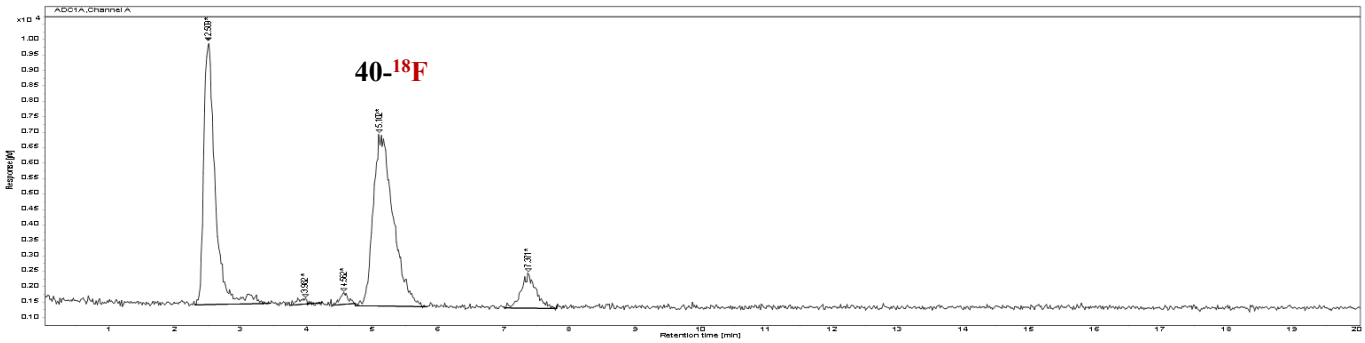
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
39	**39-^{18}F**	6.5 mCi/(6.5+0.27) mCi = 96%	40% MeCN	N.D.

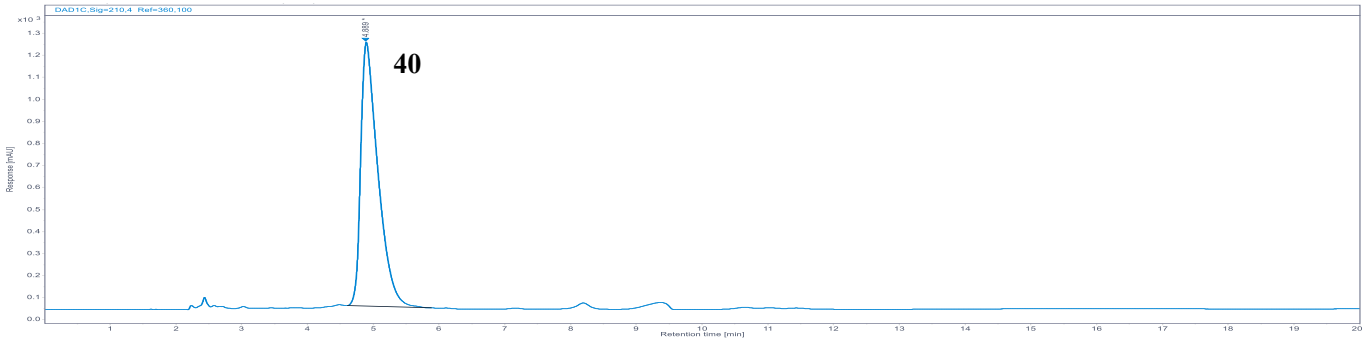
Supplementary Table 47. Elution efficiency and RCC calculation of **39-^{18}F**.



Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
40	**40-^{18}F**	13.92 mCi/(13.92+0.78) mCi = 95%	40% MeCN (column B)	49%

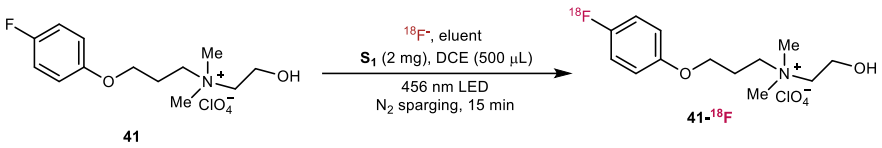
Supplementary Table 48. Elution efficiency and RCC calculation of **40-^{18}F**.





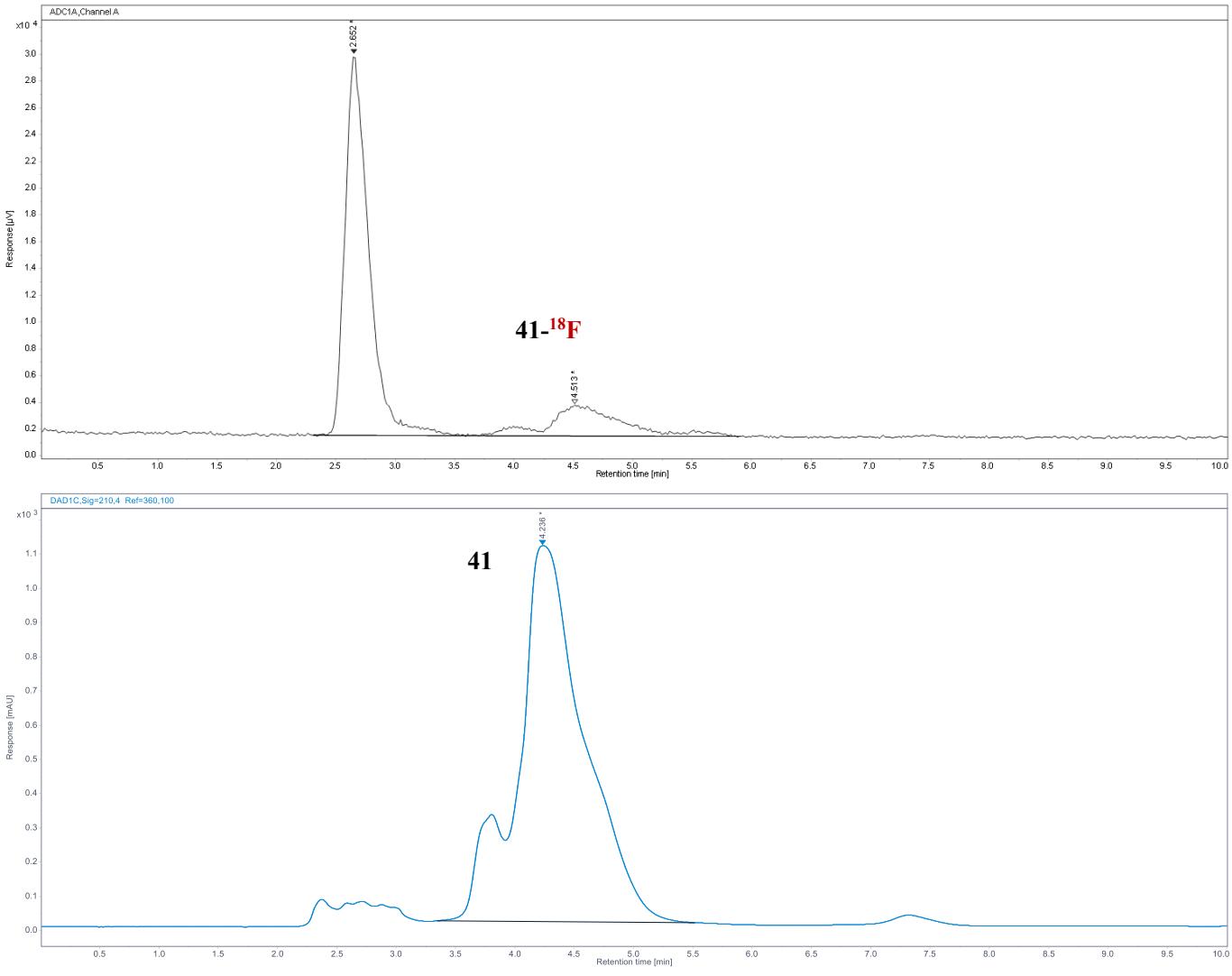
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.509	102203.473	42.187	8516.150	53.71	2.298	3.444
2	3.982	1803.592	0.744	199.569	1.26	3.752	4.243
3	4.562	3471.311	1.433	400.312	2.52	4.395	4.742
4	5.102	117480.864	**48.494**	5586.241	35.23	4.742	5.833
5	7.371	17301.347	7.142	1153.355	7.27	7.008	7.803

Supplementary Figure 44. Radio-HPLC analysis of **40-^{18}F**.



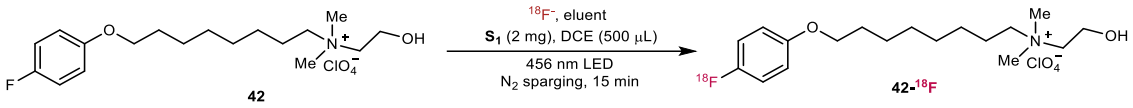
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
41	**41-^{18}F**	12.5 mCi/(12.5 + 0.7) mCi = 95%	35% MeCN (column B)	20%

Supplementary Table 49. Elution efficiency and RCC calculation of **41-^{18}F**.



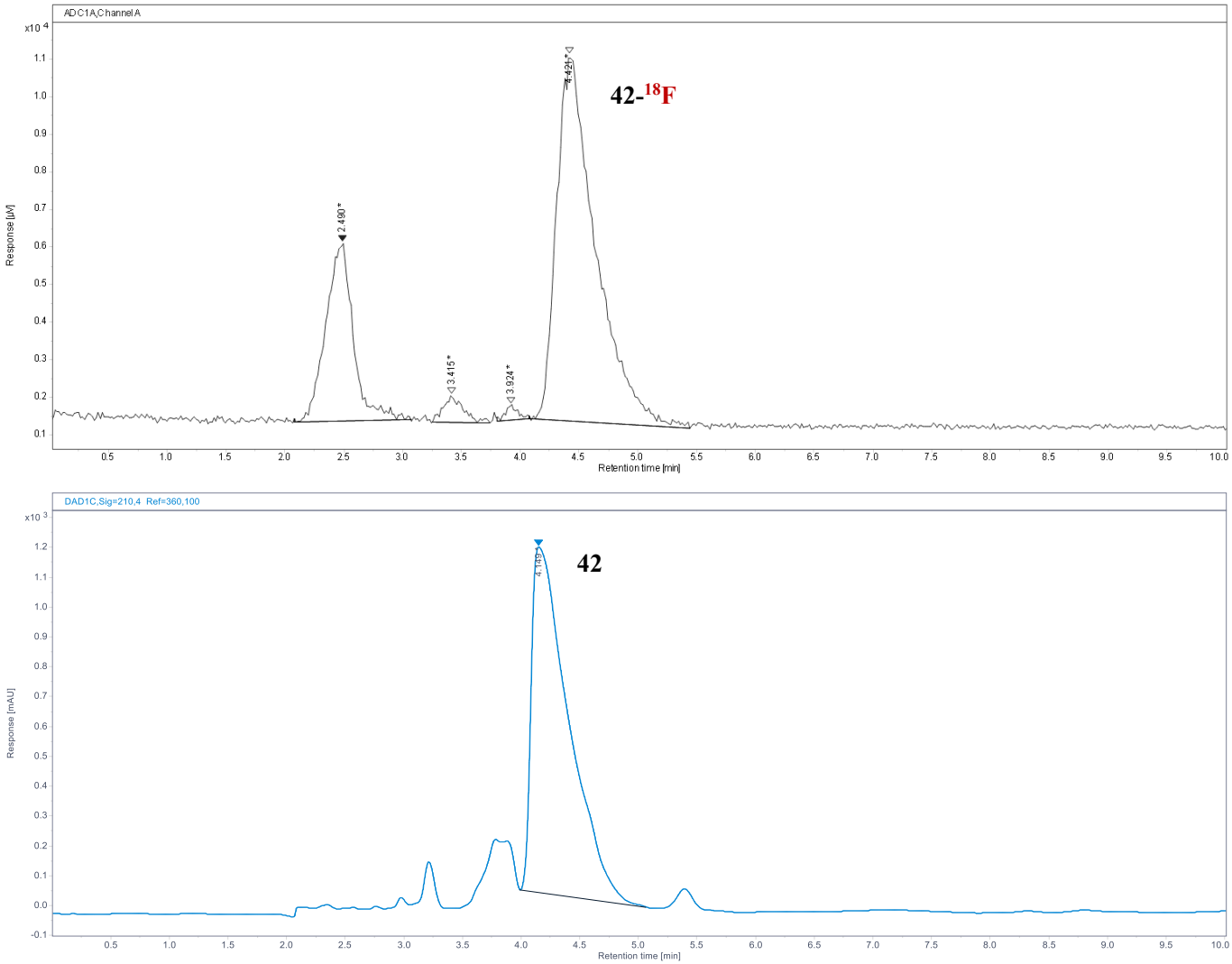
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.652	395420.034	80.332	28452.075	92.47	2.310	3.583
2	4.513	96811.367	**19.668**	2316.562	7.53	3.583	5.902

Supplementary Figure 45. Radio-HPLC analysis of **41-^{18}F**.



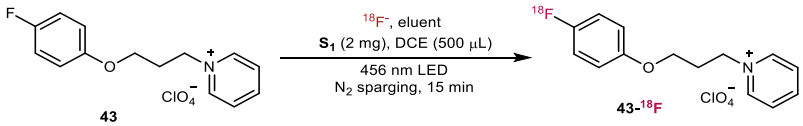
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
42	**42-^{18}F**	8.41 mCi/(8.41+0.74) mCi = 92%	60% MeCN	72%

Supplementary Table 50. Elution efficiency and RCC calculation of **42-^{18}F**.



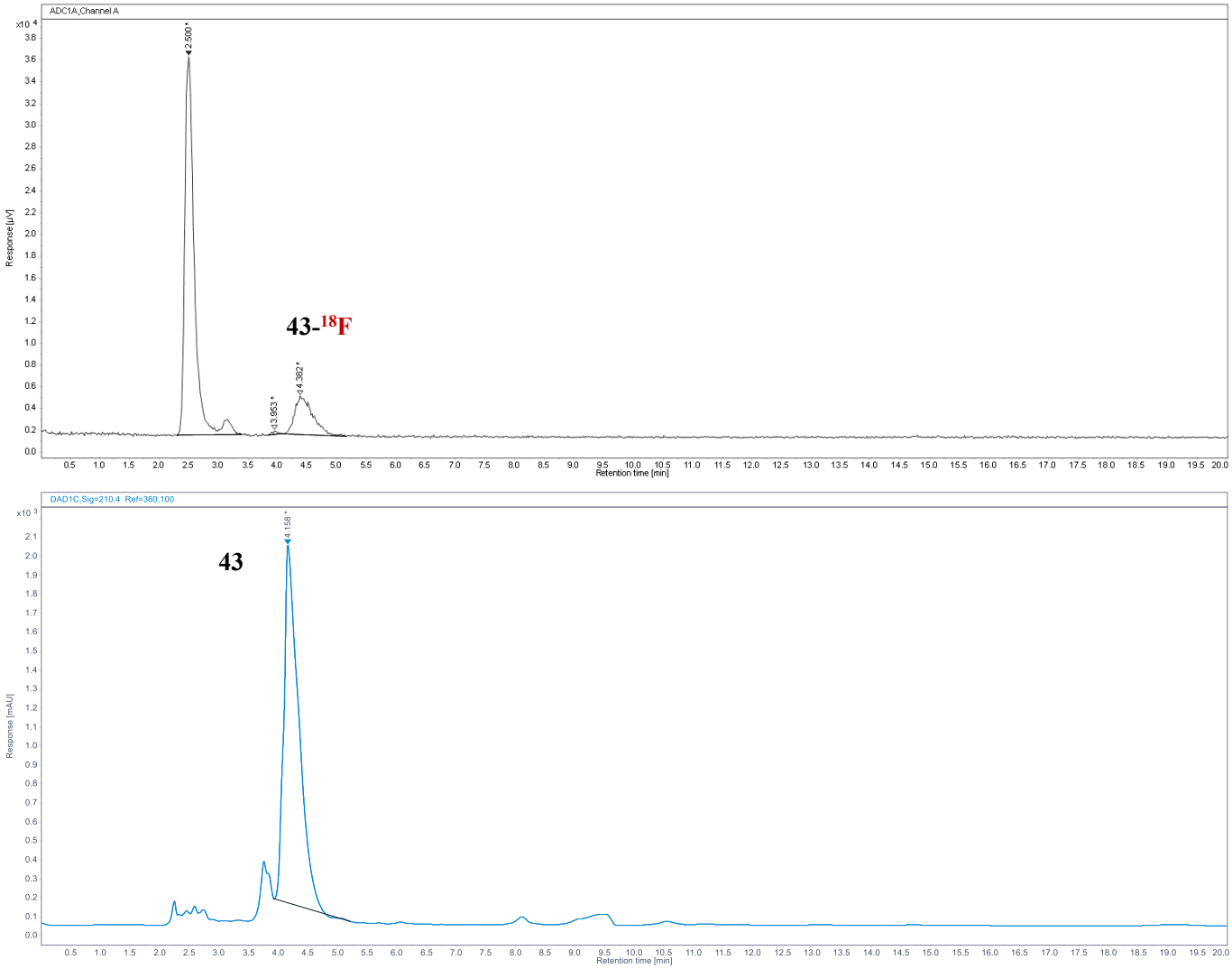
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.490	76910.277	24.695	4744.585	30.39	2.078	3.073
2	3.415	8260.146	2.652	711.557	4.56	3.251	3.743
3	3.924	2910.418	0.935	416.356	2.67	3.801	4.079
4	4.421	223356.774	**71.718**	9739.408	62.38	4.079	5.445

Supplementary Figure 46. Radio-HPLC analysis of **42-^{18}F**.



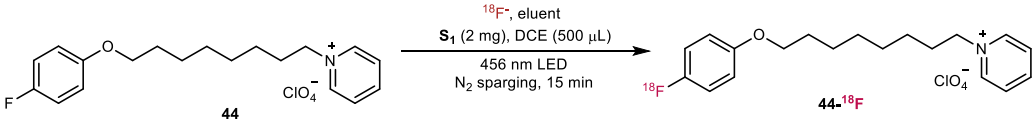
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
43	**43-^{18}F**	14.2 mCi/(14.2 + 0.58) mCi = 96%	40% MeCN (column B)	16%

Supplementary Table 51. Elution efficiency and RCC calculation of **43-^{18}F**.



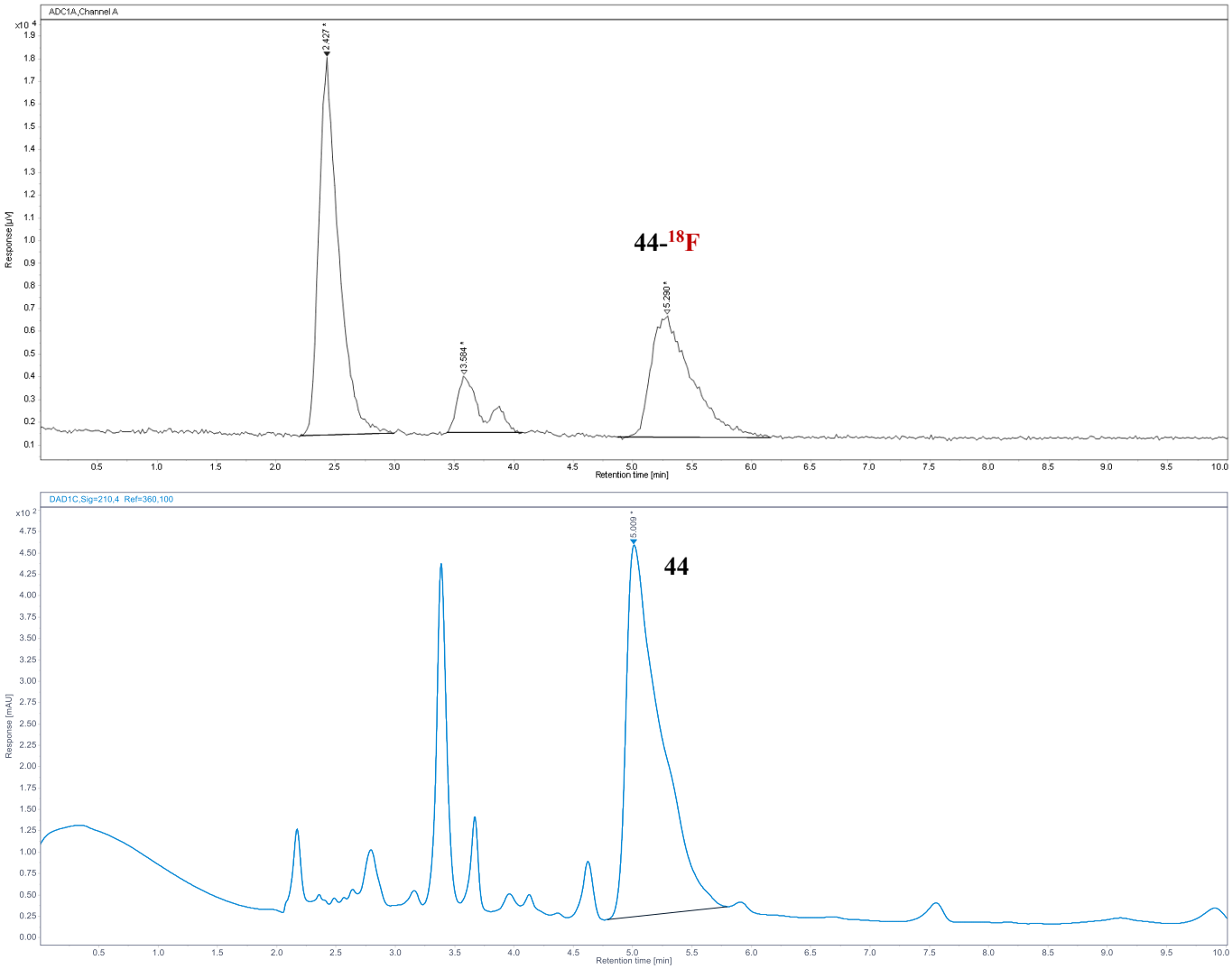
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.500	386970.106	83.624	34721.801	90.01	2.303	3.390
2	3.953	1783.256	0.385	334.662	0.87	3.846	4.059
3	4.382	73998.582	**15.991**	3518.352	9.12	4.059	5.164

Supplementary Figure 47. Radio-HPLC analysis of **43-^{18}F**.



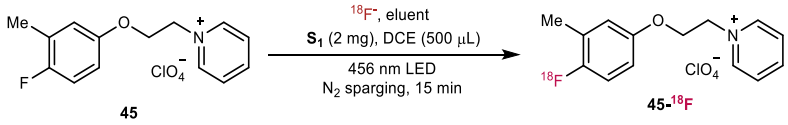
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
44	**44-^{18}F**	28.2 mCi/ (28.2 + 0.74) mCi = 97%	60% MeCN	36%

Supplementary Table 52. Elution efficiency and RCC calculation of **44-^{18}F**.



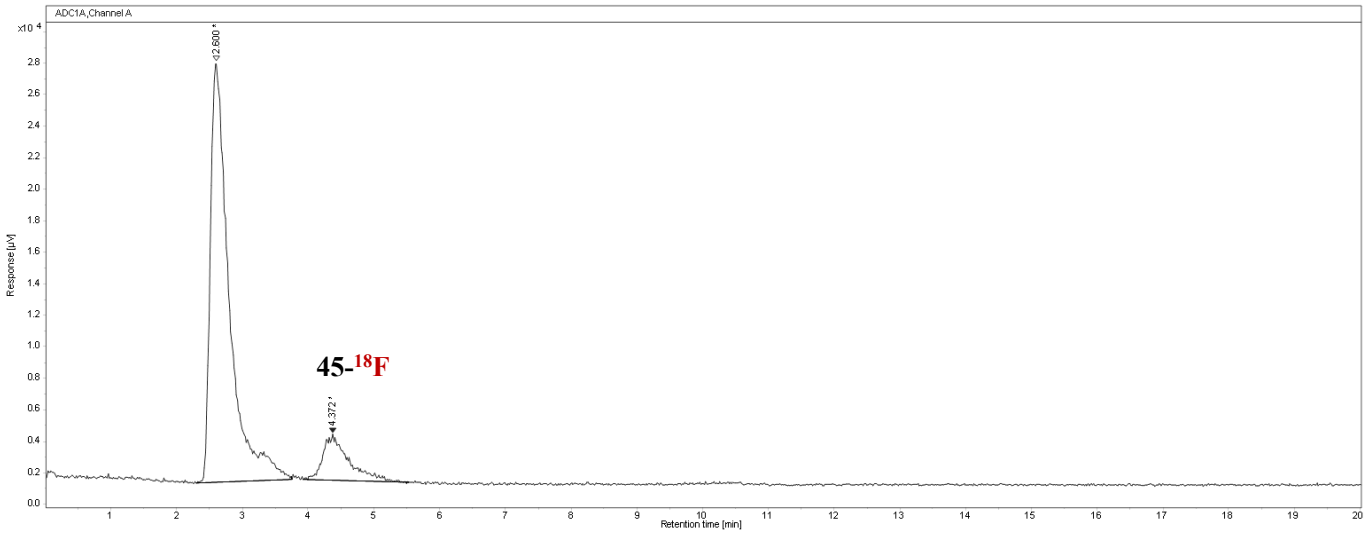
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.427	191314.144	54.097	16625.277	67.88	2.203	2.993
2	3.584	35580.953	10.061	2508.375	10.24	3.436	4.071
3	5.290	126752.522	**35.841**	5356.932	21.87	4.874	6.156

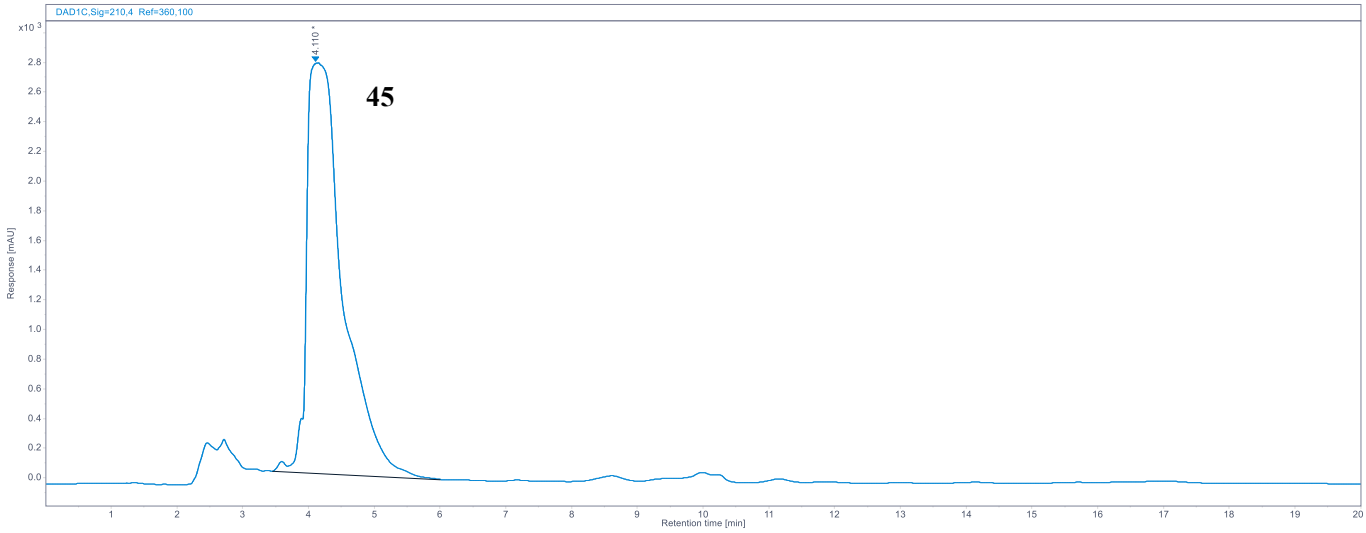
Supplementary Figure 48. Radio-HPLC analysis of **44-^{18}F**.



Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
45	**45-^{18}F**	14.3 mCi/(14.3 + 1.2) mCi = 92%	40% MeCN (column B)	13%

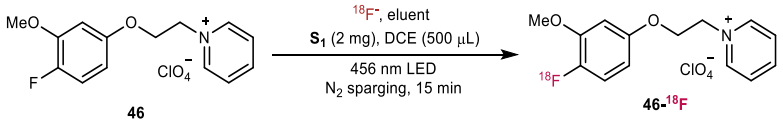
Supplementary Table 53. Elution efficiency and RCC calculation of **45-^{18}F**.





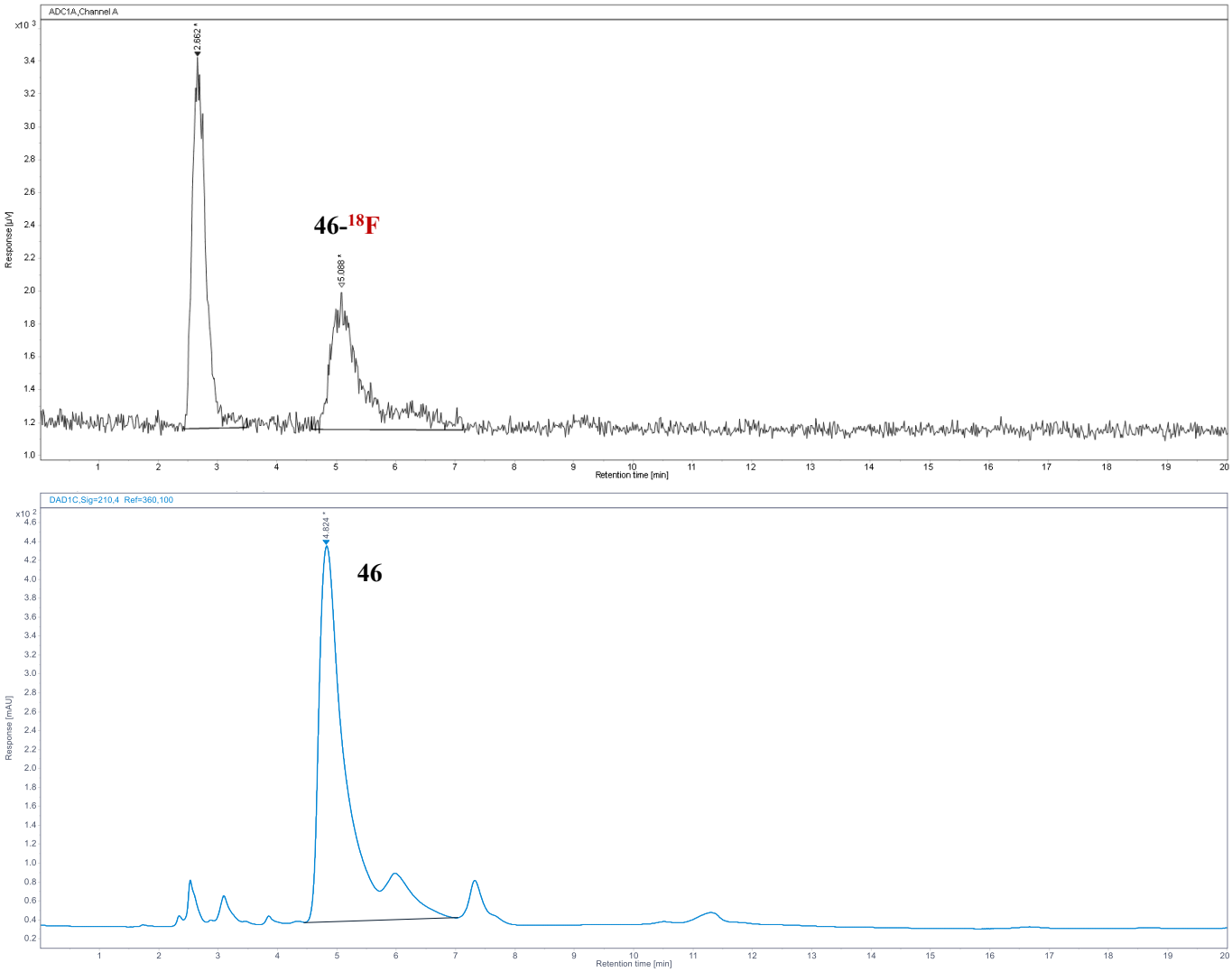
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.600	533254.271	87.316	26670.229	90.13	2.301	3.744
2	4.372	77465.468	**12.684**	2921.985	9.87	3.924	5.530

Supplementary Figure 49. Radio-HPLC analysis of **45-^{18}F**.



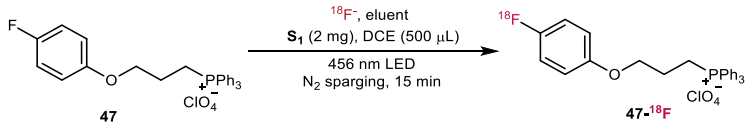
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
46	**46-^{18}F**	8.18 mCi/(8.18 + 0.23) mCi = 97%	35% MeCN (column B)	46%

Supplementary Table 54. Elution efficiency and RCC calculation of **46-^{18}F**.



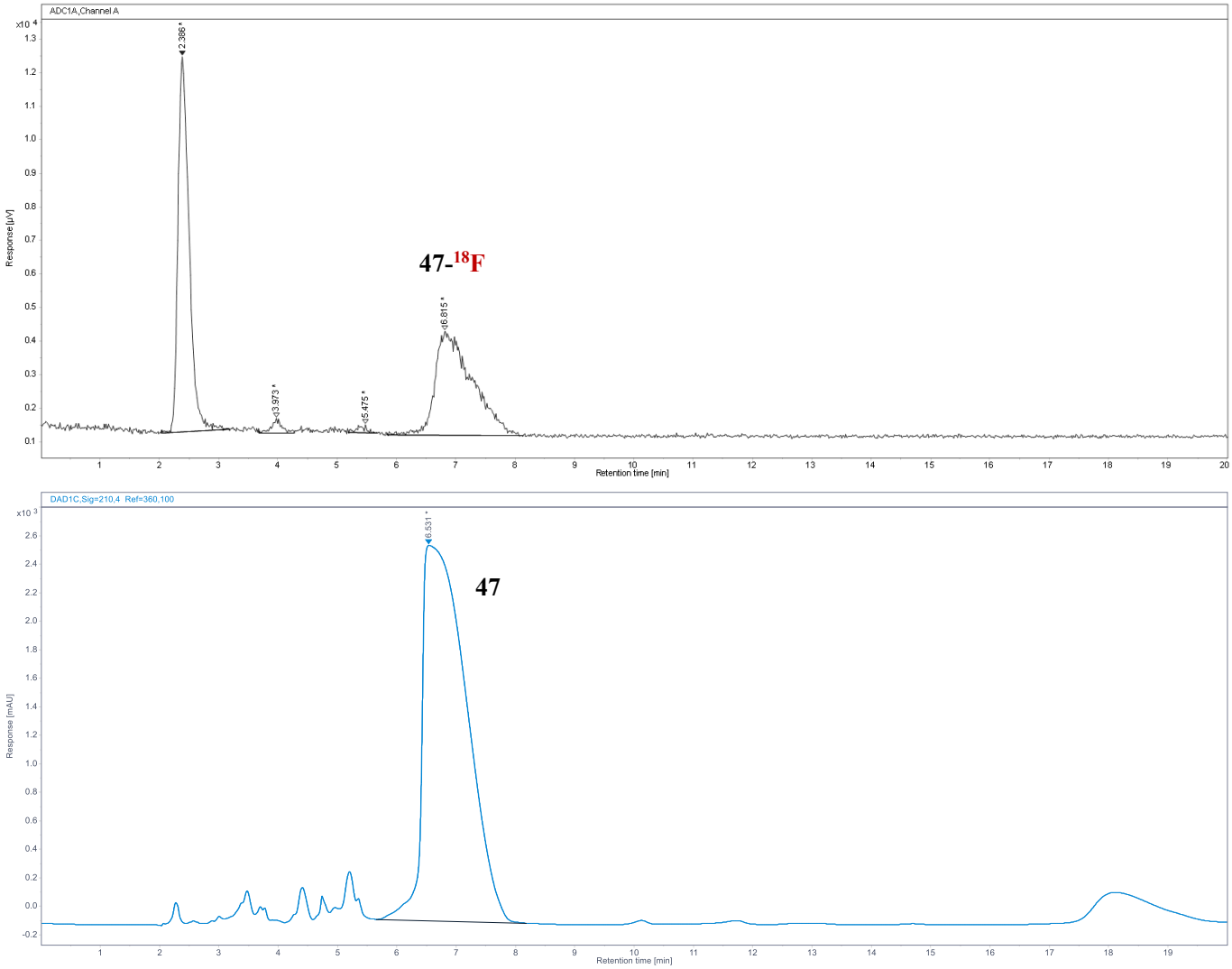
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.662	36093.611	53.891	2258.260	72.43	2.440	3.488
2	5.088	30881.122	**46.109**	859.591	27.57	4.584	7.128

Supplementary Figure 50. Radio-HPLC analysis of **46-^{18}F**.



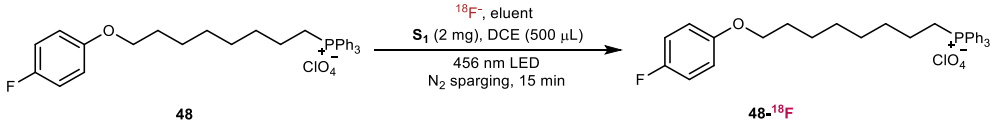
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
47	**47-^{18}F**	8.98 mCi/(8.98 + 0.56) mCi = 94%	60% MeCN(column B)	47%

Supplementary Table 55. Elution efficiency and RCC calculation of **47-^{18}F**.



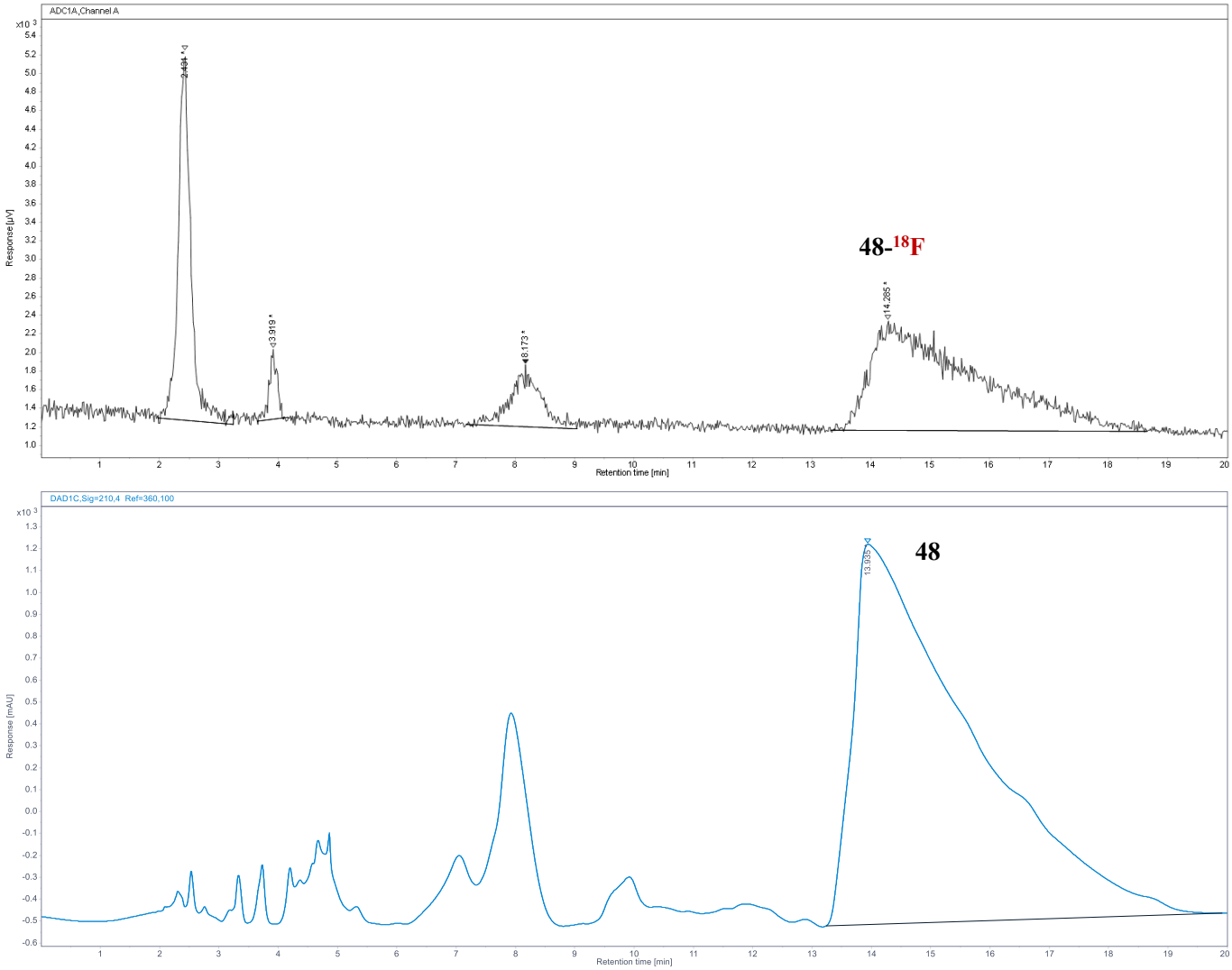
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.386	147101.620	50.989	11192.459	74.76	2.036	3.182
2	3.973	4907.057	1.701	426.626	2.85	3.685	4.274
3	5.475	2261.127	0.784	236.991	1.58	5.187	5.675
4	6.815	134229.165	**46.527**	3115.039	20.81	5.846	8.130

Supplementary Figure 51. Radio-HPLC analysis of **47-^{18}F**.



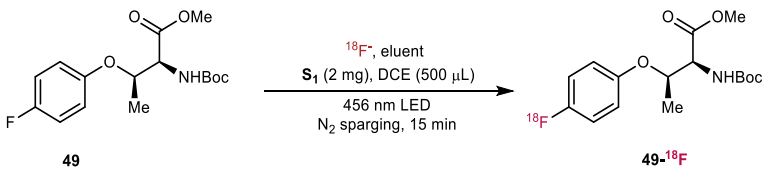
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
48	**48-^{18}F**	3.95 mCi/(3.95 + 0.17) mCi = 96%	60% MeCN	62%

Supplementary Table 56. Elution efficiency and RCC calculation of **48-^{18}F**.



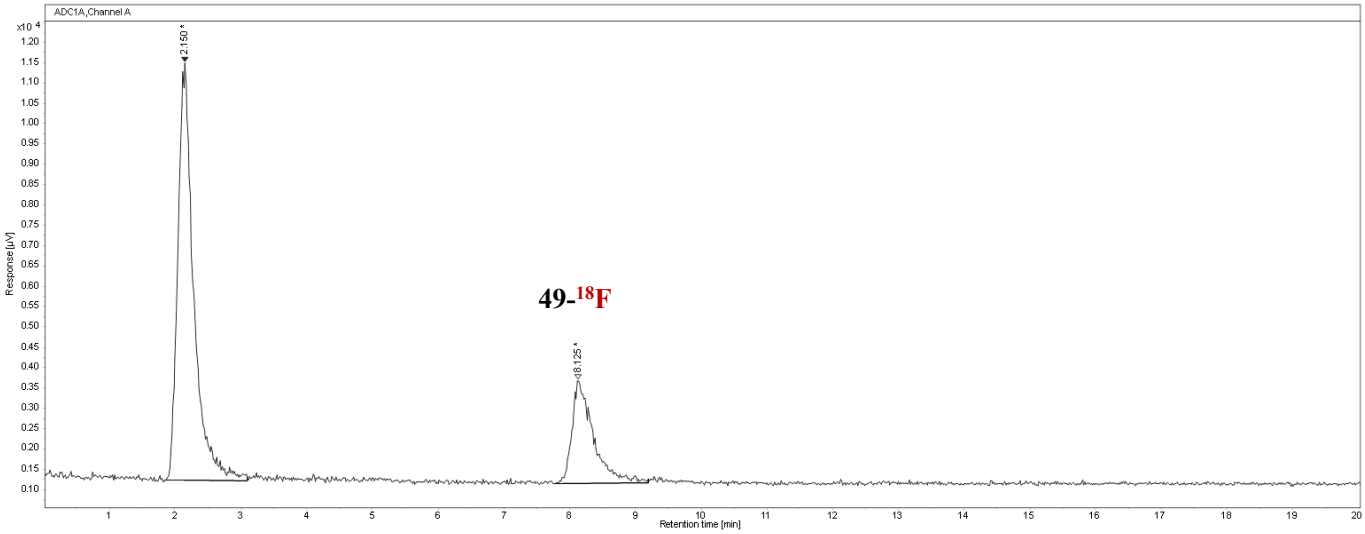
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.431	58767.153	25.499	3972.321	60.36	1.978	3.247
2	3.919	6772.879	2.939	756.058	11.49	3.647	4.171
3	8.173	22165.865	9.618	667.574	10.14	7.178	9.040
4	14.285	142762.285	**61.944**	1185.573	18.01	13.316	18.654

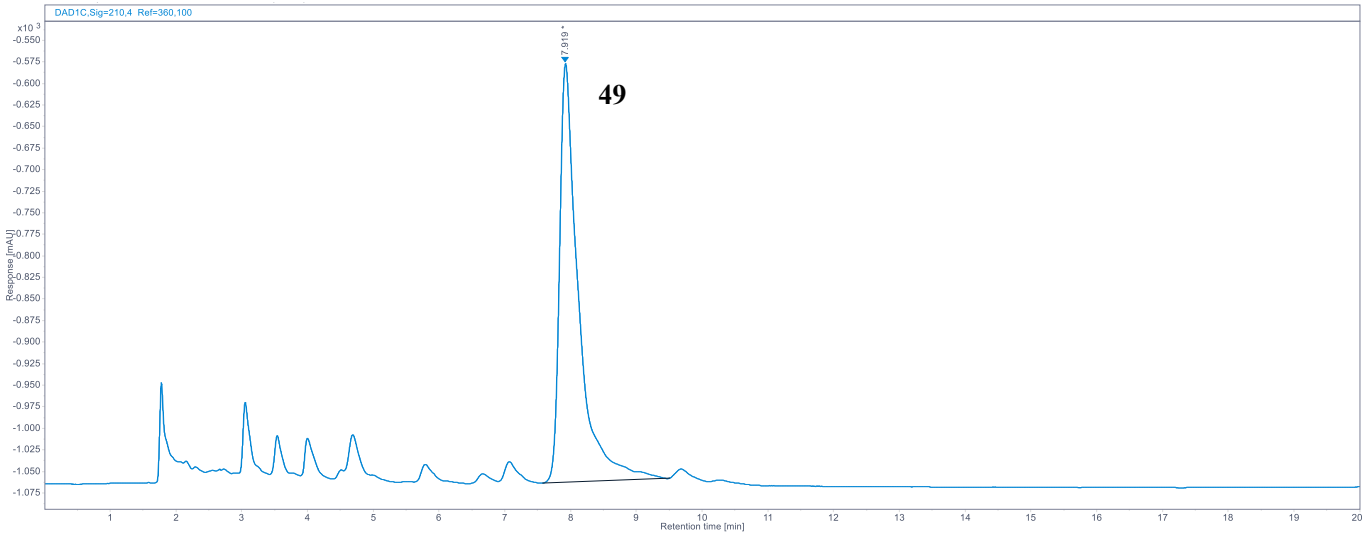
Supplementary Figure 52. Radio-HPLC analysis of **48-^{18}F**.



Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
49	**49-^{18}F**	11.23 mCi/(11.23 + 0.74) mCi = 94%	60% MeCN	25%

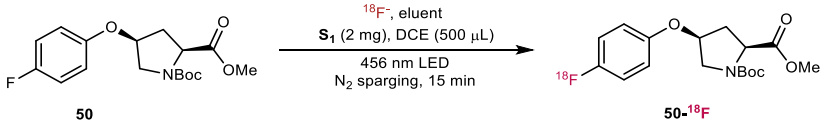
Supplementary Table 57. Elution efficiency and RCC calculation of **49-^{18}F**.





#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.150	172052.227	74.990	10258.638	80.22	1.849	3.095
2	8.125	57382.623	**25.010**	2529.306	19.78	7.779	9.199

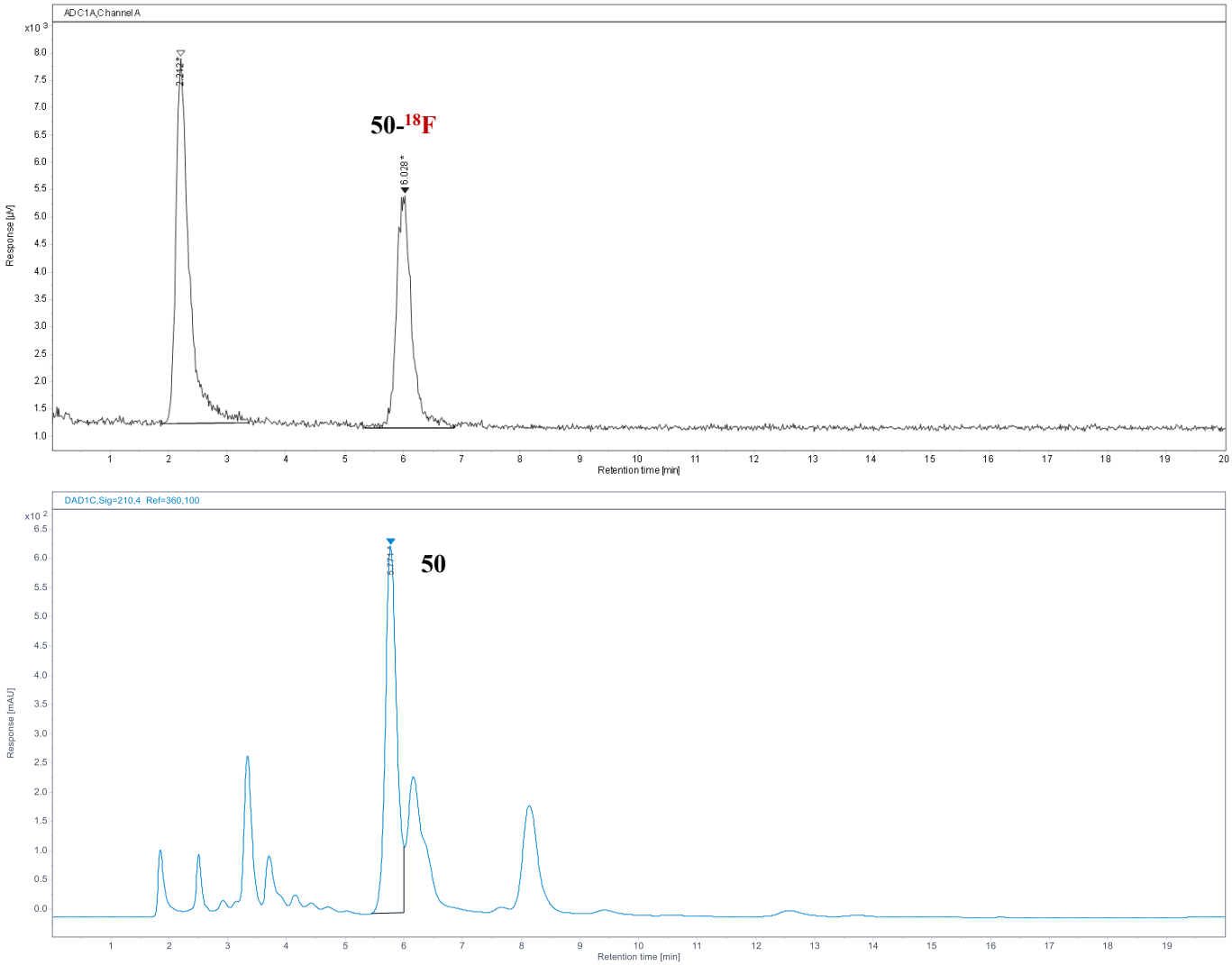
Supplementary Figure 53. Radio-HPLC analysis of **49-^{18}F**.



50 50-^{18}F

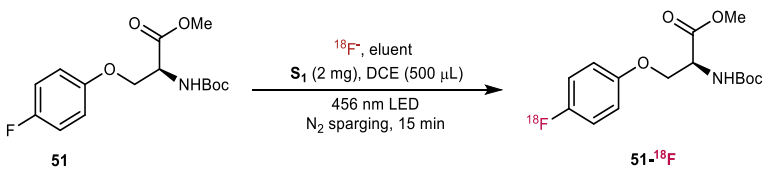
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
50	**50-^{18}F**	10.48 mCi/(10.48 + 0.2) mCi = 98%	65% MeCN	42%

Supplementary Table 58. Elution efficiency and RCC calculation of **50-^{18}F**.



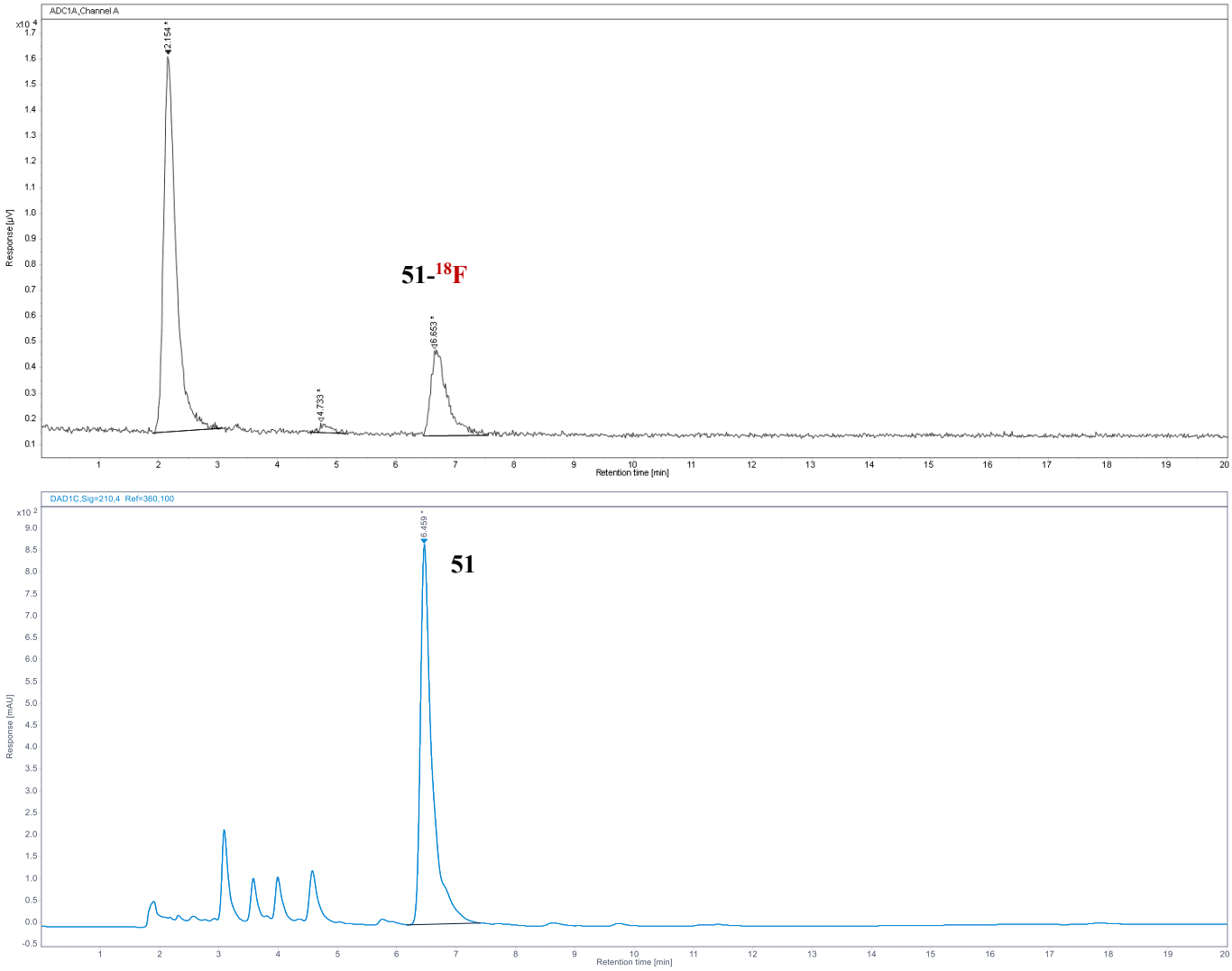
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.212	106394.107	58.026	6688.351	61.15	1.903	3.370
2	6.028	76962.017	**41.974**	4250.157	38.85	5.351	6.861

Supplementary Figure 54. Radio-HPLC analysis of **50-^{18}F**.



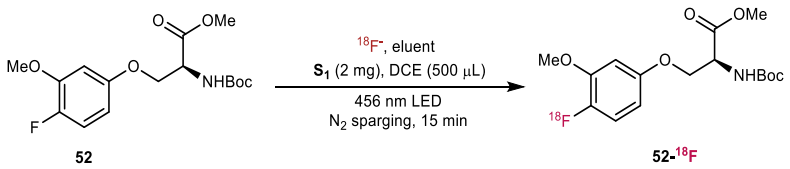
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
51	**51-^{18}F**	18.42 mCi/(18.42 + 0.36) mCi = 98%	55% MeCN	23%

Supplementary Table 59. Elution efficiency and RCC calculation of **51-^{18}F**.



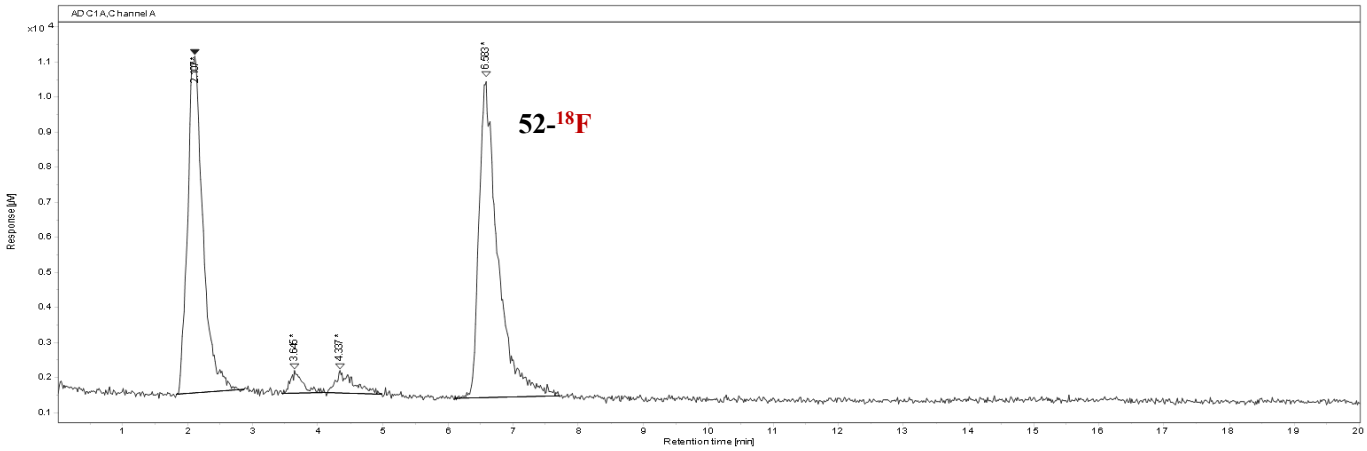
#	RT (min)	Area (µV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.154	214867.364	75.573	14659.198	79.82	1.910	3.067
2	4.733	4526.215	1.592	365.579	1.99	4.554	5.124
3	6.653	64925.701	**22.835**	3339.407	18.18	6.467	7.553

Supplementary Figure 55. Radio-HPLC analysis of **51-^{18}F**.



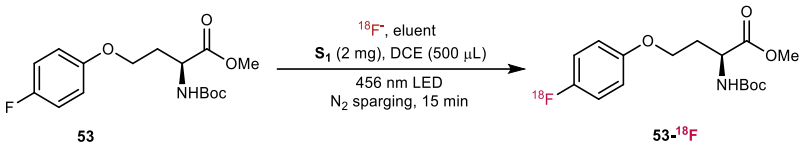
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
52	**52-^{18}F**	16.28 mCi/(16.28 + 0.42) mCi = 98%	60% MeCN	51%

Supplementary Table 60. Elution efficiency and RCC calculation of **52-^{18}F**.



#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.107	157433.175	43.640	9603.605	48.04	1.832	2.864
2	3.645	8232.535	2.282	651.690	3.26	3.452	4.124
3	4.337	12097.183	3.353	631.560	3.16	4.124	4.977
4	6.583	182988.687	**50.724**	9104.677	45.54	6.117	7.714

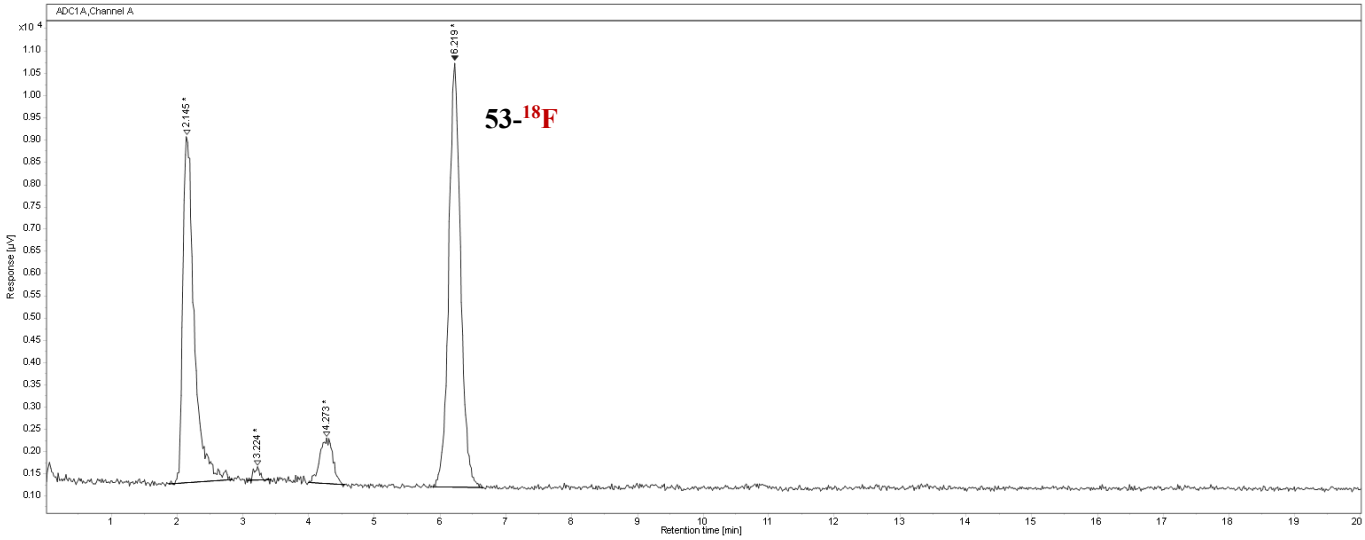
Supplementary Figure 56. Radio-HPLC analysis of **52-^{18}F**.

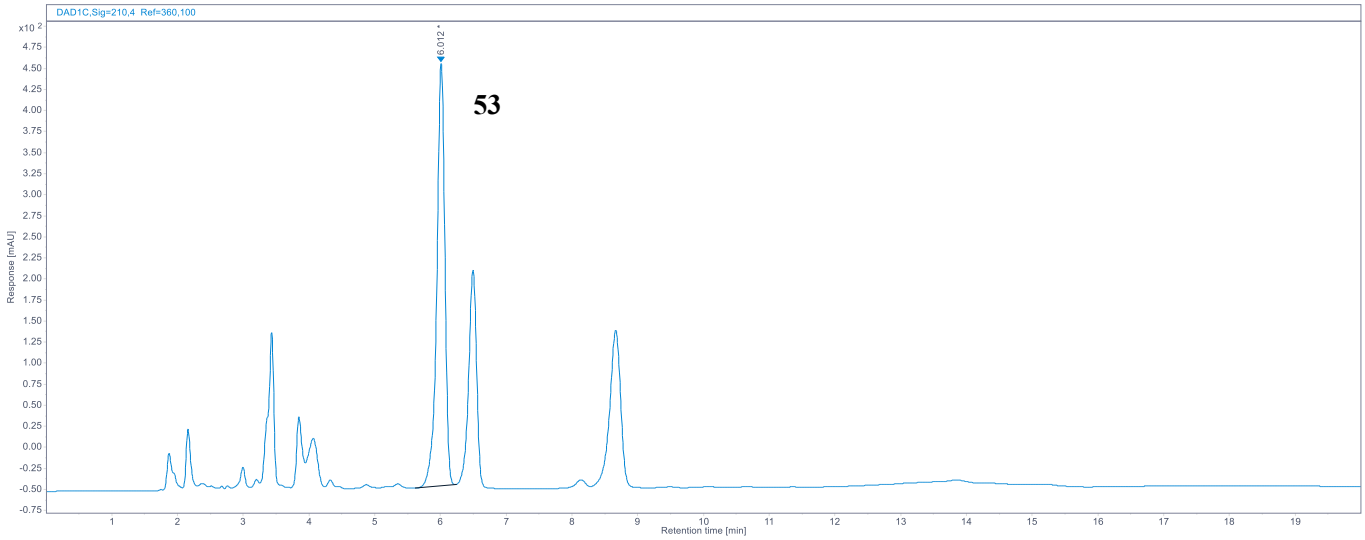


53 53-^{18}F

Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
53	**53-^{18}F**	30.8 mCi/(30.8 + 1.25) mCi = 96%	55% MeCN	52%

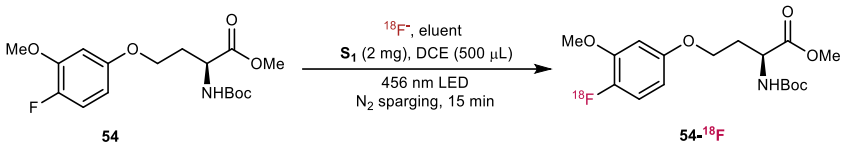
Supplementary Table 61. Elution efficiency and RCC calculation of **53-^{18}F**.





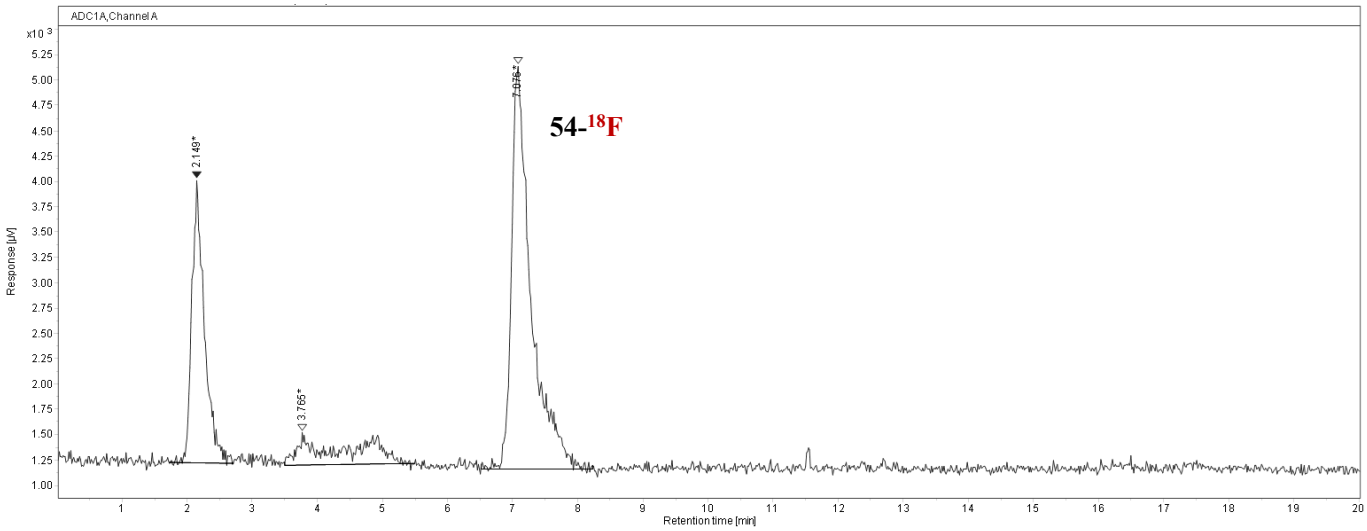
#	RT (min)	Area (µV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.145	94631.634	41.300	7786.617	41.67	1.879	2.840
2	3.224	1859.577	0.812	310.129	1.66	3.081	3.429
3	4.273	13879.321	6.057	1027.511	5.50	3.995	4.550
4	6.219	118760.069	**51.831**	9562.581	51.17	5.895	6.651

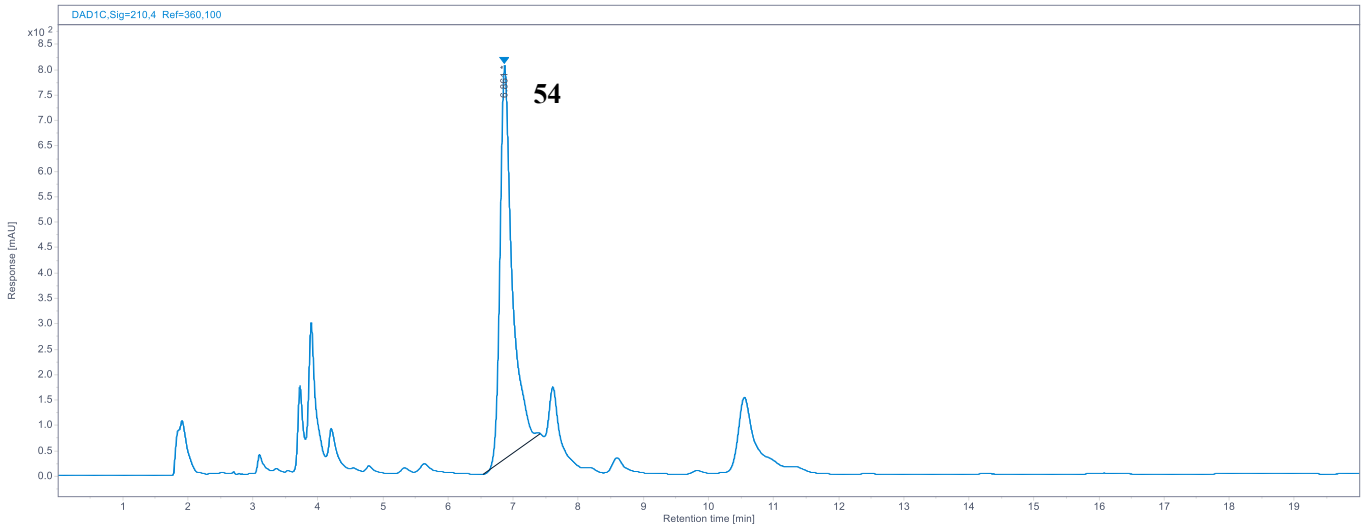
Supplementary Figure 57. Radio-HPLC analysis of **53-^{18}F**.



Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
54	**54-^{18}F**	9.31 mCi/(9.31 + 0.18) mCi = 98%	60% MeCN	61%

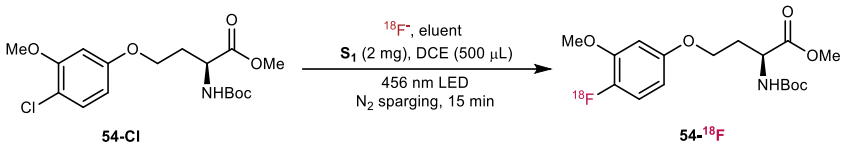
Supplementary Table 62. Elution efficiency and RCC calculation of **54-^{18}F**.





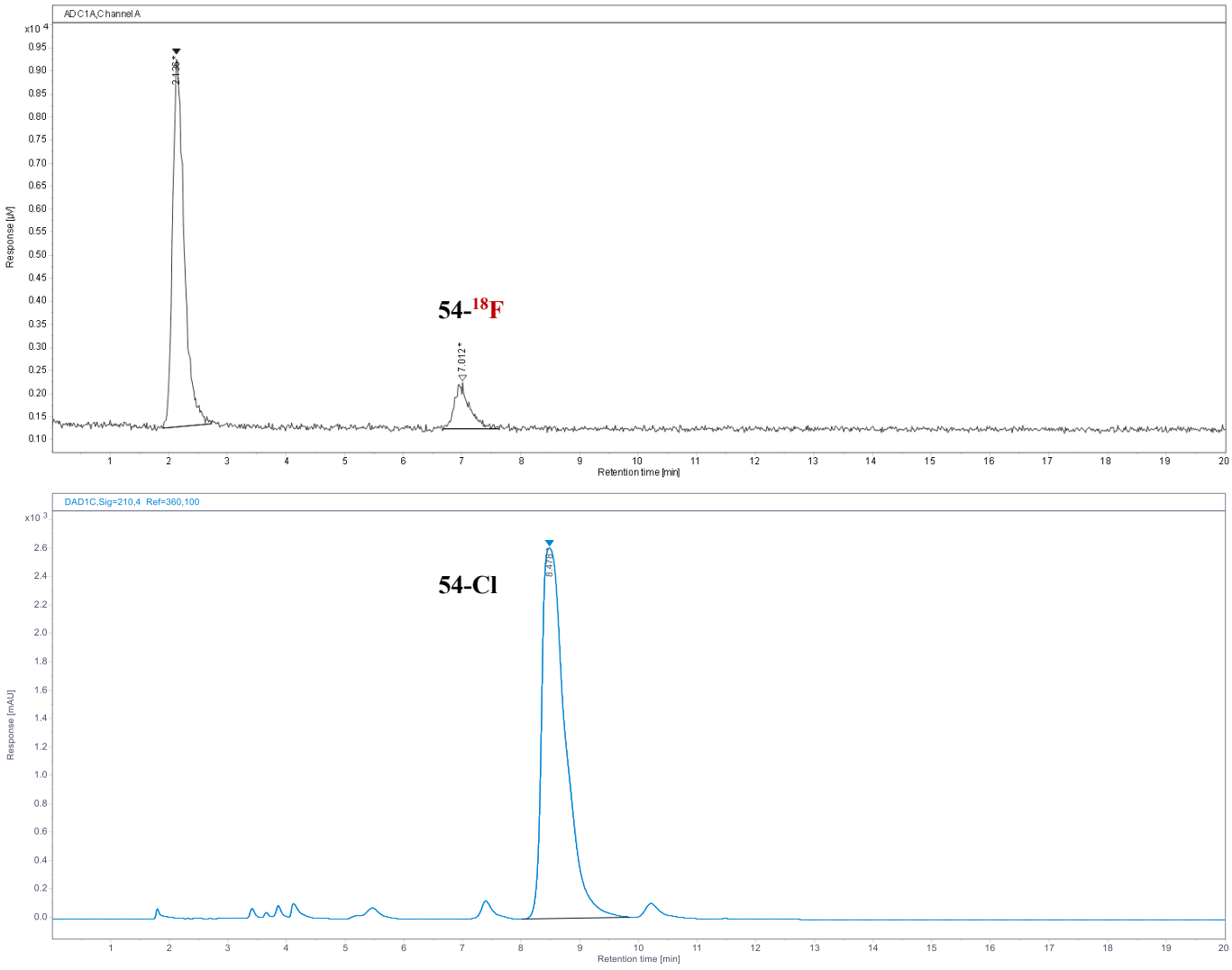
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.149	37360.795	27.719	2799.242	39.43	1.733	2.708
2	3.765	14914.523	11.066	319.345	4.50	3.494	5.485
3	7.076	82506.490	**61.215**	3980.207	56.07	6.514	8.221

Supplementary Figure 58. Radio-HPLC analysis of **54-^{18}F**.



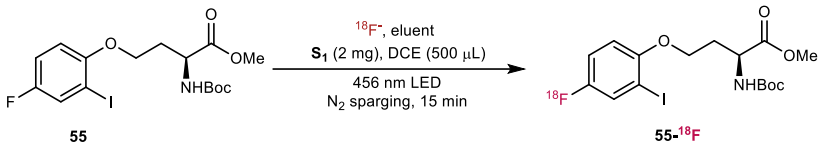
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
54-Cl	**54-^{18}F**	6.19 mCi/(6.19 + 0.12) mCi = 98%	60% MeCN	15%

Supplementary Table 63. Elution efficiency and RCC calculation of **54-^{18}F**.



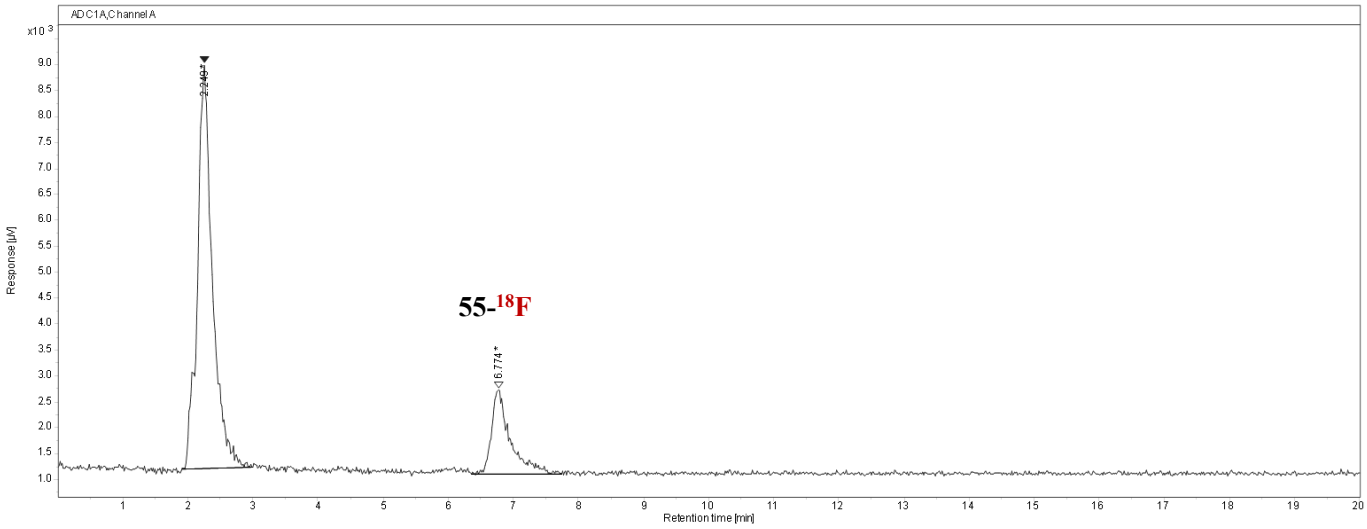
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.136	109219.868	85.530	8048.725	88.89	1.909	2.729
2	7.012	18477.442	**14.470**	1005.553	11.11	6.675	7.625

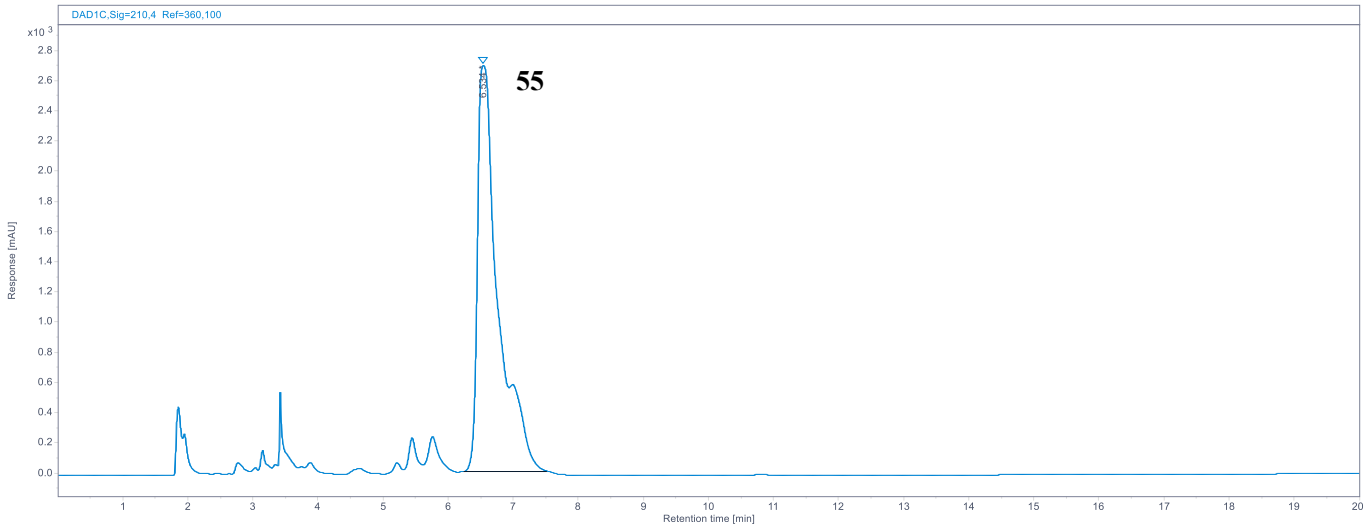
Supplementary Figure 59. Radio-HPLC analysis of **54-^{18}F**.



Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
55	**55-^{18}F**	6.71 mCi /(6.71 + 0.21) mCi = 97%	70% MeCN	21%[a]

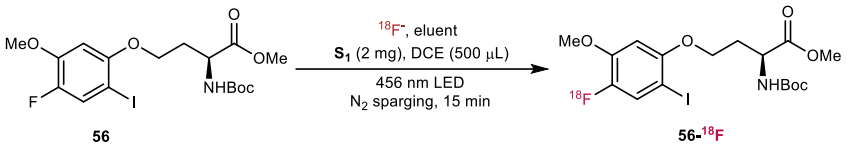
Supplementary Table 64. Elution efficiency and RCC calculation of **55-^{18}F**.a.0.02 mmol substrate





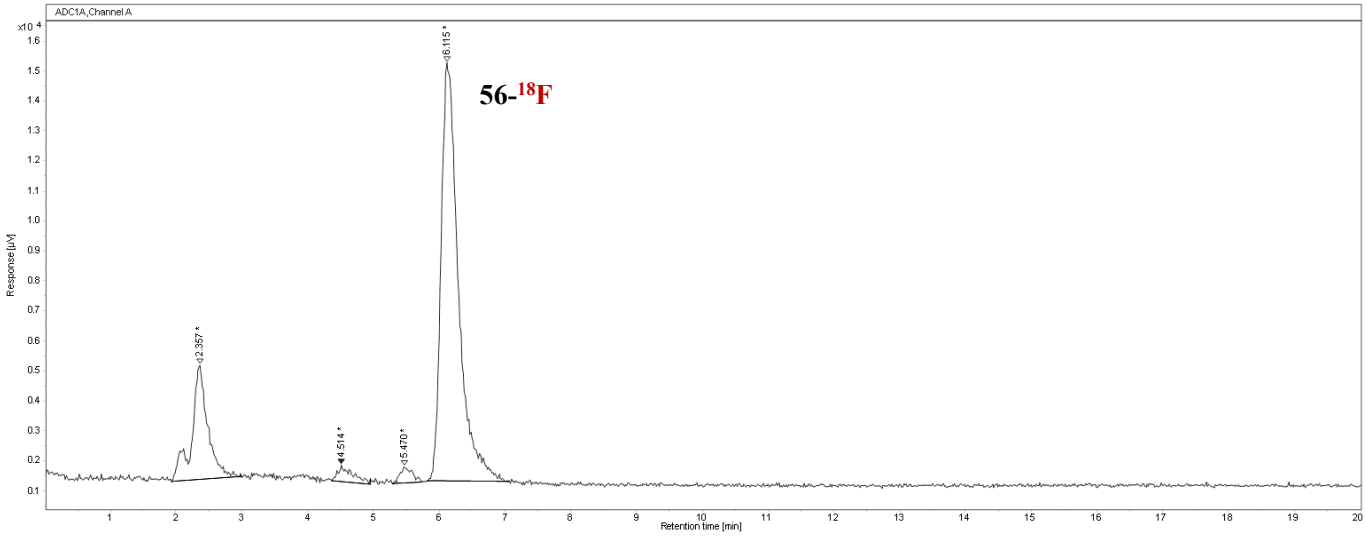
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.249	123984.497	79.469	7793.962	82.82	1.915	2.997
2	6.774	32031.697	**20.531**	1616.693	17.18	6.360	7.736

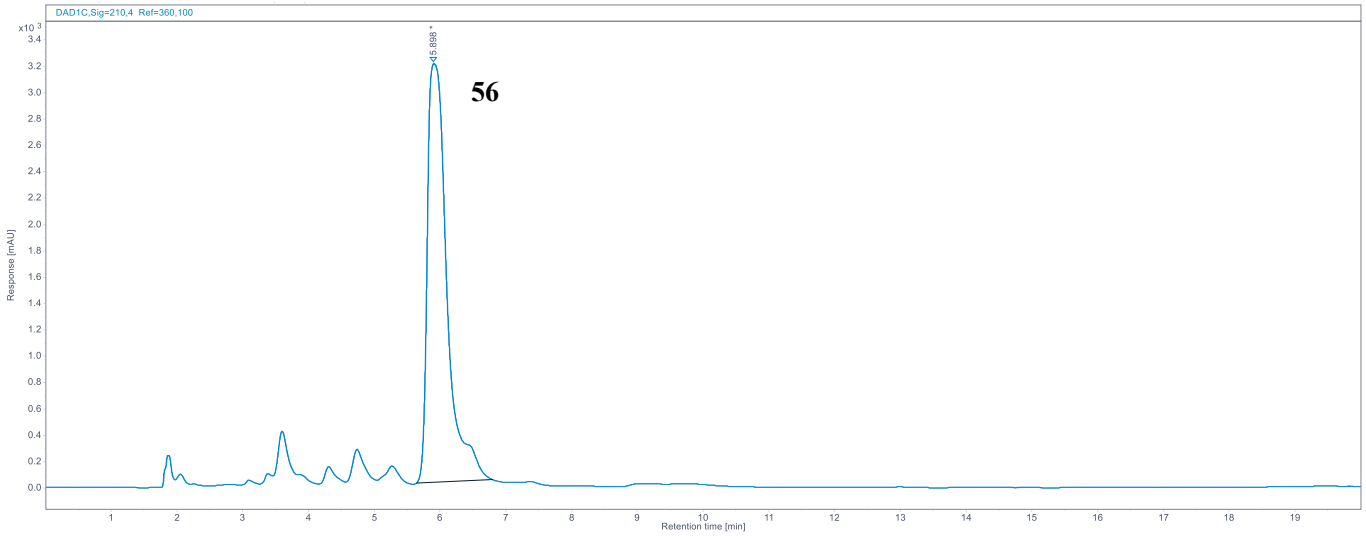
Supplementary Figure 60. Radio-HPLC analysis of **55-^{18}F**.



Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
56	**56-^{18}F**	7.45 mCi/ (7.45 + 0.3) mCi = 96%	70% MeCN	76%

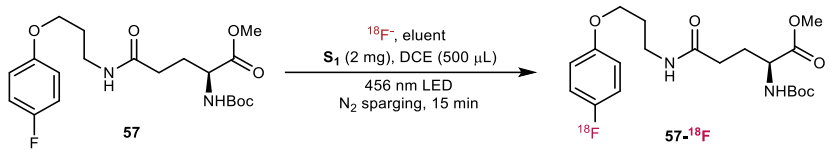
Supplementary Table 65. Elution efficiency and RCC calculation of **56-^{18}F**.





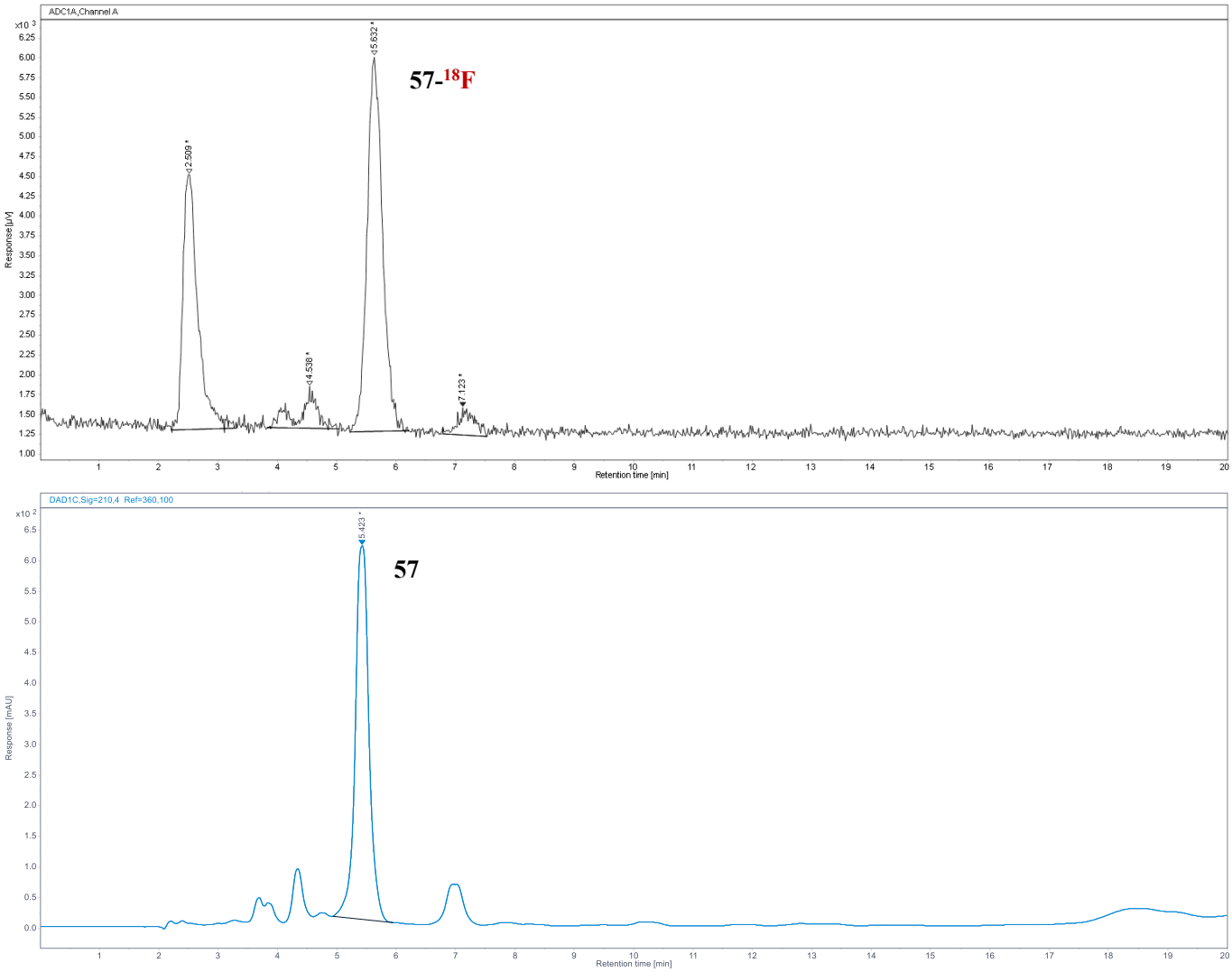
#	RT (min)	Area (µV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.357	65510.230	19.528	3833.836	20.34	1.934	2.994
2	4.514	8314.156	2.478	540.535	2.87	4.359	4.956
3	5.470	6823.166	2.034	540.838	2.87	5.290	5.739
4	6.115	254812.677	**75.959**	13935.769	73.93	5.811	7.055.

Supplementary Figure 61. Radio-HPLC analysis of **56-^{18}F**.



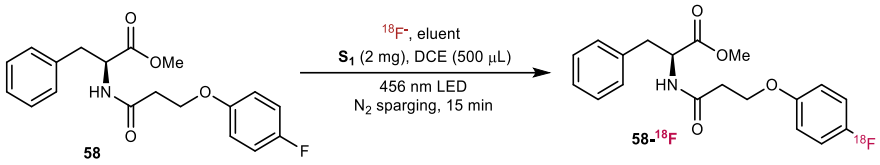
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
57	**57-^{18}F**	10.27 mCi/(10.27 + 0.7) mCi = 94%	60% MeCN (column B)	54%

Supplementary Table 66. Elution efficiency and RCC calculation of **57-^{18}F**.



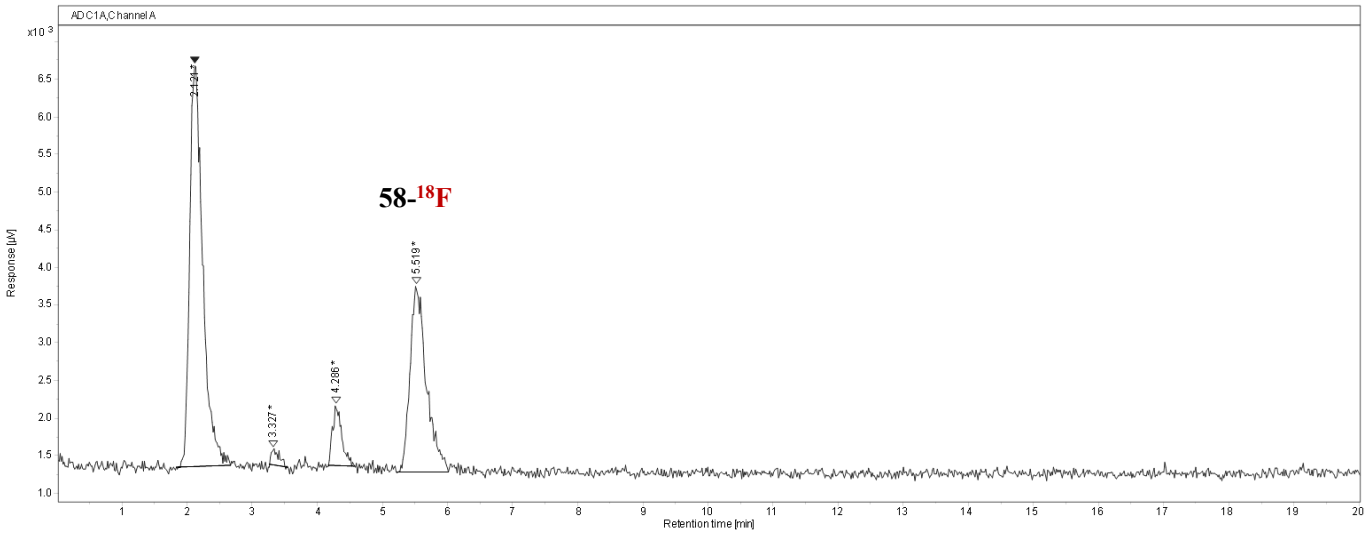
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.509	56691.679	35.596	3213.985	36.41	2.214	3.312
2	4.538	10474.257	6.577	528.594	5.99	3.834	5.042
3	5.632	85599.801	**53.747**	4732.705	53.62	5.220	6.220
4	7.123	6498.959	4.081	351.035	3.98	6.784	7.520

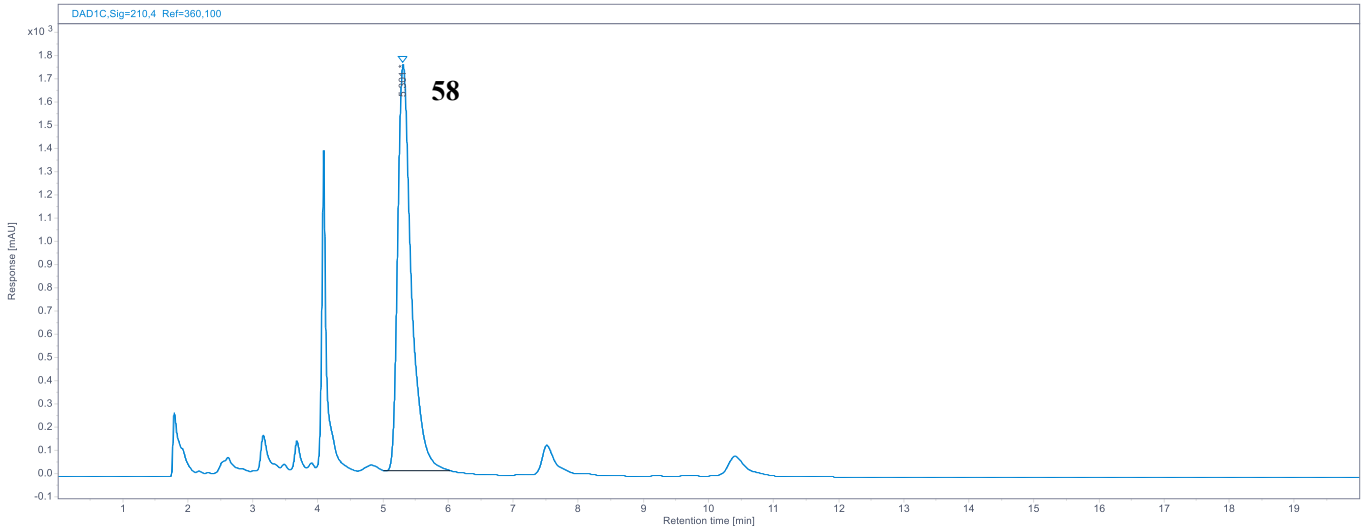
Supplementary Figure 62. Radio-HPLC analysis of **57-^{18}F**.



Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
58	**58-^{18}F**	7.39 mCi/(7.39 + 0.09) mCi = 99%	55% MeCN	34%

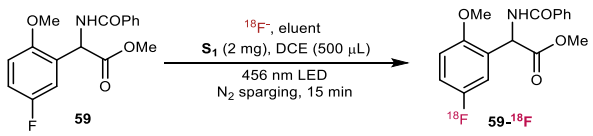
Supplementary Table 67. Elution efficiency and RCC calculation of **58-^{18}F**.





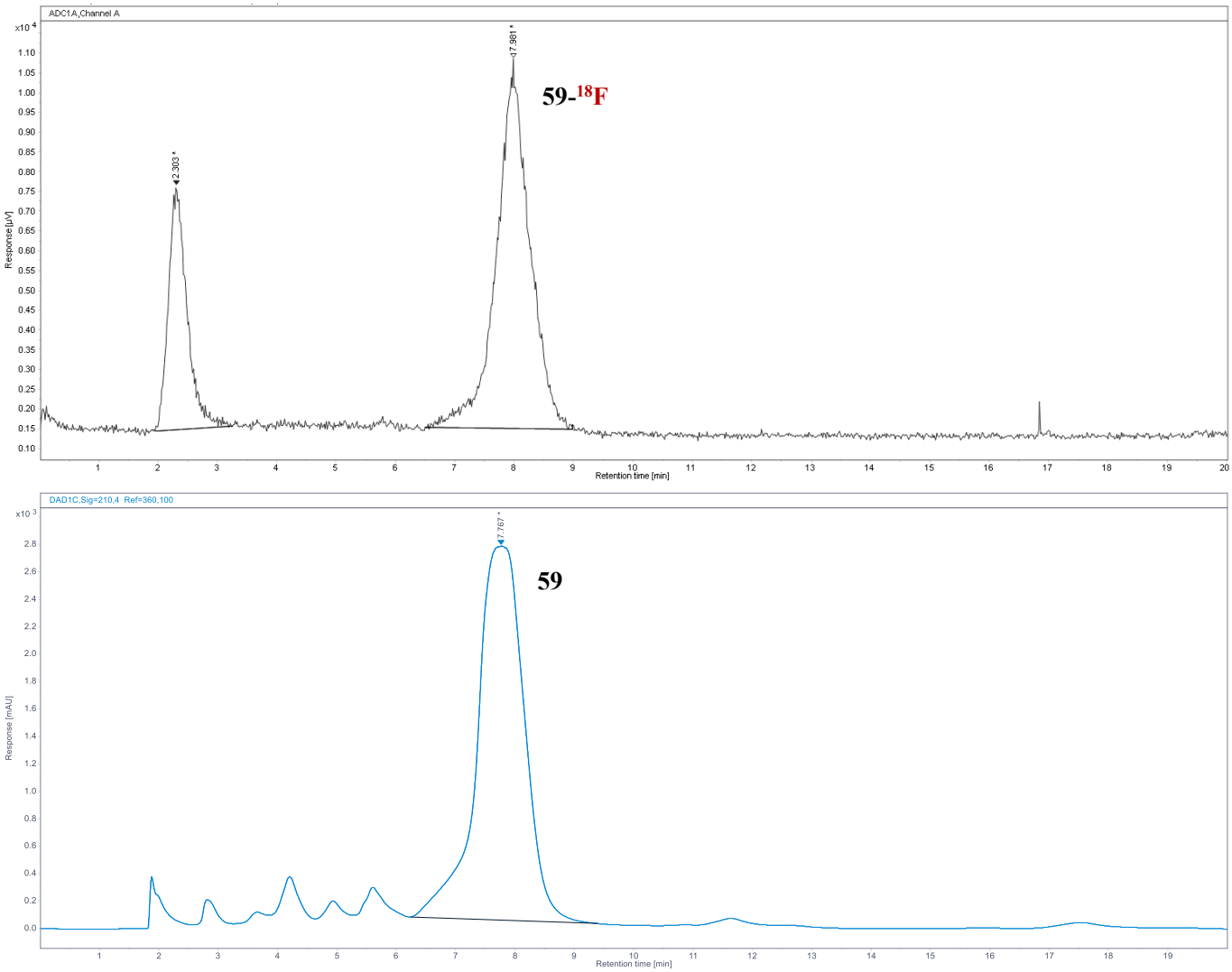
#	RT (min)	Area (µV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.121	73831.406	58.205	5336.670	60.37	1.836	2.661
2	3.327	1728.767	1.363	214.306	2.42	3.268	3.551
3	4.286	7877.012	6.210	809.553	9.16	4.165	4.578
4	5.519	43409.546	**34.222**	2479.791	28.05	5.221	6.014

Supplementary Figure 63. Radio-HPLC analysis of **58-^{18}F**.



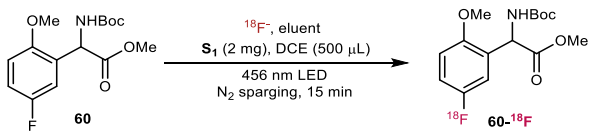
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
59	**59-^{18}F**	11.4 mCi/(11.4 + 0.43) mCi = 96%	50% MeCN	73%

Supplementary Table 68. Elution efficiency and RCC calculation of **59-^{18}F**.



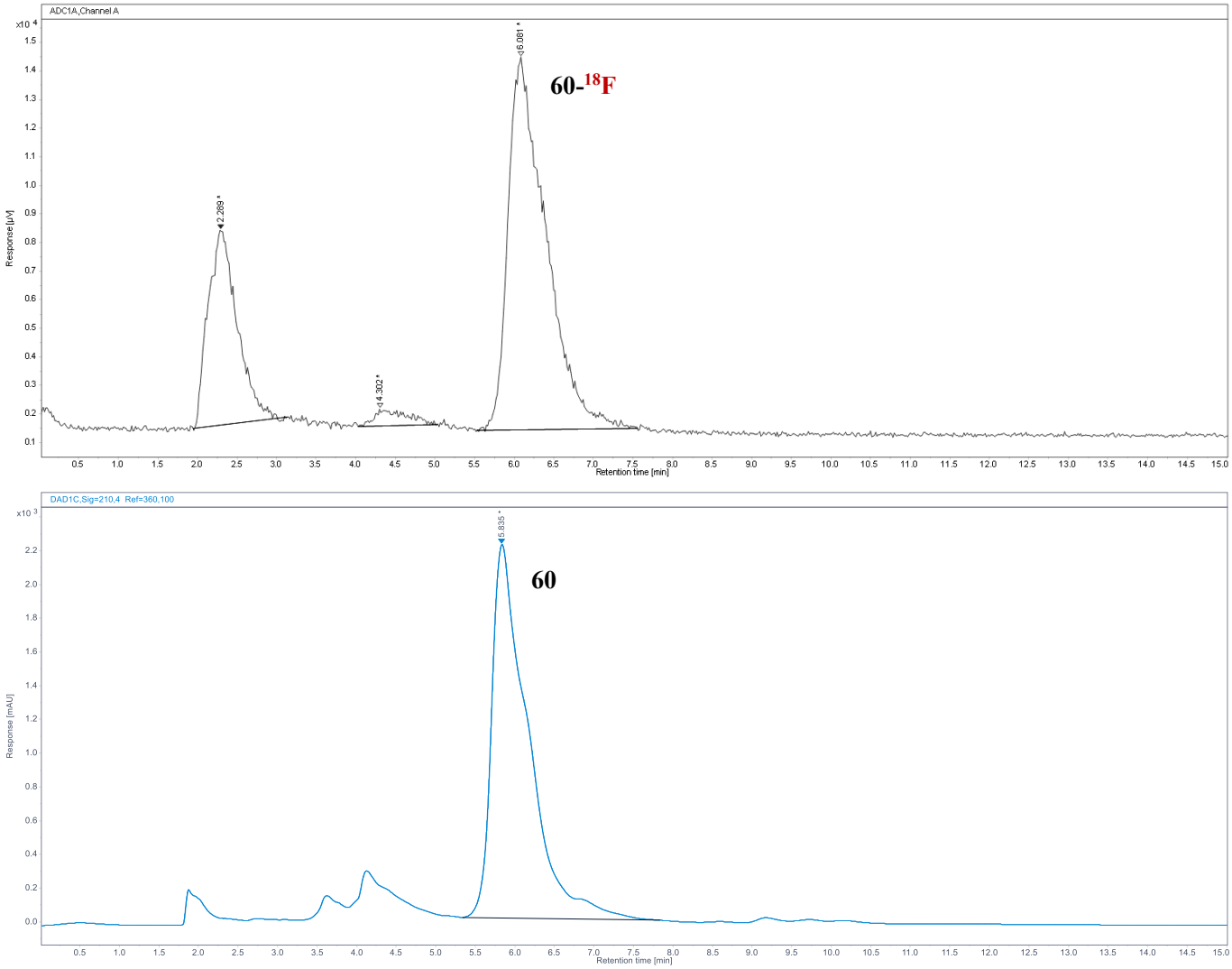
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.303	133761.189	27.134	6155.136	39.71	1.946	3.253
2	7.981	359209.066	**72.866**	9345.949	60.29	6.503	8.983

Supplementary Figure 64. Radio-HPLC analysis of **59-^{18}F**.



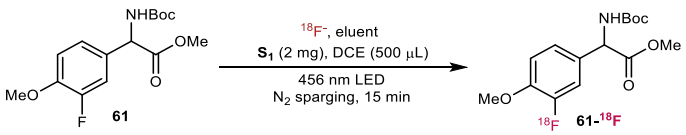
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
60	**60-^{18}F**	81 mCi/(81+17.2) mCi = 83%	60% MeCN	69%

Supplementary Table 69. Elution efficiency and RCC calculation of **60-^{18}F**.



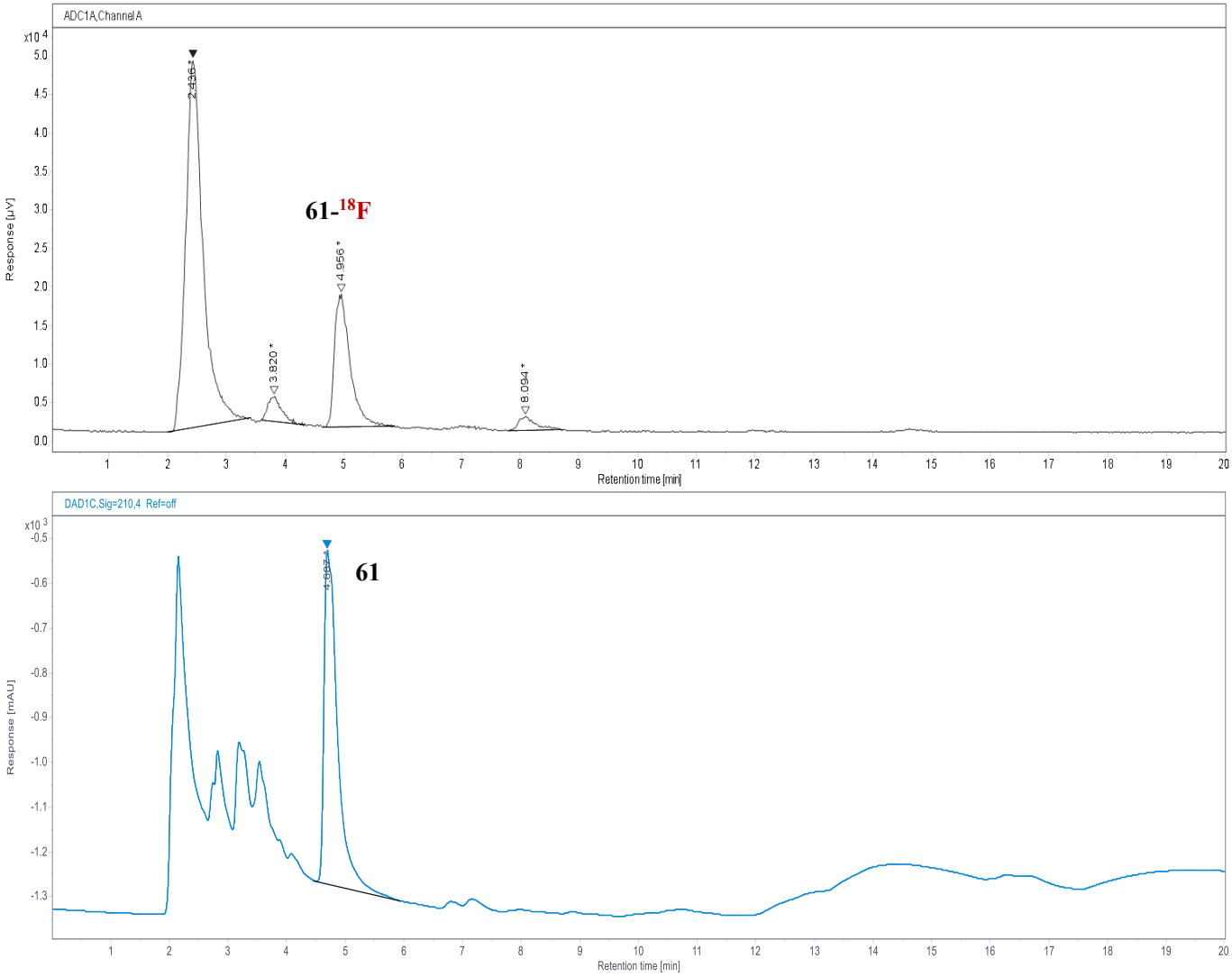
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.289	174611.945	28.009	6826.337	33.35	1.942	3.143
2	4.302	16046.255	2.574	595.193	2.91	4.030	5.029
3	6.081	432761.614	**69.417**	13044.932	63.74	5.523	7.556

Supplementary Figure 65. Radio-HPLC analysis of **60-^{18}F**.



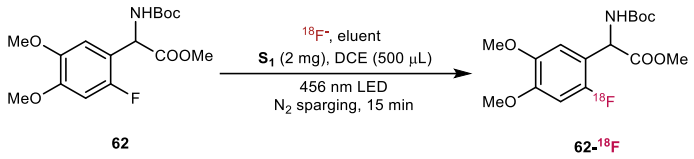
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
61	**61-^{18}F**	116.2 mCi/(116.2 + 42.4) mCi = 73%	55% MeCN	23%

Supplementary Table 70. Elution efficiency and RCC calculation of **61-^{18}F**.



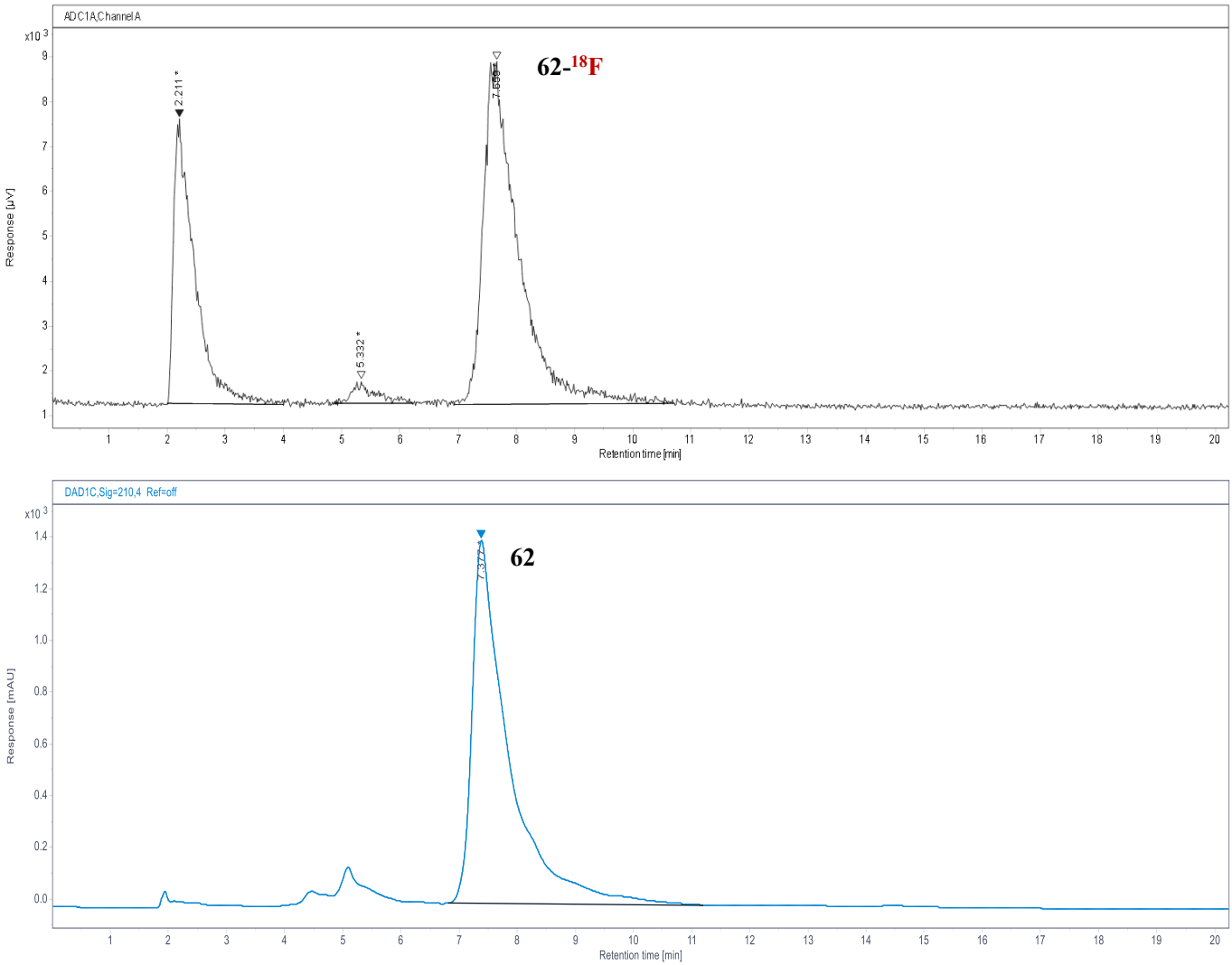
#	RT (min)	Area (μV·s)	Area%	Height (μV)	Height%	Start time (min)	End time (min)
1	2.436	980688.942	70.700	47698.989	68.02	1.998	3.409
2	3.820	55270.625	3.985	3395.141	4.84	3.587	4.330
3	4.956	315200.171	**22.723**	17165.205	24.48	4.642	5.860
4	8.094	35956.944	2.592	1868.366	2.66	7.814	8.723

Supplementary Figure 66. Radio-HPLC analysis of **61-^{18}F**.



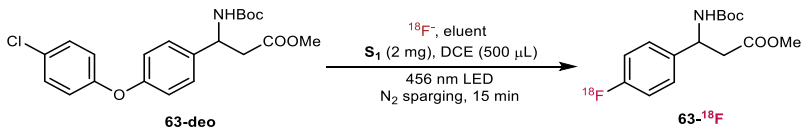
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
62	**62-^{18}F**	13.8 mCi/(13.8 + 1.1) mCi = 93%	50% MeCN	47%

Supplementary Table 71. Elution efficiency and RCC calculation of **62-^{18}F**.



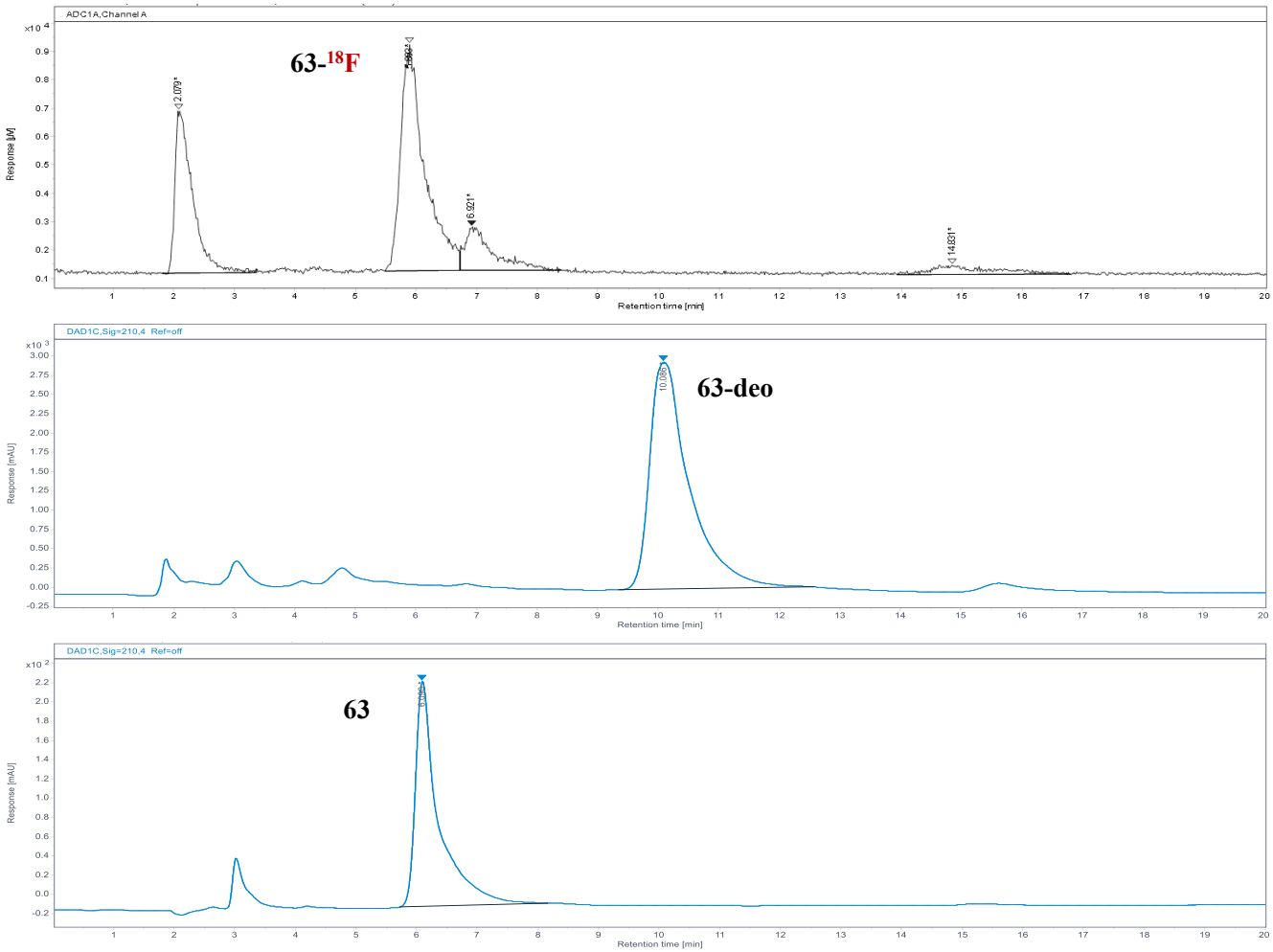
#	RT (min)	Area (μV·s)	Area%	Height (μV)	Height%	Start time (min)	Endtime (min)
1	2.211	158997.212	32.129	6354.555	…… 43.84	2.003	……3.996
2	5.332	12777.999	2.582	490.376	…… 3.38	…… 4.870	……6.219
3	7.659	323102.926	**65.289**	7648.301	…… 52.77	6.924	……10.695

Supplementary Figure 67. Radio-HPLC analysis of **62-^{18}F**.



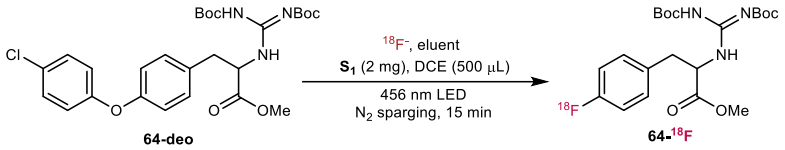
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
63-deo	**63-^{18}F**	26.5 mCi/(26.5 + 2.72) mCi= 91%	70% MeCN	54%

Supplementary Table 72. Elution efficiency and RCC calculation of **63-^{18}F**.



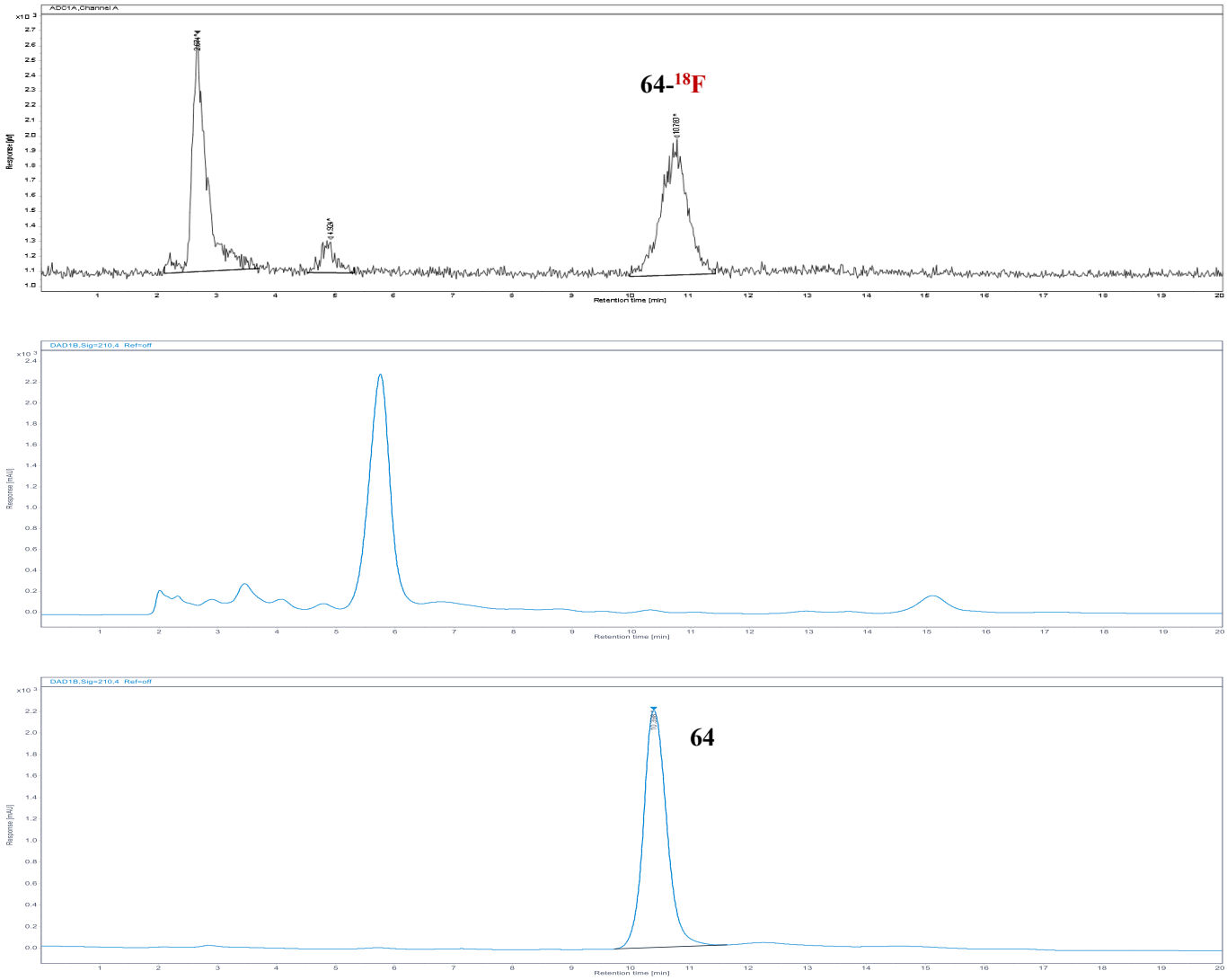
#	RT (min)	Area (μV·s)	Area%	Height (μV)	Height%	Start time (min)	End time (min)
1	2.079	116230.129	28.779	5732.540	36.87	1.813	3.371
2	5.893	217743.183	**53.915**	7974.664	51.30	5.487	6.719
3	6.921	48199.504	11.935	1519.129	9.77	6.719	8.382
4	14.831	21692.984	5.371	319.892	2.06	13.925	16.775

Supplementary Figure 68. Radio-HPLC analysis of **63-^{18}F**.



Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
64-deo	**64-^{18}F**	7.8 mCi/(7.8 + 0.16) mCi = 98%	70% MeCN	47%

Supplementary Table 73. Elution efficiency and RCC calculation of **64-^{18}F**.

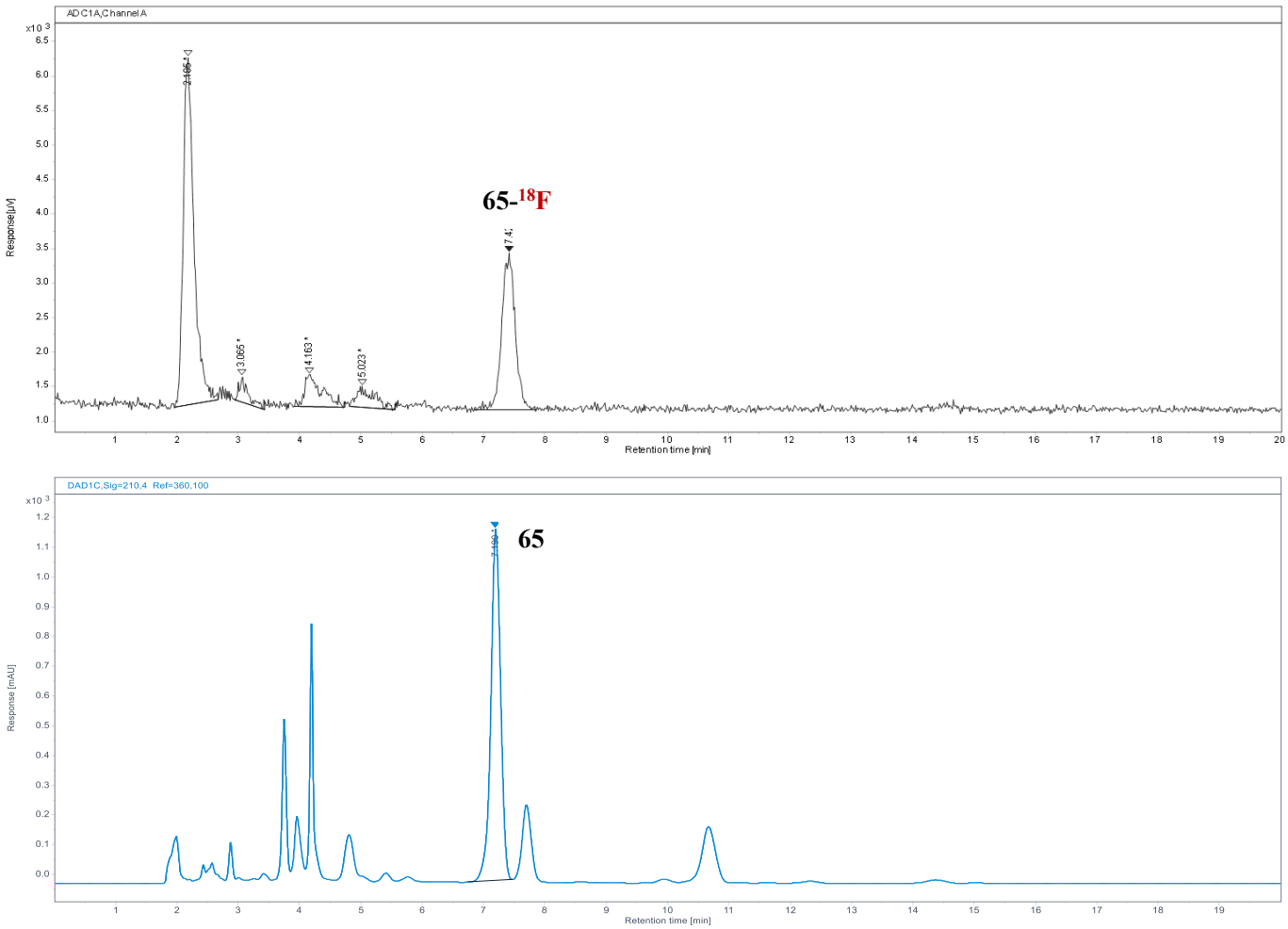


#	RT (min)	Area (µV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.674	26738.286	46.775	1578.513	58.48	2.120	3.725
2	4.924	3564.812	6.236	215.659	7.99	4.528	5.331
3	10.780	26860.535	**46.989**	905.133	33.53	9.985	11.428

Supplementary Figure 69. Radio-HPLC analysis of **64-^{18}F**.

Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
65	**65-^{18}F**	7.28 mCi/(7.28 + 0.27) mCi = 96%	60% MeCN	30%

Supplementary Table 74. Elution efficiency and RCC calculation of **65-^{18}F**.

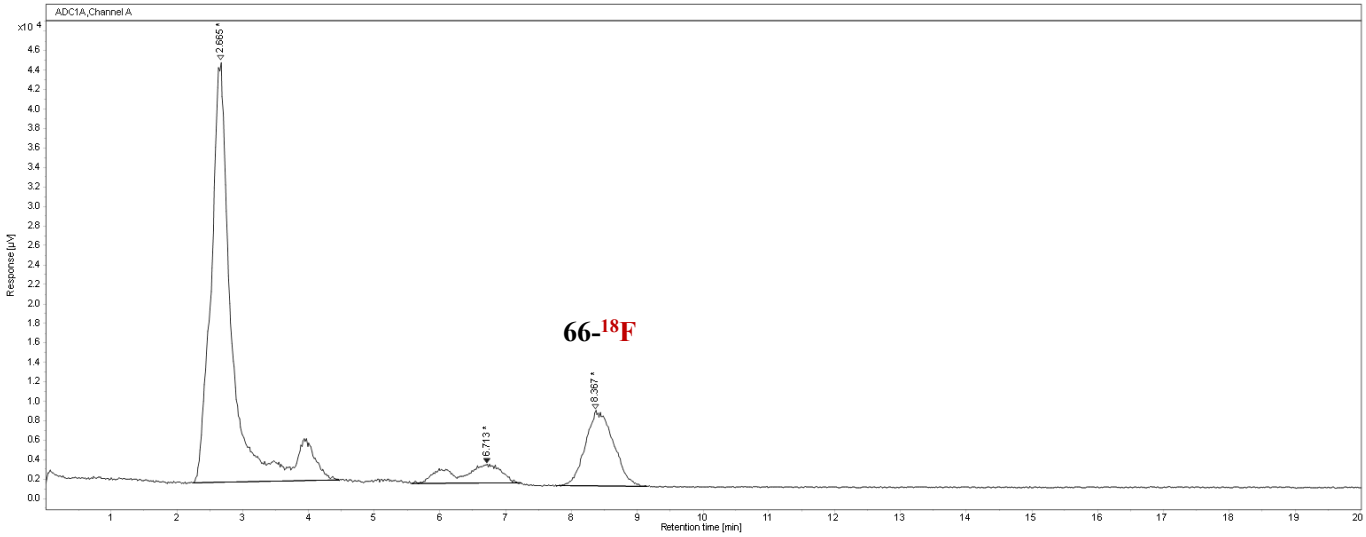


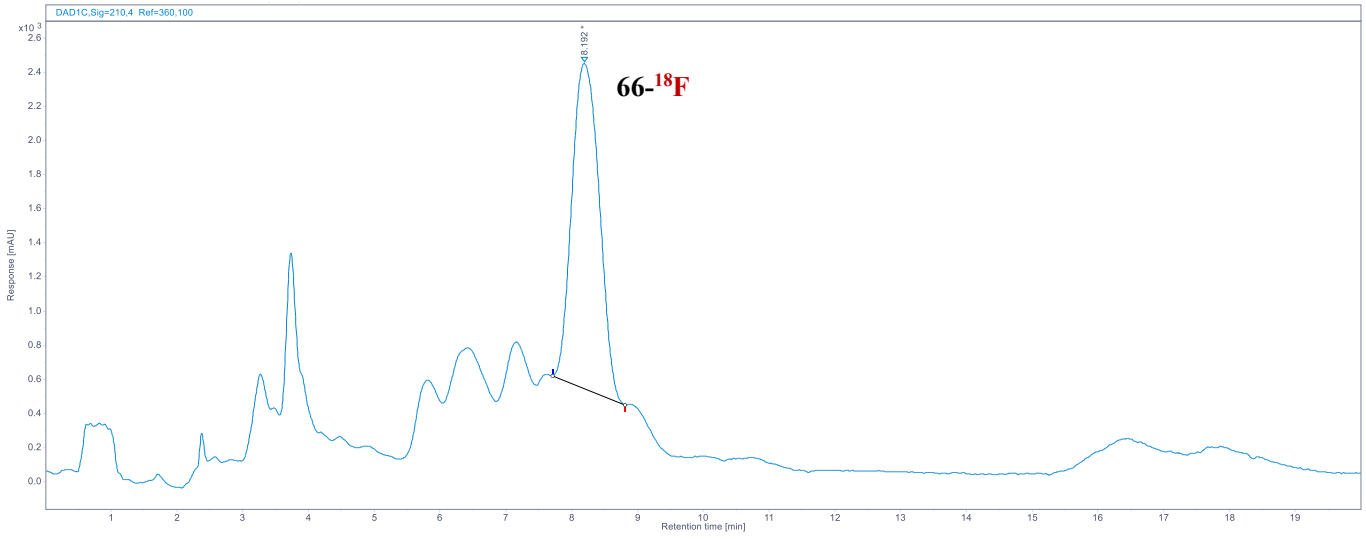
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.185	61189.261	53.483	5042.589	59.62	1.961	2.674
2	3.065	3708.392	3.241	376.098	4.45	2.947	3.435
3	4.163	9285.793	8.116	468.783	5.54	3.905	4.736
4	5.023	5785.009	5.056	305.219	3.61	4.823	5.566
5	7.423	34440.688	**30.103**	2264.499	26.78	6.849	7.862

Supplementary Figure 70. Radio-HPLC analysis of **65-^{18}F**.

Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
66	**66-^{18}F**	10.71 mCi/(10.71 + 0.47) mCi = 96%	70% MeCN	18%[a]

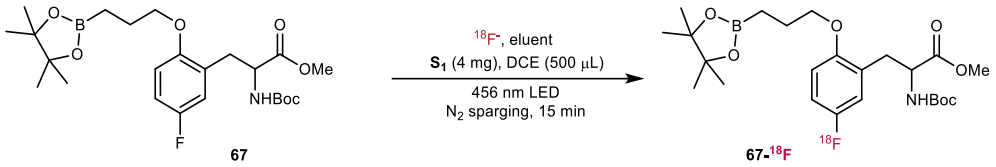
Supplementary Table 75. Elution efficiency and RCC calculation of **66-^{18}F**. a.0.02 mmol substrate.





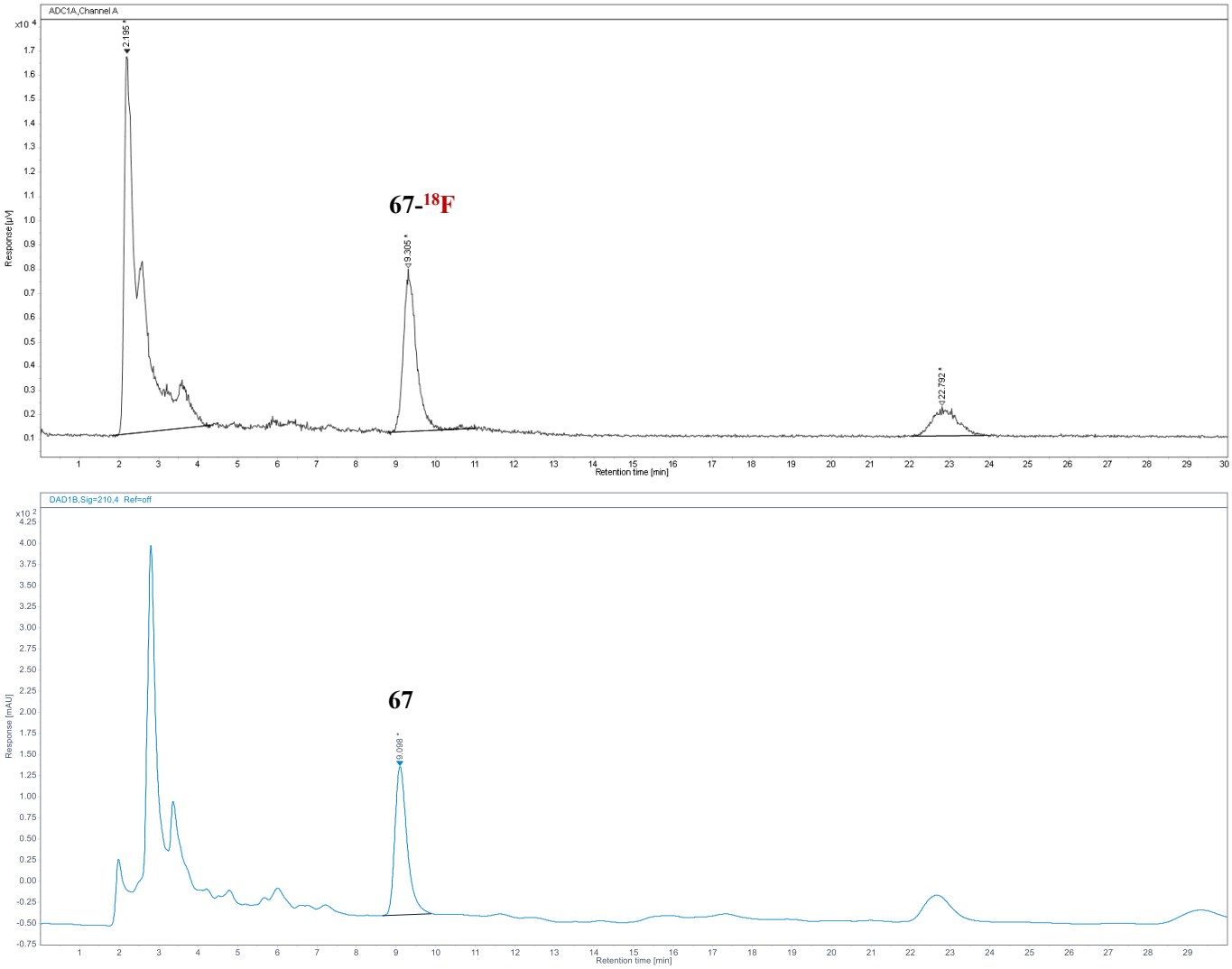
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.665	969507.183	75.050	43263.759	81.66	2.255	4.468
2	6.713	93154.711	7.211	1937.611	3.66	5.577	7.225
3	8.367	229153.647	**17.739**	7776.007	14.68	7.769	9.144

Supplementary Figure 71. Radio-HPLC analysis of **66-^{18}F**.



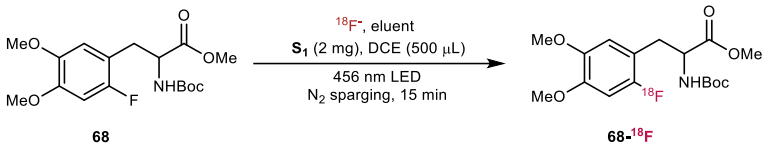
Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC
67	**67-^{18}F**	89.8 mCi/(89.8 + 9.05) mCi = 91%	70% MeCN	24%

Supplementary Table 76. Elution efficiency and RCC calculation of **67-^{18}F**.



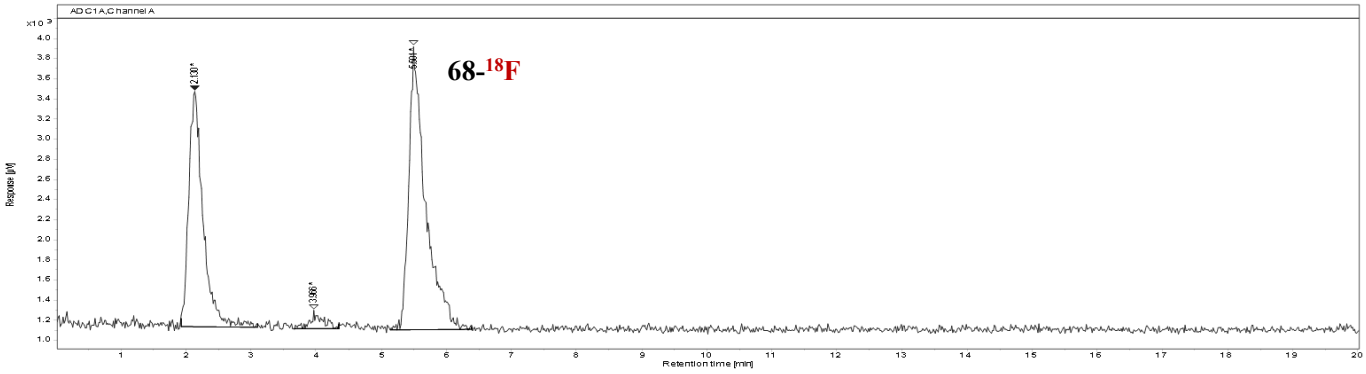
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.195	444160.213	68.388	15649.287	66.40	1.809	4.320
2	9.305	155036.219	**23.871**	6710.039	28.47	8.813	10.991
3	22.792	50275.040	7.741	1208.176	5.13	22.038	24.000

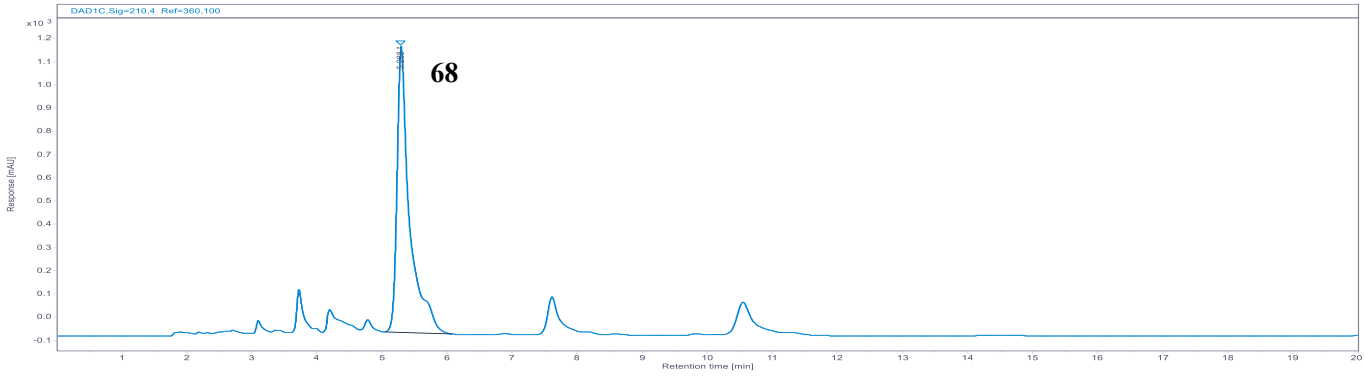
Supplementary Figure 72. Radio-HPLC analysis of **67-^{18}F**.



Substrate	Product	Elution efficiency (EE)	HPLC analysis conditions	RCC	Average RCC
68	**68-^{18}F**	8.32 mCi/(8.32 + 0.67) mCi = 93%	60% MeCN	56.8%	62±7%
		8.7 mCi/(8.7 + 0.17) mCi = 98%		75.5%	
		5.86 mCi/(5.86 + 0.1) mCi = 98%		55.9%	
		5.26 mCi/(5.26 + 0.17) mCi = 97%		57.5%	
		15.52 mCi/(15.52 + 0.29) mCi = 98%		62.7%	

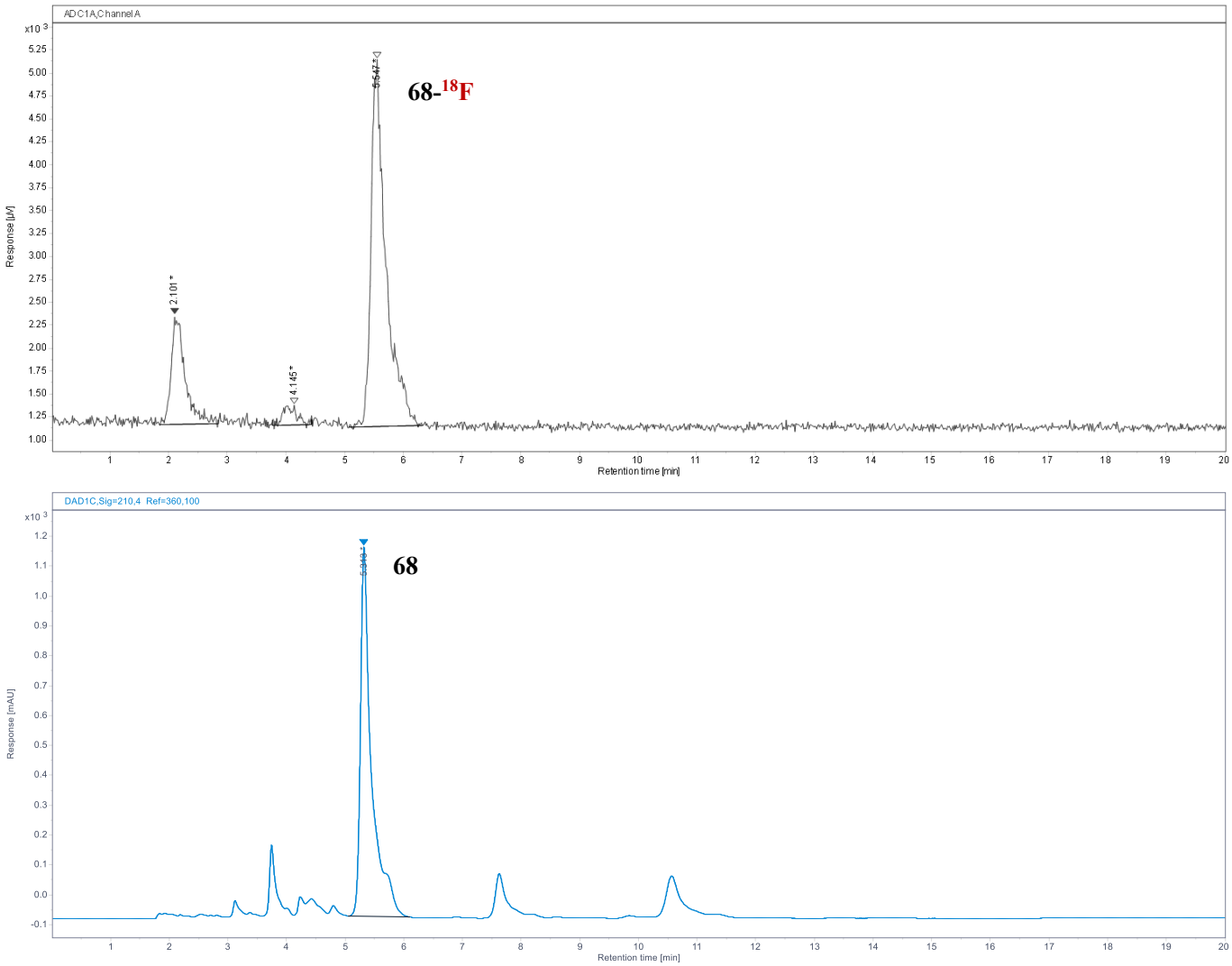
Supplementary Table 77. Elution efficiency and RCC calculation of **68-^{18}F**.





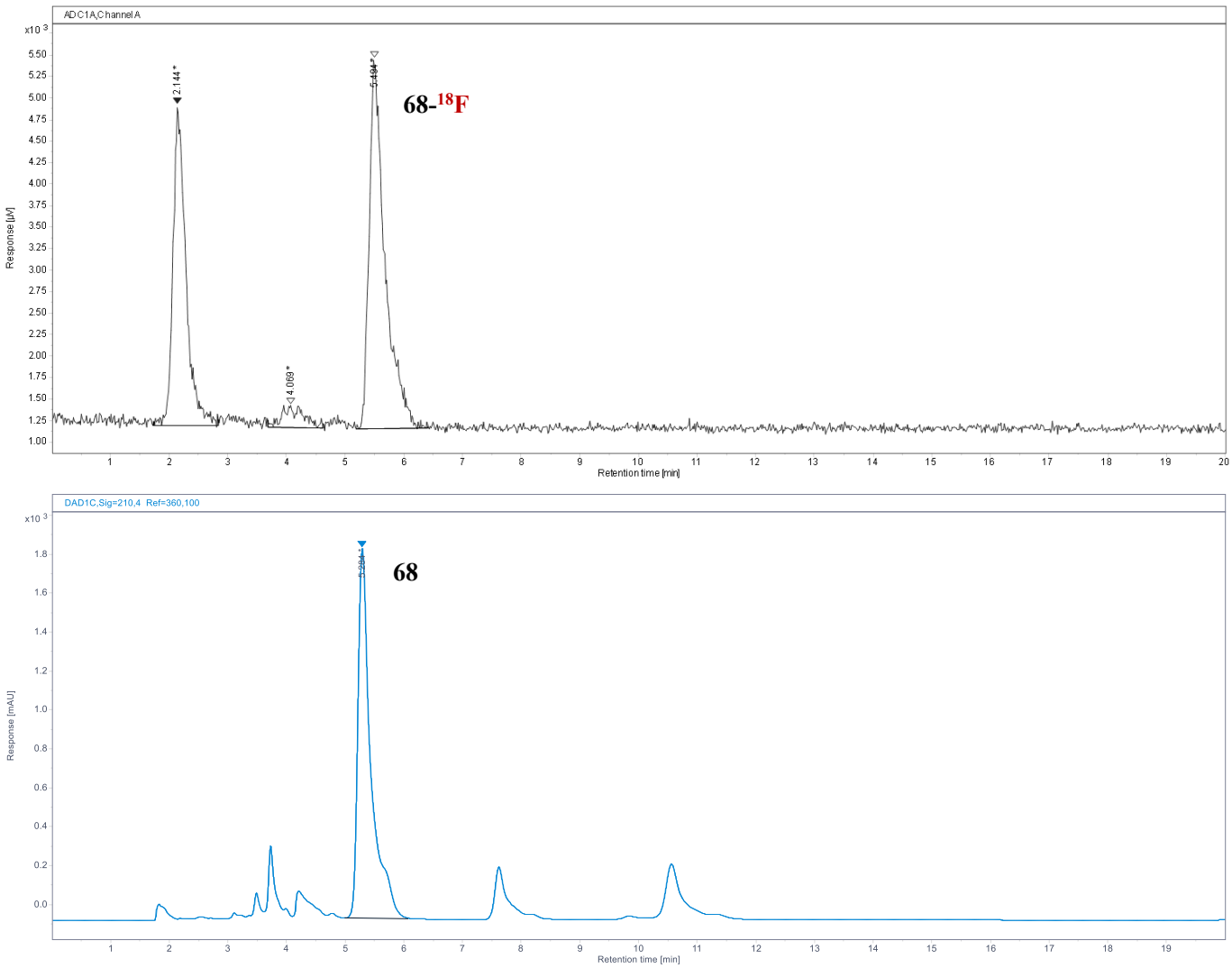
#	RT (min)	Area (μV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.130	35842.656	40.539	2335.974	43.76	1.926	3.100
2	3.966	2348.163	2.656	182.884	3.43	3.668	4.355
3	5.501	50224.684	**56.805**	2818.740	52.81	5.132	6.385

Supplementary Figure 73. Radio-HPLC analysis of **68-^{18}F**.



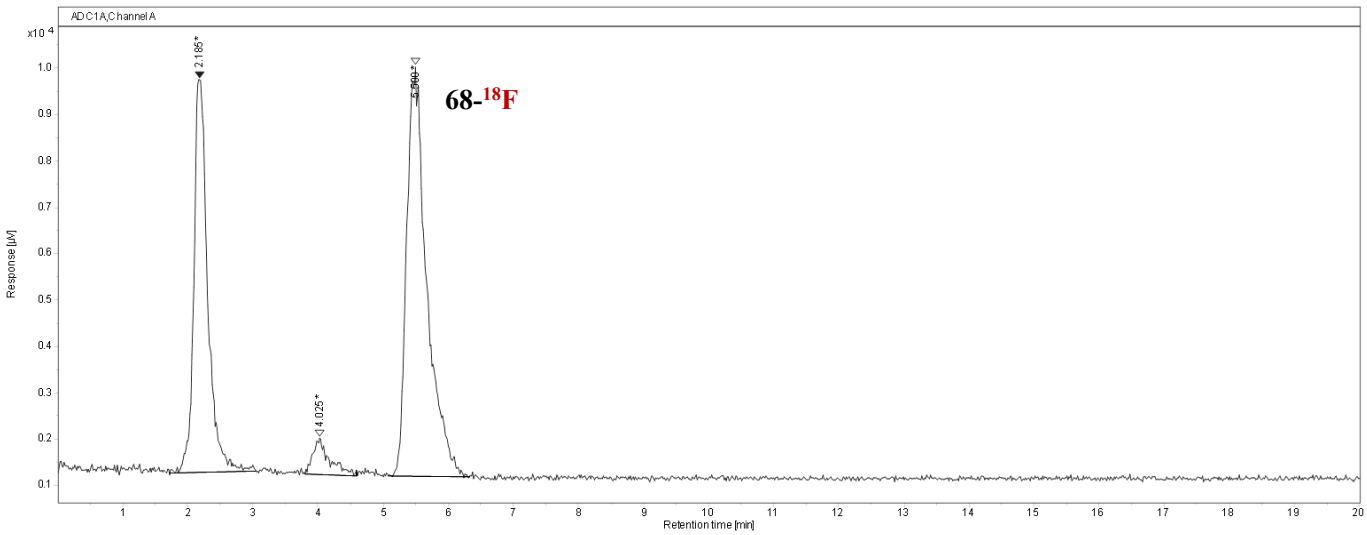
#	RT (min)	Area (µV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.101	19256.078	20.720	1185.490	21.96	1.853	2.847
2	4.145	3529.725	3.798	214.138	3.97	3.770	4.436
3	5.547	70150.740	**75.482**	3998.545	74.07	5.072	6.332

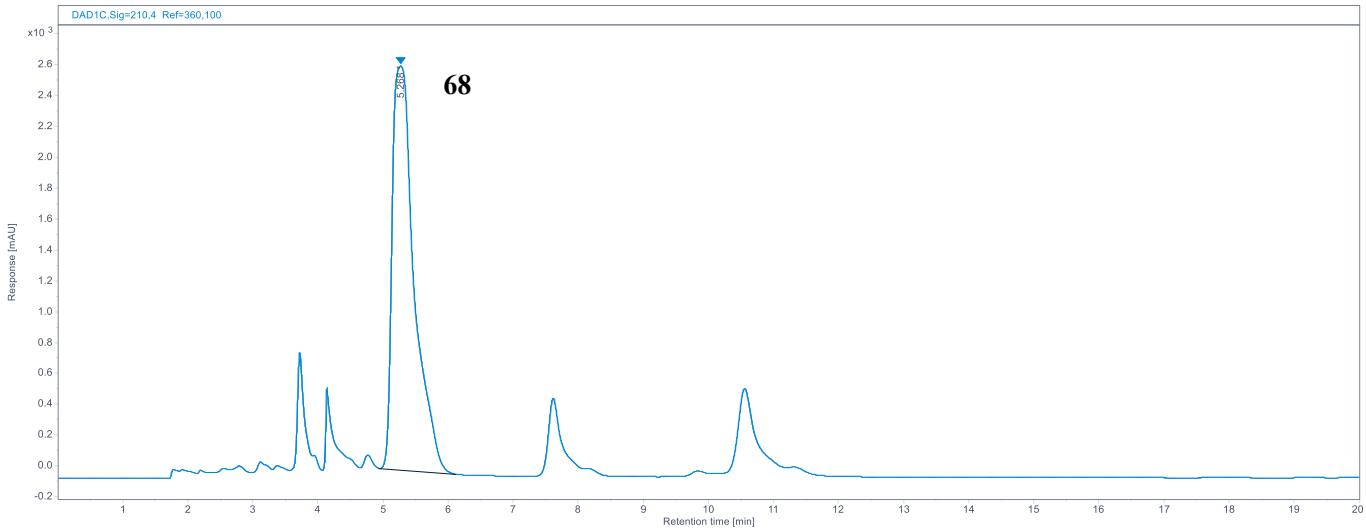
Supplementary Figure 74. Radio-HPLC analysis of **68-^{18}F**.



#	RT (min)	Area (µV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.144	57086.011	39.453	3725.865	44.95	1.740	2.838
2	4.069	6754.368	4.668	263.204	3.18	3.682	4.623
3	5.494	80853.596	**55.879**	4300.462	51.88	5.185	6.414

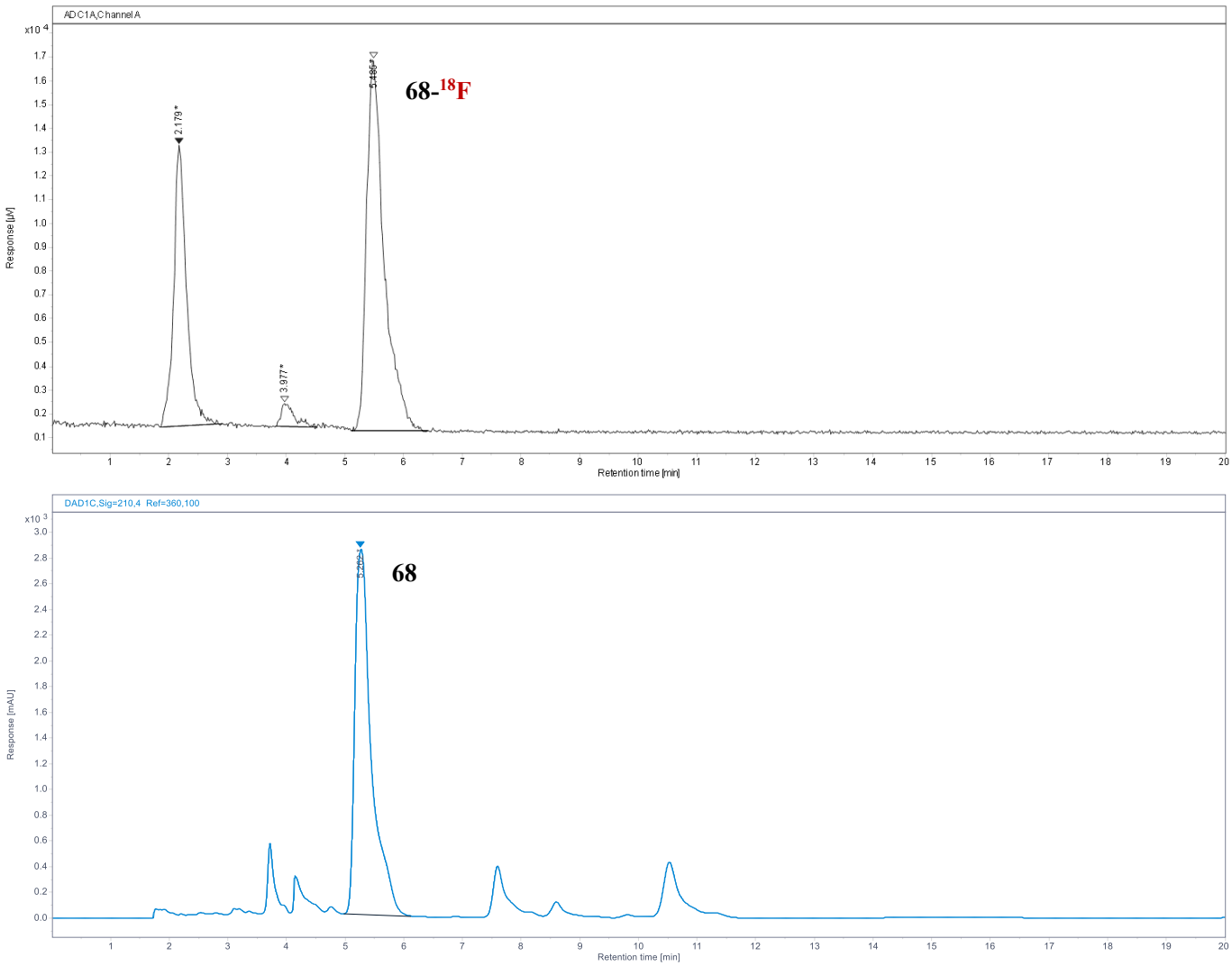
Supplementary Figure 75. Radio-HPLC analysis of **68-**^{18}**F**.





#	RT (min)	Area (µV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.185	126077.217	38.321	8477.021	46.83	1.727	3.049
2	4.025	13779.030	4.188	785.637	4.34	3.800	4.588
3	5.500	189145.662	**57.491**	8839.445	48.83	5.085	6.333

Supplementary Figure 76. Radio-HPLC analysis of **68-**^{18}**F**.



#	RT (min)	Area (µV·s)	Area%	Height	Height%	Start time (min)	End time (min)
1	2.179	178994.058	34.346	11799.772	41.55	1.843	2.915
2	3.977	15449.484	2.965	984.130	3.47	3.820	4.516
3	5.485	326704.678	**62.689**	15616.421	54.99	5.112	6.415

Supplementary Figure 77. Radio-HPLC analysis of **68-^{18}F**.

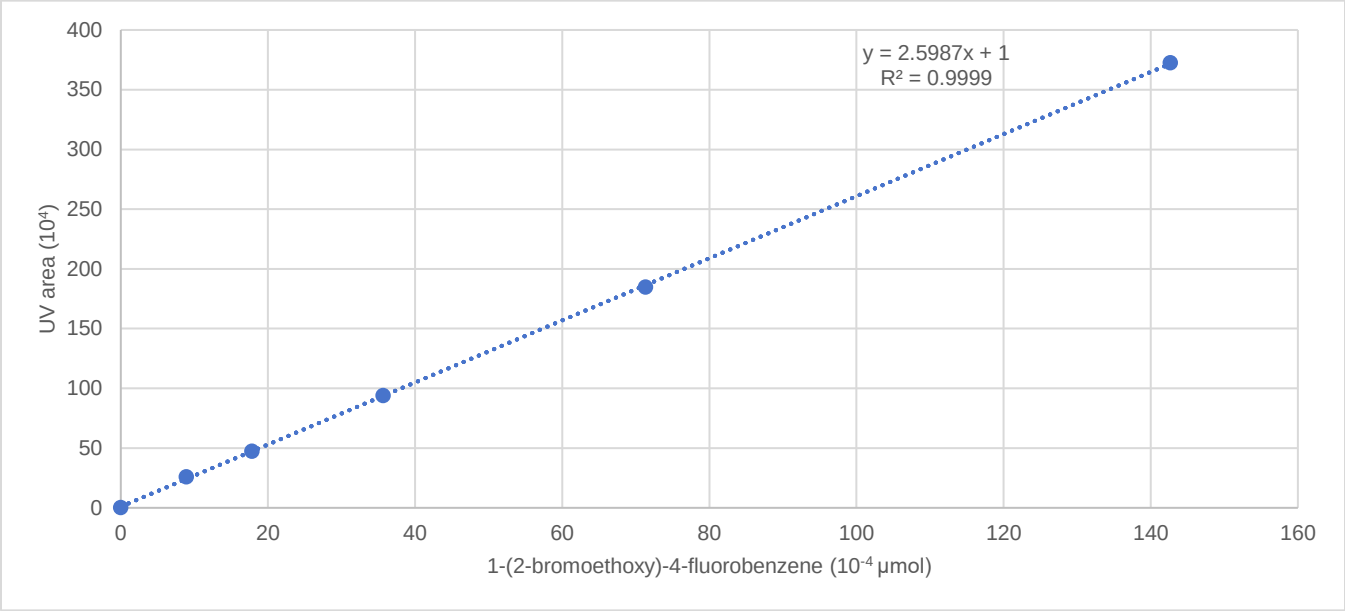
3.10 Molar activity calculation of 2-^{18}F from radiodeoxyfluorination of 2-deo

Molar activity was calculated using a standard curve of the corresponding fluorinated 1-(2-bromoethoxy)-4-fluorobenzene (2-F). 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 2-F. The radiolabeled product from the labeling reaction was collected; 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. The [^{18}F] 1-(2-bromoethoxy)-4-fluorobenzene has a molar activity of 48.47 GBq/µmol, which is decay corrected to the end of synthesis (EOS).

A

1-(2-bromoethoxy)-4-fluorobenzene (10^{-4} µmol)	UV area (10^4)
0	0
8.92	25.8960
17.83	47.3065
35.66	94.0040
71.33	184.6888
142.66	372.3726

B

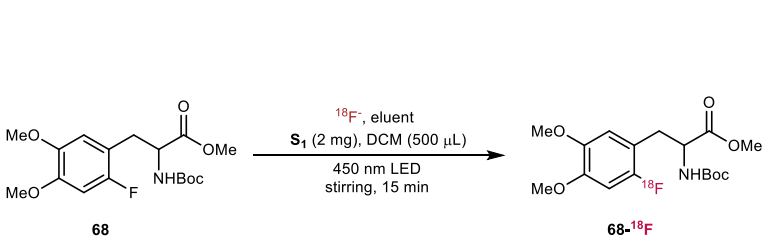


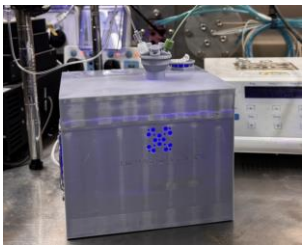
C

Entry	Decay corrected (EOS) Activity (10^{-4} GBq)	UV area (10^4)	1-(2-bromoethoxy)-4-fluorobenzene (10^{-4} µmol)	Molar activity (GBq/µmol)
1	217.1133	12.6408	4.4795	46.4682

Supplementary Figure 78. Standard curve data for 2-F(**A** and **B**) ; C. the molar activity for **2-^{18}F** calculated from parts **A** and **B**.

3.10 Scale-up ^{18}F-labelling of racemic FDOPA precursor 68 on a LED reactor



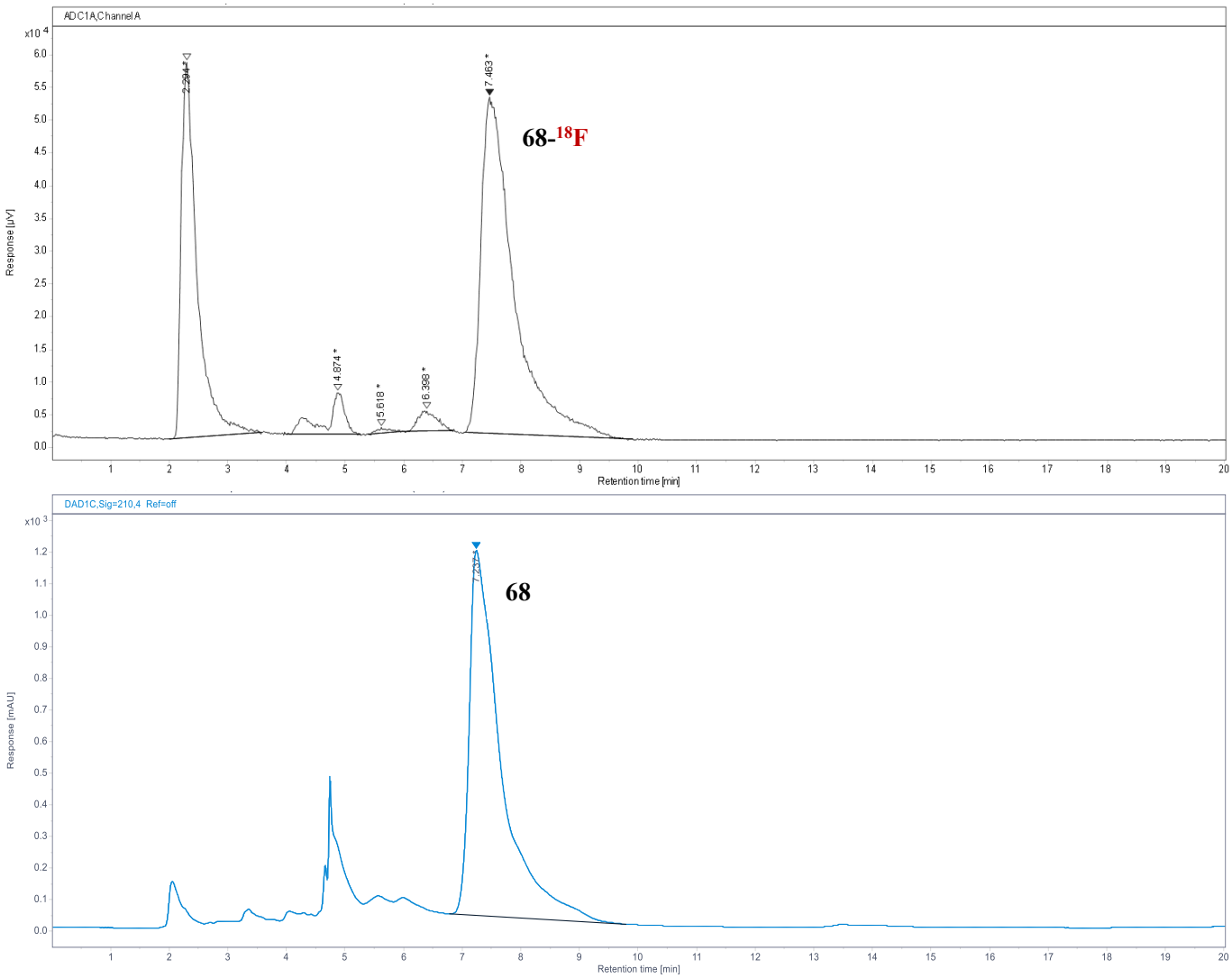


Following the genearal procedure at section **3.8**, with the standard eluent, the $^{18}F^-$ trapped on the anion exchange resin was eluted in a sealed reaction tube, which were preloaded with photocatalyst **S_1** (2 mg), substrate **68** (3.6 mg, 0.01 mmol) and DCE or DCM (500 µl) on the ProBox reactor (450 nm) as shown above. The solution was stirred under LED light irradiation for 15 min and then analyzed on the HPLC to calculate RCCs.

Substrate	Product	Solvent	Elution efficiency (EE)	HPLC analysis conditions	RCC
68	**68-^{18}F**	DCE	102.2 mCi/(102.2 + 2.01) mCi = 98%	55% MeCN (Column B)	61%
		DCM	203.96 mCi/(203.96 + 6.6) mCi = 97%		70%

Supplementary Table 78. Elution efficiency and RCC calculation of scale-up synthesis of **68-^{18}F** on the LED reactor.

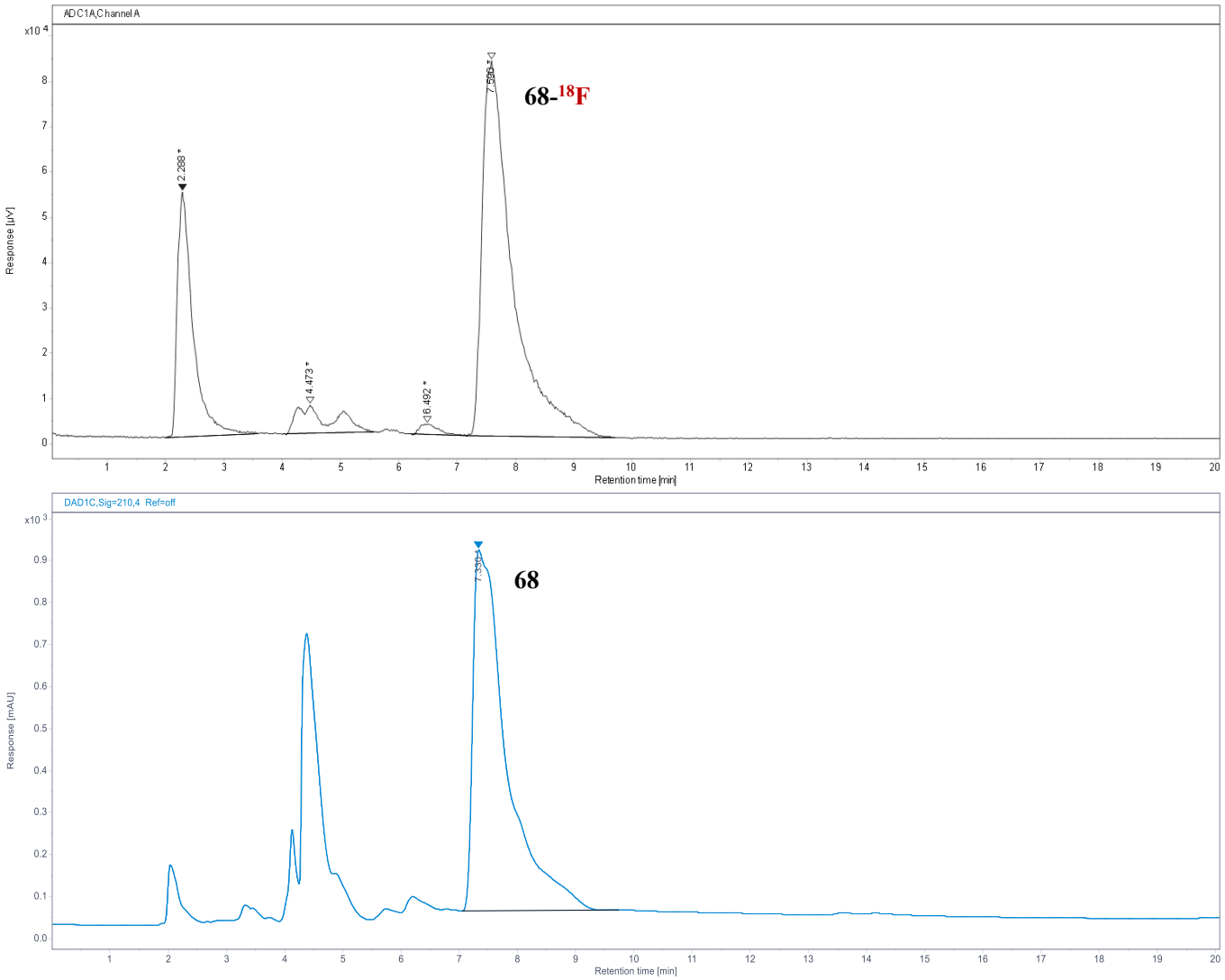
DCE as the solvent:



#	RT (min)	Area (µV·s)	Area%	Height (µV)	Height%	Start time (min)	End time (min)
1	2.294	1078443.080	32.543	57524.032	48.19	2.008	3.580
2	4.874	144167.431	4.350	6471.485	5.42	3.995	5.255
3	5.618	11272.914	0.340	814.266	0.68	5.399	5.982
4	6.398	69503.530	2.097	3122.481	2.62	5.982	6.842
5	7.463	2010533.946	**60.669**	51438.764	43.09	7.034	9.910.

Supplementary Figure 79. Radio-HPLC analysis of **68-^{18}F**.

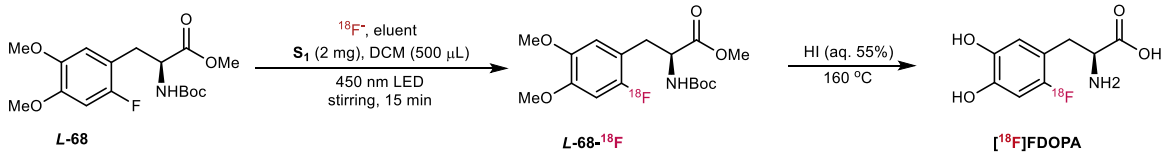
DCM as the solvent:

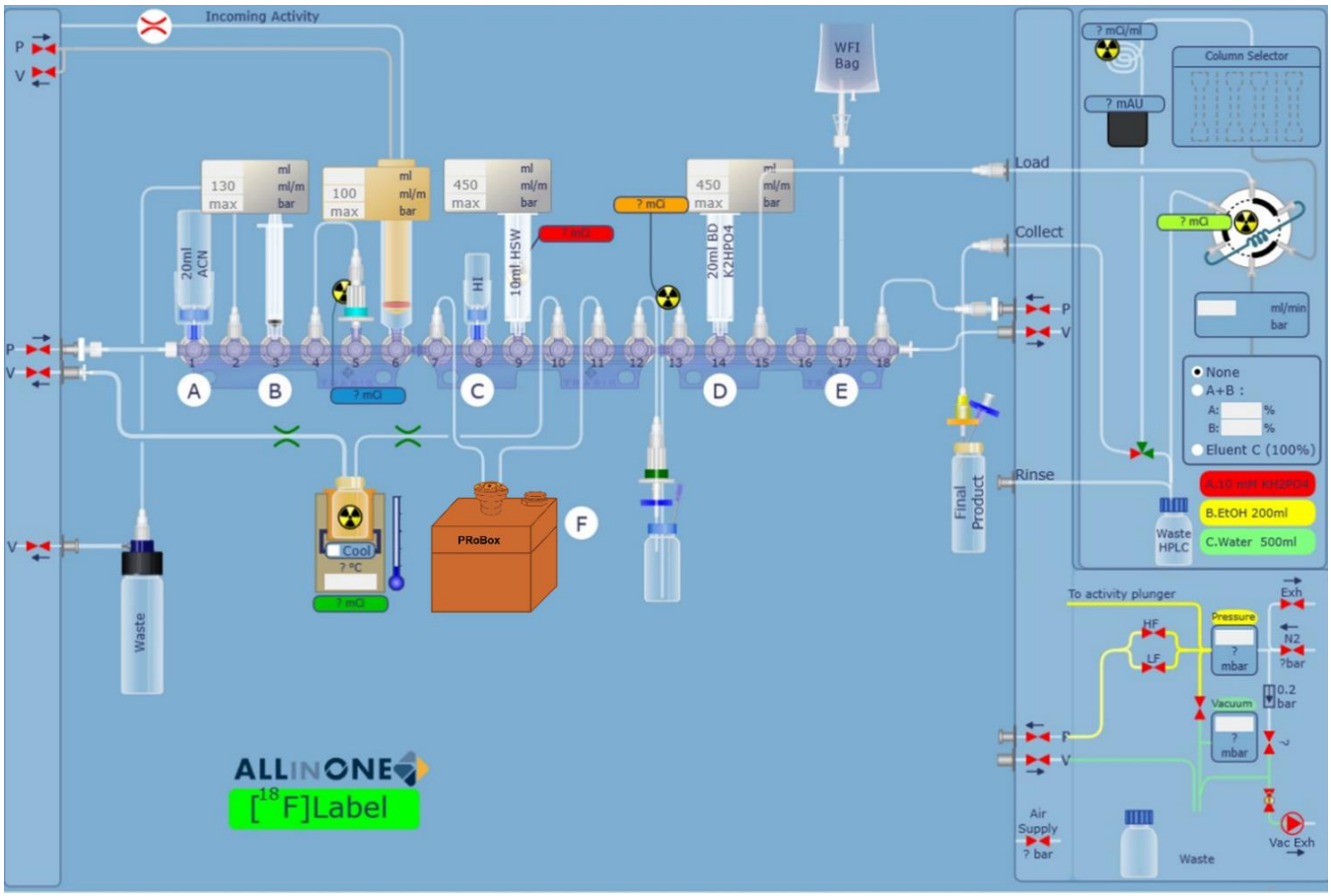


#	RT (min)	Area (µV·s)	Area%	Height (µV)	Height%	Start time (min)	End time (min)
1	2.288	992391.774	23.168	54012.137	37.18	1.995	3.568
2	4.473	256948.908	5.999	6229.063	4.29	4.013	5.571
3	6.492	51507.445	1.202	2352.515	1.62	6.179	7.173
4	7.590	2982555.425	**69.631**	82694.387	56.92	7.173	9.695

Supplementary Figure 80. Radio-HPLC analysis of **68-^{18}F**.

3.11 Automatic synthesis of [^{18}F]FDOPA





Supplementary Figure 81. Automation synthesis schematic diagram on a AllinOne radiosynthesis module

Position	Item	Composition	Qty	Container
1 (Site A)	Acetonitrile	Anhydrous acetonitrile	12 mL	20 mL clear glass vial
3 (Site B)	Eluent	^{t}BuOH	400 μL	3 mL BD syringe
		Acetonitrile	100 μL	
		TBAP (0.1 mg/μL) of MeCN solution	30 μL	
5	anion-exchange resin (KT-101)	—	1	NA
7 (Site F)	Empty reaction tube	photocatalyst **S1** (2 mg)	2 mg	ProBox
		substrate ***L*-68**	3.6 mg	
		DCM	500 μL	
8 (Site C)	HI	HI (55 wt.% in H_2O)	1 mL	4 mL clear glass vial
12	Sep-Pak Plus Long Alumina N Cartridges-1710 mg	Al_2O_3	1	NA
14 (Site D)	K_2HPO_4 solution	K_2HPO_4 solution (3 mol/L)	3 mL	20 mL BD syringe
17 (Site E)	Bag of sterile injection water	Sterile injection water	500 mL	NA

Supplementary Table 79. Details of composition in each site for ^{18}F-FDOPA synthesis on an AllinOne radiosynthesis module collecting an LED reactor (ProBox)

A schematic diagram of the AllinOne radiosynthesis module used to synthesize **[^{18}F]FDOPA** was shown in **Supplementary Figure 81**, and the details of composition in each site were listed in **Supplementary Table 79.** The automatic synthesis procedure was as follows:

Step 1: The aqueous $^{18}F^-$ solution produced by the cyclotron was delivered to the activity reservoir on position 6 (P6) of the AllinOne synthesis module and trapped through an anion-exchange resin (KT-101, P5) preconditioned with 10 mL K_2HPO4 (1 M) and 10 mL water. (P6-P5-P4-P2-Waste)

Step 2: The resin and lines were flushed under N_2 flow for 60 seconds to remove most of the water, then washed with 5 mL MeCN and flushed with N_2 for another 3 min.(P1-P9-P5-P4-P2-Waste)

Step 3: The prepared eluent was withdrawn from the 3 mL BD syringe (P3, Site B), and then was slowly (0.5 mL/min, 3 min) passed through the resin toward a sealed reaction tube, which was preloaded with photocatalyst $\mathbf{S_1}$ (2 mg), substrate ***L*-68** (3.6 mg, 0.01 mmol) which was readily obtained from chiral HPLC resolution (Column: CHIRALPAK AY-3, 4.6*100 mm; Solvents: MeOH/MeCN, **Supplementary Figure 82**) and DCM (500 μL) on the ProBox reactor (450 nm). The solution was stirred under LED light irradiation for 15 min. (P3-P4-P5-P7-ProBox reactor)

Step 4: At the end of the 15-minute reaction, the solution in the ProBox reactor was transferred into the vial located on a heater by gas pressure. Rinse the reaction tube with another 2 mL MeCN which was then transferred to the same vial. (P7-P10-heated reactor; P9-P7; P7-P10-heated reactor)

Step 5: The crude reaction solution containing the ^{18}F-labeled ***L*-68** was evaporated under vacuum and nitrogen flow using a gradient of temperature 110 ℃ for 5 min. The reactor was then actively cooled to 50 °C using a compressed air flow.

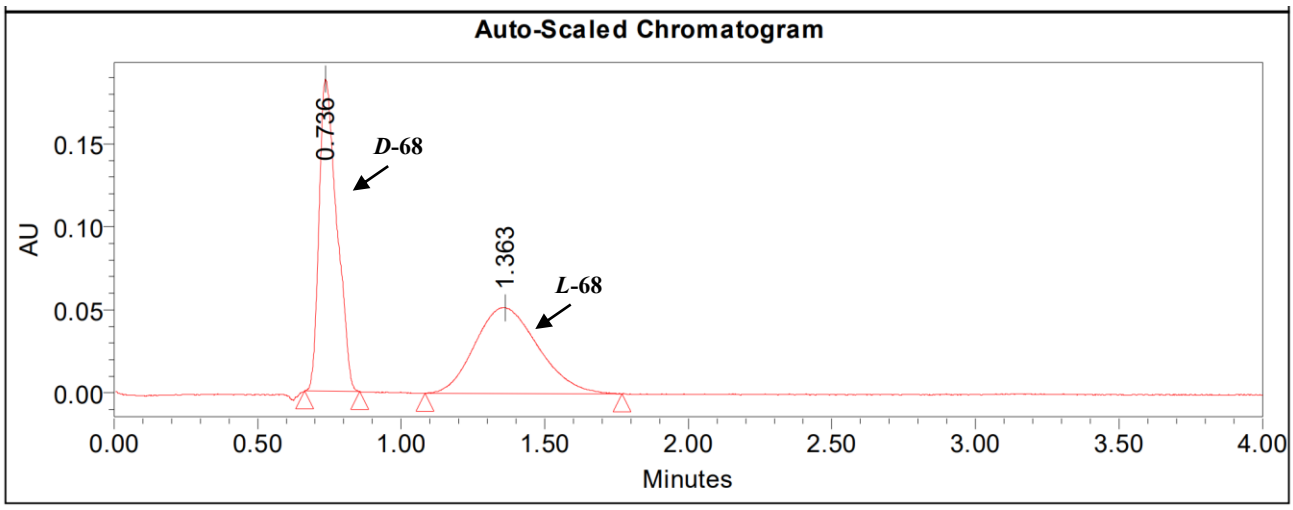
Step 6： 1 mL HI (55 wt.% in H_2O) at P8 (Site C) was then added into the vial in the heated reactor, followed by a sealed reaction at 160 °C for 15 min. The reactor was cooled to 50 °C before the reaction mixture was neutralized through the 3 mL K_2HPO4 solution (3 M) at P14 (Site D). (P14-P10)

Step 7: The crude reaction mixture (4 mL) was passed through the Alumina N cartridge (P12) pretreated with 30 mL water and a sterile nylon syringe filter to remove unreacted [^{18}F]F^- and insoluble catalyst residue before loading to HPLC. (P10-P9-P12)

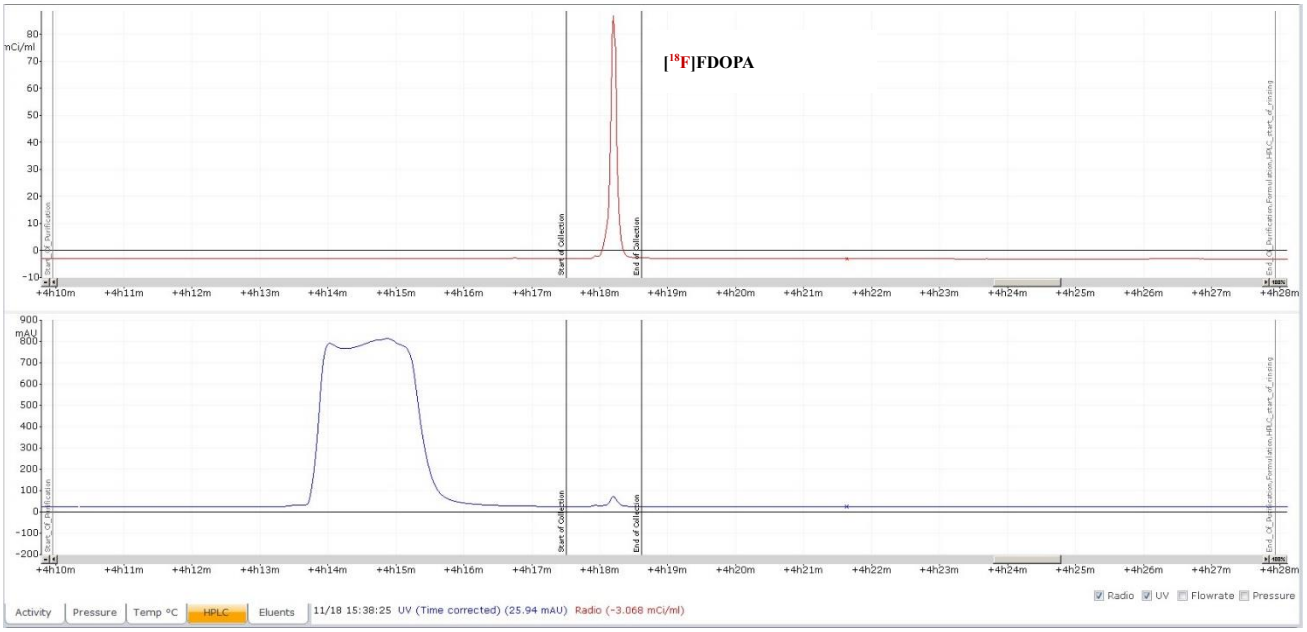
Step 8: Additionally, the reactor vial was subsequently rinsed with another 3 mL of water (P17, Site E) using the 10 mL HSW Syringe (P9), repeating step 7 to transfer the potentially remaining crude reaction mixture thoroughly. Finally, a total of 7 mL of sample was collected in the intermediate transfer vial and then loaded on the loop circle using a 20 mL BD Syringe (P14). (P17-P9-P10-P9-P12; P13-P14-P15)

Step 9: The [^{18}F]FDOPA isolated from HPLC was collected by switching the collection valve to the empty final product vial (**Supplementary Figure 83**). HPLC conditions: Phenomenex, Kinetex® 4 μm Synergi 80 Å, 250 x 10.00 mm LC Column. Mobile phase: 10 mM KH_2PO4. Flow rate: 4 mL/min.

The [^{18}F]FDOPA was successfully synthesized and isolated in 14.8% RCY (non-decay corrected) in 84 min with 99% ee on the commercial radiosynthesis module (AllinOne 4530) collecting with an LED reactor. The synthesis data was summarized in the **Supplementary Table 80.** The isolated product and the absolute configuration were confirmed by comparison with the racemic FDOPA and the clinically produced FDOPA from a commercial ^{18}F-FDOPA cassette for AllinOne (**Supplementary Figure 84**). HPLC conditions: 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. Flow rate: 1 mL/min



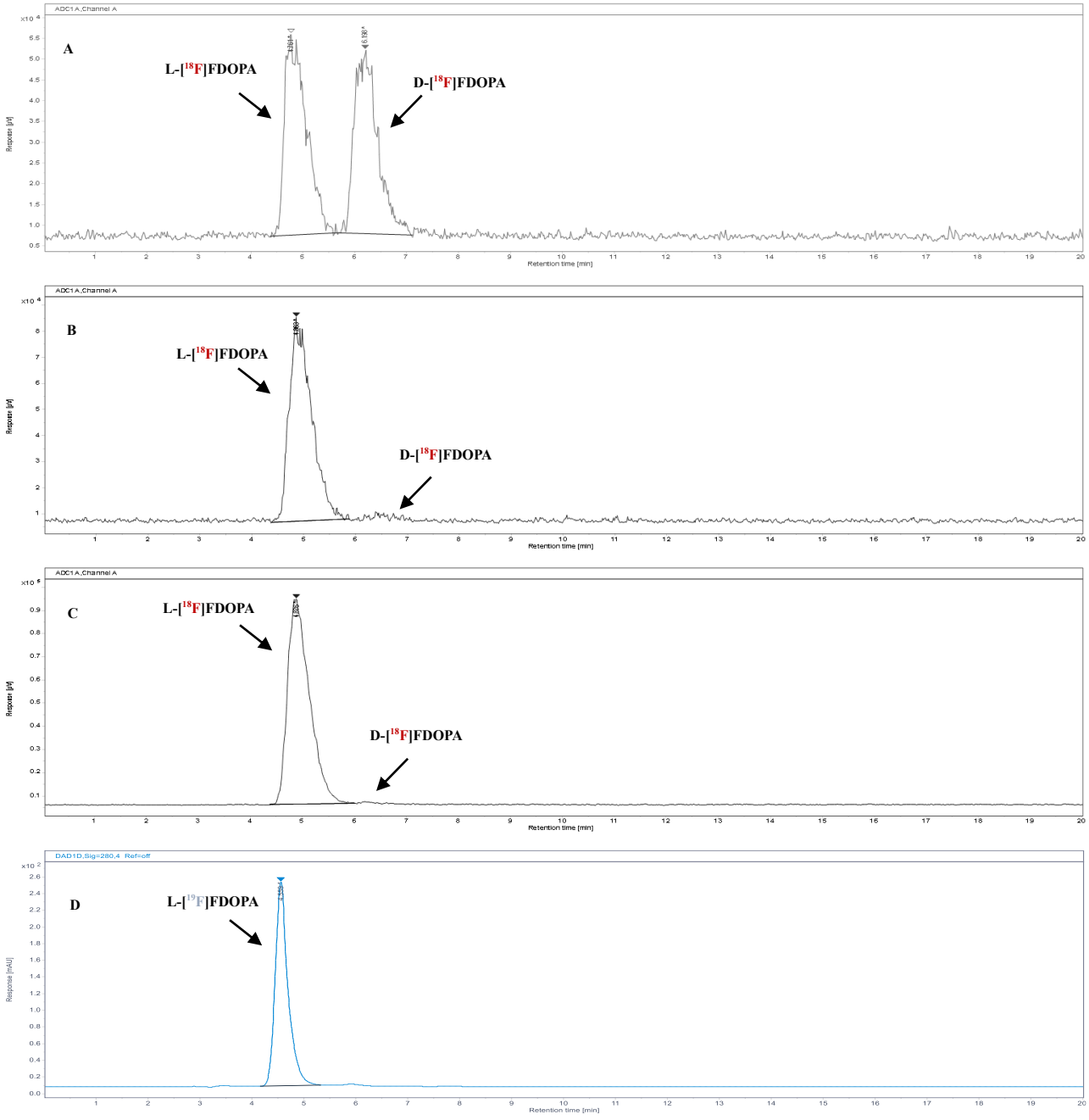
Supplementary Figure 82. Chiral HPLC resolution of **68** to provide the *L*-**68**



Supplementary Figure 83. HPLC isolation of [^{18}F]FDOPA.

Substrate	Elution efficiency (EE)	Isolated activity	RCY (non-decay corrected)	Enantiomeric excess (ee)	Synthesis time
***L*-68**	143 mCi/(143+5.9) mCi = 96%	20.7 mCi	14.8%	99%	84 min

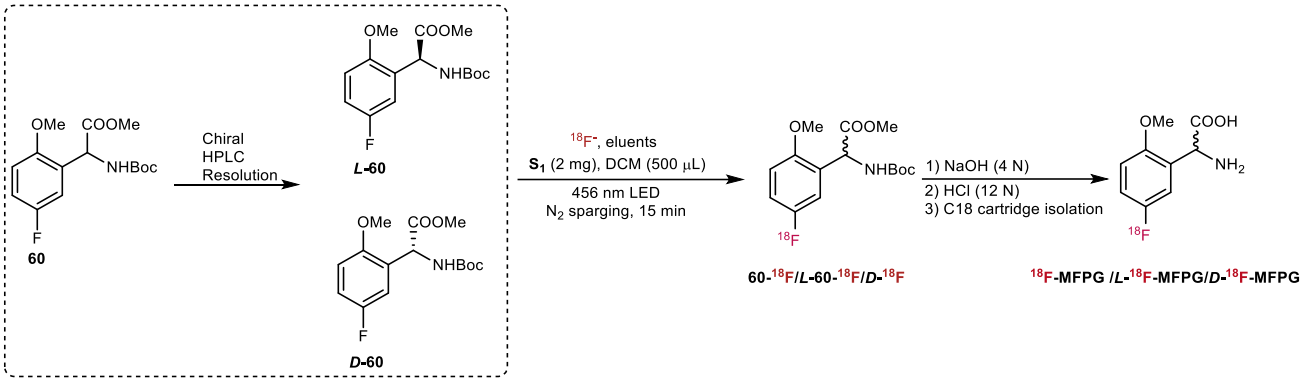
Supplementary Table 80. Automatic synthesis of **[^{18}F]FDOPA** from ***L*-68** on an AllinOne module



Supplementary Figure 84. HPLC traces for confirmation of [^{18}F]FDOPA. (A) radio-HPLC trace of racemic [^{18}F]FDOPA. (B) radio-HPLC trace of [^{18}F]FDOPA produced by a commercial AllinOne cassette. (C) [^{18}F]FDOPA produced by the azeotropic drying-free photoredox-catalyzed method. (D) UV trace (280 nm) of the [^{19}F]FDOPA.

4. PET tracer prearation and imaging study

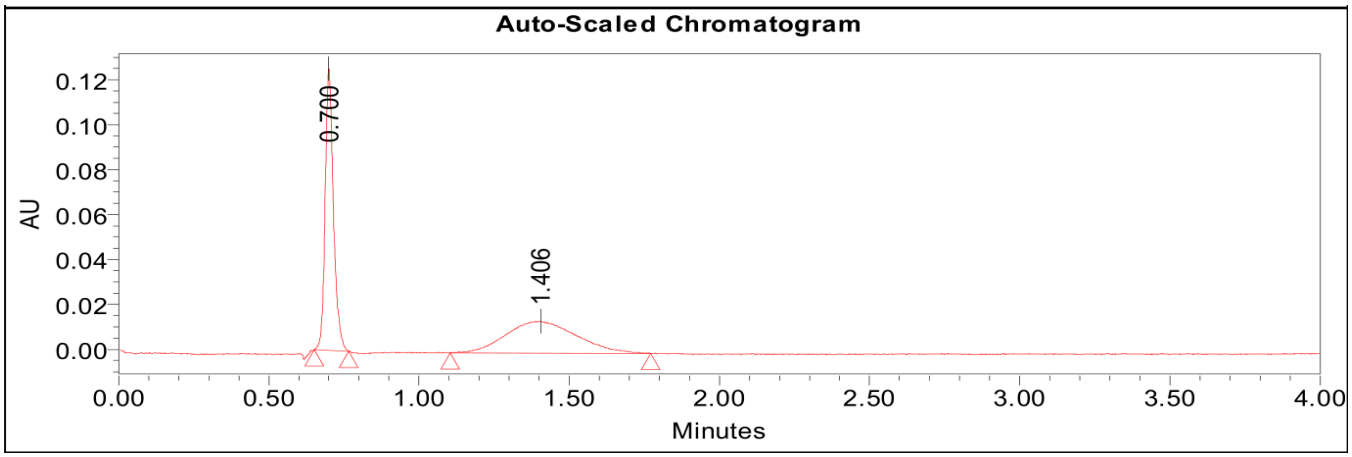
4.1 Preparation of PET tracer ^{18}F-MFPG, *L*-^{18}F-MFPG and *D*-^{18}F-MFPG



Following the general labelling procedure at section **3.8**, the substrate **60** and two enantiomers (***L*-60** and ***D*-60**) which were obtained from chiral HPLC resolution (Column: CHIRALPAK AY-3, 4.6*100mm; Solvents: MeOH/MeCN, Supplementary Figure **80**) were labelled under standard conditions with DCM as the solvent from 60 – 100 mCi $^{18}F^-$. After the irradiation, the reaction was diluted with 1 ml MeCN. The solution was passed through an aluminum cartridge (preconditioned with 5 ml 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 a sealed 5 ml V-vial preloaded with 50 µl 4N NaOH solution. The solvent was removed under 100 °C with a nitrogen stream, which generally takes 20 to 25 min. After the solvent was removed, 100 µl concentrated HCl was added into the V-vial, and the mixture was heated under 100 C for 15 min. A venting needle was then equipped before 1 ml water and 400 µl saturated $NaHCO_3$ was slowly added to the V-vial. The resulting aqueous solution was loaded on a C18 cartridge preconditioned with 5 ml EtOH and 5 ml water. The C18 cartridge was then eluted with 2.5 ml water and the solution was collected in 1.5 ml Eppendorf tubes (~500 µl each) to provide the PET tracers **^{18}F-MFPG, *L*-^{18}F-MFPG** and ***D*-^{18}F-MFPG**, respectively. The Eppendorf tube, which collected the highest dose of activity (2 – 6 mCi), was analyzed on HPLC and used for PET imaging study after the pH was adjusted to around 7 and diluted with saline solution.

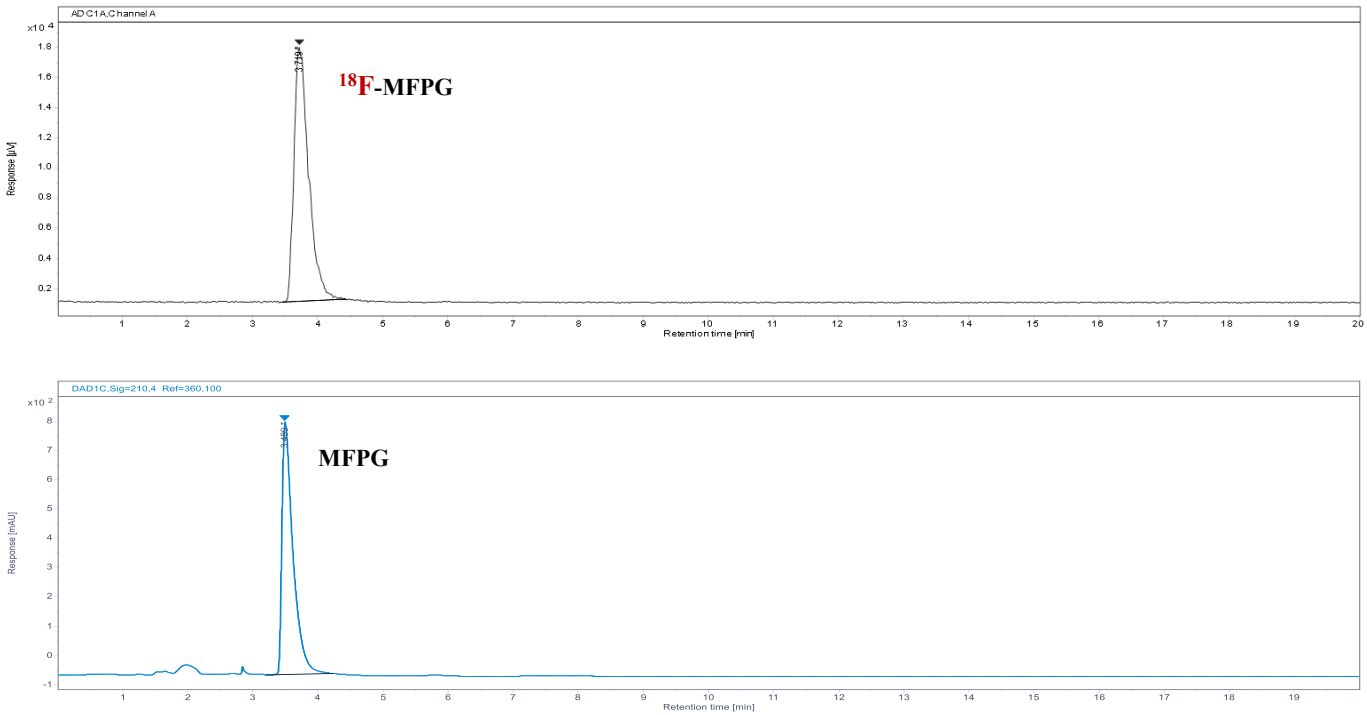
HPLC conditions for PET tracer analyzation:

Column: Phenomenex Gemini® C18 110Å column (5 µm, 4.6 × 250 mm). Solvent A: Phosphate buffer (pH = 8); Solvent B: Acetonitrile. Isocratic elution at 3% solvent B. Flow rate: 1 ml/min.



Supplementary Figure 85. Chiral HPLC resolution of **60** to provide the *L*-**60** and *D*-**60**

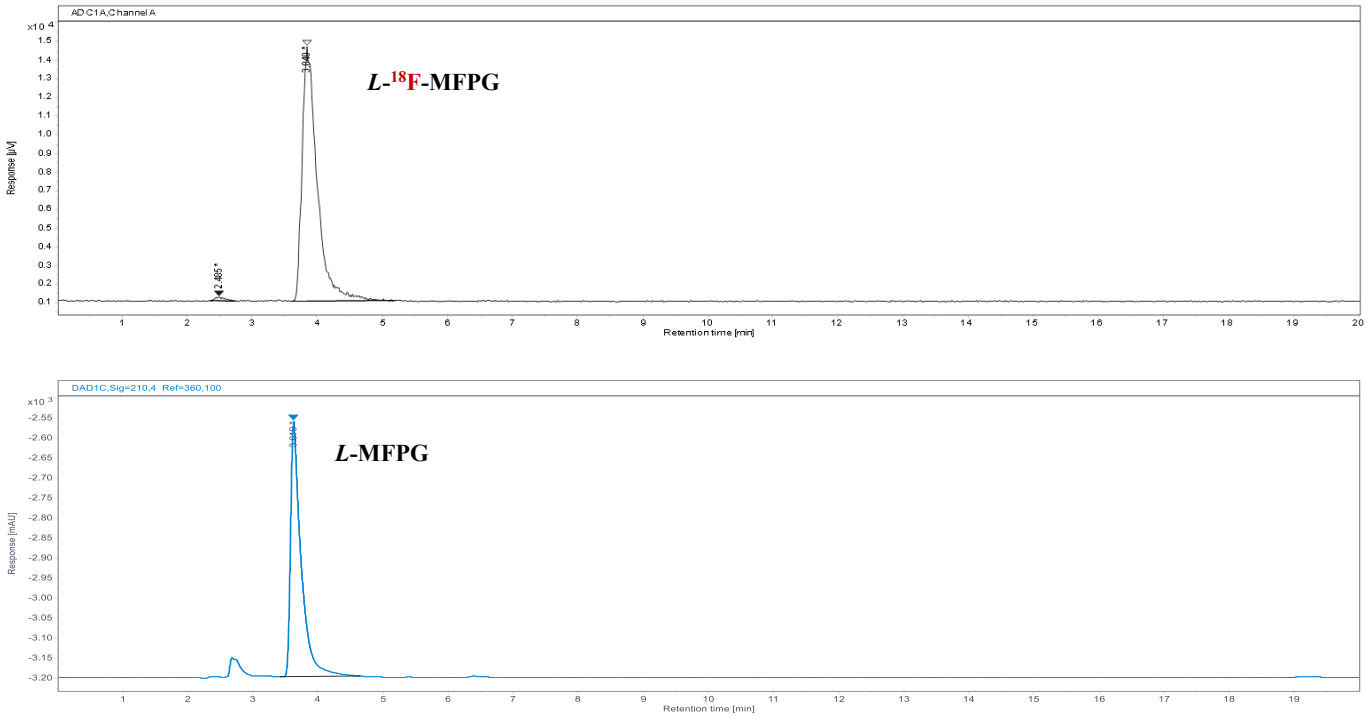
HPLC traces of ^{18}F-MFPG:



#	RT (min)	Area (µV·s)	Area%	Height (µV)	Height%	Start time (min)	End time (min)
1	3.719	264821.828	100.000	16948.991	100.00	3.424	4.432

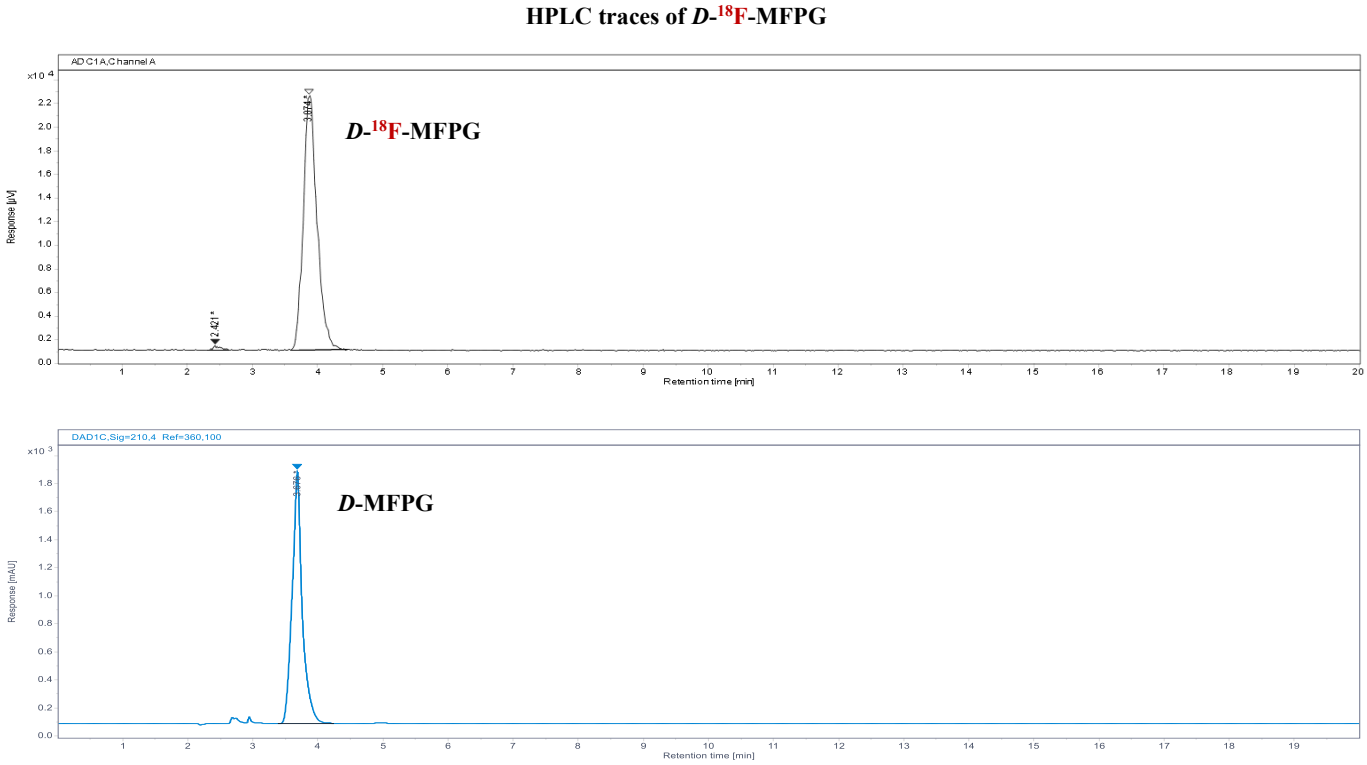
Supplementary Figure 86. Radio-HPLC analysis of ^{18}F-**MFPG**.

HPLC traces of *L*-^{18}F-MFPG



#	RT (min)	Area (μV·s)	Area%	Height (μV)	Height%	Start time (min)	End time (min)
1	2.485	1974.727	0.898	170.883	1.24	2.363	2.737
2	3.849	218037.943	99.102	13641.941	98.76	3.601	5.214

Supplementary Figure 87. Radio-HPLC analysis of ***L*-^{18}F-MFPG**



#	RT (min)	Area (μV·s)	Area%	Height (μV)	Height%	Start time (min)	End time (min)
1	2.421	2996.457	0.946	358.991	1.64	2.300	2.639
2	3.874	313802.533	99.054	21552.694	98.36	3.584	4.456

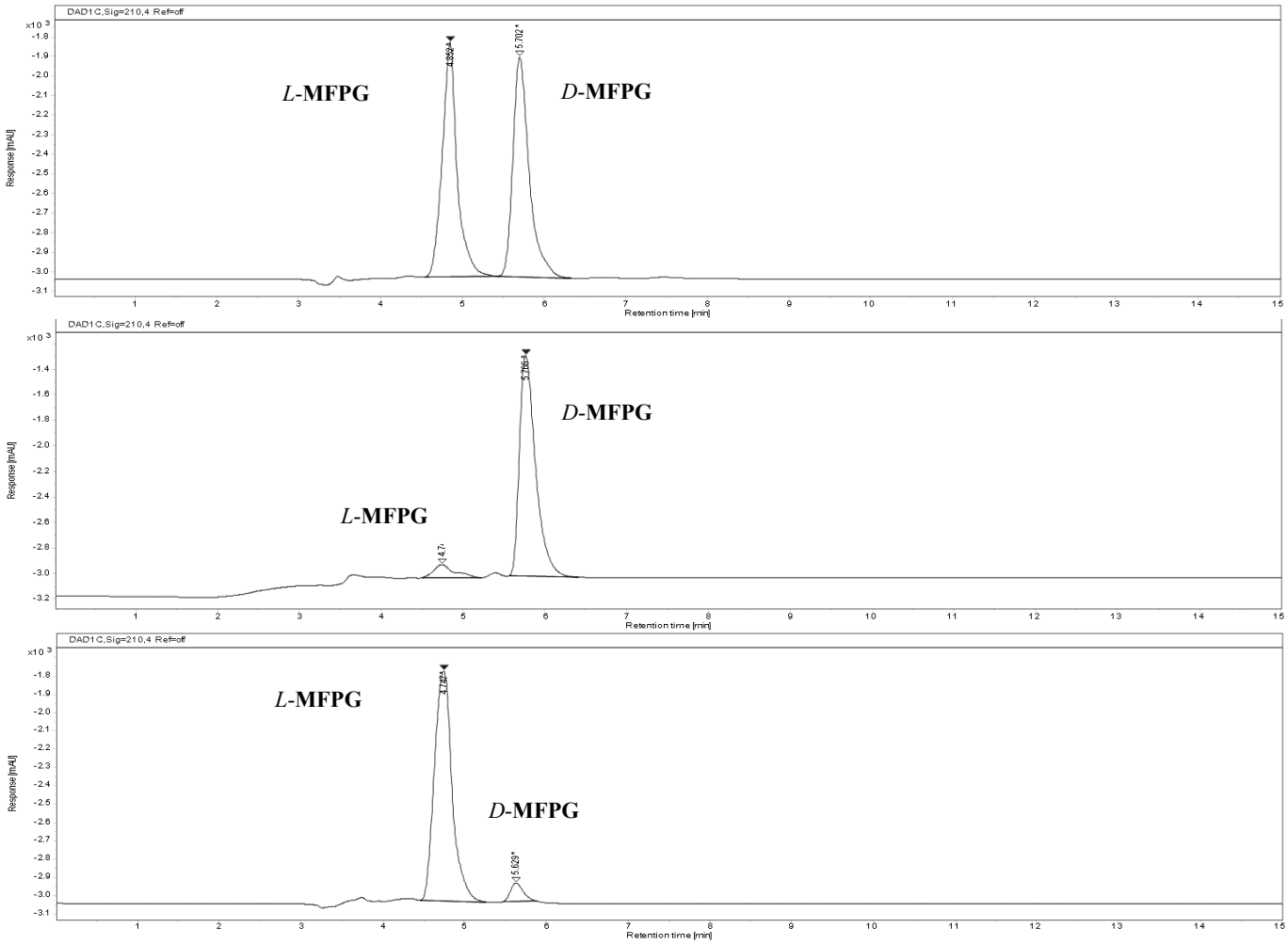
Supplementary Figure 88. Radio-HPLC analysis of ***D*-^{18}F-MFPG**

4.2 Racemization monitoring of the PET tracers

Considering that strong base and acid were used for the deprotection, the tracers after decay were analyzed on a chiral HPLC column. The HPLC UV traces demonstrated that there was no obvious racemization of the isolated ***L*-^{18}F-MFPG** and ***D*-^{18}F-MFPG** under current deprotection conditions (**Supplementary Figure 84**).

HPLC conditions:

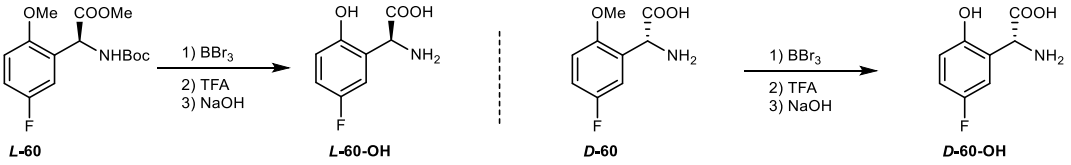
Column: Astec CHIROBIOTICR T Chiral HPLC Column, 5 μm particle size, 250 mm x 4.6 mm, SUPELCO. Mobile phase: 0.2 mL formic acid in 700 ml MeOH and 300 mL water (pH = 3.5). Flow rate: 1 ml/min



Supplementary Figure 89. Chiral HPLC analyzation of the UV trace of the tracers

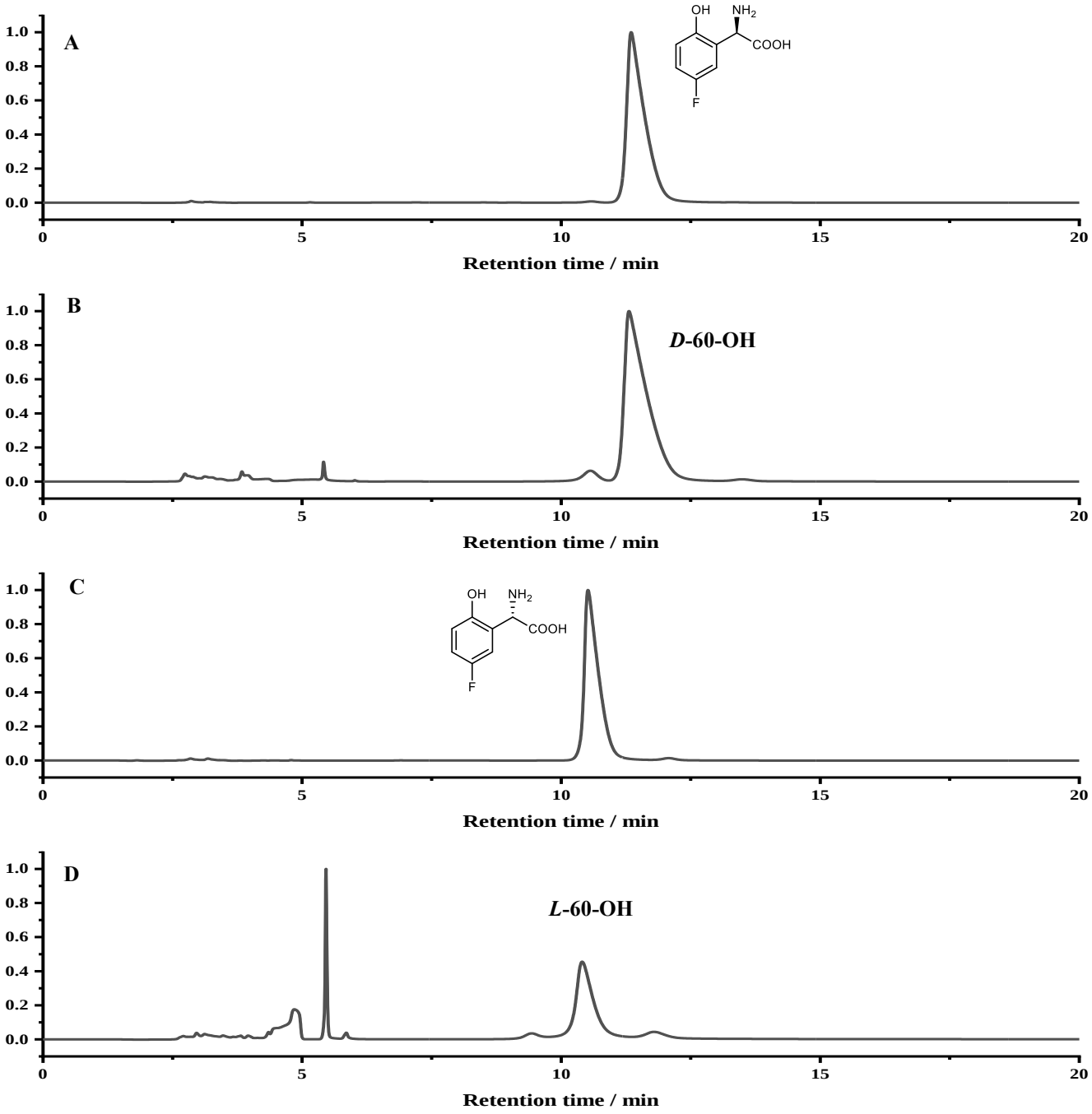
4.3 Confirmation of the absolute configuration of the two enantiomers *L*-^{18}F-MFPG and *D*-^{18}F-MFPG

The absolute configuration of the two enantiomers ***L*-^{18}F-MFPG** and ***D*-^{18}F-MFPG** were confirmed by comparision of the HPLC traces of the ***L*-60-OH** and ***D*-60-OH** with commercial standard compounds after removal of the methyl group on the oxygen (Supplementary Figure **85**).



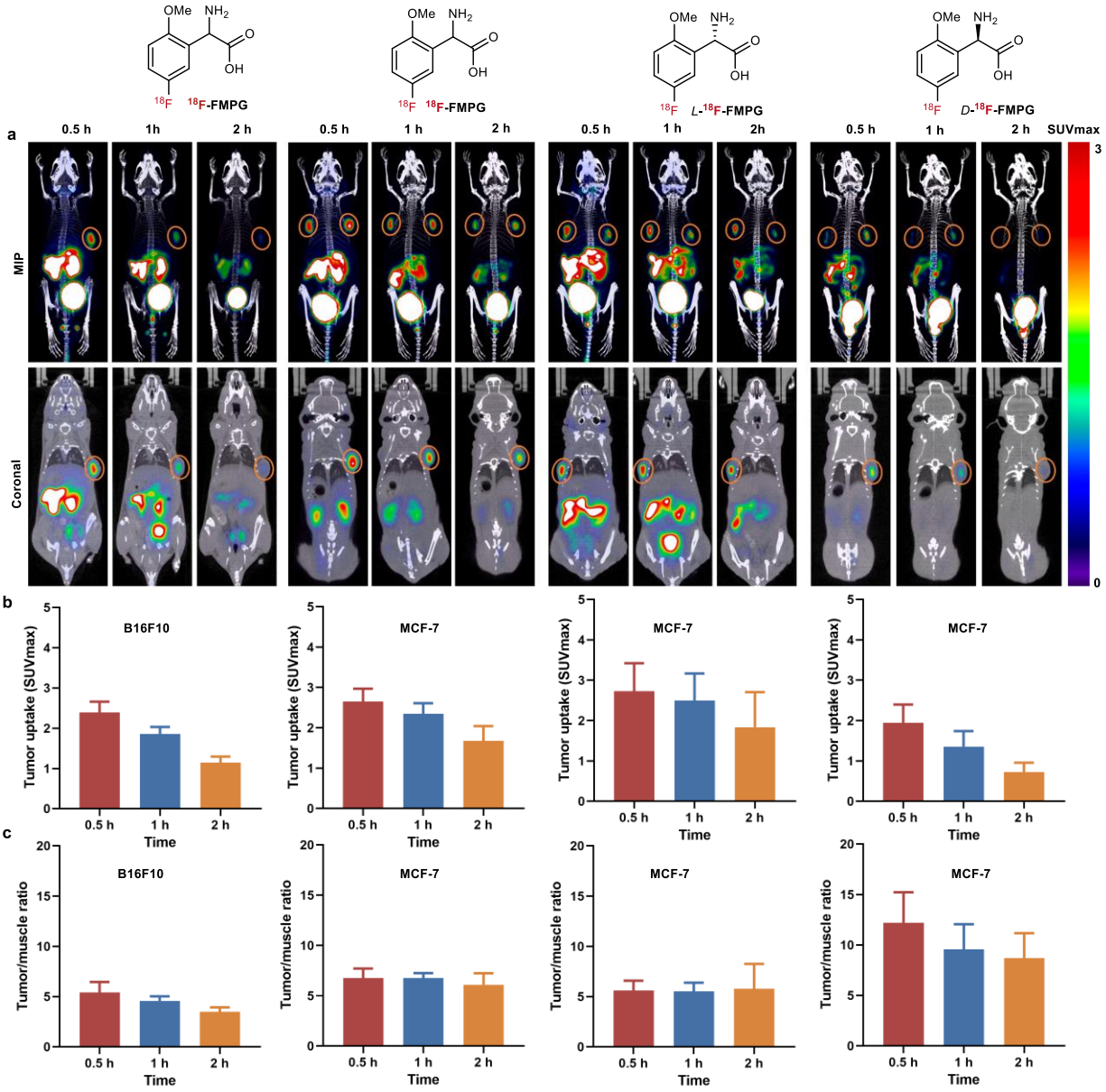
General procedure for the deprotection: the enantiomer (6.2 mg, 0.02 mmol) was dissolved in DCM (5 mL), 6.8 μL (0.06 mmol) BBr_3 was added. The mixture was stirred at room temperature for overnight and then quenched with 1 ml MeOH. The resulting solution were concentrated to remove volatile compounds. The residue was dissolved in 2 ml 10% TFA in DCM and stirred for 1h, the mixture was concentrated in vacuo. The residue was stirred in 1 ml 4 N NaOH for 1h, and then concentrated in vacuo to give the crude product of ***L*-60-OH** or ***D*-60-OH**, which were then analyzed and compared with commercial standards on

the HPLC. HPLC conditions: 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 800 ml MeOH and 200 mL water. Flow rate: 1 ml/min



Supplementary Figure 90. Confirmation of the absolute configuration of the two enantiomers by comparison with standards. Commercial standards (**A** and **C**); Compound obtained from chiral resolution after deprotection (**B** and **D**)

4.4 PET imaging studies



Supplementary Figure 91. a, PET imaging of the **^{18}F-FMPG**, *L*-**^{18}F-FMPG** and *D*-**^{18}F-FMPG** in B16F10 and MCF-7 tumour models (from left to right) at 0.5h, 1h, 2h post-injection. b, tumour uptake of **^{18}F-FMPG**, *L*-**^{18}F-FMPG** and *D*-**^{18}F-FMPG** (SUVmax) in B16F10 and MCF-7 tumour models (from left to right) at 0.5h, 1h, 2h post-injection. c, tumour/muscle ratio of **^{18}F-FMPG,** *L*-**^{18}F-FMPG** and *D*-**^{18}F-FMPG** (SUVmax) in B16F10 and MCF-7 tumour models (from left to right) at 0.5h, 1h, 2h post-injection.

All animal studies were conducted in compliance with the protocol approved by the Animal Care and Use Committees guidelines in West China Hospital and Sichuan University (Approval NO.20230515009). BALB/c nude mice and C57BL/6 mice (female, 6–8 weeks age) were used in our studies and obtained from Vital River Laboratory Animal Technology Co., Ltd. All animals were group-housed (no more than five mice per cage) at an air temperature of 24 ± 3 °C, humidity of 60 ± 4% and

a 12-h light/12-h dark cycle. Food and water were provided *ad libitum*. The female BALB/c mice were subcutaneously inoculated with MCF-7 breast cancer cells in a mixture of Matrigel (high protein concentration; Corning) and PBS (5×10^6 tumor cells in 200 μL of Matrigel/PBS (1:1)). For female C57BL/6 mice, subcutaneous tumors were generated by inoculating B16-F10 mouse melanoma cells (5×10^6 tumor cells in 100 μL PBS) suspension. Tumor size and animal weight were measured 2 times per week.When tumors were 100-200 mm^3, PET/CT images of mice were produced using an IRIS small animal PET/CT imaging system (inviscan SAS, Strasbourg, France). Each PET tracer was tested randomly in at least three mice bearing unilateral or bilateral subcutaneous tumours to obtain an average uptake value. **^{18}F-FMPG** (3.7 MBq) was administered to the B16-F10 or MCF-7 tumor-bearing mice via the tail vein. At 30 min, 1 h, and 2 h post-injection, the tumor-bearing mice were imaged with the micro-PET/CT scan under anesthesia with 2% isoflurane. Data were acquired for 15 min for each scan and reconstructed with a three-dimensional ordered-subset expectation–maximization (3D-OSEM) algorithm with a Monte Carlo-based accurate detector model. CT acquisition was performed with 50 kV, 1 mA X-ray output and a total acquisition time of 140 s. PET images were analyzed using Osirix MD software version 10.0.4 (Pixmeo SARL), and data were expressed as standard uptake values (SUV) in animals. GraphPad Prism 9.5 was used to generate bar graphs and calculate means.

5. Reference

[1] T. Verdelet, S. Benmahdjoub, B. Benmerad, M. Alami, S. Messaoudi, *J Org Chem* **2019**, *84*, 9226-9238.

[2] N. E. S. Tay, W. Chen, A. Levens, V. A. Pistritto, Z. Huang, Z. Wu, Z. Li, D. A. Nicewicz, *Nat Catal* **2020**, *3*, 734-742.

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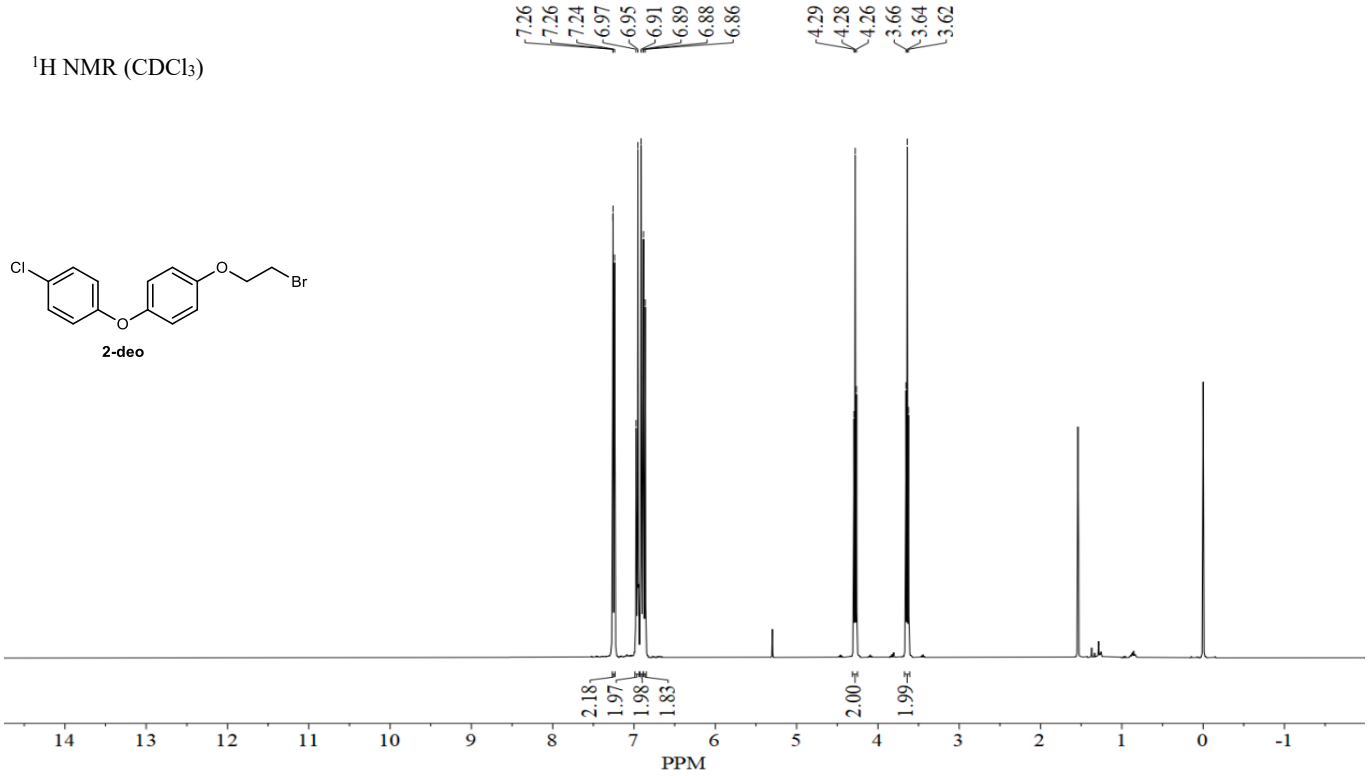
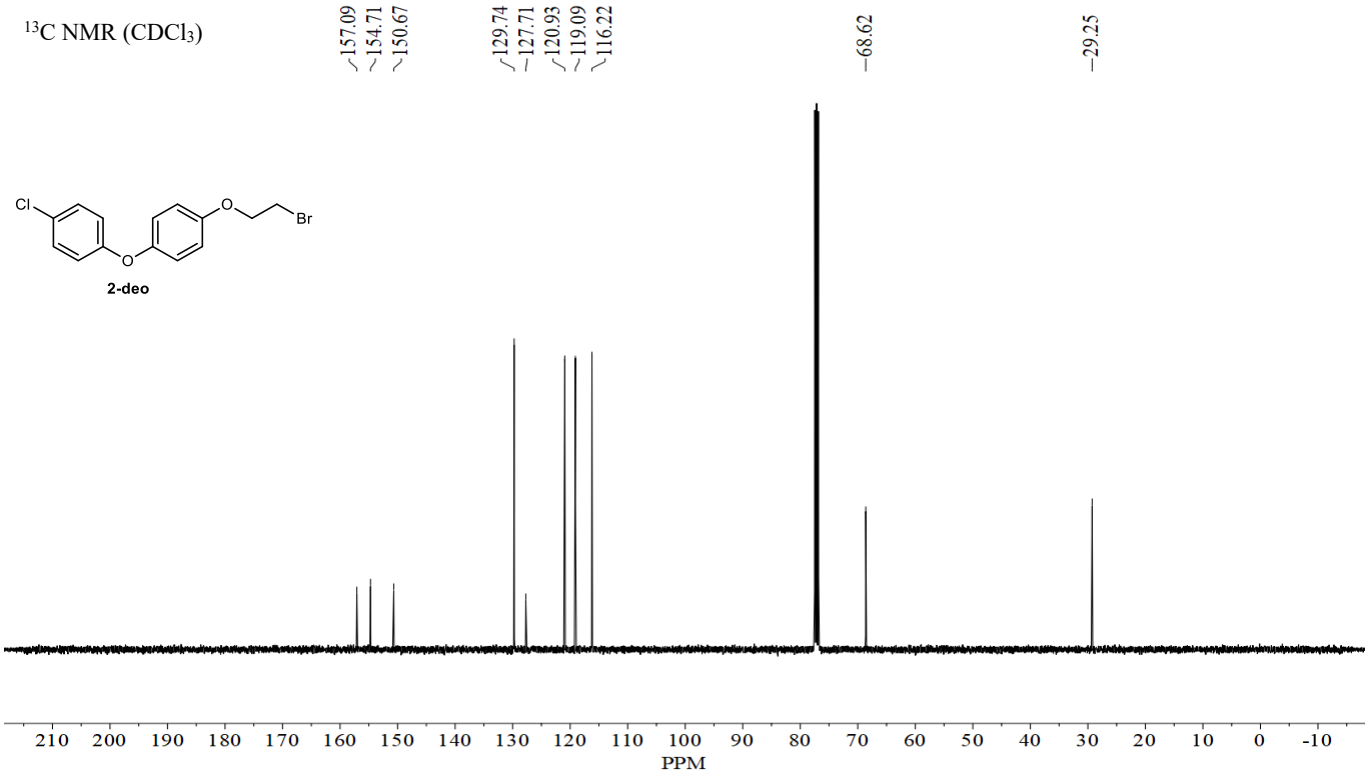
[6] W. Chen, H. Wang, N. E. S. Tay, V. A. Pistritto, K. P. Li, T. Zhang, Z. Wu, D. A. Nicewicz, Z. Li, *Nat Chem* **2022**, *14*, 216-223.

6. NMR spectra (^{1}H NMR, ^{13}C NMR, ^{19}F NMR)

^{1}H NMR ($CDCl_3$)



^{13}C NMR ($CDCl_3$)



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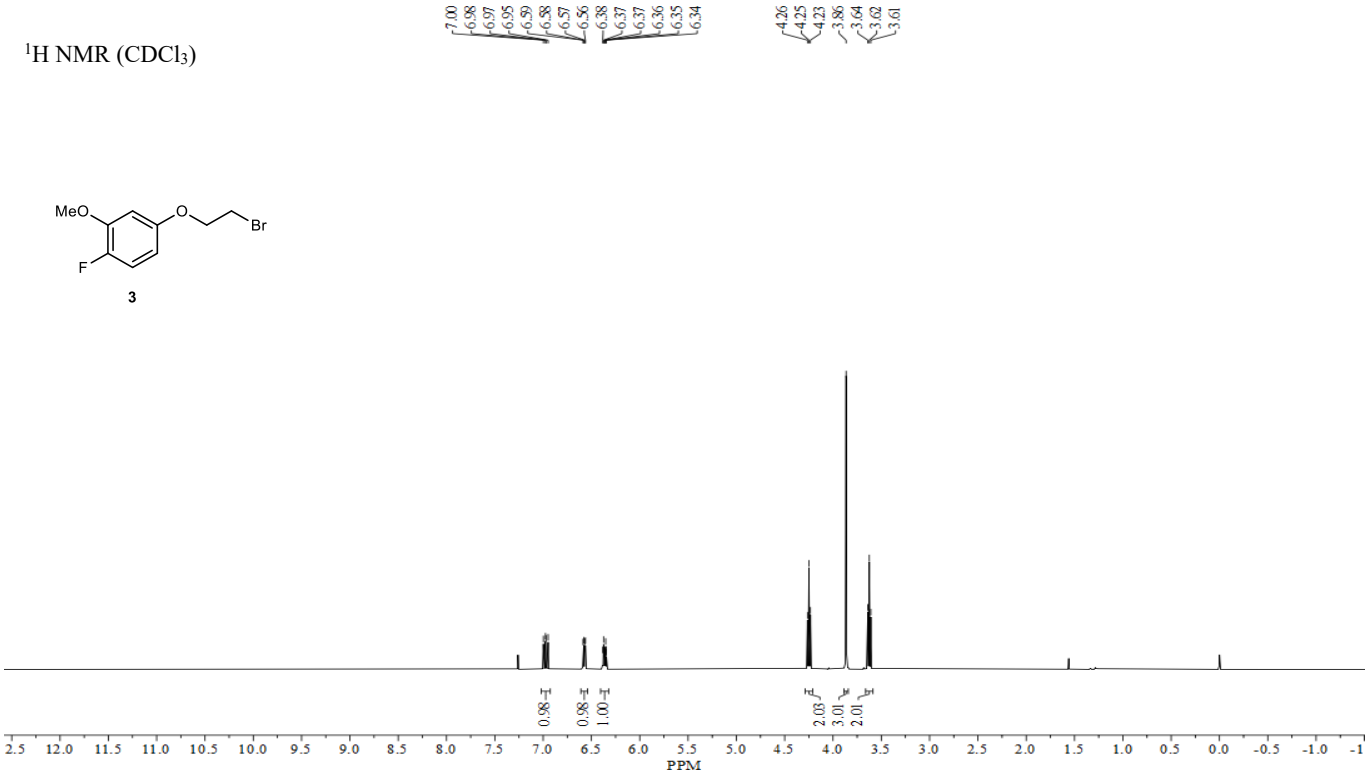
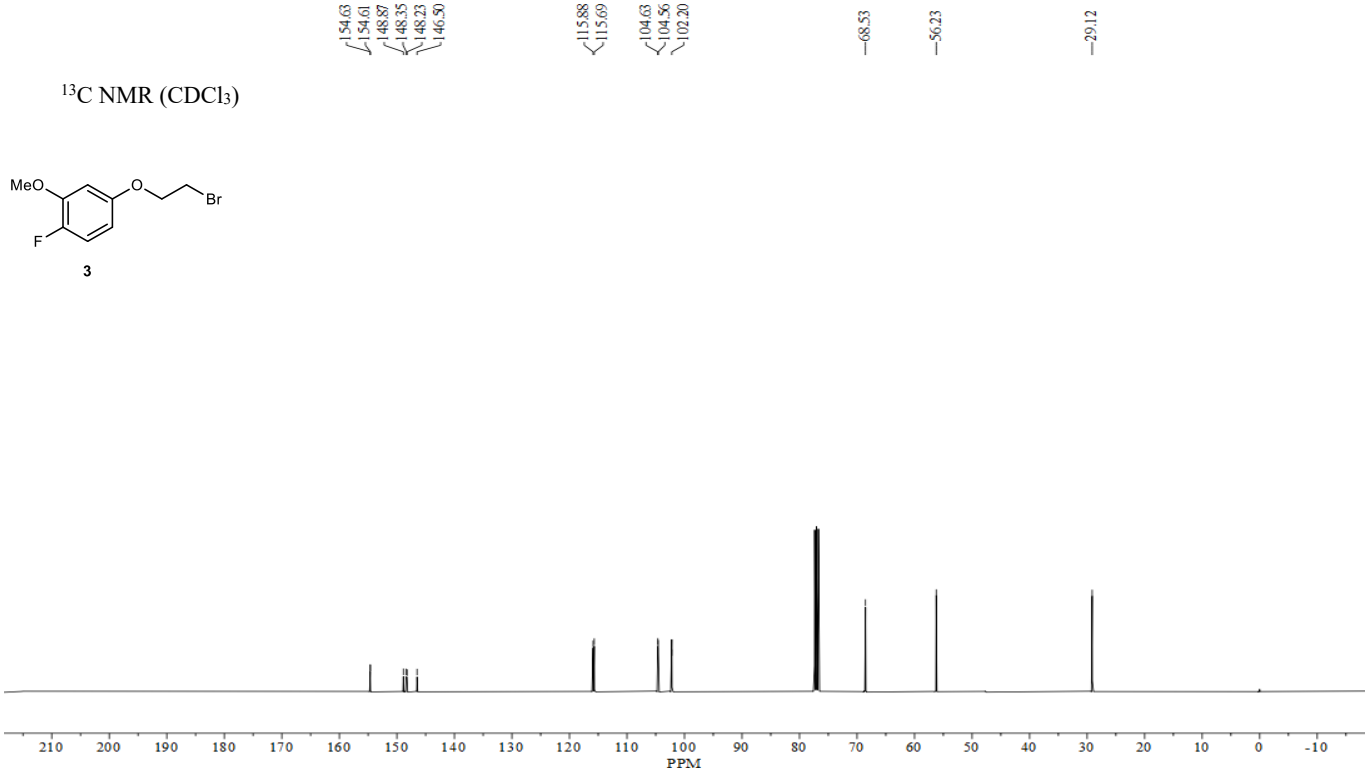
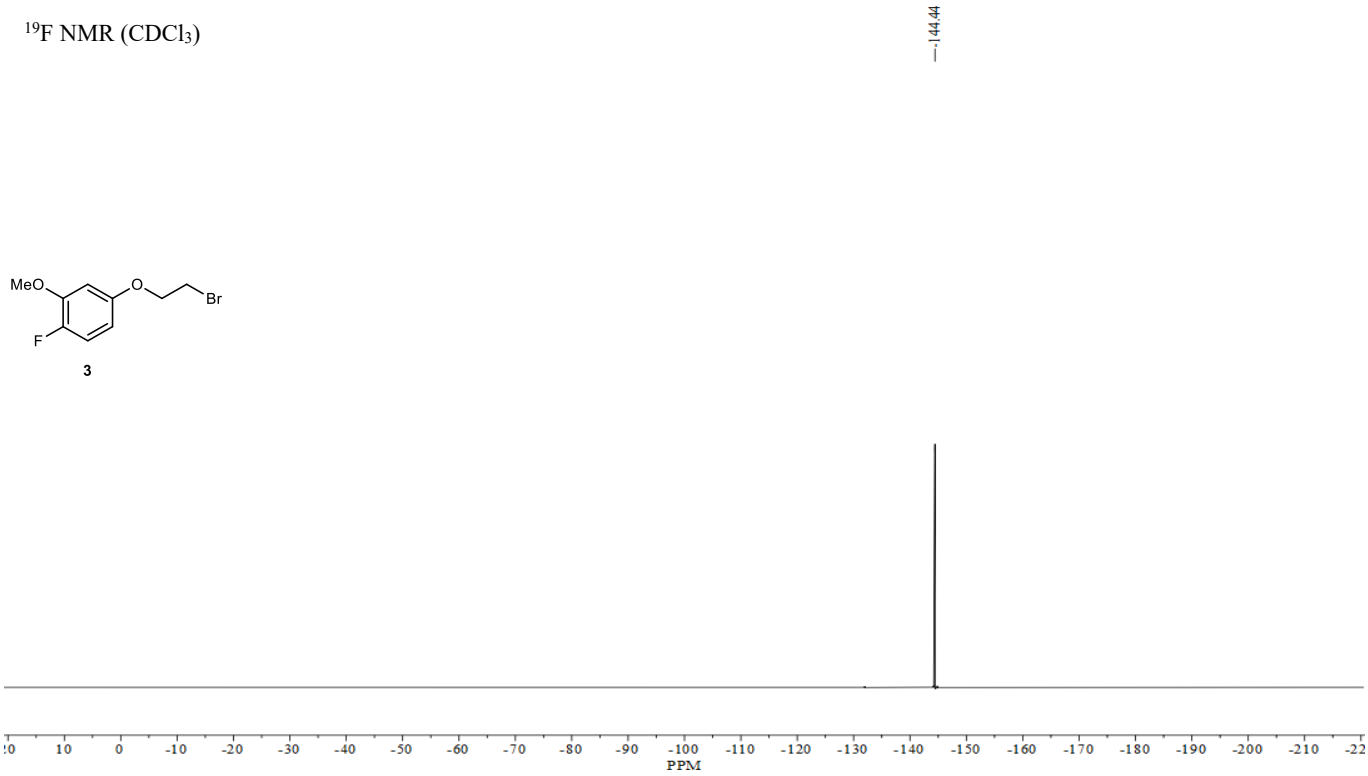




^{13}C NMR ($CDCl_3$)

^{19}F NMR ($CDCl_3$)



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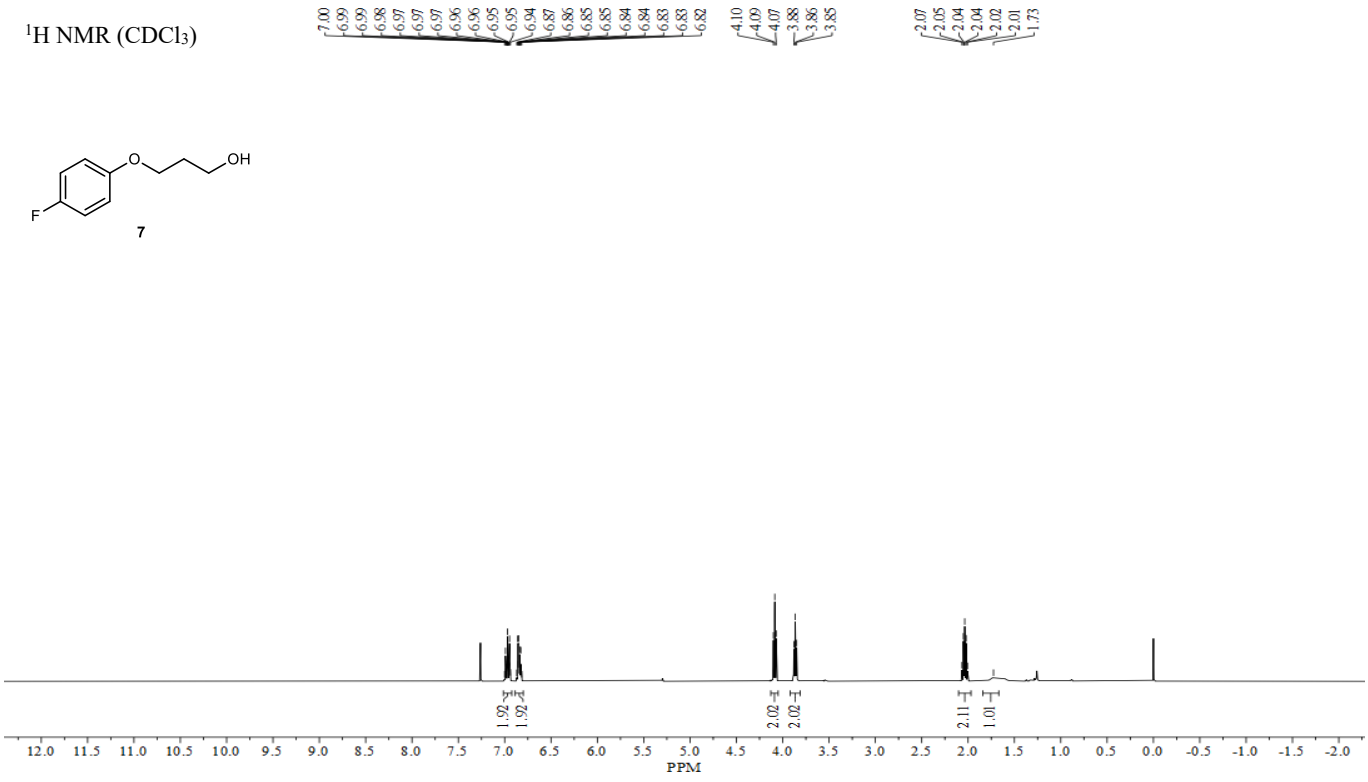

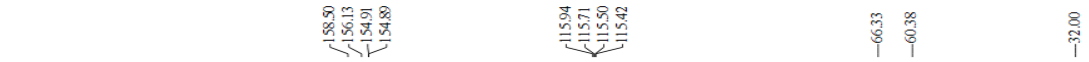

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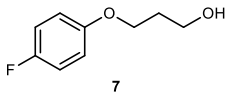

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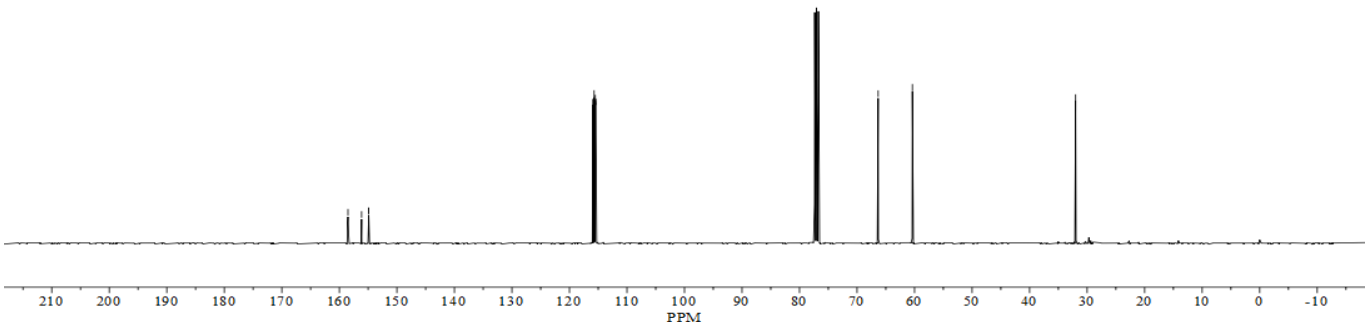

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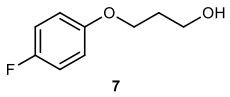

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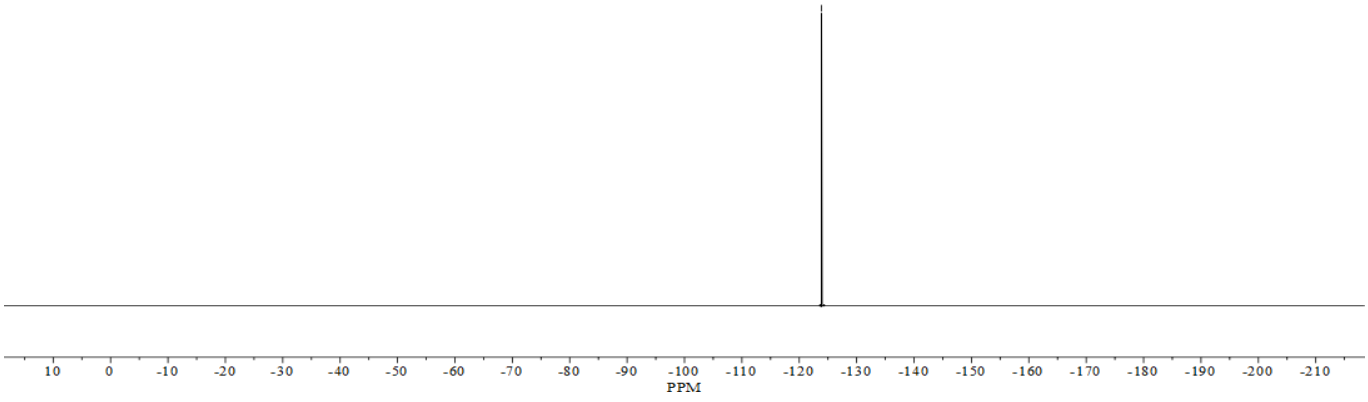

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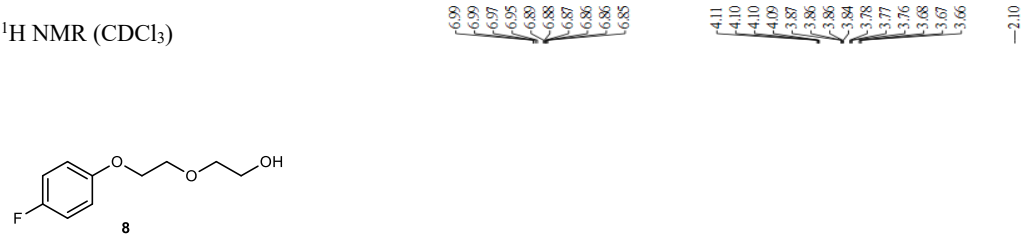

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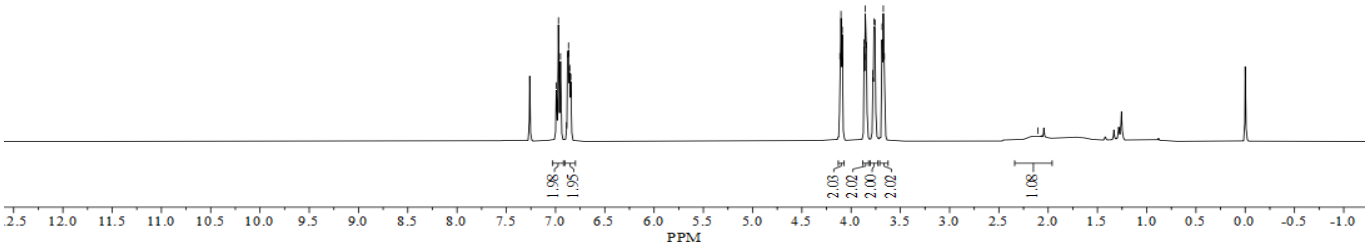

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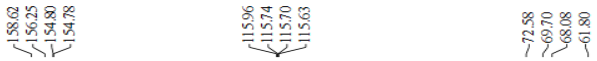

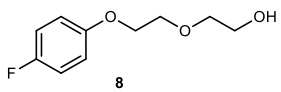

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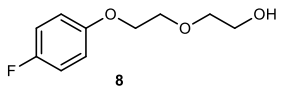

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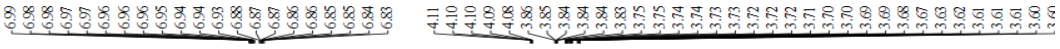

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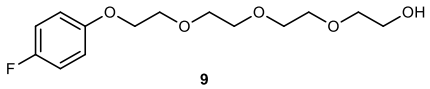

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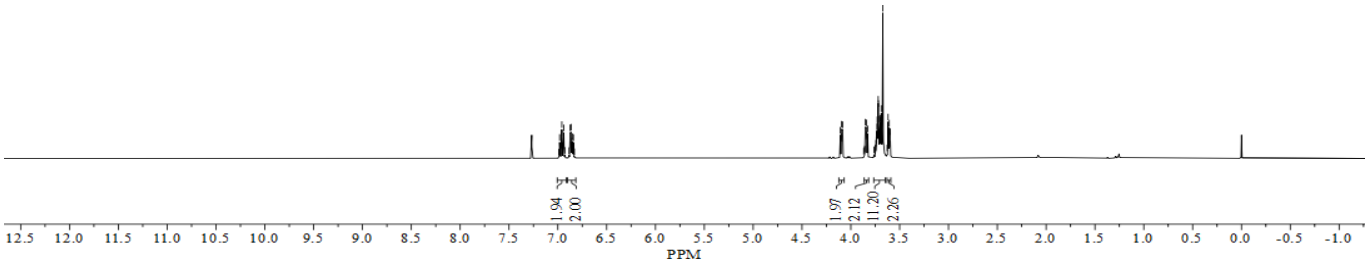

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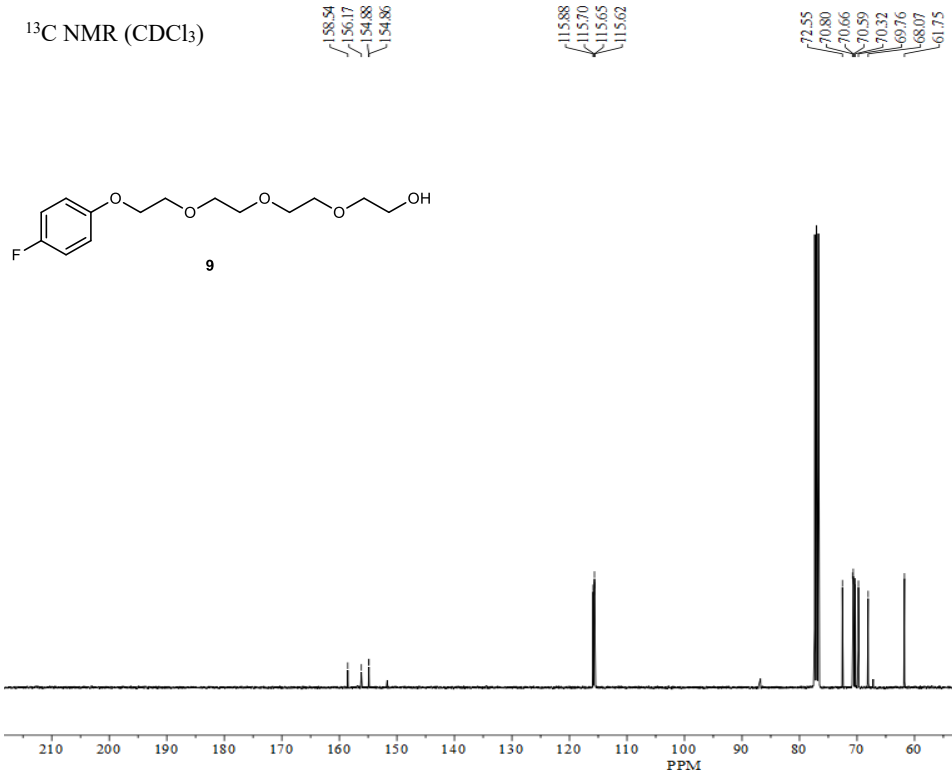

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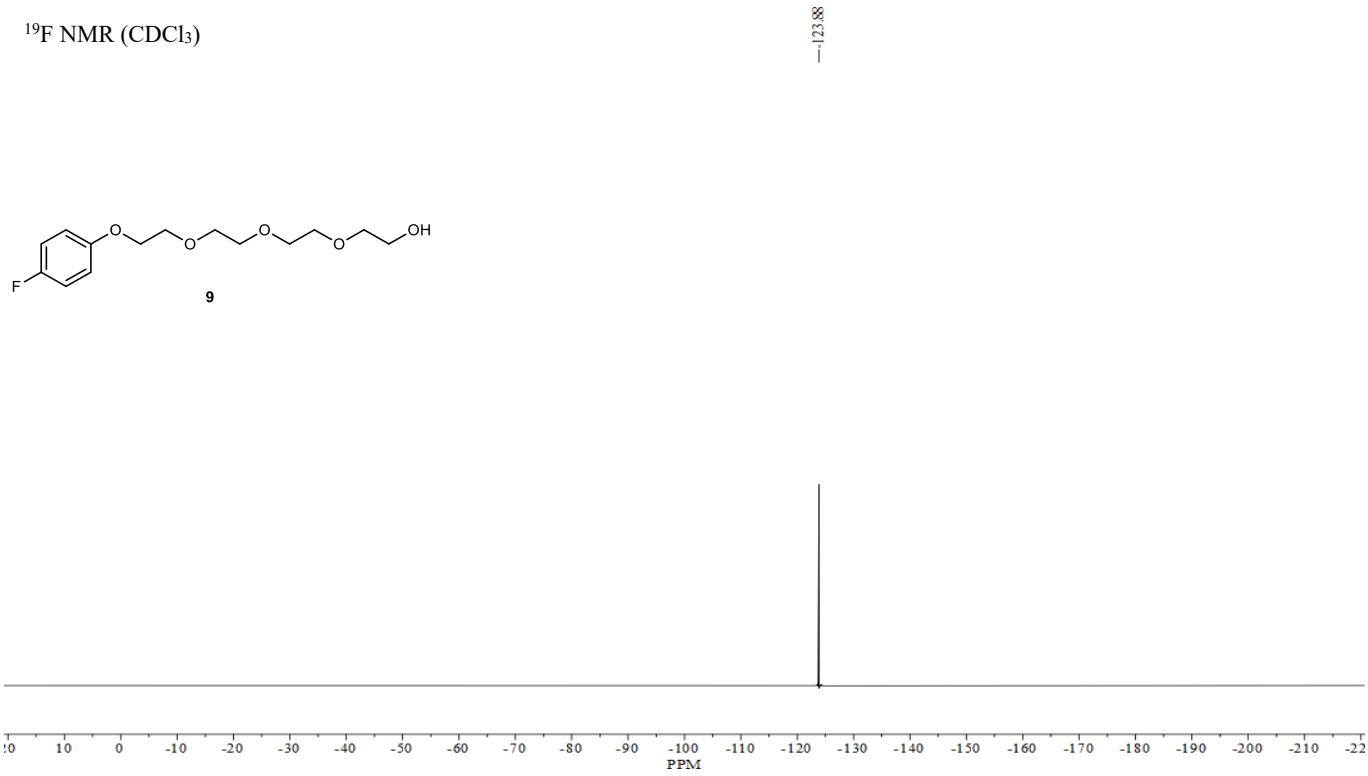

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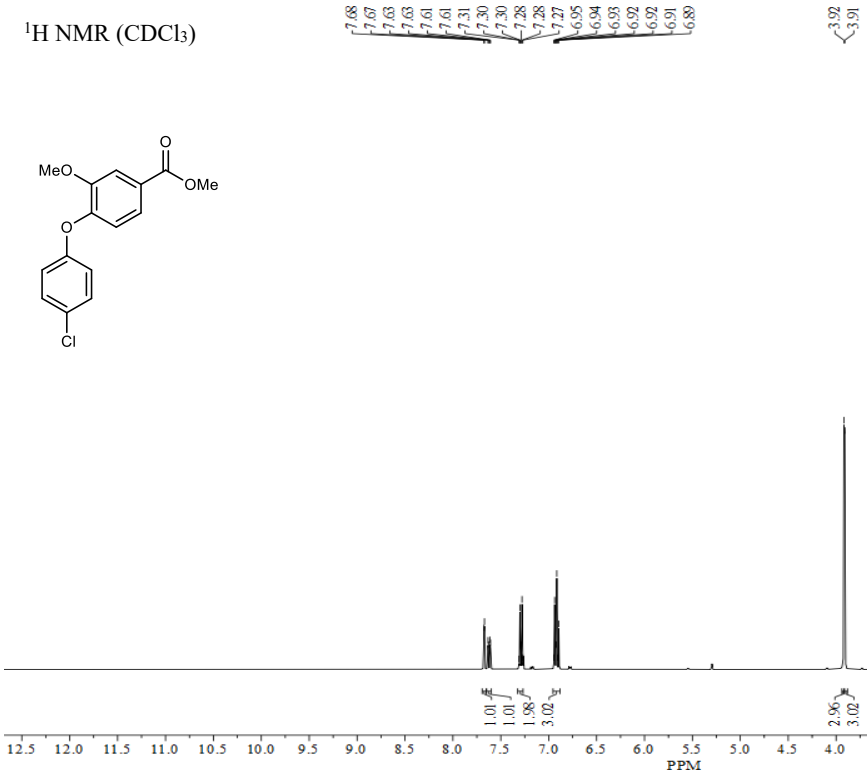

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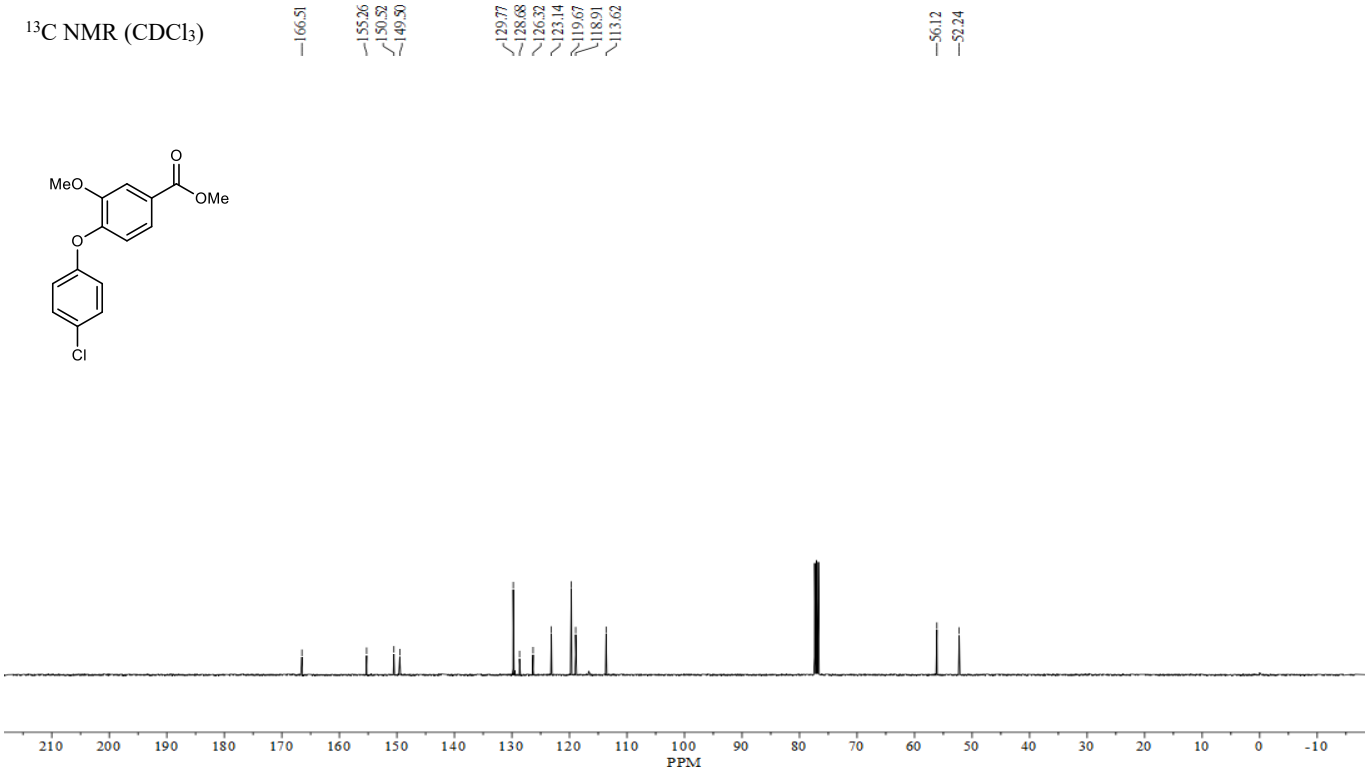

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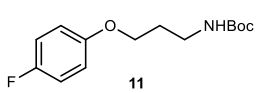

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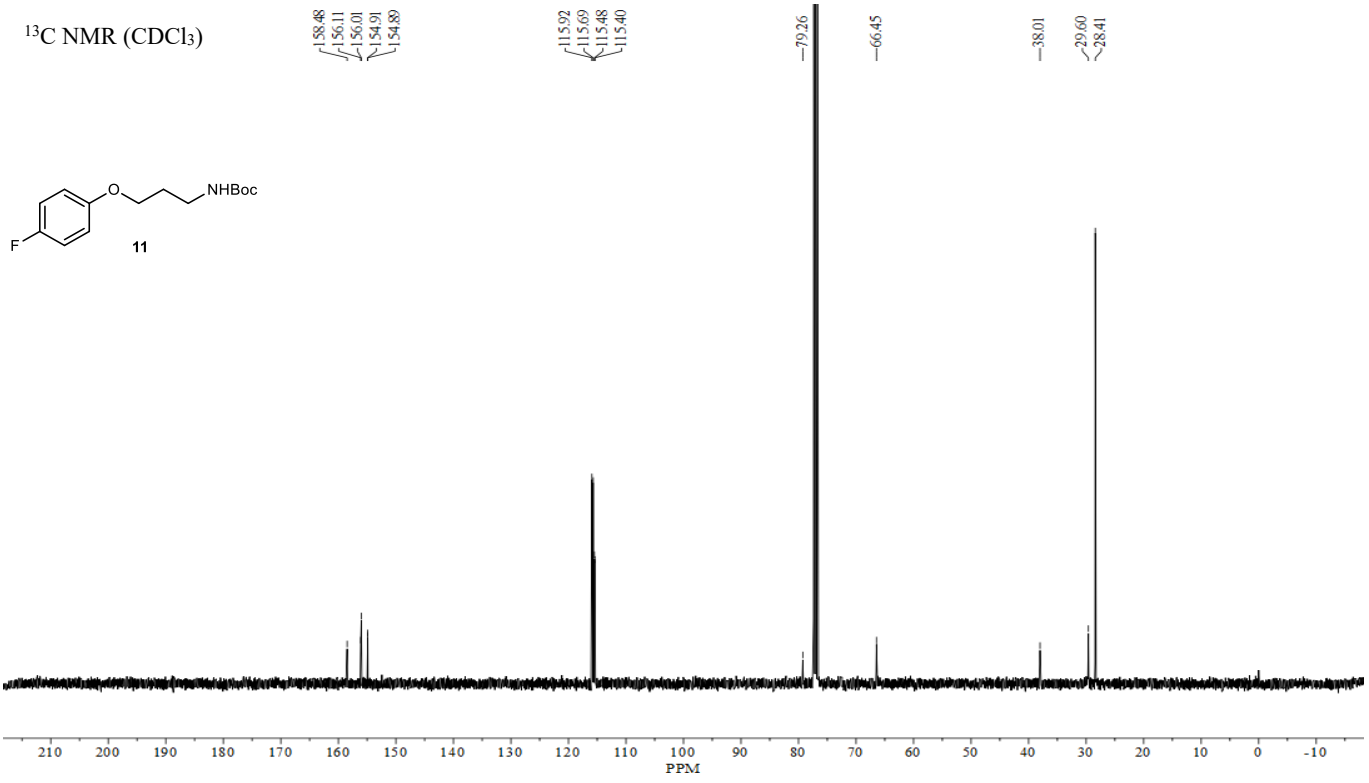

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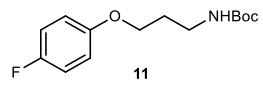

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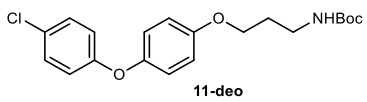

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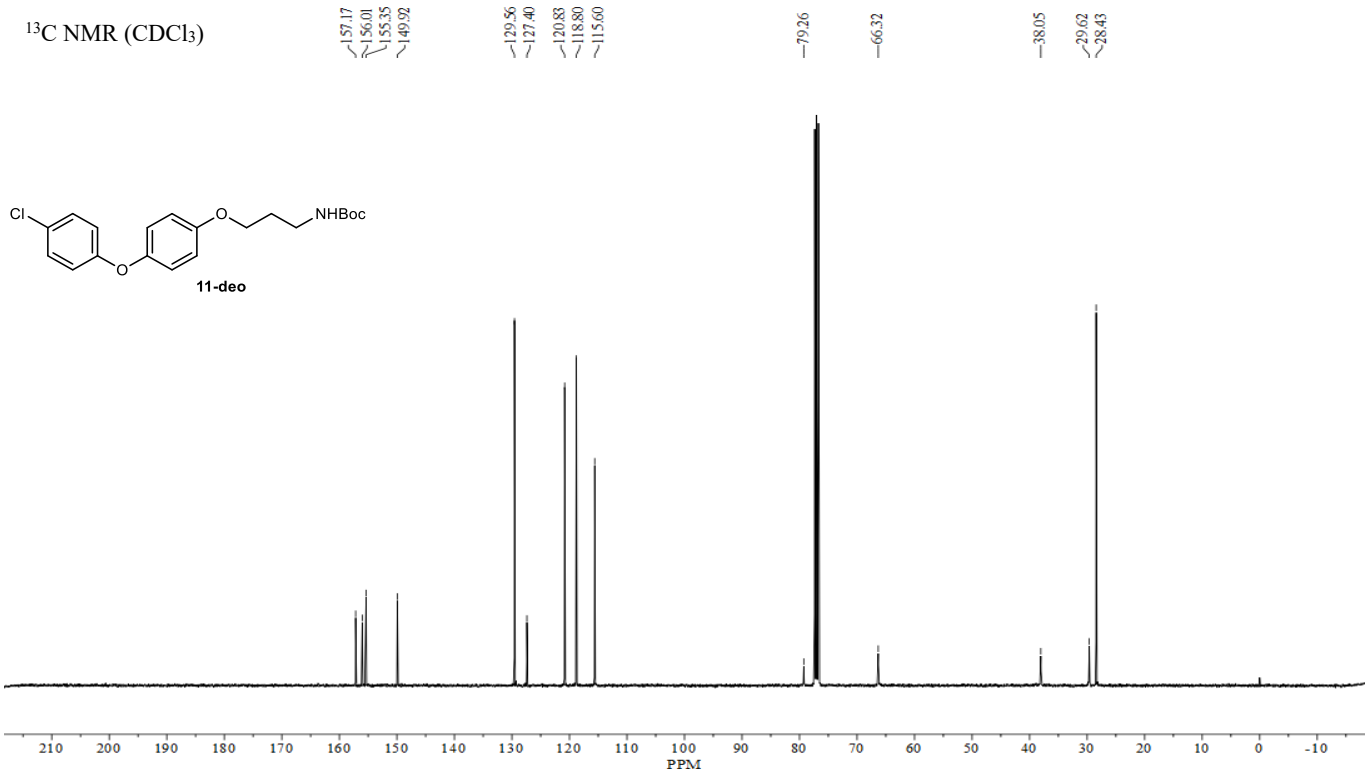

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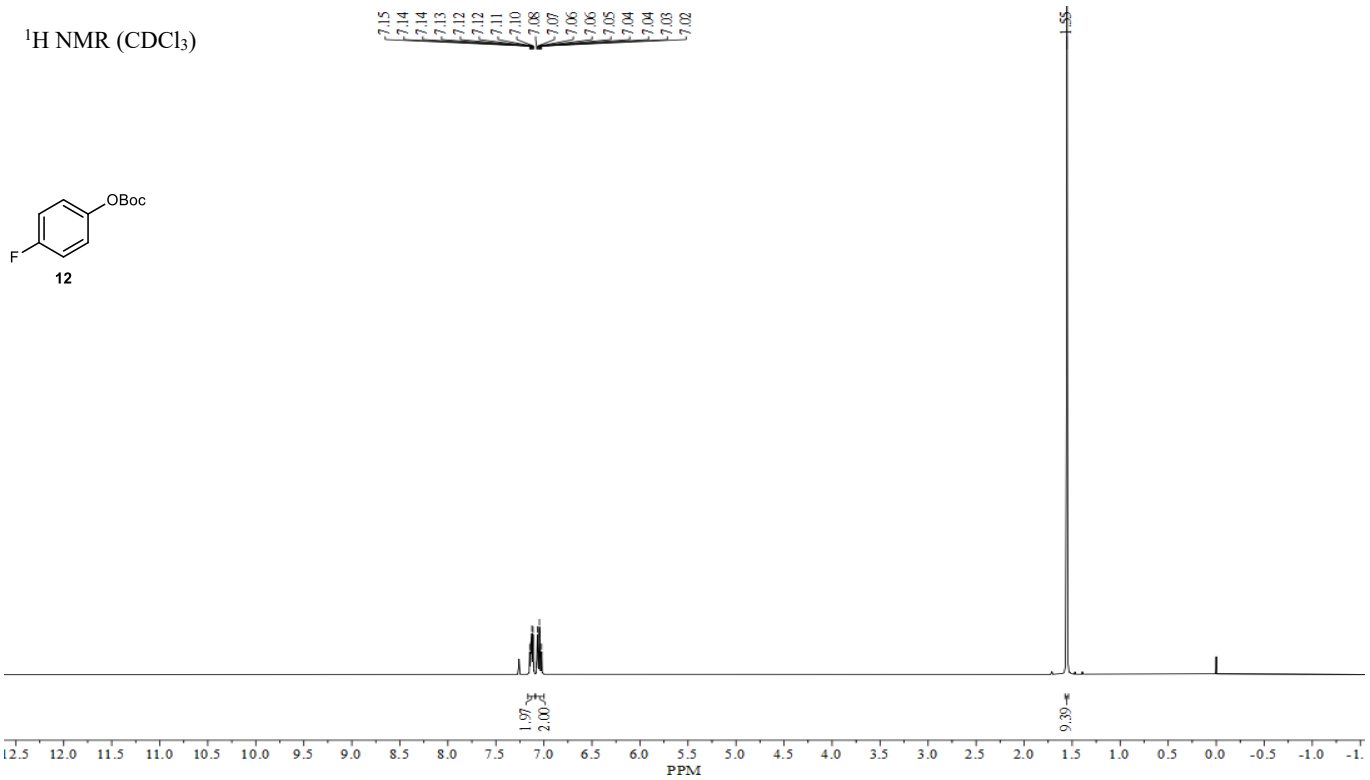

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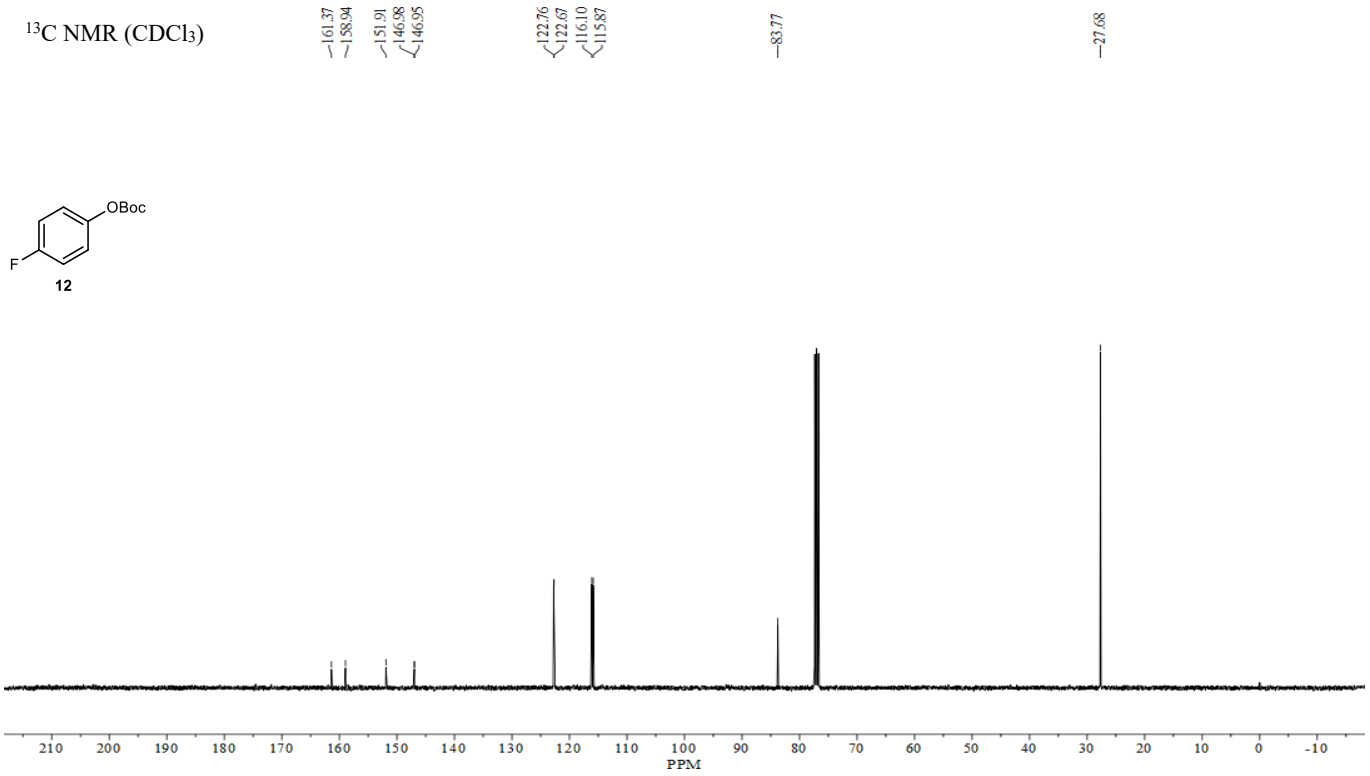
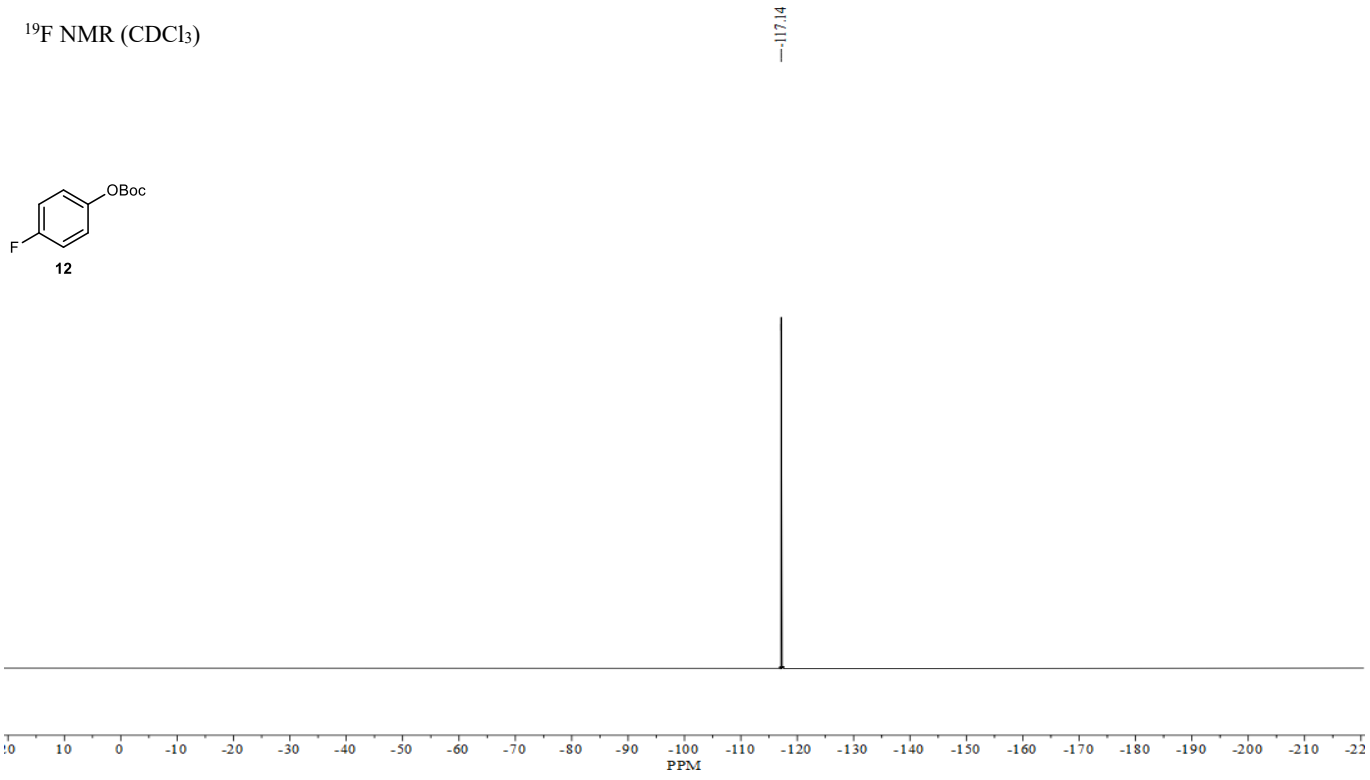
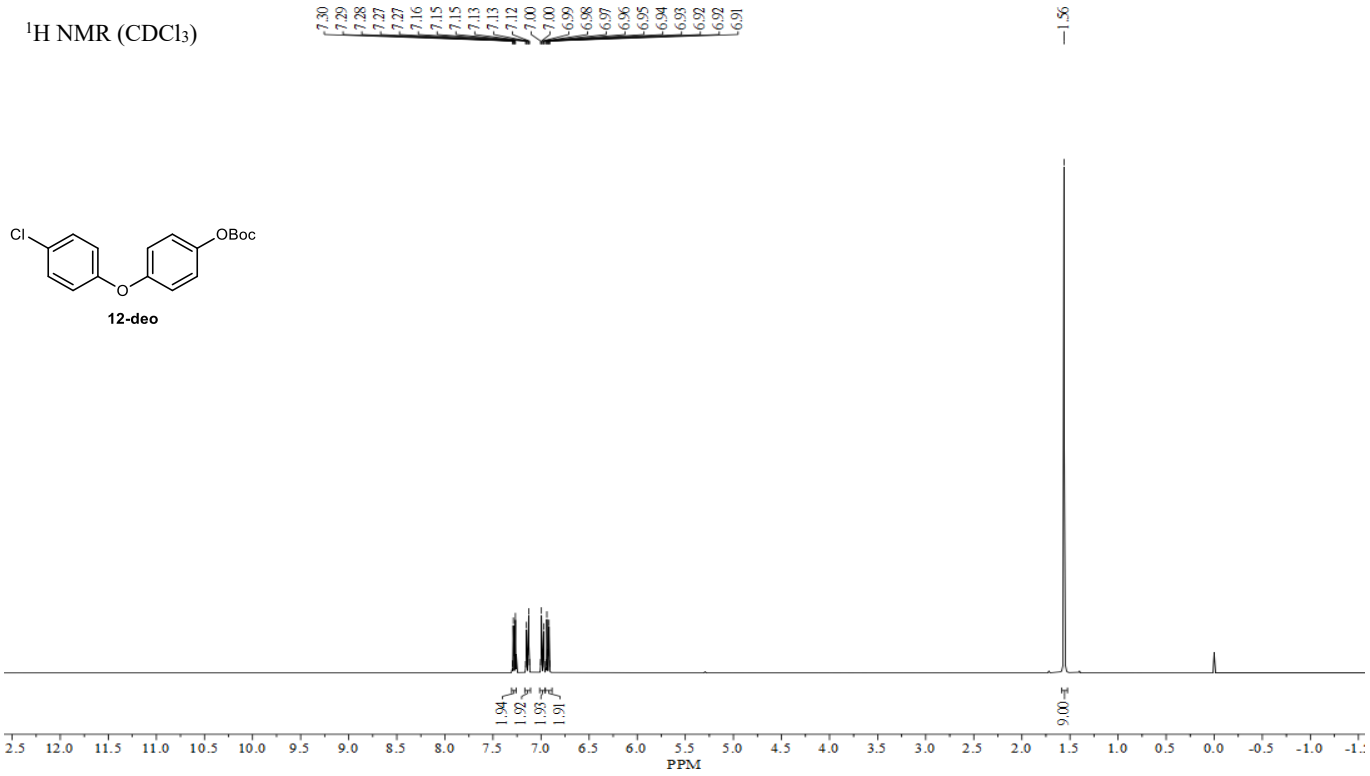


^{19}F NMR ($CDCl_3$)

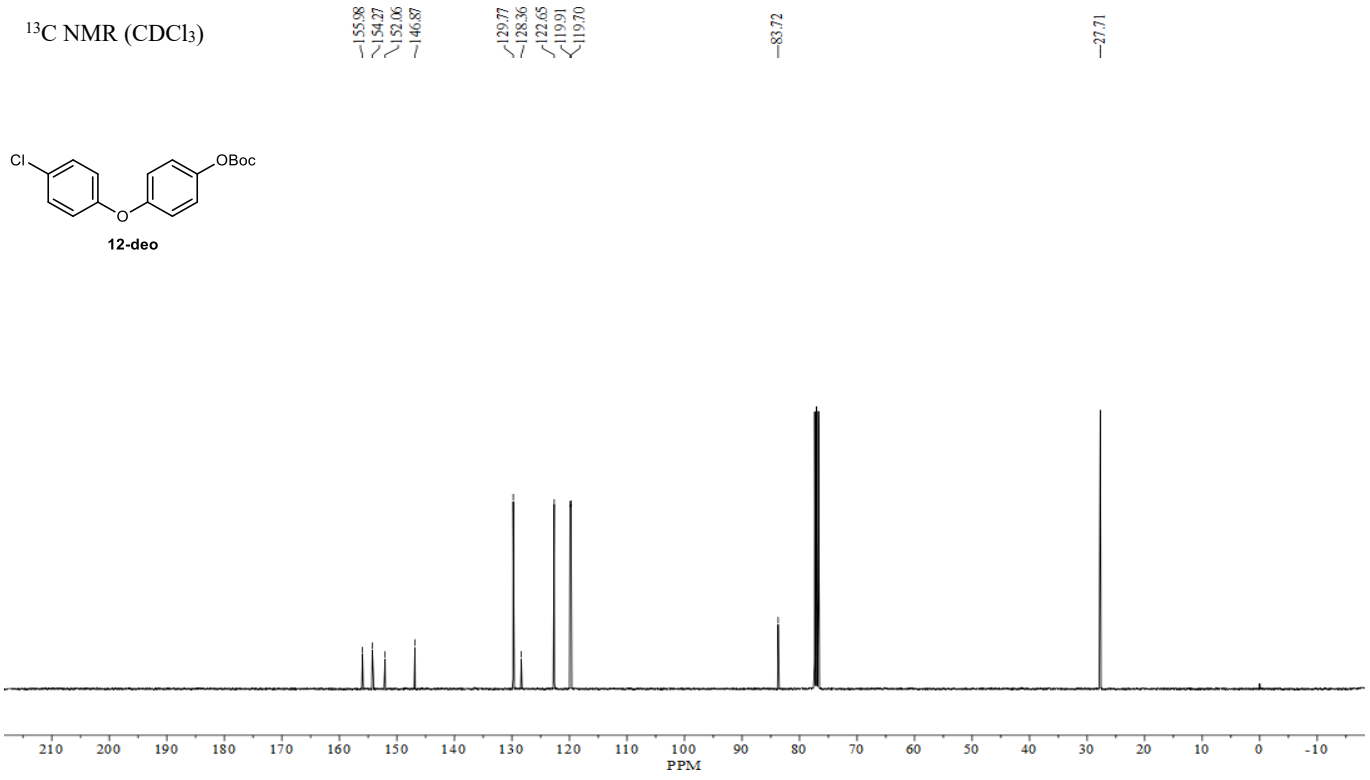


^{1}H NMR ($CDCl_3$)



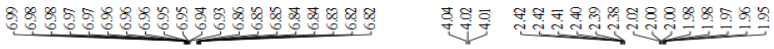
12-deo

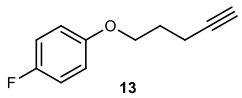
^{13}C NMR ($CDCl_3$)



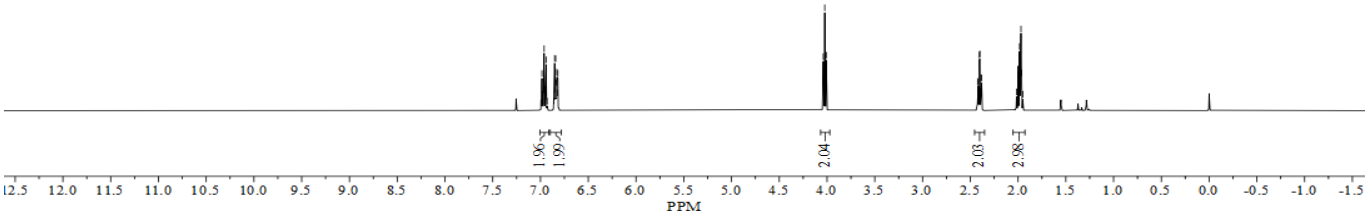
12-deo

^{1}H NMR ($CDCl_3$)

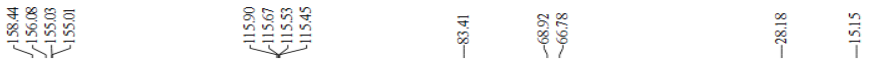


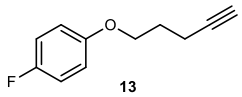


13

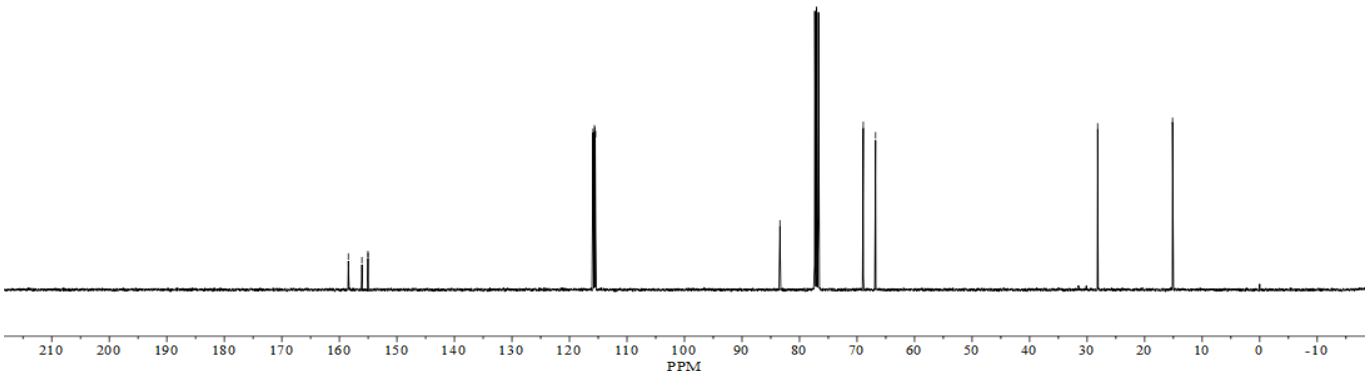


^{13}C NMR ($CDCl_3$)

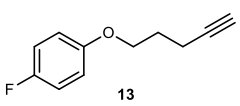




13

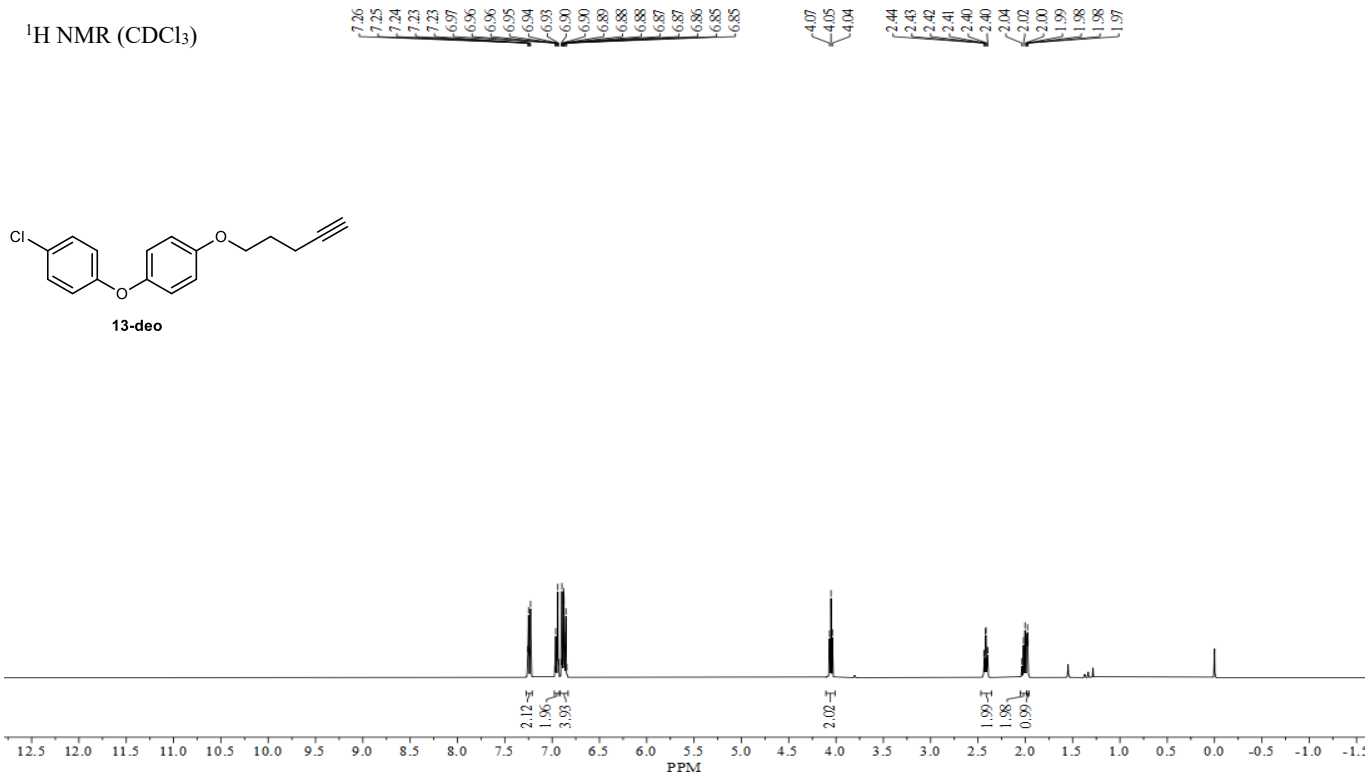


^{19}F NMR ($CDCl_3$)



13

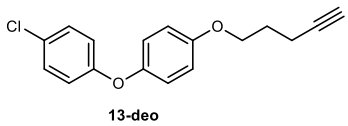
^{1}H NMR ($CDCl_3$)



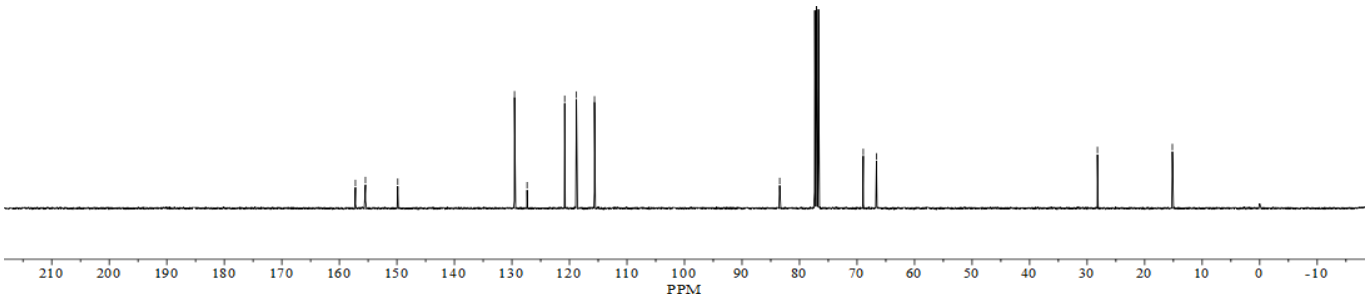
13-deo

^{13}C NMR ($CDCl_3$)

157.21
155.46
149.85
129.55
127.37
120.88
118.79
115.64
83.45
68.92
66.63
28.21
15.19

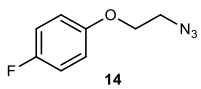


13-deo

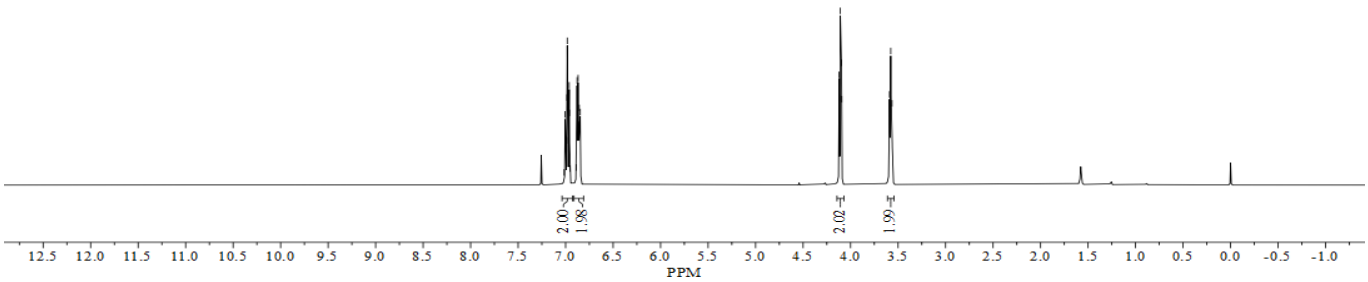


^{1}H NMR ($CDCl_3$)

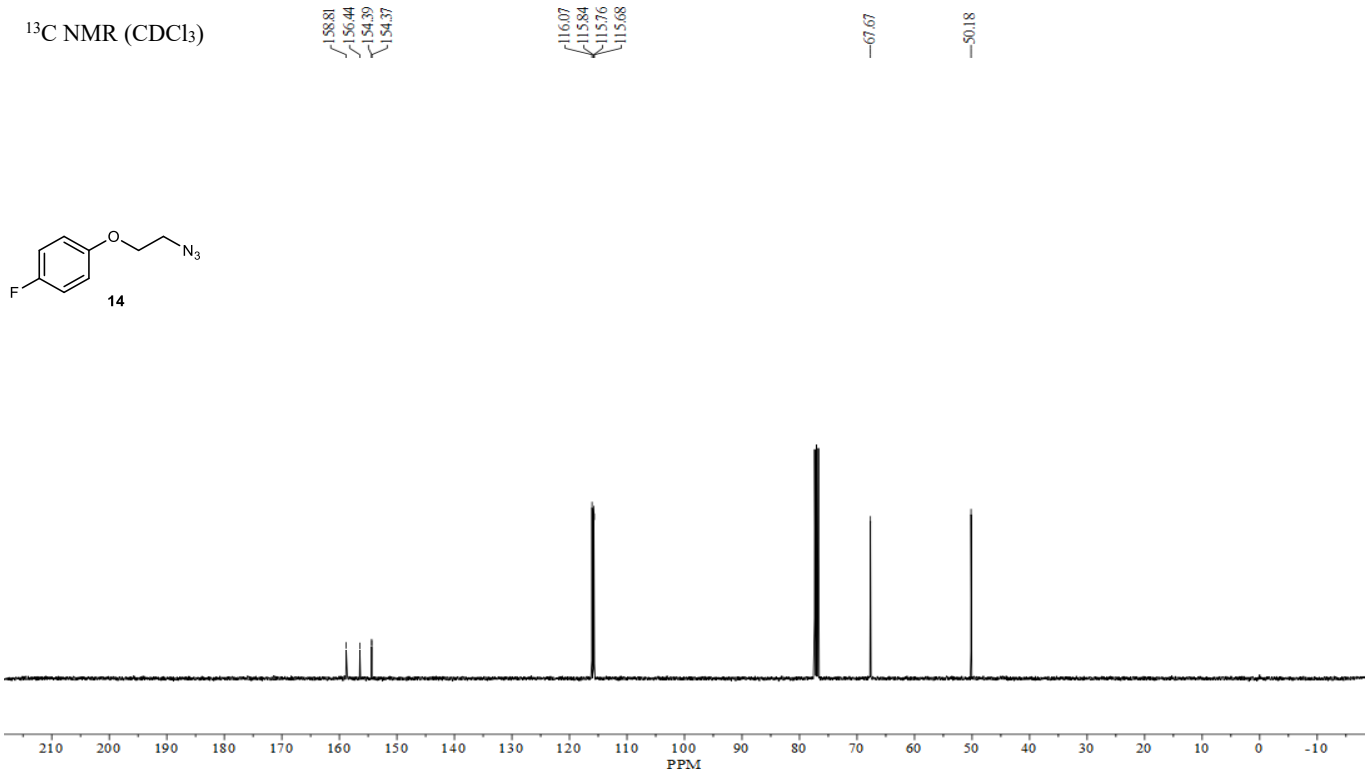
7.02
7.01
7.00
6.99
6.99
6.98
6.98
6.97
6.96
6.96
6.95
6.89
6.88
6.87
6.86
6.86
6.85
4.12
4.12
4.11
4.10
4.09
3.59
3.58
3.56



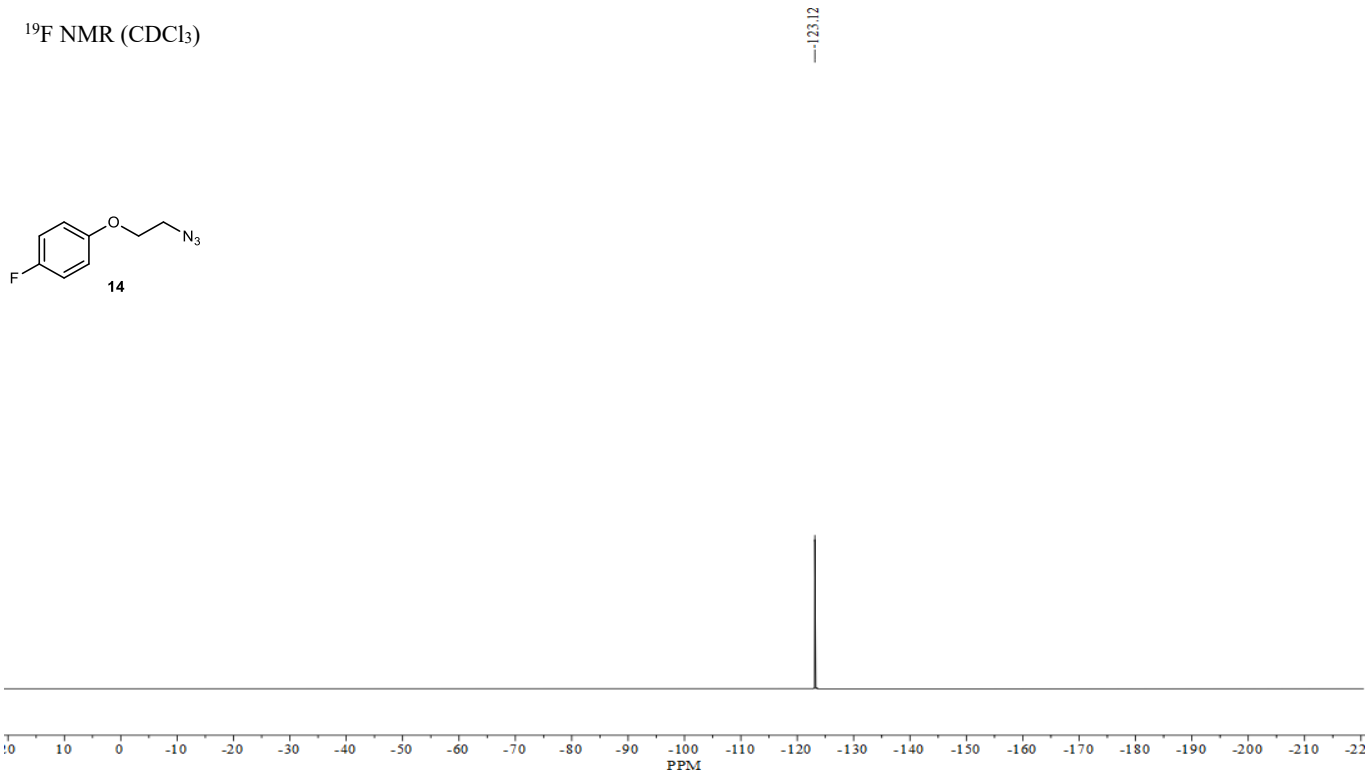
14



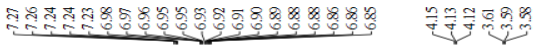
^{13}C NMR ($CDCl_3$)

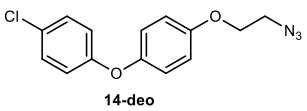


^{19}F NMR ($CDCl_3$)

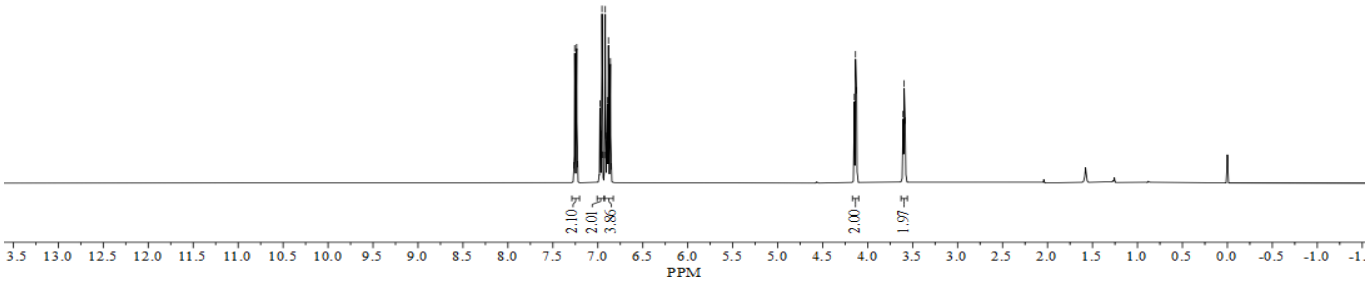


^{1}H NMR ($CDCl_3$)

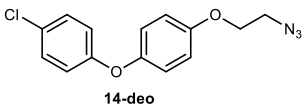




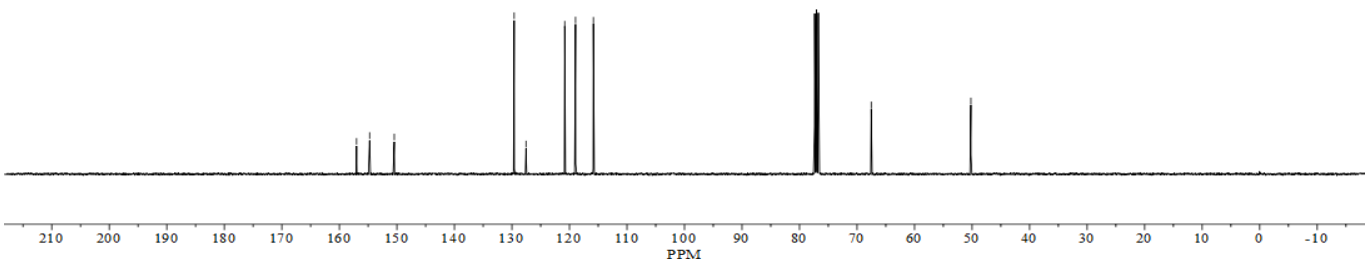
14-deo



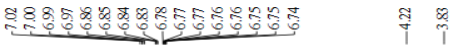
^{13}C NMR ($CDCl_3$)

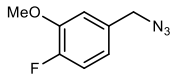


14-deo



^{1}H NMR ($CDCl_3$)





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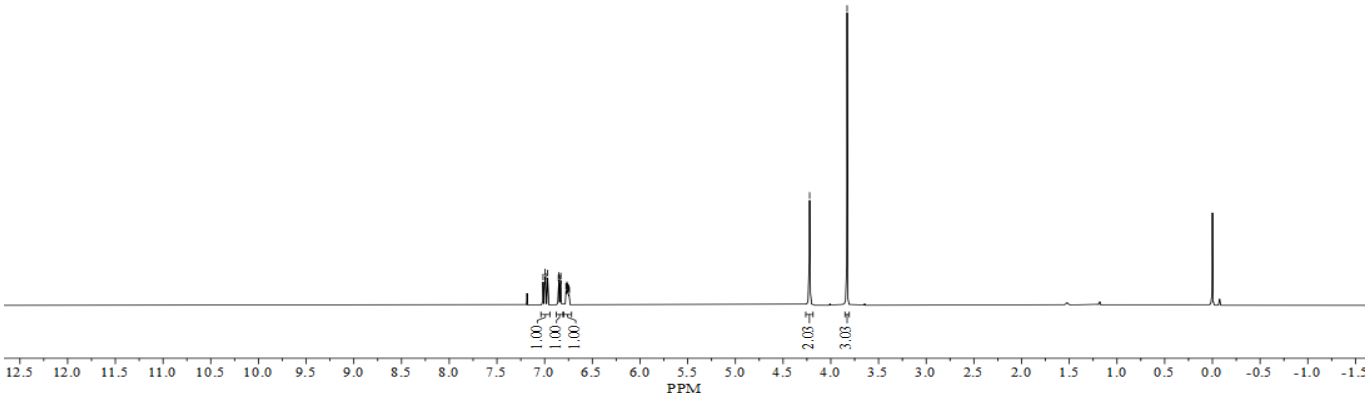
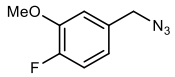
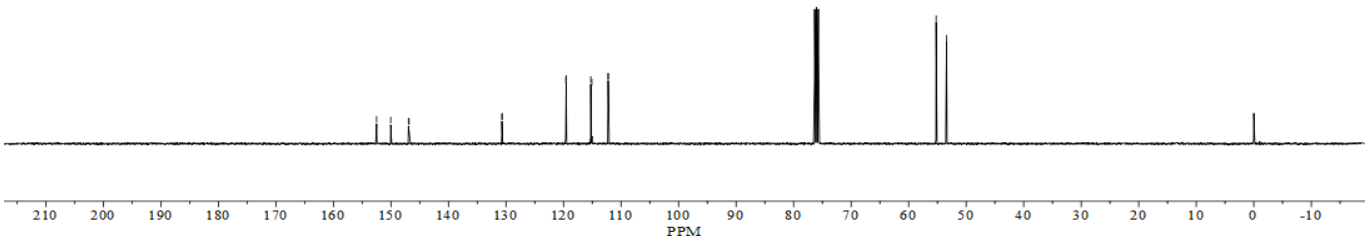


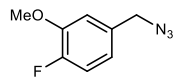
^{13}C NMR ($CDCl_3$)



15

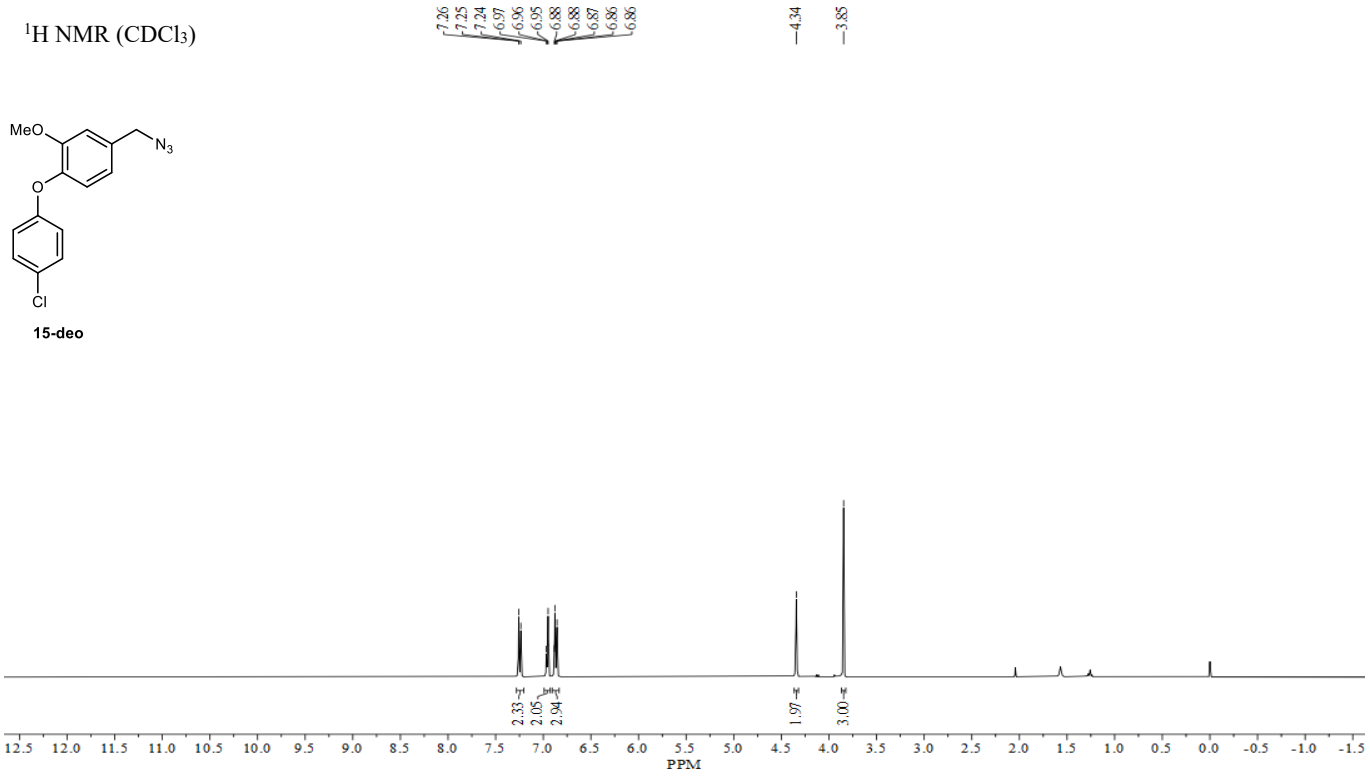


^{19}F NMR ($CDCl_3$)



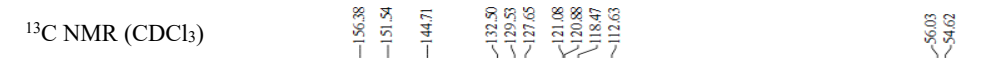
15

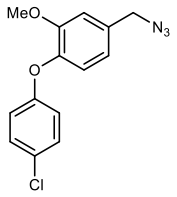
^{1}H NMR ($CDCl_3$)



15-deo

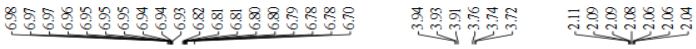
^{13}C NMR ($CDCl_3$)

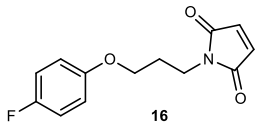




15-deo

^{1}H NMR ($CDCl_3$)





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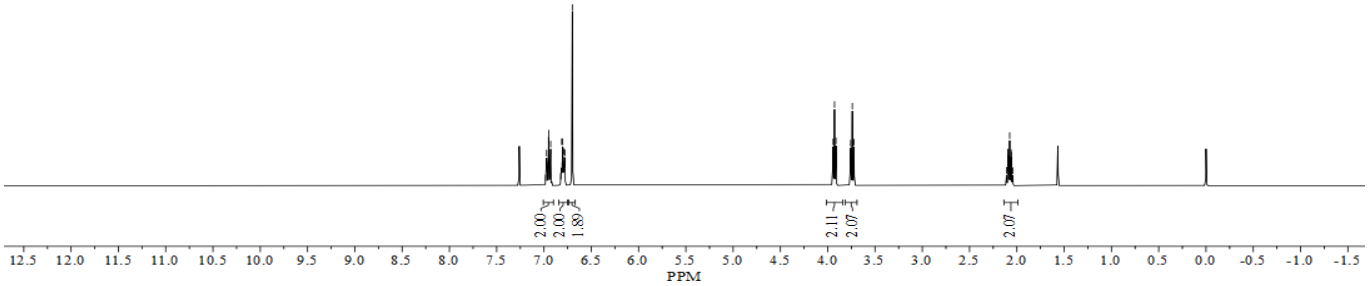
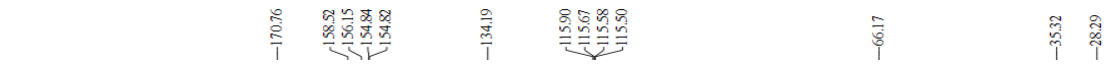
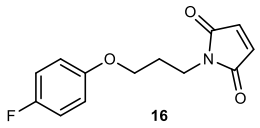
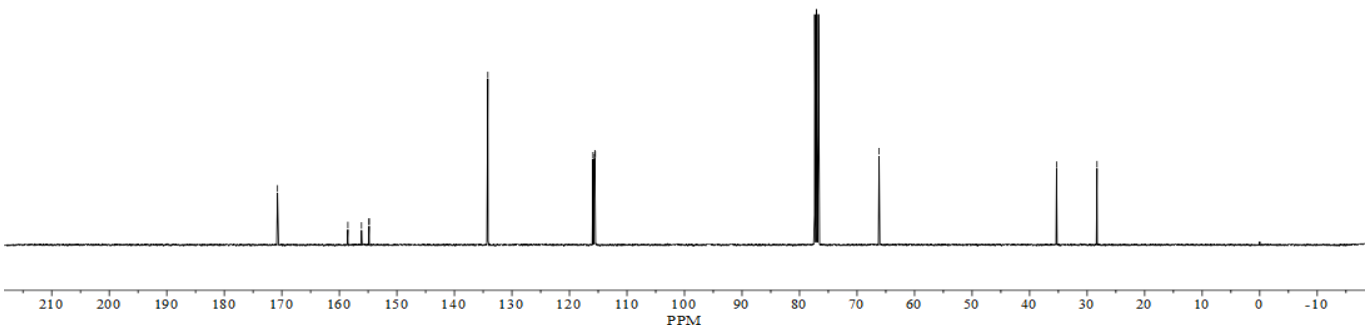




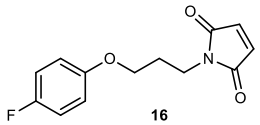
^{13}C NMR ($CDCl_3$)



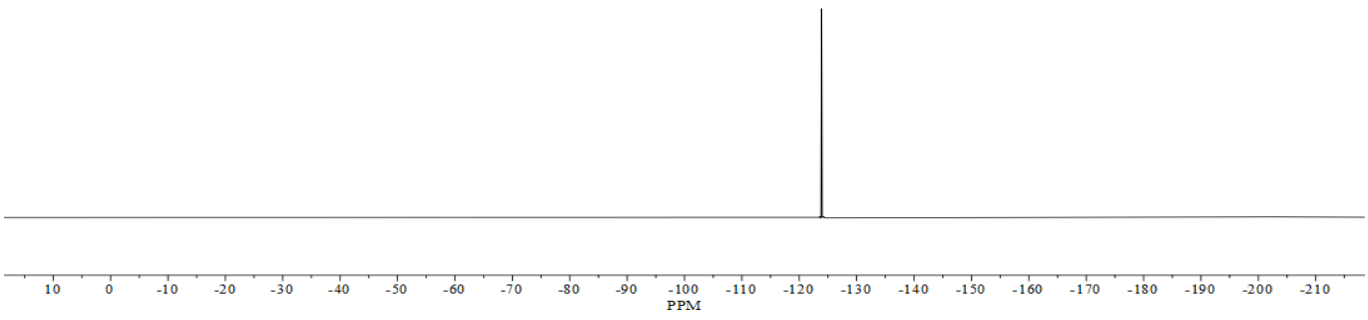
16



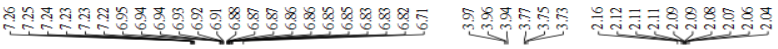
^{19}F NMR ($CDCl_3$)

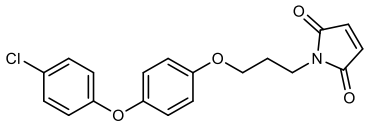


16

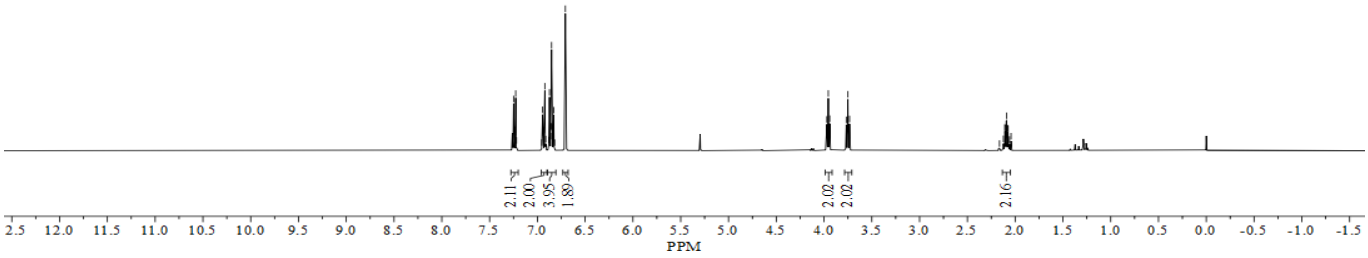


^{1}H NMR ($CDCl_3$)

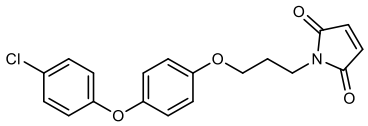




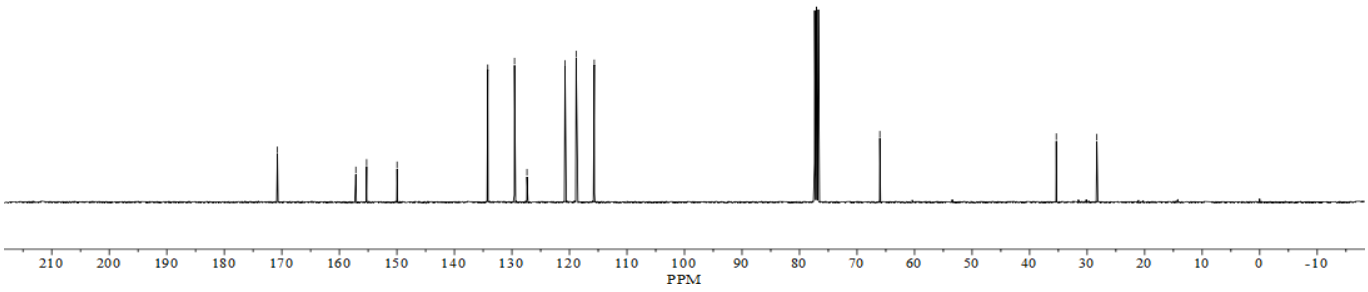
16-deo



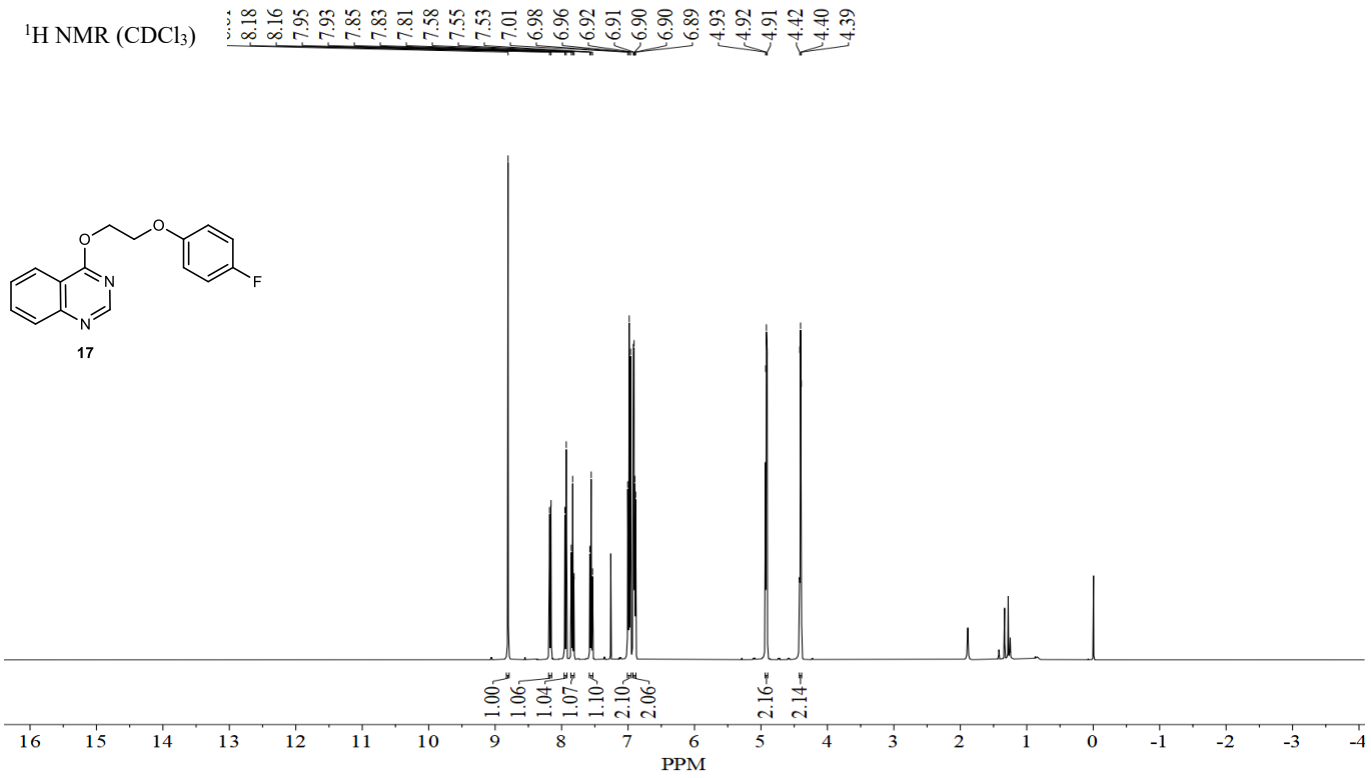
^{13}C NMR ($CDCl_3$)



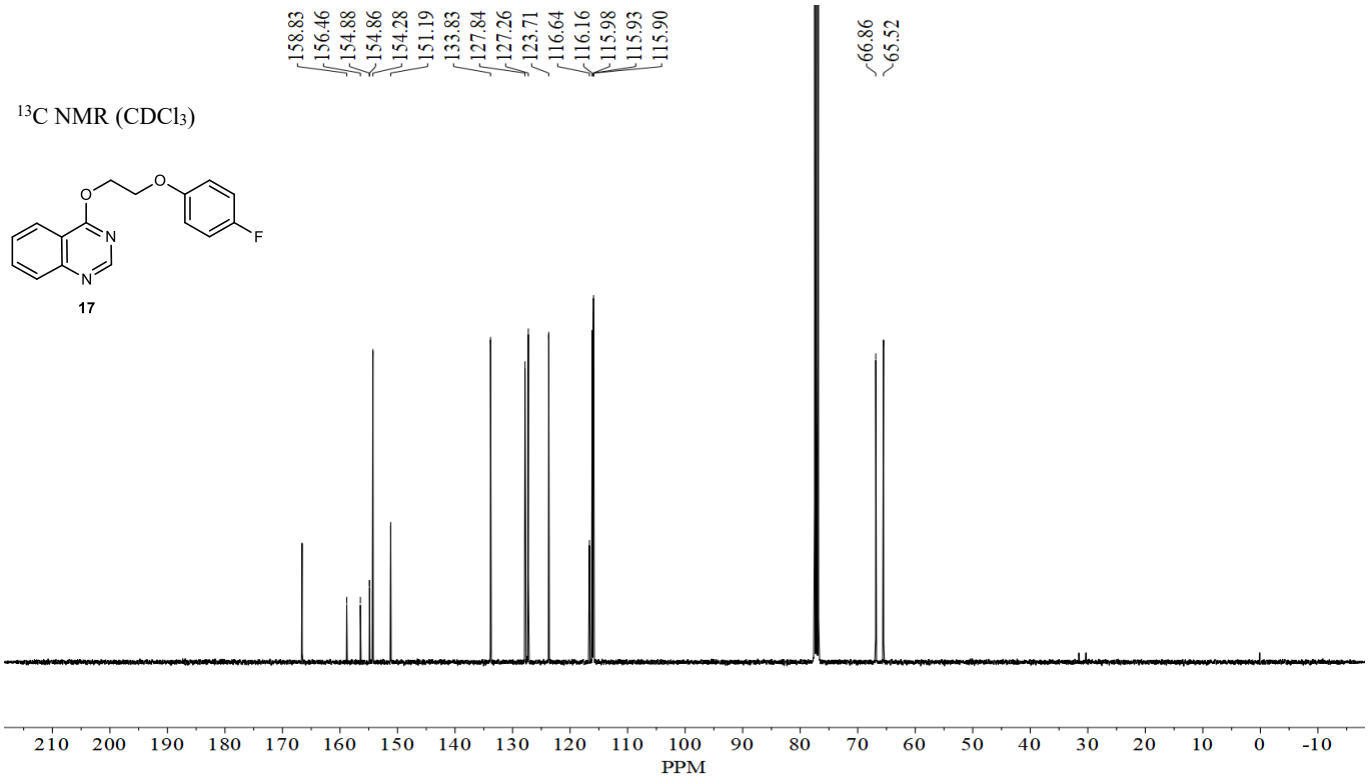
16-deo



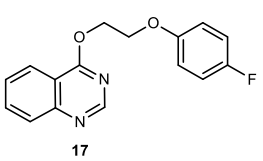
^{1}H NMR ($CDCl_3$)



^{13}C NMR ($CDCl_3$)

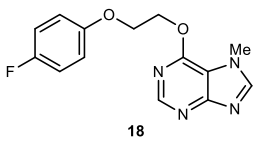


^{19}F NMR ($CDCl_3$)



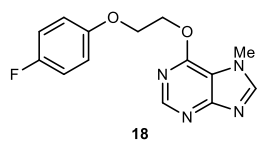
17

^{1}H NMR ($CDCl_3$)



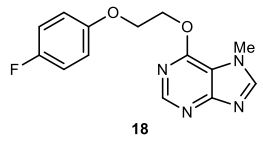
18

^{13}C NMR ($CDCl_3$)



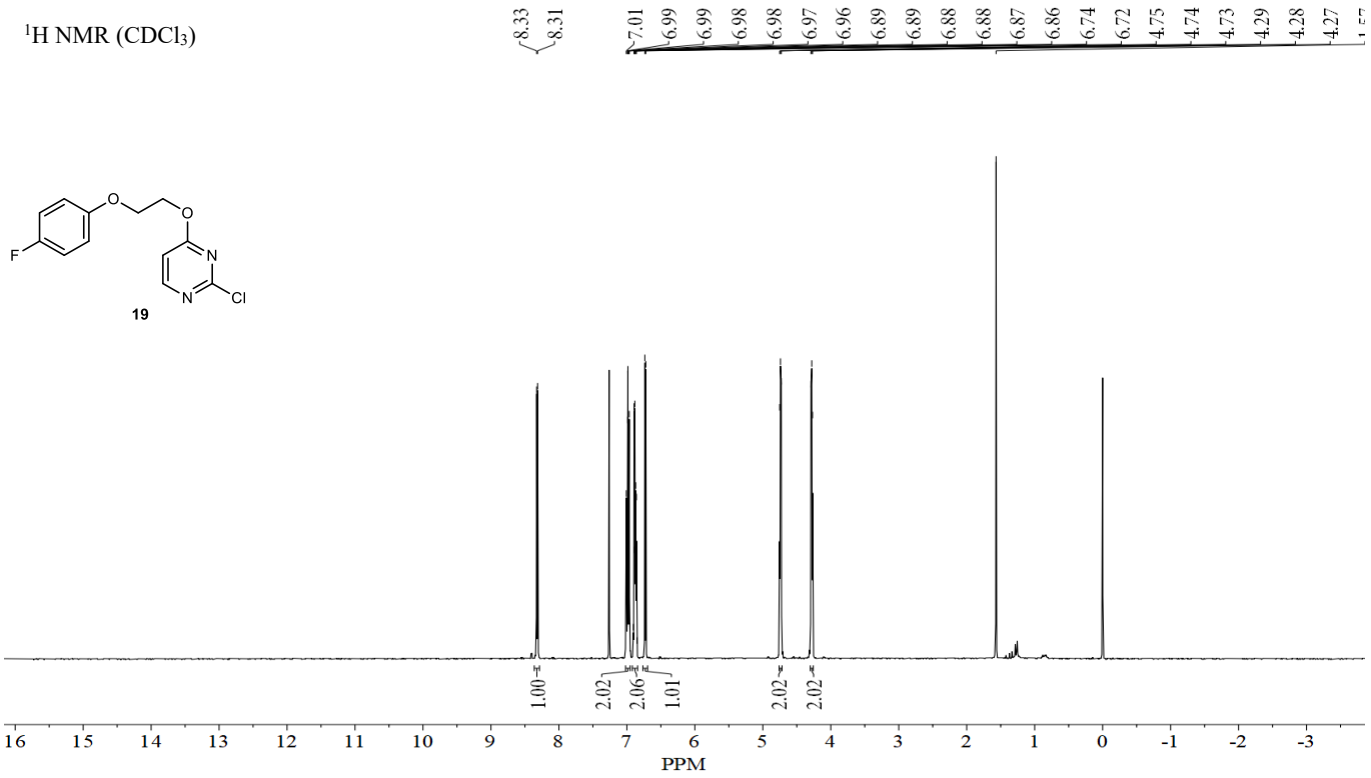
18

^{19}F NMR ($CDCl_3$)

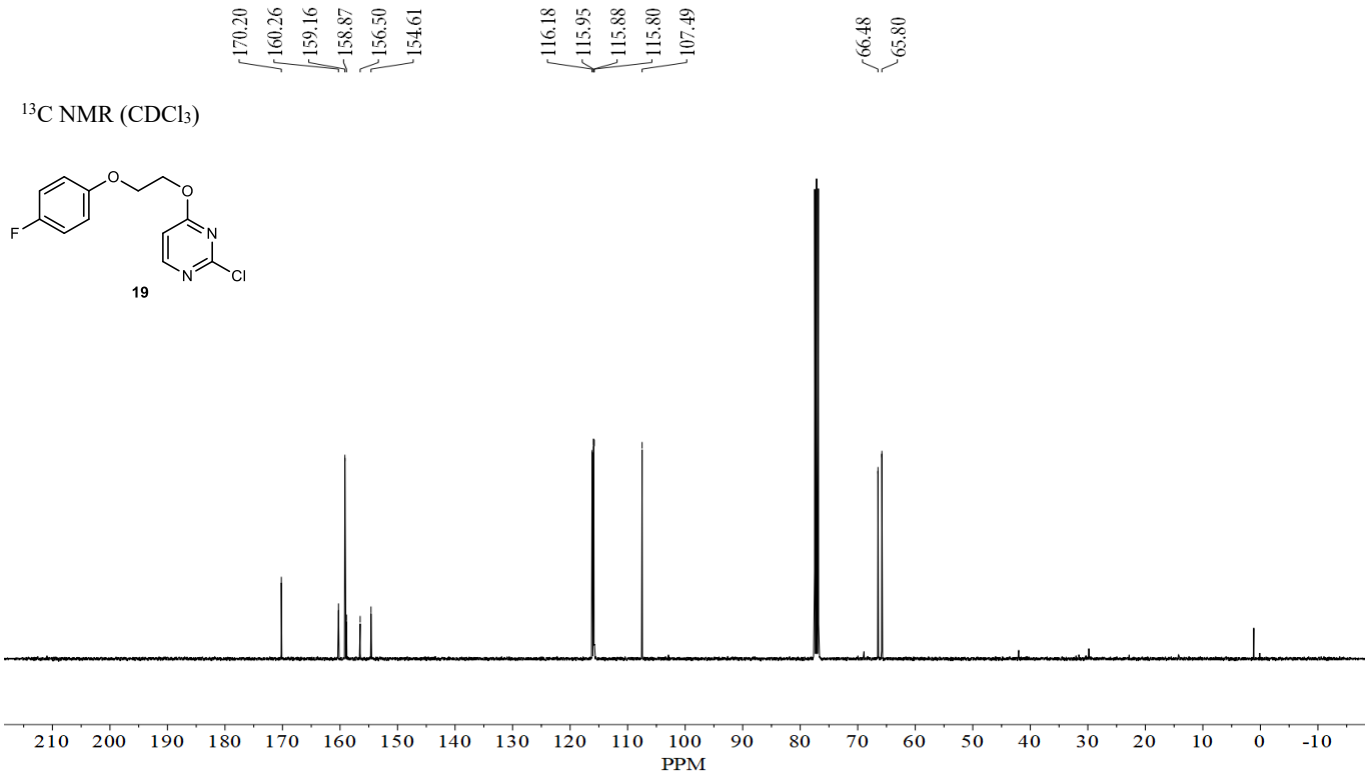


18

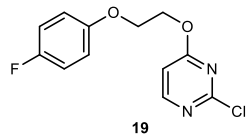
^{1}H NMR ($CDCl_3$)



^{13}C NMR ($CDCl_3$)

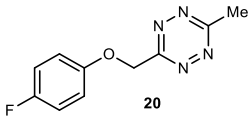


^{19}F NMR ($CDCl_3$)



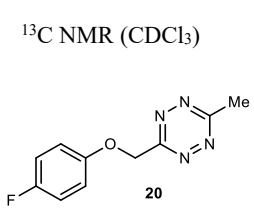
19

^{1}H NMR ($CDCl_3$)



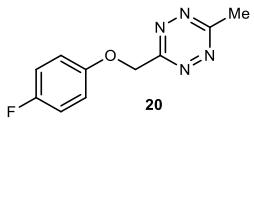
20

^{13}C NMR ($CDCl_3$)



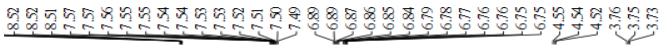
20

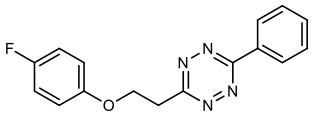
^{19}F NMR ($CDCl_3$)



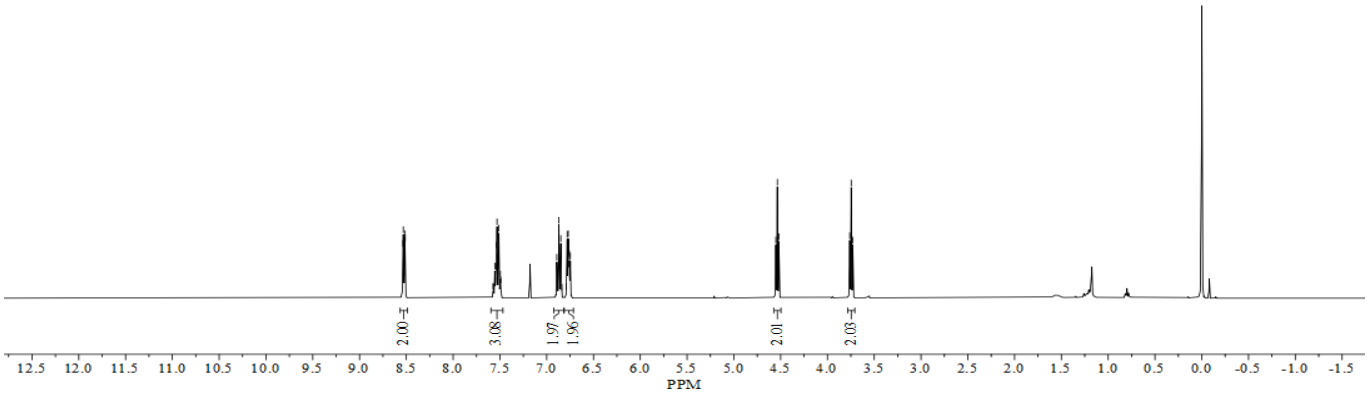
20

^{1}H NMR ($CDCl_3$)

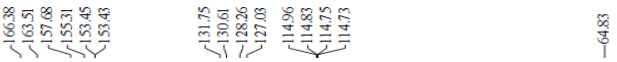


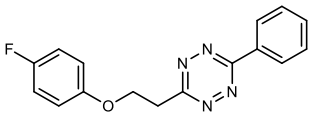


21

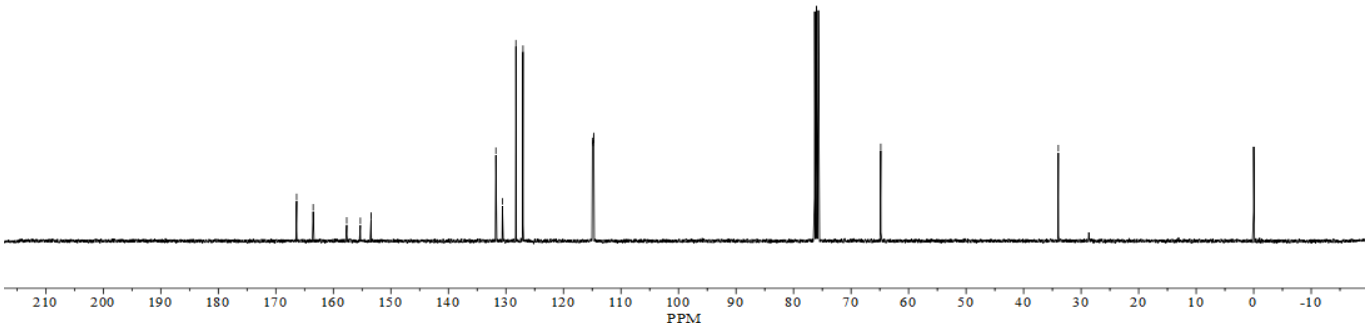


^{13}C NMR ($CDCl_3$)

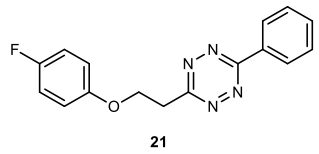




21

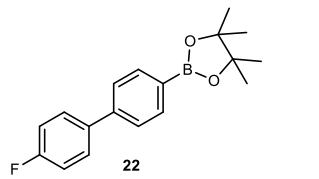


^{19}F NMR ($CDCl_3$)



21

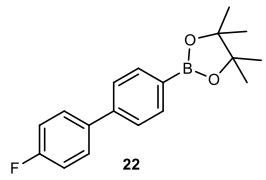
^{1}H NMR ($CDCl_3$)



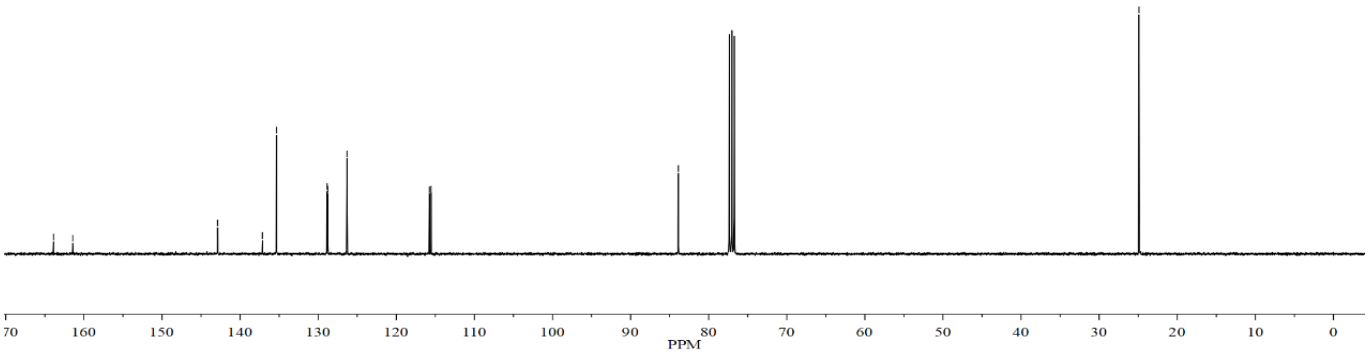
22

163.89
161.43
142.88
137.16
137.13
135.33
128.85
128.77
126.31
115.77
115.56
83.88
24.90

^{13}C NMR ($CDCl_3$)

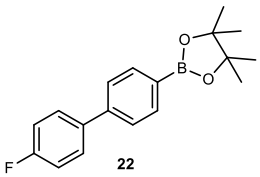


22



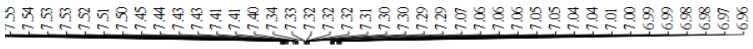
^{19}F NMR ($CDCl_3$)

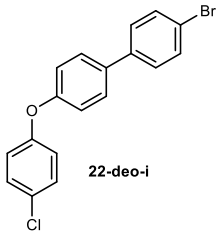
-115.31

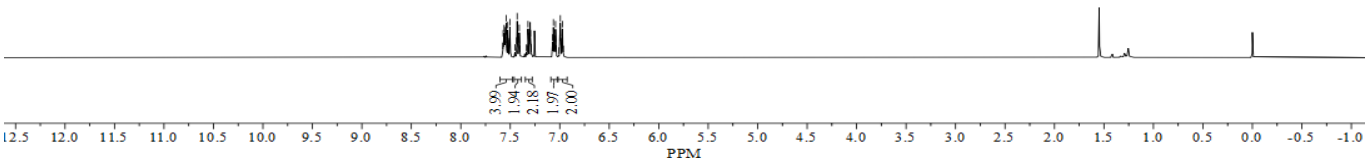


22

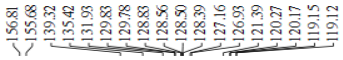
^{1}H NMR ($CDCl_3$)

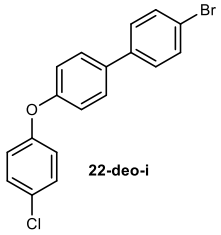




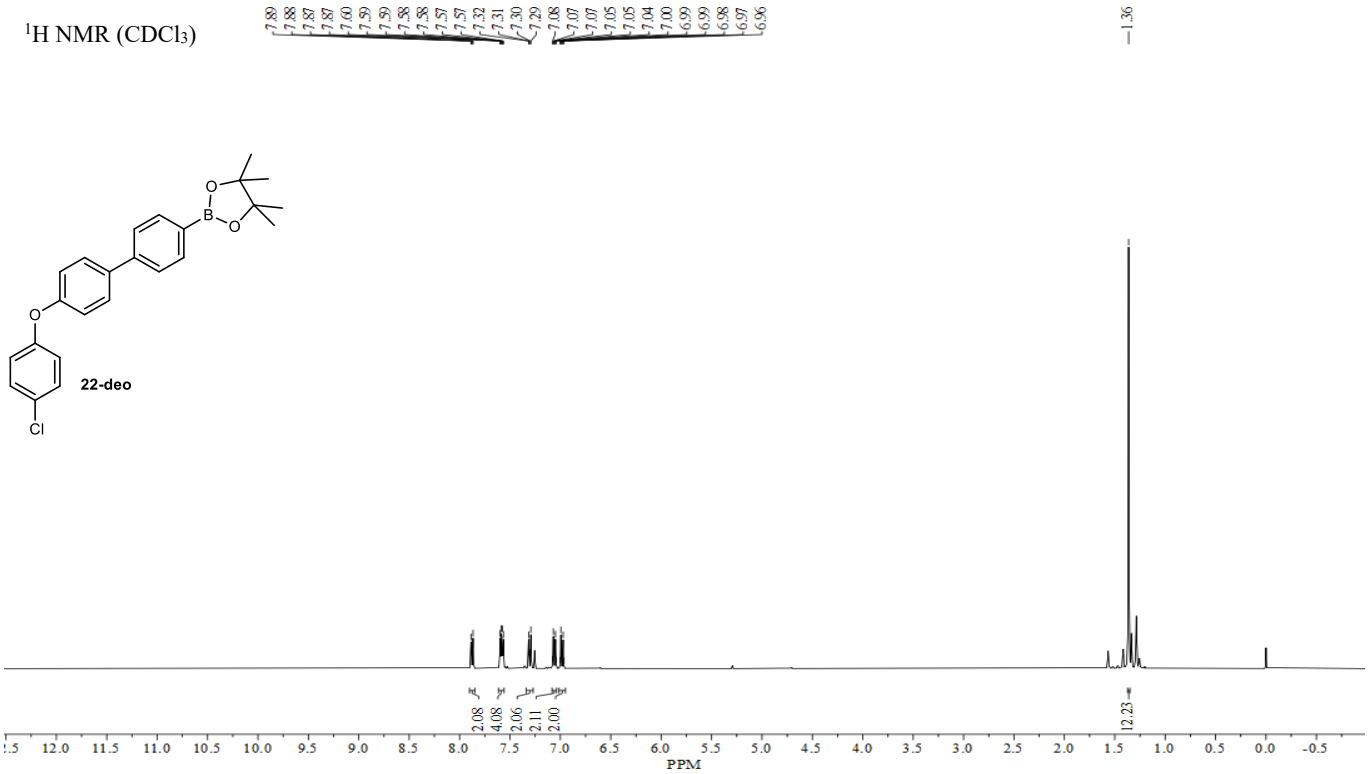


^{13}C NMR ($CDCl_3$)

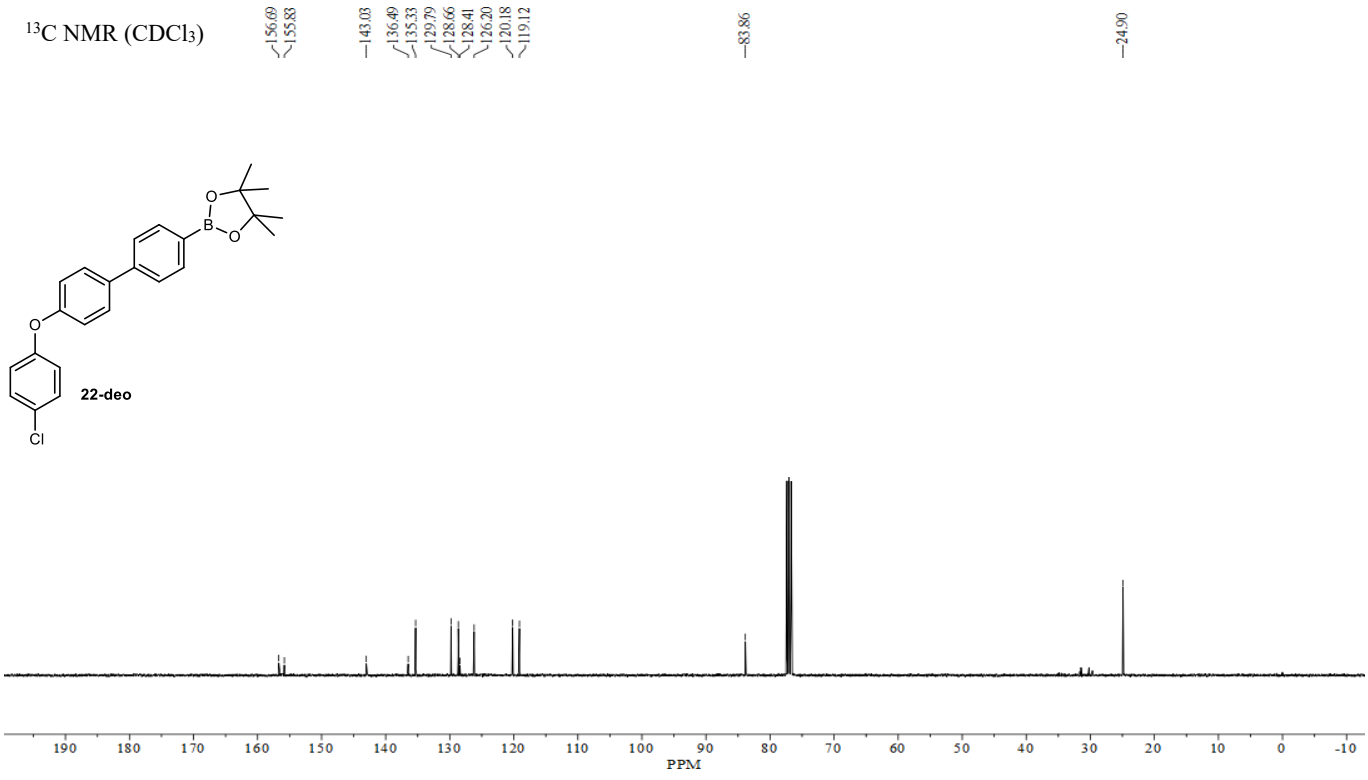




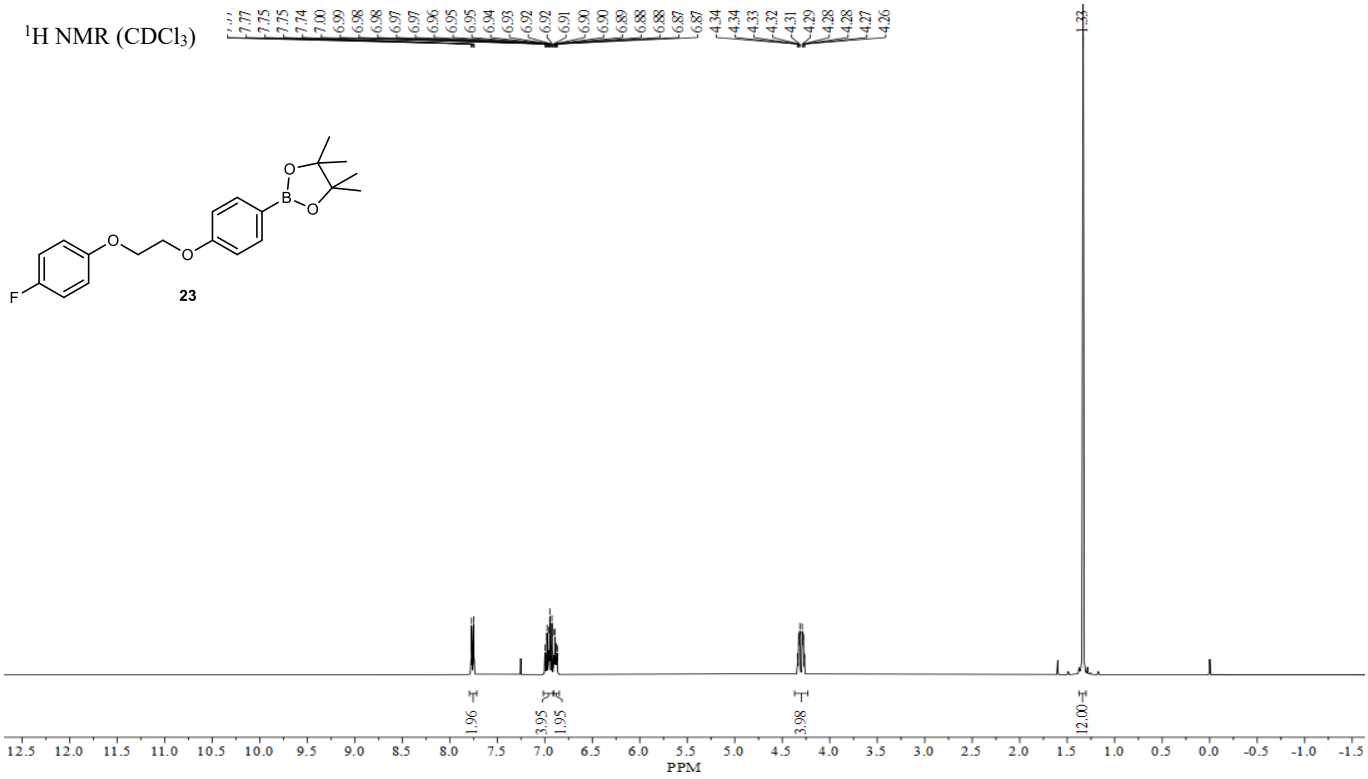
^{1}H NMR ($CDCl_3$)

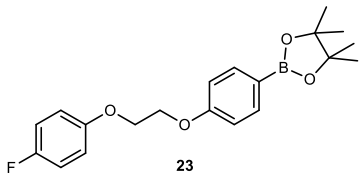


^{13}C NMR ($CDCl_3$)



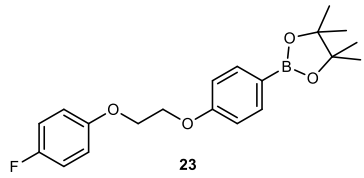
^{1}H NMR ($CDCl_3$)





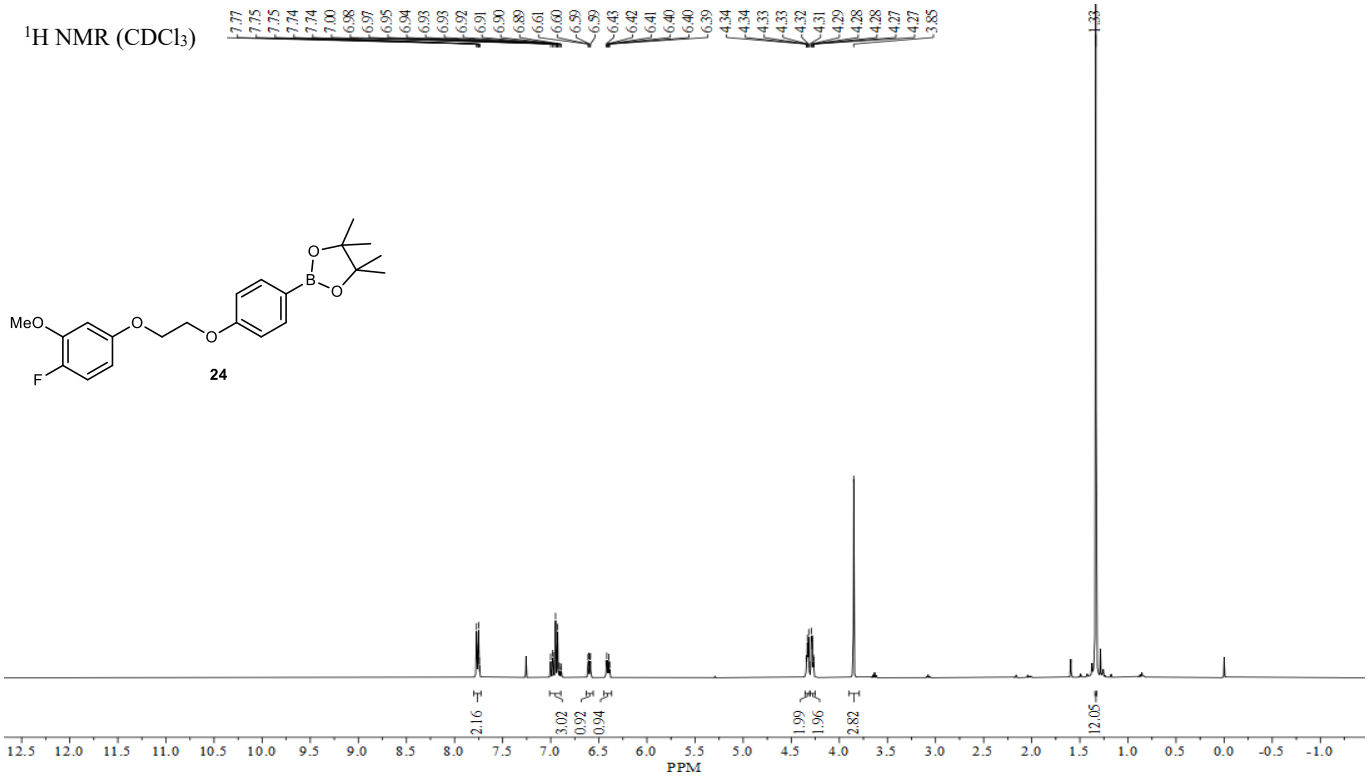
^{13}C NMR ($CDCl_3$)

^{19}F NMR ($CDCl_3$)



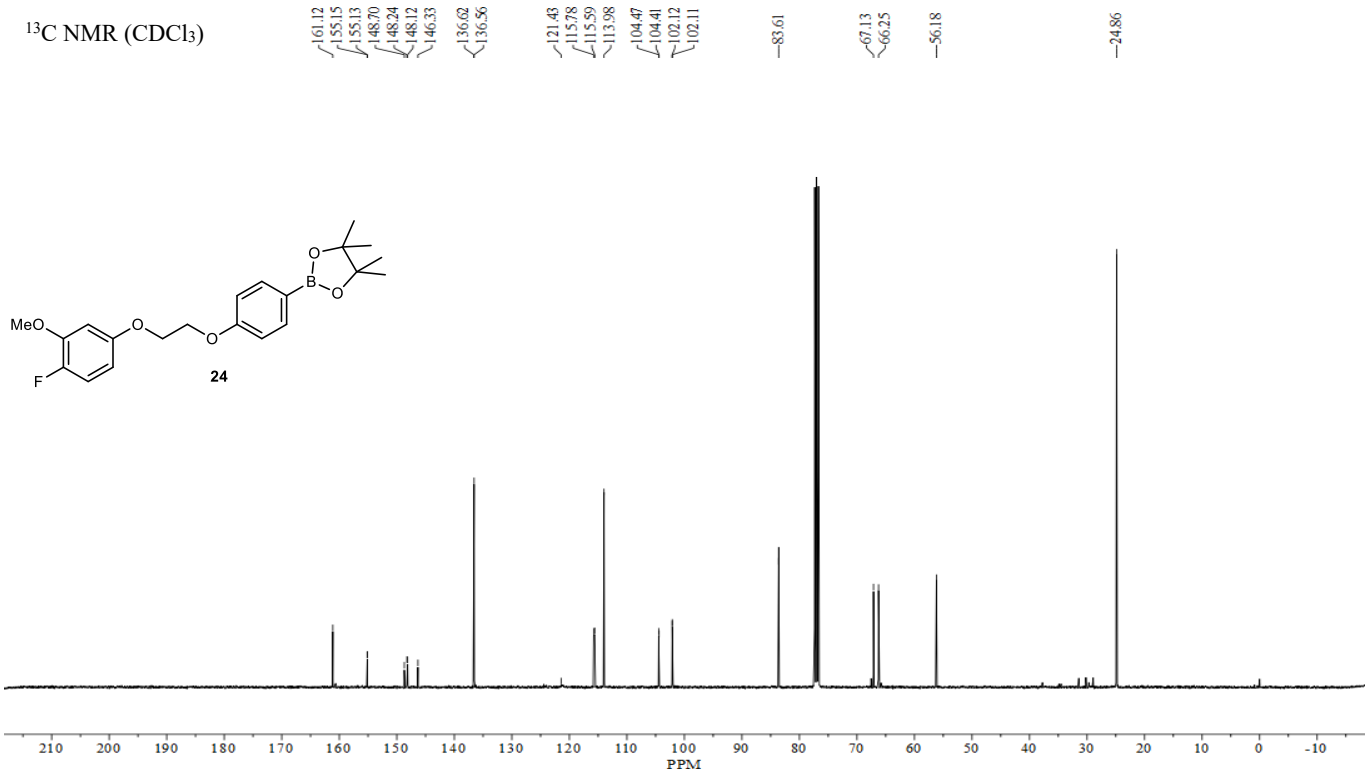
23

^{1}H NMR ($CDCl_3$)

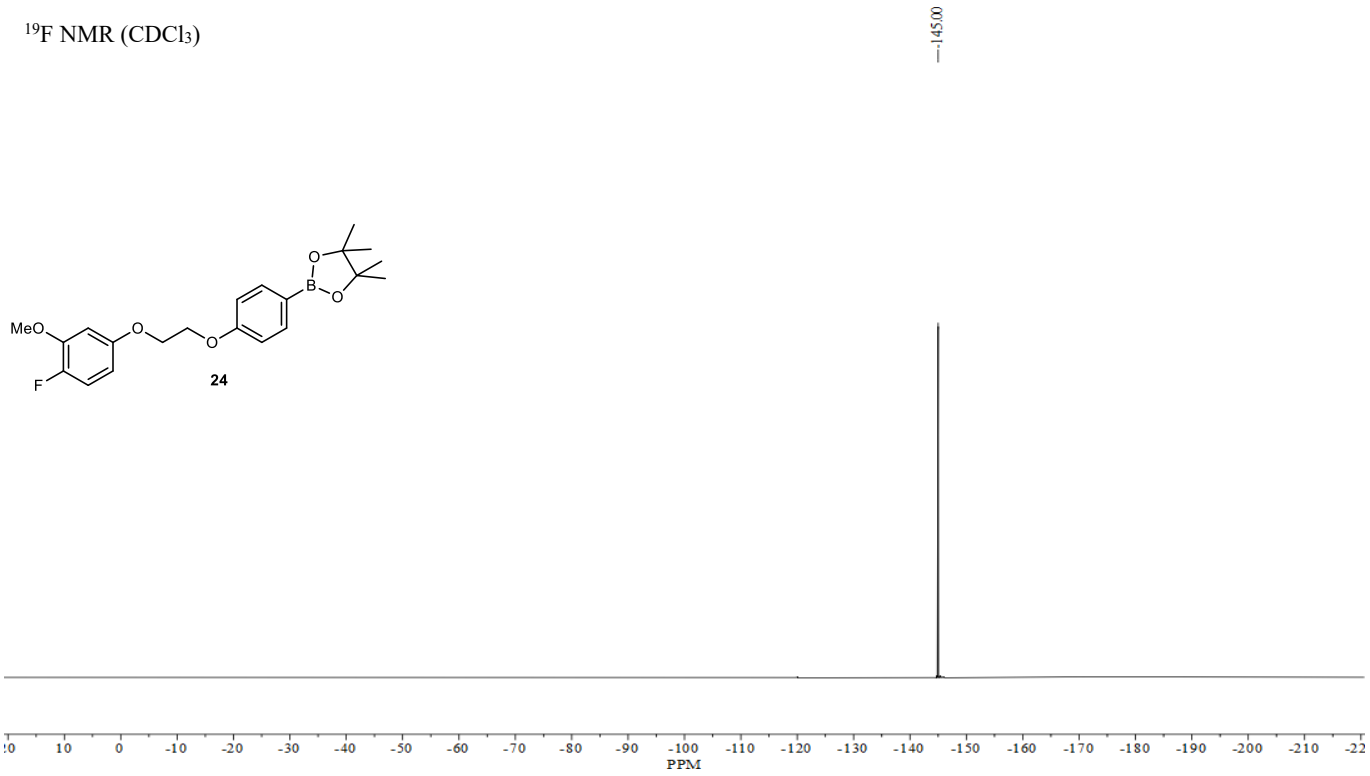


24

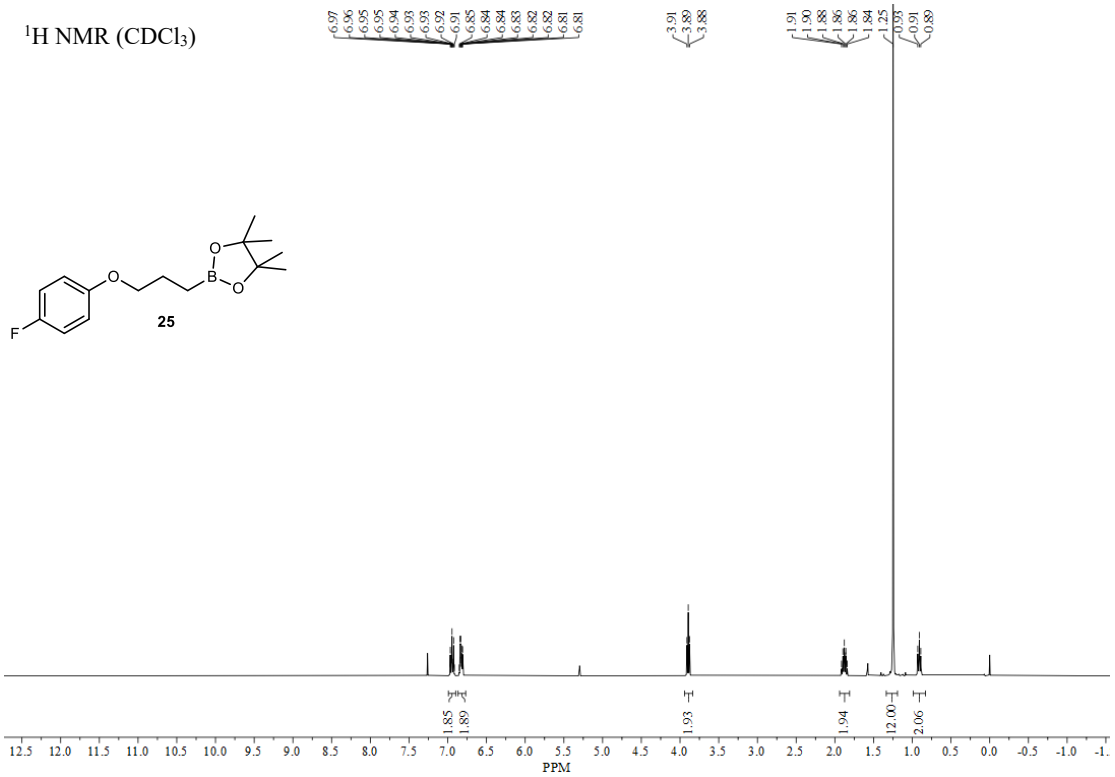
^{13}C NMR ($CDCl_3$)



^{19}F NMR ($CDCl_3$)

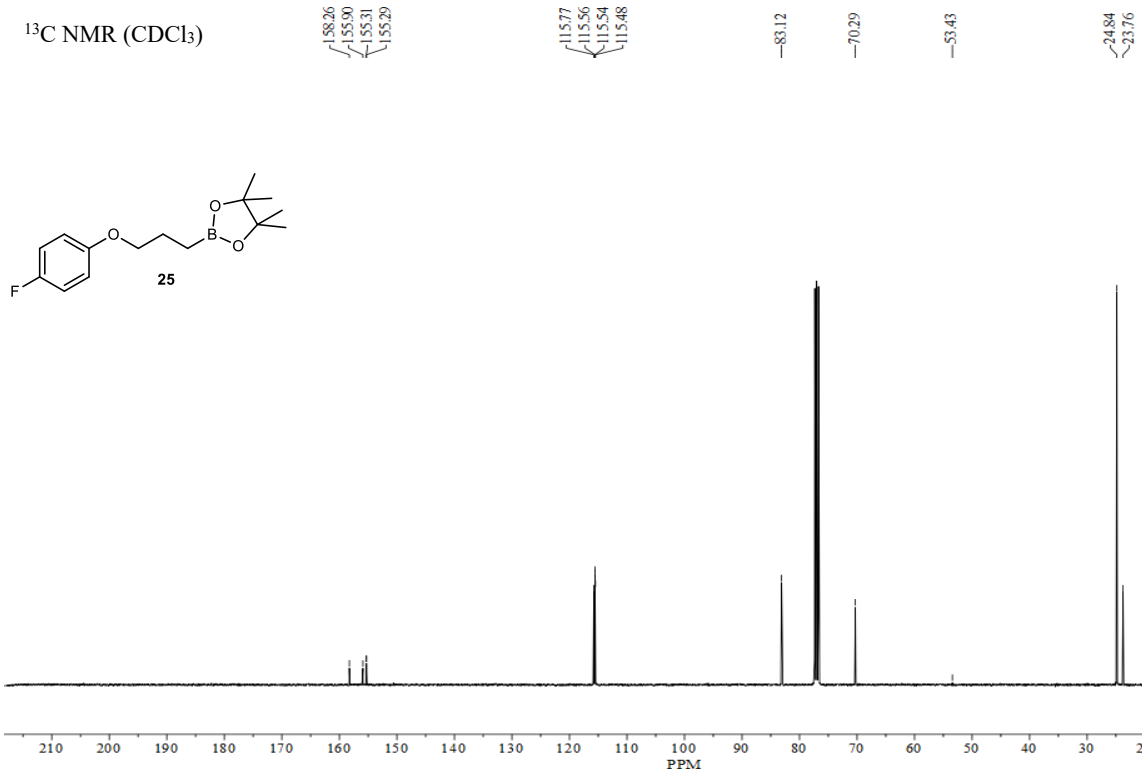


^{1}H NMR ($CDCl_3$)



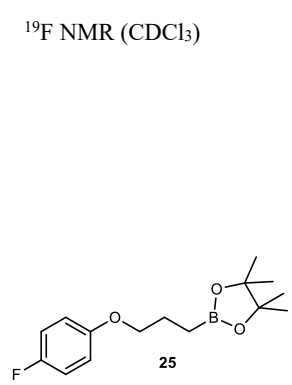
25

^{13}C NMR ($CDCl_3$)

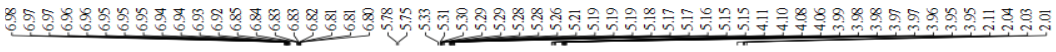


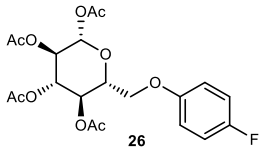
25

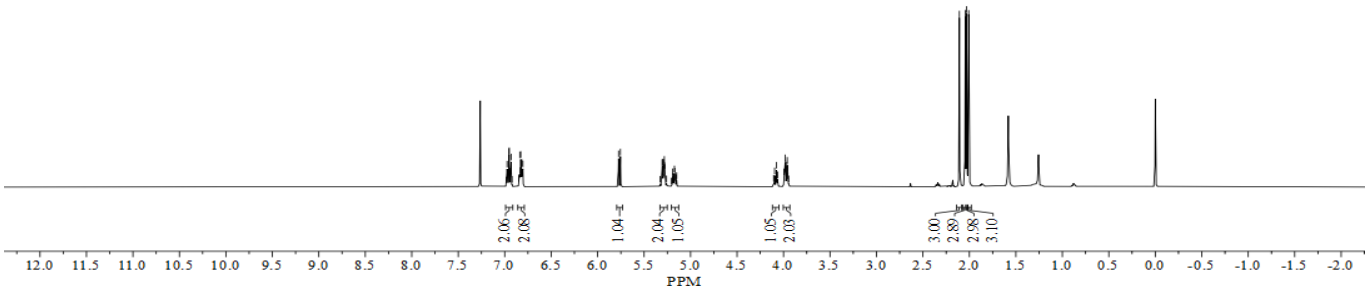
^{19}F NMR ($CDCl_3$)



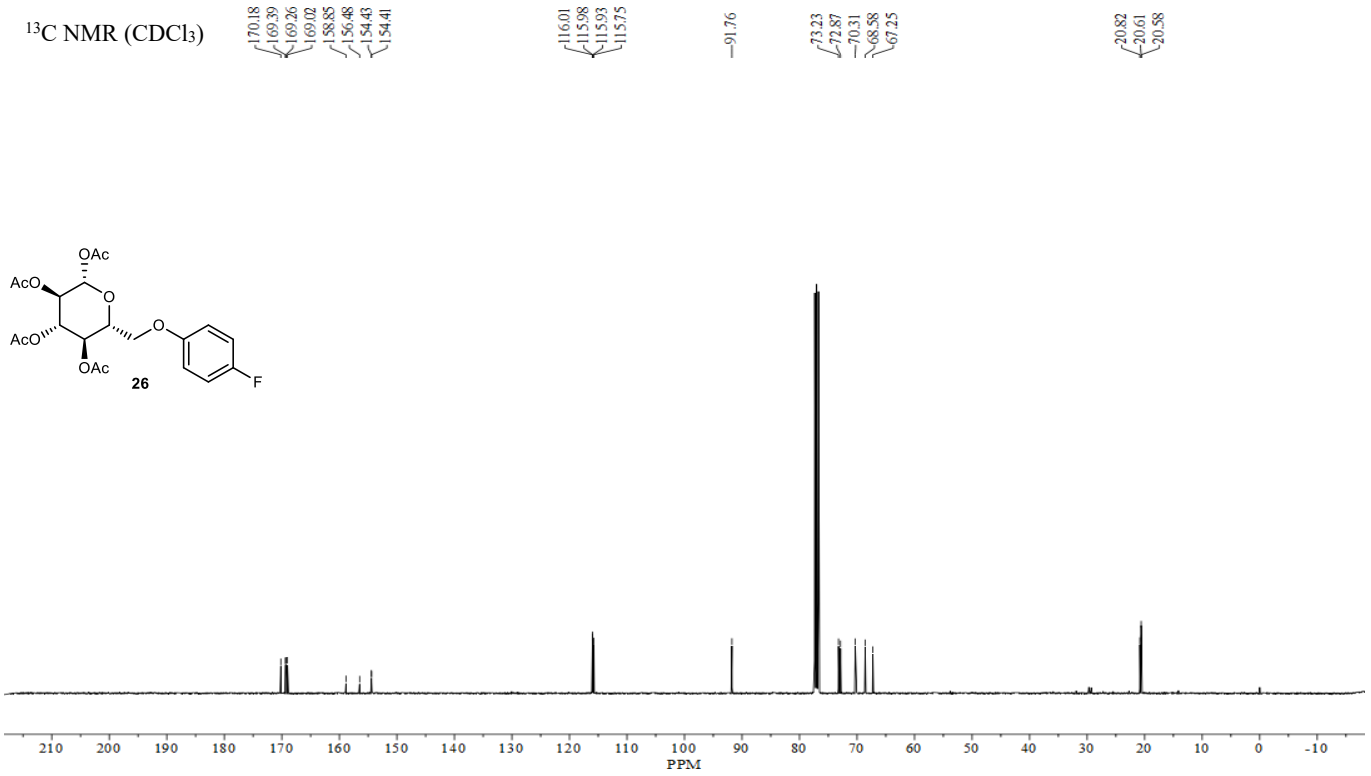
^{1}H NMR ($CDCl_3$)



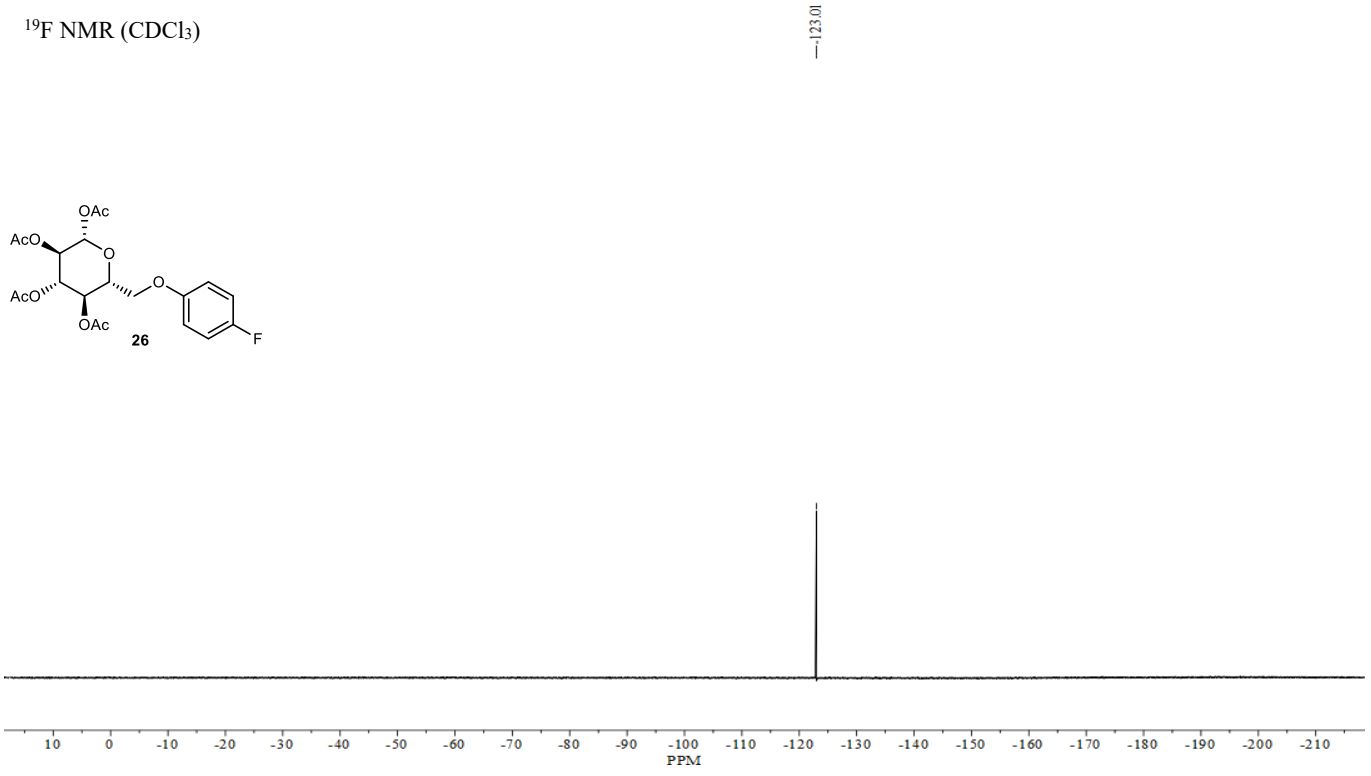




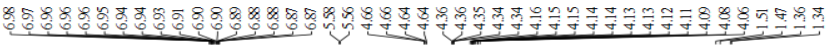
^{13}C NMR ($CDCl_3$)

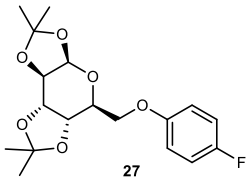


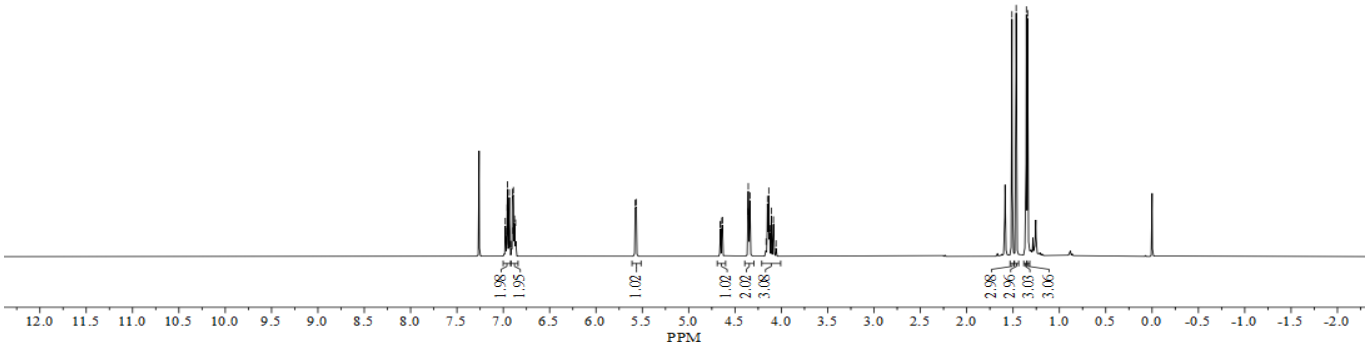
^{19}F NMR ($CDCl_3$)



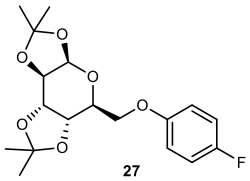
^{1}H NMR ($CDCl_3$)

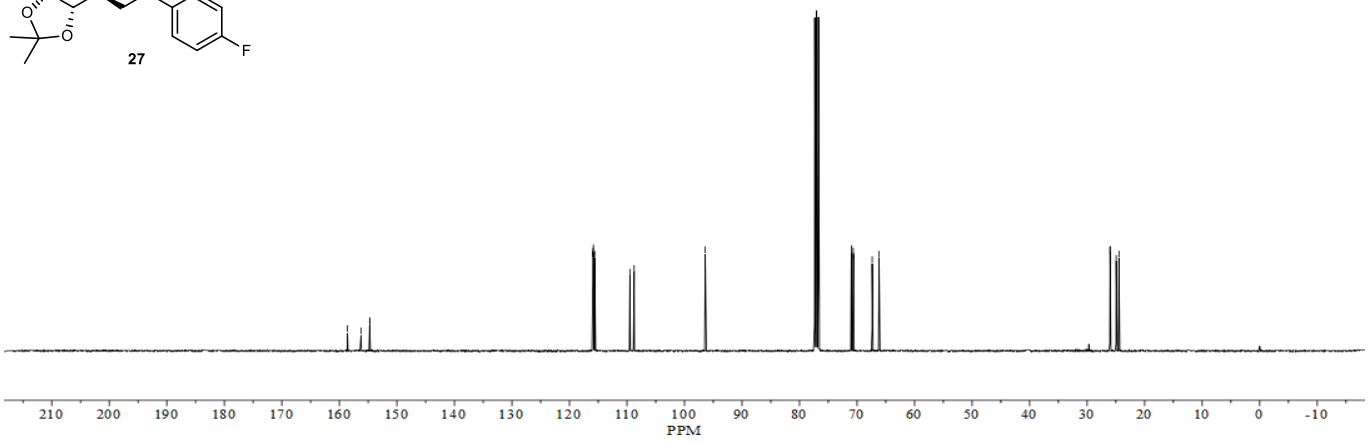




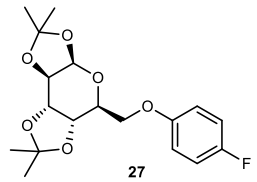


^{13}C NMR ($CDCl_3$)



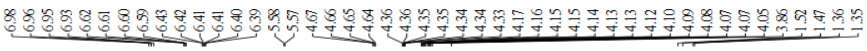


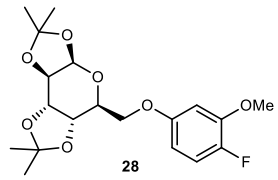
^{19}F NMR ($CDCl_3$)



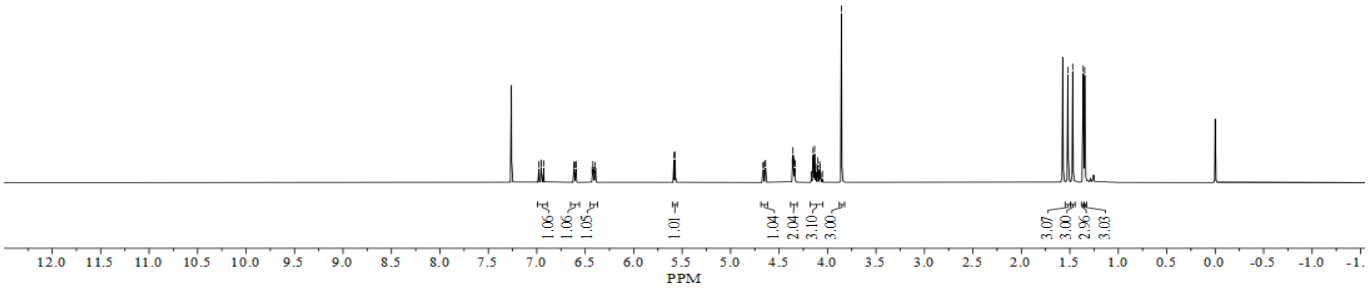
27

^{1}H NMR ($CDCl_3$)

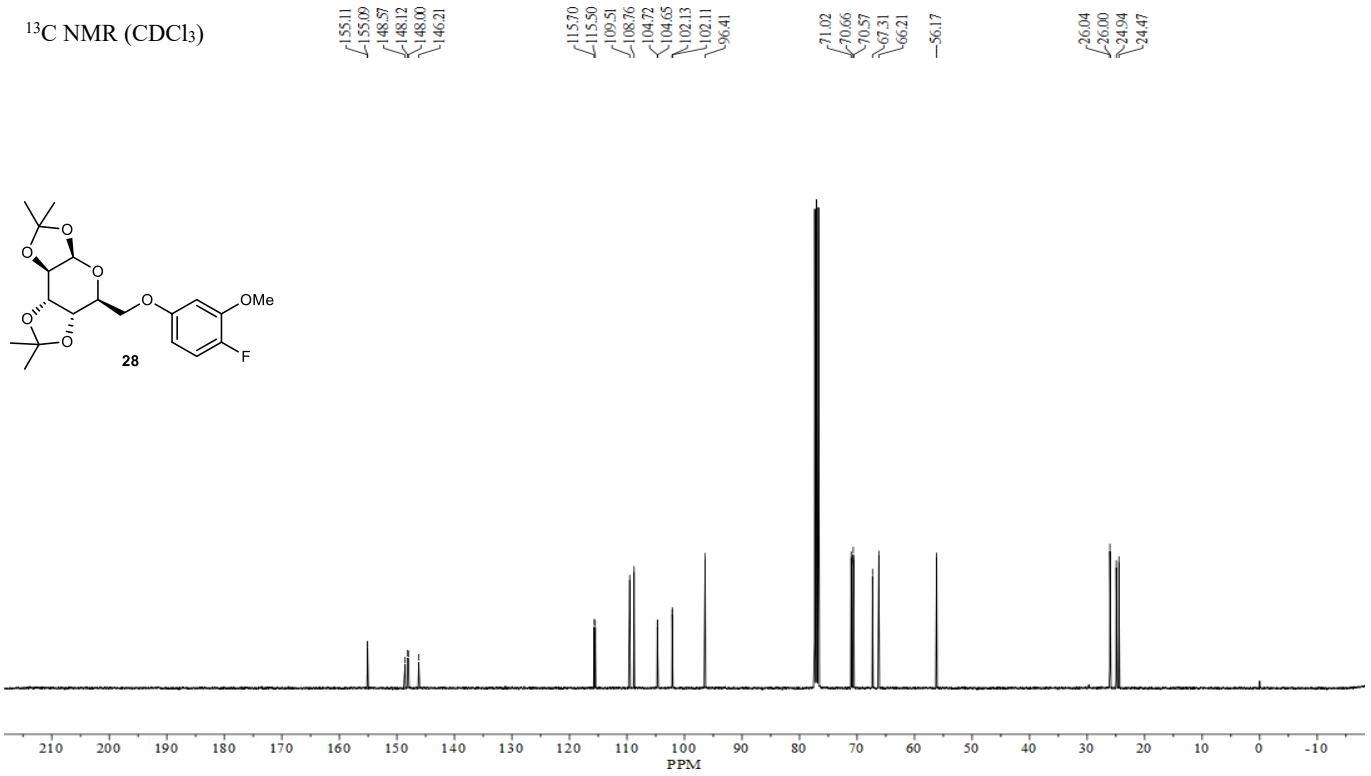




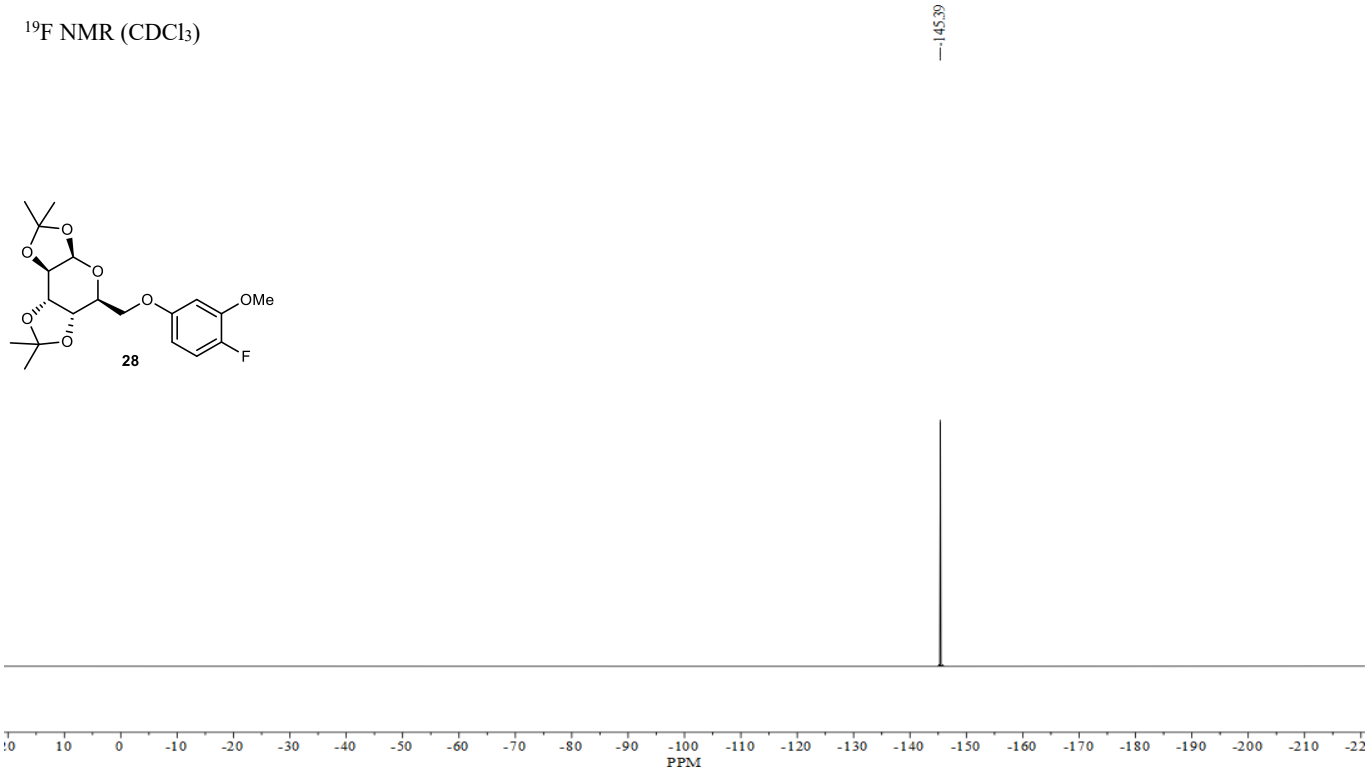
28



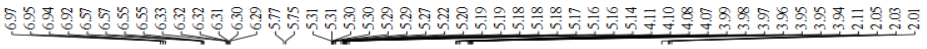
^{13}C NMR ($CDCl_3$)

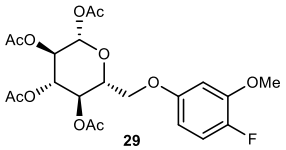


^{19}F NMR ($CDCl_3$)



^{1}H NMR ($CDCl_3$)





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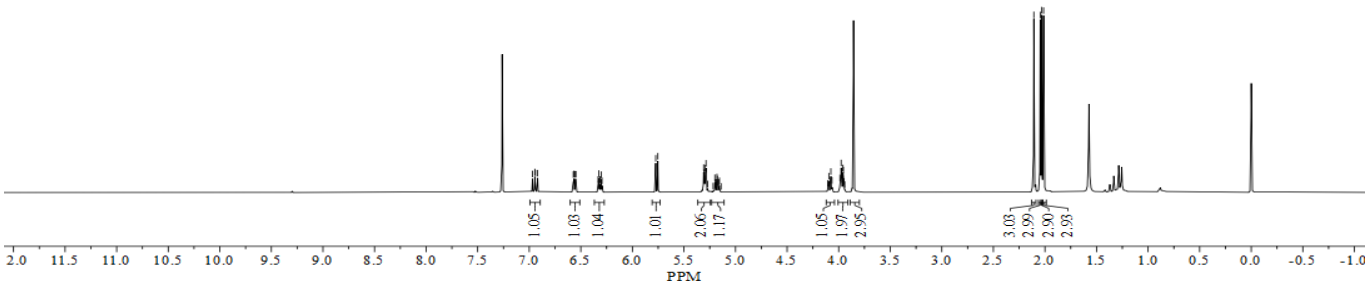
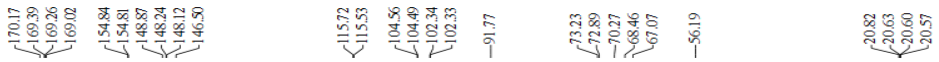
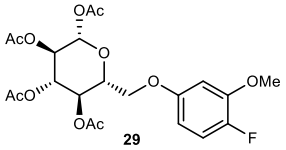


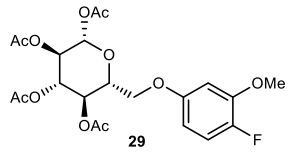
^{13}C NMR ($CDCl_3$)





29

^{19}F NMR ($CDCl_3$)



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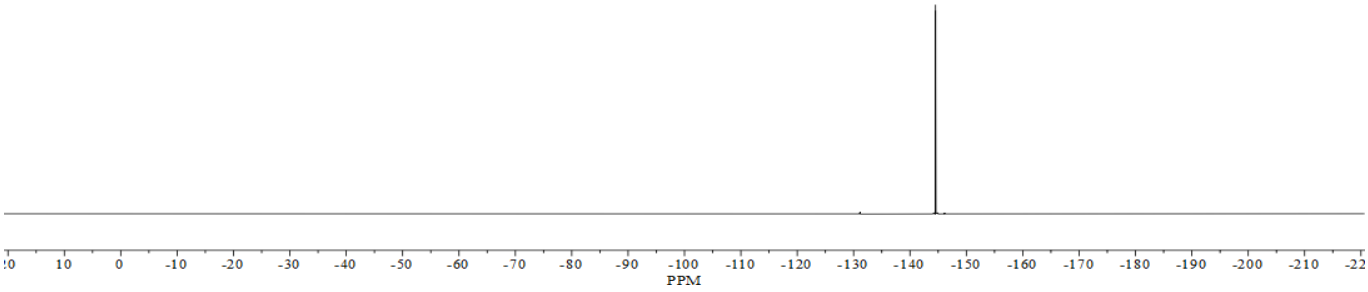
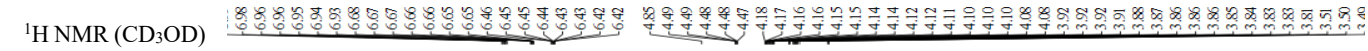
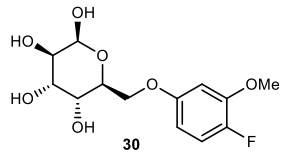


^{1}H NMR (CD_3OD)





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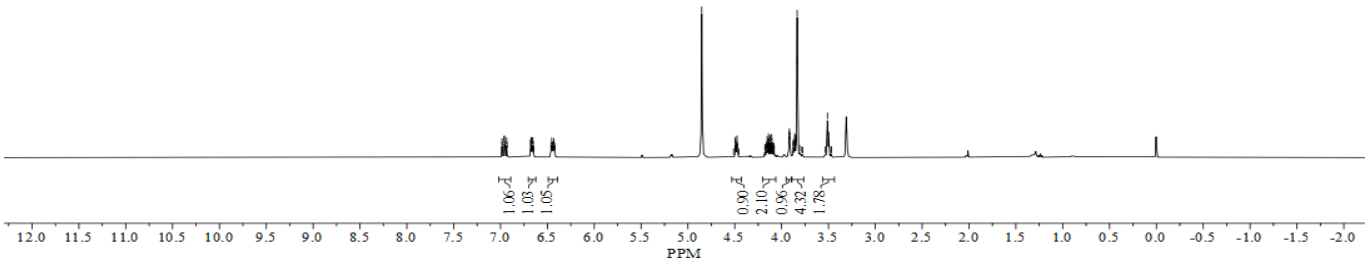
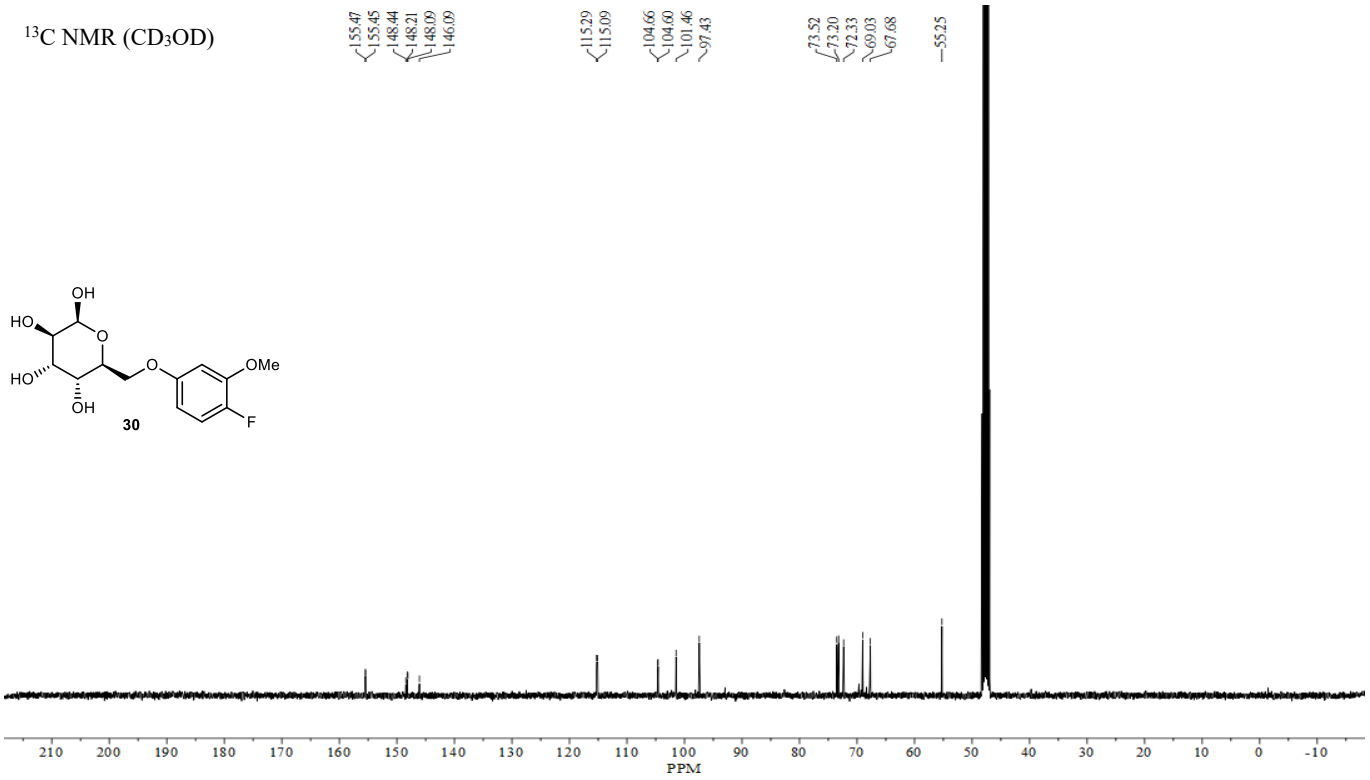


^{13}C NMR (CD_3OD)



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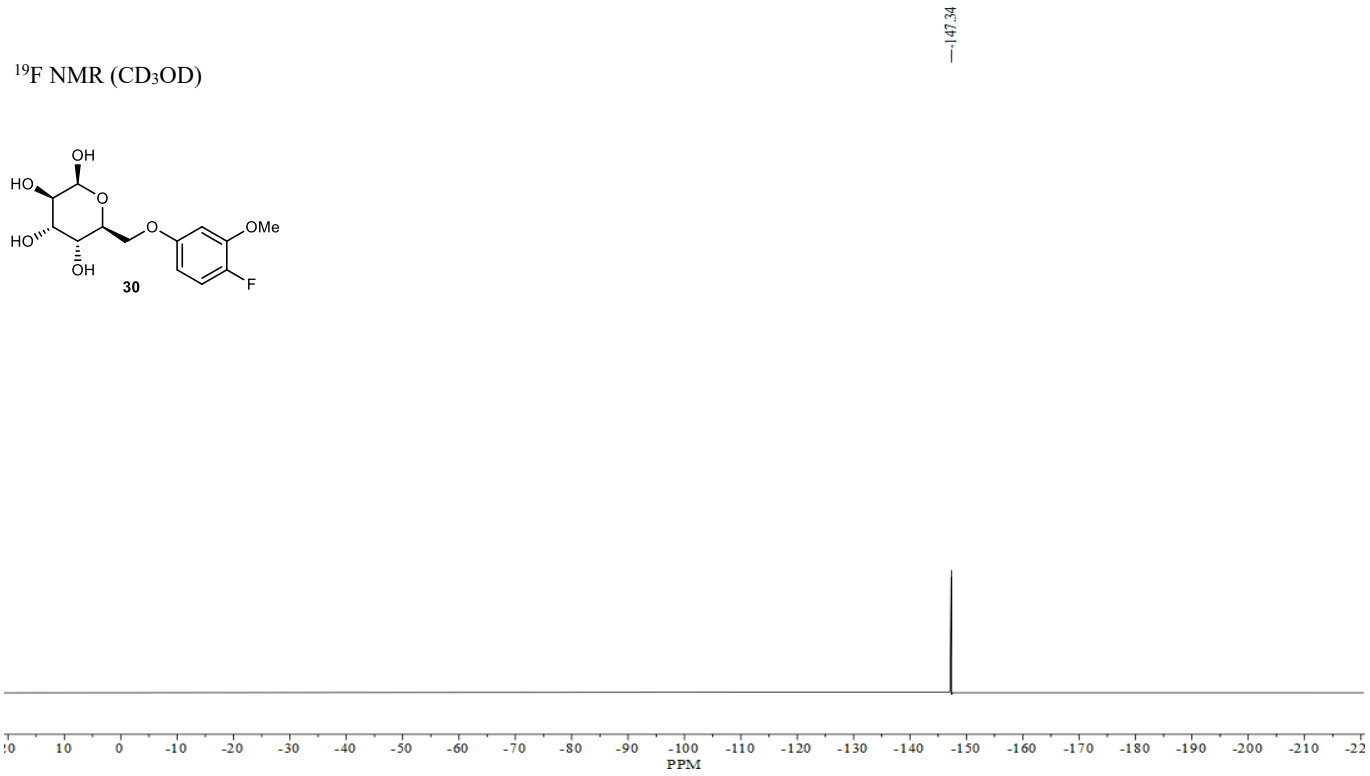
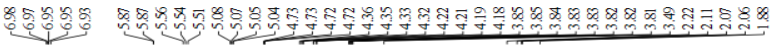
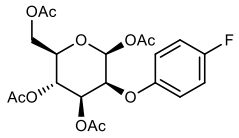
^{19}F NMR (CD_3OD)



30

^{1}H NMR ($CDCl_3$)





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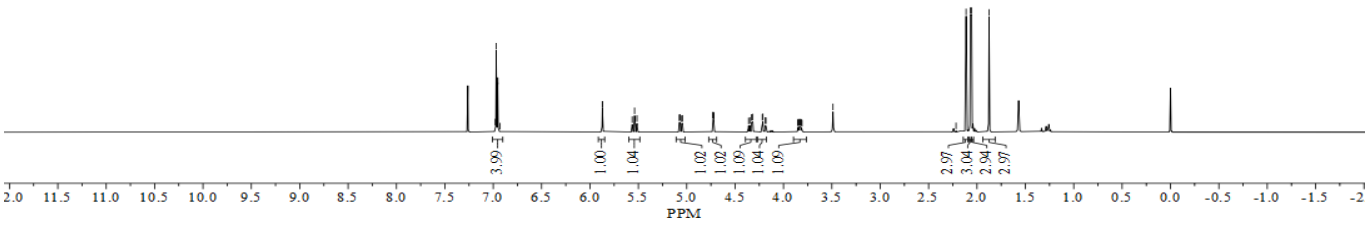
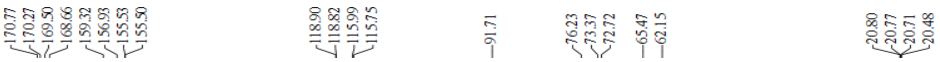
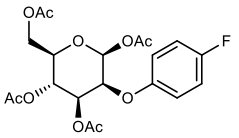
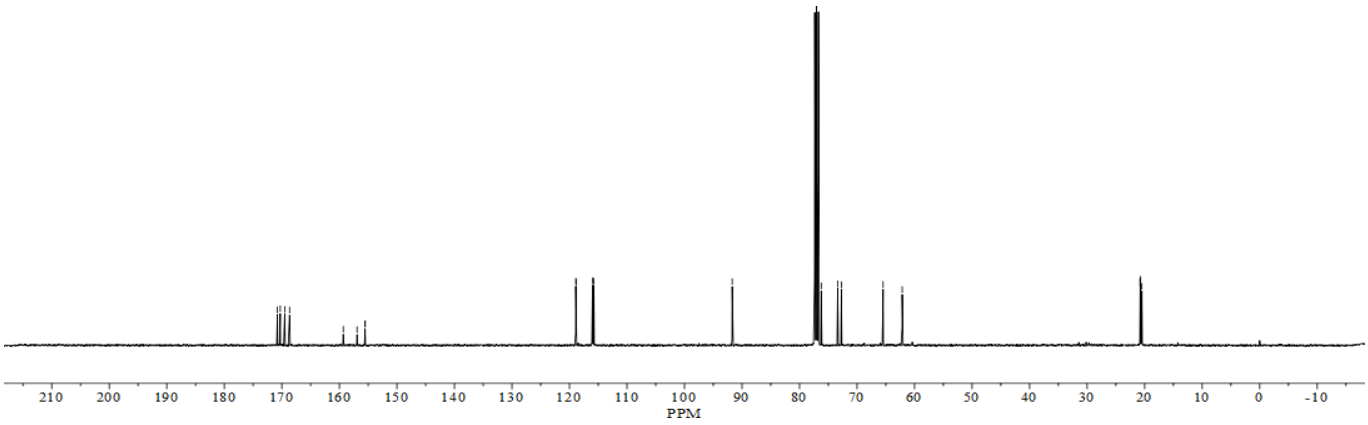




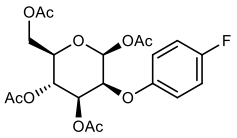
^{13}C NMR ($CDCl_3$)



31

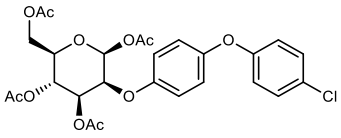


^{19}F NMR ($CDCl_3$)

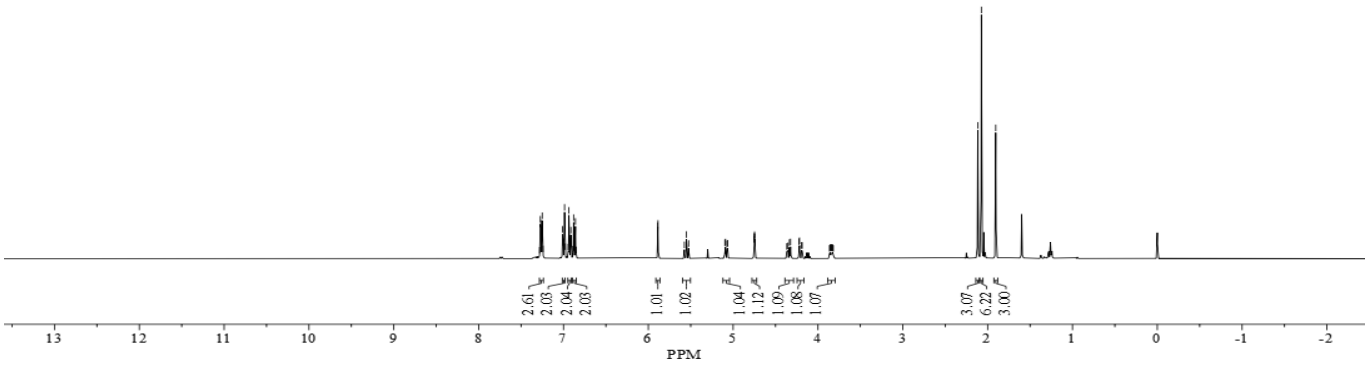


31

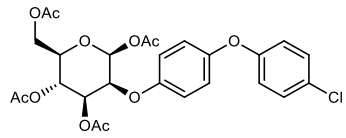
^{1}H NMR ($CDCl_3$)



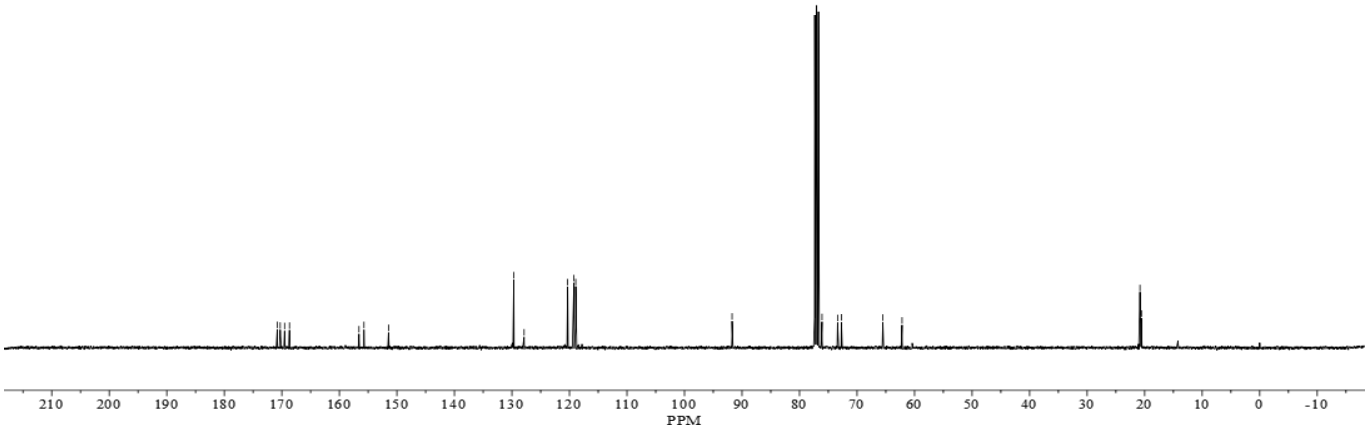
31-deo



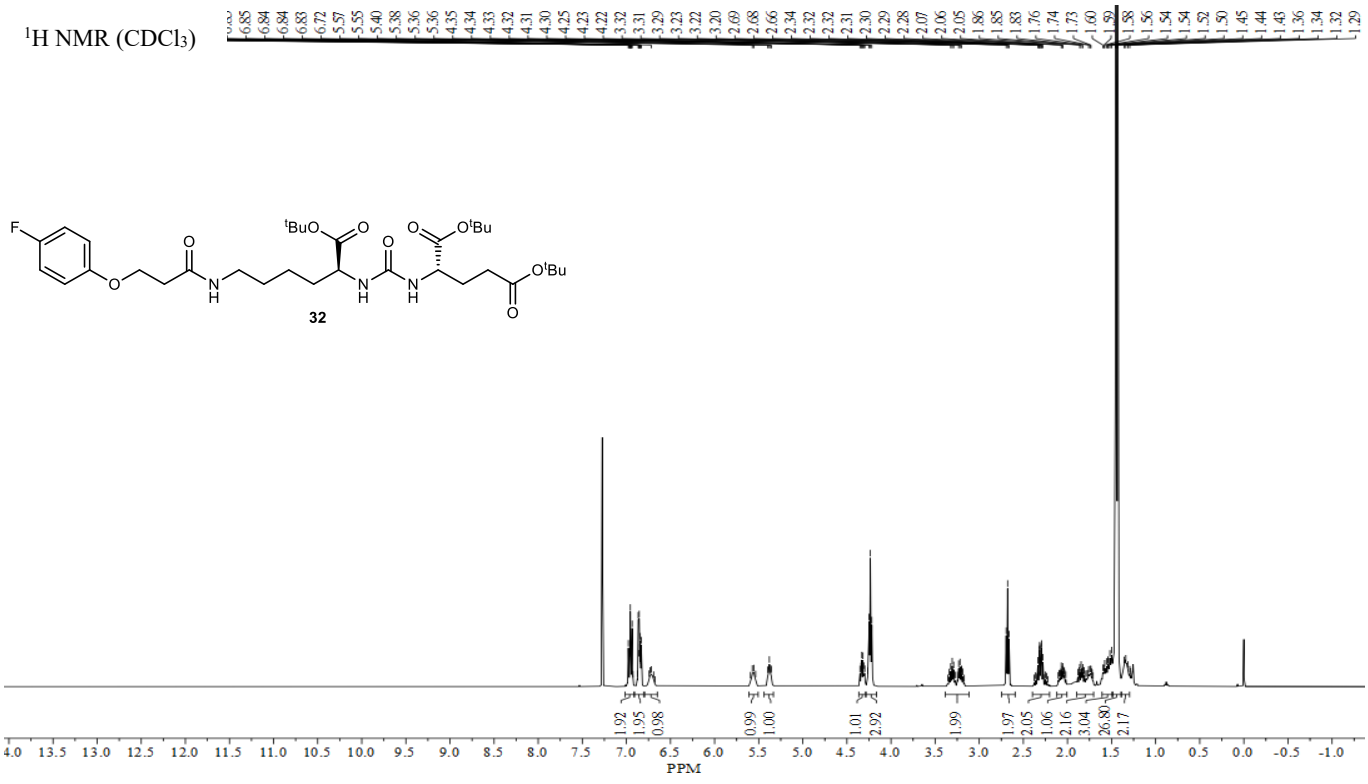
^{13}C NMR ($CDCl_3$)



31-deo

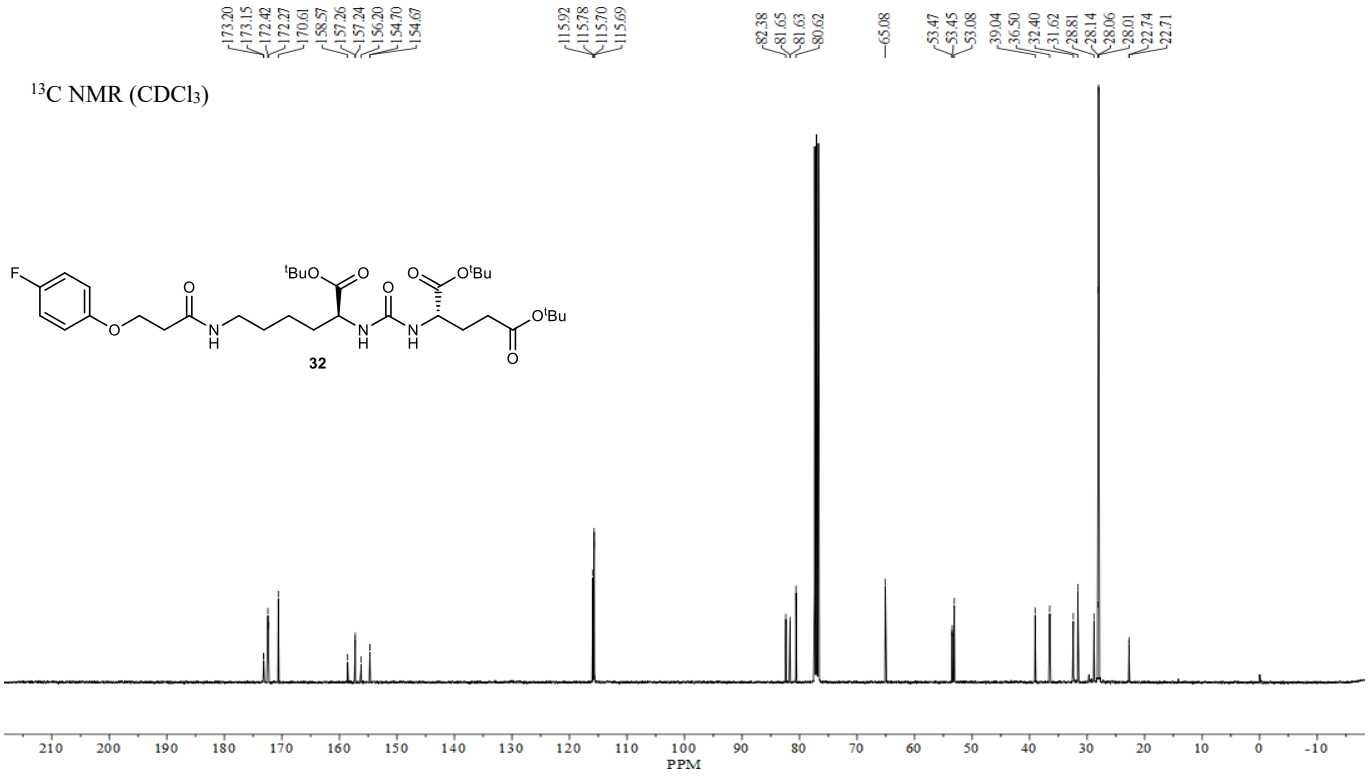


^{1}H NMR ($CDCl_3$)

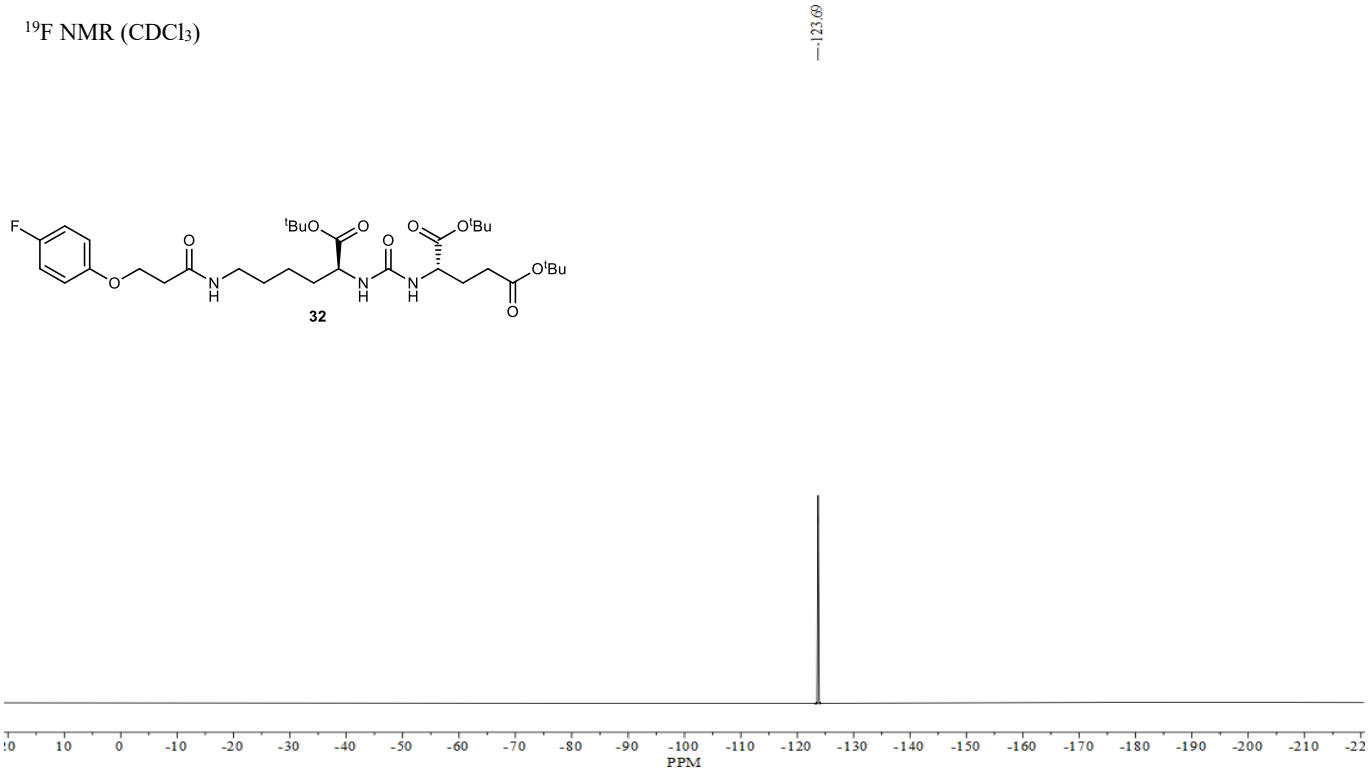


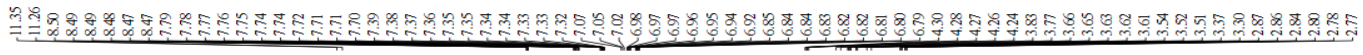
32

^{13}C NMR ($CDCl_3$)

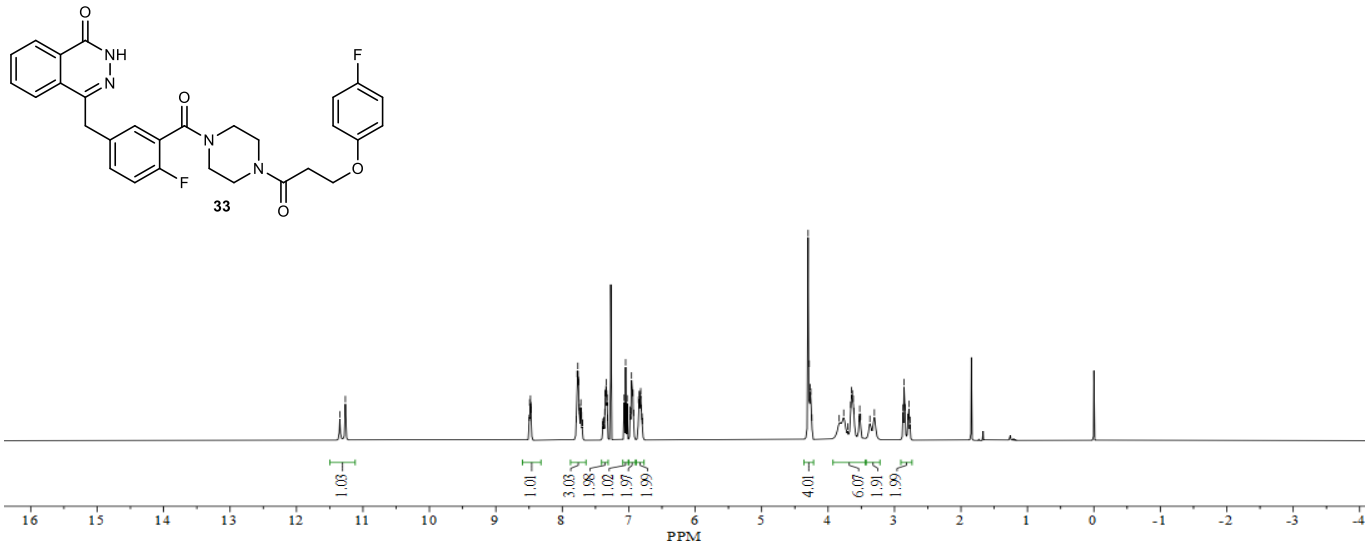


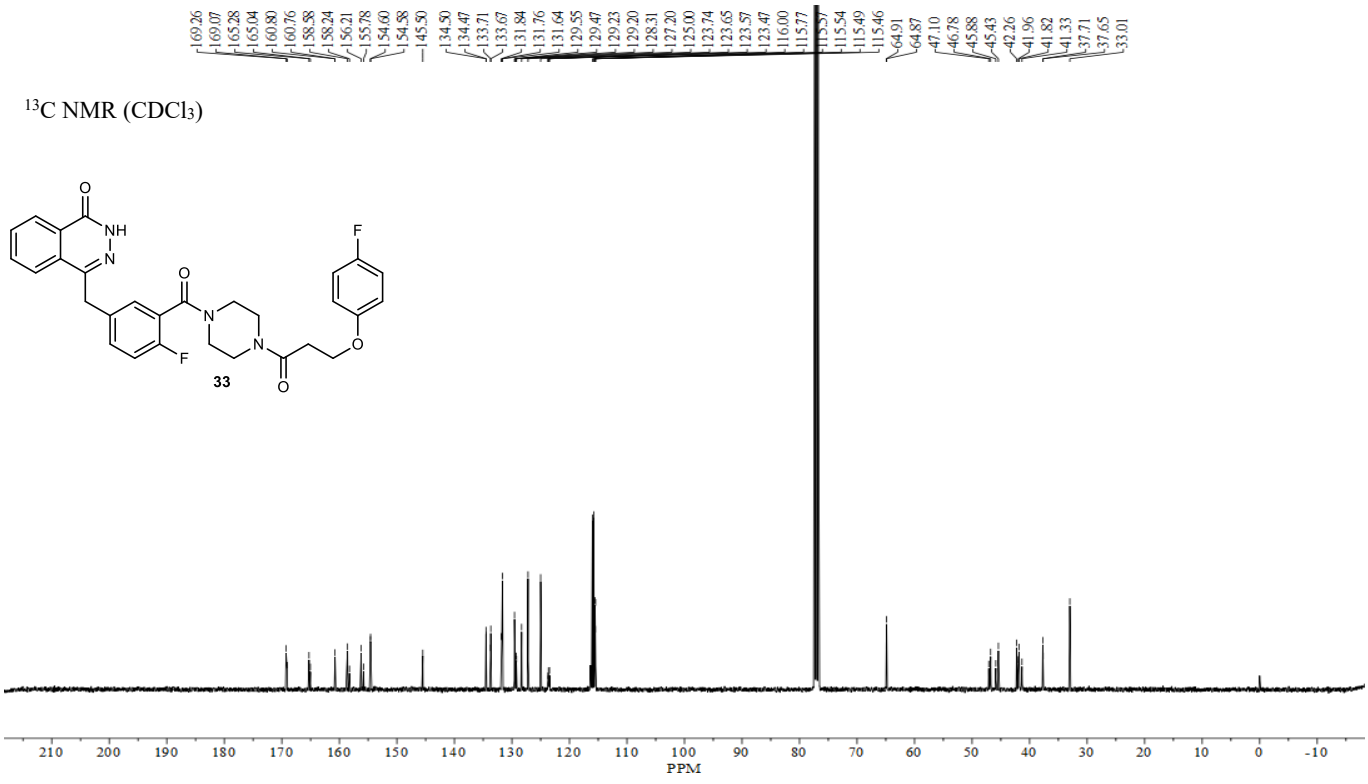
^{19}F NMR ($CDCl_3$)





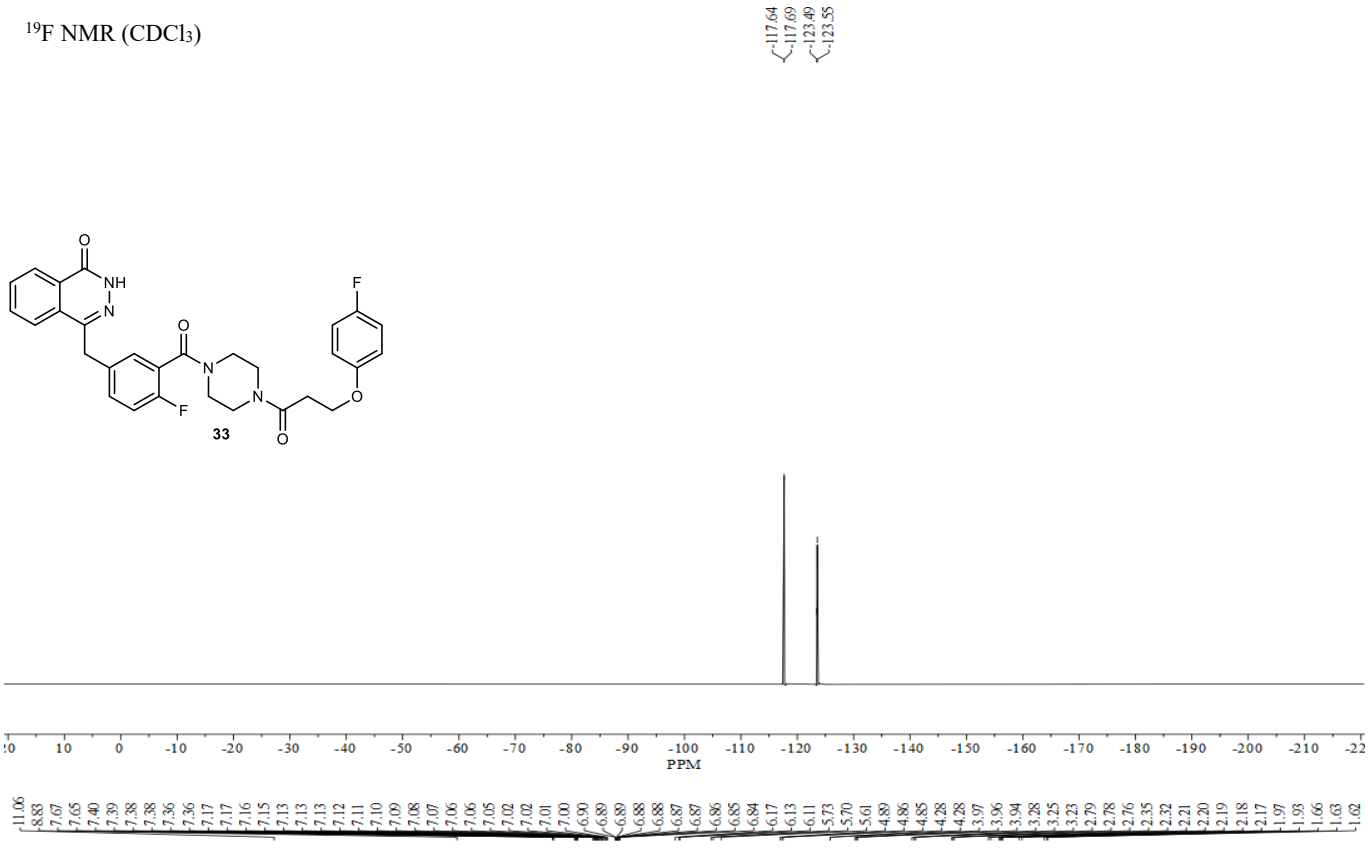
^{1}H NMR ($CDCl_3$)



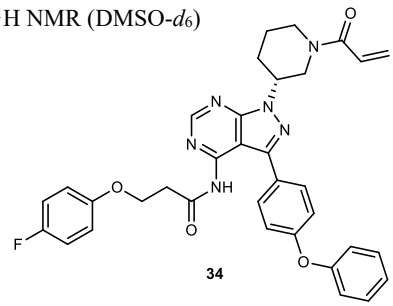


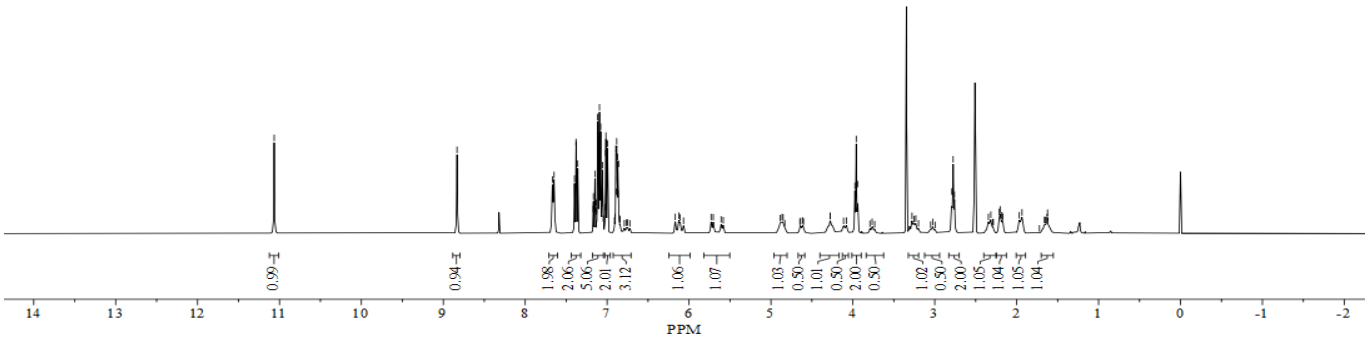
^{13}C NMR ($CDCl_3$)

^{19}F NMR ($CDCl_3$)

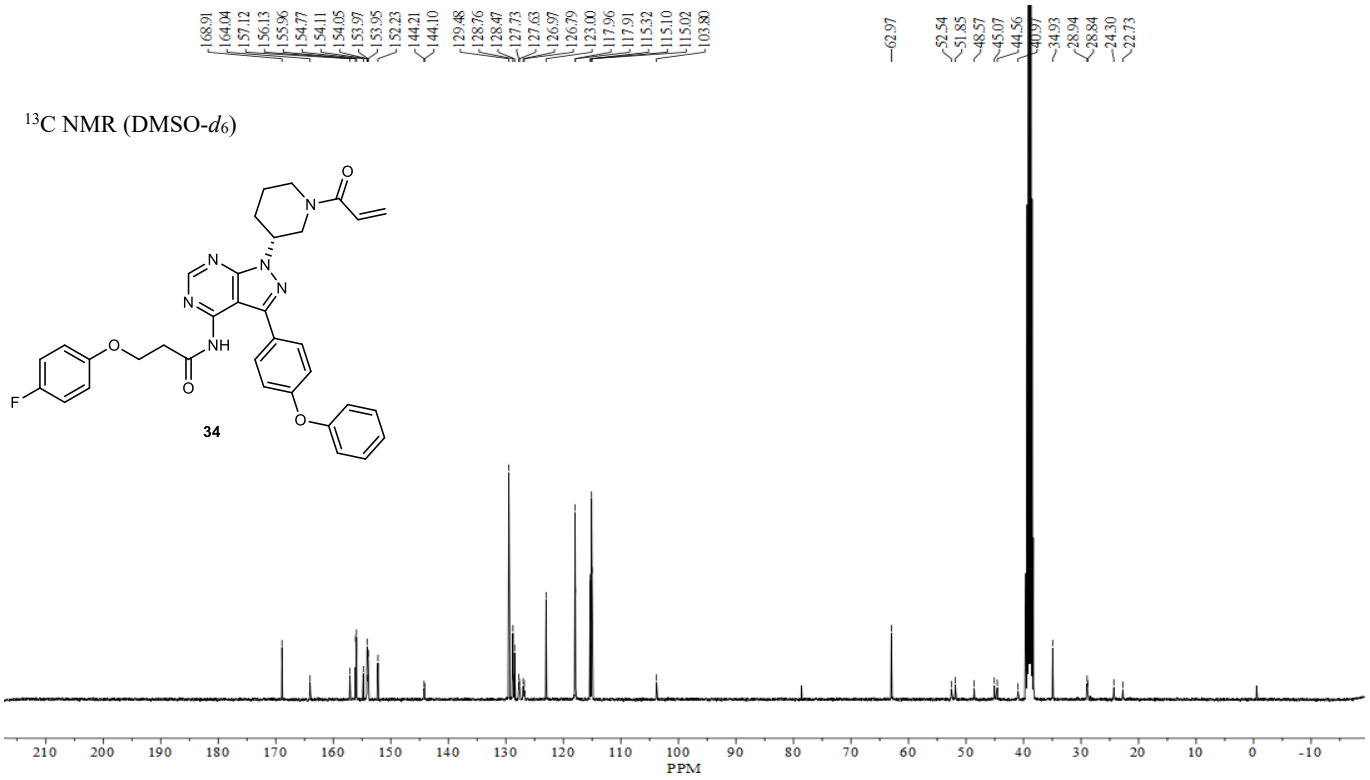


^{1}H NMR (DMSO-d_6)

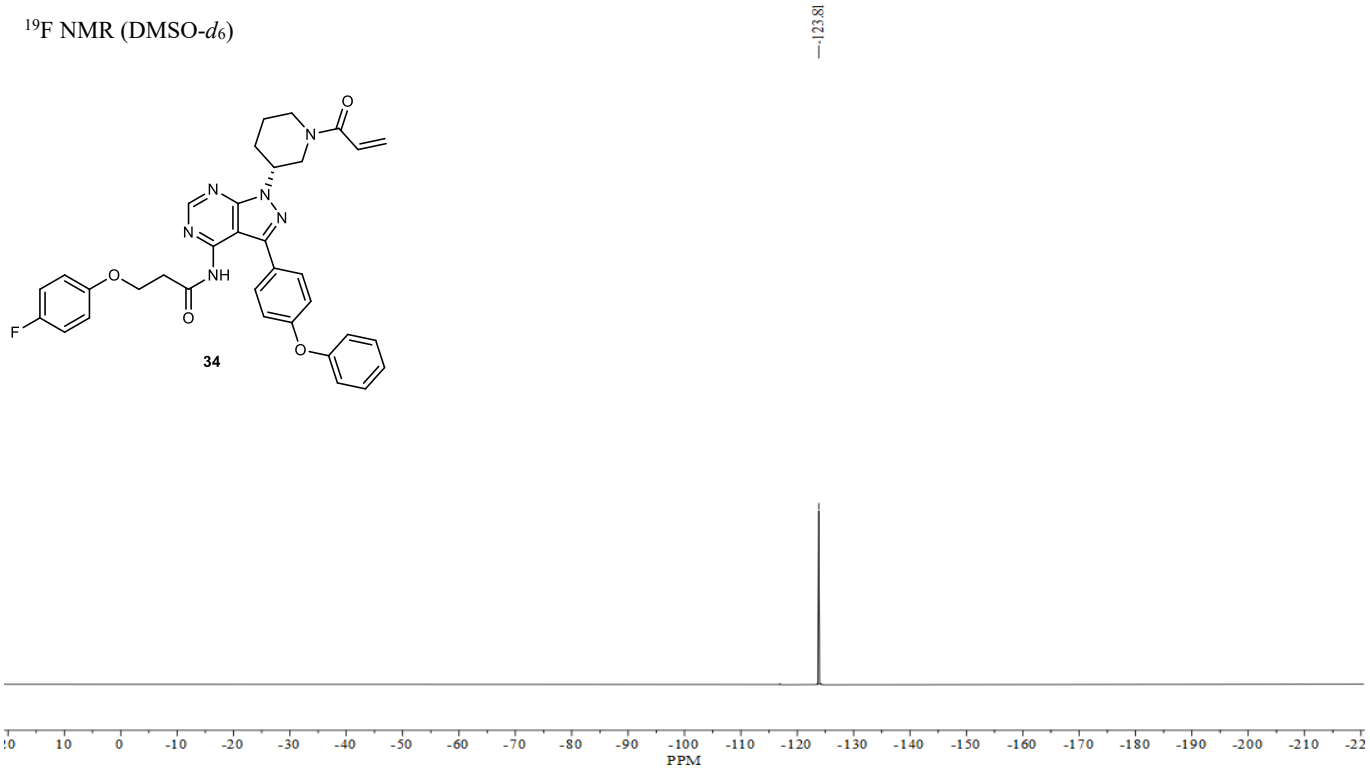


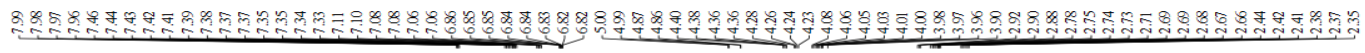


^{13}C NMR (DMSO-d_6)

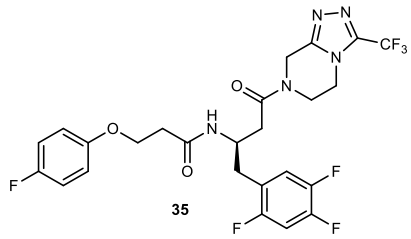


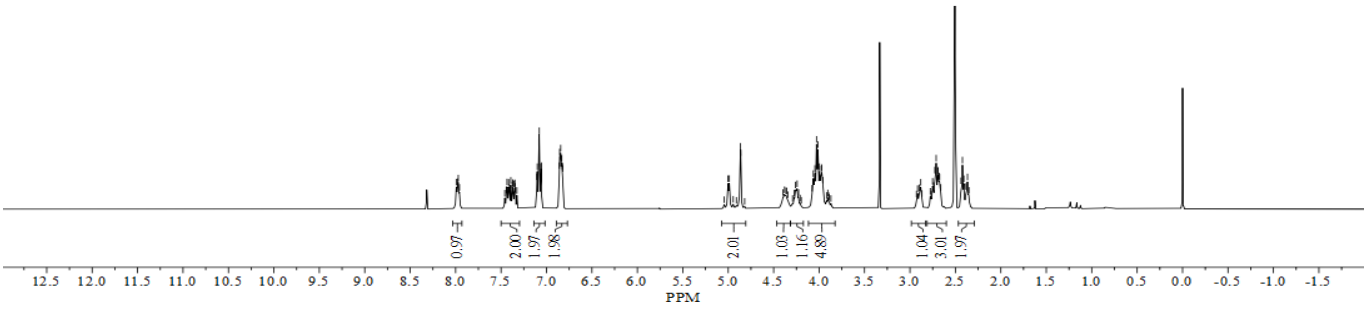
^{19}F NMR (DMSO-d_6)

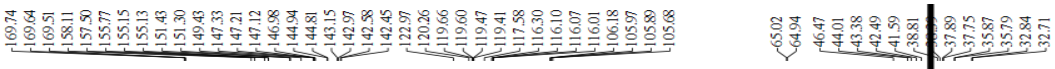




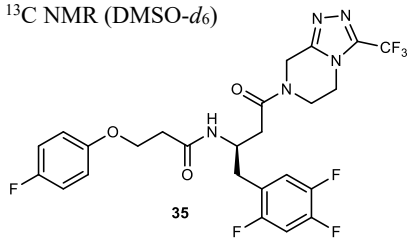
^{1}H NMR (DMSO-d_6)

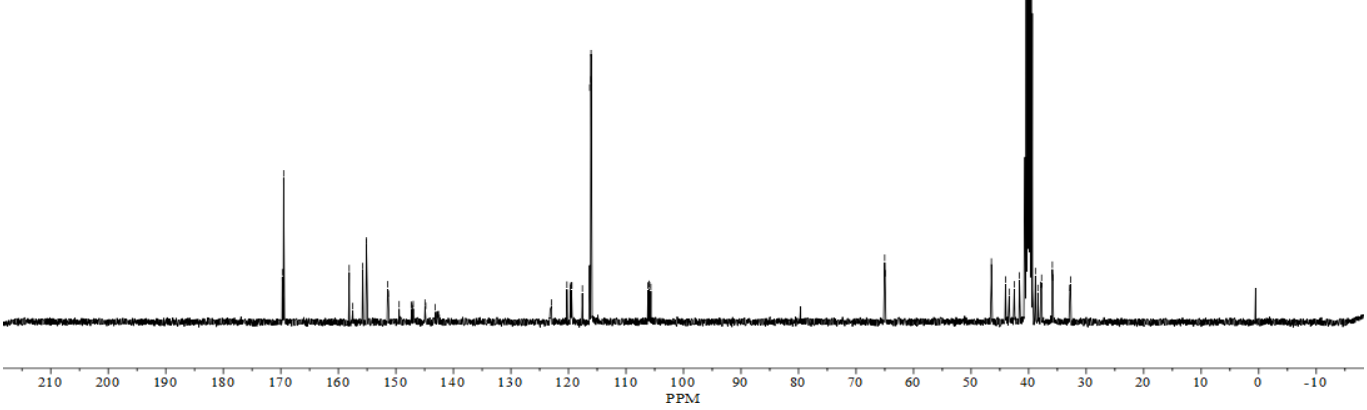




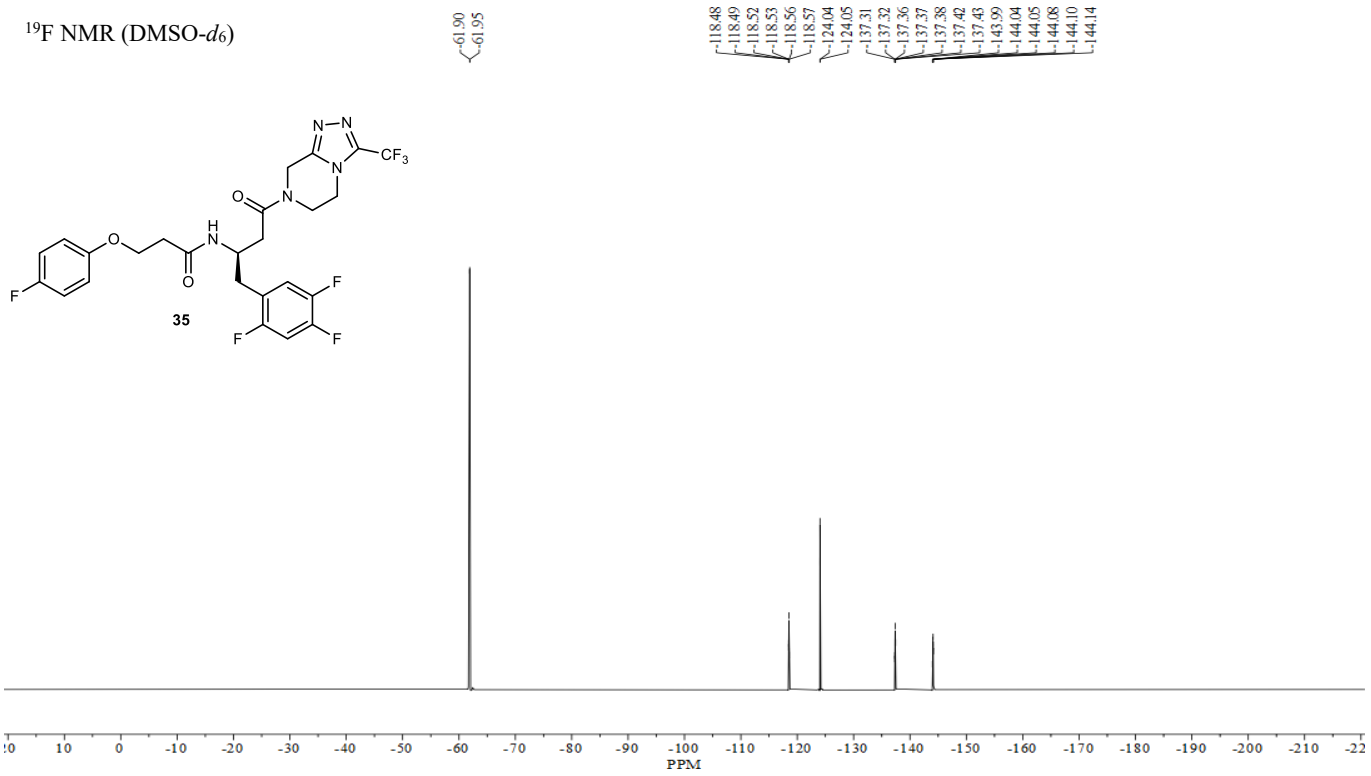


^{13}C NMR (DMSO-d_6)

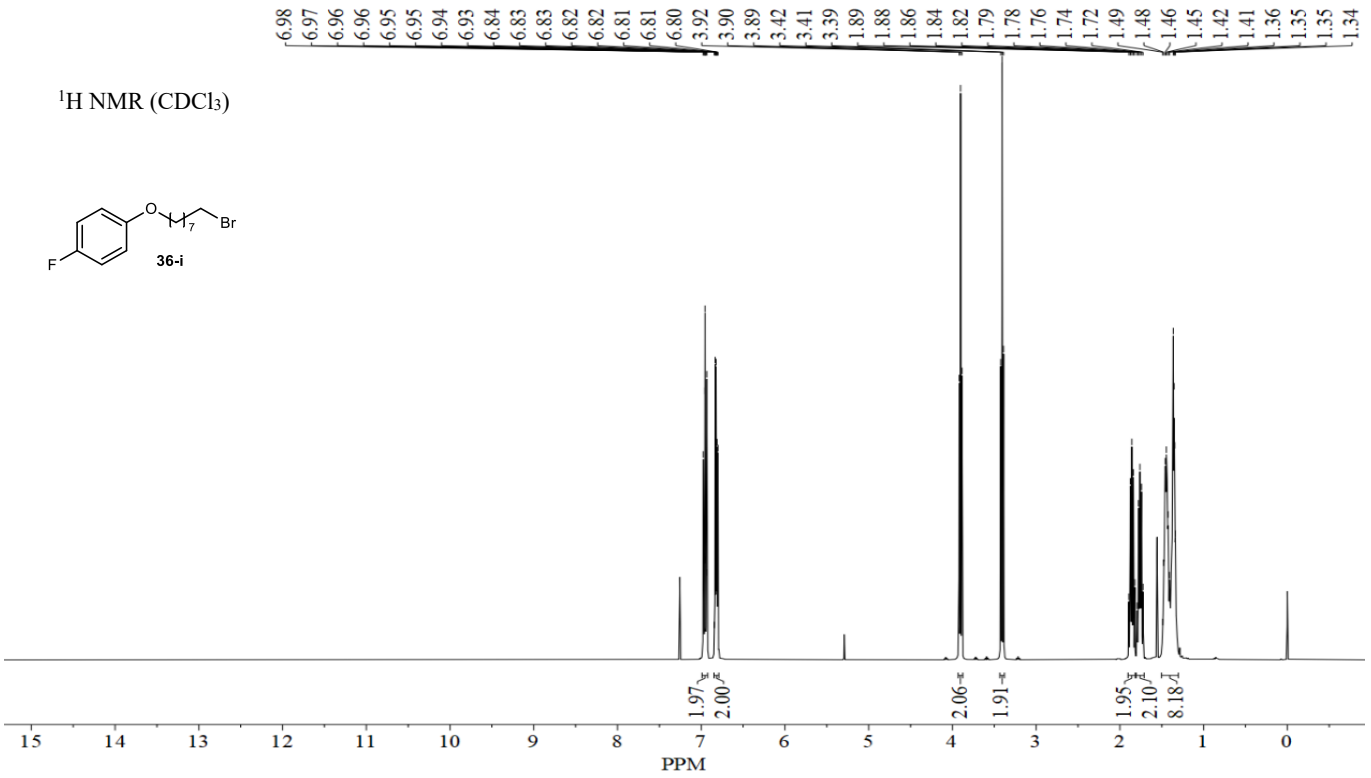




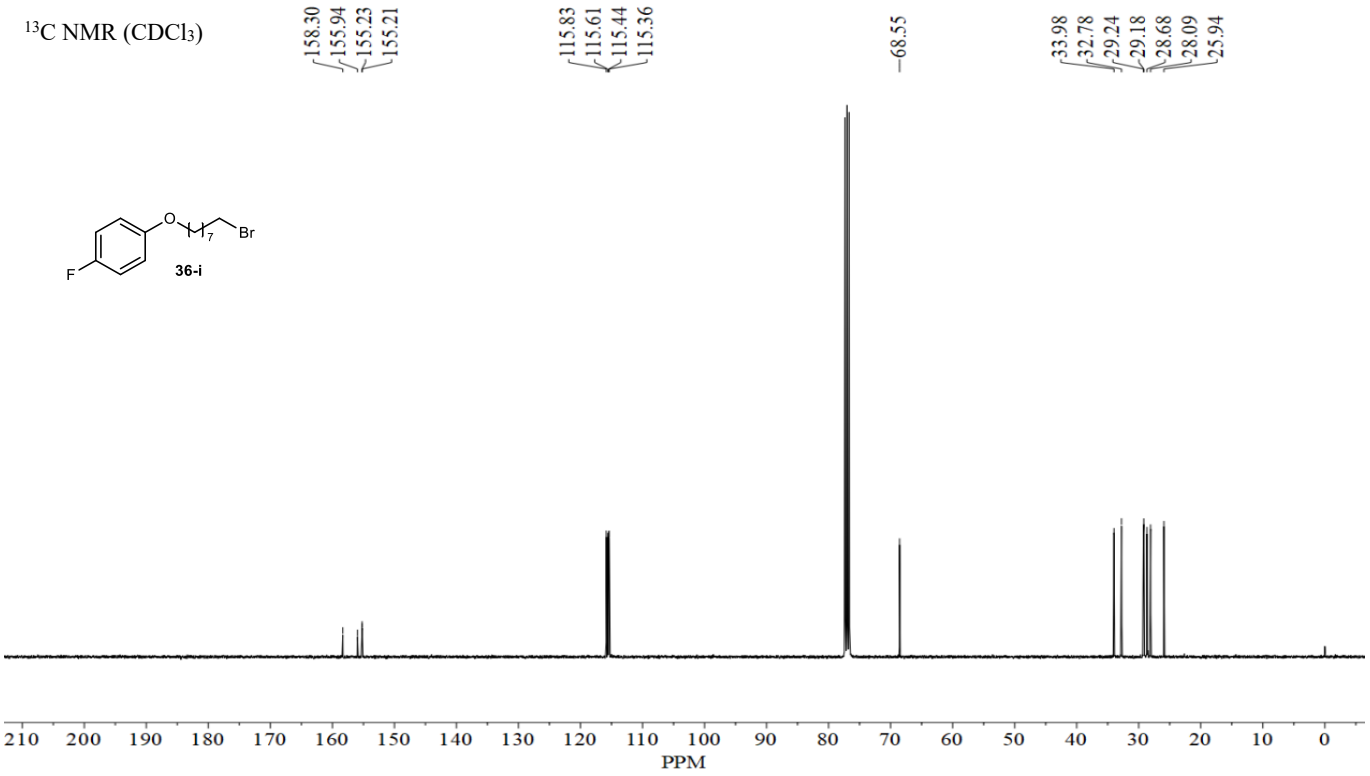
^{19}F NMR (DMSO-d_6)



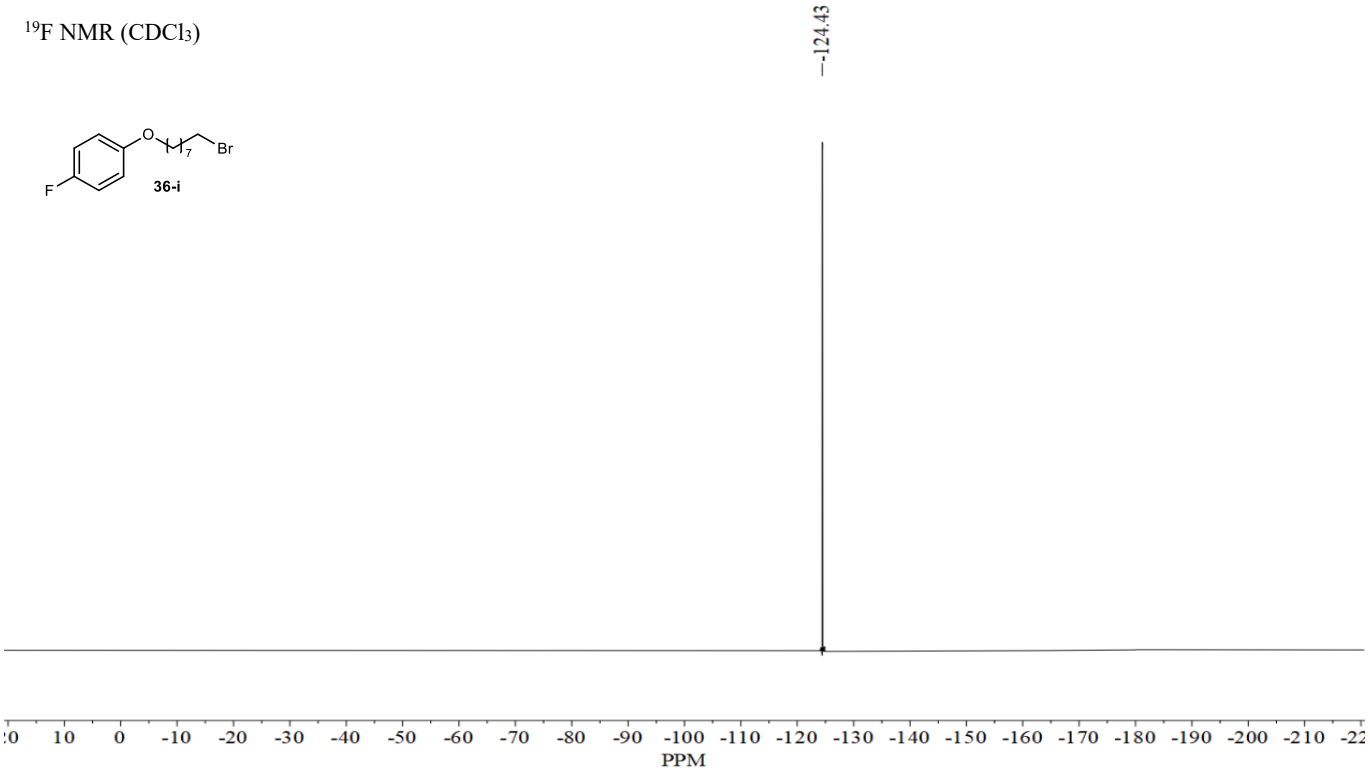
^{1}H NMR ($CDCl_3$)



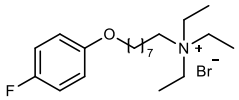
^{13}C NMR ($CDCl_3$)



^{19}F NMR ($CDCl_3$)

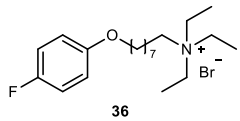


^{1}H NMR ($CDCl_3$)



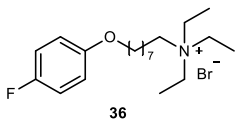
36

^{13}C NMR ($CDCl_3$)



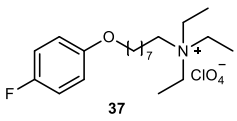
36

^{19}F NMR ($CDCl_3$)



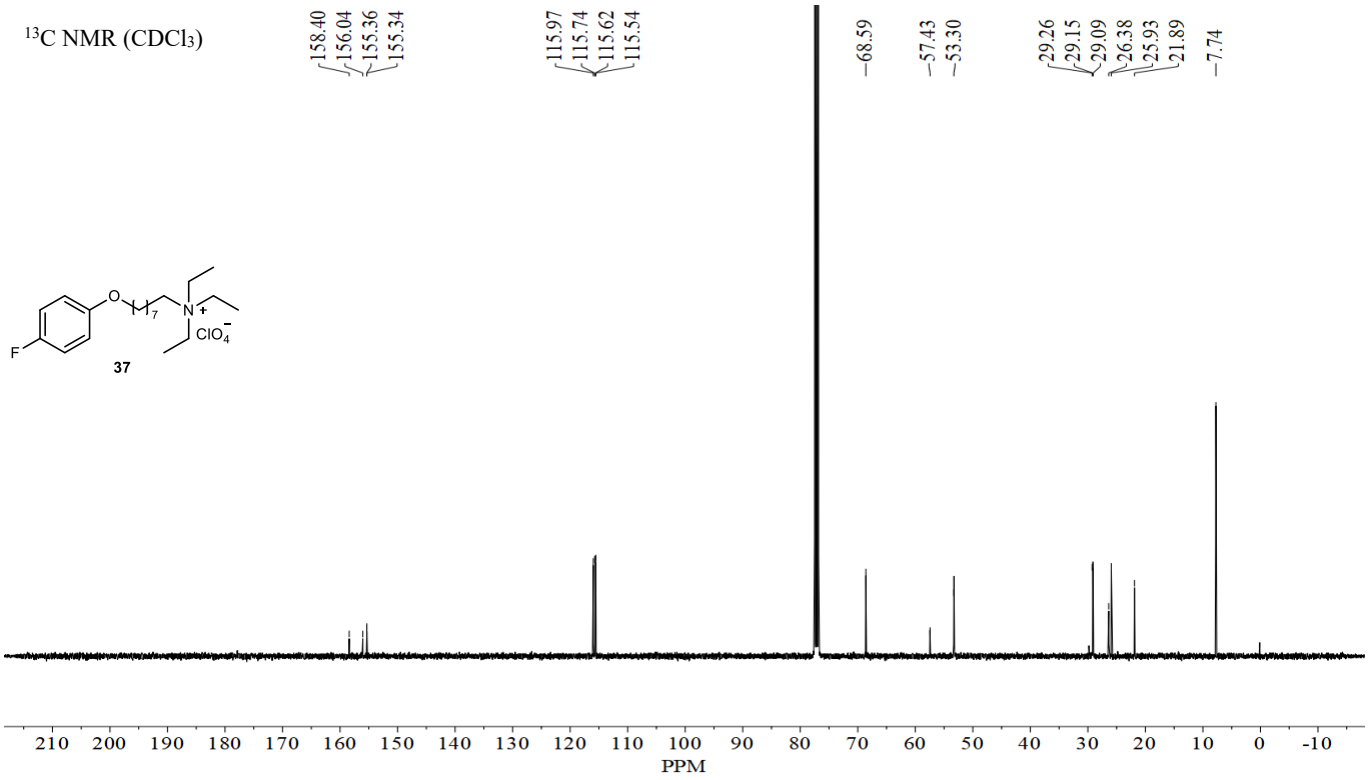
36

^{1}H NMR ($CDCl_3$)

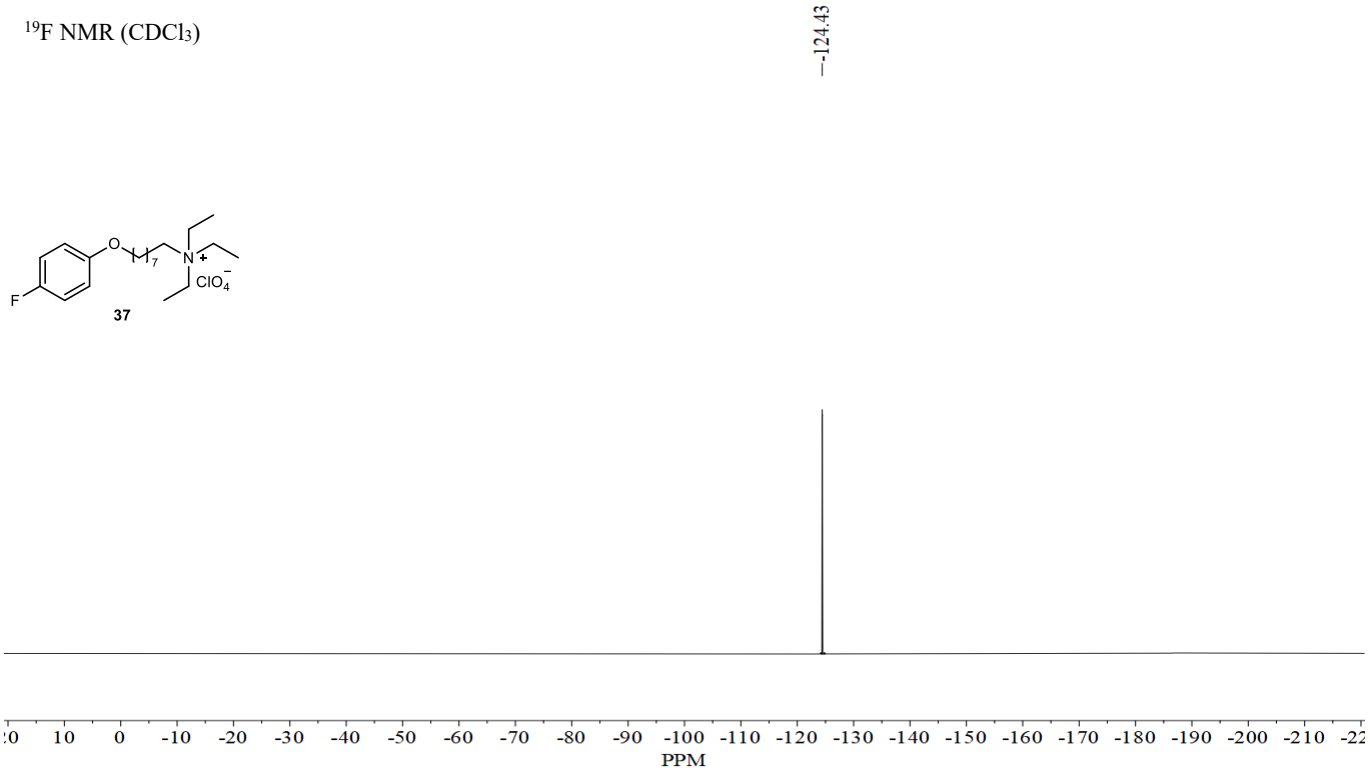


37

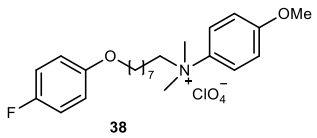
^{13}C NMR ($CDCl_3$)



^{19}F NMR ($CDCl_3$)



^{1}H NMR ($CDCl_3$)



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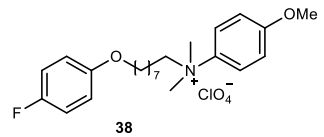
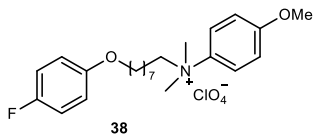


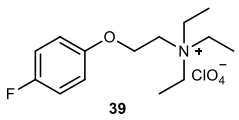
38

^{19}F NMR ($CDCl_3$)



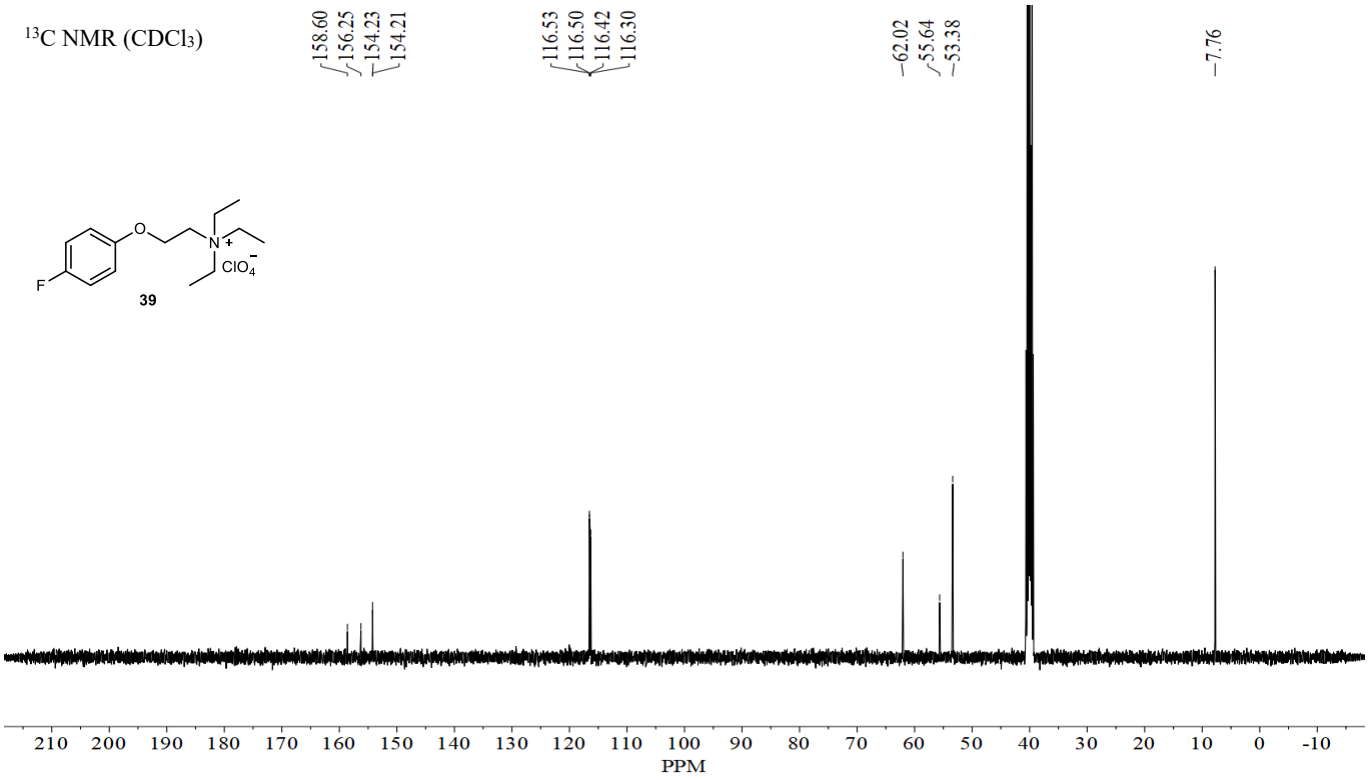
38

^{1}H NMR ($CDCl_3$)

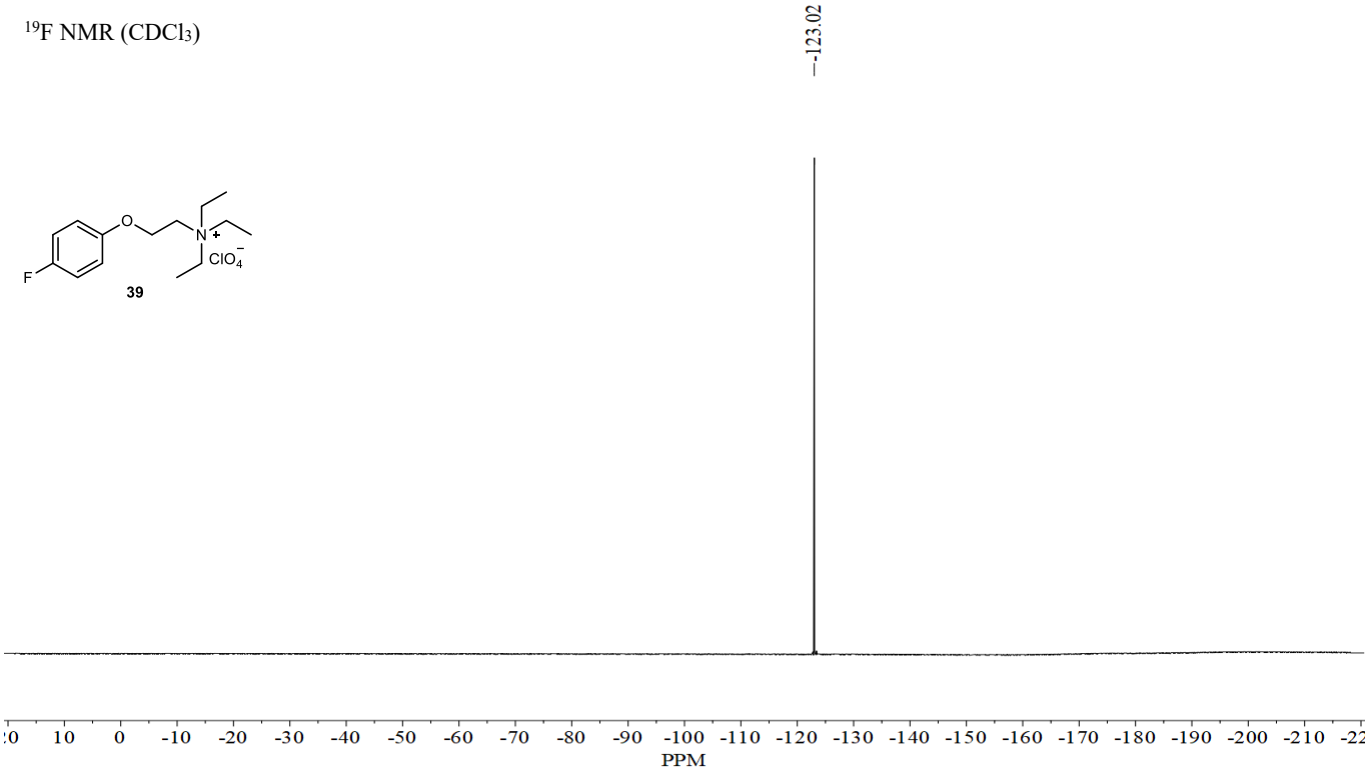


39

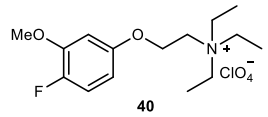
^{13}C NMR ($CDCl_3$)



^{19}F NMR ($CDCl_3$)

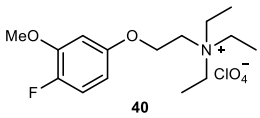


^{1}H NMR ($CDCl_3$)



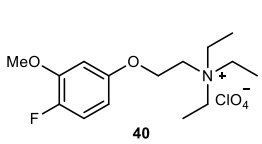
40

^{13}C NMR ($CDCl_3$)



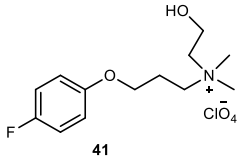
40

^{19}F NMR ($CDCl_3$)



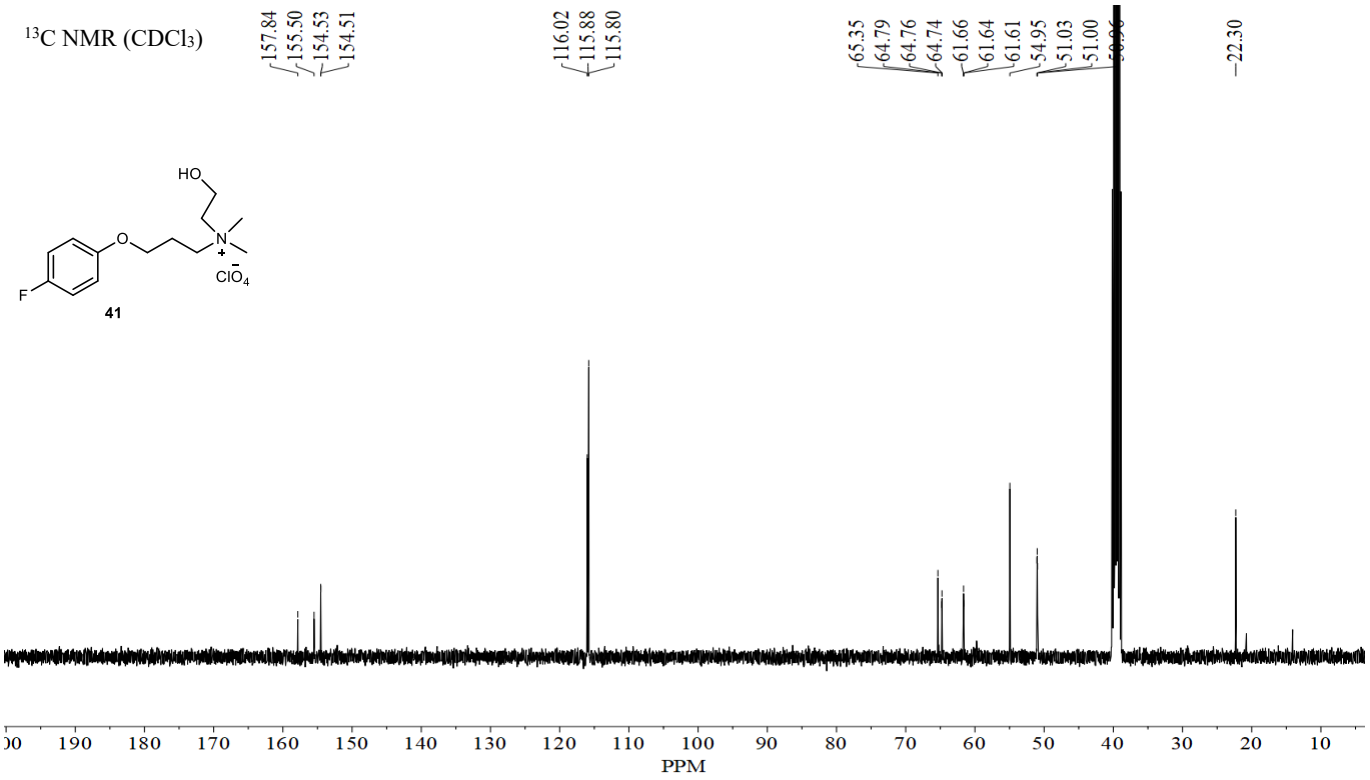
40

^{1}H NMR ($CDCl_3$)

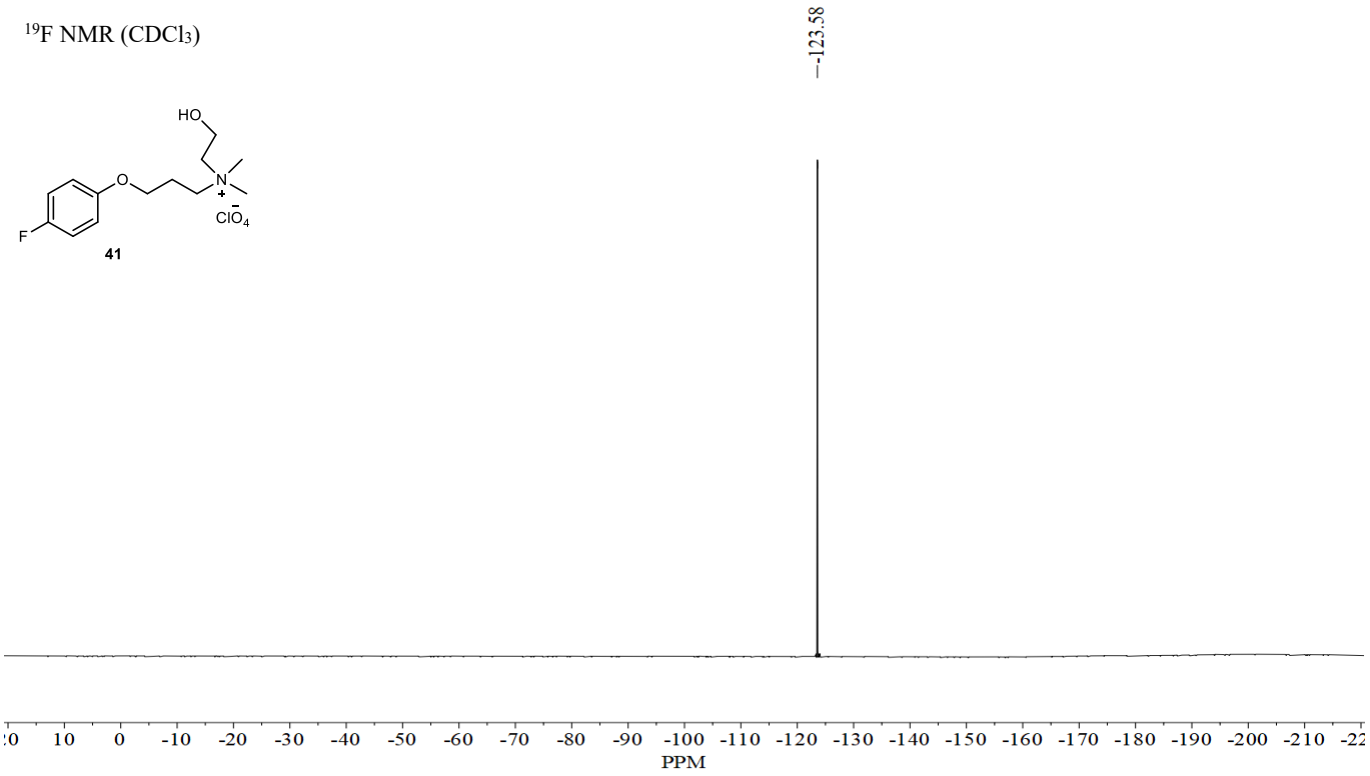


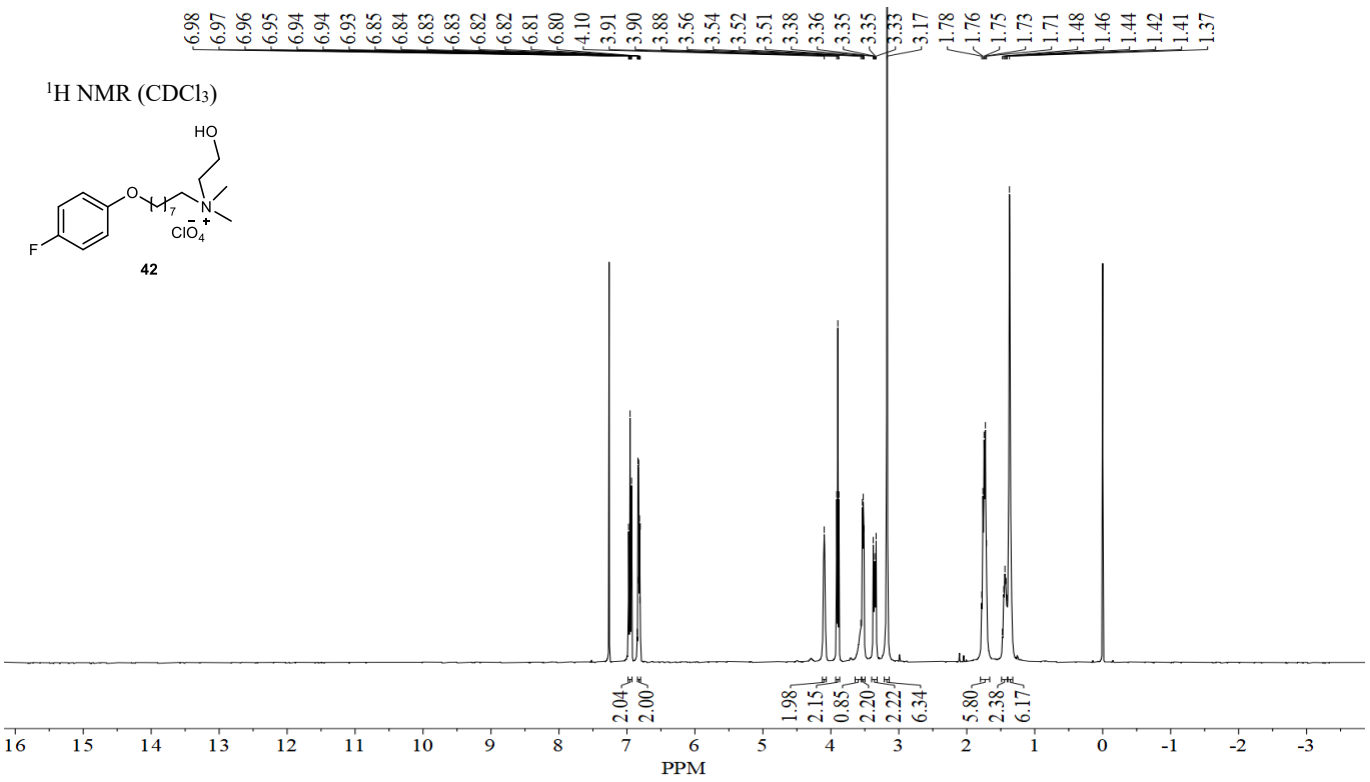
41

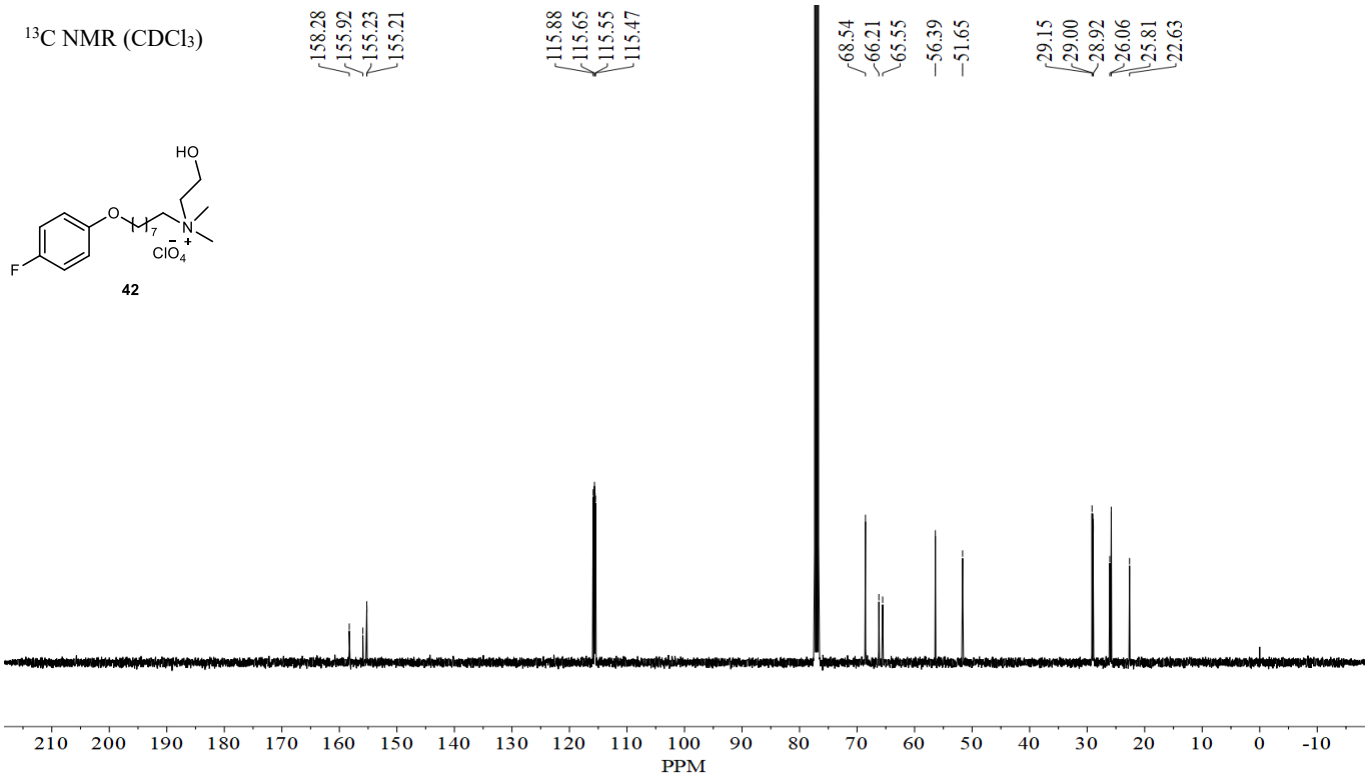
^{13}C NMR ($CDCl_3$)



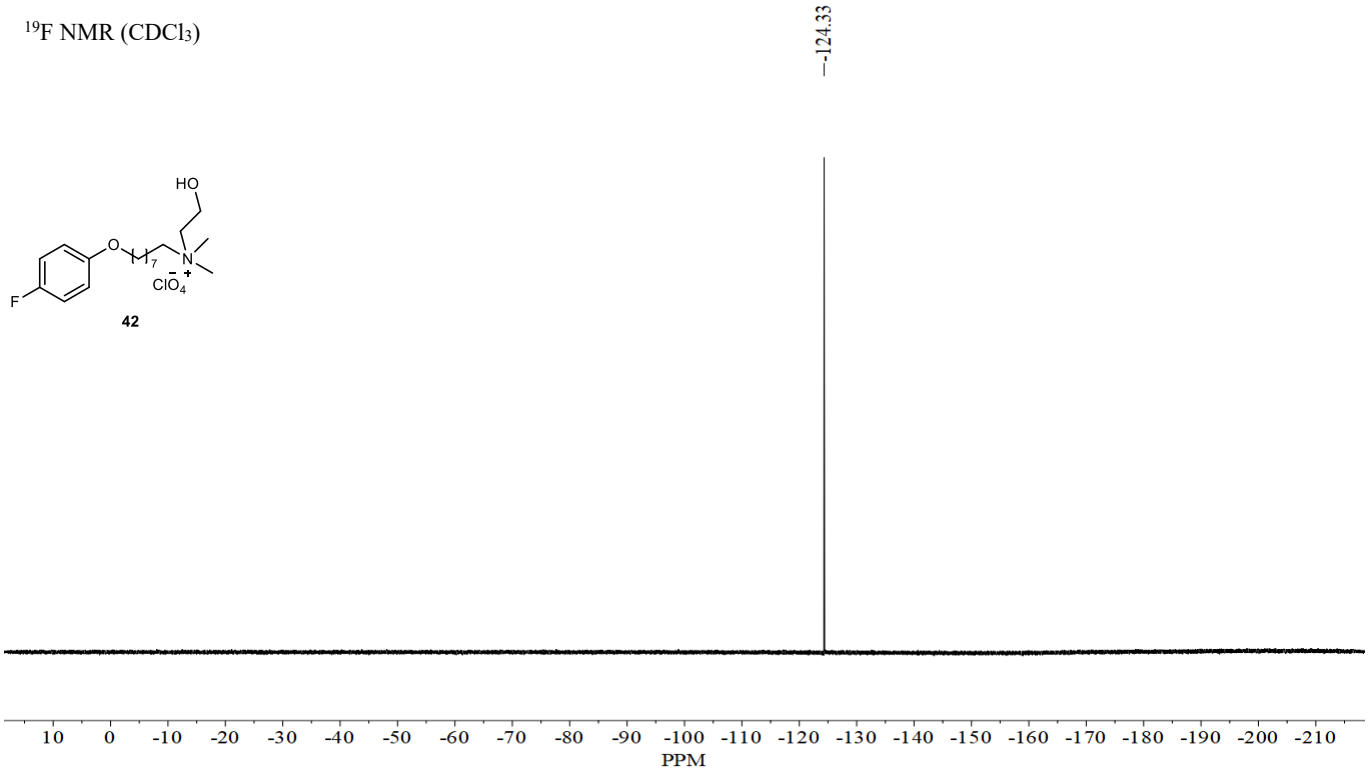
^{19}F NMR ($CDCl_3$)



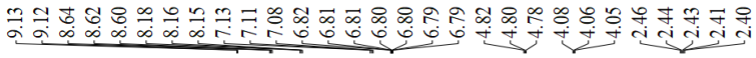

6.98 6.97 6.96 6.95 6.94 6.94 6.93 6.85 6.84 6.83 6.83 6.82 6.82 6.81 6.80 4.10 3.91 3.90 3.88 3.56 3.54 3.52 3.51 3.38 3.36 3.35 3.35 3.33 3.17 1.78 1.76 1.75 1.73 1.71 1.48 1.46 1.44 1.42 1.41 1.37
1H NMR (CDCl3)
HO
O
7
N
ClO4
F
42
2.04 2.00 1.98 2.15 0.85 2.20 2.22 6.34 5.80 2.38 6.17
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3
PPM


13C NMR (CDCl3)
158.28 155.92 155.23 155.21 115.88 115.65 115.55 115.47 68.54 66.21 65.55 56.39 51.65 29.15 29.00 28.92 26.06 25.81 22.63
HO
O
7
N
ClO4
F
42
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
PPM

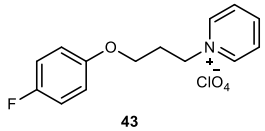
^{19}F NMR ($CDCl_3$)



42

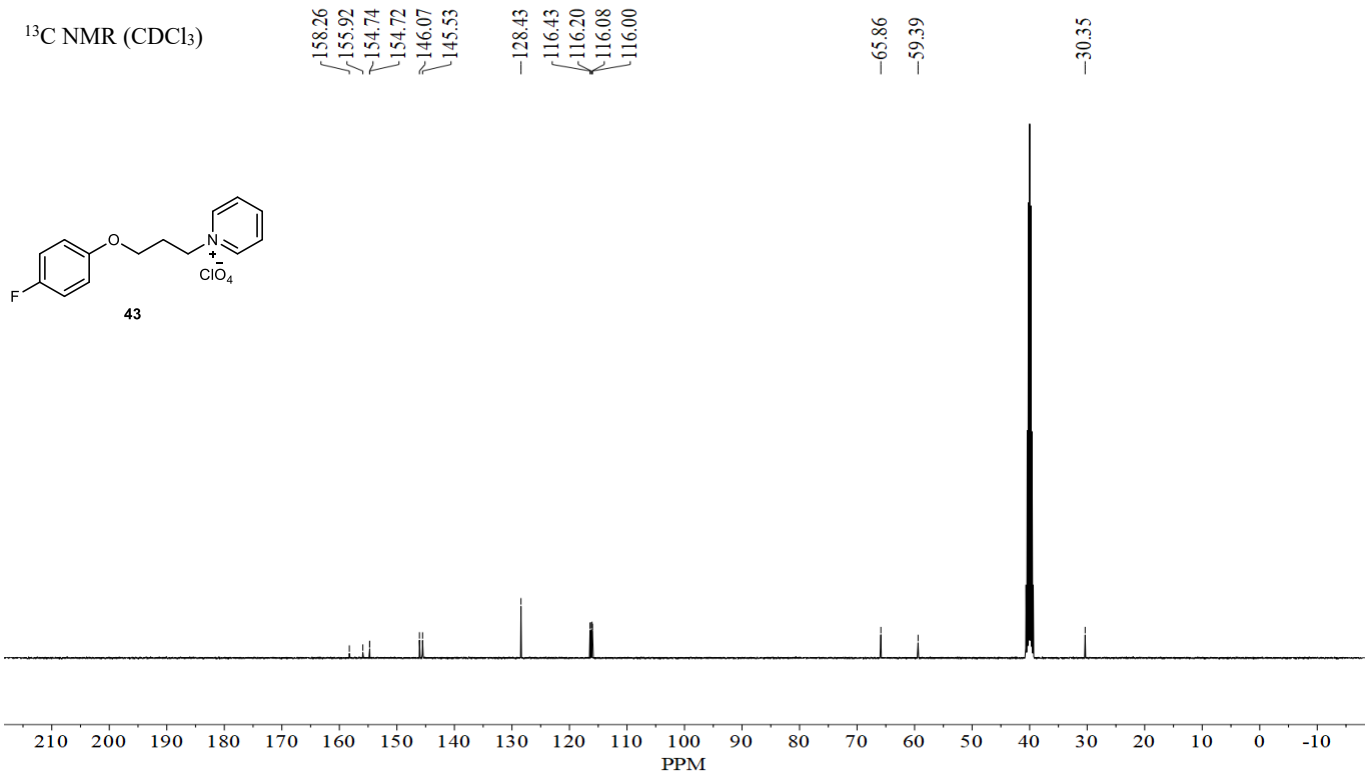


^{1}H NMR ($CDCl_3$)

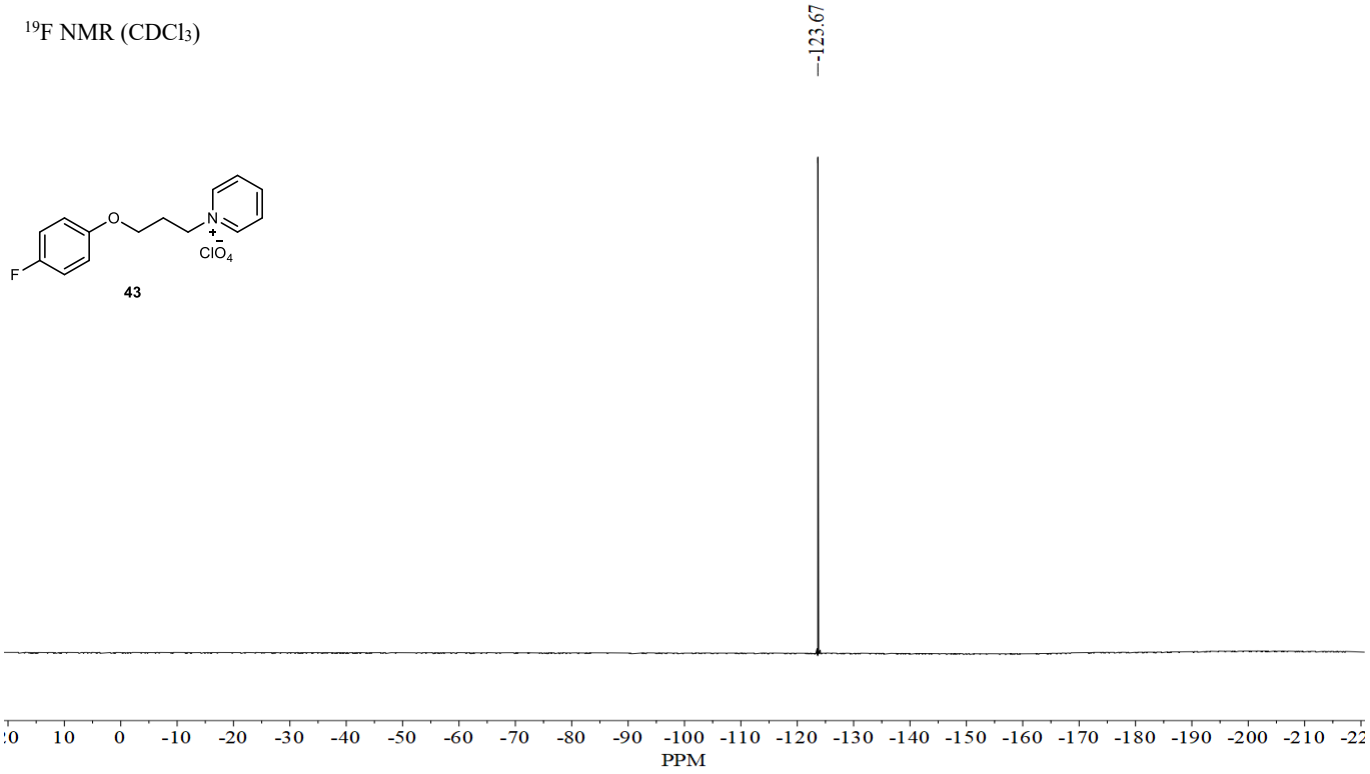


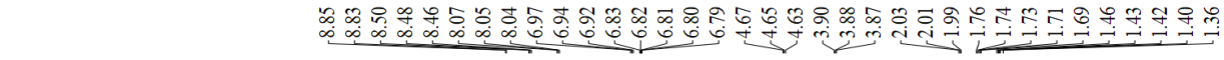
43

^{13}C NMR ($CDCl_3$)

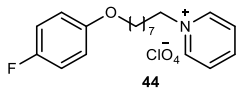


^{19}F NMR ($CDCl_3$)





^{1}H NMR ($CDCl_3$)



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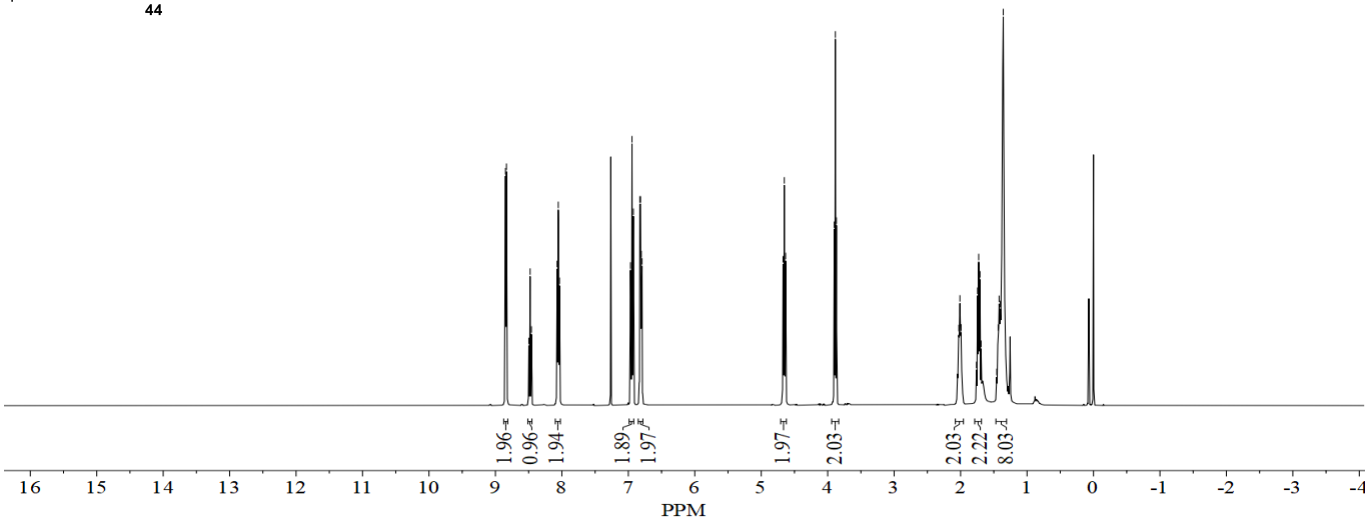
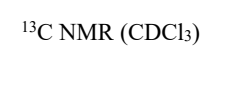


^{13}C NMR ($CDCl_3$)



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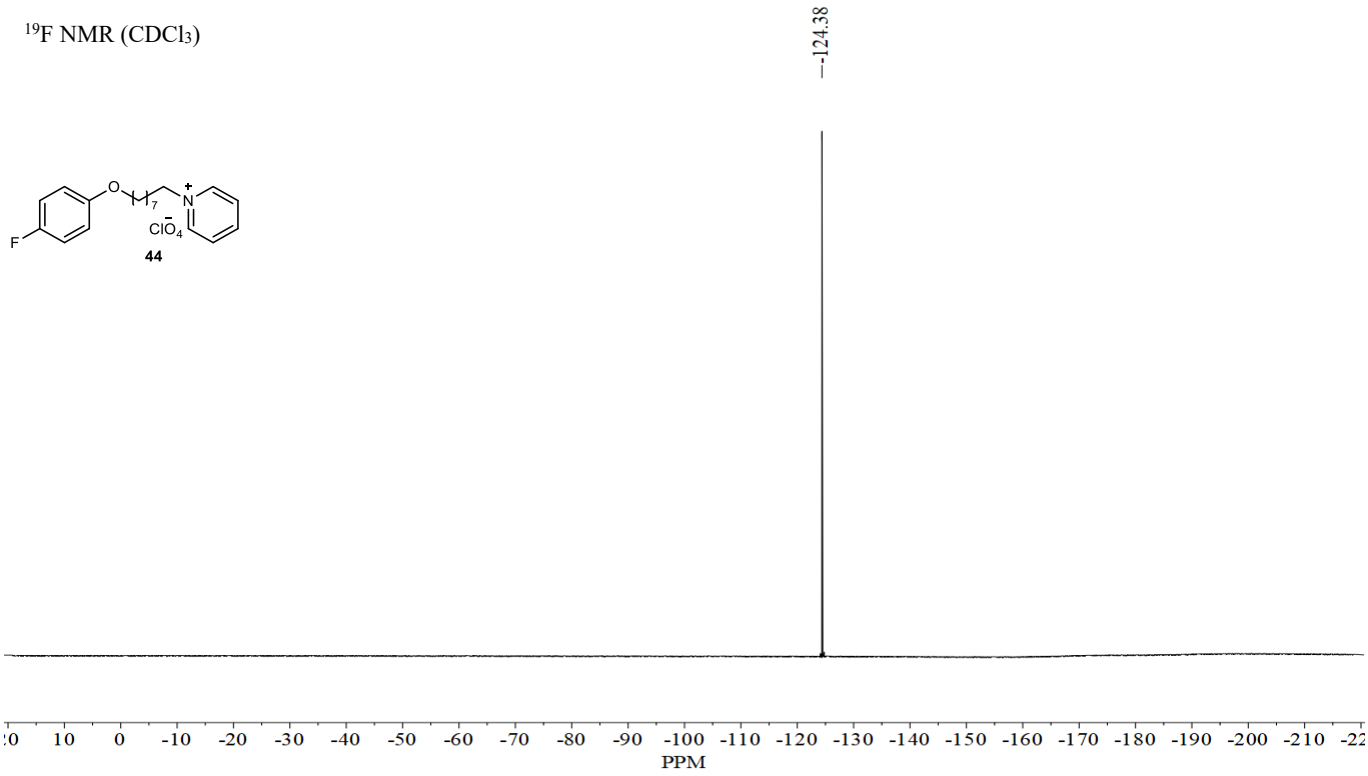
^{19}F NMR ($CDCl_3$)



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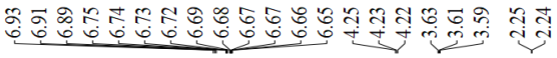
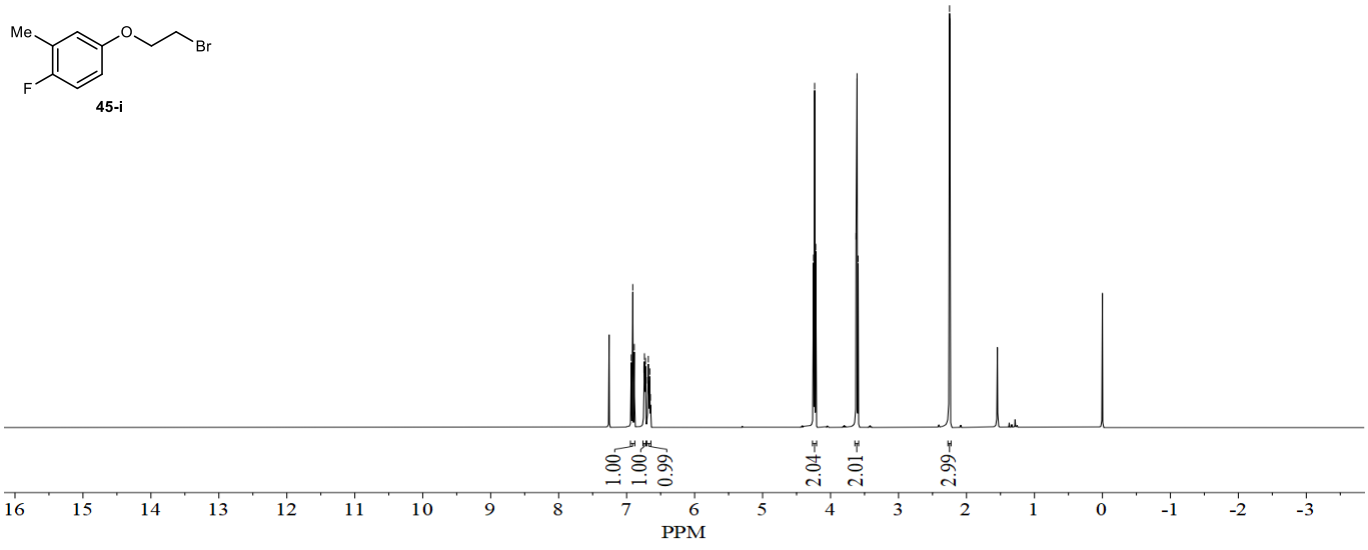
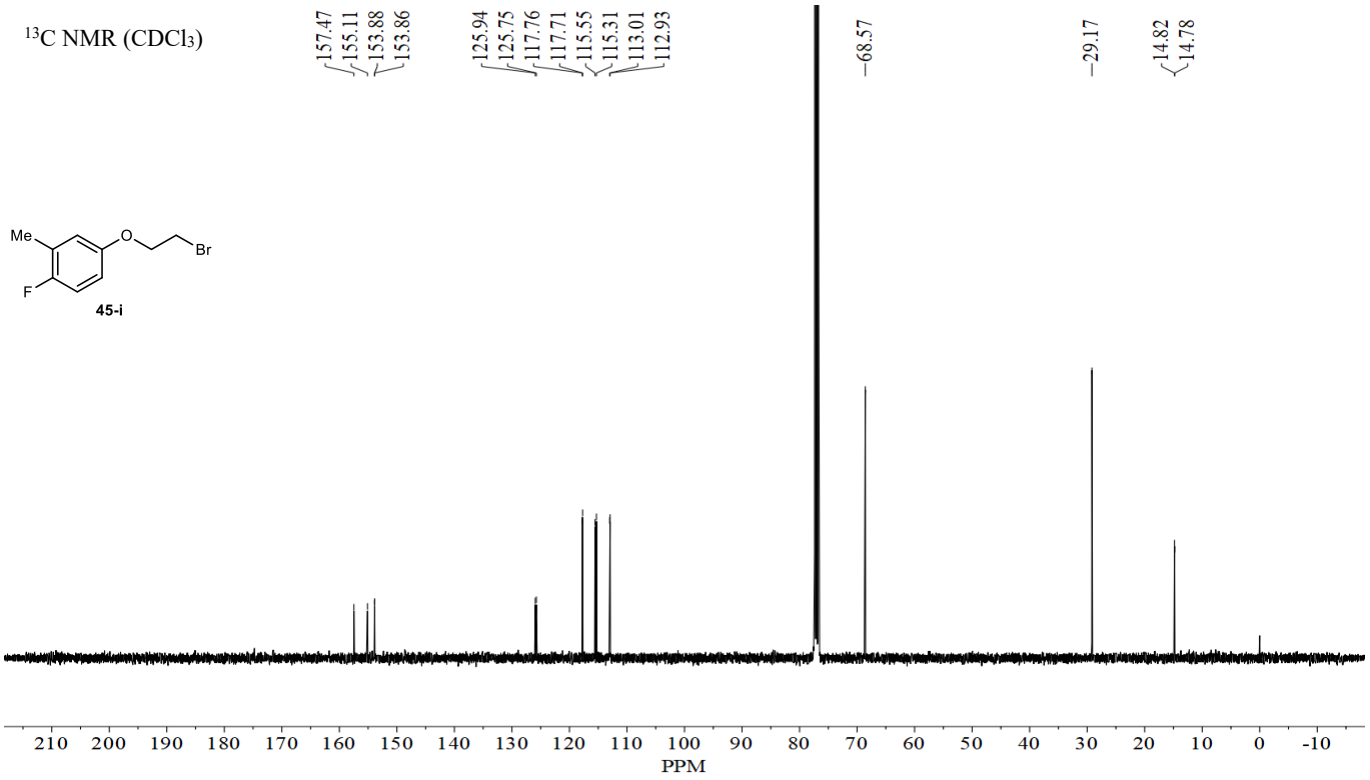


^{1}H NMR ($CDCl_3$)

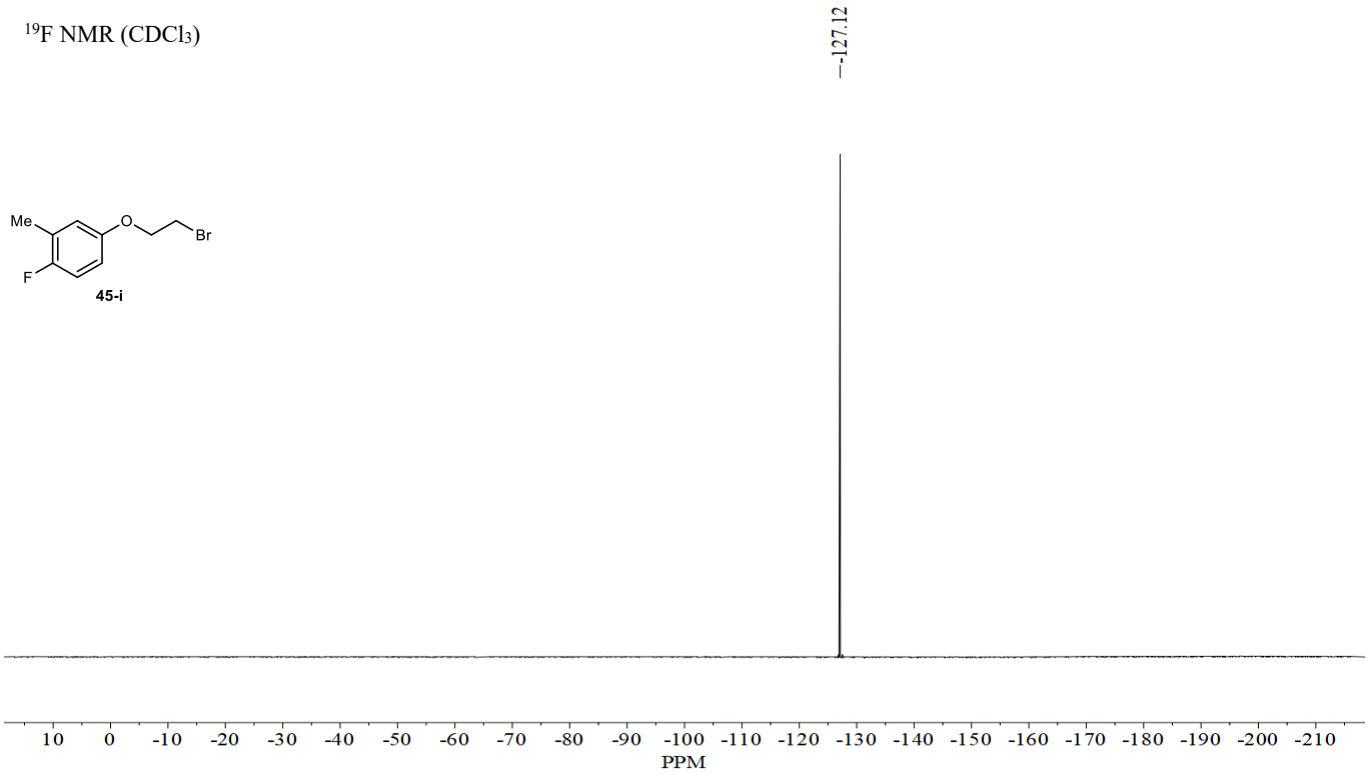


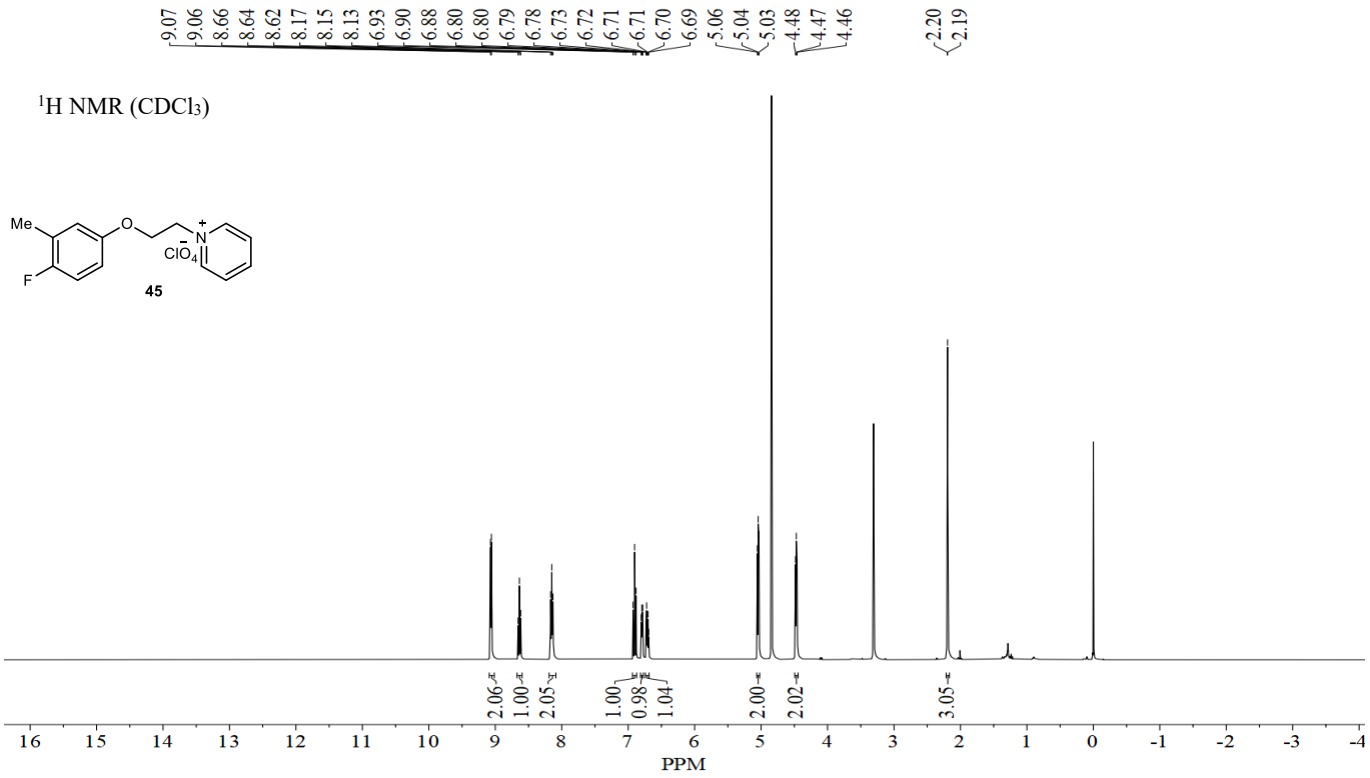
45-i

^{13}C NMR ($CDCl_3$)



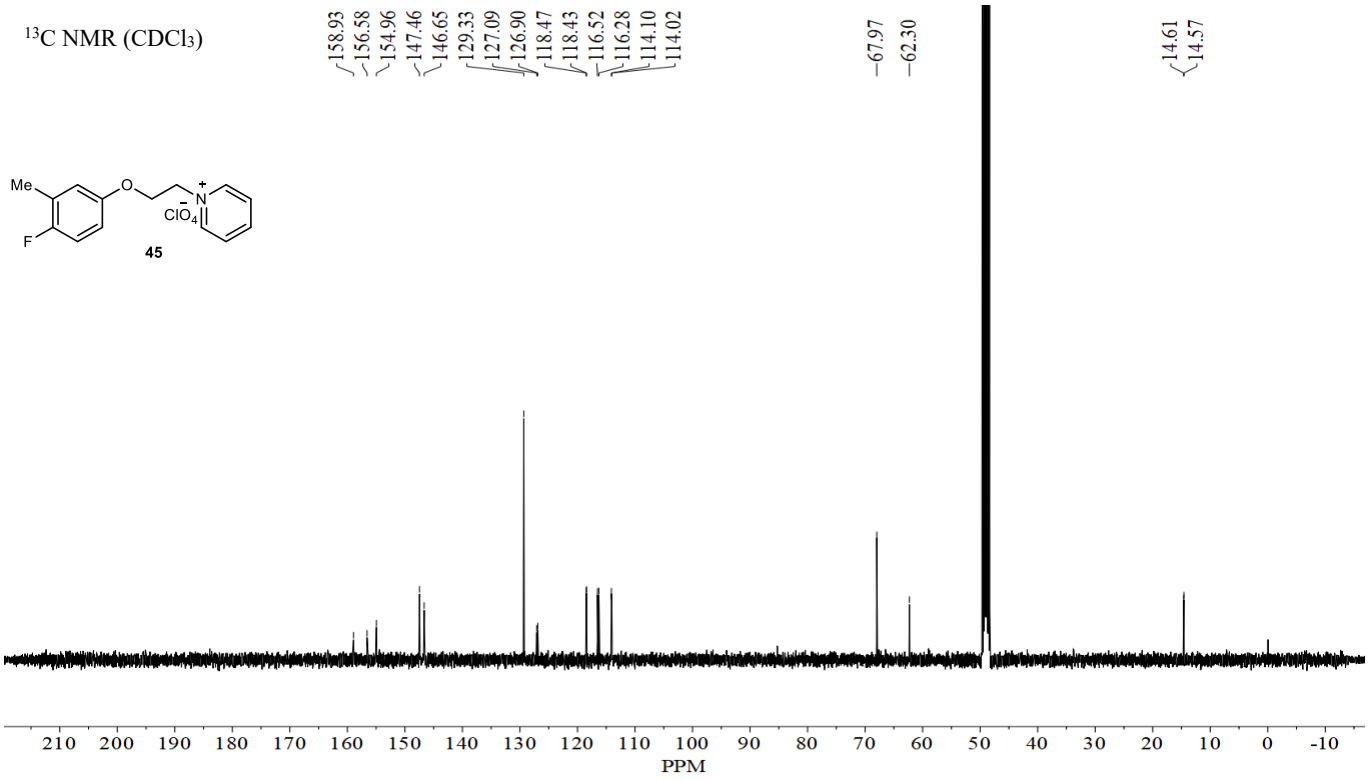
^{19}F NMR ($CDCl_3$)





^{1}H NMR ($CDCl_3$)

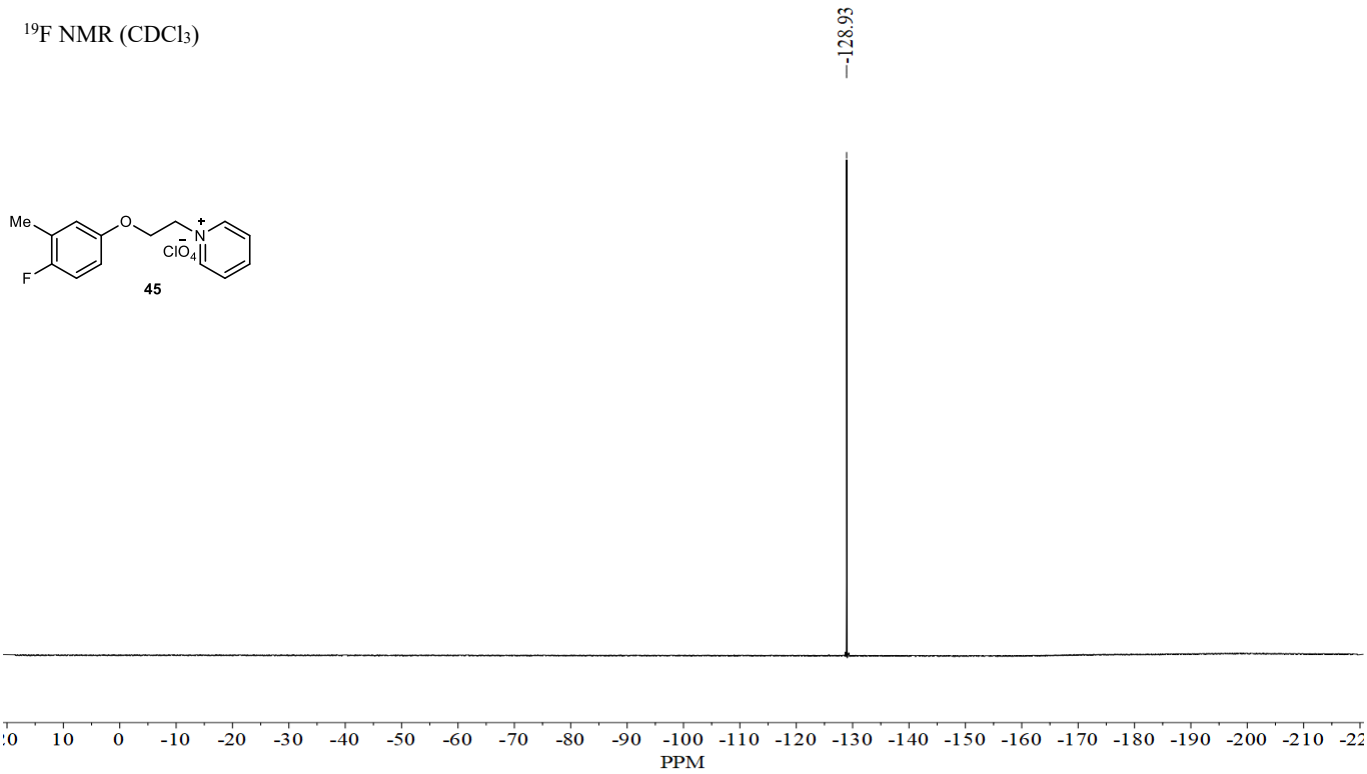
45



^{13}C NMR ($CDCl_3$)

45

^{19}F NMR ($CDCl_3$)



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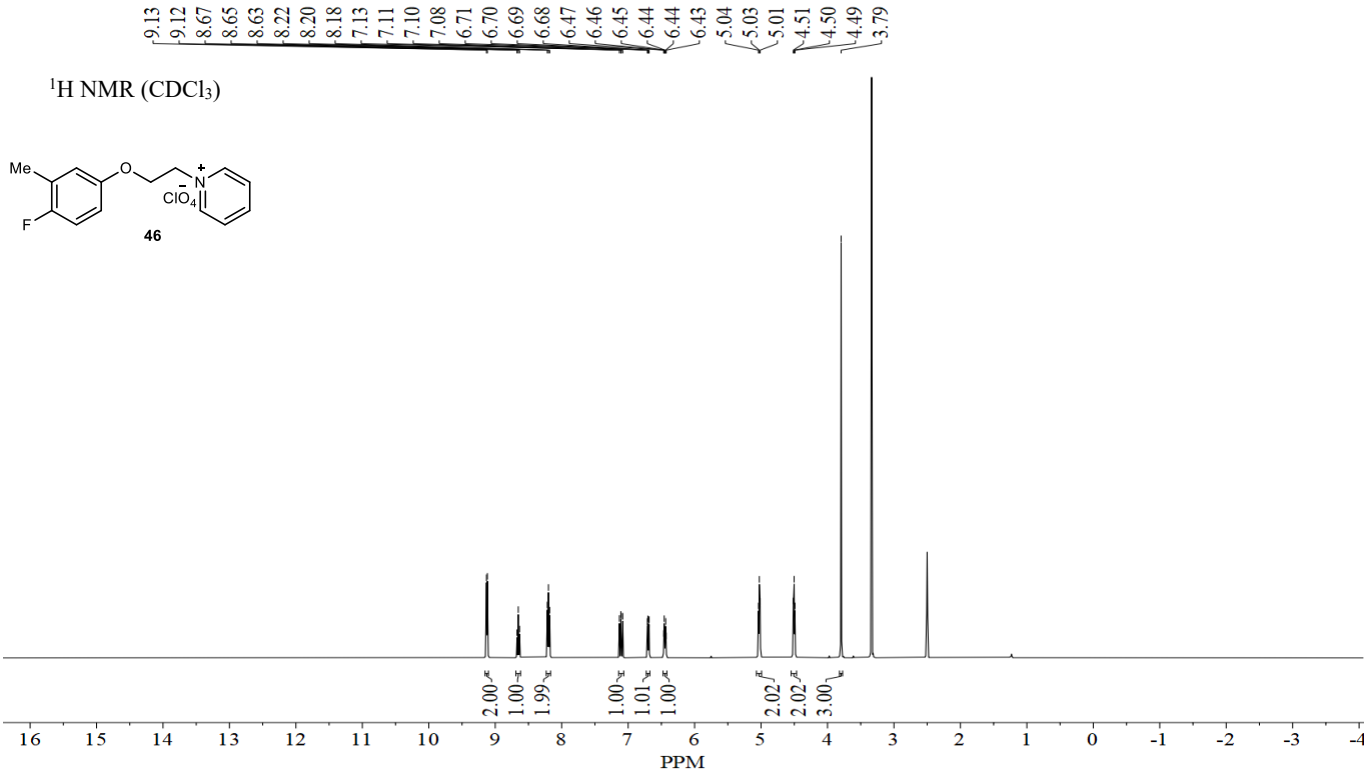
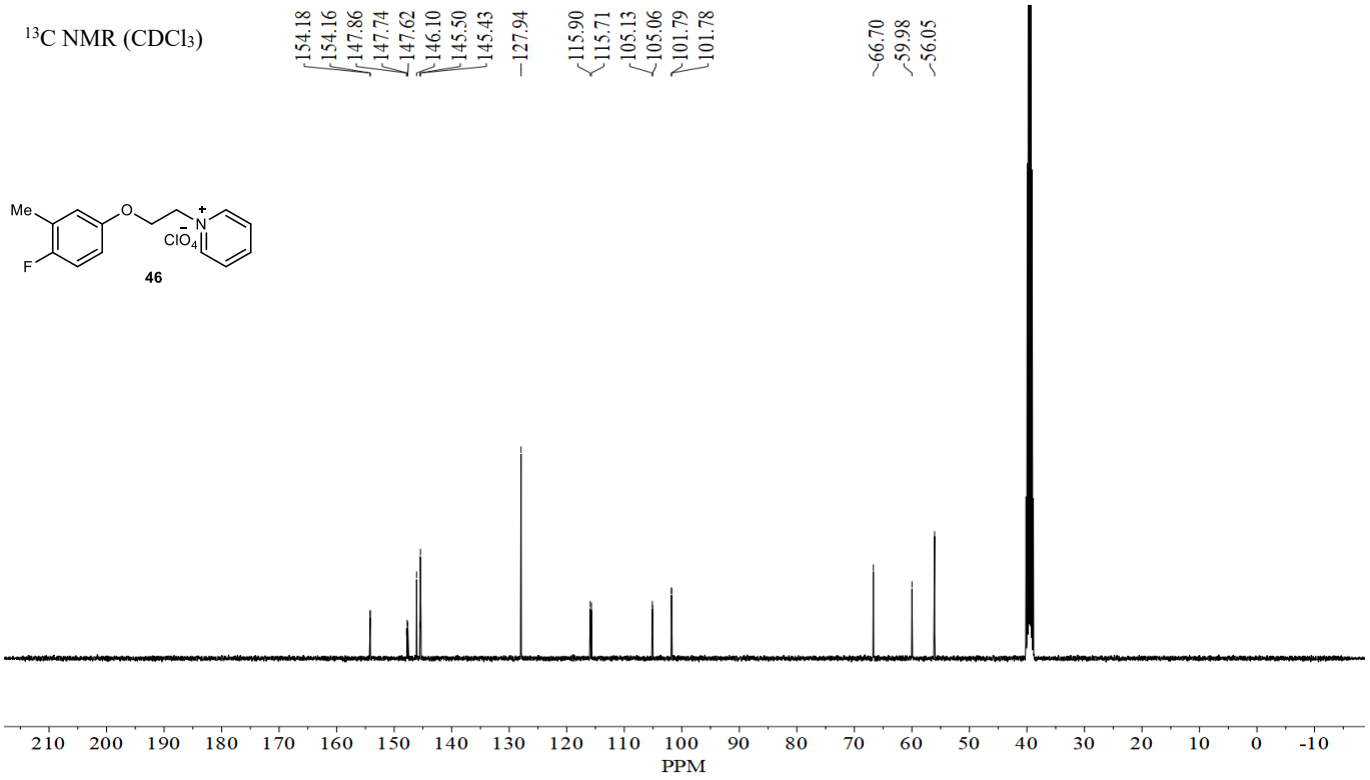
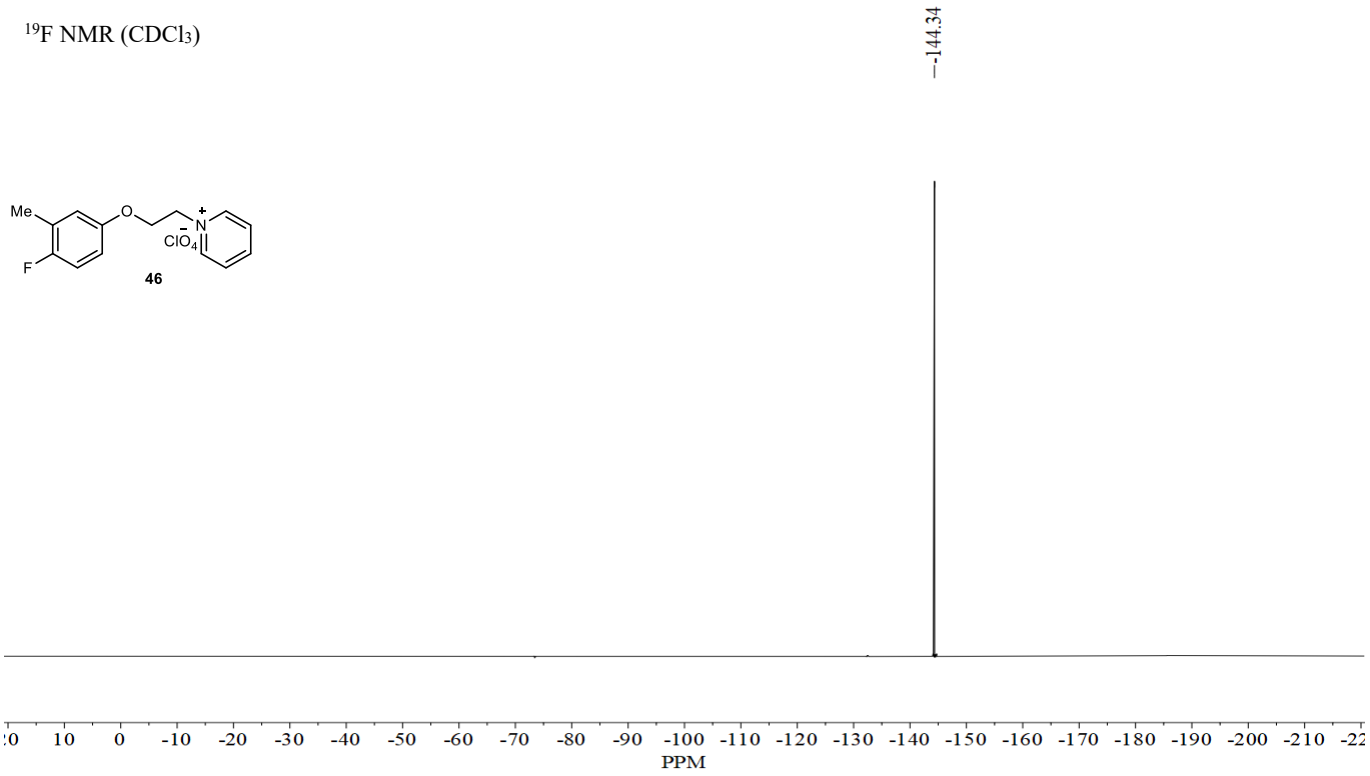


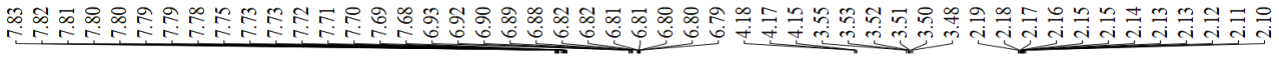
46

^{13}C NMR ($CDCl_3$)

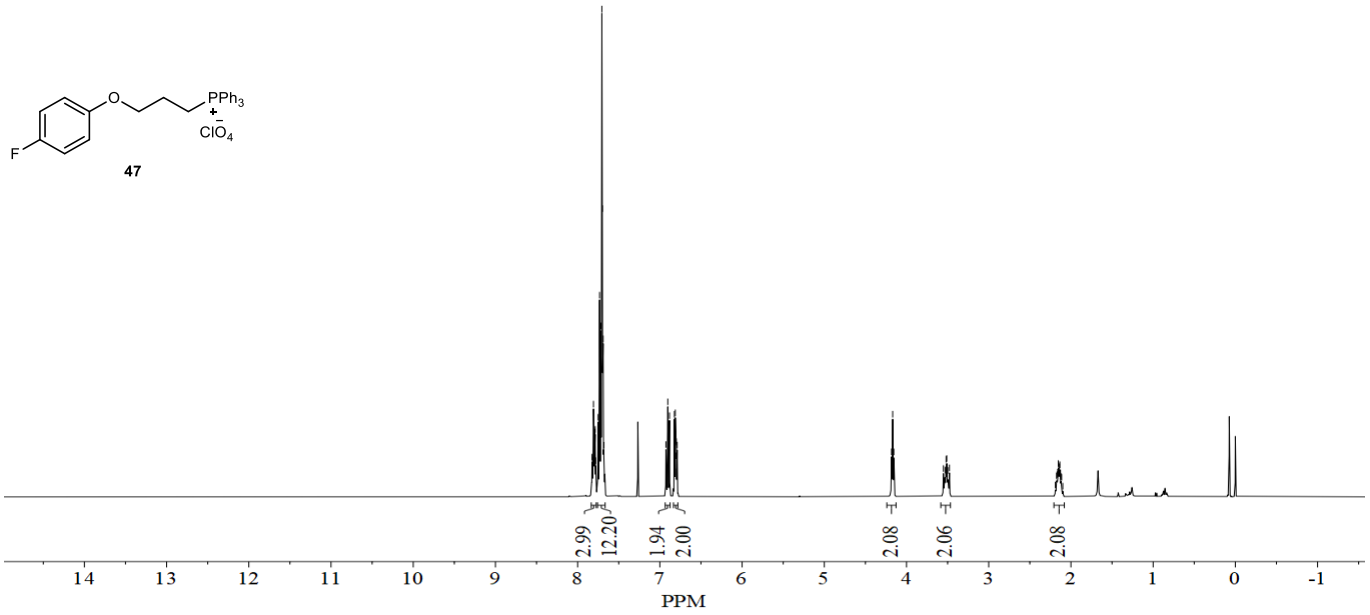


^{19}F NMR ($CDCl_3$)

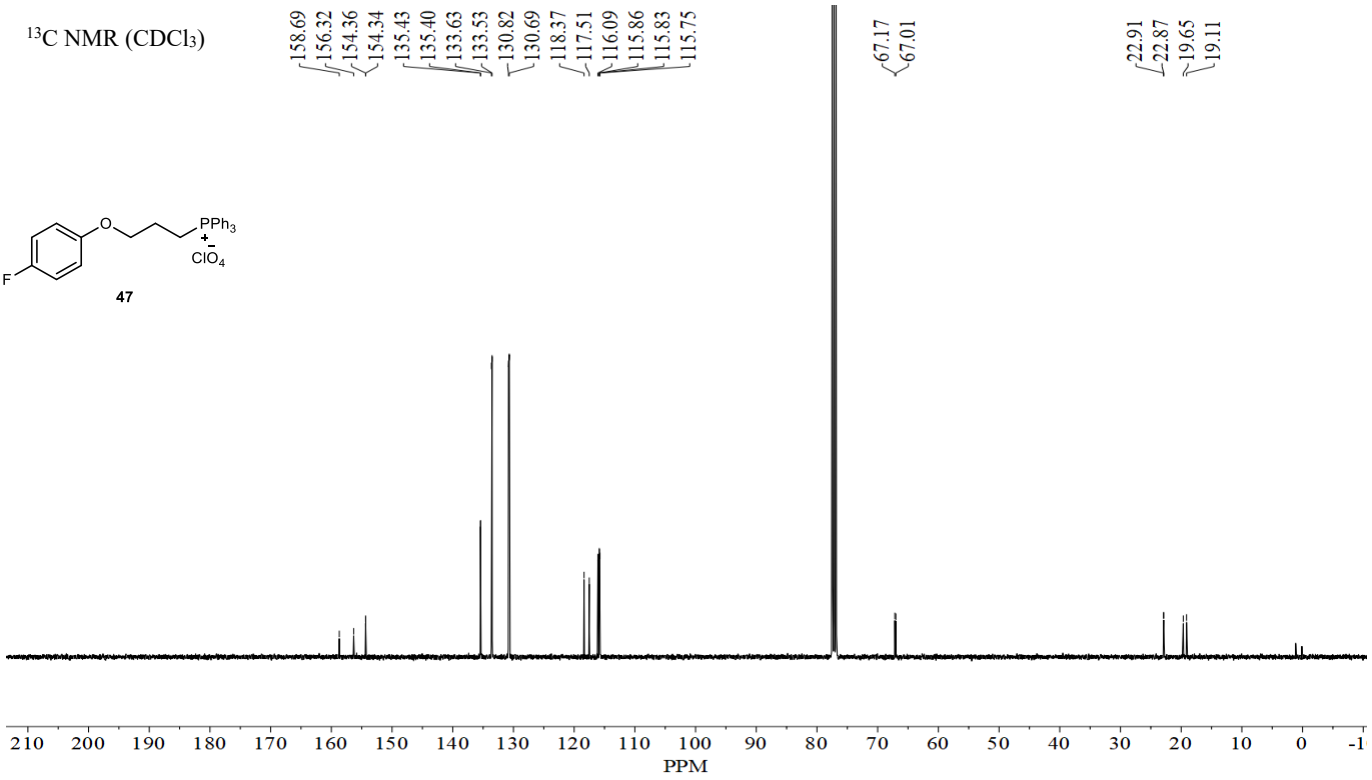




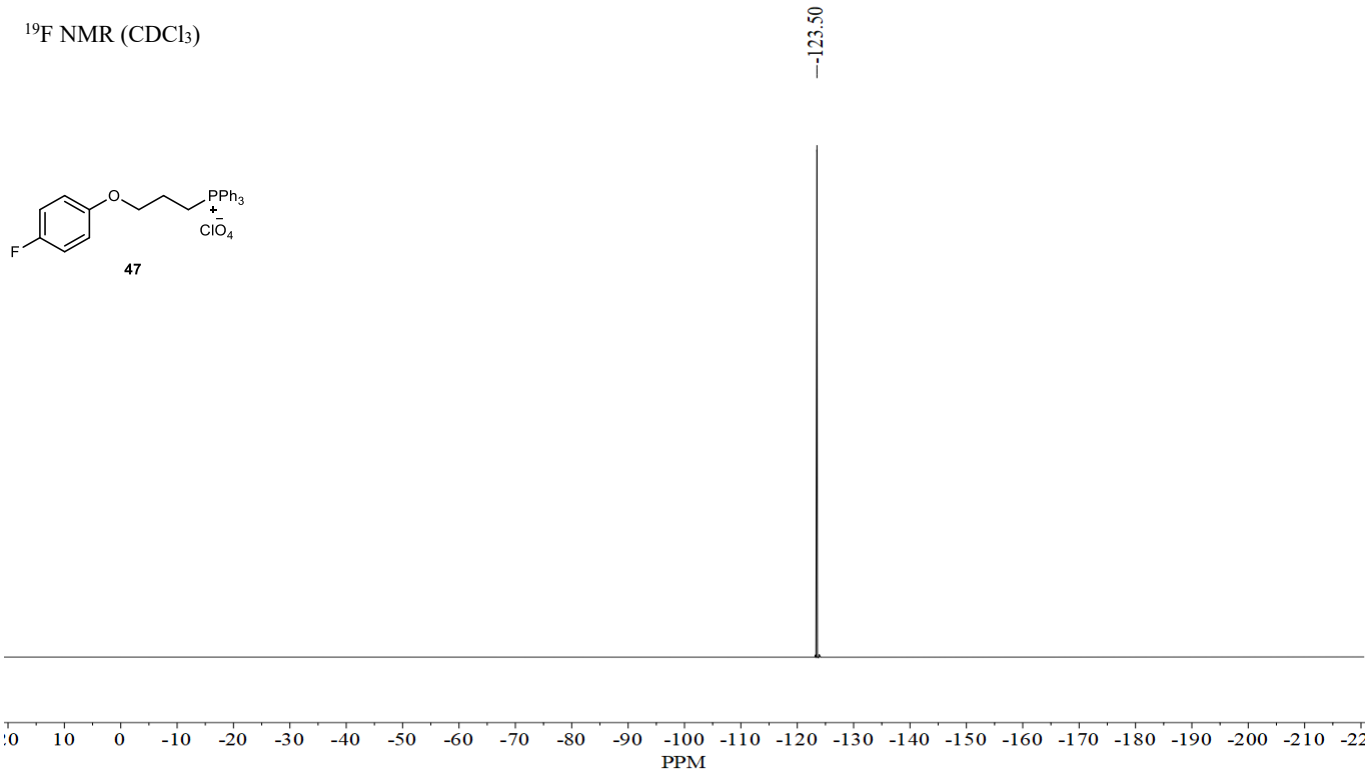
^{1}H NMR ($CDCl_3$)



^{13}C NMR ($CDCl_3$)



^{19}F NMR ($CDCl_3$)



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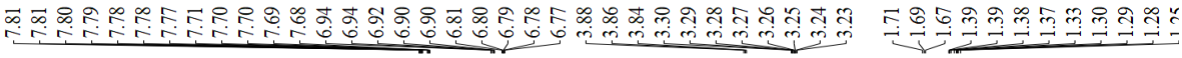
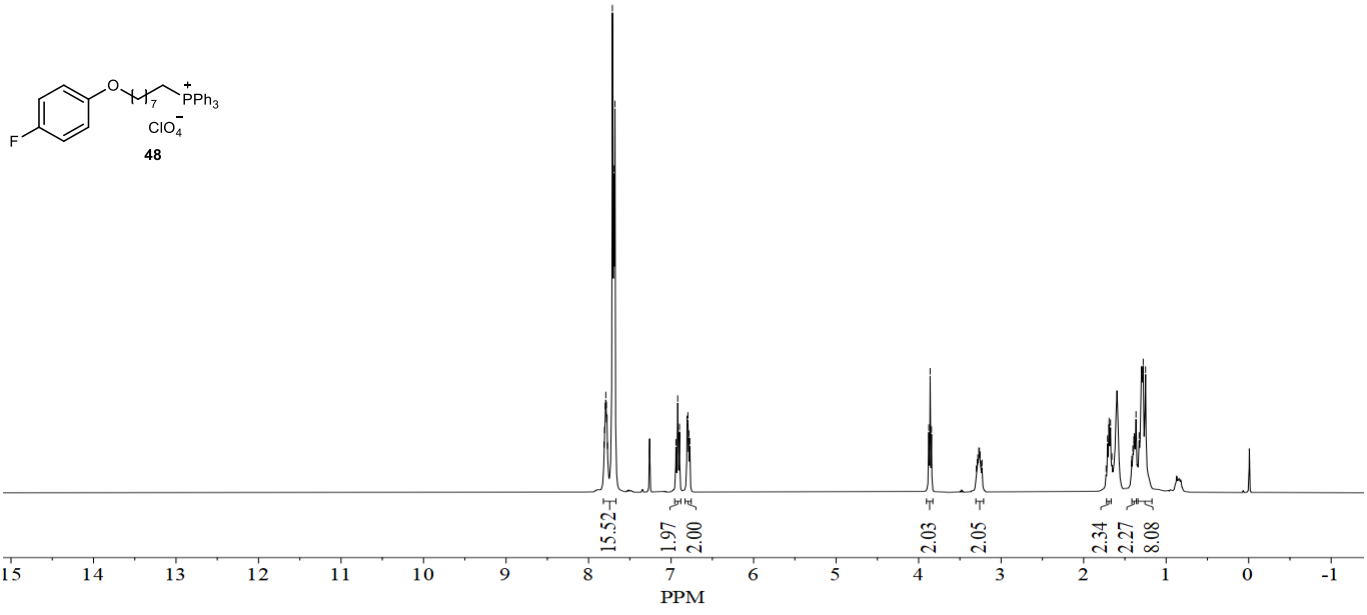
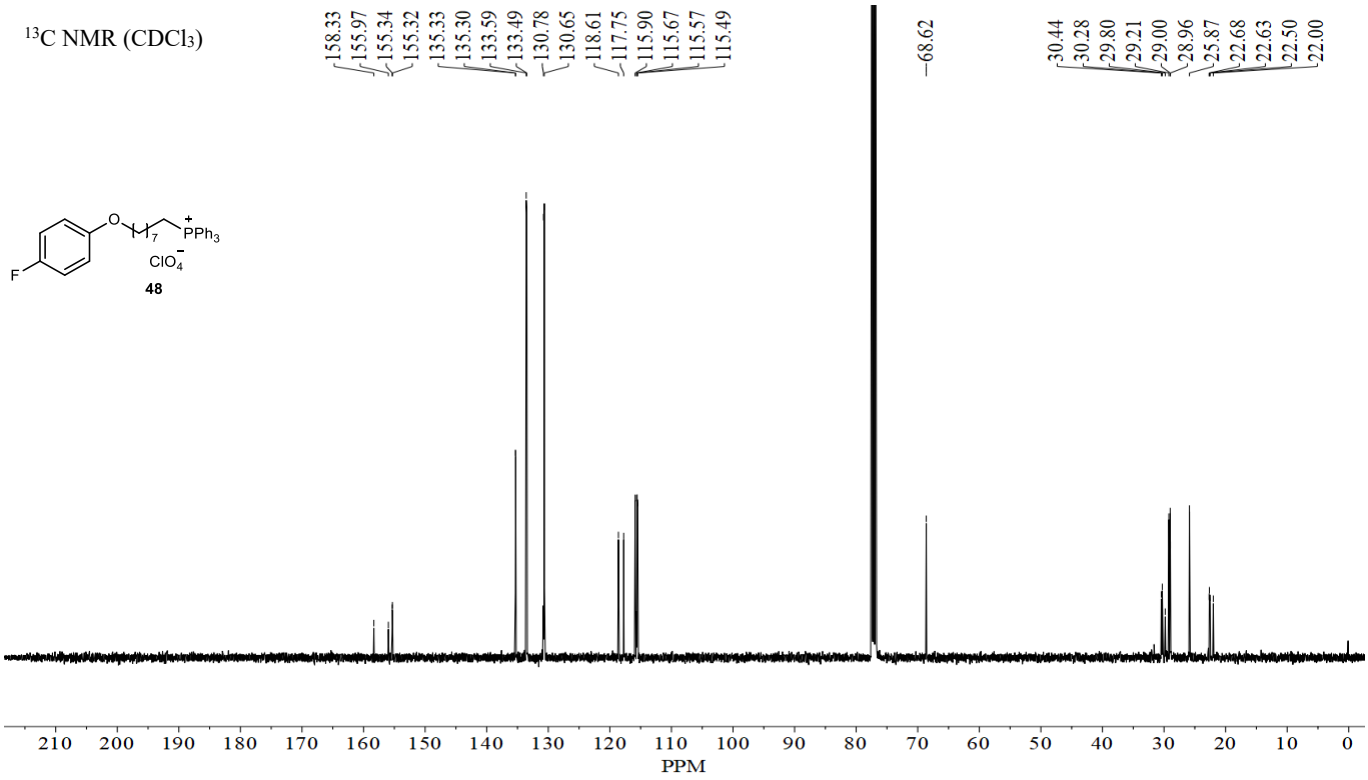


^{1}H NMR ($CDCl_3$)



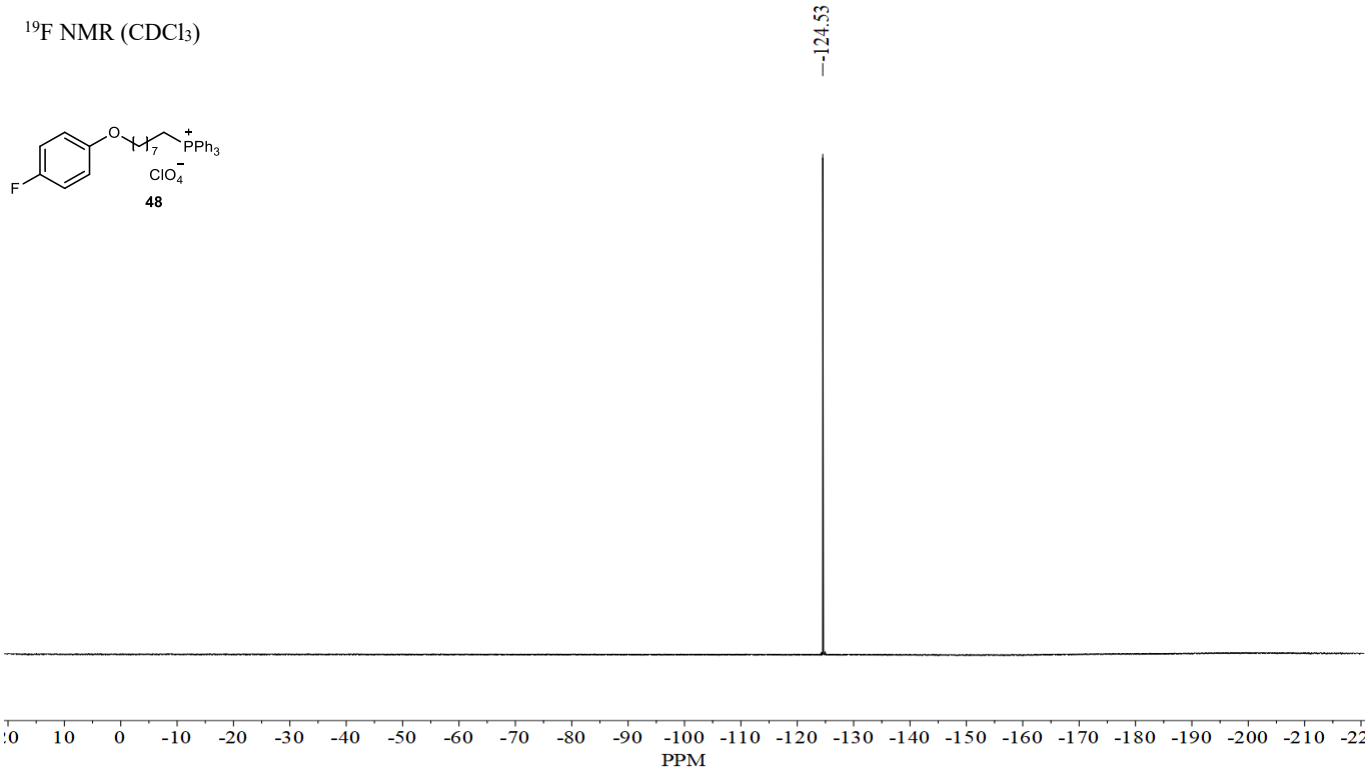
48

^{13}C NMR ($CDCl_3$)

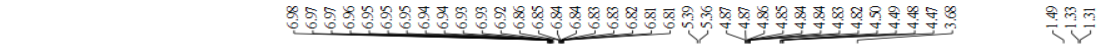


48

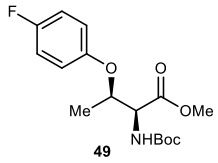
^{19}F NMR ($CDCl_3$)



48



^{1}H NMR ($CDCl_3$)



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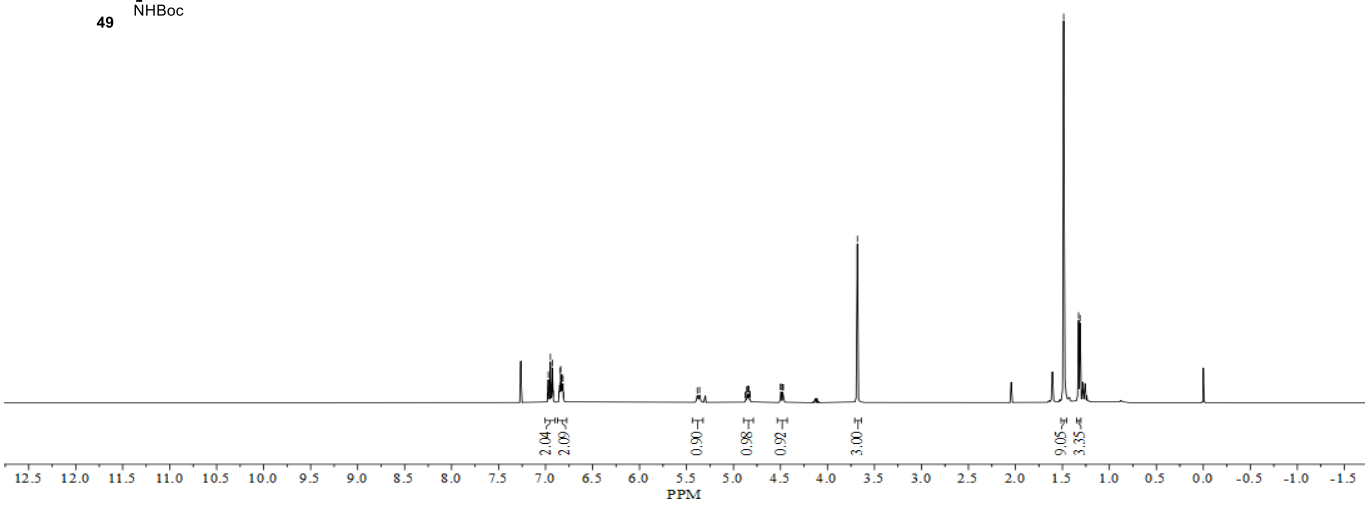

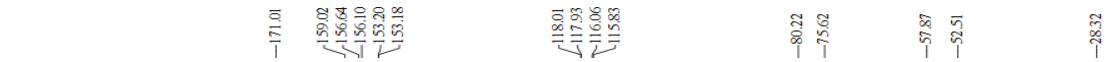

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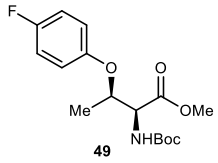

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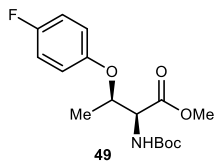
^{19}F NMR ($CDCl_3$)



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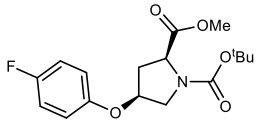
^{1}H NMR ($CDCl_3$)



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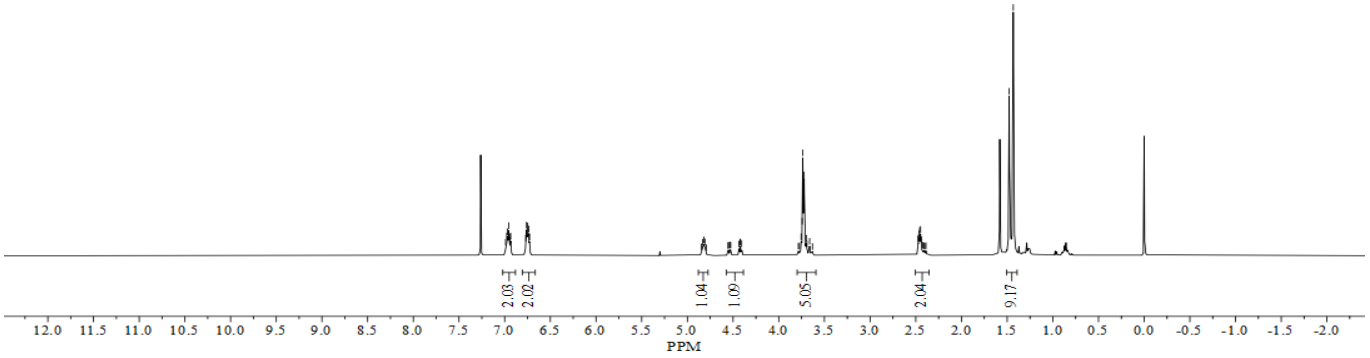
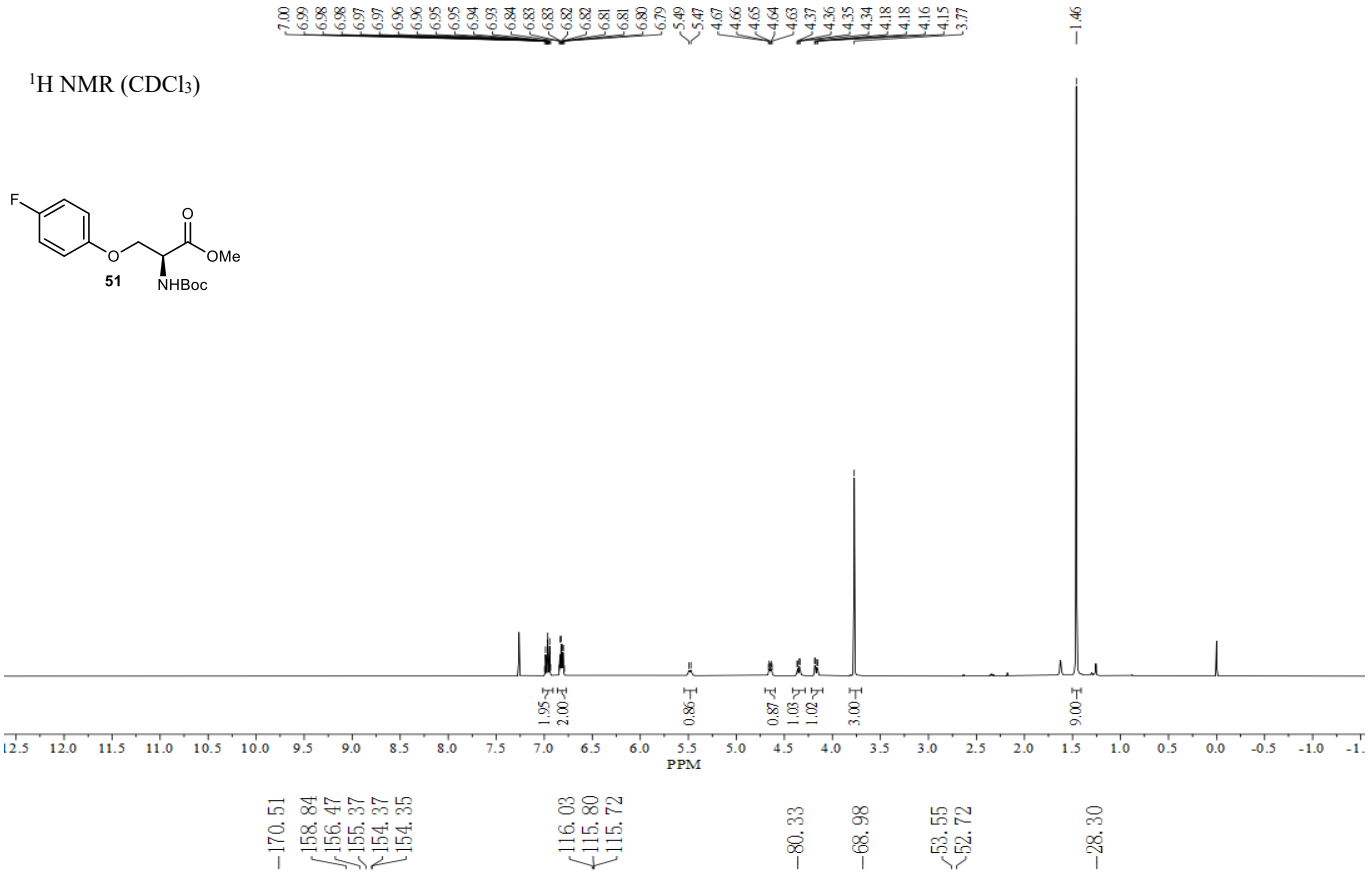
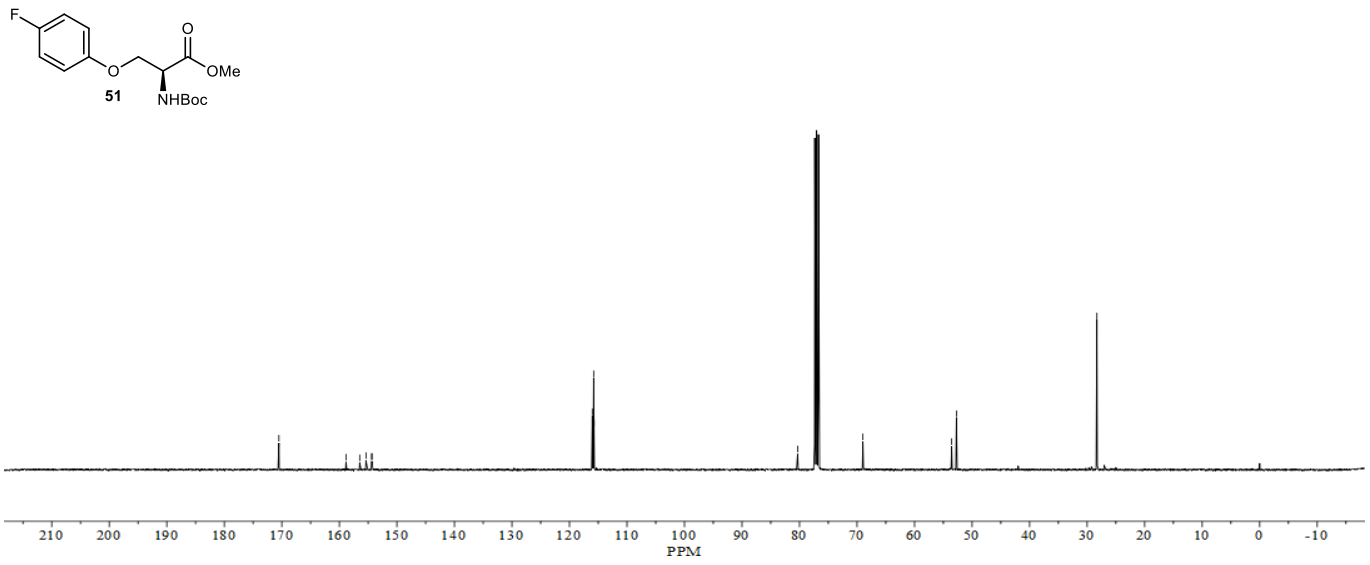


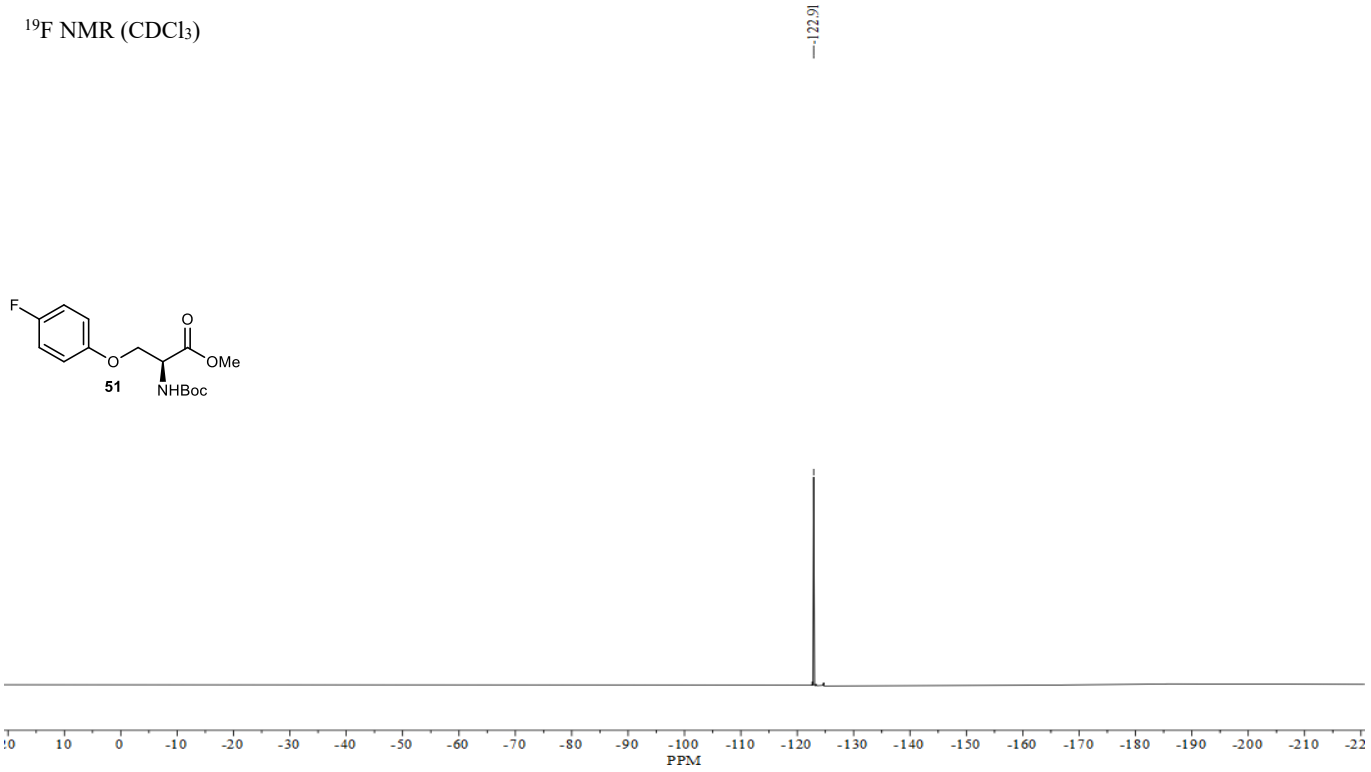
^{1}H NMR ($CDCl_3$)



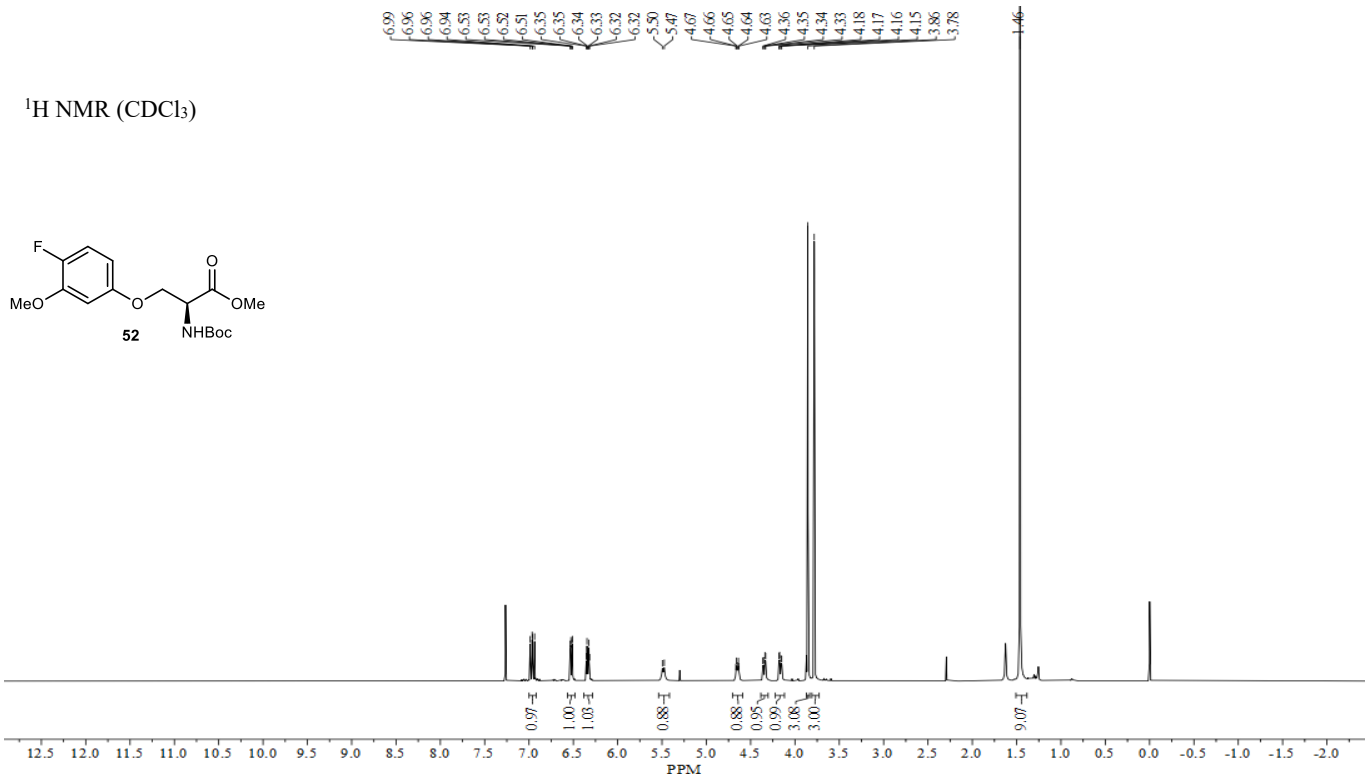
^{13}C NMR ($CDCl_3$)



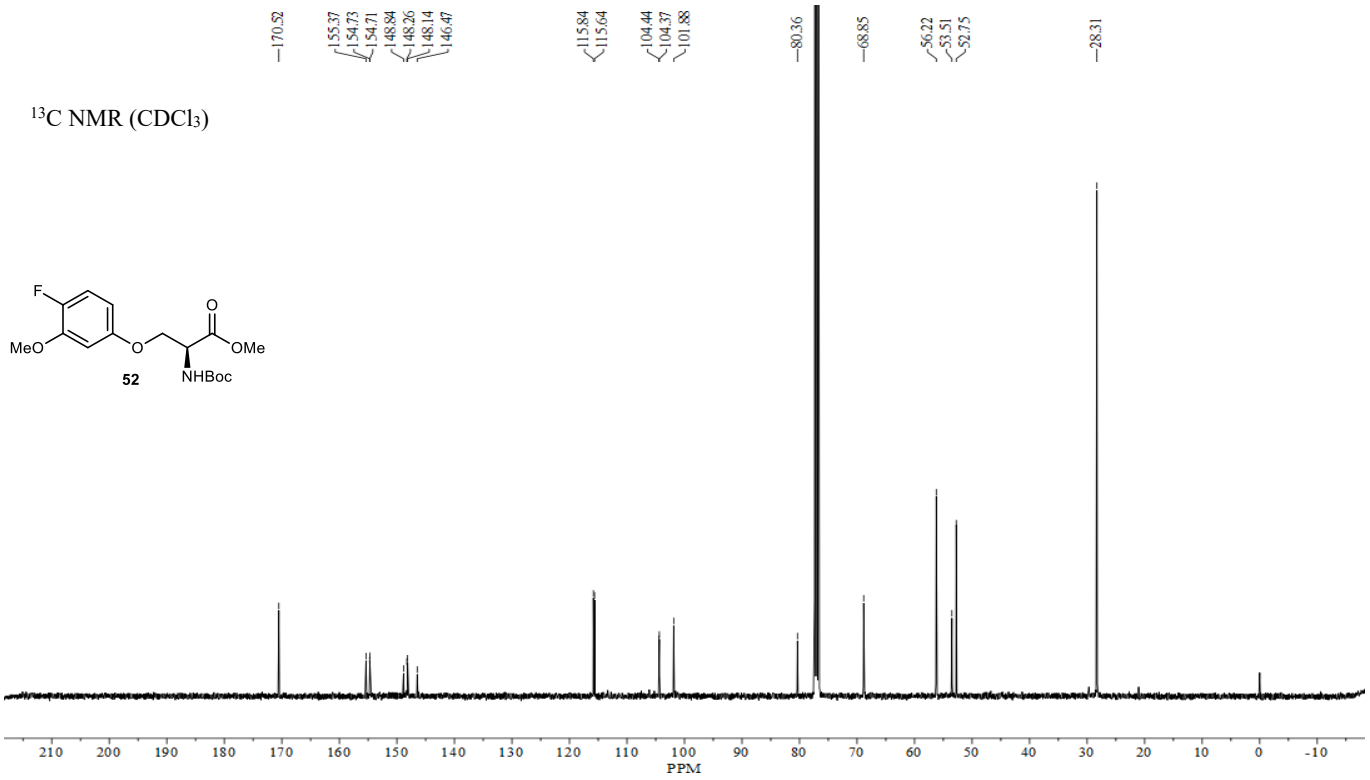
^{19}F NMR ($CDCl_3$)



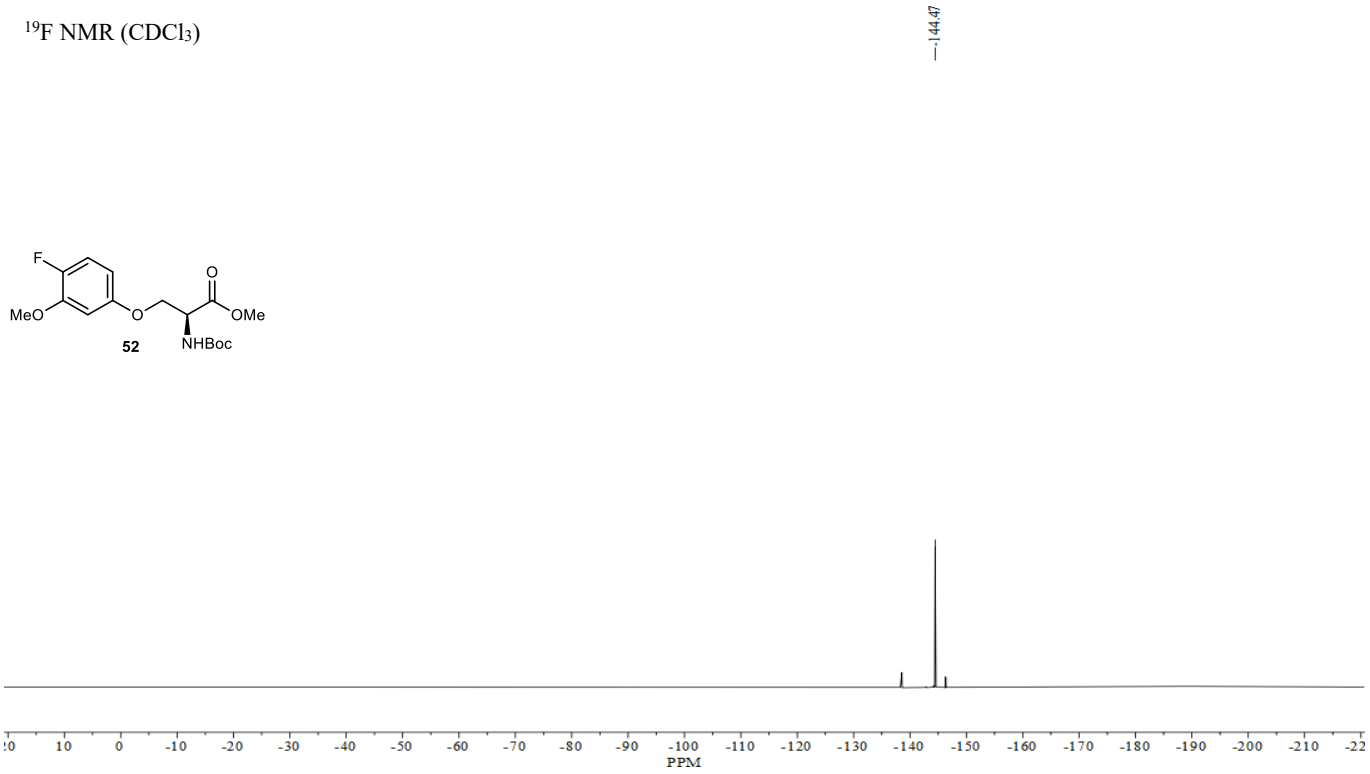
^{1}H NMR ($CDCl_3$)

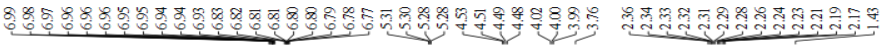


^{13}C NMR ($CDCl_3$)

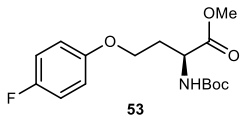


^{19}F NMR ($CDCl_3$)



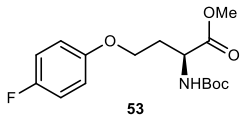


^{1}H NMR ($CDCl_3$)

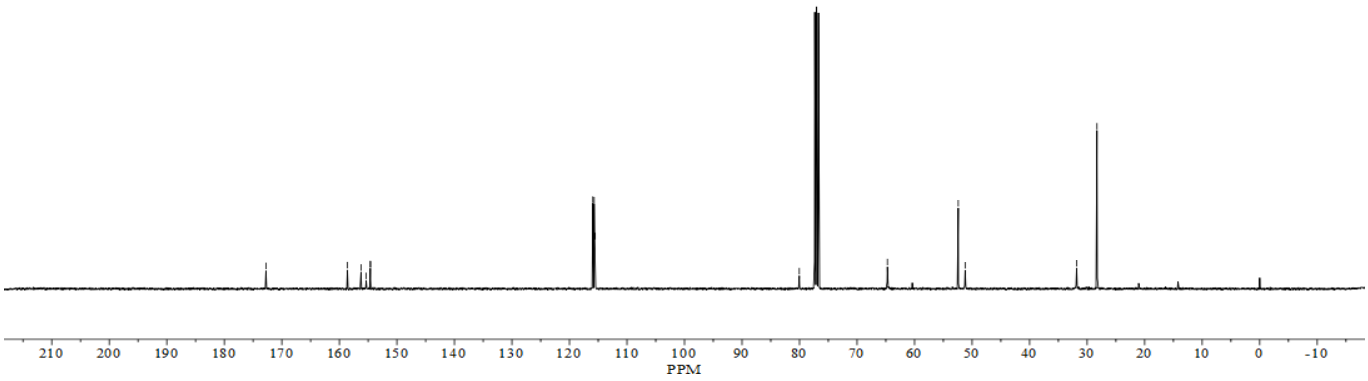


53

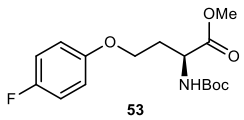
^{13}C NMR ($CDCl_3$)



53



^{19}F NMR ($CDCl_3$)



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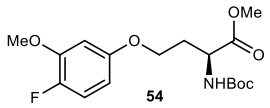
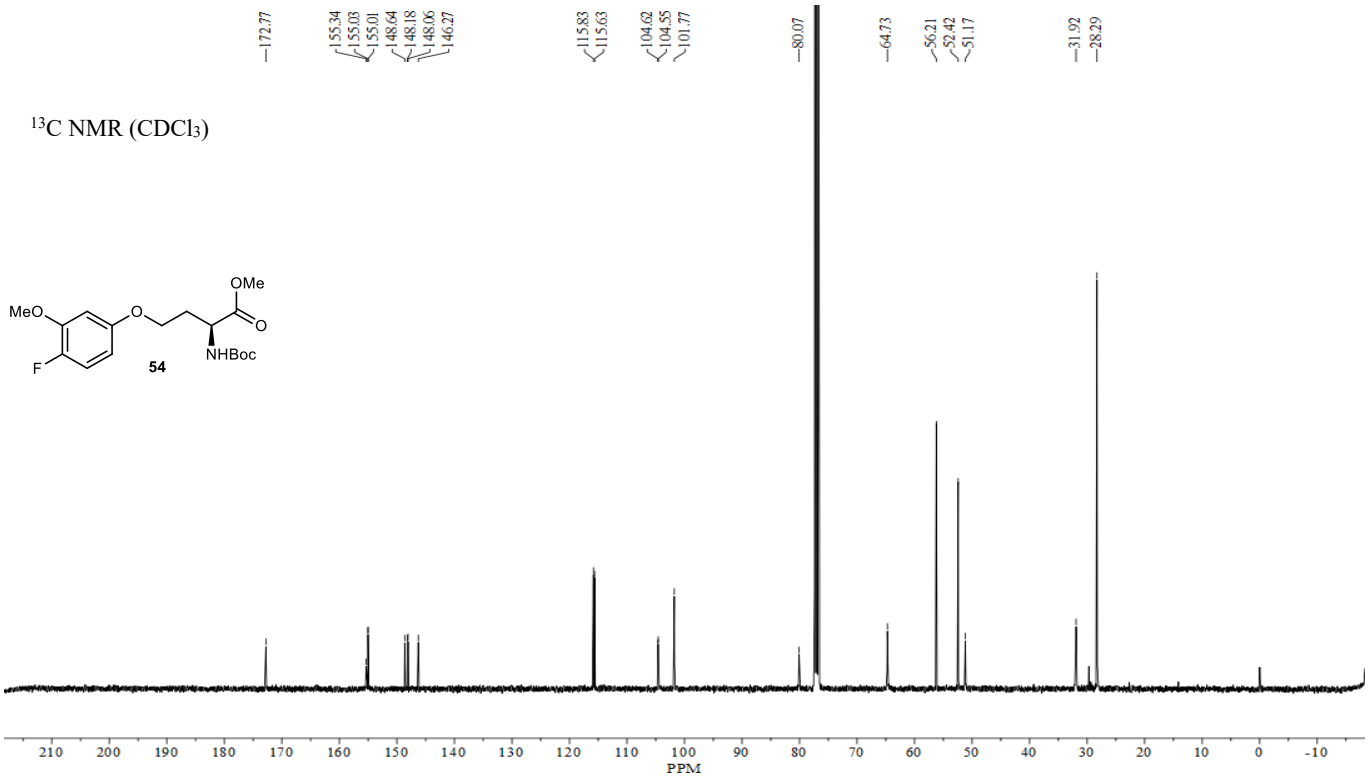
^{1}H NMR ($CDCl_3$)

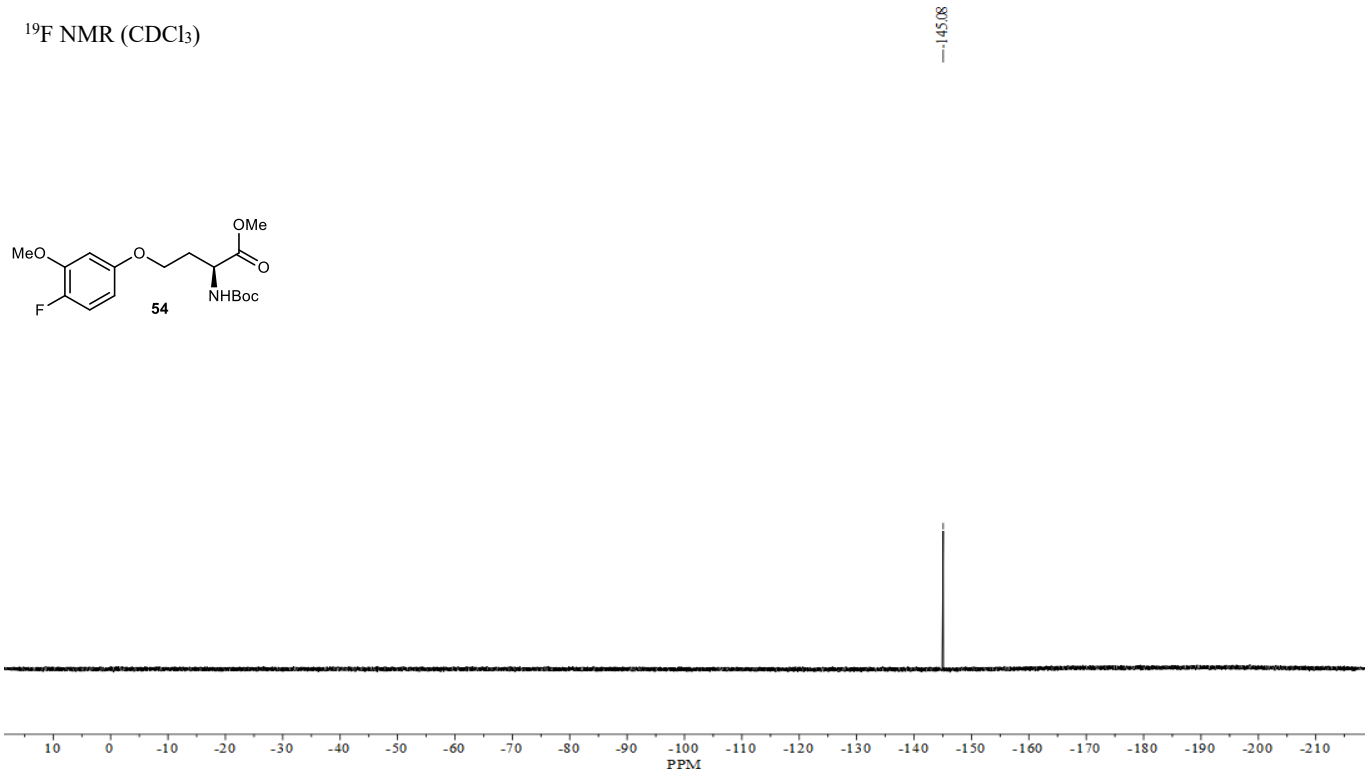


54

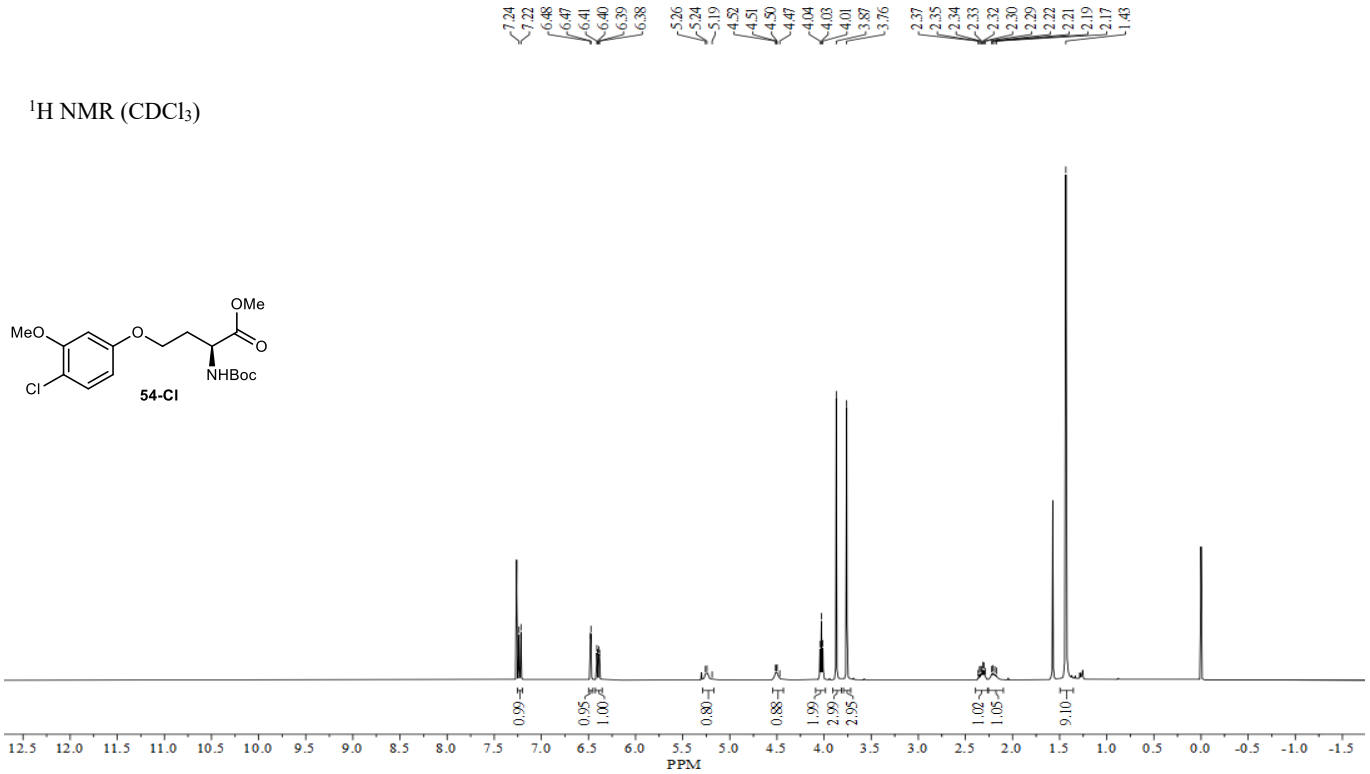
^{13}C NMR ($CDCl_3$)



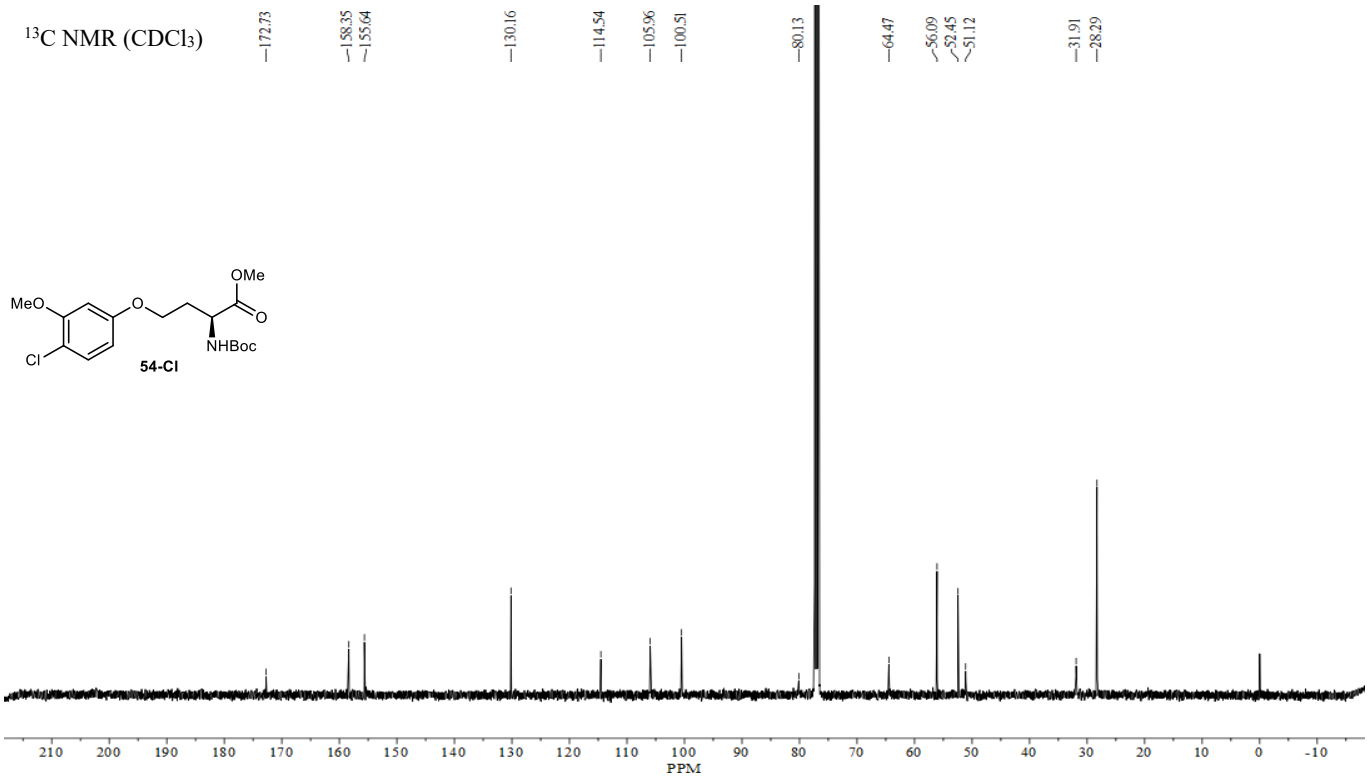
^{19}F NMR ($CDCl_3$)



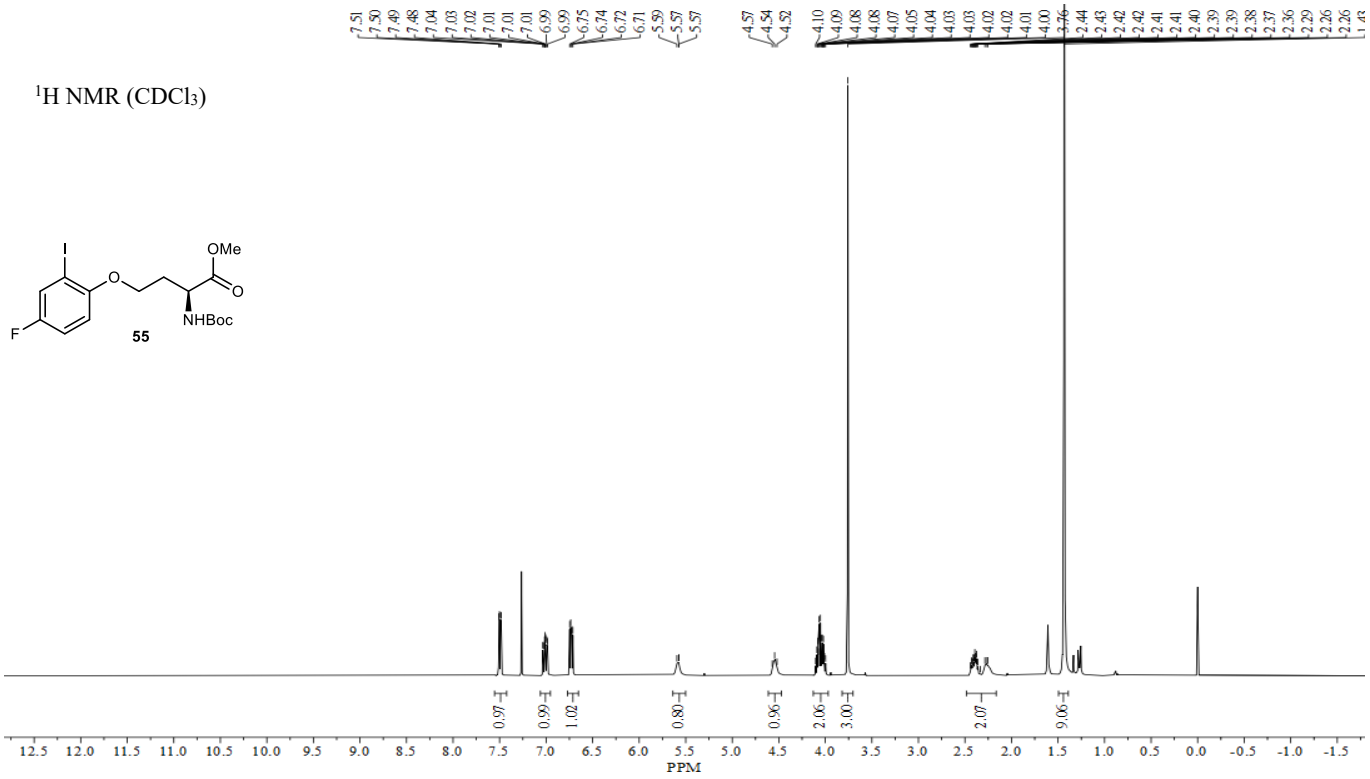
^{1}H NMR ($CDCl_3$)



^{13}C NMR ($CDCl_3$)



^{1}H NMR ($CDCl_3$)



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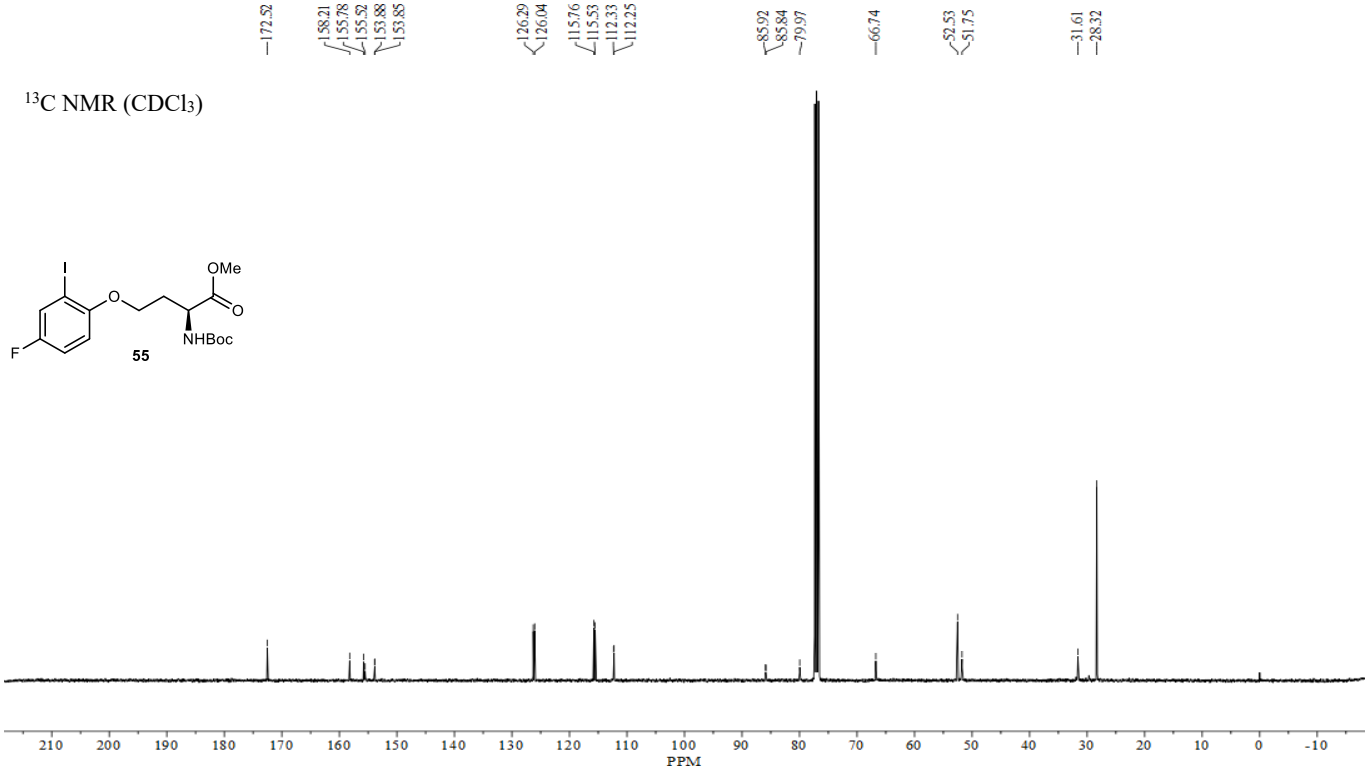
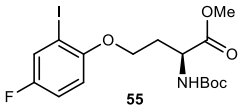
^{13}C NMR ($CDCl_3$)



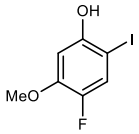
55

^{19}F NMR ($CDCl_3$)

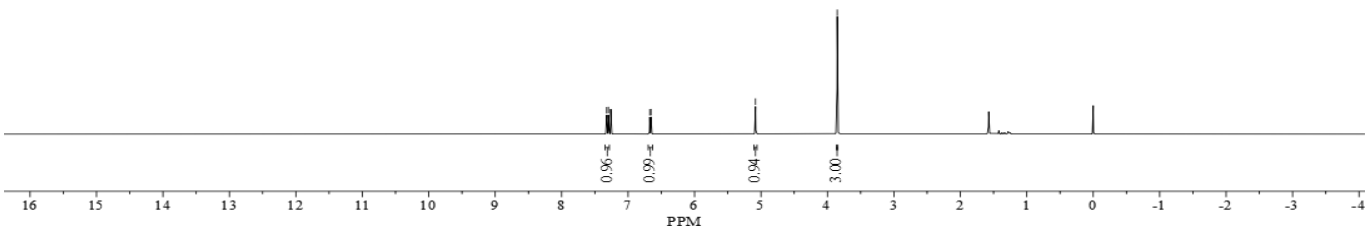


55

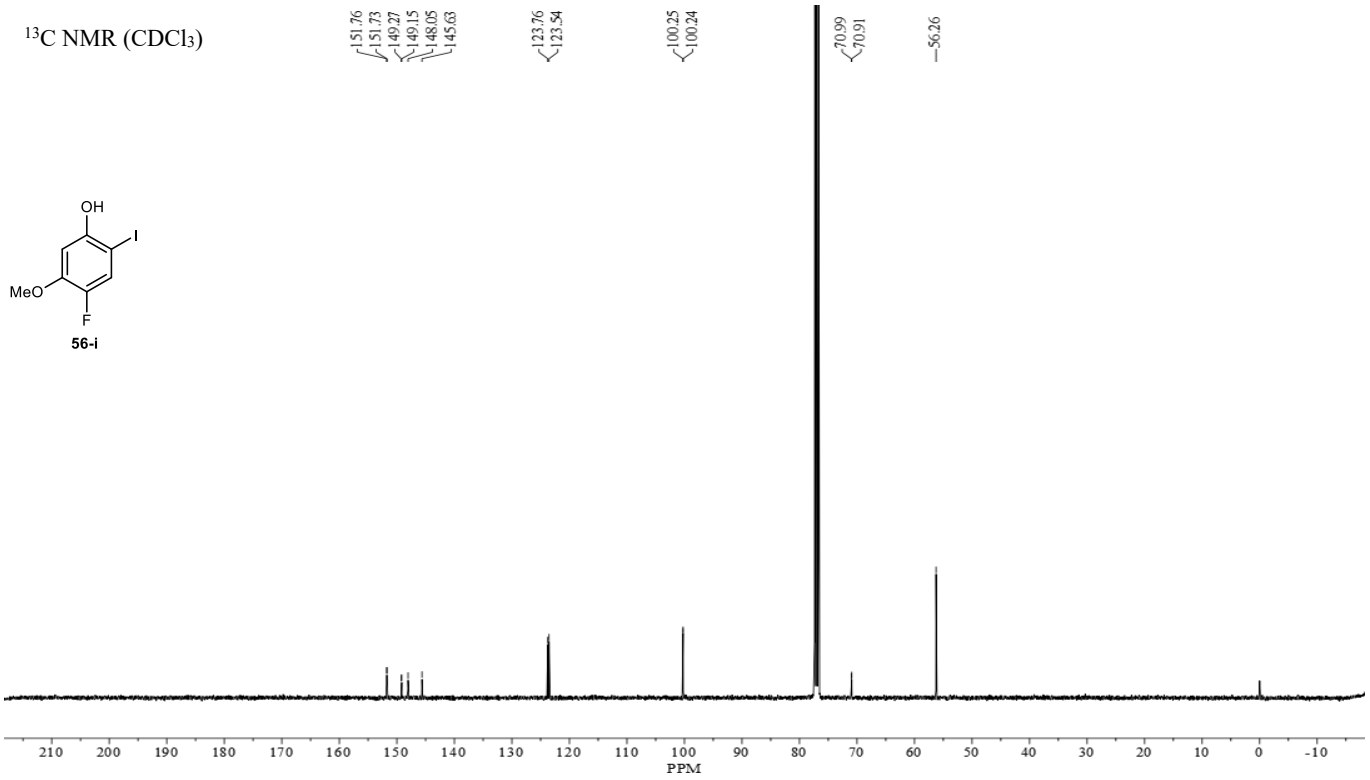
^{1}H NMR ($CDCl_3$)



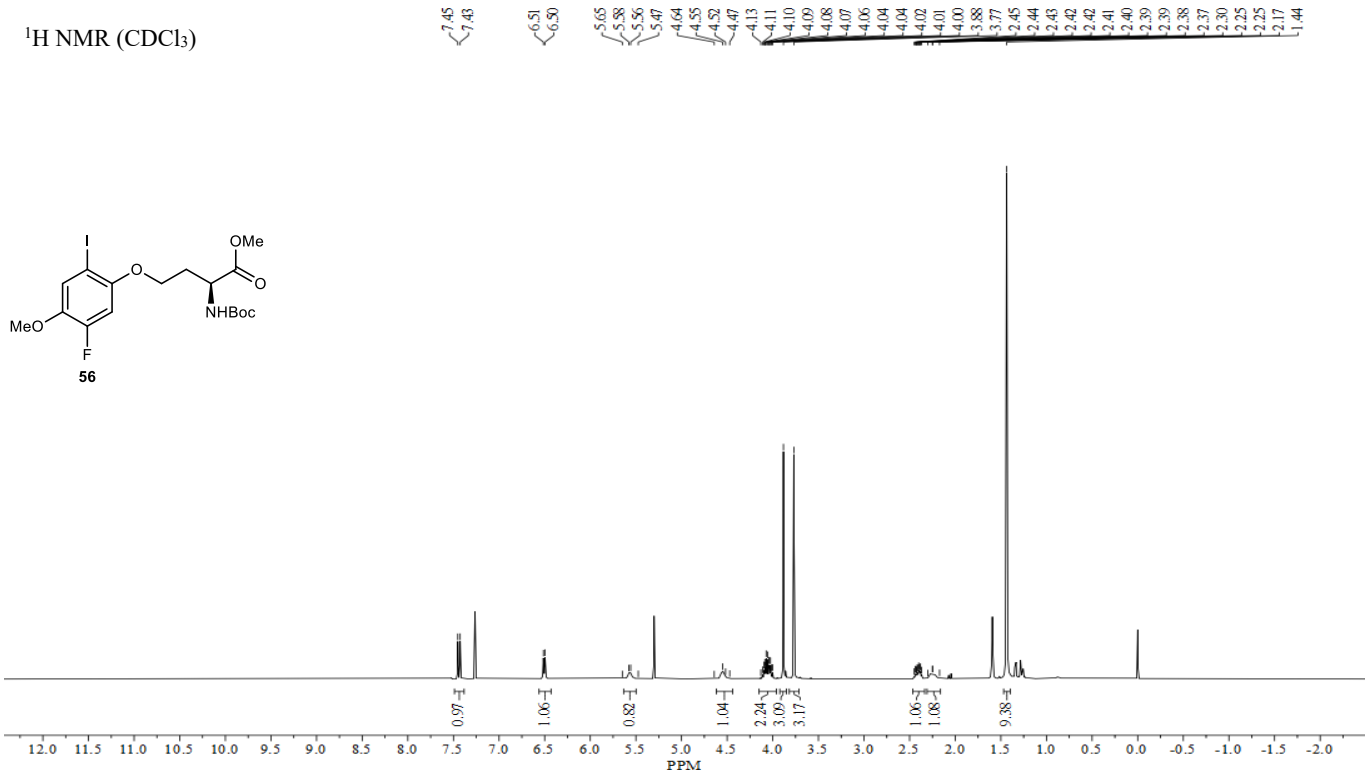
56-i



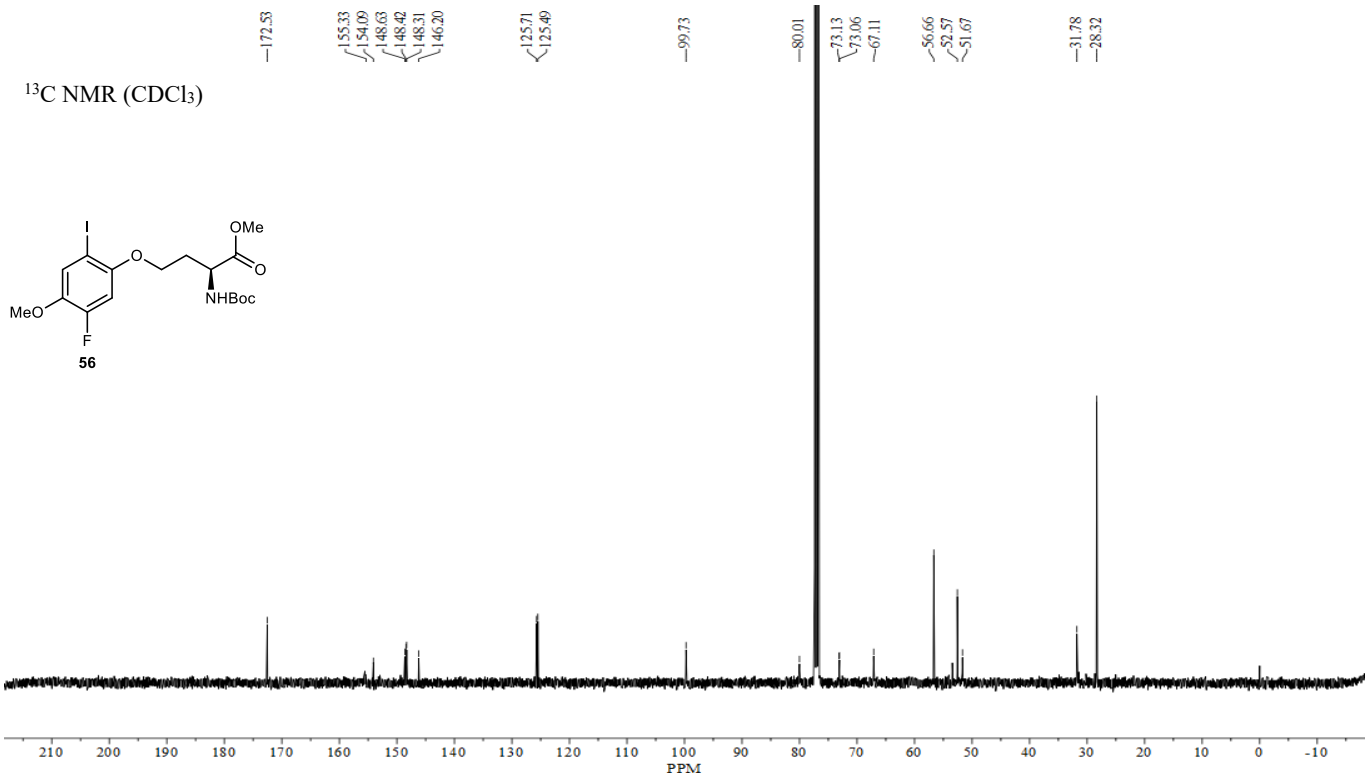
^{13}C NMR ($CDCl_3$)



^{1}H NMR ($CDCl_3$)

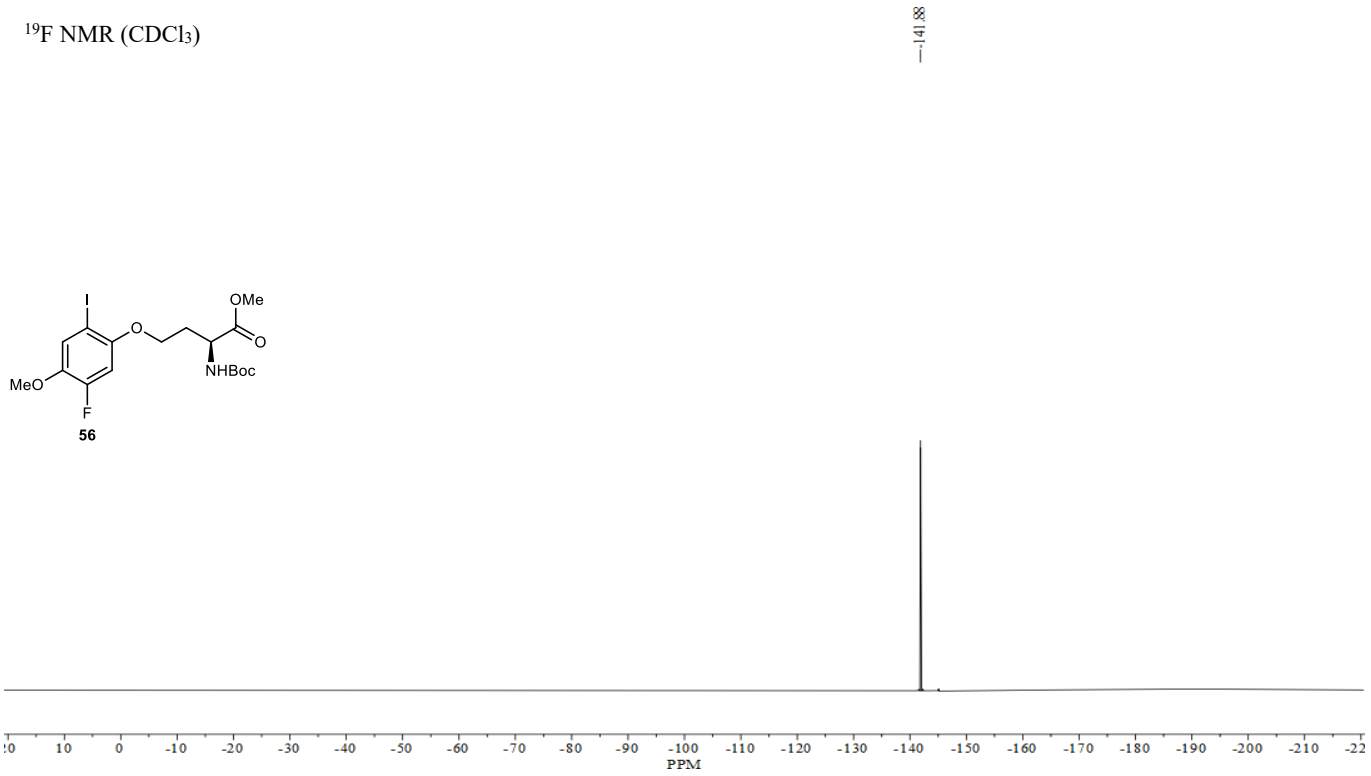


^{13}C NMR ($CDCl_3$)



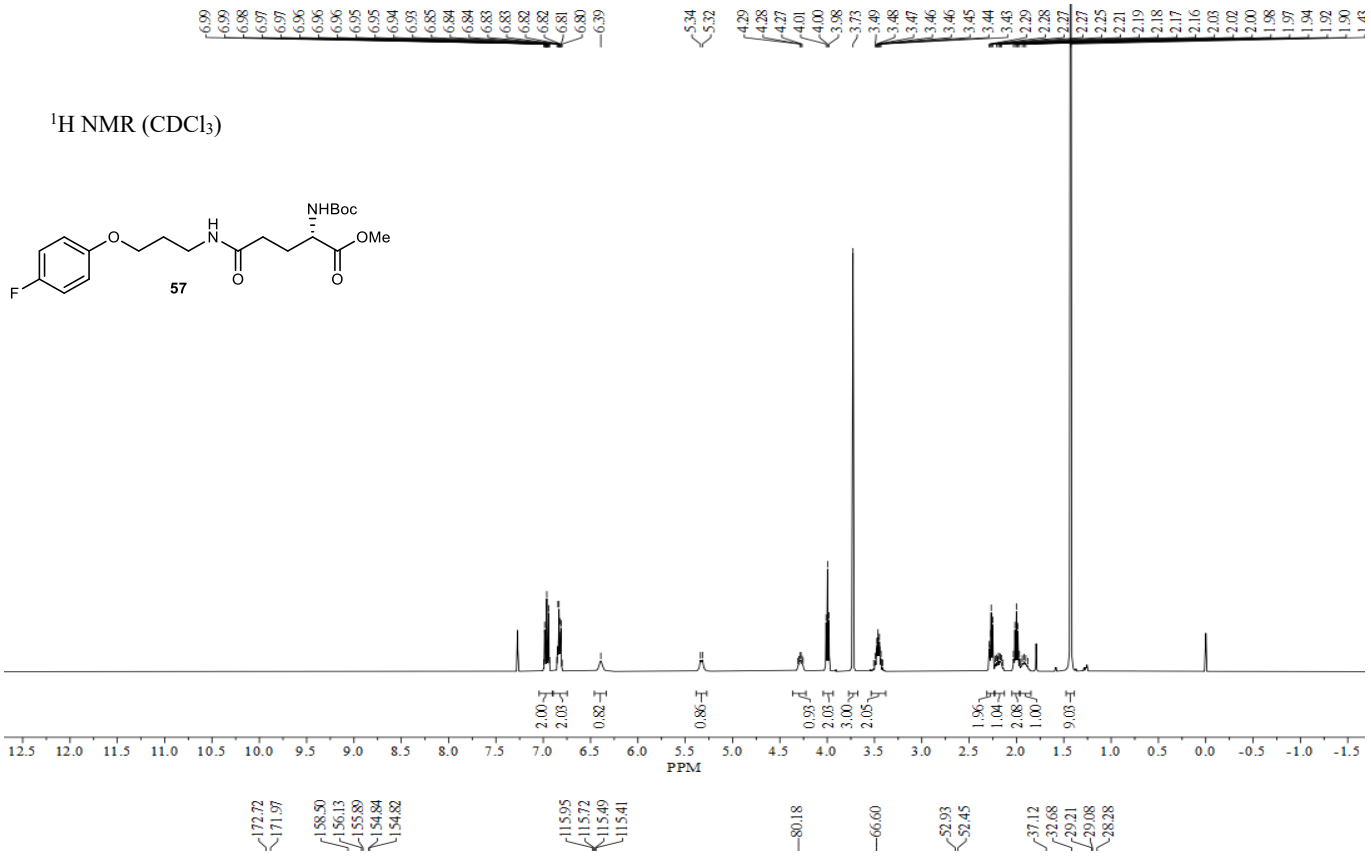
56

^{19}F NMR ($CDCl_3$)

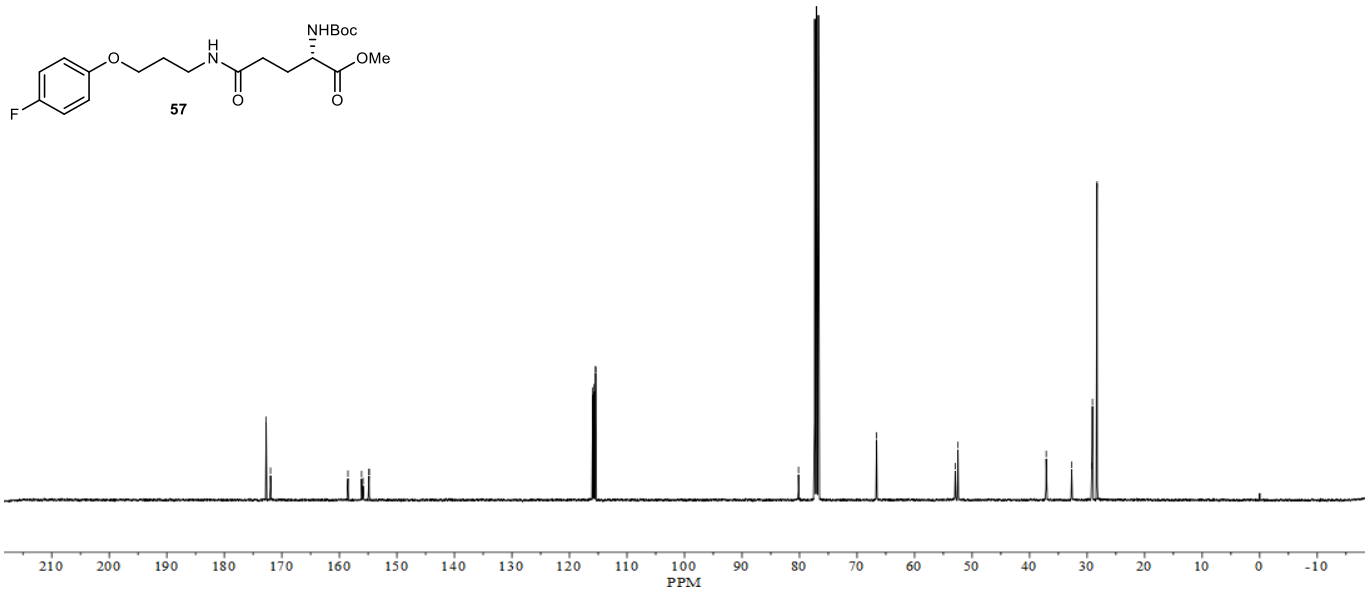


56

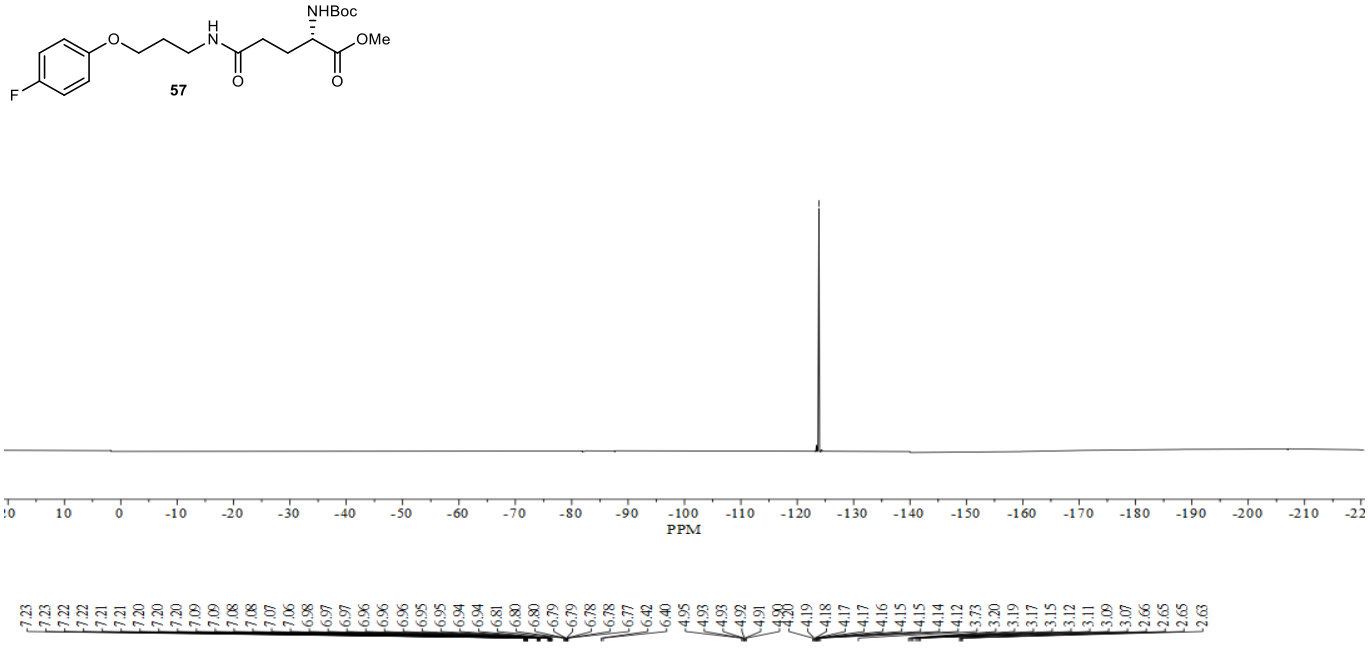
^{1}H NMR ($CDCl_3$)



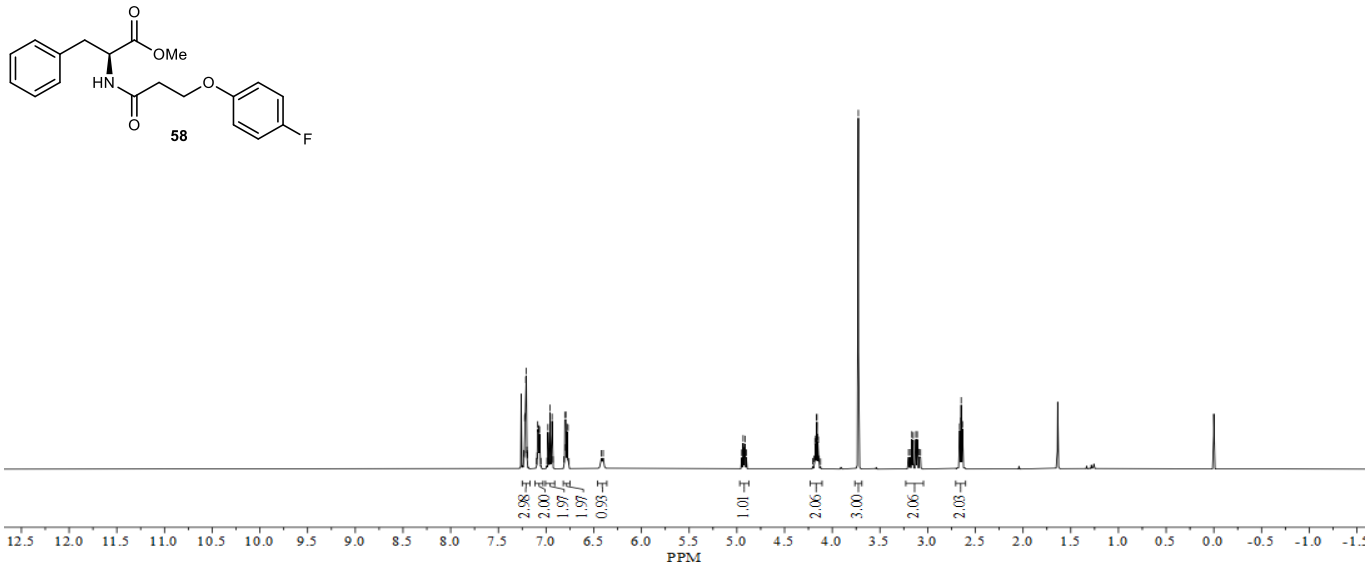
^{13}C NMR ($CDCl_3$)



^{19}F NMR ($CDCl_3$)

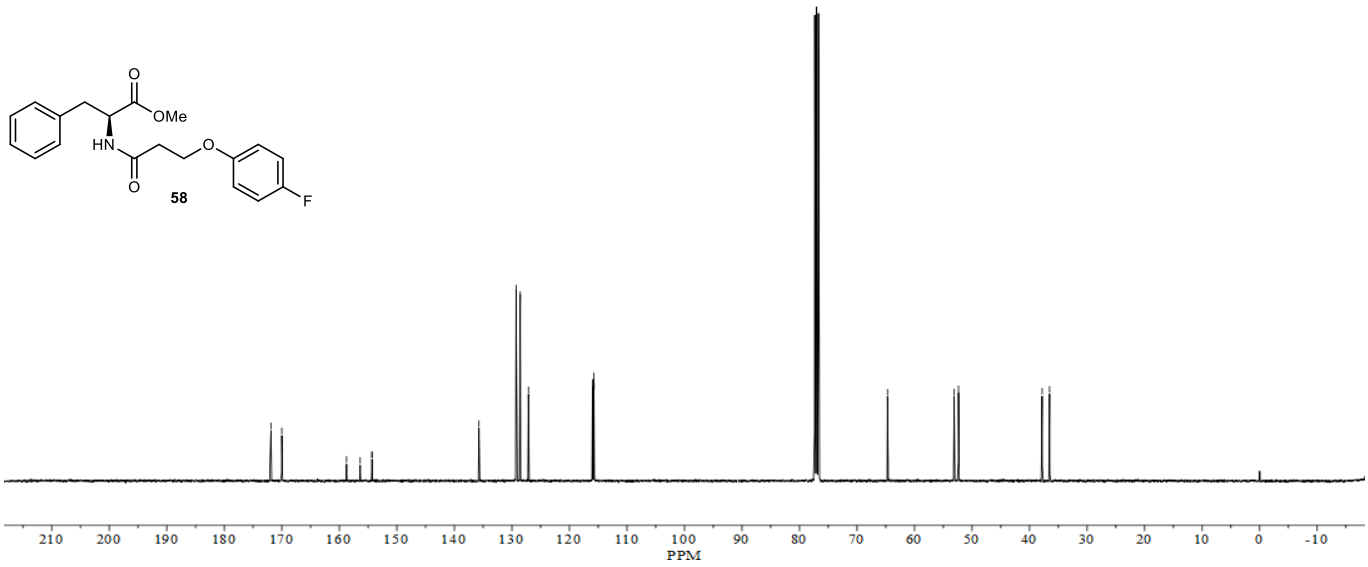


^{1}H NMR ($CDCl_3$)



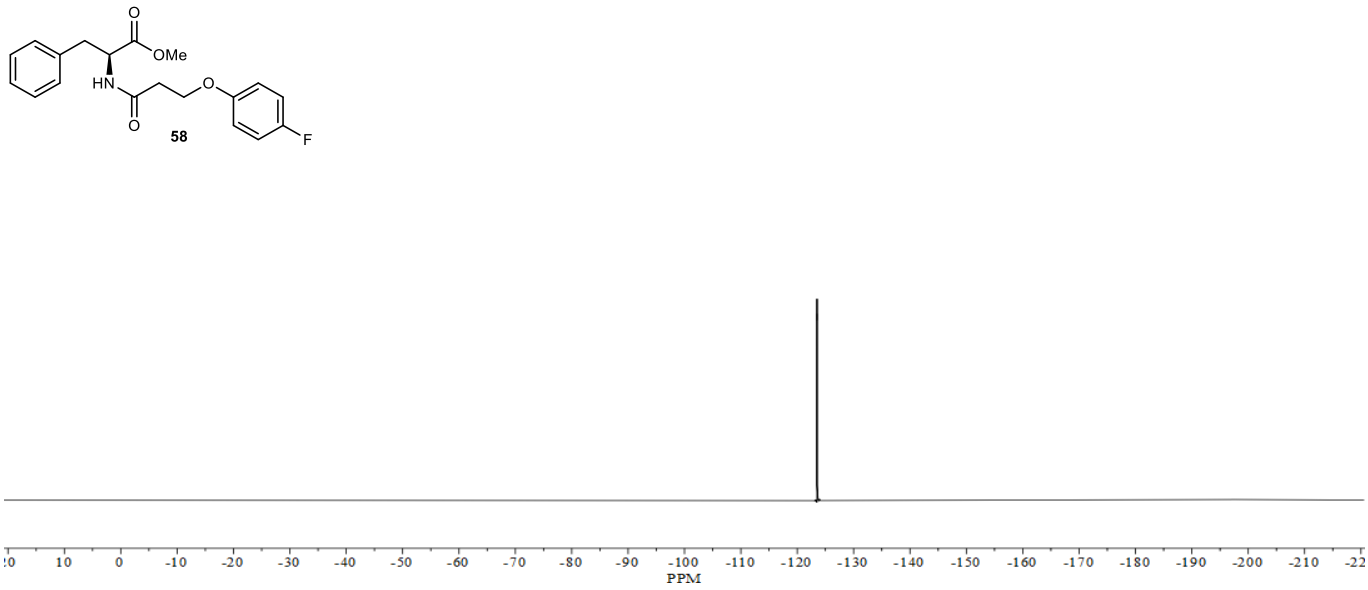
171.88
170.00
158.74
156.37
154.34
154.32
135.73
129.27
128.54
127.12
115.99
115.78
115.76
115.70
64.70
53.11
52.36
37.81
36.52

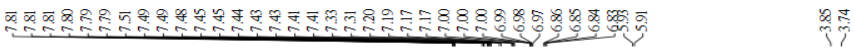
^{13}C NMR ($CDCl_3$)



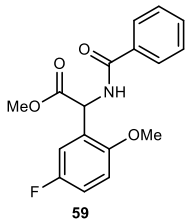
^{19}F NMR ($CDCl_3$)

-123.52

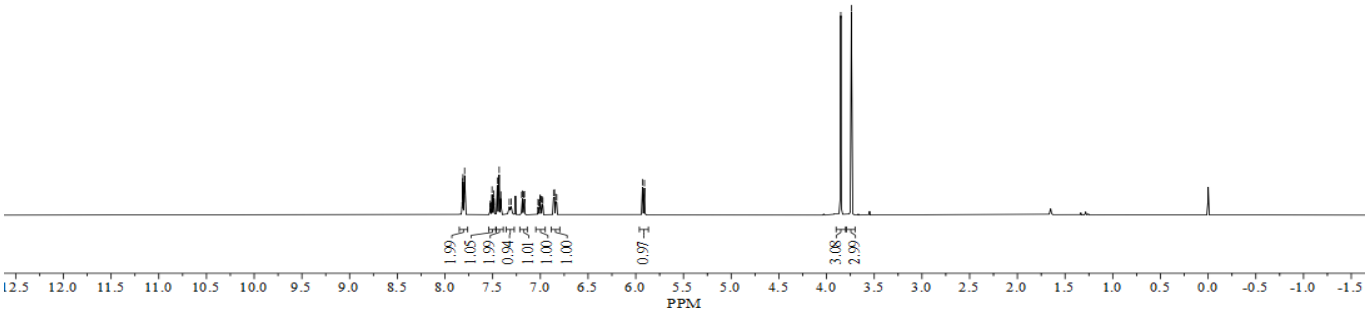


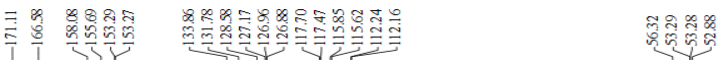


^{1}H NMR ($CDCl_3$)

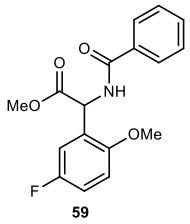


59

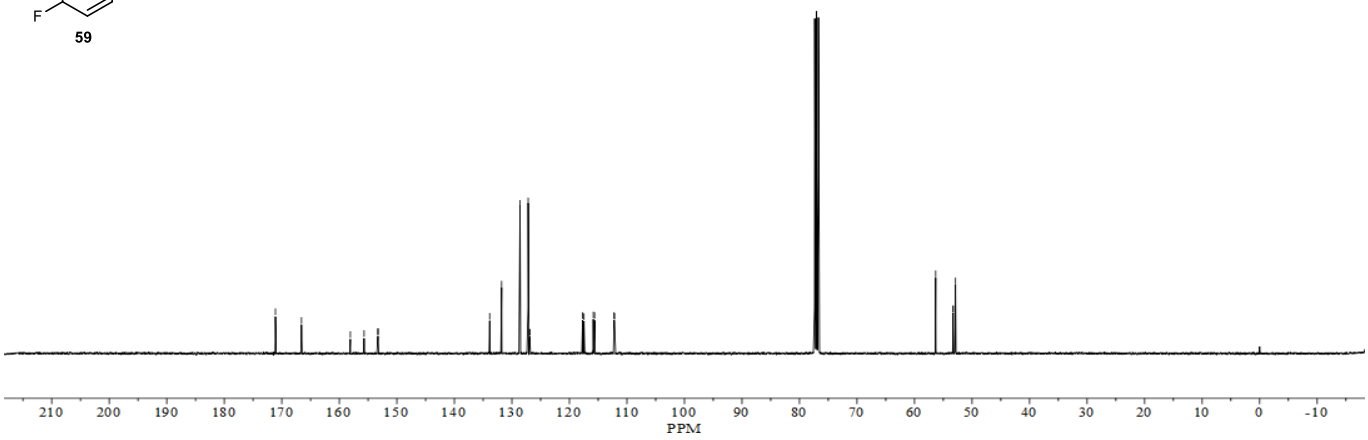




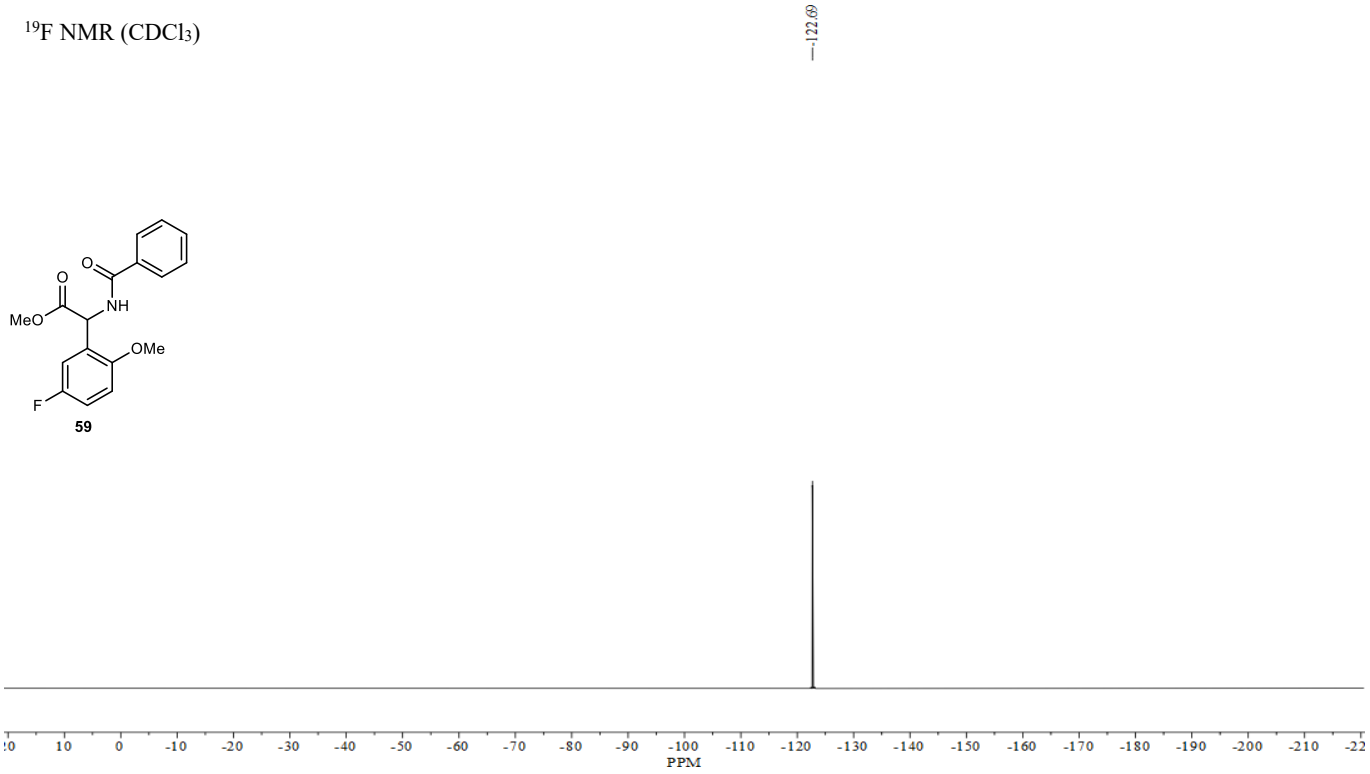
^{13}C NMR ($CDCl_3$)



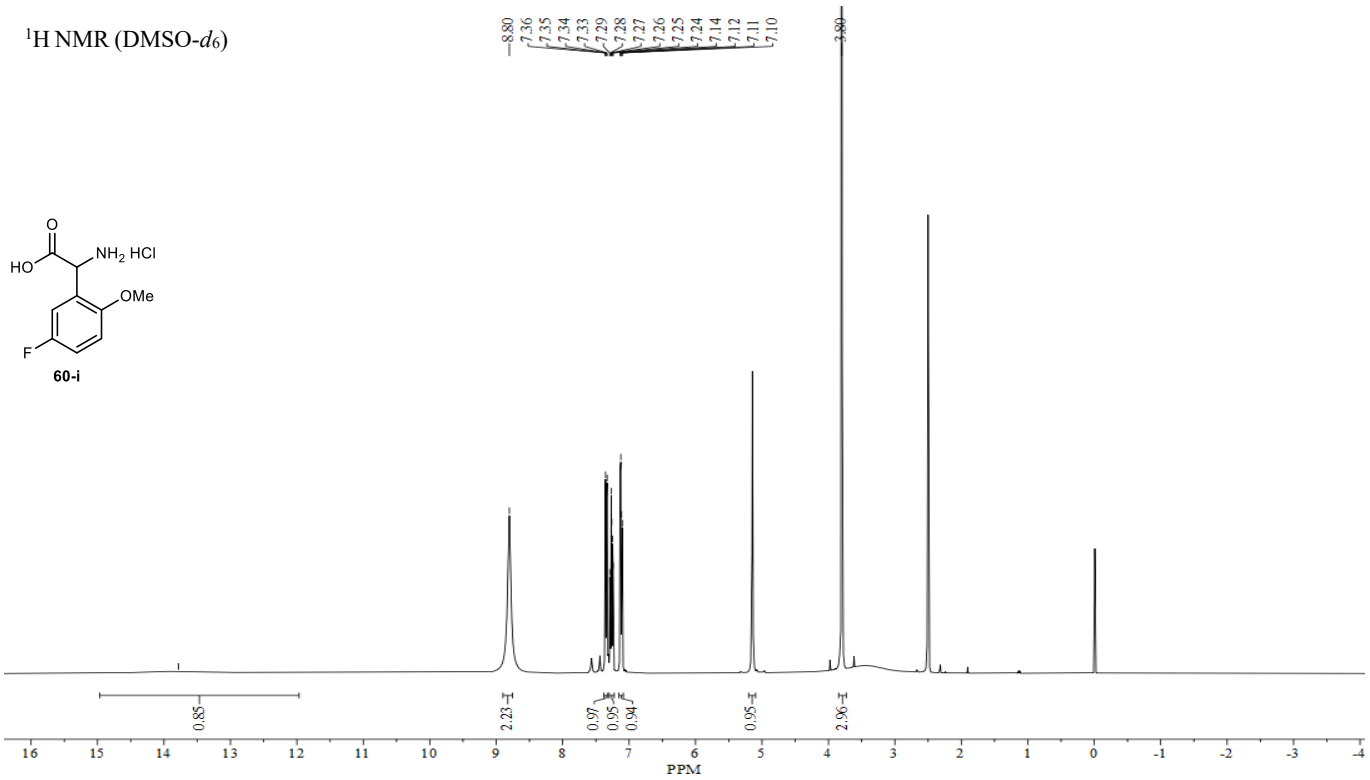
59



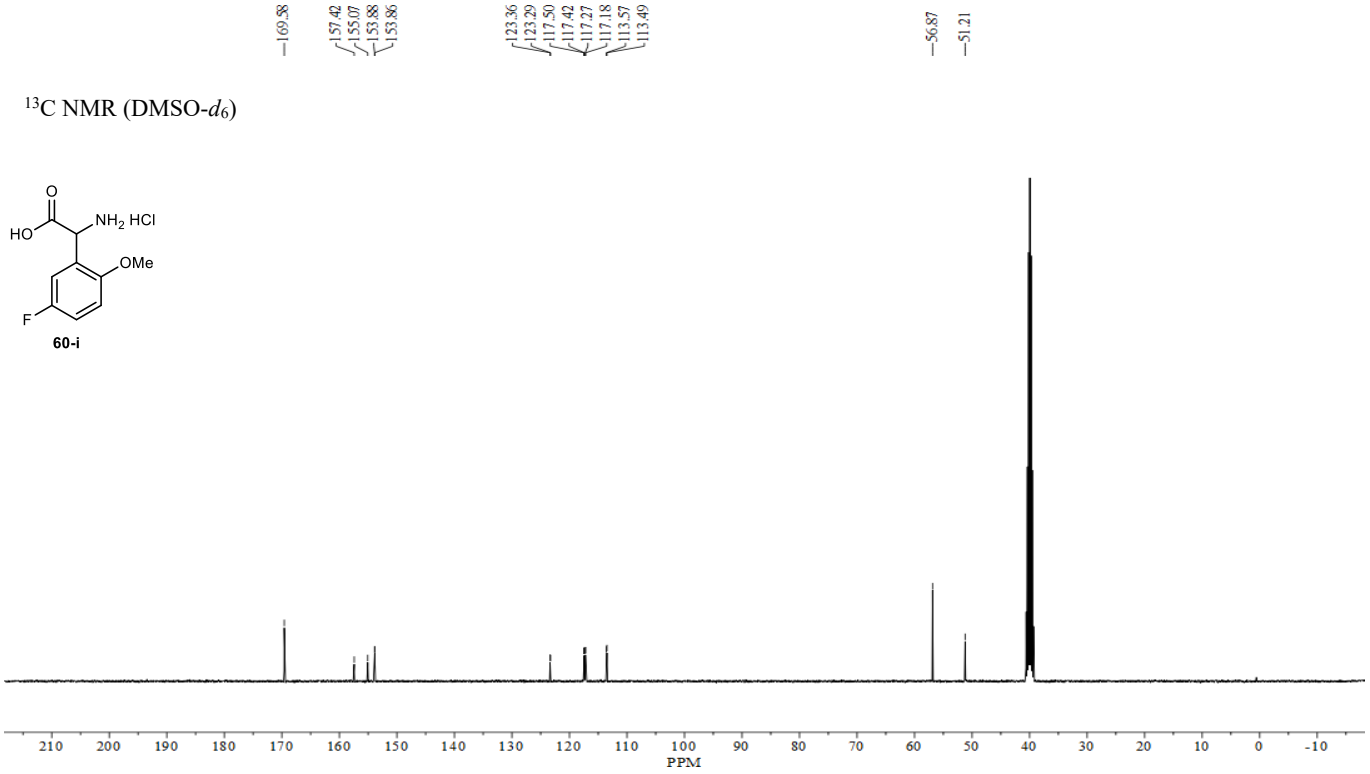
^{19}F NMR ($CDCl_3$)



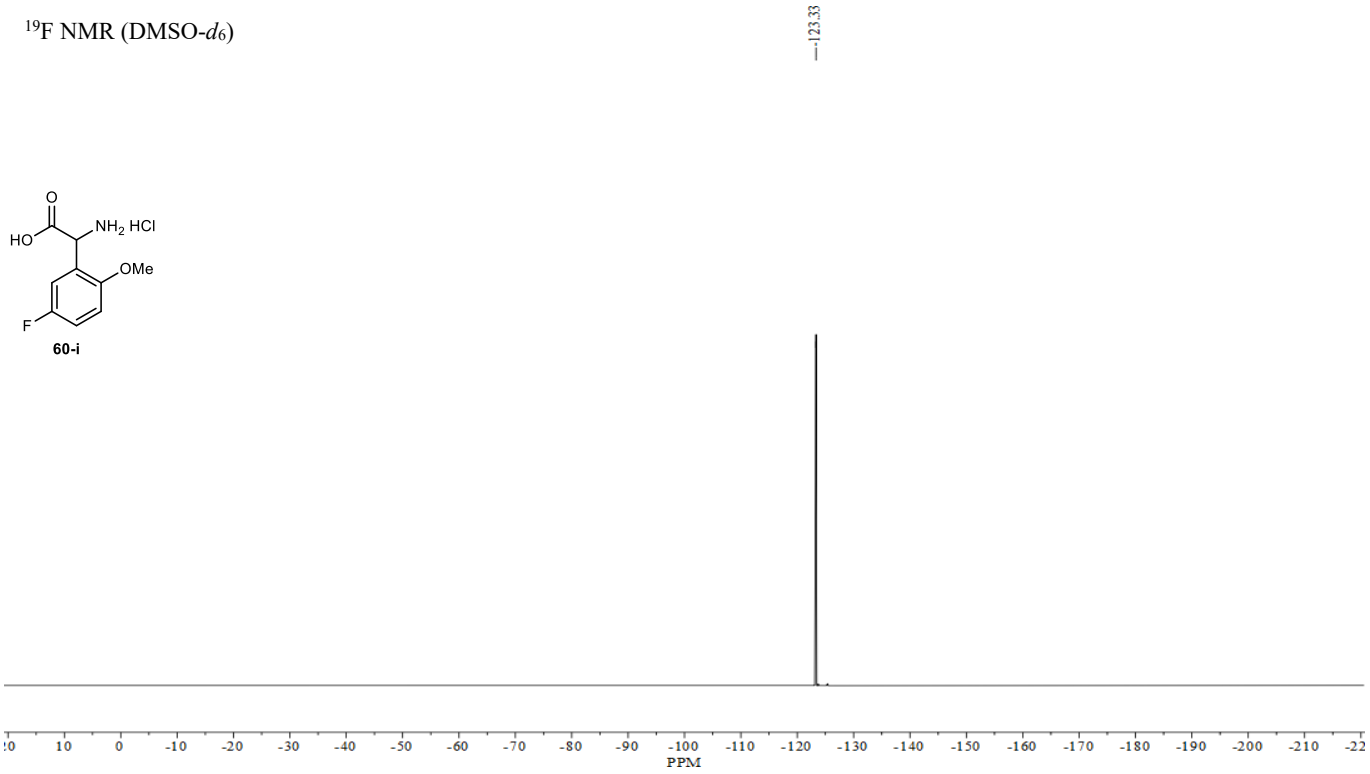
^{1}H NMR (DMSO-d_6)



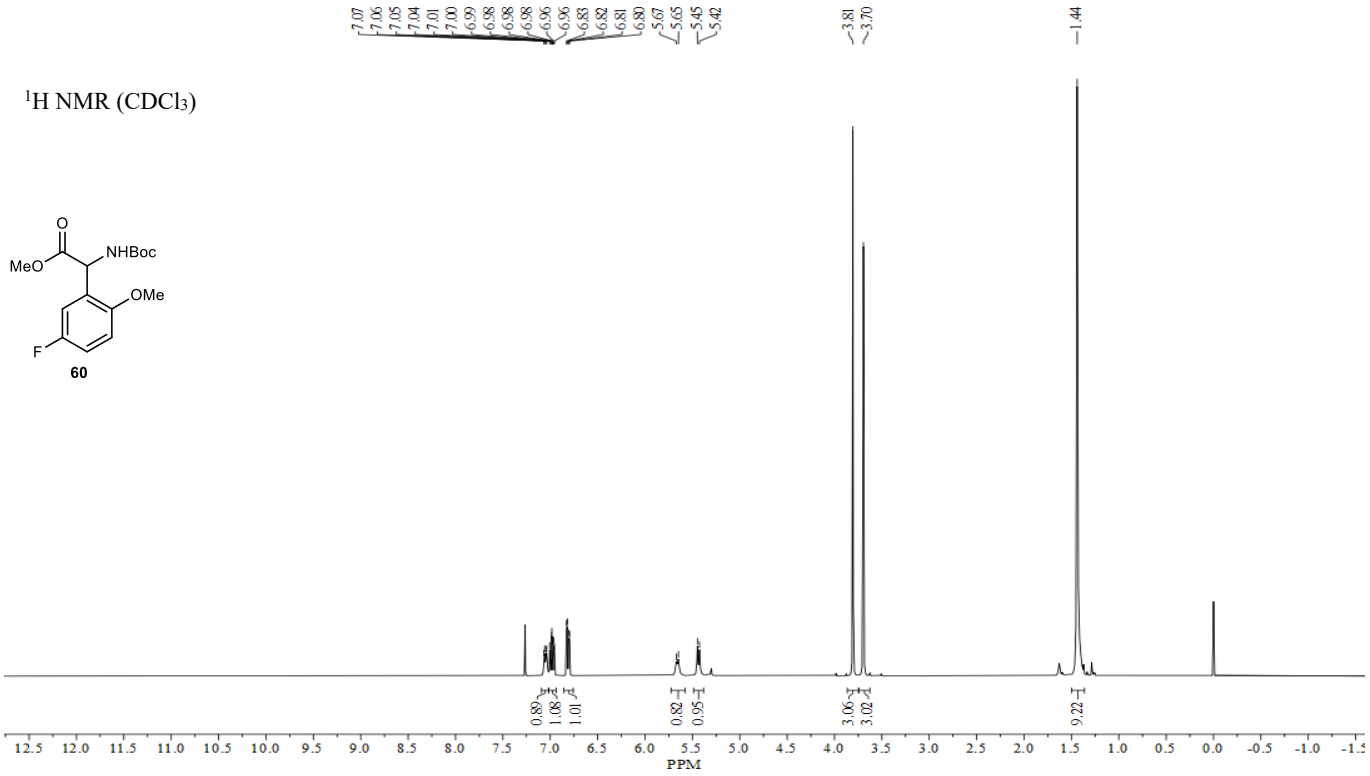
^{13}C NMR (DMSO-d_6)



^{19}F NMR (DMSO-d_6)

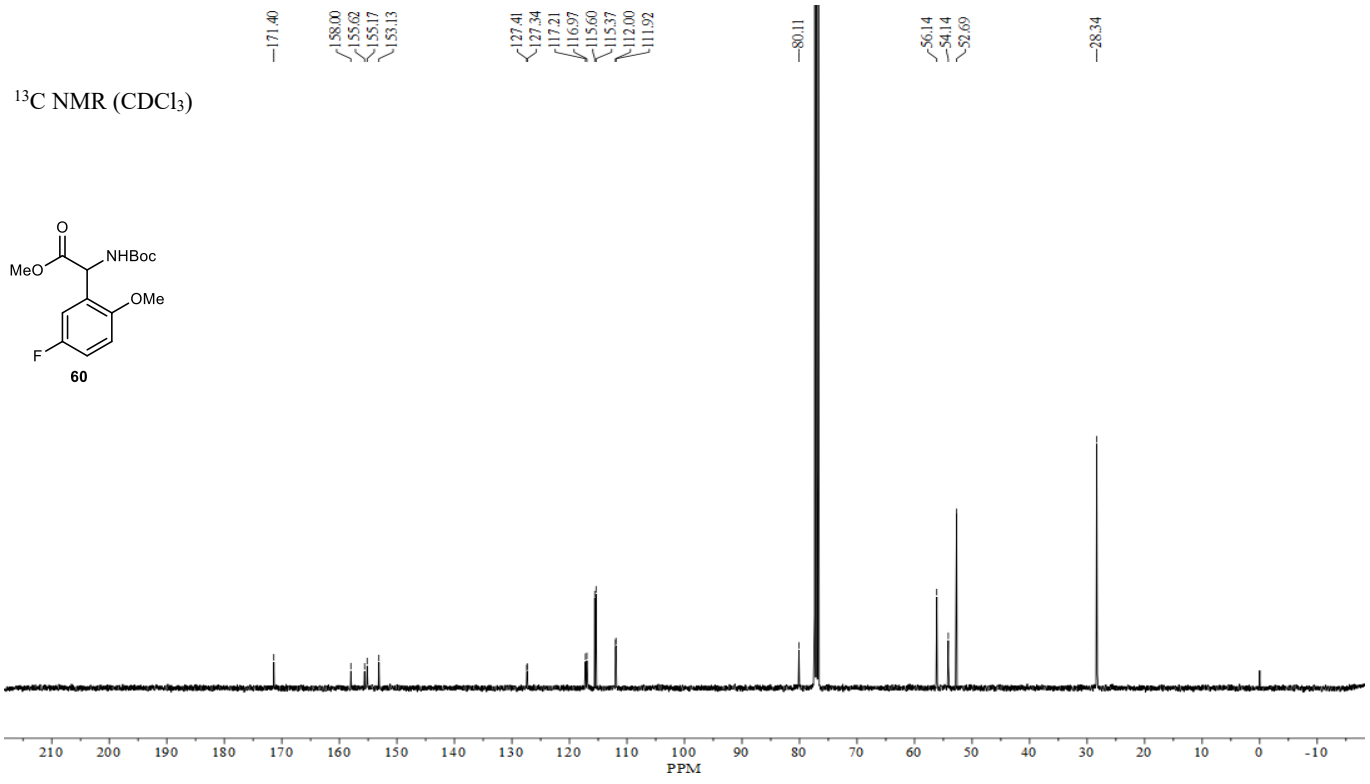


^{1}H NMR ($CDCl_3$)



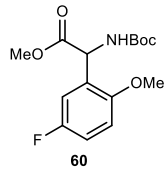
60

^{13}C NMR ($CDCl_3$)



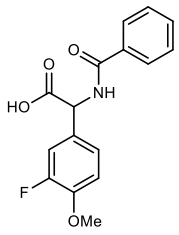
60

^{19}F NMR ($CDCl_3$)



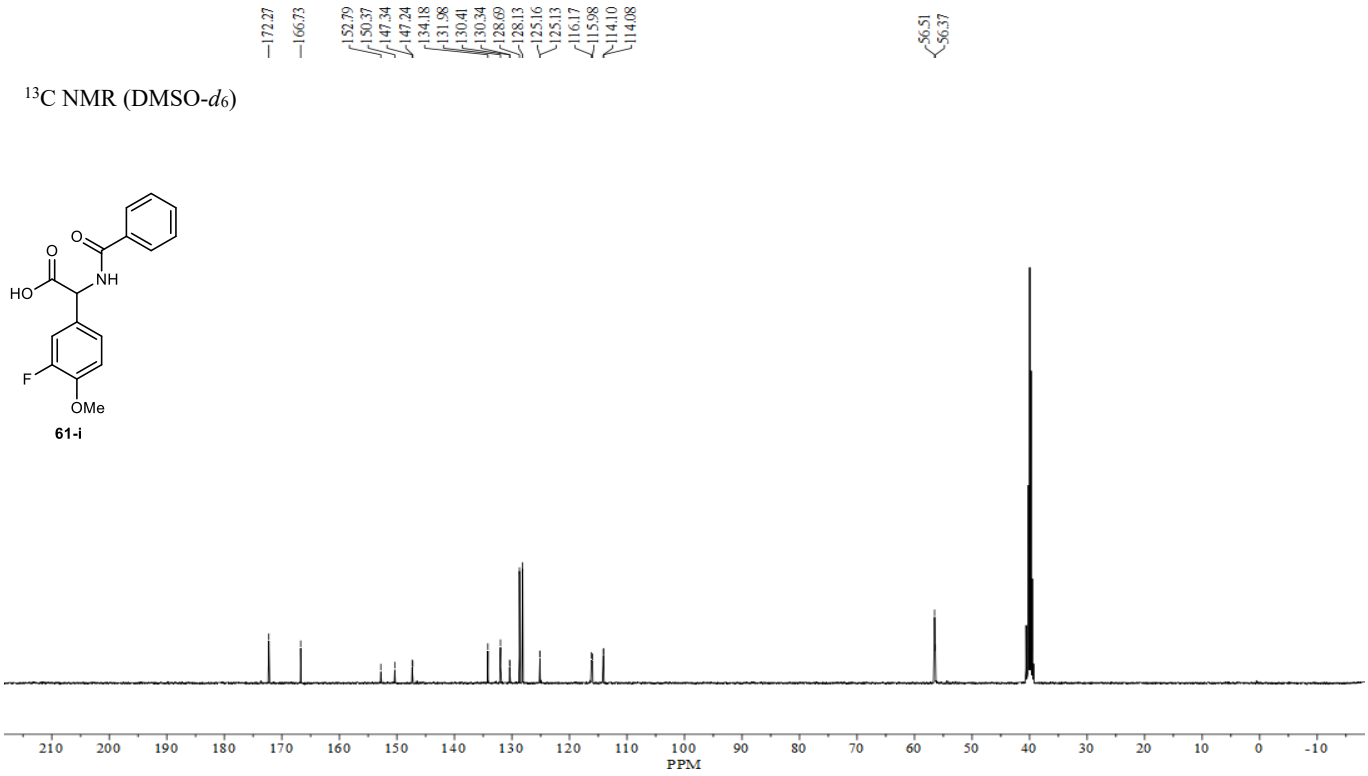
60

^{1}H NMR (DMSO-d_6)

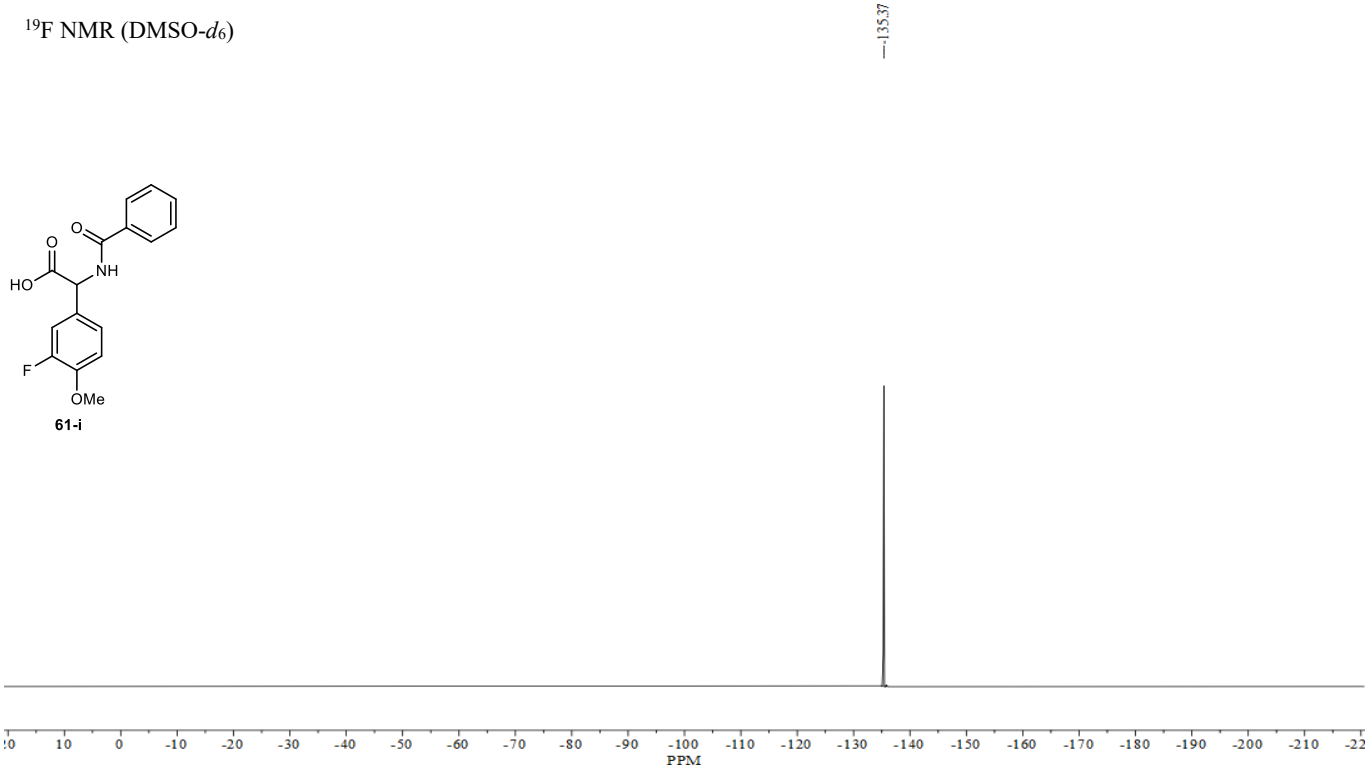


61-i

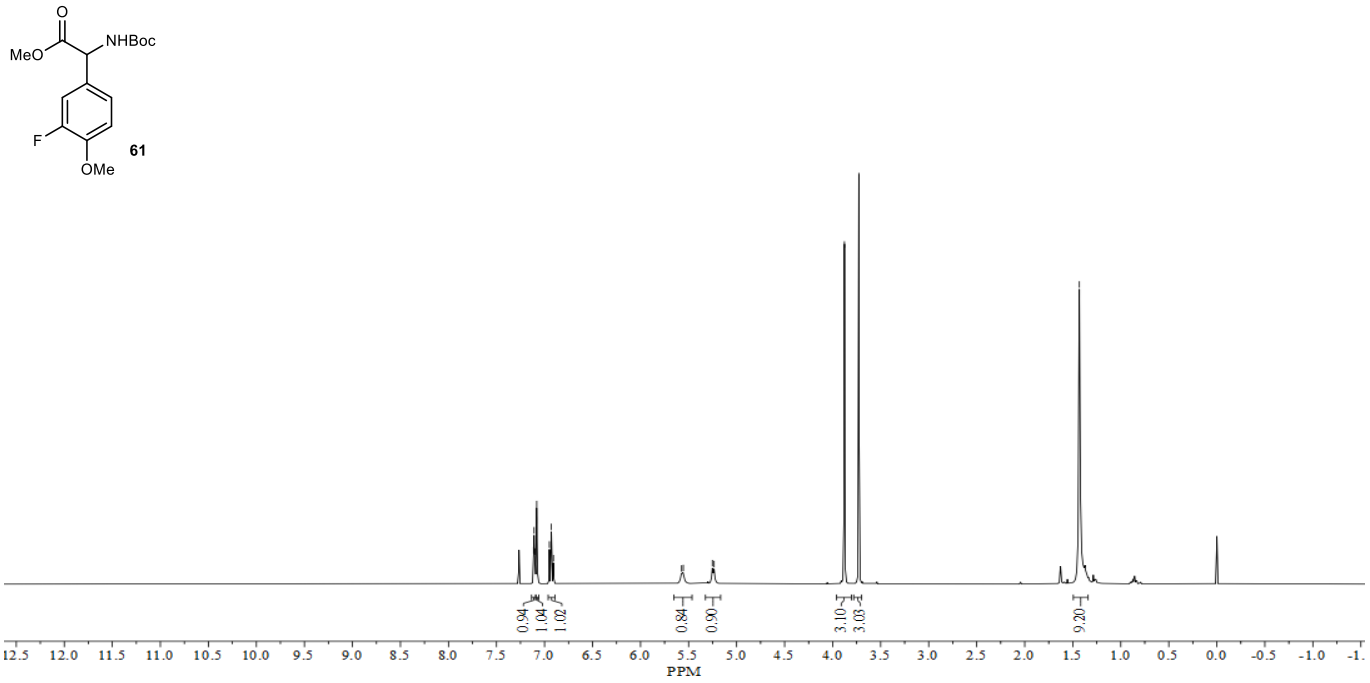
^{13}C NMR (DMSO-d_6)



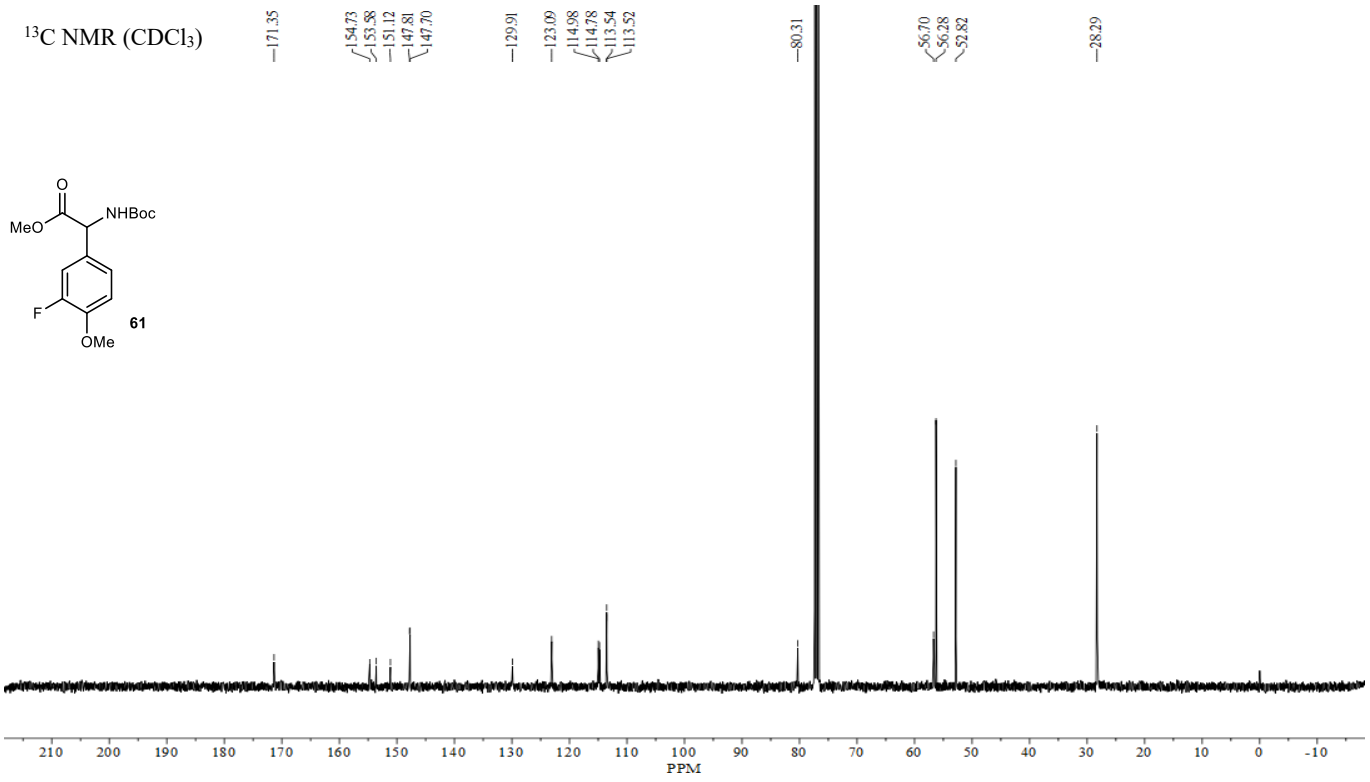
^{19}F NMR (DMSO-d_6)



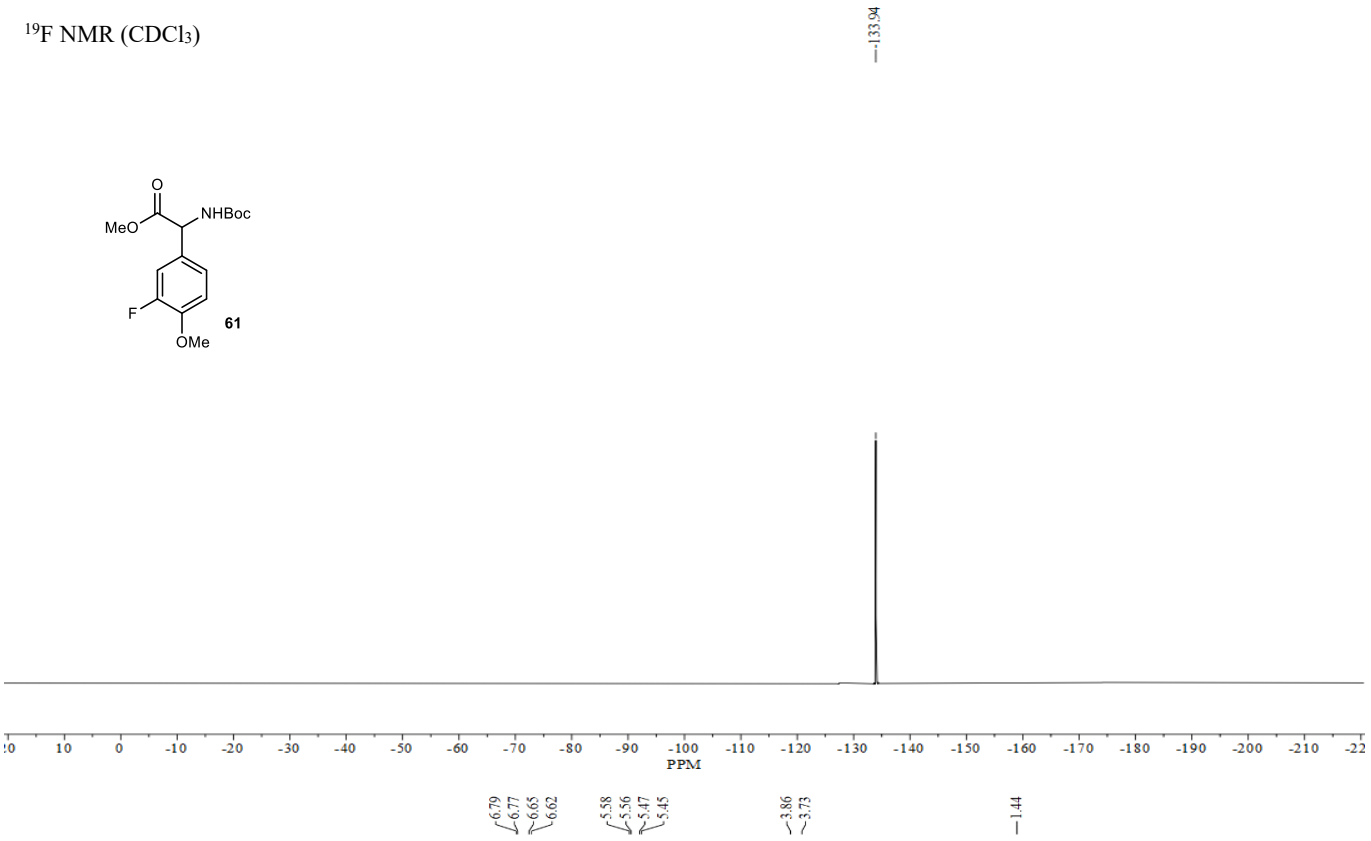
^{1}H NMR ($CDCl_3$)



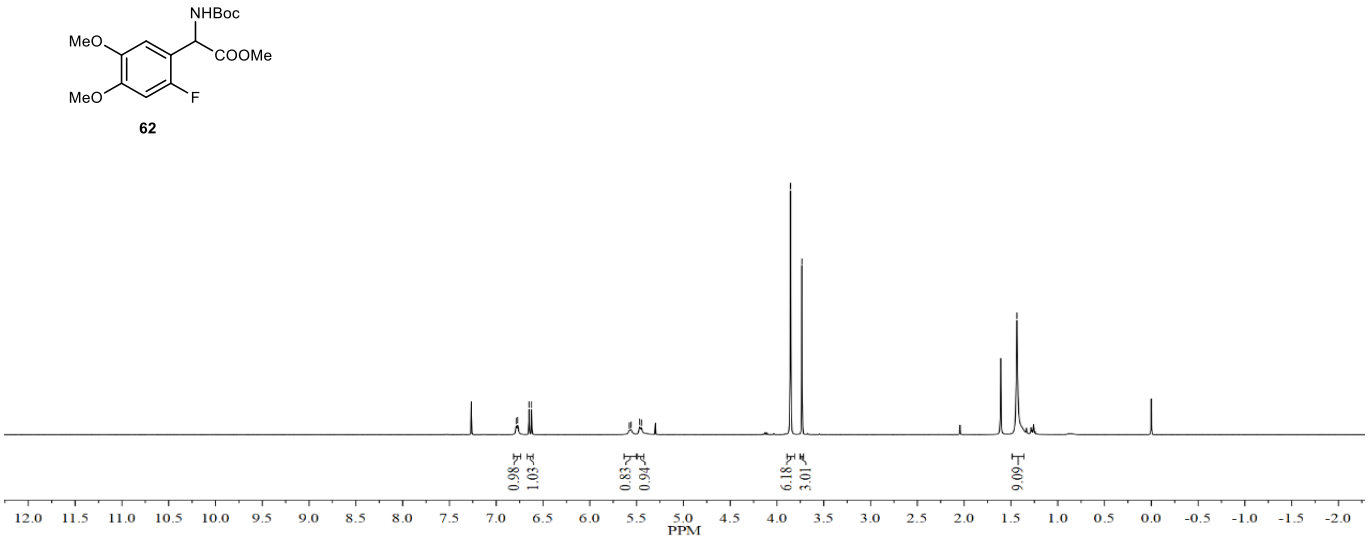
^{13}C NMR ($CDCl_3$)



^{19}F NMR ($CDCl_3$)

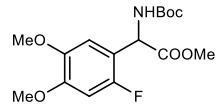


^{1}H NMR ($CDCl_3$)



171.26
155.89
154.90
153.49
149.99
149.90
145.52
114.91
111.02
100.43
100.17
80.28
77.36
77.04
76.72
56.47
56.18
52.89
52.09
28.30

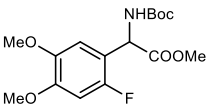
^{13}C NMR ($CDCl_3$)



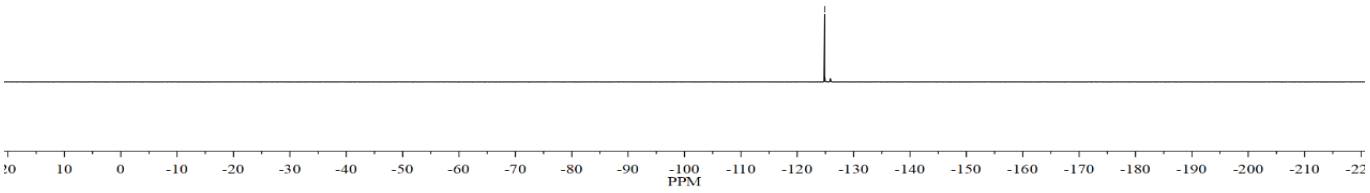
62

^{19}F NMR ($CDCl_3$)

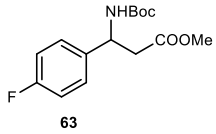
-124.84



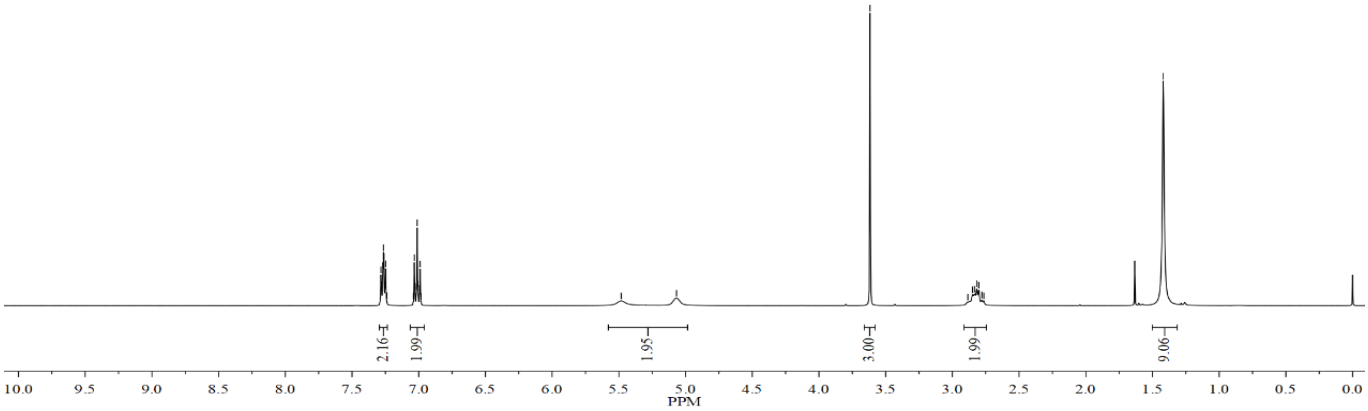
62



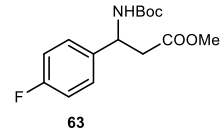
^{1}H NMR ($CDCl_3$)



63

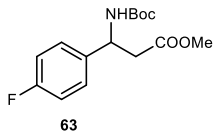


^{13}C NMR ($CDCl_3$)



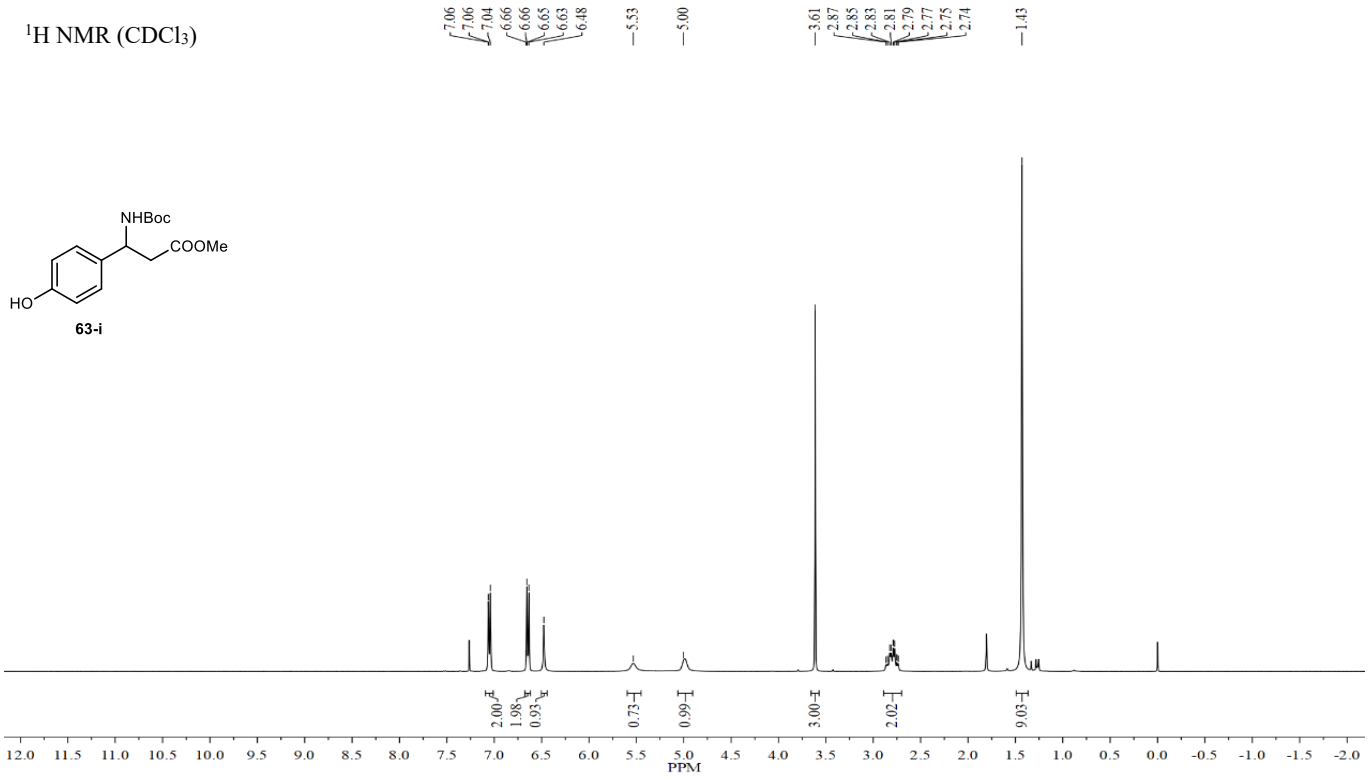
63

^{19}F NMR ($CDCl_3$)



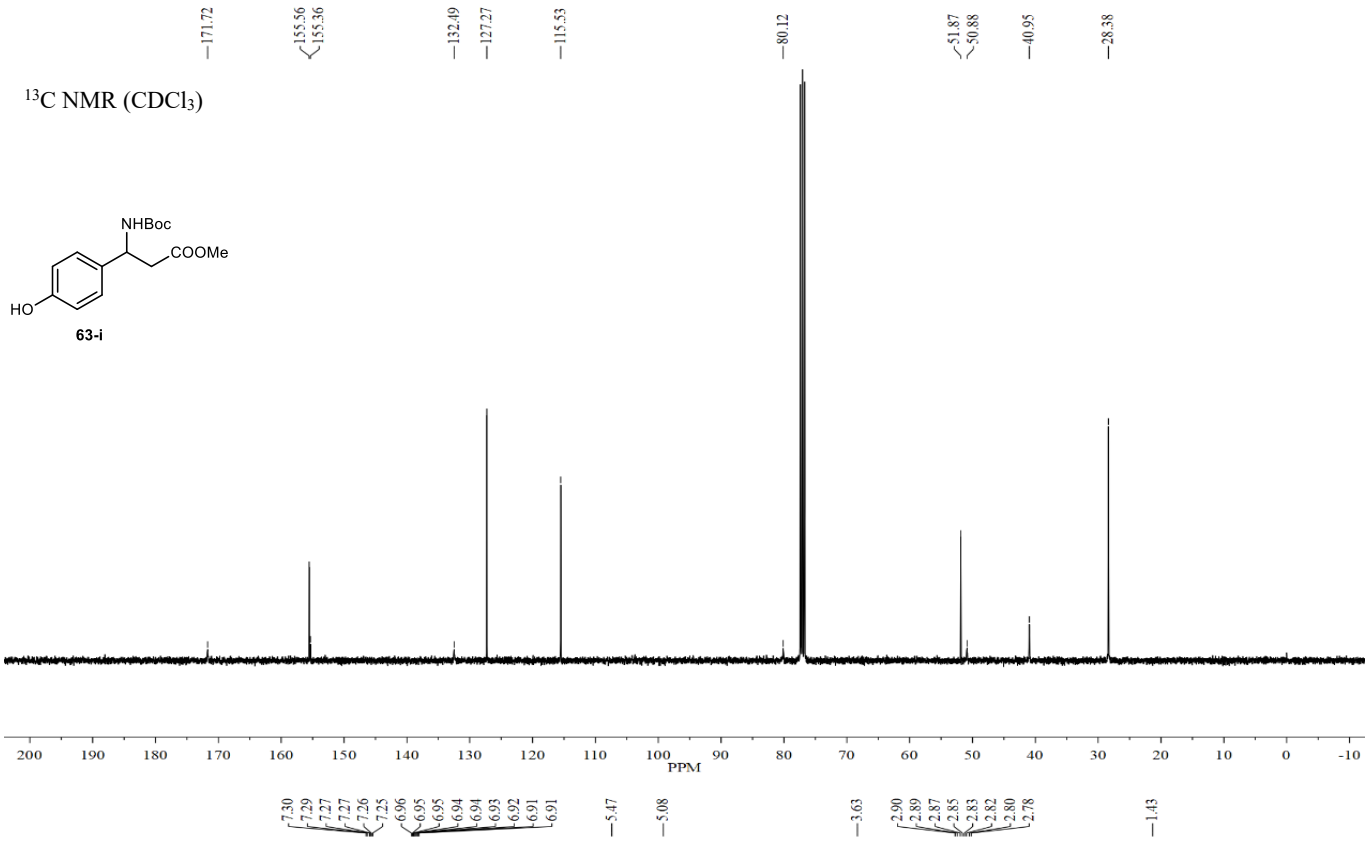
63

^{1}H NMR ($CDCl_3$)

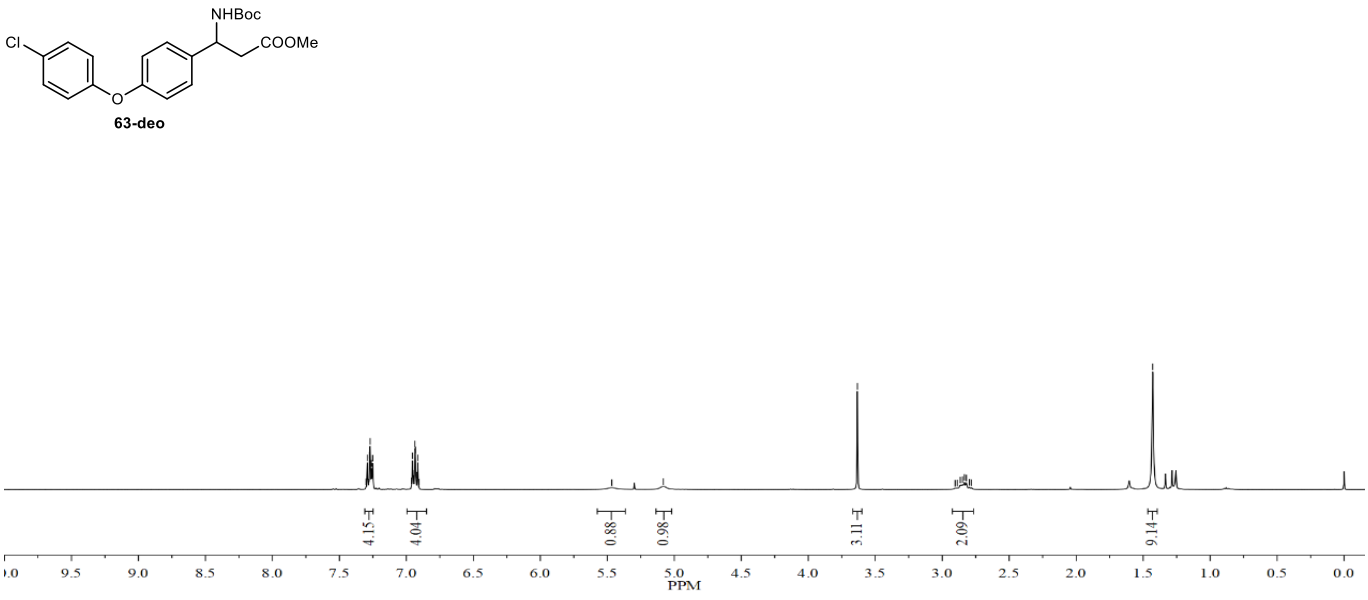


63-i

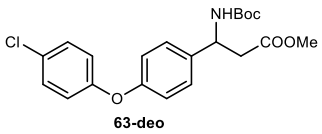
^{13}C NMR ($CDCl_3$)



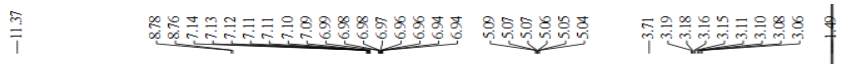
^{1}H NMR ($CDCl_3$)



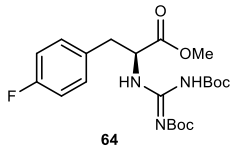
^{13}C NMR ($CDCl_3$)



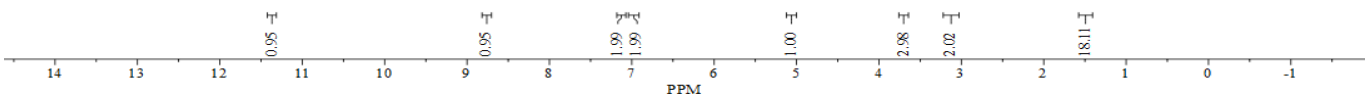
63-deo



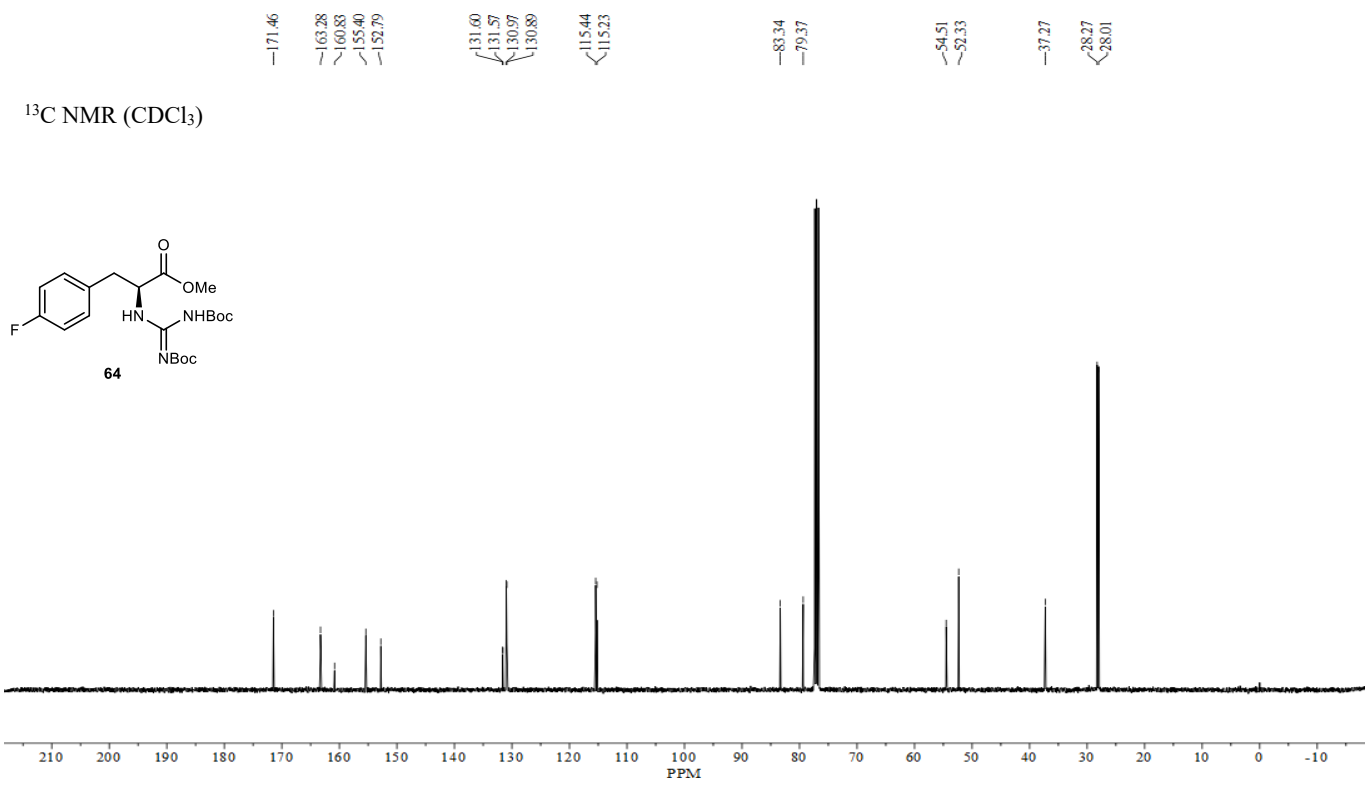
^{1}H NMR ($CDCl_3$)



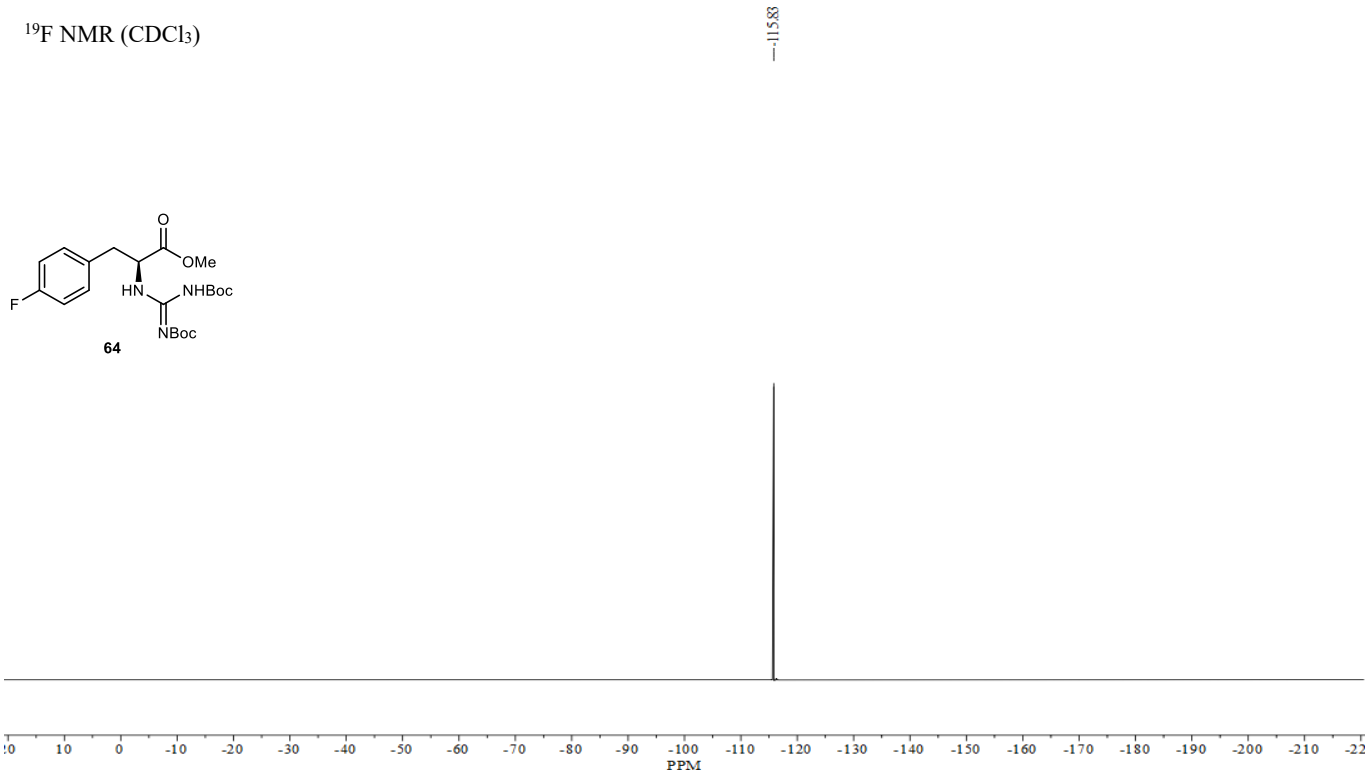
64



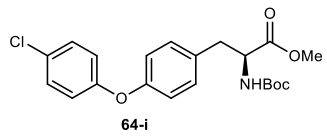
^{13}C NMR ($CDCl_3$)



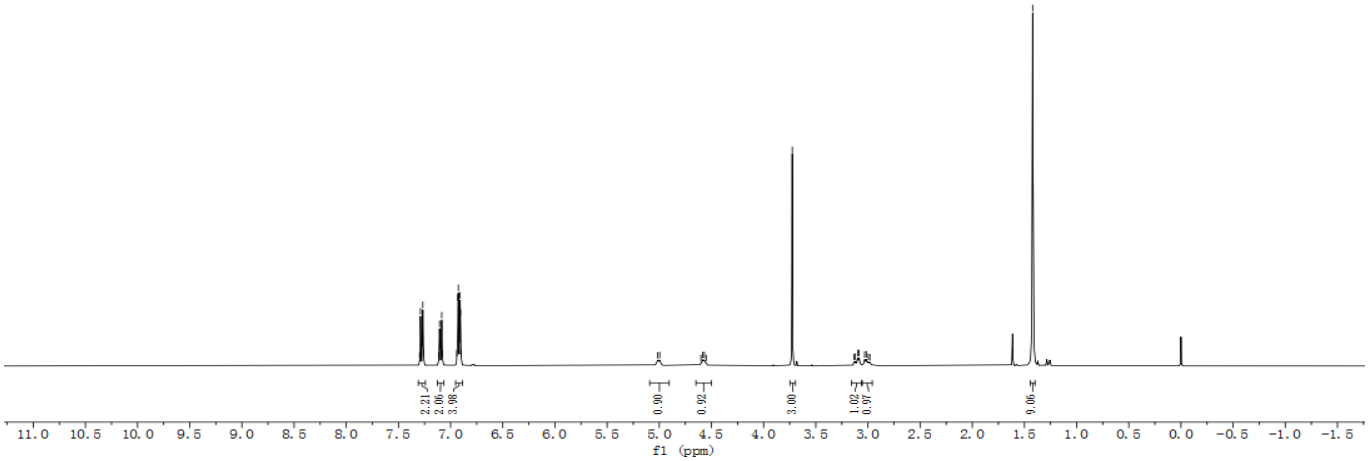
^{19}F NMR ($CDCl_3$)



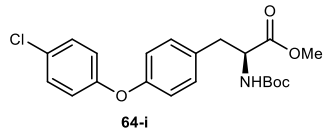
^{1}H NMR ($CDCl_3$)



64-i

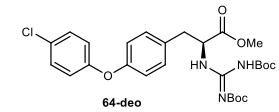


^{13}C NMR ($CDCl_3$)



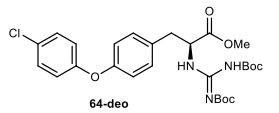
64-i

^{1}H NMR ($CDCl_3$)



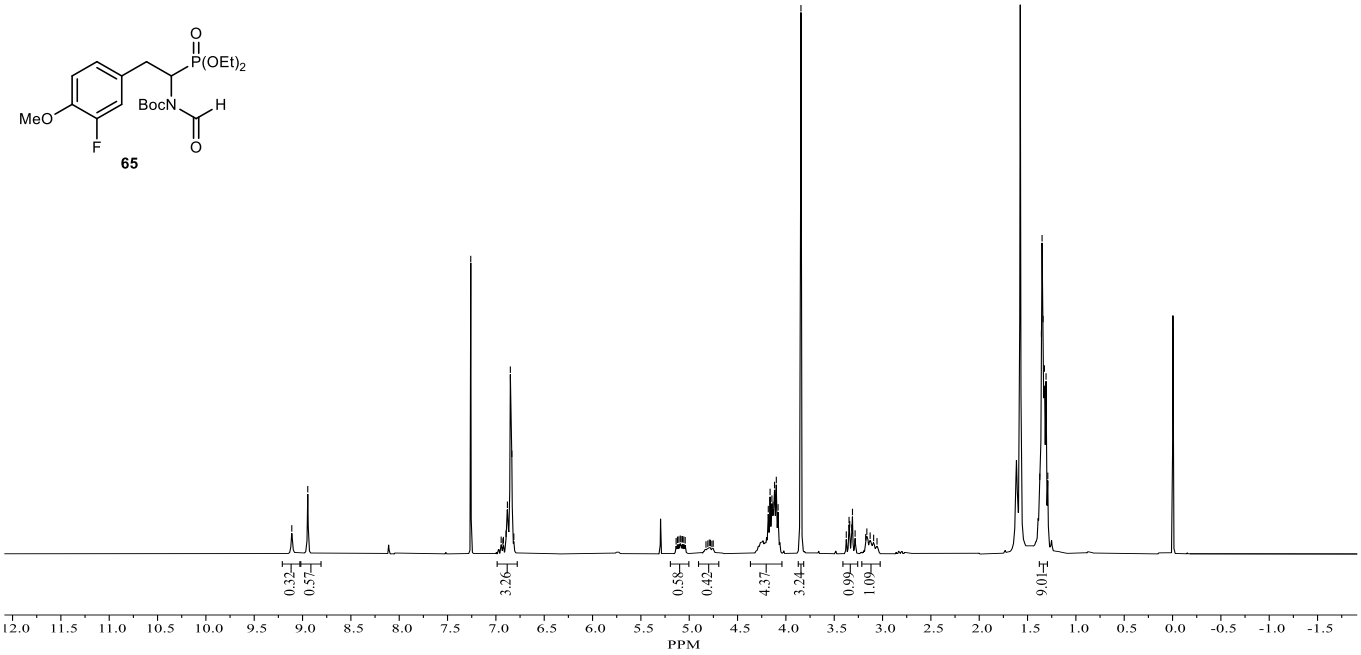
64-deo

^{13}C NMR ($CDCl_3$)

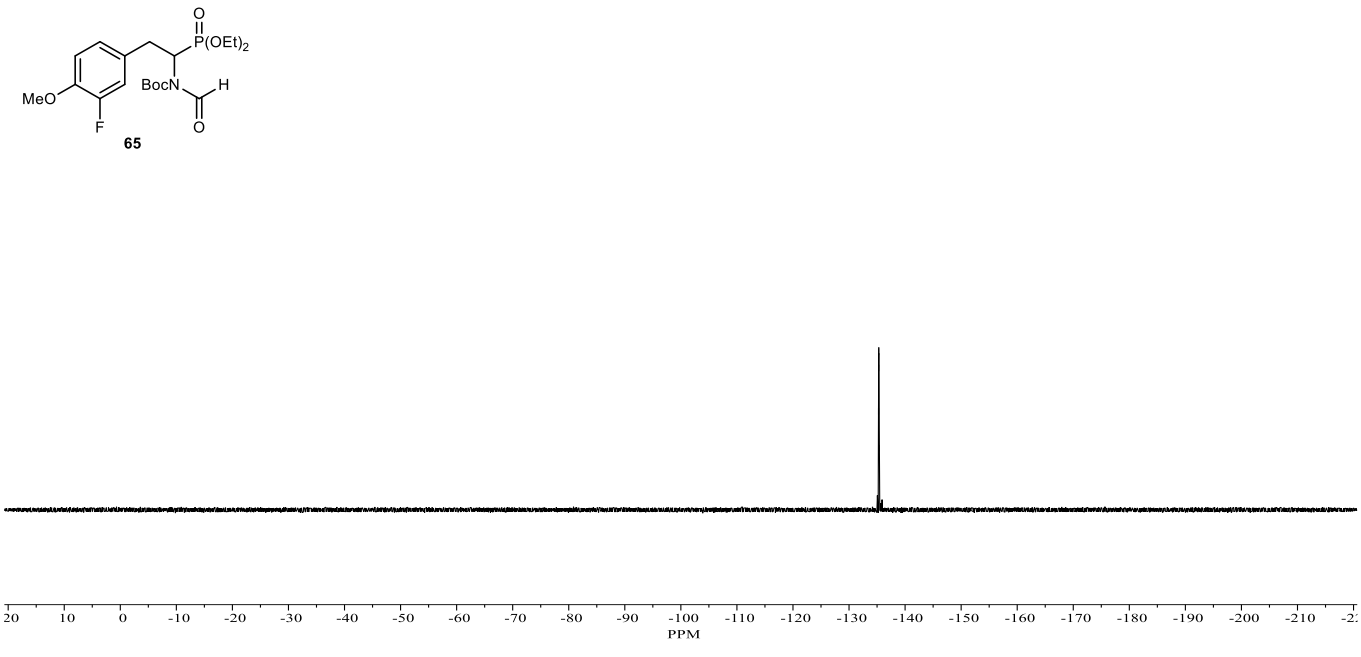


64-deo

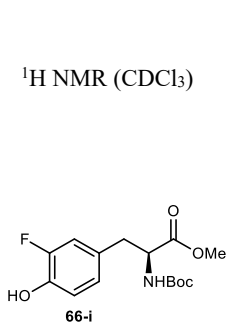
^{1}H NMR ($CDCl_3$)



^{19}F NMR ($CDCl_3$)

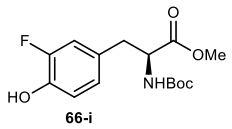


^{1}H NMR ($CDCl_3$)



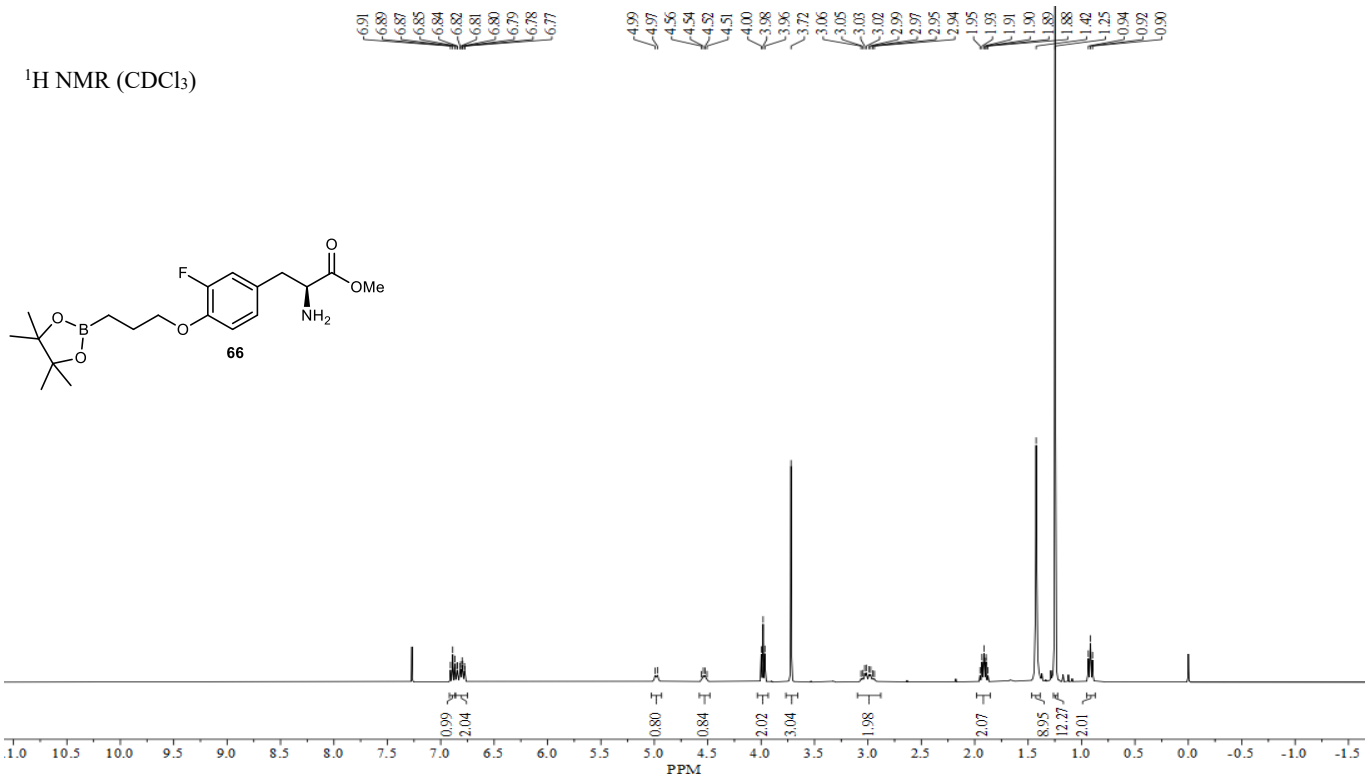
66-i

^{19}F NMR ($CDCl_3$)

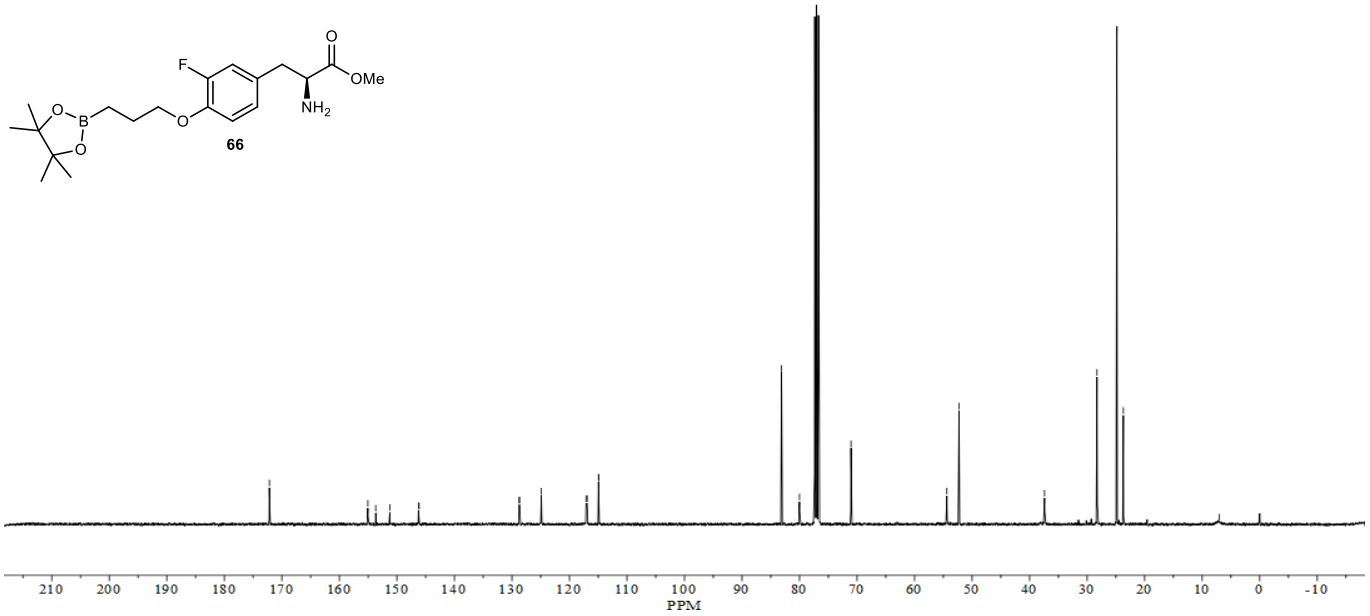


66-i

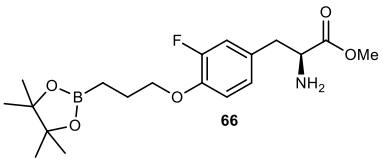
^{1}H NMR ($CDCl_3$)



^{13}C NMR ($CDCl_3$)



^{19}F NMR ($CDCl_3$)



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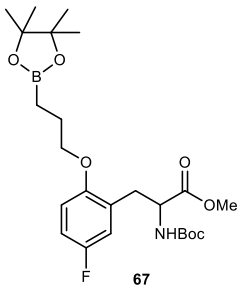
^{13}C NMR ($CDCl_3$)



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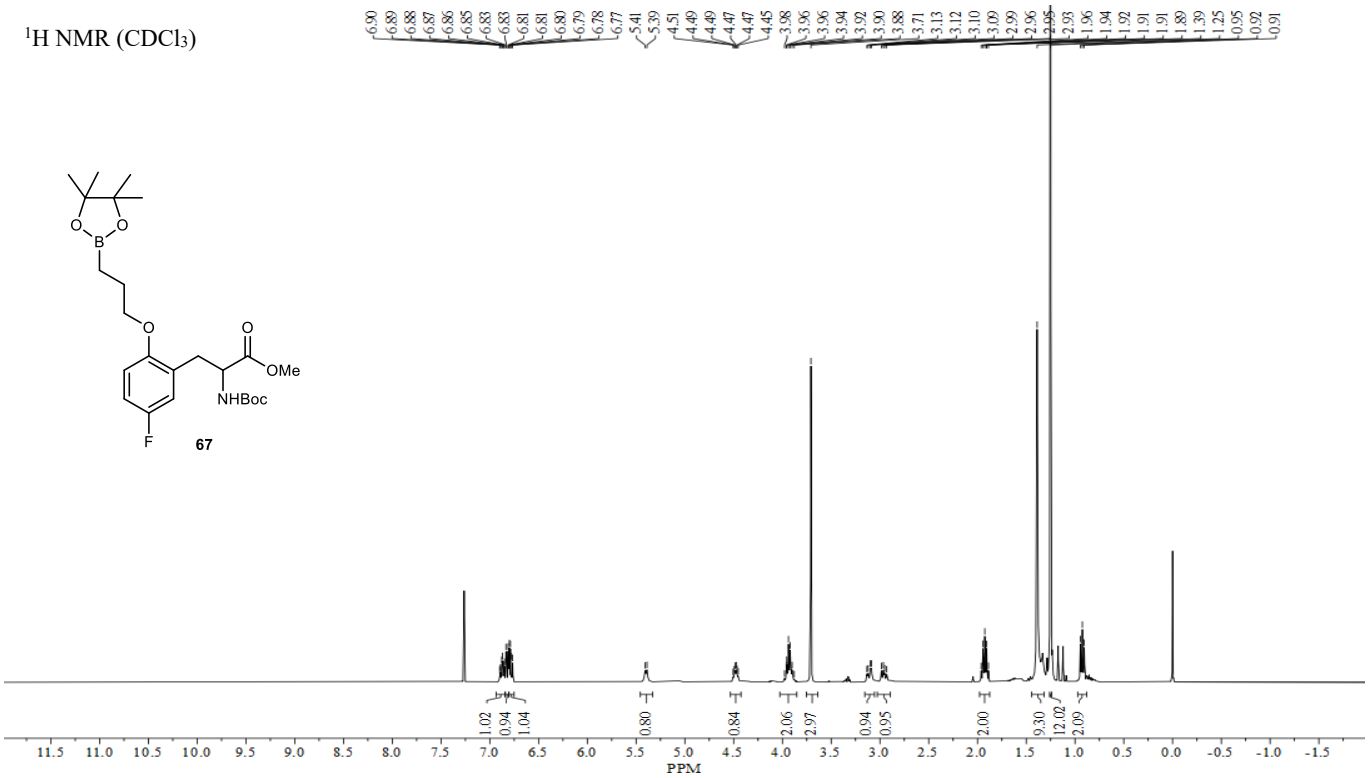
^{1}H NMR ($CDCl_3$)

^{1}H NMR ($CDCl_3$)



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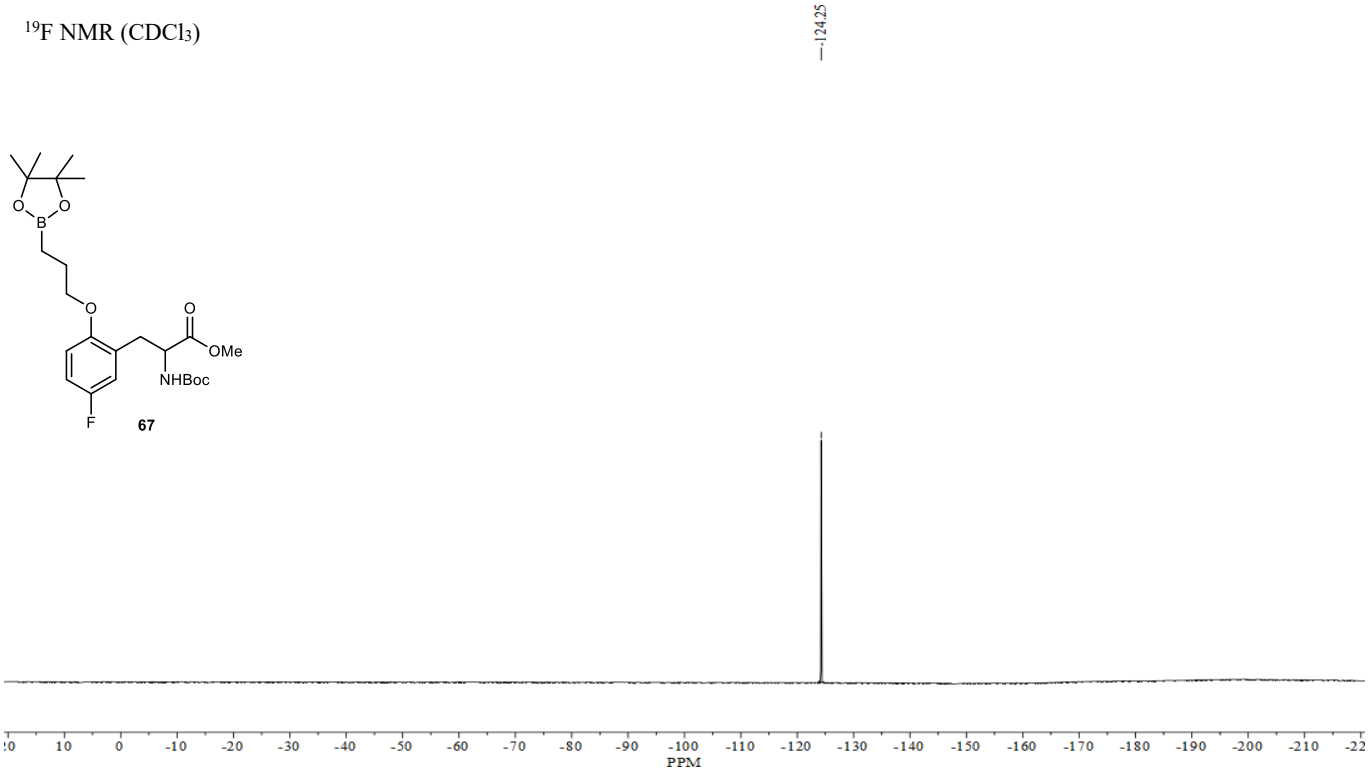
^{19}F NMR ($CDCl_3$)



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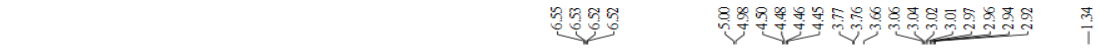
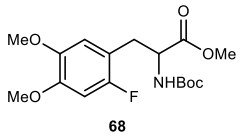


^{1}H NMR ($CDCl_3$)



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