Electronic Supplementary Information

Single-step syntheses of functionalized no-carrier-added [^{18}F]fluoroarenes as labeling synthons from diaryliodonium salts

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1. Materials

Acetonitrile (99.8%, anhydrous), chloroform (99.8%, anhydrous), and dichloromethane (99.8%, anhydrous) were purchased from Sigma-Aldrich (Milwaukee, WI) in Sure/Seal™ bottles and used in synthesis as received. *m*-CPBA (*m*-chloroperbenzoic acid), and *p*-TsOH·H_2O (*p*-toluenesulfonic acid monohydrate) were purchased from Sigma-Aldich (Milwaukee, WI). Chemicals for radiochemistry such as potassium carbonate (99%), K 2.2.2 (4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane), *N,N*-dimethylformamide (DMF, 99.8%, anhydrous; Sure/Seal™ bottle), and reference fluoroarenes were purchased from either Sigma-Aldrich (Milwaukee, WI) or Alfa Aesar (Ward Hill, MA). 4-Iodobenzophenone was obtained from Matrix Scientific (Columbia, SC). Acetonitrile (high purity solvent, Burdick & Jackson, Morristown, NJ) was used for HPLC. QMA anionic resin cartridges were supplied by ORTG (Oakdale, TN).

The following diaryliodonium tosylates were prepared as described previously[1,2]: (4-formylphenyl)(4'-methoxyphenyl)iodonium tosylate (**1a**), (3-formylphenyl)(4'-methoxyphenyl)iodonium tosylate (**2a**), (3-formylphenyl)(2'-thienyl)iodonium tosylate (**2c**), (3-formyl-6-methoxyphenyl)(4'-methoxyphenyl)iodonium tosylate (**3a**), (2-bromomethylphenyl)(4'-methoxyphenyl)iodonium tosylate (**4a**), (2-chloromethylphenyl)(4'-methoxyphenyl)iodonium tosylate (**5a**), (3-bromomethylphenyl)(4'-methoxyphenyl)iodonium tosylate (**6a**), (3-bromomethylphenyl)(2'-thienyl)iodonium tosylate (**6b**), (3-chloromethylphenyl)(4'-methoxyphenyl)iodonium tosylate (**7a**), (4-bromomethylphenyl)(4'-methoxyphenyl)iodonium tosylate (**8a**), (4-chloromethylphenyl)(4'-methoxyphenyl)iodonium tosylate (**9a**), (4-chloromethylphenyl)(2',4',6'-trimethoxyphenyl)iodonium tosylate (**9b**), [4-(methoxycarbonyl)phenyl](2'-thienyl)iodonium tosylate (**11a**), [3-(methoxycarbonyl)phenyl](4'-methoxyphenyl)iodonium tosylate (**12a**), [3-(methoxycarbonyl)phenyl](2'-thienyl)iodonium tosylate (**12b**), [3-(ethoxycarbonyl)phenyl](4'-methoxyphenyl)iodonium tosylate (**13**), and [4-(4"-bromophenylcarbonyl)-phenyl](4'-methoxyphenyl) tosylate (**15**).

2. General methods

^{1}H (400 MHz), ^{13}C (100 MHz), and ^{19}F (376 MHz) NMR spectra were recorded at room temperature on an Avance-400 spectrometer (Bruker; Billerica, MA, USA). ^{1}H and ^{13}C chemical shifts are reported in δ units downfield from the chemical shift for

tetramethylsilane, and ^{19}F NMR chemical shifts in δ units downfield from the chemical shift for $CFCl_3$. Abbreviations br, s, d, t, and m denote broad, singlet, doublet, triplet and multiplet, respectively. High resolution mass spectra (HRMS) were obtained at the Mass Spectrometry Laboratory, University of Illinois at Urbana-Champaign (Urbana, IL, USA) under electron ionization conditions using a double-focusing high-resolution mass spectrometer (Autospec; Micromass Inc., USA). Melting points were measured with a Mel-Temp melting point apparatus (Electrothermal; Fisher Scientific). No-carrier-added [^{18}F]fluoride ion was obtained through the $^{18}O(p,n)^{18}F$ nuclear reaction by irradiating [^{18}O]water (95 atom %) for 90–120 min with a proton beam (17 MeV; 20 μA) produced by a PETrace cyclotron (GE Medical Systems, Milwaukee, MI).

3. Syntheses of starting materials and reference fluoroarenes

1-(Diacetoxyiodo)naphthalene (**A**).

Peracetic acid (32 wt.% in acetic acid, 7 mL) was added dropwise to a mixture of 1-iodonaphthalene (2.54 g, 10 mmol) in acetic acid (5 mL) kept below 5 °C. The reaction mixture was allowed to reach rt and stirred overnight (*ca.* 14 h). 1-Iodonaphthalene consumption was verified with TLC (hexane, R_f = 0.5). Water (30 mL) was added to the resulting yellow solution. The aqueous layer was extracted with dichloromethane (30 mL × 2), dried over $MgSO_4$, and concentrated under reduced pressure. The residual yellow oil was triturated with Et_2O and the generated solid was filtered off and recrystallized from acetic acid to give **A** as a pale yellow solid (0.78 g, 21%); mp = 138−141 °C; ^1H-NMR ($CDCl_3$) δ 8.50 (2 H, dd, J = 0.8, 7.2 Hz, ArH), 8.14−8.09 (3 H, m, ArH), 7.91 (1 H, d, J = 8.4 Hz, ArH), 7.66−7.62 (2 H, m, ArH), 1.93 (6 H, s, Me); ^{13}C-NMR ($CDCl_3$) δ 175.5, 135.9, 132.4, 130.9, 128.5, 128.1, 127.9, 127.3, 126.5, 125.5, 19.3.

2-(Diacetoxyiodo)naphthalene (**B**).

The method for **A** was used with 2-iodonaphthalene (2.54 g, 10 mmol) to give **B** as a pale yellow solid (0.68 g, 18%); mp = 144−147 °C; ^1H-NMR ($CDCl_3$) δ 8.20 (1 H, s, ArH), 7.95−7.91 (1 H, m, ArH), 7.69 (1 H, d, J = 8.8 Hz, ArH), 7.65−7.62 (2 H, m, ArH), 7.49−7.41 (2 H, m, ArH), 1.89 (6 H, s, Me); ^{13}C-NMR ($CDCl_3$) δ 174.7, 134.2, 133.7, 131.9, 131.6, 128.4, 127.9, 126.4, 126.1, 125.2, 124.9, 17.9.

2-Fluoro-1,3,5-trimethoxybenzene (**C**).

Selectfluor® (1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane *bis*(tetrafluoroborate; 0.78 g, 2.2 mmol) was added portion-wise to a cooled (*ca*. − 40 °C) solution of 1,3,5-trimethoxybenzene (0.34 g, 2 mmol) in MeCN (20 mL). The partially frozen reaction mixture was gradually warmed to rt and then stirred for 2 h. The solvent was removed under reduced pressure and CH_2Cl_2 (20 mL) was added. The residual solid was filtered off. The filtrate was concentrated *in vacuo* and after column chromatography (silica gel; 20% EtOAc/hexane) gave **C** (R_f = 0.3) as a pale yellow solid (0.17 g, 46%); mp = 145−146 °C; ^{1}H NMR ($CDCl_3$) δ 6.15 (2 H, dt, J = 1.4, 6 Hz, ArH), 3.85 (6 H, s, 2 OMe), 3.76 (3 H, s, OMe); ^{13}C NMR ($CDCl_3$) δ 155.5 (d, $J_{C\text{-}F}$ = 3 Hz), 148.5 (d, $J_{C\text{-}F}$ = 9.1 Hz), 137.5 (d, $J_{C\text{-}F}$ = 234 Hz), 92.0, 52.3, 55.4; ^{19}F NMR ($CDCl_3$) δ −168.7 (lit.[3] δ −169.0).

Methyl 6-iodo-2-naphthoate (**D**)[4].

Hydrochloric acid (37%, 8 mL) was added dropwise from a pressure-equivalizing dropping funnel to a cold (*ca*. 0 °C) mixture of methyl 6-amino-2-naphthoate (1.03 g, 5.1 mmol) and $NaNO_2$ (0.55 g, 8 mmol) in H_2O (10 mL). The resultant yellow solution was stirred for 1 h at 0 °C. Then KI (1.5 g, 9 mmol) in H_2O (10 mL) was added dropwise with vigorous stirring, while keeping the mixture below 5 °C. After 30 min, the temperature was gradually increased to 35 °C while nitrogen evolution stopped. The mixture was filtered and the filtrate extracted with CH_2Cl_2 (30 mL × 2). The combined brown organic layers were further washed with saturated sodium thiosulfate solution (30 mL × 2) and then H_2O (30 mL) to remove iodine, dried over $MgSO_4$ and evaporated under reduced pressure. Column chromatography (silica gel; 50%/hexane) of the residue gave **D** (R_f = 0.4) as a pale yellow solid (0.74 g, 46%); mp = 162−163 °C (lit.[4] mp = 163−164 °C); ^{1}H NMR ($CDCl_3$) δ 8.55 (1 H, s, ArH), 8.29 (1 H, s, ArH), 8.07 (1 H, dd, J = 1.6, 8.4 Hz, ArH), 7.80−7.75 (2 H, m, ArH), 7.67 (1 H, d, J = 8.4 Hz, ArH), 3.98 (3 H, s, OMe); ^{13}C NMR ($CDCl_3$) δ 166.9, 136.8, 136.7, 135.4, 131.2, 130.9, 130.7, 128.0, 127.0, 126.2, 94.7, 52.4.

(6-Iodonaphthalen-2-yl)methanol (**E**).

Lithium aluminum hydride (LAH; 1.0 M, 4 mL in THF) was added dropwise from a syringe to a cooled (< 5 °C) and stirred solution of **D** in THF (15 mL). The reaction mixture was stirred for 1 h at −10 °C. H_2O (10 mL) was added carefully to quench the reaction, and then 2M Na_2CO_3 (*aq*, 10 mL). The solid was filtered off and further washed with EtOAc (20

mL). The aqueous layer was extracted with EtOAc (20 mL × 2). The combinec organic layers were dried over $MgSO_4$. Solvent was removed under reduced pressure. Column chromatography (silica gel; 20% EtOAc/hexane) of the crude residue gave **E** (R_f = 0.2) as a pale yellow solid (0.55 g, 82%); mp = 145−147 °C; ^{1}H NMR ($CDCl_3$) δ 8.22 (1 H, s, ArH), 7.85−7.81 (1 H, m, ArH), 7.71 (1 H, dd, J = 1.6, 8.4 Hz, ArH), 7.54 (1 H, d, J = 8.4 Hz, ArH), 7.48−7.46 (2 H, m, ArH), 4.84 (2 H, s, CH_2OH); ^{13}C NMR ($CDCl_3$) δ 139.1, 136.5, 134.8, 134.5, 132.1, 129.4, 127.2, 126.2, 125.9, 125.3, 91.5, 65.3.

2-(Chloromethyl)-6-iodonaphthalene (**F**).

Dichloromethane (20 mL) and compound **E** (0.54 g, 1.9 mmol) were added to a mixture of DMF (2 mL) and cyanuric chloride (0.39 g, 2.1 mmol). This mixture was stirred for 3 h at rt, and became a clear yellow solution. Consumption of **E** was monitored with TLC (20% EtOAc/hexane, R_f = 0.2). After 3 h, the reaction mixture was washed with H_2O (20 mL × 2). The organic layers were dried over $MgSO_4$. The solvent was removed in vacuo. Column chromatography (silica gel; 20% EtOAc/hexane) of the residue gave **F** (R_f = 0.2) as a white solid (0.53 g, 92%); mp = 141−142 °C; ^{1}H NMR ($CDCl_3$) δ 8.23 (1 H, s, ArH), 7.78 (1 H, s, ArH), 7.75−7.72 (2 H, m, ArH), 7.56 (1 H, d, J = 8.8 Hz, ArH), 7.71 (1 H, dd, J = 1.6, 6.8 Hz, ArH), 4.73 (2 H, s, CH_2Cl); ^{13}C NMR ($CDCl_3$) − 135.7, 134.7, 134.3, 133.8, 131.0, 128.7, 126.8, 126.7, 126.3, 91.4, 45.7.

(6-Fluoronaphthalen-2-yl)methanol (**G**).

The method for **E** was used with 6-fluoro-2-naphthoic acid (0.57 g, 3 mmol) and LAH (1.0M in THF, 5 mL). Column chromatography (silica gel; 20% EtOAc/hexane) gave **G** (R_f = 0.14) as a white solid (0.24 g, 46 %); mp = 102−103 °C; ^{1}H NMR ($CDCl_3$) δ 7.83−7.77 (3 H, m, ArH), 7.50 (1 H, d, J = 8 Hz, ArH), 7.44 (1 H, dd, J = 2.4, 7.6 Hz, ArH), 7.26 (1 H, dt, J = 2.4, 8.8 Hz, ArH), 4.84 (2 H, s, CH_2OH); ^{13}C NMR ($CDCl_3$) δ 160.7 (d, $J_{C\text{-}F}$ = 244 Hz), 137.6 (d, $J_{C\text{-}F}$ = 2 Hz), 133.6 (d, $J_{C\text{-}F}$ = 9 Hz), 130.3, 130.2 (d, $J_{C\text{-}F}$ = 9 Hz), 127.7 (d, $J_{C\text{-}F}$ = 5 Hz), 126.2, 125.4, 116.5 (d, $J_{C\text{-}F}$ = 25 Hz), 110.8 (d, $J_{C\text{-}F}$ = 20 Hz), 65.3; ^{19}F NMR ($CDCl_3$) δ −114.8.

2-(Chloromethyl)-6-fluoronaphthalene (**H**)

The method for **F** was used with **G** (0.22 g, 1.2 mmol) and cyanuric chloride (0.37 g, 2 mmol). Column chromatography (silica gel; 10% EtOAc/hexane) gave **H** (R_f = 0.56) as a

white solid (0.21 g, 88%); mp = 58−60 °C; ^{1}H NMR ($CDCl_3$) δ 7.83−7.77 (3 H, m, ArH), 7.52 (1 H, d, J = 8.8 Hz, ArH), 7.44 (1 H, dd, J = 2, 7.6 Hz, ArH), 7.23 (1 H, dt, J = 2.4, 8.8 Hz, ArH), 4.74 (2 H, s, CH_2Cl); ^{13}C NMR ($CDCl_3$) δ 172.5, 161.7 (d, $J_{C\text{-}F}$ = 246 Hz), 134.2 (d, $J_{C\text{-}F}$ = 3 Hz), 133.9 (d, $J_{C\text{-}F}$ = 9 Hz), 130.4 (d, $J_{C\text{-}F}$ = 8 Hz), 130.1, 116.8 (d, $J_{C\text{-}F}$ = 25 Hz), 110.4 (d, $J_{C\text{-}F}$ = 21 Hz), 46.4; ^{19}F NMR ($CDCl_3$) δ −113.7.

4. Syntheses of functionalized diaryliodonium salts

Method A

The following synthesis of **3b** represents Method A.

(3-Formyl-4-methoxyphenyl)(2'-thienyl)iodonium tosylate (**3b**).

p-TsOH·H_2O (0.21, 1.1 mmol) was added to a suspension of 2-(diacetoxyiodo)thiophene (0.33 g, 1.0 mmol) in MeCN (5 mL). A bright yellow solution developed instantly. A solution of 4-methoxy-3-(*tri*-*n*-butylstannyl)benzaldehyde (0.43 g, 1.0 mmol) in $CHCl_3$ (20 mL) was added and the reaction mixture was heated to 50 °C for 3 h. Consumption of the generated 2-[hydroxy(tosyloxy)iodo]thiophene was verified with KI starch paper, and the disappearance of 4-methoxy-3-(*tri*-*n*-butylstannyl)benzaldehyde with TLC (silica gel; 20% EtOAc/hexane, R_f = 0.5). The reaction mixture was cooled to rt and solvent was removed under reduced pressure. The residual yellow oil was triturated with Et_2O. The solid was filtered off, washed with Et_2O (30 mL × 2), and dried *in vacuo* for 4 h to give **3b** as a white solid (0.25 g, 48%); mp 178−179 °C; ^{1}H-NMR ($CDCl_3$) δ 9.73 (1 H, s, C*H*O-), 8.44 (1 H, d, J = 2 Hz, ArH), 7.97 (1 H, dd, J = 2, 8.4 Hz, ArH), 7.76 (1 H, dd, J = 1.6, 4 Hz, ArH), 7.51 (1 H, dd, J = 1.2, 5.2 Hz, ArH), 7.40 (2 H, dd, J = 1.6, 6.4 Hz, ArH), 7.06−6.96 (4 H, m, ArH), 4.02 (3 H, s, OMe), 2.31 (3 H, s, Me); ^{13}C-NMR ($CDCl_3$) δ 188.5, 160.8, 142.2, 140.5, 139.7, 139.0, 135.5, 135.0, 131.8, 129.2, 128.5, 125.9, 112.5, 110.3, 98.4, 57.7, 21.6; HRMS $[M-OTs]^+$ Calc'd. for $C_{12}H_{10}O_2SI$: 344.9446, Found: 344.9449.

(2-Bromomethylphenyl)(2',4',6'-trimethoxyphenyl)iodonium tosylate (**4b**).

Method A was used with 2-bromomethyl(diacetoxyiodo)benzene (0.42 g, 1.0 mmol) and 1,3,5-trimethoxybenzene (0.19 g, 1.1 mmol) and gave **4b** as a white solid (0.63 g, 99%); mp 144−147 °C; ^{1}H-NMR (MeOD-d_4) δ 8.18 (1 H, d, J = 8 Hz, ArH), 7.74−7.61 (4 H, m, ArH),

7.37 (1 H, t, *J* = 7.6 Hz, ArH), 7.20 (2 H, d, *J* = 7.6 Hz, ArH), 6.40 (2 H, s, ArH), 4.84 (2 H, s, -C*H*$_2$Br), 3.99 (6 H, s, 2 MeO), 3.88 (3 H, s, MeO), 2.35 (3 H, s, Me); ^{13}C-NMR (MeOD-d_4) δ 169.0, 161.6, 143.8, 141.9, 141.7, 139.8, 134.5, 133.5, 132.6, 129.9, 127.1, 119.1, 93.2, 85.5, 57.9, 56.9, 35.4, 21.5; HRMS [M−OTs]$^+$ Calc'd. for $C_{16}H_{17}O_3BrI$: 462.9406, Found: 462.9412.

(3-Chloromethylphenyl)(2'-thienyl)iodonium tosylate (**7b**).

Method A was used with 3-chloromethyl(diacetoxyiodo)benzene (0.30 g, 0.81 mmol) and thiophene (0.2 mL) and gave **7b** as a white solid (0.34 g, 83%); mp 141−143 ^{o}C; ^{1}H-NMR ($CDCl_3$) δ 8.01 (1 H, t, *J* = 1.2 Hz, ArH), 7.87 (1 H, dd, *J* = 0.8, 8.4 Hz, ArH), 7.81 (1 H, dd, *J* = 0.8, 3.6 Hz, ArH), 7.57 (1 H, dd, *J* = 1.2, 5.2 Hz, ArH), 7.51–7.45 (3 H, m, ArH), 7.31 (1 H, t, *J* = 8 Hz, ArH), 7.06−7.01 (3 H, m, ArH), 4.45 (2 H, s, -C*H*$_2$Cl), 2.32 (3 H, s, Me); ^{13}C-NMR ($CDCl_3$) δ 142.1, 141.1, 140.7, 139.7, 136.1, 133.9, 133.7, 131.6, 131.5, 131.0, 129.6, 128.6, 125.9, 118.8, 99.2, 44.5, 21.3; HRMS [M−OTs]$^+$ Calc'd. for $C_{11}H_9SClI$: 334.9158, Found: 334.9158.

(3-Chloromethylphenyl)(5'-methyl-2'-thienyl)iodonium tosylate (**7d**).

Method A was used with 3-chloromethyl(diacetoxyiodo)benzene (0.55 g, 1.5 mmol) and 2-methylthiophene (0.29 g, 3 mmol) and gave **7d** as a white solid (0.71 g, 94%); mp 145−146 ^{o}C; ^{1}H-NMR ($CDCl_3$) δ 7.99 (1 H, t, *J* = 1.6 Hz, ArH), 7.85 (1 H, dd, *J* = 0.8, 6.4 Hz, ArH), 7.60 (1 H, d, *J* = 3.6 Hz, ArH), 7.55 (2 H, dd, *J* = 1.6, 6.4 Hz, ArH), 7.50 (1 H, d, *J* = 8 Hz, ArH), 7.33 (1 H, t, *J* = 8 Hz, ArH), 7.08 (2 H, d, *J* = 8 Hz, ArH), 6.72 (1 H, dd, *J* = 0.8, 3.6 Hz, ArH), 4.47 (2 H, s, -C*H*$_2$Cl), 2.57 (3 H, s, Me), 2.33 (3 H, s, Me); ^{13}C-NMR ($CDCl_3$) δ 152.5, 142.2, 141.5, 141.2, 139.7, 133.4, 133.3, 131.7, 131.5, 128.6, 128.2, 126.0, 118.9, 94.6, 44.6, 21.3, 15.5; HRMS [M−OTs]$^+$ Calc'd. for $C_{12}H_{11}SClI$: 348.9315, Found: 348.9313.

(4-Bromomethylphenyl)(2',4',6'-trimethoxyphenyl)iodonium tosylate (**8b**).

Method A was used with 4-bromomethyl(diacetoxyiodo)benzene (0.092 g, 0.22 mmol) and 1,3,5-trimethoxybenzene (0.037 g, 0.23 mmol) and gave **8b** as a white solid (0.076 g, 54%); mp 161−163 ^{o}C; ^{1}H-NMR (MeOD-d_4) δ 7.91 (2 H, d, *J* = 8 Hz, ArH), 7.69 (2 H, d, *J* = 8.4 Hz, ArH), 7.50 (2 H, d, *J* = 8.4 Hz, ArH), 7.22 (2 H, d, *J* = 8 Hz, ArH), 6.42 (2 H, s, ArH), 4.56 (2 H, s, -C*H*$_2$Br), 3.97 (6 H, s, 2 MeO), 3.89 (3 H, s, MeO), 2.36 (3 H, s, Me); ^{13}C-NMR (MeOD-d_4) δ 169.0, 161.6, 144.7, 143.8, 143.8, 141.8, 136.3, 133.4, 129.9, 127.1, 115.2, 93.1,

86.4, 57.9, 56.8, 32.1, 21.5; HRMS $[M-OTs]^+$ Calc'd. for $C_{16}H_{17}O_3BrI$: 462.9406, Found: 462.9407.

1-Naphthyl(4'-methoxyphenyl)iodonium tosylate (**31**).

Method A was used with 1-(diacetoxyiodo)naphthalene (0.41 g, 1.1 mmol) and anisole (0.5 mL) and gave **31** as a beige solid (0.36 g, 61%); mp 178−180 °C; ^{1}H-NMR (MeOD-d_4) δ 8.63 (1 H, d, J = 7.6 Hz, ArH), 8.25 (2 H, d, J = 8.4 Hz, ArH), 8.09 (2 H, d, J = 9.2 Hz, ArH), 8.01 (1 H, d, J = 8 Hz, ArH), 7.82 (1 H, t, J = 8 Hz, ArH), 7.72 (3 H, t, J = 6 Hz, ArH), 7.59 (1 H, t, J = 8 Hz, ArH), 7.21 (2 H, d, J = 8 Hz, ArH), 6.97 (2 H, d, J = 8 Hz, ArH), 3.78 (3 H, s, MeO), 2.36 (3 H, s, Me); ^{13}C-NMR (MeOD-d_4) δ 164.4, 141.7, 138.7, 138.1, 136.3, 135.2, 132.6, 131.1, 130.8, 129.8, 129.5, 129.3, 128.5, 126.9, 119.4, 118.7, 104.3, 56.3, 21.3; HRMS $[M-OTs]^+$ Calc'd. for $C_{17}H_{14}OI$: 361.0089, Found: 361.0090.

2-Naphthyl(4'-methoxyphenyl)iodonium tosylate (**32**).

Method A was used with 2-(diacetoxyiodo)naphthalene (0.67 g, 1.8 mmol) and anisole (0.8 mL) and gave **32** as a pale yellow solid (0.69 g, 72%); mp 173−175 °C; ^{1}H-NMR (MeOD-d_4) δ 8.78 (1 H, s, ArH), 8.12 (2 H, d, J = 8.8 Hz, ArH), 8.05 (2 H, dd, J = 1.6, 7.2 Hz, ArH), 7.99−7.97 (3 H, m, ArH), 7.70−7.68 (4 H, m, ArH), 7.20 (2 H, d, J = 8 Hz, ArH), 7.05 (2 H, d, J = 9.2 Hz, ArH), 3.83 (3 H, s, MeO), 2.35 (3 H, s, CH_3); ^{13}C-NMR (MeOD-d_4) δ 164.5, 143.6, 141.6, 138.6, 137.2, 135.9, 135.5, 132.9, 130.6, 130.3, 129.8, 129.4, 129.2, 129.1, 126.9, 118.9, 113.3, 104.6, 56.3, 21.3; HRMS $[M-OTs]^+$ Calc'd. for $C_{17}H_{14}OI$: 361.0089, Found: 361.0094.

Method B

The following synthesis of **14** represents Method B.

[4-(Phenylcarbonyl)phenyl](4'-methoxyphenyl)iodonium tosylate (**14**):

m-CPBA (0.49 g, 2.2 mmol, 77% max. content) was added in portions to a solution of 4-iodobenzophenone (0.62 g, 2 mmol) in $CHCl_3$ (20 mL). The mixture was stirred for 15 min while it became a pale yellow solution. *p*-TsOH·H_2O (0.29 g, 1.5 mmol) was added at once, followed by anisole (1.08 g, 10 mmol). The resultant mixture was heated to 40 °C and held at this temperature for about 3 h. Consumption of the generated [hydroxy(tosyl)iodo]arene (HTIA) was verified with KI starch paper. Solvent was then removed under reduced

pressure. The residual yellow oil was triturated with Et_2O. The generated solid was washed with Et_2O (30 mL × 2) and recrystallized from MeOH-Et_2O to give **14** as a white solid (0.73 g, 62%). mp = 176−178 °C; ^{1}H-NMR (MeOD-d_4) δ 8.25 (2 H, d, J = 8.8 Hz, ArH), 8.14 (2 H, d, J = 9.2 Hz, ArH), 7.83 (2 H, d, J = 8.4 Hz, ArH), 7.76 (2 H, d, J = 7.2 Hz, ArH), 7.71-7.66 (3 H, m, ArH), 7.54 (2 H, t, J = 7.6 Hz, ArH), 7.22 (2 H, d, J = 7.6 Hz, ArH), 7.10 (2 H, d, J = 9.2 Hz, ArH), 3.87 (3 H, s, MeO), 2.36 (3 H, s, Me); ^{13}C-NMR (MeOD-d_4) δ 196.6, 164.9, 142.4, 141.8, 139.0, 137.8, 136.1, 134.7, 133.7, 131.3, 129.9, 127.1, 120.2, 119.2, 104.6, 56.6, 21.4; HRMS [M−OTs]$^+$ Calc'd. for $C_{20}H_{16}O_2I$: 415.0195, Found: 415.0192.

(6-Chloromethyl-2-naphthyl)(4'-methoxyphenyl)iodonium tosylate (**10a**).

Method B was used with 2-(chloromethyl)-6-iodonaphthalene (0.55 g, 1.8 mmol) and anisole (0.8 mL) and gave **10a** as a white solid (0.77 g, 72%); mp 193−195 °C; ^{1}H-NMR (MeOD-d_4) δ 8.77 (1 H, d, J = 1.2 Hz, ArH), 8.13−8.06 (3 H, m, ArH), 7.98−7.97 (3 H, m, ArH), 7.73−7.71 (3 H, m, ArH), 7.20 (2 H, d, J = 8 Hz, ArH), 7.02 (2 H, d, J = 8 Hz, ArH), 4.84 (2 H, s, -CH_2Cl), 3.83 (3 H, s, MeO), 2.35 (3 H, s, Me); ^{13}C-NMR (MeOD-d_4) δ 164.7, 143.8, 141.8, 140.6, 138.7, 137.1, 135.6, 133.2, 131.3, 130.2, 129.9, 129.8, 128.8, 127.1, 119.1, 113.8, 104.7, 56.5, 46.6, 21.4; HRMS [M−OTs]$^+$ Calc'd. for $C_{18}H_{15}OClI$: 408.9856, Found: 408.9868.

Anion metatheses

The preparation of **3c** is a representative example of metathesis for the synthesis of diaryliodonium chlorides.

(3-Formyl-6-methoxyphenyl)(2'-thienyl)iodonium chloride (**3c**).

3-Formyl-6-methoxyphenyl(2'-thienyl)iodonium tosylate (**3b**, 0.13 g, 0.25 mmol) was dissolved in MeCN/H_2O (*ca.*10% H_2O, v/v, 2 mL), heated to 50 °C and stirred for 5 min, to give a clear solution. Saturated NH_4Cl (*aq*) solution (3 mL) was added dropwise to the stirred solution and slowly cooled to rt. The white precipitate was filtered off, and washed with ice-cold water (5 mL) followed by Et_2O (20 mL). This product was further dried *in vacuo* for 4 h to give **3c** as a white solid (0.075 g, 78%); mp 178−180 °C; ^{1}H-NMR (DMSO-d_6) δ 9.90 (1 H, s, C*H*O), 8.77 (1 H, s, ArH), 8.13 (1 H, d, J = 8.4 Hz, ArH), 7.82 (2 H, s, ArH), 7.45 (1 H, d, J = 8.4 Hz, ArH), 7.07 (1 H, s, ArH), 4.08 (3 H, s, MeO); ^{13}C-NMR

(DMSO-d_6) δ 190.1, 159.9, 138.6, 137.4, 135.9, 135.3, 131.3, 128.9, 114.1, 112.9, 106.5, 57.6; HRMS $[M-Cl]^+$ Calc'd. for $C_{12}H_{10}O_2SI$: 344.9446, Found: 344.9448.

(4-Formylphenyl)(4'-methoxyphenyl)iodonium chloride (**1b**).

The method for **3c** was used with **1a** (0.23 g, 0.45 mmol) and gave **1b** as a white solid (0.10 g, 59%); mp 156−159 ^oC; ^1H-NMR (DMF-d_7) δ 10.10 (1 H, s, C*H*O), 8.43 (2 H, d, J = 8.4 Hz, ArH), 8.19 (2 H, d, J = 8.8 Hz, ArH), 7.45 (2H, dd, J = 1.6, 8.4 Hz, ArH), 7.06 (2 H, d, J = 9.2 Hz, ArH), 3.86 (3 H, s, MeO); ^{13}C-NMR (DMF-d_7) δ 192.6, 162.6, 137.9, 137.3, 135.5, 131.6, 129.3, 117.3, 111.8, 55.7; HRMS $[M-Cl]^+$ Calc'd. for $C_{14}H_{12}O_2I$: 338.9882, Found: 338.9881.

(3-Formylphenyl)(4'-methoxyphenyl)iodonium chloride (**2b**).

The method for **3c** was used with **2a** (0.074 g, 0.14 mmol) and gave **2b** as a white solid (0.041 g, 78%); mp 186−188 ^oC; ^1H-NMR (DMF-d_7: low solubility) δ 10.08 (1 H, s, C*H*O), 8.71 (1 H, t, J = 1.6 Hz, ArH), 8.50 (1 H, dt, J = 1.2, 5.2 Hz, ArH), 8.18 (2 H, dd, J = 2, 8.8 Hz, ArH), 8.11 (1 H, dt, J = 1.2, 5.2 Hz, ArH), 7.71 (1 H, t, J = 7.6 Hz, ArH), 7.04 (2 H, dd, J = 2, 8.8 Hz, ArH), 3.85 (3 H, s, MeO); ^{13}C-NMR (DMF-d_7: low solubility) δ 192.2, 162.6, 140.2, 138.8, 137.3, 135.0, 132.0, 131.7, 124.4, 117.2, 112.3, 55.6; HRMS $[M-Cl]^+$ Calc'd. for $C_{14}H_{12}O_2I$: 338.9882, Found: 338.9886.

(3-Formylphenyl)(2'-thienyl)iodonium chloride (**2d**).

The method for **3c** was used with (**2c**, 0.15 g, 0.31 mmol) and gave **2d** as a white solid (0.079 g, 72%); mp 178−180 ^oC; ^1H-NMR (DMF-d_7) δ 10.09 (1 H, s, C*H*O), 8.78 (1 H, t, J = 1.6 Hz, ArH), 8.53 (1 H, dt, J = 1.2, 4.8 Hz, ArH), 8.13 (1 H, dt, J = 1.2, 5.2 Hz, ArH), 7.98 (1 H, dd, J = 1.2, 2.4 Hz, ArH), 7.89 (1 H, dd, J = 1.2, 4 Hz, ArH), 7.73 (1 H, t, J = 8 Hz, ArH), 7.14 (1 H, dd, J = 3.6, 5.2 Hz, ArH); ^{13}C-NMR (DMF-d_7) δ 191.7, 139.9, 138.9, 138.7, 135.3, 134.8, 132.1, 132.0, 129.4, 125.9, 112.6; HRMS $[M-Cl]^+$ Calc'd. for $C_{11}H_8OSI$: 314.9341, Found: 314.9344.

(3-Bromomethylphenyl)(2'-thienyl)iodonium chloride (**6c**).

The method for **3c** was used with **6b** (0.40 g, 0.73 mmol) and gave **6c** as a white solid (0.25 g, 83%); mp 175−177 ^oC; ^1H-NMR (MeOD-d_4) δ 8.28 (1 H, t, J = 2 Hz, ArH), 8.09 (1 H, dq, J = 1.2, 5.2 Hz, ArH), 8.01 (1 H, dd, J = 1.2, 2.8 Hz, ArH), 7.89 (1 H, dd, J = 1.2, 5.6 Hz,

ArH), 7.73 (1 H, dd, J = 0.8, 7.6 Hz, ArH), 7.50 (1 H, t, J = 8 Hz, ArH), 7.20 (1 H, dd, J = 1.6, 5.6 Hz, ArH), 4.59 (2 H, s, -CH_2Br); ^{13}C-NMR (MeOD-d_4) δ 144.3, 142.2, 138.7, 136.2, 135.4, 134.4, 133.4, 131.0, 119.4, 100.1, 31.8; HRMS $[M-Cl]^+$ Calc'd. for $C_{11}H_9SBrI$: 378.8653, Found: 378.8656.

(3-Chloromethylphenyl)(2'-thienyl)iodonium chloride (**7c**).

The method for **3c** was used with **7b** (0.20 g, 0.4 mmol) and gave **7c** as a white solid (0.34 g, 83%); mp 187−188 ^{o}C; ^{1}H-NMR (DMSO-d_6) δ 8.29 (1 H, t, J = 1.6 Hz, ArH), 8.16 (1 H, dq, J = 0.8, 5.2 Hz, ArH), 7.88 (2 H, dq, J = 1.2, 9.6 Hz, ArH), 7.65 (1 H, d, J = 8 Hz, ArH), 7.48 (1 H, t, J = 7.6 Hz, ArH), 7.31 (1 H, dd, J = 3.6, 5.2 Hz, ArH), 4.78 (2 H, s, -CH_2Cl); ^{13}C-NMR (DMSO-d_6) δ 140.7, 138.7, 135.7, 134.3, 134.1, 131.6, 131.4, 129.2, 122.5, 108.0, 44.8; HRMS $[M-Cl]^+$ Calc'd. for $C_{11}H_9SClI$: 334.9158, Found: 334.9154.

(3-Chloromethylphenyl)(5'-methyl-2'-thienyl)iodonium chloride (**7e**).

The method for **3c** was used with **7d** (0.3 g, 0.59 mmol) and gave **7e** as a white solid (0.20 g, 88%); mp 181−182 ^{o}C; ^{1}H-NMR (MeOD-d_4) δ 8.24 (1 H, t, J = 1.6 Hz, ArH), 8.09 (1 H, dd, J = 0.8, 8 Hz, ArH), 7.81 (1 H, d, J = 3.6 Hz, ArH), 7.72 (1 H, d, J = 7.6 Hz, ArH), 7.52 (1 H, t, J = 8 Hz, ArH), 6.88 (1 H, dd, J = 1.2, 4 Hz, ArH), 4.59 (2 H, s, -CH_2Cl), 2.61 (3 H, s, Me); ^{13}C-NMR (MeOD-d_4) δ 154.5, 143.8, 142.8, 135.5, 135.3, 133.8, 133.3, 129.6, 119.6, 96.2, 45.4, 15.4; HRMS $[M-Cl]^+$ Calc'd. for $C_{12}H_{11}SClI$: 348.9315, Found: 348.9316.

(6-Chloromethyl-2-naphthyl)(4'-methoxyphenyl)iodonium chloride (**10b**).

The method for **3c** was used with **10a (**0.16 g, 0.31 mmol) and gave **10b** as a white solid (0.12 g, 78%); mp 180−183 ^{o}C; ^{1}H-NMR (DMF-d_7) δ 8.92 (1 H, s, ArH), 8.26−8.18 (3 H, m, ArH), 8.10 (2 H, d, J = 12.4 Hz, ArH), 7.76 (1 H, d, J = 8.8 Hz, ArH), 7.04 (2 H, d, J = 8.8 Hz, ArH), 5.02 (2 H, s, -CH_2Cl), 3.84 (3 H, s, MeO); ^{13}C-NMR (DMF-d_7) δ 162.3, 138.2, 136.8, 135.0, 133.9, 133.4, 130.9, 128.9, 128.2, 127.8, 120.1, 116.9, 111.1, 55.4, 46.1; HRMS $[M-Cl]^+$ Calc'd. for $C_{18}H_{15}OClI$: 408.9856, Found: 408.9845.

4. Radiochemistry

The configuration and operation of the microfluidic apparatus (NanoTek apparatus; Advion; Ithica, NY) used in this study has been described ion our previous publications.[2,3] Cyclotron-produced no-carrier-added (NCA) [^{18}F]fluoride ion (3.7−7.4 GBq) in [^{18}O]water

(250–400 μL) was first adsorbed onto a QMA anionic resin cartridge within the CE module of a NanoTek apparatus, and then released with a solution of K_2CO_3 (0.8 mg; 5 μmol) plus K 2.2.2 (4.5 mg; 11 μmol) in MeCN-H_2O (9: 1 v/v; 450 μL) into a 2-mL V-vial. The solution was dried by two cycles of azeotropic evaporation with additional MeCN (0.6 mL) under nitrogen flow at 95 ºC.

Dried $^{18}F^-$-K 2.2.2-K^+ complex (3.7−5.6 GBq) was dissolved in either MeCN or DMF. A solution of diaryliodonium salt (10 mM) was prepared in matching solvent. Each solution (280 μL) was loaded into a separate storage loop of the apparatus. For radiofluorination, each solution (10–20 μL) was infused simultaneously into the micro-reactor (4-m coiled glass silica tube; internal diameter, 100 μm; internal volume, 31.4 μL) of the apparatus at a set flow rate in the range 4–10 μL/min and at a fixed temperature. The micro-reactor output was directly quenched by dilution with MeCN-H_2O (1: 1 v/v; 3 mL) at rt. Temperature and flow rate were varied in 6−12 runs with each substrate to search for conditions giving the highest yield of [^{18}F]fluorarene. Decay-corrected radiochemical yields (RCYs) of [^{18}F]fluoroarenes were determined by reversed phase radio-HPLC on a Luna C18 column (250 × 4.6 mm i.d., 10 μm; Phenomenex, Torrance, CA). Three methods were applied for reaction mixture analysis, as follows:

Method A: For compounds **1a−3c.** Gradient elution at 1.50 mL/min with MeCN-H_2O (50: 50, v/v) with MeCN increased linearly from 50 to 80% over 7 min.

Method B: For compounds **4a−9b**, **14**, and **15**. Gradient elution at 1.75 mL/min with MeCN-H_2O (60: 40, v/v), with MeCN increased linearly from 60 to 80% over 7 min.

Method C: For compounds **10a**, and **10b**. Gradient elution at 1.75 mL/min with MeCN-H_2O (70: 30, v/v) with MeCN increased linearly from 70 to 90% over 7 min.

4.1. Radiofluorination of 31 and 32.

The radiofluorinations of **31** and **32** by the above procedure gave [^{18}F]1-fluoronaphthalene and [^{18}F]2-fluoronaphthalene in 42 and 44% RCYs, respectively, as determined by HPLC analysis. Corresponding RCYs after correction for adsorption were 34 and 39%, respectively.

References

1 J.-H. Chun and V. W. Pike, *J. Org. Chem*., 2012, **77**, 1931−1938.

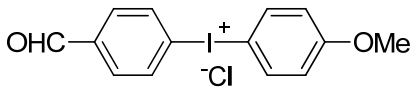
2 J.-H. Chun, S. Telu, S. Lu and V. W. Pike, *Org. Biomol. Chem.*, 2013, **11**, 5094-5099.

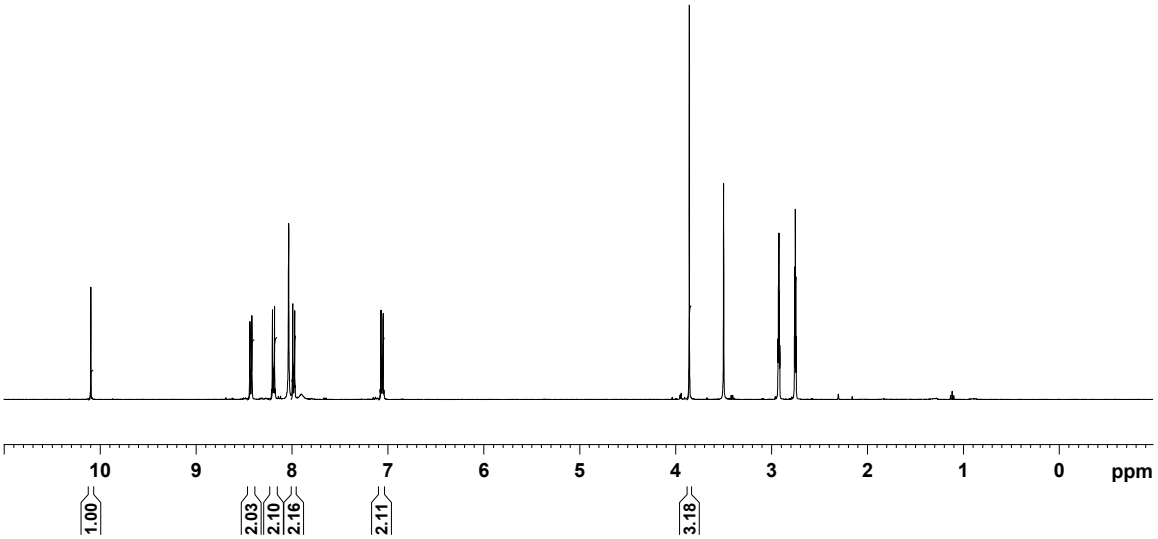
3 J. Pavlinac, M. Zupan and S. Stavber, *Molecules*, 2009, **14**, 2394−2409.

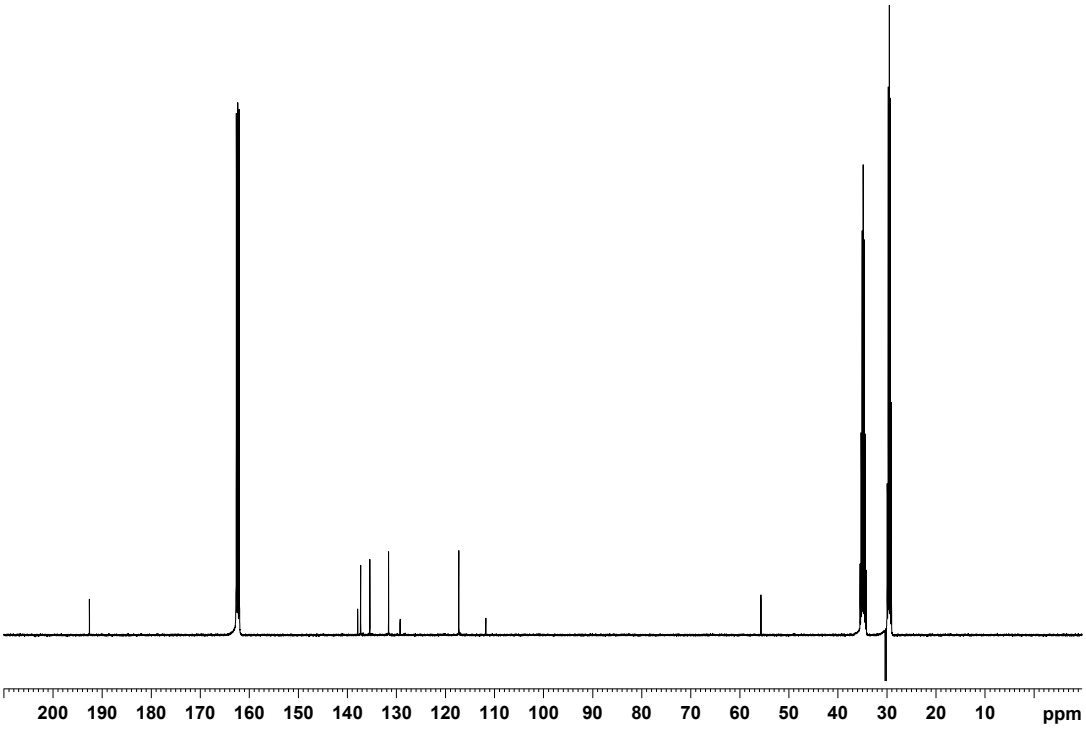
4 W. Adcock and P. R. Wells, *Aust. J. Chem.*, 1965, **18**, 1351−1364.

Appendix 1. ^{1}H and ^{13}C NMR spectra of functionalized diaryliodonium salts.

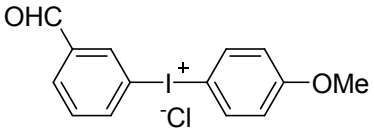
Compound **1b**

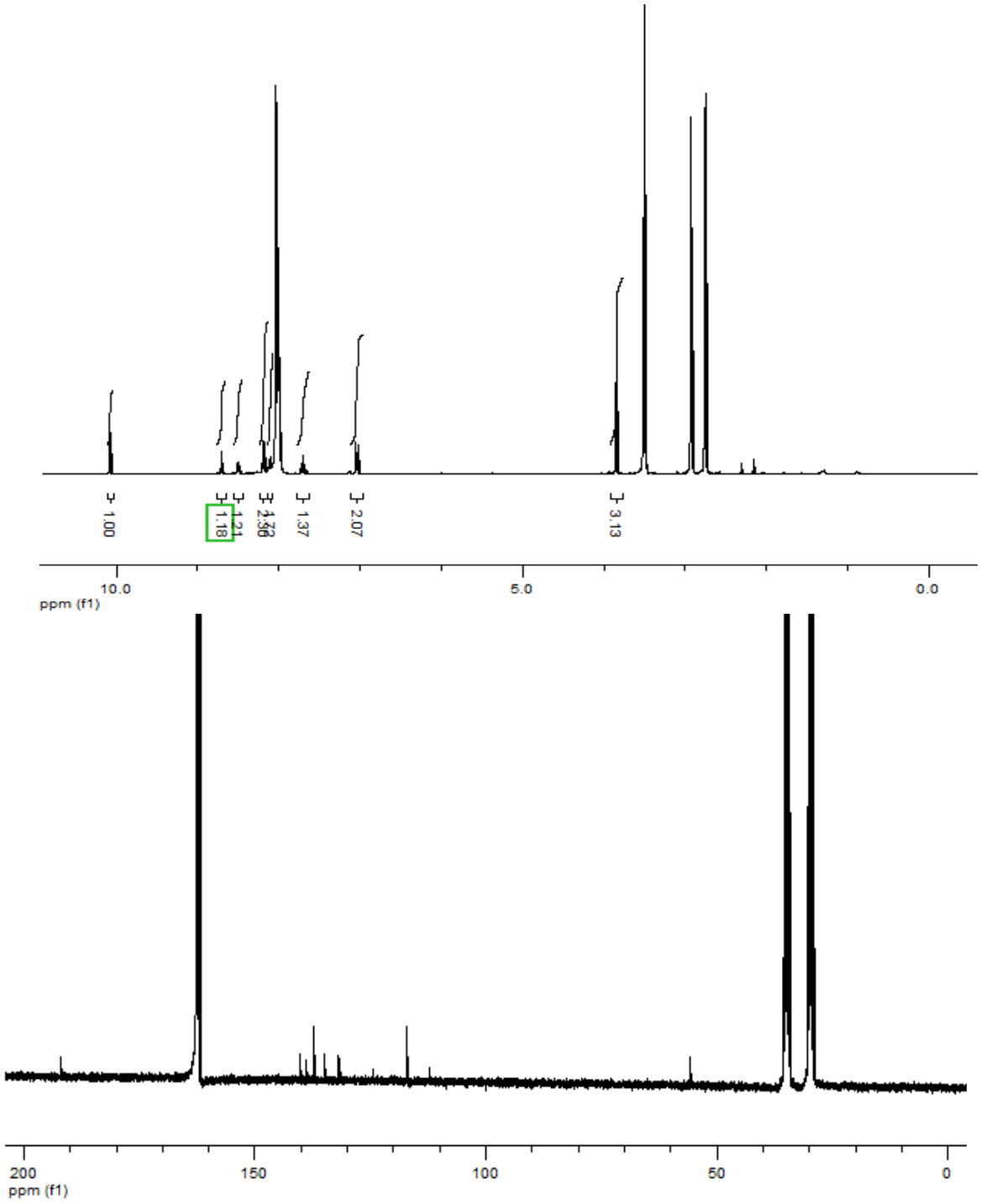




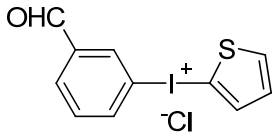


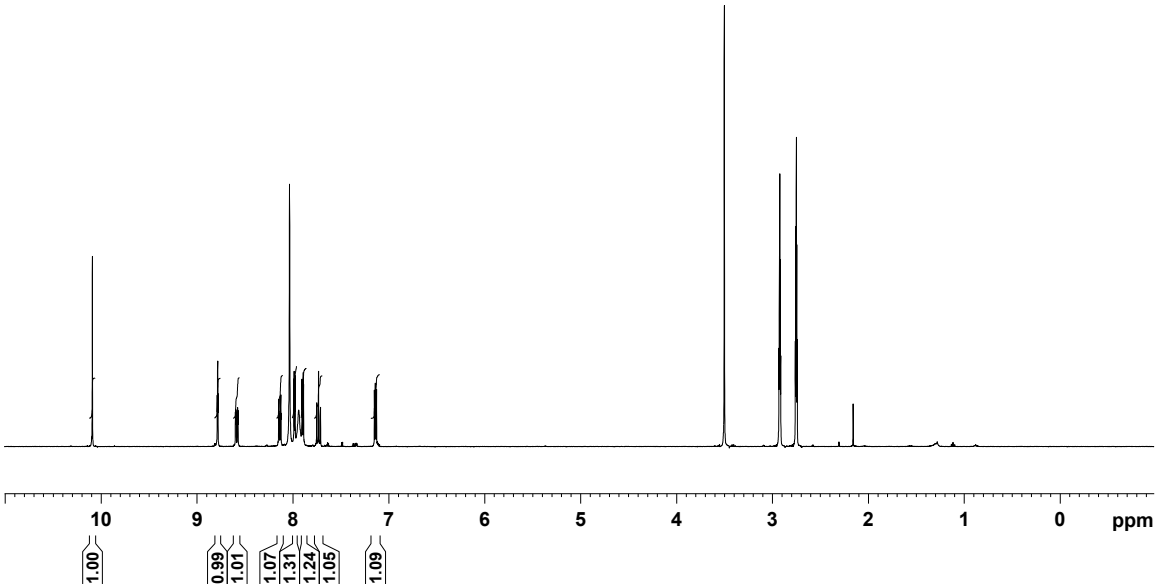
Compound **2b**

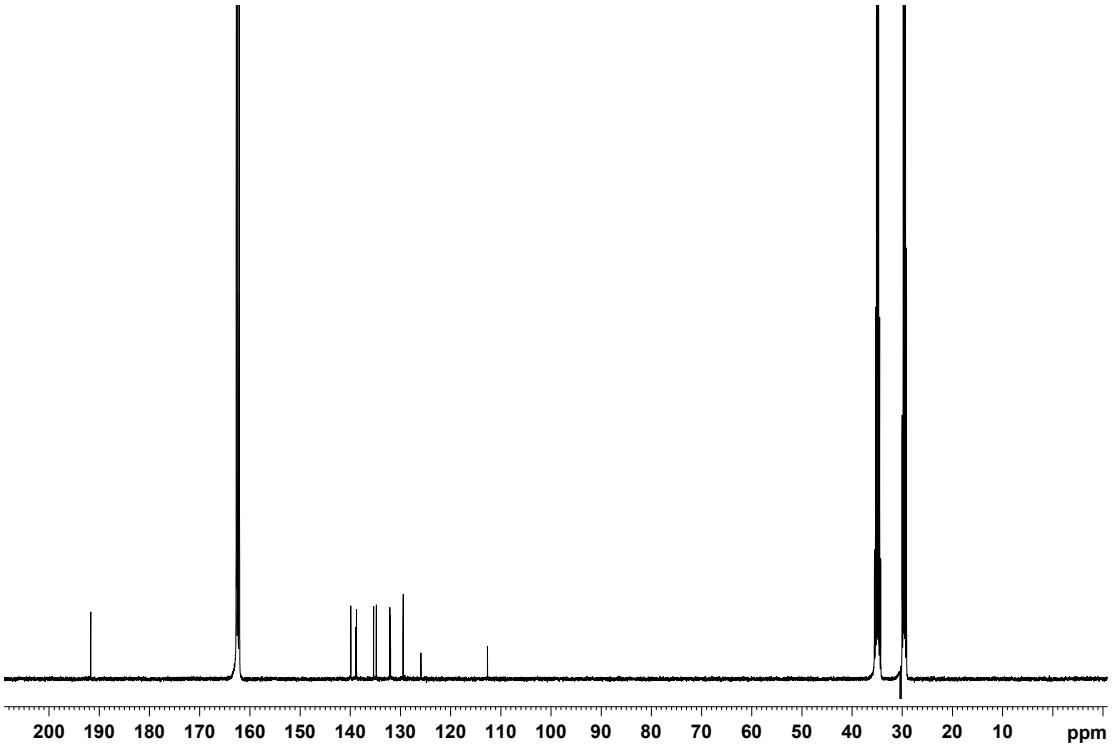




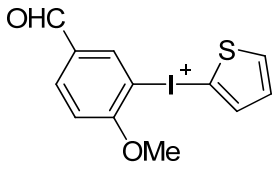
Compound **2d**

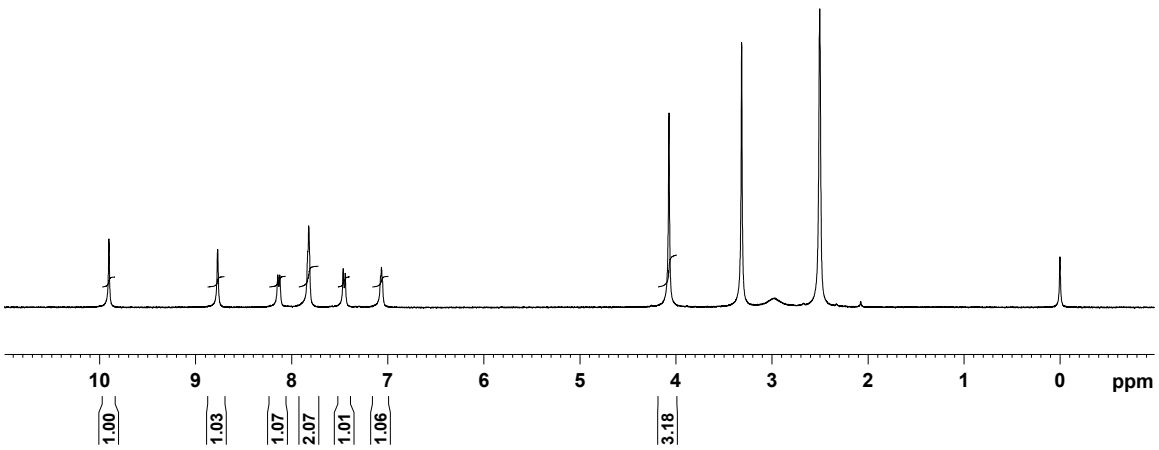


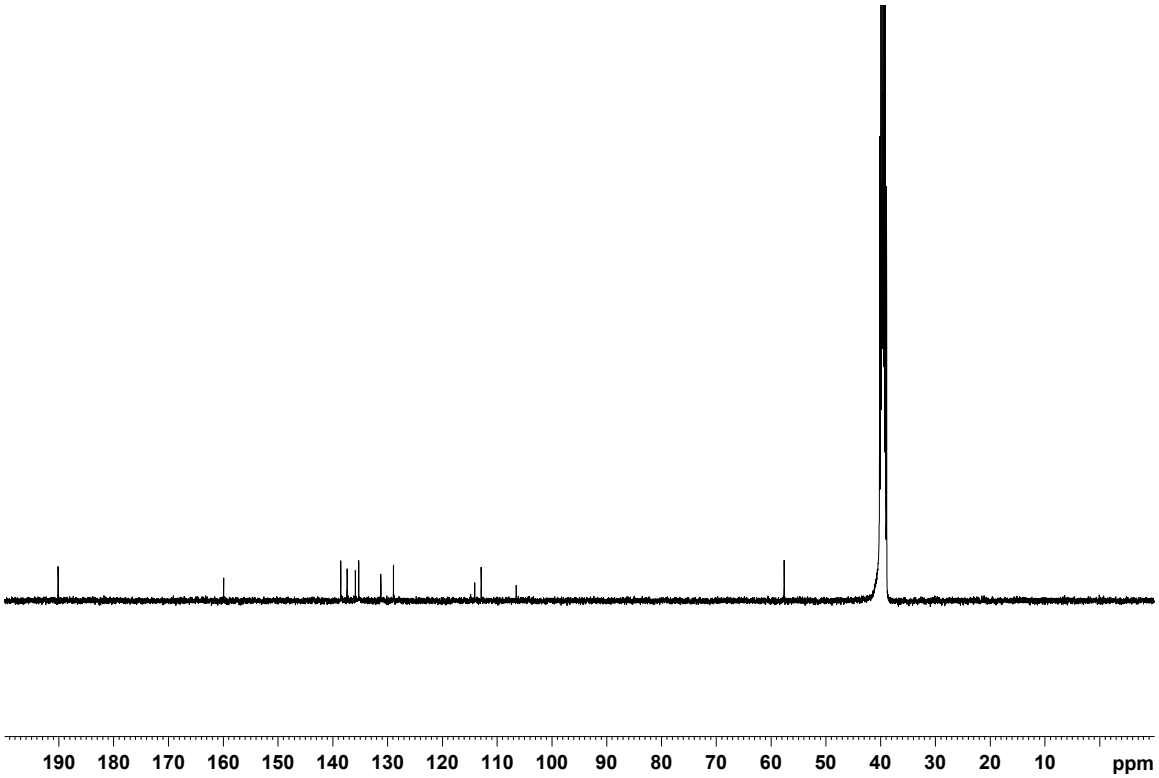




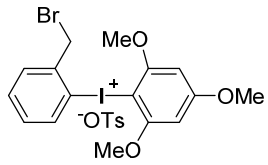
Compound **3c**

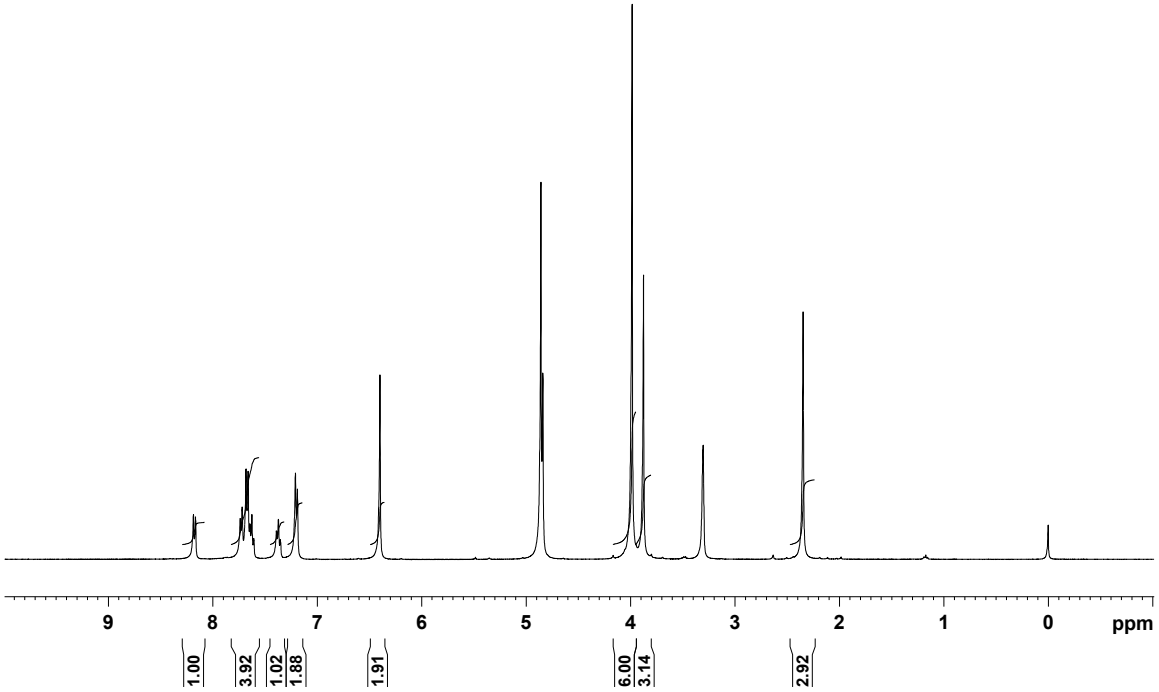


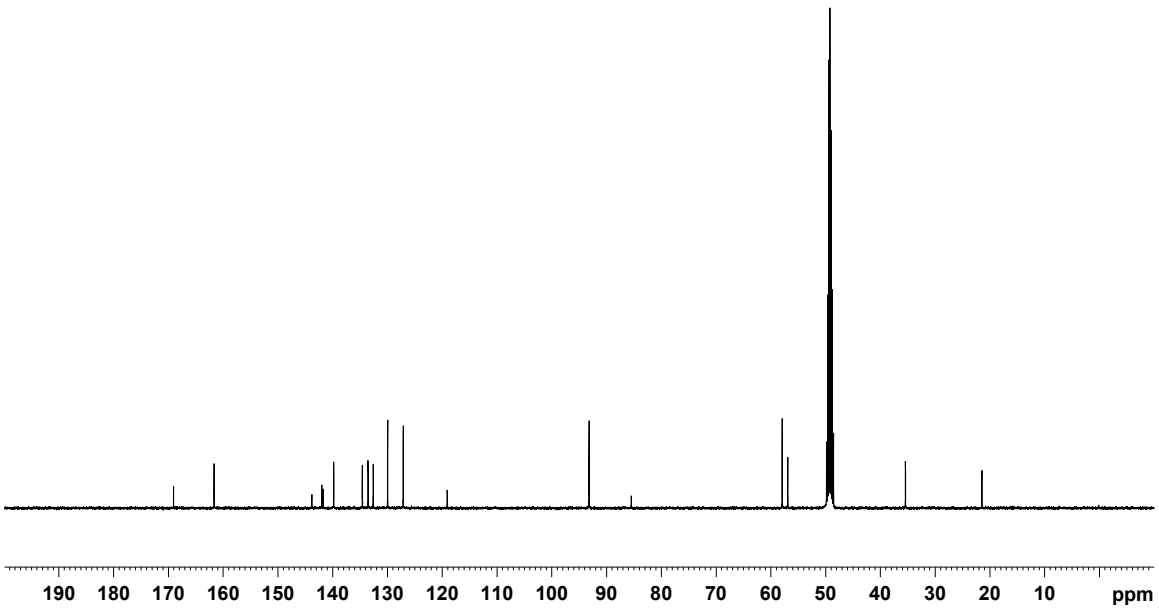




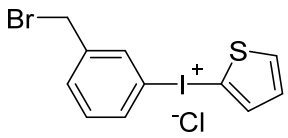
Compound **4b**

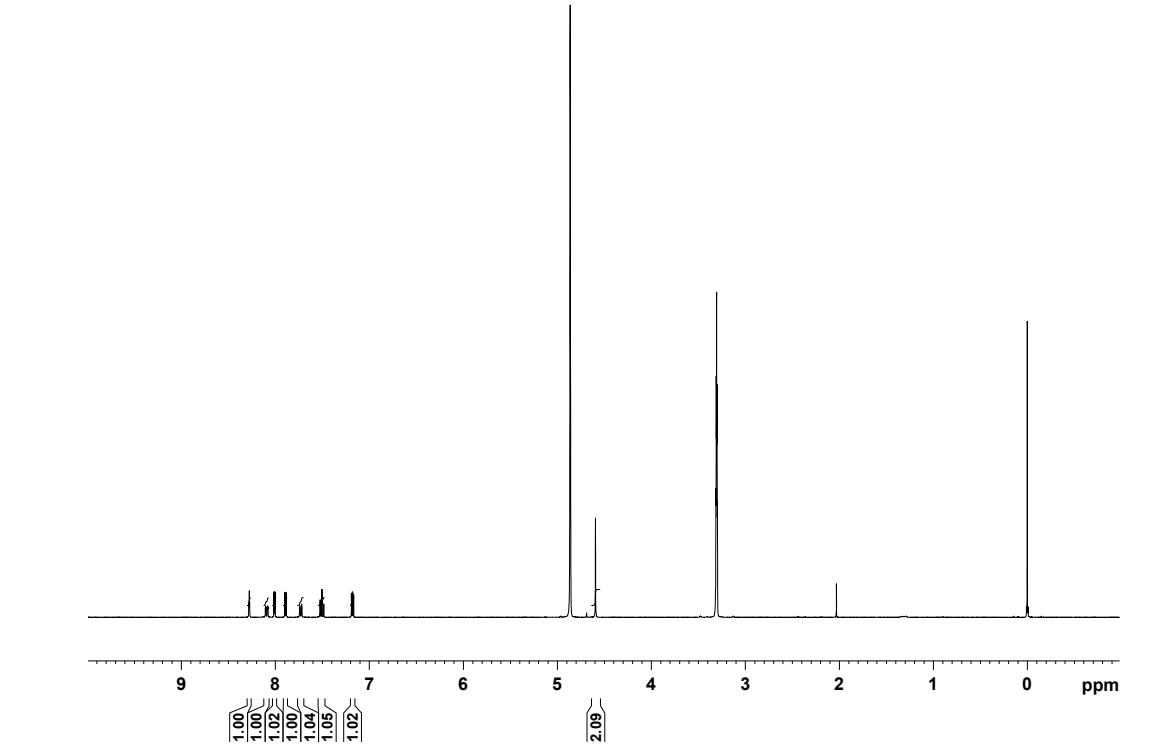


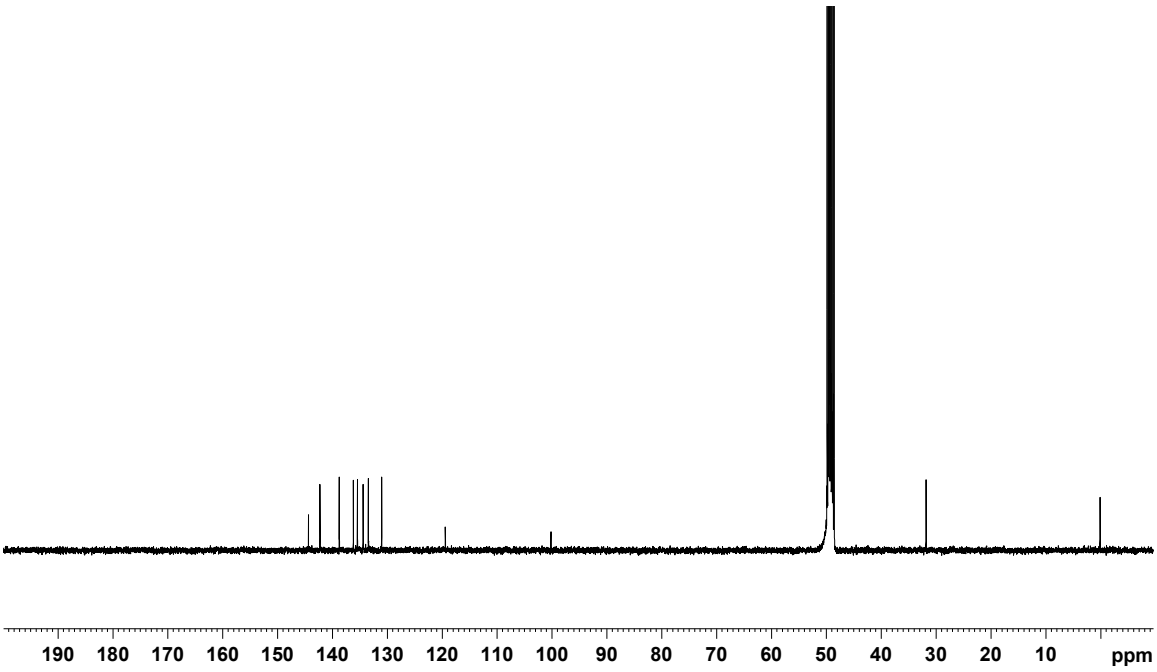




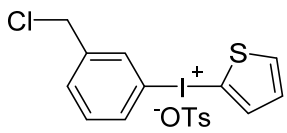
Compound **6c**

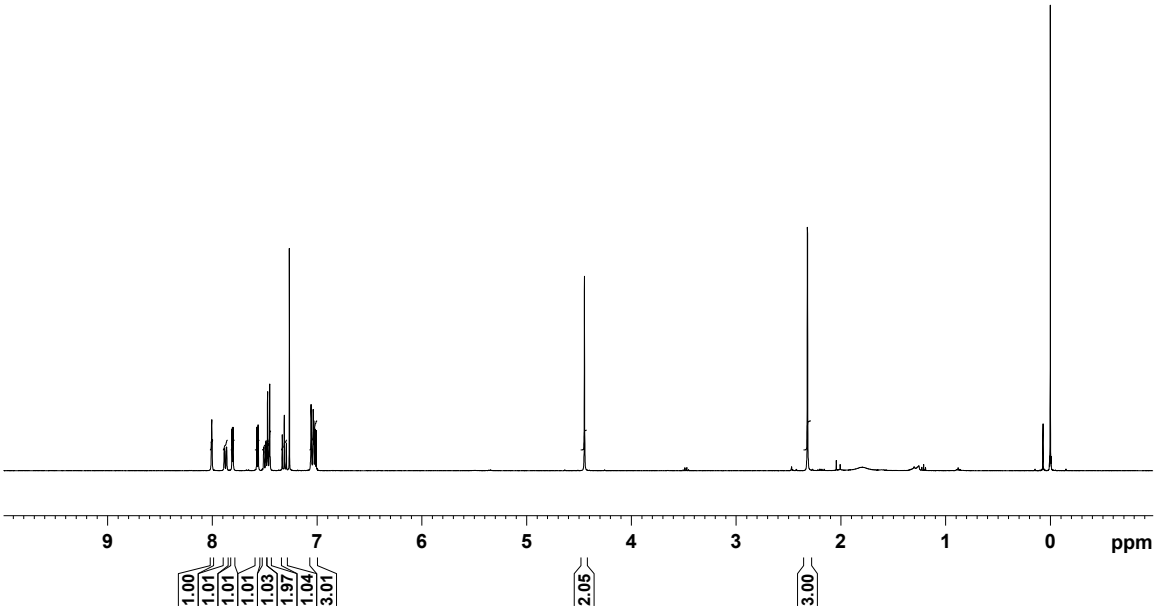


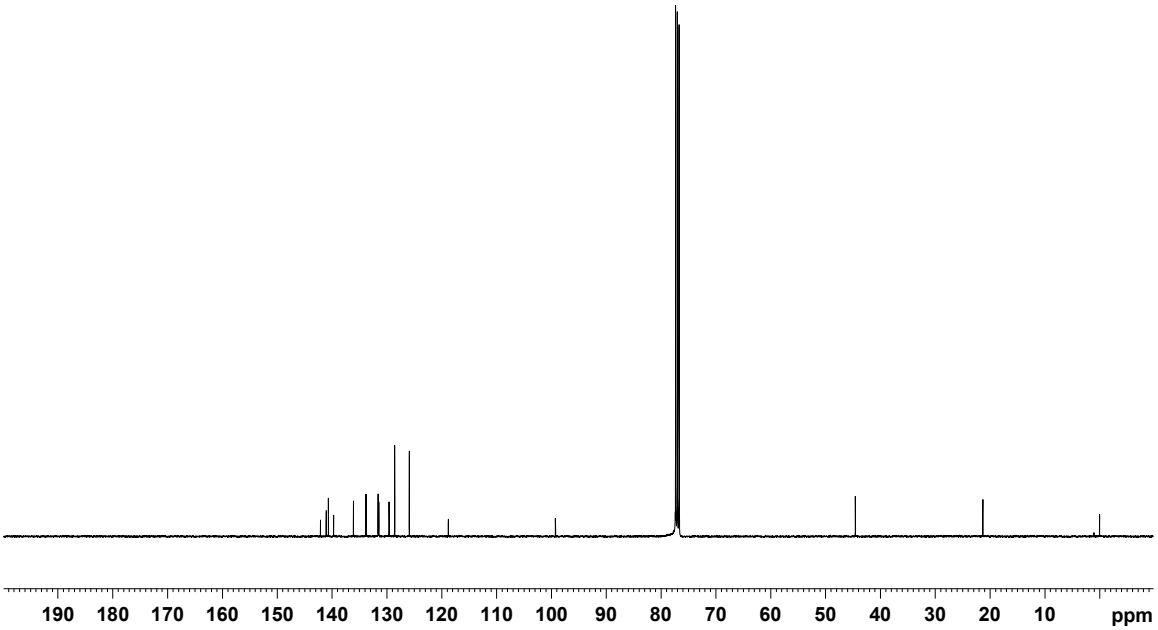




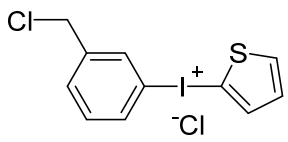
Compound **7b**

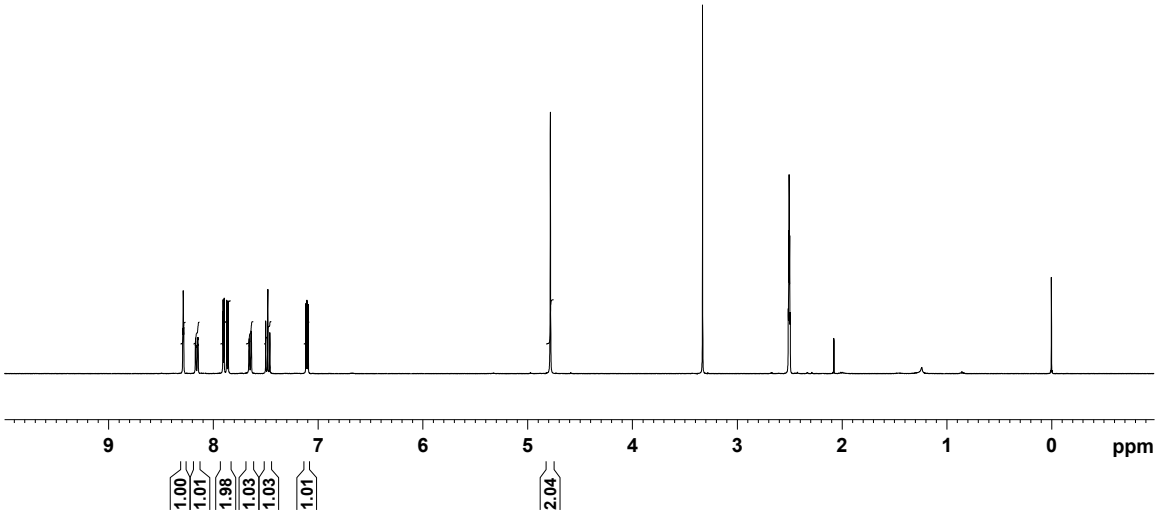


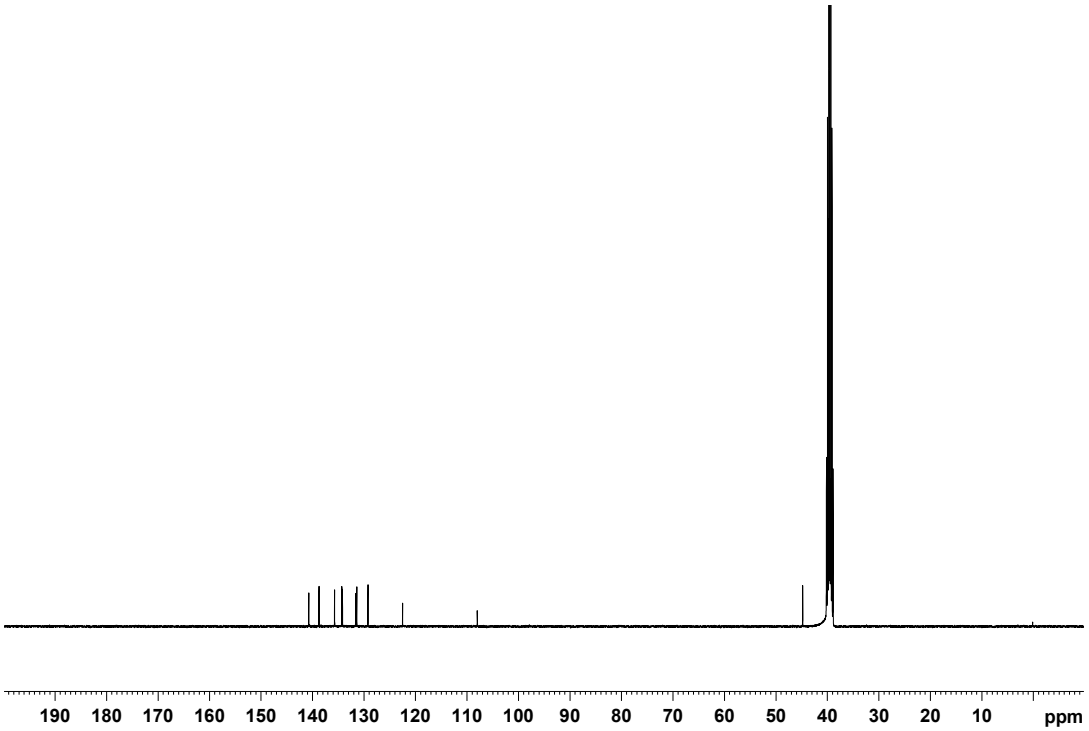




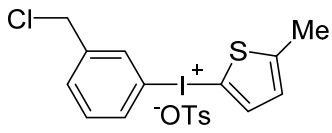
Compound **7c**

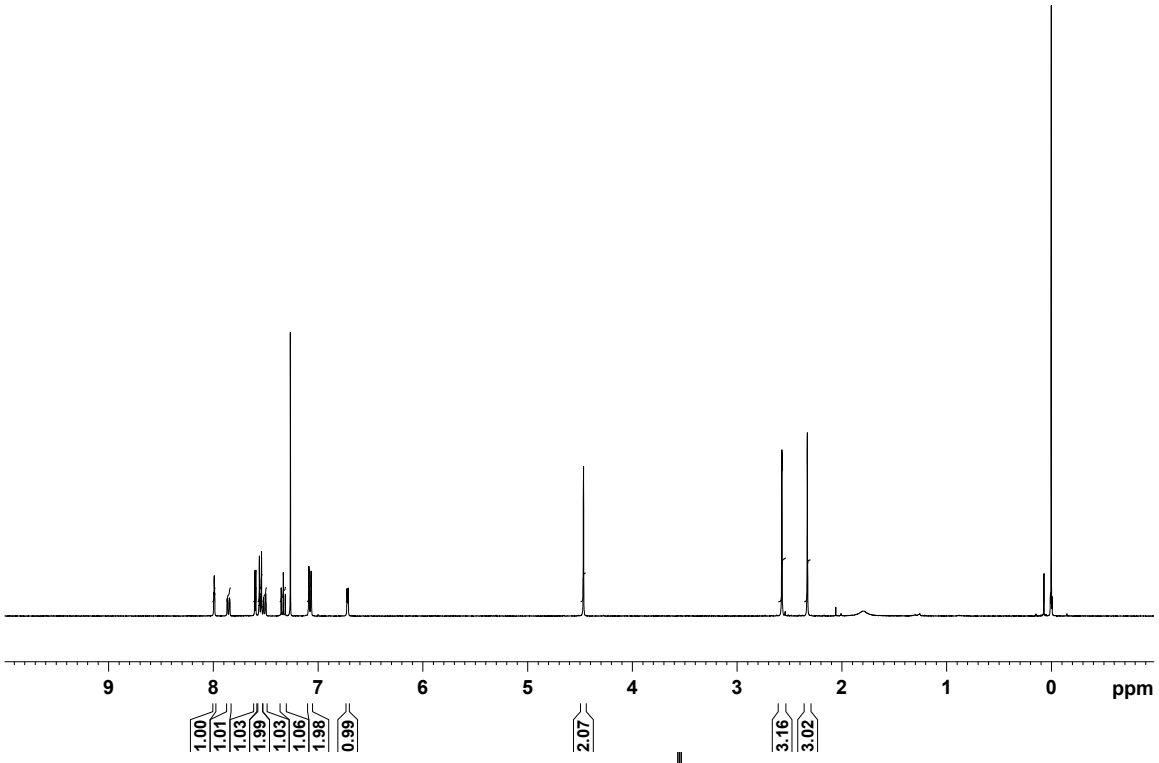


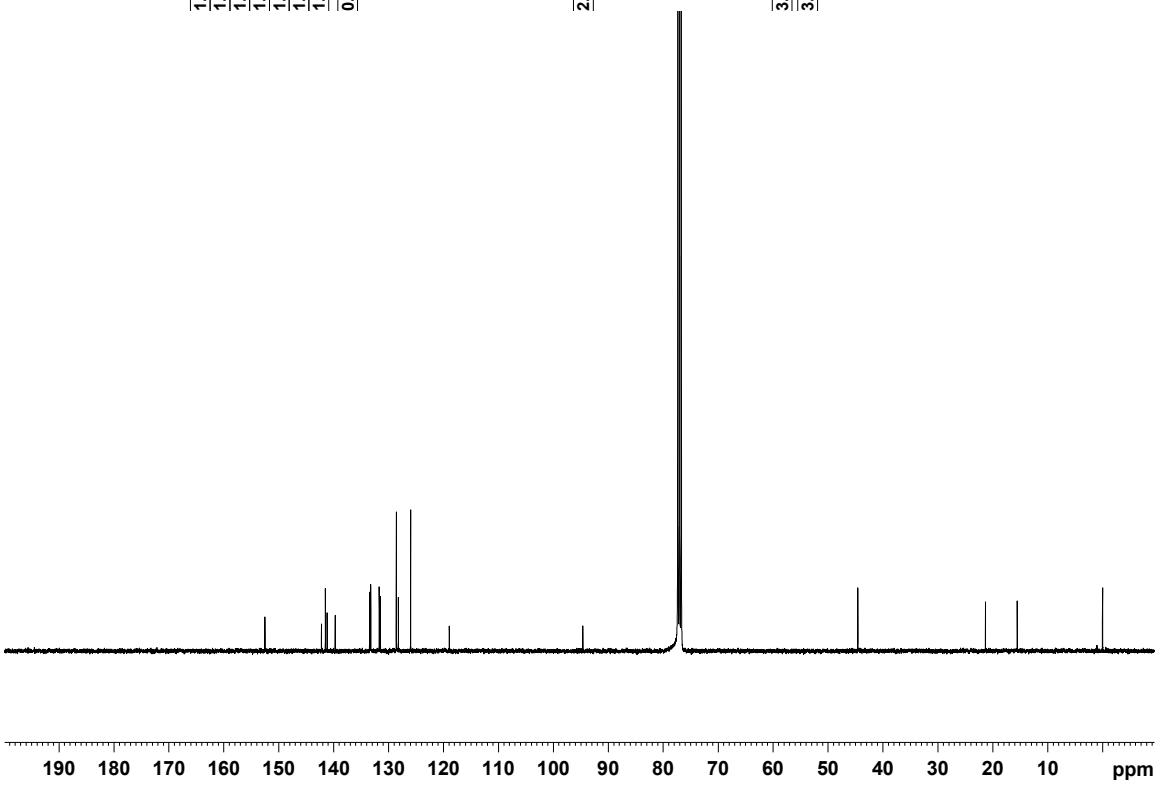




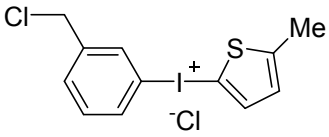
Compound **7d**

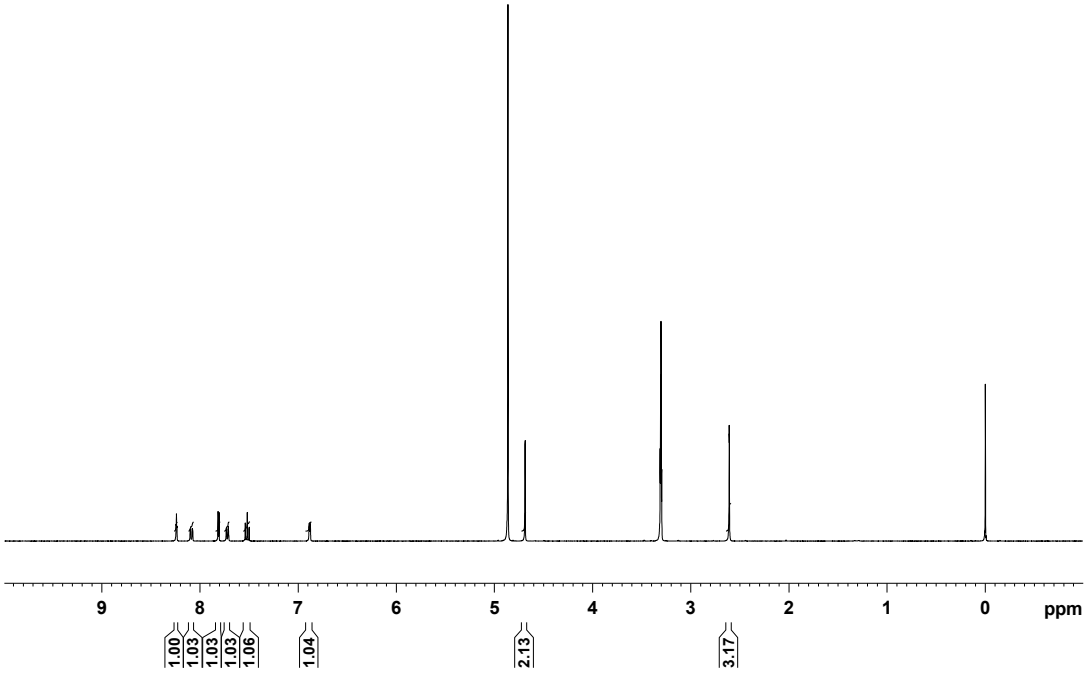


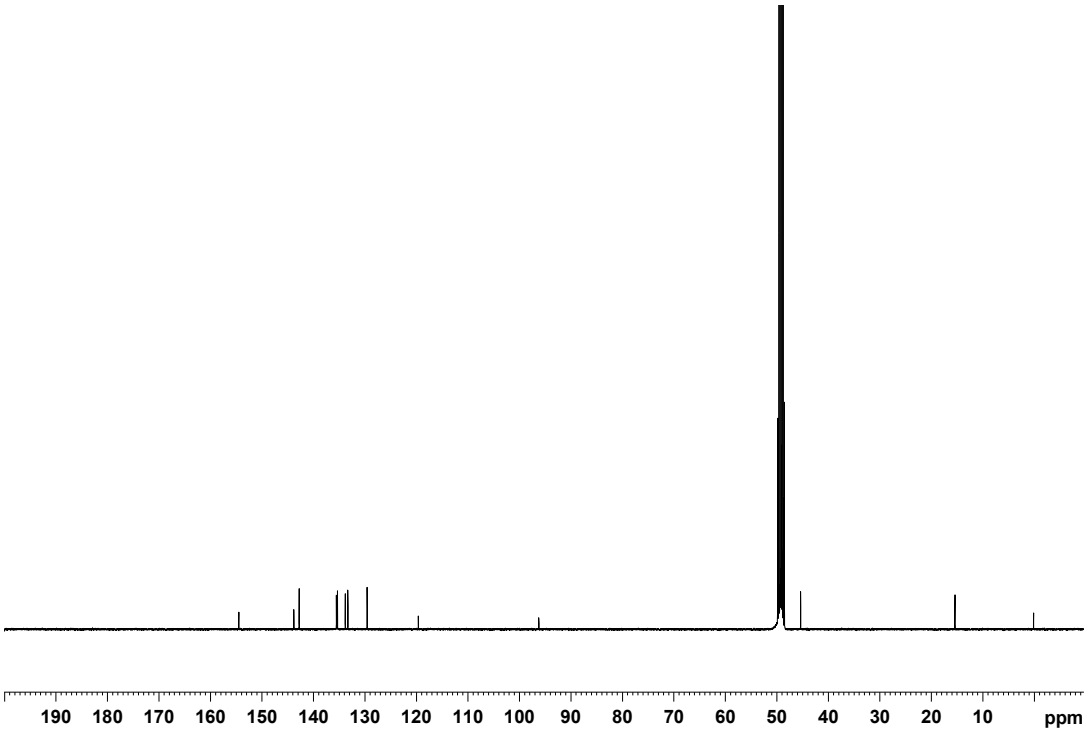




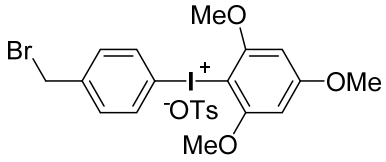
Compound **7e**

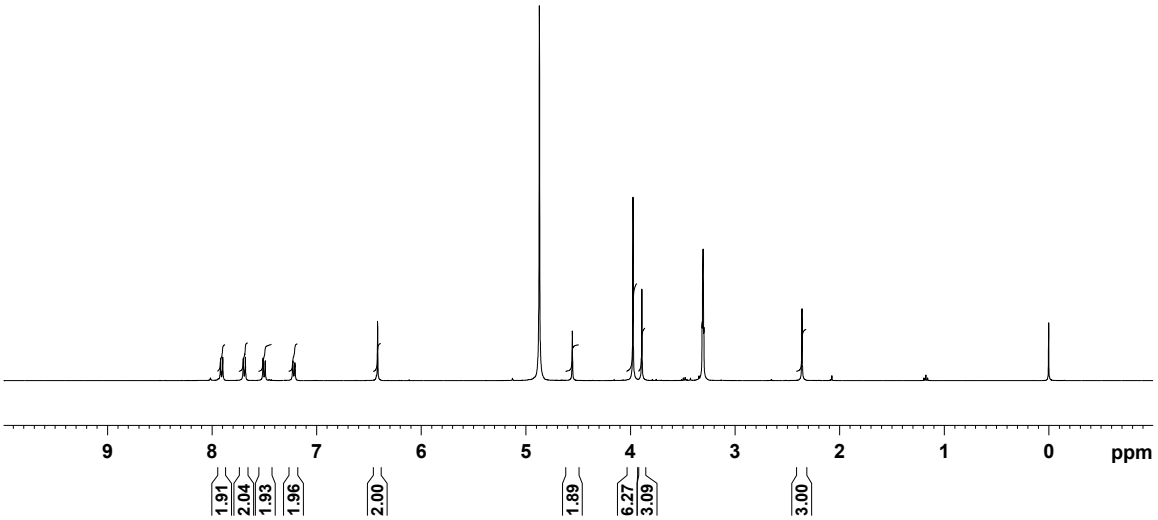


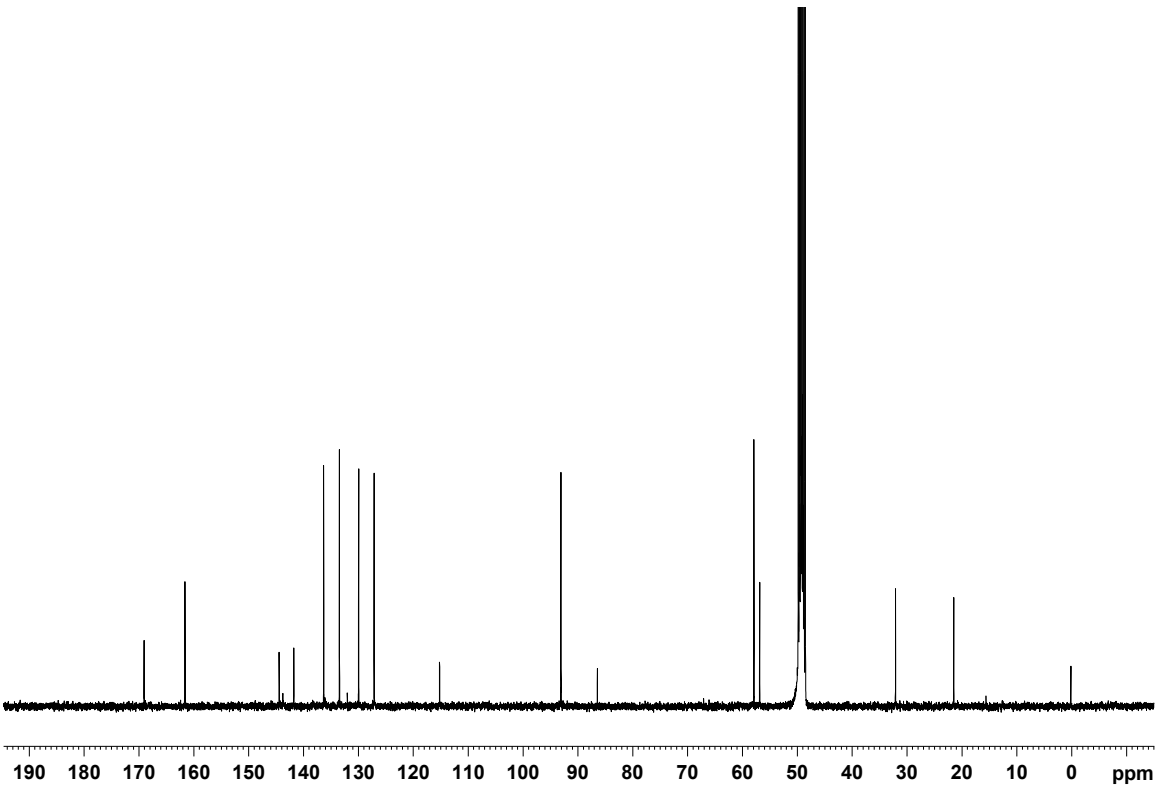




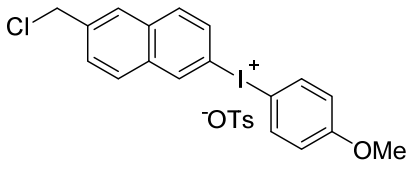
Compound **8b**

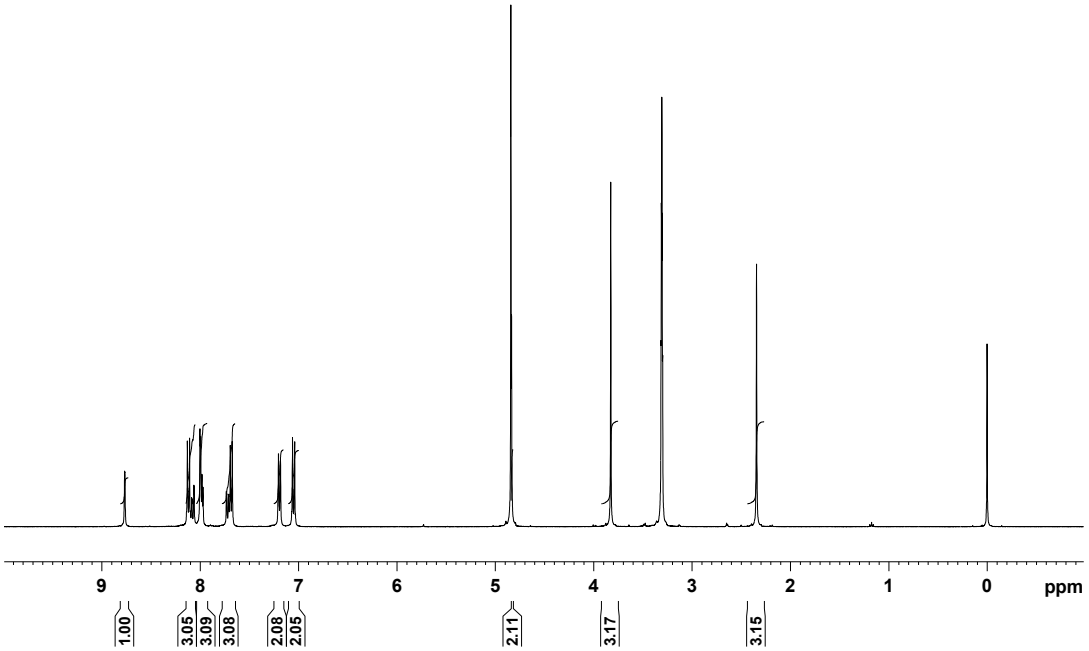


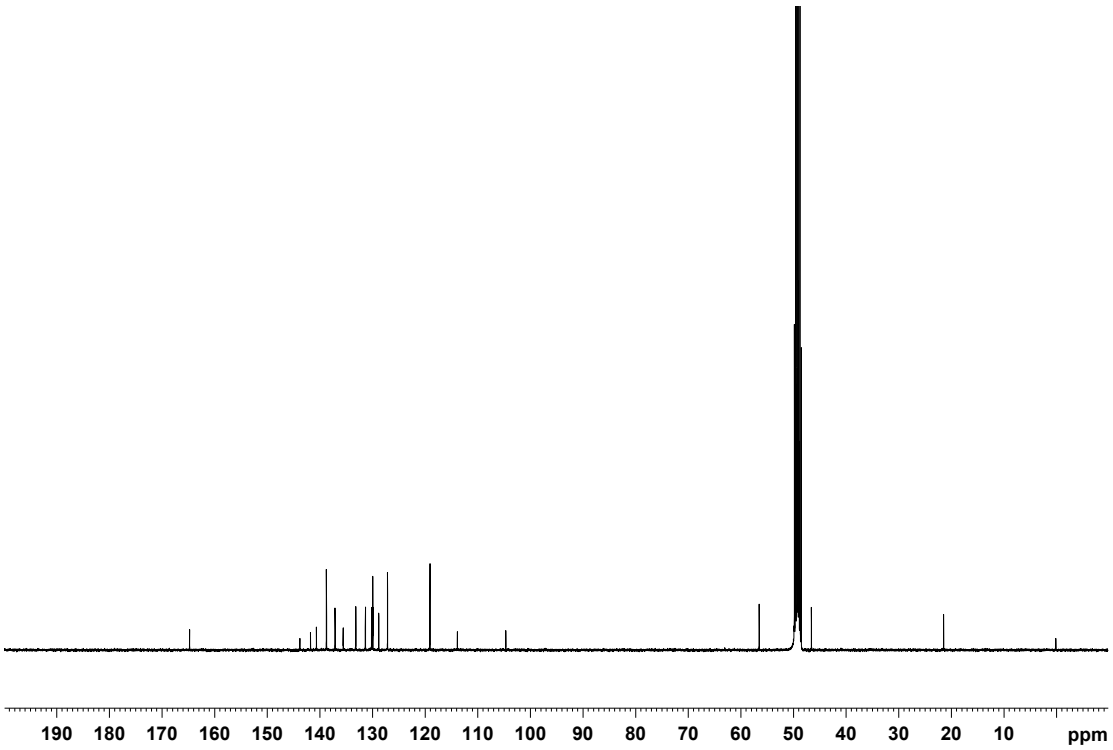




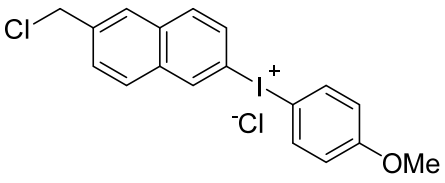
Compound **10a**

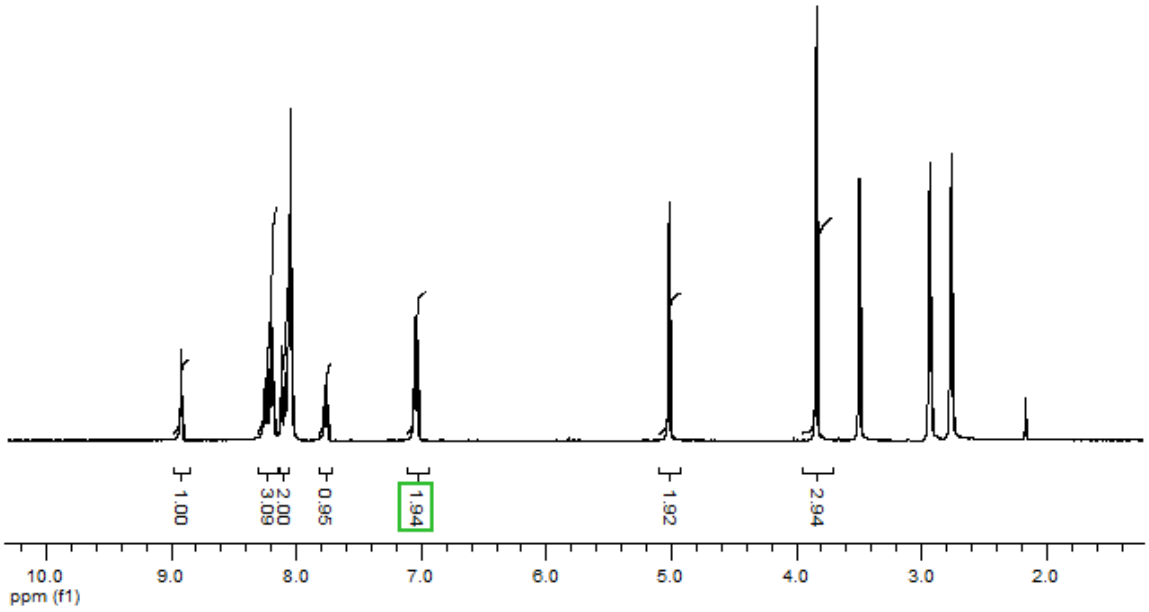


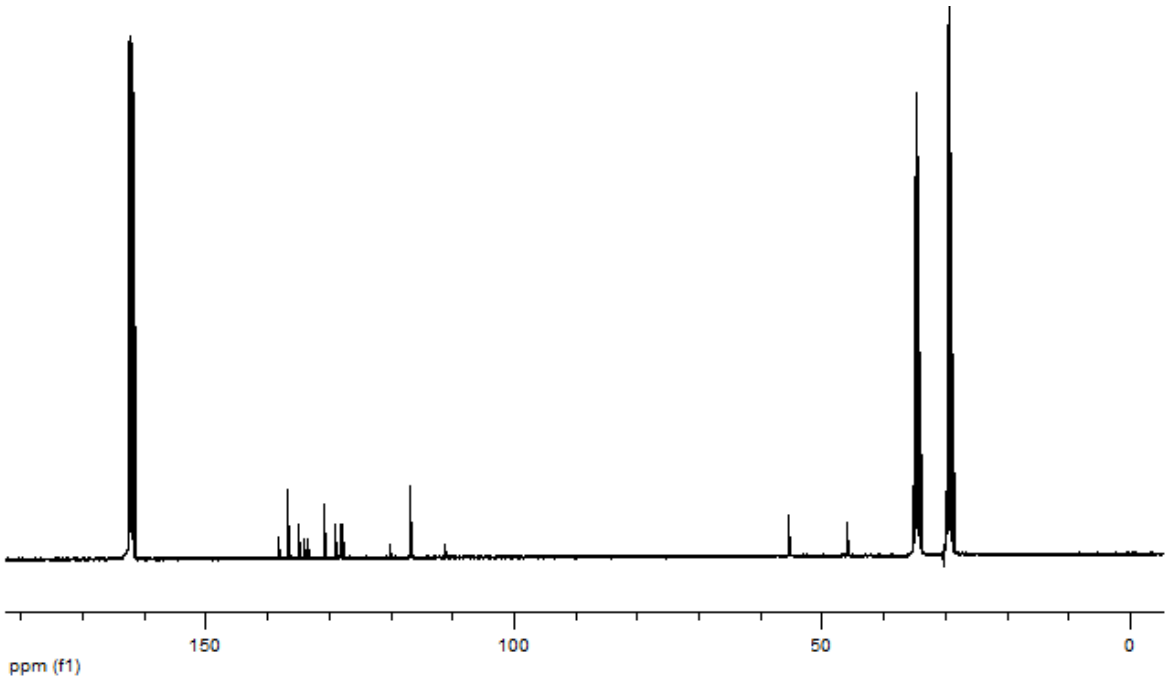




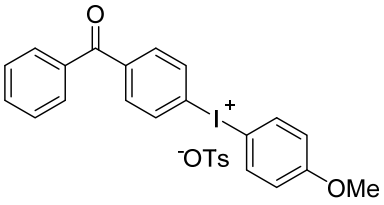
Compound **10b**

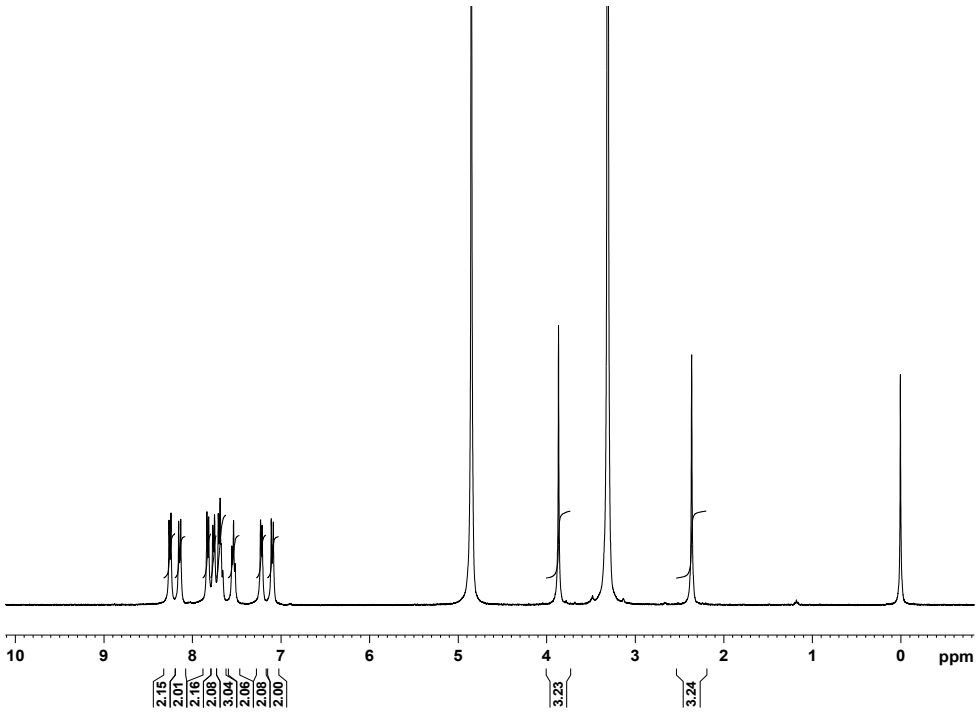


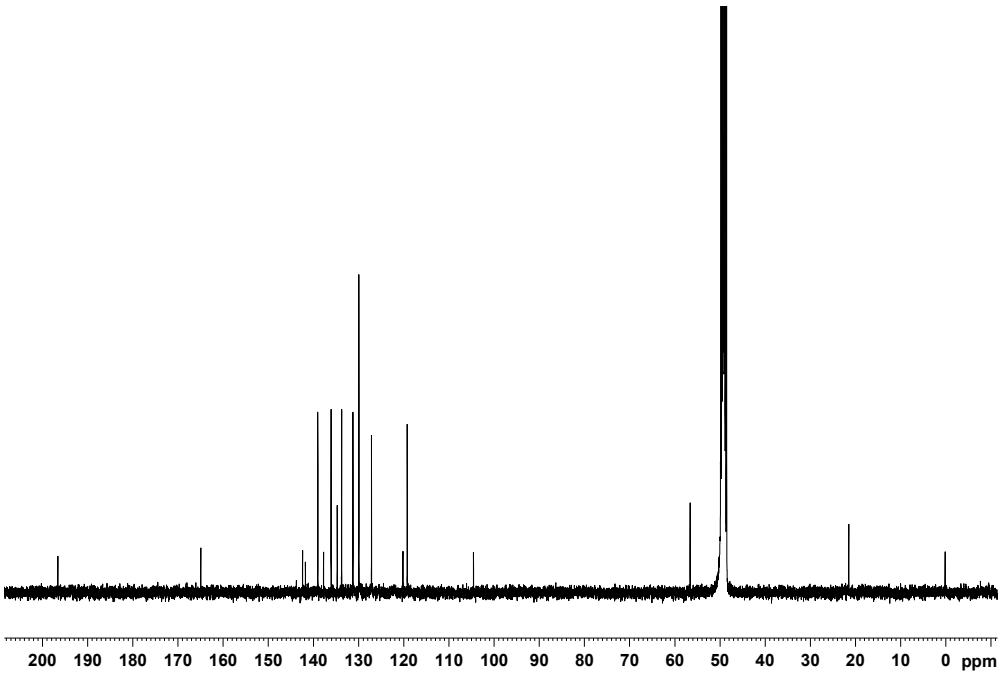




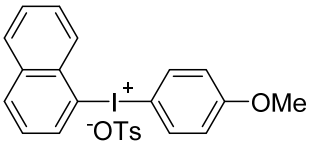
Compound **14**

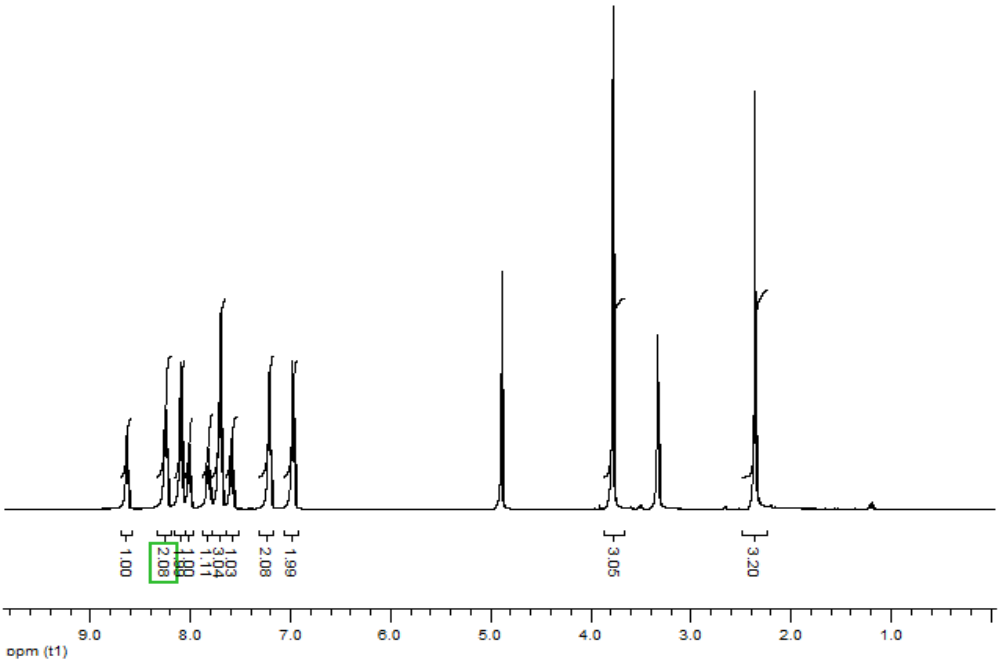


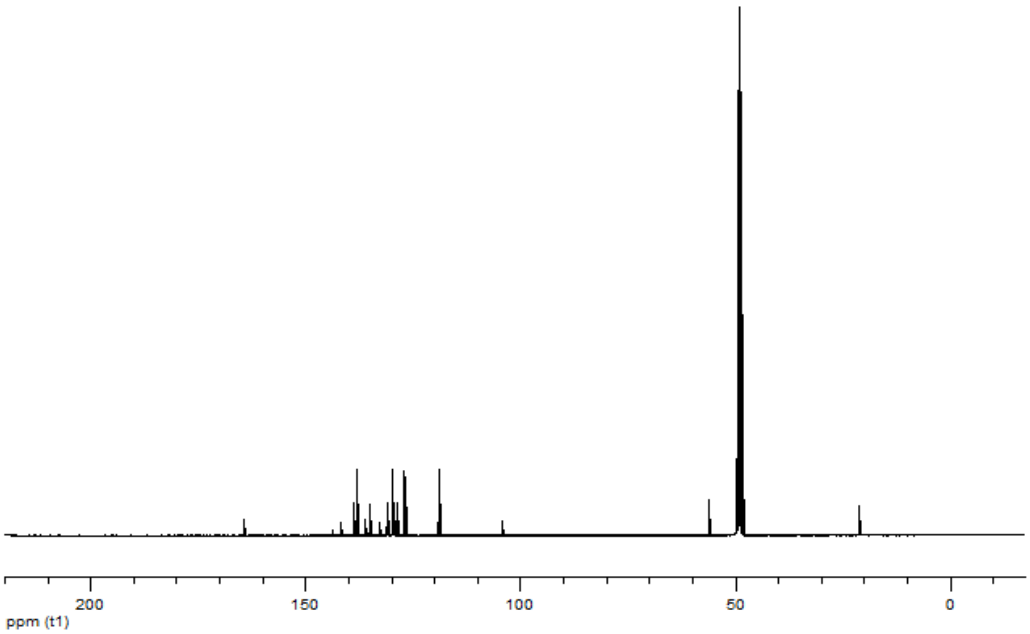




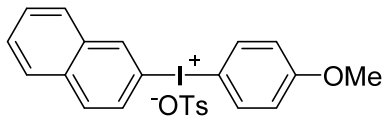
Compound **31**

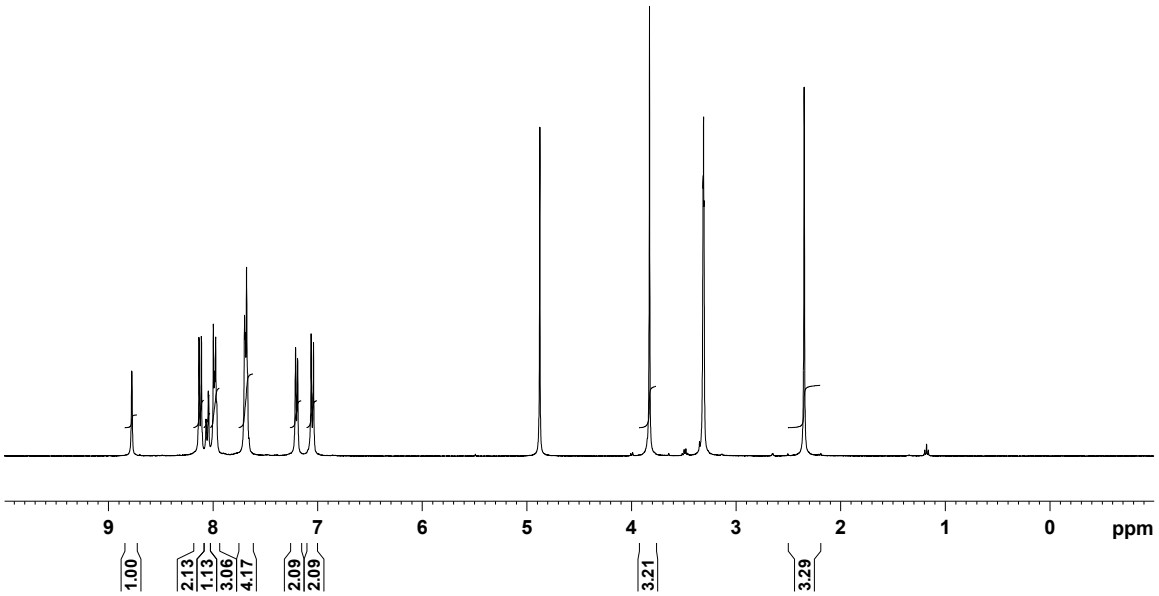


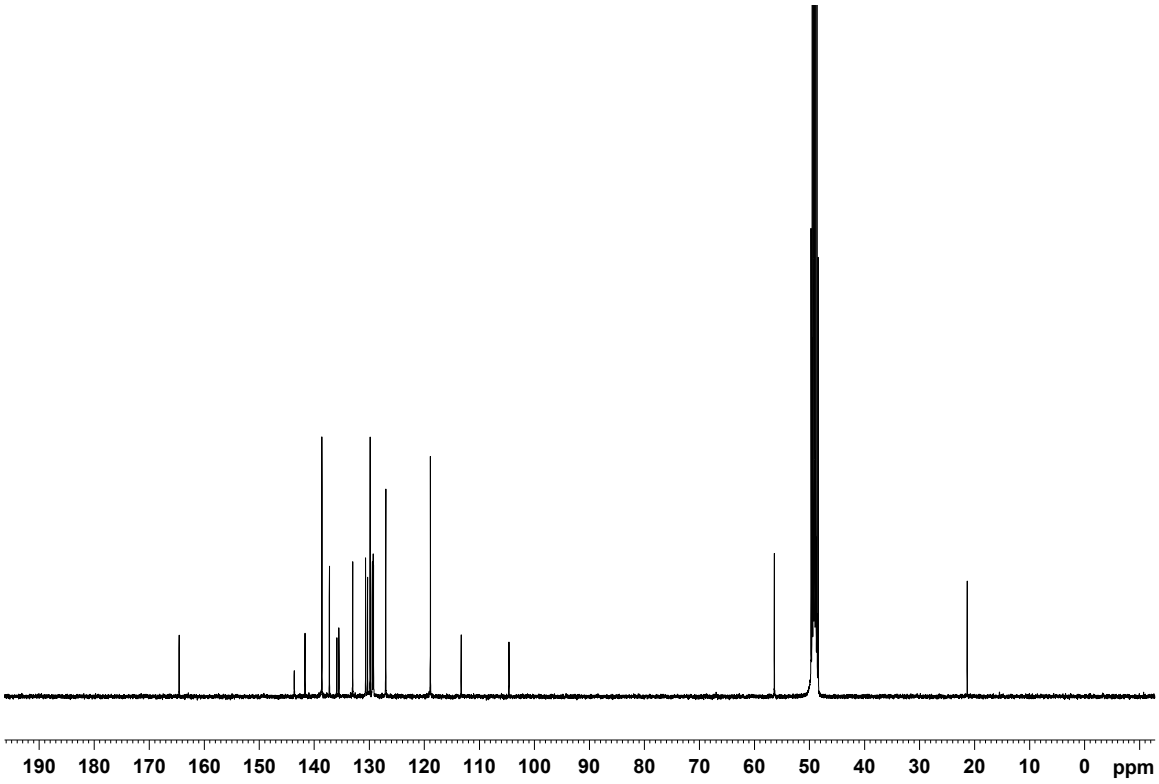




Compound **32**

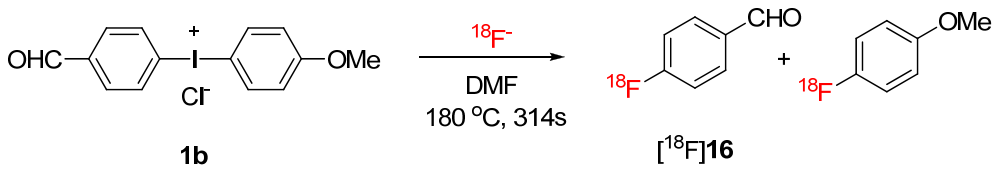




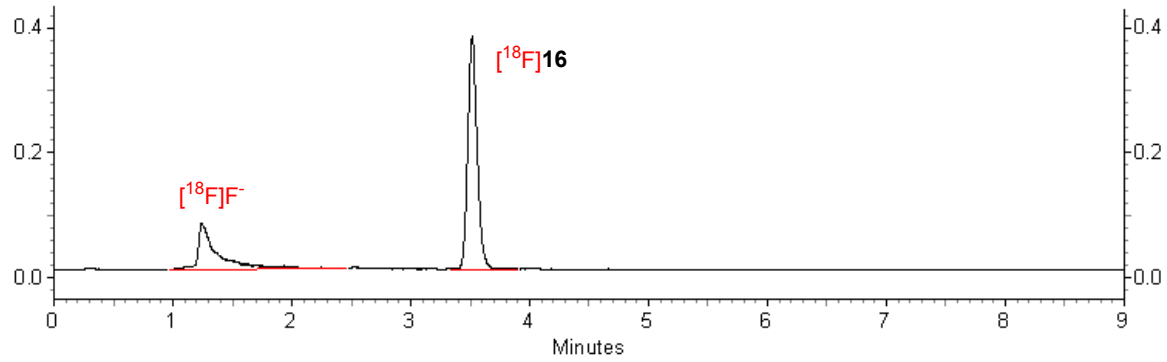


Appendix 2. Selected radio-HPLC chromatograms.

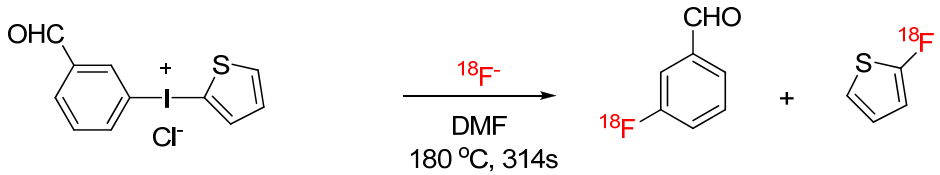
Radiofluorination of **1b**



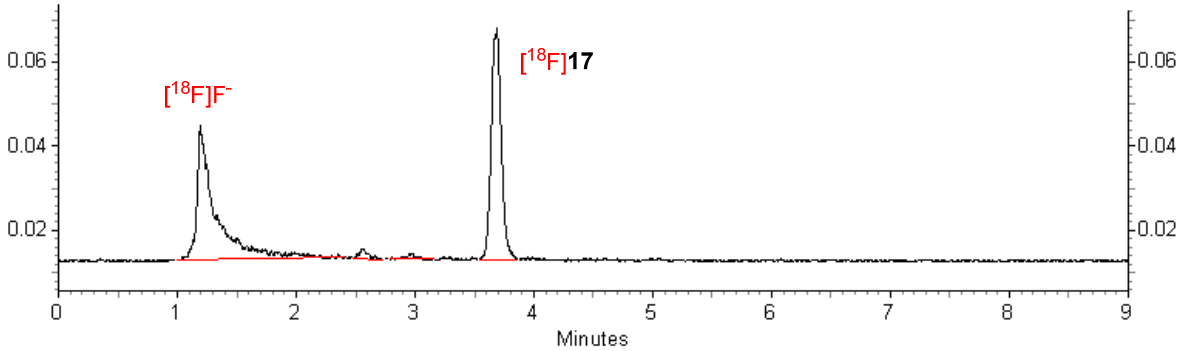
1b **[18F]16**



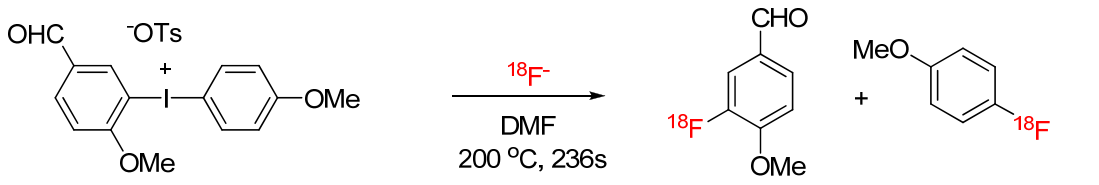
Radiofluorination of **2d**



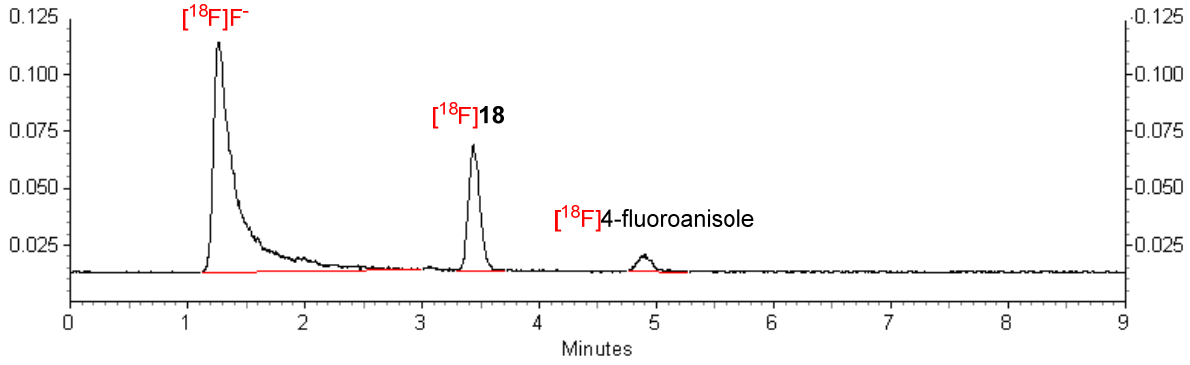
2d **[18F]17**



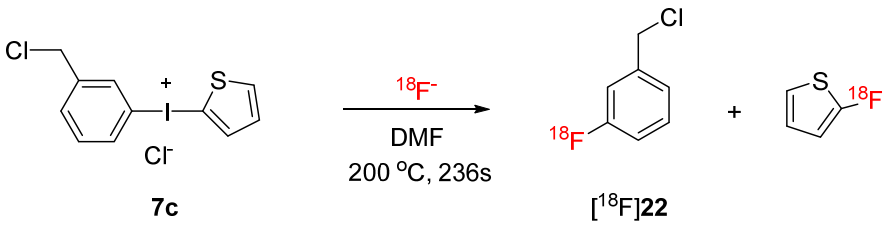
Radiofluorination of **3a**



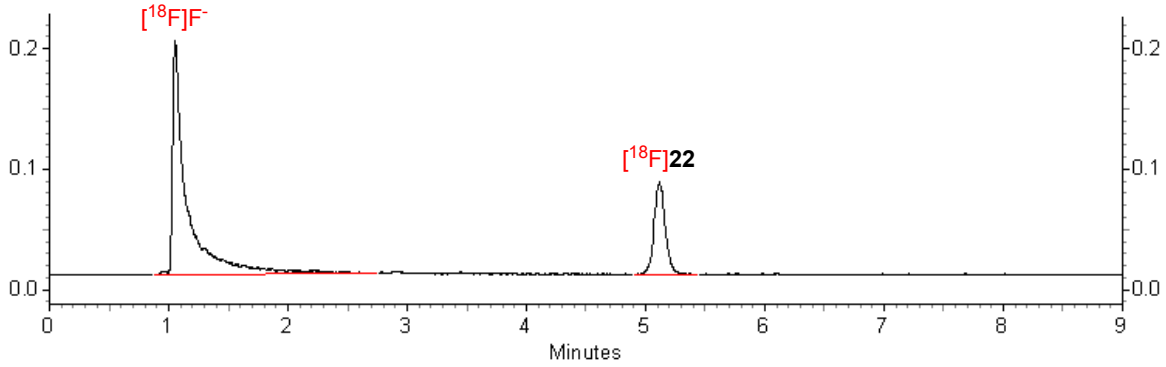
3a [18F]**18** [18F]4-fluoroanisole



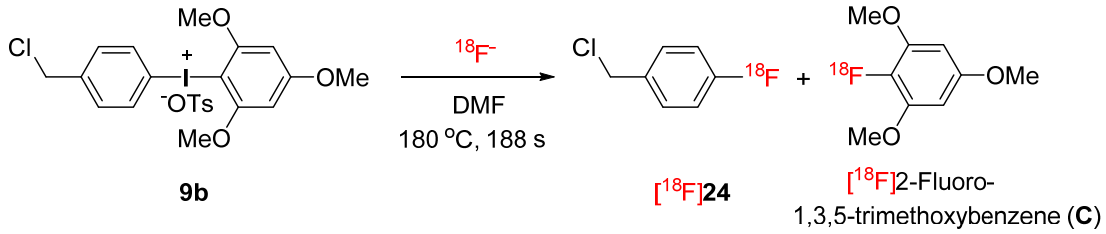
Radofluorination of **7c**



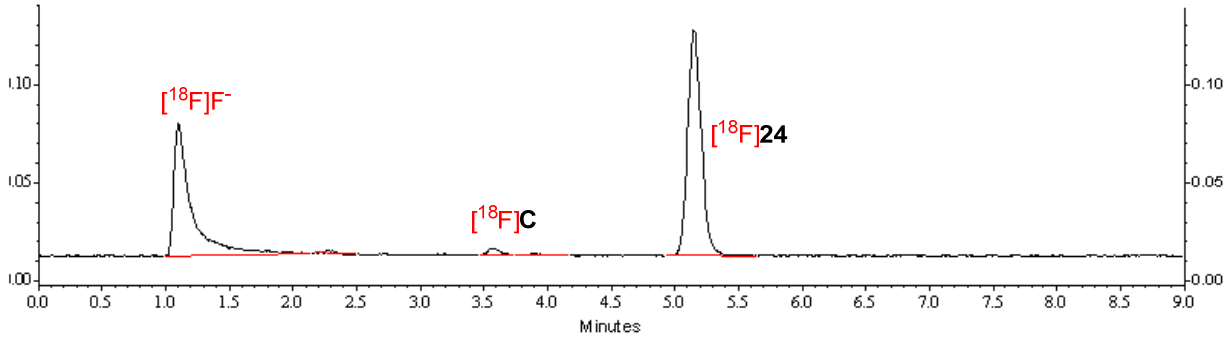
7c [18F]**22**



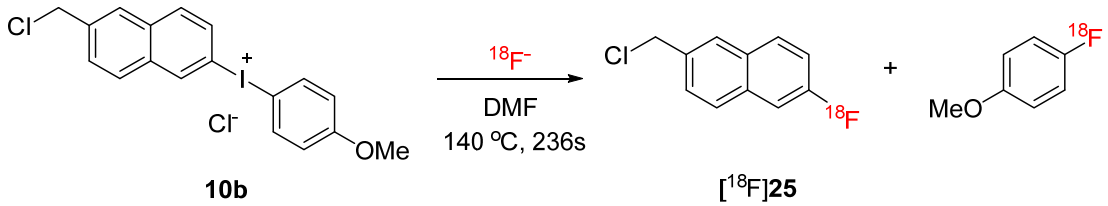
Radiofluorination of **9b**



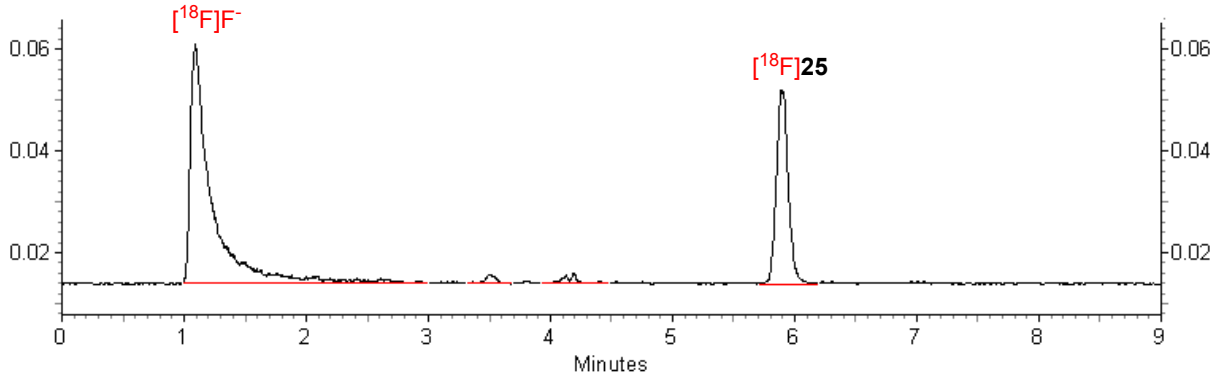
9b [18F]**24** [18F]2-Fluoro-1,3,5-trimethoxybenzene (**C**)



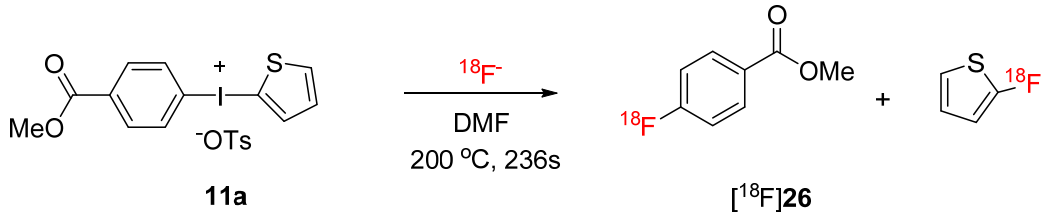
Radiofluorination of **10b**



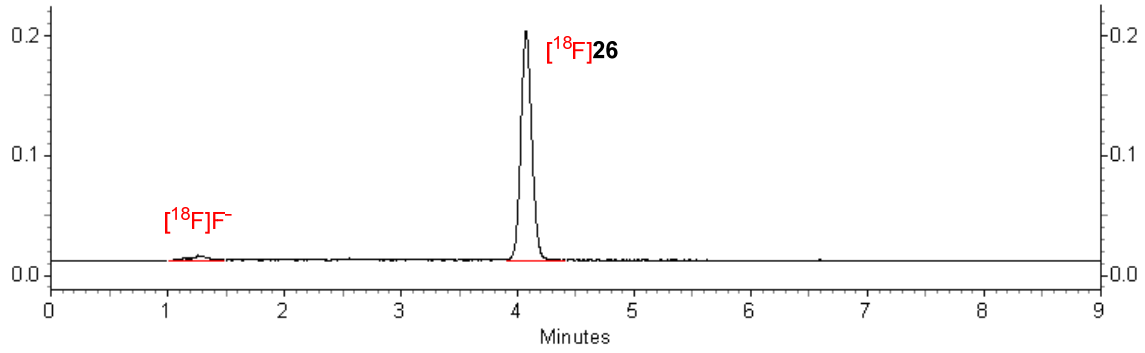
10b [18F]**25**



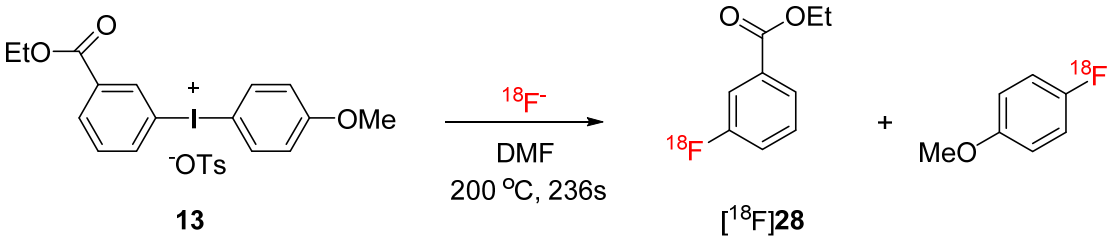
Radiofluorination of **11a**



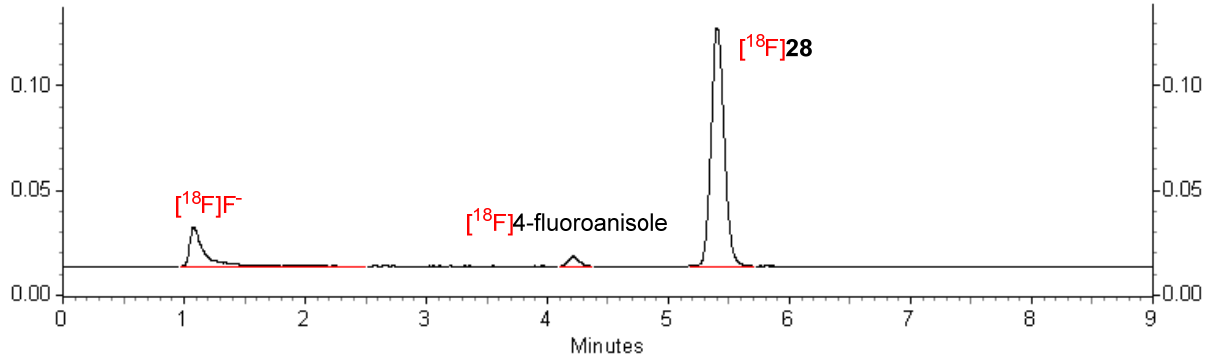
11a **[18F]26**



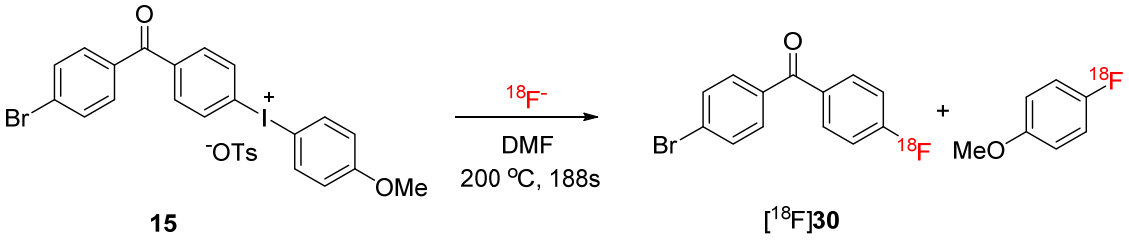
Radiofluorination of **13**



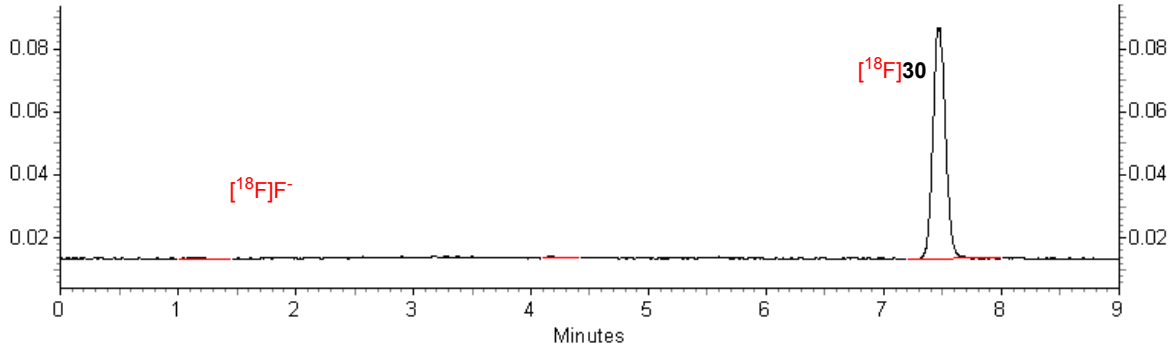
13 **[18F]28**



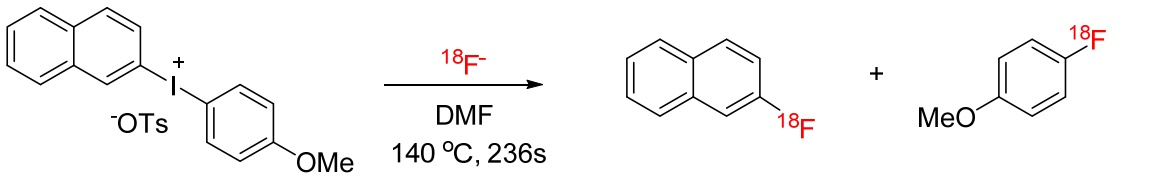
Raiofluorination of **15**



15 [^{18}F]**30**



Radiofluorination of **32**



32 [^{18}F]2-fluoronaphthalene [^{18}F]4-fluoroanisole