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Supporting Information

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A solid-phase route to ^{18}F-labeled tracers, exemplified by the synthesis of [^{18}F]2-fluoro-2-deoxy-D-glucose

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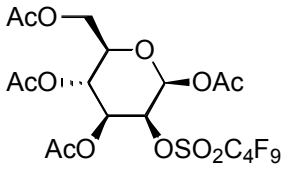
General Methods

IR spectra were recorded on a Perkin-Elmer 1600 FT-IR instrument, a Bio-Rad FTS 135 instrument using a Golden Gate adaptor or a Nicolet Impact 400 FTIR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC300 (300 and 75 MHz respectively) or a Bruker DPX400 (400 and 100 MHz respectively). Low resolution mass spectra were obtained on a Fisons VG platform single quadrupole mass spectrometer in electron spray ionisation mode. Elemental analyses were obtained from MEDAC Ltd., Egham, UK. Melting points were measured on a Gallenkamp electrothermal melting point apparatus. CH_2Cl_2 and Et_3N were distilled from calcium hydride. THF was distilled from sodium/benzophenone prior to use. CH_3OH was distilled from Mg/I_2. All other anhydrous solvents were purchased from Aldrich. All reactions were performed under a dry argon atmosphere in oven dried glassware unless stated otherwise. Sulfonic halides and anhydrides were either purchased from Aldrich or prepared by following literature methods.[1] 1,3,4,6-Tetra-*O*-acetyl-β-D-mannopyranoside was prepared following a literature procedure.[2]

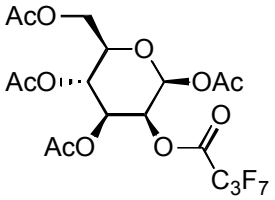
[1] P. J. Stang, M. Hanack, L. R. Subramanian, *Synthesis* **1982**, 85.
[2] V. Pozsgay, C. P. J. Glaudemans, J. B. Robbins, R. Schneerson, *Tetrahedron* **1992**, *48*, 10249.

1,3,4,6-Tetra-*O*-acetyl-2-(1,1,2,2,3,3,4,4,4-nonafluoro-butane-sulfonate)-β-D-mannopyranoside (8).[3]



To a solution of 1,3,4,6-tetra-*O*-acetyl-β-D-mannopyranoside[2] (**4**, 200 mg, 0.57 mmol) and pyridine (158 mg, 2.0 mmol) in CH_2Cl_2 (3 mL) at –30°C was added $(F_9C_4SO_2)_2O$ (785 mg, 1.35 mmol). The reaction mixture was allowed to warm to rt over 1.5 h, whereupon $NaHCO_3$ (aq) was added and the organic layer was separated, dried ($MgSO_4$) and the solvent removed in vacuo. Purification by column chromatography, eluting with Et_2O/hexanes (4:1) afforded the title compound **8** as a pale yellow oil (129 mg, 0.205 mmol, 36 %). ^{1}H NMR ($CDCl_3$) ∂ 5.93 (1H, s), 5.31 (1H, tt, *J* = 1.5, 9.9 Hz), 5.16-5.23 (2H, m), 4.25 (1H, dd, *J* = 4.8, 12.4 Hz), 4.18 (1H, dd, *J* = 2.6, 12.4 Hz), 3.84 (1H, ddd, *J* = 2.6, 4.8, 9.9 Hz), 2.16 (3H, s), 2.11 (3H, s), 2.10 (3H, s), 2.07 (3H, s); ^{13}C NMR ($CDCl_3$) ∂ 170.78, 170.00, 169.27, 168.16, 89.27, 81.63, 73.66, 69.81, 64.57, 61.73, 20.76, 20.70, 20.54; ^{19}F NMR ($CDCl_3$, ref. C_6F_6) ∂ 81.2, 51.6, 40.9, 35.9.

1,3,4,6-Tetra-*O*-acetyl-2-(perfluorobutanoate)-β-D-mannopyranoside (9).



To a mixture of AgOTf (118 mg, 0.46 mmol), $F_9C_4SO_2Cl$ (136 mg, 0.43 mmol) and pyridine (38 μL, 0.45 mmol) in THF (3 mL) was added 1,3,4,6-tetra-*O*-acetyl-β-D-mannopyranoside[2] (**5**, 100 mg, 0.287 mmol). After 2 h at rt the reaction was partitioned between Et_2O and water, and the organic layer was separated, dried ($MgSO_4$) and the solvent removed in vacuo. Purification by column chromatography, eluting with EtOAc/hexanes (1:9) afforded the title compound **9** as a pale yellow oil (70 mg, 0.132 mmol, 46 %). $[\alpha]_D$ –1.8° (c = 0.0056, $CHCl_3$); ν_{max} (neat, cm^{-1}) 1750, 1369, 1209, 1085, 1054; (^{1}H NMR ($CDCl_3$) ∂ 5.94 (1H, d, *J* = 0.8 Hz), 5.60 (1H, d, *J* = 3.0 Hz), 5.32 (1H, t, *J* = 9.9 Hz), 5.22 (1H, dd, *J* = 3.0, 9.9 Hz), 4.28 (1H, dd, *J* = 4.3, 12.4 Hz), 4.18 (1H, dd, *J* = 2.2, 12.4 Hz), 3.84 (1H, ddd, *J* = 2.2, 4.3, 9.9 Hz), 2.11 (3H, s), 2.09 (3H, s), 2.06 (3H, s), 2.02 (3H, s); ^{13}C NMR ($CDCl_3$) ∂ 170.62, 169.69, 169.20, 168.12, 89.51, 73.27, 72.84, 70.10, 64.72, 61.49, 20.57, 20.48, 20.27; ^{19}F NMR ($CDCl_3$, ref. C_6F_6) ∂ 81.3, 42.7, 35.2; MS (ES^+) *m/z* 567.2 ($[M + Na]^+$, 100 %).

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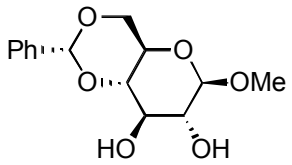
[3] (a) V. Pavliak, K. Pavol, *Carbohydr. Res.* **1991**, *210*, 333; (b) K. Hamacher, *Carbohydr. Res.* **1984**, *128*, 291.

Methyl 4,6-O-benzylidene-β-D-glucopyranoside (11).[4]



11

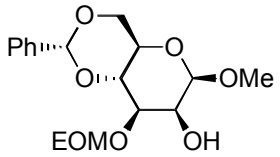
Following the method of Bundle: Methyl-β-D-glucopyranoside (5.1 g, 25 mmol), benzaldehyde dimethylacetal (15.2 g, 15 mL, 100 mmol) and 10-camphorsulfonic acid (58 mg, 0.25 mmol) were dissolved in anhydrous MeCN (75 mL) and the reaction stirred at room temperature for 4 h. Et_3N (0.5 mL) was added and the reaction filtered. The solid residue was washed with MeCN, the combined filtrates were concentrated in vacuo (~30 mL) and re-filtered. The combined solids were purified by crystallization from EtOAc: hexane and dried to afford the title compound as white crystals (**11**, 6.6 g, 93 %). Mp 198–200°C; Lit: 196.5–198°C;[4] ν_{max} (neat, cm^{-1}) 3373, 2872, 1378, 1087, 1022, 995; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50-7.45 (2H, m), 7.40-7.33 (3H, m), 5.55 (1H, s), 4.37 (1H, dd, *J* = 4.7, 10.4 Hz), 4.34 (1H, d, *J* = 8.0 Hz), 3.85 (1H, t, *J* = 10.3 Hz), 3.78 (1H, t, *J* = 10.3 Hz), 3.59 (3H, s), 3.58-3.43 (3H, m), 2.83 (1H, br), 2.69 (1H, br); ^{13}C NMR (300 MHz, DMSO-d_6) δ 137.80, 128.85, 128.03, 126.35, 104.53, 100.67, 80.63, 74.27, 72.81, 67.97, 65.78, 56.40. Spectroscopic data consistent with that reported previously in the literature.[5]

[4] D. R. Bundle, *J. Chem. Soc.-Perkin Trans. 1* **1979**, 2751.
[5] A. Roën, J. I. Padron, J. T. Vazquez, *J. Org. Chem* **2003**, *68*, 4615.

Methyl-4,6-*O*-benzylidene-3-*O*-ethoxymethyl-β-D-glucopyranoside (13).

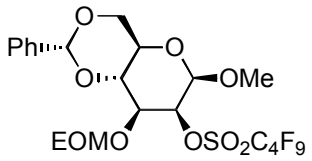
To methyl-4,6-*O*-benzylidene-β-D-glucopyranoside (**11**, 847 mg, 3.0 mmol) in anhydrous THF (40 mL) was added NaH (60 % in mineral oil, 192 mg, 4.8 mmol) and the mixture stirred, under argon, for 30 min. Chloromethylethyl ether (425 mg, 0.42 mL, 4.5 mmol) was added dropwise, and the reaction stirred at room temperature for 20 h. The reaction was quenched with methanol (0.5 mL) and concentrated *in vacuo*. The crude product was dissolved in CH_2Cl_2, washed with water and the aqueous phase extracted with CH_2Cl_2. The combined organic phase was washed with water, brine, dried (anhydrous Na_2SO_4) and concentrated *in vacuo*. Purification by silica gel column chromatography (hexane: EtOAc, 2:1) afforded three isolated products: compound **12** (white solid, 260 mg, 0.76mmol, 25 %), compound **13** (white solid, 500 mg, 49 %) and compound **14** (white solid, 82 mg, 0.21mmol, 7 %). **Data for 13:** mp 99–102 °C; $[\alpha]_D$ –11.3° (c = 0.488, $CHCl_3$); ν_{max} (neat, cm^{-1}) 3450, 2876, 1727, 1380, 1100, 1069, 1026; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50-7.30 (5H, m), 5.53 (1H, s), 4.85 (1H, d, *J* = 7.4 Hz), 4.78 (1H, d, *J* = 7.4 Hz), 4.38 (1H, d, *J* = 7.4 Hz), 4.37 (1H, dd, *J* = 5.2, 10.3 Hz), 4.00 (1H, d, *J* =1.5 Hz), 3.84-3.74 (2H, m), 3.66 (1H, t, *J* = 8.1 Hz), 3.62-3.56 (2H, m), 3.60 (3H, s), 3.58-3.40 (2H, m), 1.21 (3H, t, *J* = 6.6 Hz); ^{13}C NMR (300 MHz, $CDCl_3$) δ 137.25, 129.28, 128.40, 126.33, 104.53, 101.77, 96.68, 82.17, 79.71, 74.09, 68.86, 66.55, 64.39, 57.67, 15.02; MS (ES^+) *m/z* 363.1 ($[M + Na]^+$, 100 %); Anal. Calcd for C_{17} H_{24} O_7: C, 59.99; H, 7.11. Found: C, 59.83; H, 7.14. **Data for Methyl-4,6-*O*-benzylidene-2-*O*-ethoxymethyl-β-D-glucopyranoside (12):** mp 103-105 °C; $[\alpha]_D$ –20.8° (c = 0.606, $CHCl_3$); ν_{max} (neat, cm^{-1}) 3437, 2975, 2879, 1453, 1390, 1089, 1046, 1025; ^1H NMR (300 MHz, $CDCl_3$) δ 7.51-7.30 (5H, m), 5.56 (1H, s), 4.89 (1H, d, *J* = 6.6 Hz), 4.79 (1H, d, *J* = 7.4 Hz), 4.38 (1H, d, *J* = 7.4 Hz), 4.36 (1H, dd, *J* = 5.2, 10.3 Hz), 4.02 (1H, s), 3.85-3.75 (3H, m), 3.62-3.55 (2H, m), 3.56 (3H, s), 3.46 (1H, ddd, *J* = 4.4, 9.5, 10.3 Hz), 3.34 (1H, t, *J* = 8.1 Hz), 1.21 (3H, t, *J* = 6.6 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 137.08, 129.14, 128.26, 126.30, 103.47, 101.88, 96.67, 83.34, 80.59, 72.71, 68.70, 66.08, 64.33, 57.41, 15.01; MS (ES^+) *m/z* 363.3 $[M + Na]^+$. **Data for Methyl-4,6-*O*-benzylidene-2,3-*O*-di(ethoxymethyl)-β-D-glucopyranoside (14):** mp 73-75 °C; $[\alpha]_D$ –62.2° (c = 0.475, $CHCl_3$); ν_{max} (neat, cm^{-1}) 2975, 2880, 1455, 1390, 1095, 1046, 1028; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50-7.30 (5H, m), 5.52 (1H, s), 4.90 (1H, d, *J* = 6.6 Hz), 4.89 (2H, s), 4.83 (1H, d, *J* = 6.6 Hz), 4.36 (1H, d, *J* = 8.1 Hz), 4.35 (1H, dd, *J* = 4.4, 10.3 Hz), 3.87 (1H, t, *J* = 9.2 Hz), 3.77 (1H, t, *J* = 10.3 Hz), 3.71-3.52 (6H, m), 3.54 (3H, s), 3.43 (1H, ddd, *J* = 5.1, 9.6, 10.3 Hz), 1.22 (3H, t, *J* = 7.0 Hz), 1.05 (3H, t, *J* = 6.6 Hz); ^{13}C NMR (300 MHz, $CDCl_3$) δ: 137.35, 129.18, 128.35, 126.29, 104.73, 101.65, 95.97, 80.89, 78.13, 76.89, 68.95, 66.23, 63.98, 63.75, 57.39, 15.13, 14.91; MS (ES^+) *m/z* 421.4 ($[M + Na]^+$, 100 %).

Methyl-4,6-*O*-benzylidene-3-*O*-ethoxymethyl-β-D-mannopyranoside (15).



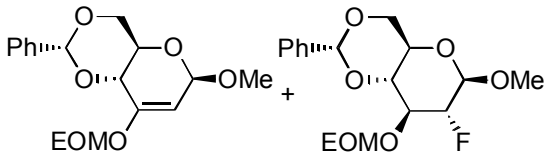
A solution methyl-4,6-*O*-benzylidene-3-*O*-ethoxymethyl-β-D-glucopyranoside (**13**, 14.0 g, 41.2 mmol) in DMSO (168 mL) and Ac_2O (84.5 mL, 0.943 mol) was stirred at room temperature for 24 h. The reaction was diluted with EtOAc (1 L) and washed with a saturated aqueous solution of K_2CO_3 (600 mL). The organic layer was separated, dried (Na_2SO_4) and concentrated to dryness in vacuo giving the crude ketone as a white solid (20 g). The crude ketone (20 g) was re-dissolved in MeOH (200 mL) and cooled to –20°C before $NaBH_4$ (1.69 g, 44.4 mmol) was added slowly, with stirring. The reaction mixture was allowed to warm to 25°C then stirred at this temperature for a further 48 h. The reaction was concentrated in vacuo to give a gum which was partitioned between EtOAc (250 mL) and saturated aqueous K_2CO_3. The organic layer was separated re-extracting the aqueous with EtOAc (2 x 100 mL). The combined organic phase was dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the resulting off-white solid by silica gel column chromatography (hexane: EtOAc, 1:3) afforded the title compound as a white solid (**15**, 10.62 g, 31.2 mmol, 76 %) in addition to some mixed fractions containing some of compound **15** (2.74 g) and pure **13** (1.54 g, 4.0 mmol, 10 %). **Data for 15:** m.p. 106–108 °C; $[\alpha]_D$ –38.7° (c = 0.375, $CHCl_3$); ν_{max} (neat, cm^{-1}) 3473, 2971, 2891, 1738, 1375, 1092, 1030; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.50-7.30 (5H, m), 5.56 (1H, s), 4.91 (1H, d, *J* = 6.9 Hz), 4.83 (1H, d, *J* = 6.9 Hz), 4.50 (1H, s), 4.34 (1H, dd, *J* = 5.2, 10.3 Hz), 4.17 (1H, dd, *J* = 1.5, 2.2 Hz), 4.06 (1H, t, *J* = 9.6 Hz), 3.91 (1H, dd, *J* = 2.9, 9.5 Hz), 3.88 (1H, t, *J* = 10.3 Hz), 3.73-3.60 (2H, m), 3.58 (3H, s), 3.40 (1H, ddd, *J* = 5.2, 9.6, 10.3 Hz), 2.59 (1H, d, *J* = 1.5 Hz), 1.17 (3H, t, *J* = 7.0 Hz); ^{13}C NMR (300 MHz, $CDCl_3$) δ 137.48, 129.15, 128.36, 126.25, 101.87, 101.50, 94.91, 77.65, 74.89, 70.56, 68.74, 67.13, 63.79, 57.50, 15.16; MS (ES^+) *m/z* 703.2 ($[2M + Na]^+$, 100 %); HRMS (ES) Calcd for $C_{17}H_{24}O_7Na$: 363.1414. Found 363.1416; Anal. Calcd for $C_{17}H_{24}O_7$: C, 59.99; H, 7.11. Found: C, 59.90; H, 7.12

Methyl-4,6-O-benzylidine-3-ethoxymethyl-2-(1,1,2,2,3,3,4,4,4-nonafluoro-butane-sulfonate)-β-D-mannopyranoside (16).



To a solution of **15** (204 mg, 0.6 mmol) in anhydrous THF (8 mL) was added NaH (60 % in mineral oil, 43 mg, 1.1 mmol) and the reaction stirred, under argon, at room temperature for 30 min. Perfluoro-*n*-butylsulfonyl fluoride (290 mg, 0.1 mmol), was added, dropwise, and the reaction stirred for a further 1.5 h. The reaction was quenched with methanol and concentrated *in vacuo*. The crude product was dissolved in CH_2Cl_2, washed with water and the aqueous phase extracted with CH_2Cl_2.The combined organic phase was washed with water, brine, dried (Na_2SO_4) and concentrated *in vacuo*. Purification by silica gel column chromatography (hexane: EtOAc, 2:1) afforded the title compound as a white solid (**16**, 233 mg, 62 %). mp 93–95 °C; $[\alpha]_D$ –56.7° (c = 0.425, $CHCl_3$); ν_{max} (film, cm^{-1}) 2944, 1714, 1410, 1353, 1197, 1143, 1078, 934; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49-7.33 (5H, m), 5.59 (1H, s), 5.15 (1H, d, *J* = 3.0 Hz), 4.87 (1H, d, *J* = 6.9 Hz), 4.78 (1H, d, *J* = 7.4 Hz), 4.62 (1H, s), 4.36 (1H, dd, *J* = 5.0, 10.9 Hz), 4.15 (1H, dd, *J* = 3.0, 9.9 Hz), 3.91 (1H, t, *J* = 9.4 Hz), 3.90 (1H, t, *J* = 10.4 Hz), 3.74-3.59 (2H, m), 3.58 (3H, s), 3.46 (1H, ddd, *J* = 4.5, 9.5, 9.9 Hz), 1.15 (3H, t, *J* = 6.9 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 137.10, 129.29, 128.37, 126.19, 101.93, 99.15, 94.09, 83.83, 77.36, 71.01, 68.44, 67.59, 63.98, 57.49, 14.99; ^{19}F NMR (300 MHz, $CDCl_3$, ref. C_6F_6) δ 81.27, 52.03, 40.89, 35.83.

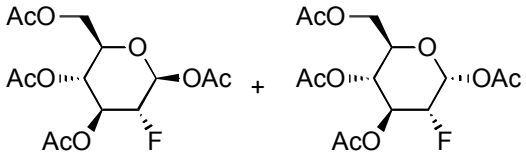
Preparation of 17 and 18.



17 **18**

A solution of **16** (124 mg, 0.20 mmol), 1,10-diaza-4,7,13,16,21,24-hexaoxabicyclo[8,8,8] hexacosan (90 mg, 0.24 mmol) and KF (14 mg, 0.24 mmol) in MeCN (4 mL) was vigorously refluxed, under argon, for 10 min. The reaction was cooled and concentrated *in vacuo*. The crude product was dissolved in CH_2Cl_2, washed with water and the aqueous phase re-extracted with CH_2Cl_2. The combined organic phase was washed with water, brine, dried (anhydrous Na_2SO_4) and concentrated *in vacuo*. Purification by silica gel column chromatography (hexane: Et_2O, 2:1) afforded compound **18** (36 mg, 53 %) and compound **17** (11 mg, 17 %). **Data for methyl-4,6-*O* -benzylidene-3-*O*-ethoxymethyl-2-deoxy-2-fluoro-β-D-glucopyranoside (18):** m.p. 44–46 °C; $[\alpha]_D$ –22.9° (c = 0.431, $CHCl_3$); ν_{max} (film, cm^{-1}) 2972, 2885, 1454, 1383, 1095, 1030; ^1H NMR (300 MHz, $CDCl_3$) δ 7.48-7.32 (5H, m), 5.53 (1H, s), 4.91 (1H, d, *J* = 6.6 Hz), 4.83 (1H, d, *J* = 6.6 Hz), 4.52 (1H, dd, *J* = 3.7, 7.7 Hz), 4.37 (1H, dd, *J* = 5.2, 10.3 Hz), 4.26 (1H, td, *J* = 7.7, 49.3 Hz), 4.09 (1H, td, *J* = 9.2, 15.4 Hz), 3.78 (1H, t, *J* = 10.3 Hz), 3.69-3.57 (3H, m), 3.60 (3H, s), 3.51-3.45 (1H, m); ^{13}C NMR (300 MHz, $CDCl_3$) δ 137.12, 129.29, 128.39, 126.25, 102.30 (d, *J* = 23.7 Hz), 101.68, 95.39, 92.55 (d, *J* = 186.8 Hz), 80.13 (d, *J* = 9.2 Hz), 75.15 (d, *J* = 18.8 Hz), 68.69, 66.38, 63.52, 57.61, 14.90; ^{19}F NMR (300 MHz, $CDCl_3$, ref. C_6F_6) δ –37.30 (ddd, *J* = 4.6, 16.2, 53.3 Hz); MS (ES^+) *m/z* 365.1 ($[M + Na]^+$, 100 %); HRMS (ES) Calcd for $C_{17}H_{23}O_6FNa$: 365.1371. Found 365.1369. **Data for methyl-4,6-*O*-benzylidene-3-*O*-ethoxymethyl-2-deoxy-β-D-erythro-hex-2-enopyranoside (17):** mp 77–79 °C; $[\alpha]_D$ +11.9° (c = 0.118, $CHCl_3$); ν_{max} (film, cm^{-1}) 2927, 2865, 1692, 1590, 1248, 1138, 1094; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50-7.34 (5H, m), 5.61 (1H, s), 5.39 (1H, dd, *J* = 1.5, 2.2 Hz), 5.10 (2H, s), 4.99 (1H, t, *J* = 1.5 Hz), 4.40 (1H, dt, *J* = 2.2, 8.1 Hz), 4.32 (1H, dd, *J* = 4.4, 9.5 Hz), 3.90 (1H, t, *J* = 9.5 Hz), 3.80 (1H, ddd, *J* = 4.4, 8.1, 10.3 Hz), 3.68 (2H, q, *J* = 7.4 Hz), 3.47 (3H, s), 1.22 (3H, t, *J* = 7.4 Hz); ^{13}C NMR (300 MHz, $CDCl_3$) δ 153.03, 137.21, 129.15, 128.37, 126.42, 102.37, 100.06, 99.73, 92.86, 74.76, 69.19, 68.94, 64.73, 54.68, 15.11; MS (ES^+) *m/z* 255.0 ($[M - C_6H_5CH + Na]^+$, 100 %), 233.1 ($[M - C_6H_5CH]^+$, 20 %)

Preparation of FDG tetraacetates [^{19}F]2 and 19.

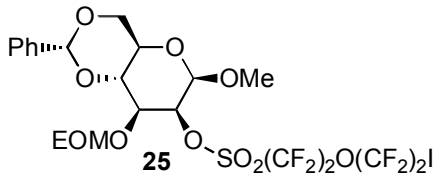


[^{19}F]-2 (36% from **18**) **19** (35% from **18**)

A solution of **18** (59 mg, 0.17 mmol) in 6 N HCl (2 mL) was refluxed at 140°C for 10 min. The reaction was concentrated *in vacuo* and Ac_2O (0.5 mL) and pyridine (1.0 mL) were added. The reaction was stirred at room temperature overnight, concentrated and purified by silica gel column chromatography (hexane: EtOAc 2:1) to afford compounds **[^{19}F]2** (22 mg, 36 %) and **19** (21 mg, 35 %). Data for **2-fluoro-2-deoxy-β-D-glucopyranoside tetraacetate [^{19}F]2:** $[\alpha]_D$ +43° (c = 0.41, CH_2Cl_2), Lit.[6] $[\alpha]_D$ +50°; ν_{max} (film, cm^{-1}) 2957, 1748, 1434, 1369, 1212, 1072, 1035; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.79 (1H, dd, *J* = 3.2, 8.1 Hz), 5.38 (1H, td, *J* = 9.6, 15.5 Hz), 5.08 (1H, t, *J* = 9.6 Hz), 4.45 (1H, ddd, *J* = 8.1, 9.6, 51 Hz), 4.30 (1H, dd, *J* = 4.4, 12.5 Hz), 4.10 (1H, dd, *J* = 2.0, 12.5 Hz), 3.87 (1H, ddd, *J* = 2.0, 4.4, 9.6 Hz), 2.19 (3H, s), 2.10 (3H, s), 2.09 (3H, s), 2.05 (3H, s); ^{13}C NMR (300 MHz, $CDCl_3$) δ 170.72, 170.04, 169.70, 168.99, 91.65 (d, *J* = 24 Hz), 88.60 (d, *J* = 192 Hz), 73.17, 73.12 (d, *J* = 19 Hz), 68.03 (d, *J* = 8 Hz), 61.75, 20.98, 20.86, 20.80, 20.71; ^{19}F NMR (282 MHz, $CDCl_3$, ref. C_6F_6) δ –39.05 (m). Spectroscopic data consistent with those reported previously in the literature.[7] **Data for 2-deoxy-2-fluoro-α-D-pyranoside tetraacetate (19):** $[\alpha]_D$ +119° (c = 0.53, CH_2Cl_2), Lit.[8] $[\alpha]_D$ +147° (c = 1.0, $CHCl_3$); ν_{max} (film, cm^{-1}) 2963, 1746, 1434, 1370, 1213, 1078, 1036; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.44 (1H, d, *J* = 4.4 Hz), 5.50 (1H, td, *J* = 9.6, 12.5 Hz), 5.08 (1H, t, *J* = 9.6 Hz), 4.66 (1H, ddd, *J* = 4.4, 9.6, 49 Hz), 4.30 (1H, dd, *J* = 4.4, 12.5 Hz), 4.13-4.00 (2H, m), 2.21 (3H, s), 2.10 (3H, s), 2.09 (3H, s), 2.05 (3H, s); ^{13}C NMR (300 MHz, $CDCl_3$) δ 170.59, 170.17, 169.50, 168.70, 88.72 (d, *J* = 22 Hz), 86.60 (d, *J* = 195 Hz), 70.97 (d, *J* = 19 Hz), 69.96, 67.83 (d, *J* = 8 Hz), 61.76, 20.88, 20.70, 20.56; ^{19}F NMR (282 MHz, $CDCl_3$, ref. C_6F_6) δ –40.64 (dd, *J* = 10, 48 Hz). Spectroscopic data consistent with those reported previously in the literature.[8]

[6] J. Adamson, A. B. Foster, L. D. Hall, R. N. Johnson, *Carbohydr. Res.* **1970**, *15*, 351.
[7] P. Kovac, H. J. C. Yeh, C. P. J. Glaudemans, *Carbohydr. Res.* **1987**, *169*, 23.
[8] K. Dax, B. I. Glanzer, G. Schulz, H. Vyplel, *Carbohydr. Res.* **1987**, *162*, 13.

Methyl-4,6-O-benzylidine-3-ethoxymethyl-2-(5-iodooctafluoro-3-oxapentane sulfonate)-β-D-mannopyranoside (25).



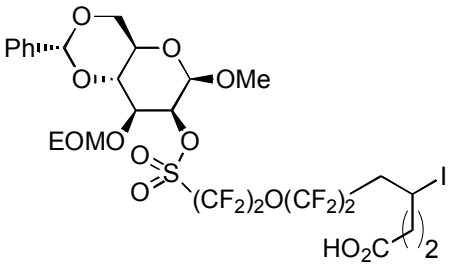
25

To methyl-4,6-*O*-benzylidene-3-*O*-ethoxy methyl-β-D-mannopyranoside (**15**, 315 mg, 0.93 mmol) in anhydrous THF (10 mL) was added NaHMDS (1.0 M solution in THF, 1.1 mL, 1.1 mmol) and the reaction stirred, under argon, at room temperature for 20 min. 5-Iodooctafluoro-3-oxapentanesulfonyl fluoride (437 mg, 1.11 mmol), was added, dropwise, and the reaction stirred for a further 45 min. The reaction was concentrated *in vacuo*, dissolved in Et_2O, washed with saturated K_2CO_3 solution and water and the aqueous phase re-extracted with Et_2O. The combined organic phase was washed with brine, dried (anhydrous $MgSO_4$) and concentrated *in vacuo*. Purification by silica gel column chromatography (hexane: EtOAc, 3:1) afforded the desired product **25** as a white solid (540 mg, 77 %). $[\alpha]_D$ –4.0° (c = 0.028, $CHCl_3$); ν_{max} (film, cm^{-1}) 2971, 2890, 1738, 1411, 1380, 1208, 1146, 1092, 1025, 915; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50-7.30 (5H, m), 5.57 (1H, s), 5.13 (1H, d, *J* = 2.9 Hz), 4.86 (1H, d, *J* = 7.4 Hz), 4.78 (1H, d, *J* = 7.4 Hz), 4.57 (1H, s), 4.34 (1H, dd, *J* = 5.1, 10.3 Hz), 4.12 (1H, dd, *J* = 2.9, 9.6 Hz), 3.94-3.82 (2H, m), 3.74-3.55 (2H, m), 3.56 (3H, s), 3.44 (1H, ddd, *J* = 4.4, 9.5, 10.3 Hz), 1.13 (3H, t, *J* = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.13, 129.28, 128.37, 126.19, 101.92, 99.16, 94.07, 83.61, 77.32, 71.04, 68.44, 67.58, 63.96, 57.50, 15.01; ^{19}F NMR (282 MHz, $CDCl_3$, ref. C_6F_6) δ 96.98, 79.97, 76.42, 48.24; MS (ES^+) *m/z* 769.1 ($[M + Na]^+$, 100 %); Anal. Calcd for $C_{21}H_{23}O_{10}F_8IS$: C, 33.79; H, 3.11. Found: C, 33.86; H, 3.13

General procedure A: the alkylation of iodide 25 to provide acids 26–29.

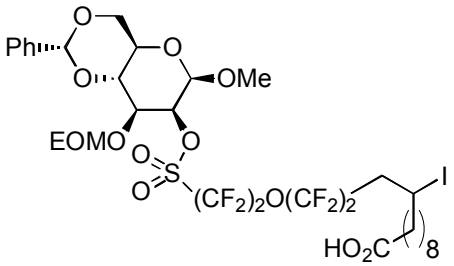
To the iodide **25** and the carboxylic acid (1.2 equiv) in MeCN was added H_2O followed by $NaHCO_3$ (1.2 equiv) and $Na_2S_2O_4$ (85 %, 1.2 equiv) and the reaction stirred at room temperature for 30 min. The reaction was concentrated *in vacuo*, dissolved in Et_2O (100 mL), washed with water (100 mL) and the aqueous phase re-extracted with Et_2O (50 mL). The combined organic phase was washed with brine (100 mL), dried ($MgSO_4$), concentrated in vacuo and purified as described.

Methyl-4,6-*O*-benzylidine-3-ethoxymethyl-2-(3-oxa-6,6,7,7,9,9,10,10-octafluoro-4-iodo-decanoic acid-10-sulfonate)-β-D-mannopyranoside (26).



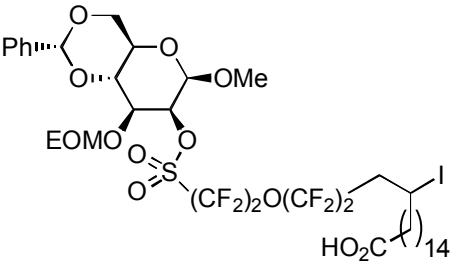
Using the general procedure **A** with the following amounts: iodide **25** (400 mg, 0.54 mmol) and 4-pentenoic acid (56 mg, 0.56 mmol) in CH_3CN (4 mL), H_2O (2 mL) with $NaHCO_3$ (59 mg, 0.70 mol) and $Na_2S_2O_4$ (85 %, 140 mg, 0.70 mmol). Purification by silica gel column chromatography eluting with EtOAc: hexane (1: 2) afforded the desired product **26** as a colourless oil (305 mg, 67 %). ν_{max} (film, cm^{-1}) 2975, 2878, 1714, 1410, 1192, 1148, 1093, 1025, 920; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50-7.25 (5H, m), 5.52 (1H, s), 5.17 (1H, d, *J* = 2.9 Hz), 4.86 (1H, d, *J* = 7.4 Hz), 4.80 (1H, d, *J* = 7.4 Hz), 4.60 (1H, s), 4.34-4.24 (2H, m), 4.09 (1H, dd, *J* = 2.9 Hz), 3.90-3.77 (2H, m), 3.70-3.50 (2H, m), 3.50 (3H, s), 3.45-3.32 (1H, m), 2.98-2.28 (4H, m), 2.18-1.90 (2H, m), 1.05 (3H, t, *J* = 7.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.32, 137.12, 129.28, 128.36, 126.20, 101.93, 99.19, 94.02, 83.66, 77.28, 71.10, 68.43, 67.61, 64.01, 57.54, 41.37, 35.14, 34.21, 19.09, 14.98; ^{19}F NMR (282 MHz, $CDCl_3$, ref. C_6F_6) δ 79.74, 72.97, 47.56, 43.89; MS (ES^-) *m/z* 844.7 ($[M]^-$, 60 %).

Methyl-4,6-*O*-benzylidine-3-ethoxymethyl-2-(3-oxa-12,12,13,13,15,15,16,16-octa fluoro-10-iodo-hexadecanoic acid-16-sulfonate)-β-D-mannopyranoside (27).



Using the general procedure A with the following amounts: iodide **25** (300 mg, 0.40 mmol) and undecylenic acid (89 mg, 0.48 mmol) in CH_3CN (2 mL), H_2O (1 mL) with $NaHCO_3$ (41 mg, 0.48 mmol) and $Na_2S_2O_4$ (85 %, 97 mg, 0.48 mmol). Purification by silica gel column chromatography twice, first eluting with CH_2Cl_2:CH_3OH (98:2), secondly eluting with CH_2Cl_2: CH_3OH (99: 1) afforded the desired product **27** as a colorless oil (200 mg, 54 %). ν_{max} (film, cm^{-1}) 2931, 2858, 1709, 1410, 1192, 1147, 1093, 1025, 919; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50-7.31 (5H, m), 5.58 (1H, s), 5.15 (1H, d, *J* = 2.9 Hz), 4.85 (1H, d, *J* = 7.4 Hz), 4.79 (1H, d, *J* = 7.4 Hz), 4.61 (1H, s), 4.40-4.25 (2H, m), 4.17 (1H, dd, *J* = 2.9, 10.3 Hz), 3.95-3.85 (2H, m), 3.75-3.60 (2H, m), 3.58 (3H, s), 3.51-3.42 (1H, m), 3.00-2.65 (2H, m), 2.35 (2H, t, *J* = 7.4 Hz), 1.90-1.30 (14H, m), 1.15 (3H, t, *J* = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.22, 136.01, 128.10, 128.18, 126.46, 102.20, 99.47, 94.26, 83.84, 77.58, 71.39, 68.71, 67.90, 64.25, 57.73, 41.65, 40.69, 34.31, 29.86, 29.53, 29.49, 29.37, 28.82, 25.04, 21.48, 15.23; ^{19}F NMR (282 MHz, $CDCl_3$, ref. C_6F_6) δ 79.78, 74.37, 47.92, 43.70; MS (ES^-) *m/z* 929.3 ($[M]^-$, 100); HRMS (ES+) Calcd for $C_{32}H_{43}O_{12}F_8ISNa$: 953.1284. Found 953.1266.

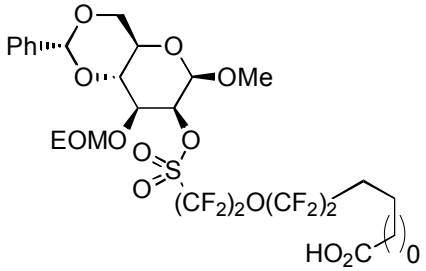
Methyl-4,6-*O*-benzylidine-3-ethoxymethyl-2-(3-oxa-18,18,19,19,21,21,22,22-octafluoro-16-iodo-docosanoic acid-22-sulfonate)-β-D-mannopyranoside (28).



Using the general procedure **A** with the following amounts: iodide **25** (1.0 g, 1.34 mmol) and 16-heptadecenoic acid (378 mg, 1.41 mmol) in CH_3CN (60 mL), H_2O (30 mL) with $NaHCO_3$ (135 mg, 1.61 mmol) and $Na_2S_2O_4$ (85 %, 322 mg, 1.61 mmol). The reaction remained cloudy and was stirred at room temperature for 1 h. Purification by silica gel column chromatography, eluting with EtOAc:hexane (1:3)

afforded the desired product **28** as a colorless oil (230 mg, 17 %). ν_{max} (film, cm^{-1}) 2927, 2855, 1725, 1412, 1194, 1149, 1096, 1026, 921; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50-7.31 (5H, m), 5.58 (1H, s), 5.15 (1H, d, *J* = 2.9 Hz), 4.86 (1H, d, *J* = 7.4 Hz), 4.80 (1H, d, *J* = 7.4 Hz), 4.63 (1H, s), 4.40-4.28 (2H, m), 4.17 (1H, dd, *J* = 2.9, 10.3 Hz), 3.97-3.87 (2H, m), 3.75-3.62 (2H, m), 3.60 (3H, s), 3.52-3.42 (1H, m), 3.00-2.70 (2H, m), 2.37 (2H, t, *J* = 7.4 Hz), 1.85-1.40 (4H, m), 1.30-1.10 (22H, m), 1.15 (3H, t, *J* = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.04, 137.56, 129.67, 128.76, 126.62, 102.36, 99.64, 94.47, 84.00, 77.59, 71.55, 68.87, 68.06, 64.41, 57.91, 42.02, 41.82, 41.62, 40.91, 34.48, 30.17, 30.14, 30.10, 29.99, 29.93, 29.81, 29.65, 29.10, 25.32, 21.79, 15.40; ^{19}F NMR (282 MHz, $CDCl_3$, ref. C_6F_6) δ 80.20, 73.14, 47.87, 43.76; MS (ES^-) *m/z* 1013.1 ($[M]^-$), 1127.5 ($[M + TFA]^-$).

Methyl-4,6-*O*-benzylidine-3-ethoxymethyl-2-(3-oxa-4,4,5,5,7,7,8,8-octafluoro-octanoic acid-8-sulfonate)-β-D-mannopyranoside (29).

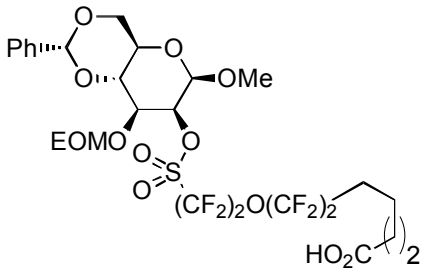


Using the general procedure **A** with the following amounts: iodide **25** (1.0 g, 1.34 mmol) and acrylic acid (101 mg, 1.41 mmol) in CH_3CN (8 mL), H_2O (4 mL) with $NaHCO_3$ (135 mg, 1.61 mmol) and $Na_2S_2O_4$ (85 %, 322 mg, 1.61 mmol). Purification by silica gel column chromatography, eluting with EtOAc: hexane (1: 4) to EtOAc: hexane (1: 0) afforded the desired product **29** as a colorless oil (419 mg, 38 %). ν_{max} (film, cm^{-1}) 2972, 1722, 1412, 1193, 1148, 1096, 1026, 921; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52-7.32 (5H, m), 5.58 (1H, s), 5.15 (1H, d, *J* = 2.9 Hz), 4.85 (1H, d, *J* = 7.4 Hz), 4.80 (1H, d, *J* = 7.4 Hz), 4.61 (1H, s), 4.30 (1H, q, *J* = 5.2 Hz), 4.16 (1H, dd, *J* = 2.9, 10.3 Hz), 3.90-3.78 (2H, m), 3.75-3.62 (2H, m), 3.58 (3H, s), 3.51-3.42 (1H, m), 2.68 (2H, t, *J* = 7.4 Hz), 2.55-2.36 (2H, m), 1.65-1.15 (3H, t, *J* = 7.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.63, 137.11, 129.31, 128.38, 126.20, 101.92, 99.19, 93.93, 83.61, 77.23, 71.09, 68.41, 67.58, 64.01, 57.54, 25.97, 25.69, 14.94; ^{19}F NMR (282 MHz, $CDCl_3$, ref. C_6F_6) δ 79.82, 73.56, 47.73, 43.27; MS (ES^-) *m/z* 804.8 ($[M + TFA]^-$, 100 %), 1382.20 ($[2M]^-$, 20 %); HRMS (ES^+) Calcd for $C_{24}H_{28}O_{12}F_8IS$ Na: 715.1066. Found 715.1068.

General procedure B: the reduction of acids 26–28 to provide acids 30–32.

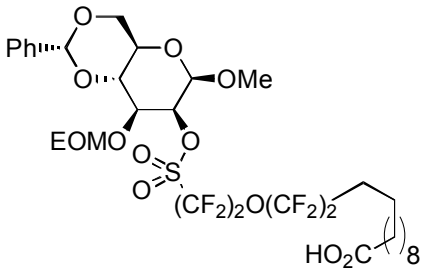
To acid (**26–28**) in Et_2O was added zinc (99.998 %, 100 mesh, 6 equiv) and AcOH and the reaction refluxed, under argon, for 3 h (bath temp = 80 °C). The reaction was allowed to cool to room temperature and filtered through celite, washing with Et_2O (3 x 30 mL). The filtrate and combined washings were concentrated to dryness *in vacuo* and purified as described.

Methyl-4,6-*O*-benzylidine-3-ethoxymethyl-2-(3-oxa-6,6,7,7,9,9,10,10-octafluoro-decanoic acid-10-sulfonate)-β-D-mannopyranoside (30).



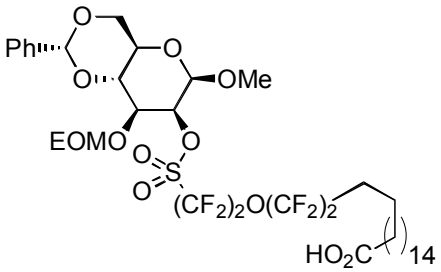
Using the general procedure **B** with the following amounts: acid **26** (300 mg, 0.36 mmol) zinc (93 mg, 1.42 mmol) in Et_2O (2 mL) and AcOH (1 mL). Purification by silica gel column chromatography, eluting with EtOAc: hexane (1: 3) afforded the desired product **30** as a colourless oil (70 mg, 27 %). ν_{max} (film, cm^{-1}) 2932, 1723, 1410, 1192, 1149, 1115, 1027, 922; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50-7.31 (5H, m), 5.58 (1H, s), 5.15 (1H, d, *J* = 2.9 Hz), 4.87 (1H, d, *J* = 7.4 Hz), 4.79 (1H, d, *J* = 7.4 Hz), 4.63 (1H, s), 4.36 (1H, q, *J* = 5.2 Hz), 4.17 (1H, dd, *J* = 2.9, 10.3 Hz), 3.95-3.86 (2H, m), 3.75-3.60 (2H, m), 3.58 (3H, s), 3.52-3.43 (1H, m), 2.42 (2H, t, *J* = 7.4 Hz), 2.20-2.00 (2H, m), 1.80-1.60 (4H, m), 1.15 (3H, t, *J* = 7.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.65, 137.11, 129.29, 128.37, 126.20, 101.92, 99.19, 93.99, 83.50, 77.27, 71.08, 68.42, 67.60, 64.00, 57.54, 33.55, 30.29, 24.16, 20.07, 14.97; ^{19}F NMR (282 MHz, $CDCl_3$, ref. C_6F_6) δ 79.72, 73.61, 47.91, 43.70; MS (ES^-) *m/z* 719.0 ($[M]^-$, 100 %), 832.9 ($[M + TFA]^-$, 40 %); HRMS (ES^+) Calcd for $C_{26}H_{32}O_{12}F_8SNa$: 743.1379. Found 743.1365.

Methyl-4,6-*O*-benzylidine-3-ethoxymethyl-2-(3-oxa-12,12,13,13,15,15,16,16-octafluoro-hexadecanoic acid-16-sulfonate)-β-D-mannopyranoside (31).



Using the general procedure **B** with the following amounts: acid **27** (190 mg, 0.20 mmol) zinc (41 mg, 0.61 mmol) in Et_2O (2 mL) and AcOH (1 mL). Purification by silica gel column chromatography, eluting with EtOAc: hexane (1: 3) afforded the desired product **31** as a colourless oil (97 mg, 59 %). ν_{max} (film, cm^{-1}) 2929, 2858, 2858, 1710, 1411, 1147, 1093, 1025, 994, 918; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50-7.31 (5H, m), 5.58 (1H, s), 5.15 (1H, d, *J* = 2.9 Hz),), 4.85 (1H, d, *J* = 7.4 Hz), 4.79 (1H, d, *J* = 7.4 Hz), 4.63 (1H, s), 4.35-4.25 (1H, q, *J* = 5.8 Hz), 4.17 (1H, dd, *J* = 2.9, 10.3 Hz), 3.95-3.86 (2H, m), 3.75-3.60 (2H, m), 3.58 (3H, s), 3.51-3.42 (1H, m), 2.35 (2H, t, *J* = 7.4 Hz), 2.15-1.90 (2H, m), 1.65-1.25 (14H, m), 1.10 (3H, t, *J* = 7.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.34, 129.39, 128.48, 126.34, 102.08, 99.38, 94.14, 83.57, 77.46, 71.31, 68.59, 67.78, 64.11, 57.58, 34.22, 30.89, 30.67, 30.45, 29.57, 29.45, 29.36, 29.30, 24.95, 20.56, 15.09; ^{19}F NMR (282 MHz, $CDCl_3$, ref. C_6F_6) δ 79.8, 74.2, 47.9, 43.5; MS (ES^-) *m/z* 803.3 ($[M]^-$, 100 %); HRMS (ES^+) Calcd for $C_{32}H_{44}O_{12}F_8SNa$: 827.2318. Found 827.2299.

Methyl-4,6-*O*-benzylidine-3-ethoxymethyl-2-(3-oxa-18,18,19,19,21,21,22,22-octafluoro-docosanoic acid-22-sulfonate)-β-D-mannopyranoside (32).

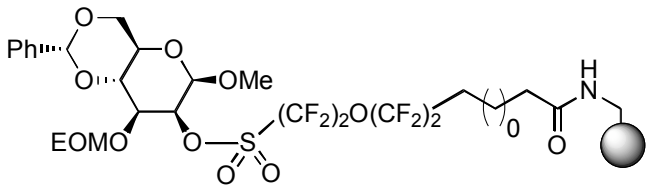


Using the general procedure **B** with the following amounts: acid **28** (200 mg, 0.20 mmol) zinc (80 mg, 1.23 mmol) in Et_2O (4 mL) and AcOH (2 mL). Purification by silica gel column chromatography, eluting with EtOAc:hexane (1:3) afforded the desired product **32** as a colourless oil (132 mg, 75 %). ν_{max} (film, cm^{-1}) 2926, 2854, 1711, 1412, 1191, 1149, 1096, 1027, 920; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50-7.35 (5H, m), 5.60 (1H, s), 5.15 (1H, d, *J* = 2.9 Hz), 4.86 (1H, d, *J* = 7.4 Hz), 4.79 (1H, d, *J* = 7.4 Hz), 4.61 (1H, s), 4.36 (1H, q, *J* = 5.1 Hz), 4.20-4.12 (1H, m), 3.95-3.85 (2H, m), 3.75-3.60 (2H, m), 3.58 (3H, s), 3.51-3.42 (1H, m), 2.37 (2H, t, *J* = 7.4 Hz), 1.70-1.55 (4H, m), 1.40-1.20 (26H, m), 1.15 (3H, t, *J* = 7.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.40, 137.07, 129.51, 128.60, 126.45, 102.19, 99.49, 94.28, 83.70, 77.58, 71.43, 68.71, 67.89, 64.29, 57.78, 34.46, 31.02, 30.80, 30.58, 30.04, 29.99, 29.84, 29.80, 29.65, 29.49, 25.17, 21.43, 20.70, 15.21; ^{19}F NMR (282 MHz, $CDCl_3$, ref. C_6F_6) δ 80.01, 74.08, 47.96, 43.34; MS (ES^-) *m/z* 887.1 ($[M]^-$, 40 %); HRMS (ES^+) Calcd for $C_{38}H_{56}O_{12}F_8SNa$: 911.3257. Found 911.3275.

General procedure C: coupling of acids 29–32 to provide resins 33–36.

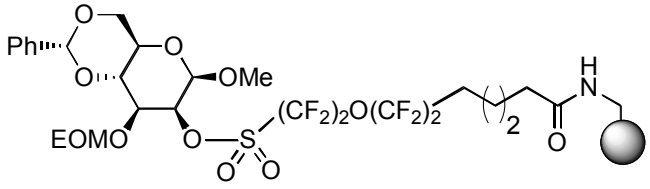
To amino-methylated polystyrene (NovaBiochem, 50-100 mesh, loading: 1.5 mmol/g) and acid (**29–32**, 1.3 equiv) in anhydrous CH_2Cl_2 was added *N,N*-diisopropylethylamine (2.6 equiv) followed by diphenylphosphoryl chloride (1.3 equiv). The reaction was stirred gently, under argon, at room temperature for 18 h. The resin was removed by filtration, washed with CH_2Cl_2 (3 x 10 mL), CH_3OH (3 x 10 mL), Et_2O (3 x 10 mL) and dried in vacuo, at 40 °C for 48 h.

Methyl-4,6-*O*-benzylidine-3-ethoxymethyl-2-(3-oxa-4,4,5,5,7,7,8,8-octafluoro-octanoic acid-8-sulfonate)-β-D-mannopyranoside polystyryl amide (33).



Using general procedure **C** with the following amounts: amino-methylated polystyrene (145 mg, 0.218 mmol), acid **29** (200 mg, 0.289 mmol) in CH_2Cl_2 (2 mL), *N,N*-diisopropylethylamine (75 mg, 100 μL, 0.579 mmol) and diphenylphosphoryl chloride (68 mg, 55 μL, 0.289 mmol). This gave the title resin **33** as a pale yellow solid (283 mg, 94 %). ν_{max} (on-bead, cm^{-1}) 2970, 1739, 1418, 1366, 1216, 1093; ^{19}F NMR (282 MHz, $CDCl_3$, ref. $CFCl_3$) δ –81.84, –87.79, –113.67, –117.96; Loading Calcd: 0.75 mmol/g. Found (F elemental analysis) 0.80 mmol/g.

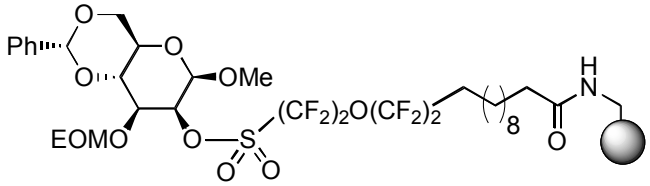
Methyl-4,6-*O*-benzylidine-3-ethoxymethyl-2-(3-oxa-6,6,7,7,9,9,10,10-octafluoro-decanoic acid-10-sulfonate)-β-D-mannopyranoside polystyryl amide (34).



Using general procedure **C** with the following amounts: amino-methylated polystyrene (45 mg, 0.067 mmol), acid **30** (58 mg, 0.289 mmol) in CH_2Cl_2 (1 mL), *N,N*-diisopropylethylamine (21 mg, 28 μL, 0.162 mmol) and diphenylphosphoryl chloride (19 mg, 16 μL, 0.081 mmol). This gave the title resin **34** as a pale yellow solid (87 mg, 99 %). ν_{max} (on-bead, cm^{-1}) 2931, 1662, 1493, 1452, 1410, 1275, 1146, 1094, 1025,

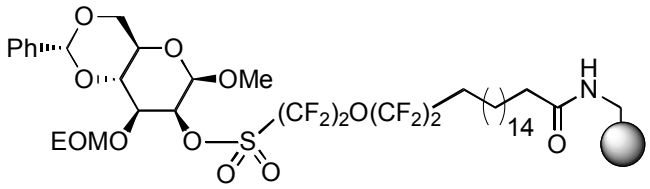
919; ^{19}F NMR (282 MHz, $CDCl_3$, ref. $CFCl_3$) δ –82.01, –88.13, –113.86, –118.23; Loading Calcd: 0.73 mmol/g. Found (F elemental analysis) 0.55 mmol/g.

Methyl-4,6-*O*-benzylidine-3-ethoxymethyl-2-(3-oxa-12,12,13,13,15,15,16,16-octafluoro-hexadecanoic acid-16-sulfonate)-β-D-mannopyranoside polystyryl amide (35).



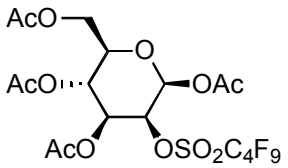
Using general procedure C with the following amounts: amino-methylated polystyrene (50g, 0.07 mmol), acid 31 (80 mg, 0.10 mmol) in CH_2Cl_2 (1 mL), *N,N*-diisopropylethylamine (35 μL, 0.20 mmol) and diphenylphosphoryl chloride (24 mg, 0.10 mmol). This gave the title resin 35 as a pale yellow solid (103 mg, 90 %). ν_{max} (on-bead, cm^{-1}) 2925, 1662, 1493, 1453, 1411, 1146, 1095, 1025; ^{19}F NMR (282 MHz, $CDCl_3$, ref. $CFCl_3$) δ –82.06, –88.14, –113.93, –118.34; Theoretical loading calcd: 0.69 mmol/g. Found (F elemental analysis) 0.59 mmol/g.

Methyl-4,6-*O*-benzylidine-3-ethoxymethyl-2-(3-oxa-18,18,19,19,21,21,22,22-octafluoro-docosanoic acid-22-sulfonate)-β-D-mannopyranoside polystyryl amide (36).

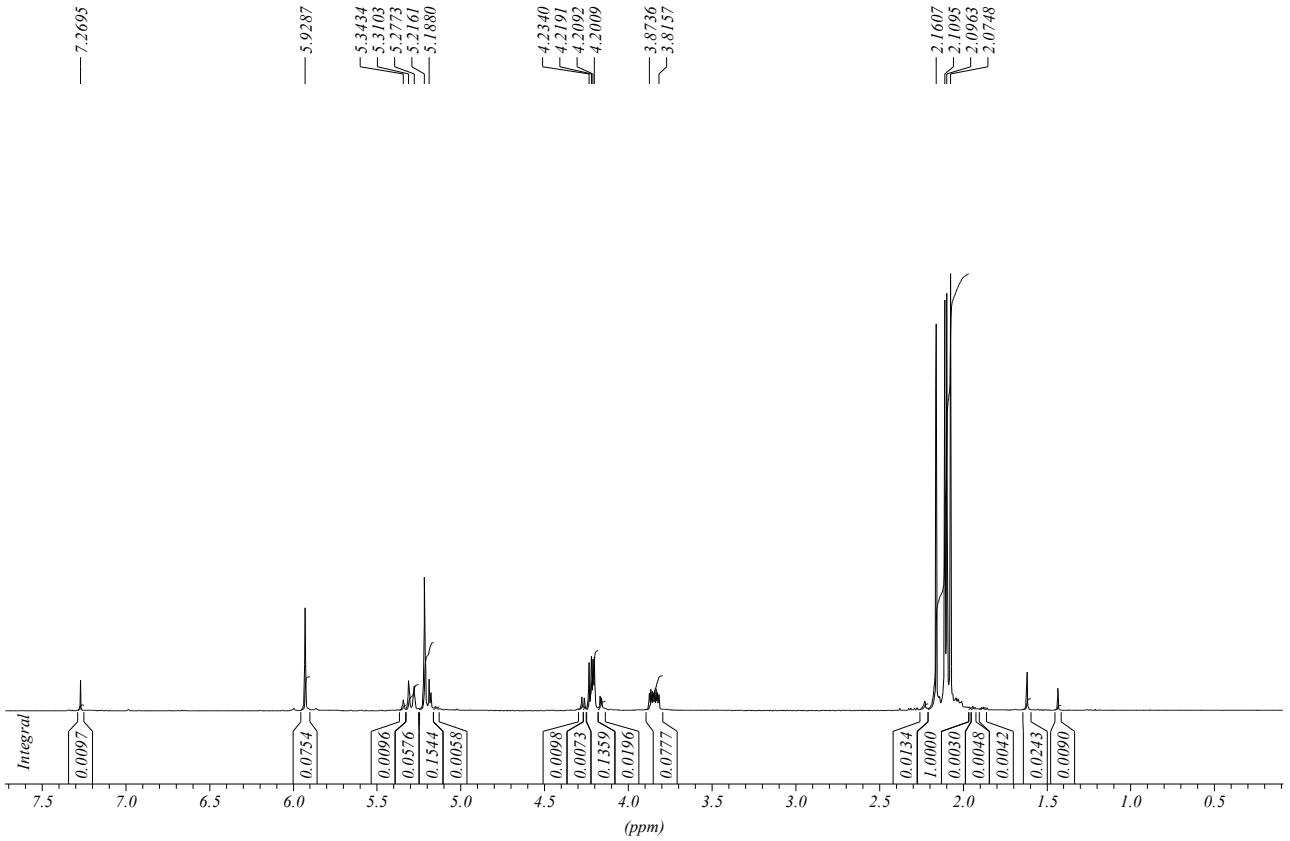


Using general procedure **C** with the following amounts: amino-methylated polystyrene (62 mg, 0.093 mmol), acid **32** (108 mg, 0.121 mmol) in CH_2Cl_2 (3 mL), *N,N* -diisopropylethylamine (42μL, 0.243 mmol) and diphenylphosphoryl chloride (29 mg, 0.121 mmol). This gave the title resin as a pale yellow solid (**36**, 136 mg, 86 %). ν_{max} (on-bead, cm^{-1}) 2925, 1662, 1493, 1453, 1411, 1146, 1095, 1025; ^{19}F NMR (282 MHz, $CDCl_3$, ref. $CFCl_3$) δ –82.06, –88.14, –113.93, –118.34; Theoretical loading calcd: 0.65 mmol/g. Found (F elemental analysis) 0.52 mmol/g.

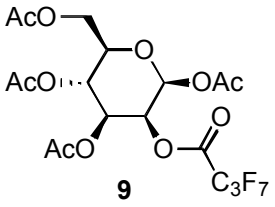
^{1}H NMR Compound **8**



8



^{1}H NMR Compound **9**



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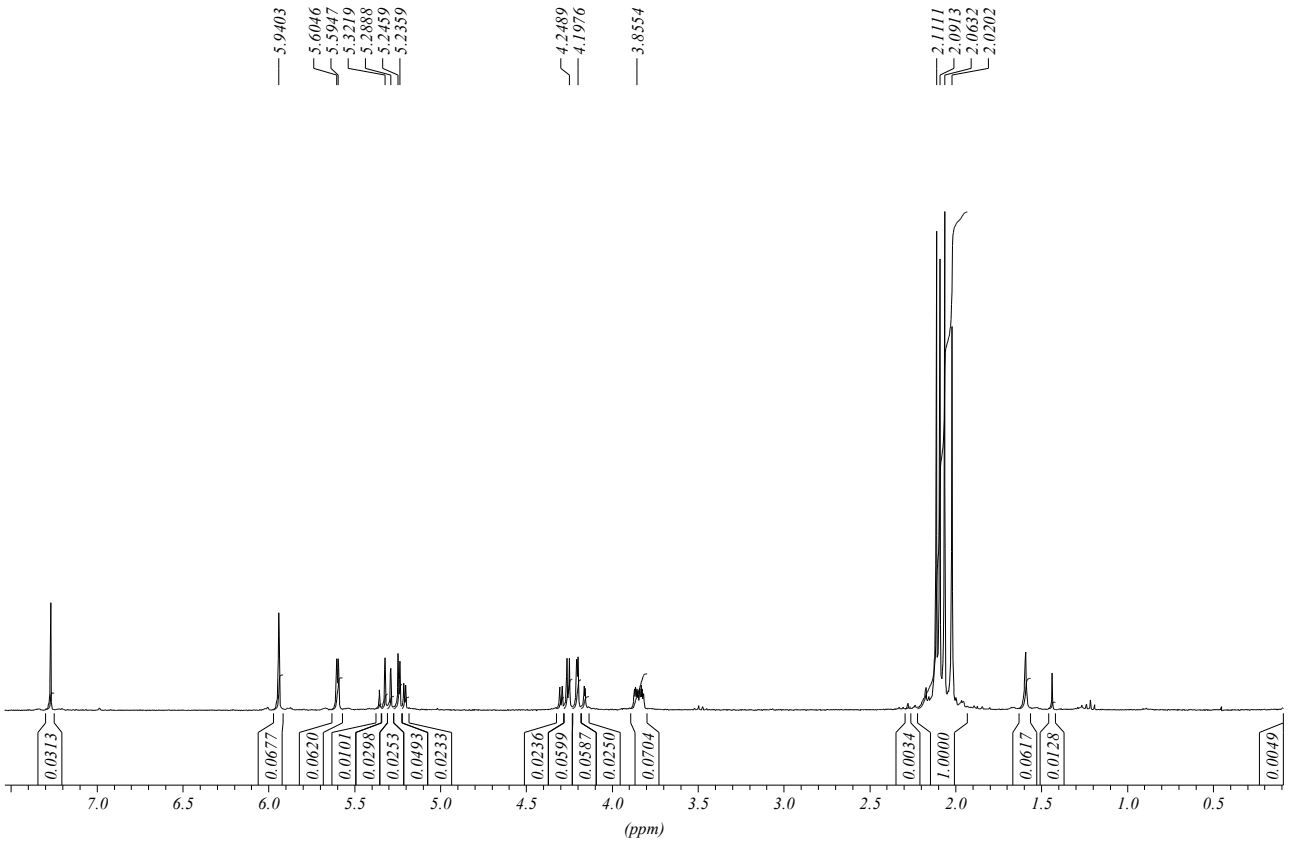
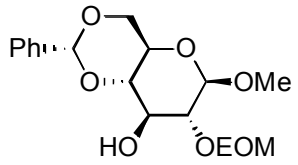


^{1}H NMR Compound **12**



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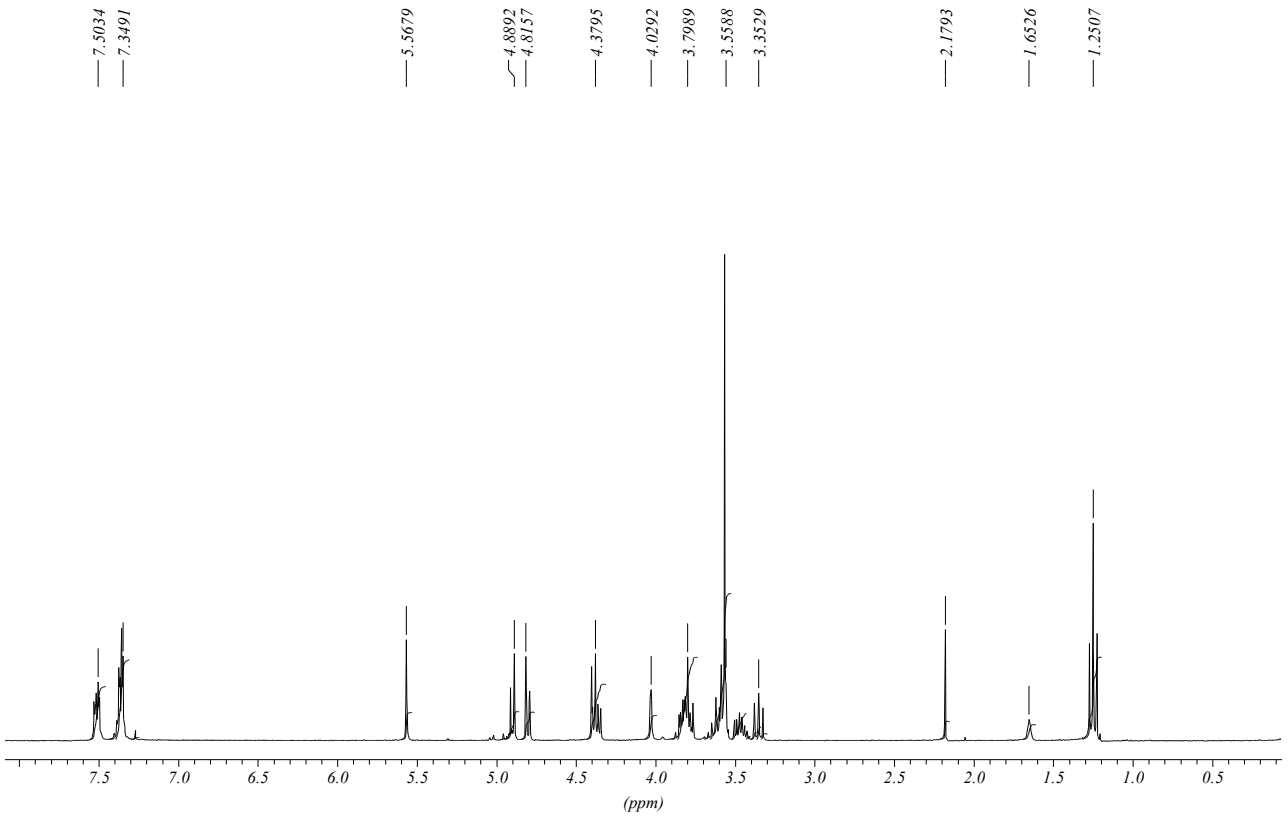
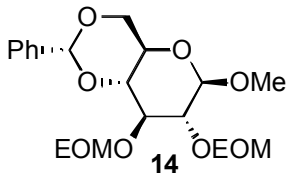
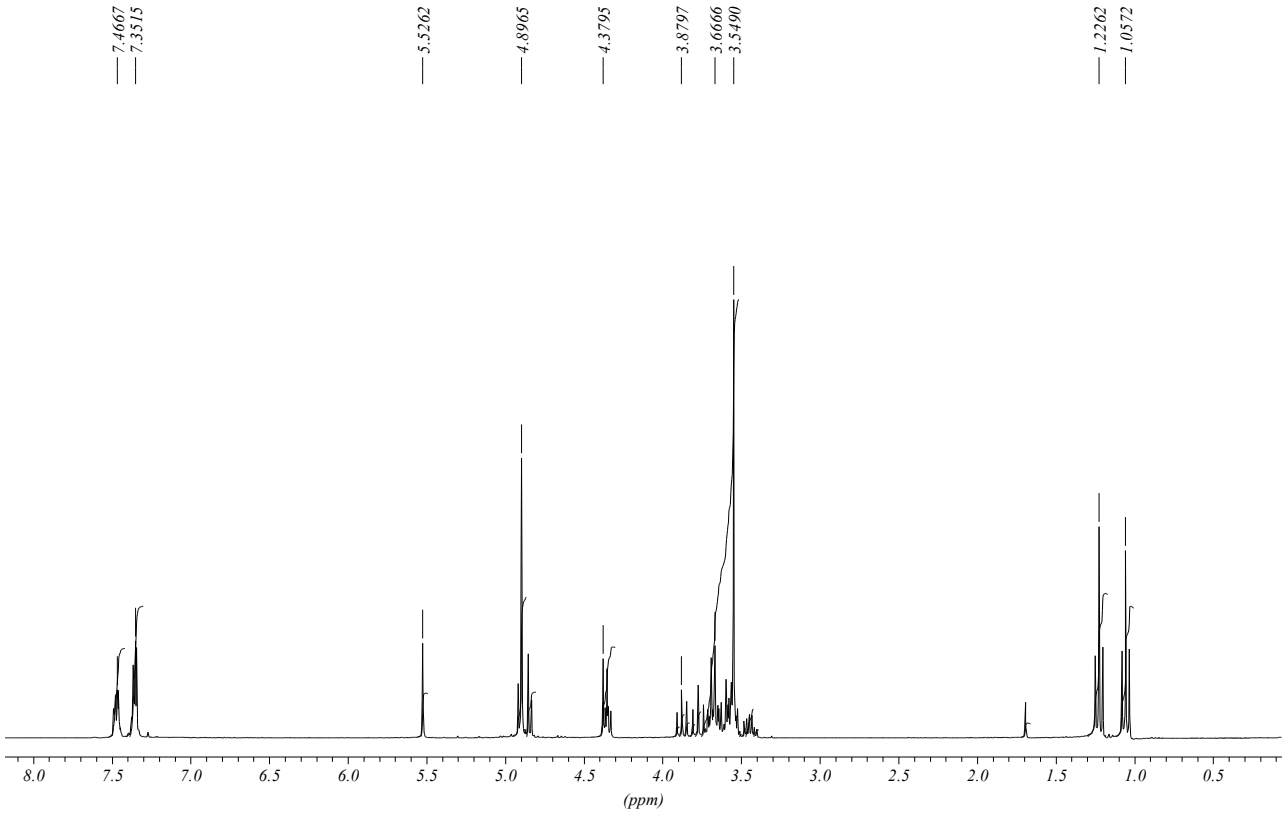


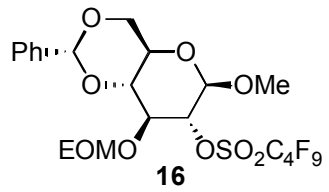
^{1}H NMR Compound 14



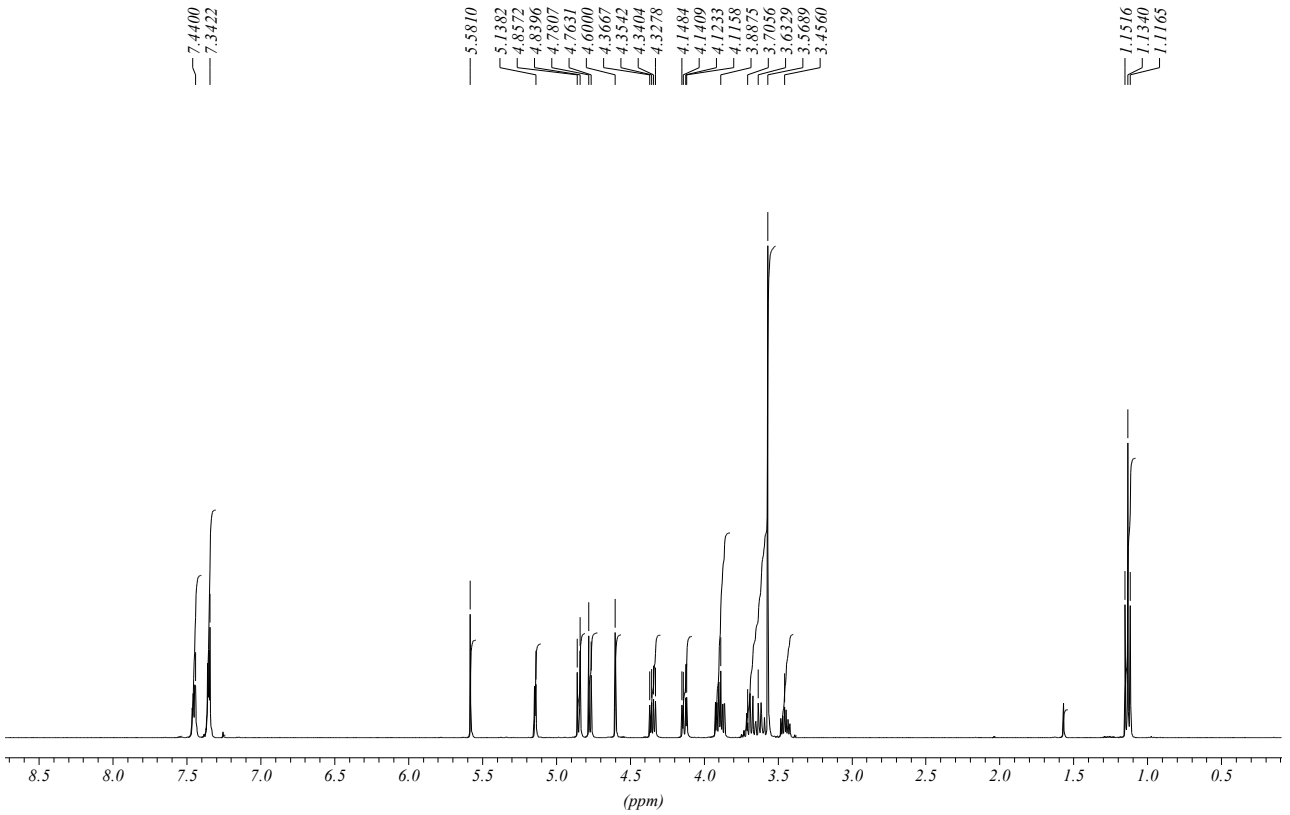
14



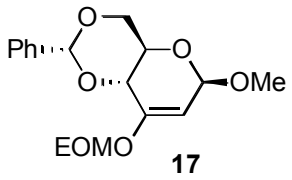
^{1}H NMR Compound 16



16



^{1}H NMR Compound **17**



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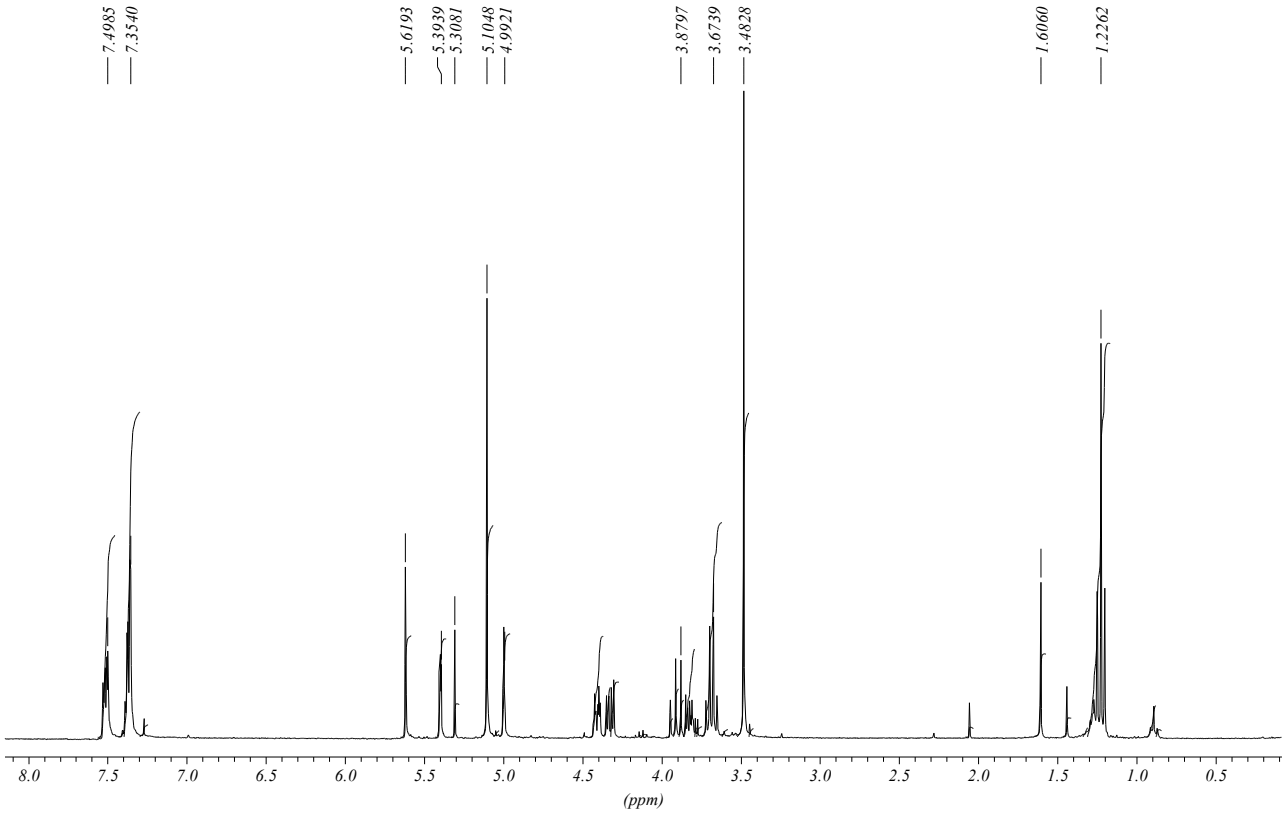
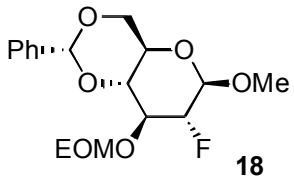
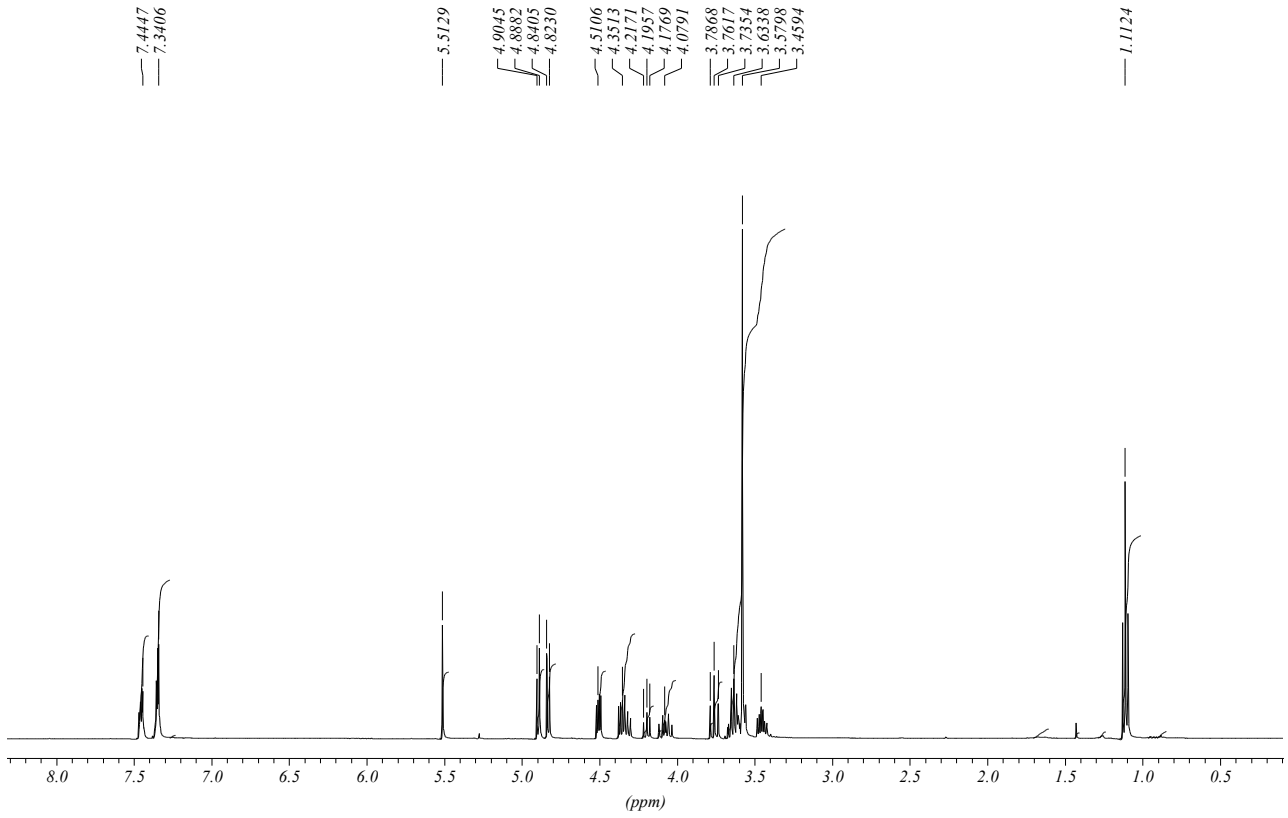


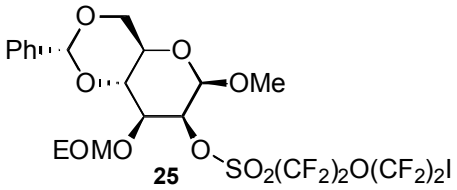
^{1}H NMR Compound **18**



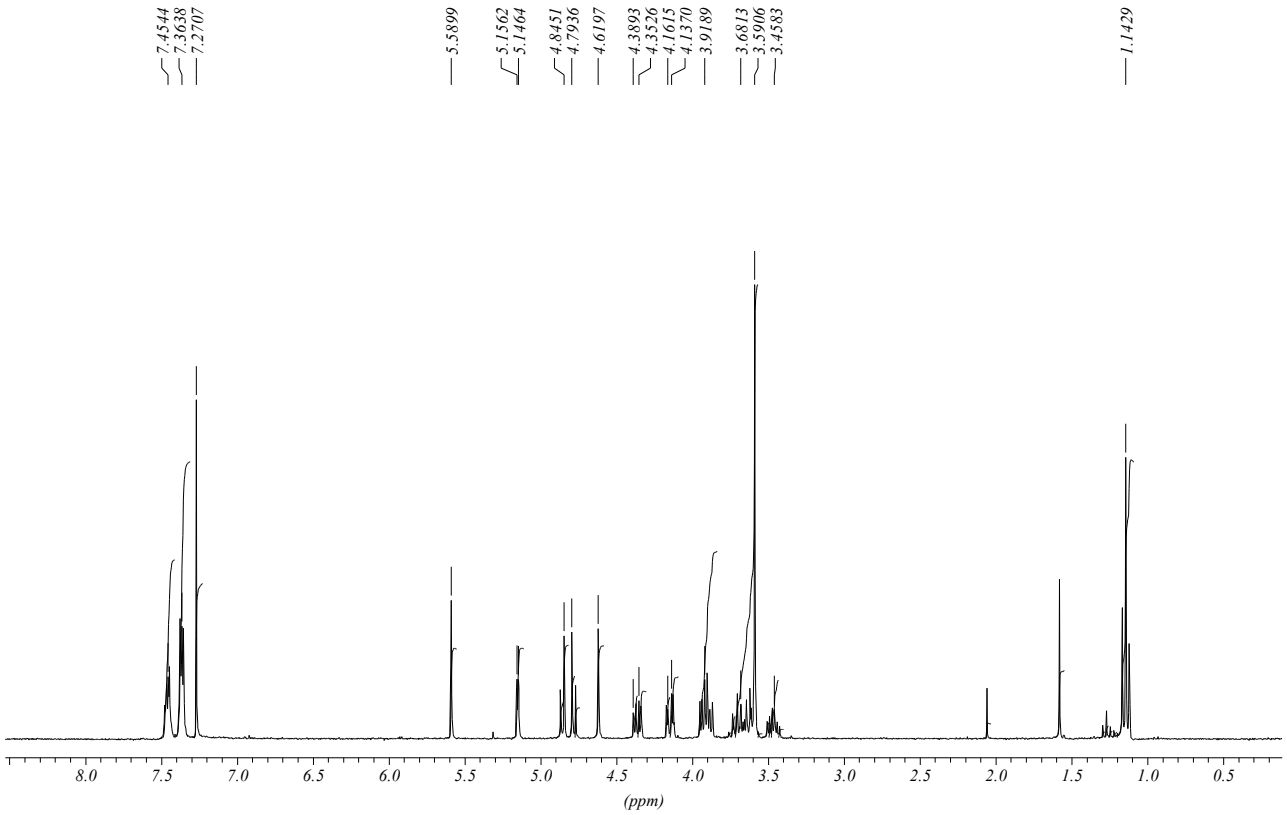
18



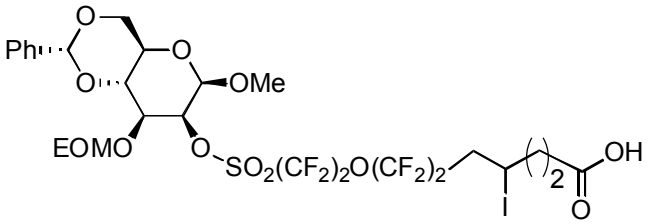
^{1}H NMR Compound ***25***

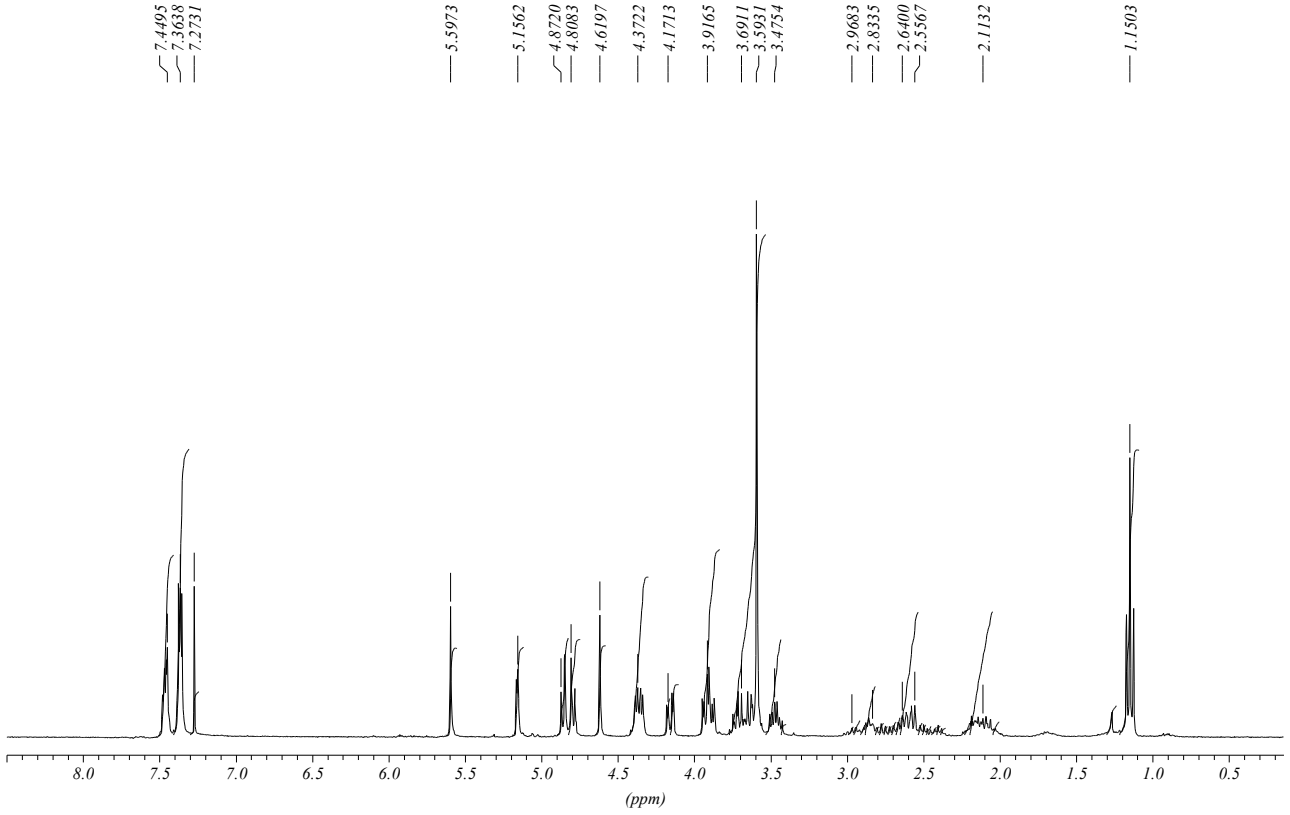


25

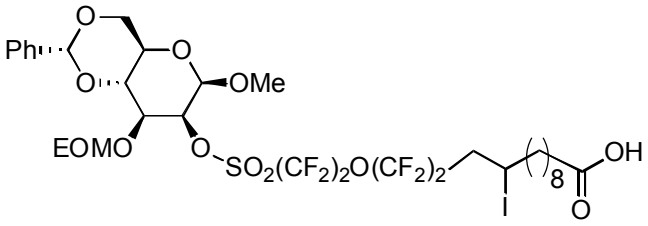


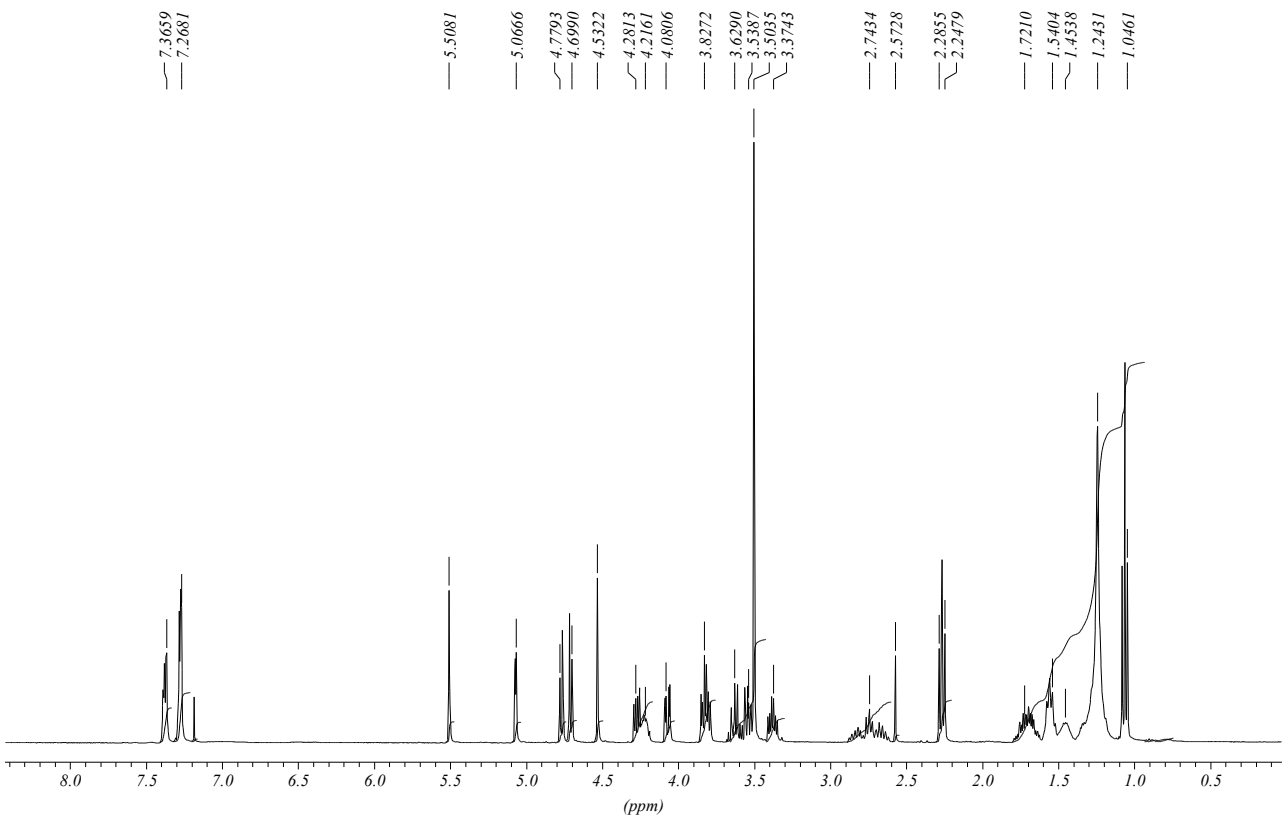
26


Ph
O
O
O
OMe
EOMO
O
SO2(CF2)2O(CF2)2
2
OH
I
O

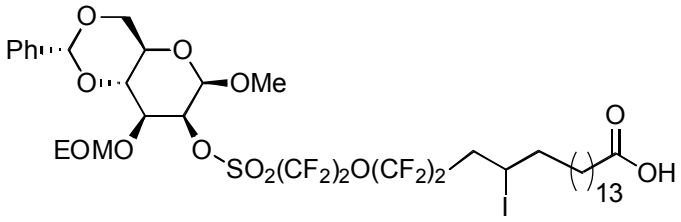

7.4495
7.3638
7.2731
5.5973
5.1562
4.8720
4.8083
4.6197
4.3722
4.1713
3.9165
3.6911
3.5931
3.4754
2.9683
2.8335
2.6400
2.5567
2.1132
1.1503
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
(ppm)

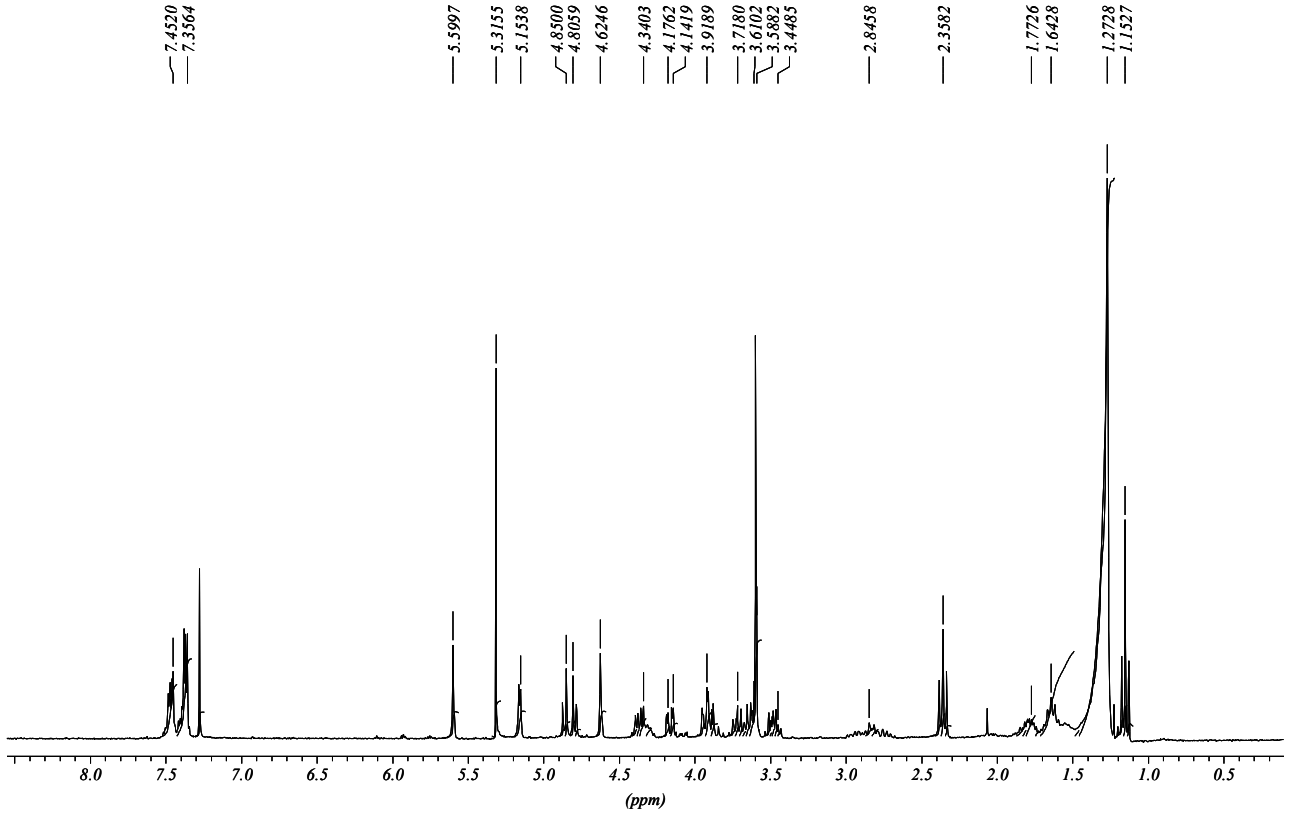
^{1}H NMR Compound **27**



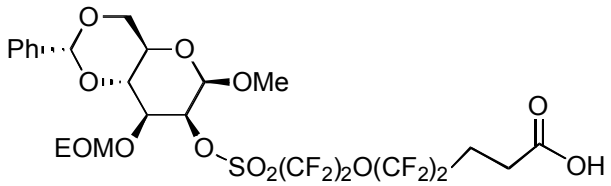


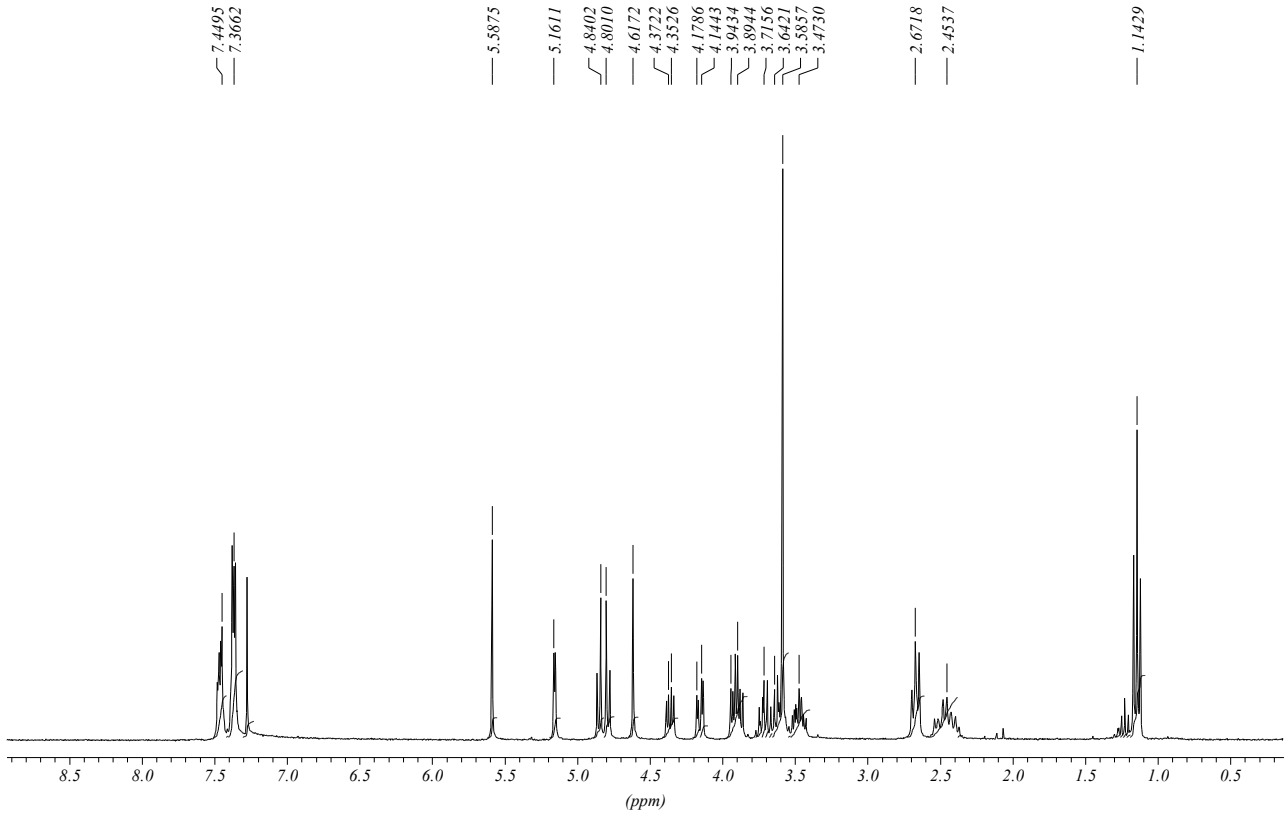
^{1}H NMR Compound 2**8**



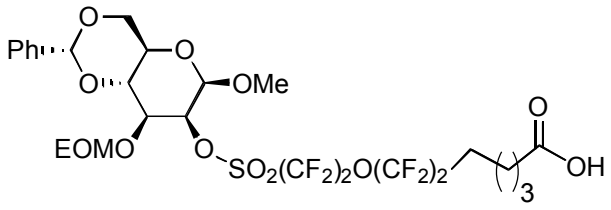


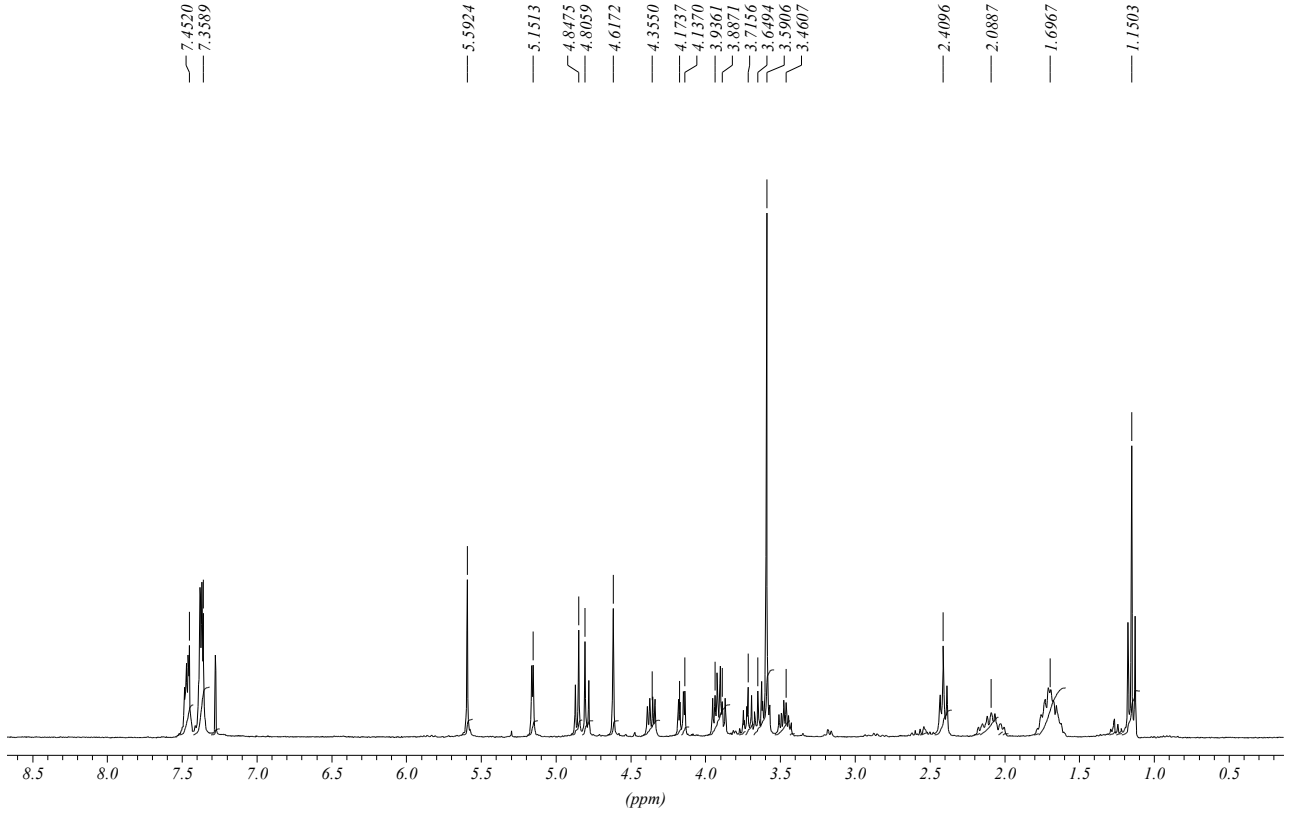
^{1}H NMR Compound **29**



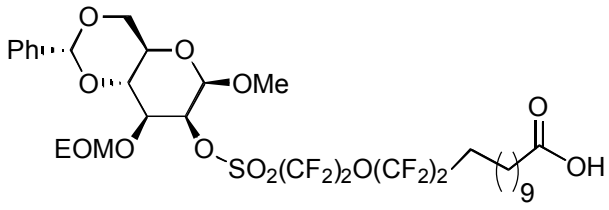


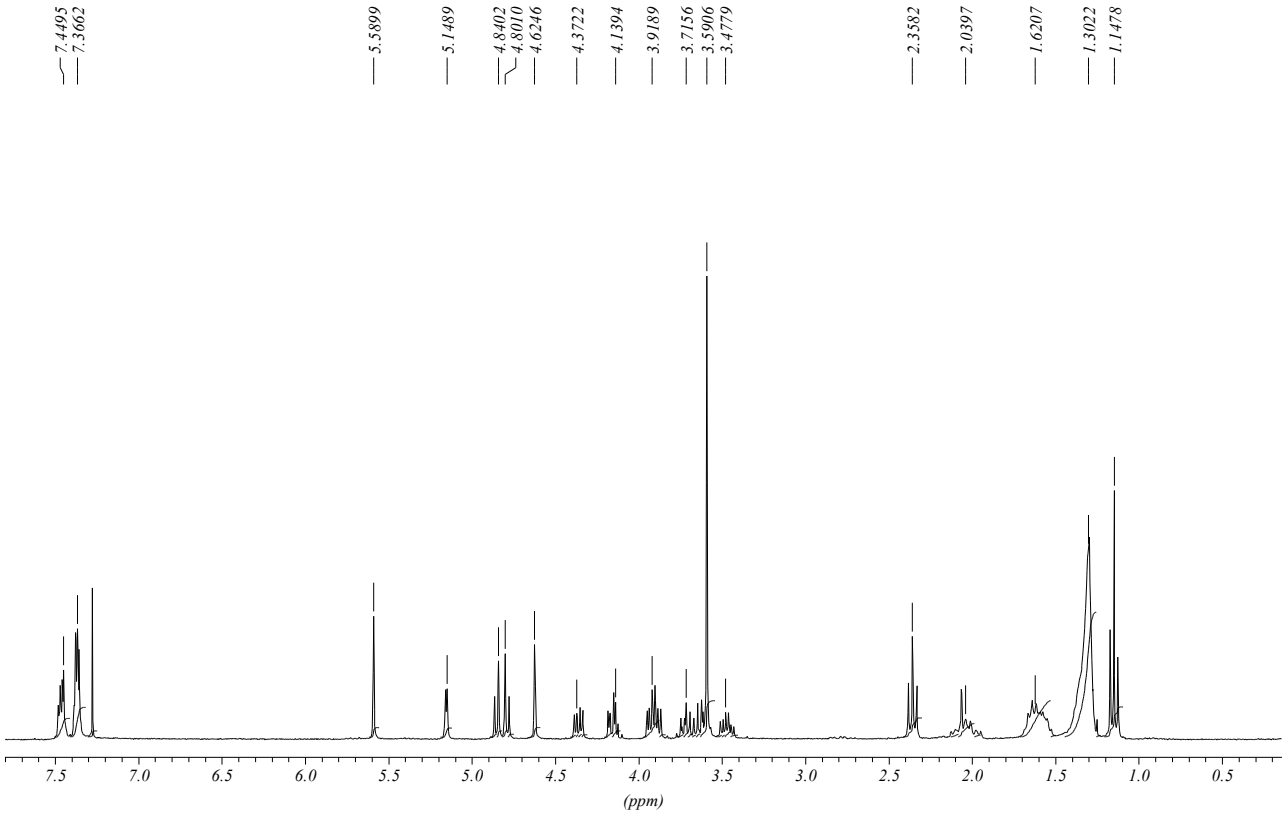
^{1}H NMR Compound **30**



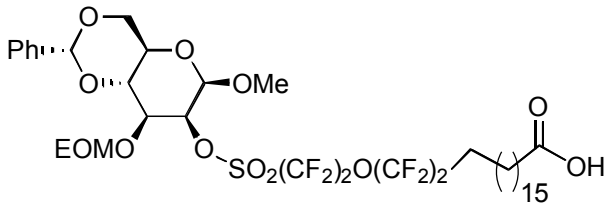


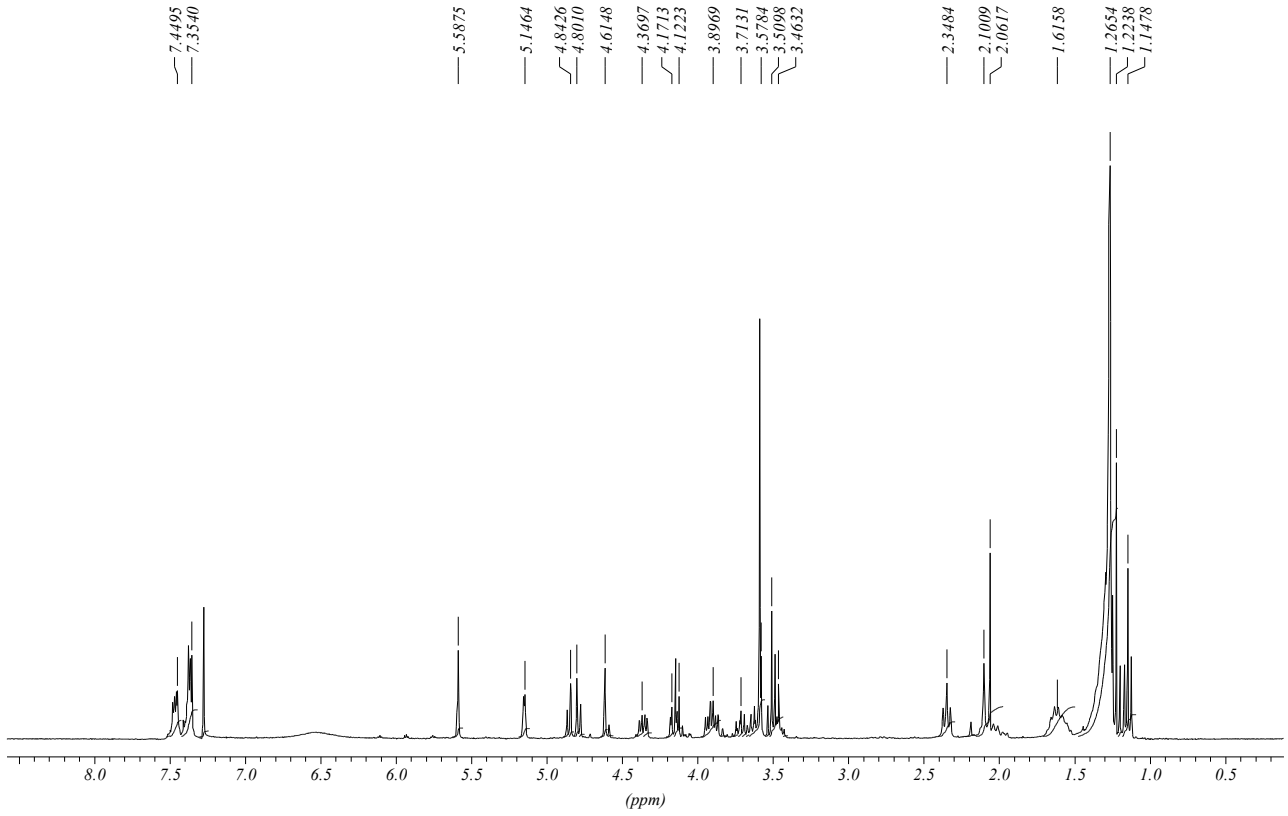
^{1}H NMR Compound **31**



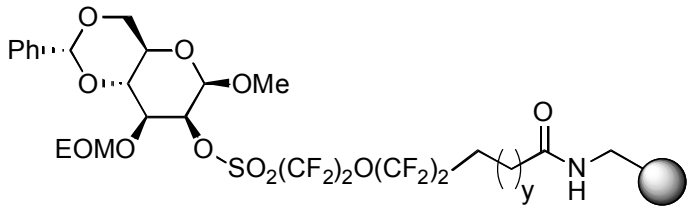


^{1}H NMR Compound **32**

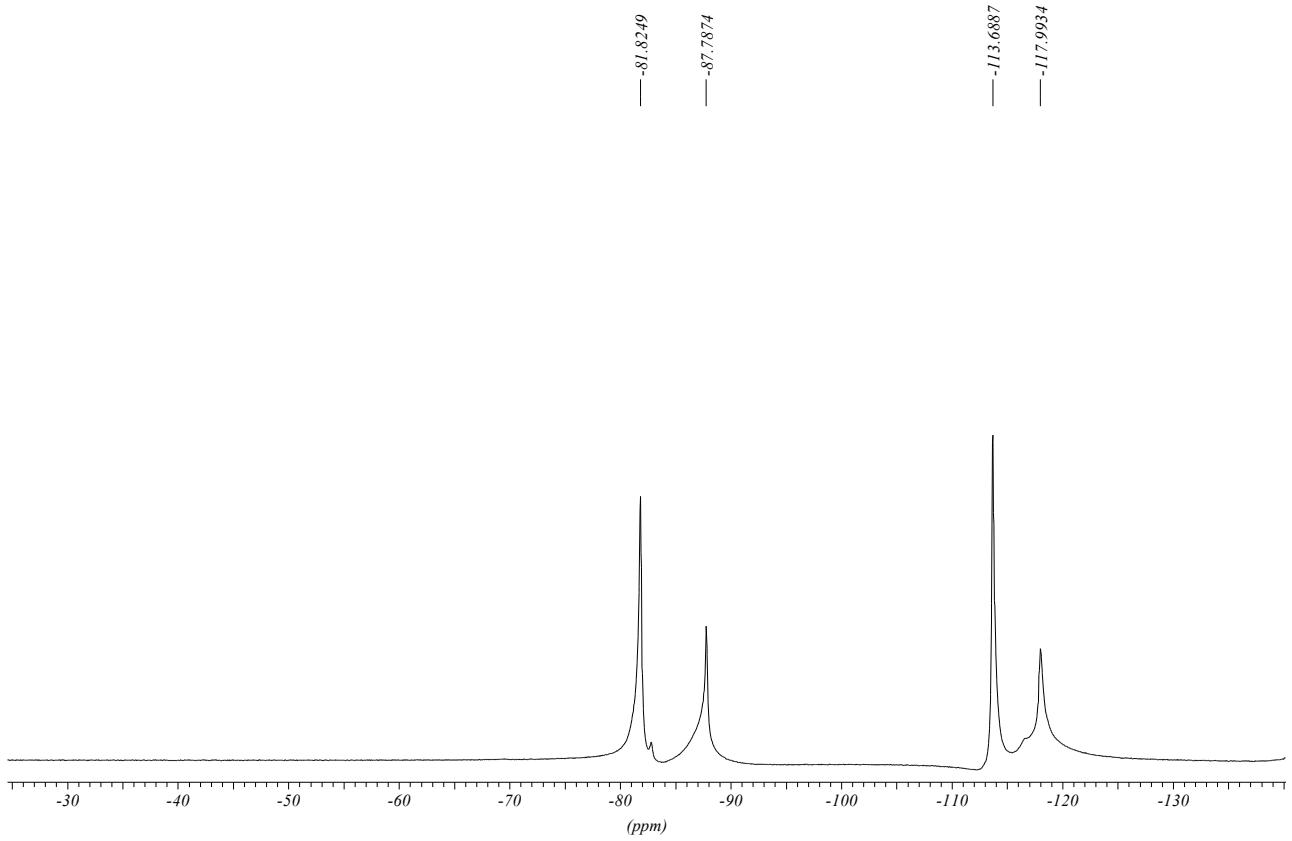




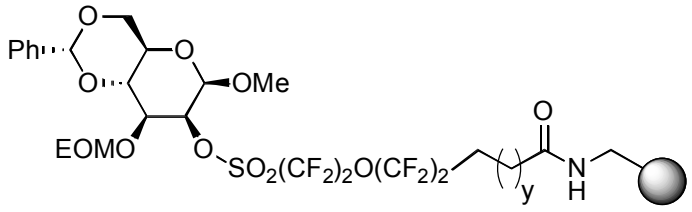
Gel-Phase ^{19}F NMR Compound **33** (Ref. $CFCl_3$)



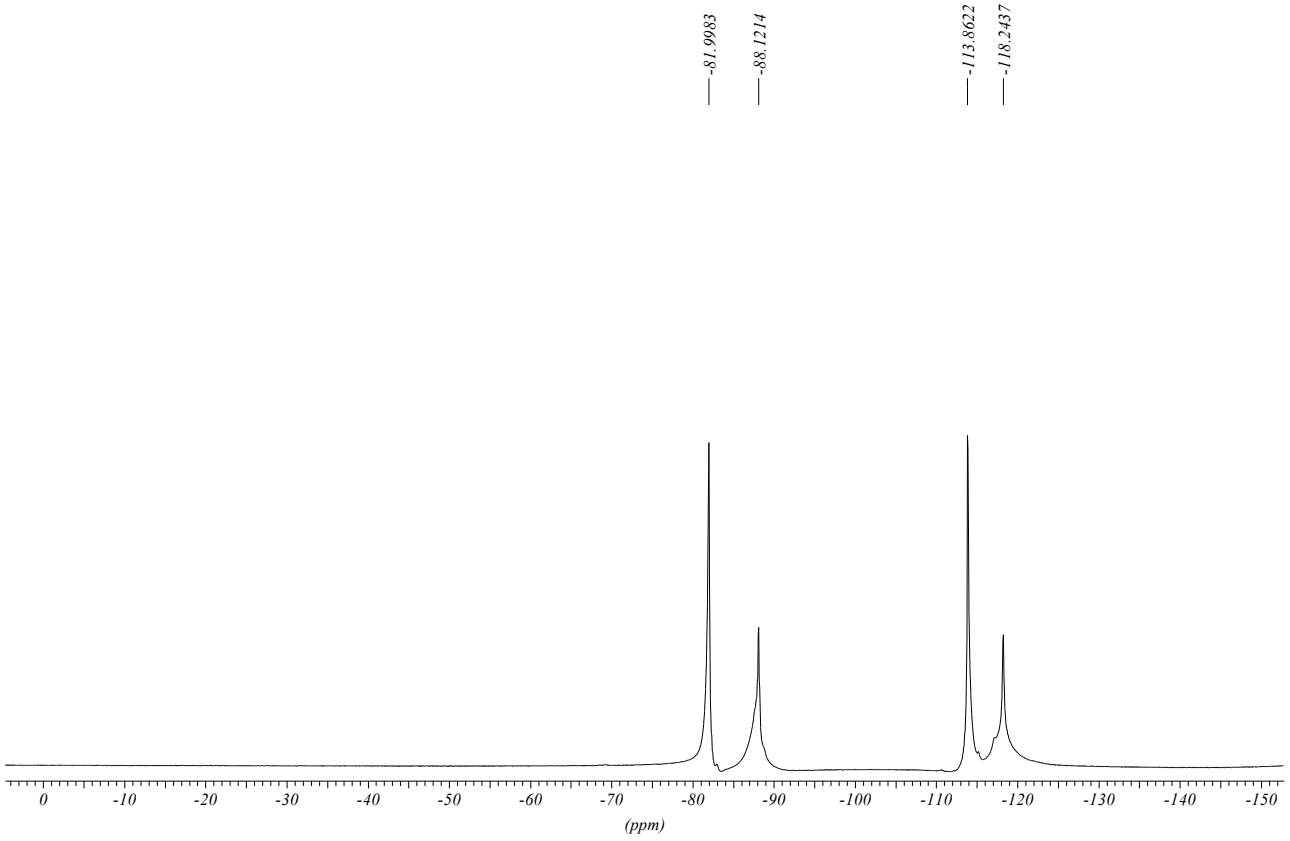
33 y = 1



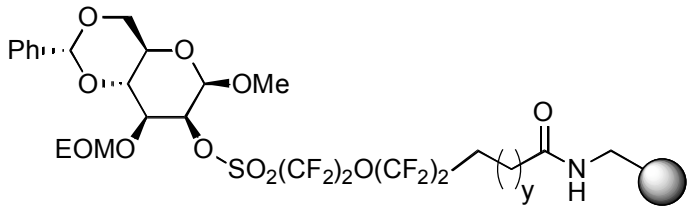
Gel-Phase ^{19}F NMR Compound **34** (Ref. $CFCl_3$)



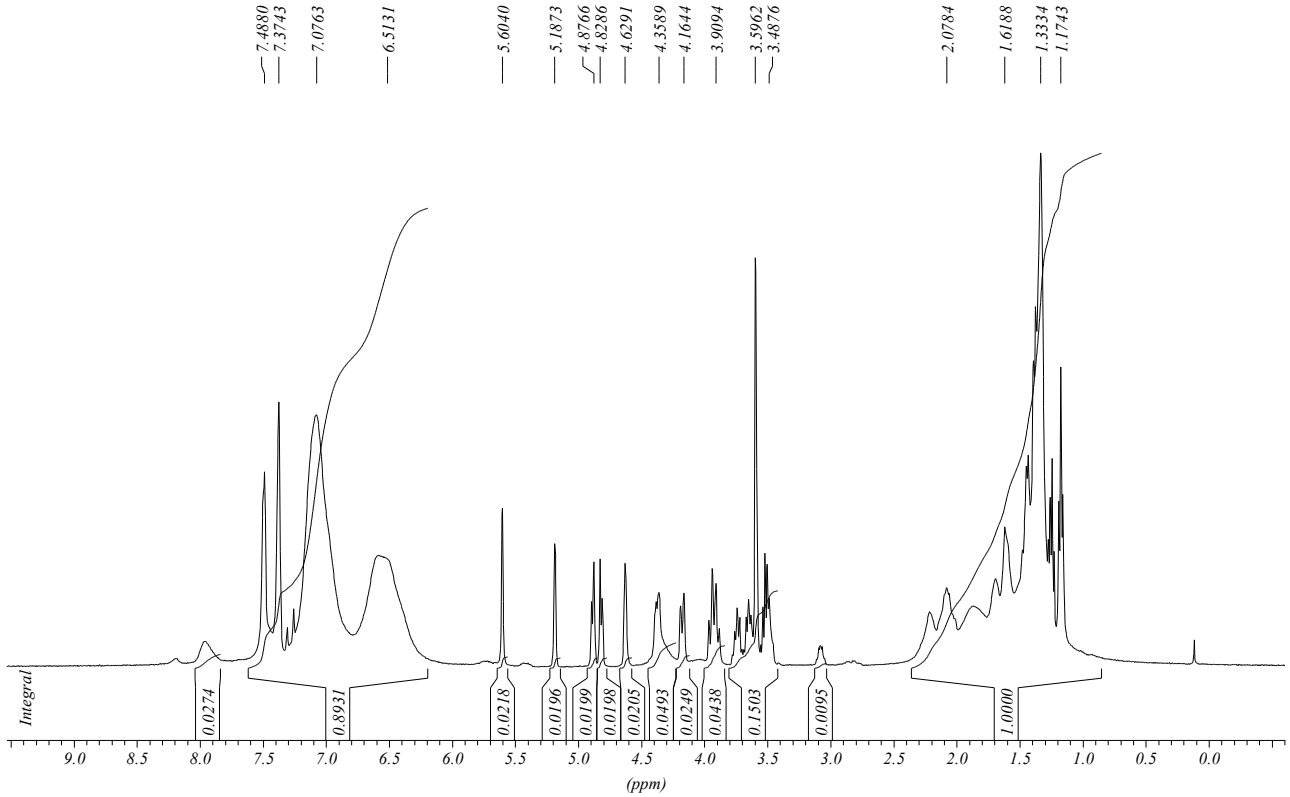
34 y = 3



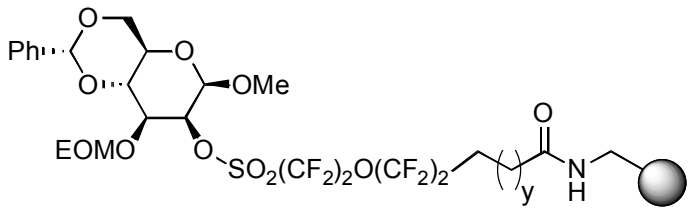
MAS ^{1}H NMR Compound **35**



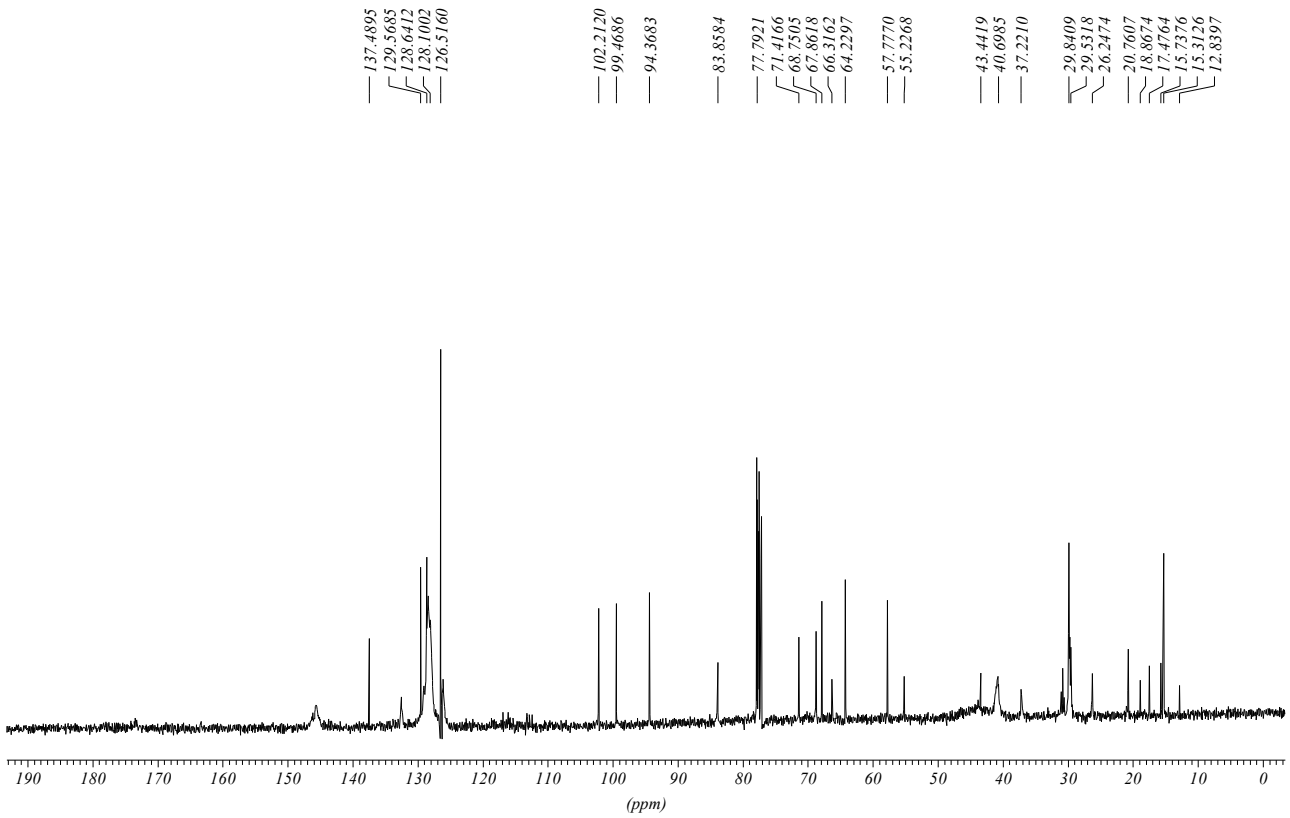
35 y = 9



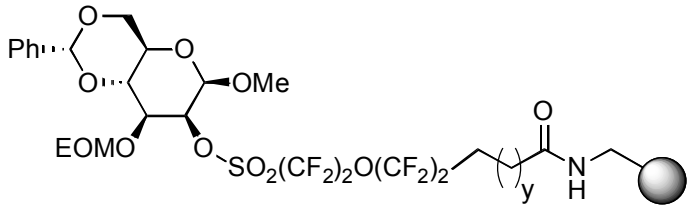
MAS ^{13}C NMR Compound **35**



35 y = 9



Gel-Phase ^{19}F NMR Compound **35** (Ref. $CFCl_3$)



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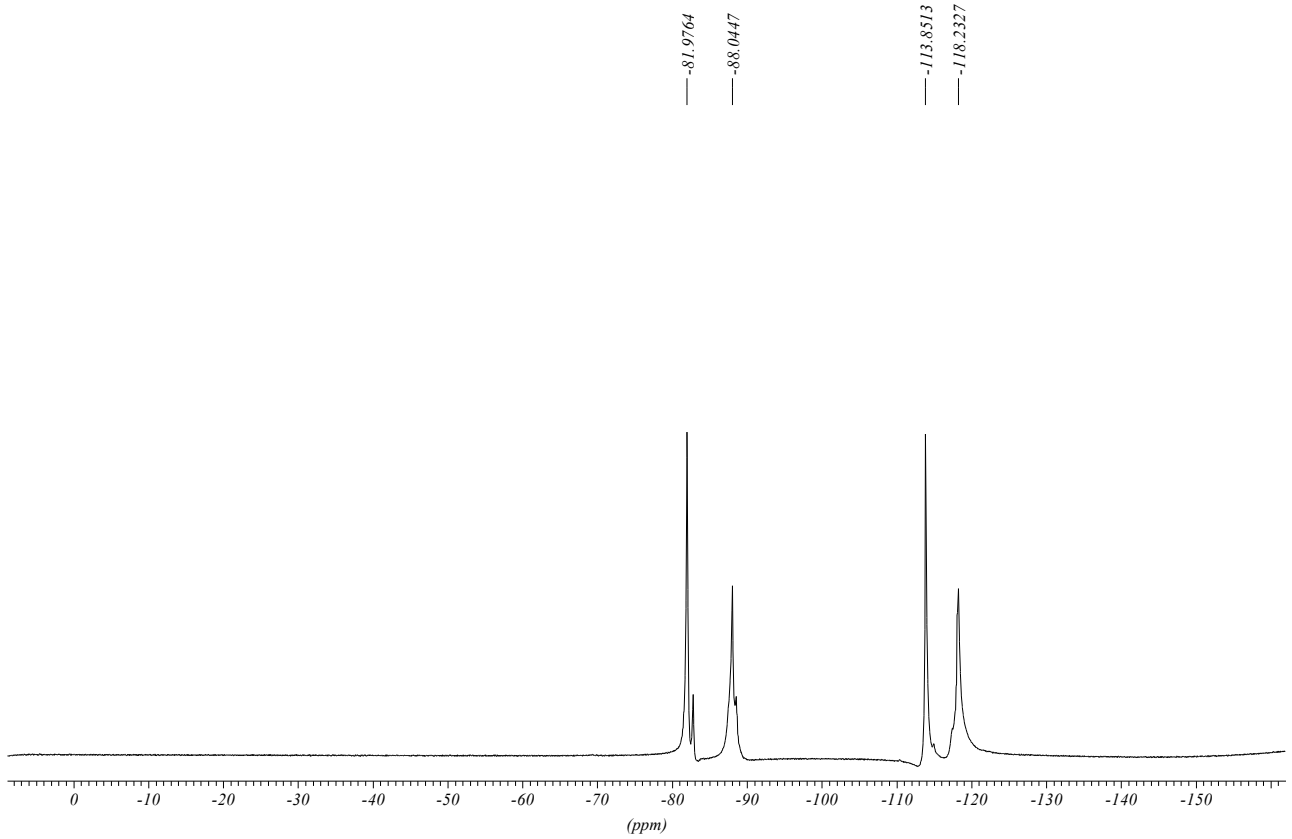
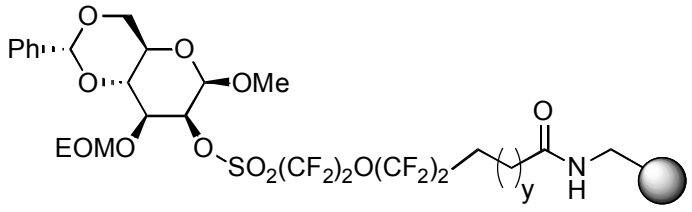
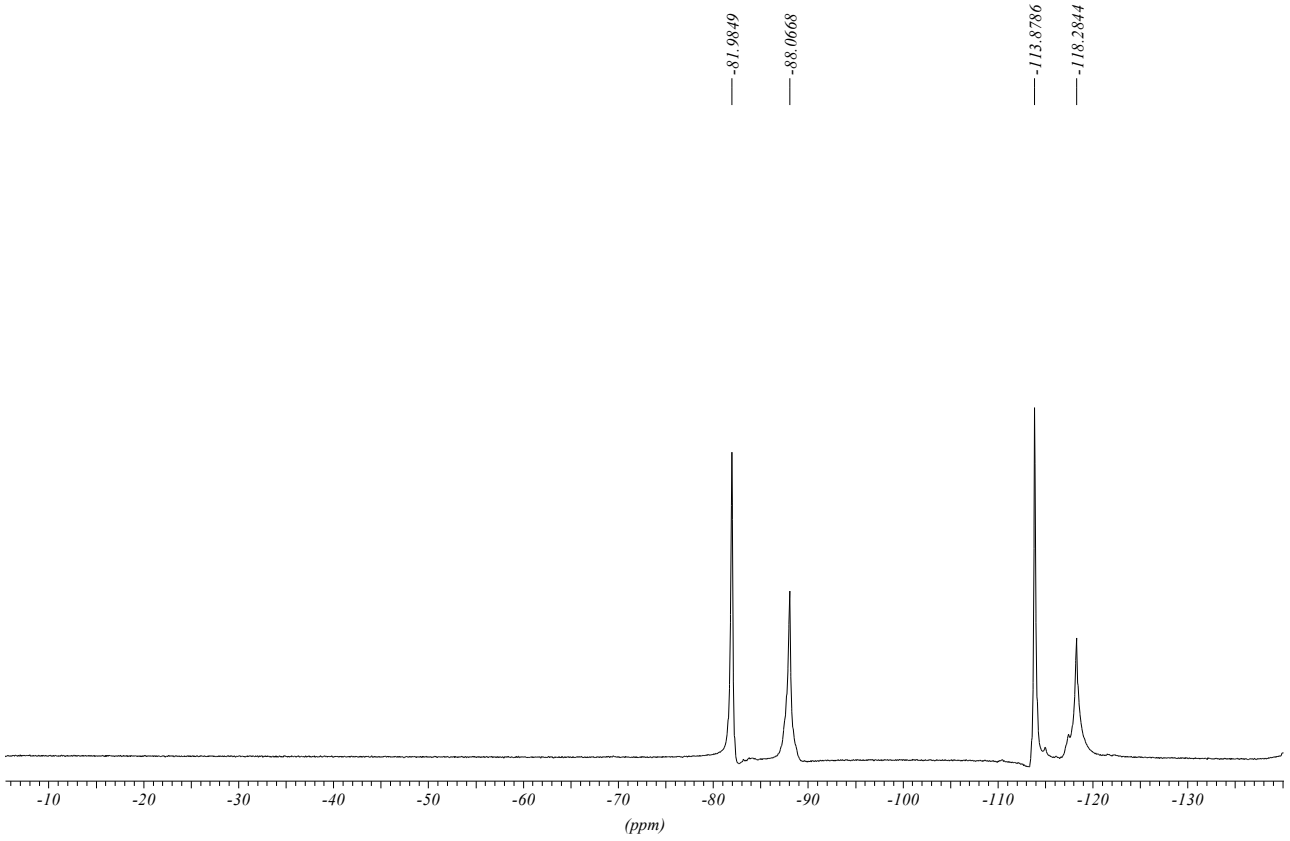


Gel-Phase ^{19}F NMR Compound **36** (Ref. $CFCl_3$)



36 y = 15



Procedure for the radiosynthesis of [^{18}F]Methyl-4,6-O-benzylidene-3-O-ethoxymethyl-2-deoxy-2-fluoro-β-D-glucopyranoside ([^{18}F]18) from a resin-bound β-D-mannose derivative (e.g. resin 35)

A carbon glass reaction vessel was placed in a brass heater and the pot lid (with three lines attached to allow evaporation, nitrogen flow, and addition of reagents) tightened down and the whole system leak tested. Kryptofix [2.2.2] (22 mg) in CH_3CN (300 μL) and K_2CO_3 (8 mg) in water (300 μL) was transferred using a plastic syringe (1 mL) into the carbon glass reaction vessel. The [^{18}F]fluoride ion (185-370 MBq) in water (0.5 – 2 mL) was added and heated to 125°C. After 15 mins three aliquots of CH_3CN (0.5 mL) were added at 1 min intervals. [^{18}F]Fluoride ion was dried up to 40 mins in total. The heater was cooled to room temperature, the pot lid removed and CH_3CN (0.2 mL) was added. The pot lid was replaced and the lines were capped off with stoppers. The heater was set at 100°C for 10 mins and the [^{18}F]fluoride ion redissolved. After cooling to room temperature the [^{18}F] fluoride ion solution (0.2 mL) was transferred to a second carbon glass reaction vessel containing the resin (20–25 mg) using a plastic syringe (1 mL). This carbon glass vessel was transferred to an ion chamber and the labeling activity measured. The carbon glass vessel was replaced in the brass heater and the capped pot lid tightened. The reaction was heated to 86°C for 4 min before cooling with compressed air. The pot lid was removed CH_3CN (1.0 mL) was added and the activity in the reaction vessel was measured. The resin was mixed and drawn up into a plastic syringe and then passed through a sintered syringe and into a collection vial. The reaction vessel was washed with a further volume of CH_3CN (0.5 mL) and passed through the sintered syringe. The activity in the collection vial, on the resin and of the sintered syringe was measured. The reaction mixture was diluted with water (1 mL), passed through a C_{18} Sep-Pak (Waters) that had been pre-conditioned with EtOH (5 mL) and water (10 mL). This solution was then passed through a silica Sep-Pak (Waters) that had been pre-conditioned with Et_2O (5 mL). The activities of all solutions were measured at each stage.

Comparison of the chemical purity of the crude protected FDG [^{18}F]18 from the resin precursor 35 against the crude protected FDG product [^{18}F]2 obtained by conventional solution synthesis.

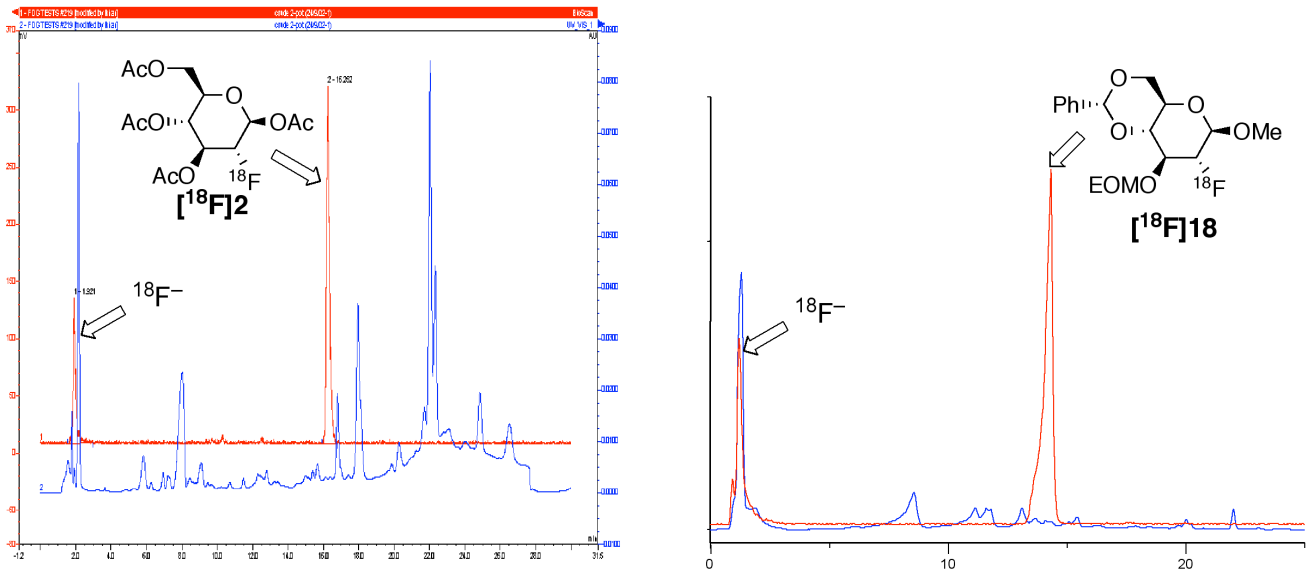


Figure. Reversed-phase HPLC chromatograms (C_{18} column) of the crude protected products **[^{18}F]2** and **[^{18}F]18** from conventional solution-phase FDG synthesis (left hand trace) and from the solid-phase precursor **35** (right hand trace). Red trace: Radioactivity; Blue trace: UV activity (210 nM).

The chromatogram on the left hand side is of the product of a conventional solution tetracetoxy manose triflate fluoridation reaction before removal of unreacted [^{18}F]fluoride ion. The blue UV trace indicates that a wide range of starting material decomposition products are produced. The red radioactive trace shows that there are only two radioactive materials present identified as fluoride running near the origin and the main radioactive peak of tetra acetoxy [^{18}F]FDG (**[^{18}F]2**).

The chromatogram on the right is of the product of fluoridation of the solid phase precursor **35**. The blue UV trace shows that apart from material eluting from the column near the origin there is little other UV active material released from the solid phase. The red radioactive trace shows that there are two radioactive materials present. The peak eluting near the origin is assigned to unreacted [^{18}F]fluoride ion and the peak near 14 minuites is assigned as the protected [^{18}F]FDG (**[^{18}F]18**)